Synthesis of Novel Aza-Sulfur(VI) Compounds

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June 2025

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A thesis submitted in partial fulfilment of the requirements for the degree of

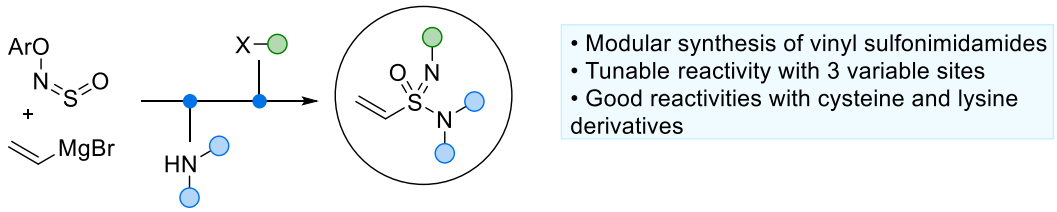
Doctor of Philosophy in Organic Chemistry

Abstract

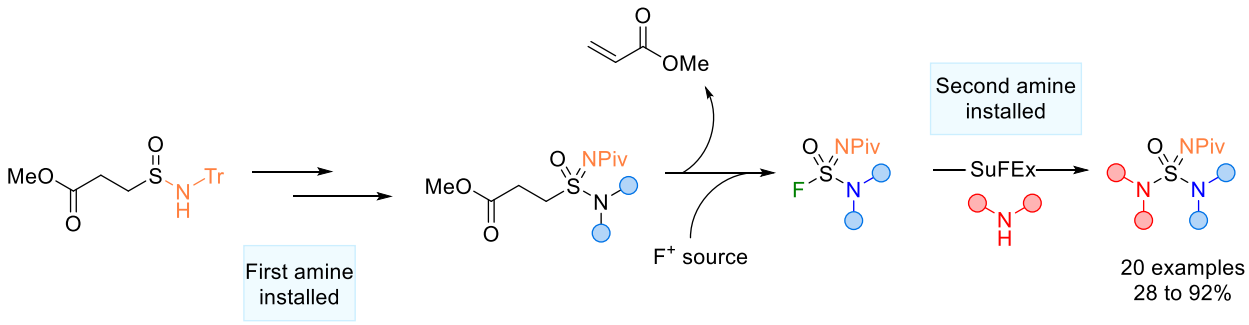
S(VI) based moieties exhibit promising pharmacological properties, and are present in over 150 FDA approved drugs currently available on the market. In this thesis, a variety of vinyl sulfonimidamides were synthesised and evaluated for their potential as bioisosteres of acrylamides. Furthermore, a novel methodology for the synthesis of rarely reported iminosulfamides was developed, employing a Lewis-acid mediated SuFEx amination system. The method enabled access to a broad variety of iminosulfamide derivatives with different amidic components.

Chapter 1 is a review introducing S(VI) functionalities, focusing on current synthetic strategies used for accessing sulfonamides, sulfonimidamides, sulfamides and iminosulfamides. The properties and application of these compounds are also described.

Chapter 2 focuses on the synthesis of *N*H vinyl sulfonimidamides, through a single-step from an aryl-ONSO reagent, a vinyl organometallic, and an appropriate amine. These vinyl sulfonimidamides have shown good reactivity towards cysteine and lysine derived nucleophiles, and the electrophilicity of these reagents can be modulated by choice of the imidic N-substituents and alkene substituents to achieve reactivity either above or below the corresponding acrylamide.



Chapter 3 describes a general and practical approach for synthesising a variety of sulfuramidimidoyl fluorides, through a key elimination/fluorination process using sulfonimidamide substrates. With the installation of electron withdrawing pivaloyl group, the reactivity of the S(VI) fluoride was enhanced, and a mild SuFEx amination reaction allowed the access to a wide variety of iminosulfamides, which were previously considered synthetically challenging.



Chapter 4 summarize the research and discusses potential areas for future work.

Chapter 5 provides experimental procedures and data for this research.

Declaration

The work described in this thesis is entirely the work of the author, except where specifically indicated. This thesis has not been previously submitted for a degree, diploma, or any other qualification at the University of Oxford or elsewhere.

Yu Tung Wong

June 2025

Acknowledgements

Firstly, I would like to express my deepest gratitude to Prof. Michael Willis for being a fantastic supervisor throughout my time at Oxford. Thank you for your invaluable guidance and creative insights into chemistry, and most importantly, for your encouragement and patience when things did not go as planned (which happens more often than not). Your support really meant a lot and help me overcome the many challenges I encoutered.

To all the past and present members of the Willis group, this is a fantastic group full of amazing people. It has been a good time in this group, thank you for all the precious memories. Special thanks to Charlie, Suzie, Mingkai, Cian, Kangtao, Di, Wyman and Matt, who proofread this thesis.

For people that I worked together in F1, you are all wonderful people, I really enjoyed the time working with you all. To Tony, thank you for taking care of me when I first joined the group, you have taught me a lot and help me familiarise with the lab. To Antoine, thank you for teaching me how to do my first waste duty. Janette, thank you for the 'welcome' door mat as my secret santa present. To Dan, really enjoyed the pub trip with you and the F1 boys. To Jonny and Ben, can't imagine how lucky I am to be able to sit next to you two in the office. You are both friendly and fun for chatting about random stuffs, and are smart and creative when discussing chemistry. To Jagadeesh, I often feel nervous when getting into new enivironment, and your friendliness helped me a lot. Loic and Damien, you are both excellent postdoc to work with. To Suzie and Josh, thank you for being the DJ and for the vibe you brought to F1, and thank you for helping to organise the lab (which I am not good at, even though I am more senior). Kangtao, you are a fun person to work with, and also an excellent flatmate and fantastic cook. Wyman, my new neighbour in the office and former senior colleague from CUHK, after 5 years and we are in the same group again, really enjoyed the time with you. Matt, it has been great time working next to you in the lab, and thank you for the marker pen 'the store request'! Cian, be more confident! You are a smart and great chemist. To all the part II and visiting students, Artem, Russell, Charlie Perry, Josh Mitchell, Em, Chris, Nerea, Lucia, Nikki, Luca, thank you for making F1 an excellent lab.

To people in F2, first of all, Charlie, thank you so much for everything, all the inspiring ideas, proofreading my manuscript, SI, thesis, powerpoint, thank you for all your help. Mingkai, you are a great friend and enthusiatic chemist, and I really enjoyed the time playing badminton together. Di, a sharp and straightfroward man, really fun to chat with you, I can ask your opions on anything and you will always give your answer without hesitation. Katherine and May, thank you for organising most of the social events and group lunch for the Willis group, which maintaine the friendships and vibe within the group. Mingyan, you are always nice and helpful, and fun to chat with. Cherry, welcome to the Willis group, I am sure you will enjoy the time staying in this wonderful group, and good luck being the 'senior DPhil' in F2. Tilby, Xinlan, Ndidi, Zexin, Nick, Aiden, Dominic, Gabby, Maia, Presiyan, Ria, Sajal, Erik, Niklas, thank you for making the Willis group an amazing place to work in. I would also like to express my gratitude also goes to the departmental service staff, especially for the staffs in NMR facility.

Lastly, I want to thank my family for all their support. No matter good or bad times, you are always by my side, giving me strength to overcome all the obstacles.

Table of Content

Abbreviations and Acronyms

Ac	acetyl
app.	apparent
aq.	Aqueous
Ar	aromatic
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
br.	broad signal
Bu	butyl
Bz	benzoyl
°C	degrees Celsius
cm^{-1}	wavenumber(s)
conc.	concentrated
d	doublet
DABCO	1,4-diazabicyclo[2.2.2]octane
DABSO	DABCO-Bis(SO2) adduct
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
decomp.	decomposition
DIPEA	*N*,*N*-diisopropylethylamine

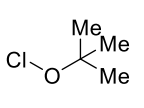
DMAP	4-dimethylaminopyridine
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
DNS	2,4-Dinitrobenzenesulfonyl
d.r.	diastereomeric ratio
E	electrophile
EDG	electron donating group
e.e.	enantiomeric excess
EI	electron ionisation
equiv.	equivalent(s)
ESI	electrospray ionisation
Et	ethyl
EWG	electron withdrawing group
FDA	food and drug administration
FT	Fourier Transform
g	gram(s)
h	hour(s)
HetAr	heteroaryl
HMDS	hexamethyldisilazane
HOBt	N-hydroxybenzotriazole

HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	hertz
Int.	intermediate
IR	infrared radiation
J	coupling constant
L	litre(s)
LRMS	low resolution mass spectrometry
µ	micro
m	multiplet/milli
M	mole(s) per litre/mega
$M^{+/-}$	molecular ion
Me	methyl
Min	minute(s)
mol	mole(s)
m.p.	melting point
Ms	methansulfonyl/mesyl
m/z	mass/charge ratio
NCS	*N*-chlorosuccinimide
n.d.	not detected

NFSI	*N*-fluorobenzenesulfonimidamide
NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
Ns	4-nitrobenzenesulfonyl
p	*para*
pent.	Pentet
Petrol	petroleum ether (boiling range 40-60 °C)
PG	protecting group
Piv	pivaloyl
PMP	*para*-methoxyphenyl
ppm	part(s) per million
Pr	propyl
q	quartet
R	generic substituent/group
rpm	revolution(s) per mintue
r.t.	room temperature
s	singlet
SAFs	sulfuramidimidoyl fluorides
sext	sextet
SuFEx	sulfur(VI)-fluoride exchange

t	tertiary
t	triplet
TBAF	tetra-n-butylammonium fluoride
t-BuSF	N,N-(diisopropylcarbamoyl)-2-methylpropane-2-sulfonimidoyl fluoride
TCCA	trichloroisocyanuric acid
Temp.	temperature
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin-layer chromatography
TMS	trimethylsilyl
t-Oct	*tert*-octyl
Tol	tolyl
Tr	trityl
Ts	tosyl
UV	ultraviolet
wt.%	percentage by weight
X	(pseudo)halide

Ligands and Chemical Structures



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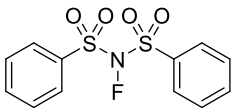

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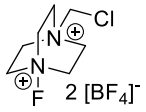

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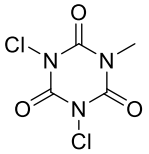

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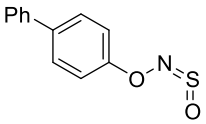
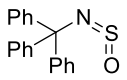
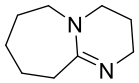


BiPhONSO

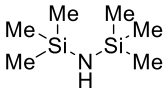


TrNSO

DABCO



DBU



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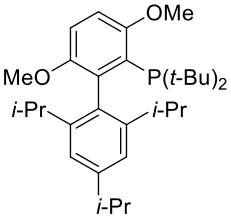


t-BuBrettPhos

Chapter 1 Introduction

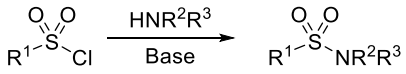
1.1 S(VI) compounds in Medicinal Chemistry

1.1.1 Sulfonamides

Sulfonamides are important structures in the pharmaceutical industry and have been used to treat various diseases for more than 80 years.[1] Up to 2024, there were more than 80 FDA approved drugs that feature a sulfonamide motif.[2, 3] They are widely considered as bioisosteres of amides, with several advantages including three dimensional geometry and better stability towards hydrolysis and metabolism.[4]

Synthesis of Sulfonamides

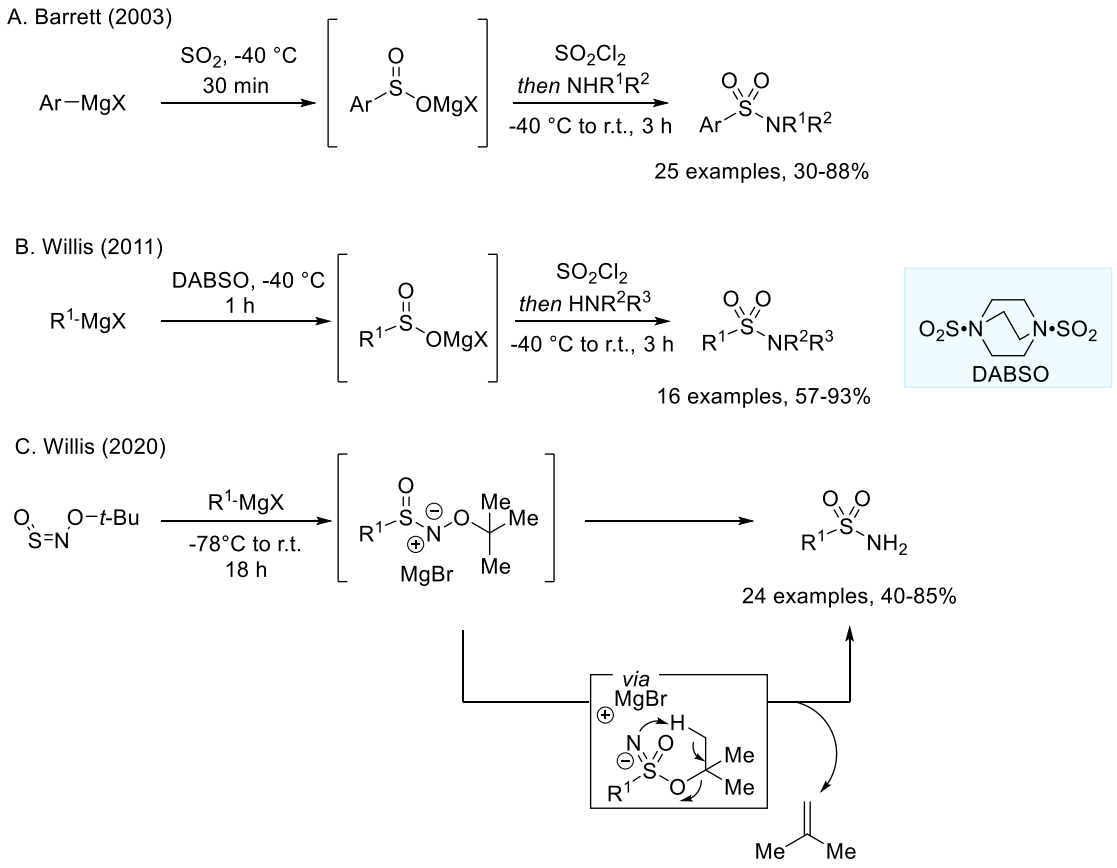
Early synthetic procedures for accessing sulfonamides heavily relied on the nucleophilic substitution reactions between amines and sulfonyl chlorides (**Scheme 1-1**).[5, 6] However, since sulfonyl chlorides are moisture sensitive,[7] and the synthetic procedures of sulfonyl chlorides often requires highly acidic reagents,[8] the scope of the reaction is limited. Sulfonamides can also be accessed through the oxidation of sulfenamides[9] or thiols[10] and disulfides with amines.[11] However, these low oxidation state sulfur(II) compounds are typically malodorous, and hence these synthetic routes tend to be avoided. To overcome this challenge, researchers have developed alternative strategies to synthesize sulfonamides, preferentially through the *in-situ* generation of sulfonyl chlorides using mild conditions.



Scheme 1-1 Synthesis of sulfonamides from sulfonyl chlorides.

In 2003, Barrett and co-workers reported a one-pot synthesis of sulfonamides through the combination of Grignard reagents with sulfur dioxide gas to form sulfinates and subsequent oxidative chlorination *in situ*

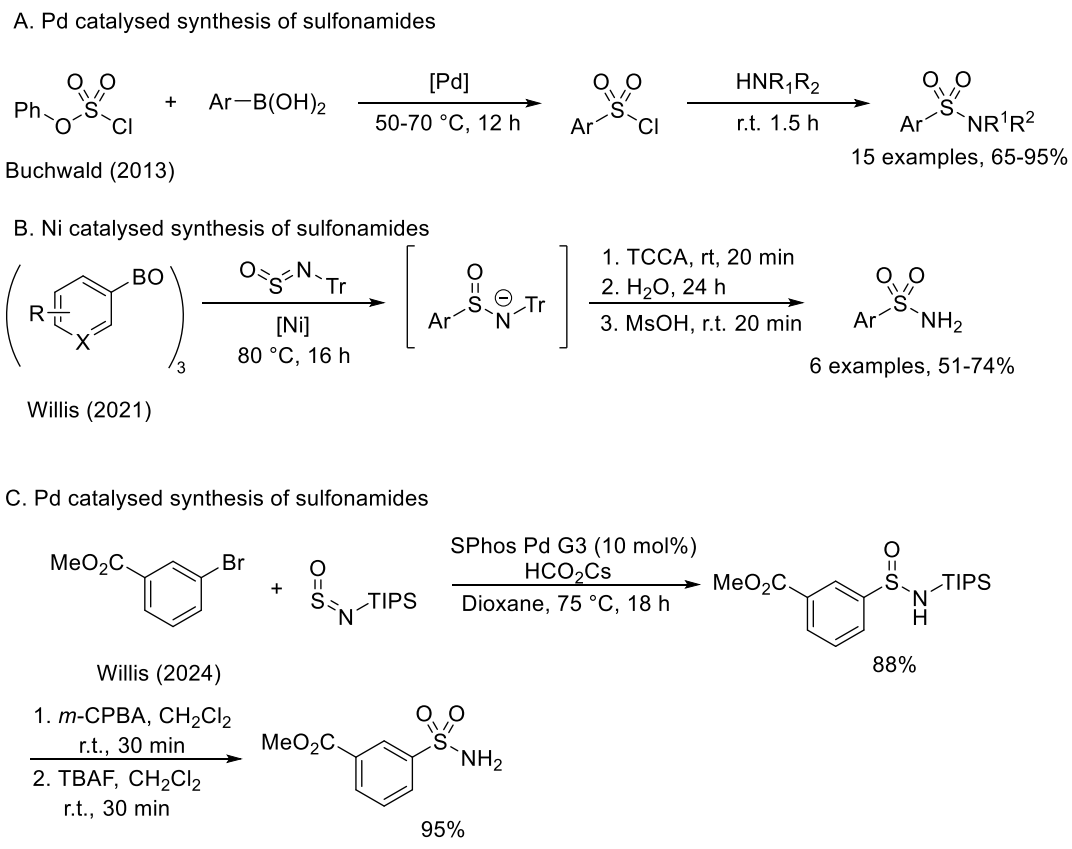
with sulfuryl chloride, followed by reaction with an amine to form the corresponding sulfonamides (**Scheme 1-2 A**).[12] To avoid the use of toxic gaseous SO_2, Willis and co-workers employed the bench stable solid SO_2 surrogate 1,4-diazabicyclo-[2.2.2]octane-bis(sulfur dioxide) (DABSO).[13] By combining Grignard reagents with DABSO, followed by the addition of sulfuryl chloride and an amine, the corresponding sulfonamides were obtained (**Scheme 1-2 B**). In 2020, the same group introduced a new sulfinylamine reagent N-sulfinyl-O-(tert-butyl)hydroxylamine (*t*-BuONSO), in combination with Grignard reagents to generate primary sulfonamides, through isobutene elimination (**Scheme 1-2 C**).[14]



Scheme 1-2 Synthesis of sulfonamides using SO_2 or SO_2 surrogates.

