New Reagents and Reactions for the Synthesis of Sulfinates and their Aza-Analogues

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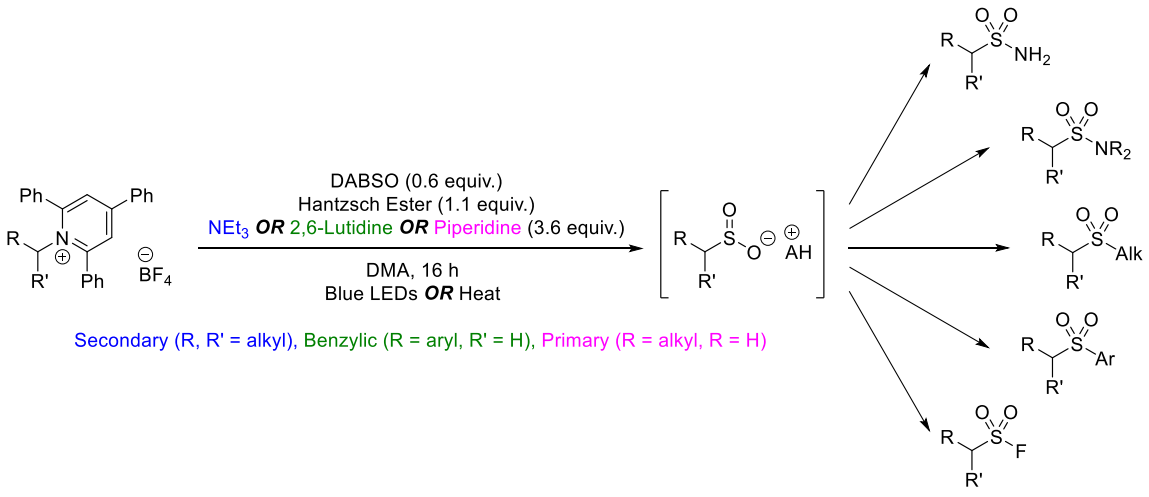
Abstract

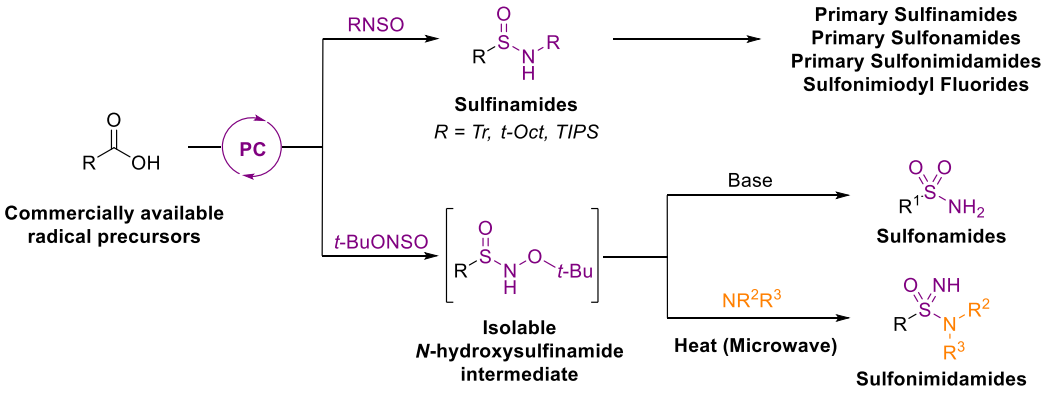
The work in this thesis documents several advances in the synthesis of S(VI) functional groups. The methods reported in this work have a focus on the reaction of radicals with sulfur dioxide and its aza-analogues to prepare S(IV) products, which can then be exploited to prepare a broad selection of S(VI) products. Furthermore, studies were carried out into the preparation of reagents that can generate reactive sulfinylamines in situ, and these were used in a variety of reactions. Finally, we were able to prepare novel sulfurdiimide reagents, and we were able to demonstrate the use of these reagents in the preparation of challenging aza-sulfur functional groups.

Chapter 1 is a literature review covering the properties, applications and synthesis of sulfur functional groups. The chemistry of sulfur dioxide surrogates, sulfinylamines and sulfurdiimides is also reviewed.

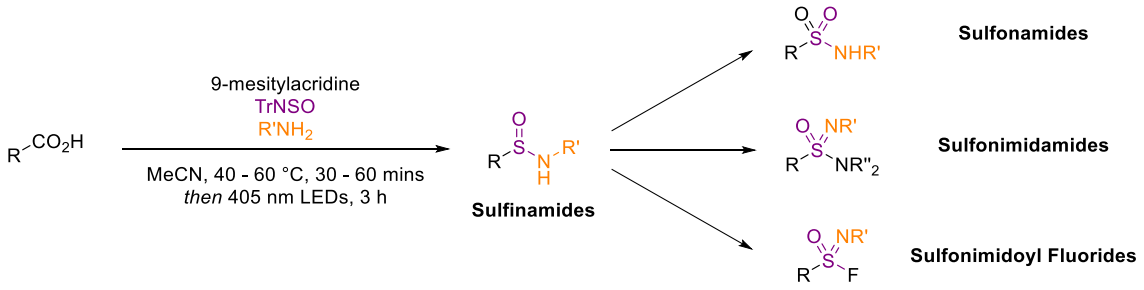
Chapter 2 describes the development of a novel method for the synthesis of alkyl sulfinates and their derivatives utilising alkyl radical addition to sulfur dioxide surrogates. This method utilises Katritzky pyridinium salts as alkyl radical precursors, which can be prepared from readily-available primary amines.



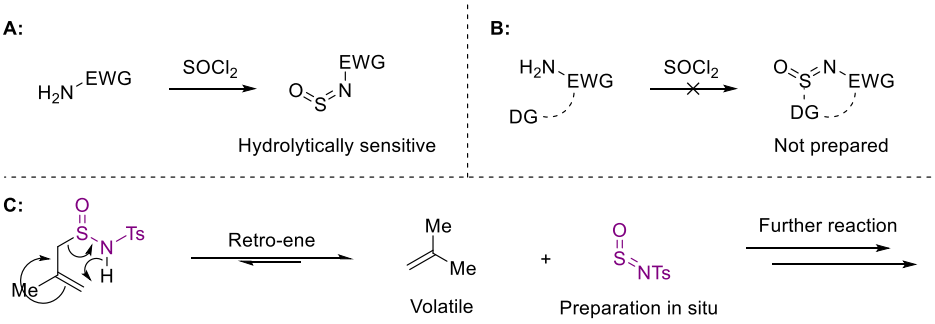
Chapter 3 describes the preparation of sulfinamide products via decarboxylative radical addition to sulfinylamine reagents and their use in the preparation of S(VI) products. This method was applied to sulfinylhydroxylamines in order to prepare *N*-alkoxysulfinamides, which were subsequently used to prepare sulfonamide and sulfonimidamide products.



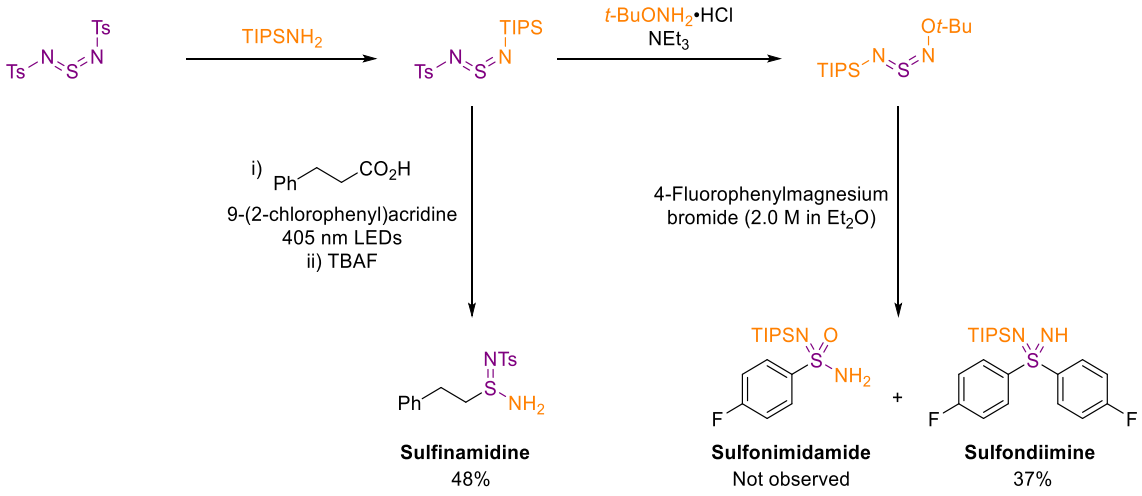
Chapter 4 describes the application of trans-sulfinylation to prepare sensitive sulfinylamines in situ. This was used in combination with our previously-developed decarboxylative reaction conditions to prepare diverse *N*-alkylated sulfinamide products.



Chapter 5 describes studies towards the development and application of bench-stable sulfinylamine reagents or sulfinylamine surrogates to support the use of existing methods and enable the development of new methods utilising hydrolytically-sensitive electron-poor sulfinylamines.



Chapter 6 describes studies towards the development of synthetic routes towards new sulfurdiimide reagents and demonstrates their reaction with alkyl radicals or organometallic reagents to prepare challenging aza-sulfur products.



C**hapter 7** presents conclusions to our research and potential future directions of study.

C**hapter 8** presents experimental data.

Declaration

I declare that the work in this thesis had not been previously submitted for a degree at the university of Oxford or any other higher education institution.

The experimental work in **Chapter 2** was carried out in collaboration with Dr Loïc Pantaine, a former postdoctoral researcher in the Willis group. The work for this chapter has also been published in Organic Letters (2021). All characterisation data given in the experimental section for this chapter is my own work, and any experiments carried out by Dr Loïc Pantaine are clearly labelled within **Chapter 2**.

The experimental work in **Chapter 3** was carried out in collaboration with Dr Jagadeesh Kalepu, a former postdoctoral researcher in the Willis group. The work for this chapter has also been prepared for publication. All characterisation data given in the experimental section for this chapter is my own work, and all experiments carried out by Dr Jagadeesh Kalepu are clearly labelled within **Chapter 3**. The X-ray crystallographic structure shown in this chapter was obtained by Dr Kirsten E. Christensen, a member of the Chemical Crystallography Group at the University of Oxford.

Preliminary experimental work in **Chapter 4** was carried out in collaboration with Mr Russell Woodger, a former MChem project student in the Willis group. The work for this will be prepared for publication in the future. All characterisation data given in the experimental section for this chapter is my own work, and all experiments carried out by with Mr Russell Woodger are clearly labelled within **Chapter 4**.

The experimental work in **Chapter 5** and **Chapter 6** were not carried out collaboratively. All results and characterisation data discussed in these chapters are my own work.

Jonathan A. Andrews, 2023

Acknowledgements

First of all, I would like to thank Mike for all of his guidance and support over the last four years. I don't think I truly appreciated how challenging a DPhil would be, but working with you and your fantastic group has enabled me to follow my interests and instincts, explore new and exciting chemistry, and pushed me to be the best chemist I could be. I am immensely proud of everything I have achieved, and despite all the challenges, setbacks, and long evenings in the lab, I couldn't have imagined doing anything different. Thank you for trusting me with this work, and I look forward to seeing where it goes.

Then I have to thank the MCW group. It has been a pleasure to work with all of you brilliant people. Whilst the group changed massively over the years, every iteration of the Willis group has been a joy to work with, from the "ATS gang," to the "F1 boys," to "the council." To Ben and Dan, the kings with whom I shared so many unforgettable luncheons, thanks for being great friends over the years and dragging me away from the lab every day for ATS and horsebox trips, it has been a pleasure boys. Thanks to Russell for being a fantastic part II and excellent friend, making my time as a supervisor exceptionally easy and providing a strong foundation from which I built up one of my favourite projects! Thanks also to Loïc and Jagadeesh for all of their efforts on the projects we collaborated on. To all the other F1 boys (and girls), for providing a fantastic place to work and chat shit, including Antoine, Janette, Ivan, Josh, Suzie, Kangtao, Damien, Charlie P, Hugh, Tony, Gwyndaf, Nicoletta, as well as those from the other place (F2), who also contributed so much to my time over the years, including Xinlan, Charlie B, Tilby, May, Terry, Katherine, Mingkai, Di, Nick, Mingyan, Zexin and Ndi.

I also need to thank Janice for all of her hard work over the years. Whilst our relationship over the years has been a little dysfunctional, and I've spent more hours than I would like trying to get you to do what you're told, everything was always harder when you weren't there, and I couldn't have achieved everything I did without you.

Thanks to Lydia, Stuart, Philip and Shannah, for great times in Temple Street. You were the best housemates. Thanks also to everyone I met through SBM. I learnt a lot, and had great times with you all during the taught course.

My time with OUTriC has also been a huge part of my time at Oxford, and I am thankful for all the good times I've spent with people from all backgrounds that have been brought together by the shared love of a sport (or three). There are far too many people to name here, but thanks to everyone I spent so many hours with on bikes, running around the track, (occasionally) swimming, drinking and arguing with at committee meetings.

Last but perhaps most of all, thanks to my fantastic family, who support me through everything, despite not having a clue what it is I do.

A final note for mum. I wish you could see all I've achieved over the last 16 years. I've gone far and done so much, and I hope you're proud.

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Abbreviations

A	Acceptor
Ac	Acetyl
Alk	Alkyl
aq.	Aqueous
Ar	Aryl
app.	Apparent
BCP	Bicyclo[1.1.1]pentane
BiPh	4-Phenylphenyl (Biphenyl)
Boc	*tert*-Butyloxycarbonyl
Bn	Benzyl
BPhen	Bathophenanthroline
br.	Broad
Bt	Benzotriazole
Bu	Butyl
CAN	Ceric Ammonium Nitrate
cat	Catecholato
Cbz	Benzyloxycarbonyl
CFL	Compact fluorescent lamp
CI	Chemical Ionisation

D	Donor
d	Doublet
DABCO	1,4-diazabicyclo[2.2.2]octane
DABSO	DABCO-SO_2 charge-transfer complex
DCE	1,2-Dichloroethane
DCM	Dichloromethane
DG	Donating Group
DIPEA	*N*,*N*-Diisopropylethylamine
DMA	*N*,*N*-Dimethylacetamide
DMAP	4-Dimethylaminopyridine
DMF	*N*,*N*-Dimethylformamide
DMC	Dimethyl carbonate
DMSO	Dimethyl sulfoxide
dr	Diastereomeric Ratio
dtbbpy	4,4'-Di-*tert*-butyl,2,2'-dipyridyl
EDA	Electron Donor-Acceptor
ee	Enantiomeric excess
equiv.	Equivalents
ESI	Electrospray Ionisation
Et	Ethyl

EWG	Electron-withdrawing group
FT	Fourier Transform
g	Gram(s)
Glu	Glutamic acid
glyme	Dimethoxyethane
h	Hour(s)
HAT	Hydrogen atom transfer
HE	Hantzsch Ester
hept	Heptet
Het	Heteroaryl
Hex	Hexyl
HFIP	Hexafluoroisopropanol
HFIPS	Hexafluoroisopropyl Sulfamate
HMDS	Hexamethyldisilazane
HPLC	High-Performance Liquid Chromatography
HRMS	High Resolution Mass Spectrometry
Hz	Hertz
i-	*iso*
IR	Infrared
J	Coupling Constant (Hz)

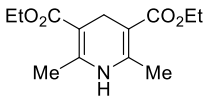
LCT	Liquid Chromatography
LED	Light Emitting Diode
LRMS	Low Resolution Mass Spectrometry
m-	*meta*-
m	Multiplet
M	Molar
*m*CPBA	*meta*-Chloroperoxybenzoic acid
Me	Methyl
MEM	2-Methoxyethoxymethyl ether
Mes	2,4,6-Trimethylphenyl (Mesityl)
mida	*N*-Methyliminodiacetic acid
mins.	Minute(s)
mol	Mole(s)
m.p.	Melting Point
Ms	Methanesulfonyl (Mesyl)
m/z	Mass to Charge Ratio
n-	*normal*-
NCS	*N*-Chlorosuccinamide
NFSI	*N*-Fluorobenzenesulfonimide
NMMSO	*N*-Methylmorpholine-SO_2 charge-transfer complex

NMP	*N*-Methyl-2-pyrrolidone
NMR	Nuclear Magnetic Resonance
Ns	4-Nitrobenzenesulfonyl (Nosyl)
Nu	Nucleophile
o-	*ortho*-
Oct	Octyl
p-	*para*-
PC	Photocatalyst
PCET	Proton Coupled Electron Transfer
PET	Photoinduced Single Electron Transfer
Petrol	Petroleum Ether (40 – 60 °C)
PG	Protecting Group
Ph	Phenyl
PIDA	Phenyliodine(III) diacetate
ppm	Parts per million
ppy	2-phenylpyridine
Pr	Propyl
Py	Pyridine
q	Quartet
quin.	Quintet

R	Generic Group/Substituent
R_f	Retention Factor
r.t.	Room Temperature
s	Singlet
SAR	Structure-Activity Relationships
sat.	Saturated
SET	Single-Electron Transfer
SMOPS	Sodium 3-methoxy-3-oxopropane-1-sulfinate
S_NAr	Nulceophilic Aromatic Substitution
t-	*tert*-
t	Triplet
TBAB	Tetrabutylammonium bromide
TBAF	Tetrabutylammonium fluoride
TCCA	Trichloroisocyanuric acid
Temp	Temperature
TEMPO	2,2,6,6-Tetramethyl-1-piperidinyloxy free radical
terpy	Terpyridine
Tf	Trifluoromethylsulfonyl
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran

TimSO	*N*-Methylpyrrolidine-SO_2 charge-transfer complex
TIPS	Triisopropylsilyl
TLC	Thin Later Chromatography
TMEDA	*N,N,N',N'*-Tetramethylethylenediamine
TMS	Trimethylsilyl
Tol	Methylphenyl (Tolyl)
TPP	Tetraphenylporphyrin
Tr	Triphenylmethyl
Ts	4-Toluenesulfonyl (Tosyl)
UV	Ultra-Violet
Val	Valine
Vis	Visible

Chemical Structures



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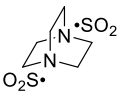

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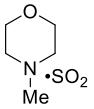
TimSO



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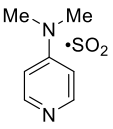

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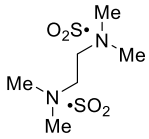

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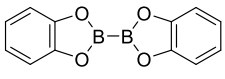

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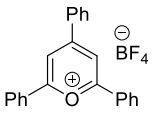

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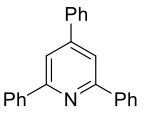

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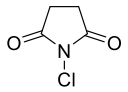

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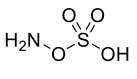

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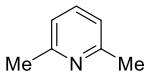

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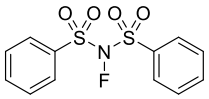

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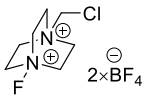

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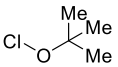

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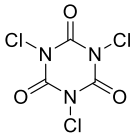

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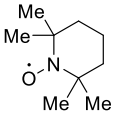

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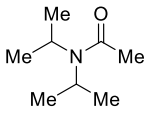
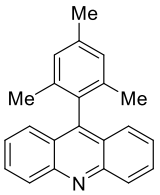
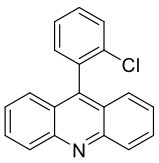


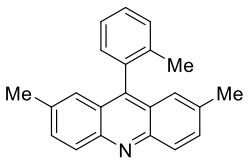
N,*N*-Diisopropyl acetamide



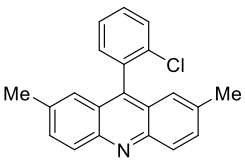
9-mesitylacridine



9-(2-chlorophenyl)acridine



2,7-dimethyl-9-(*o*-tolyl)acridine



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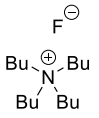

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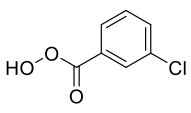
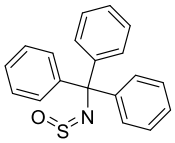


*m*CPBA



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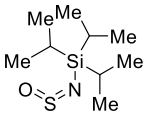

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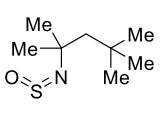
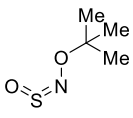


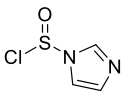
t-OctNSO



t-BuONSO



Thionyl Chloride



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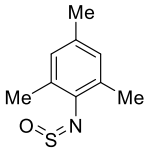

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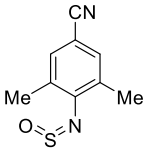

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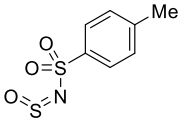
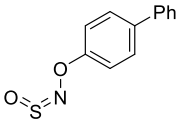
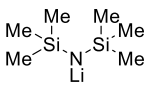


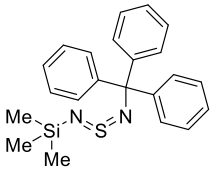
TsNSO



BiPhONSO



LiHMDS



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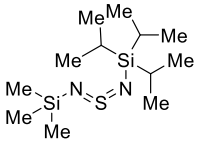

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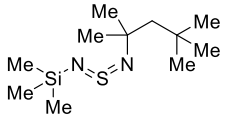

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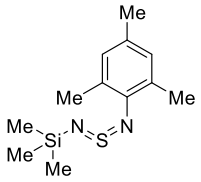
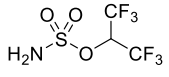


N-(trimethylsily)-*N*'-(2,4,6-trimethylphenyl)sulfur diimide (TMSNSNMes)



Hexafluoroisopropyl sulfamate (HFIPS)

Bis(*p*-toluenesulfonyl) sulfur diimide (TsNSNTs)

N-(*p*-toluenesulfonyl)-*N*'-(triisopropylsilyl)sulfur diimide (TsNSNTIPS)

N-(*tert*-butoxy)-*N*'-(triisopropylsilyl)sulfur diimide (*t*-BuONSNTIPS)

Chapter 1 - Introduction

1.1 Applications of Sulfur Containing Functional Groups

Owing to its ability to exist in multiple oxidation states, and its ability to bond to several atoms, including carbon, nitrogen, oxygen, sulfur, phosphorous, fluorine, chlorine, and occasionally others, the organic chemistry of sulfur is a vast and complex subject, characterised by a diverse array of sulfur-containing functional groups (**Figure 1.1**).



Figure 1.1. Selected sulfur-containing functional groups.

Due to their diverse structural, electronic and physical properties, sulfur-containing functional groups are found ubiquitously in biologically active molecules and biological processes.[1] Sulfur-(II) functional groups such as thiols and sulfides can be found in important molecules such as cysteine, biotin, and penicillin (**Figure 1.2**).[2] Sulfenic acids and sulfenamides are less-frequently encountered, but are often proposed as important intermediates in biological processes.[3] The oxidative lability of S(II) functional groups can often be key to their activity, but equally, can often hinder their use. [4]

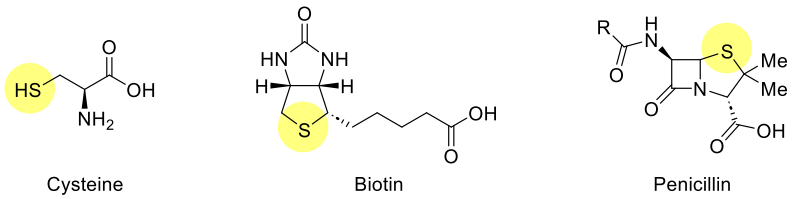


Figure 1.2. Examples of biologically-active S(II)-containing compounds.

Sulfur-(IV) functional groups are less-frequently encountered in medicinal chemistry. Much like S(II) functional groups, S(IV) can be labile to oxidative (as well as reductive) processes, which can complicate their use.[4] Further complications are encountered when it is considered that many S(IV) products are chiral. This challenge has resulted in the development of a vast array of methods for the preparation of enantioenriched sulfoxides in particular.[5] Despite these challenges, some examples of drug molecules containing S(IV) functional groups exist, usually containing a sulfoxide, such as esomeprazole, which is sold as a single enantiomer (**Figure 1.3**).[6]

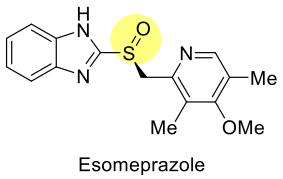


Figure 1.3. Esomeprazole as an example of a sulfoxide drug.

Given the oxidative lability of both S(II) and S(IV), it is not surprising that S(VI) functional groups are most-commonly encountered in marketed drug molecules, and of these, the majority contain the sulfonamide functional group, which is present in >10% of the best-selling small-molecule drugs, and sulfones, sulfamides and sulfates are also sometimes encountered (**Figure 1.4**).[7] Sulfonyl fluorides

are also an important S(VI) functional group, as their use in sulfur-fluoride exchange reactions (SuFEx) means they are finding application as covalent probes or warheads.[8]

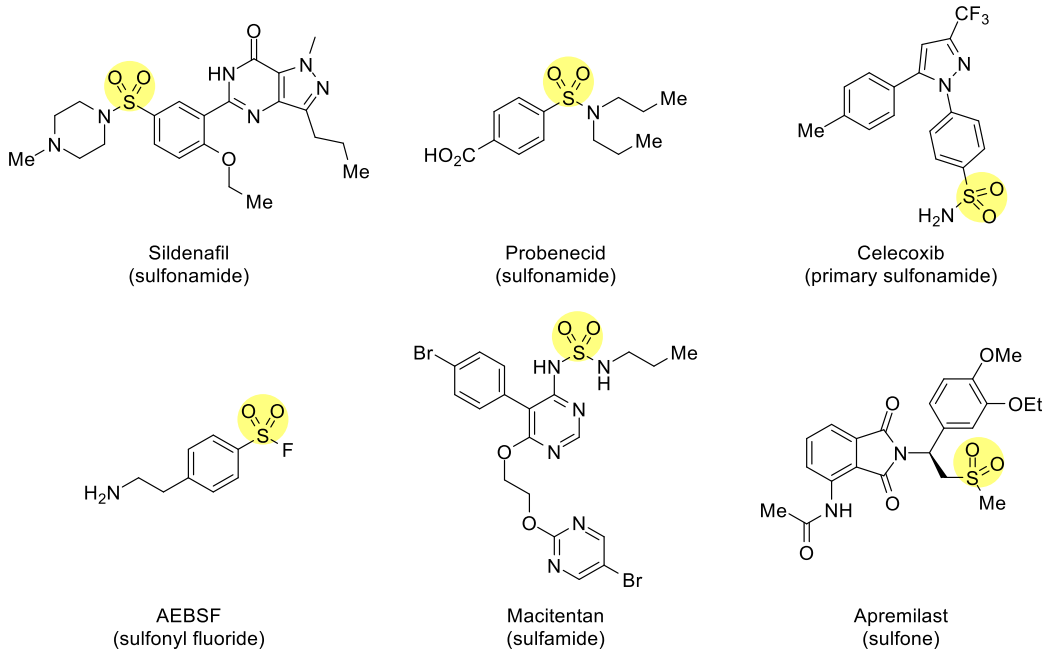


Figure 1.4. Examples of biologically-active S(VI)-containing compounds.

Whilst there are fewer examples of the use of aza-analogues of the aforementioned S(VI) functional group in biologically-active molecules, they have the potential to have significant impact in medicinal chemistry and agrochemistry, as the additional vector for functionalisation on the imidic nitrogen enables precise tailoring of the electronic and steric properties of the molecule, as well as providing a chiral centre which can further influence the specificity of drug-target interactions. Following several significant advancements in methods by which these functional groups can be accessed, their use seems to be gaining traction,[9] as evidenced by a growing number of examples in the medicinal chemistry patent literature,[10] as well as an example of a sulfoximine insecticide, Sulfoxaflor (**Figure 1.5**).[11]

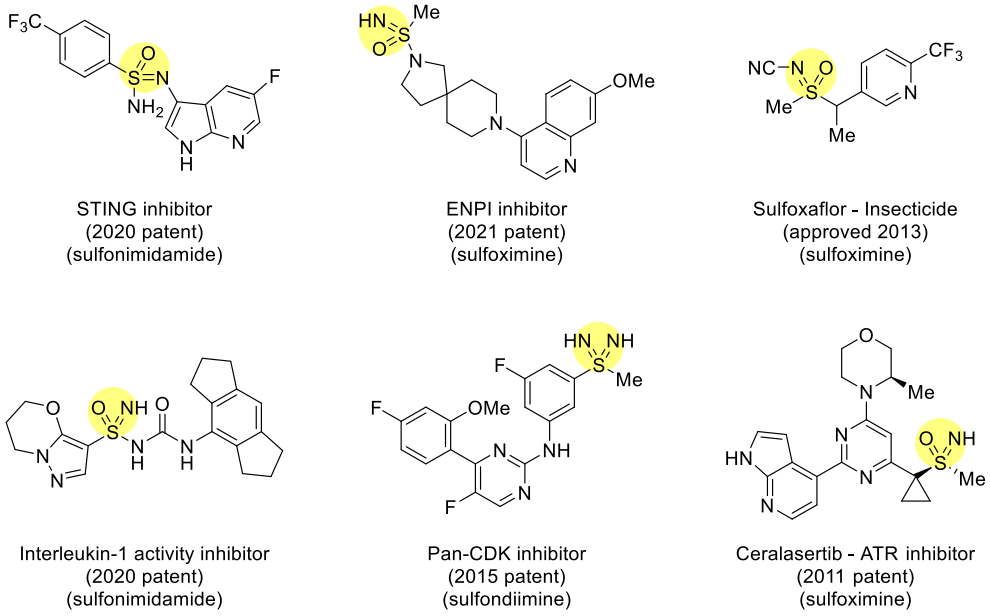
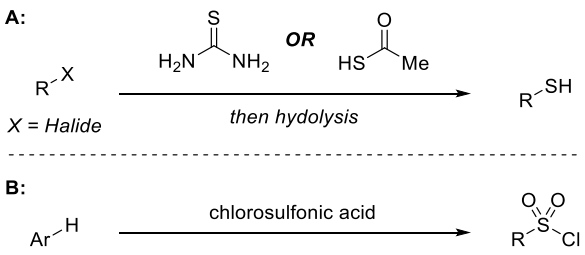


Figure 1.5. Examples of biologically-active aza-S(VI)-containing compounds.

With the demonstrated importance of S(VI) functional groups, the availability of high-yielding and versatile methods for their preparation are important for synthetic organic chemists.

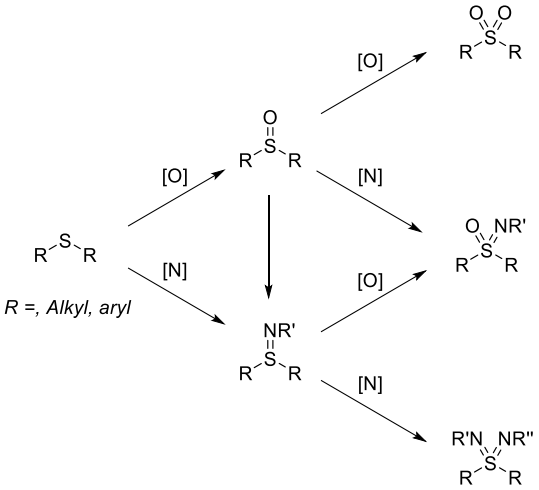
1.2 Synthesis of S(IV) and S(VI) Functional Groups

Synthetic routes to many of these sulfur-containing functional groups generally stem from more commercially available or readily-accessible functional groups such as thiols and sulfonyl chlorides. Thiols can be accessed from the reaction of electrophiles with sulfur-nucleophiles such as thiourea or thioacetic acid (**Scheme 1.1.A**). Copper-catalysed methods for the synthesis of aryl thiols have also been developed.[12] A useful method for the preparation of aryl sulfonyl chlorides is via electrophilic aromatic substitution using chlorosulfonic acid (**Scheme 1.1.B**).



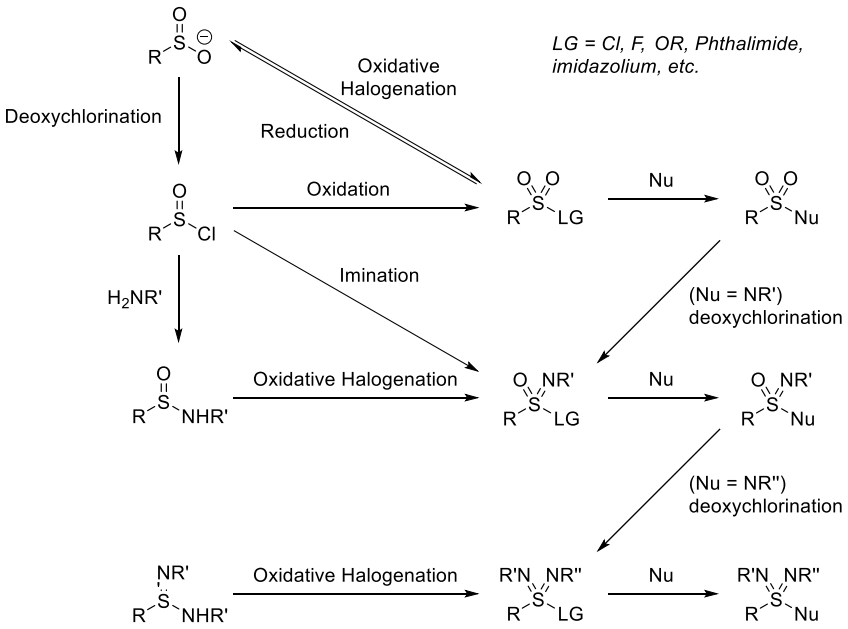
Scheme 1.1. Preparation of thiols or sulfonyl chlorides.

Oxidation of sulfides can be a useful tool for the preparation of higher-oxidation-state sulfur functional groups (**Scheme 1.2**). Similarly, imination reactions can be used to prepare aza-analogues.[13] Conversion of sulfoxides to sulfilimines has also been achieved, either using *N*-sulfinylsulfonamides or Burgess-type reagents.[14]



Scheme 1.2. Oxidations and iminations to prepare S(IV) and S(VI) products.

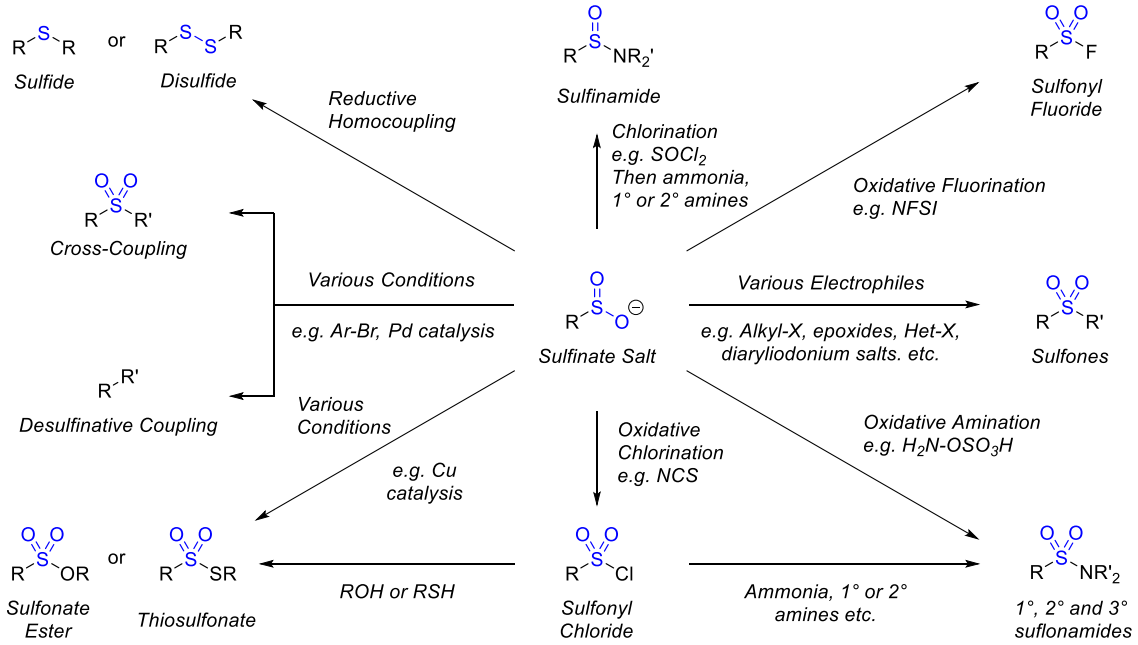
A useful method for the interconversion of sulfur functional groups is nucleophilic substitutions with functional groups containing a leaving-group (e.g. chloride) (**Scheme 1.3**). Whilst some sulfonyl chlorides are commercially available, or can be accessed as previously discussed, they can also be accessed via oxidative chlorination of sulfinate salts.[15] Aza-S(VI) halides can be similarly accessed from sulfinamides or sulfinamidines.[16] Imination of sulfinyl chlorides or deoxychlorination of sulfonamides and sulfonimidamides are alternative routes to aza-S(VI) chlorides.[17]



Scheme 1.3. Interconversion between S(IV) and S(VI) products.

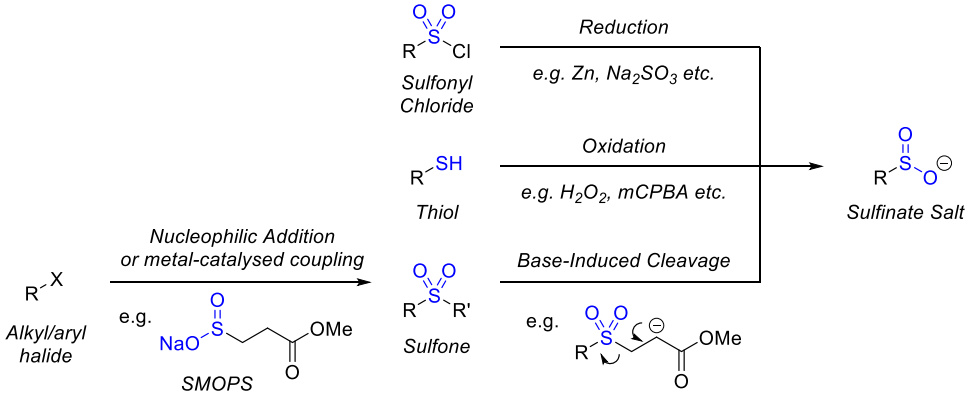
Given the discussed methods for the interconversion of S(VI) functional groups, synthetic routes can often be complicated, especially for aza-S(VI) products if preparation is needed from thiol or sulfonyl chloride starting materials. Of the available routes to S(VI) products, perhaps the most useful and versatile are oxidative functionalisations of S(IV) intermediates such as sulfinate salts, sulfinamides and sulfinamidines.[15]

Unlike sulfinic acids, which are prone to disproportionation,[18] sulfinate salts are generally stable reagents. They can readily react with C-electrophiles to prepare sulfones, F-electrophiles to prepare sulfonyl fluorides and N-electrophiles to prepare sulfonamides.[15, 19] Oxidative chlorination or fluorination can also be used to prepare sulfonyl halides which can then often be reacted directly with nucleophiles to prepare S(VI) products as demonstrated above.[15] Sulfinates have also been used in metal-catalysed Buchwald-Hartwig-type cross-couplings to prepare sulfones,[20] or in desulfinative $C(sp^2)$-$C(sp^2)$ and $C(sp^2)$-$C(sp^3)$ cross-couplings,[21] further enhancing their worth. Due to their versatility and stability, methods for the preparation of sulfinate salts are valuable for the synthesis of sulfonyl-derived products (**Scheme 1.4**).



Scheme 1.4. Versatility of sulfinate salts.

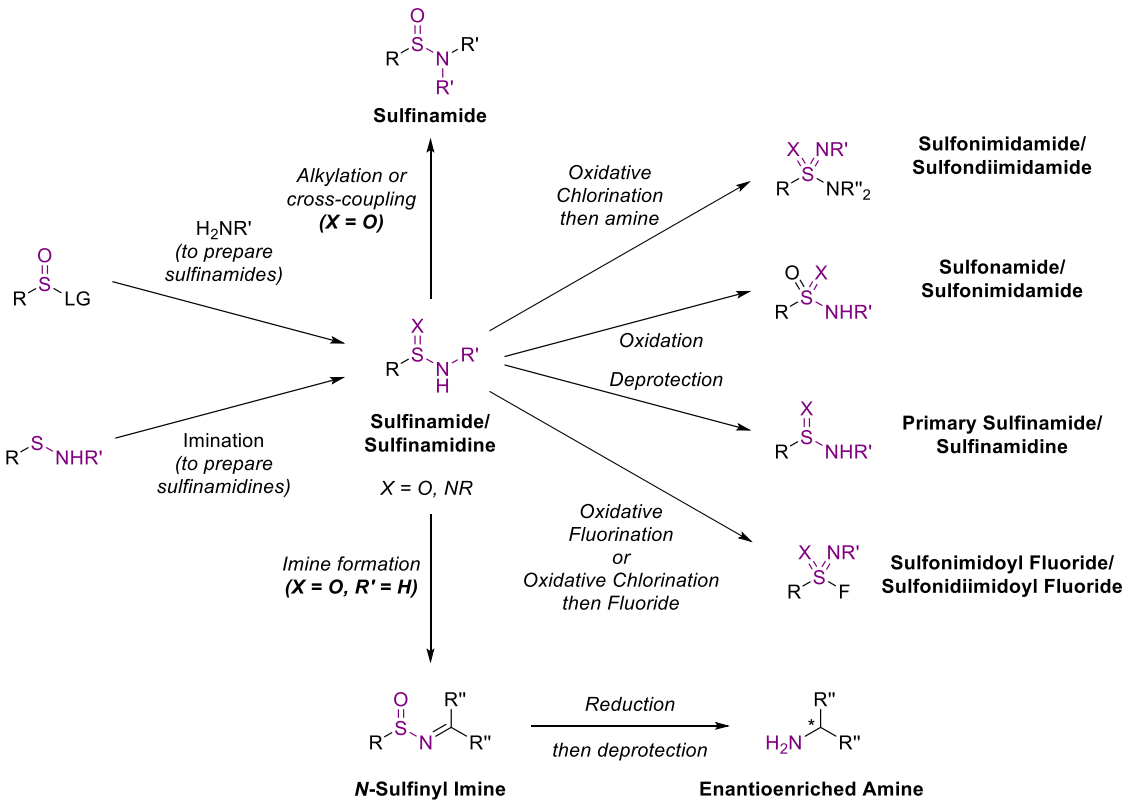
Classical methods for the preparation of sulfinates includes the oxidation of thiols or reduction of sulfonyl chlorides (**Scheme 1.5**), but more convenient processes for their preparation from more commercially-available substrates are desirable.[15, 22] One such method is the use of sulfinate transfer reagents, which reacts with electrophiles to give a sulfone intermediate, and subsequent elimination delivers the sulfinate salt.[23] The use of these reagents is limited by the availability of suitable electrophiles.



Scheme 1.5. Preparation of sulfinate salts from sulfonyl chlorides or thiols, or via the use of sulfinate transfer reagents.

Sulfinamides are also versatile intermediates for the preparation of various sulfur-containing functional groups (**Scheme 1.6**).[24] Unlike sulfinate salts, reaction with C-electrophiles or metal-

catalysed couplings usually result in functionalisation on nitrogen.[24] Sulfinamides have also been used extensively in condensation reactions with aldehydes and ketones. When using chiral sulfinamides, reaction with a ketone to form an imine and subsequent reduction can be a powerful method to access chiral amine products.[25] Sulfinamides can also be used for the preparation of other aza-sulfur products, usually via oxidative functionalisation.[26] Sulfinamidines can also be used analogously to prepare aza-sulfur products.[16a] Sulfinamides are usually prepared via nucleophilic substitution of other S(IV) products,[24] or oxidation of sulfenamides.[3b] Methods to prepare sulfinamidines are less-well developed, but one method that can be used is the imination of sulfenamides.[27]



Scheme 1.6. Versatility of sulfinamides and sulfinamidines.

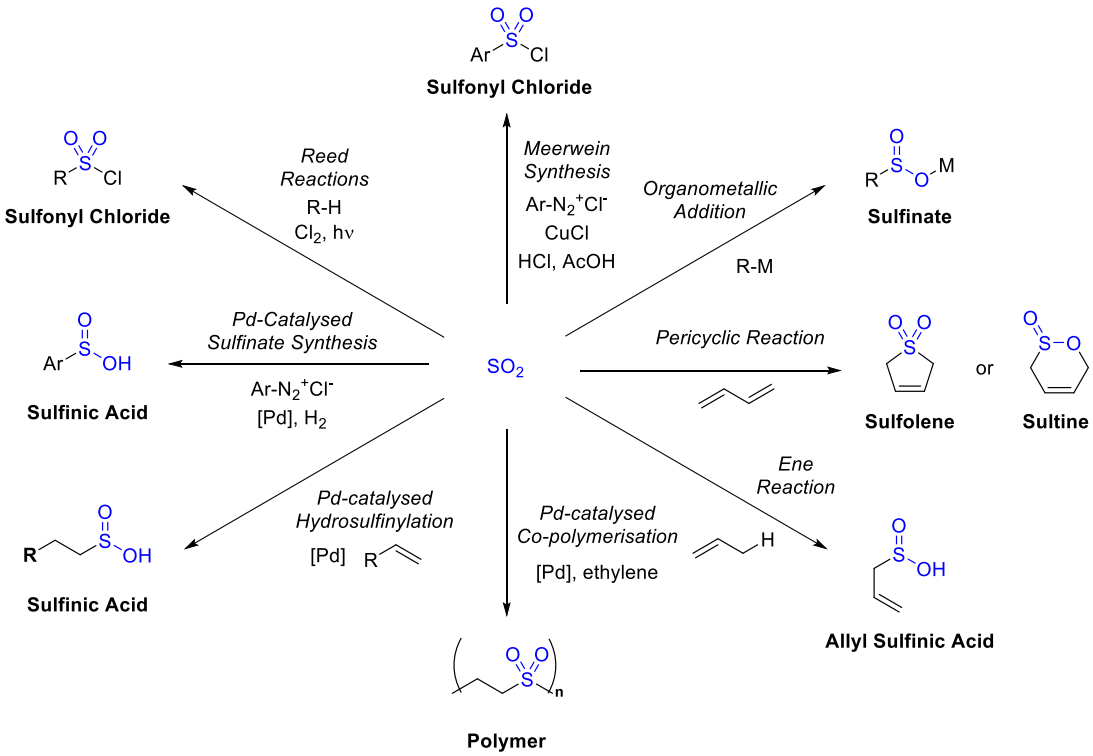
Whilst methods for the preparation of sulfinate salts, sulfinamides and sulfinamidines exist via interconversion from other sulfur functional groups, more methods for their direct preparation are desirable. Routes to these important intermediates have since been transformed through the

introduction and development of the chemistry of sulfur dioxide surrogates, sulfinylamines and sulfurdiimides.

1.3 Sulfur Dioxide

Sulfur dioxide is a cheap and widely-available commodity chemical. It is readily prepared through the aerobic combustion of elemental sulfur, and is used for the preparation of other important substances such as sulfuric acid and metal sulfites.[28] Sulfur dioxide has a varied reactivity profile, due to its high-lying HOMO and low-lying LUMO bonding giving amphoteric character (**Scheme 1.7**).[29]

Sulfur dioxide has found application in radical methods to prepare sulfonyl chlorides by Reed and Meerwein.[30] Sulfur dioxide also reacts readily in pericyclic reactions,[31] and can also be reacted with organometallic reagents to prepare sulfinate salts.[32] Sulfur dioxide has also been shown to readily form complexes with transition metals,[33] and this has been applied to some isolated examples of metal-catalysed reactions, such as palladium-catalysed alkene hydrosulfination,[34] co-polymerisation,[35] or in the preparation of sulfinic acids from aryldiazonium salts.[36] Despite the observed interaction between transition metals and sulfur dioxide, the lack of development in this field is proposed to be due to catalyst poisoning by excess SO_2.

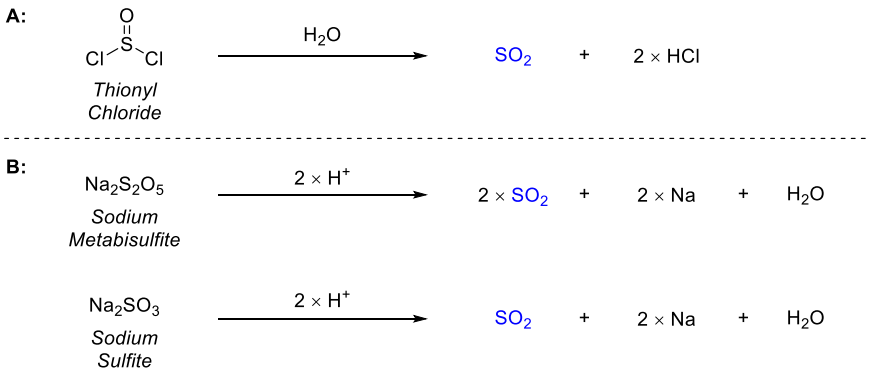


Scheme 1.7. Reactivity of sulfur dioxide.

Despite its diverse reactivity, sulfur dioxide is a toxic gas, and consequently requires the use of specialised equipment to handle it safely. Furthermore, precise control of loading is a challenge when using gaseous sulfur dioxide, and excess SO_2 can be detrimental, resulting in catalyst poisoning or overreaction. The use of solutions of sulfur dioxide of a known concentration has been used in some cases,[37] but more often, the use of sulfur dioxide surrogates has served as an effective method to introduce sulfur dioxide to reactions.

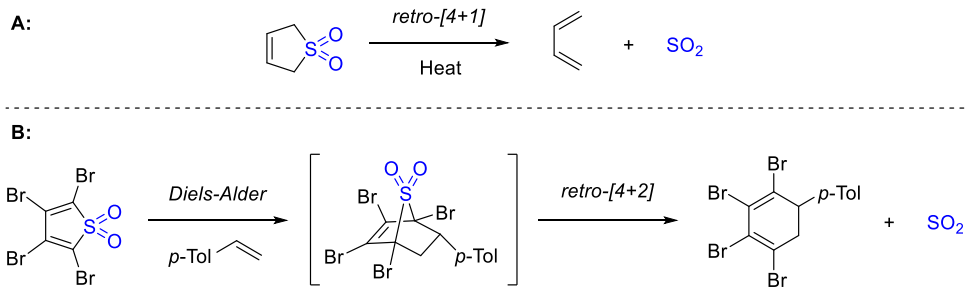
1.3.1 Sulfur Dioxide Surrogates

Several methods have been used to liberate sulfur dioxide in situ.[38] For example, the reaction of thionyl chloride with water can be used, although this method is uncommon (**Scheme 1.8.A**).[39] More common is the use of metal sulfite salts, such as sodium metabisulfite, which decompose under acidic conditions to liberate sulfur dioxide (**Scheme 1.8.B**).[40]



Scheme 1.8. A): Sulfur dioxide generation from hydrolysis of thionyl chloride. **B):** Sulfur dioxide generation from metal sulfite salts under acidic conditions.

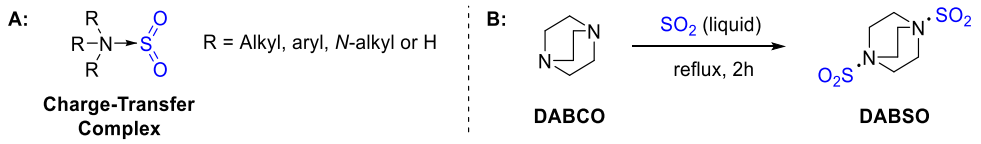
3-Sulfolene, the product of [4+2] cheletropic reaction between butadiene and sulfur dioxide, can be used to liberate sulfur dioxide at high temperatures via a retro-[4+2] reaction (**Scheme 1.9.A**).[41] Thiophene S,S-dioxides (SOGen) can also be used to liberate sulfur dioxide. These surrogates operate via Diels-Alder reaction with a styrene followed by a retro-[4+2] reaction (**Scheme 1.9.B**).[42] These surrogates are generally used in two-chamber setups, wherein gaseous sulfur dioxide is generated in one chamber and then diffuses into a second chamber where it is used in subsequent reactions.



Scheme 1.9. A): Sulfur dioxide generation from retro-[4+2] from sulfolene. **B):** Sulfur dioxide generation from SOGen.

Another important class of sulfur dioxide surrogates are amine-SO_2 charge-transfer complexes. Due to its Lewis acidity, sulfur dioxide forms 1:1 complexes with Lewis basic amine donors (**Scheme 1.10.A**). The formation of these adducts has been known since 1900,[43] but their application as sulfur dioxide surrogates in organic synthesis had been used only in isolated cases[44] until the introduction of DABSO, derived from DABCO and two molecules of SO_2, by Willis and co-workers (**Scheme 1.10.B**).[45] Amine-SO_2 charge-transfer complexes are stable under ambient conditions, and can be

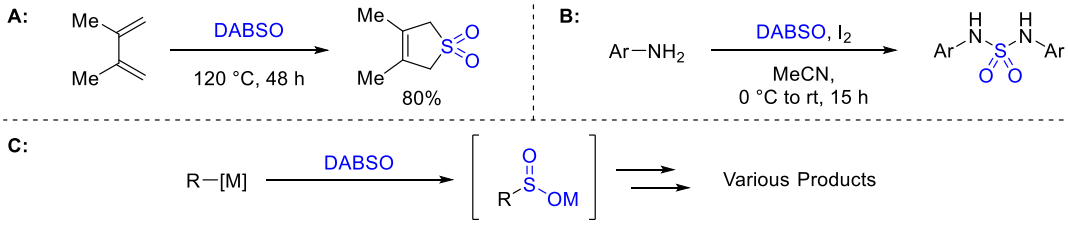
used to liberate SO_2 under mild conditions, and as a result have been used in a wide variety of reactions to prepare valuable sulfonyl-derived products.[46]



Scheme 1.10. A): Amine-SO_2 charge-transfer complexes. **B):** Synthesis of DABSO from DABCO and SO_2.

1.3.2 Reactions Using Sulfur Dioxide Surrogates

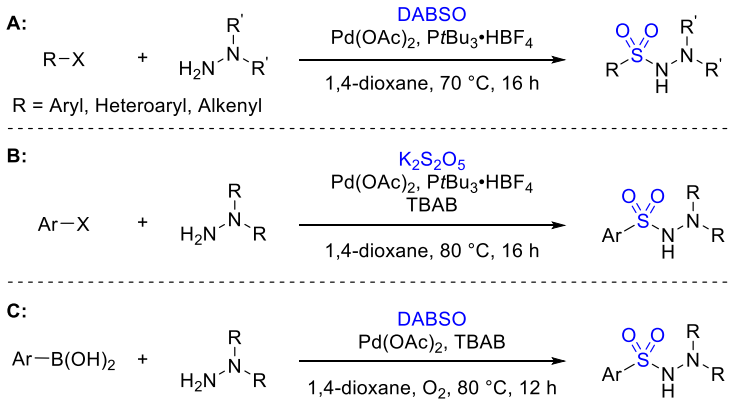
Following the introduction of sulfur dioxide surrogates, many new methods have been developed utilising SO_2 for the preparation of sulfonyl-derived products, usually using either metabisulfite salts or DABSO.[40, 46] Willis and co-workers showed that DABSO could be used as a direct replacement for SO_2 gas in cheletropic reactions to prepare sulfolene products, reactions with anilines to prepare sulfamides, or reactions with organometallic reagents to prepare sulfinate salts (**Scheme 1.11**).[47] Sulfinate salts prepared in this manner have been used in one-pot procedures to prepare a broad variety of products, including sulfones, sulfonamides, sulfoxides and sulfinamides.[48]



Scheme 1.11. A): Cheletropic reactions using DABSO. **B):** Synthesis of sulfamides using DABSO. **C):** Reaction of DABSO with organometallic reagents and subsequent derivatisation.

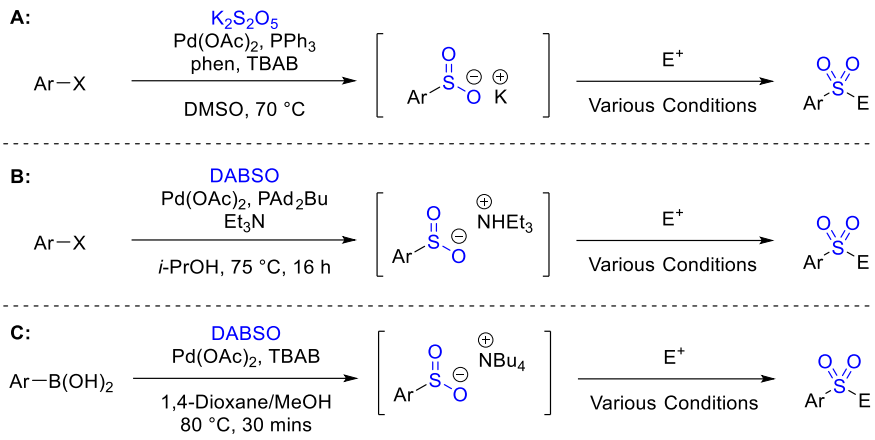
The ability to precisely control sulfur dioxide loading using SO_2 surrogates has enabled the development of several new methodologies, particularly using metal catalysis, where previously catalyst-poisoning by excess SO_2 hindered progress. Willis and co-workers initiated these studies through the development of a palladium-catalysed aminosulfonylation of aryl halides using DABSO and hydrazines (**Scheme 1.12.A**).[49] The observation that increased DABSO loading reduced product yield supports the proposed catalyst poisoning by excess SO_2. Subsequently, a similar transformation

has been developed by Wu and co-workers using potassium metabisulfite (**Scheme 1.12.B**).[50] Wu and co-workers later showed that boronic acids can also be used in aminosulfonylation reactions using DABSO and hydrazines under oxidising conditions (**Scheme 1.12.C**).[51] Procedures using alternative aryl substrates and catalysts have also been developed. [52]



Scheme 1.12. A): Pd-catalysed aminosulfonylation of aryl halides using DABSO. **B):** Pd-catalysed aminosulfonylation of aryl halides using potassium metabisulfite. **C):** Pd-catalysed aminosulfonylation of arylboronic acids using DABSO.

Willis and a group from Pfizer then independently developed palladium-catalysed methods for the synthesis of sulfinates using DABSO and $K_2S_2O_5$ (**Scheme 1.13.A-B**).[53] Both reactions required a reductant to complete the catalytic cycle, with Pfizer opting for sodium formate and Willis finding that the isopropanol solvent could serve as a reductant. Various sulfonyl derivatives were prepared using the intermediate sulfinate, including sulfones and sulfonamides. These reports were followed up by redox-neutral methods using boronic acids to prepare sulfinates (**Scheme 1.13.C**).[54] Subsequent methods utilised sulfinates prepared via metal-catalysis to develop improved methods for the synthesis of various sulfonyl derivatives, such as sulfonyl fluorides and sulfonate esters.[55] Other substrates and metal catalysts have also been used in the preparation of sulfinates and their derivatives.[56] This concept has also been used to develop copper-catalysed sulfonylative Suzuki, Hiyama and Chan-Lam couplings.[57]



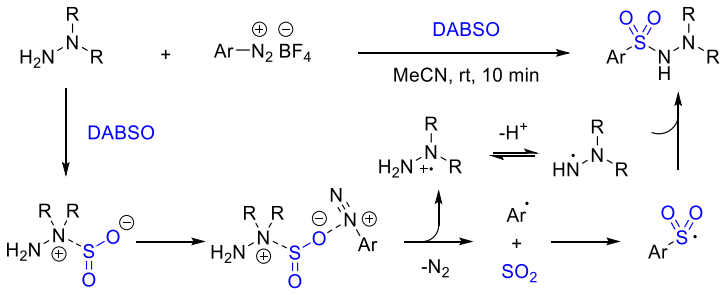
Scheme 1.13. A): Pd-catalysed sulfinylation of aryl halides using potassium metabisulfite. **B):** Pd-catalysed sulfinylation of aryl halides using DABSO. **C):** Pd-catalysed sulfinylation of arylboronic acids using DABSO.

The introduction of SO_2 surrogates and subsequent development of new reactions has transformed how synthetic organic chemists access sulfur-containing functional groups. In particular, metal-catalysed reactions have proven to be a versatile method for the preparation of aryl sulfonyl derivatives from SO_2 surrogates, however, the corresponding reactions to prepare alkyl sulfonyl derivatives are lacking. New methods are therefore needed to access these products, such as radical reactions leveraging the SOMO-philic character of SO_2.

1.3.3 Radical Reactions using Sulfur Dioxide Surrogates

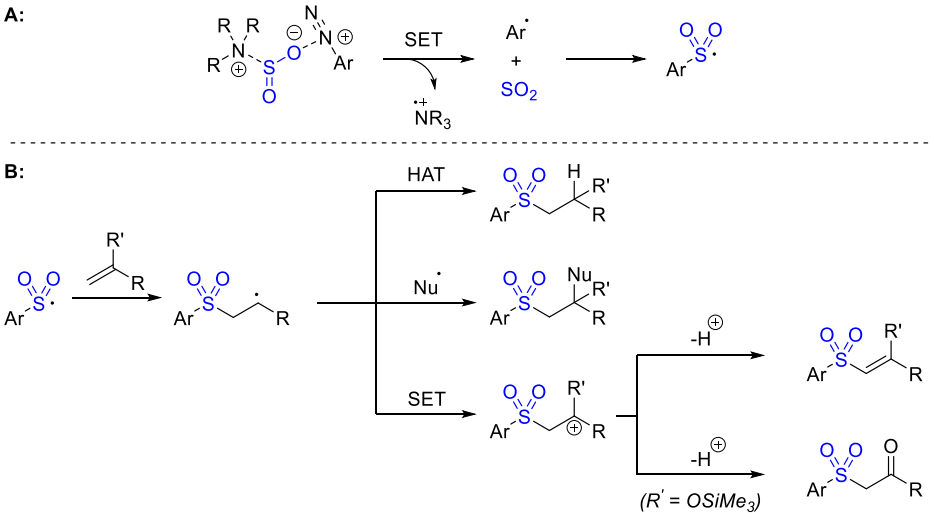
Some of the earliest uses of sulfur dioxide are the radical methods developed by Reed and Meerwein for the synthesis of sulfonyl chloride products.[30] Since the introduction of sulfur dioxide surrogates, many new radical methods have been developed for the introduction of sulfonyl-derived functional groups to organic molecules.[46, 58]

The first radical methods using SO_2 surrogates were achieved using aryldiazonium salts. The first of these methods was developed by Wu and co-workers, wherein it was found that a proposed palladium-catalysed aminosulfonylation using diazonium salts could be carried out in the absence of the palladium catalyst. A radical method was instead proposed, where a hydrazine-SO_2 charge-transfer complex is formed in situ, and electrostatic interactions between this and the aryldiazonium salts induce a charge-transfer event which initiates the reaction (**Scheme 1.14**).[59]



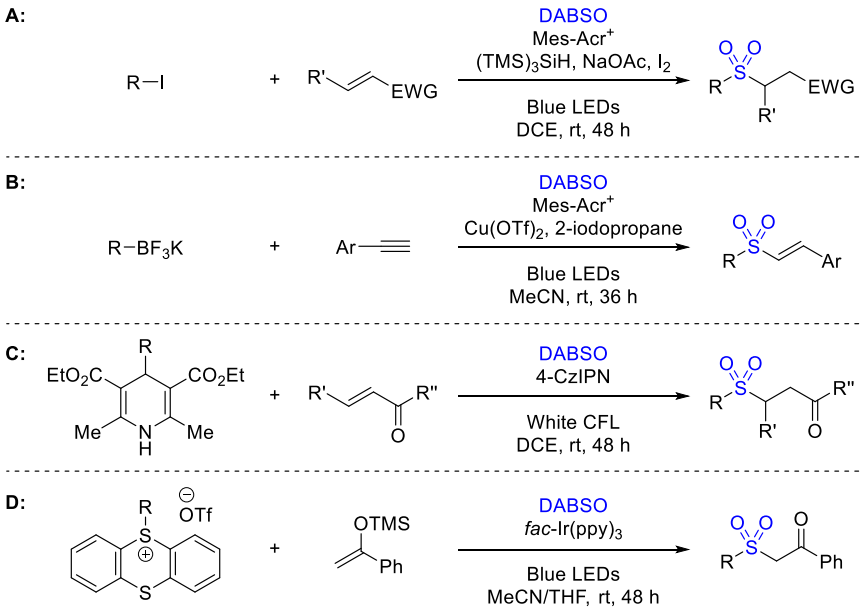
Scheme 1.14. Catalyst-free aminosulfonylation of aryldiazonium salts and proposed mechanism.

Subsequent developments enabled the trapping of the sulfonyl radical intermediate with alternative electrophiles such as alkenes and alkynes to prepare sulfone products. Initial investigations used peroxides and copper catalysis to initiate radical generation,[60] but subsequent investigations found that radicals could be generated in metal- and peroxide-free conditions via a mechanism similar to that using hydrazines, involving thermally-induced SET from DABSO to the aryldiazonium salt (**Scheme 1.15.A**).[61] Following sulfonyl radical addition to an alkene, various products can be prepared depending on the reaction conditions. HAT or trapping with an in-situ-generated radical can give alkyl products,[62] or SET can give carbocation products that can react with nucleophiles or eliminate to give an alkene.[61, 63] Alternatively, radical addition into a silyl enol ether can give β-keto sulfone products (**Scheme 1.15.B**).[64] Alkynes and various other radical traps have been used for the preparation of sulfonyl-derived products.[62d]



Scheme 1.15. **A):** Mechanism of metal-free radical generation from aryldiazonium salts. **B):** Preparation of sulfone products from sulfonyl radical addition to alkenes.

Whilst a substantial proportion of radical methods utilising SO_2 surrogates have used aryldiazonium salts, other radical precursors have also been used. For example, diaryliodonium salts and aryl halides have been used as alternative aryl radical precursors.[65] Alkyl radicals could also be generated from alkyl halides under milder conditions through the use of photocatalysts, which was used in combination with DABSO and electron-poor alkenes to give sulfone products (**Scheme 1.16.A**).[66] Various other alkyl radical precursors can also be used in combination with various photocatalysts, SO_2 surrogates and radical traps to give sulfone products. Examples of compatible radical precursors include potassium trifluoroborate salts,[67] 4-substituted Hantzsch esters[68] and thianthrenium salts (**Scheme 1.16.B-D**).[69]



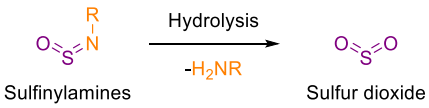
Scheme 1.16. **A):** Alkyl sulfone synthesis using alkyl iodides. **B):** Alkyl sulfone synthesis using alkyl trifluoroborate salts. **C):** Alkyl sulfone synthesis using 4-substitued Hantzsch esters. **D):** Alkyl sulfone synthesis using thianthrenium salts.

There are several further examples of methods for the synthesis of sulfur-containing functional groups via radical methods, and more methods continue to be disclosed.[46, 58] Most methods can be used only for specific substrates and access S(VI) products directly, so cannot serve as versatile methods for the synthesis of diverse sulfur-containing products. Methods to access sulfinate salts would be more versatile, but there are fewer examples of these. These are covered in detail in **Chapter 2**.

1.4 The Chemistry of Sulfinylamines

Sulfinylamines are the mono-aza analogues of sulfur dioxide. In 1878, Böttinger prepared the first known example of a sulfinylamine, *N*-sulfinylaniline, by reaction of aniline with thionyl chloride,[70] although the structure wasn't determined until 1890 by Herz and co-workers.[71] The reactivity of these interesting functional groups often mirrors that of sulfur dioxide, and as a result, they can provide access to challenging sulfur-containing functional groups.[72]

Due to their electrophilic sulfur atom, sulfinylamines are often readily-hydrolysed to sulfur dioxide and the corresponding primary amine (**Scheme 1.17**). Sulfinylamines with electron-withdrawing groups are particularly moisture-sensitive, meaning care needs to be taken upon preparation. [73] *N*-Alkylsulfinylamines are also rapidly hydrolysed, and are also prone to decomposition by other pathways, whereas *N*-arylsulfinylamines are somewhat more stable to hydrolysis, although care needs to be taken to prevent exposure to moisture for prolonged storage.



Scheme 1.17. Hydrolysis of sulfinylamines to SO_2.

The sensitivity of sulfinylamines to moisture has hindered their adoption as useful reagents, but recent work from Willis and co-workers has identified a selection of sulfinylamines that show markedly improved stability owing to steric or electronic factors (**Figure 1.6**). This has resulted in a resurgence in the use of sulfinylamines to prepare aza-sulfur functional groups.[73]

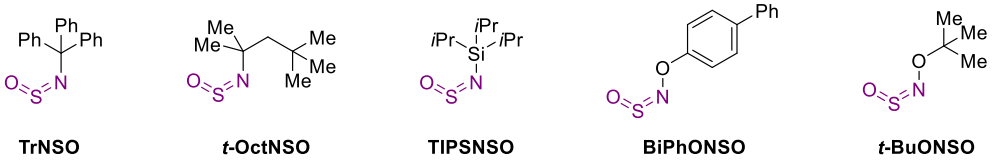
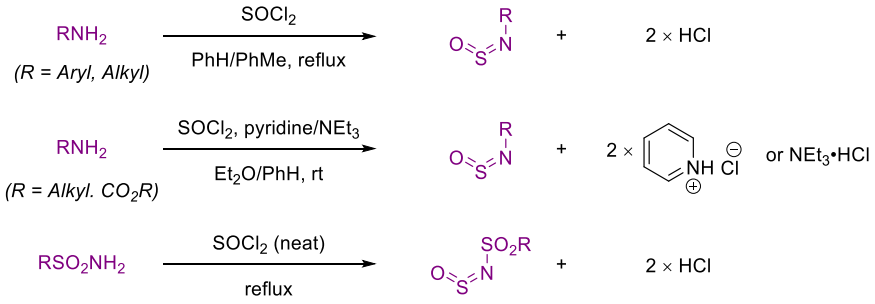


Figure 1.6. Examples of relatively moisture-stable sulfinylamines.

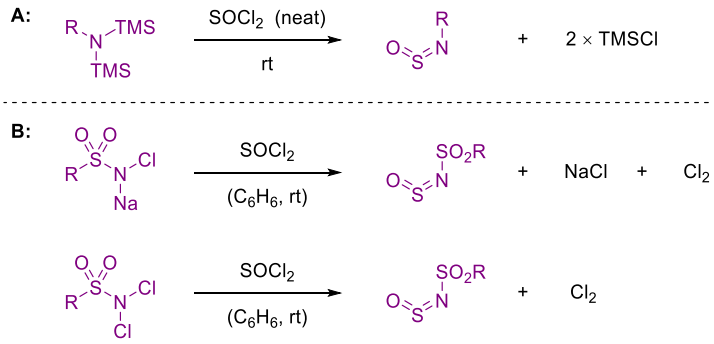
1.4.1 Preparation of Sulfinylamines

Following the seminal work by Böttinger, the reaction of amines with thionyl chloride remains the most common method for the preparation of sulfinylamines (**Scheme 1.18**).[70, 72a] High temperatures are usually used for the preparation of *N*-aryl sulfinylamines, but for more-reactive substrates such as alkylamines, or when preparing more sensitive sulfinylamines such as those derived from carbamates, the reaction can be carried out at room temperature with the addition of base.[74] *N*-Sulfinylsulfonamides, derived from primary sulfonamides, can also be prepared using thionyl chloride, but more forcing conditions are generally needed, and these sulfinylamines are usually prepared in refluxing neat thionyl chloride.[72b]



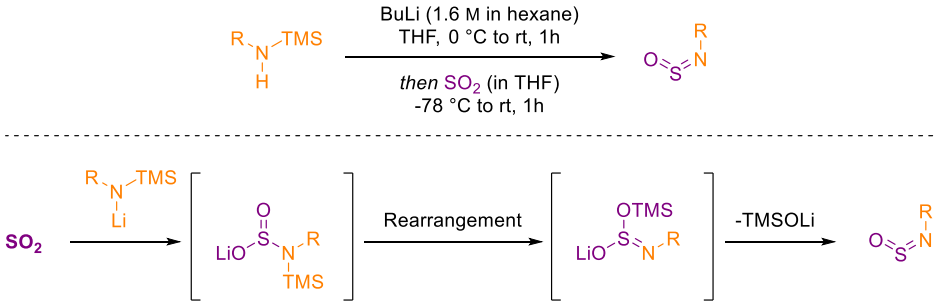
Scheme 1.18: Preparation of sulfinylamines from the corresponding amines using thionyl chloride.

Thionyl chloride can also be reacted with bis(trimethylsilyl)amines to give the corresponding sulfinylamines (**Scheme 1.19.A**).[75] Additionally, milder conditions for the preparation of *N*-sulfinylsulfonamides using thionyl chloride have also been developed, using either the sodium salts of *N*-chlorosulfonamides or *N*,*N*-dichlorosulfonamides (**Scheme 1.19.B**).[76]



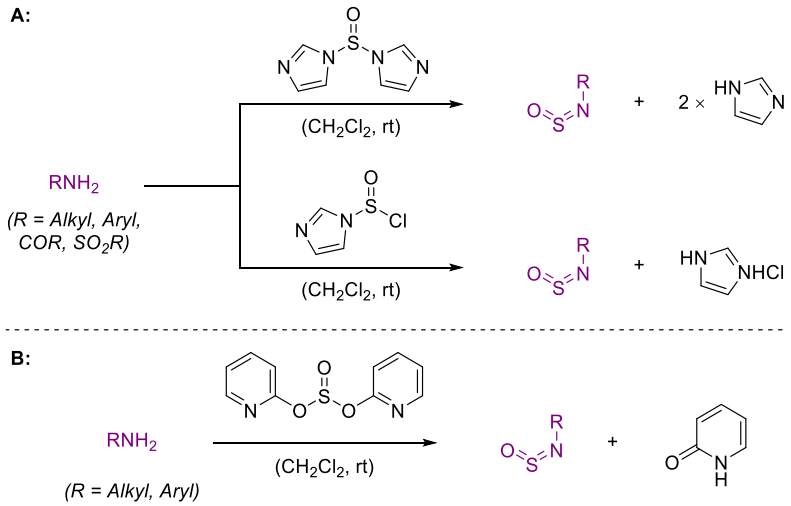
Scheme 1.19. A): Preparation of sulfinylamines using bis(trimethylsilyl)amines. **B):** Preparation of *N*-sulfinylsulfonamides from *N*-chlorosulfonamides.

An alternative procedure for the preparation of sulfinylamines involves the reaction of lithium trimethylsilylamides with gaseous sulfur dioxide.[77] Nucleophilic addition of the lithium trimethylsilylamides to SO_2, rearrangement, and loss of lithium trimethylsiloxide then gives the product sulfinylamines (**Scheme 1.20**).



Scheme 1.20. Preparation of sulfinylamines via nucleophilic addition of trimethylsilylamines to SO_2.

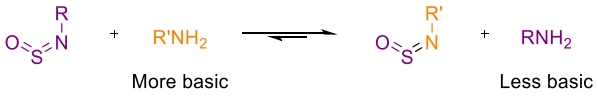
Alternative electrophiles to thionyl chloride can also be used to prepare sulfinylamines under milder conditions. For example, Kim and co-workers demonstrate the use of *N,N'*-sulfinylbisimidazole and *N*-(chlorosulfinyl)imidazole, both derived from thionyl chloride, to give sulfinylamines under mild conditions[78] These reagents give only imidazole or imidazolium hydrochloride as by-products, and can even be used for the preparation of *N*-sulfinylsulfonamides under mild reaction conditions (**Scheme 1.21.A**). Di-2-pyridyl sulfites have also been used in an analogous manner to prepare sulfinylamines under mild conditions. These reagents can also be prepared from thionyl chloride and can be stored for a short time without significant decomposition. The use of these reagents was only demonstrated for the preparation of alkyl or aryl sulfinylamines (**Scheme 1.21.B**).[79]



Scheme 1.21. A): *N,N'*-sulfinylbisimidazole and *N*-(chlorosulfinyl)imidazole reagents for the preparation of sulfinylamines. **B):** Di-2-pyridyl sulfites for the preparation of sulfinylamines.

Trans-sulfinylation is another important method by which sulfinylamines can be prepared. This involves transferring the sulfinyl group from a preformed sulfinylamine to a new primary amine. This can serve as a useful method to prepare sulfinylamines that would otherwise be sensitive to other reaction conditions used for their synthesis.[72]

Trans-sulfinylation reactions exist in equilibrium between the two sulfinylamines, and the equilibrium generally favours the formation of the sulfinylamine derived from the more basic amine. As a result, *N*-sulfinylsulfonamides are excellent reagents for trans-sulfinylation, affording the new sulfinylamine in almost quantitative yield (**Scheme 1.22**).[76, 80] This process is discussed in more detail in **Chapter 4**.

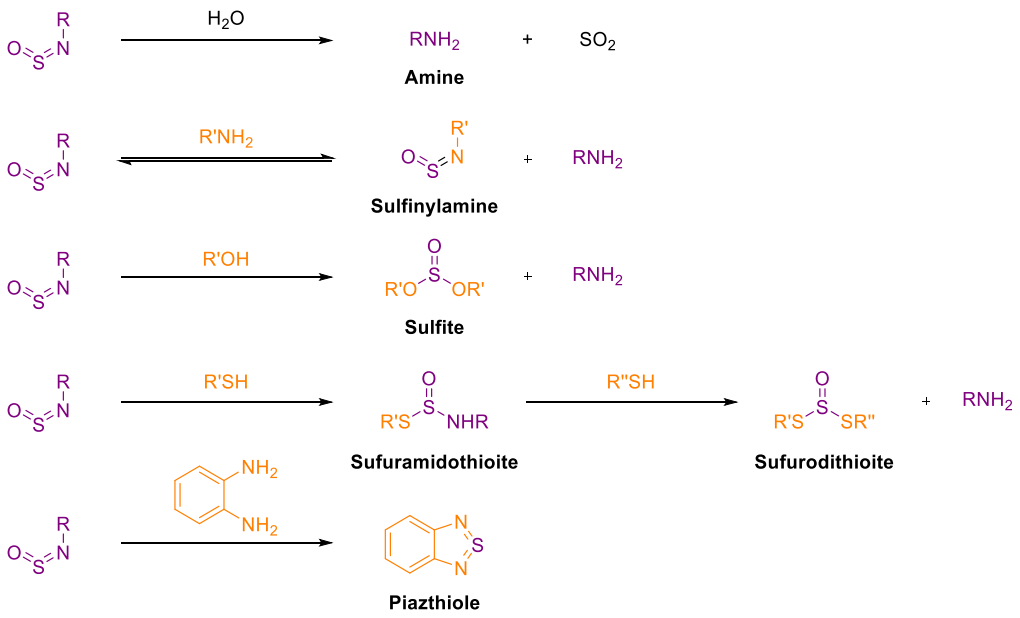


Scheme 1.22. Amine-sulfinylamine exchange equilibrium.

1.4.2 Reactions of Sulfinylamines

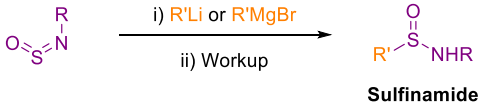
The electrophilicity of the sulfur atom in sulfinylamines is important for its reactivity. Whilst reaction with water results in hydrolysis and reaction with amines results in trans-sulfinylation, reaction with other nucleophiles can give a selection of interesting products. For example, reaction with alcohols gives sulfite products,[81] whereas reaction with thiols initially give a sulfuramidothioite, which can

then react with another thiol to give a sulfurodithioite (**Scheme 1.23**).[82] Reactions of sulfinylamines with 1,2-diamines can also be used to prepare 2,1,3-benzothiadiazole (piazthiole) products.[83]



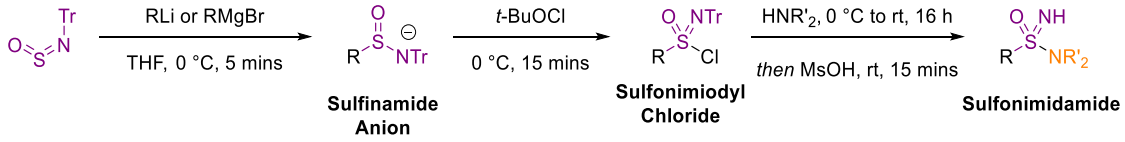
Scheme 1.23. Reaction of sulfinylamines with nucleophiles.

Sulfinylamines also react readily with organometallic reagents, which upon workup provides the corresponding sulfinamide (**Scheme 1.24**).[74, 84] Given the versatility of sulfinamides, this is an important observation, as this can provide a route towards important aza-sulfur functional groups.



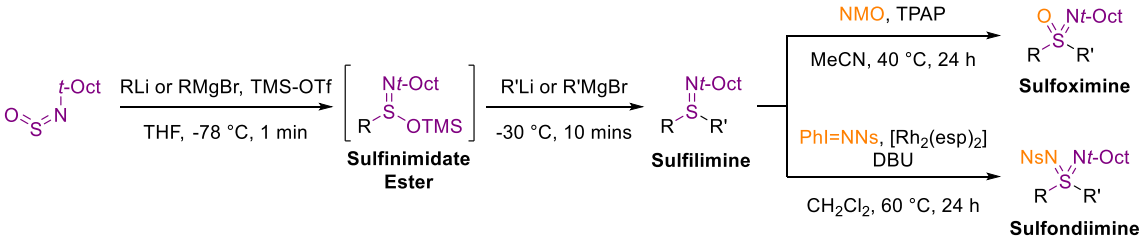
Scheme 1.24. Reaction of sulfinylamines with organometallic nucleophiles.

The Willis group utilised the addition of organometallic reagents to introduce their relatively moisture-stable sulfinylamine, TrNSO. Oxidative chlorination, reaction with amine nucleophiles and deprotection of the trityl group using methanesulfonic acid resulted in the preparation of sulfonimidamide products in a one-pot, 4-step procedure (**Scheme 1.25**).[16b]



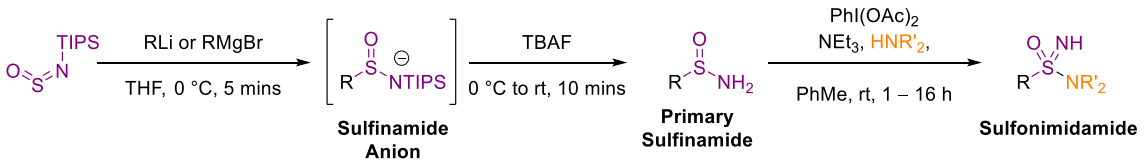
Scheme 1.25. Reaction of sulfinylamines with organometallic nucleophiles.

The sulfinylamine *t*-OctNSO was used in a procedure to prepare sulfondiimines via the addition of an organometallic reagent and trapping the anionic intermediate with TMS triflate to prepare a sulfinimidate ester. Addition of another organometallic reagent then gave a sulfilimine intermediate, from which a sulfondiimine was prepared via rhodium catalysed imination using an iminoiodinane reagent. Sulfoximines could also be prepared by oxidation of the sulfilimine intermediates. Deprotection of both protecting groups and functionalisations of the imidic nitrogens was also demonstrated (**Scheme 1.26**).[85]



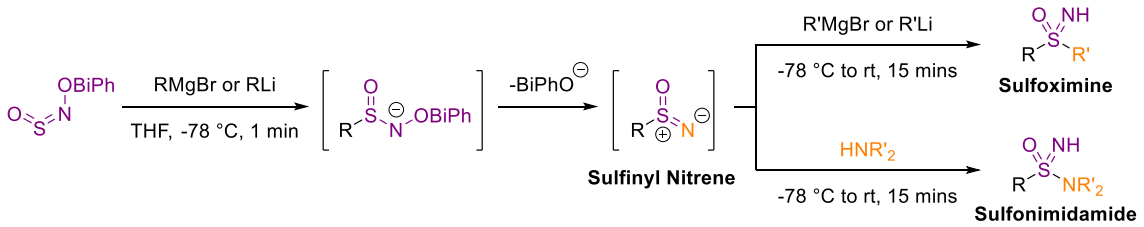
Scheme 1.26. Preparation of sulfoximines and sulfondiimines from *t*-OctNSO via oxidation or imination of a sulfilimine intermediate.

Willis and co-workers also developed an *N*-silyl sulfinylamine, TIPSNSO, which was found to be relatively-moisture stable, and owing to the ease of TIPS-deprotection using TBAF, could be used for the preparation of primary sulfinamides. An efficient 2-step procedure was then developed for the conversion of primary sulfinamides to sulfonimidamides via oxidative amination using (diacetoxyiodo)benzene (PIDA) and an amine nucleophile (**Scheme 1.27**). This resulted in an improved procedure for the rapid preparation of sulfonimidamides than that previously developed using TrNSO.



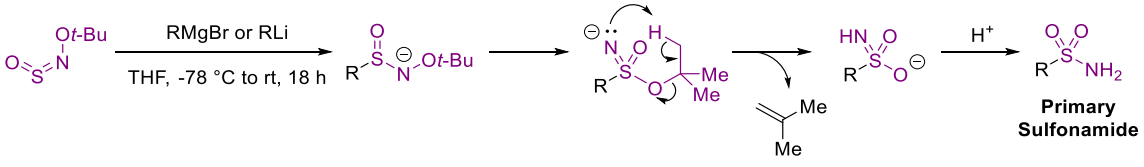
Scheme 1.27. Preparation of primary sulfinamides from TIPSNSO and subsequent oxidative amination to prepare sulfonimidamides.

The sulfinylhydroxylamine BiPhONSO was also prepared by Willis and co-workers. This sulfinylhydroxylamine was found to have good stability, and reacted readily with organometallic nucleophiles, but upon formation of the sulfinamide anion intermediate, cleavage of the weak N-O bond and loss of the phenoxide leaving group results in the formation of a sulfinyl nitrene intermediate. The authors harnessed the unique reactivity of sulfinyl nitrenes by reaction with further organometallic or amine nucleophiles to give sulfoximine or sulfonimidamide products (**Scheme 1.28**).[86]



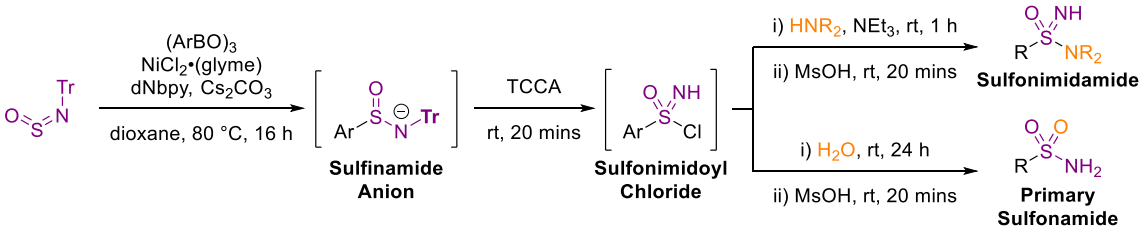
Scheme 1.28. Preparation of sulfoximines and sulfonimidamides from BiPhONSO via the formation of a sulfinyl nitrene intermediate.

Willis and co-workers also developed another sulfinylhydroxylamine, *t*-BuONSO, which can be used to access primary sulfonamides. Addition of organometallic reagents to *t*-BuONSO gives a sulfinamide anion intermediate, which rather than forming sulfinyl nitrenes, instead rearranges to a sulfinamidate ester intermediate which then liberates isobutene to give a primary sulfonamide (**Scheme 1.29**).



Scheme 1.29. Preparation of primary sulfonamides via the addition of organometallic reagents to *t*-BuONSO.

Whilst the chemistry of sulfinylamines generally mirrors that of sulfur dioxide, the only published example of a metal-catalysed reaction of sulfinylamines was disclosed by Willis and co-workers, wherein a nickel-catalysed coupling between arylboroxines and TrNSO gave sulfinamide intermediates, which were then used to prepare sulfonimidamides in a multistep sequence via oxidative chlorination, reaction with amine nucleophiles and trityl deprotection (**Scheme 1.30**).[87] Primary sulfonamides were also obtained via oxidative chlorination, hydrolysis and trityl deprotection. The use of boroxines rather than boronic acids was crucial in this reaction, as when boronic acids were used, inconsistent results were obtained, owing to the hydrolysis of TrNSO under the reaction conditions.



Scheme 1.30. Preparation of sulfonimidamides and primary sulfonamides via the nickel-catalysed coupling of boroxines with TrNSO.

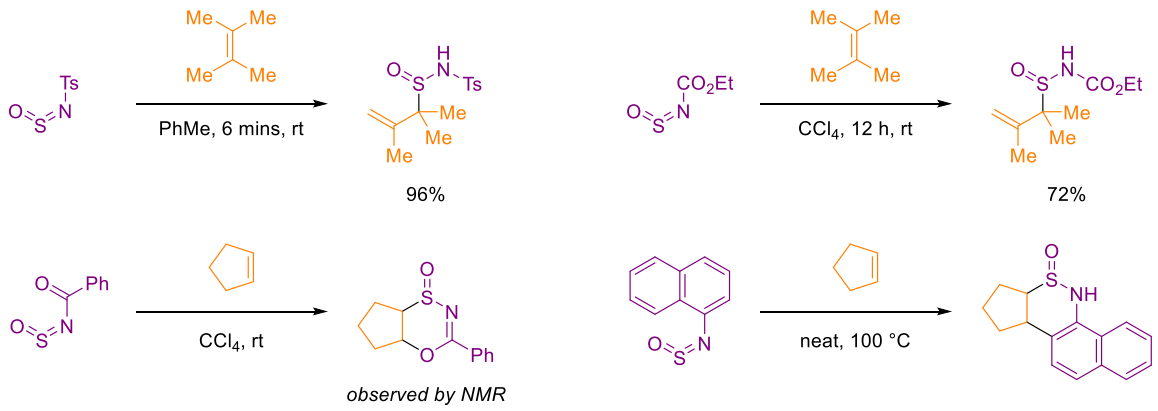
Another important reaction of sulfinylamines is in cycloaddition or ene reactions.[72b] Electron-poor sulfinylamines such as *N*-sulfinylsulfonamides react more readily in cycloaddition reactions than sulfinylanilines, which often need more forcing conditions. Cycloaddition reactions have not been observed using *N*-alkylsulfinylamines. In hetero-Diels-Alder reactions, PhNSO requires prolonged heating of the neat reactants to give the cycloaddition product in 74% yield,[88] whereas heating a solution of TsNSO and butadiene in benzene provides the corresponding cycloaddition product in 94% yield after 1 h at 50 – 60 °C.[72a, 76] (**Scheme 1.31**). An asymmetric variant of the hetero Diels-Alder was carried out by Gautun and co-workers using either TsNSO or CbzNSO.[89]



Scheme 1.31. Hetero-Diels-Alder reactions using sulfinylamines.

Sulfinylamines have also been used in cycloaddition reactions with various other substrates, such as donor-acceptor cyclopropanes,[90] ketenes,[91] and various 1,3-dipoles.[72b, 92]

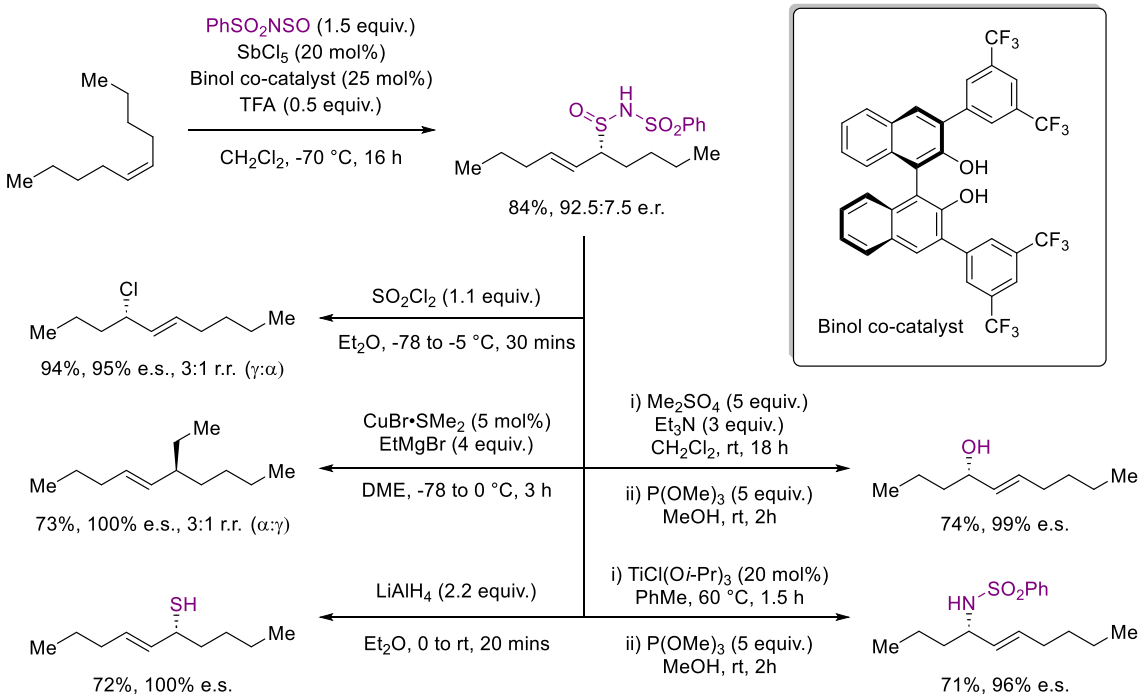
Electron-poor sulfinylamines are also excellent enophiles, readily forming ene adducts with olefins under mild conditions (**Scheme 1.32**).[93] Kresze and co-workers showed that this reaction proceeds well using both *N*-sulfinylsulfonamides and *N*-sulfinylcarbamates, with more electron-withdrawing substituents reacting at faster rate.[94] The corresponding ene-adducts from *N*-sulfinylamides were not observed, the sulfinylamine instead acting as a heterodiene, giving the [4+2] reaction products. These products were observed by NMR analysis of the reaction mixtures, but could not be isolated.[94a] Ene reactions of *N*-sulfinylanilines have not been observed in any cases. Instead, at elevated temperatures, *N*-sulfinyl-1-aminonaphthalene forms [4+2] cycloaddition adduct involving the naphthalene ring.[95] Similar products have also been observed using *N*-sulfinylaniline with norbornene.[96]



Scheme 1.32. Ene reactions using sulfinylamines.

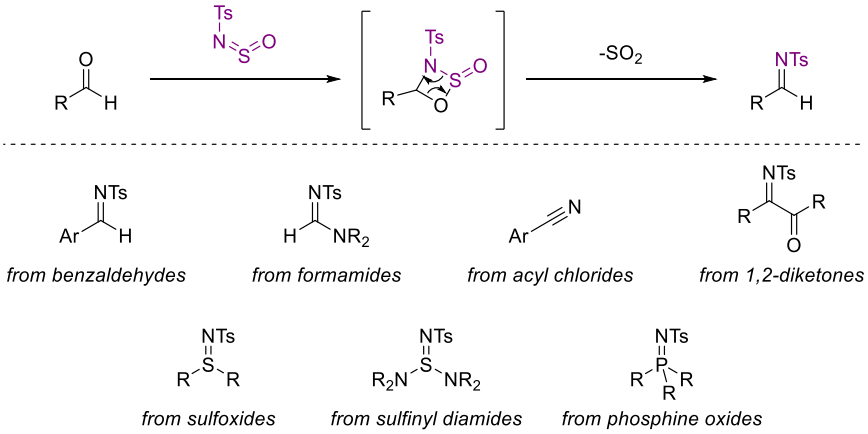
Ene reactions of sulfinylamines continue to garner interest in more recent literature. For example, a chiral Lewis acid-catalysed ene reaction of *N*-sulfinylsulfonamides with olefins was developed by Tambar and co-workers.[97] Given the high reactivity of *N*-sulfinylsulfonamides with olefins in ene reactions, low temperatures were needed to shut down the background reaction, such that only the catalysed reaction operated, giving the sulfinamide products with high enantioselectivity. Only internal cis-akenes gave good yields

and good enantioselectivity. The enantioenriched allyl sulfinamide products could be used to prepare a diverse selection of valuable chiral products (**Scheme 1.33**).



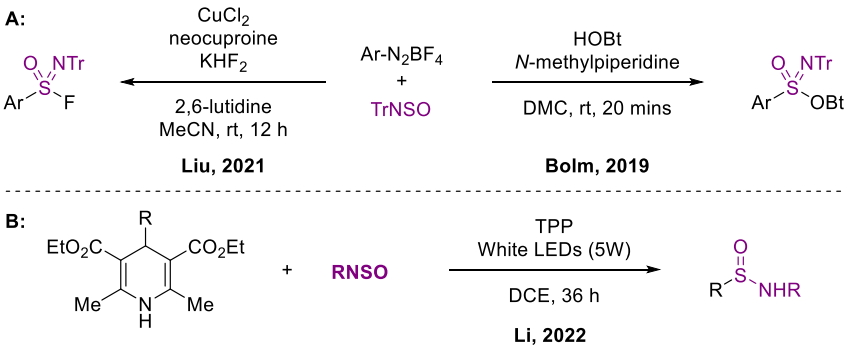
Scheme 1.33. Stereoselective ene reaction and subsequent derivatisation to enantioenriched products.

Another useful reaction of electron-poor sulfinylamines is in reactions with carbonyl compounds (benzaldehydes, formamides, acyl chlorides and 1,2-diketones), sulfoxides, sulfinyl diamides and phosphine oxides to prepare their imine derivatives.[14c, 72b, 98] The mechanisms of these reactions have not been well-studied, but have been proposed to operate similarly to a Wittig reaction via the formation of a 4-membered ring followed by a retro [2+2] to liberate SO_2 and generate the imine product (**Scheme 1.34**).



Scheme 1.34. Proposed mechanism for formation of an aldimine from an aldehyde using TsNSO, and accessible imine derivatives using related methodologies.

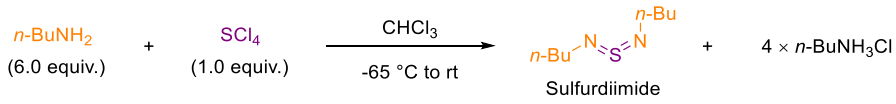
Where many methods have utilised radical addition to sulfur dioxide to prepare sulfonyl products, reactions utilising radical addition to sulfinylamines are scarce. Aryldiazonium salts were used as radical precursors by Liu and Bolm to prepare sulfonimidoyl fluoride or sulfonimidate ester products from radical addition to TrNSO (**Scheme 1.35.A**).[99] Li and co-workers used 4-substituted Hantzsch ester as alkyl radical precursors to prepare sulfinamides from sulfinylamines (**Scheme 1.35.B**).[100] These reactions are discussed in more detail in **Chapter 3**.



Scheme 1.35. A): Reactions of aryldiazonium salts with TrNSO to prepare sulfonimidoyl fluoride or sulfonimidate ester products. **B):** Preparation of sulfinamides from 4-substituted Hantzsch esters via radical addition to sulfinylamines.

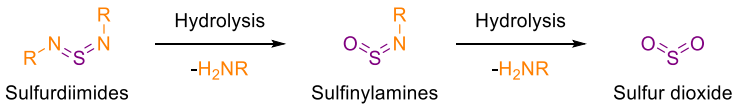
1.5 The Chemistry of Sulfurdiimides

Sulfurdiimides are the di-aza analogues of sulfur dioxide, the first example of which, dibutylsulfur diimide, was prepared by Goehring and Weis in 1956 from the reaction of 6 equivalents of butylamine with sulfur tetrachloride (**Scheme 1.36**).[101]



Scheme 1.36. First synthesis of a sulfurdiimide.

Sulfurdiimides are often more hydrolytically-sensitive than the corresponding sulfinylamines, particularly those with one or two electron-withdrawing groups (**Scheme 1.37**).[72b] Di-alkyl sulfurdiimides are also relatively moisture-sensitive and prone to decomposition, although di-*tert*-alkyl sulfurdiimides have been shown to have markedly improved stability.[102] Diaryl sulfurdiimides also slowly hydrolyse in the presence of water.



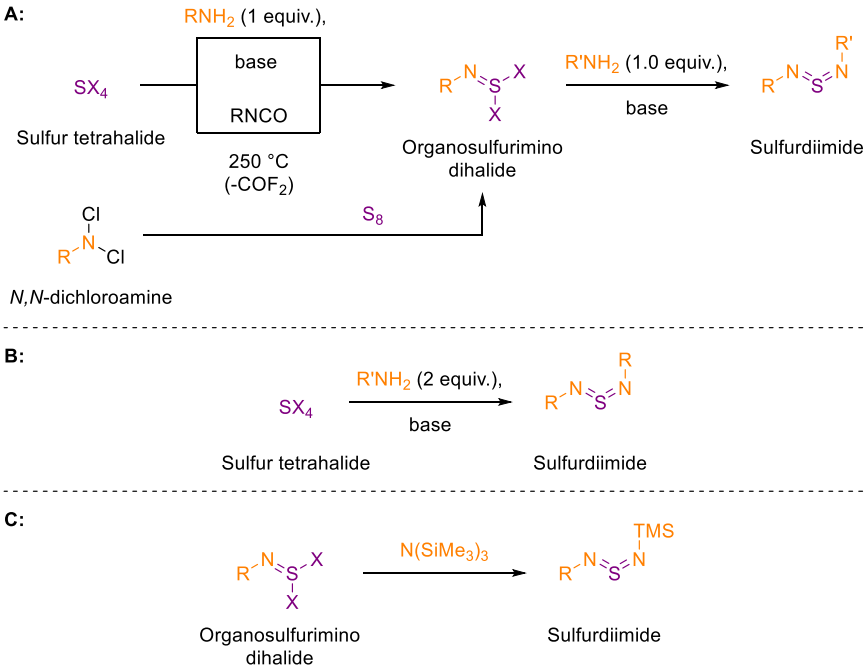
Scheme 1.37. Hydrolysis of sulfurdiimides to SO_2

The chemistry of sulfurdiimides is even less-well explored than that of sulfinylamines. This may be in part due to their hydrolytic sensitivity, as well as their preparation either requiring the use of hazardous reagents, or needing multi-step sequences. Despite this, sulfurdiimides have been shown to have interesting reactivity, often mirroring that of sulfinylamines,[72b] and they have found some recent applications in the synthesis of challenging aza-sulfur functional groups.[16a, 103]

1.5.1 Preparation of Sulfurdiimides

Where sulfinylamines can be accessed from reaction of thionyl chloride with amines, sulfurdiimides can be prepared using its aza-analogue, organoiminosulfur dichloride,[101] or organoiminosulfur difluorides,[104] which themselves are generally prepared from the reaction

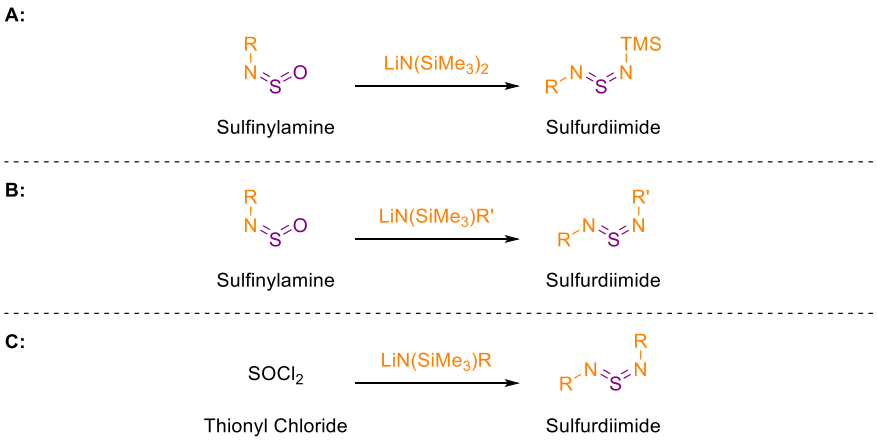
of sulfur tetrahalides with amines or isocyanates (**Scheme 1.38.A**).[101, 104-105] Organoiminosulfur dichlorides have also previously been prepared via the reaction of *N,N*-dichloroamines with elemental sulfur.[106] Symmetrical sulfurdiimides can also be accessed directly from sulfur tetrahalides with excess primary amine without the need to isolate the intermediate organoiminosulfur dihalides (**Scheme 1.38.B**). Similar to the analogous reaction of tris(trimethylsilyl)amine with thionyl chlorides, organoiminosulfur dihalides can be used instead to prepare sulfurdiimides (**Scheme 1.38.C**).[107] Due to the poor stability of sulfur tetrachloride, the more stable sulfur tetrafluoride is more commonly used in these reactions. Whilst several methods can be used for the preparation of SF_4,[108] the hazards associated with the use of this toxic gaseous reagent limit the use of these methods to prepare sulfurdiimides. Furthermore, similar to thionyl chloride, the intermediate organoiminosulfur dihalides are also moisture sensitive,[105a] and in some cases have been known to polymerise.[104a]



Scheme 1.38. A) Sulfurdiimides from sulfur tetrahalides via organoiminosulfur dihalides. B) Symmetrical sulfurdiimides directly from sulfur tetrahalides. C) Reaction of organoiminosulfur dihalides with tris(trimethylsilyl)amine.

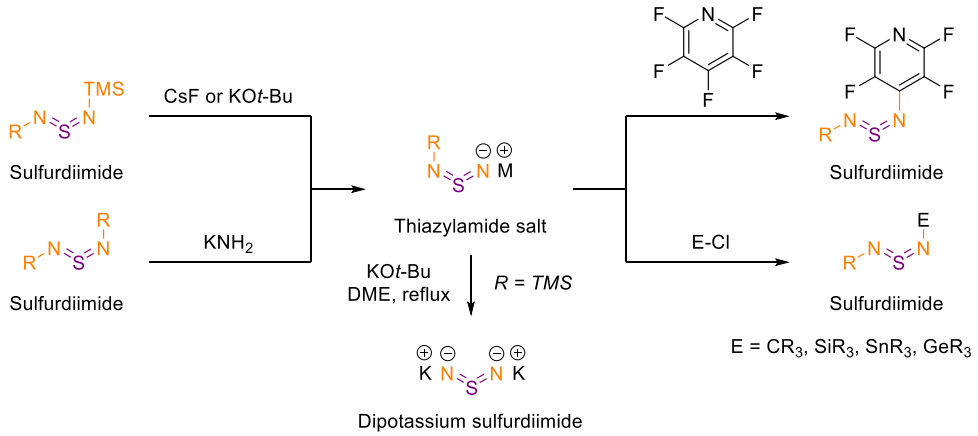
A more useful method developed by Appel and co-workers uses the reaction of sulfinylamines with lithium bis(trimethylsilyl)amide to give unsymmetrically substituted sulfurdiimides

where one of the protecting groups is TMS (**Scheme 1.39.A**).[109] Alternatively, lithium trimethylsilylamides with various alkyl or aryl substituents can be used for the preparation of sulfurdiimides, although mixtures of symmetrical and unsymmetrical sulfurdiimides is sometimes observed (**Scheme 1.39.B**).[110] The mechanism of these reactions is similar to that proposed for the preparation of sulfinylamines from lithium trimethylsilyl amides and SO_2.[77] Lithium trimethylsilyl amides can instead be reacted directly with thionyl chloride to prepare symmetrical sulfurdiimides (**Scheme 1.39.C**).[110b]



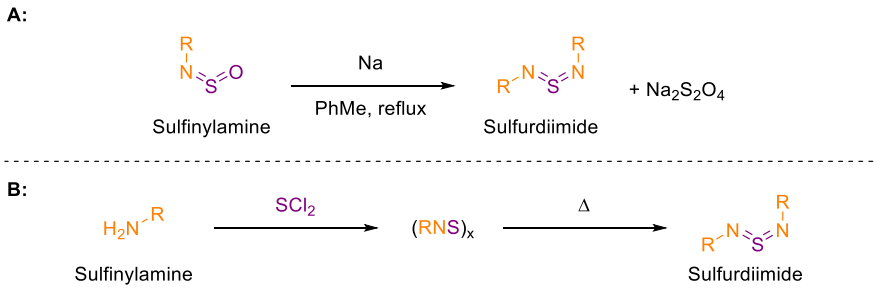
Scheme 1.39. A) Sulfurdiimides from sulfinylamines and LiHMDS. B) Sulfurdiimides from sulfinylamines and lithium trimethylsilyl amides. C) Sulfurdiimides from thionyl chloride and lithium trimethylsilyl amides.

TMS protecting groups on sulfurdiimides can be removed using either CsF or KO*t*-Bu to give the corresponding thiazylamide salts.[111] These salts can also be prepared from the reaction of potassium amide with sulfurdiimides.[112] These unstable salts have been reacted with a limited selection of electrophiles, such as heteroaryl fluorides or group 4 halides to give the corresponding sulfurdiimides.[113] The dianion can also be prepared by double deprotection of TMS groups under more harsh conditions, and these react with selected electrophiles similarly to the monoanions (**Scheme 1.40**).[114]



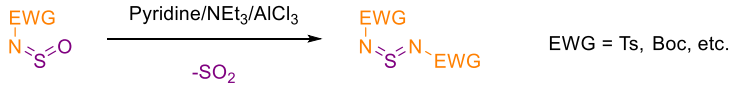
Scheme 1.40. Preparation and reactions of thiazylamide salts.

Other less-general methods for the preparation of sulfurdiimides include the reaction of sulfinylamines with sodium metal, giving sodium dithionite as a by-product (**Scheme 1.41.A**).[115] Alternatively, the reaction of tertiary amines with SCl_2 and subsequent thermal cracking of the polymeric $(RNS)_x$ compounds gives di-*tert*-alkyl sulfurdiimides (**Scheme 1.41.B**).[102]



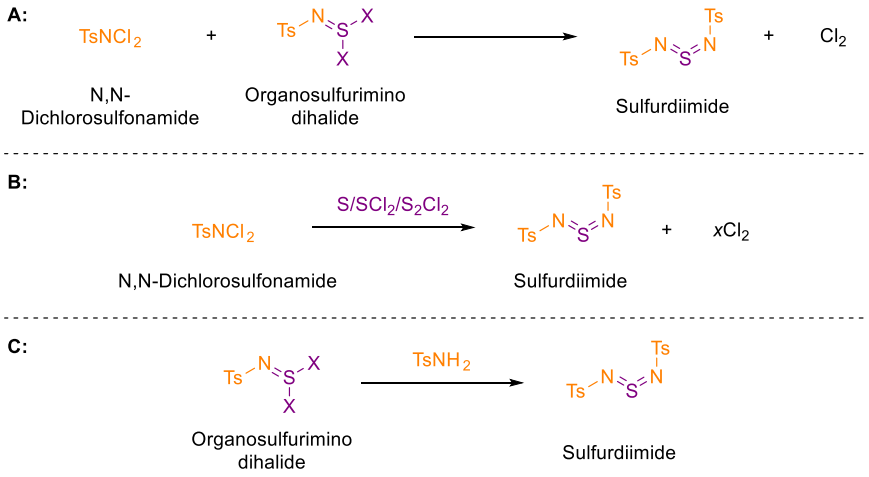
Scheme 1.41. A): Sulfurdiimides from sulfinylamines and sodium metal. **B):** Sulfurdiimides from tertiary amines and SCl_2.

An important class of sulfurdiimides are those substituted with two electron-withdrawing groups, such as disulfonylsulfurdiimides. These compounds are conveniently accessed from the reaction of the corresponding sulfinylamines with pyridine, tertiary amines or Lewis acids, liberating SO_2 (**Scheme 1.42**).[116]



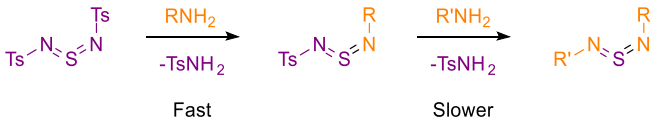
Scheme 1.42. Preparation of electron-poor sulfurdiimides synthesis from sulfinylamines.

Similar to the corresponding *N*-sulfinylsulfonamides, which can be prepared from *N*,*N*-dichlorosulfonamides and thionyl chloride, disulfonylsulfurdiimides can be prepared analogously using organoiminosulfur dihalides (**Scheme 1.43.A**).[117] *N*,*N*-Dichlorosulfonamides can also react with elemental sulfur, sulfur dichloride or disulfur dichloride to give disulfonylsulfurdiimides directly (**Scheme 1.43.B**).[117] Similar to alkyl sulfurdiimides, electron-poor sulfurdiimides can also be prepared from the reaction of organoiminosulfur dihalides and sulfonamides (**Scheme 1.43.C**).[117]



Scheme 1.43. A): Disulfonylsulfurdiimides from *N*,*N*-dichlorosulfonamides and organoiminosulfur dihalides. **B):** Disulfonylsulfurdiimides from *N*,*N*-dichlorosulfonamides and S, SCl_2 or S_2Cl_2. **C):** Disulfonylsulfurdiimides from *N*,*N*-dichlorosulfonamides and sulfonamides.

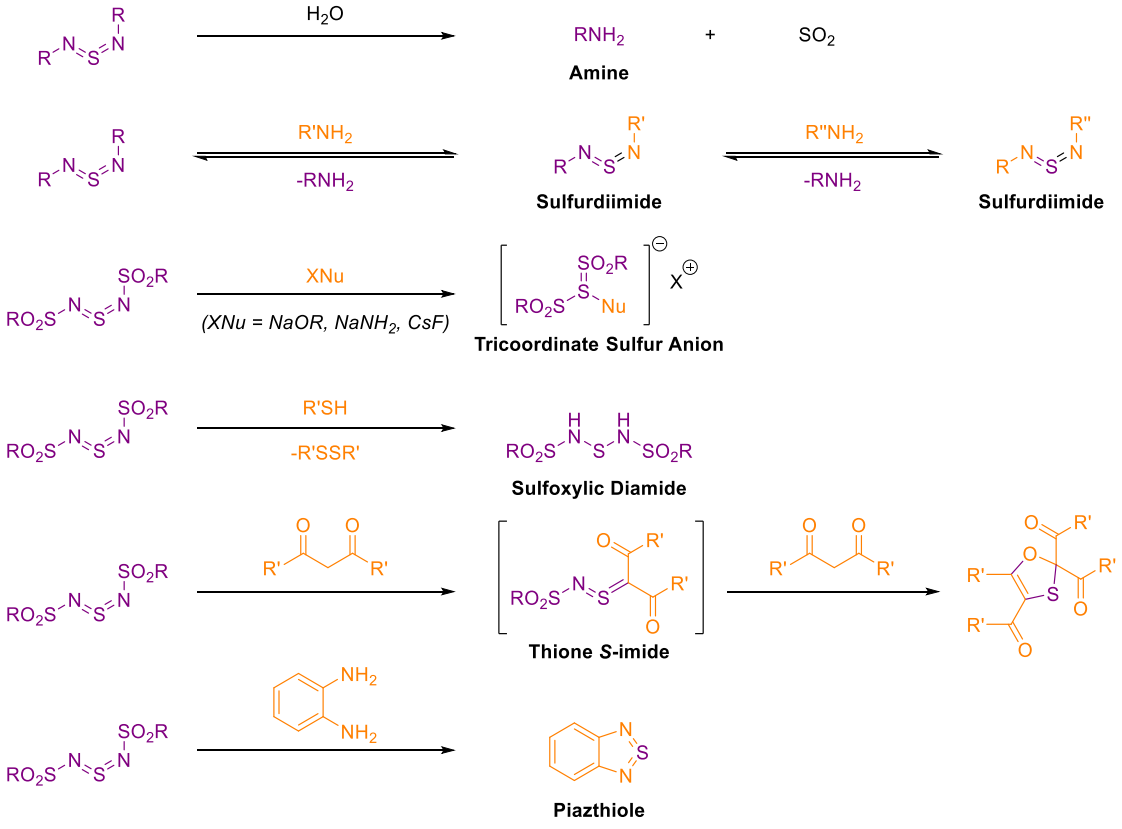
Much like sulfinylamines, sulfurdiimides can be used in trans-sulfinylation to give other sulfurdiimide products. Sulfurdiimides substituted with two electron-withdrawing groups react much faster with amines than those with one, meaning trans-sulfinylation can be done sequentially with two different amines to give unsymmetrical sulfurdiimides (**Scheme 1.44**).[118]



Scheme 1.44. Amine exchange using sulfurdiimides

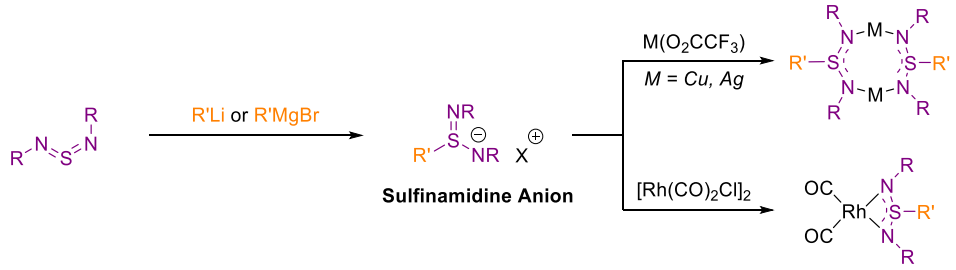
1.5.2 Reactions of Sulfurdiimides

Similar to sulfinylamines, the electrophilicity of the sulfur atom again results in the reaction of nucleophiles at sulfur (**Scheme 1.45**). Again, reaction with water results in hydrolysis and reaction with amines results in trans-sulfinylation.[118] The reactions of other nucleophiles have mostly been studied for bis-sulfinyl sulfurdiimides, which often results in the formation of surprisingly stable anionic tricoordinate sulfur compounds.[119] Reaction with thiols results in the reduction to a sulfoxylic diamide and a disulfide by-product.[120] Dicarbonyl nucleophiles can also react with sulfurdiimides, giving an intermediate thione *S*-amide intermediate, which then usually undergo further reaction.[121] Reactions with 1,2-diamines can again be used to prepare piazthiole products.[118]



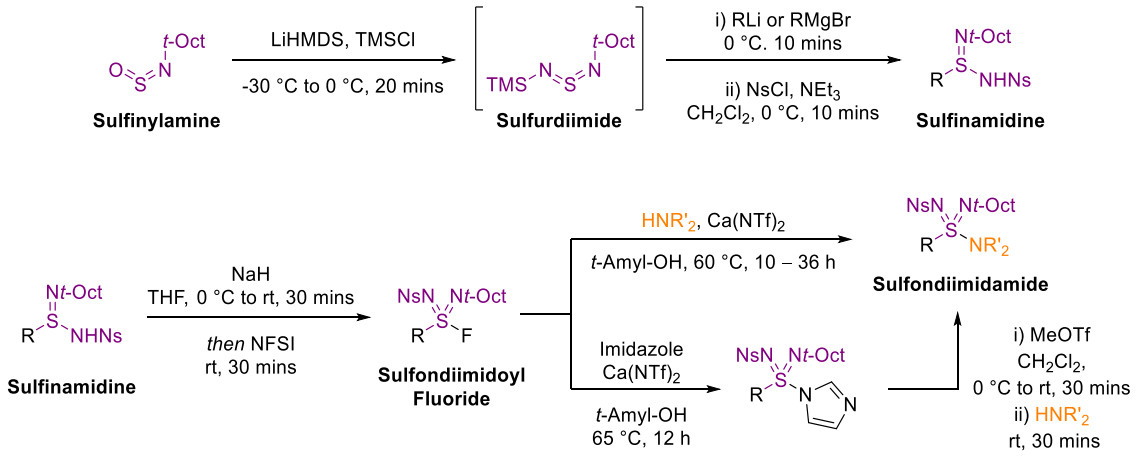
Scheme 1.45. Reaction of sulfurdiimides with nucleophiles.

The addition of organometallic reagents to sulfurdiimides is also possible, and the resulting sulfinamidine anions (often referred to as diimidosulfinates) can be used as chelating or bridging ligands with various metals (**Scheme 1.46**).[122]



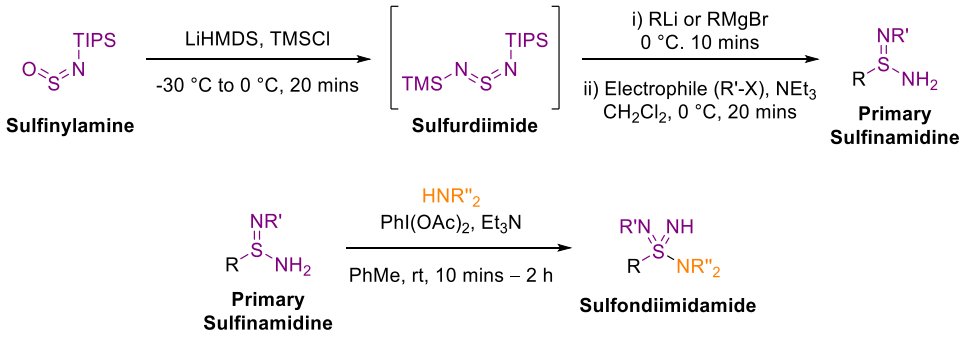
Scheme 1.46. Reaction of sulfurdiimides with organometallic reagents and subsequent complexation to metal salts.

Some recent work from the Willis group has started to explore the addition of organometallic reagents to sulfurdiimides for the synthesis of aza-S(VI) products. This has mostly focussed on the use of sulfinylamines derived from the reaction of sulfinylamines with LiHMDS. The addition of organometallic reagents to a solution of pre-formed *N*-(trimethylsilyl)-*N*'-(2,4,4-trimethylpentan-2-yl)sulfur diimide (TMSNSN*t*-Oct) and subsequent protection using nosyl chloride gave isolable sulfinamidine intermediates. Deprotonation using sodium hydride and oxidative fluorination using NFSI then gave sulfonimidoyl fluoride intermediates. These sulfonimidoyl fluorides could then be reacted with amines in the presence of calcium triflimide as a Lewis acid enabled the synthesis of sulfondiimidamides. This procedure worked well for nucleophilic secondary amines, but for less-nucleophilic examples, formation of an intermediate imidazole sulfondiimidamide, methylation and then addition of the desired amine enabled the synthesis of the desired sulfondiimidamide products (**Scheme 1.47**).[16a] Subsequent deprotection and functionalisation of the imidic nitrogen enabled the synthesis of a diverse selection of sulfondiimidamide products.



Scheme 1.47. Preparation of sulfondiimidamides via organometallic addition to sulfurdiimides, oxidative fluorination and nucleophilic amination.

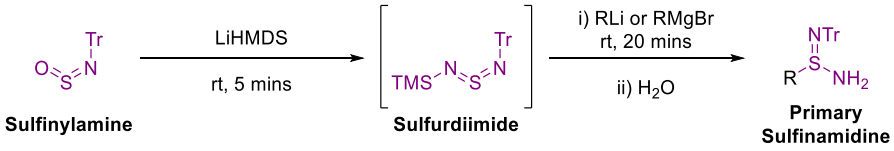
A subsequent development from the Willis group utilised *N*-(trimethylsilyl)-*N*'-(triisopropylsilyl)sulfur diimide (TMSNSNTIPS), which provided sulfinamidines which were readily functionalised and then TIPS-deprotected to give primary sulfinamidine intermediates. Oxidative amination using PIDA and an amine nucleophile then delivered sulfondiimidamides in a shorter reaction sequence (**Scheme 1.48**).[103a] This reaction was again found to work best with more-nucleophilic amines, but diversification of the *N*-protecting groups was more-readily achieved in this reaction sequence.



Scheme 1.48. Preparation of sulfondiimidamides via organometallic addition to sulfurdiimides followed oxidative amination.

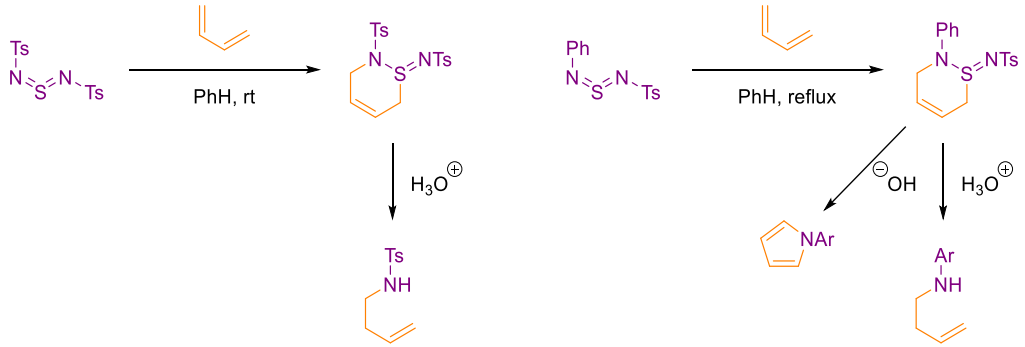
Luisi and co-workers disclosed a related procedure for the synthesis of stable *N*-trityl sulfinamidines from organometallic addition to *N*-(trimethylsilyl)-*N*'-(trityl)sulfur diimide (TMSNSNTr) and subsequent quenching with water. The authors developed a continuous

flow strategy for the synthesis of the primary sulfinamidine products, enabling the sulfurdiimide synthesis to be carried out at room temperature and without TMSCl, and the subsequent organometallic addition could be carried out at room temperature also (**Scheme 1.49**).[103b]



Scheme 1.49. Preparation of sulfondiimidamides via organometallic addition to sulfurdiimides followed oxidative amination.

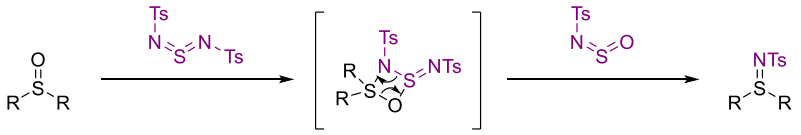
A significant amount of research has also been carried out on cycloadditions of electron-poor sulfurdiimide reagents. Much like sulfinylamines, sulfurdiimides readily undergo hetero Diels-Alder reactions with dienes, giving cyclic sulfinamidine products (**Scheme 1.50**).[123] These reactions have been also observed using unsymmetrical aryl/Ts sulfurdiimides, giving only one of the two possible regioisomers, although these require more forcing conditions to achieve good conversion.[124] The hetero Diels-Alder adducts could be hydrolysed using aqueous acid to homoallyl amine products, or in the case of the *N*-aryl product, alkaline hydrolysis can give *N*-arylpyrroles.



Scheme 1.50. Hetero-Diels-Alder reactions using sulfurdiimides.

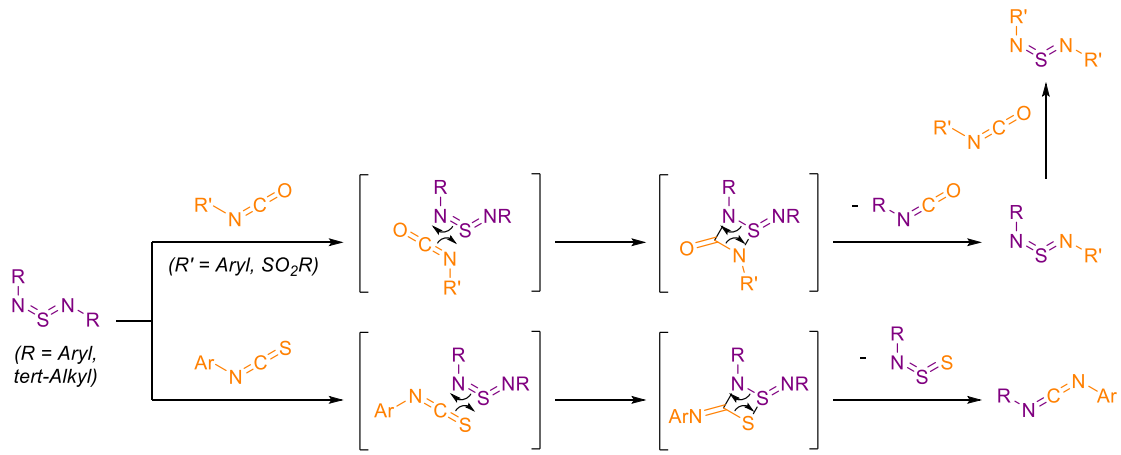
Bis-sulfonyl sulfurdiimides have also been used in cycloadditions with various other substrates, such as donor-acceptor cyclopropanes,[90] ketenes,[125] ynamides,[126] and vinyl

ethers.[127] Similar to sulfinylamines, sulfurdiimides can also react with aryl aldehydes and sulfoxides to give imines and sulfilimine products in high yields (**Scheme 1.51**).[72b, 128]



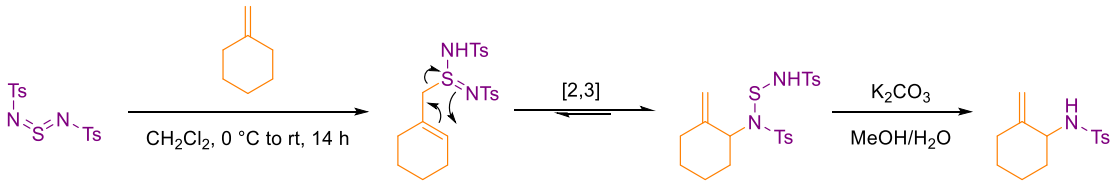
Scheme 1.51. Synthesis of sulfilimines from sulfoxides using bis-sulfonyl sulfurdiimides.

The reaction of symmetrical bis-alkyl or bis-aryl sulfurdiimides in [2+2] reactions with isocyanates and isothiocyanates are also interesting. Reactions with these reagents gave different products, with isocyanates reacting through nitrogen to give unsymmetrical sulfurdiimides (which could undergo further reaction), whereas isothiocyanates reacted through sulfur to give carbodiimides (**Scheme 1.52**).[129]



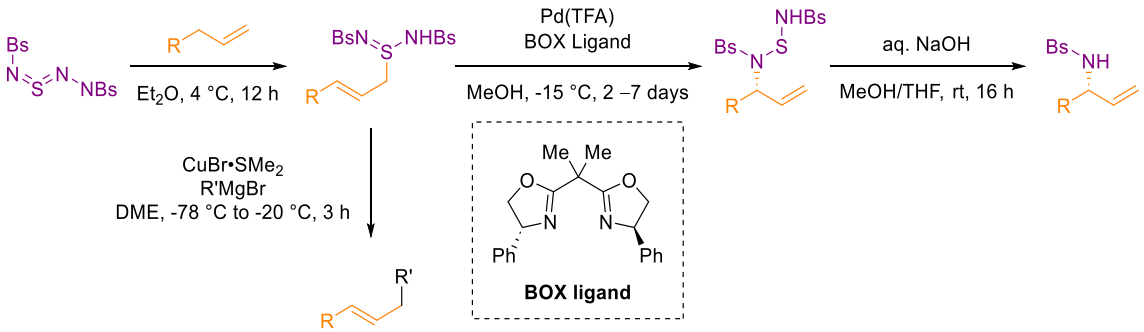
Scheme 1.52. Reactions of sulfurdiimides with isocyanates and isothiocyanates.

Electron-poor sulfurdiimides also react readily with olefins in ene reactions. Sharpless and co-workers demonstrated that where the allyl sulfinamide products from ene reactions of sulfinylamines are configurationally stable, the allyl sulfinamidine products derived from TsNSO rapidly undergo a [2,3]-rearrangement to give sulfenamides (**Scheme 1.53**).[130] These sulfenamides could then be cleaved under basic conditions to give *N*-allylic sulfonamide products.



Scheme 1.53. Hetero-Diels-Alder reactions using sulfurdiimides.

Whilst [2,3] rearrangements are usually observed for the ene adducts of *N*-sulfinylsulfonamides, Tambar and co-workers found that the allyl sulfinamidine product derived from BsNSNBs was configurationally stable at temperatures below 0 °C, and could be isolated by filtration from the reaction mixture.[131] Addition of a Pd catalyst ligated with a chiral BOX ligand catalysed the rearrangement at low temperatures, resulting in the preparation of enantioenriched sulfenamide products, which could be hydrolysed to the sulfonamide (**Scheme 1.54**). Overall, this procedure is an asymmetric allylic amination of unactivated olefins. Tambar and co-workers later disclosed the use of the sulfinamidine intermediates with organometallic nucleophiles using a copper catalyst.[132]



Scheme 1.54. Enantioselective [2,3]-rearrangement of allyl sulfinamidine intermediates or copper-catalysed reaction with organometallic reagents.

To our knowledge, there have been no reports of metal-catalysed couplings or radical addition to sulfurdiimides.

1.6 Research Aims

With the demonstrated importance of sulfur-containing functional groups, as well as the growing interest and potential applications of aza-sulfur functional groups, it is important that versatile methods are available for their access.[7c, 133] Furthermore, methods to access *S*-alkyl variants are more

scarce, but access to these functionalities is becoming increasingly important due to the trend towards more sp^3-rich molecules in the pharmaceutical industry.[134] The research presented in this thesis aims to address the observed limitations in access to sp^3-rich sulfur-containing functional groups, utilising the reactions of alkyl radicals with sulfur dioxide and its aza-analogues to access S(IV) intermediates, which could then be used in a series of derivatisation reactions to access diverse S(VI) products. Furthermore, we aimed to further support the applications of the chemistry of sulfinylamines and sulfurdiimides through the development of new, stable reagents.

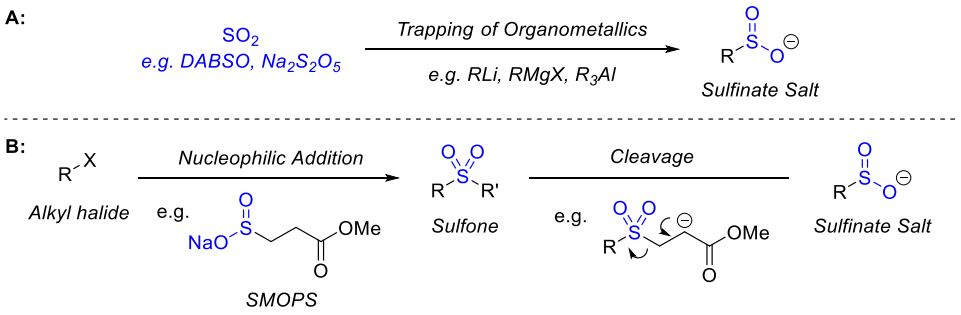
Chapter 2 - Preparation of Sulfinates using Katritzky Pyridinium Salts as Radical Precursors

2.1 Introduction

2.1.1 Alkyl Sulfinate Salts

As discussed in **Chapter 1**, sulfinate salts are versatile intermediates that can be used for the preparation of diverse sulfonyl-derived functional groups, and as a result, reliable and functional group-tolerant methods for their preparation are valuable for synthetic organic chemists. Despite the development of several methods for the preparation of sulfinate salts,[15, 38, 135] those that can be used to access alkyl variants remain underexplored.

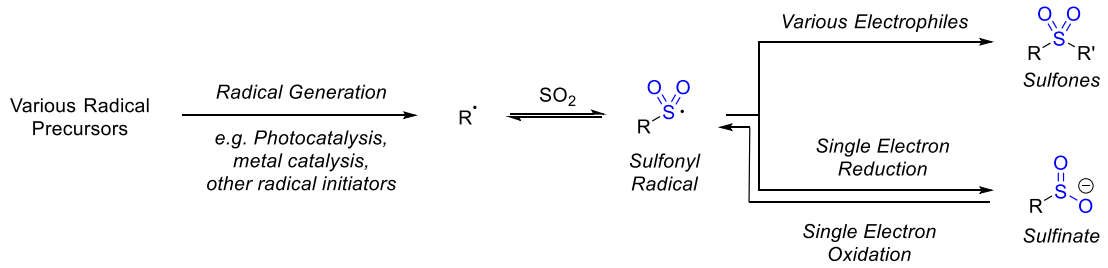
Reactions of organometallic reagents with sulfur dioxide or its surrogates can be used for the preparation of alkyl sulfinate salts, but functional group compatibility and the commercial availability of alkyl organometallic reagents limits the utility of this method (**Scheme 2.1.A**). The use of sulfinate transfer reagents such as SMOPS is a viable alternative, but is again limited by the commercial availability of suitable electrophiles (**Scheme 2.1.B**).[23a]



Scheme 2.1. A): Synthesis of sulfinates from organometallic reagents. **B):** Synthesis of sulfinates from sulfinate transfer reagents.

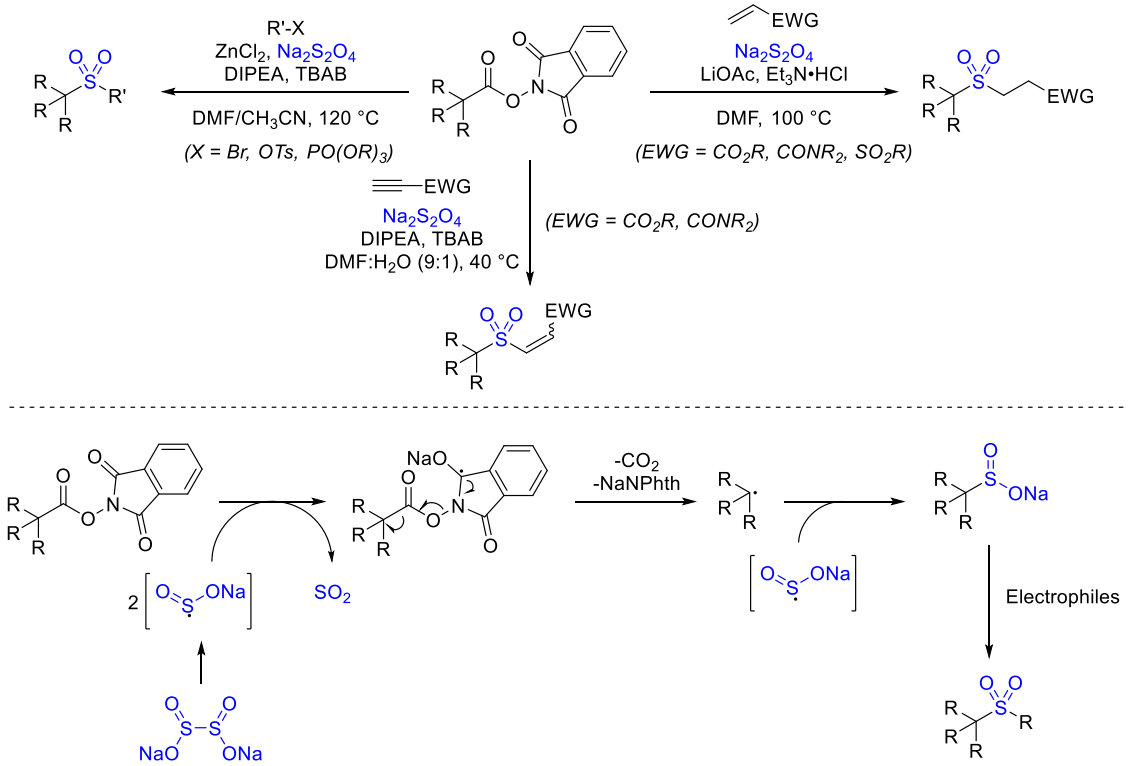
Despite the well-established reactivity of sulfur dioxide with radicals, as well as numerous methods for the preparation of alkyl radicals from diverse radical precursors,[58] methods that use alkyl radicals for the preparation of sulfinate salts are scarce. In fact, most methods involve the trapping of

intermediate sulfonyl radicals with appropriate radical traps to access sulfones or sulfonamides directly, rather than undergoing a single electron reduction to a sulfinate salt, which would be a more useful transformation (**Scheme 2.2**).[46, 58] This can be simply explained by the observation that sulfinate salts are often used as radical precursors themselves, generating alkyl radicals by single electron oxidation and subsequent C-S bond scission.[136] This presents a significant challenge when preparing radicals from one radical precursor and preventing radical formation from the sulfinate salt products.



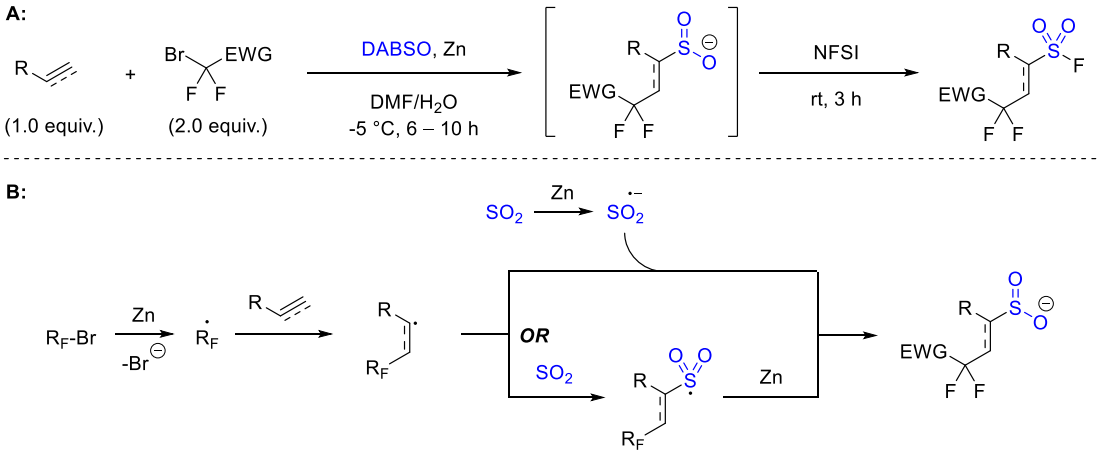
Scheme 2.2. Alternative pathways for sulfonyl radical intermediates and reversibility of sulfinate generation.

Despite the challenges of preparing sulfinate salts via radical methods, some examples have been disclosed in the literature. Jiang and co-workers developed two related methods using *N*-hydroxyphthalimide esters, sodium dithionite and various electrophiles to generate sulfones, with sulfinate salts suggested as intermediates, although these are not isolated (**Scheme 2.3**).[137] These methods rely upon homolytic cleavage of sodium dithionite to two sulfur dioxide radical anions. SET from these radical anions to the *N*-hydroxyphthalimide esters generates the alkyl radical with loss of CO_2, and this radical is then proposed to capture a second equivalent of the sulfur dioxide radical anion to give a sulfinate salt intermediate. Alkylation or conjugate addition in the reaction pot then gives the sulfone products. Whilst this method makes good use of commercially available sodium dithionite, and the *N*-hydroxyphthalimide esters are easily accessible from carboxylic acids, the scope of the reactions is somewhat limited, and the majority of examples are unfunctionalised, tertiary and/or benzylic, although some examples of secondary substrates are shown with moderate yields.



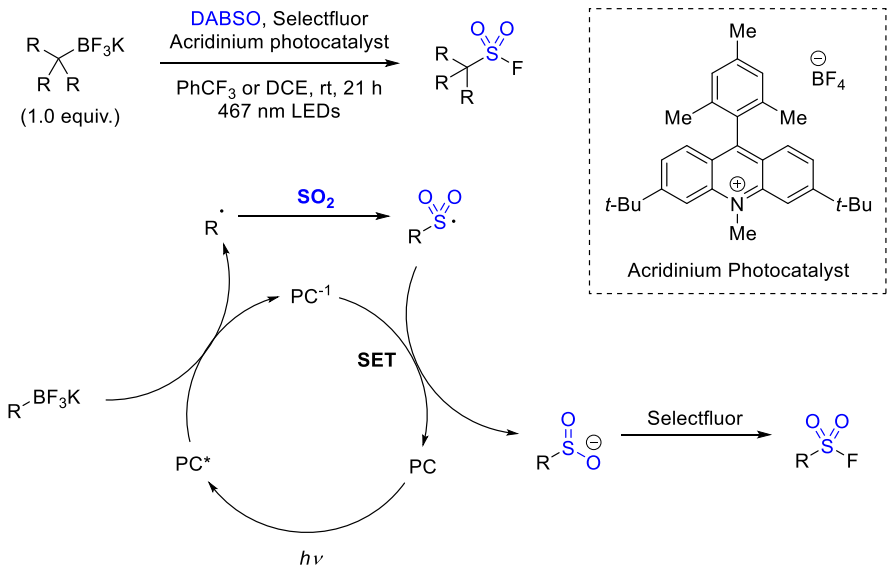
Scheme 2.3. Synthesis of sulfones via sulfinates using *N*-hydroxyphthalimide esters and sodium dithionite.

Liu and co-workers prepared sulfonyl fluorides using fluoroalkyl bromides via the formation of a sulfinate intermediate (**Scheme 2.4**).[138]. The proposed mechanism involves radical generation via SET from zinc to give the fluoroalkyl radical, which then added to an alkene or alkyne to give an alkyl or vinyl radical. The authors then propose two alternative mechanisms for the formation of the sulfinate. The first of these involves the formation of a SO_2 radical anion from the reduction of SO_2 using zinc, which combines with the alkyl or vinyl radical to give the product sulfinate. Alternatively, radical addition to SO_2 would give a sulfonyl radical, which the authors propose could be reduced by zinc to give the sulfinate product. The method was shown to tolerate a wide variety of functional groups, and a diverse selection of fluoroalkyl bromides could be used. Application to the preparation of other sulfonyl derivatives, including sulfones, sulfonate esters and sulfonyl azides was shown. This method is useful for the preparation of fluoroalkyl sulfonyl derivatives, but no examples were shown using non-fluorinated substrates.



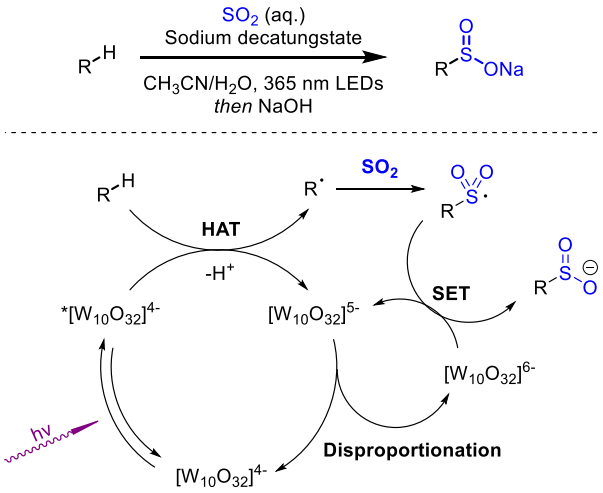
Scheme 2.4. Synthesis of sulfonyl fluorides via sulfinates using fluoroalkyl bromides and DABSO.

A recent method from Tambar and co-workers used alkyl trifluoroborate salts to prepare sulfonyl fluorides (**Scheme 2.5**).[139] Alkyl radicals are generated via reductive quenching of an excited-state acridinium photocatalyst, and subsequent addition to DABSO gave a sulfonyl radical. The authors then propose reduction of the sulfonyl radical via SET to give a sulfinate salt intermediate which is then trapped by Selectfluor to give the sulfonyl fluoride product. The reaction worked best for primary alkyl substrates, whereas secondary or tertiary substrates generally gave moderate to poor yields. This trend could be explained by the reverse reaction of the sulfinate salt to the alkyl radical being dominant when generating more-stabilised secondary or tertiary radicals. Furthermore, whilst several functional groups were tolerated, yields were moderate for these examples.



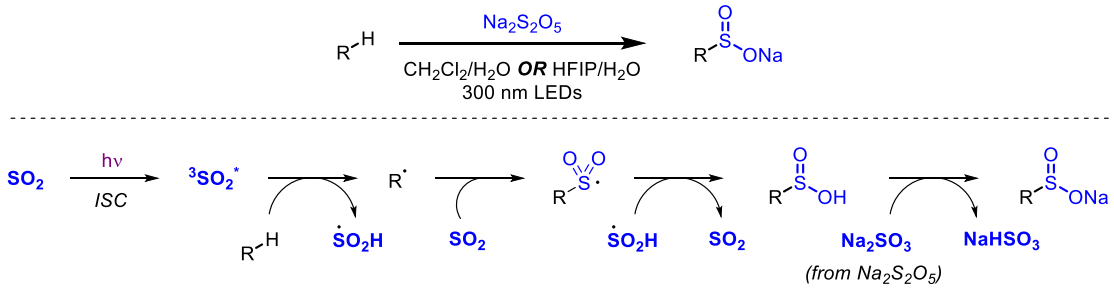
Scheme 2.5. Synthesis of sulfonyl fluorides via sulfinates using alkyl trifluoroborate salts and DABSO.

A method from MacMillan and co-workers exploits selective HAT from alkanes using singlet-excited sodium decatungstate to generate alkyl radicals, which subsequently add to SO_2 to give sulfonyl radical intermediates. SET from doubly-reduced decatungstate ($[W_{10}O_{32}]^{6-}$) gives the sulfinate salt, which is protonated under the reaction conditions (**Scheme 2.6**). This method benefits from wide availability of substrates and good functional group compatibility, but regioselectivity issues are often observed, and the reaction cannot be used effectively if the most electron-rich C-H bond is not the desired site of sulfinylation.[140]



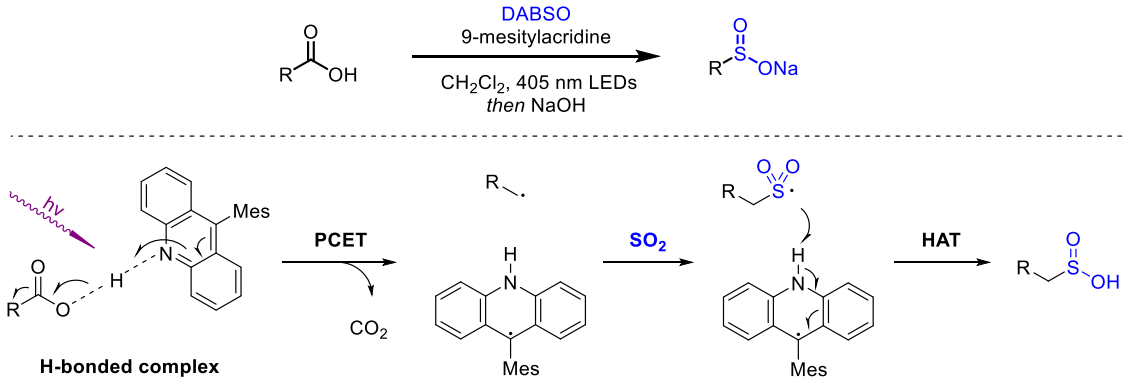
Scheme 2.6. Synthesis of sulfinates from alkanes using sodium decatungstate.

A related method from Larionov and co-workers involves direct excitation of SO_2 (derived from sodium metabisulfite) using 300 nm UV light, which undergoes intersystem crossing to form triplet-excited SO_2 and then abstracts a hydrogen atom from an alkane to form an alkyl radical, which then reacts with further SO_2 and is then reduced by a hydroxysulfinyl radical (**Scheme 2.7**).[141] This reaction has reasonable functional group compatibility, but the use of harmful UV light is a major disadvantage, and whilst regioselectivity could be controlled to some extent by choice of solvent, selective sulfinylation in complex organic molecules would be challenging using this method.



Scheme 2.7. Synthesis of sulfinates from alkanes using sodium metabisulfite and UV light.

An alternative useful method developed by Larionov and co-workers involves radical generation from carboxylic acids using acridine photocatalysts. Alkyl radicals are generated via proton-coupled electron transfer (PCET) from a singlet-excited complex between the acid and catalyst.[142] Radical addition to SO_2 and subsequent HAT gives sulfinic acids, which can subsequently be deprotonated to the sulfinate salt or functionalised in several one-pot procedures (**Scheme 2.8**).[143] This methodology shows good functional group tolerance, and will be discussed in more detail in **Chapter 3**.

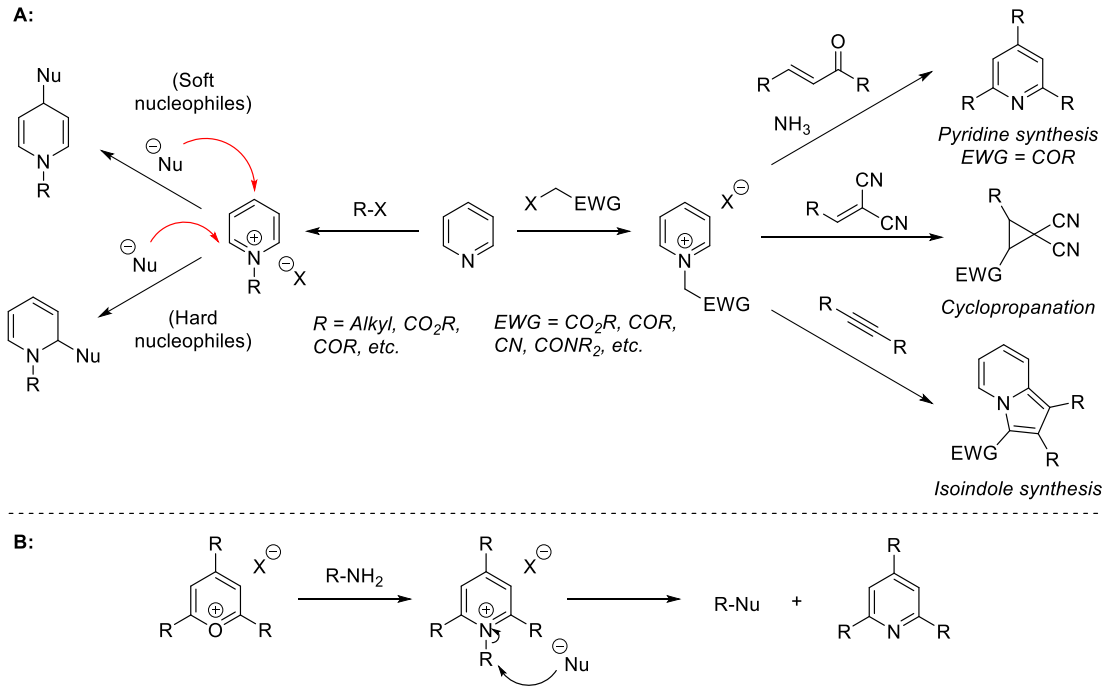


Scheme 2.8. Synthesis of sulfinates from carboxylic acids using acridine photocatalysts.

To add to the available methods for the preparation of alkyl sulfinates via the addition of alkyl radicals to SO_2, we were attracted to a number of recent reports using 2,4,6-trisubstituted pyridinium (Katritzky) salts as radical precursors.

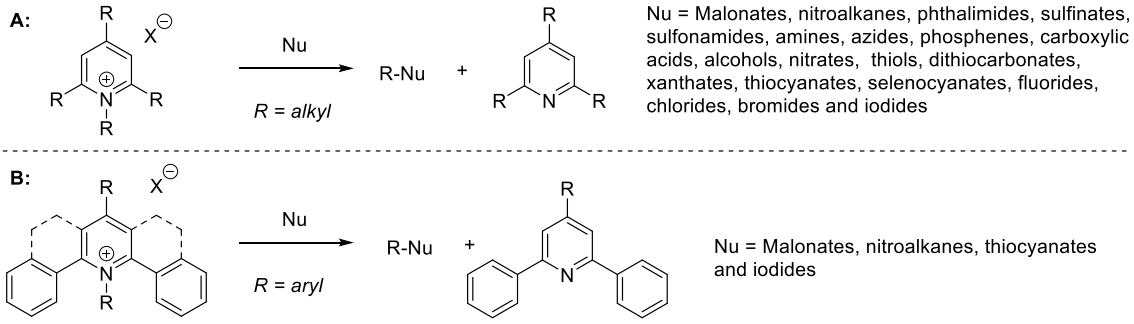
2.1.2 Katritzky Pyridinium Salts

N-Alkyl pyridinium salts are highly reactive species that have been used in a broad spectrum of reactions. Their reactivity is often characterised by nucleophilic addition to the pyridinium ring, or the formation and reaction of pyridinium ylides (**Scheme 2.9.A**).[144] Conversely, 2,4,6-trisubstituted pyridinium salts, often referred to as Katritzky salts, react preferentially with nucleophiles at the *N*-alkyl substituent due to steric hinderance on the pyridinium ring, resulting in loss of a 2,4,6-trisubstituted pyridine leaving group and transfer of the alkyl substituent (**Scheme 2.9.B**).[145]



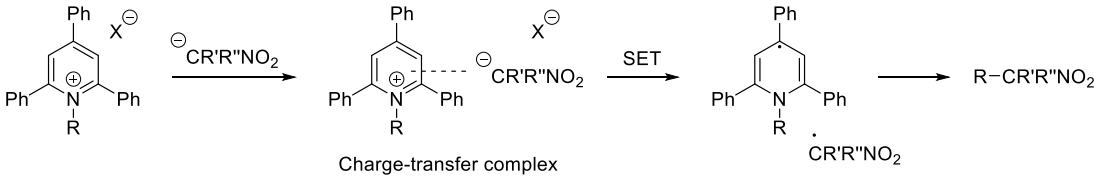
Scheme 2.9. A): Reactivity of pyridinium salts. **B):** Reactivity of 2,4,6-trisubstituted pyridinium salts.

The reaction of Katritzky salts with a broad range of nucleophiles and *N*-substituents have been studied, resulting in methods for the deaminative preparation of a broad selection of functional groups (**Scheme 2.10.A**).[145] Whilst the *N*-substituents are often alkyl, examples of substitutions involving aryl groups have also been demonstrated, although conditions are often harsh, and choice of nucleophile is more limited and sometimes requires the use of more-reactive ethylene-bridged Katritzky salts (**Scheme 2.10.B**).[146]



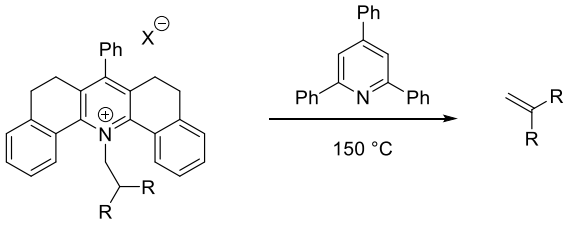
Scheme 2.10. A): Nucleophilic substitution reactions of *N*-alkyl Katritzky salts. **B):** Nucleophilic substitution reactions of *N*-aryl Katritzky salts.

The mechanisms and reaction rates of nucleophilic displacements can vary depending on the nucleophile, leaving group, and pyridinium substituents. Whilst most mechanisms are S_N1 or S_N2, there are also some isolated examples of substitution via a radical mechanism, such as when using nitroalkane anions, which form a charge-transfer complex with the Katritzky salt and subsequently undergo SET, fragmentation of the dihydropyridine radical to an alkyl radical and then radical-radical combination (**Scheme 2.11**).[147]



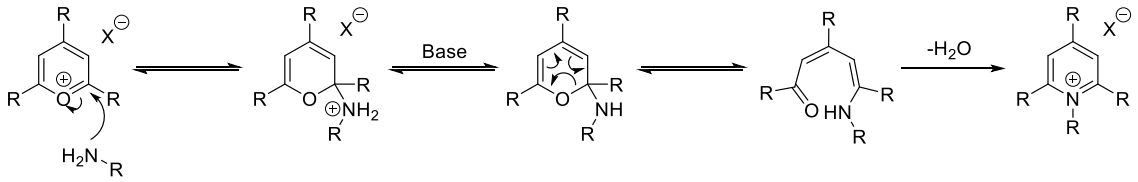
Scheme 2.11. Substitution using nitroalkane anions via a radical mechanism.

Olefins can also be prepared from Katritzky salts via E1 elimination, but unactivated substrates usually require more-reactive ethylene-bridged Katritzky salts, high temperatures and a non-nucleophilic base (**Scheme 2.12**).[148] Katritzky salts have also been used in a variety of other transformations, such as functional group interconversions and rearrangements.[145a, 149]



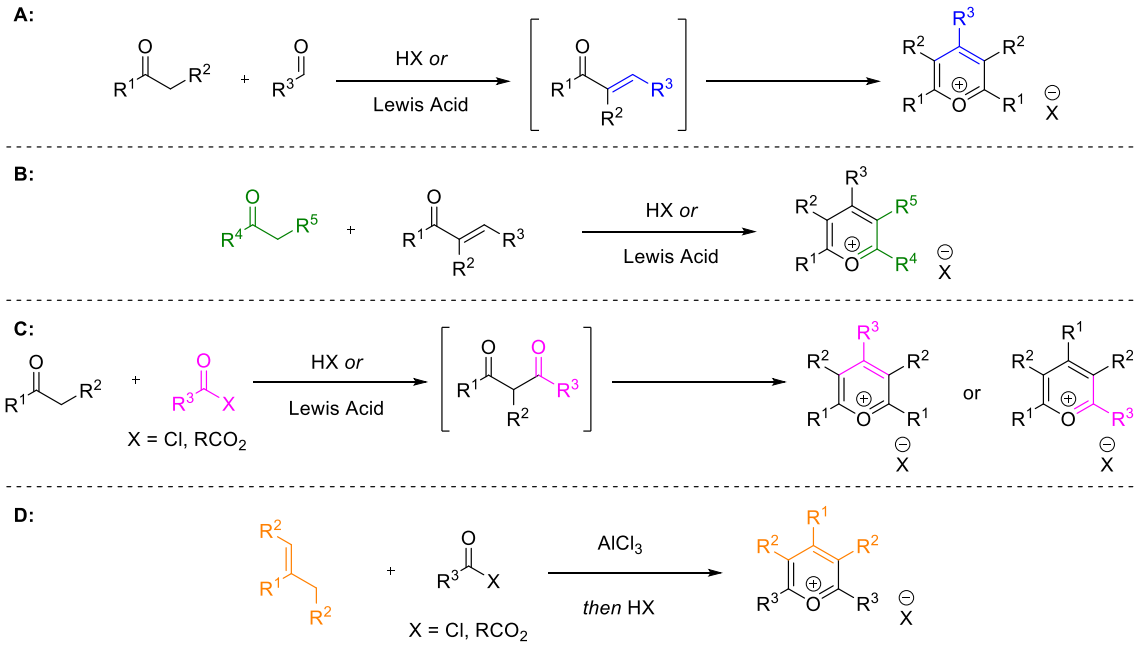
Scheme 2.12. Deaminative preparation of olefins via elimination from Katritzky salts.

Katritzky salts are readily accessed from reaction of primary amines with 2,4,6-trisubstituted pyrylium salts, via nucleophilic attack at the 2-position on the pyrylium ring, ring opening, and subsequent condensation (**Scheme 2.13**). This reaction is often high yielding, functional group-tolerant, and the corresponding Katritzky salts often crash out of solution and can therefore usually be isolated without column chromatography.



Scheme 2.13. Synthesis of Katritzky salts from pyrylium salts.

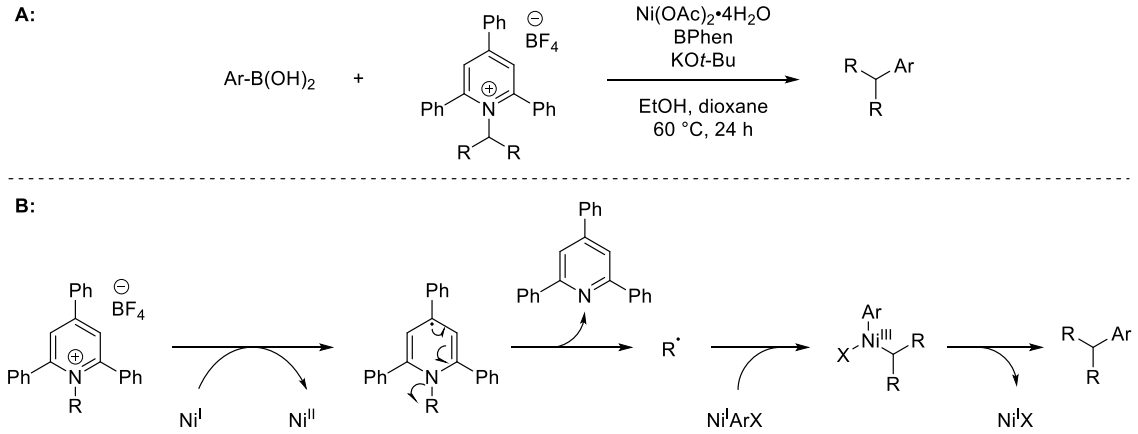
The pyrylium salt starting materials are readily accessible by a several methods.[150] Most commonly used to prepare symmetrical pyrylium salts is the reaction of two equivalents of a ketone with one equivalent of aldehyde, via the formation of an intermediate enone (**Scheme 2.14.A**). This can also be done in a stepwise fashion to enable the synthesis of unsymmetrical pyrylium salts (**Scheme 2.14.B**).[149a] Alternatively, acyl chlorides or anhydrides can be used, giving an intermediate 1,3-diketone, which reacts with another equivalent of ketone to give one of two pyrylium salt products, with the regiochemistry dependant on the electrophilicity of the 1,3-diketone (**Scheme 2.14.C**).[151] A different approach involves the $AlCl_3$-enabled reaction of olefins with two equivalents of acyl chlorides or anhydrides, giving symmetrical pyrylium salt products (**Scheme 2.14.D**).[152]



Scheme 2.14. Syntheses of pyrylium salts.

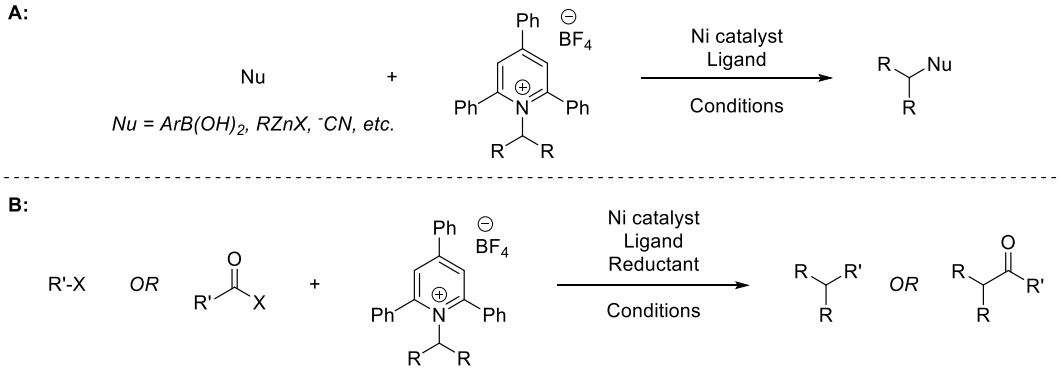
2.1.3 Katritzky Pyridinium Salts as Radical Precursors

Following the substantial work carried out on substitution reactions and functional group interconversions carried out by Katritzky and others on pyridinium salts, these interesting reagents were largely overlooked until Watson and co-workers demonstrated their use as electrophiles in a nickel-catalysed Suzuki-Miyaura-type coupling (**Scheme 2.15.A**).[153] Crucially, mechanistic studies uncovered that the key alkyl nickel intermediates were prepared in a stepwise manner rather than direct oxidative addition, via SET to generate a dihydropyridine radical, fragmentation to generate an alkyl radical and radical capture by nickel. Reductive elimination then gave the product (**Scheme 2.15.B**). This work demonstrated the potential for Katritzky salts to be used as radical precursors, prompting a renaissance in their study and use in a variety of transformations.[154]



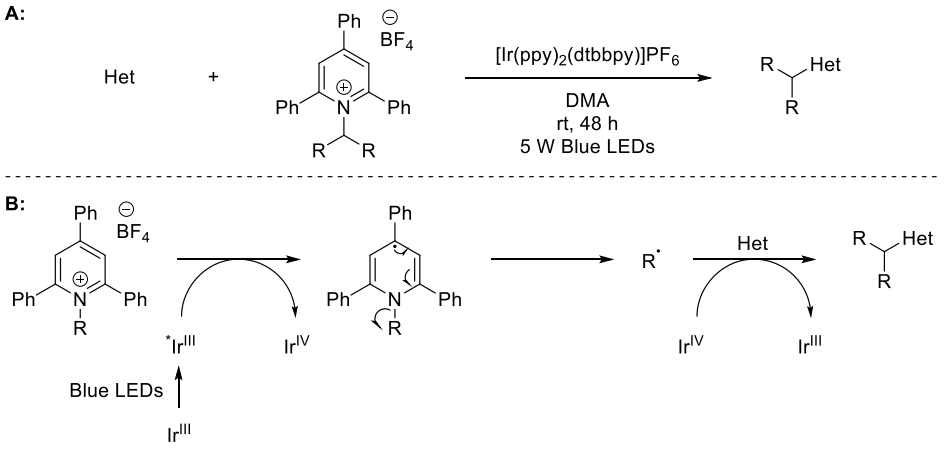
Scheme 2.15. A): Deaminative Suzuki-Miyaura reaction. **B):** Proposed mechanism.

Several further nickel-catalysed reactions have since been disclosed, from Watson and others in the field, resulting in alkyl variants of Negishi reactions, reductive cross-electrophile couplings, Sonogashira reactions, and a wide variety of other applications (**Scheme 2.16**).[155] Other metals such as copper have also been used in similar coupling reactions.[156]



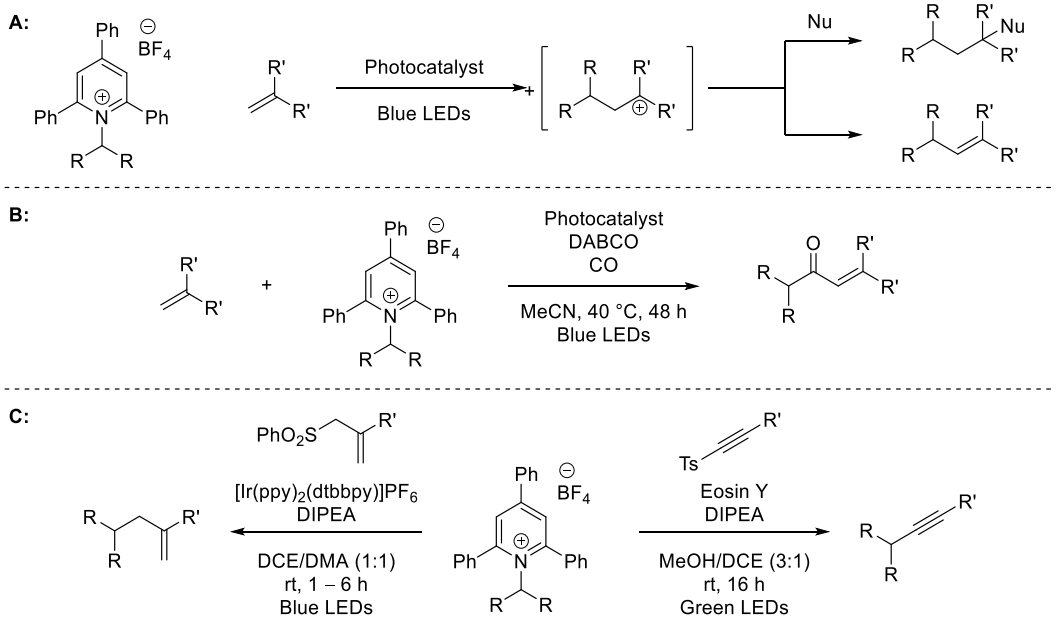
Scheme 2.16. A): Nickel-catalysed coupling of Katritzky salts with nucleophiles. **B):** Nickel-catalysed cross-electrophile couplings of Katritzky salts and alkyl, aryl or carbonyl electrophiles.

Alternative methods for achieving SET and generating alkyl radicals from Katritzky salts have also been explored. Glorius and co-workers demonstrated the use of singlet-excited photoredox catalysts, where oxidative quenching via SET to the Katritzky salt enables the generation alkyl radicals, which were then added to heterocycles, and subsequent SET gave alkylated heterocycle products (**Scheme 2.17**).[157]



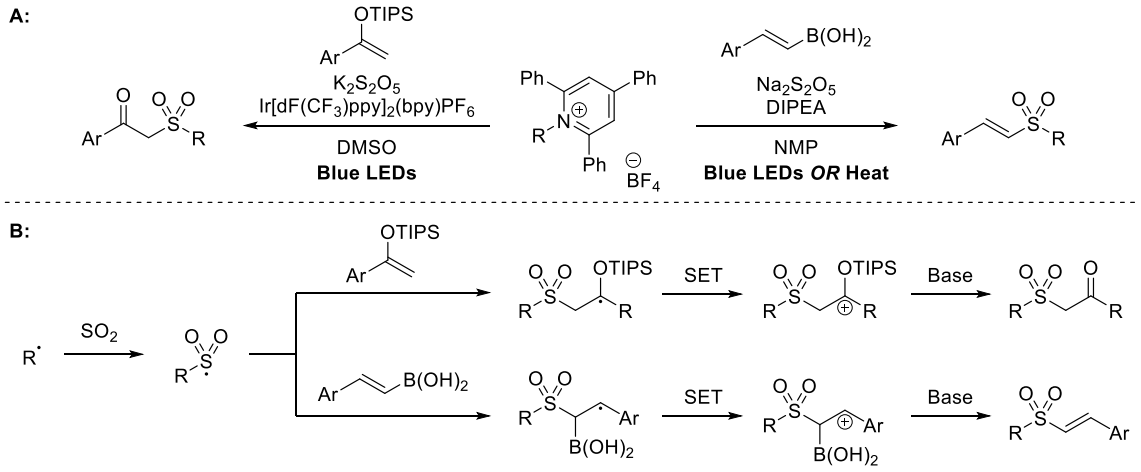
Scheme 2.17. A): Deaminative alkylation of heterocycles. **B):** Proposed mechanism.

Subsequent methods have utilised photocatalysts and Katritzky salts in a broad variety of reactions. For example, radical addition to olefins and subsequent SET gives a carbocation, which can either be trapped with nucleophiles,[158] or in the absence of nucleophiles, undergoes elimination to give Heck-type products (**Scheme 2.18.A**).[159] Carbonylative variants of these reactions have also been developed, with products formed via radical addition to carbon monoxide prior to addition to an olefin (**Scheme 2.18.B**).[159a, 160] Other variants include radical addition to allyl or alkynyl sulfones, which give allyl or alkynyl products via the loss of a sulfonyl radical (**Scheme 2.18.C**).[161]



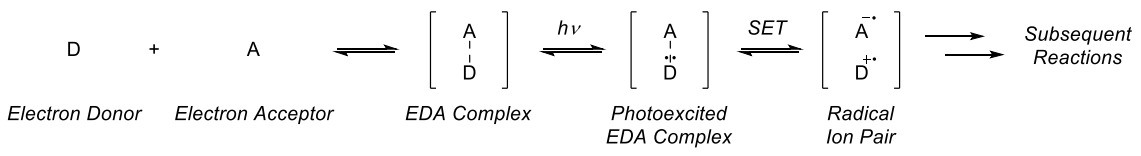
Scheme 2.18. A): Radical addition to olefins and subsequent trapping with nucleophile or elimination. **B):** Carbonylative Heck-type reaction using Katritzky salts. **C):** Deaminative allylation and alkynylation.

Crucially for our proposed reactions with SO_2, sulfonylative variants have also been developed. Wu and co-workers demonstrated addition of the intermediate sulfonyl radical with silyl enol ethers to give β-keto sulfones (**Scheme 2.19**).[162] Similarly, vinyl boronate esters can be used to give vinyl sulfones, but in this case without either a photocatalyst or metal catalyst, and can also be done in the absence of light.[163] This is an example of another prominent method of radical generation from Katritzky salts, via the formation of an electron donor-acceptor (EDA) complex.



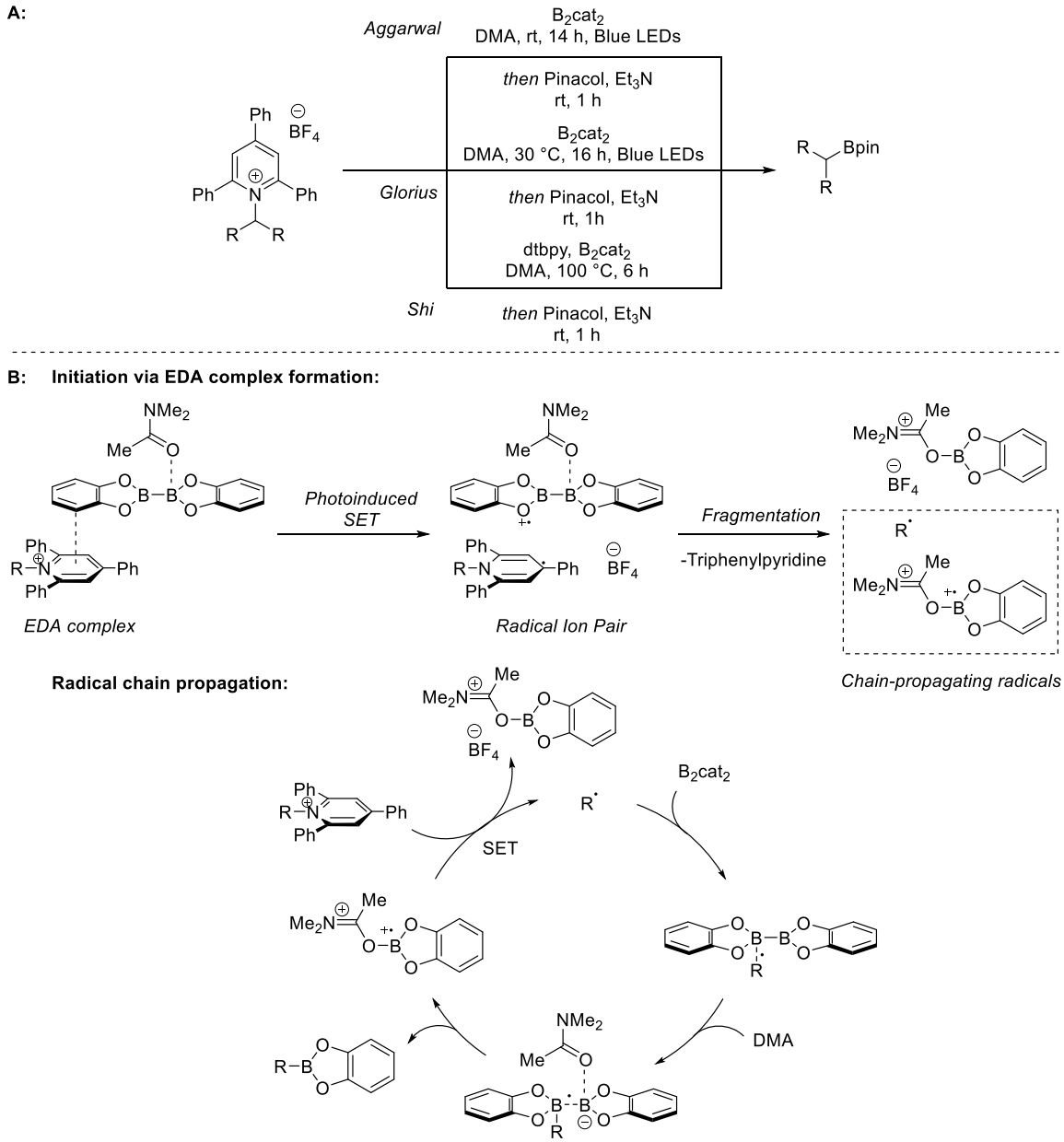
Scheme 2.19. A) Deaminative sulfonylative reactions to give sulfone products. **B)** Reaction mechanisms.

The reversible dipole-dipole interaction between electron donors and electron acceptors, usually referred to as an EDA complex, has found substantial utility in recent research.[164] This interaction results in the formation of a weak charge-transfer band, usually in the visible region, where usually the two separate components do not absorb visible light.[165] Subsequently, these EDA complexes can be promoted to a singlet excited state by light or heat, and this can induce a single electron transfer.[166] The reverse reaction is fast, but this mild method of forming radicals can be used in situations where subsequent reactions are fast, or one of the radical anions decomposes, such as through the loss of a leaving group (**Scheme 2.20**).



Scheme 2.20. EDA complex formation and absorption of visible light to generate a radical ion pair.

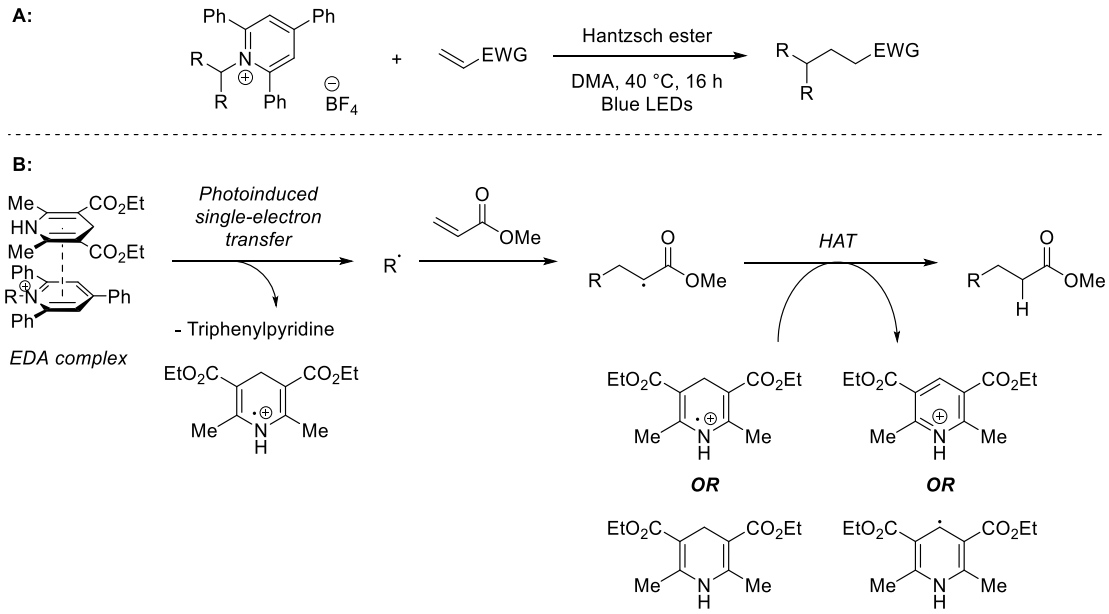
Katritzky salts make excellent substrates for radical generation via the formation of EDA complexes, due to their high electron-affinity owing to the positively-charged pyridinium ring, as well as the ability to lose the pyridine leaving group. To this end, Aggarwal and Glorius independently disclosed photoinduced deaminative borylation reactions, initiated via SET from an EDA complex between the Katritzky salt and an adduct between B_2cat_2 and DMA (**Scheme 2.21.A**).[167] Following initial radical generation via EDA complex formation, a chain propagation mechanism is then proposed (**Scheme 2.21.B**). Similarly, Shi and co-workers developed a thermally-induced variant, with otherwise similar conditions, but with thermally-induced SET.[168]



Scheme 2.21. A): Deaminative borylation. **B):** Proposed mechanism of radical borylation.

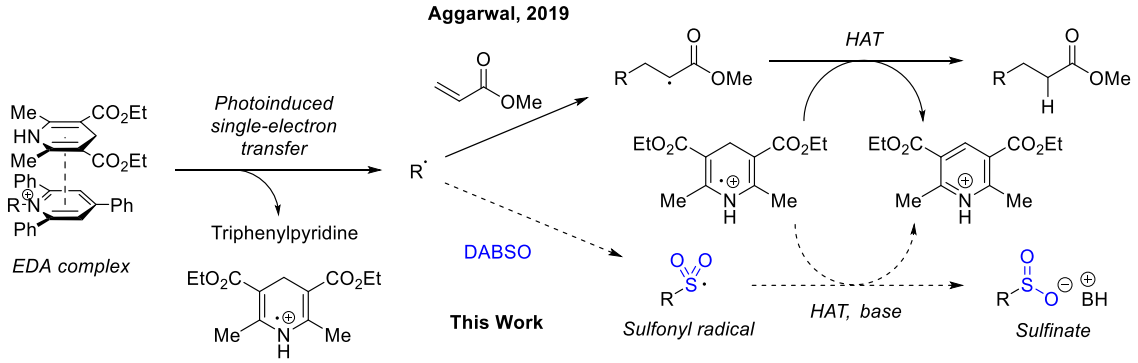
Following this work, the formation of EDA complexes with many electron-donors, such as thiols, amines, heterocycles, acrylamides, carbonates, xanthates and dithiocarbamates, has been used to prepare useful products from Katritzky salts.[161c, 169]

Aggarwal and co-workers developed a method for the preparation of Giese products from Katritzky salts and electron-deficient alkenes, using Hantzsch ester as both an electron-donor and a reductant (**Scheme 2.22.A**).[170] This reaction proceeds via EDA complex formation and subsequent photoinduced alkyl radical generation, giving a dihydropyridine radical cation as a by-product. The alkyl radicals then add to the electron-deficient alkene, and subsequent HAT with either the dihydropyridine radical or another equivalent of Hantzsch ester gives the Giese product (**Scheme 2.22.B**).



Scheme 2.22. A): Deaminative Giese reaction via EDA complex formation using Hantzsch ester. **B):** Proposed mechanism.

As the use of Hantzsch ester enables a net-reductive transformation without metal or photoredox catalysts, we proposed that we could adapt this method to prepare alkyl sulfinates via radical addition to SO_2, as we suggested that the HAT step would give a sulfinic acid in situ, and the reverse oxidation would not occur under the reaction conditions (**Scheme 2.23**).

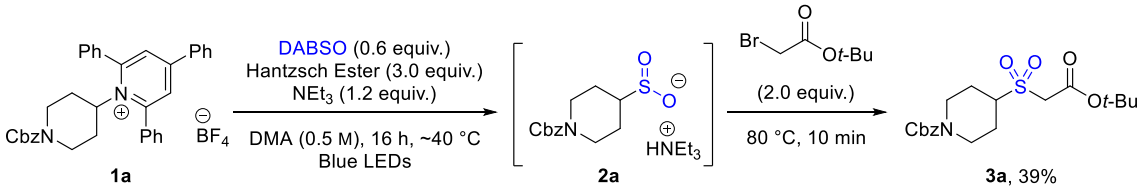


Scheme 2.23. Comparison between deaminative Giese reaction and proposed deaminative sulfinylation reaction.

2.2 Results and Discussion

2.2.1 Reaction Optimisation

We initiated our investigations using Katritzky salt **1a** as a model substrate, adapting conditions from Aggarwal and co-workers,[170] using DABSO as the SO_2 source and Et_3N to deprotonate the forming sulfinic acid to give a sulfinate product (**Scheme 2.24**). We were pleased to observe the formation of products consistent with sulfinate **2a** in the reaction mixture, and following alkylation using *tert*-butyl bromoacetate, sulfone **3a** was obtained in 39% yield.

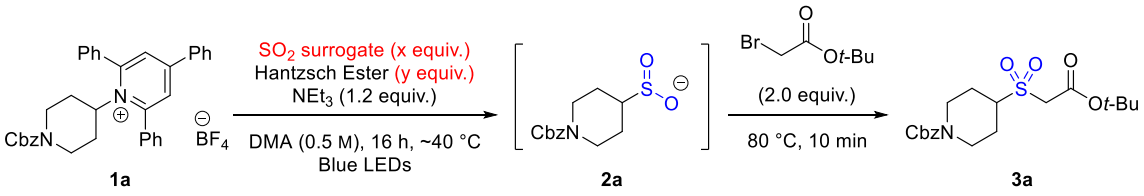


Scheme 2.24. Synthesis of sulfone **3a** from Katritzky salt **1a** via sulfinate **2a**.

We initiated our optimisation by studying the influence of Hantzsch ester loading, as we noted that 3.0 equivalents were not completely soluble, which we anticipated could impact the yield. We were pleased to observe that 1.1 equivalents of Hantzsch ester gave a slightly improved yield of 46%, and this lower loading would be used in subsequent optimisation (**Table 2.1**). We also studied the effect of using alternative SO_2-surrogates. Sodium metabisulfite could be used to give sulfone **3a** in 62% yield, whereas potassium metabisulfite gave a slightly lower 49% yield. Alternative amine-SO_2 charge-transfer complexes were also studied, including *N*-methylpyrrolidine·SO_2 (TimSO), *N*-

methylmorpholine·SO_2 (NMMSO), DMAP·SO_2 and TMEDA·$(SO_2)_2$, which all gave yields ranging between 74% and 81%. We would continue to study all of these SO_2-surrogates during ongoing optimisation studies, as whilst these alternative amine-SO_2 charge-transfer complexes give improved yields, they are not commercially available, which makes their use less favourable. All the SO_2-surrogates tested gave better yields with 1.1 equivalents of Hantzsch ester than with 3.0 equivalents, but it was also noted that a low yield of sulfone was obtained even with no Hantzsch ester present, other than when using DABSO. Tertiary amines have been noted to form EDA complexes with Katritzky salts, resulting in radical formation in the absence of Hantzsch ester, which may explain how some product can be generated for these examples.[170]

Table 2.1. Exploring SO_2 surrogates and Hantzsch ester loading for secondary alkyl substrate **1a**.



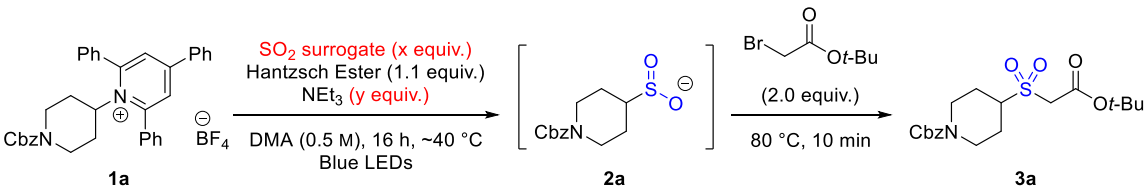
		SO_2 surrogate						
		DABSO (0.6 equiv.)	**$Na_2S_2O_5$ (1.2 equiv.)**	**$K_2S_2O_5$ (1.2 equiv.)**	**TimSO (1.2 equiv.)**	**NMMSO (1.2 equiv.)**	**DMAP.SO_2 (1.2 equiv.)**	**TMEDA.$(SO_2)_2$ (0.6 equiv.)**
Hantzsch Ester (equiv.)	0	0%	18%	-	24%	15%	15%	15%
	0.5	-	40%	-	65%	-	47%	44%
	1.1	46%	62%	49%	78%	81%	79%	74%
	3	39%	31%	41%	71%	60%	64%	72%

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

We found that the loading of base had a significant influence on the yield of sulfone **3a** (**Table 2.2**). This was particularly noteworthy when using DABSO as the SO_2 surrogate, where increasing loading of triethylamine from 1.2 to 2.4 to 3.6 equivalents increased the yield to 82%. The yield using sodium metabisulfite also improved substantially to 75% when using 3.6 equivalents of triethylamine, whereas the yield using other amine-SO_2 charge-transfer complexes showed no significant dependence on triethylamine loading, which may be due to extra tertiary amine already being present as the SO_2 is consumed. The importance of additional tertiary amine may suggest the formation of a ternary EDA complex, which results in a bathochromic shift and an increase in the absorbance of the

EDA complex, which results in more light being absorbed and therefore a faster generation of the alkyl radicals.[170] The highest yield was now obtained using DABSO as the SO_2-surrogate, and 3.6 equivalents of triethylamine would now be used in subsequent optimisation studies.

Table 2.2. Exploring SO_2 surrogates and triethylamine loading for secondary alkyl substrate **1a**.

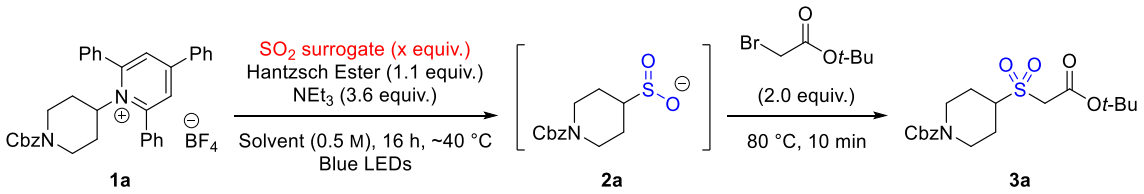


		SO_2 surrogate						
		DABSO (0.6 equiv.)	**$Na_2S_2O_5$ (1.2 equiv.)**	**$K_2S_2O_5$ (1.2 equiv.)**	**TimSO (1.2 equiv.)**	**NMMSO (1.2 equiv.)**	**DMAP.SO_2 (1.2 equiv.)**	**TMEDA.$(SO_2)_2$ (0.6 equiv.)**
NEt_3 (equiv.)	0	0%	0%	-	39%	65%	24%	7%
	0.5	-	63%	-	79%	-	66%	56%
	1.2	46%	62%	49%	78%	81%	79%	74%
	2.4	73%	72%	-	73%	75%	79%	70%
	3.6	82%	75%	-	76%	78%	75%	75%

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

DMA is often used as the solvent in reactions where Katritzky salts are used as radical precursors. In some cases, the presence of DMA has been proposed to be mechanistically important, as exemplified by Aggarwal and co-workers where DMA forms and adduct with B_2cat_2 ,and is subsequently involved in the EDA complex.[167a] The high boiling point of DMA is disadvantageous when removing solvent, so we screened a selection of alternative solvents for use in our reaction. We found that the highest yields of sulfone **3a** were obtained using DMA or DMF as the solvent (**Table 2.3**). DMSO also gave a good 66% yield, and several other solvents gave yields below 60%. Similar results were obtained using sodium metabisulfite and TimSO, although anomalously, acetonitrile gave a good 72% yield when using TimSO. Following these studies, DMA was retained as the optimum solvent.

Table 2.3. Exploring SO_2 surrogates and solvent for secondary alkyl substrate **1a**.

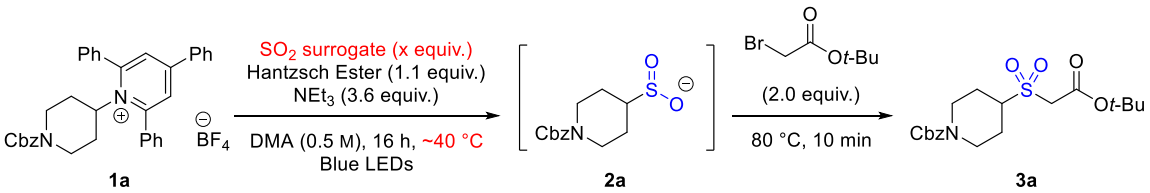


		SO_2 surrogate		
		DABSO (0.6 equiv.)	**$Na_2S_2O_5$ (1.2 equiv.)**	**TimSO (1.2 equiv.)**
Solvent	DMA	81%	70%	81%
	DMF	75%	69%	77%
	Acetonitrile	29%	12%	72%
	1,4-Dioxane	41%	23%	51%
	DMSO	66%	-	-
	DCM	55%	-	-
	Acetone	53%	-	-
	Methanol	53%	-	-

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

It was noted by Aggarwal and co-workers that improved yields were obtained when the reactions were warmed by the heat generated from the blue LED strips, which gave an ambient reaction temperature of 40 °C. This was emulated during our optimisation studies up to this point by wrapping the apparatus with aluminium foil and not using fan cooling. Removing the foil and using fan-cooling gave an ambient temperature of ~30 °C, and comparable yields of sulfone **3a** were obtained at this temperature (**Table 2.4**). A small drop in yield was observed when using sodium metabisulfite at this lower temperature, which may be due to poorer solubility or slower liberation of SO_2.

Table 2.4. Exploring reaction temperature for secondary alkyl substrate **1a**.

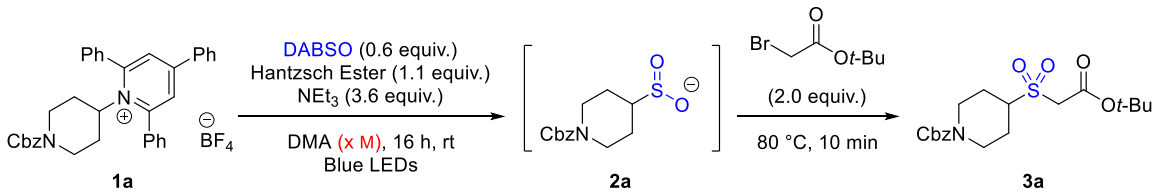


	SO_2 surrogate	
	DABSO (0.6 equiv.)	**$Na_2S_2O_5$ (1.2 equiv.)**
~ 40 °C (vents sealed)	81%	75%
~ 30 °C (vents open with fan cooling)	81%	62%

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

We then studied the effect of reaction concentration by varying the amount of solvent used (**Table 2.5**). We found that yields were comparable for concentrations between 1 M and 0.33 M, but was reduced slightly at 0.25 M to 66%. We continued to use 0.5 M during the optimisation, as this solubilised all the reagents well whilst not impeding purification of the products.

Table 2.5. Concentration screen for secondary alkyl substrate **1a**.



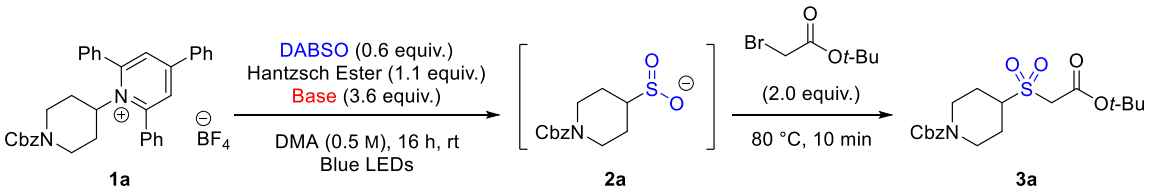
1a **2a** **3a**

Volume DMA	Yield
0.2 mL (1 M)	75%
0.3 mL (0.67 M)	73%
0.4 mL (0.5 M)	76%
0.5 mL (0.4 M)	77%
0.6 mL (0.33 M)	76%
0.8 mL (0.25 M)	66%

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

Given that the loading of base was found to be important in improving the yield of sulfone **3a**, we studied the impact of using different bases (**Table 2.6**). DIPEA gave comparable yields to triethylamine, whereas the other tertiary amines, *N*-methylmorpholine and DABCO, gave slightly lower yields. Morpholine was found to give a slightly higher 84% yield, whereas the more-hindered 2,6-lutidine gave only 6% yield. Some inorganic bases also gave good yields, with sodium and potassium carbonate giving 59% and 60% respectively, and potassium phosphate giving 62%. These higher-yielding inorganic bases have also been found to form EDA complexes, which may explain the good yields in these cases.[169f] Whilst piperidine gave a slightly improved yield, we anticipated issues regarding other functionalisations of the intermediate sulfinate, such as the formation of sulfonamides, so we retained triethylamine as the optimum base.

Table 2.6. Exploring bases for secondary alkyl substrate **1a**.



1a **2a** **3a**

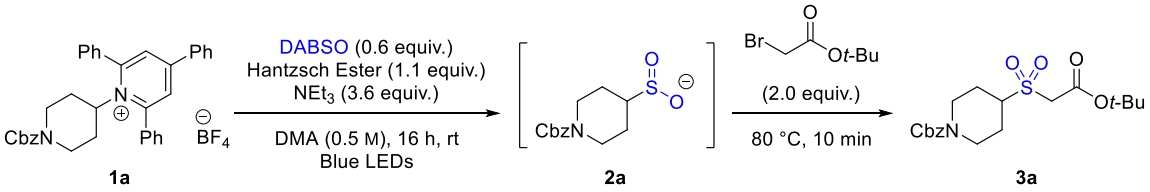
Base	Yield
Triethylamine	81%
DIPEA	81%
Morpholine	84%
N-methylmorpholine	62%
2,6-lutidine	6%
DABCO	68%

Base	Yield
KO*t*-Bu	0%
NaO*t*-Bu	4%
Na_2CO_3	59%
K_2CO_3	60%
Cs_2CO_3	18%
K_3PO_4	62%
NaOH	11%

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

With optimised conditions in hand, we carried out some control reactions to study their impact on the yield of sulfone **3a** (**Table 2.7**). Without light present, only traces of sulfone product were observed (**Table 2.7, entry 2**), but were surprised to observe that at a higher temperature of 60 °C, reactivity was restored, giving an excellent yield of 80% (**Table 2.7, entry 3**). This result demonstrates that there is also a thermal pathway for the key SET step to occur, consistent with some other examples of radical generation via thermally-induced SET from EDA complexes with Katritzky salts.[161c, 168, 171] The effect of moisture and air on sulfone yield was also studied to determine the robustness of the reaction. Using vigorously dried and degassed solvent gave 83% yield (**Table 2.7, entry 4**). Using solvent which had not been dried, but had been degassed, gave only a slight drop to 79% yield (**Table 2.7, entry 5**), whereas adding 20 µL water to the reaction gave a further small drop to 73% yield (**Table 2.7, entry 6**). These results demonstrate that the presence of water has only a small impact on the yield of sulfone **3a**. Carrying out the reaction in degassed, dry solvent with air in the reaction headspace gave 81% yield, whereas using solvent that had been sparged with air gave 80% yield (**Table 2.7, entries 7 and 8**). These results demonstrate that the presence of oxygen has negligible impact on the yield of the reaction.

Table 2.7. Variations from the optimised conditions for secondary alkyl substrate **1a**.

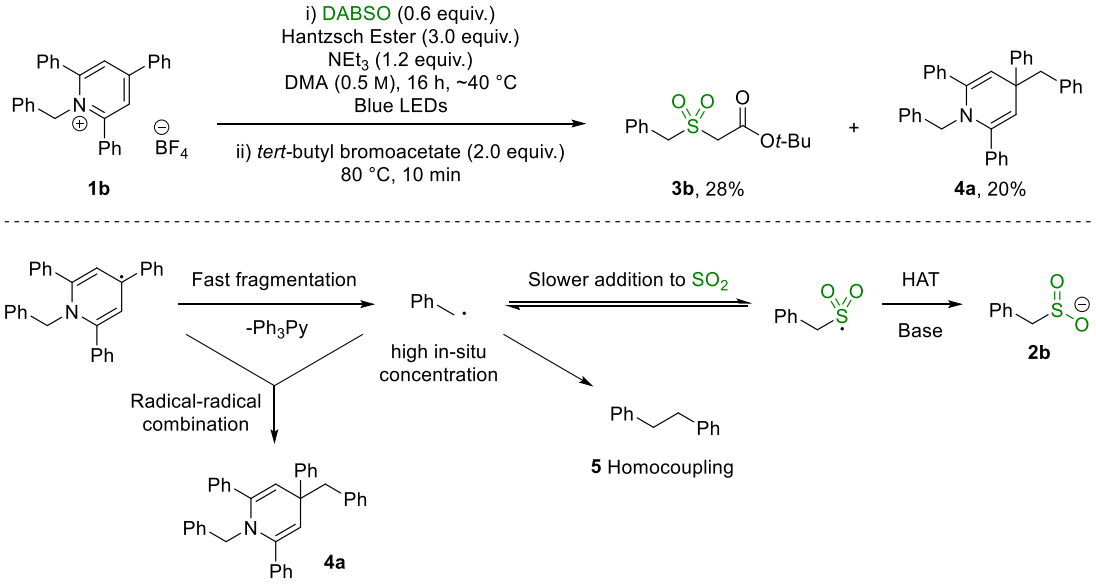


1a **2a** **3a**

Entry	Modifications	Yield
1	None	82%
2	Dark, 30 °C	Trace
3	Dark, 60 °C	80%
4	Rigorously dry and degassed solvents	83%
5	Degassed, DMA from bottle	79%
6	Degassed, DMA + 5% H_2O	73%
7	Under air, degassed dry DMA	81%
8	Dry DMA sparged with air	80%

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

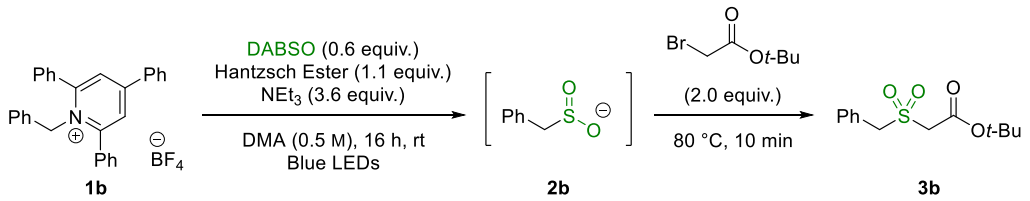
All the studies up to this point have used secondary alkyl substrates. When using Katritzky salt **1b**, derived from benzylamine, the sulfone **3b** was obtained in only 28% yield, alongside dihydropyridine **4a** in 20% yield. 1,2-Diphenylethane **5** was also observed, but wasn't isolated (**Scheme 2.25**). The rate of fragmentation of the relatively-stable dihydropyridine radical intermediate is highly dependent on the stability of the forming alkyl radical. In the case of benzylic substrates, the forming benzylic radical is much more stable than secondary alkyl radicals, so occurs much faster. If the rate of fragmentation is much faster than their reaction with SO_2, there will be a high in-situ concentration of benzylic radical, which can result in side-reactions, such as homocoupling to give **5**, and reaction with the dihydropyridine radical to give dihydropyridine **4a**. We wished to improve the yields for these substrates, so further optimisation was needed.



Scheme 2.25. Synthesis of benzyl sulfone **3b** from Katritzky salt and side-product formation.

We realised that we needed to reduce the rate of formation of the dihydropyridine radical, which would in turn reduce the in-situ concentration of benzylic radical and therefore the yield of the side-products. Following the observation that a higher loading of triethylamine increased the rate of reaction, likely due to the formation of a ternary EDA complex, we reasoned that reducing the loading of triethylamine may help reduce the rate of benzylic radical generation. Removing the triethylamine completely gave 9% yield of **3b**, likely due to the requirement for triethylamine to deprotonate the intermediate sulfinic acid (**Table 2.8, entry 2**). Using 1.2 equivalents of triethylamine gave 27% yield, comparable to that obtained using 3.6 equivalents (**Table 2.8, entry 3**). We considered whether increasing the loading of DABSO to 2.4 equivalents would increase the rate of benzylic radical addition to SO_2, but yields were comparable to that obtained using 1.2 equivalents (**Table 2.8, entry 4**). Carrying out the reaction at a lower 0.25 M concentration improved the yield somewhat to 47% (**Table 2.8, entry 5**). Lowering the light intensity gave a negligible increase in yield to 31% (**Table 2.8, entry 6**). Using sodium metabisulfite instead of DABSO lowered the yield further to 7%, likely due to poorer solubility (**Table 2.8, entry 7**). Finally, removing Hantzsch ester prevented reaction completely (**Table 2.8. entry 8**).

Table 2.8. Initial optimisation studies for benzylic substrate **1b**.



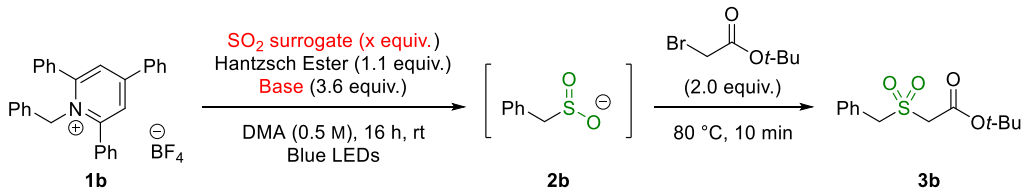
1b **2b** **3b**

Entry	Modifications	Yield
1	None	28%
2	No NEt_3	9%
3	1.2 equiv. NEt_3	27%
4	2.4 equiv. DABSO	27%
5	2x Dilution (0.8 mL, 0.25 M)	47%
6	Lower light intensity	31%
7	$Na_2S_2O_5$ instead of DABSO	7%
8	No Hantzsch Ester	0%

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

We then opted to screen a selection of bases, as we reasoned that more-hindered bases would be less-able to form a ternary EDA complex, thus lowering the absorption of the EDA complex and reducing the rate of SET, whilst still enabling deprotonation of the sulfinic acid intermediate (**Table 2.9**). Using the more-hindered DIPEA gave an improvement in yield to 46%, but 2,2,6,6-tetramethylpiperidine gave only 20% yield. Pyridine-derived bases gave much better results. Pyridine itself gave only 17% yield, but 2,6-lutidine and 2,4,6-collidine gave 83% and 82% yield respectively. 2,6-Di-*tert*-butylpyridine was likely too-hindered, giving 0% yield. Interestingly, when sodium metabisulfite was used as the SO_2-surrogate, comparable yields were obtained both in the presence and absence of 2,6-lutidine, giving 67% and 70% yield of the sulfone respectively. This may be due to deprotonation of the sulfinic acid intermediate by the sodium sulfite formed upon liberation of SO_2 from sodium metabisulfite.[40a]

Table 2.10. Base screen for benzylic substrate **1b**.

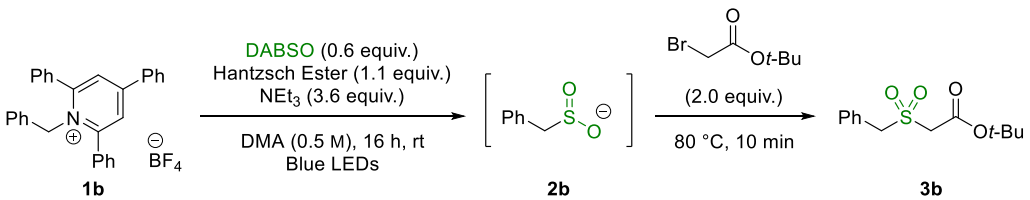


		SO_2 surrogate	
		DABSO (0.6 equiv.)	$Na_2S_2O_5$ (1.2 equiv.)
Additive	None	9%	70%
	Triethylamine	28%	7%
	DIPEA	46%	-
	2,2,6,6-tetramethylpiperidine	20%	-
	Pyridine	17%	-
	2,6-lutidine	83%	67%
	2,4,6-collidine	82%	-
	2,6-di-*tert*-butylpyridine	0%	-

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

The use of 3.6 equivalents of 2,6-lutidine was observed to give better yields of sulfone **3b** than 1.2 or 2.4 equivalents, giving 68% and 79% yield respectively (**Table 2.11**). These conditions can again be used to give sulfone **3b** in the absence of light, this time at low temperatures, giving 84% yield at 40 °C.

Table 2.11. Variations from the optimised conditions for benzylic substrate **1b**.

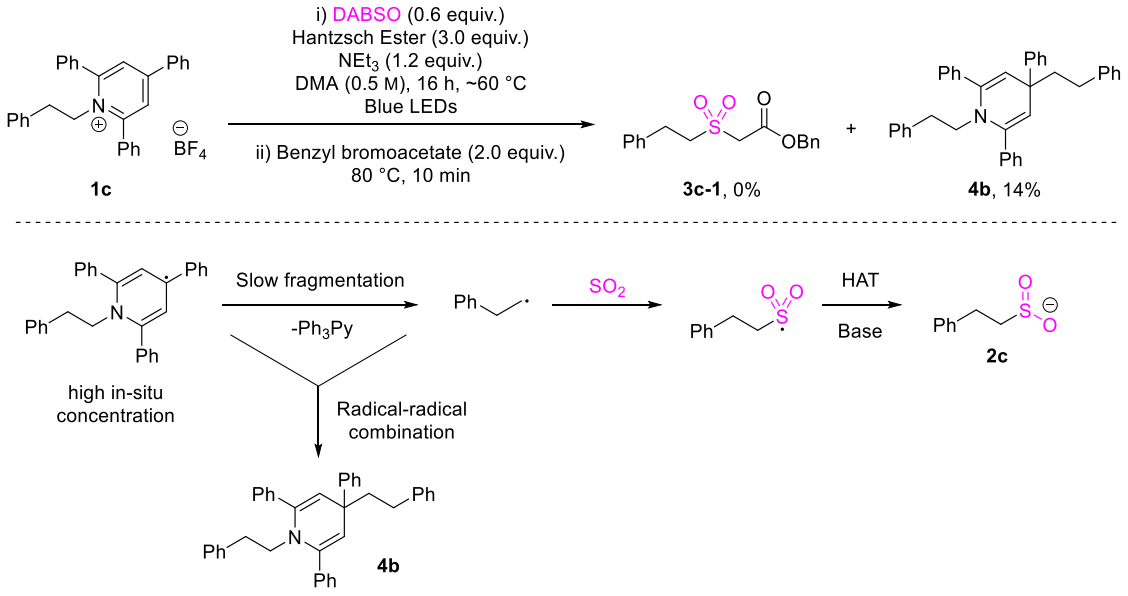


Modifications	Yield
None	83%
1.2 equiv. 2.6-lutidine	68%
2.4 equiv. 2,6-lutidine	79%
Dark, 30 °C	54%
Dark, 40 °C	84%

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

Contrary to benzyl radicals, primary alkyl radicals are much less stable than the dihydropyridine radical intermediate, resulting in a higher barrier to fragmentation. As a result, when using Katritzky salt **1c**, derived from phenethylamine, no reaction was observed in the previously-optimised

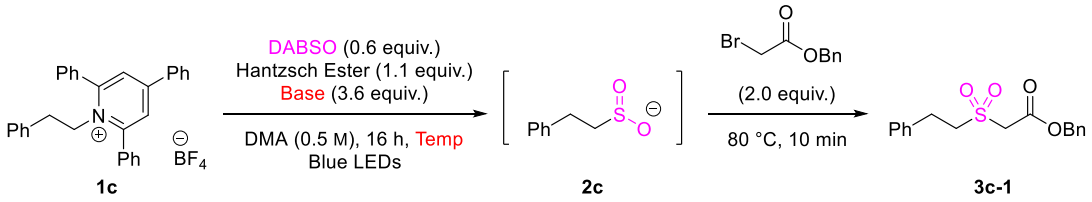
conditions. When the ambient temperature was increased to 60 °C, some consumption of Katritzky salt **1c** was observed, but whilst sulfone **3c-1** was not observed, dihydropyridine **4b** was isolated in 14% yield (**Scheme 2.26**). We reasoned that the photoexcited EDA complex would still undergo SET to give the dihydropyridine radical, which due to the slow fragmentation will exist in relatively high concentration. When primary radicals are generated, they are then likely to react with the dihydropyridine radical instead of SO_2, giving the dihydropyridine side-product **4b** and preventing the formation of the sulfinate **2c**. We again needed to re-optimise to enable access to this important class of substrates.



Scheme 2.26. Synthesis of benzyl sulfone **3c-1** from Katritzky salt and side-product formation.

Given the importance of the base in both of the previous optimisation studies, we screened a selection of bases, but product **3c-1** was only observed when secondary amines were used (**Table 2.12**). These yields ranged from 33% when using morpholine to 57% when using piperidine. A further increase to 74% yield was obtained when using piperidine with an ambient reaction temperature of 80 °C, but no further increase in yield was obtained at 90 °C. The other secondary amines screened at 80 °C gave more varied results, with some giving a drop in yield. The good yields using piperidine were encouraging, but the setup used to achieve these higher temperatures, involving wrapping LED strips inside a vial placed in an oil bath, gave inconsistent yields, so further optimisation was needed.

Table 2.12. Base and temperature screen for primary alkyl substrate **1c**.

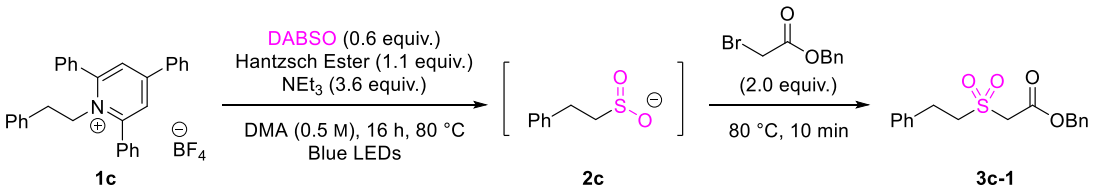


		Temperature			
		Ambient Temp (30 °C)	60 °C	80 °C	90 °C
Base	Triethylamine	0%	0%	Trace	-
	Morpholine	0%	33%	28%	-
	Pyrroline	0%	51%	58%	-
	Piperidine	-	57%	74%	72%
	Diethylamine	-	47%	-	-
	Diisopropylamine	-	43%	23%	-
	Dicyclohexylamine	-	37%	-	-
	N-methylpiperazine	-	49%	-	-
	2,6-lutidine	-	0%	-	-
	tert-butylamine	-	0%	-	-
	n-butylamine	-	0%	-	-
	DBU	0%	0%	-	-
	2,2,6,6-tetramethylguanidine	-	0%	-	-
	DMAP	-	0%	-	-

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

As the previously optimised conditions could be carried out in the absence of light, with thermally-induced SET, we expected that if the reaction of primary substrates could be done thermally, it would provide a more consistent reaction with a more reproducible setup. Pleasingly, upon removal of light with the reaction at 80 °C, only a small drop in yield to 67% was obtained (**Table 2.13, entry 2**). Under these reaction conditions, we re-tested morpholine and pyrrolidine, which gave lower yields of 28% and 58% respectively (**Table 2.13, entries 3 and 4**). Increasing the temperature further to 90 °C gave a slight improvement to 76% yield (**Table 2.13, entry 5**). Sodium metabisulfite could again be used instead of DABSO to give 69% yield. Finally, removing Hantzsch ester under these reaction conditions gave only 9% yield.

Table 2.13. Variations from the optimised conditions for primary alkyl substrate **1c**.

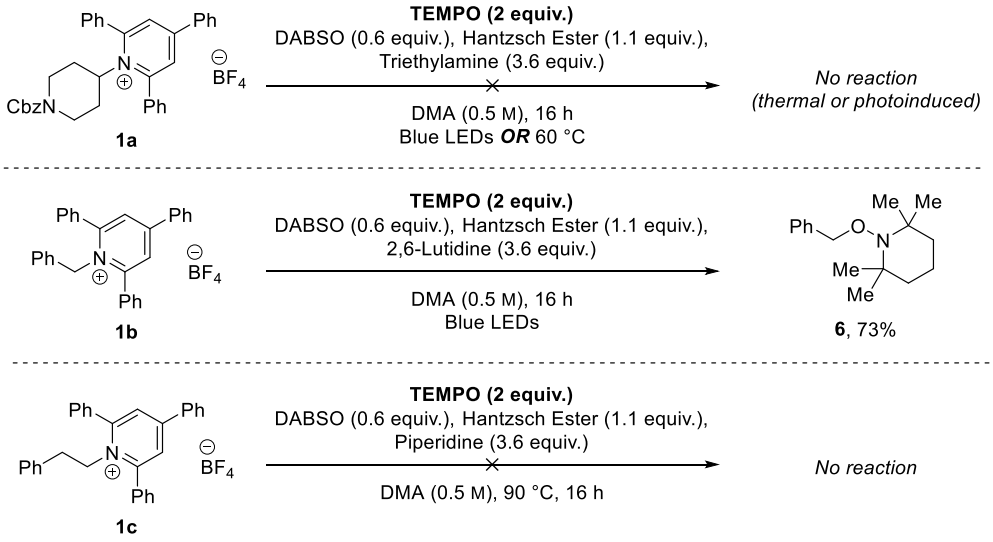


Entry	Modifications	Yield
1	None	74%
2	Dark	67%
3	Dark, morpholine	28%
4	Dark, pyrrolidine	58%
5	Dark, 90 °C	76%
6	Dark, $Na_2S_2O_5$ instead of DABSO	69%
7	Dark, no Hantzsch ester	9%

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

2.2.3 Mechanistic Experiments

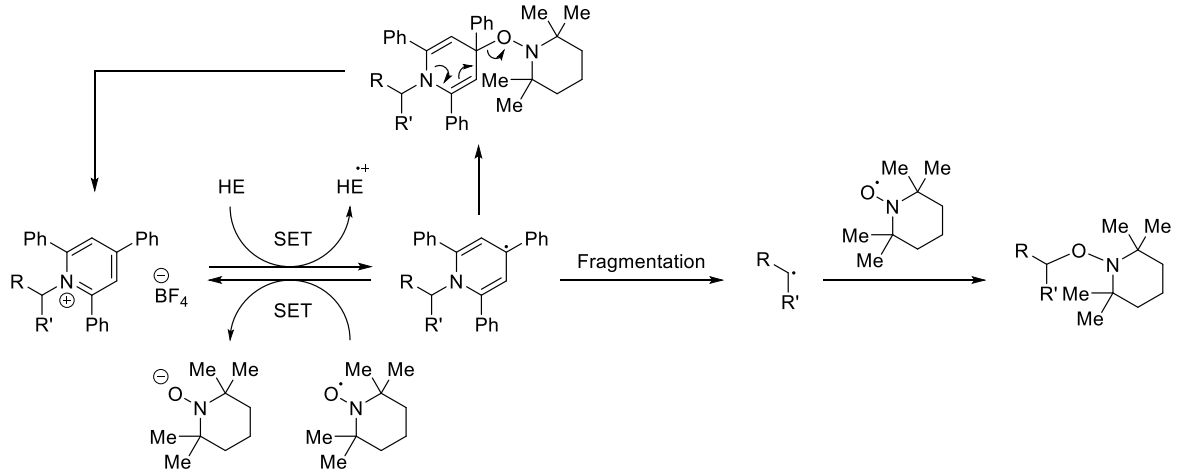
To probe the reaction mechanism and to justify observations during the optimisation of the reaction, we carried out mechanistic studies. We found that addition of TEMPO inhibited the reaction when using secondary or primary alkyl substrates **1a** and **1c**, but complete conversion was observed using benzylic substrate **1b**, giving adduct **6** in 73% yield (**Scheme 2.27**).



Scheme 2.27. Formation of adducts using TEMPO.

This difference in reactivity is likely due to the difference in rate of fragmentation of the different substrates. We propose that the dihydropyridine radical forms under these reaction conditions, but if

fragmentation is slow, the dihydropyridine radical is quenched prior to fragmentation, either by SET or radical combination with TEMPO, regenerating the Katritzky salt starting material and therefore inhibiting the reaction (**Scheme 2.28**).



Scheme 2.28. Competing reactions of dihydropyridine radical: fragmentation or reaction with TEMPO

In order to investigate EDA complex formation in our reaction mixtures, UV/vis absorption studies were performed on individual reaction components and mixtures to observe bathochromic shifts in absorption associated with complex formation.

In agreement with observations by Aggarwal and co-workers,[170] the UV/vis absorption spectra of binary mixtures of Katritzky salt **1a** and either Hantzsch ester or triethylamine showed a significant bathochromic shift and an increase in absorption when compared to the spectra of the separate components, indicating the formation of EDA complexes. The ternary mixture of **1a**, Hantzsch ester and triethylamine showed a further bathochromic shift, indicating the formation of a ternary EDA complex, which explains why additional triethylamine was found to be important in giving high yields of the sulfinate product (**Figure 2.1**).

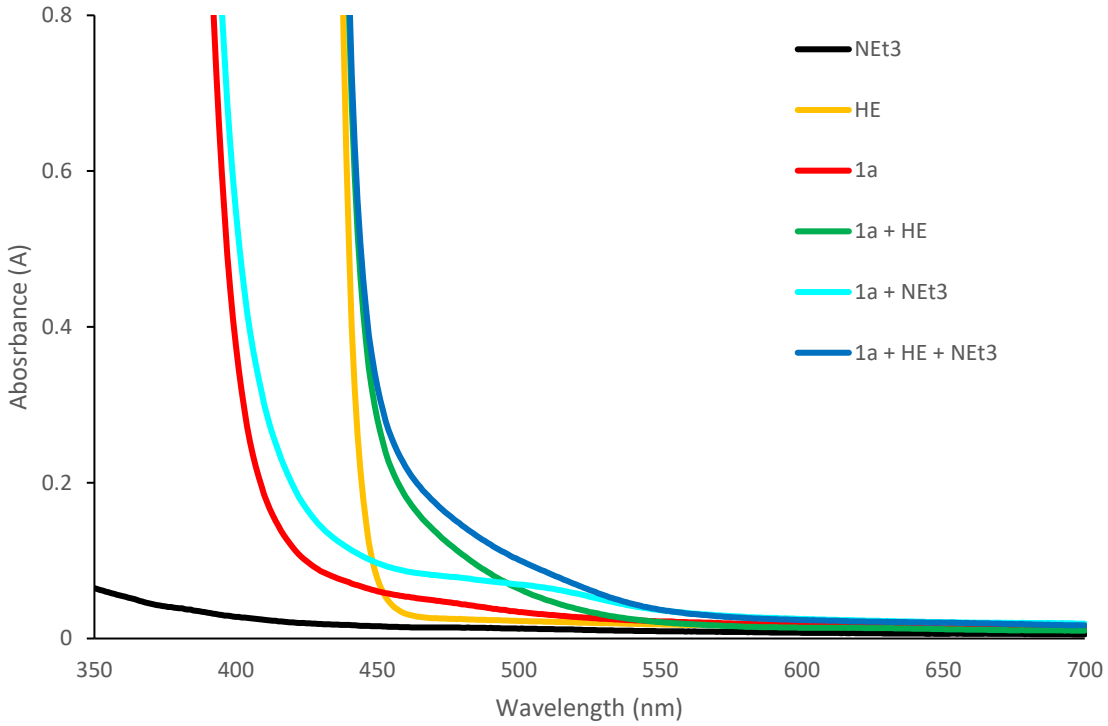


Figure 2.1. UV/vis absorbance spectra for components of reaction mixture for Katritzky salt **1a**. Concentration of solutions: Katritzky salt **1a** (0.1 M) Hantzsch Ester (0.11 M) NEt_3 (0.36 M).

For benzylic substrate **1b**, the absorption spectrum of the ternary mixture of **1b**, Hantzsch ester and 2,6-lutidine appeared to be identical to that of the binary mixture of **1b** and Hantzsch ester, which supports the hypothesis that 2,6-lutidine does not form a ternary EDA complex whilst still acting as a base to deprotonate the sulfinic acid intermediate (**Figure 2.2**). As a ternary EDA complex does not form, SET and thus benzylic radical generation occurs at a reduced rate, resulting in a higher yield of the sulfinate and lower yield of side-products.

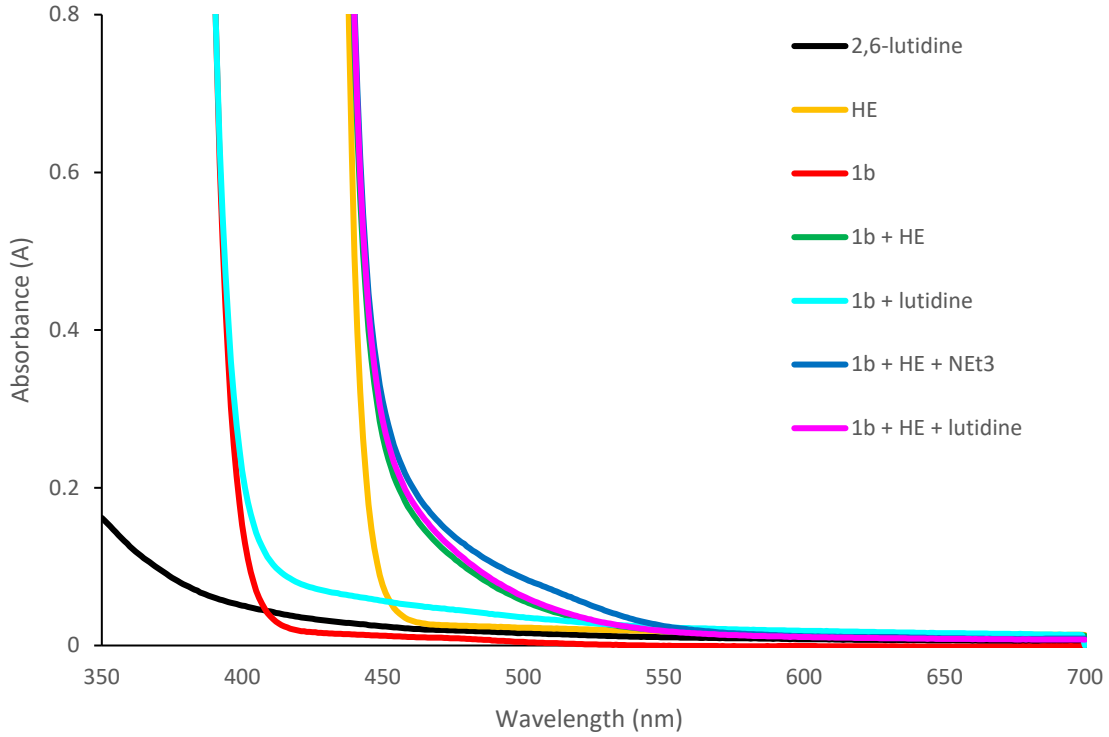


Figure 2.2. UV/vis absorbance spectra for components of reaction mixture for Katritzky salt **1b**. Concentration of solutions: Katritzky salts **1b** (0.1 M), Hantzsch Ester (0.11 M), NEt_3 (0.36 M), 2,6-lutidine (0.36 M).

For primary substrate **1c**, the spectrum of the ternary mixture of **1c**, Hantzsch ester and piperidine showed a further bathochromic shift and increase in absorbance compared to that using Et_3N (**Figure 2.3**). Previous studies have reported a stronger interaction between secondary amines donors and electron-acceptors in EDA complexes compared to that using tertiary amines.[165b-d] This may contribute to the increased reactivity observed when using piperidine with the primary substrates.

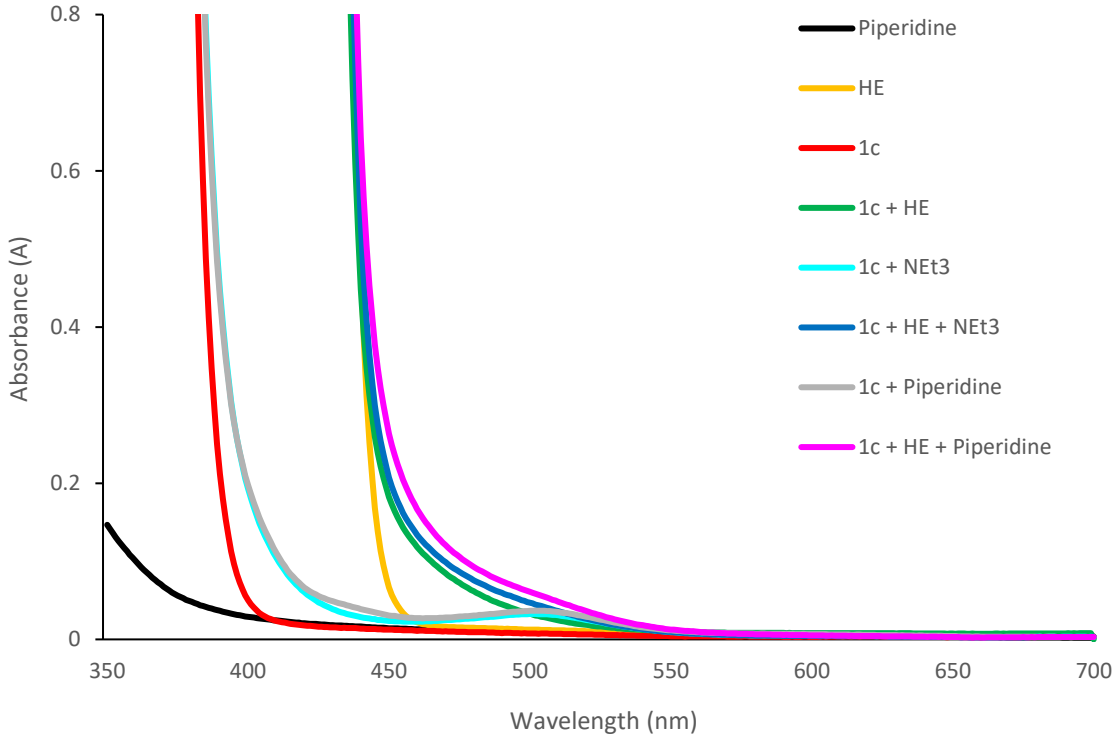
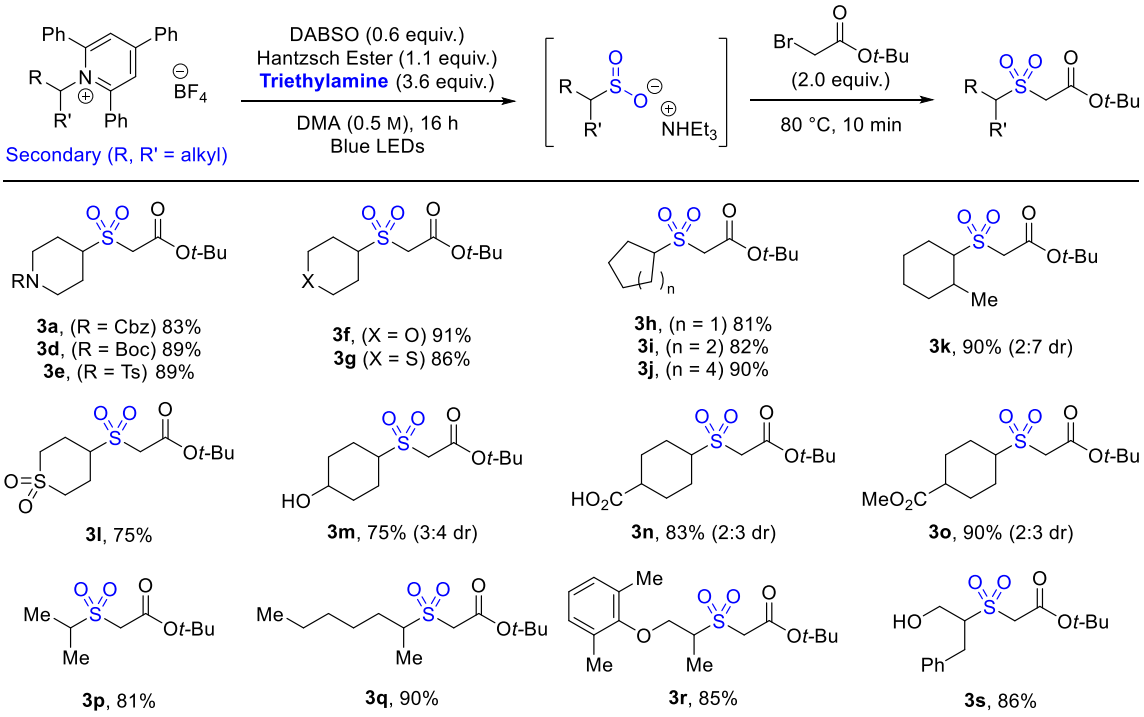


Figure 2.3. UV/vis absorbance spectra for components of reaction mixture for Katritzky salt **1c**. Concentration of solutions: Katritzky salts **1c** (0.1 M), Hantzsch Ester (0.11 M), NEt_3 (0.36 M), piperidine (0.36 M).

2.2.3 Primary Amine Scope

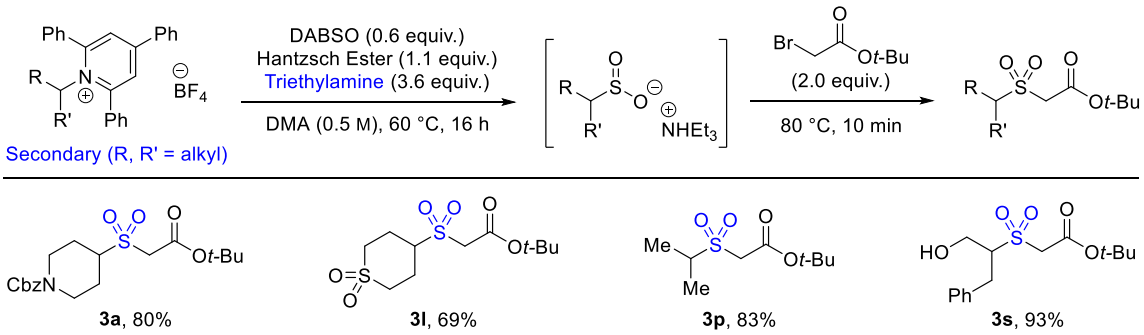
With optimised reaction conditions in hand, we began exploring the scope of the reaction. The scope of secondary alkyl substrates was carried out by Dr. Loïc Pantaine (a previous post-doc in our group) (**Table 2.14**). We were pleased to find that the reaction tolerates protected amines, (**3a**, **3d** and **3e**), tetrahydrofuran (**3f**), tetrahydrothiopyran (**3g**) and tetrahydrothiopyran 1,1-dioxide (**3l**), all giving excellent yields. Varied steric properties were also tolerated with non-cyclic substrates (**3p** and **3q**), cyclic substrates with ring sizes from 5-8 (**3h**, **3i** and **3j**), and an ortho-methyl substituent (**3k**) giving the corresponding sulfone products in excellent yields. Protic functionalities such alcohol (**3m**) and carboxylic acid (**3n**), as well as electrophilic functionalities such as ester (**3o**), could be prepared in high yields using our method. These products would be challenging to prepare using non-radical methods such as reactions of organometallic reagents with DABSO. We could also use this method to prepare sulfone derivatives of biologically-relevant substrates, such as the drug molecule: mexiletine (**3r**), as well as phenylalaninol (**3s**), both giving the corresponding products in good yields.

Table 2.14. Scope of sulfone products from secondary-alkyl substrates. All experiments carried out by Dr Loïc Pantaine.

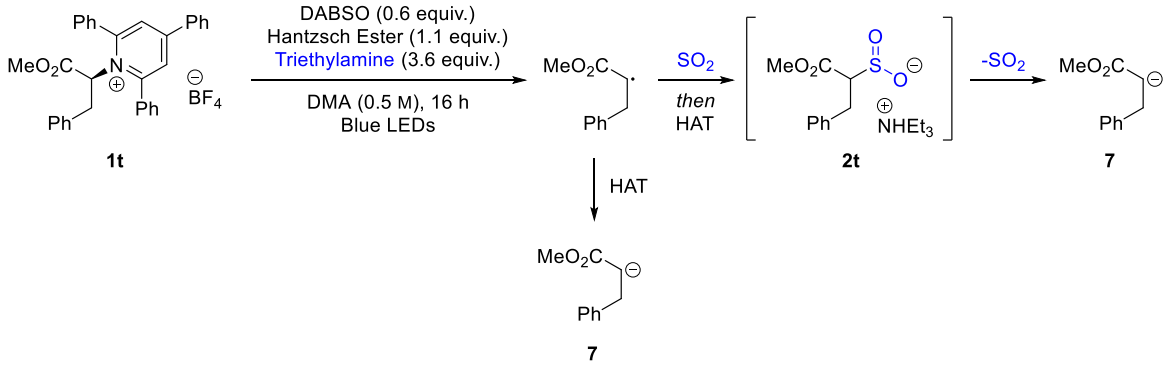


We also tested four of the above substrates using the thermal conditions without light, and found that the product sulfones could be obtained in yields comparable to those obtained using blue LEDs to initiate the reactions (**Table 2.15**).

Table 2.15. Sulfone products from secondary-alkyl substrates using thermal conditions. All experiments carried out by Dr Loïc Pantaine.

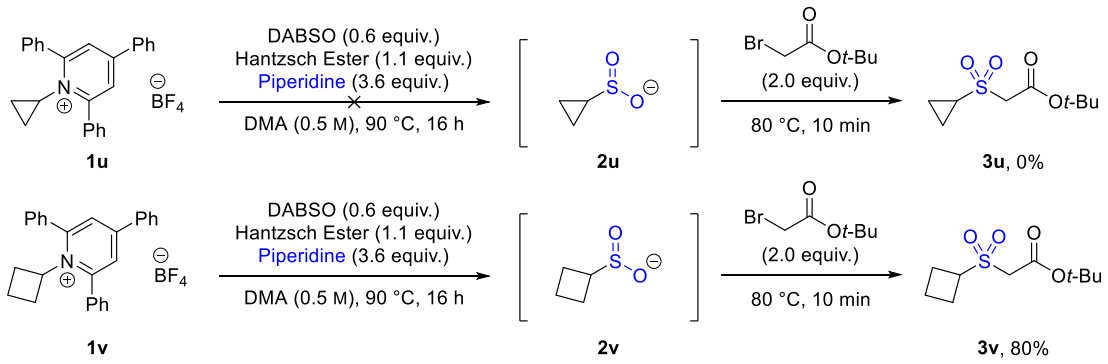


Using substrate **1t**, derived from phenylalanine methyl ester, none of the corresponding sulfone was observed. Instead, methyl 3-phenylpropionate **7** was observed in the crude reaction mixture, which indicated either loss of SO_2 from the intermediate sulfinate **2t** to give the ester enolate or reduction of the α-carboxy radical by Hantzsch ester (**Scheme 2.29**).[170]



Scheme 2.29. Decomposition of amino ester-derived sulfinates to ester enolate.

Cyclopropyl and cyclobutyl substrates **1u** and **1v** gave none of the corresponding sulfone products **3u** and **3v** under the standard reaction conditions. This can be explained by their radical stabilities, where the cyclobutyl radical is closer in stability to primary alkyl radicals than it is to secondary alkyl radicals, whereas the cyclopropyl radical is even less stable.[172] Given this observation, we applied the optimised conditions for primary alkyl substrates to these examples. Whilst the cyclopropyl product **3u** still wasn't observed using these conditions, the cyclobutyl product **3v** could be isolated in 80% yield (**Scheme 2.30**).

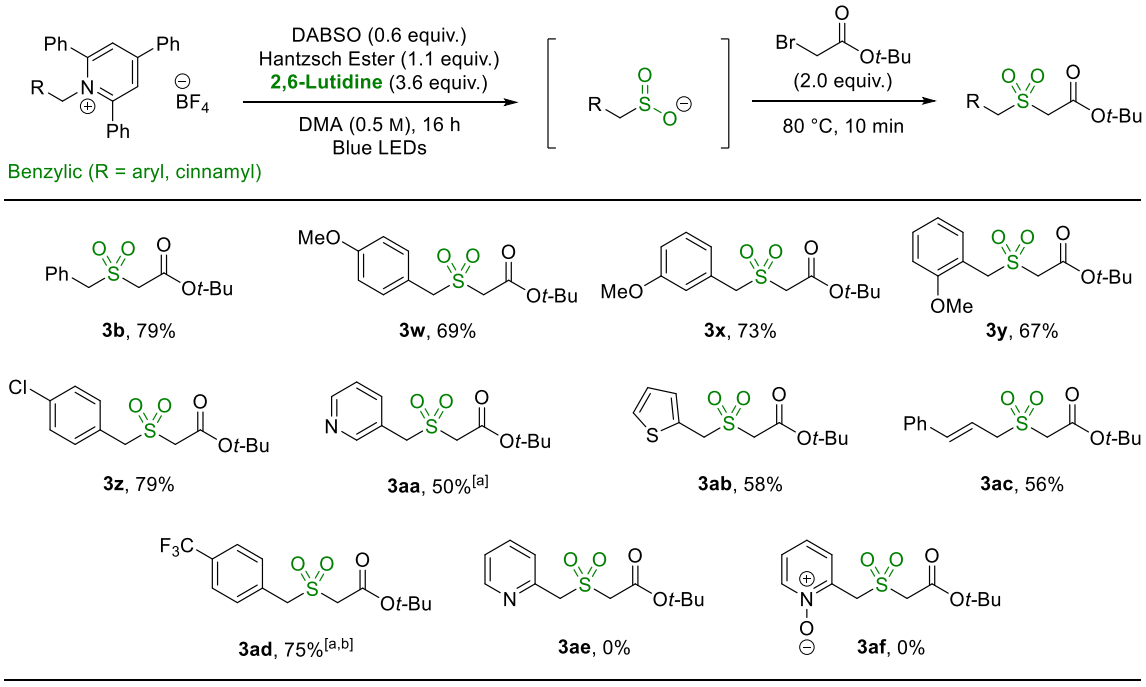


Scheme 2.30. Reactions of cyclopropyl and cyclobutyl substrates.

We then assessed the scope of benzylic substrates that could be used under the optimised reaction conditions using 2,6-lutidine (**Table 2.16**). Electron-donating methoxy substituents were well tolerated, and this could be moved around the ring giving comparable yields in all cases (**3w**, **3x** and **3y**). Chloride (**3z**) could also be used, providing a handle for further reactivity. Pyridine (**3aa**) and thiophene (**3ab**) heterocycles could also be tolerated, giving the corresponding sulfone products in moderate yields. Cinnamyl amines could also be used to give sulfone **3ac** using these conditions.

Electron-withdrawing substituents were less-well tolerated, likely due to loss of SO_2 from the intermediate sulfinate to give a stabilised benzylic anion. Trifluoromethyl sulfone **3ad** could be prepared in good yield, but a shorter reaction time and lower alkylation temperature were needed to minimise decomposition of the intermediate sulfinate. Sulfone **3ae** could not be isolated, which is consistent with previous studies in the Willis group demonstrating that the corresponding sulfinates rapidly liberate SO_2. The same result was obtained when preparing the *N*-oxide derivative **3af**.

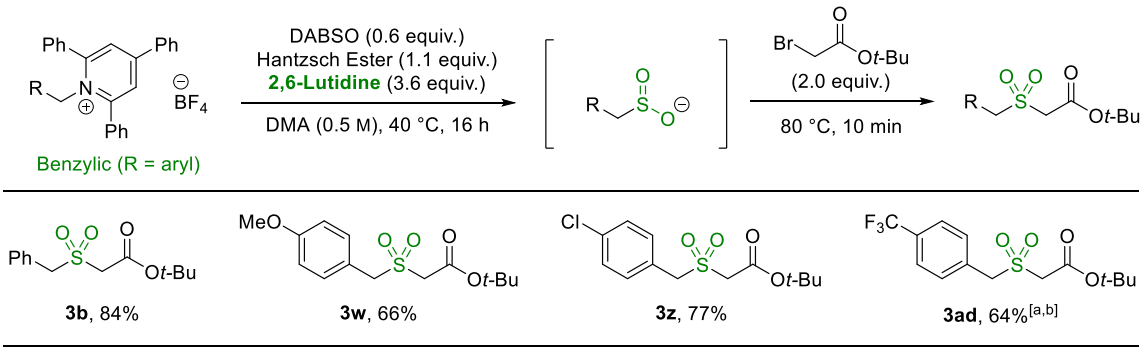
Table 2.16. Scope of sulfone products from benzylic substrates.



[a] Step 2: r.t., 5 h. [b] Step 1: 8-hour reaction time.

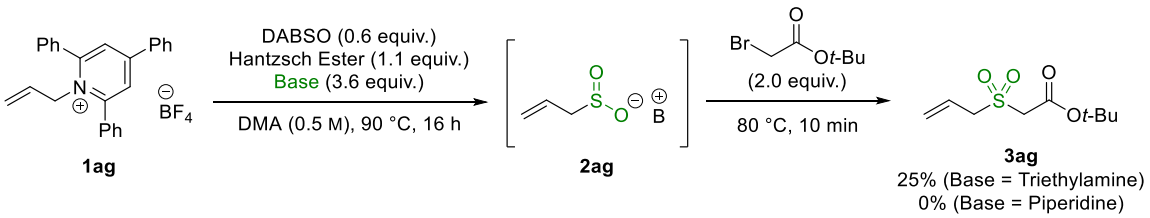
We again tested four of the above substrates using the thermal conditions without light, and found that again that yields of the sulfone products were generally comparable to those obtained using light (**Table 2.17**). Shorter reaction times and reduced alkylation temperature was again used for trifluoromethyl example **3ad**, but the slight drop in yield in this case was likely due to a slightly increased rate of sulfinate decomposition at the higher reaction temperature.

Table 2.17. Sulfone products from benzylic substrates using thermal conditions.



[a] Step 2: r.t., 5 h. [b] Step 1: 8-hour reaction time.

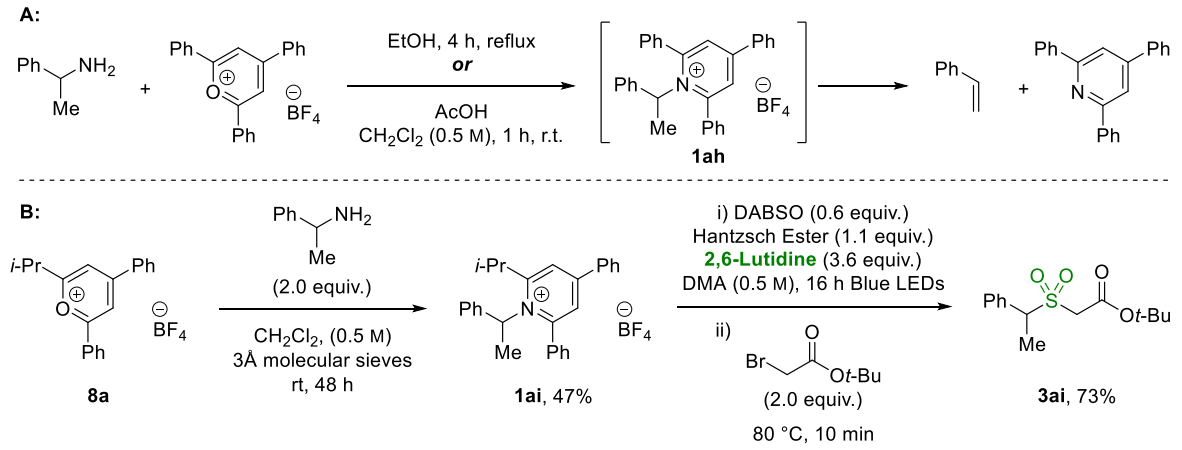
Having obtained a good yield for cinnamyl example **3ac** under the optimised reaction conditions, we were surprised to find that allyl sulfone **3ag** could not be generated using the same reaction conditions, despite full consumption of the Katritzky salt **1ag**. Conversely, allyl sulfone **3ag** could be isolated using the conditions optimised for secondary-alkyl substrates using triethylamine, albeit in a low 25% yield (**Scheme 2.31**). Previous studies in the Willis group have found that reactions involving the formation of allyl sulfinates are often low-yielding, which is attributed to the decomposition of the sulfinate under the reaction conditions. In this case, the cation identity may be significant, with triethylamine forming a more stable sulfinate salt than 2,6-lutidine.



Scheme 2.31. Reactions of allyl substrate **1ag**.

The Katritzky salt **1ah**, derived from α-methylbenzylamine, is known to decompose upon preparation to give styrene and 2,4,6-triphenylpyridine (**Scheme 2.32.A**).[173] The 2-isopropyl analogue **1ai** however has been previously reported by Katritzky and co-workers,[174] and pleasingly, this substrate could be used with no further modification of the reaction conditions to give sulfone **3ai** in 73% yield (**Scheme 2.32.B**). This enables access to secondary benzylic substrates, but also demonstrates that

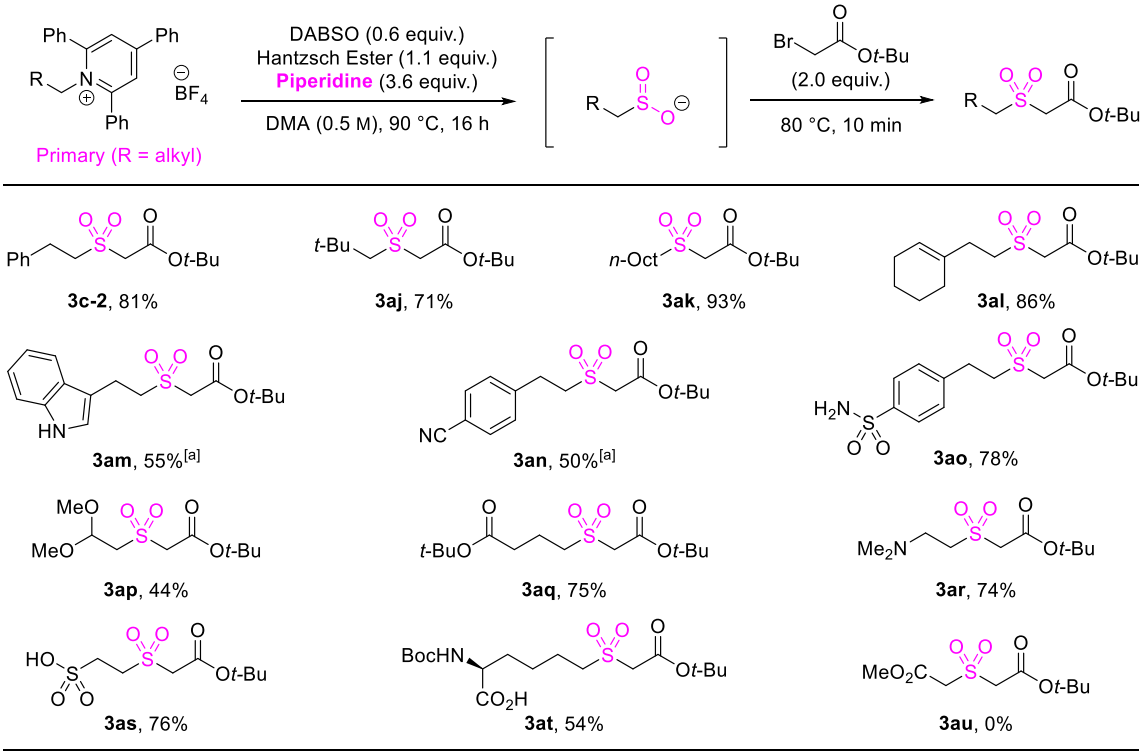
the 2,4,6-triphenyl substitution pattern is not necessary in order to generate the dihydropyridine radical or to enable fragmentation to the alkyl radical.



Scheme 2.32. A): Decomposition of pyridinium **1ah** upon preparation. **B):** Preparation and use of 2-isopropyl analogue **1ai** and its use to prepare sulfone **3ai**.

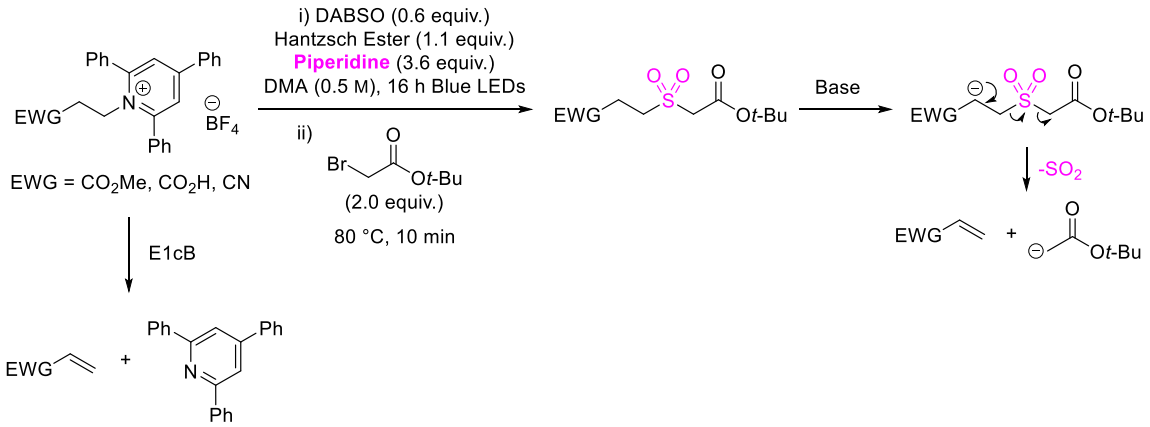
We then assessed the scope of primary substrates compatible with the optimised conditions using piperidine (**Table 2.18**). Sulfones containing a hindered neopentyl substituent (**3aj**) and long aliphatic octyl chain (**3ak**) were obtained in good yields under the reaction conditions. Due to the commercial availability of diverse primary amine substrates, we were able to demonstrate excellent functional group compatibility of these conditions, tolerating alkene (**3al**), indole (**3am**), nitrile (**3an**), primary sulfonamide (**3ao**), acetal (**3ap**), *tert*-butyl ester (**3aq**), tertiary amine (**3ar**), and sulfonic acid (**3as**) functional groups, giving good to excellent yields. Using these conditions, the lysine side-chain could be functionalised to give an unnatural amino ester product **3at**. Similar to the observations using phenylalanine methyl ester, glutamine methyl ester showed full consumption of the Katritzky salt starting material, but none of the desired sulfinate **2au** was observed, likely due to the liberation of SO_2 from the sulfinate intermediate. Improved yields of nitrile and indole substrates **3am** and **3an** were obtained if alkylation was carried out at a lower temperature.

Table 2.18. Scope of sulfone products from primary-alkyl substrates.



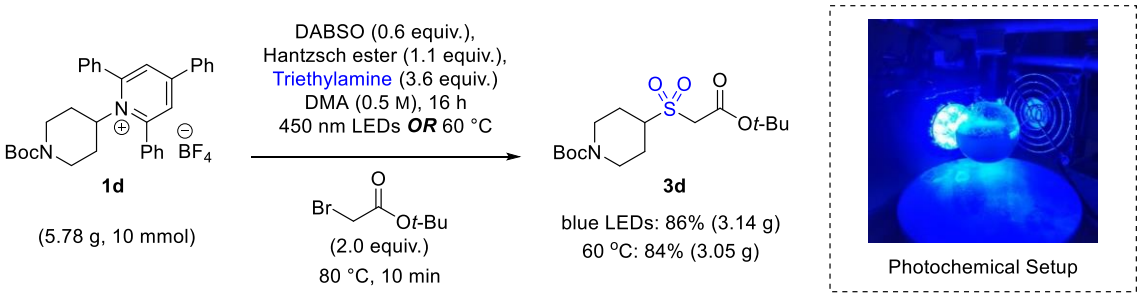
[a] Step 2: r.t., 5 h.

Substrates with β-electron withdrawing groups, such as esters, nitriles, and even carboxylic acid (**1av**, **1aw** and **1ax**), gave 0% yield of the desired sulfone products. This may be due to either decomposition of the Katritzky salt via an E1cB mechanism under the rection conditions or decomposition of the sulfone product to the sulfinate,[175] which itself would liberate SO_2 to form the ester enolate (**Scheme 2.33**). This reasoning may also explain the observation the observed increased yield for sulfone **3an** when the alkylation was carried out at a lower temperature.



Scheme 2.33. Decomposition of sulfones with β-electron-withdrawing groups.

We carried out the reaction on a 10 mmol scale with both photochemically and thermally induced SET in order to demonstrate the application of this chemistry to large-scale synthesis. We were pleased to find that without modification to the reaction conditions, sulfone **3d** could be isolated in 86% using blue LEDs and 84% with the reaction carried out at 60 °C, compared to 89% on a 0.2 mmol scale (**Scheme 2.34**).



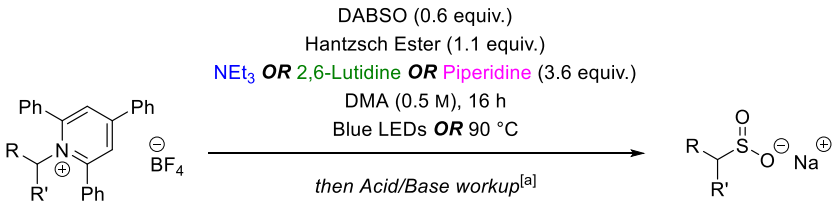
Scheme 2.34. Scale-up reaction.

2.2.4. Sulfinate Derivatisation

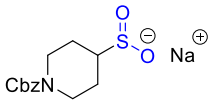
Having demonstrated that the amine component could be varied to give a wide selection of sulfone products, we then wished to show that we could use this method to prepare a selection of other sulfonyl derivatives.

We began by first demonstrating that the sulfinate intermediate could also be isolated. Purification of sulfinates can be challenging, and whilst we found that the sulfinate could be isolated purification by flash-column chromatography, the yield was poor, and less than one equivalent of the expected ammonium cation was observed, which we rationalised was likely due to cation exchange with trace impurities in the silica gel. To give improved yields of the sulfinate with a known countercation, we opted to isolate the sulfinate by acid workup followed by extraction of the sulfinate using 10% aqueous Na_2CO_3 solution. Using this method, we were able to isolate sodium sulfinate salts **9a**, **9b** and **9c** in good yields (**Table 2.19**).

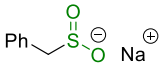
Table 2.19. Preparation of sodium sulfinate salts.



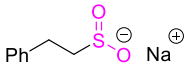
Secondary (R, R' = alkyl), Benzylic (R = aryl, R' = H), Primary (R = alkyl, R = H)



9a, 82%[b]



9b, 77%[c]

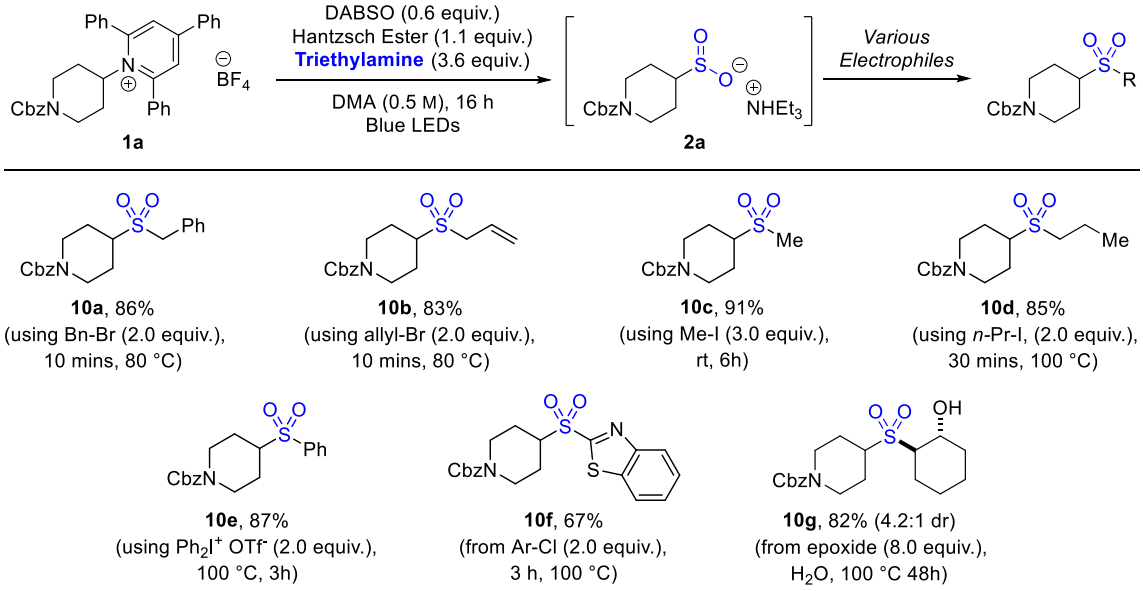


9c, 87%[d]

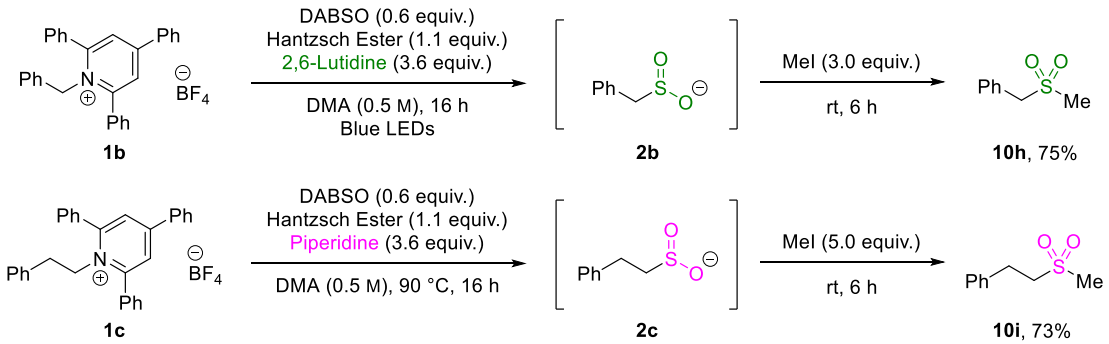
[a] After step 1: acidify using 2 M aq. H_3PO_4, extraction using 3 × 10% aq. Na_2CO_3, solvent removed from combined aqueous phase and extraction using boiling EtOH × 3. [b] Using triethylamine and Blue LEDs. [c] Using 2,6-lutidine and Blue LEDs. [d] Using piperidine at 90 °C.

We then showed that other C-electrophiles could be used in a one-pot procedure to prepare a selection of sulfones (**Table 2.20**). Activated electrophiles such as benzyl and allyl bromide could be used in the same conditions as those using *tert*-butyl bromoacetate to give sulfones **10a** and **10b** in 86% and 83% yield respectively. Methylation using methyl iodide gave sulfone **10c** in an excellent 91% yield, but alkylation was carried out at a lower temperature due to the low boiling point of methyl iodide. Propyl iodide could also be used, although a slightly higher temperature was needed to good yields of propyl sulfone **10d**. Aryl electrophiles such as diphenyliodonium triflate could be used to give phenyl sulfone **10e** in 87% yield. Sulfone products could also be obtained by an S_NAr reaction, such as with 2-chlorobenzothiazole, which gave sulfone **10f** in good yield. Finally, the sulfinate could be reacted with epoxides such as cyclohexene oxide to give β-hydroxysulfone **10g**. We were surprised to observe two diastereomers in the reaction, which could be due to epimerisation or initial epoxide ring-opening using DABCO or triethylamine, and subsequent S_N2 using the sulfinate salt. We found this could be suppressed somewhat by dilution with H_2O, although 8.0 equivalents of epoxide and 100 °C was then needed to achieve good conversion under these conditions to give sulfone **10g** in 82% yield with 4.2:1 dr.

Table 2.20. One-pot reaction with various electrophiles to give sulfones.



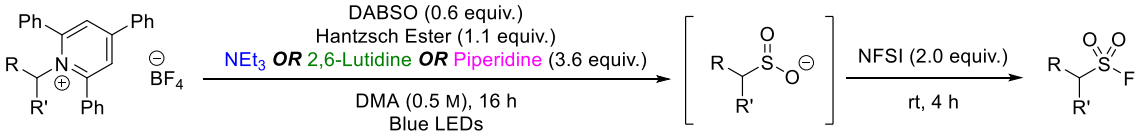
We then demonstrated that other sulfones could be prepared from sulfinates prepared in conditions using 2,6-lutidine or piperidine (**Scheme 2.35**). Methyl sulfone **10h** could be prepared in 75% yield from benzyl sulfinate **2b** with no modification of the reaction conditions, whereas the preparation of methyl sulfone **10i** from primary alkyl sulfinate **2c** needed 5.0 equivalents of methyl iodide to give a yield of 73%, likely due to competing alkylation of piperidine.



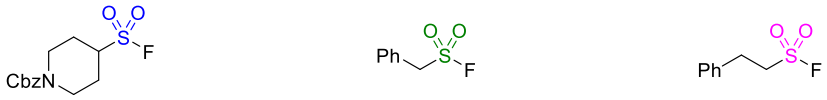
Scheme 2.35. Preparation of methyl sulfones from benzylic and primary alkyl substrates.

Sulfonyl fluorides could be readily prepared by addition of NFSI to the reaction mixture. Using identical reaction conditions, sulfonyl fluorides **11a**, **11b** and **11c** could all be prepared in good yields (**Table 2.21**).

Table 2.21. One-pot reaction with NFSI to give sulfonyl fluorides.



Secondary (R, R' = alkyl), Benzylic (R = aryl, R' = H), Primary (R = alkyl, R = H)

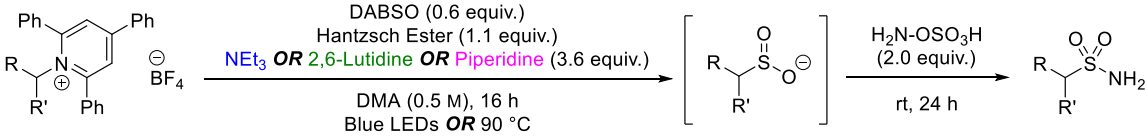


11a, 85% **11b**, 75% **11c**, 81%

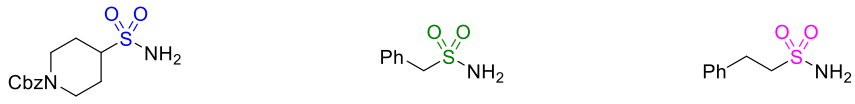
[a] Using triethylamine and Blue LEDs. [b] Using 2,6-lutidine and Blue LEDs. [c] Using piperidine at 90 °C.

Primary sulfonamides can be prepared from sulfinates using hydroxylamine-*O*-sulfonic acid (**Table 2.22**).[19a] Addition of hydroxylamine-*O*-sulfonic acid to the crude reaction mixture from secondary Katritzky salt **1a** gave primary sulfonamide **12a** in 88% yield. The same reaction with benzyl Katritzky salt **1b** gave a poor yield of primary sulfonamide **12b** due to 2,6-lutidine reacting with hydroxylamine-*O*-sulfonic acid.[176] Removing 2,6-lutidine using an acid workup prevented this, giving sulfonamide **12b** in 74% yield. Alternatively, conditions using sodium metabisulfite, where 2,6-lutidine is not needed, could be used without the requirement for a workup, giving sulfonamide **12b** in 69% yield. Finally, addition of hydroxylamine-*O*-sulfonic acid to the crude reaction mixture from primary Katritzky salt **1c** gave primary sulfonamide **12c** in 71% yield, despite the competing reaction with piperidine to give 1-aminopiperidine.[176]

Table 2.22. Reaction with hydroxylamine-*O*-sulfonic acid to give primary sulfonamides.



Secondary (R, R' = alkyl), Benzylic (R = aryl, R' = H), Primary (R = alkyl, R = H)

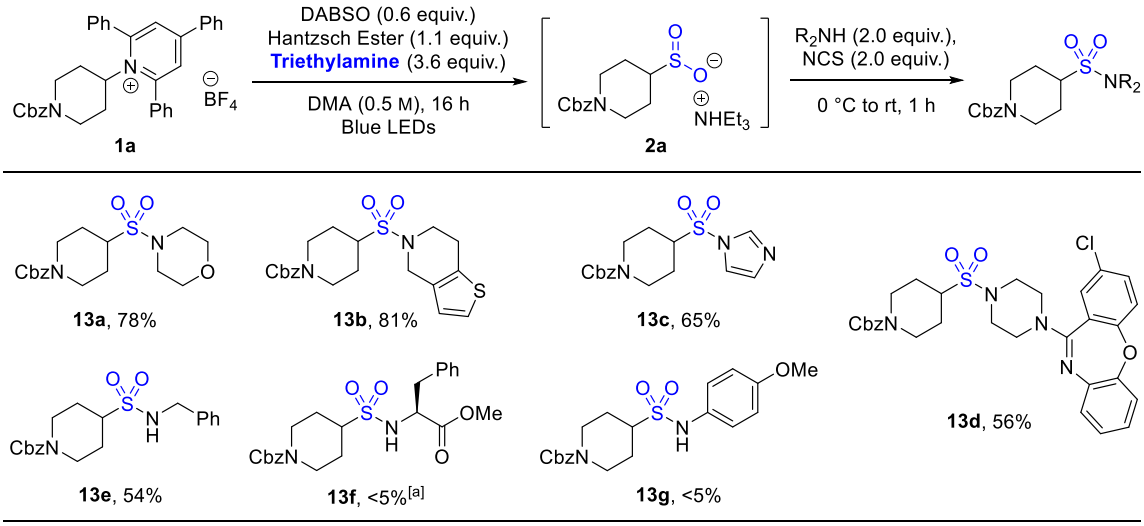


12a, 88%[a] **12b**, 74%[b], 69%[c] **12c**, 71%[d]

[a] Using triethylamine and Blue LEDs. [b] Using 2,6-lutidine and Blue LEDs, After step 1: acidify using 2 M aq. H_3PO_4, extract using CH_2Cl_2 × 3, combine organic phases and add DIPEA. [c] $Na_2S_2O_5$ instead of DABSO, no 2,6-lutidine, using Blue LEDs. [d] Using piperidine at 90 °C.

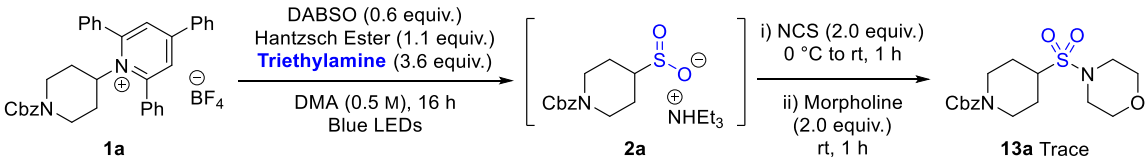
Sulfonamides could be prepared via oxidative chlorination of the intermediate sulfinate **2a** using NCS to prepare a sulfonyl chloride intermediate and reaction with an amine nucleophile in a one-pot procedure (**Table 2.23**). Good yields were obtained using nucleophilic amines such as morpholine (**13a**), 4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine (a fragment of Clopidogrel) (**13b**) and Amoxapine (**13c**), as well as heterocyclic nucleophiles such as imidazole (**13d**). However, poorer yields were obtained when using less-nucleophilic amines, such as benzylamine, which gave 54% of the corresponding sulfonamide **13e**. Furthermore, only traces of the desired sulfonamide products were obtained when using phenylalanine methyl ester (**13f**) or *p*-anisidine (**13g**).

Table 2.23. One-pot preparation of sulfonamides via oxidative chlorination.



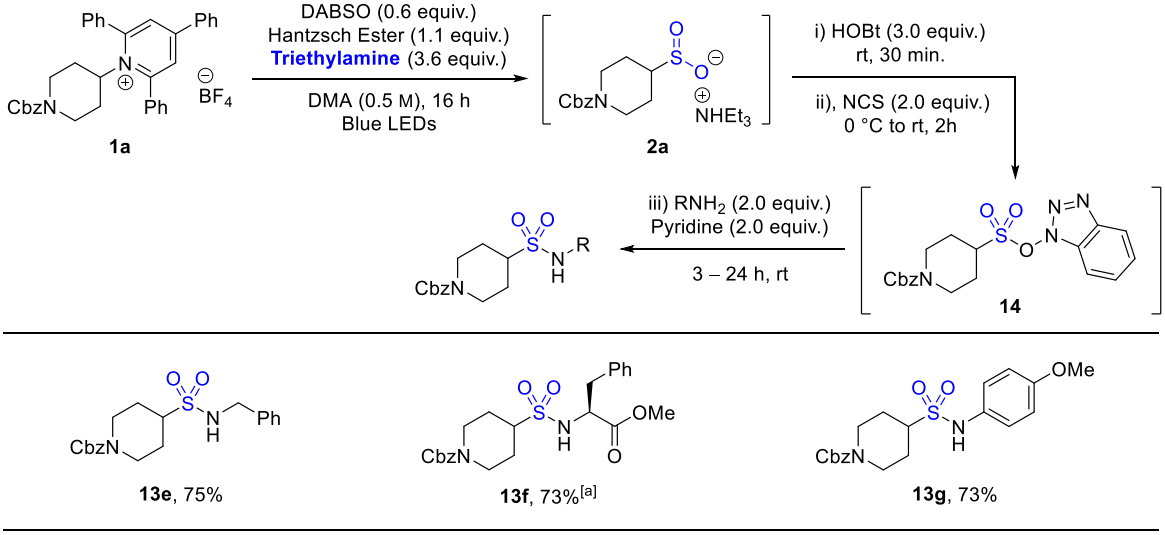
[a] From stirred solution of amine HCl salt (2.0 equiv.) with DIPEA (2.0 equiv.) in 0.2 mL DMA

We wished to be able to access these sulfonamides derived from less-nucleophilic amines in improved yields. We found that if the sulfonyl chloride is generated using NCS and left to stir for 1 h prior to addition of morpholine, only traces of the desired sulfonamide **13a** was observed (**Scheme 2.36**). This allowed us to conclude that the sulfonyl chloride decomposes in the reaction mixture, which results in poorer yields with less-nucleophilic amines where addition to the sulfonyl chloride is slower.



Scheme 2.36. Delayed addition of morpholine to sulfonyl chloride to give sulfonamide **13a**.

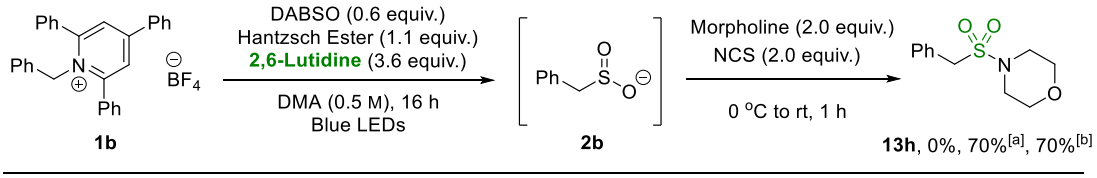
In order to address this, we opted to intercept the sulfonyl chloride with HOBt, as we expected that the product HOBt sulfonate ester **14** would be more robust under the reaction conditions, but could still be reacted with amine nucleophiles to give the desired sulfonamide products.[177] Pleasingly, we found that if HOBt was added and left to deprotonate for 30 mins, and then NCS was added, good conversion to the sulfonate ester was observed. Subsequent addition of the amine and pyridine then gave the sulfonamide products (**Table 2.24**). Using this procedure, benzylamine could be reacted with the HOBt sulfonate ester for 3 h to give an improved yield of 75% of sulfonamide **13e**. Addition of a pre-stirred solution of L-Alanine methyl ester hydrochloride with DIPEA to the sulfonate ester gave the corresponding sulfonamide **13f** in 73% yield and 98% ee after 40 h reaction. Finally, *p*-anisidine could also be used, giving sulfonamide **13g** in 73% yield after 24 h.



[a] From stirred solution of amine HCl salt (2.0 equiv.) with DIPEA (2.0 equiv.) in 0.2 mL DMA

Table 2.24. One-pot preparation of sulfonamides via oxidative chlorination.

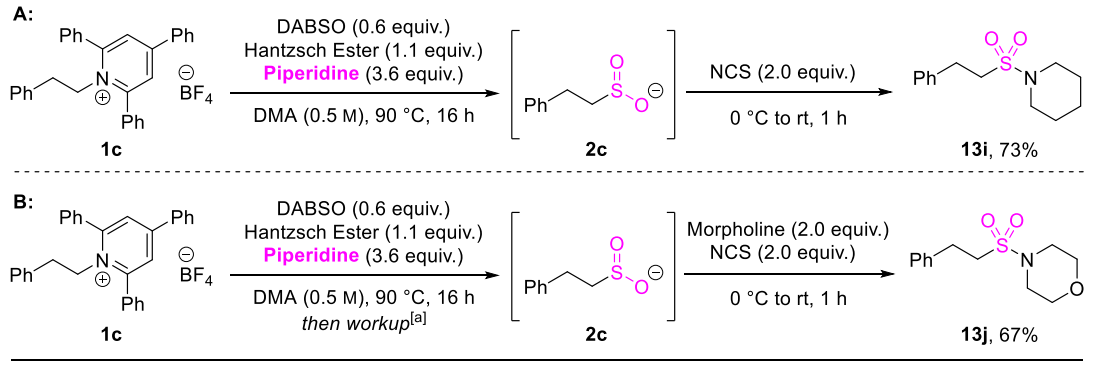
Addition of NCS and morpholine to the reaction mixture from benzyl Katritzky salt **1b** failed to give the desired sulfonamide **13h**, which may be due to side-reactions of the sulfonyl chloride with 2,6-lutidine (**Scheme 2.37**). Again removing 2,6-lutidine using an acid workup prior to addition of NCS and morpholine resulted in the formation sulfonamide **13h** in 70% yield. Alternatively, sodium metabisulfite can be used instead of DABSO and 2,6-lutidine, which enabled the preparation of sulfonamide **13h** in 70% yield without workup in a one-pot procedure.



[a] After step 1: acidify using 2 M aq. H_3PO_4, extract using CH_2Cl_2 × 3, combine organic phases and add DIPEA.
[b] $Na_2S_2O_5$ instead of DABSO, no 2,6-lutidine

Scheme 2.37. Synthesis of sulfonamides from benzylic substrates.

Addition of NCS to the reaction mixture from primary Katritzky salt **1c** gave sulfonamide **13i**, from reaction of piperidine with the sulfonyl chloride, in 73% yield. To enable the formation of other sulfonamides, piperidine was removed using an acid workup prior to addition of NCS and amine (**Scheme 2.38**). Using this procedure, sulfonamide **13j** was isolated in 67% yield.

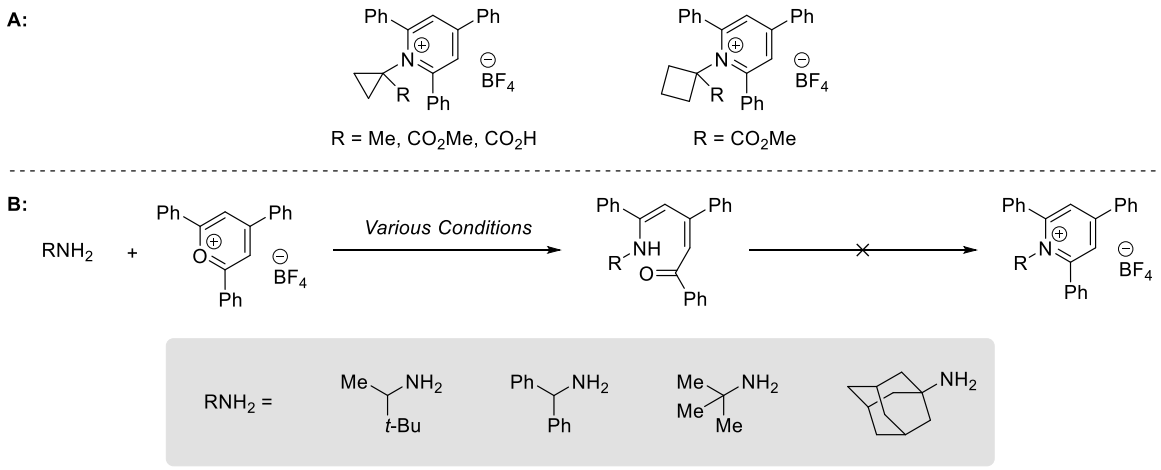


[a] After step 1: acidify using 2 M aq. H_3PO_4, extract using CH_2Cl_2 × 3, combine organic phases and add DIPEA.

Scheme 2.38. A: Synthesis of sulfonamides from primary substrates using piperidine. **B:** Synthesis of sulfonamides from primary substrates using other amines with acid workup.

2.3 Katritzky Salts from Sterically Hindered Amines

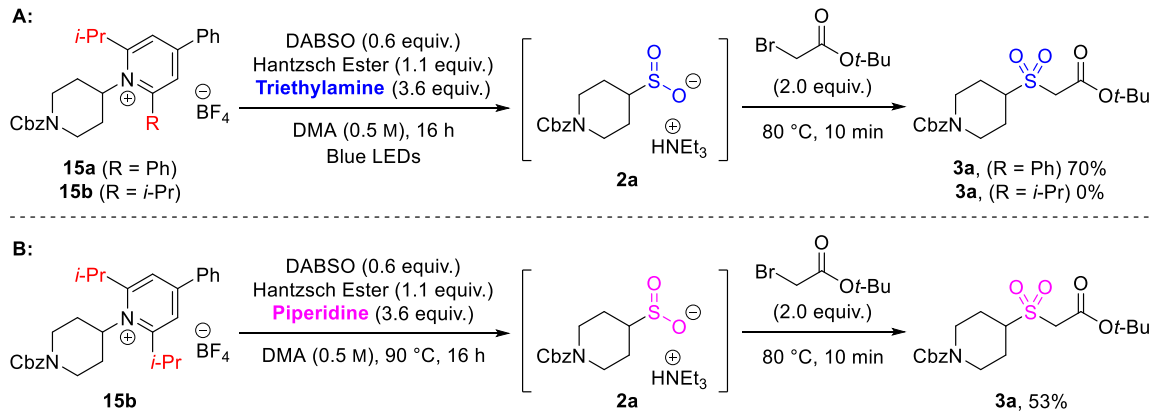
One limitation in the use of Katritzky salts as radical precursors is that it cannot be used for sterically-hindered substrates. There are very few examples of the preparation of Katritzky salts derived from α-tertiary amines, which are almost exclusively derived from cyclopropyl or cyclobutyl amines (**Scheme 2.39.A**).[155m, 168, 169d, 178] We attempted to prepare several Katritzky salts derived from a selection of tertiary amines and sterically-demanding α-secondary amines, but observed either no reaction or the formation of the ring-opened Zincke aldehyde-type intermediates (**Scheme 2.39.B**).



Scheme 2.39. A): Literature examples of Katritzky salts derived from α-tertiary amines. **B):** Attempted preparation of hindered Katritzky salts.

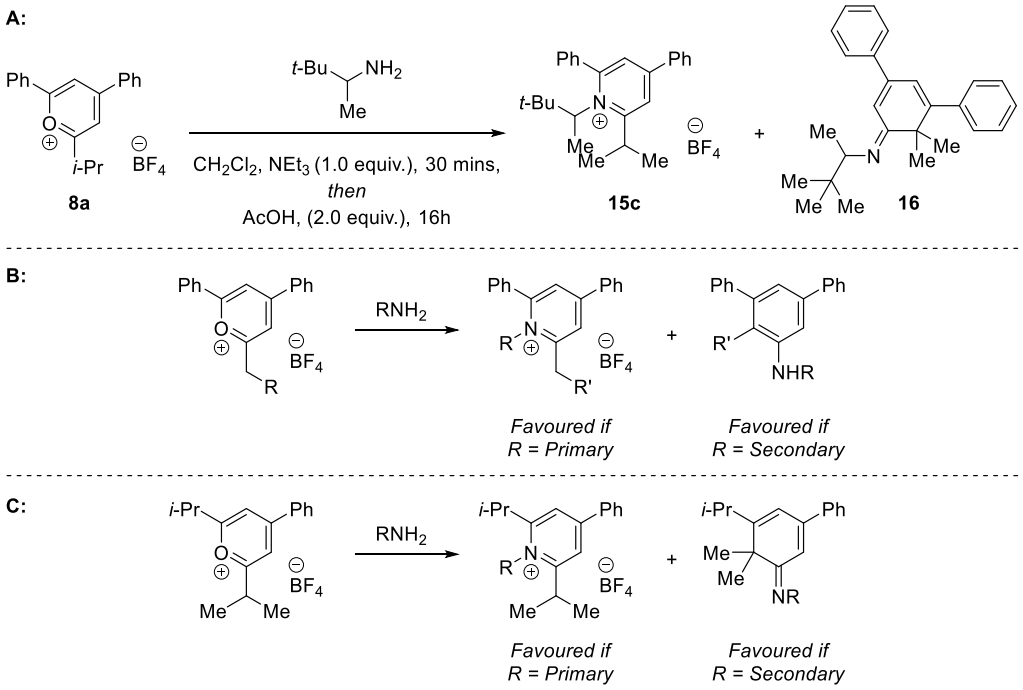
Having determined that the 2,4,6-triphenyl substitution pattern could be modified whilst preserving reactivity, we envisaged that we could prepare Katritzky salts from hindered amines if less sterically-demanding substituents could be used in the 2- and 6- positions whilst maintaining reactivity.

We initiated these studies by preparing the 2-isopropyl and 2,6-diisopropyl analogues of our optimum substrate **1a** to study their reactivity. We found that the mono-isopropyl Katritzky salt **15a** gave the sulfone product **3a** in 70% yield using standard conditions, whereas the di-isopropyl analogue **15b** showed no conversion and gave 0% yield of the sulfone product (**Scheme 2.40.A**). However, applying the conditions optimised for primary alkyl substrates to the di-isopropyl analogue **15b** gave 53% yield of the sulfone product **3a** (**Scheme 2.40.B**).



Scheme 2.40. A): Reactivity of mono- and di-isopropyl Katritzky salts **15a** and **15b** using standard conditions. **B):** Reactivity of di-isopropyl Katritzky salt **15b** in conditions used for primary alkyl substrates.

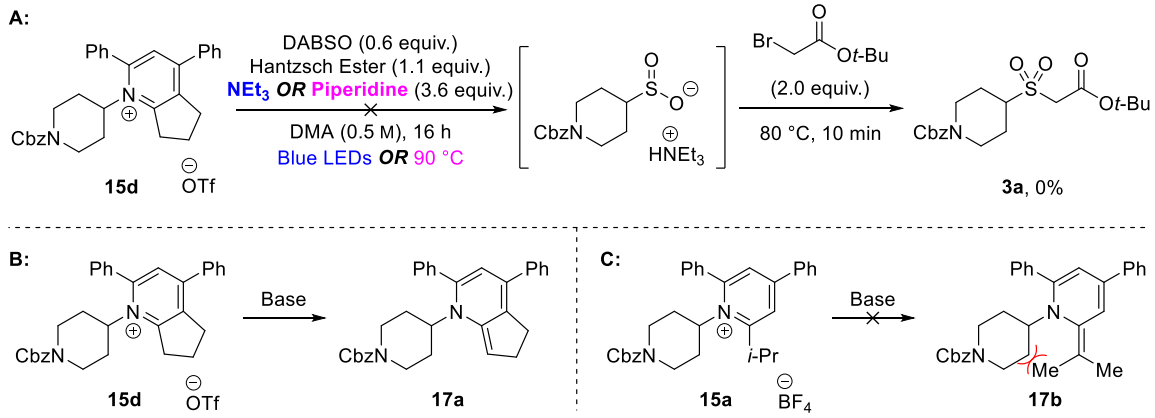
Having established the reactivity of these Katritzky salt analogues, we attempted to prepare the mono-isopropyl Katritzky salt **15c** using 3,3-dimethyl-2-butylamine. We were surprised to find that the expected Katritzky salt was not found, but instead peaks consistent with a different cyclisation product **16** were observed (**Scheme 2.41.A**). The reaction of pyrylium salts with primary-alkyl substituents in the 2- or 6- position can often form the aniline product from reaction with more-hindered primary amines, with the formation of a benzene ring as a driving force (**Scheme 2.42.B**),[179] but similar cyclisations have also been observed for 2,6-diisopropyl Katritzky salts with more-hindered amines, despite the formation of non-aromatic products (**Scheme 2.43.C**).[180]



Scheme 2.43. A): Observed reactivity of pyrylium salt **8a** with 3,3-dimethyl-2-butylamine. **B):** Formation of anilines from 2-alkyl pyrylium salts. **C):** Formation of dienes from 2-isopropyl Katritzky salts.

We therefore needed to consider substrates that would be less-hindered, but also have a higher barrier to cyclisation, which we expected we could achieve using bicyclic Katritzky salts. We prepared Katritzky salt **15d** to explore its reactivity, but observed no reaction upon applying our optimised reaction conditions using triethylamine using blue LEDs or piperidine at 90 °C (**Scheme 2.44.A**). This observed lack of reactivity may be due to deprotonation of the α-proton under the reaction conditions to give anhydrobase **17a**, which has been observed by Katritzky and co-workers (**Scheme**

2.44.B).[181] This isn't observed for 2-isopropyl substrates due to steric hinderance between the *N*-substituent and one of the methyl groups when planar (**Scheme 2.44.C**).[174]



Scheme 2.44. A): Reactivity of bicyclic Katritzky salt **15d B):** Formation of anhydrobase **17a** from Katitzky salt **15d**. **C):** Hindered formation of anhydrobase **17b** from Katitzky salt **15a**.

With the availability of other radical methods for the synthesis of alkyl sulfinates which were compatible with hindered substrates, alongside the increasingly lengthy preparations of the pyrylium salts and cost of starting materials, further studies towards the preparation of Katritzky salts derived from hindered amines were not carried out.

2.4 Reaction with TrNSO

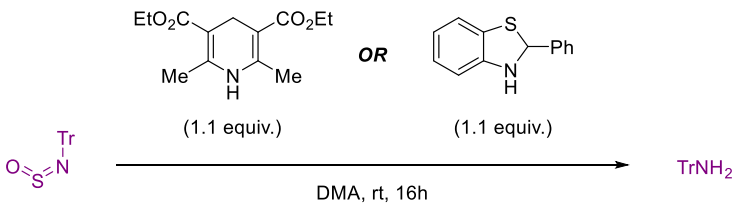
Given that alkyl radicals are also known to react with sulfinylamines,[100] we wished to determine whether our optimised reaction conditions could be used with TrNSO to give sulfinamide **18**. To our surprise, none of the desired sulfinamide product was obtained, and complete hydrolysis of TrNSO was observed (**Scheme 2.45**).



Scheme 2.45. Attempted synthesis of sulfinamide **18** from Katritzky salt **1a** using TrNSO.

Further studies showed that stirring TrNSO and Hantzsch ester for 16 h also resulted in complete conversion to trityl amine, whereas minimal hydrolysis was observed when stirring with other

components of the reaction mixture. The same result was observed using 2-phenyl-2,3-dihydrobenzo[*d*]thiazole, which we found could be used instead of Hantzsch ester in our previous conditions to prepare sufinates from Katritzky salts (**Scheme 2.46**).



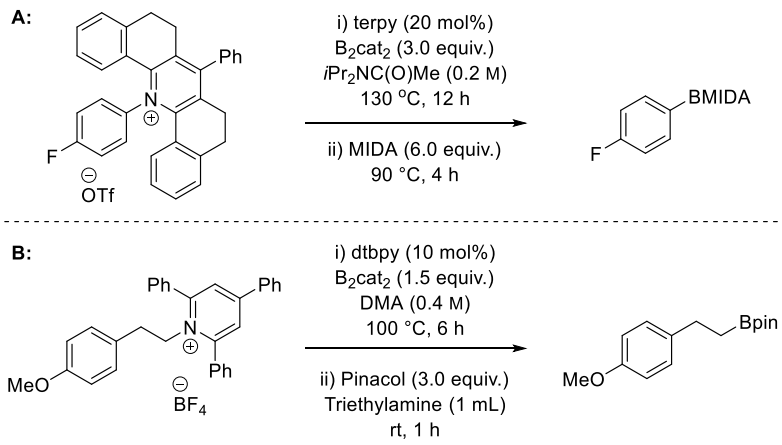
Scheme 2.46. Observed formation of tritylamime from TrNSO.

These studies showed that this methodology is unlikely to be compatible with sulfinylamines due to their poor stability in the presence of hydrogen atom donors. Other methods of radical generation would be needed to enable this transformation, an example of which is discussed in **Chapter 3**.

2.5 *N*-Aryl Katritzky Salts

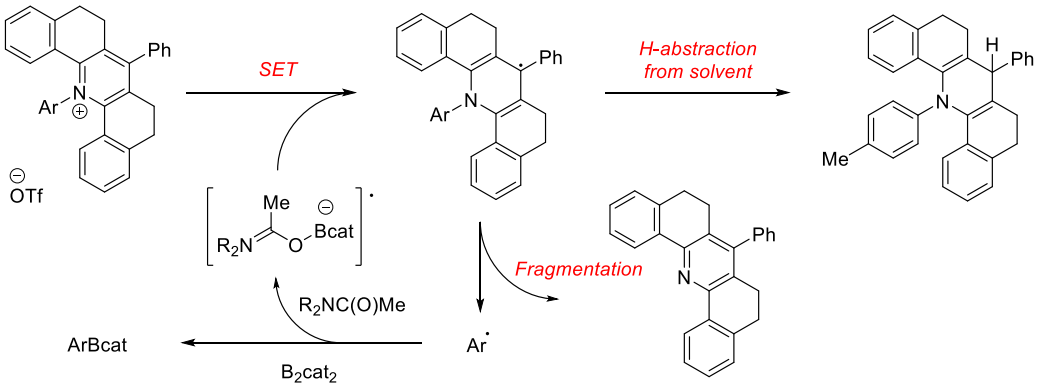
We also proposed that another extension of this work would be its application to the generation of aryl sulfinates from *N*-aryl pyridinium via the formation of aryl radicals. This would provide an alternative to methods using aryl bromides or boronic acids for the synthesis of aryl sulfinates.

Following several methods using *N*-alkyl Katritzky salts to prepare boronic esters,[167-168] Cornella and co-workers showed that pentacyclic *N*-aryl Katritzky salts can be used to analogously prepare arylboronic esters (**Scheme 2.47.A**).[171] The conditions used and proposed mechanism are similar to those developed by Shi and co-workers (**Scheme 2.47.B**).[168]



Scheme 2.47. A): Deaminative synthesis of arylboronic esters by Cornella and co-workers. **B):** Deaminative synthesis of alkylboronic esters by Shi and co-workers.

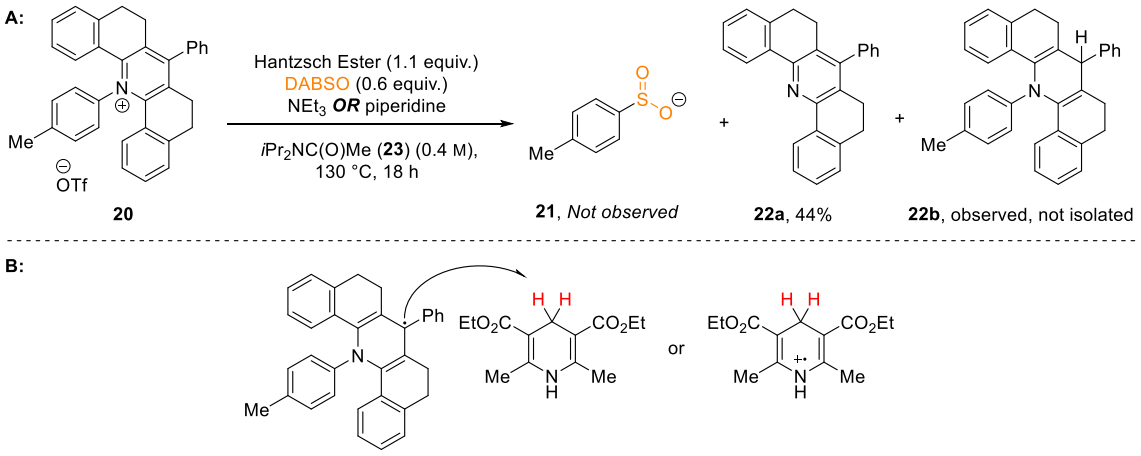
These methods rely upon thermally-induced SET from complexes of B_2cat_2, and then fragmentation generates the aryl radicals, which then react with further B_2cat_2 to give the boronic ester (**Scheme 2.48**). The pentacyclic Katritzky salts used by Cornella and co-workers are essential to give good yields, as the ethylene groups constrain the structure resulting in a relatively strained pyridine ring. Liberation of the aryl radical from the dihydropyridine radical results in the formation of a thermodynamically more stable pyridine by-product, acting as the driving force.[171] Cornella observed that the dihydropyridine radical can abstract a proton from the solvent if DMA is used, but found that the use of the more-hindered *N*,*N*-diisopropylacetamide **23** hinders this process.



Scheme 2.48. Proposed mechanism for the deaminative borylation of *N*-aryl Katritzky salts.

We applied modified conditions based on our previous work to the pentacyclic Katritzky salt **20** using Hantzsch Ester and a base. None of the desired sulfinate **21** was observed, but the

consumption of Katritzky salt **20** and the generation of pyridine **22a** in 44% yield indicated that the desired aryl radicals were being generated (**Scheme 2.49.A**). Furthermore, peaks consistent with dihydropyridine side-product **22b** were observed, despite using *N*,*N*-diisopropylacetamide **23** as the solvent. The formation of this side-product in our reaction indicated that the dihydropyridine radical was abstracting protons from another source, such as Hantzsch ester (**Scheme 2.49.B**).



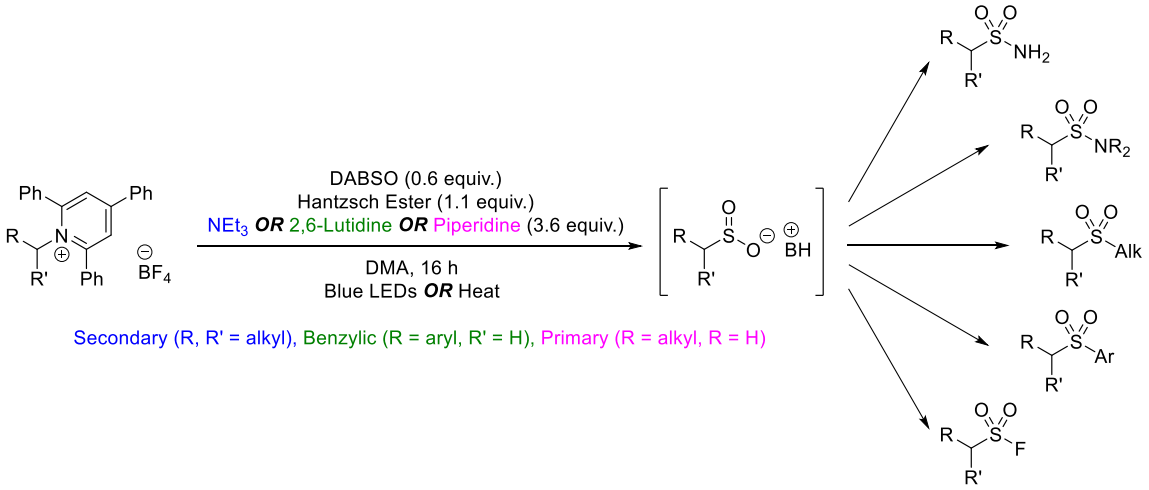
Scheme 2.49. A): Attempted deaminative synthesis of aryl sulfinate **21**. **B):** HAT from Hantzsch ester or its radical cation to dihydropyridine radical.

Various alternative reaction conditions were tried, such as various bases, solvents, and SO_2 surrogates, but none of the desired product and the same side-products were observed in all cases. Substituting Hantzsch ester for other single-electron donors, such as dihydrobenzothiazoles, dithiocarbonyl compounds,[169c] sodium dithionite,[137a] Zn and Mg, all gave comparable results or no reaction. Following these results, no further studies were carried out using this system.

2.6 Conclusions and Future Work

In conclusion, we have developed a general, scalable synthesis of alkyl sulfinates from primary amines via Katritzky pyridinium salts. We demonstrated the application of this method to the synthesis of a variety of sulfones, sulfonamides and sulfonyl fluorides (>60 examples), and carried

out UV/vis and radical trapping studies to probe the mechanism and explain the observations made during the optimisation of the reaction (**Scheme 2.50**).



Scheme 2.50. Deaminative synthesis of sulfinates and their derivatives.

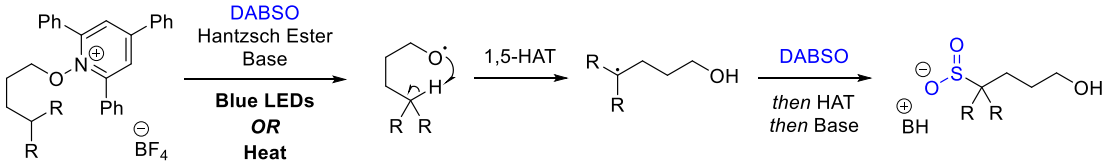
We explored the synthesis of a selection of less-sterically congested pyrylium salts with the goal of preparing Katritzky salts with more-hindered amines for use in our reaction. Undesired reactivity of these substrates and increasingly laborious synthesis of desired targets resulted in the proposed reactions being less-favourable than alternative methods of radical generation.

We attempted to apply the optimised reaction conditions to sulfinylamine reagents, but found the sulfinylamines to be unstable under the reaction conditions, so alternative methods would be needed for this transformation to take place.

Finally, we carried out preliminary investigations on pentacyclic Katritzky salts that have been shown to generate aryl radicals, with the goal of developing conditions to prepare aryl sulfinate salts. Unfortunately, whilst aryl radical generation was observed, the desired products were not observed due to competing side-reactions.

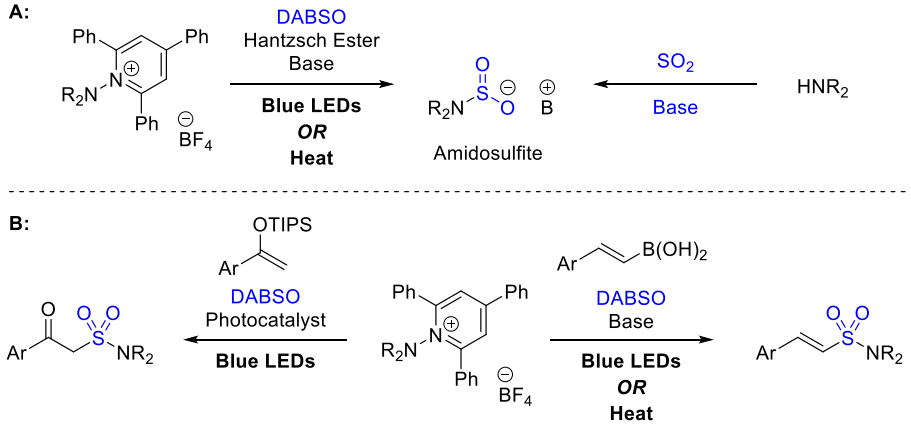
Future work could focus on further applications of Katritzky salts for the synthesis of sulfinates. For example, *N*-alkoxy Katritzky salts can be used to generate *O*-centred radicals, which can then undergo 1,5-HAT to give more-stable alkyl radicals.[182] This process could be combined with radical addition

to SO_2 to give complex sulfinate products, as well as a route towards tertiary alkyl sulfinates (**Scheme 2.51**).



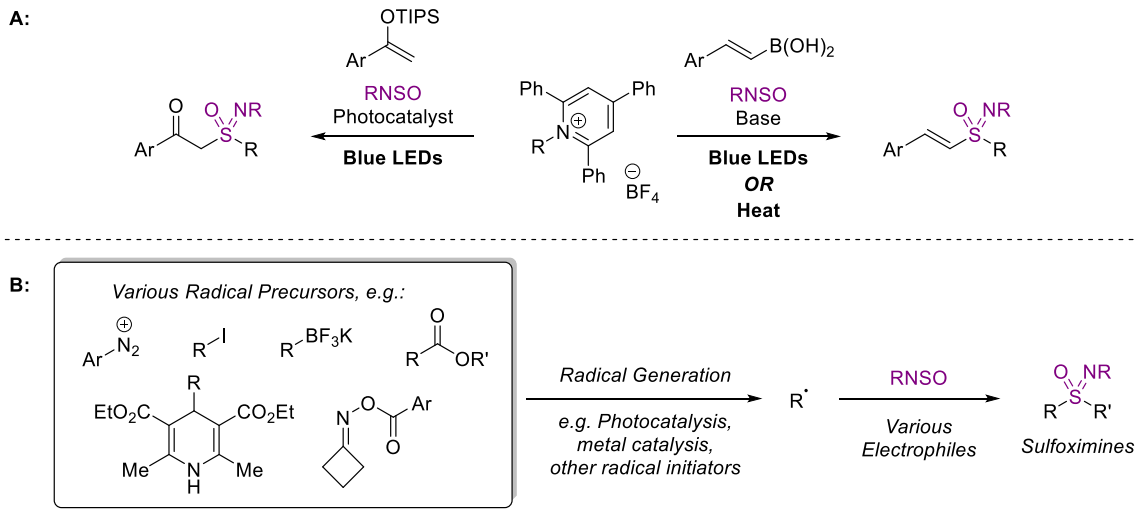
Scheme 2.51. Proposed synthesis of tertiary alkyl sulfinates from *N*-alkoxy Katritzky salts via 1,5-HAT.

N-Centred radicals can also be generated from *N*-amino Katritzky salts, and these radicals have been used in reactions with various electrophiles as well as in nickel-catalysed couplings.[183] Use of these reagents in our previous conditions could be used to prepare amidosulfites, but these reagents can also be simply prepared from reaction of secondary amines with SO_2 (**Scheme 2.52.A**).[184] *N*-alkyl Katritzky salts could instead be used in methods such as that developed by Wu and co-workers to prepare sulfonamides from silyl enol ethers or vinylboronic acids (**Scheme 2.52.B**).[162-163]



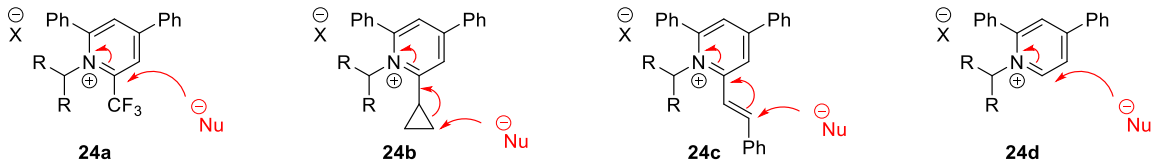
Scheme 2.52. A) Proposed synthesis of amidosulfites from *N*-amino Katritzky salts. **B)** Proposed synthesis of sulfonamides from *N*-amino Katritzky salts.

Whilst sulfinylamines were incompatible with radical generation using Hantzsch ester, other radical generation methods may be compatible, and as a result, application of methods such as those developed by Wu and co-workers could again be used here, in this case to prepare sulfoximine products (**Scheme 2.53.A**).[58a] Similarly, methods using other radical precursors to generate sulfonyl derivatives via radical addition to SO_2 could be modified for use with sulfinylamines, enabling access to various sulfoximine products (**Scheme 2.53.B**).[46, 58]



Scheme 2.53. A) Proposed synthesis of sulfoximines from Katritzky salts and sulfinylamines. **B)** Proposed synthesis of sulfoxides from various radical precursors and sulfinylamines.

Whilst other methods are available for the preparation of sulfinates with hindered alkyl substituents,[140, 143c] the preparation of Katritzky salts using hindered amines may be useful in other methodologies. For these studies, further examples of Katritzky salts that are less-hindered and unable to form the anydrobase or aniline side-products need to be explored. Some examples that could be considered include 2-trifluoromethyl (**24a**), 2-cyclopropyl (**24b**), 2-styryl (**24c**) and 2-unsubstituted (**24d**) Katritzky salts (**Scheme 2.54**). These Katritzky salts may be more reactive with nucleophiles due to increased electrophilicity (**24a**), or the availability of less-hindered electrophilic sites (**24b**, **24c** and **24d**), which may impact their preparation and use.



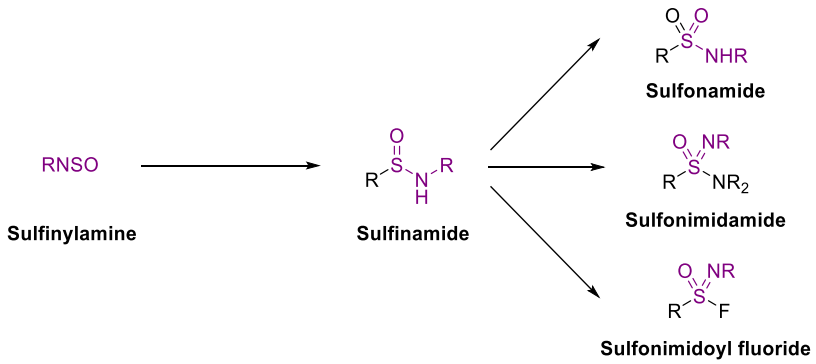
Scheme 2.54. Proposed Katritzky salts and their reactivity with nucleophiles.

Chapter 3 - Preparation of Sulfinamides using Carboxylic Acids as Radical Precursors

3.1 Introduction

3.1.1 Radical Addition to Sulfinylamines

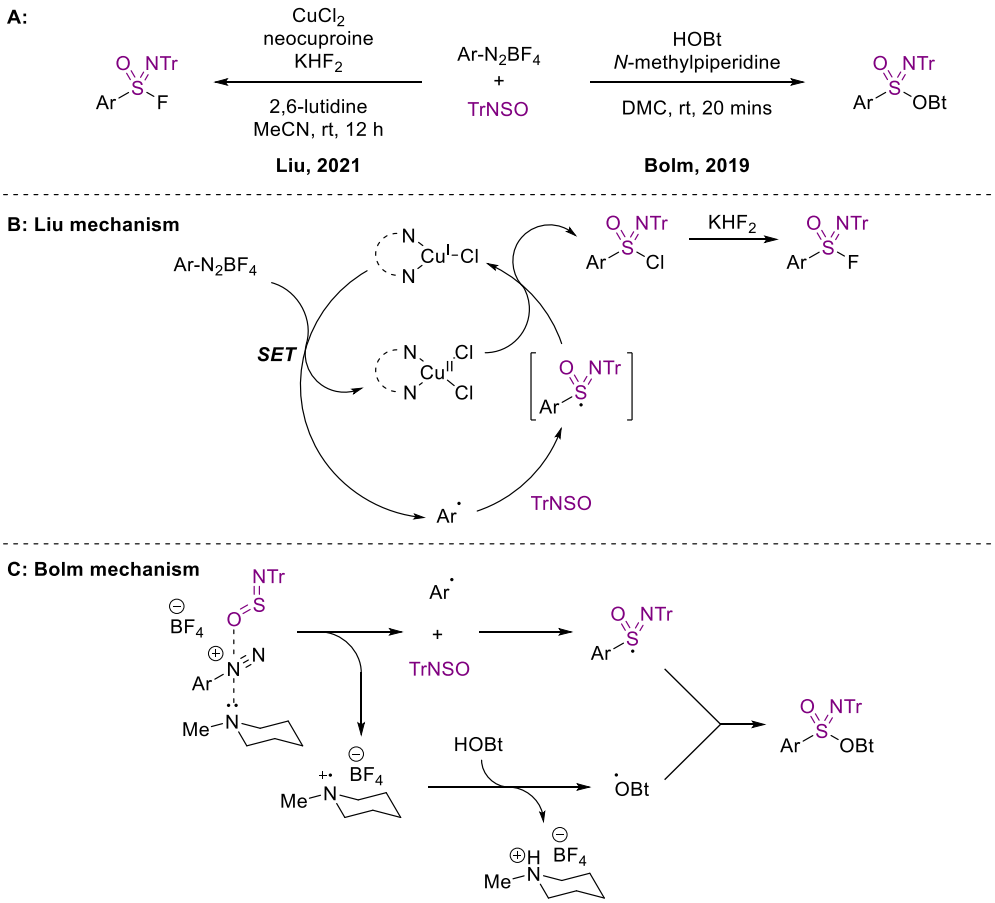
Sulfinamides, the mono-aza analogues of sulfinic acids, have useful applications in the preparation of aza-sulfur products. Analogously to preparations of sulfinates from SO_2, sulfinylamines can be used for the preparation of sulfinamides (**Scheme 3.1**).



Scheme 3.1. Preparation of sulfinamides and their derivatives using sulfinylamines.

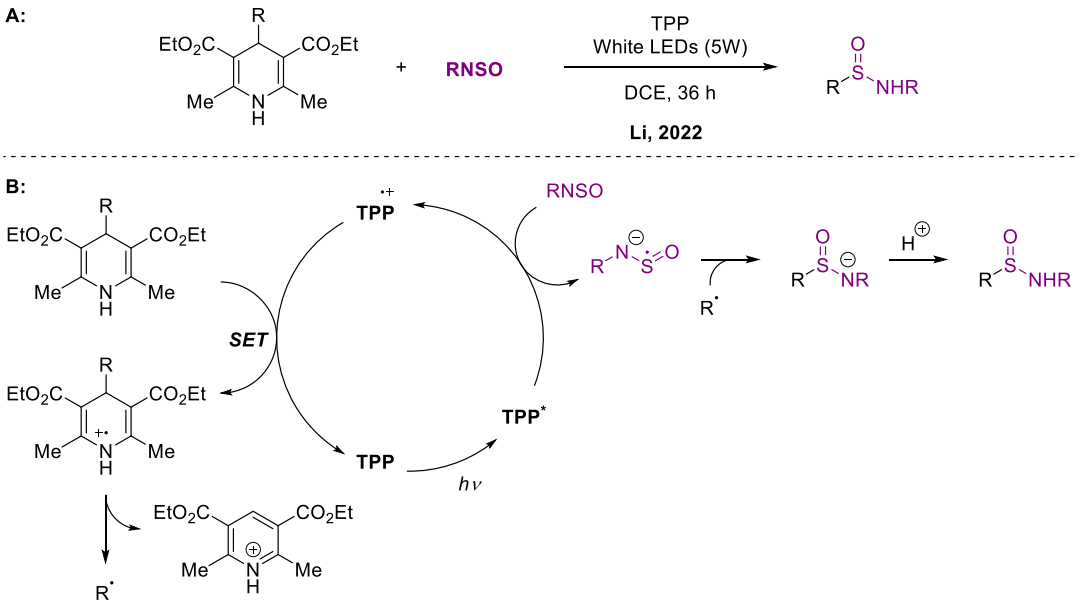
Reactions of organometallic reagents or metal-catalysed couplings of boronic acids with sulfinylamines has been used to prepare sulfinamides from sulfinylamines, but the versatility of these reactions, particularly for the synthesis of alkyl variants, is limited.[73] We proposed that the addition of alkyl radicals to sulfinylamines could provide a more versatile method for the preparation of alkyl sulfinamides.

Radical addition to sulfinylamines has been demonstrated in a few cases. Aryl radicals derived from aryldiazonium salts were used by Liu and Bolm, giving sulfonimidoyl fluoride or sulfonimidate esters, respectively, via radical addition to TrNSO and subsequent trapping of the forming sulfonimidoyl radical (**Scheme 3.2**).[99]



Scheme 3.2. A): Reactions of aryldiazonium salts with TrNSO. **B):** Mechanism of sulfonimidoyl fluoride synthesis. **C):** Mechanism of HOBt sulfonimidate ester synthesis.

To prepare alkyl sulfinamides via radical methods, Zhao and Li demonstrated that 4-substituted Hantzsch ester radical precursors can be used (**Scheme 3.3.A**).[100] This reaction is proposed to proceed via oxidative quenching of a singlet-excited TPP photocatalyst to give a sulfinylamine radical anion from a sulfinylamine. The oxidised TPP then undergoes SET with the Hantzsch ester to give a radical cation, which then liberates an alkyl radical. Reaction of the alkyl radical with the sulfinylamine radical anion then gives a sulfinamide anion which is protonated under the reaction conditions (**Scheme 3.3.B**). Whilst this method succeeds in preparing alkyl sulfinamides from sulfinylamines via a radical method, the reaction uses only a limited selection of Hantzsch ester substrates, and few functional groups are shown to be compatible with the reaction, indicating either poor functional group tolerance or demonstrating the limited availability of the Hantzsch esters or aldehydes from which they are prepared.



Scheme 3.3. A): Preparation of sulfinamides from substituted 4-Hantzsch esters. **B):** Proposed mechanism.

With the demonstrated use of alkyl radical generation to prepare sulfinamides from sulfinylamines, we wished to develop a more general and functional group-tolerant procedure for the synthesis of sulfinamides. Ideally, we wanted to achieve this using radical precursors that have good commercial availability and broad structural diversity.

Whilst Katritzky salts, derived from widely available primary amines, would fulfil the desired criteria, previously-optimised deaminative reaction conditions were incompatible with sulfinylamines, giving hydrolysed sulfinylamines under the reaction conditions (**Scheme 3.4**).

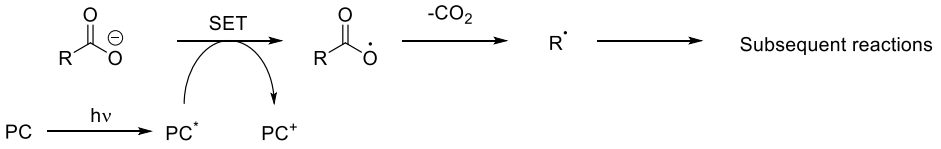


Scheme 3.4. Attempted synthesis of sulfinamide **18** from Katritzky salt **1a** using TrNSO.

3.1.2 Carboxylic Acids as Radical Precursors

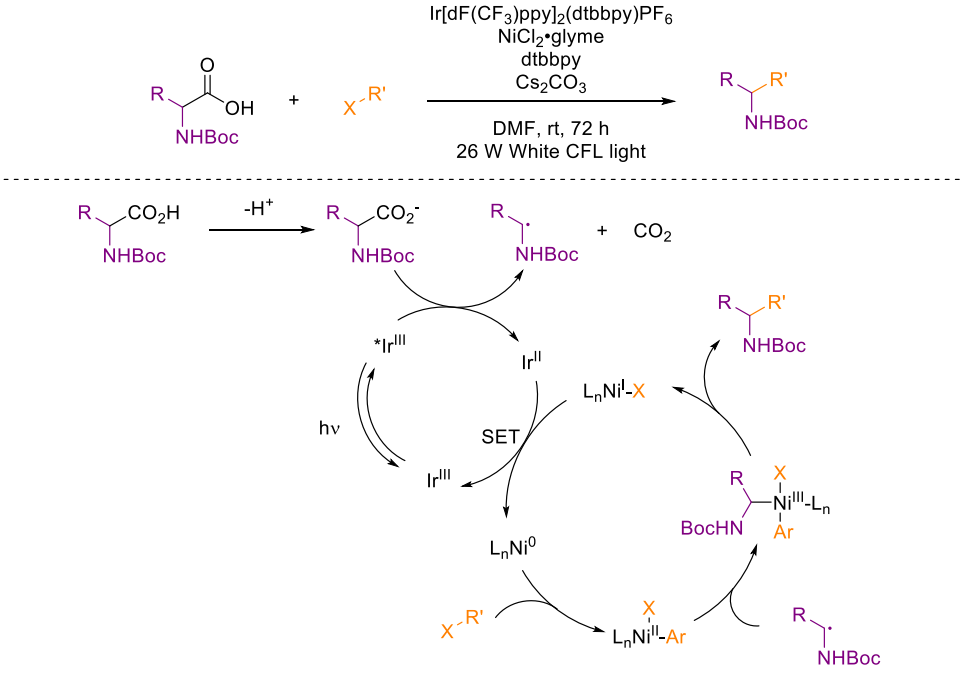
An alternative family of radical precursors that have excellent commercially availability and can also be used without prior activation are carboxylic acids.[185] Radical generation from carboxylic acids usually operates via single-electron oxidation of a carboxylate anion, often via reductive quenching of a singlet-excited photocatalyst (often using acridinium, iridium or ruthenium photocatalysts)[186]

to form a carboxy radical. Loss of CO_2 then gives an alkyl radical that can be used in subsequent reactions (**Scheme 3.5**).[187]



Scheme 3.5. Radical generation by decarboxylation.

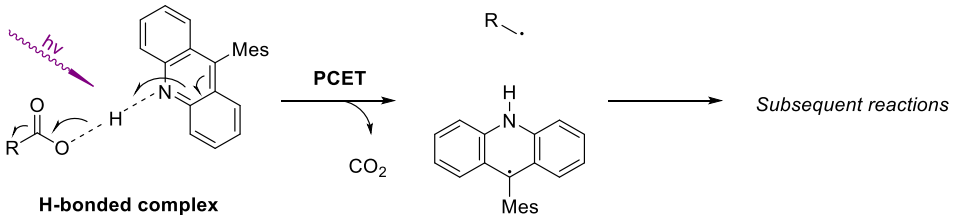
The application of this chemistry can be exemplified by work from MacMillan and co-workers, wherein radicals derived from photocatalysed decarboxylation are intercepted by a nickel co-catalyst, enabling a C(sp^2)-C(sp^3) cross-coupling with aryl bromides (**Scheme 3.6**).[187b]



Scheme 3.6. Decarboxylative nickel/photoredox catalysed C(sp^2)-C(sp^3) cross-coupling.

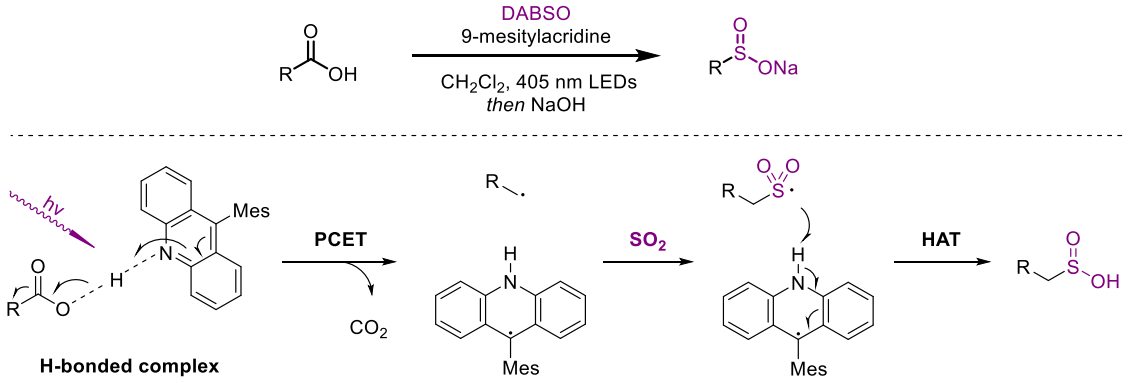
Whilst many powerful methods have been developed using this catalytic platform, there are some limitations. Most importantly, these reactions usually work best when generating relatively-stable α-amino, α-oxo or benzylic radicals.[185] Some methods can also be applied to the preparation of unstabilised secondary alkyl radicals, but methods that can be used for the preparation of unstabilised primary alkyl radicals are scarce, and yields are often moderate in these cases,[188] although in-situ pre-activation has been used to address these issues in some cases.[189]

An alternative approach for the generation of alkyl radicals, initially developed by Oda and co-workers, is the use of acridine photocatalysts.[190] Whilst higher loading of these photocatalysts is often needed,[191] they have proven to be effective at preparing alkyl radicals, including unstabilised primary alkyl radicals, using mild conditions, enabling the use of broadly available and diversely functionalised carboxylic acids. Radical generation using these photocatalysts is mechanistically distinct, and deprotonation of the carboxylic acid is not needed. Instead, radicals are generated via the formation of a photoactive H-bonded complex between the acridine and the carboxylic acid, which absorbs visible light, and the singlet-excited H-bonded complex then undergoes proton-coupled electron transfer (PCET) and decarboxylation to give the alkyl radical (**Scheme 3.7**).[190a]



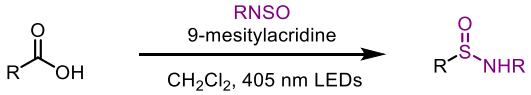
Scheme 3.7. Radical generation using acridine photocatalysts.

This catalytic regime has been used in several methodologies,[142, 192] and crucially for our proposed studies, Larionov and co-workers applied acridine photocatalysts in a preparation of sulfinates from carboxylic acids.[143c] In this method, radical addition to SO_2 and subsequent HAT gives sulfinic acids, which can then be deprotonated in a second step using a base to give a sulfinate salt product (**Scheme 3.8**). This methodology shows good steric and functional group tolerance, can be used for primary, secondary and tertiary carboxylic acids, and various one-pot derivatisations were demonstrated for the preparation of various sulfonyl derivatives.[143]



Scheme 3.8. Synthesis of sulfinates from carboxylic acids using acridine photocatalysts.

We proposed that given the demonstrated use of acridine catalysts to make sulfinic acids from carboxylic acids under mild conditions, as well as the known reactivity of sulfinylamines with radicals,[99-100] we could develop a related method for the preparation of sulfinamides (**Scheme 3.9**).

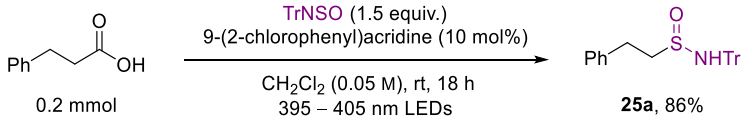


Scheme 3.9. Synthesis of sulfinates from carboxylic acids using acridine photocatalysts.

3.2 Results and Discussion

3.2.1 Previous Work

Dr Jagadeesh Kalepu (a former post-doc in the group) demonstrated that the proposed reaction was feasible, using hydrocinnamic acid, TrNSO and 9-(2-chlorophenyl)acridine **(PC1)** in dichloromethane with irradiation by 395 – 405 nm LEDs to give the desired sulfinamide product **25a** in 86% yield (**Scheme 3.10**).

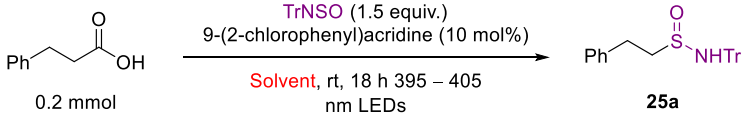


Scheme 3.10. Preparation of sulfinamide **25a** via decarboxylative radical addition to TrNSO.

Dr Kalepu further optimised the reaction, and the key findings can be found in **Table 3.1**, **Table 3.2** and **Table 3.3**. Reaction concentration was first varied, where it was found that more concentrated reactions gave lower yields, whereas less-concentrated reactions gave comparable yields to those

obtained at 0.05 M (**Table 3.1, entries 1 – 5**). Alternative solvents could also be used in the reaction to give good yields, but dichloromethane remained the optimum solvent (**Table 3.1, entries 6 – 11**). Some solvents were found to be incompatible with the reaction showing no conversion and 0% yield, which we reasoned was due to the formation of an acridinium carboxylate salt rather than the catalytically active H-bonded complex (**Table 3.1, entries 12 – 15**).

Table 3.1. Optimisation of solvent and concentration. All entries performed by Dr Jagadeesh Kalepu.



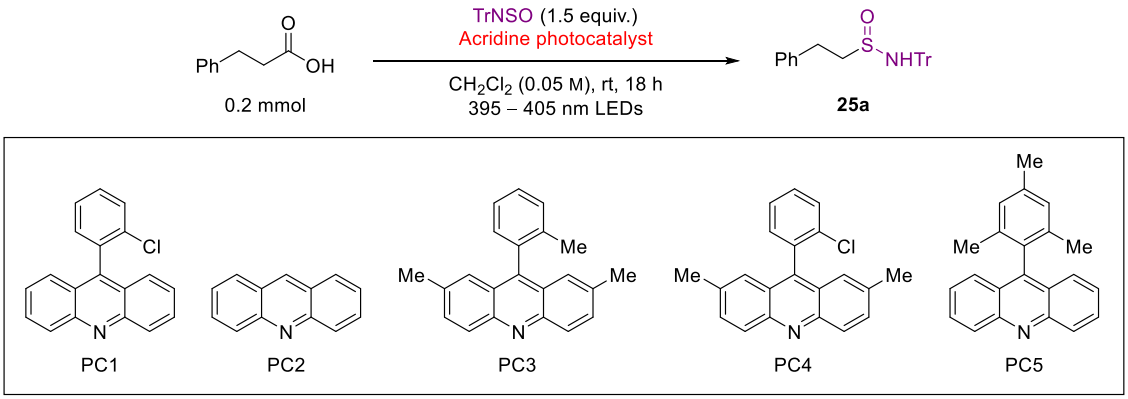
Entry	Solvent	Solvent Volume (mL)	Concentration ($moldm^{-3}$)	Yield
1	CH_2Cl_2	1.0	0.2	63%
2	CH_2Cl_2	2.0	0.1	67%
3	**CH_2Cl_2**	**4.0**	**0.05**	**86%**
4	CH_2Cl_2	6.0	0.033	85%
5	CH_2Cl_2	8.0	0.025	83%
6	1,2-Dichloroethane	4.0	0.05	79%
7	$CHCl_3$	4.0	0.05	48%
8	α,α,α-Trifluorotoluene	4.0	0.05	65%
9	Acetone	4.0	0.05	58%
10	Acetonitrile	4.0	0.05	62%
11	Cyclohexane	4.0	0.05	32%
12	DMF	4.0	0.05	0%
13	DMSO	4.0	0.05	0%
14	EtOH	4.0	0.05	0%
15	THF	4.0	0.05	0%

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

Photocatalyst loading was then explored. Using 5 mol% catalyst gave incomplete conversion and a lower 51% yield (**Table 3.2, entry 1**), whereas increasing the loading to 20 mol% gave a small increase to 93% yield (**Table 3.2, entry 3**). We also explored alternative photocatalysts, although examples including photocatalysts (**PC2 – 4**) gave a lower yield than **PC1** at 10 mol% (**Table 3.2, entries 4 – 6**). The more-hindered 9-mesitylacridine (**PC5**) gave an improved yield of 98%, meaning catalyst loading could be kept at 10 mol% (**Table 3.2, entry 7**). These studies are consistent with observations by Larionov,[143a] as well as studies by Dilman demonstrating that whilst many of these

acridine photocatalysts have relatively-low turnover numbers, this is improved somewhat by the inclusion of sterically-hindered substituents in the 9-position of the acridine.[191]

Table 3.2. Optimisation of photocatalyst and photocatalyst loading. All entries performed by Dr Jagadeesh Kalepu.

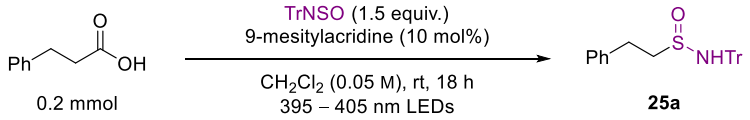


Entry	Photocatalyst	Photocatalst loading (mol%)	Conversion	Yield
1	PC1	5	52%	51%
2	PC1	10	100%	86% (88%)[a]
3	PC1	20	100%	93%
4	PC2	10	70%	50%
5	PC3	10	80%	58%
6	PC4	10	100%	70%
7	**PC5**	**10**	**100%**	**98% (96%)[a]**

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard. [a]Isolated Yield.

Control reactions were then carried out to study their impact on the yield of sulfinamide **25a** (**Table 3.3**). Removing photocatalyst or light was found to give no reaction (**Table 3.3, entries 2 and 3**). Similarly, removing light but heating the reaction gave no conversion, indicating there isn't a thermal pathway for the reaction (**Table 3.3, entry 4**). Using solvent which had not been dried showed that the presence of water has only a small impact on the yield, giving 83% of sulfinamide **25a** (**Table 3.3, entry 5**). Carrying out the reaction in dry solvent which had been sparged with air showed a substantial drop in conversion to 57% and gave only 29% yield of product. (**Table 3.3, entry 6**). The use of wet solvent under air gave a poor 41% conversion and 16% yield (**Table 3.3, entry 7**). These results demonstrate that the reaction is sensitive to the presence of oxygen.

Table 3.3. Control reactions. All entries performed by Dr Jagadeesh Kalepu.

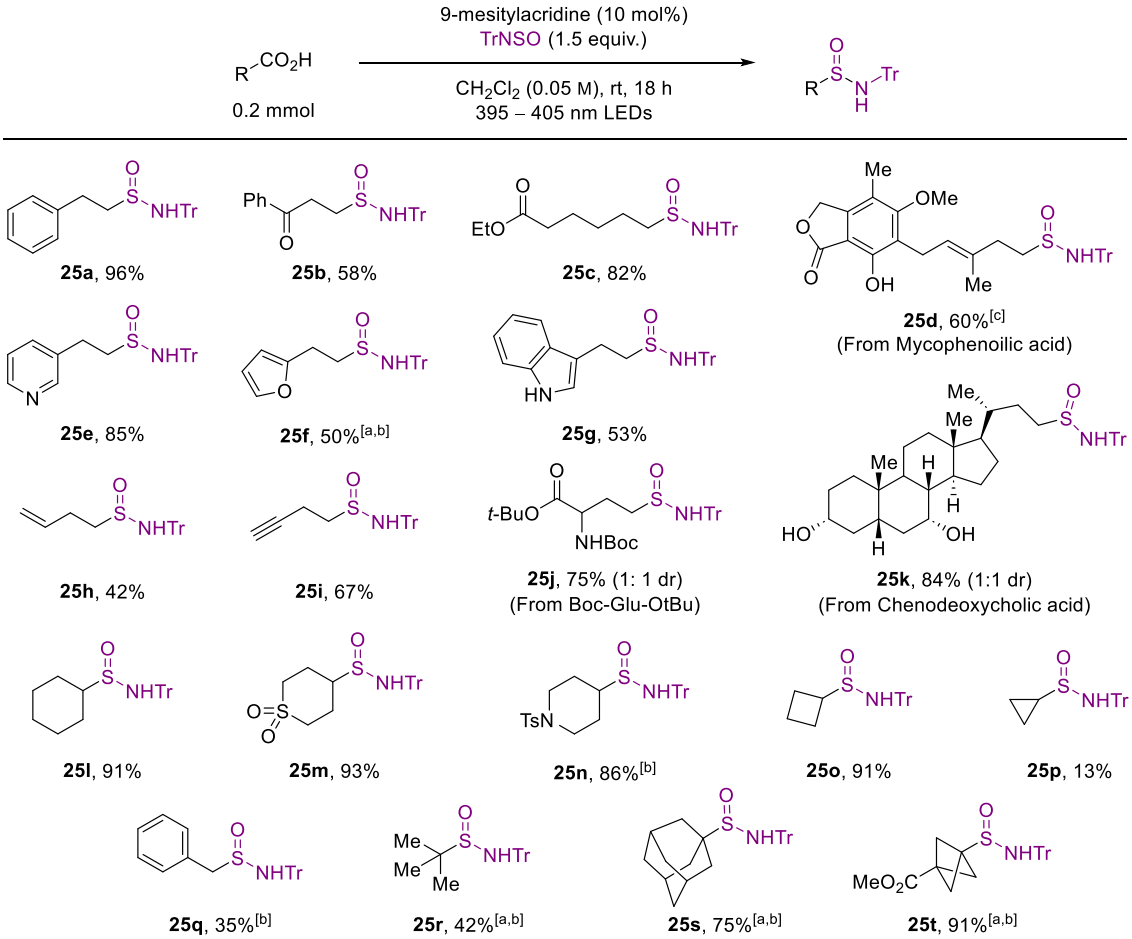


Entry	Modifications	Conversion	Yield
1	**None**	**100%**	**98% (96%)[a]**
2	No photocatalyst	0%	0%
3	No light	0%	0%
4	No light, heat to 40 °C	0%	0%
5	CH_2Cl_2 from bottle, sparged with N_2	100%	83%
6	Dry CH_2Cl_2, solvent sparged with air	57%	29%
7	CH_2Cl_2 from bottle, sparged with air	41%	16%

0.2 mmol scale, yields calculated from HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.
[a]Isolated Yield.

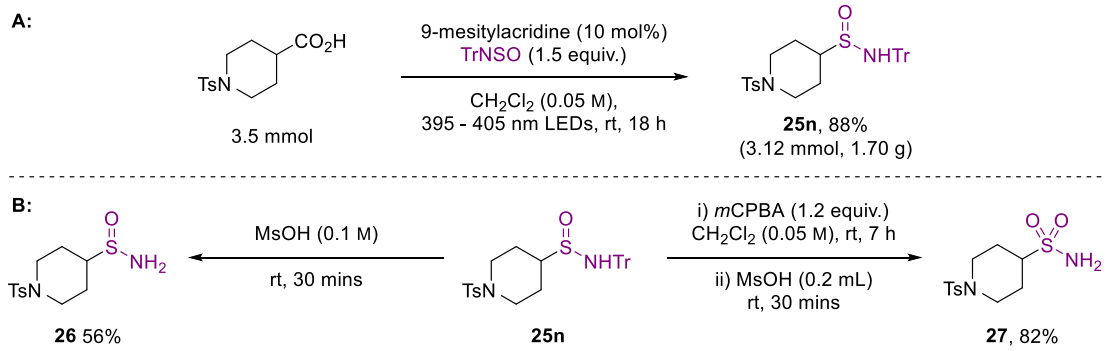
With optimised conditions in hand, Dr Kalepu then assessed the scope of the reaction with respect to the carboxylic acid, representative examples of which are shown in **Table 3.4**. The reaction was found to be broadly functional group-tolerant, with primary alkyl substates containing ketone (**25b**), ester (**25c**), heterocycles (**25e**, **25f** and **25g**), alkene and alkyne (**25h** and **25i**) functional groups all tolerated giving moderate to excellent yields. The application of this method to late-stage functionalisation was also demonstrated through the use of densely-functionalised biologically-active molecules such as amino acid derivative Boc-Glu-O*t*-Bu (**25j**), the drug molecule Mycophenolic acid (**25d**), and the natural product Chenodeoxycholic acid (**25k**), all giving the corresponding sulfinamides in good yields. Secondary alkyl substrates also gave the corresponding sulfinamides in excellent yields (**25l**, **25m** and **25n**), including examples with strained rings, such as cyclobutyl sulfinamide (**25o**) in excellent yield and cyclopropyl sulfinamide (**25p**) in poor yield. Benzylic substrates (**25q**) could also be used, but only moderate yields could be obtained, likely due to homocoupling of the benzylic radical. Attempts to improve this yield were unsuccessful. Tertiary alkyl substrates could also be used, with *tert*-butyl sulfinamide (**25r**) obtained in moderate yield, whereas the more rigid adamantane and BCP examples (**25s** and **25t**) gave excellent yields.

Table 3.4. Selected carboxylic acid scope examples. All entries performed by Dr Jagadeesh Kalepu.



[a] Carboxylic acid (0.3 mmol), TrNSO (0.2 mmol). [b] CH_2Cl_2 (1 mL, 0.2 M). [c] 9-mesitylacridine (20 mol%). Isolated yields.

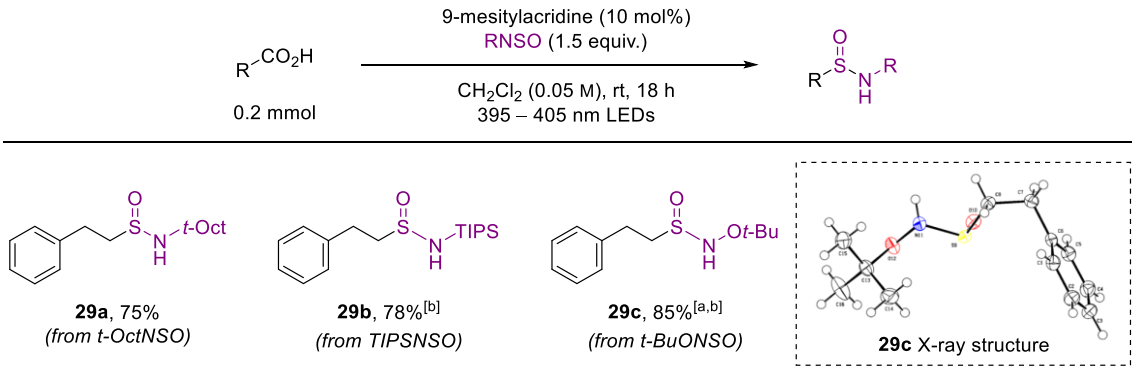
Dr Kalepu showed that the reaction was scalable, preparing sulfinamide **25n** in 88% yield on 1.0 g scale (**Scheme 3.11.A**). Using the isolated *N*-protected sulfinamide product **25n**, Dr Kalepu also demonstrated that deprotection using methanesulfonic acid could be used to prepare primary sulfinamide **26** in good yield, or alternatively, primary sulfonamide **27** could be obtained in excellent yield by oxidation using *m*CPBA followed by deprotection (**Scheme 3.11.B**).



Scheme 3.11. A): 1.0 g scale reaction. **B):** Preparation of primary sulfinamide **26** and primary sulfonamide **27** from isolated sulfinamide **25n**. All entries performed by Dr Jagadeesh Kalepu.

The scope of the reaction with respect to the sulfinylamine component was also assessed using a selection of sulfinylamines developed within our group that show good hydrolytic stability (**Table 3.5**).[26, 85, 193] The *t*-octyl and TIPS-protected sulfinamides **28a** and **29b** could be prepared from the corresponding sulfinylamines in good yields. The *N*-alkoxysulfinamide **29c**, derived from the sulfinylhydroxylamine *t*-BuONSO, could also be prepared in excellent yield. The structure of this product was confirmed by single-crystal x-ray analysis.

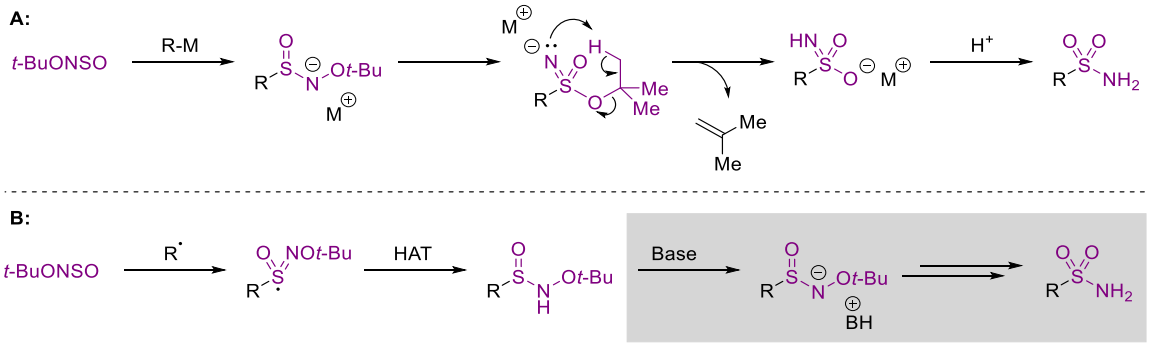
Table 3.5. Sulfinylamine scope examples. All entries performed by Dr Jagadeesh Kalepu. X-ray structural data collected by Dr Kirsten E. Christensen.



[a] Carboxylic acid (0.3 mmol), Sulfinylamine (0.2 mmol). [b] CH_2Cl_2 (2 mL). Isolated yields.

The observed *N*-alkoxysulfinamide product **29c** from reaction with *t*-BuONSO was unexpected, as its reaction with organometallic reagents usually gives primary sulfonamide products. The formation of primary sulfonamides is thought to occur via a rearrangement of the sulfinamide anion intermediate to a sulfinamidate ester intermediate and the liberation of isobutene (**Scheme 3.12.A**).[193] In this work

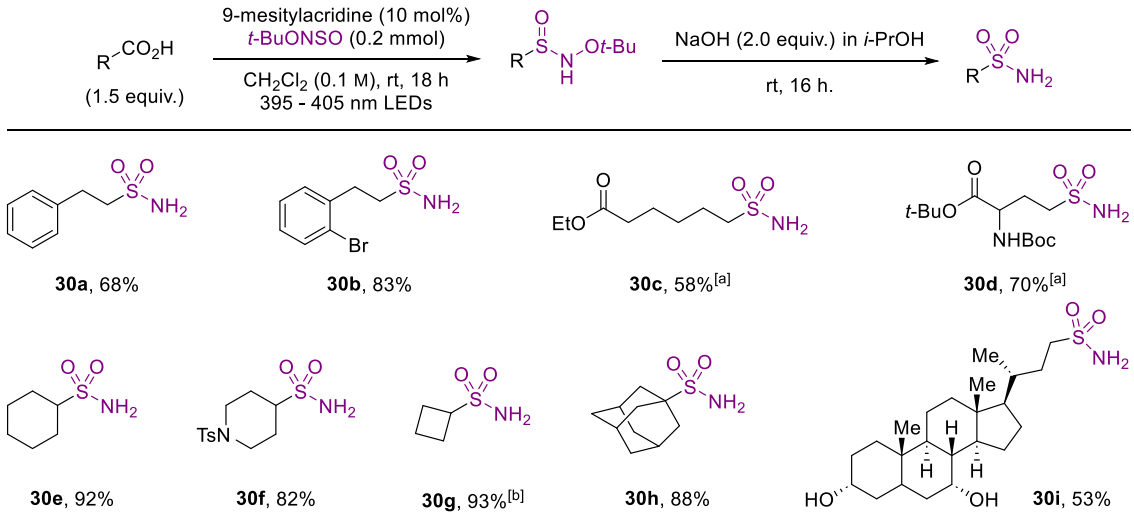
however, the sulfinamide anion is not an intermediate, as HAT to the sulfonimidoyl radical intermediate directly gives the observed *N*-alkoxysulfinamide. Given this observation, we expected that the primary sulfonamides could be accessed via deprotonation of the *N*-alkoxysulfinamide product (**Scheme 3.12.B**).



Scheme 3.12. A): Reaction of organometallic reagents with *t*-BuONSO. **B):** Reaction of radicals with *t*-BuONSO and proposed deprotonation to prepare primary sulfinamides.

Following the proposed reaction procedure, the desired primary sulfonamides could be prepared by the addition of a solution of sodium hydroxide in isopropanol to the crude reaction mixture. Alternatively, sodium hydride could be used to give the same primary sulfonamide products, which was found to be beneficial for substrates containing esters that are susceptible to hydrolysis. These conditions could again be used with primary, secondary and tertiary substrates, with good functional group compatibility, giving the corresponding primary sulfonamides in good to excellent yields (**Table 3.6**).

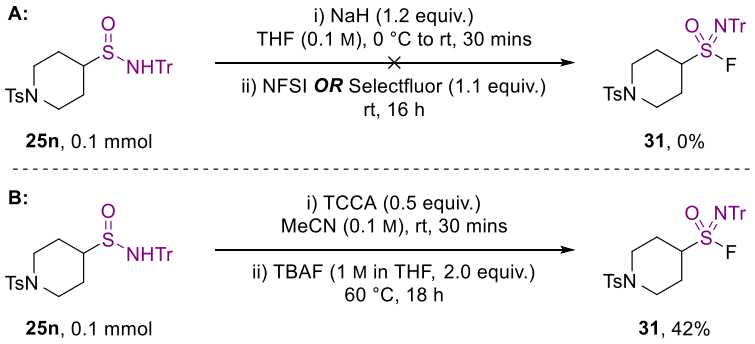
Table 3.6. Primary sulfonamide scope. All entries performed by Dr Jagadeesh Kalepu.



[a] Second Step: NaH (1.3 equiv.), THF (2 mL), 0 °C - rt, 3 h. [b] 9-Mesitylacridine (20 mol%). Isolated yields.

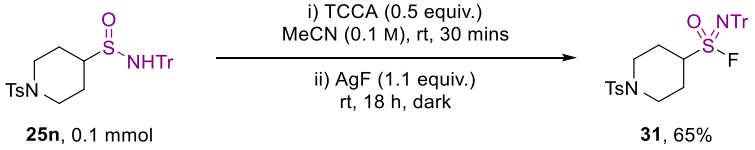
3.2.2 Sulfinamide Derivatisation

To further demonstrate the utility of this decarboxylative sulfinamidation, we wished to establish reaction conditions using which we could prepare sulfonimidoyl fluorides and sulfonimidamides. In the literature, sulfonimidoyl fluorides are prepared from sulfinamides either by oxidative fluorination, using reagents such as Selectfluor,[194] or via oxidative chlorination to form a sulfonimidoyl chloride followed by reaction with a fluoride.[87, 195] Using sulfinamide **25n**, we were unsuccessful in preparing sulfonimidoyl fluoride **31** via deprotonation using sodium hydride followed by reaction with Selectfluor or NFSI (**Scheme 3.13.A**). Conversely, oxidative chlorination using trichloroisocyanuric acid (TCCA) followed by reaction with tetrabutylammonium fluoride (TBAF) gave the desired sulfonimidoyl fluoride **31**, but only in a moderate 42% yield (**Scheme 3.13.B**). Using *t*-BuOCl instead of TCCA, and KF or KHF_2 instead of TBAF (with or without the addition of crown ethers), gave no improvement in yield. Similarly, different solvents such as THF or dichloromethane gave no improvement in yield.



Scheme 3.13. A): Attempted oxidative fluorination to prepare sulfonimidoyl fluoride **31**. **B):** Oxidative chlorination and nucleophilic fluorination to prepare sulfonimidoyl fluoride **31**.

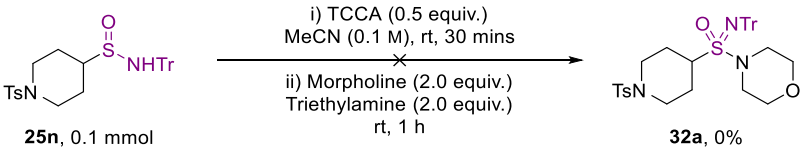
Most literature procedures for the preparation of sulfonimidoyl fluorides from sulfinamides use *S*-aryl examples. In a literature example by Bolm and co-workers, sulfonimidoyl fluoride products were obtained via oxidative chlorination using *t*-BuOCl followed by fluorination using KF with 18-crown-6, and similarly, *S*-alkyl examples were also found to give poor yields.[196] Bolm proposed that competing deprotonation of the acidic α-protons by the fluoride could explain this yield, reasoning that similar observations were made by Johnson in analogous reactions of sulfonimidoyl chlorides.[197] Bolm identified alternative conditions using AgF that gave improved yields of the sulfonimidoyl fluorides in these cases, likely due to the formation of silver chloride acting as the driving force. We applied these conditions to our system, and were pleased to find an improved yield of 65% of sulfonimidoyl fluoride **31** (**Scheme 3.14**).



Scheme 3.14. Oxidative chlorination and fluorination using AgF to prepare sulfonimidoyl fluoride **31**.

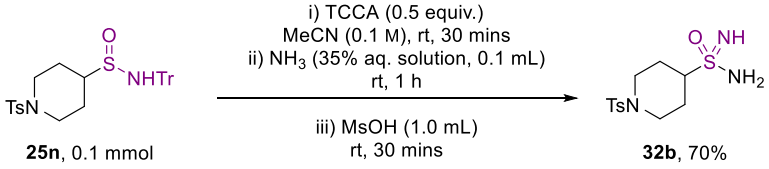
We also wished to prepare sulfonimidamides via the formation of the sulfonimidoyl chloride using TCCA followed by reaction with an amine nucleophile. However, following addition of morpholine and triethylamine to the reaction mixture, we were surprised to find that we were unable to identify the desired sulfonimidamide product **32a** (**Scheme 3.15**). In a related procedure, Willis and co-workers showed that sulfonimidamides derived from *S*-alkyl sulfinamides were obtained in much

lower yields than the corresponding *S*-aryl examples.[16b] Deprotonation of the acidic α-protons could again contribute to these lower yields, but the poorer electrophilicity of *S*-alkyl sulfonimidoyl chloride intermediates due to electron-donation as well as increased steric hinderance to nucleophilic substitution may also be a factor.



Scheme 3.15. Attempted preparation of sulfonimidamide **32a** via oxidative chlorination and nucleophilic amination.

We instead attempted to react the intermediate sulfonimidoyl chloride with a solution of ammonia, and were pleased that following trityl-deprotection using methanesulfonic acid, we could isolate the primary sulfonimidamide **32b** in 70% yield (**Scheme 3.16**). The good yield for this less-hindered nucleophile supports the hypothesis that steric hinderance to nucleophilic attack at the sulfur centre contributes to the poorer yields when using more-hindered secondary amine nucleophiles.



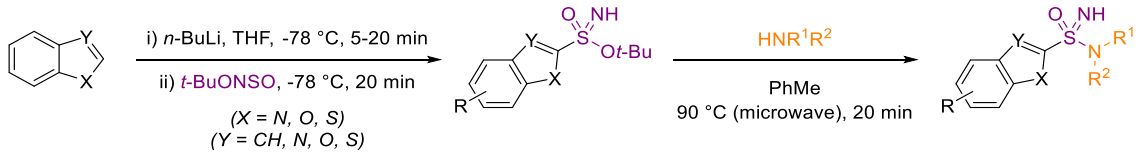
Scheme 3.16. Preparation of primary sulfonimidamide **32b** via oxidative chlorination and nucleophilic amination using ammonia.

Whilst we were pleased that the primary sulfonimidamide **32b** could be obtained, access to diverse sulfonimidamides was an important goal of this work, so alternative methods for their preparation would have to be considered.

3.2.3 Preparation of Sulfonimidamides from *N*-Alkoxysulfinamides

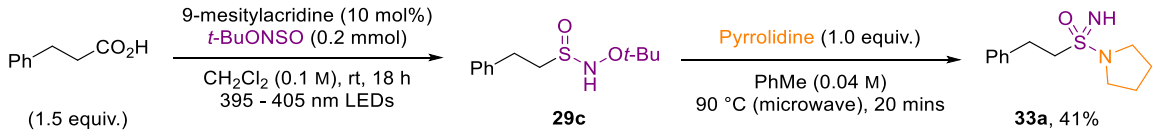
Following the observation that we could obtain *N*-alkoxysulfinamides from radical addition to sulfinylhydroxylamines, we wished to determine whether we could utilise these intermediates in the preparation of sulfonimidamides. We were inspired by a report from Tummanapalli and co-workers,

in which they prepare sulfonimidamides from heteroaryl lithium reagents.[198] In this work, a stable intermediate is formed rather than the expected primary sulfonamide, which the authors propose to be a sulfonimidate ester. The authors use this intermediate to form sulfonimidamide products via reaction with an amine nucleophile with heating in a microwave initiator (**Scheme 3.17**).



Scheme 3.17. Preparation of sulfonimidamides from heteroaryl lithium reagents

Whilst Tummanapalli and co-workers proposed sulfonimidate ester intermediates rather than *N*-alkoxysulfinamides, we envisaged that we could use a similar procedure to prepare sulfonimidamides. We were pleased to find that following our decarboxylative reaction with *t*-BuONSO to give the *N*-alkoxysulfinamide intermediate **29c**, a solvent swap to toluene, addition of pyrrolidine and heating the reaction in a microwave initiator at 90 °C for 20 mins gave sulfonimidamide **33a** in 41% yield (**Scheme 3.18**).

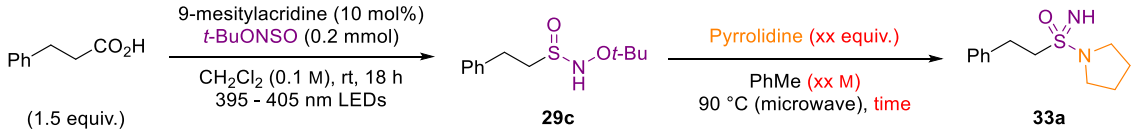


Scheme 3.18. Microwave-assisted preparation of sulfonimidamide **33a** via an *N*-alkoxysulfinamide **29c**.

We then commenced optimising the reaction conditions (**Table 3.7**). We found that a small increase in yield of **33a** was obtained in a more-concentrated reaction (**Table 3.7, entry 2**). At this concentration, we also explored longer reaction times and a higher reaction temperature, but a small drop in yield was obtained in these cases (**Table 3.7, entries 3 and 4**). We also explored the impact of varying the loading of pyrrolidine, and when using 2.0 equivalents, a significant increase to 71% was obtained (**Table 3.7, entry 5**). A further increase to 3.0 equivalents showed no further improvement, with a slight drop to 67% (**Table 3.7, entry 6**). Combining the higher loading of pyrrolidine and a higher reaction temperature gave the optimised conditions with 72% yield (**Table**

3.7, entry 7). Finally, we attempted the reaction with heating at 90 °C for 18 h on a stirrer hotplate, but a poor 17% yield was obtained, indicating that heating using a microwave initiator was important (**Table 3.7, entry 8**).

Table 3.7. Optimisation of sulfonimidamide synthesis **33a** using pyrrolidine.

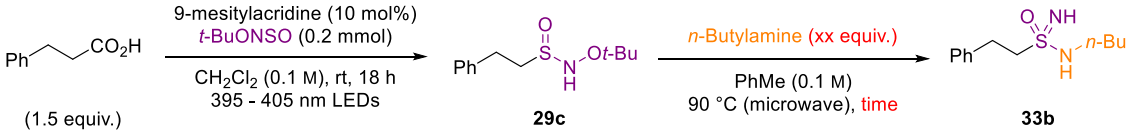


Entry	Solvent volume (mL)	Concentration ($moldm^{-3}$)	Equivalents pyrrolidine	Other Changes	Yield
1	5.0	0.04	1.0	-	41%
2	2.0	0.1	1.0	-	55%
3	2.0	0.1	1.0	40 mins reaction time	49%
4	2.0	0.1	1.0	100 °C reaction temperature	50%
5	5.0	0.04	2.0	-	71%
6	5.0	0.04	3.0	-	67%
7	**2.0**	**0.1**	**2.0**	**-**	**72%**
8	2.0	0.1	2.0	90 °C heating on hotplate, 18 h	17%

0.2 mmol scale. Isolated Yields

Whilst Tummanapalli showed that less-nucleophilic primary amines gave comparable yields to secondary amines in their reaction, we obtained only a moderate 39% yield of sulfonimidamide **33b** when using *n*-butylamine with our optimised reaction conditions (**Table 3.8, entry 1**). A longer 1-hour reaction time gave a slight improvement to 45% yield (**Table 3.8, entry 2**). Increasing the loading of *n*-butylamine to 5.0 equivalents increased the yield substantially to 64% (**Table 3.8, entry 3**). A longer reaction time again increased the yield slightly to 68% (**Table 3.8, entry 4**). Increasing the amine loading further to 10 equivalents gave the optimum yield of 70% (**Table 3.8, entry 5**), which gave the optimised conditions that would be used for lower-yielding examples.

Table 3.8. Optimisation of sulfonimidamide **33b** synthesis using *n*-butylamine.

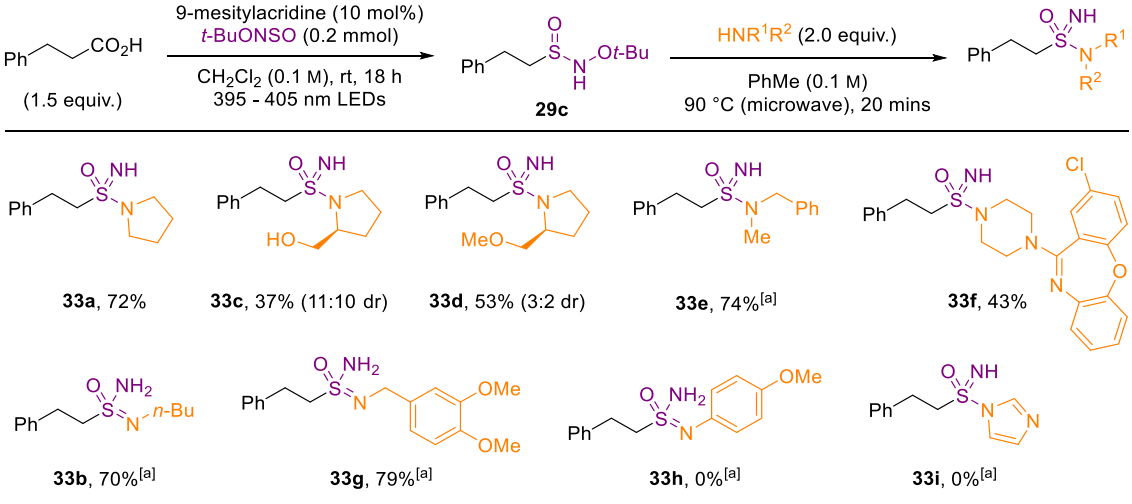


Entry	Equivalents *n*-butylamine	Reaction time (mins)	Yield
1	2.0	20	39%
2	2.0	60	45%
3	5.0	20	64%
4	5.0	60	68%
5	10.0	20	70%

0.2 mmol scale. Isolated Yields

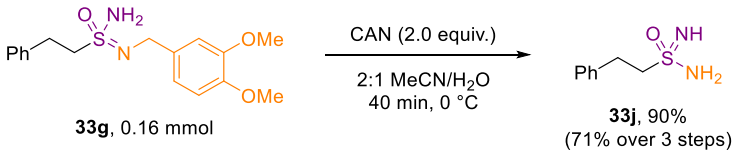
With optimised conditions in hand, we assessed the scope of the reaction with respect to the amine component (**Table 3.9**). We were pleased to find that diverse amine nucleophiles were compatible with the reaction. Prolinol (**33c**) and its *O*-methylated derivative (**33d**), gave moderate yields, and the increased yields for the methylated example indicates that the presence of an unprotected alcohol is detrimental. The drug molecule Amoxapine could also be used in the reaction to give a moderate yield of the product sulfonimidamide **33e**. 10 equivalents of amine were needed to give sulfonimidamides **3b**, **3f** and **3g** in good yields. *p*-Toluidine and imidazole could not be used to give the corresponding sulfonimidamides **3h** and **3i** using these reaction conditions.

Table 3.9. Sulfonimidamide amine scope.



[a] HNR^1R^2 (10 equiv.). Isolated Yields.

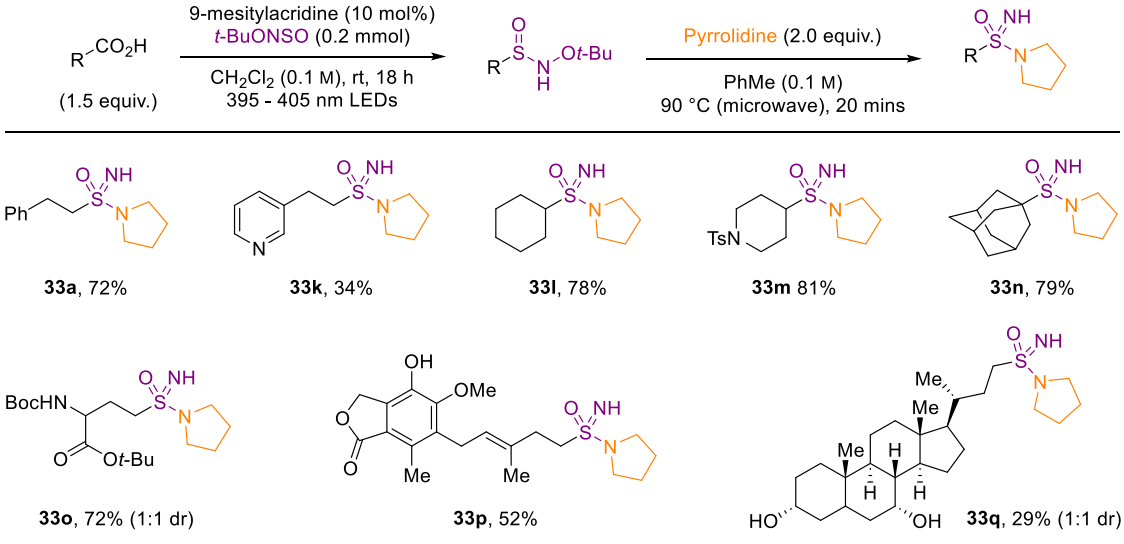
Ammonia was found to be incompatible with the process, but we were able to use the isolated sulfinamide **33g**, derived from 3,4-dimethoxybenzylamine, to prepare primary sulfinamide **33j** in 90% yield (71% over the 3 reaction steps) via deprotection using ceric ammonium nitrate (CAN) (**Scheme 3.19**).



Scheme 3.19. Preparation of primary sulfonimidamide **33j** from sulfinamide **33g**.

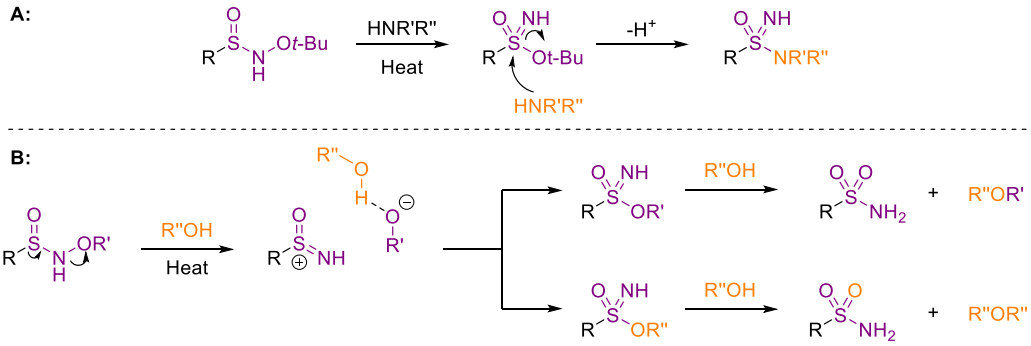
We then assessed the scope with respect to the carboxylic acid, using pyrrolidine as the amine nucleophile (**Table 3.10**). We were pleased to find that diverse carboxylic acids were compatible with the reaction, giving good yields for primary alkyl (**33a** and **33k**), secondary alkyl (**33l** and **33m**) and tertiary alkyl (**33n**) substrates. Furthermore, we were again able to demonstrate the application of the reaction to biologically relevant substrates such as the amino acid, Boc-Glu-O*t*-Bu (**33o**), the drug molecule mycophenolic acid (**33p**) and the natural product chenodeoxycholic acid (**33q**), giving the corresponding sulfonimidamide products in moderate to good yields.

Table 3.10. Sulfonimidamide carboxylic acid scope.



Isolated Yields.

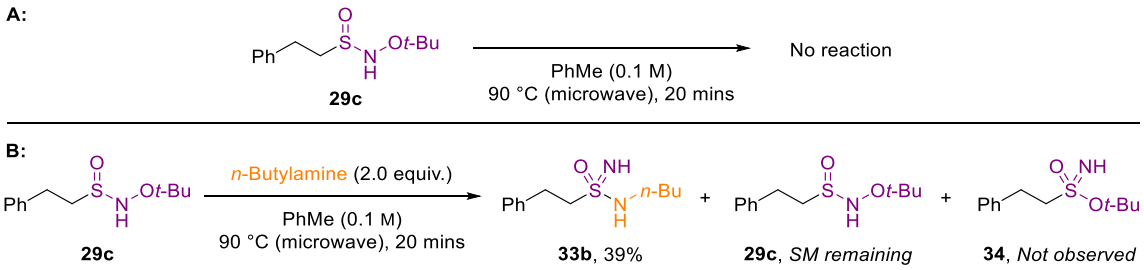
We were intrigued by the mechanism by which the sulfonimidamide products are formed in the reaction. Tummanapalli and co-workers propose the formation of a sulfonimidate ester intermediate, from which nucleophilic attack by the amine would presumably give the sulfonimidamide product (**Scheme 3.20.A**). In their studies of the 1,2-rearrangments of *N*-alkoxysulfinamides to sulfonimidate esters, Maricich and co-workers propose the formation of a sulfinyl nitrene intermediate via loss of an alkoxide (stabilised by H-bonding to the alcohol solvent).[199] Recombination of the alkoxide with the sulfinyl nitrene then gives the sulfonimidate ester intermediate, which can be used to alkylate nucleophiles such as alcohols. Cross-over to form the sulfonimidate ester with the alcohol solvent was also observed, verified by the formation of the symmetrical ether products from nucleophilic addition of the alcohol solvent on the sulfonimidate ester *O*-alkyl substituent (**Scheme 3.20.B**). Other nucleophiles such as DMSO have also been shown to competitively react with the sulfinyl nitrene intermediates prepared under similar conditions.[200]



Scheme 3.20. A): Nucleophilic addition to sulfonimidate ester intermediate **B):** 1,2-Rearrangement of *N*-alkoxysulfinamides via sulfinyl nitrene intermediates and cross-over product formation.

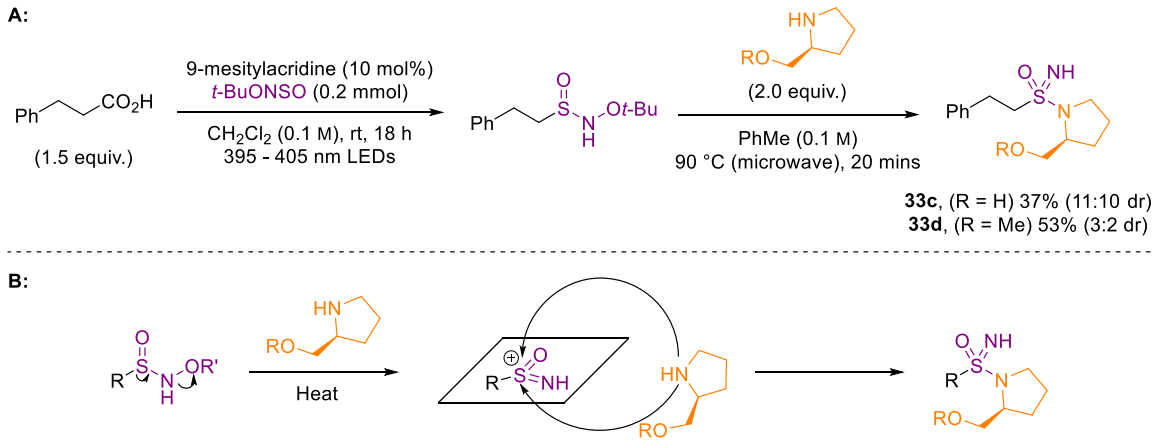
We observed no evidence for the formation of a sulfonimidate ester intermediate **34** in our work. Furthermore, heating the reactions without an amine nucleophile or with one equivalent of DIPEA result in no consumption of the *N*-alkoxysulfinamide **29c**, supporting the proposal by Maricich that the presence of a H-bond donor aids the loss of the alkoxide leaving group (**Scheme 3.21.A**). Reaction with 2.0 equivalents of the less-nucleophilic *n*-butylamine gave a poorer yield of the sulfonimidamide product **33b**, but also returned some of the starting material, indicating that the nucleophilicity of the

amine is also important (**Scheme 3.21.B**). The nucleophilicity of the amine wouldn't be expected to impact the formation of a sulfinyl nitrene based on the mechanism proposed by Maricich.[199]



Scheme 3.21. A): No reaction without amine present. **B):** Incomplete conversion shows unreacted *N*-alkoxysulfinamide **29c** but no sulfonimidate ester **34**.

Some mechanistic insight can also be gained from the preparation of sulfonimidamides **33c** and **33d** from chiral amines, wherein diastereoselectivity is observed from racemic *N*-alkoxysulfinamide **29c** (**Scheme 3.22.A**). This indicates the formation of an achiral intermediate, such as a sulfinyl nitrene, which likely reacts preferentially on one face with chiral amines to give the observed diastereoselectivity (**Scheme 3.22.B**).

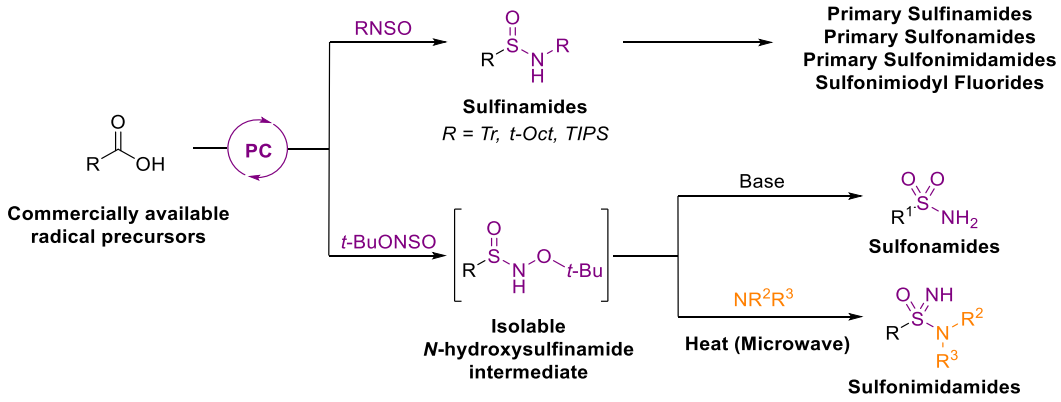


Scheme 3.22. A): Diastereoselectivity using chiral amines. **B):** Nucleophilic addition of chiral amine to either face of achiral sulfinyl nitrene intermediate.

Whilst some of our results support the potential formation of a sulfinyl nitrene intermediate, further mechanistic studies, as well as computational studies, are likely needed to further elucidate the mechanism.

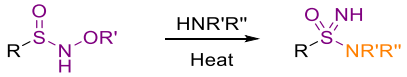
3.3 Conclusions and Future Work

In conclusion, in collaboration with Dr Jagadeesh Kalepu, we have developed a general method for the preparation of sulfinamides from readily available carboxylic acids and sulfinylamines. This method shows excellent functional group tolerance, and can be used for primary, secondary and tertiary alkyl substrates. Furthermore, we developed conditions for the preparation of primary sulfinamides, primary sulfonamides, primary sulfonimidamides and sulfonimidoyl fluorides from the sulfinamide products. Using the sulfinylhydroxylamine *t*-BuONSO gave *N*-alkoxysulfinamide products, which could be used to prepare either sulfonamides by deprotonation with a base, or sulfonimidamides by heating with an amine nucleophile (**Scheme 3.33**).



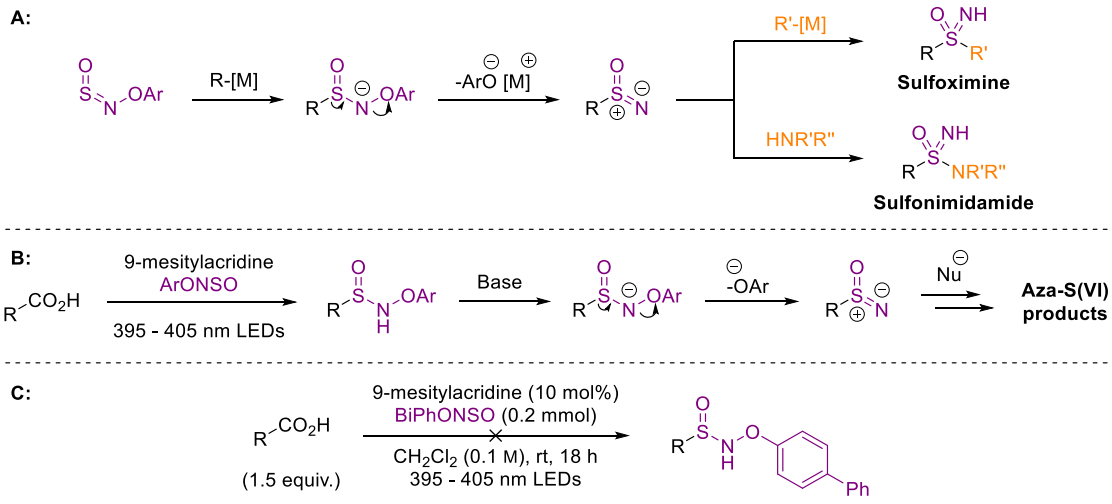
Scheme 3.33. Decarboxylative preparation of sulfinamides and *N*-alkoxysulfinamides and subsequent reactions to diverse S(VI) products.

Whilst the functional group tolerance for the preparation of sulfonimidamides from *N*-alkoxysulfinamides was good, yields for less-nucleophilic amines required high loadings of amines, which would be prohibitive when using valuable amines. Furthermore, good yields could only be obtained using microwave heating, which would present challenges if the reaction needed to be carried out on a large scale. The work from Maricich and co-workers demonstrates that sulfinyl nitrenes could also be prepared from various *N*-alkoxysulfinamides,[199-200] and exploring the impact of varying the alkoxide leaving group may enable the preparation of sulfonimidamides in improved yields with less-nucleophilic amines (**Scheme 3.34**).



Scheme 3.34. Exploration of different *O*-alkyl substituents for the preparation of sulfonimidamide products.

Previous studies from the Willis group also show that the reaction of sulfinyhydroxylamines functionalised with electron-withdrawn phenoxide leaving groups (such as BiPhONSO) with organometallic reactions can be used to give sulfinyl nitrenes under cryogenic conditions. These were then used to prepare sulfoximines or sulfonimidamides via addition of an additional organometallic reagent or amine nucleophile (**Scheme 3.35.A**).[86] Following radical addition to *O*-aryl sulfinylhydroxylamines, sulfinyl nitrenes could hypothetically be prepared under mild conditions via deprotonation of the *N*-phenoxysulfinamide intermediates, and subsequent addition of various nucleophiles could then be used to prepare various aza-S(VI) products (**Scheme 3.35.B**). Preliminary investigations by Dr. Jagadeesh Kalepu found that radical addition to BiPhONSO gave a complicated reaction mixture, and the desired sulfinamide product could not be identified, but exploration of alternative aryl substituents may enable the preparation and use of *N*-phenoxysulfinamides (**Scheme 3.35.C**).



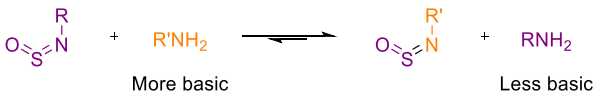
Scheme 3.35. A): Sulfinyl nitrenes from organometallic addition to *O*-aryl sulfinylhydroxylamines. **B):** Proposed preparation of *N*-phenoxysulfinamides and subsequent deprotonation to form sulfinyl nitrenes. **C):** Attempted preparation of an *N*-phenoxysulfinamides from BiPhONSO performed by Dr Jagadeesh Kalepu.

Chapter 4 - Exploiting Trans-Sulfinylation to Prepare Diverse *N*-Substituted Sulfinamides

4.1 Introduction

"Trans-sulfinylation," the process by which a sulfinyl group can be transposed from one primary amine to another, is often cited as a useful method for the preparation of sensitive sulfinylamines (**Scheme 4.1**).[72]

The position of this equilibrium between the two sulfinylamines can be correlated to the basicity of the two amine components, and at equilibrium, the major sulfinylamine component will be that formed from the more basic amine. As a result, using *N*-sulfinylsulfonamides in this trans-sulfinylation procedure with primary amines, hydroxylamines, and hydrazines provides almost exclusively the exchanged sulfinylamine product due to the low basicity of sulfonamides.[76, 80]



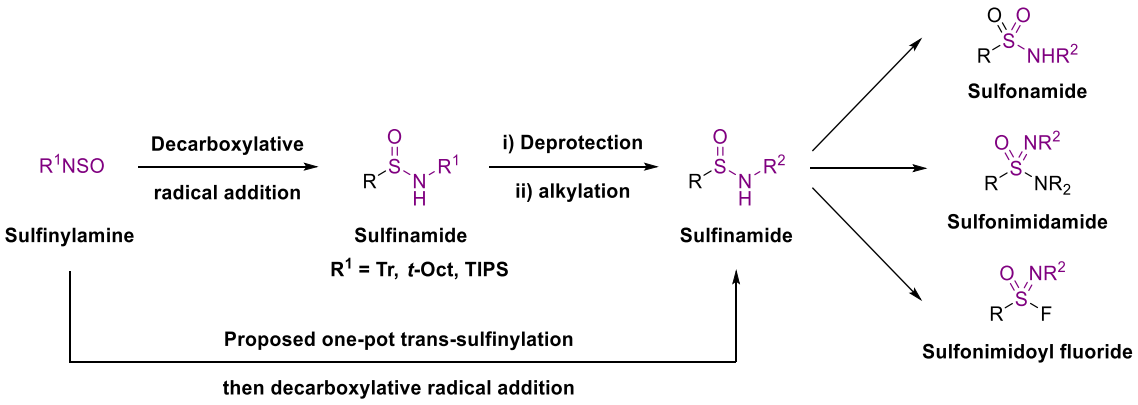
Scheme 4.1. Amine-sulfinylamine exchange equilibrium.

There are very few cases where trans-sulfinylation has been exploited in the literature, other than some isolated examples for the preparation of some exotic heterocycles.[80b, 201] This is because the sulfinylamine reagents generally used for trans-sulfinylation, such as *N*-sulfinylanilines and *N*-sulfinylsulfonamides, are moisture sensitive and require precautions when preparing, purifying and handling to ensure they are not exposed to water. Furthermore, the generation of one equivalent of amine or sulfonamide by-product is a notable disadvantage, as purification is required in many cases to use the sulfinylamine in subsequent reactions, for example with organometallic reagents.

During his DPhil studies, Dr. Thomas Q. Davies (a former DPhil student in the group) noted that this exchange process also occurred with TrNSO upon addition of butylamine, reaching a ratio of 2.5:1

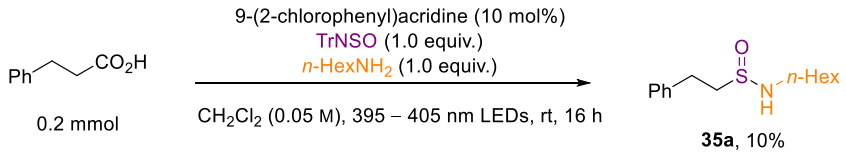
BuNSO:TrNSO after 3 hours at room temperature in $CDCl_3$ as the solvent, demonstrating the decreased basicity of tritylamine compared to that of other primary amines. The use of TrNSO has many advantages compared to other sulfinylamine reagents used for trans-sulfinylation, as it is relatively moisture-insensitive, and commercially available.

Using the decarboxylative radical addition procedure described in **Chapter 3**, we can readily prepare alkyl sulfinamides and their derivatives. However, the preparation of differentially *N*-alkylated products requires removal of the protecting group followed by alkylation, resulting in two additional steps to prepare the desired products (**Scheme 4.2**). A more convenient method would be to use sulfinylamines pre-functionalised with the desired alkyl substituent, however, preparation of a new sulfinylamine each time is not practical.



Scheme 4.2. Routes to differentially alkylated sulfinamides and their derivatives.

This concept provided an opportunity to showcase the use of TrNSO to prepare the desired sulfinylamine via trans-sulfinylation, followed by radical addition. We expected the radical addition process to be insensitive to the presence of the tritylamine by-product, enabling the procedure to be carried out without purification of the sulfinylamine. Preliminary investigations by Dr Jagadeesh Kalepu demonstrated the feasibility of this procedure, isolating 10% of *N*-hexyl sulfinamide **35a** following the addition of 1.0 equivalent of hexylamine to the previously optimised reaction conditions (**Scheme 4.3**).



Scheme 4.3. Preparation of *N*-hexylsulfinamide **35a** via in-situ trans-sulfinylation and radical addition. Reaction performed by Dr Jagadeesh Kalepu.

4.2 Results and Discussion

4.2.1 Previous Work

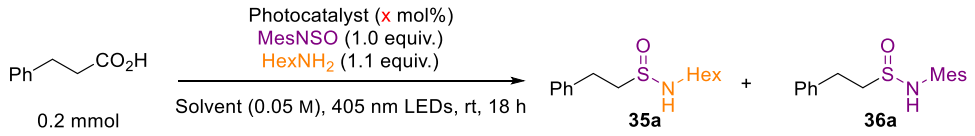
Mr Russell Woodger (a former MChem project student in the group) carried out the initial optimisation of this procedure. Early studies were carried out using *N*-sulfinylmesidine (MesNSO). It was expected that due to the lower pK_{aH} of mesidine compared to that of tritylamine, the equilibrium would favour the formation of the desired sulfinylamine. MesNSO was found to have improved hydrolytic stability compared to PhNSO, and was found to give a slightly higher yield of the trans-sulfinylation product at equilibrium.

Key findings for the optimisation are found in **Table 4.1** and **Table 4.2**; full details can be found in Mr Woodger's thesis. Several solvents gave comparable yields of sulfinamide **35a**, including dichloromethane, DCE, MeCN and EtOAc (**Table 4.1, entries 1 – 4**). Similar to the parent reaction discussed in **Chapter 3**, solvents such as DMSO, Et_2O and DMF (**Table 4.1, entries 5 – 7**) gave poor conversion, which was attributed to the carboxylic acid and acridine photocatalyst preferentially forming an ion pair rather than the photoactive H-bonded complex. Using toluene (**Table 4.1, entry 8**) gave moderate conversion and yields, which is likely due to the formation of a cloudy solution due to poor solubility, resulting in poorer light transmission through the reaction mixture and thus lower yields. Dichloromethane was chosen as the solvent of choice as it showed the highest consumption of the acid.

Varying catalysts and catalyst loading was explored in order to improve conversion. Using 50 mol% of **PC1** (**Table 4.1, entry 9**) was found to improve product yields and conversion of acid, although some still remained. Using **PC5** (**Table 4.1, entry 10**) also improved yields and conversion, and

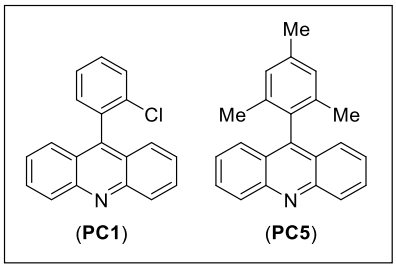
increasing loading to 20 mol% (**Table 4.1, entry 11**) gave full conversion and a 44% yield of sulfinamide **35a**. Using different light sources was also investigated, and it was noted that a more powerful HepatoChem EvoluChem^{TM} 18 W 405 nm LED lamp (**Table 4.1, entry 12**) gave an improved yield of sulfinamide **35a**, as well as reaching completion in a much shorter 3 h reaction time. This reaction setup was used in subsequent studies.

Table 4.1. Optimisation of solvent and photocatalyst. All entries performed by Mr Russell Woodger.



Entry	Solvent	Catalyst	Catalyst loading (mol%)	Yield (%)		Acid remaining (%)
				Sulfinamide 35a	Sulfinamide 36a	
1	CH_2Cl_2	**PC1**	10	18	31	33
2	DCE	**PC1**	10	22	31	48
3	MeCN	**PC1**	10	23	17	42
4	EtOAc	**PC1**	10	24	24	52
5	DMSO	**PC1**	10	0	0	79
6	Et_2O	**PC1**	10	6	5	62
7	DMF	**PC1**	10	0	0	100
8	Toluene	**PC1**	10	13	27	60
9	CH_2Cl_2	**PC1**	50	40	21	15
10	CH_2Cl_2	**PC5**	10	29	28	23
11	CH_2Cl_2	**PC5**	20	44	27	0
12[a]	CH_2Cl_2	**PC5**	20	53	28	0

[a]Reaction carried out using Hepatochem 405 nm lamp, 3 h reaction time.
Yields determined by HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard



Whilst yields were now up to 53%, and reaction was now reaching full conversion, substantial amounts of sulfinamide **35a**, derived from MesNSO, was still observed. NMR experiments were conducted to monitor the rate of trans-sulfinylation (**Figure 4.1**). For MesNSO, 1.5 h was needed for the equilibrium of 2:1 HexNSO:MesNSO to be established (**Figure 4.1.B**). For TrNSO, equilibration was much slower, reaching only 1:1.2 HexNSO:TrNSO after 3 h (**Figure 4.1.A**). If radical generation

is initiated before the equilibrium is established, the forming radicals are more likely to react with MesNSO, which results in a higher yield of *N*-mesityl product **38a**.

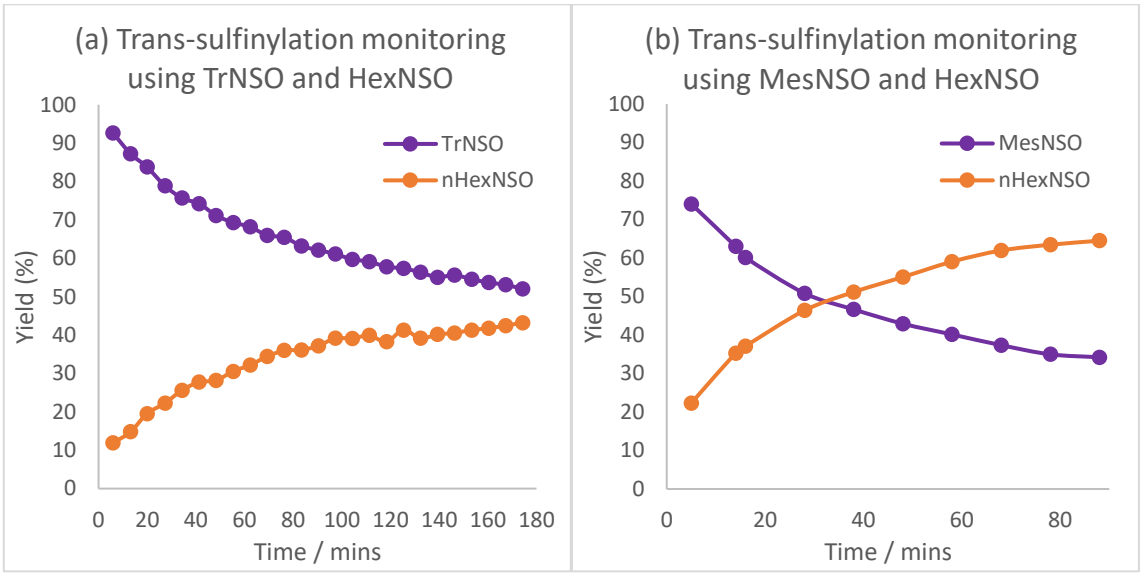
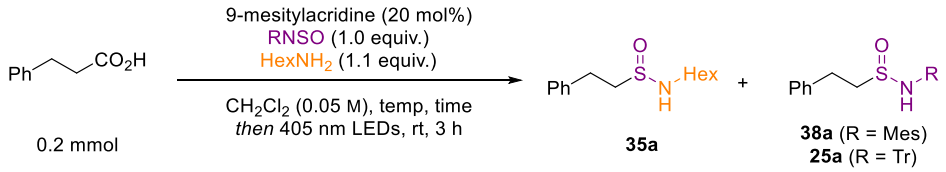


Figure 4.1. Comparison of the rates of trans-sulfinylation with HexNSO for TrNSO (a) and MesNSO (b). Experiments performed by Mr Russell Woodger.

Stirring the reaction for 30 mins at room temperature prior to irradiation gave a slightly improved yield of the hexyl product **35a** and slightly lower yield of the mesityl side-product **38a** (**Table 4.2, entry 3**). Stirring at 40 °C for 30 mins (**Table 4.2, entry 5**) improved the yield further to 68%, and stirring at 60 °C improved it even further to 71% (**Table 4.2, entry 7**). Despite TrNSO needing a longer time to reach equilibrium than MesNSO, pre-stirring the trans-sulfinylation reaction with TrNSO at elevated temperatures improved yield of sulfinamide **35a** substantially from 45% without pre-stirring (**Table 4.2, entry 8**) to 62% with 30 mins stirring at 40 °C (**Table 4.2, entry 10**). Increasing the temperature to 60 °C improved the yield of sulfinamide **35a** even further to 68%, and gave only 2% of the trityl side-product **25a** (**Table 4.2, entry 12**). Both TrNSO and MesNSO gave optimum yields with 30 mins pre-stirring at 60 °C.

Table 4.2. Optimisation of pre-equilibrium conditions. All entries performed by Mr Russell Woodger.



Entry	Sulfinylamine	Pre-equilibrium temperature	Pre-equilibrium time	Yield (%)	
				Sulfinamide 35a	Sulfinamide 38a or 25a
1	MesNSO	rt	0 min	53	28
2	MesNSO	rt	15 min	52	28
3	MesNSO	rt	30 min	57	22
4	MesNSO	40 °C	15 min	67	14
5	MesNSO	40 °C	30 min	68	13
6	MesNSO	60 °C	15 min	71	9
7	MesNSO	60 °C	30 min	71	10
8	TrNSO	rt	0 min	45	21
9	TrNSO	40 °C	15 min	59	7
10	TrNSO	40 °C	30 min	62	4
11	TrNSO	60 °C	15 min	67	3
12	TrNSO	60 °C	30 min	68	2

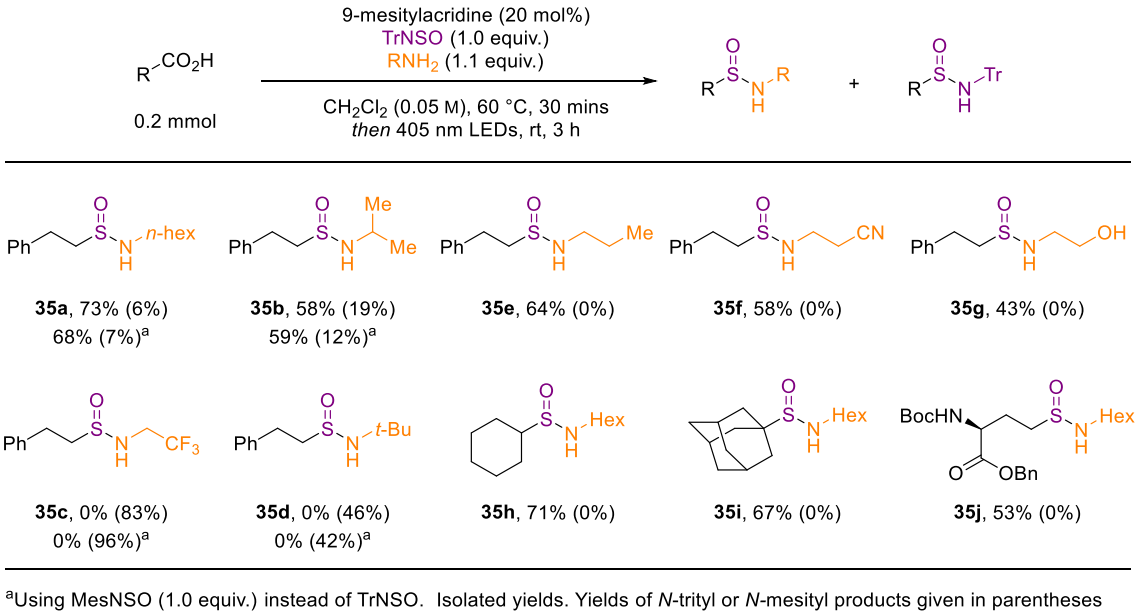
Yields determined by HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard

With optimum conditions in hand, Mr Woodger assessed the scope of the reaction (**Table 4.3**). Both TrNSO and MesNSO gave comparable isolated yields of *N*-hexyl and *N*-isopropyl sulfinamides **35a** and **35b**. Less nucleophilic amines: 2,2,2-trifluoroethylamine and *tert*-butylamine, were also subjected to the reaction conditions. None of the exchange products **35c** and **35d** were isolated in either case, and high yields of *N*-trityl and *N*-mesityl products were isolated in all cases.

These results established that for the primary amines tested, there was no major advantage to either sulfinylamine in the trans-sulfinylation. As a result, only TrNSO was used in subsequent scoping due to its commercial availability.

Despite its volatility, propylamine was used to prepare sulfinamide **35e** in good yield. Nitrile groups and even unprotected alcohols were tolerated in the reaction to give sulfinamides **35f** and **35g** in good yields. Cyclohexyl and adamantyl sulfinamides **35h** and **35i** could both be obtained in good yields, demonstrating that more sterically demanding radicals are also compatible. Finally, sulfinamide **35j**, derived from Boc-Glu-OBn, could be prepared in good yield, demonstrating the applicability of this methodology to the functionalisation of more complex carboxylic acids.

Table 4.3. Preliminary scope. All entries performed by Mr Russell Woodger.



[a]Using MesNSO (1.0 equiv.) instead of TrNSO. Isolated yields. Yields of *N*-trityl or *N*-mesityl products given in parentheses

4.2.2 Reaction Re-Optimisation

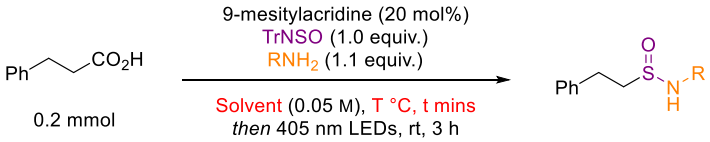
Following the initial studies by Mr Woodger, we decided that further optimisation would be necessary to address some issues. Firstly, the reaction solvent is heated to above its boiling point during pre-equilibrium, meaning a pressure tube is necessary. We wished to reassess solvents in order to remove this requirement. Secondly, we wished to improve the yields obtained for sulfinamides derived from α-secondary amines such as isopropylamine, the yield for which was lower than expected in the previously optimised conditions. We reasoned that reassessing pre-equilibrium time and temperature may help improve yields for these substrates.

Reaction conditions were re-optimised using *n*-hexylamine, isopropylamine and benzylamine as model amine substrates. Upon repeating the reactions for the three substrates with 30 min equilibrium at both 40 °C and 60 °C, it was noted that the yield of **37a** from hexylamine was identical in both cases, meaning 40 °C would be sufficient for α-primary amines (**Table 4.4, entry 1 and 2**). Isopropylamine gave a lower yield of sulfinamide **37b** at 40 °C, likely due to a slower trans-sulfinylation, meaning pre-equilibrium at 60 °C or higher is important for α-secondary amines. Finally, benzylamine gave a higher yield of sulfinamide **37c** at 40 °C than at 60 °C. More discolouration was noted at the higher temperature, indicating that the forming BnNSO may be

unstable under the reaction conditions at 60 °C. Pre-equilibrium at room temperature for 2 h gave slightly poorer yields for both hexylamine and benzylamine (**Table 4.4, entry 3**).

Following the observation that higher temperatures were still needed for α-secondary amines, MeCN was considered as an alternative reaction solvent, which had previously given comparable product yields in the optimisation carried out by Mr Woodger. Using MeCN with 30 mins pre-equilibrium at 40 °C (**Table 4.4, entry 4**), hexylamine gave comparable yields of **37a** to that using dichloromethane. However, no benzyl sulfinamide product **37c** was observed using benzylamine. For isopropylamine, slightly improved yields of **37b** were obtained in MeCN with 30 mins pre-equilibrium at 60 °C (**Table 4.4, entry 5**). Further improvements were observed when increasing pre-equilibrium time to 1 h, giving 67% yield (**Table 4.4, entry 6**). Increasing the pre-equilibrium temperature further to 80 °C for 30 mins gave a poorer yield than that obtained at 60 °C (**Table 4.4, entry 7**). Finally, switching to DCE as the solvent gave poorer yields at 60 °C than MeCN for both 30 mins and 1 h pre-equilibrium (**Table 4.4, entry 8 and 9**). Following these studies, MeCN was chosen as the optimum solvent, but in cases where the forming sulfinylamine was unstable in the reaction solvent, such as when using benzylamine, dichloromethane would be used instead. 30 mins at 40 °C pre-equilibrium is sufficient for α-primary amines, but for α-secondary amines, 1 h at 60 °C would be used.

Table 4.4. Re-optimisation of reaction solvent and pre-equilibrium.



Entry	Solvent	Pre-equilibrium temperature	Pre-equilibrium time	Yield (%) R = *n*-hexylamine	isopropylamine	benzylamine
1	CH_2Cl_2	60 °C	30 mins	74	55	41
2	CH_2Cl_2	40 °C	30 mins	74	22	58
3	CH_2Cl_2	rt	2 h	69	-	54
4	MeCN	40 °C	30 mins	75	-	0
5	MeCN	60 °C	30 mins	-	59	-
6	MeCN	60 °C	1h	-	67	-
7	MeCN	80 °C	30 mins	-	61	-
8	DCE	60 °C	30 mins	-	45	-
9	DCE	60 °C	1 h	-	54	-

[a]Yields determined by HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard

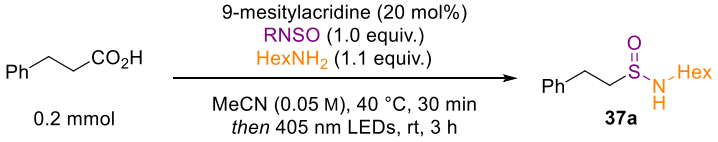
We then tested a wider selection of sulfinylamine reagents in place of TrNSO (**Table 4.5**). When using *tert*-OctNSO, a large amount of precipitate formed during the pre-equilibrium step. As a result, the reaction progressed slowly, giving only 39% of the exchange product **37a** after 18 h irradiation, with 53% starting material remaining (**Table 4.5, entry 2**). When using TIPSNSO, no exchange product **37a** was observed, and the reaction gave only the *N*-TIPS product (**Table 4.5, entry 3**).

N-Sulfinylaniline **38a** gave comparable yields of the exchange product to TrNSO, demonstrating that it could be a viable alternative, however, its increased moisture-sensitivity made its use more cumbersome (**Table 4.5, entry 4**). MesNSO was again tested under the new reaction conditions, and as before gave a good yield of the exchange product **37a** (**Table 4.5, entry 5**).

Sulfinylamines derived from anilines containing electron-withdrawing groups are generally very moisture sensitive, but in spite of this, may improve yields for amines with a lower pK_{aH} in our procedure due to the lower pK_{aH} of the aniline, therefore favouring trans-sulfinylation. Given the improved hydrolytic stability of MesNSO compared to that of PhNSO, likely due to the steric influence of the ortho-methyl substituents, we hypothesised that adding ortho-methyl substituents to anilines featuring electron-withdrawing groups would stabilise the corresponding sulfinylamine. To test this hypothesis, we prepared *N*-sulfinyl-4-cyano-2,6-dimethylaniline **38b**, which was found to be moisture insensitive under ambient conditions. We then tested this reagent in the reaction and found that it gave the exchange product **37a** in 51% yield (**Table 4.5, entry 6**).

Finally, we prepared and tested *N*-sulfinyl-*p*-toluenesulfonamide (TsNSO, **38c**), which is highly moisture-sensitive, but is known to be an excellent sulfinylation reagent due to the low pK_{aH} of *p*-toluenesulfonamide (**Table 4.5, entry 7**). TsNSO was added as a solution in dichloromethane, and dichloromethane was used as the reaction solvent. The exchange product **37a** was obtained in 38% yield. This low yield may be explained by decomposition of TsNSO in the reaction conditions prior to trans-sulfinylation with hexylamine.

Table 4.5. Testing a selection of sulfinylamines.

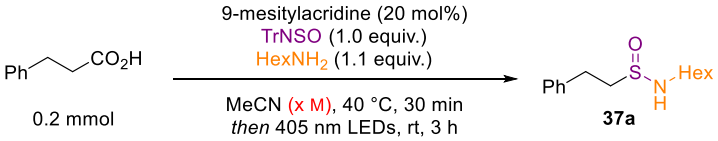


Entry	R =	Yield (%)
1	Tr	73
2	*t*-Octyl	39[a]
3	TIPS	0
4	Ph	74
5	Mes	68
6	4-cyano-2,6-dimethylphenyl	51
7	Ts	38[b]

[a]18 h reaction time. [b]DCM used as solvent, TsNSO added as 0.33 M solution in DCM.
Yields determined by HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard

We then studied the effect of concentration on the yield of sulfinamide **37a** (**Table 4.6**). At a higher concentration, yield was comparable to that obtained using 4 mL solvent (**Table 4.6, entries 2 and 3**).

Table 4.6. Optimisation of reaction concentration.

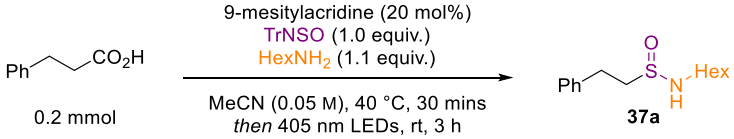


Entry	Volume	Concentration	Yield (%)
1	1 mL	0.2 M	73
2	2 mL	0.1 M	74
3	4 mL	0.05 M	73

Yields determined by HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard

Several control experiments were carried out in order to probe the sensitivity of the reaction to air and water (**Table 4.7**). A substantial drop to 45% was observed when reaction solvent was sparged with air (**Table 4.7, entry 2**), showing similar sensitivity to the parent reaction discussed in **Chapter 3**. The reaction also showed a substantial drop to 30% when using HPLC-grade solvent which had not been dried (**Table 4.7, entry 3**). A combination of air and wet solvent gave a poor yield of 19% (**Table 4.7, entry 4**). These results indicate that care has to be taken to exclude air and water from these reactions in order to obtain optimum yields.

Table 4.7. Control experiments.



Entry	Modification	Yield (%)
1	None	75
2	Dry MeCN, solvent sparged with air	45
3	"Wet" HPLC grade solvent, sparged with N_2	30
4	"Wet" solvent, under air	19

[a]Yields determined by HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard

4.2.3 Primary Amine Scope

With optimised conditions in hand, we recommenced exploration of the scope with respect to the primary amine component, firstly using α-primary amines with 30 mins pre-equilibrium at 40 °C (**Table 4.8**).

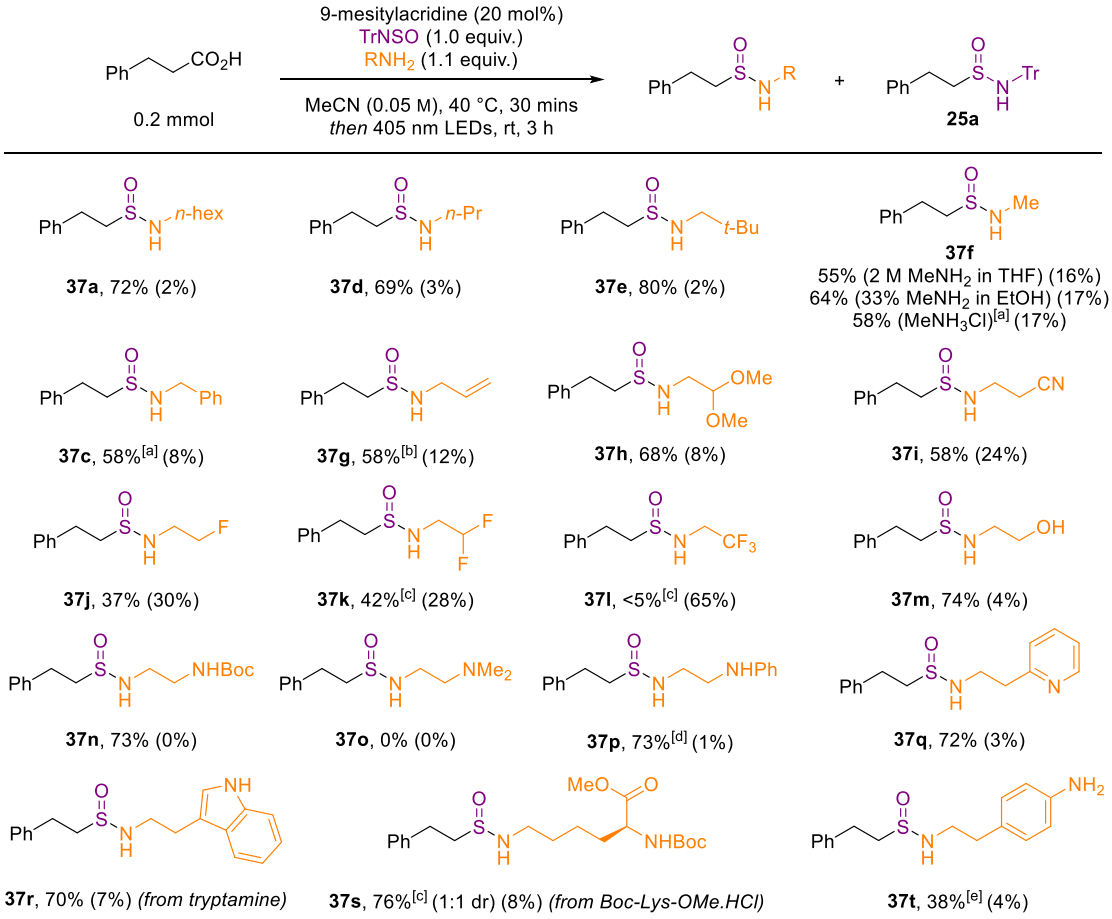
Good yields were obtained irrespective of steric environments, as demonstrated by straight-chain examples **37a** and **37d**, as well as more hindered β-tertiary substrates such as neopentylamine, giving sulfinamide **37e** in good yield. Solutions of methylamine could also be used to prepare the *N*-methyl product **37f**. Solutions in both THF and EtOH were found to be suitable, despite both of these solvents giving no product yield when used as the reaction solvent. The hydrochloride salt could also be used, provided that 1.1 equivalents of triethylamine was added, to give the sulfinamide product in good yield, with no further modifications needed. Yields of the methylamine product were notably lower than the longer-chain alkylamine products, and higher yields of the *N*-trityl product **25a** were observed. This may be justified by the absence of additional electron-donating alkyl substituents, slightly lowering the basicity of the amine, and thus shifting the trans-sulfinylation equilibrium towards TrNSO.

Both benzylamine and allylamine were not compatible with the reaction when MeCN was used as the reaction solvent, likely due to the poor stability of the forming sulfinylamines under the reaction conditions. dichloromethane was used instead, which gave the *N*-benzyl and *N*-allyl products **37c** and **37g** in good yields, respectively.

The reaction was found to be tolerant of varied functional groups, including acetals (**37h**), methyl esters (**37s**) and nitriles (**37i**). Protic functional groups were also well tolerated, including carbamates (**37n** and **37s**), indole (**37r**), and alcohol (**37m**), which gave an improved yield of 74% compared to the 43% obtained with dichloromethane as the solvent.

Substrates containing tertiary amines (**37o**) resulted in no conversion, likely due to the competing interaction between the tertiary amine and the carboxylic acid, rather than the photoactive H-bonded complex with the acridine catalyst. Less-basic amines, however, such as *N*-alkylaniline**s**, gave full conversion, albeit with a slightly longer reaction time of 5 h, to give a good yield of sulfinamide **37p**. Sulfinamide **37t**, derived from a primary amine also featuring an aniline functional group, resulted in full conversion under standard conditions, but gave only moderate yields. This lower yield could be due to the formation of sulfinamides derived from exchange with the aniline, or exchange with both amines, however, these proposed products were not isolated from the complicated reaction mixture. Pyridines were also well-tolerated, giving sulfinamide **37q** in good yield.

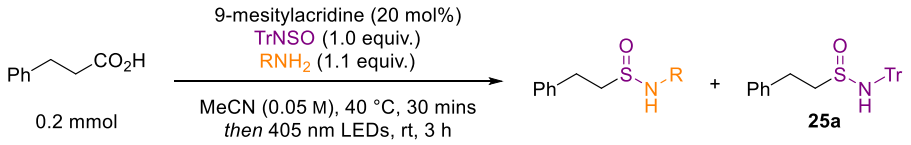
Table 4.8. α-Primary amine scope.



Isolated yields. [a] From HCl salt, added NEt_3 (1.1 equiv.). [b] CH_2Cl_2 used as solvent. [c] 1 h pre-heating at 60 °C. [d] 5 h irradiation. [e] 18 h pre-heating.
Yield of **25a** given in parentheses, calculated by HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

Yields of sulfinamide products containing proximal inductively electron-withdrawing functional groups such as nitrile **37i** or fluorides **37j**, **37k** and **37l** gave lower yields of the exchange products, and higher yields of the trityl product **25a** (**Table 4.9**). A correlation can be observed between the pK_{aH} of the amines and the yield of the exchange product,[202] which can again be justified by the trans-sulfinylation equilibrium lying more in favour of TrNSO for amines with a lower pK_{aH}. Based on this trend, the yield obtained from reaction of 2-fluoroethylamine is lower than expected, which may be due to instability of the forming sulfinylamine under the reaction conditions.

Table 4.9. Correlating pK_{aH} and yield for amines with proximal electron-withdrawing groups.



Entry	RNH_2	pK_{aH} (H_2O)	Yield (%) R =	
			Trans-sulfinylation[a]	Sulfinamide 25a[b]
1	*n*-hexylamine	10.64[c]	72	2
2	2-fluoroethylamine	9.19[d]	37	30
3	3-aminopropionitrile	7.80[e]	58	24
4[f]	2,2,-difluoroethylamine	7.45[d]	42	28
5[f]	2,2,2-trilfuoroethylamine	5.40[d]	<5	65

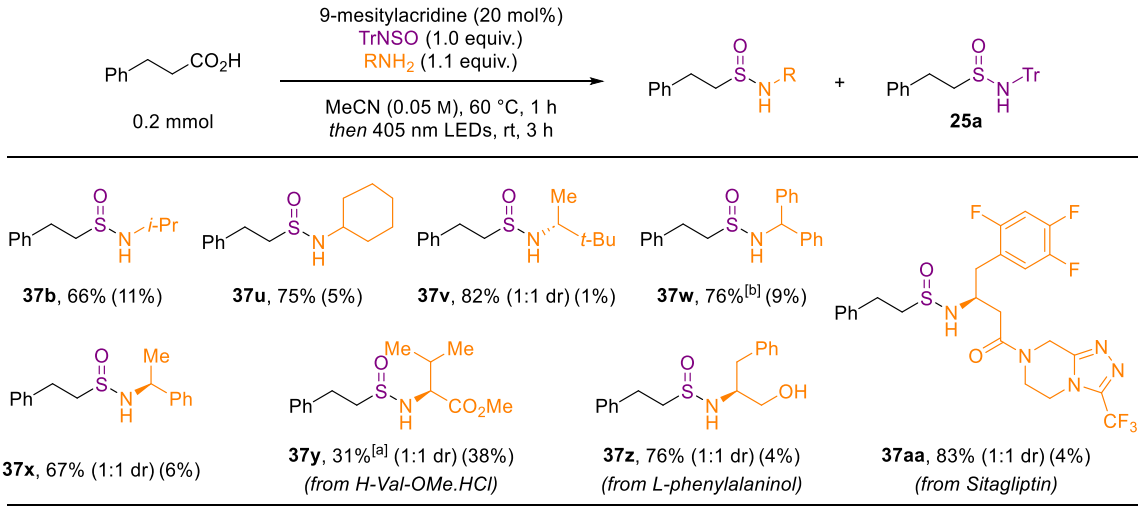
[a] Isolated yields. [b] Yield determined by HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard. [c] Ref[202a]. [d] Ref[202b]. [e] Ref[202c]. [f]1 h pre-heating at 60 °C.

We then investigated a selection of α-secondary amines with 1 h pre-equilibrium at 60 °C to determine the generality of the conditions developed using isopropylamine (**Table 4.10**).

Both cyclic and acyclic alkyl groups were tolerated, as demonstrated by examples **37b** and **37u** being obtained in good yields. Furthermore, highly sterically congested amines could be tolerated, for example giving sulfinamide **37v** in an excellent 82% yield. Sulfinamide **37x** was obtained in 67% yield from α-methylbenzylamine without any modifications, whereas sulfinamide **37w**, derived from benzyhydrylamine, gave only 50% yield using MeCN as the solvent. An improved yield of 76% was obtained when using DCE as the solvent, which may be due to decomposition of the *N*-sulfinylbenzyhydrylamine in the reaction conditions, similar to the observations when using benzylamine.

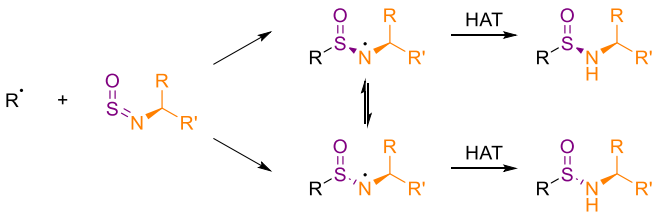
Amino acid esters were also compatible with the reaction, albeit giving moderate yields of the exchange product **37y** derived from H-Val-OMe hydrochloride. The moderate yield is likely due to electron-withdrawing ester lowering the pK_{aH}, resulting in the trans-sulfinylation equilibrium shifting towards TrNSO rather than trans-sulfinylation product. Using phenylalaninol gave a good yield of sulfinylamine product **37z**, and the densely functionalised drug molecule, Sitagliptin, also gave an excellent yield of sulfinamide product **37aa**, demonstrating the potential for this methodology to be used in late-stage functionalisation of amine-containing drug molecules.

Table 4.10. α-Secondary amine scope.



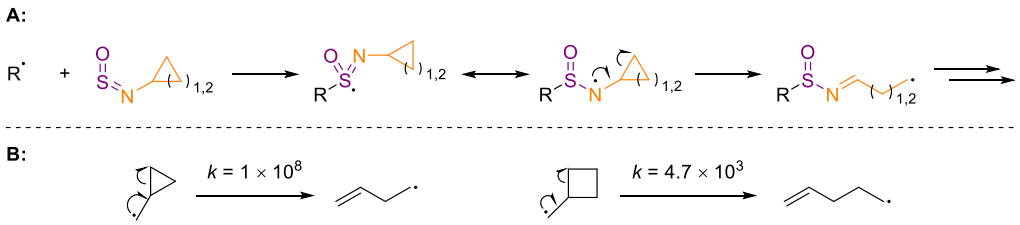
Isolated yields. [a] From HCl salt, added NEt_3 (1.1 equiv.). [b] DCE used as solvent.
Yield of **25a** given in parentheses, calculated by HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

All amines containing a stereocentre gave the corresponding sulfinamides with a dr of 1:1, indicating that either there is no strong preference for radical addition to either face of the sulfinylamine, or that the formed sulfonimidoyl radical rapidly racemises prior to HAT (**Scheme 4.4**).



Scheme 4.4. Radical addition to enantioenriched sulfinylamines.

Cyclopropyl and cyclobutylamine gave none of the desired sulfinamide products **37ab** and **37ac**, which we proposed was due to ring-opening of the strained rings to give an alkyl radical, which could then undergo further reaction (**Scheme 4.5.A**). The rate of cyclobutane ring-opening is much slower than that of cyclopropane (**Scheme 4.5.B**),[203] so the observed reactivity of cyclobutylamine indicates that the sulfonimidoyl radical intermediate is relatively long-lived.



Scheme 4.5. A): Ring-opening of *N*-cyclopropyl and cyclobutyl sulfonimidoyl radical intermediates. **B):** Rates of cyclopropyl and cyclobutyl ring opening.

In order to test the limits of the trans-sulfinylation using TrNSO, we then explored a selection of more challenging substrates. (**Table 4.11**).

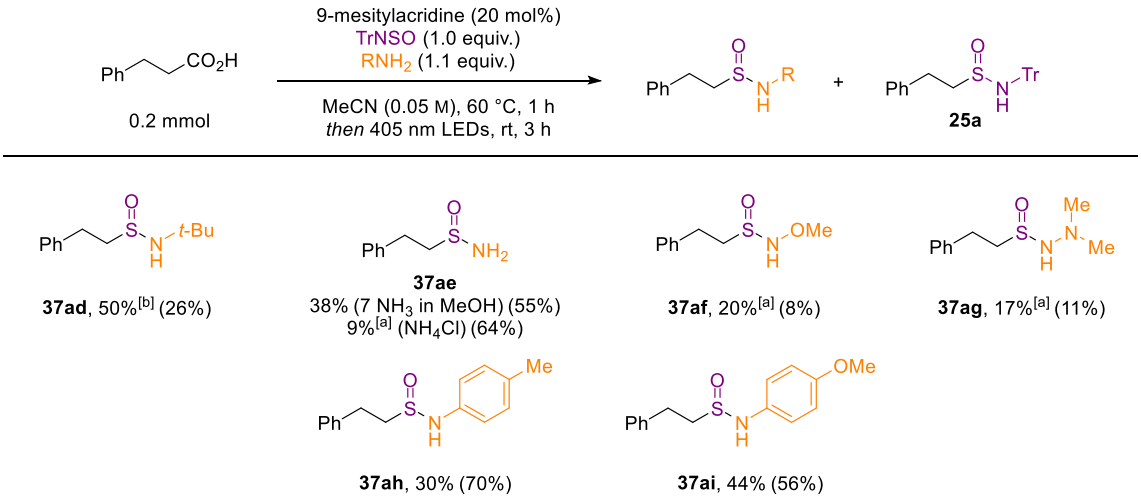
Sulfinylamines derived from α-tertiary alkyl amines often show improved hydrolytic stability, and are often easily prepared and purified.[16b, 85] However, the simplest example of this class, *N*-sulfinyl-*tert*-butylamine, is relatively volatile, meaning care has to be taken during purification.[78] This provided an excellent opportunity to test if these poorly-nucleophilic amines could be used in a trans-sulfinylation with TrNSO. Under the conditions used for α-secondary amines, only trace product **37ad** was observed, and a large amount of precipitate, presumably the ammonium-carboxylate salt, formed. Switching the solvent to DCE and substantially increasing the pre-equilibrium time and temperature to 18 h at 80 °C resulted in 50% yield of sulfinamide **37ad**, with just 26% of the trityl product **25a** observed.

The simplest substrate for the trans-sulfinylation reaction would be ammonia, however, thionylimide (HNSO), usually prepared from thionyl chloride and ammonia in the gas phase, rapidly polymerises in its pure form above – 70 °C,[204] and as a result is rarely used, with the majority of studies using it to prepare transition-metal-bonded NSO complexes.[205] We wished to determine whether a primary sulfinamide **37ae** could be prepared via the preparation of a dilute solution of HNSO in our reaction mixture by trans-sulfinylation, followed by radical addition. We were pleased to observe that the use of a 7 M solution of ammonia in methanol gave the primary sulfinamide **37ae** in a moderate 38% yield. Ammonium chloride could also be used with addition of triethylamine; however, the yield was only 9% in this case.

Our previous studies in **Chapter 3** show that radical addition to *N*-sulfinylhydroxylamines can be used to prepare *N*-alkoxysulfinamide products. We wished to determine whether an *O*-alkylhydroxylamine could be used to prepare the *N*-sulfinylhydroxylamine via trans-sulfinylation, and similarly, whether hydrazines could be used to prepare *N*-sulfinylhydrazines. Despite the observed stability of *N*-sulfinylhydroxylamines and *N*-sulfinylhydrozylamines,[193, 206] trans-sulfinylation using *O*-methylhydroxylamine and *N*,*N*-dimethylhydrazine gave poor yields of the corresponding sulfinamide **37af** and **37ag**, even after a longer 18 h pre-equilibration at 60 °C.

Finally, we subjected *p*-toluidine and *p*-anisidine to the reaction conditions, and found that the *N*-arylsulfinamides **37ah** and **37ai** could be prepared in moderate yields, with a higher yield obtained for *p*-anisidine due to its higher basicity.

Table 4.11. Hindered and less-basic amine scope.



Isolated yields. [a] From HCl salt, added NEt_3 (1.1 equiv.). [b] DCE used as solvent, 18 h at 80 °C pre-heating. [c] 18 h pre-heating at 60 °C
Yield of **25a** given in parentheses, calculated by HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

4.2.4 Re-visiting alternative sulfinylamines for poorly yielding amines

It would beneficial to have conditions to prepare the exchange products in improved yields for less-basic, lower-yielding amine examples. Given the influence of the sulfinylamine component on the trans-sulfinylation equilibrium, we decided to explore alternative sulfinylamine reagents in the reaction with poorly-yielding amines.

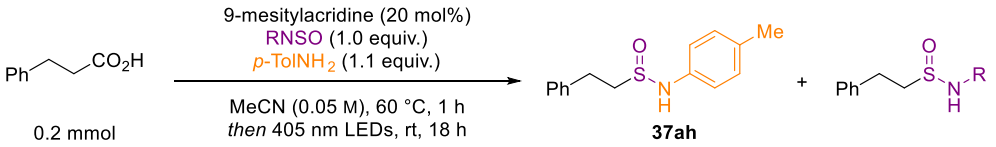
Firstly, we studied *p*-toluidine, which gave 30% yield of the exchange product **37ah** when using TrNSO (**Table 4.12, entry 1**). We studied the equilibrium position for 1:1 mixtures of *p*-toluidine with both MesNSO and *N*-sulfinyl-4-cyano-2,6-dimethylaniline **38b** in $CDCl_3$ by monitoring the ratio of the two sulfinylamines by NMR analysis. It was noted during these studies that after heating at 40 °C overnight, very little trans-sulfinylation occurred using the poorly-nucleophilic *p*-toluidine. Addition of 1.0 equivalent of acetic acid resulted in a significant acceleration of the process, with equilibrium being reached within 1 h at 40 °C for MesNSO. This indicates that acid in our reaction helps catalyse the trans-sulfinylation reaction, as well as acting as the source of alkyl radicals.

At equilibrium, the ratio of *p*-TolNSO:MesNSO was found to be 2:1, whereas for *N*-sulfinyl-4-cyano-2,6-dimethylaniline **38b**, there was a larger proportion of *p*-TolNSO present, with a ratio of 7:1 obtained, although this required overnight heating at 40 °C to establish the equilibrium.

Following these encouraging studies, we used these sulfinylamines in the radical reaction, and were pleased that when using MesNSO, we obtained an improved 50% yield of the exchange sulfinamide **37ah**, as well as 30% of the *N*-mesityl product **39a**, although a longer 18 h reaction time was needed for complete consumption of the carboxylic acid starting material (**Table 4.12, entry 2**).

Using *N*-sulfinyl-4-cyano-2,6-dimethylaniline **38b**, we were surprised to obtain only 27% yield of the exchange product **37ah**, and 55% yield of the nitrile product **39b** (**Table 4.12, entry 3**). Given the longer equilibrium time in the NMR studies, we repeated the reaction with a longer 18 h pre-equilibrium. We obtained an improved 43% yield of exchange product **37ah**, but the 2:1 ratio of the products was still some inconsistent with the 7:1 ratio of the sulfinylamines observed by NMR. Furthermore, the overall yield of the two sulfinamides had decreased, which may indicate that *N*-sulfinyl-4-cyano-2,6-dimethylaniline **38b** is somewhat sensitive under the reaction conditions. Due to this result, no further studies were carried for this system, but we were encouraged that the yield of sulfinamides derived from less-basic amines could be increased by modifying the sulfinylamine.

Table 4.12. Testing a selection of sulfinylamines for trans-sulfinylation using *p*-toluidine.

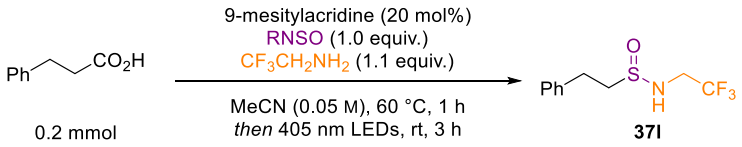


Entry	R =	Yield (%)	
		Sulfinamide 37ah	Sulfinamide 38a or 38b
1[a]	Tr	30	70[b]
2	Mes	50	30
3	4-cyano-2,6-dimethylphenyl	27	55
4[c]	4-cyano-2,6-dimethylphenyl	43	21

[a] 3 h reaction time. [b] Yield calculated by HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard. [c] 24h pre-equilibrium. Isolated yields.

Following these encouraging results, we also decided to carry out further studies using 2,2,2-trifluoroethylamine, which gave only trace product **37l** in the previously optimised conditions (**Table 4.13**). Both TrNSO and MesNSO gave 4% yield of the sulfinamide product **37l** as determined by ^{19}F NMR analysis of the crude reaction mixture (**Table 4.13, entries 1 and 2**). A small boost in yield to 6% was obtained when using *N*-sulfinyl-4-cyano-2,6-dimethylaniline **38b** (**Table 4.13, entry 3**). A solution of TsNSO in dichloromethane was also tested, but only gave 9% yield of the exchange product **37b** (**Table 4.13, entry 4**). One justification for the lower yield with TsNSO may be due to decomposition of TsNSO in the reaction conditions prior to trans-sulfinylation. These yields were still too low to give useful amounts of the desired product. Further efforts to improve the procedure for the synthesis of sulfinamide **37l** are discussed in **Chapter 5**.

Table 4.13. Testing a selection of sulfinylamines for trans-sulfinylation using 2,2,2-trifluoroethylamine to give sulfinamide **37l**.



Entry	R =	Yield (%)
1	Tr	4
2	Mes	4
3	4-cyano-2,6-dimethylphenyl	6
4	Ts	9[a]

[a] CH_2Cl_2 used as solvent, TsNSO added as 0.33 M solution in CH_2Cl_2.
Yields determined by quantitative ^{19}F NMR analysis using 1,4-difluorobenzene as an internal standard

4.2.5 Trans-Sulfinylation Catalysed by Carboxylic Acids

Following the observation that the presence of acid accelerated the rate of trans-sulfinylation using aniline nucleophiles and *N*-sulfinylanilines, we decided to monitor the rate of exchange of TrNSO with *n*-hexylamine with the addition of 1.0 equivalent of acetic acid in order to observe the same accelerated rate. In this study, an equilibrium ratio of 4:1 *n*-HexNSO:TrNSO is reached in 150 mins, whereas in the absence of acid, only 1:1.2 *n*-HexNSO to TrNSO is reached in the same time (**Figure 4.2**). This study therefore confirms that trans-sulfinylation is likely catalysed by the presence of the carboxylic acid substrate, which explains why no further improvement on yield is obtained if pre-equilibrium of longer than 3 hours at room temperature is used.

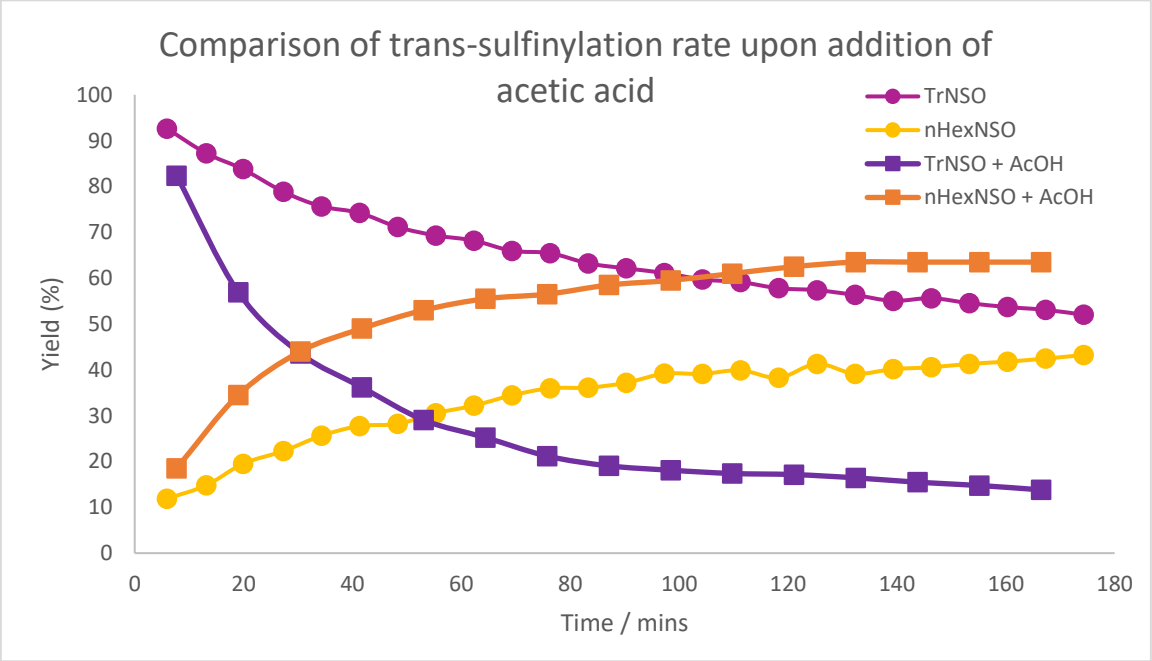


Figure 4.2. Comparison of the rates of trans-sulfinylation for *n*-HexNSO and TrNSO in the presence and absence of 1.0 equiv. acetic acid.

4.2.6 Carboxylic Acid Scope

We then turned to variations on the carboxylic acid radical precursor (**Table 4.14**). We chose *N*-Boc-ethylenediamine as the amine component, as it can be used to introduce a handle for further functionalisation via deprotection to the primary amine.

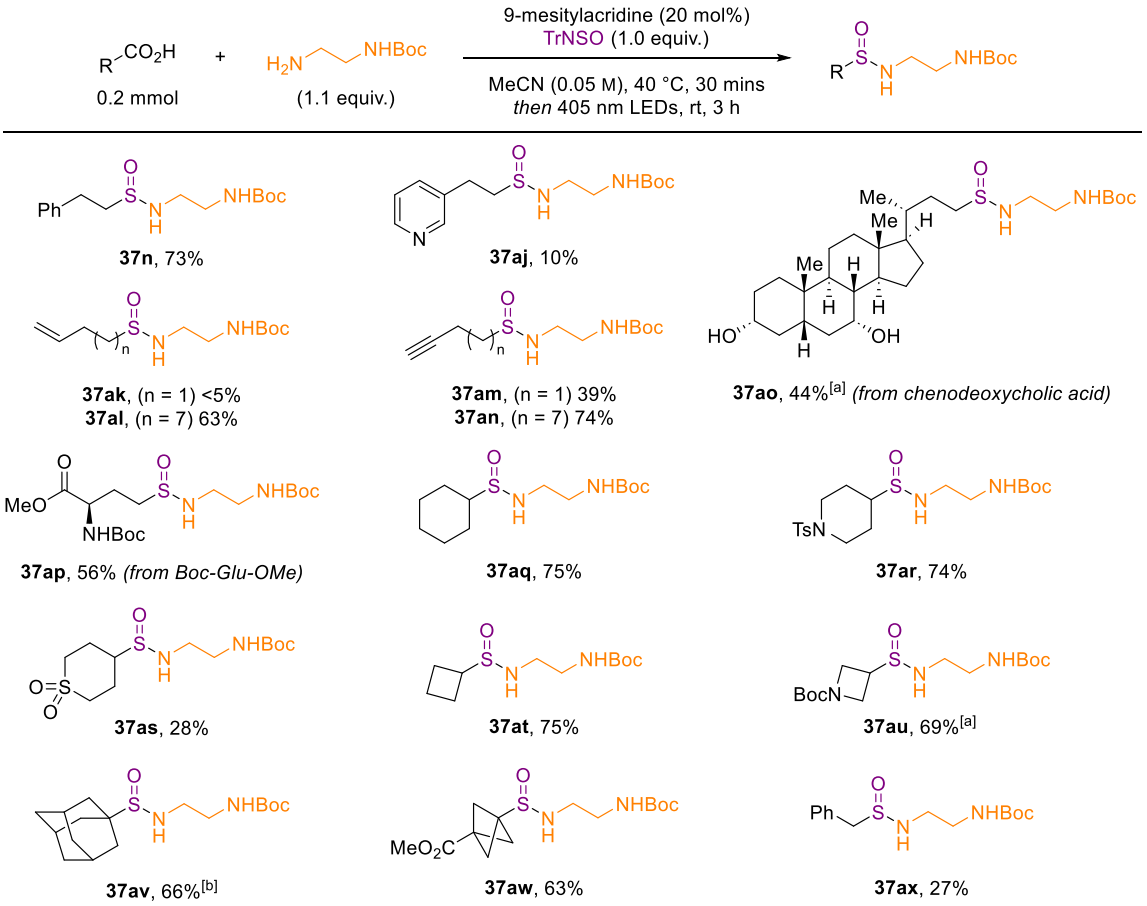
A poor yield was obtained for sulfinamide **37aj**, which we proposed may be due to Minisci-type reactivity of the sulfonimidoyl radical intermediate with the pyridine ring. Similarly, only trace alkene **37ak** was observed, whereas a moderate 39% yield of alkyne **37am** could be isolated. These substrates gave improved yields when preparing *N*-trityl products, so we hypothesised that the bulky trityl group inhibited cyclisation onto the alkene or alkyne in these cases. Instead, we proposed that a longer alkyl chain would result in a slower rate of cyclisation, and we were pleased to find that 10-undecenoic acid and 10-undecynoic acid gave the desired sulfinamide products in 63% and 74% yield, respectively (**37al** and **37an**).

We were also able to demonstrate that densely-functionalised biologically-relevant molecules could be used in this method. The acid side-chain of the protected amino acid Boc-Glu-OMe could be used to prepare sulfinamide **37ap** in good 56% yield and 1:1 dr, and the natural product chenodeoxycholic acid gave the corresponding sulfinamide product **37ao** in a moderate 44% yield and 1:1 dr. Whilst yields were more modest than those obtained using TrNSO, these results demonstrate that this methodology could be used in late-stage functionalisation of a molecule, enabling the exploration of structure-activity relationships dependant on the amine component.

Secondary alkyl substrates **37aq** and **37ar** were obtained in excellent yield, whereas sultone **37as** was obtained in a poor 10% yield. Strained cyclobutyl and azetidine rings could also be used in this reaction to give sulfinamides **37at** and **37au** in good yields. Tertiary alkyl substrates could also be used to obtained adamantyl sulfinamide **37av** and BCP **37aw** in good yields.

Phenylacetic acid could be used to give the corresponding sulfinamide product **37ax** in moderate yield. This lower yield may be due to competing side-reactions of the relatively stable benzyl radical, such as radical recombination, as observed in **Chapters 2 and 3**.

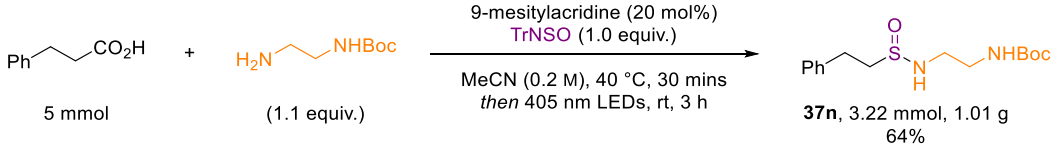
Table 4.14. Carboxylic acid scope



Isolated yields. [a] CH_2Cl_2 used as solvent. [b] MeCN:CH_2Cl_2 (1:1) used as solvent.

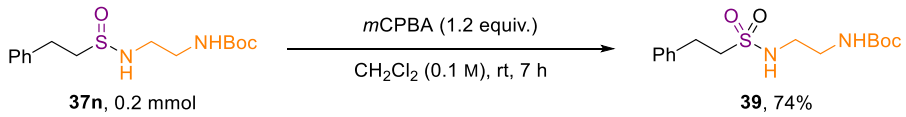
4.2.7 Scale-Up and Sulfinamide Derivatisation

We then wished to assess the scalability of the reaction. To ensure efficient irradiation of the whole reaction mixture, we opted to carry out the reaction at a higher concentration of 0.2 M, instead of the usual 0.05 M, which our optimisation showed had negligible impact on the yield on 0.2 mmol scale. We were pleased to find the reaction worked well for the preparation of sulfinamide **37n** on a 5 mmol scale, albeit with a slight drop in yield to 64% from the 73% yield obtained on 0.2 mmol (**Scheme 4.6**).



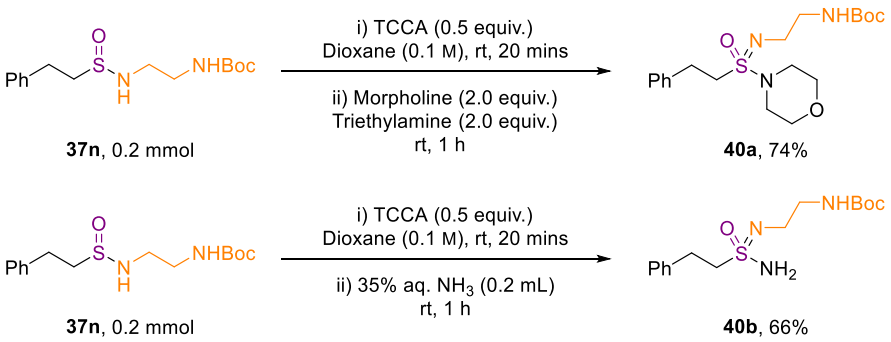
Scheme 4.6. Scale-up reaction.

With over 1 g of sulfinamide **37n** in hand, we explored its utility in the synthesis of a selection of S(VI) products. Firstly, we prepared a sulfonamide via oxidation using *m*CPBA. The product sulfonamide **39** was obtained in 74% yield using identical conditions to those used in **Chapter 3** (**Scheme 4.7**).



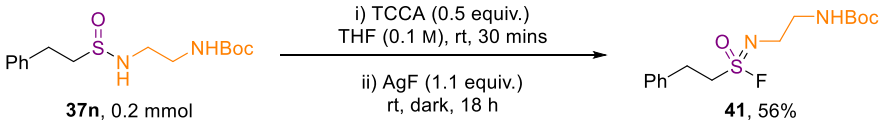
Scheme 4.7. Synthesis of sulfonamide **39** from sulfinamide **37n**.

Sulfonimidamides could be prepared from sulfinamide **37n** via oxidative chlorination to prepare the intermediate sulfonimidoyl chloride, followed by nucleophilic substitution using the appropriate amine. The sulfonimidoyl chloride was readily prepared using TCCA, and subsequent addition of morpholine and triethylamine gave sulfonimidamide **40a** in 74% yield. We also showed that we could prepare primary sulfonimidamide **40b** in 66% yield by treating the same sulfonimidoyl chloride with an aqueous solution of ammonia (**Scheme 4.8**).



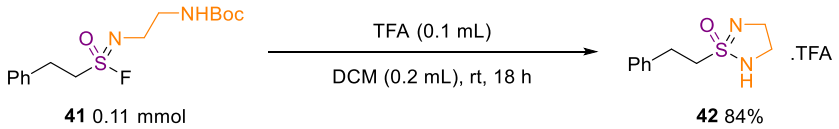
Scheme 4.8. Sulfonimidamide synthesis from sulfinamide **37n** via sulfonimidoyl chloride.

We then turned to the formation of sulfonimidoyl fluorides, via initial preparation of a sulfonimidoyl chloride, again using TCCA, followed by halogen exchange using a nucleophilic fluoride source. Similar to our previous work in **Chapter 3**, as well as work by Bolm and co-workers,[196] silver fluoride was found to be the optimum fluoride source, providing sulfonimidoyl fluoride **41** in 56% yield (**Scheme 4.9**).



Scheme 4.9. Sulfonimidoyl fluoride **41** synthesis from sulfinamide **37n** via sulfonimidoyl chloride.

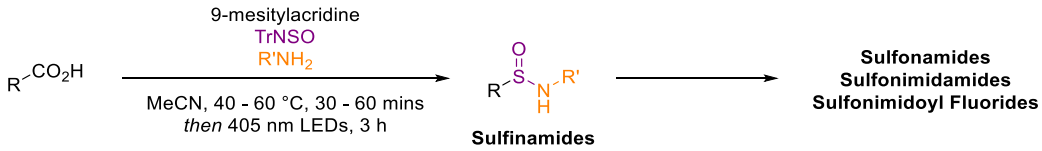
With sulfonimidoyl fluoride **41** available, we were uniquely positioned to prepare a cyclic sulfonimidamide via Boc-deprotection and subsequent nucleophilic substitution of the amine onto the sulfonimidoyl fluoride. There was good precedent for such a reaction, as in a previous report, Boc-protected amines have been deprotected and cyclised with a sulfonyl fluoride in a one-pot procedure using TFA.[207] Using these conditions, we isolated the cyclic sulfonimidamide **42** in 84% yield as the TFA salt (**Scheme 4.10**).



Scheme 4.10. One-pot deprotection and cyclisation to prepare cyclic sulfonimidamide **42** from sulfonyl fluoride **41**.

4.3 Conclusions and future work

In summary, we have developed a route to diverse *N*-alkylated alkyl sulfinamides, derived from in situ trans-sulfinylation to prepare sensitive sulfinylamine reagents, followed by radical addition. This procedure enables the synthesis of these challenging sulfinamide products in one step from commercially available reagents, and enables the synthesis of varied S(VI) products (**Scheme 4.11**).



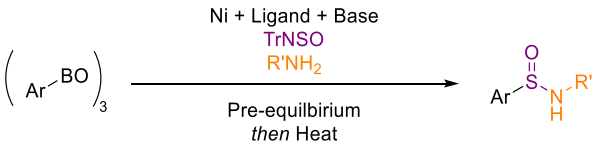
Scheme 4.11. Decarboxylative preparation of diverse *N*-substituted sulfinamides via in situ trans-sulfinylation.

We showed the versatility of this reaction using diversely functionalised primary amines, and developed conditions for its use with α-primary, α-secondary and α-tertiary amines, as well as anilines

and even ammonia. We also demonstrated the use of varied carboxylic acids, with a particular focus on the use of densely-functionalised, biologically relevant molecules, with the notion that this procedure could be used in a medicinal chemistry context for late-stage functionalisation of a carboxylic acid, enabling exploration of SAR with varied amine components (or vice versa).

We showed preliminary data suggesting that the yield of lower-yielding examples could be improved by changing the sulfinylamine reagent. Further studies could focus on optimising the reactions using these reagents, which would further expand the compounds accessible using this reaction.

Applying trans-sulfinylation to other reactions would also be highly valuable. Previous work within the Willis group has demonstrated the preparation of sulfinamides by a nickel-catalysed coupling of aryl boroxines with TrNSO.[87] Addition of an equivalent of primary amine may enable trans-sulfinylation prior to coupling with the boroxine, enabling access to varied aryl sulfinamides (**Scheme 4.12**). This proposed reaction presents several challenges, such as water sensitivity (given the sensitivity of the reaction with TrNSO), as well as whether the additional equivalent of primary amine would be tolerated, and whether a competing Chan-Lam-type couplings of the boroxine with the primary amine could be avoided. However, this still presents an excellent opportunity to showcase the potential of trans-sulfinylation as a useful method to prepare diversely *N*-alkylated S(IV) and S(VI) products.



Scheme 4.12. Proposed one-pot preparation of diversely *N*-alkylated aryl sulfinamides via trans-sulfinylation followed by nickel-catalysed coupling with aryl boroxines.

Chapter 5 - Studies Towards New Sulfinylamine Reagents

5.1 Introduction

Whilst the use of new, more hydrolytically stable sulfinylamines has enabled the development of many useful methodologies for the preparation of sulfur (IV) and (VI) products,[73] there are still some benefits to the use of more reactive, more hydrolytically-sensitive sulfinylamines, such as *N*-sulfinylsulfonamides, *N*-sulfinylcarbamates, *N*-sulfinylamides and *N*-sulfinylsulfamides (**Figure 5.1**).

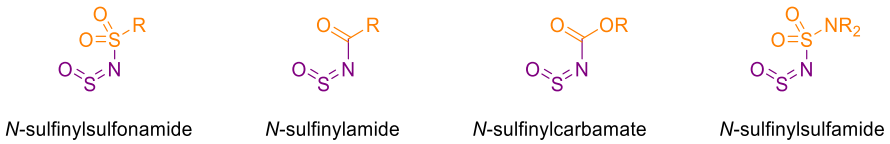
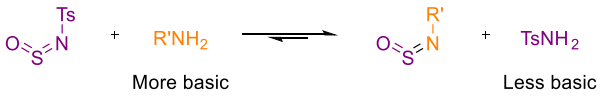


Figure 5.1. Electron-poor sulfinylamines.

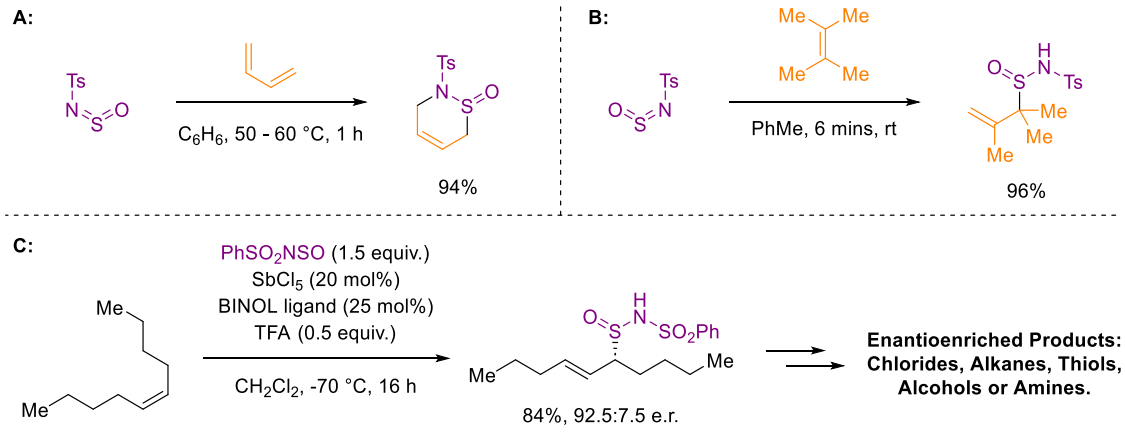
Firstly, as discussed in **Chapter 4**, *N*-sulfinylsulfonamides are excellent trans-sulfinylation reagents, enabling the preparation of challenging sulfinylamines, even those derived from poorly basic primary amines, in high yields (**Scheme 5.1**).[72b] Preparing these sulfinylamines in high yields may have benefits for future applications of trans-sulfinylation in the preparation of S(IV) and S(VI) products.



Scheme 5.1. Amine exchange using TsNSO.

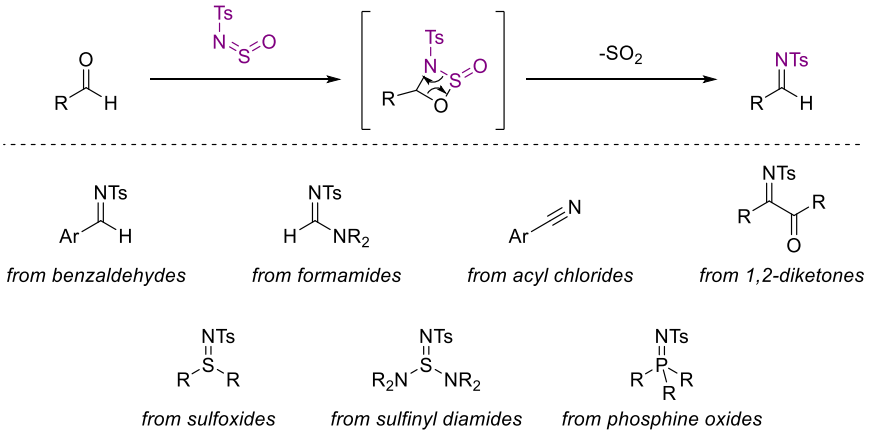
The reactivity of electron-poor sulfinylamines such as *N*-sulfinylsulfonamides enables other modes of reactivity that are either substantially slower or do not happen with sulfinylamines derived from anilines or alkyl amines. These methods could prove useful in modern chemistry, such as the use of hetero Diels-Alder cycloadditions to prepare interesting heterocyclic scaffolds,[72, 76] (**Scheme 5.2.A**) or ene reactions to prepare versatile allyl sulfinamide products

(**Scheme 5.2.B**).[93] The chiral Lewis acid-catalysed ene reactions developed by Tambar and co-workers demonstrates the potential applications of these reactive sulfinylamines in the preparation of various enantioenriched products from olefins (**Scheme 5.2.C**).[97]



Scheme 5.2. Hetero-Diels-Alder reactions using sulfinylamines.

The preparation of imine derivatives of carbonyl, sulfinyl or phosphine oxide functional groups is also a useful transformation that hasn't been well-utilised (**Scheme 5.3**).[14c, 72b, 98]



Scheme 5.3. Preparation of imine derivatives of carbonyl, sulfinyl or phosphine oxide functional groups.

The application of the unique and diverse chemistry associated with electron-poor sulfinylamines is limited by the challenges associated with their preparation, long-term storage and use due to their moisture sensitivity. This chapter discusses preliminary studies towards the preparation of more-stable analogues or precursors of these important reagents.

5.2 Stabilisation via the Formation of Intramolecular Charge-Transfer Complexes

5.2.1 Introduction

Sulfur dioxide readily forms stable charge-transfer complexes with electron-donors such as primary amines. The formation of such charge-transfer complexes such as DABSO has enabled the use of sulfur dioxide in organic synthesis whilst avoiding the challenges associated with handling the toxic gaseous reagent.[47, 49]

The analogous formation of stable charge-transfer complexes between amines and sulfinylamines could be an attractive solution to the sensitivity of sulfinylamine reagents. Coordination of an electron-donor to the sulfur centre of the sulfinylamine would reduce the partial positive-charge, which could decrease its reactivity with nucleophiles such as water (**Figure 5.2**).

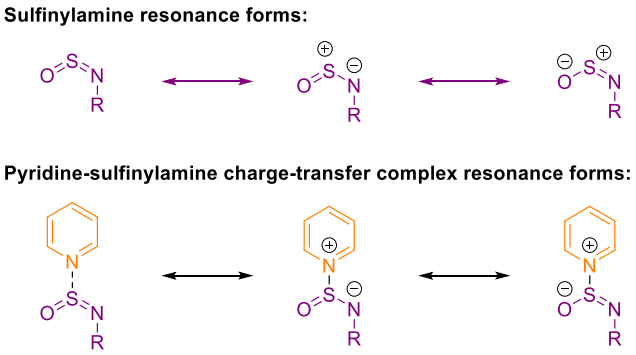
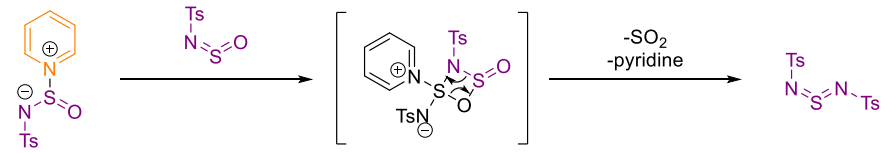


Figure 5.2. Resonance structures of sulfinylamines and their charge-transfer complexes.

In practice, there are no isolated examples of stable charge-transfer complexes of sulfinylamines. The formation of charge-transfer complexes between *N*-sulfinylanilines and pyridines has been observed spectroscopically by ^{17}O NMR studies, where a shift in the sulfinylamine oxygen peak is attributed to coordination of the pyridine nitrogen to sulfur.[208] The oxygen peak was also found to be insensitive to substitution on the aryl ring, which is justified by the complexation of pyridine interrupting the conjugation of the oxygen with the aryl ring.

Interactions of electron-poor sulfinylamines, such as *N*-sulfinylsulfonamides, with tertiary amines or pyridine results in the formation of the corresponding sulfurdiimide from two equivalents of the sulfinylamine, with loss of SO_2.[116] Whilst the mechanism of this transformation has not been well-studied, the structural similarity of the pyridine-sulfinylamine charge-transfer complex to sulfinyl diamides, which form the imine analogue following reaction with *N*-sulfinylsulfonamides, indicate that this charge-transfer complex may be mechanistically important (**Scheme 5.4**).



Scheme 5.4. Proposed mechanism for sulfurdiimide synthesis from sulfinylamines via formation of a pyridine-sulfinylamine charge-transfer complex.

We wished to determine whether we could prepare electron-poor sulfinylamines functionalised with a pendant electron-donating group, such as a tertiary amine or pyridine. Our hypothesis was that if such sulfinylamines could be prepared, coordination of the electron-donating group would enable the formation of an intramolecular charge-transfer complex, which would stabilise the sulfinylamine by electron-donation to the electrophilic sulfur atom.

Formation of these intramolecular charge-transfer complexes would require the sulfinylamine to switch from the generally preferred *Z*-configuration,[209] stabilised by donation of the N-lone pair into the S-O σ* orbital and donation of the S-lone pair into the N-R σ* orbital,[86] to the less-favoured *E*-conformation, which has been inferred as the reactive component in some reactions,[210] and which we propose would be stabilised by the charge-transfer complex formation (**Figure 5.3**).

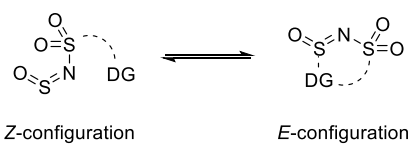
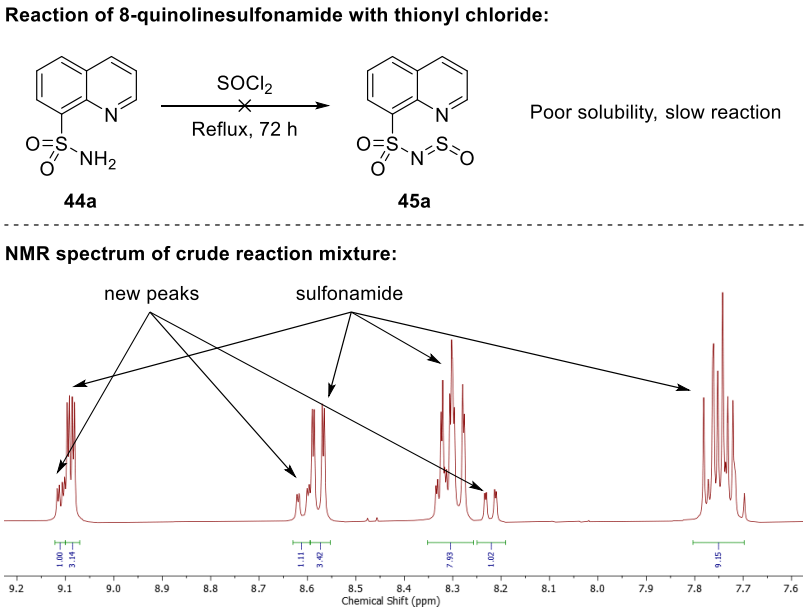


Figure 5.3. Configurations of proposed sulfinylamines functionalised with pendant electron-donating functional groups.

If these proposed sulfinylamines could be prepared, and were stable, we aimed to determine whether they could be used in similar reactions to other electron-poor sulfinylamines, owing to the reversible nature of the charge-transfer complex formation.

5.2.2 Results and Discussion

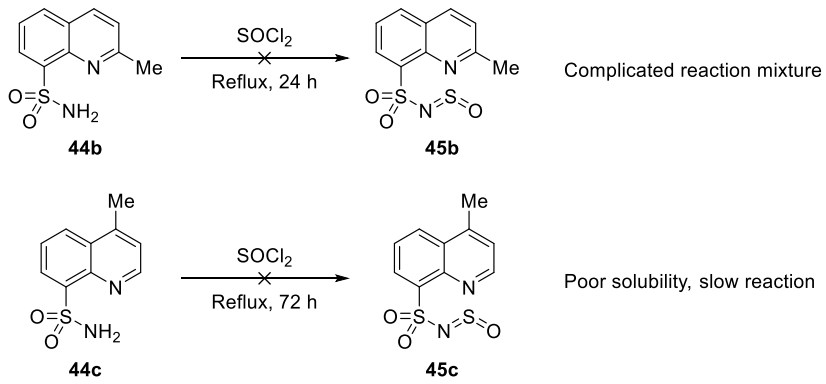
We expected that a 6-membered ring would enable the most favourable interaction between the electron-donor and the sulfinylamine, so we began our studies by preparing 8-quinolinesulfonamide **44a** from the commercially available 8-quinolinesulfonyl chloride **43a**. Upon refluxing the sulfonamide in thionyl chloride new peaks were observed in the NMR spectra of the crude reaction mixture, however, conversion was very slow, reaching a ratio of 3:1 starting material to product after 24 hours (**Scheme 5.5**). Even after 72 hours, the reaction had only reached a ratio of 1:1, and efforts to isolate the product **45a** from the starting material were unsuccessful.



Scheme 5.5. Attempted synthesis of (*N*-sulfinyl)-8-quinolinesulfonamide and NMR spectrum of the crude reaction mixture.

We noticed that 8-quinolinesulfonamide had very poor solubility in the reaction mixture. In order to improve the solubility, we explored alkyl substitution on the quinoline ring (**Scheme 5.6**). The sulfonamides **44b** and **44c** were prepared from the corresponding sulfonyl chlorides **43b** and **43c**, which were readily prepared by chlorosulfonylation of the quinoline starting materials. Methyl

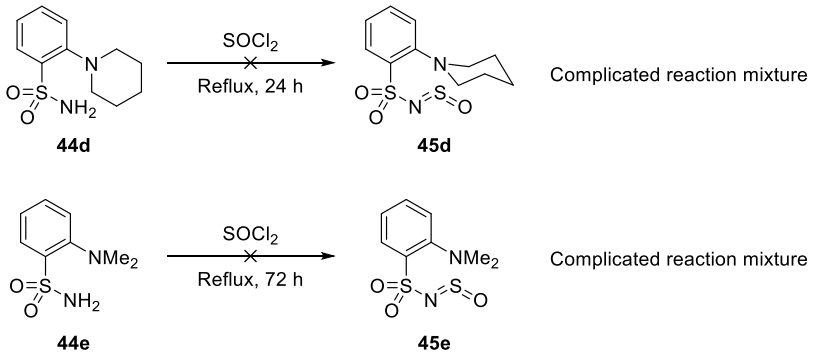
substitution in the 2-position (**44b**) resulted in improved solubility, but reaction with thionyl chloride gave a complicated reaction mixture, and no products could be isolated. The 4-methyl-substituted analogue (**44c**) was also found to have poor solubility, and whilst new peaks were observed upon reaction with thionyl chloride, a ratio of just 3:1 starting material to product was obtained after 72 hours.



Scheme 5.6. Attempted synthesis of methylated analogues of (*N*-sulfinyl)-8-quinolinesulfonamide.

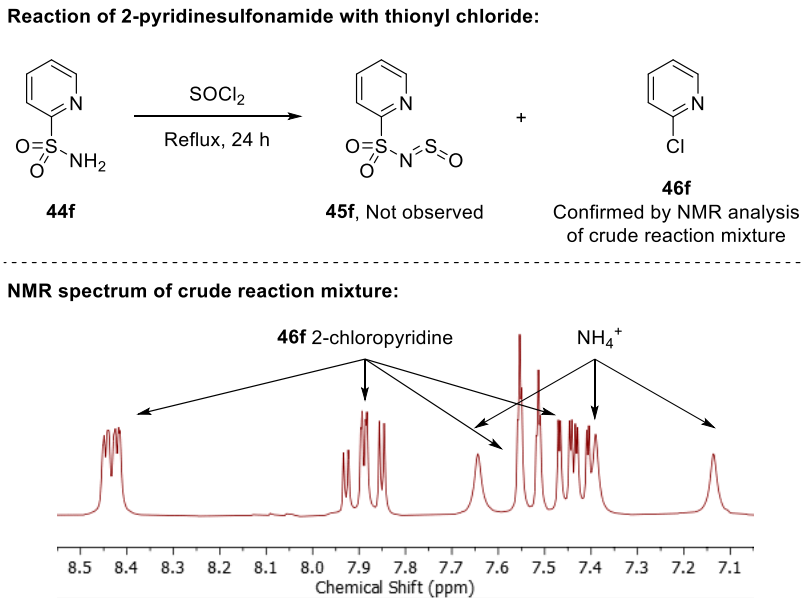
These studies demonstrated that the use of the 8-quinolinesulfonamides scaffold was not practical for the formation of the corresponding sulfinylamines. Whilst alternative substitution, or even alternative heterocycles could be explored, substrate preparation was a limiting factor.

To explore alternative electron-donors, we prepared benzene sulfonamides substituted with tertiary amines in the 2-position (**44d** and **44e**). These examples showed improved solubility compared to the quinoline examples, and showed full consumption of starting material, but the crude reaction mixtures were complicated and no sulfinylamine products could be identified (**Scheme 5.7**).



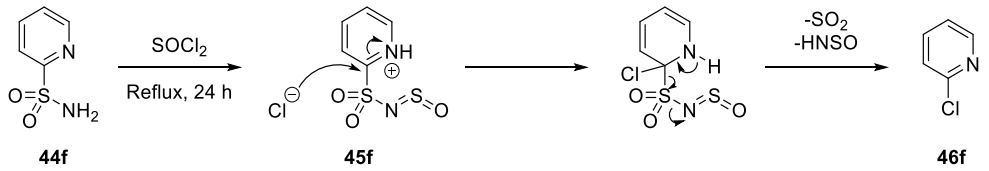
Scheme 5.7. Attempted synthesis of sulfinylamines from 2-aminobenzenesulfonamides.

We then opted to explore 2-pyridinesulfonamides, which would form a 5-membered intramolecular charge-transfer complex. Refluxing 2-pyridinesulfonamide **44f** in thionyl chloride resulted in complete consumption of starting material, and gave clean conversion to a new product. We were surprised however to observe peaks consistent with an ammonium salt, in the form of a triplet at 7.4 ppm. Further analysis demonstrated that the product was not the desired *N*-sulfinylsulfonamide **45f**, but was in fact 2-chloropyridine **46f**, verified by spiking the NMR sample with an authentic sample of 2-chloropyridine (**Scheme 5.6**).



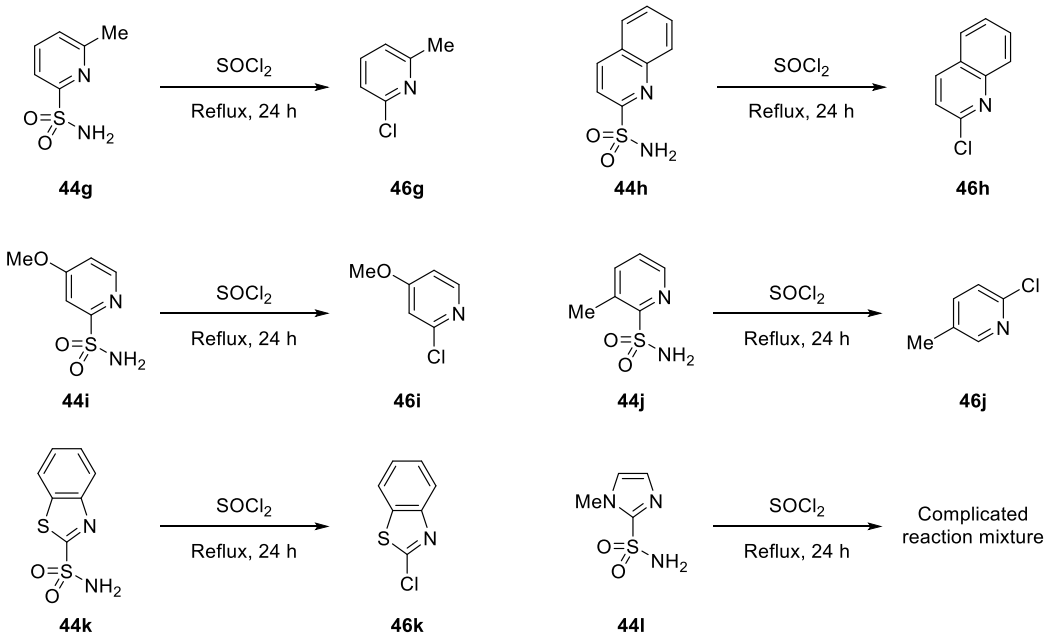
Scheme 5.6. Reaction of 2-pyridinesulfonamide **44f** with thionyl chloride to give 2-chloropyridine **46f** and NMR spectrum of the crude reaction mixture.

The mechanism for this unusual transformation is unclear, but we propose that the initial formation of the *N*-sulfinylsulfonamide **45f** occurs in the reaction, and subsequent addition of chloride ipso to the sulfinylsulfonamide in an S_NAr-type mechanism, likely mediated by protonation of the pyridine,[211] results in the loss of sulfur dioxide and a thiazate anion (NSO^-), which would be protonated to give HNSO (**Scheme 5.7**). The hydrolysis of HNSO could then explain the formation of the observed ammonium salt.



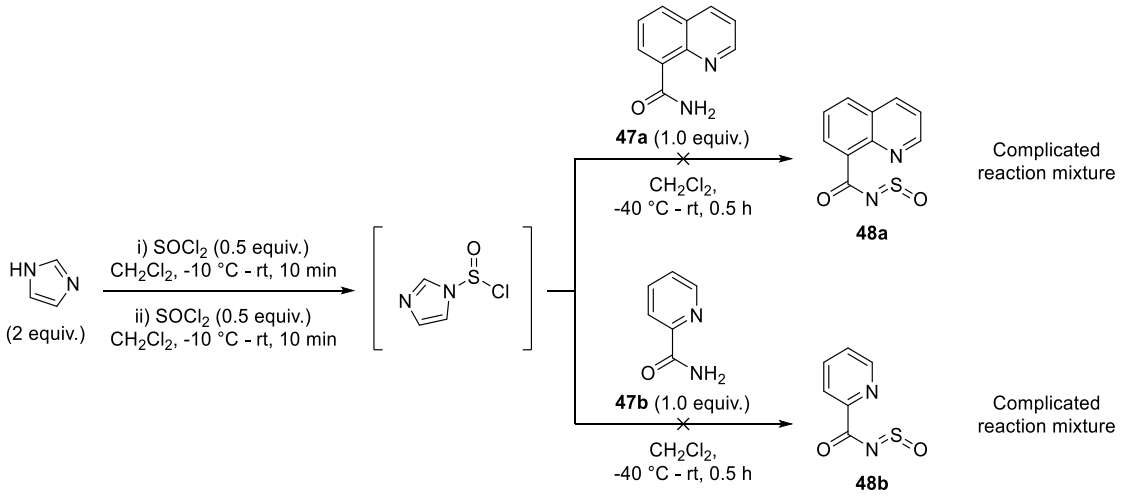
Scheme 5.7. Proposed mechanism for 2-chloropyridine synthesis from 2-pyridinesulfonamide.

Other analogues of 2-pyridinesulfonamide also formed the corresponding chlorides, all verified by spiking the crude NMR sample with an authentic sample of the 2-chloropyridine product (**Scheme 5.8**). We proposed that electron-donating functional groups would hinder the S_NAr substrate, but found that 2-chloro-4-methoxypyridine **46i** was formed from the corresponding sulfonamide **44i**. Surprisingly, addition of a methyl substituent to the 3-position of the sulfonamide (**44j**) resulted in addition of chloride in the 6-position rather than the 2-position as would be expected by an S_NAr-type mechanism (**46j**). This may indicate that an alternative mechanism is operating in this case. We also carried out the reaction with 2-benzothiazolesulfonamide **44k** and 1-methyl-1*H*-imidazole-2-sulfonamide **44l**. The benzothiazole example gave the corresponding chloride **46k** (verified by NMR analysis), whereas the imidazole gave a complicated reaction mixture.



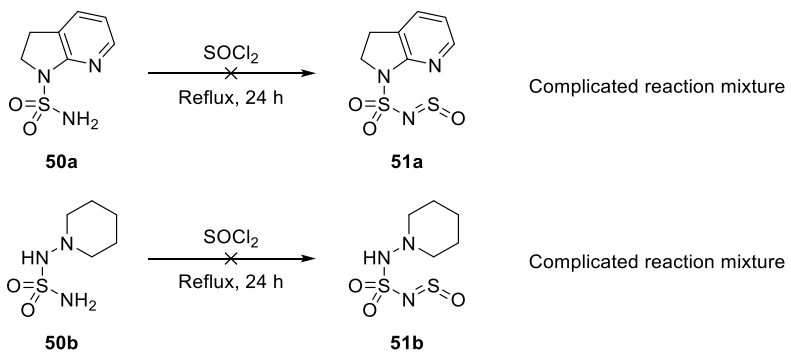
Scheme 5.8. Reaction of analogues of 2-pyridinesulfonamide with thionyl chloride to give the corresponding chlorides.

We also explored the use of *N*-sulfinylamides, the preparation of which generally requires milder conditions than those used for *N*-sulfinylsulfonamides, as decomposition is usually observed when using classical conditions.[212] Reactions of both 8-quinoline-carboxamide **47a** and picolinamide **47b** with *N*-(chlorosulfinyl)imidazole, a reagent that can be used for the preparation of *N*-sulfinylamides at room temperature,[78] gave complicated reaction mixtures, and the corresponding sulfinylamines could not be identified or isolated (**Scheme 5.9**).



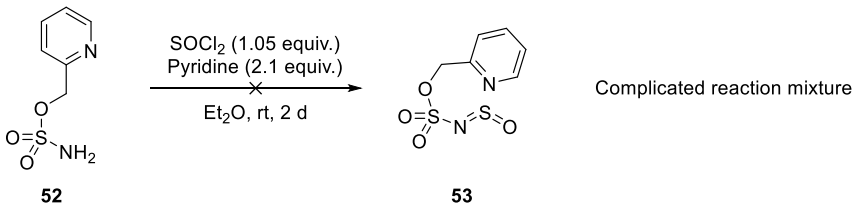
Scheme 5.9. Attempted synthesis of *N*-sulfinylamides.

N-Sulfinylsulfamides can also be prepared using similar conditions to those used to make *N*-sulfinylsulfonamides.[213] Sulfamides **50a** and **50b** were prepared using hexafluoroisopropyl sulfamate (HFIPS) **49** and 7-azaindoline and 1-aminopiperidine respectively.[214] Both examples, upon reaction with thionyl chloride at reflux, gave complicated reaction mixtures, and the corresponding sulfinylamines could not be identified or isolated (**Scheme 5.10**).



Scheme 5.10. Attempted synthesis of *N*-sulfinylsulfamides.

We postulated that the 2-pyridine analogue of benzylcarbamate, prepared from reaction of benzyl alcohol with (trimethylsilyl)isocyanate, could form a 7-membered intramolecular charge-transfer complex. The conditions used to prepare CbzNSO gave a complicated reaction mixture when using carbamate **52**,[215] and the *N*-sulfinylcarbamate **53** could not be identified (Scheme **5.11**).



Scheme 5.11. Attempted synthesis of *N*-sulfinylcarbamate.

5.2.3 Conclusions

Whilst several variations in electron-donor and sulfinylamine functional group were explored, no examples of the corresponding sulfinylamines could be isolated, and therefore no data on the feasibility of stabilising the sulfinylamine by charge-transfer complex formation could be obtained. Whilst further permutations of some of these ideas could be studied, the synthesis of substrates could become restrictive. As a result, alternative approaches to enabling the use of electron-poor sulfinylamines need to be considered.

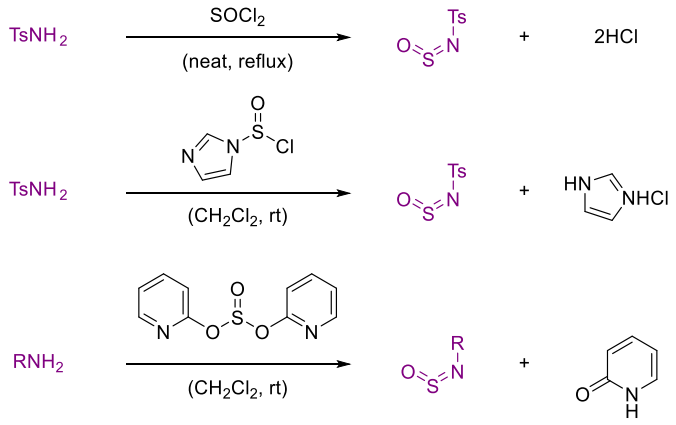
5.3 In-situ Generation of *N*-Sulfinylsulfonamides via a Retro-Ene Reaction

5.3.1 Introduction

Our previous studies into the formation of intramolecular charge-transfer complexes in order to stabilise these electron-poor sulfinylamines were unsuccessful, giving complex reaction mixtures or undesired products. Instead, we considered that the preparation of *N*-sulfinylsulfonamides in situ would be a more practical alternative.

Due to the poor nucleophilicity of primary sulfonamides, harsh conditions or highly electrophilic reagents are usually needed to prepare the corresponding *N*-sulfinylsulfonamides. Reaction with thionyl chloride also liberates HCl, which we proposed

would be detrimental for many reactions, so we concluded that in situ preparation of *N*-sulfinylsulfonamides using this method would not be practical. In situ preparation using alternative electrophiles such as *N*-(chlorosulfinyl)imidazole or di-2-pyridyl sulfites was also considered, as these reagents can be used under milder conditions and do not liberate HCl, but these reagents are also moisture sensitive so may not be amenable to long-term storage (**Scheme 5.12**).[78-79]

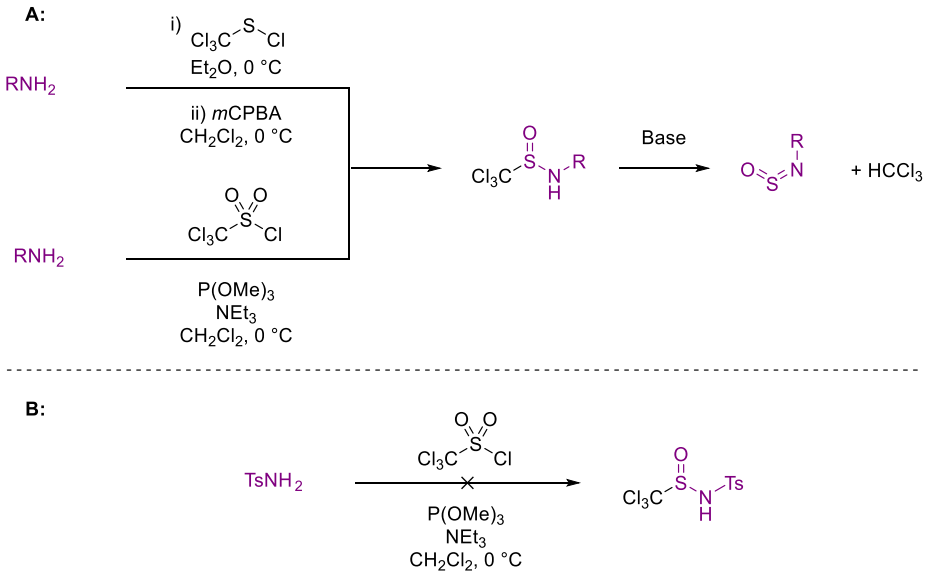


Scheme 5.12. Conditions for the preparation of TsNSO using thionyl chloride or other electrophiles.

We instead proposed that the use of alternative, bench-stable precursors that could liberate the sulfinylamine reagent without the need for nucleophilic addition of the primary sulfonamide would provide a more practical method for their in-situ preparation.

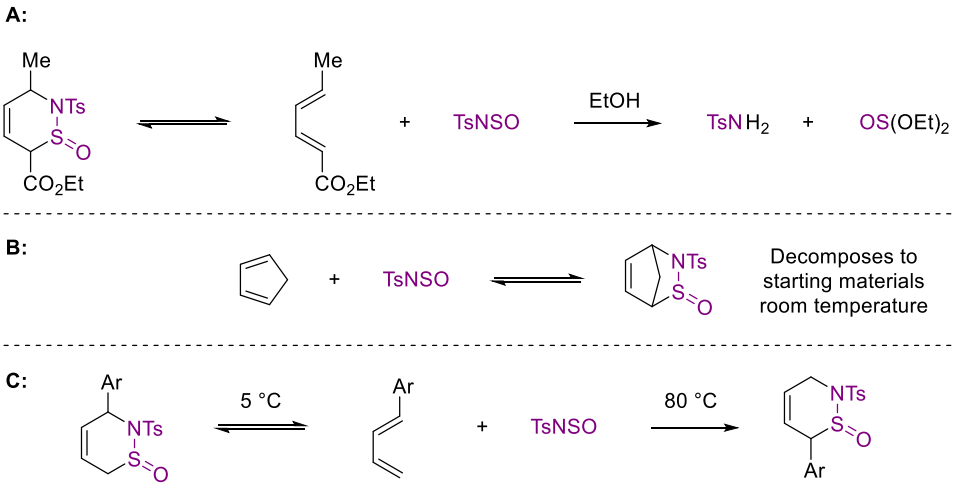
One appealing approach for the in-situ preparation of sulfinylamines was developed by Braverman and co-workers. In this work, base-induced β-elimination of chloroform from trichloromethanesulfinamides quantitatively generates sulfinylamines, which were then used in subsequent Diels-Alder reactions (**Scheme 5.13.A**).[216] These trichloromethanesulfinamides could be prepared by two different routes, and could be readily purified by column chromatography. However, this method was only demonstrated using a small selection of anilines and primary amines, and no examples of electron-poor sulfinylamines were prepared. Unfortunately, we were unsuccessful in preparing the *N*-tosyl sulfinamide using trichloromethylsulfonyl chloride, which we attributed to the decomposition

of the acidic sulfinamide product under the basic reaction conditions (**Scheme 5.13.B**). Trichloromethylsulfenyl chloride is a restricted chemical, meaning alternative methods for the preparation of the sulfinamide could not be explored.



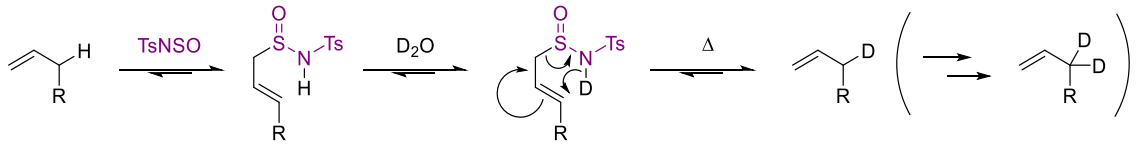
Scheme 5.13. A): Sulfinylamine synthesis via β-elimination of chloroform from trichloromethanesulfinamides. **B):** attempted application to TsNSO.

An alternative approach to sulfinylamines involves their well-established reactivity in cycloaddition reactions. The Diels-Alder reaction of *N*-sulfinylsulfonamides has been shown to be reversible in some cases, for example, Kresze and co-workers demonstrated that the adduct derived from ethyl sorbate and TsNSO was shown to decompose to its starting materials upon heating in ethanol, resulting in the formation of diethylsulfite (**Scheme 5.14.A**).[72a] Furthermore, they also found that the adduct formed from reaction of TsNSO with cyclopentadiene was found to only be isolable at low temperatures, decomposing back to the reactants at room temperature (**Scheme 5.14.B**). Finally, reaction of 1-arylbutadienes with TsNSO at low temperatures gives the kinetic product, whereas heating the reaction gives the regioisomeric thermodynamic product, where the steric hinderance between the Ar and Ts substituents are minimised (**Scheme 5.14.C**).[72b]



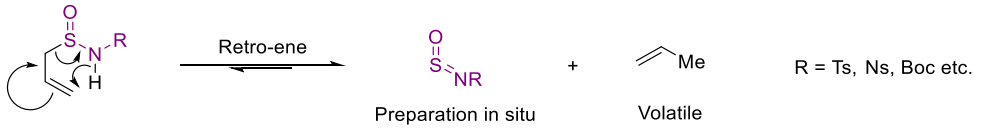
Scheme 5.14. Examples of reversible formation of Diels-Alder adducts of TsNSO.

Ene-reactions of *N*-sulfinylsulfonamides have also been shown to be reversible. Sharpless and co-workers observed that the ene-adduct of β-pinene and TsNSO slowly decomposed back to β-pinene over a few days in moist air or upon heating. This process was applied to enable allylic deuteration or tritiation via addition of either D_2O or T_2O which exchange with the sulfinamide proton, and subsequent heating results in a retro-ene reaction giving the deuterated or tritiated olefin (**Scheme 5.15**). Even in the presence of D_2O or T_2O, which would rapidly hydrolyse the TsNSO by-product, multiple deuterations or tritiations are sometimes observed owing to multiple forward and reverse ene-reactions.



Scheme 5.15 Allylic deuteration via the reversible formation of ene-adducts.

The reversibility of these reactions established the hypothesis that cycloaddition adducts could be used to liberate sulfinylamines for use in other reactions. We initiated our studies with the retro-ene reaction, as we proposed that the use of volatile alkenes may favour the liberation of the sulfinylamine (**Scheme 5.16**).



Scheme 5.16. Proposed retro-ene strategy to prepare hydrolytically unstable sulfinylamines.

5.3.2 Results and Discussion

In order to test our proposed strategy, we chose *N*-tosyl allyl sulfinamide **55a** as a model substrate, which would liberate TsNSO and propylene. We proposed several routes for the preparation of these sulfinamides that would avoid the use of TsNSO.

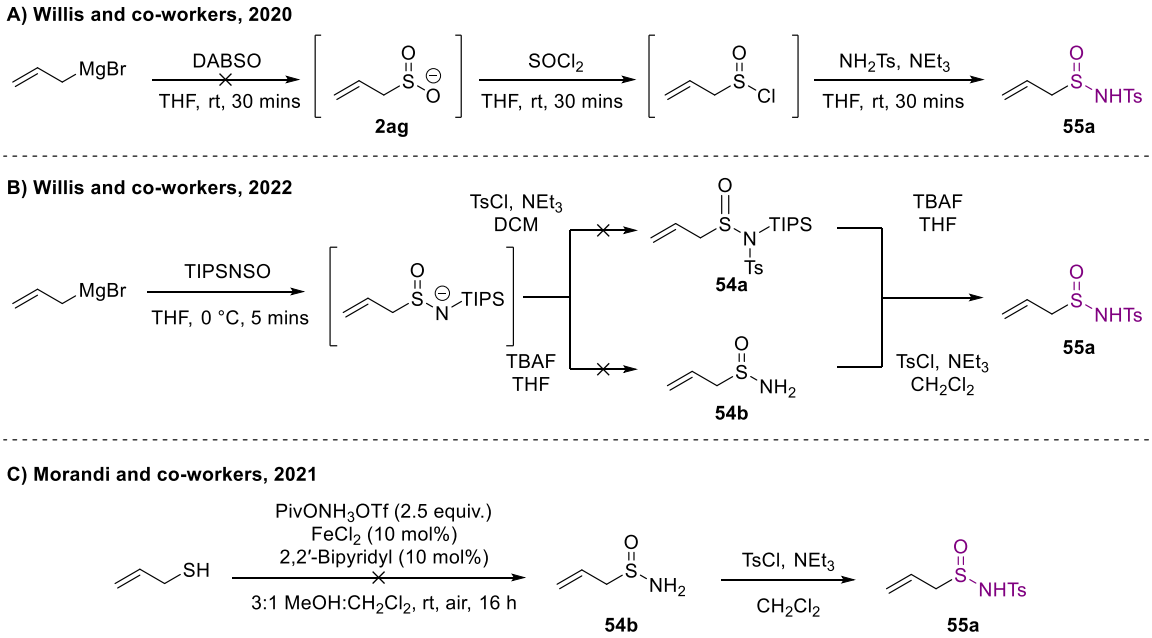
Our first route involved the initial preparation of allyl sulfinate **2ag** from allyl Grignard addition to DABSO.[48h] Subsequent in situ sulfinyl chloride preparation using $SOCl_2$ and reaction with *p*-methylphenylsulfonamide would then give the desired sulfinamide **55a** (**Scheme 5.17.A**). Previous studies in the Willis group have shown allyl sulfinates to be challenging substrates, and poor yields are often obtained for reactions involving its preparation. Consistent with these findings, no product was obtained for reactions carried out using this route.

An alternative route involves the addition of allyl Grignard to TIPSNSO.[26] Subsequent protection TIPS deprotection followed by Ts protection would give the desired sulfinamide products (**Scheme 5.17.B**). The TIPS-protected sulfinamide was generated smoothly from reaction with allyl Grignard, verified by NMR analysis of the crude reaction mixture, but only traces of the desired primary sulfinamide **54b** product was observed upon deprotection using TBAF. Instead, we proposed that initial protection with TsCl followed by TIPS protection may provide a good alternative, but the TIPS-protected sulfinamide was found to be unreactive under a variety of conditions, and with a variety of alternative protecting groups, likely due to steric hinderance.

Both of the previous routes involve the formation of anionic allyl S(IV) intermediates. Allyl sulfoxides undergo [2,3]-rearrangements to form allyl sulfenates in a Mislow–Braverman–

Evans rearrangement.[217] Similar rearrangements of allyl sulfinates or allyl sulfinamide anions may explain their poor stability and therefore the poor yields of the corresponding sulfinamide products in these reactions.

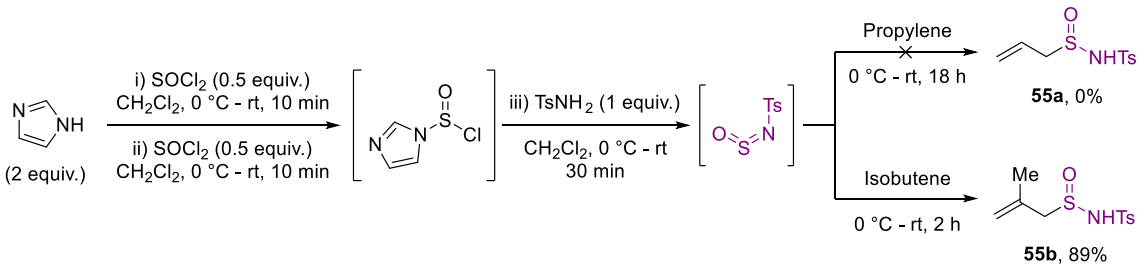
An alternative preparation of primary sulfinamides via iron-catalysed amino-oxidation of thiols was developed by Morandi and co-workers.[218] This route avoids the generation of anionic sulfinamide intermediates, and was used by Morandi to prepare the desired primary allyl sulfinamide **54b** in a moderate 45% yield from allyl thiol. Unfortunately, we were unable to reproduce this yield, and <5% was obtained in all cases (**Scheme 5.17.C**).



Scheme 5.17. Proposed routes to *N*-tosyl sulfinamides.

Following these unsuccessful preparations of the desired allyl sulfinamides, we resorted to their preparation via an ene reaction with TsNSO. TsNSO was prepared from *N*-(chlorosulfinyl)imidazole, but sparging the resulting crude reaction mixture with propylene failed to give the allyl sulfinamide product **55a**. However, isobutene gas successfully gave the corresponding ene adduct **55b** in 89% yield (**Scheme 5.18**). This ene-adduct was isolated from solution with ~20% $TsNH_2$ impurity. Column chromatography was found to be unsuitable for purification of this ene adduct, as substantial product degradation was observed. It was unclear

whether it was resulting in hydrolysis, or a [2,3]-rearrangement. Recrystallisation to give product with <5% $TsNH_2$ impurity was possible, but care was needed to prevent degradation upon heating. The ene-adduct **55b** was found to be a stable solid under ambient conditions, which could be weighed into reactions without the concern of hydrolysis, and could be stored in a freezer under air for several months without degradation.



Scheme 5.18. Preparation *N*-tosyl allyl sulfinamides via ene reaction of TsNSO.

Upon NMR analysis of ene adduct **55b** in $CDCl_3$, we were pleased to observe the degradation of the sulfinamide, and the appearance of peaks consistent with isobutene (**Figure 5.4**).

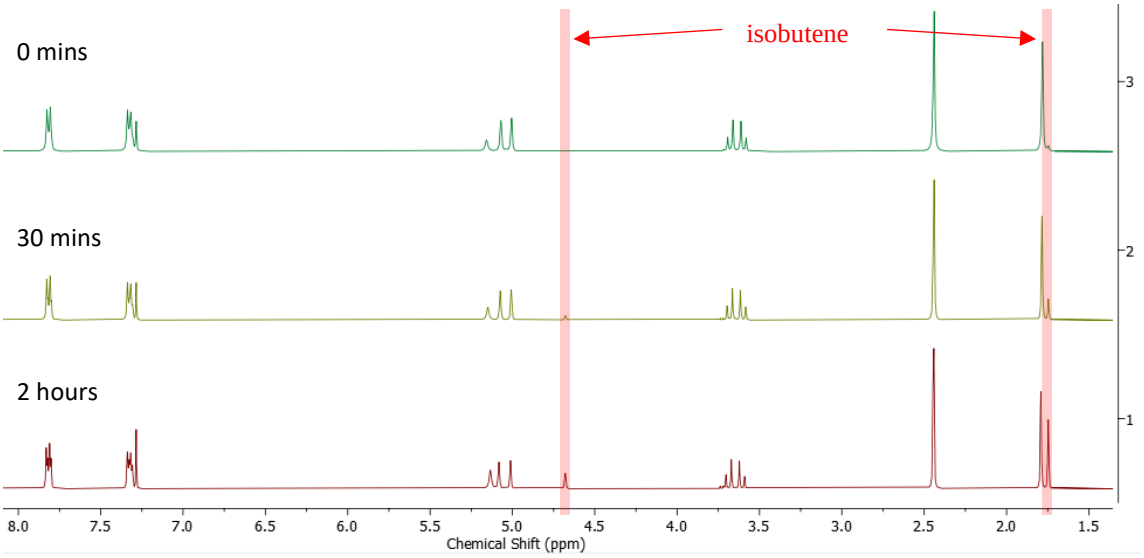
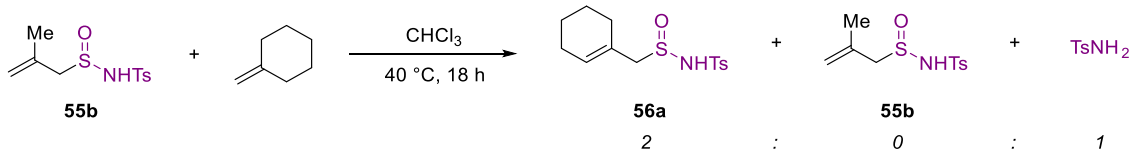


Figure 5.4. NMR of ene adduct **55b** showing liberation of isobutene.

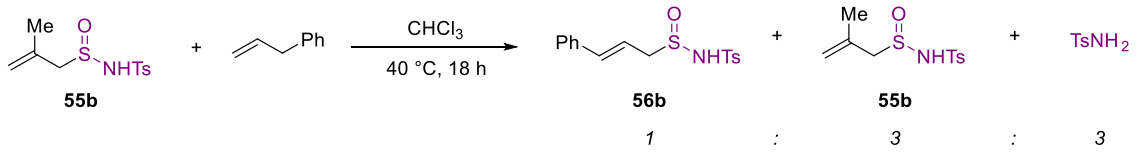
With the observation that ene-adduct **55b** liberates isobutene under mild conditions, we wished to determine whether we could utilise the liberated TsNSO in a reaction, such as an ene-reaction with a more reactive olefin. We added methylene cyclohexane to a solution of ene-adduct **55b** in chloroform and heated the reaction mixture to 40 °C overnight. ^{1}H NMR

analysis of the crude reaction mixture showed complete consumption of ene-adduct **55b** and formation of the new ene adduct **56a** and $TsNH_2$ in a 2:1 ratio (**Scheme 5.19**).



Scheme 5.19. Transfer-ene reaction using methylene cyclohexane and ene adduct **55b**.

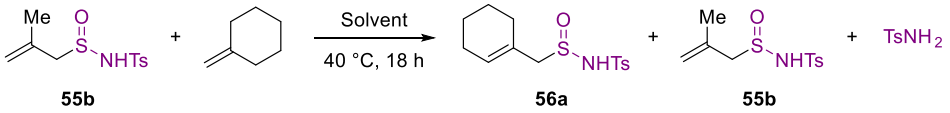
To determine whether the volatility of isobutene could enable the transfer ene-reaction with a less reactive olefin, we repeated the above experiment with allylbenzene. In this reaction, both allylbenzene and isobutene adducts **56b** and **55b** were observed in a 1:3 ratio (**Scheme 5.20**). It is likely that due to its high solubility, isobutene reacts with TsNSO in competition with the less-reactive allylbenzene.



Scheme 5.20. Transfer-ene reaction using allylbenzene and ene adduct **55b**.

For this chemistry to find application in other reactions, we needed to explore the solvent-dependence of the transformation. A selection of 6 solvents with varied properties were tested in the transfer-ene reaction with methylene cyclohexane (**Table 5.1**). Significant hydrolysis to $TsNH_2$ was observed in all cases, but we were pleased to observe complete conversion of sulfinamide **55b** into sulfinamide **56a** in DCE and $CHCl_3$ (**Table 5.1, entries 2 and** 3), as well as in toluene (**Table 5.1, entry 1**), despite poor solubility of the ene-adduct in this case. More polar solvents gave poorer results. Incomplete consumption conversion to sulfinamide **56a** was observed when using MeCN (**Table 5.1, entry 5**), whereas, no conversion was observed when using THF or DMF as the reaction solvent (**Table 5.1, entries 4 and 6**).

Table 5.1. Testing a selection of solvents for transfer-ene reaction.



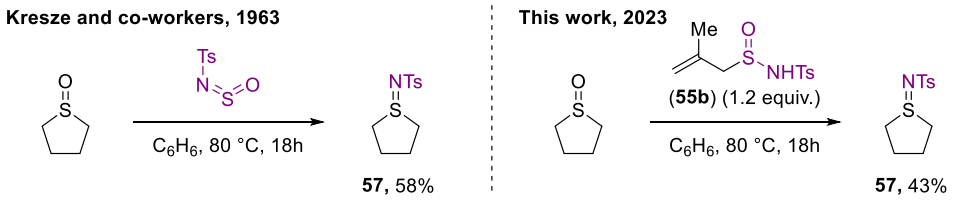
55b **56a** **55b**

Entry	Solvent	Yield (%)		
		Sulfinamide 56a	Sulfinamide 55b	$TsNH_2$
1	Toluene	44	0	48
2	DCE	55	0	45
3	$CHCl_3$	35	0	65
4	THF	0	44	56
5	MeCN	40	13	47
6	DMF	0	67	33

Yields determined by NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

The results of the solvent screen demonstrate that ene-adducts can be used to liberate TsNSO in a variety of solvents, and as a result, we wished to determine whether it can be used to replace TsNSO in previously-developed reactions.

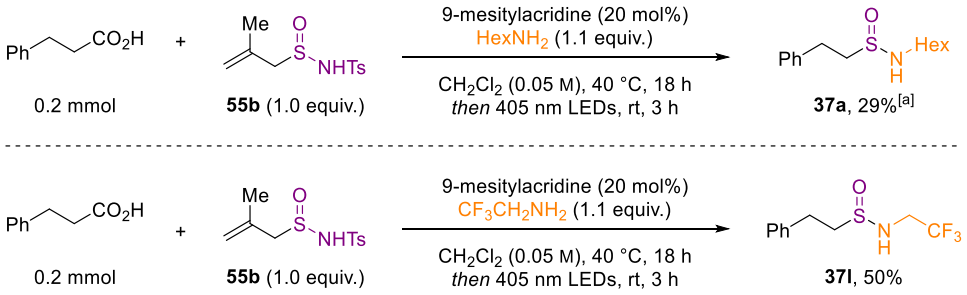
We previously discussed the reaction of TsNSO with carbonyl compounds and sulfoxides. These useful transformations could have significant applications in modern chemistry, such as the formation of challenging chiral sulfilimines from readily accessible chiral sulfoxides. Kresze and co-workers showed that reaction of TsNSO with tetrahydrothiophene 1-oxide gave the corresponding sulfilimine **57** in 58% yield.[14c] Using our ene-adduct instead of TsNSO under the same reaction conditions, we were pleased to obtain sulfilimine **57** in 43% yield (**Scheme 5.21**).



Scheme 5.21. Sulfilimine synthesis from sulfoxides using TsNSO and ene adduct.

Finally, we applied the ene adduct to trans-sulfinylation. Alkyl sulfinylamines are not known to undergo ene-reactions, and therefore alkyl sulfinylamines generated from exchange with TsNSO liberated in situ can be used directly in subsequent reactions. We therefore expected

that this could be used in the decarboxylative trans-sulfinylation reaction discussed in **Chapter 4**. We explored this reaction using both hexylamine and 2,2,2-trifluoroethylamine, and performed the retro-ene/trans-sulfinylation step overnight at 40 °C. Unfortunately, poor conversion was observed for hexylamine, and only 29% of the product **37a** was obtained, lower than that obtained using TsNSO. We proposed that the acidic sulfinamide proton in the ene-adduct may be deprotonated, preventing the retro-ene reaction and therefore giving a poorer yield than expected. However, using the less-basic 2,2,2-trifluoroethylamine substrate gave 50% yield of the exchange product **37l**, substantially higher than the yield obtained using TsNSO, perhaps due to slow release of TsNSO from the ene-adduct (**Scheme 5.22**).



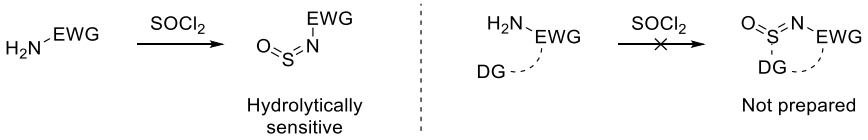
[a] Yield calculated by HPLC analysis using 1,3,5-triisopropylbenzene as an internal standard.

Scheme 5.22. Retro-ene/trans-sulfinylation reaction to prepare sulfinamide products from carboxylic acids.

5.4 Conclusions and future work

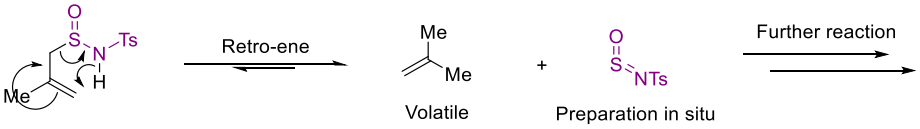
In summary, we have explored the chemistry of electron-poor sulfinylamines with the goal of generating new bench-stable sulfinylamines or precursors in order to facilitate the development of new methods.

We first prepared a selection of substrates that could be used for the preparation of sulfinylamines functionalised with a pendant electron-donating group that that would enable the formation of an intramolecular charge-transfer complex. Our studies concluded that the corresponding sulfinylamines could not be prepared, and either gave complicated reaction mixtures or no conversion (**Scheme 5.23**).



Scheme 5.23. Proposed sulfinylamines with a pendant electron-donating group.

We then focussed on the development of precursors that would liberate sulfinylamines in situ. We found that adducts derived from ene-reactions of TsNSO and olefins could be used to liberate TsNSO under mild conditions, and could therefore be used in place of TsNSO in reactions (**Scheme 5.24**).



Scheme 5.24. Proposed retro-ene strategy to prepare hydrolytically unstable sulfinylamines in situ.

Further work is needed with the use of ene-adducts to liberate sulfinylamines. The ene-adduct derived from isobutene was found to hydrolyse during reactions even without the formation of TsNSO, as demonstrated during the transfer-ene reactions in different reaction solvents. Furthermore, purification of the isobutene ene-adduct was challenging, as it was found to decompose on silica and upon heating during attempted recrystallisations. Varying the olefin component may improve stability to hydrolysis by steric hinderance α- to the sulfinamide, or prevent [2,3]-rearrangement by substitution on the terminal alkene. Variation of the protecting group may also be important as varying the steric or electronic properties here may also improve the stability (**Figure 5.5**).

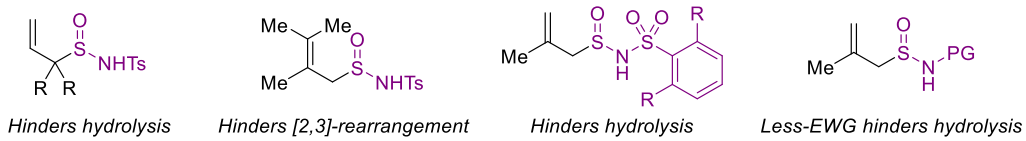
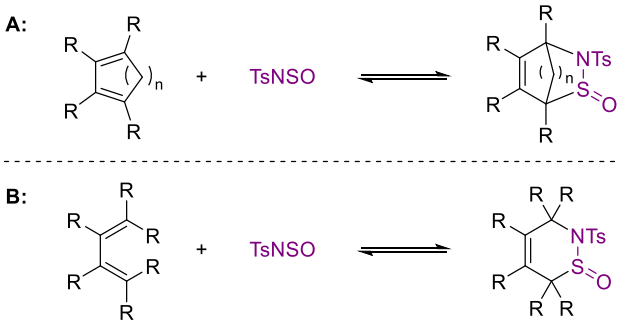


Figure 5.5. Proposed variations of ene adducts to improve stability

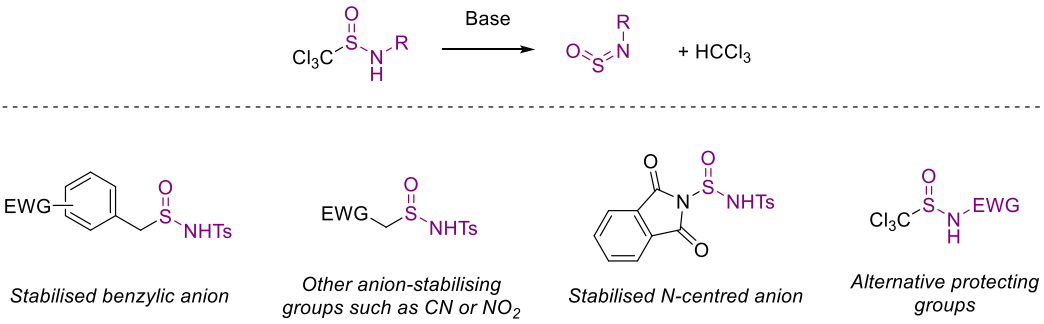
The acidity of the sulfinylamine proton may also be disadvantageous for some reactions, as demonstrated by the trans-sulfinylation example. The Diels-Alder adducts of sulfinylamines do not have these acidic protons, so may be a good alternative to the ene-adducts. The Diels-Alder adduct derived from cyclopentadiene liberates TsNSO at room temperature, but studying alternative

substitution or diene ring sizes may improve their stability. Alternatively, studying Diels-Alder adducts derived from acyclic dienes may also provide useful sulfinylamine precursors (**Scheme 5.25**).



Scheme 5.25. Proposed retro-Diels-Alder strategy to prepare sulfinylamines in situ.

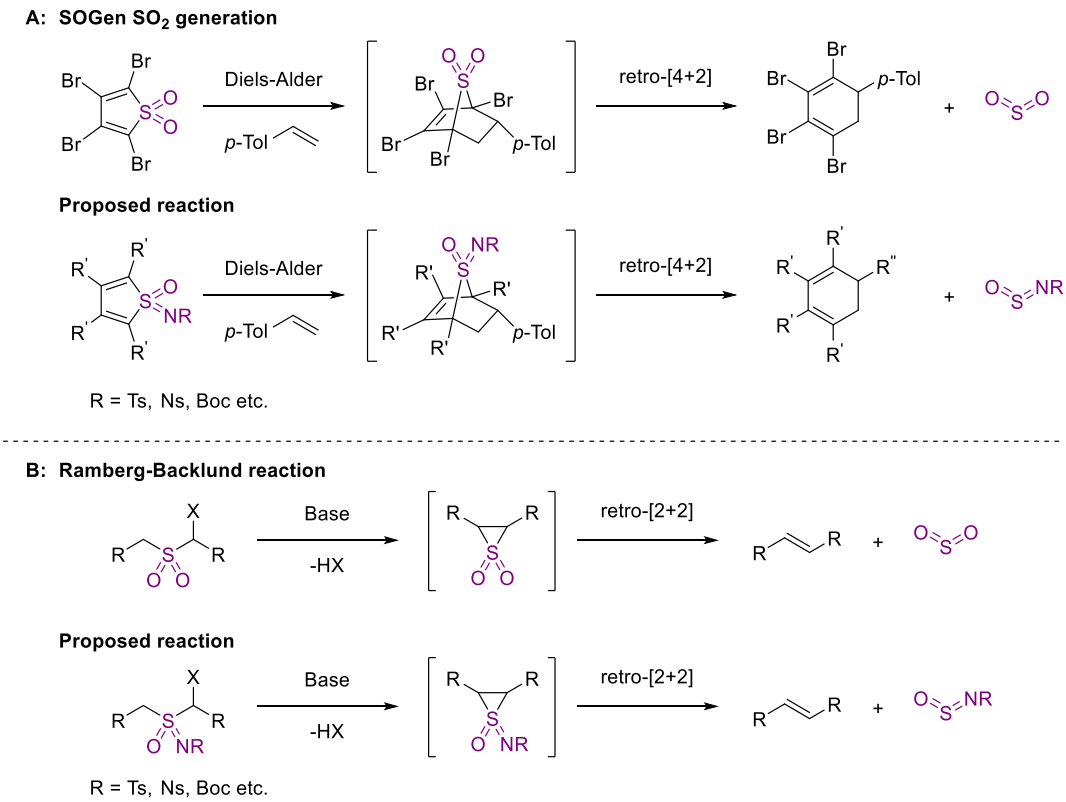
Methods that quantitively generate the sulfinylamine may also be more useful for some reactions. Whilst the attempted synthesis of *N*-tosyl trichloromethanesulfinamide was unsuccessful, further studies should be carried out to prepare similar substrates. The base-induced β-elimination relies upon the leaving group ability of the trichloromethyl anion. Alternative carbon or heteroatom leaving groups could be explored which may improve the synthesis of these sulfinylamine precursors as well as avoid the use of the restricted trichloromethylsulfenyl chloride reagent. Previous studies within the Willis group have found several sulfinates that rapidly liberate SO_2, so the analogous sulfinamides may provide a good starting point for these studies. Alternatively, different protecting groups could also be explored (**Scheme 5.26**).



Scheme 5.26. Proposed base-induced β-elimination substrates to generate sulfinylamines in situ

Analogies to other processes that liberate SO_2 may also be helpful in developing new methods of generating sulfinylamines. Lian and co-workers developed SOGen, a bench-stable solid that liberates

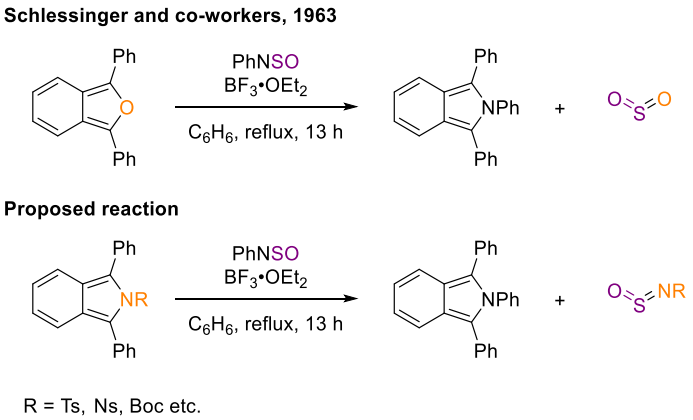
SO_2 following a Diels-Alder reaction and subsequent retro-cycloaddition (**Scheme 5.27.A**).[42] Some preliminary studies on the preparation of aza-analogues of this reagent were carried out in the Willis group by Dr Thomas Davies, but the substrates were found to be challenging to prepare. However, these substrates could still be useful, and recent advances in aza-sulfur chemistry may help with their preparation. However, competitive Diels-Alder of the sulfinylamine products with the diene by-products may complicate the use of these reagents. Alternatively, the Ramberg-Backlünd reaction involves conversion of an α-halo sulfone into an alkene via base-assisted generation of a thiirane dioxide,[219] and retro-[2+2] liberating SO_2. The preparation of α-halo sulfoximines could enable a similar reaction liberating sulfinylamines (**Scheme 5.2.7.B**). Choice of base to prevent reaction with the sulfinylamine as well as substituent choice to prevent ene reactions would be important in these reactions.



Scheme 5.27. A): Proposed aza-SOGen reagents **B):** Proposed aza-Ramberg-Backlünd reaction

Another proposal involves the reaction of sulfinylamines with 1,3-diphenylisobenzofuran discovered by Schlessinger and co-workers.[220] The expected Diels-Alder reaction with PhNSO occurs upon

heating, and subsequent rearrangement and liberation of SO_2 then occurs. The same reaction with *N*-protected isoindoles may liberate sensitive sulfinylamines without the need for their preparation (**Scheme 5.28**).



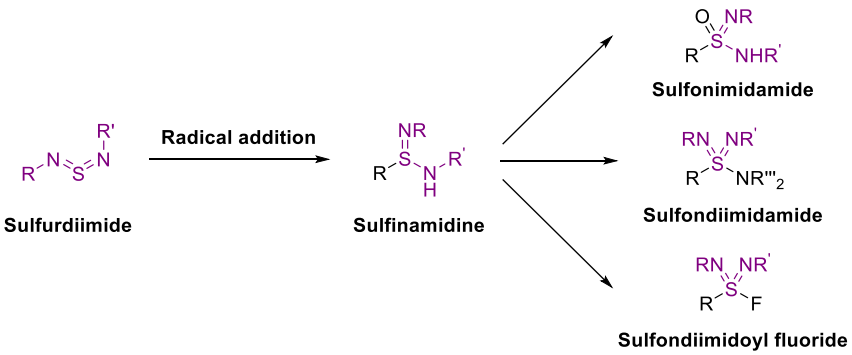
Scheme 5.28. Proposed synthesis of sulfinylamines via Dies-Alder with protected isoindoles.

Chapter 6 - The Preparation and Use of New Unsymmetrical Sulfurdiimide Reagents

6.1 Introduction

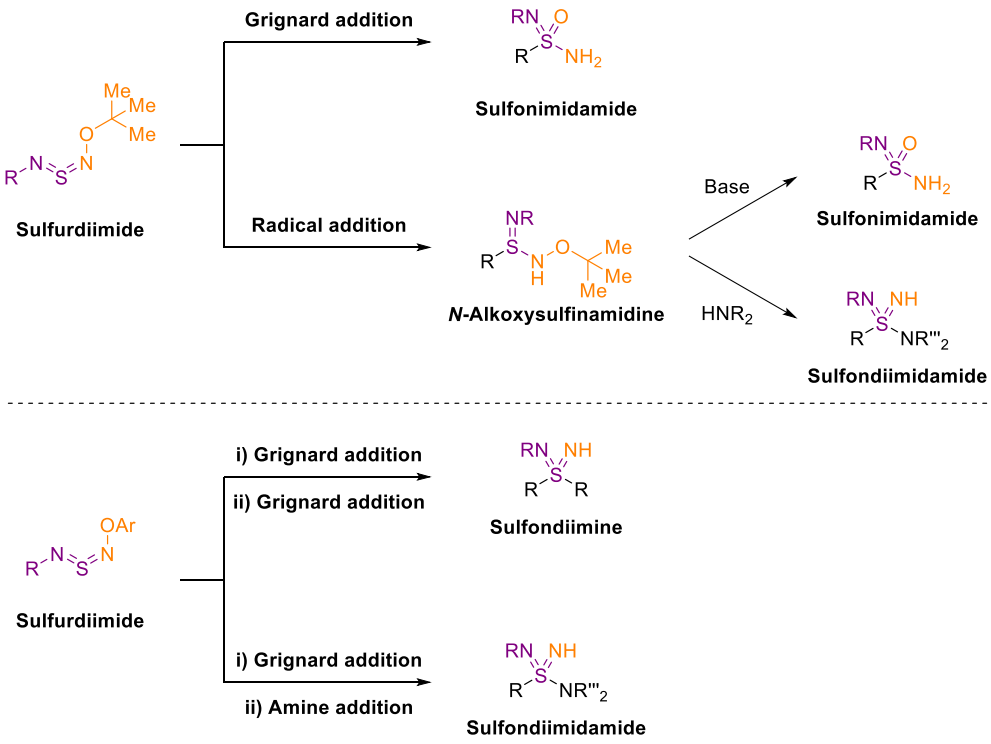
New methods utilising sulfinylamine reagents have become increasingly prevalent in the literature in recent years, in part due to the development of bench-stable sulfinylamine reagents such as TrNSO.[73] The analogous chemistry of sulfurdiimides, the di-aza analogues of SO_2, has been less-well explored in recent literature.

Following our previous studies, we reasoned that an important development would be to demonstrate the addition of radicals to sulfurdiimides, which has not yet been demonstrated. This would provide a novel route to alkyl sulfinamide products, which have useful applications for the synthesis of challenging aza-sulfur products (**Scheme 6.1**).



Scheme 6.1. Radical addition to give sulfinamidines and subsequent derivatisations.

Additionally, we wished to use our experience in the preparation of sulfurdiimide reagents to access aza-analogues of useful sulfinylhydroxylamine reagents such as *t*-BuONSO. If these reagents could be accessed, we hoped that they could be used analogously to prepare primary sulfonimidamides, sulfondiimidamides and sulfondiimines (**Scheme 6.2**).

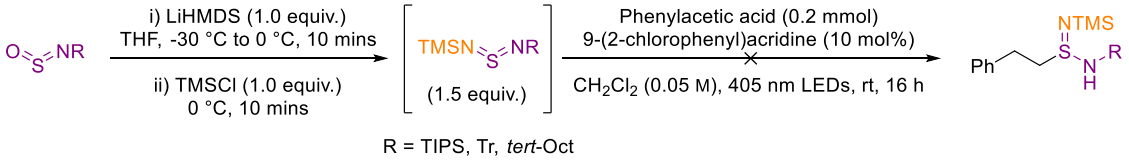


Scheme 6.2. Aza-analogues of sulfinylhydroxylamine reagents and proposed reactivity.

6.2 Results and Discussion

6.2.1 Radical Addition to Sulfurdiimides

We initiated our studies by preparing a selection of sulfurdiimide reagents in situ from the reaction of LiHMDS with our available sulfinylamine reagents.[109] We then used our optimised conditions from **Chapter 3** with the goal of preparing sulfinamidines, but none of the expected product or TMS-deprotected product was observed and carboxylic acid starting material was returned in all cases (**Scheme 6.3**).



Scheme 6.3. Attempted radical addition to sulfurdiimides to give sulfinamidines.

We proposed that the two electron-donating nitrogen substituents increase the electron density at sulfur, meaning it reacts less readily with the nucleophilic alkyl radicals. The increased steric hinderance due to the requirement for one of the substituents to be in a trans

configuration may also impact the reactivity of these reagents. We therefore expected that making the sulfurdiimide more electrophilic by swapping one of the protecting groups for an electron-withdrawing group would improve its reactivity with alkyl radicals. These reagents with only one electron-withdrawing group have been noted to be less-reactive with nucleophiles than those with two electron-withdrawing groups (**Figure 6.1**).[72b, 117] We hoped therefore that these intermediate unsymmetrical sulfurdiimides would be less moisture-sensitive, and therefore more practical for use in our proposed radical reactions.

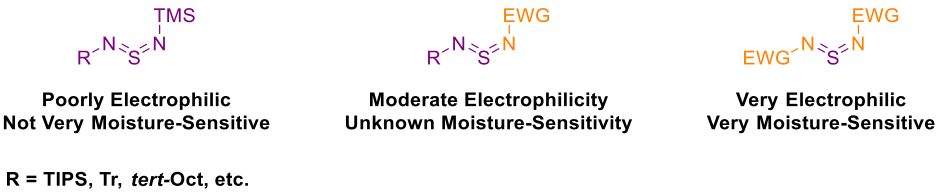
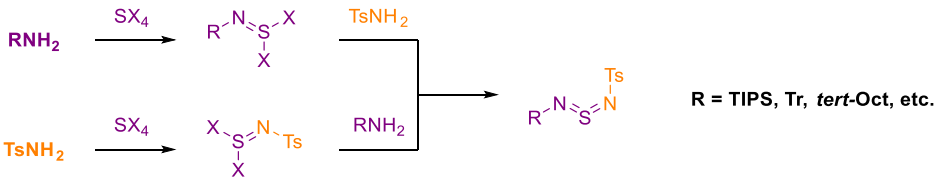


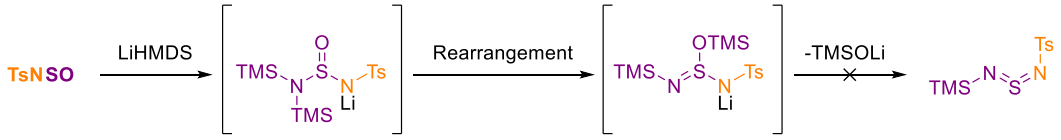
Figure 6.1. Proposed reactivity of sulfurdiimide reagents.

For these studies, we opted for Ts as the electron-withdrawing substituent, as the chemistry for the preparation and use of these sulfurdiimides has been relatively well-studied.[72b] Very few examples of these intermediate sulfurdiimides have been prepared in the literature. One method that has been used in a few cases is the reaction of nucleophiles with organoiminosulfur dihalides (**Scheme 6.4**).[221] The preparation of these reagents usually involves the use of SF_4, which is a toxic gaseous reagent that liberates HF, or SCl_4, which is an unstable solid. We reasoned that this route would be unsuitable for use without stringent safety precautions, which would limit its utility. Furthermore, the use of SF_4 would likely not be compatible with silyl-protected amines, which we have found to be useful for reactions of sulfinylamines and sulfurdiimides.[26, 103a]



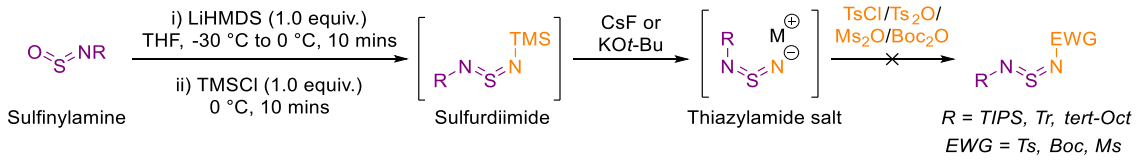
Scheme 6.4. Proposed preparation of sulfurdiimides from organoiminosulfur dihalides.

We considered the reaction of LiHMDS with TsNSO, which we hoped would give the TMS/Ts-protected sulfurdiimide. Whilst consumption of TsNSO was observed, no product consistent with the desired sulfurdiimide was detected. We postulated that due to negative charge-stabilisation by the electron-withdrawing Ts, the intermediate adduct from LiHMDS addition (or the rearranged intermediate) does not readily decompose to the sulfurdiimide, and other decomposition pathways dominate (**Scheme 6.5**).[109]



Scheme 6.5. Attempted preparation of TMSNSNTs via reaction of LiHMDS with TsNSO.

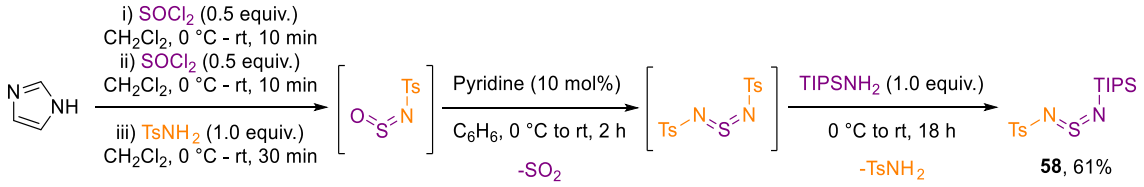
Considering that TMS-protected sulfurdiimides can be readily accessed from LiHMDS reaction with sulfinylamines, we proposed that TMS-deprotection using either KO*t*-Bu or CsF followed by reaction with various electrophiles could provide a route to the desired sulfurdiimide products. Consumption of TMS-protected sulfurdiimide starting materials was observed in all cases, and yellow precipitate was observed, consistent with the preparation of the thiazylamide salt. Unfortunately, subsequent reaction with various electrophiles in a one-pot procedure was unsuccessful in giving the desired sulfurdiimide. The thiazylamide salts were also found to be too unstable to isolate by filtration. There are very few literature examples of electrophiles that have been reacted with thiazylamide intermediates, and these studies confirm that this method is not general for reactions with diverse electrophiles to prepare sulfurdiimides (**Scheme 6.6**).



Scheme 6.5. Attempted preparation of sulfurdiimides via TMS deprotection and reaction with various electrophiles.

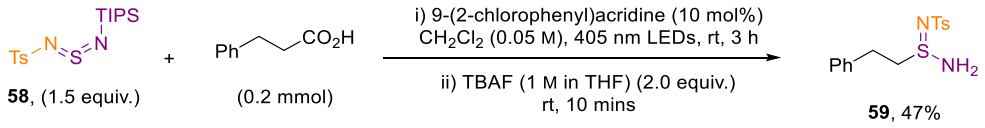
The method that has been used most often for the preparation of these intermediate sulfurdiimide reagents is the reaction of disulfonyl sulfurdiimides with one equivalent of a primary amine

nucleophile.[118] We thus prepared TsNSNTs from TsNSO using pyridine, and subsequently added one equivalent of $TIPSNH_2$. We were pleased to observe conversion to a new product, consistent with the desired TIPSNSNTs product **58** (**Scheme 6.6**). This sulfurdiimide was found to be quite moisture sensitive, and was not stable to silica column chromatography, but was found to be soluble in pentane, and so could be separated from many of the reaction impurities. Sulfurdiimide **58** was isolated in 61% yield, but contained 33% $TIPSNH_2$ impurity.



Scheme 6.6. Amine exchange to give TIPSNSNTs.

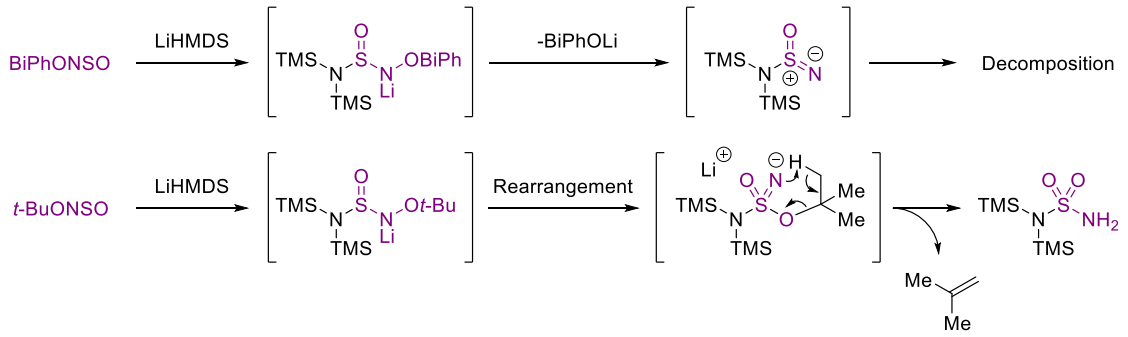
With sulfurdiimide **58** in hand, we proceeded to test radical addition using the conditions developed in **Chapter 3**. We were pleased to observe full consumption of the carboxylic acid starting material, and a new product was observed. Subsequent TIPS-deprotection using TBAF gave the desired sulfinamidine product **59** in 47% yield, representing the first known radical addition to sulfurdiimides (**Scheme 6.7**).



Scheme 6.7. Preparation of sulfinamidine **59** by radical addition to sulfurdiimide **58**.

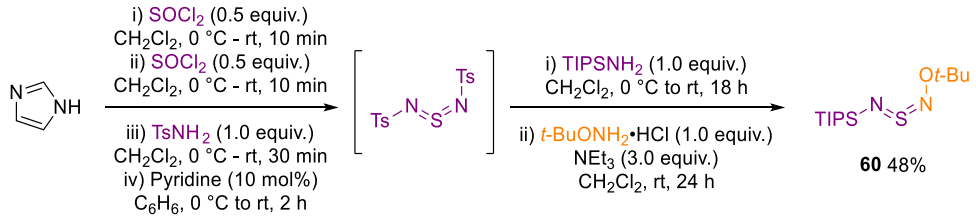
6.2.2 Aza-Analogues of Sulfinylhydroxylamines

Previous efforts from the Willis group to synthesise aza-analogues of sulfinylhydroxylamines, "thiazylhydroxylamines," via addition of LiHMDS to *t*-BuONSO or BiPhONSO were unsuccessful. It is possible that either cleavage of the N-O bond to give a sulfinyl nitrene-type intermediate, or rearrangement to a sulfamide, as may be the case for *t*-BuONSO, outcompete the formation of the desired sulfurdiimides (**Scheme 6.8**).



Scheme 6.8. Proposed decomposition pathways during sulfurdiimide synthesis from sulfinylhydroxylamines.

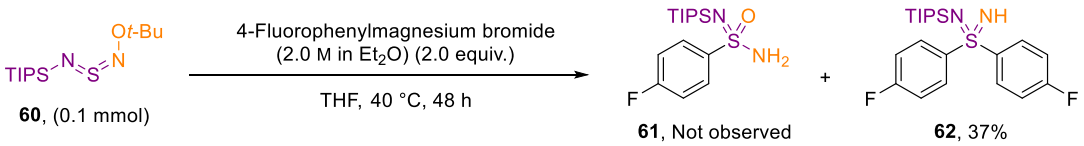
With our recent experience in the preparation and use of TsNSNTs in amine-exchange reactions, we proposed that we could carry out two sequential amine-exchange steps, one of which using a hydroxylamine, to prepare the desired sulfurdiimide products. Following an identical sequence to that used in the preparation of TIPSNSNTs **58**, followed by addition of free-based *O-tert*-butylhydroxylamine, we were pleased to observe the formation of the desired sulfurdiimide **60**, which could be extraction from the crude material using pentane, but was also found to be stable on silica during column chromatography. Following this procedure, we isolated the desired sulfurdiimide product **60** in 48% yield (**Scheme 6.9**).



Scheme 6.9. Double amine exchange with TsNSNTs to give sulfurdiimide **60**.

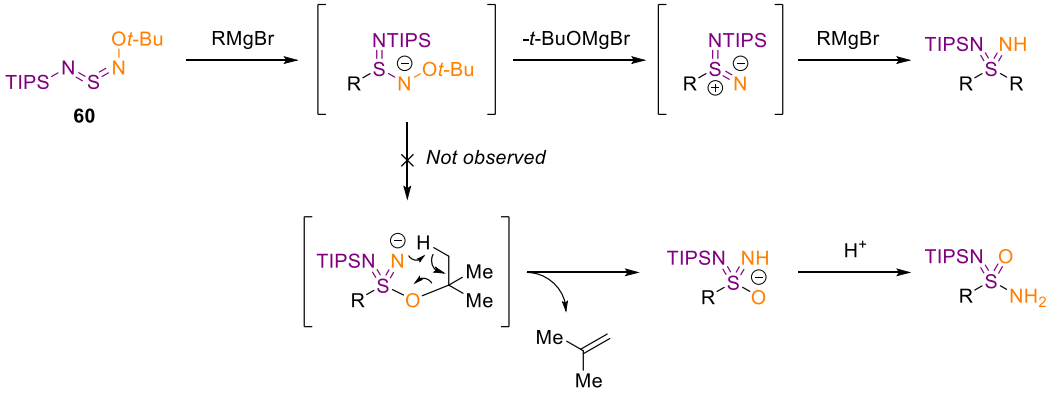
With sulfurdiimide **60** in hand, we wished to determine whether Grignard addition would provide the corresponding sulfonimidamide **61**, which we expected would form via a mechanism analogous to that observed when using *t*-BuONSO.[193] We were pleased to observe the formation of new products by TLC, but were surprised that the sulfurdiimide **60** was still present. Even after heating the reaction to 40 °C, incomplete consumption of the sulfurdiimide **60** was observed. At this point, the reaction was quenched and the new products were isolated. We were surprised to find that none of the expected

sulfonimidamide **61** was obtained, but instead, 37% of the symmetrical sulfondiimine **62** was isolated (**Scheme 6.10**).



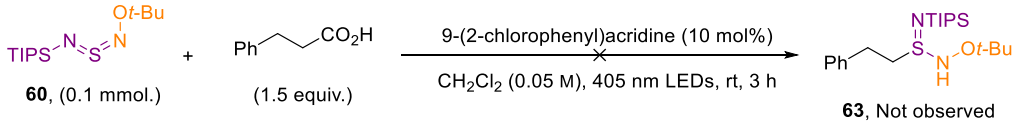
Scheme 6.10. Grignard addition to sulfurdiimide **60** to give sulfondiimine **62**.

We propose that this sulfondiimine **62** was generated through a similar mechanism to reactions with BiPhONSO, where a sulfinyl nitrene-type intermediate is formed through loss of *tert*-butoxide, which is then trapped by an additional equivalent of Grignard reagent (**Scheme 6.11**).[86] We proposed that the steric interaction between the TIPS protecting group and the tert-butoxy substituent may be the cause of this unexpected reactivity, as the rearrangement of the *N*-alkoxysulfinamidine to the sulfondiimidate ester intermediate prior to loss of isobutene would increase the steric interaction, meaning loss of *tert*-butoxide becomes the more favoured pathway.



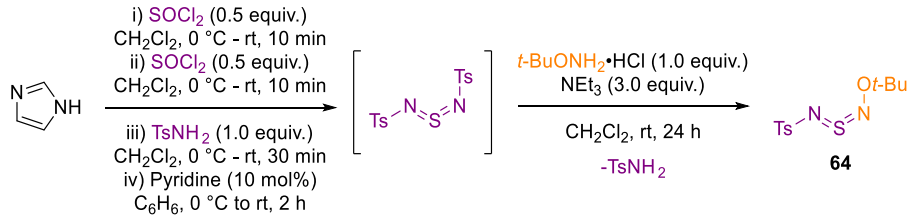
Scheme 6.11. Competing pathways from sulfinamidine anion intermediate to sulfondiimine or sulfonimidamide.

We also tested radical addition to sulfurdiimide **60** using our previously-developed decarboxylative reaction conditions. As expected, given the findings of radical addition to other electron-rich sulfurdiimides, none of the desired *N*-alkoxysulfinamidine product **63** was observed and carboxylic acid starting material was returned (**Scheme 6.12**).



Scheme 6.12. Attempted preparation of *N*-alkoxysulfinamidine **63** by radical addition to sulfurdiimide **60**.

We attempted to prepare TsNSNO*t*-Bu, which we hoped would be compatible with the decarboxylative radical reaction to give the *N*-alkoxysulfinamidine. Whilst peaks consistent with the desired sulfurdiimide **64** were observed in the crude material by NMR spectroscopy, attempts to isolate the product were unsuccessful, as it was found to be unstable on silica, and couldn't be separated from remaining $TsNH_2$ and triethylammonium hydrochloride (**Scheme 6.13**).

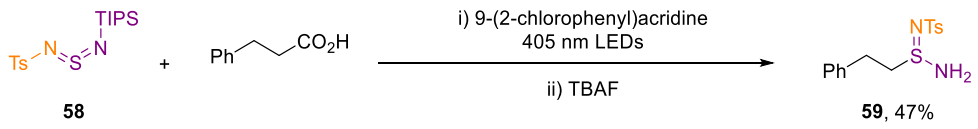


Scheme 6.13. Amine exchange to give sulfurdiimide **64**.

6.3 Conclusions and future work

In summary, we have explored the chemistry of sulfurdiimides, developing routes for the synthesis of new reagents and demonstrated their novel reactivity.

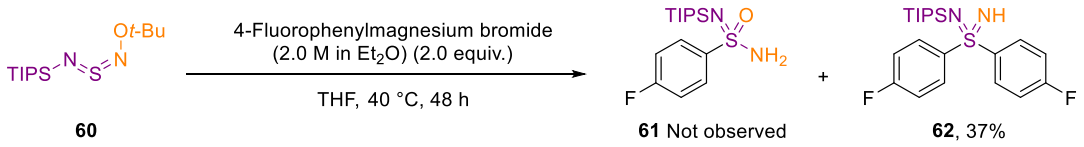
Firstly, we found that whilst radical addition to electron-rich sulfurdiimides was unsuccessful in our decarboxylative reaction conditions, we demonstrated the first example of radical addition to sulfurdiimides to give sulfinamidines through the use of a more electron-poor sulfurdiimide **58** (**Scheme 6.14**).



Scheme 6.14. Preparation of sulfinamidine 59 by radical addition to sulfurdiimide **58**.

We then further utilised amine exchange with TsNSNTs to prepare the first example of thiazylhydroxylamine reagent **60**, which is the mono aza-analogue of sulfinylhydroxylamines. This

reagent had excellent stability, but also surprising reactivity, where Grignard addition gave a sulfondiimine product **62**, apparently via the formation of a nitrene intermediate, rather than the expected sulfonimidamide **61** (**Scheme 6.15**).



60 **61** Not observed **62**, 37%

Scheme 6.15. Grignard addition to sulfurdiimide **60** to give sulfondiimine **62**.

The demonstration that radical addition to sulfurdiimides can be achieved if an electron-withdrawing protecting group is employed is an important development. However, it is likely that sulfurdiimide **58** is too moisture-sensitive to make it a practical reagent to prepare and use, so other examples of sulfurdiimides need to be evaluated. Important factors to consider would include varying the electron-withdrawing group, as this would impact both the moisture-sensitivity and the reactivity of the sulfurdiimides with radicals. Steric properties of both amines could also be varied to study the effect on moisture-sensitivity (**Figure 6.2**).

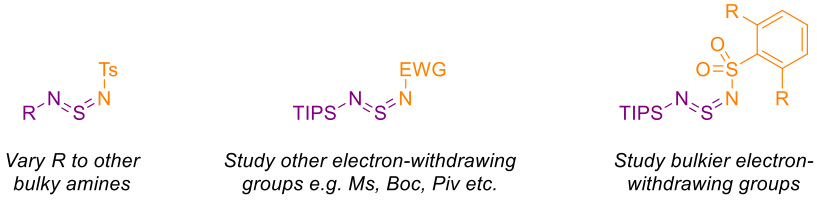
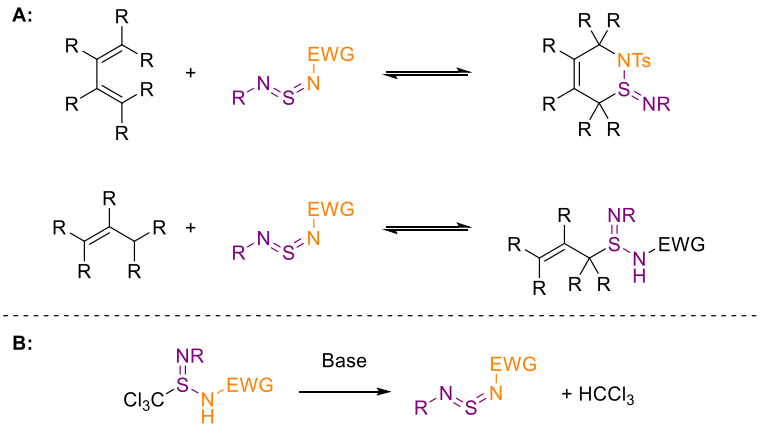


Figure 6.2. Proposed variations of sulfurdiimides to improve moisture-sensitivity.

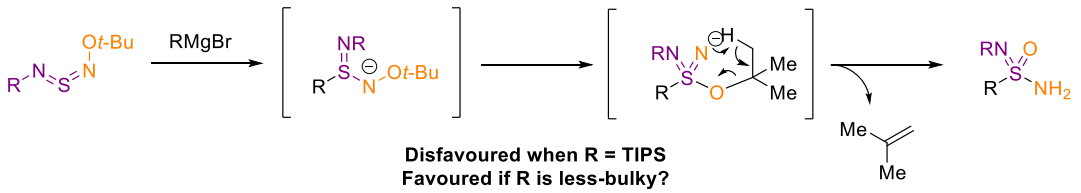
If moisture-sensitivity of sulfurdiimides remains an issue, precursors that would liberate the sulfurdiimide in situ could be considered. Sulfurdiimides with one aryl substituent and Ts have been used in Diels-Alder reactions, although higher temperatures are often needed to prepare the adduct.[124] Ene reactions have not been studied with these sulfurdiimides, but the use of either adduct could be considered as precursors to sulfurdiimides, in a similar manner to the ene adducts of TsNSO studied in **Chapter 5** (**Scheme 6.16.A**). Alternatively, base-induced β-elimination reactions, such as those discussed in **Chapter 5**, could be considered.[216] Sulfinamidines functionalised with anion-

stabilising groups such as -CCl_3 could be prepared via oxidative imination of sulfenamides. Reaction with base would then give the sulfurdiimide in situ (**Scheme 6.16.B**).



Scheme 6.16. A): Proposed reversible Diels-Alder or ene-adducts **B):** Proposed base-induced β-elimination to give sulfurdiimides in situ.

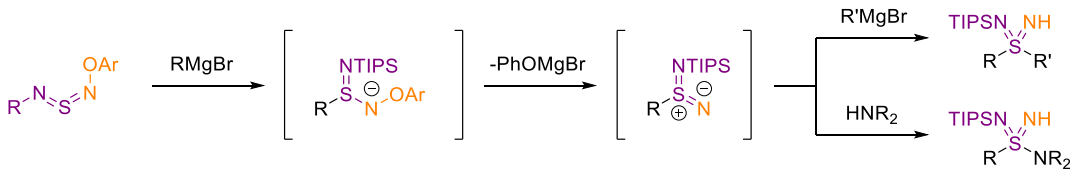
Further optimisation is needed to enable the synthesis of sulfonimidamides from NSNO compounds. The bulky TIPS group likely disfavours the rearrangement to the sulfondiimidate ester intermediate that is needed to give the sulfonimidamide. If less-bulky substituents such as benzyl give stable sulfurdiimide reagents, these may enable the desired transformation, and may also improve the rate of the additional organometallic addition (**Scheme 6.17**).



Scheme 6.17. Proposed variations of sulfurdiimides to favour formation of sulfonimidamides.

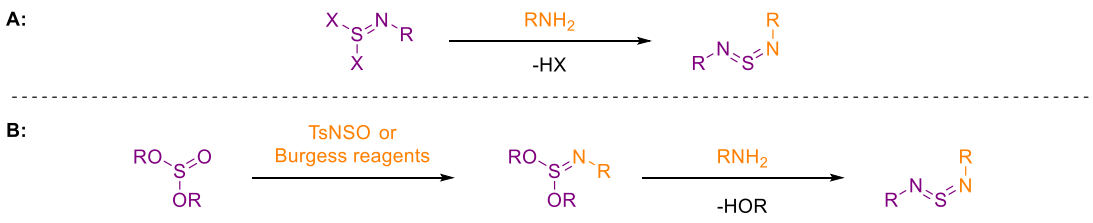
On the other hand, optimising the sulfurdiimide reagents to improve the formation of the nitrene intermediate, and subsequently the sulfondiimine products, would also be useful. A faster reaction would be needed to enable sequential addition of the first organometallic reagent at low temperature, followed by addition of a different organometallic or amine. Again, the bulky TIPS group likely impacts the rate of reaction, so less-bulky substituents may be beneficial. Substituting *O-tert*-butylhydroxylamine for other hydroxylamines would also reduce steric congestion. Use of

O-arylhydroxylamines, particularly with electron-withdrawing substituents would reduce the electron density at sulfur as well as improving the leaving group ability of the alkoxide, favouring the formation of the nitrene (**Scheme 6.18**).



Scheme 6.18. Proposed variations of sulfurdiimides to favour formation of nitrene.

Finally, whilst we were able to utilise amine-exchange with TsNSNTS to prepare sulfurdiimides in moderate yields, the procedure is lengthy, poorly atom-economic, and requires the preparation of several sensitive reagents. Alternative, shorter routes for the preparation of these reagents would be more convenient. We reasoned that the use of organoiminosulfur dihalides is inconvenient as their preparation usually requires the use of hazardous reagents such as SF_4 or SCl_4.[222] The development of alternative routes to these reagents would make them more practical for their use in sulfurdiimide synthesis (**Scheme 6.19.A**). The liberation of HF or HCl is also an issue with these reagents, as it may be incompatible with some substituents. Sulfurimidites could be considered as alternative reagents to prepare sulfurdiimides, similar to the use of sulfites in the preparation of sulfinylamines.[79] The only literature examples of their preparation involves reaction of organoiminosulfur dihalides with alcohols,[222a] so alternative methods for their preparation would again be needed. TsNSO and Burgess-type reagents have been used to prepare sulfilimines from sulfoxides.[14] Application of similar reactions to readily-accessible sulfites may enable the formation of these reagents without the use of organoiminosulfur dihalides (**Scheme 6.19.B**).



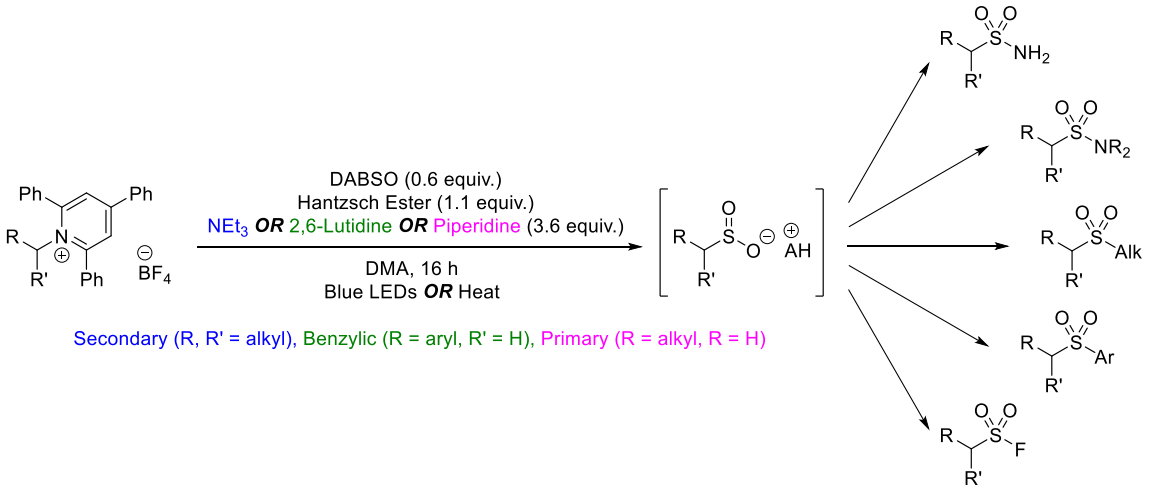
Scheme 6.19. A): Preparation of sulfurdiimides from organoiminosulfur dihalides. **B):** Proposed synthesis of sulfurimidites from sulfites and TsNSO or Burgess-type reagents and their use to prepare sulfurdiimides.

Chapter 7 - Conclusions and Future Work

7.1 Conclusions

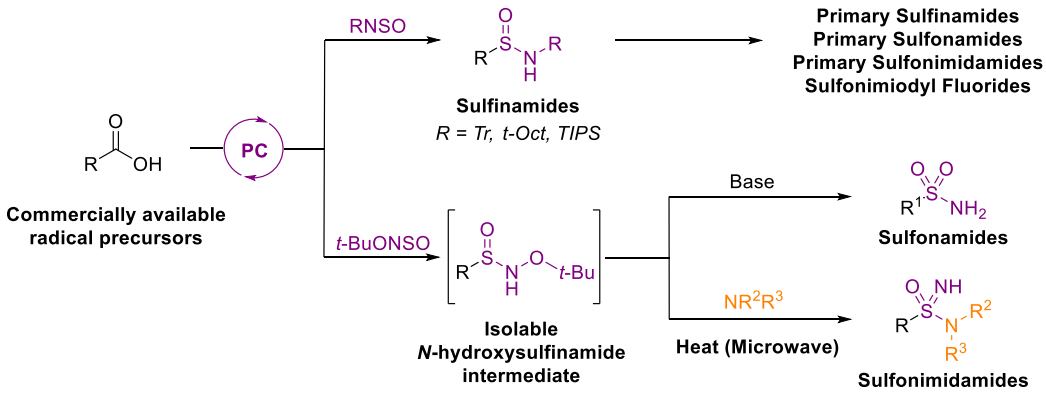
Sulfonyl-containing functional groups, including sulfones, sulfonamides and sulfonyl fluorides continue to make tremendous impact on medicinal chemistry.[7c] Additionally, the introduction of new, versatile methods to access their aza-analogues, such as sulfoximines, sulfonimidamides, sulfonimidoyl fluorides, and even their di-aza analogues, such as sulfondiimines, sulfondiimidamides and sulfondiimidoyl fluorides, has resulted in a growth in their use in synthetic organic chemistry.[133] Furthermore, the trend towards more-sp^3-rich molecules in drug discovery increases the need for efficient methods to access *S*-alkyl variants of these important functional groups.[134] To this end, the research presented in this thesis details the successful development of new, versatile, and reliable methods for the preparation of diverse *S*-alkyl sulfur-containing functional groups from readily accessible substates, focusing on the reactions of alkyl radicals with sulfur dioxide and its aza-analogues. Furthermore, we have made significant progress in the development of new reagents that we believe will have significant impact on the future work in this field.

We initiated our studies focusing on the addition of alkyl radicals to sulfur dioxide, using DABSO as a solid surrogate, in order to prepare alkyl sulfinates. We successfully developed a method for the preparation of diverse sulfinates and their derivatives from readily available primary amines, via the formation of Katritzky pyridinium salts, with radical generation initiated by visible light or heating (**Scheme 7.1**).[223] Conditions were developed to give good yields for α-secondary, α-primary and benzylic substrates, and subsequent conditions for the preparation of sulfones, sulfonamides and sulfonyl fluorides were developed. Studies towards further applications of this work to tertiary alkyl substrates, aryl substrates or addition to sulfinylamines were unsuccessful.



Scheme 7.1. Deaminative synthesis of sulfinates and their derivatives.

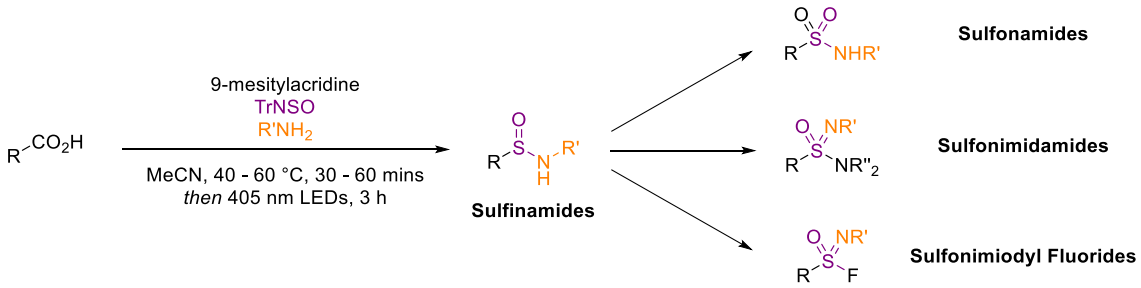
Following these studies, we turned our attention to radical addition to sulfinylamines, which has been underexplored in the literature. In collaboration with Dr Jagadeesh Kalepu, we developed a decarboxylative synthesis of *S*-alkyl sulfinamides using a selection of relatively hydrolytically-stable sulfinylamine reagents. Conditions for derivatisation of the sulfinamide products to primary sulfinamides, sulfonamides and sulfonimidamides as well as sulfonimidoyl fluorides were then developed. Furthermore, application of this methodology to the sulfinylhydroxylamine, *t*-BuONSO, resulted in the generation of *N*-alkoxysulfinamides. We were able to utilise these intermediates in the preparation of primary sulfonamides and sulfonimidamides (**Scheme 7.2**).



Scheme 7.2. Decarboxylative preparation of sulfinamides and *N*-alkoxysulfinamides and subsequent reactions to diverse S(VI) products.

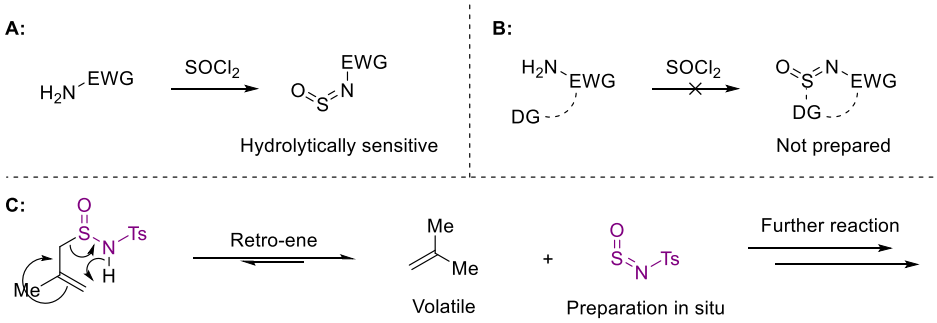
Despite our previous studies enabling the preparation of *N*-protected sulfinamides in excellent yields, we anticipated challenges if differentially *N*-alkylated products are desired, as their preparation would

require laborious multistep sequences, and the required alkylations are often substrate-dependant and poor-yielding. Furthermore, preparation of the corresponding sulfinylamine reagents would not be practical, as most of these are highly hydrolytically sensitive. In collaboration with Mr Russell Woodger, we exploited trans-sulfinylation to prepare these sensitive sulfinylamines in situ, and application of modified reaction conditions from our previous decarboxylative studies enabled the preparation of diverse *N*-alkyl sulfinamide products from the combination of readily available carboxylic acids, primary amines and bench-stable sulfinylamine reagents (**Scheme 7.3**).



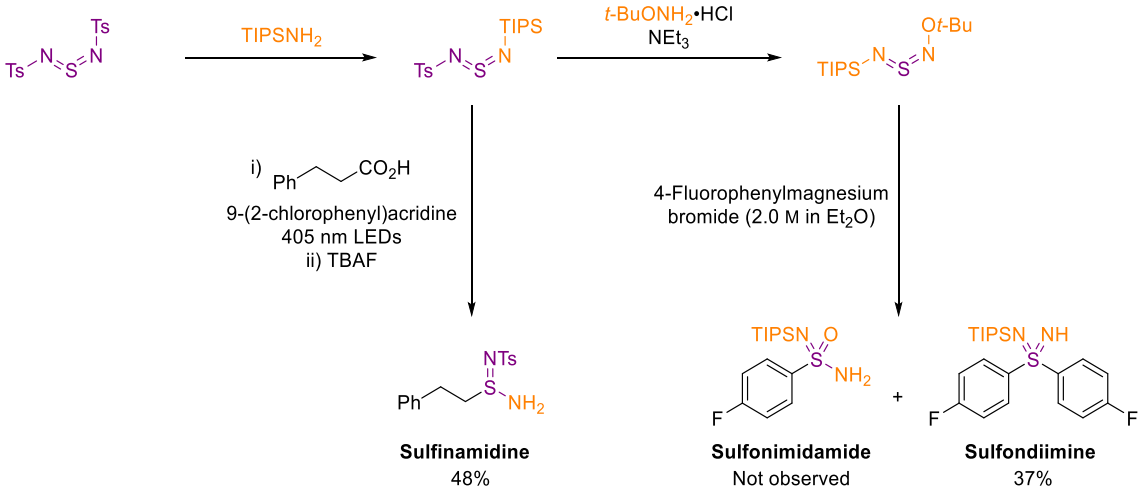
Scheme 7.3. Decarboxylative preparation of diverse *N*-substituted sulfinamides via in situ trans-sulfinylation.

We then focussed on harnessing the reactivity of more moisture-sensitive sulfinylamine reagents, such as the *N*-sulfinylsulfonamide, TsNSO, as they can be used in useful reactions such as cycloadditions which cannot be achieved using more electron-rich sulfinylamines (**Scheme 7.4.A**).[72] We reasoned that the moisture sensitivity of these reagents presents a barrier to the development and use of new reactions, so instead, we considered ways in which we could prepare *N*-sulfinylsulfonamides in situ from more-stable precursors, or analogues that could be stabilised by other mechanisms. The proposed formation of intramolecular charge-transfer complex to stabilise *N*-sulfinylsulfonamides was unsuccessful, as we were unable to prepare the desired reagents (**Scheme 7.4.B**). Instead, we utilised the reactions of *N*-sulfinylsulfonamides with olefins to give relatively-stable ene-adducts. The reversibility of the ene reaction meant that these adducts could be used to liberate sulfinylamines in situ, and we explored the utility of these reagents in a selection of reactions (**Scheme 7.4.C**).[93b]



Scheme 7.4. A: Preparation of *N*-sulfinylsulfonamides and their hydrolytic sensitivity. **B:** Failed preparation of *N*-sulfinysulfonamides with a pendant electron-donating group **C:** Retro-ene strategy to prepare hydrolytically unstable sulfinylamines in situ.

We then explored the chemistry of sulfurdiimide reagents, with the goal of demonstrating radical addition, as well as the preparation of aza-analogues of sulfinylhydroxylamines. With respect to radical addition, we found that electron-rich sulfurdiimides could not be used with the previously-developed decarboxylative radical reaction. Instead, we prepared sulfurdiimides functionalised with an electron-withdrawing group, which we found could be used in our decarboxylative methodology to give sulfinamidine products, representing the first example of radical addition to sulfurdiimides to our knowledge. These reagents were prepared by amine exchange with disulfonylsulfurdiimides.[72b, 118] A second amine exchange reaction with *O*-*tert*-butylhydroxylamine enabled the preparation of the desired aza-analogues of sulfinylhydroxylamines. Rather than the expected reactivity to give sulfonimidamides, we instead found that these reagents generated nitrene intermediates, resulting in the formation of symmetrical sulfondiimine products (**Scheme 7.5**).

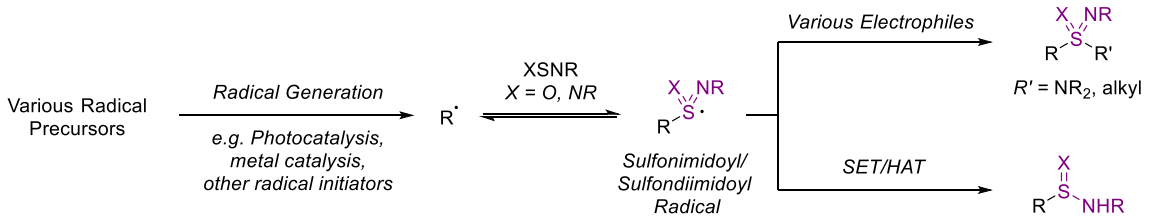


Scheme 7.5. Mono- and bis- amine exchange to prepare novel sulfurdiimide reagents, and subsequent radical reactivity and reaction with Grignard reagents to give sulfinamidine and sulfondiimine products, respectively.

7.2 Future Work

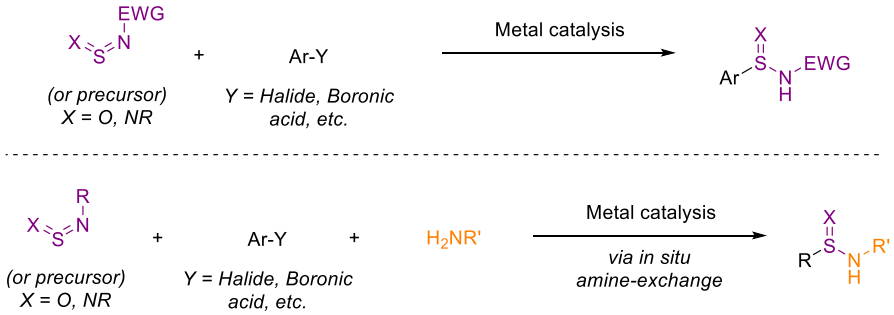
Suggestions for new avenues of investigation stemming from each of the projects presented in this thesis are discussed at the end of each chapter. More generally, however, further exploration of the chemistry of sulfinylamine and sulfurdiimide reagents, perhaps as bench-stable precursors in the case of more moisture-sensitive examples, is bound to provide new and useful methods for the synthesis of aza-sulfur functional groups.

In addition to the methods presented in this thesis, further developments in radical methodologies to access aza-sulfur products from alternative precursors may improve the accessibility of this chemistry. Furthermore, the radical chemistry of sulfurdiimides that has now been demonstrated needs further work, as the improved access to sulfinamidines and their derivatives from readily-accessible materials has the potential to have a significant impact in the use of these products in synthetic organic chemistry (**Scheme 7.6**).



Scheme 7.6. Aza-sulfur products from radical addition to sulfinylamines or sulfurdiimides.

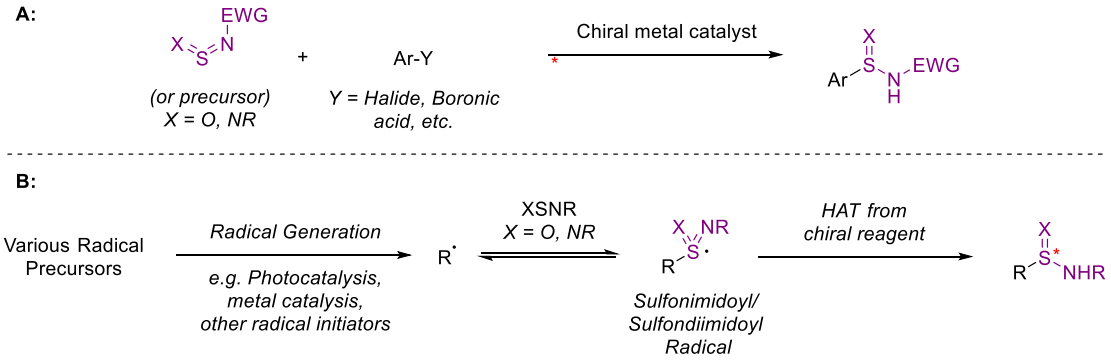
The metal-catalysed reactions of sulfinylamines are also underexplored in the literature, and current examples using TrNSO and other more-stable electron-rich sulfinylamines require high temperatures, and hydrolysis of sulfinylamine reagents under these conditions is a challenge.[87] Use of more electron-poor and less-hindered sulfinylamines may enable milder reaction conditions. Alternatively, trans-sulfinylation would give less-sterically hindered sulfinylamines, which may enable reaction under milder conditions, and would also improve access to more diverse sulfinamides. Furthermore, metal-catalysed couplings of sulfurdiimides have yet to be achieved, perhaps in part due to the more readily-accessible electron-rich and sterically-hindered examples being incompatible with metal catalysis. Access to more electron-poor and less-hindered examples may enable this chemistry to be explored, further enabling the preparation of sulfinamidines and their derivatives (**Scheme 7.7**).



Scheme 7.7. Metal-catalysed reactions with electron-poor sulfinylamines or sulfinylamines derived from trans-sulfinylation.

Finally, given the chiral nature of aza-S(IV) and S(VI) products, methods for the preparation of enantioenriched examples are highly sought after. Milder conditions for metal-catalysed couplings may enable one route to enantioenriched products by the application of chiral

ligands and catalysts (**Scheme 7.8.A**). Alternatively, given the observed application of HAT reagents and catalysts for the preparation of S(IV) products by radical methods, chiral variants of these reagents and their impact on enantioselectivity of the reactions would be an interesting avenue of investigation (**Scheme 7.8.B**).



Scheme 7.8. A): Access to chiral sulfinamides or sulfinamidines by metal-catalysed cross-coupling with chiral metal catalysts. **B):** Access to chiral sulfinamides or sulfinamidines via HAT from chiral reagents or catalysts.

There are surely many exciting developments in the field of aza-sulfur chemistry to be made in the near future, perhaps some of those derived from the work presented in this thesis, and these developments are sure to have a substantial impact on the use and application of aza-sulfur functional groups in biologically active molecules in years to come.

Chapter 8.0 - Experimental Data and Procedures

8.1 General Information

8.1.1. General Considerations

Reactions were performed under inert nitrogen atmosphere with anhydrous solvent unless otherwise stated. Reagents were purchased from Sigma-Aldrich, Fisher Scientific, Fluorochem, Tokyo Chemical Industry UK or Strem Chemicals and were used as supplied unless otherwise stated. Other solvents, if stated as anhydrous, were collected fresh from an in-house solvent purification system, which involves passing the solvent through anhydrous alumina columns. Glassware was oven-dried, and allowed to cool to rt under nitrogen. Cooling to 0 °C was achieved using ice-water bath. Reactions were monitored by HPLC analysis and/or thin layer chromatography (TLC) using pre-coated aluminium-backed silica plates (Merck Kieselgel 60 F254). Plates were visualised under ultraviolet light (254 nm) followed by staining with $KMnO_4$, phosphomolybdic acid or ninhydrin stains. Flash column chromatography was carried out using Geduran® Si 60, 40-63 micron silica gel; the compound to be purified was either loaded as an oil or concentrated solution. Petrol refers to the fraction of light Petroleum ether boiling in the range 40-60 °C.

Reactions using a microwave reactor were conducted using a Biotage® Initiator+ microwave synthesizer.

^{1}H NMR spectra were obtained using a Bruker AVIII HD 400 (400 MHz), AVII 500 (500 MHz), AVIII HD 500 (500 MHz) NEO 600 (600 MHz) spectrometer using the residual solvent as an internal standard. ^{13}C NMR spectra were obtained on a Bruker AVIII HD 400 (101 MHz), AVII 500 (126 MHz), AVIII HD 500 (126 MHz) or NEO 600 (151 MHz) spectrometer using the ^{1}H decoupling method and the residual solvent as an internal standard. Acquisitions were carried out at rt unless otherwise stated. Chemical shifts (δ) are reported in parts per million (ppm) from the residual solvent peak and coupling constants (*J*) were given in Hertz (Hz). Proton multiplicity is assigned using the

following abbreviations: singlet (s), doublet (d), triplet (t), quartet (q), quintet (p), multiplet (m), broad (br), apparent (app.).

Low resolution ESI mass spectra were recorded on a Waters LCT premier spectrometer. High resolution mass spectra were recorded either on a Bruker MicroTOF spectrometer under electrospray ionization conditions (ESI), a Waters LCT Premier spectrometer under the conditions of chemical ionization (CI) by the internal service at Chemistry Research Laboratory, University of Oxford, or a Waters BioAccord system. Samples for mass spectra were prepared as 1.0 mg/mL solution in MeOH (LRMS, HRMS-ESI) or submitted neat (HRMS-CI). Values quoted are a ratio of mass to charge in Daltons. High resolution values are calculated to four decimal places from the molecular formula, all found within a tolerance of five ppm. Melting point values were found using a Reich Melting Point Apparatus and are reported uncorrected. Infrared spectra were determined using neat samples with a Brüker Tensor 27 FT-IR spectrometer with an internal range of 600-4000 cm^{-1} and all absorptions are given in wavenumbers (cm^{-1}).

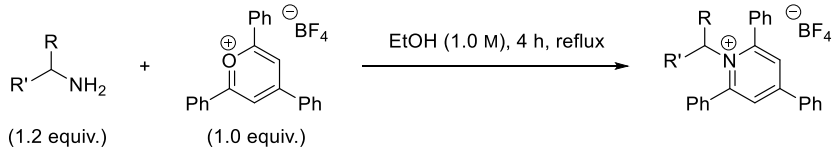
8.1.2. HPLC yields

The HPLC data was obtained from an Agilent Technologies 1200 series HPLC Hypersol ODS, 5.0 μm column (100 × 4.0 mm) using an extended 12 min method H_2O (0.1 % v/v H_3PO_4): MeCN (10 – 95% (9 min) to 100% (10.5 min) to 10% (12 min)). HPLC yields for the ligand screening were obtained via a standard calibration curve using authentic desired product and 1,3,5-triisopropylbenzene as an internal standard. Yields were calculated from absorbances at 210 nm. The method was verified by product isolation which gave a result ± 2%.

8.2 Experimental for Chapter 2

8.2.1 General Procedures

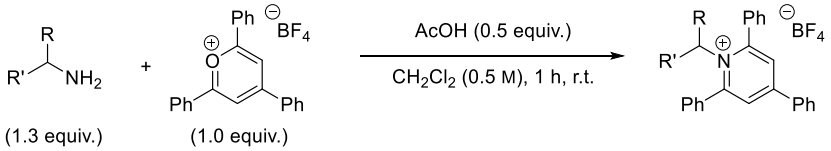
General Procedure A: Synthesis of Katritzky pyridinium salts.



According to the procedure described by Watson and co-workers,[153] the specified primary amine (1.2 equiv.) was added to a suspension of 2,4,6-triphenylpyrylium tetrafluoroborate (1.0 equiv.) and EtOH (1.0 M) in a round bottom flask. The flask was fitted with a reflux condenser and the mixture was stirred and heated to reflux in an aluminium heating block for 4 h. The mixture was then allowed to cool to rt. If product precipitation occurred, the solid was filtered, washed with EtOH (×3), then Et_2O (×3), and dried under high vacuum. If this did not occur, the solution was diluted with Et_2O (2 – 3 × the volume of EtOH used) and vigorously stirred for 1 h to induce precipitation. The resulting solid pyridinium salt was filtered and washed with Et_2O (×3). If product precipitation failed to occur at this point, the reaction mixture was subjected to flash column chromatography, eluting with 0 – 10% acetone/CH_2Cl_2 to afford the Katritzky salt product.

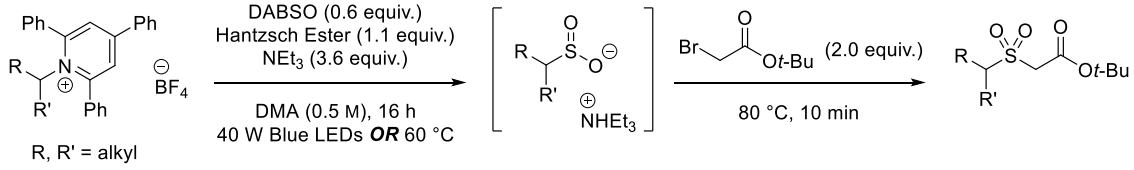
The corresponding amine hydrochloride salts can also be used by following a modified procedure: Et_3N (1.2 equiv.) was added to a mixture of the amine hydrochloride salt (1.2 equiv.) in EtOH (1.0 M). The mixture was then stirred for 30 mins at rt. 2,4,6-Triphenylpyrylium tetrafluoroborate (1.0 equiv.) was then added and the reaction was heated to reflux for 4 h. The workup procedure was analogous to that described above, but precipitated product was washed with water (×3) prior to being washed with EtOH and Et_2O as before.

General Procedure B: Alternative conditions for the synthesis of Katritzky pyridinium salts.



According to the procedure described by Gabrielson and co-workers,[224] 2,4,6-triphenylpyrylium tetrafluoroborate (1.0 equiv.) was added over 10 min to a stirred solution of the specified primary amine (1.3 equiv.) and AcOH (0.5 equiv.) in CH_2Cl_2 (0.5 M) in a round bottom flask. The reaction mixture was stirred at rt for 3 h. If product precipitation occurred, the solid was filtered, washed with EtOH (×3), then Et_2O (×3), and dried under high vacuum. If product precipitation did not occur, solvent was removed *in vacuo*, the residue dissolved in boiling EtOH and the resulting solution vigorously stirred before being cooled to rt. If product precipitation still did not occur, the solution was diluted with Et_2O (2 – 3 × volume of EtOH used) and vigorously stirred for 1 h to induce precipitation. The resulting solid pyridinium salt was filtered and washed with Et_2O (×3).

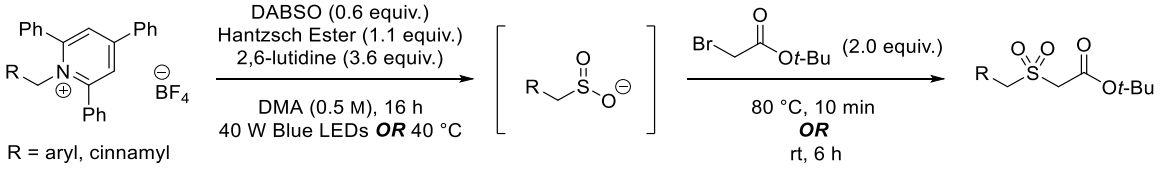
General Procedure C: Synthesis of sulfones using secondary alkyl Katritzky salts



Hantzsch ester (1.1 equiv.), DABSO (0.6 equiv.) and Katritzky pyridinium salt (1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, anhydrous DMA (0.5 M) was then added, followed by degassed, anhydrous triethylamine (3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation (**General Procedure C-1**, see **Figure S1** for experimental setups for 0.20 mmol and 10 mmol reactions) or heated to 60 °C in an aluminium heating block (**General Procedure C-2**) for 16 h. *tert*-Butylbromoacetate (2.0 equiv.) was then added and the reaction was heated to 80 °C in an aluminium heating block for 10 min. The reaction mixture was cooled to rt. Without workup, the

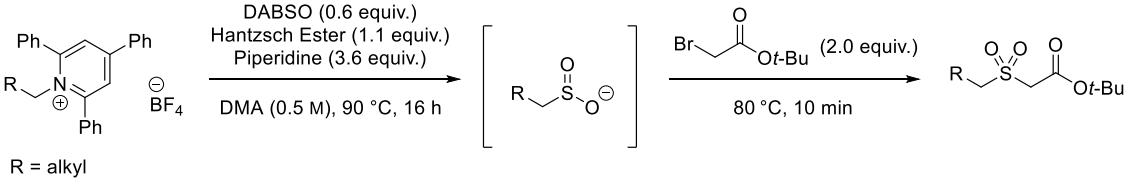
crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography to afford the sulfone product.

General Procedure D: Synthesis of sulfones using benzylic Katritzky salts



Hantzsch ester (1.1 equiv.), DABSO (0.6 equiv.) and Katritzky pyridinium salt (1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, anhydrous DMA (0.5 M) was then added, followed by degassed, anhydrous 2,6-lutidine (3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation (**General Procedure D-1**, see **Figure S1** for experimental setup) or heated to 40 °C in an aluminium heating block (**General Procedure D-2**) for 16 h. *tert*-Butylbromoacetate (2.0 equiv.) was then added and the reaction was heated to 80 °C in an aluminium heating block for 10 min or at rt for 6 hours. The reaction mixture was cooled to rt. Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography to afford the sulfone product.

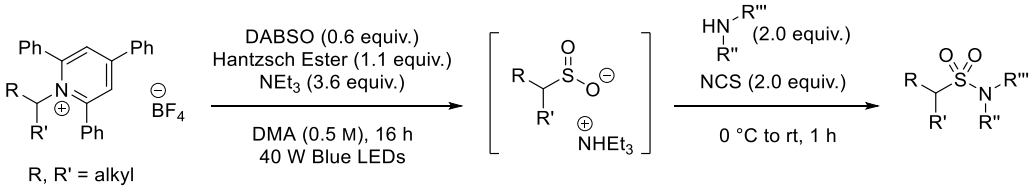
General Procedure E: Synthesis of sulfones using primary Katritzky salts



Hantzsch ester (1.1 equiv.), DABSO (0.6 equiv.) and Katritzky pyridinium salt (1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.5 M) was then added, followed by degassed, dry piperidine (3.6 equiv.). The reaction was heated to 90 °C in an aluminium heating block for 16 h. *tert*-butylbromoacetate (2.0 equiv.) was then added and the reaction heated to 80 °C in an aluminium

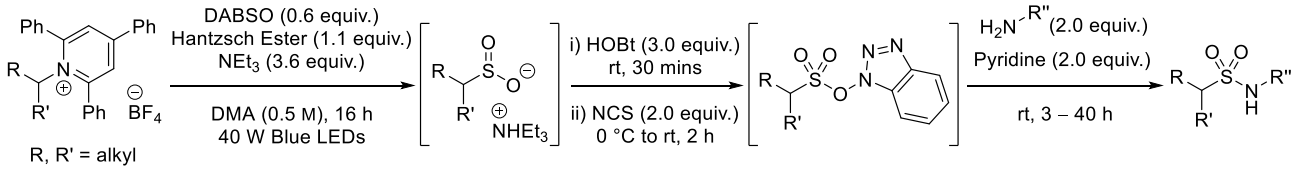
heating block for 10 min. The reaction mixture was cooled to rt. Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography to afford the sulfone product.

General Procedure F: Synthesis of tertiary Sulfonamides



Hantzsch ester (1.1 equiv.), DABSO (0.6 equiv.) and Katritzky pyridinium salt (1 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.5 M) was then added, followed by degassed, dry triethylamine (3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). After cooling the solution to 0 °C, amine (1.5 equiv.) and NCS (1.5 equiv.) were added and the reaction was stirred at rt for 1 h. The reaction mixture was cooled to rt. Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography to afford the sulfonamide product.

General Procedure G: Secondary Sulfonamides



Hantzsch ester (1.1 equiv.), DABSO (0.6 equiv.) and Katritzky pyridinium salt (1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.5 M) was then added, followed by degassed, dry triethylamine (3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). HOBt hydrate (80%) (3.0 equiv.) was then added and the reaction stirred at rt for 30 mins. After cooling the solution to 0 °C, NCS (2.0 equiv.) was added and the

reaction was stirred at rt for 2 h. Pyridine (2.0 equiv.) and primary amine (2.0 equiv.) were then added and the reaction stirred at rt until completion (determined by TLC). Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography to afford the sulfonamide product.

8.2.2 Photochemical Reaction Setup

Blue LEDs, where specified, comprised a 40 W Kessil A160WE "Tuna Blue" aquarium LAMP or HepatoChem EvoluChem™ 450PF 18 W 450 – 455 nm LED spotlight. 0.20 mmol scale reactions were carried out in 1.9 mL sample vials, fitted with a B14 Suba Seal® septum mounted in a EvoluChem™ PhotoRedOx Box device. 10 mmol scale reactions were carried out in a round bottom flask. Fan cooling was used during reactions to give an internal temperature of ~30 °C.

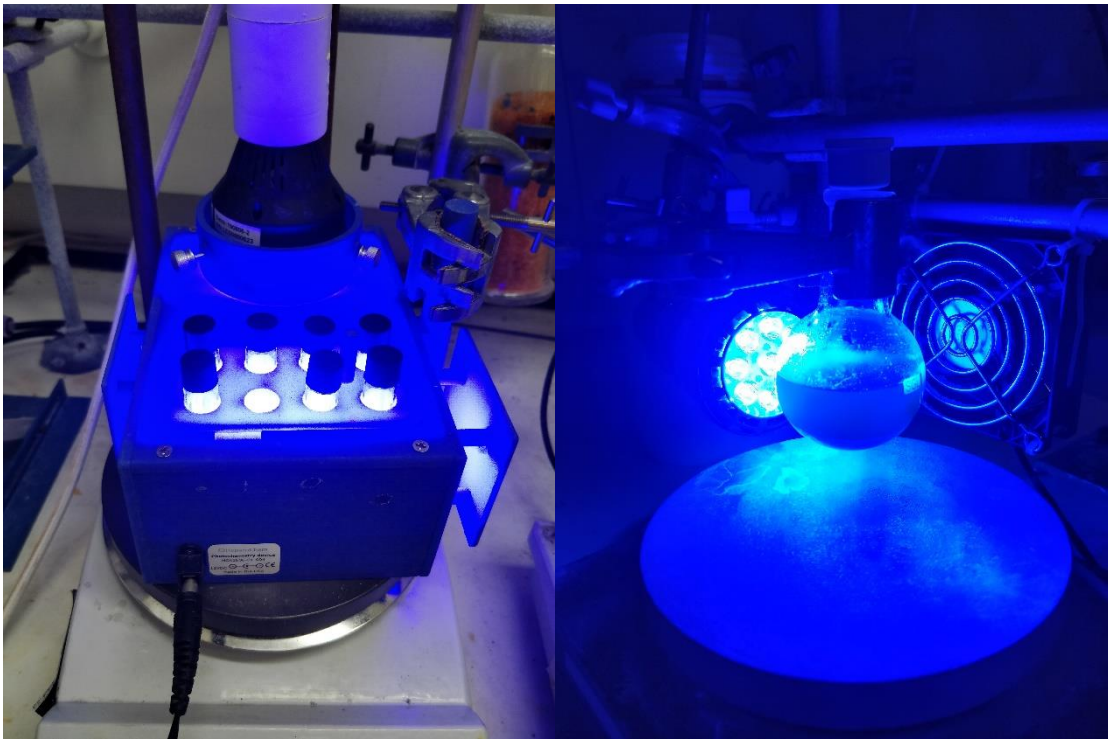
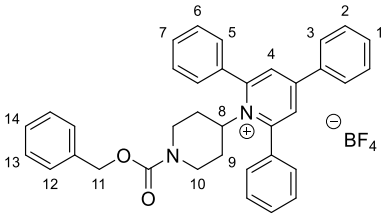


Figure S4. Left: Photobox used for 0.20 mmol scale reactions. Right: Reaction setup for 10 mmol scale reactions.

8.2.3 Katritzky salt data

1-(1-((Benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1a)

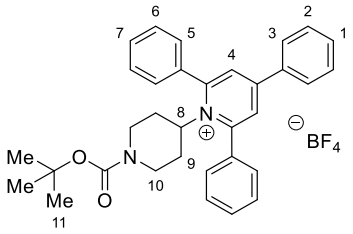


Prepared according to **General Procedure A** using benzyl 4-aminopiperidine-1-carboxylate (2.81 g, 12 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (2.97 g, 7.5 mmol, 1.0 equiv.) in ethanol (7.5 mL). Katritzky salt **1a** was isolated as a white solid (3.54 g, 5.8 mmol, 77%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 2H, NC*H*, Ar*H*), 7.78 – 7.69 (m, 6H, Ar*H*), 7.64 – 7.43 (m, 9H, Ar*H*), 7.38 – 7.28 (m, 3H, Ar*H*), 7.24 – 7.17 (m, 2H, Ar*H*), 4.95 (s, 2H, C(11)H_2), 4.79 (tt, *J* = 12.3, 3.0 Hz, 1H, C(8)*H*), 4.18 – 3.85 (br. m, 2H, 2×C(10)*H*H), 2.35 – 1.94 (m, 4H, 2×C(10)H*H* & 2×C(9)H*H*), 1.82 – 1.57 (br. m, 2H, C(9)*H*H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.3, 155.7, 154.9, 136.4, 134.1, 133.8, 132.2, 131.3, 129.8, 129.4, 129.2, 128.7, 128.5, 128.3, 127.9, 69.7, 67.4, 44.4, 32.6 (br.) *(one signal missing due to signal broadening)*; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -152.95 (minor, $^{10}BF_4$), -153.00 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 525.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{36}H_{33}N_2O_2^+$ $[M\text{-}BF_4]^+$ = 525.2537, Found = 525.2529.