Alternative approaches can be carried out using transition metal catalyzed reactions, using either S(IV) or S(VI) reagents. Buchwald and co-workers developed an alternative pathway for accessing aryl

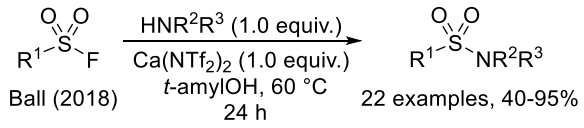
sulfonamides, through a Pd-catalyzed regioselective Suzuki-Miyaura cross coupling reaction between phenyl chlorosulfate and aryl boronic acids to give sulfonyl chlorides, followed by the addition of primary or secondary amines to form the corresponding sulfonamides (**Scheme 1-3 A**).[15] In 2021, Willis and co-workers also reported a Ni(II) catalyzed addition of hetero(aryl) boroxines to *N*-sulfinyltritylamine (TrNSO), followed by oxidative chlorination with trichloroisocyanuric acid (TCCA) and subsequent hydrolysis and acid deprotection to form the primary sulfonamide (**Scheme 1-3 B**).[16] Alternatively, palladium-catalysed addition of aryl halides to *N*-triisopropylsilyl sulfinylamine (TIPSNSO), followed by oxidation with *m*-CPBA and TBAF deprotection forms corresponding primary sulfonamide (**Scheme 1-3 C**).



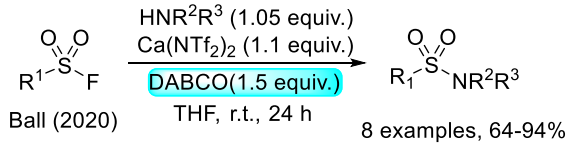
Scheme 1-3 Synthesis of sulfonamdes through transition metal catalysed reactions.

Another important approach to access sulfonamides and many other S(VI) compounds is through S(VI) fluoride intermediates such as sulfonyl fluorides. Although sulfonyl chlorides have been reliable intermediates for accessing sulfonamides, S(VI) chlorides are often highly moisture sensitive and unstable toward reduction when a carbon nucleophile is employed.[17] To address these limitations, Sharpless and co-workers re-introduced the concept of sulfur(VI) fluoride exchange (SuFEx) chemistry and suggested their potential in click chemistry, based on the unique reactivity and stability of sulfur(VI) fluorides.[18] The stability of sulfonyl fluorides can be attributed to the increased bond strengths of S-F(81±2 kcal mol^{-1}) relative to S-Cl(46±4 kcal mol^{-1}).[19] Given the stability of the S(VI)-F bond, the nucleophilic substitution reactions of sulfonyl fluorides often require excess amines with elevated temperature[20, 21] or strong bases.[22] In 2018, Ball and Ende reported the Lewis acid mediated sulfur(VI)-fluoride exchange using stochiometric calcium bistriflimide to synthesise sulfonamides (**Scheme 1-4 A**).[23] Although the reaction is base-free and does not require excess equivalents of amines, elevated temperatures are still required. In 2020, the same group reported the second generation of $Ca(NTf_2)_2$ mediated SuFEx reactions adding DABCO as a base, allowing the amine substitution to proceed at room temperature (**Scheme 1-4 B**).[24] In 2024, they published detailed mechanistic studies on this $Ca(NTf_2)_2$ mediated reaction, in which they suggested that the Ca^{2+} activates the sulfur(VI) fluoride by stabilizing the negative charges at the leaving fluoride and oxygen during the SuFEx process, while the DABCO acts as Brønsted base to activate the amine (**Scheme 1-5**).[25] The drawback of this synthetic method is that stoichiometric amount of Lewis acid were required, due to catalyst poisoning from the fluoride ion. The catalytic efficiency was found to be improved, through elevated temperature to facilitate the breaking of Ca-F bond and silyl additives as fluoride scavengers.[25] Based on this finding, they reported another synthetic stategy, employing silylamines as nucleophiles with elevated temperatures which enabled the reduction of catalyst loading to 10 mol% (**Scheme 1-4 C**).[26] Ball and co-workers also studied the effect of varying Lewis acids. Although other commercial available Lewis acids including $Ca(OTf)_2$ and $LiNTf_2$ can also be applied to the SuFEx reaction, $Ca(NTf_2)_2$ remained the best performing catalysts (**Scheme 1-4 D**).[26]

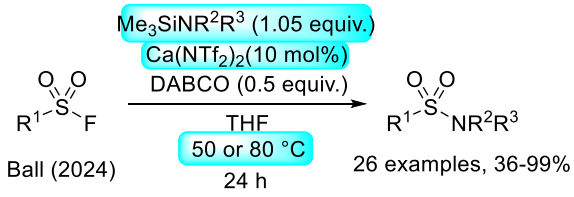
A. Generation 1 $Ca(NTf_2)_2$ activated SuFEx



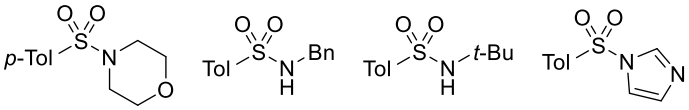
B. Generation 2 $Ca(NTf_2)_2$ activated SuFEx



C. Generation 3 $Ca(NTf_2)_2$ catalysed SuFEx

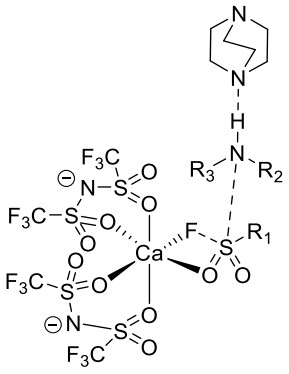


D. Varying Lewis acids with different TMS amine



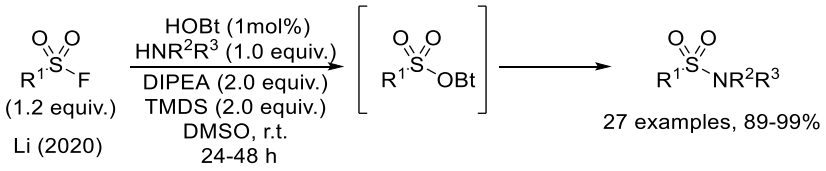
$Ca(NTf_2)_2$ (10 mol%)	81%	82%	86%	71%
$Ca(OTf)_2$ (10 mol%)	89%	64%	61%	70%
$LiNTf_2$ (10 mol%)	88%	68%	65%	41%

Scheme 1-4 $Ca(NTf_2)_2$ activated SuFEx reactions to access sulfonamides.



Scheme 1-5 Proposed mechanism for $Ca(NTf_2)_2$ and DABCO catalysed SuFEx.

Apart from Lewis acids, SuFEx reactions can also be promoted by a combination of 1-hydroxybenzotriazole (HOBt) with a silicon additive 1,1,3,3-tetramethyldisiloxane (TMDS) to access sulfonamides. The reaction pathway starts with the nucleophilic attack of $^{-}$OBt to the sulfonyl fluoride forming an activated intermediate, followed by amidation to form corresponding sulfonamides; good functional group tolerance has been achieved (**Scheme 1-6**).[27]



Scheme 1-6 HOBt catalysed SuFEx to access sulfonamides.

Applications of Sulfonamides in Drugs

Sulfonamides have proven to be an important class of bioactive compound in the pharmaceutical industry. The first commercially available sulfonamide drug Prontosil (**Figure 1-1**) was discovered in 1932.[28] Since then, numerous bioactive compounds containing sulfonamide moieties have been disclosed, possessing

antibacterial,[29] anticancer,[30] diuretic,[31] hypoglycemic,[32] antithyroid,[33] or protease inhibitory activity.[34] In 2016, sulfonamides were present in 15% of the top 100 best-selling drugs, including Sildenafil, Sulfadiazine and Probenecid (**Figure 1-1**). [35] Sulfonamides are structurally related to amides, but afford unique physicochemical properties, such as higher aqueous solubility, polarity and increased hydrogen bond binding affinity.[36-38] This is contributed by its tetrahedral geometry with an additional oxygen atom, used as a hydrogen bond acceptor.[39] There have been various examples of sulfonamide analogues of amide inhibitors, which show excellent biological activities,[39-42] including a carbohydrate based quorum sensing inhibitor in which replacing the amide moiety to a sufonamide motif gave 12-fold better activity.[43]

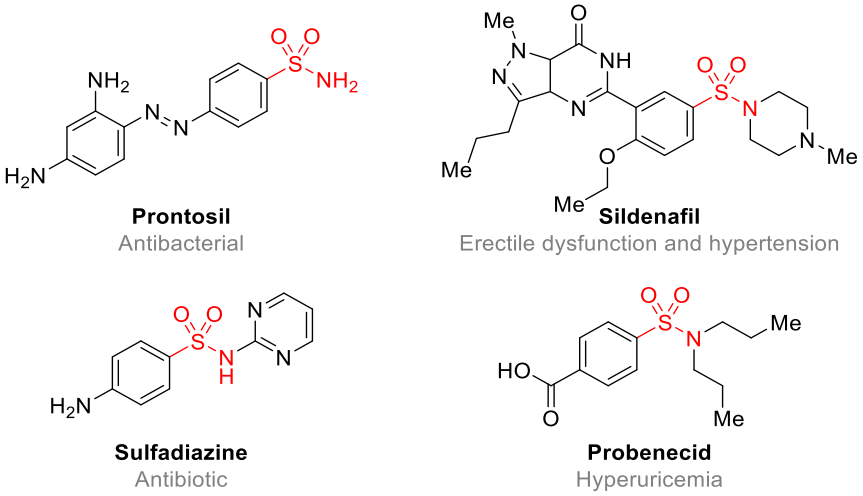


Figure 1-1 Examples of marketed drugs containing sulfonamide motifs.

The strong electron withdrawing nature of sulfonamides also brings benefits when constructing electrophilic warheads. For instance, vinyl sulfonamides have been considered as the potential bioisosteres of acrylamides, which are one of the most abundant motifs in covalent inhibitors and occupy 10% of the FDA approved covalent warhead to date.[44] Compared with acrylamides, vinyl sulfonamides are more electrophilic due to the stronger electron-withdrawing nature from the sulfonyl group, thus having higher reactivity toward nucleophilic amino acids.[45] Indeed, vinyl sulfonamides have been considered as covalent

warheads targeting cysteine in proteins, and have been found in various covalent inhibitors including a USP7 inhibitor,[46] a KRAS inhibitor[47] and a ERK2 inhibitor (**Figure 1-2**).[48] These α,β-unsaturated sulfonamides motifs can be easily synthesized by reacting 2-chloroethansulfonyl chloride with secondary amines, in the presence of triethylamine (**Scheme 1-7**).[49] Recent studies from Nomura and co-workers also revealed a vinyl sulfonamide based protein degrader, which shows superior performance over other common covalent groups (**Figure 1-2**).[50] Additionally, Armstrong and co-workers recently reported a study using vinyl sulfonamides for irreversible tethering.[51] Biochemical assays showed that ethylene glycol linked vinyl sulfonamides have intrinsic reactivity, and that the reactivity of the electrophiles can be modulated by the linker (**Figure 1-3**).

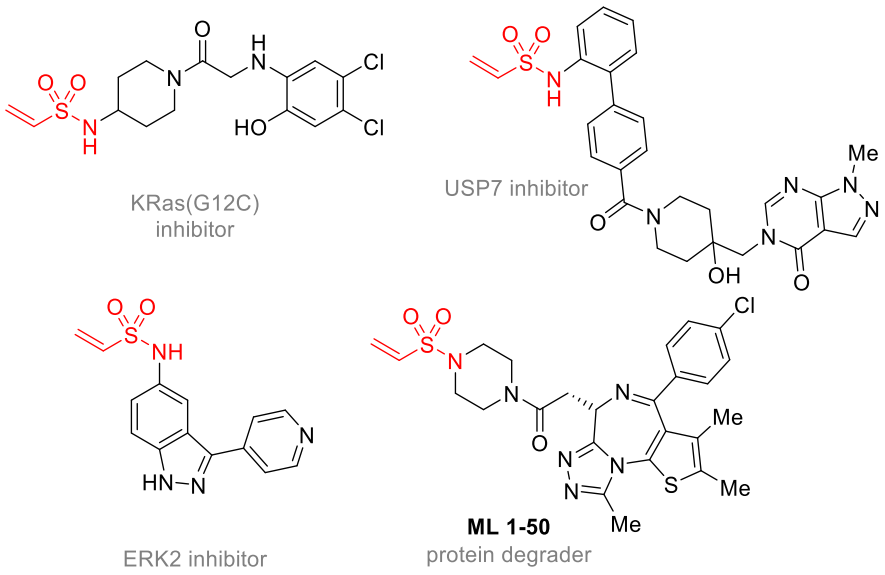
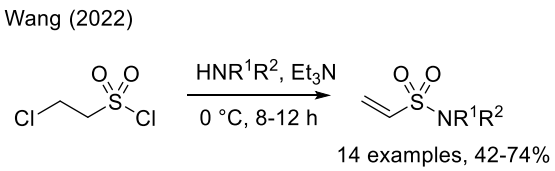


Figure 1-2 Examples of covalent inhibitors containing a vinyl sulfonamide warhead.



Scheme 1-7 Synthesis of vinyl sulfonamides.

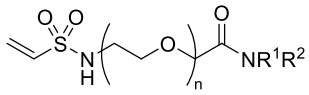


Figure 1-3 Polyethylene glycol linked vinyl sulfonamide.

Sulfonamides in the Agrochemical Industry

Organosulfur compounds are also essential for crop protection, with more than 30% of agrochemicals containing at least one sulfur atom.[52,53] Sulfonamides are popular chemical compound for designing agrochemicals, and can be commonly found in herbicides or fungicides. For instance, Asulam (**Figure 1-4**), a commercial aryl sulfonamide herbicide was described in 1965 and used in agriculture for control of stubborn weeds.[54] It has very low environmental and toxicological impact, and is rapidly degraded in soil thus possessing low chronic toxicity.[55]

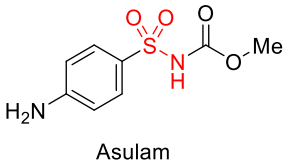


Figure 1-4 Structure of herbicide Asulam.

1.1.2 Sulfonimidamides

Despite the significance of sulfonamides in medicinal chemistry, their mono-aza analogues, sulfonimidamides were rarely explored until recently.[56] A significant reason for this is the lack of quick and robust synthetic methods to prepare these molecules.[57] Compared with sulfonamides, sulfonimidamides possess several interesting desirable features. The replacement of an oxygen to a nitrogen atom introduces a configurationally stable stereogenic center at sulfur,[58, 59] which is an increasingly important structural feature for designing selective, bioactive molecules.[56] Sulfonimidamides can also undergo tautomerism

through proton transfer between the amidic and imidic nitrogen atoms, allowing both nitrogen atoms to be hydrogen bond donors or acceptors.[56] This tautomerism can be controlled by the choice of substituent on the nitrogen atoms.[60] The imine nitrogen atom is both basic and nucleophilic, therefore it can be functionalized to tune the physicochemical and biological properties of the molecule (**Figure 1-5)**.[61] Research shows that by differing the *N*-substituents on sulfonimidamides, their pharmacokinetic parameters, including liphophilicity, dissociation constants, and aqueous solubility can be changed significantly.[62] There have been various studies on the biological properties of sulfonimidamides and they have been proven to be potential bioisosteres of structures like sulfonamides or imidazoles.[63-65]

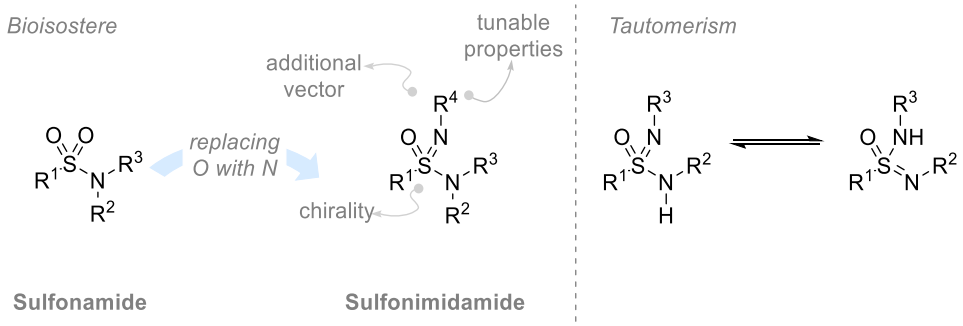
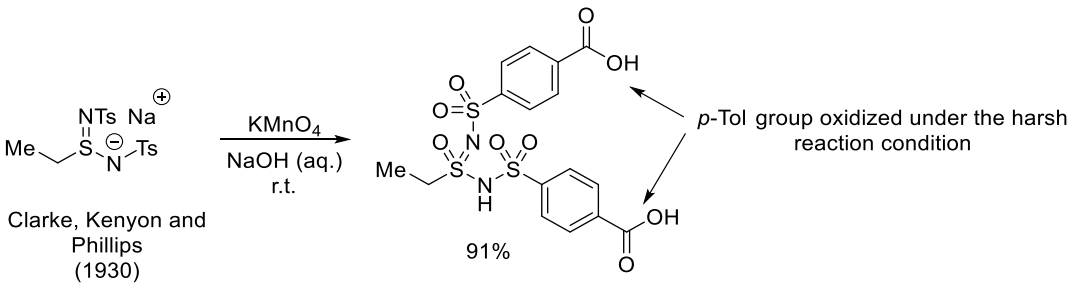


Figure 1-5 Structure and properties of sulfonimidamides.

Synthesis of Sulfonimidamides

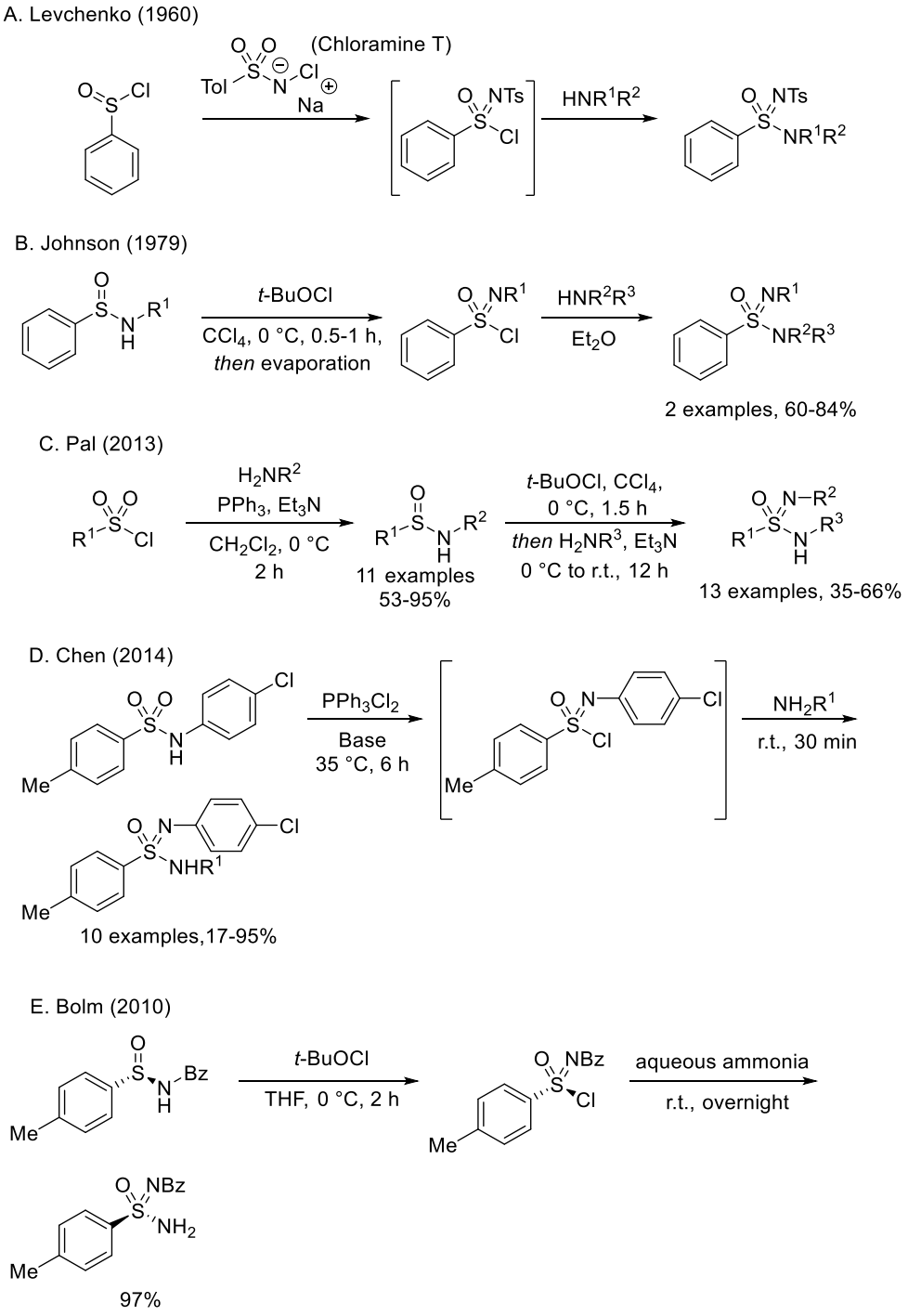
The first example of sulfonimidamide synthesis was reported in 1930 by Clarke, Kenyon and Phillips, through the reaction of potassium permanganate with a sulfinamidine salt (**Scheme 1-8**).[66] However, the harsh reaction conditions required limited the uptake of this synthetic strategy.



Scheme 1-8 First example of sulfonimidamide synthesis.

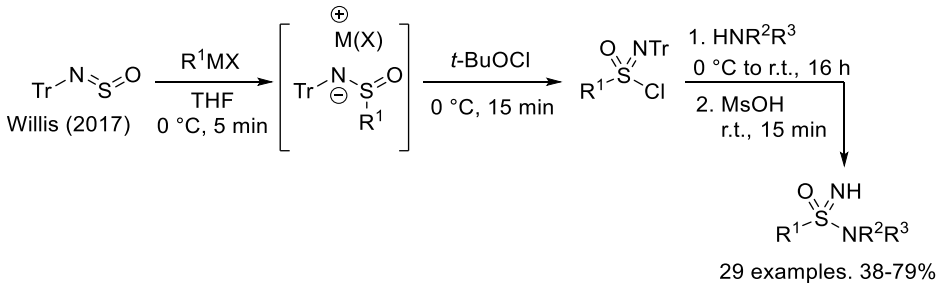
In 1960, Levchenko and co-workers established a more general synthetic route to access sulfonimidamides, through the transformation of sulfinyl chlorides (which are unstable and have to be used immediately) into sulfonimidoyl chlorides, followed by nucleophilic substitution with an amine (**Scheme 1-9 A**).[67] However, the use of highly sensitive sulfinyl chlorides, and the instability of *N*-alkyl or *N*-aryl chloroamines, limited the application of this synthetic strategy. In 1969, Johnson and co-workers reported an alternative strategy starting from the oxidative chlorination of bench-stable sulfinamides with *tert*-butyl hypochlorite to form sulfonimidoyl chlorides, followed by solvent swap and addition of an amine to form corresponding sulfonimidamides (**Scheme 1-9 B**).[68] This procedure is still widely used for preparing sulfonimidoyl chlorides because of the clean and simple experimental procedure, with other chlorinating agents such as *N*-chlorosuccinimide (NCS) and trichloroisocyanuric acid (TCCA) also being used.[69-71] In 1992, Roy reported the synthesis of sulfonimidamides, by deoxychlorination of *N*-silyated sulfonamides to sulfonimidoyl chlorides using PPh_3Cl_2 and subsequent reaction with amines.[72] In 2013, Pal and co-workers reported the conversion of sulfonyl chlorides to sulfonimidamides, through a reductive amine coupling strategy to generate sulfinamides, which underwent oxidative chlorination and subsequent amination formed the corresponding sulfonimidamides (**Scheme 1-9 C**).[73] A similar strategy was later employed by Chen and co-worker in 2014, converting sulfonamides to sulfonimidamides in one-pot (**Scheme 1-9 D**).[74] Note that Johnson,[75] Reggelin[76] and Bolm[70] have shown the retention of configuration for the oxidative chlorination step. They suggested that the nucleophilic displacement of the sulfonimidoyl chloride with

ammonia occurred with inversion of configuration, and this hypothesis was later confirmed by Bolm and co-workers (**Scheme 1-9 E**).[70]



Scheme 1-9 Synthesis of sulfonimidamides through sulfonimidoyl chloride intermediates.

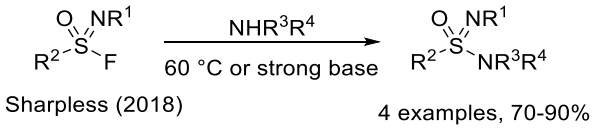
One of the major disadvantages of above synthetic routes is the limited availability of sulfinamides and sulfonamides. Although significant progress in the synthesis of sulfinamides from thiols, disulfides or sulfonyl chlorides[77, 78] had been achieved, the procedures typically involve unstable sulfinyl chlorides intermediate, and the R^1 group on sulfur is determined by the initial choice of thiol or sulfonyl chlorides. To tackle this problem, Willis and co-workers reported a one-pot synthesis of sulfonimidamides in 2017, using a sulfinylamine reagent, TrNSO, as the N=S=O linchpin (**Scheme 1-10**).[79] By reacting TrNSO with commercial available organometallic reagents, followed by chlorination of the anionic sulfinamide intermediate with *tert*-butyl hypochlorite and subsequent reaction with amine, formed the corresponding sulfonimidamides, which can be deprotected with methanesulfonic acid to generate N-H sulfonimidamides in a one-pot sequence.



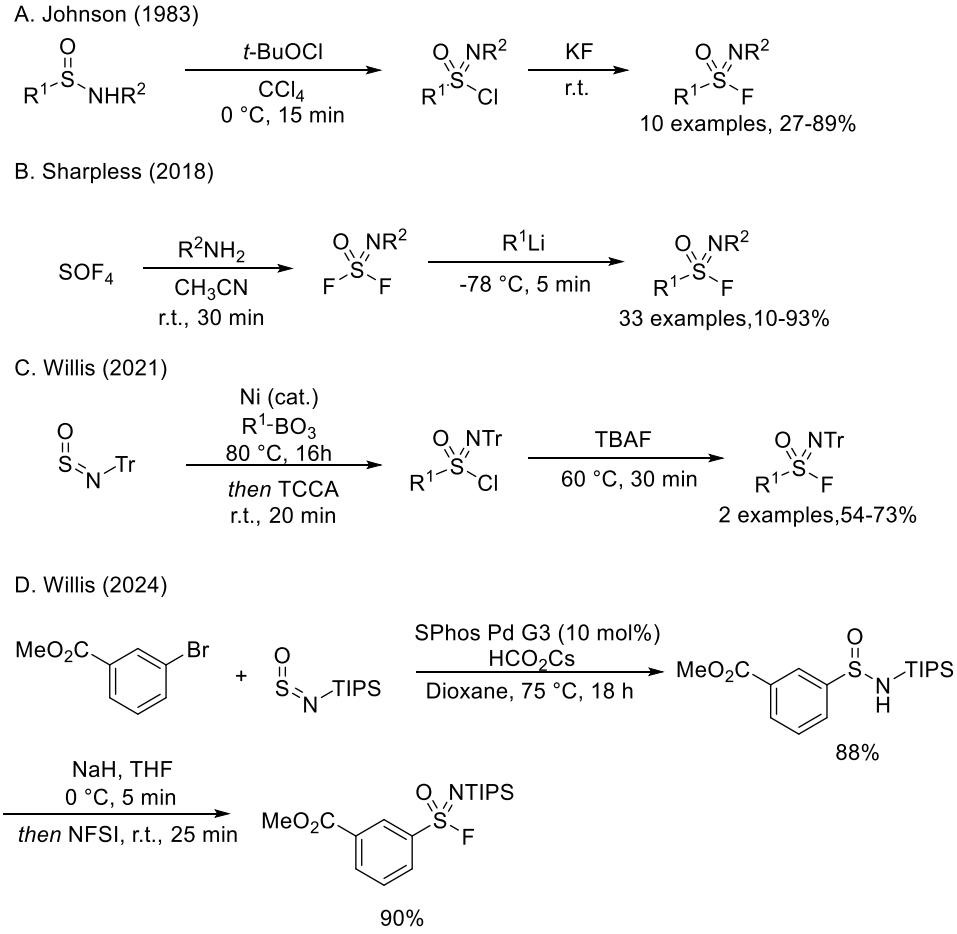
Scheme 1-10 One pot synthesis of sulfonimidamides from TrNSO.

Because of the inherent instability of S(VI) chlorides, most of them cannot not be stored and must therefore be generated and used *in situ*. To overcome this limitation, researchers have shifted their focus toward sulfonimidoyl fluorides, which offer improved stability and broader synthetic utility. Similar to that of sulfonyl fluorides, mono-aza analogues sulfonimidoyl fluorides can be used for synthesising sulfonimidamides. Sharpless and co-workers utilized SuFEx chemistry, through nucleophilic substitution with amines to form sulfonimidamides (**Scheme 1-11**).[80] The key intermediate sulfonimidoyl fluorides were synthesized through reacting thionyl tetrafluoride with primary amines to form iminosulfur oxydifluorides,

followed by treatment with organolithium reagents to give sulfonimidoyl fluorides. Alternative methods for accessing sulfonimidoyl fluorides includes the oxidative chlorination of sulfinamides, followed by halogen exchange with a suitable fluoride source.[81] Recently, more reliable and modular synthetic strategies of sulfonimidoyl fluorides were developed through *N*-sulfinylamines such as TrNSO[16] and TIPSNSO.[82]

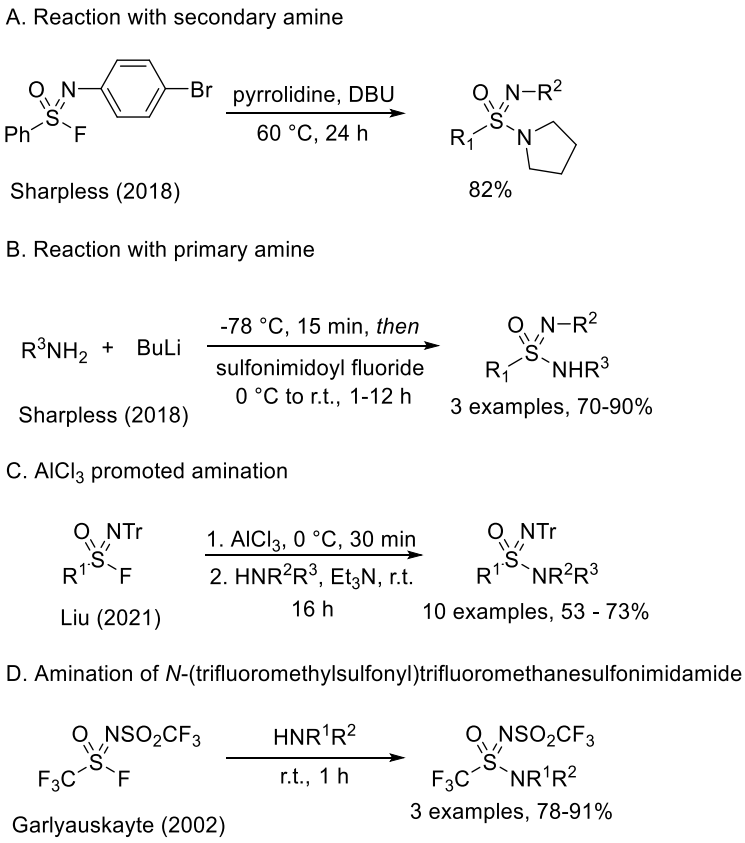


Scheme 1-11 Synthesis of sulfonimidamides from sulfonimidoyl fluorides.



Scheme 1-12 Synthesis of sulfonimidoyl fluorides.

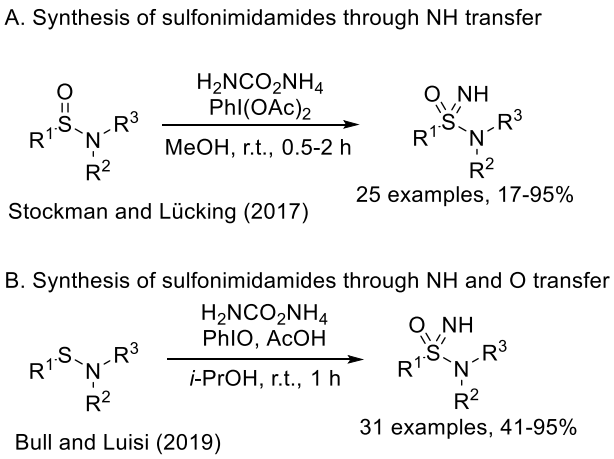
The reactions of sulfonimidoyl fluoride with nitrogen nucleophiles often requires relatively harsh conditions, which involves elevated temperature or strong base (**Scheme 1-13 A and B**).[80] Liu and co-workers showed that pre-treatment of sulfonimidoyl fluorides with $AlCl_3$ facilitates the reaction to proceed at room temperature (**Scheme 1-13 C**), although this method has little uptake due to functional group incompatability issues.[83] The reactivity of sulfonimidoyl fluorides can also be enhanced by installing electron withdrawing groups on the carbon and nitrogen substituent, in which the amination can occur under room temperature (**Scheme 1-13 D**).[84]



Scheme 1-13 SuFEx amination of sulfonimidoyl fluoride.