Data is consistent with the literature.[155k]

1-(1-(*tert*-Butoxycarbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1d)

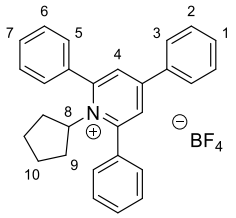


Prepared according to **General Procedure A** using *tert*-butyl 4-aminopiperidine-1-carboxylate (1.20 g, 6.0 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (1.98 g, 5.0 mmol, 1.0 equiv.) in ethanol (5.0 mL). Katritzky salt **1d** was isolated as a white solid (2.18 g, 3.8 mmol, 75%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 2H, Ar*H*), 7.77 – 7.70 (m, 6H, Ar*H*), 7.63 – 7.44 (m, 9H, Ar*H*), 4.78 (br. tt, *J* = 12.4, 3.0 Hz, 1H, C(8)*H*), 4.12 – 3.72 (br. m, 2H, 2×C(10)H*H*), 2.34 – 1.92 (br. m, 4H, 2×C(10)H*H* & C(9)H*H*), 1.81 – 1.55 (br. m, 2H, C(9)*H*H), 1.31 (s, 9H, 3×C(11)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.3, 155.5, 154.3, 134.0, 133.9, 132.1, 131.2, 129.7, 129.4, 129.1, 128.4, 128.3, 80.2, 70.0, 45.0 (br.), 32.8 (br.), 28.4 *(one signal missing due to signal broadening)*; **^{19}F NMR** (377 MHz, CDCl3) δ -152.99 (minor, $^{10}BF_4$), -153.06 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 491.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{33}H_{35}N_2O_2^+$ $[M\text{-}BF_4]^+$ = 491.2693, Found = 491.2682.

Data is consistent with the literature.[153]

1-Cyclopentyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1h)

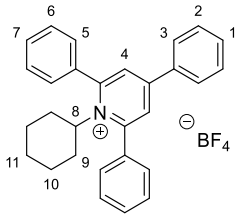


Prepared according to **General Procedure A** using cyclopentylamine (118 µL, 1.2 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (396 mg, 1.0 mmol, 1.0 equiv.) in ethanol (1.0 mL). Katritzky salt **1h** was isolated as a white solid (187 mg, 0.40 mmol, 40%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.70 (m, 8H, Ar*H*), 7.64 – 7.54 (m, 6H, Ar*H*), 7.54 – 7.43 (m, 3H, Ar*H*), 5.05 (p, *J* = 8.8 Hz, 1H, C(8)*H*), 2.29 – 2.15 (m, 2H, 2×C(9)*H*H), 2.09 – 1.95 (m, 2H, 2×C(9)H*H*), 1.24 – 1.09 (m, 2H, C(10)*H*H), 1.01 – 0.87 (m, 2H, C(10)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.9, 155.1, 134.3, 134.1, 132.1, 130.9, 129.7, 129.1, 128.4, 128.4, 70.8, 33.9, 24.7; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.36 (minor, $^{10}BF_4$), -153.42 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 376.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{28}H_{26}N^+$ $[M\text{-}BF_4]^+$ = 376.2062, Found = 376.2062.

Data is consistent with the literature.[157]

1-Cyclohexyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1i)



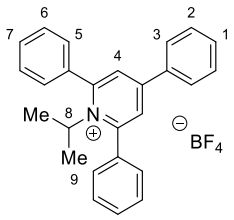
Prepared according to **General Procedure A** using cyclohexylamine (275 µL, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1i** was isolated as a white solid (441 mg, 0.92 mmol, 46%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 2H, Ar*H*), 7.77 – 7.69 (m, 6H, Ar*H*), 7.65 – 7.52 (m, 6H, Ar*H*), 7.55 – 7.40 (m, 3H, Ar*H*), 4.61 (tt, *J* = 12.2, 2.9 Hz, 1H, C(8)*H*), 2.12 (d, *J* = 11.9 Hz, 2H,

2×C(9)*H*H), 1.57 (dt, *J* = 13.5, 3.3 Hz, 2H, 2×C(9)H*H*), 1.47 (qd, *J* = 12.1, 3.4 Hz, 2H, 2×C(10)*H*H), 1.34 (br. d, *J* = 13.9 Hz, 1H, C(11)*H*H), 0.74 (d, *J* = 12.9 Hz, 2H, 2×C(10)H*H*), 0.60 (qt, *J* = 13.2, 3.5 Hz, 1H, C(11)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.2, 155.1, 134.2, 134.1, 132.0, 131.0, 129.7, 129.5, 128.9, 128.4, 128.2, 72.1, 33.7, 26.6, 24.7; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.27 (minor, $^{10}BF_4$), -153.32 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 390.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{29}H_{28}N^+$ $[M\text{-}BF_4]^+$ = 390.2216, Found = 390.2261.

Data is consistent with the literature.[153]

1-Isopropyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1p)

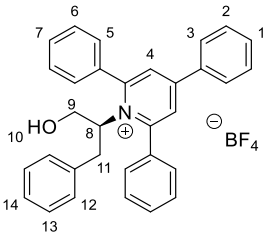


Prepared according to **General Procedure A** using isopropylamine (102 µL, 1.2 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (396 mg, 1.0 mmol, 1.0 equiv.) in ethanol (1.0 mL). Katritzky salt **1p** was isolated as a white solid (231 mg, 0.53 mmol, 53%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.68 (m, 8H, Ar*H*), 7.64 – 7.40 (m, 9H, Ar*H*), 5.11 (hept, *J* = 7.0 Hz, 1H, C(8)*H*), 1.35 (d, *J* = 7.0 Hz, 6H, 2×C(9)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.2, 155.3, 134.2, 134.0, 132.0, 131.0, 129.7, 129.6, 129.0, 128.5, 128.4, 62.8, 23.5; **^{19}F NMR** (377 MHz, CDCl3) δ -153.24 (minor, $^{10}BF_4$), -153.29 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 350.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{26}H_{24}N^+$ $[M\text{-}BF_4]^+$ = 350.1903, Found = 350.1900.

Data is consistent with the literature.[157]

(*S*)-1-(1-Hydroxy-3-phenylpropan-2-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1s)

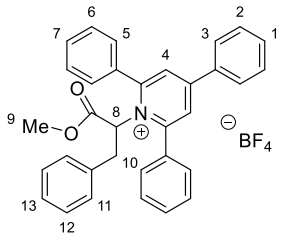


Prepared according to **General Procedure A** using L-phenylalaninol (182 mg, 1.2 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (396 mg, 1.0 mmol, 1.0 equiv.) in ethanol (1.0 mL). Katritzky salt **1s** was isolated as a white solid (402 mg, 0.76 mmol, 76%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 7.70 (m, 7H, Ar*H*), 7.72 – 7.37 (m, 9H, Ar*H*), 7.20 – 7.01 (m, 4H, Ar*H*), 6.59 (d, *J* = 7.0 Hz, 2H, Ar*H*), 5.43 – 5.31 (m, 1H, C(8)*H*), 3.78 – 3.62 (m, 2H, C(9)*H*H & O(10)*H*), 3.53 (dd, *J* = 10.2, 6.0 Hz, 1H, C(9)H*H*), 3.23 (dd, *J* = 14.1, 6.5 Hz, 1H, C(11)H*H*), 2.50 (dd, *J* = 14.1, 8.1 Hz, 1H, C(11)*H*H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.2, 135.7, 133.7, 133.6 (br.), 132.5, 131.2 (br.), 130.2, 129.9, 129.2, 129.1, 128.7, 128.4, 127.6, 73.3, 62.6, 38.5 *(two signals missing due to signal broadening)*; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -152.88 (minor, $^{10}BF_4$), -152.94 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 442.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{32}H_{28}NO^+$ $[M\text{-}BF_4]^+$ = 442.2165, Found = 442.2162.

Data is consistent with the literature.[161a]

(*S*)-1-(1-Methoxy-1-oxo-3-phenylpropan-2-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1t)



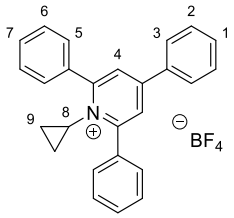
Prepared according to **General Procedure A** using L-phenylalanine methyl ester hydrochloride (259 mg, 1.2 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (396 mg, 1.0 mmol,

1.0 equiv.) in ethanol (1.0 mL) and triethylamine (167 µL, 1.2 mmol, 1.2 equiv.). Katritzky salt **1t** was isolated as a pale-yellow solid (138 mg, 0.25 mmol, 25%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 2H, Ar*H*), 7.90 – 7.72 (m, 4H, Ar*H*), 7.67 – 7.45 (m, 11H, Ar*H*), 7.16 – 7.03 (m, 3H, Ar*H*), 6.78 (dd, *J* = 7.6, 1.7 Hz, 2H, Ar*H*), 5.66 (dd, *J* = 8.2, 3.7 Hz, 1H, C(8)*H*), 3.69 (s, 3H, C(9)H_3), 3.52 (dd, *J* = 14.5, 3.7 Hz, 1H, C(10)H*H*), 2.90 (dd, *J* = 14.4, 8.3 Hz, 1H, C(10)*H*H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.3, 157.3, 157.0, 136.6, 134.0, 132.5, 132.5, 131.6, 129.9, 129.7, 129.3, 129.2, 128.7, 128.1, 127.3, 70.4, 53.8, 37.9 *(one signal missing due to signal broadening)*; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.07 (minor, $^{10}BF_4$), -153.13 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 470.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{33}H_{28}NO_2^+$ $[M\text{-}BF_4]^+$ = 470.2115, Found = 470.2112.

Data is consistent with the literature.[157]

1-cyclopropyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1u)

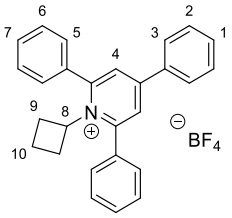


Prepared according to **General Procedure A** using cyclopropylamine (166 µL, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1 equiv.) in ethanol (2.0 mL). Katritzky salt **1u** was isolated as a pale purple solid (539 mg, 1.2 mmol, 62%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.82 (m, 6H, Ar*H*), 7.76 (app. dt, *J* = 6.5, 1.5 Hz, 2H, Ar*H*), 7.62 – 7.47 (m, 9H, Ar*H*), 4.18 – 4.08 (m, 1H, C(8)*H*), 0.66 – 0.54 (m, 4H, 2×C(9)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.4, 156.5, 134.5, 134.0, 132.1, 131.1, 129.8, 129.6, 129.3, 128.3, 126.1, 41.7, 13.9; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.44 (minor, $^{10}BF_4$), -153.50 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 348.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{26}H_{22}N^+$ $[M\text{-}BF_4]^+$ = 348.1747, Found = 348.1745.

Data is consistent with the literature.[2]

1-Cyclobutyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1v)

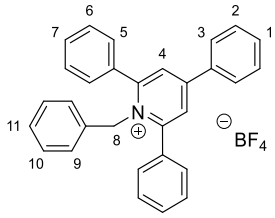


Prepared according to **General Procedure A** using cyclobutylamine (103 µL, 1.2 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (396 mg, 1.0 mmol, 1.0 equiv.) in ethanol (1.0 mL). Katritzky salt **1v** was isolated as a pale-yellow powder (333 mg, 0.74 mmol, 74%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 8.0, 1.5 Hz, 4H, Ar*H*), 7.84 (s, 3H, Ar*H*), 7.82 – 7.77 (m, 4H, Ar*H*), 7.64 – 7.48 (m, 9H, Ar*H*), 5.67 – 5.52 (m, 1H, C(8)*H*), 1.91 – 1.73 (m, 2H, 2×C(9)*H*H), 1.36 – 1.11 (m, 4H, 2×C(9)H*H* & C(10)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.5, 155.6, 134.2, 134.2, 132.2, 131.6, 129.9, 129.7, 129.5, 128.2, 126.3, 64.4, 33.2, 14.3; **^{19}F NMR** (377 MHz, CDCl3) δ -153.07 (minor, $^{10}BF_4$), -153.13 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 362.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{27}H_{24}N^+$ $[M\text{-}BF_4]^+$ = 362.1903, Found = 362.1922.

Data is consistent with the literature.[155j]

1-Benzyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1b)

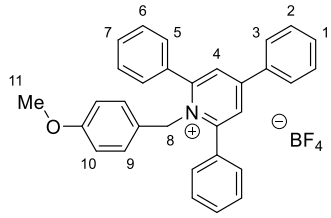


Prepared according to **General Procedure A** using benzylamine (655 µL, 6.0 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (1.98 g, 5.0 mmol, 1.0 equiv.) in ethanol (5.0 mL). Katritzky salt **1b** was isolated as a white solid (2.01 g, 4.1 mmol, 83%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 2H, Ar*H*), 7.85 – 7.78 (m, 2H, Ar*H*), 7.64 (d, *J* = 6.7 Hz, 4H, Ar*H*), 7.61 – 7.42 (m, 9H, Ar*H*), 7.21 – 7.12 (m, 1H, Ar*H*), 7.13 – 7.06 (m, 2H, Ar*H*), 6.46 (d, *J* = 7.4 Hz, 2H, Ar*H*), 5.77 (s, 2H, C(8)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.8, 156.5, 134.4, 134.0, 132.9, 132.5, 131.1, 130.0, 129.3, 129.2, 129.0, 128.4, 128.3, 126.7, 126.4, 58.4; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.13 (minor, $^{10}BF_4$), -153.19 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 398.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{30}H_{24}N^+$ $[M\text{-}BF_4]^+$ = 398.1903, Found = 398.1902.

Data is consistent with the literature.[167a]

1-(4-Methoxybenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1w)

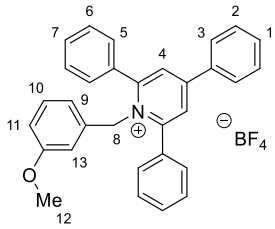


Prepared according to **General Procedure B** using 4-methozybenzylamine (340 µL, 2.6 mmol, 1.3 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in CH_2Cl_2 (4.0 mL) and acetic acid (57 µL, 1.0 mmol, 0.5 equiv.). The crude product was recrystallised from EtOH to Katritzky salt **1w** as a white solid (748 mg, 1.5 mmol, 73%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 2H, Ar*H*), 7.78 (dt, *J* = 6.8, 1.3 Hz, 2H, Ar*H*), 7.65 (br. d, *J* = 6.4 Hz, 4H, Ar*H*), 7.57 – 7.46 (m, 9H, Ar*H*), 6.64 – 6.56 (m, 2H, Ar*H*), 6.34 (d, *J* = 8.5 Hz, 2H, Ar*H*), 5.70 (s, 2H, C(8)H_2), 3.70 (s, 3H, C(11)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.6, 157.6, 156.3, 133.9, 133.0, 132.5, 131.1, 129.9, 129.3, 129.3, 128.3, 127.9, 126.7, 126.1, 114.3, 58.0, 55.4; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.00 (minor, $^{10}BF_4$), -153.06 (major, $^{11}BF_4$); **HRMS** (ESI, *m/z*): Calc. for $C_{31}H_{26}NO^+$ $[M\text{-}BF_4]^+$ = 428.2009, Found = 428.2007.

Data is consistent with the literature.[161a]

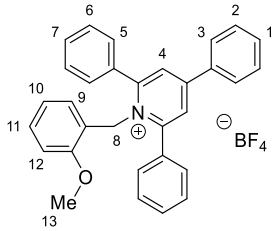
1-(3-Methoxybenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1x)



Prepared according to **General Procedure B** using 3-methozybenzylamine (333 µL, 2.6 mmol, 1.3 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in CH_2Cl_2 (4.0 mL) and acetic acid (57 µL, 1.0 mmol, 0.5 equiv.). The crude product was recrystallised from EtOH to give Katritzky salt **1x** as a white solid (785 mg, 1.5 mmol, 76%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 2H, Ar*H*), 7.80 (dt, *J* = 6.7, 1.4 Hz, 2H, Ar*H*), 7.65 (d, *J* = 6.6 Hz, 4H, Ar*H*), 7.61 – 7.42 (m, 9H, Ar*H*), 7.03 (t, *J* = 8.0 Hz, 1H, Ar*H*), 6.69 (dd, *J* = 8.2, 2.1 Hz, 1H, Ar*H*), 6.09 – 6.03 (m, 1H, Ar*H*), 5.96 (t, *J* = 2.0 Hz, 1H, Ar*H*), 5.73 (s, 2H, C(8)H_2), 3.61 (s, 3H, C(12)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.9, 157.7, 156.4, 135.8, 133.9, 132.9, 132.5, 131.1, 130.0, 129.9, 129.3, 129.3, 128.3, 126.6, 118.4, 113.8, 112.3, 58.3, 55.3; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.06 (minor, $^{10}BF_4$), -153.11 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 428.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{31}H_{26}NO^+$ $[M\text{-}BF_4]^+$ = 428.2009, Found = 428.2011; **IR** (thin film, ν_{max} /cm^{-1}) 2981, 2888, 1620, 1493, 1264, 1150, 1056; **Melting point =** 89 – 92 °C.

1-(2-Methoxybenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1y)



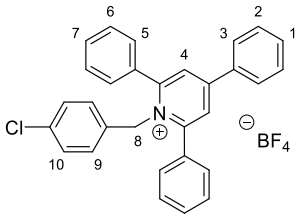
Prepared according to **General Procedure B** using 2-methozybenzylamine (339 µL, 2.6 mmol, 1.3 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in CH_2Cl_2

(4.0 mL) and acetic acid (57 µL, 1.0 mmol, 0.5 equiv.). The crude product was recrystallised from EtOH to give Katritzky salt **1y** as a white solid (897 mg, 1.7 mmol, 87%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 2H, Ar*H*), 7.80 (dq, *J* = 6.5, 2.2 Hz, 2H, Ar*H*), 7.63 (dd, *J* = 7.8, 1.6 Hz, 4H, Ar*H*), 7.58 – 7.40 (m, 9H, Ar*H*), 7.10 (td, *J* = 8.3, 1.6 Hz, 1H, Ar*H*), 6.65 – 6.54 (m, 2H, Ar*H*), 6.27 (dd, *J* = 7.6, 1.3 Hz, 1H, Ar*H*), 5.72 (s, 2H, C(8)H_2), 3.46 (s, 3H, C(13)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.1, 156.5, 156.0, 134.0, 133.3, 132.4, 130.9, 129.9, 129.9, 129.2, 129.2, 128.6, 128.2, 126.3, 122.4, 120.6, 110.4, 55.8, 55.2; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.15 (minor, $^{10}BF_4$), -153.20 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 428.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{31}H_{26}NO^+$ $[M\text{-}BF_4]^+$ = 428.2009, Found = 428.2009.

Data is consistent with the literature.[170]

1-(4-Chlorobenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1z)

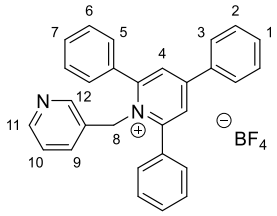


Prepared according to **General Procedure A** using 4-(chloromethyl)methanamine (292 µL, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1z** was isolated as a white solid (869 mg, 1.7 mmol, 84%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 2H, Ar*H*), 7.82 – 7.75 (m, 2H, Ar*H*), 7.69 – 7.62 (m, 4H, Ar*H*), 7.62 – 7.43 (m, 9H, Ar*H*), 7.11 – 7.03 (m, 2H, Ar*H*), 6.46 – 6.38 (m, 2H, Ar*H*), 5.74 (s, 2H, C(8)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.6, 156.7, 134.5, 133.9, 132.8, 132.7, 132.6, 131.3, 130.0, 129.4, 129.2, 129.1, 128.3, 127.8, 126.8, 57.7; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -152.84 (minor, $^{10}BF_4$), -152.90 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 432.2, 434.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{30}H_{23}{}^{35}ClN^+$ $[M\text{-}BF_4]^+$ = 432.1514, Found = 432.1517, Calc. for $C_{30}H_{23}{}^{37}ClN^+$ $[M\text{-}BF_4]^+$ = 434.1486, Found = 434.1488.

Data is consistent with the literature.[167a]

2,4,6-Triphenyl-1-(pyridin-3-ylmethyl)pyridin-1-ium tetrafluoroborate (1aa)

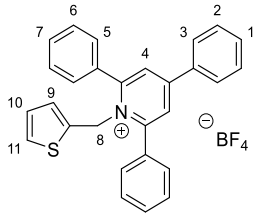


Prepared according to **General Procedure A** using 3-picolylamine (244 µL, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1aa** was isolated as a white solid (762 mg, 1.6 mmol, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (dd, *J* = 4.8, 1.3 Hz, 1H, Ar*H*), 7.91 (s, 2H, Ar*H*), 7.79 – 7.73 (m, 2H, Ar*H*), 7.70 – 7.62 (m, 5H. Ar*H*), 7.60 – 7.43 (m, 9H, Ar*H*), 7.06 (dd, *J* = 7.8, 4.8 Hz, 1H, Ar*H*), 6.93 – 6.86 (m, 1H, Ar*H*), 5.81 (s, 2H, C(8)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.5, 156.9, 149.6, 147.6, 134.6, 133.8, 132.7, 132.6, 131.4, 130.0, 129.94, 129.5, 129.2, 128.3, 126.9, 123.9, 56.1; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -152.63 (minor, $^{10}BF_4$), -152.68 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 399.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{29}H_{23}N_2^+$ $[M\text{-}BF_4]^+$ = 399.1856, Found = 399.1855.

Data is consistent with the literature.[155a]

2,4,6-Triphenyl-1-(thiophen-2-ylmethyl)pyridin-1-ium tetrafluoroborate (1ab)

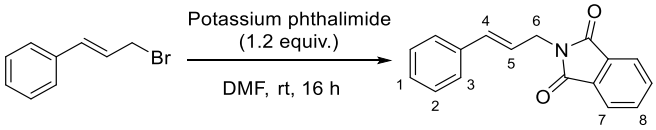


Prepared according to a modified **General Procedure A** using 2-thiophenemethylamine (267 µL, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.)

in ethanol (2.0 mL), stirred at rt overnight. Katritzky salt **1ab** was isolated as a white solid (708 mg, 1.4 mmol, 72%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 2H, Ar*H*), 7.81 – 7.71 (m, 6H, Ar*H*), 7.62 – 7.48 (m, 9H, Ar*H*), 7.11 (dd, *J* = 5.1, 1.1 Hz, 1H, Ar*H*), 6.68 (dd, *J* = 5.1, 3.6 Hz, 1H, Ar*H*), 6.03 (d, *J* = 2.7 Hz, 1H, Ar*H*), 5.95 (s, 2H, C(8)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.4, 156.5, 135.3, 133.8, 132.7, 132.6, 131.3, 130.0, 129.43, 129.40, 128.3, 128.1, 127.0, 126.8, 53.8 *(one signal missing due to signal overlap)*; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -152.98 (minor, $^{10}BF_4$), -153.03 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 404.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{28}H_{22}NS^+$ $[M\text{-}BF_4]^+$ = 404.1467, Found = 404.1470; **IR** (thin film, ν_{max} /cm^{-1}) 3063, 3037, 1619, 1562, 1053, 759, 701; **Melting point =** 131 – 134 °C.

2-[(*E*)-3-Phenyl-allyl]-isoindole-1,3-dione (1ac-1)

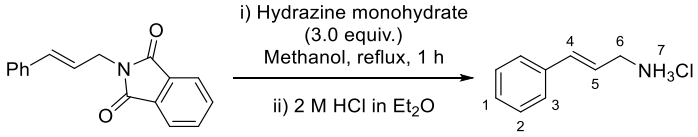


Prepared according to a modified procedure by Jørgensen and co-workers.[2] To a solution of cinnamyl bromide (1.97 g, 10.0 mmol, 1.0 equiv.) anhydrous DMF (25 mL) was added potassium phthalimide (2.22 g, 12 mmol, 1.2 equiv.) in one portion. The reaction mixture was stirred at rt for 16 h. The reaction was diluted with diethyl ether (75 mL), washed with brine (4 × 25 mL), dried using $MgSO_4$, filtered and concentrated in vacuo. The resulting pale orange solid was recrystallised from toluene to afford 2-[(*E*)-3-phenyl-allyl]-isoindole-1,3-dione **1ac-1** as colourless crystals (2.32 g, 8.8 mmol, 88%).

R_f = 0.28 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 – 7.81 (m, 2H, Ar*H*), 7.77 – 7.67 (m, 2H, Ar*H*), 7.39 – 7.16 (m, 5H, Ar*H*), 6.66 (dt, *J* = 15.8, 1.3 Hz, 1H, C(4)*H*), 6.26 (dt, *J* = 15.8, 6.5 Hz, 1H, C(5)*H*), 4.45 (dd, *J* = 6.5, 1.3 Hz, 2H, C(6)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.1, 136.4, 134.1, 134.0, 132.3, 128.7, 128.0, 126.7, 123.5, 122.9, 39.8; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{14}NO_2^+$ $[M+H]^+$ = 264.1019, Found = 264.1021.

Data is consistent with the literature.[225]

(*E*)-3-Phenylprop-2-en-1-aminium chloride (1ac-2)

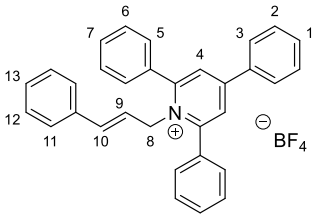


Prepared according to a modified procedure by Jørgensen and co-workers.[2] To a solution of 2-[(*E*)-3-phenyl-allyl]-isoindole-1,3-dione **1ac-1** (2.24 g, 8.5 mmol, 1.0 equiv.) in methanol (35 mL) was added hydrazine monohydrate (1.24 mL, 25.5 mmol, 3.0 equiv.). The reaction mixture was heated to reflux with vigorous stirring under N_2 for 1 h. The reaction mixture was cooled to 0 °C and the precipitate was filtered off. The filtrate was concentrated in vacuo and the resulting mixture resuspended in Et_2O (50 mL), filtered and the filtrate concentrated in vacuo. The resultant yellow oil was dissolved in ethanol (10 mL) and converted into the hydrochloride using 2.0 M HCl in Et_2O (25 mL, 0.5 mol, 5.9 equiv.). The mixture was concentrated in vacuo and the crude product was recrystallised from toluene to give (*E*)-3-phenylprop-2-en-1-ammonium chloride **1ac-2** as colourless needles (526 mg, 3.1 mmol, 37%).

^{1}H NMR (400 MHz, Methanol-d_4) δ 7.46 (dt, *J* = 8.2, 2.3 Hz, 2H, Ar*H*), 7.39 – 7.25 (m, 3H, Ar*H*), 6.82 (d, *J* = 15.9 Hz, 1H, C(4)*H*), 6.31 (dt, *J* = 15.9, 6.9 Hz, 1H, C(5)*H*), 3.72 (d, *J* = 6.8 Hz, 2H, C(6)H_2); **^{13}C NMR** (101 MHz, Methanol-d_4) δ 137.8, 137.1, 129.8, 129.6, 127.8, 121.2, 42.5.

Data is consistent with the literature.[225]

1-Cinnamyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1ac-3)

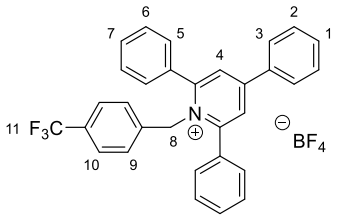


Prepared according to **General Procedure B** using (*E*)-3-phenylprop-2-en-1-ammonium chloride **1ac-2** (407 mg, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in CH_2Cl_2 (4.0 mL), triethylamine (335 µL, 2.4 mmol, 1.2 equiv.) and acetic acid (57 µL, 1.0 mmol, 0.5 equiv.). Katritzky salt **1ac-3** was isolated as a white solid (278 mg, 0.54 mmol, 27%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 2H, Ar*H*), 7.83 – 7.75 (m, 6H, Ar*H*), 7.63 – 7.49 (m, 9H, Ar*H*), 7.29 – 7.23 (m, 3H, Ar*H*), 7.12 – 7.05 (m, 2H, Ar*H*), 5.76 (dt, *J* = 15.8, 6.3 Hz, 1H, C(9)*H*), 5.62 (d, *J* = 15.8 Hz, 1H, C(10)*H*), 5.23 (dd, *J* = 6.4, 1.3 Hz, 2H, C(8)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.1, 156.3, 136.4, 135.0, 134.1, 132.9, 132.3, 131.2, 129.9, 129.4, 128.9, 128.8, 128.4, 128.3, 126.8, 126.8, 120.4, 57.4; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.21 (minor, $^{10}BF_4$), -153.27 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 424.2, $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{32}H_{26}N^+$ $[M\text{-}BF_4]^+$ = 424.2060, Found = 424.2053.

Data is consistent with the literature.[226]

2,4,6-Triphenyl-1-(4-(trifluoromethyl)benzyl)pyridin-1-ium tetrafluoroborate (1ad)

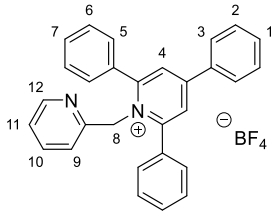


Prepared according to **General Procedure A** using 4-(trifluoromethyl)benzylamine (342 µL, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1ad** was isolated as a white solid (854 mg, 1.5 mmol, 77%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 2H, Ar*H*), 7.77 (d, *J* = 7.7 Hz, 2H, Ar*H*), 7.64 (d, *J* = 7.0 Hz, 4H, Ar*H*), 7.56 (t, *J* = 7.3 Hz, 1H, Ar*H*), 7.47 (dt, *J* = 23.5, 7.2 Hz, 8H, Ar*H*), 7.35 (d, *J* = 8.2 Hz, 2H, Ar*H*), 6.64 (d, *J* = 8.1 Hz, 2H, Ar*H*), 5.83 (s, 2H, C(8)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.6, 156.9, 138.1, 133.8, 132.7, 132.6, 131.3, 130.6 (q, *J* = 33.0 Hz), 129.9, 129.4, 129.2, 128.4, 126.9, 126.8, 125.9 (q, *J* = 3.5 Hz), 123.7 (q, *J* = 272.5 Hz), 57.8; **^{19}F NMR** (377 MHz, $CDCl_3$) δ 62.78, -152.61 (minor, $^{10}BF_4$), -152.66 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 466.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{31}H_{23}F_3N^+$ $[M\text{-}BF_4]^+$ = 466.1777, Found = 466.1768.

Data is consistent with the literature.[161a]

2,4,6-triphenyl-1-(pyridin-2-ylmethyl)pyridin-1-ium tetrafluoroborate (1ae)

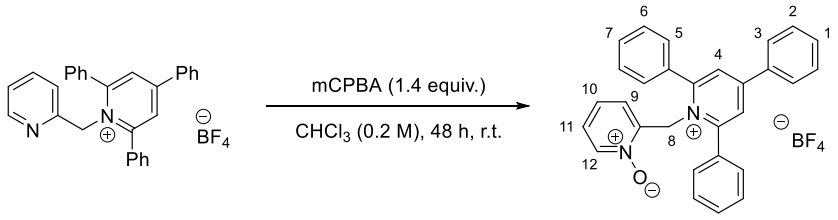


Prepared according to **General Procedure A** using 2-picolylamine (374 µL, 3.6 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (1.19 g, 3.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1ae** was isolated as a white powder (842 mg, 1.7 mmol, 58%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (ddd, *J* = 5.0, 1.7, 1.0 Hz, 1H, Ar*H*), 7.93 (s, 2H, Ar*H*), 7.82 (dq, *J* = 6.4, 2.3, 2.0 Hz, 2H, Ar*H*), 7.64 – 7.51 (m, 7H, Ar*H*), 7.49 – 7.33 (m, 7H, Ar*H*), 7.14 (dd, *J* = 6.6, 4.9 Hz, 1H, Ar*H*), 6.51 (d, *J* = 7.8 Hz, 1H, Ar*H*), 5.77 (s, 2H, C(8)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.7, 156.0, 153.4, 149.3, 136.9, 134.2, 133.1, 132.3, 130.9, 129.9, 129.0, 128.2, 126.2, 123.2, 121.9, 59.1 *(one signal missing due to signal overlap)*; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.28 (minor, $^{10}BF_4$), -153.34 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 399.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{29}H_{23}N_2^+$ $[M\text{-}BF_4]^+$ = 399.1856, Found = 399.1858.

Data is consistent with the literature.[5]

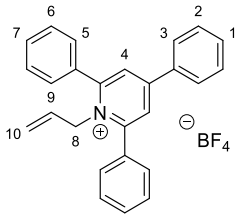
2-((2,4,6-Triphenylpyridin-1-ium-1-yl)methyl)pyridine 1-oxide tetrafluoroborate (1af)



To a solution of 2,4,6-triphenyl-1-(pyridin-2-ylmethyl)pyridin-1-ium tetrafluoroborate **1af** (973 mg, 2.0 mmol, 1.0 equiv.) in $CHCl_3$ (10 mL) was added mCPBA (483 mg, 2.8 mmol, 1.4 equiv.). The reaction mixture was stirred at rt for 48 h. After completion, the reaction mixture was quenched with 10% aqueous solution of Na_2SO_3. The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ (4 × 10 mL) and water (2 × 25 mL), dried using $MgSO_4$ and solvent was removed in vacuo. The crude product was recrystallized from hot ethanol to give Katritzky salt **1af** as a white solid (425 mg, 0.85 mmol, 42%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 2H, Ar*H*), 7.85 (d, *J* = 6.2 Hz, 1H, Ar*H*), 7.81 – 7.73 (m, 6H, Ar*H*), 7.61 – 7.49 (m, 9H, Ar*H*), 7.05 (ddd, *J* = 8.2, 6.5, 1.9 Hz, 1H, Ar*H*), 6.81 (td, *J* = 7.8, 1.0 Hz, 1H, Ar*H*), 6.52 (dd, *J* = 7.9, 1.7 Hz, 1H, Ar*H*), 5.99 (s, 2H, C(8)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.0, 156.3, 142.9, 138.9, 133.9, 133.4, 132.5, 131.5, 129.9, 129.7, 129.2, 128.5, 128.2, 126.0, 125.9, 56.5 (*1 aromatic carbon signal is not observed due to signal overlap*); **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.36 (minor, $^{10}BF_4$), -153.41 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 415.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{29}H_{23}N_2O^+$ $[M\text{-}BF_4]^+$ = 415.1805, Found = 415.1801; **IR** (thin film, ν_{max} /cm^{-1}) 3062, 1621, 1562, 1440, 1252, 1056; **Melting point =** 185 – 188 °C.

1-Allyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1ag)

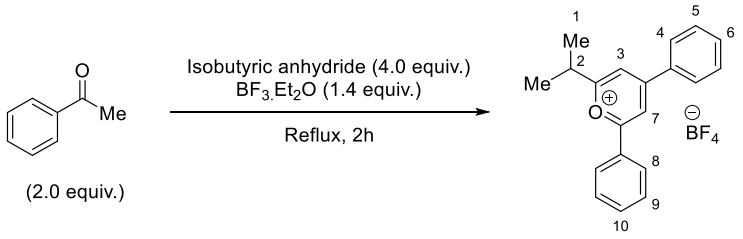


Prepared according to **General Procedure A** using allylamine (180 µL, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1 equiv.) in ethanol (2.0 mL). Katritzky salt **1ag** was isolated as a white solid (519 mg, 1.2 mmol, 60%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 2H, Ar*H*), 7.81 – 7.72 (m, 6H, Ar*H*), 7.63 – 7.48 (m, 9H, Ar*H*), 5.53 (ddt, *J* = 15.7, 10.1, 5.4 Hz, 1H, C(9)*H*), 5.13 – 5.05 (m, 3H, C(8)H_2 and C(10)*H*H), 4.52 (d, *J* = 17.2 Hz, 1H, C(10)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.2, 156.3, 134.1, 132.7, 132.4, 131.2, 130.6, 129.9, 129.3, 129.3, 128.3, 126.8, 120.2, 57.2; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.32 (minor, $^{10}BF_4$), -153.38 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 348.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{26}H_{22}N^+$ $[M\text{-}BF_4]^+$ = 348.1747, Found = 348.1745.

Data is consistent with the literature.[3]

2-Isopropyl-4,6-diphenylpyrylium tetrafluoroborate (8a)



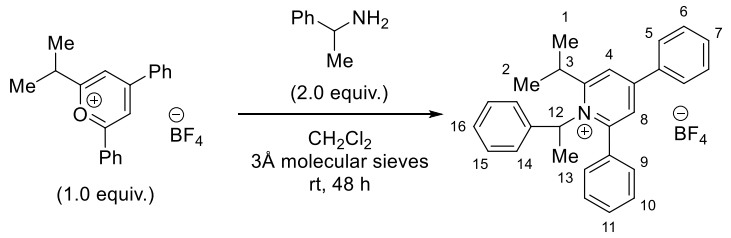
According to the procedure described by Boiko and co-workers,[227] a mixture of acetophenone (4.66 mL, 40 mmol, 2.0 equiv.), isobutyric anhydride (13.3 mL, 80 mmol, 4.0 equiv.) and $BF_3{\cdot}Et_2O$ (3.45 mL, 28 mmol, 1.4 equiv.) was refluxed for 2 h. The hot mixture was then poured into EtOAc and boiled for 5 mins. The solid pyrylium was then filtered and washed with boiling EtOAc. The

solid product was then recrystalised from methanol to give 2-isopropyl-4,6-diphenylpyrylium tetrafluoroborate **8a** as bright yellow crystals (5.20 g, 14 mmol, 72%).

^{1}H NMR (400 MHz, Acetone-d_6) δ 9.15 (d, *J* = 1.8 Hz, 1H, Ar*H*), 8.61 (d, *J* = 1.7 Hz, 1H, Ar*H*), 8.58 – 8.51 (m, 2H, Ar*H*), 8.50 – 8.42 (m, 2H, Ar*H*), 7.92 – 7.83 (m, 2H, Ar*H*), 7.83 – 7.72 (m, 4H, Ar*H*), 3.79 (hept, *J* = 6.9 Hz, 1H, C(2)*H*), 1.67 (d, *J* = 6.9 Hz, 6H, 2×C(1)H_3); **^{13}C NMR** (101 MHz, Acetone-d_6) δ 185.1, 173.1, 167.9, 136.2, 136.1, 133.8, 131.0, 130.9, 130.7, 130.2, 129.5, 117.7, 116.3, 35.7, 20.6; **^{19}F NMR** (377 MHz, Acetone-d_6) δ -148.28 (minor, $^{10}BF_4$), -148.34 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 275.1 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{20}H_{19}^+$ $[M\text{-}BF_4]^+$ = 275.1430, Found = 275.1431.

Data is consistent with the literature.[174]

2-Isopropyl-4,6-diphenyl-1-(1-phenylethyl)pyridin-1-ium tetrafluoroborate (1ai)



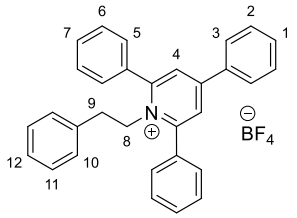
According to the procedure described by Katritzky and co-workers,[174] 1-phenylethanamine (356 µL, 2.76 mmol, 2.0 equiv.) and 2-isopropyl-4,6-diphenylpyrylium tetrafluoroborate **8a** (500 mg, 1.38 mmol, 1.0 equiv.) were stirred in CH_2Cl_2 (20 mL) over 3Å molecular sieves for 48 h at rt. Diethyl ether was then added and the resulting crude product was filtered. Recrystallisation from EtOH then gave Katritzky salt **1ai** as a white crystalline solid (302.3 mg, 0.65 mmol, 47%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 2.3 Hz, 1H, Ar*H*), 7.90 – 7.75 (m, 4H, Ar*H*), 7.69 – 7.48 (m, 7H, Ar*H*), 7.43 (t, *J* = 7.6 Hz, 2H, Ar*H*), 7.34 (t, *J* = 7.1 Hz, 1H, Ar*H*), 7.11 (d, *J* = 7.9 Hz, 2H, Ar*H*), 6.24 (q, *J* = 7.0 Hz, 1H, C(12)*H*), 3.32 (app. p, *J* = 6.6 Hz, 1H, C(3)*H*), 2.14 (d, *J* = 7.2 Hz, 3H, C(13)H_3), 1.47 (d, *J* = 7.0 Hz, 3H, C(2)H_3), 0.74 (d, *J* = 6.1 Hz, 3H, C(1)H_3); **^{13}C NMR**

(101 MHz, $CDCl_3$) δ 166.7, 156.7, 156.6, 138.0, 134.3, 133.9, 132.1, 131.2, 130.0, 129.8, 129.7, 129.0, 128.9, 128.4, 127.8, 126.0, 125.4, 64.7, 32.4, 24.0, 22.1, 18.*6 (note: for isopropyl substituent, 3 peaks were found instead of 2 due to restricted rotation)*; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -152.98 (minor, $^{10}BF_4$), -153.03 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 378.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{28}H_{28}N^+$ $[M\text{-}BF_4]^+$ = 378.2216, Found = 378.2211.

Data is consistent with the literature.[174]

1-Phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1c)

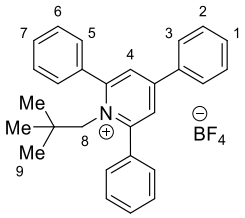


Prepared according to **General Procedure A** using phenethylamine (756 µL, 6.0 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (1.98 g, 5.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1c** was isolated as a white solid (2.39 g, 4.8 mmol, 96%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 2H, Ar*H*), 7.81 (dt, *J* = 6.5, 1.5 Hz, 6H, Ar*H*), 7.70 – 7.50 (m, 9H, Ar*H*), 7.18 – 7.11 (m, 1H, Ar*H*), 7.11 – 7.03 (m, 2H, Ar*H*), 6.34 – 6.28 (m, 2H, Ar*H*), 4.72 – 4.63 (m, 2H, C(8)H_2), 2.76 – 2.68 (m, 2H, C(9)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.8, 156.2, 135.3, 134.2, 132.9, 132.3, 131.3, 129.9, 129.5, 129.3, 129.0, 128.34, 128.32, 127.5, 126.9, 56.0, 35.8; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.27 (minor, $^{10}BF_4$), -153.33 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 412.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{31}H_{26}N^+$ $[M\text{-}BF_4]^+$ = 412.2060, Found = 412.2062.

Data is consistent with the literature.[153]

1-Neopentyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1aj)

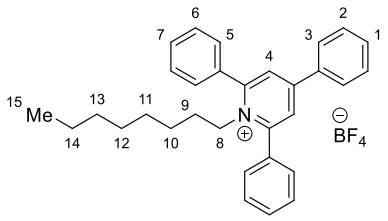


Prepared according to **General Procedure A** using neopentylamine (283 µL, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1aj** was isolated as a white solid (671 mg, 1.4 mmol, 72%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 – 8.11 (m, 2H, Ar*H*), 7.91 (s, 2H, Ar*H*), 7.82 (dd, *J* = 7.8, 1.7 Hz, 2H, Ar*H*), 7.69 – 7.50 (m, 11H, Ar*H*), 5.02 (s, 2H, C(8)H_2), 0.46 (s, 9H, 3×C(9)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.1, 155.7, 134.5, 133.6, 132.7, 131.5, 130.5, 130.0, 129.7, 128.3, 126.7, 64.0, 35.6, 29.0; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -152.92 (minor, $^{10}BF_4$), -152.97 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 378.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{31}H_{34}N^+$ $[M\text{-}BF_4]^+$ = 378.2216, Found = 378.2228.

Data is consistent with the literature.[173]

1-Octyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1ak)



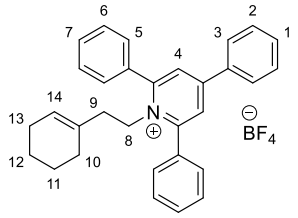
Prepared according to **General Procedure A** using octylamine (397 µL, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1ak** was isolated as a white solid (737 g, 1.5 mmol, 73%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 2H, Ar*H*), 7.82 – 7.76 (m, 4H, Ar*H*), 7.76 – 7.71 (m, 2H, Ar*H*), 7.63 – 7.56 (m, 6H, Ar*H*), 7.57 – 7.45 (m, 3H, Ar*H*), 4.44 – 4.35 (m, 2H, C(8)H_2), 1.43 (dq, *J*

= 8.2, 5.2 Hz, 2H, C(9)H_2), 1.13 (p, J = 7.2 Hz, 2H, C(14)H_2), 1.00 (dq, J = 9.0, 6.7 Hz, 2H, C(13)H_2), 0.95 – 0.85 (m, 2H, C(12)H_2), 0.80 (t, J = 7.3 Hz, 3H, C(15)H_3), 0.78 – 0.69 (m, 4H, C(10)H_2 & C(11)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.6, 155.8, 134.2, 132.9, 132.2, 131.1, 129.8, 129.4, 129.2, 128.2, 126.8, 54.9, 31.5, 29.7, 28.6, 28.0, 26.1, 22.6, 14.1; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.38 (minor, $^{10}BF_4$), -153.44 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{31}H_{34}N^+$ $[M\text{-}BF_4]^+$ = 420.2662, Found = 420.2668.

Data is consistent with the literature.[228]

1-(2-(Cyclohex-1-en-1-yl)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1al)

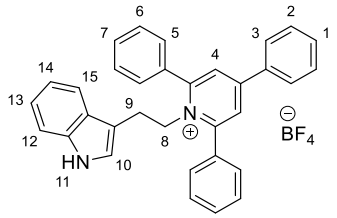


Prepared according to **General Procedure A** using 2-(1-cyclohexenyl)-ethylamine (335 µL, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1al** was isolated as a white solid (883 mg, 1.8 mmol, 88%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 – 7.78 (m, 6H, Ar*H*), 7.76 – 7.70 (m, 2H, Ar*H*), 7.63 – 7.57 (m, 6H, Ar*H*), 7.56 – 7.45 (m, 3H, Ar*H*), 4.84 – 4.78 (m, 1H, C(14)*H*), 4.47 – 4.38 (m, 2H, C(8)H_2), 2.05 – 1.97 (m, 2H, C(9)H_2), 1.76 – 1.66 (m, 2H, C(10)H_2), 1.31 (app. p, J = 3.1 Hz, 4H, C(11)H_2 & C(12)H_2), 1.15 – 1.05 (m, 2H, C(13)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.6, 155.8, 134.2, 132.9, 132.2, 131.8, 131.1, 129.8, 129.4, 129.3, 128.2, 126.8, 125.6, 54.3, 38.3, 27.2, 25.1, 22.4, 21.7; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.36 (minor, $^{10}BF_4$), -153.41 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 416.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{31}H_{30}N^+$ $[M\text{-}BF_4]^+$ = 416.2349, Found = 416.2349.

Data is consistent with the literature.[167a]

1-(2-(1*H*-Indol-3-yl)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1am)

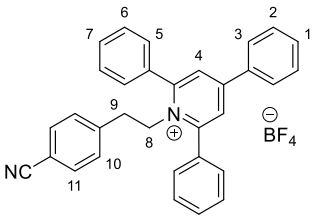


Prepared according to **General Procedure A** using tryptamine (385 mg, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1am** was isolated as a white solid (528 mg, 0.98 mmol, 49%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.81 (s, 1H, N(11)*H*), 8.47 (s, 2H, Ar*H*), 8.26 (d, *J* = 7.2 Hz, 2H, Ar*H*), 7.88 – 7.58 (m, 14H, Ar*H*), 7.27 (d, *J* = 8.1 Hz, 1H, Ar*H*), 6.99 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.71 (t, *J* = 7.4 Hz, 1H, Ar*H*), 6.53 (s, 1H, Ar*H*), 6.30 (d, *J* = 7.9 Hz, 1H, Ar*H*), 4.63 – 4.51 (m, 2H, C(8)H_2), 2.82 – 2.71 (m, 2H, C(9)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.1, 154.2, 136.0, 133.2, 133.1, 132.4, 130.9, 129.6, 129.3, 129.1, 128.7, 126.3, 126.0, 123.0, 121.3, 118.5, 117.0, 111.5, 108.0, 55.3, 25.1; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -148.22 (minor, $^{10}BF_4$), -148.28 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 451.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{33}H_{27}N_2^+$ $[M\text{-}BF_4]^+$ = 451.2169, Found = 451.2164.

Data is consistent with the literature.[167a]

1-(4-Cyanophenethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1an)

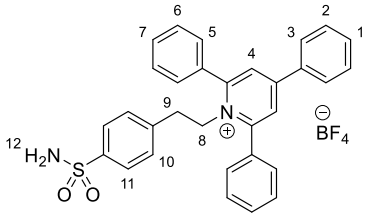


Prepared according to **General Procedure A** using 4-Cyanophenylethylamine hydrochloride (438 mg, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL) and triethylamine (335 µL, 2.4 mmol, 1.2 mmol). Katritzky salt **1an** was isolated as a white solid (472 mg, 0.90 mmol, 45%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 2H, Ar*H*), 7.85 – 7.78 (m, 4H, Ar*H*), 7.76 – 7.70 (m, 2H, Ar*H*), 7.69 – 7.58 (m, 6H, Ar*H*), 7.58 – 7.52 (m, 1H, Ar*H*), 7.51 – 7.44 (m, 2H, Ar*H*), 7.31 (d, *J* = 8.3 Hz, 2H, Ar*H*), 6.37 (d, *J* = 8.3 Hz, 2H, Ar*H*), 4.64 – 4.50 (m, 2H, C(8)H_2), 2.89 – 2.74 (m, 2H, C(9)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.5, 141.0, 134.1, 132.7, 132.6, 132.4, 131.4, 129.8, 129.6, 129.2, 129.1, 128.3, 127.0, 118.4, 111.3, 55.1, 35.6; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -152.82 (minor, $^{10}BF_4$), -152.87 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 437.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{32}H_{25}N_2^+$ $[M\text{-}BF_4]^+$ = 437.2012, Found = 437.2027.

Data is consistent with the literature.[167a]

2,4,6-Triphenyl-1-(4-sulfamoylphenethyl)pyridin-1-ium tetrafluoroborate (1ao)

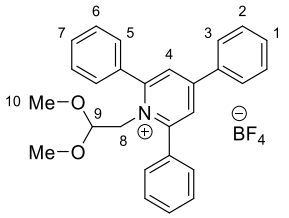


Prepared according to **General Procedure A** using 4-(2-aminoethyl)benzenesulfonamide (481 mg, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1ao** was isolated as a white solid (1.06 g, 1.8 mmol, 92%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.48 (s, 2H, Ar*H*), 8.30 – 8.23 (m, 2H, Ar*H*), 7.80 – 7.60 (m, 13H, Ar*H*), 7.54 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.33 (s, 2H, N(12)H_2), 6.60 (d, *J* = 8.3 Hz, 2H, Ar*H*), 4.61 (t, *J* = 7.4 Hz, 2H, C(8)H_2), 2.70 (t, *J* = 7.3 Hz, 2H, C(9)H_2); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 156.2, 154.5, 143.1, 139.7, 133.1, 132.9, 132.5, 131.0, 129.6, 129.3, 129.2, 128.8, 128.7, 126.1, 126.0, 55.3, 34.3; **^{19}F NMR** (377 MHz, DMSO-d_6) δ -148.25 (minor, $^{10}BF_4$), -148.31 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 491.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{31}H_{27}N_2O_2S^+$ $[M\text{-}BF_4]^+$ = 491.1788, Found = 491.1782.

Data is consistent with the literature.[167a]

1-(2,2-Dimethoxyethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1ap)

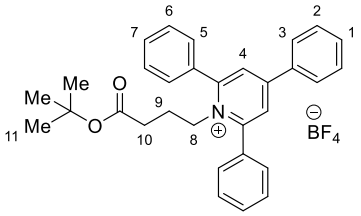


Prepared according to **General Procedure A** using aminoacetaldehyde dimethyl acetal (261 µL, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1ap** was isolated as a white solid (820 mg, 1.7 mmol, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 2H, Ar*H*), 7.85 – 7.75 (m, 6H, Ar*H*), 7.64 – 7.49 (m, 9H, Ar*H*), 4.77 (d, *J* = 5.4 Hz, 2H, C(8)H_2), 3.95 (t, *J* = 5.4 Hz, 1H, C(9)*H*), 2.92 (s, 6H, 2×C(10)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.8, 156.1, 133.9, 133.3, 132.5, 131.2, 129.9, 129.8, 129.4, 128.3, 126.4, 101.2, 55.2, 54.9; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.15 (minor, $^{10}BF_4$), -153.20 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 396.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{27}H_{26}NO_2^+$ $[M\text{-}BF_4]^+$ = 396.1958, Found = 396.1958.

Data is consistent with the literature.[229]

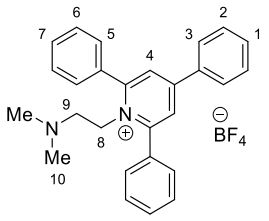
1-(4-(*tert*-Butoxy)-4-oxobutyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1aq)



Prepared according to **General Procedure A** using *tert*-butyl 4-aminobutanoate hydrochloride (470 mg, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL) and triethylamine (335 µL, 2.4 mmol, 1.2 mmol). Katritzky salt **1aq** was isolated as a white solid (610 mg, 1.1 mmol, 57%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 2H, Ar*H*), 7.85 – 7.79 (m, 4H, Ar*H*), 7.79 – 7.73 (m, 2H, Ar*H*), 7.65 – 7.59 (m, 6H, Ar*H*), 7.57 – 7.48 (m, 3H, Ar*H*), 4.51 (t, *J* = 7.7 Hz, 2H, C(8)H_2), 1.76 – 1.67 (m, 4H, C(9)H_2 & C(10)H_2), 1.26 (s, 9H, 3×C(11)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.7, 156.8, 156.1, 134.2, 132.9, 132.2, 131.2, 129.8, 129.5, 129.2, 128.3, 127.0, 81.1, 54.4, 32.2, 28.0, 25.2; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.34 (minor, $^{10}BF_4$), -153.39 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 450.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{31}H_{32}NO_2^+$ $[M\text{-}BF_4]^+$ = 450.2428, Found = 450.2429, **IR** (thin film, ν_{max} /cm^{-1}) 3063, 2980, 1723, 1623, 1154, 1054, 704; **Melting point =** 163 – 165 °C.

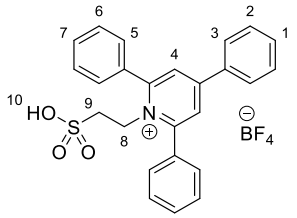
1-(2-(Dimethylamino)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1ar)



Prepared according to **General Procedure A** using *N*,*N*-dimethylethylenediamine (258 µL, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1ar** was isolated as a pale-yellow solid (836 mg, 1.8 mmol, 90%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.47 (s, 2H, Ar*H*), 8.31 – 8.23 (m, 2H, Ar*H*), 7.94 – 7.86 (m, 4H, Ar*H*), 7.76 – 7.58 (m, 9H, Ar*H*), 4.48 (t, *J* = 7.0 Hz, 2H, C(8)H_2), 2.20 (t, *J* = 7.0 Hz, 2H, C(9)H_2), 1.62 (s, 6H, 2×C(10)H_3); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 156.4, 154.2, 133.1, 133.1, 132.4, 131.0, 129.6, 129.5, 129.1, 128.7, 125.9, 56.8, 51.9, 44.3; **^{19}F NMR** (377 MHz, DMSO-d_6) δ -153.11 (minor, $^{10}BF_4$), -153.16 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 379.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{27}H_{27}N_2^+$ $[M\text{-}BF_4]^+$ = 379.2169, Found = 379.2169, **IR** (thin film, ν_{max} /cm^{-1}) 3063, 2829, 2779, 1621, 1564, 1054, 703; **Melting point =** 260 – 264 °C.

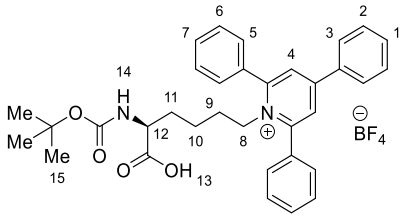
2,4,6-Triphenyl-1-(2-sulfoethyl)pyridin-1-ium tetrafluoroborate (1as)



Prepared according to **General Procedure A** using taurine (300 mg, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). A few drops of triethylamine were added to solubilise the taurine. Purification by flash column chromatography (0 – 100% Acetone in CH_2Cl_2) afforded Katritzky salt **1as** as an off-white solid (727 mg, 1.4 mmol, 72%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.38 (s, 2H, Ar*H*), 8.31 (s, 1H, O(10)*H*), 8.24 (d, *J* = 7.2 Hz, 2H, Ar*H*), 7.90 – 7.81 (m, 4H, Ar*H*), 7.73 – 7.56 (m, 9H, Ar*H*), 4.75 – 4.65 (m, 2H, C(8)H_2), 2.47 – 2.39 (m, 2H, C(9)H_2); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 156.6, 153.9, 133.2, 133.1, 132.3, 130.8, 129.5, 129.3, 129.0, 128.6, 125.9, 52.3, 48.9; **^{19}F NMR** (377 MHz, DMSO-d_6) δ -148.23 (minor, $^{10}BF_4$), -148.29 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 416.0 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{25}H_{22}NO_3S^+$ $[M\text{-}BF_4]^+$ = 416.1315, Found = 416.1313, **IR** (thin film, ν_{max} /cm^{-1}) 3406, 3058, 1620, 1563, 1179, 1029, 701; **Melting point =** 252 – 254 °C (decomposition).

(*S*)-1-(5-((*tert*-Butoxycarbonyl)amino)-5-carboxypentyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1at)

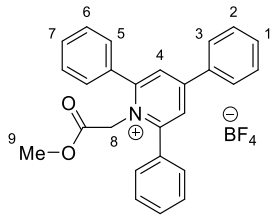


Prepared according to **General Procedure A** using N_α-(*tert*-butoxycarbonyl)-L-lysine (591 mg, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1at** was isolated as a white solid (835 mg, 1.3 mmol, 67%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 2H, Ar*H*), 7.79 – 7.67 (m, 6H, Ar*H*), 7.61 – 7.40 (m, 9H, Ar*H*), 6.84 (s, 1H, O(13)*H*), 5.03 (d, *J* = 7.7 Hz, 1H, N(14)*H*), 4.42 – 4.28 (m, 2H, C(8)H_2), 3.95 – 3.83 (m, 1H, C(12)*H*), 1.50 – 1.40 (m, 2H, C(10)H_2), 1.37 (s, 9H, 3×C(15)H_3), 1.27 – 1.16 (m, 1H, C(11)*H*H), 1.08 (dq, *J* = 13.6, 6.8 Hz, 1H, C(11)H*H*), 0.85 – 0.69 (m, 2H, C(9)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.8, 156.6, 155.8, 155.6, 134.1, 132.8, 132.2, 131.3, 129.8, 129.5, 129.1, 128.2, 126.8, 54.5, 52.9, 29.2, 28.4, 22.0; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -152.19 (minor, $^{10}BF_4$), -152.24 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 537.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{34}H_{37}N_2O_4^+$ $[M\text{-}BF_4]^+$ = 537.2748, Found = 537.2745.

Data is consistent with the literature.[167a]

1-(2-Methoxy-2-oxoethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1au)

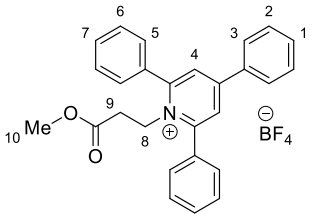


Prepared according to **General Procedure A** using glycine methyl ester hydrochloride (301 mg, 2.4 mmol, 1.2 equiv.), 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) and triethylamine (335 µL, 2.4 mmol, 1.2 equiv.) in ethanol (2.0 mL). Katritzky salt **1au** was isolated as a white solid (543 mg, 1.2 mmol, 58%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 2H, Ar*H*), 7.84 – 7.50 (m, 15H, Ar*H*), 5.10 (s, 2H, C(8)H_2), 3.54 (s, 3H, C(9)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.4, 157.4, 157.1, 133.9, 132.6, 132.2, 131.5, 129.9, 129.5, 129.0, 128.3, 126.3, 56.3, 53.4; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.31 (minor, $^{10}BF_4$), -153.36 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 380.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{26}H_{22}NO_2^+$ $[M\text{-}BF_4]^+$ = 380.1645, Found = 380.1649.

Data is consistent with the literature.[4]

1-(3-Methoxy-3-oxopropyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1av)

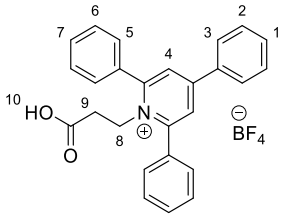


Prepared according to **General Procedure A** using β-alanine methyl ester hydrochloride (335 mg, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL) and triethylamine (335 µL, 2.4 mmol, 1.2 mmol). Katritzky salt **1av** was isolated as a white solid (482 mg, 1.0 mmol, 50%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 2H, Ar*H*), 7.82 – 7.73 (m, 6H, Ar*H*), 7.63 – 7.47 (m, 9H, Ar*H*), 4.79 – 4.70 (m, 2H, C(8)H_2), 3.43 (s, 3H, C(10)H_3), 2.57 – 2.48 (m, 2H, C(9)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.5, 156.9, 156.6, 134.2, 132.7, 132.3, 131.4, 129.8, 129.7, 129.2, 128.4, 127.1, 52.2, 50.3, 33.0; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -152.94 (minor, $^{10}BF_4$), -152.99 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 394.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{27}H_{24}NO_2^+$ $[M\text{-}BF_4]^+$ = 394.1802, Found = 394.1805.

Data is consistent with the literature.[230]

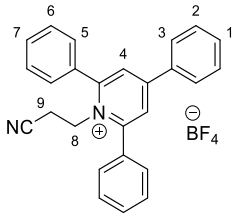
1-(2-Carboxyethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1aw)



Prepared according to **General Procedure A** using β-alanine (214 mg, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1aw** was isolated as a white solid (610 mg, 1.3 mmol, 65%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.46 (s, 2H, Ar*H*), 8.26 (d, *J* = 7.3 Hz, 2H, Ar*H*), 7.84 (s, 4H, Ar*H*), 7.76 – 7.57 (m, 9H, Ar*H*), 4.54 (t, *J* = 7.5 Hz, 2H, C(8)H_2), 2.33 (t, *J* = 7.5 Hz, 2H, C(9)H_2); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 170.2, 156.4, 154.3, 133.1, 133.0, 132.4, 131.0, 129.6, 129.2, 129.1, 128.7, 125.9, 50.7, 33.09; **^{19}F NMR** (377 MHz, DMSO-d_6) δ -148.24 (minor, $^{10}BF_4$), -148.30 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 380.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{26}H_{22}NO_2^+$ $[M\text{-}BF_4]^+$ = 380.1645, Found = 380.1644; **IR** (thin film, ν_{max} /cm^{-1}) 3486, 3000, 2885, 1729, 1623, 1165, 1056; **Melting point =** 151 – 154 °C.

1-(2-Cyanoethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1ax)

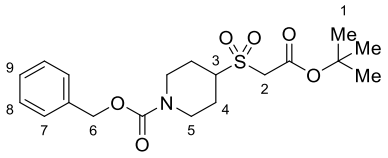


Prepared according to **General Procedure A** using 3-aminopropionitrile (177 µL, 2.4 mmol, 1.2 equiv.) and 2,4,6-triphenylpyrylium tetrafluoroborate (792 mg, 2.0 mmol, 1.0 equiv.) in ethanol (2.0 mL). Katritzky salt **1ax** was isolated as a white solid (646 mg, 1.4 mmol, 72%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 2H, Ar*H*), 7.87 – 7.81 (m, 4H, Ar*H*), 7.77 – 7.71 (m, 2H, Ar*H*), 7.69 – 7.55 (m, 7H, Ar*H*), 7.55 – 7.48 (m, 2H, Ar*H*), 4.81 (t, *J* = 7.5 Hz, 2H, C(8)H_2), 2.56 – 2.47 (m, 2H, C(9)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.2, 157.0, 133.8, 132.7, 132.1, 131.8, 130.0, 129.9, 129.3, 128.4, 127.2, 115.3, 49.3, 17.3; **^{19}F NMR** (377 MHz, CDCl3) δ -152.37 (minor, $^{10}BF_4$), -152.43 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 361.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{26}H_{21}N_2^+$ $[M\text{-}BF_4]^+$ = 361.1699, Found = 361.1695; **IR** (thin film, ν_{max} /cm^{-1}) 3062, 3035, 1622, 1550, 1057, 763, 697; **Melting point =** 141 – 144 °C.

8.2.4 Sulfone data

Benzyl 4-((2-(*tert*-butoxy)-2-oxoethyl)sulfonyl)piperidine-1-carboxylate (3a)

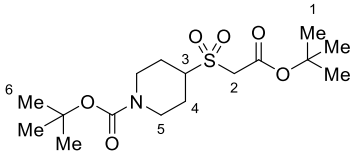


Prepared according to **General Procedure C-1** using 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (123 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), triethylamine (102 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (20 – 30% EtOAc in Petrol) afforded sulfone **3a** as a colourless oil (66.1 mg, 0.17 mmol, 83%).

Also prepared according to **General Procedure C-2**, affording the title product (66.1 mg, 0.17 mmol**,** 83%).

R$_f$ = 0.14 (30% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 5H, Ar*H*), 5.13 (s, 2H, C(6)H_2), 4.48 – 4.25 (br. m, 2H, 2×C(5)*H*H), 3.86 (s, 2H, C(2)H_2), 3.52 (tt, *J* = 12.0, 3.8 Hz, 1H, C(3)*H*), 2.98 – 2.75 (br. m, 2H, 2×C(5)H*H*), 2.11 (br. d, *J* = 12.8 Hz, 2H, 2×C(4)*H*H), 1.81 (qd, *J* = 12.0, 4.4 Hz, 2H, 2×C(4)*H*H), 1.50 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2, 155.1, 136.6, 128.7, 128.3, 128.2, 84.5, 67.6, 59.0, 56.1, 42.8, 28.0, 24.3; **HRMS** (ESI, *m/z*): Calc. for $C_{19}H_{26}NO_6S^-$ $[M-H]^-$ = 396.1484, Found = 396.1484; **IR** (thin film, ν_{max} /cm^{-1}) 2980, 2939, 1698, 1432, 1320, 1215, 1119.

***tert*-Butyl 4-((2-(*tert*-butoxy)-2-oxoethyl)sulfonyl)piperidine-1-carboxylate (3d)**



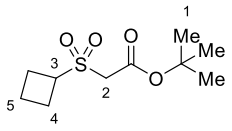
Prepared according to **General Procedure C-1** using 1-(1-(*tert*-butoxycarbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1d** (5.78 g, 10 mmol, 1.0 equiv.), Hantzsch ester (2.79 g, 11 mmol, 1.1 equiv.), triethylamine (5.02 mL, 36 mmol, 3.6 equiv.), DABSO (1.44 g, 6.0 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (2.95 mL, 20 mmol, 2.0 equiv.) in DMA (20 mL). Solvent was removed in vacuo by forming an azeotrope with toluene prior to purification by flash column chromatography (20 – 30% EtOAc in Petrol) afforded sulfone **3d** as an off- white solid (3.14 g, 8.6 mmol, 86%).

Also prepared according to **General Procedure C-2** on a 10 mmol scale, affording sulfone **3d** as an off-white solid (3.05 g, 8.4 mmol, 84%, respectively).

R_f = 0.30 (30% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.29 (app. br. s, 2H, 2×C(5)*H*H), 3.86 (s, 2H, C(2)H_2), 3.48 (tt, *J* = 12.0, 3.7 Hz, 1H, C(3)*H*), 2.76 (app. br. s, 2H, 2×C(5)H*H*), 2.09 (app. br. d, *J* = 13.3 Hz, 2H, 2×C(4)*H*H), 1.86 – 1.71 (m, 2H, 2×C(4)*H*H), 1.50 (s, 9H, 3×C(1/6)H_3), 1.45 (s, 9H, 3×C(6/1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2, 154.4, 84.4, 80.3, 59.3, 56.0, 42.6 (br.), 28.5, 28.0, 24.4; **LRMS** (ESI, *m/z*): 386.2 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{16}H_{29}NO_6SNa^+$ $[M+Na]^+$ = 386.1608, Found = 386.1610.

Data is consistent with the literature.[48d]

***tert*-Butyl 2-(cyclobutylsulfonyl)acetate (3v)**

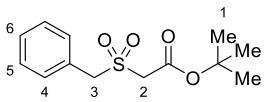


Prepared according to **General Procedure E** using 1-(1-cyclobutyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1v** (89.9 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash

column chromatography (20% EtOAc in Petrol) afforded sulfone **3v** as a colourless oil (37.7 mg, 0.16 mmol, 80%).

R_f = 0.26 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.15 (pd, *J* = 8.4, 0.7 Hz, 1H, C(3)*H*), 3.73 (s, 2H, C(2)H_2), 2.65 – 2.50 (m, 2H, 2×C(4)*H*H), 2.37 – 2.24 (m, 2H, 2×C(4)H*H*), 2.16 – 1.97 (m, 2H, C(5)H_2), 1.48 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.1, 84.0, 56.9, 54.7, 27.9, 22.5, 17.1; **LRMS** (ESI, *m/z*): 257.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{10}H_{18}O_4SNa^+$ $[M+Na]^+$ = 257.0818, Found = 257.0820; **IR** (thin film, ν_{max} /cm^{-1}) 2981, 2950, 1728, 1370. 1322, 1133, 1100.

***tert*-Butyl 2-(benzylsulfonyl)acetate (3b)**



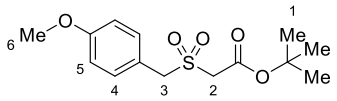
Prepared according to **General Procedure D-1** using 1-benzyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1b** (97.1 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), 2,6-lutidine (83 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (5 – 10% EtOAc in Petrol) afforded sulfone **3b** as a white crystalline solid (44.5 mg, 0.16 mmol, 82%).

Also prepared according to **General Procedure D-2**, affording sulfone **3b** (45.3 mg, 0.17 mmol, 84%).

R_f = 0.14 (10% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 – 7.47 (m, 2H, Ar*H*), 7.44 – 7.39 (m, 3H, Ar*H*), 4.50 (s, 2H, C(3)H_2), 3.68 (s, 2H, C(2)H_2), 1.55 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.5, 131.1, 129.4, 129.3, 128.1, 84.39, 59.5, 55.8, 28.1, 28.0; **LRMS** (ESI, *m/z*): 293.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{13}H_{18}O_4SNa^+$ $[M+Na]^+$ = 293.0818, Found = 293.0818.

Data is consistent with the literature.[48d]

***tert*-Butyl 2-((4-methoxybenzyl)sulfonyl)acetate (3w)**

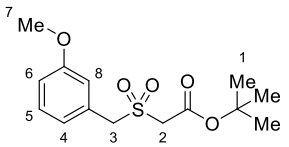


Prepared according to **General Procedure D-1** using 1-(4-methoxybenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1w** (103.1 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), 2,6-lutidine (83 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (10 – 20% EtOAc in Petrol) afforded sulfone **3w** as an off-white solid (41.3 mg,0.14 mmol, 69%).

Also prepared according to **General Procedure D-2**, affording sulfone **3w** as an off-white solid (39.8 mg, 0.13 mmol, 66%).

R_f = 0.22 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 2H, Ar*H*), 6.96 – 6.89 (m, 2H, Ar*H*), 4.43 (s, 2H, C(3)H_2), 3.81 (s, 3H, C(6)H_3), 3.66 (s, 2H, C(2)H_2), 1.54 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.5, 160.5, 132.3, 119.9, 114.7, 84.3, 58.8, 55.6, 55.5, 28.1; **LRMS** (ESI, *m/z*): 323.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{20}O_5SNa^+$ $[M+Na]^+$ = 323.0924, Found = 323.0923; **IR** (thin film, ν_{max} /cm^{-1}) 2980, 2936, 1728, 1514, 1326, 1252, 1162; **Melting point =** 61 – 63 °C.

***tert*-Butyl 2-((3-methoxybenzyl)sulfonyl)acetate (3x)**

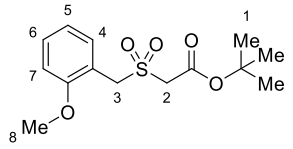


Prepared according to **General Procedure D-1** using 1-(3-methoxybenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1x** (103.1 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), 2,6-lutidine (83 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash

column chromatography (10 – 20% EtOAc in Petrol) afforded sulfone **3x** as a colourless oil (43.7 mg, 0.15 mmol, 73%).

R_f = 0.15 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 1H, Ar*H*), 7.09 – 7.01 (m, 2H, Ar*H*), 6.93 (ddd, *J* = 8.4, 2.6, 1.0 Hz, 1H, Ar*H*), 4.46 (s, 2H, C(3)H_2), 3.81 (s, 3H, C(7)H_3), 3.69 (s, 2H, C(2)H_2), 1.54 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.4, 160.1, 130.2, 129.4, 123.2, 116.4, 115.0, 84.3, 59.4, 55.8, 55.4, 28.0; **LRMS** (ESI, *m/z*): 323.0 $[M+Na]^+$, 299.0 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{20}O_5SNa^+$ $[M+Na]^+$ = 323.0924, Found = 323.0922; **IR** (thin film, ν_{max} /cm^{-1}) 2980, 2938, 1727, 1491, 1325, 1121, 695.

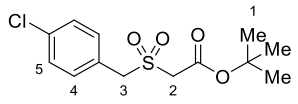
***tert*-Butyl 2-((2-methoxybenzyl)sulfonyl)acetate (3y)**



Prepared according to **General Procedure D-1** using 1-(2-methoxybenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1y** (103.1 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), 2,6-lutidine (83 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (10 – 20% EtOAc in Petrol) afforded sulfone **3y** as an off-white solid (40.0 mg, 0.13 mmol, 67%).

R_f = 0.19 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 7.5, 1.7 Hz, 1H, Ar*H*), 7.36 (ddd, *J* = 8.3, 7.5, 1.8 Hz, 1H, Ar*H*), 6.99 (td, *J* = 7.5, 1.1 Hz, 1H, Ar*H*), 6.94 (dd, *J* = 8.3, 1.1 Hz, 1H, Ar*H*), 4.59 (s, 2H, C(3)H_2), 3.86 (s, 3H, C(8)H_3), 3.81 (s, 2H, C(2)H_2), 1.53 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2, 158.0, 132.8, 130.9, 121.2, 116.5, 111.4, 84.0, 57.3, 55.8, 54.3, 28.0; **LRMS** (ESI, *m/z*): 323.0 $[M+Na]^+$, 299.0 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{20}O_5SNa^+$ $[M+Na]^+$ = 323.0924, Found = 323.0923; **IR** (thin film, ν_{max} /cm^{-1}) 2980, 2934, 1730, 1496, 1325, 1252, 1131; **Melting point =** 71 – 74 °C.

***tert*-Butyl 2-((4-chlorobenzyl)sulfonyl)acetate (3z)**

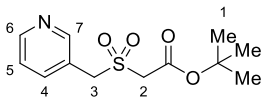


Prepared according to **General Procedure D-1** using 1-(4-chlorobenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1z** (104.0 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), 2,6-lutidine (83 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (10 – 20% EtOAc in Petrol) afforded sulfone **3z** as an off-white solid (48.1 mg, 0.16 mmol, 79%).

Also prepared according to **General Procedure D-2**, affording sulfone **3z** as an off-white solid (46.7 mg, 0.15 mmol, 77%).

R_f = 0.32 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 – 7.41 (m, 2H, Ar*H*), 7.40 – 7.34 (m, 2H, Ar*H*), 4.47 (s, 2H, C(3)H_2), 3.68 (s, 2H, C(2)H_2), 1.53 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.4, 135.7, 132.4, 129.5, 126.5, 84.5, 58.6, 56.0, 28.0; **LRMS** (ESI, *m/z*): 303.0, 305.0 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{13}H_{17}{}^{35}ClO_4SNa^+$ $[M+Na]^+$ = 327.0428, Found = 327.0428, Calc. for $C_{13}H_{17}{}^{37}ClO_4SNa^+$ $[M+Na]^+$ = 329.0398, Found = 329.0398; **IR** (thin film, ν_{max} /cm^{-1}) 2981, 2936, 1727, 1493, 1327, 1097, 834; **Melting point =** 103 – 105 °C.

***tert*-Butyl 2-((pyridin-3-ylmethyl)sulfonyl)acetate (3aa)**

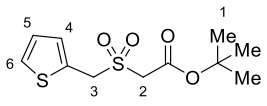


Prepared according to **General Procedure D-1** using 2,4,6-triphenyl-1-(pyridin-3-ylmethyl)pyridin-1-ium tetrafluoroborate **1aa** (97.3 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), 2,6-lutidine (83 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). The alkylation step

was carried out at rt for 5 h. Purification by flash column chromatography (60% EtOAc in Petrol) afforded sulfone **3aa** as an off-white solid (27.1 mg, 0.10 mmol, 50%).

R_f = 0.17 (60% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) 8.75 – 8.62 (m, 2H, Ar*H*), 7.86 (dt, *J* = 7.8, 1.8 Hz, 1H, Ar*H*), 7.36 (dd, *J* = 7.8, 4.8 Hz, 1H, Ar*H*), 4.52 (s, 2H, C(3)H_2), 3.70 (s, 2H, C(2)H_2), 1.54 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2, 151.7, 150.7, 138.6, 124.3, 124.0, 84.8, 56.6, 56.3, 28.0; **LRMS** (ESI, *m/z*): 272.0 $[M+H]^+$, 270.0 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{12}H_{18}NO_4S^+$ $[M+H]^+$ = 272.0951, Found = 272.0949; **IR** (thin film, ν_{max} /cm^{-1}) 2982, 2934, 1727, 1326, 1160, 1119, 713; **Melting point =** 124 – 126 °C.

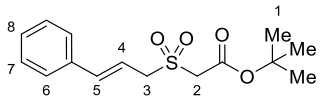
***tert*-Butyl 2-((thiophen-2-ylmethyl)sulfonyl)acetate (3ab)**



Prepared according to **General Procedure D-1** using 2,4,6-triphenyl-1-(thiophen-2-ylmethyl)pyridin-1-ium tetrafluoroborate **1ab** (98.3 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), 2,6-lutidine (83 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and tert-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (10 – 20% EtOAc in Petrol) afforded sulfone **3ab** as a colourless oil (31.9 mg, 0.12 mmol, 58%).

R_f = 0.25 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 5.2, 1.3 Hz, 1H, Ar*H*), 7.25 (dd, *J* = 2.1, 1.3 Hz, 1H, Ar*H*), 7.07 (dd, *J* = 5.2, 3.5 Hz, 1H, Ar*H*), 4.71 (s, 2H, C(3)H_2), 3.76 (s, 2H, C(2)H_2), 1.54 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.3, 130.9, 128.6, 128.3, 127.8, 84.6, 55.3, 54.1, 28.0; **LRMS** (ESI, *m/z*): 299.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{11}H_{16}O_4S_2Na^+$ $[M+Na]^+$ = 299.0382, Found = 299.0383; **IR** (thin film, ν_{max} /cm^{-1}) 2980, 2934, 1728, 1328, 1256, 1139, 712.

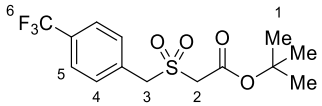
***tert*-Butyl 2-(cinnamylsulfonyl)acetate (3ac)**



Prepared according to **General Procedure D-1** using 1-cinnamyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1ac** (102.3 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), 2,6-lutidine (83 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (10 – 20% EtOAc in Petrol) afforded sulfone **3ac** as an off-white solid (48.1 mg, 0.16 mmol, 79%).

R_f = 0.33 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.40 (m, 2H, Ar*H*), 7.38 – 7.28 (m, 3H, Ar*H*), 6.82 (d, *J* = 15.9 Hz, 1H, C(5)*H*), 6.26 (dt, *J* = 15.7, 7.7 Hz, 1H, C(4)*H*), 4.13 (d, *J* = 7.6 Hz, 2H, C(3)H_2), 3.88 (s, 2H, C(2)H_2), 1.53 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.3, 140.0, 135.6, 129.0, 128.9, 127.0, 115.3, 84.3, 57.5, 56.2, 28.0; **LRMS** (ESI, *m/z*): 319.0 $[M+Na]^+$); **HRMS** (ESI, *m/z*): Calc. for $C_{15}H_{20}O_4SNa^+$ $[M+Na]^+$ = 319.0975, Found = 319.0975; **IR** (thin film, ν_{max} /cm^{-1}) 2981, 2935, 1728, 1370, 1325, 1131, 1102, 753; **Melting point =** 83 – 85 °C.

***tert*-Butyl 2-((4-(trifluoromethyl)benzyl)sulfonyl)acetate (3ad)**

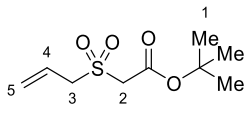


Prepared according to **General Procedure D-1** using 2,4,6-triphenyl-1-(4-(trifluoromethyl)benzyl)pyridin-1-ium tetrafluoroborate **1ad** (110.6 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), 2,6-lutidine (83 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). The sulfinylation step was left for a shorter time of 8 h, followed by the alkylation step at rt for 5 h. Purification by flash column chromatography (10 – 20% EtOAc in Petrol) afforded sulfone **3ad** as an off-white solid (50.9 mg, 0.15 mmol, 75%).

Also prepared according to **General Procedure D-2**, using a shorter reaction time of 8 h, followed by a rt alkylation for 5 h, affording sulfone **3ad** as an off-white solid (43.0 mg, 0.13 mmol, 64%).

R_f = 0.29 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.64 (d, *J* = 8.3 Hz, 2H, Ar*H*), 4.57 (s, 2H, C(3)H_2), 3.70 (s, 2H, C(2)H_2), 1.54 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.4, 131.9, 131.6, 131.5 (q, J_{CF} = 32.5 Hz), 126.1 (q, J_{CF} = 3.5 Hz), 123.9 (q, J_{CF} = 272.5 Hz), 84.7, 58.8, 56.4, 28.0; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -62.9; **LRMS** (ESI, *m/z*): 337.0 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{16}F_3O_4S^-$ $[M-H]^-$ = 337.0716, Found = 337.0731; **IR** (thin film, ν_{max} /cm^{-1}) 2992, 2937, 1728, 1318, 1165, 1131, 1069; **Melting point =** 103 – 106 °C.

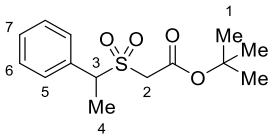
***tert*-Butyl 2-(allylsulfonyl)acetate (3ag)**



Prepared according to **General Procedure C-1** using 1-allyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1ag** (87.1 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), triethylamine (102 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (5 – 10% EtOAc in Petrol) afforded sulfone **3ag** as a colourless oil (11.2 mg, 0.05 mmol, 25%).

R_f = 0.16 (10% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.95 (ddt, *J* = 17.5, 10.1, 7.4 Hz, 1H, C(4)H_2), 5.61 – 5.51 (m, 2H, C(5)H_2), 3.97 (d, *J* = 7.4 Hz, 2H, C(3)H_2), 3.85 (s, 2H, C(2)H_2), 1.51 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2, 125.7, 125.1, 84.3, 57.8, 56.2, 28.0; **LRMS** (ESI, *m/z*): 243.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_9H_{16}O_4S^+$ $[M+Na]^+$ = 243.0662, Found = 243.0663; **IR** (thin film, ν_{max} /cm^{-1}) 2982, 1728, 1371, 1325, 1134, 942.

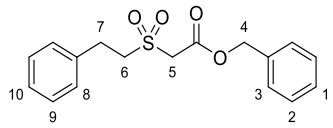
tert-butyl 2-((1-phenylethyl)sulfonyl)acetate (3ai)



Prepared according to **General Procedure D-1** using 2-Isopropyl-4,6-diphenyl-1-(1-phenylethyl)pyridin-1-ium tetrafluoroborate **1ai** (93.1 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), 2,6-lutidine (83 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (5 – 10% EtOAc in Petrol) afforded sulfone **3ai** as a colourless oil (41.9 mg, 1.5 mmol, 74%).

R_f = 0.19 (10% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 – 7.50 (m, 2H, Ar*H*), 7.43 – 7.37 (m, 3H, Ar*H*), 4.74 (q, *J* = 7.2 Hz, 1H, C(3)*H*), 3.65 (d, *J* = 14.8 Hz, 1H, C(2)*H*H), 3.56 (d, *J* = 14.8 Hz, 1H, C(2)H*H*), 1.80 (d, *J* = 7.2 Hz, 3H, C(4)H_3), 1.52 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.5, 134.4, 129.5, 129.4, 129.2, 84.1, 62.9, 55.3, 28.1, 13.3; **LRMS** (ESI, *m/z*): 307.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{20}O_4SNa^+$ $[M+Na]^+$ = 307.0975, Found = 307.0974; **IR** (thin film, ν_{max} /cm^{-1}) 2981, 2939, 1729, 1456, 1370, 1323, 1154.

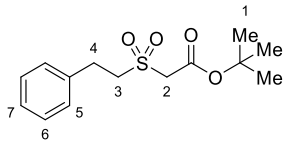
Benzyl 2-(phenethylsulfonyl)acetate (3c-1)



Prepared according to **General Procedure E** using 1-phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1c** (99.9 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and benzyl 2-bromoacetate (63 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (10 – 20% EtOAc in Petrol) afforded sulfone **3c-1** as a colourless oil (53.1 mg, 0.17 mmol, 83%).

R_f = 0.17 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.35 (m, 5H, Ar*H*), 7.35 – 7.22 (m, 3H, Ar*H*), 7.20 – 7.15 (m, 2H, Ar*H*), 5.23 (s, 2H, C(4)H_2), 3.90 (s, 2H, C(5)H_2), 3.55 – 3.47 (m, 2H, C(7)H_2), 3.19 – 3.11 (m, 2H, C(6)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.9, 137.1, 134.5, 129.1, 129.0, 128.9, 128.7, 128.7, 127.3, 68.5, 57.7, 54.9, 28.3; **LRMS** (ESI, *m/z*): 341.0 $[M+Na]^+$, 317.0 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{18}O_4SNa^+$ $[M+Na]^+$ = 341.0818, Found = 341.0819; **IR** (thin film, ν_{max} /cm^{-1}) 2942, 1737, 1455, 1317, 1111, 749, 697.

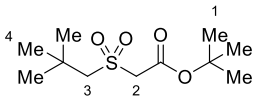
***tert*-Butyl 2-(phenethylsulfonyl)acetate (3c-2)**



Prepared according to **General Procedure E** using 1-phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1c** (99.9 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (10 – 20% EtOAc in Petrol) afforded sulfone **3c-2** as an off-white solid (40.4 mg, 0.14 mmol, 71%).

R_f = 0.41 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 2H, Ar*H*), 7.29 – 7.22 (m, 3H, Ar*H*), 3.78 (s, 2H, C(2)H_2), 3.59 – 3.50 (m, 2H, C(4)H_2), 3.22 – 3.13 (m, 2H, C(3)H_2), 1.50 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2, 137.4, 129.1, 128.7, 127.3, 84.3, 58.8, 54.8, 28.4, 28.0; **LRMS** (ESI, *m/z*): 307.0 $[M+Na]^+$, 283.0 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{20}O_4SNa^+$ $[M+Na]^+$ = 307.0975, Found = 307.0973; **IR** (thin film, ν_{max} /cm^{-1}) 2981, 2937, 1729, 1319, 1159, 1102, 700; **Melting point =** 61 – 64 °C.

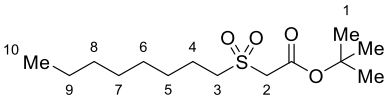
***tert*-Butyl 2-(neopentylsulfonyl)acetate (3aj)**



Prepared according to **General Procedure E** using 1-neopentyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1aj** (93.1 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (70% CH_2Cl_2 in Petrol) afforded sulfone **3aj** as a pale-yellow oil (35.7 mg, 0.14 mmol, 71%).

R_f = 0.4 (70% CH_2Cl_2 in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.82 (s, 2H, C(2)H_2), 3.23 (s, 2H, C(3)H_2), 1.51 (s, 9H, 3×C(1)H_3), 1.22 (s, 9H, 3×C(4)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.5, 84.1, 64.5, 61.9, 32.3, 29.9, 28.0; **LRMS** (ESI, *m/z*): 273.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{11}H_{22}O_4SNa^+$ $[M+Na]^+$ = 273.1131, Found = 273.1133; **IR** (thin film, ν_{max} /cm^{-1}) 2959, 1480, 1730, 1370, 1324, 1135, 1098.

***tert*-Butyl 2-(octylsulfonyl)acetate (3ak)**

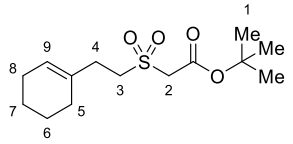


Prepared according to **General Procedure E** using 1-octyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1ak** (101.5 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (70 – 80% CH_2Cl_2 in Petrol) afforded sulfone **3ak** as a colourless oil (40.4 mg, 0.14 mmol, 71%).

R_f = 0.47 (80% CH_2Cl_2 in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.84 (s, 2H, C(2)H_2), 3.27 – 3.17 (m, 2H**,** C(3)H_2), 1.93 – 1.78 (m, 2H C(4)H_2), 1.50 (s, 9H, 3×C(1)H_3), 1.44 (q, J = 7.3 Hz, 2H,

C(5)H_2), 1.36 – 1.22 (m, 8H, C(6)H_2, C(7)H_2, C(8)H_2 & C(9)H_2), 0.92 – 0.84 (m, 3H, C(10)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.3, 84.2, 58.6, 53.7, 31.8, 29.1, 29.0, 28.5, 28.0, 22.7, 22.1, 14.2; **LRMS** (ESI, *m/z*): 315.2 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{28}O_4SNa^+$ $[M+Na]^+$ = 315.1601, Found = 315.1600; **IR** (thin film, ν_{max} /cm^{-1}) 2927, 2857, 1730, 1370, 1323, 1135, 1101.

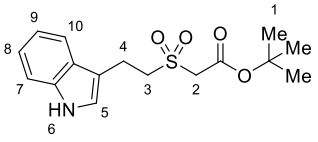
***tert*-Butyl 2-((2-(cyclohex-1-en-1-yl)ethyl)sulfonyl)acetate (3al)**



Prepared according to **General Procedure E** using 1-(2-(cyclohex-1-en-1-yl)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1al** (100.7 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (70 – 80% CH_2Cl_2 in Petrol) afforded sulfone **3al** as a colourless oil (49.5 mg, 0.17 mmol, 86%).

R_f = 0.34 (70% CH_2Cl_2 in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.53 (s, 1H, C(9)*H*), 3.85 (s, 2H, C(2)H_2), 3.37 – 3.27 (m, 2H, C(3)H_2), 2.52 – 2.41 (m, 2H, C(4)H_2), 2.05 – 1.88 (m, 4H, C(8)H_2 & C(5)H_2), 1.67 – 1.52 (m, 4H, C(6)H_2 & C(7)H_2), 1.50 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2, 133.5, 124.1, 84.2, 58.8, 52.2, 30.2, 28.2, 28.0, 25.3, 22.8, 22.3; **LRMS** (ESI, *m/z*): 311.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{24}O_4SNa^+$ $[M+Na]^+$ = 311.1288, Found = 311.1288; **IR** (thin film, ν_{max} /cm^{-1}) 2978, 2934, 1729, 1370, 1323, 1163, 1136.

***tert*-Butyl 2-((2-(1*H*-indol-3-yl)ethyl)sulfonyl)acetate (3am)**

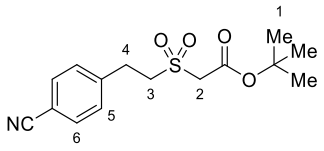


Prepared according to **General Procedure E** using 1-(2-(1*H*-indol-3-yl)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1am** (107.7 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester

(55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (20 – 30% EtOAc in Petrol) afforded sulfone **3am** as a colourless oil (35.6 mg, 0.11 mmol, 55%).

R_f = 0.19 (30% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 (s, 1H, N(6)*H*), 7.66 – 7.59 (m, 1H, Ar*H*), 7.39 (dt, *J* = 7.9, 0.8 Hz, 1H, Ar*H*), 7.23 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H, Ar*H*), 7.16 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H, Ar*H*), 7.09 (d, *J* = 2.4 Hz, 1H, Ar*H*), 3.81 (s, 2H, C(2)H_2), 3.69 – 3.58 (m, 2H, C(4)H_2), 3.42 – 3.31 (m, 2H, C(3)H_2), 1.48 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2, 136.5, 126.8, 122.7, 122.3, 120.0, 118.6, 111.8, 111.5, 84.3, 58.9, 53.9, 28.0, 18.6; **LRMS** (ESI, *m/z*): 346.0 $[M+Na]^+$, 322.0 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{16}H_{21}NO_4SNa^+$ $[M+Na]^+$ = 346.1084, Found = 346.1084; **IR** (thin film, ν_{max} /cm^{-1}) 3413, 2979, 2934, 1724, 1317, 1095, 741.

***tert*-Butyl 2-((4-cyanophenethyl)sulfonyl)acetate (3an)**

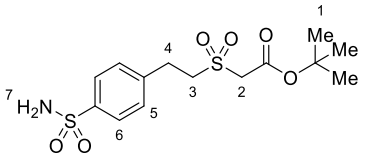


Prepared according to **General Procedure E** using 1-(4-cyanophenethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1an** (104.9 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (40 – 50% Et_2O in Petrol) afforded sulfone **3an** as a white crystalline solid (30.8 mg, 0.10 mmol, 50%).

R_f = 0.14 (50% Et_2O in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 – 7.60 (m, 2H, Ar*H*), 7.38 (d, *J* = 8.3 Hz, 2H, Ar*H*), 3.85 (s, 2H, C(2)H_2), 3.58 – 3.51 (m, 2H, C(4)H_2), 3.27 – 3.20 (m, 2H, C(3)H_2), 1.50 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2, 143.0, 132.8, 129.5, 118.7, 111.4, 84.7, 59.0, 53.9, 28.2, 28.0; **LRMS** (ESI, *m/z*): 332.0 $[M+Na]^+$, 308.1 $[M-H]^-$; **HRMS** (ESI, *m/z*):

Calc. for $C_{15}H_{19}O_4NSNa^+$ $[M+Na]^+$ = 332.0927, Found = 332.0927; **IR** (thin film, ν_{max} /cm^{-1}) 2980, 2937, 2229, 1729, 1371, 1329, 1161; **Melting point =** 117 – 119 °C.

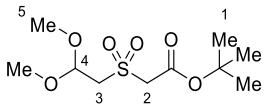
***tert*-Butyl 2-((4-sulfamoylphenethyl)sulfonyl)acetate (3ao)**



Prepared according to **General Procedure E** using 2,4,6-triphenyl-1-(4-sulfamoylphenethyl)pyridin-1-ium tetrafluoroborate **1ao** (115.7 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (40 – 50% EtOAc in Petrol) afforded sulfone **3ao** as a white crystalline solid (56.4 mg, 0.16 mmol, 78%).

R$_f$ = 0.26 (50% EtOAc in Petrol); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.76 (d, J = 8.3 Hz, 2H, Ar*H*), 7.48 (d, J = 8.3 Hz, 2H, Ar*H*), 7.32 (s, 2H, N(7)H_2), 4.31 (s, 2H, C(2)H_2), 3.63 – 3.57 (m, 2H, C(4)H_2), 3.16 – 3.09 (m, 2H, C(3)H_2), 1.43 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 162.3, 142.6, 142.4, 129.1, 126.0, 82.9, 58.2, 53.7, 27.6, 27.1; **LRMS** (ESI, *m/z*): 386.0 $[M+Na]^+$, 362.0 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{21}NO_6S_2Na^+$ $[M+Na]^+$ = 386.0702, Found = 386.0702; **IR** (thin film, ν_{max} /cm^{-1}) 3357, 3267, 2937, 1726, 1311, 1160, 1096; **Melting point =** 135 – 137 °C.

***tert*-Butyl 2-((2,2-dimethoxyethyl)sulfonyl)acetate (3ap)**

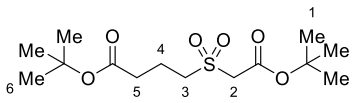


Prepared according to **General Procedure E** using 1-(2,2-dimethoxyethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1ap** (96.7 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash

column chromatography (20% EtOAc in Petrol) afforded sulfone **3ap** as a colourless oil (23.5 mg, 0.09 mmol, 44%).

R_f = 0.24 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.88 (t, *J* = 5.6 Hz, 1H, C(4)*H*), 4.01 (s, 2H, C(2)H_2), 3.57 (d, *J* = 5.6 Hz, 2H, C(3)H_2), 3.41 (s, 6H, 2×C(5)H_3), 1.50 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.3, 99.7, 84.1, 59.3, 55.3, 54.1, 28.0; **LRMS** (ESI, *m/z*): 291.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{10}H_{20}O_6SNa^+$ $[M+Na]^+$ = 291.0873, Found = 291.0873; **IR** (thin film, ν_{max} /cm^{-1}) 2981, 2938, 1730, 1371, 1325, 1110, 1070.

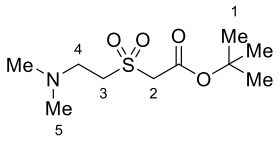
***tert*-Butyl 4-((2-(tert-butoxy)-2-oxoethyl)sulfonyl)butanoate (3aq)**



Prepared according to **General Procedure E** using 1-(4-(*tert*-butoxy)-4-oxobutyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1aq** (107.5 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (50% Et_2O in Petrol) afforded sulfone **3aq** as a colourless oil (48.2 mg, 0.15 mmol, 75%).

R_f = 0.4 (50% Et_2O in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.87 (s, 2H, C(2)H_2), 3.34 – 3.28 (m, 2H, C(3)H_2), 2.42 (t, *J* = 7.1 Hz, 2H, C(5)H_2), 2.19 – 2.08 (m, 2H, C(4)H_2), 1.49 (s, 9H, 3×C(1)H_3), 1.44 (s, 9H, 3×C(6)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 162.1, 84.3, 81.1, 58.7, 52.7, 33.6, 28.2, 28.0, 17.8; **LRMS** (ESI, *m/z*): 345.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{26}O_6SNa^+$ $[M+Na]^+$ = 345.1342, Found = 345.1342; **IR** (thin film, ν_{max} /cm^{-1}) 2979, 2936, 1722, 1369, 1323, 1155, 1132.

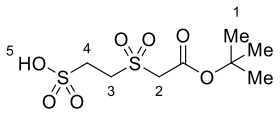
tert-Butyl 2-((2-(dimethylamino)ethyl)sulfonyl)acetate (3ar)



Prepared according to **General Procedure E** using 1-(2-(dimethylamino)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1ar** (93.3 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (0 – 2% MeOH in EtOAc) afforded sulfone **3ar** as a white solid (37.4 mg, 0.15 mmol, 74%).

R_f = 0.28 (2% MeOH in EtOAc); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 4.30 (s, 2H, C(2)H_2), 3.39 (t, J = 6.7 Hz, 2H, C(3)H_2), 2.68 (t, J = 6.7 Hz, 2H, C(4)H_2), 2.17 (s, 6H, 2×C(5)H_3), 1.44 (s, 9H, 3×C(1)H_3); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 162.3, 82.6, 59.2, 52.0, 50.5, 44.7, 27.5; **LRMS** (ESI, *m/z*): 252.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{10}H_{22}NO_4S^+$ $[M+H]^+$ = 252.1264, Found = 252.1265; **IR** (thin film, ν_{max} /cm^{-1}) 2927, 1728, 1571, 1371, 1306, 1060, 1020; **Melting point =** 205 **°C** (decomposition).

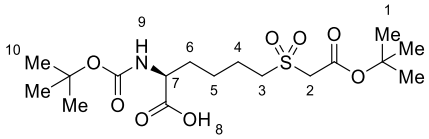
2-((2-(_tert_-butoxy)-2-oxoethyl)sulfonyl)ethane-1-sulfonic acid (3as)



Prepared according to **General Procedure E** using 2,4,6-triphenyl-1-(2-sulfoethyl)pyridin-1-ium tetrafluoroborate **1as** (100.7 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (0 – 2% AcOH in 5% MeOH in EtOAc) afforded sulfone **3as** as a white crystalline solid (43.7 mg, 0.15 mmol, 76%).

R_f = 0.08 (5% MeOH in EtOAc with 2% AcOH); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 4.33 (s, 2H, C(2)H_2), 3.53 – 3.46 (m, 2H, C(3)H_2), 2.80 – 2.74 (m, 2H, C(4)H_2), 1.44 (s, 9H, 3×C(1)H_3) *(O(5)H signal not observed)*; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 162.3, 82.7, 58.2, 50.5, 42.9, 27.5; **LRMS** (ESI, *m/z*): 287.0 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_8H_{15}O_7S_2^-$ $[M-H]^-$ = 287.0265, Found = 287.0260; **IR** (thin film, ν_{max} /cm^{-1}) 3423, 2984, 1731, 1564, 1416, 1320, 1206; **Melting point** = 49 – 51 °C.

(*S*)-6-((2-(*tert*-Butoxy)-2-oxoethyl)sulfonyl)-2-((*tert*-butoxycarbonyl)amino)hexanoic acid (3at)

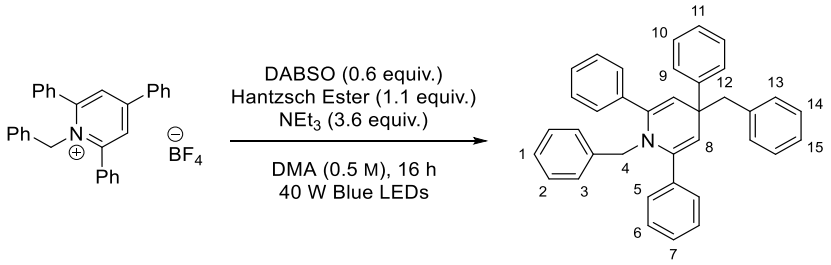


Prepared according to **General Procedure E** using (*S*)-1-(5-((*tert*-butoxycarbonyl)amino)-5-carboxypentyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1at** (124.9 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), piperidine (71 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and *tert*-butyl 2-bromoacetate (59 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (50% EtOAc in Petrol with 2% AcOH) afforded sulfone **3at** as a colourless oil (56.4 mg, 0.16 mmol, 78%).

R_f = 0.21 (50% EtOAc in Petrol with 2% AcOH); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.78 (s, 1H, O(8)*H*), 5.16 (d, *J* = 7.9 Hz, 1H, N(9)*H*), 4.42 – 4.08 (m, 1H, C(7)*H*), 3.87(s, 2H, C(2)H_2) 3.34 – 3.16 (m, 2H, C(3)H_2), 2.00 – 1.82 (m, 3H, C(6)*H*H & C(4)H_2), 1.82 – 1.67 (m, 1H, C(6)H*H*), 1.66 – 1.53 (m, 2H, C(5)H_2), 1.50 (s, 9H, 3×C(1)H_3), 1.44 (s, 9H, 3×C(10)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.9, 162.3, 155.9, 84.4, 80.4, 58.6, 53.2, 31.9, 29.7, 28.5, 28.0, 24.3, 21.6; **LRMS** (ESI, *m/z*): 408.1 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{30}NO_8S^-$ $[M-H]^-$ = 408.1698, Found = 408.1692; **IR** (thin film, ν_{max} /cm^{-1}) 3350, 2979, 2935, 1716, 1370, 1327, 1162.

8.2.5 Characterisation of side-products and TEMPO products

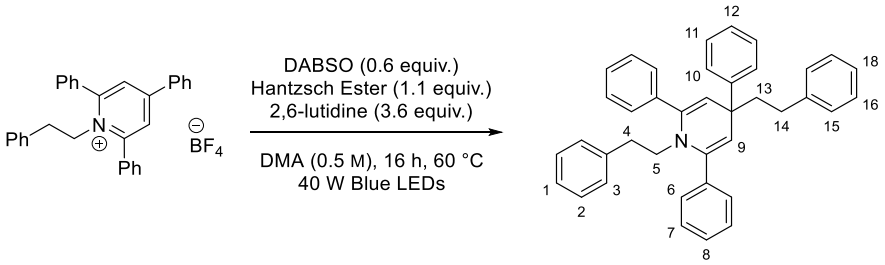
1,4-Dibenzyl-2,4,6-triphenyl-1,4-dihydropyridine (4a)



Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-benzyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1b** (97.1 mg, 0.20 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL, 0.5 M) was then added, followed by degassed, dry triethylamine (102 μL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (20% CH_2Cl_2 in Petrol) to afford dihydropyridine **4a** as a colourless oil (9.6 mg, 0.04 mmol, 20%).

R_f = 0.27 (20% CH_2Cl_2 in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 – 7.46 (m, 4H, Ar*H*), 7.43 – 7.32 (m, 6H, Ar*H*), 7.24 – 7.19 (m, 4H, Ar*H*), 7.15 – 6.99 (m, 5H, Ar*H*), 6.99 – 6.93 (m, 2H, Ar*H*), 6.70 (dt, *J* = 7.9, 2.4 Hz, 2H, Ar*H*), 6.65 – 6.60 (m, 2H, Ar*H*), 5.12 (s, 2H, 2×C(8)*H*), 4.18 (s, 2H, C(4)H_2), 2.93 (s, 2H, C(12)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.9, 142.5, 138.3, 138.3, 137.6, 131.0, 128.5, 128.4, 128.3, 128.1, 128.1, 127.9, 127.4, 127.1, 127.0, 125.9, 125.4, 114.3, 51.9, 51.6, 44.6; **LRMS** (ESI, *m/z*) 490.2 $[M+H]^+$; **HRMS** (ESI, *m/z*) Calc. for $C_{37}H_{32}N^+$ $[M+H]^+$ = 490.2529, found 490.2529; **IR** (thin film, ν_{max} /cm^{-1}) 3028, 1655, 1600, 1494, 1446, 1387, 698.

1,4-Diphenethyl-2,4,6-triphenyl-1,4-dihydropyridine (4b)

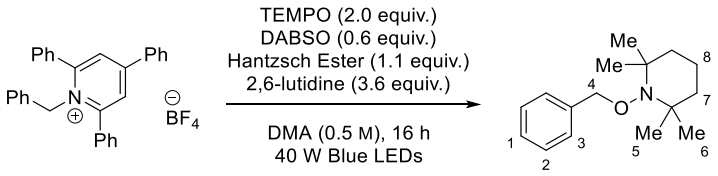


Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1c** (99.9 mg, 0.20 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL, 0.5 M) was then added, followed by degassed, dry triethylamine (102 μL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation at 60 °C for 16 h (see **Figure S1** for experimental setup). Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (20% CH_2Cl_2 in Petrol) to afford dihydropyridine **4b** as a colourless oil (83 mg, 0.03 mmol, 14%).

R_f = 0.27 (20% CH_2Cl_2 in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 – 7.51 (m, 6H, Ar*H*), 7.46 – 7.32 (m, 8H, Ar*H*), 7.25 – 7.08 (m, 6H, Ar*H*), 7.02 – 6.94 (m, 3H, Ar*H*), 6.47 (dt, *J* = 7.3, 3.6 Hz, 2H, Ar*H*), 5.17 (s, 2H, 2×C(9)*H*), 3.29 – 3.17 (m, 2H, C(5)H_2), 2.72 – 2.62 (m, 2H, C(14)H_2), 2.37 – 2.26 (m, 2H, C(4)H_2), 2.19 – 2.10 (m, 2H, C(13)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.5, 143.2, 139.3, 138.2, 128.6, 128.5, 128.5, 128.4, 128.2, 128.2, 128.2, 126.5, 125.9, 125.7, 125.7, 113.4, 50.1, 46.8, 44.0, 34.9, 32.8; **LRMS** (ESI, *m/z*) 518.2 $[M+H]^+$; **HRMS** (ESI, *m/z*) Calc. for $C_{39}H_{36}N^+$ $[M+H]^+$ = 518.2842, found 518.2842.

Data is consistent with the literature.[170]

1-(Benzyloxy)-2,2,6,6-tetramethylpiperidine (6)



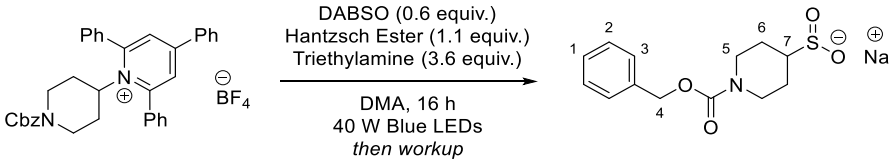
Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.), 1-benzyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1b** (97.1 mg, 0.20 mmol, 1.0 equiv.) and TEMPO (62.5 mg, 0.40 mmol, 2.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL, 0.5 M) was then added, followed by degassed, dry 2,6-lutidine (84 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). `Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography Purification by flash column chromatography (3% Et_2O in Petrol) to afforded TEMPO adduct **6** as a colourless oil (36.1 mg, 0.15 mmol, 73%).

R_f = 0.25 (3% Et_2O in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.33 (m, 4H, Ar*H*), 7.32 – 7.27 (m, 1H, Ar*H*), 4.85 (s, 2H, C(4)H_2), 1.68 – 1.33 (m, 6H, 2×C(7)H_3 & C(8)H_3), 1.28 (s, 6H, 2×C(5)H_3), 1.18 (s, 6H, 2×C(6)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.5, 128.4, 127.6, 127.4, 78.9, 60.2, 39.9, 33.3, 20.5, 17.3; **LRMS** (ESI, *m/z)* 248.2 $[M+H]^+$; **HRMS** (ESI, *m/z*) Calc. for $C_{16}H_{26}NO^+$ $[M+H]^+$ = 284.2009, found 284.2010.

Data is consistent with the literature. [231]

8.2.6 Sulfinate data

Sodium 1-((benzyloxy)carbonyl)piperidine-4-sulfinate (9a)

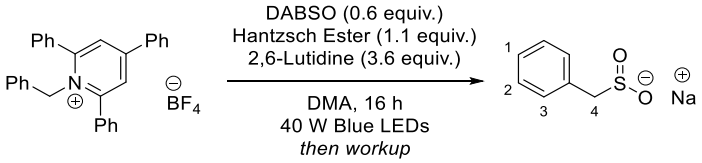


Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry triethylamine (102 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). Upon completion, aq. H_3PO_4 (5 mL, 2M) and brine (12 mL) were added to the mixture. The mixture was then extracted with Et_2O (2 × 10 mL). The combined organic phases were washed with further aq. H_3PO_4 (5 mL, 2 M) and brine (12 mL), and then extracted with a 10% Na_2CO_3 solution (3×10 mL). The aqueous layer was concentrated in vacuo by forming an azeotrope with MeCN. EtOH (20 mL) was added, and the mixture refluxed for 10 mins. The mixture was then cooled to 0 °C, filtered through a P4 frit and the residue washed with cold EtOH. The extraction process was repeated, and the combined extracts evaporated in vacuo to afford sodium sulfinate **9a** as a white solid (50.2 mg, 0.16 mmol, 82%).

^{1}H NMR (400 MHz, Methanol-d_4) δ 7.42 – 7.24 (m, 5H, Ar*H*), 5.11 (s, 2H, C(4)H_2), 4.21 (d, *J* = 13.3 Hz, 2H, 2×C(5)*H*H), 2.97 – 2.77 (m, 2H, 2×C(5)H*H*), 2.02 (tt, *J* = 11.8, 4.0 Hz, 1H, C(7)*H*), 1.95 – 1.85 (m, 2H, 2×C(6)*H*H), 1.43 (qd, *J* = 12.4, 4.5 Hz, 2H, 2×C(6)H*H*); **^{13}C NMR** (101 MHz, Methanol-d_4) δ 156.9, 138.2, 129.5, 129.1, 128.8, 68.2, 65.2, 44.8, 25.4; **LRMS** (ESI, *m/z*) 282.0 $[M\text{-}Na]^-$; **HRMS** (ESI, *m/z*) Calc. for

$C_{13}H_{16}NO_4S^-$ [M-Na]$^-$ = 282.0806, found 282.0800; **IR** (thin film, ν_{max} /cm^{-1}) 3379, 2951, 1677, 1624, 1471, 1395; **Melting point** = 268 – 271 °C (decomposition).

Sodium phenylmethanesulfinate (2b)

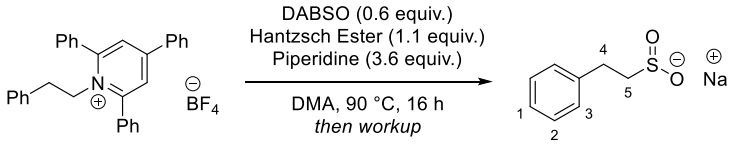


Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-benzyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1b** (97.1 mg, 0.20 mmol, 1.0 equiv.), were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry 2,6-lutidine (84 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). Upon completion, aq. H_3PO_4 (5 mL, 2M) and brine (12 mL) were added to the mixture. The mixture was then extracted with Et_2O (2 × 10 mL). The combined organic phases were washed with further aq. H_3PO_4 (5 mL, 2 M) and brine (12 mL), and then extracted with a 10% Na_2CO_3 solution (3×10 mL). The aqueous layer was concentrated in vacuo by forming an azeotrope with MeCN. EtOH (20 mL) was added, and the mixture refluxed for 10 mins. The mixture was then cooled to 0 °C, filtered through a P4 frit and the residue washed with cold EtOH. The extraction process was repeated, and the combined extracts evaporated in vacuo to afford sodium sulfinate **9b** as a white solid (27.3 mg, 0.15 mmol, 77%).

^{1}H NMR (400 MHz, Methanol-d_4) δ 7.30 – 7.25 (m, 4H, Ar*H*), 7.23 – 7.17 (m, 1H, Ar*H*), 3.51 (s, 2H, C(4)H_2); **^{13}C NMR** (101 MHz, Methanol-d_4) δ 134.7, 130.9, 129.2, 127.7, 70.9; **LRMS** (ESI, *m/z*) 155.0 [M-Na]$^-$ 155.0; **HRMS** (ESI, *m/z*) Calc. for $C_7H_7O_2S^-$ [M-Na]$^-$ = 155.0172, found 155.0161.

Data is consistent with the literature.[23c]

Sodium 2-phenylethane-1-sulfinate (2c)



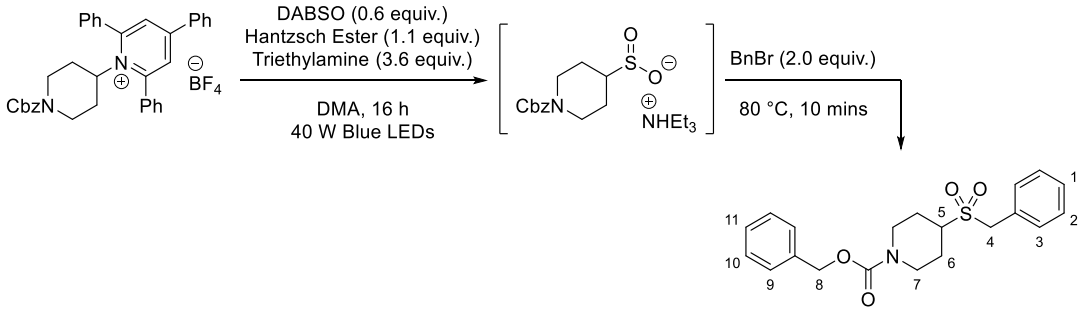
Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1c** (100 mg, 0.2 mmol, 1.0 equiv.), were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry piperidine (71 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred at 90 **°C** for 16 h. Upon completion, aq. H_3PO_4 (5 mL, 2M) and brine (12 mL) were added to the mixture. The mixture was then extracted with Et_2O (2 × 10 mL). The combined organic phases were washed with further aq. H_3PO_4 (5 mL, 2 M) and brine (12 mL), and then extracted with a 10% Na_2CO_3 solution (3×10 mL). The aqueous layer was concentrated in vacuo by forming an azeotrope with MeCN. EtOH (20 mL) was added, and the mixture refluxed for 10 mins. The mixture was then cooled to 0 °C, filtered through a P4 frit and the residue washed with cold EtOH. The extraction process was repeated, and the combined extracts evaporated in vacuo to afford sodium sulfinate **9c** as a white solid (33.3 mg, 0.17 mmol, 87%).

^{1}H NMR (400 MHz, Methanol-d_4) δ 7.29 – 7.20 (m, 4H, Ar*H*), 7.18 – 7.11 (m, 1H, Ar*H*), 2.94 – 2.85 (m, 2H, C(4)H_2), 2.57 – 2.48 (m, 2H, C(5)H_2); **^{13}C NMR** (101 MHz, Methanol-d_4) δ 142.5, 129.4, 126.9, 64.6, 29.7 (*1 aromatic carbon signal is not observed due to signal overlap*); **LRMS** (ESI, *m/z*) 169.0 $[M\text{-}Na]^-$; **HRMS** (ESI, *m/z*) Calc. for $C_8H_9O_2S^-$ $[M\text{-}Na]^-$ = 169.0329, found 169.0317.

Data is consistent with the literature.[23c]

8.2.7 Sulfinate derivatisation data

Benzyl 4-(benzylsulfonyl)piperidine-1-carboxylate (10a)

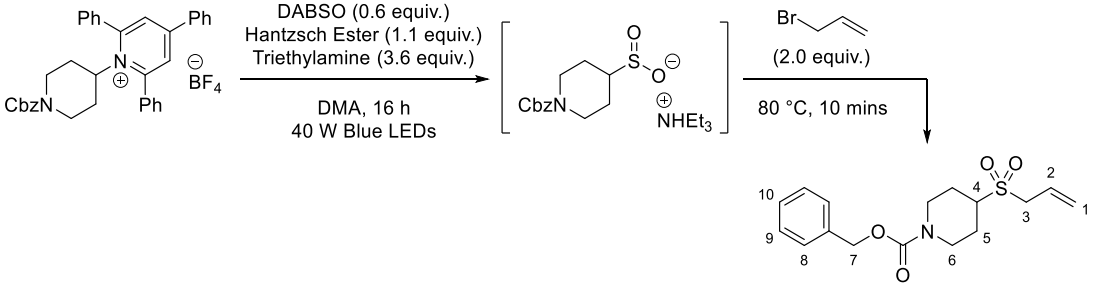


Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry triethylamine (102 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). Benzyl bromide (48 µL, 0.4 mmol, 2.0 equiv.) was then added and the reaction stirred at 80 °C for 10 min. The reaction was cooled to rt, and without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (40% EtOAc in Petrol) to afford sulfone **10a** as a colourless oil (63.9 mg, 0.17 mmol, 86%).

R_f = 0.16 (40% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 – 7.28 (m, 10H, Ar*H*), 5.12 (s, 2H, C(8)H_2), 4.30 (br. s, 2H, 2×C(7)*H*H), 4.20 (s, 2H, C(4)H_2), 2.91 (tt, *J* = 11.8, 3.7 Hz, 1H, C(5)*H*), 2.75 (br. s, 2H, 2×C(7)H*H*), 2.02 (br. d, *J* = 11.0 Hz, 2H, 2×C(6)*H*H), 1.88 – 1.69 (br. m, 2H, 2×C(6)*H*H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.9, 136.4, 130.6, 129.1, 128.6, 128.5, 128.2, 128.0, 127.4, 67.4, 57.1, 56.6, 42.6, 24.5; **LRMS** (ESI, *m/z*): 396.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{20}H_{24}NO_4S^+$ $[M+H]^+$ =

374.1420, Found = 374.1420; **IR** (thin film, ν_{max} /cm^{-1}) 2931, 2868, 1690, 1430, 1309, 1213, 1116.

Benzyl 4-(allylsulfonyl)piperidine-1-carboxylate (10b)

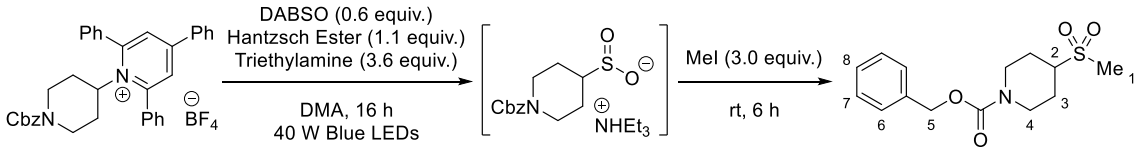


Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry triethylamine (102 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). Allyl bromide (35 µL, 0.4 mmol, 2.0 equiv.) was then added and the reaction stirred at 80 °C for 10 min. The reaction was cooled to rt, and without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (40% EtOAc in Petrol) to afford sulfone **10b** as a colourless oil (53.6 mg, 0.17 mmol, 83%).

R$_f$ = 0.14 (40% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 5H, Ar*H*), 5.91 (ddt, *J* = 17.4, 10.2, 7.3 Hz, 1H, C(2)*H*), 5.54 – 5.38 (m, 2H, C(1)H_2), 5.12 (s, 2H, C(7)H_2), 4.34 (br. s, 2H, 2×C(6)*H*H), 3.70 (d, *J* = 7.3 Hz, 2H, C(3)H_2), 3.09 (tt, *J* = 11.9, 3.8 Hz, 1H, C(4)*H*), 2.81(br. s, 2H, 2×C(6)H*H*), 2.05 (br. d, *J* = 12.4 Hz, 2H, 2×C(5)*H*H), 1.89 – 1.70 (br. m, 2H, 2×C(5)*H*H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.0, 136.5, 128.6, 128.2, 128.0, 124.7, 124.7, 67.5, 57.4, 55.0, 42.7, 24.4; **LRMS** (ESI, *m/z*): 346.0 [M+Na]$^+$;

HRMS (ESI, *m/z*): Calc. for $C_{16}H_{21}NO_4SNa^+$ $[M+Na]^+$ = 346.1084, Found = 346.1084; **IR** (thin film, ν_{max} /cm^{-1}) 2926, 2864, 1692, 1425, 1311, 1212, 1130.

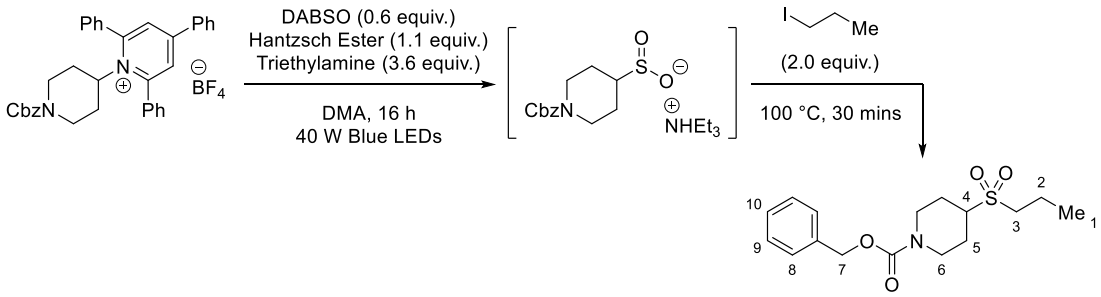
Benzyl 4-(methylsulfonyl)piperidine-1-carboxylate (10c)



Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry triethylamine (102 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). Methyl iodide (40 µL, 0.6 mmol, 3.0 equiv.) was then added and the reaction stirred at rt for 6 h. Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (70% EtOAc in Petrol) to afford sulfone **10c** as a colourless oil (53.9 mg, 0.18 mmol, 91%).

R_f = 0.27 (70% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.29 (m, 5H, Ar*H*), 5.12 (s, 2H, C(5)H_2), 4.38 (br. s, 2H, 2×C(4)*H*H), 2.98 (tt, *J* = 12.1, 3.7 Hz, 1H, C(2)*H*), 2.82 (s, 5H, 2×C(4)H*H* & C(1)H_3), 2.13 (br. d, *J* = 12.7 Hz, 2H, 2×C(3)*H*H), 1.81 – 1.64 (m, 2H, 2×C(3)*H*H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.0, 136.5, 128.6, 128.3, 128.1, 67.5, 60.5, 42.8, 37.4, 25.0; **LRMS** (ESI, *m/z*): 320.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{20}NO_4S^+$ $[M+H]^+$ = 298.1108, Found = 298.1109; **IR** (thin film, ν_{max} /cm^{-1}) 2930, 2863, 1692, 1431, 1303, 1261, 1213.

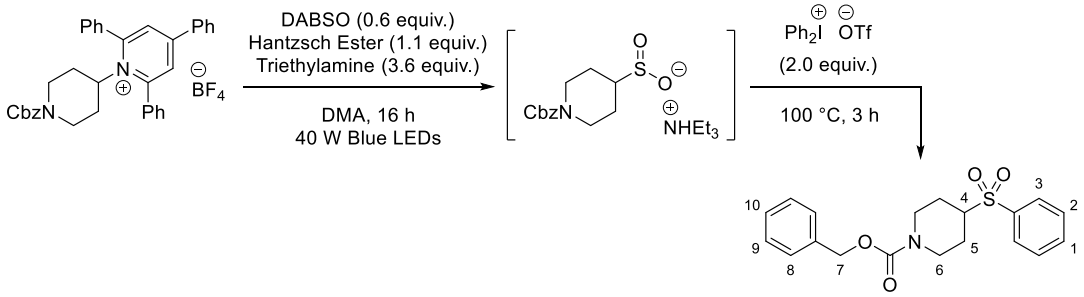
Benzyl 4-(propylsulfonyl)piperidine-1-carboxylate (10d)



Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry triethylamine (102 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). 1-Iodopropane (40 µL, 0.4 mmol, 2.0 equiv.) was then added and the reaction stirred at 100 °C for 30 min. The reaction was cooled to rt, and without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (50% EtOAc in Petrol) to afford sulfone **10d** as a colourless oil (55.3 mg, 0.17 mmol, 85%).

R_f = 0.26 (50% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 5H, Ar*H*), 5.13 (s, 2H, C(7)H_2), 4.37 (br. s, 2H, 2×C(6)*H*H), 2.98 (tt, *J* = 12.0, 3.7 Hz, 1H, C(4)*H*), 2.92 – 2.74 (m, 4H, 2×C(6)H*H* & C(3)H_2), 2.09 (br. d, *J* = 12.8 Hz, 2H, 2×C(5)*H*H), 1.96 – 1.84 (m, 2H, C(2)H_2), 1.84 – 1.71 (m, 2H, 2×C(5)*H*H), 1.09 (t, *J* = 7.4 Hz, 3H, C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.1, 136.5, 128.7, 128.3, 128.2, 67.6, 59.0, 51.4, 42.9, 24.7, 15.2, 13.4; **LRMS** (ESI, *m/z*): 348.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{16}H_{23}NO_4SNa^+$ $[M-Na]^+$ = 348.1240, Found = 348.1241; **IR** (thin film, ν_{max} /cm^{-1}) 2967, 2935, 1693, 1429, 1262, 1212, 1130.

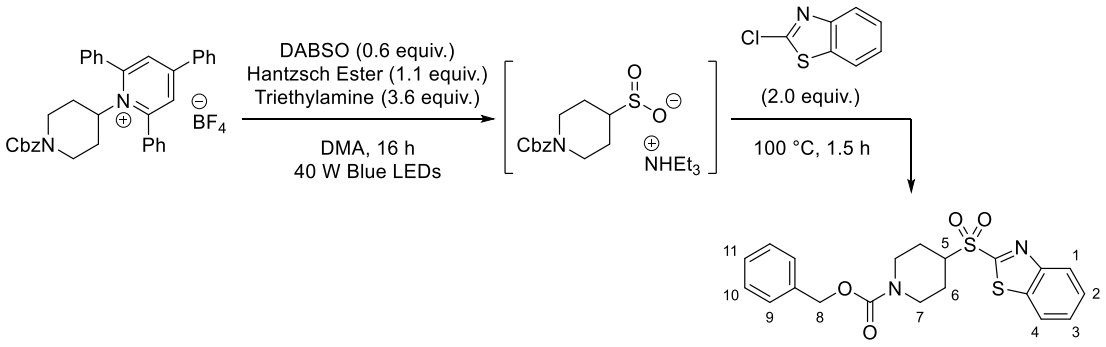
Benzyl 4-(phenylsulfonyl)piperidine-1-carboxylate (10e)



Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry triethylamine (102 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). Diphenyliodonium triflate (172 mg, 0.4 mmol, 2.0 equiv.) was then added and the reaction stirred at 100 °C for 3 h. The reaction was cooled to rt, and without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (30% EtOAc in Petrol) to afford sulfone **10e** as a colourless oil (62.5 mg, 0.17 mmol, 87%).

R_f = 0.12 (30% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (dt, *J* = 8.5, 1.7 Hz, 2H, Ar*H*), 7.73 – 7.65 (m, 1H, Ar*H*), 7.63 – 7.54 (m, 2H, Ar*H*), 7.41 – 7.28 (m, 5H, Ar*H*), 5.10 (s, 2H, C(7)H_2), 4.31 (br. s, 2H, 2×C(6)*H*H), 3.05 (tt, *J* = 12.1, 3.7 Hz, 1H, C(4)*H*), 2.74 (s, 2H, 2×C(6)H*H*), 2.01 (br. d, *J* = 12.9 Hz, 2H, 2×C(5)*H*H), 1.63 (qd, *J* = 12.5, 4.5 Hz, 2H, 2×C(5)*H*H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.0, 136.7, 136.6, 134.2, 129.4, 129.3, 128.7, 128.3, 128.1, 67.6, 61.7, 42.9, 25.2; **LRMS** (ESI, *m/z*): 382.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{19}H_{21}NO_4SNa^+$ $[M+Na]^+$ = 382.1084, Found = 382.1083; **IR** (thin film, ν_{max} /cm^{-1}) 2932, 2861, 1698, 1447, 1306, 1214, 1146.

Benzyl 4-(benzo[d]thiazol-2-ylsulfonyl)piperidine-1-carboxylate (10f)

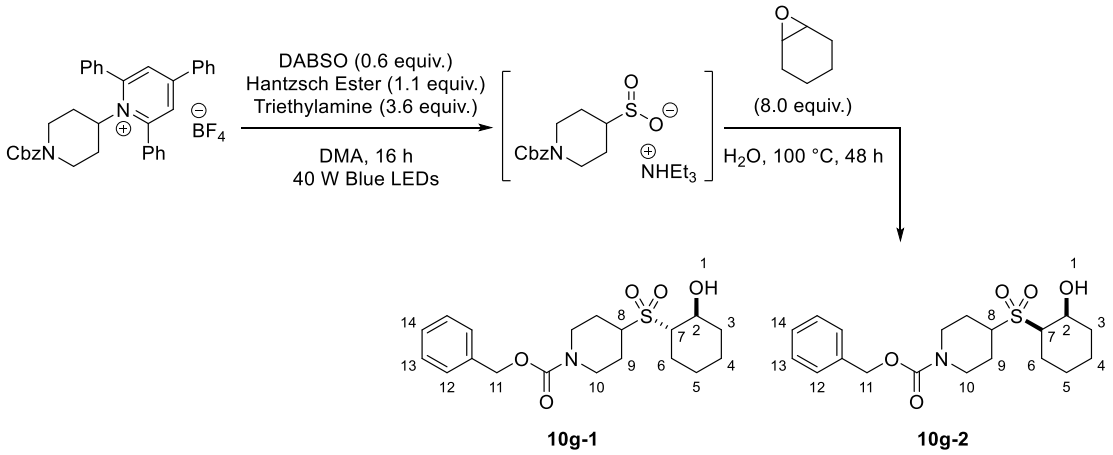


Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry triethylamine (102 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). 2-Chlorobenzothiazole (50 µL, 0.4 mmol, 2.0 equiv.) was then added and the reaction stirred at 100 °C for 1.5 h. The reaction was cooled to rt, and without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (30% EtOAc in Petrol) to afford sulfone **10f** as a colourless oil (57.8 mg, 0.14 mmol, 69%).

R_f = 0.16 (30% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 – 8.21 (m, 1H, Ar*H*), 8.06 – 8.00 (m, 1H, Ar*H*), 7.70 – 7.58 (m, 2H, Ar*H*), 7.40 – 7.27 (m, 5H, Ar*H*), 5.11 (s, 2H, C(8)H_2), 4.35 (br. s, 2H, 2×C(7)*H*H), 3.64 (tt, *J* = 11.9, 3.7 Hz, 1H, C(5)*H*), 2.85 (br. s, 2H, 2×C(7)H*H*), 2.23 – 2.10 (br. m, 2H, 2×C(6)*H*H), 1.88 (qd, *J* = 12.5, 4.5 Hz, 2H, 2×C(6)*H*H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.3, 155.0, 153.0, 137.1, 136.5, 128.6, 128.3, 128.3, 128.1, 127.9, 125.7, 122.4, 67.6, 61.1, 42.8, 24.8; **LRMS** (ESI, *m/z*): 439.0

$[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{20}H_{20}N_2O_4S_2Na^+$ $[M+Na]^+$ = 439.0757, Found = 439.0756; **IR** (thin film, ν_{max} /cm^{-1}) 2930, 2864, 1690, 1423, 1324, 1213, 1144.

Benzyl 4-((2-hydroxycyclohexyl)sulfonyl)piperidine-1-carboxylate (10g)



Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry triethylamine (102 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). Cyclohexene oxide (162 µL, 1.6 mmol, 8.0 equiv.) and water (0.5 mL) was then added and the reaction stirred at 100 °C for 48 h. The reaction was cooled to rt, and the reaction partitioned between EtOAc and water. The organic layer was washed with water, brine, dried using $MgSO_4$ and solvent removed in vacuo. The crude reaction mixture was loaded onto silica gel and purified by flash column chromatography (50-60% EtOAc in Petrol) to afford the title product as two diastereomers **10g-1** (50.5 mg, 0.13 mmol, 66%) and **10g-2** (12.0 mg, 0.03 mmol, 16%) as colourless oils (82% total).

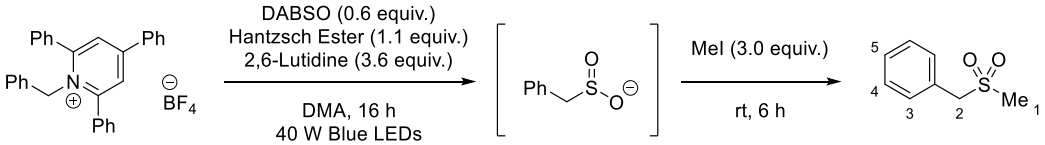
10g-1

R_f = 0.25 (60% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 5H, Ar*H*), 5.12 (s, 2H, C(11)H_2), 4.34 (br. s, 2H, 2×C(10)*H*H), 4.05 – 3.94 (br. m, 1H, C(2)*H*), 3.43 (br. s, 1H, C(7)*H*), 3.21-2.90 (br. m, 2H, O(1)*H* & C(8)*H*), 2.90 – 2.72 (m, 2H, 2×C(10)H*H*), 2.21 – 2.04 (br. m, 4H, C(3)*H*H, C(6)*H*H & 2×C(9)*H*H), 1.92 – 1.70 (br. m, 4H, C(5)*H*H, C(6)H*H* & 2×C(9)H*H*), 1.55 (qd, *J* = 13.1, 3.8 Hz, 1H, C(4)*H*H), 1.41 – 1.19 (m, 3H, C(3)H*H*, C(4)H*H* & C(5)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.1, 136.6, 128.7, 128.3, 128.1, 69.2, 67.5, 63.3, 59.9, 43.0, 42.8, 35.2, 25.0, 24.7, 23.9, 23.7; **LRMS** (ESI, *m/z*): 404.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{19}H_{27}NO_5SNa^+$ $[M+Na]^+$ = 404.1502, Found = 404.1497; **IR** (thin film, ν_{max} /cm^{-1}) 3464, 2936, 2860, 1702, 1452, 1215, 1131.

10g-2

R_f = 0.12 (60% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 5H, Ar*H*), 5.13 (s, 2H, C(11)H_2), 4.29 (br. s, 2H, 2H, 2×C(10)*H*H), 3.95 (ddd, *J* = 11.3, 8.8, 4.7 Hz, 1H, C(2)*H*), 3.67-3.54 (m, 1H, C(7)*H*), 2.96 – 2.71 (m, 3H, 2×C(10)H*H* & C(8)*H*), 2.20 (d, *J* = 3.3 Hz, 1H, O(1)*H*), 2.15 – 1.93 (m, 4H, C(3)*H*H, C(6)*H*H & 2×C(9)*H*H), 1.79 – 1.63 (m, 4H, C(4)*H*H, C(5)*H*H & 2×C(9)H*H*), 1.52 (qd, *J* = 12.7, 4.0 Hz, 1H, C(3)H*H*), 1.36 – 1.22 (m, 3H, C(4)H*H*, C(5)H*H* & C(6)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.2, 136.7, 128.7, 128.2, 128.1, 85.8, 73.4, 67.5, 62.1, 43.2, 33.4, 32.3, 24.3, 24.1, 23.8; **LRMS** (ESI, *m/z*): 404.2 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{19}H_{27}NO_5SNa^+$ $[M+Na]^+$ = 404.1502; **IR** (thin film, ν_{max} /cm^{-1}) 3362, 2937, 2861, 1701, 1452, 1215, 1119.

((Methylsulfonyl)methyl)benzene (10h)



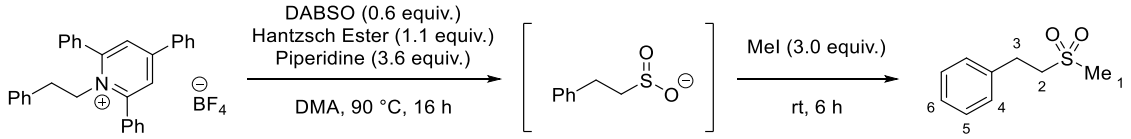
Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-benzyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1b** (97.1 mg,

0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry 2,6-lutidine (83 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). Methyl iodide (40 µL, 0.6 mmol, 3.0 equiv.) was then added and the reaction stirred at rt for 6 h. Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (40% EtOAc in Petrol) to afford sulfone **10h** as a white solid (25.6 mg, 0.15 mmol, 75%).

R_f = 0.25 (40% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 – 7.35 (m, 5H Ar*H*), 4.25 (s, 2H. C(2)H_2), 2.75 (s, 3H, C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 130.6, 129.2, 128.4, 61.4, 39.1; **LRMS** (ESI, *m/z*): 193.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_8H_{10}O_2SNa^+$ $[M+Na]^+$ = 193.0294, Found = 193.0297.

Data is consistent with the literature.[23c]

(2-(Methylsulfonyl)ethyl)benzene (10i)



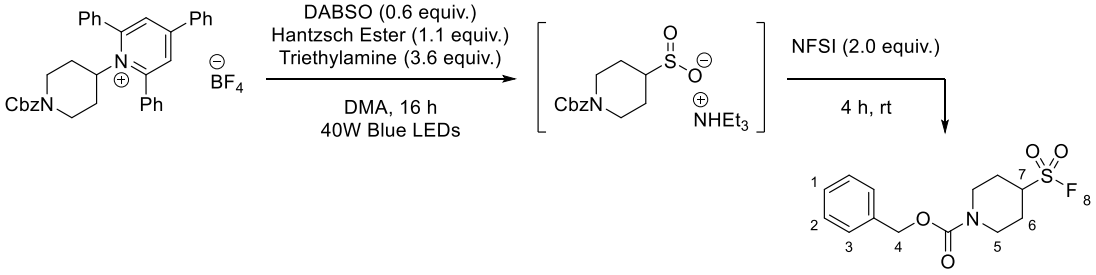
Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1c** (99.9 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry piperidine (71 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred at 90 **°C** for 16 h. Methyl iodide (62 µL, 1.0 mmol, 5.0 equiv.) was then added and the reaction stirred at rt for 6 h. Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column

chromatography (30% EtOAc in Petrol) to afford sulfone **10i** as a white solid (26.8 mg, 0.15 mmol, 73%).

R_f = 0.22 (30% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 2H, Ar*H*), 7.29 – 7.21 (m, 3H, Ar*H*), 3.34 – 3.26 (m, 2H, C(2)H_2), 3.21 – 3.12 (m, 2H, C(3)H_2), 2.82 (s, 3H, C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.5, 129.1, 128.5, 127.3, 56.3, 41.1, 28.7; **LRMS** (ESI, *m/z*): 207.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_9H_{12}O_2SNa^+$ $[M+Na]^+$ = 207.0450, Found = 207.0453.

Data is consistent with the literature.[23c]

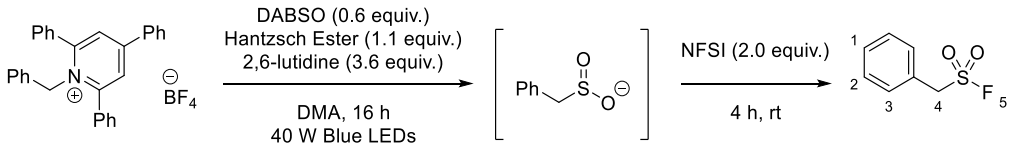
Benzyl 4-(fluorosulfonyl)piperidine-1-carboxylate (11a)



Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry triethylamine (102 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). NFSI (126.1 mg, 0.4 mmol, 2.0 equiv) was then added and the reaction stirred at rt for 4 h. Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (100% CH_2Cl_2) to afford sulfonyl fluoride **11a** as a white crystalline solid (51.4 mg, 0.17 mmol, 85%).

R_f = 0.23 (100% CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.29 (m, 5H, Ar*H*), 5.14 (s, 2H, C(4)H_2), 4.46 – 4.23 (br. s, 2H, 2×C(5)*H*H), 3.47 (ttd, *J* = 11.8, 3.8, 1.9 Hz, 1H, C(7)*H*), 3.01 – 2.79 (br. m, 2H, 2×C(5)H*H*), 2.24 (br. d, *J* = 12.0 Hz, 2H, 2×C(6)*H*H), 1.90 (br. qd, *J* = 11.6, 4.2 Hz, 2H, 2×C(6)H*H*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.9, 136.3, 128.7, 128.4, 128.2, 67.8, 58.9 (d, J_{CF} = 15.1 Hz), 42.5, 25.9; **^{19}F NMR** (377 MHz, $CDCl_3$) δ 42.3; **HRMS** (ESI, *m/z*): Calc. for $C_{13}H_{16}FNO_4SNa^+$ $[M+Na]^+$ = 324.0676, Found = 324.0677; **IR** (thin film, ν_{max} /cm^{-1}) 2938, 2868, 1698, 1400, 1183, 1015, 760; **Melting point =** 87 – 89 °C.

Phenylmethanesulfonyl fluoride (11b)



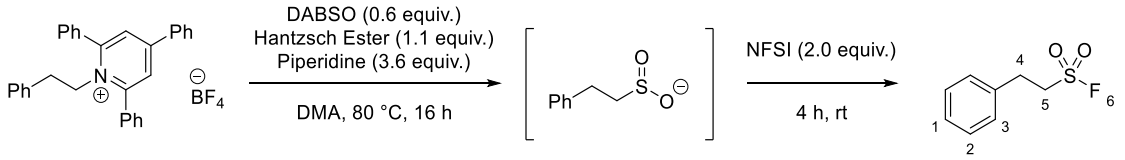
Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-benzyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1b** (97.1 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry 2,6-lutidine (84 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). NFSI (126.1 mg, 0.4 mmol, 2.0 equiv.) was then added and the reaction stirred at rt for 4 h. Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (5% EtOAc in Petrol) to afford sulfonyl fluoride **11b** as a white crystalline solid (26.1 mg, 0.15 mmol, 75%).

R_f = 0.23 (100% CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.51 – 7.40 (m, 5H, Ar*H*), 4.60 (d, *J* = 3.2 Hz, 2H, C(4)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 130.8, 130.0, 129.4, 125.6,

57.0 (d, J_{CF} = 18.0 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ 51.4 (t, *J* = 3.5 Hz); **HRMS** (ESI, *m/z*) *Mass not found.*

Data is consistent with the literature.[55b]

2-Phenylethane-1-sulfonyl fluoride (11c)

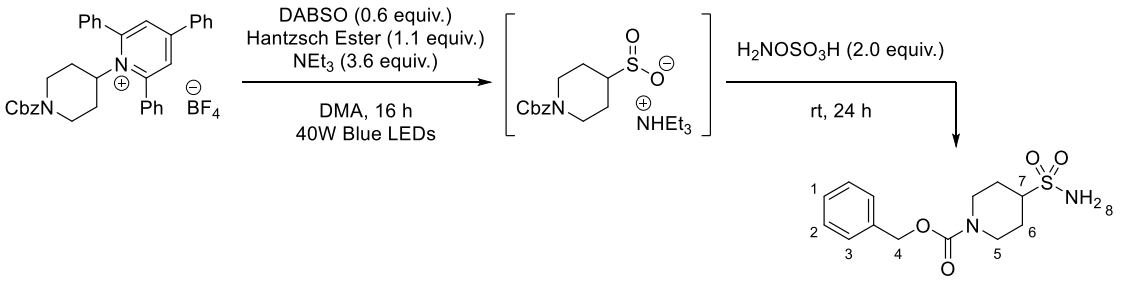


Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1c** (100 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry piperidine (71 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred at 90 **°C** for 16 h. NFSI (126.1 mg, 0.4 mmol, 2.0 equiv.) was then added and the reaction stirred at rt for 4 h. Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (3 – 5% EtOAc in Petrol) to afford sulfonyl fluoride **11c** as a white crystalline solid (30.5 mg, 0.16 mmol, 80%).

R_f = 0.15 (5% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 3H, Ar*H*), 7.25 – 7.19 (m, 2H, Ar*H*), 3.68 – 3.58 (m, 2H, C(5)H_2), 3.29 – 3.19 (m, 2H, C(4)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 136.1, 129.3, 128.5, 127.8, 52.3 (d, *J* = 16.0 Hz), 29.8; **^{19}F NMR** (377 MHz, $CDCl_3$) δ 53.2 (t, *J* = 4.5 Hz); **HRMS** (ESI, *m/z*) *Mass not found.*

Data is consistent with the literature.[232]

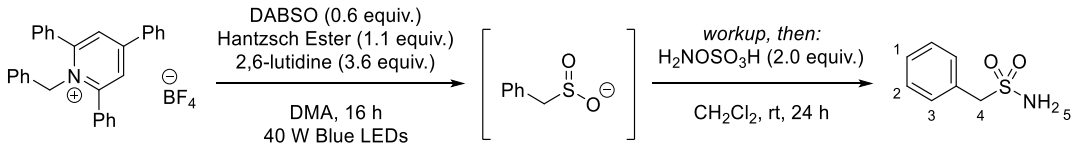
Benzyl 4-sulfamoylpiperidine-1-carboxylate (12a)



Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry triethylamine (102 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). Hydroxylamine-*O*-sulfonic acid (45.2 mg, 0.4 mmol, 2.0 equiv.) was then added and the reaction stirred at rt for 24 h. Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (60% EtOAc in Petrol) to afford primary sulfonamide **12a** as a colourless oil (52.6 mg, 0.18 mmol, 88%).

R_f = 0.19 (60% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 5H, Ar*H*), 5.13 (s, 2H, C(4)H_2), 4.48 (s, 2H, N(8)H_2), 4.37 (br. m, 2H, 2×C(5)*H*H), 3.08 (tt, *J* = 12.0, 3.7 Hz, 1H, C(7)*H*), 2.90 – 2.74 (m, 2H, 2×C(5)H*H*), 2.19 (br. d, *J* = 12.9 Hz, 2H, 2×C(6)*H*H), 1.81 – 1.66 (m, 2H, 2×C(6)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.2, 136.6, 128.7, 128.3, 128.1, 67.6, 60.7, 43.0, 26.2; **LRMS** (ESI, *m/z*): 321.0 $[M+Na]^+$, 297.0 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{13}H_{18}N_2O_4SNa^+$ $[M+Na]^+$ = 321.0879, Found = 321.0877; **IR** (thin film, ν_{max} /cm^{-1}) 3249, 2960, 1679, 1436, 1323, 1279, 1218. 1142; **Melting point =** 126 – 129 °C.

Phenylmethanesulfonamide (12b)



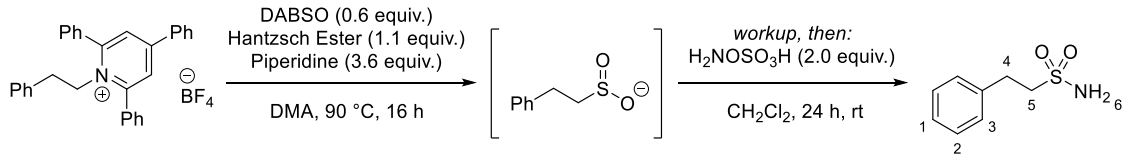
Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-benzyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1b** (97.1 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry 2,6-lutidine (84 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). Upon completion, aq. H_3PO_4 (3.0 mL, 2M) and brine (1.0 mL) were added to the mixture. The mixture was then extracted with CH_2Cl_2 (3 × 2.0 mL). The combined organic phase was transferred to a round-bottom flask and DIPEA (3 equiv.) was added. Hydroxylamine-*O*-sulfonic acid (45.2 mg, 0.4 mmol, 2.0 equiv.) and sodium acetate (32.8 mg, 0.4 mmol, 2.0 equiv.) were then added and the reaction stirred at rt for 24 h. The reaction mixture was concentrated *in* vacuo, and the crude reaction mixture was then loaded directly to silica gel and purified by flash column chromatography (40% EtOAc in Petrol) to afford primary sulfonamide **12b** as a white crystalline solid (25.3 mg, 0.15 mmol, 74%).

Also prepared according a modified procedure using $Na_2S_2O_5$ (45.6 mg, 0.24 mmol, 1.2 equiv.) instead of DABSO, and no 2,6-lutidine was added. Hydroxylamine-*O*-sulfonic acid (45.2 mg, 0.4 mmol, 2.0 equiv.) and sodium acetate (32.8 mg, 0.4 mmol, 2.0 equiv.) were added to the crude reaction mixture without workup, affording primary sulfonamide **12b** as a white crystalline solid (23.5 mg, 0.14 mmol, 69%).

R_f = 0.23 (40% EtOAc in Petrol); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.43 – 7.31 (m, 5H, Ar*H*), 6.83 (s, 2H, N(5)H_2), 4.26 (s, 2H, C(4)H_2); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 130.8, 130.8, 128.3, 127.9, 60.2; **LRMS** (ESI, *m/z*): 170.0 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_7H_8NO_2S^-$ $[M-H]^-$ = 170.0281, Found = 170.0276.

Data is consistent with the literature.[233]

2-Phenylethane-1-sulfonamide (12c)

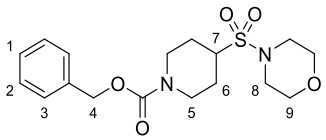


Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1b** (99.9 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry piperidine (71 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred at 90 **°C** for 16 h. Upon completion, aq. H_3PO_4 (3.0 mL, 2 M) and brine (1.0 mL) were added to the mixture. The mixture was then extracted with CH_2Cl_2 (3 × 2.0 mL). The combined organic phase was transferred to a round-bottom flask and DIPEA (3 equiv.) was added. Hydroxylamine-*O*-sulfonic acid (45.2 mg, 0.4 mmol, 2.0 equiv.) and sodium acetate (32.8 mg, 0.4 mmol, 2.0 equiv.) were then added and the reaction stirred at rt for 24 h. The reaction mixture was concentrated *in* vacuo, and the crude reaction mixture was then loaded directly to silica gel and purified by flash column chromatography (40% EtOAc in Petrol) to afford primary sulfonamide **12c** as a white crystalline solid (26.3 mg, 0.14 mmol, 71%).

R_f = 0.25 (40% EtOAc in Petrol); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.36 – 7.17 (m, 5H, Ar*H*), 6.87 (s, 2H, N(6)H_2), 3.28 – 3.20 (m, 2H, C(4)H_2), 3.04 – 2.96 (m, 2H, C(5)H_2); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 138.8, 128.6, 128.3, 126.4, 55.5, 29.6; **LRMS** (ESI, *m/z*): 184.1 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_8H_{10}NO_2S^-$ $[M-H]^-$ = 184.0438, Found = 184.0434.

Data is consistent with the literature.[234]

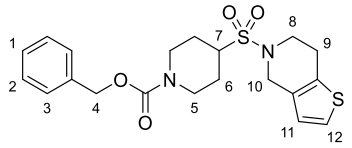
Benzyl 4-(morpholinosulfonyl)piperidine-1-carboxylate (13a)



Prepared according to **General Procedure F** using 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), triethylamine (102 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.), NCS (53.4 mg, 0.4 mmol, 2.0 equiv.) and morpholine (34.5 μL, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (60% EtOAc in Petrol) afforded sulfonamide **13a** as a colourless oil (66.1 mg, 0.17 mmol, 83%).

R_f = 0.23 (60% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 5H, Ar*H*), 5.13 (s, 2H, C(4)H_2), 4.33 (br. s, 2H, 2×C(5)*H*H), 3.81 – 3.68 (m, 4H, 2×C(9)H_2), 3.42 – 3.30 (m, 4H, 2×C(8)H_2), 3.06 (tt, *J* = 11.9, 3.7 Hz, 1H, C(7)*H*), 2.80 (br. s, 2H, 2×C(5)H*H*), 2.06 (d, *J* = 12.6 Hz, 2H, 2×C(6)*H*H), 1.73 (qd, *J* = 12.4, 4.1 Hz, 2H, 2×C(6)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.1, 136.6, 128.7, 128.3, 128.2, 67.6, 67.2, 59.5, 46.6, 43.0, 26.1; **LRMS** (ESI, *m/z*): 391.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{24}N_2O_5SNa^+$ $[M+Na]^+$ = 391.1298; found 391.1299; **IR** (thin film, ν_{max} /cm^{-1}) 2918, 2861, 1775, 1705, 1431, 1179, 953; **Melting point =** 101 – 104 °C.

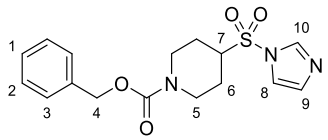
Benzyl 4-((6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl)sulfonyl)piperidine-1-carboxylate (13b)



Prepared according to **General Procedure F** using 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), triethylamine (102 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.), NCS (53.4 mg, 0.4 mmol, 2.0 equiv.) and 4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine (55.7 mg, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (20 – 30% EtOAc in Petrol) afforded sulfonamide **13b** as a colourless oil (68.2 mg, 0.16 mmol, 81%).

R_f = 0.18 (30% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.29 (m, 5H. Ar*H*), 7.14 (d, *J* = 5.2 Hz, 1H, Ar*H*), 6.75 (d, *J* = 5.2 Hz, 1H, Ar*H*), 5.12 (s, 2H, C(4)H_2), 4.45 (s, 2H, C(10)H_2), 4.31 (br. s, 2H, 2×C(5)*H*H), 3.66 (t, *J* = 5.7 Hz, 2H, C(8)H_2), 3.10 (tt, *J* = 11.9, 3.6 Hz, 1H, C(7)*H*), 2.92 (t, *J* = 5.6 Hz, 2H, C(9)H_2), 2.91-2.67 (br. m, 2H, C(5)H*H*), 2.10 – 2.01 (br. m, 2H, 2×C(6)*H*H), 1.83 – 1.66 (br. m, 2H, 2×C(6)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.0, 136.5, 133.0, 131.1, 128.6, 128.2, 128.1, 124.6, 123.8, 67.4, 59.9, 46.0, 44.1, 43.0, 26.1, 25.9.; **LRMS** (ESI, *m/z*): 443.2 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{20}H_{24}N_2O_4S_2Na^+$ $[M+Na]^+$ = 443.1070, Found = 443.1068; **IR** (thin film, ν_{max} /cm^{-1}) 2960, 2861, 1695, 1430, 1318, 1215, 1139.

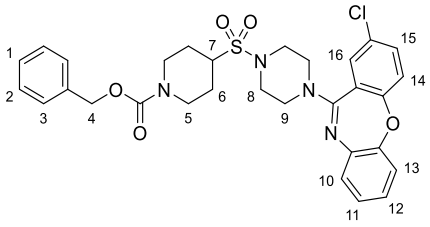
Benzyl 4-((1*H*-imidazol-1-yl)sulfonyl)piperidine-1-carboxylate (13c)



Prepared according to **General Procedure F** using 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), triethylamine (102 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.), NCS (53.4 mg, 0.4 mmol, 2.0 equiv.) and imidazole (27.2 mg, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (70% EtOAc in Petrol) afforded sulfonamide **13c** as a colourless oil (68.2 mg, 0.13 mmol, 66%).

R_f = 0.19 (70% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (s, 1H, Ar*H*), 7.34 – 7.20 (m, 5H, Ar*H*), 7.19 (t, *J* = 1.3 Hz, 1H, Ar*H*), 7.15 – 7.08 (m, 1H, Ar*H*), 5.04 (s, 2H, C(4)H_2), 4.27 (br. s, 2H, 2×C(5)*H*H), 3.24 (tt, *J* = 12.0, 3.6 Hz, 1H, C(7)*H*), 2.70 (br. s, 2H, 2×C(5)H*H*), 1.92 (br. d, *J* = 12.4 Hz, 2H, 2×C(6)*H*H), 1.67 – 1.54 (m, 2H, 2×C(6)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.9, 137.5, 136.3, 131.6, 128.7, 128.4, 128.2, 118.4, 67.8, 62.8, 42.6, 25.7; **LRMS** (ESI, *m/z*): 350.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{16}H_{20}N_3O_4S^+$ $[M+H]^+$ = 350.1169, Found = 350.1168; **IR** (thin film, ν_{max} /cm^{-1}) 3123, 2960, 1696, 1430, 1376, 1219, 1168.

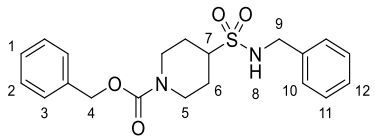
Benzyl 4-((4-(2-chlorodibenzo[*b,f*][1,4]oxazepin-11-yl)piperazin-1-yl)sulfonyl)piperidine-1-carboxylate (13d)



Prepared according to **General Procedure F** using 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.2 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), triethylamine (102 μL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.), NCS (53.4 mg, 0.4 mmol, 2.0 equiv.) and Amoxapine (125.5 mg, 0.4 mmol, 2.0 equiv.) in DMA (0.4 mL). Purification by flash column chromatography (20 – 30% EtOAc in Petrol) afforded sulfonamide **13d** as a colourless oil (66.9 mg, 0.11 mmol, 56%).

R_f = 0.18 (30% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 8.7, 2.6 Hz, 1H, Ar*H*), 7.38 – 7.28 (m, 6H, Ar*H*), 7.20 (d, *J* = 8.7 Hz, 1H, Ar*H*), 7.17 – 7.07 (m, 3H, Ar*H*), 7.06 – 6.99 (m, 1H, Ar*H*), 5.13 (s, 2H, C(4)H_2), 4.33 (br. s, 2H, 2×C(5)*H*H), 3.60 (br. s, 4H, 2×C(9)H_2), 3.47 (br. s, 4H, 2×C(8)H_2), 3.08 (tt, *J* = 11.9, 3.5 Hz, 1H, C(7)*H*), 2.79 (br. s, 2H, 2×C(5)H*H*), 2.07 (br. d, *J* = 12.2 Hz, 2H, 2×C(6)*H*H), 1.84 – 1.64 (br. m, 2H, 2×C(6)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.5, 158.5, 155.0, 151.8, 139.7, 136.6, 133.1, 130.6, 128.9, 128.7, 128.3, 128.1, 127.2, 126.0, 125.2, 124.8, 123.0, 120.3, 67.5, 59.6, 48.1, 46.0, 43.0, 26.1; **LRMS** (ESI, *m/z*): 595.2 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{30}H_{32}Cl^{35}N_4O_5S^+$ $[M+H]^+$ = 595.1776; found 595.1770; **IR** (thin film, ν_{max} /cm^{-1}) 2929, 2858, 1698, 1587, 1471, 1215, 1143.

Benzyl 4-(*N*-benzylsulfamoyl)piperidine-1-carboxylate (13e)



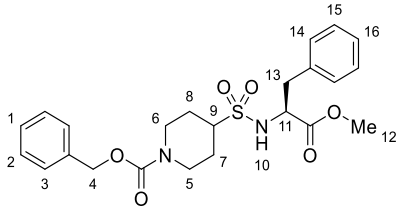
Prepared according to **General Procedure F** using 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.20 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), triethylamine (102 µL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.), NCS (53.4 mg, 0.40 mmol, 2.0 equiv.) and benzylamine (44 µL, 0.40 mmol, 2.0 equiv.) in DMA (0.4 mL, 0.5 M). Following addition of the amine, the reaction was stirred for 3 h until full consumption of the sulfonate ester was observed. Purification by flash column chromatography (40% EtOAc in Petrol) afforded sulfonamide **13e** as a white solid (41.9 mg, 0.11 mmol, 54%).

Also prepared according to **General Procedure G** using 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.20 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), triethylamine (102 µL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.), HOBt (80%) (101.3 mg, 0.60 mmol, 3.0 equiv.), NCS (53.4 mg, 0.40 mmol, 2.0 equiv.), benzylamine (44 µL, 0.40 mmol, 2.0 equiv.) and pyridine (32 µL, 0.40 mmol, 2.0 equiv.) in DMA (0.4 mL, 0.5 M). Following addition of the amine, the reaction was stirred for 3 h until full consumption of the sulfonate ester was observed. Purification by flash column chromatography (40% EtOAc in Petrol) afforded sulfonamide **13e** as a white solid (58.6 mg, 0.15 mmol, 75%).

R_f = 0.18 (40% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 10H, Ar*H*), 5.11 (s, 2H, C(4)H_2), 4.88 (br. s, 1H, N(8)*H*), 4.36 – 4.17 (br. m, 4H, 2×C(5)*H*H &

C(9)H_2), 2.83 (tt, J = 11.9, 3.6 Hz, 1H, C(7)*H*), 2.67 (app. br. s, 2H, 2×C(5)H*H*), 2.03 (app. br. d, J = 12.4 Hz, 2H, 2×C(6)*H*H), 1.75 – 1.59 (br. m, 2H, 2×C(5)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.1, 137.3, 136.5, 128.9, 128.6, 128.2, 128.2, 128.1, 128.0, 67.5, 59.9, 47.6, 42.9, 25.9; **LRMS** (ESI, *m/z*): 411.2 $[M+Na]^+$, 387.2 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{20}H_{25}N_2O_4S^+$ $[M+H]^+$ = 389.1530; found 389.1523; **IR** (thin film, ν_{max} /cm^{-1}) 3256, 2980, 1684, 1435, 1319, 1217, 1141; **Melting point =** 121 – 124 °C.

Benzyl (*S*)-4-(*N*-(1-methoxy-1-oxo-3-phenylpropan-2-yl)sulfamoyl)piperidine-1-carboxylate (13f)

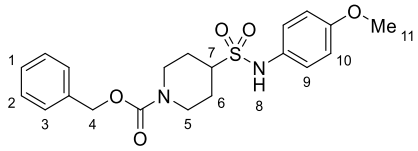


Prepared according to **General Procedure G** using 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.20 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), triethylamine (102 µL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.), HOBt (80%) (101.3 mg, 0.60 mmol, 3.0 equiv.), NCS (53.4 mg, 0.40 mmol, 2.0 equiv.), L-Alanine methyl ester hydrochloride (55.8 mg, 0.40 mmol, 2.0 equiv.) and pyridine (32 µL, 0.40 mmol, 2.0 equiv.) in DMA (0.4 mL, 0.5 M). Following addition of the amine, the reaction was stirred for 40 h until full consumption of the sulfonate ester was observed. Purification by flash column chromatography (40% EtOAc in Petrol) afforded sulfonamide **13f** as a pale-yellow oil (67.5 mg, 0.15 mmol, 73%).

R_f = 0.18 (40% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.06 (m, 10H, Ar*H*), 5.03 (s, 2H, C(4)H_2), 4.86 (d, J = 9.7 Hz, 1H, N(10)*H*), 4.21 (td, J = 9.1, 4.7 Hz, 1H, C(11)*H*), 4.07 (app. br. s, 2H, C(5)*H*H & C(6)*H*H), 3.69 (s, 3H, C(12)H_3), 3.09 (dd, J =

13.8, 4.7 Hz, 1H, C(13)*H*H), 2.82 (dd, *J* = 13.8, 8.9 Hz, 1H, C(13)H*H*), 2.46 (app. br. s, 3H, C(5)H*H*, C(6)H*H* & C(9)*H*), 1.78 (app. br. d, *J* = 12.3 Hz, 1H, C(7/8)*H*H), 1.65 (app. br. d, *J* = 12.7 Hz, 1H, C(8/7)*H*H), 1.41 (qd, *J* = 12.4, 4.5 Hz, 1H, C(7/8)H*H*), 1.29 (qd, *J* = 12.5, 4.5 Hz, 1H, C(8/7)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.4, 155.0, 136.6, 136.0, 129.6, 128.9, 128.7, 128.3, 128.1, 127.6, 67.5, 60.2, 58.0, 52.9, 42.8, 42.8, 39.6, 25.5 *(note: for piperidine ring, 4 peaks were found instead of 3 due to the loss of symmetry caused by chiral sulfur atom)*; **LRMS** (ESI, *m/z*): 483.2 $[M+Na]^+$, 459.1 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{23}H_{29}N_2O_6S^+$ $[M+H]^+$ = 461.1741; found 461.1740; **IR** (thin film, ν_{max} /cm^{-1}) 3251, 2957, 1745, 1704, 1434, 1279, 1217; **ee** (determined by chiral SFC using a Chiralpak® IC column, 1500 psi, 30 °C; flow: 1.5 mL/min; 1.0 – 30% MeOH in 5.0 min): 98% ee (major enantiomer t_R = 4.305 min, minor enantiomer t_R = 4.497 min); $[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ -13.0° (c = 1.0, $CHCl_3$).

Benzyl 4-(*N*-(4-methoxyphenyl)sulfamoyl)piperidine-1-carboxylate (13g)

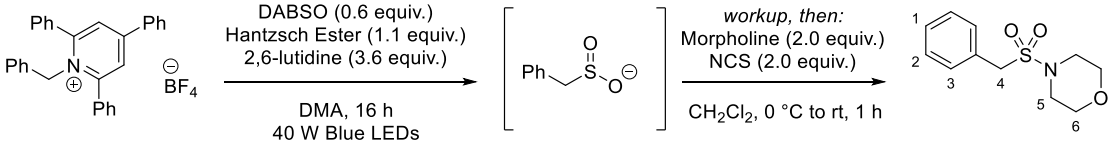


Prepared according to **General Procedure G** using 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1a** (122.5 mg, 0.20 mmol, 1.0 equiv.), Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), triethylamine (102 µL, 0.72 mmol, 3.6 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.), HOBt (80%) (101.3 mg, 0.60 mmol, 3.0 equiv.), NCS (53.4 mg, 0.40 mmol, 2.0 equiv.) and *p*-anisidine (49.3 mg, 0.40 mmol, 2.0 equiv.) and pyridine (32 µL, 0.40 mmol, 2.0 equiv.) in DMA (0.4 mL, 0.5 M). Following addition of the amine, the reaction was stirred for 24 h until full consumption of the sulfonate ester was observed. Purification by flash column

chromatography (70 – 80% Et_2O in Petrol) afforded sulfonamide **13g** as an off-white solid (64.3 mg, 0.16 mmol, 79%).

R_f = 0.2 (40% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 5H, Ar*H*), 7.21 – 7.14 (m, 2H, Ar*H*), 6.88 – 6.83 (m, 2H, Ar*H*), 5.11 (s, 2H, C(4)H_2), 4.28 (app. br. s, 2H, 2×C(5)*H*H), 3.79 (s, 3H, C(11)H_3), 3.09 (tt, *J* = 11.8, 3.7 Hz, 1H, C(7)*H*), 2.75 (app. br. s, 2H, 2×C(5)H*H*), 2.07 (app. br. d, *J* = 11.5 Hz, 2H, 2×C(6)*H*H), 1.87 – 1.69 (br. m, 2H, 2×C(6)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.9, 155.1, 136.5, 129.3, 128.7, 128.3, 128.1, 124.2, 114.9, 67.6, 58.0, 55.6, 42.9, 25.9; **LRMS** (ESI, *m/z*): 427.0 $[M+Na]^+$, 403.0 $[M-H]^-$; **HRMS** (ESI, *m/z*): Calc. for $C_{20}H_{24}N_2O_5SNa^+$ $[M+Na]^+$ = 427.1298; found 427.1300; **IR** (thin film, ν_{max} /cm^{-1}) 3250, 2960, 1675, 1510, 1280, 1213, 1147; **Melting point =** 104 – 107 °C.

1-(Benzylsulfonyl)morpholine (13h)



Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-benzyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1b** (97.1 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry 2,6-lutidine (84 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred under 450 nm blue LED irradiation for 16 h (see **Figure S1** for experimental setup). Upon completion, aq. H_3PO_4 (3.0 mL, 2 M) and brine (1.0 mL) were added to the mixture. The mixture was then extracted with CH_2Cl_2 (3 × 2.0 mL). The combined organic phase was transferred to a round-bottom flask and DIPEA (3 equiv.) was added. NCS (53.4 mg, 0.4 mmol, 2.0 equiv.) and morpholine (34.5 µL,

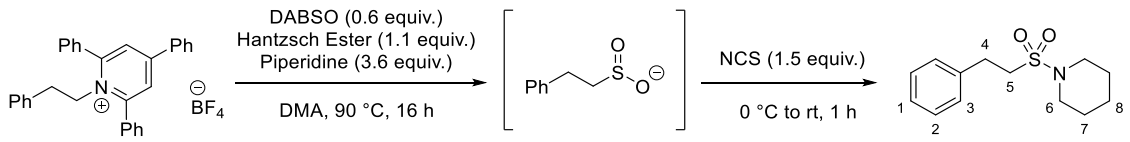
0.4 mmol, 2.0 equiv.) were added and the reaction stirred at rt for 1 h. The crude reaction mixture was concentrated *in* vacuo, and the crude reaction mixture was then loaded directly to silica gel and purified by flash column chromatography (30% EtOAc in Petrol) to afford sulfonamide **13h** as a white crystalline solid (33.8 mg, 0.14 mmol, 70%).

Also prepared according a modified procedure using $Na_2S_2O_5$ (45.6 mg, 0.24 mmol, 1.2 equiv.) instead of DABSO, and no 2,6-lutidine was added. NCS (53.4 mg, 0.4 mmol, 2.0 equiv.) and morpholine (34.5 µL, 0.4 mmol, 2.0 equiv.) were added to the crude reaction mixture without workup, affording sulfonamide **13h** as a white crystalline solid (33.9 mg, 0.14 mmol, 70%).

R_f = 0.18 (30% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 – 7.32 (m, 5H, Ar*H*), 4.23 (s, 2H, C(4)H_2), 3.61 (t, *J* = 4.6 Hz, 4H, 2×C(6)H_2), 3.10 (t, *J* = 4.6 Hz, 4H, 2×C(6)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 130.8, 129.0, 129.0, 128.7, 66.8, 56.9, 46.2; **LRMS** (ESI, *m/z*): 264.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{11}H_{16}NO_3S^+$ $[M+H]^+$ = 242.0845, Found = 242.0847.

Data is consistent with the literature.[235]

1-(Phenethylsulfonyl)piperidine (13i)



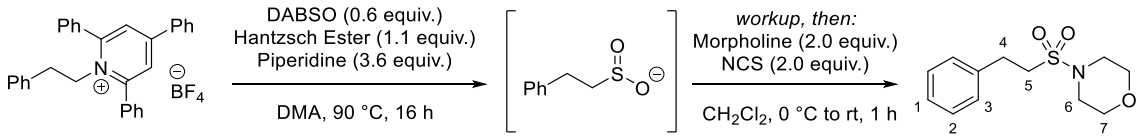
Hantzsch ester (55.7 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1c** (99.9 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry piperidine (71 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred at 90 °**C** for 16 h. After cooling the solution to 0 °C,

NCS (53.4 mg, 0.4 mmol, 2.0 equiv.) was added and the reaction stirred at rt for 1 h. Without workup, the crude reaction mixture was loaded directly to silica gel and purified by flash column chromatography (70 – 80% CH_2Cl_2 in Petrol) to afford sulfonamide **13i** as a white crystalline solid (37.1 mg, 0.15 mmol, 73%).

R_f = 0.28 (80% CH_2Cl_2 in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 2H, Ar*H*), 7.27 – 7.18 (m, 3H, Ar*H*), 3.28 – 3.21 (m, 4H, 2×C(6)H_2), 3.17 – 3.08 (m, 4H, C(4)H_2 & C(5)H_2), 1.70 – 1.60 (m, 4H, 2×C(7)H_2), 1.60 – 1.52 (m, 2H, C(8)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.5, 129.0, 128.5, 127.0, 50.9, 46.8, 29.5, 25.8, 24.0; **LRMS** (ESI, *m/z*): 254.2 $[M+H]^+$, 276.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{13}H_{20}NO_2S^+$ $[M+H]^+$ = 254.1209, Found = 254.1209.

Data is consistent with the literature.[236]

4-(Phenethylsulfonyl)morpholine (13j)



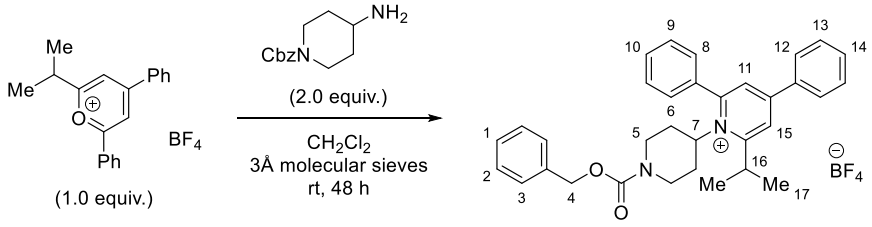
Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 1-phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate **1c** (100 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry DMA (0.4 mL) was then added, followed by degassed, dry piperidine (71 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred at 90 **°C** for 16 h. Upon completion, aq. H_3PO_4 (3.0 mL, 2 M) and brine (1.0 mL) were added to the mixture. The mixture was then extracted with CH_2Cl_2 (3 × 2.0 mL). The combined organic phase was transferred to a round-bottom flask and DIPEA (3 equiv.) was added. NCS (53.4 mg, 0.4 mmol, 2.0 equiv.) and morpholine (34.5 µL, 0.4 mmol, 2.0 equiv.) were added and the reaction

stirred at rt for 1 h. The crude reaction mixture was concentrated *in* vacuo, and the crude reaction mixture was then loaded directly to silica gel and purified by flash column chromatography (30% EtOAc in Petrol) to afford sulfonamide **13j** as a white crystalline solid (34.3 mg, 0.13 mmol, 67%).

R_f = 0.24 (30% CH_2Cl_2 in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 2H, Ar*H*), 7.29 – 7.19 (m, 3H, Ar*H*), 3.83 – 3.67 (m, 4H, 2×C(7)H_2), 3.34 – 3.22 (m, 4H, 2×C(6)H_2), 3.22 – 3.08 (m, 4H, C(4)H_2 & C(5)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.1, 129.0, 128.5, 127.1, 66.7, 50.5, 45.9, 29.4; **LRMS** (ESI, *m/z*): 278.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{12}H_{18}NO_3S^+$ $[M+H]^+$ = 256.1002, Found = 256.1003; **IR** (thin film, ν_{max} /cm^{-1}) 2920, 2857, 1453, 1323, 1156, 1111, 949; **Melting point =** 78 – 80 °C.

8.2.8 New Pyrylium and Pyrydinium For Hindered Amines Data

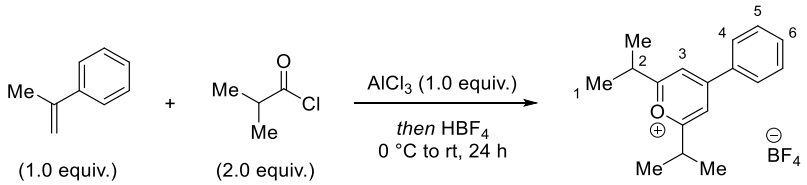
1-(1-((Benzyloxy)carbonyl)piperidin-4-yl)-2-isopropyl-4,6-diphenylpyridin-1-ium tetrafluoroborate (15a)



According to the procedure described by Katritzky and co-workers,[174] benzyl 4-aminopiperidine-1-carboxylate (647 mg, 2.76 mmol, 2.0 equiv.) and 2-isopropyl-4,6-diphenylpyrylium tetrafluoroborate **8a** (500 mg, 1.38 mmol, 1.0 equiv.) were stirred in CH_2Cl_2 (20 mL) over 3Å molecular sieves for 48 h at rt. Diethyl ether was then added to give the crude product. Purification by flash column chromatography (10% Acetone in CH_2Cl_2) afforded Katritzky salt **15a** as an off-white solid (79.6 mg, 0.14 mmol, 10%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 2.2 Hz, 1H, Ar*H*), 7.80 – 7.45 (m, 11H, Ar*H*), 7.35 (q, *J* = 4.5 Hz, 5H, Ar*H*), 5.11 (s, 2H, C(4)H_2), 4.92 (app. br. s, 1H, C(7)*H*), 4.33 (s, 2H, 2×C(5)*H*H), 3.71 (hept, *J* = 6.6 Hz, 1H, C(16)*H*), 2.56 – 2.07 (m, 6H, 2×C(5)H*H* & 2×C(6)H_2), 1.55 (d, *J* = 6.6 Hz, 6H, 2×C(17)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.3, 156.7, 155.0, 136.4, 134.5, 134.3, 132.0, 131.2, 129.8, 128.7, 128.4, 128.28, 128.25, 67.7, 67.1, 44.2, 32.1, 30.9, 23.9 (*4 aromatic carbon signals are not observed due to signal overlap*); **^{19}F NMR** (377 MHz, $CDCl_3$) δ -153.10 (minor, $^{10}BF_4$), -153.15 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 491.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{33}H_{35}N_2O_2^+$ $[M\text{-}BF_4]^+$ = 491.2693, Found = 491.2691; **IR** (thin film, ν_{max} /cm^{-1}) 2940, 1698, 1625, 1417, 1238, 1055; **Melting point =** 100 °C (decomp.).

2,6-Diisopropyl-4-phenylpyrylium tetrafluoroborate (8b)

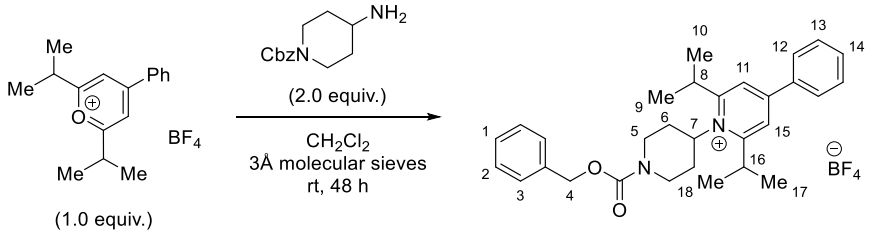


According to the procedure described by Katritzky and co-workers,[174] α-methylstyrene (3.1 mL, 24 mmol, 1.0 equiv.) was added slowly at 0 °C, with stirring, to a suspension of anhydrous aluminium chloride (3.2 g, 24 mmol) in isobutyryl chloride (5.0 mL, 48 mmol, 2.0 equiv.). The reaction was then stirred at rt for 24 h, after which ice (50 g) and 2 M aq. HCl (50 mL) were added and impurities were extracted with diethyl ether (l00 mL). Fluoroboric acid (6 mL of a 40% aqueous solution) was added and the mixture extracted with CH_2Cl_2 (2 × 200 mL). The combined organic extracts were dried using $MgSO_4$ and solvent removed in vacuo. Diethyl ether was added to the residue, upon which the product crashed out as a pale-brown solid. The product was the recrystallised from methanol to give pyrylium salt **8b** as a beige solid (3.53 g, 11 mmol, 45%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.4 Hz, 4H, Ar*H*), 7.65 (t, *J* = 7.4 Hz, 1H, Ar*H*), 7.57 (t, *J* = 7.6 Hz, 2H, Ar*H*), 3.56 (hept, *J* = 6.9 Hz, 2H, 2×C(2)*H*), 1.47 (d, *J* = 6.9 Hz, 12H, 4×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.9, 168.0, 135.4, 132.4, 130.3, 129.9, 116.7, 34.8, 20.3; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -152.68 (minor, $^{10}BF_4$), -153.73 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 241.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{21}O^+$ $[M\text{-}BF_4]^+$ = 241.1587, Found = 241.1589.

Data is consistent with the literature.[174]

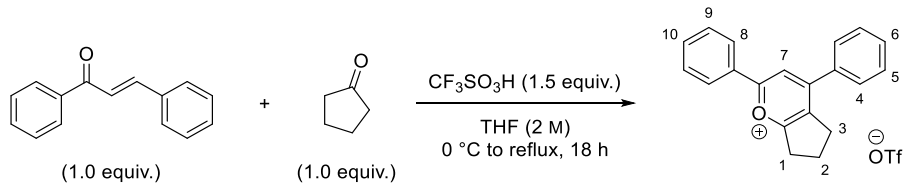
1-(1-((Benzyloxy)carbonyl)piperidin-4-yl)-2,6-diisopropyl-4-phenylpyridin-1-ium tetrafluoroborate (15b)



According to the procedure described by Katritzky and co-workers,[174] benzyl 4-aminopiperidine-1-carboxylate (713 mg, 3.04 mmol, 2.0 equiv.) and 2,6-diisopropyl-4-phenylpyrylium tetrafluoroborate **8b** (500 mg, 1.52 mmol, 1.0 equiv.) were stirred in CH_2Cl_2 (20 mL) over 3Å molecular sieves for 48 h at rt. Diethyl ether was then added, upon which Katritzky salt **15b** precipitated out of solution as an off-white solid (461 mg, 0.85 mmol, 56%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.70 (m, 4H, Ar*H*), 7.67 – 7.49 (m, 3H, Ar*H*), 7.46 – 7.30 (m, 5H, Ar*H*), 5.37 (app. br. s, 1H, C(7)*H*), 5.17 (s, 2H, C(4)H_2), 4.43 (app. br. s, 2H, 2×C(5)*H*H), 3.90 – 3.66 (m, 2H, C(8)*H* & C(16)*H*), 3.90 – 3.66 (m, 2H, 2×C(5)H*H*), 2.34 (s, 4H, 2×C(6)H_2), 1.58 – 1.39 (m, 12H, C(9)H_3, C(10)H_3, C(17)H_3 & C(18)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.6, 165.1, 156.4, 155.2, 136.5, 134.4, 132.2, 130.0, 128.7, 128.4, 128.3, 128.0, 123.2, 121.9, 67.7, 62.6, 43.9, 32.7, 32.3, 30.9, 24.1, 23.3 *(note: for isopropyl substituents, 4 peaks were found instead of 2 due to restricted rotation)*; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -152.70 (minor, $^{10}BF_4$), -152.76 (major, $^{11}BF_4$); **LRMS** (ESI, *m/z*): 457.2 $[M\text{-}BF_4]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{30}H_{37}N_2O_2^+$ $[M\text{-}BF_4]^+$ = 457.2850, Found = 457.2847; **IR** (thin film, ν_{max} /cm^{-1}) 2973, 1696, 1628, 1425, 1241, 1052; **Melting point =** 179 – 182 °C.

2,4-Diphenyl-6,7-dihydro-5*H*-cyclopenta[*b*]pyran-1-ium trifluoromethanesulfonate (8c)

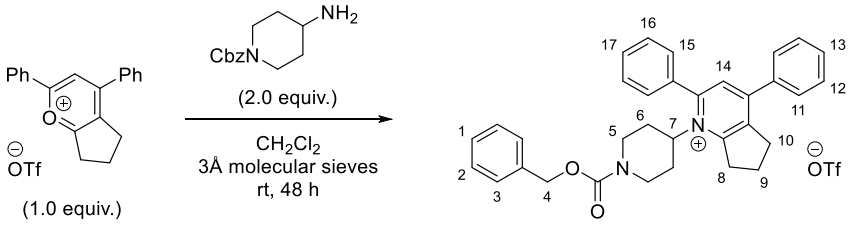


According to a procedure described by Cornella and co-workers,[6] chalcone (5.2 g, 25 mmol, 1.0 equiv.) was added to a Schlenk flask fitted with a reflux condenser. The system was sealed, evacuated and backfilled with N_2 (× 3). Cyclopentanone (2.22 mL, 25 mmol, 1.0 equiv.) and dry THF (13 mL) were then added and the reaction was cooled to 0 °C. Trifluoromethanesulfonic acid (3.31 mL, 15 mmol, 1.5 equiv.) was added dropwise with stirring. The reaction mixture was then heated to reflux and stirred for 18 h. The reaction was cooled and the solid precipitate was collected by filtration, washed with Et_2O three times and dried under high vacuum to afford pyrylium salt **8c** as an off-white solid (1.96 g, 4.6 mmol, 19%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H, Ar*H*), 8.17 – 8.11 (m, 2H, Ar*H*), 7.87 (dd, *J* = 7.9, 1.6 Hz, 2H, Ar*H*), 7.68 – 7.50 (m, 6H, Ar*H*), 3.57 (t, *J* = 7.9 Hz, 2H, C(1)H_2), 3.36 (t, *J* = 7.4 Hz, 2H, C(3)H_2), 2.43 (app. p, *J* = 7.7 Hz, 2H, C(2)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.4, 170.5, 164.3, 135.7, 134.7, 133.8, 133.5, 130.03, 130.00, 129.9, 128.7, 128.3, 33.2, 30.2, 21.6; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -78.31; **LRMS** (ESI, *m/z*): 273.0 $[M\text{-}OTf]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{21}H_{17}O^+$ $[M\text{-}OTf]^+$ = 273.1274, Found = 273.1276.

Data is consistent with the literature.[174]

1-(1-((Benzyloxy)carbonyl)piperidin-4-yl)-2,4-diphenyl-6,7-dihydro-5*H*-cyclopenta[*b*]pyridin-1-ium trifluoromethanesulfonate (15d)

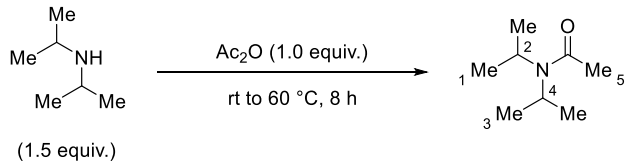


According to the procedure described by Katritzky and co-workers,[174] benzyl 4-aminopiperidine-1-carboxylate (469 mg, 2.0 mmol, 2.0 equiv.) and 2,4-diphenyl-6,7-dihydro-5*H*-cyclopenta[*b*]pyran-1-ium **8c** (422 mg, 1.0 mmol, 1.0 equiv.) were stirred in CH_2Cl_2 (20 mL) over 3Å molecular sieves for 48 h at rt. Diethyl ether was then added, upon which Katritzky salt **15d** precipitated out of solution as an off-white solid (354 mg, 0.55 mmol, 55%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.43 (m, 11H, Ar*H*), 7.40 – 7.28 (m, 5H, Ar*H*), 5.10 (s, 2H, C(4)H_2), 4.76 (app. br. s, 1H, C(7)*H*), 4.29 (app. br. s, 2H, 2×C(5)*H*H), 3.57 (app. br. s, 2H, C(8)H_2), 3.23 (app. br. s, 2H, C(10)H_2), 2.67 – 1.97 (br. m, 8H, 2×C(5)H*H*, 2×C(6)H_2 & C(9)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.0, 153.8, 153.4, 136.4, 135.2, 133.4, 131.1, 130.8, 129.5, 129.2, 128.74, 128.69, 128.3, 128.2, 120.7 (q, *J* = 320.9 Hz), 67.6, 43.8, 35.3, 30.8, 29.8, 24.7 *(1 aromatic and 1 aliphatic signal missing due to signal broadening)*; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -78.27; **LRMS** (ESI, *m/z*): 489.2 $[M\text{-}OTf]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{34}H_{33}N_2O_2^+$ $[M\text{-}OTf]^+$ = 489.2537, Found = 489.2527; **IR** (thin film, ν_{max} /cm^{-1}) 2956, 1697, 1614, 1431, 1262, 1148, 1030; **Melting point =** 104 – 107 °C.

8.2.9 Reactions of *N*-Aryl Katritzky Salts Data

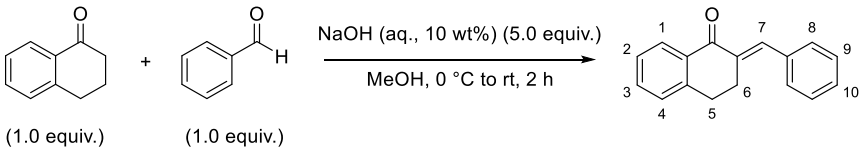
N,*N*-Diisopropylacetamide (23)



According to the procedure described by Cornella and co-workers,[6] diisopropylamine (84.1 mL, 0.6 mol, 1.5 equiv.) was added to a 250 mL RBF. With water bath cooling, acetic anhydride (37.8 mL, 0.4 mol, 1.0 equiv.) was added via dropping funnel. The reaction mixture was then stirred at 60 °C for 8 h. The reaction mixture was then cooled to rt, and water (50 mL) was added to the mixture to dissolve the ammonium salt. The aqueous layer was extracted with Et_2O (150 mL). The organic layer was then washed with water (50 mL), added into a one-necked flask and neutralized with saturated Na_2CO_3 solution under stirring, upon which CO_2 was released and a solid crashed out from the aqueous phase. The organic layer was dried using Na_2SO_4, filtered and solvent was removed in vacuo to give amide **23** as a colourless liquid (47.6 g, 0.33 mol, 83%). The product was found to be analytically pure, and was used in subsequent reactions without further purification

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (hept, *J* = 6.7 Hz, 1H, C(2)*H*), 3.52 (s, 1H, C(4)*H*), 2.06 (s, 3H, C(5)H_3), 1.35 (d, *J* = 6.8 Hz, 6H, 2×C(1)H_3), 1.19 (d, *J* = 6.8 Hz, 6H, 2×C(3)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.7, 49.4, 45.6, 24.0, 21.1, 20.7; **HRMS** (ESI, *m/z*): Calc. for $C_8H_{17}NONa^+$ $[M+Na]^+$ = 166.1202, Found = 166.1205.

(*E*)-2-Benzylidene-3,4-dihydronaphthalen-1(2*H*)-one (19a)

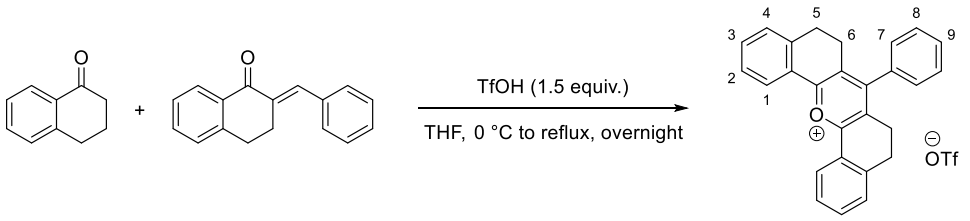


According to the procedure described by Cornella and co-workers,[6] benzaldehyde (2.03 mL, 20 mmol, 1.0 equiv.) and α-tetralone (2.66 mL, 20 mmol, 1.0 equiv.) were dissolved in methanol (20 mL). The reaction was cooled to 0 °C, to which aqueous NaOH solution (40 mL, 100 mmol, 10 wt%, 5.0 equiv.) was added. The reaction mixture was allowed to warm to rt and the reaction stirred for 2 h. The solid precipitate was collected by filtration, washed with cool MeOH and dried under high vacuum to give chalcone **19a** as a white solid (2.70 g, 12 mmol, 58%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 7.8, 1.1 Hz, 1H, Ar*H*), 7.88 (s, 1H, C(7)*H*), 7.54 – 7.30 (m, 7H, Ar*H*), 7.27 – 7.24 (m, 1H, Ar*H*), 3.14 (td, *J* = 6.5, 1.7 Hz, 2H, C(6)H_2), 3.00 – 2.92 (m, 2H, C(7)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 188.1, 143.4, 136.8, 136.0, 135.6, 133.6, 133.4, 130.0, 128.7, 128.6, 128.4, 128.3, 127.2, 29.0, 27.4; **LRMS** (ESI, *m/z*): 235.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{14}O^+$ $[M+H]^+$ = 235.1117, = Found = 235.1118.

Data is consistent with the literature.[171]

7-Phenyl-5,6,8,9-tetrahydrodibenzo[*c*,*h*]xanthen-14-ium trifluoromethanesulfonate (19b)

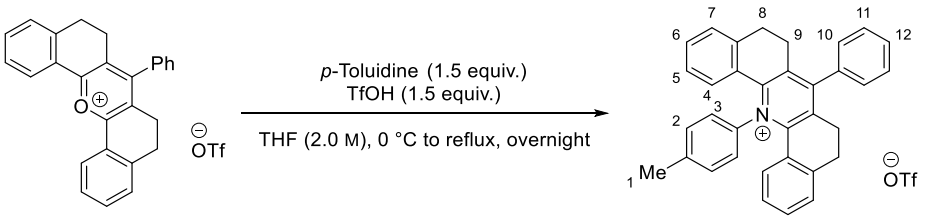


According to the procedure described by Cornella and co-workers,[6] (*E*)-2-benzylidene-3,4-dihydronaphthalen-1(2*H*)-one **19a** (2.34 g, 10 mmol, 1.0 equiv.) was added to a Schlenk flask fitted with a reflux condenser. The system was sealed, evacuated and backfilled with N_2 (× 3). 1-tetralone (1.47 g, 10 mmol, 1.0 equiv.) were dissolved in dry THF (5.0 mL) were added successively. The reaction was cooled to 0 °C, to which trifluoromethanesulfonic acid (1.32 mL, 15 mmol, 1.5 equiv.) was added dropwise with stirring. The reaction mixture was then heated to reflux and stirred for 18 h. The reaction was cooled and the solid precipitate was collected by filtration, washed with Et_2O three times and dried under high vacuum to give pyrylium salt **19b** as a yellow solid (2.61 g, 5.1 mmol, 51%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.43 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.79 – 7.60 (m, 7H, Ar*H*), 7.56 – 7.47 (m, 4H, Ar*H*), 3.07 (t, *J* = 7.5 Hz, 4H, 2×C(6)H_2), 2.88 (t, *J* = 7.5 Hz, 4H, 2×C(5)H_2); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 165.1, 164.3, 141.5, 135.2, 132.6, 130.4, 130.1, 129.3, 129.0, 128.4, 127.4, 126.2, 125.6, 122.2 (q, *J* = 322.2 Hz), 25.6, 24.1; **^{19}F NMR** (377 MHz, DMSO-d_6) δ -77.71; **LRMS** (ESI, *m/z*): 361.2 $[M\text{-}OTf]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{27}H_{21}O^+$ $[M\text{-}OTf]^+$ = 361.1587, Found = 361.1590.

Data is consistent with the literature.[6]

7-Phenyl-14-(*p*-tolyl)-5,6,8,9-tetrahydrodibenzo[*c,h*]acridin-14-ium trifluoromethanesulfonate (20)

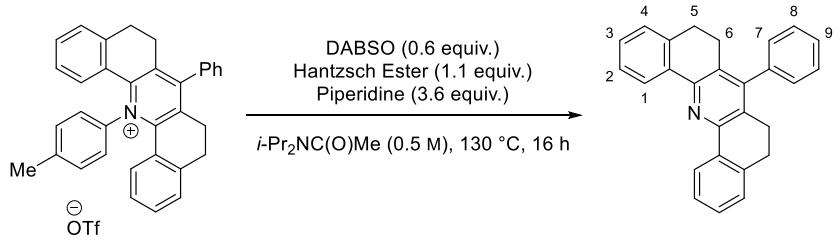


According to the procedure described by Cornella and co-workers,[6] 7-phenyl-5,6,8,9-tetrahydrodibenzo[*c,h*]xanthen-14-ium trifluoromethanesulfonate **19b** (1.53 mg, 3.0 mmol, 1.0 equiv.) and *p*-toluidine (482 mg, 4.5 mmol, 1.5 equiv.) were added to a Schlenk flask fitted with a reflux condenser. The system was sealed, evacuated and backfilled with N_2 (× 3). Ethanol (20 mL) was added and the mixture was stirred and heated to reflux for 4 h. The mixture was then allowed to cool to rt. Precipitated product was collected by filtration, washed with EtOH (3 × 25 mL), then Et_2O (3 × 25 mL), and dried under high vacuum. Katritzky salt **20** was isolated as a white powder (987 mg, 1.6 mmol, 55%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.64 (q, *J* = 7.6 Hz, 3H, Ar*H*), 7.55 – 7.41 (m, 6H, Ar*H*), 7.33 (dd, *J* = 7.4, 4.8 Hz, 4H, Ar*H*), 6.96 (t, *J* = 7.6 Hz, 2H, Ar*H*), 6.53 (d, *J* = 8.1 Hz, 2H, Ar*H*), 3.01 – 2.82 (m, 4H, 2×C(9)H_2), 2.82 – 2.63 (m, 4H, 2×C(8)H_2), 2.40 (s, 3H, C(1)H_3); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 154.2, 147.9, 142.0, 141.1, 138.2, 138.1, 134.1, 130.6, 130.3, 129.7, 129.3, 129.2, 129.1, 128.2, 127.9, 127.1, 125.9, 120.7 (q, *J* = 322.6 Hz), 27.9, 27.3, 20.8; **^{19}F NMR** (377 MHz, DMSO-d_6) δ -77.72; **LRMS** (ESI, *m/z*): 450.2 $[M\text{-}OTf]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{34}H_{28}N^+$ $[M\text{-}OTf]^+$ = 450.2216, Found = 450.2216.

Data is consistent with the literature.[6]

7-Phenyl-5,6,8,9-tetrahydrodibenzo[*c*,*h*]acridine (22a)



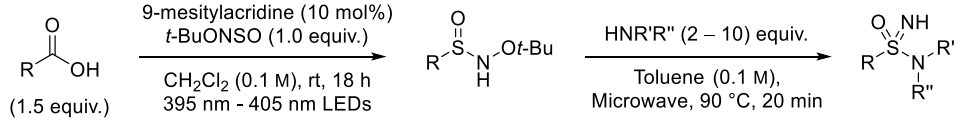
Hantzsch ester (55.2 mg, 0.22 mmol, 1.1 equiv.), DABSO (28.8 mg, 0.12 mmol, 0.6 equiv.) and 7-phenyl-14-(*p*-tolyl)-5,6,8,9-tetrahydrodibenzo[*c*,*h*]acridin-14-ium trifluoromethanesulfonate **20** (120 mg, 0.2 mmol, 1.0 equiv.) were added to an oven-dried 1.9 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Degassed, dry *N*,*N*-diisopropylacetamide **23** (0.4 mL) was then added, followed by degassed, dry piperidine (71 µL, 0.72 mmol, 3.6 equiv.). The reaction was stirred at 130 °C for 16 h. The reaction mixture was cooled to rt. Without workup, the crude reaction mixture was loaded directly onto silica gel and purified by flash column chromatography (10 – 20% CH_2Cl_2 in Petrol) to afford pyridine **22a** as an off-white solid (31.7 mg, 0.09 mmol, 44%).

R_f = 0.16 (20% CH_2Cl_2 in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (dd, *J* = 7.7, 1.0 Hz, 2H, Ar*H*), 7.51 (ddd, *J* = 7.5, 6.3, 1.3 Hz, 2H, Ar*H*), 7.48 – 7.39 (m, 3H, Ar*H*), 7.33 (td, *J* = 7.4, 1.4 Hz, 2H, Ar*H*), 7.25 – 7.17 (m, 4H, Ar*H*), 2.96 – 2.78 (m, 4H, 2×C(6)H_2), 2.67 (dd, *J* = 8.6, 5.9 Hz, 4H, 2×C(5)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.2, 147.6, 138.1, 137.9, 135.5, 128.9, 128.81, 128.79, 128.7, 127.7, 127.6, 127.1, 125.4, 28.3, 25.9; **LRMS** (ESI, *m/z*): 360.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{27}H_{23}N^+$ $[M+H]^+$ = 360.1747, Found = 360.1761.

Data is consistent with the literature.[149a]

8.3 Experimental for Chapter 3

8.3.1 General Procedures



General Procedure H: Carboxylic acid (1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (1.0 equiv.), and 9-mesitylacridine (**PC5**) (10 mol%) were weighed into an oven-dried 10 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Dry CH_2Cl_2 (0.1 M) was then added and the reaction was stirred under 395 – 405 nm LED irradiation (See **Figure S2** for experimental setup) with fan cooling for 18 h. After completion of the reaction (determined by TLC), solvent was removed under a stream of nitrogen, and the crude material was then dissolved in dry toluene (0.1 M), and amine (2.0 – 10 equiv.) was then added. The microwave vial was sealed with a rubber septum and heated to 90 °C in a microwave initiator for 20 mins. Upon completion, the reaction mixture was concentrated and purified using silica gel flash column chromatography.

8.3.2 Photochemical Reaction Setup

395 – 405 nm LEDs, where specified, comprised of 10 W LED strips wrapped inside a crystallising dish. 0.20 mmol scale reactions were carried out in 8 mL sample vials, sealed with a screw cap and Parafilm. Fan cooling was used during reactions to give an internal temperature of ~22 °C.

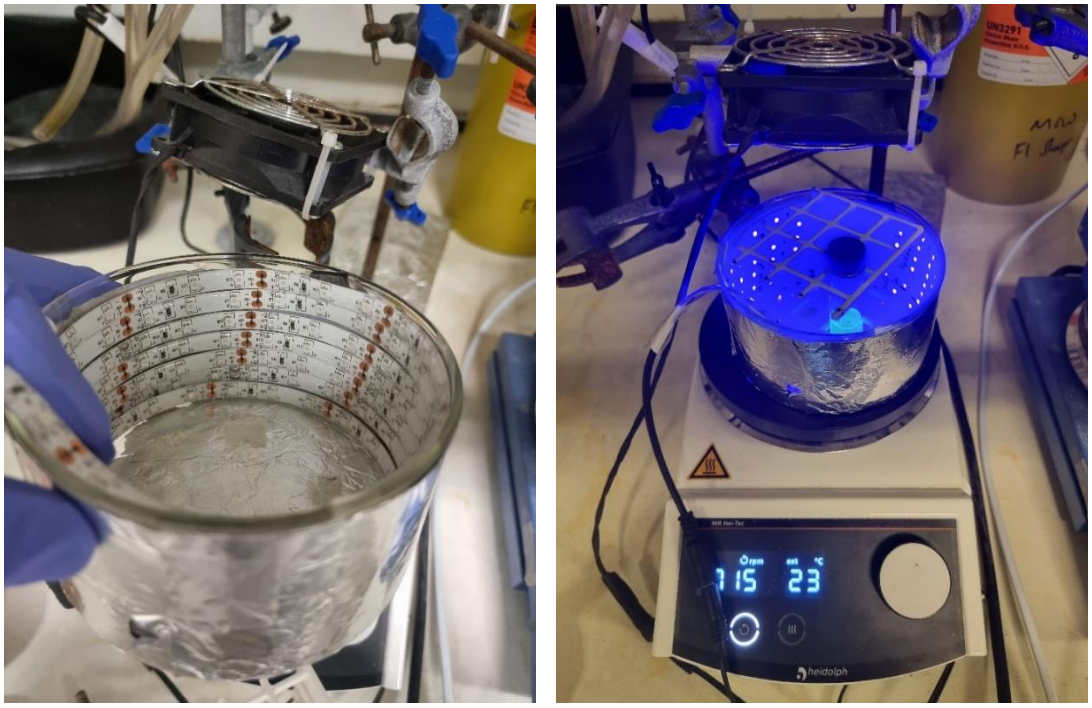
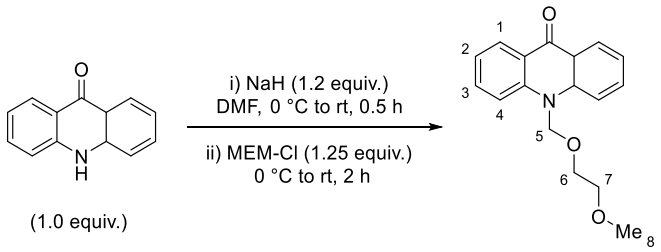


Figure S2. Left: LED strips wrapped inside crystallisation dish. Right: Reaction setup for 0.20 mmol reactions.

8.3.3 Catalyst Synthesis

N-(2-Methoxyethoxymethyl)-9-acridone (PC5-I)

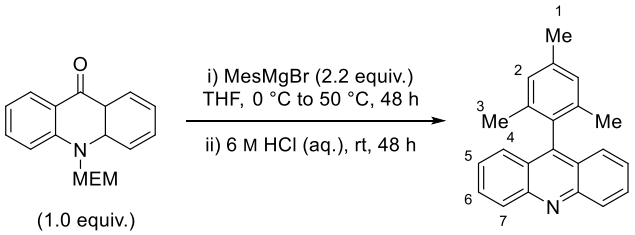


According to a modified procedure from Fukuzumi and co-workers,[237] 9-acridone (5.0 g, 25.6 mmol, 1.0 equiv.) was added to an oven-dried round-bottom flask, and dry DMF (50 mL) was then added. The resulting solution was cooled to 0 °C and NaH (60% in mineral oil) (1.23 g, 30.7 mmol, 1.2 equiv.) was then added in portions. The reaction was allowed to warm to rt and stirred for 30 mins. The reaction mixture was then cooled to 0 °C, and 2-methoxy-ethoxymethyl chloride (3.66 mL, 32.0 mmol, 1.25 equiv.) was then added dropwise. The reaction was allowed to warm to rt and stirred for 2 h. The reaction mixture was quenched with water (40 mL) and stirred for a further 30 mins. The crude product was extracted using ethyl acetate (3 × 50 mL). The combined organic layers were washed with water, brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was purified by silica gel flash column chromatography (1 – 2% MeOH in CH_2Cl_2) afforded acridone **PC5-I** as an off-white solid (4.18 g, 14.8 mmol, 57%).

R_f = 0.45 (2% MeOH in CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) 8.57 – 8.49 (m, 2H, Ar*H*), 7.78 – 7.67 (m, 4H, Ar*H*), 7.33 (ddd, *J* = 8.0, 5.9, 2.0 Hz, 2H, Ar*H*), 5.82 (s, 2H, C(5)H_2), 3.92 – 3.79 (m, 2H, C(6 or 7)H_2), 3.67 – 3.62 (m, 2H, C(7 or 6)H_2), 3.44 (s, 3H, C(8)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.6, 142.6, 134.1, 127.8, 122.6, 122.3, 115.4, 77.3, 72.4, 67.5, 59.4; **LRMS** (ESI^+, *m/z*) 284.1 $[M+H]^+$; **HRMS** (ESI^+, *m/z*): Calc. for $C_{17}H_{20}NO_3$ $[M+H]^+$ 284.1281, Found: 284.1282.

Data is consistent with the literature.[237]

9-Mesitylacridine (PC5)



According to a modified procedure from Verhoeven and co-workers,[238] *N*-(2-methoxy-ethoxymethyl)-9-acridone **PC5-I** (2.83 g, 10 mmol, 1.0 equiv.) was added to an oven-dried RBF, and dissolved in dry THF (500 mL), and the resulting solution was sparged with N_2 for 5 mins. The resulting solution was then cooled to 0 °C, and 2-mesitylmagnesium bromide (1.0 M in THF) (22 mL, 22 mmol, 2.2 equiv.) was then added dropwise. The reaction mixture was allowed to warm to rt and then heated to 50 °C and stirred for 48 h. The reaction was then cooled to rt and 6 M aqueous HCl solution (75 mL) was then added. The reaction mixture was then heated to 50 °C and stirred for a further 48 h. The reaction was then cooled to rt, basified with saturated aqueous $NaHCO_3$ solution and extracted with $CHCl_3$ (3×200 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was purification by silica gel flash column chromatography (2 – 7.5% EtOAc in Petrol) to give acridine **PC5** as an off-white solid (1.67 mg, 5.6 mmol, 56%).

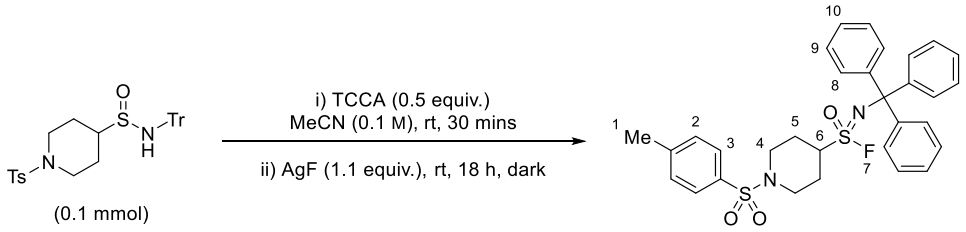
R_f = 0.25 (10% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.77 (ddd, *J* = 8.7, 6.5, 1.5 Hz, 2H, Ar*H*), 7.55 – 7.48 (m, 2H, Ar*H*), 7.40 (ddd, *J* = 8.7, 6.5, 1.1 Hz, 2H, Ar*H*), 7.09 (s, 2H, Ar*H*), 2.45 (s, 3H, C(1)H_3), 1.71 (s, 6H, 2×C(2)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.2, 138.2, 136.8, 130.3, 130.0, 128.5, 126.2, 126.0,

125.2, 21.4, 20.1; **LRMS** (ESI^+, *m/z*) 298.2 $[M+H]^+$; **HRMS** (ESI^+, *m/z*): Calc. for $C_{22}H_{20}N$ $[M+H]^+$ 298.1590, Found: 298.1586.

Data is consistent with the literature.[238]

8.3.4 Sulfinamide Derivatisation

1-Tosyl-*N*-tritylpiperidine-4-sulfonimidoyl fluoride (31)

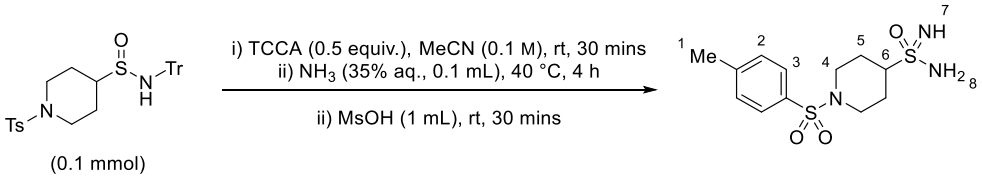


1-Tosyl-*N*-tritylpiperidine-4-sulfinamide **25n** (54.5 mg, 0.1 mmol, 1.0 equiv.) was weighed into an oven-dried 10 mL reaction vial, sealed, evacuated and back-filled with N_2 (×3). Dry MeCN (1.0 mL) was then added. Trichloroisocyanuric acid (11.6 mg, 0.05 mmol, 0.5 equiv.) was added under a cone of nitrogen, the vial re-sealed and the reaction was stirred at rt for 30 mins. AgF (14.0 mg, 0.11 mmol, 1.1 equiv.) was then added under a cone of nitrogen, the vial re-sealed and the reaction was stirred at rt for 18 h (protected from light using aluminium foil). After completion of the reaction (determined by TLC), the reaction mixture was concentrated in vacuo, and the crude reaction mixture was purified by silica gel flash column chromatography (60 – 70% CH_2Cl_2 in Petrol) to afford sulfonimidoyl fluoride **31** as a white solid (36.5 mg, 0.07 mmol, 65%).

R_f = 0.26 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.25 (dddd, *J* = 14.2, 8.6, 7.0, 5.0 Hz, 17H, Ar*H*), 3.94 (d, *J* = 12.3 Hz, 2H, 2×C(4)*H*H), 3.17 (tt, *J* = 11.9, 3.4 Hz, 1H, C(6)*H*), 2.38 (s, 3H, C(1)H_3), 2.37 – 2.27 (m, 4H, 2×C(4)H*H* and 2×C(5)*H*H), 2.21 – 2.01 (m, 2H, 2×C(5)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 146.2 (d, *J* = 4.3 Hz), 144.2, 133.0, 130.0, 128.8, 127.9, 127.8, 127.2, 73.6 (d, *J* = 4.4 Hz), 61.8 (d, *J* = 21.1 Hz), 45.1, 26.8, 26.4, 21.7 *(note: for piperidine ring, 4 peaks were found instead of 3 due to the loss of symmetry caused by chiral sulfur atom)*; **^{19}F NMR** (377 MHz, $CDCl_3$) δ 68.24; **HRMS** (ESI, *m/z*): Calc. for $C_{31}H_{31}FN_2O_3S_2Na$

$[M+Na]^+$ = 585.1655, Found = 585.1644; **IR** (thin film, ν_{max}/cm^{-1}) 2958, 2928, 2856, 1449, 1344 1169; **Melting point** = 216 – 218 °C.

1-Tosylpiperidine-4-sulfonimidamide (32b)



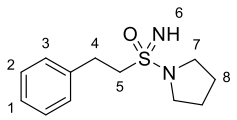
1-Tosyl-*N*-tritylpiperidine-4-sulfinamide **25n** (54.5 mg, 0.1 mmol, 1.0 equiv.) was weighed into an oven-dried 10 mL reaction vial, sealed, evacuated and back-filled with N_2 (×3). Dry MeCN (1.0 mL) was then added. Trichloroisocyanuric acid (0.05 mmol, 11.6 mg) was added under a cone of N_2, the vial re-sealed and the reaction was stirred at rt for 30 mins. 35% aqueous NH_3 (0.1 mL) was then added and the reaction was stirred at 40 °C for 4 h. The reaction was cooled to rt and methanesulfonic acid (1.0 mL) was added dropwise and the mixture was stirred at rt for 30 mins. After completion of the reaction (determined by TLC), the reaction mixture was then neutralized with saturated aq. $NaHCO_3$ and extracted with EtOAc (4×20 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude reaction mixture was purified by silica gel flash column chromatography (0 – 2% MeOH in EtOAc) to afford sulfonimidamide **32b** as a white solid (22.2 mg, 0.07 mmol, 70%).

R_f = 0.16 (2% MeOH in EtOAc); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.62 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.44 (d, *J* = 8.0 Hz, 2H, Ar*H*), 5.51 (br. s, 3H, N(7)*H* and N(8)H_2), 3.73 (d, *J* = 11.7 Hz, 2H, 2×C(4)*H*H), 2.77 (tt, *J* = 11.8, 3.7 Hz, 1H, C(6)*H*), 2.40 (s, 3H, C(1)H_3), 2.25 (td, *J* = 12.3, 2.3 Hz, 2H, 2×C(4)H*H*), 2.12 – 2.05 (m, 2H, 2×C(5)*H*H), 1.64 (qd, *J* = 12.7, 4.2 Hz, 2H, 2×C(5)H*H*); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 143.6, 132.8, 129.9, 127.4, 59.0, 44.9, 25.9, 21.0; **LRMS** (ESI, *m/z*) 318.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for

$C_{12}H_{20}N_3O_3S_2$ $[M+H]^+$ = 318.0941, Found = 318.0937; **IR** (thin film, ν_{max}/cm^{-1}) 3296, 3042, 2942, 1333, 1249, 1159; **Melting point** = 157 – 159 °C.

8.3.5 Sulfonimidamide Synthesis from *N*-Alkoxy sulfinamides

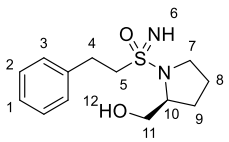
1-(2-Phenylethylsulfonimidoyl)pyrrolidine (33a)



Prepared according to **General Procedure H** using hydrocinnamic acid (45.1 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol, 1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). Pyrrolidine (32.8 µL, 0.4 mmol, 2.0 equiv.) in toluene (2.0 mL) was used in the second step. Purification by silica gel flash column chromatography (90 – 100% EtOAc in Petrol) afforded sulfonimidamide **33a** as a colourless oil (34.2 mg, 0.14 mmol, 72%).

R_f = 0.27 (90% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 2H, Ar*H*), 7.25 – 7.19 (m, 3H, Ar*H*), 3.37 – 3.26 (m, 5H, C(5)*H*H and 2×C(8)H_2), 3.22 – 3.03 (m, 3H, C(4)H_2 & C(5)H*H*), 2.26 (br. s, 1H, N(6)*H*), 1.97 – 1.81 (m, 4H, 2×C(8)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.7, 128.9, 128.6, 126.9, 50.8, 48.5, 30.1, 26.1; **LRMS** (ESI, *m/z*) 239.0 $[M+H]^+$, 261.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{12}H_{19}N_2OS$ $[M+H]^+$ = 239.1213, Found = 239.1213; **IR** (thin film, ν_{max}/cm^{-1}) 3273, 2973, 2875, 1497, 1455, 1240.

((2*S*)-1-(2-Phenylethylsulfonimidoyl)pyrrolidin-2-yl)methanol (33c)

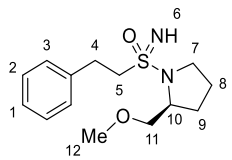


Prepared according to **General Procedure H** using hydrocinnamic acid (45.1 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol,

1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). L-prolinol (39.1 µL, 0.4 mmol, 2.0 equiv.) in toluene (2.0 mL) was used in the second step. Purification by silica gel flash column chromatography (100% EtOAc) afforded sulfonimidamide **33c** as a pale-yellow gum (19.8 mg, 0.07 mmol, 37%, 11:10 inseparable mixture of diastereomers).

R_f = 0.21 (100% EtOAc); **^{1}H NMR** (600 MHz, $CDCl_3$, asterisk denotes signals arising from minor diastereomer) δ 7.35 – 7.30 (m, 2H, Ar*H*), 7.27 – 7.22 (m, 3H, Ar*H*), 3.99 – 3.92 (m, 0.55H, C(10)*H*), 3.90 – 3.80 (m, 0.5H, C(10)*H*)*, 3.66 – 3.30 (m, 5H, C(5)*H*H, C(7)H_2 and C(11)H_2), 3.28 – 3.14 (m, 3H, C(4)H_2 and C(5)H*H*), 2.62 (app. br. s, 2H, N(6)*H* and O(12)*H*), 2.07 – 1.98 (m, 1H, C(9)*H*H), 1.98 – 1.88 (m, 1H, C(8)*H*H), 1.86 – 1.77 (m, 1H, C(8)H*H*), 1.78 – 1.66 (m, 1H, C(9)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$, 11:10 mix of diastereomers, asterisk denotes signals arising from minor diastereomer) δ 138.3, 138.2*, 129.1*, 129.0, 128.67, 128.65*, 127.14*, 127.09, 66.7, 66.3*, 62.4*, 62.0, 51.9, 51.5*, 50.2, 50.1*, 30.04, 30.01*, 29.54*, 29.50, 25.3, 24.8*; **LRMS** (ESI, *m/z*) 269.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{13}H_{21}N_2O_2S$ $[M+H]^+$ = 269.1318, Found = 269.1319; **IR** (thin film, ν_{max}/cm^{-1}) 3299, 2935. 2873, 1497, 1455, 1237.

(2*S*)-2-(Methoxymethyl)-1-(2-phenylethylsulfonimidoyl)pyrrolidine (33d)

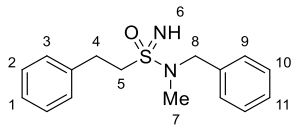


Prepared according to **General Procedure H** using hydrocinnamic acid (45.1 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol, 1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). *O*-Methyl-L-prolinol (49.4 µL, 0.4 mmol, 2.0 equiv.) in toluene (2.0 mL) was used in the

second step. Purification by silica gel flash column chromatography (70 – 80% EtOAc in Petrol) afforded sulfonimidamide **33d** as a colourless oil (29.9 mg, 0.11 mmol, 53%, 3:2 inseparable mixture of diastereomers).

R_f = 0.24 (70% EtOAc in Petrol); **^{1}H NMR** (600 MHz, $CDCl_3$, asterisk denotes signals arising from minor diastereomer) δ 7.34 – 7.29 (m, 2H, Ar*H*), 7.26 – 7.18 (m, 3H, Ar*H*), 3.97 – 3.92 (m, 0.6H, C(10)*H*), 3.92 – 3.87 (m, 0.4H, C(10)*H*)*, 3.54 – 3.00 (m, 11H, C(4)H_2, C(5)H_2, C(7)H_2, C(11)H_2 and C(12)H_3), 2.70 – 2.43 (br. m, 1H, N(6)*H*), 1.98 – 1.89 (m, 2.4H, C(8)H_2 and C(9)H_2), 1.90 – 1.81 (m, 1.6H, C(8)H_2 and C(9)H_2)*; **^{13}C NMR** (151 MHz, $CDCl_3$, 3:2 mix of diastereomers, asterisk denotes signals arising from minor diastereomer) δ 138.8, 138.7*, 128.9, 128.6, 126.88*, 126.87, 75.62, 75.59*, 59.17*, 59.16, 59.1*, 58.9, 51.5, 51.3*, 49.8*, 49.5, 30.4, 30.1*, 29.2*, 29.0, 24.9, 24.8* *(2 carbon signals are unresolved from the corresponding signals in the other diastereomer)*; **LRMS** (ESI, *m/z*) 283.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{23}N_2O_2S$ $[M+H]^+$ = 283.1475, Found = 283.1474; **IR** (thin film, ν_{max}/cm^{-1}) 3271, 2927, 2875, 1455, 1244, 1109.

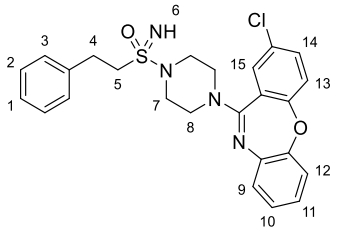
***N*-Benzyl-*N*-methyl-2-phenylethane-1-sulfonimidamide (33e)**



Prepared according to **General Procedure H** using hydrocinnamic acid (45.1 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol, 1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). *N*-Methylbenzylamine (258 µL, 2.0 mmol, 10 equiv.) in toluene (2.0 mL) was used in the second step. Purification by silica gel flash column chromatography (30 – 40% EtOAc in Petrol) afforded sulfonimidamide **33e** as a colourless oil (42.8 mg, 0.15 mmol, 74%).

R_f = 0.25 (40% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.19 (m, 7H, Ar*H*), 7.22 – 7.13 (m, 3H, Ar*H*), 4.33 (d, *J* = 14.4 Hz, 1H, C(8)*H*H), 4.27 (d, *J* = 14.4 Hz, 1H, C(8)H*H*), 3.34 – 3.23 (m, 1H, C(4)*H*H), 3.19 – 3.02 (m, 3H, C(4)H*H* and C(5)H_2), 2.74 (s, 3H, C(7)H_3), 2.33 (s, 1H, N(6)*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.5, 136.7, 129.0, 128.9, 128.6, 128.2, 128.0, 127.0, 54.8, 51.8, 35.4, 30.1; **LRMS** (ESI, *m/z*) 289.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{16}H_{21}N_2OS$ $[M+H]^+$ = 289.1368, Found = 289.1368; **IR** (thin film, ν_{max}/cm^{-1}) 3316, 3062, 3028, 1496, 1455, 1243.

2-Chloro-11-(4-(2-phenylethylsulfonimidoyl)piperazin-1-yl)dibenzo[*b*,*f*][1,4]oxazepine (33f)

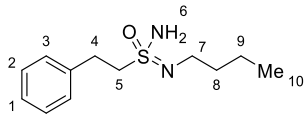


Prepared according to **General Procedure H** using hydrocinnamic acid (45.1 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol, 1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). Amoxapine (126 mg, 0.4 mmol, 2.0 equiv.) in toluene (2.0 mL) was used in the second step. Purification by silica gel flash column chromatography (50 – 60% EtOAc in Petrol) afforded sulfonimidamide **33f** as a colourless oil (41.0 mg, 0.09 mmol, 43%).

R_f = 0.28 (50% EtOAc in Petrol); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 (dd, J = 8.7, 2.5 Hz, 1H, Ar*H*), 7.34 – 7.29 (m, 2H, Ar*H*), 7.28 (d, *J* = 2.5 Hz, 1H, Ar*H*), 7.26 – 7.22 (m, 3H, Ar*H*), 7.20 (d, *J* = 8.7 Hz, 1H, Ar*H*), 7.18 – 7.15 (m, 1H, Ar*H*), 7.12 – 7.08 (m, 2H, Ar*H*), 7.05 – 7.00 (m, 1H, Ar*H*), 3.61 (app. br. s, 4H, 2×C(7)H_2), 3.40 (app. br. s, 4H, 2×C(8)H_2), 3.29 (td, *J* = 11.9, 5.0 Hz, 1H, C(5)*H*H), 3.25 – 3.15 (m, 2H, C(4)H_2), 3.08 (td, *J* = 11.7,

4.9 Hz, 1H, C(5)H*H*), 2.28 (br. s, 1H, N(6)*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.5, 158.6, 151.9, 139.8, 138.4, 133.0, 130.6, 129.0, 128.9, 128.6, 127.3, 127.1, 126.0, 125.2, 124.9, 123.0, 120.3, 50.6, 47.9, 46.4, 29.8; **LRMS** (ESI, *m/z*) 481.1, 483.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{25}H_{26}{}^{35}ClN_4O_2S$ $[M+H]^+$ 481.1460, Found: 481.1460, Calc. for $C_{25}H_{26}{}^{37}ClN_4O_2S$ $[M+H]^+$ = 483.1432, Found = 483.1429; **IR** (thin film, ν_{max}/cm^{-1}) 3331, 2981, 2853, 1602, 1588, 1243.

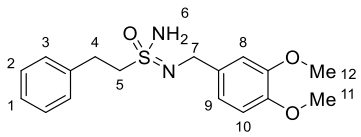
***N′*-Butyl-2-phenylethane-1-sulfonimidamide (33b)**



Prepared according to **General Procedure H** using hydrocinnamic acid (45.1 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol, 1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). Butylamine (198 µL, 2.0 mmol, 10 equiv.) in toluene (2.0 mL) was used in the second step. Purification by silica gel flash column chromatography (50% EtOAc in Petrol) afforded sulfonimidamide **33b** as a colourless oil (33.5 mg, 0.14 mmol, 70%).

R_f = 0.29 (50% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 2H, Ar*H*), 7.28 – 7.22 (m, 3H, Ar*H*), 3.45 – 3.24 (m, 2H, C(5)H_2), 3.21 – 3.10 (m, 2H, C(4)H_2), 3.02 – 2.74 (m, 4H, N(6)H_2 and C(7)H_2), 1.46 – 1.23 (m, 4H, C(8)H_2 and C(9)H_2), 0.90 (t, *J* = 7.2 Hz, 3H, C(10)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.3, 129.0, 128.6, 127.1, 54.2, 43.7, 32.5, 30.6, 20.0, 13.8; **LRMS** (ESI, *m/z*) 241.2 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{12}H_{21}N_2OS$ $[M+H]^+$ = 241.1369, Found = 241.1370; **IR** (thin film, ν_{max}/cm^{-1}) 3264, 2958, 2933 2871, 1455, 1237.

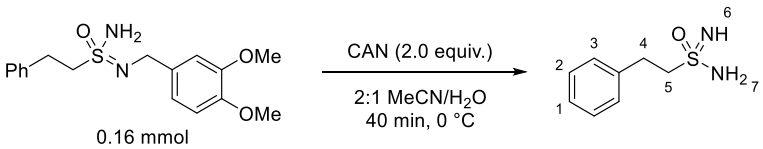
N'-(3,4-Dimethoxybenzyl)-2-phenylethane-1-sulfonimidamide (33g)



Prepared according to **General Procedure H** using hydrocinnamic acid (45.1 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol, 1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). 3,4-Dimethoxybenzylamine (302 µL, 2.0 mmol, 10 equiv.) in toluene (2.0 mL) was used in the second step. Purification by silica gel flash column chromatography (70 – 80% EtOAc in Petrol) afforded sulfonimidamide **33g** as a colourless oil (52.9 mg, 0.16 mmol, 79%).

R_f = 0.28 (70% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 2H, Ar*H*), 7.25 – 7.19 (m, 1H, Ar*H*), 7.14 – 7.09 (m, 2H, Ar*H*), 6.82 – 6.78 (m, 3H, Ar*H*), 4.13 (d, *J* = 14.1 Hz, 1H, C(7)*H*H), 4.09 (d, *J* = 14.1 Hz, 1H, C(7)H*H*), 3.85 (s, 6H, C(11/12)H_3 and C(12/11)H_3), 3.46 (s, 2H, N(6)H_2), 3.30 – 3.23 (m, 2H, C(5)H_2), 3.11 – 3.04 (m, 2H, C(4)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.3, 148.9, 138.1, 130.1, 128.9, 128.5, 127.0, 120.3, 111.4, 111.3, 56.1, 54.9, 47.8, 30.5; **LRMS** (ESI, *m/z*): 335.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{23}N_2O_3S$ $[M+H]^+$ = 335.1424, Found = 335.1425; **IR** (thin film, ν_{max}/cm^{-1}) 3277, 2936, 2836, 1515, 1262, 1239.

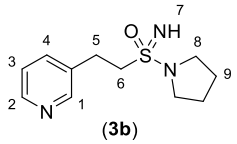
2-Phenylethane-1-sulfonimidamide (33j)



To a solution of *N'*-(3,4-Dimethoxybenzyl)-2-phenylethane-1-sulfonimidamide **33g** (52.9 mg, 0.158 mmol, 1.0 equiv.) in MeCN (1.6 mL) and water (800 µL) cooled to 0 °C was added ceric ammonium nitrate (173 mg, 0.316 mmol, 2.0 equiv.). The reaction was stirred at the same temperature for 1h. Solvent was removed in vacuo, and purification of the crude residue by silica gel flash column chromatography (80 – 100% EtOAc in Petrol, then 0 – 5% MeOH in EtOAc) afforded sulfonimidamide **33j** as an off-white solid (26.2 mg, 0.14 mmol, 90%).

R_f = 0.17 (100% EtOAc); **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.34 – 7.25 (m, 4H, Ar*H*), 7.25 – 7.20 (m, 1H, Ar*H*), 3.41 – 3.35 (m, 2H, C(5)H_2), 3.17 – 3.11 (m, 2H, C(4)H_2) *(note: N(6)H and N(7)H_2 not observed due to H/D exchange)*; **^{13}C NMR** (101 MHz, Methanol-d_4) δ 139.9, 129.8, 129.5, 127.7, 59.0, 31.6; **LRMS** (ESI, *m/z*) 185.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_8H_{13}N_2OS$ $[M+H]^+$ = 185.0743, Found = 185.0742; **IR** (thin film, ν_{max}/cm^{-1}) 3510, 3279. 2923, 1637, 1254, 1034; **Melting point** = 54 °C (decomp.).

3-(2-(Pyrrolidine-1-sulfonimidoyl)ethyl)pyridine (33k)

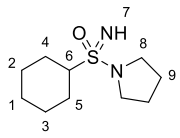


(**3b**)

Prepared according to **General Procedure H** using 3-pyridinepropanoic acid (45.3 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol, 1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). Pyrrolidine (32.8 µL, 0.4 mmol, 2.0 equiv.) in toluene (2.0 mL) was used in the second step. Purification by silica gel flash column chromatography (5 – 10% MeOH in EtOAc) afforded sulfonimidamide **33k** as a pale-yellow oil (16.1 mg, 0.07 mmol, 34%).

R_f = 0.14 (10% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.57 – 8.44 (m, 2H, Ar*H*), 7.63 – 7.53 (m, 1H, Ar*H*), 7.26 – 7.21 (m, 1H, Ar*H*), 3.37 – 3.24 (m, 5H, C(6)*H*H and 2×C(8)H_2), 3.25 – 3.16 (m, 2H, C(4)H_2), 3.15 – 3.05 (m, 1H, C(6)H*H*), 2.32 (br. s, 1H, N(7)*H*), 1.96 – 1.81 (m, 4H, 2×C(9)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.9, 148.4, 136.2, 134.3, 123.7, 50.2, 48.4, 27.5, 26.1; **LRMS** (ESI, *m/z*) 240.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{11}H_{18}N_3OS$ $[M+H]^+$ = 240.1166, Found = 240.1165; **IR** (thin film, ν_{max}/cm^{-1}) 3276, 2955, 2878, 1480, 1426, 1239.

1-(Cyclohexanesulfonimidoyl)pyrrolidine (33l)

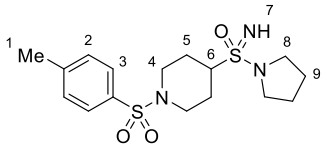


Prepared according to **General Procedure H** using cyclohexanecarboxylic acid (38.5 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol, 1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). Pyrrolidine (32.8 µL, 0.4 mmol, 2.0 equiv.) in toluene (2.0 mL) was used in the second step. Purification by silica gel flash column chromatography (100% EtOAc) afforded sulfonimidamide **33l** as a colourless oil (33.7 mg, 0.16 mmol, 78%).

R_f = 0.27 (100% EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.55 – 3.27 (m, 5H, C(6)*H* and 2×C(8)H_2), 2.29 (br. d, *J* = 12.2 Hz, 1H, C(4/5)*H*H), 2.11 (br. d, *J* = 12.2 Hz, 1H, C(5/4)*H*H), 2.03 – 1.81 (m, 6H, C(2/3)*H*H, N(7)*H* and 2×C(9)H_2), 1.76 – 1.53 (m, 3H, C(3/2)*H*H, C(4)H*H* and C(5)H*H*), 1.43 – 1.10 (m, 4H, C(1)H_2, C(2)H*H* and C(3)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 61.8, 48.5, 27.4, 26.6, 26.1, 25.53, 25.51, 25.3 *(note: for cyclohexane ring, 6 peaks were found instead of 4 due to the loss of symmetry caused by chiral sulfur atom)*; **LRMS** (ESI, *m/z*) 217.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for

$C_{10}H_{21}N_2OS$ $[M+H]^+$ = 217.1369, Found = 217.1370; **IR** (thin film, ν_{max}/cm^{-1}) 3262, 2934, 2857, 1452, 1236, 1009.

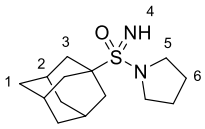
4-(Pyrrolidine-1-sulfonimidoyl)-1-tosylpiperidine (33m)



Prepared according to **General Procedure H** using 1-tosylpiperidine-4-carboxylic acid (85.0 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol, 1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). Pyrrolidine (32.8 µL, 0.4 mmol, 2.0 equiv.) in toluene (2.0 mL) was used in the second step. Purification by silica gel flash column chromatography (100% EtOAc) afforded sulfonimidamide **33m** as a pale-yellow solid (60.0 mg, 0.16 mmol, 81%).

R_f = 0.17 (100% EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 – 7.58 (m, 2H, Ar*H*), 7.31 (d, *J* = 7.9 Hz, 2H, Ar*H*), 3.95 – 3.84 (m, 2H, 2×C(4)*H*H), 3.30 (tt, *J* = 6.7, 3.4 Hz, 4H, 2×C(8)H_2), 2.91 (tt, *J* = 12.0, 3.7 Hz, 1H, C(6)*H*), 2.42 (s, 3H, C(1)H_3), 2.35 (br. s, 1H, N(7)*H*), 2.27 (td, *J* = 12.2, 1.9 Hz, 2H, 2×C(4)H*H*), 2.22 – 2.08 (m, 2H, 2×C(5)*H*H), 2.00 – 1.80 (m, 6H, 2×C(5)H*H* and 2×C(9)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.9, 133.2, 129.9, 127.7, 59.5, 48.8, 45.41, 45.37, 26.3, 26.2, 26.1, 21.6 *(note: for piperidine ring, 5 peaks were found instead of 3 due to the loss of symmetry caused by chiral sulfur atom)*; **LRMS** (ESI, *m/z*) 372.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{16}H_{26}N_3O_3S_2$ $[M+H]^+$ = 372.1410, Found = 372.1410; **IR** (thin film, ν_{max}/cm^{-1}) 3299, 2935, 2849, 1333, 1243, 1163; **Melting point** = 124 – 126 °C.;

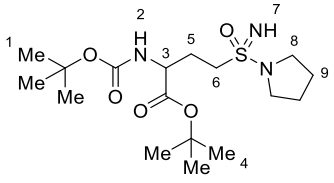
1-((3*s*,5*s*,7*s*)-Adamantane-1-sulfonimidoyl)pyrrolidine (33n)



Prepared according to **General Procedure H** using 1-adamantanecarboxylic acid (54.1 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol, 1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). Pyrrolidine (32.8 µL, 0.4 mmol, 2.0 equiv.) in toluene (2.0 mL) was used in the second step. Purification by silica gel flash column chromatography (70 – 80% EtOAc in Petrol) afforded sulfonimidamide **33n** as a white solid (42.1 mg, 0.16 mmol, 79%).

R_f = 0.27 (70% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.42 (tq, *J* = 7.4, 3.3 Hz, 4H, 2×C(5)H_2), 2.56 (br. s, 1H, N(4)*H*), 2.13 (br. s, 3H, 3×C(2)*H*), 2.08 (br. app. d, *J* = 2.8 Hz, 6H, 3×C(3)H_2), 1.94 – 1.83 (m, 4H, 2×C(6)H_2), 1.69 (br. s, 6H, 3×C(1)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 63.7, 49.9, 36.7, 36.1, 28.7, 26.3; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{25}N_2OS$ $[M+H]^+$ = 269.1682, Found = 269.1684; **IR** (thin film, ν_{max}/cm^{-1}) 3275, 2908. 2851, 1454, 1231, 999; **Melting point** = 82 – 84 °C

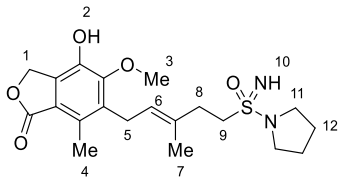
***tert*-Butyl 2-((*tert*-butoxycarbonyl)amino)-4-(pyrrolidine-1-sulfonimidoyl)butanoate (33o)**



Prepared according to **General Procedure H** using Boc-DL-Glu-O*t*-Bu (54.1 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol, 1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). Pyrrolidine (32.8 µL, 0.4 mmol, 2.0 equiv.) in toluene (2.0 mL) was used in the second step. Purification by silica gel flash column chromatography (70 – 80% EtOAc in Petrol) afforded sulfonimidamide **33o** as a colourless oil (50.8 mg, 0.13 mmol, 65%, 1:1 inseparable mixture of diastereomers).

R_f = 0.25 (80% EtOAc in Petrol); **^{1}H NMR** (600 MHz, Acetone-d_6, 1:1 mix of diastereomers) δ 4.22 – 4.02 (m, 1H, C(3)*H*), 3.35 – 3.23 (m, 4H, 2×C(8)H_2), 3.14 (ddd, J = 13.6, 10.4, 5.5 Hz, 0.5H, C(6)*H*H, diastereomer A), 3.12 – 2.99 (m, 1H, C(6)H_2, diastereomer B), 2.96 (ddd, J = 14.1, 10.5, 5.0 Hz, 0.5H, C(6)H*H*, diastereomer A), 2.37 – 2.25 (m, 1H, C(6)*H*H), 2.20 – 2.09 (m, 1H, C(6)H*H*), 2.09 – 2.06 (m, 2H, N(2)*H* and N(7)*H*), 1.95 – 1.82 (m, 4H, 2×C(9)H_2), 1.46 (s, 9H, 3×C(1/4)H_3), 1.41 (s, 9H, 3×C(4/1)H_3); **^{13}C NMR** (151 MHz, Acetone-d_6, 1:1 mix of diastereomers) δ 171.8, 156.5, 81.8, 79.3, 54.24, 54.21, 48.9, 46.3, 46.2, 28.6, 28.2, 27.12, 27.09, 26.5 *(8 carbon signals are unresolved from the corresponding signals in the other diastereomer)*; **LRMS** (ESI, *m/z*) 392.2 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{33}N_3O_5SNa$ $[M+Na]^+$ = 392.2214, Found = 392.2212; **IR** (thin film, ν_{max}/cm^{-1}) 3310, 2976, 2933, 1710, 1518, 1367.

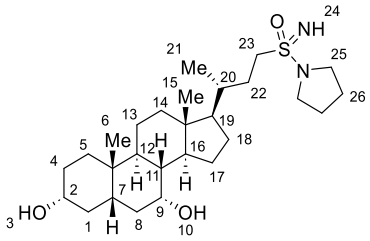
(*E*)-4-Hydroxy-5-methoxy-7-methyl-6-(3-methyl-5-(pyrrolidine-1-sulfonimidoyl)pent-2-en-1-yl)isobenzofuran-1(3*H*)-one (33p)



Prepared according to **General Procedure H** using mycophenolic acid (96.1 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol, 1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). Pyrrolidine (32.8 µL, 0.4 mmol, 2.0 equiv.) in toluene (2.0 mL) was used in the second step. Purification by silica gel flash column chromatography (0 – 10% MeOH in EtOAc) afforded sulfonimidamide **33p** as a colourless gum (42.6 mg, 0.1 mmol, 52%).

R_f = 0.18 (100% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.33 – 5.25 (m, 1H, C(6)*H*), 5.18 (s, 2H, C(1)H_2), 3.75 (s, 3H, C(3)H_3), 3.37 (d, *J* = 7.0 Hz, 2H, C(5)H_5), 3.34 – 3.23 (m, 4H, 2×C(11)H_2), 3.09 (ddd, *J* = 13.2, 11.3, 5.7 Hz, 1H, C(9)*H*H), 2.95 (ddd, *J* = 13.3, 11.0, 5.7 Hz, 1H, C(9)H*H*), 2.49 (tq, *J* = 14.3, 7.1 Hz, 2H, C(8)H_2), 2.13 (s, 3H, C(4)H_3), 1.94 – 1.85 (m, 4H, 2×C(12)H_2), 1.81 (s, 3H, C(7)H_3) *(O(2)H signal not observed)*; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.0, 163.8, 153.7, 144.3, 132.6, 124.0, 121.9, 116.9, 106.5, 70.2, 61.1, 48.4, 48.3, 33.4, 26.0, 22.7, 16.4, 11.7; **LRMS** (ESI, *m/z*) 409.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{20}H_{29}N_2O_5S$ $[M+H]^+$ = 409.1792, Found = 409.1790; **IR** (thin film, ν_{max}/cm^{-1}) 3423, 2943, 1734, 1620, 1456, 1099.

(3*R*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-Dimethyl-17-((2*R*)-4-(pyrrolidine-1-sulfonimidoyl)butan-2-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7-diol (33q)



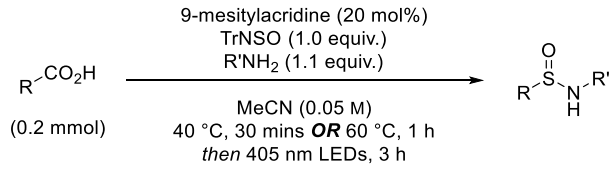
Prepared according to **General Procedure H** using chenodeoxycholic acid (118 mg, 0.3 mmol, 1.5 equiv.), *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine (27.0 mg, 0.2 mmol,

1.0 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL). Pyrrolidine (32.8 µL, 0.4 mmol, 2.0 equiv.) in toluene (2.0 mL) was used in the second step. Purification by silica gel flash column chromatography (5 – 10% MeOH in EtOAc) afforded sulfonimidamide **33q** as a colourless gum (28.0 mg, 0.06 mmol, 29%, 1:1 inseparable mixture of diastereomers).

R_f = 0.20 (5% MeOH in EtOAc); **^{1}H NMR** (600 MHz, $CDCl_3$, 1:1 mix of diastereomers) δ 3.89 – 3.80 (m, 1H, C(9)*H*), 3.48 – 3.42 (m, 1H, C(2)*H*), 3.39 – 3.28 (m, 4H, 2×C(25)H_2), 3.13 (td, *J* = 12.8, 4.7 Hz, 0.5H, C(23)*H*H, diastereomer A), 3.05 – 2.94 (m, 1H, C(23)H_2, diastereomer B), 2.88 – 2.80 (m, 0.5H, C(23)H*H* diastereomer A), 2.20 (q, *J* = 13.0 Hz, 1H, C(1)*H*H), 2.05 – 1.87 (m, 9H, C(8)*H*H, C(14)*H*H, C(17)*H*H, C(22)*H*H, N(24)*H* and 2×C(26)H_2), 1.86 – 1.79 (m, 2H, C(5)*H*H and C(11)*H*), 1.75 – 1.22 (m, 15H, C(1)H*H*, O(3)*H*, C(4)H_2, C(7)*H*, C(8)H*H*, O(10)*H*, C(12)*H*, C(13)H_2, C(16)*H*, C(17)H*H* C(18)*H*H, C(20)*H* and C(22)H*H*), 1.21 – 1.09 (m, 3H, C(14)*H*H, C(18)H*H* and C(19)*H*), 1.01 – 0.92 (m, 4H, C(5)H*H* and C(21)H_3), 0.90 (s, 3H, C(6)H_3), 0.66 (s, 3H, C(15)H_3); **^{13}C NMR** (151 MHz, $CDCl_3$, 1:1 mix of diastereomers) δ 72.1, 68.6, 55.7, 55.60, 50.59, 50.57, 48.49, 48.48, 47.0, 42.9, 41.6, 40.0, 39.7, 39.6, 39.54, 35.46, 35.19, 35.18, 35.1, 34.83, 34.81, 33.0, 30.8, 29.5, 29.4, 28.31, 28.29, 26.1, 23.8, 22.9, 20.7, 18.7, 18.6, 11.9 *(16 carbon signals are unresolved from the corresponding signals in the other diastereomer)*; **LRMS** (ESI, *m/z*) 481.3 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{27}H_{49}N_2O_3S$ $[M+H]^+$ = 481.3458, Found = 481.3458; **IR** (thin film, ν_{max}/cm^{-1}) 3365, 2930, 2866, 1449, 1239, 1110.

8.4 Experimental for Chapter 4

8.4.1 General Procedures



General Procedure I: Carboxylic acid (0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine (11.9 mg, 0.04 mmol, 20 mol%) and primary amine (if solid) (0.22 mmol, 1.1 equiv.) were weighed into an oven-dried 10 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Dry MeCN (4.0 mL), followed by primary amine (if liquid) (0.22 mmol, 1.1 equiv.) was then added. The reaction was heated to 40 °C and stirred for 30 mins (for α-primary amines, **General Procedure I-1**), or 60 °C and stirred for 1.0 hour (for α-secondary amines, **General Procedure I-2**) in a pre-heated aluminium heating block. The reaction vial was then removed from the heating block, and stirred under 405 nm LED irradiation with fan cooling for 3 h (See **Figure S3** for experimental setup). Upon completion (determined by TLC), the reaction mixture was concentrated in vacuo and purified using silica gel flash column chromatography.

Notes:

1. The corresponding primary amine hydrochloride salts can also be used, with addition of triethylamine (1.1 equiv.) after addition of reaction solvent. No further modifications are needed.
2. In some cases, precipitate formed upon addition of the primary amine. This often solubilised during the pre-heating step. In some cases, precipitate was still present following the heating step, or precipitated out as the reaction cooled in the photoreactor. The reaction in these cases would often proceed smoothly in the

indicated reaction setup (**Figure S3**), and the reaction slowly became homogenous during the 3 h, with no requirement for further modification.

3. In rare cases where precipitate formation impeded reactivity, which was usually indicated by precipitate formation preventing efficient stirring, modification of the solvent system, usually to chlorinated solvents such as CH_2Cl_2 or DCE, improved solubility and thus enabled the reactions to proceed smoothly.
4. Individual variations from the general procedure are noted for each example.

8.4.2 Photochemical Reaction Setup

405 nm LEDs, where specified, comprised a HepatoChem EvoluChem™ 405PF 18 W 405 nm LED spotlight. 0.20 mmol scale reactions were carried out in 2-5 mL microwave reaction vials, fitted with an aluminium seal with a blue PTFE/white silicone setum, mounted in a EvoluChem™ PhotoRedOx Box device. 5.0 mmol scale reactions were carried out in a round bottom flask. Fan cooling was used during reactions to give an internal temperature of ~30 °C.

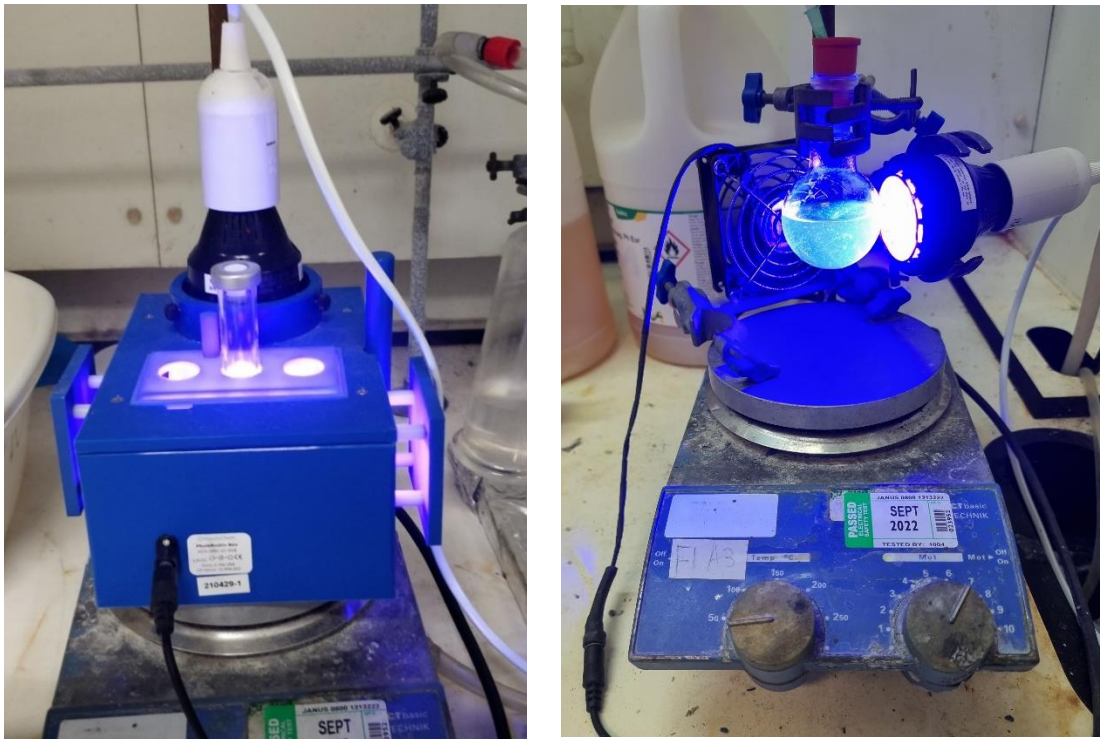
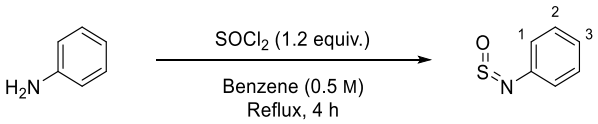


Figure S3. Left: Photobox used for 0.20 mmol scale reactions. Right: Reaction setup for 5.0 mmol scale reactions.

8.4.3 Sulfinylamine Synthesis

***N*-sulfinylaniline (38a)**:

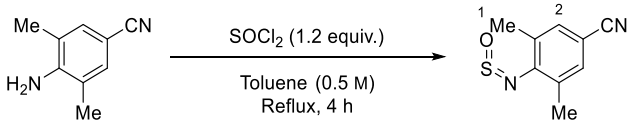


Prepared according to the procedure described by Kresze and co-workers.[72a] An oven-dried two-necked flask equipped with a reflux condenser was sealed with rubber septa, evacuated and backfilled with N_2 (× 3). Aniline (456 µL, 5.0 mmol, 1.0 equiv.) and dry benzene (10 mL) were then added and the reaction was cooled to 0 °C. Thionyl chloride (435 µL, 6.0 mmol, 1.2 equiv.) was then added dropwise with stirring, and the reaction was then warmed to rt. The reaction was then stirred at reflux for 4 h, and then cooled to rt. Solvent was then removed in vacuo to give *N*-sulfinylaniline **38a** as a brown oil (409 mg, 2.95 mmol, 59%). The product was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.80 (m, 2H, Ar*H*), 7.51 – 7.36 (m, 3H, Ar*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.8, 130.7, 129.4, 127.3.

Data is consistent with the literature.[216]

***N*-Sulfinyl-4-cyano-2,6-dimethylaniline (38b)**:

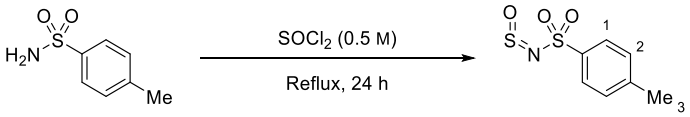


Prepared according to the procedure described by Kresze and co-workers.[72a] 4-Amino-3,5-dimethylbenzonitrile (731 mg, 5.0 mmol, 1.0 equiv.) was weighed into an oven-dried two-necked flask equipped with a reflux condenser. The reaction vessel was then sealed with rubber septa, evacuated and backfilled with N_2 (× 3). Dry toluene (10 mL) was then

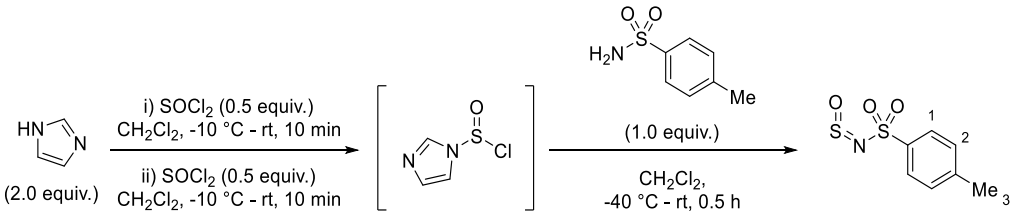
added and the reaction cooled to 0 °C. Thionyl chloride (435 µL, 6.0 mmol, 1.2 equiv.) was then added dropwise with stirring, and the reaction was then warmed to rt. The reaction was then stirred at reflux for 4 h, and then cooled to rt. Solvent was then removed in vacuo to give *N*-sulfinyl-4-cyano-2,6-dimethylaniline **38b** as a yellow solid (932 mg, 4.85 mmol, 97%). The product was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 2H, 2×C(2)*H*), 2.28 (s, 6H, 2×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.8, 131.8, 130.6, 118.6, 110.4, 19.3; **HRMS** (ESI, *m/z*): Calc. for $C_9H_9N_2OS$ $[M+H]^+$ = 193.0432, Found = 193.0430; **IR** (thin film, ν_{max}/cm^{-1}) 2222, 1314, 1286, 1181, 1143, 884; **Melting point** = 107 – 109 °C.

***N*-Sulfinyl-4-toluenesulfonamide (38c)**:



Prepared according to a modified procedure described by Kresze and co-workers.[72b] 4-toluenesulfonamide (1.71 g, 10 mmol, 1.0 equiv.) was weighed into an oven-dried two-necked flask equipped with a reflux condenser. The reaction vessel was then sealed with rubber septa, evacuated and backfilled with N_2 (× 3). Thionyl chloride (20 mL) was then added and the reaction was then stirred at reflux for 24 h, and then cooled to rt. Solvent was then removed in vacuo to give *N*-sulfinyl-4-toluenesulfonamide **38c** as a yellow solid (1.96 g, 62% pure as determined by ^{1}H NMR spectroscopy, 6.1 mmol, 61% yield). The product was used without further purification.



Also prepared according to a procedure described by Yong and co-workers.[78] . Imidazole (1.36 g, 20 mmol, 2.0 equiv.) was weighed into an oven-dried round-bottom flask. The reaction vessel was then sealed with rubber septum, evacuated and backfilled with N_2 (× 3). Dry CH_2Cl_2 (20 mL) was then added and the reaction cooled to -10 °C. Thionyl chloride (362 µL, 5.0 mmol, 0.5 equiv.) was then added dropwise, and the reaction was then warmed to rt and stirred for 10 mins. The resultant suspension was filtered and the filtrate added to an oven-dried round-bottom flask. The headspace was flushed with argon, sealed with a rubber septum, and the reaction cooled to -10 °C. Thionyl chloride (362 µL, 5.0 mmol, 0.5 equiv.) was then added dropwise, and the reaction was then warmed to rt and stirred for 10 mins. 4-Toluenesulfonamide (1.71 g, 10 mmol, 1.0 equiv.) was weighed into a separate oven-dried two-necked flask equipped with a reflux condenser. Dry CH_2Cl_2 (20 mL) was then added and the reaction cooled to -40 °C. The prepared *N*-(chlorosulfinyl)imidazole solution from the previous step was then added dropwise to the 4-toluenesulfonamide suspension, and the resulting solution was stirred at rt for 1 h. The reaction was filtered through a cannula filter to give a ~0.33 M solution of *N*-sulfinyl-4-toluenesulfonamide **38c** in CH_2Cl_2, which was used without further purification.

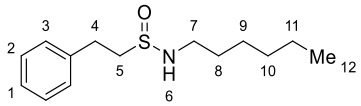
^{1}H NMR (400 MHz, C_6D_6) δ 7.81 (d, *J* = 8.4 Hz, 2H, Ar*H*), 6.66 (d, *J* = 8.0 Hz, 2H, Ar*H*), 1.79 (s, 3H, C(3)H_3).

Data is consistent with the literature.[239]

Note: *N*-sulfinylmesidine was prepared by Mr. Russell Woodger, and full characterisation is included in his part II thesis.[240]

8.4.4 Primary Amine Scope

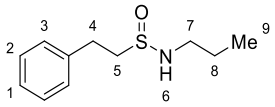
***N*-Hexyl-2-phenylethane-1-sulfinamide (37a)**:



Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and hexylamine (29.1 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (40 – 50% EtOAc in Petrol) afforded sulfinamide **37a** as a pale-yellow oil (36.7 mg, 0.14 mmol, 72%).

R_f = 0.32 (50% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.17 (m, 5H, Ar*H*), 3.72 (s, 1H, N(6)*H*), 3.11 (app. q, *J* = 6.8 Hz, 2H, C(7)H_2), 3.06 – 2.91 (m, 4H, C(4)H_2 and C(5)H_2), 1.60 – 1.50 (m, 2H, C(8)H_2), 1.41 – 1.21 (m, 6H, C(9)H_2, C(10)H_2 and C(11)H_2), 0.95 – 0.81 (m, 3H, C(12)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.1, 128.9, 128.6, 126.8, 56.6, 43.1, 31.6, 30.9, 29.6, 26.6, 22.7, 14.1; **LRMS** (ESI, *m/z*): 254.2 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{24}NOS$ $[M+H]^+$ = 254.1573, Found = 254.1569; **IR** (thin film, ν_{max}/cm^{-1}) 2930, 1455, 1164, 1041, 741, 700.

2-Phenyl-*N*-propylethane-1-sulfinamide (37d):

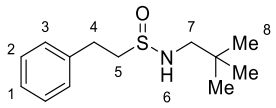


Prepared according to **General Procedure I=1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and propylamine (18.1 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column

chromatography (70 – 80% EtOAc in Petrol) afforded sulfinamide **37d** as a pale-yellow oil (29.3 mg, 0.14 mmol, 69%).

R_f = 0.4 (80% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) 7.35 – 7.18 (m, 5H, Ar*H*), 3.91 (t, *J* = 6.0 Hz, 1H, N(6)*H*), 3.14 – 2.89 (m, 6H, C(4)H_2, C(5)H_2 and C(7)H_2), 1.58 (tq, *J* = 7.4, 7.4 Hz, 2H, C(8)H_2), 0.93 (t, *J* = 7.4 Hz, 3H, C(9)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.1, 128.8, 128.6, 126.7, 56.5, 44.9, 29.6, 24.2, 11.5; **LRMS** (ESI, *m/z*): 212.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{11}H_{18}NOS$ $[M+H]^+$ = 212.1104, Found = 212.1105; **IR** (thin film, ν_{max}/cm^{-1}) 3192, 1497, 1455, 1049, 751, 698.

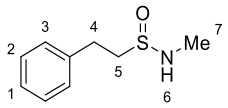
***N*-Neopentyl-2-phenylethane-1-sulfinamide (37e)**:



Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and neopentylamine (25.9 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (50 – 60% EtOAc in Petrol) afforded sulfinamide **37e** as an off-white solid (38.1 mg, 0.16 mmol, 80%).

R_f = 0.17 (50% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2H, Ar*H*), 7.25 – 7.19 (m, 3H, Ar*H*), 3.92 (t, *J* = 7.1 Hz, 1H, N(6)*H*), 3.13 – 2.95 (m, 4H, C(4)H_2 and C(5)H_2), 2.92 (dd, *J* = 12.6, 6.3 Hz, 1H, C(7)*H*H), 2.80 (dd, *J* = 12.6, 8.0 Hz, 1H, C(7)H*H*), 0.90 (s, 9H, 3×C(8)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.1, 128.9, 128.6, 126.8, 56.7, 55.4, 31.8, 29.7, 27.3; **LRMS** (ESI, *m/z*): 262.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{13}H_{21}NOSNa$ $[M+Na]^+$ = 262.1236, Found = 262.1229; **IR** (thin film, ν_{max}/cm^{-1}) 3200, 2955, 2867, 1478, 1051, 698; **Melting point** = 84 – 86 °C.

***N*-Methyl-2-phenylethane-1-sulfinamide (37f)**:



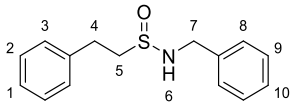
Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and 2.0 M methylamine in THF (0.11 mL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (100% EtOAc in Petrol) afforded sulfinamide **37f** as a pale-yellow oil (20.2 mg, 0.11 mmol, 55%).

Also prepared according to **General Procedure I-1** using 33% methylamine in ethanol (27.5 µL, 0.22 mmol, 1.1 equiv.) to afford sulfinamide **37f** as a pale-yellow oil (23.5 mg, 0.13 mmol, 64%).

Also prepared according to **General Procedure I-1** using methylamine hydrochloride (14.9 mg, 0.22 mmol, 1.1 equiv.) and triethylamine (30.7 µL, 0.22 mmol, 1.1 equiv.) to afford sulfinamide **37f** as a pale-yellow oil (21.4 mg, 0.12 mmol, 58%).

R_f = 0.34 (100% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 2H. Ar*H*), 7.26 – 7.19 (m, 3H, Ar*H*), 3.90 (q, *J* = 5.4 Hz, 1H, N(6)*H*), 3.08 – 2.92 (m, 4H, C(4)H_2 and C(5)H_2), 2.77 (d, *J* = 5.6 Hz, 3H, C(7)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.0, 128.8, 128.6, 126.8, 55.4, 29.6, 27.5; **LRMS** (ESI, *m/z*): 206.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_9H_{14}NOS$ $[M+H]^+$ = 184.0791, Found = 184.0794; **IR** (thin film, ν_{max}/cm^{-1}) 3214, 2918, 1497, 1455, 1048.

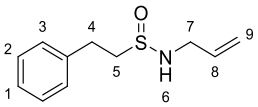
***N*-Benzyl-2-phenylethane-1-sulfinamide (37c)**:



Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and benzylamine (24.0 µL, 0.22 mmol, 1.1 equiv.) in CH_2Cl_2 (4.0 mL). Purification by silica gel flash column chromatography (40 – 70% EtOAc in Petrol) afforded sulfinamide **37c** as a pale-yellow oil (30.0 mg, 0.12 mmol, 58%).

R_f = 0.27 (50% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 – 7.09 (m, 10H, Ar*H*), 4.26 – 4.15 (m, 2H, C(7)H_2), 4.07 (t, *J* = 6.0 Hz, 1H, N(6)*H*), 3.06 – 2.86 (m, 4H, C(4)H_2 and C(5)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.9, 138.1, 128.9, 128.6, 128.31, 127.9, 126.8, 56.5, 46.5, 29.6 (*1 aromatic carbon signal is not observed due to signal overlap*); **LRMS** (ESI, *m/z*): 260.1 $[M+H]^+$, 282.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{15}H_{18}NOS$ $[M+H]^+$ = 260.1104, Found = 260.1112; **IR** (thin film, ν_{max}/cm^{-1}) 3718, 3029, 2920, 1497, 1455, 1050; **Melting point** = 75 – 77 °C.

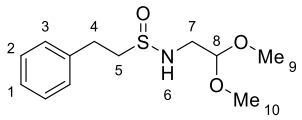
***N*-Allyl-2-phenylethane-1-sulfinamide (37g)**:



Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and allylamine (16.5 µL, 0.22 mmol, 1.1 equiv.) in CH_2Cl_2 (4.0 mL). Purification by silica gel flash column chromatography (50 – 60% EtOAc in Petrol) afforded sulfinamide **37g** as a pale-yellow oil (24.2 mg, 0.12 mmol, 58%).

R_f = 0.29 (60% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 2H, Ar*H*), 7.27 – 7.19 (m, 3H, Ar*H*), 5.91 (ddt, *J* = 17.1, 10.2, 5.9 Hz, 1H, C(8)*H*), 5.26 (dq, *J* = 17.1, 1.6 Hz, 1H, C(9)*H*H), 5.17 (dq, *J* = 10.2, 1.3 Hz, 1H, C(9)H*H*), 4.00 (t, *J* = 6.0 Hz, 1H, N(6)*H*), 3.83 – 3.64 (m, 2H, C(7)H_2), 3.13 – 2.93 (m, 4H, C(4)H_2 and C(5)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.0, 134.9, 128.9, 128.6, 126.8, 117.6, 56.5, 45.6, 29.6; **LRMS** (ESI, *m/z*): 210.1 $[M+H]^+$, 232.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{11}H_{15}NOSNa$ $[M+Na]^+$ = 232.0767, Found = 232.0763; **IR** (thin film, ν_{max}/cm^{-1}) 3198, 2918, 1497, 1455, 1053, 923.

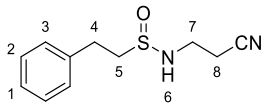
***N*-(2,2-Dimethoxyethyl)-2-phenylethane-1-sulfinamide (37h)**:



Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and 2,2-dimethoxyethylamine (24.0 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (80 – 90% EtOAc in Petrol) afforded sulfinamide **37h** as a pale-yellow oil (34.9 mg, 0.14 mmol, 68%).

R_f = 0.27 (80% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.26 (m, 2H, Ar*H*), 7.22 (t, *J* = 6.7 Hz, 3H, Ar*H*), 4.49 (t, J = 5.5 Hz, 1H, C(8)*H*), 4.09 (t, *J* = 6.4 Hz, 1H, N(6)*H*), 3.39 (s, 3H, C(9/10)H_3), 3.38 (s, 3H, C(9/10)H_3), 3.31 – 3.12 (m, 2H, C(7)H_2), 3.11 – 2.89 (m, 4H, C(4)H_2 and C(5)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.9, 128.8, 128.6, 126.8, 103.5, 56.5, 54.5, 54.4, 44.4, 29.6; **LRMS** (ESI, *m/z*): 280.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{12}H_{19}NO_3SNa$ $[M+Na]^+$ = 280.0978, Found = 280.0974; **IR** (thin film, ν_{max}/cm^{-1}) 3215, 2935, 1454, 1130, 1053, 699.

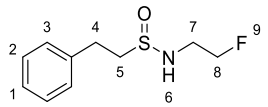
***N*-(2-Cyanoethyl)-2-phenylethane-1-sulfinamide (37i)**:



Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and 3-aminopropionitrile (16.1 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (0 – 2% MeOH in EtOAc) afforded sulfinamide **37i** as a colourless oil (26.0 mg, 0.12 mmol, 58%).

R_f = 0.25 (100% EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 2H, Ar*H*), 7.27 – 7.20 (m, 3H, Ar*H*), 4.58 (t, *J* = 6.6 Hz, 1H, N(6)*H*), 3.48 – 3.35 (m, 2H, C(7)H_2), 3.17 – 2.96 (m, 4H, C(4)H_2 and C(5)H_2), 2.62 (t, *J* = 6.5 Hz, 2H, C(8)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.6, 128.9, 128.6, 126.9, 117.8, 56.9, 40.1, 29.4, 20.4; **LRMS** (ESI, *m/z*): 223.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{11}H_{15}N_2OS$ $[M+H]^+$ = 223.0900, Found = 223.0900; **IR** (thin film, ν_{max}/cm^{-1}) 3189, 2927, 1455, 1046, 753, 699.

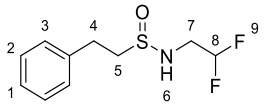
***N*-(2-Fluoroethyl)-2-phenylethane-1-sulfinamide (37j)**:



Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%), 2-fluoroethylamine hydrochloride (21.9 mg, 0.22 mmol, 1.1 equiv.) and triethylamine (30.7 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (80 – 100% EtOAc in Petrol) afforded sulfinamide **37j** as a colourless oil (16.1 mg, 0.07 mmol, 37%).

R_f = 0.16 (80% EtOAc in Petrol); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 2H, Ar*H*), 7.27 – 7.20 (m, 3H, Ar*H*), 4.65 – 4.45 (m, 2H, C(8)H_2), 4.22 (t, *J* = 6.0 Hz, 1H, N(6)*H*), 3.53 – 3.32 (m, 2H, C(7)H_2), 3.13 – 2.94 (m, 4H, C(4)H_2 and C(5)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.8, 128.9, 128.7, 126.9, 83.4 (d, *J* = 168.3 Hz), 56.8, 43.7 (d, *J* = 20.5 Hz), 29.5; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -224.07 (tdd, *J* = 47.1, 28.0, 25.6 Hz), **LRMS** (ESI, *m/z*): 238.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{10}H_{14}FNOSNa$ $[M+Na]^+$ = 238.0672, Found = 238.0661; **IR** (thin film, ν_{max}/cm^{-1}) 3192, 2919, 1455, 1044, 927, 700.

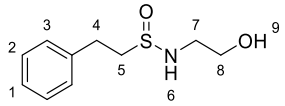
***N*-(2,2-Difluoroethyl)-2-phenylethane-1-sulfinamide (37k)**:



Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%), 2,2-difluoroethylamine (21.9 mg, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (86% EtOAc in Petrol) afforded sulfinamide **37k** as a colourless oil (19.6 mg, 0.08 mmol, 42%).

R_f = 0.21 (60% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 2H, Ar*H*), 7.27 – 7.17 (m, 3H, Ar*H*), 5.90 (tt, *J* = 55.9, 4.1 Hz, 1H, C(8)*H*), 4.28 (t, *J* = 6.9 Hz, 1H, N(6)*H*), 3.56 – 3.34 (m, 2H, C(7)H_2), 3.12 – 2.94 (m, 4H, C(4)H_2 and C(5)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.6, 129.0, 128.6, 127.0, 114.6 (t, *J* = 241.9 Hz), 56.9, 45.8 (t, *J* = 26.2 Hz), 29.4; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -122.78 (dtd, *J* = 56.0, 14.6, 6.2 Hz); **LRMS** (ESI, *m/z*): 256.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{10}H_{13}F_2NOSNa$ $[M+Na]^+$ = 256.0578, Found = 256.0570; **IR** (thin film, ν_{max}/cm^{-1}) 3196, 2924, 1455, 1062, 906, 699.

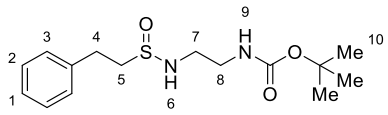
***N*-(2-Hydroxyethyl)-2-phenylethane-1-sulfinamide (37m)**:



Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and ethanolamine (13.3 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (0 – 2% MeOH in Petrol) afforded sulfinamide **37m** as an off-white solid (31.6 mg, 0.15 mmol, 74%).

R_f = 0.25 (2% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2H, Ar*H*), 7.26 – 7.18 (m, 3H, Ar*H*), 4.70 (t, *J* = 6.4 Hz, 1H, N(6)*H*), 4.00 (s, 1H, O(9)*H*), 3.75 – 3.62 (m, 2H, C(8)H_2), 3.42 – 3.28 (m, 1H, C(7)*H*H), 3.28 – 3.18 (m, 1H, C(7)H*H*), 3.16 – 3.04 (m, 2H, C(5)H_2), 3.04 – 2.88 (m, 2H, C(4)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.7, 128.9, 128.6, 126.9, 62.2, 55.6, 46.9, 29.7; **LRMS** (ESI, *m/z*): 236.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{10}H_{16}NO_2S$ $[M+H]^+$ = 214.0896, Found = 214.0898; **IR** (thin film, ν_{max}/cm^{-1}) 3237, 2925, 2871, 1455, 1040, 699; **Melting point** = 64 – 66 °C.

***tert*-Butyl (2-((phenethylsulfinyl)amino)ethyl)carbamate (37n)**:

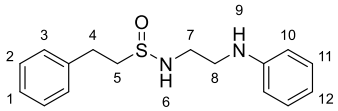


Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (0 – 2% MeOH in EtOAc) afforded sulfinamide **37n** as an off-white solid (45.6 mg, 0.15 mmol, 73%).

Also prepared on a 5.0 mmol scale according to **General Procedure I-1** using hydrocinnamic acid (751 mg, 5.0 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (1.53 g, 5.0 mmol, 1.0 equiv.), 9-mesitylacridine (297 mg, 1.0 mmol, 20 mol%) and *N*-Boc-ethylenediamine (950 µL, 0.22 mmol, 1.1 equiv.) in MeCN (25.0 mL). Purification by silica gel flash column chromatography (0 – 2% MeOH in EtOAc) afforded sulfinamide **37n** as an off-white solid (1.01 g, 3.2 mmol, 64%).

R_f = 0.24 (100% EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 2H, Ar*H*), 7.26 – 7.19 (m, 3H, Ar*H*), 5.16 (s, 1H, N(9)*H*), 4.26 – 4.17 (m, 1H, N(6)*H*), 3.39 – 3.16 (m, 4H, C(7)H_2 and C(8)H_2), 3.10 – 2.93 (m, 4H, C(4)H_2 and C(5)H_2), 1.43 (s, 9H, 3×C(10)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.4, 138.8, 128.8, 128.5, 126.8, 79.7, 56.4, 43.8, 41.3, 29.5, 28.4; **LRMS** (ESI, *m/z*): 335.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{15}H_{24}N_2O_3SNa$ $[M+Na]^+$ = 335.1400, Found = 335.1415; **IR** (thin film, ν_{max}/cm^{-1}) 3295, 2871, 1695, 1525, 1172, 1047; **Melting point** = 78 – 80 °C.

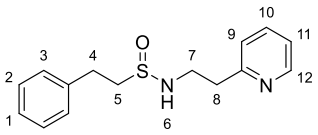
2-Phenyl-*N*-(2-(phenylamino)ethyl)ethane-1-sulfinamide (37p):



Prepared according to a modified **General Procedure I-1**, where the reaction mixture was irradiated with 405 nm LEDs for an extended time of 5 h, using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-phenylethylenediamine (28.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (80 – 90% EtOAc in Petrol) afforded sulfinamide **37p** as a white solid (42.3 mg, 0.15 mmol, 73%).

R_f = 0.2 (80% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 2H, Ar*H*), 7.27 – 7.14 (m, 5H, Ar*H*), 6.73 (tt, *J* = 7.4, 1.0 Hz, 1H, Ar*H*), 6.67 – 6.60 (m, 2H, Ar*H*), 4.31 – 4.17 (m, 2H, N(6)*H* and N(9)*H*), 3.45 – 3.27 (m, 4H, C(7)H_2 and C(8)H_2), 3.09 – 2.93 (m, 4H, C(4)H_2 and C(5)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.9, 138.9, 129.5, 128.9, 128.6, 126.9, 117.9, 113.2, 56.5, 44.4, 42.9, 29.6; **LRMS** (ESI, *m/z*): 311.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{16}H_{20}N_2OSNa$ $[M+Na]^+$ = 311.1189, Found = 311.1183; **IR** (thin film, ν_{max}/cm^{-1}) 3333, 3197, 2922, 1603, 1499, 1046; **Melting point** = 91 – 93 °C.

2-Phenyl-*N*-(2-(pyridin-2-yl)ethyl)ethane-1-sulfinamide (37q):

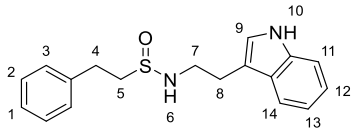


Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and 2-(2-pyridyl)ethylamine (26.3 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (0 – 10% MeOH in EtOAc) afforded sulfinamide **37q** as an off-white solid (39.3 mg, 0.14 mmol, 72%).

R_f = 0.22 (10% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.51 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H, Py*H*), 7.60 (app. td, *J* = 7.7, 1.8 Hz, 1H, Py*H*), 7.32 – 7.26 (m, 2H, Ar*H*), 7.24 – 7.10 (m, 5H, Ar*H* and Py*H*), 4.79 (t, *J* = 5.7 Hz, 1H, N(6)*H*), 3.55 (app. q, *J* = 6.4 Hz, 2H, C(7)H_2), 3.14 – 3.04 (m, 2H, C(8)H_2), 3.04 – 2.97 (m, 2H, C(5)H_5), 2.97 – 2.87 (m, 2H, C(4)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.2, 149.3, 139.1, 136.7, 128.8, 128.6, 126.7, 123.7, 121.8, 56.3, 42.5, 38.5, 29.6; **LRMS** (ESI, *m/z*): 275.1 $[M+H]^+$; **HRMS** (ESI,

m/z): Calc. for $C_{15}H_{19}N_2OS$ $[M+H]^+$ = 275.1213, Found = 275.1213; **IR** (thin film, ν_{max}/cm^{-1}) 3187, 2926, 1594, 1437, 1051, 753.

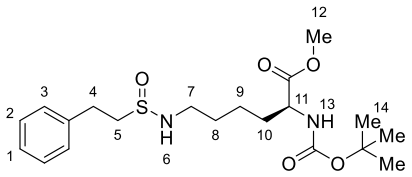
***N*-(2-(1*H*-Indol-3-yl)ethyl)-2-phenylethane-1-sulfinamide (37r)**:



Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and tryptamine (35.2 mg, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (80% EtOAc in Petrol) afforded sulfinamide **37r** as a light-brown gum (44.0 mg, 0.14 mmol, 70%).

R_f = 0.24 (80% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (s, 1H, N(10)*H*), 7.63 – 7.57 (m, 1H, Ar*H*), 7.38 (dt, *J* = 8.1, 0.9 Hz, 1H, Ar*H*), 7.30 (tt, *J* = 8.1, 1.7 Hz, 2H, Ar*H*), 7.26 – 7.10 (m, 5H, Ar*H*), 7.04 (d, *J* = 2.3 Hz, 1H, C(9)*H*), 3.88 (t, *J* = 6.3 Hz, 1H, N(6)*H*), 3.56 – 3.39 (m, 2H, C(7)H_2), 3.10 – 3.02 (m, 2H, C(8)H_2), 3.02 – 2.87 (m, 4H, C(4)H_2 and C(5)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.9, 136.5, 128.8, 128.6, 127.4, 126.7, 122.7, 122.2, 119.5, 118.7, 112.2, 111.5, 56.3, 43.4, 29.6, 26.8; **LRMS** (ESI, *m/z*): 335.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{18}H_{20}N_2OSNa$ $[M+Na]^+$ = 335.1189, Found = 335.1191; **IR** (thin film, ν_{max}/cm^{-1}) 3263, 2923, 1456, 1042, 743, 699.

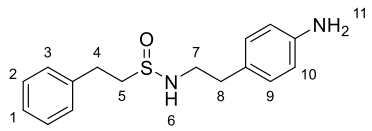
Methyl N^2-(*tert*-butoxycarbonyl)-N^6-(phenethylsulfinyl)-*L*-lysinate (37s):



Prepared according to **General Procedure I-1** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%), Boc-*L*-Lys-OMe hydrochloride (65.3 mg, 0.22 mmol, 1.1 equiv.) and triethylamine (30.7 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (80 – 90% EtOAc in Petrol) afforded sulfinamide **37s** as a pale-brown oil (62.8 mg, 0.15 mmol, 76%, 1:1 mixture of inseparable diastereomers).

R_f = 0.23 (80% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 2H, Ar*H*), 7.25 – 7.18 (m, 3H, Ar*H*), 5.14 (t, *J* = 7.1 Hz, 1H, N(13)*H*), 4.28 (q, *J* = 7.9 Hz, 1H, C(11)*H*), 4.00 (t, *J* = 6.4 Hz, 1H, N(6)*H*), 3.71 (app. d, *J* = 0.6 Hz, 3H, C(12)H_3), 3.09 (app. q, *J* = 6.8 Hz, 2H, C(7)H_2), 3.06 – 2.90 (m, 4H, C(4)H_2 and C(5)H_2), 1.86 – 1.70 (m, 1H, C(10)*H*H), 1.68 – 1.50 (m, 3H, C(8)H_2 and C(10)H*H*), 1.44 – 1.34 (m, 11H, C(9)H_2 and 3×C(14)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.4, 155.5, 139.0, 128.8, 128.6, 126.8, 80.0, 56.4, 53.2, 52.4, 42.8, 42.7, 32.5, 30.3, 29.6, 28.4, 22.7 *(15 carbon signals are unresolved from the corresponding signals in the other diastereomer);* **LRMS** (ESI, *m/z*): 413.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{20}H_{33}N_2O_5S$ $[M+H]^+$ = 413.2105, Found = 413.2109; **IR** (thin film, ν_{max}/cm^{-1}) 3247, 2933, 1743, 1709, 1366, 1167, 1048.

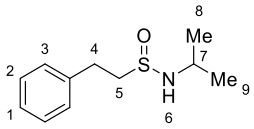
***N*-(4-Aminophenethyl)-2-phenylethane-1-sulfinamide (37t)**:



Prepared according to a modified **General Procedure I-1**, where the reaction mixture was pre-heated at 40 °C for 18 h prior to irradiation, using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and 4-(2-aminoethyl)aniline (29.0 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (100% EtOAc) afforded sulfinamide **37t** as a brown oil (22.2 mg, 0.08 mmol, 38%).

R_f = 0.24 (100% EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 2H, Ar*H*), 7.26 – 7.16 (m, 3H, Ar*H*), 6.98 (d, *J* = 8.3 Hz, 2H, Ar*H*), 6.68 – 6.59 (m, 2H, Ar*H*), 3.77 (t, *J* = 6.3 Hz, 1H, N(6)*H*), 3.63 (br. s, 2H, N(11)H_2), 3.33 (app. q, *J* = 6.8 Hz, 2H, C(7)H_2), 3.02 – 2.89 (m, 4H, C(4)H_2 and C(5)H_2), 2.84 – 2.69 (m, 2H, C(8)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.1, 139.1, 129.9, 128.8, 128.6, 128.2, 126.8, 115.5, 56.6, 44.5, 36.3, 29.6; **LRMS** (ESI, *m/z*): 289.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{16}H_{21}N_2OS$ $[M+H]^+$ = 289.1369, Found = 289.1358; **IR** (thin film, ν_{max}/cm^{-1}) 3214, 2927, 1627, 1519, 1285, 1050.

***N*-Isopropyl-2-phenylethane-1-sulfinamide (37b)**:

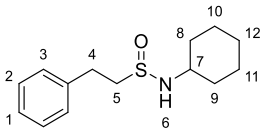


Prepared according to **General Procedure I-2** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-

mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and isopropylamine (18.7 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (60 – 70% EtOAc in Petrol) afforded sulfinamide **37b** as a pale-yellow oil (27.8 mg, 0.13 mmol, 66%).

R_f = 0.26 (60% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 2H, Ar*H*), 7.25 – 7.18 (m, 3H, Ar*H*), 3.65 (d, *J* = 5.2 Hz, 1H, N(6)*H*), 3.64 – 3.52 (m, 1H, C(7)*H*), 3.06 – 2.92 (m, 4H, C(4)H_2 and C(5)H_2), 1.23 (d, *J* = 6.4 Hz, 3H, C(8/9)H_3), 1.19 (d, *J* = 6.3 Hz, 3H, C(8/9)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.1, 128.8, 128.6, 126.8, 57.5, 46.7, 29.5, 25.0, 23.9; **LRMS** (ESI, *m/z*): 212.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{11}H_{18}NOS$ $[M+H]^+$ = 212.1104, Found = 212.1105; **IR** (thin film, ν_{max}/cm^{-1}) 3184, 2967, 1455, 1048, 983, 698.

***N*-Cyclohexyl-2-phenylethane-1-sulfinamide (37u)**:

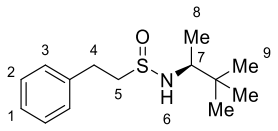


Prepared according to **General Procedure I-2** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and cyclohexylamine (25.2 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (70 – 80% EtOAc in Petrol) afforded sulfinamide **37u** as a pale-yellow oil (37.8 mg, 0.15 mmol, 75%).

R_f = 0.19 (70% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H, Ar*H*), 7.26 – 7.17 (m, 3H, Ar*H*), 3.73 (d, *J* = 5.3 Hz, 1H, N(6)*H*), 3.28 – 3.17 (m, 1H, C(7)*H*), 3.06 – 2.94 (m, 4H, C(4)H_2 and C(5)H_2), 2.08 – 1.90 (m, 2H, C(8)$H_{eq}H_{ax}$ and C(9)$H_{eq}H_{ax}$), 1.78 – 1.66 (m, 2H, C(10)$H_{eq}H_{ax}$ and C(11)$H_{eq}H_{ax}$), 1.65 – 1.53 (m, 1H, C(12)$H_{eq}H_{ax}$),

1.36 – 1.11 (m, 5H, C(8)H$_{eq}$*H$_{ax}$*, C(9)H$_{eq}$*H$_{ax}$*, C(10)H$_{eq}$*H$_{ax}$*, C(11)H$_{eq}$*H$_{ax}$* and C(12)H$_{eq}$*H$_{ax}$*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.1, 128.8, 128.6, 126.7, 57.5, 53.7, 35.5, 34.4, 29.6, 25.5, 24.9, 24.8; **LRMS** (ESI, *m/z*): 252.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{22}NOS$ $[M+H]^+$ = 252.1417, Found = 252.1416; **IR** (thin film, ν_{max}/cm^{-1}) 3181, 2931, 2855, 1453, 1048, 698; **Melting point** = 65 – 67 °C.

***N*-((*R*)-3,3-Dimethylbutan-2-yl)-2-phenylethane-1-sulfinamide (37v)**:

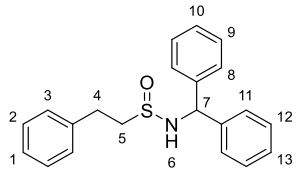


Prepared according to **General Procedure I-2** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and (*R*)-(-)-3,3-dimethyl-2-butylamine (29.2 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (50 – 60% EtOAc in Petrol) afforded sulfinamide **37v** as an off-white solid (41.4 mg, 0.16 mmol, 82%, 1:1 mixture of inseparable diastereomers).

R$_f$ = 0.22 (50% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 2H, Ar*H*), 7.26 – 7.18 (m, 3H, Ar*H*), 3.76 (d, *J* = 5.7 Hz, 0.5H, N(6)*H (diastereomer A)*), 3.37 (d, *J* = 9.2 Hz, 0.5H, N(6)*H diastereomer B*), 3.17 (app. p, *J* = 6.5 Hz, 0.5H, C(7)*H (diastereomer A)*), 3.12 – 2.90 (m, 4.5H, C(4)*H*$_2$, C(5)*H*$_2$ and C(7)*H (diastereomer B)*), 1.23 (d, *J* = 6.8 Hz, 1.5H, C(8)*H*$_3$ *(diastereomer B)*), 1.17 (d, *J* = 6.6 Hz, 1.5H, C(8)*H*$_3$ *(diastereomer A)*), 0.89 (s, 4.5H, C(8)*H*$_3$ *(diastereomer A or B)*), 0.85 (s, 4.5H, C(8)*H*$_3$ *(diastereomer B or A)*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.2, 128.8, 128.63, 128.61, 126.8, 62.1, 58.1, 58.0, 57.1, 35.0, 34.3, 29.7, 29.5, 26.3, 26.2, 18.8, 17.1 *(3 carbon signals are unresolved from the corresponding signals in the other diastereomer)*; **LRMS** (ESI, *m/z*): 254.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{24}NOS$ $[M+H]^+$ = 254.1573, Found

= 254.1570; **IR** (thin film, ν_{max}/cm^{-1}) 3201, 2961, 2870, 1455, 1051, 698; **Melting point** = 67 – 69 °C.

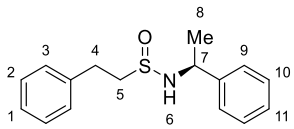
***N*-Benzhydryl-2-phenylethane-1-sulfinamide (37w)**:



Prepared according to **General Procedure I-2** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and benzyhydrylamine (37.9 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (30% EtOAc in cyclohexane) afforded sulfinamide **37w** as an off-white solid (50.8 mg, 0.15 mmol, 76%).

R$_f$ = 0.17 (30% EtOAc in cyclohexane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.16 (m, 13H, Ar*H*), 7.11 – 7.04 (m, 2H, Ar*H*), 5.75 (d, *J* = 3.2 Hz, 1H, C(7)*H*), 4.41 (d, *J* = 3.2 Hz, 1H, N(6)*H*), 3.09 – 2.83 (m, 4H, C(4)H_2, and C(5)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.4, 141.6, 138.9, 129.0, 128.8, 128.6, 128.1, 128.0, 127.9, 127.5, 126.8, 59.7, 56.9, 29.5 *(1 aromatic carbon signal is not observed due to signal overlap)*; **LRMS** (ESI, *m/z*): 358.1 [M+Na]$^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{21}H_{21}NOS$ [M+Na]$^+$ = 358.1236, Found = 358.1242; **IR** (thin film, ν_{max}/cm^{-1}) 3172, 3028, 1494, 1454, 1053, 698; **Melting point** = 95 – 97 °C.

2-Phenyl-*N*-((*S*)-1-phenylethyl)ethane-1-sulfinamide (37x):



Prepared according to **General Procedure I-2** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and (*S*)-(−)-α-methylbenzylamine (28.4 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (60 – 70% EtOAc in Petrol) afforded sulfinamide **37x** as two separable diastereomers **37x-1** (18.2 mg, 0.07 mmol, 33%) as a colourless gum and **37x-2** (18.2 mg, 0.07 mmol, 33%) as an off-white solid (67% total).