Apart from the conventional routes which proceed through the sulfonimidoyl chloride or fluoride intermediates, another strategy for synthesizing sulfonimidamides was reported by Stockman and Lücking

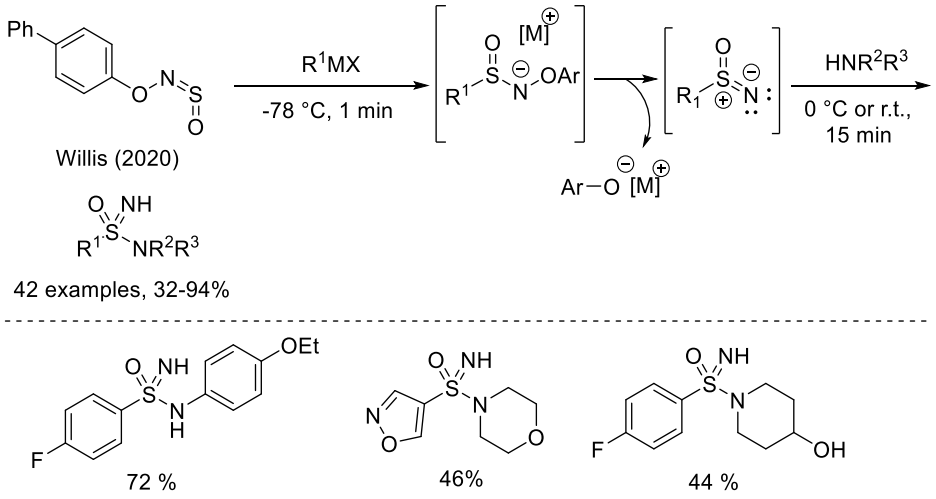
in 2017 (**Scheme 1-14 A**).[85] By applying the NH-transfer method, previously developed by Bull and co-workers[86] for sulfoxides on sulfinamides, the desired sulfonimidamides could be synthesized. However, the reaction was limited to the use of tertiary sulfinamides, since the reactions of primary and secondary sulfinamides resulted in sulfonimidates.[85] Bull and co-workers further developed a new one-pot NH and O transfer reaction to access sulfonimidamides using sulfenamides as starting materials, which are bench-stable and can be readily prepared from disulfides and amine (**Scheme 1-14 B**).[87]



Scheme 1-14 Synthesis of sulfonimidamides through NH transfer.

Most of the common routes for synthesising sulfonimidamides requires an external oxidant to form the sulfonimidoyl chlorides or fluorides from S(IV) species. Willis and co-workers envisioned that by reacting sulfinylamine reagents with carbon nucleophiles, if an appropriate leaving group is present on the nitrogen, a reactive sulfinyl nitrene intermediate would be formed. Thus, they reported a new synthetic route, using BiPhONSO, a sulfinylhydroxylamine reagent, to access sulfoximines and sulfonimidamides (**Scheme 1-15**).[88] Through the addition of Grignard reagents, a sulfinyl nitrene intermediate is formed by the N-O bond cleavage, which subsequently reacted with an amine to form the corresponding *N*-H sulfonimidamides. The key intermediate involved a sulfinyl nitrene, which was formed by the N-O bond cleavage. This

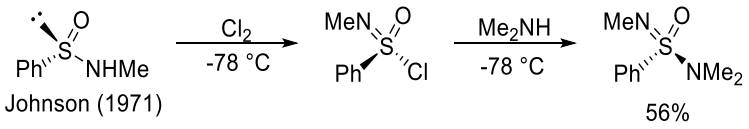
synthetic strategy tolerates a wide range of functional groups, including bulky amines, primary amines, anilines and various heterocycles.



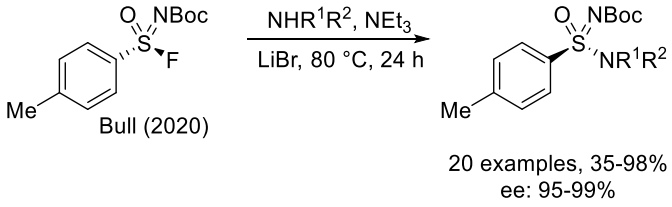
Scheme 1-15 One-pot synthesis of sulfonimidamides using BiPhONSO.

Enantioenriched Sulfonimidamides

Since sulfonimidamides contain a stereogenic center, the synthesis of enantioenriched sulfonimidamides has been an attractive area for researchers. The most reliable way for accessing enantiopure sulfonimidamides typically employs optically active sulfinyl derivatives.[89] Johnson and co-workers reported the first synthesis of optically active sulfonimidamides in 1971, through the chlorination of sulfinamides, followed by reaction with dimethylamine (**Scheme 1-16**).[75] Bull and co-workers also reported the synthesis of enantioenriched sulfonimidamides through stereospecific SuFEx reactions, using LiBr as the fluoride scavenger to prevent the racemisation of sulfonimidoyl fluoride caused by nucleophilic attack of excess fluoride ions (**Scheme 1-17**).[90]

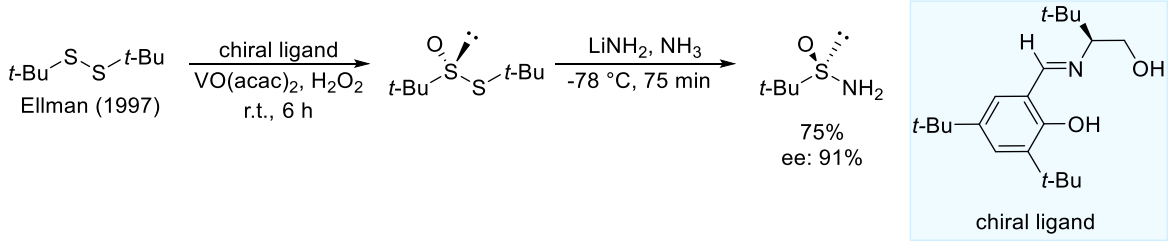


Scheme 1-16 First example of enantioenriched sulfonimidamide synthesis.



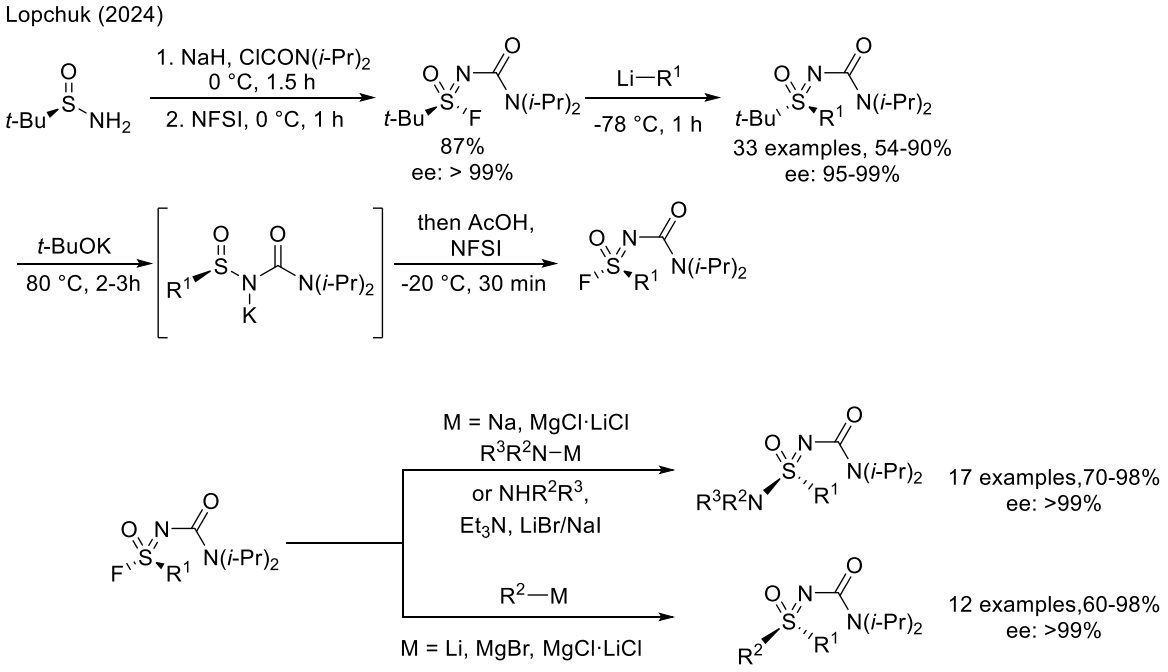
Scheme 1-17 Synthesis of enantioenriched sulfonimidamides through stereospecific SuFEx reactions.

Among the accessible enantiopure sulfinamides, *tert*-butanesulfinamide, known as the Ellman auxiliary, is one of the most commonly used intermediates for synthesising chiral S(IV) and S(VI) compounds.[89] Ellman and co-workers reported the asymmetric synthesis of enantiopure *tert*-butanesulfinamide in 1997, starting from the catalytic asymmetric oxidation of *tert*-butyl disulfide in the presence of vanadium catalysts and Schiff-base chiral ligands to access the enantiopure thiosulfinate intermediate, followed by the addition of lithium amide in ammonia, affording the desired enantioenriched sulfinamide from achiral starting material (**Scheme 1-18**).[91]



Scheme 1-18 Synthesis of Ellman auxiliary (*tert*-butanesulfinamide).

Employing the Ellman auxiliary, Lopchuk and co-workers synthesized the enantiopure bifunctional S(VI) transfer reagent *N*,*N*-(diisopropylcarbamoyl)-2-methylpropane-2-sulfonimidoyl fluoride (*t*-BuSF), an enantiopure sulfonimidoyl fluoride which undergoes SuFEx reactions with organolithium reagents to generate chiral sulfoximines. Enantioenriched *tert*-butyl sulfoximines can then be reduced to S(IV) species with *t*-BuOK to generate the sulfinyl urea intermediates, which undergo subsequent fluorination with NFSI to form enantiopure sulfonimidoyl fluorides in one-pot. The corresponding sulfonimidoyl fluorides then react with organometallic reagents or amine nucleophiles, providing the enantiopure sulfoximine or sulfonimidamides, respectively (**Scheme 1-19**).[92]



Scheme 1-19 Accessing sulfonimidamides and sulfoximine through bifunctional S(VI) transfer reagent.

Application of Sulfonimidamides in Medicinal Chemistry

The first reported biological activity study for sulfonimidamides was conducted by Johnson and co-workers in 1979. They synthesized the sulfonimidamide analogues of hyperglycaemic agent tolbutamide and sulfadiazine, but they did not exhibit sufficient activities to be of interest as antibacterials.[93] In 1997, Toth and co-workers synthesized the sulfonimidamide analogues of antitumor sulfonyl urea LY181984. Although the plasma exposure of the sulfonimidamide analogue was much lower than the parent drug after oral administration, it could be dosed at non-toxic levels and produced significant antitumor activity. One interesting finding was that only the (-)-enantiomer of the analogue shows antitumor activities, and the (+)-enantiomer also produced different metabolite (**Figure 1-6**). This suggested that the chirality of sulfonimidamides indeed has a significant effect on their biological properties.[94]

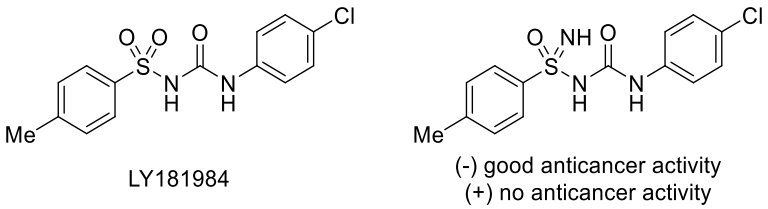


Figure 1-6 Sulfonimidamide analogue of an antitumor sulfonyl urea.

With the huge potential shown by sulfonimidamides in drug development, there have been numerous studies on the biological activities of sulfonimidamides, and they have been shown to exhibit a wide range of inhibitory activities, including Na^+/H^+ transporter,[95] γ-Secretase[63] and dipeptidyl peptidase-IV.[96]

Although sulfonimidamides have yet to been found in any approved drug, there is already a NLRP3 inhibitor containing sulfonimidamide motif, which is currently in phase II clinical trials (**Figure 1-7**). The in-human study suggested that DFV890 has good permeability, safety and tolerability, and has the potential to be a clinically effective oral NLRP3 inhibitor, warranting further clinical evaluation. [97]

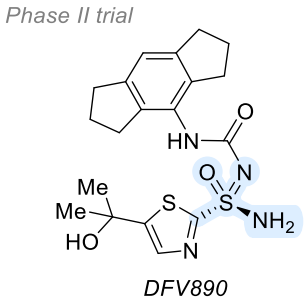
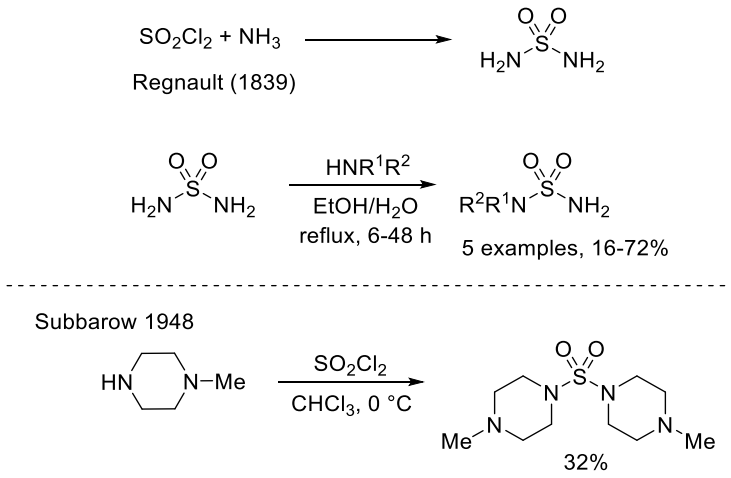


Figure 1-7 NLRP3 inhibitor containing sulfonimidamide motif.

1.1.3 Sulfamides

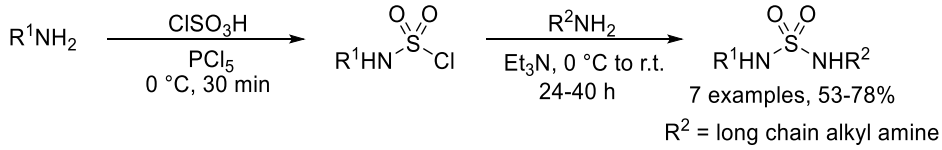
Synthesis of Sulfamides

Sulfamides, in which the carbon substituent of sulfonamides is replaced by a nitrogen substituent, are important analogues of sulfonamides. In general, the synthesis of sulfamides relies on nucleophilic substitution of amines with sulfuryl chloride or a sulfamoyl chloride. The earliest synthetic method for accessing sulfamides was reported in 1839 by Regnault (**Scheme 1-20**),[98] through the reaction of sulfuryl chloride and gaseous ammonia. The *N*-primary, *N'*-primary sulfamide generated (which is now commercially available) can undergo amide exchange reactions to form non-symmetric sulfamides.[99, 100] Alternatively, sulfuryl chloride could react with excess amine to form symmetric sulfamide.[101]



Scheme 1-20 Synthesis of sulfamides and amide exchange.

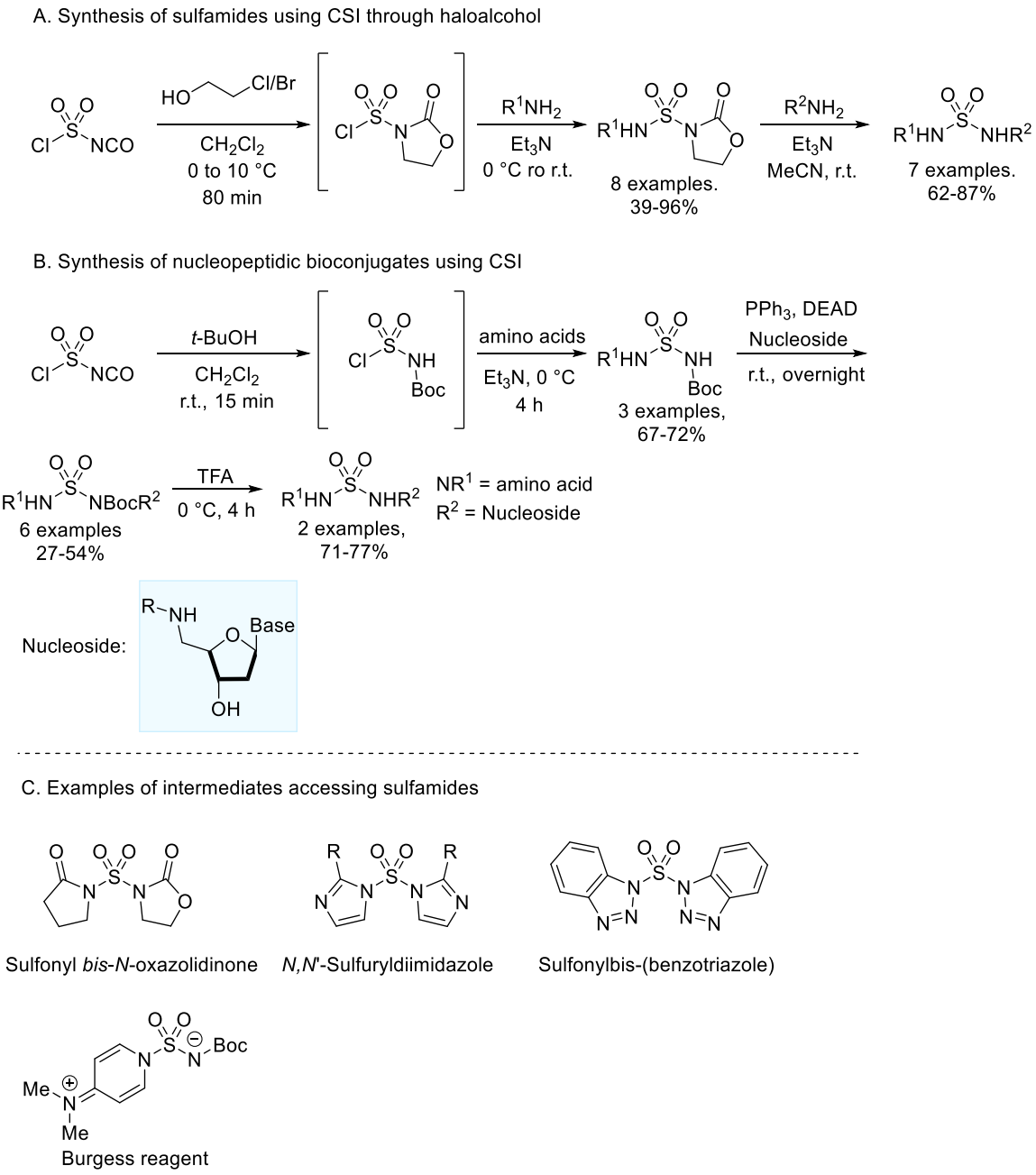
Although sulfuryl chloride is an efficient reagent for accessing symmetrical sulfamides, sulfamoyl chlorides are essential intermediates for constructing unsymmetrical sulfamides. In 1976, Lechinsky and co-workers reported the synthesis of *N*-alkyl sulfamoyl chlorides, by treating primary or secondary amines with a combination of chlorosulfonic acid and phosphorus pentachloride.[102] This sulfamoyl chloride intermediate was later utilized by Goya and Fonseca to synthesis sulfamide derived analogues of long chain oleyl ethanolamide (**Scheme 1-21**).[99]



Scheme 1-21 Synthesis of sulfamides using chlorosulfonic acid.

Another important route for synthesising non-symmetric sulfamides is through the use of chlorosulfonyl isocyanate (CSI), which is a commercially available reagent. CSI can be treated with 2-bromo or 2-chloroethanol to give *N*-sulfamoyloxazolidinones, via addition to the isocyanate and subsequent ring

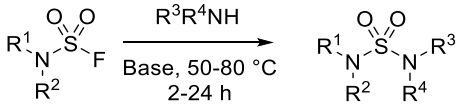
closure. This intermediate reacts *in situ* with a primary amine to displace the chloride, followed by addition of a second primary amine to form the corresponding sulfamides (**Scheme 1-22 A**).[103] CSI can also react with *tert*-butanol to form a sulfamoyl chloride intermediate, followed by an amine addition and subsequent Mitsunobu reaction of the Boc-*N*H sulfamide and acidic deprotection to form corresponding sulfamides. Montero and Imbach employed this synthetic route to synthesize nucleopeptidic bioconjugates that contain a sulfamide bridge (**Scheme 1-22 B**).[104] Some other reliable intermediates to access sulfamides include sulfonyl *bis*-*N*-oxazolidinone,[105] *N*,*N'*- sulfuryldimidazole,[106] sulfonylbis(benzotriazole)[107] and Burgess reagent (**Scheme 1-22 C**).[108] These intermediates are either commercially available or derived from sulfinyl chloride, and are stable to storage.



Scheme 1-22 Synthesis of sulfamides using CSI and related intermediates.

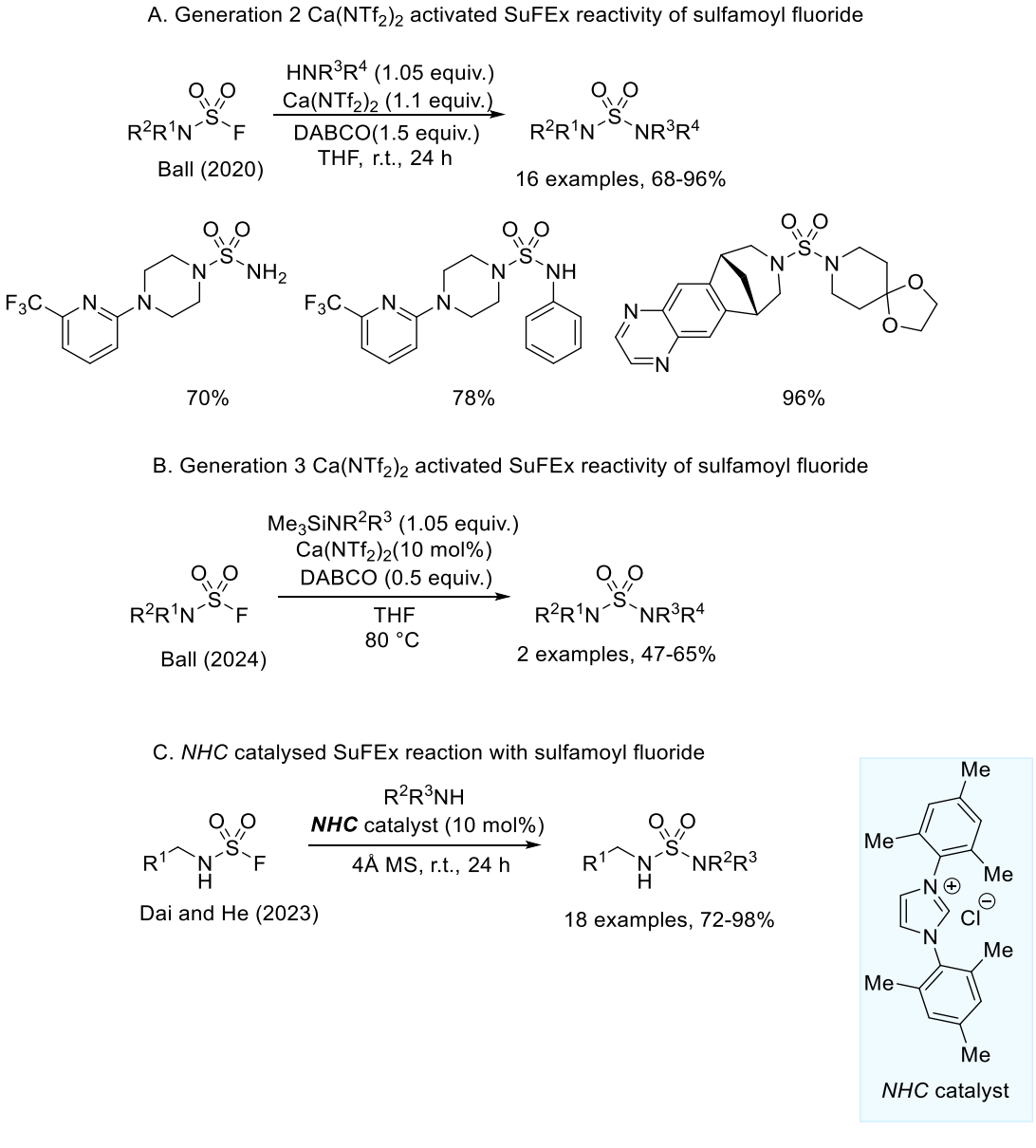
Similar to their chloride derivatives, sulfamoyl fluorides reacts with amines to form sulfamides. Compared with sulfonyl fluorides, the resonance donating nitrogen atom reduces the electrophilicity of the sulfur atom,

which leads to reduced reactivity,[24] thus the nucleophilic amine substitution reactions often require harsher conditions than used for sulfonyl fluorides.[80, 109]



Scheme 1-23 General reaction condition for sulfamoyl fluorides reaction with amines.

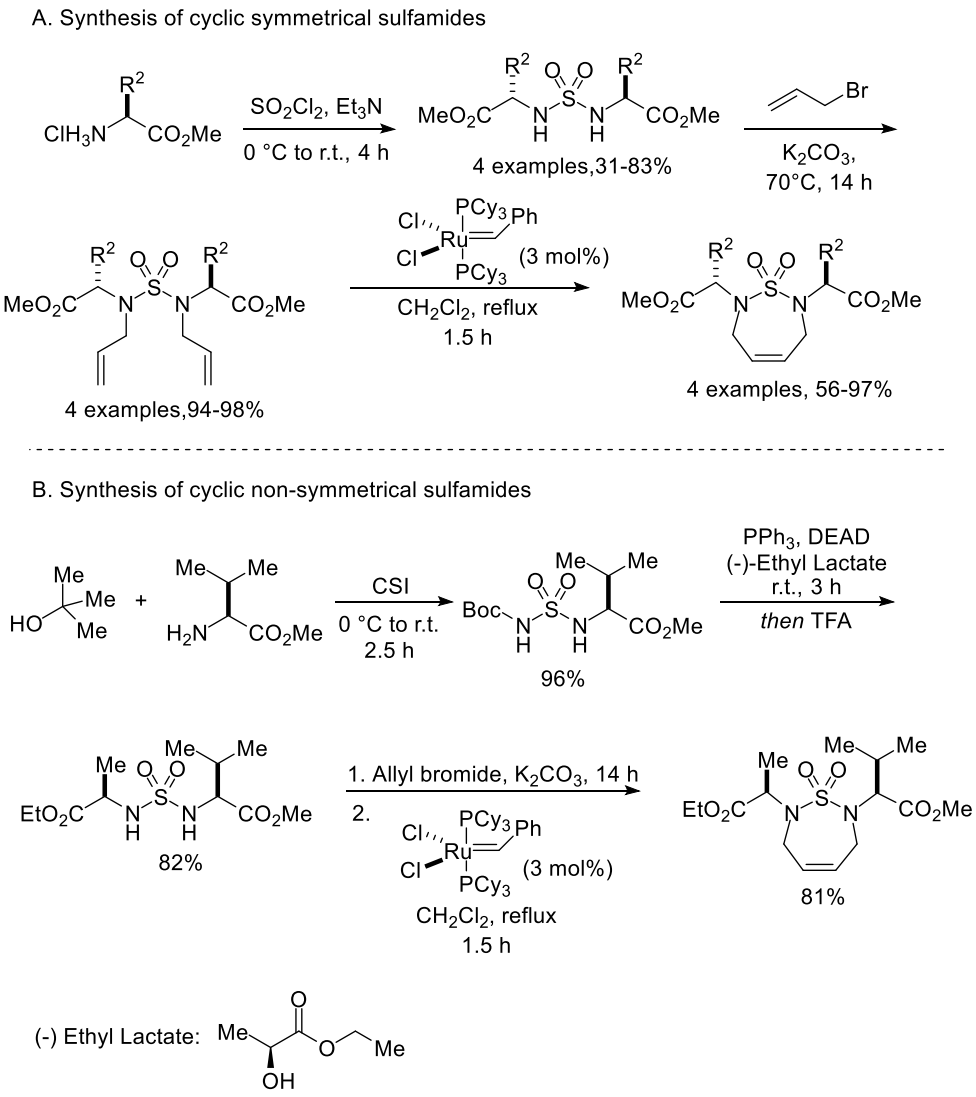
As mentioned previously, Ball and co-workers reported a calcium triflimide activated sulfonamide synthesis from sulfonyl fluorides (**Scheme 1-4 A**).[23] However, when they applied the same conditions with sulfamoyl fluorides, the reaction did not go to full conversion even using excess amounts of amines. With further investigation, aforementioned second generation of $Ca(NTf_2)_2$ mediated SuFEx reaction, utilising DABCO, can be applied to sulfamoyl fluorides and fluorosulfates at room temperature **(Scheme 1-24 A**).[24] Although stochiometric $Ca(NTf_2)_2$ is employed, the catalyst loading of $Ca(NTf_2)_2$ can be lowered to 10 mol% by heating and employing silylamines (**Scheme 1-24 B**).[26] Dai and He reported another SuFEx reaction of sulfamoyl fluorides at room temperature, using *N*-heterocyclic carbenes (NHC) as Brønsted base in combination with amines to access sulfamides, with molecular sieves used to abstract the HF generated from the reaction (**Scheme 1-24 C**).[110] However, aromatic and secondary aliphatic amine derived sulfamoyl fluoride were not amenable to this synthetic strategy.



Scheme 1-24 Lewis acid and NHC catalysed SuFEx reaction of sulfamoyl fluorides.

Similar to acyclic sulfamides, cyclic sulfamides can be synthesized from SO_2Cl_2 or CSI. For instance, Hanson and co-workers reported the synthesis of amino acid derived C_2-symmetric sulfamides using SO_2Cl_2. By reacting excess amino ester with SO_2Cl_2, followed by diallyation and ring closing metathesis using Grubbs catalyst gave the corresponding symmetrical cyclic sulfamides (**Scheme 1-25 A**).[111] They

also described a synthetic strategy for unsymmetrical cyclic sulfamides, through reacting CSI with *t*-BuOH and amino esters to form sulfamoyl chloride intermediates, followed by regioselective Mitsunobu reaction, acidic deprotection, diallylation and ring closing metathesis to obtain the unsymmetric cyclic sulfamide (**Scheme 1-25 B**).[111]



Scheme 1-25 Synthesis of cyclic sulfamides.

Applications of Sulfamides

With two nitrogen atoms attached, sulfamides offer huge structural diversity with up to four different amidic substituents possible. Because of its highly polarized nature, the water solubility and bioavailability of a drug can be increased by incorporating a sulfamide moiety.[112] Sulfamide motifs have shown potent inhibition in diseases associated with proteolytic enzymes, serine protease, HIV protease and noroviruses.[113-115] Plentiful examples of marketed drugs contain a sulfamide motif which plays a key role in their biological activity, including Doripenem,[116] Quinagolide,[117] Macitentan[118] and Famotidine (Figure 1-8).[119] Unlike sulfonamides, sulfamide can be used to synthesise both symmetrical or nonsymmetrical inhibitors, and have shown distinct property and structure-activity relationships compared with corresponding ureas.[120, 121] The HN-SO_2-NH motif of cyclic sulfamide HIV protease inhibitors was found to substitute an essential water molecule for catalysis with aspartate residues, thus facilitating the inhibition of the protease.[122]

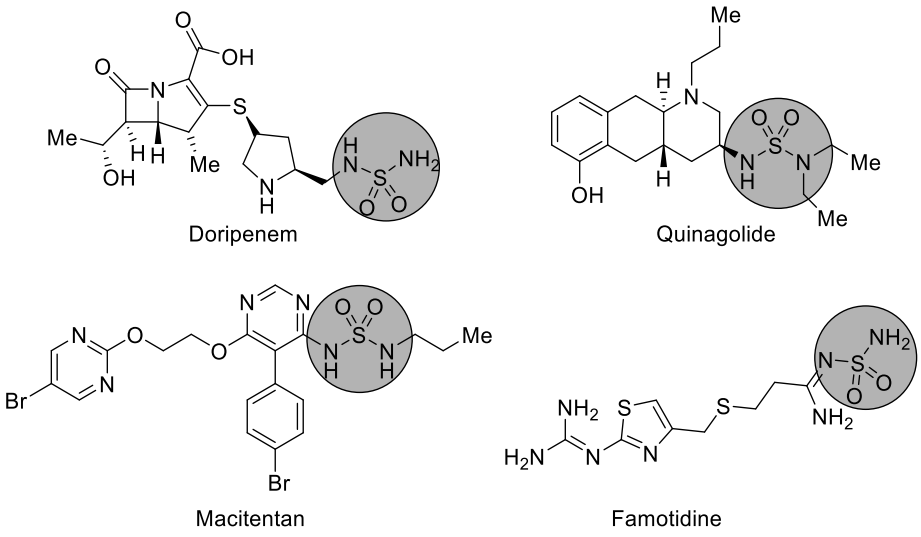
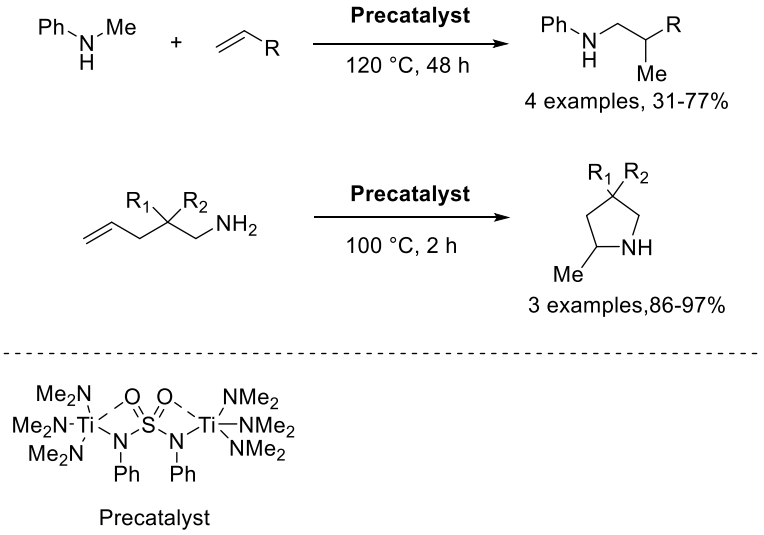


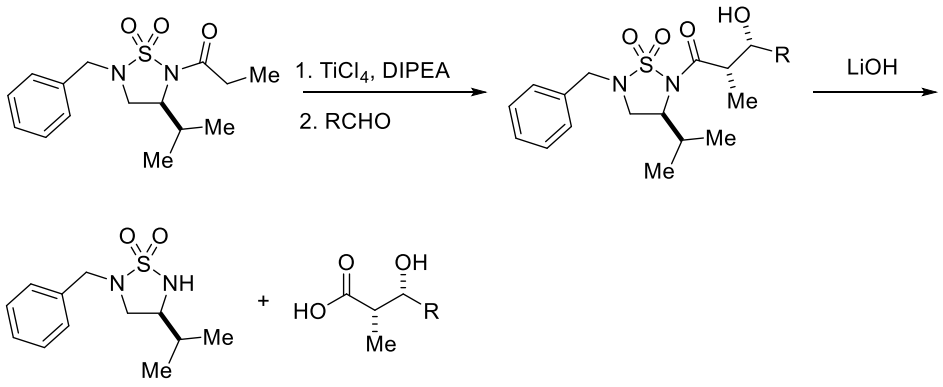
Figure 1-8 Examples of marketed drugs containing sulfamide motifs.

Apart from medicinal chemistry, sulfamides are often used as catalysts or ligands in organic synthesis. For instance, Doye and co-workers employed titanium complexes with sulfamide ligands as precatalysts for

hydroaminoalkylation and hydroamination reactions (**Scheme 1-26**).[123] Sulfamides containing chiral amidic components can also act as chiral auxiliary for asymmetric synthesis. Dewynter and co-workers reported a synthetic route using a cyclic sulfamide which can act as a chiral auxiliary to access diastereo-controlled aldol products. These can be hydrolysed with LiOH to form the corresponding β-hydroxy acids (**Scheme 1-27**).[124]



Scheme 1-26 Sulfamide as ligand for hydroaminoalkylation and hydroamination.