37x-1

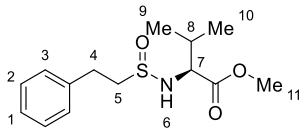
R_f = 0.25 (60% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.23 (m, 7H, Ar*H*), 7.22 – 7.17 (m, 1H, Ar*H*), 7.14 – 7.07 (m, 2H, Ar*H*), 4.67 (qd, *J* = 6.6, 3.5 Hz, 1H, C(7)*H*), 4.06 (d, *J* = 3.1 Hz, 1H, N(6)*H*), 3.01 – 2.84 (m, 4H, C(4)H_2, and C(5)H_2), 1.51 (d, *J* = 6.6 Hz, 3H, C(8)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.3, 139.0, 128.9, 128.8, 128.6, 127.9, 126.8, 126.6, 56.8, 51.8, 29.5, 23.8; **LRMS** (ESI, *m/z*): 274.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{16}H_{20}NOS$ $[M+H]^+$ = 274.1260, Found = 274.1261; **IR** (thin film, ν_{max}/cm^{-1}) 3190, 2926, 1495, 1454, 1049, 699; $[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ 4.7° (c = 0.5, $CHCl_3$).

37x-2

R_f = 0.16 (60% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 7H, Ar*H*), 7.25 – 7.16 (m, 3H, Ar*H*), 4.60 (qd, *J* = 6.7, 4.1 Hz, 1H, C(7)*H*), 3.90 (d, *J* = 3.7 Hz, 1H, N(6)*H*), 3.10 – 2.93 (m, 4H, C(4)H_2, and C(5)H_2), 1.54 (d, *J* = 6.7 Hz, 3H, C(8)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.2, 139.0, 128.9, 128.8, 128.6, 127.8, 126.9, 126.8, 57.7, 54.4, 29.4, 25.1; **LRMS** (ESI, *m/z*): 274.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for

$C_{16}H_{20}NOS$ $[M+H]^+$ = 274.1260, Found = 274.1252; **IR** (thin film, ν_{max}/cm^{-1}) 3179, 2926,1496,1454, 1049, 699; **Melting point** = 91 – 93 °C; $[\alpha]_D^{25}$ -57.0° (c = 0.5, $CHCl_3$).

Methyl (phenethylsulfinyl)-*L*-valinate (37y):

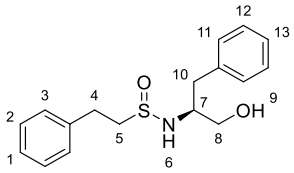


Prepared according to **General Procedure I-2** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%), H-Val-OMe hydrochloride (36.9 mg, 0.22 mmol, 1.1 equiv.) and triethylamine (30.7 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (50 – 60% EtOAc in Petrol) afforded sulfinamide **37y** as a colourless oil (17.8 mg, 0.06 mmol, 31%, 1:1 mixture of inseparable diastereomers).

R_f = 0.18 (50% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 2H, Ar*H*), 7.26 – 7.19 (m, 3H, Ar*H*), 4.58 (d, *J* = 9.9 Hz, 0.5H, N(6)*H (diastereomer A)*), 4.50 (d, *J* = 8.4 Hz, 0.5H, N(6)*H (diastereomer B)*), 3.83 (dd, *J* = 9.9, 5.3 Hz, 0.5H, C(7)*H (diastereomer A)*), 3.78 – 3.71 (m, 3.5H, C(7)*H (diastereomer B)* and C(11)H_3), 3.18 – 2.91 (m, 4H, C(4)H_2, and C(5)H_2), 2.13 – 2.01 (m, 1H, C(8)*H*), 1.00 (d, *J* = 6.8 Hz, 1.5H, C(9/10)H_3 *(diastereomer A)*), 0.95 (d, *J* = 6.8 Hz, 3H, C(10/9)H_3), 0.87 (d, *J* = 6.8 Hz, 1.5H, C(9/10)H_3 *(diastereomer B*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.6, 173.5, 138.9, 128.9, 128.6, 126.9, 126.8, 63.0, 58.9, 57.6, 56.4, 52.6, 52.5, 32.2, 31.9, 29.7, 29.4, 19.3, 19.2, 18.2, 17.5 *(3 carbon signals are unresolved from the corresponding signals in the other diastereomer)*; **LRMS** (ESI, *m/z*): 306.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for

$C_{14}H_{21}NO_3SNa$ $[M+Na]^+$ = 306.1134, Found = 306.1130; **IR** (thin film, ν_{max}/cm^{-1}) 3206, 2962, 1741, 1455, 1204, 1062.

***N*-((*S*)-1-Hydroxy-3-phenylpropan-2-yl)-2-phenylethane-1-sulfinamide (37z)**:



Prepared according to **General Procedure I-2** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *L*-phenylalaninol (33.3 mg, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (90 – 100% EtOAc in Petrol, then 0 – 5% MeOH in EtOAc) afforded sulfinamide **37z** as two separable diastereomers **37z-1** (23.2 mg, 0.08 mmol, 38%) as a white solid and **37-2** (23.1 mg, 0.08 mmol, 38%) as a colourless gum (76% total).

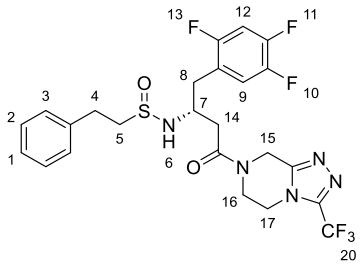
37z-1

R_f = 0.25 (90% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 4H, Ar*H*), 7.25 – 7.17 (m, 4H, Ar*H*), 7.09 (d, *J* = 7.1 Hz, 2H, Ar*H*), 4.23 (d, *J* = 7.8 Hz, 1H, N(6)*H*), 3.92 (br. s, 1H, O(9)*H*), 3.78 – 3.65 (m, 2H, C(7)*H* and C(8)*H*H), 3.54 – 3.44 (m, 1H, C(8)H*H*), 2.97 – 2.64 (m, 6H, C(4)H_2, C(5)H_2 and C(10)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.7, 137.7, 129.5, 128.8, 128.8, 128.5, 127.0, 126.9, 65.6, 58.2, 54.8, 38.5, 29.4; **LRMS** (ESI, *m/z*): 326.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{21}N_2OSNa$ $[M+Na]^+$ = 326.1185, Found = 326.1187; **IR** (thin film, ν_{max}/cm^{-1}) 3208, 3029, 1497, 1455, 1043, 749; **Melting point** = 103 – 105 °C; $[\alpha]_D^{25}$ -10.8° (c = 1.0, $CHCl_3$).

37z-2

R_f = 0.14 (90% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 4H, Ar*H*), 7.25 – 7.19 (m, 2H, Ar*H*), 7.19 – 7.14 (m, 2H, Ar*H*), 7.13 – 7.08 (m, 2H, Ar*H*), 4.31 (d, *J* = 9.0 Hz, 1H, N(6)*H*), 3.90 – 3.70 (m, 2H, C(8)H*H* and O(9)*H*), 3.60 – 3.45 (m, 2H, C(7)*H* and C(8)*H*H), 3.07 – 2.96 (m, 2H, C(5)H_2), 2.91 – 2.72 (m, 4H, C(4)H_2 and C(10)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.8, 137.8, 129.5, 128.9, 128.64, 128.61, 126.9, 126.8, 65.7, 61.4, 57.6, 39.3, 29.6; **LRMS** (ESI, *m/z*): 326.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{21}N_2OSNa$ $[M+Na]^+$ = 326.1185, Found = 326.1195; **IR** (thin film, ν_{max}/cm^{-1}) 3214, 3029, 1497, 1455, 1046, 756; $[\alpha]_D^{25}$ -7.8° (c = 1.0, $CHCl_3$).

***N*-((*R*)-4-Oxo-4-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-*a*]pyrazin-7(8*H*)-yl)-1-(2,4,5-trifluorophenyl)butan-2-yl)-2-phenylethane-1-sulfinamide (37aa)**:



Prepared according to **General Procedure I-2** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and Sitagliptin (89.6 mg, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (2 – 10% MeOH in EtOAc) afforded sulfinamide **37aa** as two separable diastereomers **37aa-1** (23.2 mg, 0.08 mmol, 38%) as a white solid and **37aa-2** (23.1 mg, 0.08 mmol, 38%) as a colourless gum (76% total).

37aa-1

R_f = 0.21 (2% MeOH in EtOAc); **^{1}H NMR** (600 MHz, DMSO-d_6) δ 7.52 – 7.46 (m, 1H, Ar*H*), 7.43 (p, *J* = 9.3 Hz, 1H, Ar*H*), 7.26 (t, *J* = 7.5 Hz, 2H, Ar*H*), 7.19 (t, *J* = 7.3 Hz, 1H,

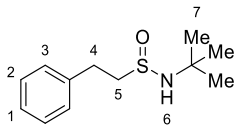
Ar*H*), 7.14 – 7.10 (m, 2H, Ar*H*), 6.19 (app. dd, *J* = 8.6, 5.1 Hz, 1H, N(6)*H*), 4.99 (app. dd, *J* = 21.3, 17.0 Hz, 0.85H, C(15)H_2 *(minor rotamer)*), 4.86 (app. dd, *J* = 21.6, 17.5 Hz, 1.15H, C(15)H_2 *(major rotamer)*), 4.24 (t, *J* = 5.1 Hz, 1.15H, C(17)H_2 *(major rotamer)*), 4.13 – 4.02 (m, 0.85H, C(17)H_2 *(minor rotamer)*), 4.02 – 3.83 (m, 3H, C(7)*H* and C(16)H_2), 2.97 – 2.90 (m, 1H, C(8)*H*H), 2.90 – 2.71 (m, 4H, C(5)H_2, C(8)H*H* and C(14)*H*H), 2.60 (dd, *J* = 21.3, 17.0 Hz, 3H, C(4)H_2, C(14)H*H*); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 169.5, 156.0 (dd, *J* = 241.8, 9.5 Hz), 150.93 *(major rotamer)*, 150.85 *(minor rotamer)*, 147.9 (dt, *J* = 246.9, 13.7 Hz), 145.8 (dd, *J* = 241.1, 12.0 Hz), 142.4 (app. qd, *J* = 38.7, 15.3 Hz), 139.3, 128.4, 128.2, 126.2, 122.7 – 122.1 (m), 120.1 – 119.4 (m), 118.4 (q, *J* = 270.1 Hz), 105.5 (dd, *J* = 29.3, 21.0 Hz), 55.3 *(minor rotamer)*, 55.2 *(major rotamer)*, 52.2 *(minor rotamer)*, 52.1 *(major rotamer)*, 43.6 *(major rotamer)*, 43.0 *(minor rotamer)*, 42.0 *(minor rotamer)*, 41.2 *(major rotamer)*, 38.9 *(minor rotamer)*, 38.7 *(major rotamer)*, 38.4 *(major rotamer)*, 37.5 *(minor rotamer)*, 34.6 *(minor rotamer)*, 34.3 *(major rotamer)*, 28.95; **^{19}F NMR** (565 MHz, DMSO-d_6) δ -61.91, -118.39 (m), -136.89 – -137.40 (m), -143.25 – -144.28 (m); **LRMS** (ESI, *m/z*): 560.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{24}H_{24}F_6N_5O_2S$ $[M+H]^+$ = 560.1549, Found = 560.1540; **IR** (thin film, ν_{max}/cm^{-1}) 3444, 2927, 1656, 1521, 1212, 1166; $[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ 1.2° (c = 1.0, $CHCl_3$).

37aa-2

R_f = 0.14 (2% MeOH in EtOAc); **^{1}H NMR** (600 MHz, DMSO-d_6) δ 7.50 – 7.40 (m, 2H, Ar*H*), 7.26 (t, *J* = 7.5 Hz, 2H, Ar*H*), 7.19 (t, *J* = 7.4 Hz, 1H, Ar*H*), 7.11 – 7.06 (m, 2H Ar*H*), 6.13 (app. dd, *J* = 13.9, 9.6 Hz, 1H, N(6)*H*), 5.05 (d, *J* = 16.9 Hz, 0.4H, C(15)*H*H, *(minor rotamer)*), 4.96 (d, *J* = 16.9 Hz, 0.4H, C(15)H*H*, *(minor rotamer)*), 4.91 (d, *J* = 17.1 Hz, 0.6H, C(15)*H*H, *(major rotamer)*), 4.84 (d, *J* = 17.1 Hz, 0.6H, C(15)H*H*, *(major rotamer)*), 4.25 (t, *J* = 5.2 Hz, 1.2H, C(17)H_2 *(major rotamer)*), 4.16 – 3.91 (m, 2.4H, C(16)H_2 *(major rotamer)*, C(16)*H*H *(minor rotamer)* and C(17)H_2 *(minor rotamer)*), 3.89

– 3.77 (m, 1.4H, C(7)*H* and C(16)H*H (minor rotamer)*), 2.94 – 2.72 (m, 5H, C(5)H_2, C(8)H_2 and C(14)*H*H), 2.70 – 2.55 (m, 3H, C(4)H_2 and C(14)H*H*); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 169.5 *(minor rotamer)*, 169.4 *(major rotamer)*, 155.9 (dd, *J* = 242.6, 8.8 Hz), 151.0 *(major rotamer)*, 150.9 *(major rotamer)*, 147.8 (dt, *J* = 246.9, 13.4 Hz), 145.7 (dd, *J* = 239.8, 11.4 Hz), 142.4 (app. qd, *J* = 37.9, 7.3 Hz), 139.4, 128.4, 128.2, 126.2, 123.1 – 122.6 (m), 119.6 (app. dt, *J* = 16.9, 4.7 Hz), 118.5 (q, *J* = 270.0 Hz), 105.5 (dd, *J* = 29.3, 21.0 Hz), 56.0 *(major rotamer)*, 55.9 *(minor rotamer)*, 53.9 *(minor rotamer)*, 53.7 *(major rotamer)*, 43.6 *(major rotamer)*, 42.9 *(minor rotamer)*, 42.0 *(minor rotamer)*, 41.3 *(major rotamer)*, 38.8, 38.4 *(major rotamer)*, 37.6 *(minor rotamer)*, 34.9 *(minor rotamer)*, 34.7 *(major rotamer)*, 29.0 *(major rotamer)*, 28.9 *(minor rotamer)*; **^{19}F NMR** (565 MHz, DMSO-d_6) δ -61.86 *(minor rotamer)*, -61.89 *(major rotamer)*, 118.32 – -118.49 (m), -137.16 – -137.31 (m), -144.04 – -144.20 (m); **LRMS** (ESI, *m/z*): 560.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{24}H_{24}F_6N_5O_2S$ $[M+H]^+$ = 560.1549, Found = 560.1542; **IR** (thin film, ν_{max}/cm^{-1}) 3455, 2937, 1656, 1522, 1278, 1213, 1167; $[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ 1.8° (c = 1.0, $CHCl_3$).

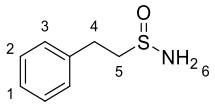
***N*-(*tert*-Butyl)-2-phenylethane-1-sulfinamide (37ad)**:



Prepared according to a modified **General Procedure I-2**, where the reaction mixture was pre-heated at 80 °C for 18 h prior to irradiation, using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *tert*-butylamine (23.1 µL, 0.22 mmol, 1.1 equiv.) in DCE (4.0 mL). Purification by silica gel flash column chromatography (70 – 80% EtOAc in Petrol) afforded sulfinamide **37ad** as a white solid (22.4 mg, 0.1 mmol, 50%).

R_f = 0.17 (70% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H, Ar*H*), 7.25 – 7.19 (m, 3H, Ar*H*), 3.60 (s, 1H, N(6)*H*), 3.03 – 2.91 (m, 4H, C(4)H_2 and C(5)H_2), 1.30 (s, 9H, 3×C(7)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.2, 128.8, 128.7, 126.7, 58.5, 54.0, 31.2, 29.6; **LRMS** (ESI, *m/z*): 248.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{12}H_{19}NOSNa$ $[M+Na]^+$ = 248.1080, Found = 248.1068; **IR** (thin film, ν_{max}/cm^{-1}) 3191, 2972, 1367, 1235, 1043, 699; **Melting point** = 63 – 65 °C.

2-Phenylethane-1-sulfinamide (37ae):

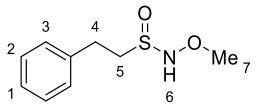


Prepared according to **General Procedure I-2** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and 7.0 M ammonia in methanol (31.4 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (0 – 2% methanol in EtOAc) afforded sulfinamide **37ae** as a colourless crystalline solid (12.8 mg, 0.08 mmol, 38%).

Also prepared according to **General Procedure I-2** using ammonium chloride (11.8 mg, 0.22 mmol, 1.1 equiv.) and triethylamine (30.7 µL, 0.22 mmol, 1.1 equiv.) to afford sulfinamide **37ae** as a colourless crystalline solid (3.1 mg, 0.02 mmol, 9%).

R_f = 0.14 (2% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 2H, Ar*H*), 7.28 – 7.20 (m, 3H, Ar*H*), 4.22 (s, 2H, N(6)H_2), 3.13 – 2.97 (m, 4H, C(4)H_2, and C(5)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.9, 128.9, 128.6, 126.9, 58.7, 29.2; **LRMS** (ESI, *m/z*): 170.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_8H_{12}NOS$ $[M+H]^+$ = 170.0634, Found = 170.0635; **IR** (thin film, ν_{max}/cm^{-1}) 3213, 3107, 1056, 1026, 724, 698; **Melting point** = 77 – 79 °C.

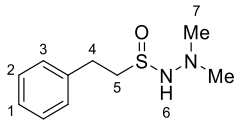
***N*-Methoxy-2-phenylethane-1-sulfinamide (37af)**:



Prepared according to a modified **General Procedure I-2**, where the reaction mixture was pre-heated at 80 °C for 18 h prior to irradiation, using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%), *O*-methylhydroxylamine hydrochloride (18.4 mg, 0.22 mmol, 1.1 equiv.) and triethylamine (30.7 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (40 – 60% EtOAc in Petrol) afforded sulfinamide **3af** as a colourless oil (8.1 mg, 0.04 mmol, 20%).

R_f = 0.18 (50% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (s, 1H, N(6)*H*), 7.36 – 7.29 (m, 2H, Ar*H*), 7.28 – 7.22 (m, 3H, Ar*H*), 3.72 (s, 3H, C(7)H_3), 3.16 – 3.10 (m, 2H, C(5)H_2), 3.08 – 2.99 (m, 2H, C(4)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.7, 129.0, 128.7, 127.0, 64.6, 52.0, 29.1; **LRMS** (ESI, *m/z*): 200.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_9H_{14}NO_2S$ $[M+H]^+$ = 200.0740, Found = 200.0740; **IR** (thin film, ν_{max}/cm^{-1}) 3088, 2939, 1498, 1456, 1087, 1038.

***N*',*N*'-Dimethyl-2-phenylethane-1-sulfinohydrazide (37ag)**:

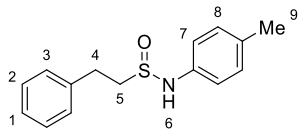


Prepared according to a modified **General Procedure I-2**, where the reaction mixture was pre-heated at 60 °C for 18 h prior to irradiation, using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-

mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*,*N*-dimethylhydrazine (16.7 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (100% EtOAc) afforded sulfinamide **37ag** as a colourless oil (7.4 mg, 0.03 mmol, 17%).

R_f = 0.15 (100% EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 2H, Ar*H*), 7.25 – 7.20 (m, 3H, Ar*H*), 4.64 (s, 1H, N(6)*H*), 3.19 – 3.12 (m, 2H, C(5)H_2), 3.04 – 2.90 (m, 2H, C(4)H_2), 2.62 (s, 6H, 2×C(7)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.3, 128.9, 128.7, 126.8, 53.3, 51.0, 29.6; **IR** (thin film, ν_{max}/cm^{-1}) 3136, 2849, 1455, 1060, 853, 752; **HRMS** (ESI, *m/z*) *Mass not found.*

2-Phenyl-*N*-(*p*-tolyl)ethane-1-sulfinamide (37ah):



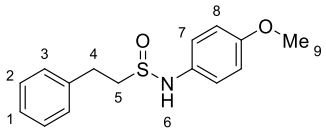
Prepared according to **General Procedure I-2** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *p*-toluidine (23.6 mg, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (40 – 50% EtOAc in Petrol) afforded sulfinamide **37ah** as an off-white solid (15.5 mg, 0.06 mmol, 30%).

Also prepared according to a modified **General Procedure I-2**, where the reaction mixture was irradiated for 18 h, using *N*-sulfinylmesidine (36.3 mg, 0.2 mmol, 1.0 equiv.) instead of *N*-sulfinyltritylamine. Purification by silica gel flash column chromatography (5 – 10% EtOAc in CH_2Cl_2) afforded sulfinamide **37ah** as an off-white solid (26.2 mg, 0.1 mmol, 50%).

Also prepared according to a modified **General Procedure I-2**, where the reaction mixture was pre-heated at 60 °C for 24 h and irradiated for 18 h, using *N*-sulfinyl-4-cyano-2,6-dimethylaniline **38b** (38.4 mg, 0.2 mmol, 1.0 equiv.) instead of *N*-sulfinyltritylamine. Purification by silica gel flash column chromatography (5 – 10% EtOAc in CH_2Cl_2) afforded sulfinamide **37ah** as an off-white solid (22.2 mg, 0.09 mmol, 43%).

R_f = 0.27 (50% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 2H, Ar*H*), 7.29 – 7.23 (m, 1H, Ar*H*), 7.24 – 7.16 (m, 2H, Ar*H*), 7.06 (d, *J* = 8.1 Hz, 2H, Ar*H*), 6.98 – 6.90 (m, 2H, Ar*H*), 6.77 (br. s, 1H, N(6)*H*), 3.33 – 3.20 (m, 2H, C(5)H_2), 3.10 – 3.02 (m, 2H, C(4)H_2), 2.30 (s, 3H, C(9)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.7, 138.5, 133.2, 130.1, 128.9, 128.7, 126.9, 119.3, 57.0, 29.6, 20.8; **LRMS** (ESI, *m/z*): 260.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{15}H_{18}NOS$ $[M+H]^+$ = 260.1104, Found = 260.1115; **IR** (thin film, ν_{max}/cm^{-1}) 3152, 2921, 1515, 1055, 1039, 825; **Melting point** = 138 – 140 °C.

***N*-(4-Methoxyphenyl)-2-phenylethane-1-sulfinamide (37ai)**:



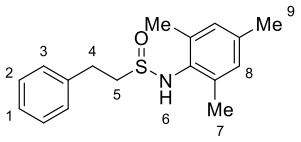
Prepared according to **General Procedure I-2** using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *p*-anisidine (27.1 mg, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (20% EtOAc in CH_2Cl_2) afforded sulfinamide **37ai** as an off-white solid (24.4 mg, 0.09 mmol, 44%).

R_f = 0.18 (20% EtOAc in CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 2H, Ar*H*), 7.30 – 7.26 (m, 1H, Ar*H*), 7.26 – 7.19 (m, 2H, Ar*H*), 7.06 – 6.99 (m, 2H, Ar*H*), 6.87

– 6.78 (m, 2H, Ar*H*), 6.49 (br. s, 1H, N(6)*H*), 3.79 (s, 3H, C(9)H_3), 3.31 – 3.16 (m, 2H, C(5)H_2), 3.13 – 3.02 (m, 2H, C(4)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.7, 138.8, 133.6, 128.9, 128.7, 126.9, 122.4, 114.8, 56.8, 55.6, 29.6; **LRMS** (ESI, *m/z*): 298.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{15}H_{18}NO_2SNa$ $[M+Na]^+$ = 298.0872, Found = 298.0880; **IR** (thin film, ν_{max}/cm^{-1}) 3156, 2934, 1511, 1244, 1050, 1037; **Melting point** = 98 – 100 °C.

8.4.5 Side-Product Characterisation

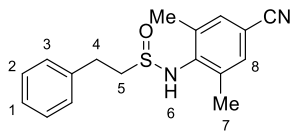
***N*-Mesityl-2-phenylethane-1-sulfinamide (39a)**:



Prepared according to a modified **General Procedure I-2**, where the reaction mixture was irradiated for 18 h, using hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine (11.9 mg, 0.04 mmol, 20 mol%), *N*-sulfinylmesidine **PC5** (36.3 mg, 0.2 mmol, 1.0 equiv.) and *p*-toluidine (23.6 mg, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (0 – 10% EtOAc in CH_2Cl_2) afforded sulfinamide **39a** as an off-white solid (17.4 mg, 0.06 mmol, 30%).

R_f = 0.36 (100% CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.23 (m, 5H, Ar*H*), 6.87 (s, 2H, Ar*H*), 5.31 (s, 1H, N(6)*H*), 3.33 – 3.11 (m, 4H, C(4)H_2 and C(5)H_2), 2.28 (s, 6H, 2×C(7)H_3), 2.25 (s, 3H, C(9)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.0, 135.9, 134.8, 133.7, 129.6, 129.0, 128.7, 126.9, 58.1, 29.2, 20.9, 19.1; **LRMS** (ESI, *m/z*): 310.2 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{21}NOSNa$ $[M+Na]^+$ = 310.1236, Found = 310.1236; **IR** (thin film, ν_{max}/cm^{-1}) 3152, 2921, 1515, 1055, 1039, 825; **Melting point** = 116 – 118 °C.

***N*-(4-Cyano-2,6-dimethylphenyl)-2-phenylethane-1-sulfinamide (39b)**:



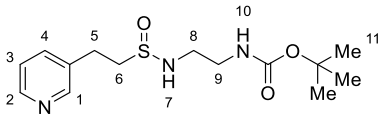
Prepared according to a modified **General Procedure I-2**, where the reaction mixture was pre-heated at 60 °C for 24 h and irradiated for 18 h, using hydrocinnamic acid (30.0 mg,

0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%), *N*-sulfinyl-4-cyano-2,6-dimethylaniline (38.4 mg, 0.2 mmol, 1.0 equiv.) and *p*-toluidine (23.6 mg, 0.22 mmol, 1.1 equiv.). Purification by silica gel flash column chromatography (0 – 10% EtOAc in CH_2Cl_2) afforded sulfinamide **39b** as an off-white solid (12.0 mg, 0.04 mmol, 21%).

R_f = 0.40 (100% CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 7H, Ar*H*), 5.58 (br. s, 1H, N(9)*H*), 3.40 – 3.11 (m, 4H, C(4)H_2 and C(5)H_2), 2.32 (s, 6H, 2×C(7)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.3, 138.5, 134.1, 132.6, 129.1, 128.7, 127.2, 118.9, 109.2, 58.1, 28.8, 19.1; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{18}N_2OSNa$ $[M+Na]^+$ = 321.1032, Found = 321.1034; **IR** (thin film, ν_{max}/cm^{-1}) 3391, 3029, 1633, 1491, 1181, 1041; **Melting point** = 86 °C (decomp.).

8.4.6 Carboxylic Acid Scope

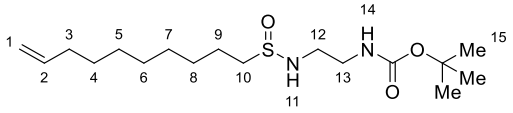
***tert*-Butyl (2-(((2-(pyridin-3-yl)ethyl)sulfinyl)amino)ethyl)carbamate (37aj)**:



Prepared according to **General Procedure I-1** using 3-(pyridin-3-yl)propanoic acid (30.2 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (10 – 15% MeOH in EtOAc) afforded sulfinamide **37aj** as a colourless oil (6.1 mg, 0.02 mmol, 10%).

R_f = 0.18 (15% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 – 8.46 (m, 2H, Ar*H*), 7.56 (dt, *J* = 7.8, 1.9 Hz, 1H, Ar*H*), 7.25 – 7.22 (m, 1H, Ar*H*), 5.12 (s, 1H, N(10)*H*), 4.33 (s, 1H, N(7)*H*), 3.38 – 3.17 (m, 4H, C(8)H_2 & C(9)H_2), 3.08 – 2.95 (m, *J* = 5.5 Hz, 4H, C(5)H_2 & C(6)H_2), 1.43 (s, 9H, 3×C(11)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.5, 150.0, 148.4, 136.2, 134.4, 123.7, 87.0, 55.9, 44.0, 41.4, 28.5, 27.0; **LRMS** (ESI, *m/z*): 336.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{23}N_3O_3SNa$ $[M+Na]^+$ = 336.1352, Found = 336.1351; **IR** (thin film, ν_{max}/cm^{-1}) 3316, 2942, 1701, 1525, 1172, 1047.

***tert*-Butyl (2-((dec-9-en-1-ylsulfinyl)amino)ethyl)carbamate (37al)**:

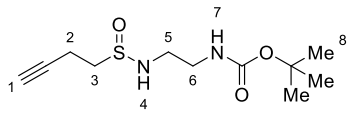


Prepared according to **General Procedure I-1** using 10-undecenoic acid (36.9 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine

(34.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (100% EtOAc) afforded sulfinamide **37al** as a colourless oil (44.0 mg, 0.13 mmol, 63%).

R_f = 0.23 (100% EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.78 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H, C(2)*H*), 5.27 (s, 1H, N(14)*H*), 4.96 (dq, *J* = 17.1, 1.6 Hz, 1H, C(1)*H*H), 4.90 (ddt, *J* = 10.2, 2.2, 1.2 Hz, 1H, C(1)H*H*), 4.31 (s, 1H, N(11)*H*), 3.35 – 3.14 (m, 4H, C(12)H_2 & C(13)H_2), 2.79 – 2.65 (m, 2H, C(10)H_2), 2.05 – 1.97 (m, 2H, C(3)H_2), 1.69 – 1.58 (m, 2H, C(9)H_2), 1.48 – 1.20 (m, 19H, C(4)H_2, C(5)H_2, C(6)H_2, C(7)H_2, C(8)H_2 & 3×C(15)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.4, 139.2, 114.3, 79.6, 55.4, 43.8, 41.4, 33.8, 29.3, 29.3, 29.1, 28.9, 28.7, 28.5, 23.3; **LRMS** (ESI, *m/z*): 347.2 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{35}N_2O_3S$ $[M+H]^+$ = 347.2363, Found = 347.2370; **IR** (thin film, ν_{max}/cm^{-1}) 3294, 2929, 1715, 1524, 1175, 1046.

***tert*-Butyl (2-((but-3-yn-1-ylsulfinyl)amino)ethyl)carbamate (37am)**:

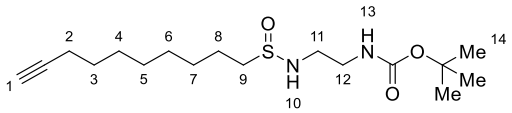


Prepared according to **General Procedure I-1** using 4-pentynoic acid (19.6 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (0 – 2% MeOH in EtOAc) afforded sulfinamide **37am** as a colourless oil (20.4 mg, 0.08 mmol, 39%).

R_f = 0.23 (2% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.21 (br. s, 1H, N(7)*H*), 4.53 (br. s, 1H, N(4)*H*), 3.33 – 3.16 (m, 4H, C(8)H_2 and C(9)H_2), 2.96 – 2.89 (m, 2H,

C(3)H_2), 2.65 – 2.48 (m, 2H, C(2)H_2), 2.06 (t, J = 2.7 Hz, 1H, C(1)H), 1.43 (s, 9H, 3×C(8)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.5, 81.0, 79.8, 70.6, 53.1, 43.9, 41.4, 28.5, 13.4; **LRMS** (ESI, *m/z*): 283.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{11}H_{20}N_2O_3SNa$ $[M+Na]^+$ = 283.1087, Found = 283.1089; **IR** (thin film, ν_{max}/cm^{-1}) 3305, 2984, 1707, 1530, 1280, 1175.

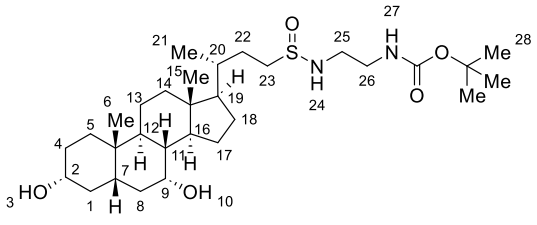
***tert*-Butyl (2-((dec-9-yn-1-ylsulfinyl)amino)ethyl)carbamate (37an)**:



Prepared according to **General Procedure I-1** using 10-undecynoic acid (36.5 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (0 – 2% MeOH in EtOAc) afforded sulfinamide **37an** as a blue oil (51.0 mg, 0.15 mmol, 74%).

R_f = 0.21 (100% EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.29 (s, 1H, N(13)H), 4.36 (s, 1H, N(10)H), 3.28 – 3.11 (m, 4H, C(11)H_2 & C(12)H_2), 2.71 (td, J = 7.4, 4.0 Hz, 2H, C(9)H_2), 2.14 (td, J = 7.0, 2.6 Hz, 2H, C(2)H_2), 1.91 (t, J = 2.6 Hz, 1H, C(1)H), 1.62 (p, J = 7.5 Hz, 2H, C(8)H_2), 1.53 – 1.24 (m, 19H, C(3)H_2, C(4)H_2, C(5)H_2, C(6)H_2, C(7)H_2 & 3×C(14)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.4, 84.7, 79.5, 68.3, 55.3, 43.7, 41.3, 29.2, 28.9, 28.7, 28.6, 28.5, 28.4, 23.3, 18.4; **LRMS** (ESI, *m/z*): 367.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{32}N_2O_3SNa$ $[M+Na]^+$ = 367.2026, Found = 367.2037; **IR** (thin film, ν_{max}/cm^{-1}) 3296, 2932, 1699, 1526, 1172, 1047.

***tert*-Butyl (2-((((*R*)-3-((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3,7-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)butyl)sulfinyl)amino)ethyl)carbamate (37ao)**:

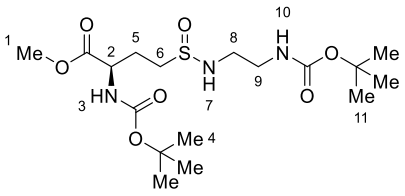


Prepared according to **General Procedure I-1** using chenodeoxycholic acid (78.5 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in CH_2Cl_2 (4.0 mL). Purification by silica gel flash column chromatography (5 – 10% MeOH in EtOAc) afforded sulfinamide **37ao** as a white solid (43.1 mg, 0.09 mmol, 44%).

R_f = 0.13 (5% MeOH in EtOAc); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.25 (s, 1H, N(17)*H*), 4.23 (s, 1H, N(24)*H*), 3.88 – 3.81 (m, 1H, C(9)*H*), 3.50 – 3.40 (m, 1H, C(2)*H*), 3.38 – 3.15 (m, 4H, C(25)H_2 & C(26)H_2), 2.86 – 2.73 (m, 1H, C(23)*H*H), 2.73 – 2.60 (m, 1H, C(23)H*H*), 2.20 (q, *J* = 12.4 Hz, 1H, C(1)*H*), 2.04 – 1.59 (m, 11H, C(1)H*H*, O(3)*H*, C(4)*H*H, C(5)*H*H, C(8)*H*H, O(10)*H*, C(14)*H*H, C(16)*H*, C(17)*H*H, C(18)*H*H & C(22)*H*H), 1.59 – 1.21 (m, 19H, C(4)*H*H, C(7)*H*, C(8)*H*H, C(11)*H*H, C(12)*H*, C(13)H_2, C(17)H*H*, C(20)*H*, C(22)H*H* & 3×C(28)H_3)), 1.21 – 1.07 (m, 3H, C(14)H*H*, C(18)H*H* & C(19)*H*), 1.01 – 0.92 (m, 4H, C(5)H*H* & C(21)H_3), 0.89 (s, 3H, C(6)H_3), 0.66 (d, *J* = 2.6 Hz, 3H, C(15)H_3); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.5, 79.7, 72.1, 68.53 *(diastereomer A)*, 68.52 *(diastereomer B)*, 55.87 *(diastereomer A)*, 55.85 *(diastereomer B)*, 52.7 *(diastereomer A)*, 52.6 *(diastereomer B)*, 50.6, 43.9 *(diastereomer A)*, 43.8 *(diastereomer B)*, 42.9, 41.64 *(diastereomer A)*, 41.62 *(diastereomer B)*, 41.4, 40.0, 39.8, 39.6, 35.48 *(diastereomer A)*,

35.47 *(diastereomer B)*, 35.4 *(diastereomer A)*, 35.3 *(diastereomer B)*, 35.2, 34.83 *(diastereomer A)*, 34.82 *(diastereomer B)*, 33.0, 30.8, 29.4 *(diastereomer A)*, 29.1 *(diastereomer B)*, 28.6, 28.4, 23.8, 22.9, 20.7, 18.7, 11.93 *(diastereomer A)*, 11.92 *(diastereomer B) (18 carbon signals are unresolved from the corresponding signals in the other diastereomer)*; **LRMS** (ESI, *m/z*): 577.2 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{30}H_{54}N_2O_5SNa$ $[M+Na]^+$ = 577.3646, Found = 577.3659; **IR** (thin film, ν_{max}/cm^{-1}) 3361, 2931, 1696, 1171, 910, 734.

Methyl (2*R*)-2-((*tert*-butoxycarbonyl)amino)-4-(((2-((*tert*-butoxycarbonyl)amino)ethyl)amino)sulfinyl)butanoate (37ap):

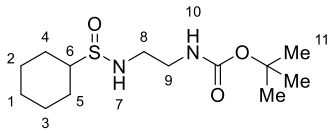


Prepared according to **General Procedure I-1** using Boc-Glu-OMe (52.3 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (0 – 2% MeOH in EtOAc) afforded sulfinamide **37ap** as a colourless oil (47.6 mg, 0.11 mmol, 56%, 1:1 mixture of inseparable diastereomers).

R_f = 0.25 (100% EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.50 – 5.21 (m, 2H, N(3)*H* and N(10)*H*), 4.57 (d, *J* = 24.6 Hz, 1H, N(7)*H*), 4.48 – 4.31 (m, 1H, C(2)*H*), 3.74 (s, 3H, C(1)H_3), 3.39 – 3.12 (m, 4H, C(8)H_2 and C(9)H_2), 2.93 – 2.72 (m, 2H, C(6)H_2), 2.15 (dq, *J* = 25.7, 8.2 Hz, 1H, C(5)*H*H), 2.06 – 1.89 (m, 1H, C(5)H*H*), 1.44 – 1.39 (m, 18H, 3×C(4)H_3 and 3×C(11)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.4 *(diastereomer A)*, 172.3 *(diastereomer B)*, 156.4, 155.7 *(diastereomer A)*, 155.6 *(diastereomer B)*, 80.5

(diastereomer A), 80.4 *(diastereomer B)*, 79.6, 52.7, 52.4, 51.1 *(diastereomer A)*, 51.0 *(diastereomer B)*, 44.1 *(diastereomer A)*, 43.9 *(diastereomer B)*, 41.4, 28.5, 28.4, 26.8 (diastereomer A), 26.5 (diastereomer B); **LRMS** (ESI, *m/z*): 446.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{33}N_3O_7SNa$ $[M+Na]^+$ = 446.1931, Found = 446.1932; **IR** (thin film, ν_{max}/cm^{-1}) 3351, 2984, 1714, 1529, 1368, 1174.

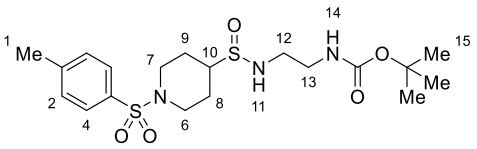
***tert*-Butyl (2-((cyclohexylsulfinyl)amino)ethyl)carbamate (37aq)**:



Prepared according to **General Procedure I-1** using cyclohexanecarboxylic acid (25.6 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (0 – 5% MeOH in EtOAc) afforded sulfinamide **37aq** as a white solid (43.4 mg, 0.15 mmol, 75%).

R_f = 0.26 (5% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.28 (br. s, 1H, N(10)*H*), 4.13 (br. s, 1H, N(7)*H*), 3.40 – 3.13 (m, 4H, C(8)H_2 and C(9)H_2), 2.53 (tt, *J* = 11.2, 3.7 Hz, 1H, C(6)*H*), 2.08 – 1.99 (m, 1H, C(4/5)*H*H), 1.99 – 1.90 (m, 1H, C(5/4)*H*H), 1.90 – 1.75 (m, 2H, C(2/3)*H*H and C(3/2)*H*H), 1.69 – 1.61 (m, 1H, C(1)*H*H), 1.48 – 1.16 (m, 14H, C(1)H*H*, C(2)H*H*, C(3)H*H*, C(4)H*H*, C(5)H*H* and 3×C(11)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.4, 79.5, 62.0, 44.4, 41.4, 28.5, 26.4, 26.2, 25.6, 25.4, 25.3 *(note: for cyclohexane ring, 6 peaks were found instead of 4 due to the loss of symmetry caused by chiral sulfur atom)*; **LRMS** (ESI, *m/z*): 313.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{13}H_{26}N_2O_3SNa$ $[M+Na]^+$ = 313.1556, Found = 313.1565; **IR** (thin film, ν_{max}/cm^{-1}) 3259, 2933, 1695, 1528, 1175, 1041; **Melting point** = 101 – 103 °C.

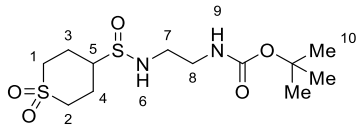
***tert*-Butyl (2-(((1-tosylpiperidin-4-yl)sulfinyl)amino)ethyl)carbamate (37ar)**:



Prepared according to **General Procedure I-1** using 1-tosylpiperidine-4-carboxylic acid (56.7 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (0 – 2% MeOH in EtOAc) afforded sulfinamide **37ar** as a white solid (66.0 mg, 0.15 mmol, 74%).

R_f = 0.23 (2% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.31 (d, *J* = 7.9 Hz, 2H, Ar*H*), 5.17 (br. s, 1H, N(14)*H*), 4.30 (br. t, *J* = 5.6 Hz, 1H, N(11)*H*), 3.78 – 3.64 (m, 2H, C(6)*H*H and C(7)*H*H), 3.30 – 3.08 (m, 4H, C(12)H_2 and C(13)H_2), 2.52 – 2.36 (m, 6H, C(1)H_3, C(6)H*H*, C(7)H*H* and C(10)*H*), 2.11 – 2.01 (m, 1H, C(8/9)*H*H), 2.00 – 1.91 (m, 1H, C(9/8)*H*H), 1.82 – 1.61 (m, 2H, C(8)H*H* and C(9)H*H*), 1.39 (s, 9H, 3×C(15)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.5, 143.9, 133.0, 129.9, 127.7, 79.7, 58.9, 45.4, 45.3, 43.9, 41.3, 28.5, 25.7, 25.3, 21.6 *(note: for piperidine ring, 5 peaks were found instead of 3 due to the loss of symmetry caused by chiral sulfur atom)*; **LRMS** (ESI, *m/z*): 468.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{19}H_{31}N_3O_5S_2Na$ $[M+Na]^+$ = 468.1597, Found = 468.1601; **IR** (thin film, ν_{max}/cm^{-1}) 3296, 2980, 1704, 1524, 1164, 1056; **Melting point** = 161 – 163 °C.

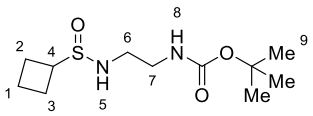
***tert*-Butyl (2-(((1,1-dioxidotetrahydro-2*H*-thiopyran-4-yl)sulfinyl)amino)ethyl)carbamate (37as)**:



Prepared according to **General Procedure I-1** using tetrahydro-2*H*-thiopyran-4-carboxylic acid 1,1-dioxide (35.6 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (5 – 10% MeOH in EtOAc) afforded sulfinamide **37as** as a colourless oil (19.0 mg, 0.06 mmol, 28%).

R_f = 0.11 (5% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.05 (s, 1H, N(9)*H*), 4.43 (t, *J* = 5.6 Hz, 1H, N(6)*H*), 3.36 – 3.11 (m, 6H, C(1)*H*H, C(2)*H*H, C(7)H_2 & C(8)H_2), 3.08 – 2.96 (m, 2H, C(1)H*H* & C(2)H*H*), 2.75 (tt, *J* = 9.9, 3.5 Hz, 1H, C(5)*H*), 2.55 – 2.42 (m, 2H, C(3)*H*H & C(4)*H*H), 2.42 – 2.20 (m, 2H, C(3)H*H* & C(4)H*H*), 1.43 (s, 9H, 3×C(10)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.7, 80.1, 58.2, 49.8, 44.1, 41.4, 28.5, 24.8, 24.4 *(note: for sultone ring, 4 peaks were found instead of 3 due to the loss of symmetry caused by chiral sulfur atom)*; **LRMS** (ESI, *m/z*): 363.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{12}H_{24}N_2O_5S_2Na$ $[M+Na]^+$ = 363.1019, Found = 363.1025; **IR** (thin film, ν_{max}/cm^{-1}) 3356, 2985, 1702, 1524, 1294, 1122.

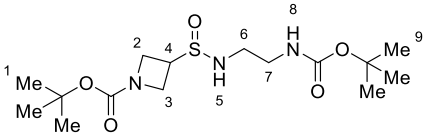
***tert*-Butyl (2-((cyclobutylsulfinyl)amino)ethyl)carbamate (37at)**:



Prepared according to **General Procedure I-1** using cyclobutanecarboxylic acid (19.1 µL, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (0 – 2% MeOH in EtOAc) afforded sulfinamide **37at** as a colourless oil (39.6 mg, 0.15 mmol, 75%).

R_f = 0.22 (2% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.24 (s, 1H, N(8)*H*), 3.97 (t, *J* = 5.9 Hz, 1H, N(5)*H*), 3.49 (p, *J* = 8.1 Hz, 1H, C(4)*H*), 3.33 – 3.10 (m, 4H, C(6)H_2 & C(7)H_2), 2.59 – 2.45 (m, 1H, C(2)*H*H), 2.30 – 2.08 (m, 3H, C(2)H*H* & C(1)H_2), 2.08 – 1.88 (m, 2H, C(3)H_2), 1.41 (s, 9H, 3×C(9)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.4, 79.6, 56.0, 44.4, 41.4, 28.5, 23.0, 20.8, 17.7 *(note: for cyclobutyl ring, 4 peaks were found instead of 3 due to the loss of symmetry caused by chiral sulfur atom)*; **LRMS** (ESI, *m/z*): 285.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{11}H_{22}N_2O_3SNa$ $[M+Na]^+$ = 285.1243, Found = 285.1237; **IR** (thin film, ν_{max}/cm^{-1}) 3264, 2979, 1694, 1525, 1171, 1048.

***tert*-Butyl 3-(((2-((*tert*-butoxycarbonyl)amino)ethyl)amino)sulfinyl)azetidine-1-carboxylate (37au)**:

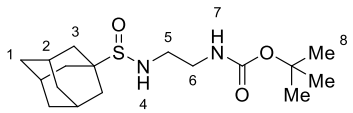


Prepared according to **General Procedure I-1** using 1-(*tert*-butoxycarbonyl)azetidine-3-carboxylic acid (40.2 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg,

0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in CH_2Cl_2 (4.0 mL). Purification by silica gel flash column chromatography (2 – 5% MeOH in EtOAc) afforded sulfinamide **37au** as a colourless oil (49.9 mg, 0.14 mmol, 69%).

R_f = 0.17 (2% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.20 (t, *J* = 5.5 Hz, 1H, N(8)*H*), 4.50 (t, *J* = 5.6 Hz, 1H, N(5)*H*), 4.24 (dd, *J* = 9.6, 5.2 Hz, 1H, C(2)*H*H), 4.17 – 4.05 (m, 2H, C(2)H*H* & C(3)*H*H), 3.94 (dd, *J* = 9.8, 5.3 Hz, 1H, C(3)H*H*), 3.63 (tt, *J* = 8.3, 5.2 Hz, 1H, C(4)*H*), 3.33 – 3.10 (m, 4H, C(6)H_2 & C(7)H_2), 1.42 (s, 9H, 3×C(1/9)H_3), 1.41 (s, 9H, 3×C(9/1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.6, 156.0, 80.4, 79.8, 50.2, 49.7 (br.), 44.1, 41.3, 28.5, 28.4; **LRMS** (ESI, *m/z*): 386.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{15}H_{29}N_3O_5SNa$ $[M+Na]^+$ = 386.1720, Found = 386.1716; **IR** (thin film, ν_{max}/cm^{-1}) 3335, 2977, 1702, 1526, 1394, 1167.

***tert*-Butyl (2-((((3*s*,5*s*,7*s*)-adamantan-1-yl)sulfinyl)amino)ethyl)carbamate (3av)**:

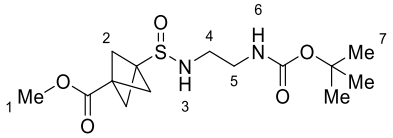


Prepared according to **General Procedure I-1** using 1-adamantanecarboxylic acid (36.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (2.0 mL) and CH_2Cl_2 (2.0 mL). Purification by silica gel flash column chromatography (0 – 2% MeOH in EtOAc) afforded sulfinamide **3av** as a colourless oil (45.3 mg, 0.13 mmol, 66%).

R_f = 0.24 (2% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.17 (br. s, 1H, N(7)*H*), 3.66 (br. t, *J* = 5.7 Hz, 1H, N(4)*H*), 3.42 – 3.18 (m, 4H, C(5)H_2 and C(6)H_2), 2.14 (s, 3H,

3×C(1)*H*), 1.91 – 1.63 (m, 12H, 3×C(3)H_2 and 3×C(3)H_2), 1.42 (s, 9H, 3×C(8)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.2, 79.4, 57.6, 46.2, 41.5, 36.4, 34.8, 28.6, 28.4; **LRMS** (ESI, *m/z*): 365.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{17}H_{30}N_2O_3SNa$ $[M+Na]^+$ = 365.1869, Found = 365.1885; **IR** (thin film, ν_{max}/cm^{-1}) 3307, 2910, 1697, 1526, 1173, 1034.

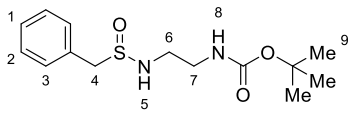
Methyl 3-(((2-((*tert*-butoxycarbonyl)amino)ethyl)amino)sulfinyl)bicyclo[1.1.1]pentane-1-carboxylate (37aw):



Prepared according to **General Procedure I-1** using 3-(methoxycarbonyl)bicyclo[1.1.1]pentane-1-carboxylic acid (34.0 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (2 – 5% MeOH in EtOAc) afforded sulfinamide **37aw** as a colourless oil (42.0 mg, 0.13 mmol, 63%).

R_f = 0.29 (5% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.15 (br. s, 1H, N(6)*H*), 4.11 (br. t, J = 5.6 Hz, 1H, N(3)*H*), 3.70 (s, 3H, C(1)H_3), 3.42 – 3.19 (m, 4H, C(4)H_2 and C(5)H_2), 2.31 (s, 6H, 3×C(2)H_2), 1.43 (s, 9H, 3×C(7)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.0, 156.5, 79.8, 52.2, 51.8, 50.9, 45.3, 41.5, 37.1, 28.5; **LRMS** (ESI, *m/z*): 355.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{24}N_2O_5SNa$ $[M+Na]^+$ = 355.1298, Found = 355.1304; **IR** (thin film, ν_{max}/cm^{-1}) 3304, 2978, 1714, 1523, 1211, 1167.

***tert*-Butyl (2-((benzylsulfinyl)amino)ethyl)carbamatecarbamate (37ax)**:

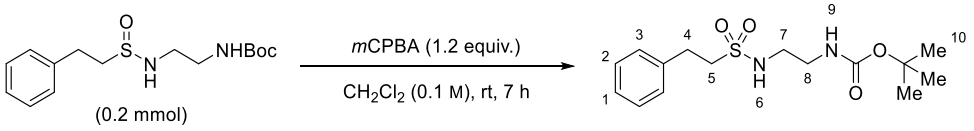


Prepared according to **General Procedure I-1** using phenylacetic acid (27.2 mg, 0.2 mmol, 1.0 equiv.), *N*-sulfinyltritylamine (61.1 mg, 0.2 mmol, 1.0 equiv.), 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) and *N*-Boc-ethylenediamine (34.8 µL, 0.22 mmol, 1.1 equiv.) in MeCN (4.0 mL). Purification by silica gel flash column chromatography (100% EtOAc) afforded sulfinamide **37ax** as a colourless oil (16.0 mg, 0.05 mmol, 27%).

R_f = 0.2 (100% EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.27 (m, 5H, Ar*H*), 4.97 (br. s, 1H, N(8)*H*), 4.10 – 3.88 (m, 3H, C(4)H_2 and N(5)*H*), 3.31 – 3.10 (m, 4H, C(6)H_2 and C(7)H_2), 1.43 (s, 9H, 3×C(9)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.3, 130.6, 129.4, 129.0, 128.5, 79.6, 61.1, 44.2, 41.4, 28.5; **LRMS** (ESI, *m/z*): 321.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{22}N_2O_3S$ $[M+Na]^+$ = 321.1243, Found = 321.1241; **IR** (thin film, ν_{max}/cm^{-1}) 3277, 2936, 1711, 1456, 1175, 1050.

8.4.7 Derivatisations

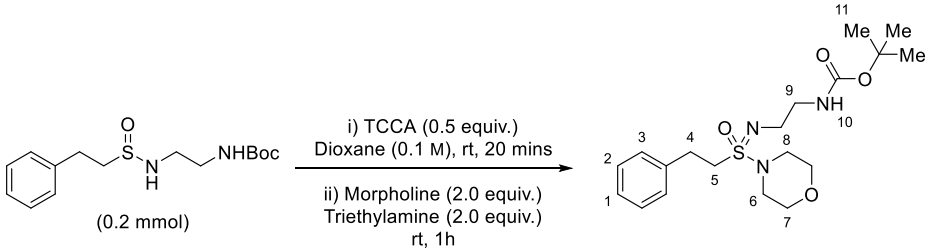
***tert*-Butyl (2-((2-phenylethyl)sulfonamido)ethyl)carbamate (39)**:



tert-Butyl (2-((phenethylsulfinyl)amino)ethyl)carbamate **37n** (62.5 mg, 0.2 mmol, 1.0 equiv.) was added to a round-bottom flask, and dissolved in CH_2Cl_2 (2.0 mL). *m*-CPBA (60% by weight) (0.24 mmol, 69.0 mg) was then added, and the reaction was stirred at rt for 7 h. After completion of the reaction (determined by TLC), the reaction mixture was neutralized with saturated aq. $NaHCO_3$ and extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude reaction mixture was purified by silica gel flash column chromatography (40% EtOAc in Petrol) to afford sulfonamide **39** as a colourless oil (48.6 mg, 0.15 mmol, 74%).

R_f = 0.24 (40% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 2H, Ar*H*), 7.26 – 7.19 (m, 3H, Ar*H*), 5.14 – 4.97 (br. m, 2H, N(6)*H* and N(9)*H*), 3.33 – 3.20 (m, 4H, C(5)H_2 and C(8)H_2), 3.20 – 3.05 (m, 4H, C(4)H_2 and C(7)H_2), 1.42 (s, 9H, 3×C(9)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.6, 138.0, 129.0, 128.5, 127.1, 80.0, 53.9, 43.7, 40.9, 30.0, 28.5; **LRMS** (ESI, *m/z*): 351.1 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{15}H_{24}N_2O_4S$ $[M+Na]^+$ = 351.1349, Found = 351.1351; **IR** (thin film, ν_{max}/cm^{-1}) 3299, 3030, 1695, 1521, 1320, 1149.

***tert*-Butyl (2-((morpholino(oxo)(phenethyl)-λ^6-sulfaneylidene)amino)ethyl)carbamate (40a)**:

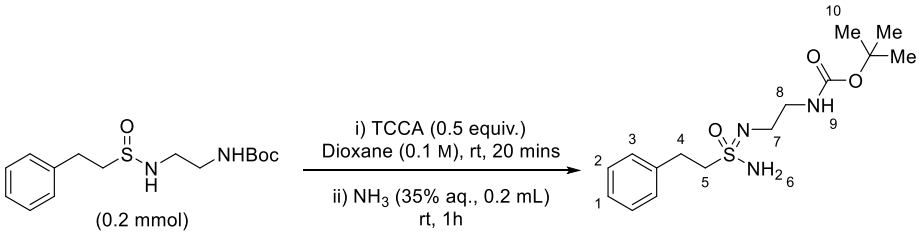


tert-Butyl (2-((phenethylsulfinyl)amino)ethyl)carbamate **37n** (62.5 mg, 0.2 mmol, 1.0 equiv.) was weighed into an oven-dried 10 mL reaction vial, sealed, evacuated and back-filled with N_2 (×3). Dry THF (2.0 mL) was then added. TCCA (23.2 mg, 0.1 mmol, 0.5 equiv.) was added under a cone of nitrogen, the vial re-sealed and the reaction was stirred at rt for 20 mins. Morpholine (35 µL, 0.4 mmol, 2.0 equiv.) and triethylamine (56 µL, 0.4 mmol, 2.0 equiv.) were then added and the reaction was stirred at rt for 1 h. After completion of the reaction (determined by TLC), water (20 mL) was added to the reaction mixture and the product was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude reaction mixture was purified by silica gel flash column chromatography (100% EtOAc) to afford sulfonimidamide **40a** as a colourless oil (58.9 mg, 0.15 mmol, 74%).

R_f = 0.2 (100% EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 2H, Ar*H*), 7.25 – 7.19 (m, 3H, Ar*H*), 5.04 (br. s, 1H, N(10)*H*), 3.70 (t, *J* = 4.7 Hz, 4H, 2×C(7)H_2), 3.29 – 3.07 (m, 10H, C(4)H_2, C(5)*H*H, 2×C(6)H_2, C(8)*H*H and C(9)H_2), 3.07 – 2.94 (m, 2H, C(5)H*H* and C(8)H*H*), 1.43 (s, 9H, 3×C(11)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.1, 138.3, 128.9, 128.5, 127.0, 79.1, 66.8, 50.5, 46.7, 42.5, 41.8, 29.5, 28.5; **LRMS** (ESI, *m/z*):

398.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{19}H_{32}N_3O_4S$ $[M+Na]^+$ = 398.2108, Found = 398.2112; **IR** (thin film, ν_{max}/cm^{-1}) 3367, 2976, 1709, 1510, 1255, 1169, 937.

***tert*-Butyl (2-((amino(oxo)(phenethyl)-λ^6-sulfaneylidene)amino)ethyl)carbamate (40b)**:

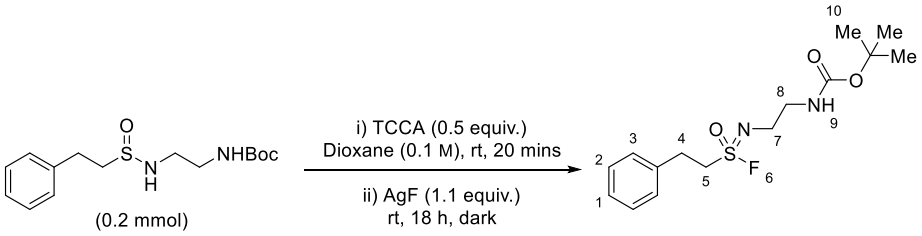


tert-Butyl (2-((phenethylsulfinyl)amino)ethyl)carbamate **37n** (62.5 mg, 0.2 mmol, 1.0 equiv.) was weighed into an oven-dried 10 mL reaction vial, sealed, evacuated and back-filled with N_2 (×3). Dry THF (2.0 mL) was then added. TCCA (23.2 mg, 0.1 mmol, 0.5 equiv.) was added under a cone of nitrogen, the vial re-sealed and the reaction was stirred at rt for 20 mins. 35% aq NH_3 (0.1 mL) was then added and the reaction was stirred at rt for 1 h. After completion of the reaction (determined by TLC), water (20 mL) was added and the product was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude reaction mixture was purified by silica gel flash column chromatography (100% EtOAc) to afford sulfonimidamide **40b** as a white solid (42.9 mg, 0.13 mmol, 65%).

R_f = 0.18 (100% EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H, Ar*H*), 7.25 – 7.19 (m, 3H, Ar*H*), 5.08 (br. s, 1H, N(9)*H*), 3.81 (br. s, 2H, N(6)H_2), 3.39 – 3.25 (m, 2H, C(5)H_2), 3.25 – 3.17 (m, 2H, C(8)H_2), 3.17 – 3.07 (m, 4H, C(4)H_2 and C(7)H_2), 1.41 (s, 9H, 3×C(10)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.5, 138.2, 129.0, 128.6, 127.0, 79.9, 54.9, 44.1, 41.0, 30.5, 28.5; **LRMS** (ESI, *m/z*): 328.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc.

for $C_{15}H_{26}N_3O_3S$ $[M+H]^+$ = 328.1689, Found = 328.1683; **IR** (thin film, ν_{max}/cm^{-1}) 3265, 3029, 1695, 1524, 1251, 1173; **Melting point** = 80 – 82 °C.

***tert*-Butyl (2-((fluoro(oxo)(phenethyl)-λ^6-sulfaneylidene)amino)ethyl)carbamate (41)**:

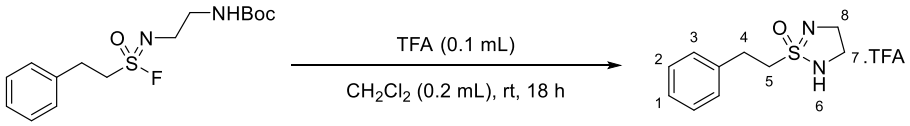


tert-Butyl (2-((phenethylsulfinyl)amino)ethyl)carbamate **37n** (62.5 mg, 0.2 mmol, 1.0 equiv.) was weighed into an oven-dried 10 mL reaction vial, sealed, evacuated and back-filled with N_2 (×3). Dry THF (2.0 mL) was then added. TCCA (23.2 mg, 0.1 mmol, 0.5 equiv.) was added under a cone of nitrogen, the vial re-sealed and the reaction was stirred at rt for 20 mins. AgF (27.9 mg, 0.22 mmol, 1.1 equiv.) was then added under a cone of nitrogen, the vial re-sealed and the reaction was stirred at rt 18 h (protected from light using aluminium foil). After completion of the reaction (determined by TLC), the reaction mixture was concentrated in vacuo, and the crude reaction mixture was purified by silica gel flash column chromatography (20% EtOAc in Petrol) to afford sulfonimidoyl fluoride **41** as a pale-yellow oil (37.3 mg, 0.11 mmol, 56%).

R_f = 0.19 (20% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 2H, Ar*H*), 7.29 – 7.25 (m, 1H, Ar*H*), 7.24 – 7.20 (m, 2H, Ar*H*), 4.79 (br. s, 1H, N(9)*H*), 3.60 (ddd, *J* = 10.5, 6.5, 2.0 Hz, 2H, C(5)H_2), 3.38 (dt, *J* = 8.6, 5.7 Hz, 2H, C(7)H_2), 3.33 – 3.18 (m, 4H, C(4)H_2 and C(8)H_2), 1.45 (s, 9H, 3×C(10)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.0, 136.8, 129.1, 128.5, 127.4, 79.4, 54.23 (d, *J* = 20.2 Hz), 43.2, 42.0, 30.2, 28.5; **^{19}F NMR** (377 MHz, $CDCl_3$) δ 76.29 (t, *J* = 8.1 Hz); **LRMS** (ESI, *m/z*): 353.0 $[M+Na]^+$; **HRMS**

(ESI, *m/z*): Calc. for $C_{15}H_{23}FN_2O_3SNa$ $[M+Na]^+$ = 353.1306, Found = 353.1315; **IR** (thin film, ν_{max}/cm^{-1}) 3367, 2935, 1711, 1515, 1329, 1173.

1-Phenethyl-3,4-dihydro-2*H*-1λ^6,2,5-thiadiazole 1-oxide trifluoroacetic acid salt (42):



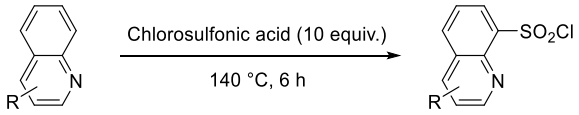
tert-Butyl (2-((fluoro(oxo)(phenethyl)-λ^6-sulfaneylidene)amino)ethyl)carbamate **41** (37.3 mg, 0.11 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (0.2 mL). TFA (0.1 mL) was then added and the reaction was stirred at rt for 18 h. After completion of the reaction (determined by TLC), the reaction mixture was concentrated in vacuo, and the crude reaction mixture was purified by silica gel flash column chromatography (5 – 15% MeOH in EtOAc) to afford the trifluoroacetic acid salt of sulfonimidamide **42** as a colourless gum (30.8 mg, 0.17 mmol, 84%).

R_f = 0.17 (15% MeOH in EtOAc); **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.34 – 7.25 (m, 4H, Ar*H*), 7.25 – 7.19 (m, 1H, Ar*H*), 3.40 – 3.32 (m, 4H, C(5)H_2 and C(8)H_2), 3.12 – 3.02 (m, 4H, C(4)H_2 and C(7)H_2) *(N(6)H signal not observed due to D-H exchange)*; **^{13}C NMR** (101 MHz, Methanol-d_4) δ 163.0, 139.6, 129.8, 129.5, 127.8, 118.2 (q, J = 292.9 Hz), 54.0, 41.5, 41.1, 30.7; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -76.95; **HRMS** (ESI, *m/z*): Calc. for $C_{12}H_{16}F_3N_2O_3S$ $[M+H]^+$ = 211.0900, Found = 211.0903; **IR** (thin film, ν_{max}/cm^{-1}) 3433, 2927, 1683, 1498, 1209, 1139.

8.5 Experimental for Chapter 5

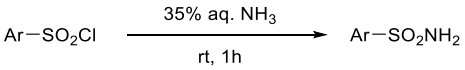
8.5.1 General Procedures

General Procedure J



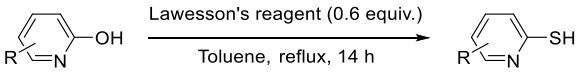
Quinoline (1 equiv.) was added to a round-bottom flask equipped with a condenser. Chlorosulfonic acid (10 equiv.) was then slowly added at 0 °C. The reaction was then heated to 140 °C for 6 h. Upon completion, the reaction was cooled to rt, and the reaction mixture was added dropwise to crushed ice. The precipitate was filtered and washed with ice water (×3) and dried under vacuum to give analytically pure product.

General Procedure K



Sulfonyl chloride (1.0 equiv.) was suspended in 35% aqueous ammonia solution (50 equiv.) at 0 °C, then warmed to rt and stirred for 1h. The excess ammonia was removed under reduced pressure, 10 mL water was added and the resulting precipitate was filtered and washed with water (×3) to give analytically pure product.

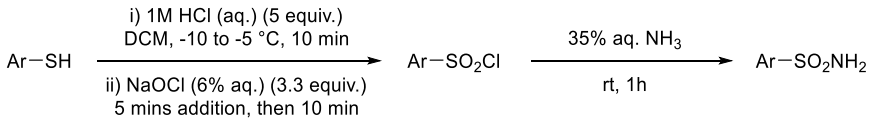
General Procedure L



2-Hydroxypyridine (1.0 equiv.) and Lawesson's reagent (0.6 equiv.) were added to a round-bottom flask equipped with a condenser. Toluene (0.17 M) was then added and the reaction stirred at reflux for 14 hours. The reaction was then cooled, and quenched with a

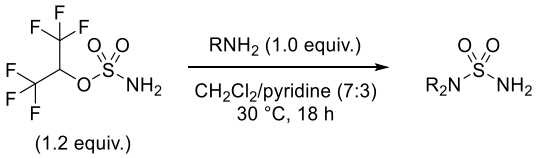
2.5 M aqueous NaOH solution (15 equiv.). The aqueous layer was separated and washed with diethyl ether (120 mL). The aqueous layer was then acidified using AcOH (120 mL), and extracted using CH_2Cl_2 (×3). The combined organic extracts were washed with brine (50 mL), dried using $MgSO_4$, filtered, and solvent removed in vacuo. Toluene (×2) was added and solvent removed in vacuo to remove residual AcOH. The product was used in the next step without further purification.

General Procedure M



CH_2Cl_2 (0.2 M) and 1.0 M aqueous HCl (5.0 equiv.) were added to a round-bottom flask, and the suspension was cooled to -5 to -10 °C. Heteroaryl thiol was then added and the resulting yellow mixture was stirred for 10 min, then NaOCl (6% solution, 4.2 equiv.) was added dropwise over 5.0 min. After the addition, the mixture was stirred for 10 min at the same temperature and decanted to a separatory funnel. The aqueous layer was washed twice with CH_2Cl_2 and the organic layers were combined and solvent removed in vacuo. The crude material was then suspended in 35% aqueous ammonia solution (25 equiv.) at 0 °C, then warmed to rt and stirred for 1h. Ammonia was then removed in vacuo and the precipitate filtered to give the crude product. The crude product was then purified by recrystallisation or silica gel flash column chromatography as required.

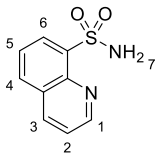
General Procedure N



Prepared according to a procedure described by Magolan and co-workers.[214] Amine (1.0 equiv.) was added to an oven-dried round-bottom flask, and dissolved in dry CH_2Cl_2 and pyridine (7:3, 0.1 M). HFIPS **(49)** (1.2 equiv.) was then added and the resulting reaction mixture was stirred at 30 °C for 18 h. The reaction mixture was then cooled, concentrated in vacuo and purified using silica gel flash column chromatography.

8.5.2 Intramolecular charge-transfer complex compounds

Quinoline-8-sulfonamide (44a):

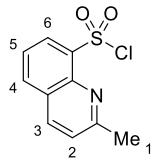


Prepared according to **General Procedure K** using 8-quinolinesulfonyl chloride (569 mg, 2.5 mmol, 1.0 equiv.) and 35% aqueous ammonia solution (12.5 mL, 125 mmol, 50 equiv.). Sulfonamide **44a** was isolated as a white solid (839 mg, 2.0 mmol, 81%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.08 (dd, *J* = 4.2, 1.8 Hz, 1H, Ar*H*), 8.56 (dd, *J* = 8.4, 1.7 Hz, 1H, Ar*H*), 8.29 (ddd, *J* = 10.7, 7.8, 1.4 Hz, 2H, Ar*H*), 7.79 – 7.69 (m, 2H, Ar*H*), 7.25 (s, 2H, N(7)H_2); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 151.2, 142.6, 139.3, 137.1, 133.0, 128.5, 128.4, 125.7, 122.4; **LRMS** (ESI, *m/z*): 209.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_9H_9N_2O_2S$ $[M+H]^+$ = 209.0379, Found = 209.0375.

Data is consistent with the literature.[241]

2-Methylquinoline-8-sulfonyl chloride (43b):



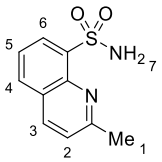
(**xx**)

Prepared according to **General Procedure J** using 2-methylquinoline (1.35 mL, 10 mmol, 1.0 equiv.) and chlorosulfonic acid (6.65 mL, 100 mmol, 10 equiv.). Sulfonyl chloride **43b** was isolated as an off-white solid (1.02 g, 4.2 mmol, 42%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.19 (d, *J* = 8.6 Hz, 1H, Ar*H*), 8.41 (d, *J* = 7.8 Hz, 2H, Ar*H*), 8.09 (d, *J* = 8.6 Hz, 1H, Ar*H*), 7.97 (t, *J* = 7.8 Hz, 1H, Ar*H*), 3.04 (dt, s, 3H, C(1)H_3); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 158.4, 146.8, 135.9, 132.7, 132.3, 130.9, 128.9, 126.8,

124.0, 22.0; **IR** (thin film, ν_{max}/cm^{-1}) 3079, 1643, 1537, 1244, 1174, 1050; **Melting point** = 301 °C (decomp); **HRMS** (ESI, *m/z*) *Mass not found.*

2-Methylquinoline-8-sulfonamide (44b):

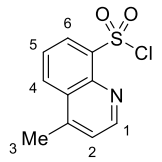


(**xx**)

Prepared according to **General Procedure K** using 2-methylquinoline-8-sulfonamide (967 mg, 4.0 mmol, 1.0 equiv.) and 35% aqueous ammonia solution (20 mL, 200 mmol, 50 equiv.). Sulfonamide **44b** was isolated as a white solid (763 mg, 3.4 mmol, 86%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.42 (d, *J* = 8.2 Hz, 1H, Ar*H*), 8.28 – 8.17 (m, 2H, Ar*H*), 7.67 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.59 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.20 (s, 2H, N(7)H_2), 2.77 (s, 3H, C(1)H_3); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 160.31, 142.1, 138.5, 137.0, 132.7, 128.1, 126.8, 124.7, 123.2, 25.3; **LRMS** (ESI, *m/z*): 223.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{10}H_{11}N_2O_2S$ $[M+H]^+$ = 223.0536, Found = 223.0525; **IR** (thin film, ν_{max}/cm^{-1}) 3346, 3252, 1324, 1162, 1142, 839; **Melting point** = 162 – 164 °C.

4-Methylquinoline-8-sulfonyl chloride (43c):



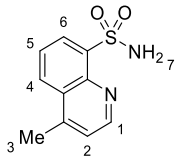
(**xx**)

Prepared according to **General Procedure J** using 4-methylquinoline (1.32 mL, 10 mmol, 1.0 equiv.) and chlorosulfonic acid (6.65 mL, 100 mmol, 10 equiv.). Sulfonyl chloride **43c** was isolated as a white solid (1.97 g, 8.1 mmol, 81%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.25 (d, *J* = 5.8 Hz, 1H, Ar*H*), 8.51 (dd, *J* = 8.5, 1.2 Hz, 1H, Ar*H*), 8.44 (dd, *J* = 7.3, 1.2 Hz, 1H, Ar*H*), 8.07 (d, *J* = 5.7 Hz, 1H, Ar*H*), 7.99 (dd, *J*

= 8.4, 7.4 Hz, 1H, Ar*H*), 3.01 (s, 3H, C(3)H_3); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.7, 145.4, 137.4, 132.3, 132.2, 128.9, 128.4, 127.6, 123.0, 20.2; **IR** (thin film, ν_{max}/cm^{-1}) 3086, 1626, 1604, 1231, 1216, 1040; **Melting point** = 305 °C (decomp); **HRMS** (ESI, *m/z*) *Mass not found.*

4-Methylquinoline-8-sulfonamide (44c):

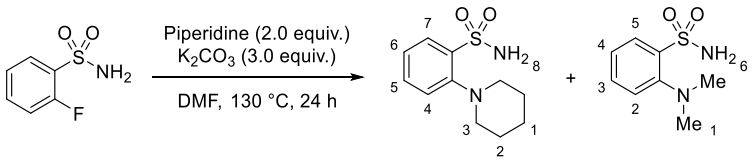


(**xx**)

Prepared according to **General Procedure K** using 4-methylquinoline-8-sulfonamide (1.21 g, 5.0 mmol, 1.0 equiv.) and 35% aqueous ammonia solution (25 mL, 250 mmol, 50 equiv.). Sulfonamide **44c** was isolated as a white solid (822 mg, 3.7 mmol, 74%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.91 (d, *J* = 4.1 Hz, 1H, Ar*H*), 8.39 (d, *J* = 8.2 Hz, 1H, Ar*H*), 8.30 (d, *J* = 7.0 Hz, 1H, Ar*H*), 7.76 (t, *J* = 7.8 Hz, 1H, Ar*H*), 7.55 (d, *J* = 3.6 Hz, 1H, Ar*H*), 7.24 (s, 2H, N(7)H_2), 2.75 (s, 3H, C(3)H_3); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 150.7, 145.7, 142.5, 139.7, 129.3, 128.4, 128.1, 125.3, 122.9, 18.5; **LRMS** (ESI, *m/z*): 223.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{10}H_{11}N_2O_2S$ $[M+H]^+$ = 223.0536, Found = 223.0526; **IR** (thin film, ν_{max}/cm^{-1}) 3025, 2835, 1436, 1322, 1033; **Melting point** = 226 – 228 °C.

2-(Piperidin-1-yl)benzenesulfonamide (44d) and 2-(dimethylamino)benzenesulfonamide (44e):



Prepared according to a modified procedure described by Yan and co-workers.[242] To a suspension of K_2CO_3 (1.04 g, 7.5 mmol, 3.0 equiv.) in DMF (5.0 mL) was added 2-fluorobenzenesulfonamide (569 mg, 2.5 mmol, 1.0 equiv.) and piperidine (494 µL, 5.0 mmol, 2.0 equiv.). The reaction mixture was stirred at 130 °C for 24 h, and then cooled to rt. The crude reaction mixture was poured into water (100 mL) and extracted using EtOAc (3×mL). The combined organic layers were dried using $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel flash column chromatography (20 – 30% EtOAc in Petrol) afforded sulfonamide **44d** as a white solid (229 mg, 0.73 mmol, 29%) and sulfonamide **44e** as a white solid (263 mg, 1.0 mmol, 40%).

2-(Piperidin-1-yl)benzenesulfonamide (44d):

R_f = 0.29 (30% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 7.9, 1.5 Hz, 1H, Ar*H*), 7.55 (td, *J* = 7.9, 1.6 Hz, 1H, Ar*H*), 7.42 – 7.37 (m, 1H, Ar*H*), 7.31 – 7.23 (m, 1H, Ar*H*), 5.81 (s, 2H, N(8)H_2), 3.39 – 2.61 (br. m, 4H, 2×C(3)H_2), 1.85 – 1.70 (br. m, 4H, 2×C(2)H_2), 1.68 – 1.48 (br. m, 2H, C(1)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.6, 138.7, 133.7, 127.8, 125.5, 123.9, 55.3, 27.0, 24.0; **LRMS** (ESI, *m/z*): 241.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{11}H_{17}N_2O_2S$ $[M+H]^+$ = 241.1005, Found = 241.1000.

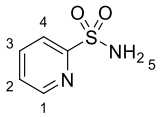
Data is consistent with the literature.[242]

2-(Dimethylamino)benzenesulfonamide (44e):

R_f = 0.18 (30% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 7.9, 1.6 Hz, 1H, Ar*H*), 7.57 (ddd, *J* = 8.0, 7.3, 1.6 Hz, 1H, Ar*H*), 7.45 (dd, *J* = 8.1, 1.0 Hz, 1H, Ar*H*),

7.31 – 7.25 (m, 1H, Ar*H*), 5.72 (s, 2H, N(6)H_2), 2.80 (s, 6H, 2×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.0, 138.6, 133.8, 127.8, 125.6, 123.4, 46.4; **LRMS** (ESI, *m/z*): 201.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_8H_{13}N_2O_2S$ $[M+H]^+$ = 201.0692, Found = 201.0697; **IR** (thin film, ν_{max}/cm^{-1}) 3268, 2946, 1477, 1335, 1165, 773; **Melting point** = 93 – 95 °C.

Pyridine-2-sulfonamide (44f):

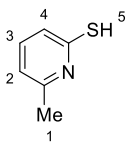


Prepared according to **General Procedure M** using 2-mercaptopyridine (2.23 g, 20 mmol, 1.0 equiv.), 1.0 M aqueous HCl (100 mL, 100 mmol, 5.0 equiv.), 6% aqueous NaOCl solution (104 mL, 41.9 mmol, 4.2 equiv.) in CH_2Cl_2 (100 mL), followed by 35% aqueous ammonia solution (50 mL, 500 mmol, 25 equiv.). Purification by recrystallisation from EtOAc and hexane afforded sulfonamide **44f** as a white solid (1.41 g, 9.0 mmol, 45%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.71 (ddd, *J* = 4.7, 1.7, 0.9 Hz, 1H, Ar*H*), 8.06 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 7.93 (dt, *J* = 7.9, 1.0 Hz, 1H, Ar*H*), 7.64 (ddd, *J* = 7.6, 4.7, 1.1 Hz, 1H, Ar*H*), 7.46 (s, 2H, N(6)H_2); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.8, 149.7, 138.6, 126.7, 120.5; **LRMS** (ESI, *m/z*): 181.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_5H_6N_2O_2SNa$ $[M+Na]^+$ = 181.0042, Found = 181.0036.

Data is consistent with the literature.[243]

6-Methylpyridine-2-thiol (43g):



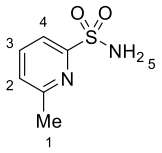
Prepared according to **General Procedure L** using 2-hydroxy-6-methylpyridine (2.43 g, 22.3 mmol, 1.0 equiv.), Lawesson's reagent (5.46 g, 13.5 mmol, 0.6 equiv.) in toluene

(131 mL), followed by 2.5 M aqueous NaOH solution (13.4 mL, 335 mmol, 15 equiv.). Thiol **43g** was isolated as a yellow solid (2.27 g, 18.1 mmol, 81%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 13.74 (s, 1H, S(5)*H*), 7.29 – 7.17 (m, 2H, Ar*H*), 6.45 (d, *J* = 6.8 Hz, 1H, Ar*H*), 2.37 (s, 3H, C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.0, 148.7, 138.5, 130.7, 114.0, 18.7; **LRMS** (ESI, *m/z*): 126.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for C_6H_8NS $[M+H]^+$ = 126.0372, Found = 126.0371.

Data is consistent with the literature.[244]

6-Methylpyridine-2-sulfonamide (44g):

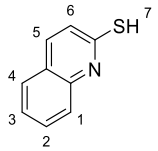


Prepared according to **General Procedure M** using 2-mercapto-6-methylpyridine (3.44 g, 20 mmol, 1.0 equiv.), 1.0 M aqueous HCl (100 mL, 100 mmol, 5.0 equiv.), 6% aqueous NaOCl solution (104 mL, 41.9 mmol, 4.2 equiv.) in CH_2Cl_2 (100 mL), followed by 35% aqueous ammonia solution (50 mL, 500 mmol, 25 equiv.). The precipitate was washed with water (×3) to give analytically pure sulfonamide **44g** as a white solid (326 mg, 2.0 mmol, 10%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.93 (t, *J* = 7.8 Hz, 1H, Ar*H*), 7.74 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.48 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.41 (s, 2H, N(6)H_2), 2.55 (s, 3H, C(1)H_3); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.2, 158.7, 138.5, 126.2, 117.6, 23.8; **LRMS** (ESI, *m/z*): 195.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_6H_8N_2O_2SNa$ $[M+Na]^+$ = 195.0199, Found = 195.0201.

Data is consistent with the literature.[245]

Quinoline-2-thiol (43h):

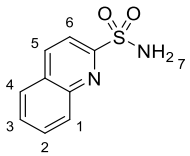


Prepared according to **General Procedure L** using quinoline-2-ol (1.45 g, 10 mmol, 1.0 equiv.), Lawesson's reagent (2.43 g, 6.0 mmol, 0.6 equiv.) in toluene (60 mL), followed by 2.5 M aqueous NaOH solution (6.0 mL, 300 mmol, 15 equiv.). Thiol **43h** was isolated as a yellow solid (1.46 g, 9.0 mmol, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.99 (s, 1H, S(7)*H*), 7.73 – 7.55 (m, 4H, Ar*H*), 7.48 (d, *J* = 9.1 Hz, 1H, Ar*H*), 7.40 – 7.31 (m, 1H, Ar*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 180.7, 139.2, 135.9, 131.7, 131.3, 128.0, 125.1, 123.2, 116.4; **LRMS** (ESI, *m/z*): 162.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for C_9H_8NS $[M+H]^+$ = 162.0372, Found = 162.0373.

Data is consistent with the literature.[246]

Quinoline-2-sulfonamide (44h):



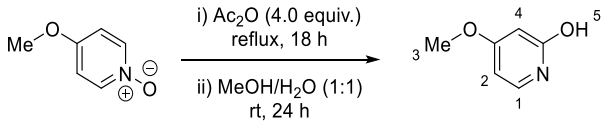
Prepared according to **General Procedure M** using quinoline-2-thiol (1.45 g, 9.0 mmol, 1.0 equiv.), 1.0 M aqueous HCl (45 mL, 45 mmol, 5.0 equiv.), 6% aqueous NaOCl solution (46.8 mL, 18.9 mmol, 4.2 equiv.) in CH_2Cl_2 (45 mL), followed by 35% aqueous ammonia solution (22.5 mL, 225 mmol, 25 equiv.). The precipitate was washed with water (×3) to give analytically pure sulfonamide **44h** as a white solid (153 mg, 0.72 mmol, 8%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.68 (d, *J* = 8.5 Hz, 1H, Ar*H*), 8.13 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.04 (d, *J* = 8.6 Hz, 1H, Ar*H*), 7.93 (ddd, *J* = 8.5, 6.7, 1.2 Hz, 1H, Ar*H*), 7.82 – 7.74 (m, 1H, Ar*H*), 7.65 (s, 2H, N(7)H_2); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.6, 146.1,

139.1, 131.3, 129.0, 128.7, 128.3, 128.3, 117.3; **LRMS** (ESI, *m/z*): 209.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_9H_9N_2O_2S$ $[M+H]^+$ = 209.0379, Found = 209.0369

Data is consistent with the literature.[241]

4-Methoxypyridine-2-ol (43i-1):

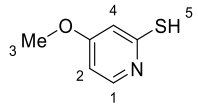


4-Methoxypyridine *N*-oxide (3.00 g, 24 mmol, 1.0 equiv.) was added to a round-bottom flask, and was dissolved in acetic anhydride (90 mL, 96 mmol, 4.0 equiv.). The resulting solution was refluxed for 18 h. The solvent was then removed in vacuo, and the residue was dissolved in methanol (30 mL) and water (30 mL) and stirred for 24 h at rt. The solvent was removed in vacuo and the crude material purified by silica gel flash column chromatography (5 – 10% MeOH in CH_2Cl_2) to afford pyridine **43i-1** as a pale-orange solid (1.31 g, 10.6 mmol, 44%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 13.08 – 12.54 (m, 1H, O(5)*H*), 7.22 (d, *J* = 7.3 Hz, 1H, Ar*H*), 5.98 (dd, *J* = 7.3, 2.5 Hz, 1H, Ar*H*), 5.89 (d, *J* = 2.5 Hz, 1H, Ar*H*), 3.78 (s, 3H, C(3)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) 170.0, 167.4, 134.8, 101.5, 97.2, 55.5; **LRMS** (ESI, *m/z*): 126.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_6H_8NO_2$ $[M+H]^+$ = 126.0550, Found = 126.0551.

Data is consistent with the literature.[247]

4-Methoxypyridine-2-thiol (43i-2):

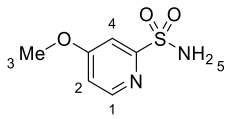


Prepared according to **General Procedure L** using 4-methoxypyridine-2-ol **43i-1** (1.25 g, 10 mmol, 1.0 equiv.), Lawesson's reagent (2.43 g, 6.0 mmol, 0.6 equiv.) in toluene (60 mL), followed by 2.5 M aqueous NaOH solution (6.0 mL, 150 mmol, 15 equiv.). Thiol **43i-2** was isolated as a yellow solid (915 mg, 6.5 mmol, 65%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.81 (br. s, 1H, S(5)*H*), 7.53 (t, *J* = 5.8 Hz, 1H, Ar*H*), 6.77 (d, *J* = 2.6 Hz, 1H, Ar*H*), 6.39 (dd, *J* = 7.1, 2.6 Hz, 1H, Ar*H*), 3.80 (s, 3H, C(3)H_3); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 178.6, 165.6, 138.6, 112.0, 105.0, 55.9; **LRMS** (ESI, *m/z*): 142.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for C_6H_8NOS $[M+H]^+$ = 142.0321, Found = 142.0316.

Data is consistent with the literature.[248]

4-Methoxypyridine-2-sulfonamide (44i):

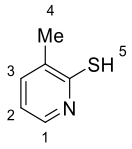


Prepared according to **General Procedure M** using 4-methoxypyridine-2-thiol (1.25 g, 6.0 mmol, 1.0 equiv.), 1.0 M aqueous HCl (30 mL, 30 mmol, 5.0 equiv.), 6% aqueous NaOCl solution (31.2 mL, 25.2 mmol, 4.2 equiv.) in CH_2Cl_2 (30 mL), followed by 35% aqueous ammonia solution (15 mL, 25 mmol, 25 equiv.). The precipitate was washed with water (×3) to give analytically pure sulfonamide **44i** as a white solid (293 mg, 1.6 mmol, 26%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.52 (d, *J* = 5.6 Hz, 1H, Ar*H*), 7.50 – 7.39 (m, 3H, Ar*H* and N(5)H_2), 7.19 (dd, *J* = 5.6, 2.5 Hz, 1H, Ar*H*), 3.91 (s, 3H, C(3)H_3); **^{13}C NMR**

(101 MHz, DMSO-d_6) δ 166.5, 161.4, 151.0, 112.3, 106.7, 56.1; **LRMS** (ESI, *m/z*): 211.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_6H_8N_2O_3SNa$ $[M+Na]^+$ = 211.0148, Found = 211.0145; **IR** (thin film, ν_{max}/cm^{-1}) 2954, 1739, 1492, 1225, 1158, 829; **Melting point** = 157 °C (decomp).

3-Methylpyridine-2-thiol (43j):

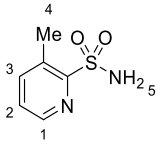


Prepared according to **General Procedure L** using 2-hydroxy-3-methylpyridine (2.18 g, 20 mmol, 1.0 equiv.), Lawesson's reagent (4.85 g, 12 mmol, 0.6 equiv.) in toluene (120 mL), followed by 2.5 M aqueous NaOH solution (12 mL, 300 mmol, 15 equiv.). Thiol **43j** was isolated as a yellow solid (1.55 g, 12.4 mmol, 62%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.34 (br. s, 1H, S(5)*H*), 7.49 (s, 1H, Ar*H*), 7.32 – 7.25 (m, 1H, Ar*H*), 7.20 (d, *J* = 8.7 Hz, 1H, Ar*H*), 2.08 (s, 3H, C(4)H_3); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 175.0, 139.6, 136.0, 132.5, 122.2, 16.5; **LRMS** (ESI, *m/z*): 126.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for C_6H_8NS $[M+H]^+$ = 126.0372, Found = 126.0374.

Data is consistent with the literature.[244]

3-Methylpyridine-2-sulfonamide (44j):



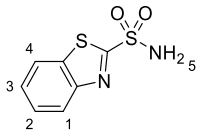
Prepared according to **General Procedure M** using 3-methylpyridine-2-thiol (1.50 g, 12 mmol, 1.0 equiv.), 1.0 M aqueous HCl (60 mL, 60 mmol, 5.0 equiv.), 6% aqueous NaOCl solution (62.4 mL, 41.9 mmol, 4.2 equiv.) in CH_2Cl_2 (60 mL), followed by 35% aqueous ammonia solution (30 mL, 300 mmol, 25 equiv.). The precipitate was washed

with water (×3) to give analytically pure sulfonamide **44j** as a white solid (931 mg, 5.4 mmol, 45%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.57 – 8.52 (m, 1H, Ar*H*), 7.89 – 7.78 (m, 2H, Ar*H*), 7.39 (s, 2H, N(5)H_2), 2.39 (s, 3H, C(4)H_3); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 157.3, 149.8, 138.4, 136.7, 120.1, 17.9; **LRMS** (ESI, *m/z*): 195.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_6H_8N_2O_2SNa$ $[M+Na]^+$ = 195.0199, Found = 195.0201.

Data is consistent with the literature.[249]

Benzo[*d*]thiazole-2-sulfonamide (44k):

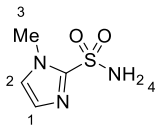


Prepared according to **General Procedure M** using 2-mercaptobenzothiazole (3.35 g, 20 mmol, 1.0 equiv.), 1.0 M aqueous HCl (100 mL, 100 mmol, 5.0 equiv.), 6% aqueous NaOCl solution (104 mL, 41.9 mmol, 4.2 equiv.) in CH_2Cl_2 (100 mL), followed by 35% aqueous ammonia solution (50 mL, 500 mmol, 25 equiv.). Purification by silica gel flash column chromatography (40 – 60% EtOAc in Petrol) afforded sulfonamide **44k** as a white solid (193 mg, 1.0 mmol, 5%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.35 (s, 2H, N(5)H_2), 8.30 – 8.23 (m, 1H, Ar*H*), 8.21 – 8.14 (m, 1H, Ar*H*), 7.72 – 7.59 (m, 2H, Ar*H*); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 169.4, 151.8, 135.7, 127.6, 127.5, 124.2, 123.2; **LRMS** (ESI, *m/z*): 236.9 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_7H_6N_2O_2S_2Na$ $[M+Na]^+$ = 236.9763, Found = 236.9756.

Data is consistent with the literature.[250]

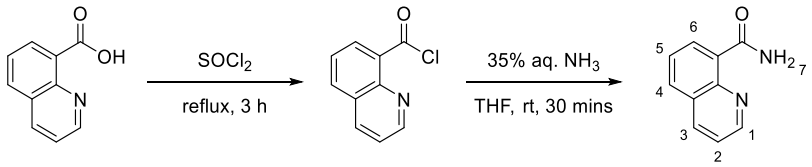
1-Methyl-1*H*-imidazole-2-sulfonamide (44l):



Prepared according to **General Procedure K** using 1-methylimidazole-2-sulfonyl chloride (903 mg, 5.0 mmol, 1.0 equiv.) and 35% aqueous ammonia solution (25 mL, 250 mmol, 50 equiv.). Sulfonamide **44l** was isolated as a white solid (585 mg, 3.7 mmol, 73%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.84 (s, 2H, N(4)H_2), 7.36 (d, J = 0.9 Hz, 1H, ArH), 6.98 (d, J = 1.1 Hz, 1H, ArH), 3.83 (s, 3H, C(3)H_3); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 145.4, 126.7, 125.4, 34.4; **LRMS** (ESI, *m/z*): 184.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_4H_7N_3O_2SNa$ $[M+Na]^+$ = 184.0151, Found = 184.0157; **IR** (thin film, ν_{max}/cm^{-1}) 3023, 2842, 1744, 1349, 1189, 1152; **Melting point** = 112 – 114 °C.

Quinoline-8-carboxamide (47a):

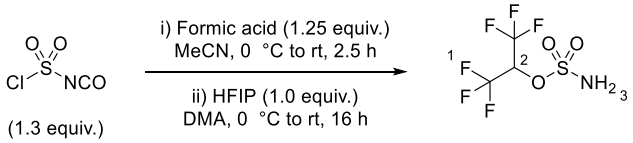


Thionyl chloride (10 mL) was added to an oven-dried round-bottom flask, and cooled to 0 °C. 8-Quinolinecarboxylic acid (1.73 g, 10 mmol, 1.0 equiv.) was then added portionwise, and the reaction mixture was warmed to rt and stirred for 3 h. The crude reaction mixture was then concentrated in vacuo, and the residue was dissolved in THF (25 mL). The reaction mixture was cooled to 0 °C, and 35% aqueous ammonia solution (25 mL, 250 mmol, 100 equiv.) was added. The crude reaction mixture was then concentrated in vacuo, the residue suspended in water and filtered. Purification by silica gel flash column chromatography (30 – 50% EtOAc in CH_2Cl_2) afforded amide **47a** as a white solid (557 mg, 3.2 mmol, 32%).

R_f = 0.25 (40% EtOAc in CH_2Cl_2); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.21 (s, 1H, N(7)*H*H), 9.03 (d, *J* = 3.6 Hz, 1H, Ar*H*), 8.56 (dd, *J* = 18.6, 7.8 Hz, 2H, Ar*H*), 8.19 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.93 (s, 1H, N(7)H*H*), 7.74 (t, *J* = 7.7 Hz, 1H, Ar*H*), 7.66 (dd, *J* = 8.0, 4.1 Hz, 1H, Ar*H*); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 166.4, 150.4, 144.8, 137.9, 132.8, 132.4, 129.5, 128.3, 126.3, 121.5; **LRMS** (ESI, *m/z*): 173.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{10}H_9N_2O$ $[M+H]^+$ = 173.0709, Found = 173.0702.

Data is consistent with the literature.[251]

1,1,1,3,3,3-Hexafluoropropan-2-yl sulfamate (HFIPS) (49):

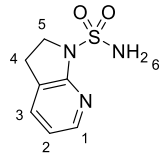


Prepared according to a procedure described by Magolan and co-workers.[214] Chlorosulfonyl isocyanate (2.01 mL, 22.8 mmol, 1.3 equiv.) was added to an oven-dried round-bottom flask, and dissolved in dry MeCN (2.0 mL). The solution was cooled to 0 °C, and formic acid (826 μL, 21.9 mmol, 1.25 equiv.) was added over a period of 5.0 mins with stirring, and then stirred for a further 10 mins at the same temperature. The reaction mixture was then warmed to rt and stirred for a further 2.5 h. The reaction mixture was then cooled to 0 °C, and a solution of HFIP (1.84 mL, 17.5 mmol, 1.0 equiv.) in DMA (2.0 mL) was added dropwise. The resulting reaction mixture was stirred at the same temperature for 10 mins, and then warmed to rt and stirred for a further 16 h. The reaction was then quenched with the slow addition of H_2O (5.0 mL) and transferred to a separatory funnel with additional H_2O (5.0 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic extracts were washed with H_2O (4 × 10 mL), brine (10 mL), and 10% LiCl (2 × 5.0 mL), dried over $MgSO_4$, and concentrated in vacuo to provide sulfamate **49** as a white solid (2.26 g, 8.9 mmol, 51%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.50 (s, 2H, N(3)H_2), 6.21 (hept, J = 6.1 Hz, 1H, C(2)H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 120.67 (qd, J = 282.6, 3.3 Hz), 70.88 (hept, J = 33.9 Hz);**^{19}F NMR** (377 MHz, DMSO-d_6) δ -72.40 (d, J = 6.1 Hz); **HRMS** (ESI, *m/z*) *Mass not found.*

Data is consistent with the literature.[214]

2,3-Dihydro-1*H*-pyrrolo[2,3-*b*]pyridine-1-sulfonamide (50a):

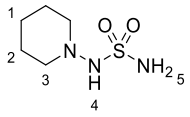


Prepared according to **General Procedure N** using 7-azaindoline (240 mg, 2.0 mmol, 1.0 equiv.), HFIPS **49** (593 mg, 2.4 mmol, 1.2 equiv.), CH_2Cl_2 (14 mL) and pyridine (6.0 mL). Purification by silica gel flash column chromatography (60% EtOAc in Petrol) afforded sulfamide **50a** as a white solid (202 mg, 1.0 mmol, 51%).

R_f = 0.25 (60% EtOAc in Petrol); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.10 – 8.01 (m, 1H, ArH), 7.58 (dd, J = 7.3, 1.4 Hz, 1H, ArH), 7.22 (s, 2H, N(6)H_2), 6.91 (dd, J = 7.3, 5.2 Hz, 1H, ArH), 3.87 (t, J = 8.3 Hz, 2H, C(5)H_2), 3.04 (t, J = 8.3 Hz, 2H, C(4)H_2); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 157.2, 145.9, 133.1, 124.5, 117.3, 48.6, 24.8; **LRMS** (ESI, *m/z*): 200.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_7H_{10}N_3O_2S$ $[M+H]^+$ = 200.0488, Found = 200.0483.

Data is consistent with the literature.[252]

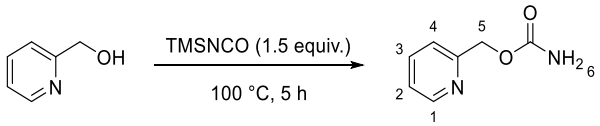
***N*-1-Piperidinylsulfamide (50b):**



Prepared according to **General Procedure N** using 1-aminopiperidine (216 µL, 2.0 mmol, 1.0 equiv.), HFIPS (593 mg, 2.4 mmol, 1.2 equiv.), CH_2Cl_2 (14 mL) and pyridine (6.0 mL). Purification by silica gel flash column chromatography (20% EtOAc in CH_2Cl_2) afforded sulfamide **50b** as a white solid (82.0 mg, 0.46 mmol, 23%).

R_f = 0.36 (20% EtOAc in CH_2Cl_2); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 6.64 (s, 2H, N(5)H_2), 2.96 – 2.88 (m, 4H, 2×C(3)H_2), 1.56 (app. p, J = 5.8 Hz, 4H, 2×C(2)H), 1.48 – 1.37 (m, 2H, C(1)H_2) *(N(4)H signal not observed)*; **^{13}C NMR** (101 MHz, DMSO-d_6) δ 46.6, 24.6, 23.3; **IR** (thin film, ν_{max}/cm^{-1}) 3354, 3263, 1364, 1348, 1168, 927; **Melting point** = 108 – 110 °C; **HRMS** (ESI, *m/z*) *Mass not found.*

Pyridin-2-ylmethyl carbamate (52):



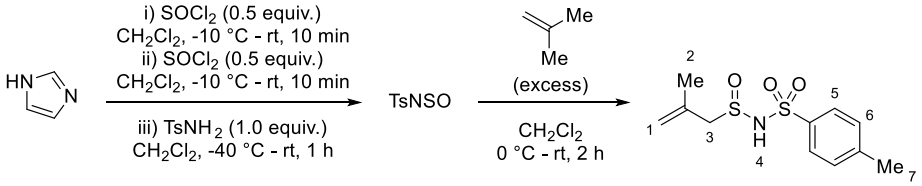
Trimethylsilyl isocyanate (965 µL, 15 mmol, 1.5 equiv.) and 2-pyridinemethanol (2.10 mL, 10 mmol, 1.0 equiv.) were added to an oven-dried round-bottom flask. The resulting mixture was stirred at 100 °C for 5 h. The reaction mixture was cooled to rt, and the resulting crystals were filtered and washed with toluene to give the pure product carbamate **52** as an off-white solid (551 mg, 3.6 mmol, 36%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.62 – 8.49 (m, 1H, ArH), 7.84 (td, J = 7.7, 1.8 Hz, 1H, ArH), 7.43 (d, J = 7.8 Hz, 1H, ArH), 7.39 – 7.32 (m, 1H, ArH), 7.20 (s, 2H, N(6)H_2), 5.20 (s, 2H, C(5)H_2); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 155.5, 153.5, 149.2, 137.0, 123.1, 121.4, 66.8; **LRMS** (ESI, *m/z*): 153.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_7H_9N_2O_2$

$[M+H]^+$ = 153.0659, Found = 153.0652; **IR** (thin film, ν_{max}/cm^{-1}) 3354, 3263, 1364, 1348, 1168, 927; **Melting point** = 161 – 163 °C.

8.5.3 In-situ generation of *N*-sulfinylsulfonamides via a retro-ene reaction compounds

4-Methyl-*N*-((2-methylallyl)sulfinyl)benzenesulfonamide (55b):

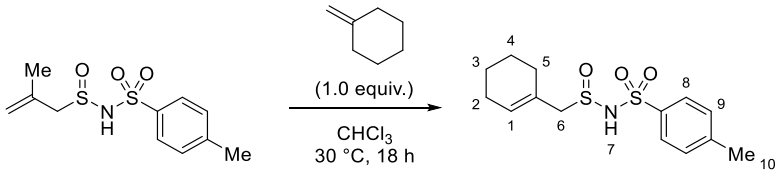


Imidazole (681 mg, 10 mmol, 2.0 equiv.) was added to an oven-dried round-bottom flask, sealed with rubber septa, evacuated and backfilled with N_2 (× 3). CH_2Cl_2 (10 mL) was then added and the resulting solution was cooled to -10 °C. Thionyl chloride (181 μL, 2.5 mmol, 0.5 equiv.) was then added, and the resulting reaction mixture was stirred at rt for 10 min. The reaction mixture was filtered through a sinter into a further oven-dried round-bottom flask under N_2. The filtrate was then cooled to -10 °C, and thionyl chloride (181 μL, 2.5 mmol, 0.5 equiv.) was added and the resulting reaction mixture was stirred at rt for 10 min. The reaction mixture was then added dropwise to a suspension of *p*-toluenesulfonamide (856 mg, 5.0 mmol, 1.0 equiv.) in CH_2Cl_2 (5.0 mL) under argon at -40 °C and the resulting reaction mixture was stirred at rt for 1h. The reaction mixture was then filtered through a cannula filter by cannula filtration into an oven-dried round-bottom flask filled with argon and washed with CH_2Cl_2 (5.0 mL). The filtrate was cooled to 0 °C and sparged with isobutylene gas for 5.0 mins, before stirring at rt for 2 h. Solvent was removed in vacuo. Cooling recrystallisation from EtOAc/cyclohexane gave sulfinamide **55b** as a white powder (1.21 g, 4.5 mmol, 89%).

^{1}H NMR (400 MHz, Acetone-d_6) δ 7.76 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.18 (d, *J* = 8.0 Hz, 2H Ar*H*), 4.88 – 4.80 (m, 1H, C(1)*H*H), 4.78 – 4.73 (m, 1H, C(1)H*H*), 4.29 (br. s, 1H, N(4)*H*), 3.47 (d, *J* = 12.2 Hz, 1H, C(3)*H*H), 3.39 (d, *J* = 12.3 Hz, 1H, C(3)H*H*), 2.34 (s, 3H, C(7)H_3), 1.60 (s, 3H, C(2)H_3); **^{13}C NMR** (101 MHz, Acetone-d_6) δ 143.7, 141.3, 137.9, 129.4, 127.6, 116.8, 67.1, 23.4, 21.3; **LRMS** (ESI, *m/z*): 296.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc.

for $C_{11}H_{15}NO_3S_2Na$ $[M+Na]^+$ = 296.0386, Found = 296.0384; **IR** (thin film, ν_{max}/cm^{-1}) 3070, 1377, 1330, 1167, 1092, 816; **Melting point** = 68 – 70 °C.

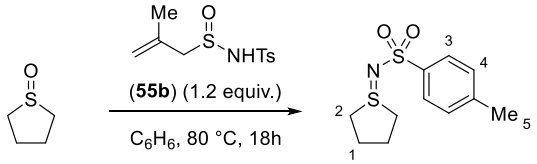
***N*-((Cyclohex-1-en-1-ylmethyl)sulfinyl)-4-methylbenzenesulfonamide (56a):**



4-Methyl-*N*-((2-methylallyl)sulfinyl)benzenesulfonamide **55b** (54.7 mg, 0.2 mmol, 1.0 equiv.) was added to oven-dried 10 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Dry $CHCl_3$ (1.0 mL) and methylenecyclohexane (24 µL, 0.2 mmol, 1.0 equiv.) were added and the resulting stirred at 30 °C for 18 h. Solvent was removed in vacuo, and purification by silica gel flash column chromatography (10% MeOH in EtOAc) afforded sulfinamide **56a** as a white solid (39.5 mg, 0.13 mmol, 63%).

R_f = 0.12 (10% MeOH in EtOAc); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.58 – 7.53 (m, 2H, Ar*H*), 7.15 (d, *J* = 7.9 Hz, 2H, Ar*H*), 5.45 (s, 1H, C(1)*H*), 3.01 – 2.90 (m, 2H, C(6)H_2), 2.30 (s, 3H, C(10)H_3), 1.97 – 1.81 (m, 4H, C(2)H_2 & C(5)H_2), 1.48 – 1.34 (m, 4H, C(3)H_2 & C(4)H_2); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 138.7, 134.8, 130.4, 128.2, 126.0, 125.7, 67.7, 28.7, 24.8, 22.2, 21.5, 20.8 *(one signal missing due to signal overlap)*; **LRMS** (ESI, *m/z*): 336.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{14}H_{19}NO_3S_2Na$ $[M+Na]^+$ = 336.0699, Found = 336.0689; **IR** (thin film, ν_{max}/cm^{-1}) 3496, 2926, 1249, 1136, 1091, 985; **Melting point** = 189 °C (decomposition).

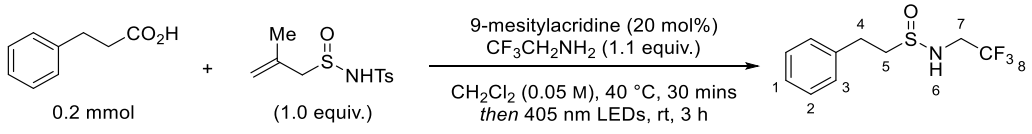
4-Methyl-*N*-(tetrahydro-1λ^4-thiophen-1-ylidene)benzenesulfonamide (57):



4-Methyl-*N*-((2-methylallyl)sulfinyl)benzenesulfonamide **55b** (65.6 mg, 0.24 mmol, 1.2 equiv.) was added to oven-dried 10 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Dry benzene (1.0 mL) and tetrahydrothiophene 1-oxide (18 µL, 0.2 mmol, 1.0 equiv.) was added and the resulting stirred at 80 °C for 18 h. Solvent was removed in vacuo, and purification by silica gel flash column chromatography (0 – 5% MeOH in EtOAc) afforded sulfilimine **57** as a white solid (22.2 mg, 0.09 mmol, 43%).

R$_f$ = 0.19 (5% MeOH in EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.21 (d, *J* = 7.9 Hz, 2H, Ar*H*), 3.16 – 3.05 (m, 2H, 2×C(2)*H*H), 3.02 – 2.93 (m, 2H, 2×C(2)H*H*), 2.49 – 2.38 (m, 2H, 2×C(1)*H*H), 2.37 (s, 3H, C(5)*H*$_3$), 2.05 – 1.93 (m, 2H, 2×C(1)H*H*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.8, 141.4, 129.4, 126.4, 51.4, 26.5, 21.5; **LRMS** (ESI, *m/z*): 258.0 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{11}H_{16}NO_2S_2$ $[M+H]^+$ = 258.0617, Found = 258.0616; **IR** (thin film, ν_{max}/cm^{-1}) 2945, 1277, 1141, 1084, 976, 749. Data is consistent with the literature.[14c]

2-Phenyl-*N*-(2,2,2-trifluoroethyl)ethane-1-sulfinamide (37l):



Hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), 4-methyl-*N*-((2-methylallyl)sulfinyl)benzenesulfonamide **55b** (54.7 mg, 0.2 mmol, 1.0 equiv.) and 9-mesitylacridine **PC5** (11.9 mg, 0.04 mmol, 20 mol%) were weighed into an oven-dried

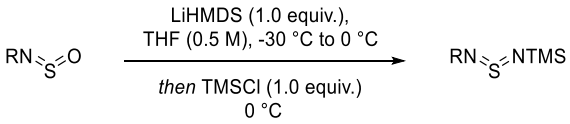
10 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Dry CH_2Cl_2 (4.0 mL), followed by 2,2,2-trifluoroethylamine (17.3 µL, 0.22 mmol, 1.1 equiv.). The reaction was then heated to 40 °C and stirred for 18 h in a pre-heated aluminium heating block. The reaction vial was then removed from the heating block, and stirred under 405 nm LED irradiation (See **Figure S3** for experimental setup) with fan cooling for 3 h. The reaction mixture was then concentrated in vacuo and purification by silica gel flash column chromatography (60% EtOAc in Petrol) afforded sulfinamide **37l** as a pale-yellow oil (24.9 mg, 0.1 mmol, 50%).

R_f = 0.2 (60% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2H, Ar*H*), 7.28 – 7.17 (m, 3H, Ar*H*), 4.69 (t, *J* = 7.1 Hz, 1H, N(6)*H*), 3.82 – 3.65 (m, 1H, C(7)*H*H), 3.65 – 3.49 (m, 1H, C(7)H*H*), 3.17 – 2.95 (m, 4H, C(4)H_2 and C(5)H_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.5, 129.0, 128.6, 127.0, 124.3 (q, *J* = 277.9 Hz), 57.4, 44.9 (q, *J* = 34.5 Hz), 29.4; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -72.68 (t, *J* = 9.0 Hz); **LRMS** (ESI, *m/z*): 274.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{10}H_{12}F_3NOSNa$ $[M+Na]^+$ = 274.0481, Found = 274.0481; **IR** (thin film, ν_{max}/cm^{-1}) 3170, 2921, 1298, 1273, 1161, 1059.

8.6 Experimental for Chapter 6

8.6.1 General Procedures

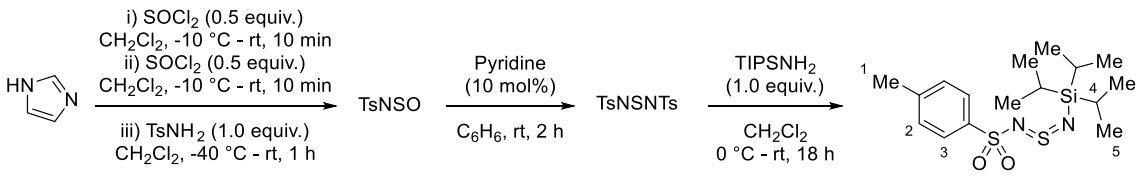
General Procedure O



Prepared according to the procedure described by Willis and co-workers.[16a] Sulfinylamine (1.0 equiv.) was dissolved in anhydrous THF (0.5 M) in an oven-dried round-bottom flask and was sparged with N_2 for 5.0 mins. The reaction mixture was cooled to -30 °C before LiHMDS solution (1.0 M in THF) (1.0 equiv.) was then added dropwise and the reaction stirred at the same temperature for 5.0 min. The reaction was then warmed to 0 °C and stirred for a further 5.0 min. TMSCl (1.0 equiv.) was then added and the reaction was stirred at 0 °C for 10 min. The reaction was then warmed to rt and solvent removed in vacuo. The residue was then suspended in diethyl ether and the resulting suspension filtered to remove lithium salts. Solvent was then removed in vacuo to give the product sulfurdiimide. Sulfurdiimides were used in subsequent reactions without further purification.

8.6.2 Sulfurdiimide Data

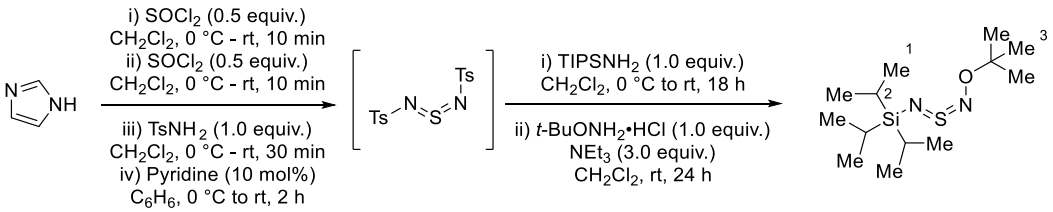
4-Methyl-*N*-(((triisopropylsilyl)imino)-λ⁴-sulfaneylidene)benzenesulfonamide (58):



Imidazole (681 mg, 10 mmol, 2.0 equiv.) was added to an oven-dried round-bottom flask, sealed with rubber septa, evacuated and backfilled with N_2 (× 3). CH_2Cl_2 (10 mL) was then added and the resulting solution was cooled to -10 °C. Thionyl chloride (181 µL, 2.5 mmol, 0.5 equiv.) was then added, and the resulting reaction mixture was stirred at rt for 10 min. The reaction mixture was filtered through a sinter into a further oven-dried round-bottom flask under N_2. The filtrate was then cooled to -10 °C, and thionyl chloride (181 µL, 2.5 mmol, 0.5 equiv.) was added and the resulting reaction mixture was stirred at rt for 10 min. The reaction mixture was then added dropwise to a suspension of *p*-toluenesulfonamide (856 mg, 5.0 mmol, 1.0 equiv.) in CH_2Cl_2 (10 mL) under argon at -40 °C and the resulting reaction mixture was stirred at rt for 1h. The reaction mixture was then filtered through a cannula filter by cannula filtration into an oven-dried round-bottom flask filled with argon and washed with CH_2Cl_2 (5.0 mL). Solvent was removed in vacuo and the crude TsNSO was redissolved in benzene (10 mL). Pyridine (40.3 µL, 0.5 mmol, 10 mol%) was added, and the reaction stirred until precipitated TsNSNTs was observed. The reaction was stirred for a further 2 h, and then cooled to 0 °C. A solution of $TIPSNH_2$ (433 mg, 2.5 mmol, 1.0 equiv.) in CH_2Cl_2 (10 mL) was then added dropwise, and the reaction stirred at rt for 18 h. Solvent was removed in vacuo, and the crude reside suspended in dry pentane (50 mL). The resulting suspension was filtered through a sinter and the resulting filtrate concentrated in vacuo to give the product sulfurdiimide **58** as a yellow oil (655.8 mg, 3.1 mmol, 61%, 33% $TIPSNH_2$ impurity).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.79 (m, 2H, Ar*H*), 7.31 (br. d, *J* = 8.0 Hz, 2H, Ar*H*), 2.43 (s, 3H, C(1)H_3), 1.32 – 1.26 (m, 3H, 3×C(4)H_3), 1.05 (d, *J* = 7.4 Hz, 18H, 6×C(5)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.2, 138.2, 129.8, 127.1, 21.8, 18.0, 12.4; **IR** (thin film, ν_{max}/cm^{-1}) 2947, 2869, 1465, 1331, 1162, 669; **HRMS** (ESI, *m/z*) *Mass not found.*

_O_-(_tert_-Butyl)-_N_-(((triisopropylsilyl)imino)- λ^4-sulfaneylidene)hydroxylamine (60):



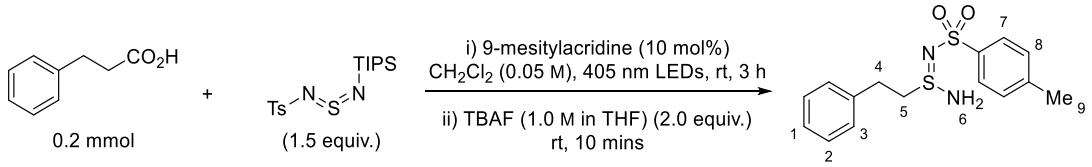
Imidazole (681 mg, 10 mmol, 2.0 equiv.) was added to an oven-dried round-bottom flask, sealed with rubber septa, evacuated and backfilled with N_2 (× 3). CH_2Cl_2 (10 mL) was then added and the resulting solution was cooled to -10 °C. Thionyl chloride (181 µL, 2.5 mmol, 0.5 equiv.) was then added, and the resulting reaction mixture was stirred at rt for 10 min. The reaction mixture was filtered through a sinter into a further oven-dried round-bottom flask under N_2. The filtrate was then cooled to -10 °C, and thionyl chloride (181 µL, 2.5 mmol, 0.5 equiv.) was added and the resulting reaction mixture was stirred at rt for 10 min. The reaction mixture was then added dropwise to a suspension of *p*-toluenesulfonamide (856 mg, 5.0 mmol, 1.0 equiv.) in CH_2Cl_2 (10 mL) under argon at -40 °C and the resulting reaction mixture was stirred at rt for 1 h. The reaction mixture was then filtered through a cannula filter by cannula filtration into an oven-dried round-bottom flask filled with argon and washed with CH_2Cl_2 (5.0 mL). Solvent was removed in vacuo and the crude TsNSO was redissolved in benzene (10 mL). Pyridine (40.3 µL, 0.5 mmol, 10 mol%) was added, and the reaction stirred until precipitated TsNSNTs was observed. The reaction was stirred for a further 2 h, and then cooled to 0 °C. A solution of $TIPSNH_2$ (433 mg, 2.5 mmol, 1.0 equiv.) in CH_2Cl_2 (10 mL) was then added dropwise, and the reaction stirred at rt for 18 h. In a separate oven-dried round bottom flask, *O*-(*tert*-

butyl)hydroxylamine hydrochloride (314 mg, 2.5 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (10 mL) and cooled to 0 °C. Triethylamine (1.04 mL, 7.5 mmol, 3.0 equiv.) was then added and a white solid precipitated. The sulfurdiimide solution was then transferred by syringe to the solution of hydroxylamine, and the resulting reaction mixture stirred at rt for 24 h. Solvent was removed in vacuo, and the crude reside suspended in dry pentane (50 mL). The resulting suspension was filtered through a sinter and the resulting filtrate concentrated in vacuo. The crude reaction mixture was purified by silica gel flash column chromatography (100% pentane) to afford sulfurdiimide **60** as a pale-yellow oil (346 mg, 1.2 mmol, 48%).

R_f = 0.61 (100% pentane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.32 (s, 9H, 3×C(3)H_3), 1.23 – 1.13 (m, 3H, 3×C(2)*H*), 1.04 (d, *J* = 7.1 Hz, 18H, 6×C(1)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 83.6, 27.2, 18.4, 13.4; **IR** (thin film, ν_{max}/cm^{-1}) 2944, 2867, 1465, 1298, 1000, 883; **HRMS** (ESI, *m/z*) *Mass not found.*

8.6.3 Product Data

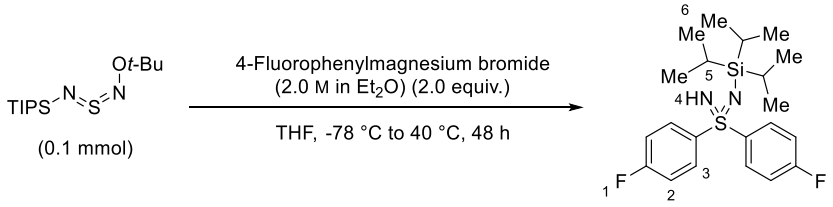
(*Z*)-*N*-(Amino(phenethyl)-λ⁴-sulfaneylidene)-4-methylbenzenesulfonamide (59):



Hydrocinnamic acid (30.0 mg, 0.2 mmol, 1.0 equiv.), 4-methyl-*N*-(((triisopropylsilyl)imino)-λ⁴-sulfaneylidene)benzenesulfonamide **58** (112 mg, 0.3 mmol, 1.5 equiv.) and 9-mesitylacridine **PC5** (5.9 mg, 0.02 mmol, 10 mol%) were weighed into an oven-dried 10 mL reaction vial. The vial was then sealed with a rubber septum, evacuated and backfilled with N_2 (× 3). Dry CH_2Cl_2 (4.0 mL) was added and the reaction. stirred under 405 nm LED irradiation (See **Figure S3** for experimental setup) with fan cooling for 3 h. TBAF (1.0 M in THF) (0.4 mL, 0.4 mmol, 2.0 equiv.) was then added and the reaction stirred at rt for 10 mins. After completion of the reaction (determined by TLC), saturated brine (20 mL) was added and the product was extracted with EtOAc (3×20 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude reaction mixture was purified by silica gel flash column chromatography (70 – 80% EtOAc in Petrol) to afford sulfinamidine **59** as an off-white solid (30.4 mg, 0.09 mmol, 47%).

R_f = 0.25 (80% EtOAc in Petrol); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 – 7.74 (m, 2H, Ar*H*), 7.26 – 7.18 (m, 5H, Ar*H*), 7.01 – 6.95 (m, 2H, Ar*H*), 4.84 (s, 2H, N(6)H_2), 3.53 – 3.36 (m, 2H, C(5)H_2), 2.98 – 2.82 (m, 2H, C(4)H_2), 2.40 (s, 3H, C(9)H_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.2, 141.4, 137.4, 129.5, 128.9, 128.6, 127.1, 126.3, 53.9, 29.8, 21.6; **LRMS** (ESI, *m/z*): 345.0 $[M+Na]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{15}H_{18}N_2O_2S_2Na$ $[M+Na]^+$ = 345.0702, Found = 345.0700; **IR** (thin film, ν_{max}/cm^{-1}) 3328, 2930, 1278, 1141, 1089, 989; **Melting point** = 114 – 116 °C.

1,1-Bis(4-fluorophenyl)-*N*-(triisopropylsilyl)-λ^6-sulfanediimine (62):



O-(*tert*-Butyl)-*N*-(((triisopropylsilyl)imino)- λ^4-sulfaneylidene)hydroxylamine **60** (29.1 mg, 0.1 mmol, 1.0 equiv.) was added to an oven-dried 10 mL reaction vial, dissolved in dry THF (0.5 mL) and cooled to -78 °C. 4-Fluorophenylmagnesium bromide solution (2 M in Et_2O) (0.1 mL, 0.2 mmol, 2.0 equiv.) was added dropwise and the reaction warmed to rt. The reaction was then stirred at 40 °C h in an aluminium heating block for 48 h. The reaction was quenched with 10% aqueous NH_4Cl solution (10 mL) and the product was extracted with EtOAc (3×20 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude reaction mixture was purified by silica gel flash column chromatography (0 – 10% EtOAc in petrol) to afford sulfondiimine **62** as a pale-brown oil (15.0 mg, 0.04 mmol, 37%).

R_f = 0.24 (10% EtOAc in pentane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 – 8.04 (m, 4H), 7.11 – 7.03 (m, 4H), 2.33 (s, 1H), 1.15 – 1.06 (m, 3H), 1.03 (d, *J* = 6.4 Hz, 18H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.49 (d, *J* = 252.9 Hz), 144.29 (d, *J* = 2.7 Hz), 129.92 (d, *J* = 9.1 Hz), 115.79 (d, *J* = 22.4 Hz), 18.70, 13.48; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -108.63 (tt, *J* = 8.4, 5.2 Hz); **LRMS** (ESI, *m/z*): 409.1 $[M+H]^+$; **HRMS** (ESI, *m/z*): Calc. for $C_{21}H_{31}F_2N_2SSi$ $[M+H]^+$ = 409.1940, Found = 409.1951; **IR** (thin film, ν_{max}/cm^{-1}) 2943, 2865, 1590, 1490, 1266, 1230.

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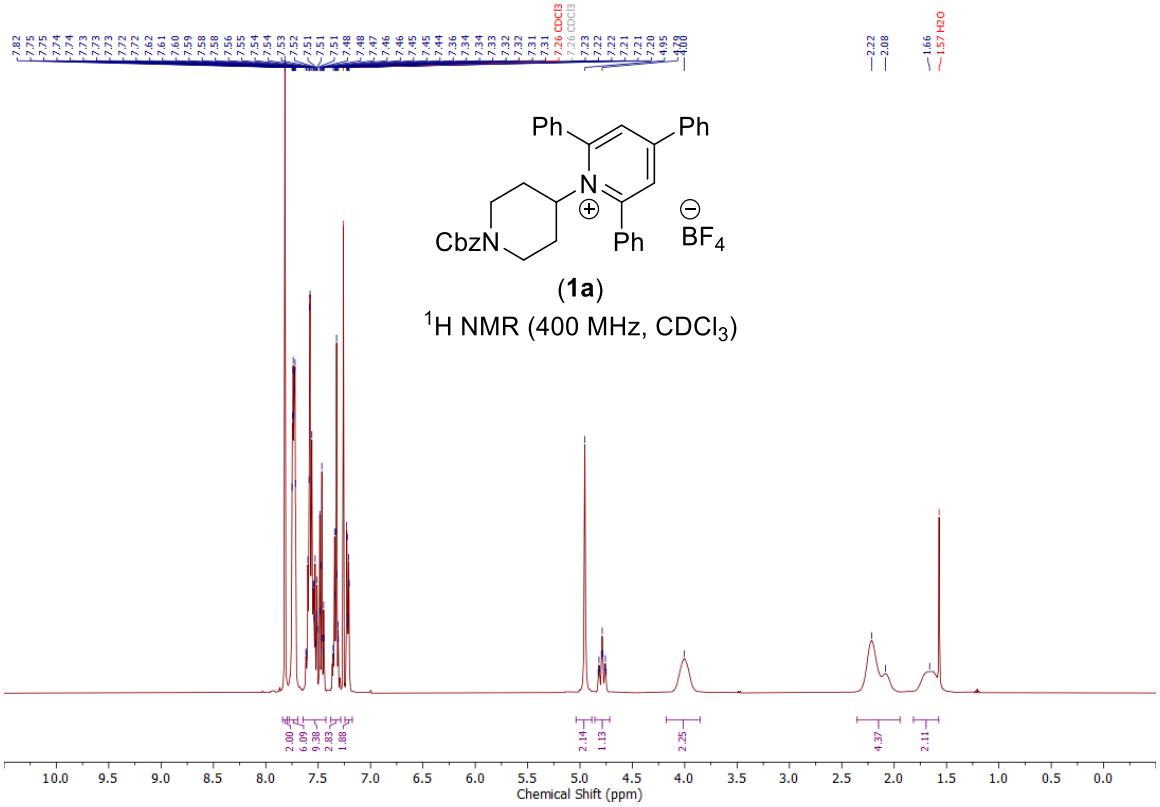
Appendix

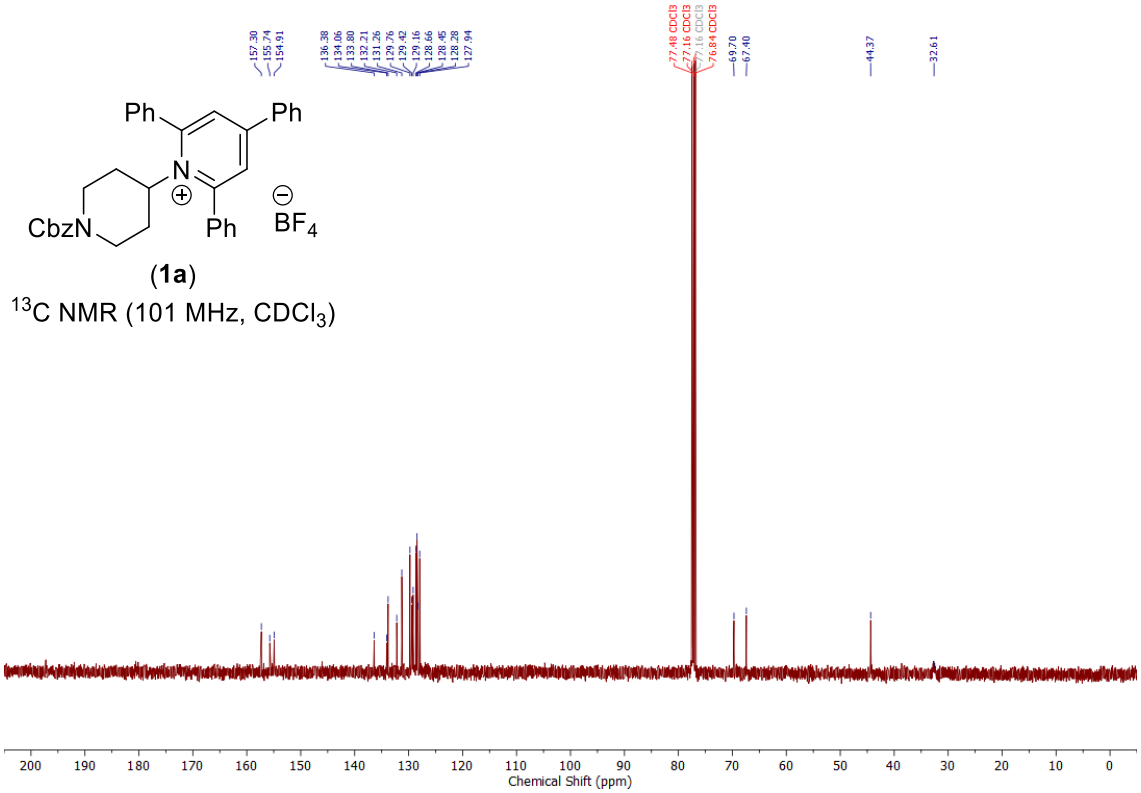
10.1 NMR Spectra for Chapter 2

NMR spectra of 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1a)



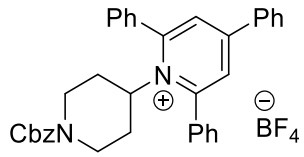
(**1a**)

^{1}H NMR (400 MHz, $CDCl_3$)



(**1a**)

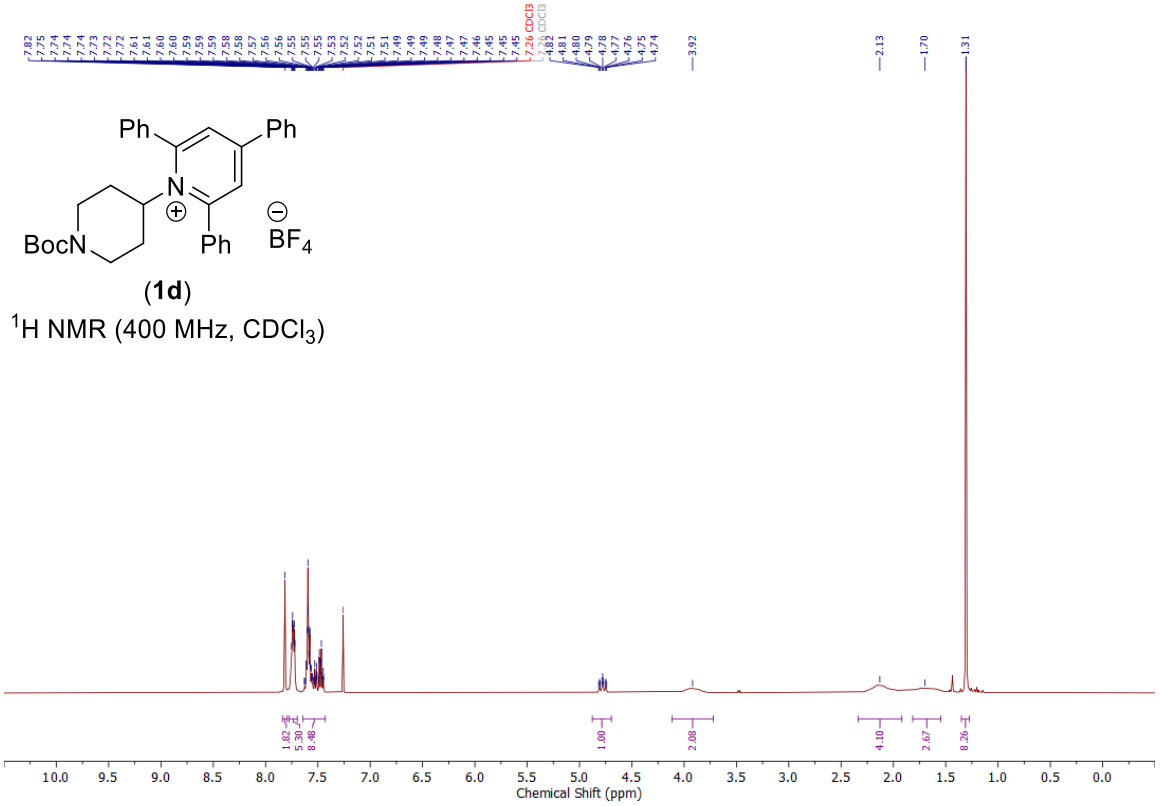
^{13}C NMR (101 MHz, $CDCl_3$)



(**1a**)

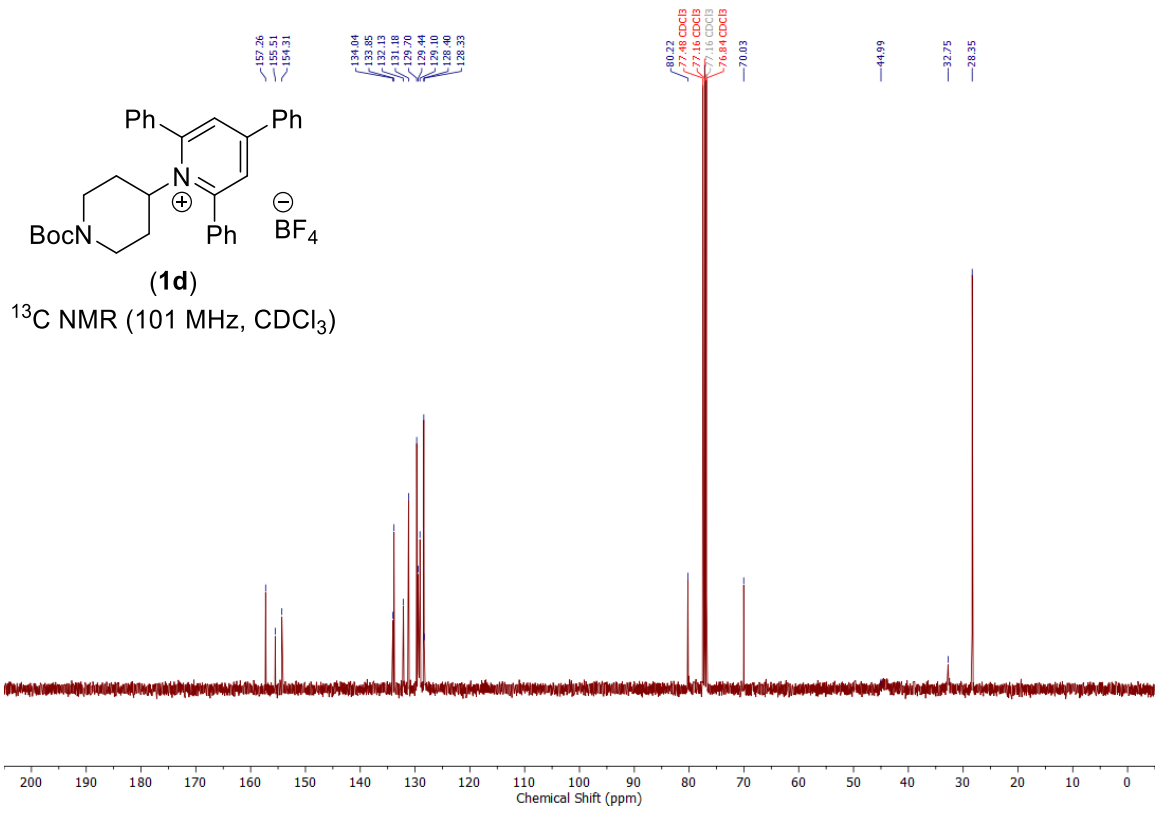
^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(1-(*tert*-butoxycarbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1d)



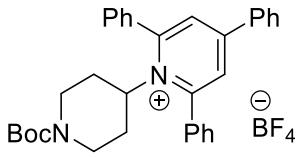
(**1d**)

^{1}H NMR (400 MHz, $CDCl_3$)



(**1d**)

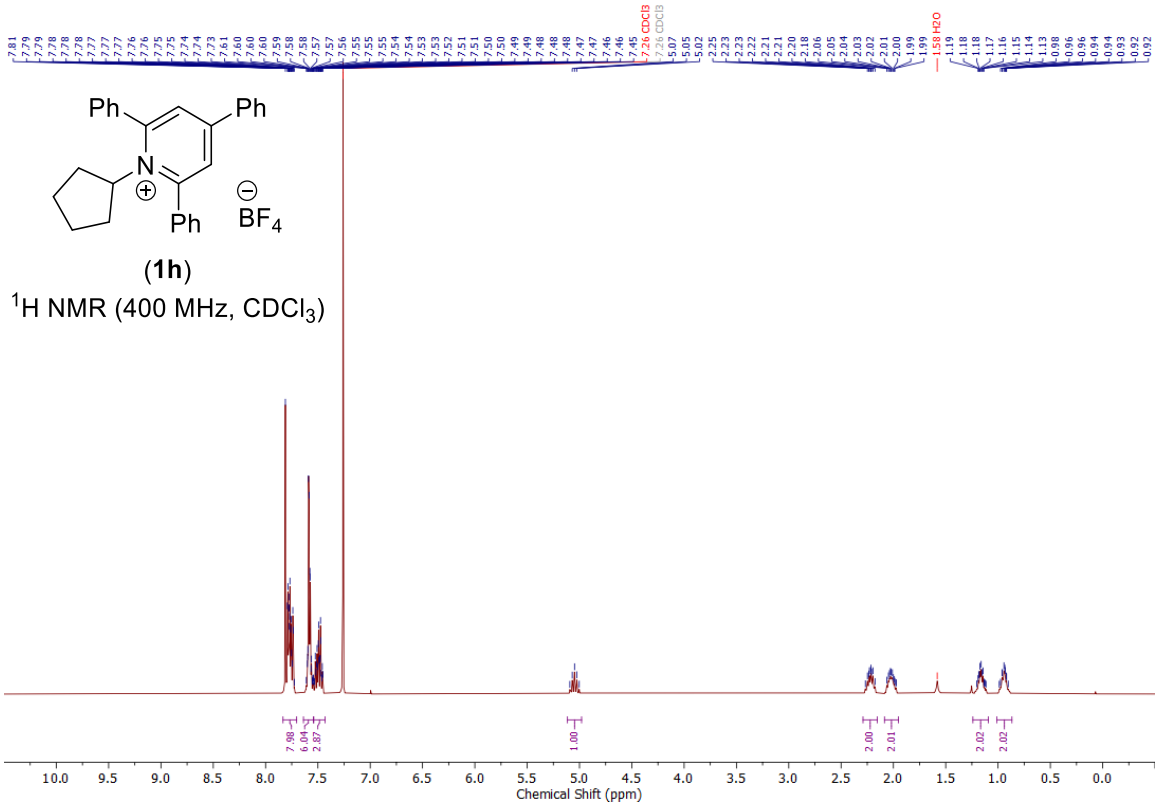
^{13}C NMR (101 MHz, $CDCl_3$)

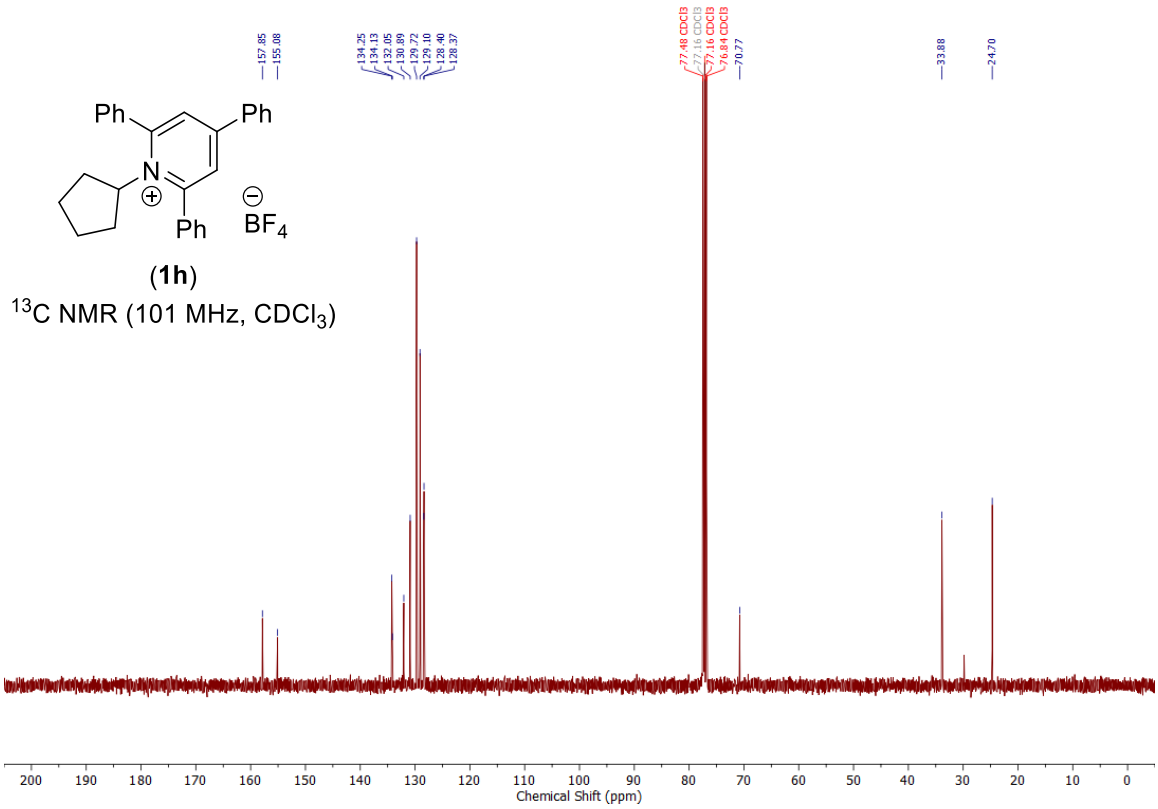


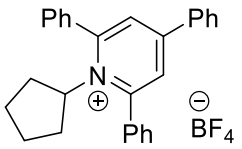
(**1d**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-cyclopentyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1h)



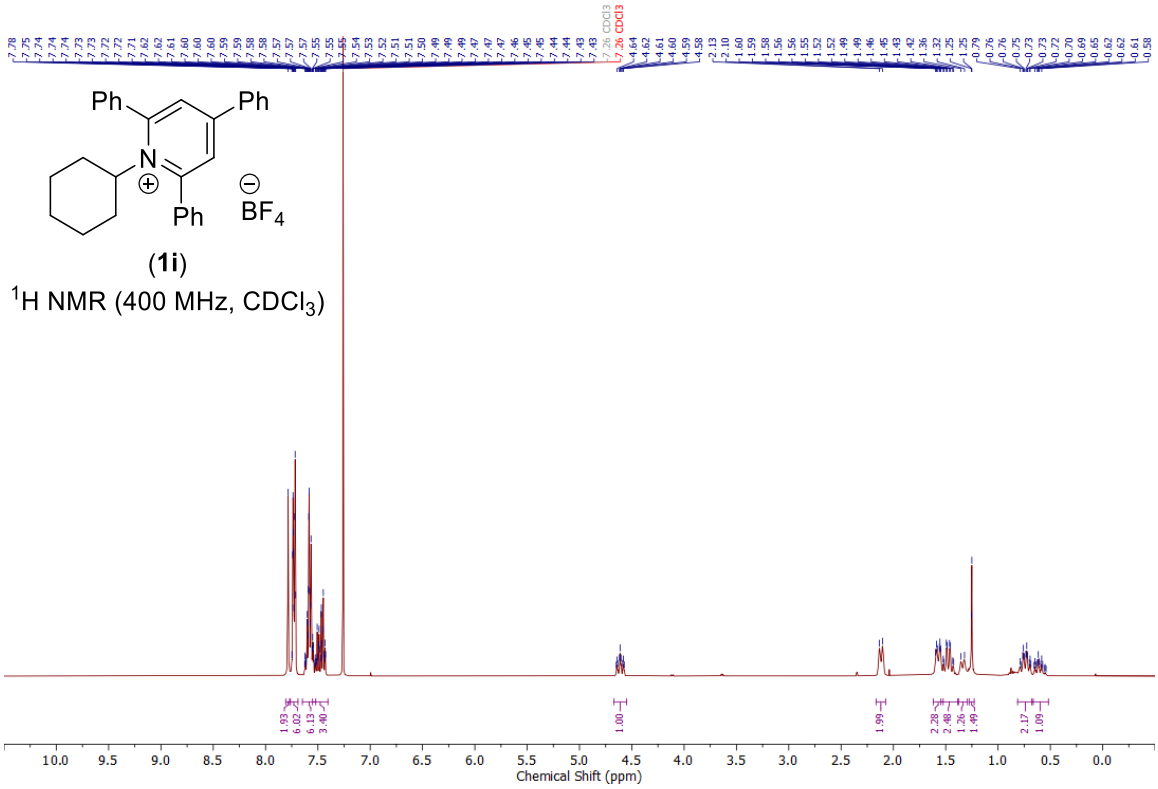


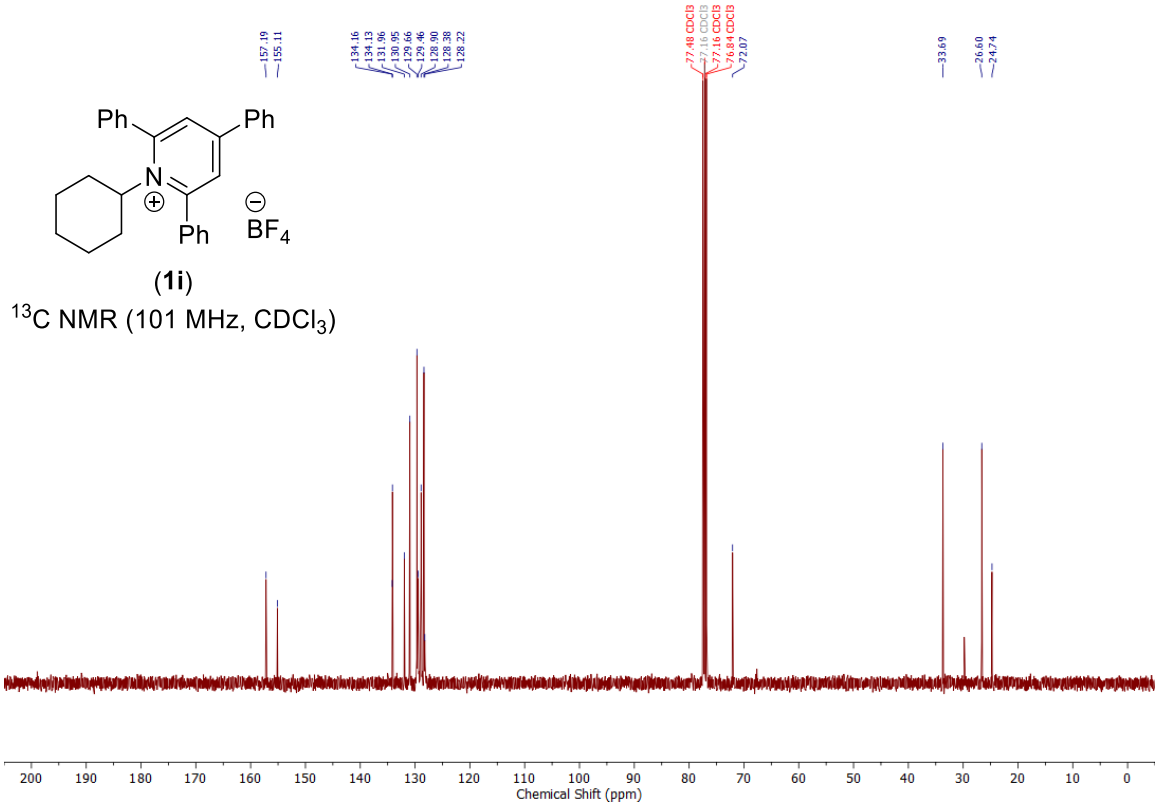


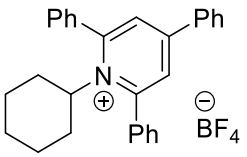
(**1h**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-cyclohexyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1i)



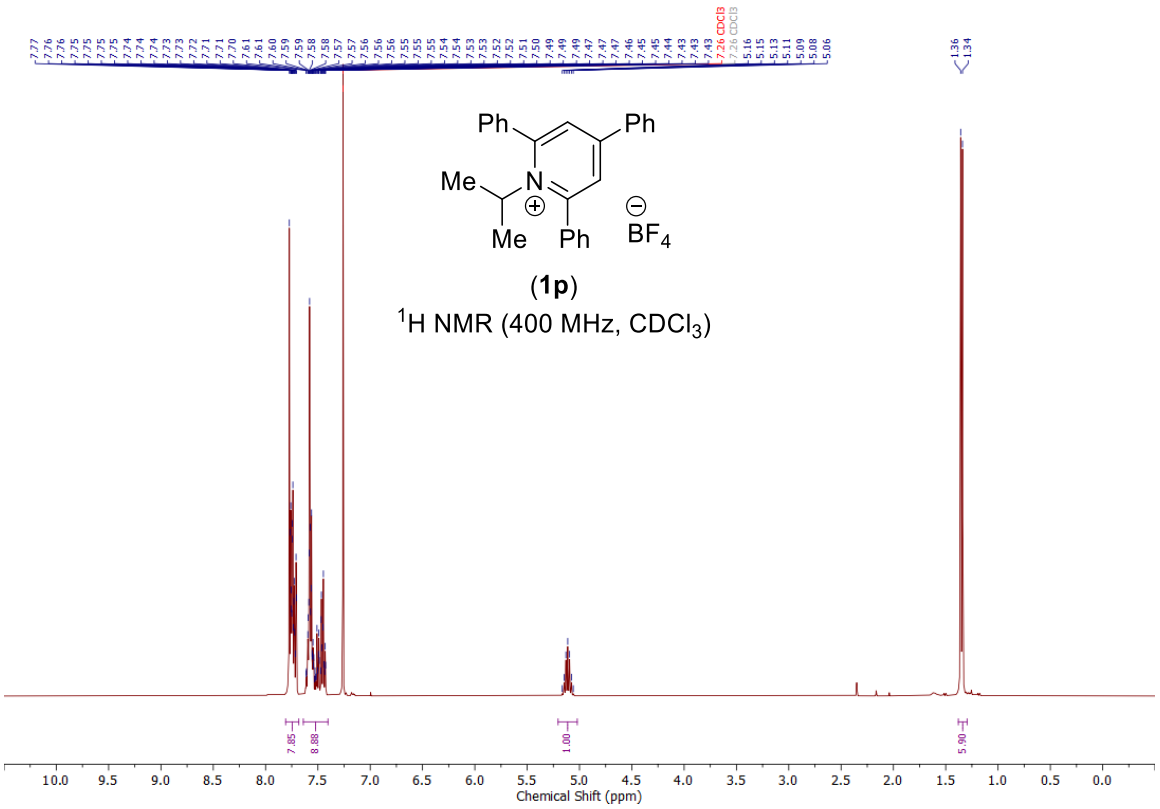


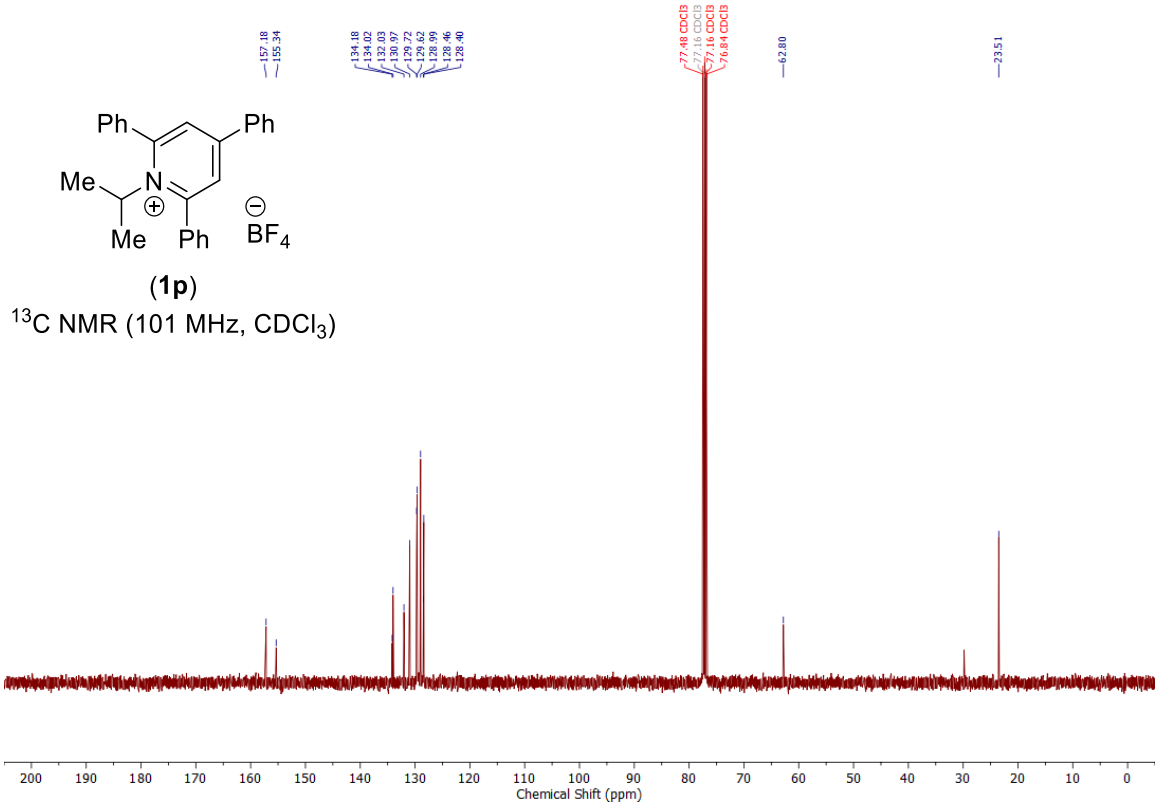


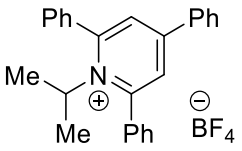
(**1i**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-isopropyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1p)



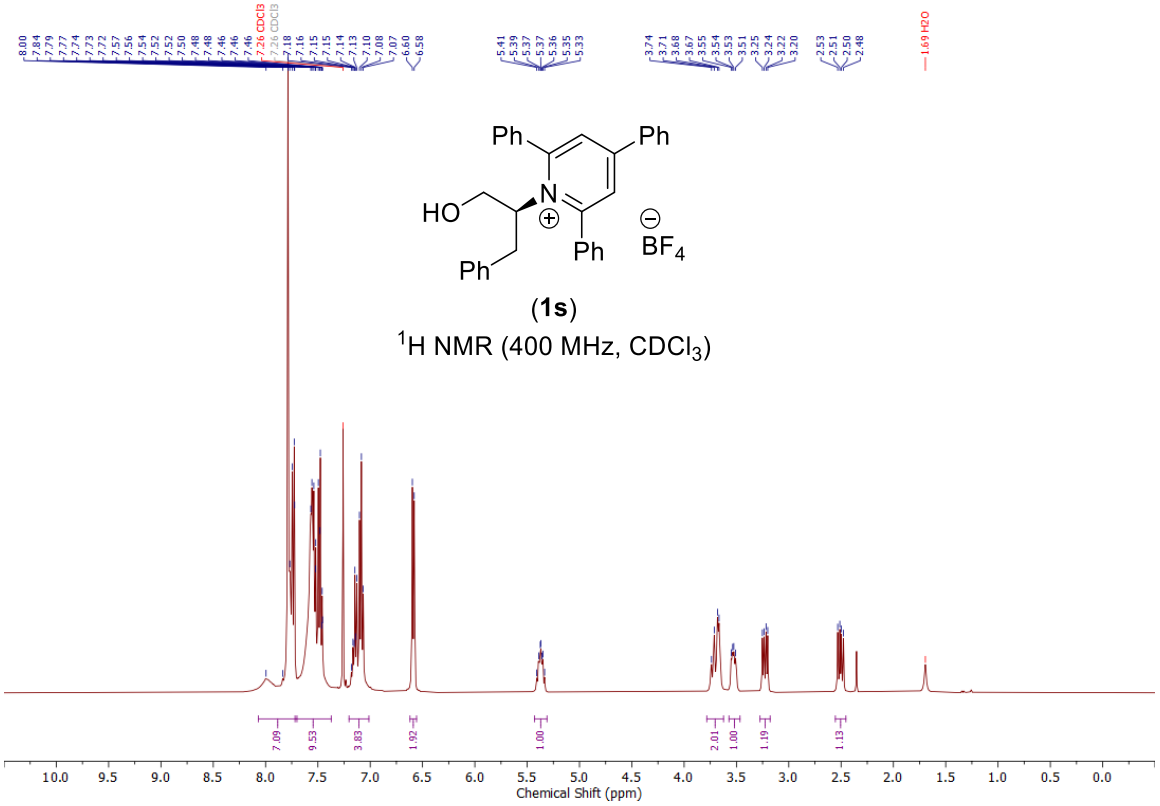


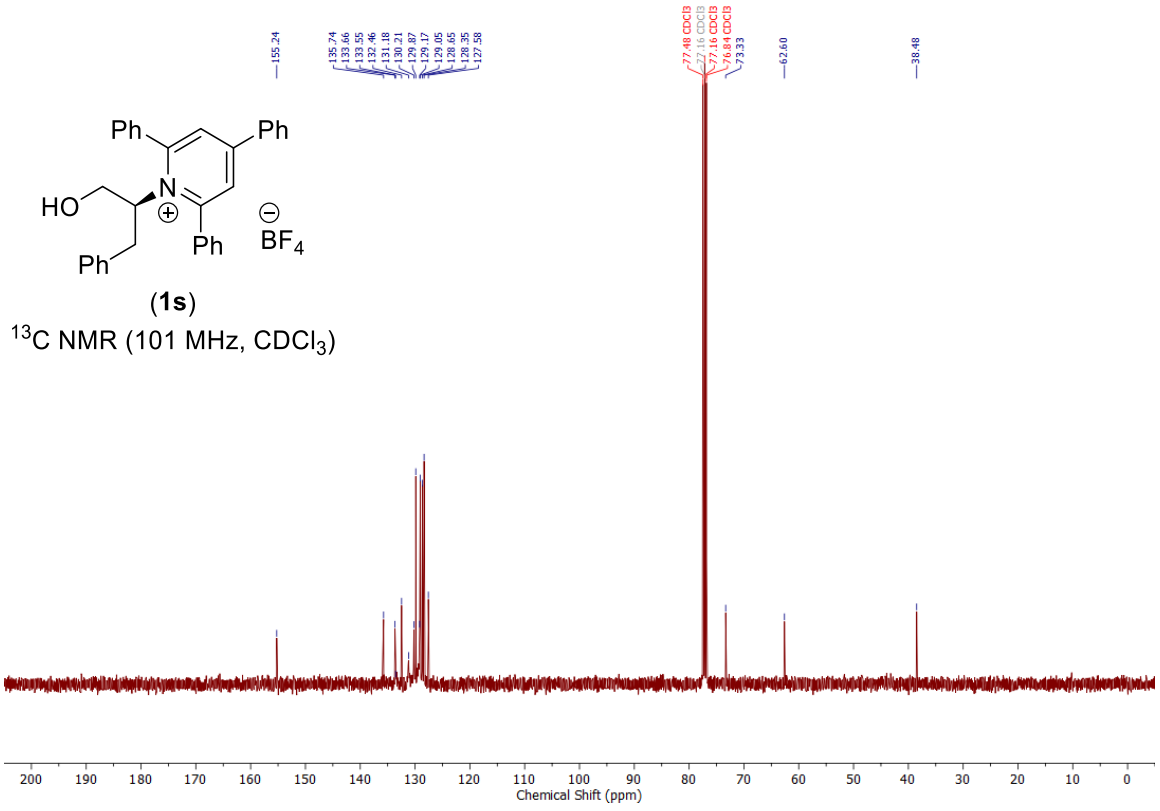


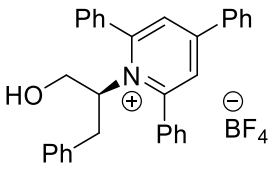
(**1p**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of (*S*)-1-(1-hydroxy-3-phenylpropan-2-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1s)



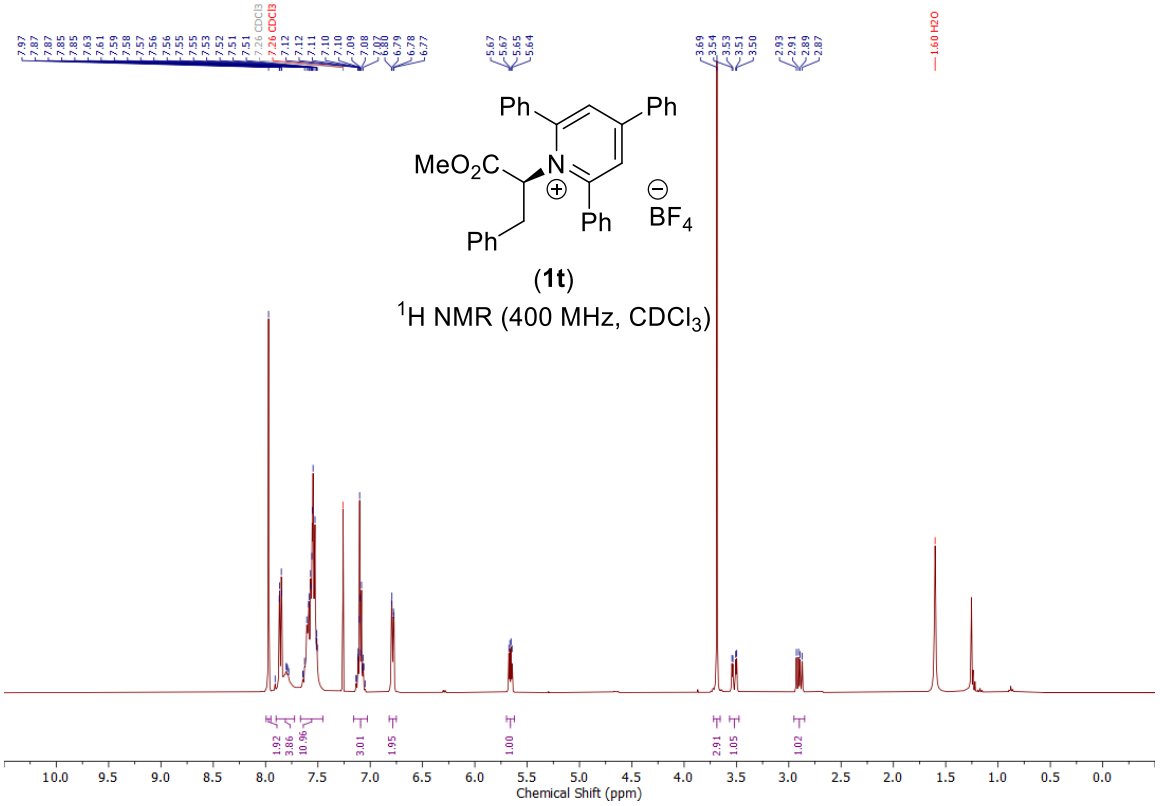


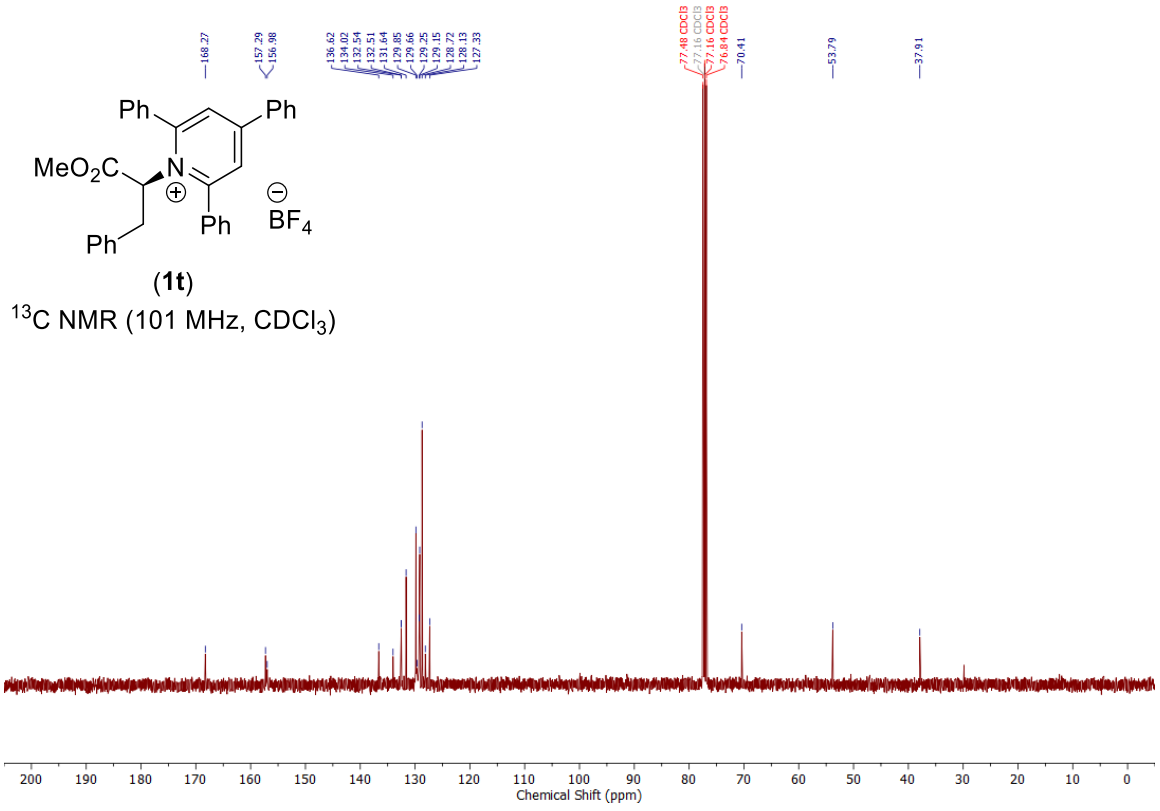


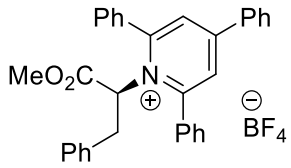
(**1s**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of (*S*)-1-(1-methoxy-1-oxo-3-phenylpropan-2-yl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1t)



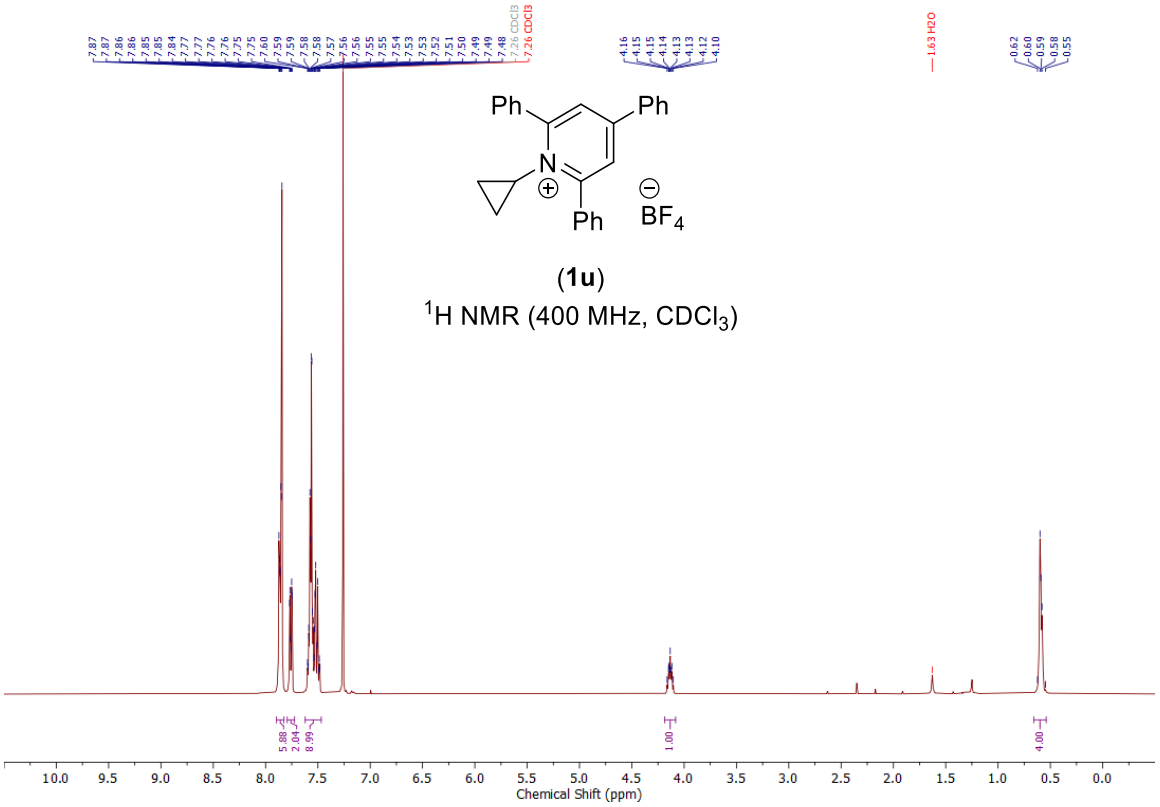




(**1t**)

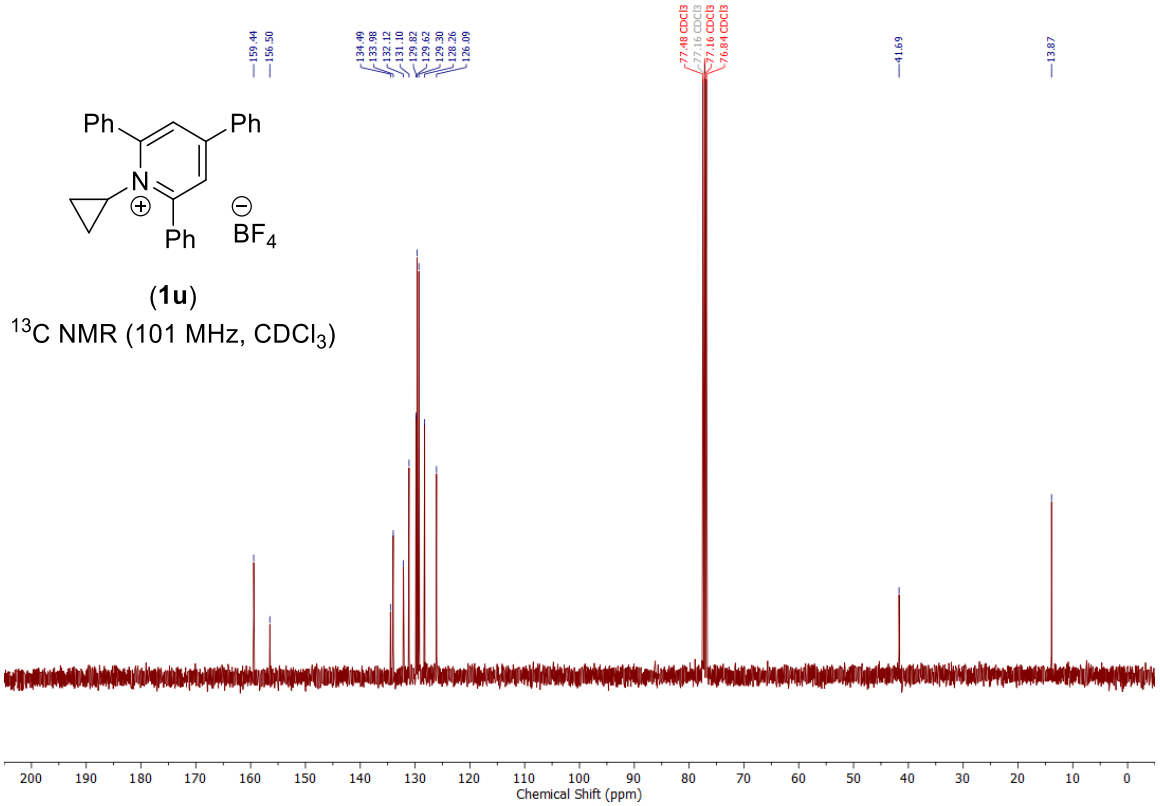
^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-cyclopropyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1u)



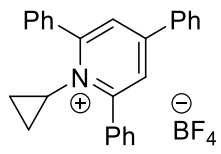
(**1u**)

^{1}H NMR (400 MHz, $CDCl_3$)



(**1u**)

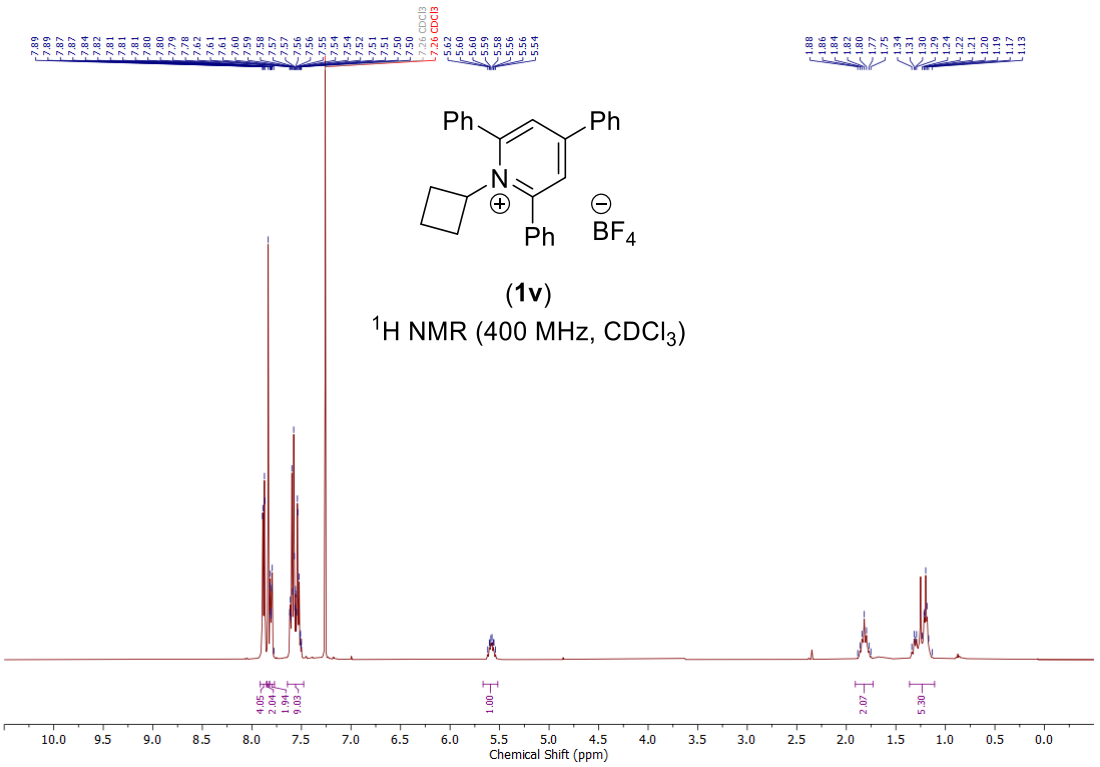
^{13}C NMR (101 MHz, $CDCl_3$)

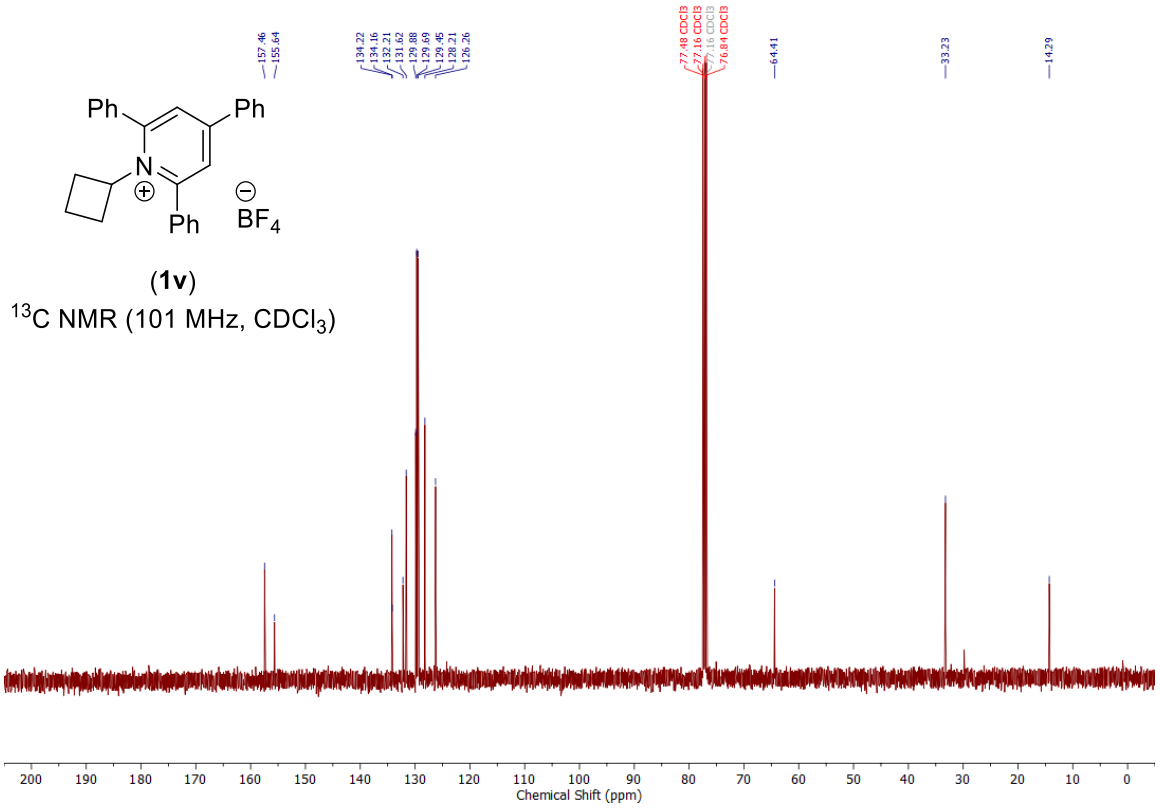


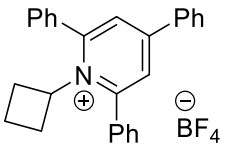
(**1u**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-cyclobutyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1v)



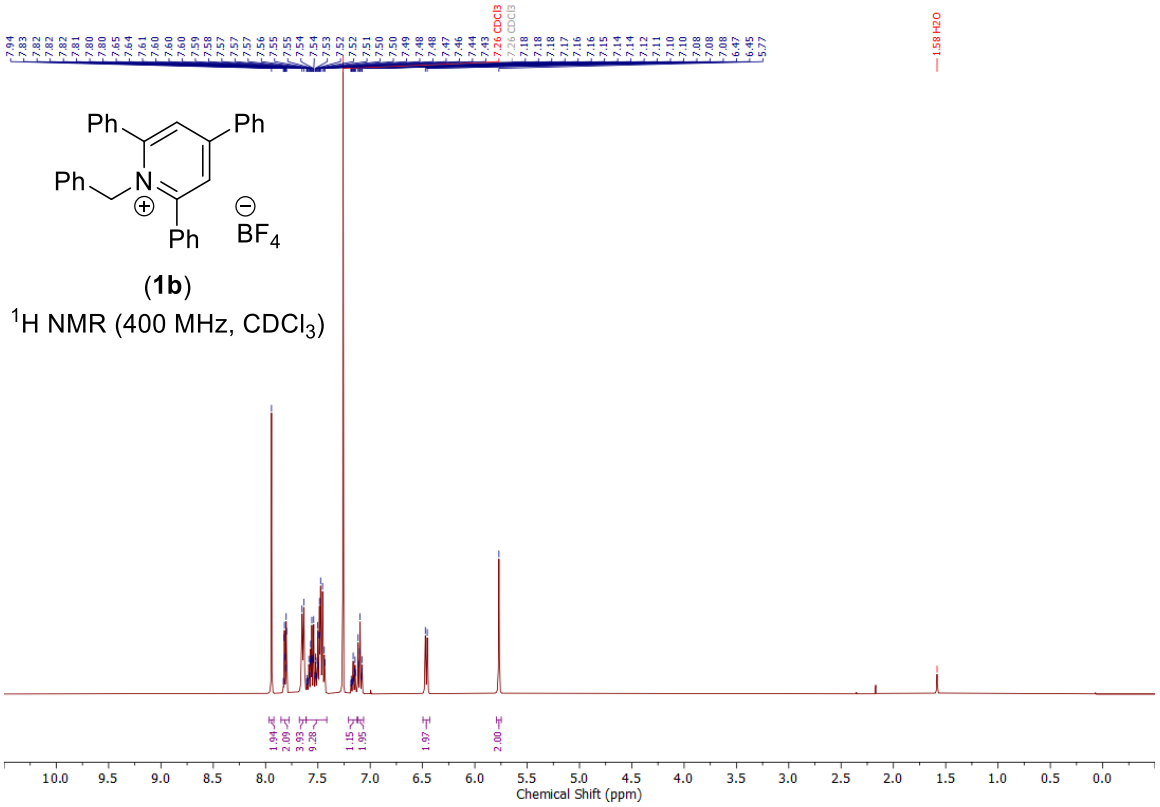


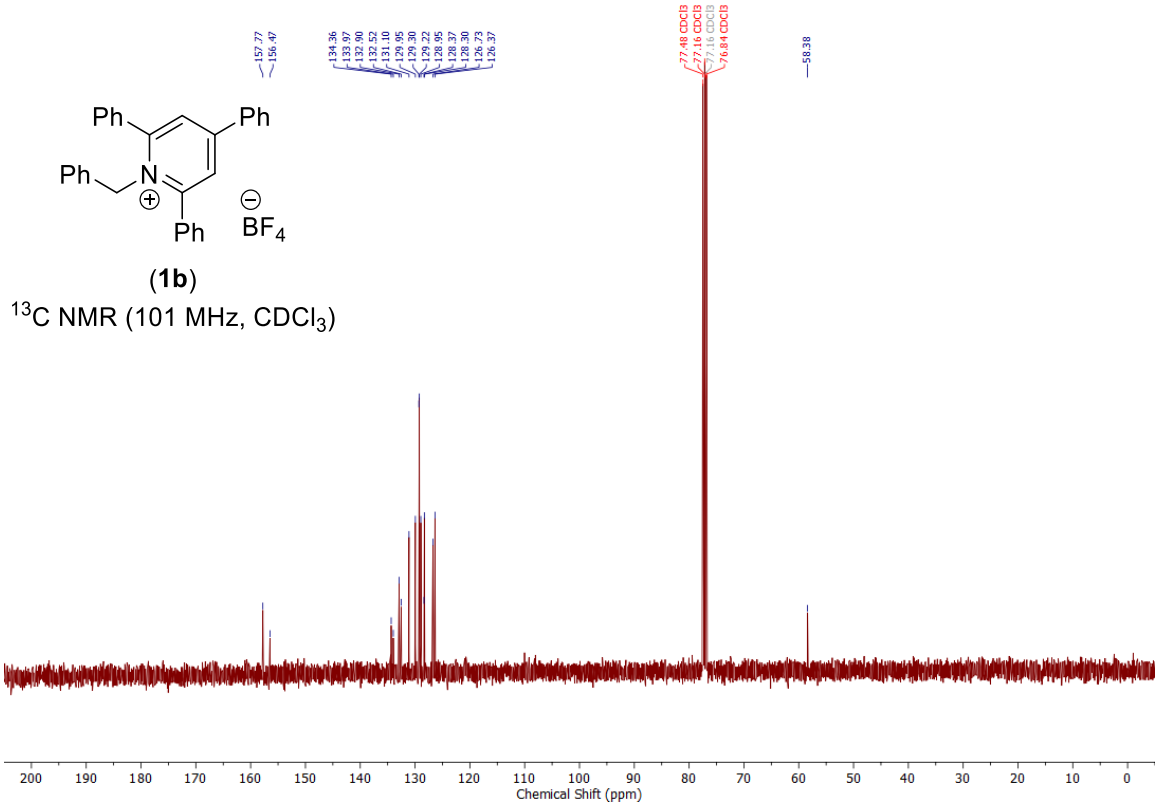


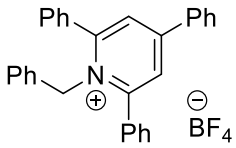
(**1v**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-benzyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1b)



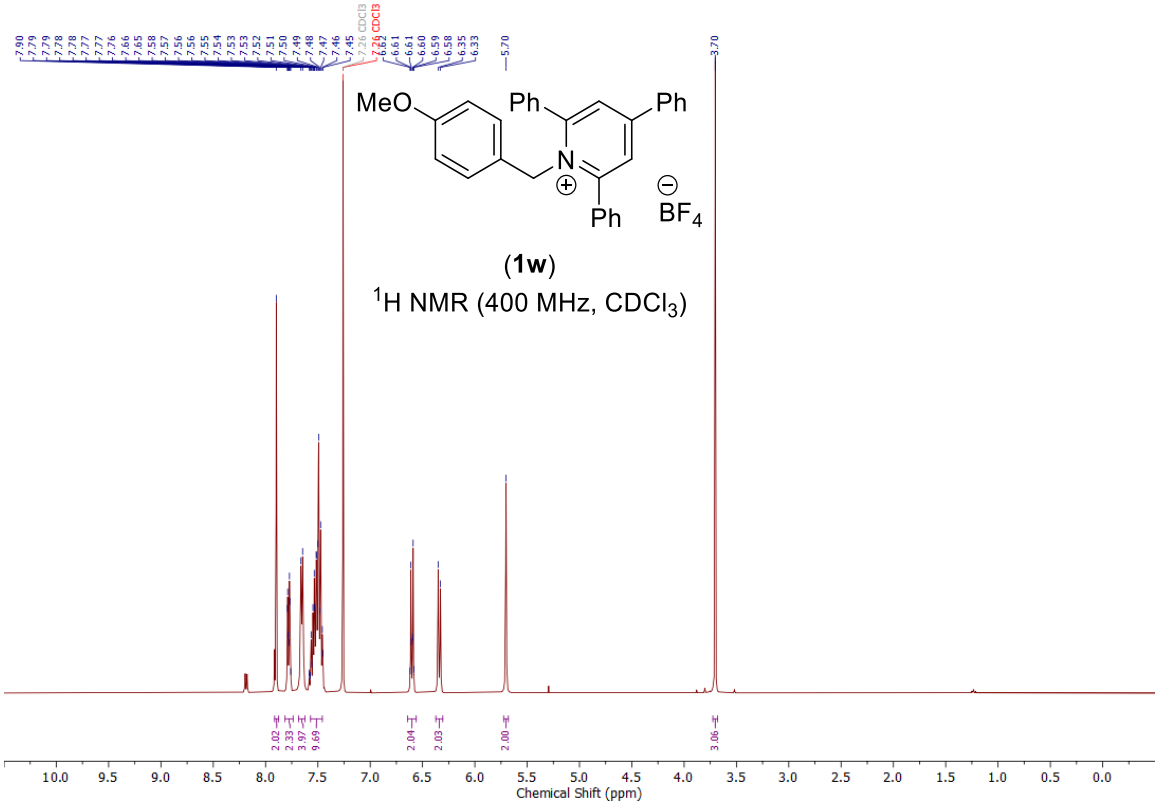


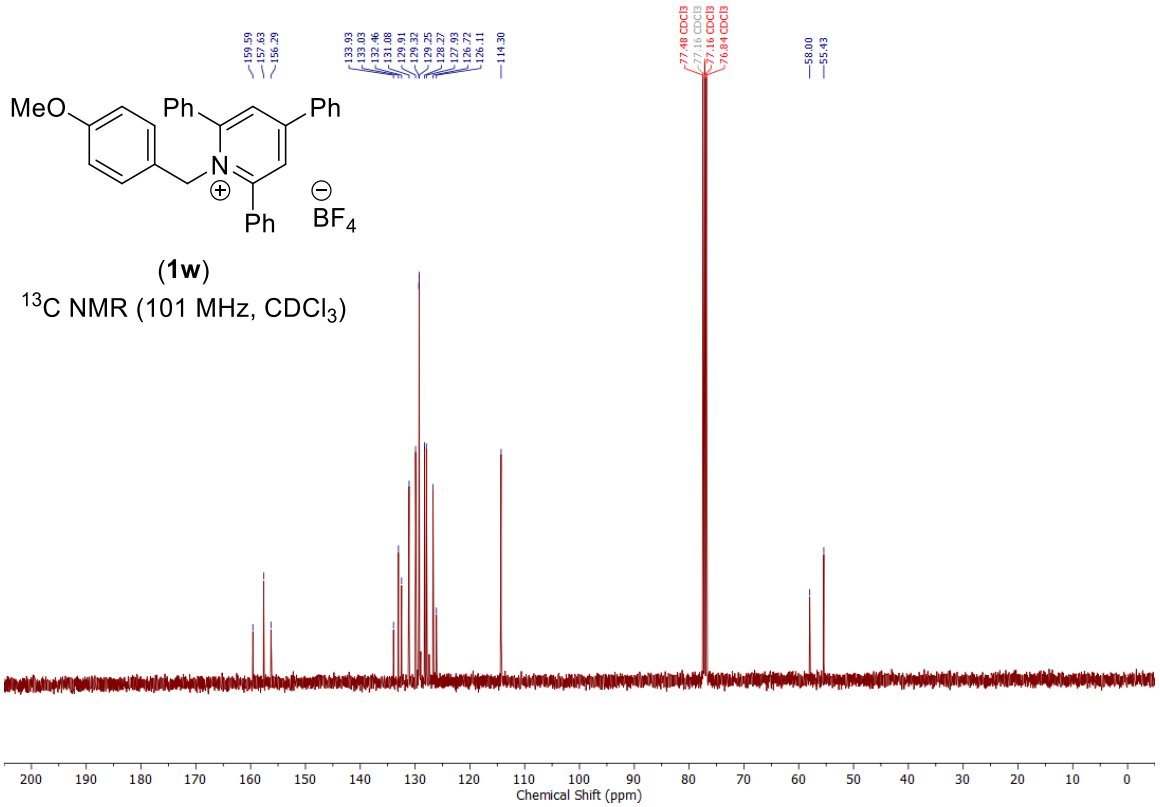


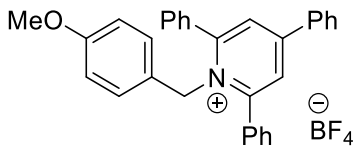
(**1b**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(4-methoxybenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1w)



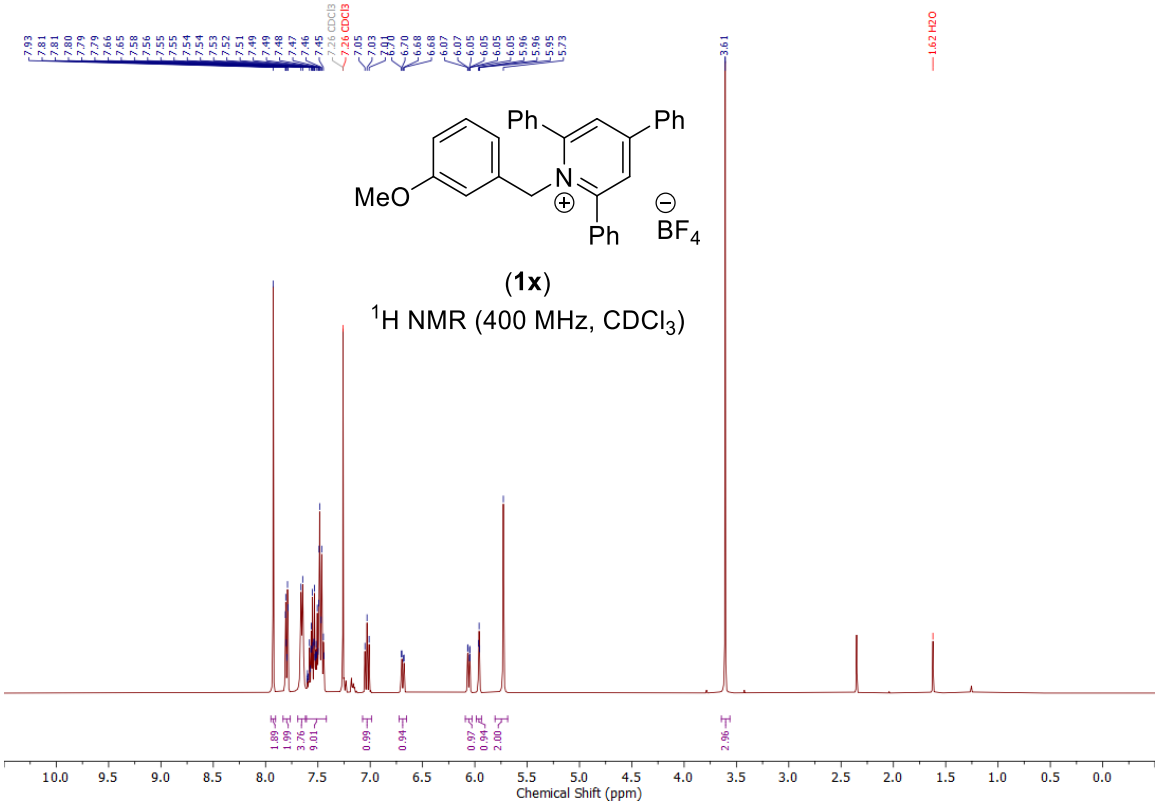


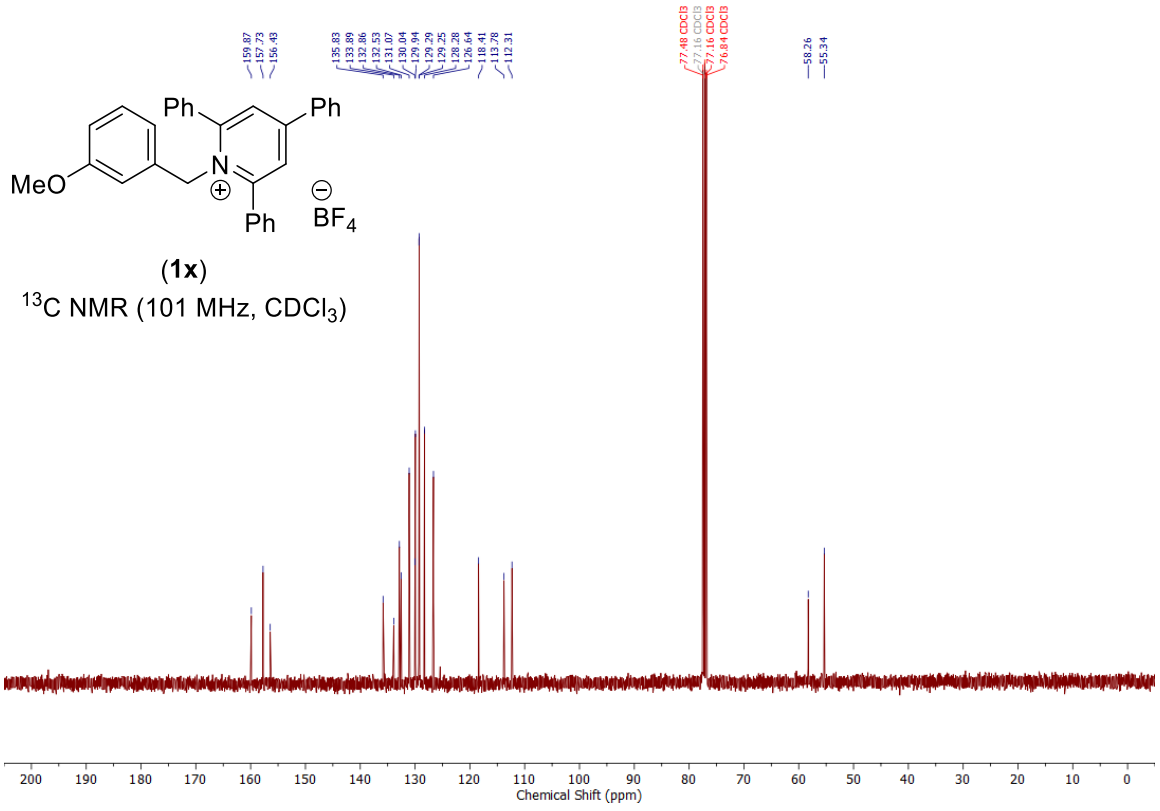


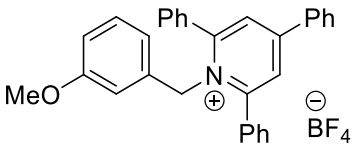
(**1w**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(3-methoxybenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1x)



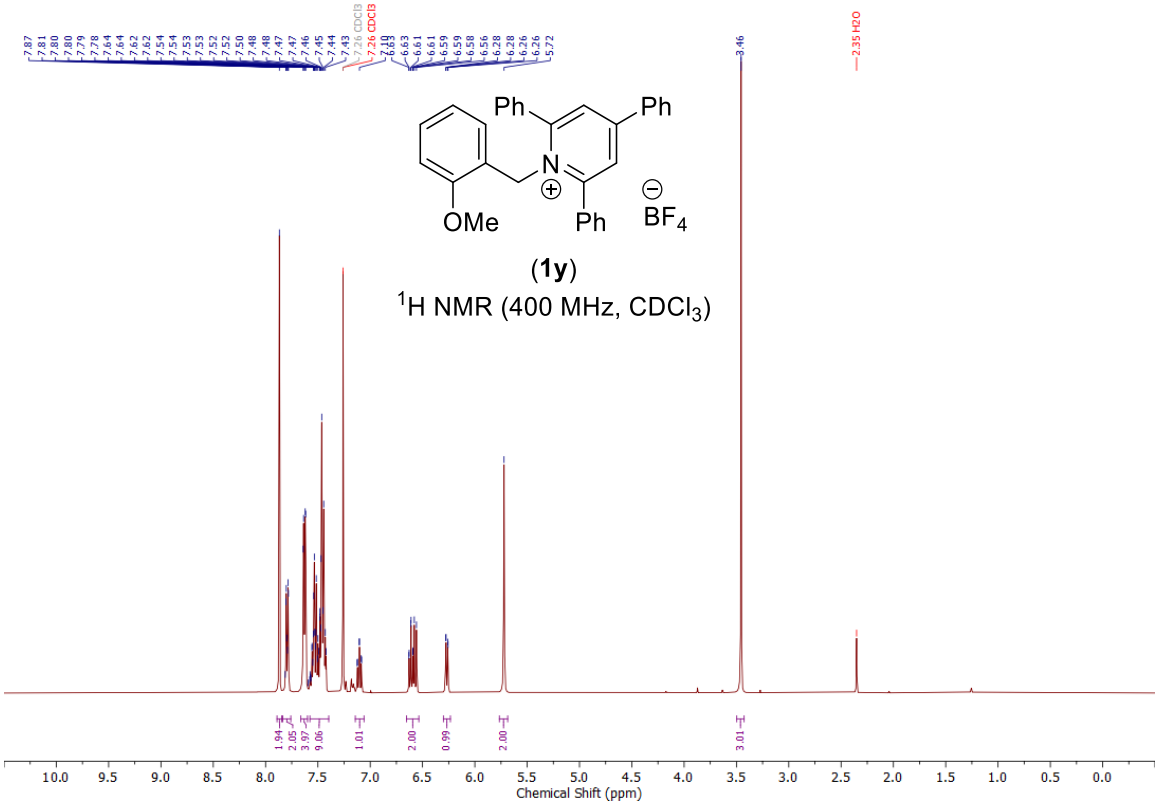


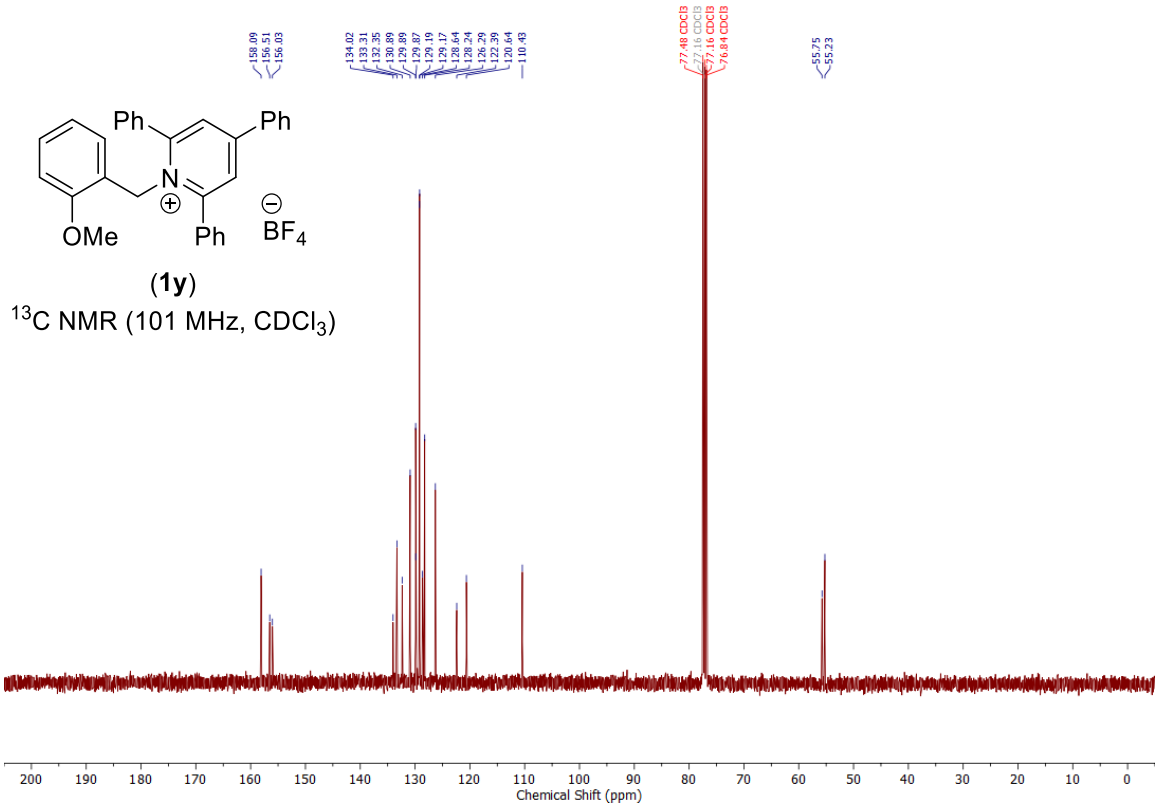


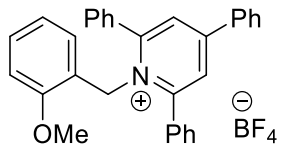
(**1x**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(2-methoxybenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1y)



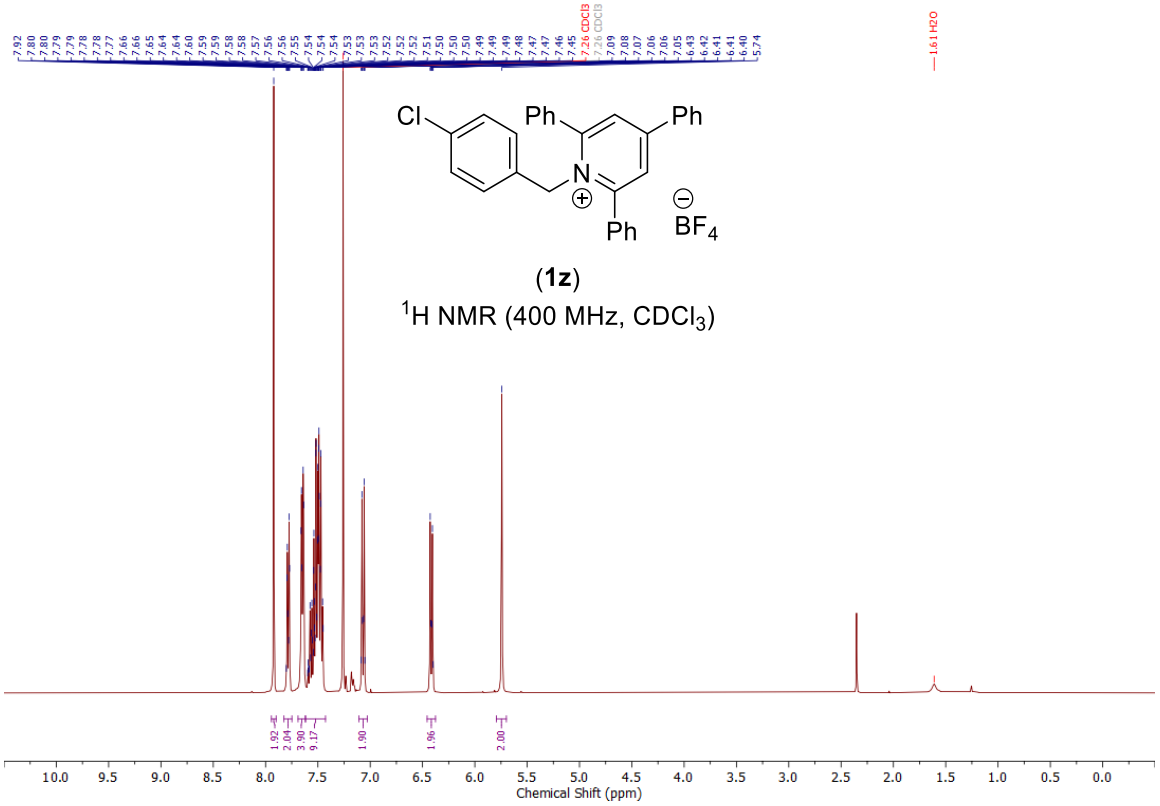


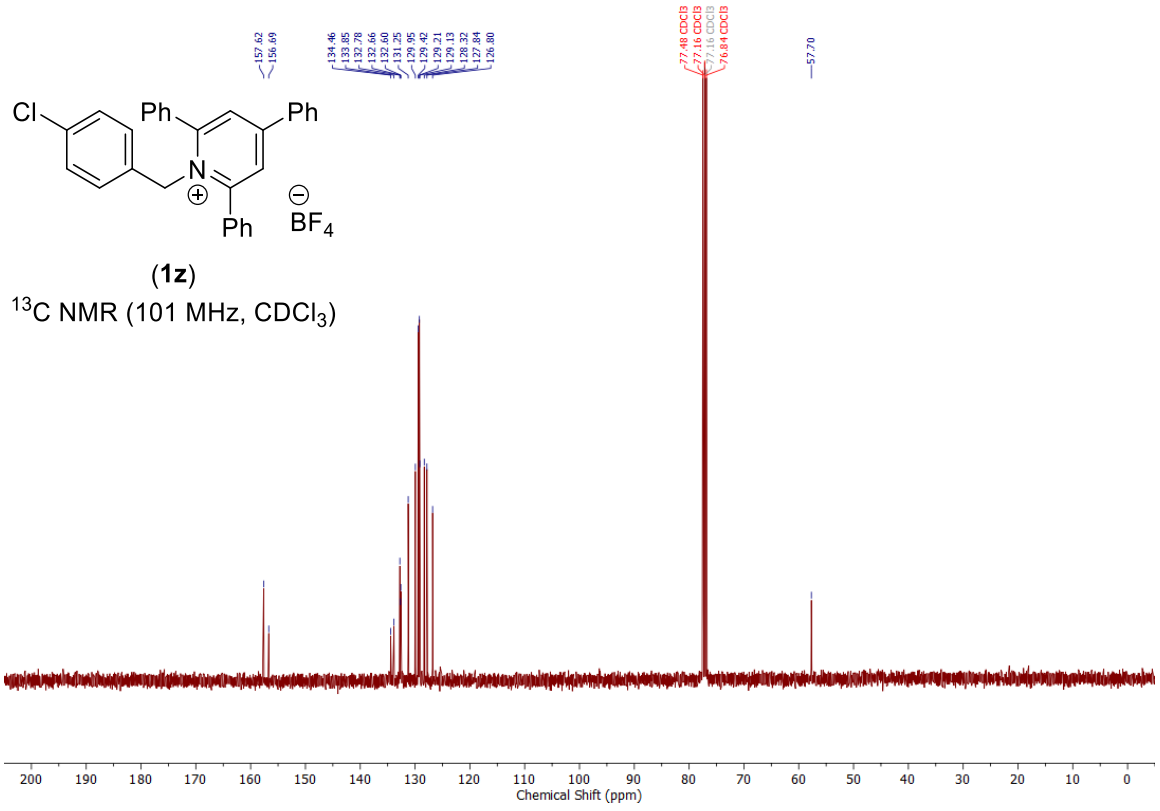


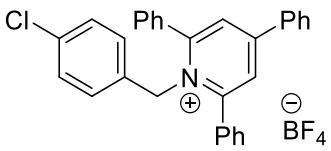
(**1y**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(4-chlorobenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1z)



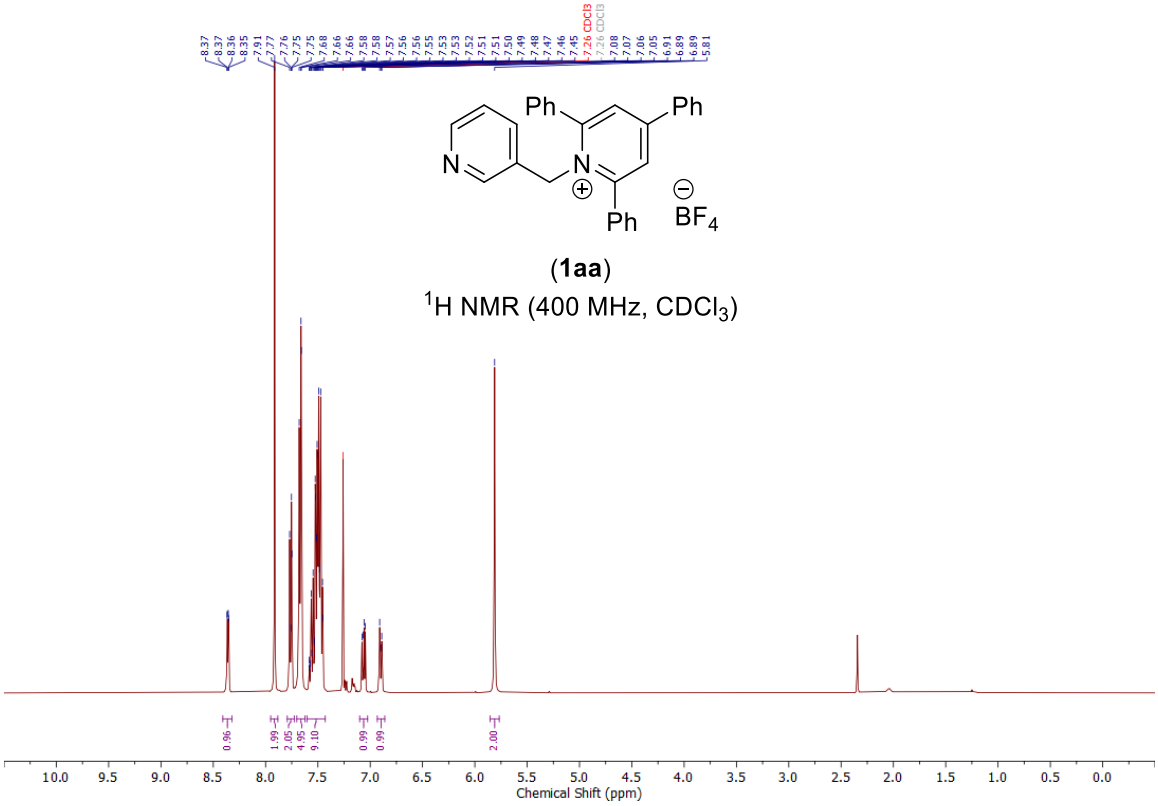


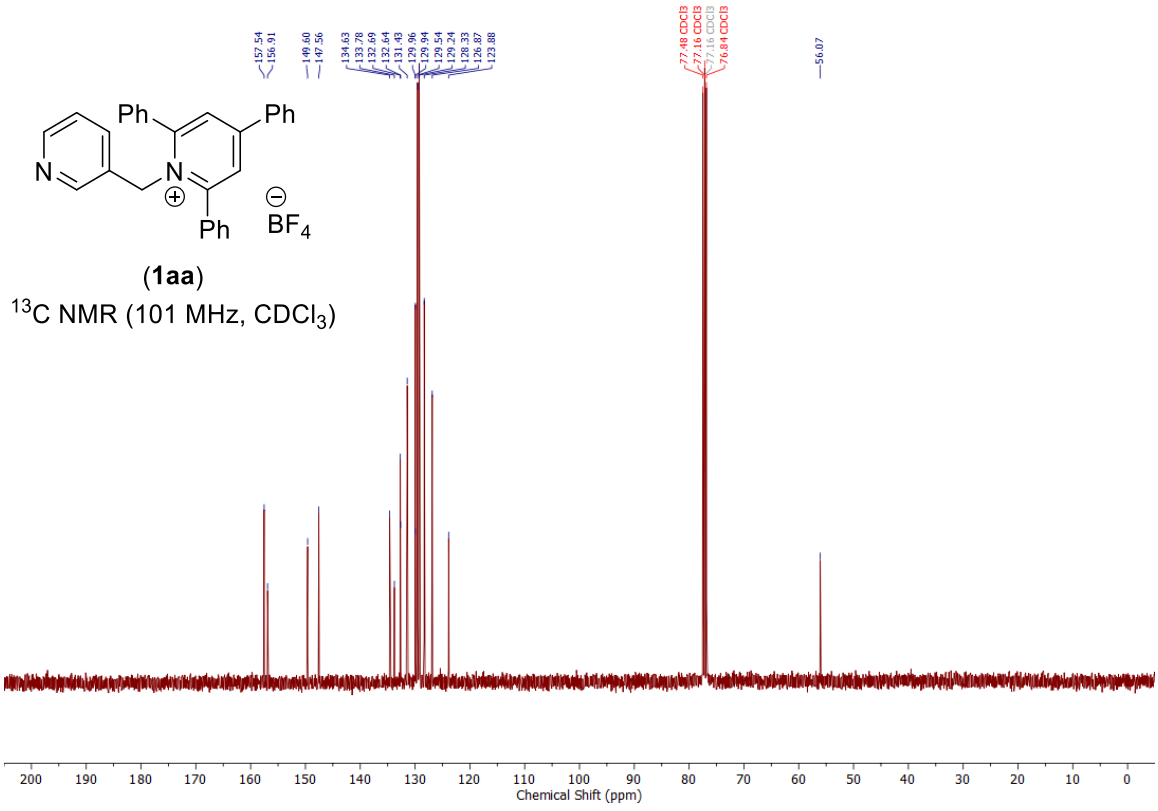


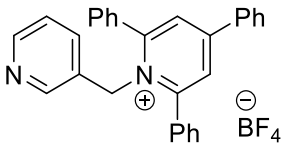
(**1z**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 2,4,6-triphenyl-1-(pyridin-3-ylmethyl)pyridin-1-ium tetrafluoroborate (1aa)



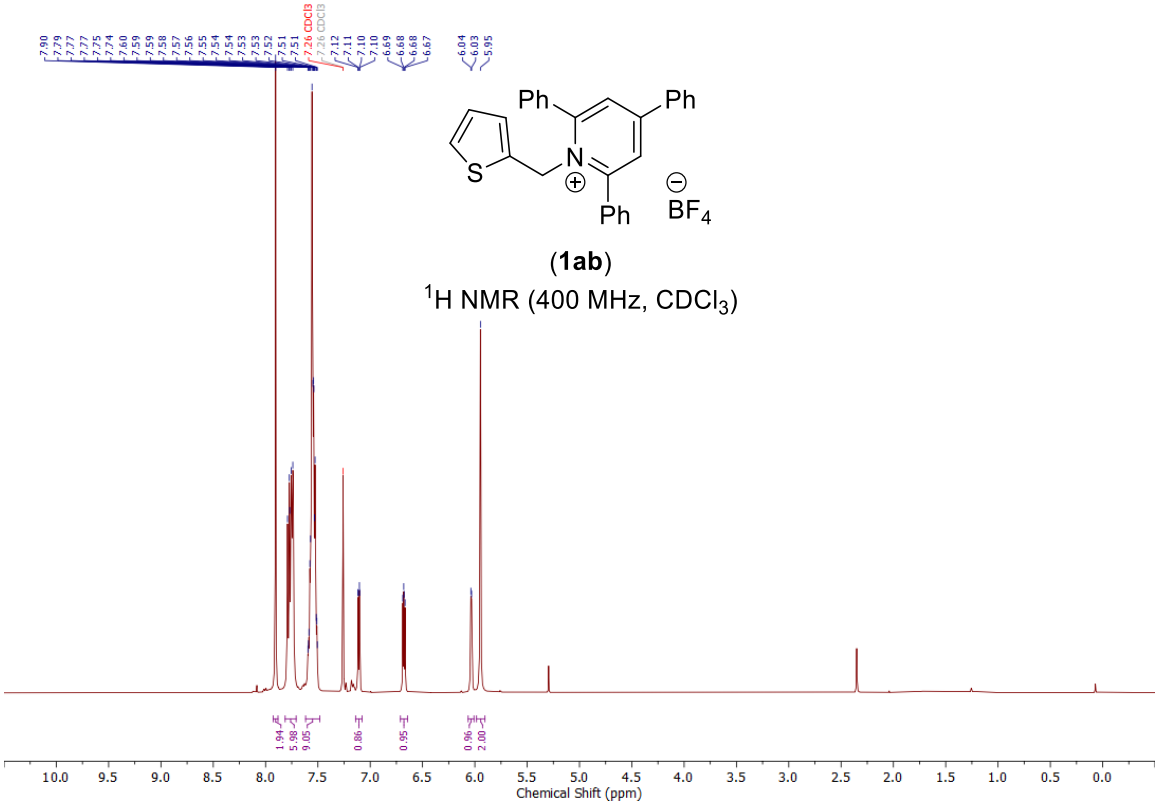


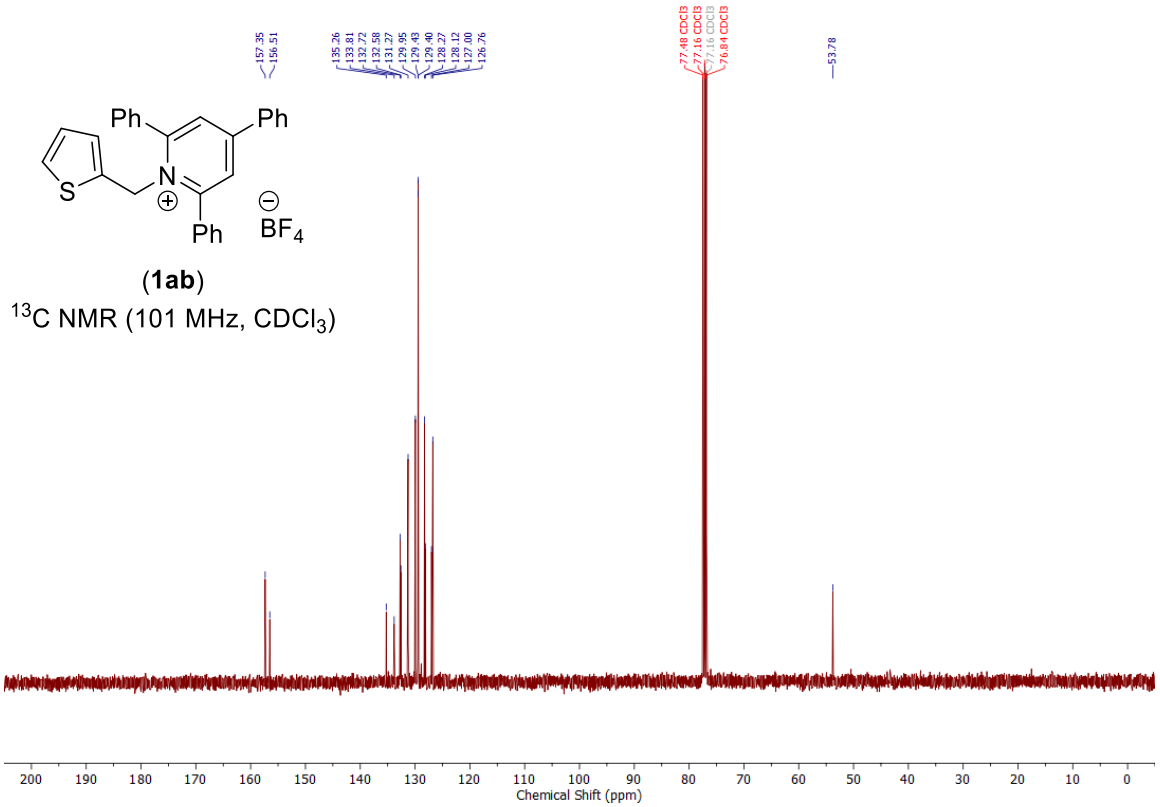


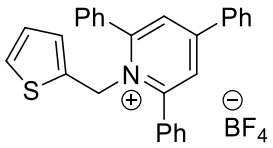
(**1aa**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 2,4,6-triphenyl-1-(thiophen-2-ylmethyl)pyridin-1-ium tetrafluoroborate (1ab)



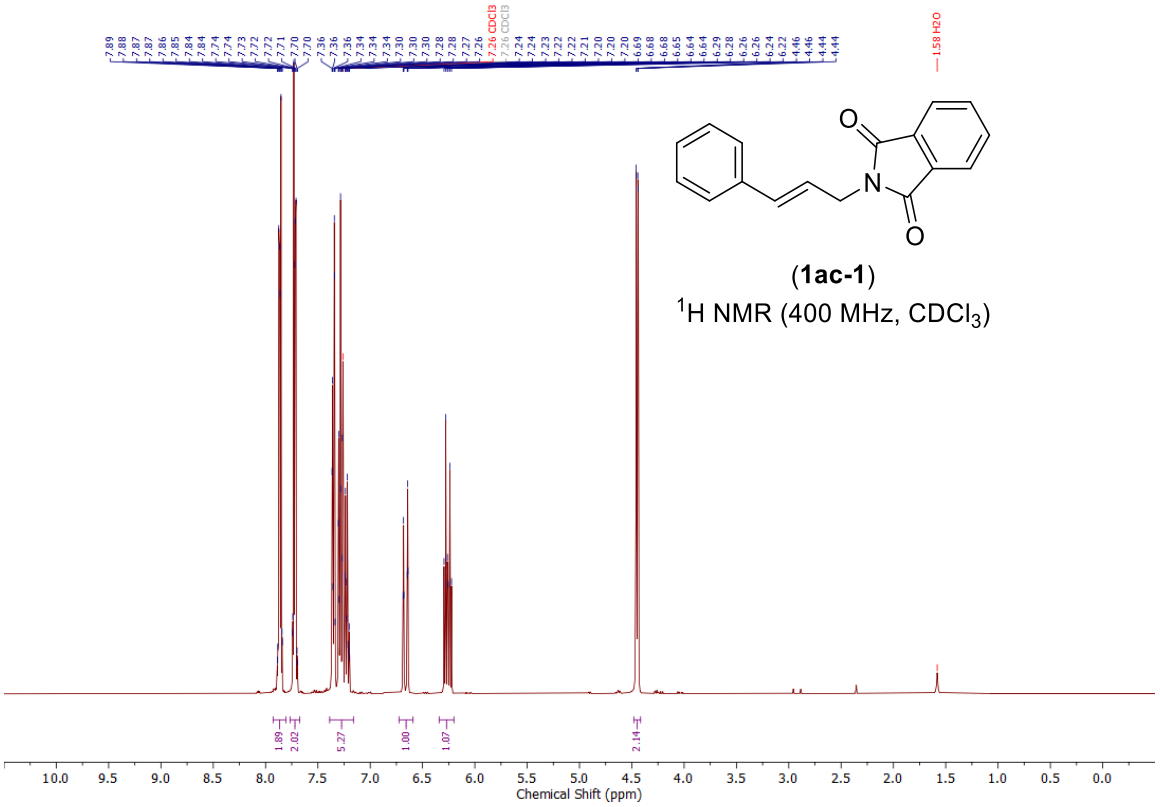


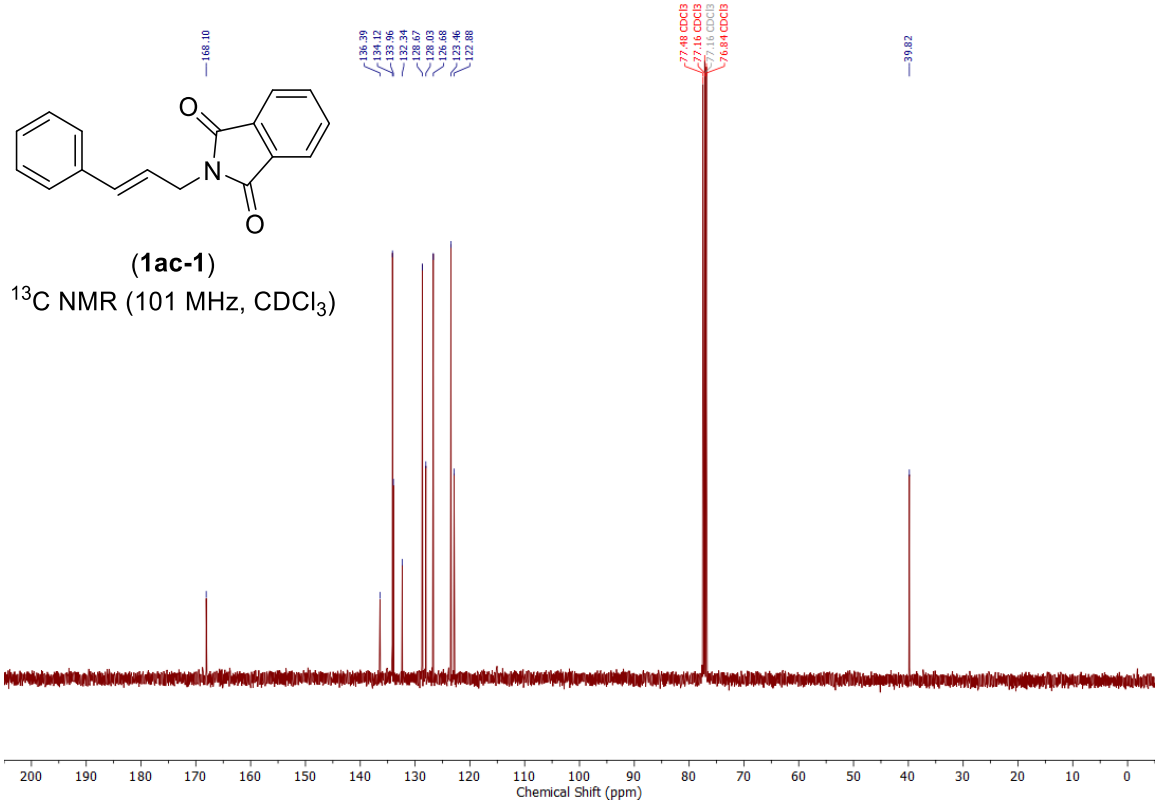


(**1ab**)

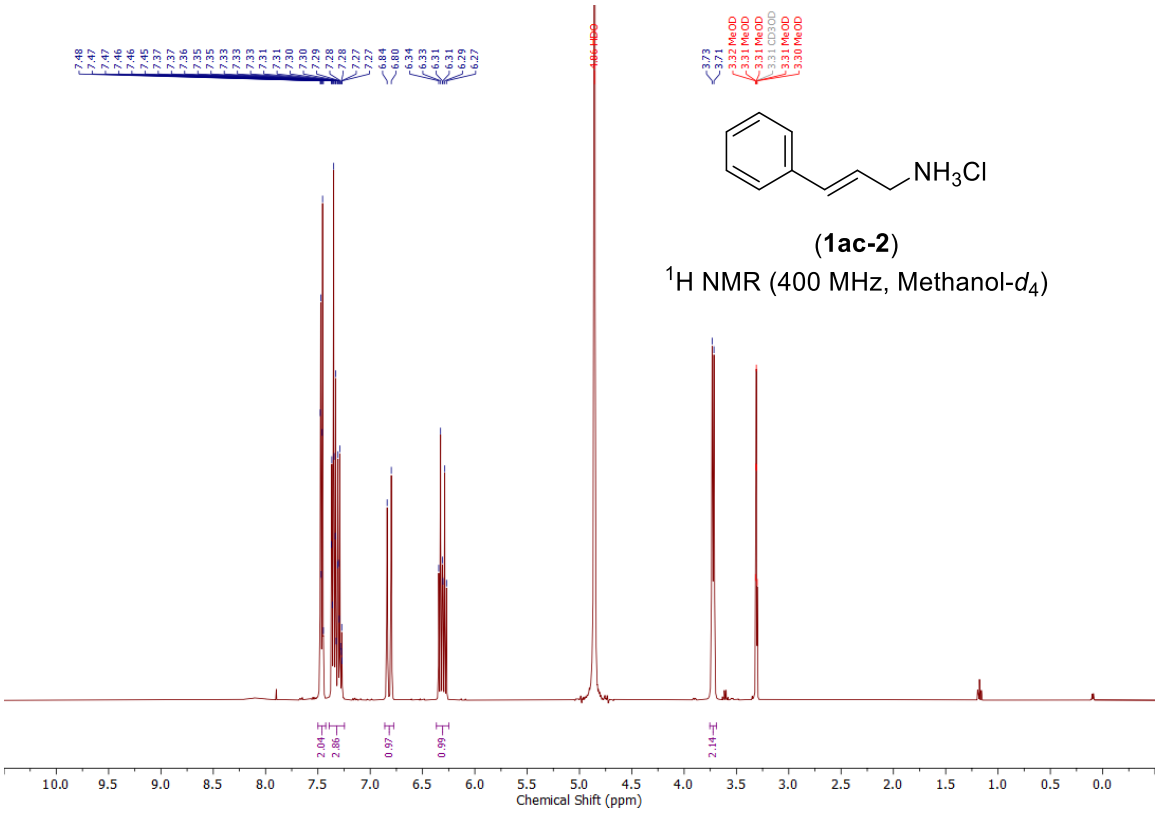
^{19}F NMR (377 MHz, $CDCl_3$)

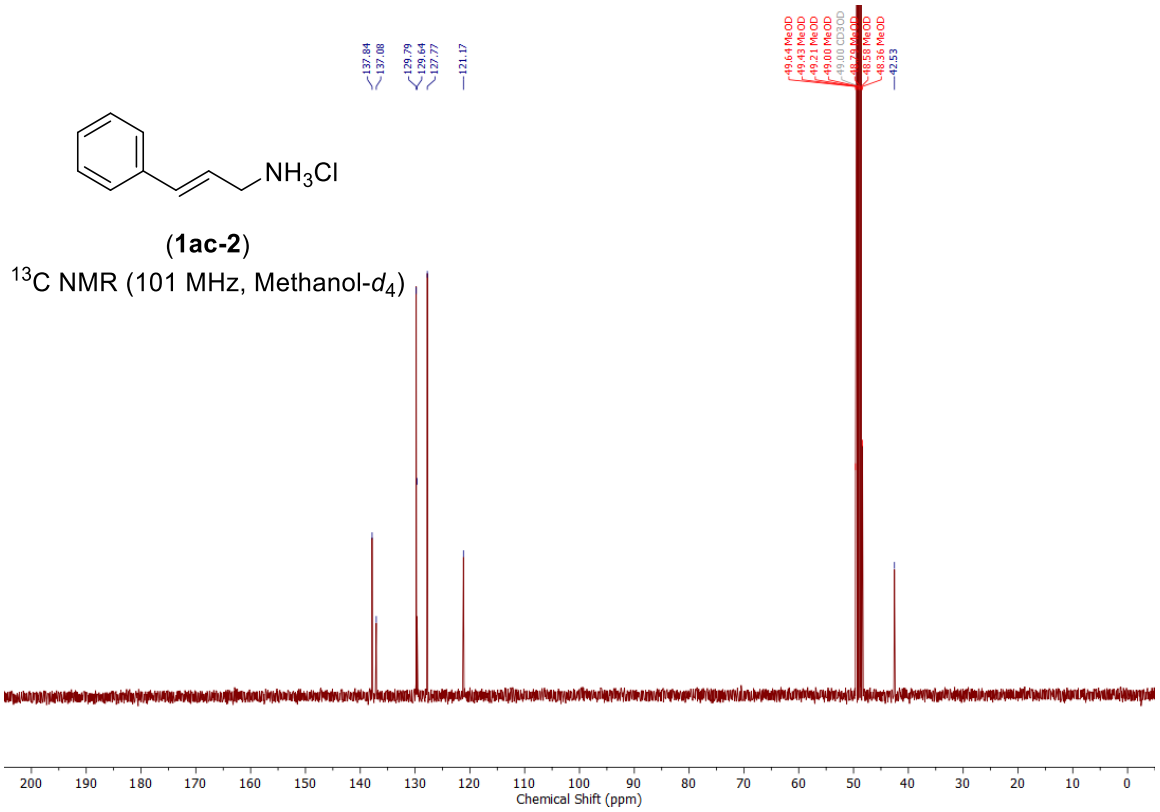
NMR spectra of 2-cinnamylisoindoline-1,3-dione (1ac-1)



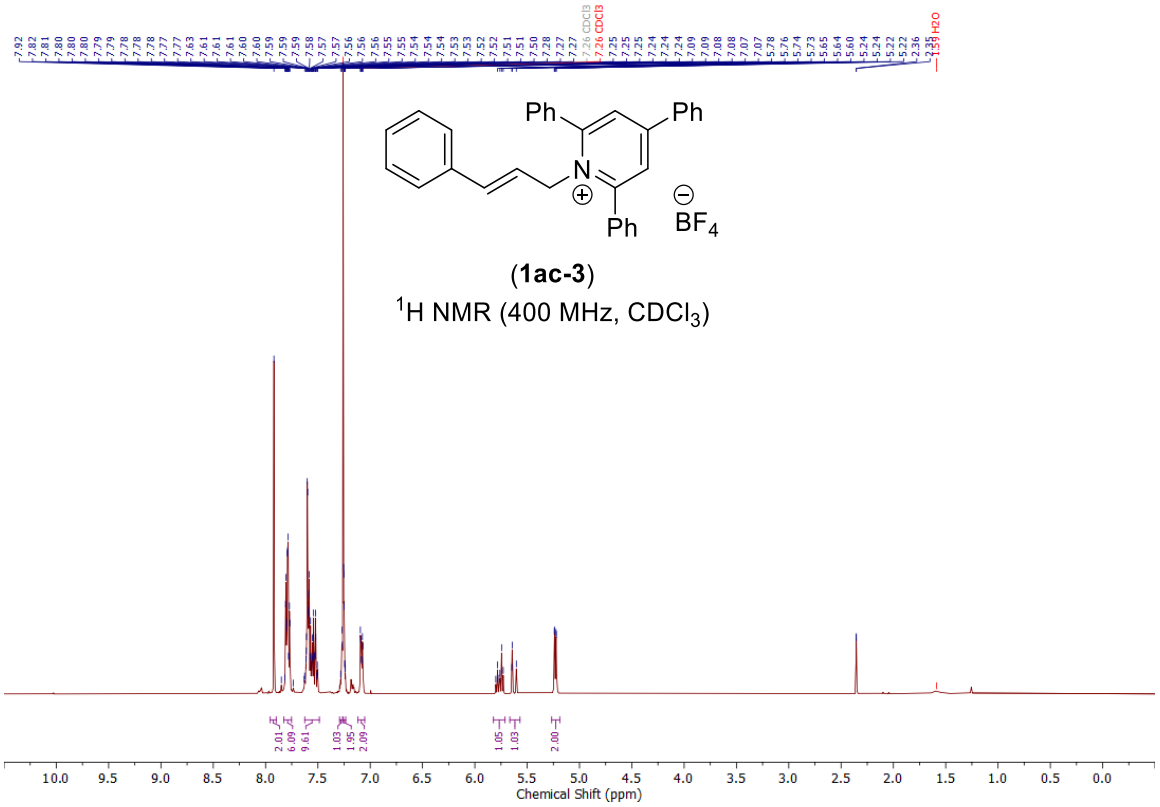


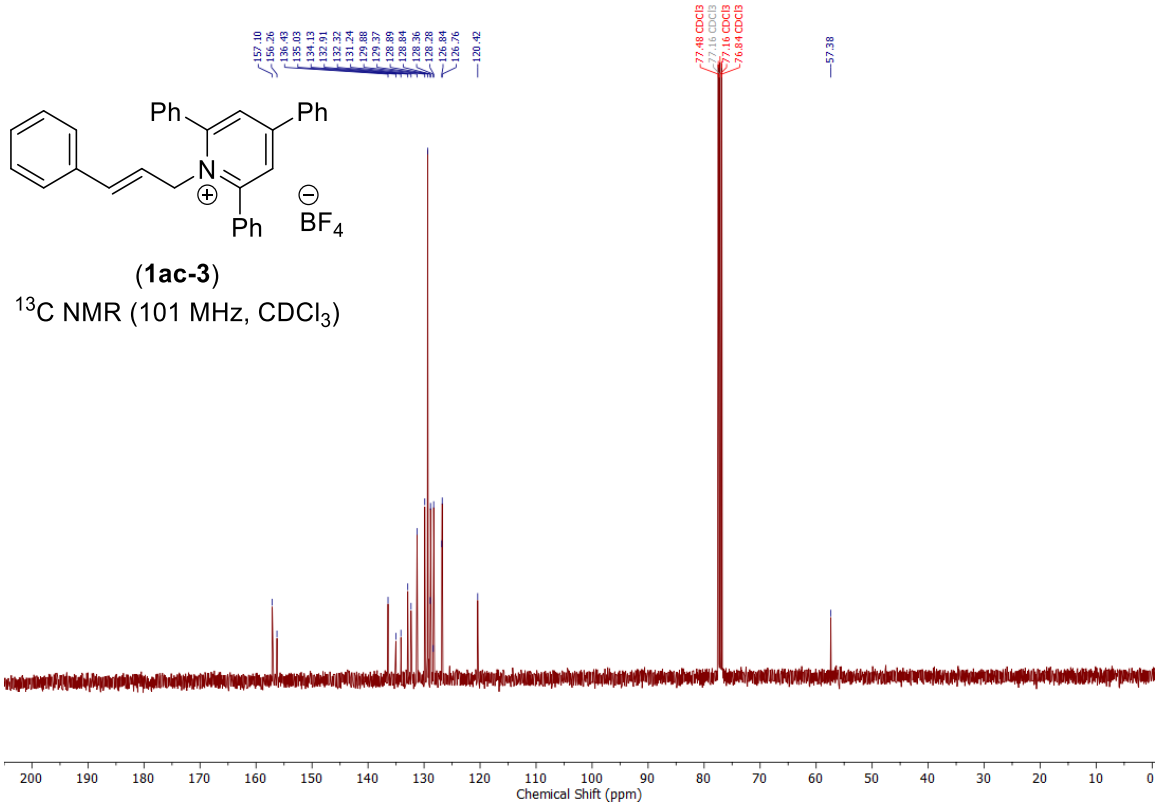
NMR spectra of (*E*)-3-phenylprop-2-en-1-aminium chloride (1ac-2)

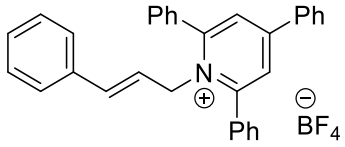




NMR spectra of 1-cinnamyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1ac-3)



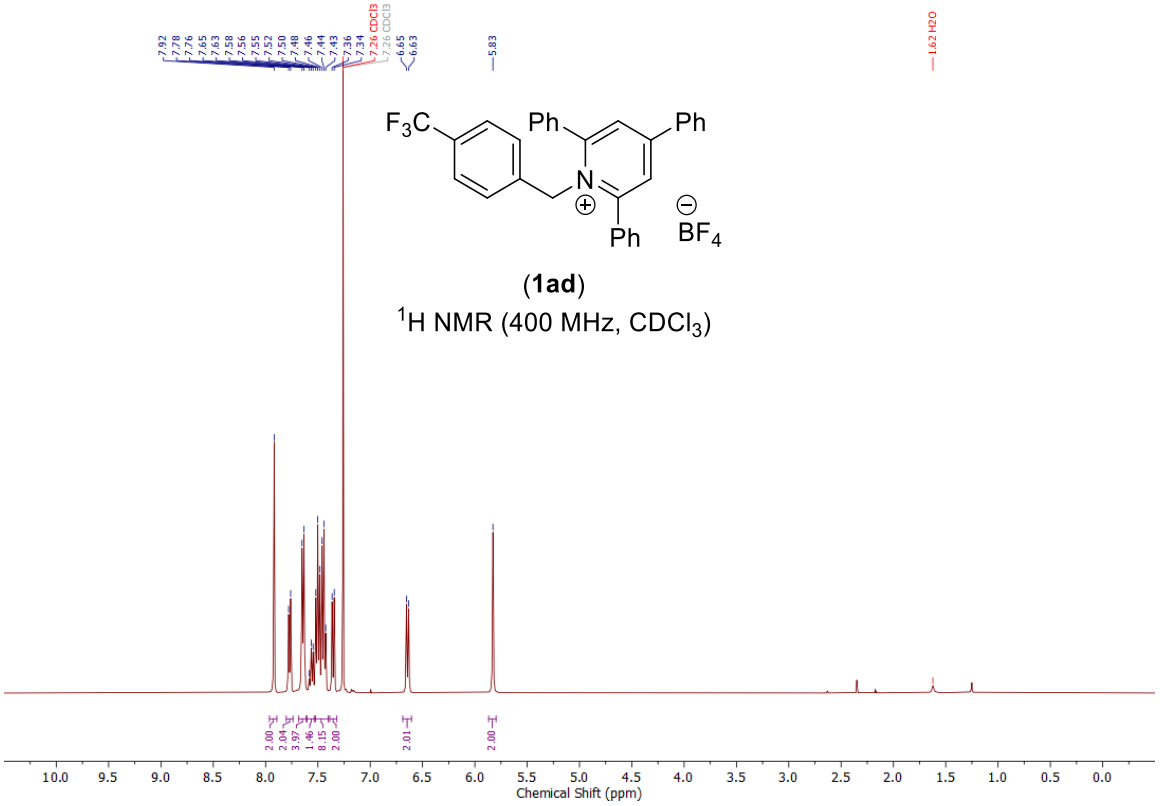


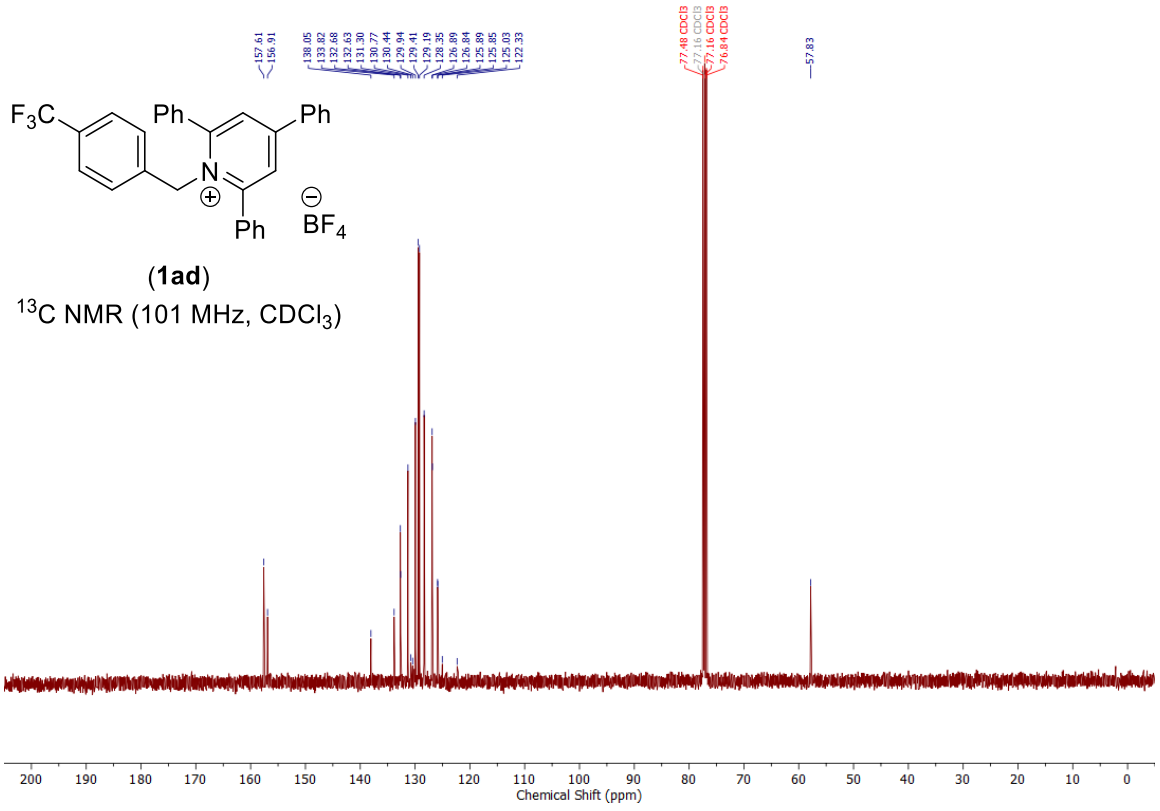


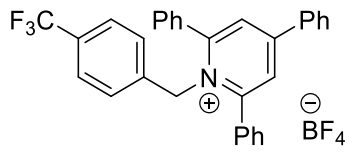
(**1ac-3**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 2,4,6-triphenyl-1-(4-(trifluoromethyl)benzyl)pyridin-1-ium tetrafluoroborate (1ad)



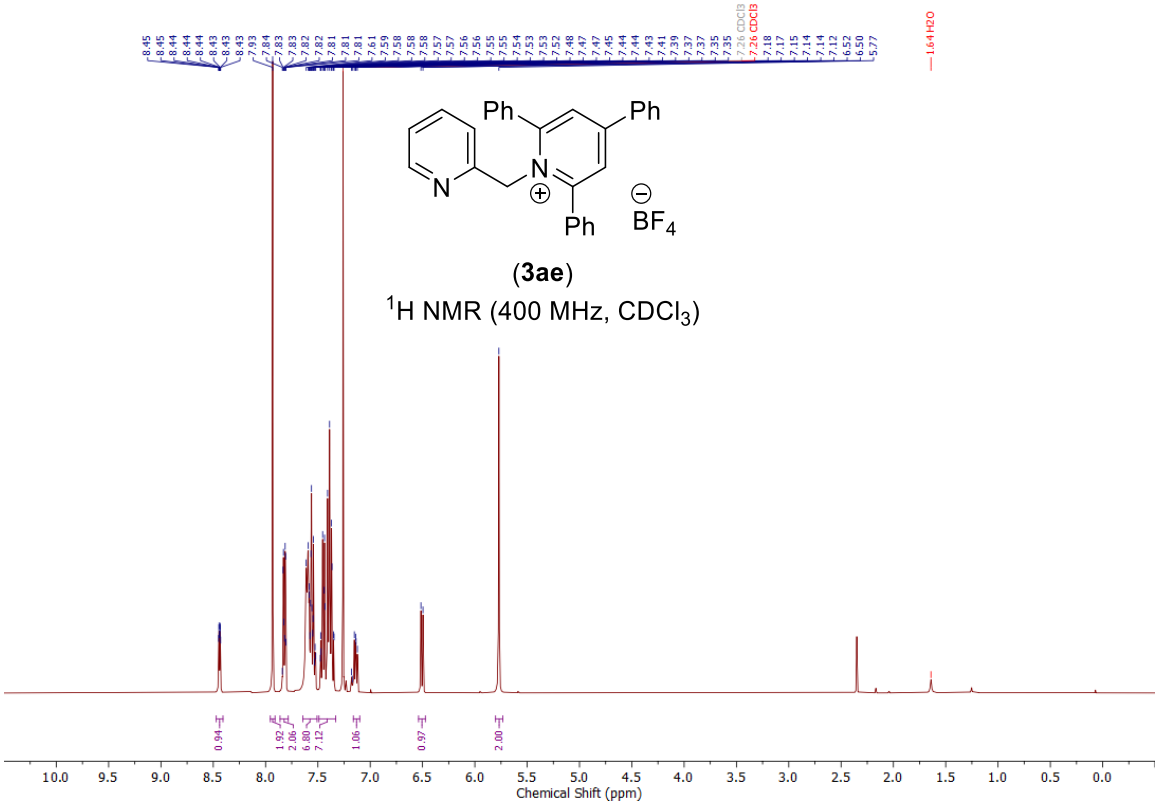




(**1ad**)

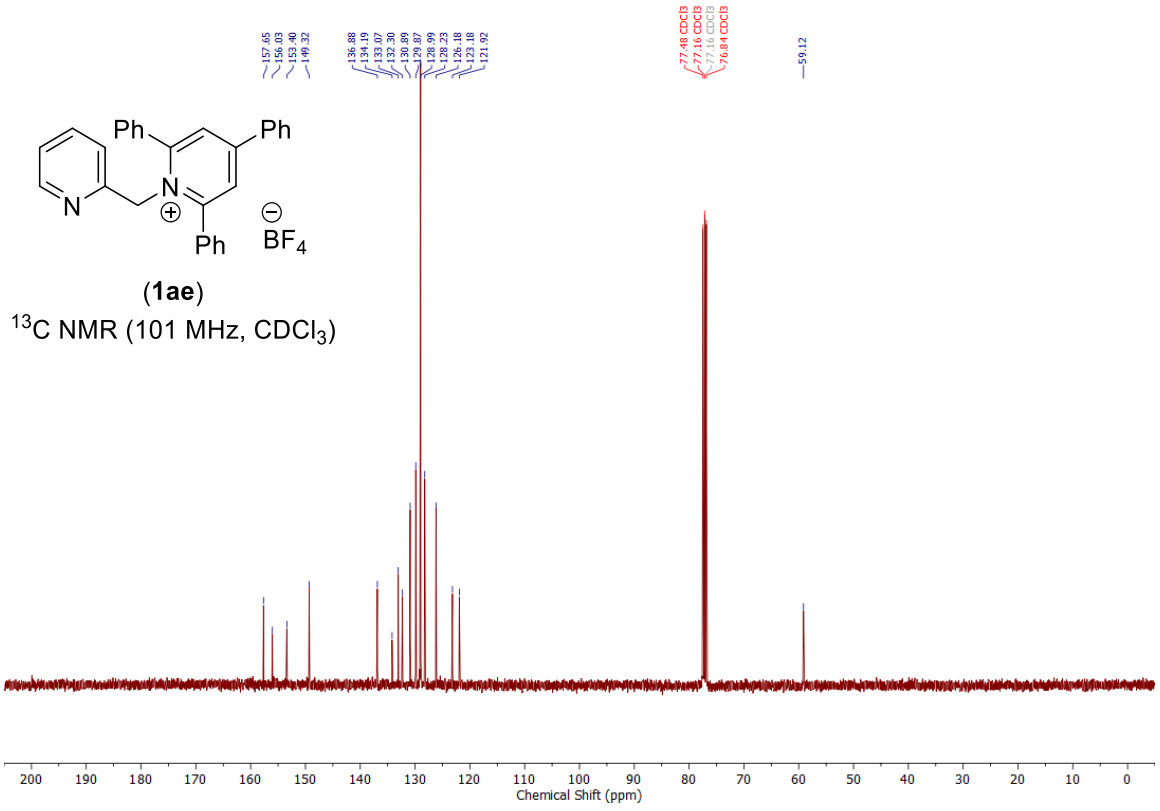
^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 2,4,6-triphenyl-1-(pyridin-2-ylmethyl)pyridin-1-ium tetrafluoroborate (1ae)



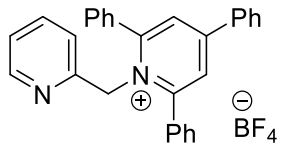
(**3ae**)

^{1}H NMR (400 MHz, $CDCl_3$)



(**1ae**)

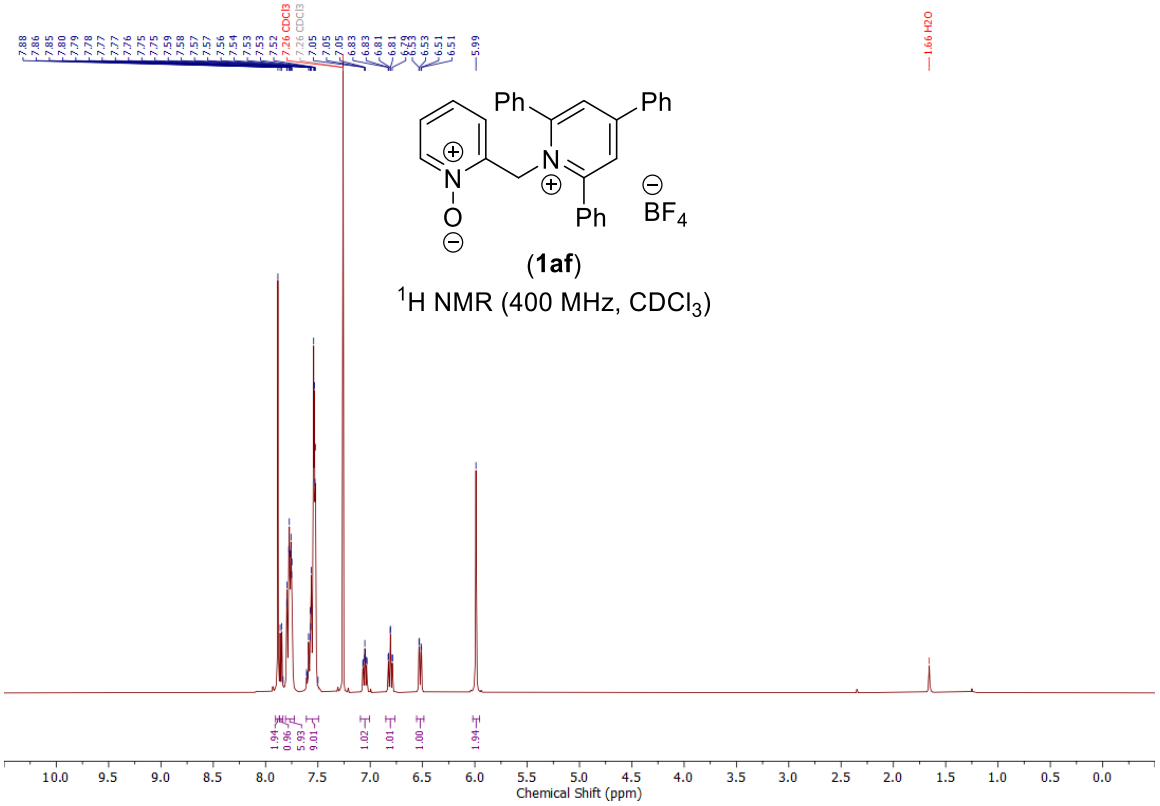
^{13}C NMR (101 MHz, $CDCl_3$)

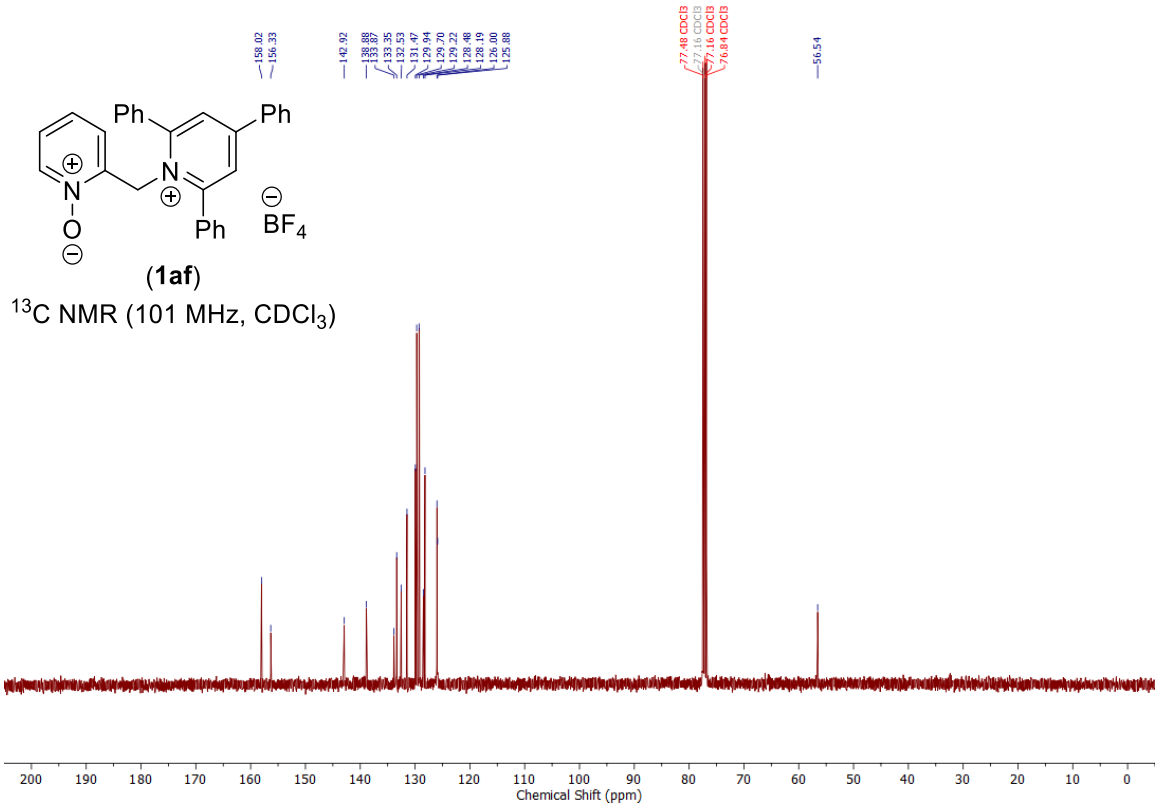


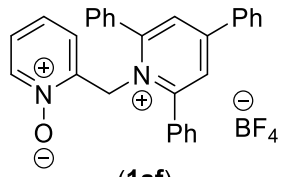
(**1ae**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 2-((2,4,6-triphenylpyridin-1-ium-1-yl)methyl)pyridine 1-oxide tetrafluoroborate (1af)



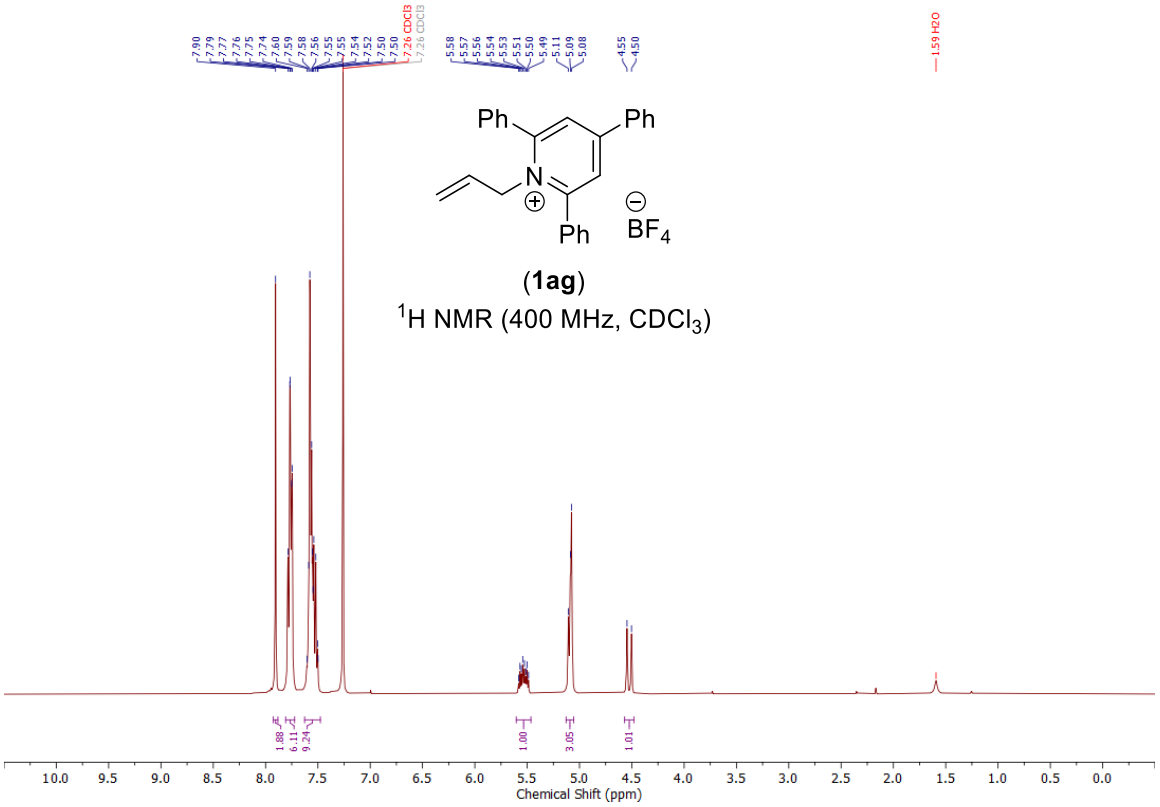


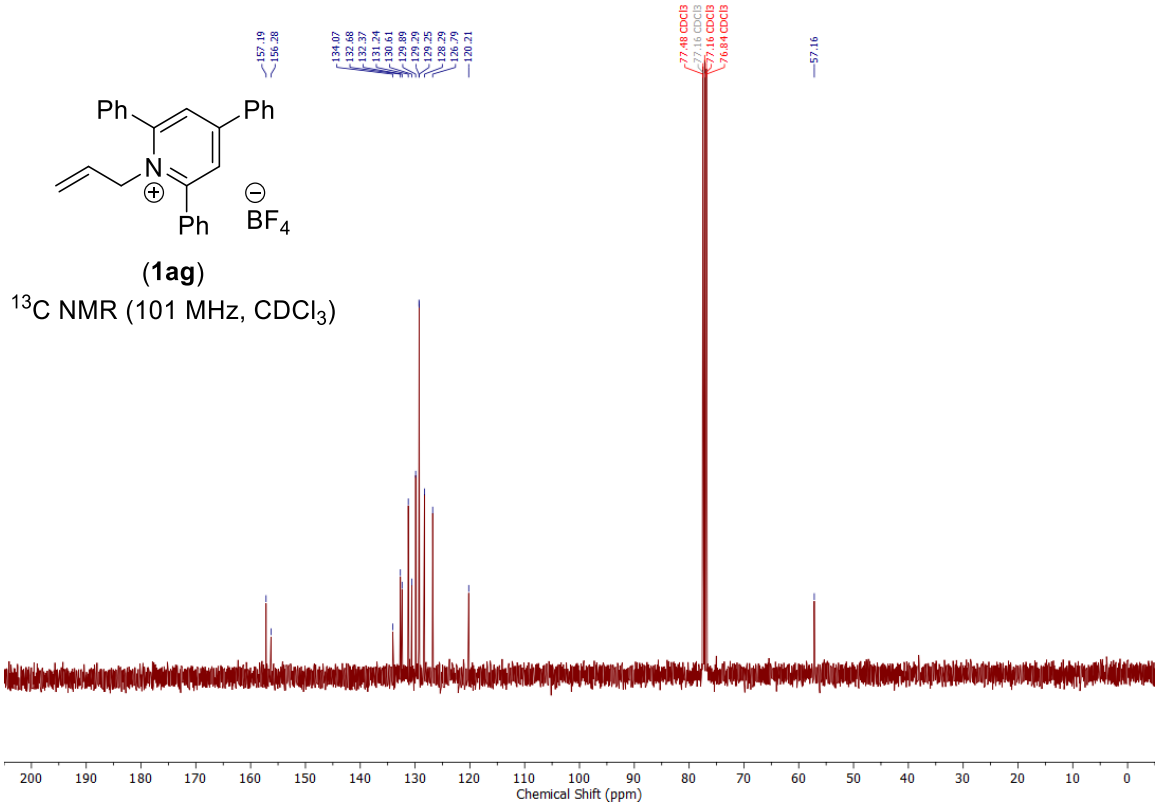


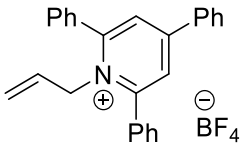
(**1af**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-allyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1ac)



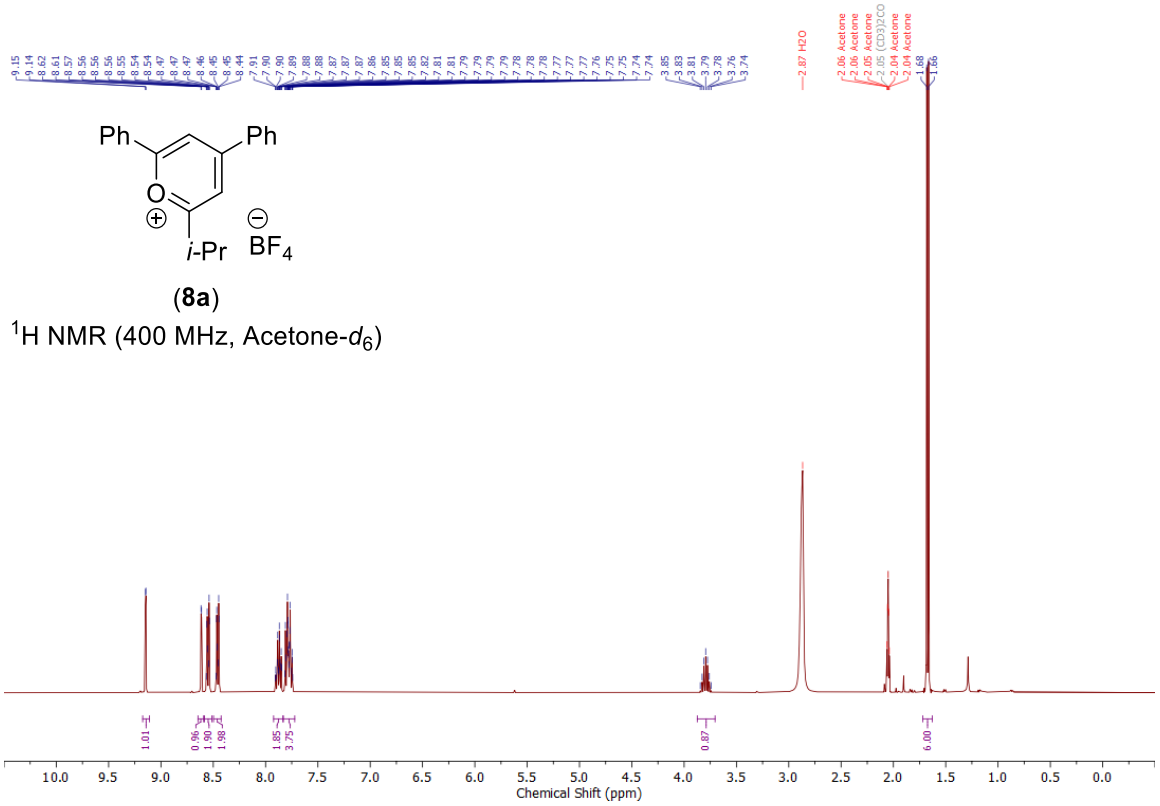




(**1ag**)

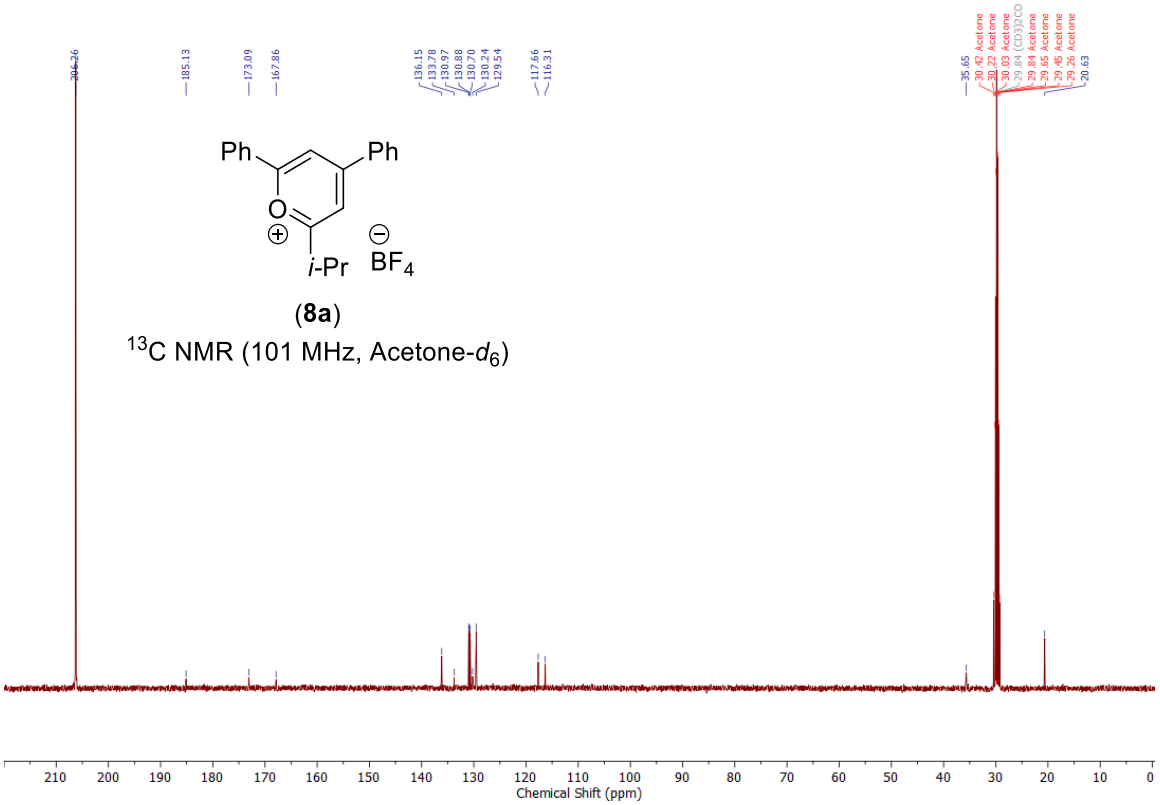
^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 2-isopropyl-4,6-diphenylpyrylium tetrafluoroborate (8a)



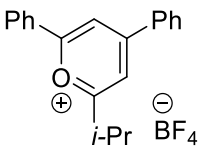
(**8a**)

^{1}H NMR (400 MHz, Acetone-d_6)



(**8a**)

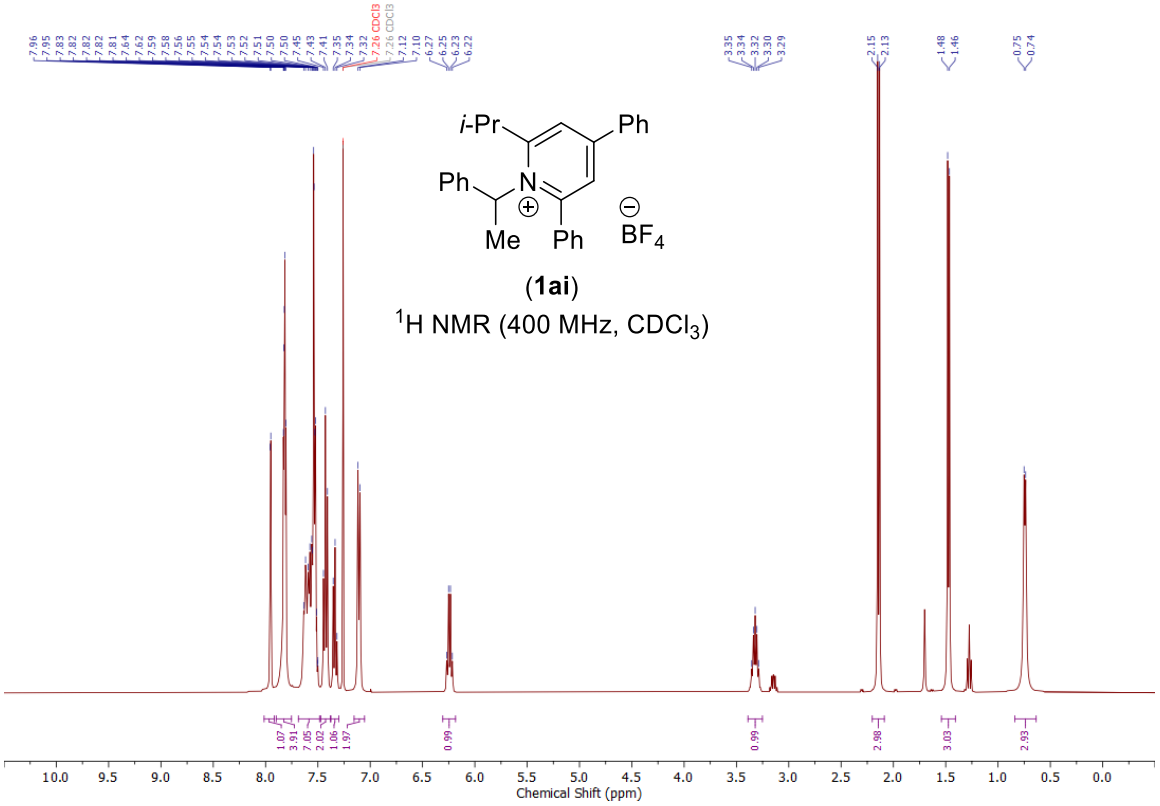
^{13}C NMR (101 MHz, Acetone-d_6)

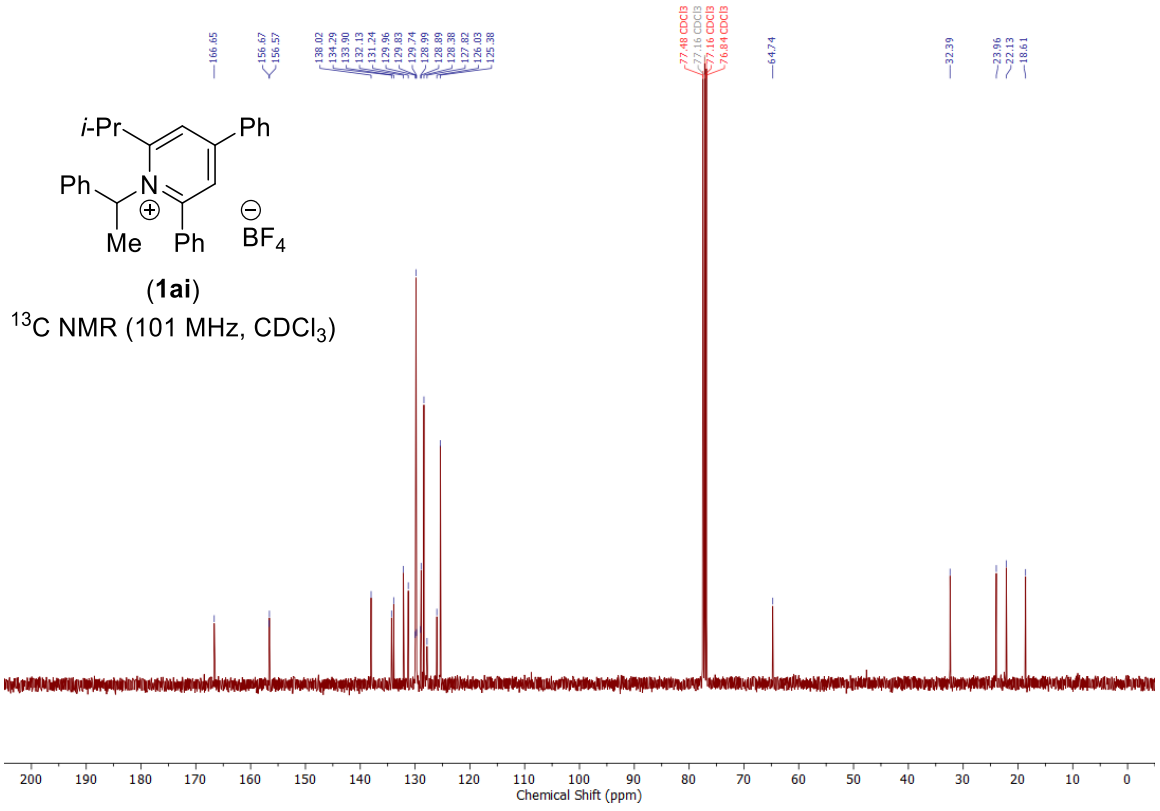


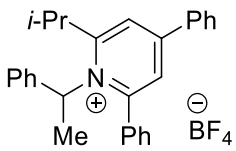
(**8a**)

^{19}f NMR (377 MHz, Acetone-d_6)

NMR spectra of 2-isopropyl-4,6-diphenyl-1-(1-phenylethyl)pyridin-1-ium tetrafluoroborate (1ai)



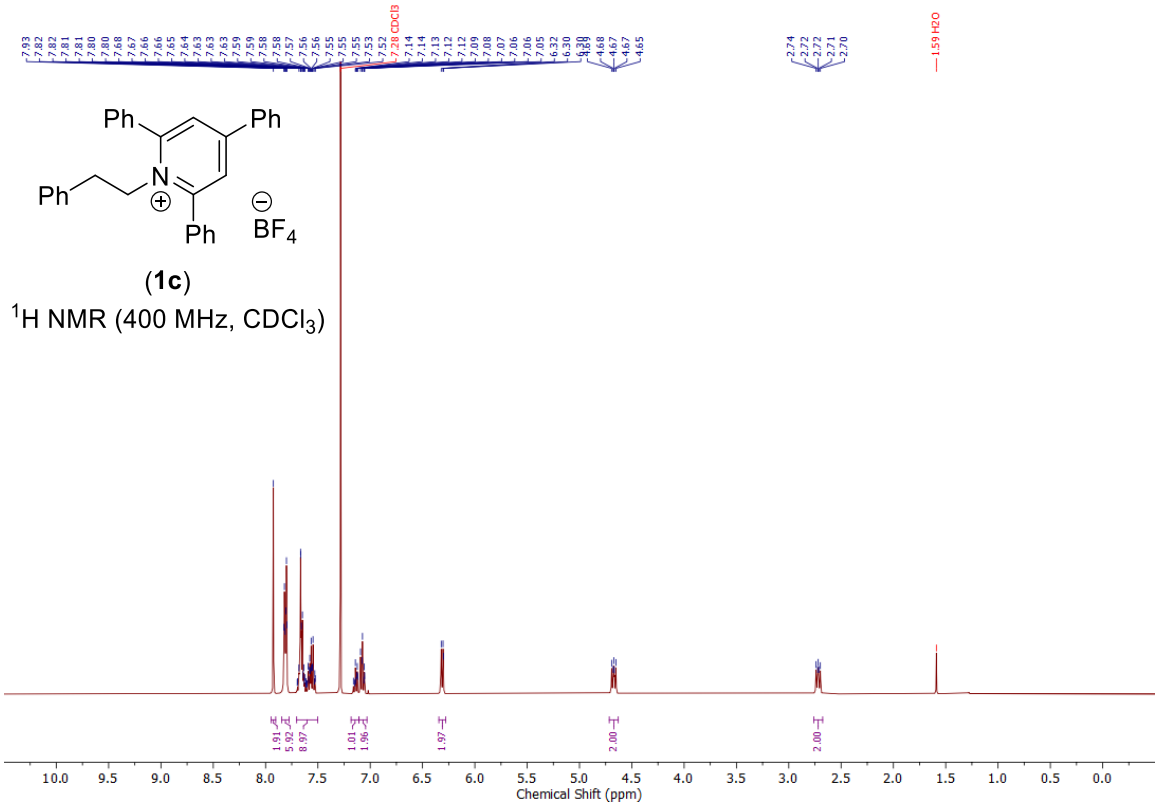




(**1ai**)

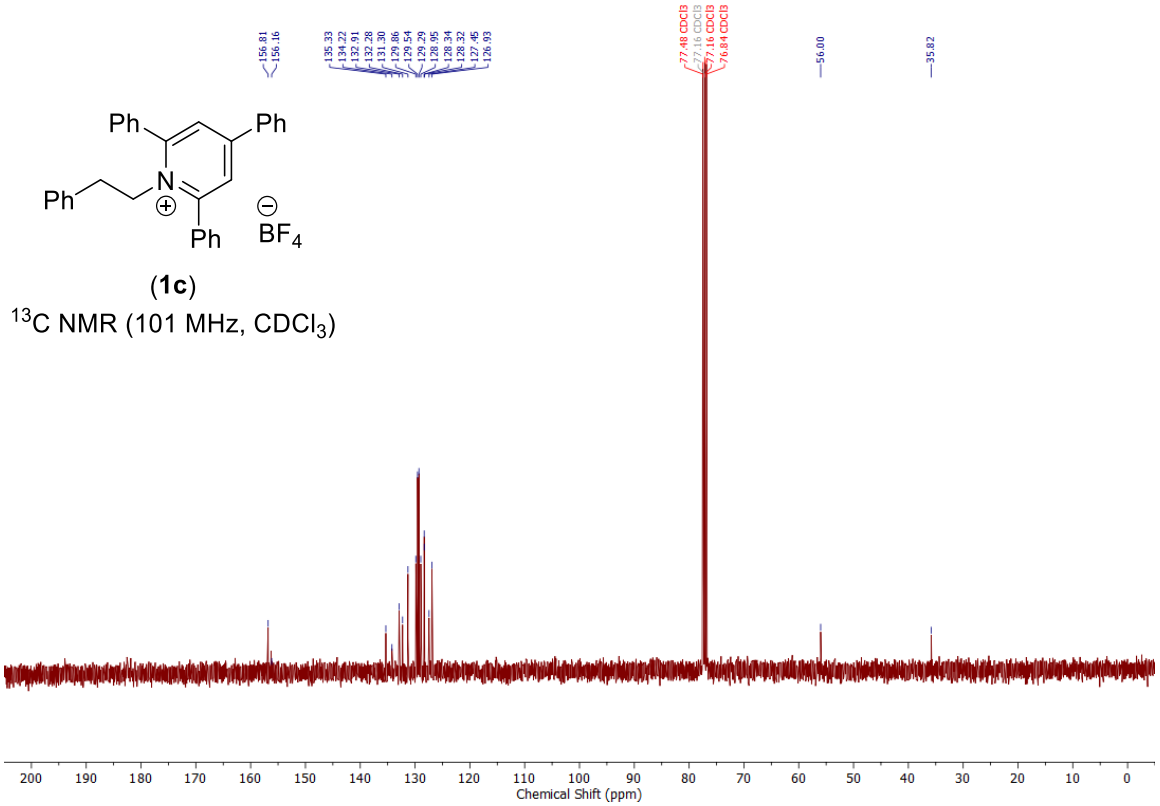
^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-phenethyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1c)



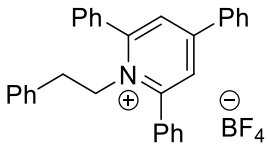
(**1c**)

^{1}H NMR (400 MHz, $CDCl_3$)



(**1c**)

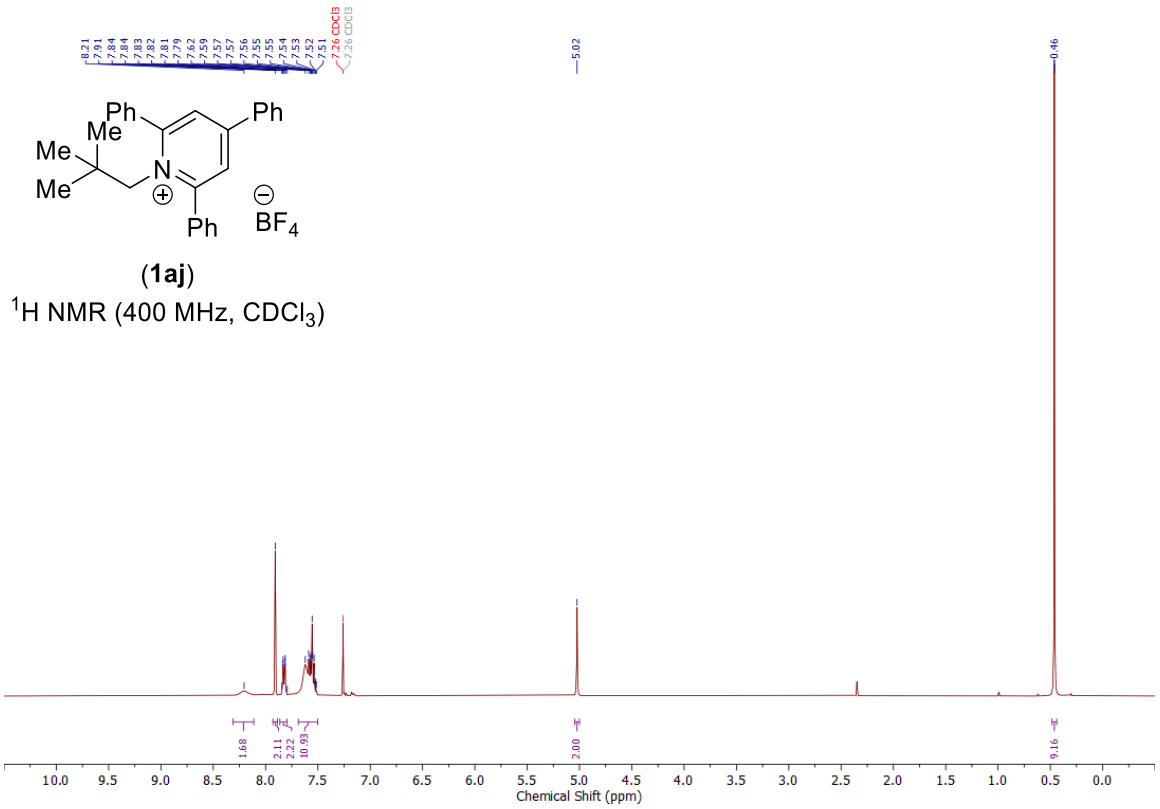
^{13}C NMR (101 MHz, $CDCl_3$)



(**1c**)

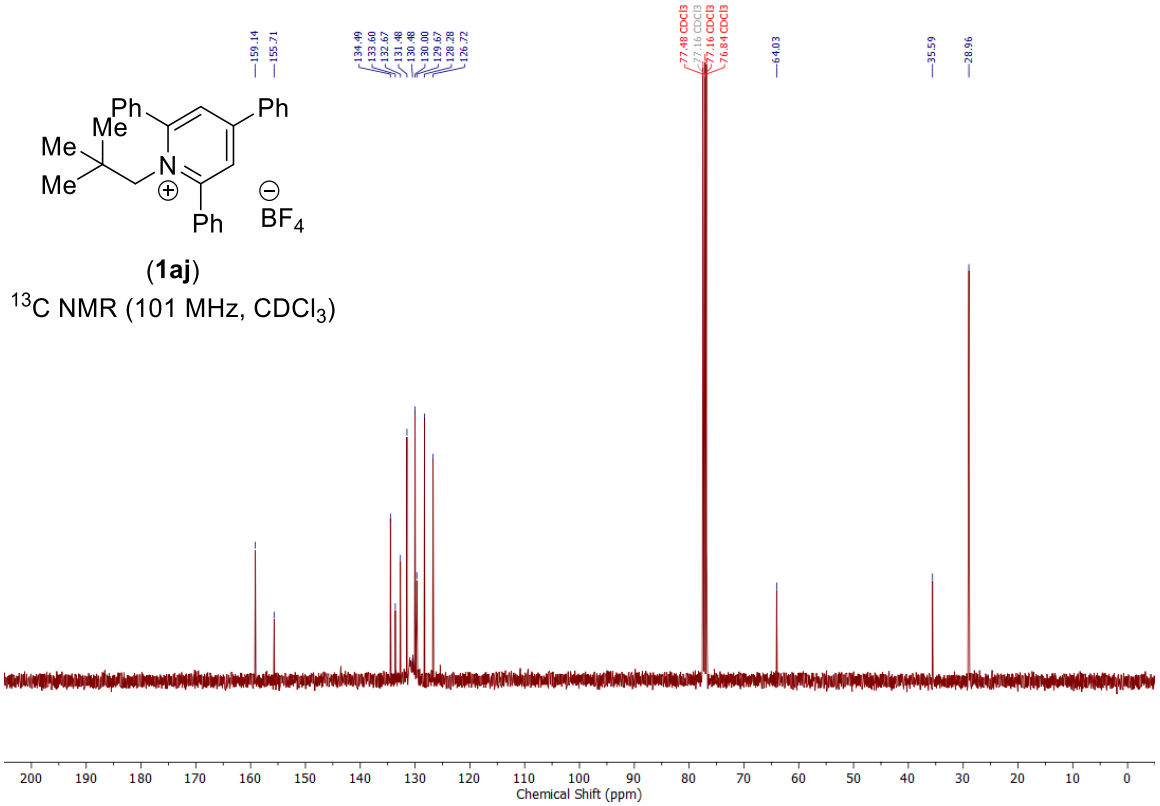
^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-neopentyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1aj)



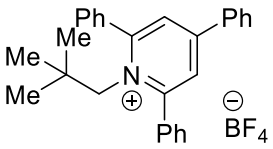
(**1aj**)

^{1}H NMR (400 MHz, $CDCl_3$)



(**1aj**)

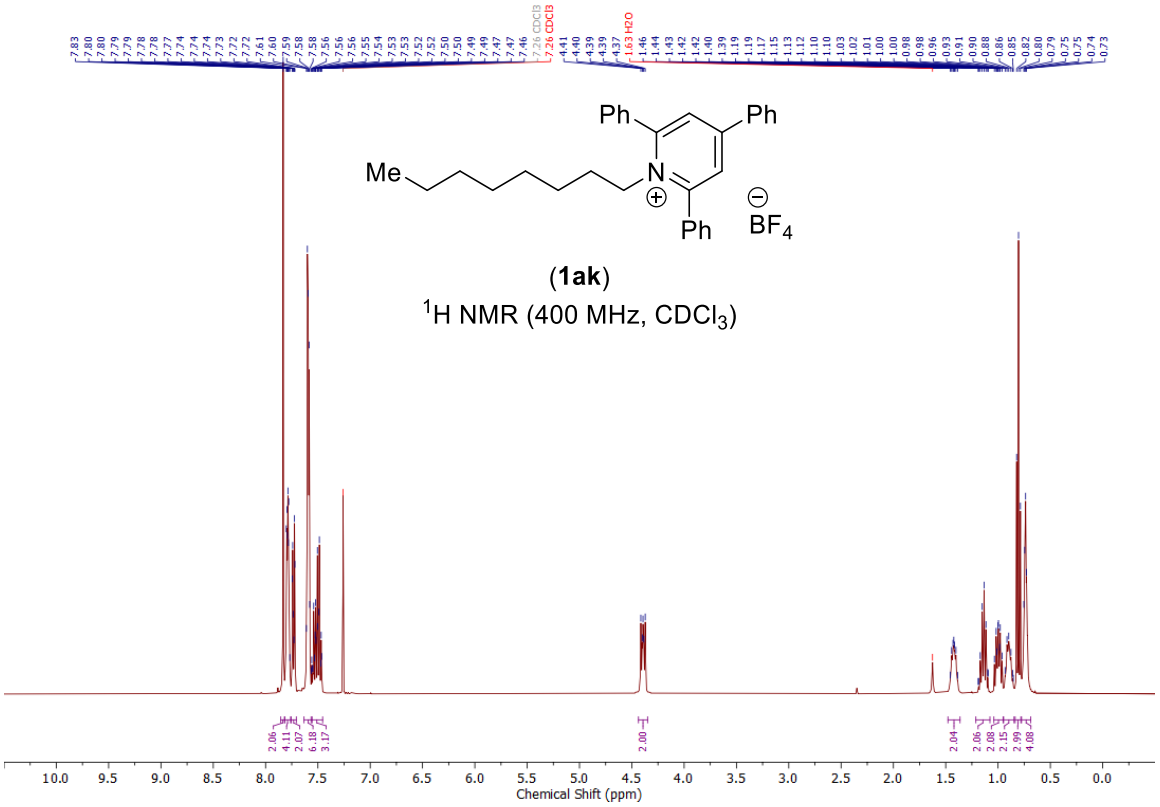
^{13}C NMR (101 MHz, $CDCl_3$)

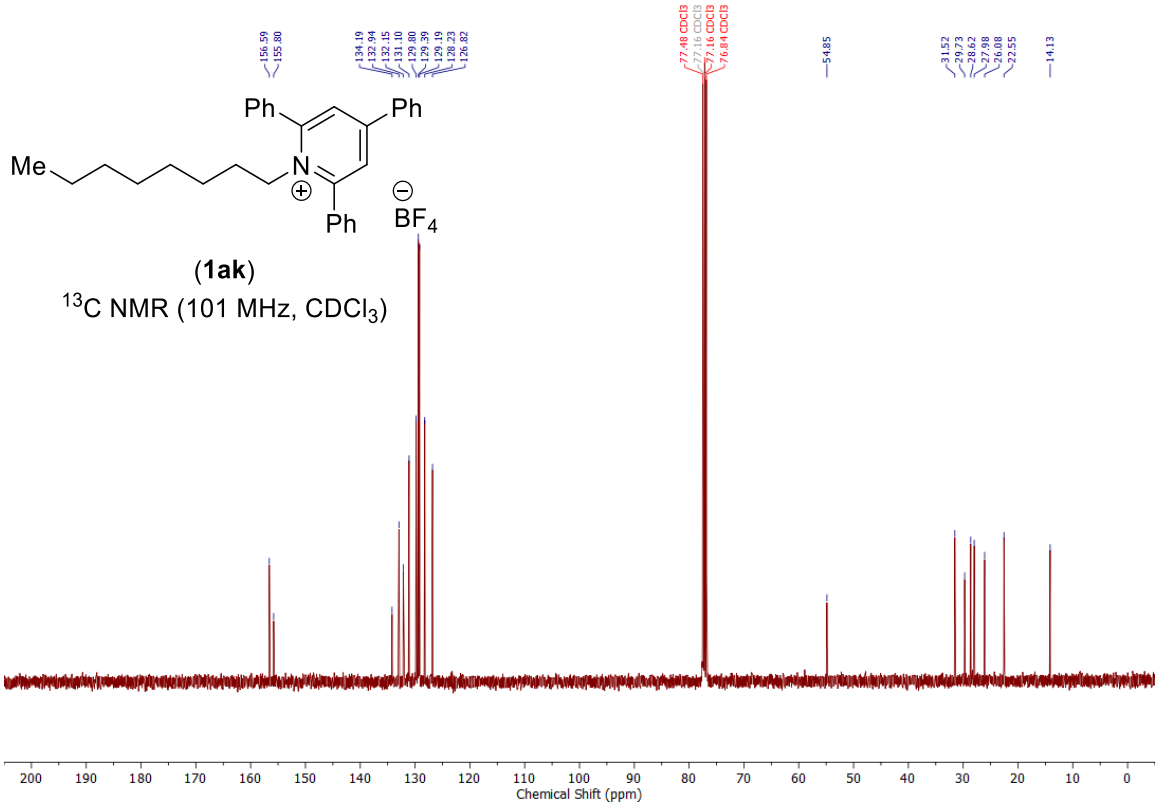


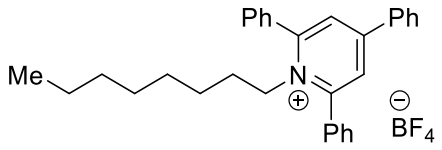
(**1aj**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-octyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1ak)



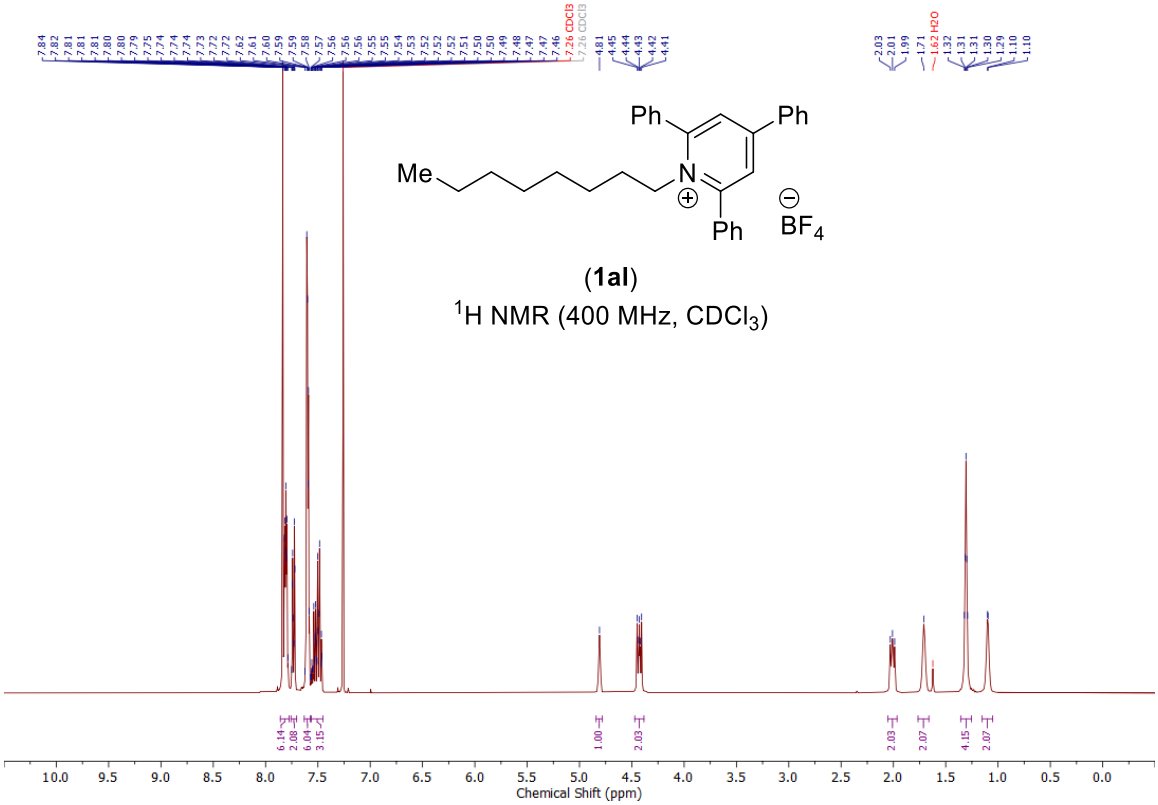


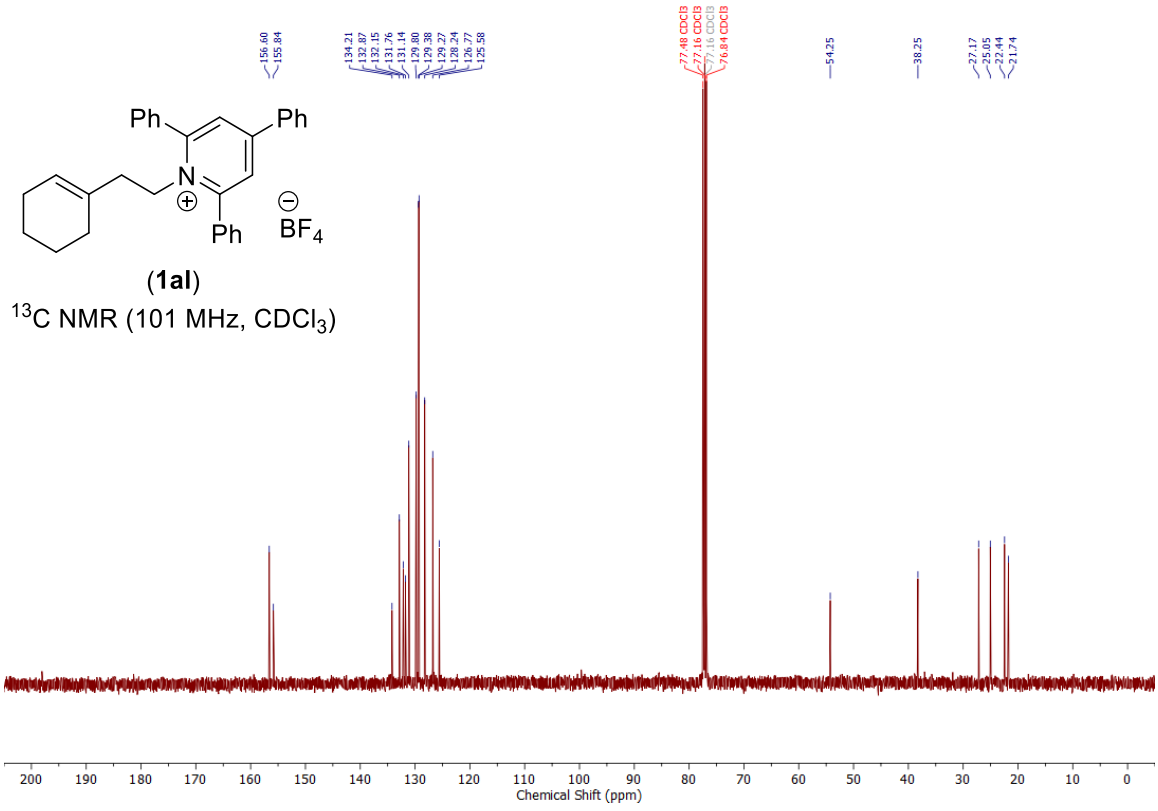


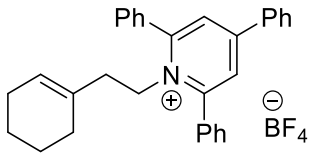
(**1ak**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(2-(cyclohex-1-en-1-yl)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1al)



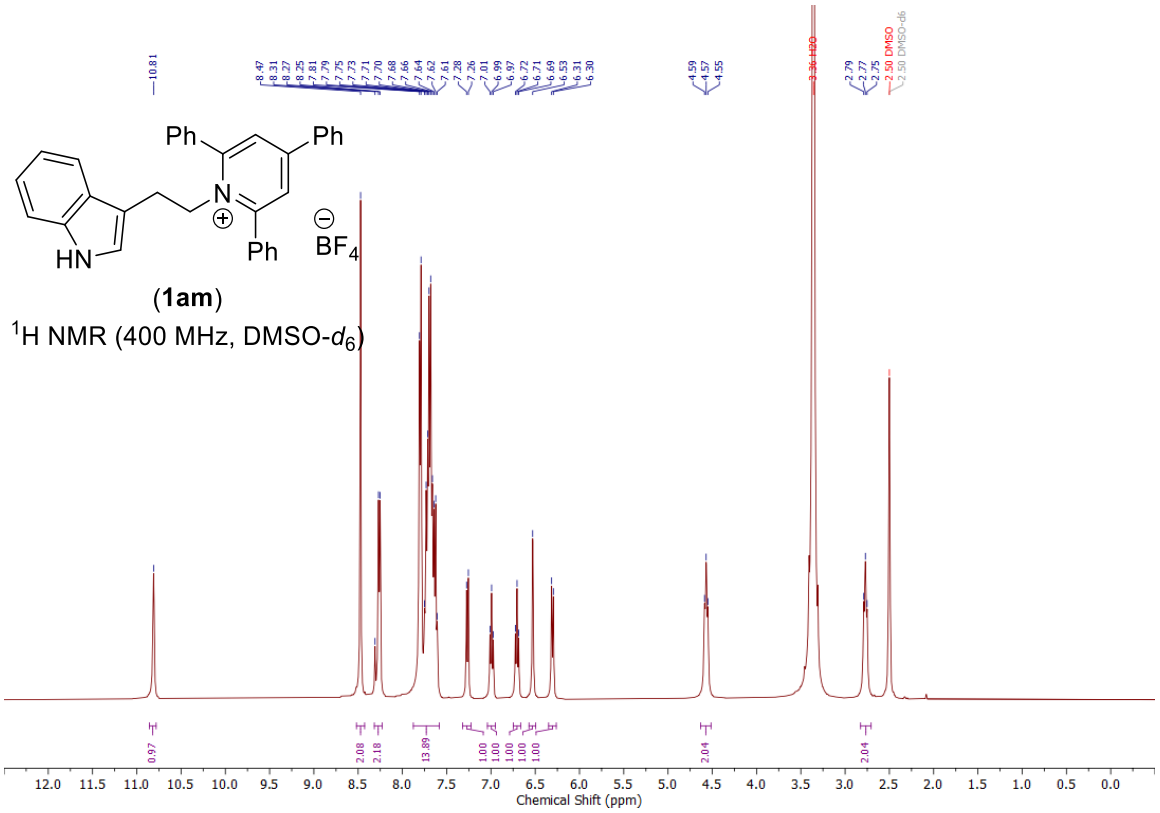


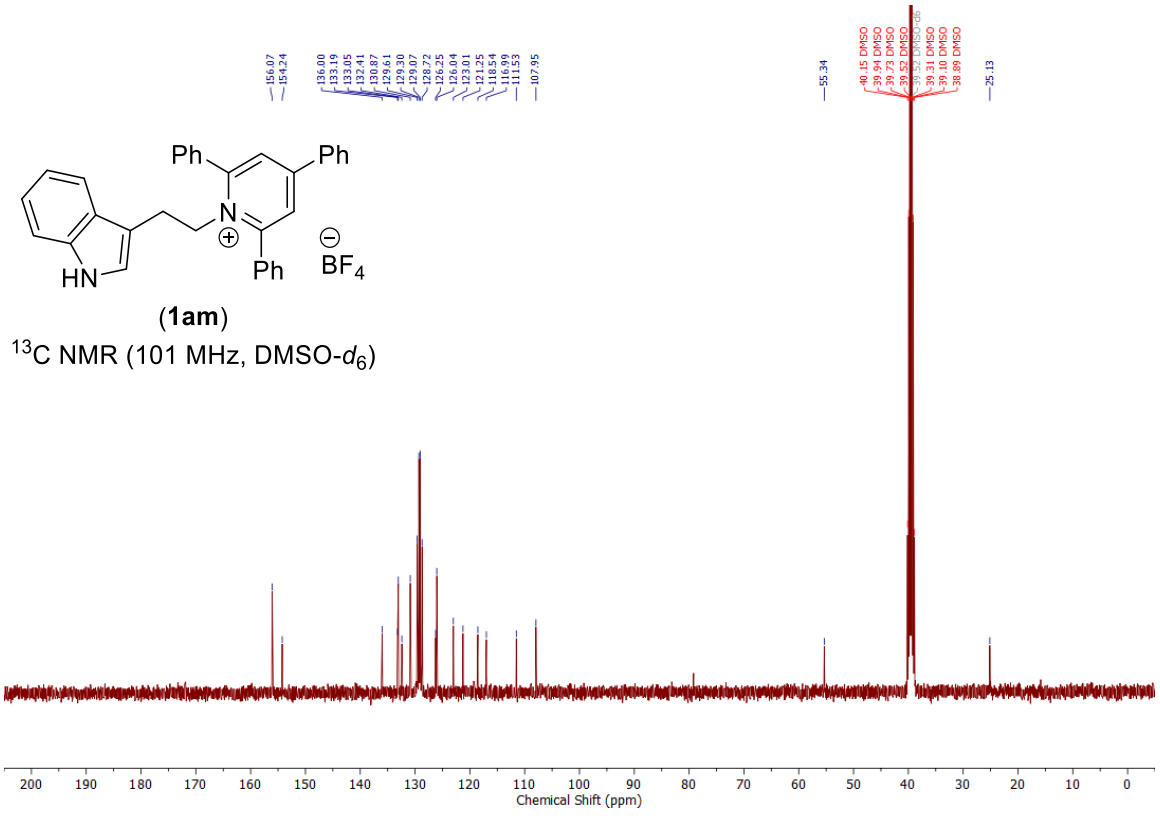


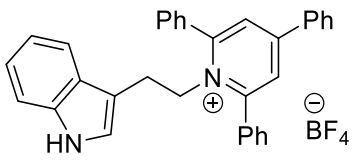
(**1al**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(2-(1*H*-indol-3-yl)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1am)



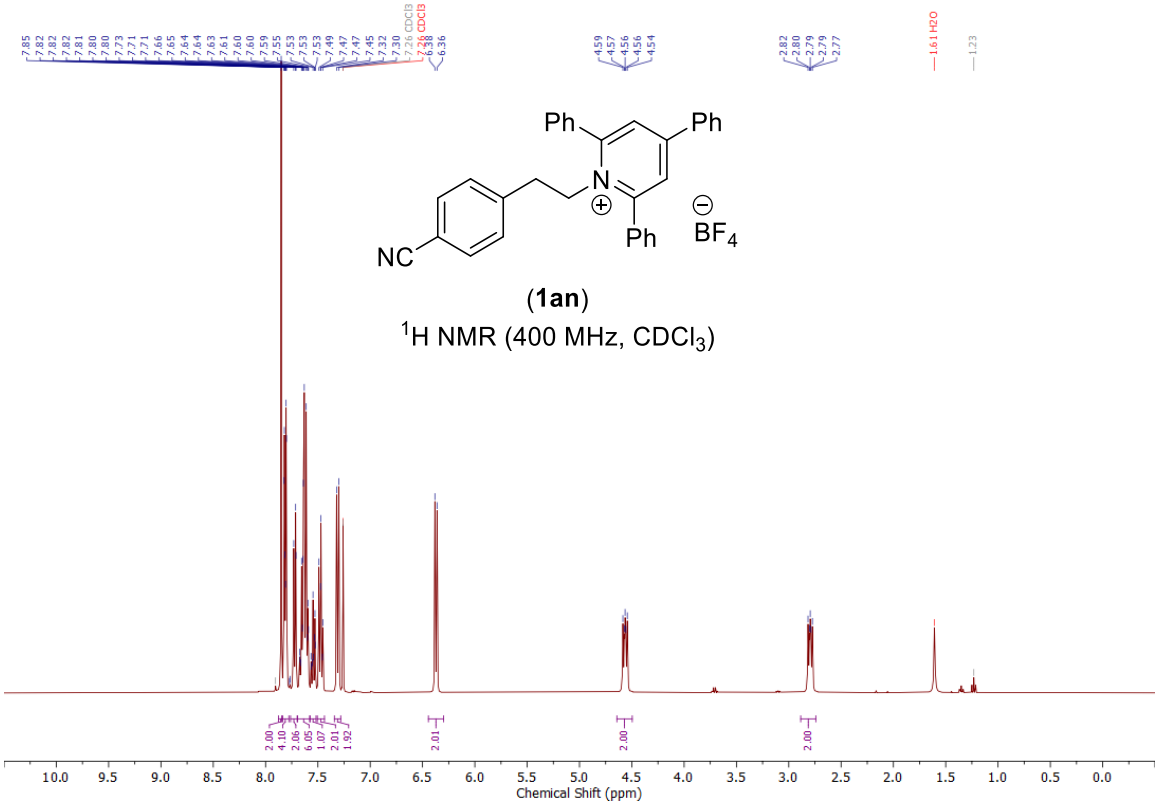


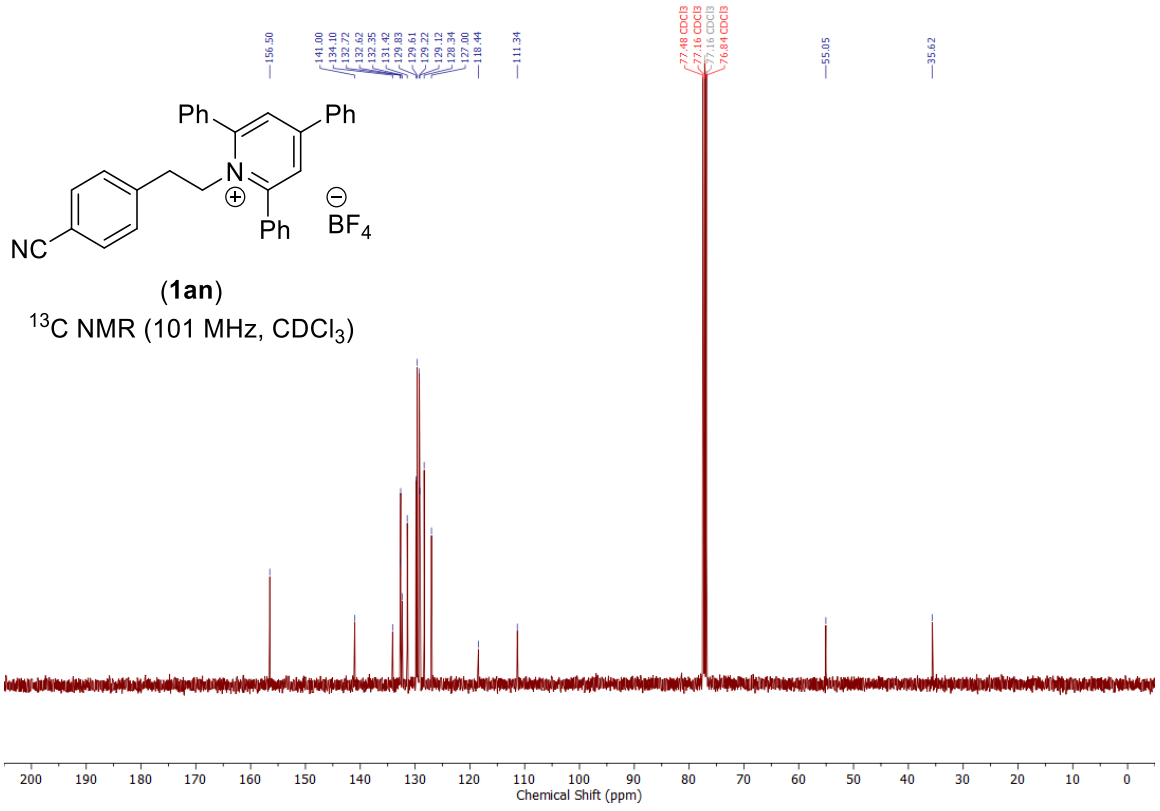


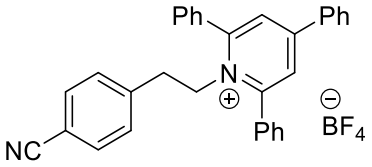
(**1am**)

^{19}F NMR (377 MHz, DMSO-d_6)

NMR spectra of 1-(4-cyanophenethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1an)



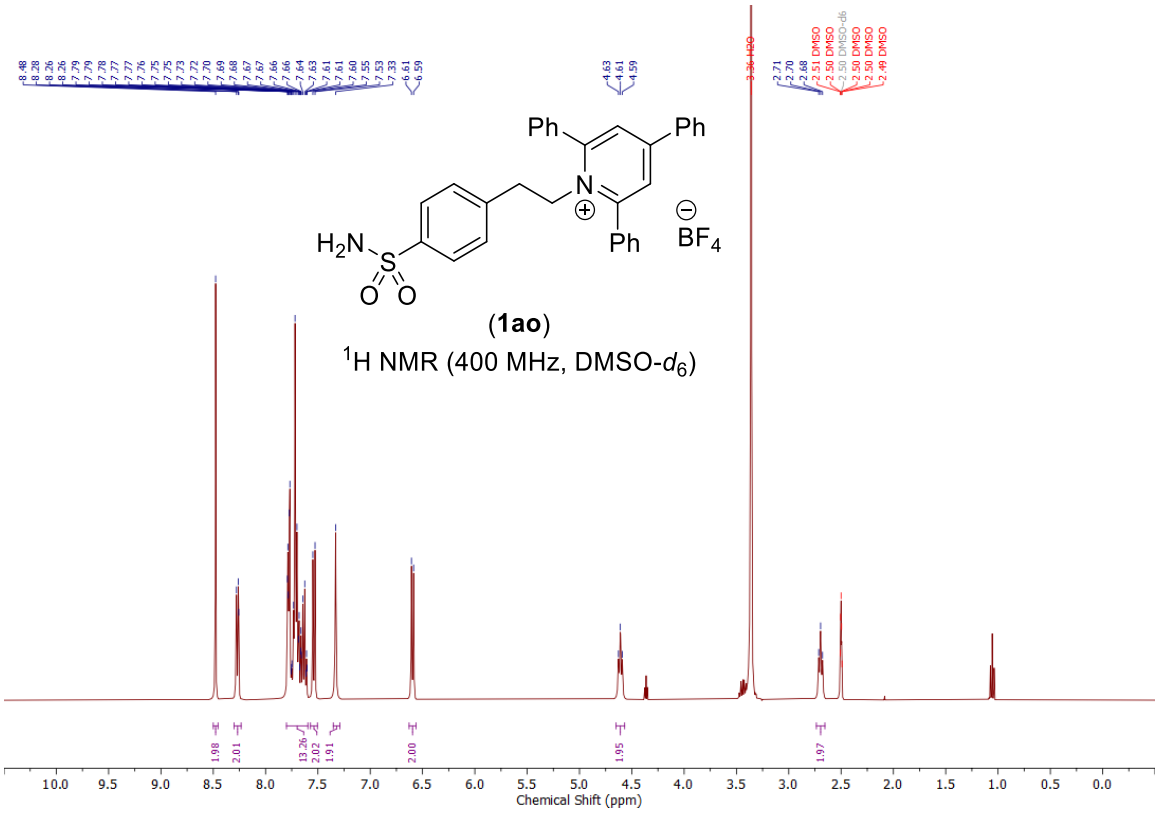


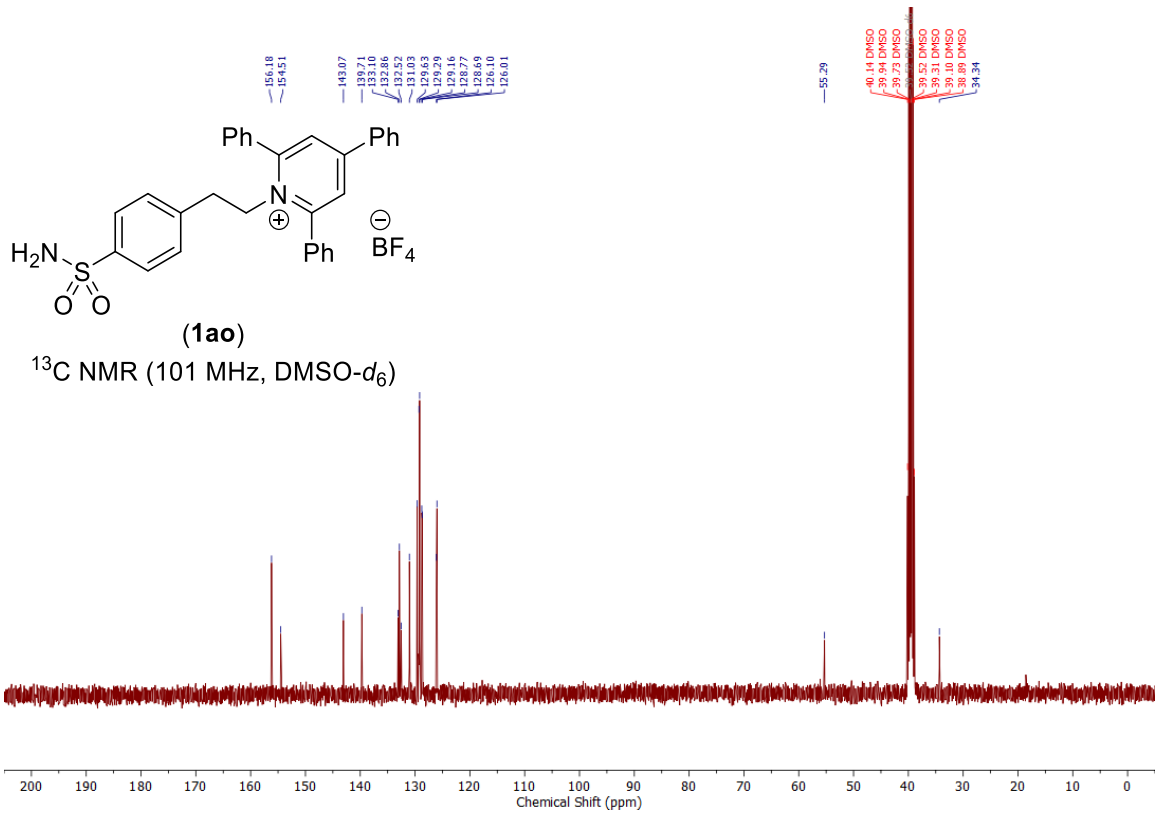


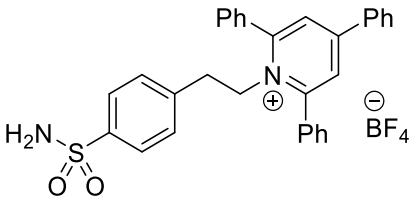
(**1an**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 2,4,6-triphenyl-1-(4-sulfamoylphenethyl)pyridin-1-ium tetrafluoroborate (1ao)



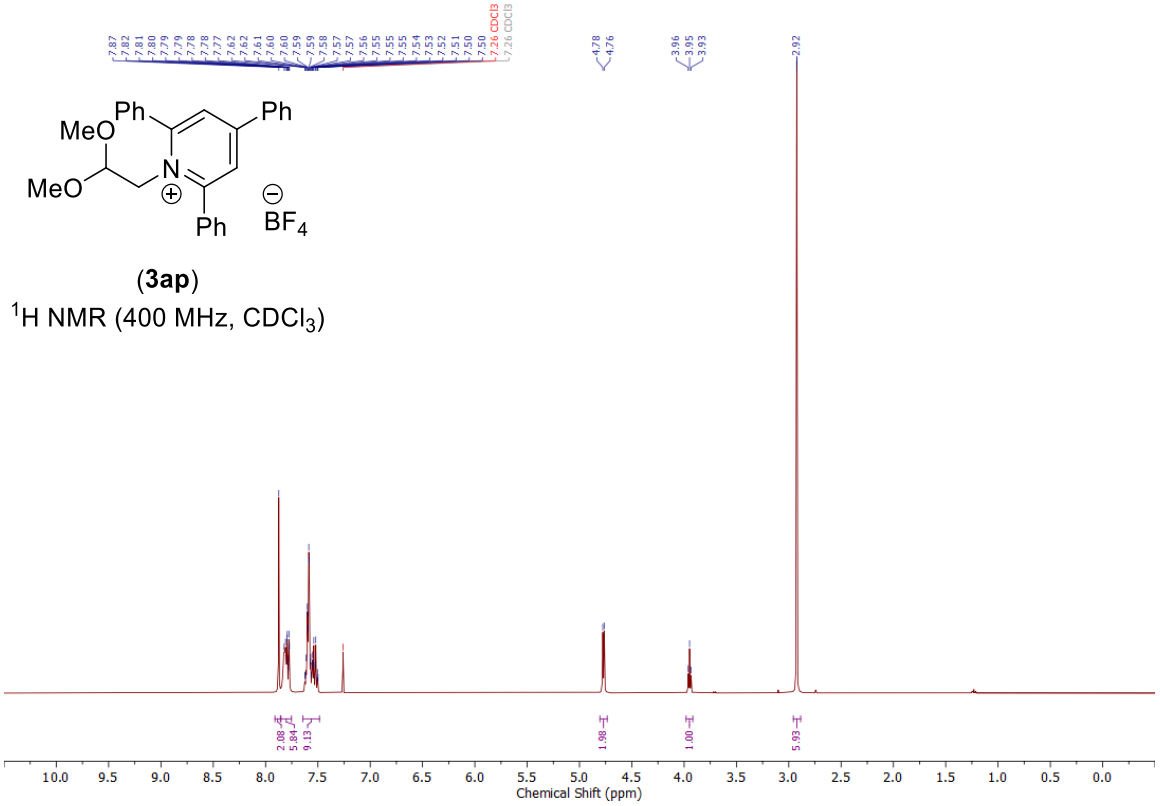




(**1ao**)

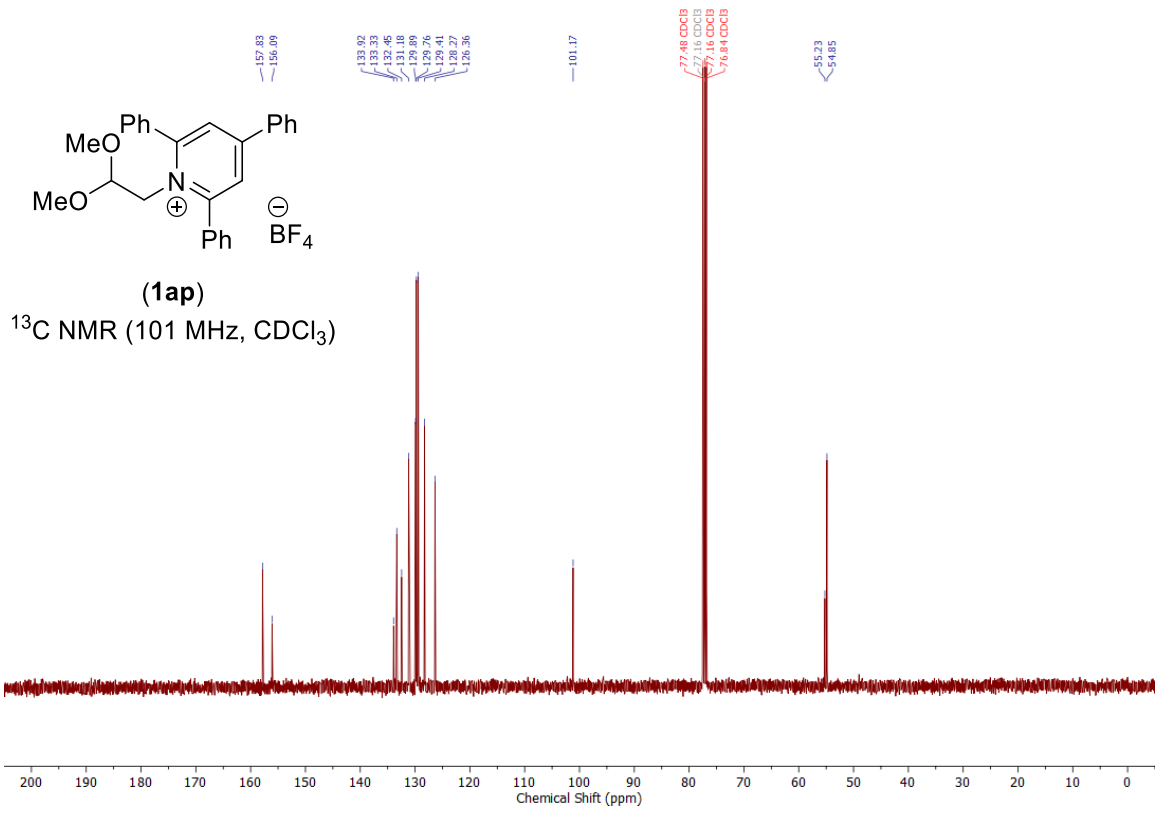
^{19}F NMR (377 MHz, DMSO-d_6)

NMR spectra of 1-(2,2-dimethoxyethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1ap)



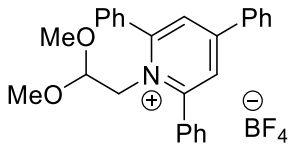
(**3ap**)

^{1}H NMR (400 MHz, $CDCl_3$)



(**1ap**)

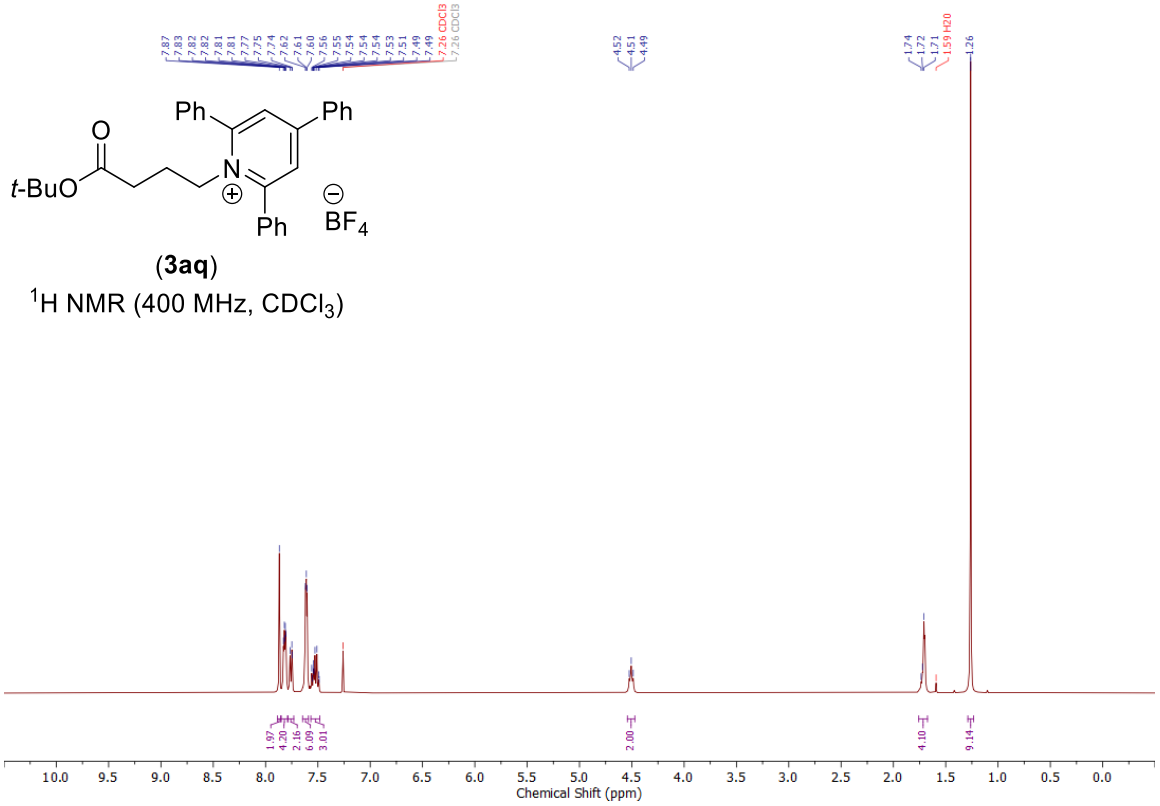
^{13}C NMR (101 MHz, $CDCl_3$)

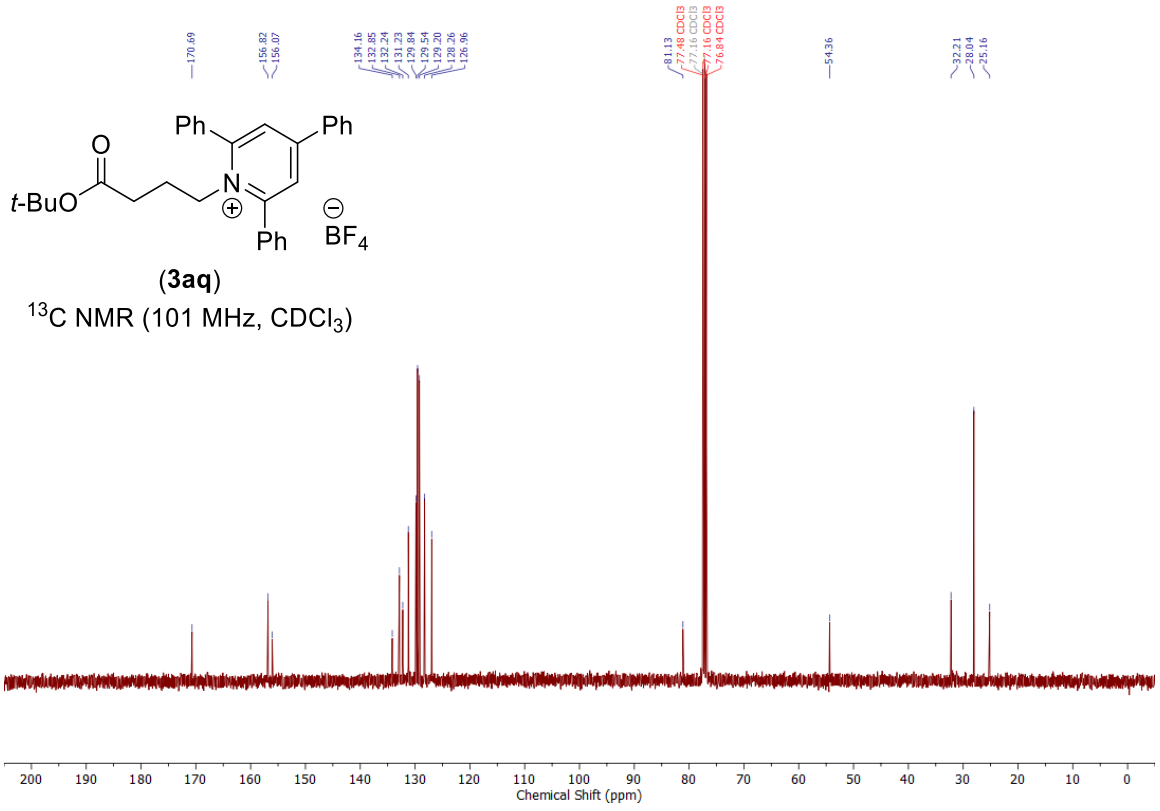


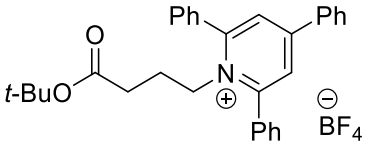
(**1ap**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(4-(*tert*-butoxy)-4-oxobutyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1aq)



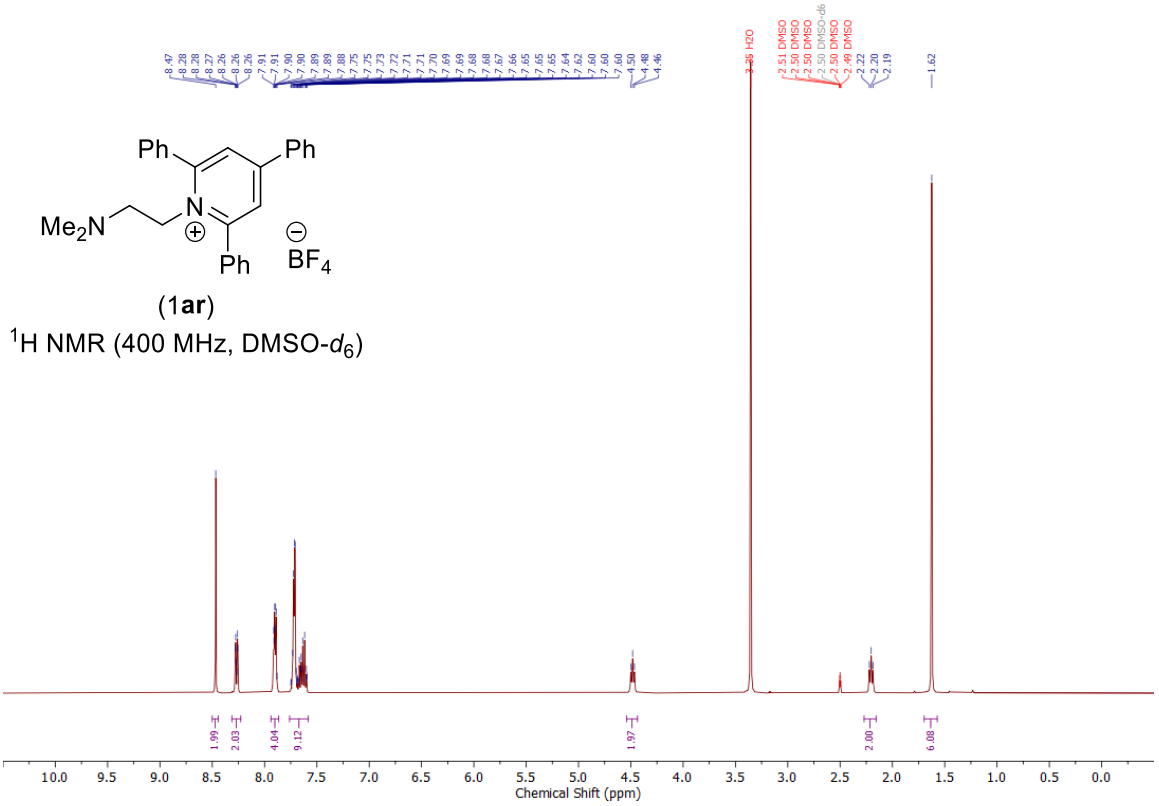




(**1aq**)

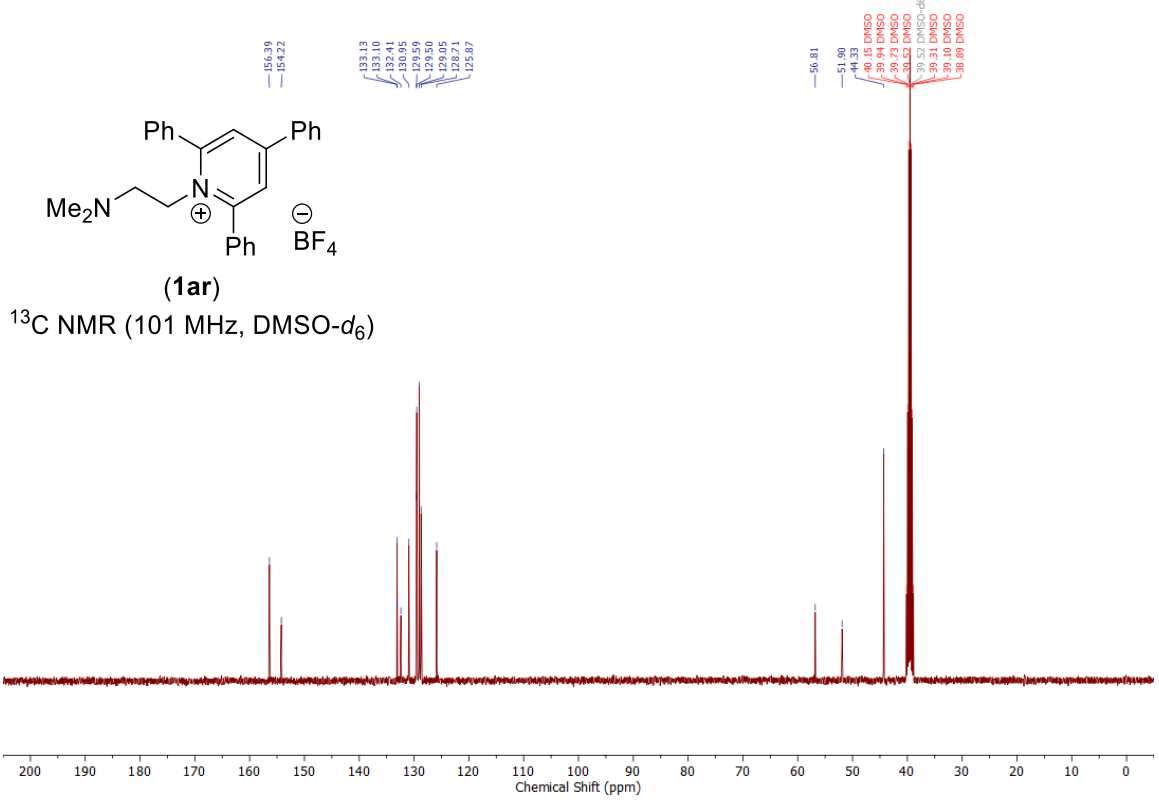
^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(2-(dimethylamino)ethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1ar)



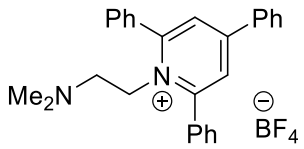
(**1ar**)

^{1}H NMR (400 MHz, DMSO-d_6)



(**1ar**)

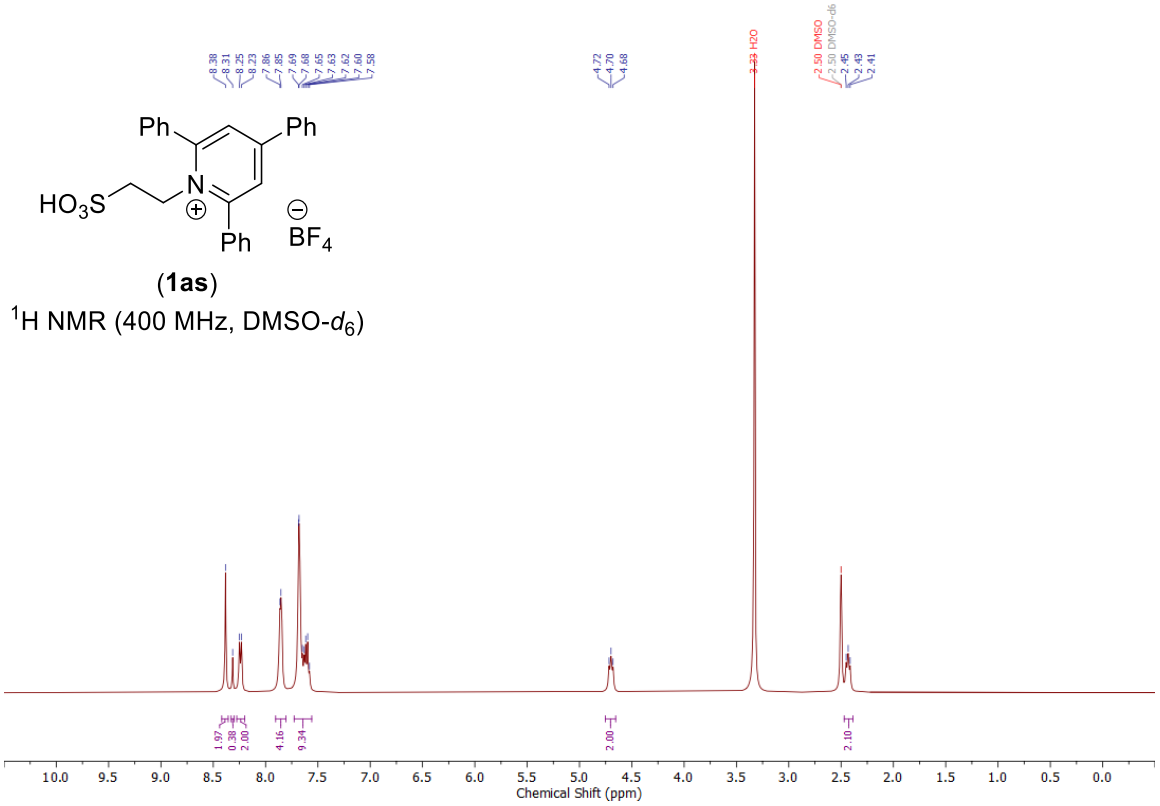
^{13}C NMR (101 MHz, DMSO-d_6)



(**1ar**)

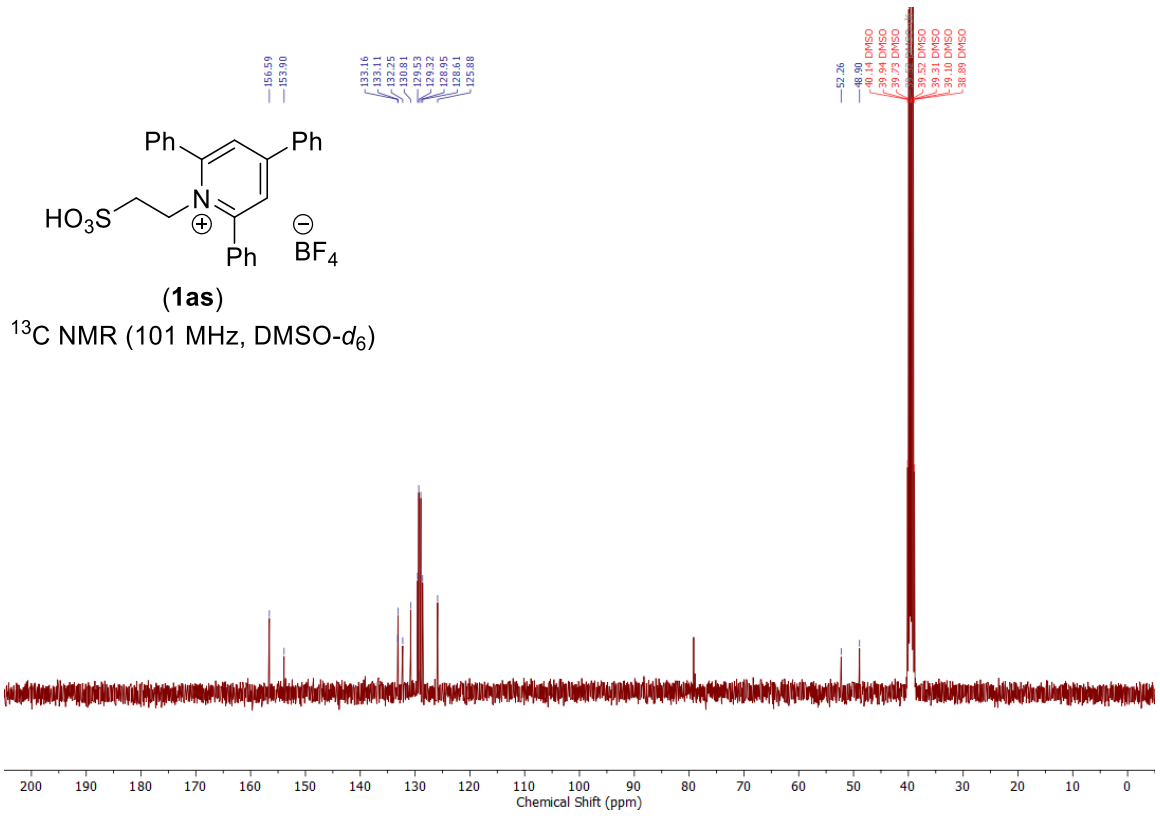
^{19}F NMR (377 MHz, DMSO-d_6)

NMR spectra of 2,4,6-triphenyl-1-(2-sulfoethyl)pyridin-1-ium tetrafluoroborate (1as)



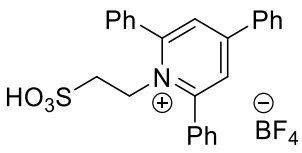
(**1as**)

^{1}H NMR (400 MHz, DMSO-d_6)



(**1as**)

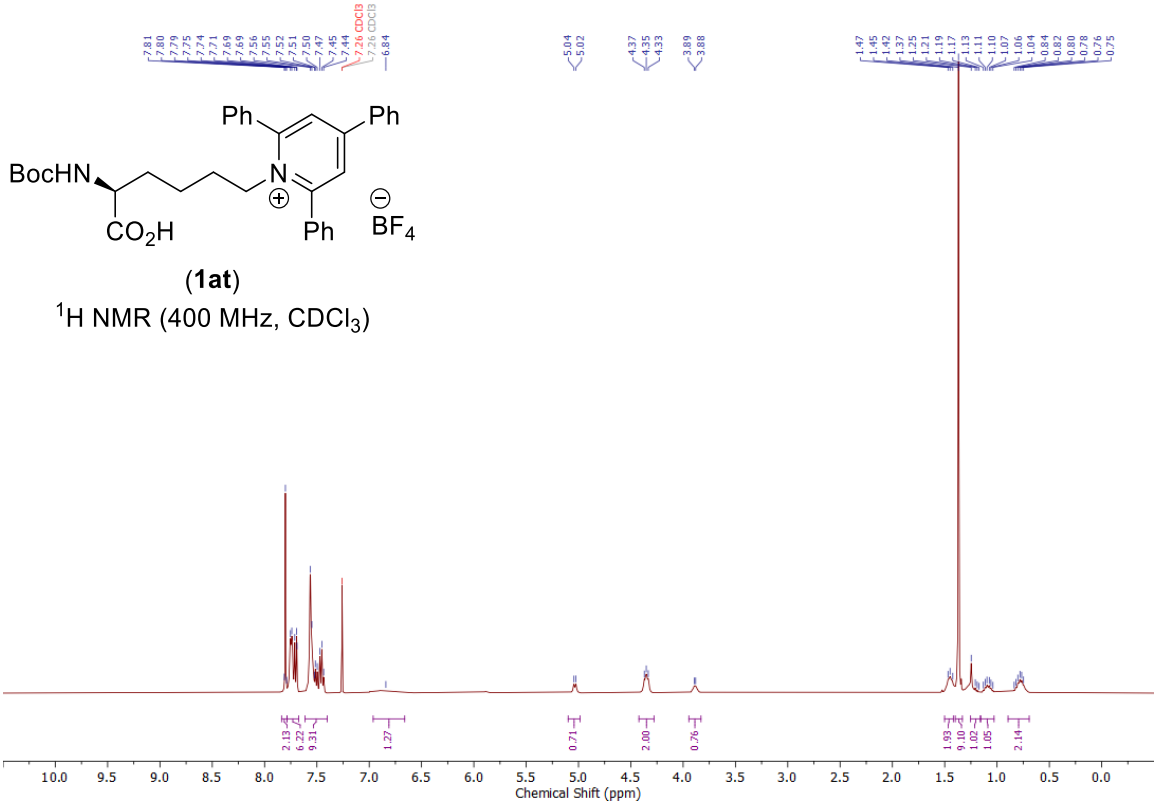
^{13}C NMR (101 MHz, DMSO-d_6)



(**1as**)

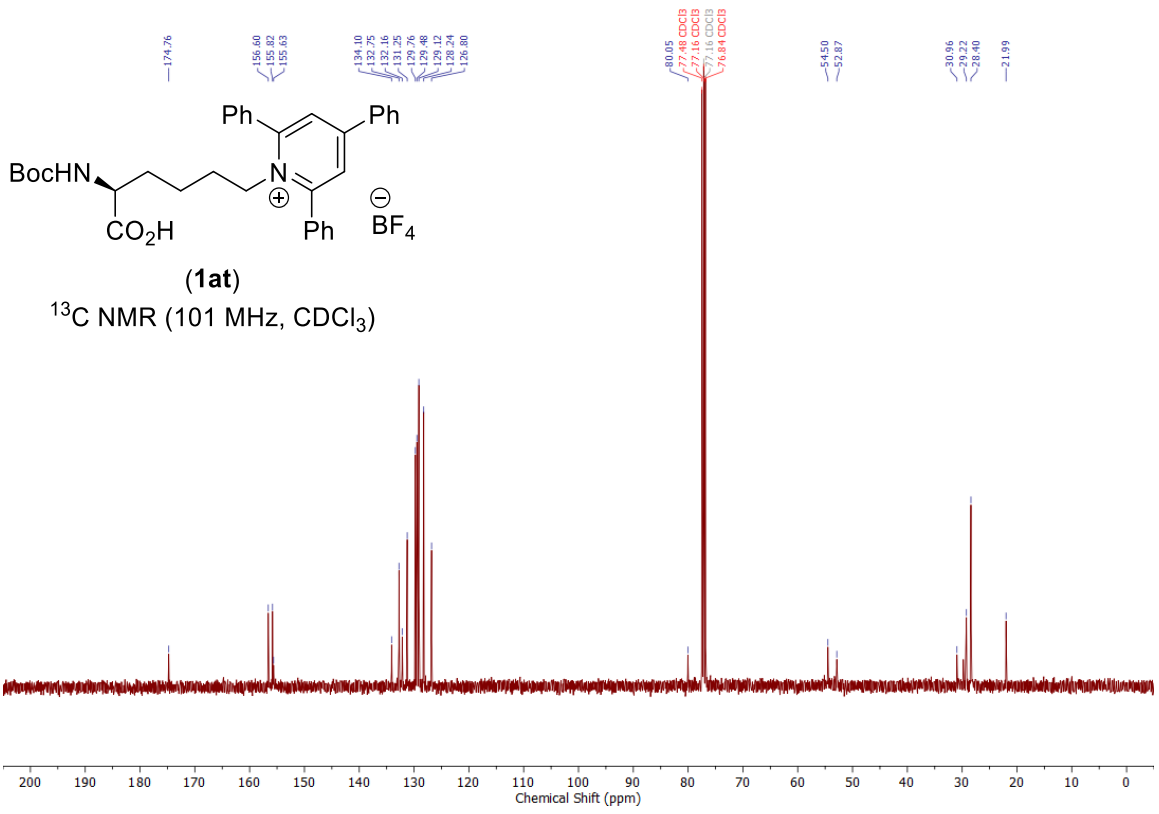
^{19}F NMR (377 MHz, DMSO-d_6)

NMR spectra of (*S*)-1-(5-((*tert*-butoxycarbonyl)amino)-5-carboxypentyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1at)



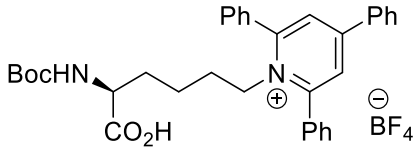
(**1at**)

^{1}H NMR (400 MHz, $CDCl_3$)



(**1at**)

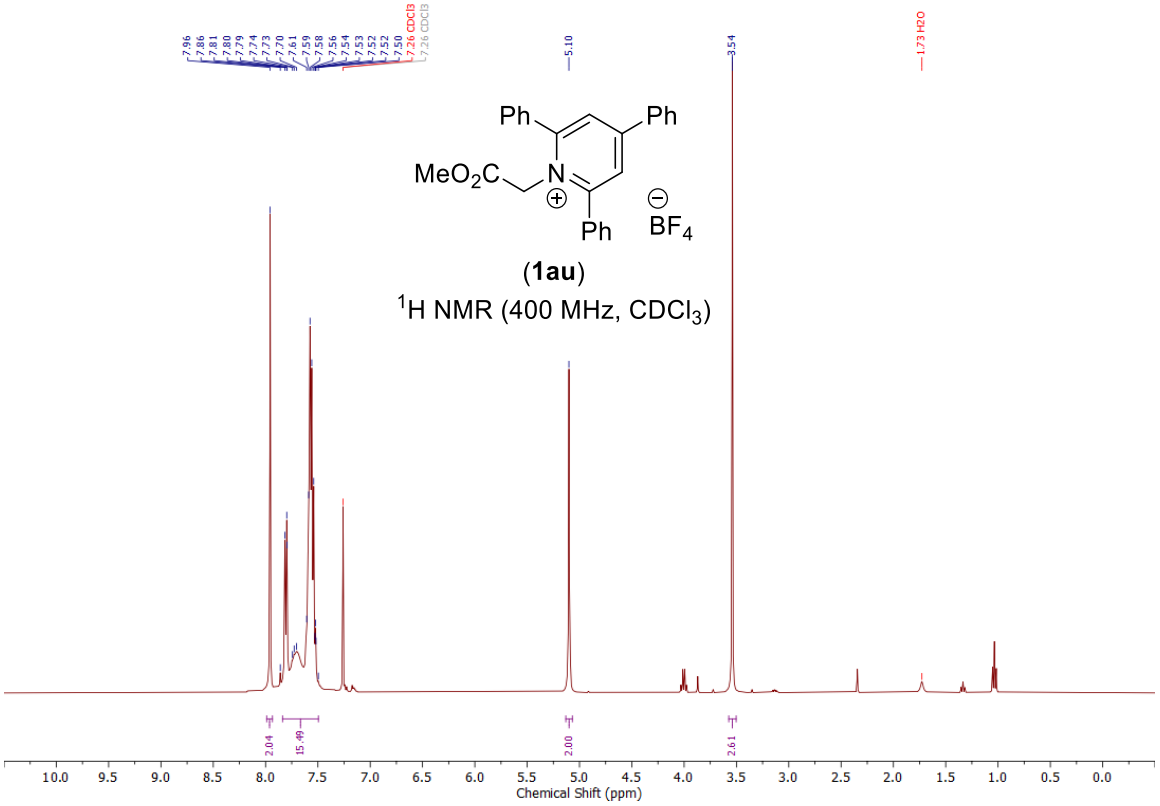
^{13}C NMR (101 MHz, $CDCl_3$)

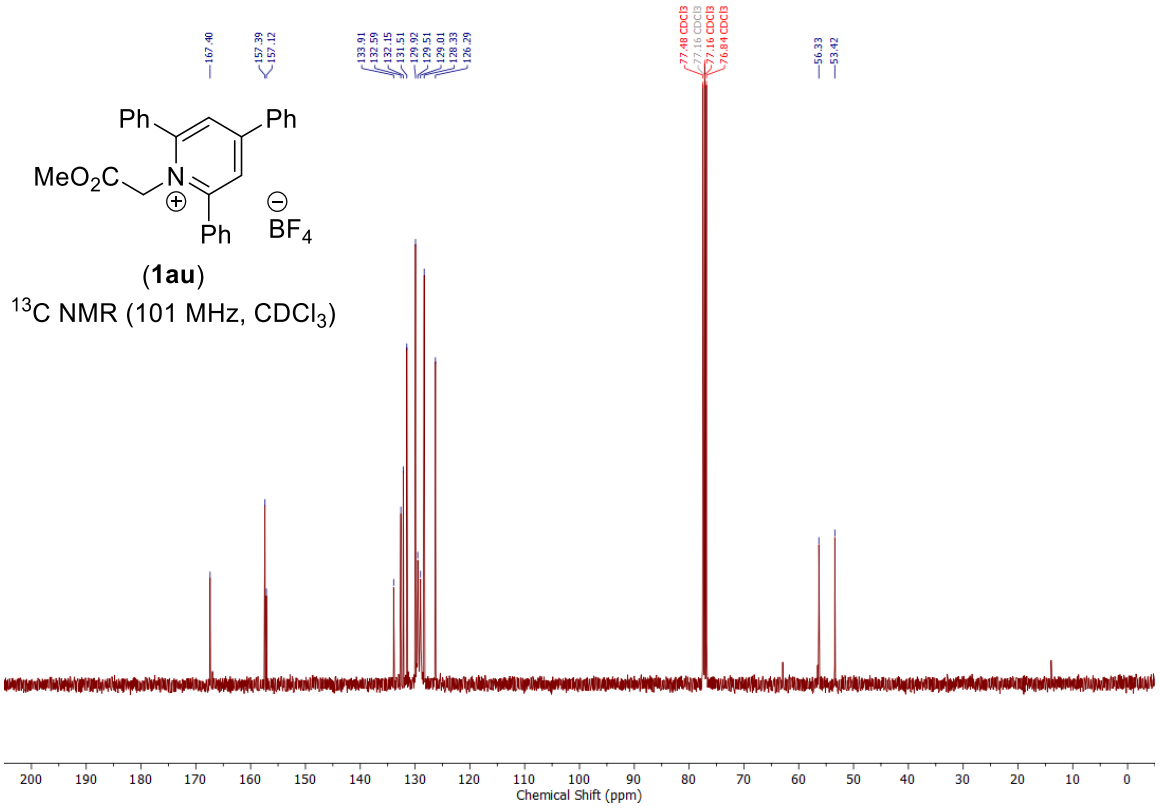


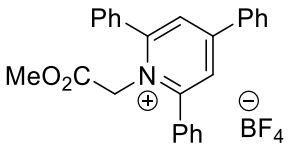
(**1at**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(2-methoxy-2-oxoethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1au)



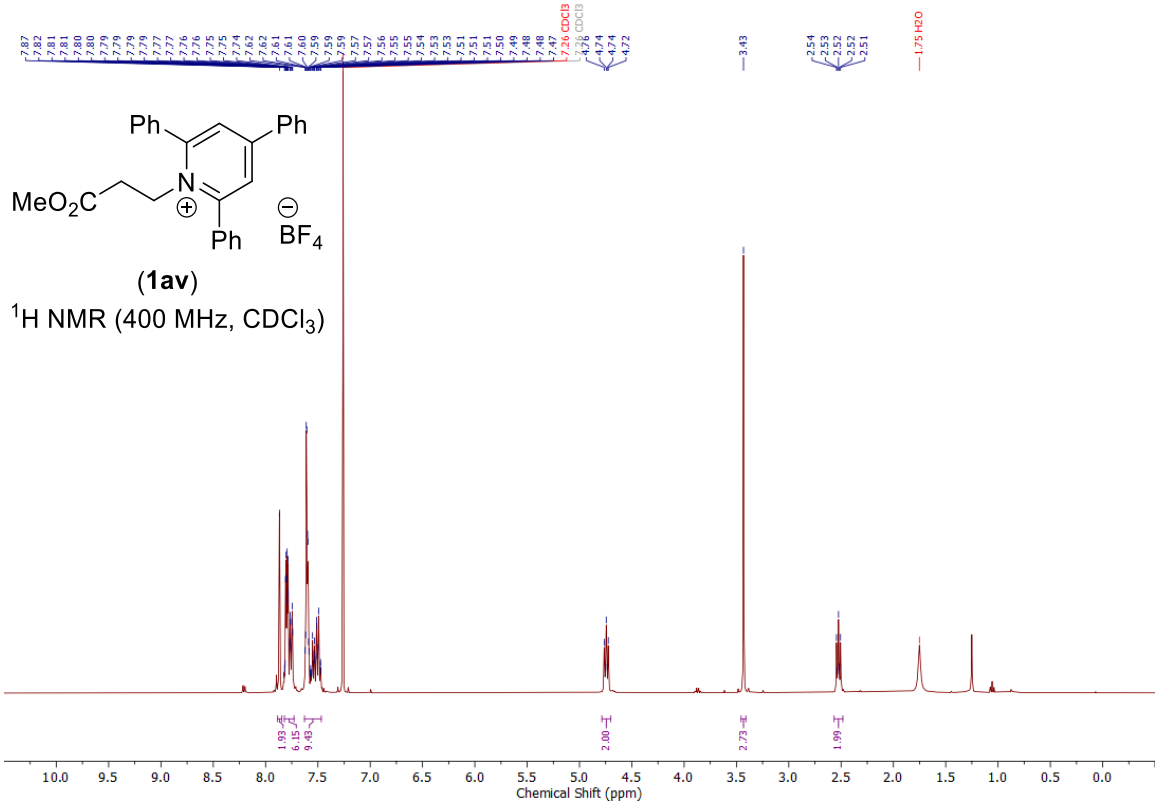


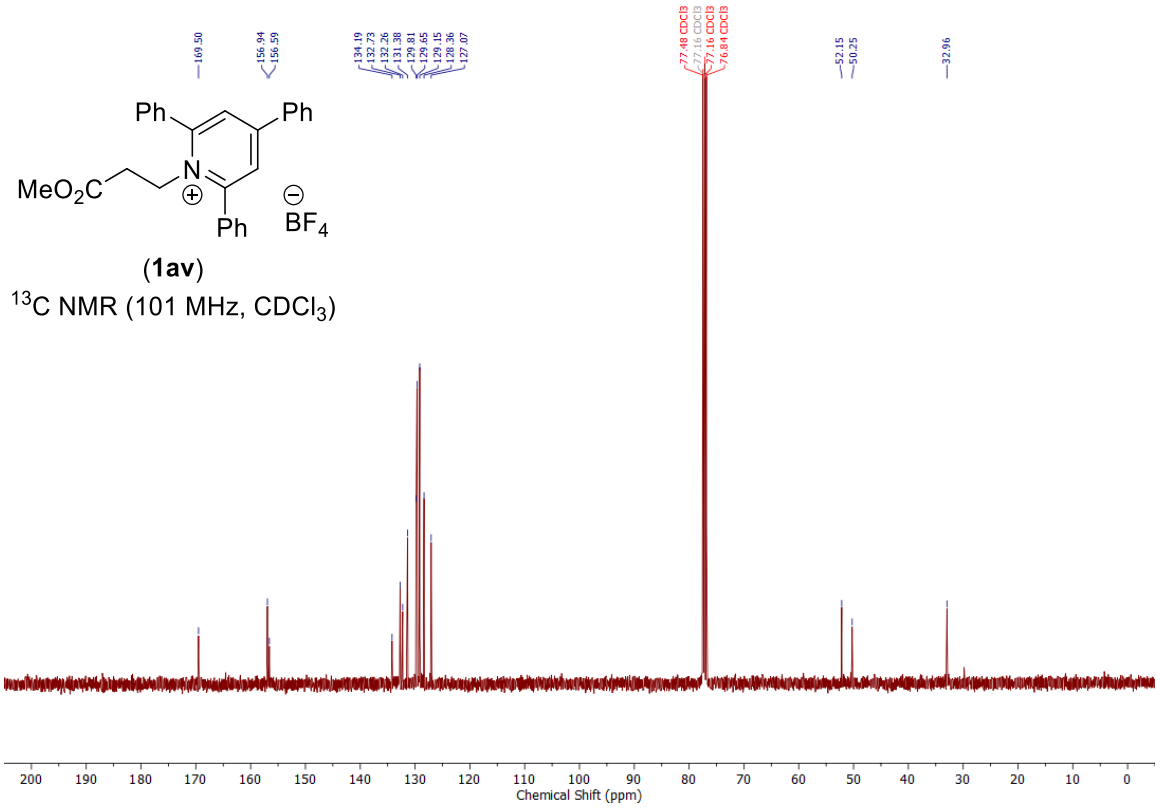


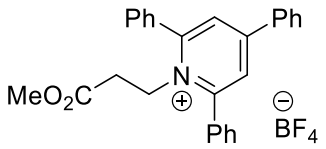
(**1au**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(3-methoxy-3-oxopropyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1av)



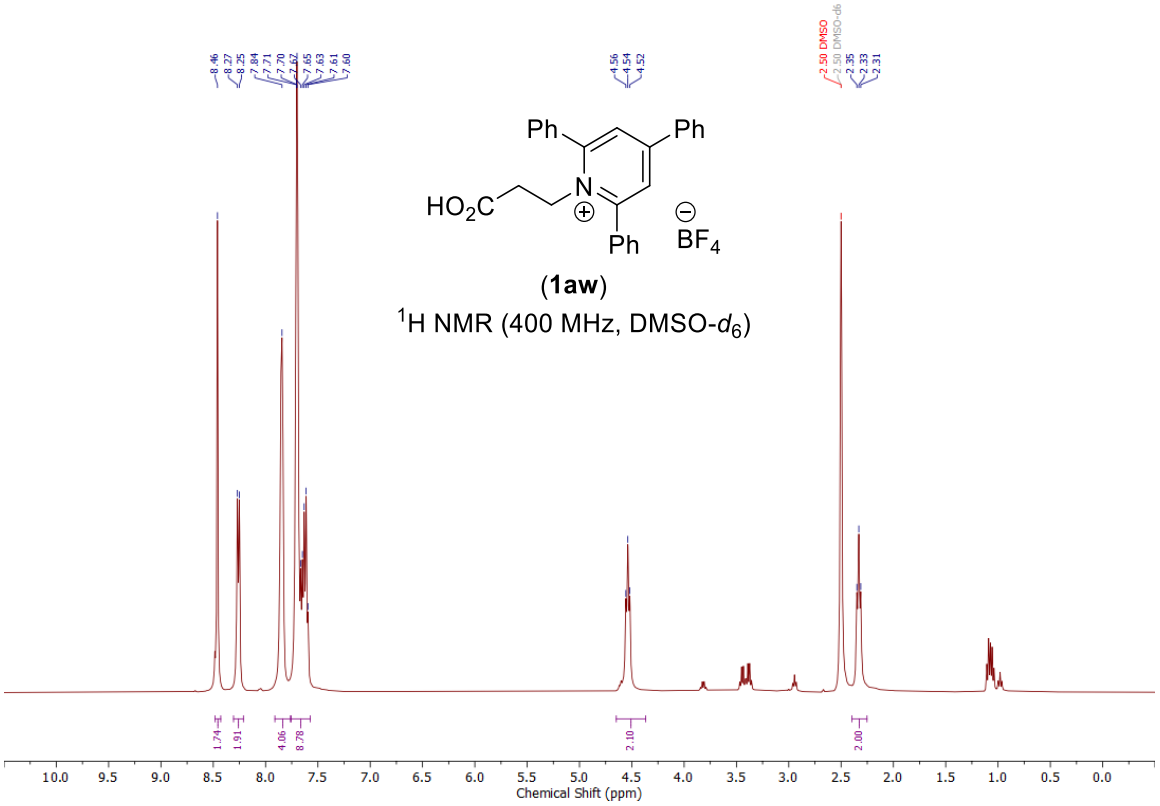


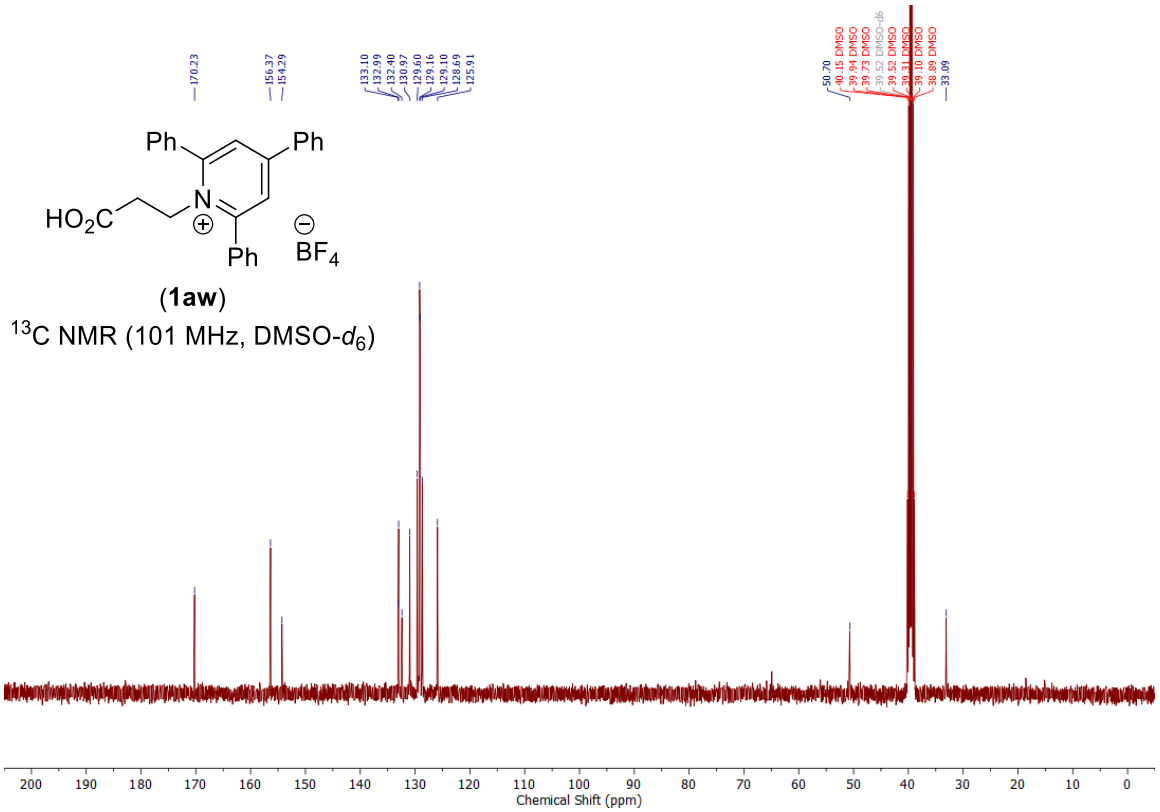


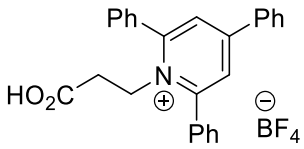
(**1av**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(2-carboxyethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1aw)



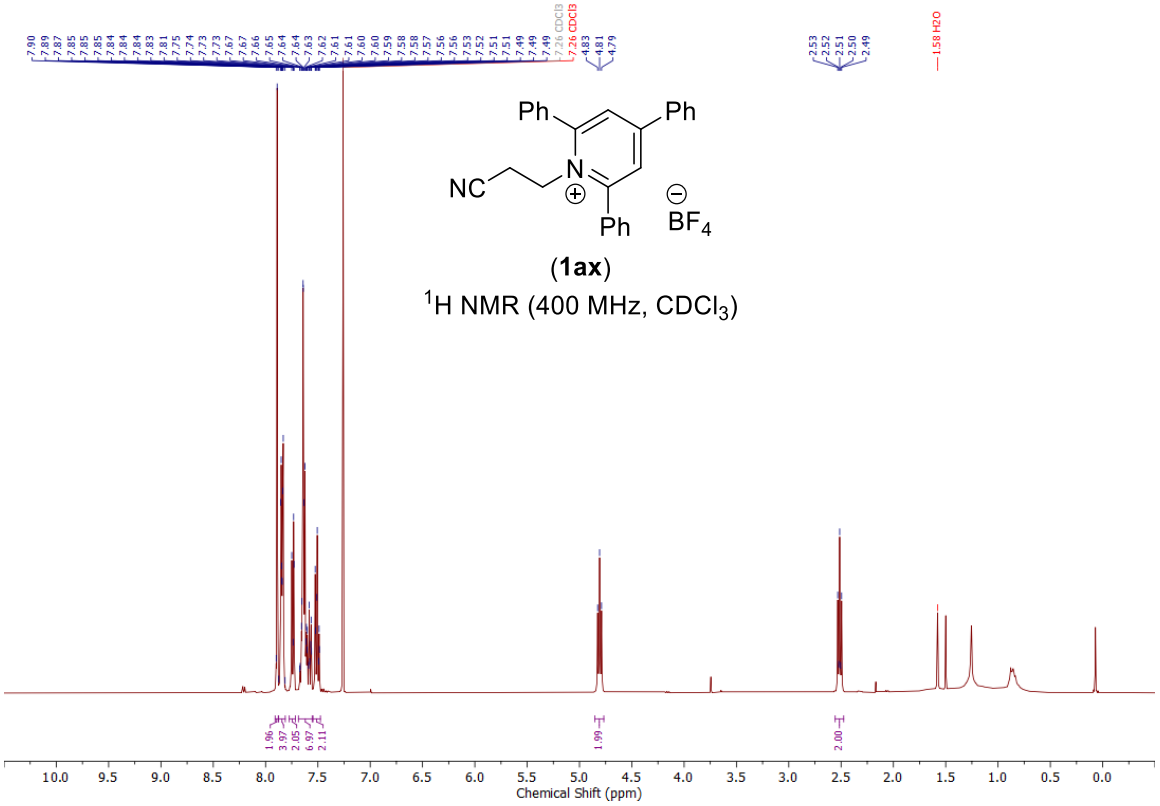


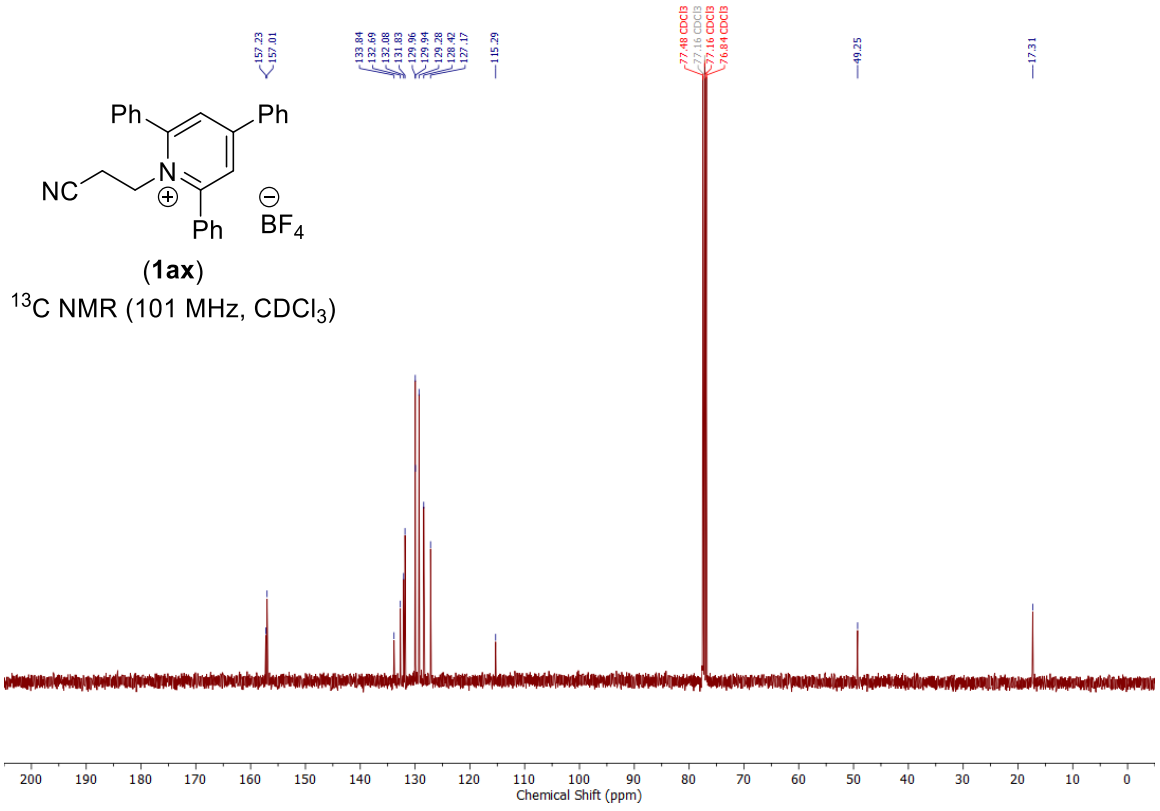


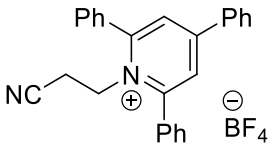
(**1aw**)

^{19}F NMR (377 MHz, DMSO-d_6)

NMR spectra of 1-(2-cyanoethyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (1ax)



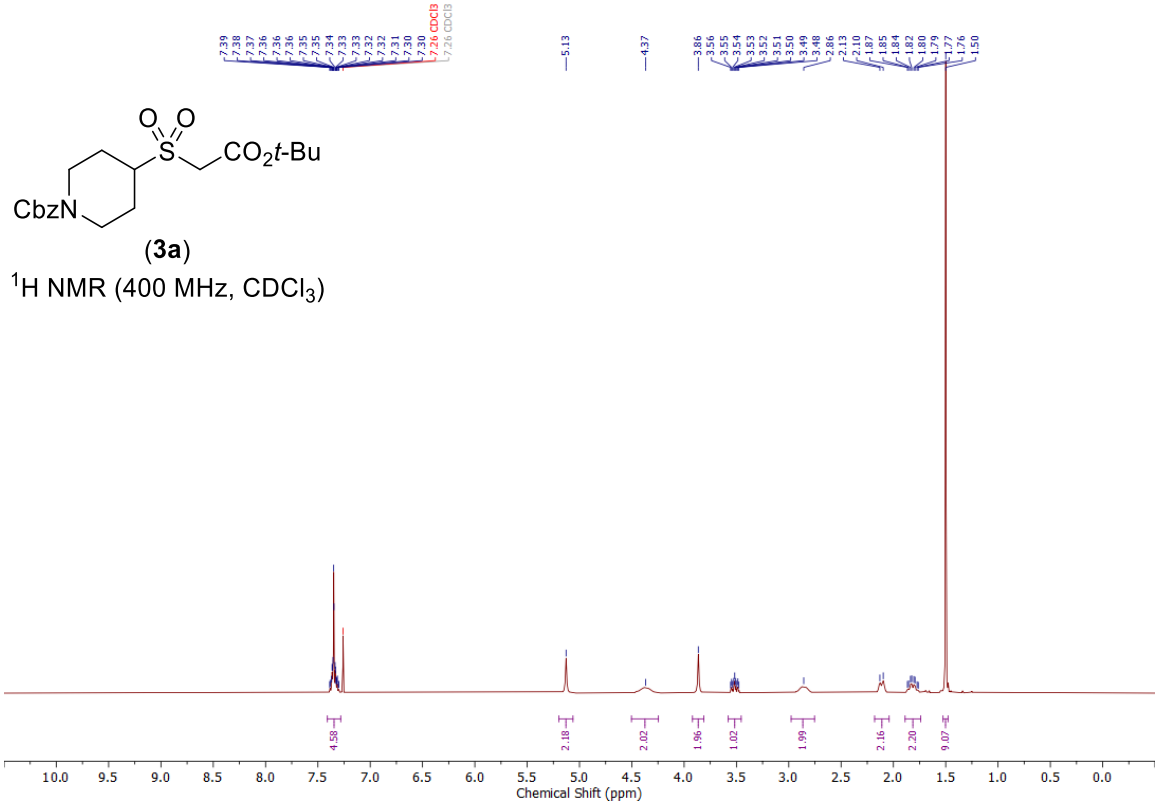




(**1ax**)

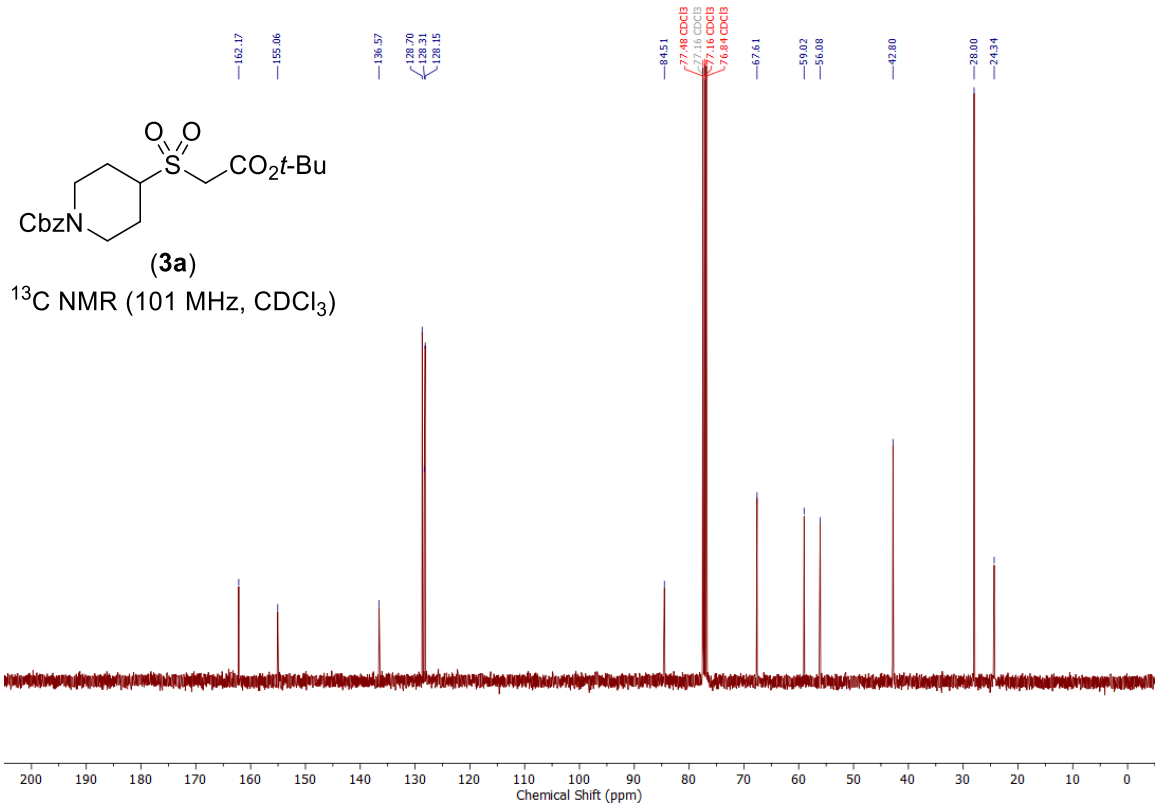
^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of benzyl 4-((2-(*tert*-butoxy)-2-oxoethyl)sulfonyl)piperidine-1-carboxylate (3a)



(**3a**)

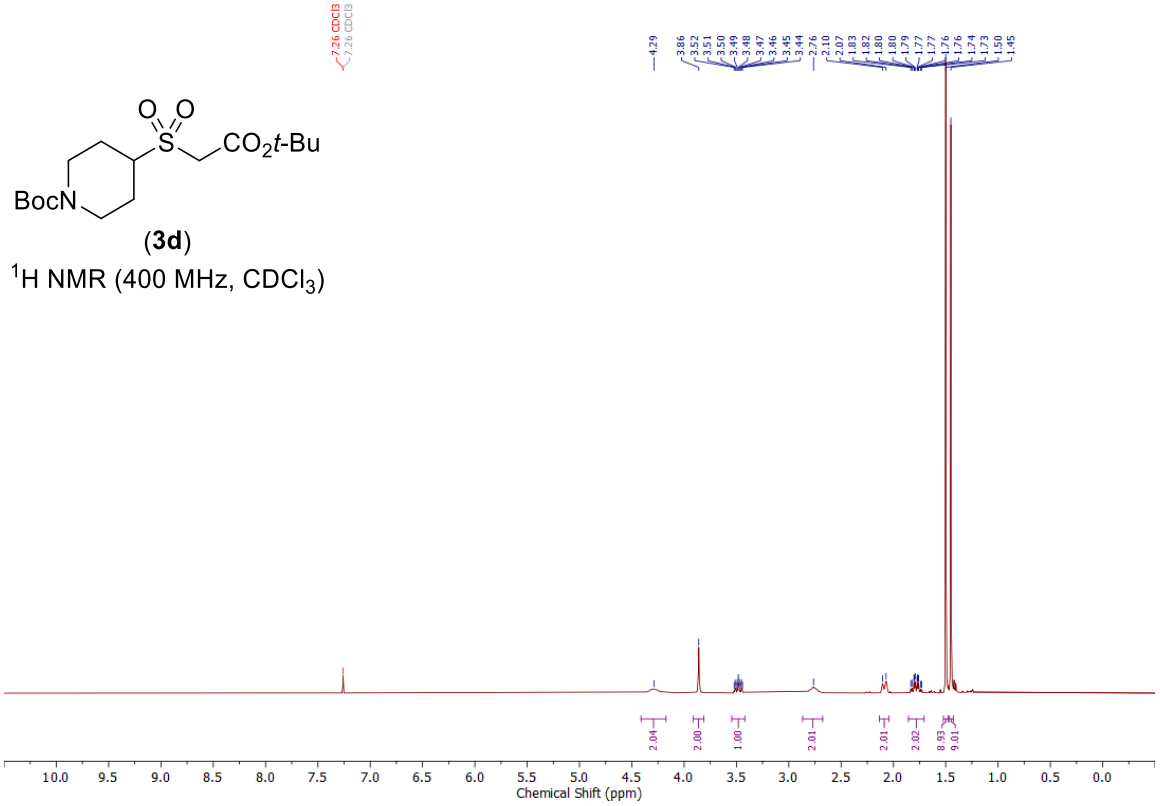
^{1}H NMR (400 MHz, $CDCl_3$)

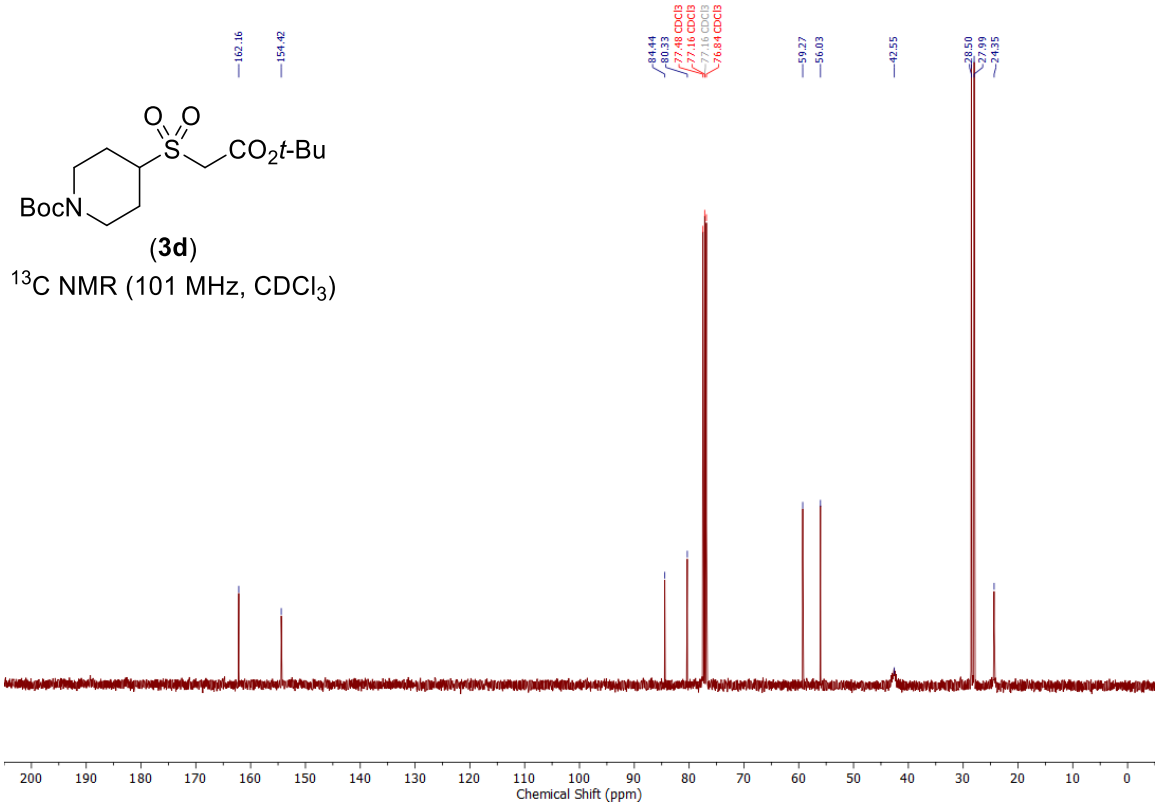


(**3a**)

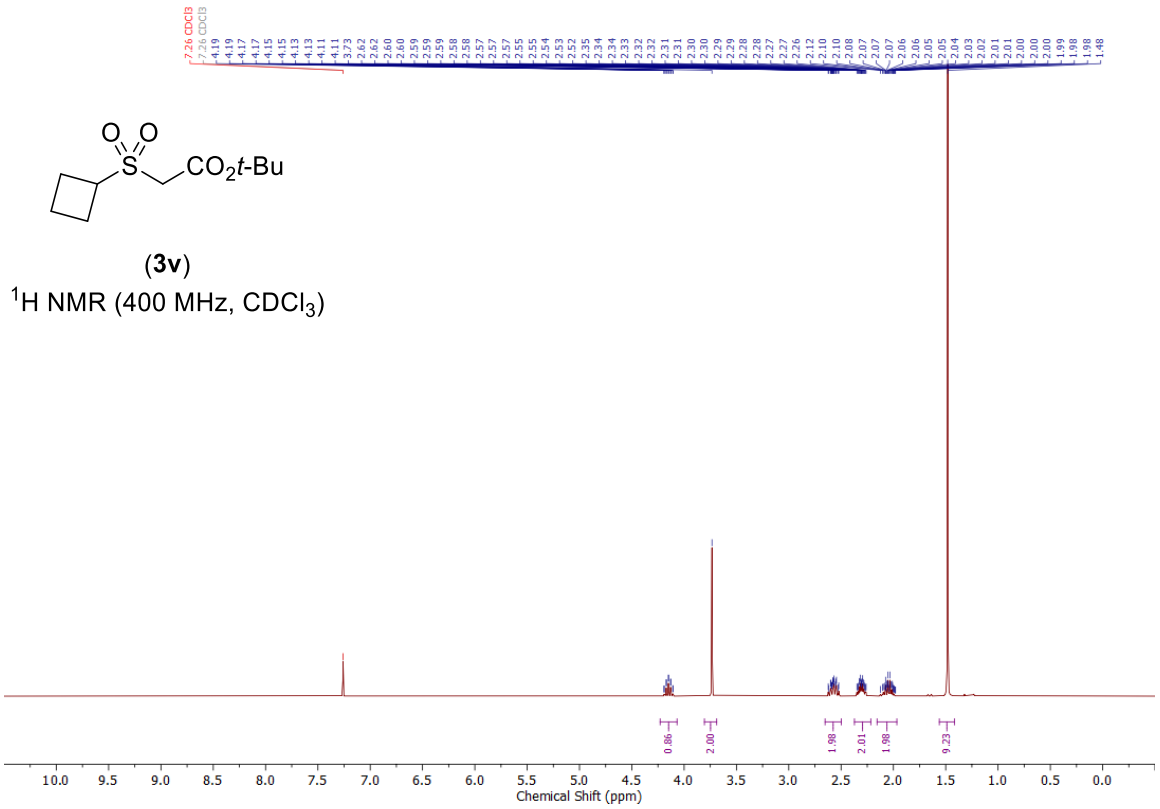
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 4-((2-(*tert*-butoxy)-2-oxoethyl)sulfonyl)piperidine-1-carboxylate (3d)

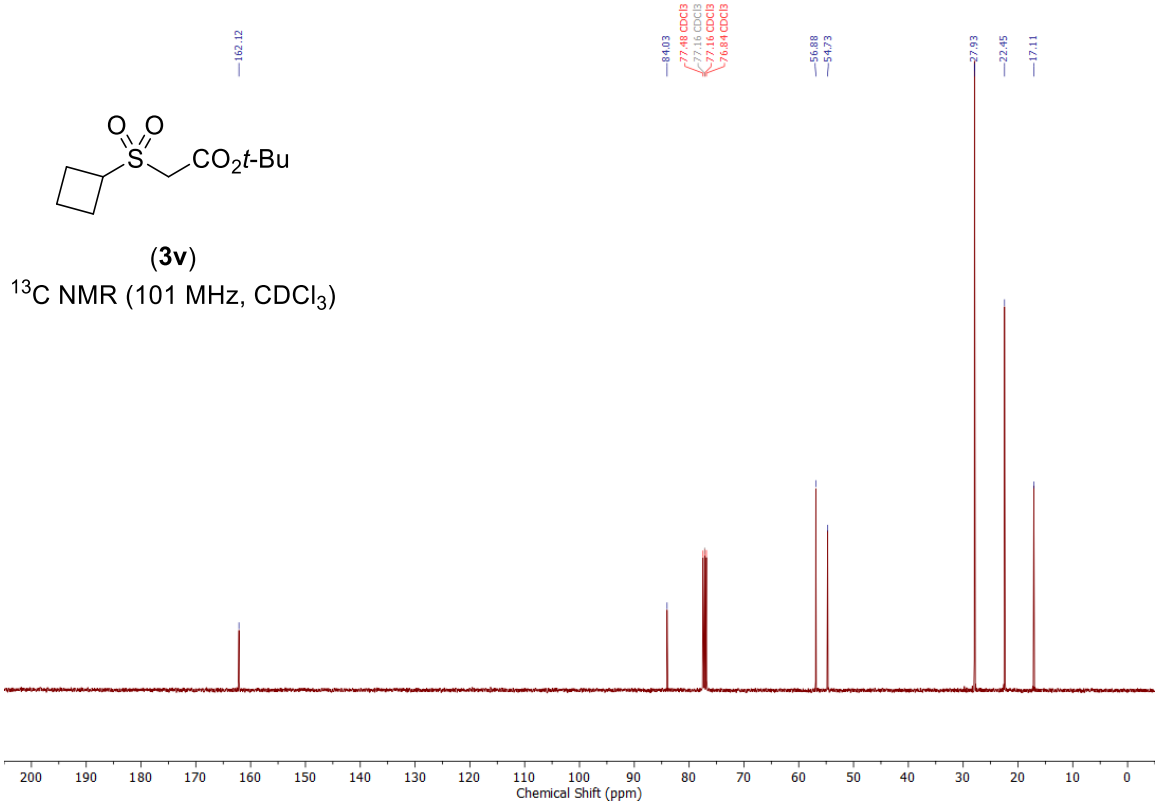




NMR spectra of *tert*-butyl 2-(cyclobutylsulfonyl)acetate (3v)

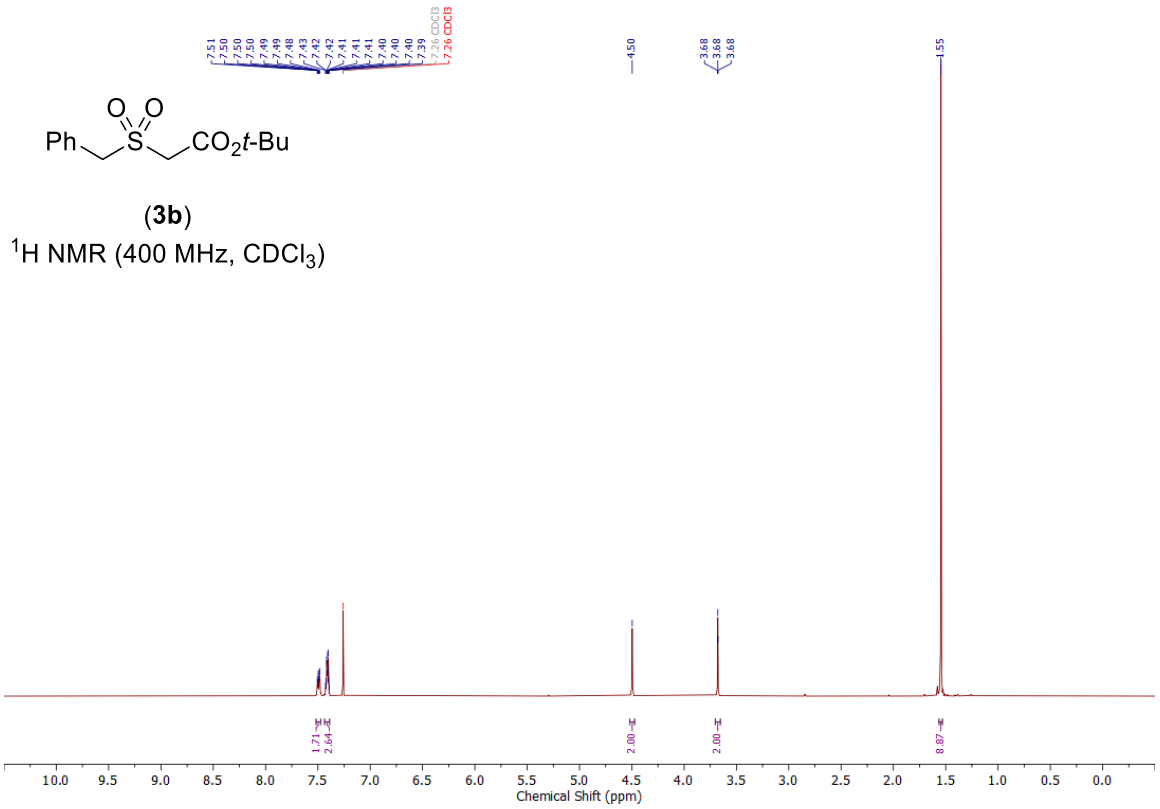


(**3v**)
^{1}H NMR (400 MHz, $CDCl_3$)

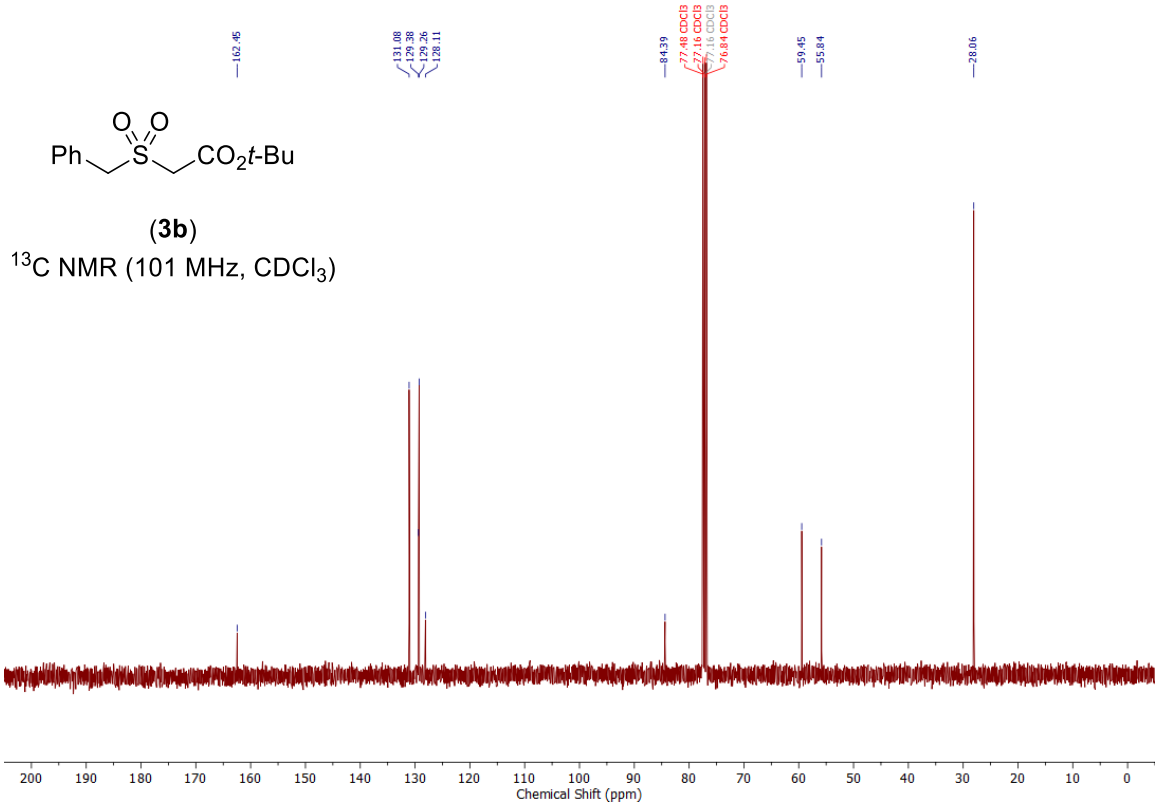


(**3v**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-(benzylsulfonyl)acetate (3b)

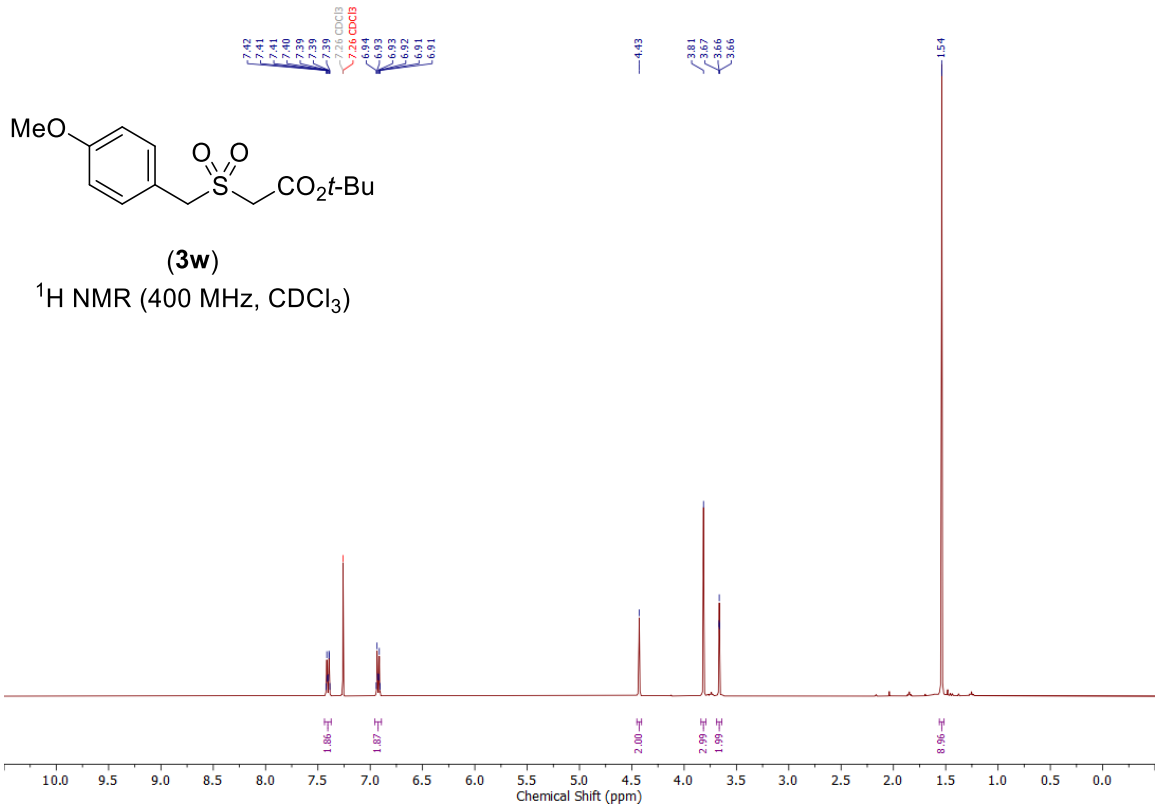


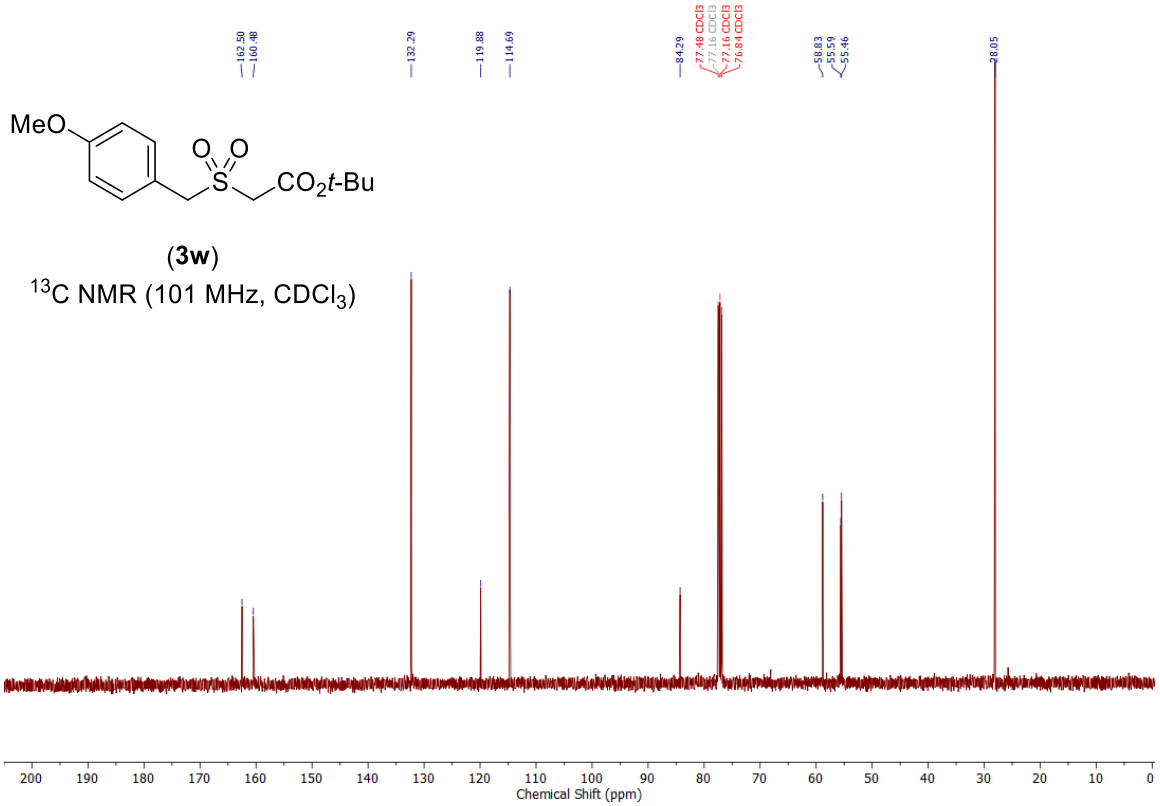
(**3b**)
^{1}H NMR (400 MHz, $CDCl_3$)



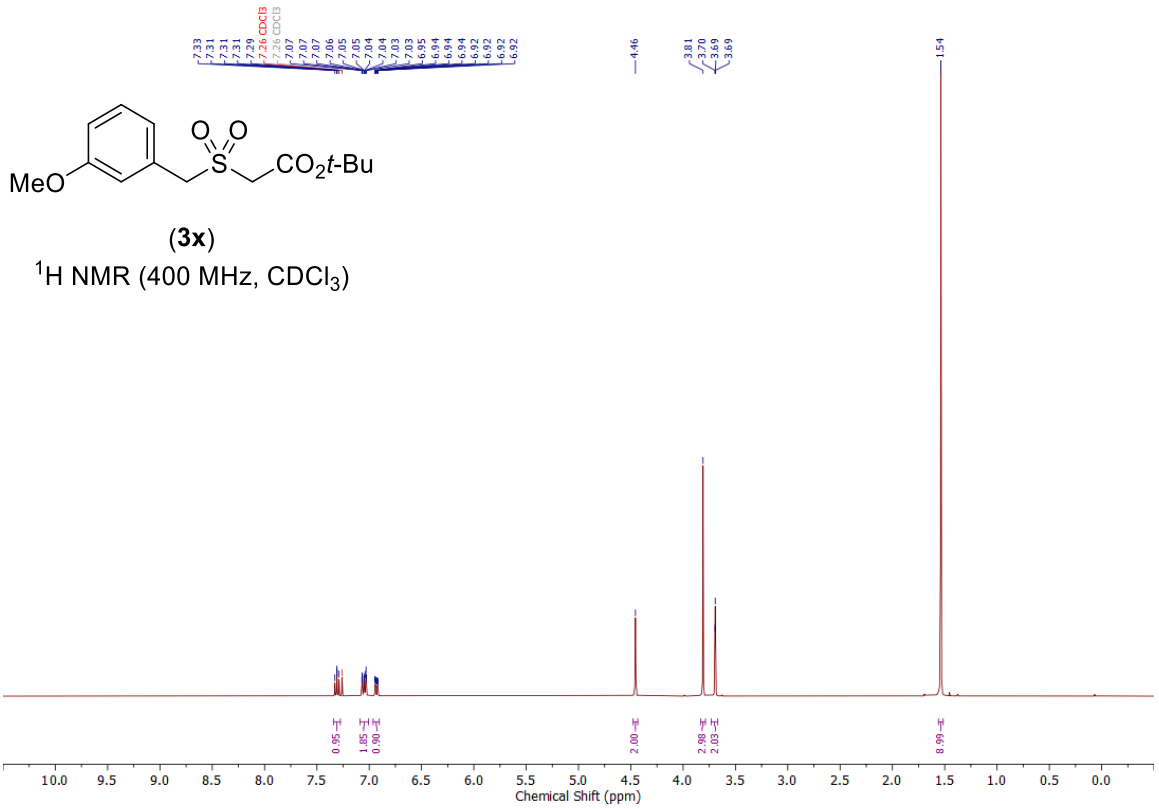
(**3b**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-((4-methoxybenzyl)sulfonyl)acetate (3w)



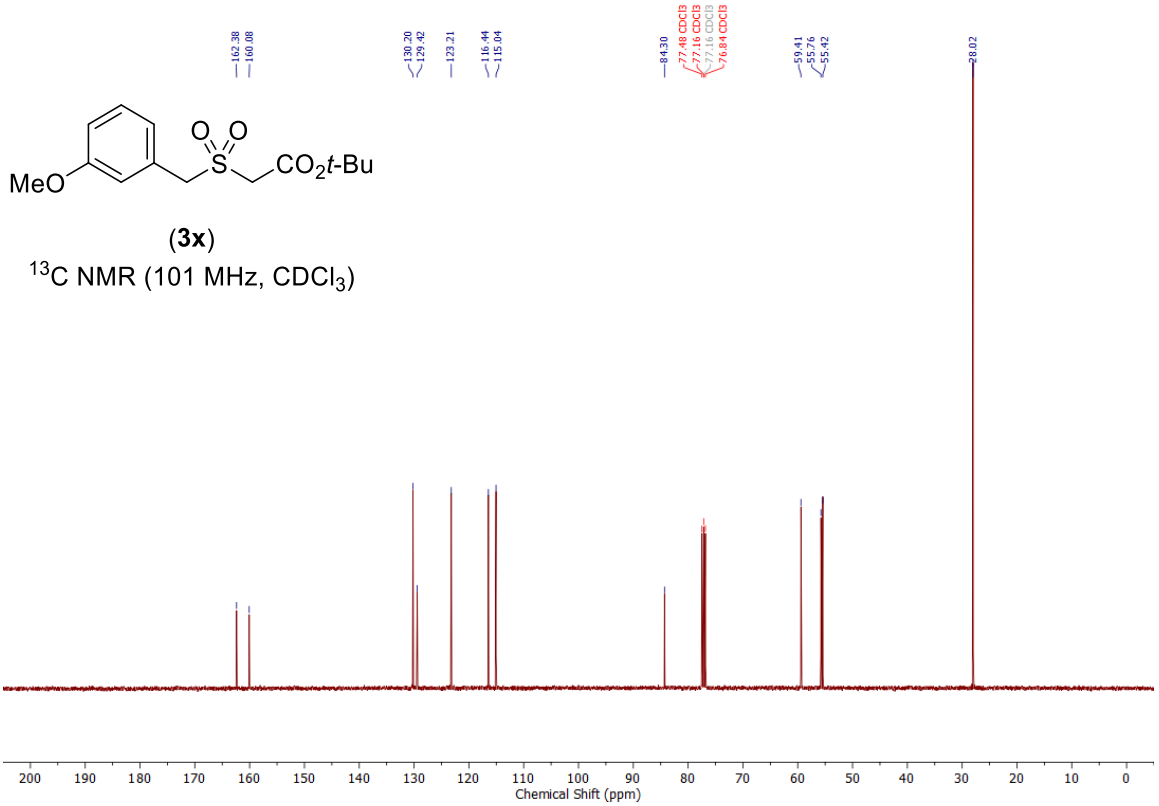


NMR spectra of *tert*-butyl 2-((3-methoxybenzyl)sulfonyl)acetate (3x)



(**3x**)

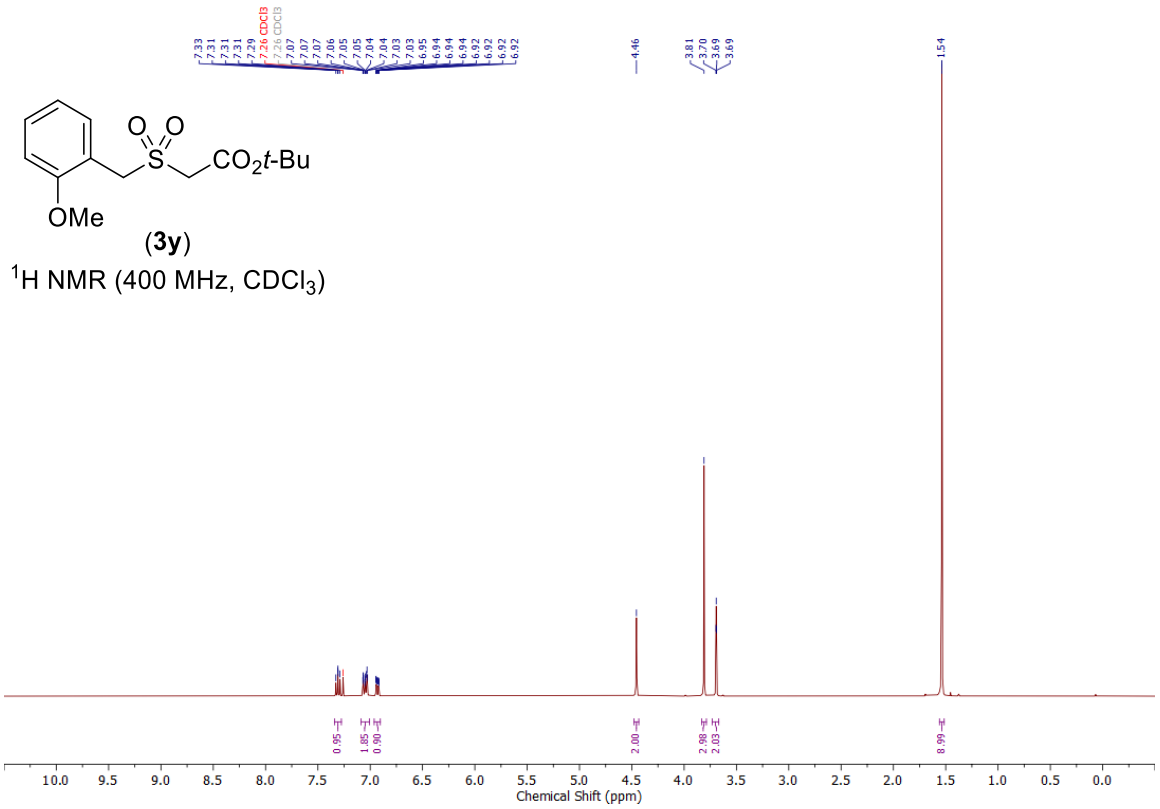
^{1}H NMR (400 MHz, $CDCl_3$)



(**3x**)

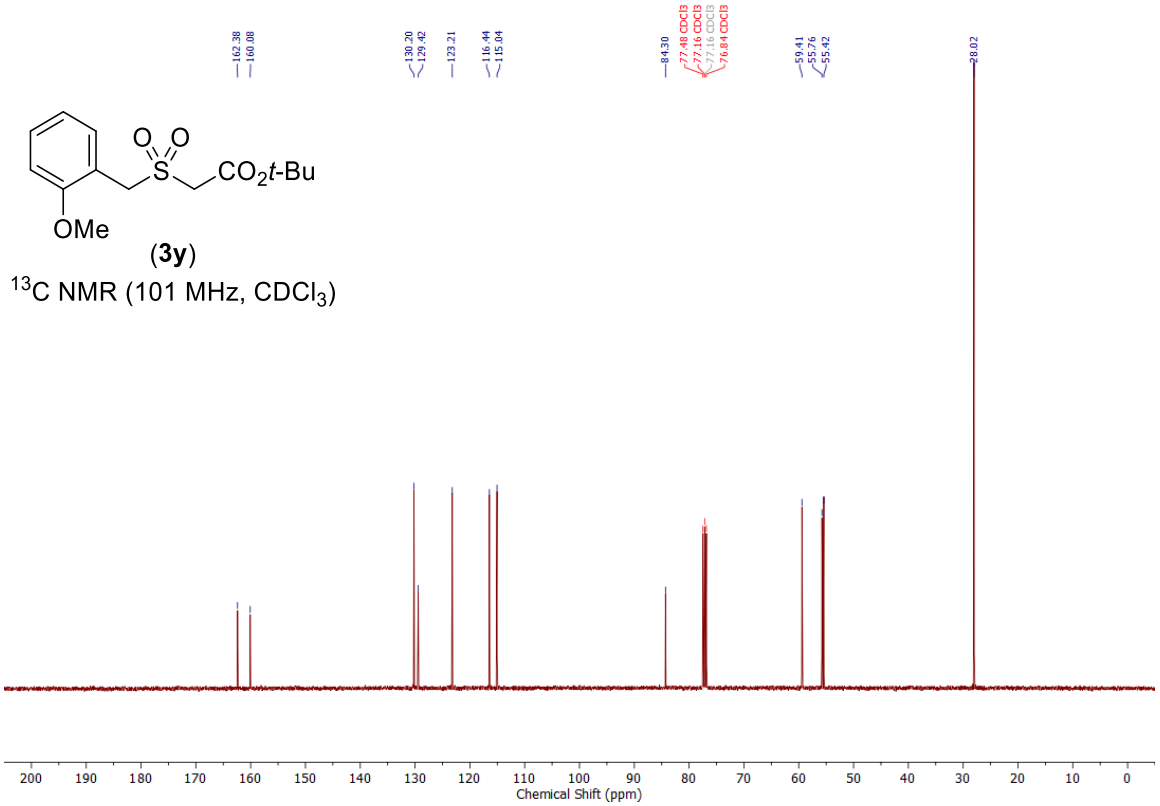
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-((2-methoxybenzyl)sulfonyl)acetate (3y)



(**3y**)

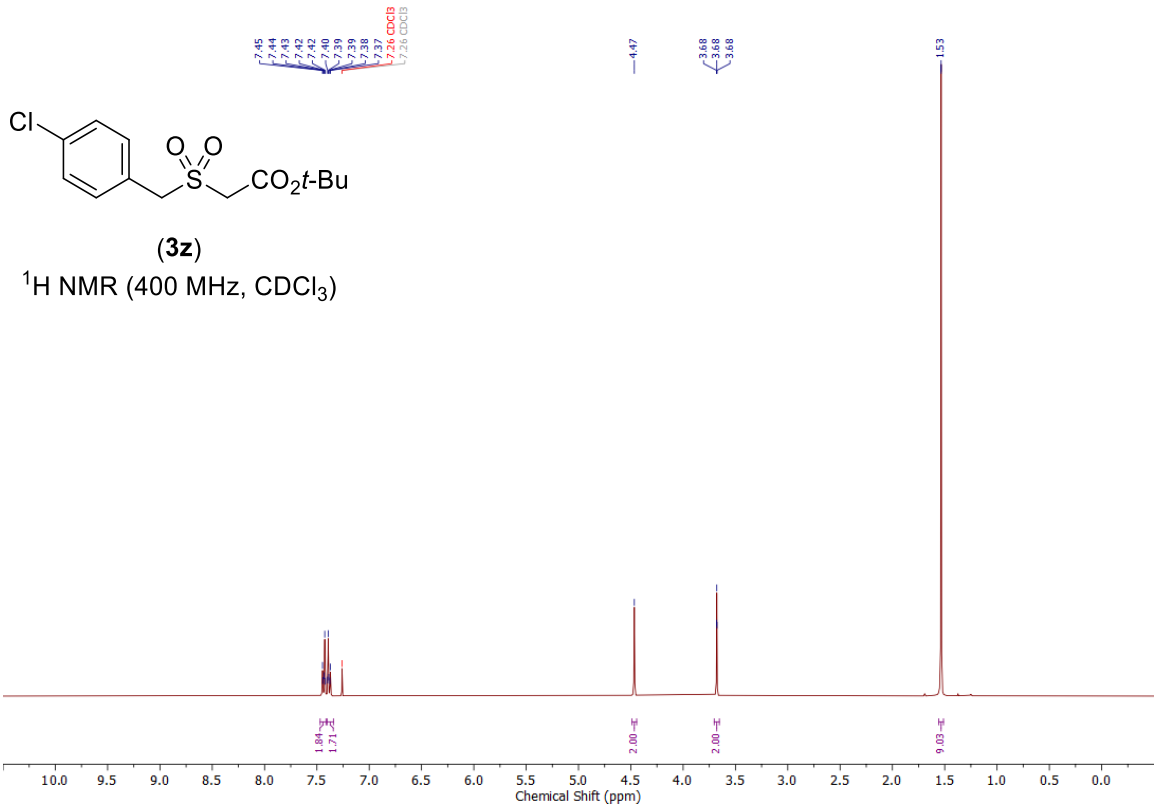
^{1}H NMR (400 MHz, $CDCl_3$)



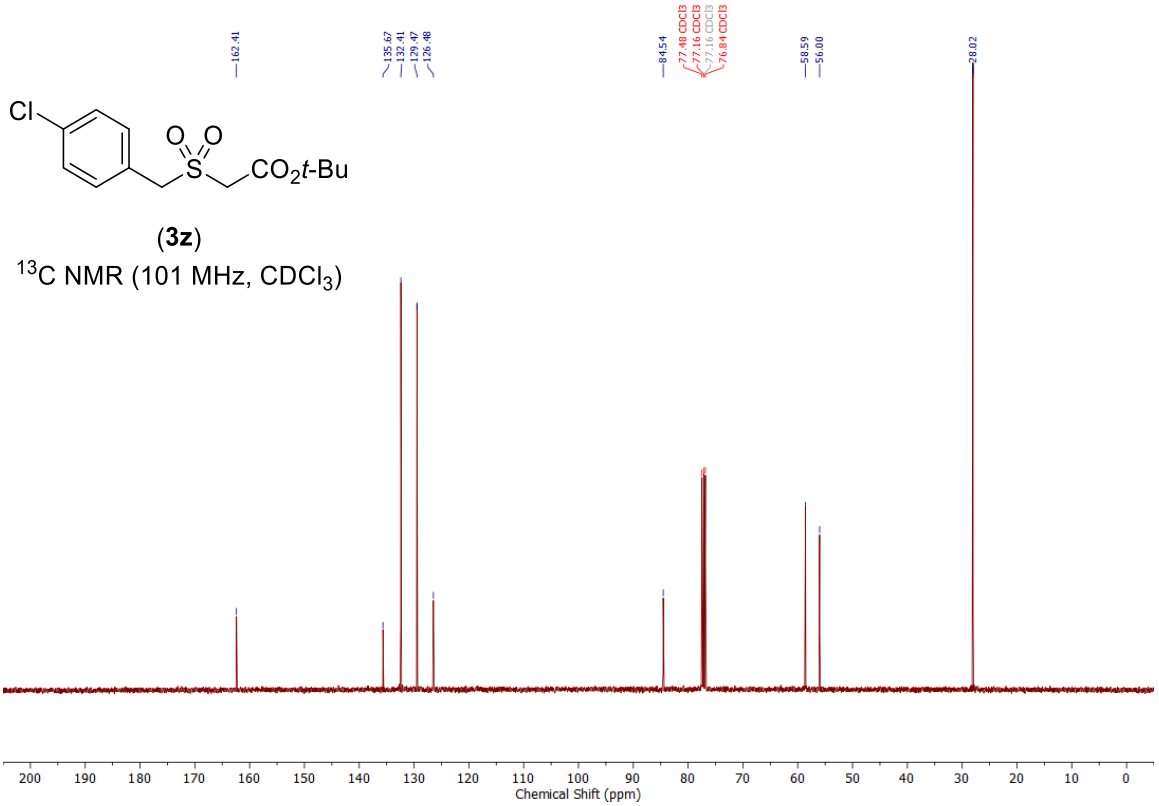
(**3y**)

^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-((4-chlorobenzyl)sulfonyl)acetate (3z)

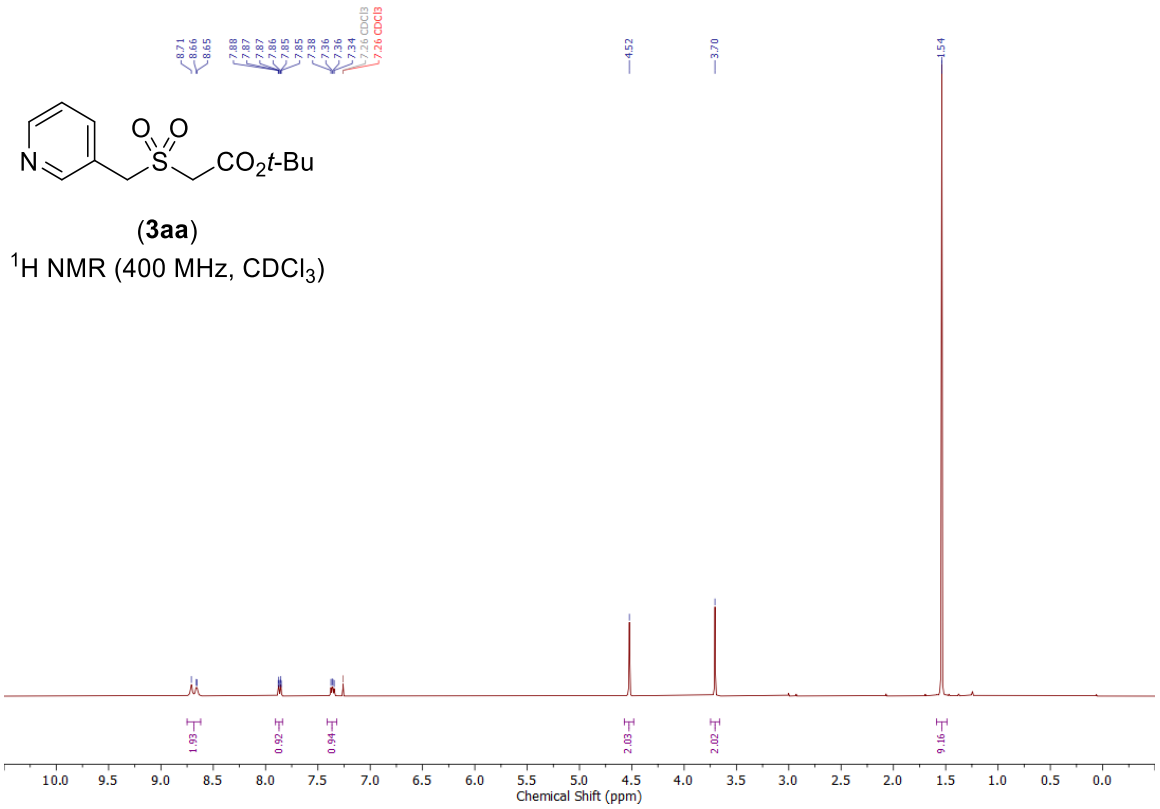


(**3z**)
^{1}H NMR (400 MHz, $CDCl_3$)

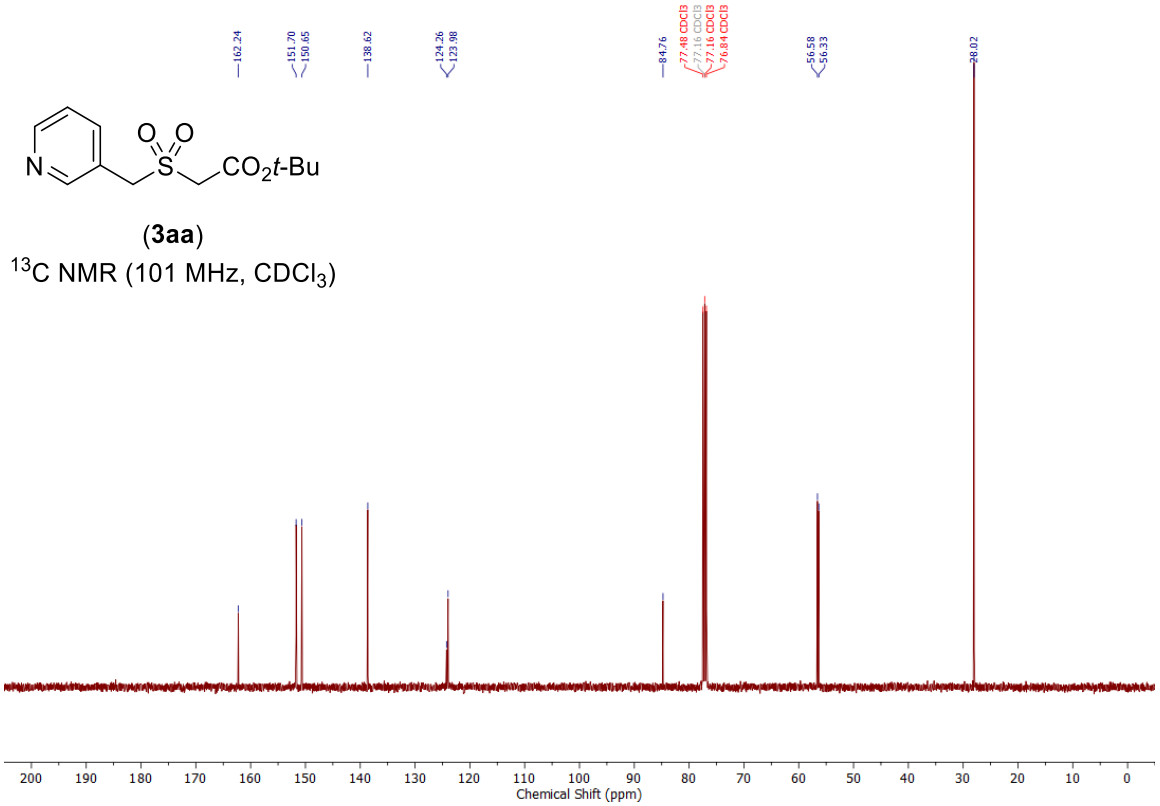


(**3z**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-((pyridin-3-ylmethyl)sulfonyl)acetate (3aa)

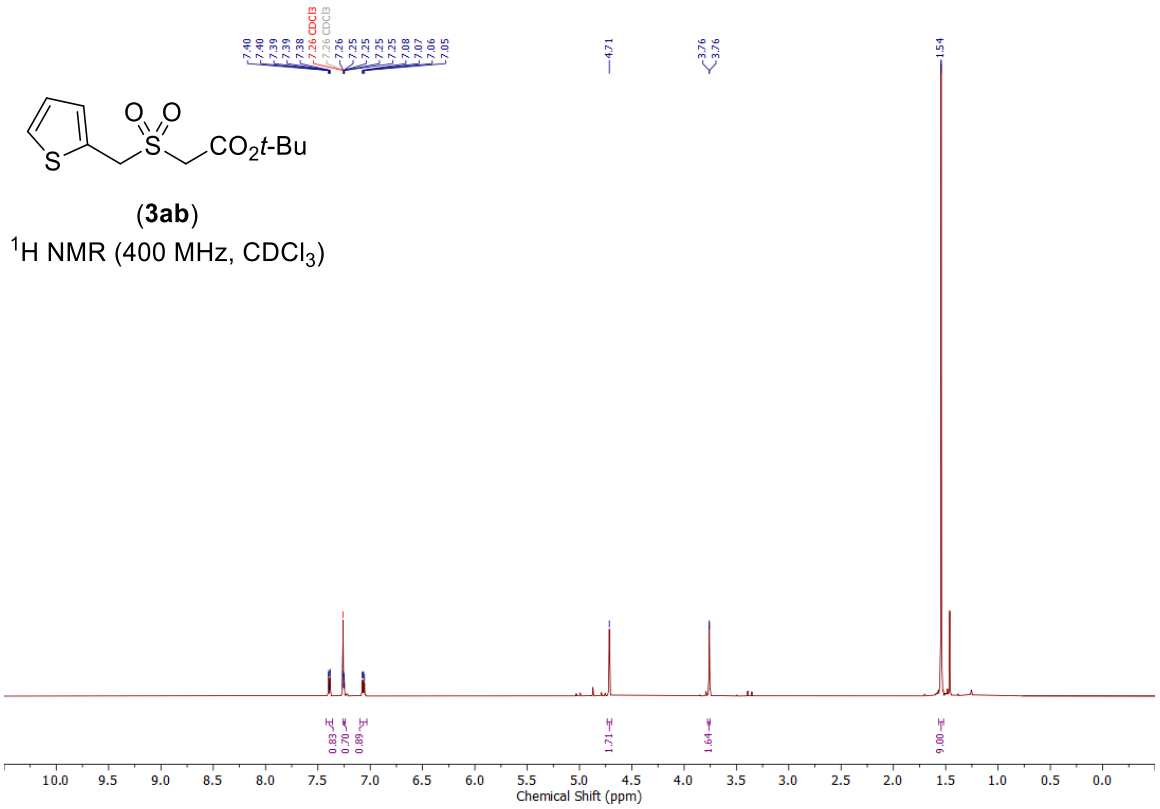


(**3aa**)
^{1}H NMR (400 MHz, $CDCl_3$)

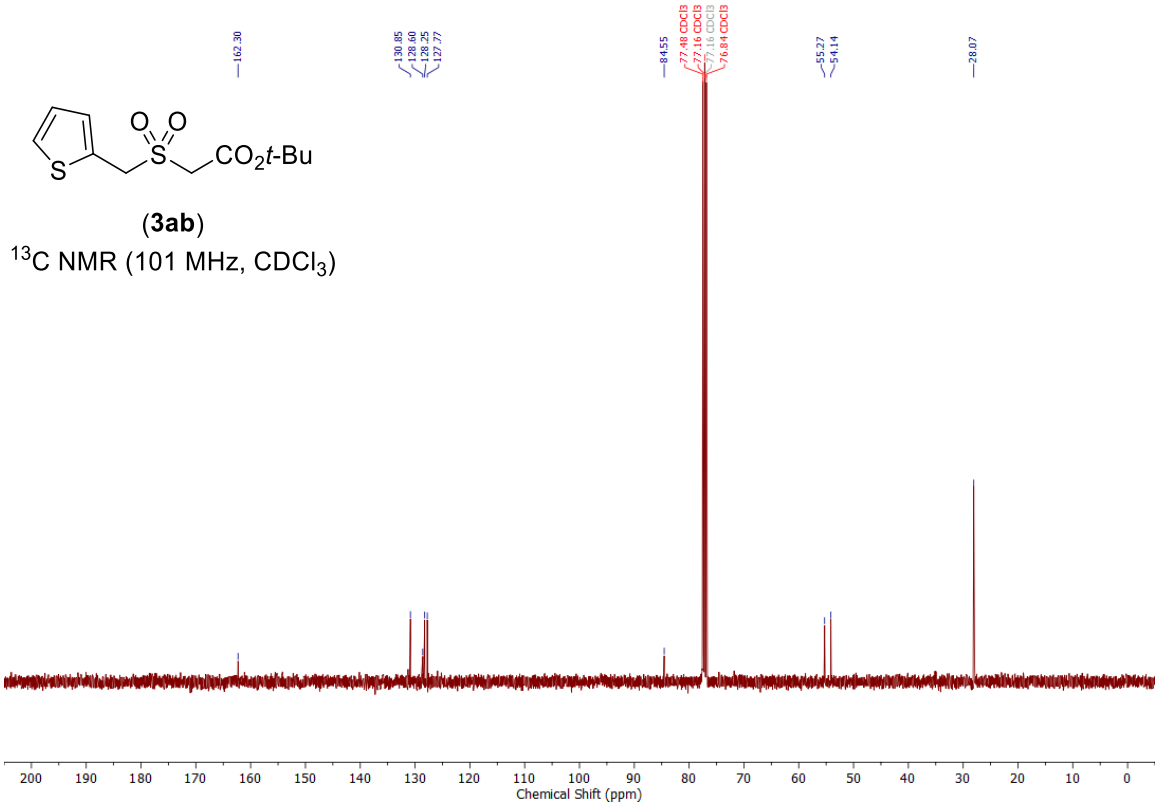


(**3aa**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-((thiophen-2-ylmethyl)sulfonyl)acetate (3ab)

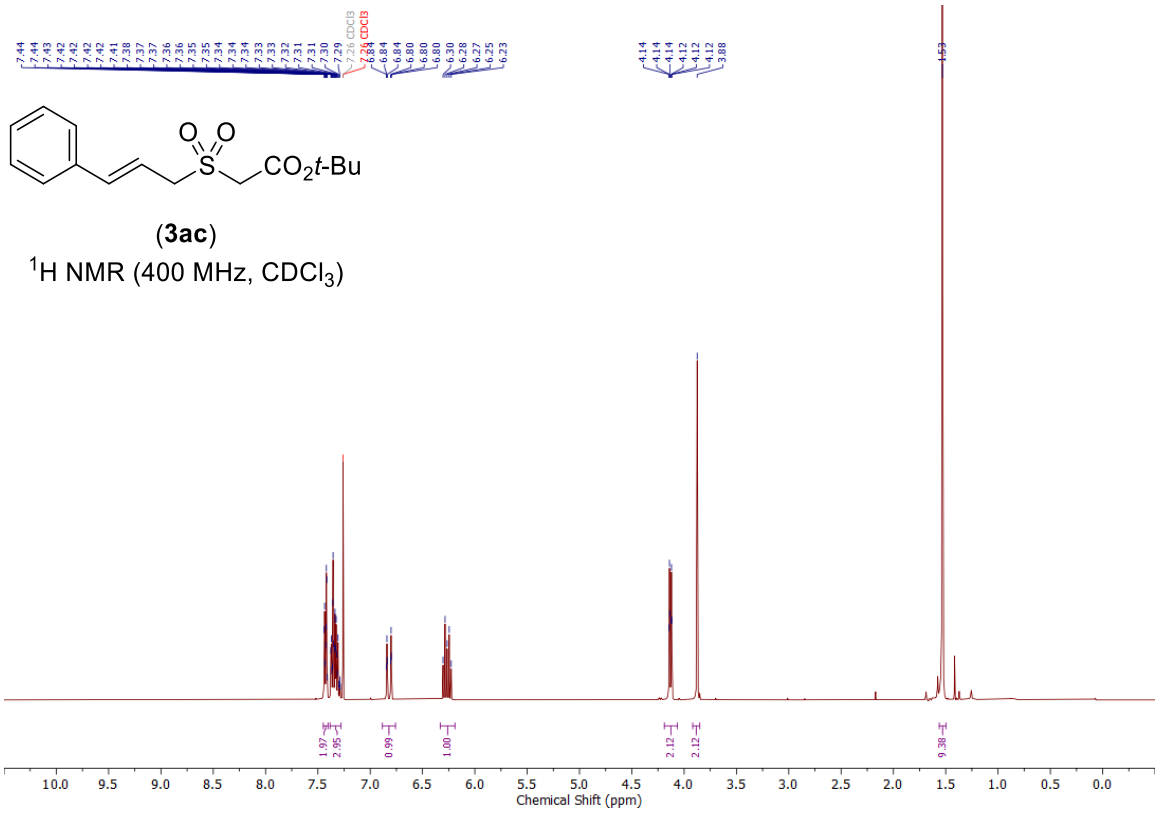


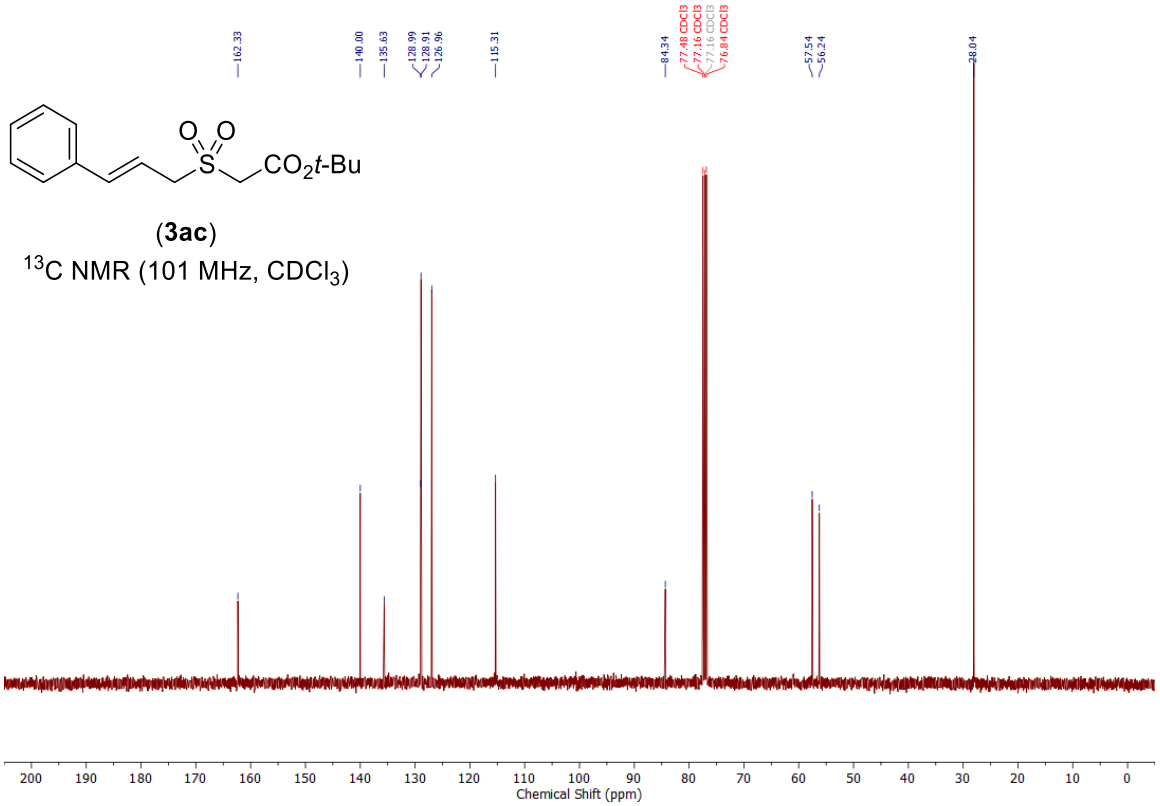
(**3ab**)
^{1}H NMR (400 MHz, $CDCl_3$)



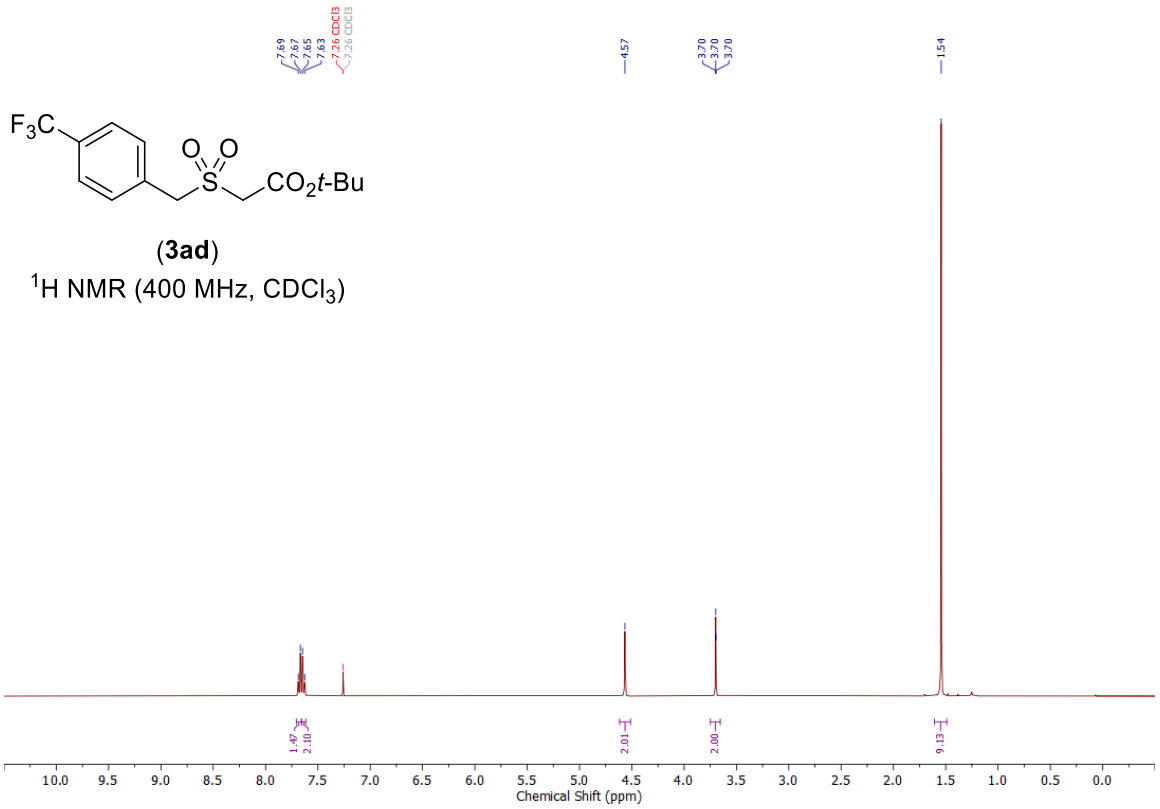
(**3ab**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-(cinnamylsulfonyl)acetate (3ac)

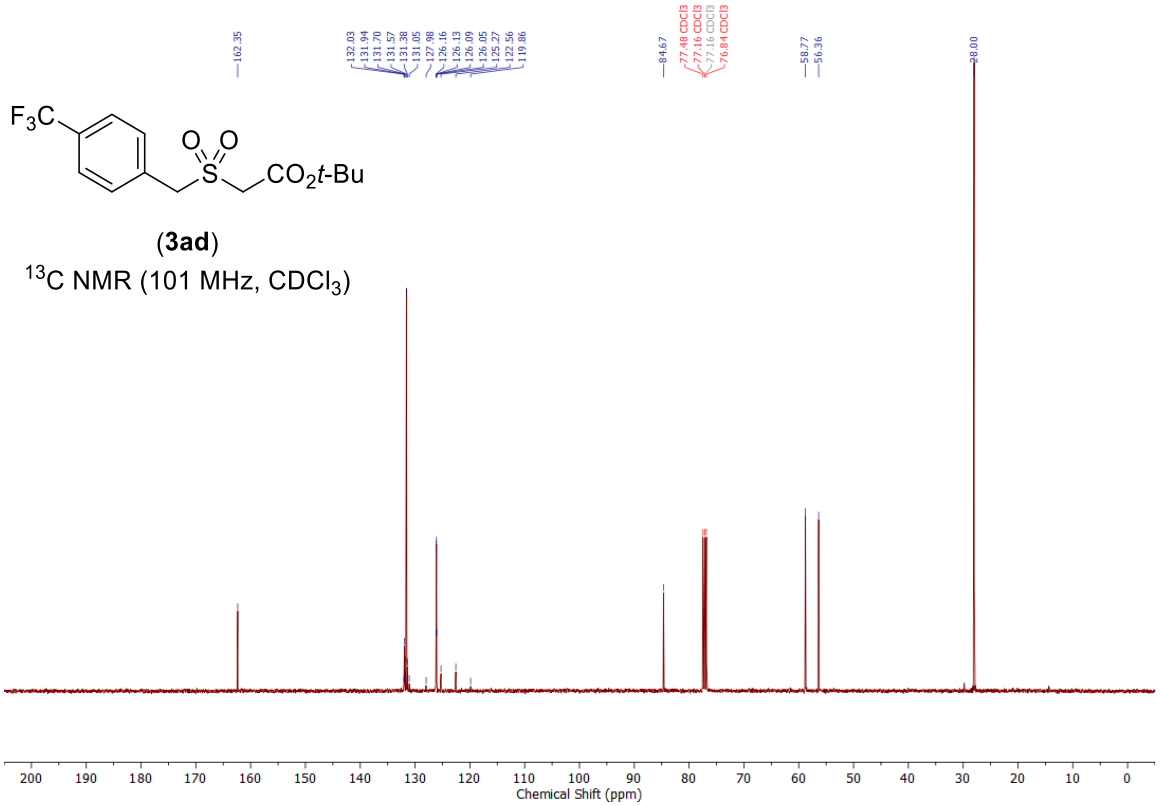




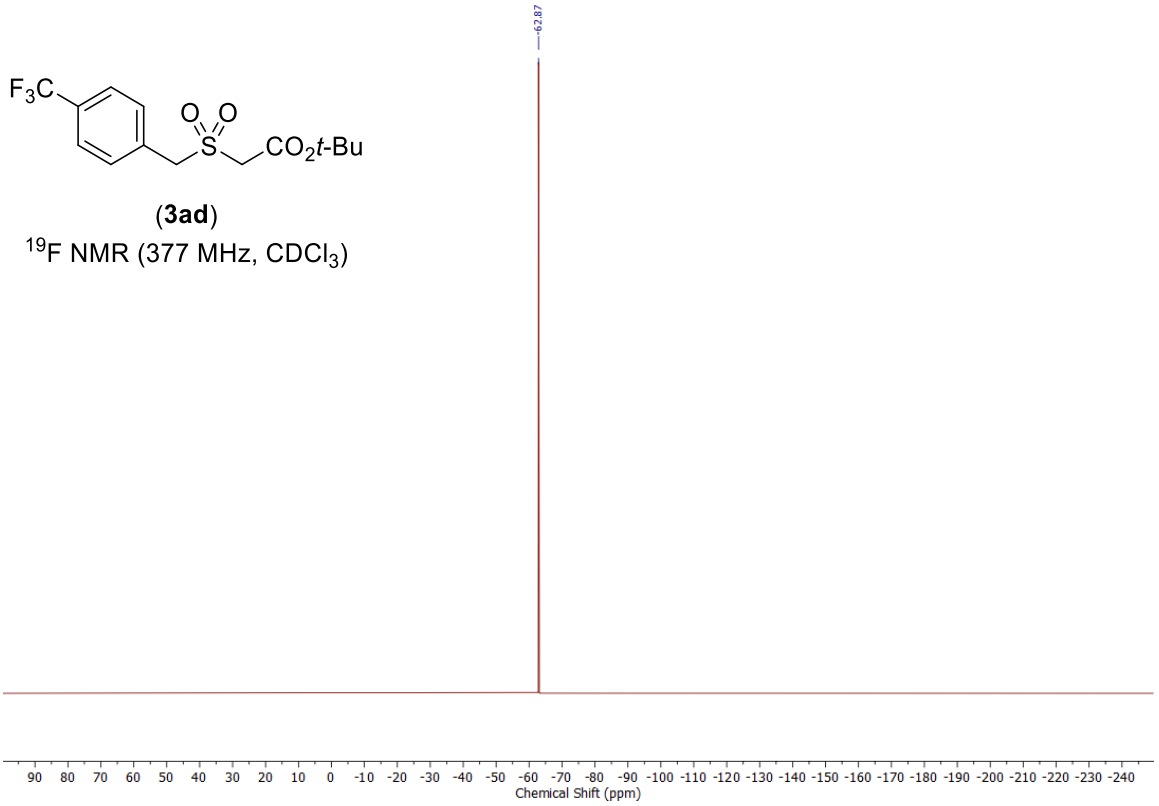
NMR spectra of *tert*-butyl 2-((4-(trifluoromethyl)benzyl)sulfonyl)acetate (3ad)



(**3ad**)
^{1}H NMR (400 MHz, $CDCl_3$)



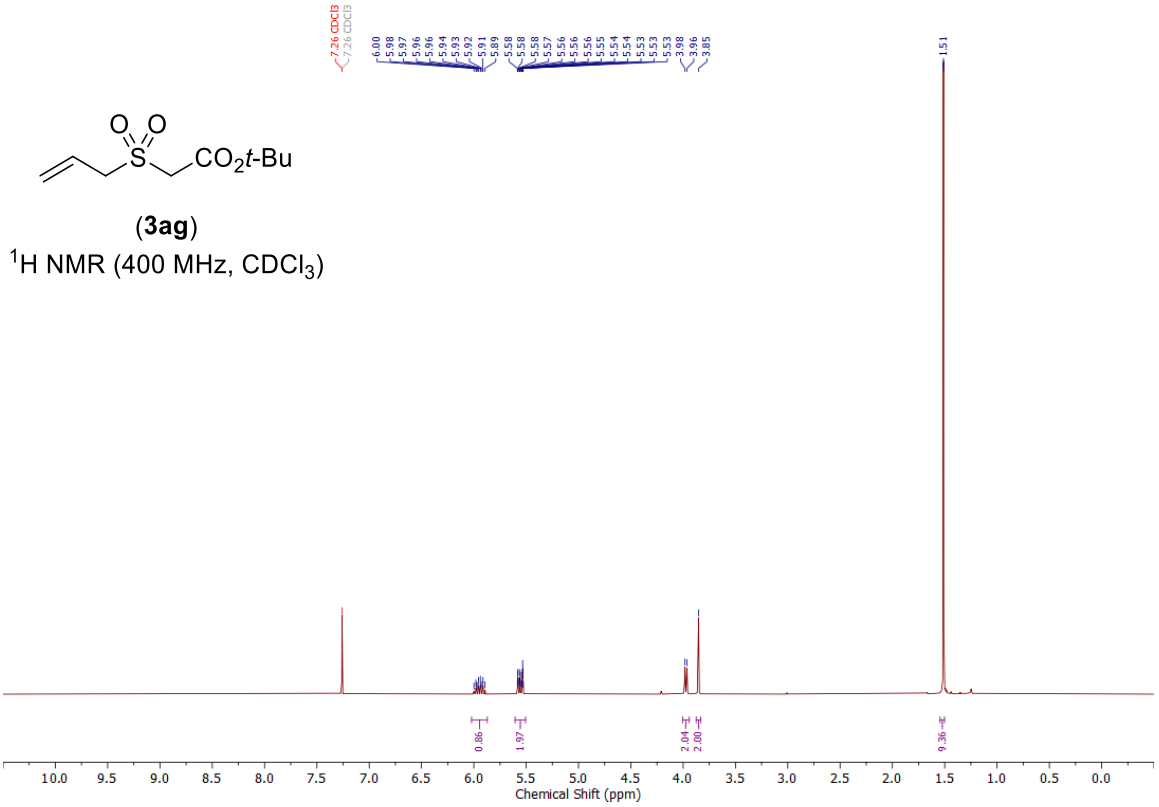
(**3ad**)
^{13}C NMR (101 MHz, $CDCl_3$)



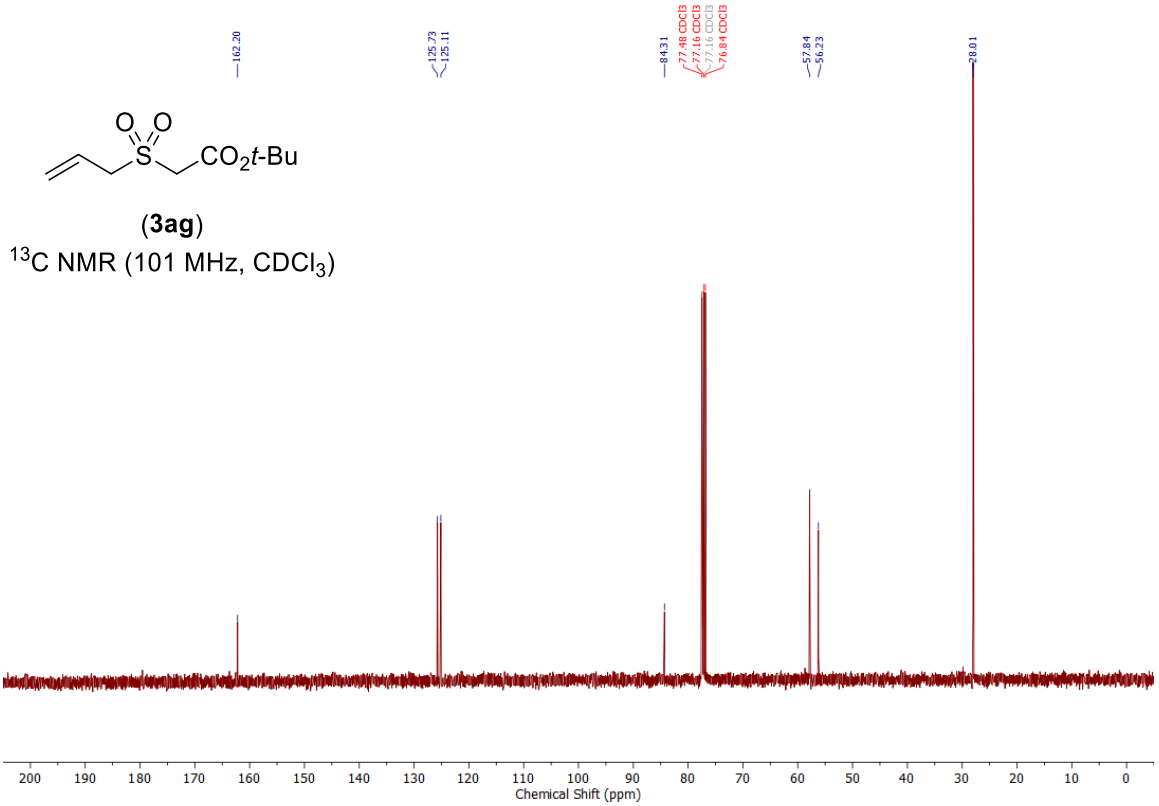
(**3ad**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-(allylsulfonyl)acetate (3ag)

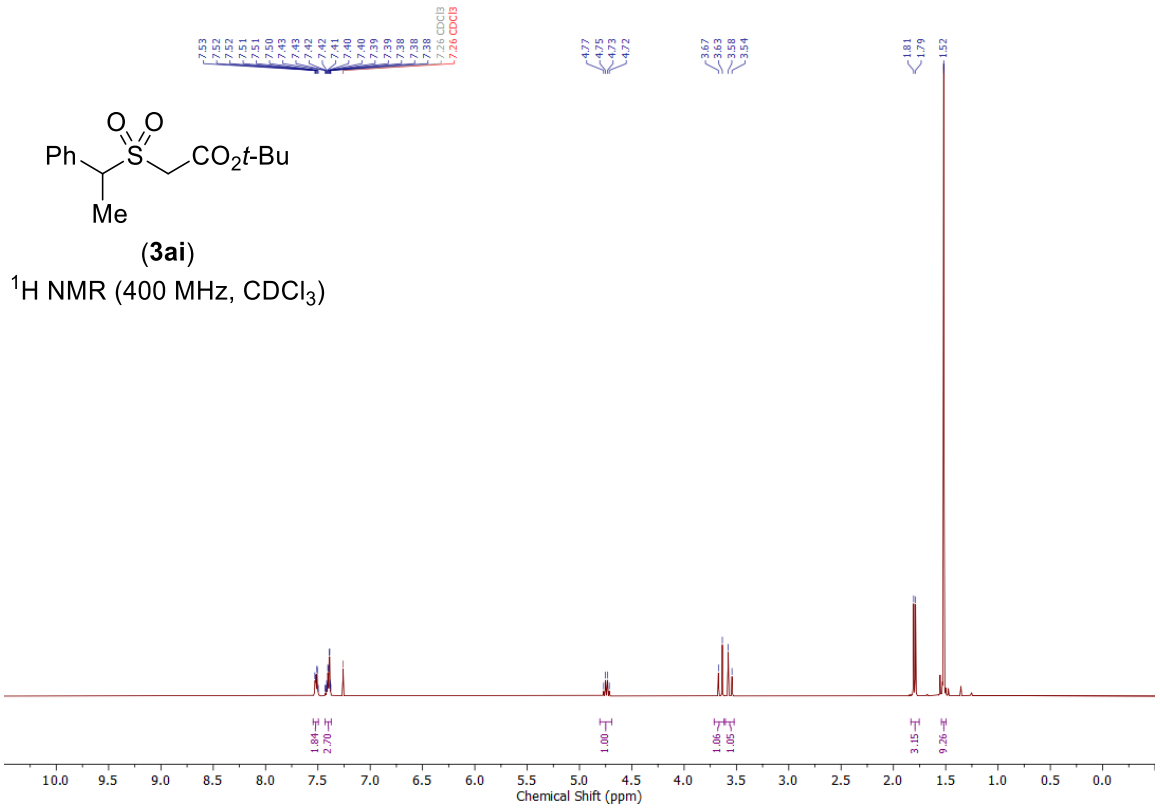


(**3ag**)
^{1}H NMR (400 MHz, $CDCl_3$)



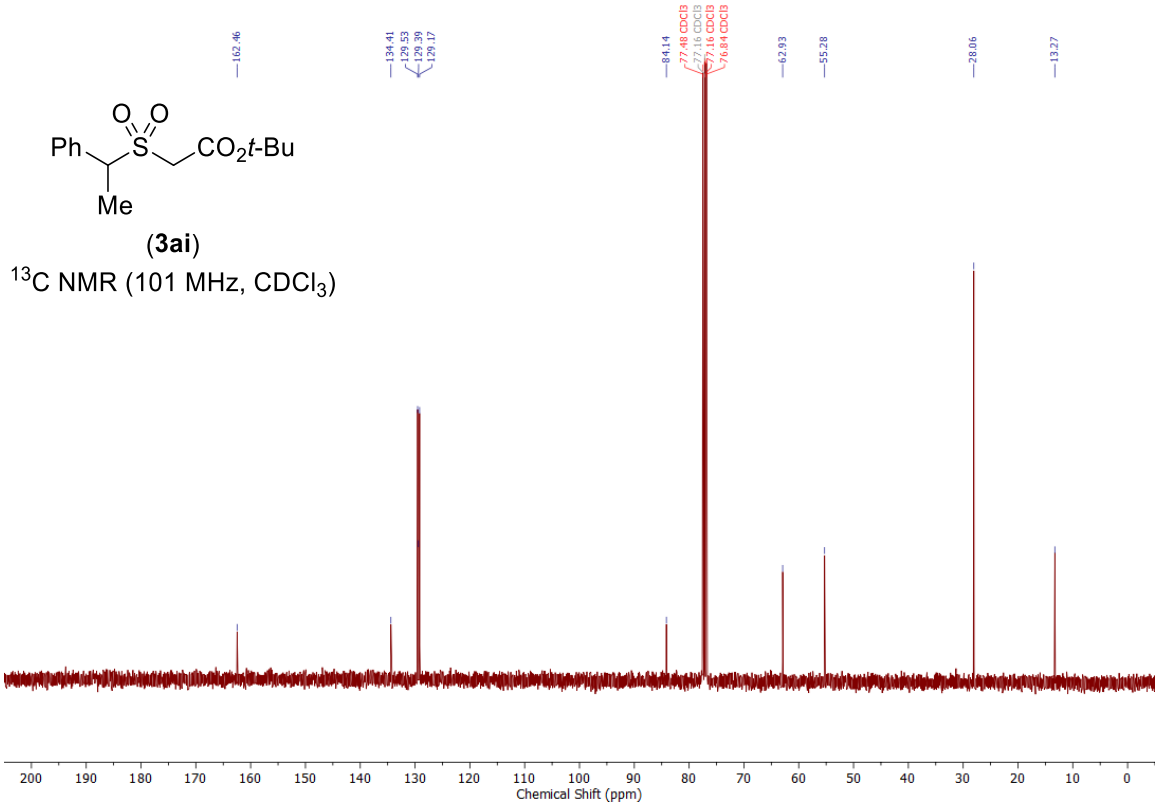
(**3ag**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-((1-phenylethyl)sulfonyl)acetate (3ai)



(**3ai**)

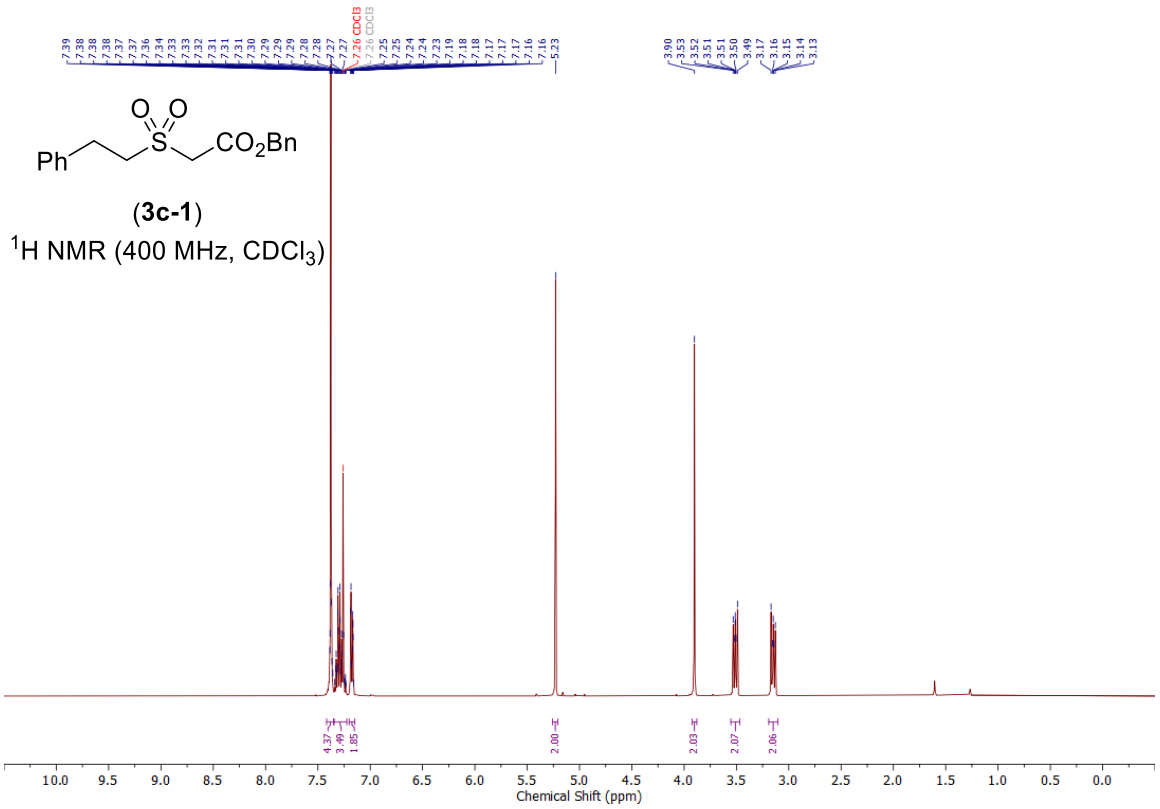
^{1}H NMR (400 MHz, $CDCl_3$)

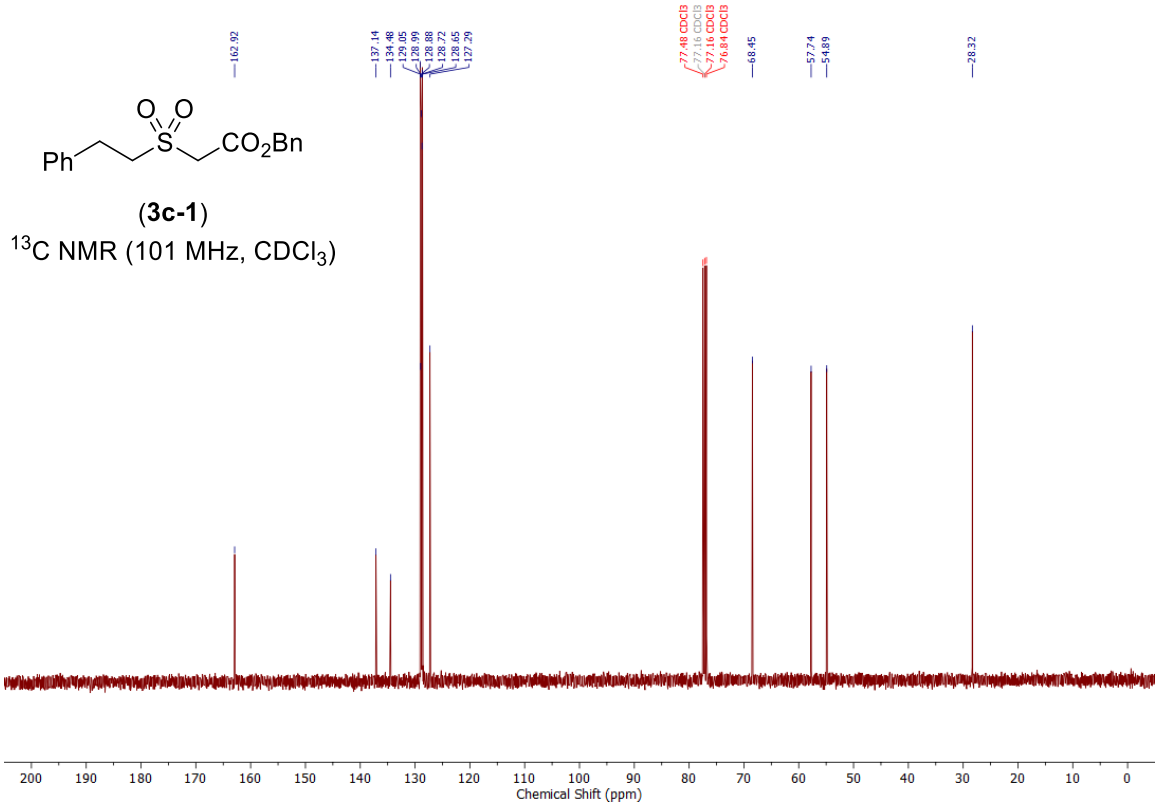


(**3ai**)

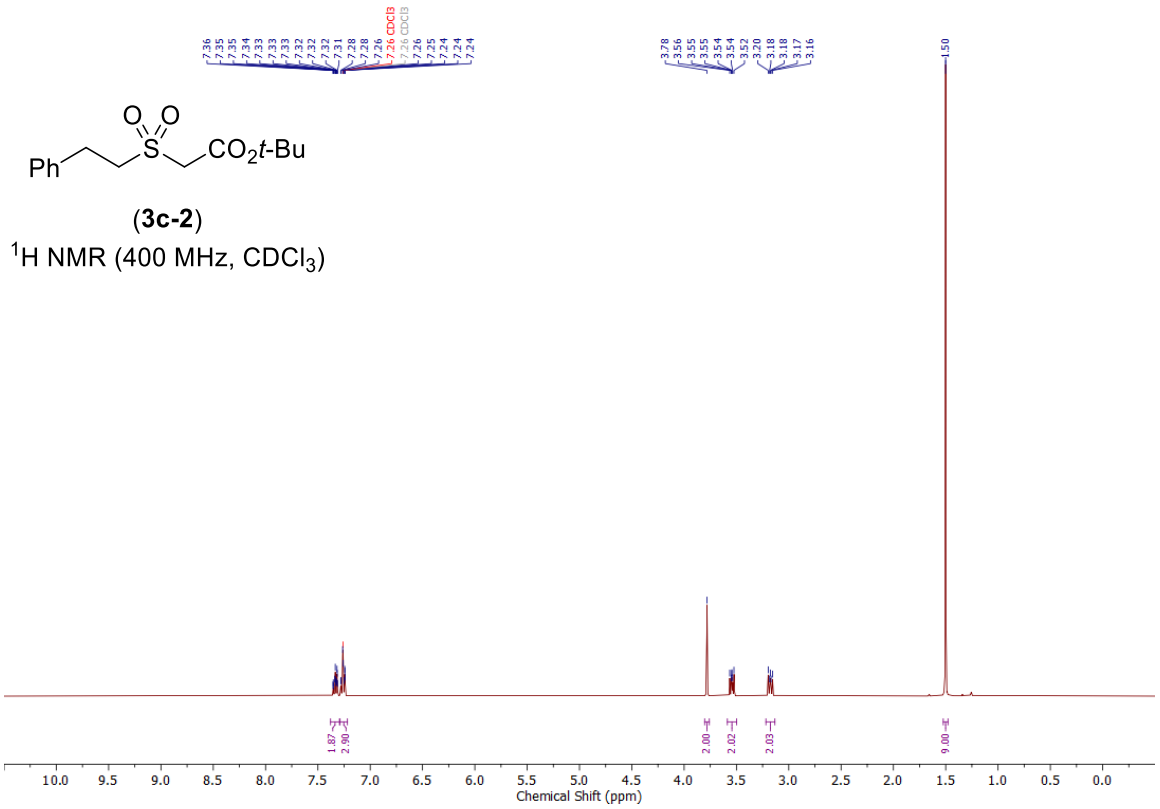
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of benzyl 2-(phenethylsulfonyl)acetate (3c-1)

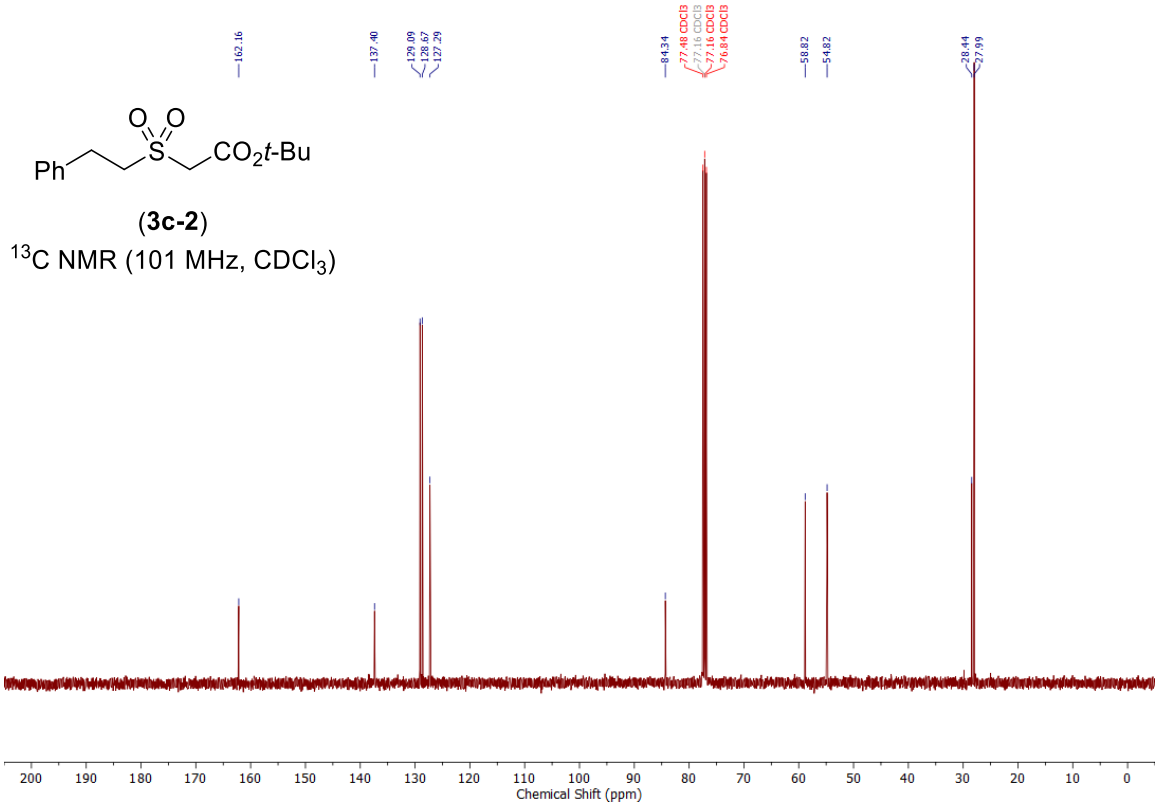




NMR spectra of *tert*-butyl 2-(phenethylsulfonyl)acetate (3c-2)

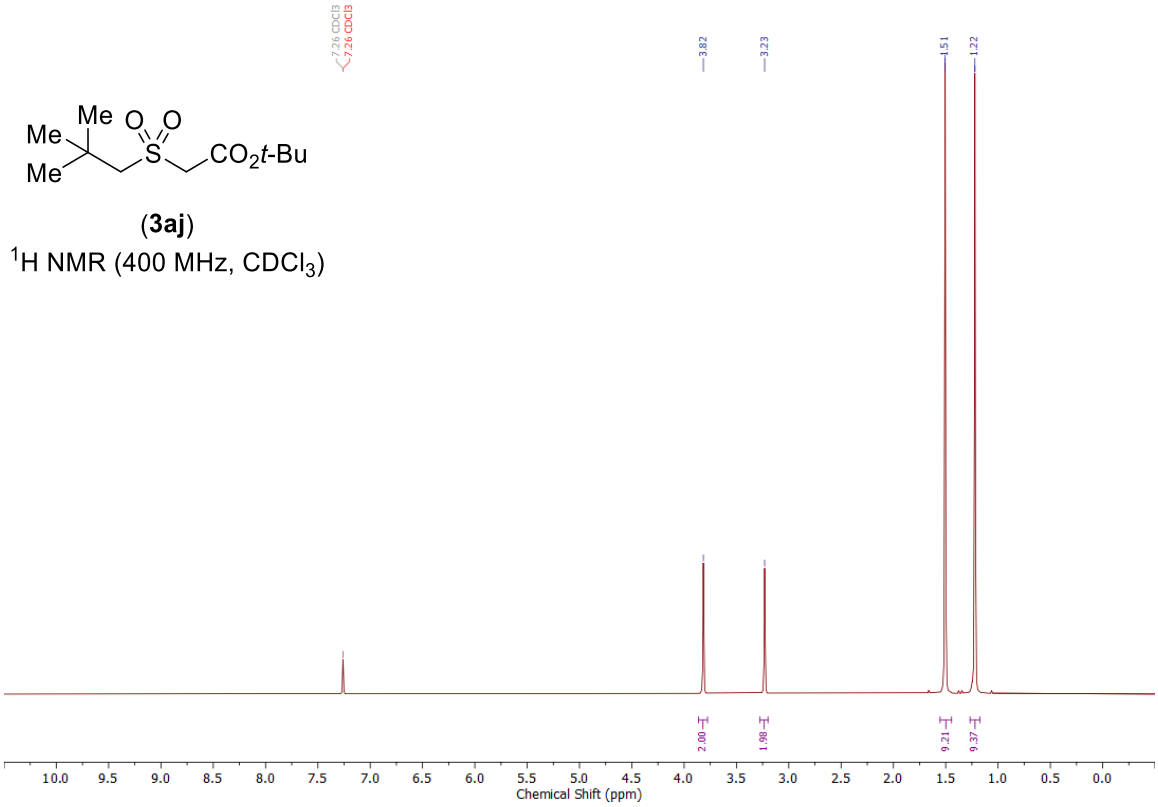


(**3c-2**)
^{1}H NMR (400 MHz, $CDCl_3$)

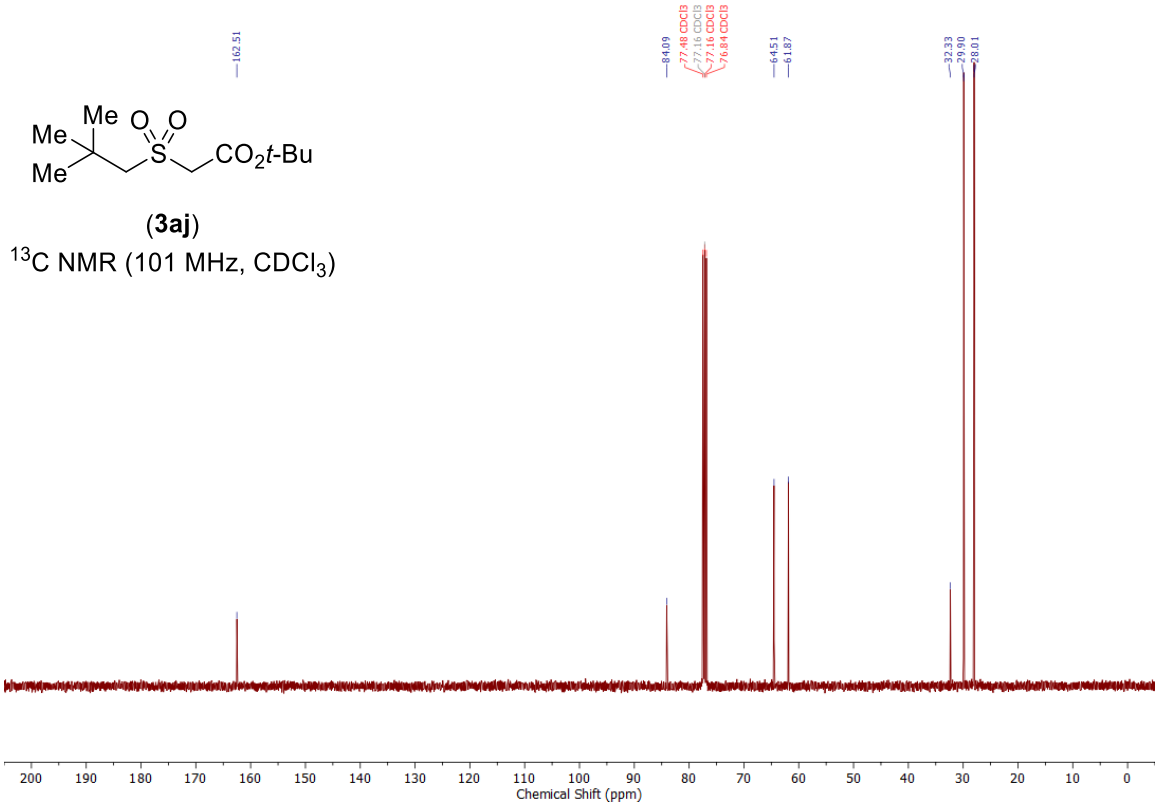


(**3c-2**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-(neopentylsulfonyl)acetate (3aj)

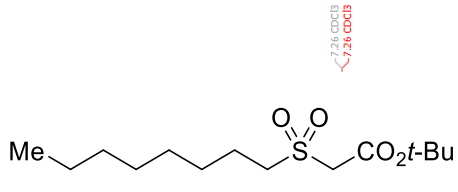


(**3aj**)
^{1}H NMR (400 MHz, $CDCl_3$)



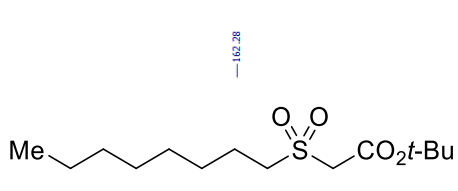
(**3aj**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-(octylsulfonyl)acetate (3ak)



(**3ak**)

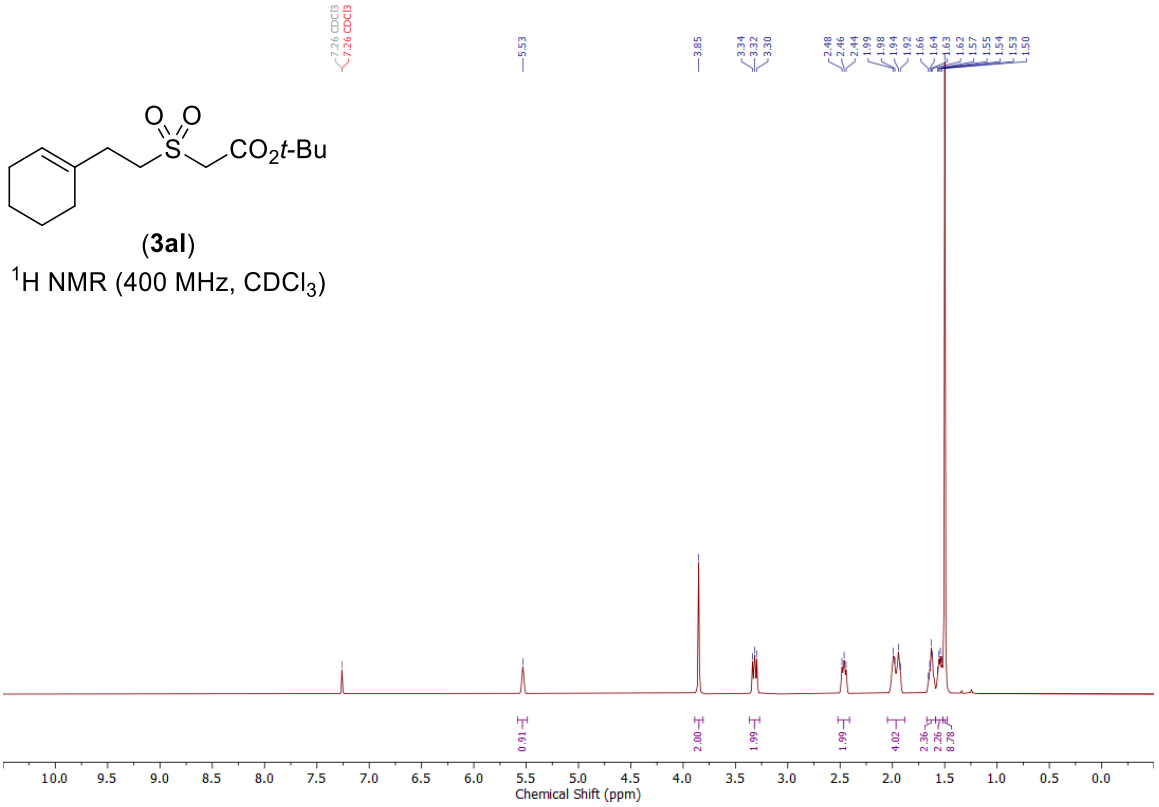
^{1}H NMR (400 MHz, $CDCl_3$)



(**3ak**)

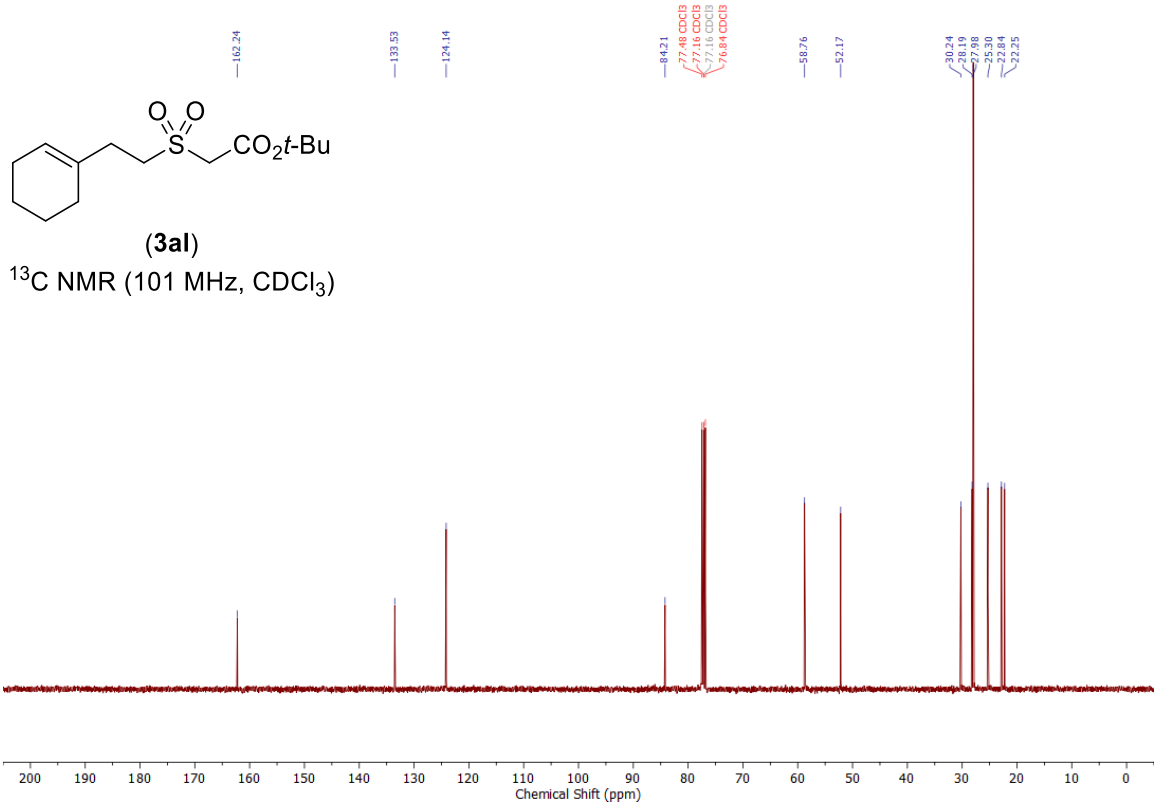
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-((2-(cyclohex-1-en-1-yl)ethyl)sulfonyl)acetate (3al)



(**3al**)

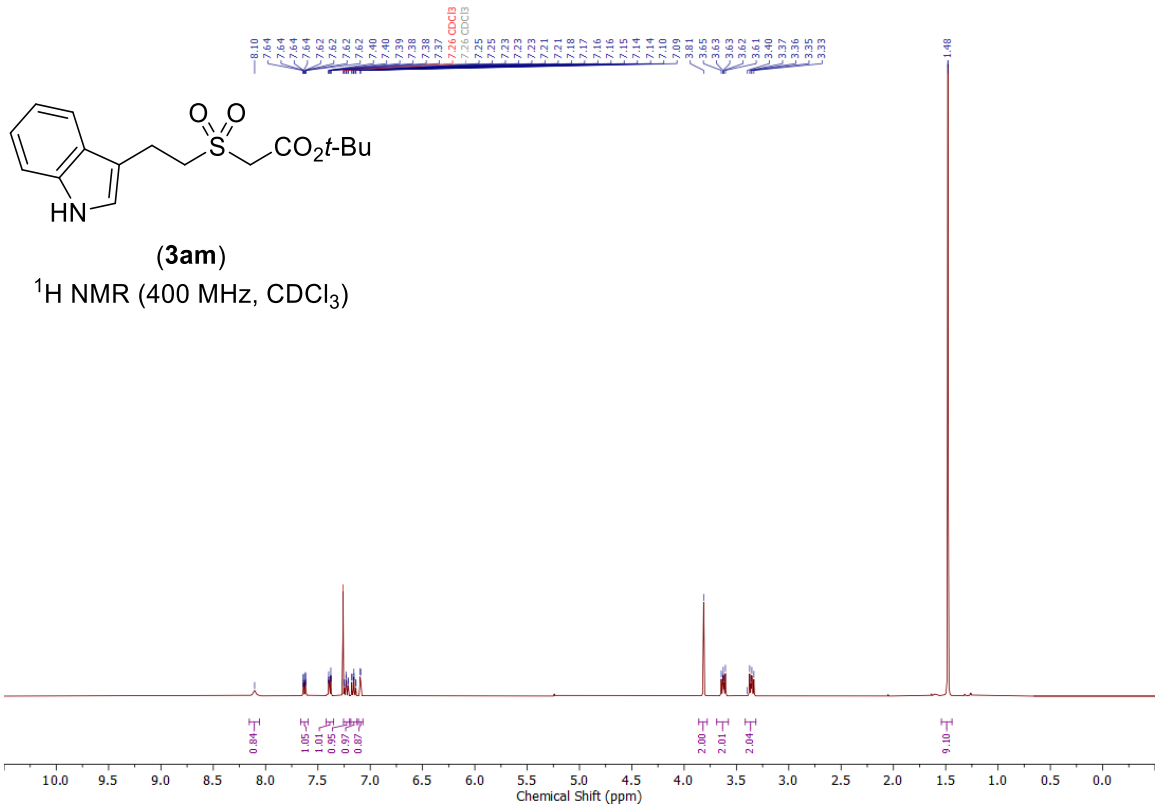
^{1}H NMR (400 MHz, $CDCl_3$)



(**3al**)

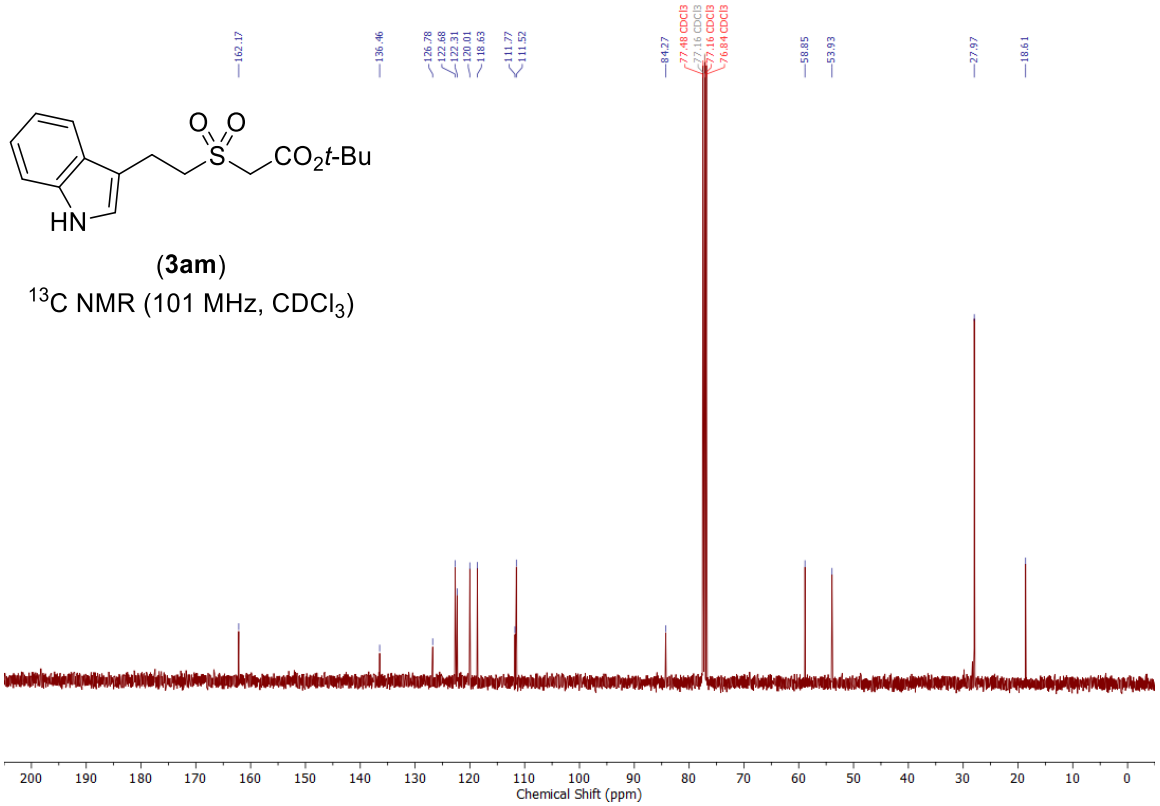
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-((2-(1*H*-indol-3-yl)ethyl)sulfonyl)acetate (3am)



(**3am**)

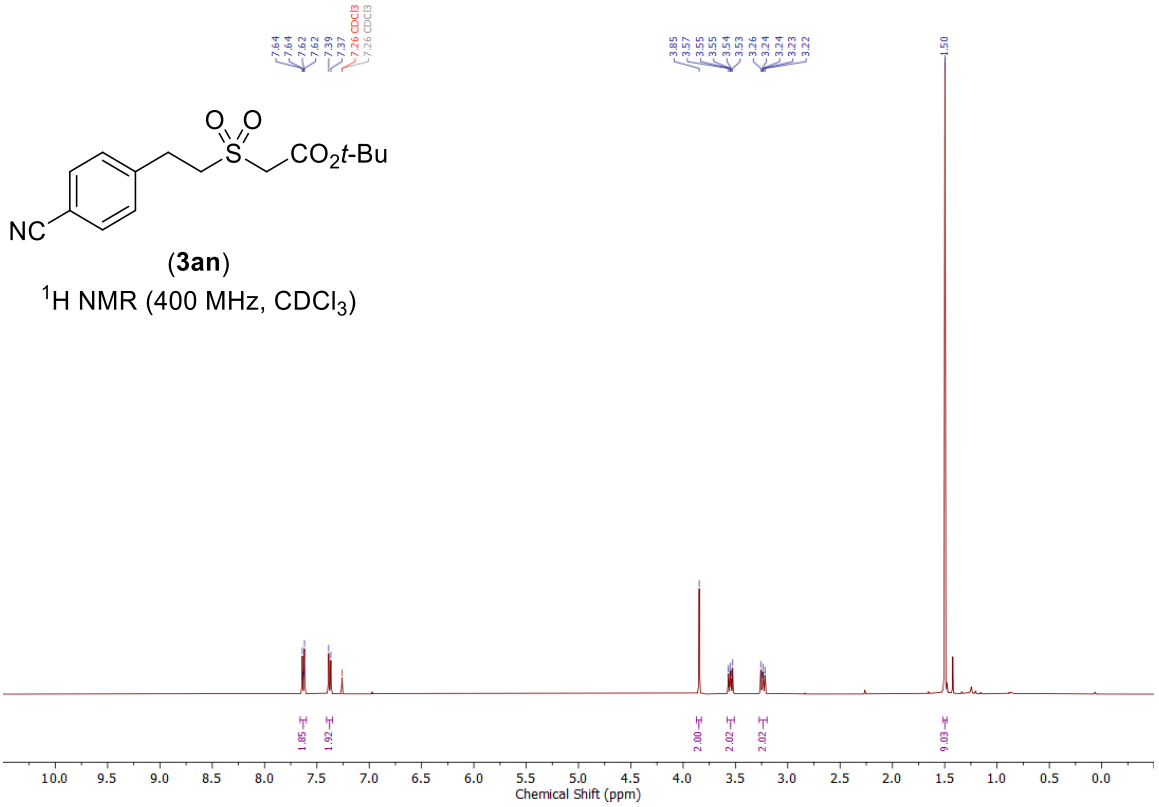
^{1}H NMR (400 MHz, $CDCl_3$)

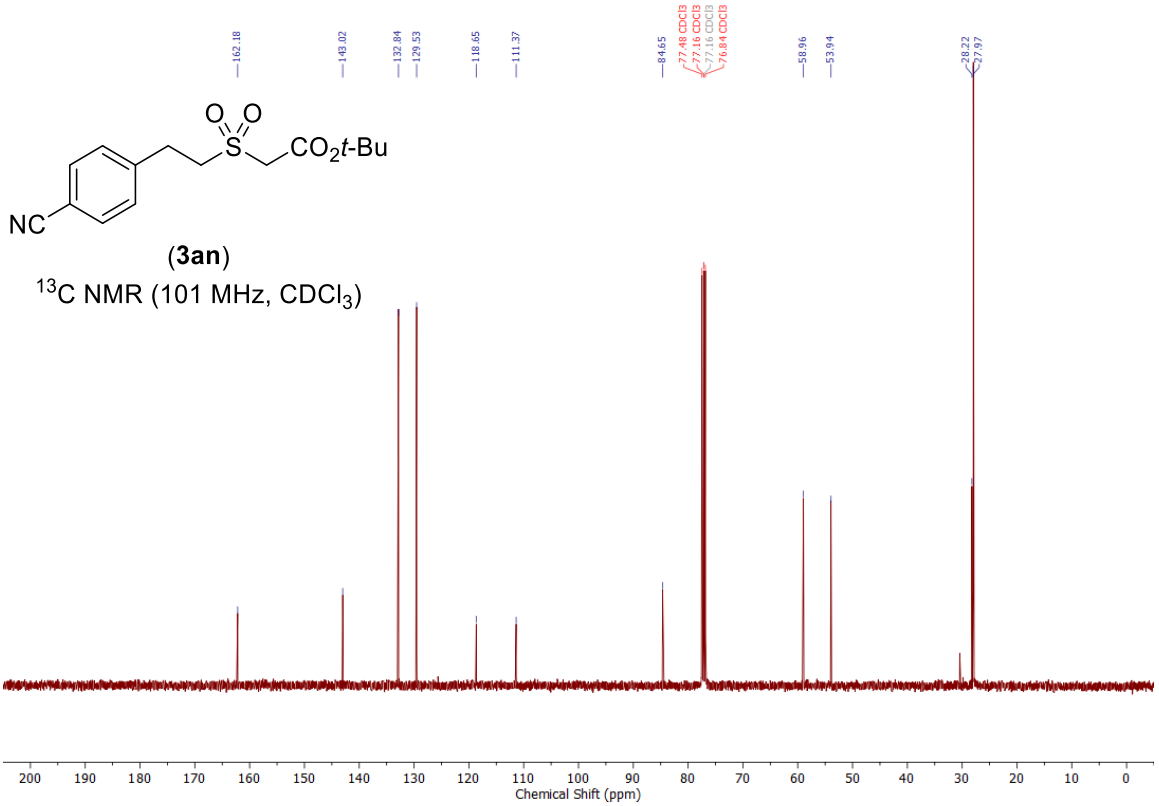


(**3am**)

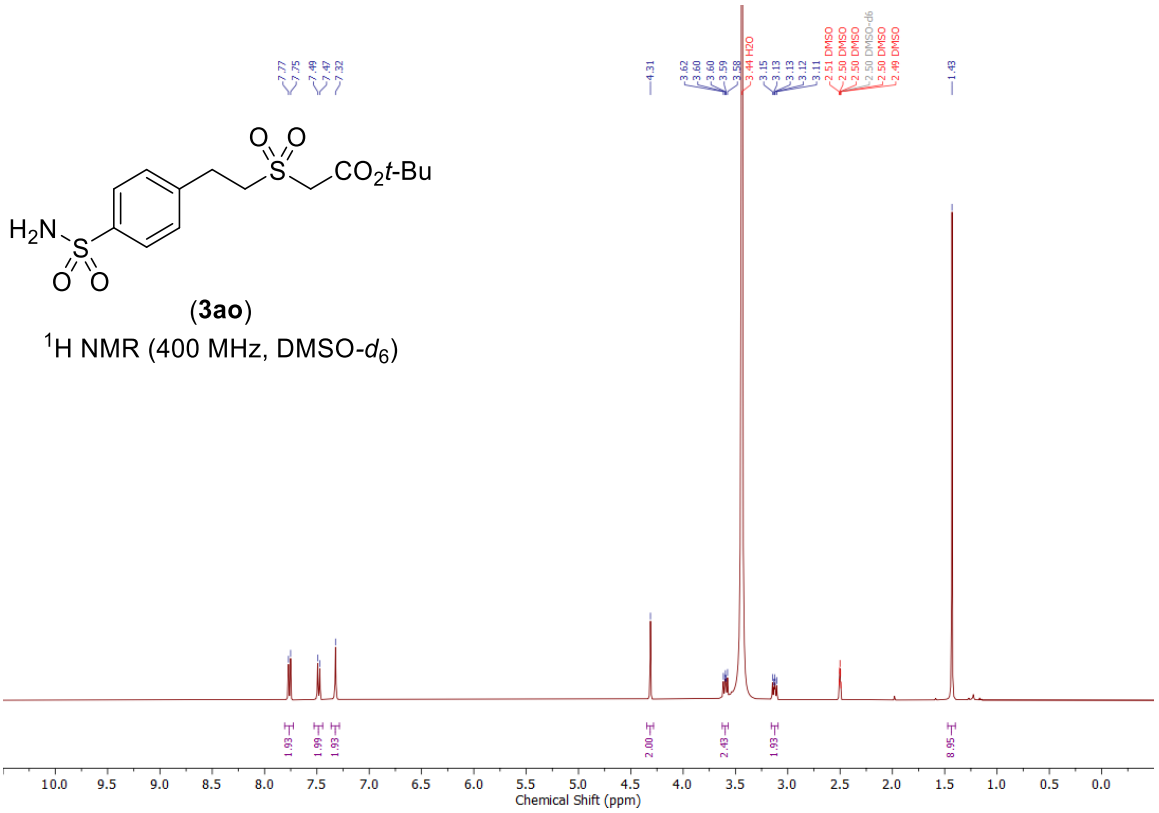
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-((4-cyanophenethyl)sulfonyl)acetate (3an)



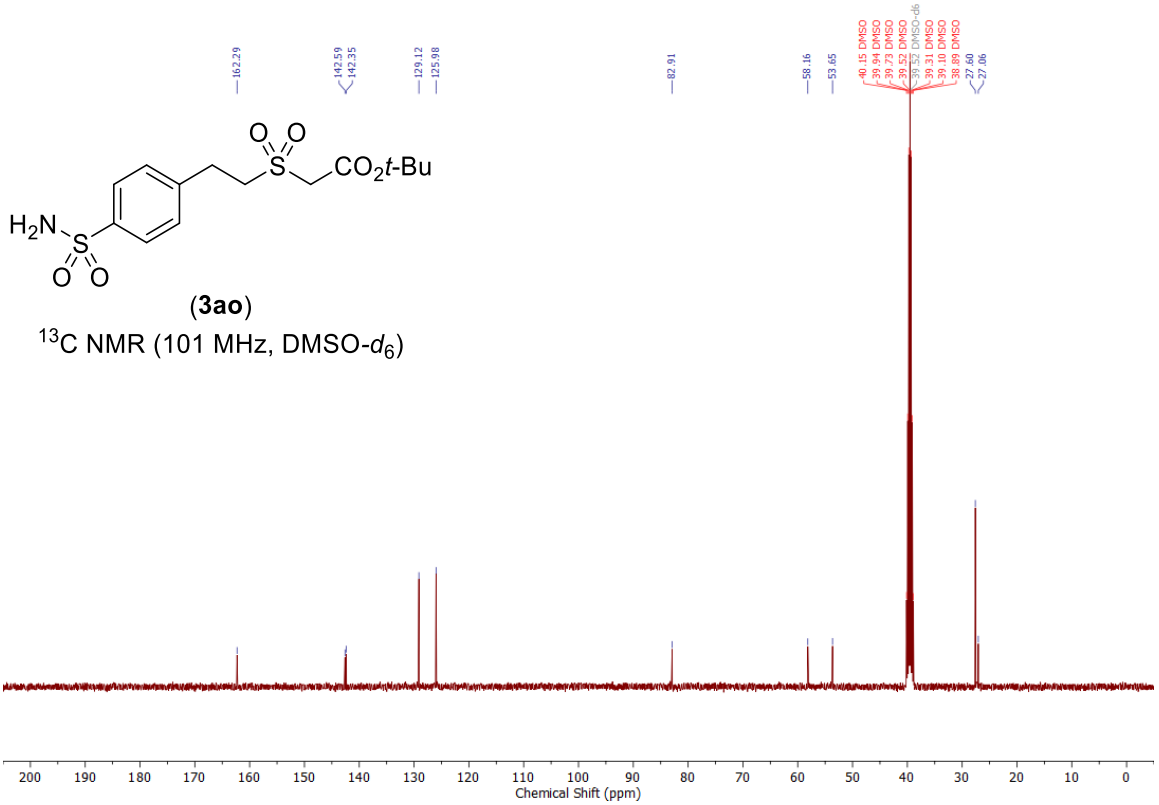


NMR spectra of *tert*-butyl 2-((4-sulfamoylphenethyl)sulfonyl)acetate (3ao)



(**3ao**)

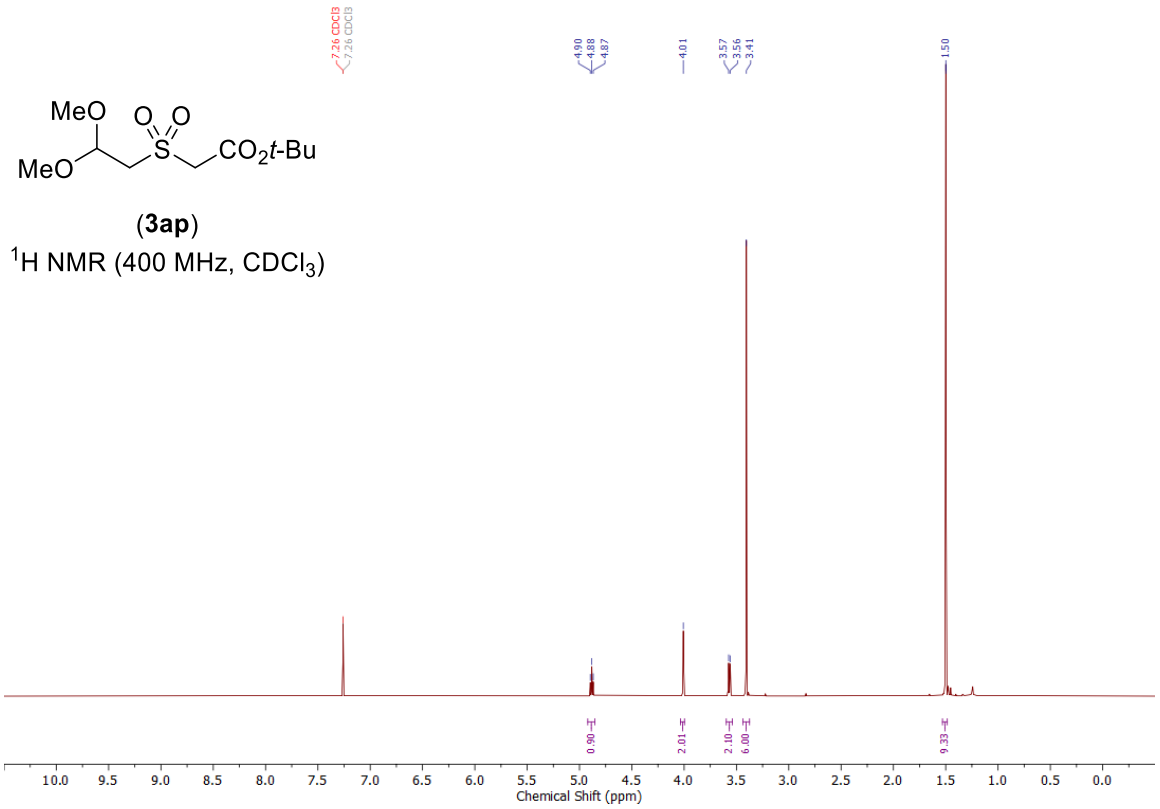
^{1}H NMR (400 MHz, DMSO-d_6)



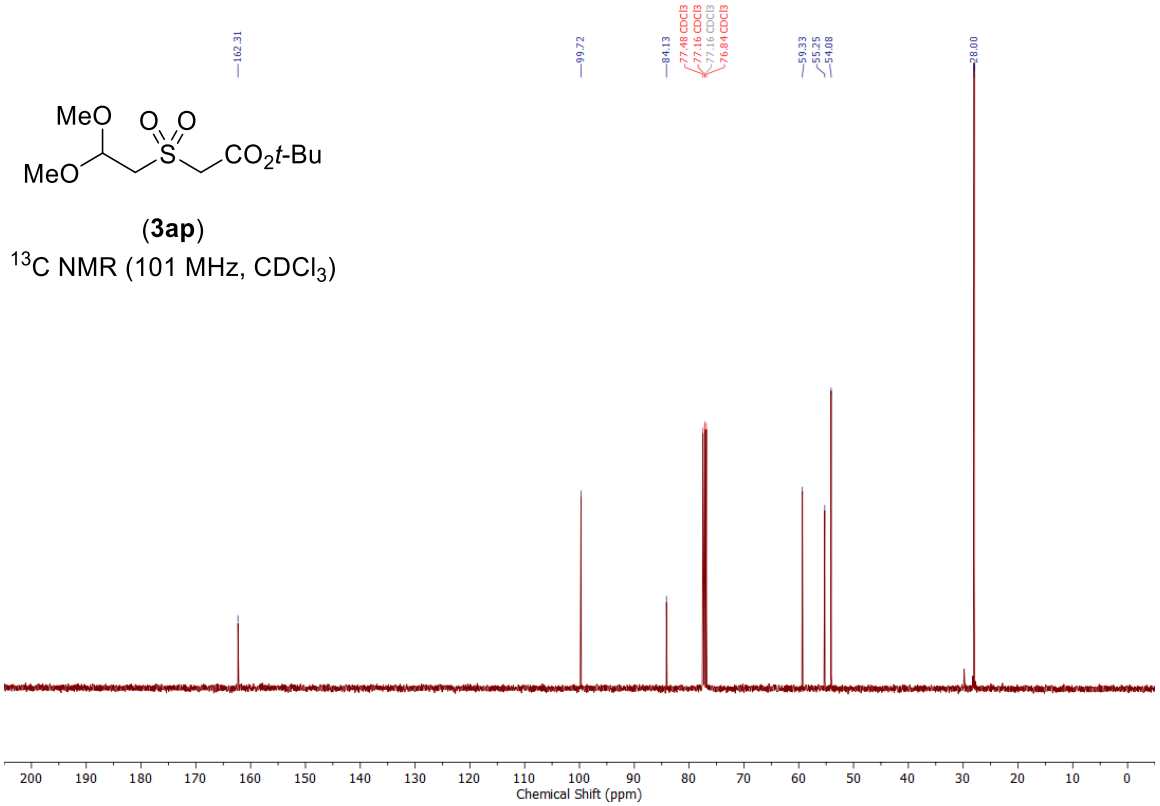
(**3ao**)

^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of *tert*-butyl 2-((2,2-dimethoxyethyl)sulfonyl)acetate (3ap)

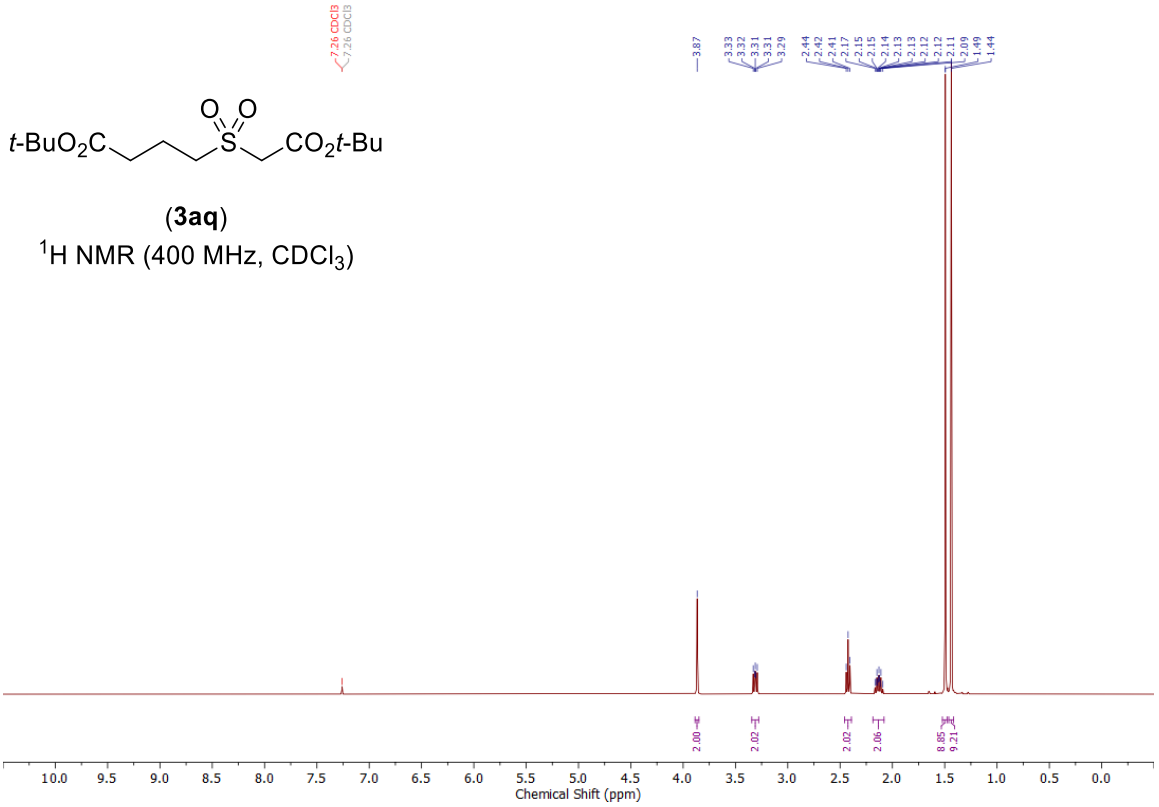


(**3ap**)
^{1}H NMR (400 MHz, $CDCl_3$)

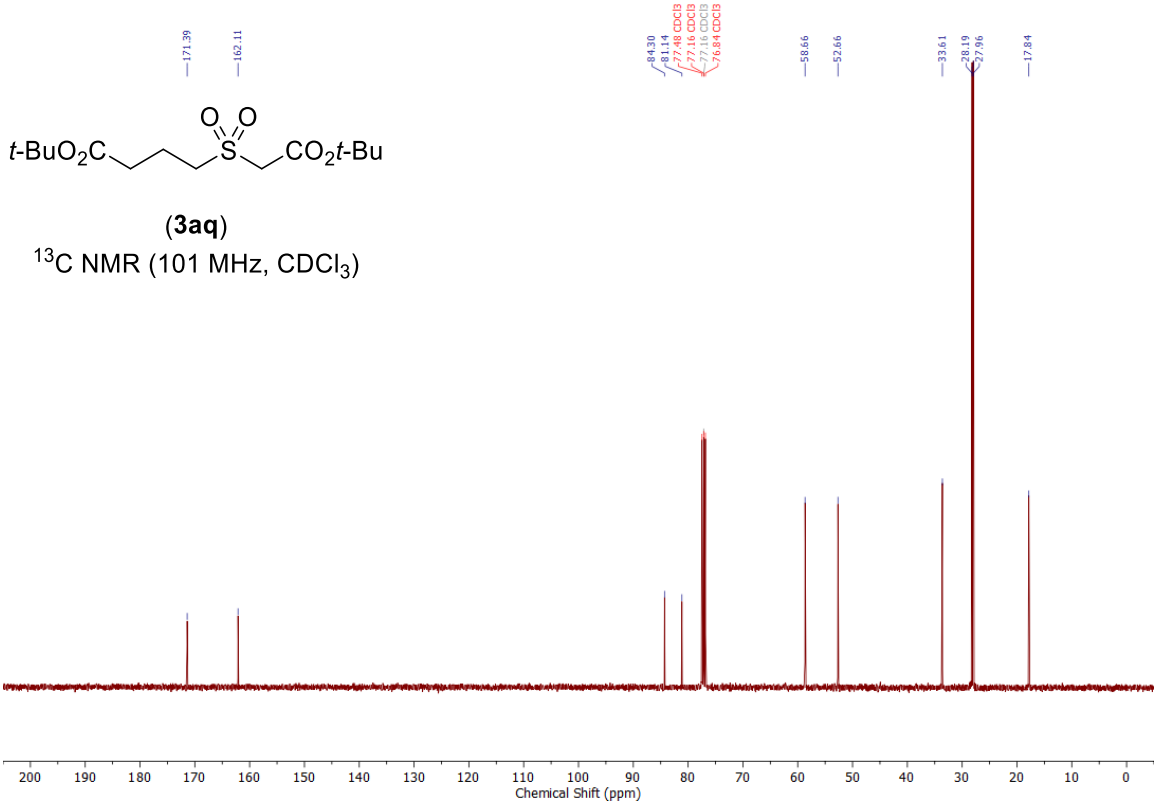


(**3ap**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 4-((2-(tert-butoxy)-2-oxoethyl)sulfonyl)butanoate (3aq)

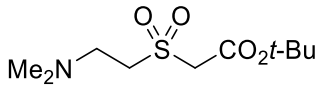


(**3aq**)
^{1}H NMR (400 MHz, $CDCl_3$)



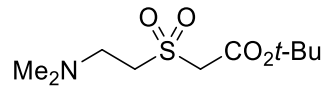
(**3aq**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-((2-(dimethylamino)ethyl)sulfonyl)acetate (3ar)



(**3ar**)

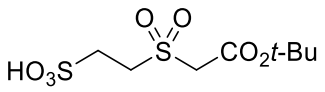
^{1}H NMR (400 MHz, DMSO-d_6)



(**3ar**)

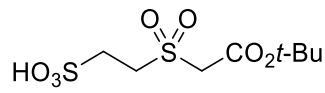
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of 2-((2-(*tert*-butoxy)-2-oxoethyl)sulfonyl)ethane-1-sulfonic acid (3as)



(**3as**)

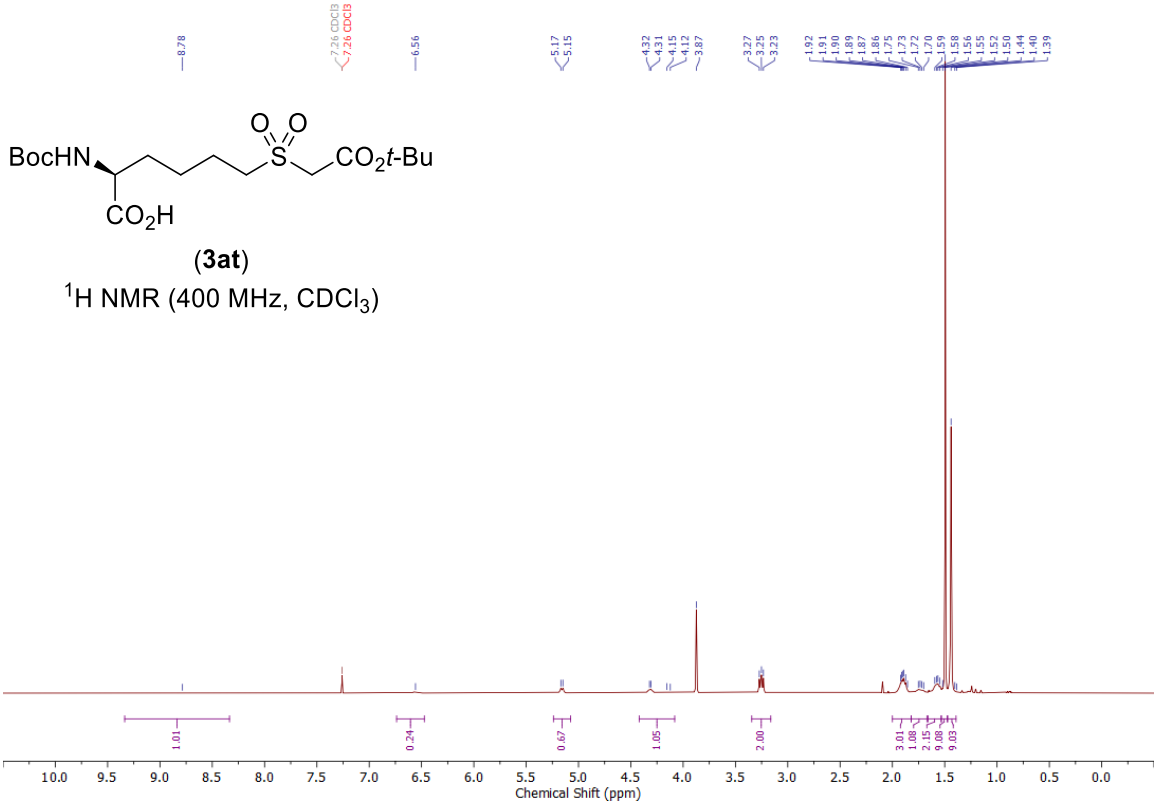
^{1}H NMR (400 MHz, DMSO-d_6)



(**3as**)

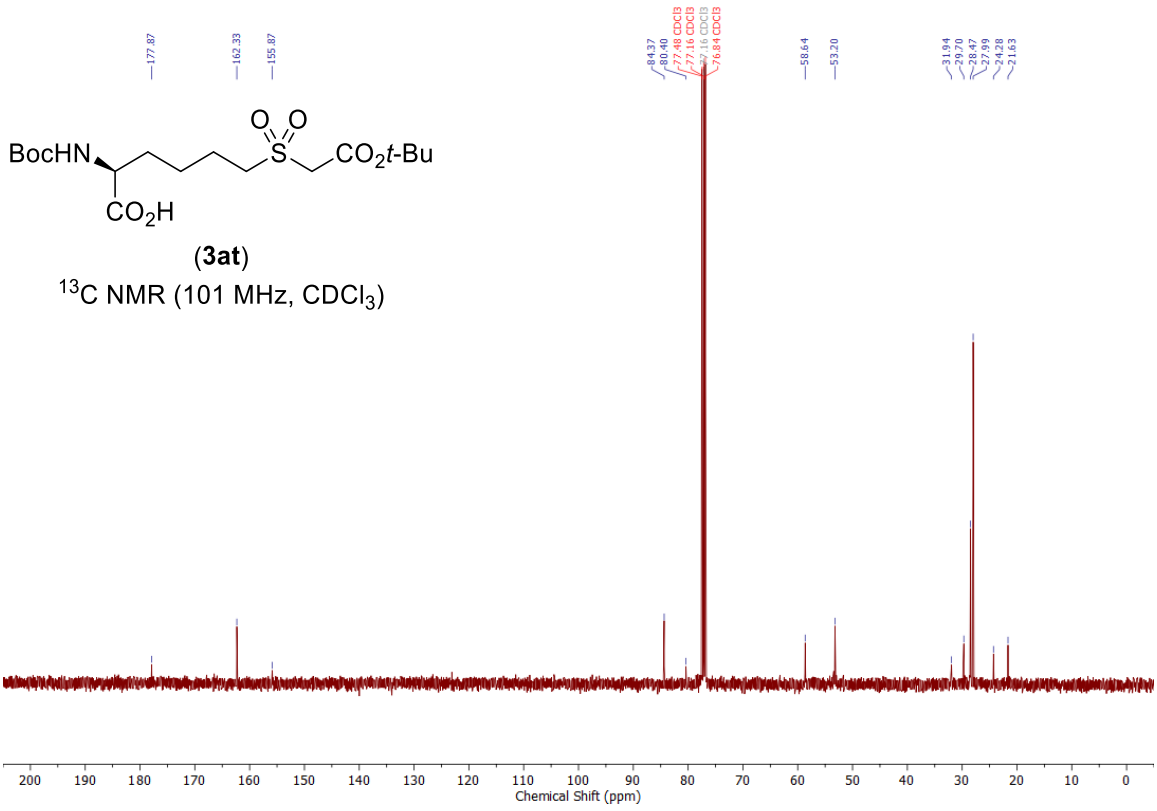
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of (*S*)-6-((2-(*tert*-butoxy)-2-oxoethyl)sulfonyl)-2-((*tert*-butoxycarbonyl)amino)hexanoic acid (3at)



(**3at**)

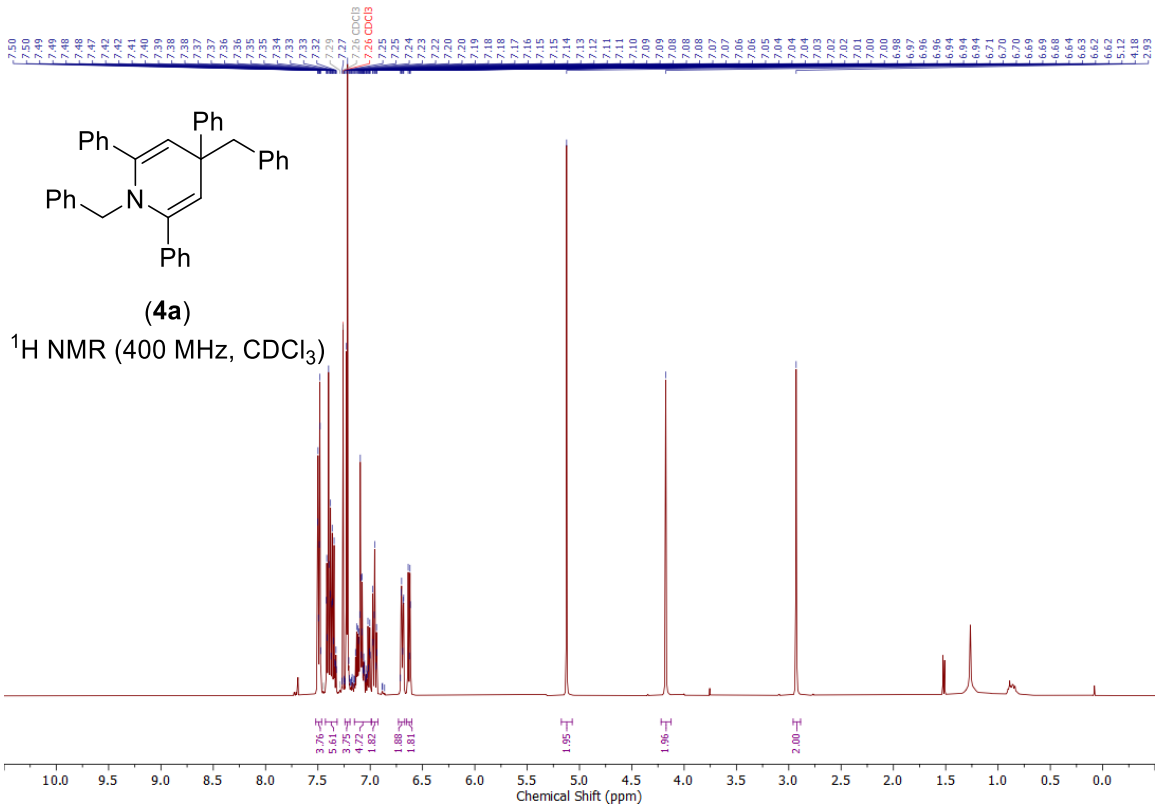
^{1}H NMR (400 MHz, $CDCl_3$)

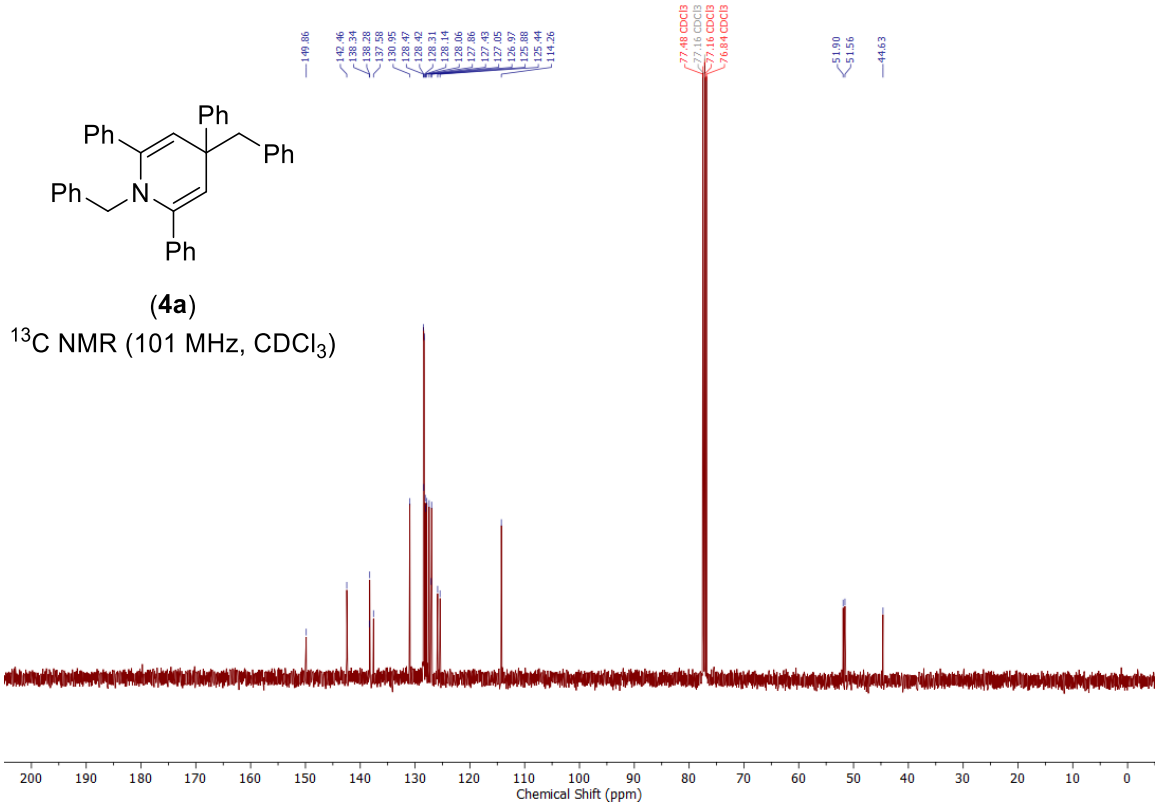


(**3at**)

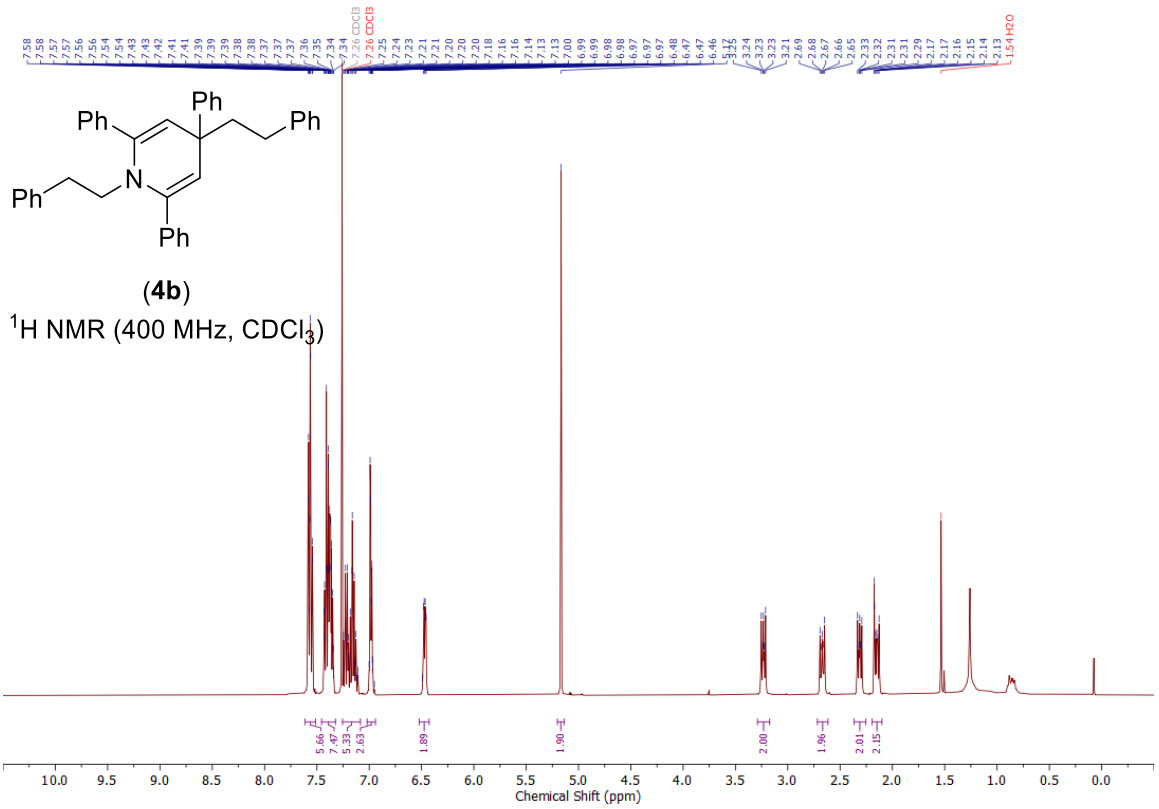
^{13}C NMR (101 MHz, $CDCl_3$)

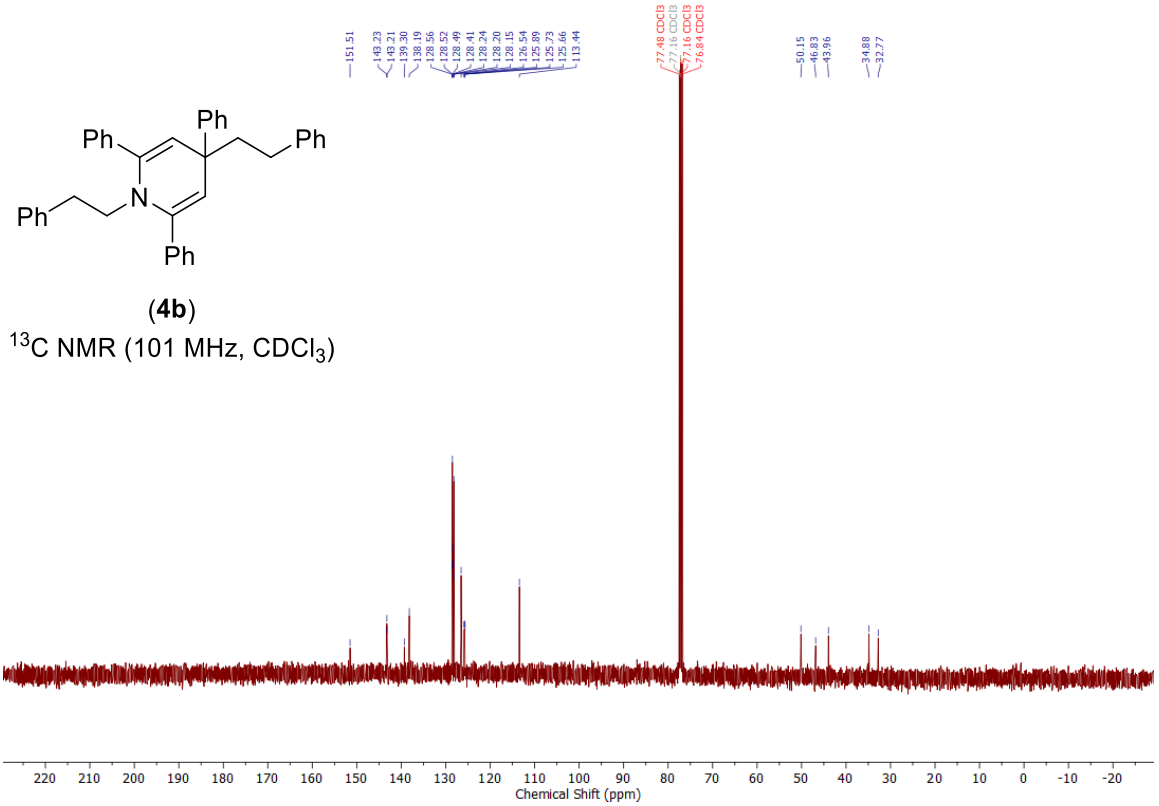
NMR spectra of 1,4-dibenzyl-2,4,6-triphenyl-1,4-dihydropyridine (4a)



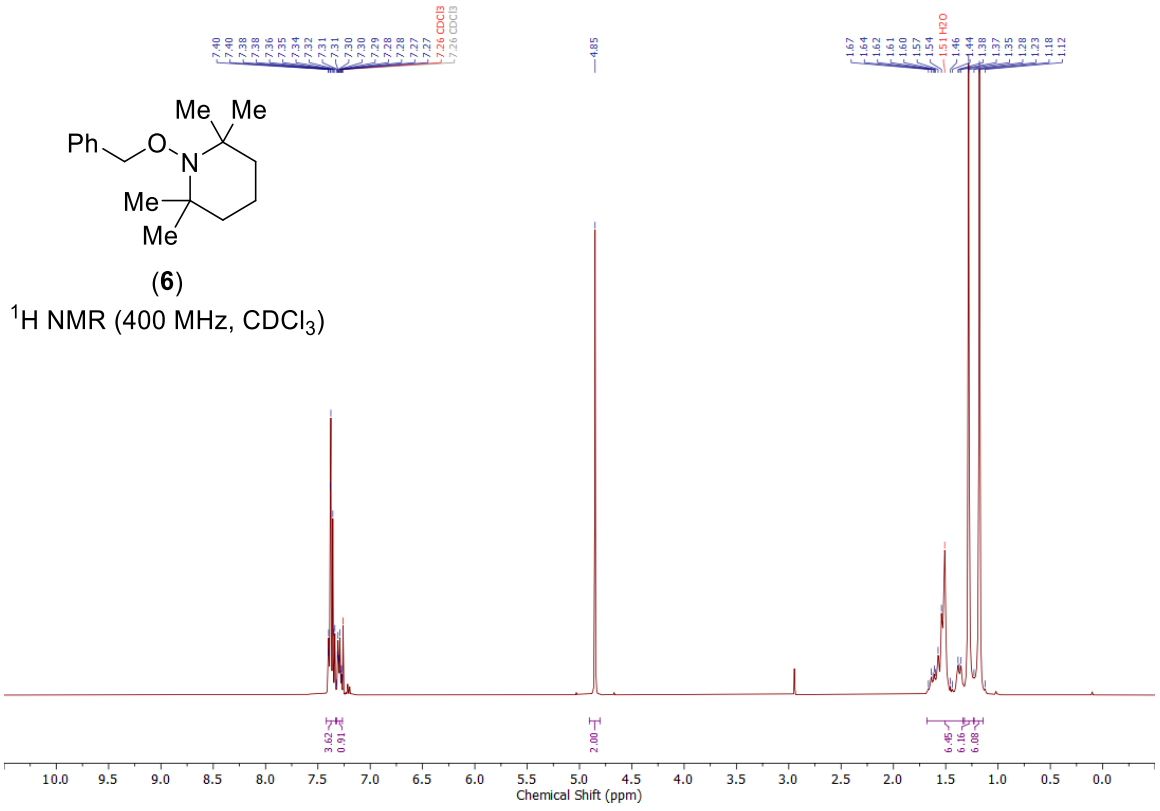


NMR spectra of 1,4-diphenethyl-2,4,6-triphenyl-1,4-dihydropyridine (4b)



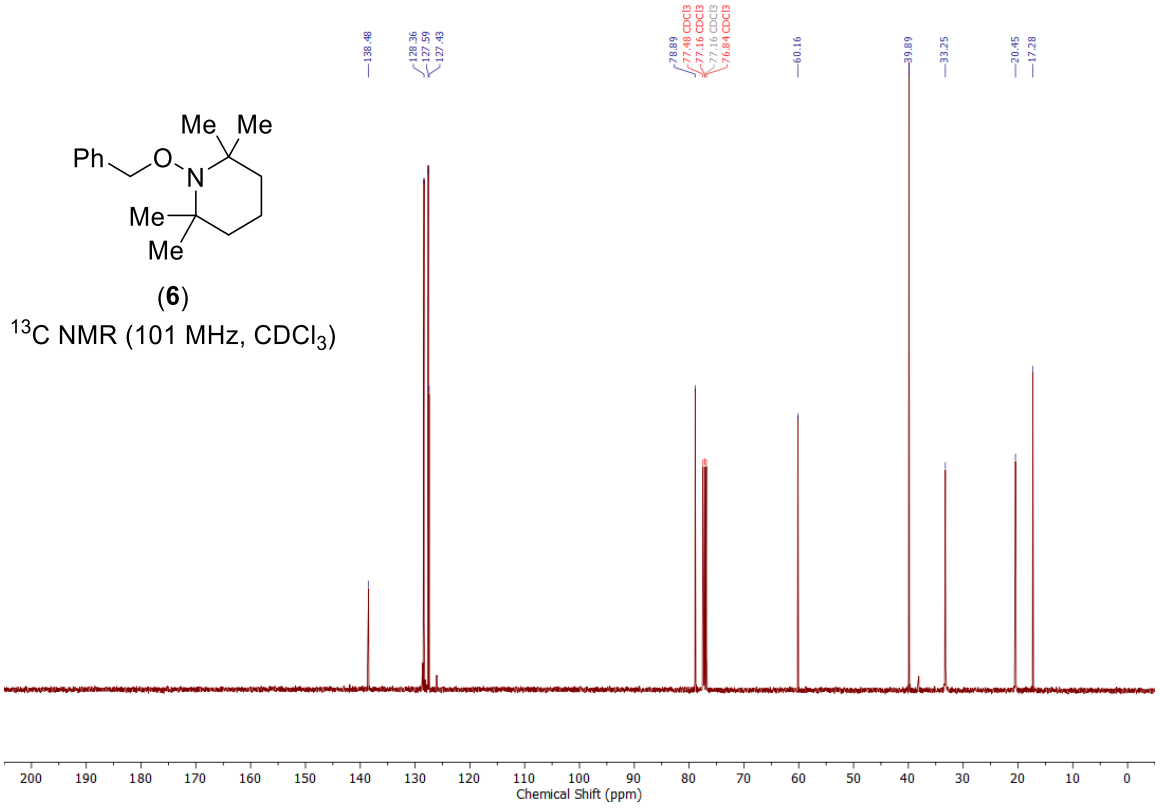


NMR spectra of 1-(benzyloxy)-2,2,6,6-tetramethylpiperidine (6)



(**6**)

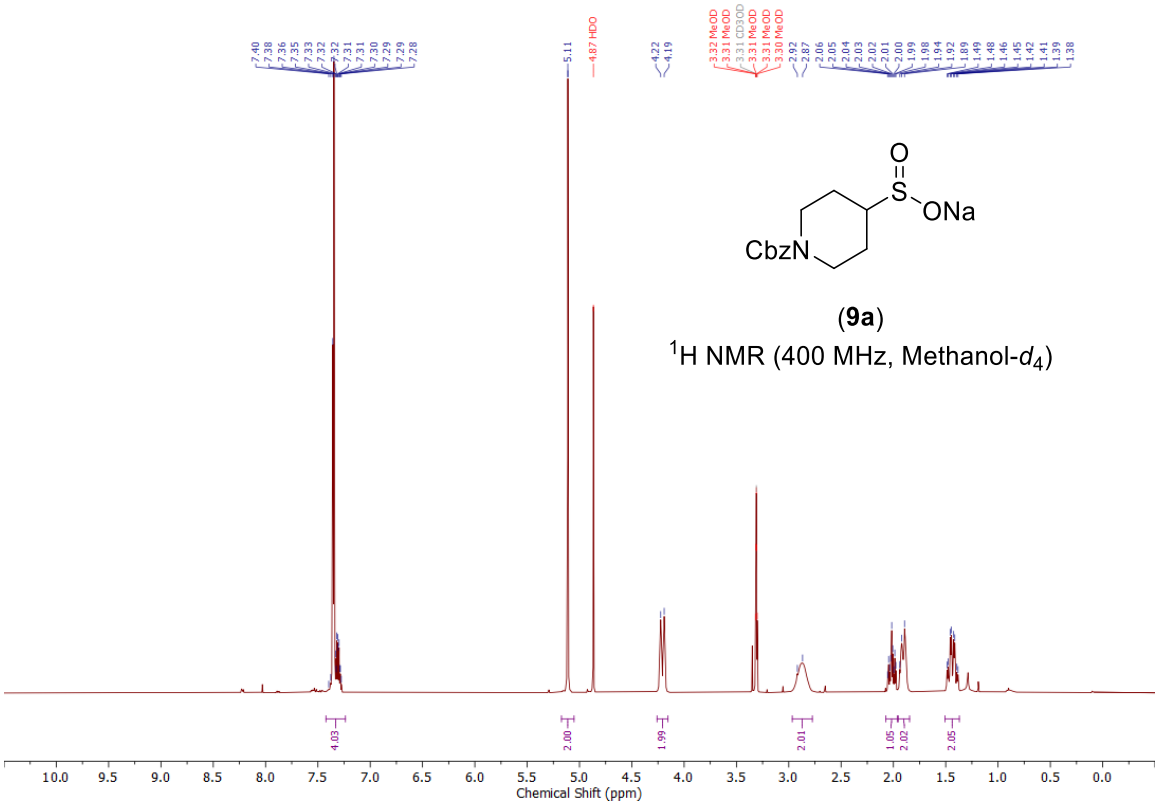
^{1}H NMR (400 MHz, $CDCl_3$)



(**6**)

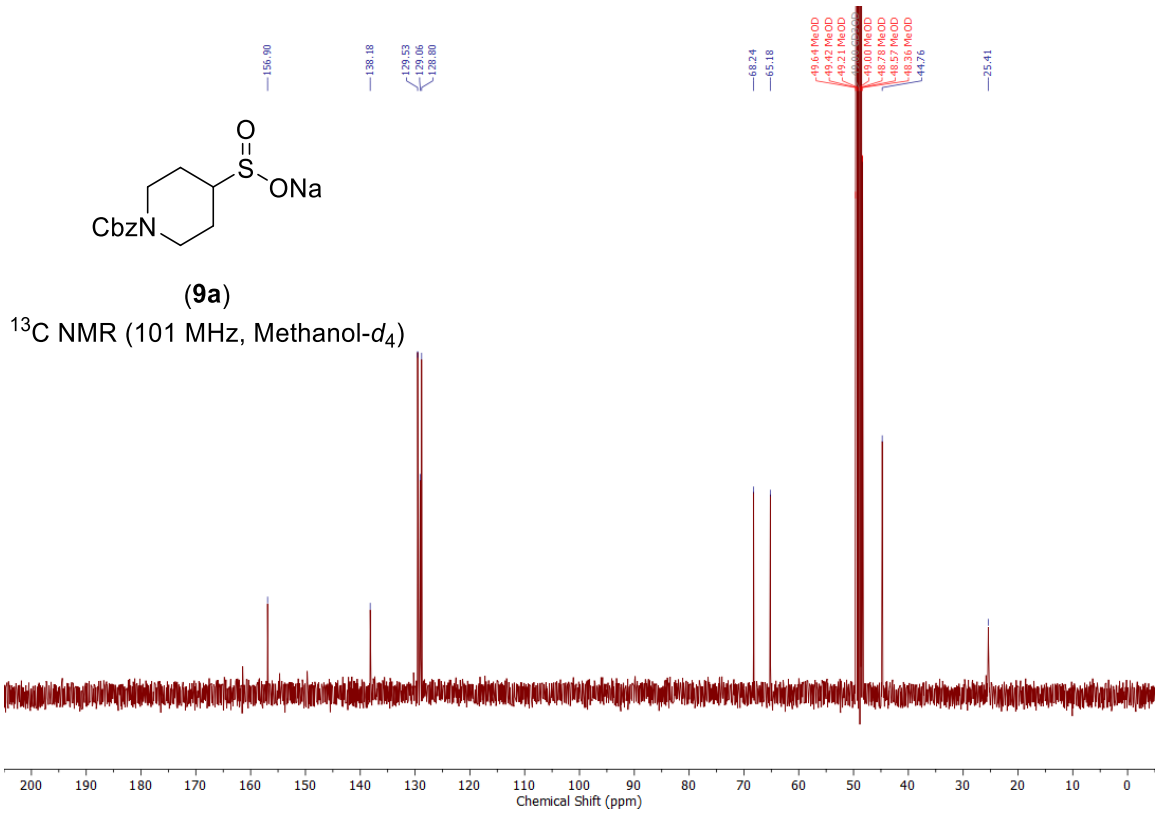
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of sodium 1-((benzyloxy)carbonyl)piperidine-4-sulfinate (9a)



(**9a**)

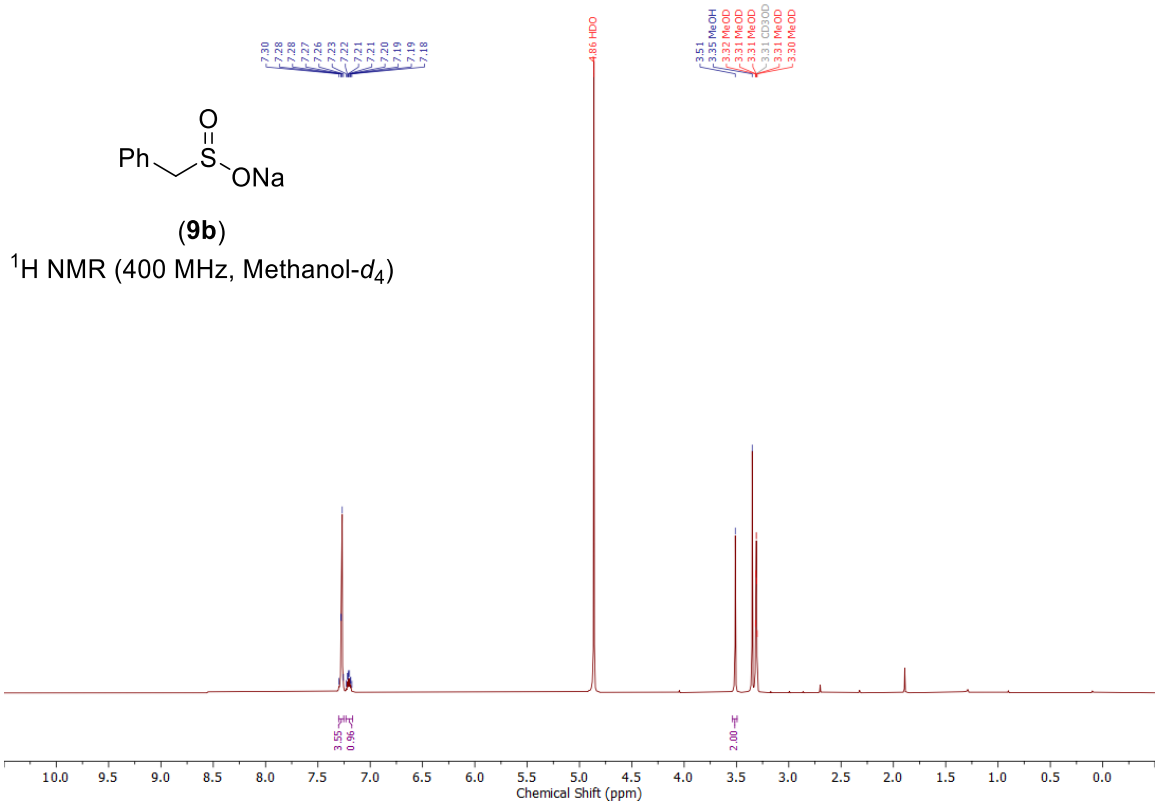
^{1}H NMR (400 MHz, Methanol-d_4)

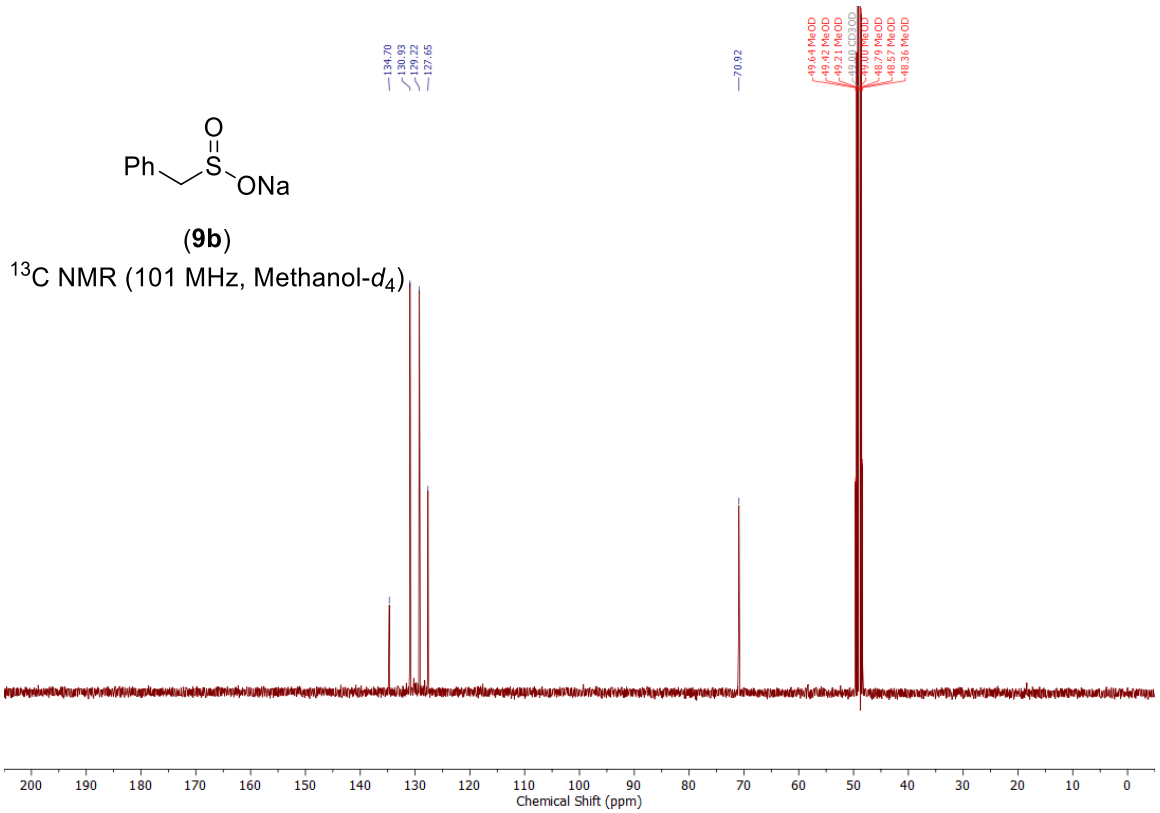


(**9a**)

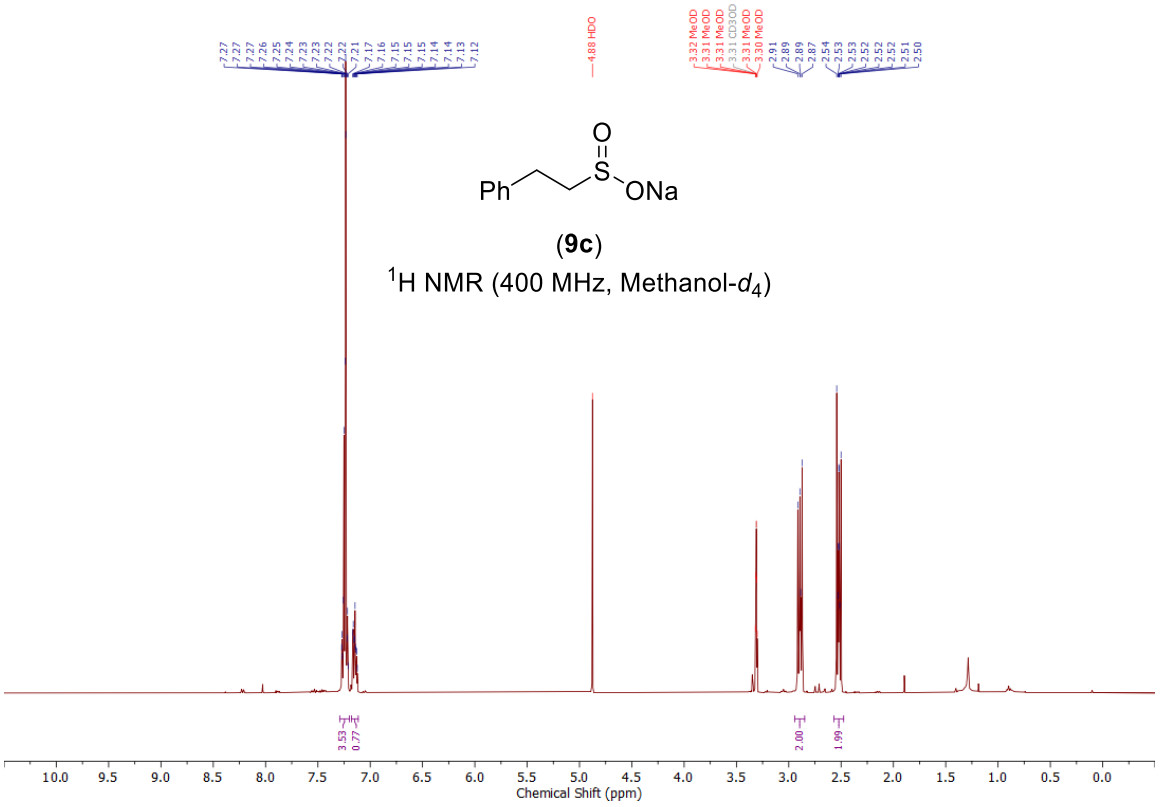
^{13}C NMR (101 MHz, Methanol-d_4)

NMR spectra of sodium phenylmethanesulfinate (9b)



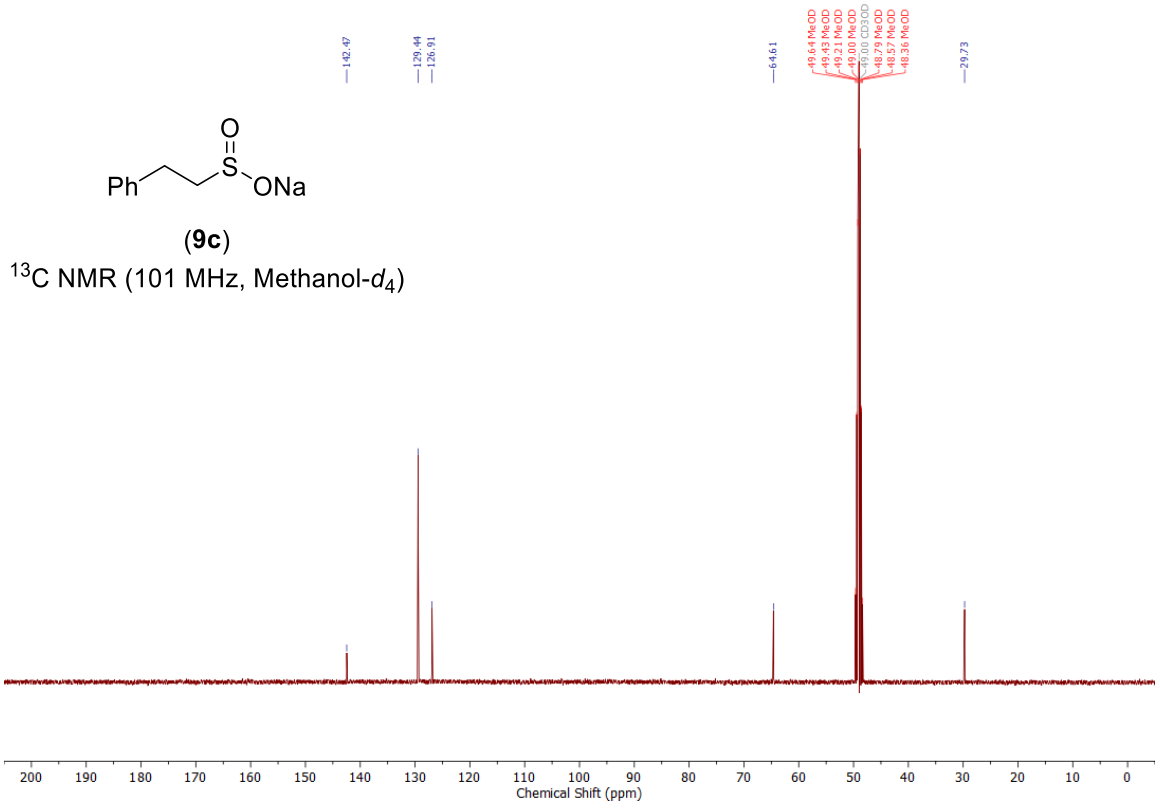


NMR spectra of sodium 2-phenylethane-1-sulfinate (9c)



(**9c**)

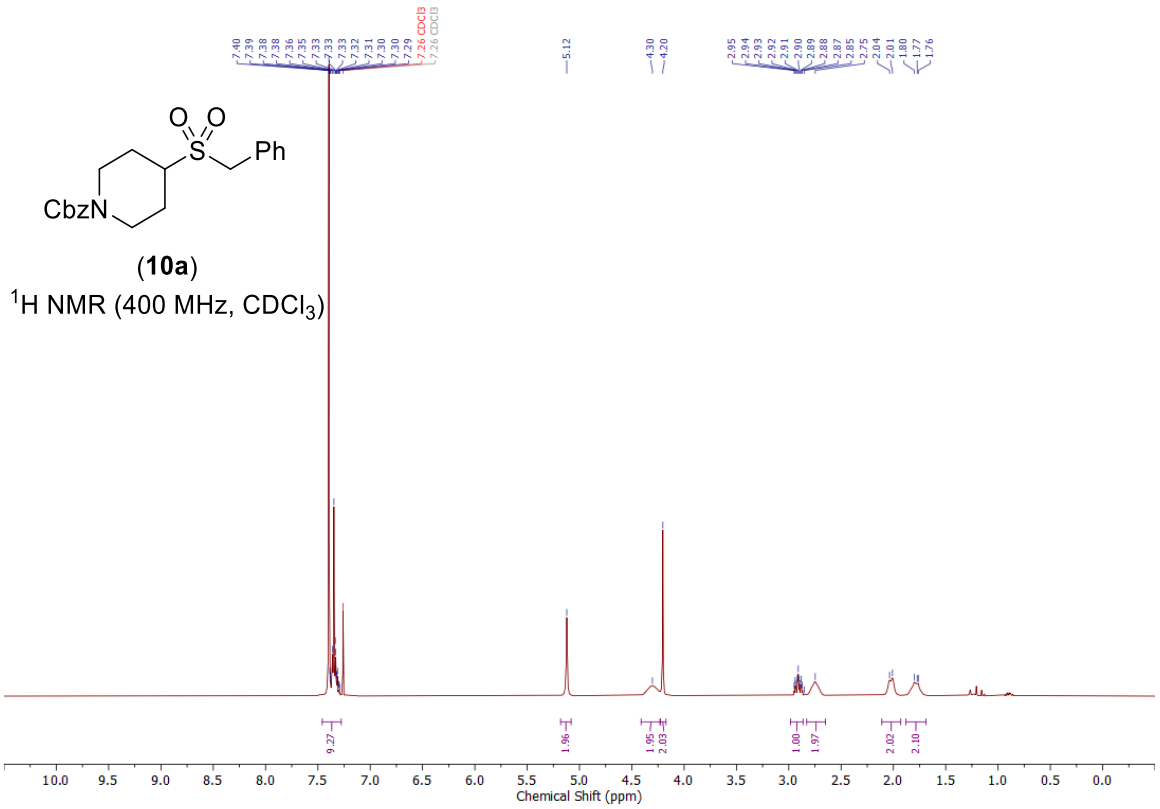
^{1}H NMR (400 MHz, Methanol-d_4)

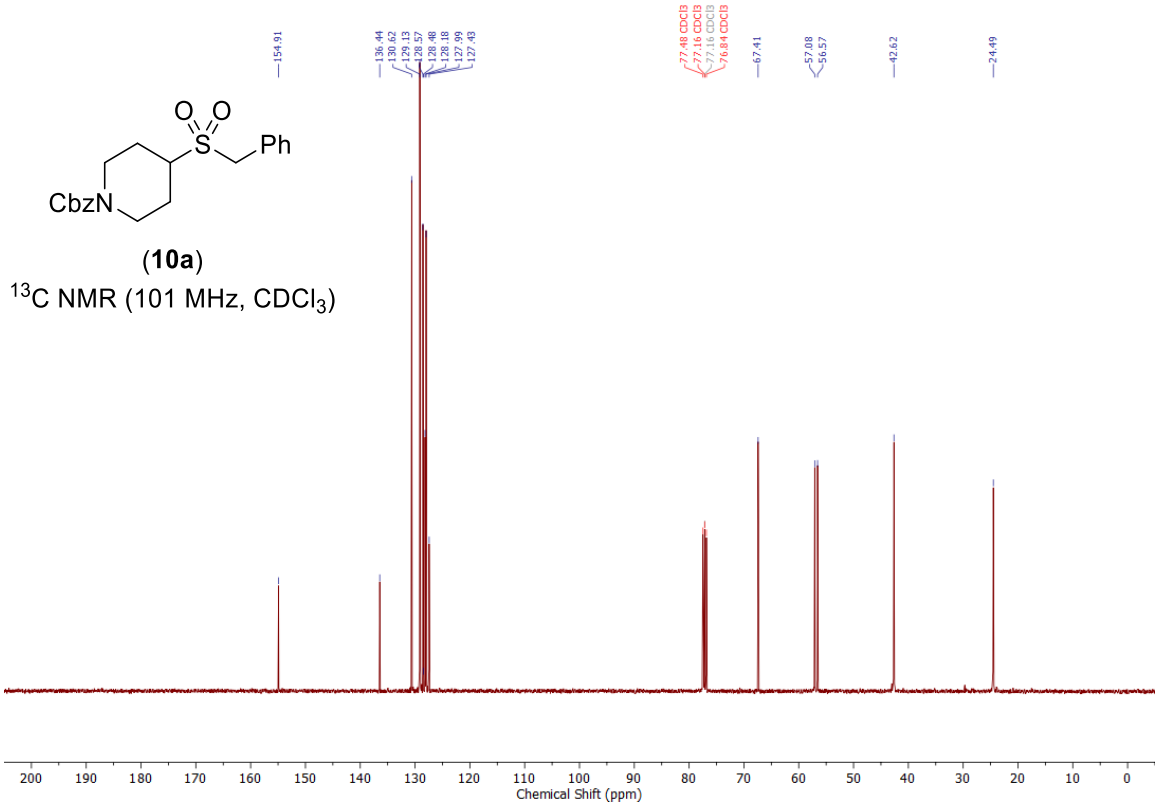


(**9c**)

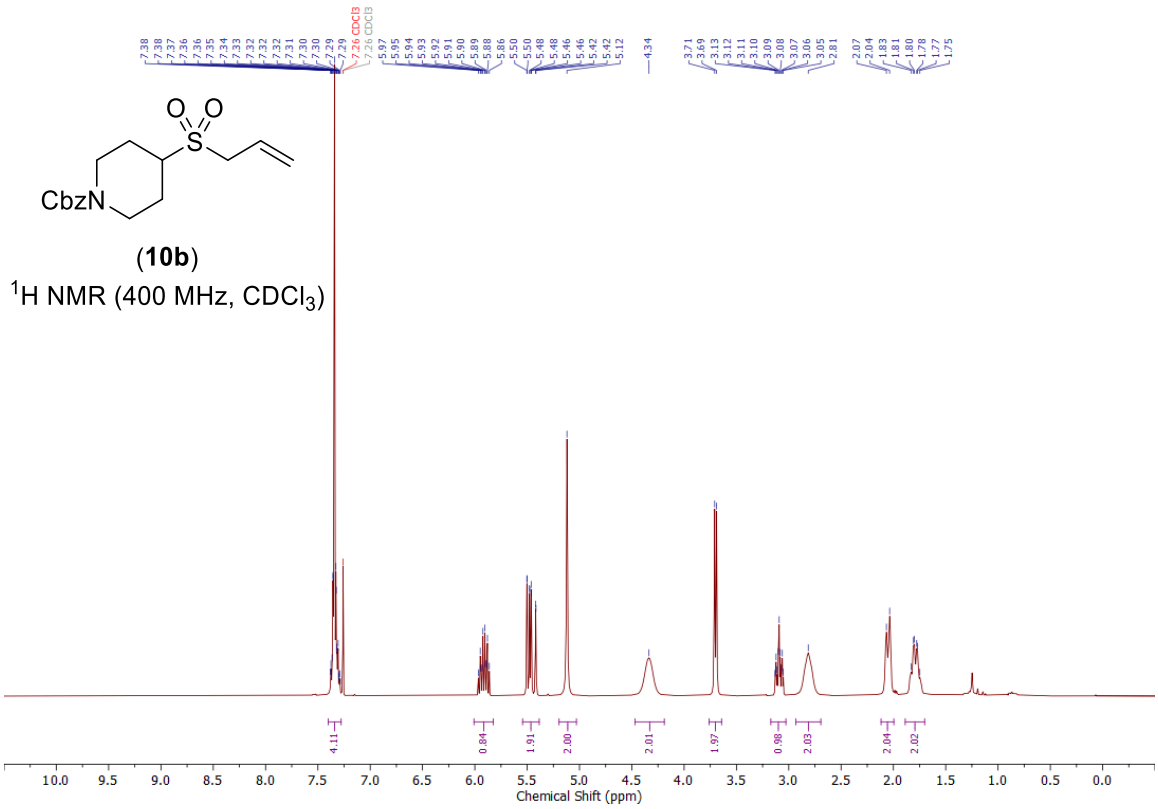
^{13}C NMR (101 MHz, Methanol-d_4)

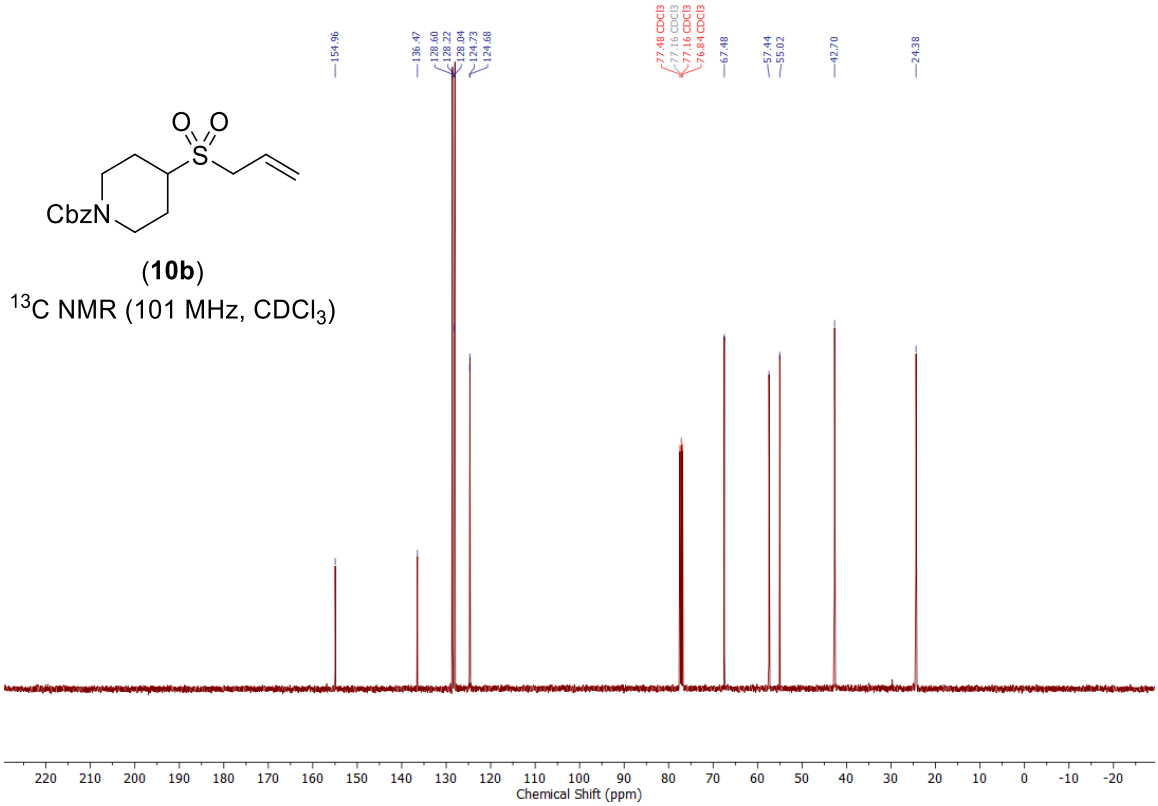
NMR spectra of benzyl 4-(benzylsulfonyl)piperidine-1-carboxylate (10a)



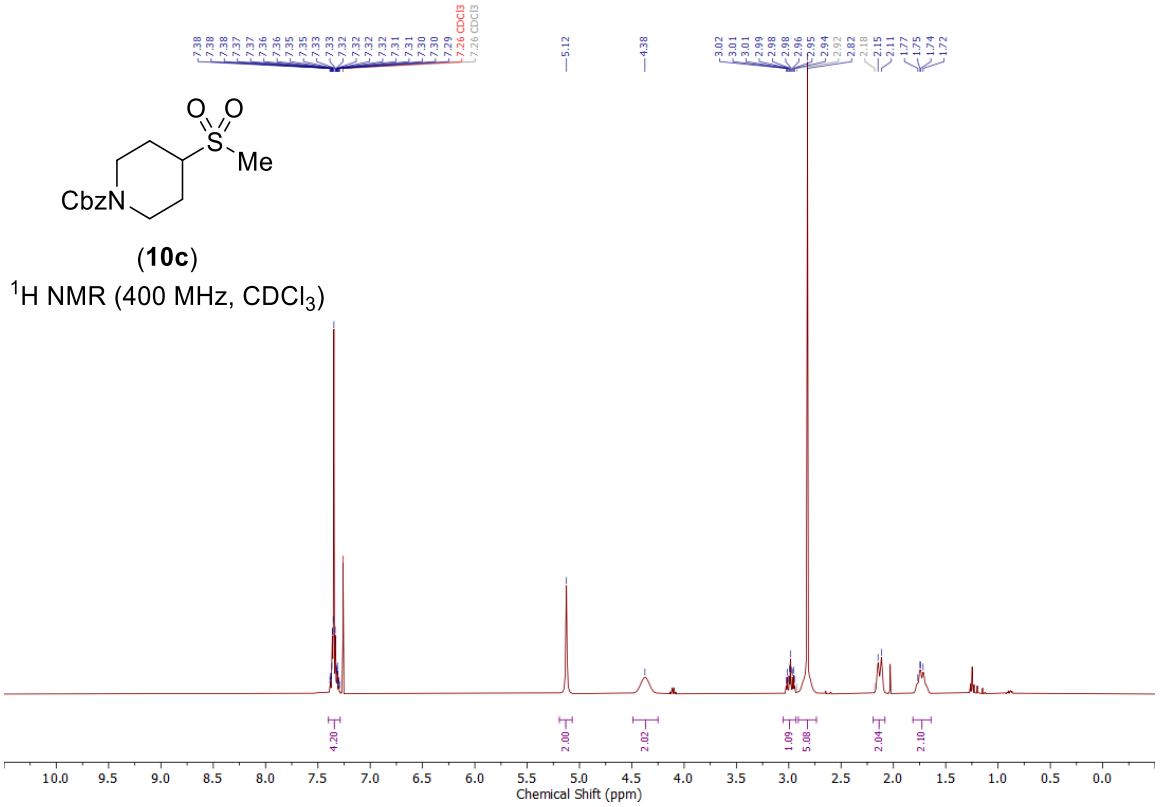


NMR spectra of benzyl 4-(allylsulfonyl)piperidine-1-carboxylate (10b)