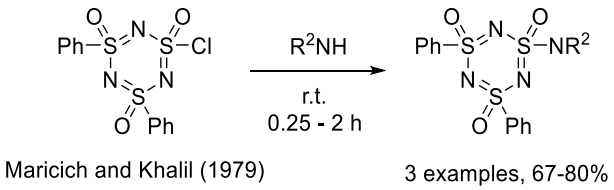


Scheme 1-27 Sulfamide as chiral auxillary for asymmetric synthesis.

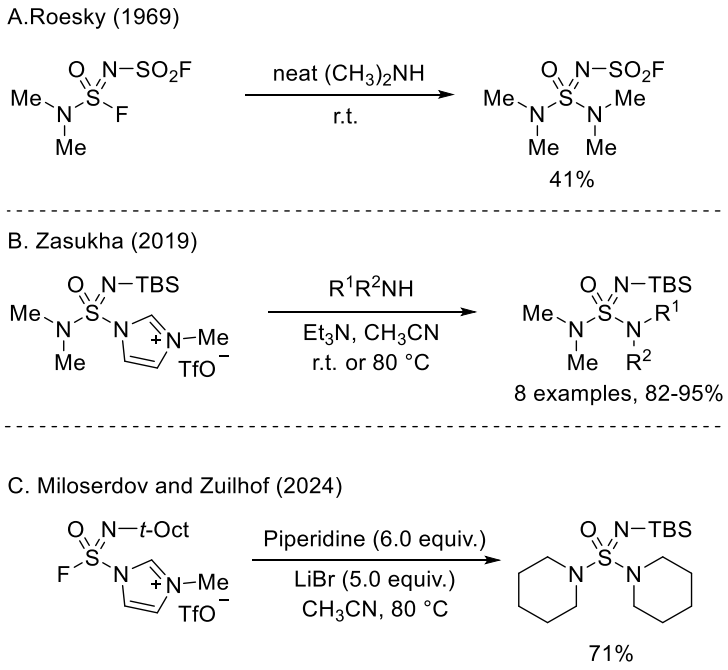
1.1.4 Iminosulfamides

Synthesis of Iminosulfamides

Despite the wide application of sulfamides, the aza-analogue of sulfamides, iminosulfamides, have remained largely underexplored, likely due to a paucity of methods for their synthesis. The earliest examples of an iminosulfamide was reported by Roesky in 1969, through the SuFEx reaction of sulfuramidimidoyl fluorides with neat dimethylamine (**Scheme 1-29 A**). Maricich and Khalil also reported a synthetic strategy in 1979, through reaction of sulfuramidimidoyl chlorides with secondary amines.[125] There were a few synthetic examples of iminosulfamides reported afterward, but they are mostly in six-membered heterocyclic structure and often with only with limited examples.[126, 127] In 2019, Zasukha and co-workers provide a significant breakthrough, using a 1-sulfamimidoyl-3-methylimidazolium intermediate, synthesising 9 examples of iminosulfamides (**Scheme 1-29 B**).[128] These bench-stable reagents are accessed from reaction of *N*-(*tert*-butyldimethylsilyl) derived sulfamide with *in situ* generated Ph_3PCl_2, followed by amine substitution with imidazole and subsequent methylation using MeOTf. Miloserdov and Zuilhof also showed an example of iminosulfamide synthesis by reacting the imidazolium salt of 2-methylimidazole-1-(N-tert-octyl)sulfonimidoyl fluoride with excess piperidine and LiBr to form the corresponding iminosulfamide (**Scheme 1-29 C**).[129]



Scheme 1-28 Synthesis of iminosulfamdies through reaction of iminosulfonimidoyl chloride.



Scheme 1-29 Synthesis of iminosulfamides through imidazolium intermediate.

Application of Iminosulfamides

Although there are to date no examples of marketed drugs containing an iminosulfamide motif, studies have shown that they exhibit a range of potential biological activities, including anticancer, anti-inflammatory, antifibrotic and sodium channel inhibition.[130-134] It was also reported that iminosulfamides can also be used for synthesizing organic electronic devices, which gave the highest external quantum efficiency among the selected heterocyclic compounds.[135]

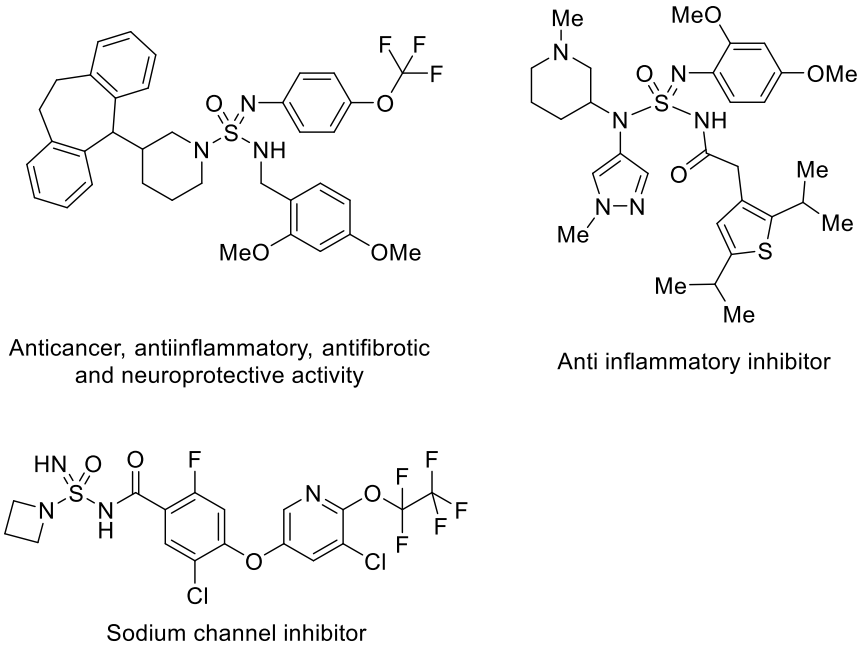


Figure 1-9 Inhibitors containing iminosulfamide motif.

1.2 Summary and Research Aims

This introduction has described various synthetic strategies for accessing several important S(VI) compounds. Sulfonamides are well explored moieties and have become an essential part in the pharmaceutical industry. Their aza-analogues, sulfonimidamides, have demonstrated huge potential with distinct biological activity and pharmacokinetic properties, but are yet to appear in a marketed drug. In chapter 2 of this thesis, vinyl sulfonimidamides are chosen to explore their potential as bioisosteres of acrylamides, through reactivity and kinetic studies.

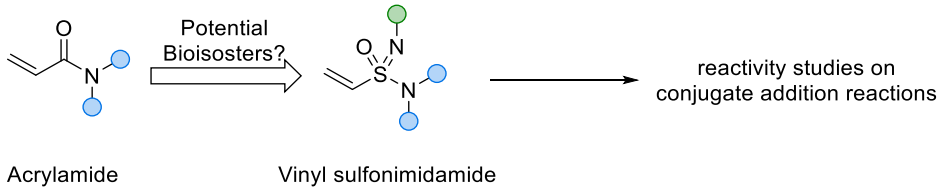


Figure 1-10 Research aim (Chapter 2).

On the other hand, although sulfamides can be readily synthesized through different methods, the synthesis of iminosulfamides remains underexplored, with only limited literature precedents and limited scope. In chapter 3 of this thesis, a new synthetic strategy is described to access iminosulfamides through iminosulfonimidoyl fluoride intermediates. The installation of an amine to the sulfinamide combined with the SuFEx reactions allows the access to a wide range of iminosulfamides with different functionalities.

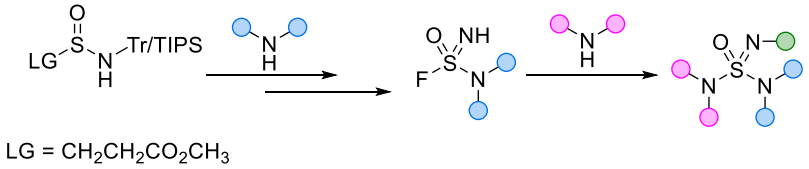


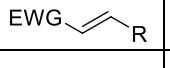
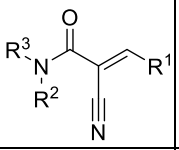
Figure 1-11 Research aim (Chapter 3).

Chapter 2 Synthesis and Functionalisation of Vinyl Sulfonimidamides and Their Potential as Electrophilic Warheads

2.1 Origin of Project and Previous work

Covalent inhibitors are small molecules that inactivate their target through covalent linkage. Despite having the advantage of high drug potency, long residence time and decreased drug resistance rate,[136] the pharmaceutical industry had tended to avoid the use of covalent inhibitors due to their potential off-target effects associated with toxicity. To address this potential drawback, a new approach was taken to develop covalent drugs, through targeting non-catalytic nucleophiles in proteins. The covalent inhibitors developed, referred to as 'targeted covalent inhibitors', contain a non-covalent binding site which specifically targets the desired site, enhancing its selectivity and minimizing the potential for toxicity due to off-target effects.[137] Covalent warheads react with nucleophilic amino acid residues on targeted proteins through 1,2- or 1,4-additions. The modification can be reversible or irreversible, depending on the type of warhead (**Table 2-1**).[138-144] Among the covalent warheads reported in CAS Content Collection, more than 45% contain an α,β-unsaturated carbonyl, which react with targeted residues through a Michael addition.[145]

Table 2-1 Selected examples of covalent warheads.

Warhead	Target residue(s)	Mode of modification
	Cys	Irreversible
	Cys	Reversible
	Ser, Lys	Irreversible
	Cys, Lys, Thr, His	Irreversible
	Ser, Thr, Lys, Tyr	Irreversible

Of the over 10,000 covalent inhibitors present in the Covalent inhibitor Database,[146] over 50% have a mechanism of action as Michael addition. Within this group, acrylamides are the most popular warhead used, which can be found in 15 approved drugs[146] and occupy 10% of FDA-approved covalent warheads.[44] Acrylamide based drugs exhibit a wide range of biological activities, including anticancer,[147] antiviral,[148] antibacterial,[149] anti-inflammatory,[150] and antidiabetic activities.[151] There have been studies that investigate the difference in reactivity of acrylamides with cysteine or glutathione (GSH) by altering the nitrogen substituent or employing α- or β-substituted alkenes.[45, 152, 153] For instance, the KRAS inhibitor, adagrasib, was found to have minimal GSH metabolism and improved bioavailability by the incorporation of a 2-fluoroacrylamide moiety.[154]

As mentioned in chapter 1 (**Figure 1-2**), vinyl sulfonamides have been considered as a more electrophilic alternative of acrylamide, and have proven to be active covalent warheads.[46-48] However, the reactivity of both acrylamide and vinyl sulfonamides are limited to the variation of the amidic *N*-substituent or the substitution group on the alkene. On the other hand, the mono-aza analogue of sulfonamides, sulfonimidamides, with the presence of the imidic nitrogen, provides opportunities for the tuning of

physiochemical and biological properties of these molecules (**Figure 2-1**). We envisioned that vinyl sulfonimidamides could act as a potential bioisosteres of acrylamide and vinyl sulfonamides.

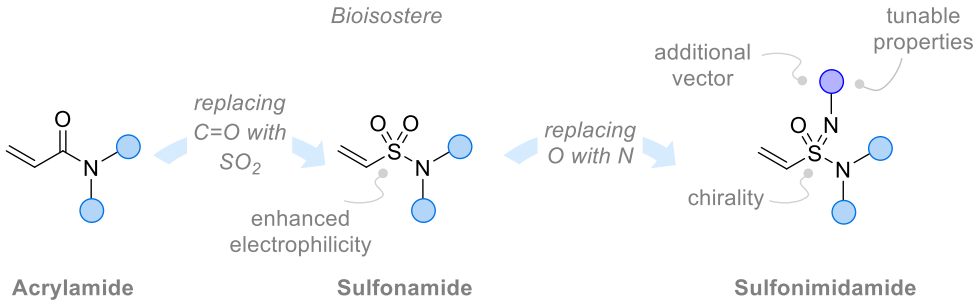
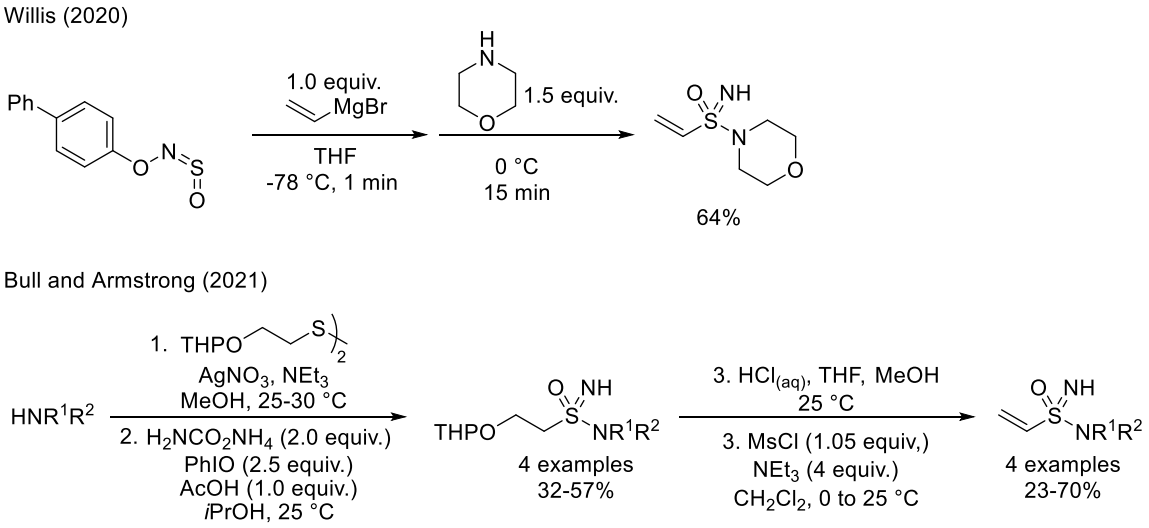
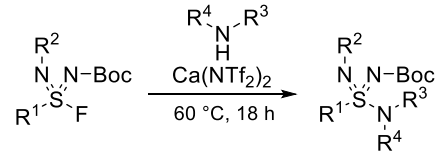


Figure 2-1 Sulfonamide and sulfonimidamide as potential bioisosteres of acrylamide.

In 2020, Willis and co-workers published the first synthetic example of vinyl sulfonimidamides, using BiPhONSO, vinyl magnesium bromide and morpholine (**Scheme 2-1**).[88] Bull and Armstrong also synthesised a series of these compounds and showcased the stability and configuration of vinyl sulfonimidamides.[155] Given that vinyl sulfonamides have already been proven as potential covalent warheads (**Figure 1-2**), we envisioned that vinyl sulfonimidamides could also act as bioisosteres of acrylamides. At the time this project was initiated, there were very few precedents in the literature, highlighting the novelty and unexplored potential of this compound class. Willis and Co-workers in 2024 reported a modular synthesis of sulfondiimidoyl fluorides, which undergoes SuFEX reaction to generate sulfondiimidamide and sulfondiimine. They described that by replacing the imidic substituent R^2 to an electron withdrawing urea group, the reactivity of the sulfondiimidoyl fluorides increased significantly (**Scheme 2-2**). [61] Given that the nitrogen substituent on aza S(VI) reagents has demonstrated to have a marked effect on reactivity with nucleophilic species, we were interested in evaluating this in the context of vinyl sulfonimidamides.



Scheme 2-1 Examples of the synthesis of vinyl sulfonimidamides.



Willis (2024)

	Morpholine	Butylamine	Cyclobutyl amine
R^2 = Si(*i*-Pr)$_3$	82%	0%	0%
R^2 = morpholine urea	95%	81%	92%

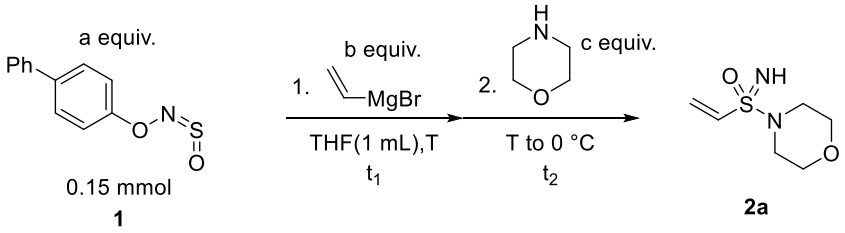
Scheme 2-2 Effects of nitrogen substituent on the reactivity of aza(SVI) compounds .

2.2 Synthesis of Vinyl Sulfonimidamides

The initial work of the project focused on the synthesis of vinyl sulfonimidamides with different amine components, employing the one-pot synthetic strategy mentioned above (**Scheme 2-1**).[88] Literature conditions were initially trialled, with a moderate yield (50%) of **2a** obtained using BiPhONSO **1**, vinyl magnesium bromide and morpholine (Table 2-2 Optimization table for the synthesis of vinyl sulfonimidamides.**Table 2-2**). Since the resulting product **2a** consists of an electrophilic vinyl group it could react with any unconsumed nucleophilic amine. By reducing the reaction time and the number of

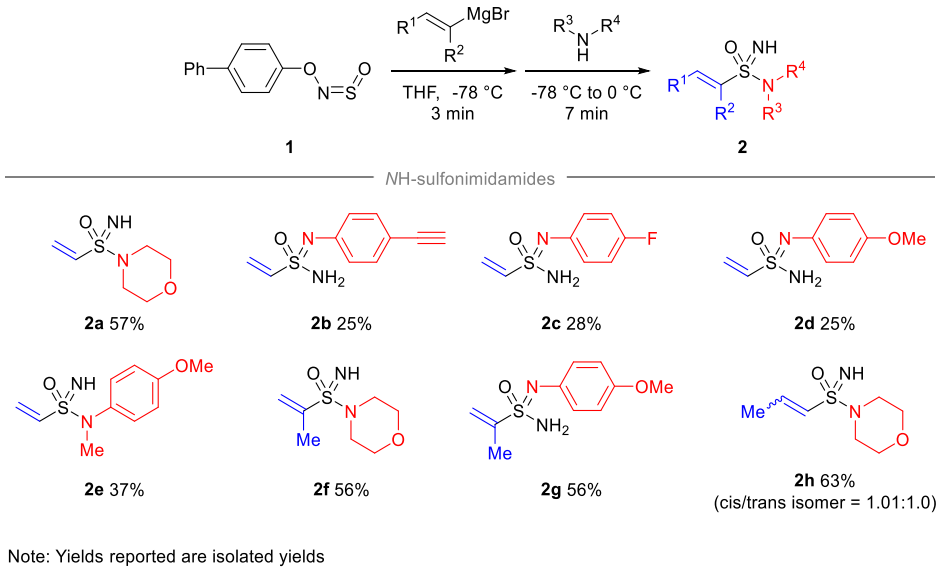
equivalents of morpholine, the reaction yield improved slightly to 57% (**Table 2-2 entry 10**). With the optimised conditions, vinyl sulfonimidamides with different aniline derivatives were synthesised, but with lower yields compared with the morpholine derivative (**Scheme 2-3**). Using isopropenylmagnesium bromide or 1-propenylmagnesium bromide generated the corresponding α or β-methyl substituted products (**Scheme 2-3**).