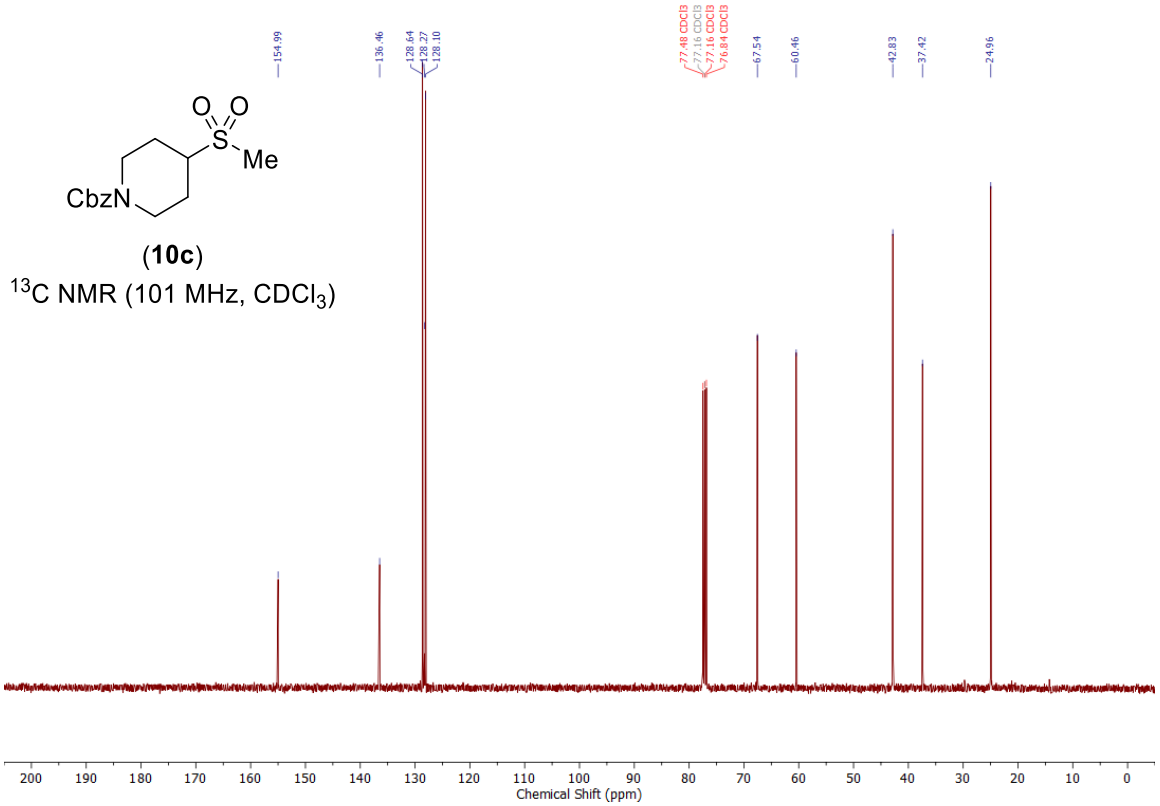


NMR spectra of benzyl 4-(methylsulfonyl)piperidine-1-carboxylate (10c)



(**10c**)

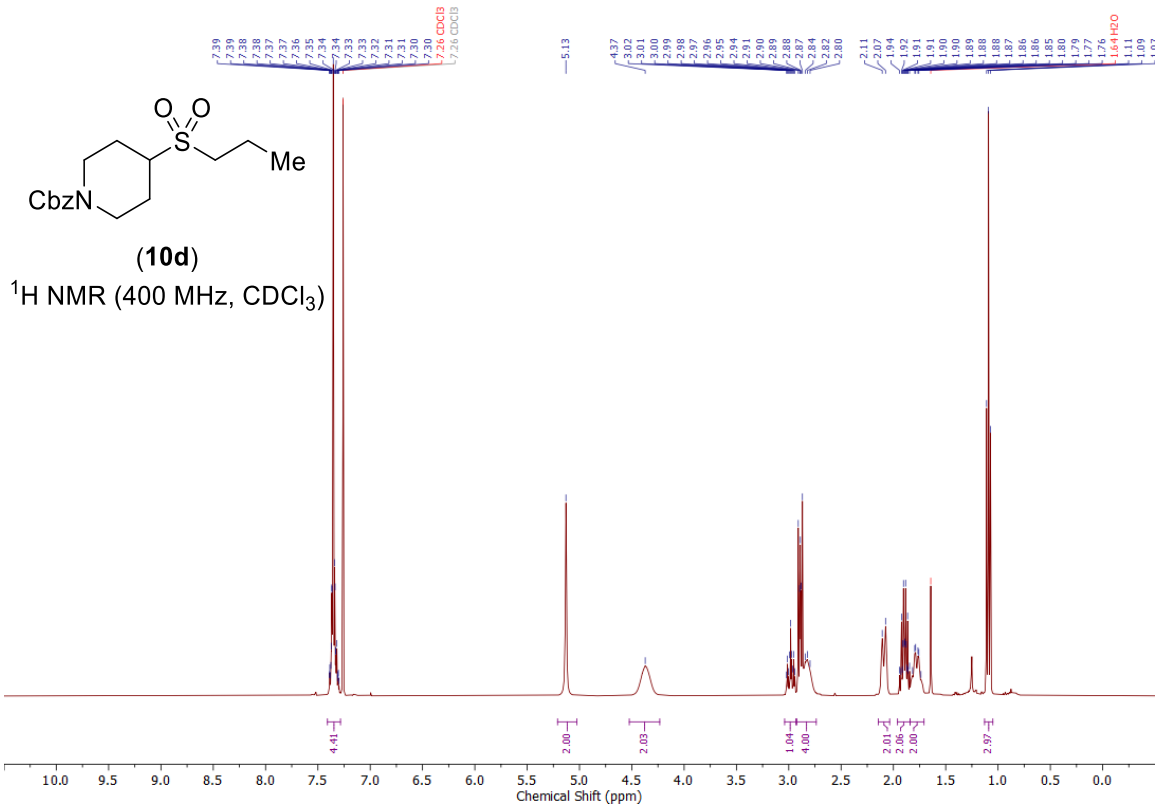
^{1}H NMR (400 MHz, $CDCl_3$)

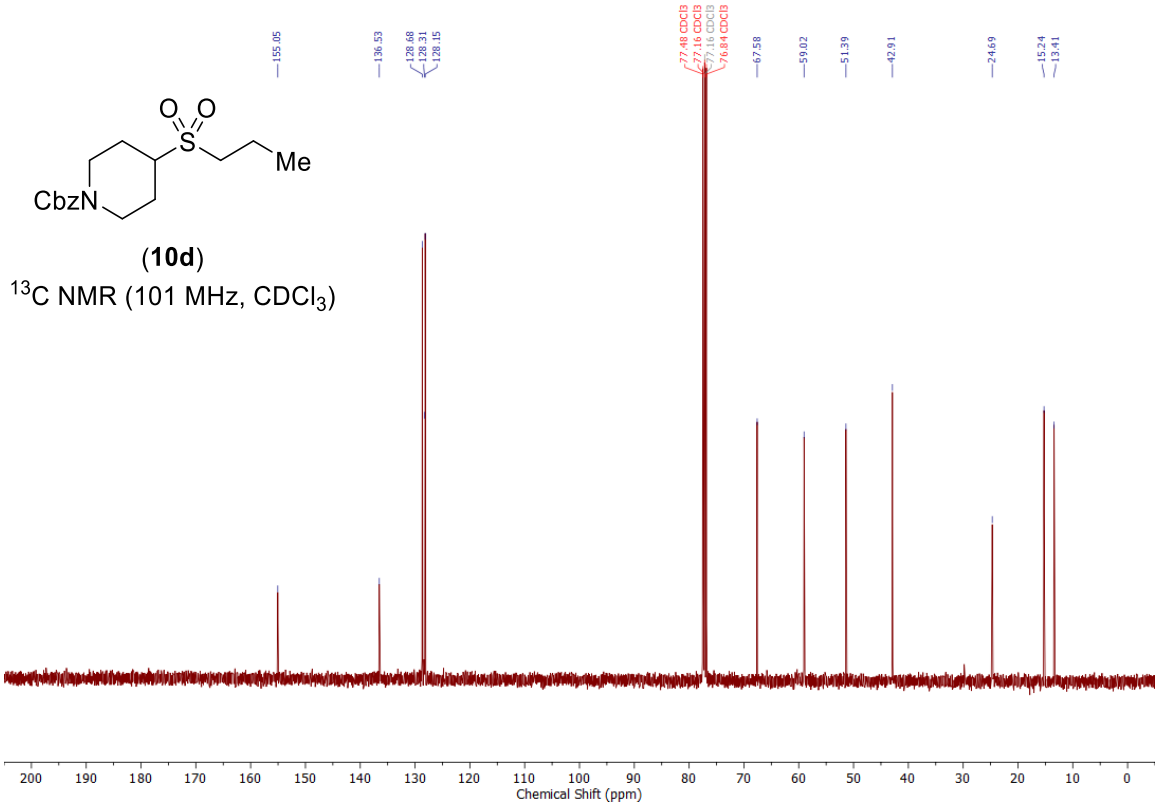


(**10c**)

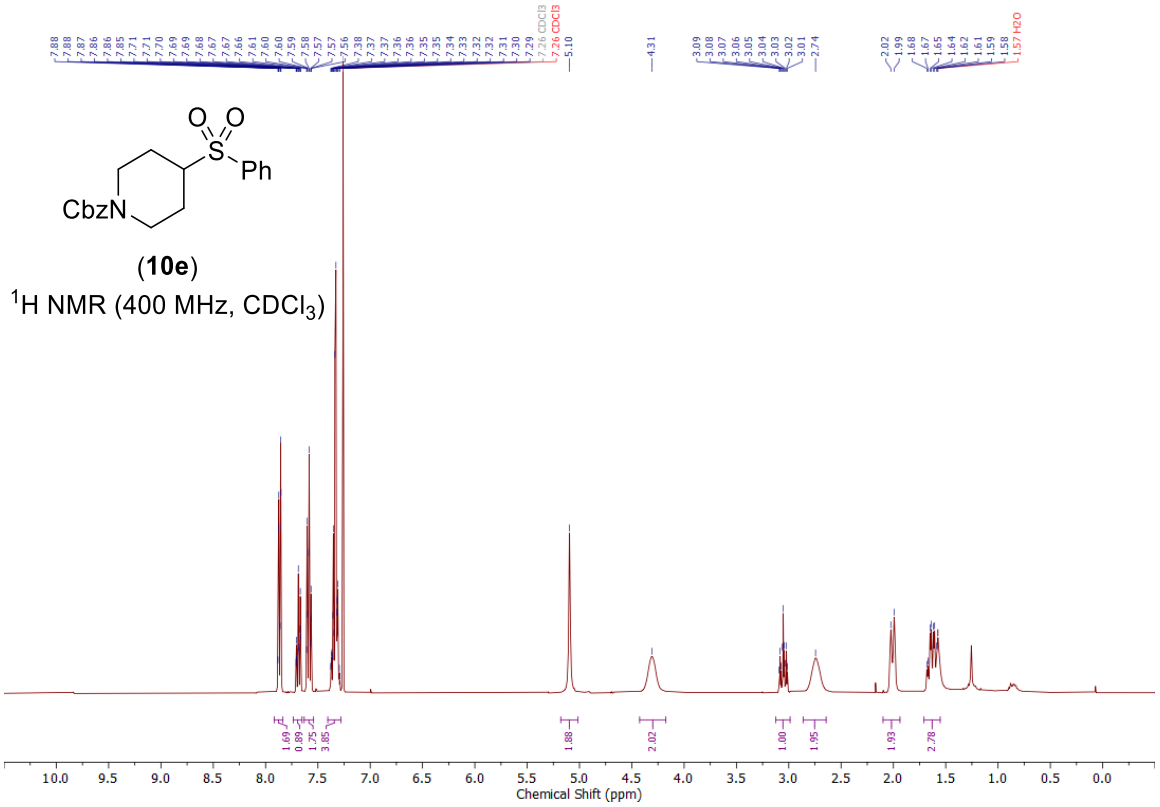
^{13}C NMR (101 MHz, $CDCl_3$)

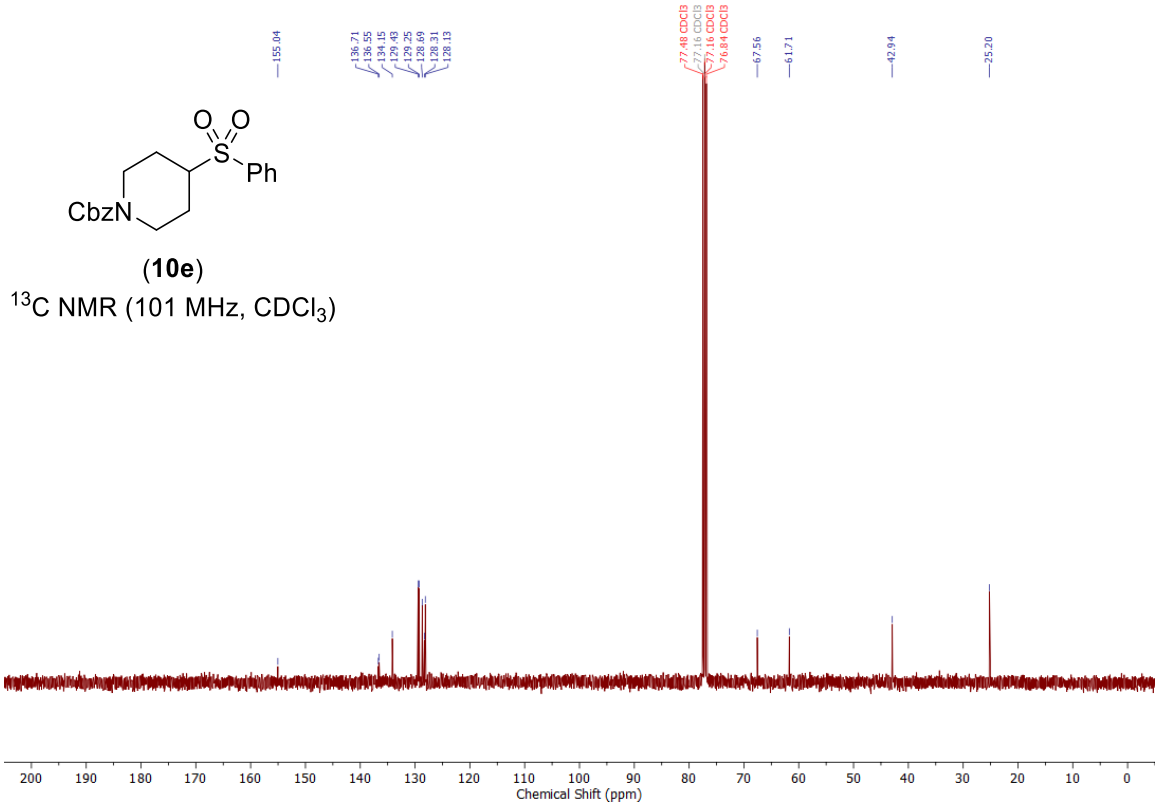
NMR spectra of benzyl 4-(propylsulfonyl)piperidine-1-carboxylate (10d)



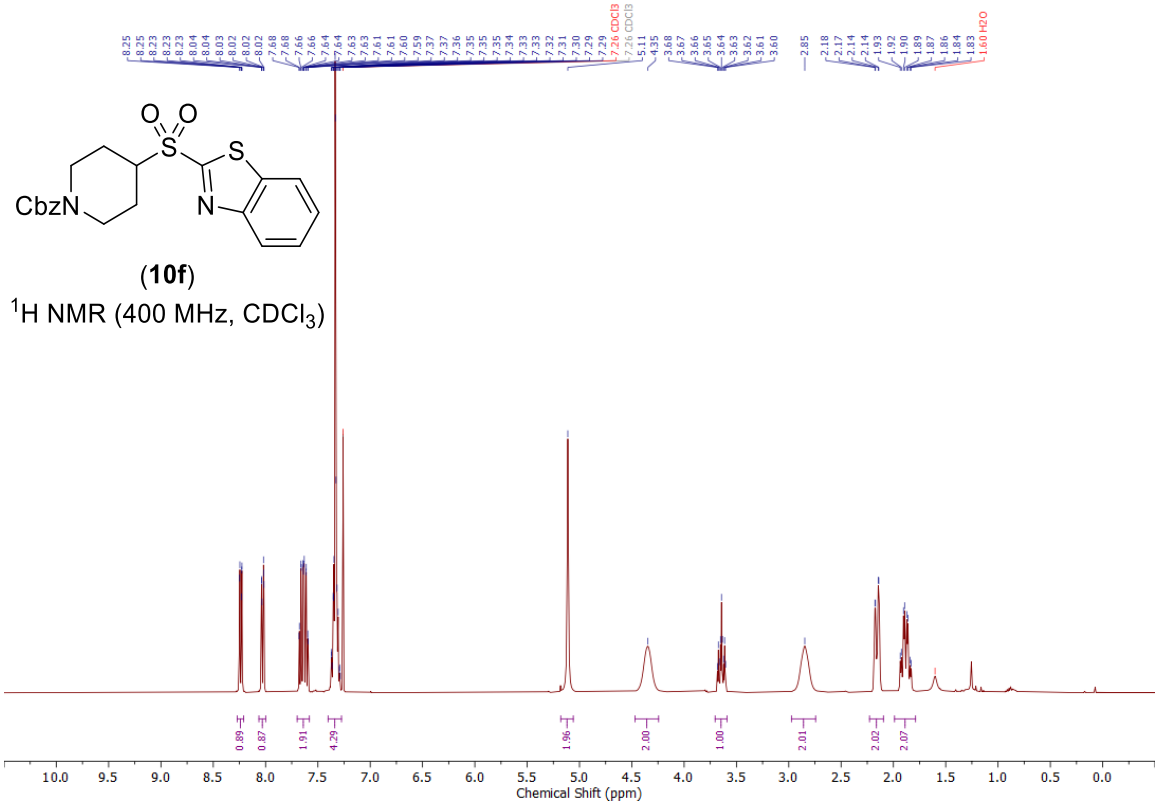


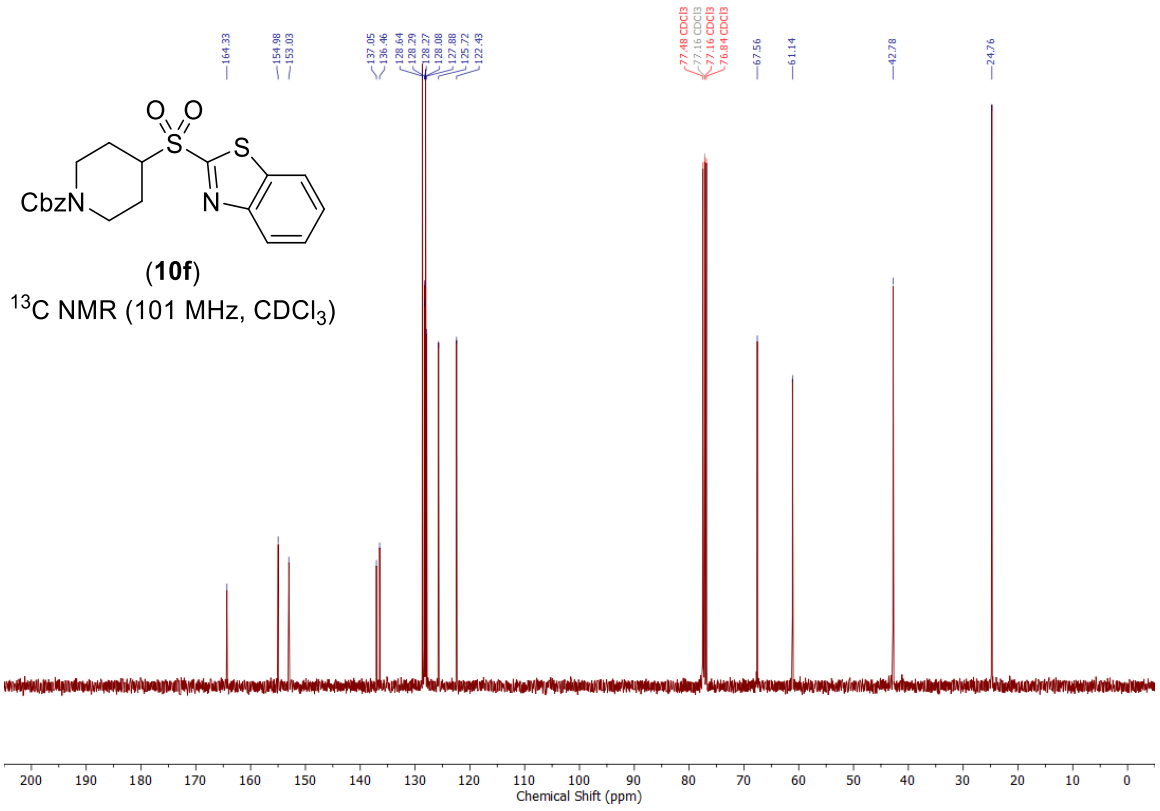
NMR spectra of benzyl 4-(phenylsulfonyl)piperidine-1-carboxylate (10e)



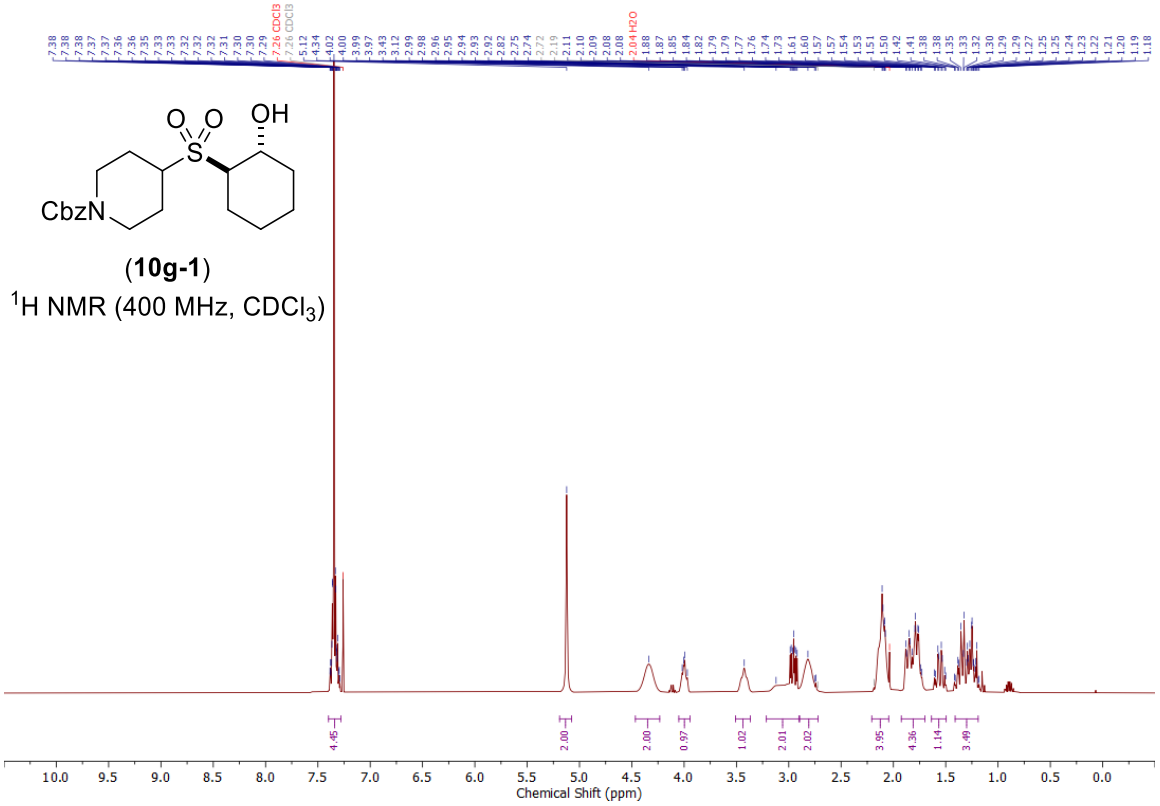


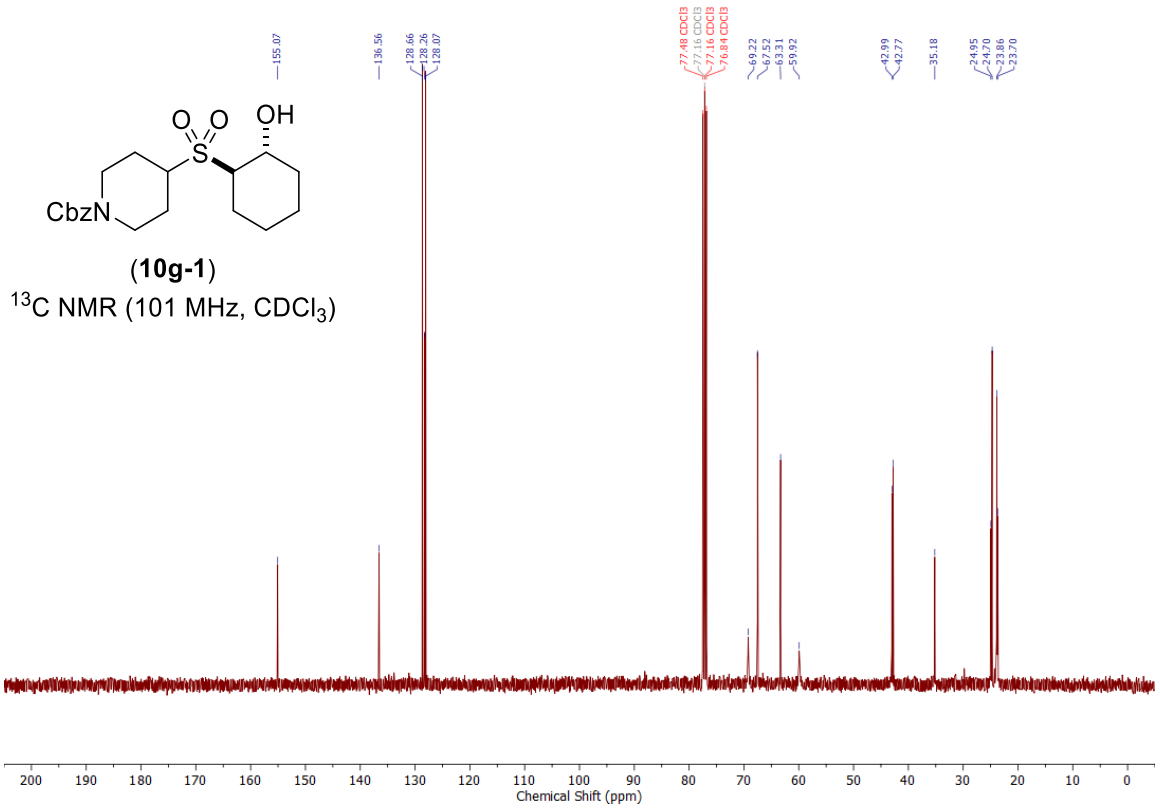
NMR spectra of benzyl 4-(benzo[*d*]thiazol-2-ylsulfonyl)piperidine-1-carboxylate (10f)



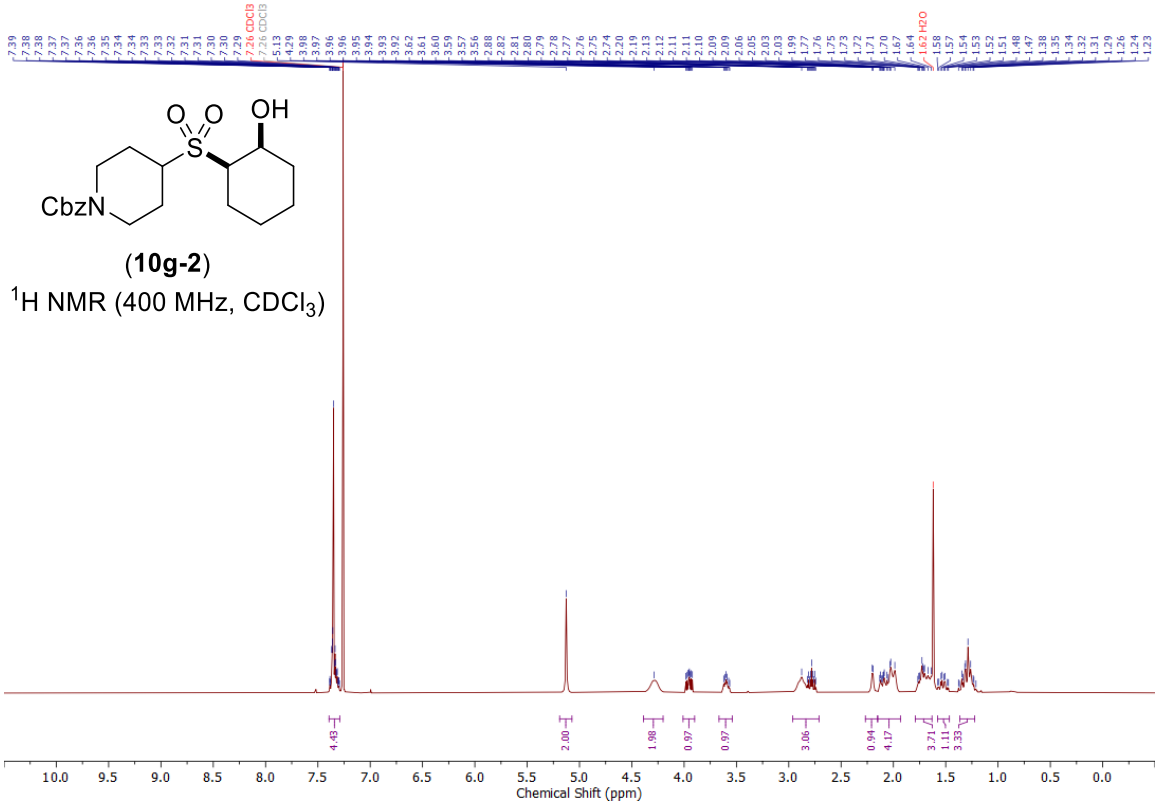


NMR spectra of benzyl 4-((2-hydroxycyclohexyl)sulfonyl)piperidine-1-carboxylate (10g-1)

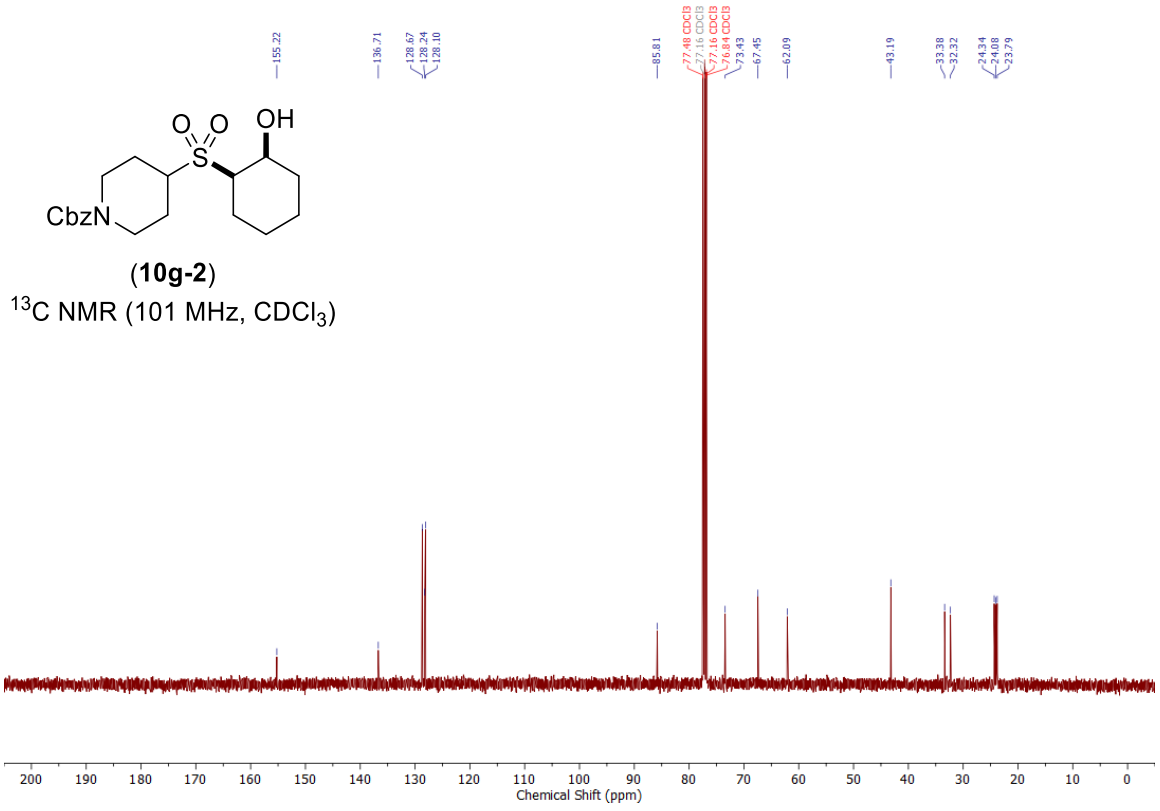




NMR spectra of benzyl 4-((2-hydroxycyclohexyl)sulfonyl)piperidine-1-carboxylate (10g-2)

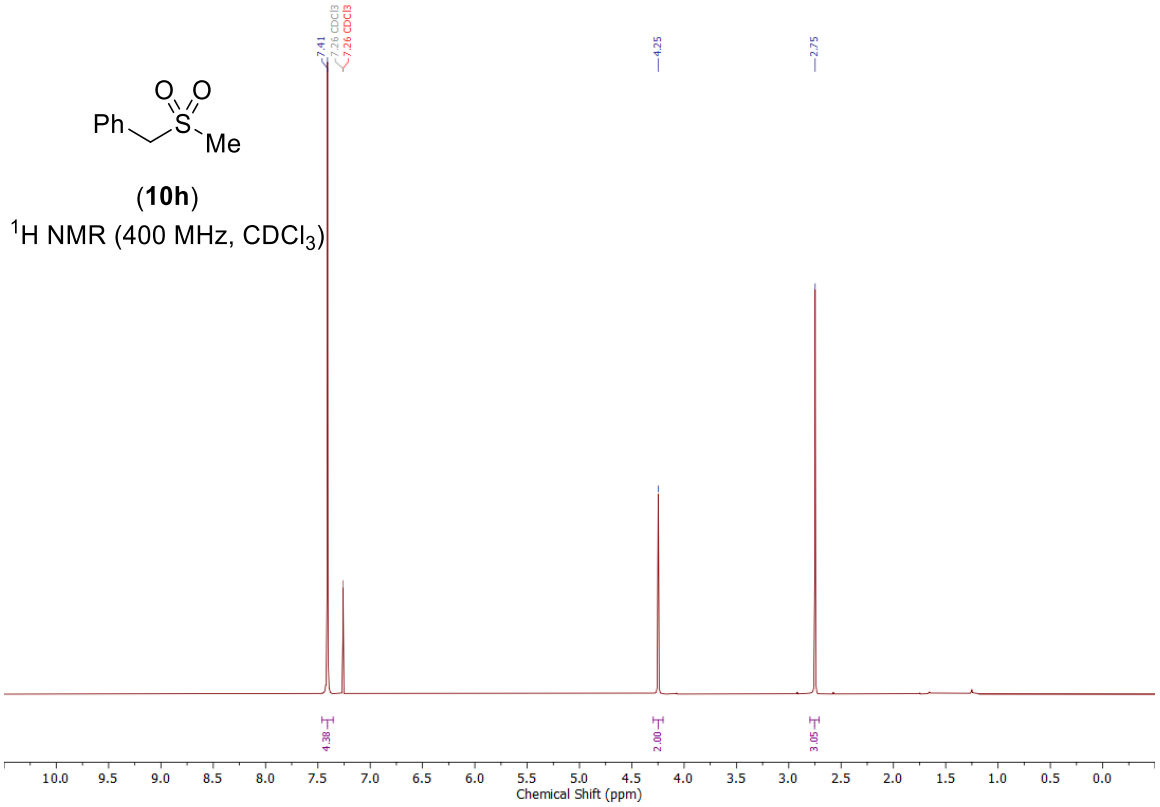


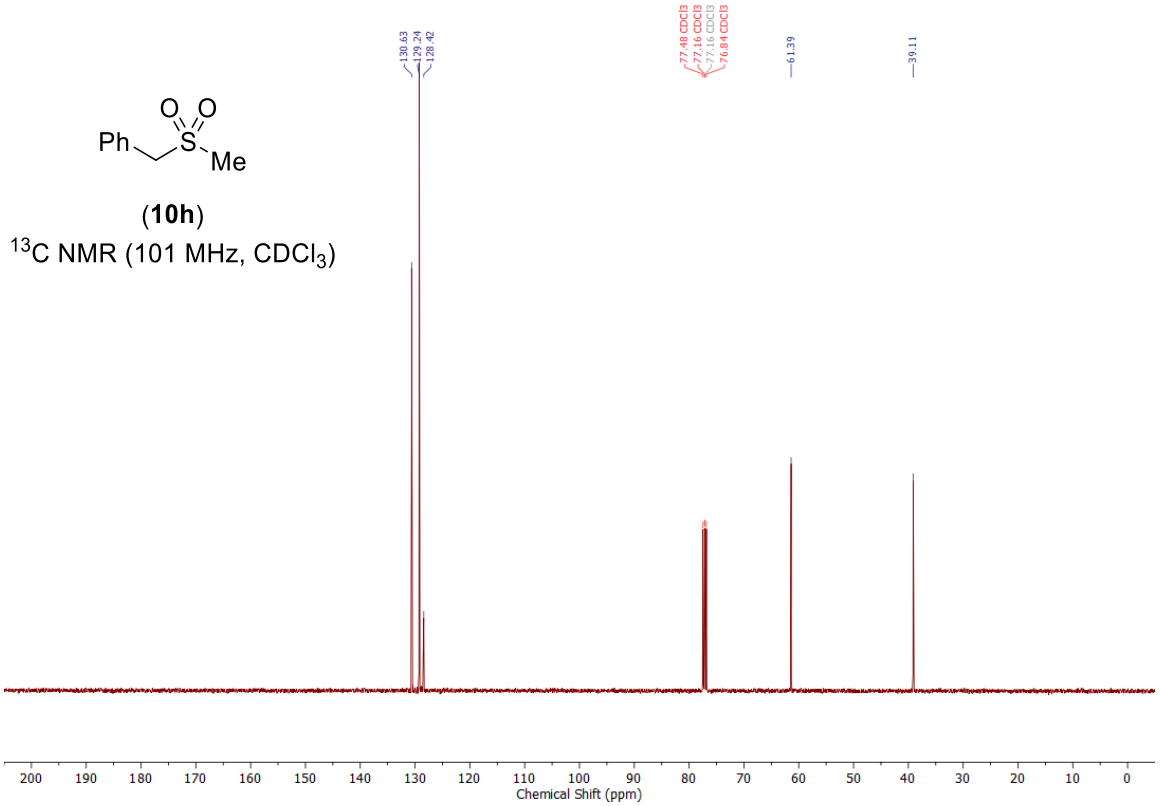
(**10g-2**)
^{1}H NMR (400 MHz, $CDCl_3$)



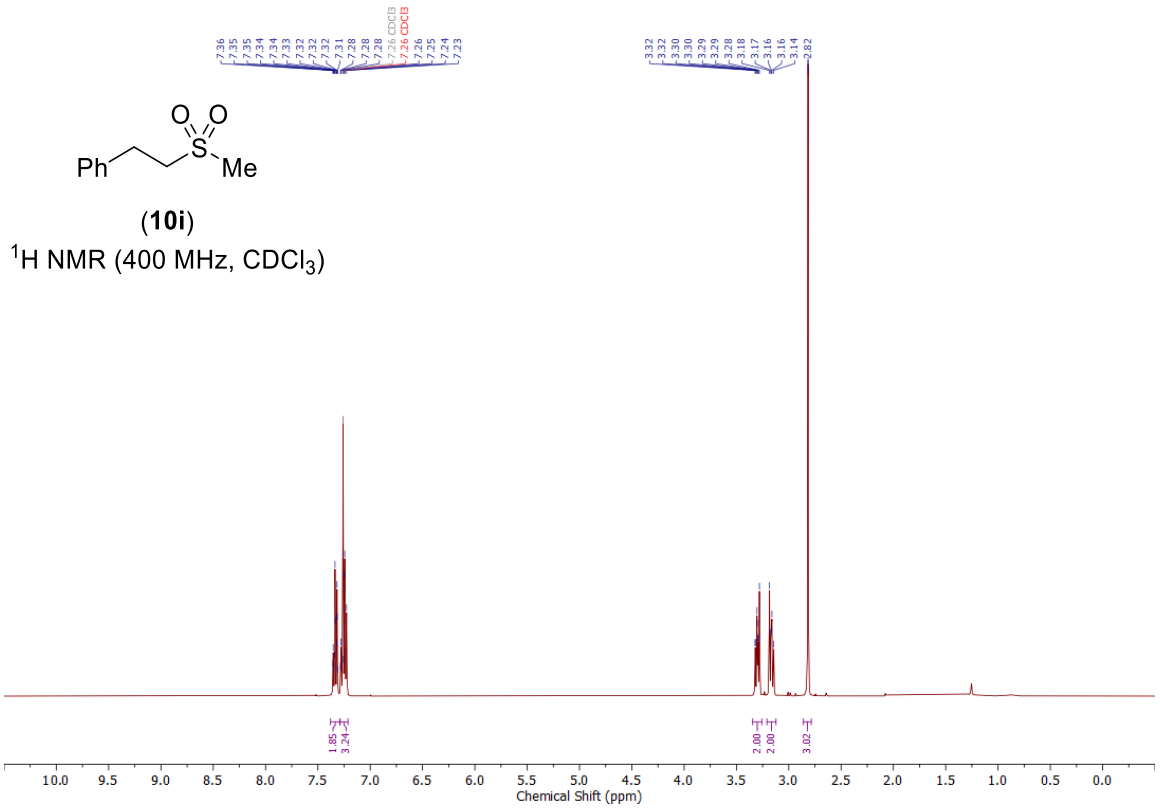
(**10g-2**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of ((methylsulfonyl)methyl)benzene (10h)



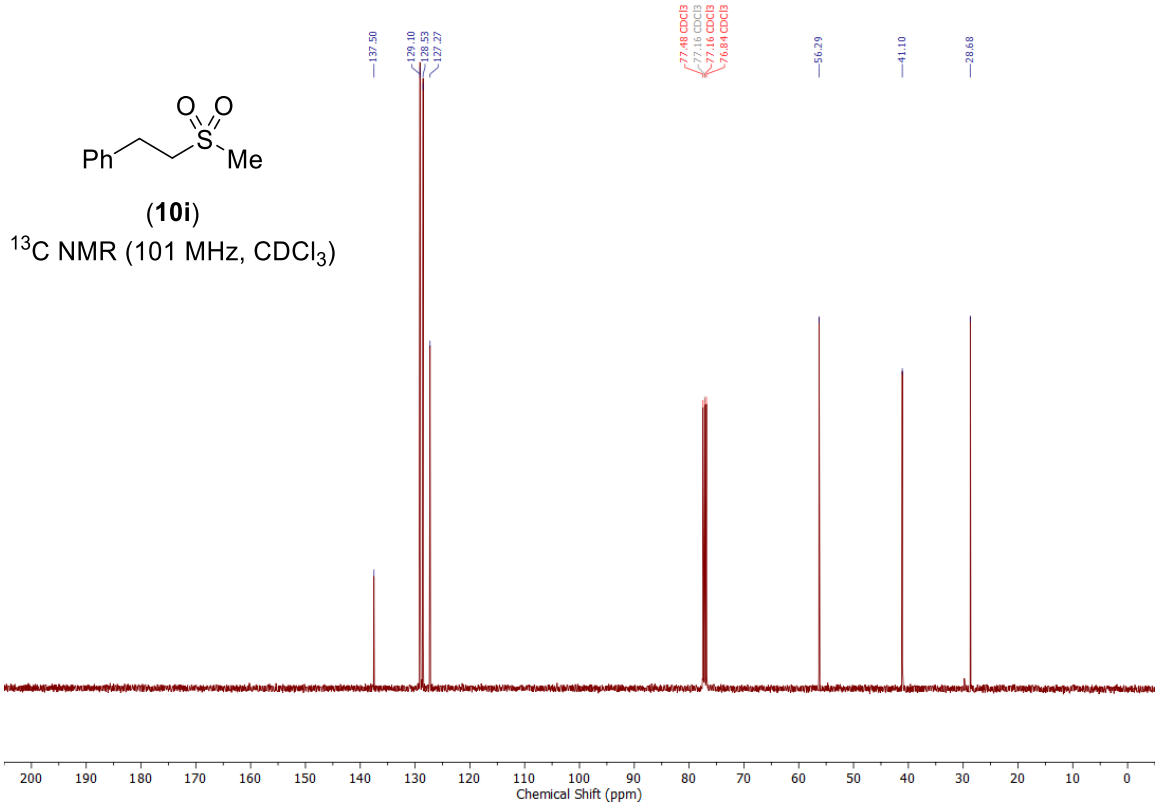


NMR spectra of (2-(methylsulfonyl)ethyl)benzene (10i)



(**10i**)

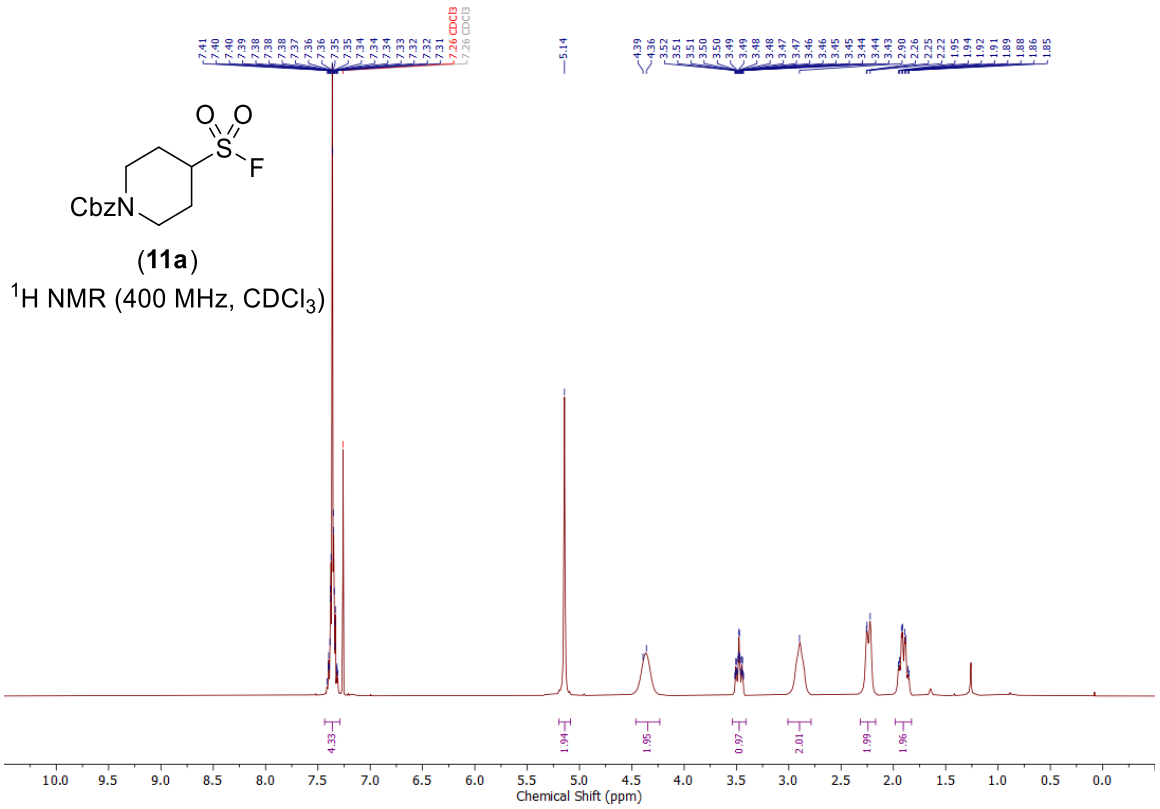
^{1}H NMR (400 MHz, $CDCl_3$)

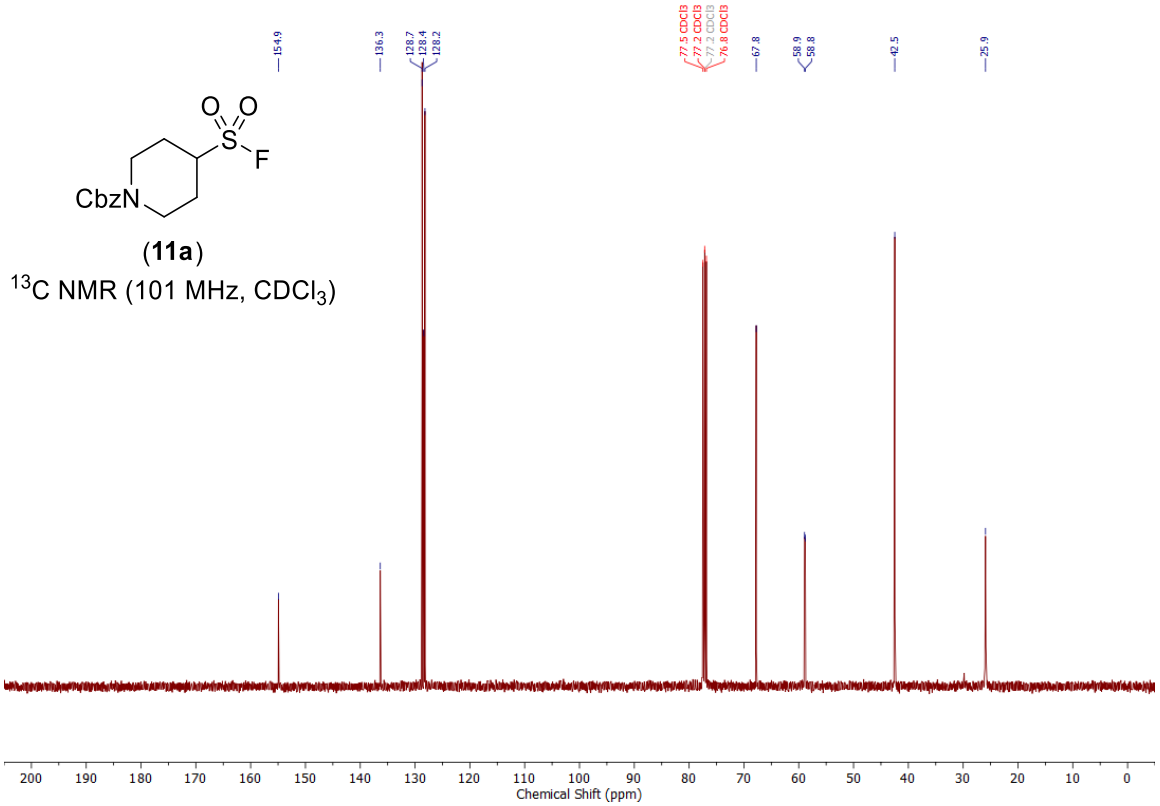


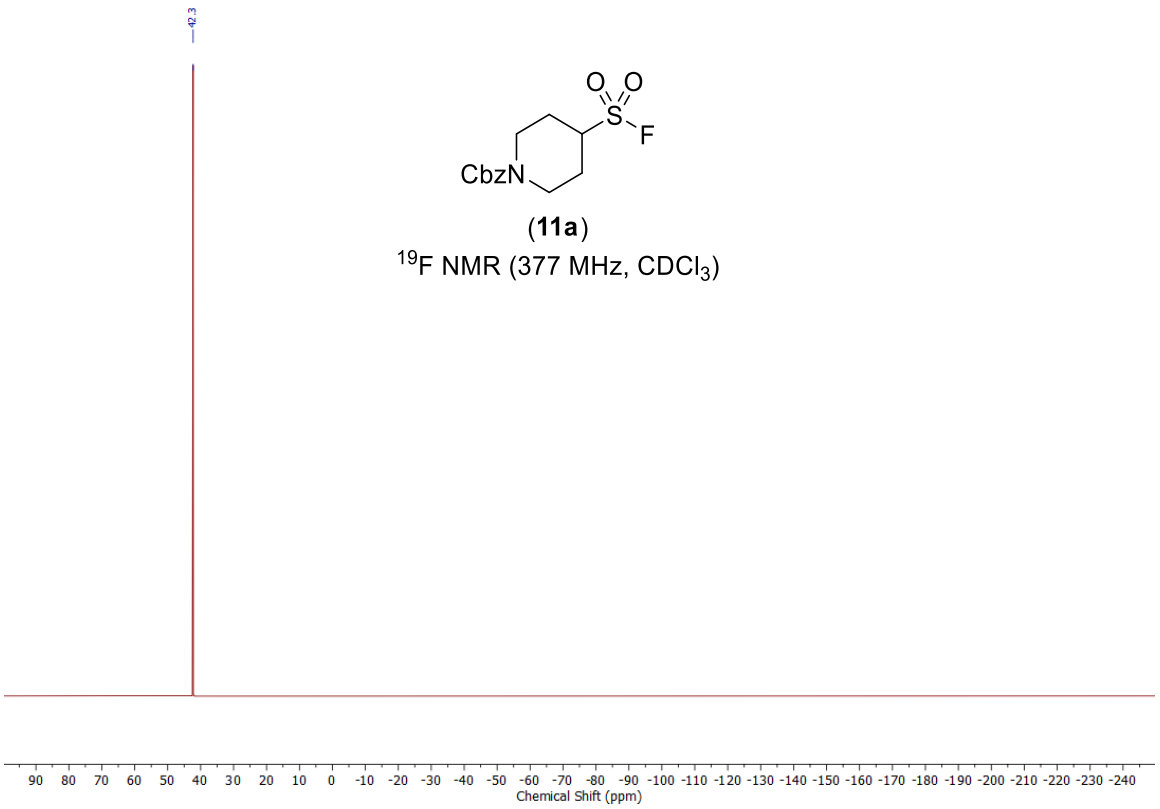
(**10i**)

^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of benzyl 4-(fluorosulfonyl)piperidine-1-carboxylate (11a)



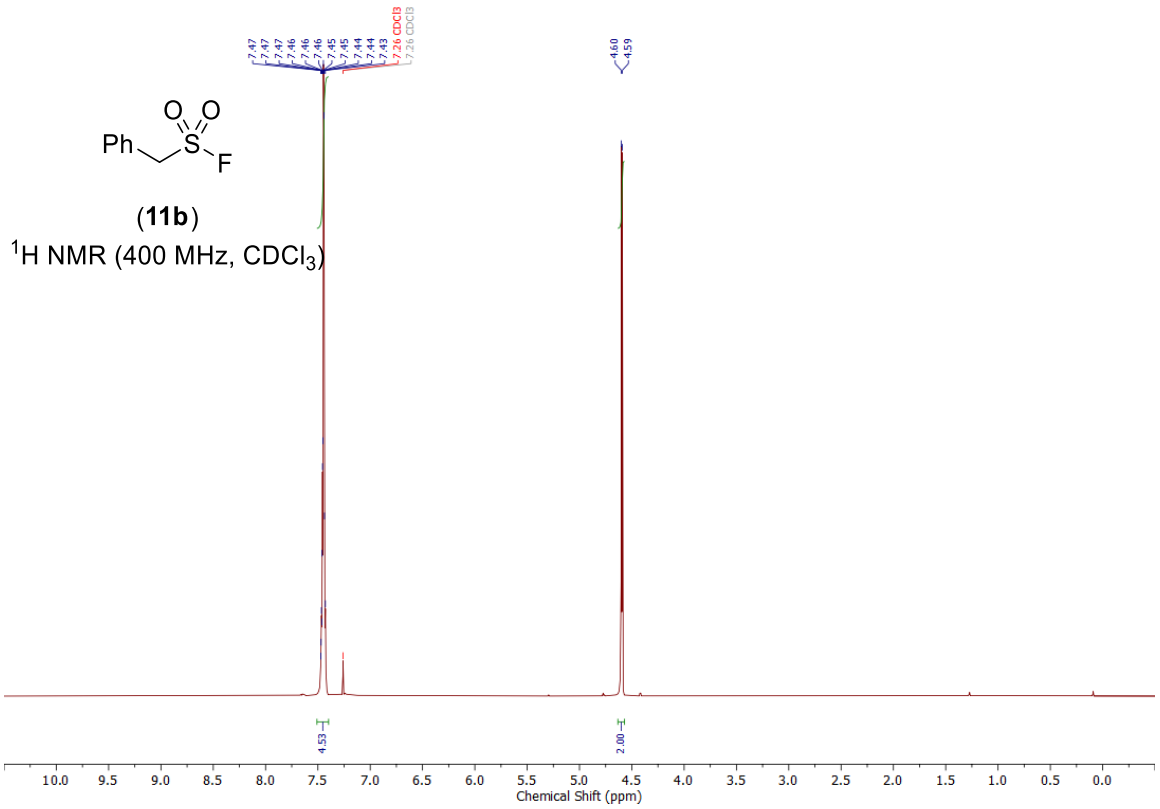


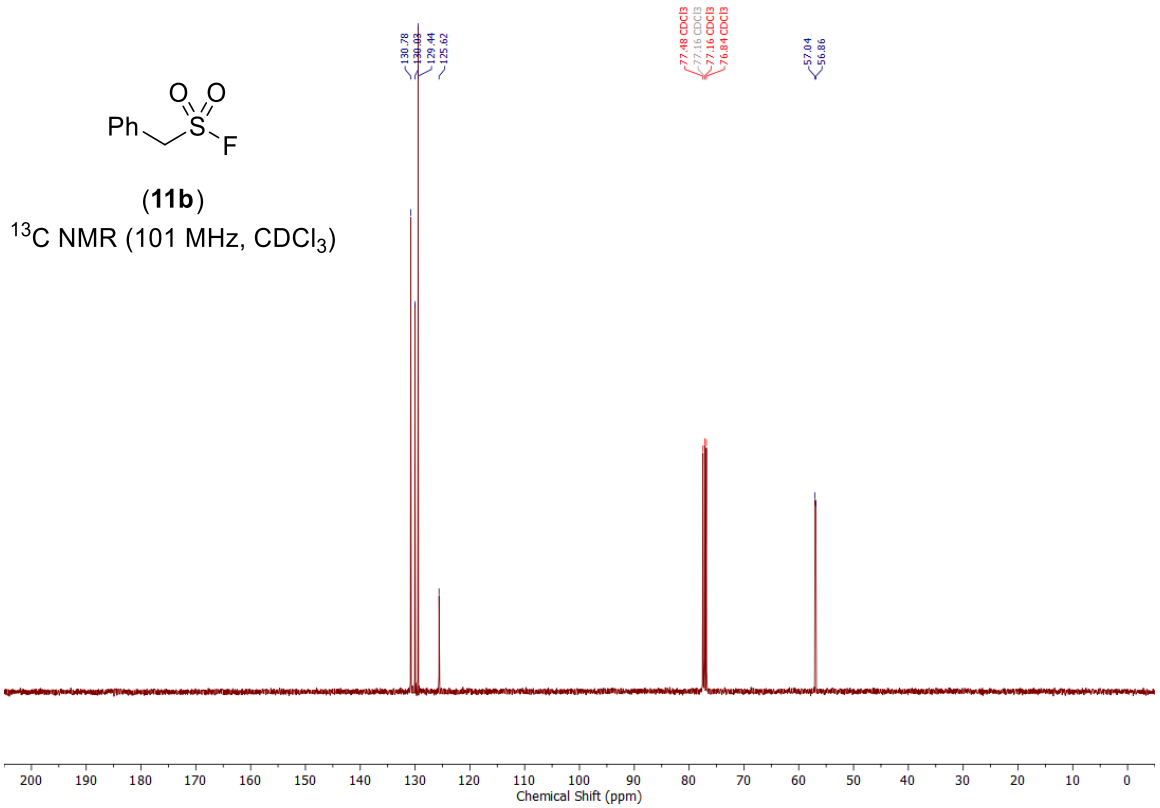


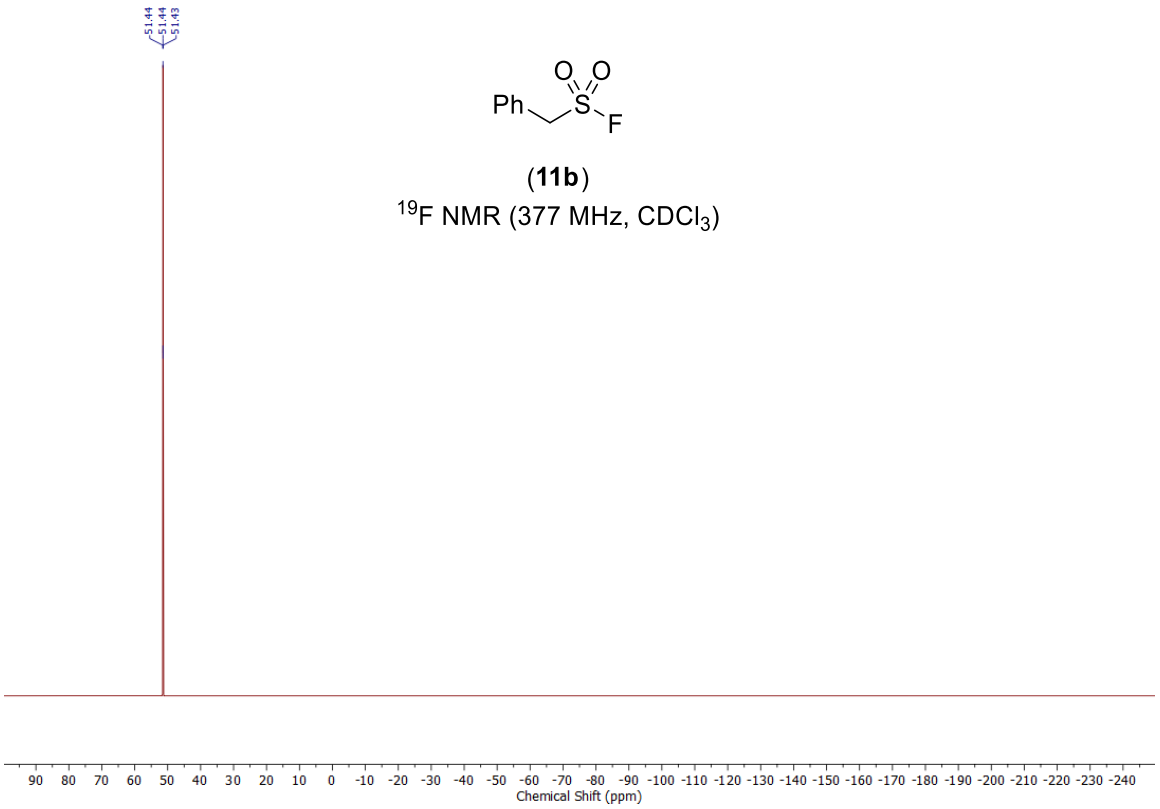
(**11a**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of phenylmethanesulfonyl fluoride (11b)



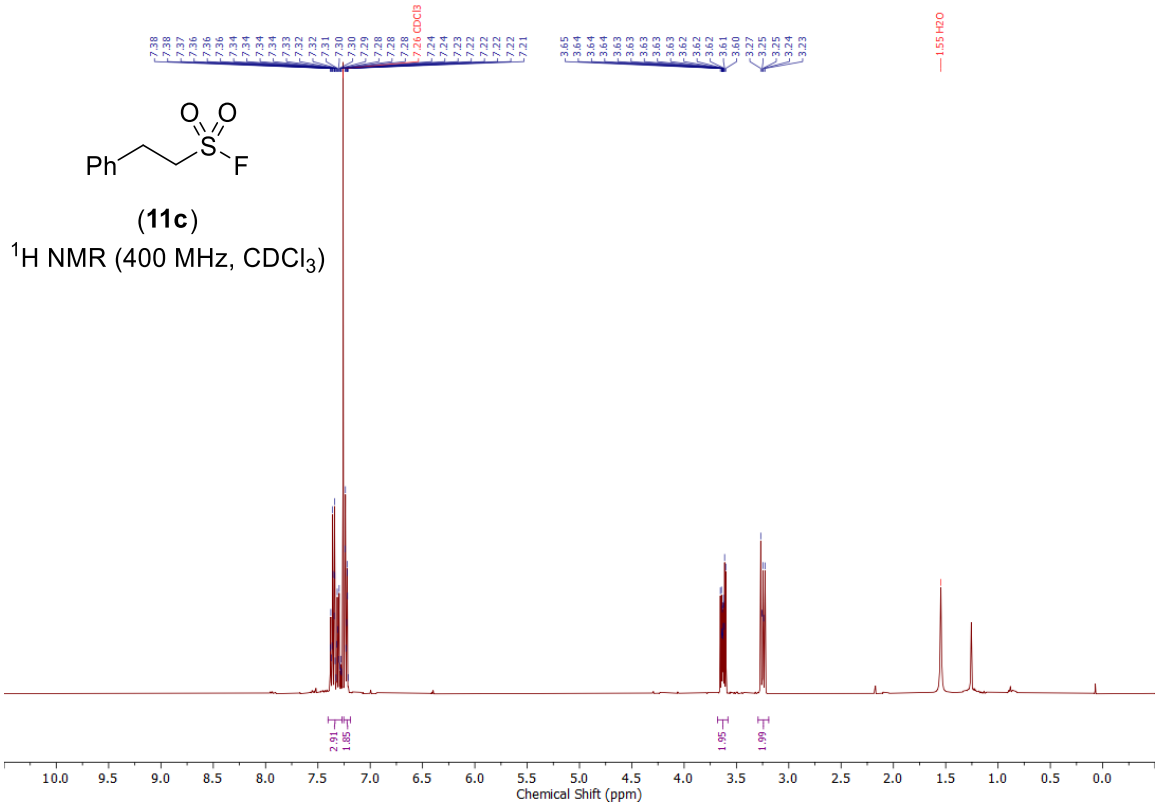


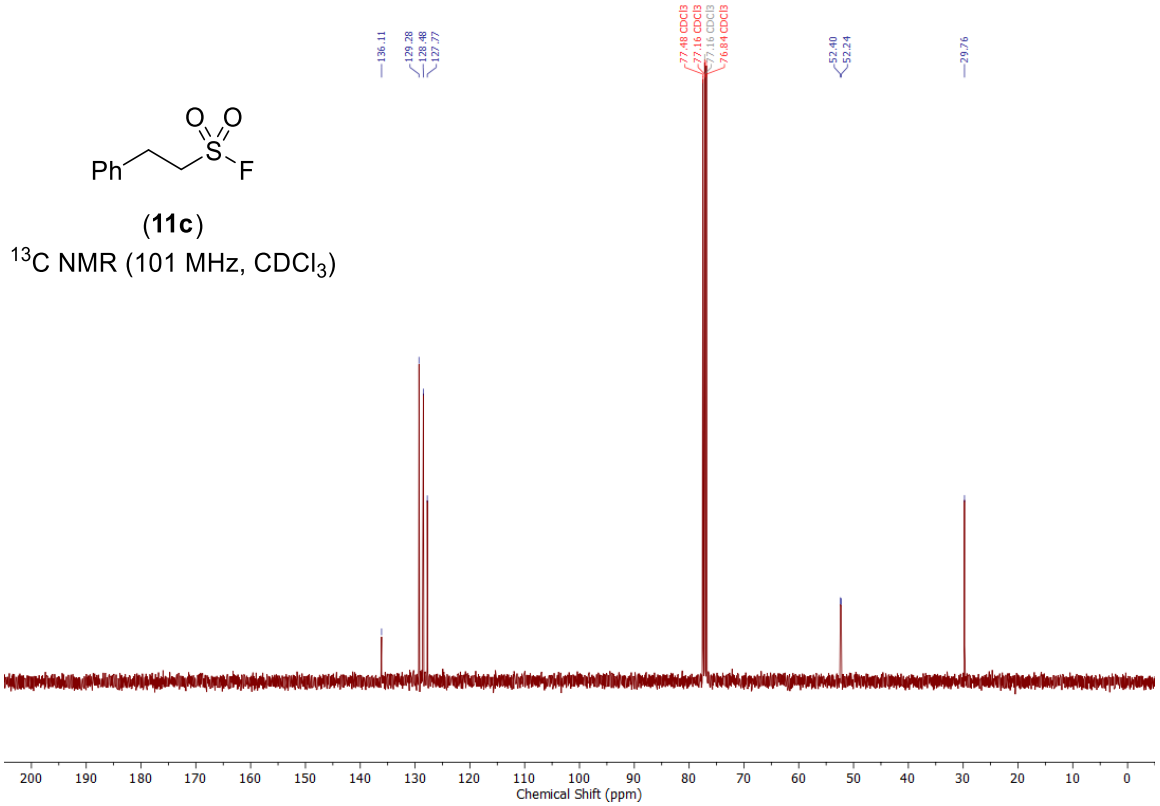


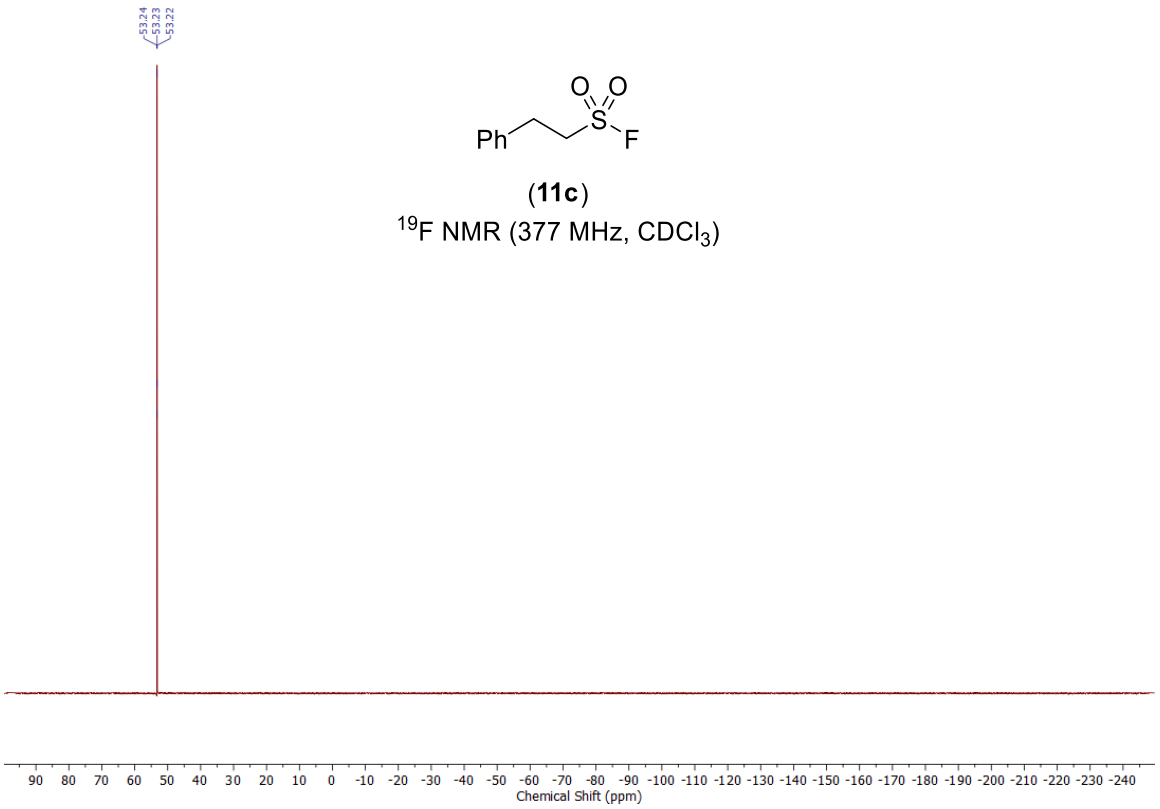
(**11b**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 2-phenylethane-1-sulfonyl fluoride (11c)



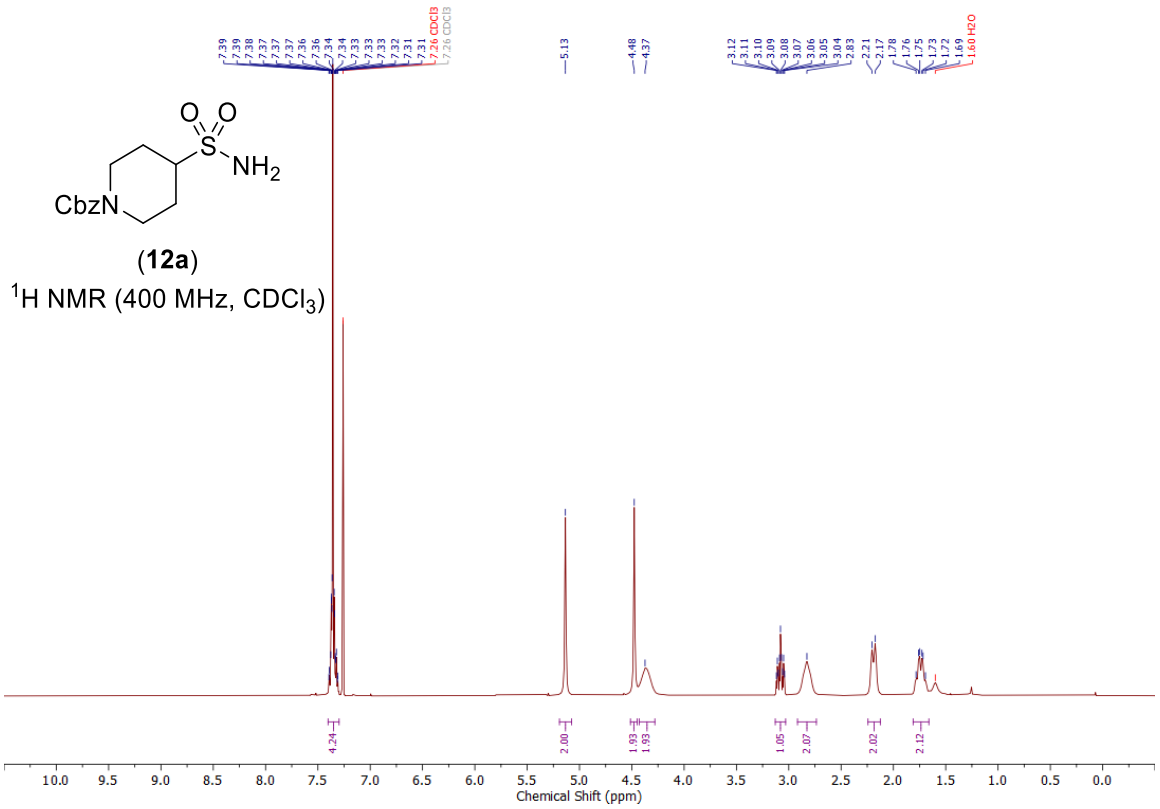


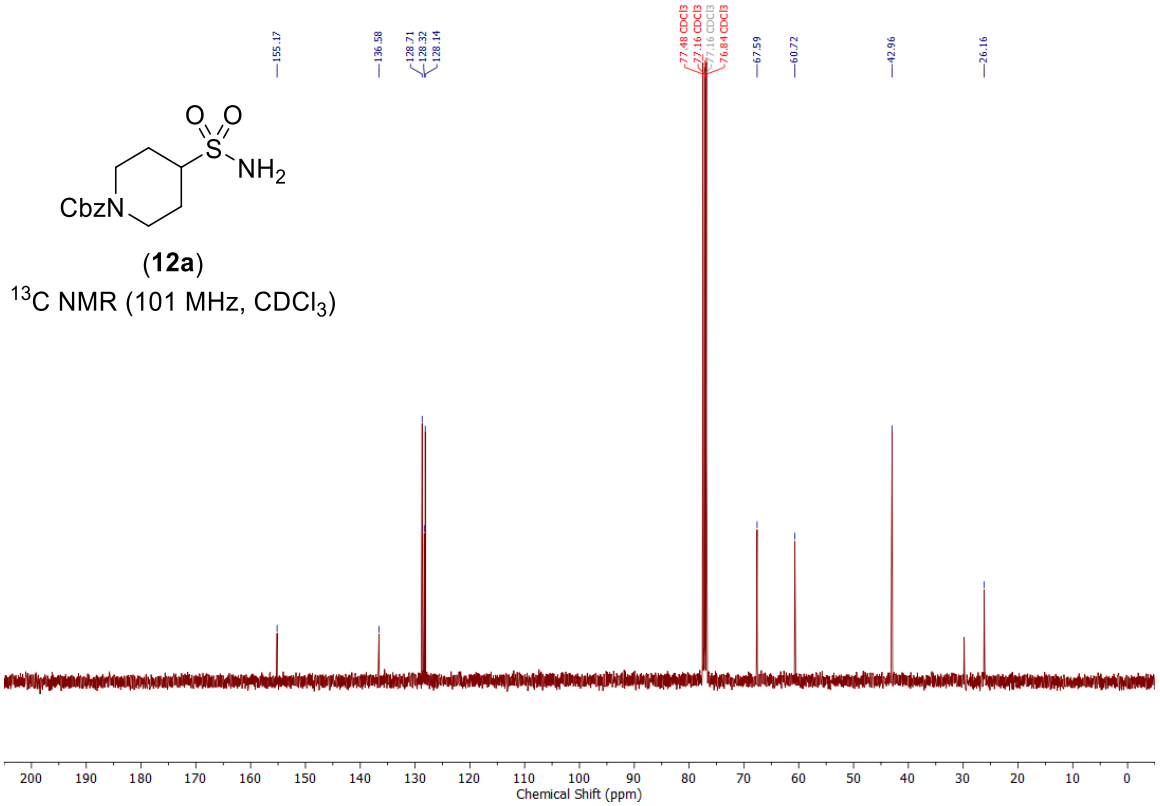


(**11c**)

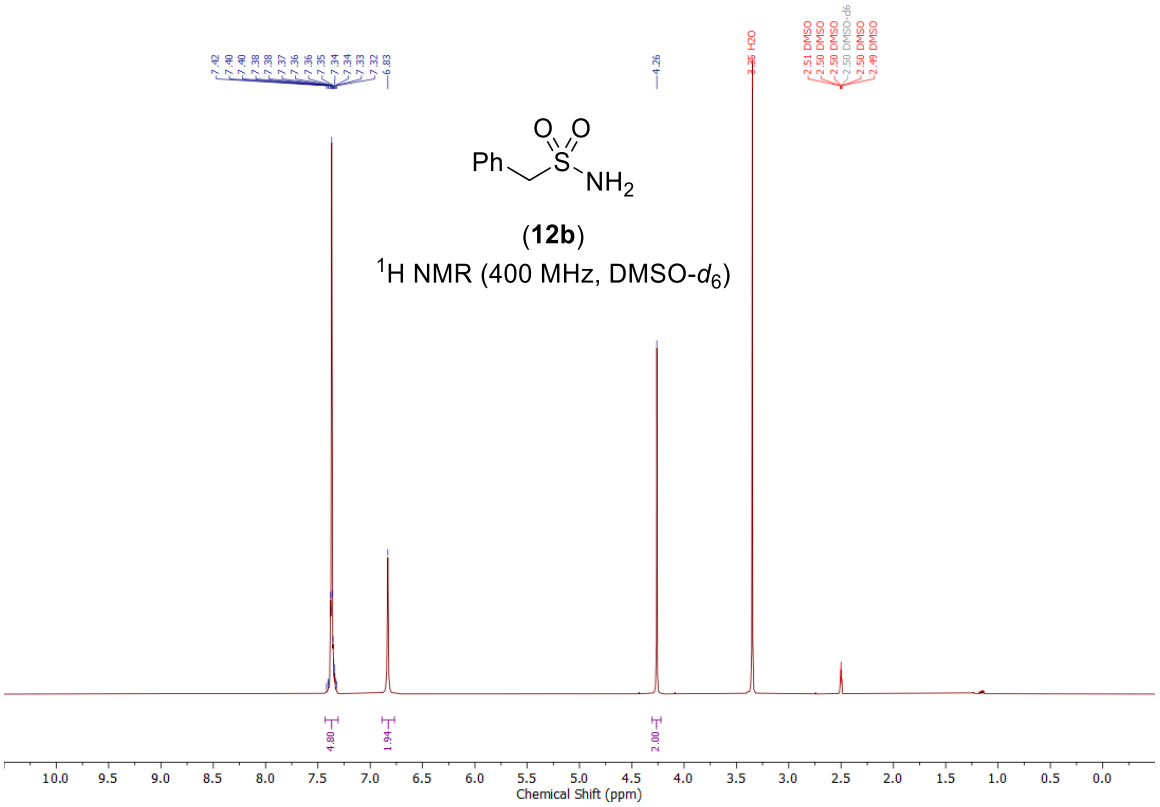
^{19}F NMR (377 MHz, $CDCl_3$)

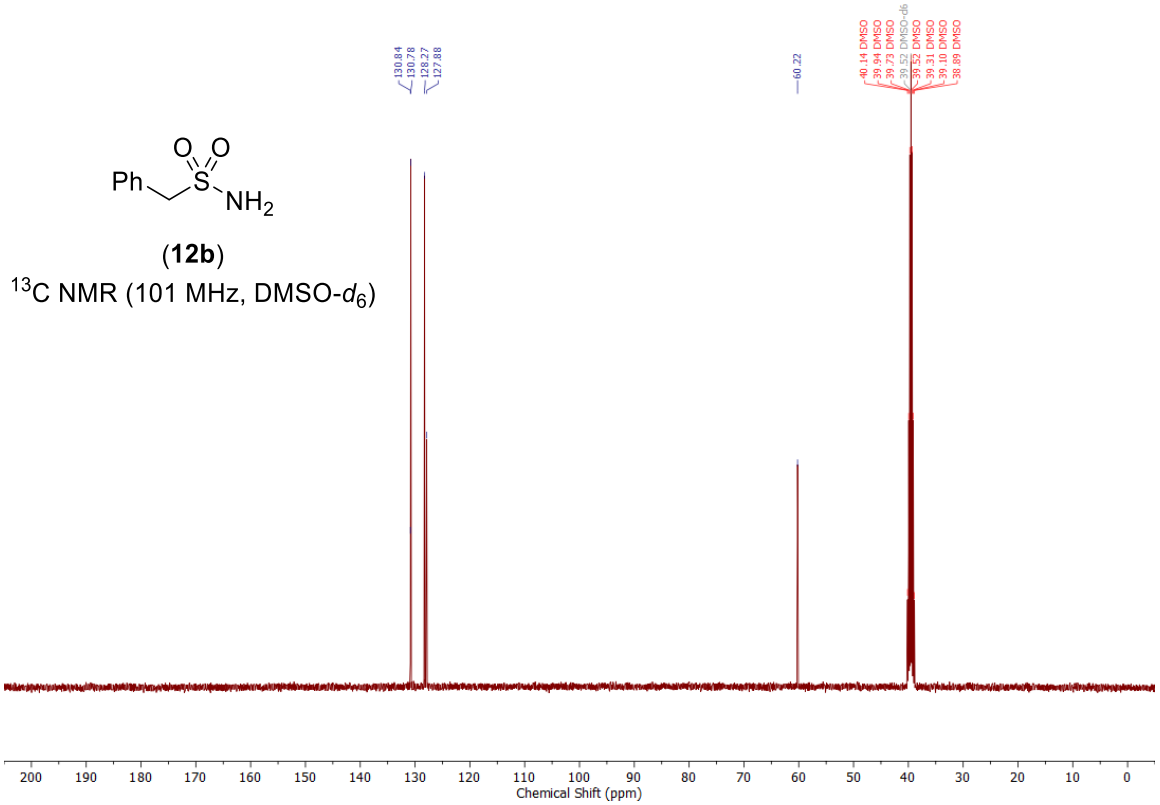
NMR spectra of benzyl 4-sulfamoylpiperidine-1-carboxylate (12a)



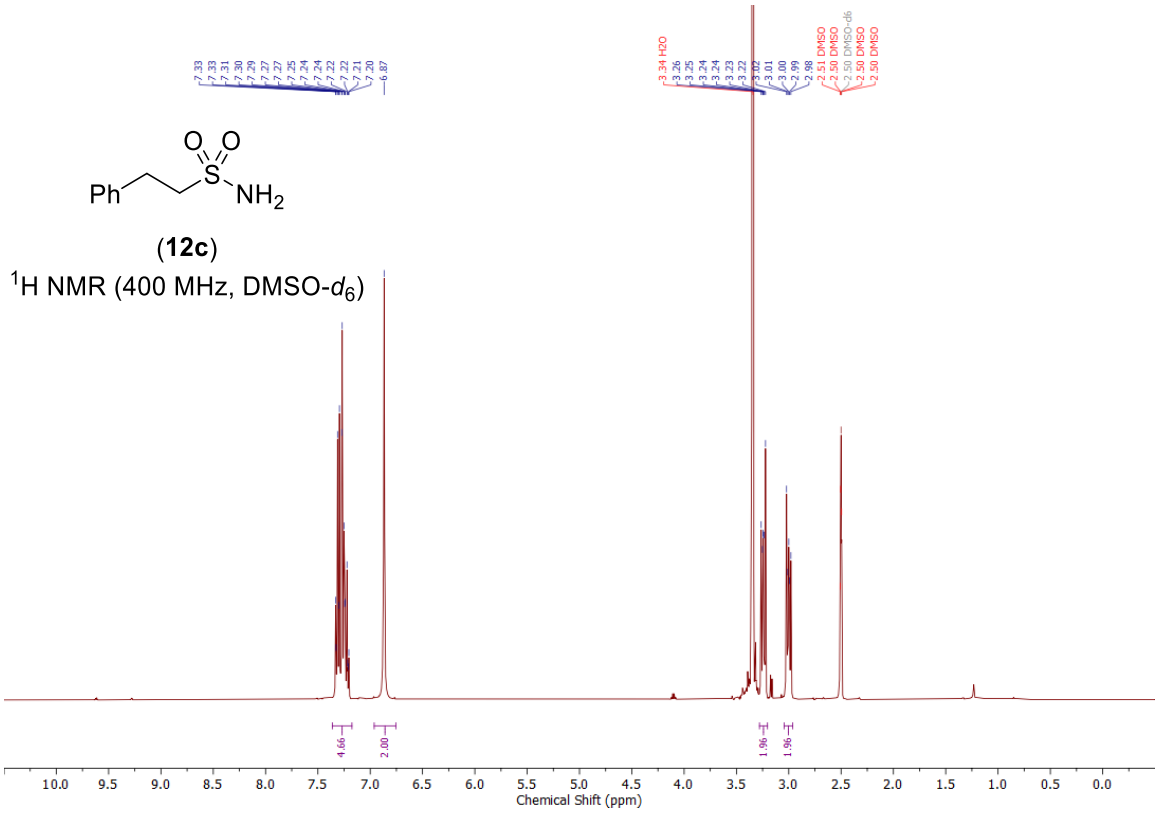


NMR spectra of phenylmethanesulfonamide (12b)

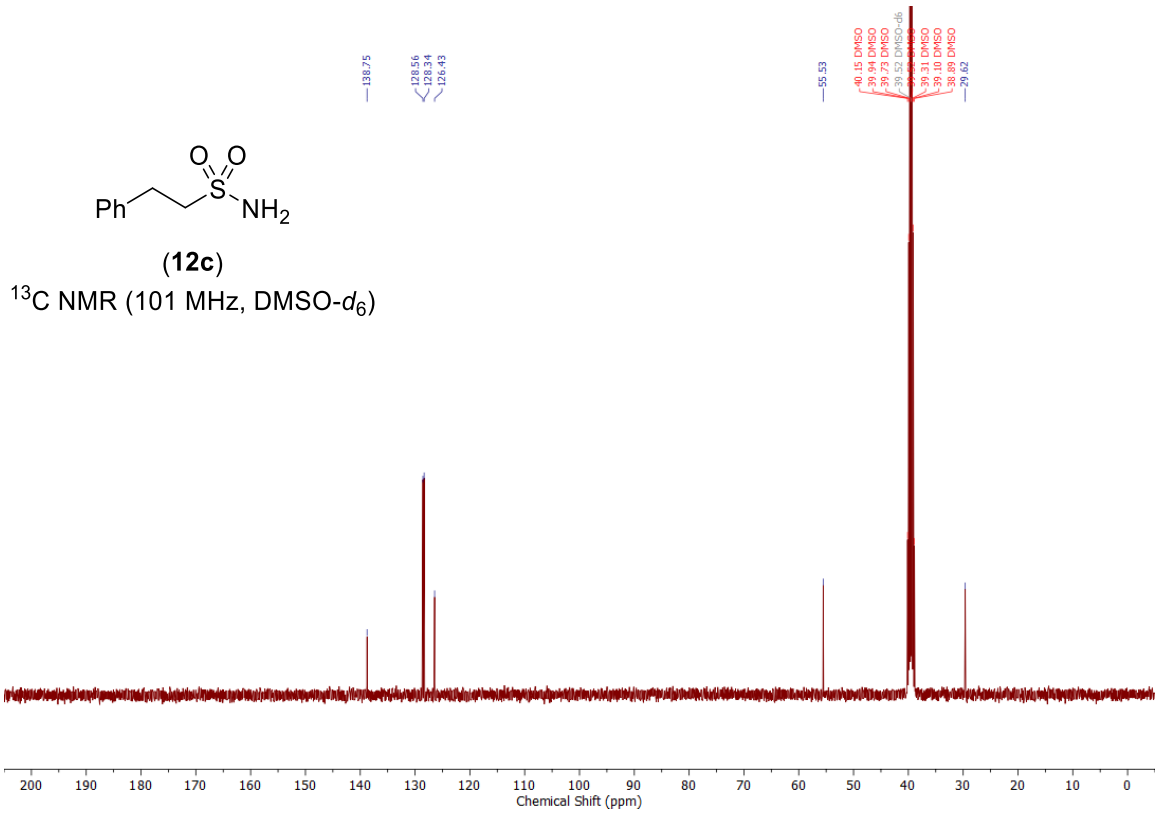




NMR spectra of 2-phenylethane-1-sulfonamide (12c)

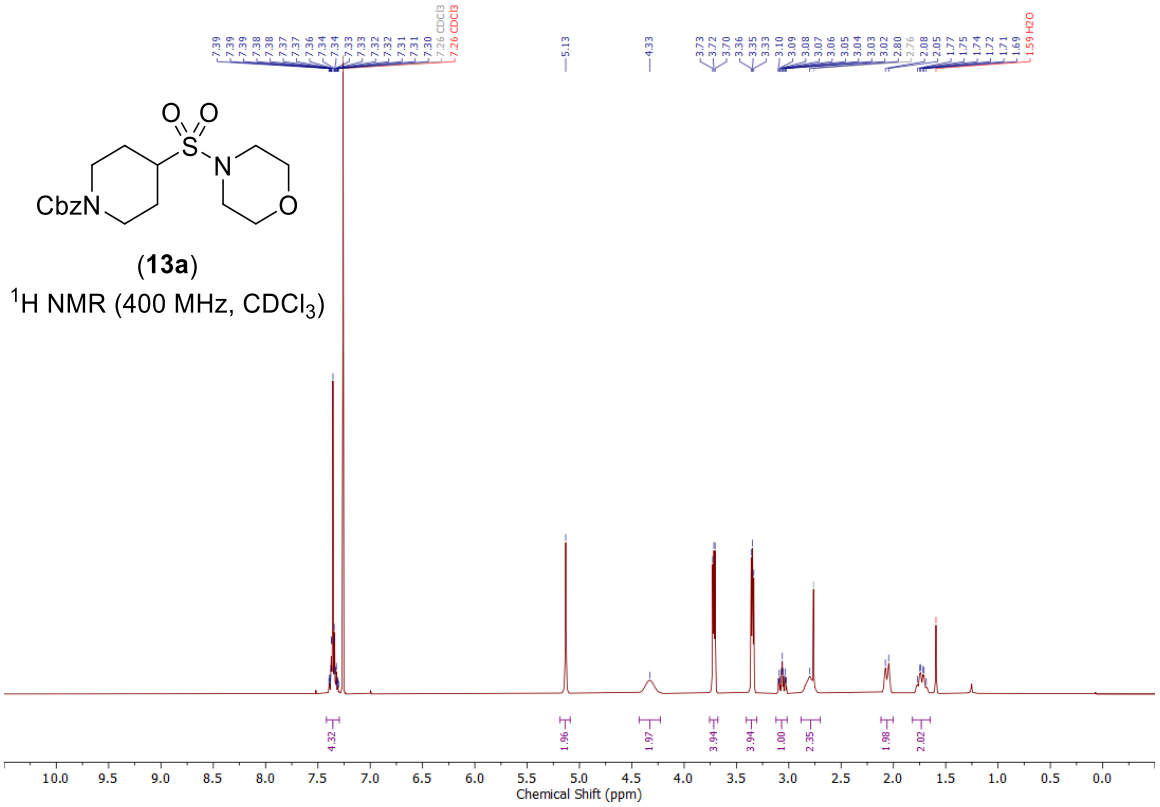


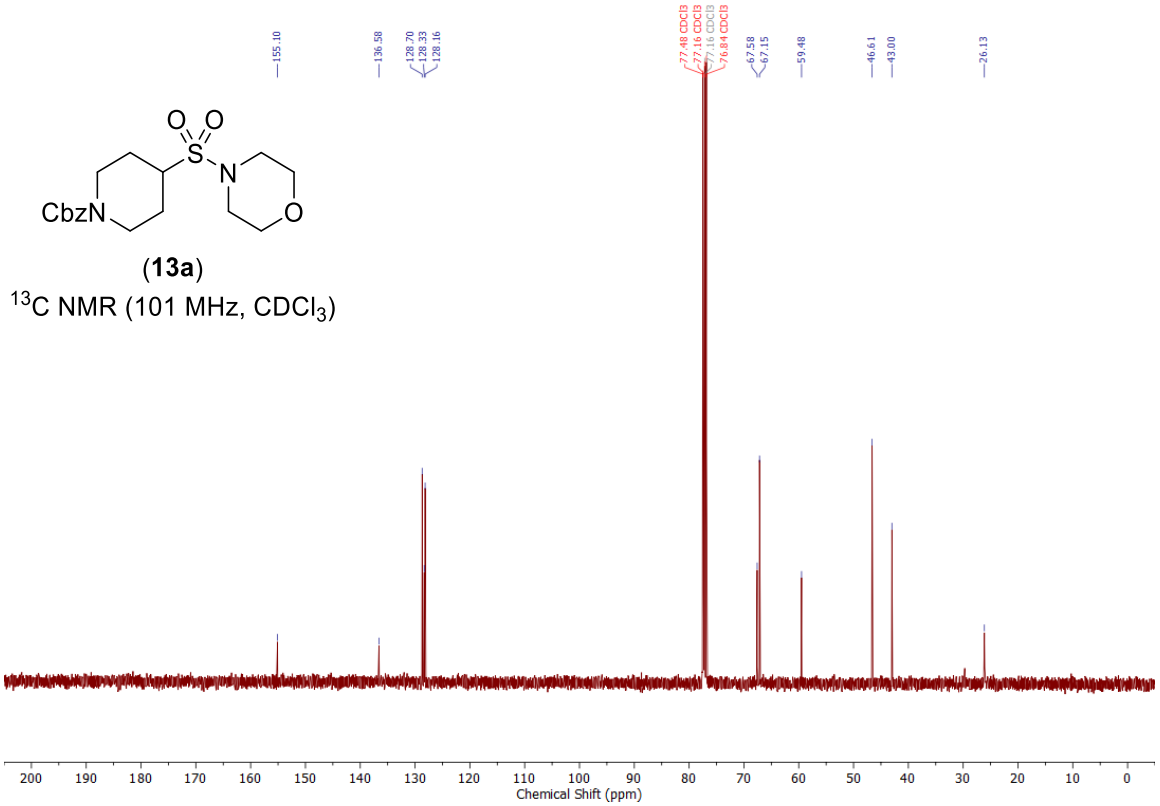
(**12c**)
^{1}H NMR (400 MHz, DMSO-d_6)



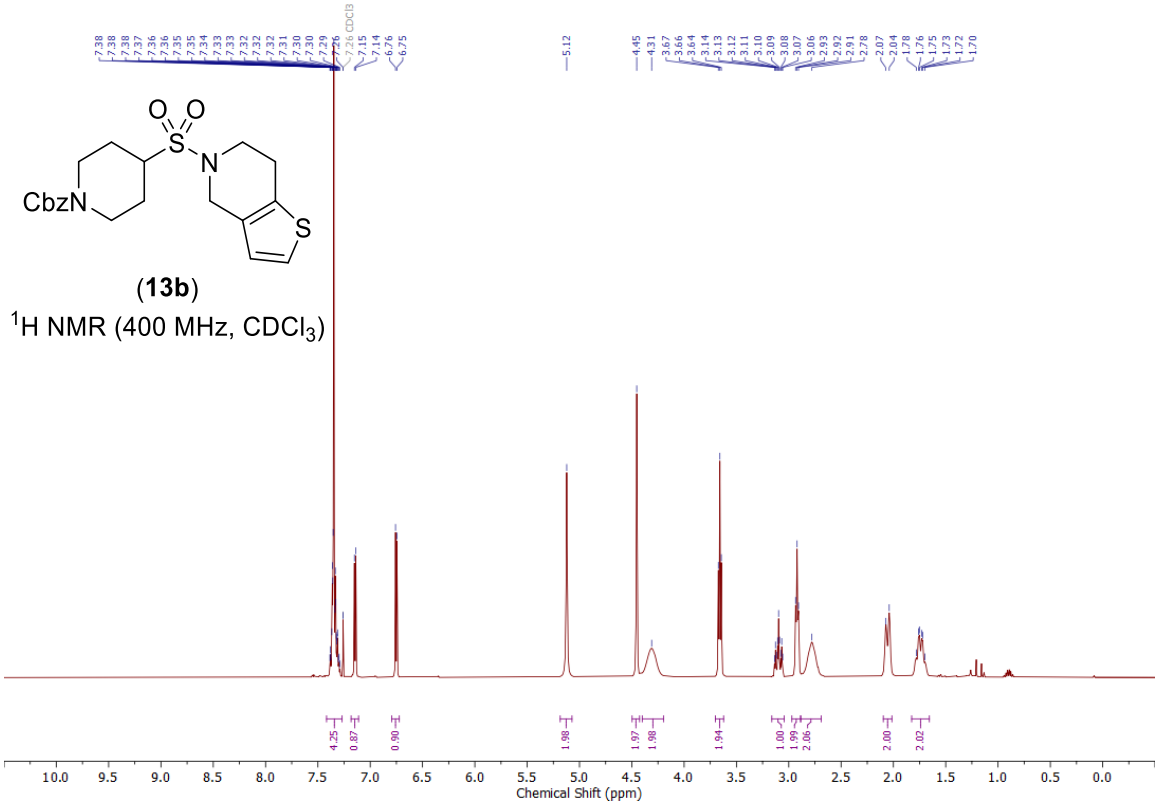
(**12c**)
^{13}C NMR (101 MHz, DMSO-d_6)

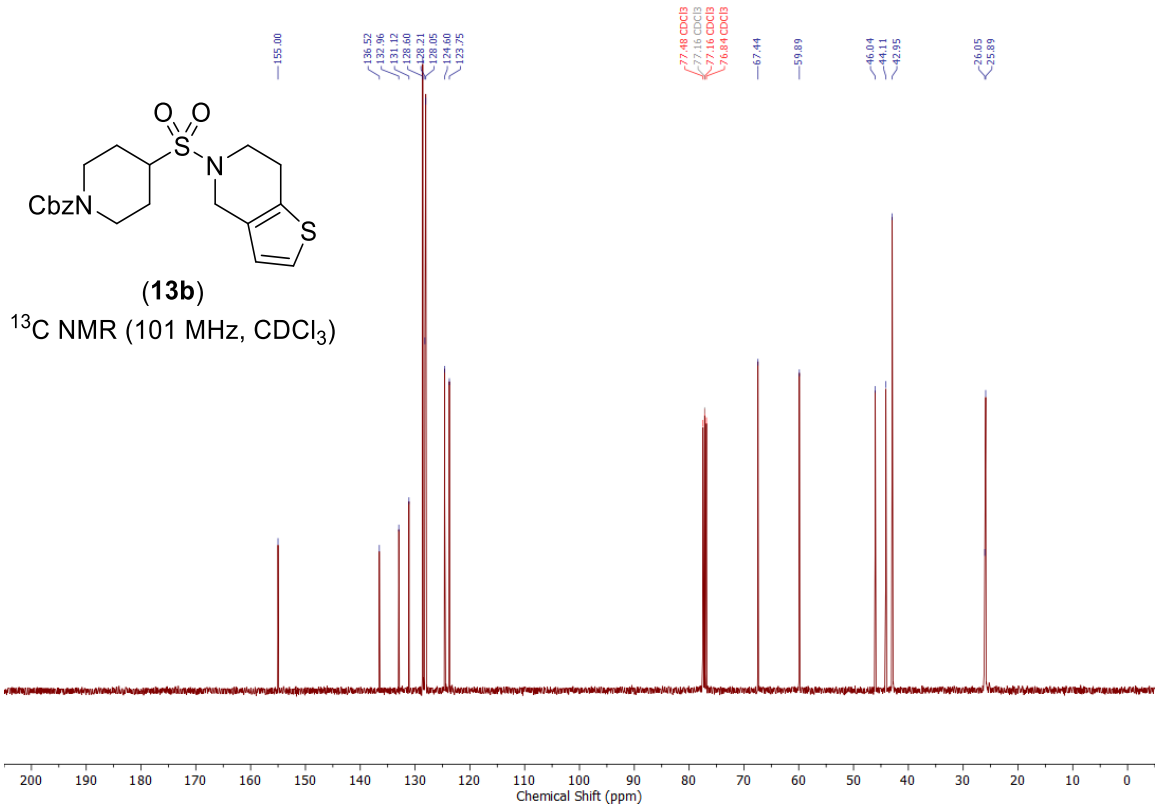
NMR spectra of benzyl 4-(morpholinosulfonyl)piperidine-1-carboxylate (13a)



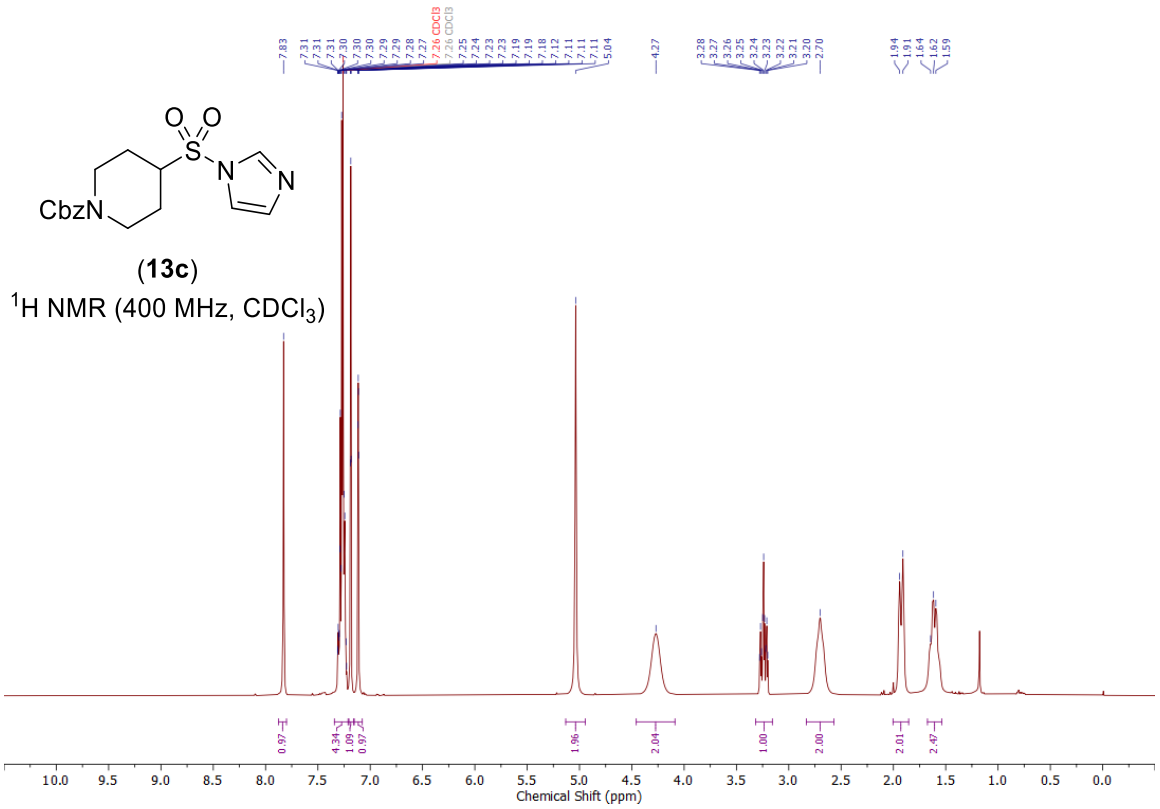


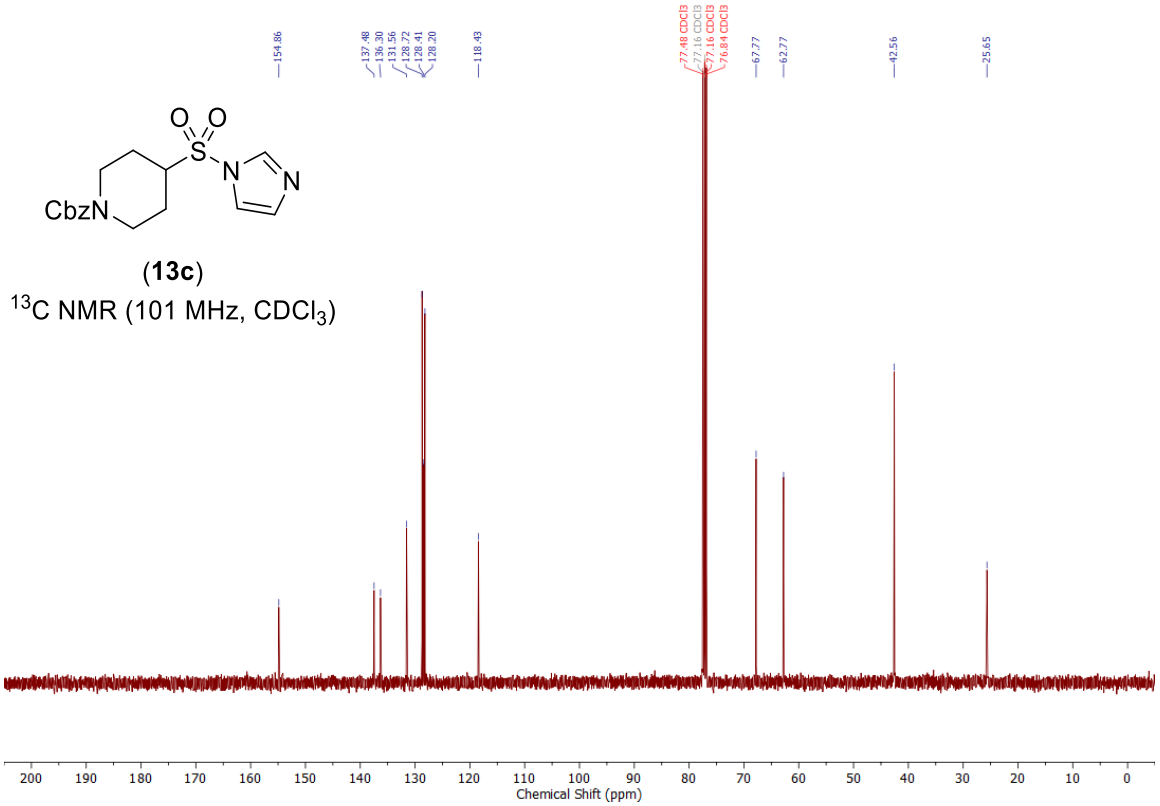
NMR spectra of benzyl 4-((6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl)sulfonyl)piperidine-1-carboxylate (13b)



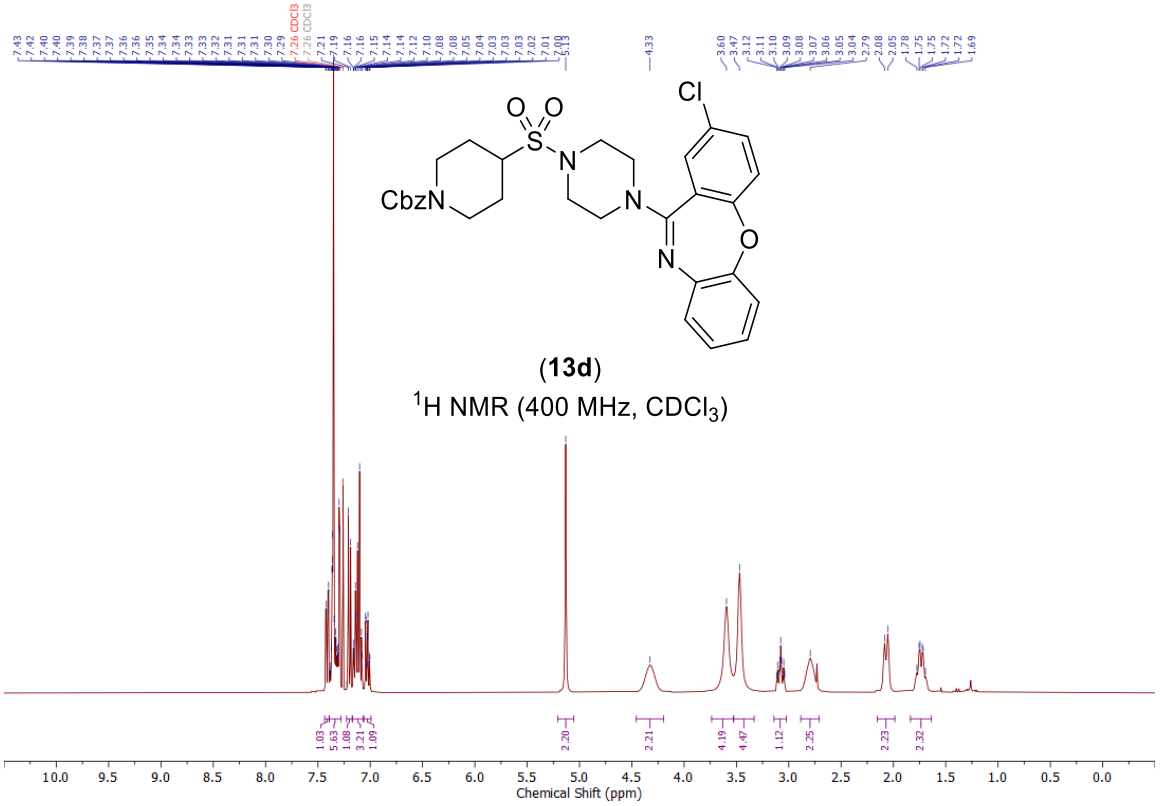


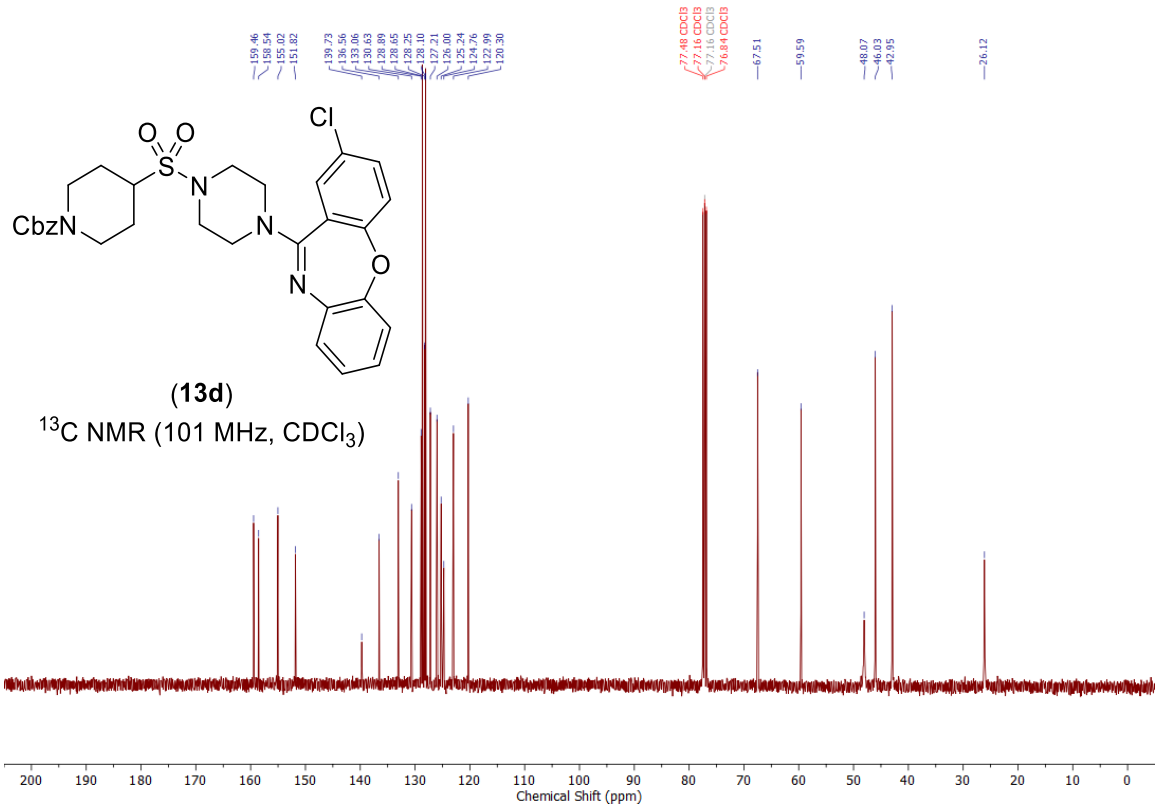
NMR spectra of benzyl 4-((1*H*-imidazol-1-yl)sulfonyl)piperidine-1-carboxylate (13c)



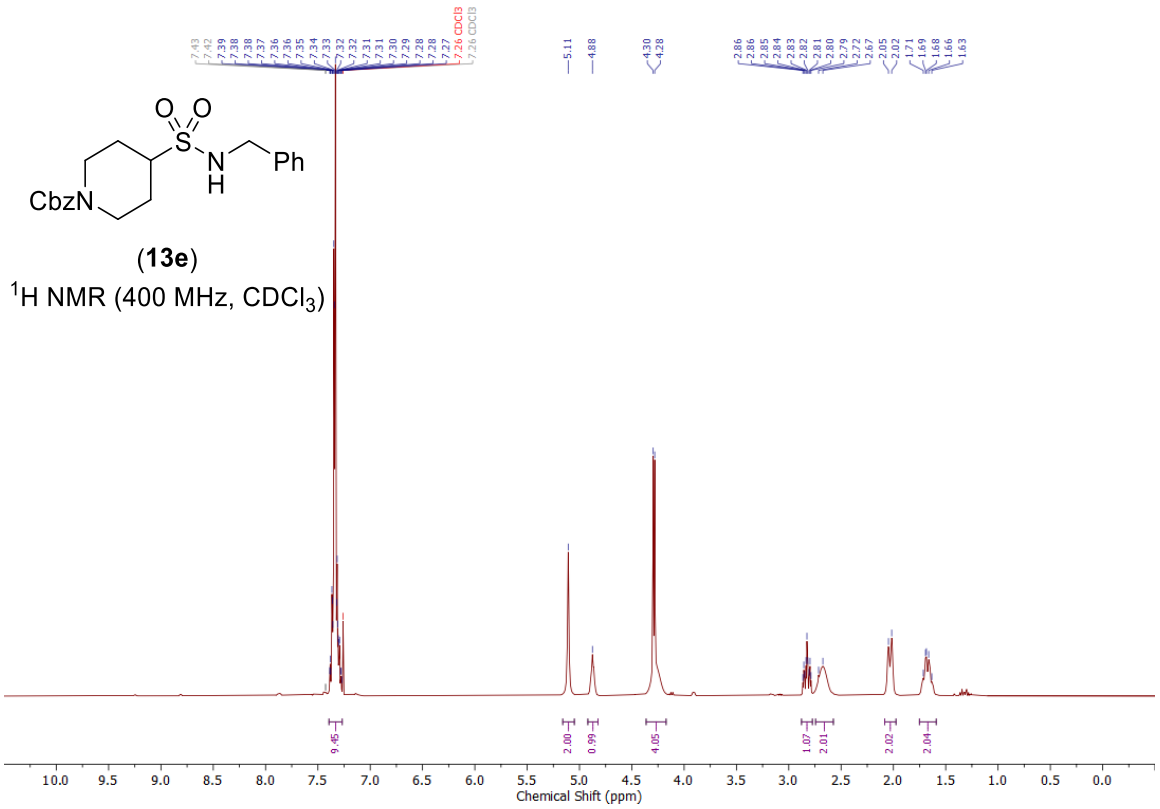


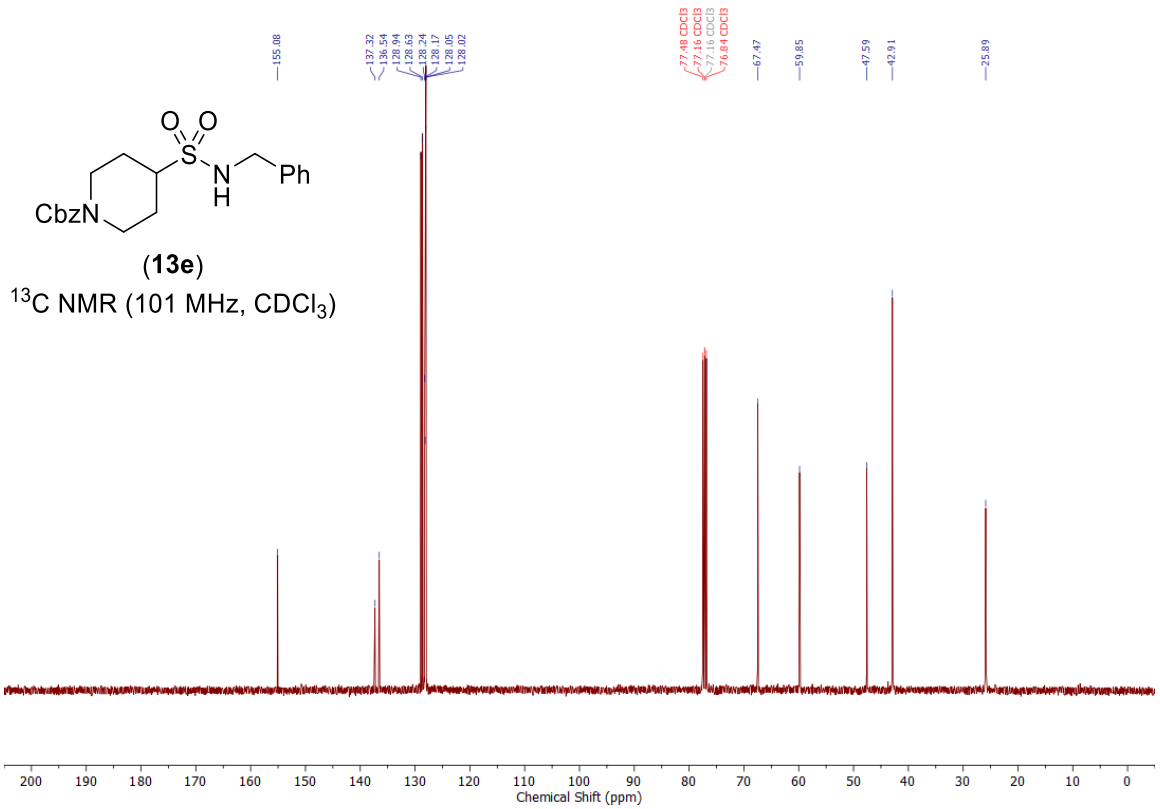
NMR spectra of benzyl 4-((4-(2-chlorodibenzo[*b,f*][1,4]oxazepin-11-yl)piperazin-1-yl)sulfonyl)piperidine-1-carboxylate (13d)



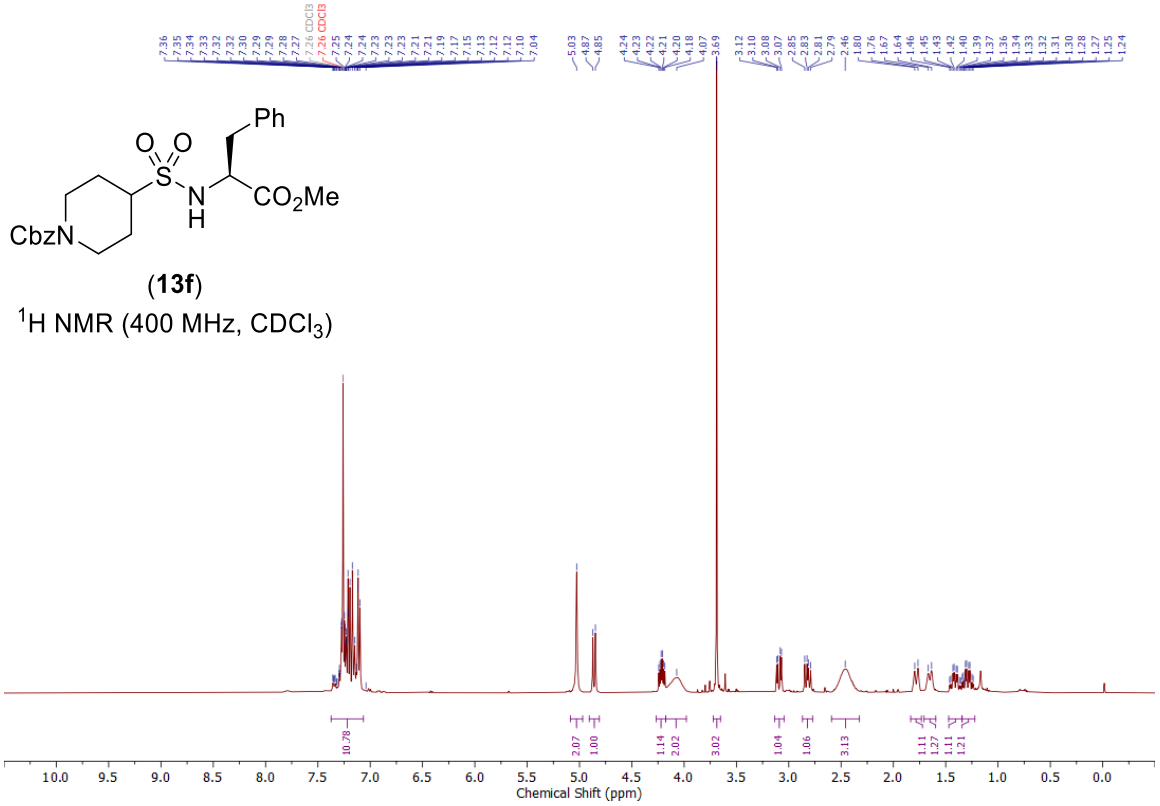


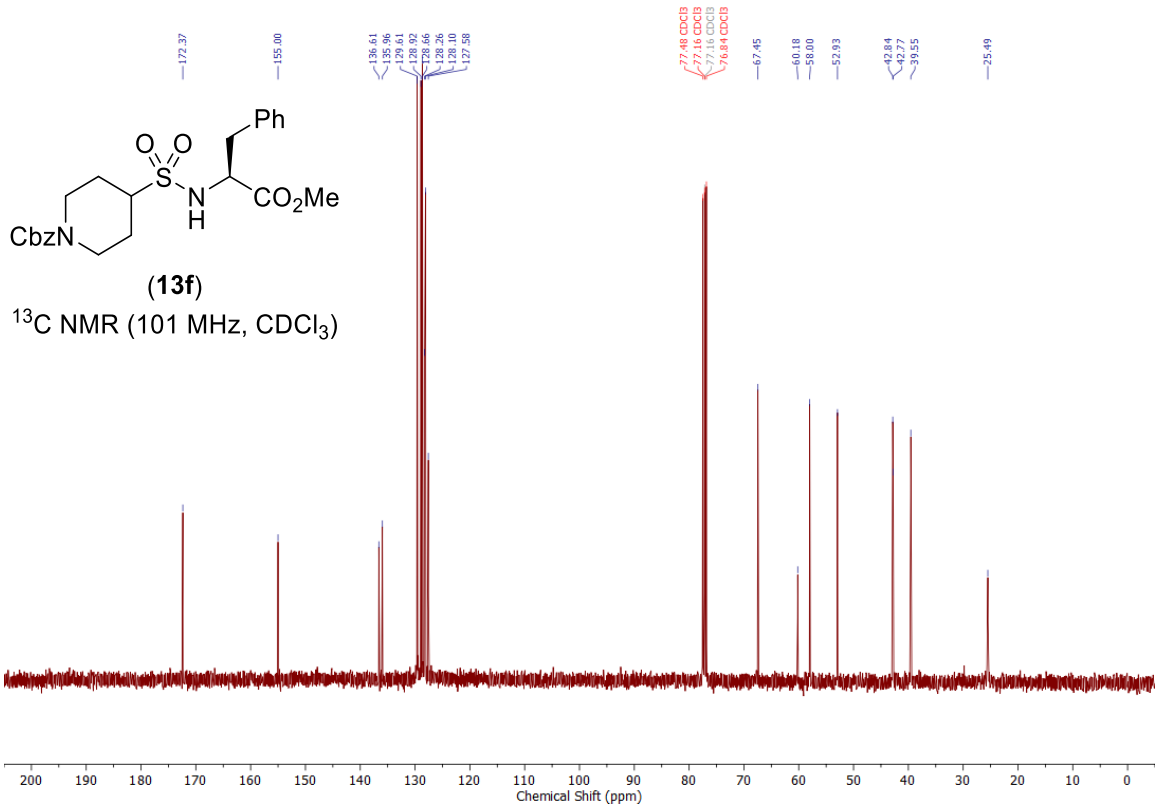
NMR spectra of benzyl 4-(*N*-benzylsulfamoyl)piperidine-1-carboxylate (13e)



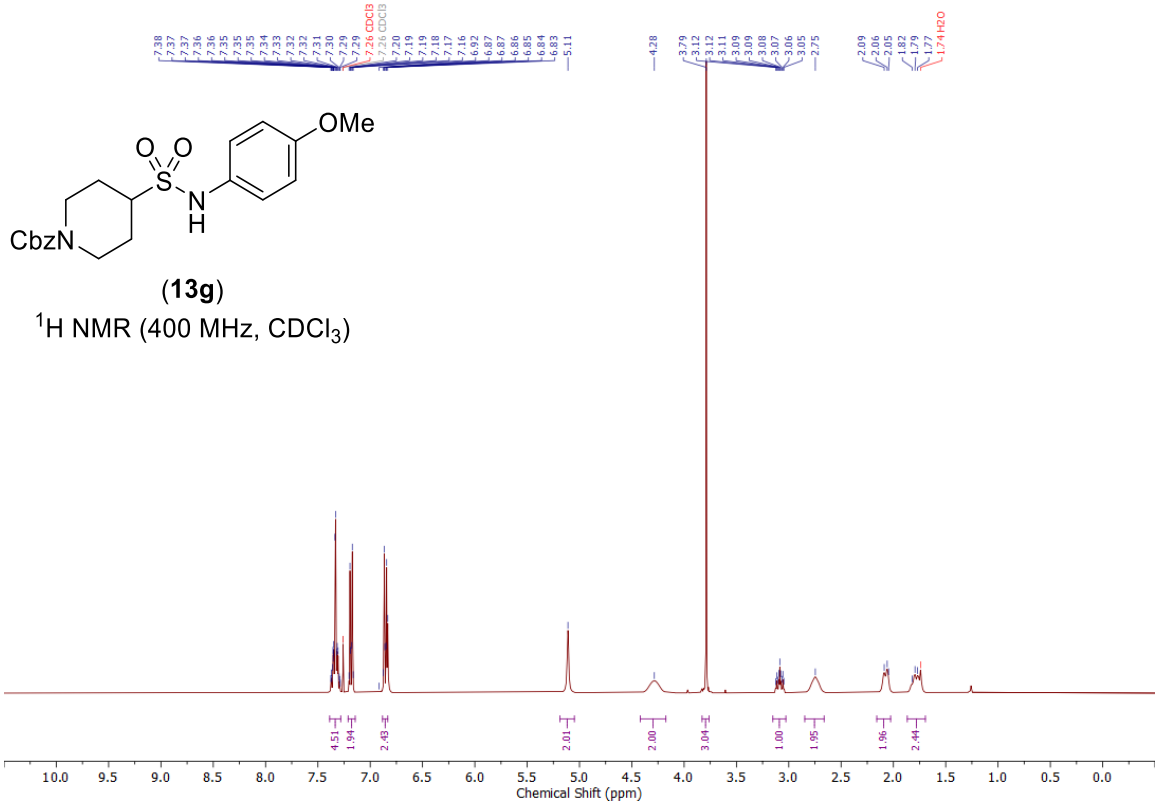


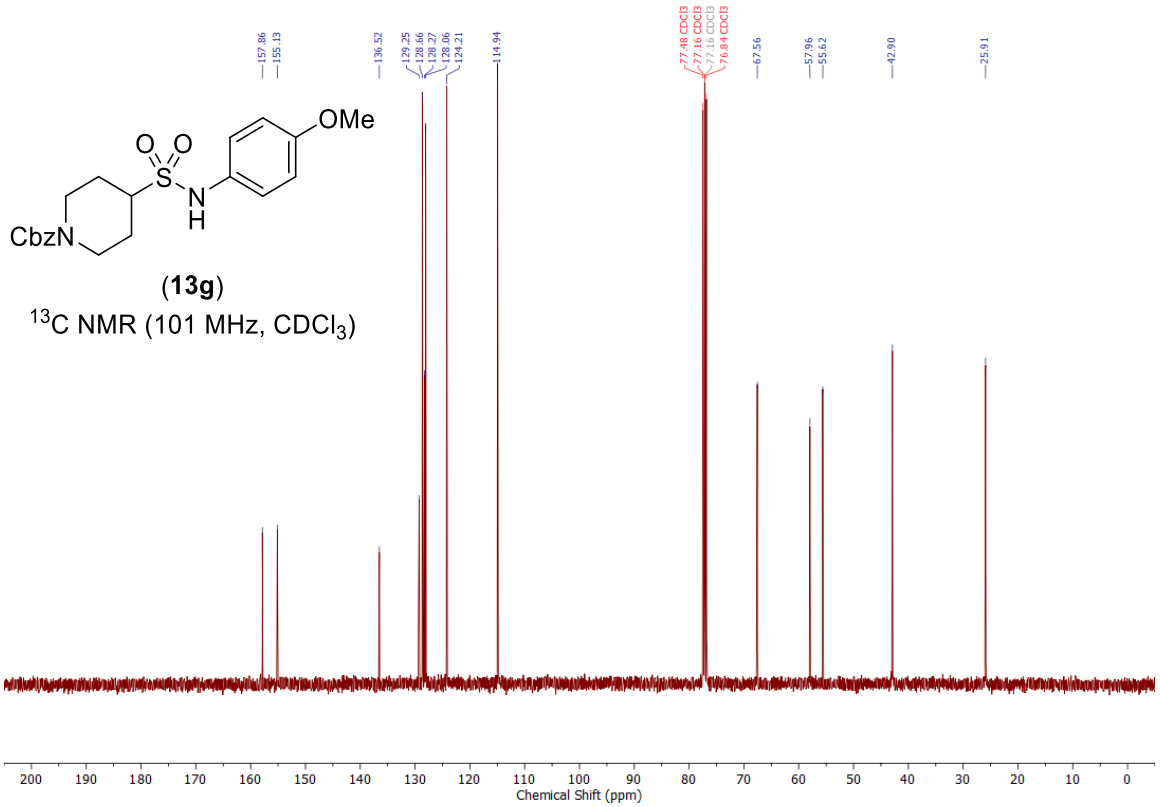
NMR spectra of benzyl (*S*)-4-(*N*-(1-methoxy-1-oxo-3-phenylpropan-2-yl)sulfamoyl)piperidine-1-carboxylate (13f)



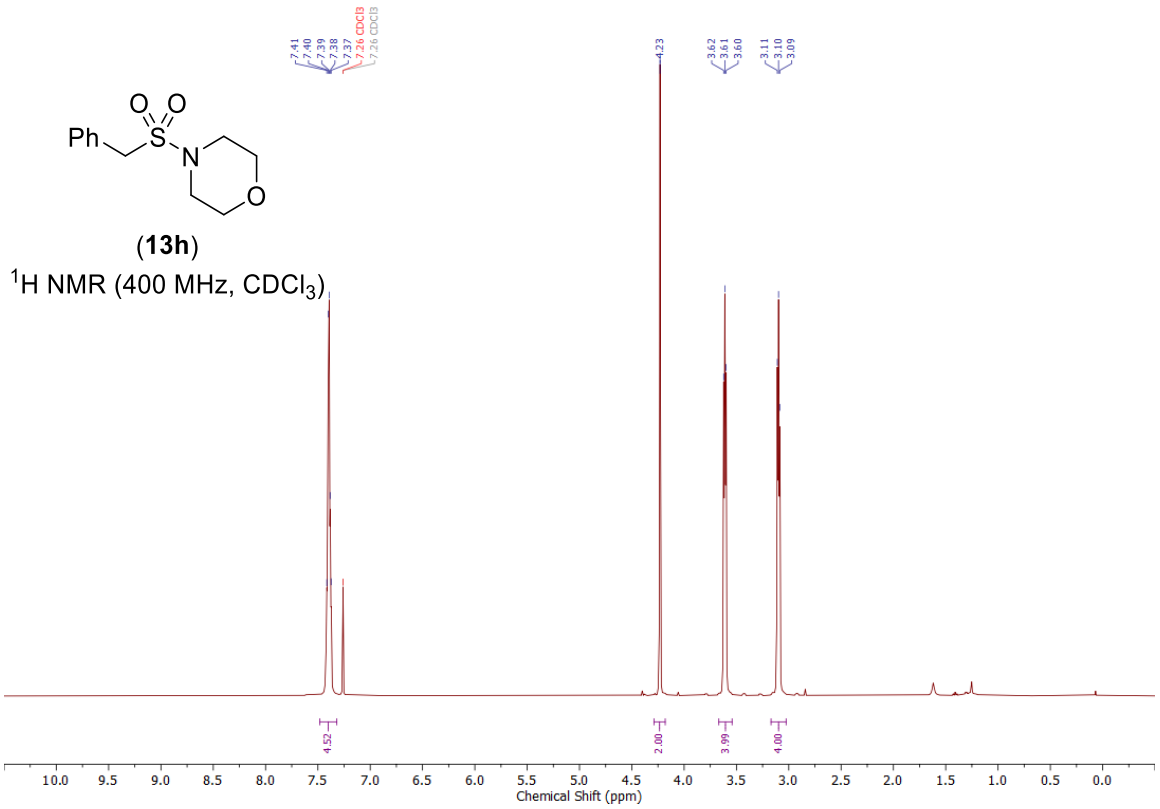


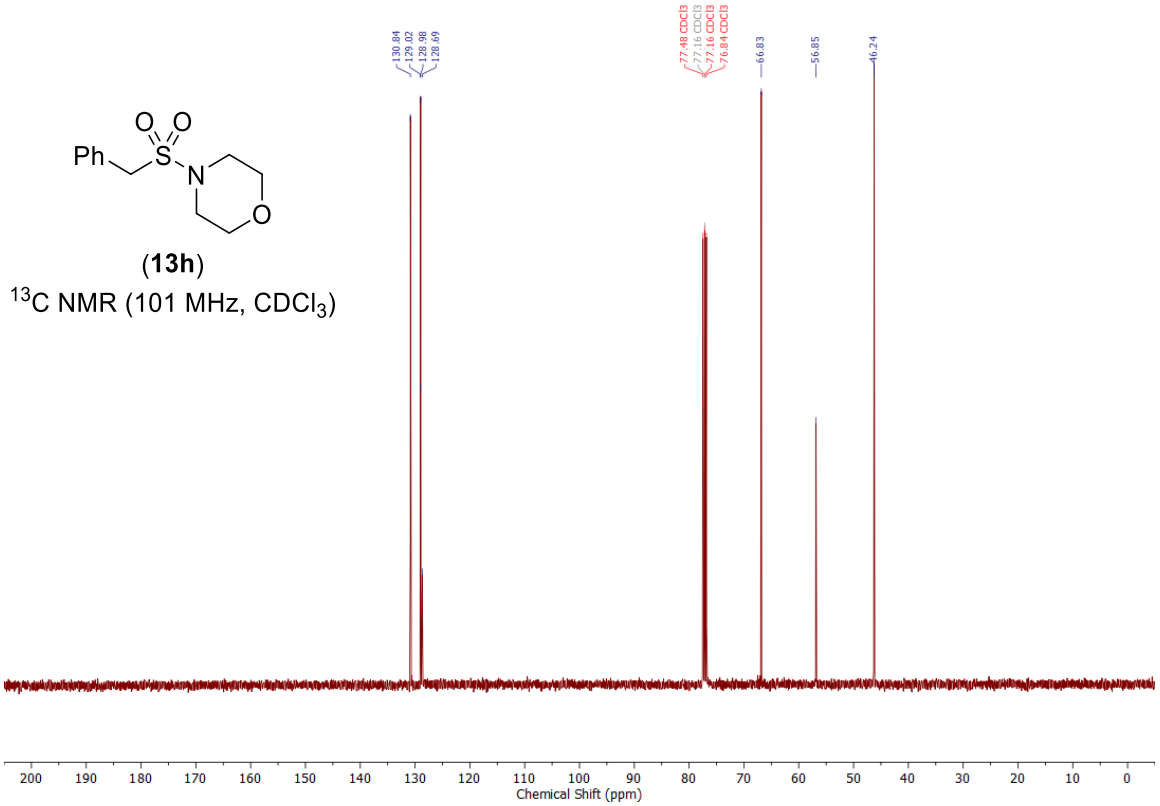
NMR spectra of benzyl 4-(*N*-(4-methoxyphenyl)sulfamoyl)piperidine-1-carboxylate (13g)



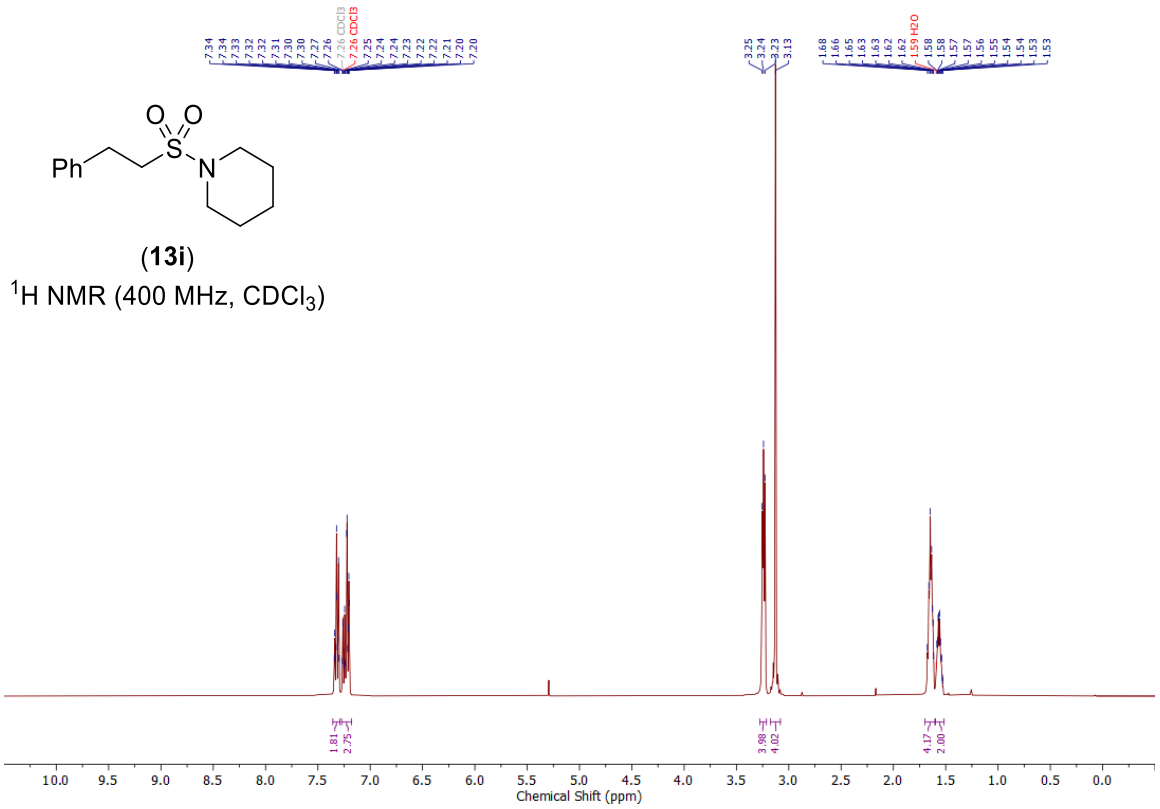


NMR spectra of 1-(benzylsulfonyl)morpholine (13h)



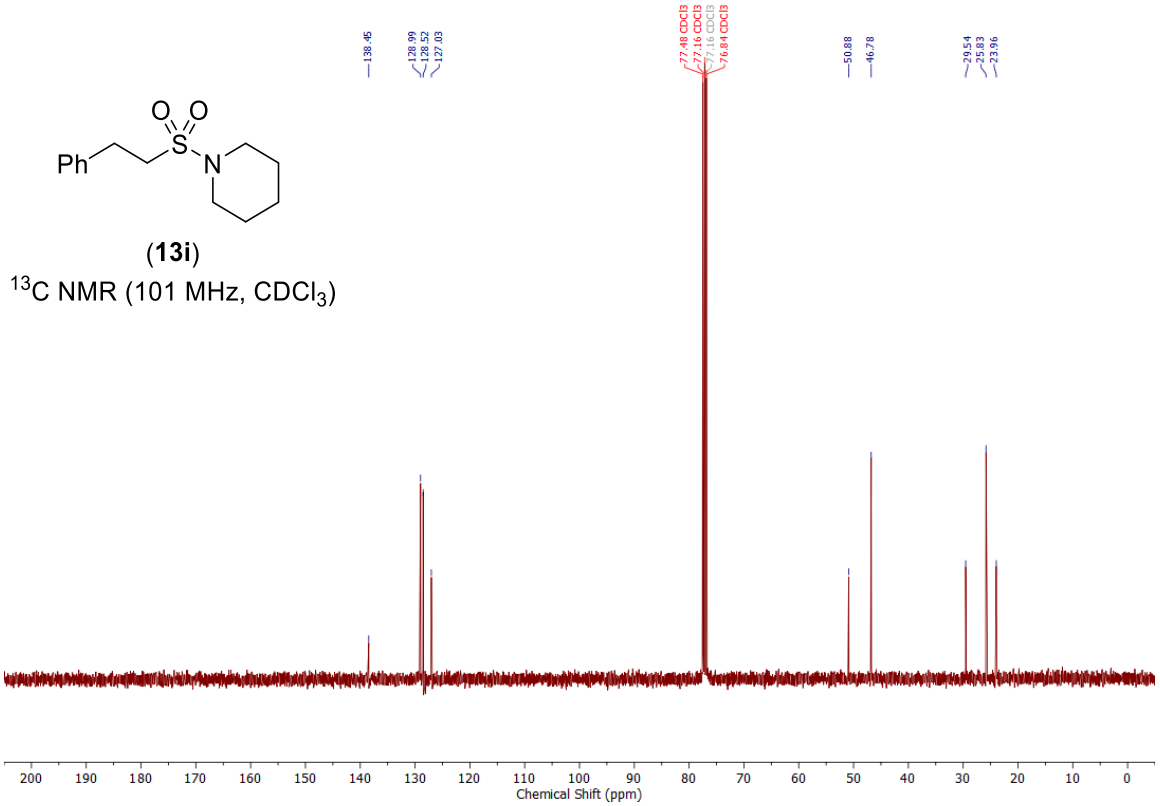


NMR spectra of 1-(phenethylsulfonyl)piperidine (13i)



(**13i**)

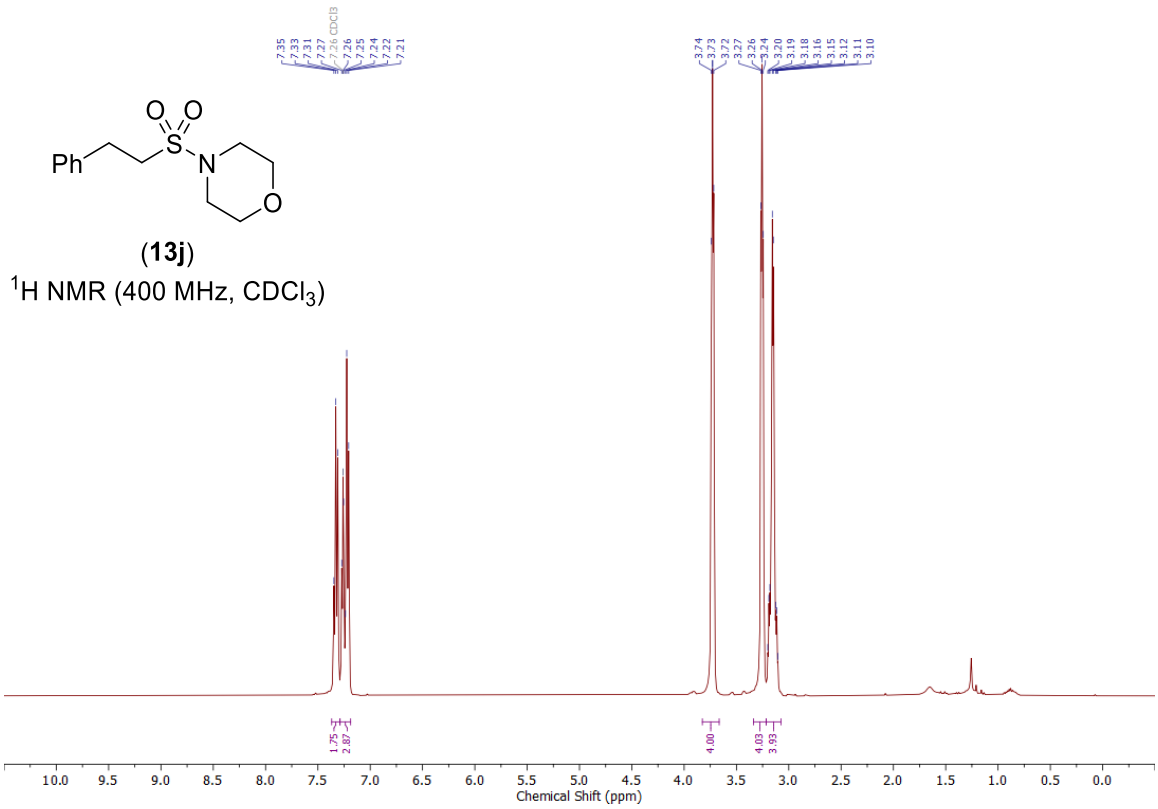
^{1}H NMR (400 MHz, $CDCl_3$)

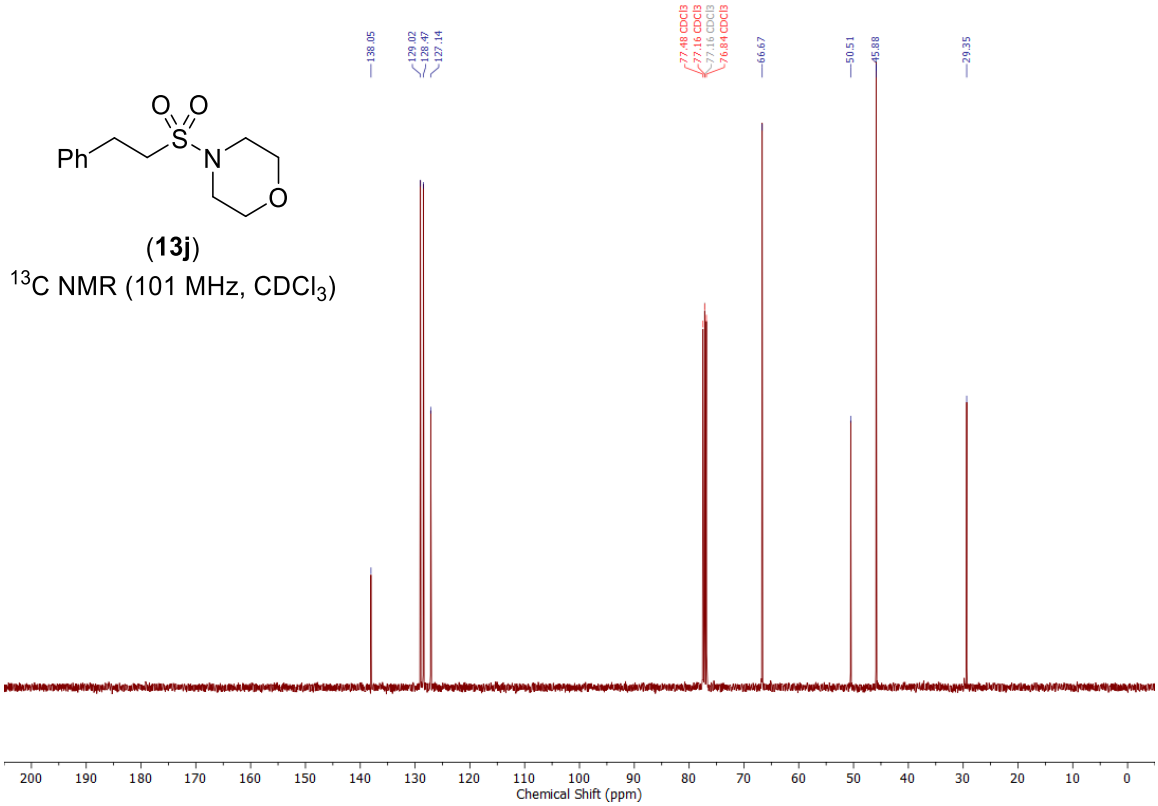


(**13i**)

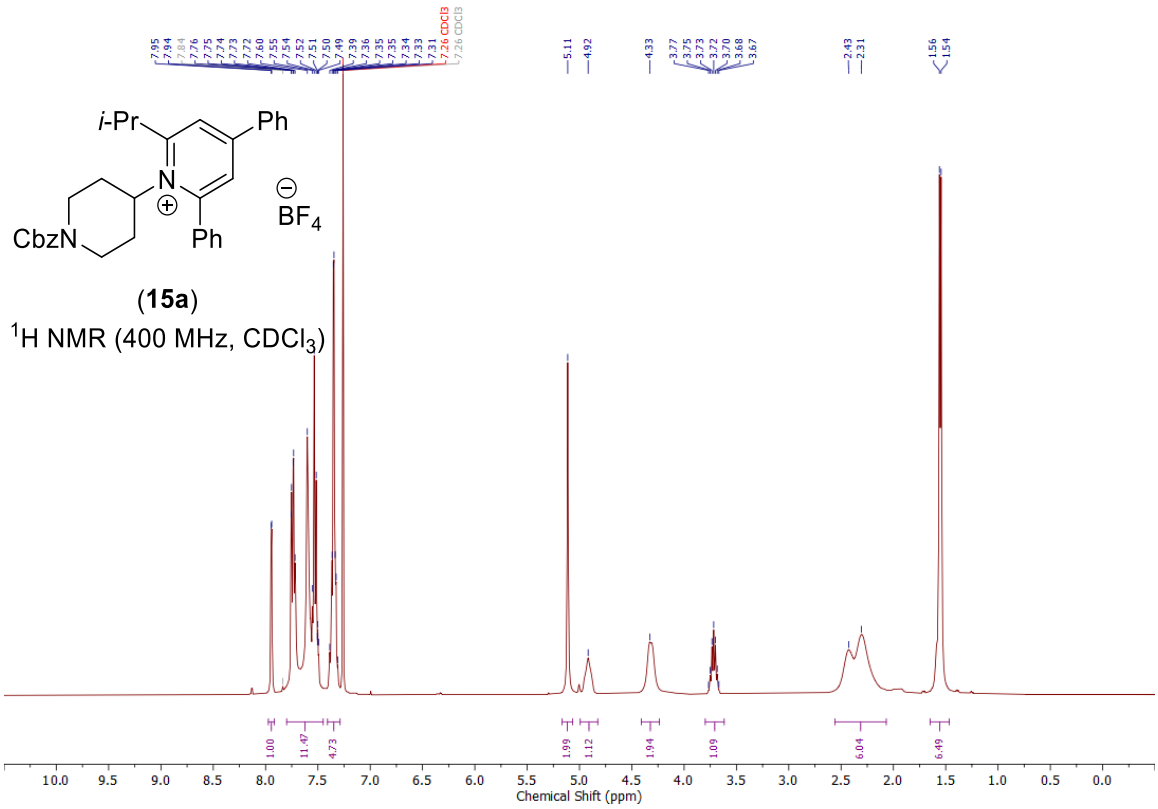
^{13}C NMR (101 MHz, $CDCl_3$)

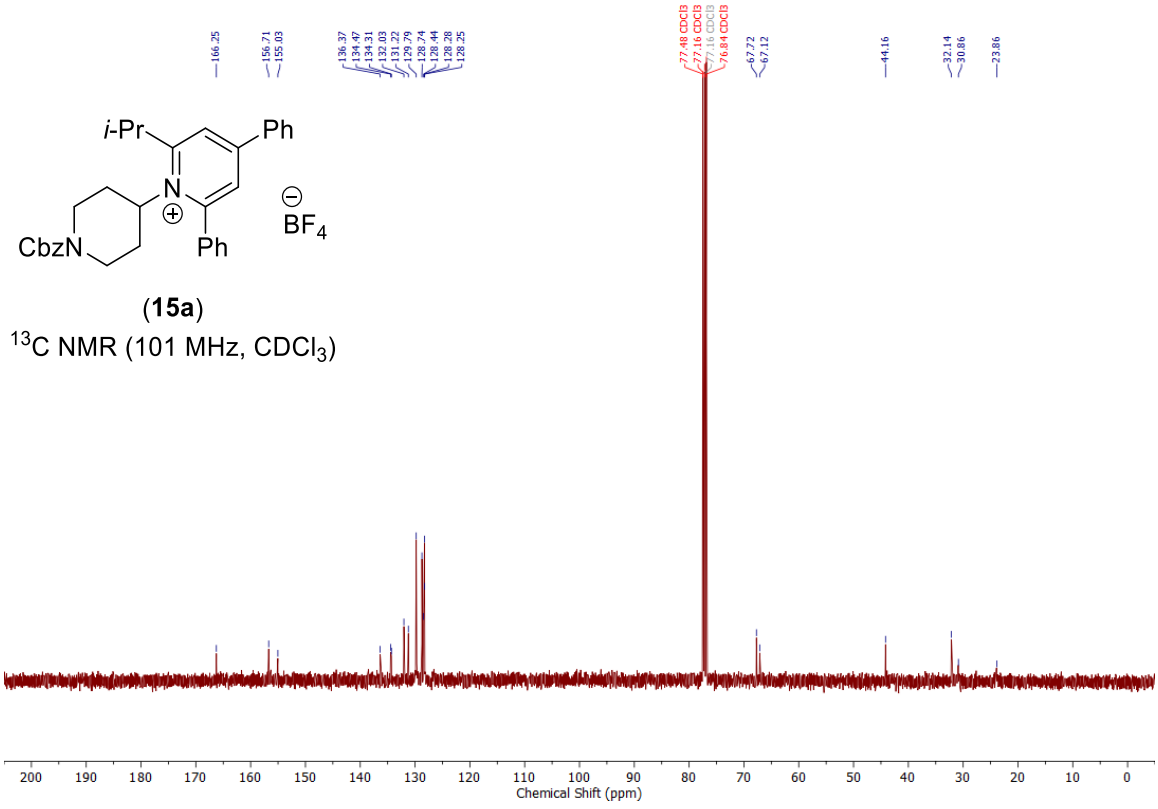
NMR spectra of 4-(phenethylsulfonyl)morpholine (13j)

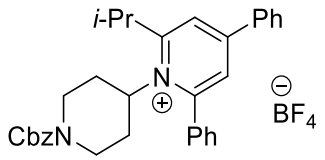




NMR spectra of 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2-isopropyl-4,6-diphenylpyridin-1-ium tetrafluoroborate (15a)



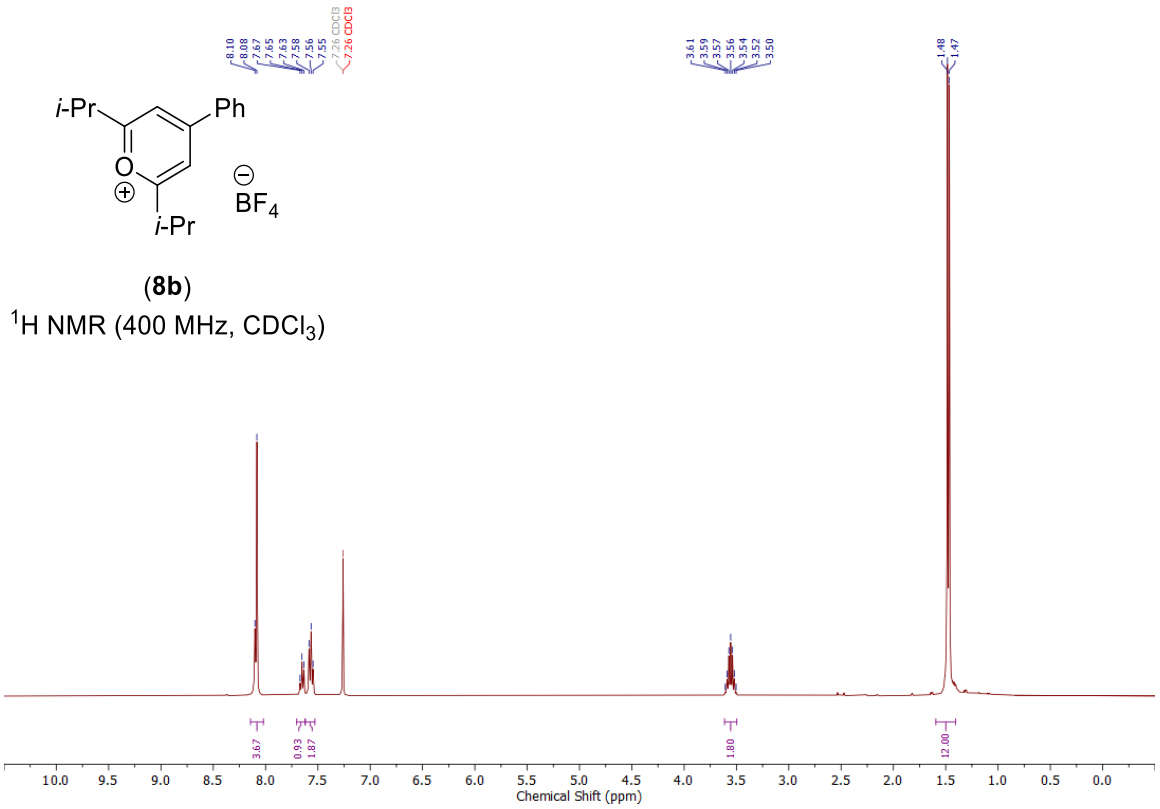




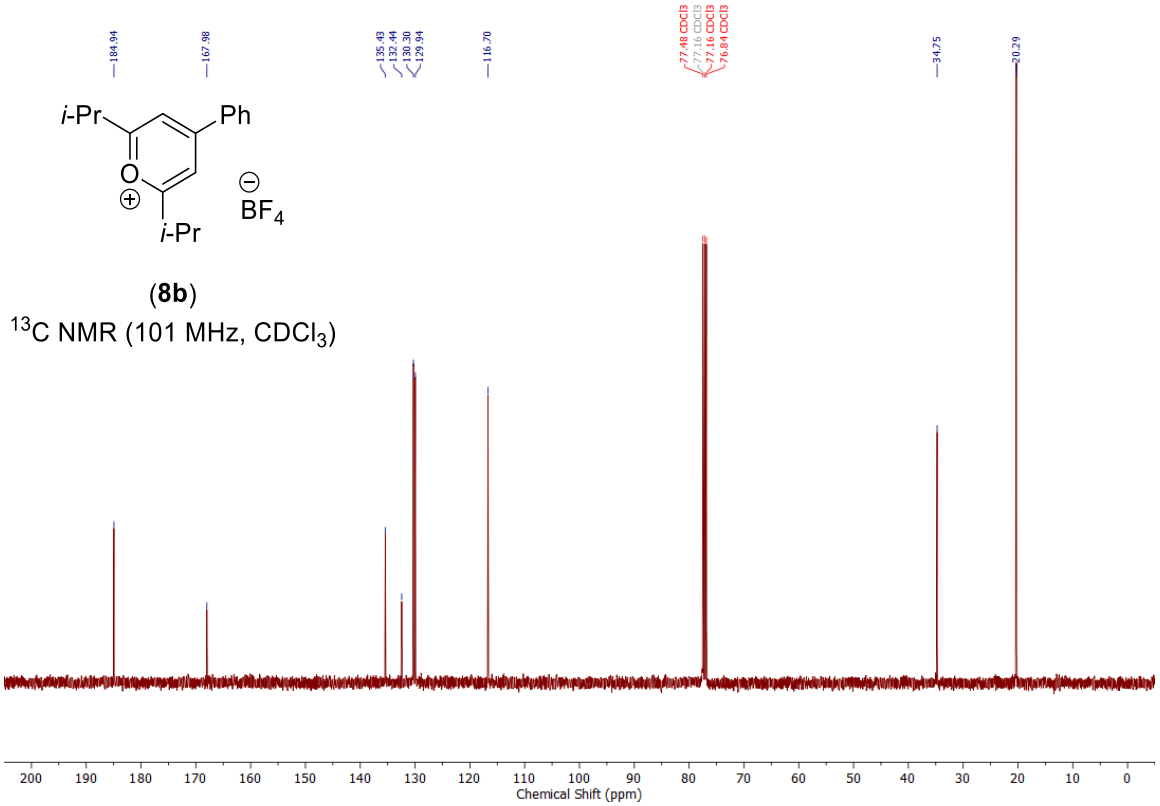
(**15a**)

^{19}F NMR (377 MHz, $CDCl_3$)

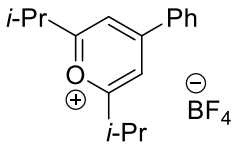
NMR spectra of 2,6-diisopropyl-4-phenylpyrylium tetrafluoroborate (8b)



(**8b**)
^{1}H NMR (400 MHz, $CDCl_3$)



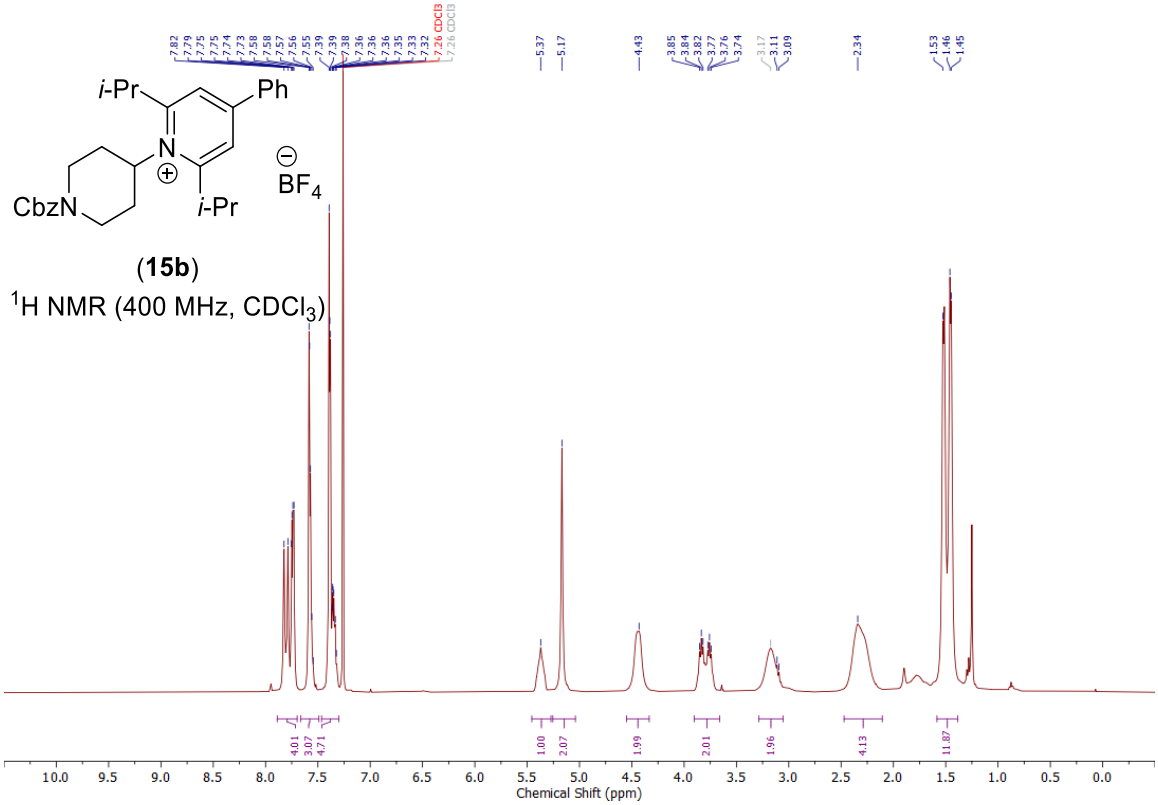
(**8b**)
^{13}C NMR (101 MHz, $CDCl_3$)

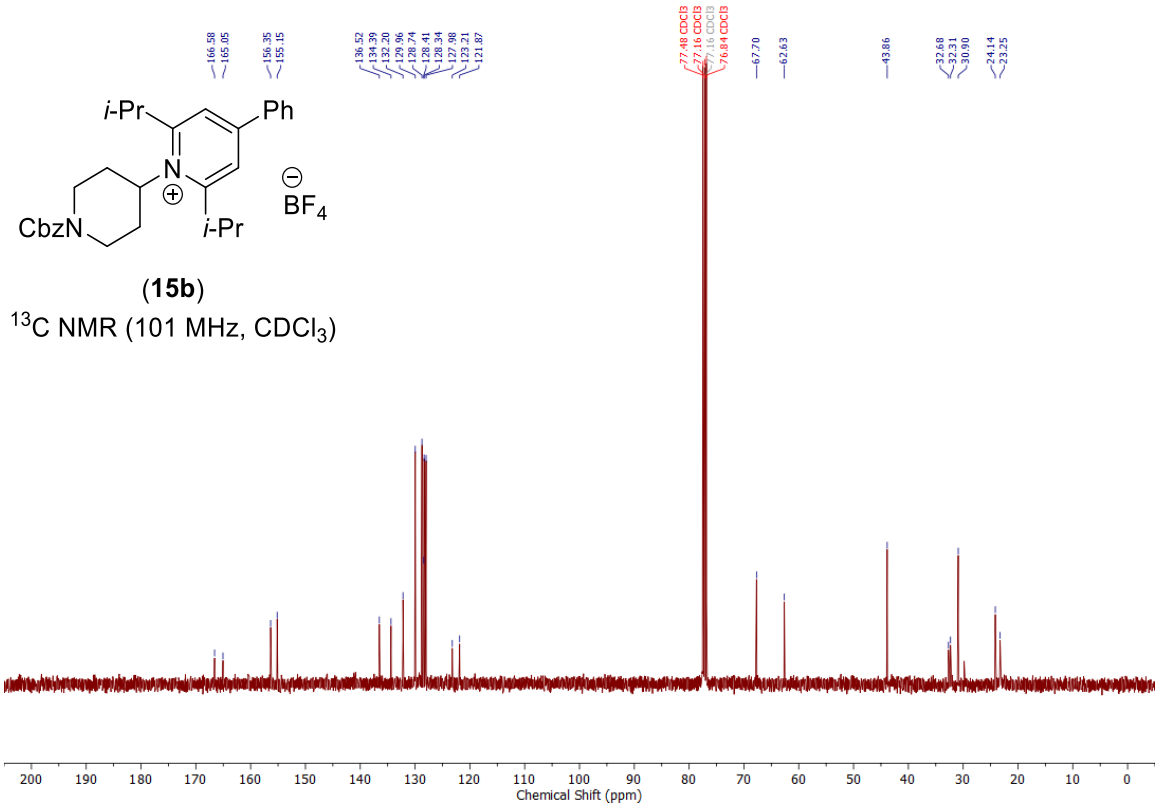


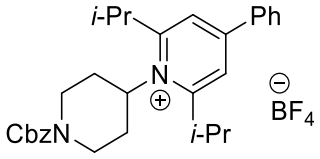
(**8b**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,6-diisopropyl-4-phenylpyridin-1-ium tetrafluoroborate (15b)



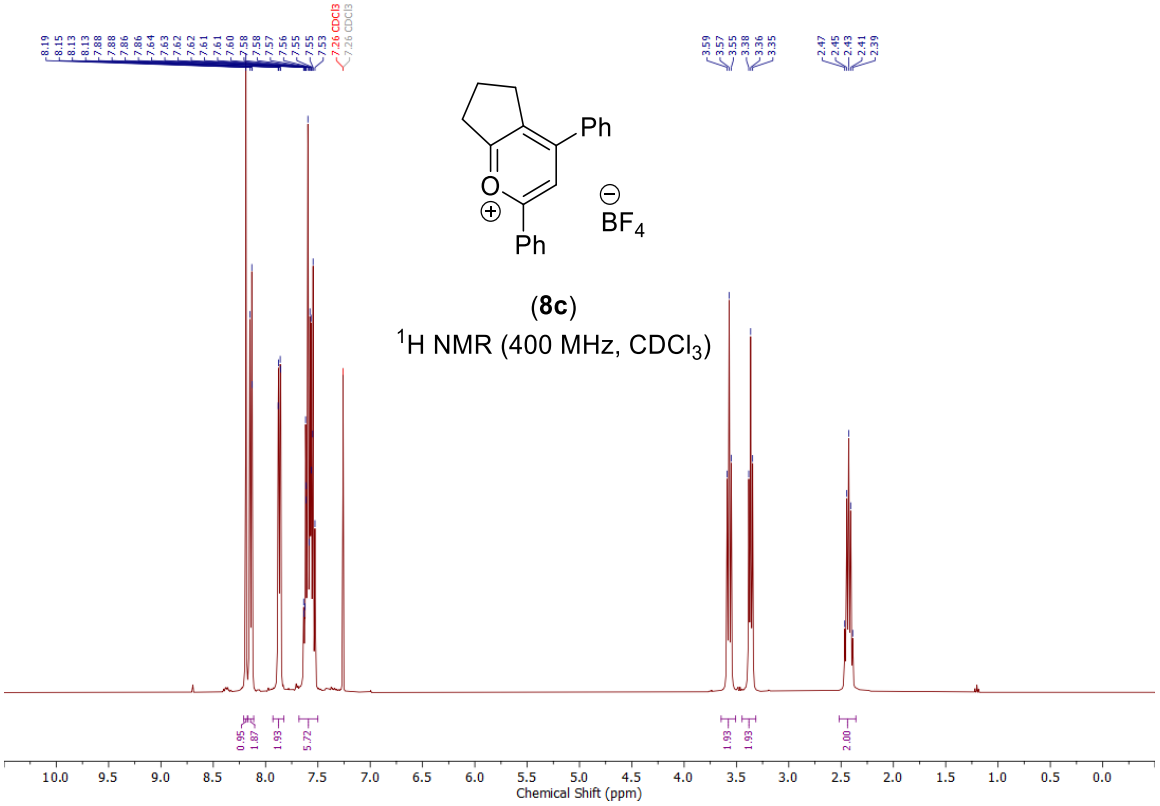


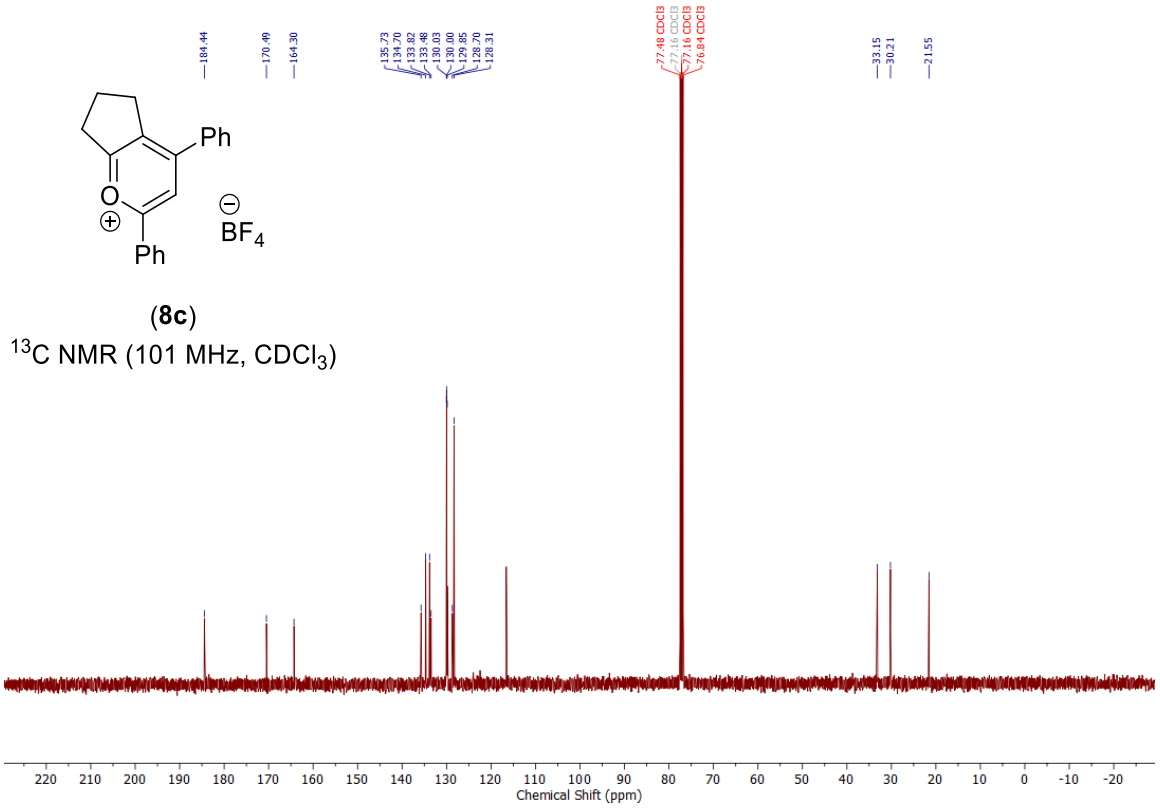


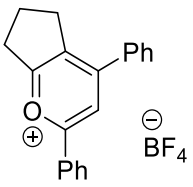
(**15b**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 2,4-diphenyl-6,7-dihydro-5*H*-cyclopenta[*b*]pyran-1-ium trifluoromethanesulfonate (8c)



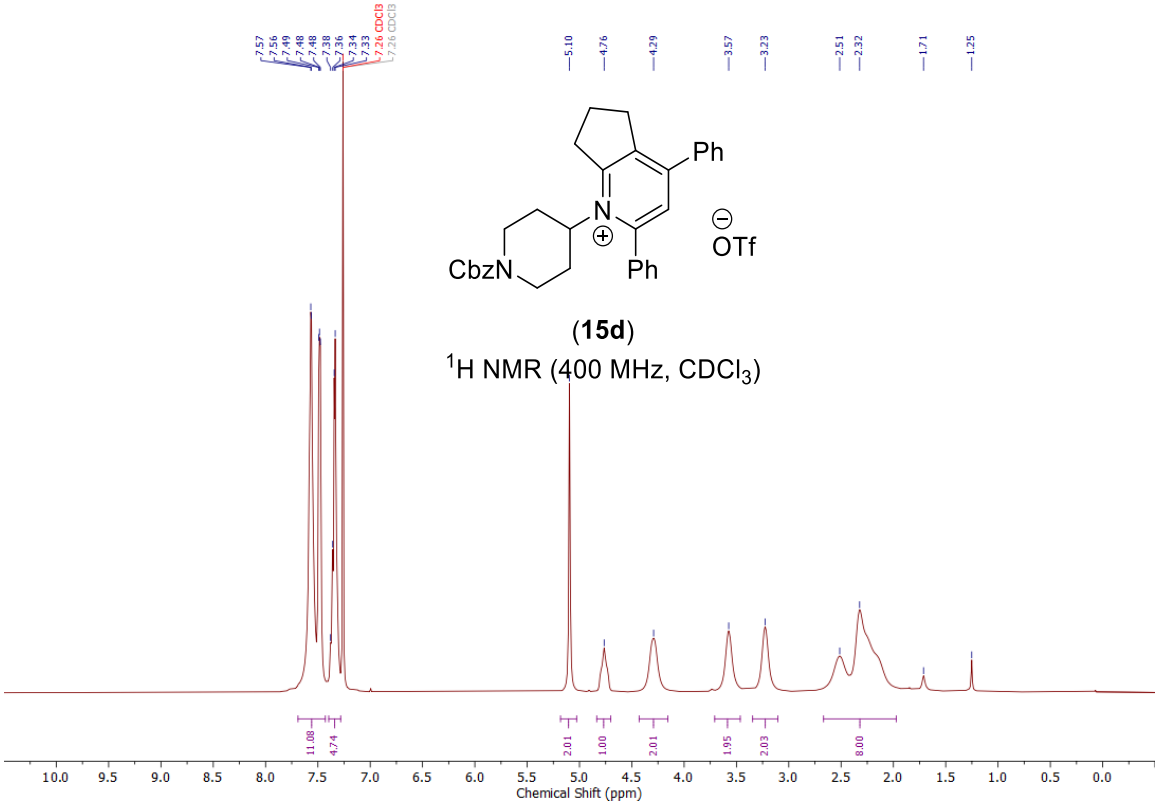


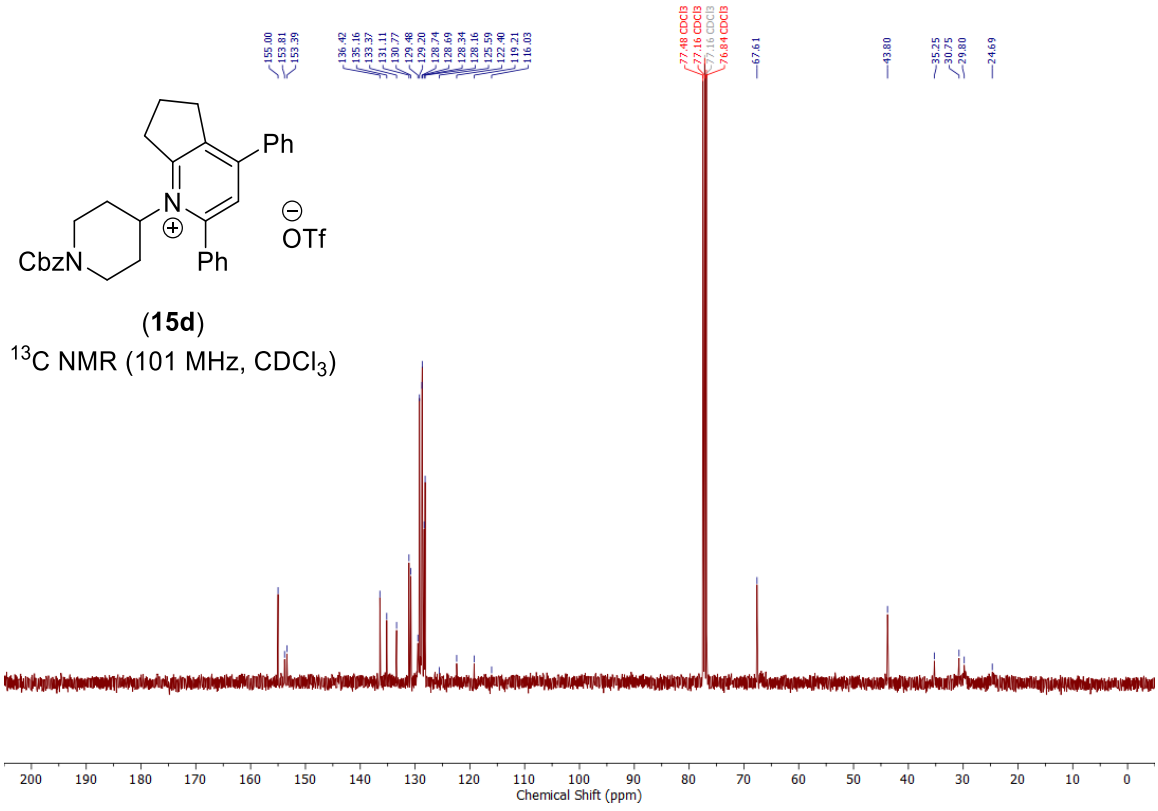


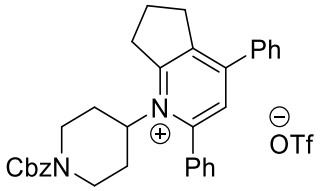
(**8c**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,4-diphenyl-6,7-dihydro-5*H*-cyclopenta[*b*]pyridin-1-ium trifluoromethanesulfonate (15d)



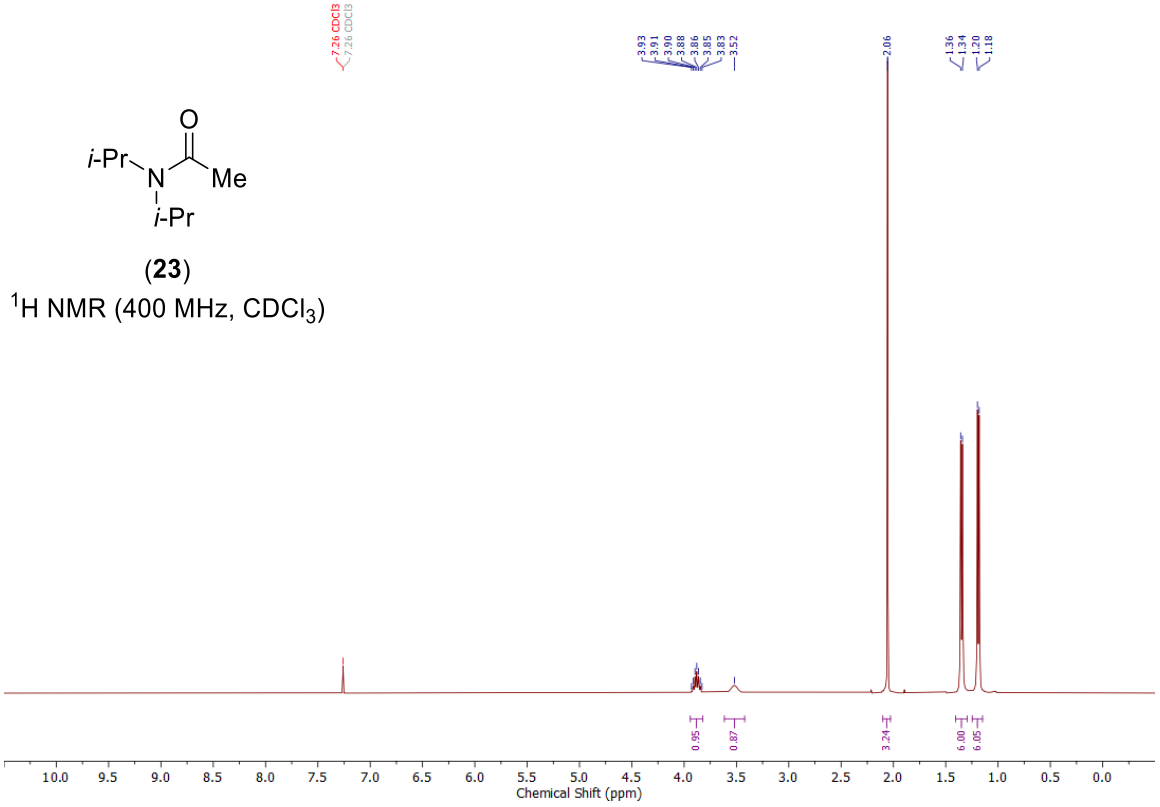


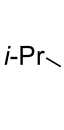


(**15d**)

^{19}F NMR (101 MHz, $CDCl_3$)

NMR spectra of *N,N*-diisopropylacetamide (23)





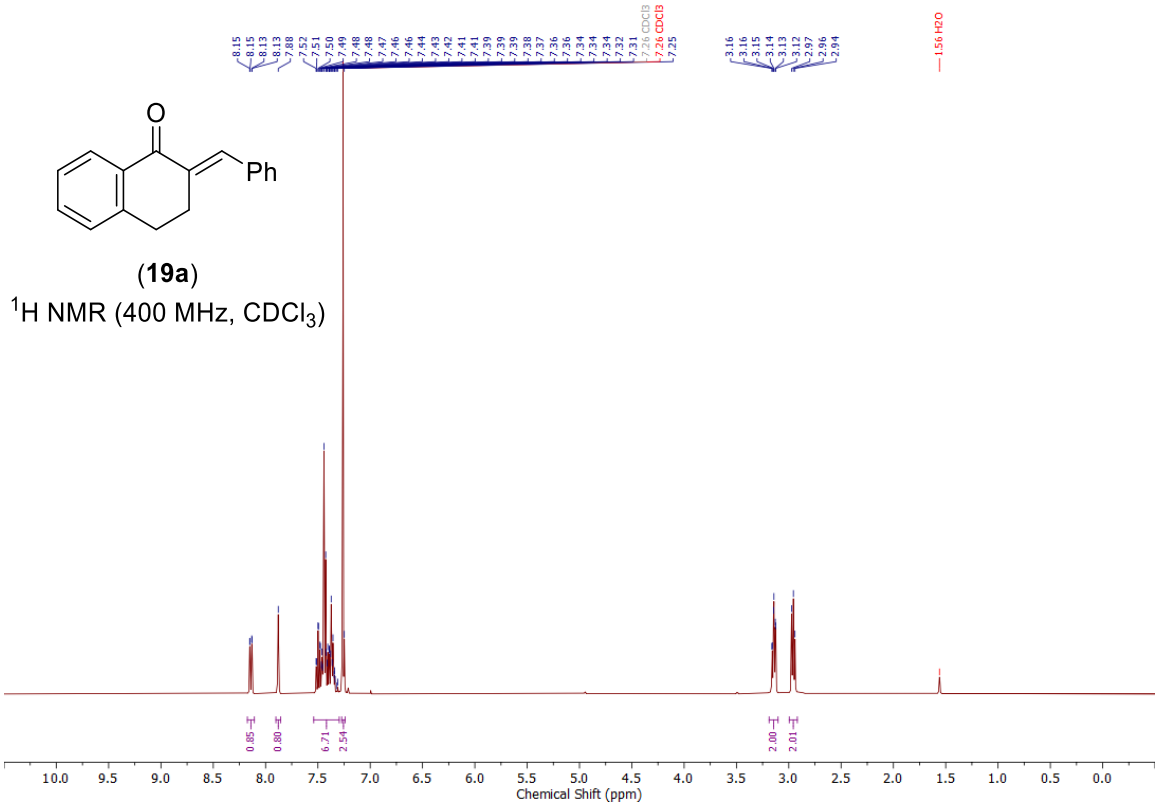
(**23**)

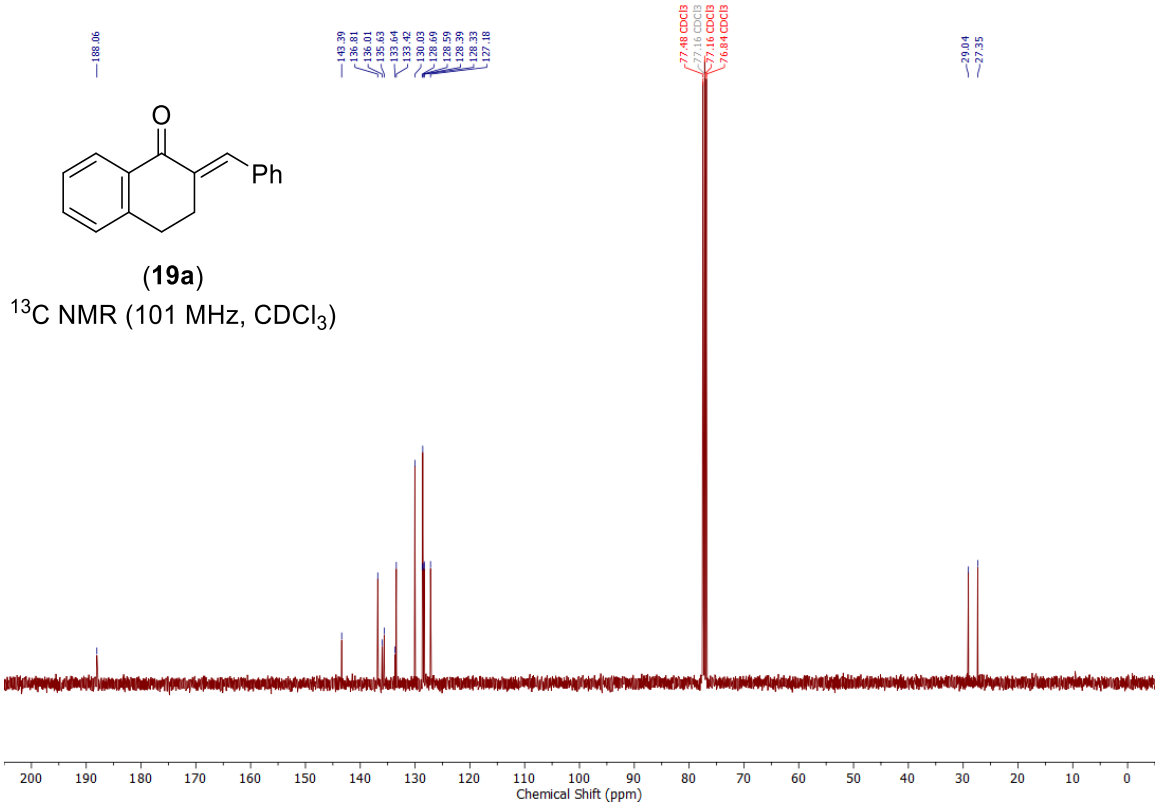
^{1}H NMR (400 MHz, $CDCl_3$)

(**23**)

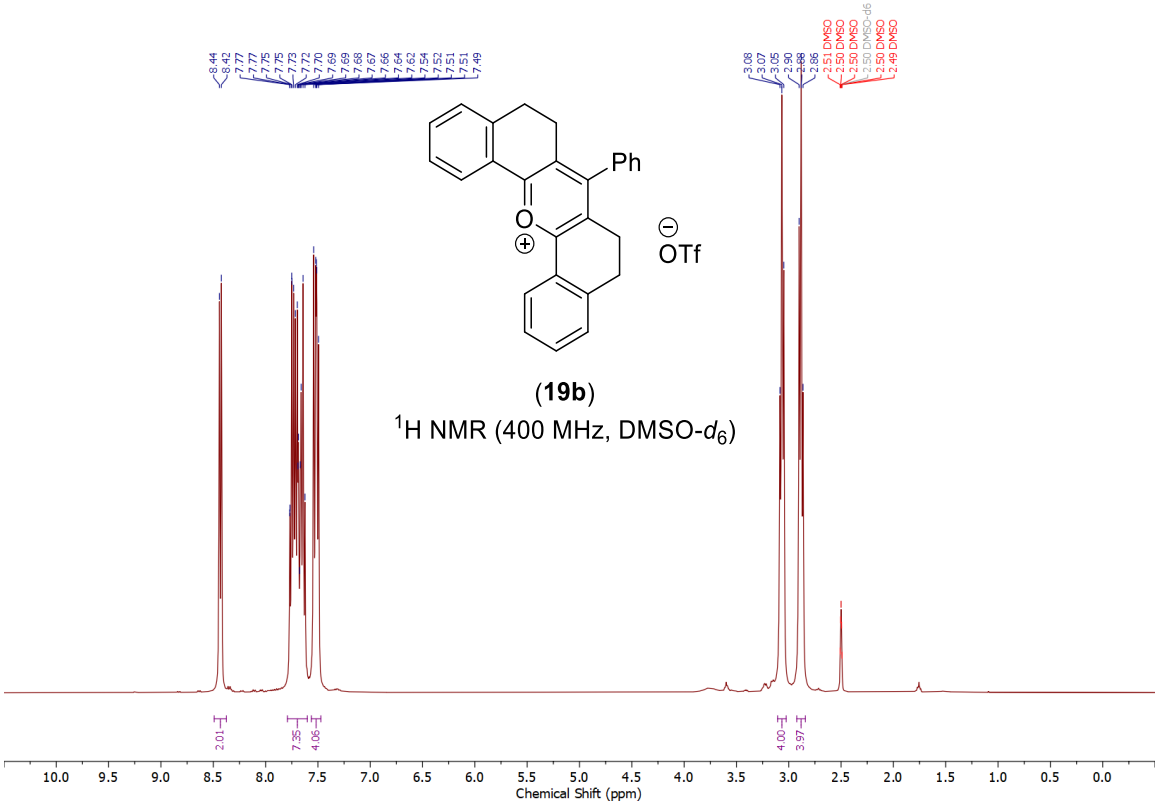
^{13}C NMR (101 MHz, $CDCl_3$)

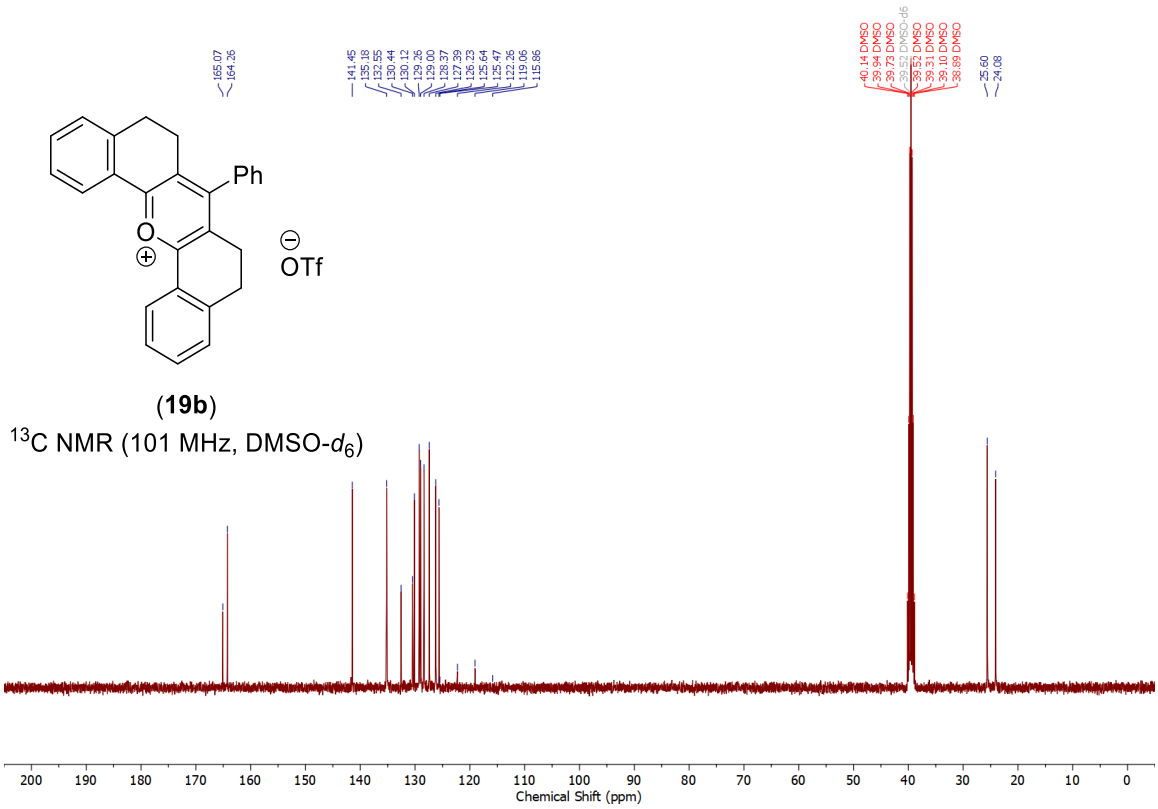
NMR spectra of (*E*)-2-benzylidene-3,4-dihydronaphthalen-1(2*H*)-one (19a)

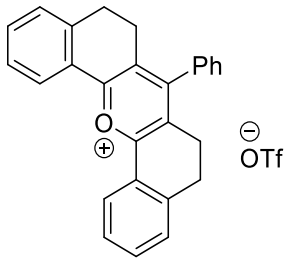




NMR spectra of 7-phenyl-5,6,8,9-tetrahydrodibenzo[*c*,*h*]xanthen-14-ium trifluoromethanesulfonate (19b)



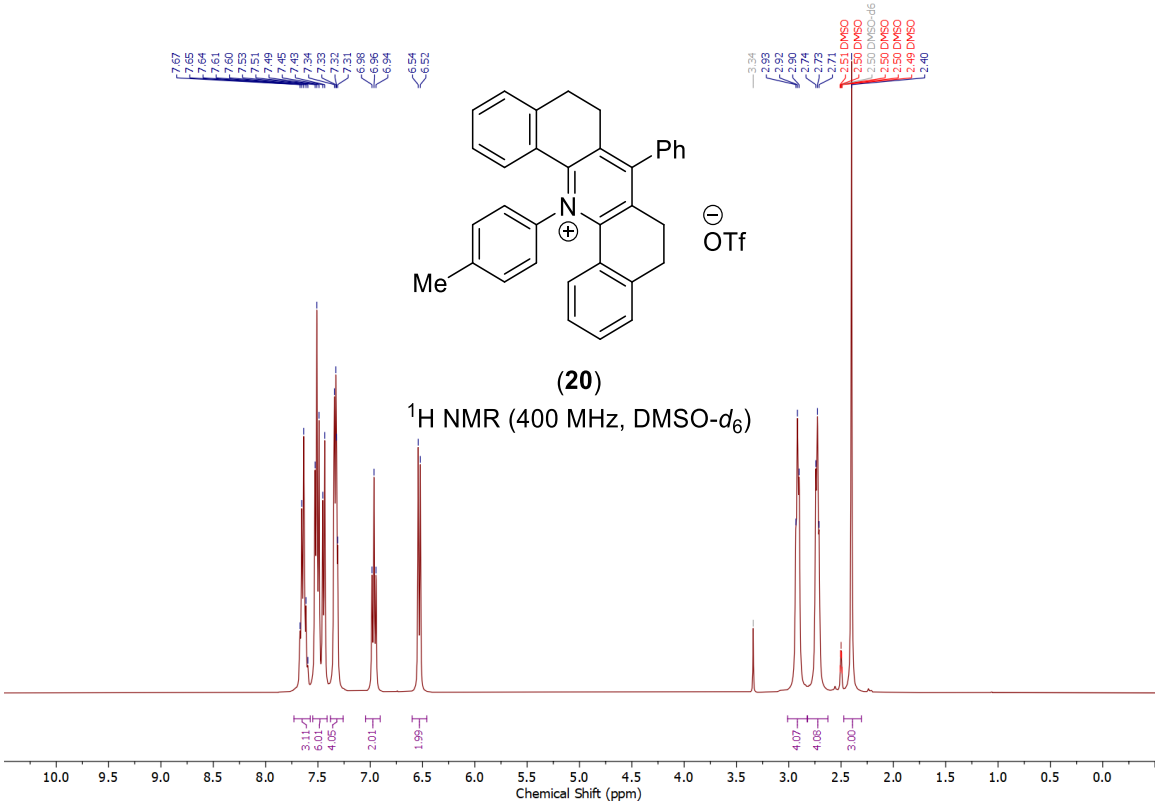


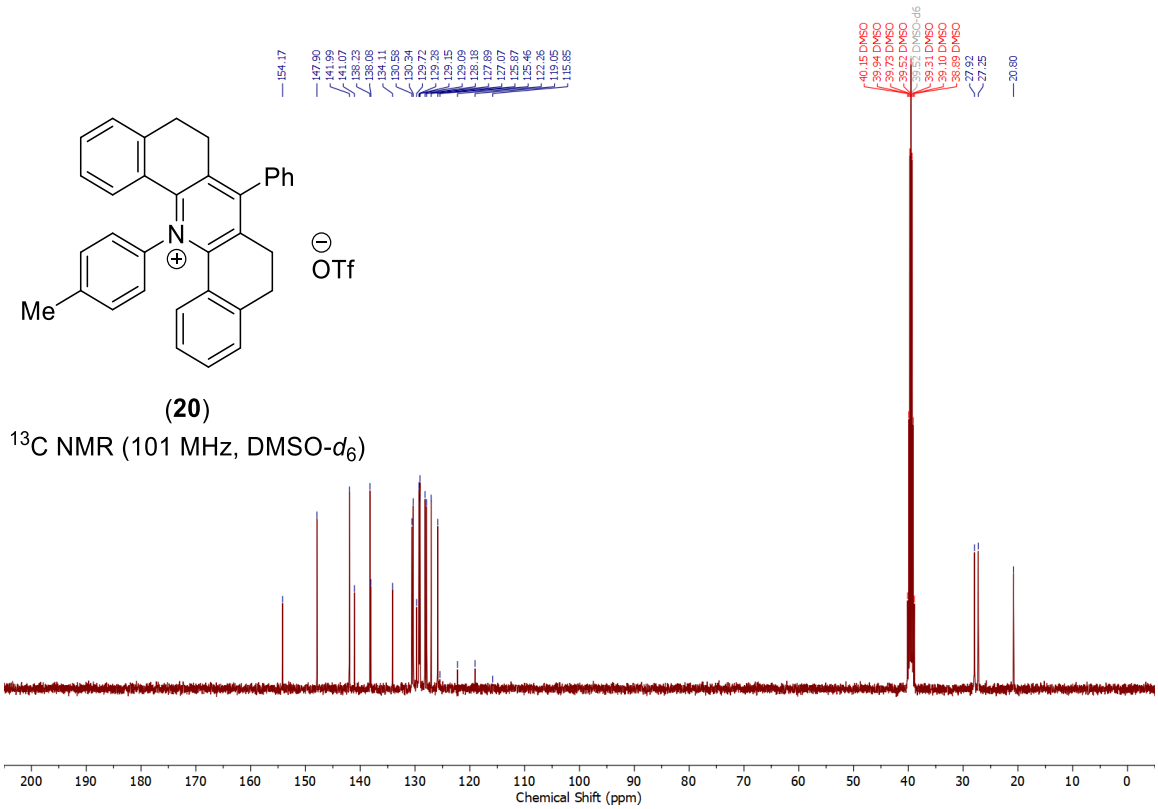


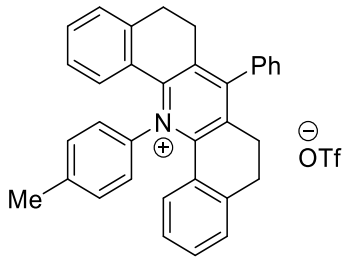
(**19b**)

^{19}F NMR (377 MHz, DMSO-d_6)

NMR spectra of 7-phenyl-14-(*p*-tolyl)-5,6,8,9-tetrahydrodibenzo[*c*,*h*]acridin-14-ium trifluoromethanesulfonate (20)



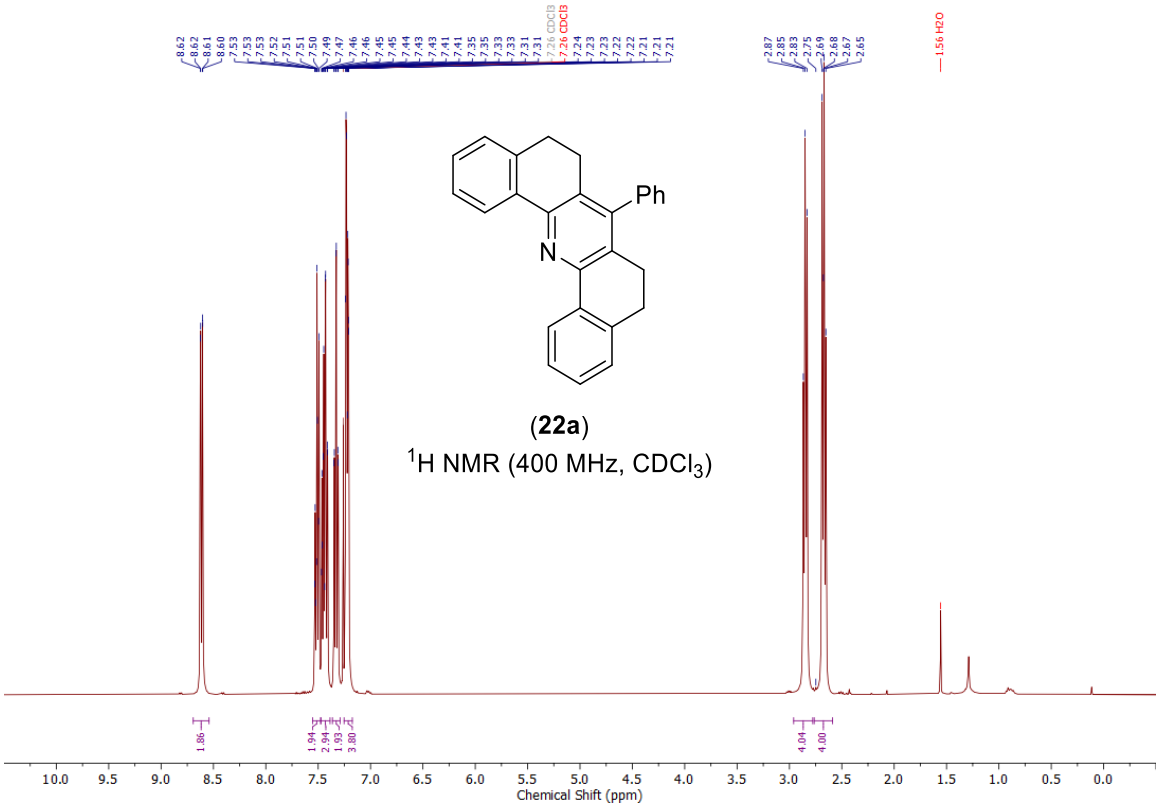


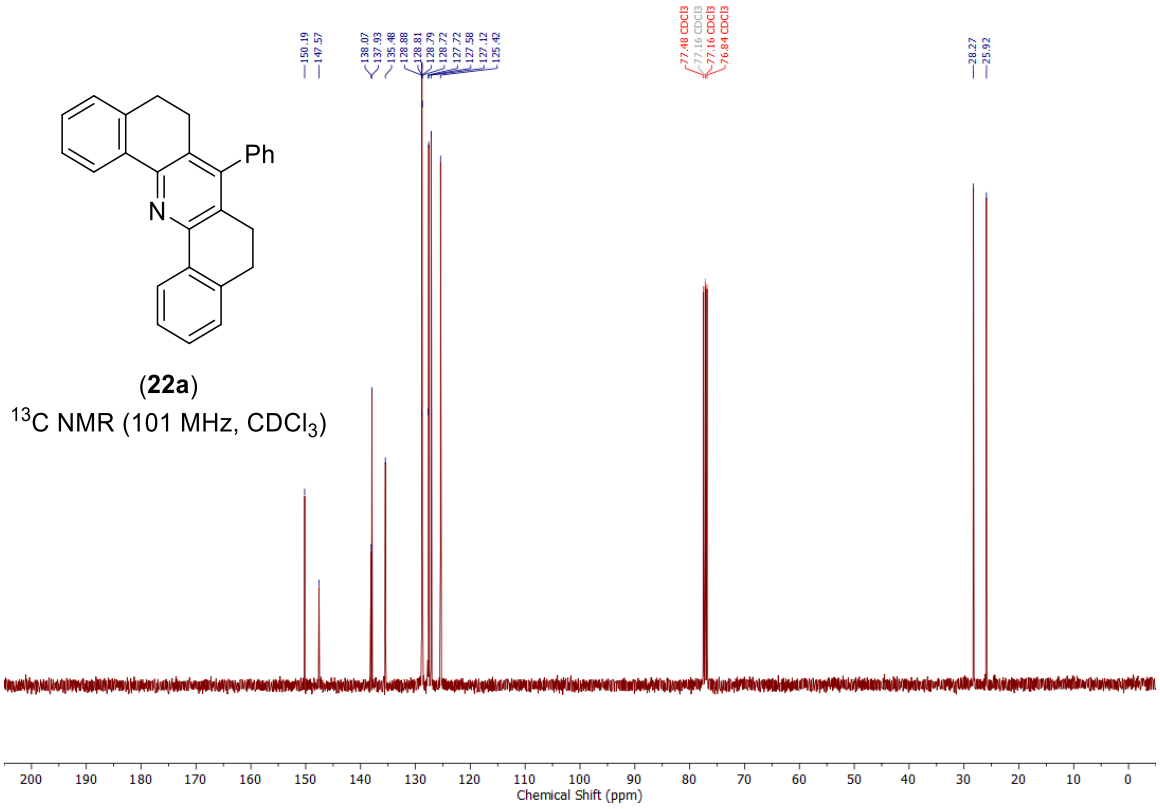


(**20**)

^{19}F NMR (377 MHz, DMSO-d_6)

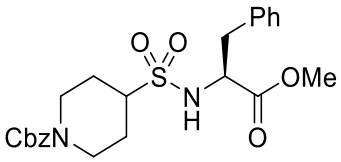
NMR spectra of 7-phenyl-5,6,8,9-tetrahydrodibenzo[*c*,*h*]acridine (22a)





10.2 Chiral HPLC Traces for Chapter 2

Benzyl (*S*)-4-(*N*-(1-methoxy-1-oxopropan-2-yl)sulfamoyl)piperidine-1-carboxylate (13f)



ee determined by chiral SFC using a Chiralpak® IC column, 1500 psi, 30 °C; flow: 1.5 mL/min; 1-30% MeOH in 5 min, 98% ee (major enantiomer t_R = 4.305 min, minor enantiomer t_R = 4.497 min).

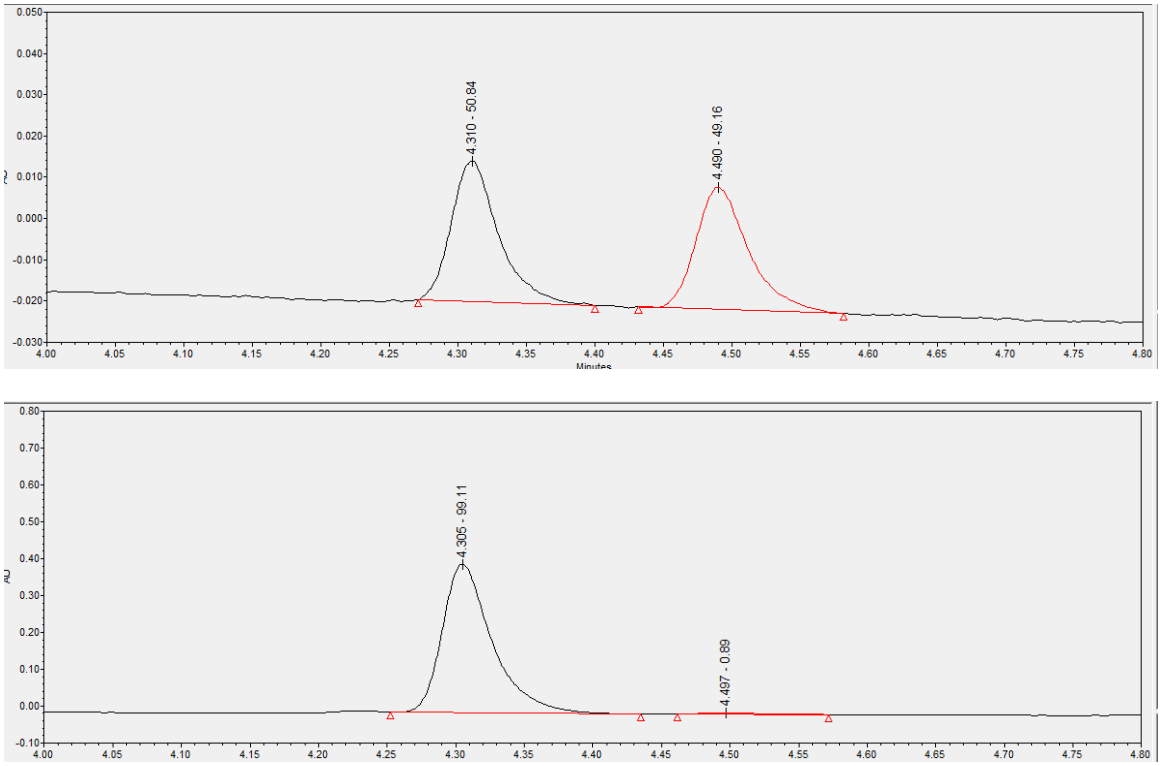
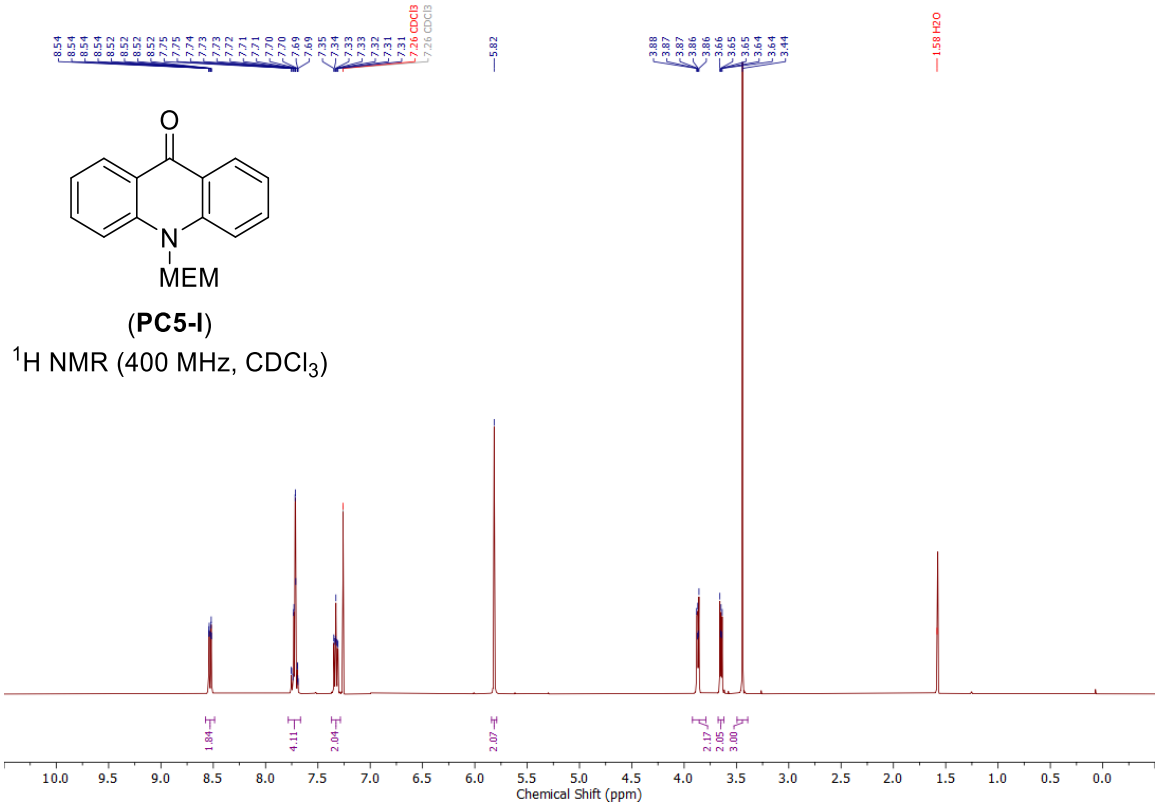
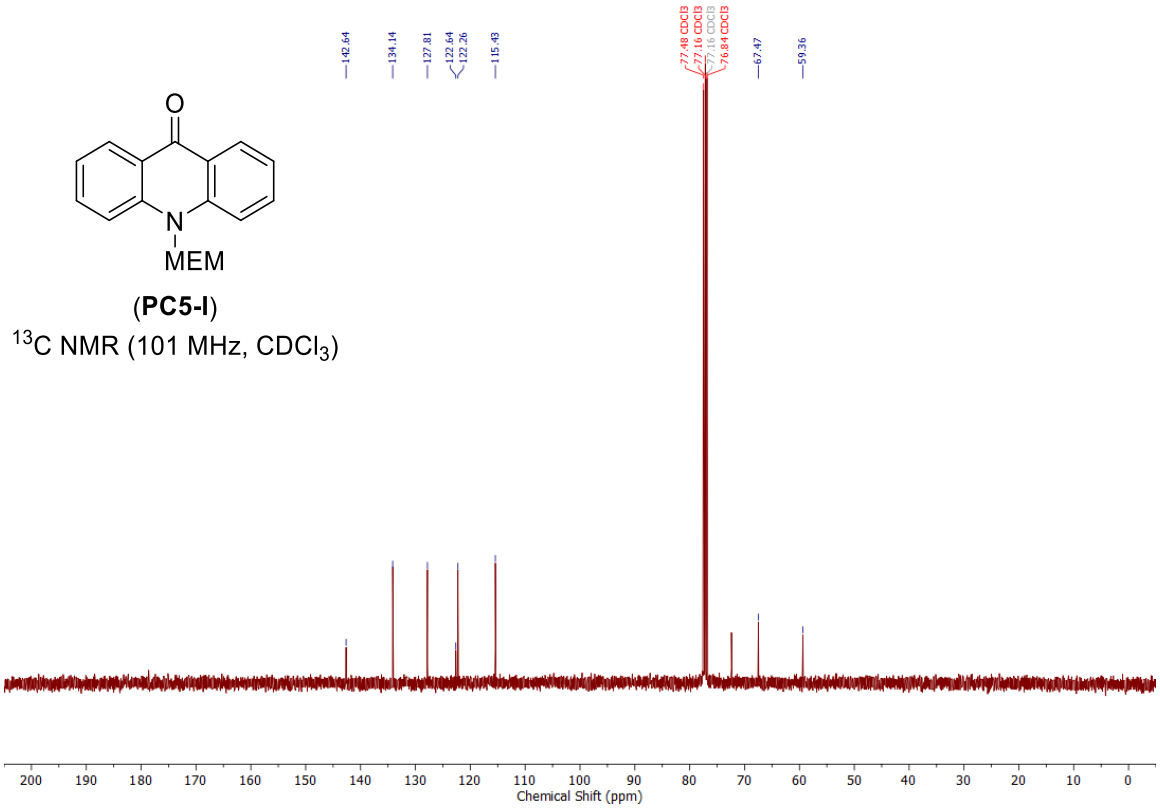


Figure S4: SFC traces of racemic (±)-**13f** (top) and enantioenriched **13f** (bottom).

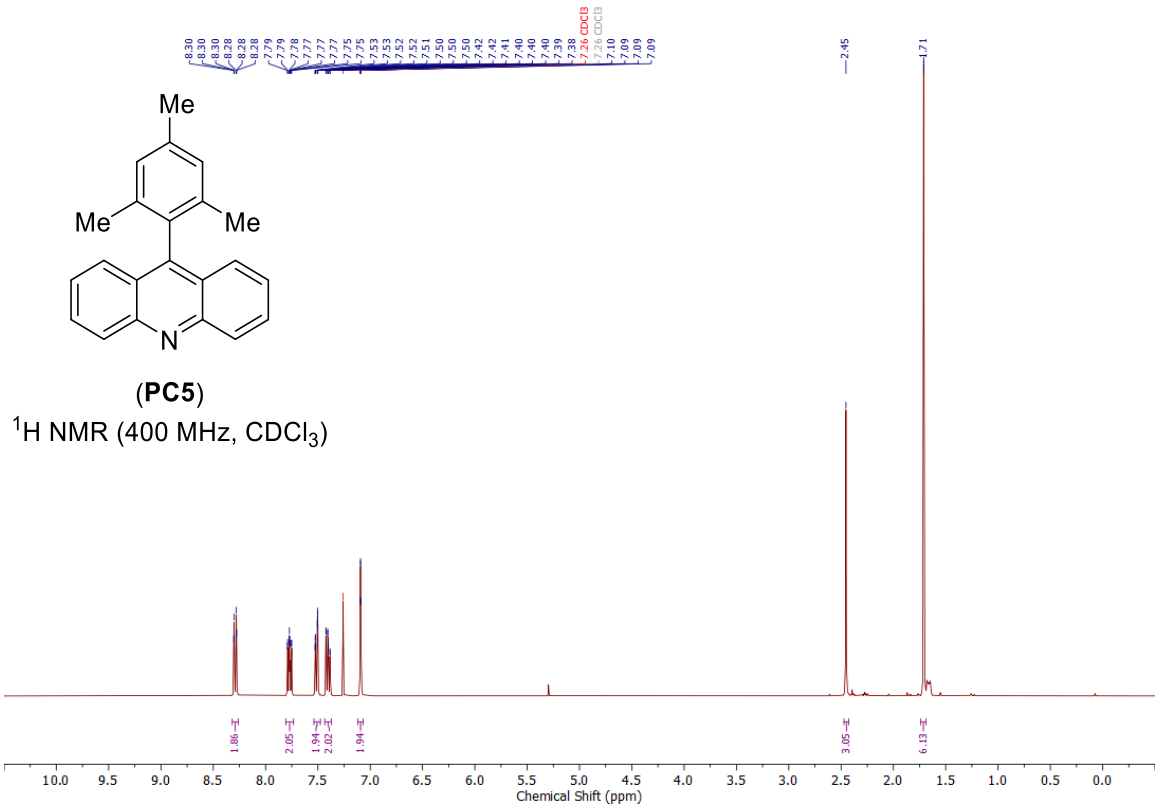
10.3 NMR Spectra for Chapter 3

NMR spectra of *N*-(2-methoxyethoxymethyl)-9-acridone (PC5-I)



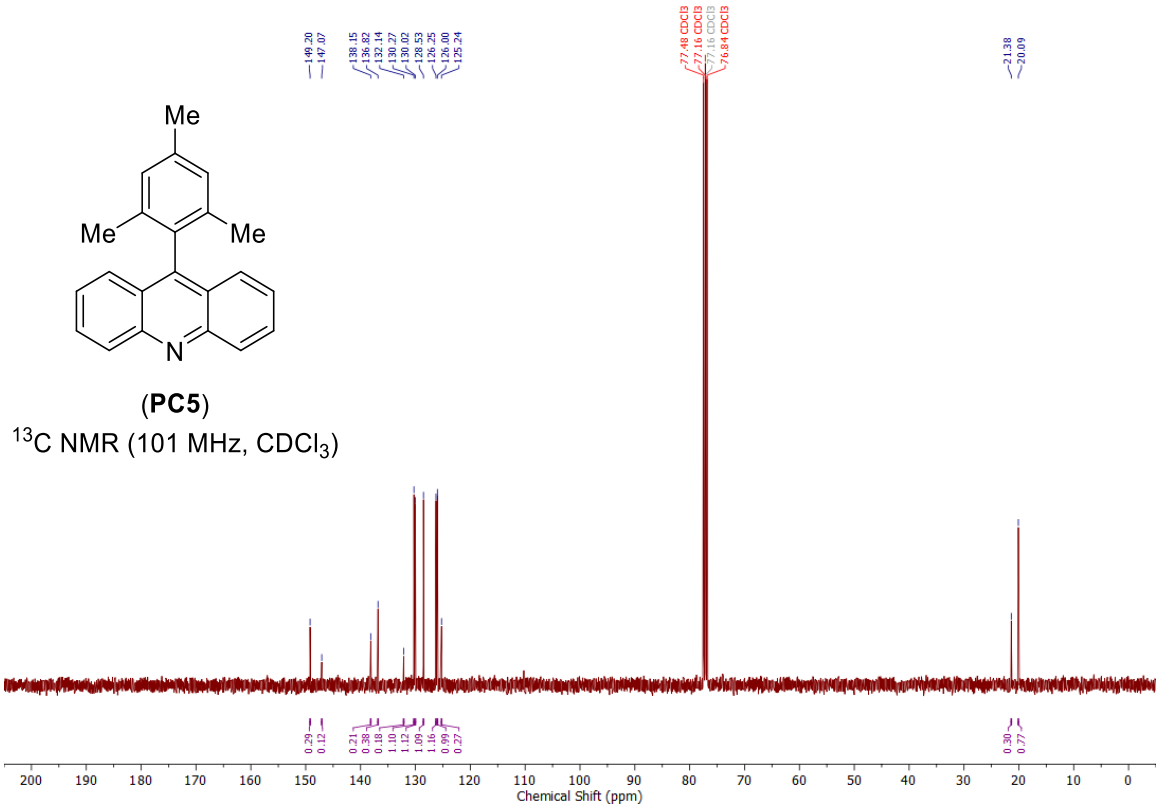


NMR spectra of 9-mesitylacridine (PC5)



(**PC5**)

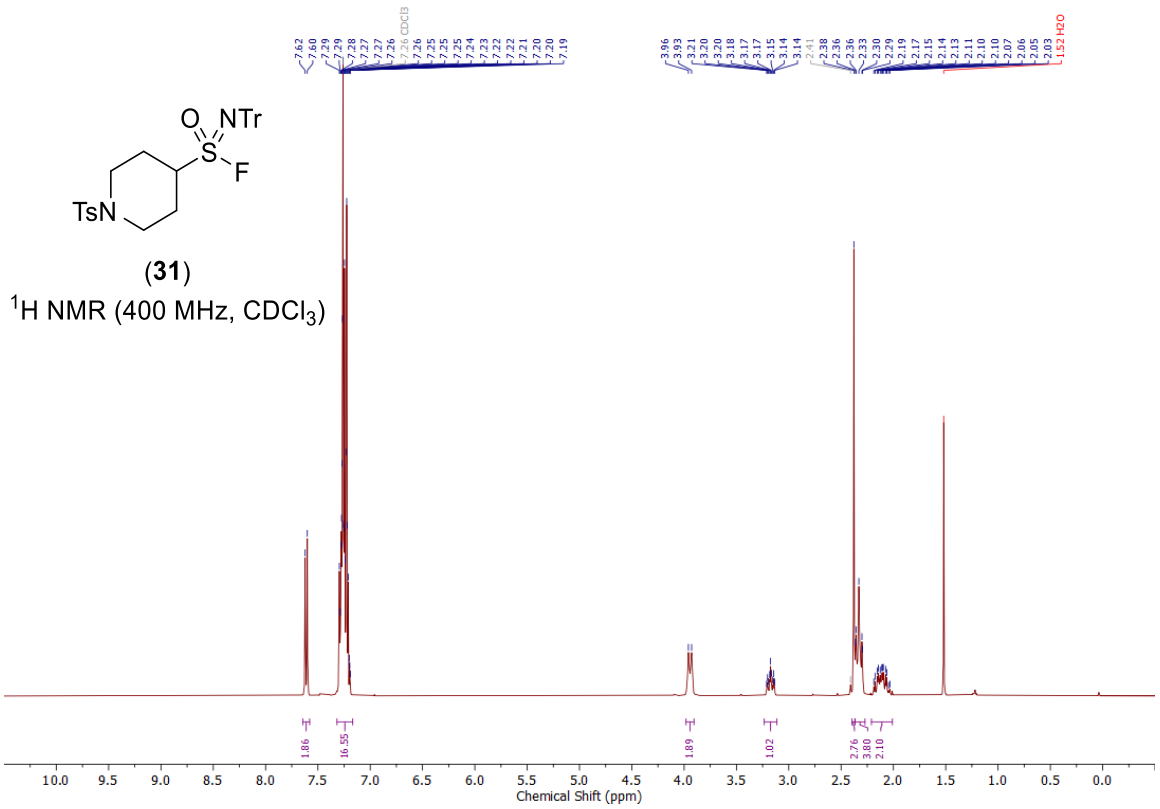
^{1}H NMR (400 MHz, $CDCl_3$)



(**PC5**)

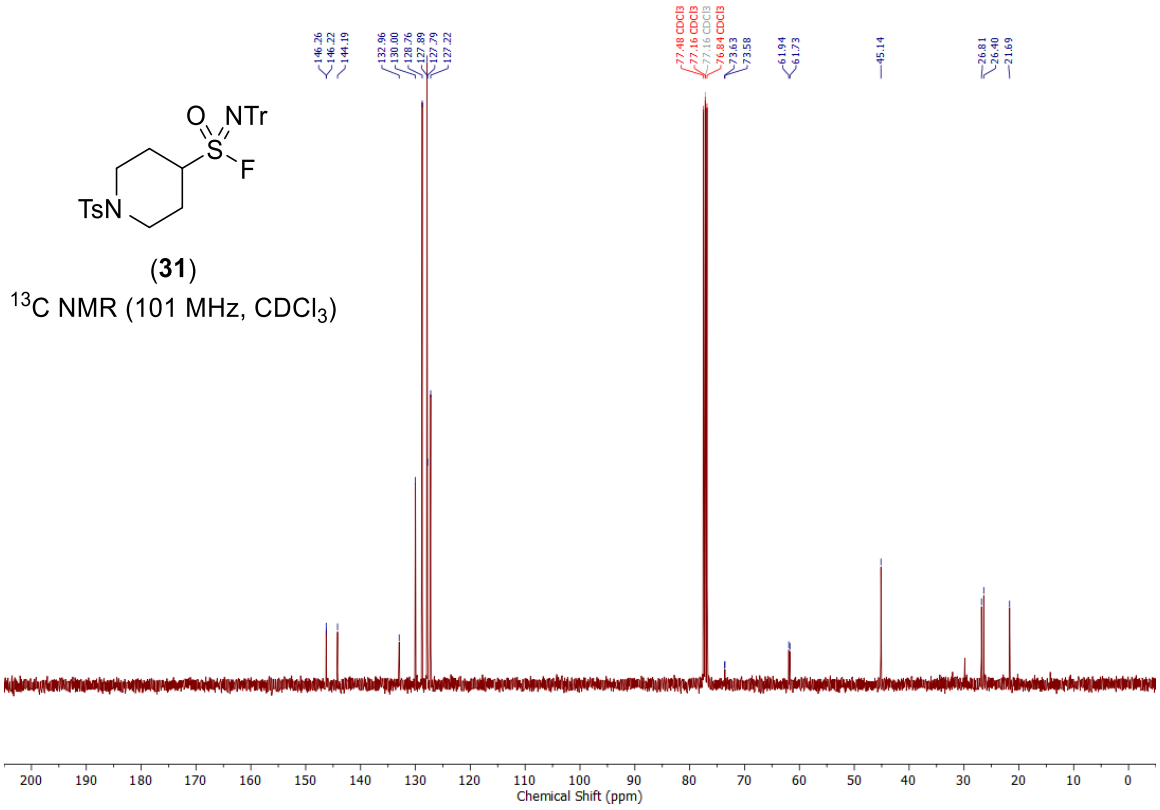
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of 1-tosyl-*N*-tritylpiperidine-4-sulfonimidoyl fluoride (31)



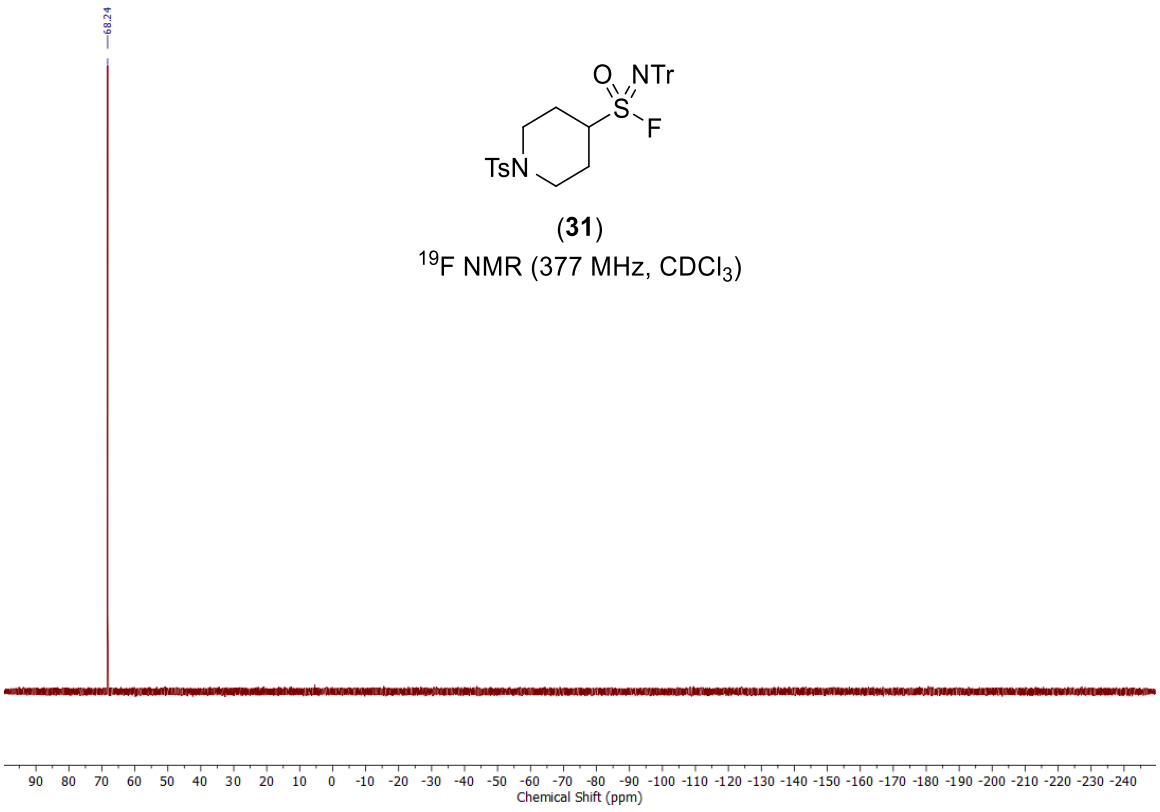
(**31**)

^{1}H NMR (400 MHz, $CDCl_3$)



(**31**)

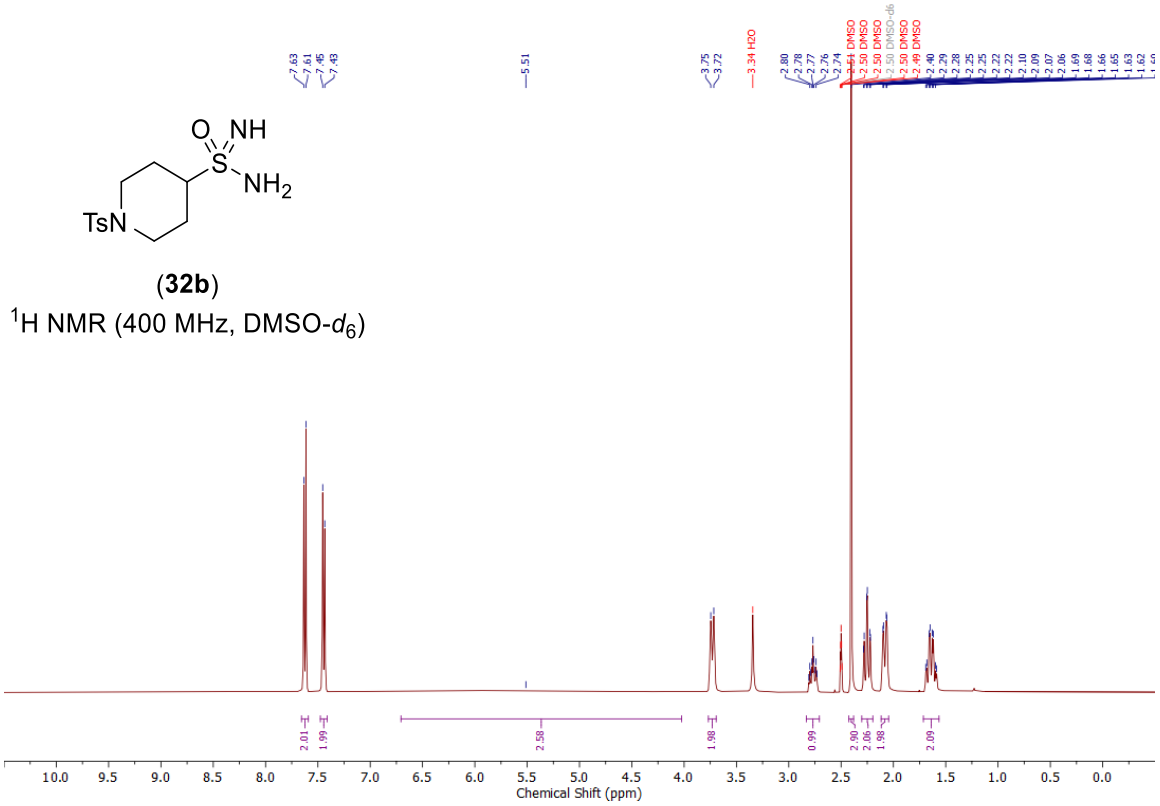
^{13}C NMR (101 MHz, $CDCl_3$)



(**31**)

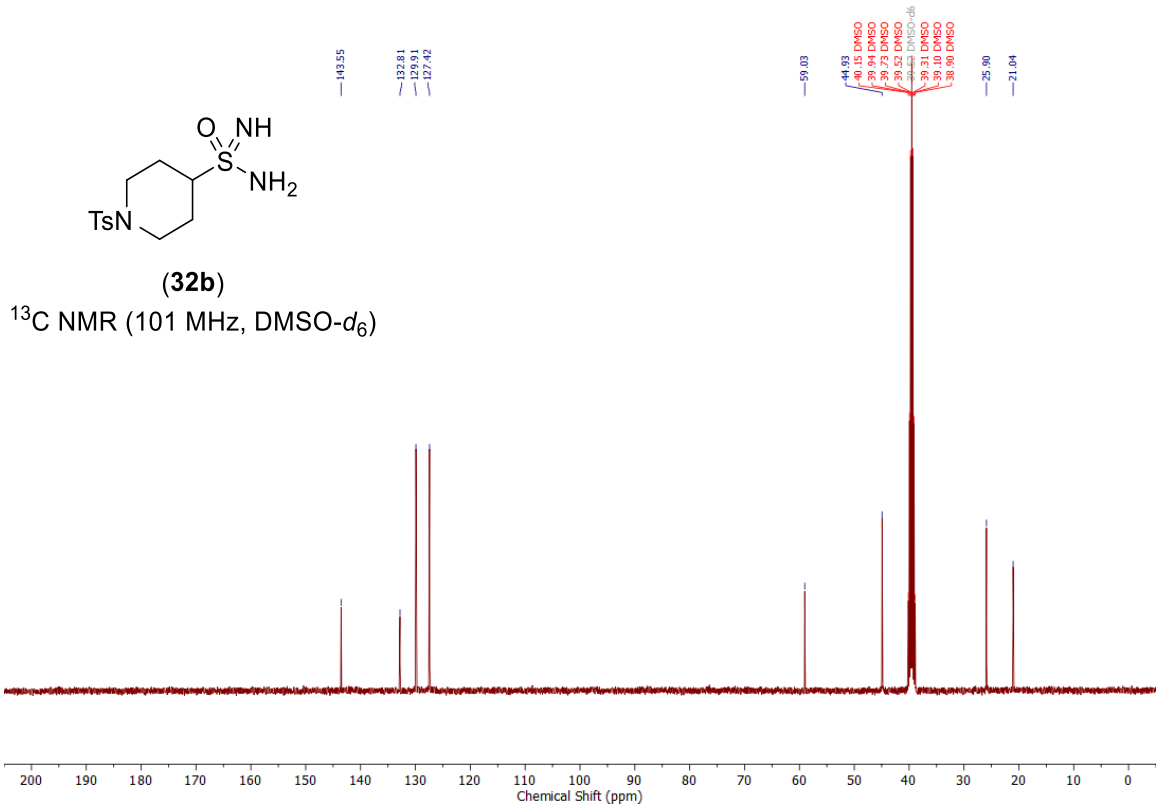
^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-tosylpiperidine-4-sulfonimidamide (32b)



(**32b**)

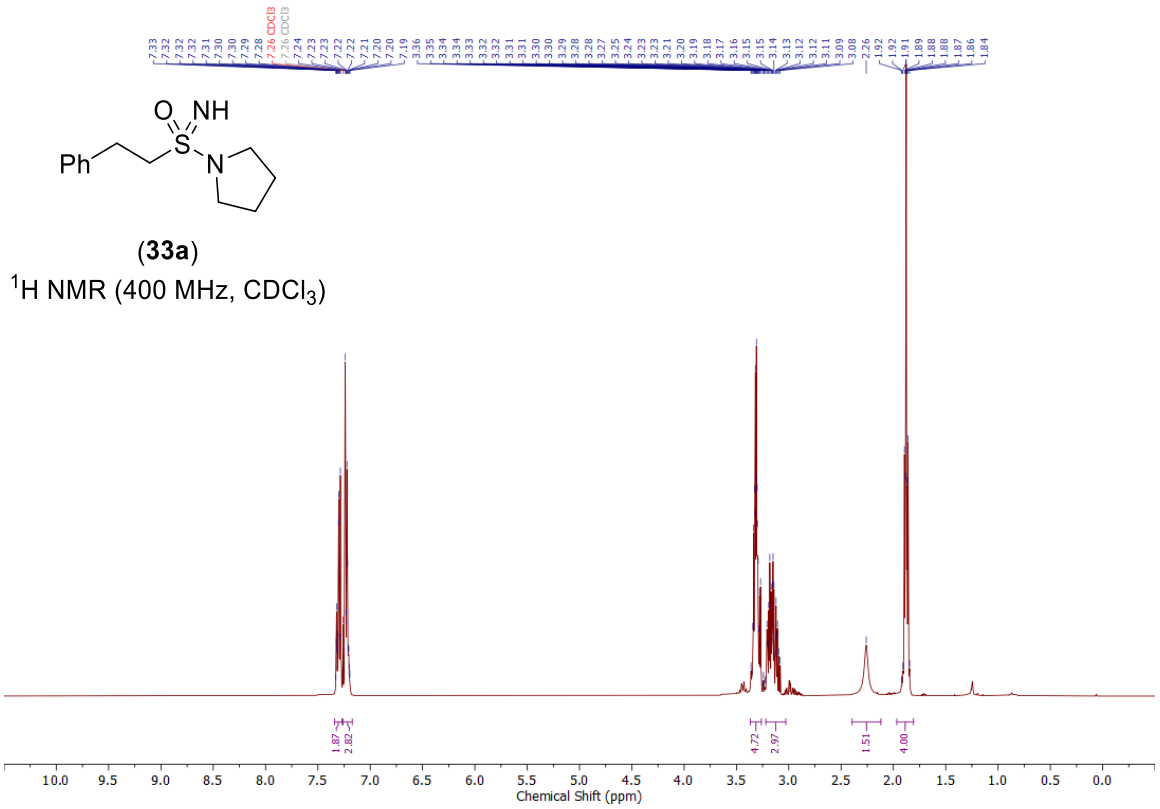
^{1}H NMR (400 MHz, DMSO-d_6)



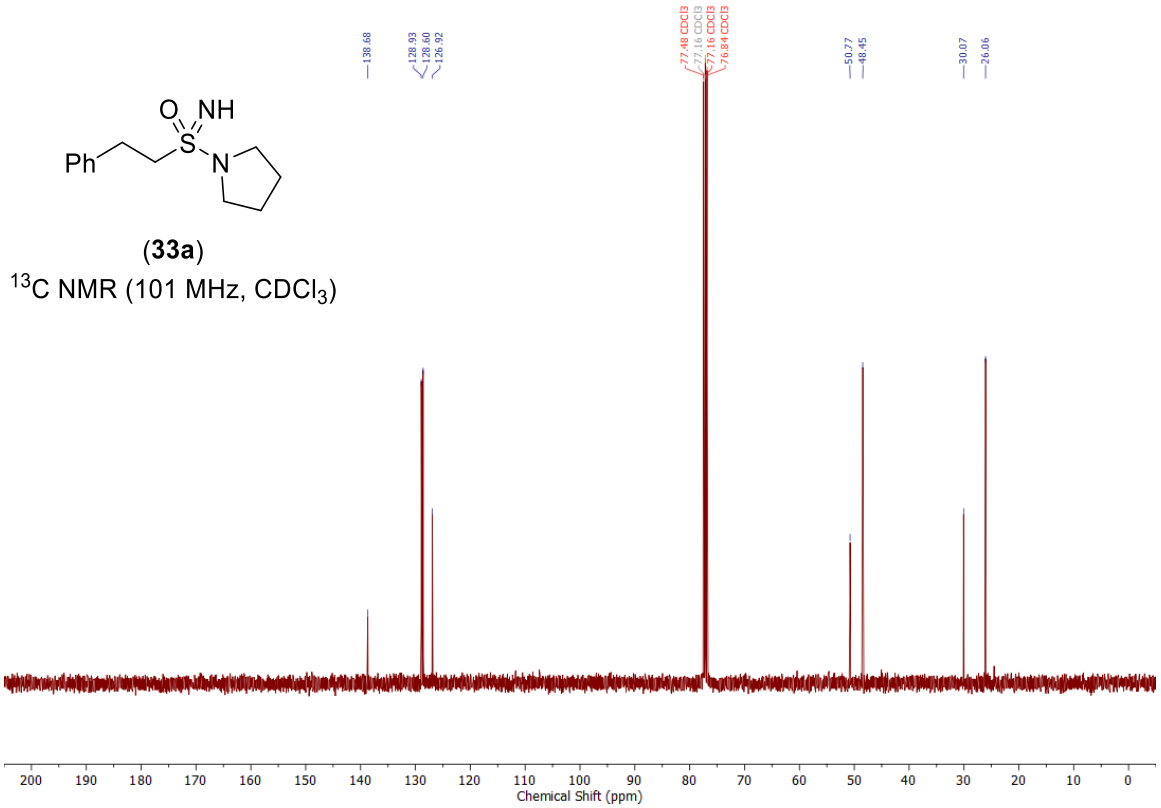
(**32b**)

^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of 1-(2-phenylethylsulfonimidoyl)pyrrolidine (33a)

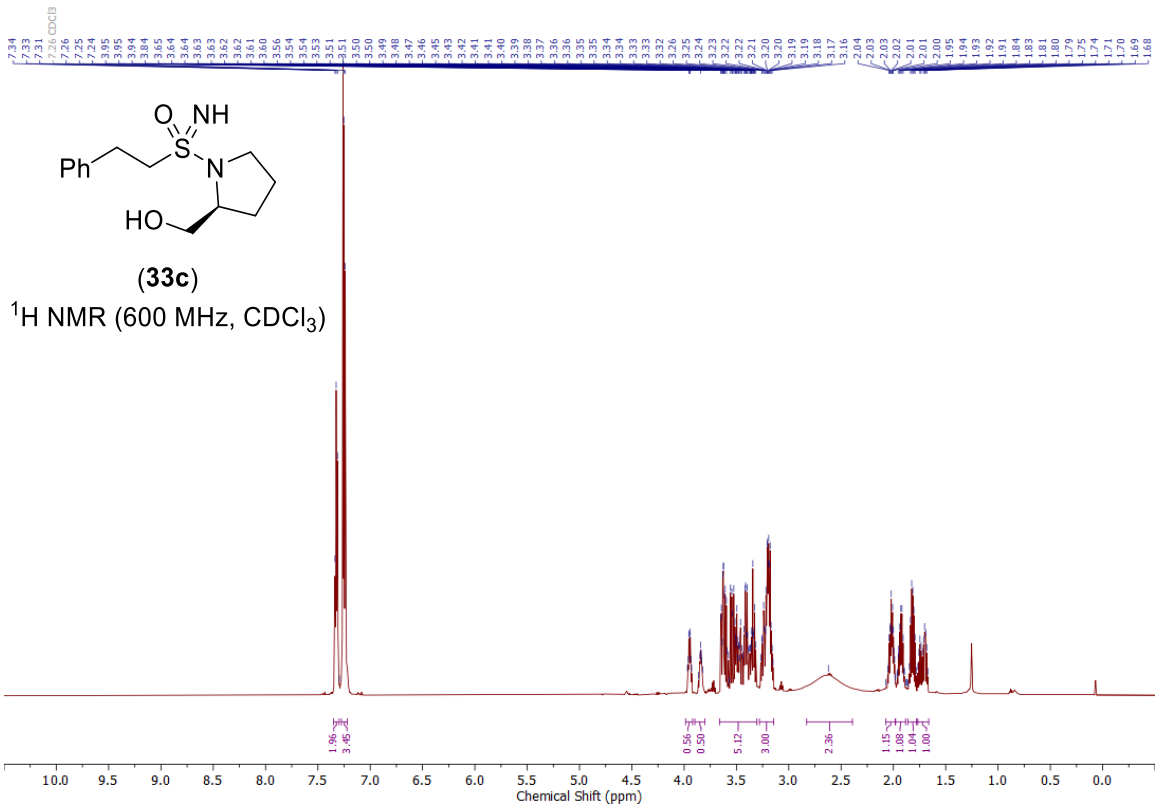


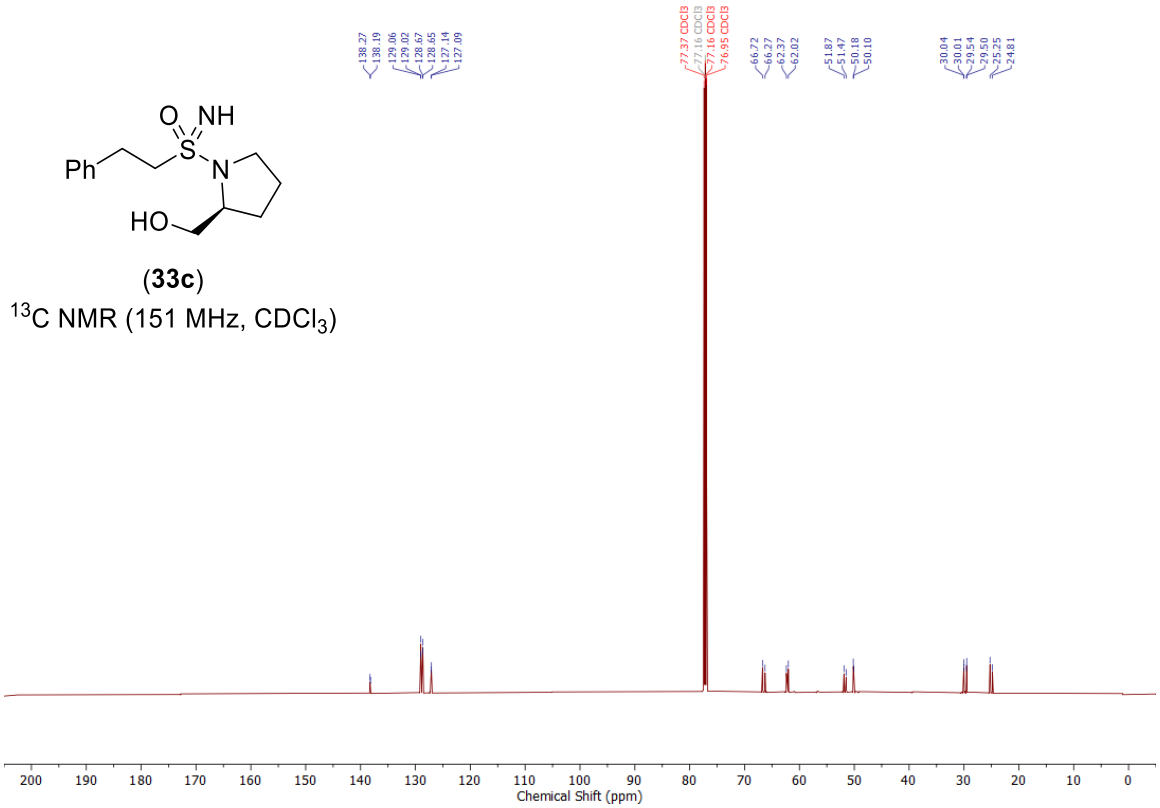
(**33a**)
^{1}H NMR (400 MHz, $CDCl_3$)



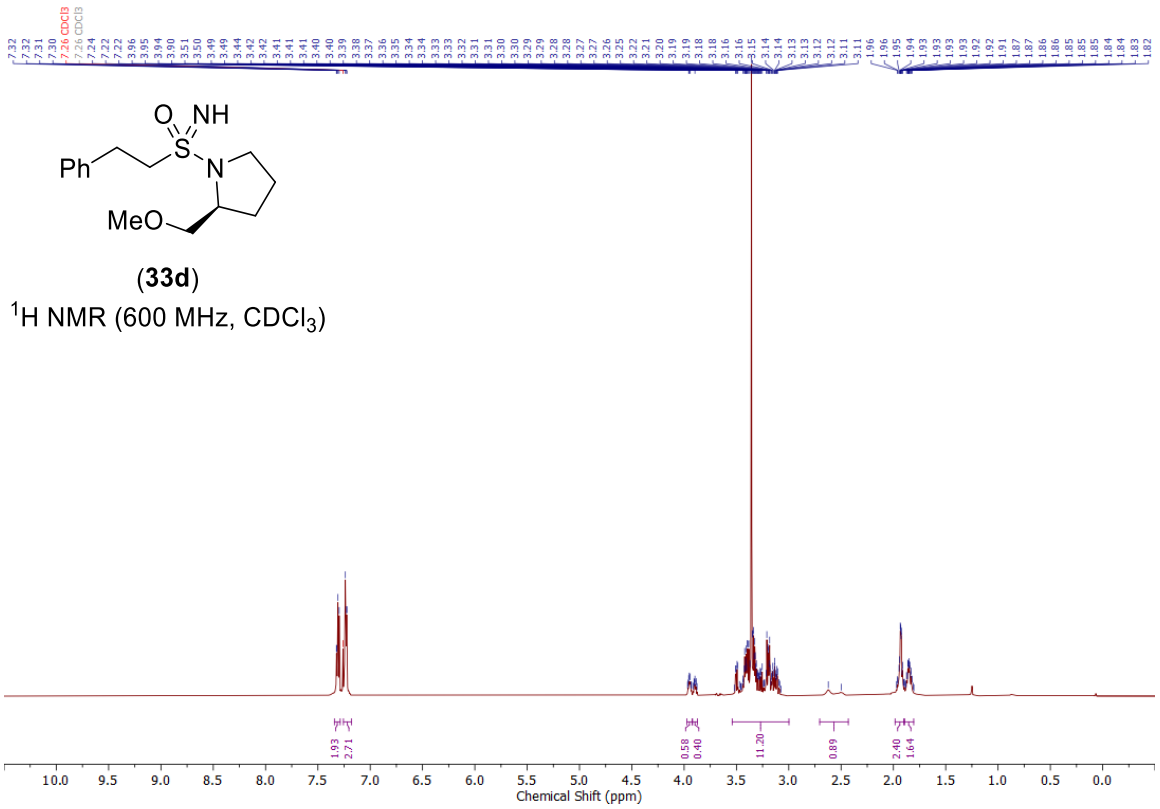
(**33a**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of ((2*S*)-1-(2-phenylethylsulfonimidoyl)pyrrolidin-2-yl)methanol (33c)

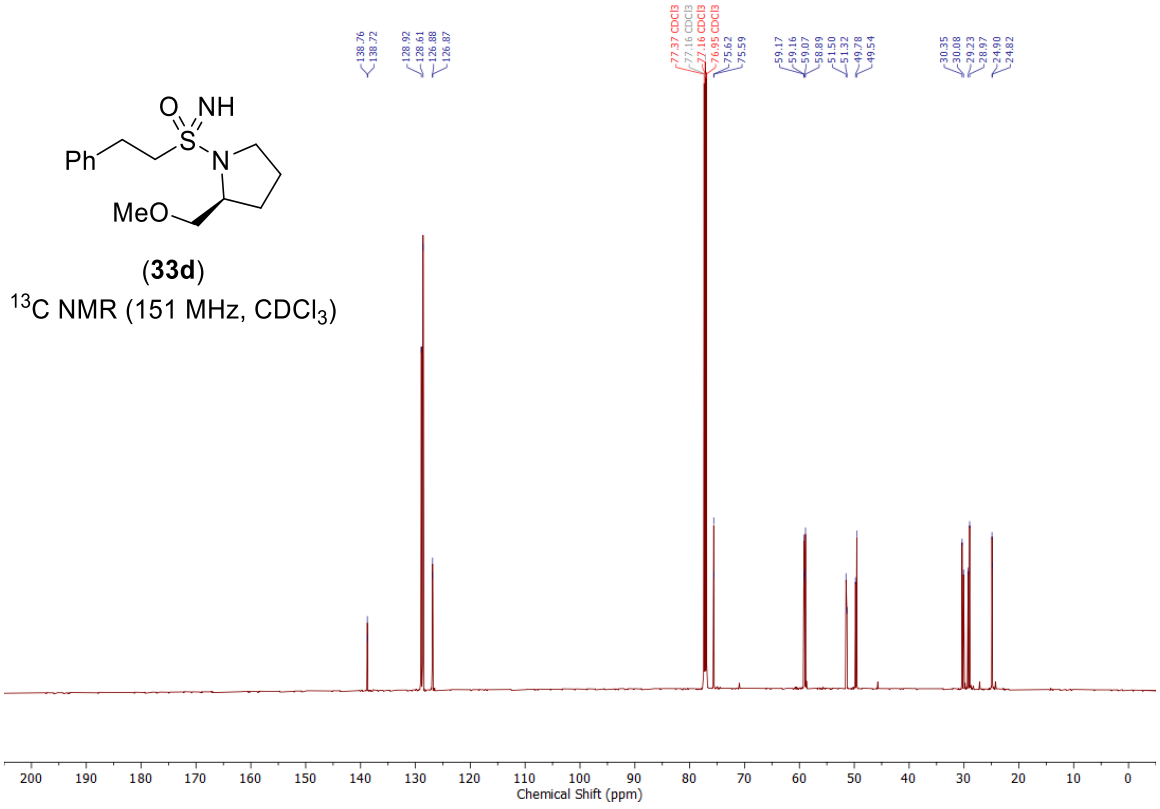




NMR spectra of (2*S*)-2-(methoxymethyl)-1-(2-phenylethylsulfonimidoyl)pyrrolidine (33d)

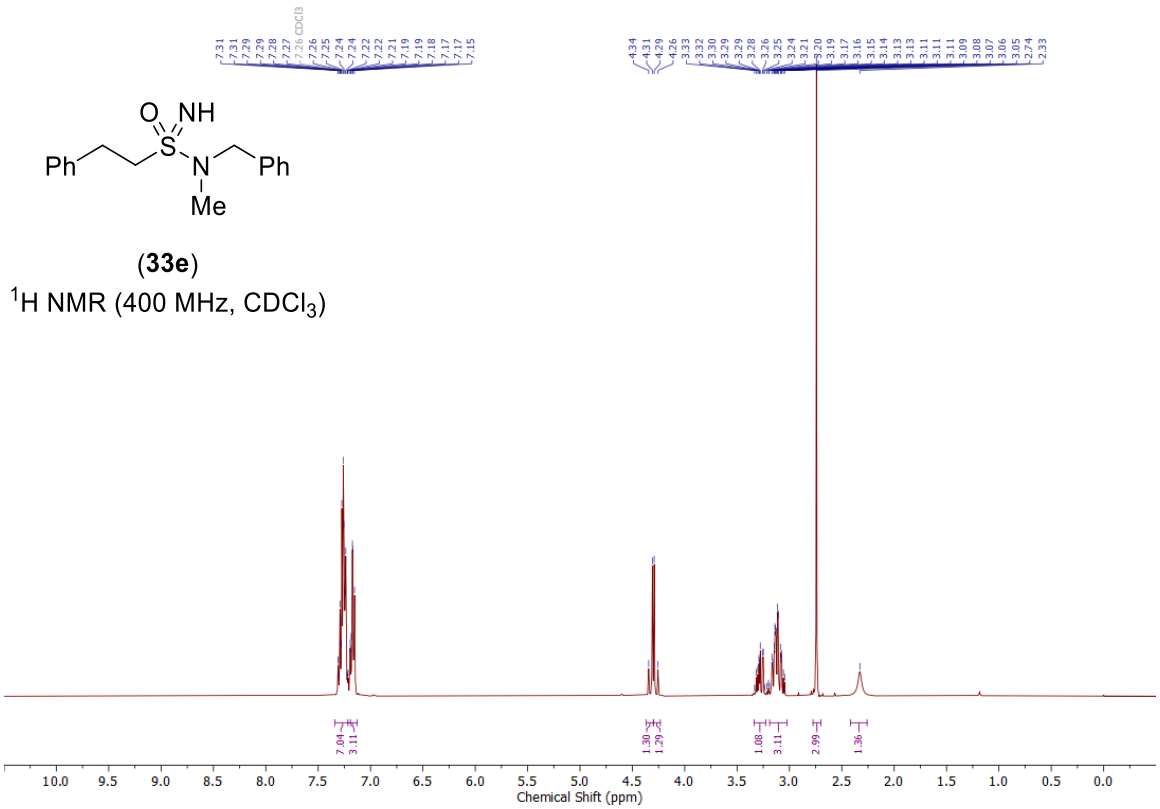


(**33d**)
^{1}H NMR (600 MHz, $CDCl_3$)



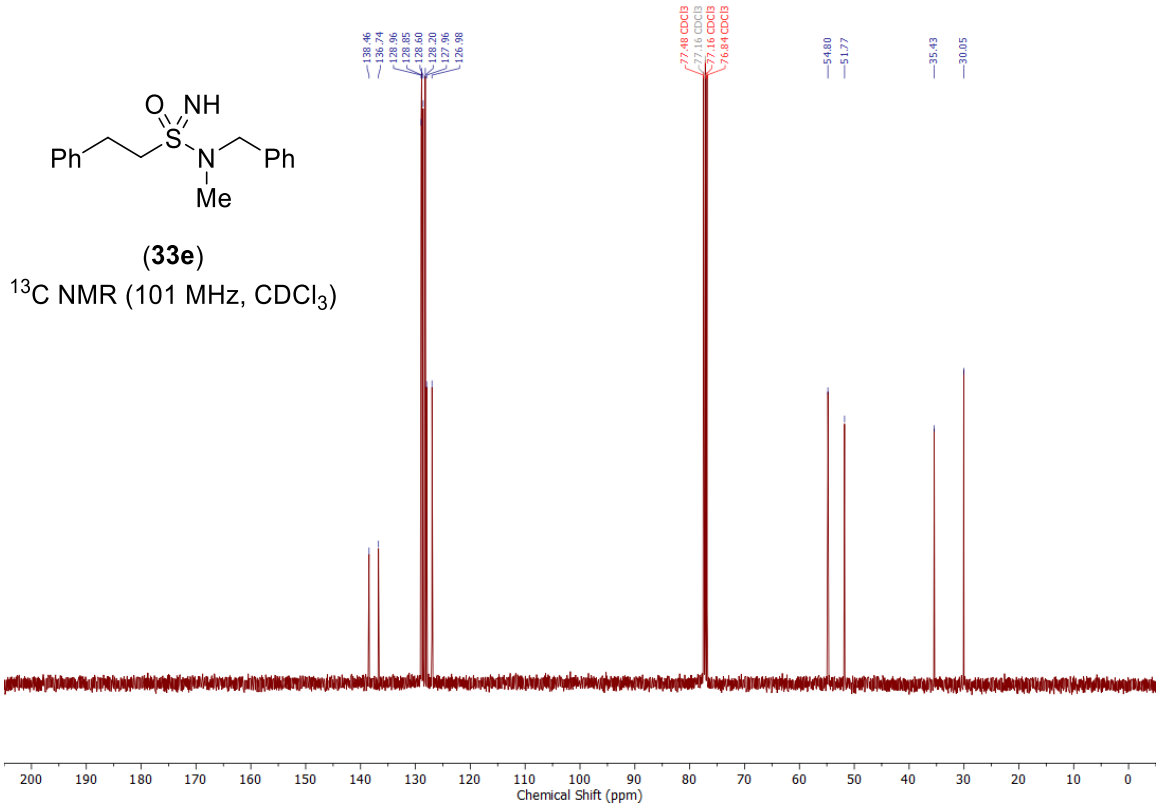
(**33d**)
^{13}C NMR (151 MHz, $CDCl_3$)

NMR spectra of *N*-benzyl-*N*-methyl-2-phenylethane-1-sulfonimidamide (33e)



(**33e**)

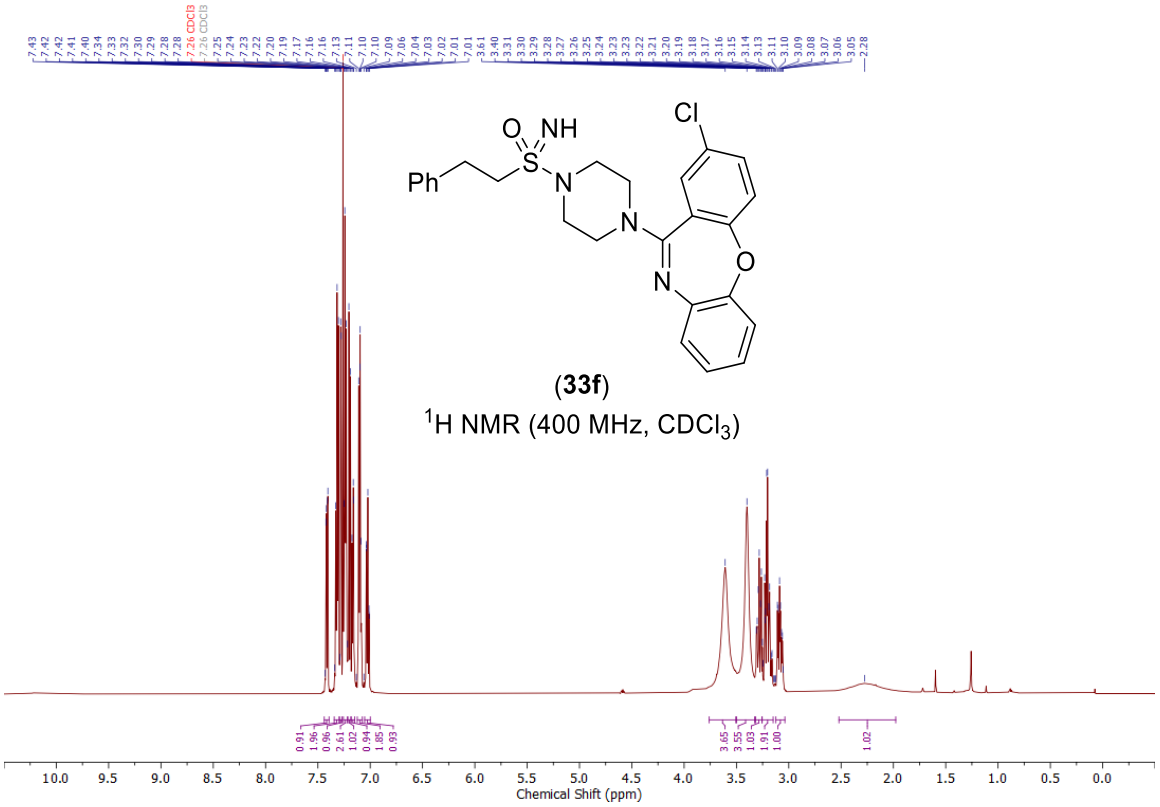
^{1}H NMR (400 MHz, $CDCl_3$)

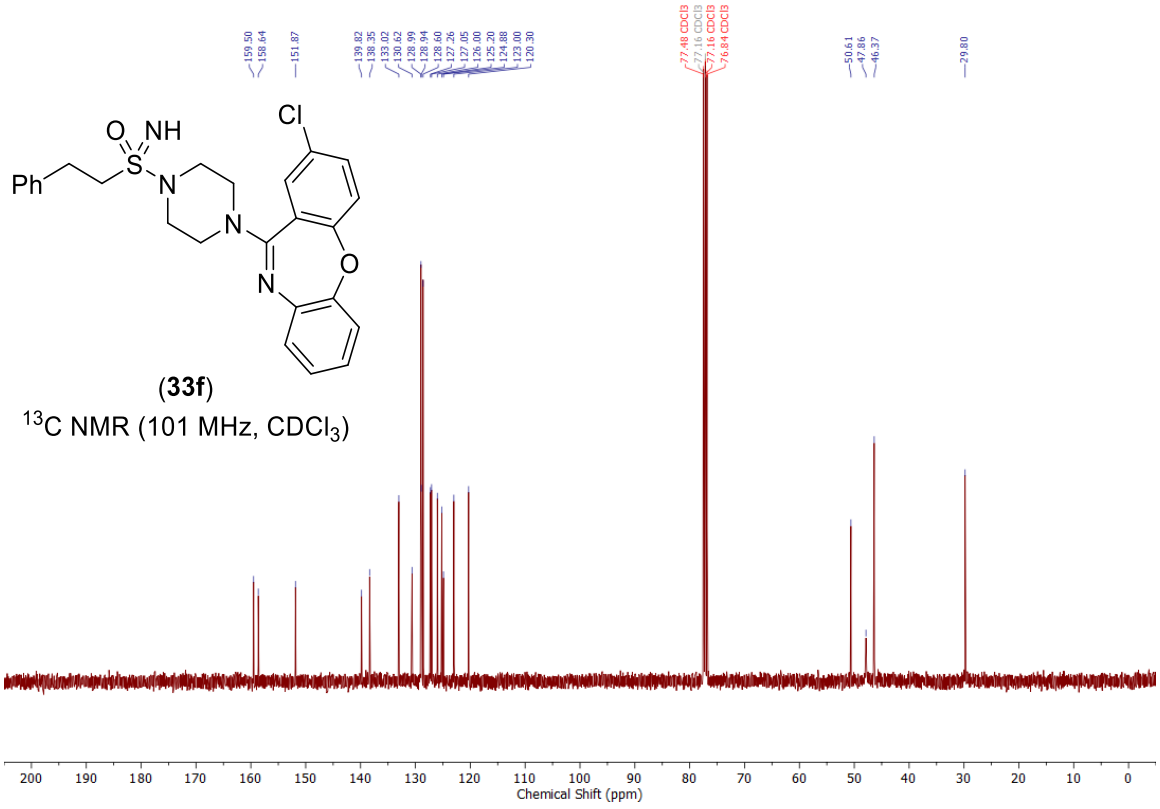


(**33e**)

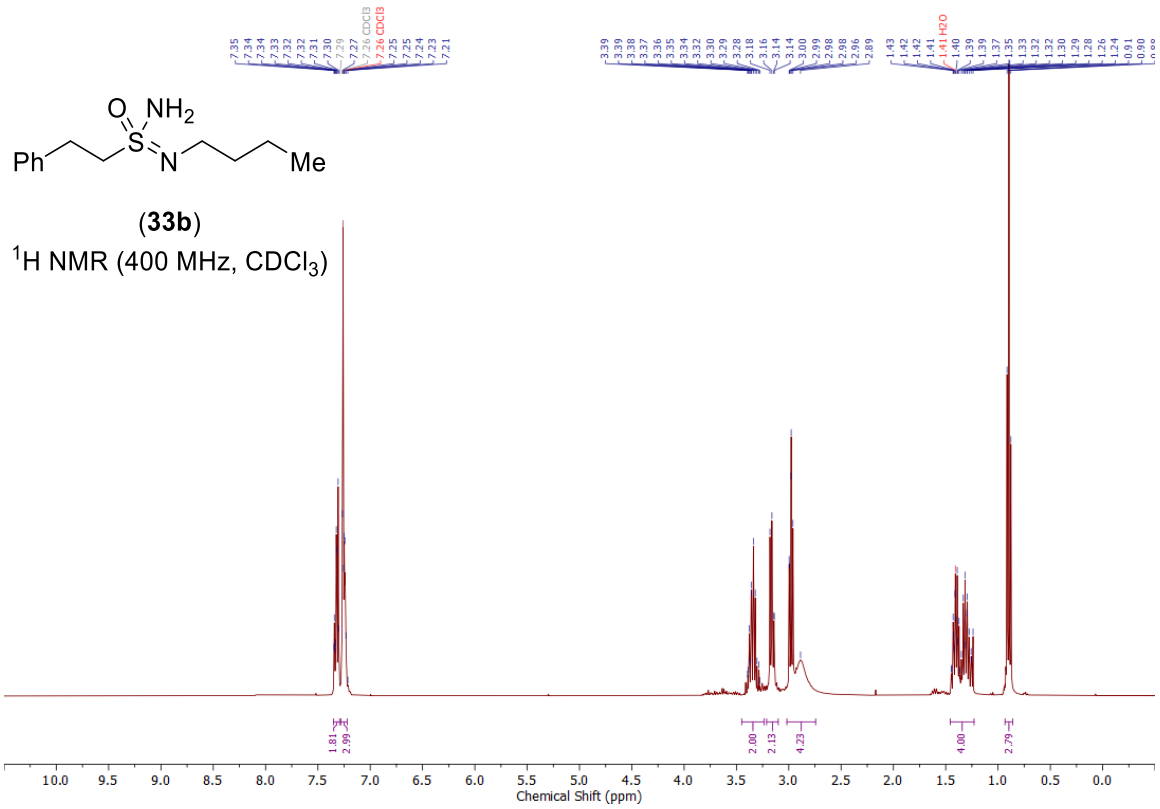
^{13}C NMR (101 MHz, $CDCl_3$)

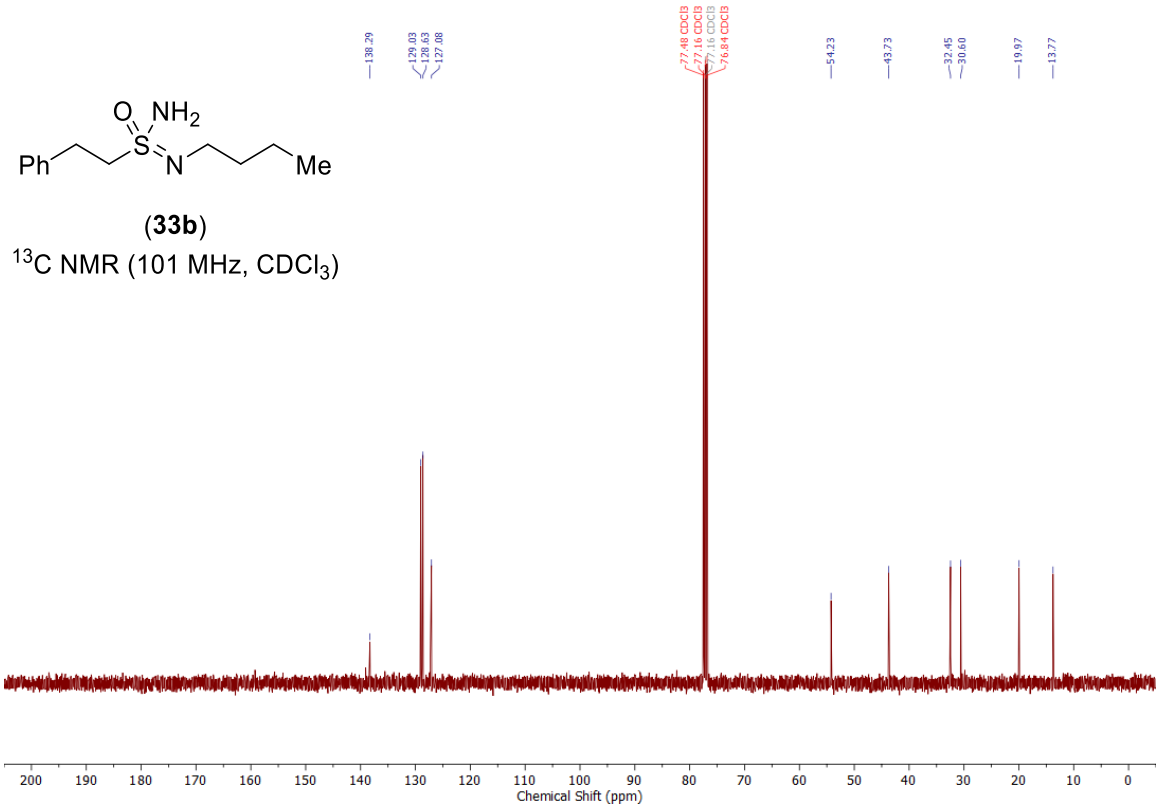
NMR spectra of 2-chloro-11-(4-(2-phenylethylsulfonimidoyl)piperazin-1-yl)dibenzo[*b*,*f*][1,4]oxazepine (33f)



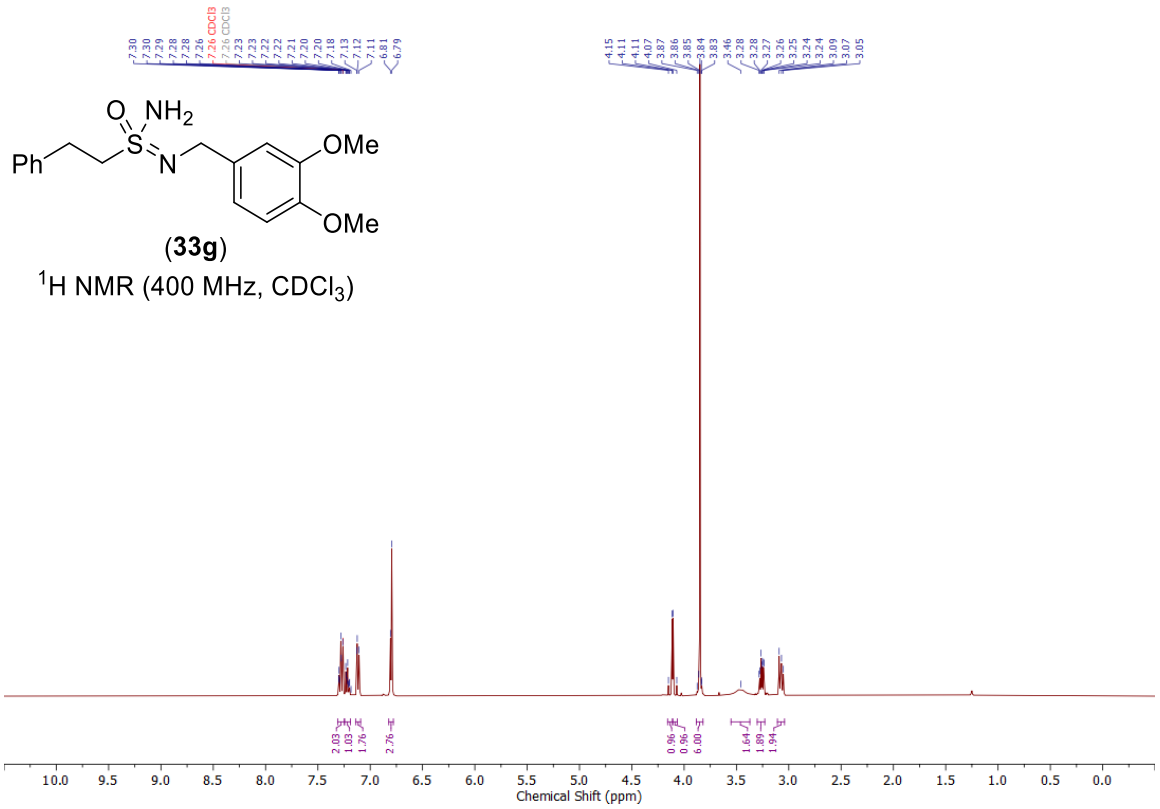


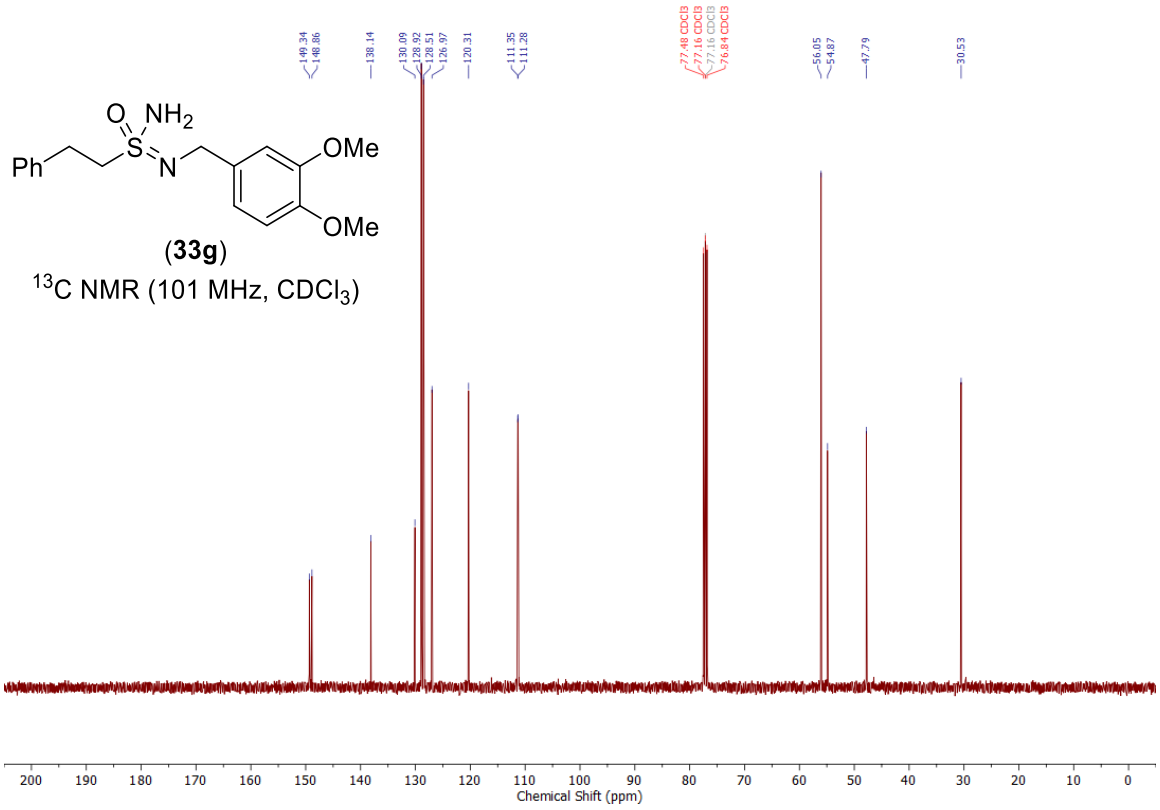
NMR spectra of *N′*-butyl-2-phenylethane-1-sulfonimidamide (33b)



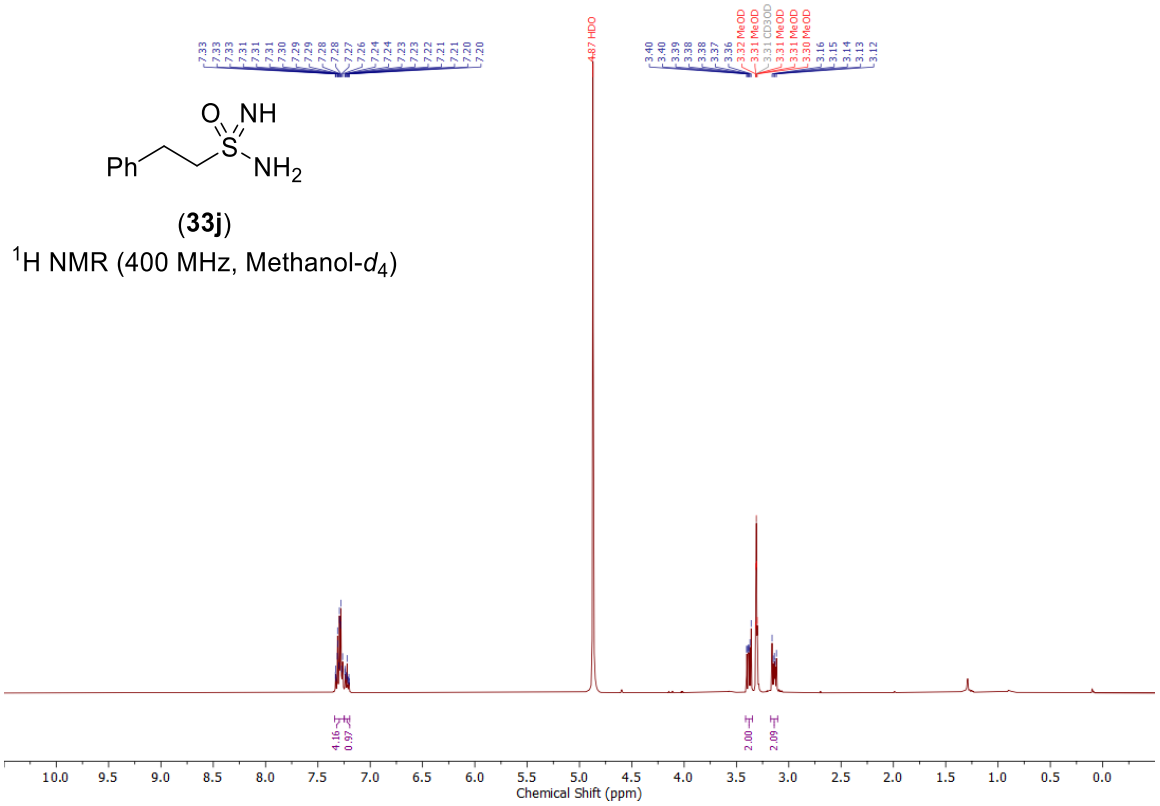


NMR spectra of *N′*-(3,4-dimethoxybenzyl)-2-phenylethane-1-sulfonimidamide (33g)



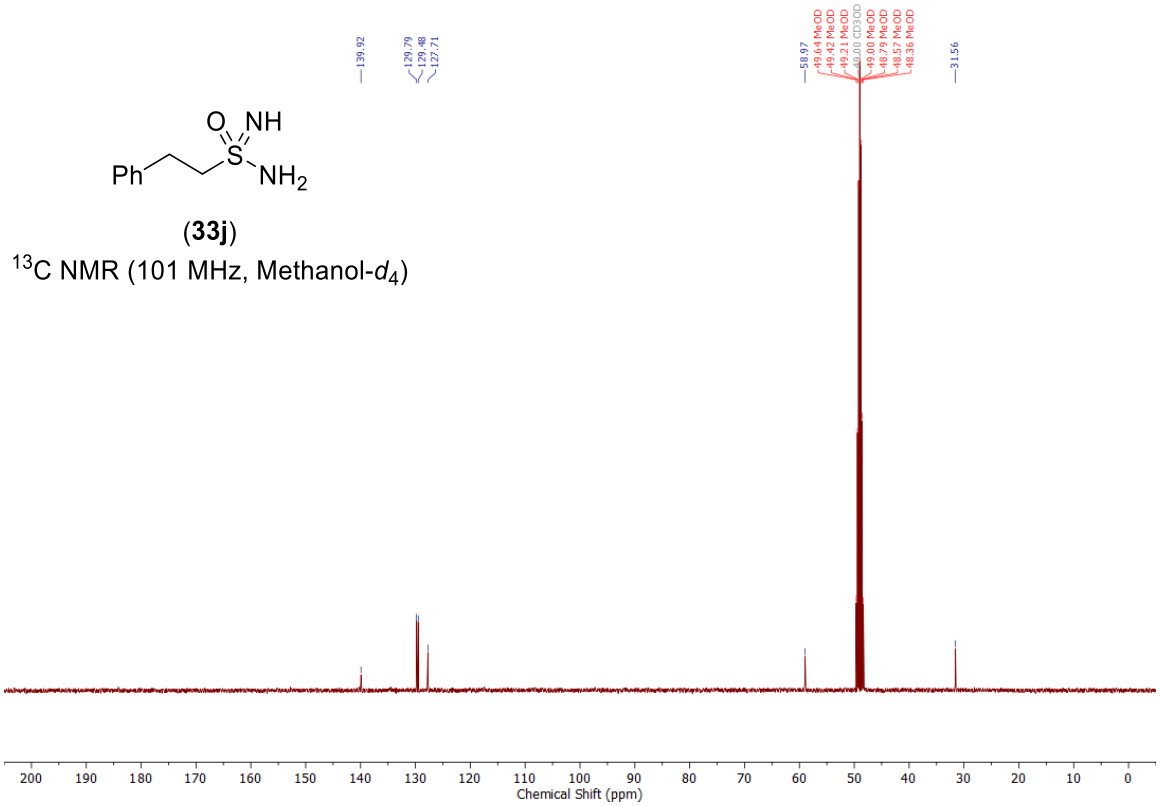


NMR spectra of 2-phenylethane-1-sulfonimidamide (33j)



(**33j**)

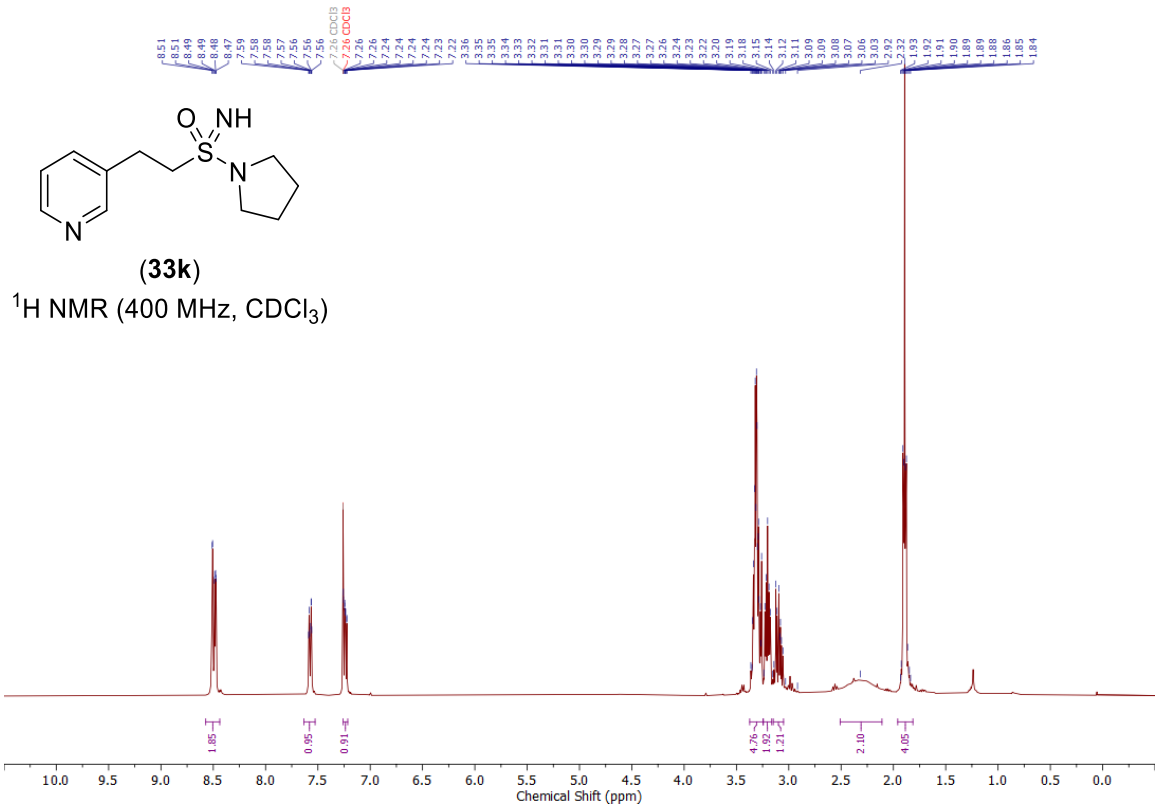
^{1}H NMR (400 MHz, Methanol-d_4)

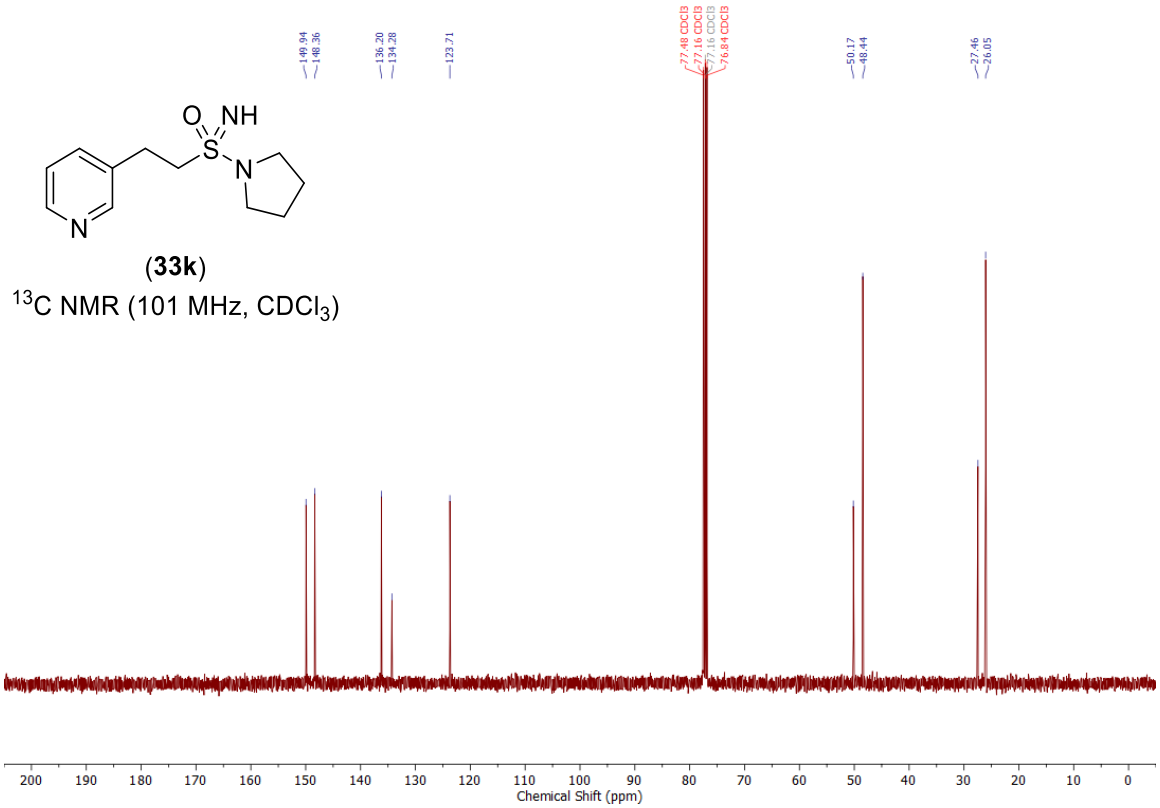


(**33j**)

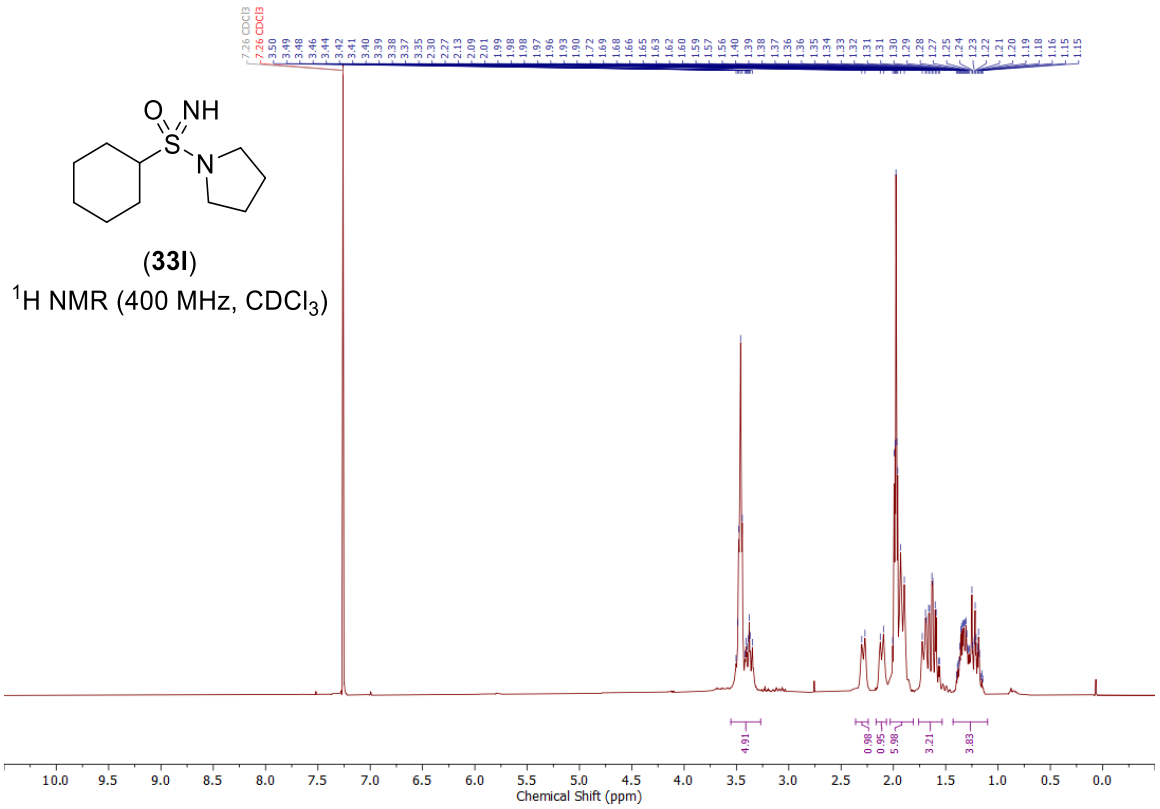
^{13}C NMR (101 MHz, Methanol-d_4)

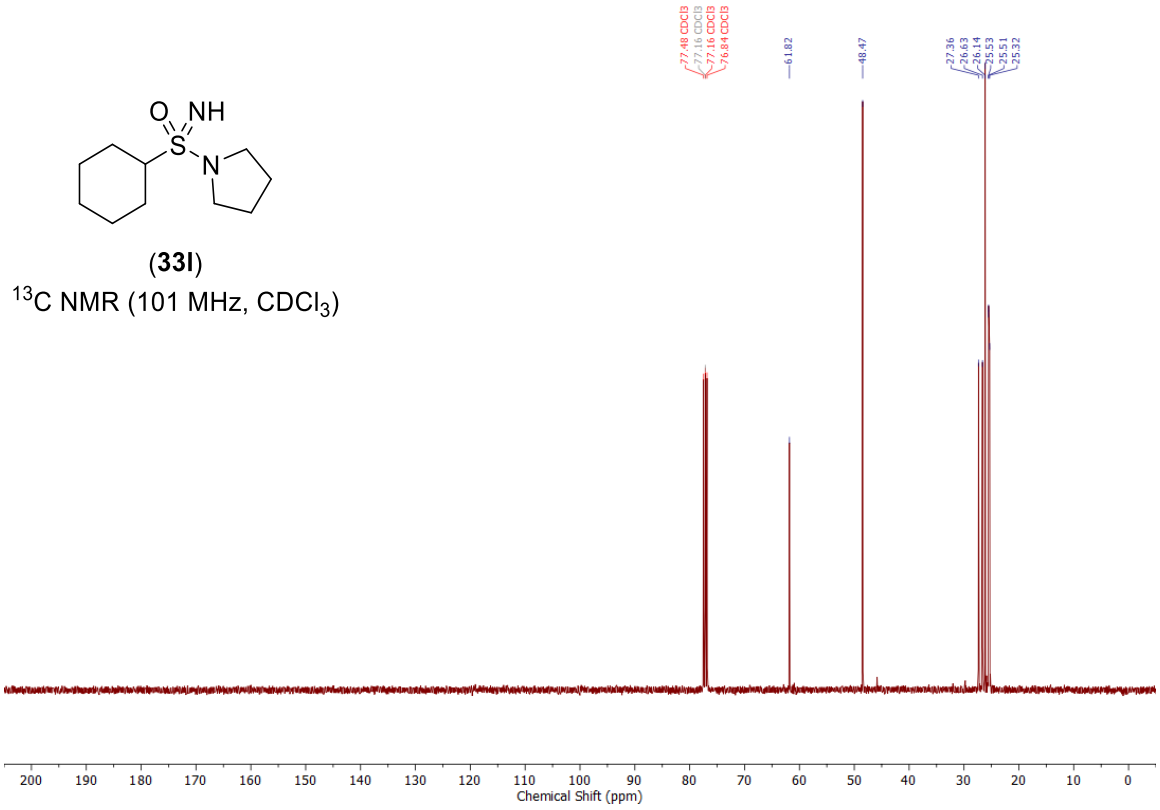
NMR spectra of 3-(2-(pyrrolidine-1-sulfonimidoyl)ethyl)pyridine (33k)



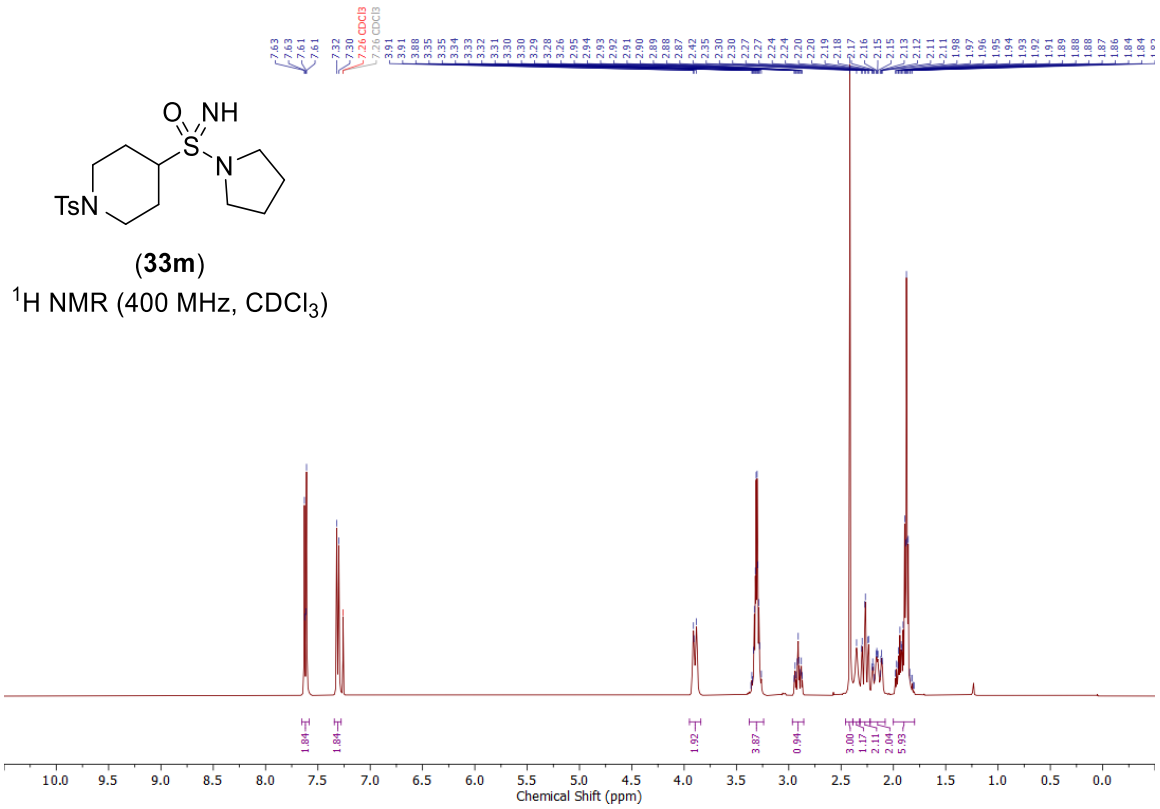


NMR spectra of 1-(cyclohexanesulfonimidoyl)pyrrolidine (33l)



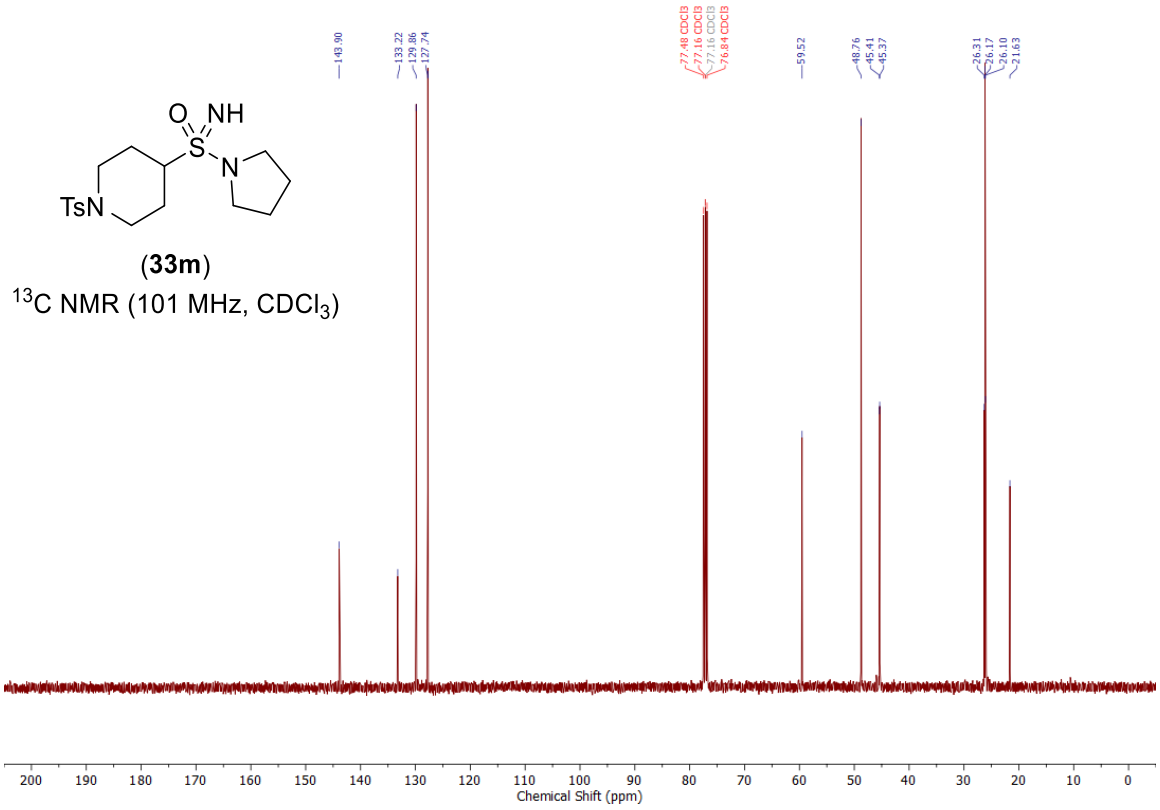


NMR spectra of 4-(pyrrolidine-1-sulfonimidoyl)-1-tosylpiperidine (33m)



(**33m**)

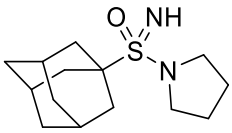
^{1}H NMR (400 MHz, $CDCl_3$)



(**33m**)

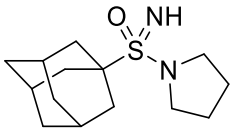
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of 1-((3*s*,5*s*,7*s*)-adamantane-1-sulfonimidoyl)pyrrolidine (33n)



(**33n**)

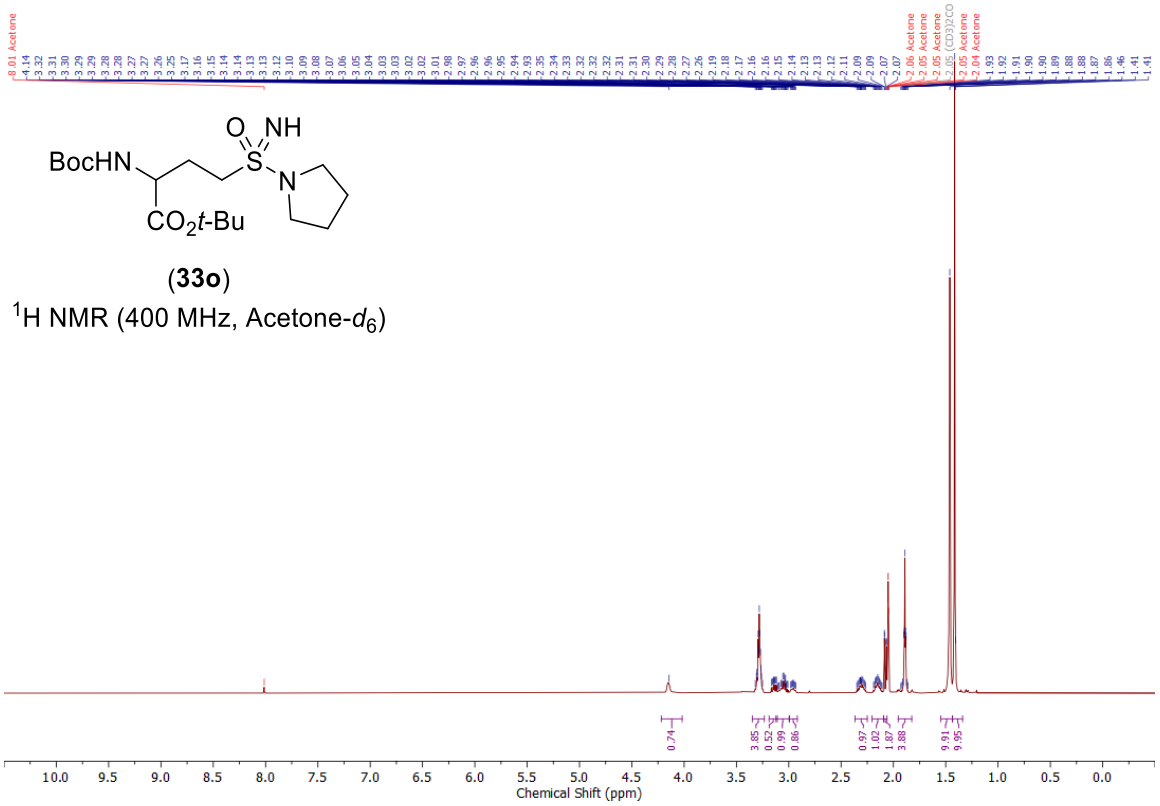
^{1}H NMR (400 MHz, $CDCl_3$)



(**33n**)

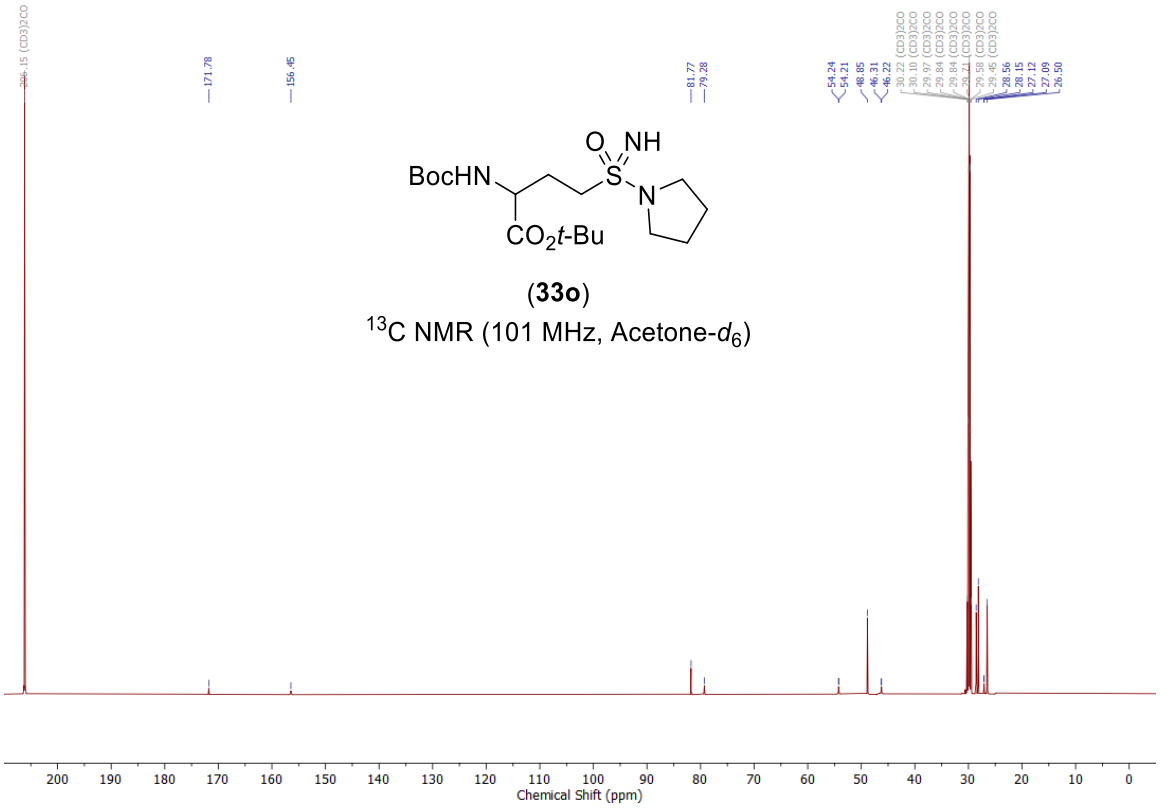
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(pyrrolidine-1-sulfonimidoyl)butanoate (33o)



(**33o**)

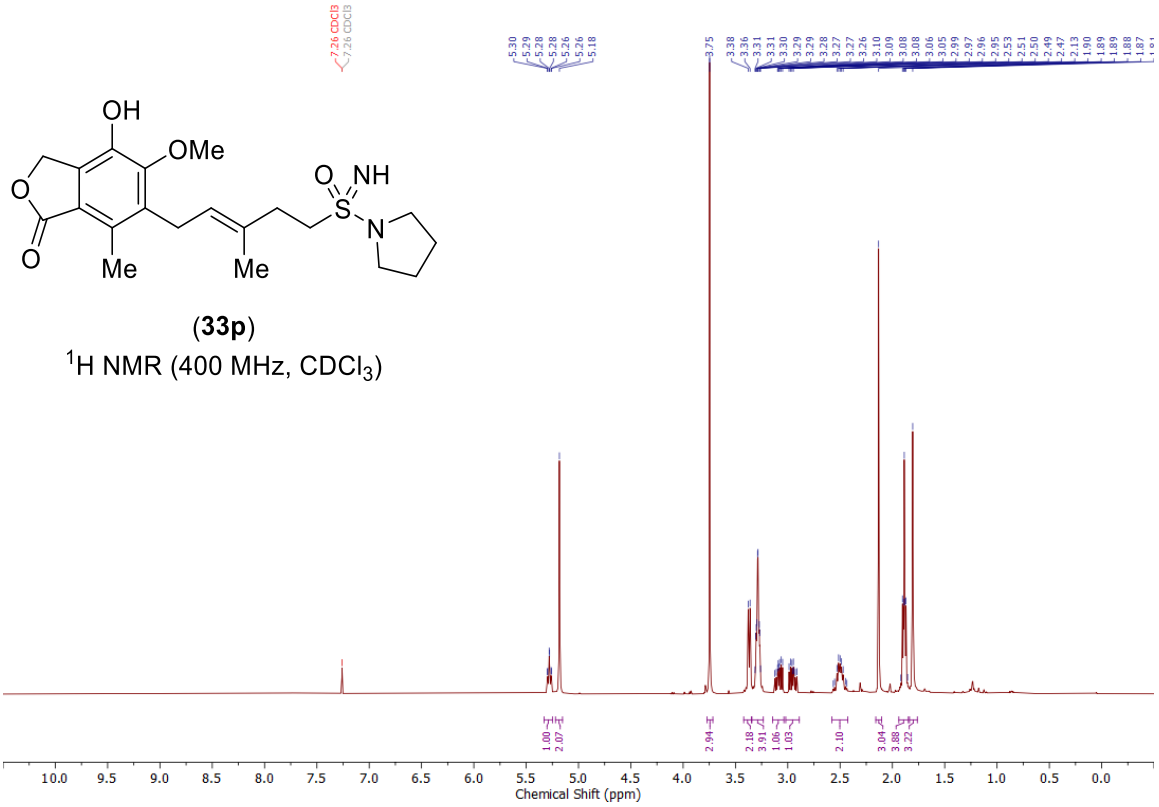
^{1}H NMR (400 MHz, Acetone-d_6)



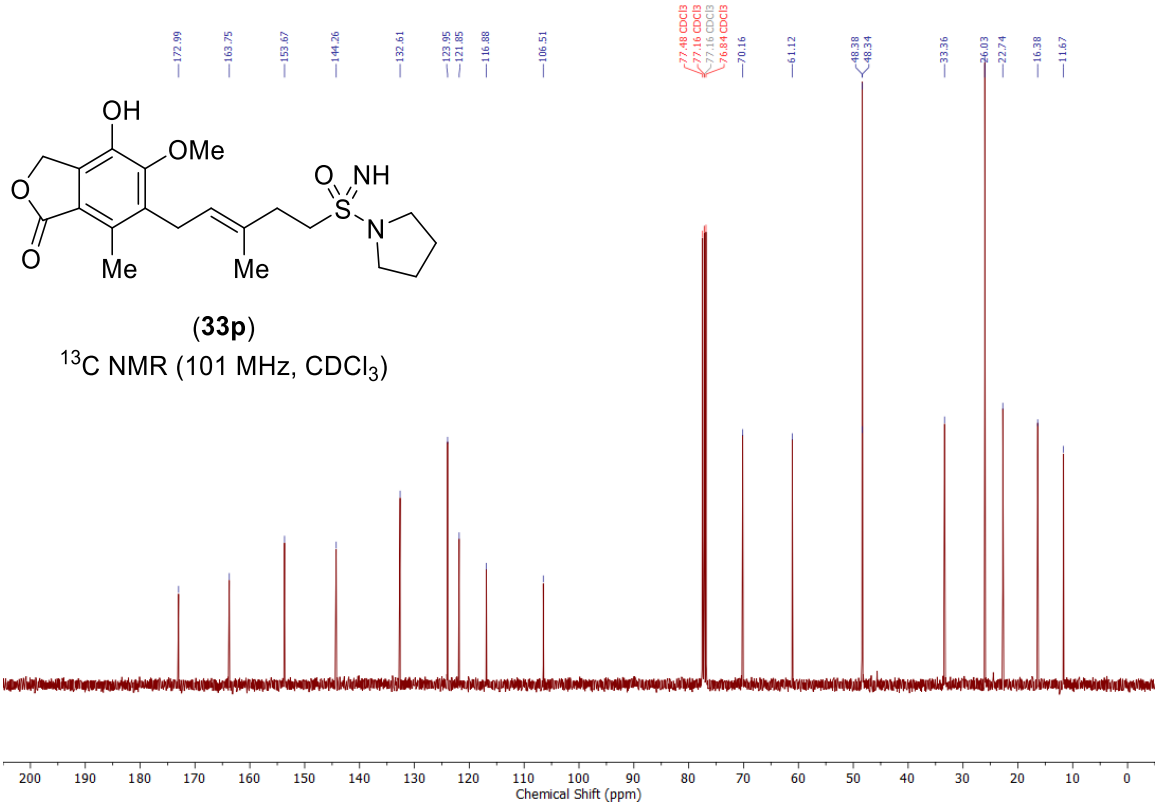
(**33o**)

^{13}C NMR (101 MHz, Acetone-d_6)

NMR spectra of (*E*)-4-hydroxy-5-methoxy-7-methyl-6-(3-methyl-5-(pyrrolidine-1-sulfonimidoyl)pent-2-en-1-yl)isobenzofuran-1(3*H*)-one (33p)

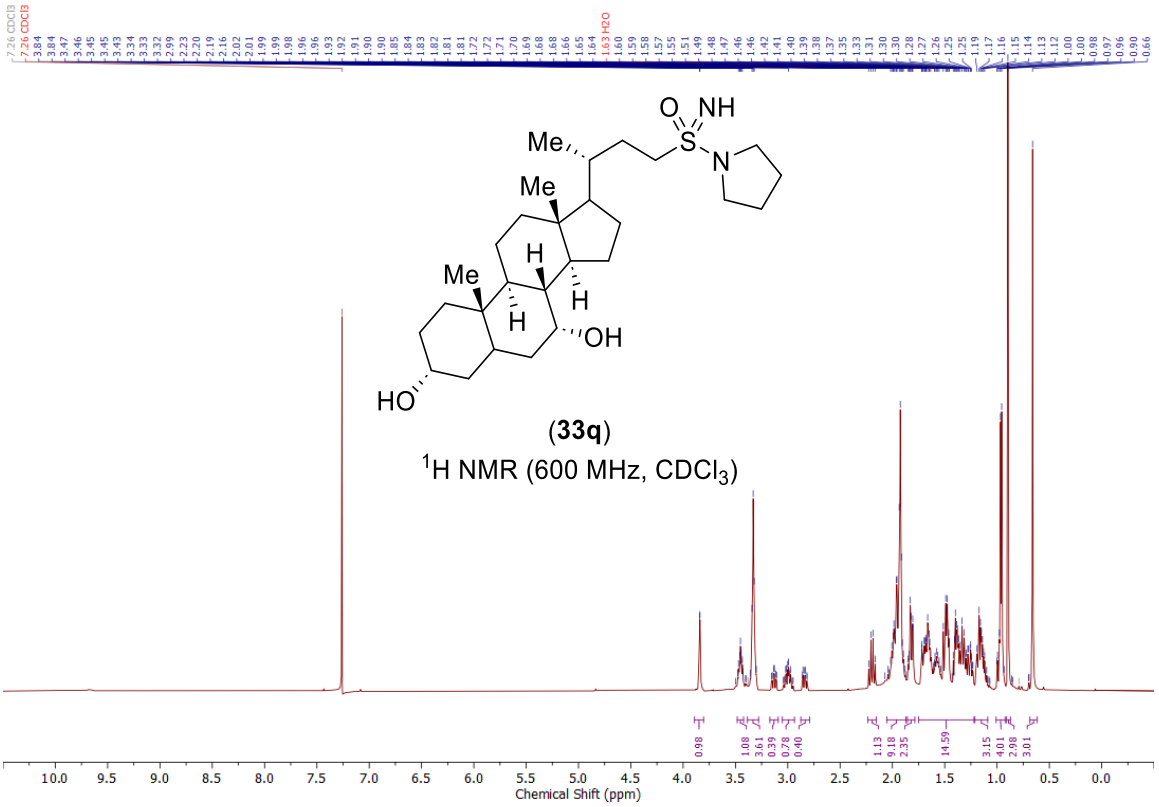


(**33p**)
^{1}H NMR (400 MHz, $CDCl_3$)



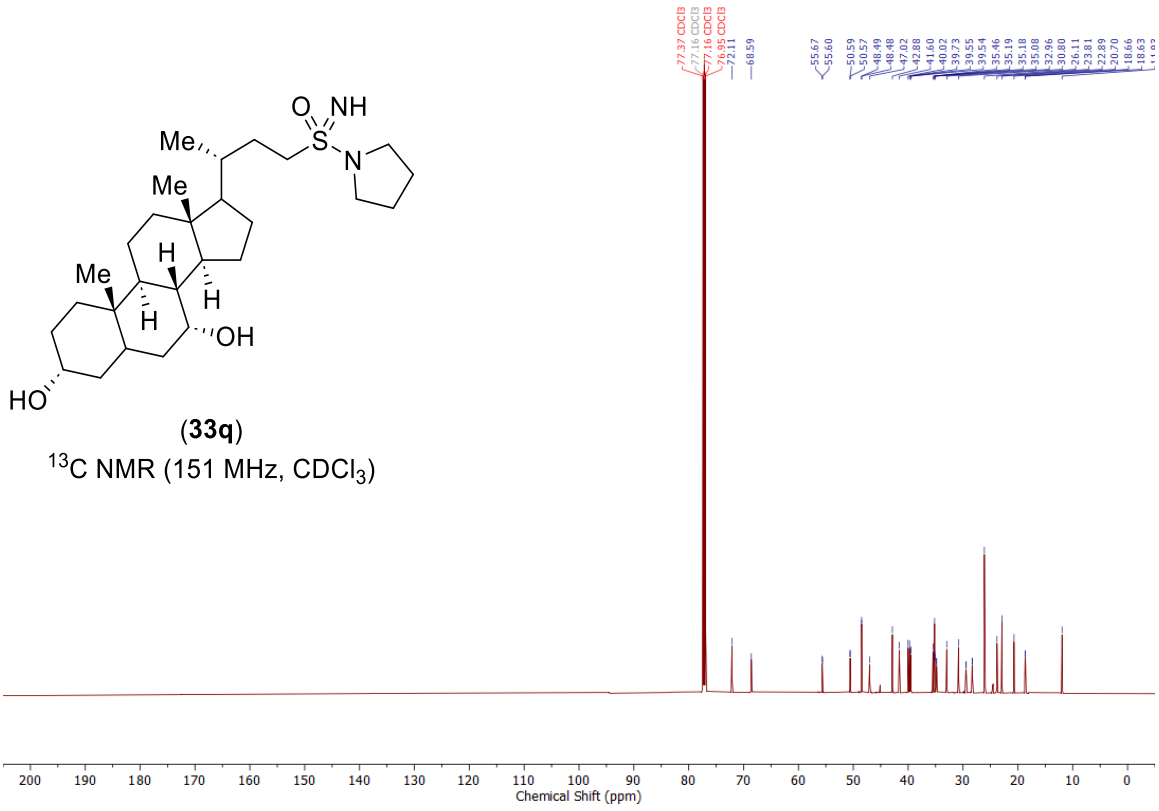
(**33p**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of (3*R*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((2*R*)-4-(pyrrolidine-1-sulfonimidoyl)butan-2-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7-diol (33q)



(**33q**)

^{1}H NMR (600 MHz, $CDCl_3$)

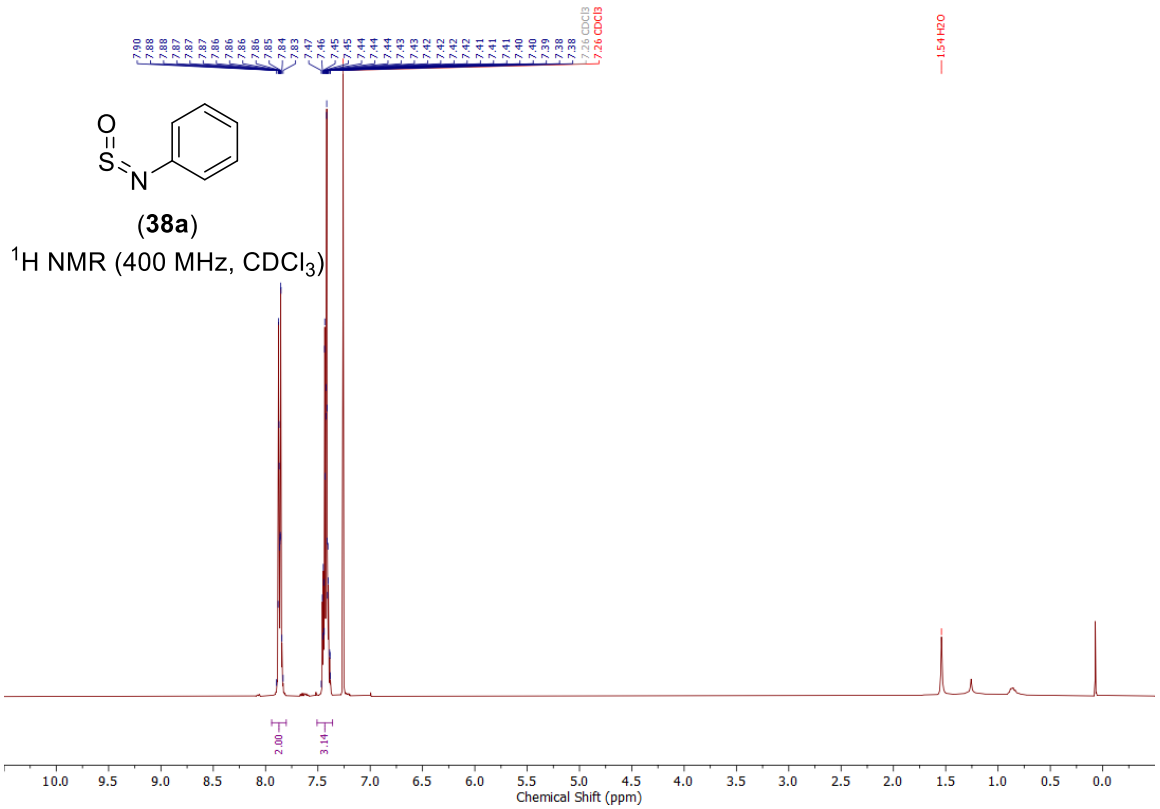


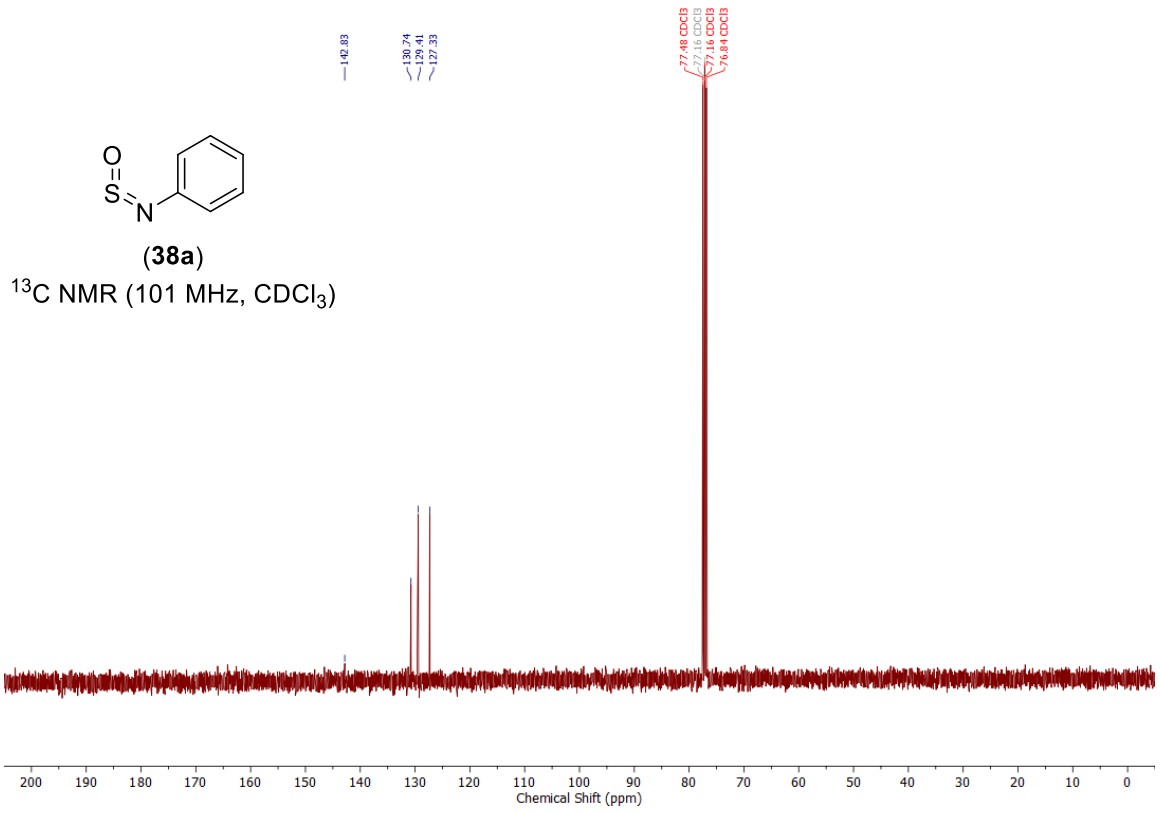
(**33q**)

^{13}C NMR (151 MHz, $CDCl_3$)

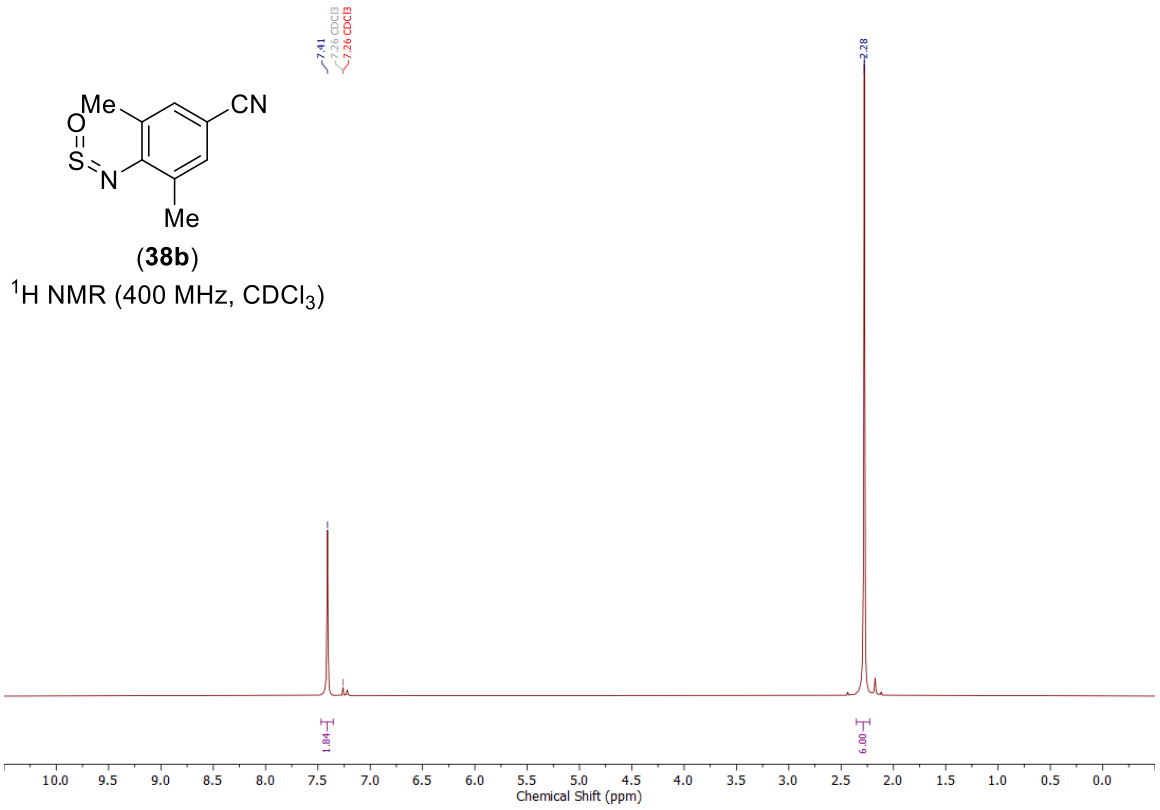
10.4 NMR Spectra for Chapter 4

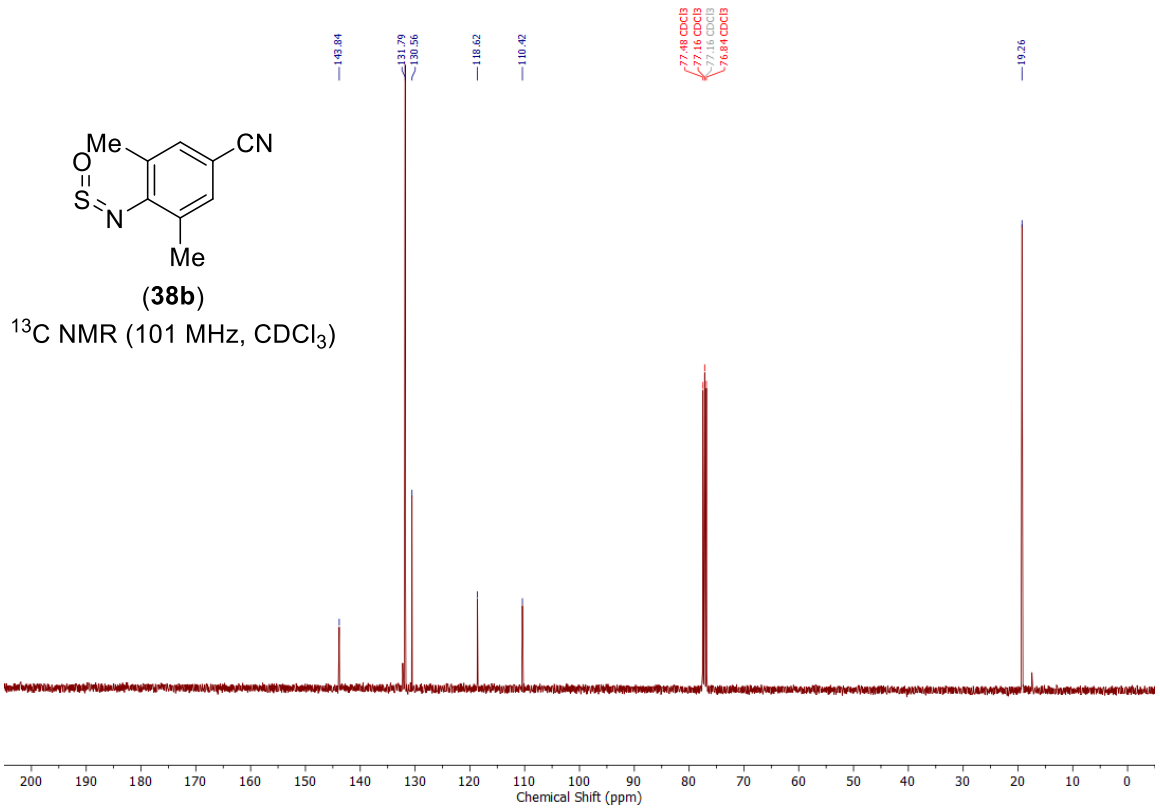
NMR spectra of *N*-sulfinylaniline (38a)



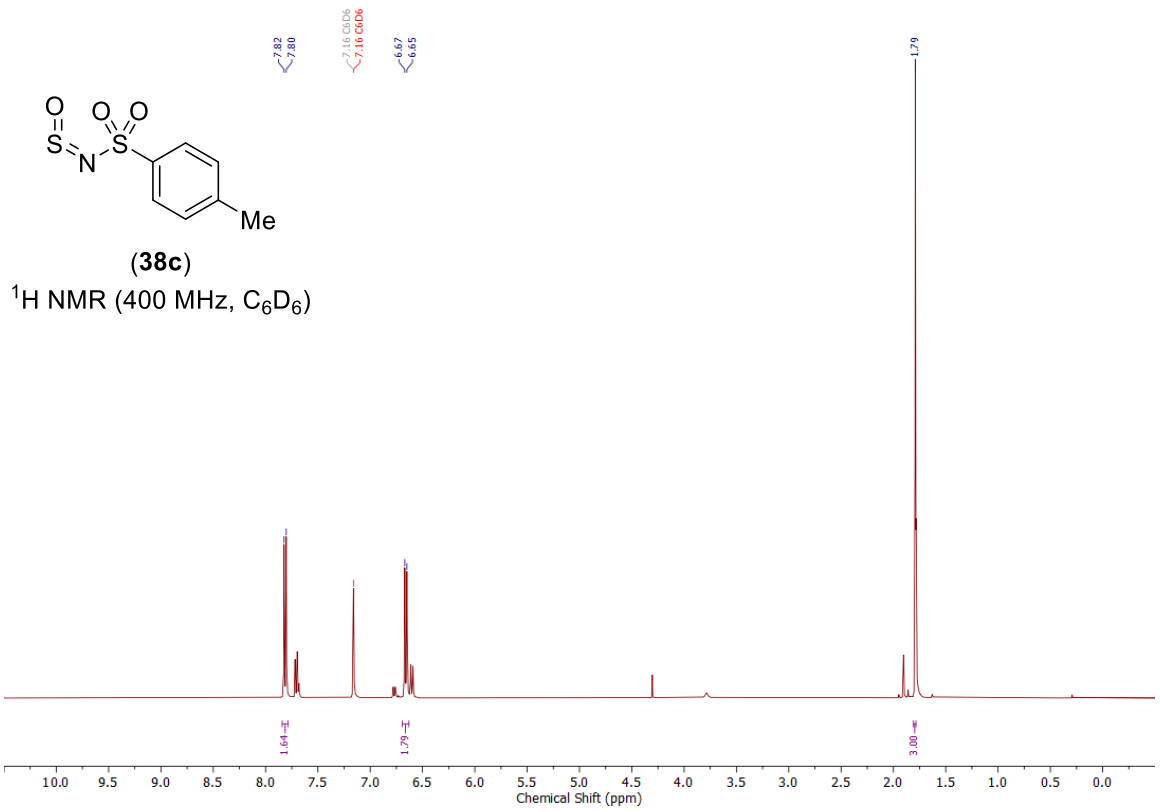


NMR spectra of *N*-sulfinyl-4-cyano-2,6-dimethylaniline (38b):

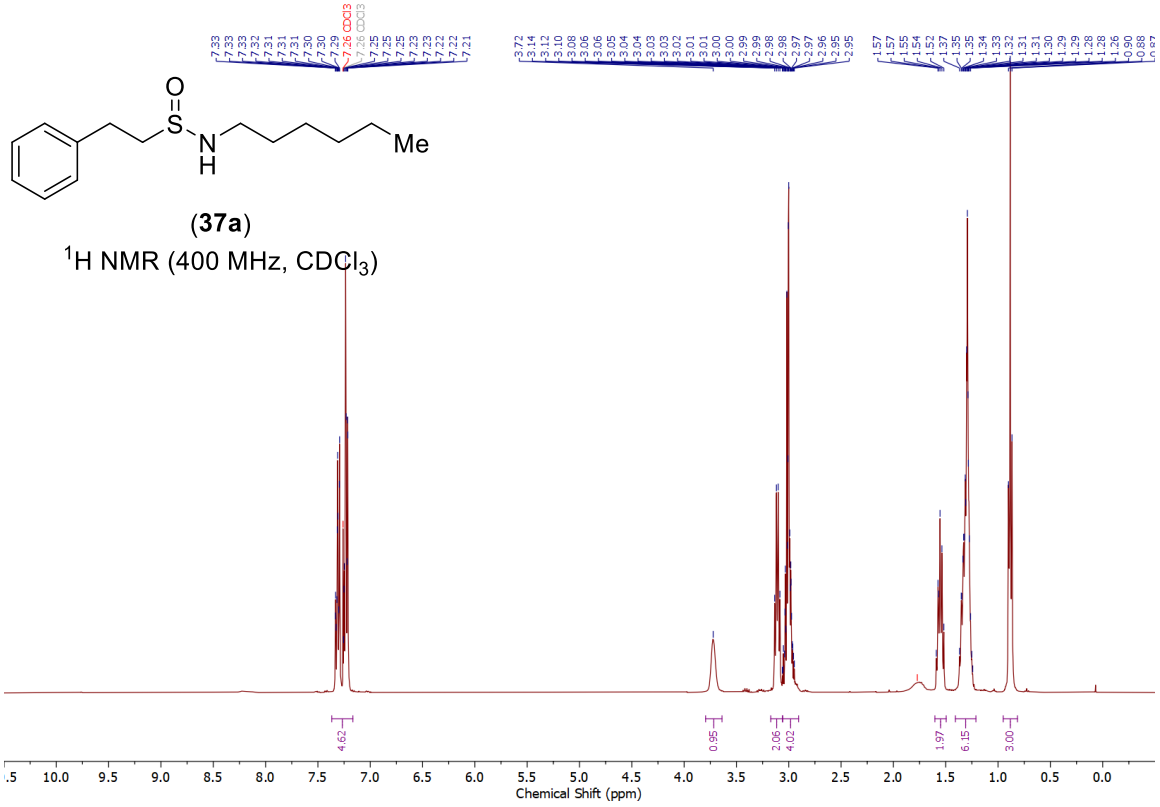


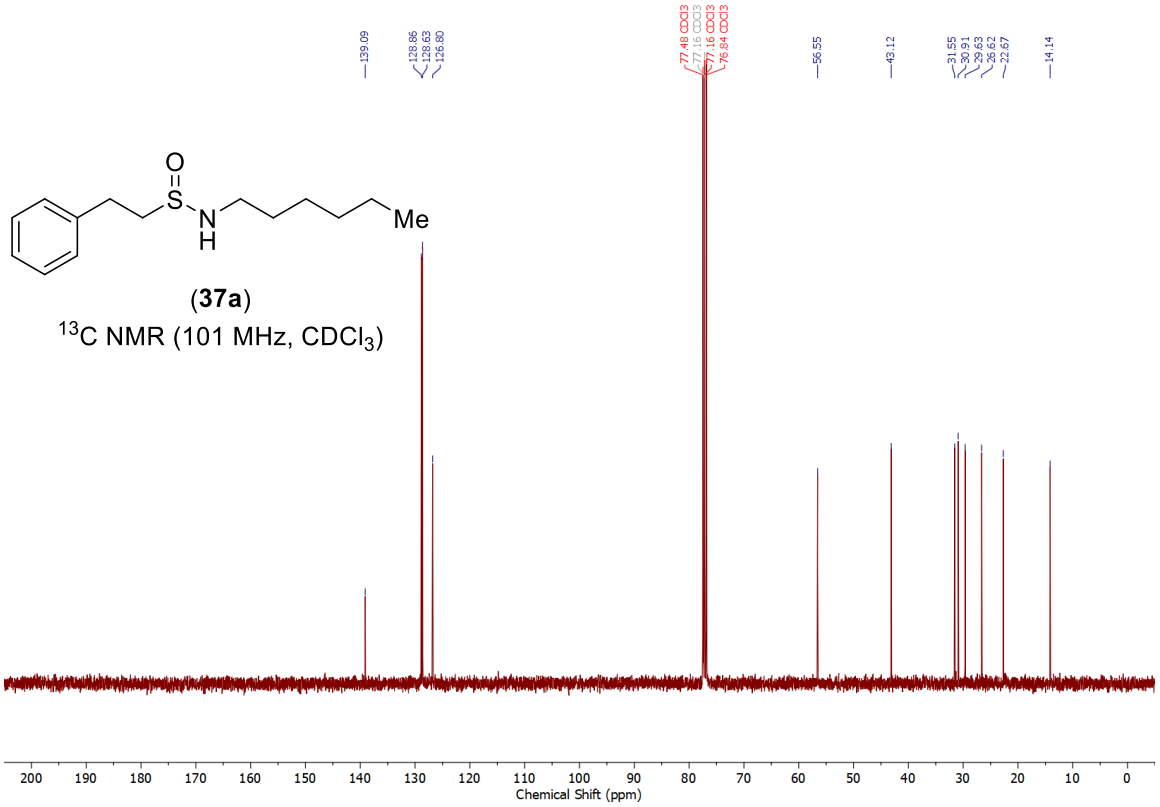


NMR spectra of *N*-sulfinyl-4-toluenesulfonamide (38c):

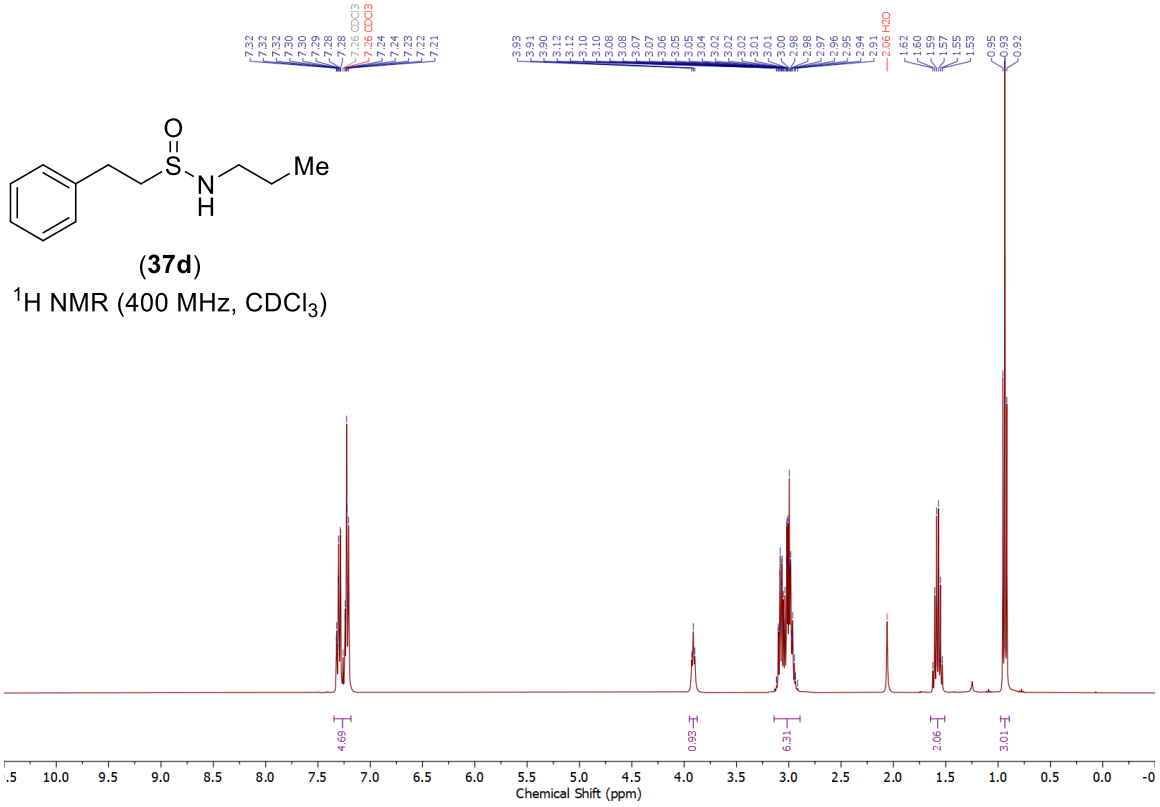


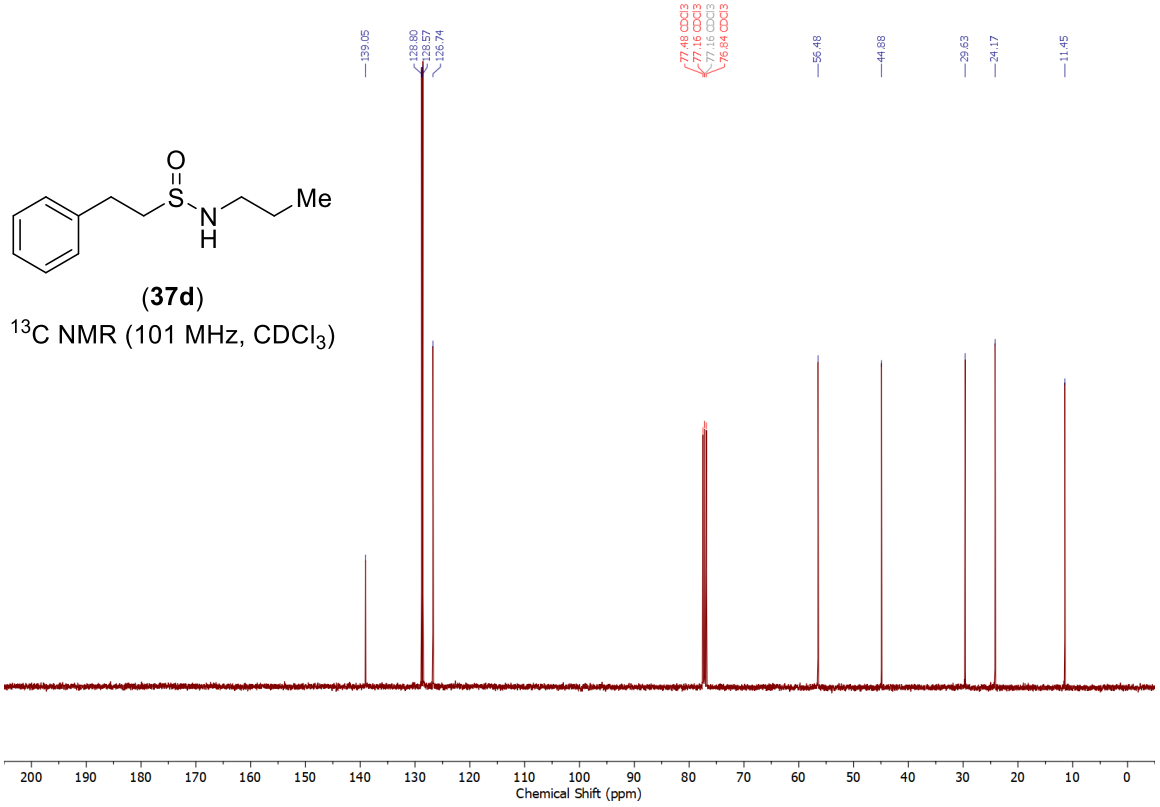
NMR spectra of *N*-hexyl-2-phenylethane-1-sulfinamide (37a):



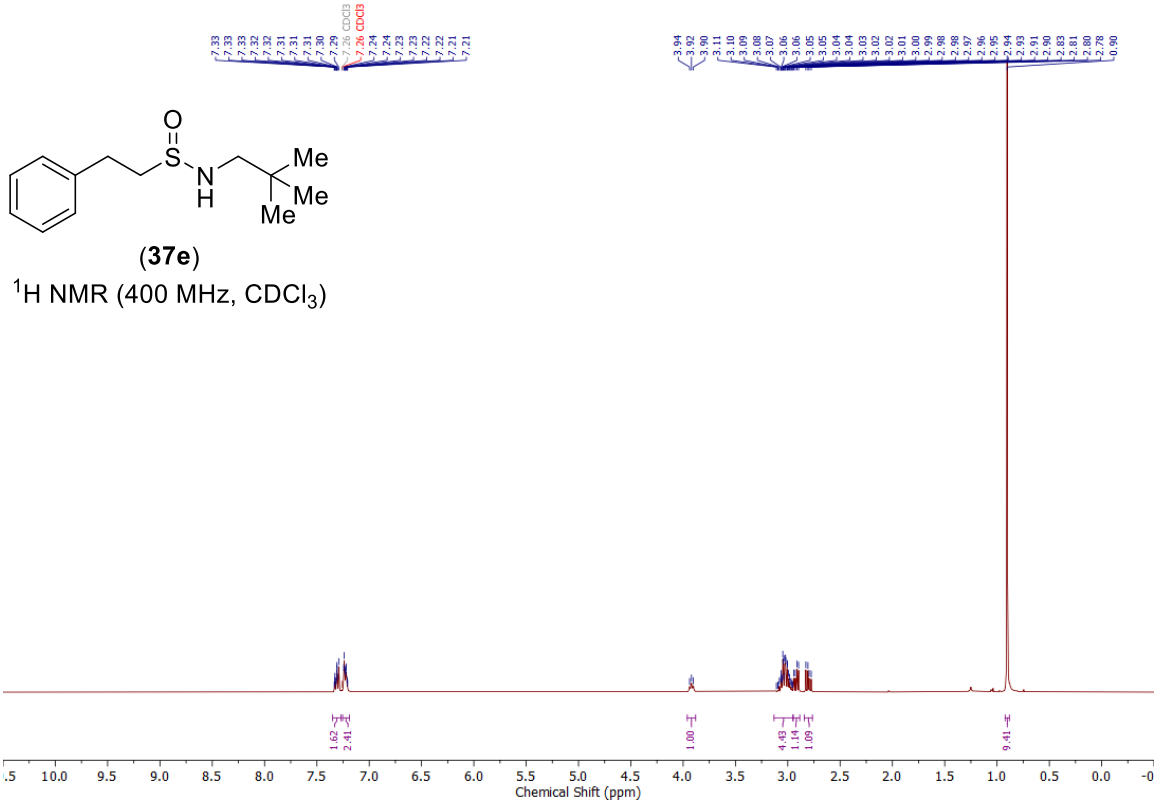


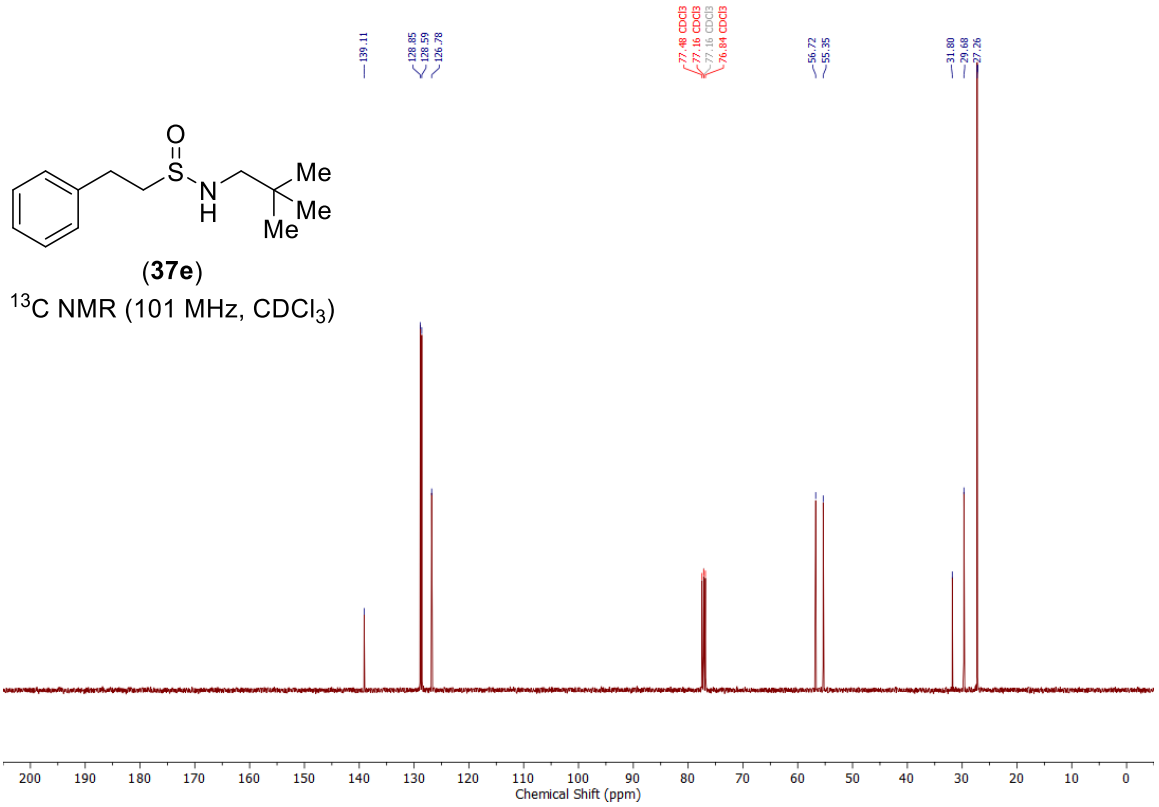
NMR spectra of 2-phenyl-*N*-propylethane-1-sulfinamide (37d):



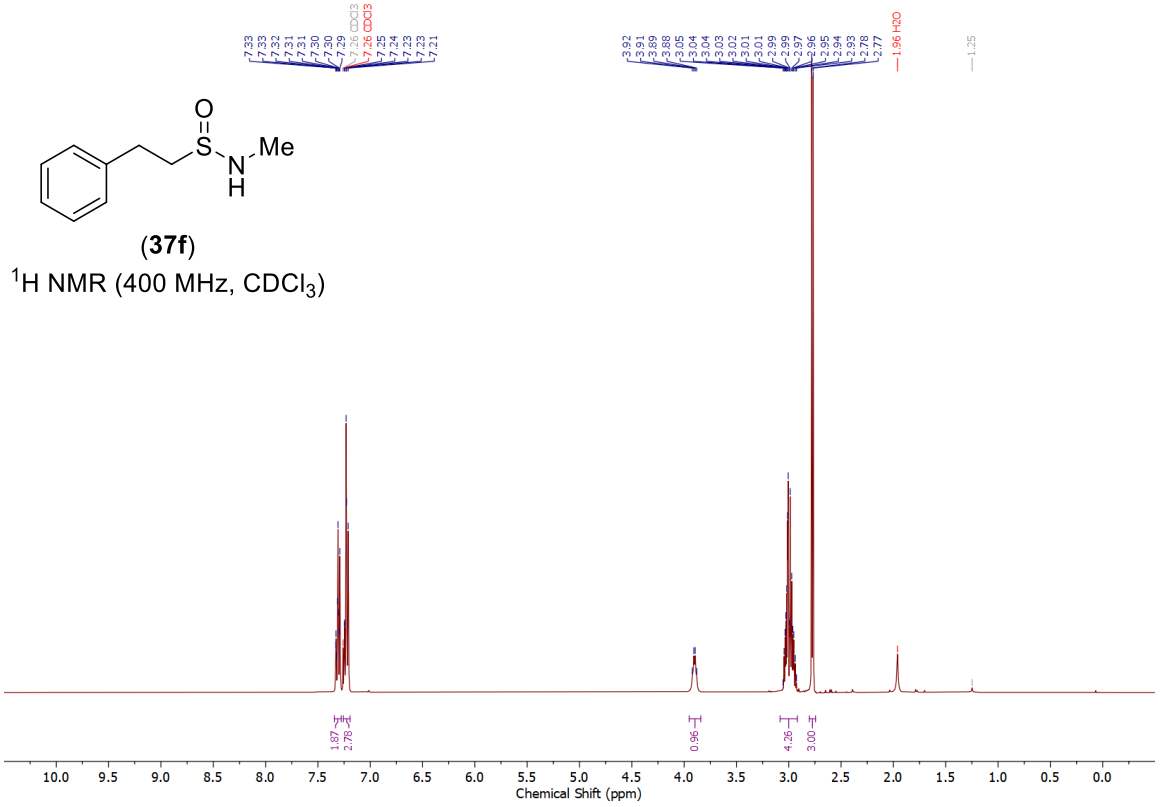


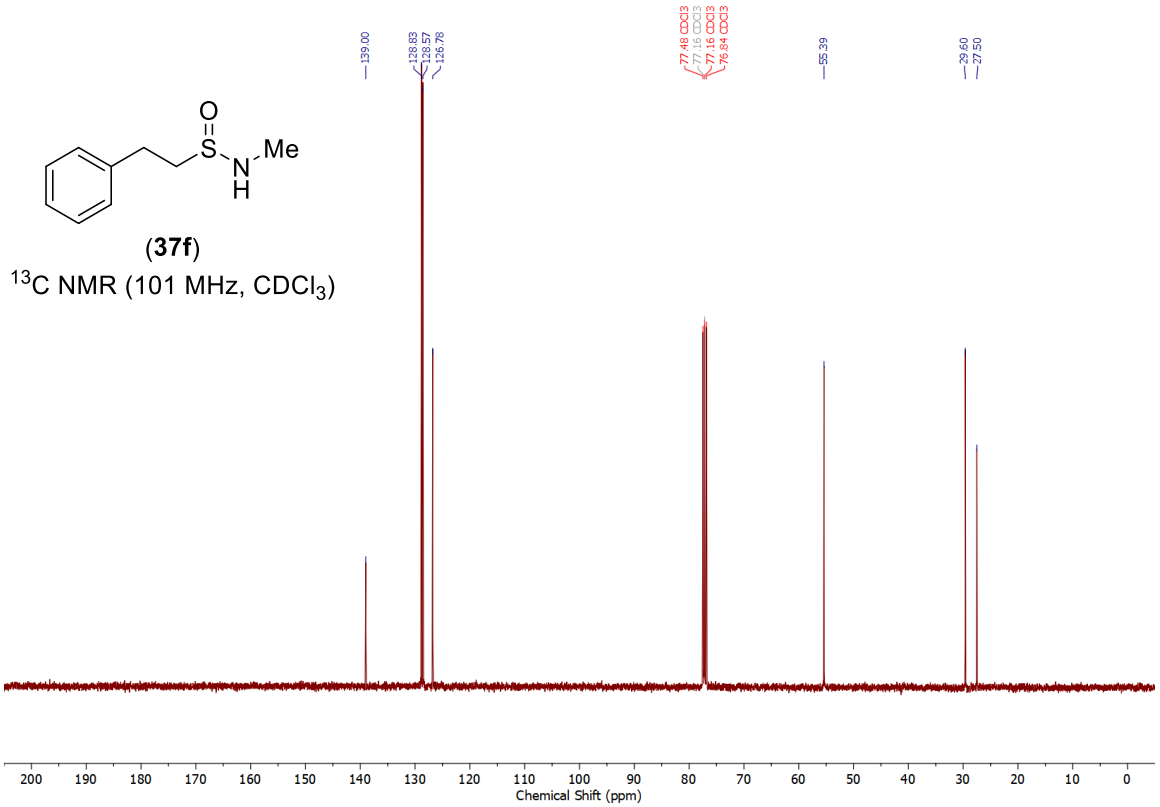
NMR spectra of *N*-neopentyl-2-phenylethane-1-sulfinamide (37e):



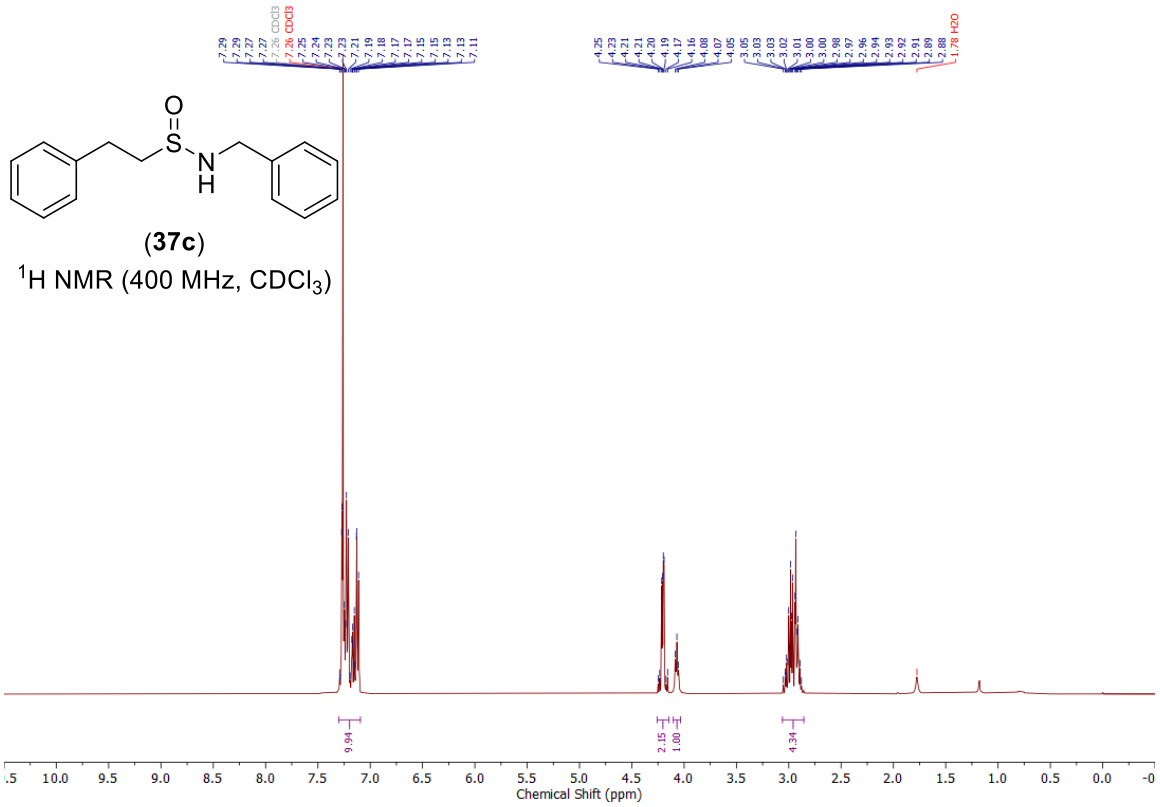


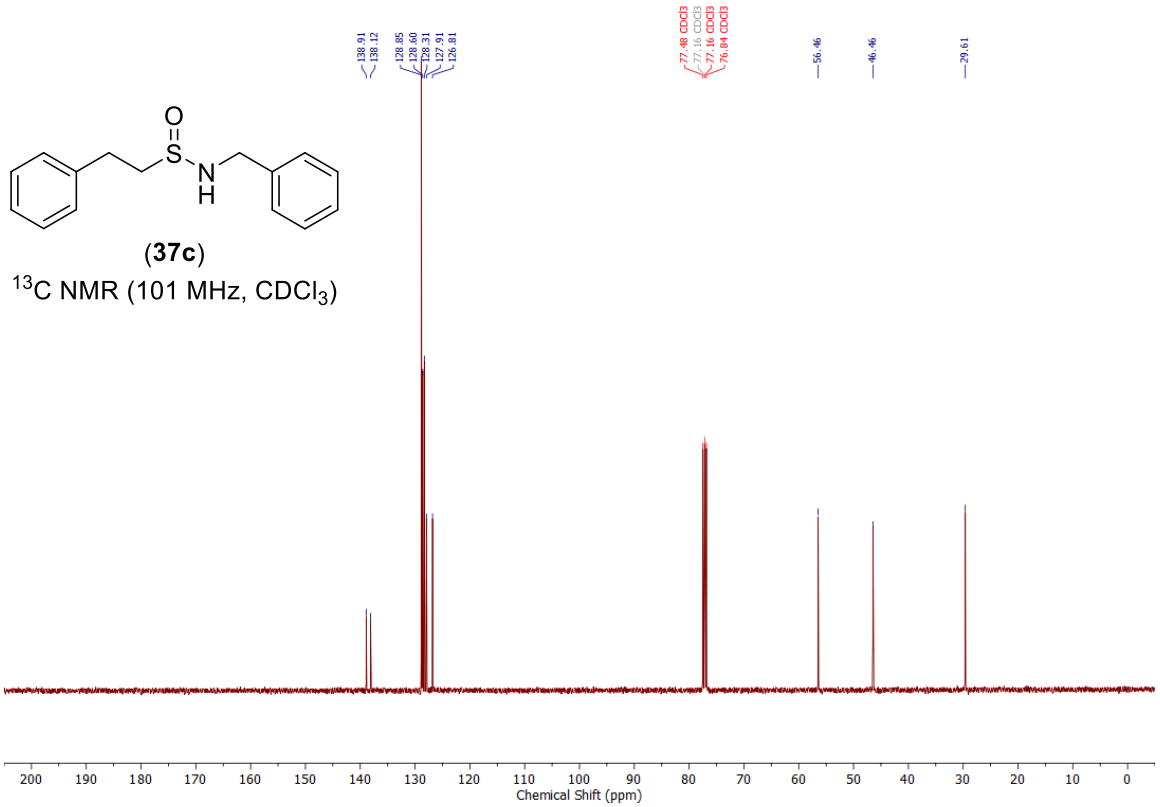
NMR spectra of *N*-methyl-2-phenylethane-1-sulfinamide (37f):



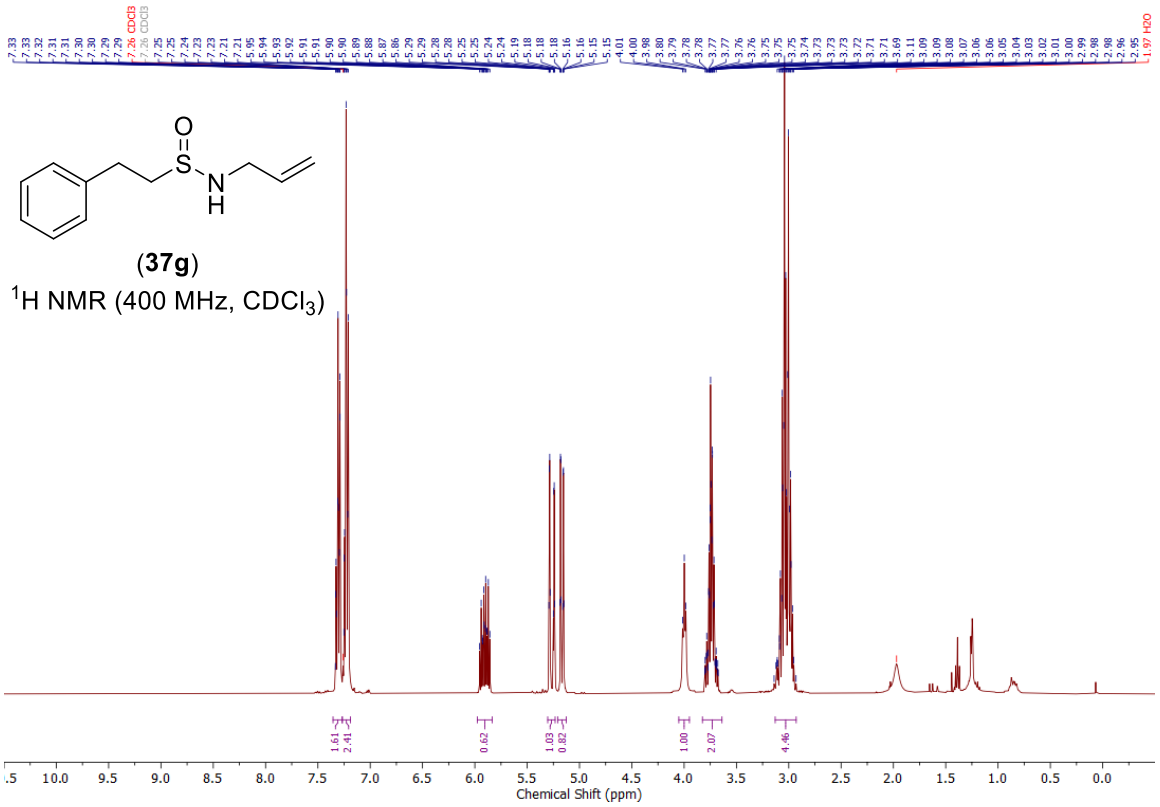


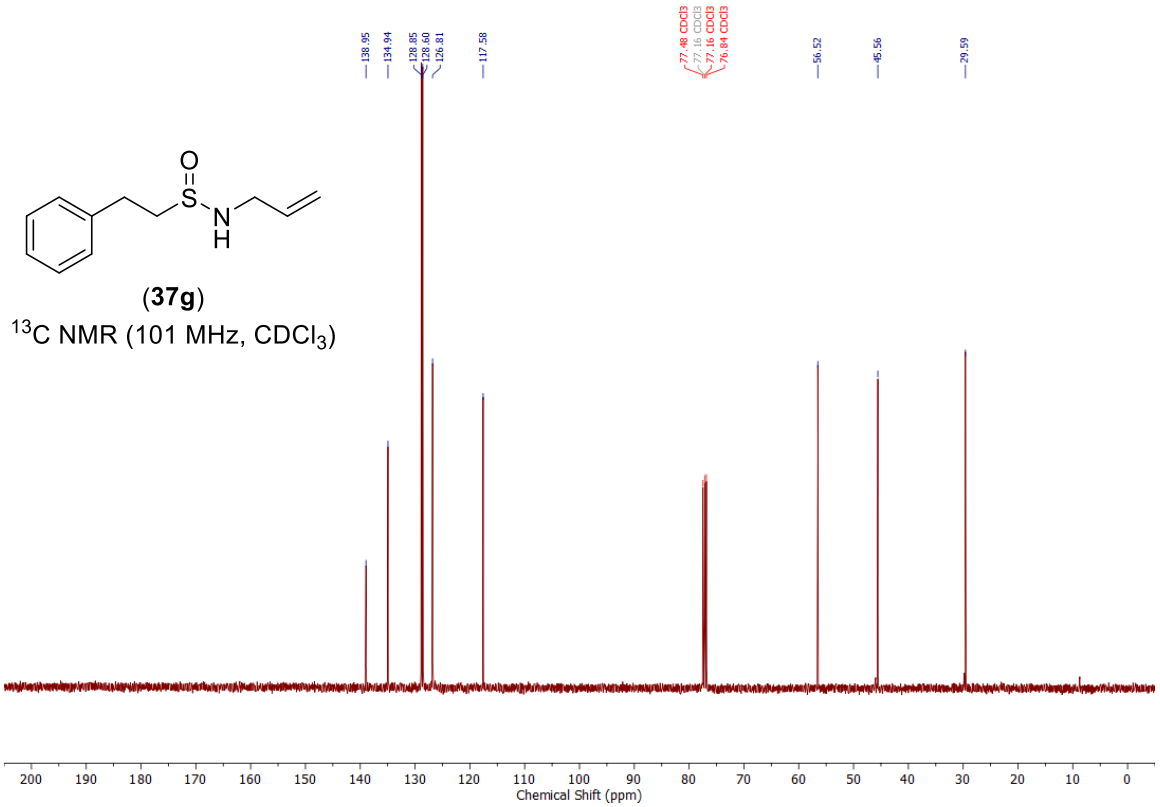
NMR spectra of *N*-benzyl-2-phenylethane-1-sulfinamide (37c):



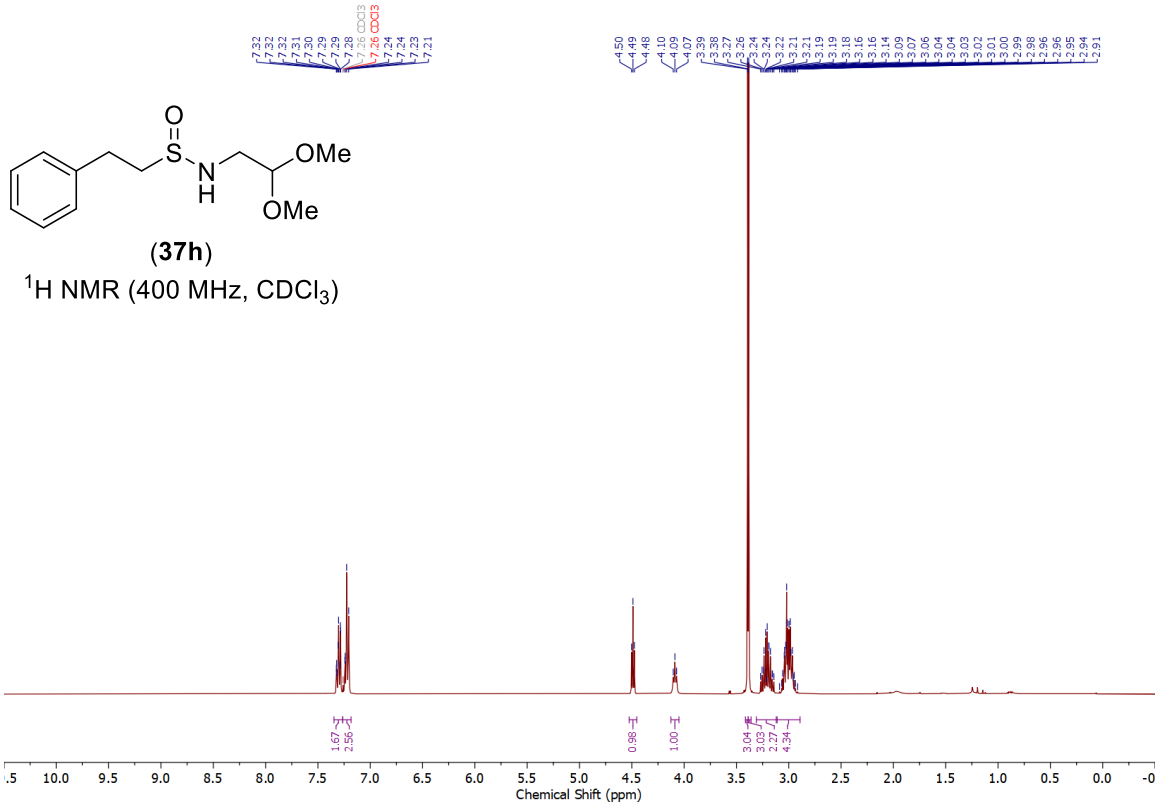


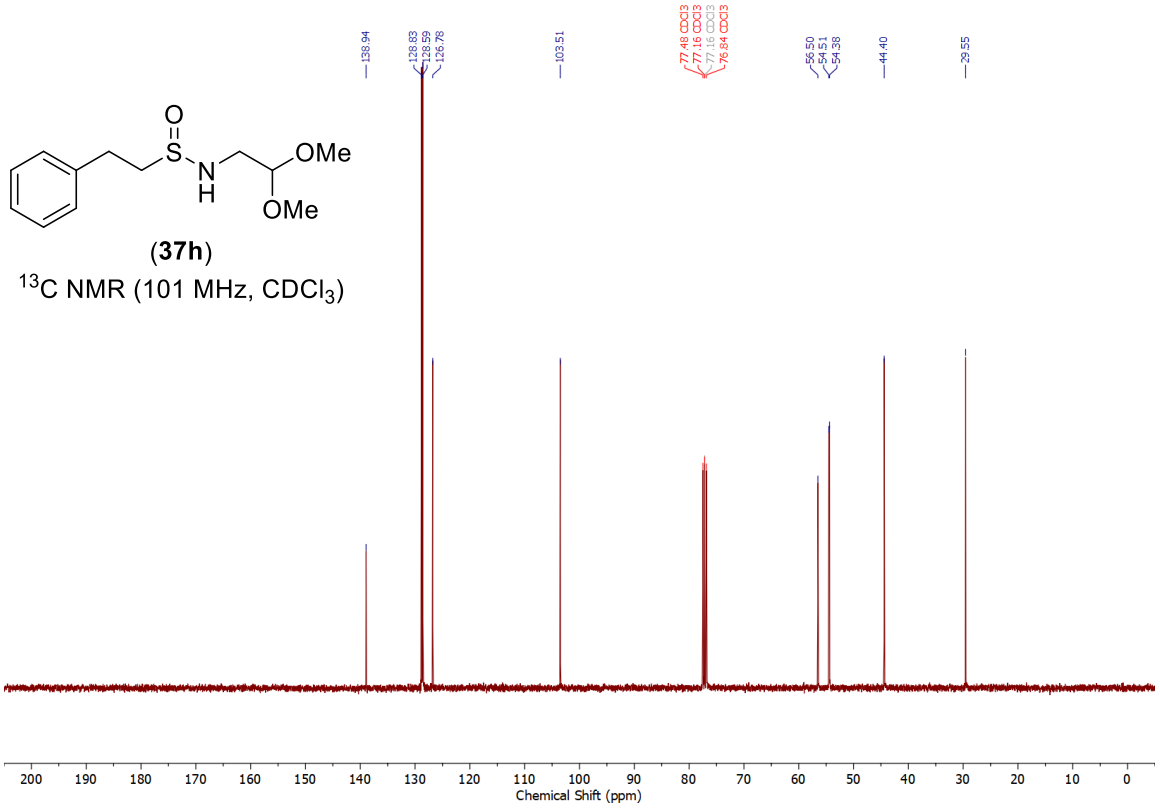
NMR spectra of *N*-allyl-2-phenylethane-1-sulfinamide (37g):



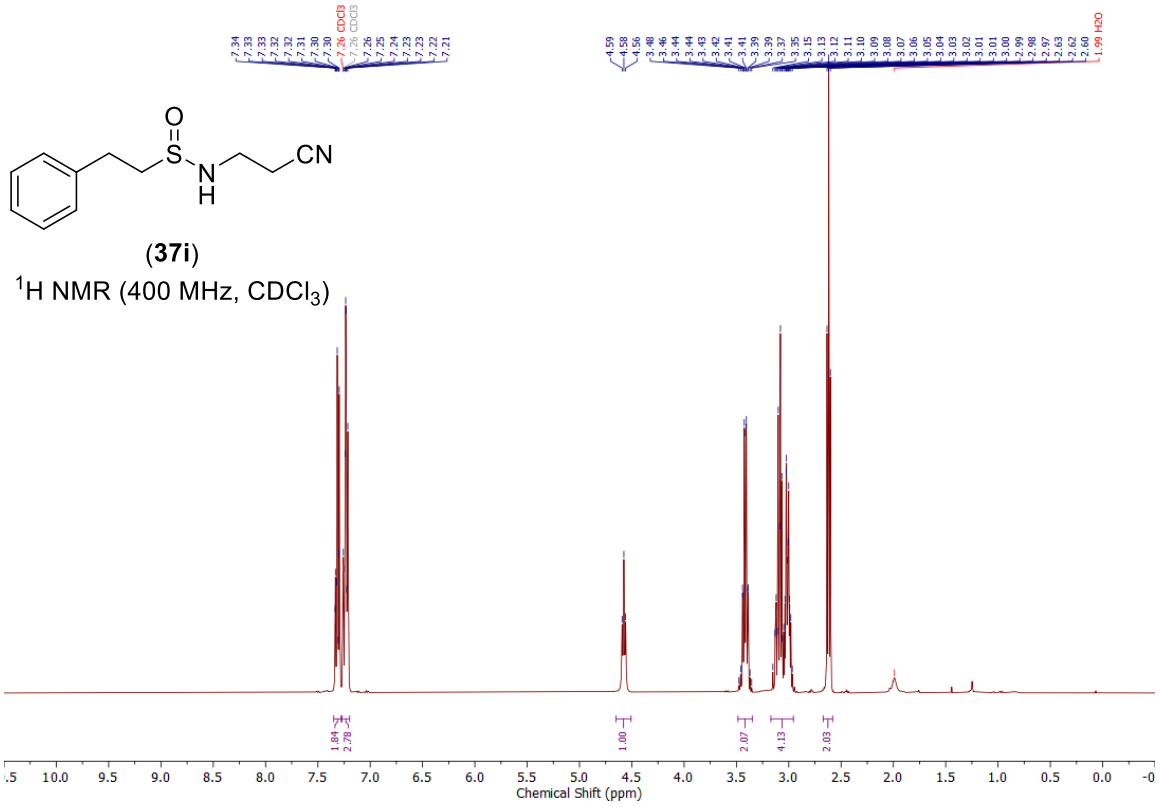


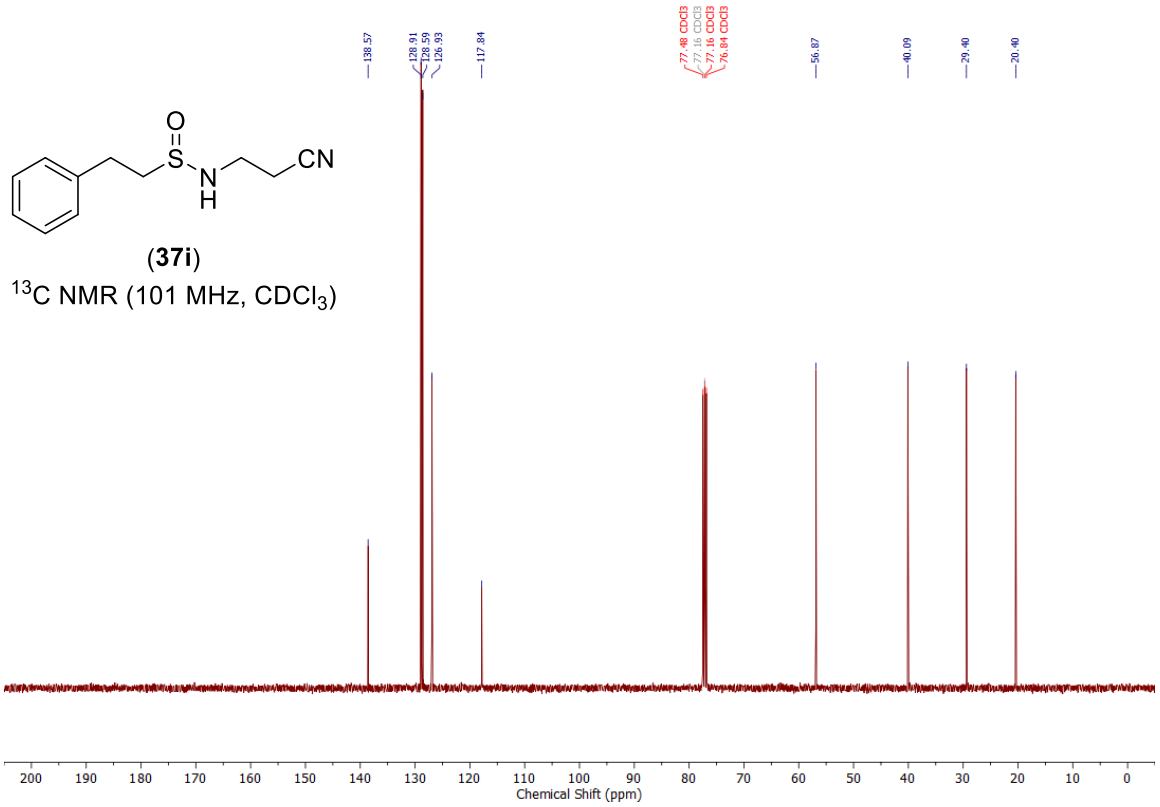
NMR spectra of *N*-(2,2-dimethoxyethyl)-2-phenylethane-1-sulfinamide (37h)



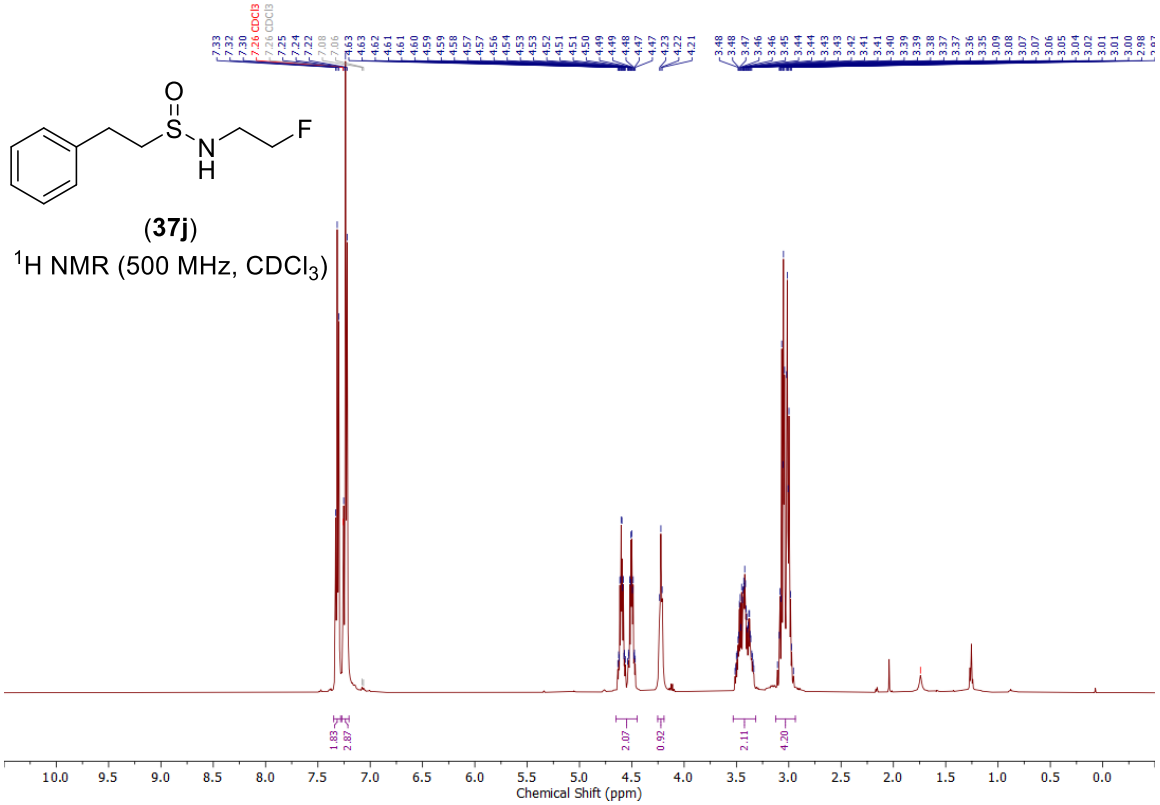


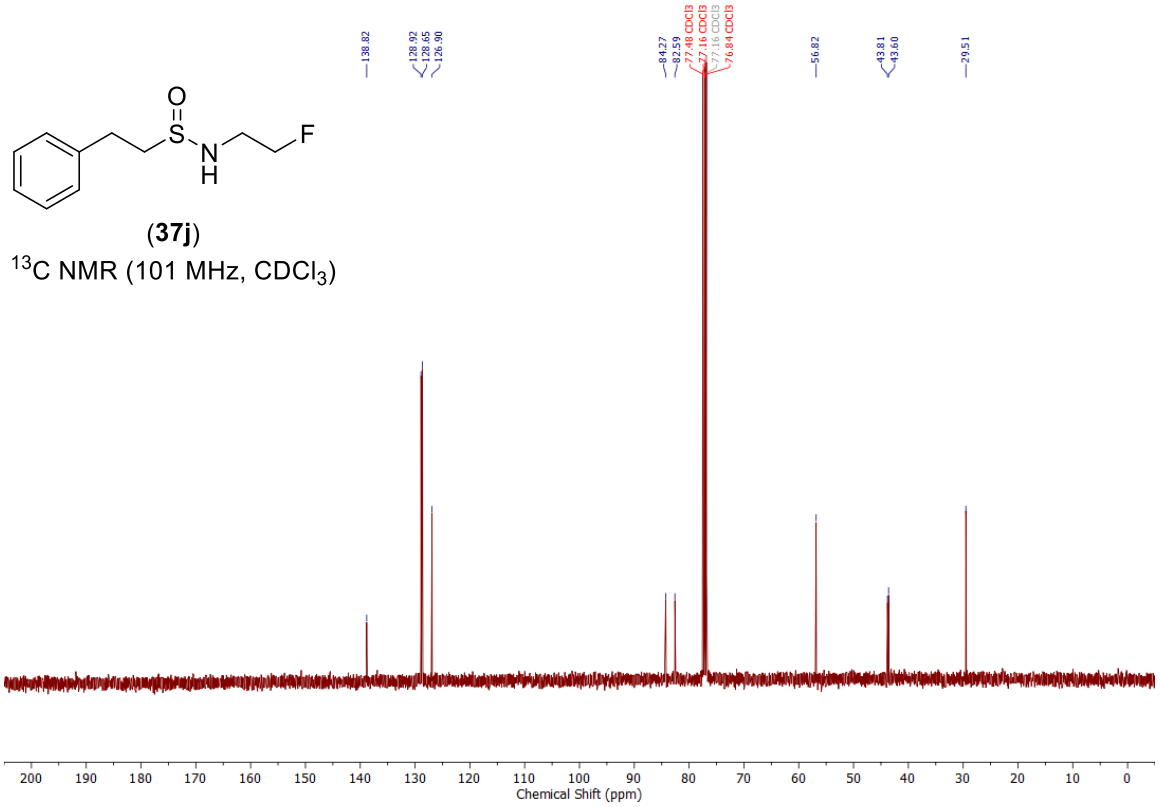
NMR spectra of *N*-(2-cyanoethyl)-2-phenylethane-1-sulfinamide (37i):

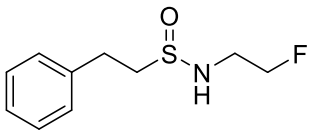




NMR spectra of *N*-(2-fluoroethyl)-2-phenylethane-1-sulfinamide (37j):



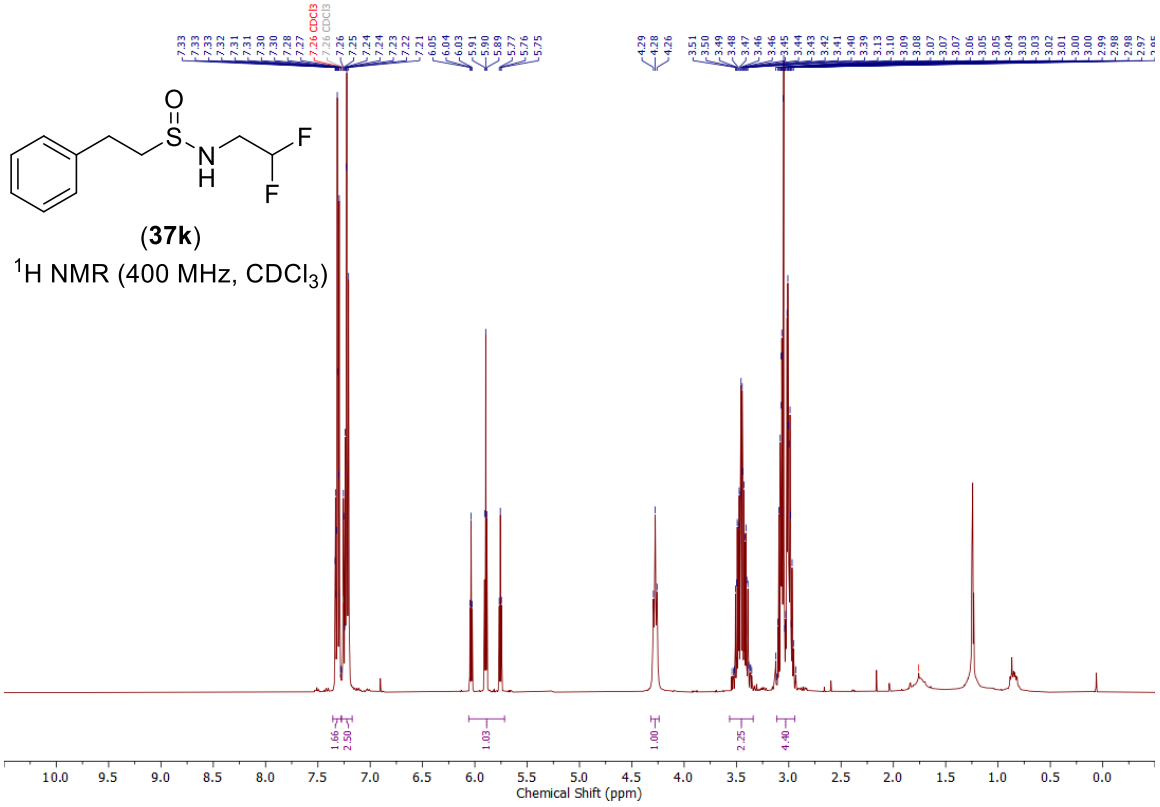


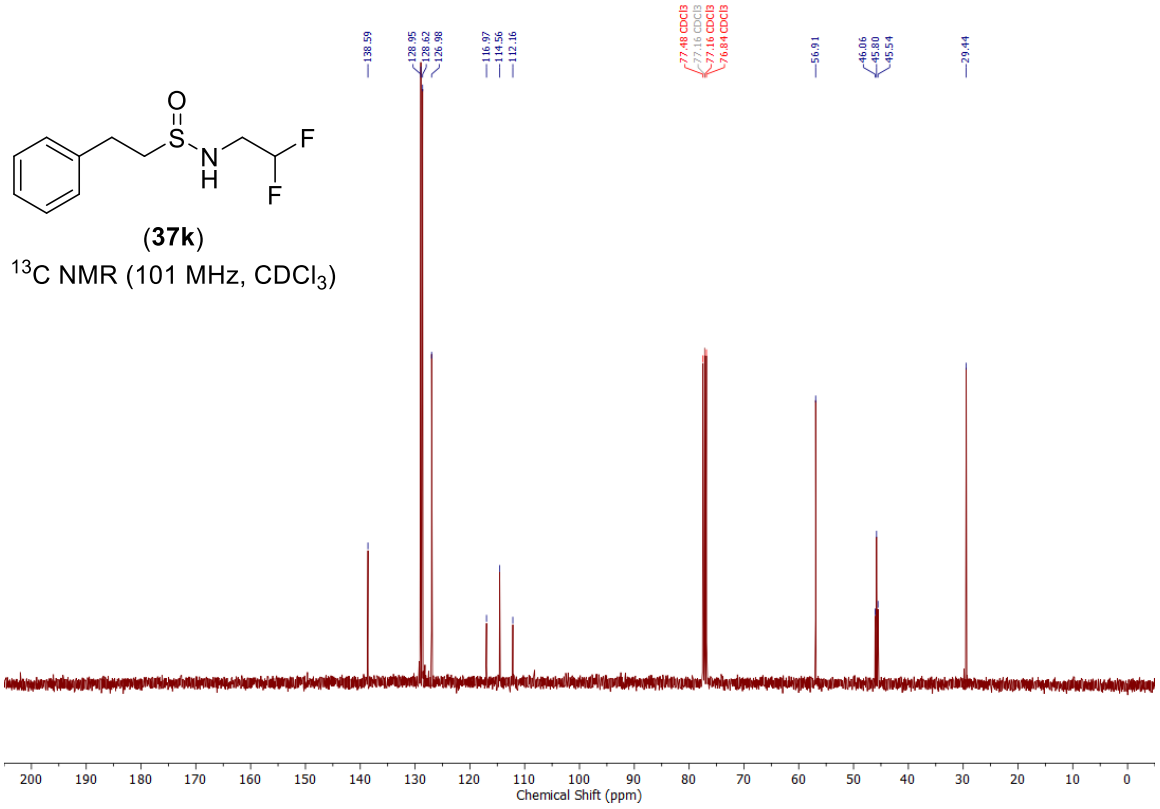


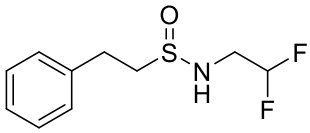
(**37j**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of *N*-(2,2-difluoroethyl)-2-phenylethane-1-sulfinamide (37k):



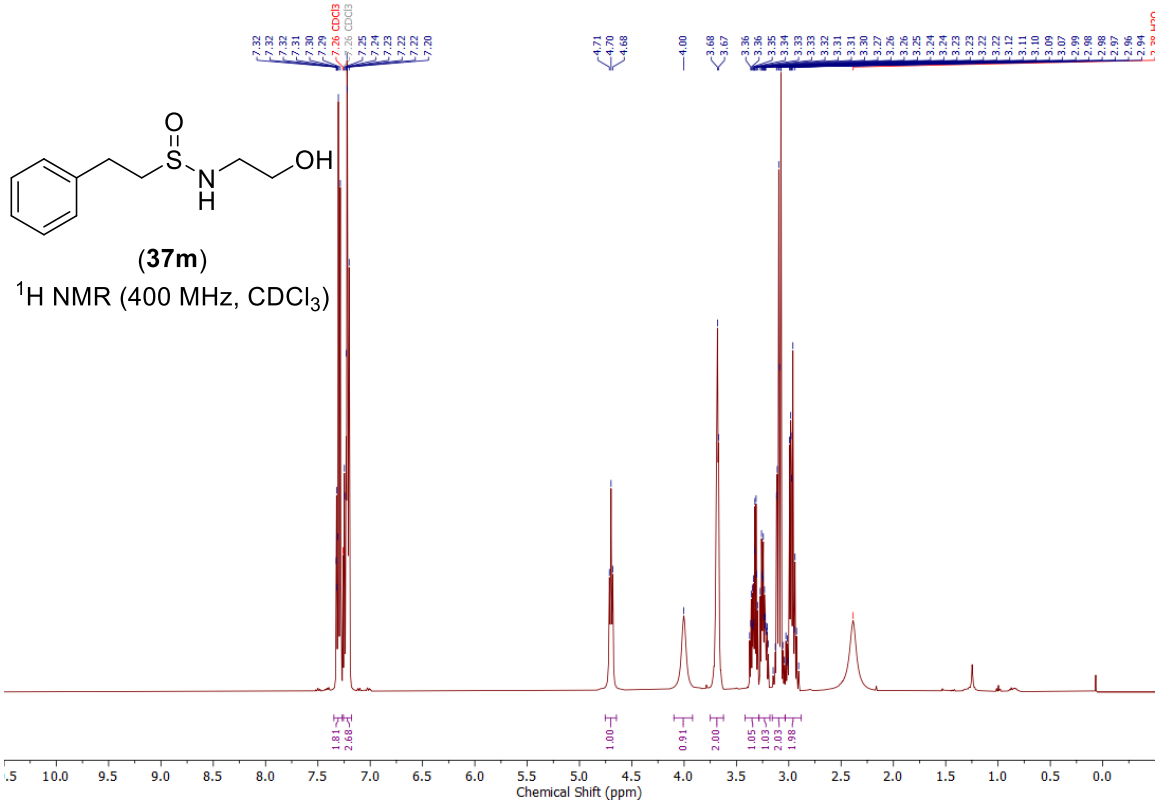


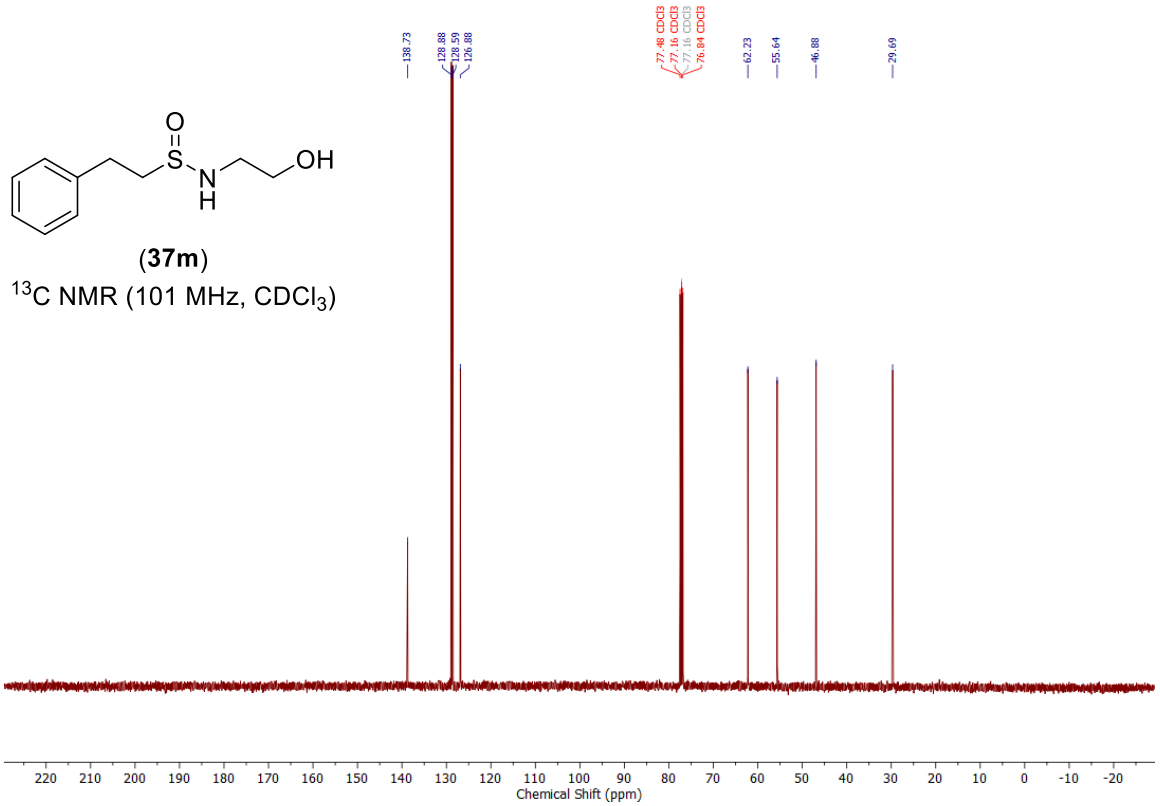


(**37k**)

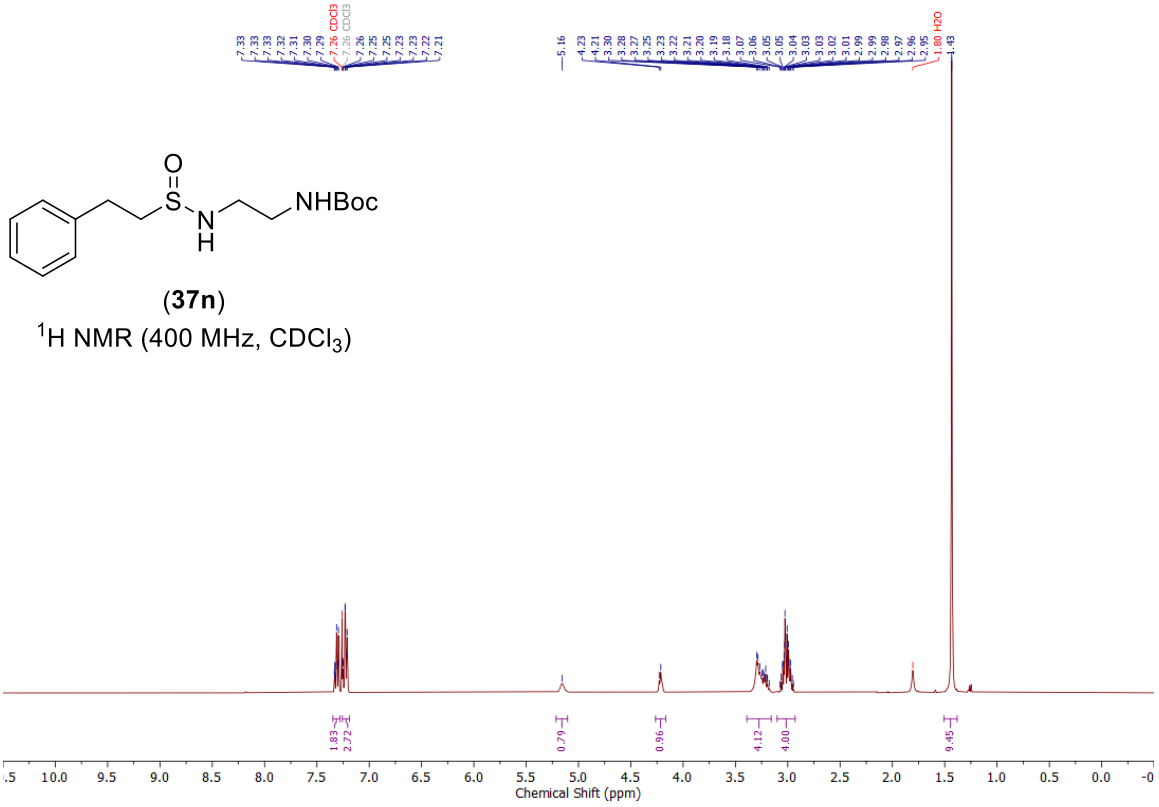
^{19}F NMR (377 MHz, $CDCl_3$)

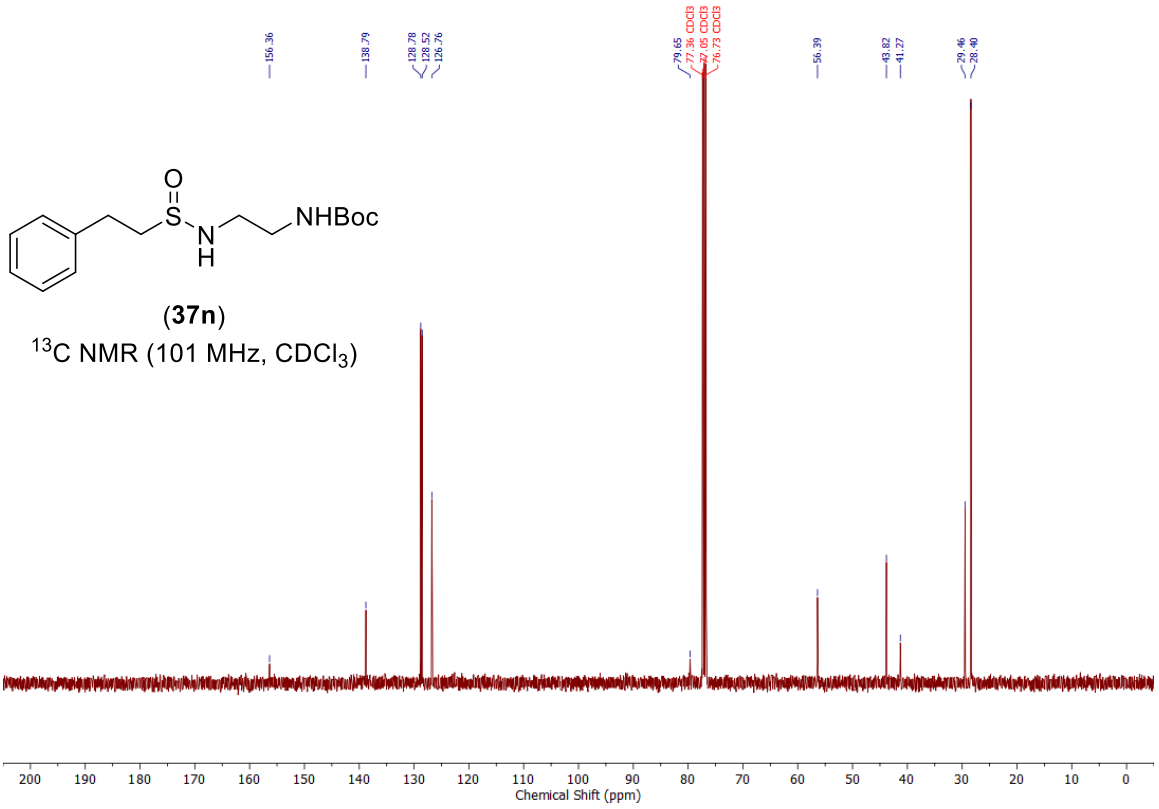
NMR spectra of *N*-(2-hydroxyethyl)-2-phenylethane-1-sulfinamide (37m):



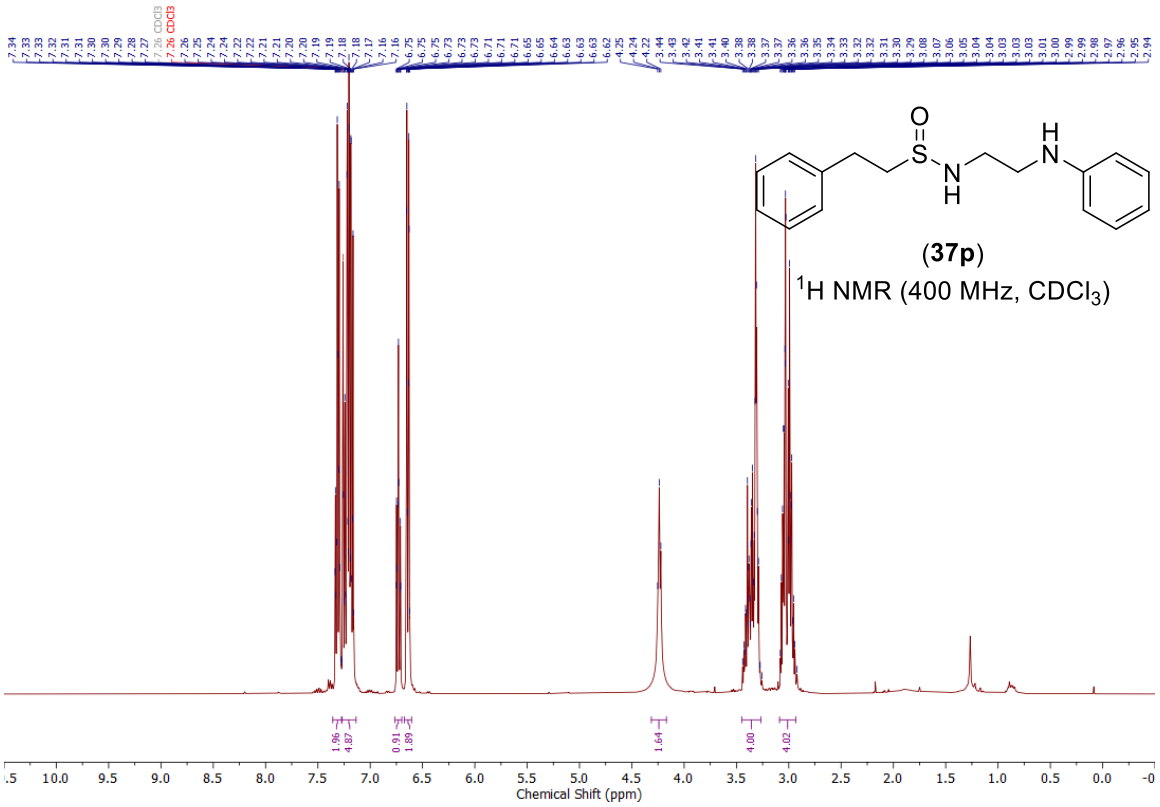


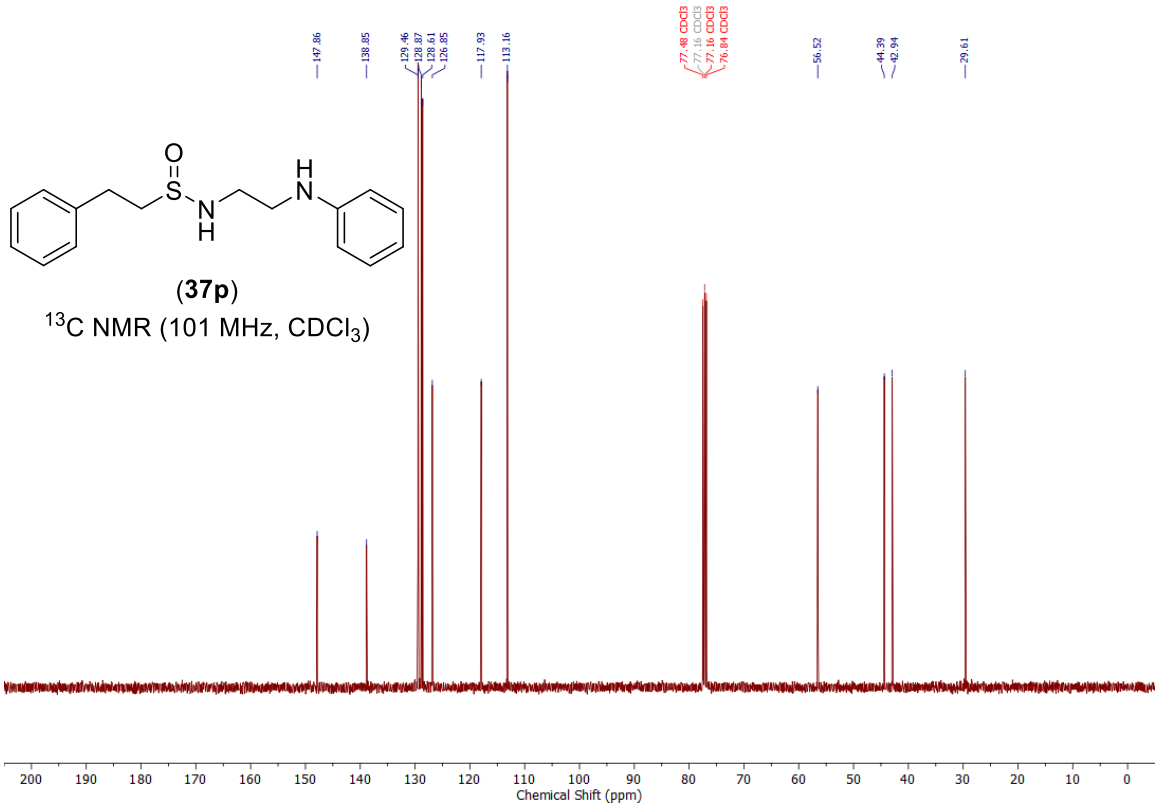
NMR spectra of *tert*-butyl (2-((phenethylsulfinyl)amino)ethyl)carbamate (37n):



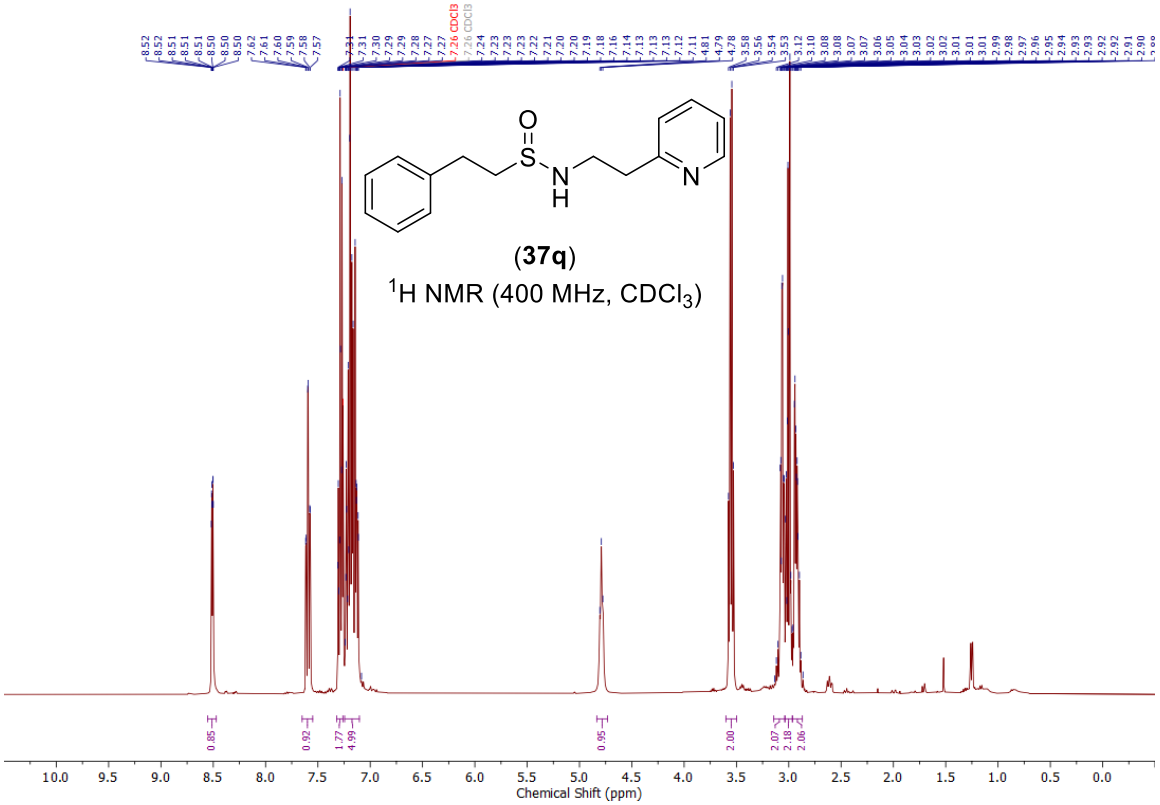


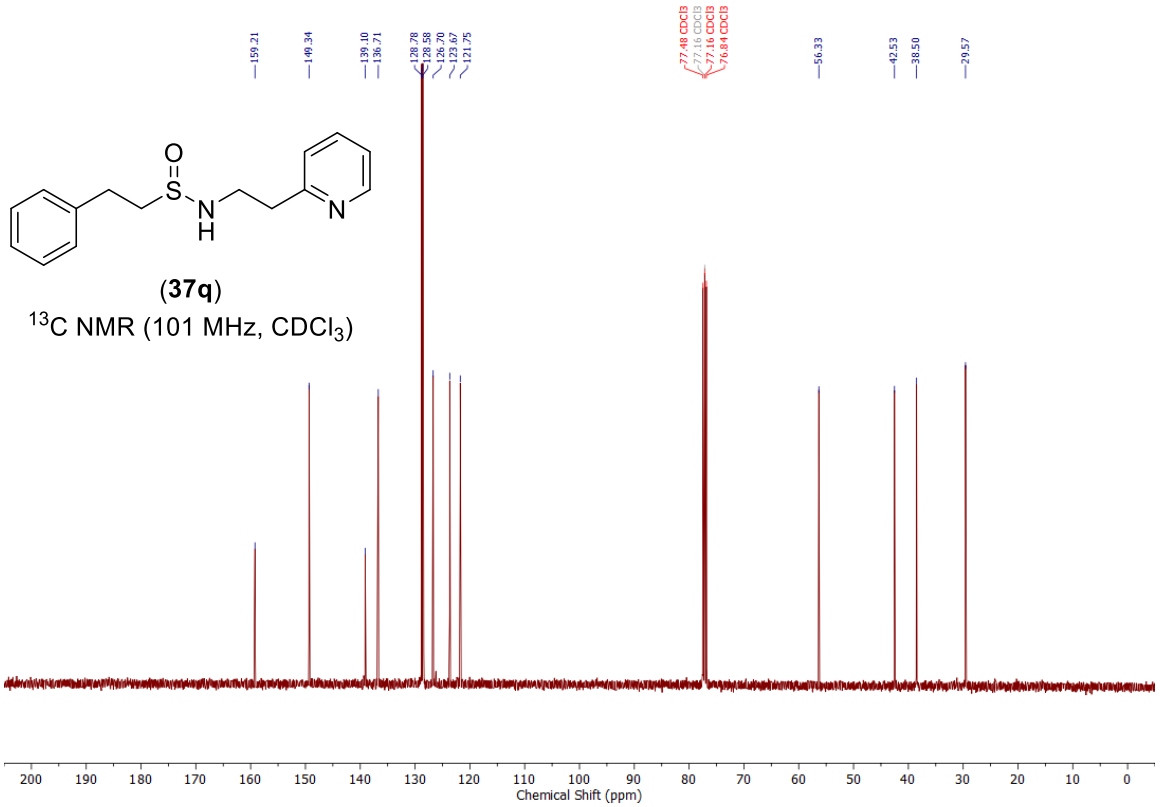
NMR spectra of 2-phenyl-*N*-(2-(phenylamino)ethyl)ethane-1-sulfinamide (37p):



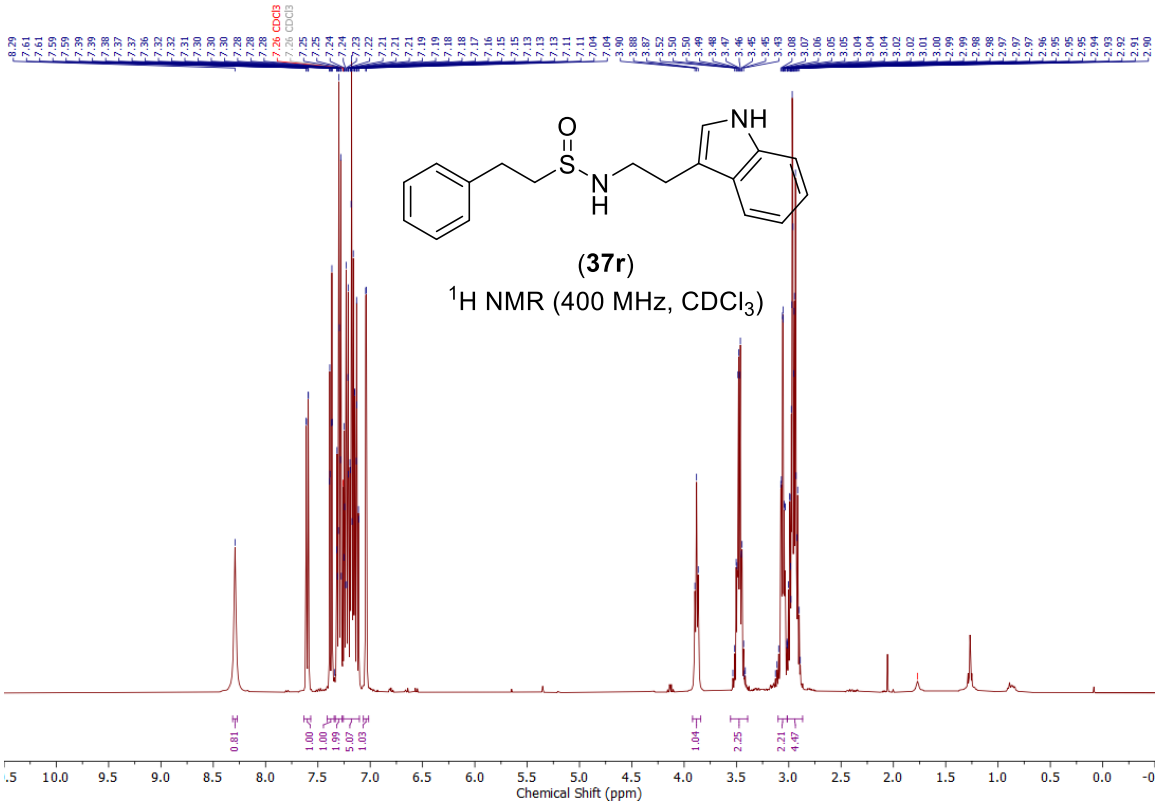


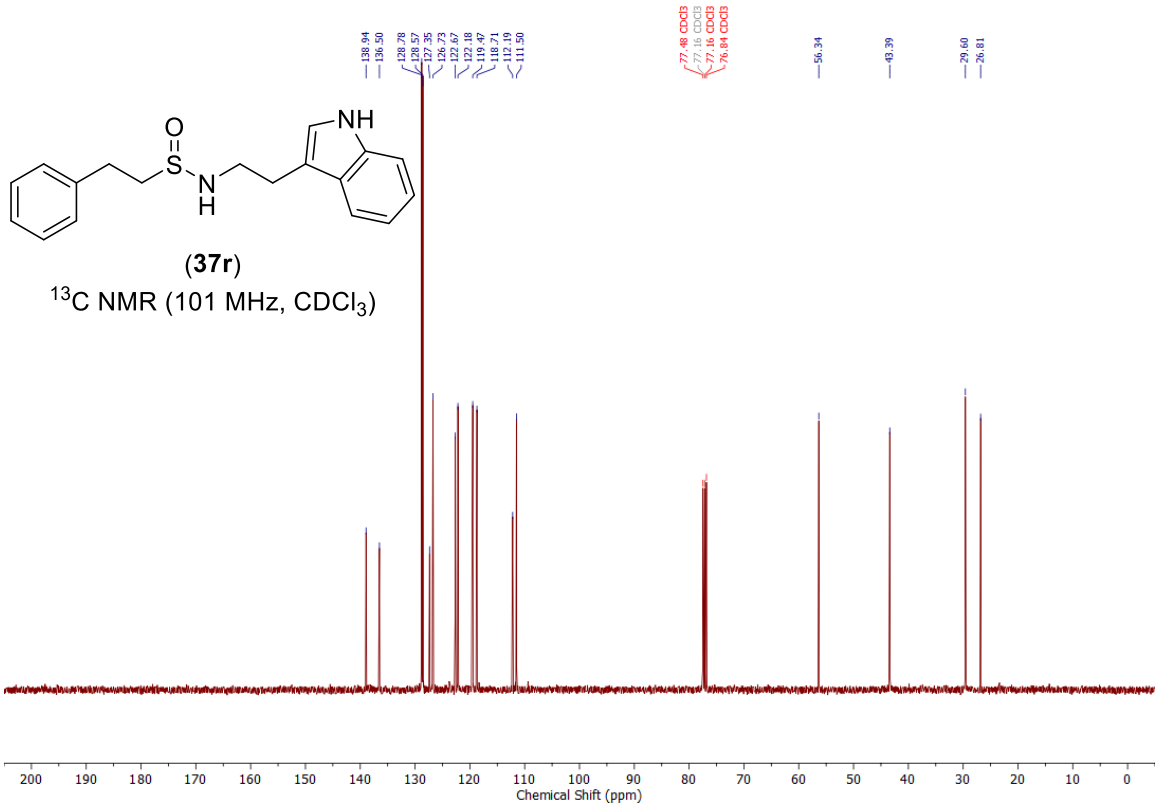
NMR spectra of 2-phenyl-*N*-(2-(pyridin-2-yl)ethyl)ethane-1-sulfinamide (37q):



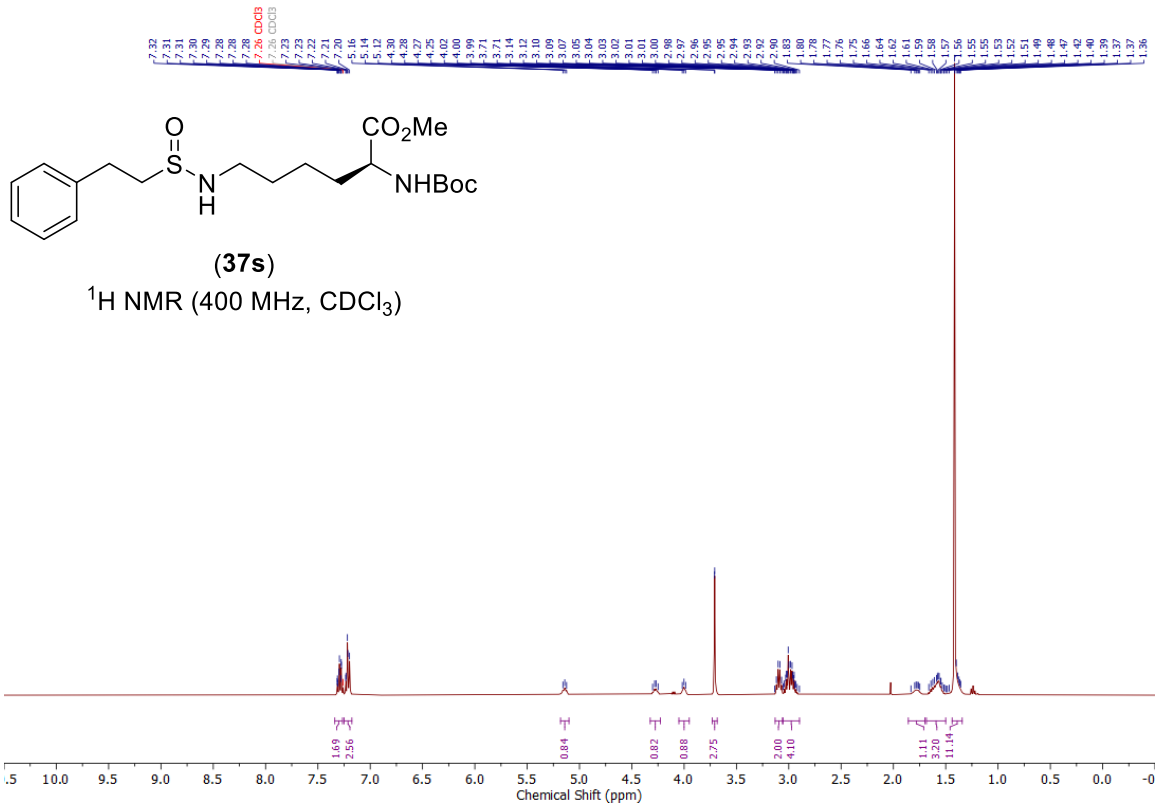


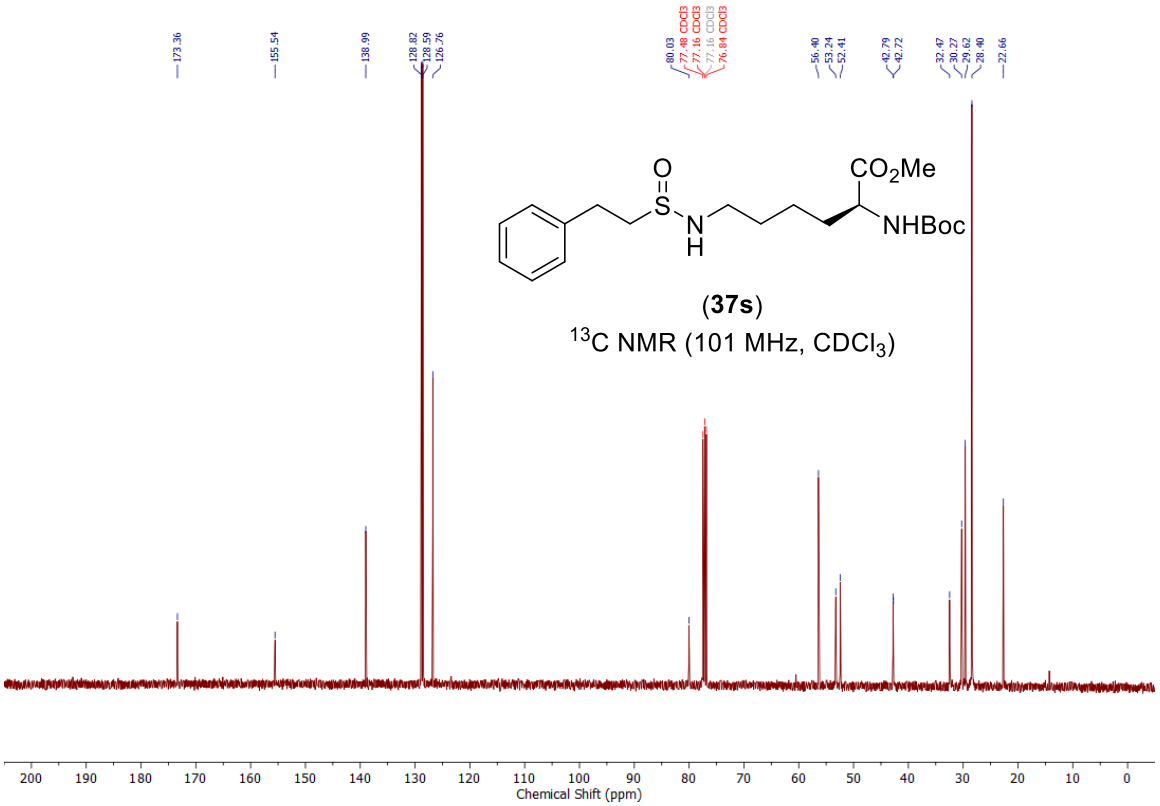
NMR spectra of *N*-(2-(1*H*-indol-3-yl)ethyl)-2-phenylethane-1-sulfinamide (37r):



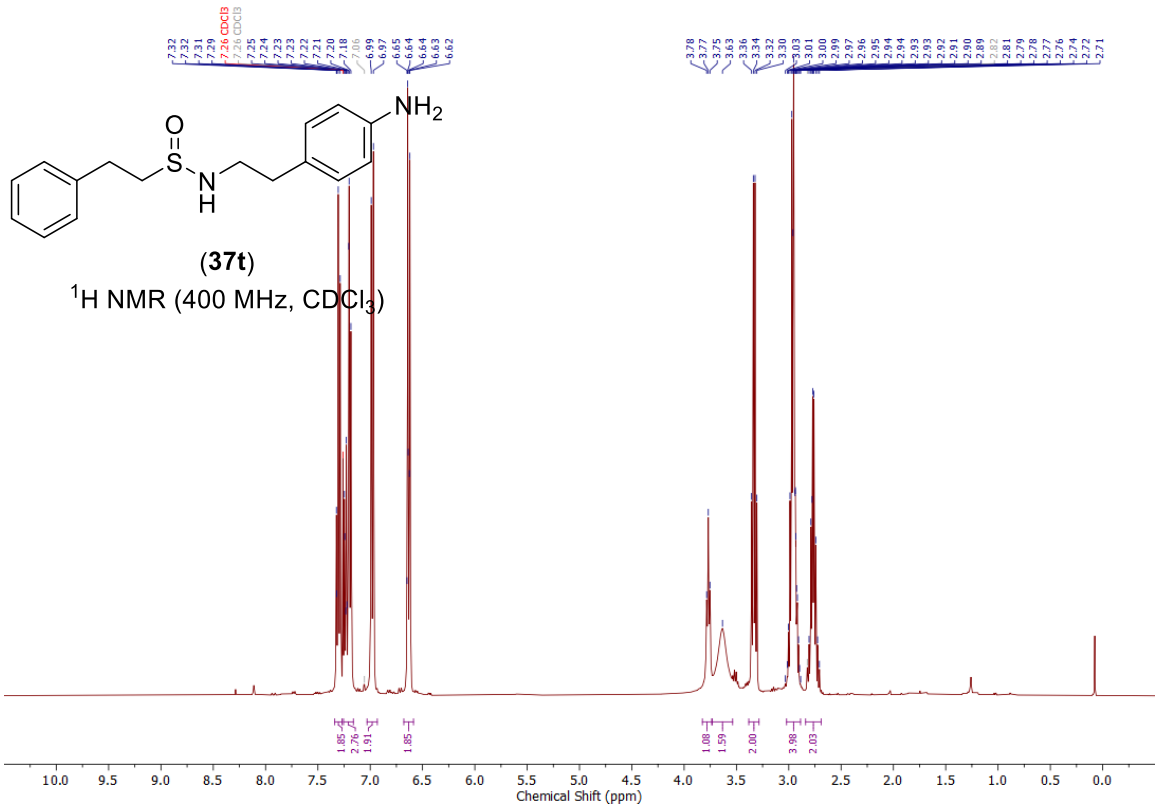


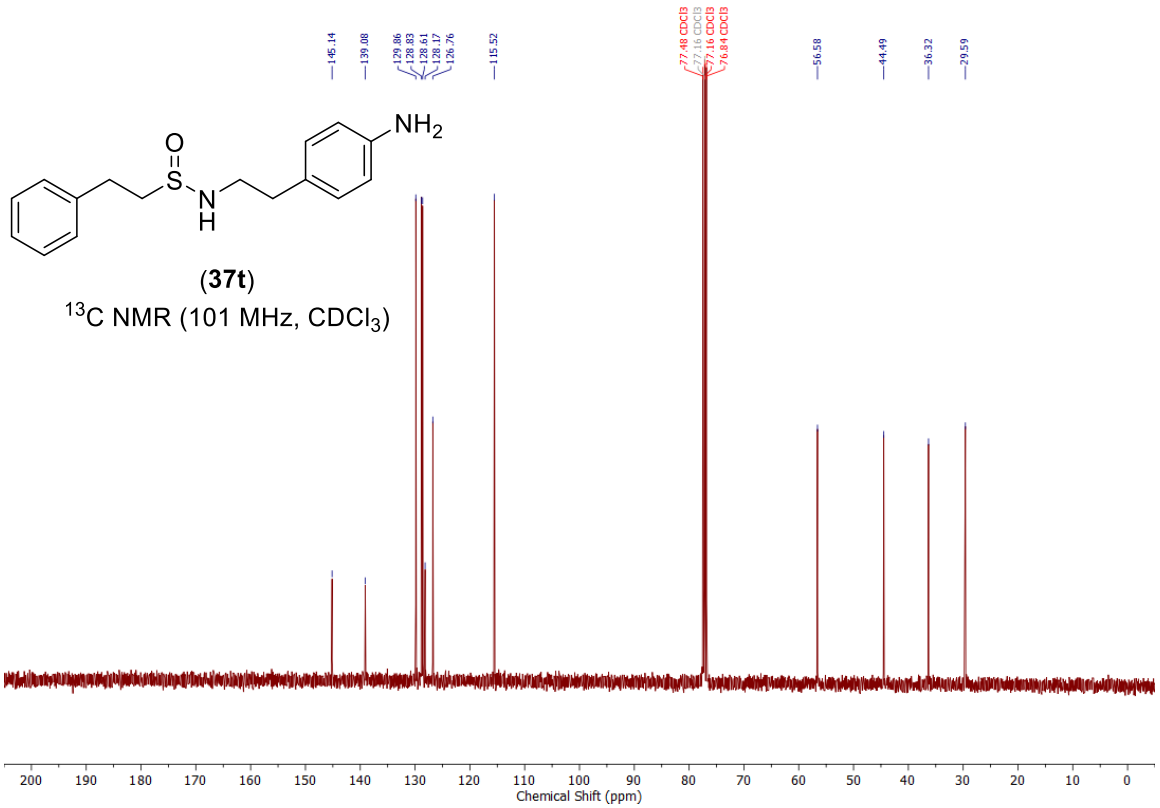
NMR spectra of methyl N^2-(*tert*-butoxycarbonyl)-N^6-(phenethylsulfinyl)-*L*-lysinate (37s):



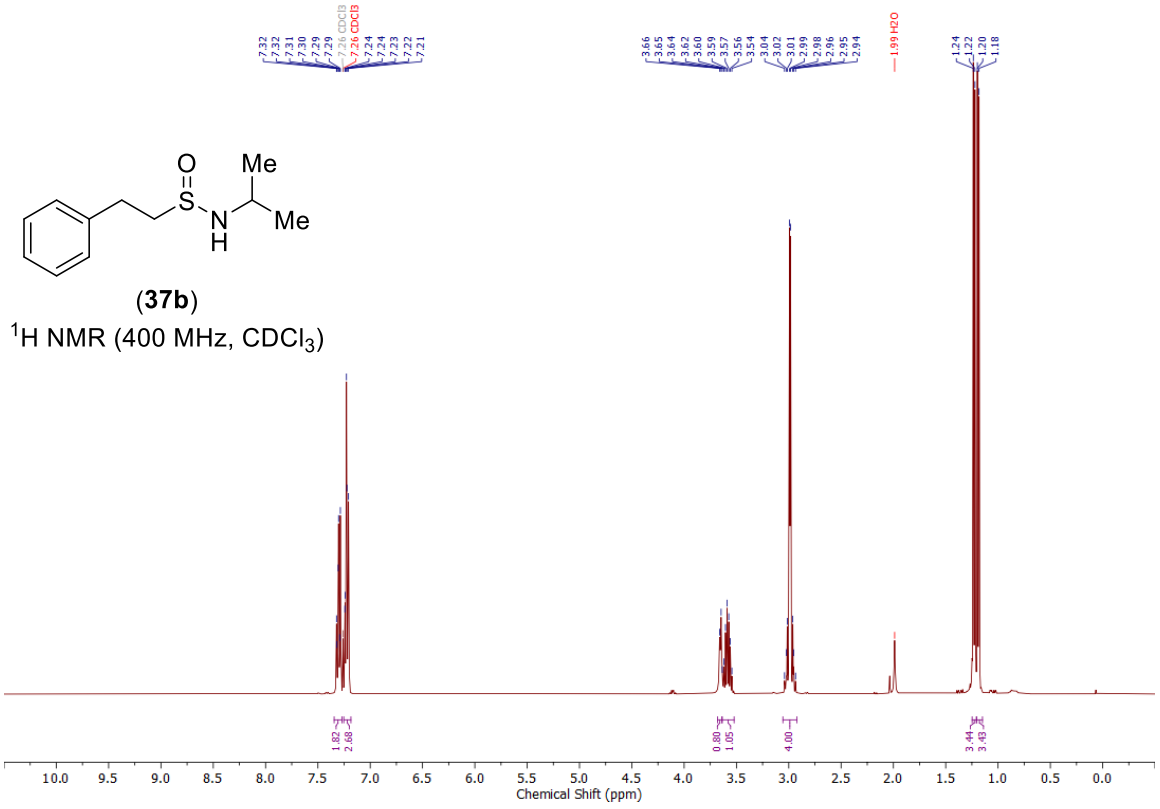


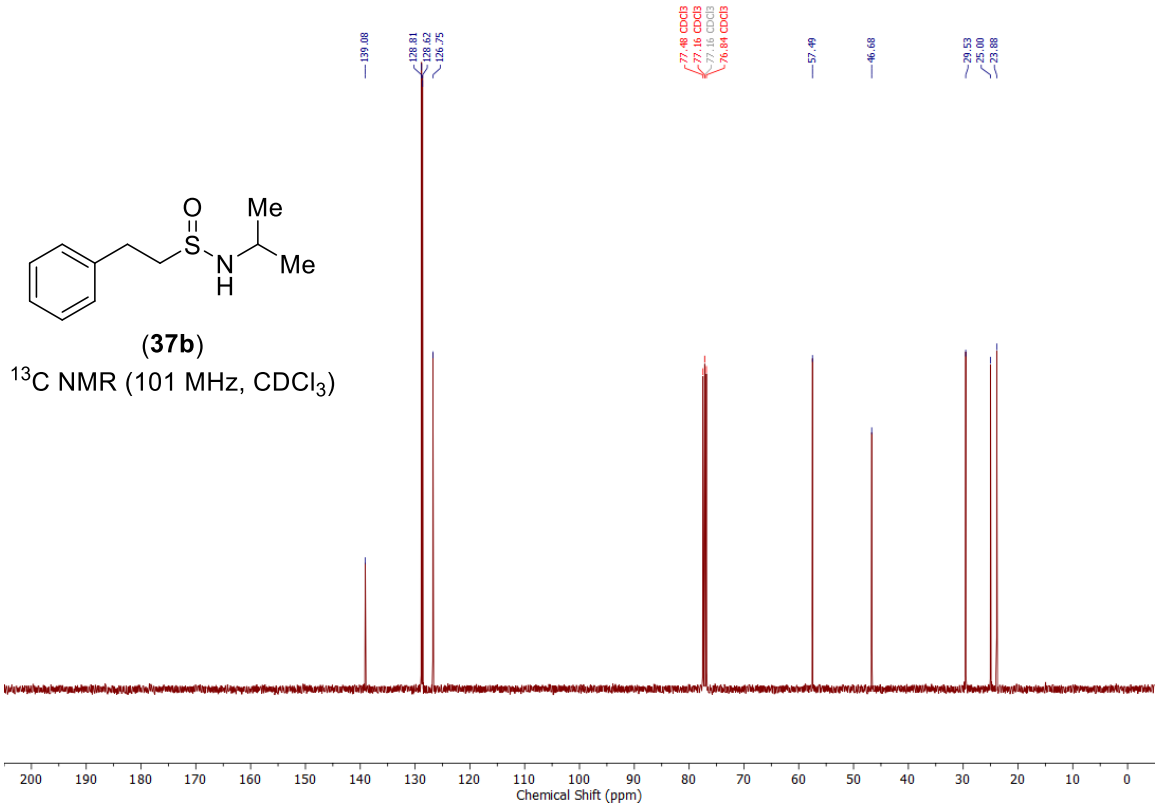
NMR spectra of *N*-(4-aminophenethyl)-2-phenylethane-1-sulfinamide (37t):



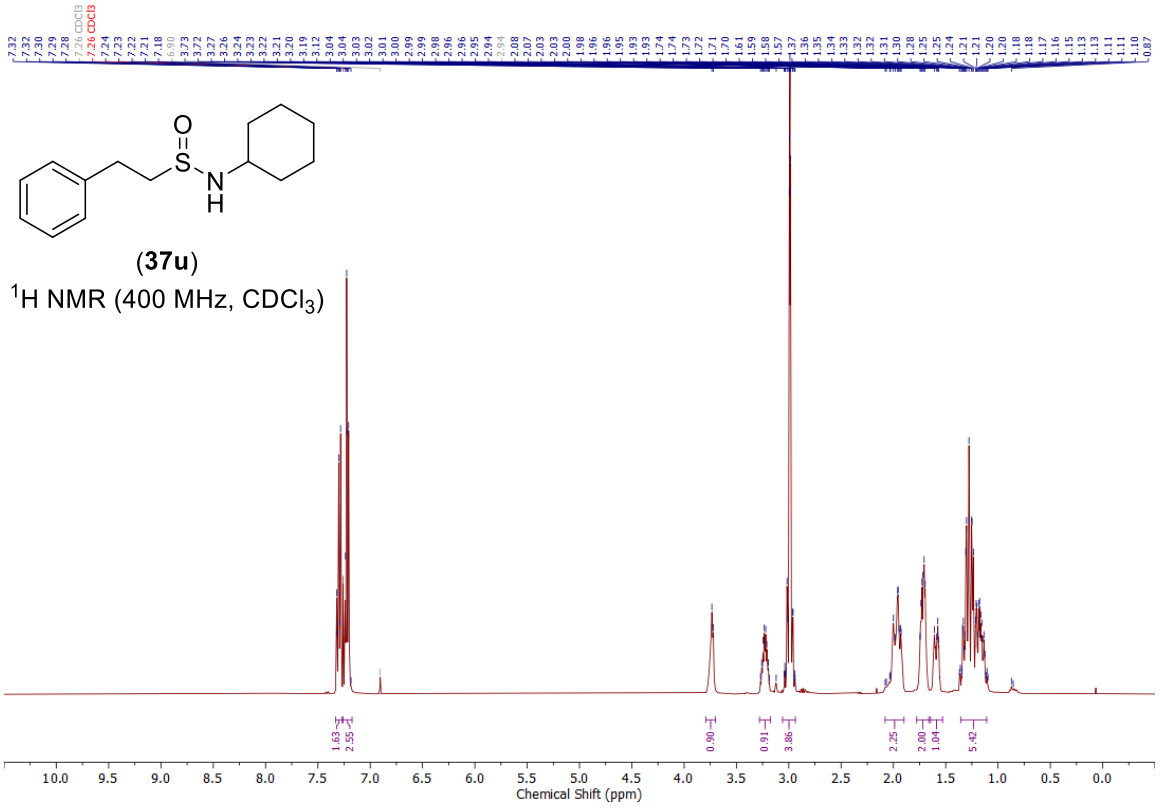


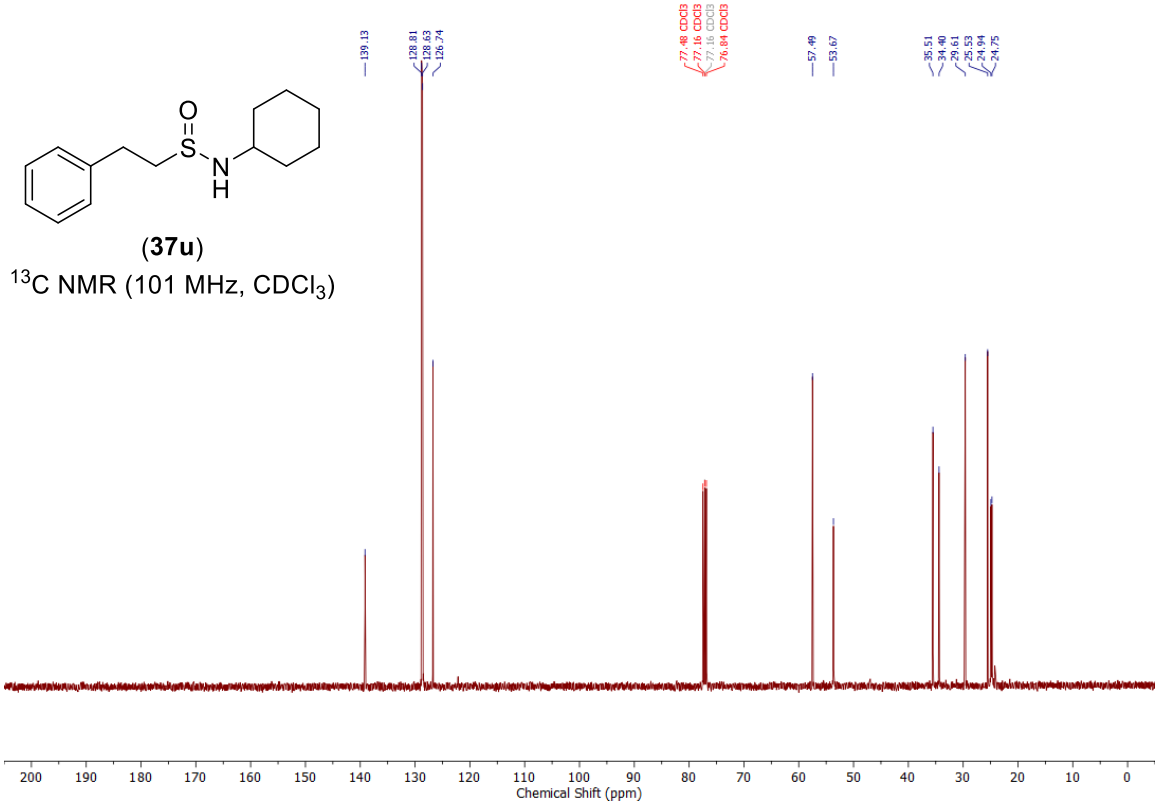
NMR spectra of *N*-isopropyl-2-phenylethane-1-sulfinamide (37b):



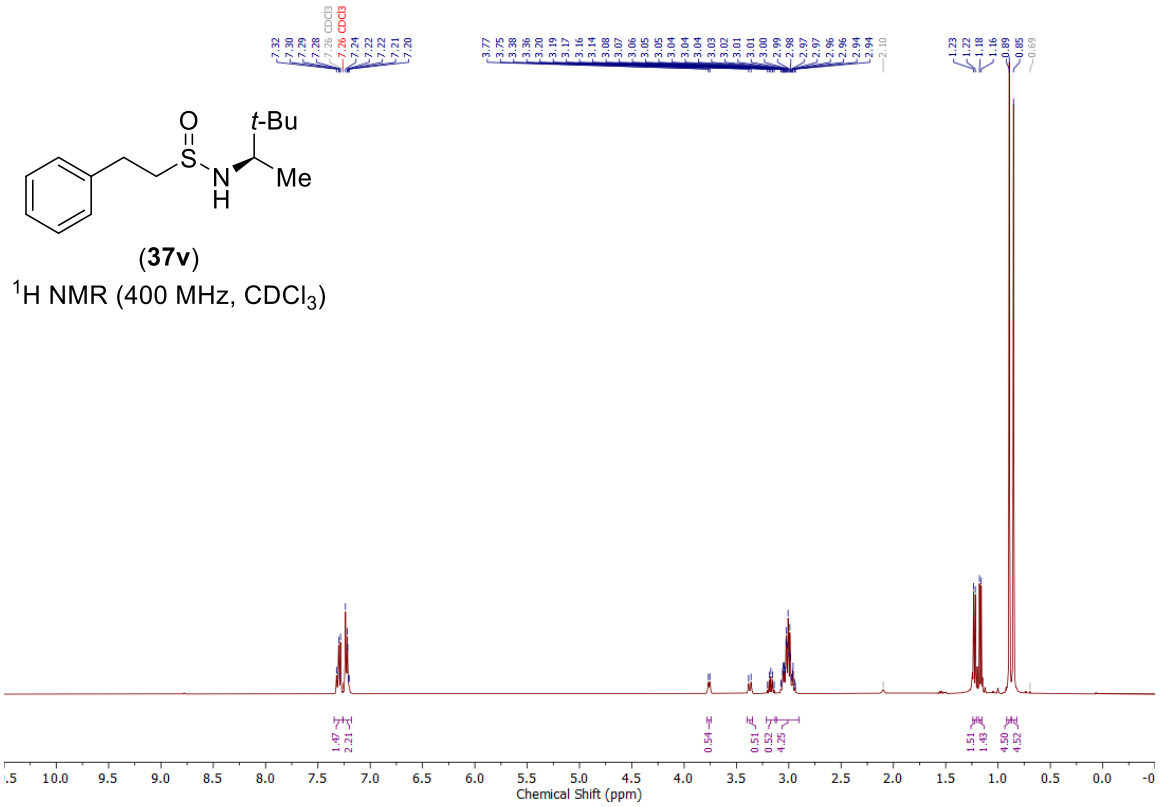


NMR spectra of *N*-cyclohexyl-2-phenylethane-1-sulfinamide (37u):



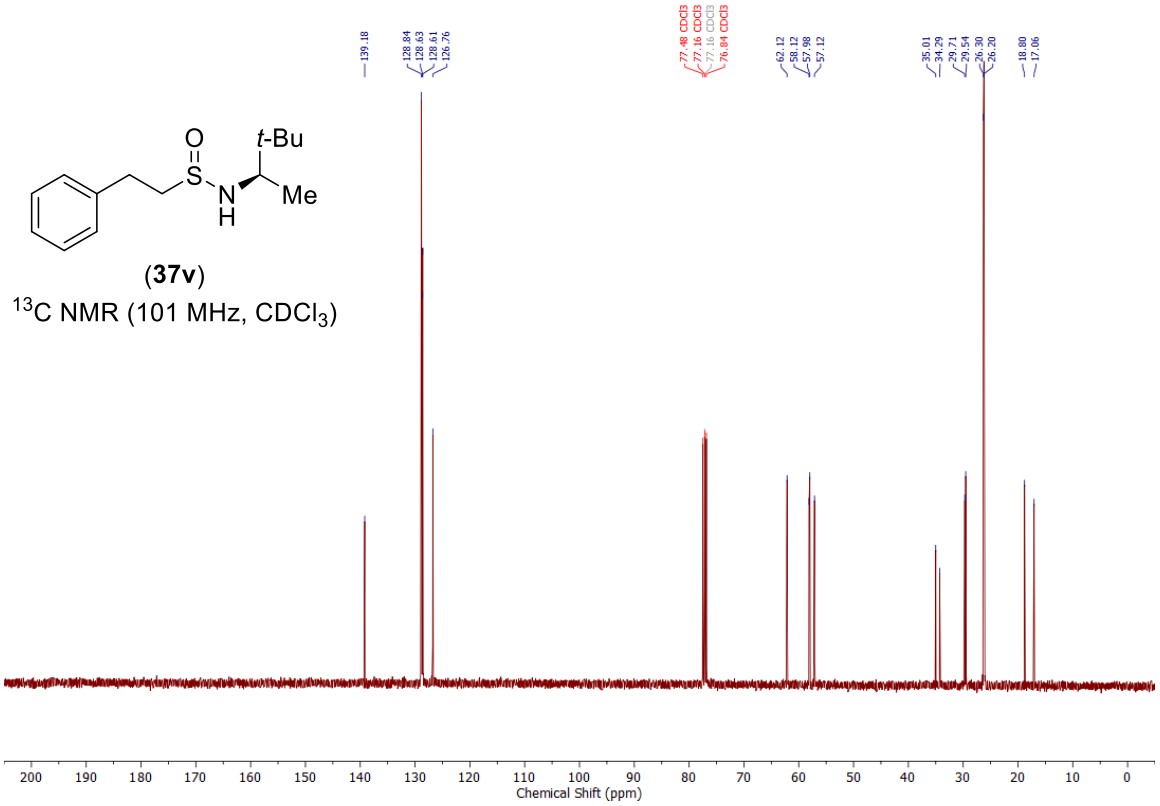


NMR spectra of *N*-((*R*)-3,3-dimethylbutan-2-yl)-2-phenylethane-1-sulfinamide (37v):



(**37v**)

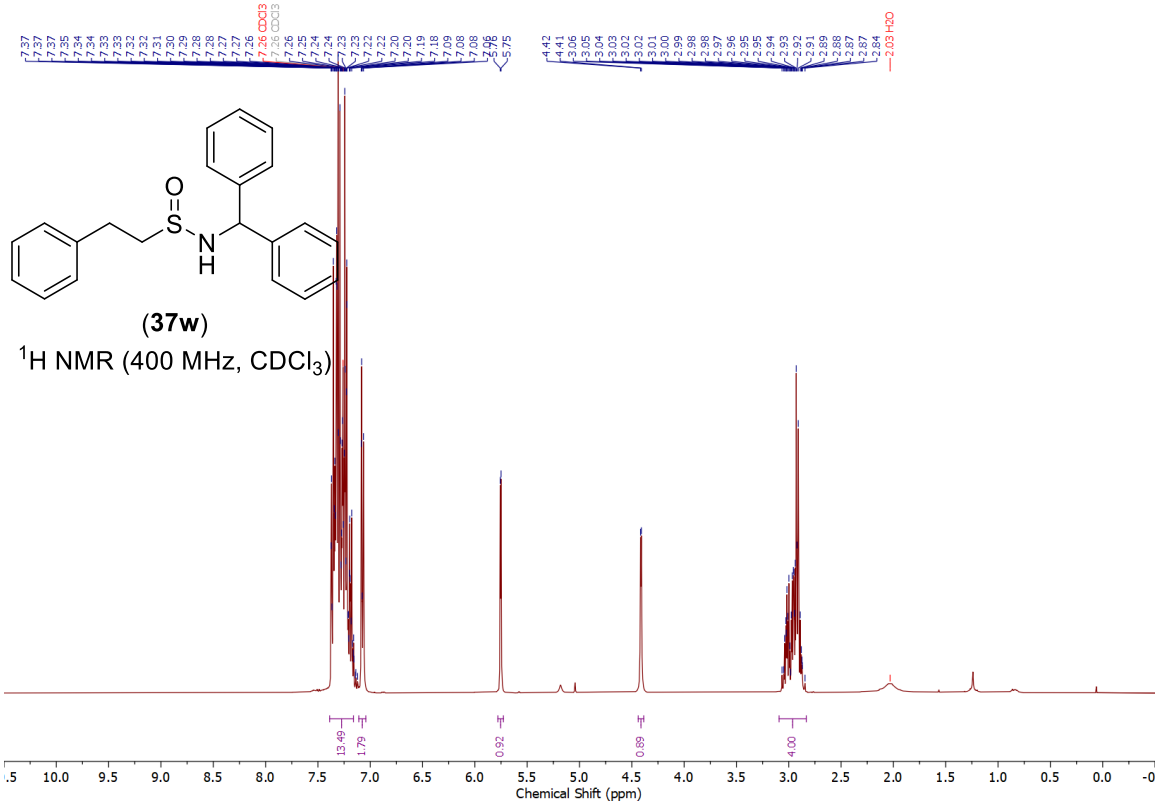
^{1}H NMR (400 MHz, $CDCl_3$)

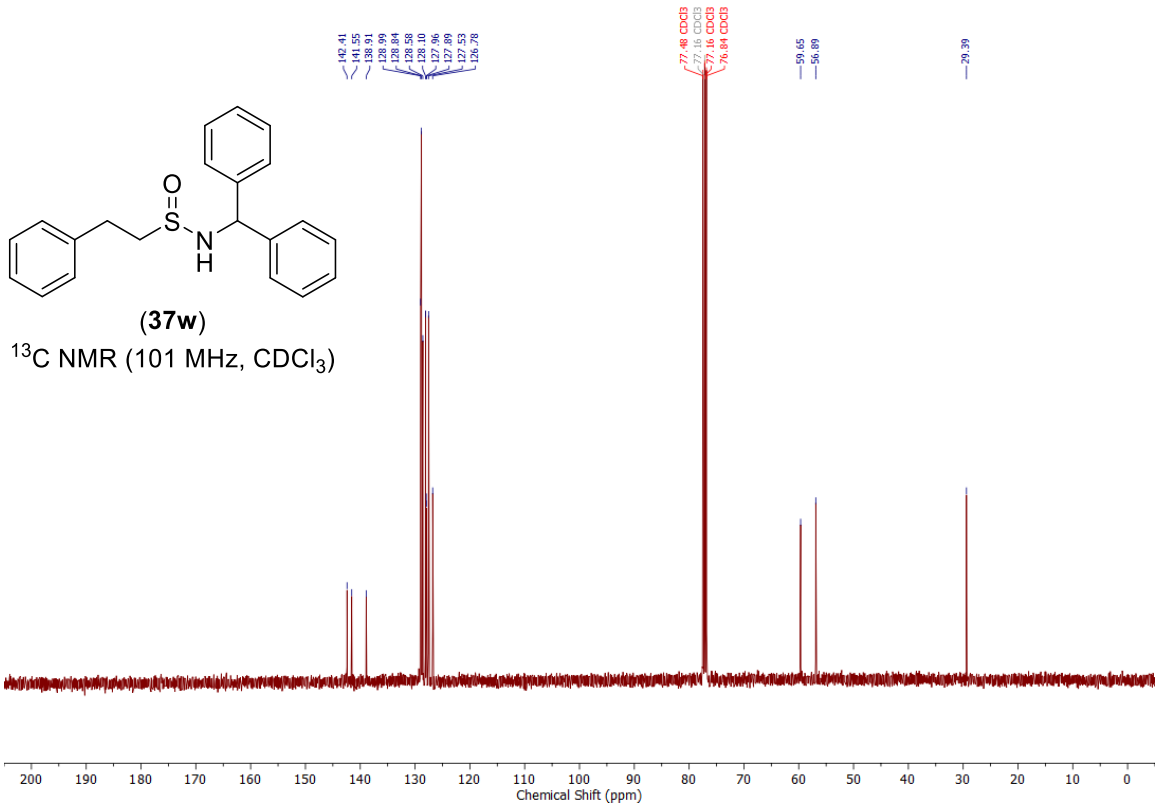


(**37v**)

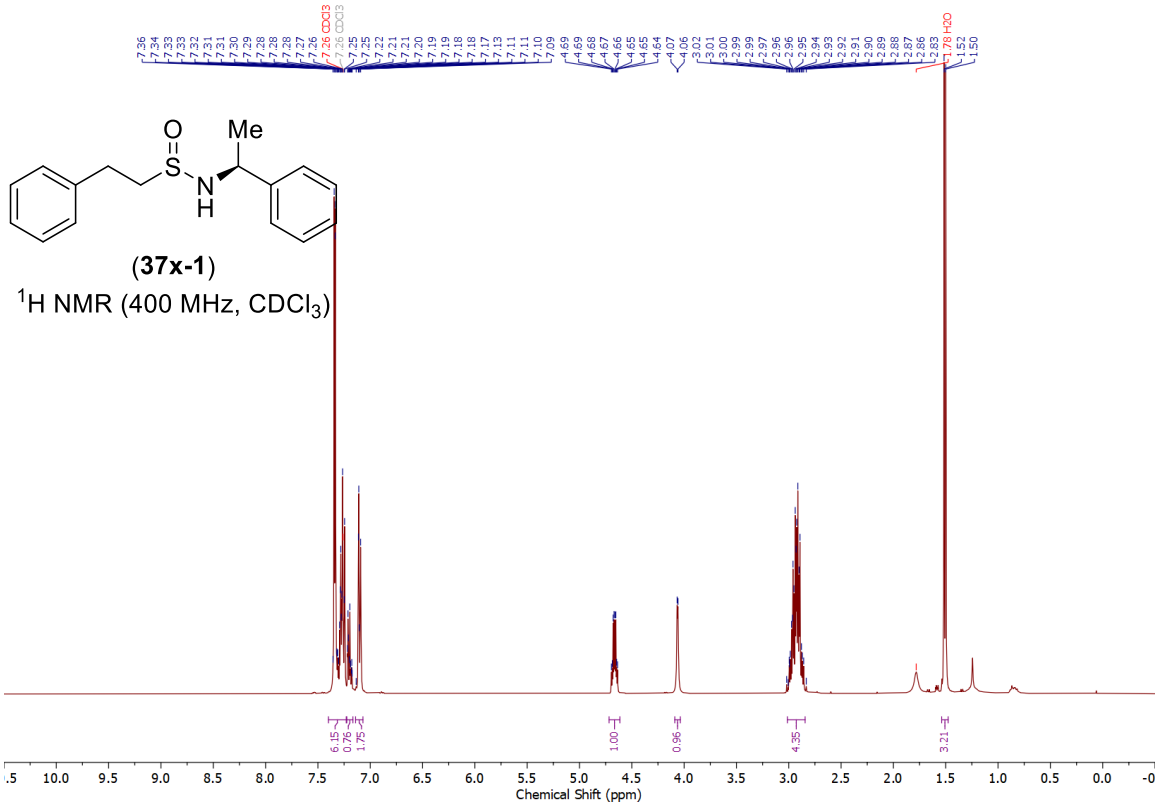
^{13}C NMR (101 MHz, $CDCl_3$)

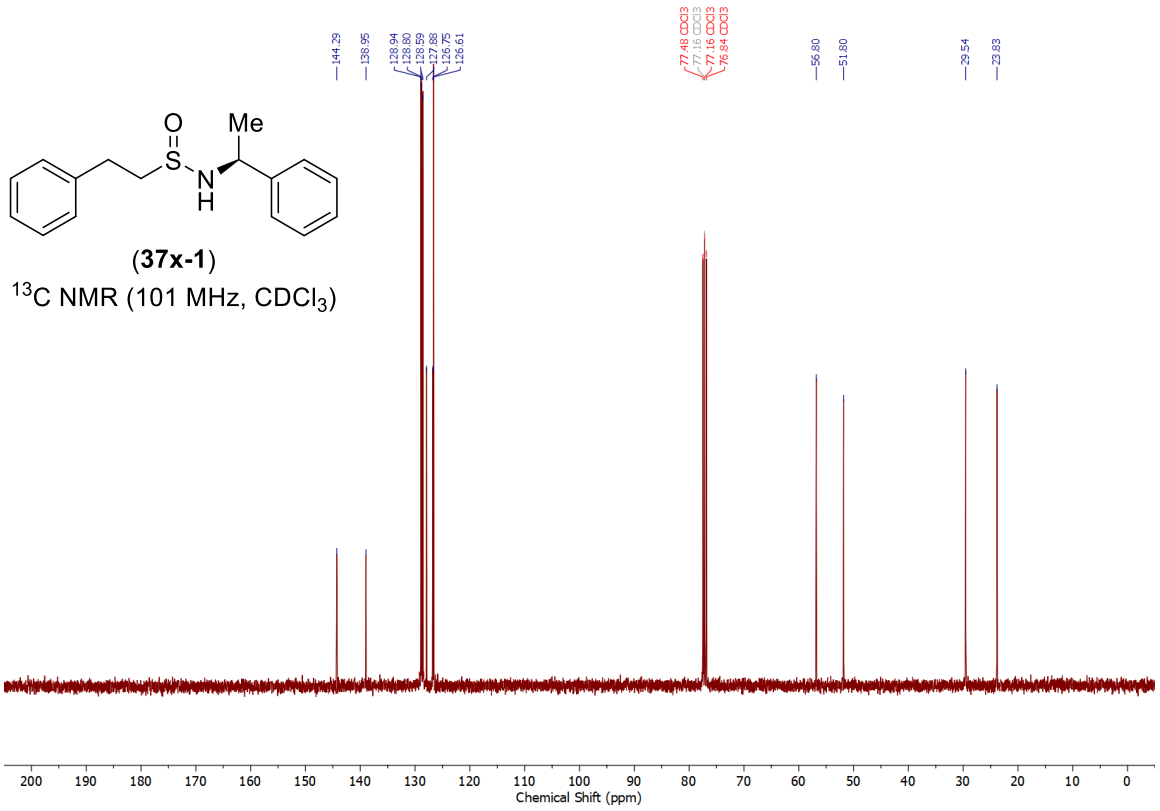
NMR spectra of *N*-benzhydryl-2-phenylethane-1-sulfinamide (37w):



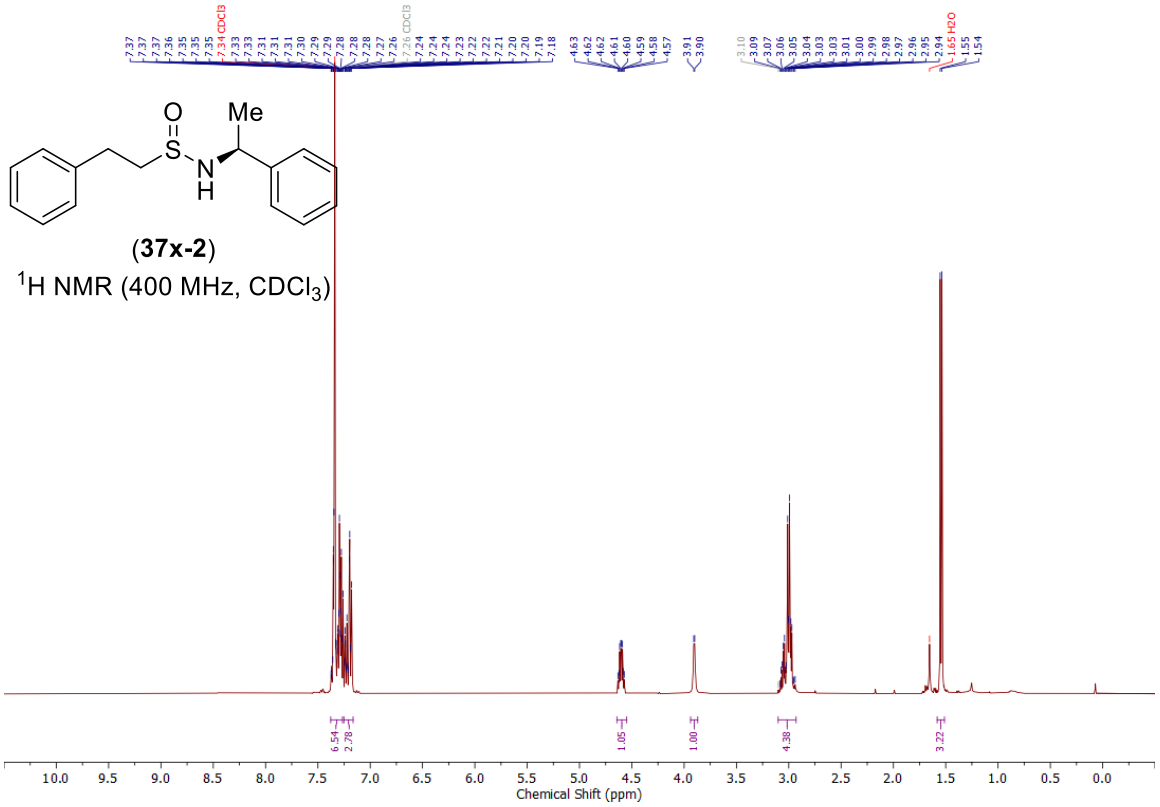


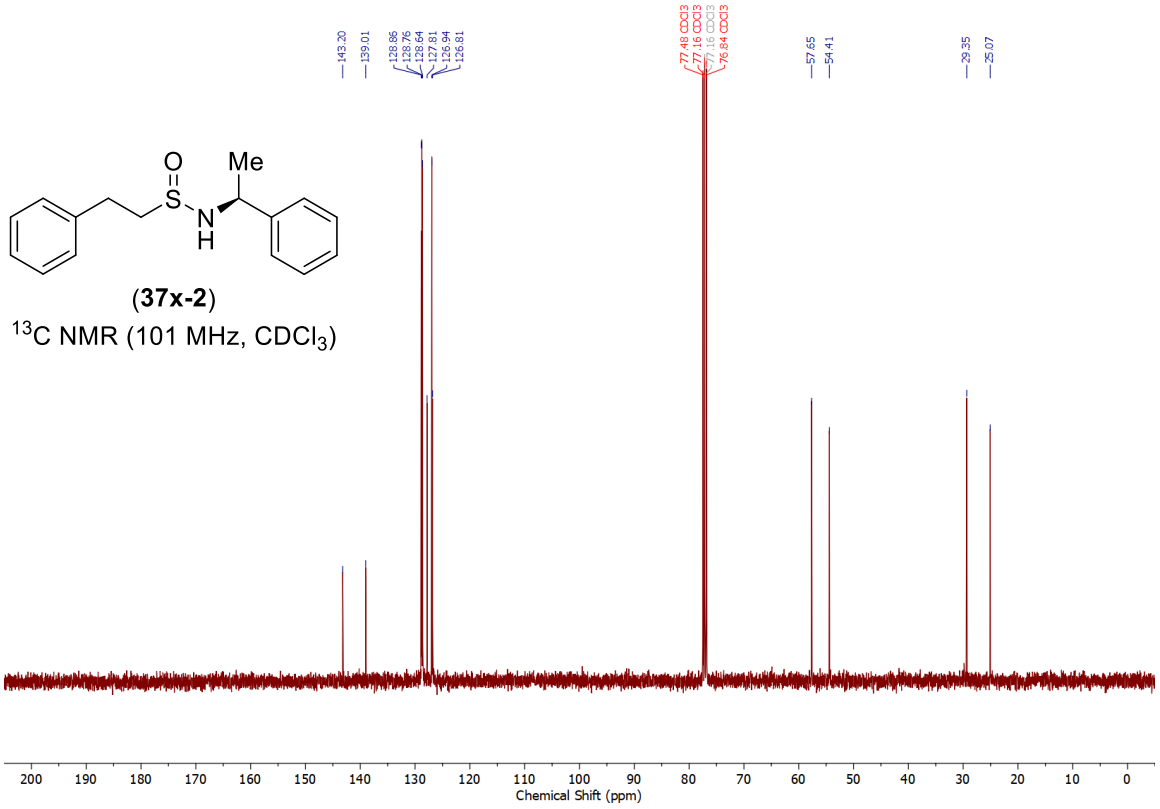
NMR spectra of 2-phenyl-*N*-((*S*)-1-phenylethyl)ethane-1-sulfinamide (37x-1):



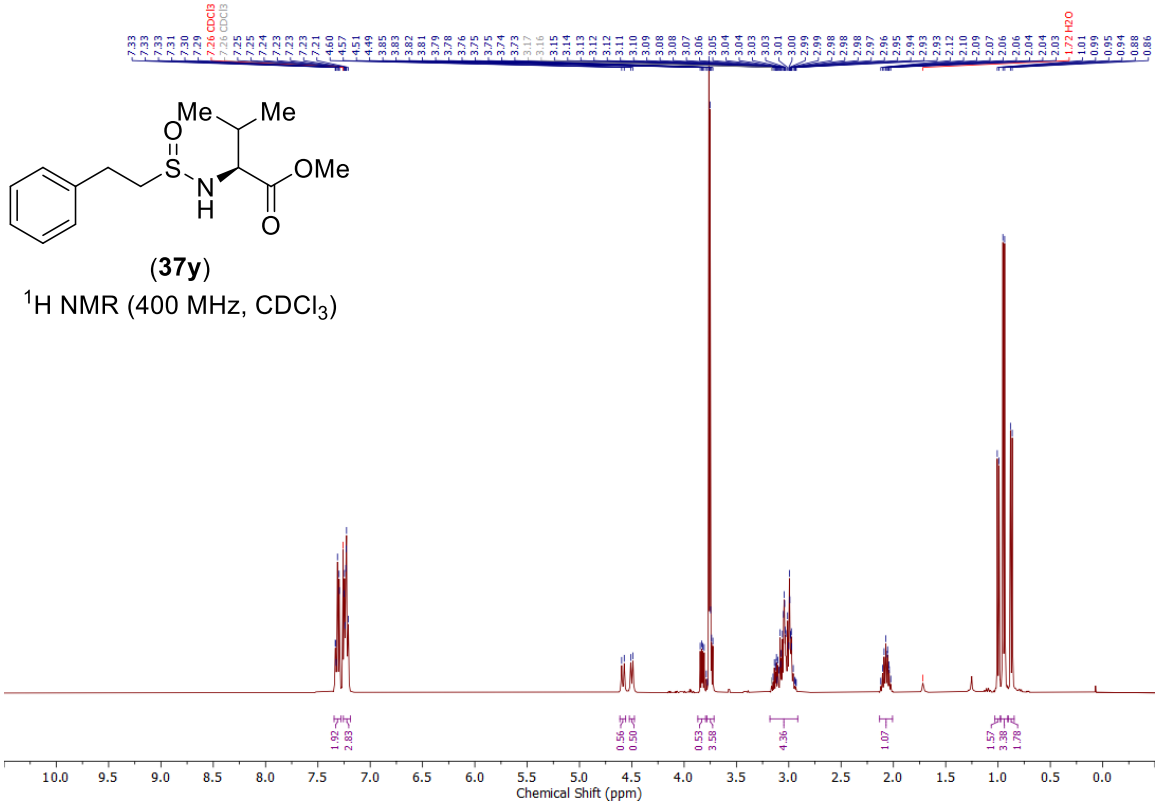


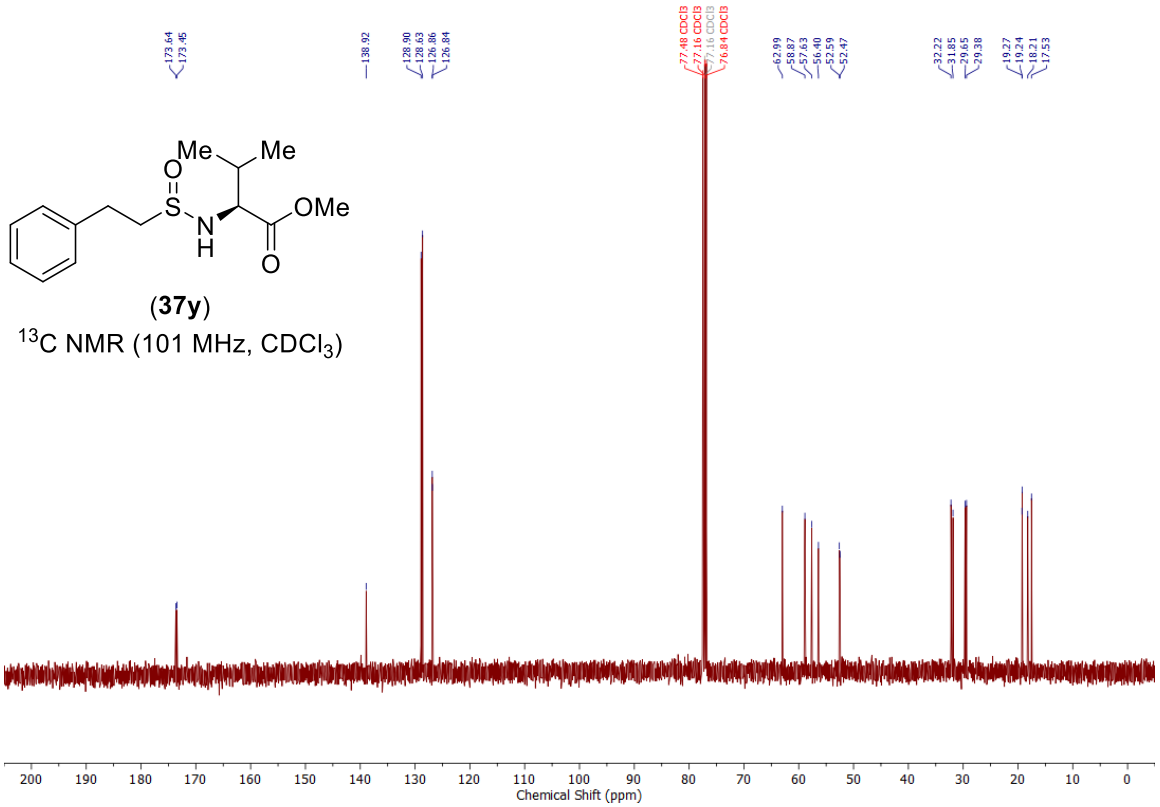
NMR spectra of 2-phenyl-*N*-((*S*)-1-phenylethyl)ethane-1-sulfinamide (37x-2):



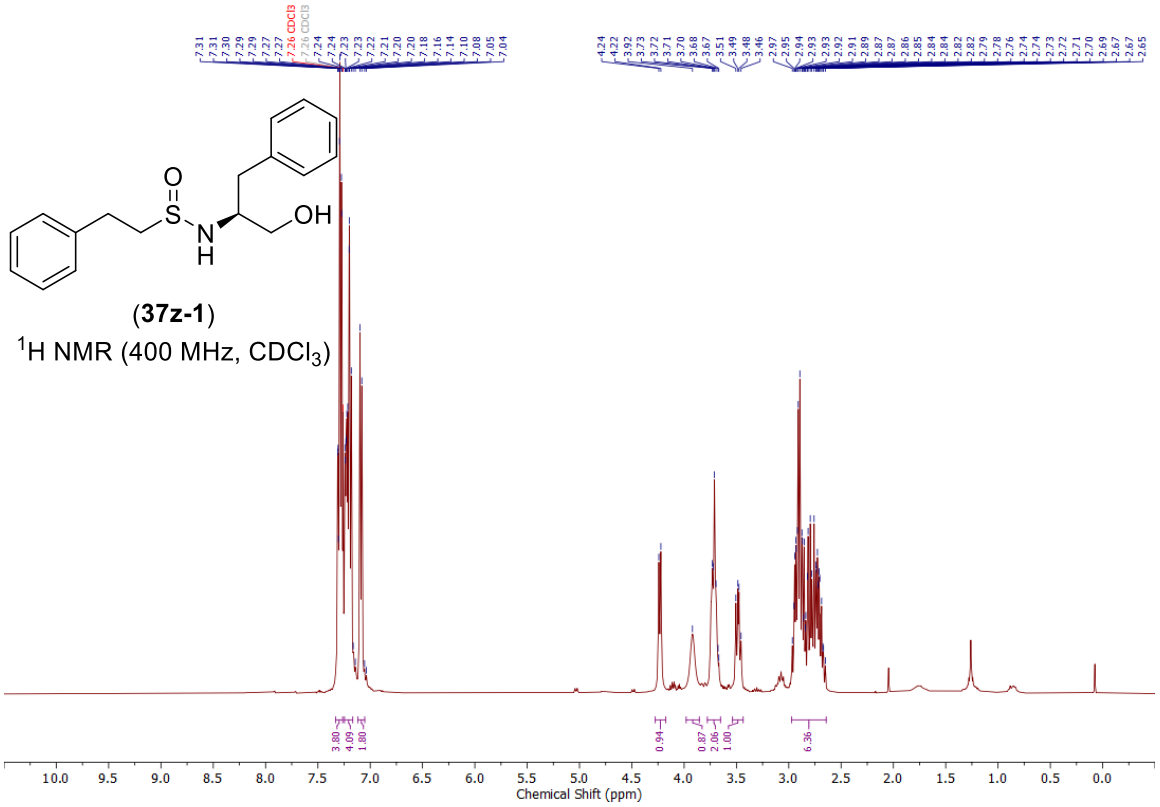


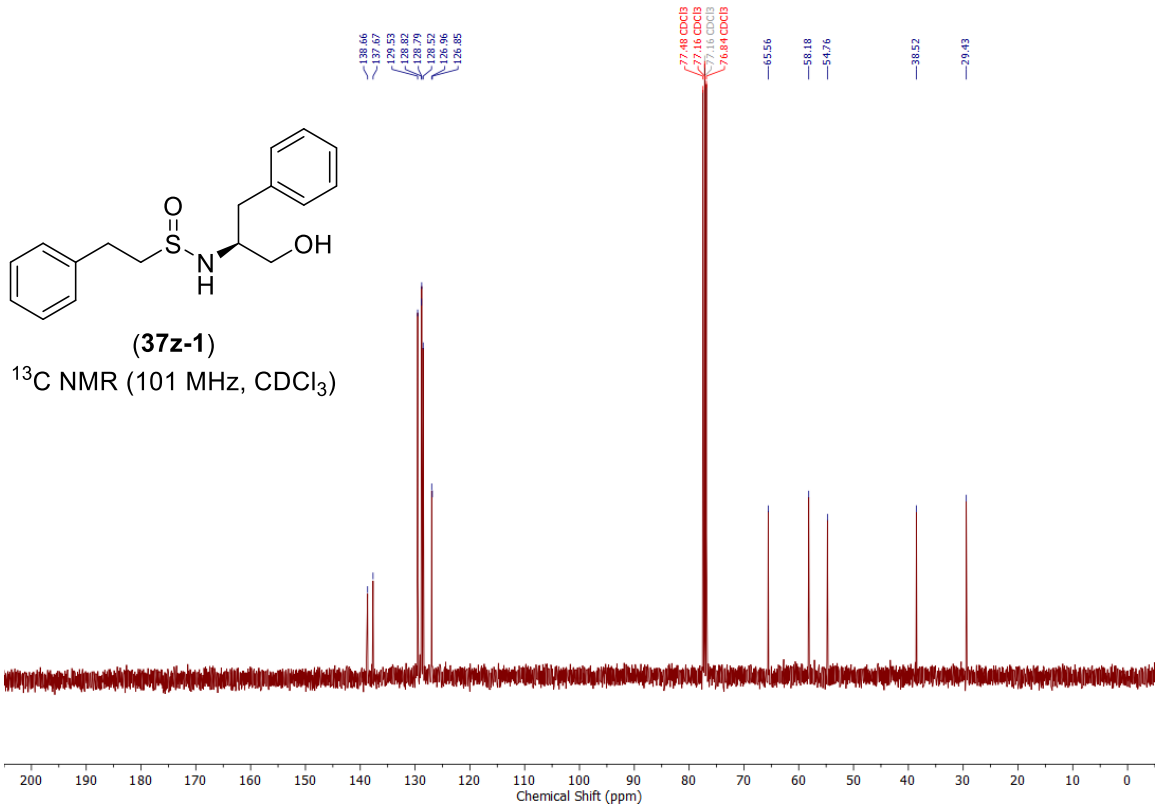
NMR spectra of methyl (phenethylsulfinyl)-*L*-valinate (37y):



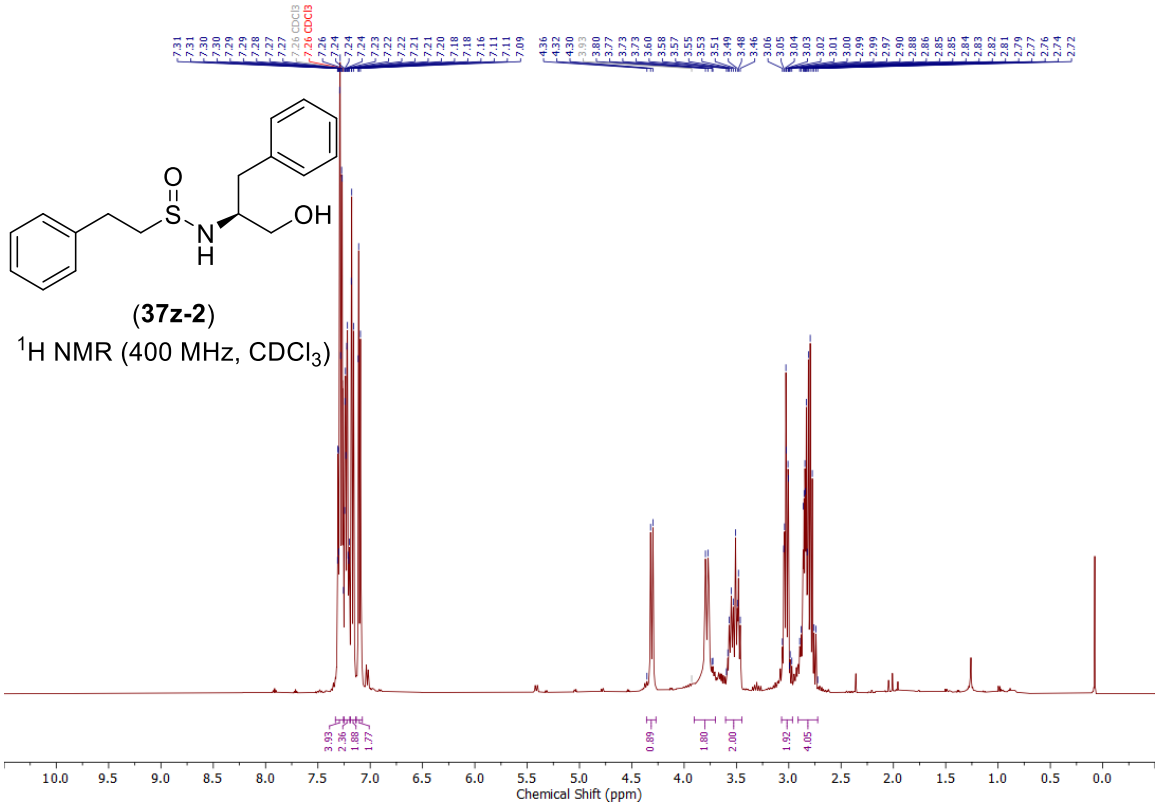


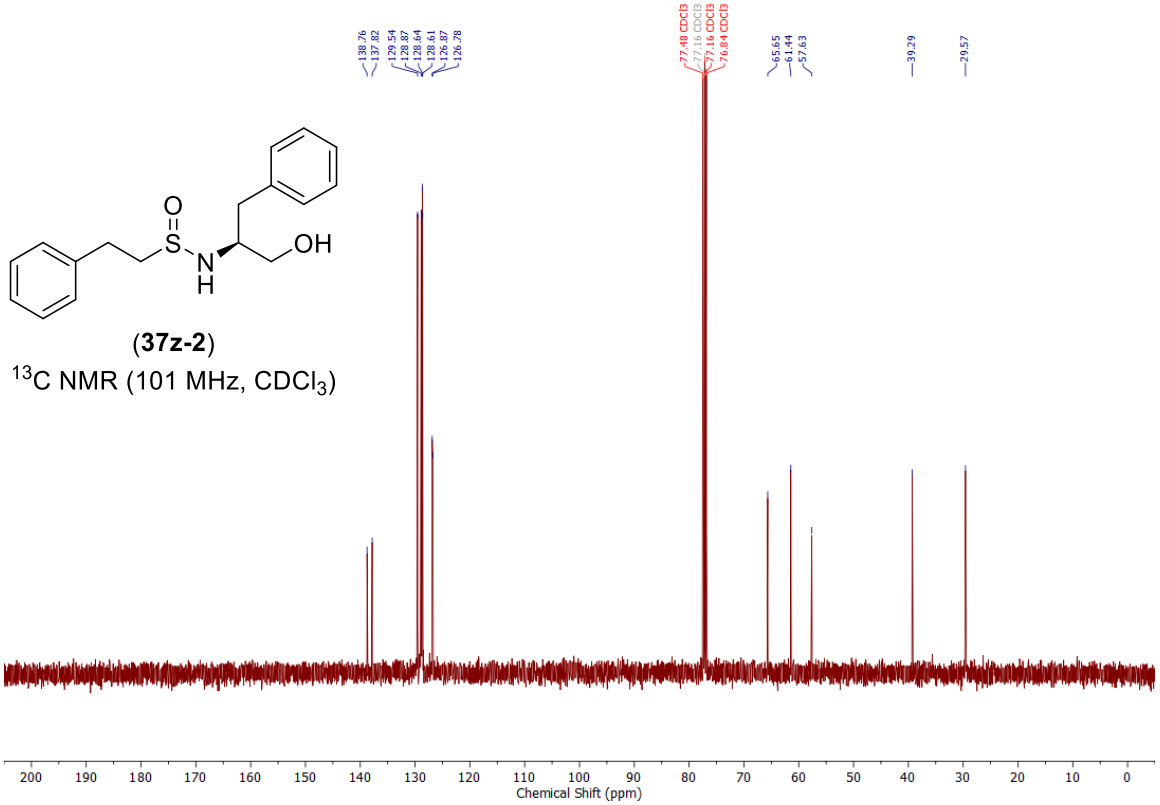
NMR spectra of *N*-((*S*)-1-hydroxy-3-phenylpropan-2-yl)-2-phenylethane-1-sulfinamide (37z-1):



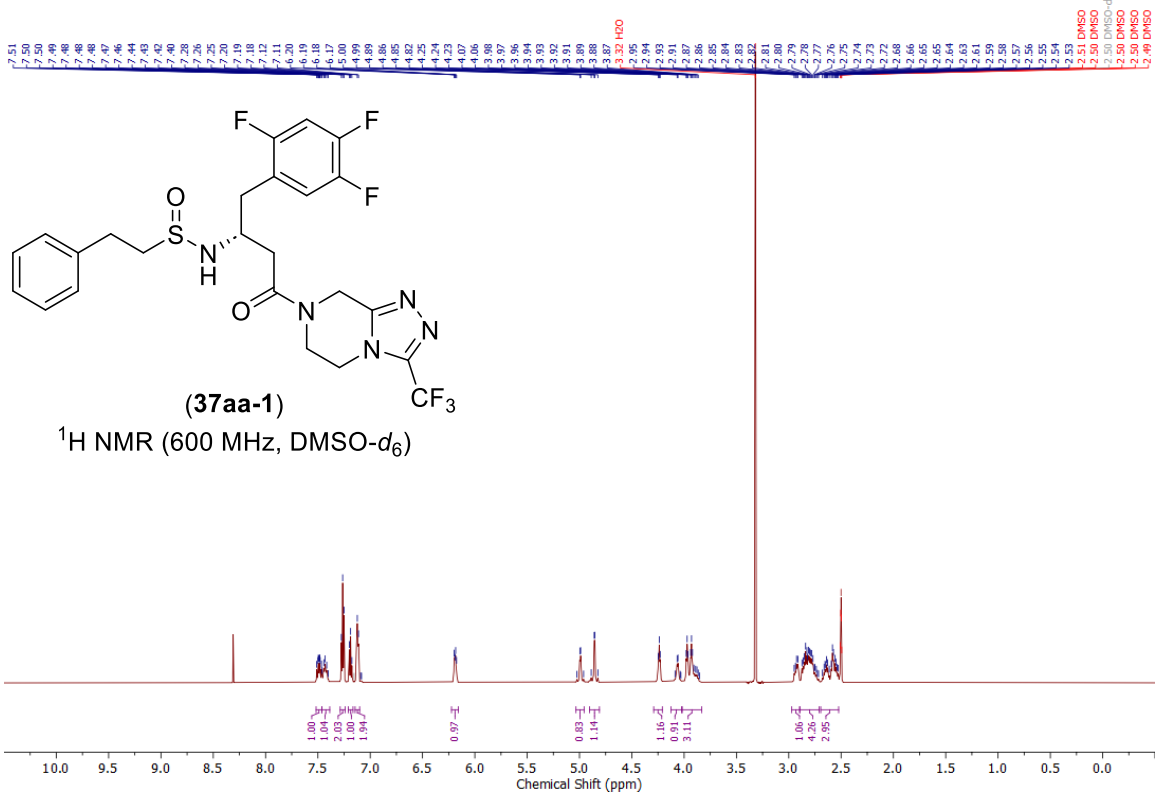


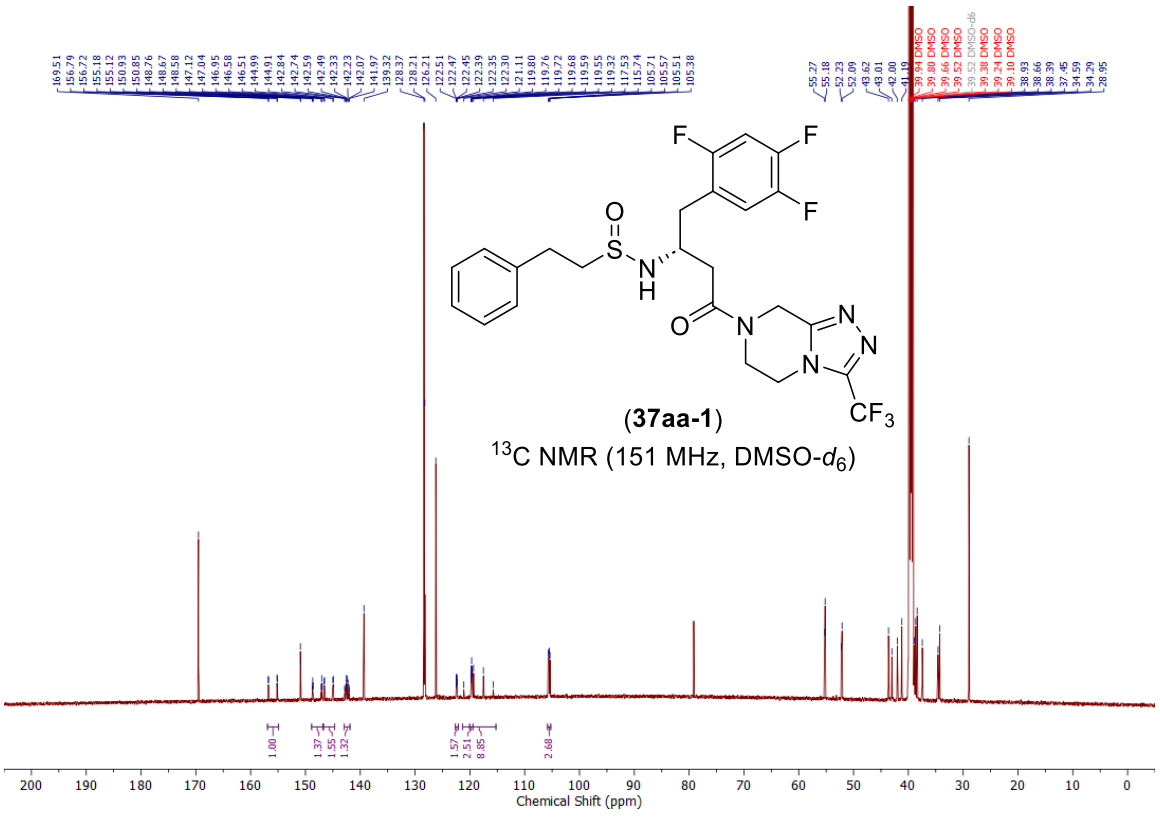
NMR spectra of *N*-((*S*)-1-hydroxy-3-phenylpropan-2-yl)-2-phenylethane-1-sulfinamide (37z-2):

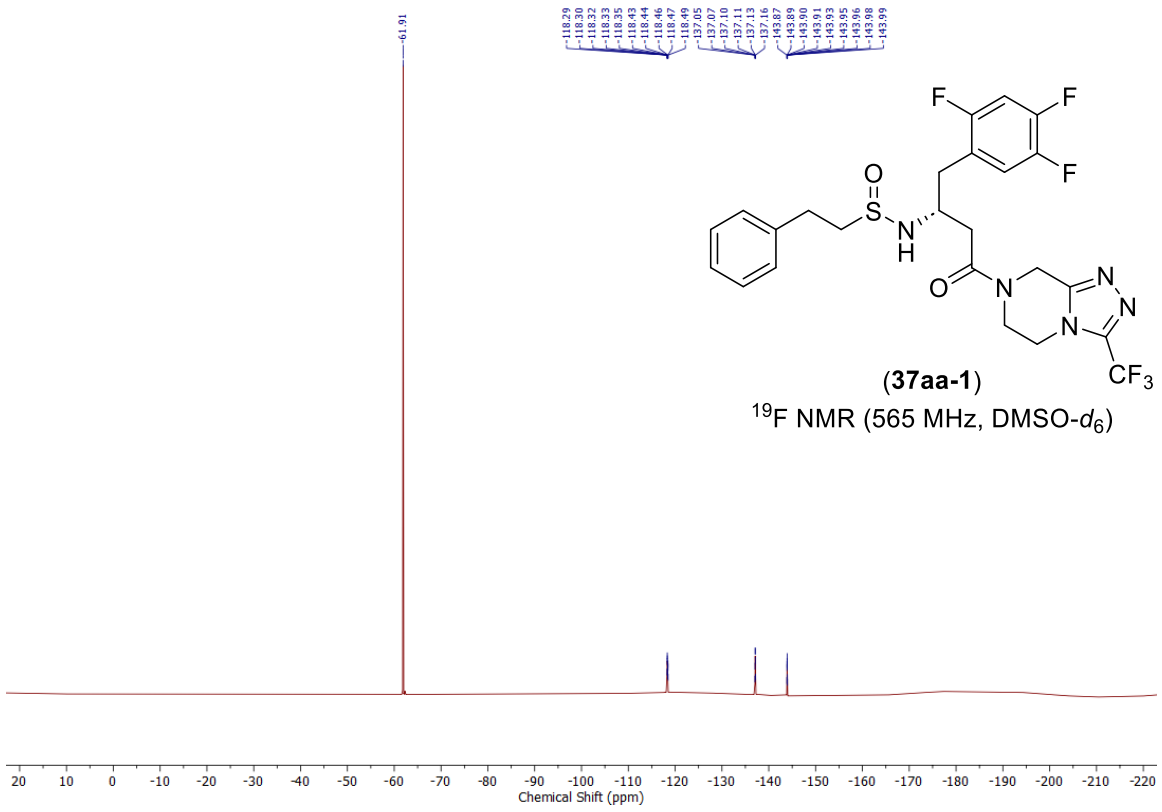




NMR spectra of *N*-((*R*)-4-Oxo-4-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-*a*]pyrazin-7(8*H*)-yl)-1-(2,4,5-trifluorophenyl)butan-2-yl)-2-phenylethane-1-sulfinamide (37aa-1)



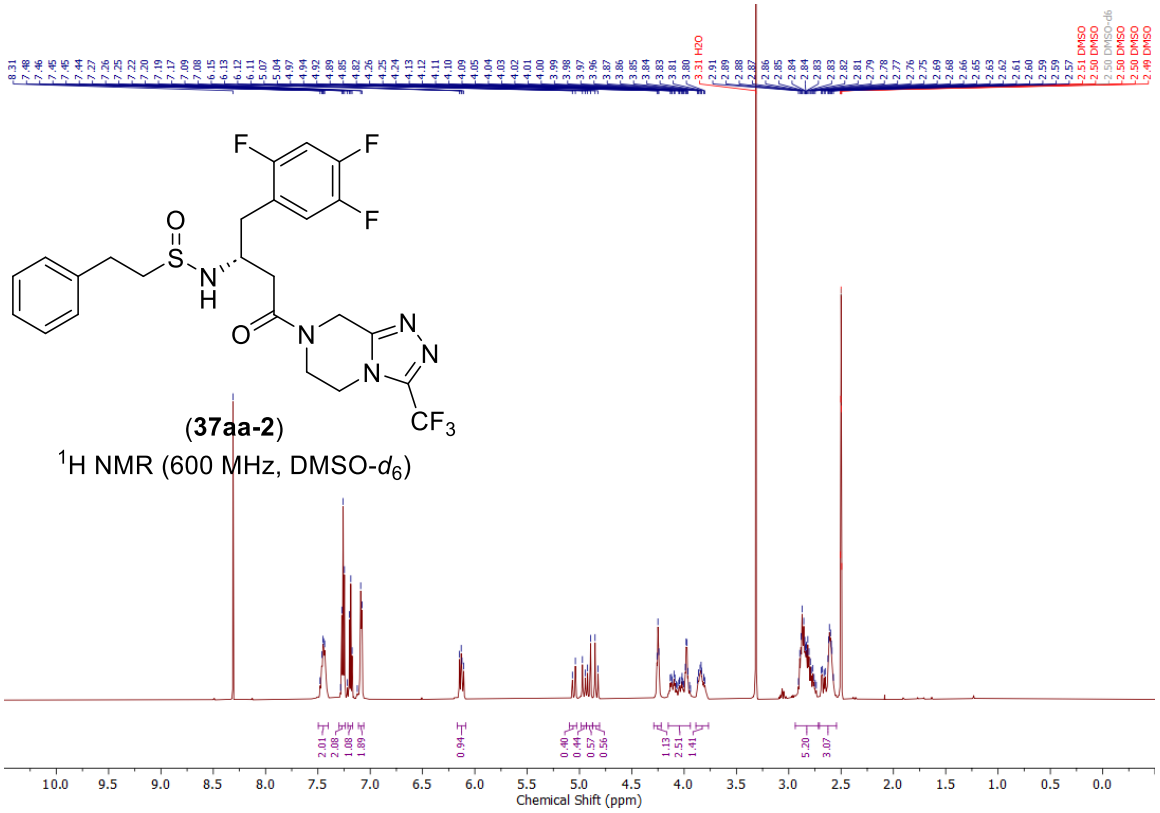


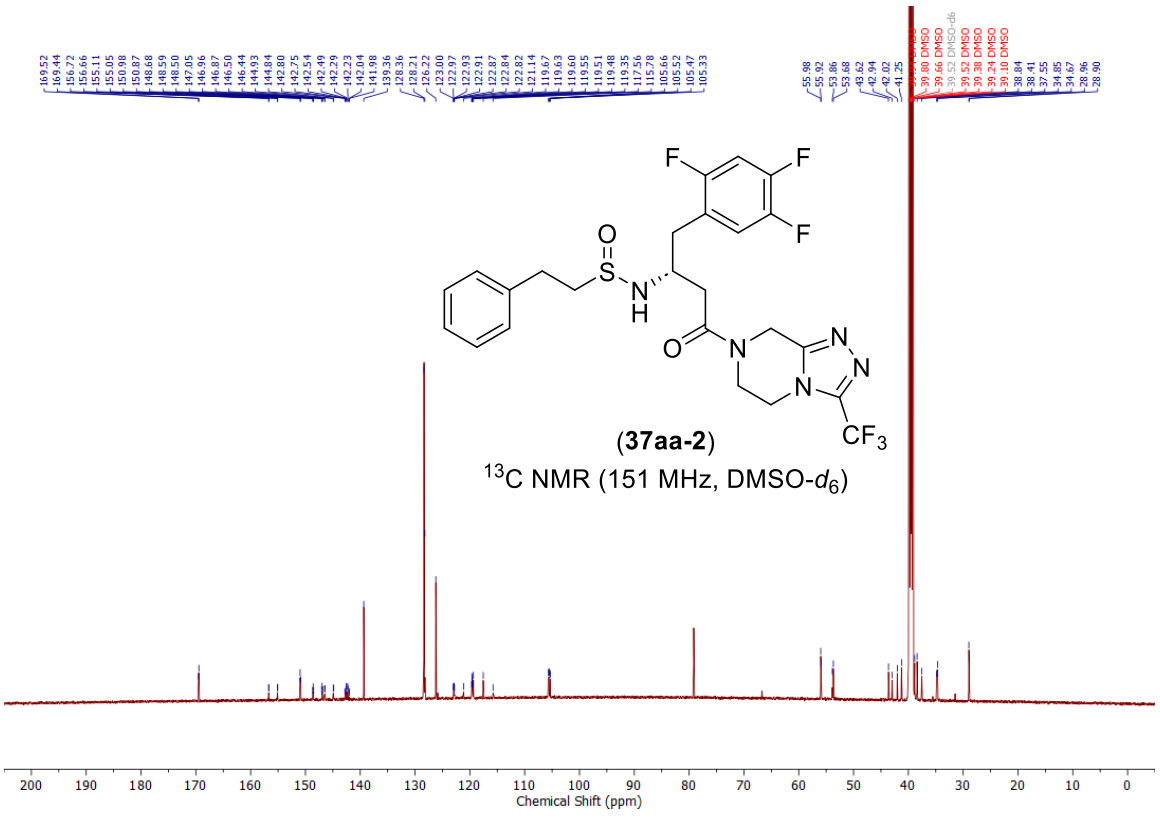


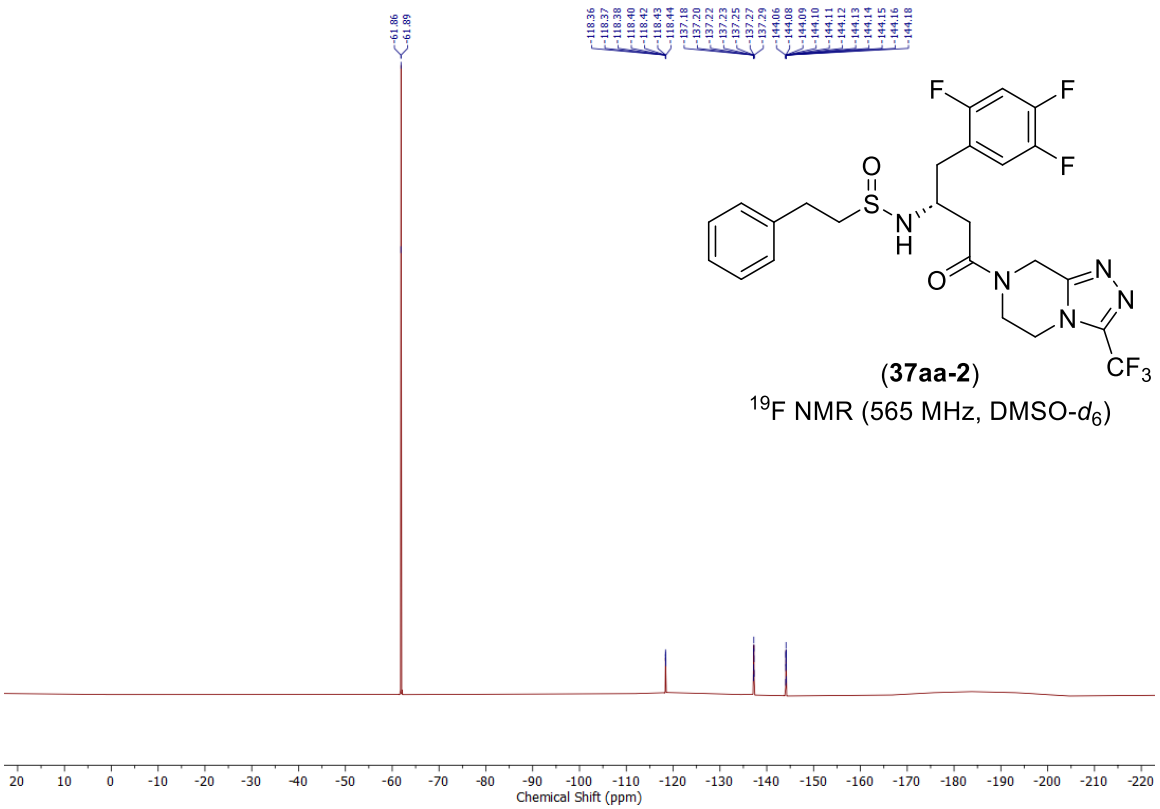
(**37aa-1**)

^{19}F NMR (565 MHz, DMSO-d_6)

NMR spectra of *N*-((*R*)-4-Oxo-4-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-*a*]pyrazin-7(8*H*)-yl)-1-(2,4,5-trifluorophenyl)butan-2-yl)-2-phenylethane-1-sulfinamide (37aa-2)



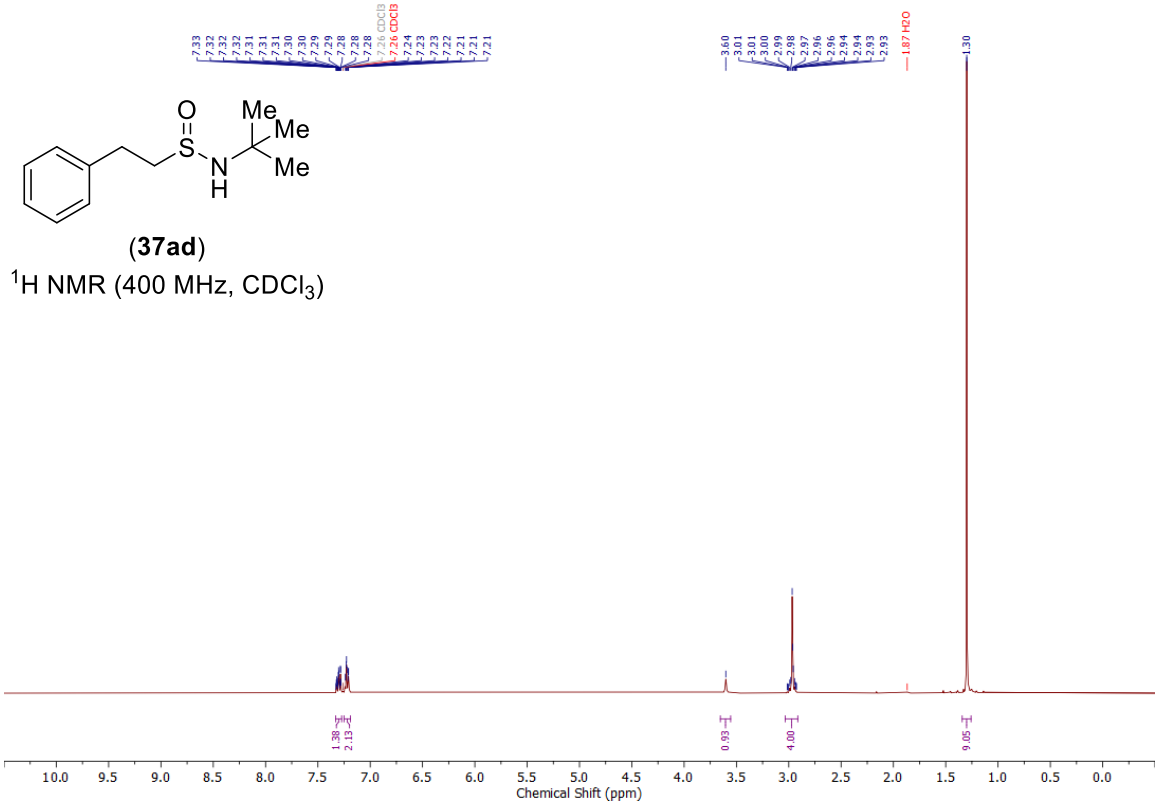


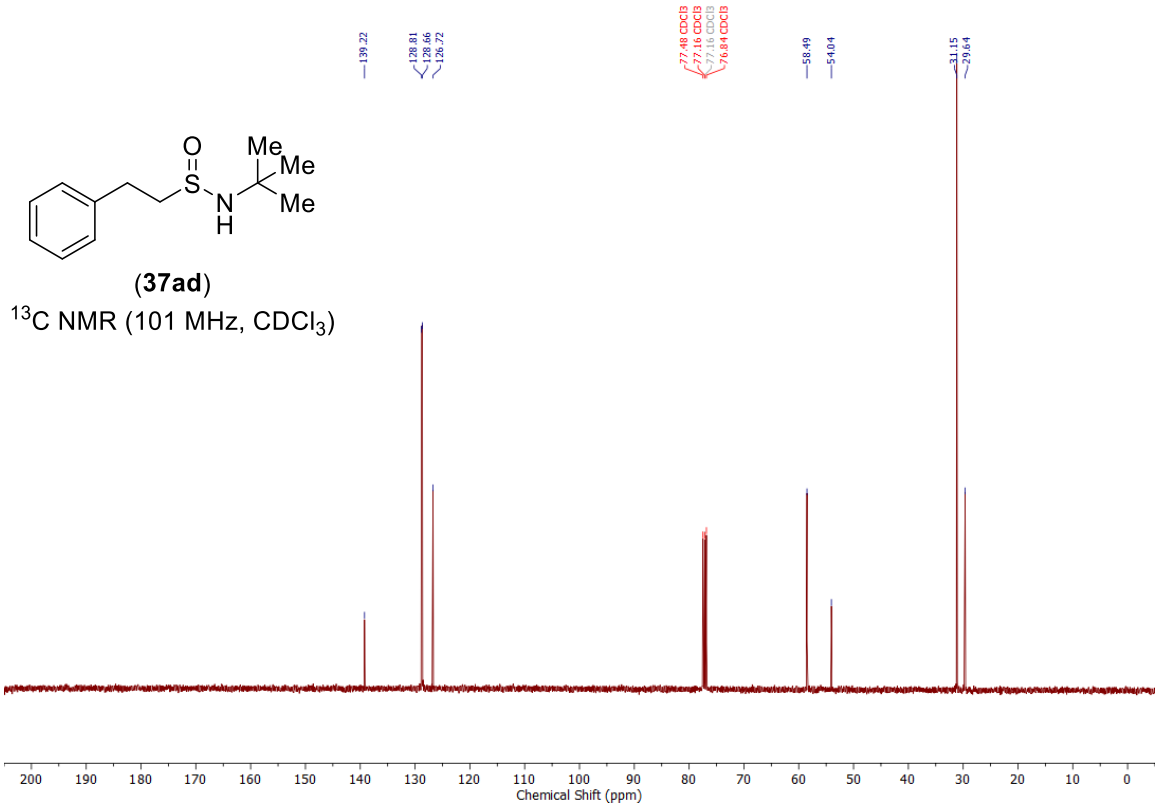


(**37aa-2**)

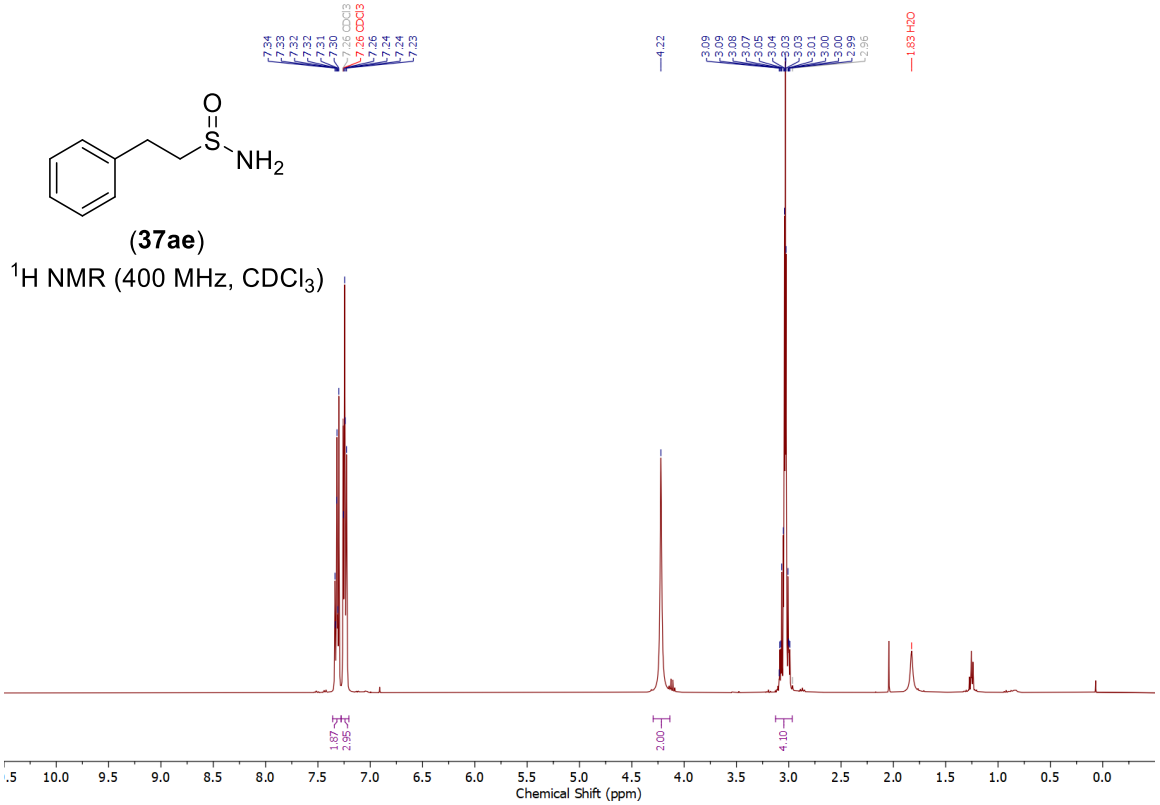
^{19}F NMR (565 MHz, DMSO-d_6)

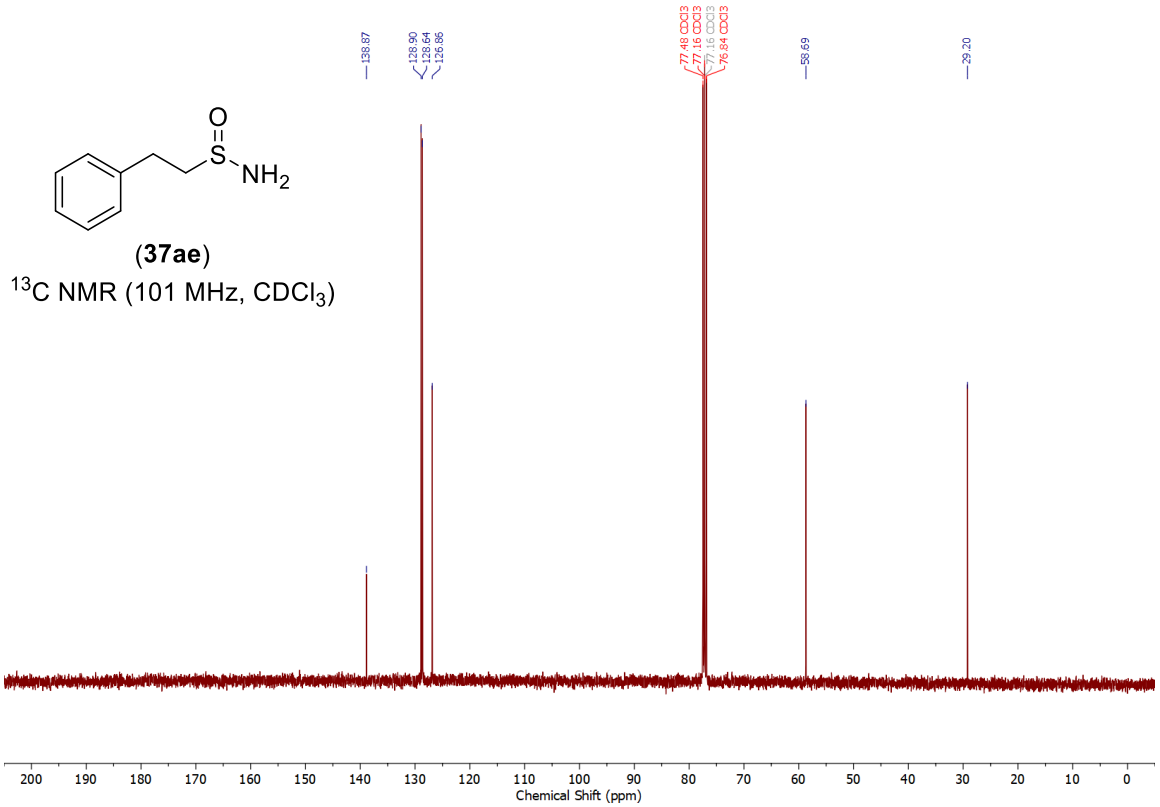
NMR spectra of *N*-(*tert*-butyl)-2-phenylethane-1-sulfinamide (37ad):



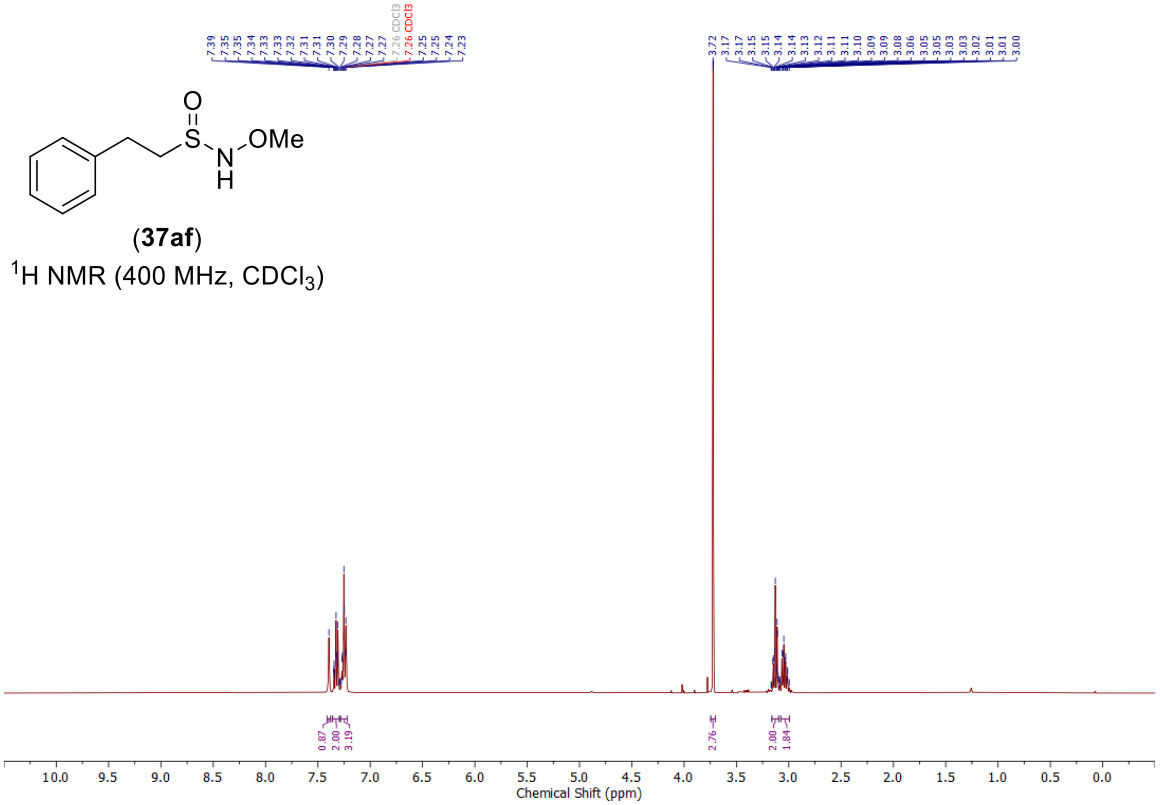


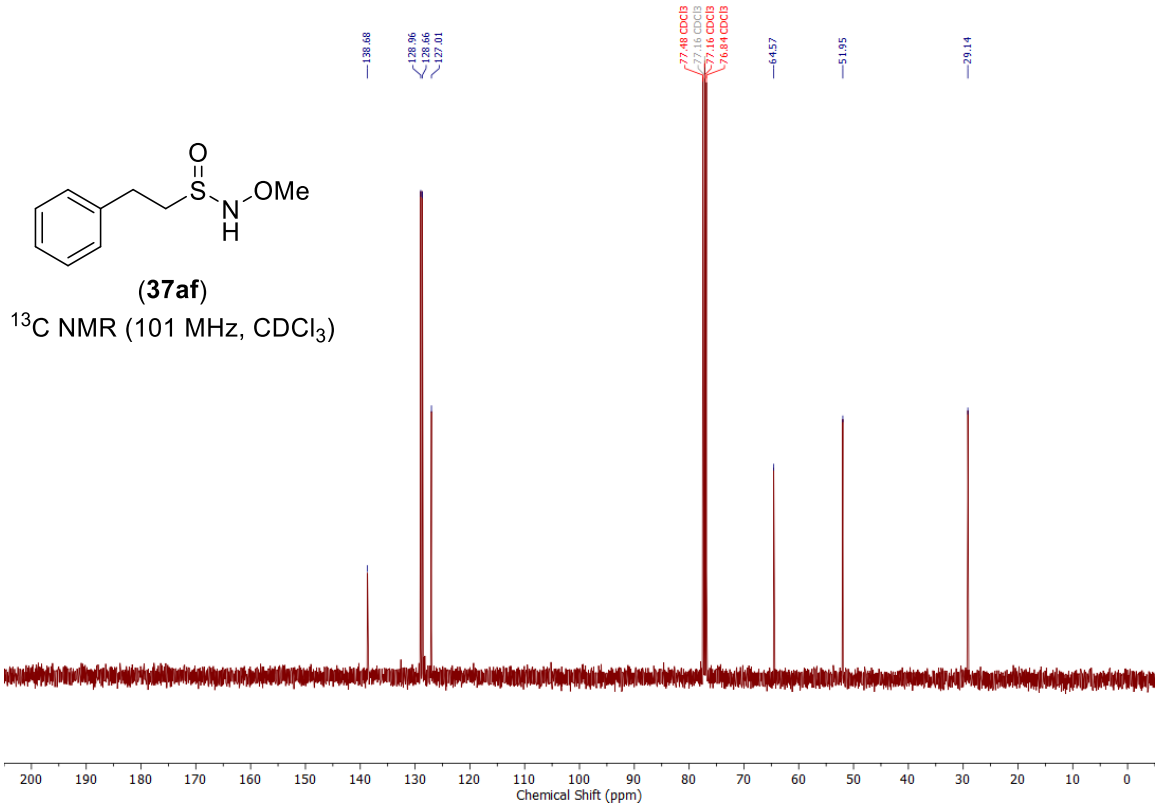
NMR spectra of 2-phenylethane-1-sulfinamide (37ae):



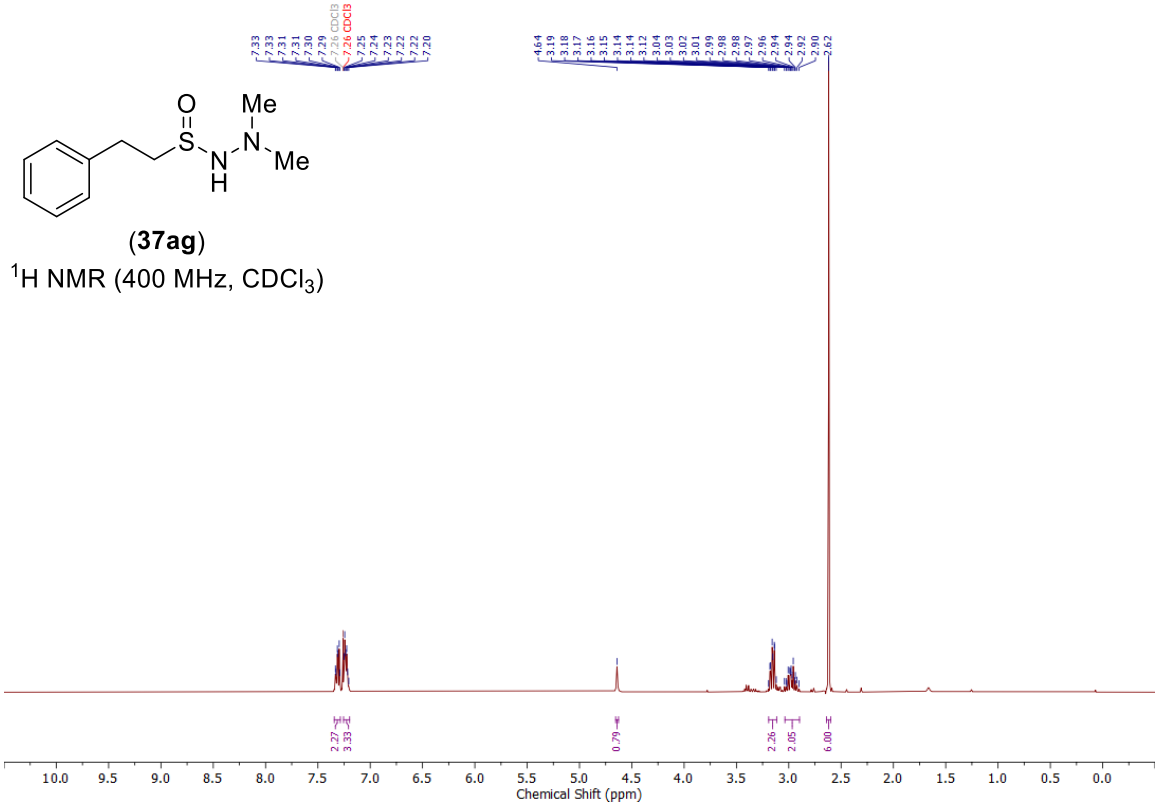


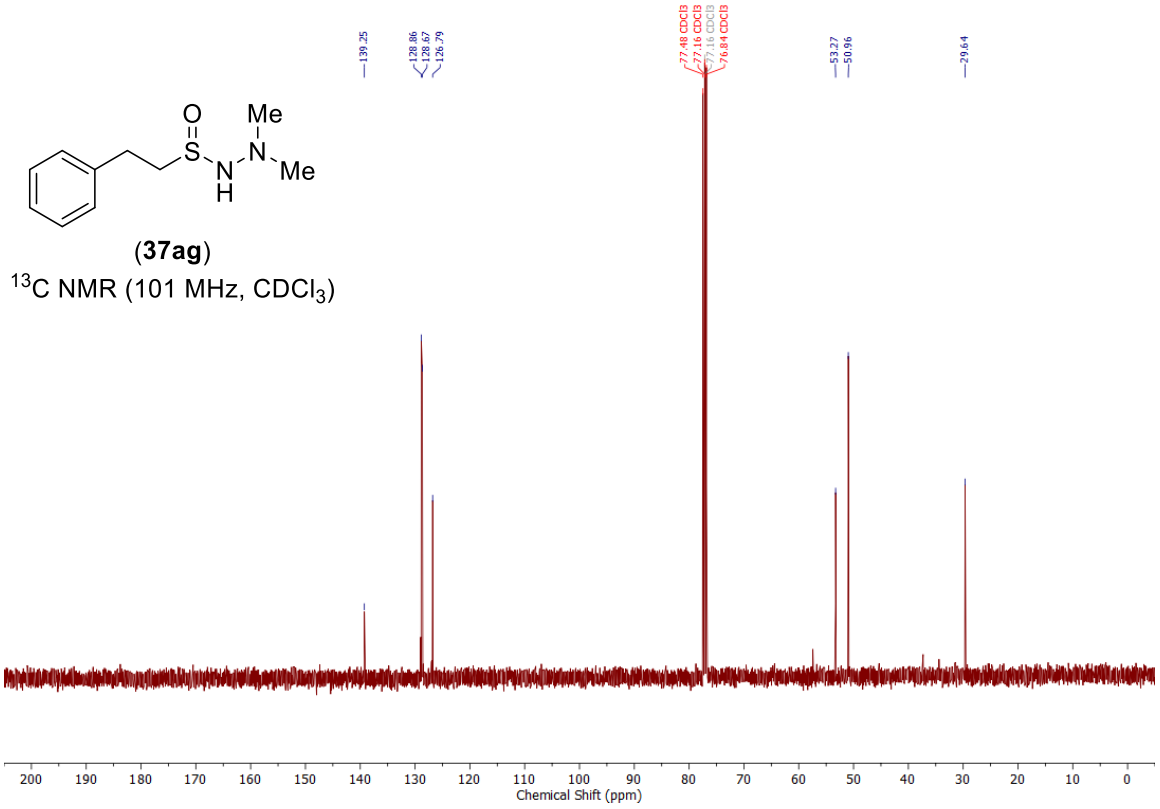
NMR spectra of *N*-methoxy-2-phenylethane-1-sulfinamide (37af):



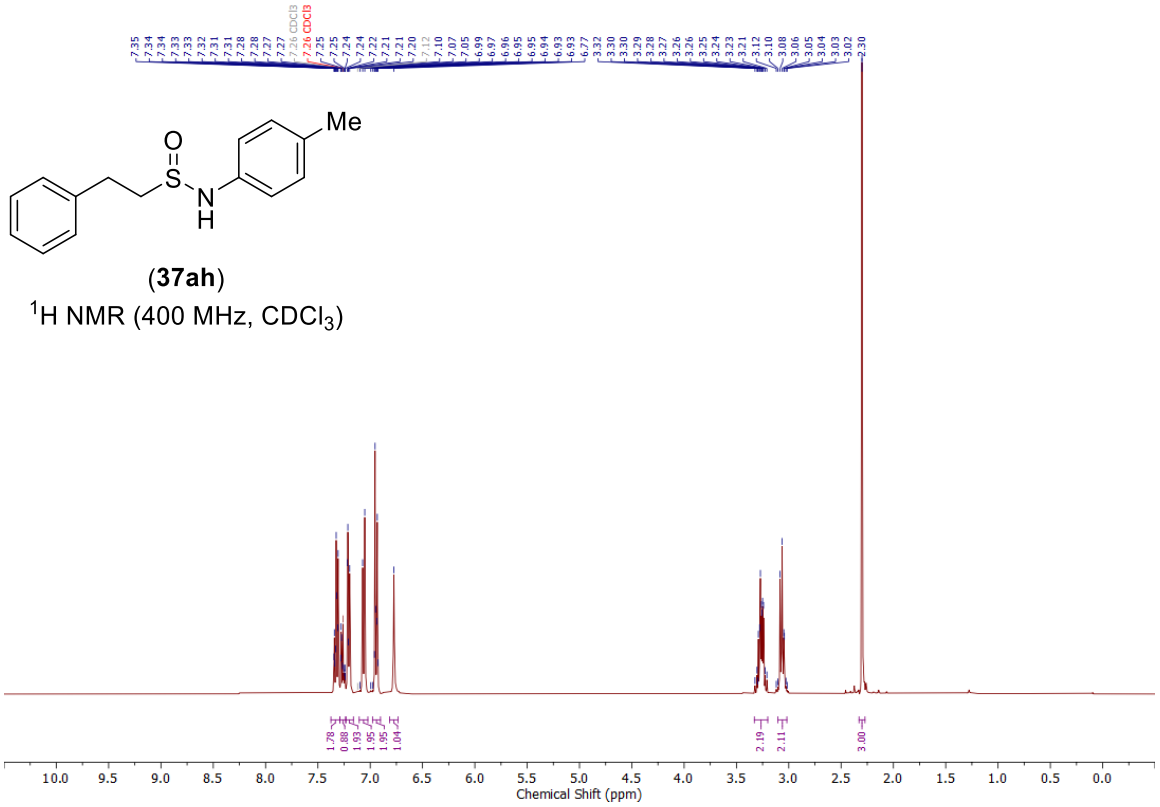


NMR spectra of *N*',*N*'-dimethyl-2-phenylethane-1-sulfinohydrazide (37ag):



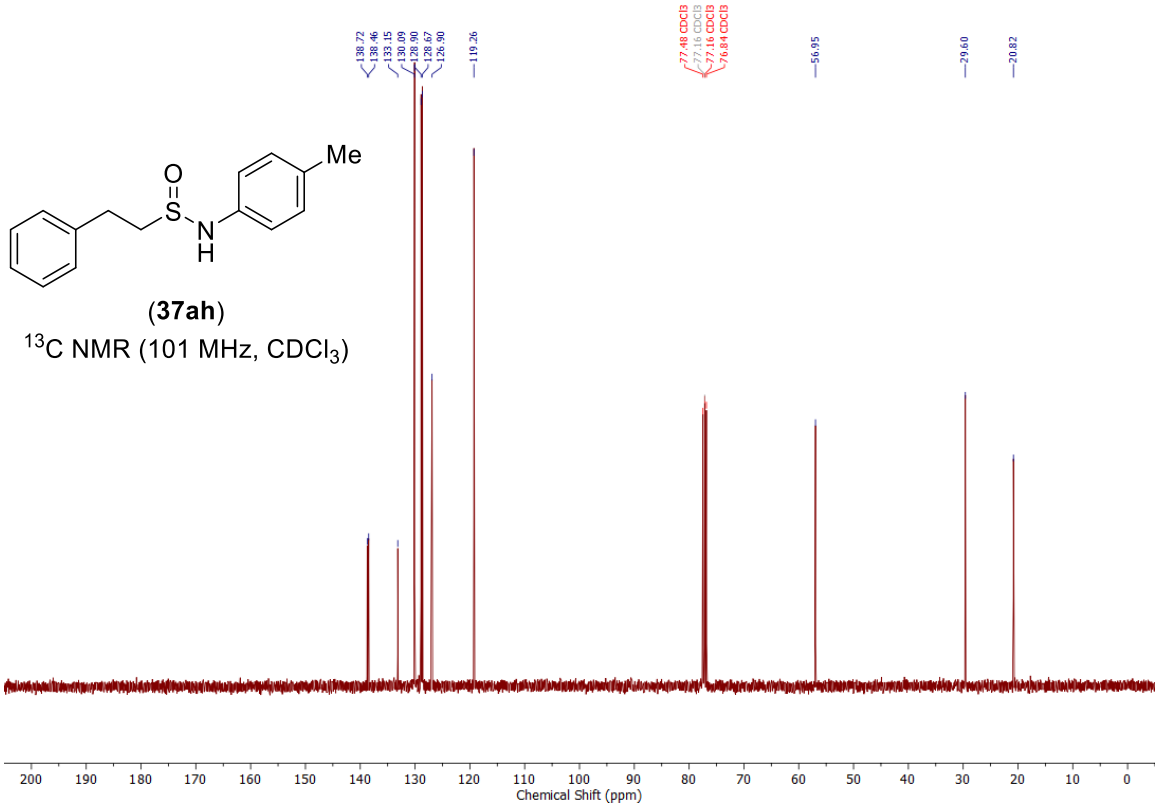


NMR spectra of 2-phenyl-*N*-(*p*-tolyl)ethane-1-sulfinamide (37ah):



(**37ah**)

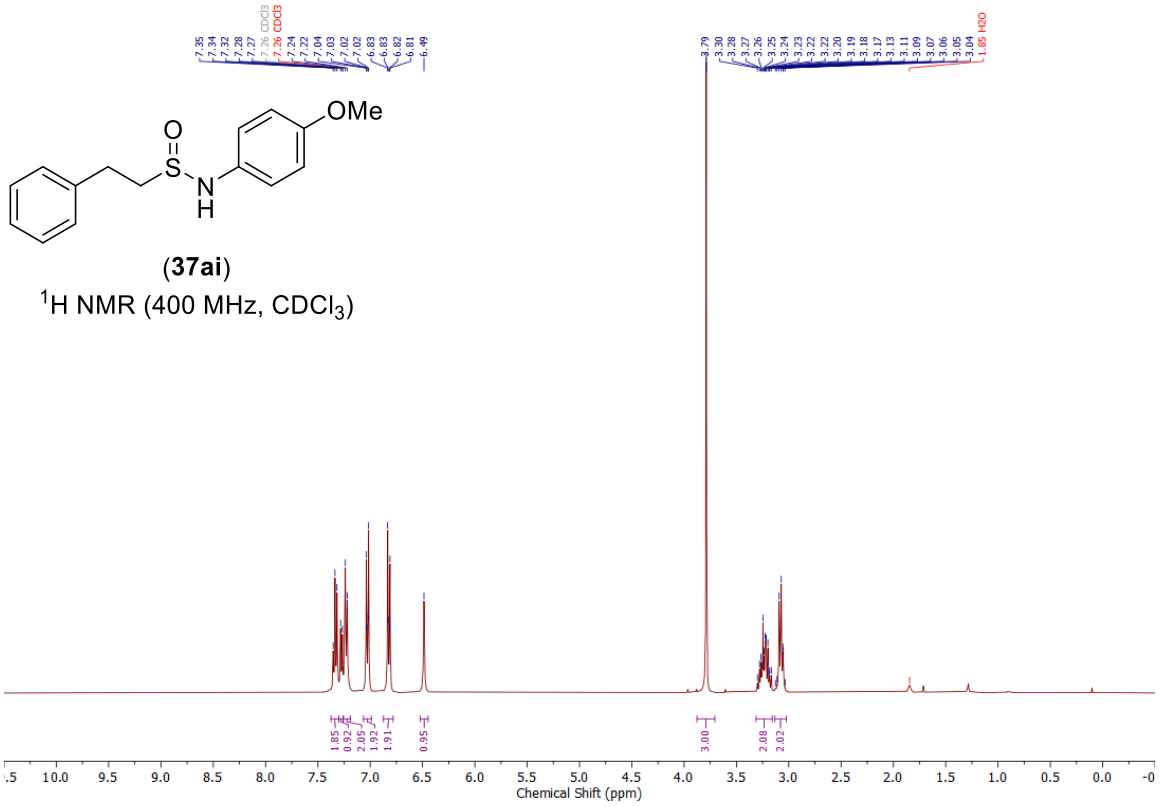
^{1}H NMR (400 MHz, $CDCl_3$)

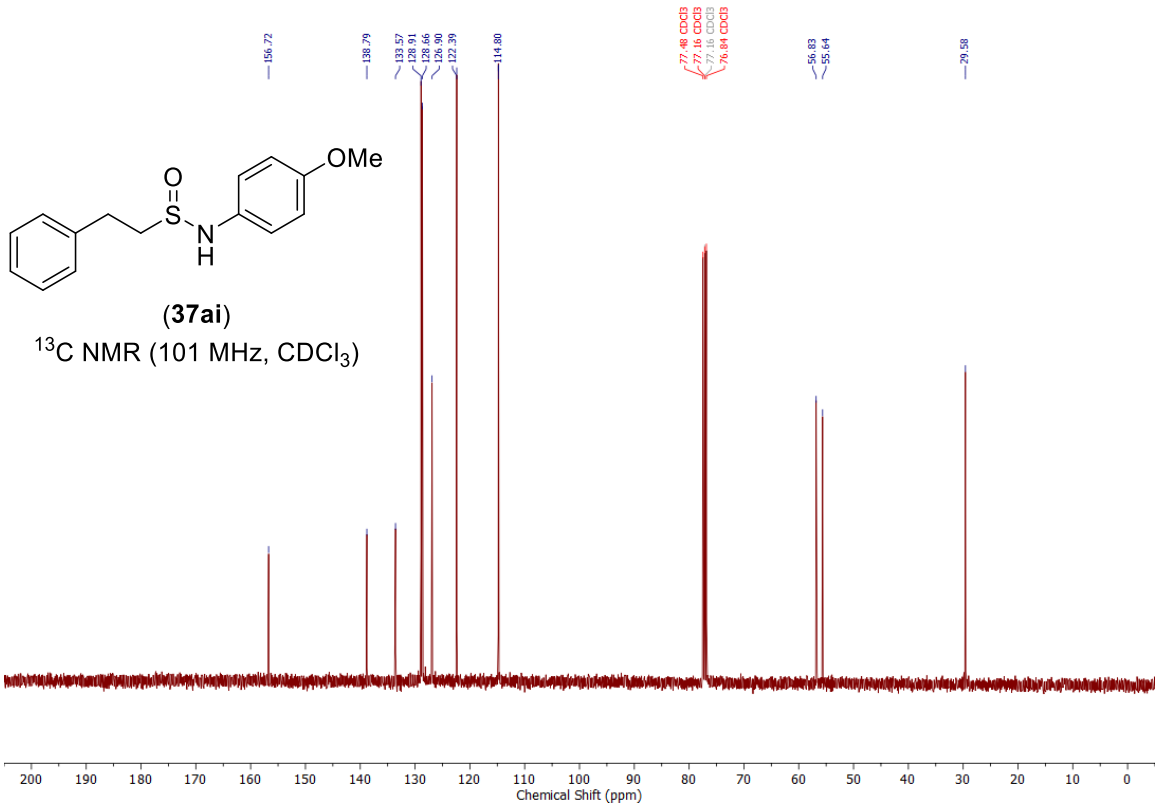


(**37ah**)

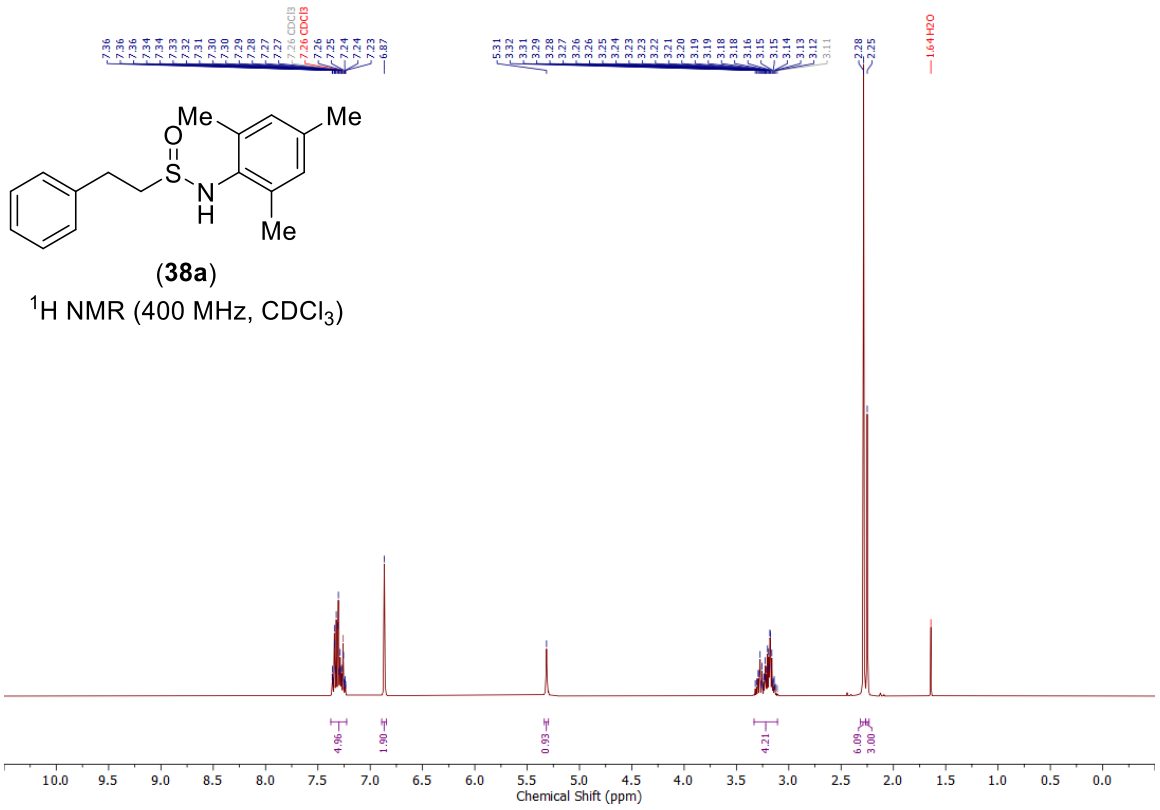
^{13}C NMR (101 MHz, $CDCl_3$)

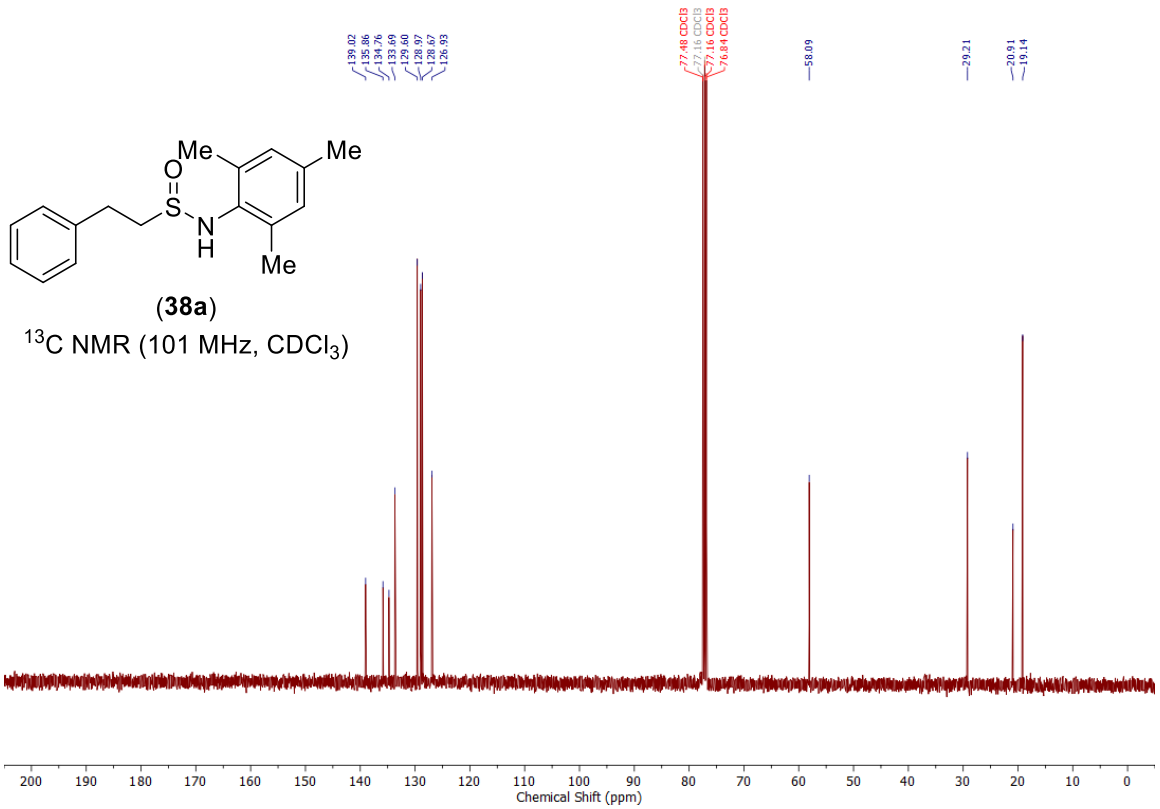
NMR spectra of *N*-(4-methoxyphenyl)-2-phenylethane-1-sulfinamide (37ai):



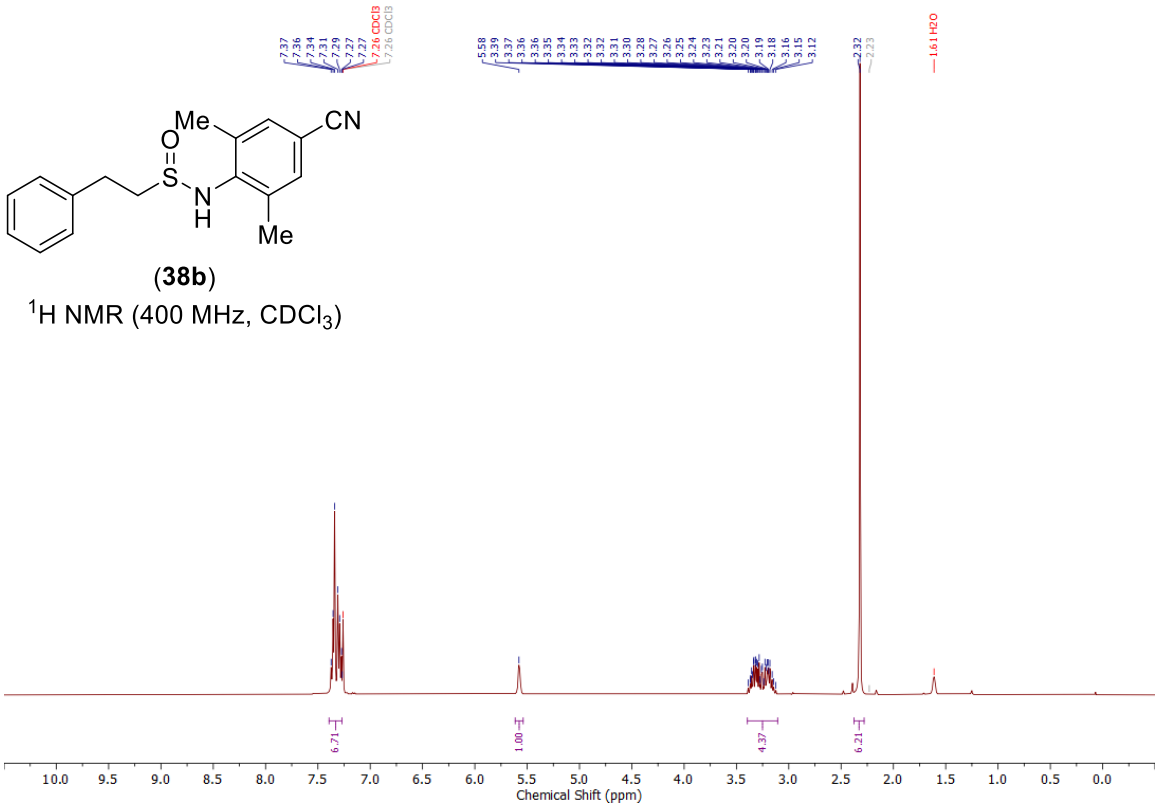


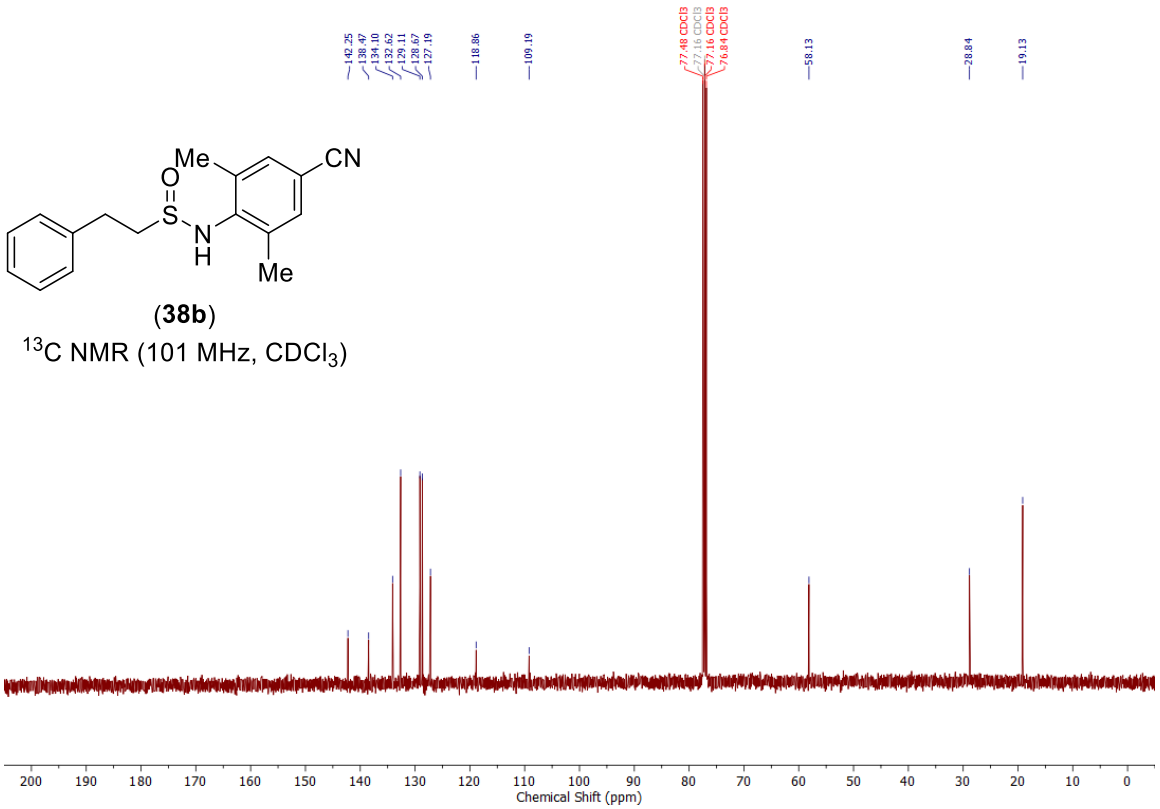
NMR spectra of *N*-mesityl-2-phenylethane-1-sulfinamide (38a):



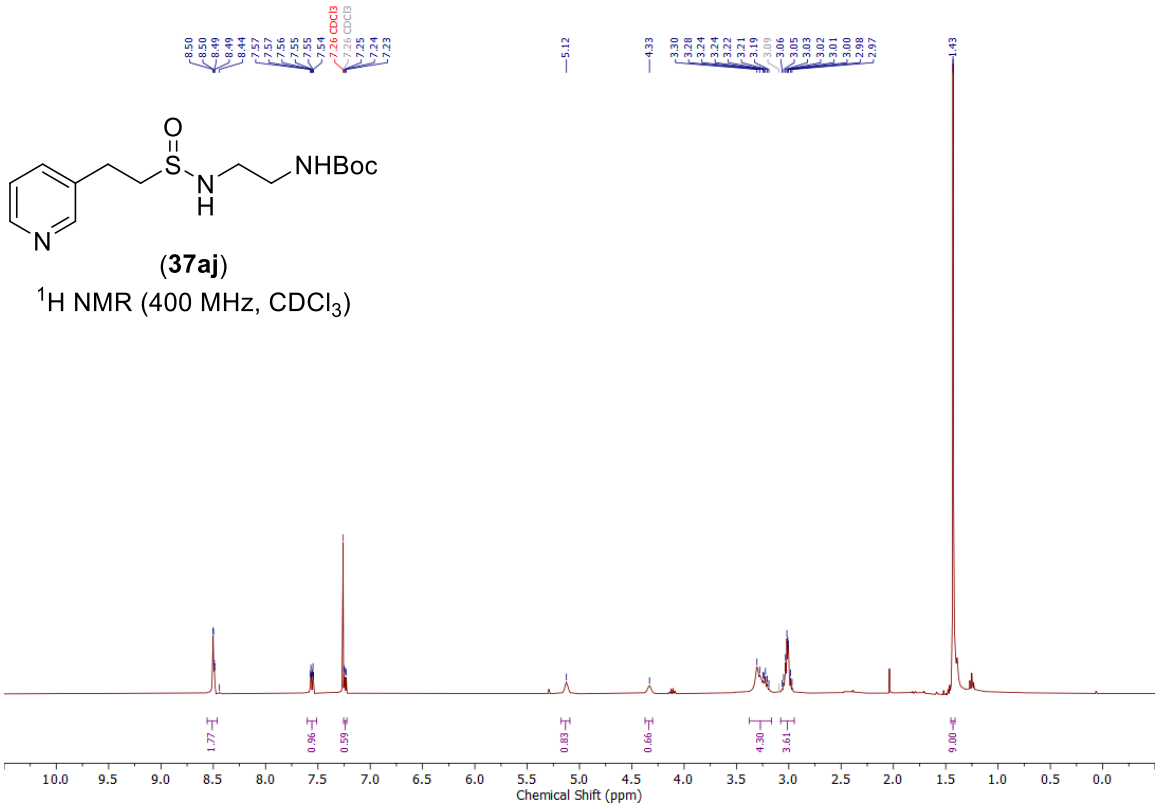


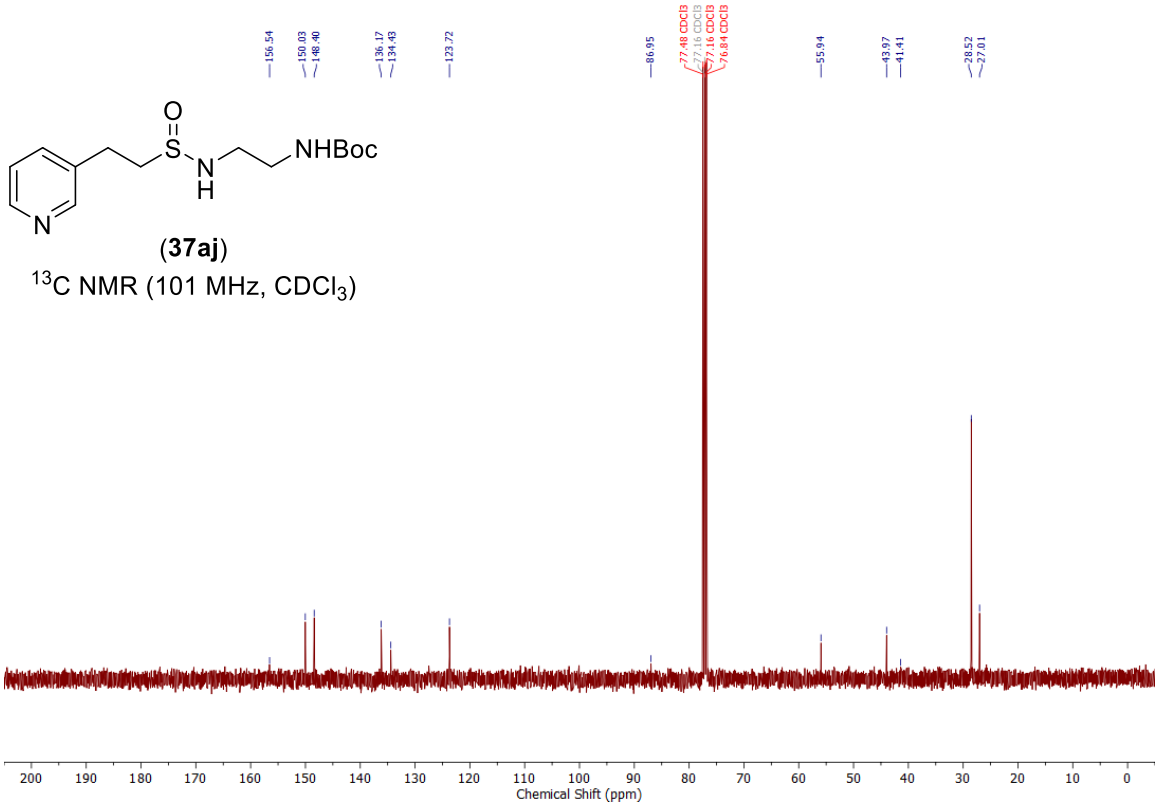
NMR spectra of *N*-(4-cyano-2,6-dimethylphenyl)-2-phenylethane-1-sulfinamide (38b):



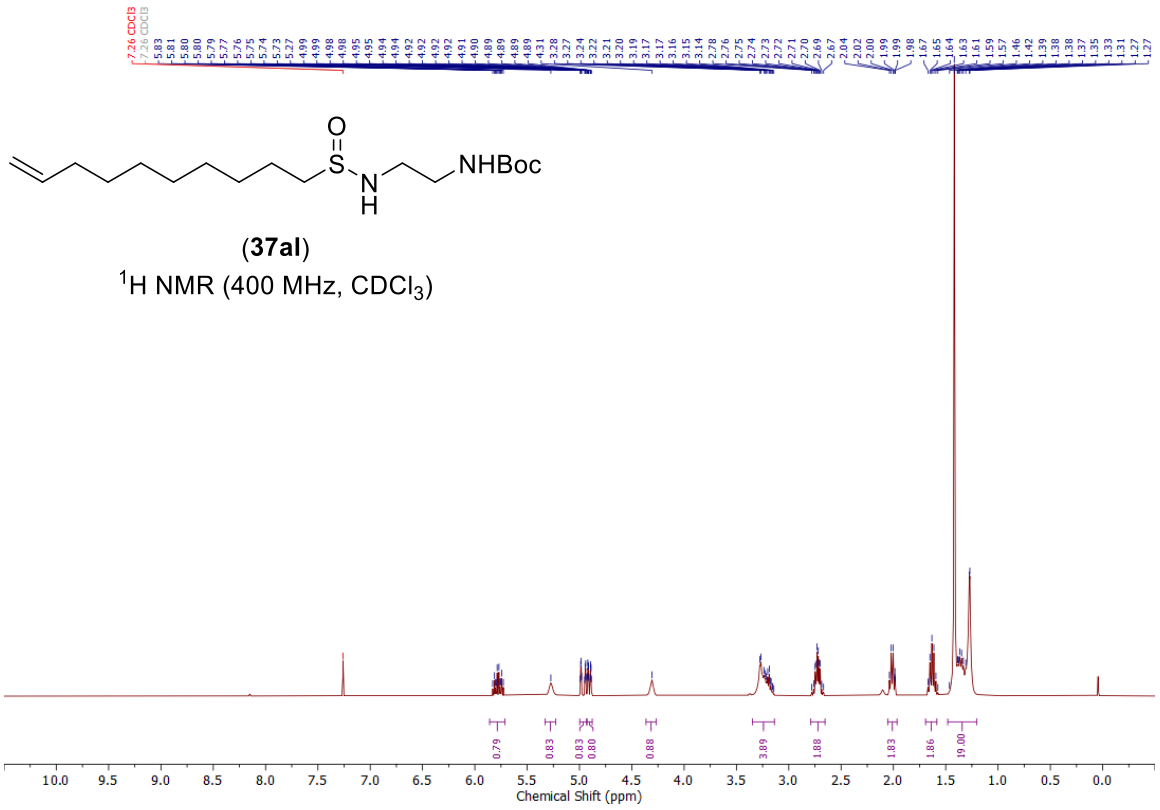


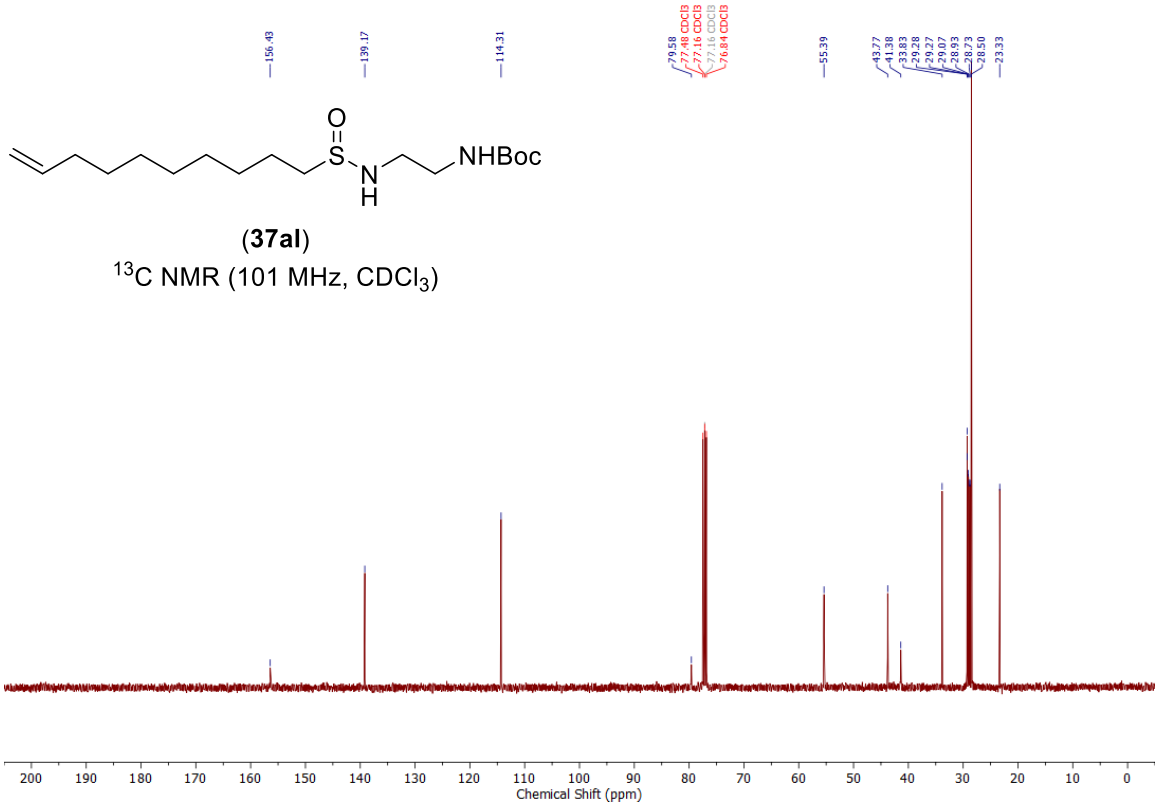
NMR spectra of *tert*-butyl (2-(((2-(pyridin-3-yl)ethyl)sulfinyl)amino)ethyl)carbamate (37aj):



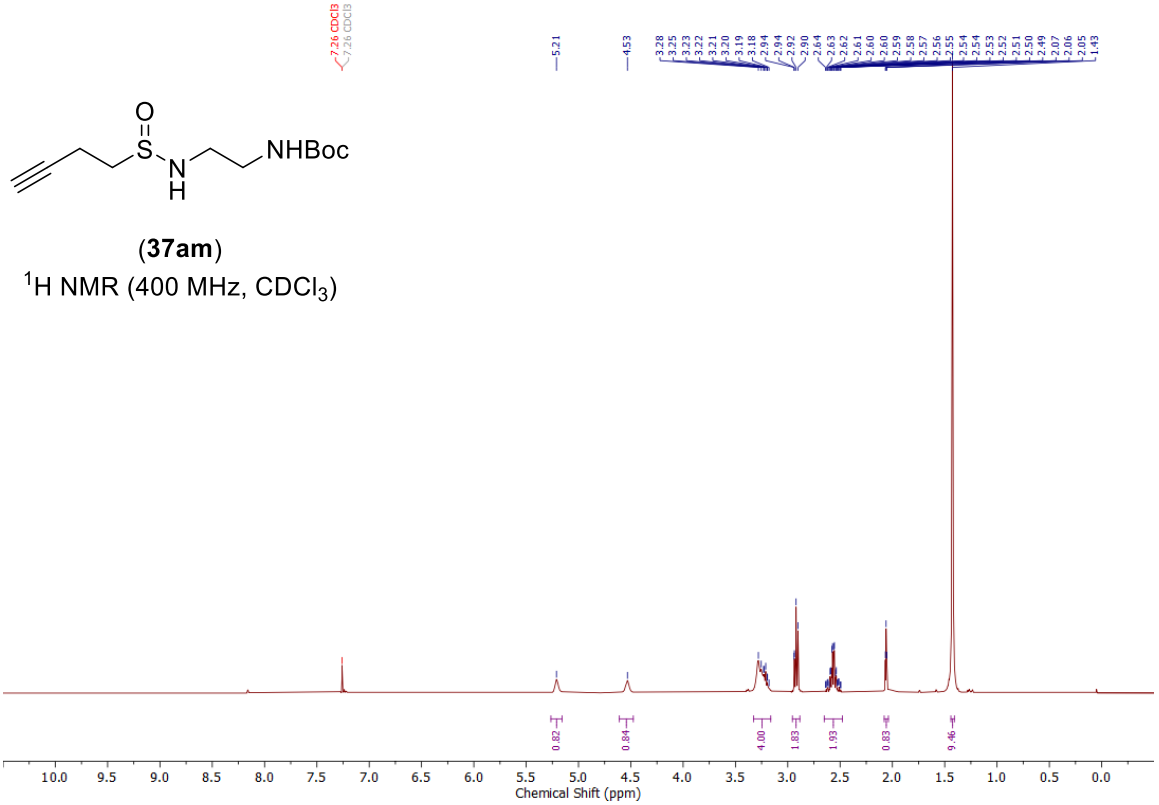


NMR spectra of *tert*-butyl (2-((dec-9-en-1-ylsulfinyl)amino)ethyl)carbamate (37al):

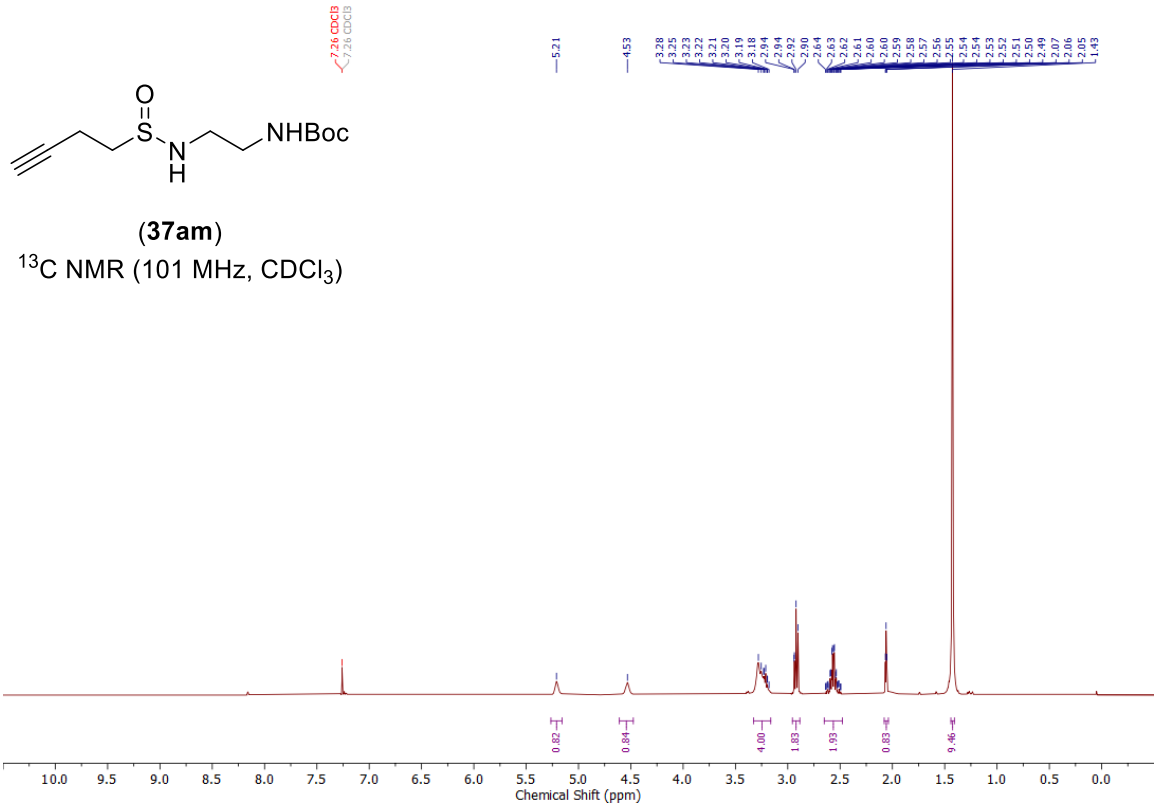




NMR spectra of *tert*-Butyl (2-((but-3-yn-1-ylsulfinyl)amino)ethyl)carbamate (37am):