Table 2-2 Optimization table for the synthesis of vinyl sulfonimidamides.



entry	t_1 (min)	t_2 (min)	T °C	a	b	c	Yield[a]
1	1	15	-78	1.0	1.0	1.5	50%
2	3	15	-78	1.0	1.0	1.5	51%
3	5	15	-78	1.0	1.0	1.5	47%
4	3	3	-78	1.0	1.0	1.5	47%
5	3	5	-78	1.0	1.0	1.5	47%
6	3	7	-78	1.0	1.0	1.5	52%
7	3	9	-78	1.0	1.0	1.5	52%
8	3	7	-78	1.0	1.1	1.5	47%
9	3	7	-78	1.0	1.0	1	43%
10	3	7	-78	1.0	1.0	1.2	57%
11	3	7	-78	1.0	1.0	2	19%
12	3	7	-50	1.0	1.0	1.2	49%
13	3	7	-60	1.0	1.0	1.2	49%
14	3	7	-78	1.1	1.0	1.32	55%
15	3	7	-78	1.5	1.0	1.8	43%

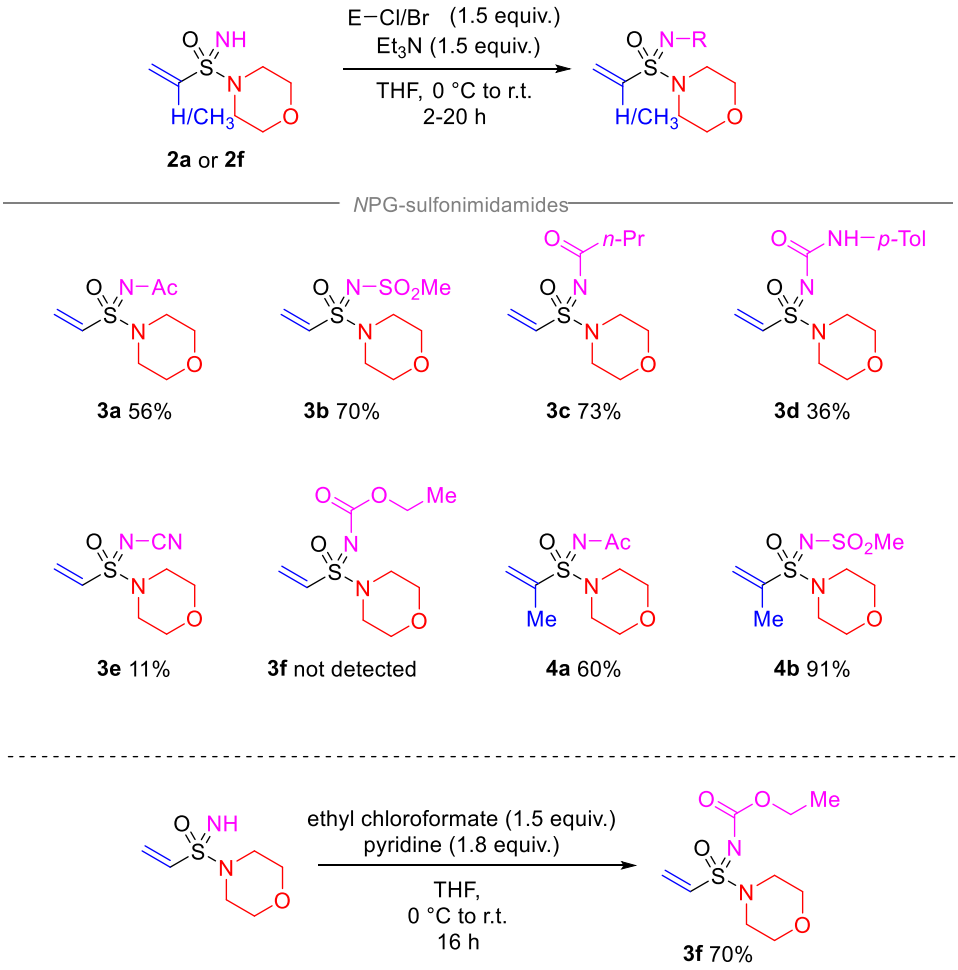
[a] Determined by quantitative ^{1}H NMR yield using methyl 3,5-dinitrobenzoate as an internal standard



Scheme 2-3 Synthesis of *N*-H sulfonimidamides from BiPhONSO.

2.3 *N*-Functionalisations

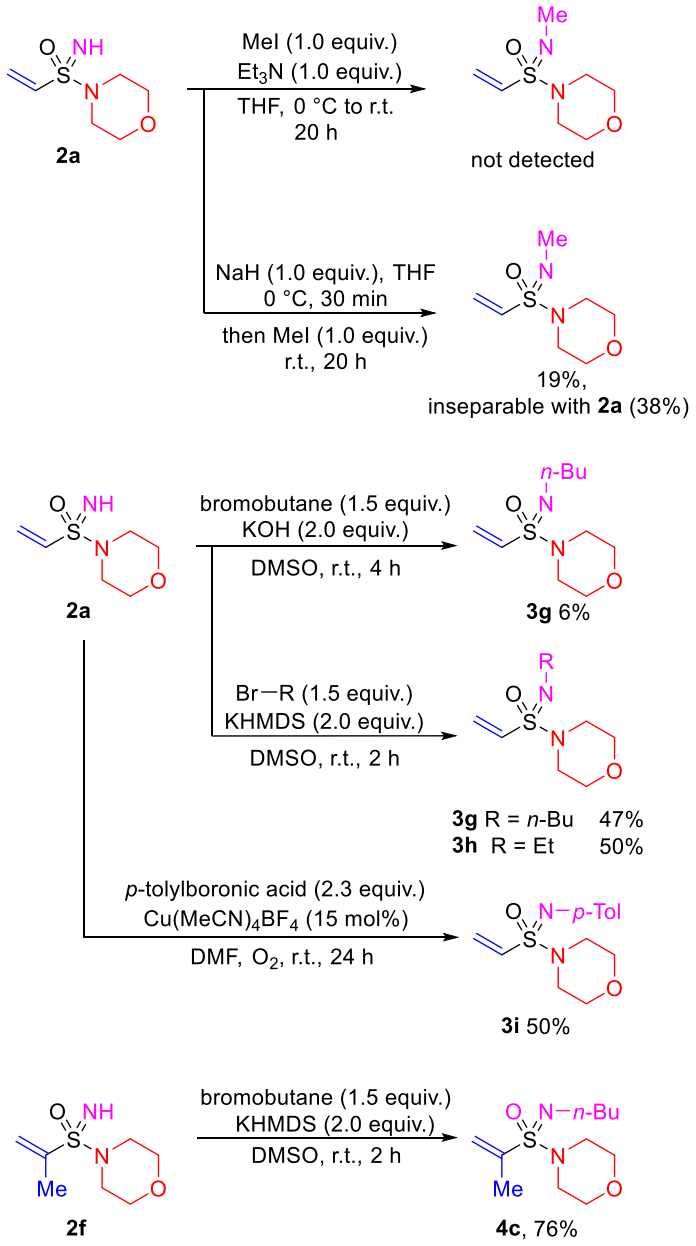
The morpholine derivatives **2a** could be easily functionalised by treatment with appropriate electrophiles and bases. Electron withdrawing groups including acetyl (**3a, 4a**), mesyl (**3b, 4b**), urea (**3d**) and nitrile (**3e**) could be installed by reacting with the corresponding electrophile in the presence of triethylamine (**Scheme 2-4**). An exception to this is ethyl chloroformate (**3f**); however, simply replacing triethylamine with pyridine gave the corresponding carbamate product **3f** in good yield (70%) (**Scheme 2-4**). Similar reaction conditions could be applied to the α-methyl derivative **2f** to access the *N*-functionalised product **4a** and **4b** in improved yield, potentially due to the increased stability of the electrophilic vinyl group.



Scheme 2-4 *N*-functionalisation of 2a and 2f.

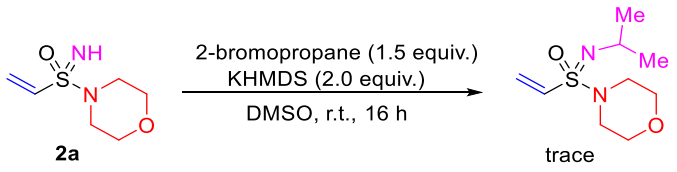
Initial attempts for *N*-alkyl protection using iodomethane in the presence of triethylamine did not result in the formation of the desired product, with most of the starting material being recovered. To facilitate the nucleophilic substitution reaction, NaH was used to deprotonate the imidic proton, followed by the addition of iodomethane generating the corresponding product in low yield (19%) which was inseparable with the starting material (38%). Applying the conditions adapted from Lücking and co-workers,[156] using bromobutane and KOH gave the corresponding product **3g** in poor yield (6%), with full consumption of starting materials. Suspecting that the low yield might result from the nucleophilic attack at the vinyl group by hydroxide ions, we decided to use a strong non-nucleophilic base. Treating **2a** with bromobutane or bromomethane while switching the base to KHMDS gave the desired product **3g** or **3h** in a moderate yield

(47%). Applying the same reaction condition on the α-methyl derivative **2f** afforded corresponding product **4c** in a good yield (76%). In addition, *N*-aryl derivative **3i** could be accessed by utilizing a reported Cu-mediated Chan-Lam coupling procedure.[157]

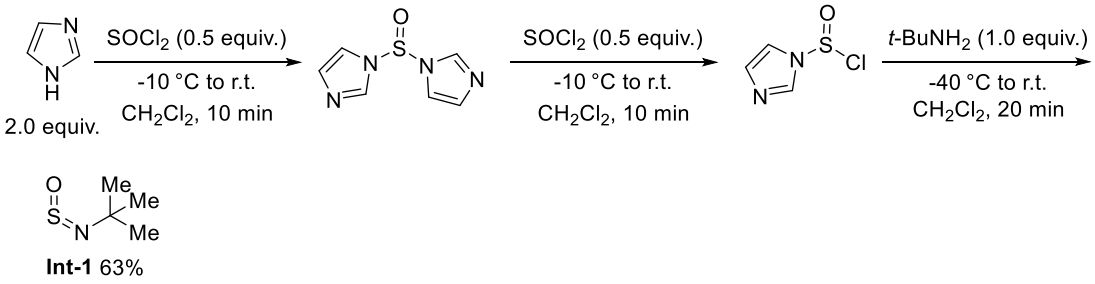


Scheme 2-5 *N*-Alkylation and arylation of *N*-H sulfonimidamides 2a and 2f.

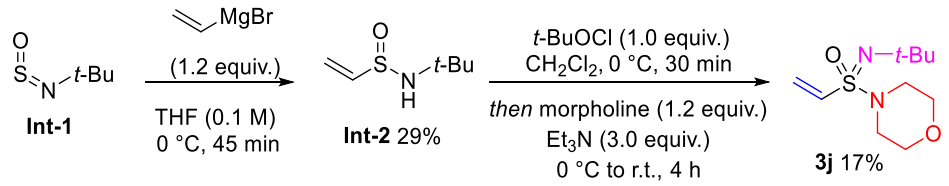
The installation of a sterically bulky functional group was found to be much more challenging. Treating **2a** with 2-bromopropane gave only trace amounts of product (**Scheme 2-6**), with decomposition of the starting material observed with prolonged reaction time. Since the direct installation of bulky functionality was unsuccessful, an alternative synthetic route was employed to access the *N*-*tert*-butyl derivative, proceeding from *N*-*tert*-butyl sulfinylamine **Int-1**, which can be synthesized using a procedure reported by Kim and co-workers (**Scheme 2-7**).[158] Treating the *N*-*tert*-butyl sulfinylamine with vinylmagnesium bromide generated sulfinamide **Int-2**, which followed by oxidative chlorination and amine substitution gave the *N*-*tert*-butyl derivative **3j** (**Scheme 2-8**).



Scheme 2-6 Reaction of 2a with 2-bromopropane.

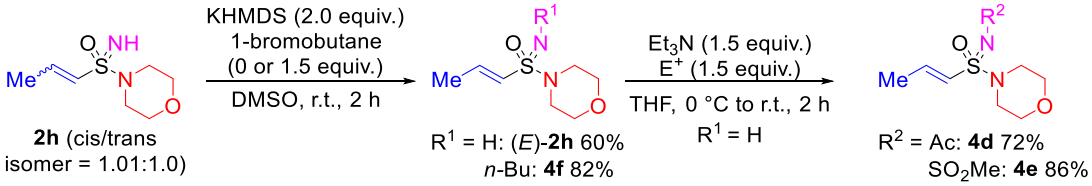


Scheme 2-7 Synthesis of N-*tert*-butyl sulfinylamine.



Scheme 2-8 Synthesis of *N*-*t*-Bu sulfonimidamide 3j.

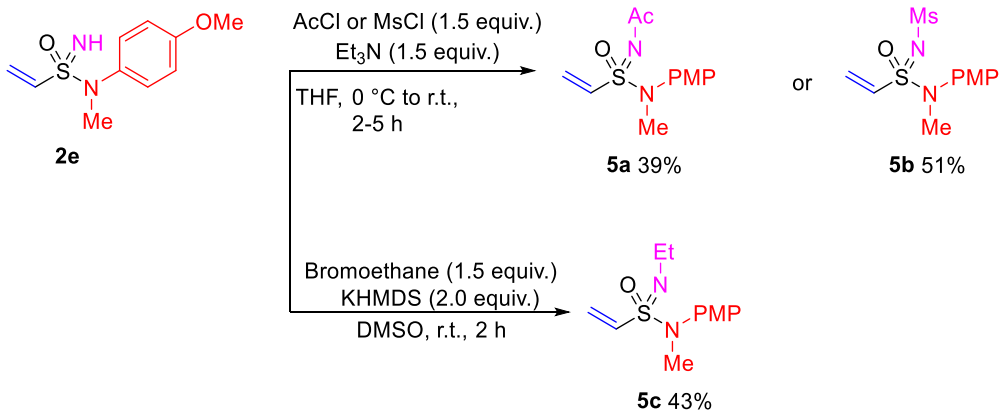
Although the β-methyl substituted vinyl sulfonimidamide **2h** was isolated as a mixture of isomers, it undergoes base catalysed geometric isomerisation. Similar processes have been previously described for sulfides, sulfoxides and sulfones[159] to give the (*E*)-isomer **(*E*)-2h**. With the presence of 1-bromobutane as electrophile, the *n*-butyl substituted product **4f** as only the (*E*)-isomer was obtained in high yield (82%). With the single isomer **(*E*)-2h** obtained, functionalisation of the imidic nitrogen was carried out through treatment with triethylamine and acetyl chloride or methanesulfonyl chloride to generate products **4d** and **4e** in high yield, with no observed isomerisation.



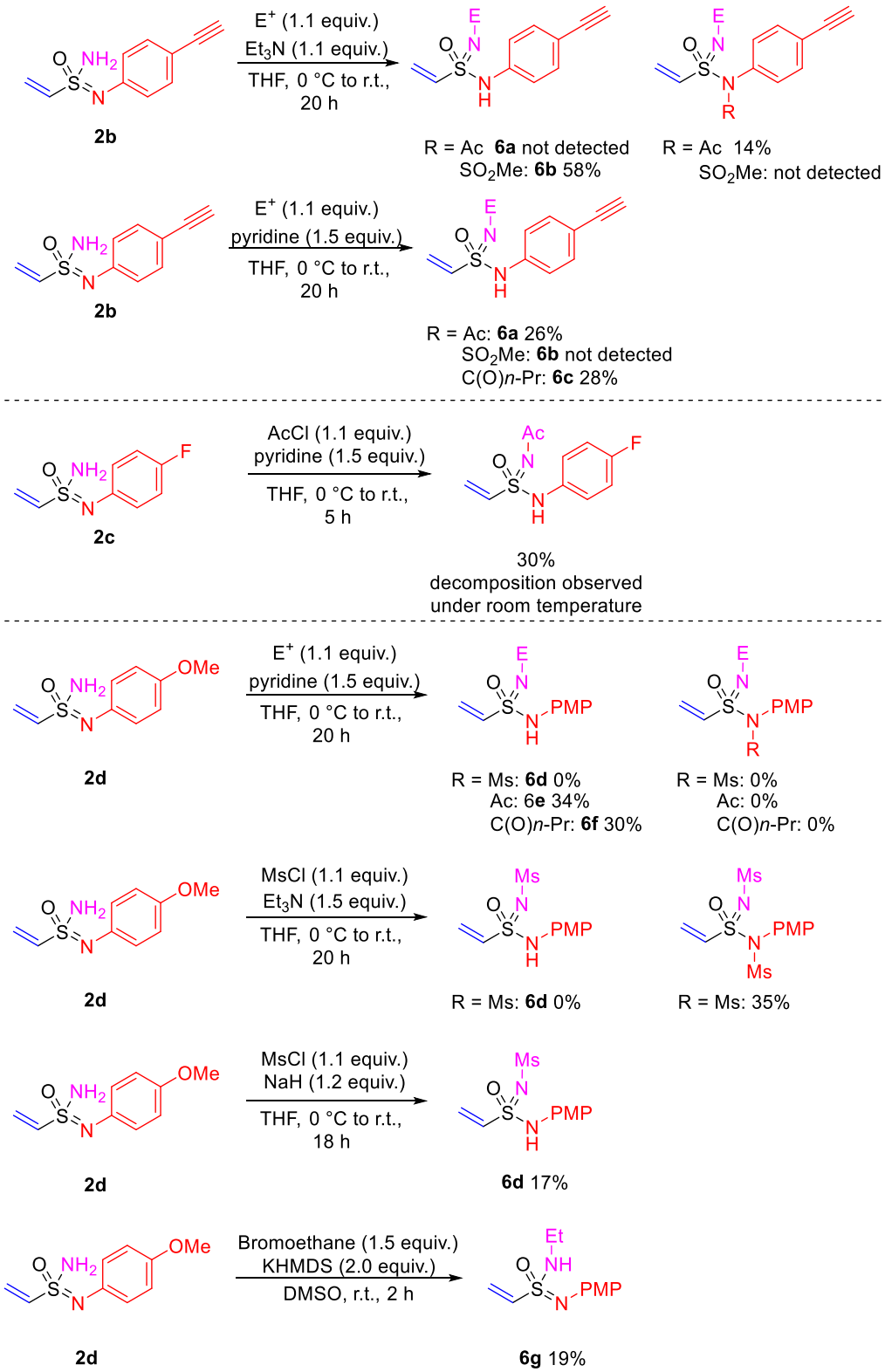
Scheme 2-9 Isomerisation and *N*-functionalisation of 2h.