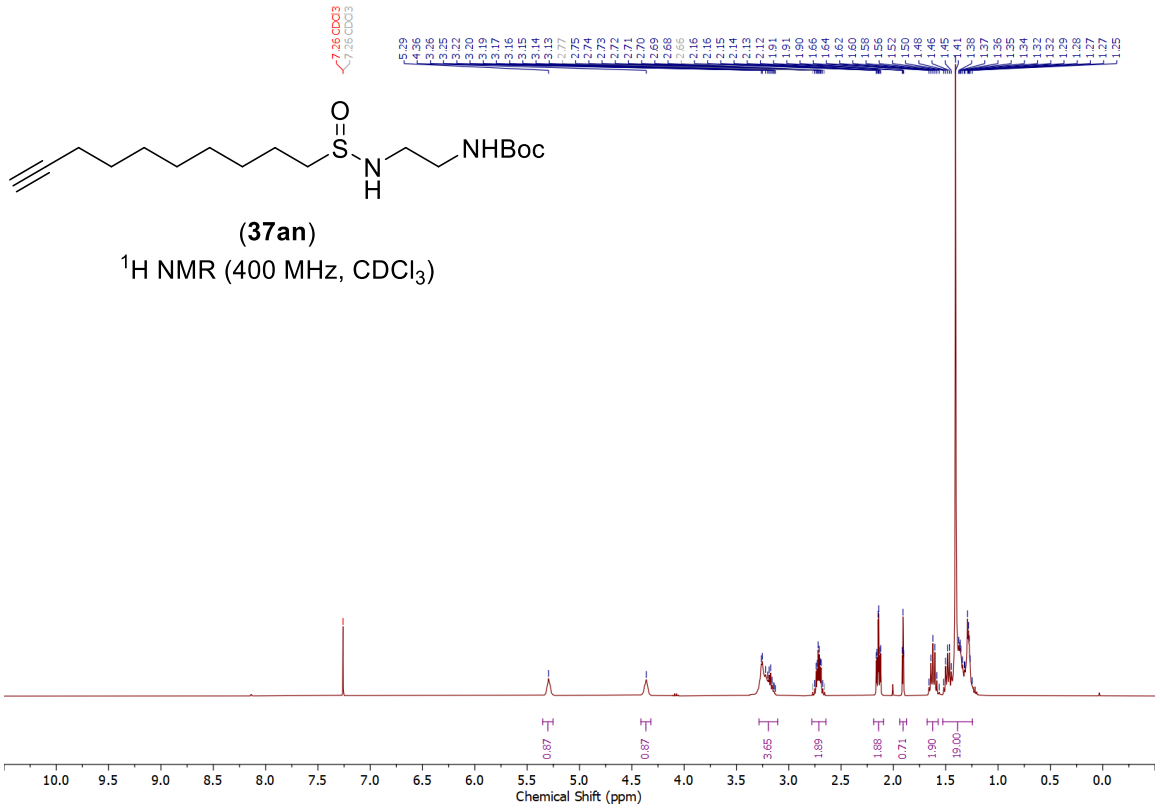


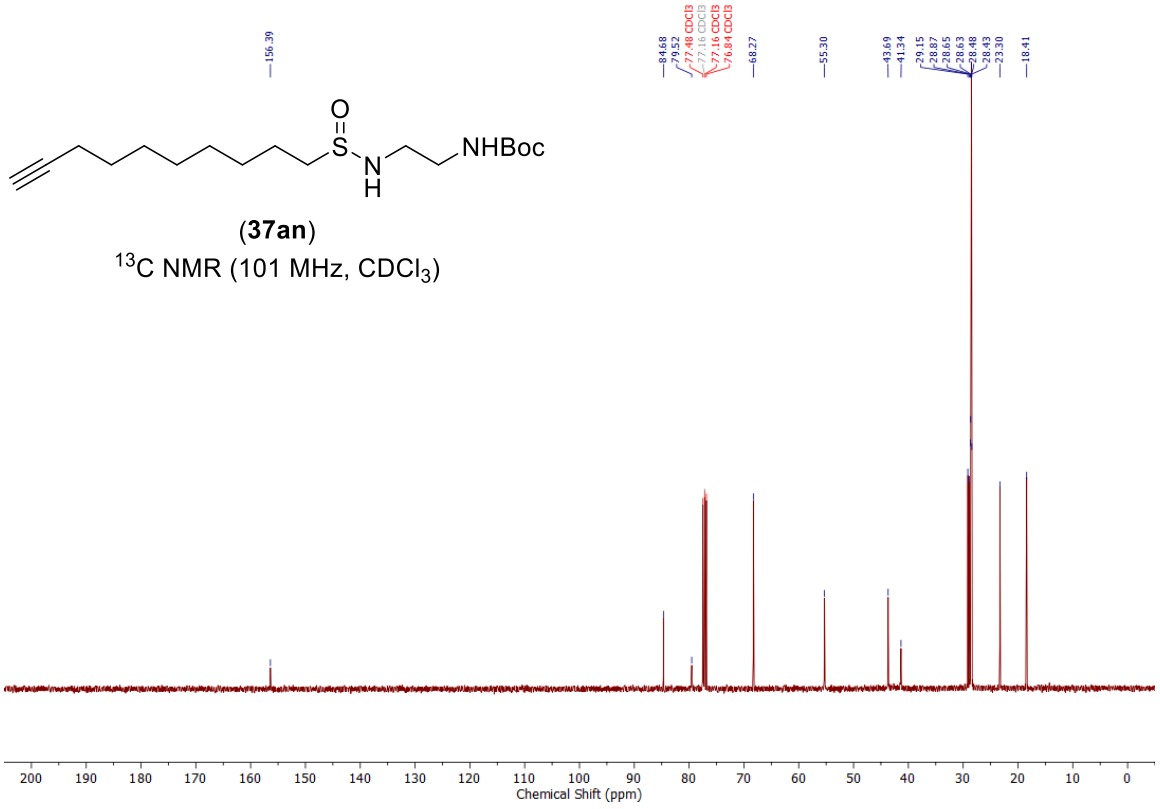
(**37am**)
^{1}H NMR (400 MHz, $CDCl_3$)



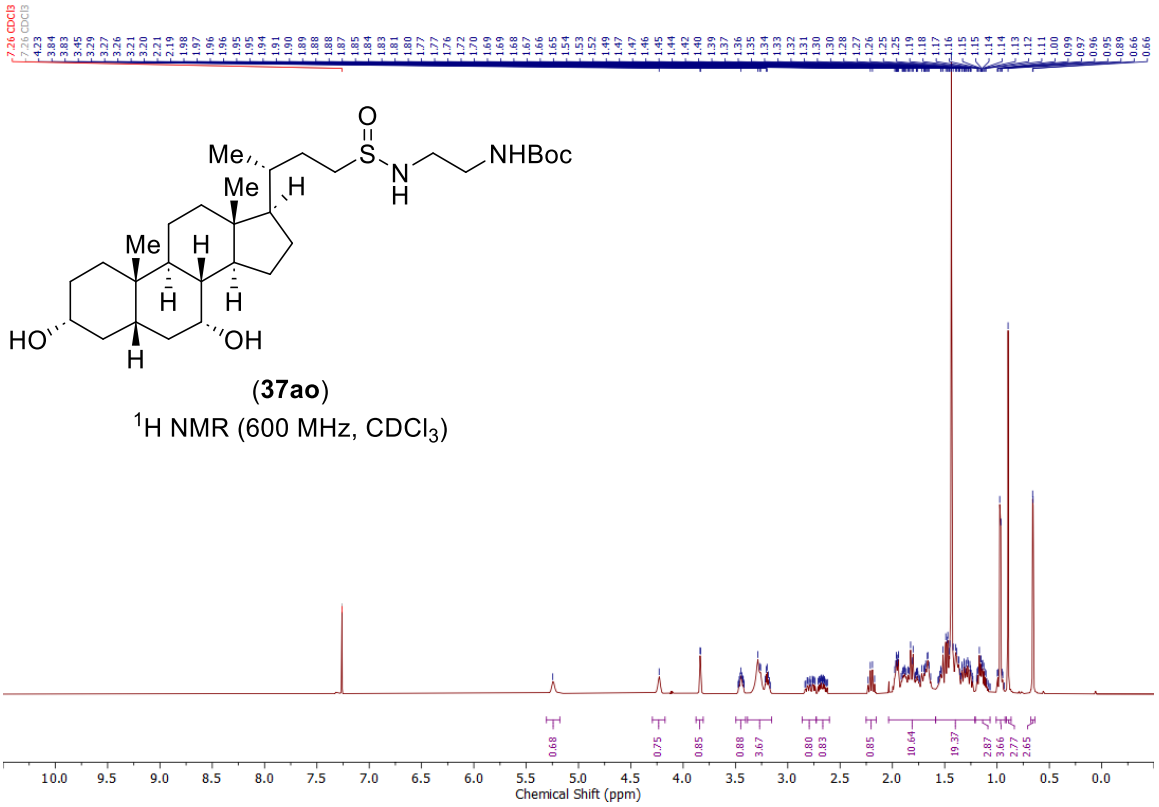
(**37am**)
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl (2-((dec-9-yn-1-ylsulfinyl)amino)ethyl)carbamate (37an):



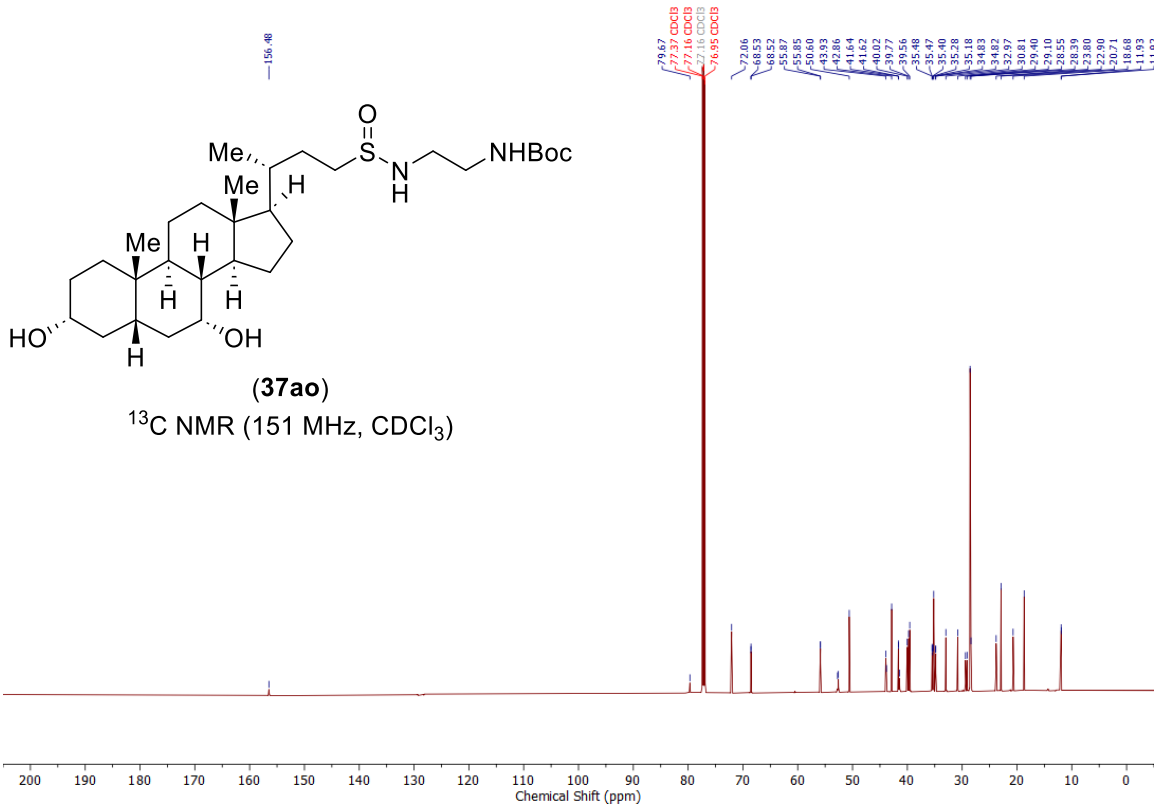


NMR spectra of *tert*-butyl (2-((((*R*)-3-((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3,7-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)butyl)sulfinyl)amino)ethyl)carbamate (37ao):



(**37ao**)

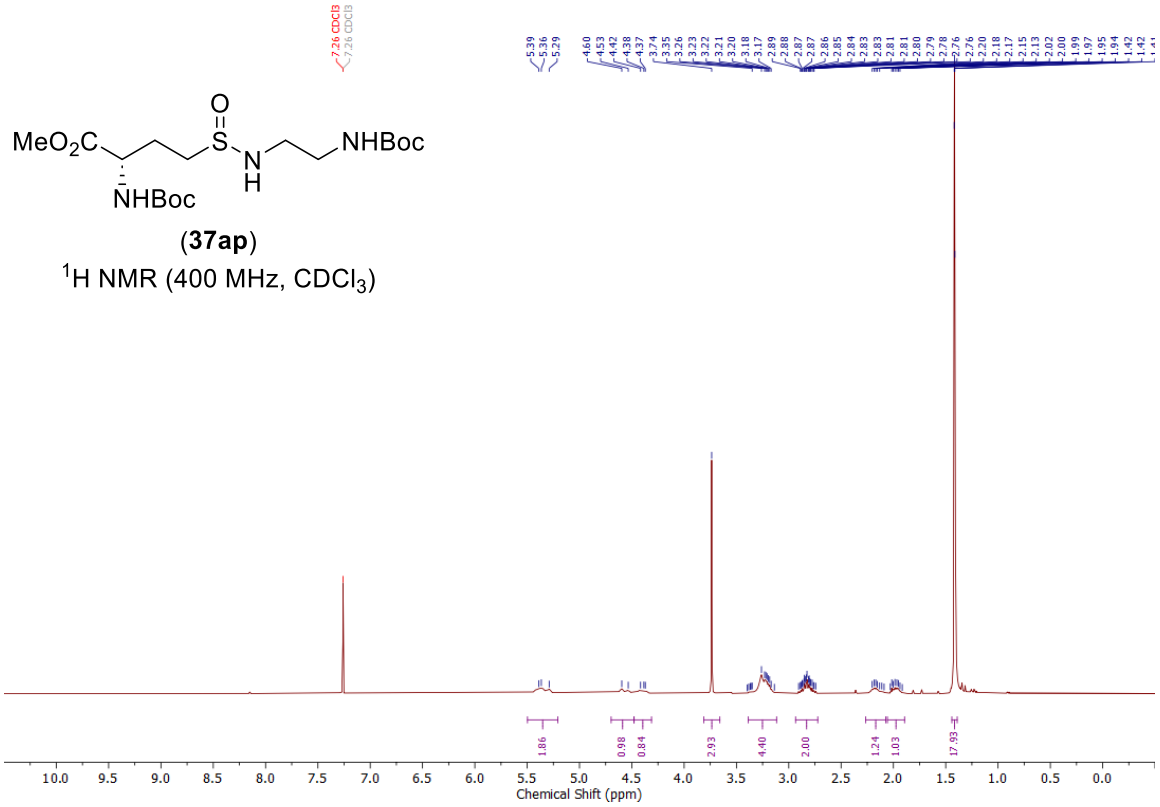
^{1}H NMR (600 MHz, $CDCl_3$)



(**37ao**)

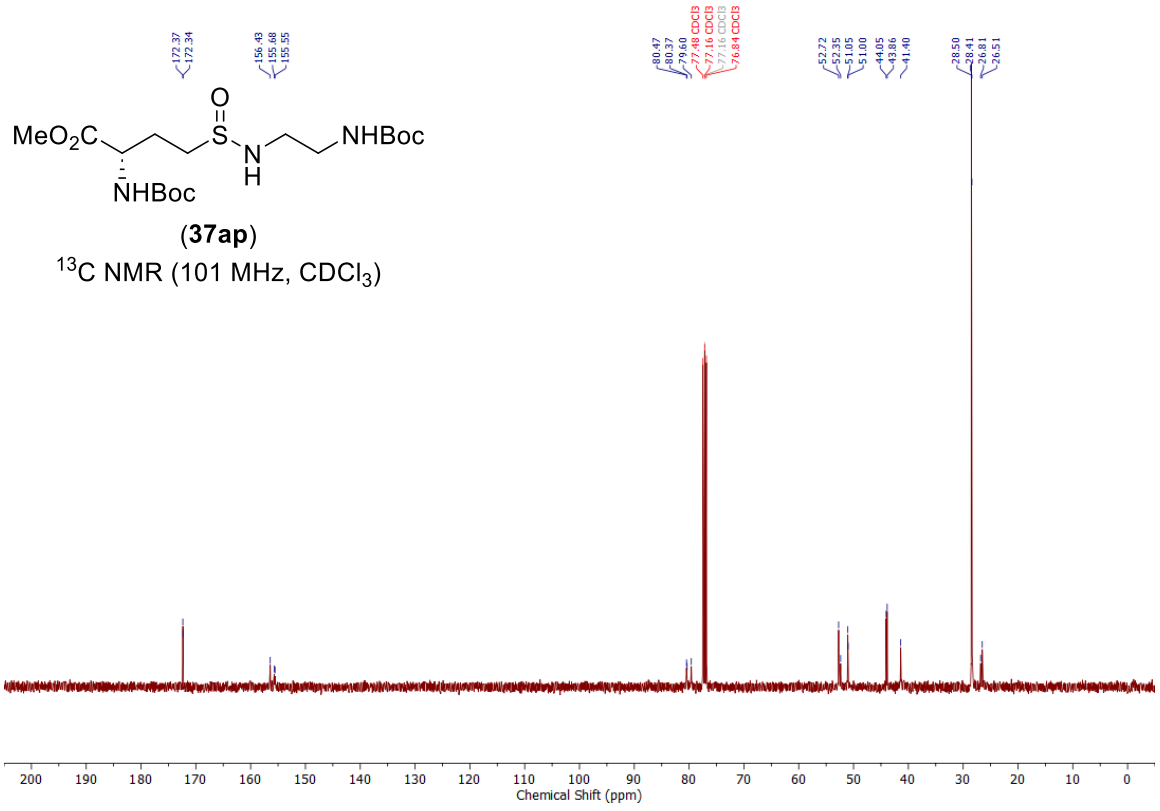
^{13}C NMR (151 MHz, $CDCl_3$)

NMR spectra of methyl (2*R*)-2-((*tert*-butoxycarbonyl)amino)-4-(((2-((*tert*-butoxycarbonyl)amino)ethyl)amino)sulfinyl)butanoate (37ap):



(**37ap**)

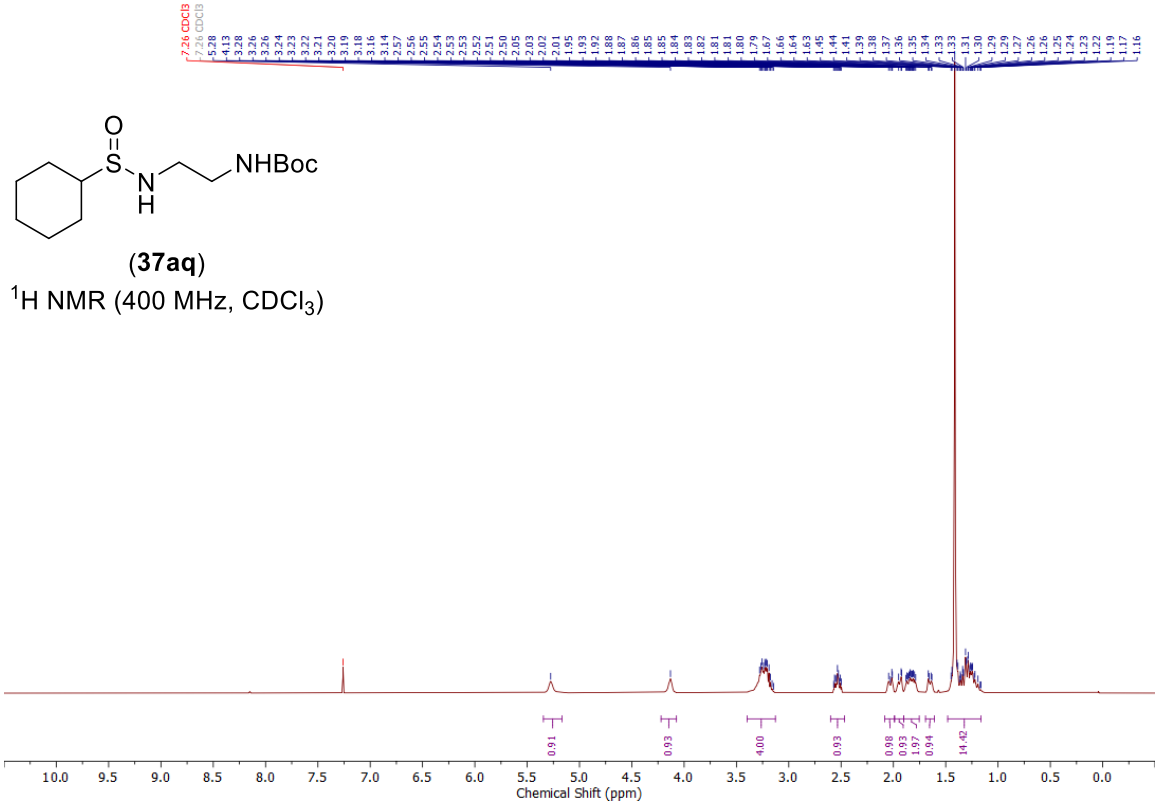
^{1}H NMR (400 MHz, $CDCl_3$)



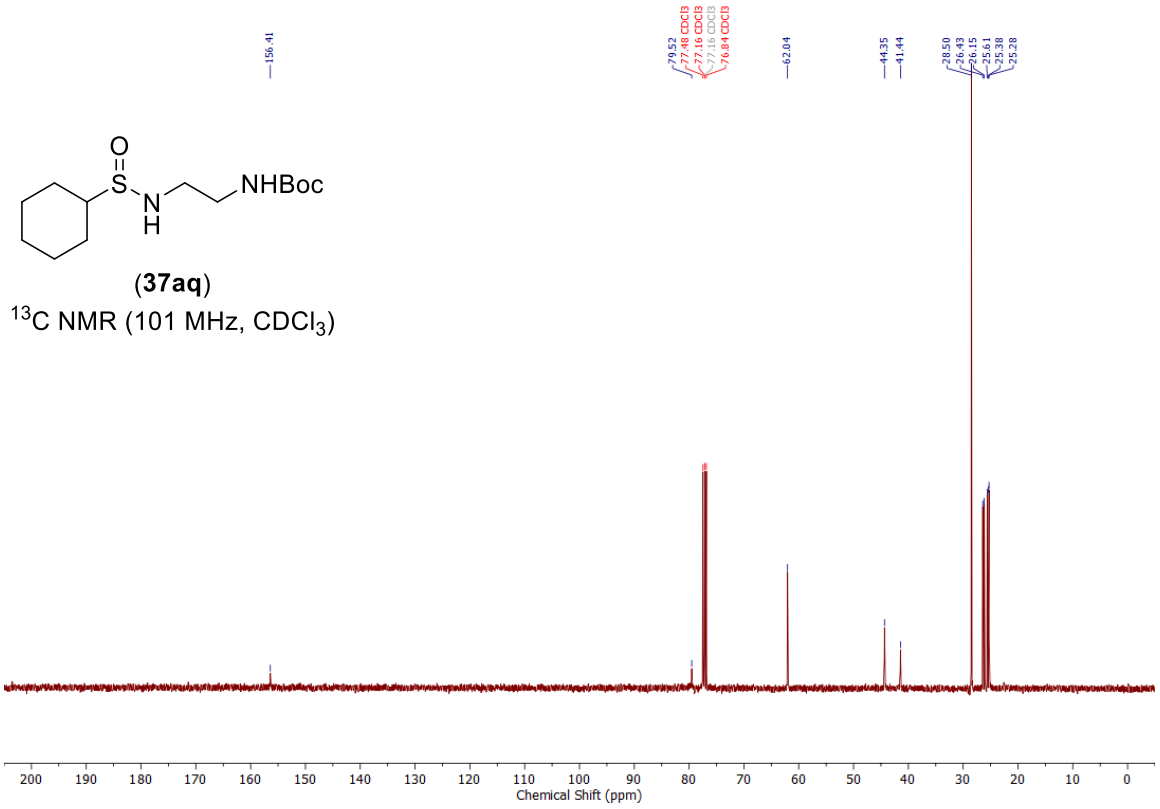
(**37ap**)

^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of *tert*-butyl (2-((cyclohexylsulfinyl)amino)ethyl)carbamate (37aq):

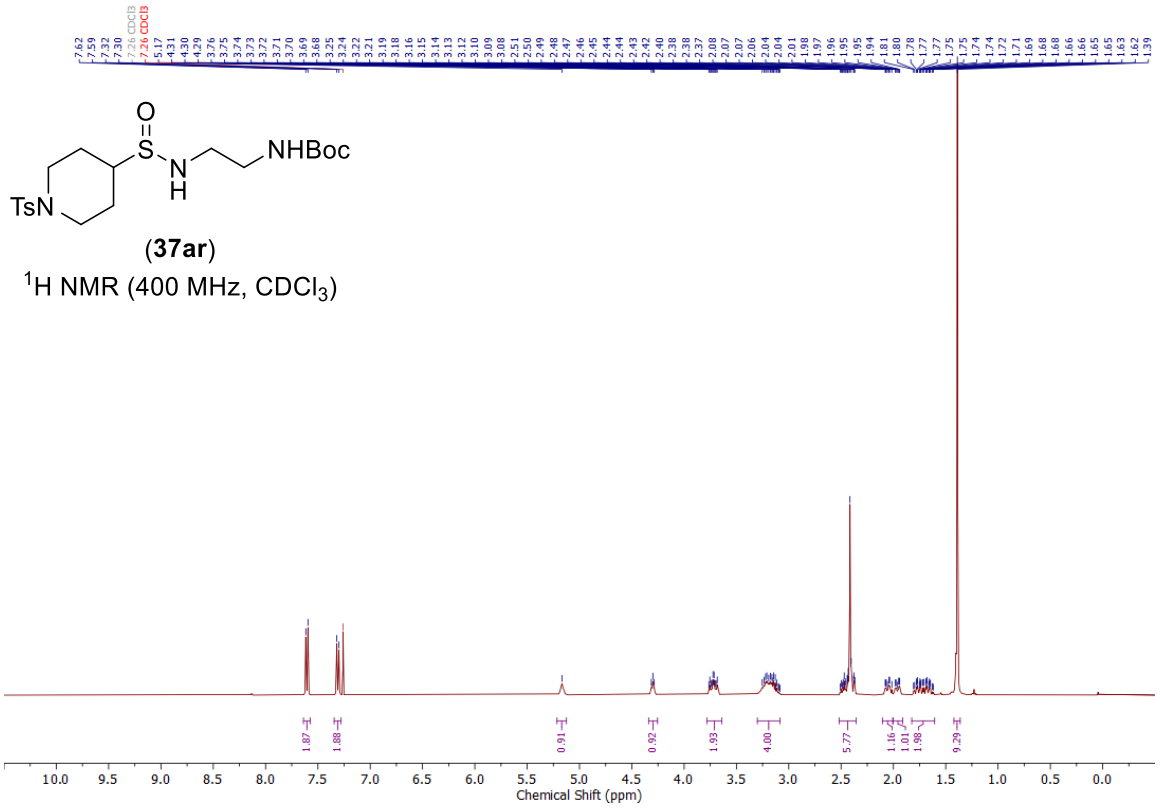


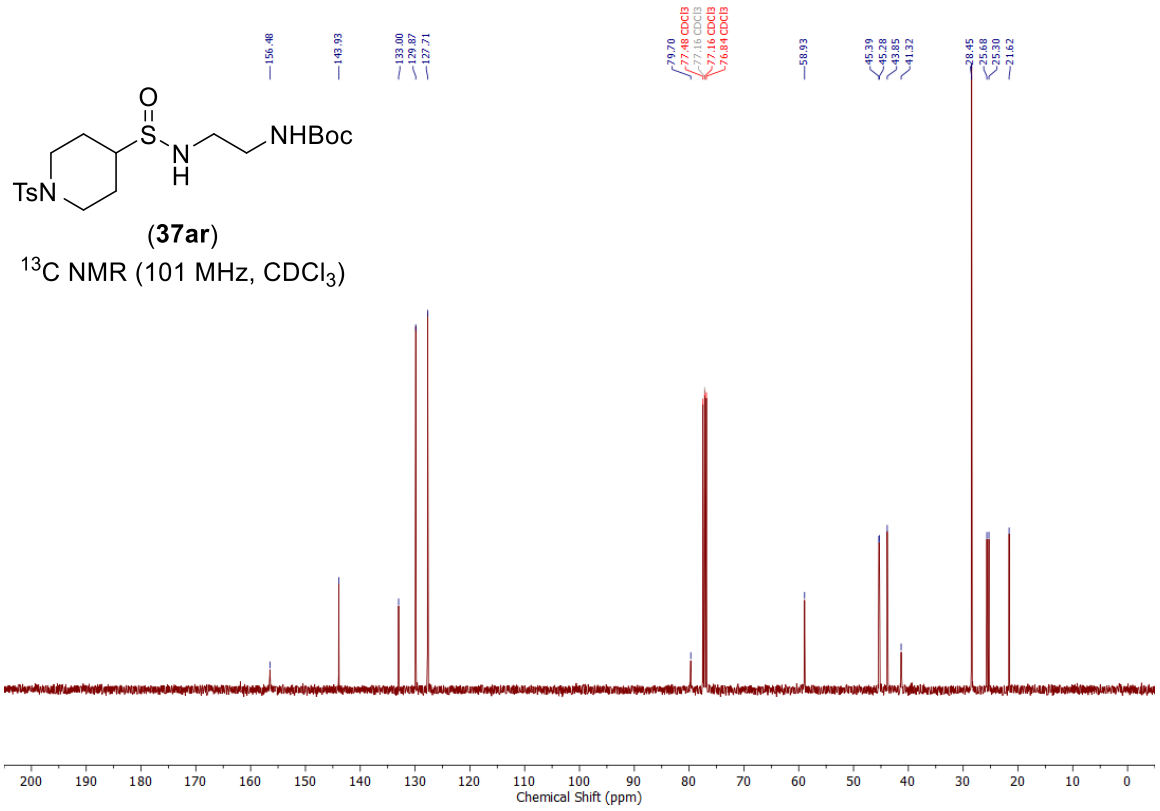
(**37aq**)
^{1}H NMR (400 MHz, $CDCl_3$)



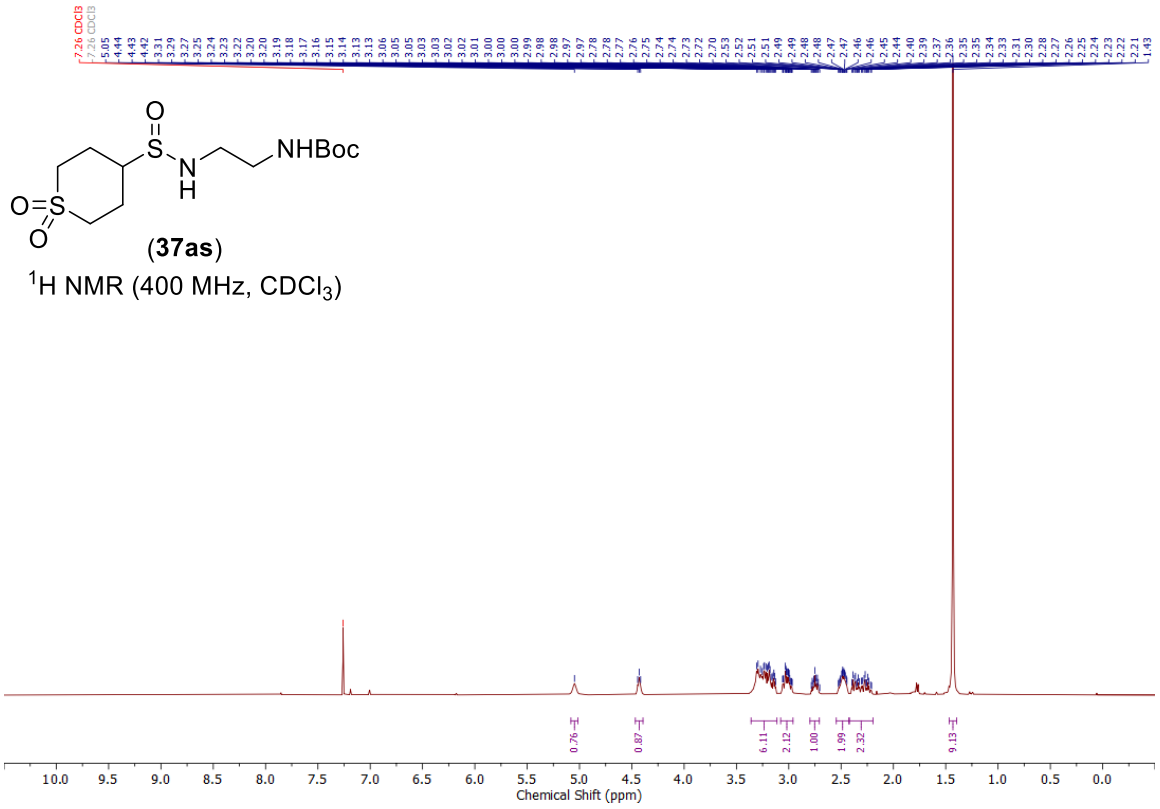
(**37aq**)
^{13}C NMR (101 MHz, $CDCl_3$)

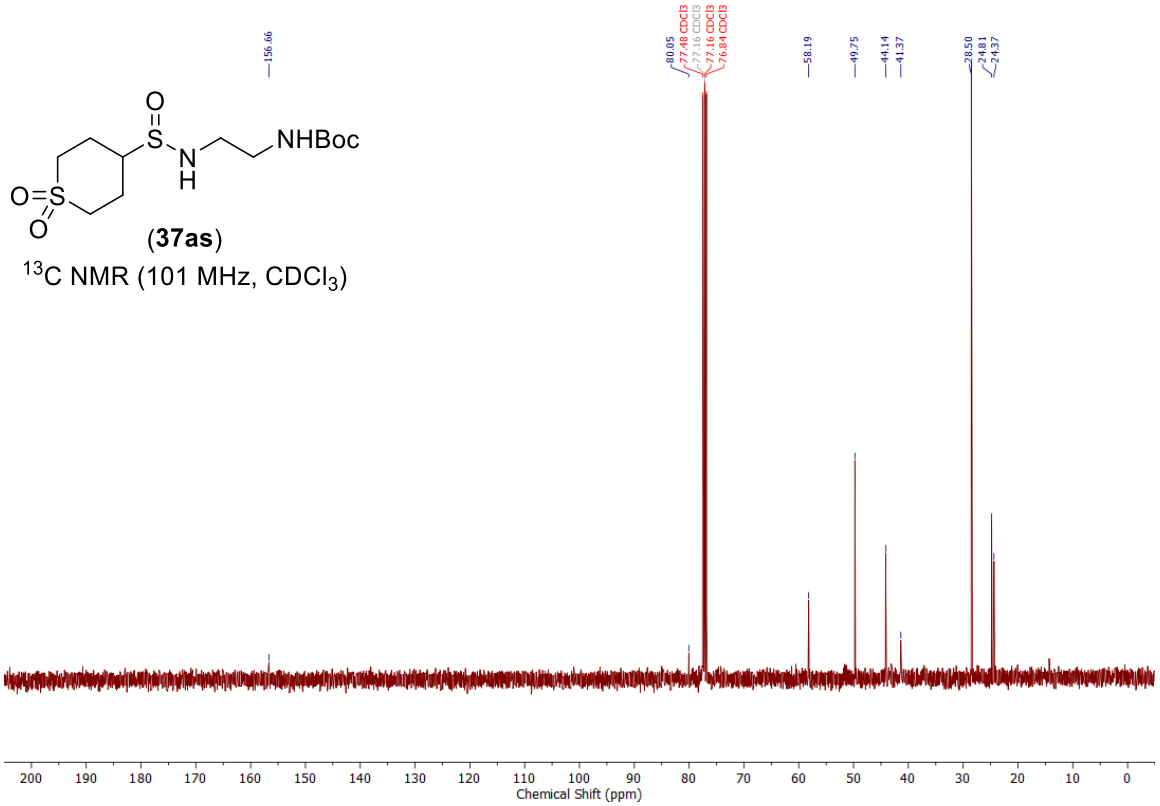
NMR spectra of *tert*-Butyl (2-(((1-tosylpiperidin-4-yl)sulfinyl)amino)ethyl)carbamate (37ar):



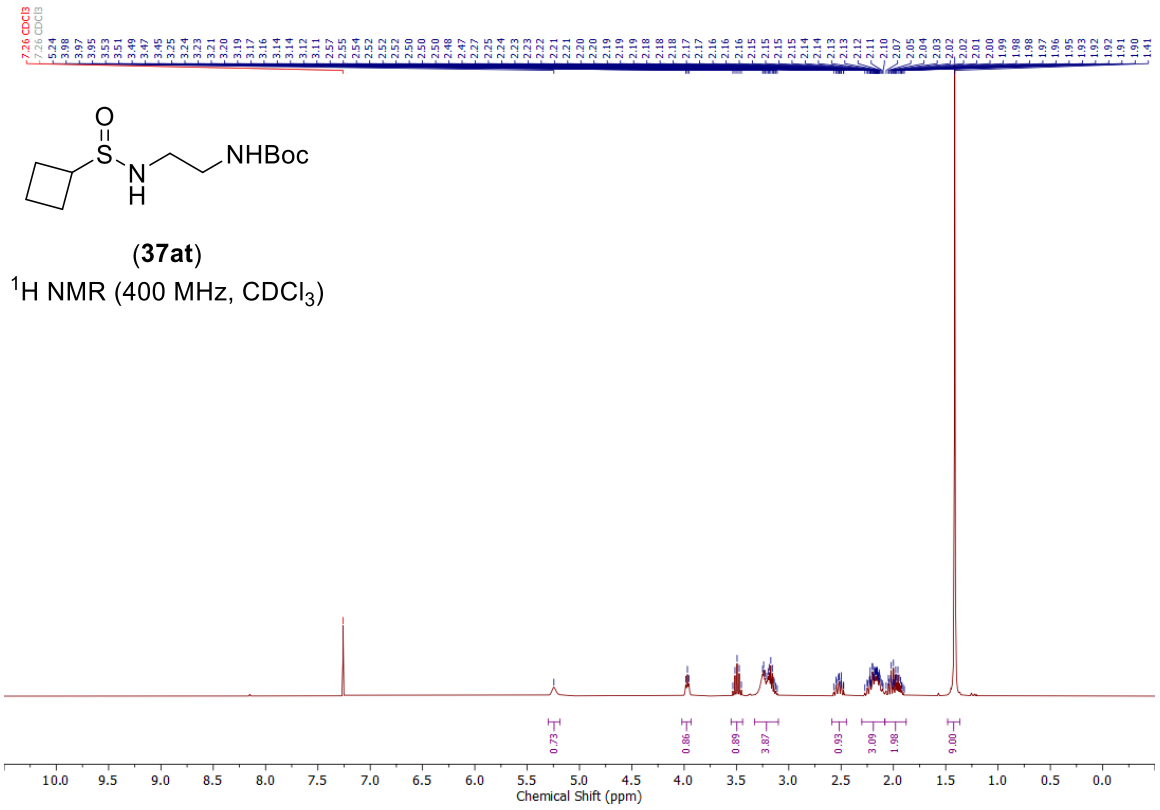


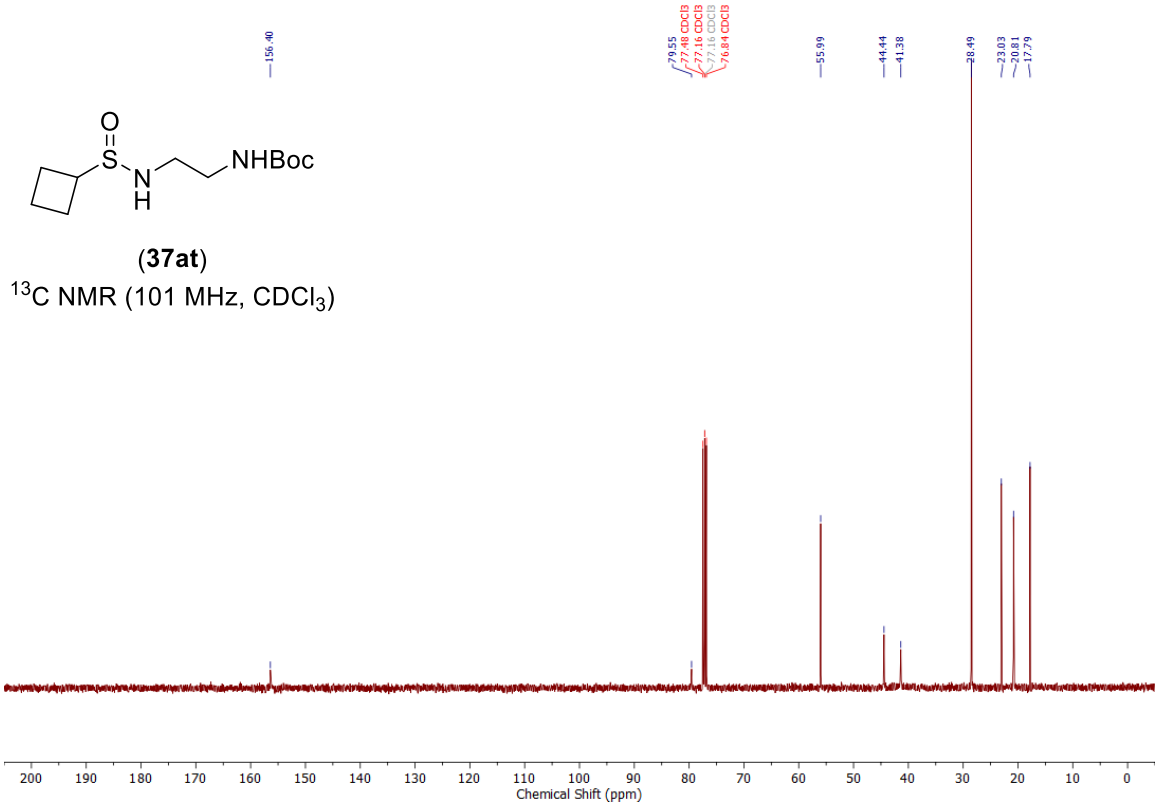
NMR spectra of *tert*-butyl (2-(((1,1-dioxidotetrahydro-2*H*-thiopyran-4-yl)sulfinyl)amino)ethyl)carbamate (37as):



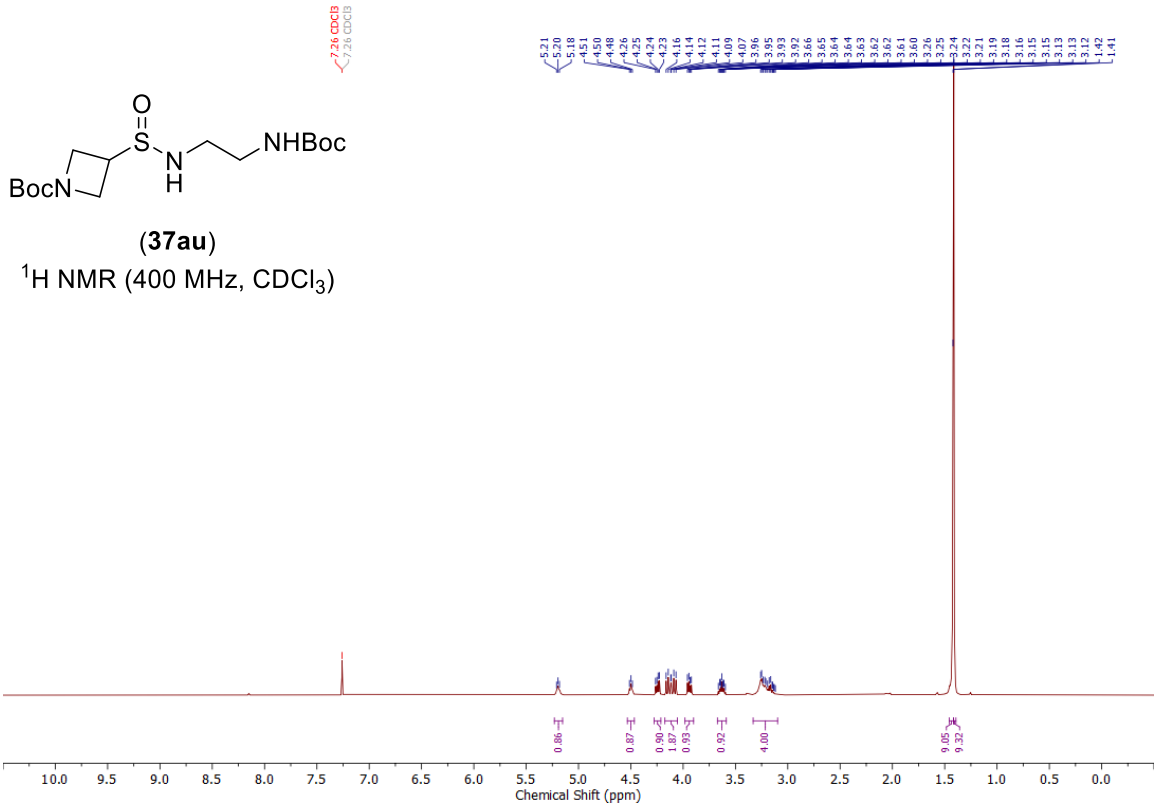


NMR spectra of *tert*-butyl (2-((cyclobutylsulfinyl)amino)ethyl)carbamate (37at):

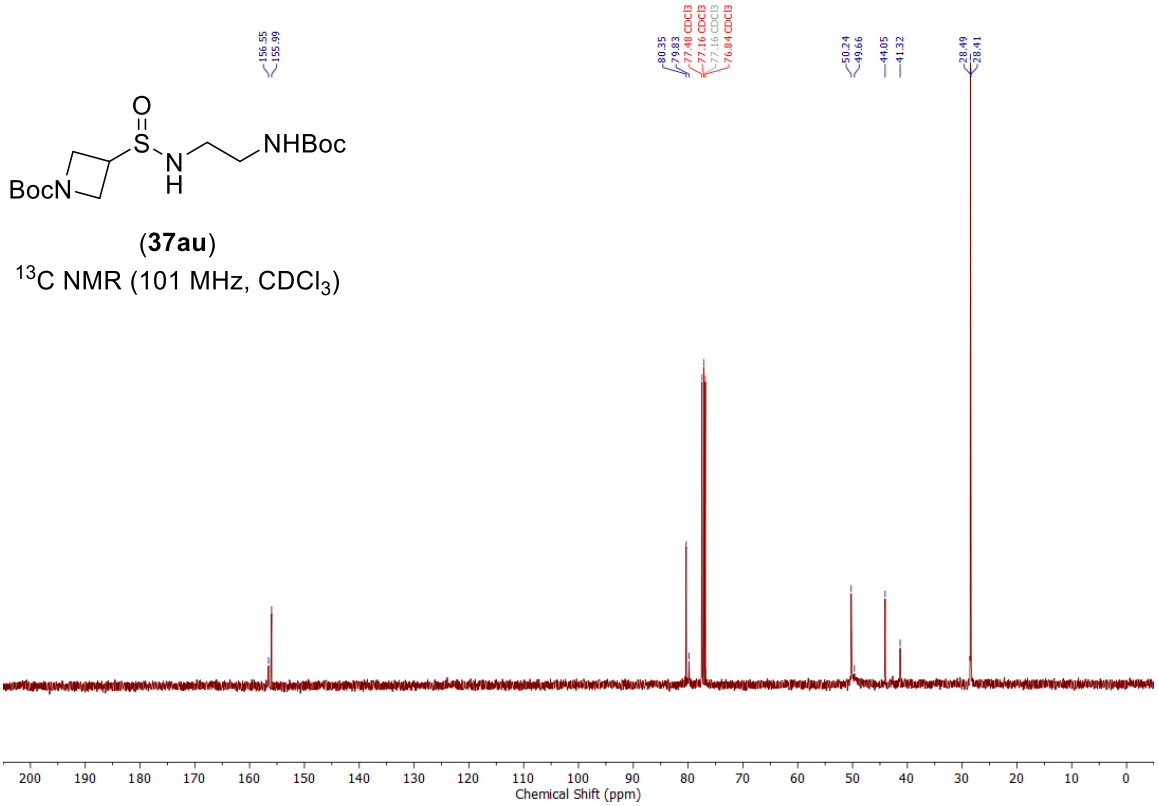




NMR spectra of *tert*-butyl 3-(((2-((*tert*-butoxycarbonyl)amino)ethyl)amino)sulfinyl)azetidine-1-carboxylate (37au):

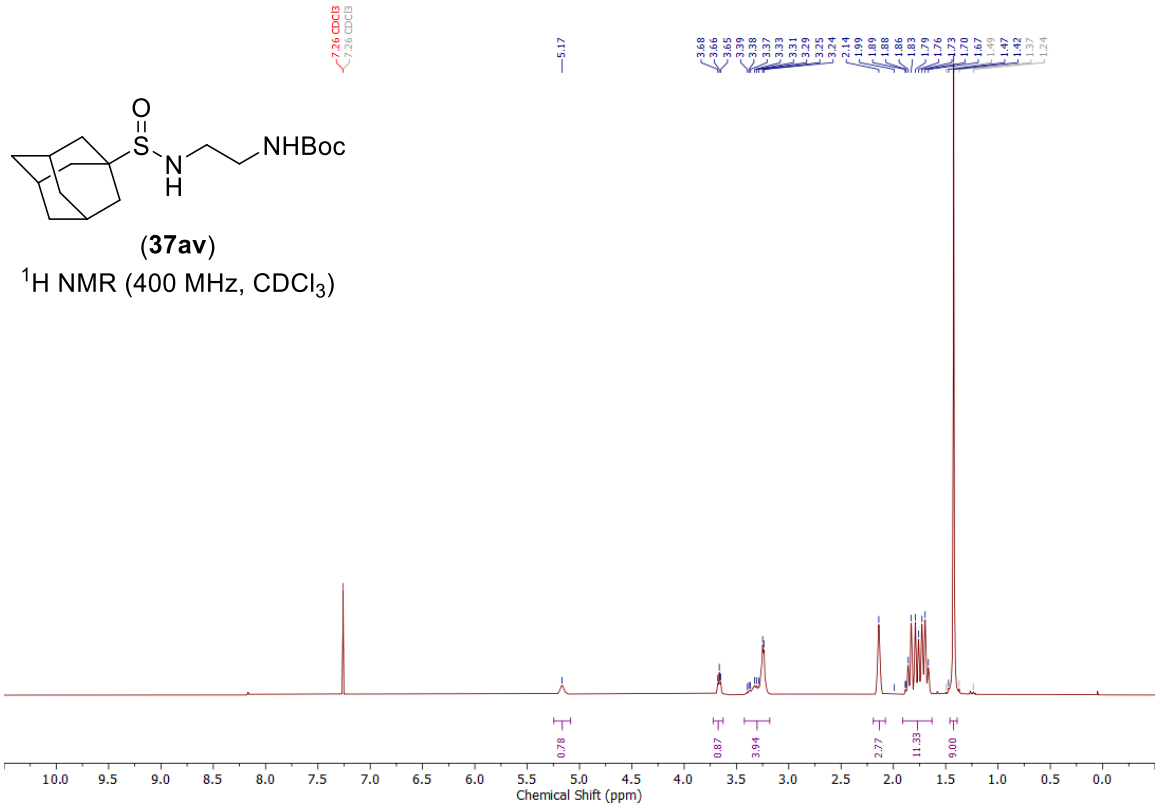


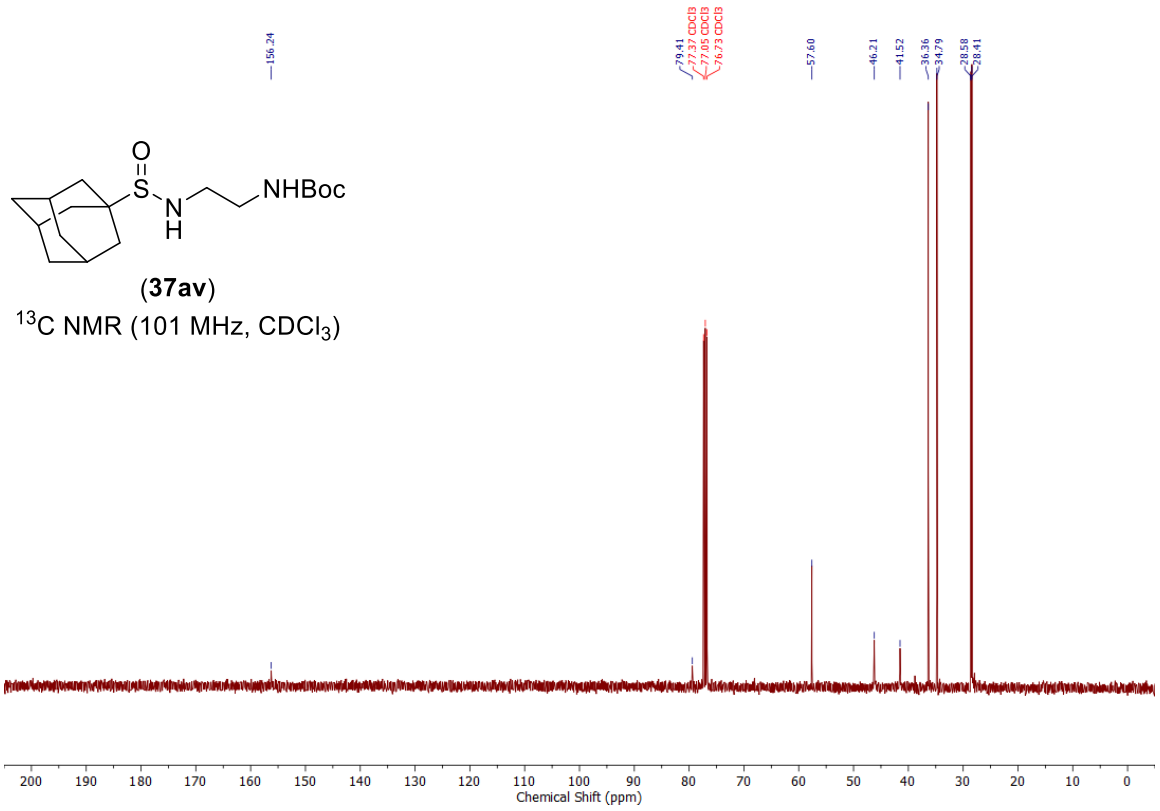
(**37au**)
^{1}H NMR (400 MHz, $CDCl_3$)



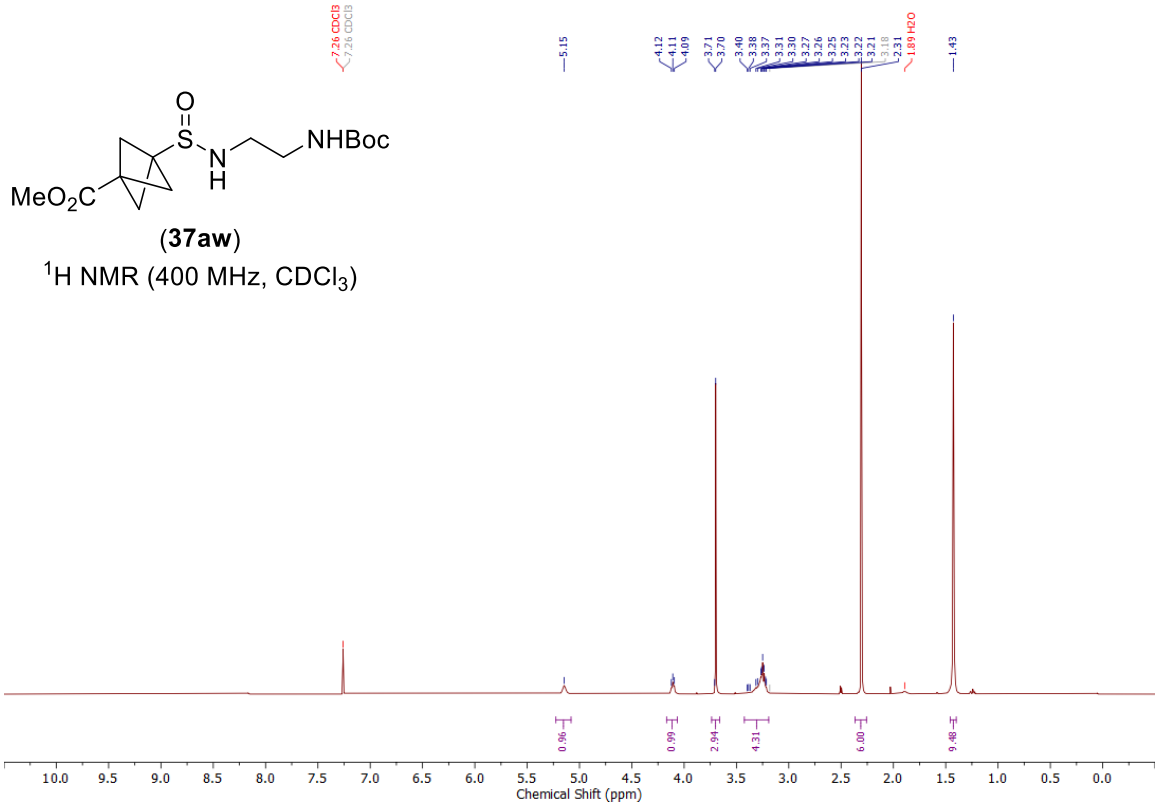
(**37au**)
^{13}C NMR (101 MHz, $CDCl_3$)

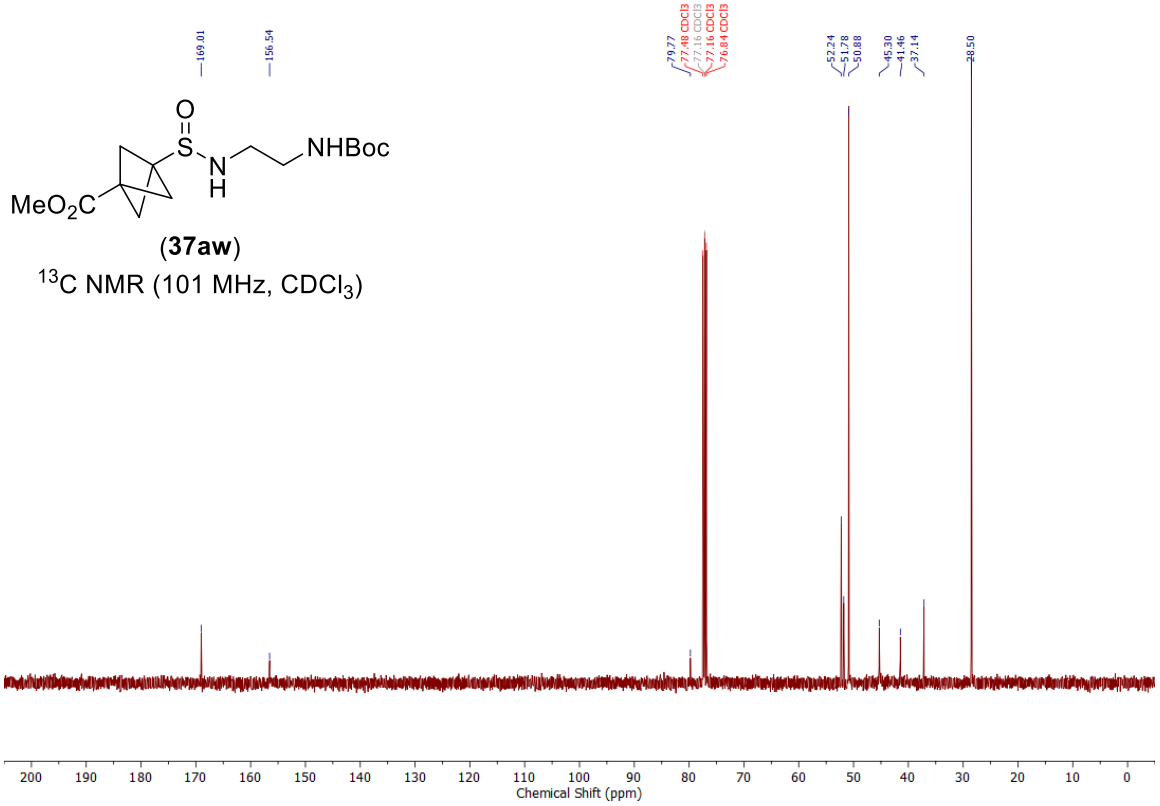
NMR spectra of *tert*-butyl (2-((((3*s*,5*s*,7*s*)-adamantan-1-yl)sulfinyl)amino)ethyl)carbamate (37av):



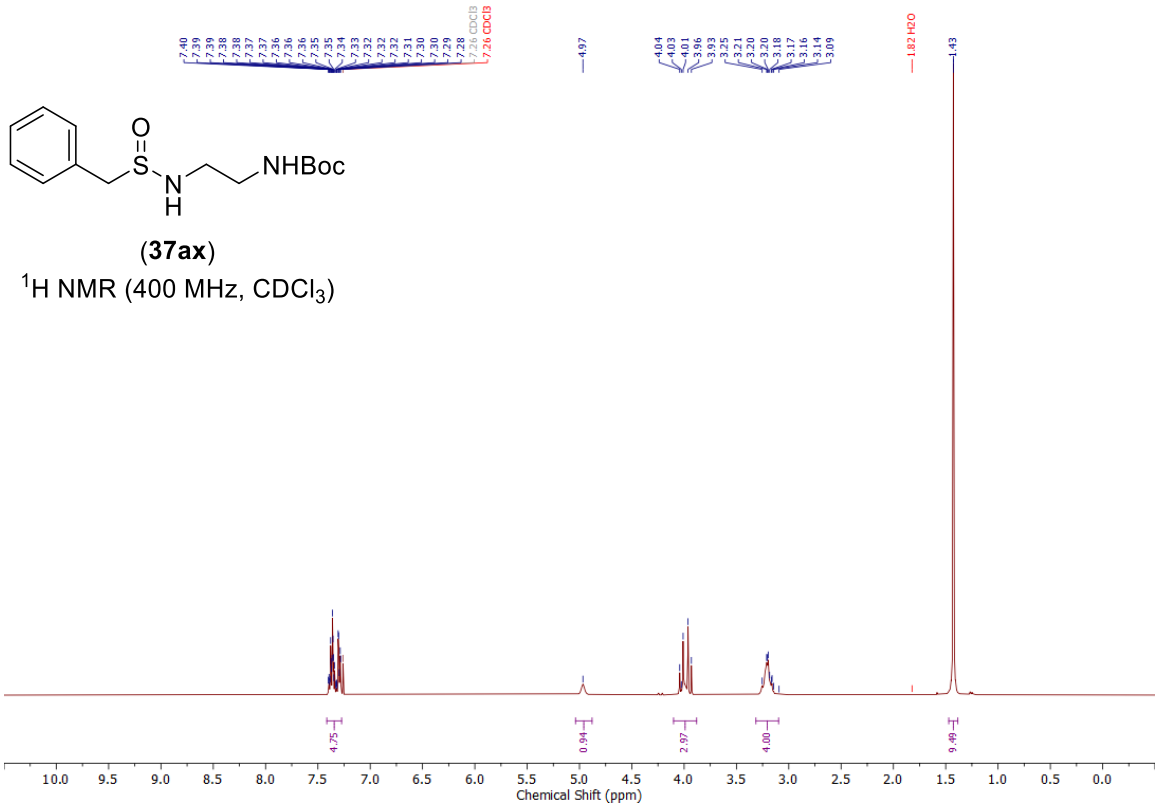


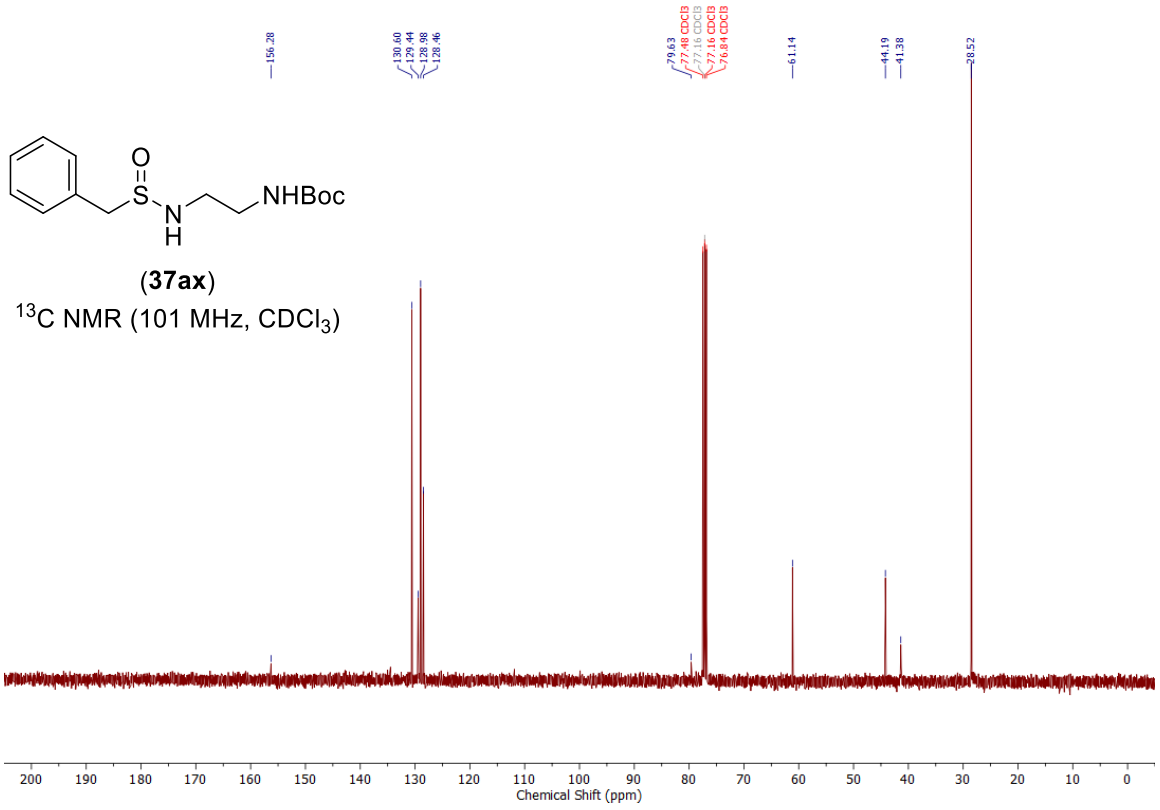
NMR spectra of methyl 3-(((2-((*tert*-butoxycarbonyl)amino)ethyl)amino)sulfinyl)bicyclo[1.1.1]pentane-1-carboxylate (37aw):



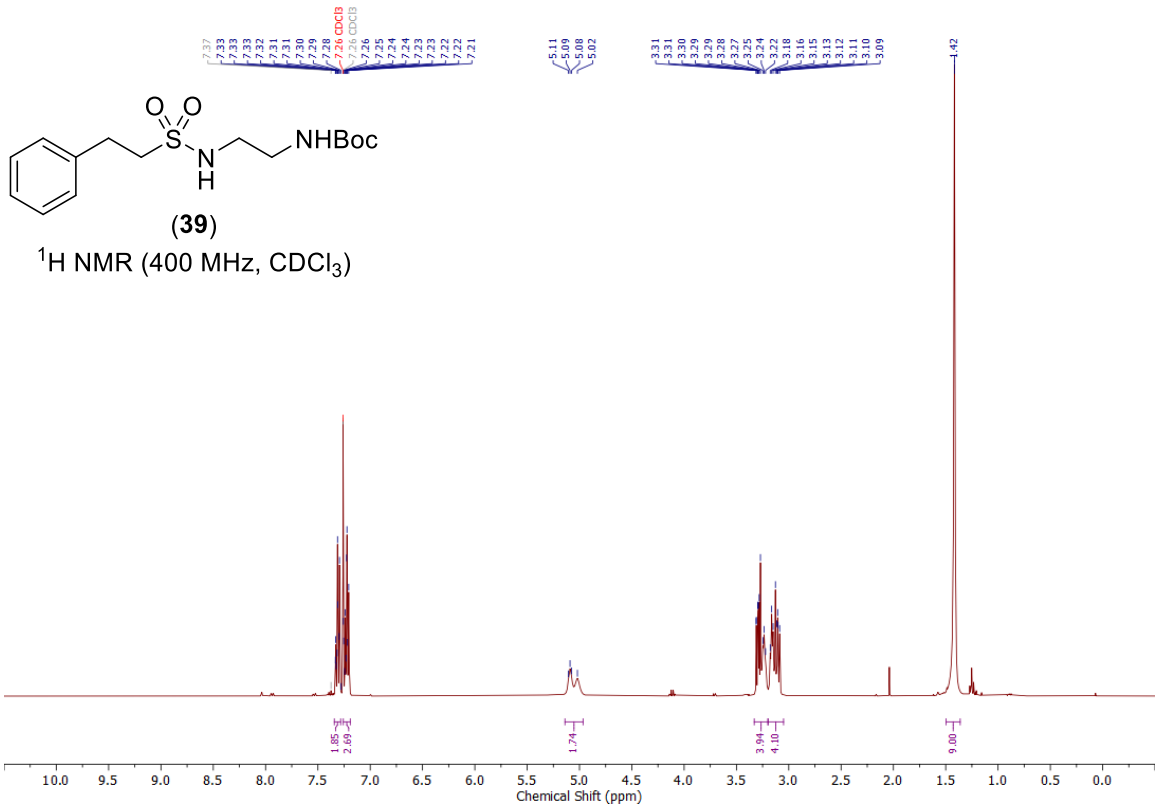


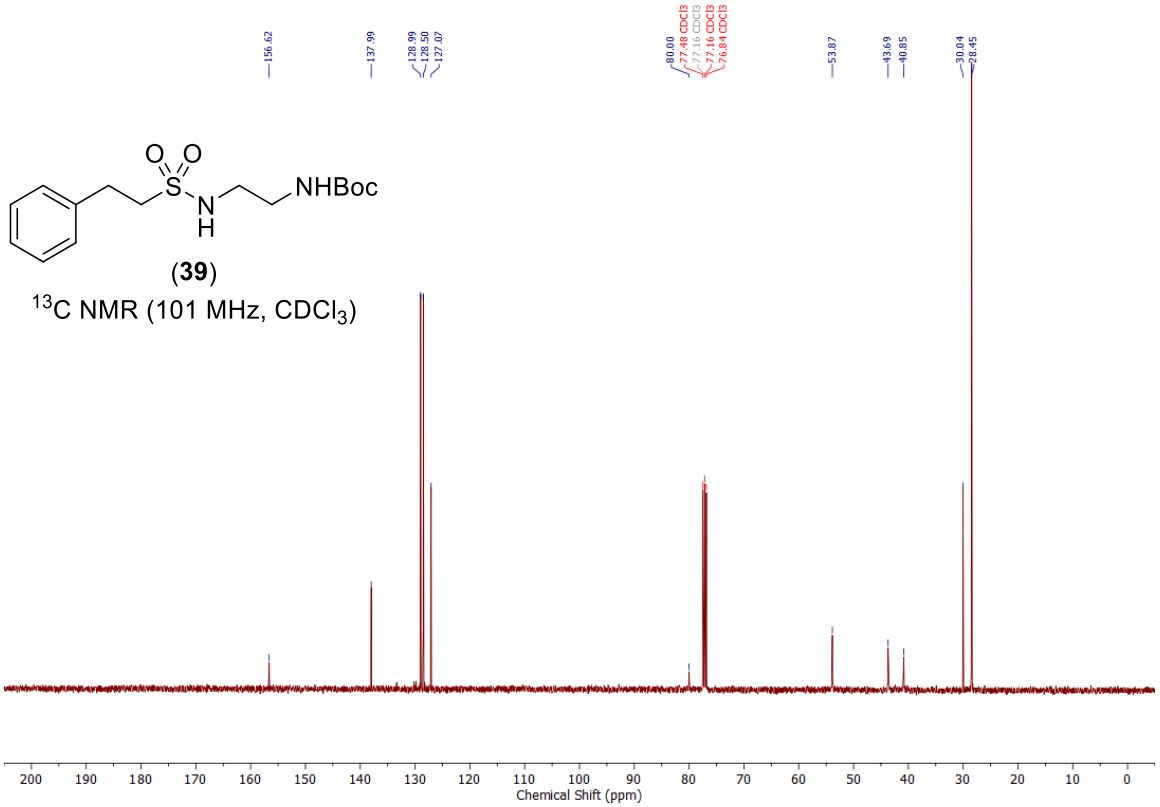
NMR spectra of *tert*-butyl (2-((benzylsulfinyl)amino)ethyl)carbamatecarbamate (37ax):



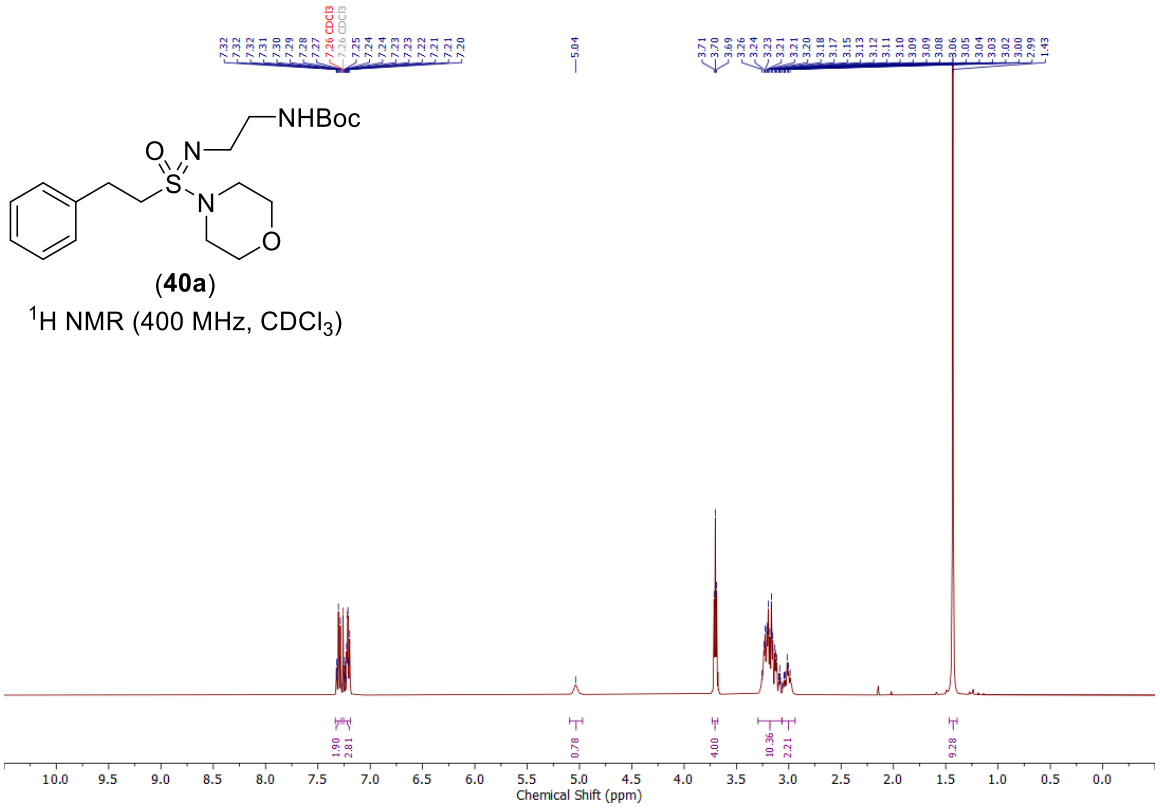


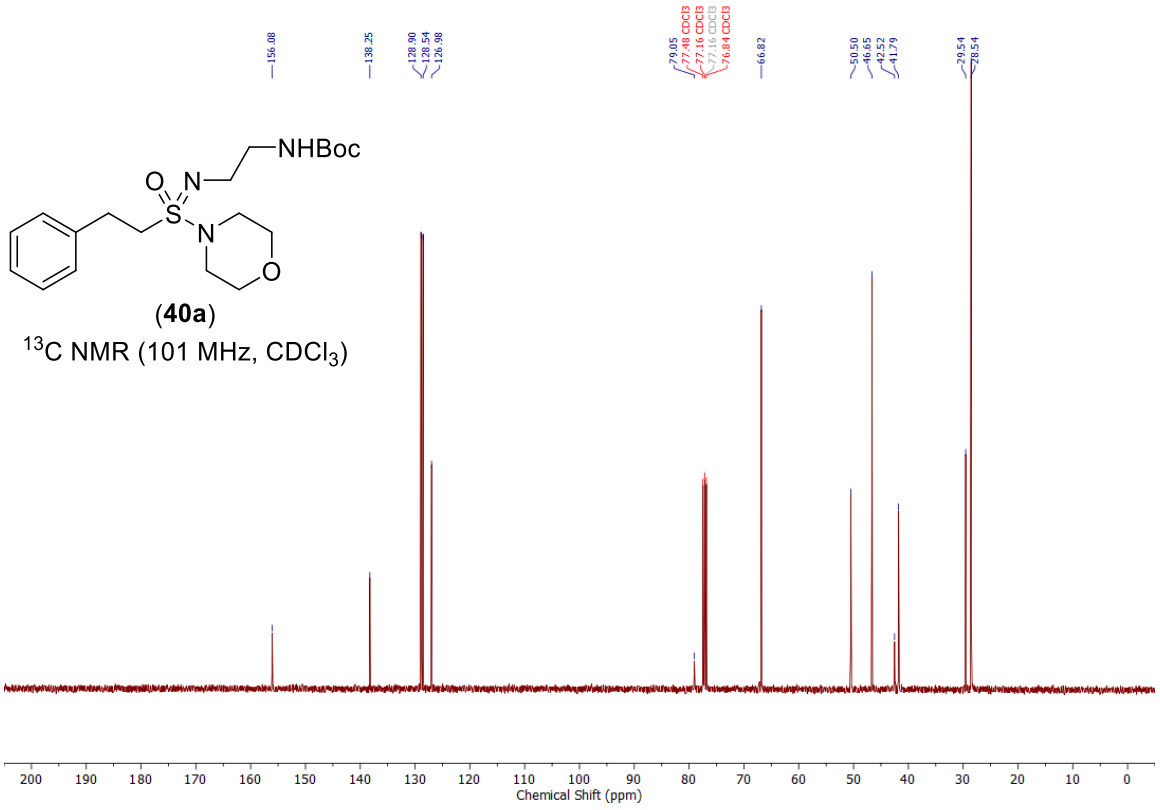
NMR spectra of *tert*-Butyl (2-((2-phenylethyl)sulfonamido)ethyl)carbamate (39):



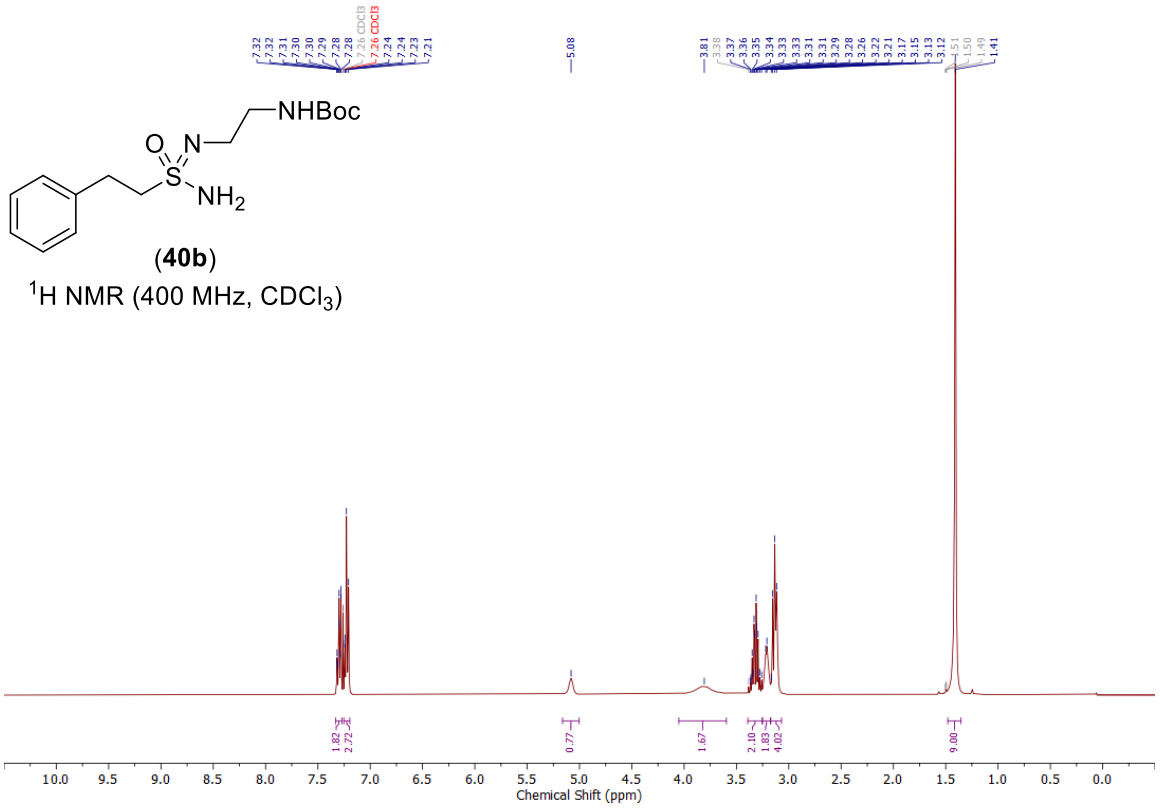


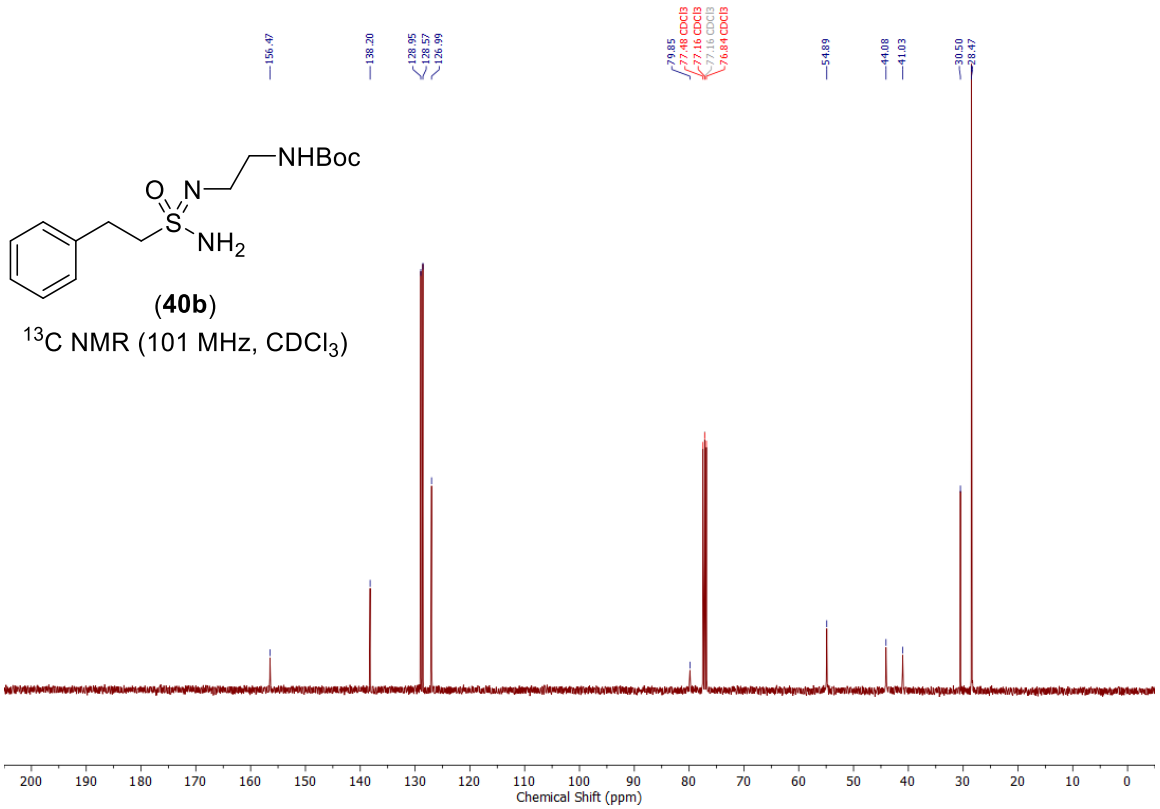
NMR spectra of *tert*-Butyl (2-((morpholino(oxo)(phenethyl)-λ^6-sulfaneylidene)amino)ethyl)carbamate (40a):



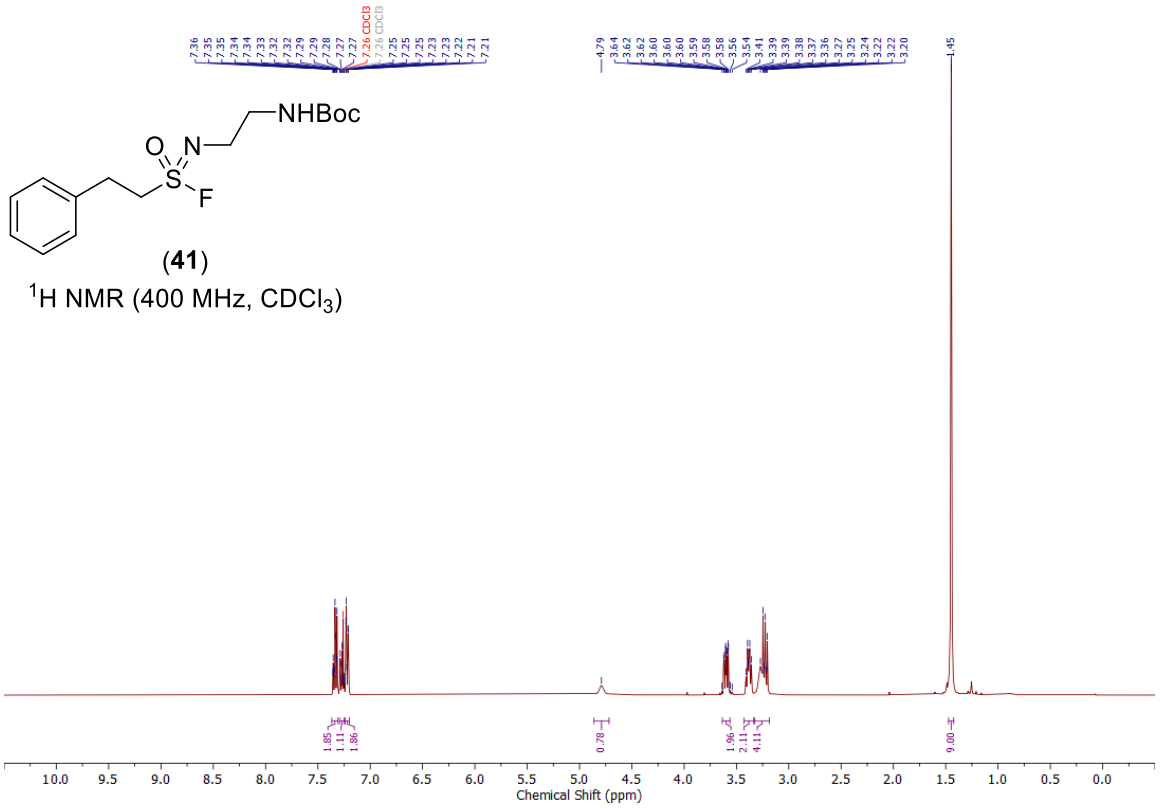


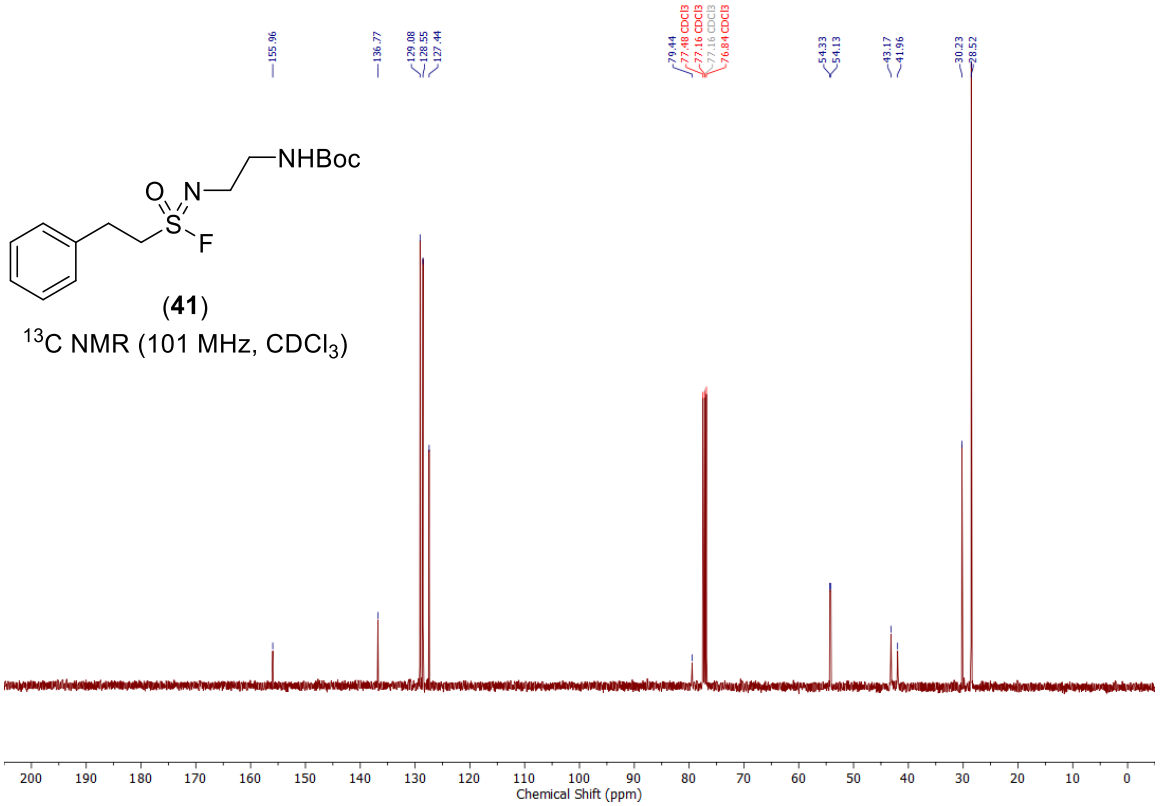
NMR spectra of *tert*-Butyl (2-((amino(oxo)(phenethyl)-λ^6-sulfaneylidene)amino)ethyl)carbamate (40b):

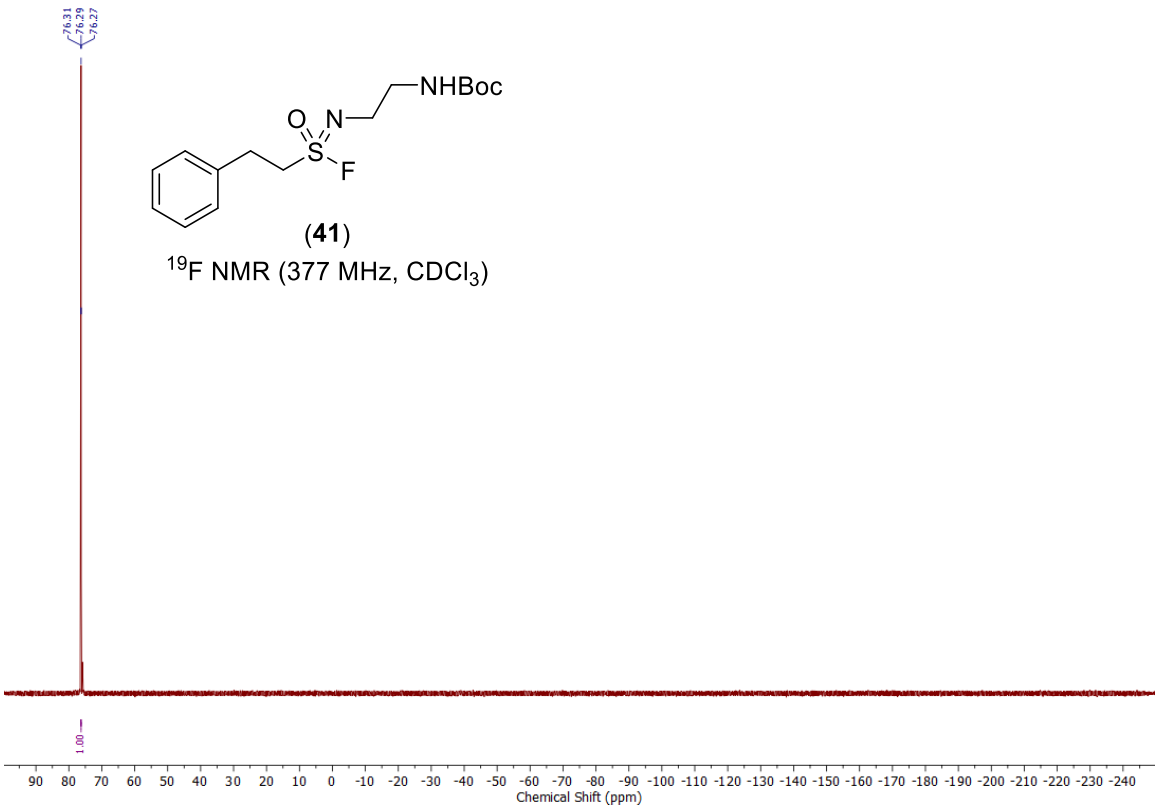




NMR spectra of *tert*-Butyl (2-((fluoro(oxo)(phenethyl)-λ^6-sulfaneylidene)amino)ethyl)carbamate (41):



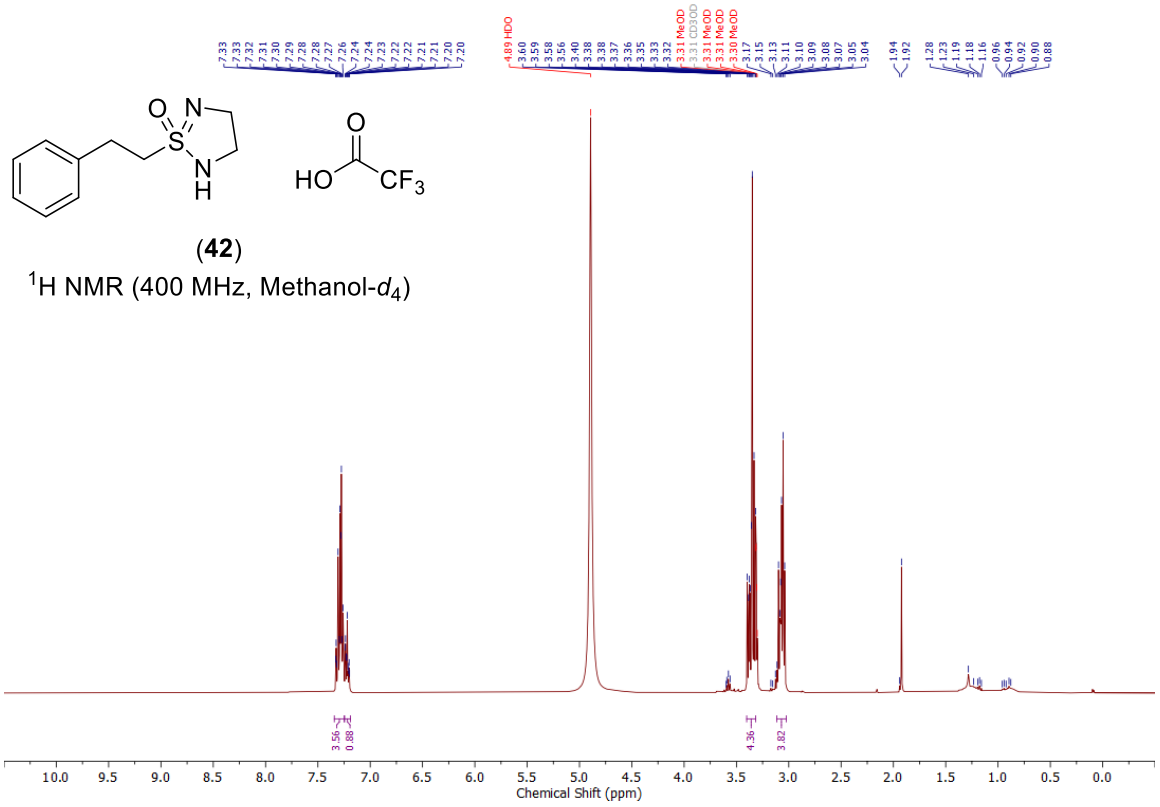


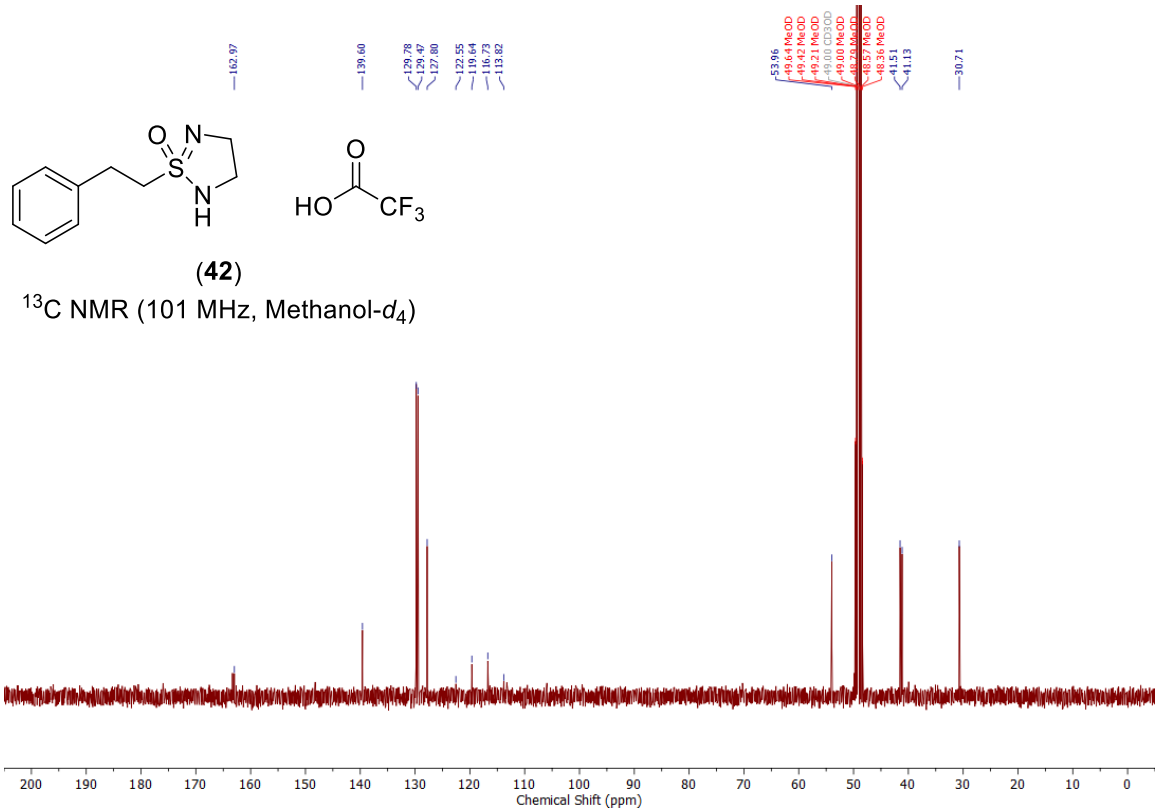


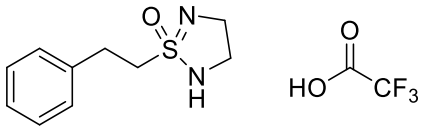
(**41**)

^{19}F NMR (377 MHz, $CDCl_3$)

NMR spectra of 1-phenethyl-3,4-dihydro-2*H*-1λ^6,2,5-thiadiazole 1-oxide trifluoroacetic acid salt (42):





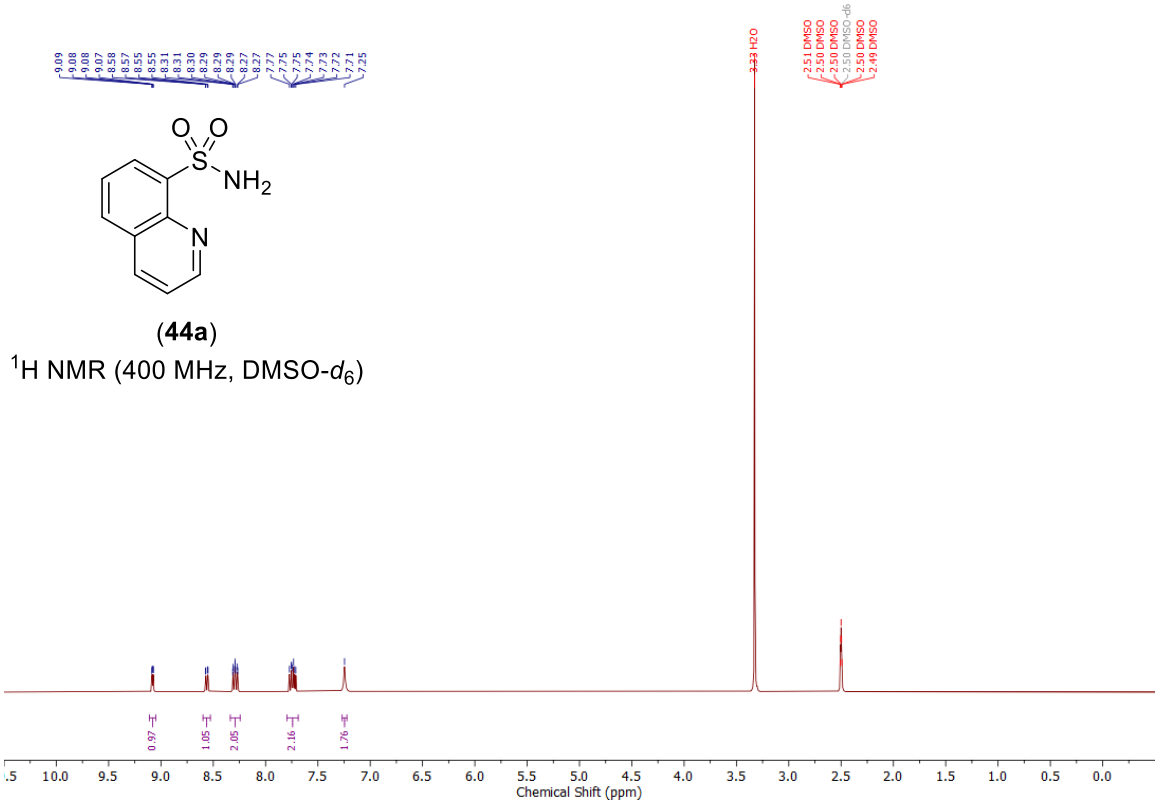


(**42**)

^{19}F NMR (377 MHz, Methanol-d_4)

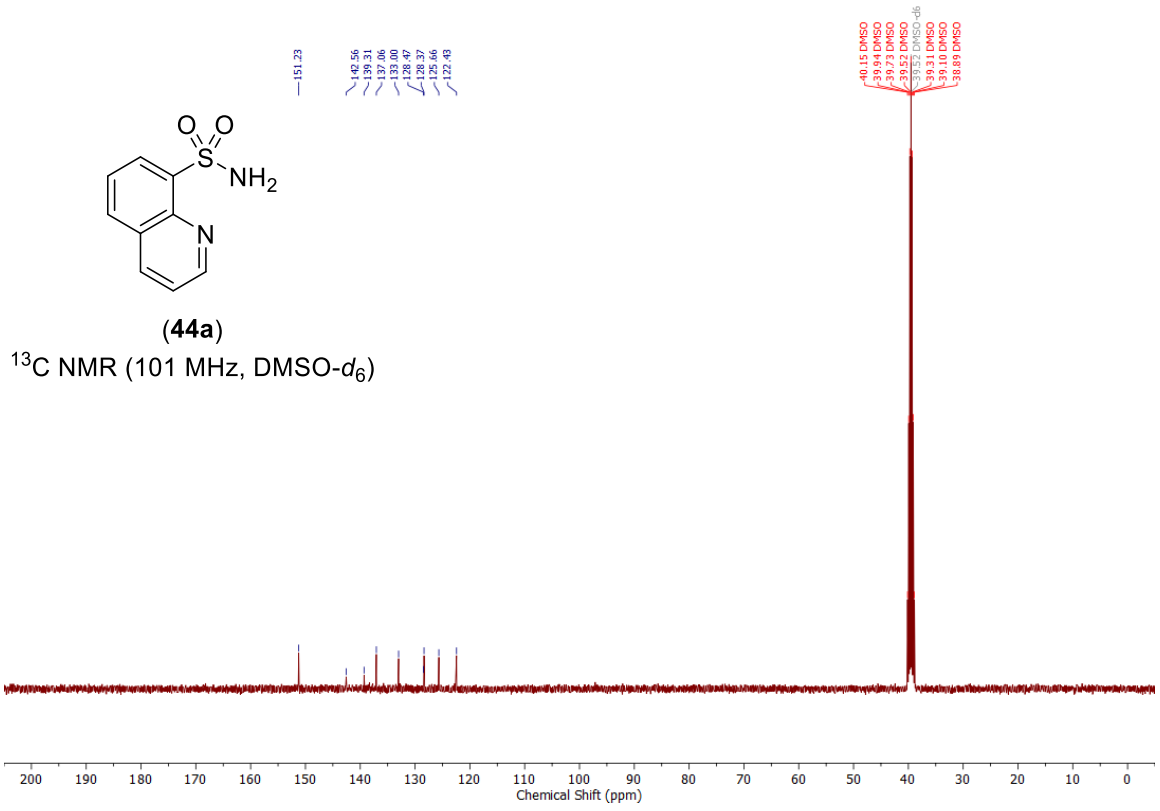
10.5 NMR Spectra for Chapter 5

NMR spectra of quinoline-8-sulfonamide (44a):



(**44a**)

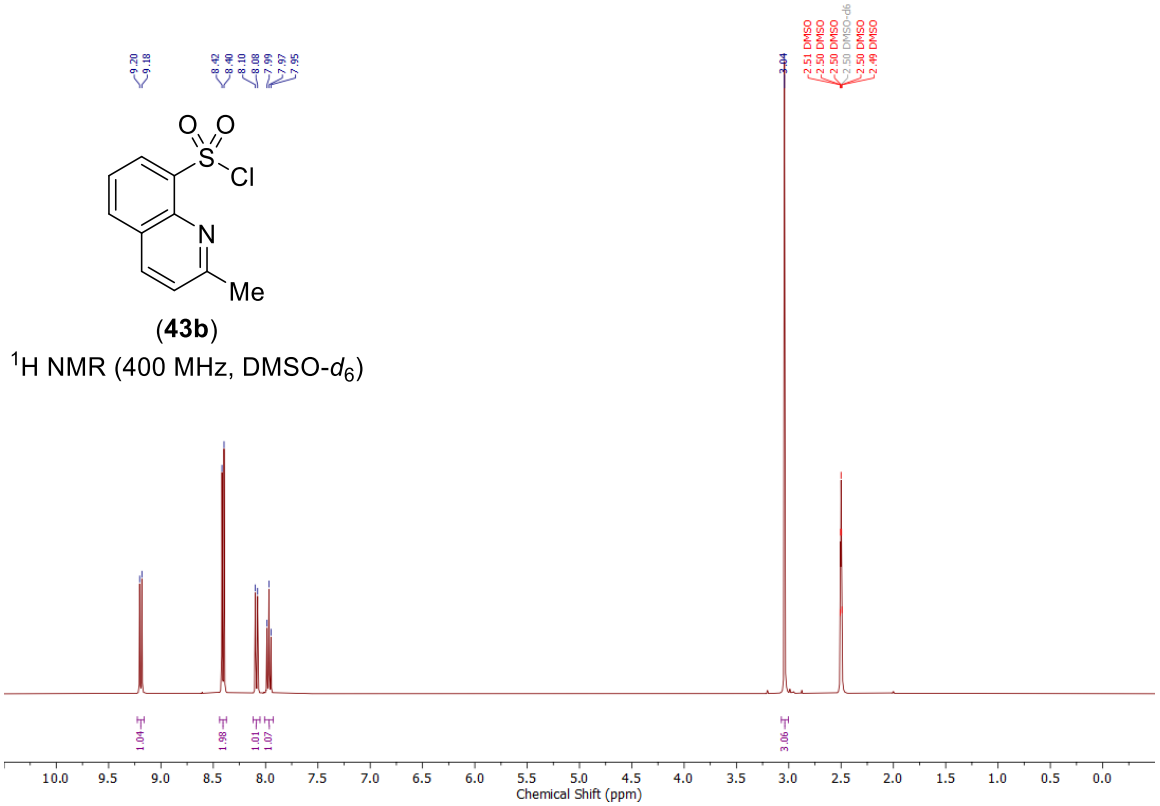
^{1}H NMR (400 MHz, DMSO-d_6)



(**44a**)

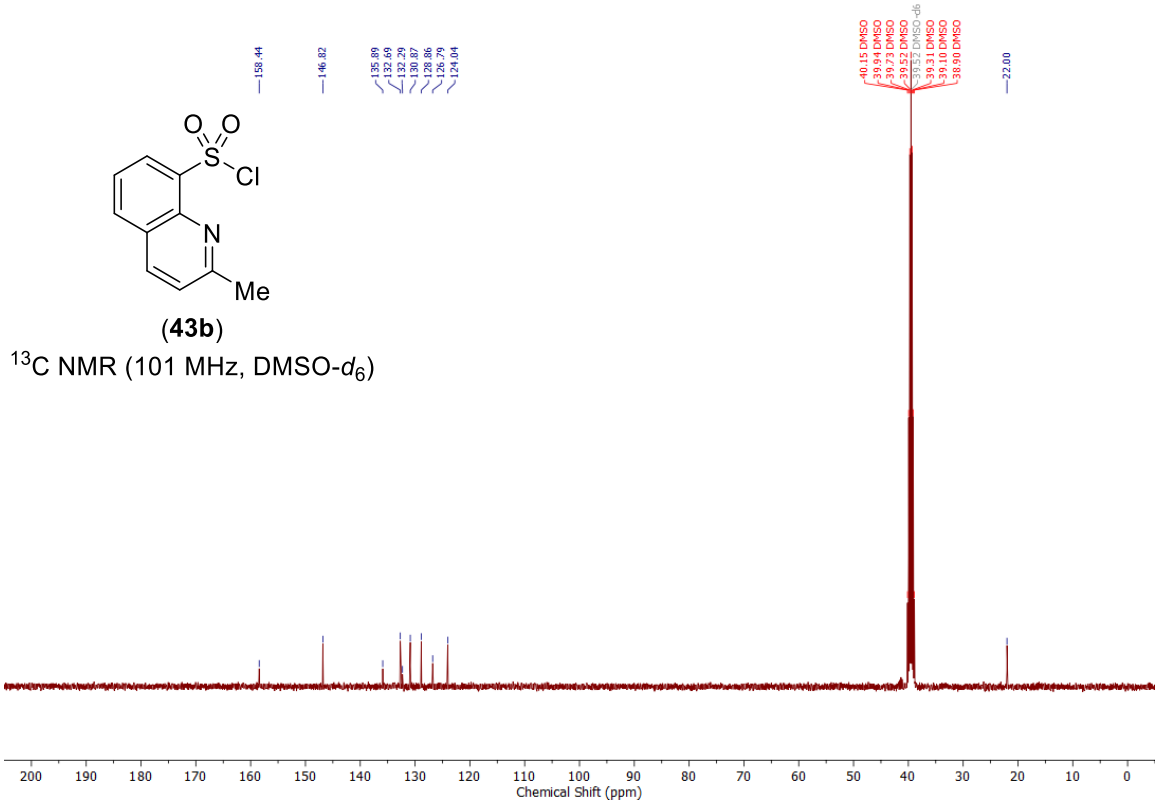
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of 2-methylquinoline-8-sulfonyl chloride (43b):



(**43b**)

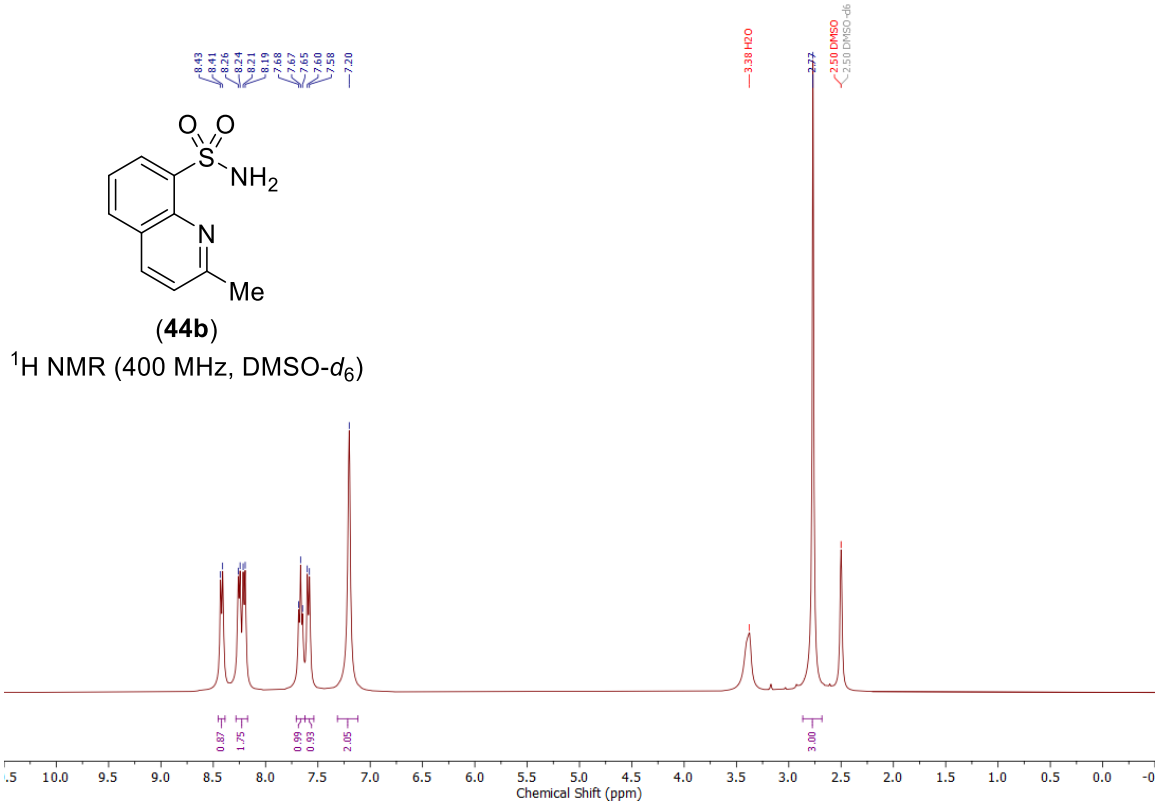
^{1}H NMR (400 MHz, DMSO-d_6)



(**43b**)

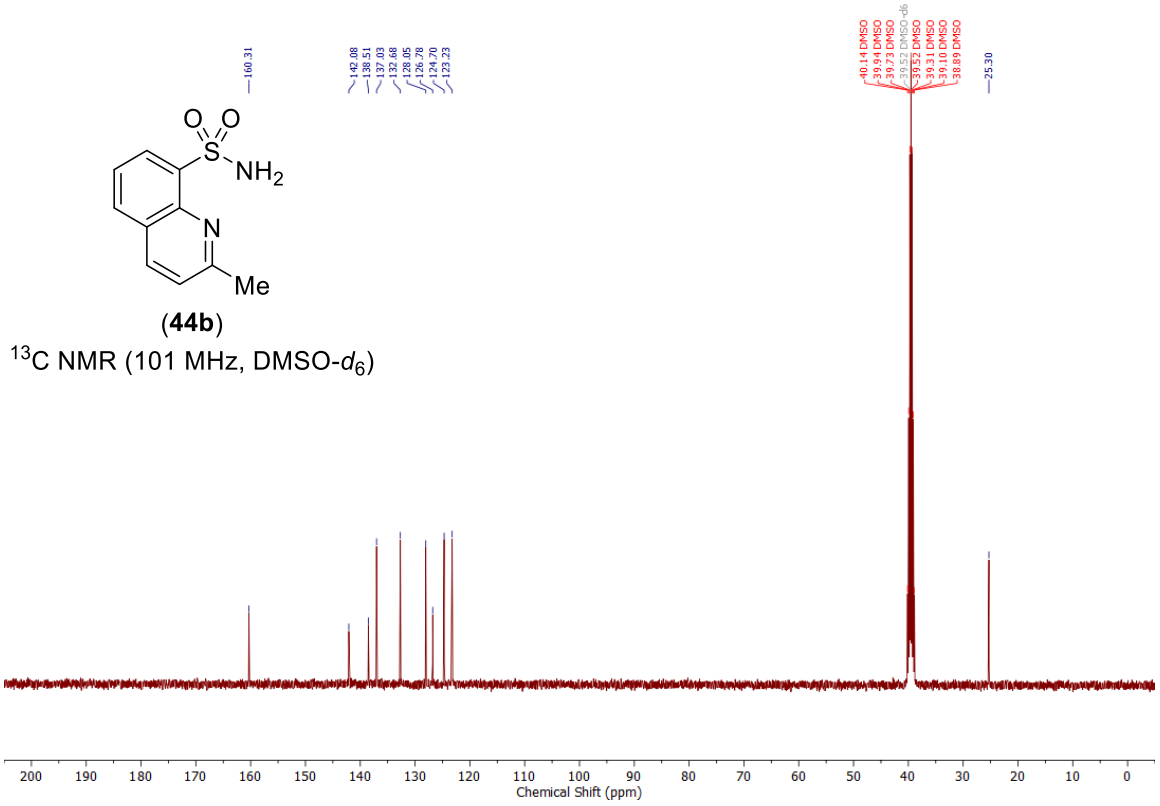
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of 2-methylquinoline-8-sulfonamide (44b):



(**44b**)

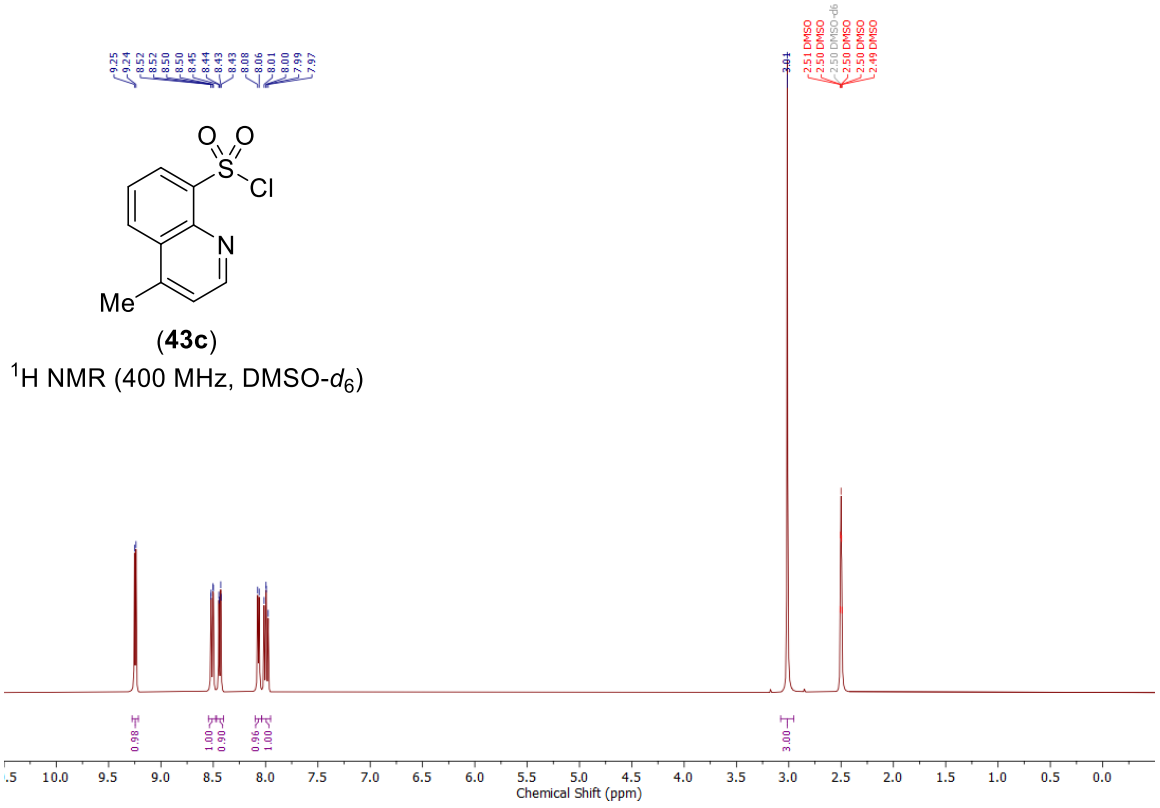
^{1}H NMR (400 MHz, DMSO-d_6)



(**44b**)

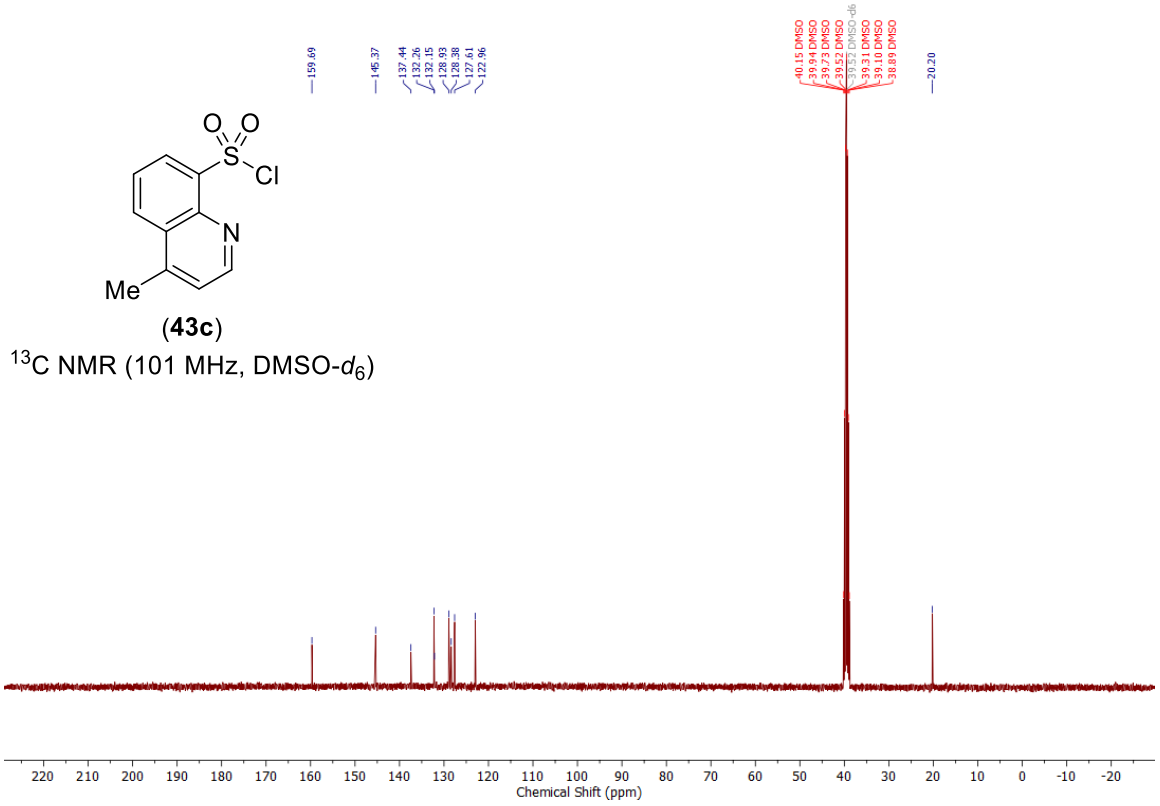
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of 4-methylquinoline-8-sulfonyl chloride (43c):



(**43c**)

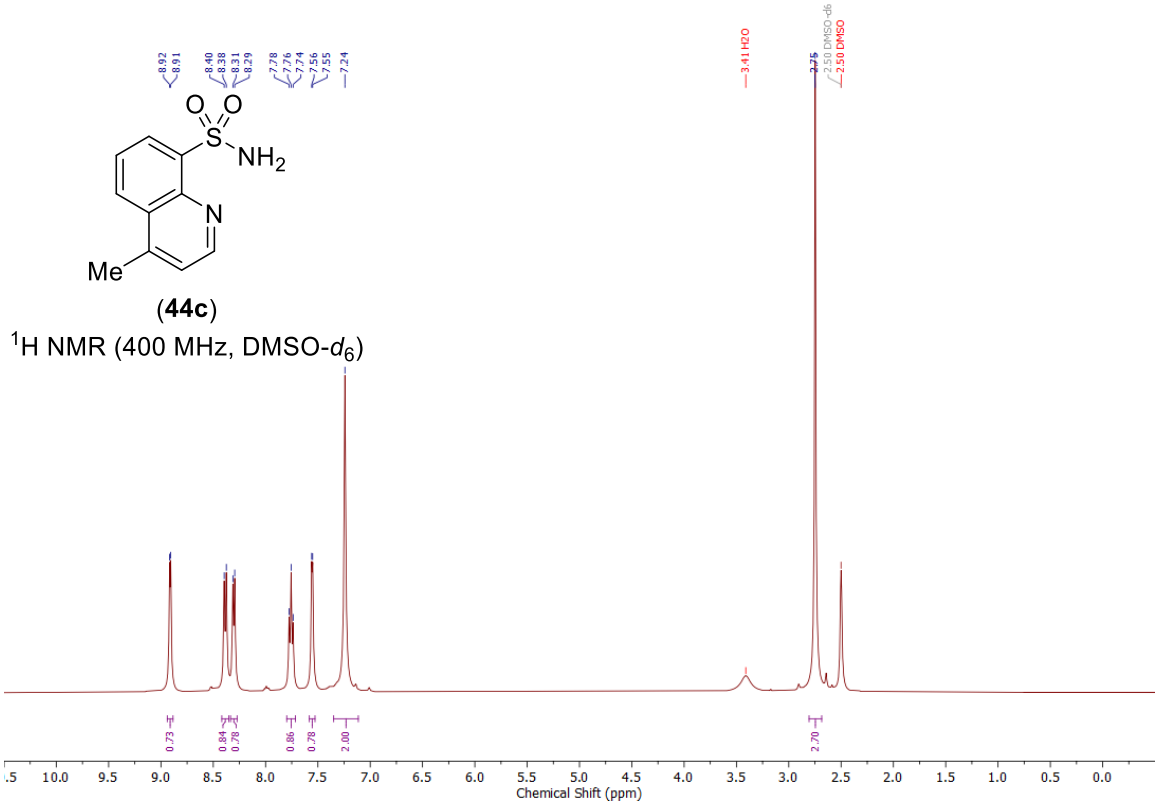
^{1}H NMR (400 MHz, DMSO-d_6)



(**43c**)

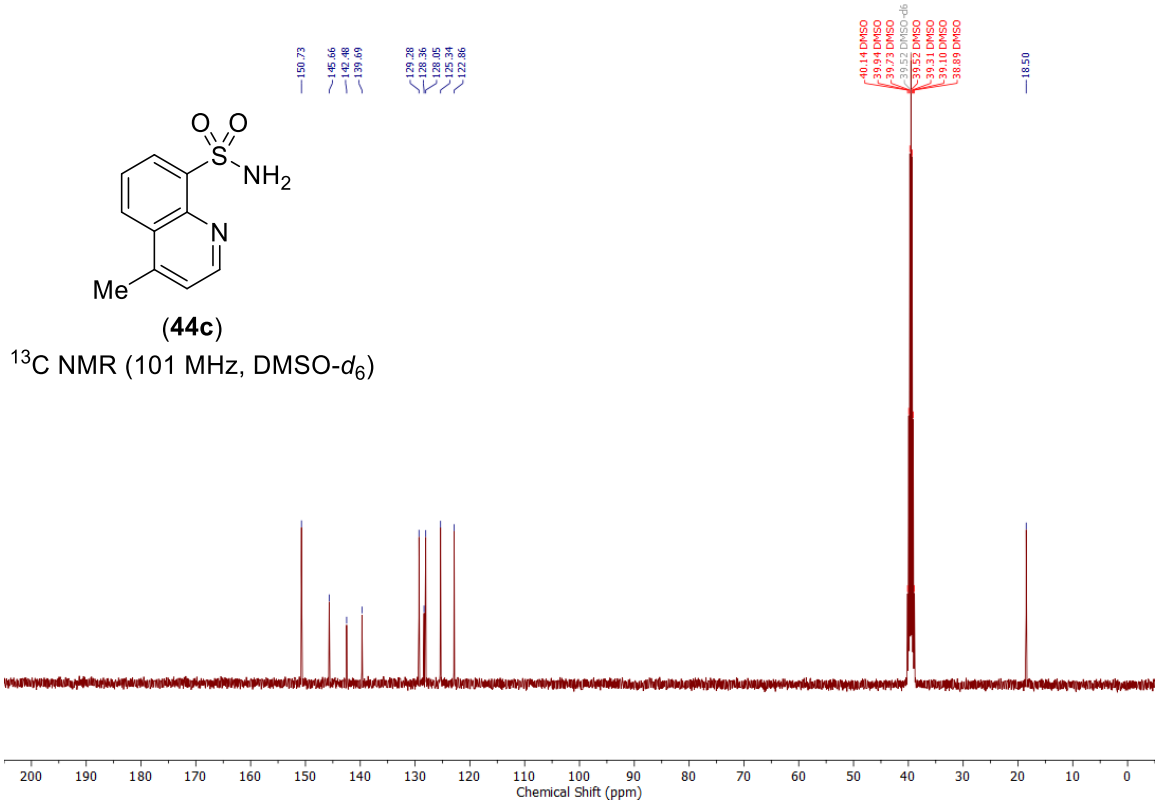
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of 4-methylquinoline-8-sulfonamide (44c):



(**44c**)

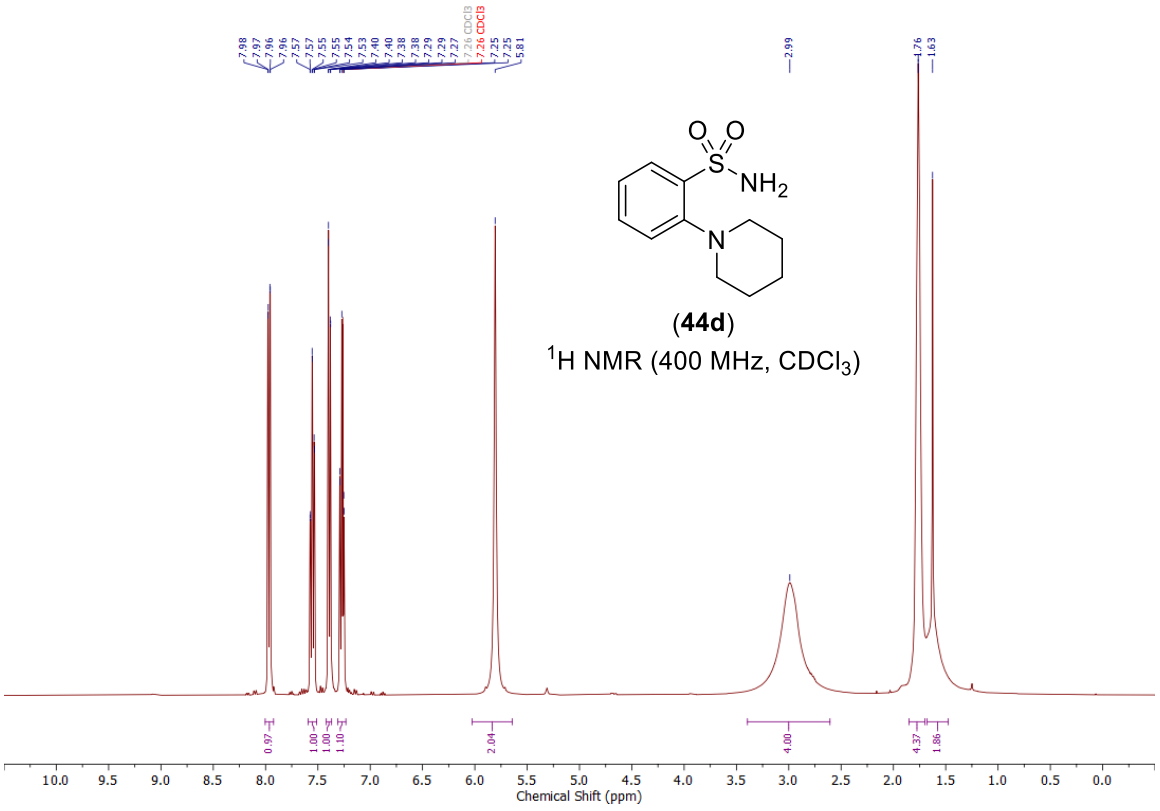
^{1}H NMR (400 MHz, DMSO-d_6)

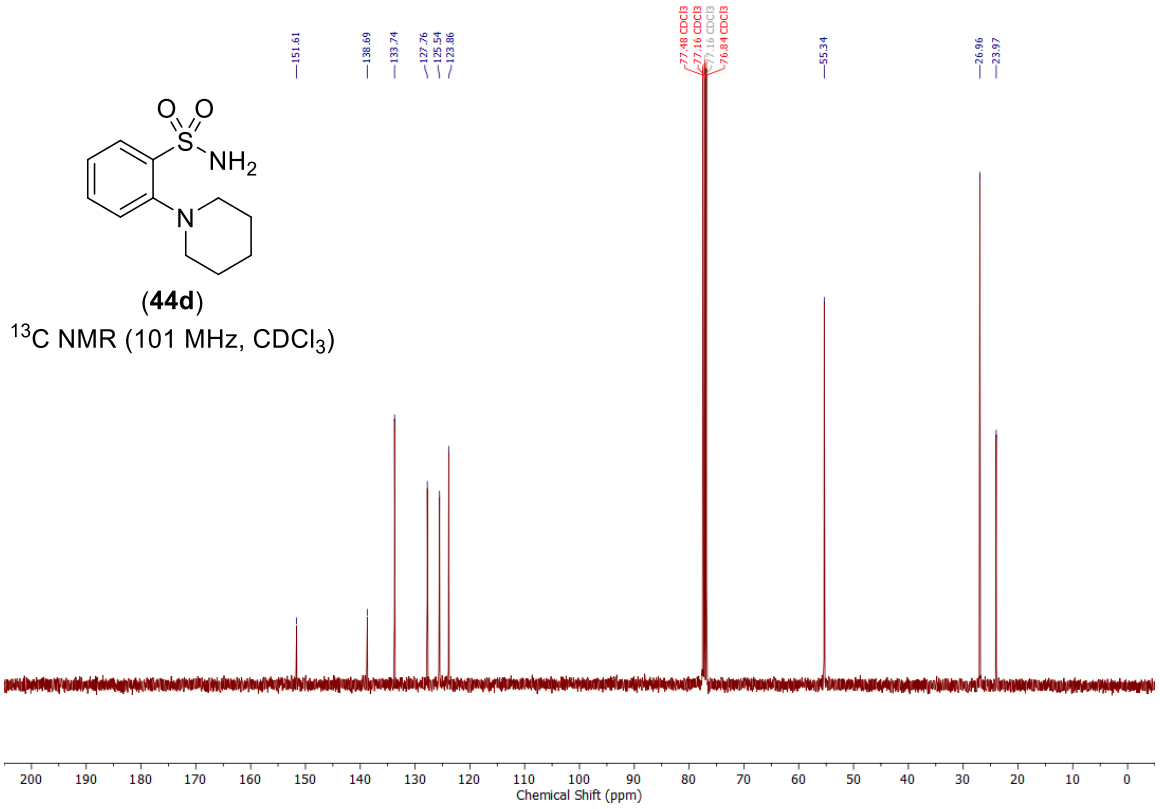


(**44c**)

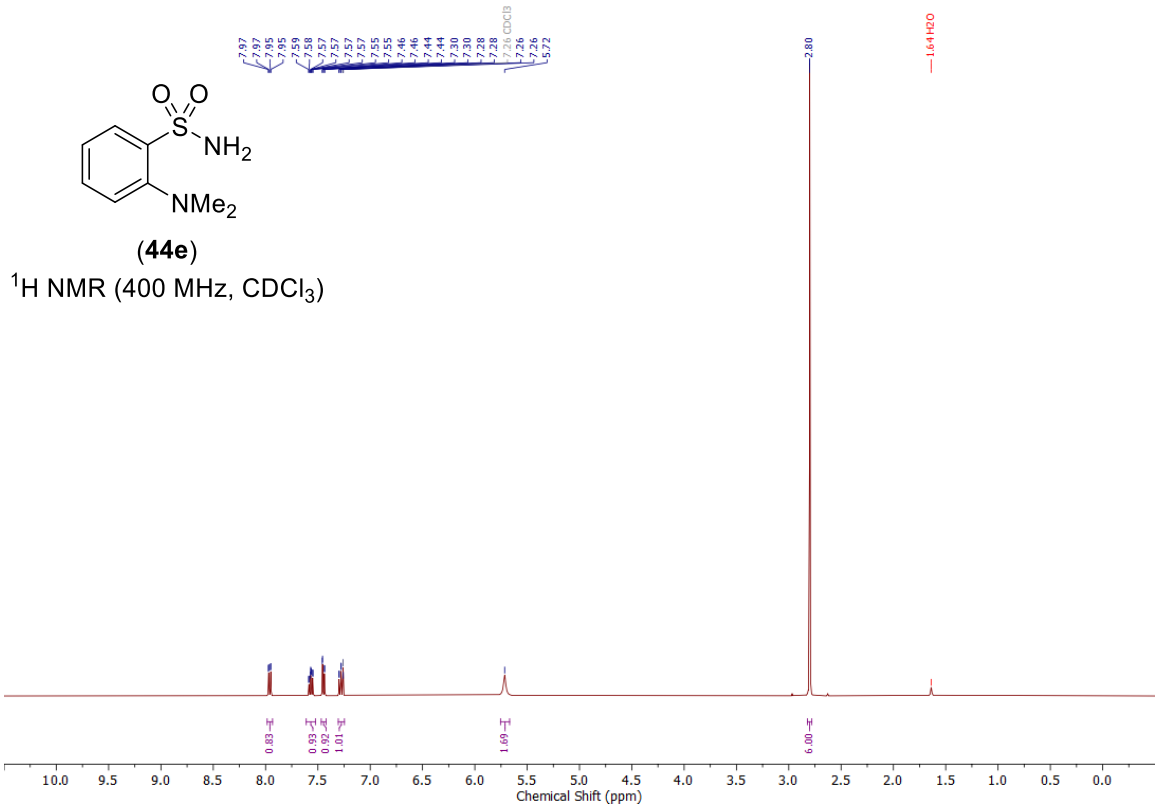
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of 2-(piperidin-1-yl)benzenesulfonamide (44d):



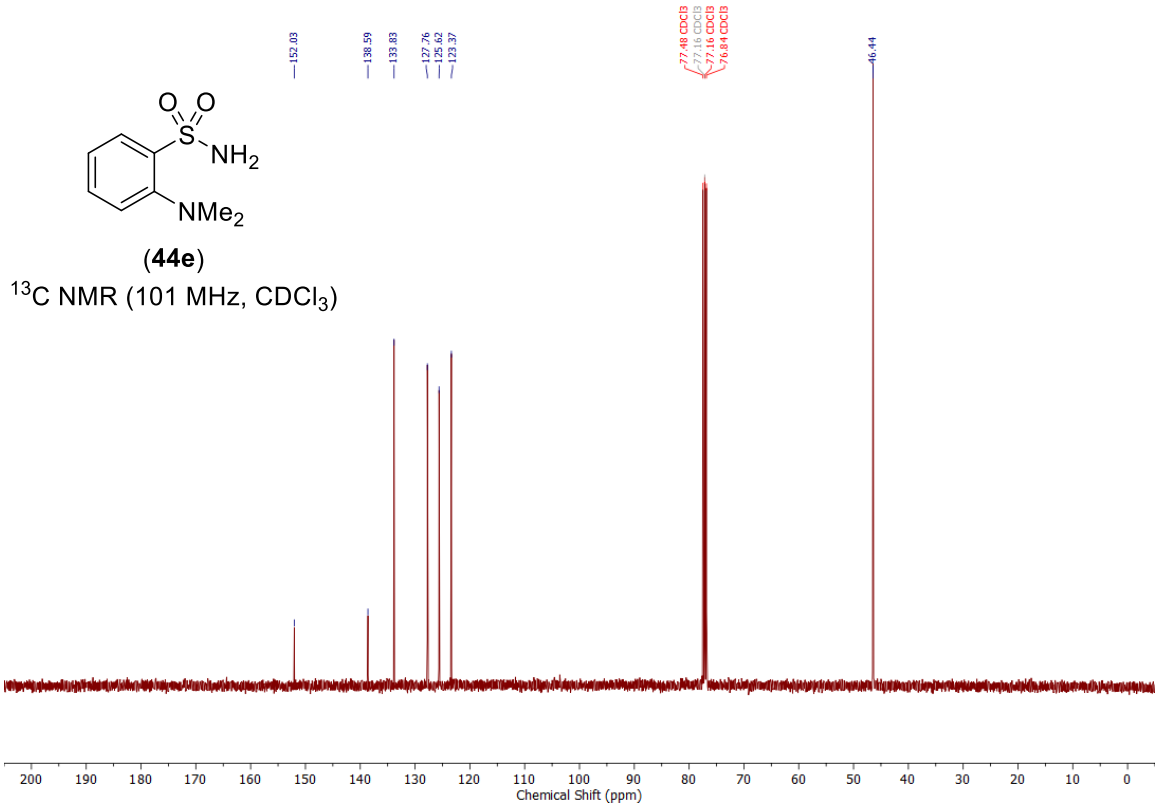


NMR spectra of 2-(dimethylamino)benzenesulfonamide (44e):



(**44e**)

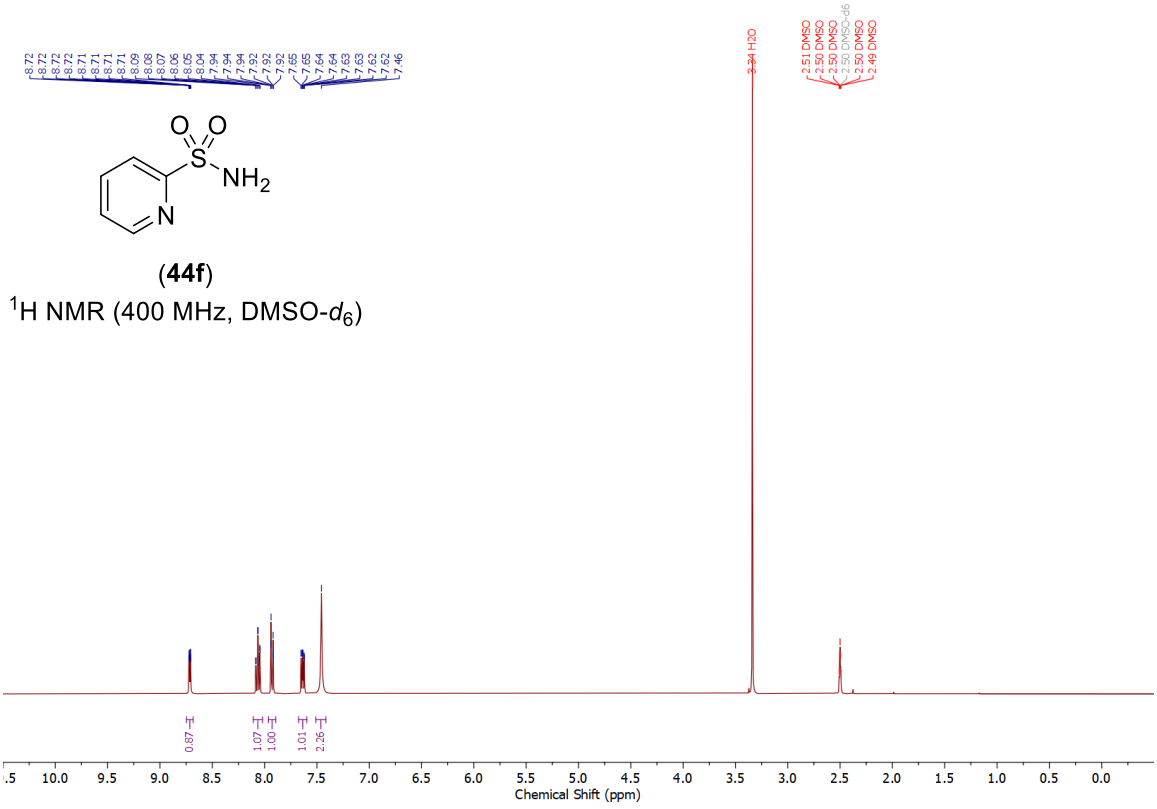
^{1}H NMR (400 MHz, $CDCl_3$)



(**44e**)

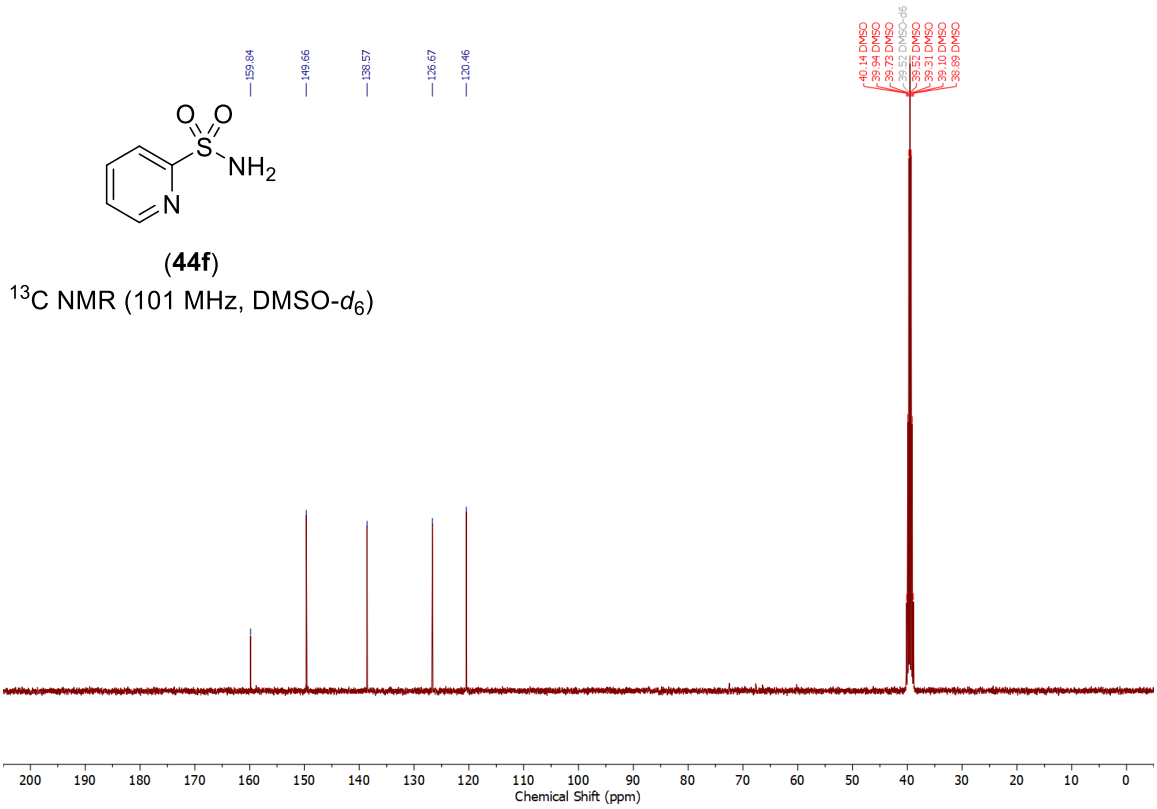
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of pyridine-2-sulfonamide (44f):



(**44f**)

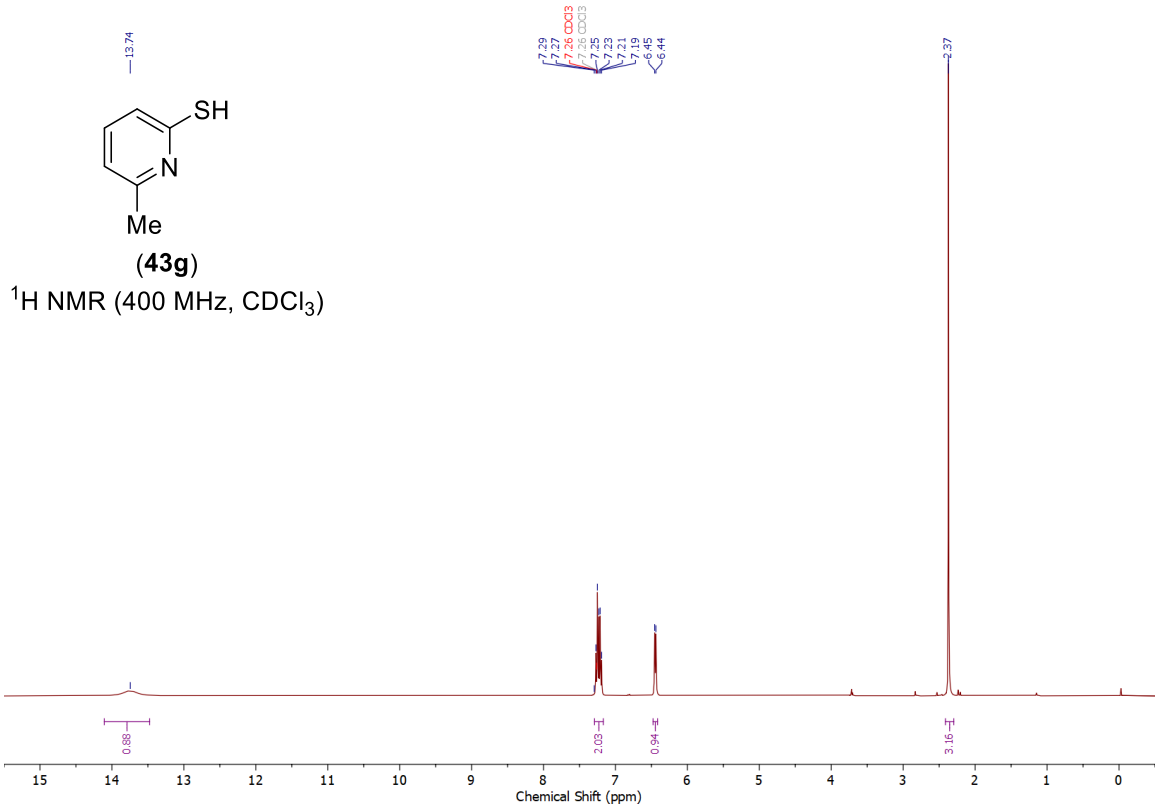
^{1}H NMR (400 MHz, DMSO-d_6)



(**44f**)

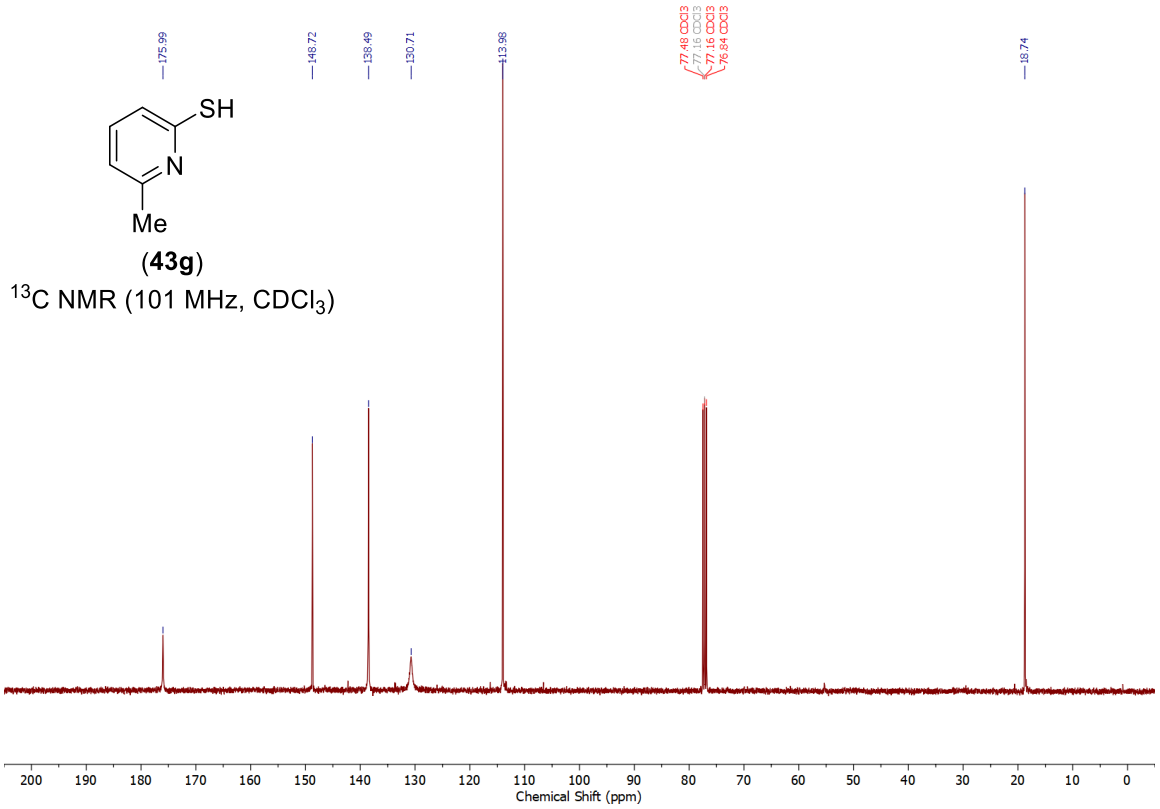
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of 6-methylpyridine-2-thiol (43g):



(**43g**)

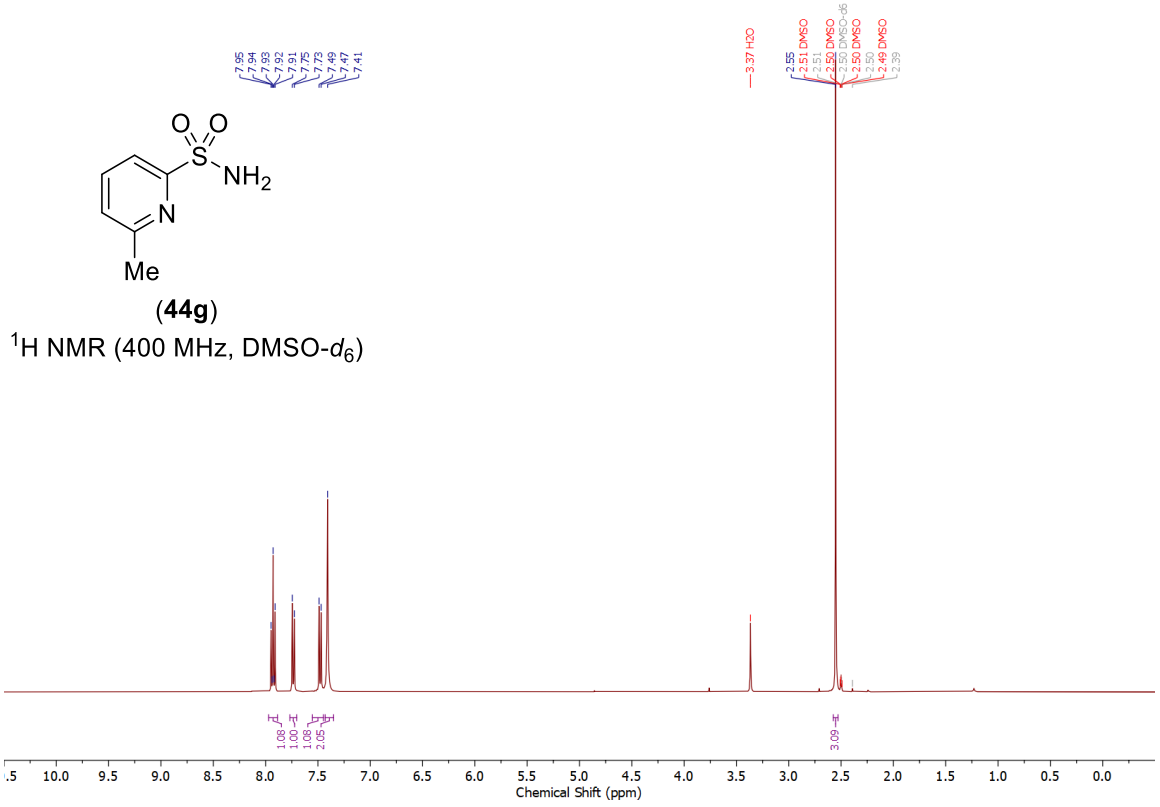
^{1}H NMR (400 MHz, $CDCl_3$)



(**43g**)

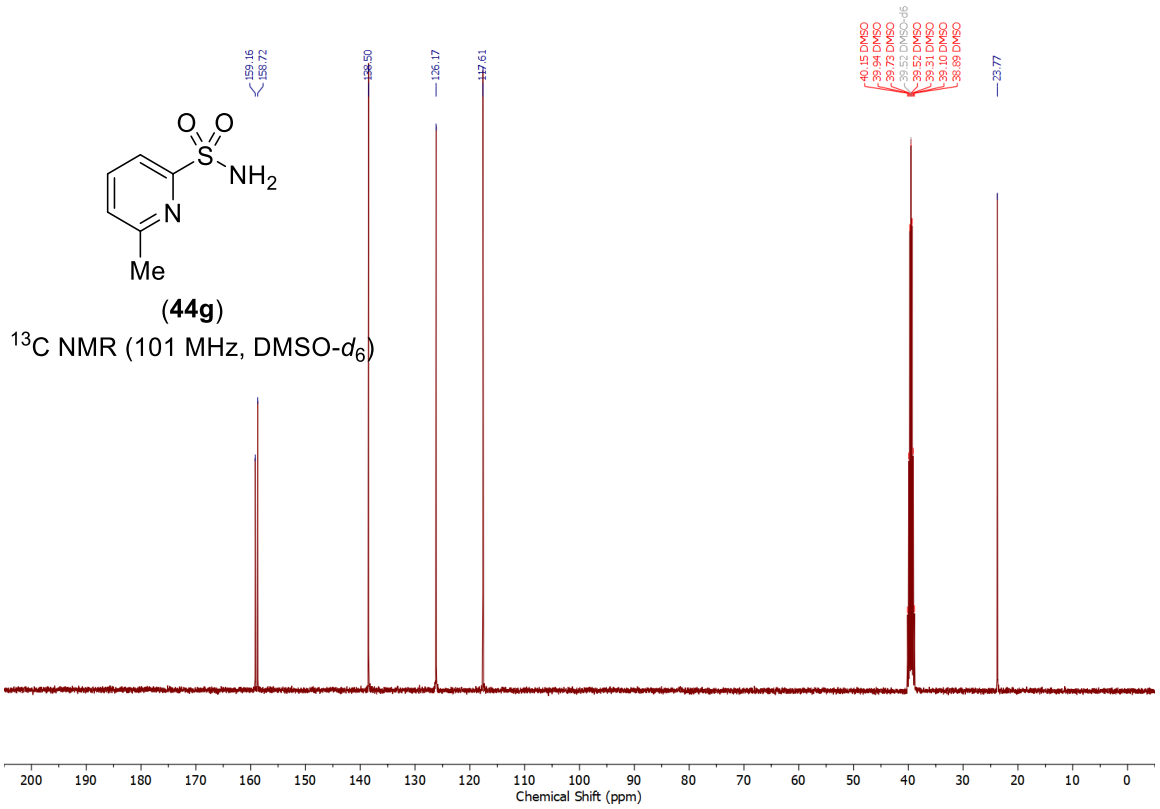
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of 6-methylpyridine-2-sulfonamide (44g):



(**44g**)

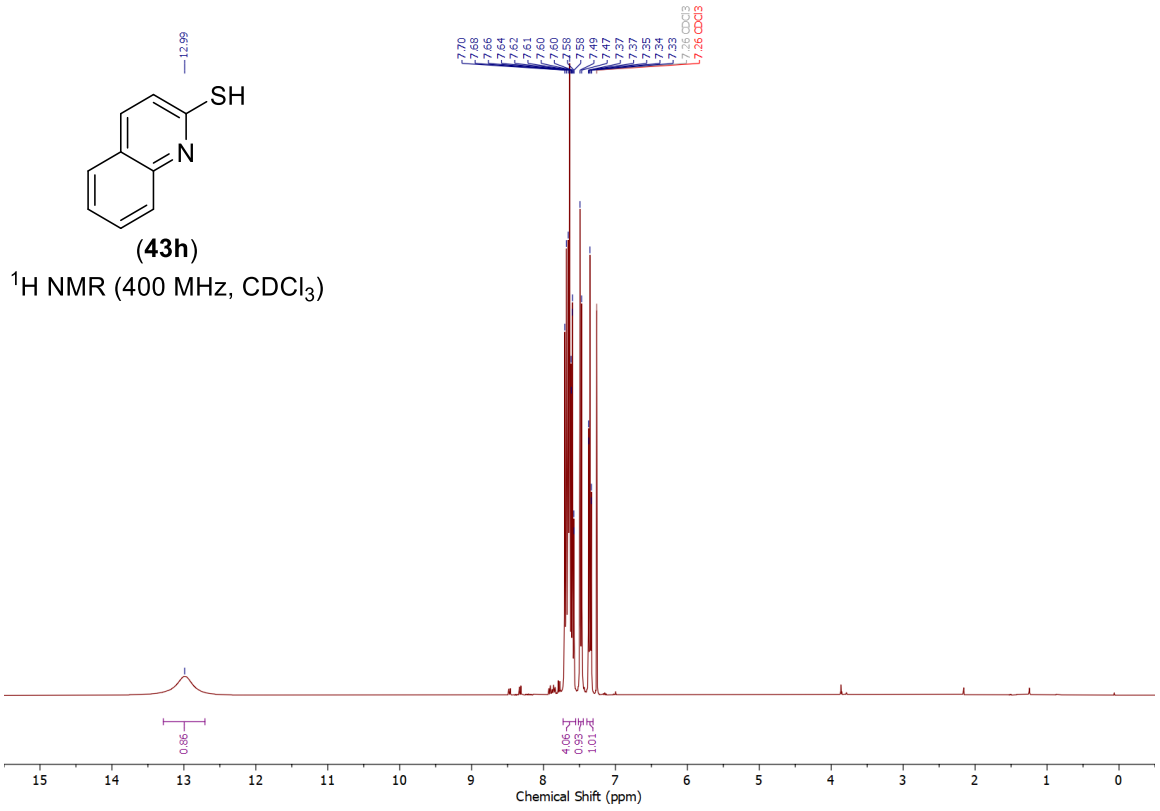
^{1}H NMR (400 MHz, DMSO-d_6)



(**44g**)

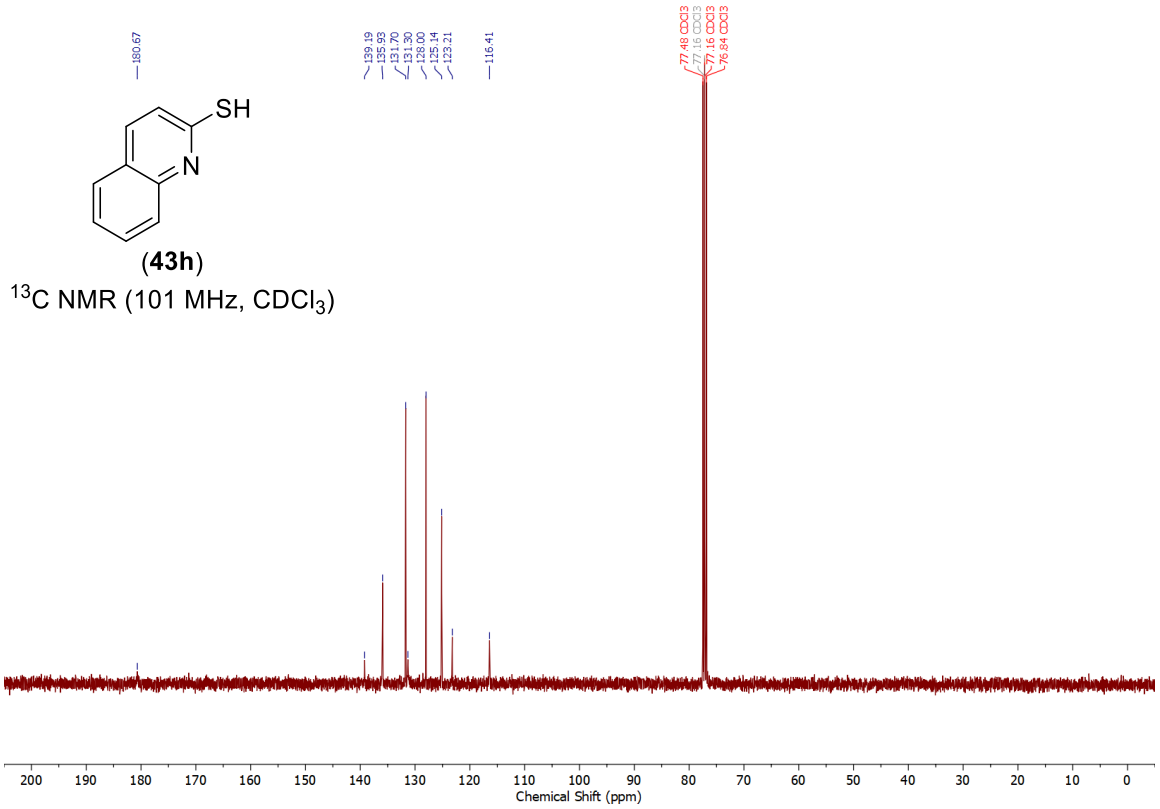
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of quinoline-2-thiol (43h):



(**43h**)

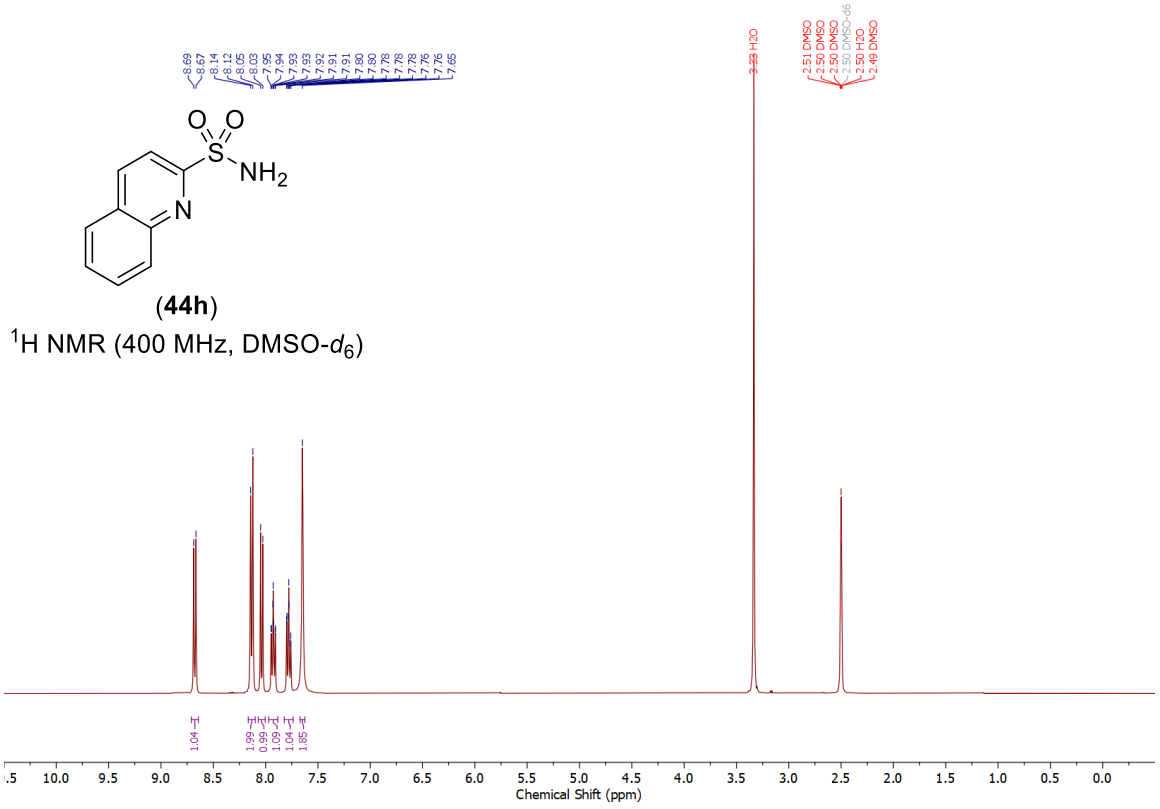
^{1}H NMR (400 MHz, $CDCl_3$)



(**43h**)

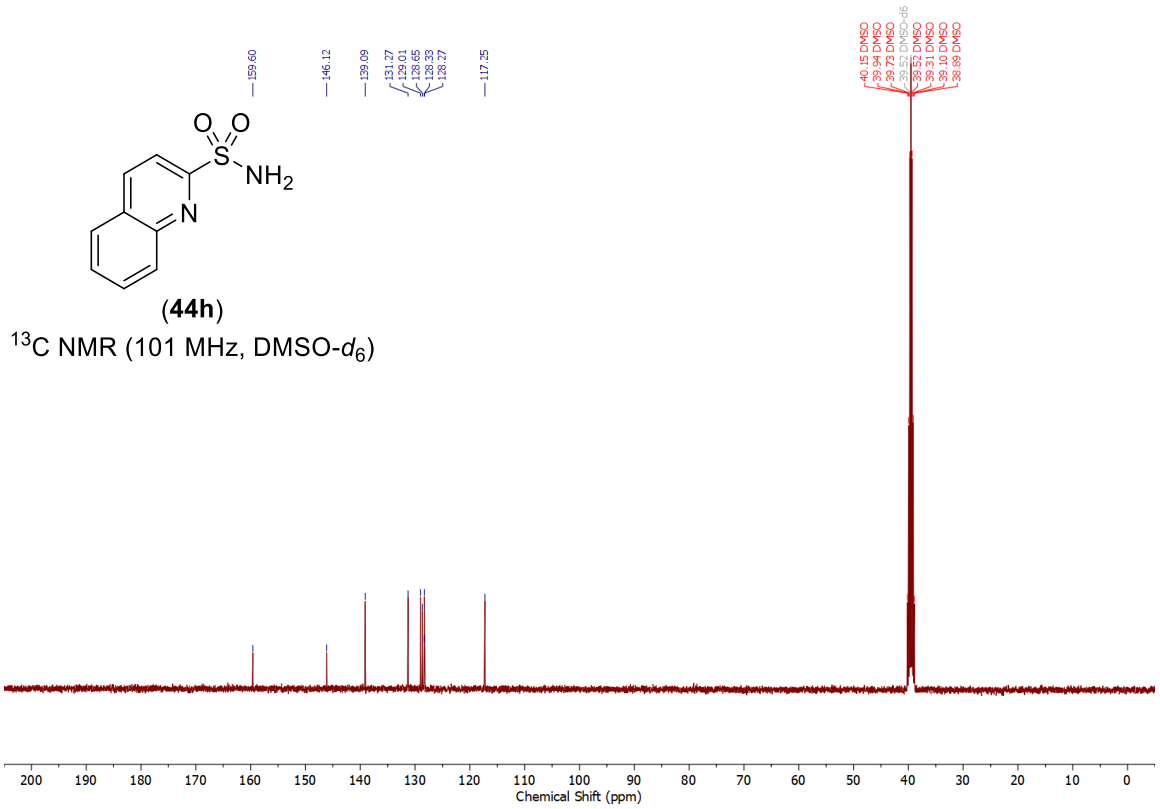
^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of quinoline-2-sulfonamide (44h):



(**44h**)

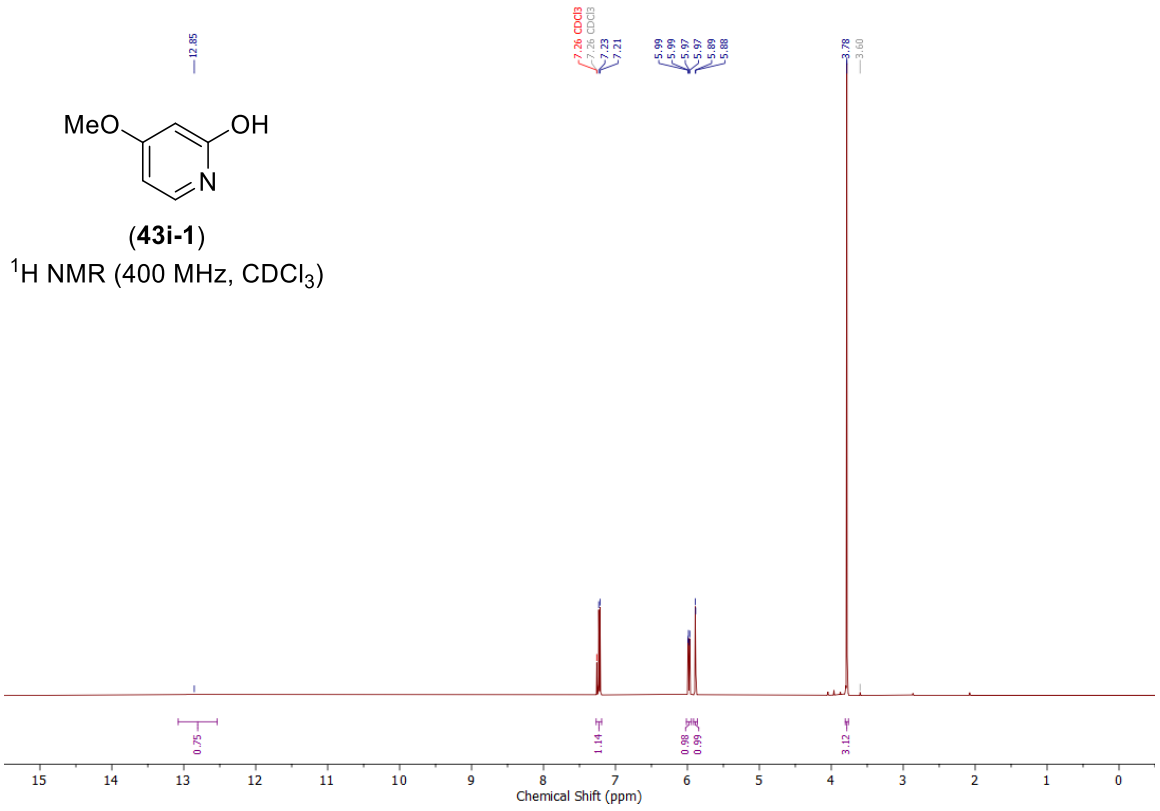
^{1}H NMR (400 MHz, DMSO-d_6)



(**44h**)

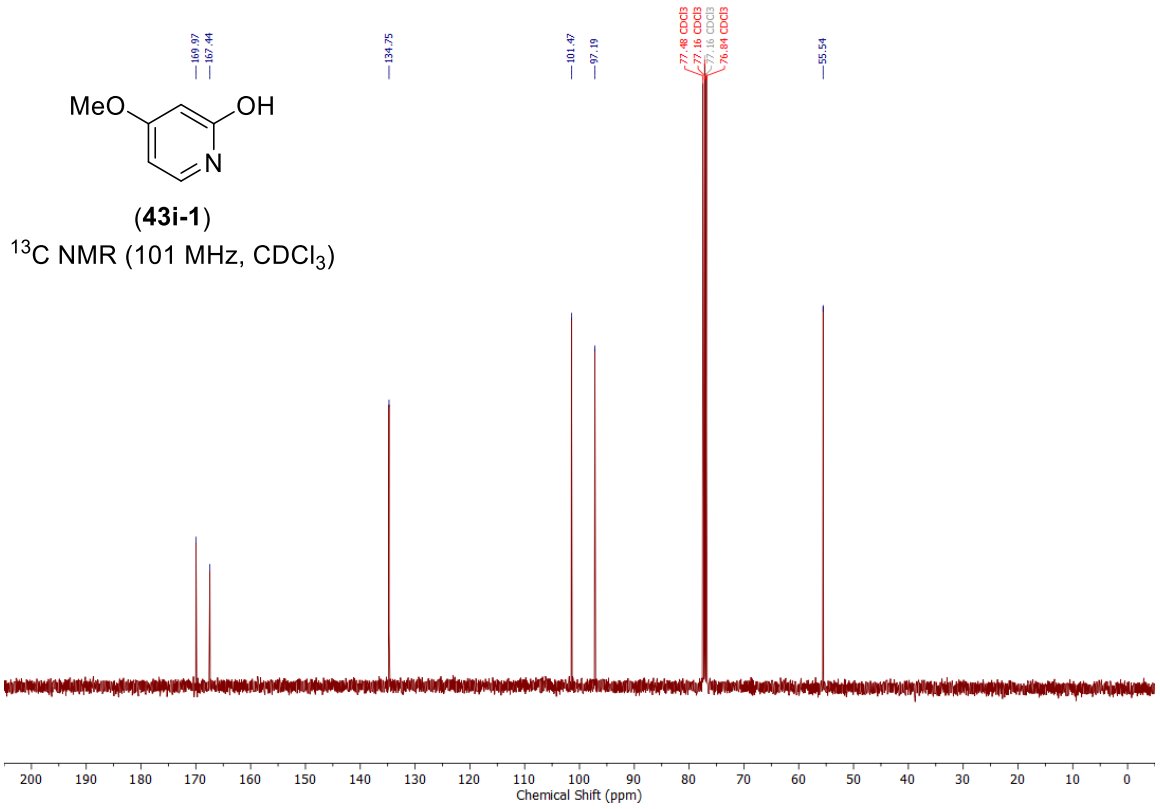
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of 4-methoxypyridine-2-ol (43i-1):



(**43i-1**)

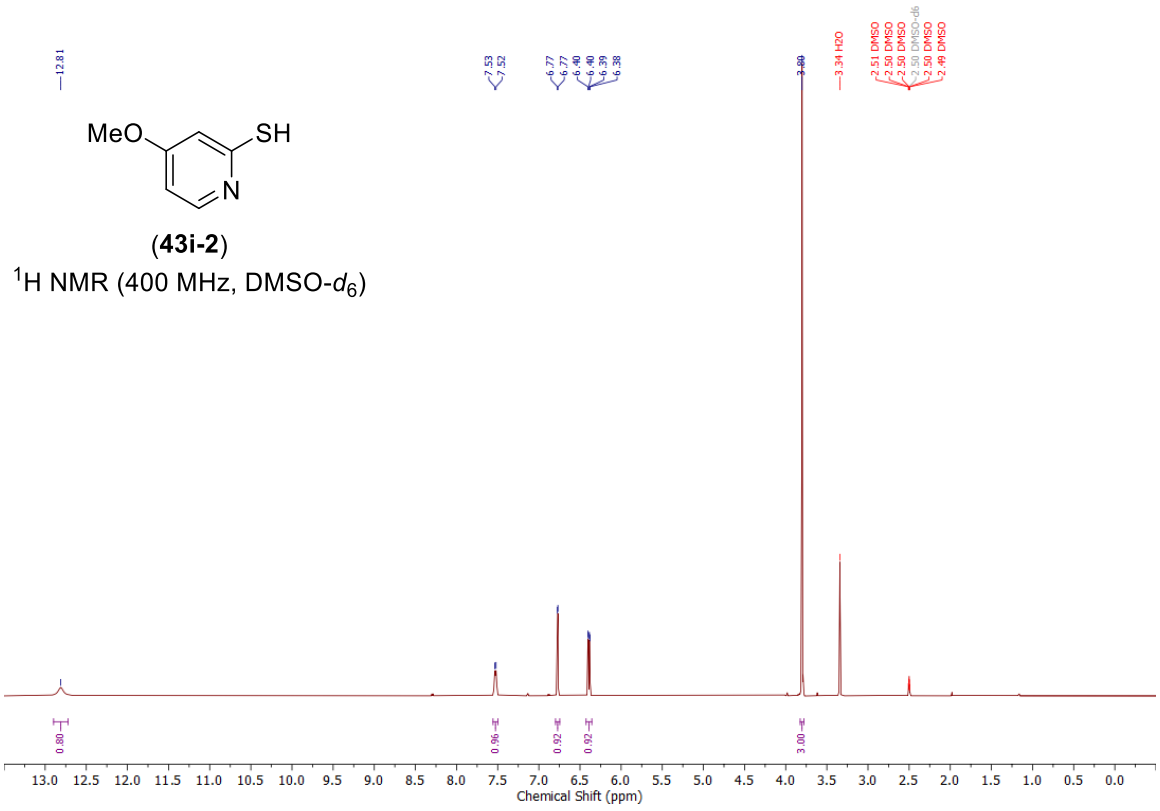
^{1}H NMR (400 MHz, $CDCl_3$)



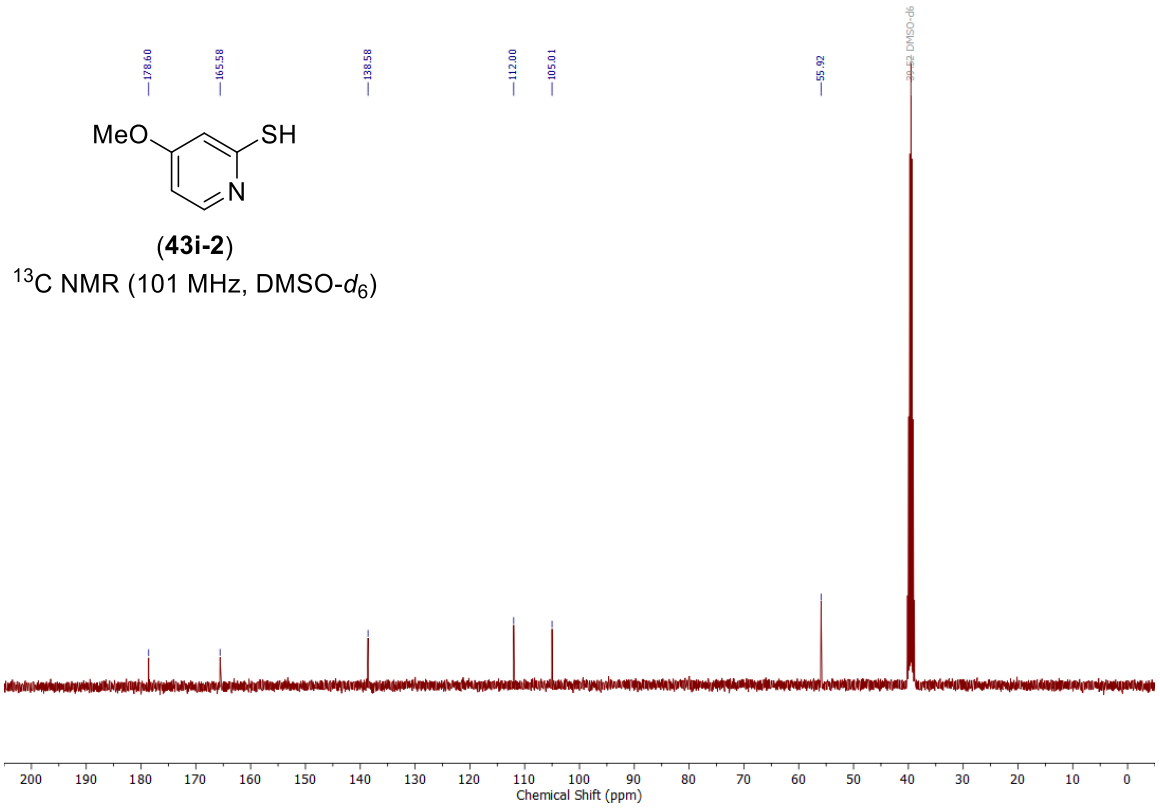
(**43i-1**)

^{13}C NMR (101 MHz, $CDCl_3$)

NMR spectra of 4-methoxypyridine-2-thiol (43i-2):

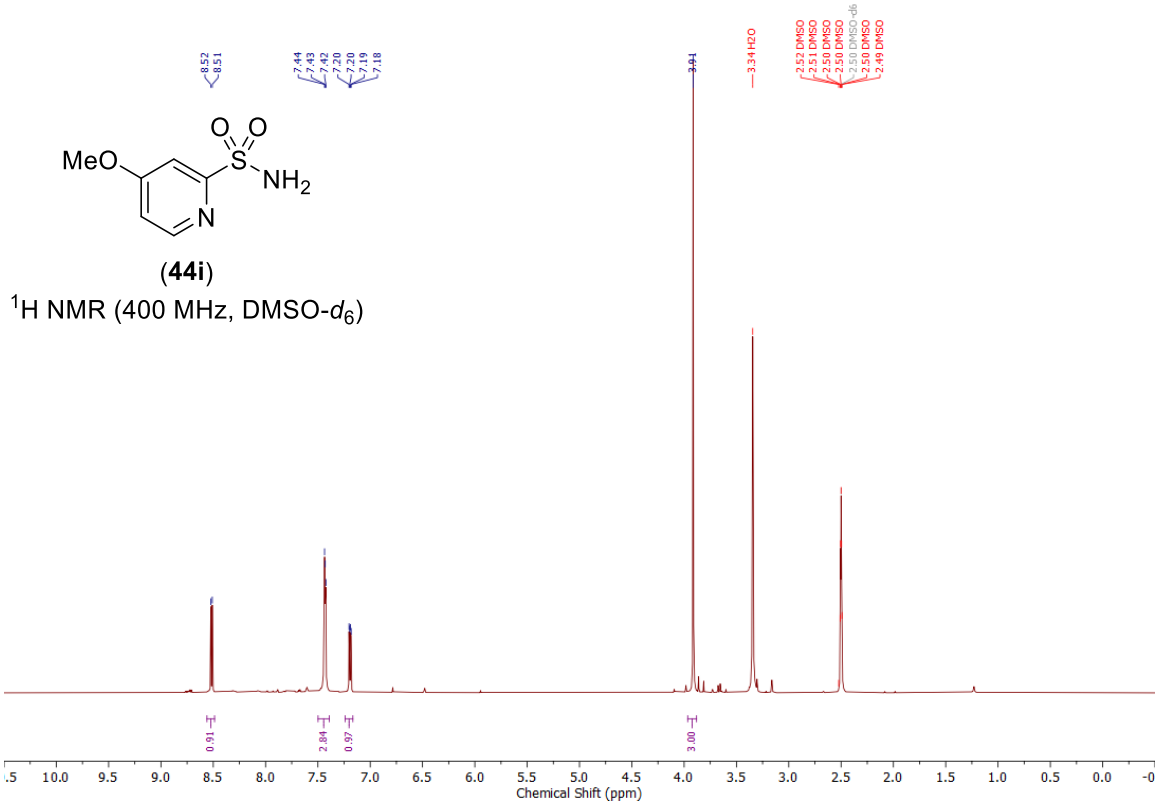


(**43i-2**)
^{1}H NMR (400 MHz, DMSO-d_6)



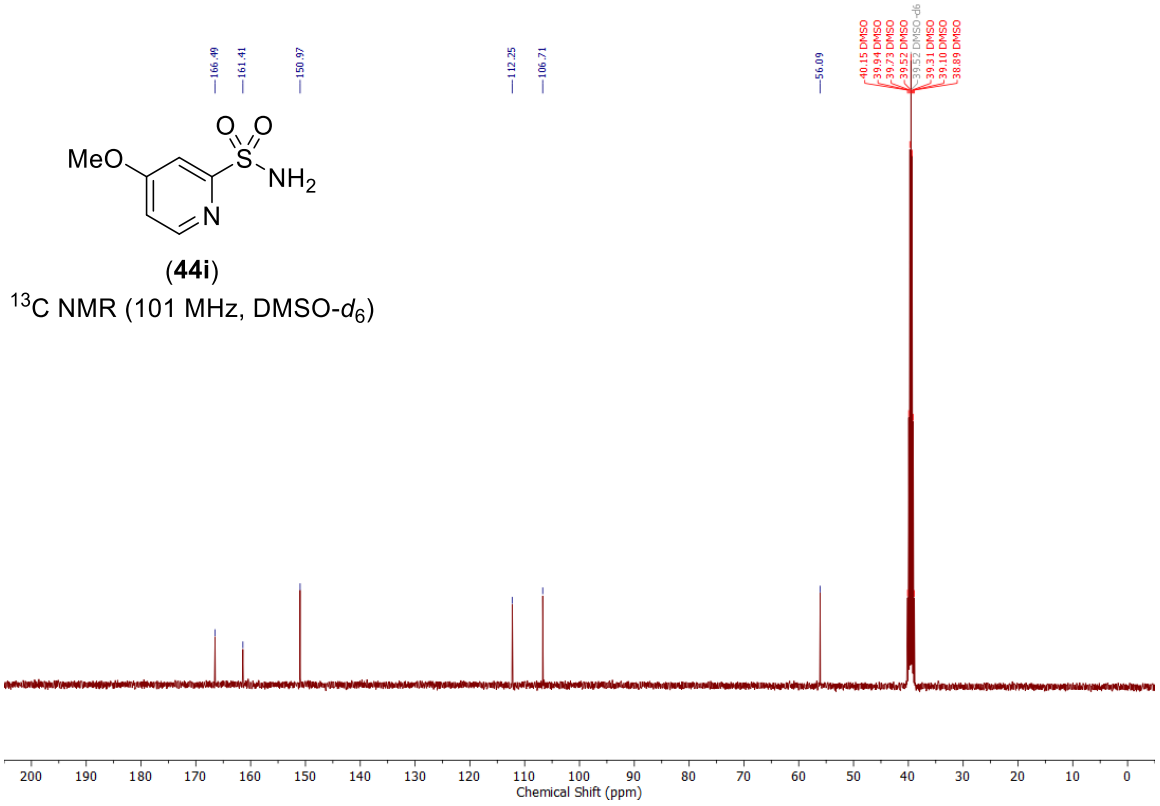
(**43i-2**)
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of 4-methoxypyridine-2-sulfonamide (44i):



(**44i**)

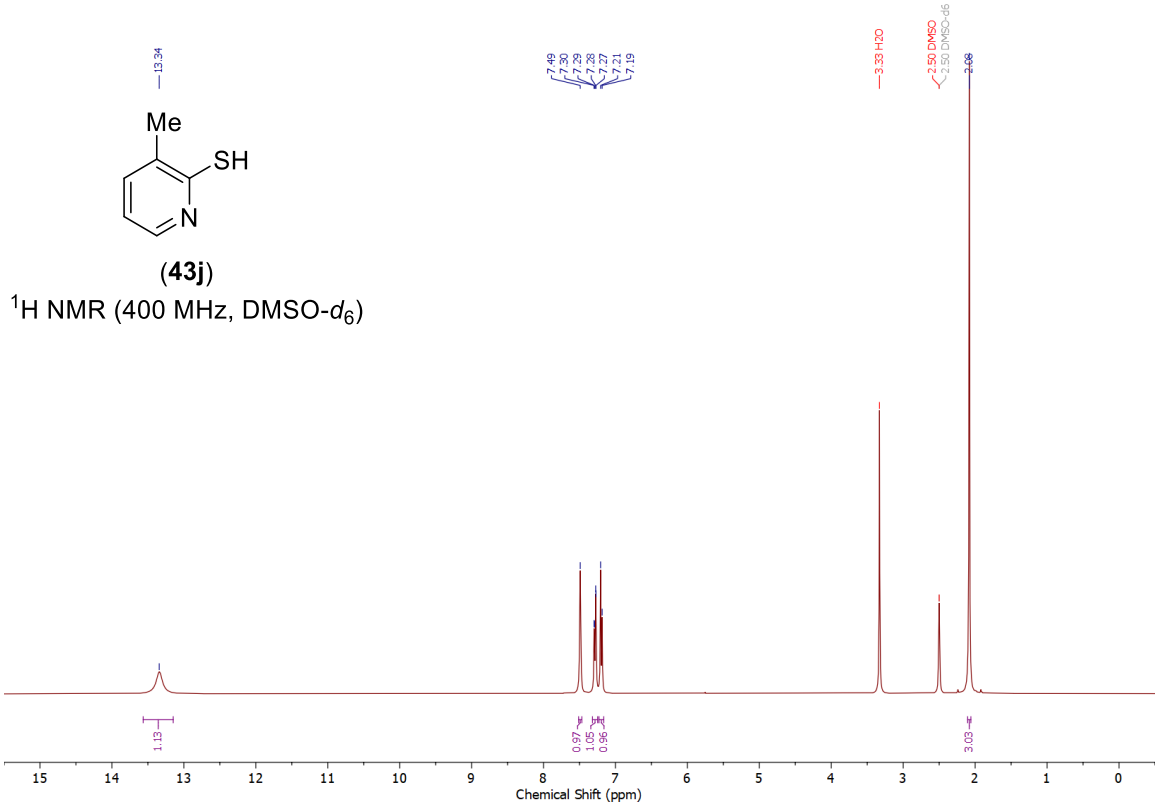
^{1}H NMR (400 MHz, DMSO-d_6)



(**44i**)

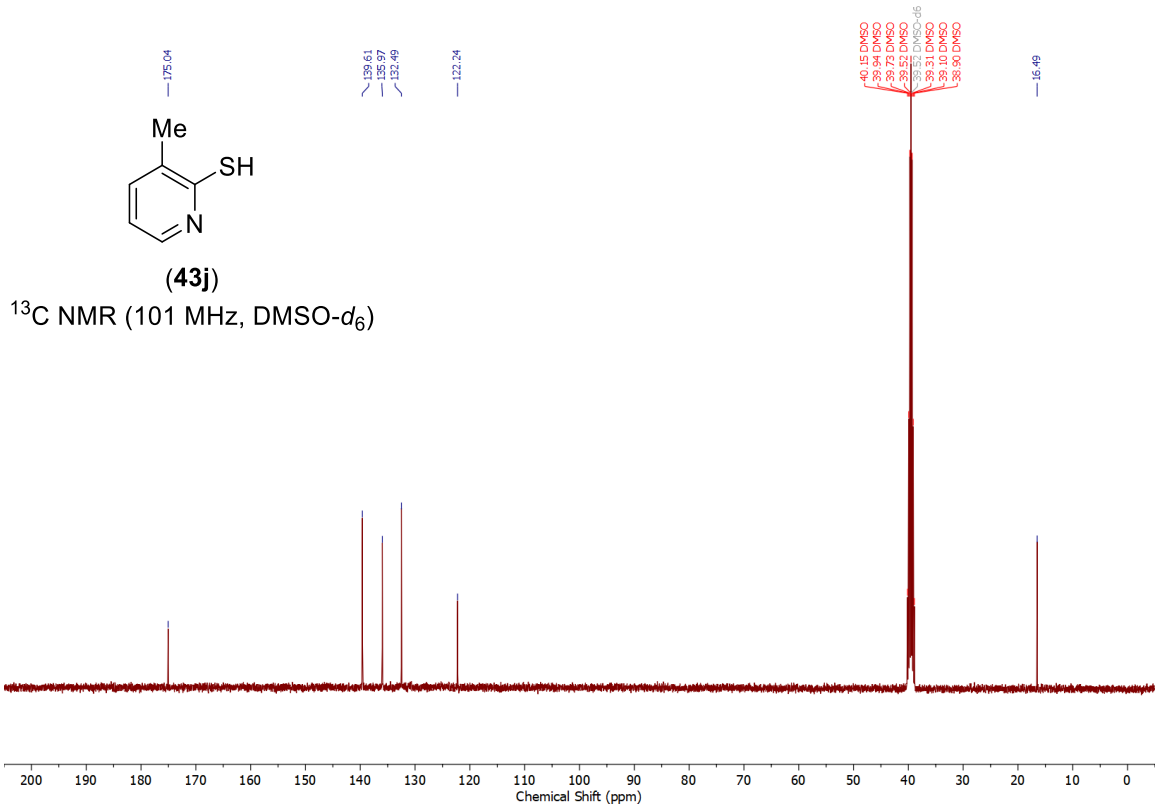
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of 3-methylpyridine-2-thiol (43j):



(**43j**)

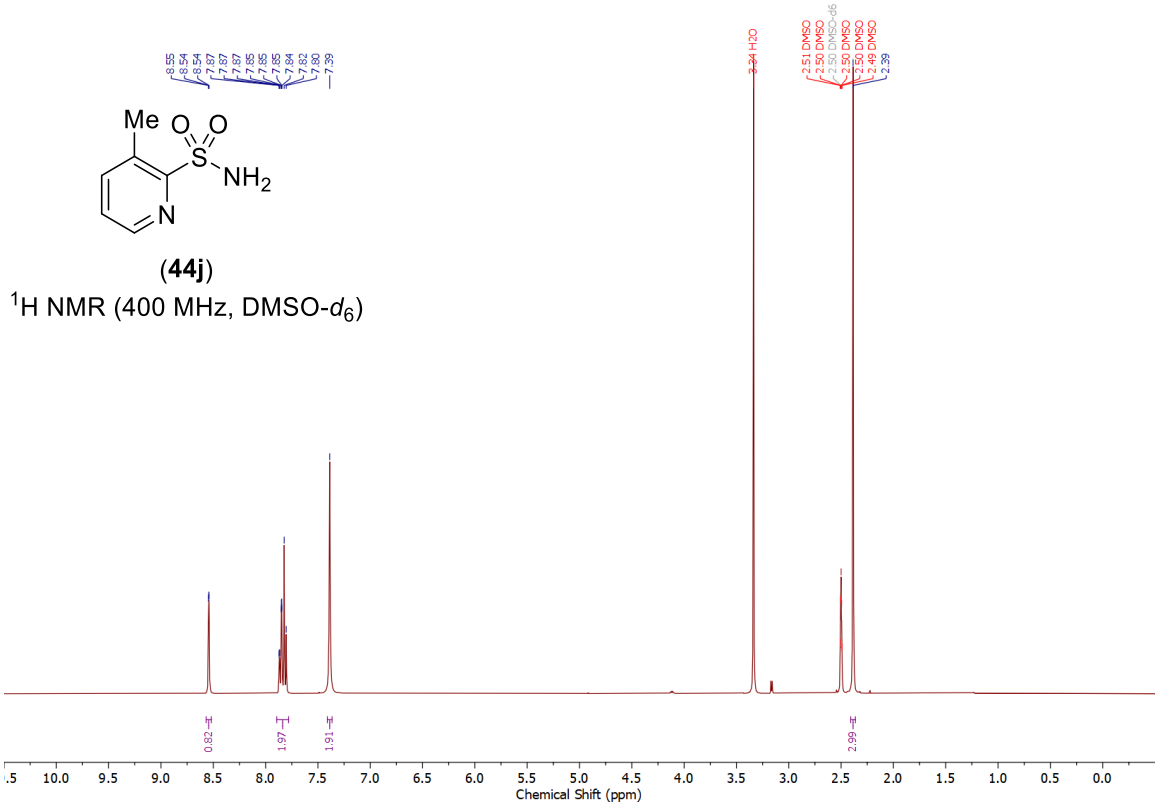
^{1}H NMR (400 MHz, DMSO-d_6)



(**43j**)

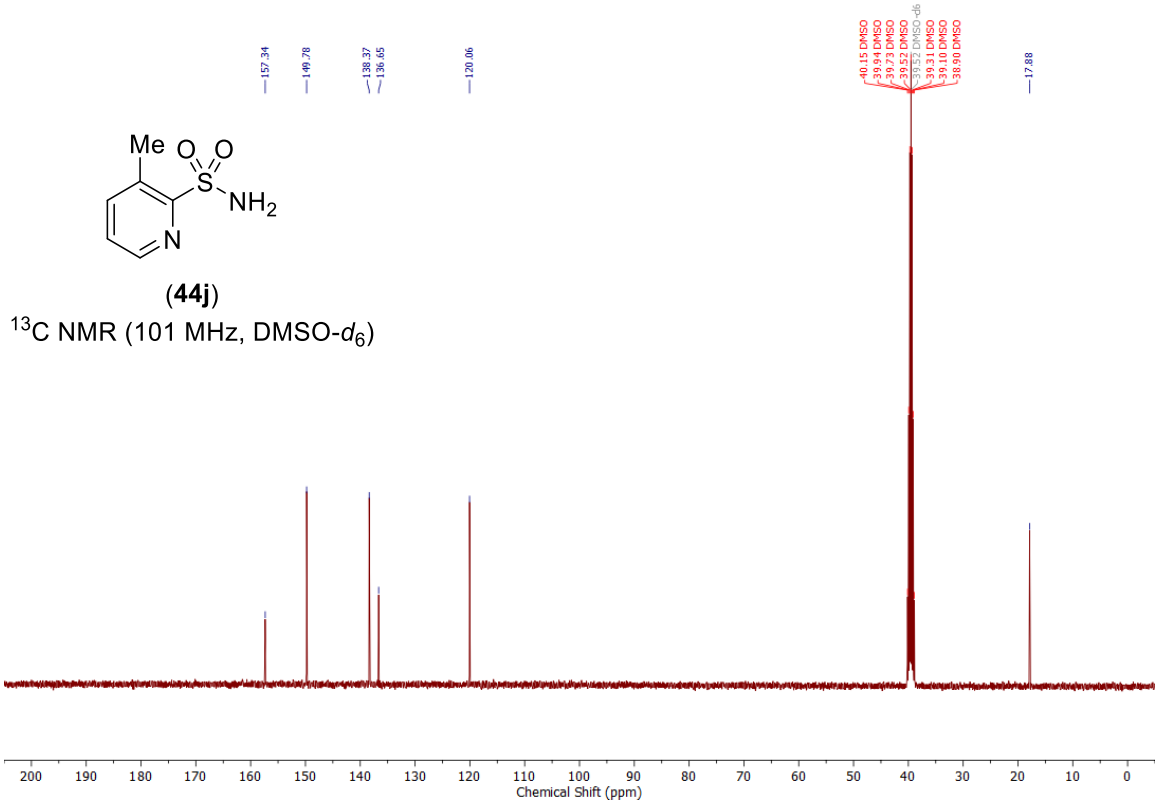
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of 3-methylpyridine-2-sulfonamide (44j):



(**44j**)

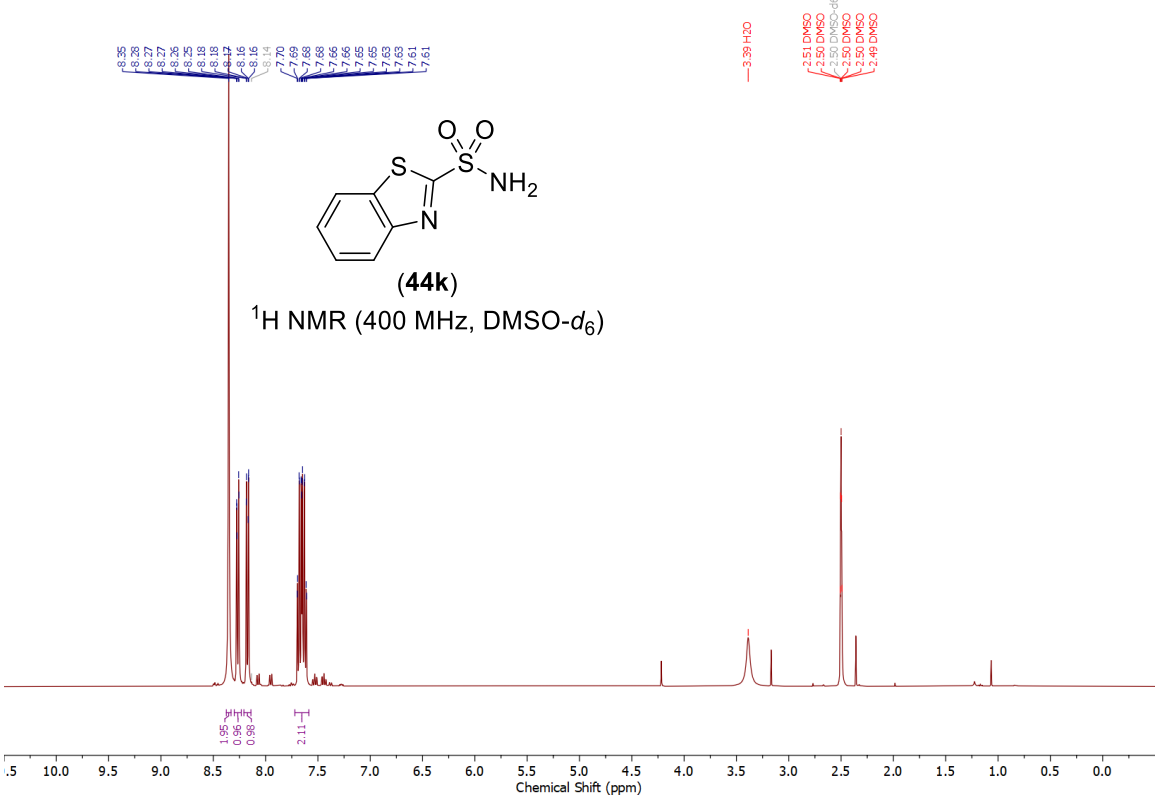
^{1}H NMR (400 MHz, DMSO-d_6)

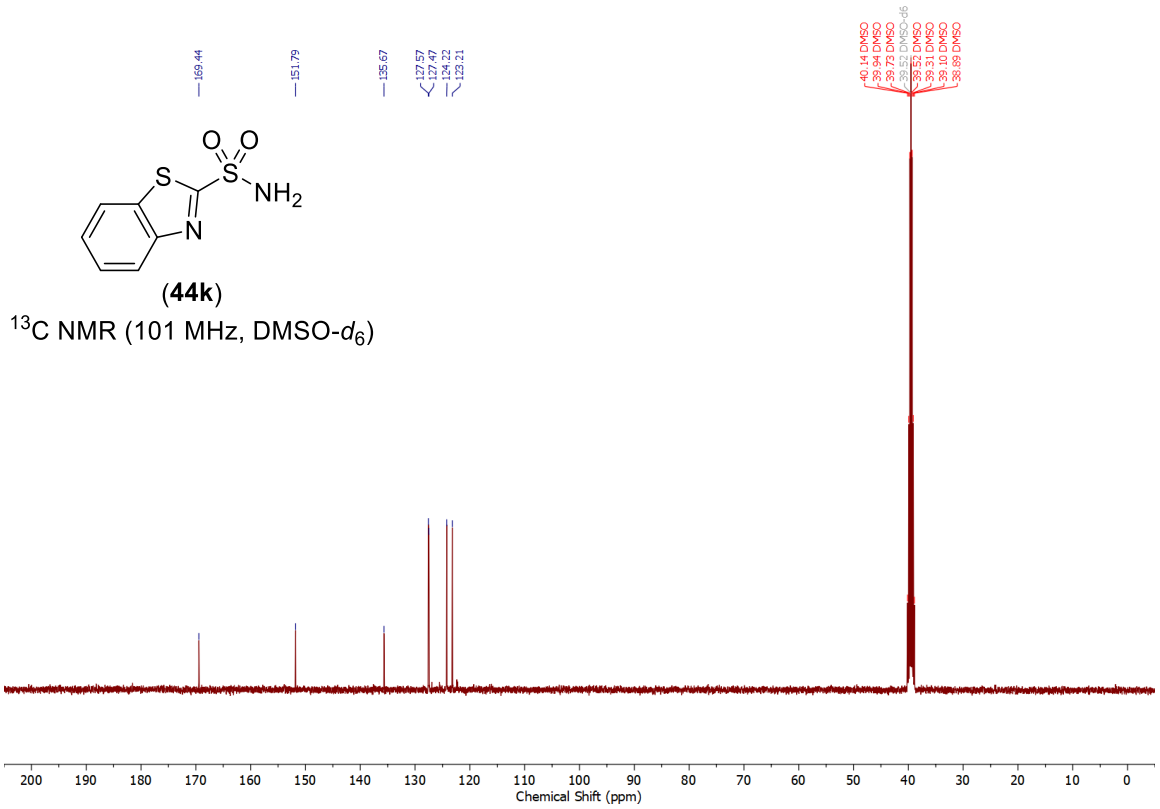


(**44j**)

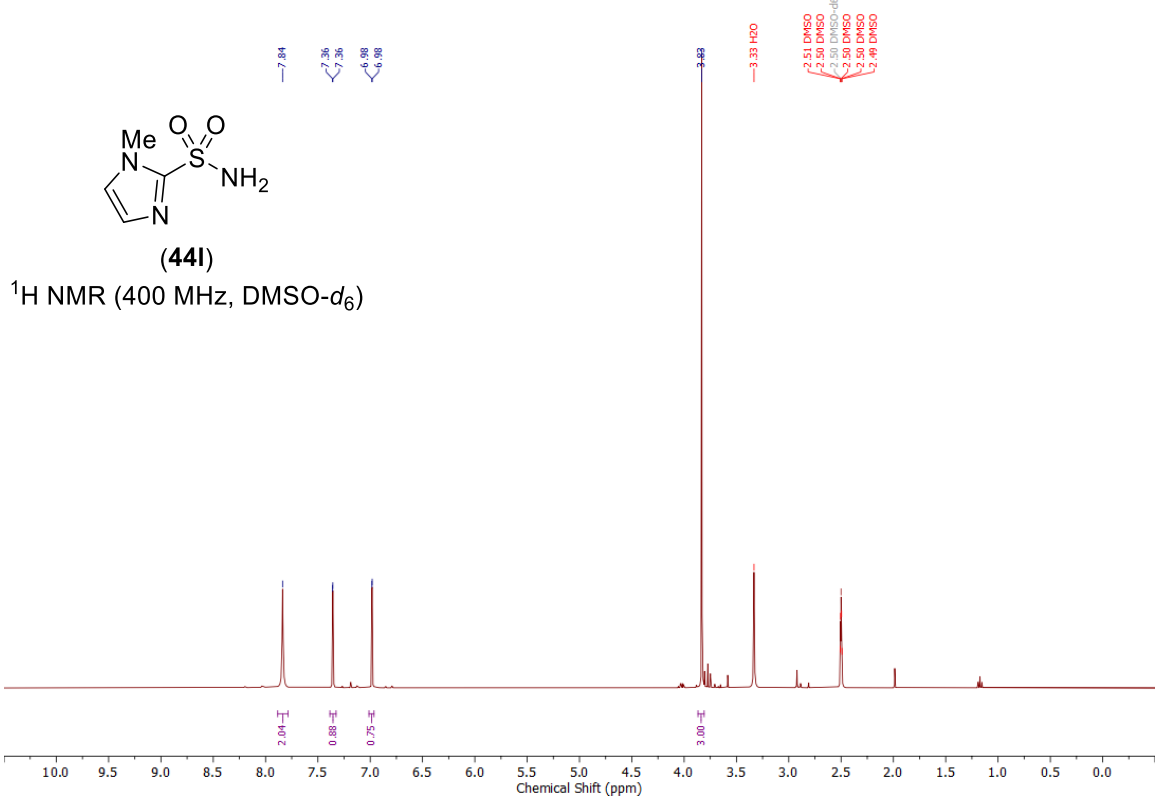
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of benzo[*d*]thiazole-2-sulfonamide (44k):



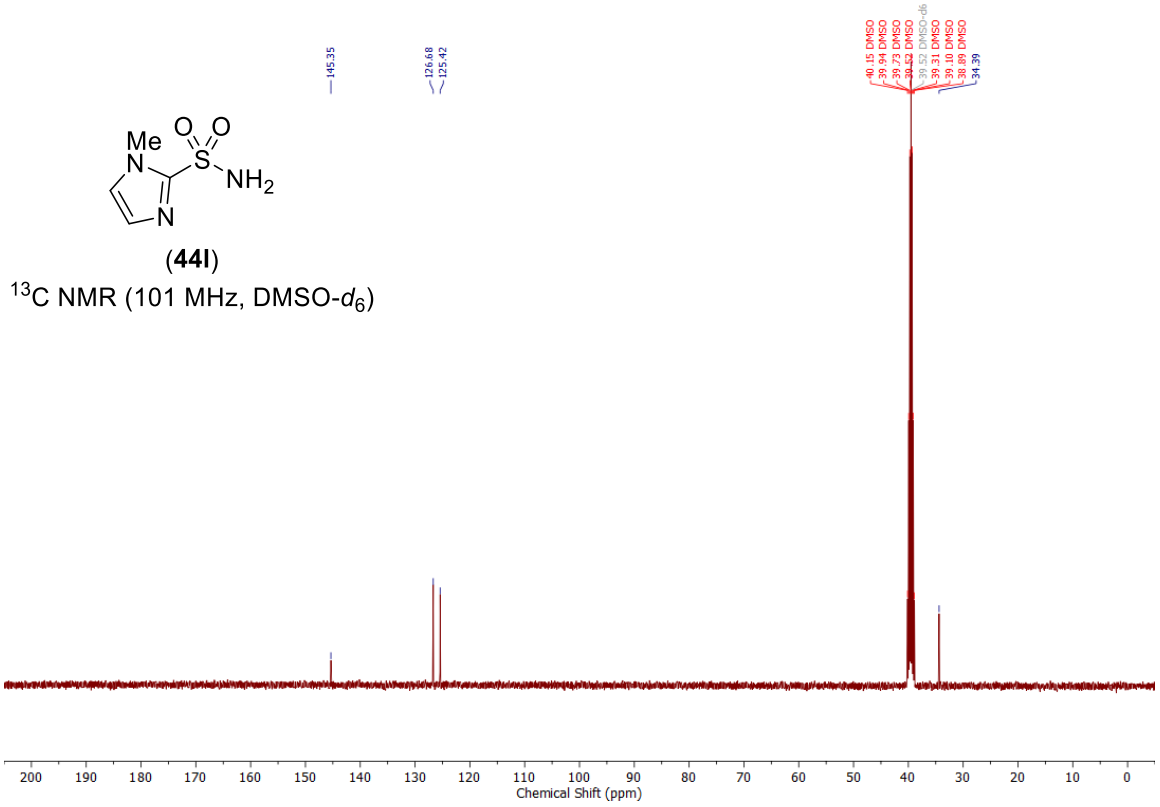


NMR spectra of 1-methyl-1*H*-imidazole-2-sulfonamide (44l):



(**44l**)

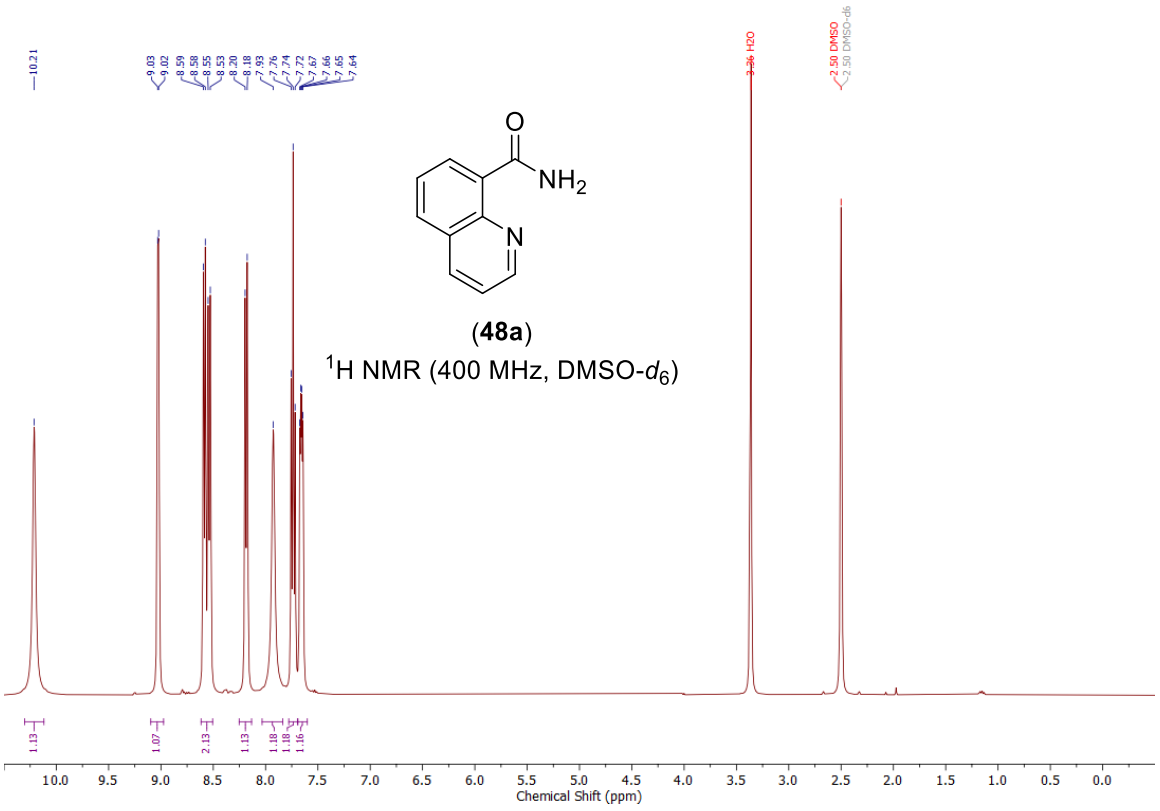
^{1}H NMR (400 MHz, DMSO-d_6)

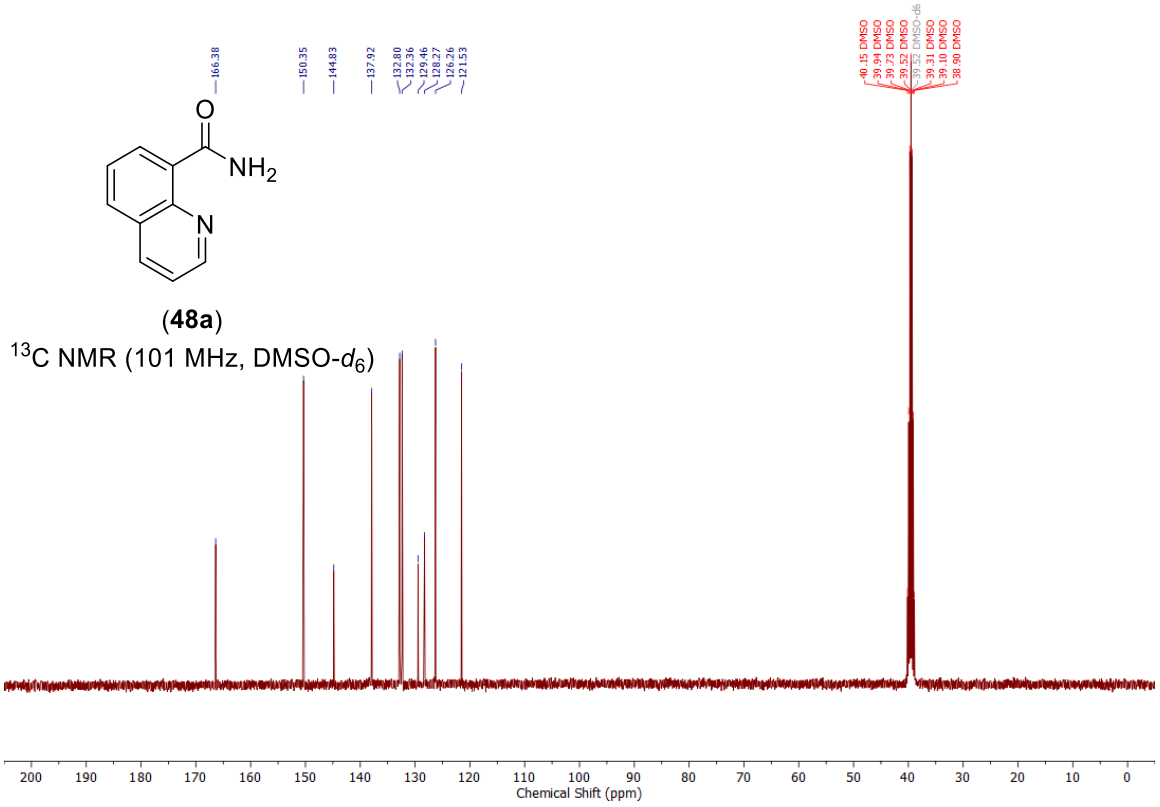


(**44l**)

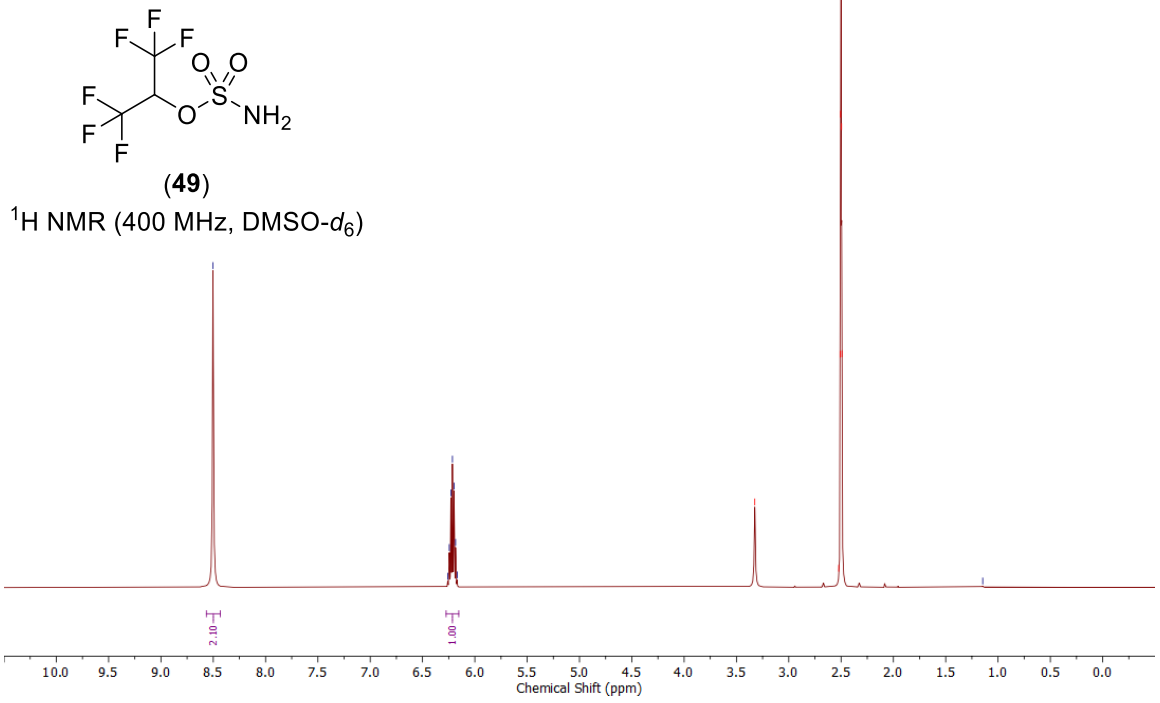
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of quinoline-8-carboxamide (48a):



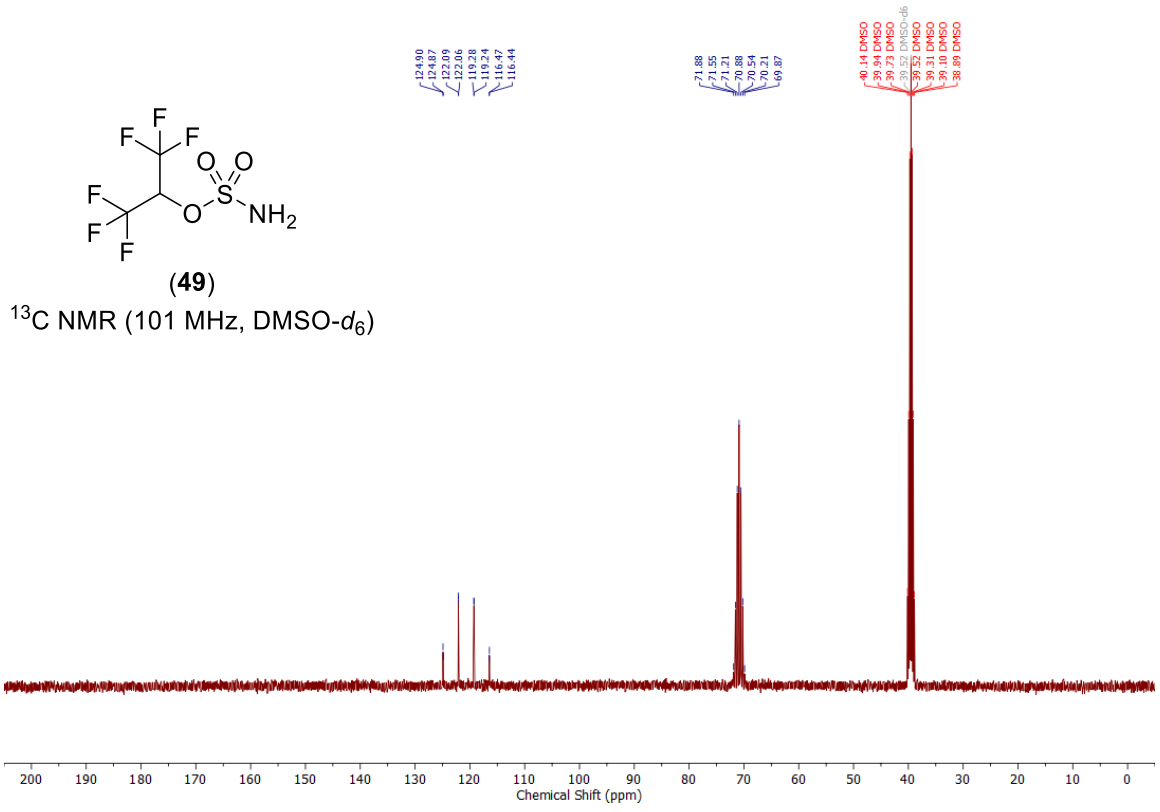


NMR spectra of 1,1,1,3,3,3-hexafluoropropan-2-yl sulfamate (HFIPS) (49):



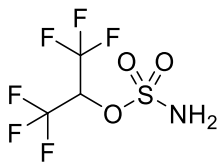
(**49**)

^{1}H NMR (400 MHz, DMSO-d_6)



(**49**)

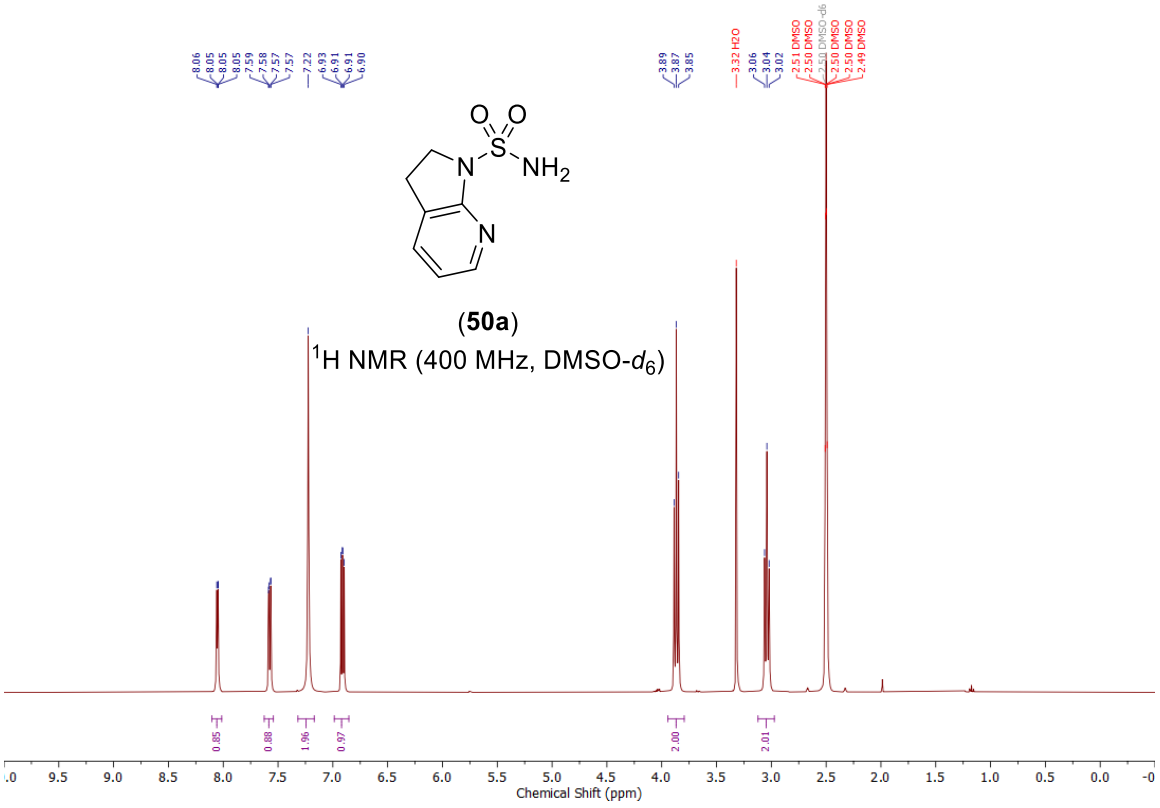
^{13}C NMR (101 MHz, DMSO-d_6)

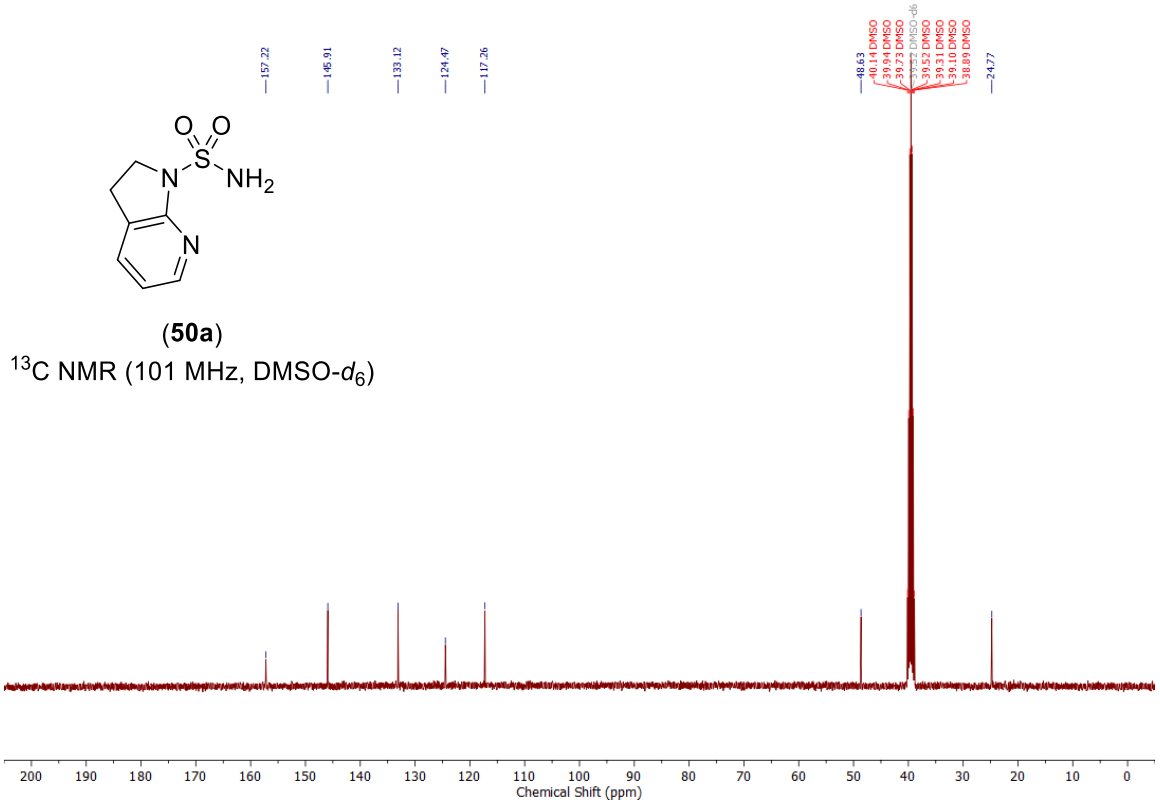


(**49**)

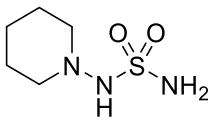
^{19}F NMR (377 MHz, DMSO-d_6)

NMR spectra of 2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyridine-1-sulfonamide (50a):



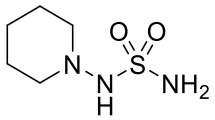


NMR spectra of *N*-1-piperidinylsulfamide (50b):



(**50b**)

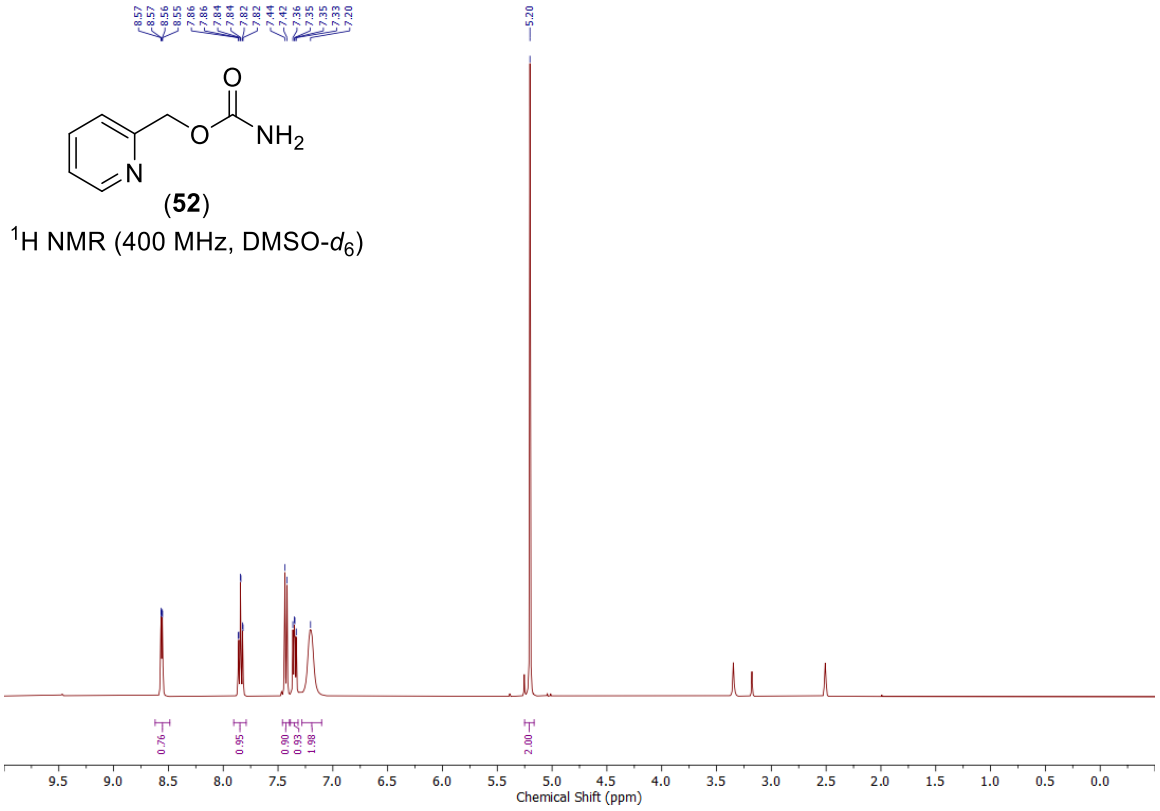
^{1}H NMR (400 MHz, DMSO-d_6)



(**50b**)

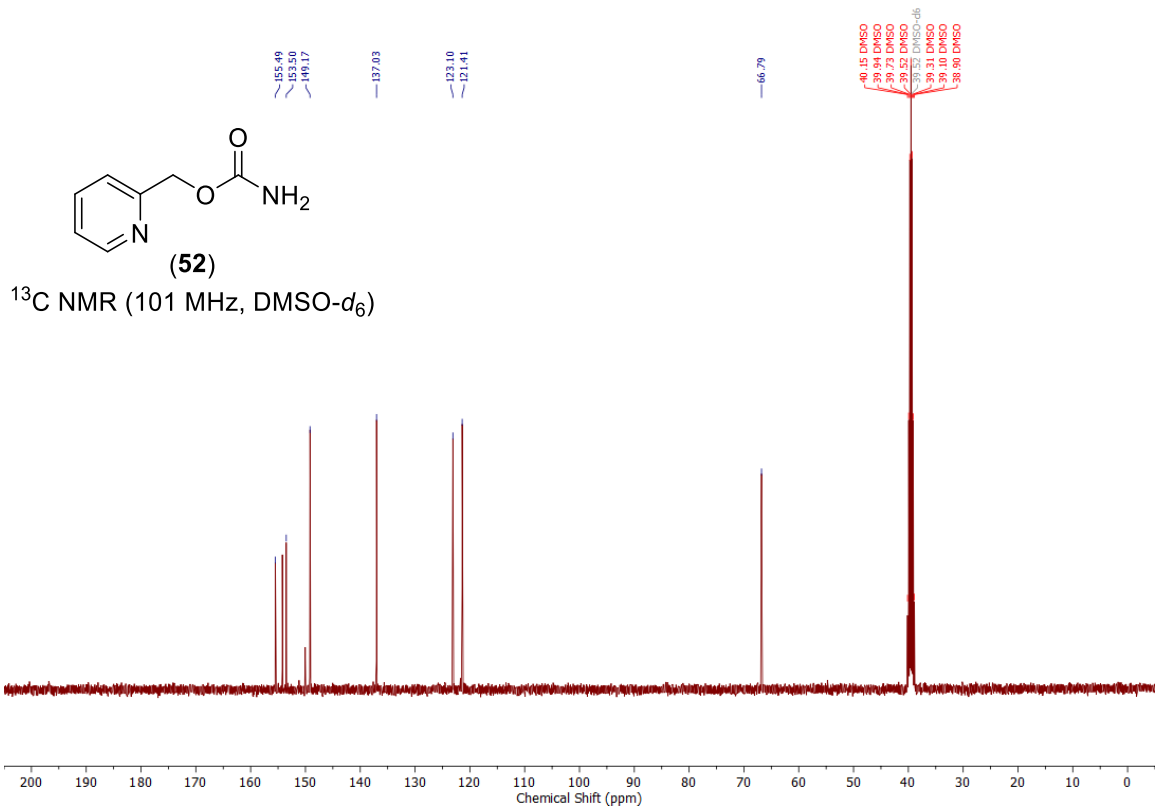
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of pyridin-2-ylmethyl carbamate (52):



(**52**)

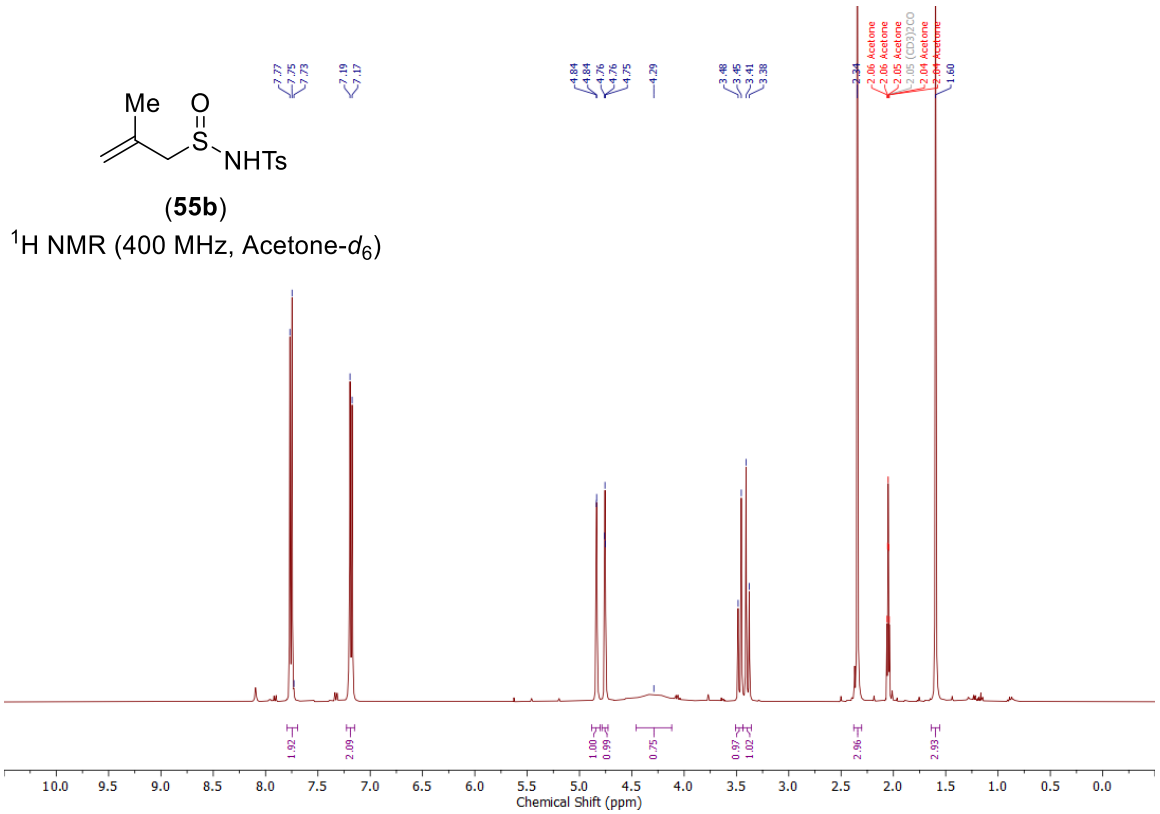
^{1}H NMR (400 MHz, DMSO-d_6)



(**52**)

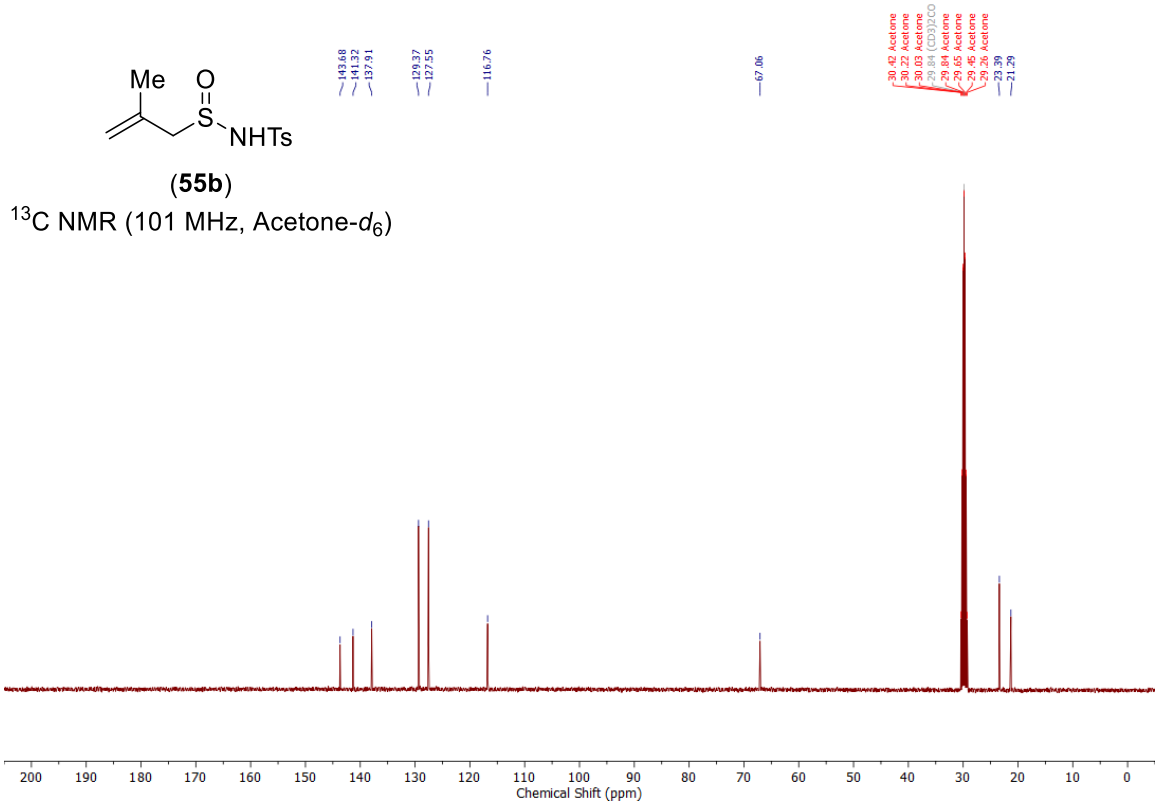
^{13}C NMR (101 MHz, DMSO-d_6)

NMR spectra of 4-methyl-*N*-((2-methylallyl)sulfinyl)benzenesulfonamide (55b):



(**55b**)

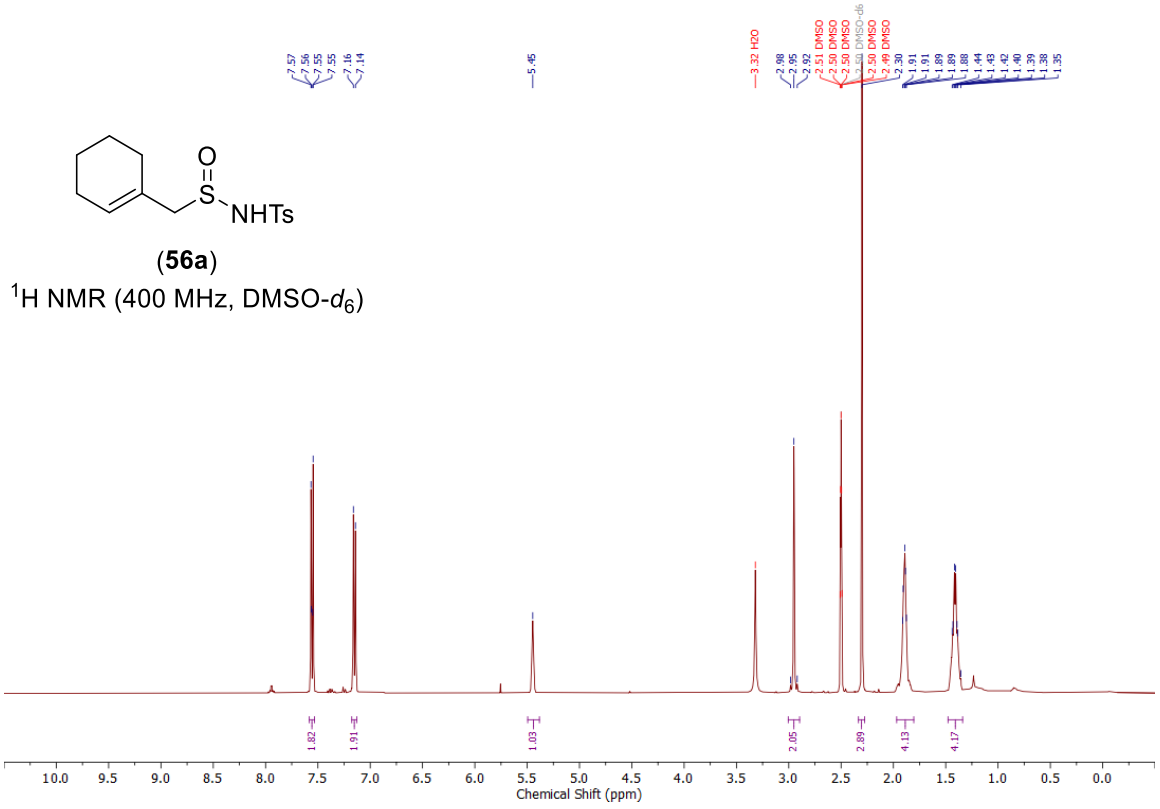
^{1}H NMR (400 MHz, Acetone-d_6)



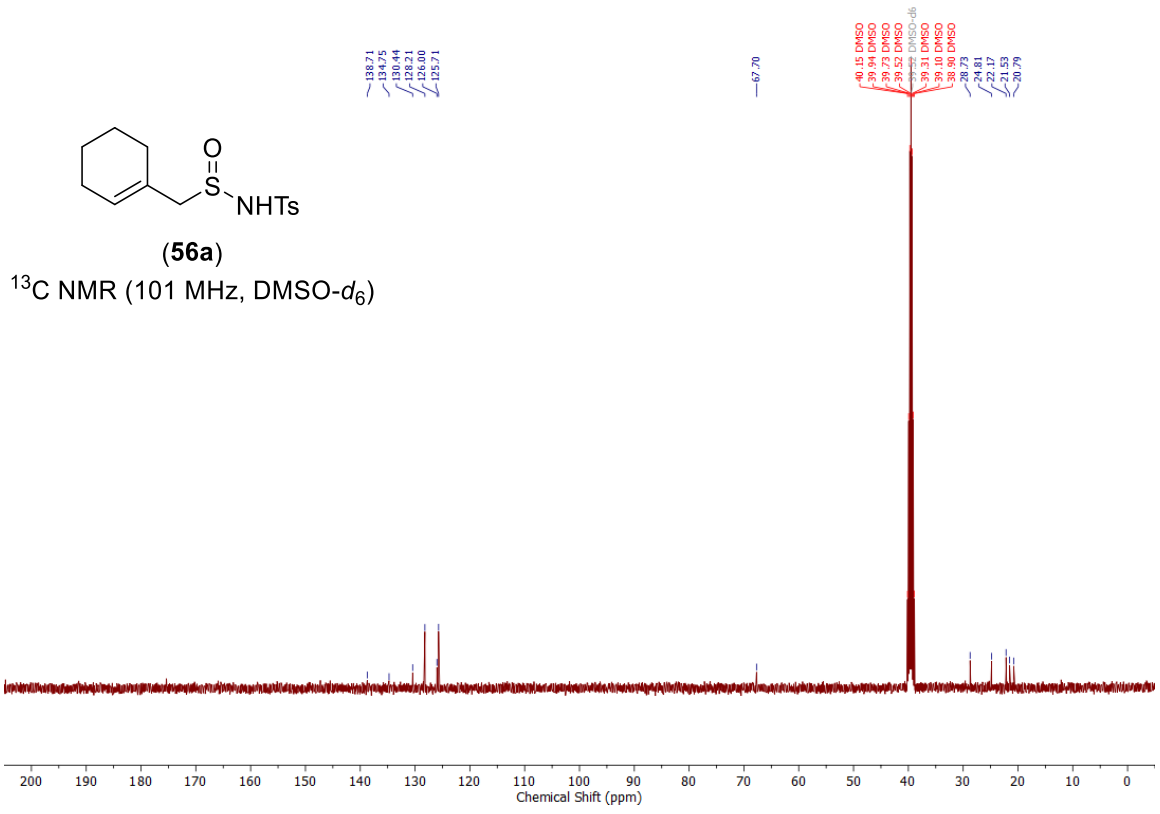
(**55b**)

^{13}C NMR (101 MHz, Acetone-d_6)

_N_-((Cyclohex-1-en-1-ylmethyl)sulfinyl)-4-methylbenzenesulfonamide (56a):

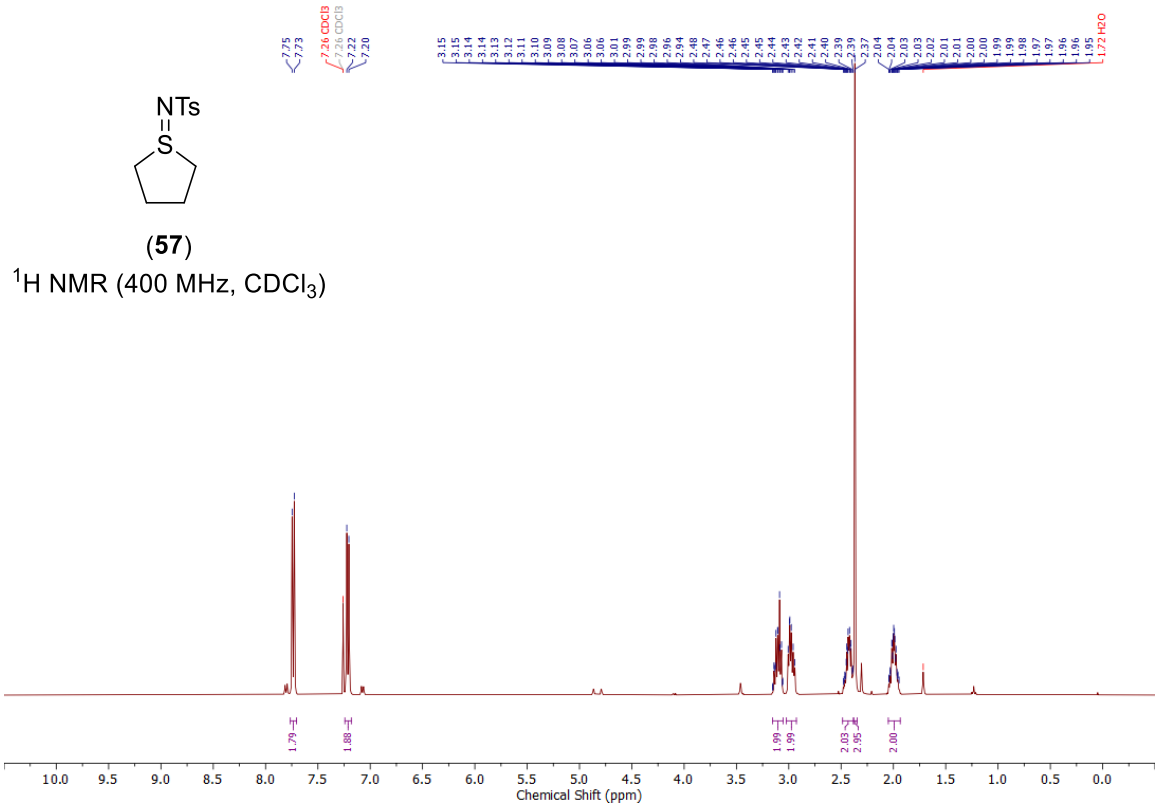


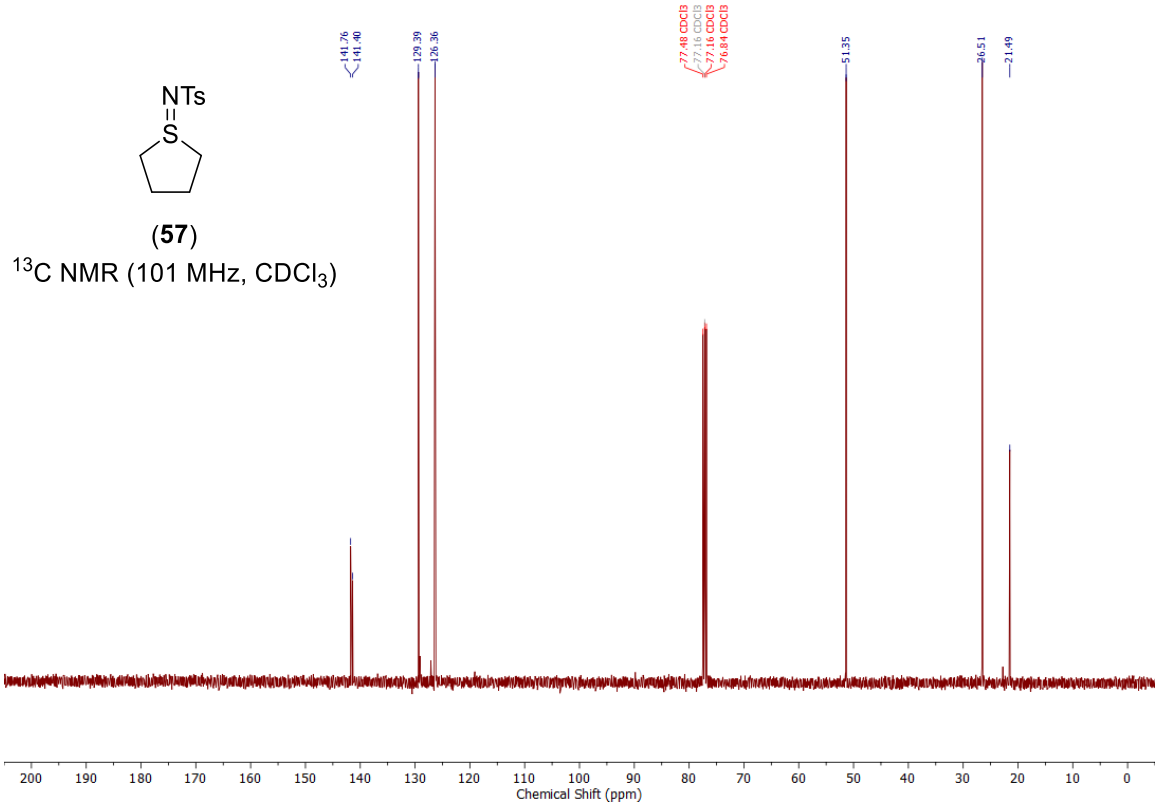
(**56a**)
^{1}H NMR (400 MHz, DMSO-d_6)



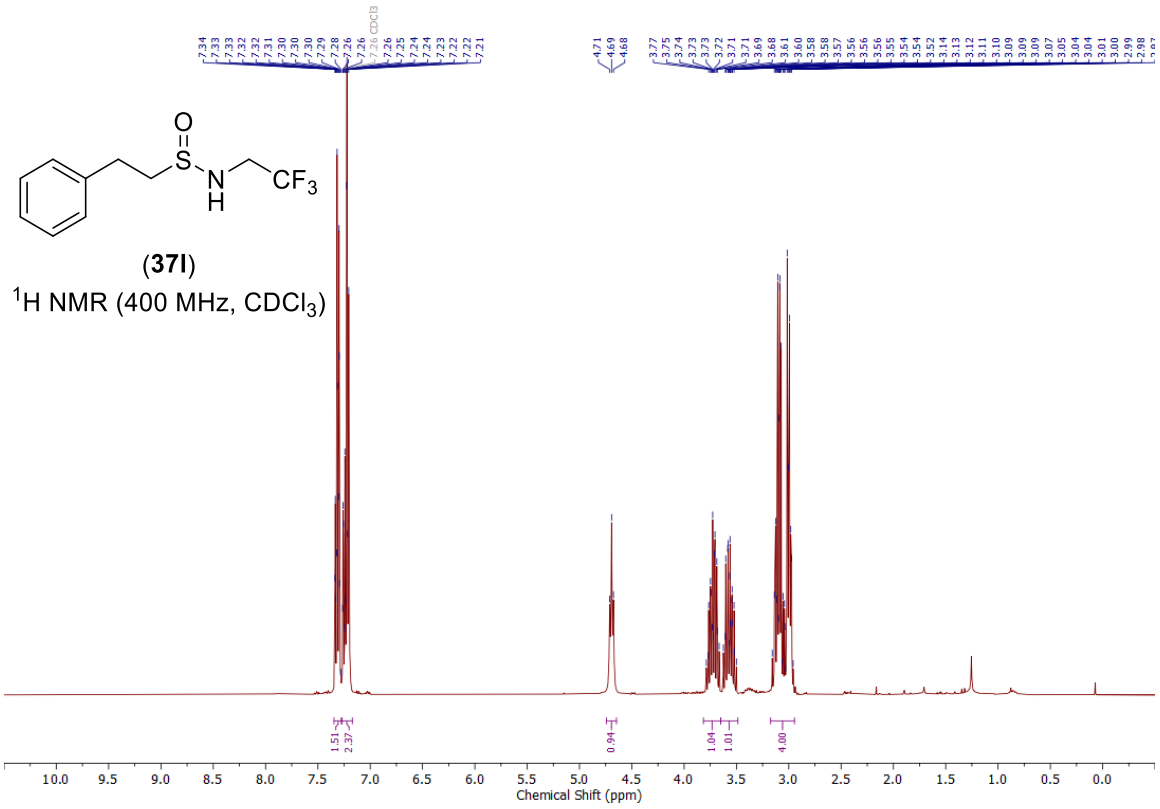
(**56a**)
^{13}C NMR (101 MHz, DMSO-d_6)

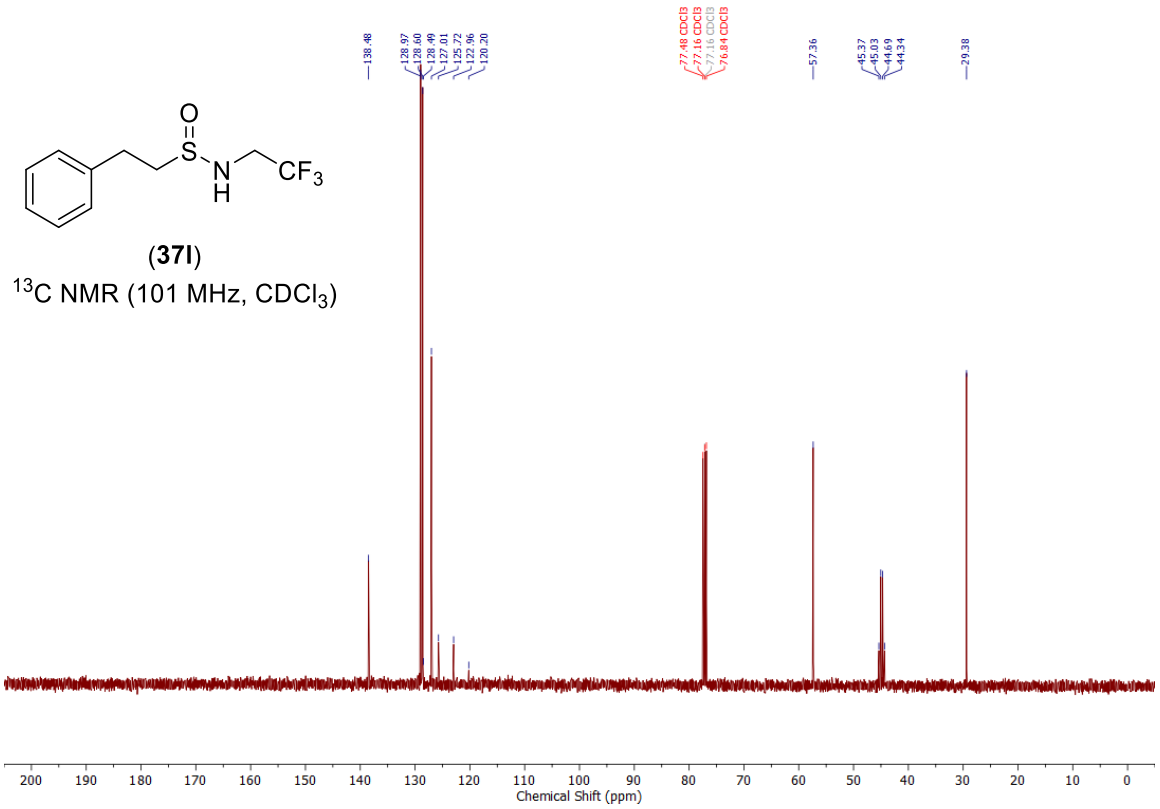
NMR spectra of 4-methyl-*N*-(tetrahydro-1λ^4-thiophen-1-ylidene)benzenesulfonamide (57):

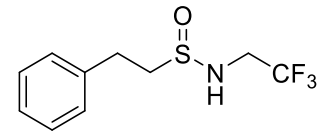




NMR spectra of 2-phenyl-*N*-(2,2,2-trifluoroethyl)ethane-1-sulfinamide (37l):





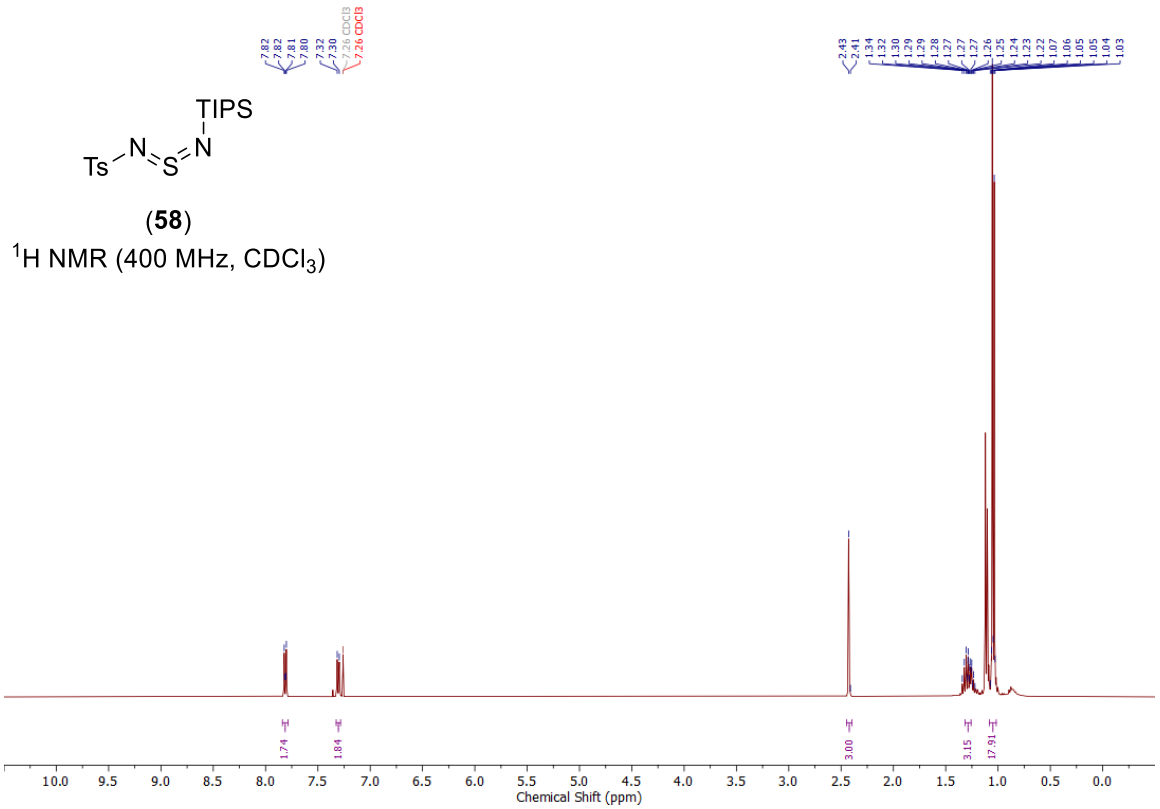


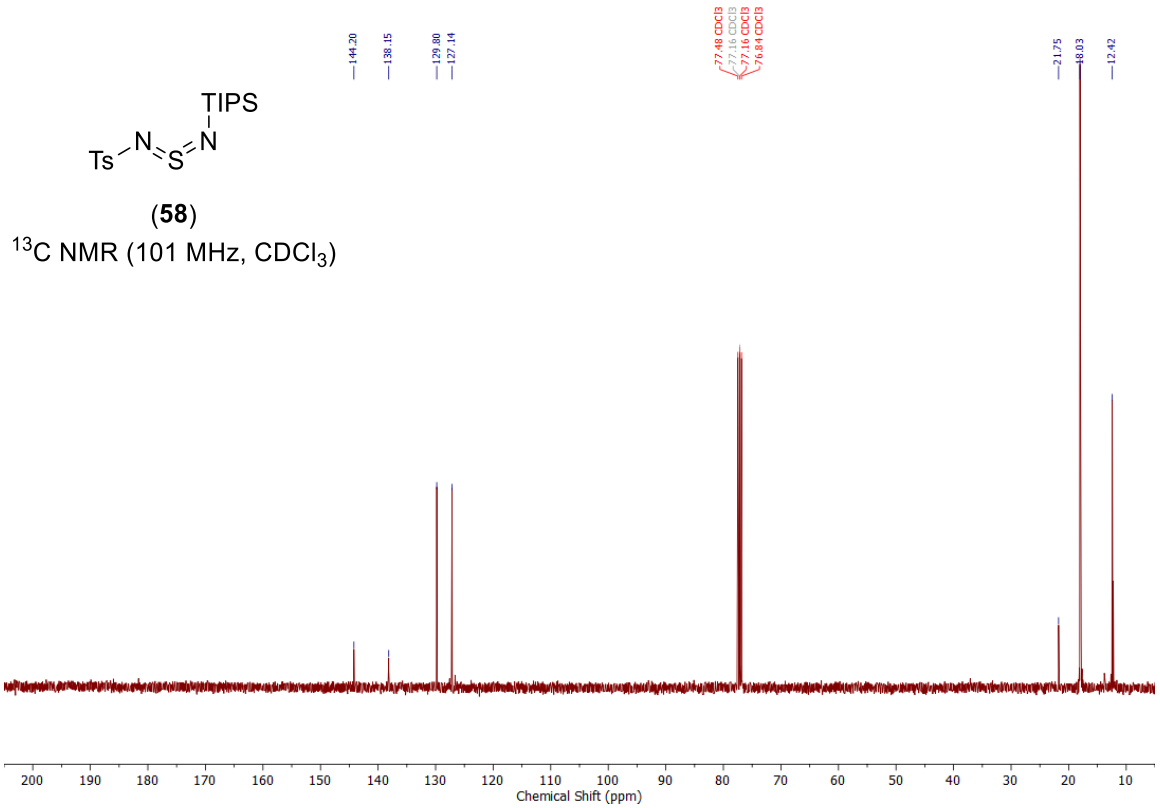
(**37l**)

^{19}F NMR (377 MHz, $CDCl_3$)

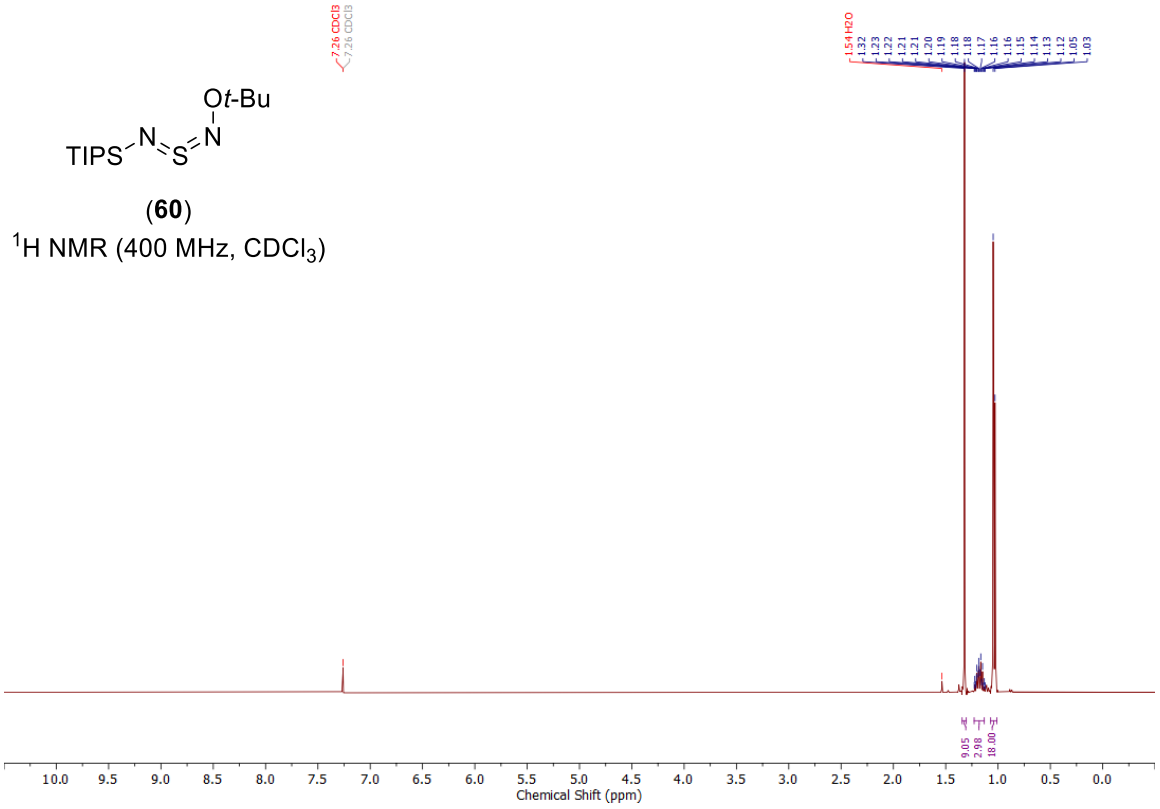
10.6 NMR Spectra for Chapter 6

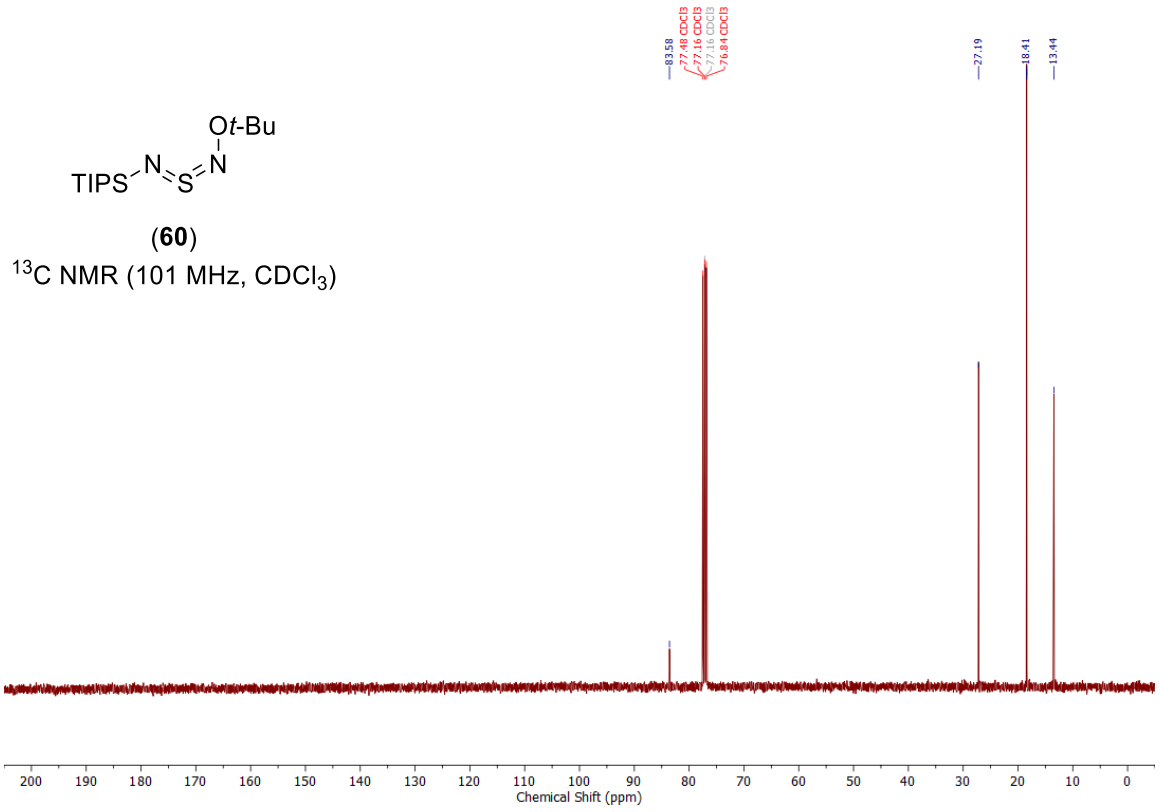
NMR spectra of 4-methyl-*N*-(((triisopropylsilyl)imino)-λ⁴-sulfaneylidene)benzenesulfonamide (58):



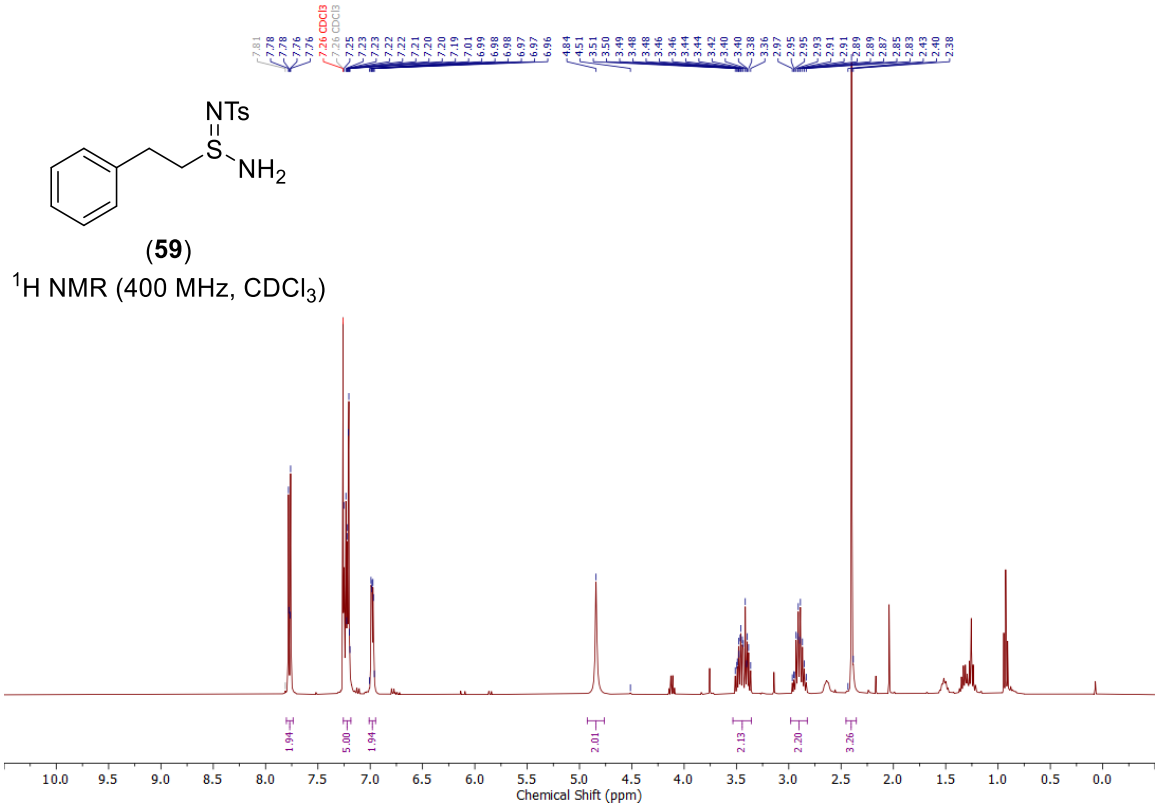


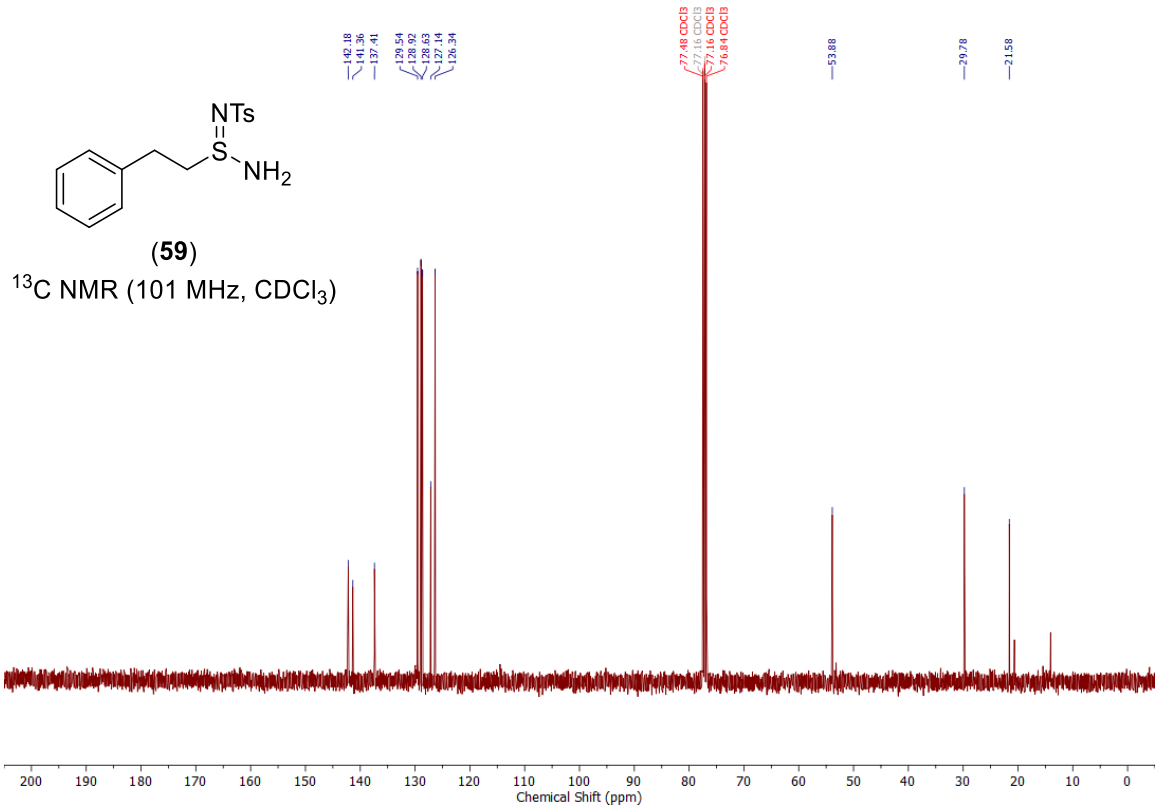
NMR spectra of *O*-(*tert*-butyl)-*N*-(((triisopropylsilyl)imino)- λ^4-sulfaneylidene)hydroxylamine (60):



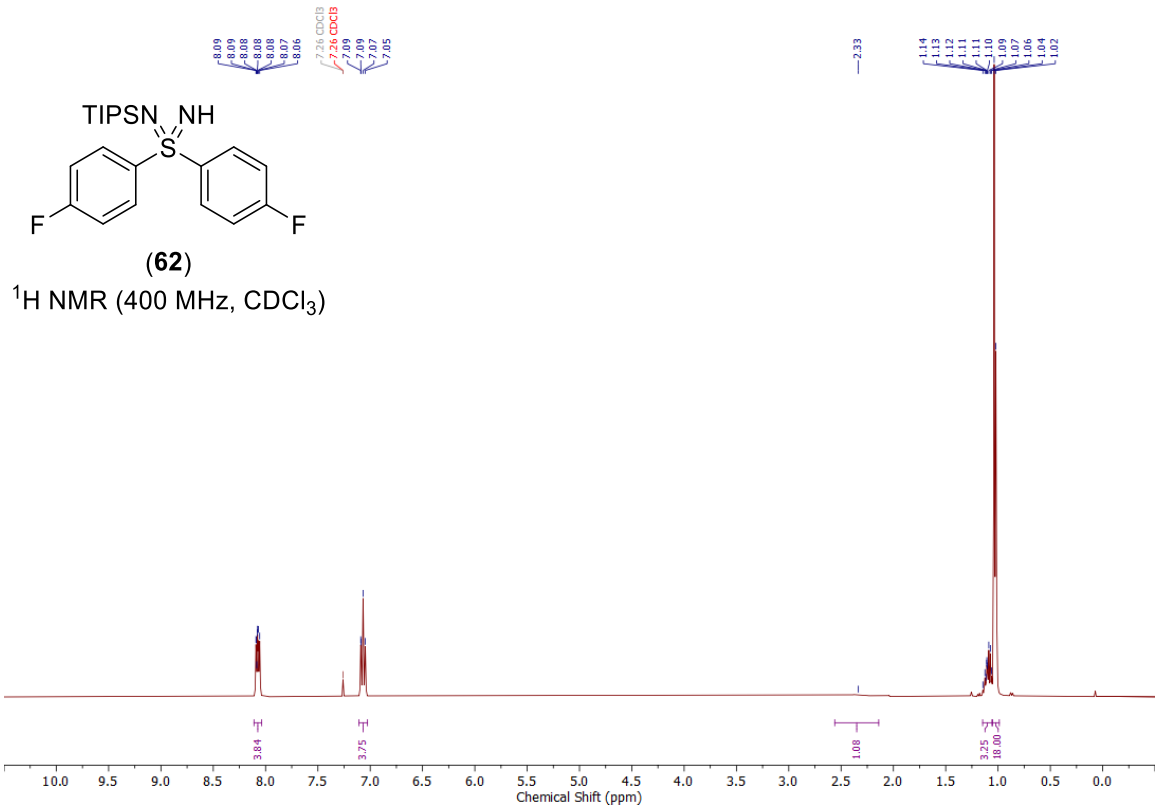


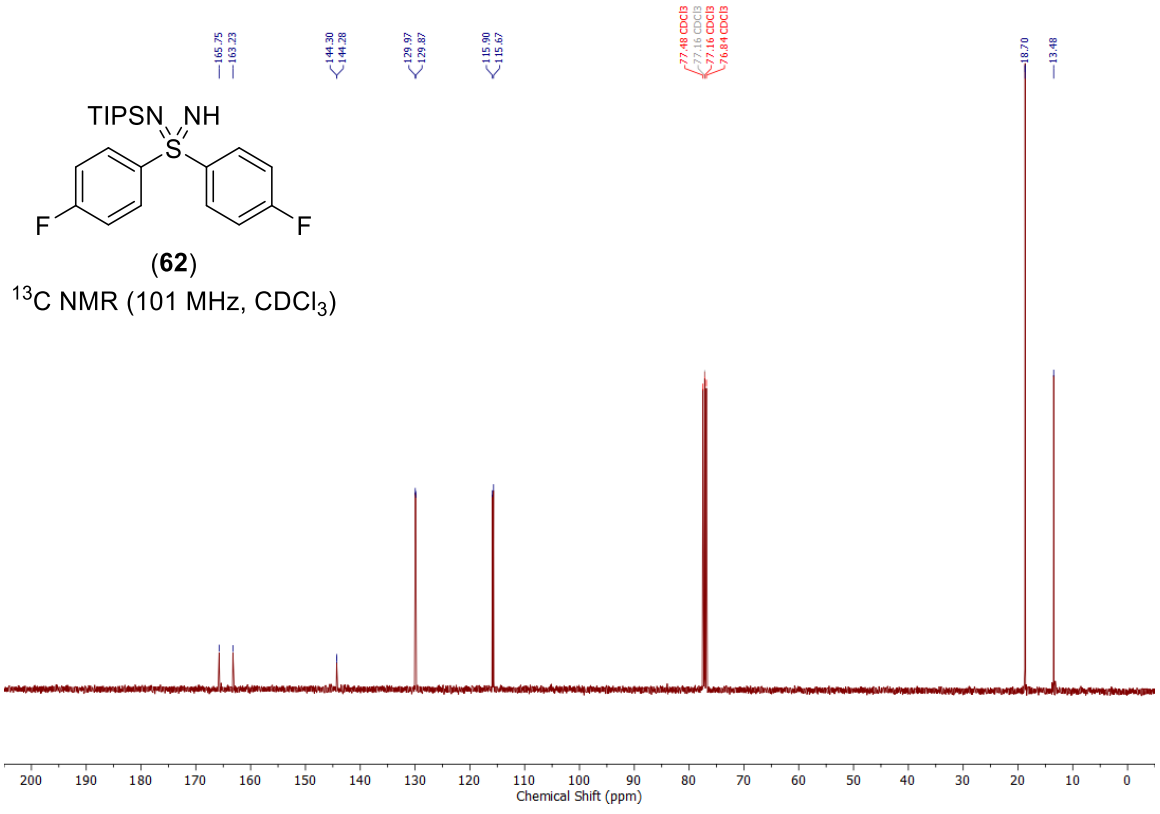
NMR spectra of (*Z*)-*N*-(Amino(phenethyl)-λ^4-sulfaneylidene)-4-methylbenzenesulfonamide (59):

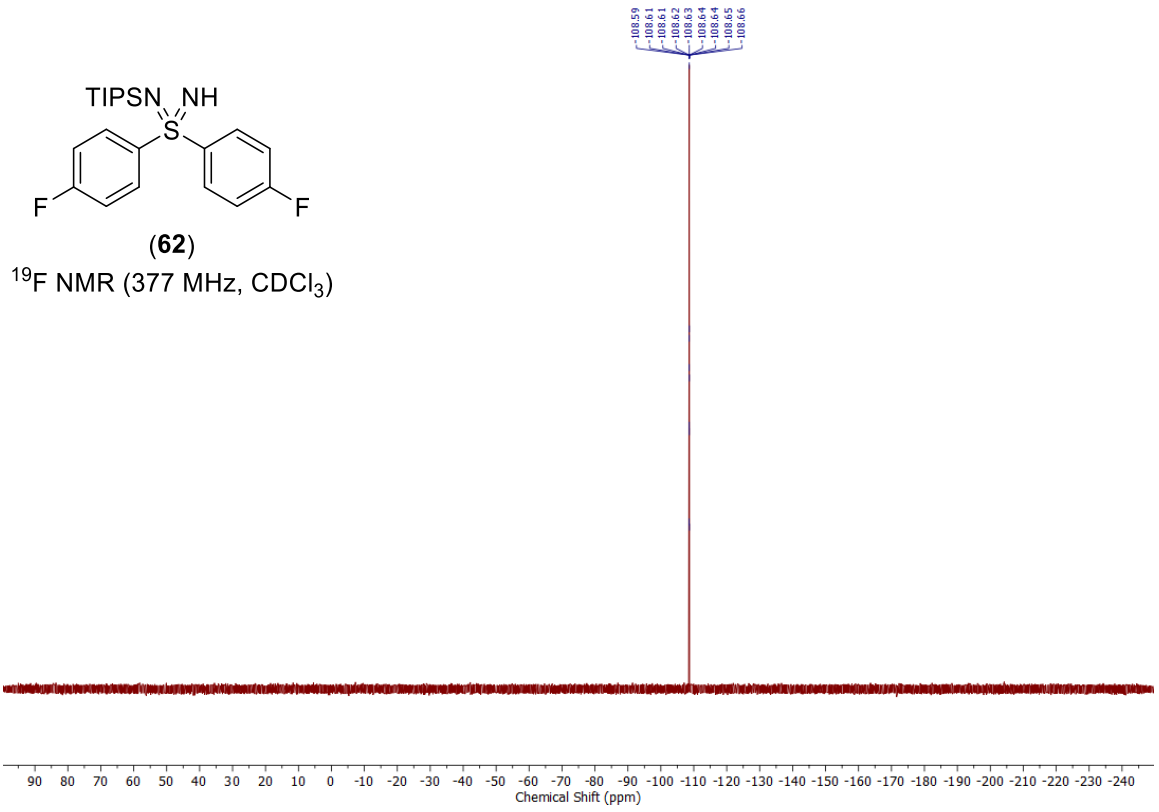




NMR spectra of 1,1-bis(4-fluorophenyl)-*N*-(triisopropylsilyl)-λ^6-sulfanediimine (62):







(**62**)

^{19}F NMR (377 MHz, $CDCl_3$)