The functionalisation of secondary aniline derivative **2e** proceeded under the same reaction conditions in moderate yields (39-51%) (**Scheme 2-10**). However, primary aniline derived **2b**, **2c** and **2d** were more challenging to functionalise, due to the presence of two amidic protons, which led to di-substituted products or addition at the vinyl group under basic conditions**.** In addition, the reactivities of the imidic nitrogen are also greatly affected by the substituent on the aniline. When **2b** was treated with acetyl chloride in the presence of triethylamine, desired product **6a** was not detected, with only double acetylated product

observed, while the mesylation of **2c** with triethylamine went smoothly in moderate yield (**6b**, 58%). By switching the base to pyridine, the desired mono-substituted product **6a** and **6c** could be obtained. Similarly, **2c** could react with acetyl chloride in the presence of pyridine to give the mono-acylated product. Although the electron-withdrawing groups were successfully installed, decompositions of **2b** and **2c** derivatives at room temperature were observed, potentially due to the increased reactivity of the vinyl group. Thus, we switched our focus on the more electron-rich *p*-anisidine derivative **2d**. Acetyl and butyryl functional groups were successfully installed in a similar manner to give **6e** and **6f**, but the desired mesylated product **6d** was not observed with either triethylamine or pyridine. Deprotonation using NaH, followed by the addition of methanesulfonyl chloride gave the product **6d** in low yield (17%). Similar to the morpholine derivatives **2a** and **2f**, an ethyl group could be installed by reacting **2d** with bromoethane in the presence of KHMDS.



Scheme 2-10 *N*-functionalisation of 2e.

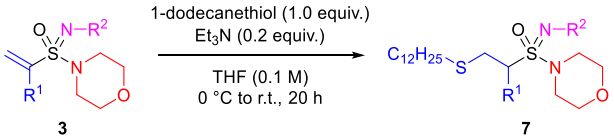


Note: Compounds are depicted in their most probable tautomeric forms. Attempts to unambiguously charaterise the exact tautomeric form using NMR spectroscopy were unsuccessful

Scheme 2-11 *N*-functionalisation of 2b, 2c and 2d.

2.4 Reactivity Studies with Conjugate Addition

With a broad range of functionalised sulfonimidamides in hand, reactivity studies towards conjugate addition were carried out using 1-dodecanethiol. Reactions were performed in THF for 20 hours. The influence of the *N*-substituent was pronounced, with yields ranging from 7 to 84% for the vinyl examples (**Scheme 2-12**). In general, installing an electron-withdrawing group enhanced the reactivity of the vinyl group. This is typified by *N*-sulfonyl sulfonimidamide **3b**, which gave the highest yield of 84%. Of note is electron-donating *N*-butyl and *N*-ethyl examples (**7h**, **7i**), which exhibit greatly enhanced reactivities under compared with the unsubstituted **2a**. We speculate that this may be due to the enhanced basicity of the imidic nitrogen which catalysed the reaction as Brønsted base. The α-methyl substituted sulfonimidamides showed poor reactivity (**7j - 7l**), which is in agreement with previous studies on α-substituted acrylamides.[160] In addition, competition reactions in the presence of an acrylamide analogue, 4-acryloylmorpholine (**8**, 1.0 equiv.) were performed to benchmark the reactivities of these *N*-functionalised sulfonimidamides. The yield obtained from these cases was consistent (yields in parenthesis, **7a**, **7c** and **7h**), showcasing the enhanced reactivity of these functionalities compared with acrylamide.



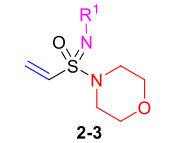
Entry	R^1	R^2	Cmpd.	Yield
1	H	H	**7a**	16%(15%)[a]
2	H	Ac	**7b**	18%
3	H	Ms	**7c**	84% (81%)[a]
4	H	C(O)*n*-Pr	**7d**	27%
5	H	C(O)NHTol	**7e**	75%
6	H	CO_2Et	**7f**	26%
7	H	p-Tol	**7g**	7%
8	H	*n*-Bu	**7h**	74% (76%)[a]
9	H	Et	**7i**	75%
10	Me	H	**7j**	2%
11	Me	Ms	**7k**	6%
12	Me	*n*-Bu	**7l**	3%

[a] In the presence of 1.0 equiv. of acrylamide 8.

Scheme 2-12 Conjugate addition reactions of alkenyl sulfonimidamides 3 with 1-dodecanethiol.

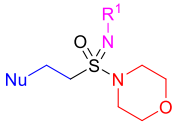
The reactivity of vinyl sulfonimidamides was next examined with a series of protected amino acid derivatives, using the *N*-H, *N*-Ms and *N*-*n*-Bu examples as the electrophiles. Similar to what had been observed with 1-dodecanethiol, the *N*-Ms substrate **3b** provided a high yield (89%) for the addition product with the cysteine derivative. The *N*-*n*-Bu substrate **3g** had comparable reactivity (86%) to the *N*-Ms substrate **3b**, while the *N*-H substrate **2a** showed lower reactivity (54%). The result was consistent when performed with stoichiometric or sub-stochiometric quantities of triethylamine (0.2 equiv., yields in parenthesis). The selected vinyl sulfonimidamides also reacted readily with a lysine derivative, with the *N*-Ms substrate **3b** providing the adduct in excellent yield (98%). The reaction of the lysine derivatives with *N*-H (**2a**) or *N*-*n*-butyl (**3g**) substrate gave a mixture of mono- (**10a** and **10c**) and bis- addition products. All these substrates were unreactive towards serine derivative Boc-(L)-Ser-OMe, with >90% starting material recovery and no desired product observed.

To further investigate the reactivity of the vinyl sulfonimidamides with amino acid derivatives, we next performed a series of competition experiments. Sulfonimidamides **2a**, **3b** and **3g** were reacted with a 1:1 mixture of protected lysine and cysteine nucleophiles respectively and the yields of addition products were measured. The most electrophilic *N*-Ms derivative gave the cysteine adduct as the major product (72%), with 25% of lysine adduct as the minor product. The *N*-H substrate reacted preferentially with the cysteine nucleophile (70%), with a small amount of mono- (8%) and bis-lysine addition (4%) products. Finally, the *N*-*n*-Bu substrate showed good selectivity for cysteine, with only 7% of lysine addition product isolated.



2-3

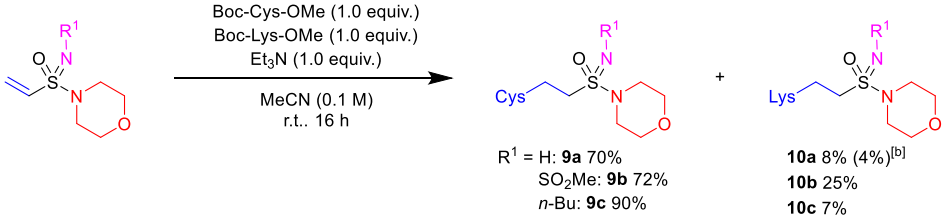
Amino acid (1.0 equiv.)
Et_3N (0.2-2.0 equiv.)
MeCN (0.1 M)
r.t., 16 h



9-11

R^1	Amino acid	Product	Yield
H		**9a**	54% (53%)[a]
Ms	Boc-Cys-OMe	**9b**	89% (87%)[a]
n-Bu		**9c**	86% (85%)[a]
H		**10a**	53% (13%)[b]
Ms	Boc-Lys-OMe·HCl	**10b**	98%
n-Bu		**10c**	34% (20%)[b]
H		**11a**	0%
Ms	Boc-Ser-OMe	**11b**	0%
n-Bu		**11c**	0%

Competition experiment:



R^1 = H: **9a** 70%
SO_2Me: **9b** 72%
n-Bu: **9c** 90%

10a 8% (4%)[b]
10b 25%
10c 7%

[a] Et3N (0.2 equiv.) was used; [b] yield for double addition product (formed by lysing reacting with two vinyl sulfonimidamides)

Scheme 2-13 Conjugate addition reaction of vinyl sulfonimidamides 2-3 with amino acid derivatives.

2.5 Kinetic Studies with Glutathione

We next examined the reactivity of vinyl sulfonimidamides under biologically relevant conditions, using glutathione (GSH) as a nucleophile at pH 7.3. The rate constant (k) and half-life ($t_{1/2}$) was determined based on the rate of disappearance of the starting material, as monitored by ^{1}H NMR spectroscopy. Control experiments using acrylamide **8** and sulfonimidamide **2a** confirmed only GSH-dependent reactivity. Due to the rapid reaction rate, the half-life of the majority of substrates was calculated using second-order kinetics, except for the half-life for the unfunctionalized α-Me and β-Me-substituted sulfonimidamide derivatives (**2f** and (*E*)-**2h**), which was determined with pseudo-first-order kinetics using six equivalents of GSH. 4-Acryloylmorpholine **8** and vinyl sulfonamide **12** were included as substrates to benchmark the reactivity of the vinyl sulfonimidamides under these reaction conditions. The half-life measured for the reaction of GSH and 4-acryloylmorpholine **8** (3.91 h) under these conditions is faster than that reported by Bauer and co-workers[161] (13.8 h, 1 mM electrophile, 10 mM GSH, 70 mM phosphate buffer (pH = 7.4), 30% MeCN at 37 °C), and this is likely due to the differences in experimental parameters (**for detailed experimental parameters see Experimental Section, 5.2.10**).

The half-life calculated for the unfunctionalised *N*H sulfonimidamide **2a** was 576 s, showcasing vastly enhanced reactivity compared with the acrylamide analogue **8** (14,091 s), although this was slower than the sulfonamide **12** (238 s). Installation of electron-withdrawing groups on the imidic nitrogen significantly enhanced the reactivity of sulfonimidamides. In all cases, the reaction for these functionalised sulfonimidamides with GSH exhibit extremely fast kinetics, with half-lives measured of less than 1 minute. The reaction rate for the conjugate addition compares favourably even to the fastest cysteine conjugation reactions reported, such as those using maleimide, iodoacetamide and chlorooxime electrophiles.[162] The half-life for the mesylated derivative **3b** was too fast to be determined, while the half-life of the acylated sulfonimidamide **3a** was measured as 1.01 s, which to the best of our knowledge is the shortest half-life recorded in reaction with GSH, showcasing the enhanced reactivity of the Michael acceptor.[161] Butyryl **3c** ($t_{1/2}$ = 9.88 s), urea **3d** ($t_{1/2}$ = 28.8 s) and carbamate **3f** ($t_{1/2}$ = 4.22 s) derivatives also demonstrated

significantly enhanced reactivities compared to that of the sulfonamide **12**. There was a positive correlation between the rate of the reaction and an increase in the β-carbon ^{13}C NMR shift for the sulfonimidamides featuring electron-withdrawing groups (**Figure 2-2**). The excellent reactivity of these compounds with sulfur-based nucleophiles suggests potential applications in peptide labelling and quantification of cysteine in proteomic studies.[163]

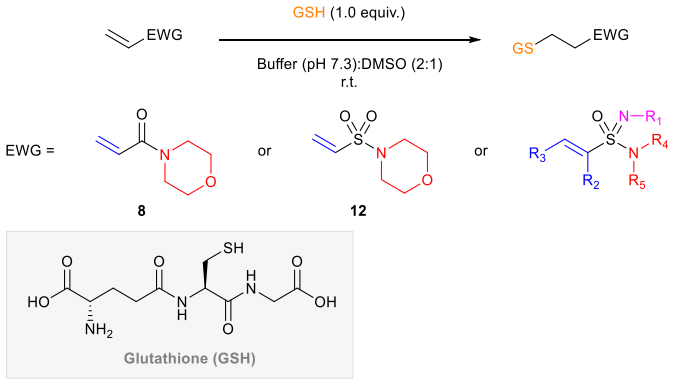
Reaction for *N*-alkyl derivatives **3g** and **3h** proceeded at a slower rate ($t_{1/2}$ = 162 and 161 s) compared with those with an electron-withdrawing group incorporated (**3a-d, 3f**), but were still enhanced relative to sulfonamide **12**. Substrate **3j** which contains an electron-donating and sterically bulky *tert*-butyl substituent showed reduced reactivity ($t_{1/2}$ = 403 s), while the aryl derivative **3i** showed similar reactivity ($t_{1/2}$ = 532 s) compared to the *N*H derivative **2a**.

To investigate the effect of substituents on the alkene towards the reaction rates with GSH, we examined the α- and β-methylated alkenyl sulfonimidamide derivatives with varying imidic *N*-substituents. The methyl substitution at α-position (**4a-c**) greatly reduced the reactivity of the substrates with GSH relative to the unsubstituted vinyl examples (**3a**, **3b** and **3g**), which agrees with the result of the study conducted by Birkholz and co-worker on acrylamide.[164] *N*-Ms (**4b**, $t_{1/2}$ = 249 s), *N*-Ac (**4a**, $t_{1/2}$ = 4680 s) and *N*-*n*-Bu (**4c**, $t_{1/2}$ = 11023 s) derivatives all showed a half-life an order of magnitude slower than their vinyl counterparts, and are more comparable to the reactivity of sulfonamide and acrylamide warheads. Similarly, the methyl substitution at β-position of vinyl group (**4d-f**) reduces the reaction rate with GSH ($t_{1/2}$ = 218 to 9307 s). This can be attributed to steric hindrance introduced by the methyl group near the site of nucleophilic attack and deactivation of alkene electrophile through hyperconjugation from adjacent methyl gourp. In all examples, the β-methylated alkenyl sulfonimidamides are more reactive than the α-methyl derivatives.

The final parameter we explored was the effect of amidic *N*-substituent. Although the *N*-methylanisidine derivative **2e** decomposed under the reaction conditions, its *N*-functionalised derivatives (**5a-c**) showed comparable reactivity with the morpholine derivatives. However, the primary anisidine derived substrates

(**6d**, **6e**, **6g**) displayed reduced reactivity relative to the tertiary derivatives (**5a-5c**). The order of reactivities based on imidic substituent was also altered for this class of substrates; Ac > Ms > Et > NH. The reduced reactivity and scrambling of substituent effect are in contrast to what has been observed for acrylamide substrates,[45] and are likely due to the tautomerism observed with *N*-aryl sulfonimidamides.

Table 2-3 Kinetic studies of vinyl sulfonimidamides with glutathione.



Compound	R^1	R^2	R^3	NR^4R^5	Kinetic	Half-life (s)
2a	H	H	H	Morpholine	Second order	576
3a	Ac	H	H	Morpholine	Second order	1.01
3b	Ms	H	H	Morpholine	Second order	n.d.[a]
3c	Butyryl	H	H	Morpholine	Second order	9.88
3d	*p*-Tolyl urea	H	H	Morpholine	Second order	28.8
3f	CO_2Et	H	H	Morpholine	Second order	4.22
3g	*n*-Bu	H	H	Morpholine	Second order	162
3h	Et	H	H	Morpholine	Second order	161
3i	*p*-Tol	H	H	Morpholine	Second order	532
3j	*t*-Bu	H	H	Morpholine	Second order	403
2d	H	H	H	PMP[b]	Second order	1065
6d	Ms	H	H	PMP[b]	Second order	274
6e	Ac	H	H	PMP[b]	Second order	81.7
6g	Et	H	H	PMP[b]	Second order	842
2e	H	H	H	*N*Me-PMP	Second order	n.d.[c]
5a	Ms	H	H	*N*Me-PMP	Second order	n.d.[a]
5b	Ac	H	H	*N*Me-PMP	Second order	3.20
5c	Et	H	H	*N*Me-PMP	Second order	196
2f[d]	H	Me	H	Morpholine	Pseudo-first order	35873
4a	Ac	Me	H	Morpholine	Second order	4680
4b	Ms	Me	H	Morpholine	Second order	249
4c	*n*-Bu	Me	H	Morpholine	Second order	11023
(***E***)-**2h**[d]	H	H	Me	Morpholine	Pseudo-first order	16379
4d	Ac	H	Me	Morpholine	Second order	1549
4e	Ms	H	Me	Morpholine	Second order	218
4f	*n*-Bu	H	Me	Morpholine	Second order	9307
8	-	-	-	-	Second order	14091
12	-	-	-	-	Second order	238

[a] Too fast to be determined. [b] *p*-Anisidine [c] Decomposition of starting material observed. [d] 6.0 equiv. GSH used.

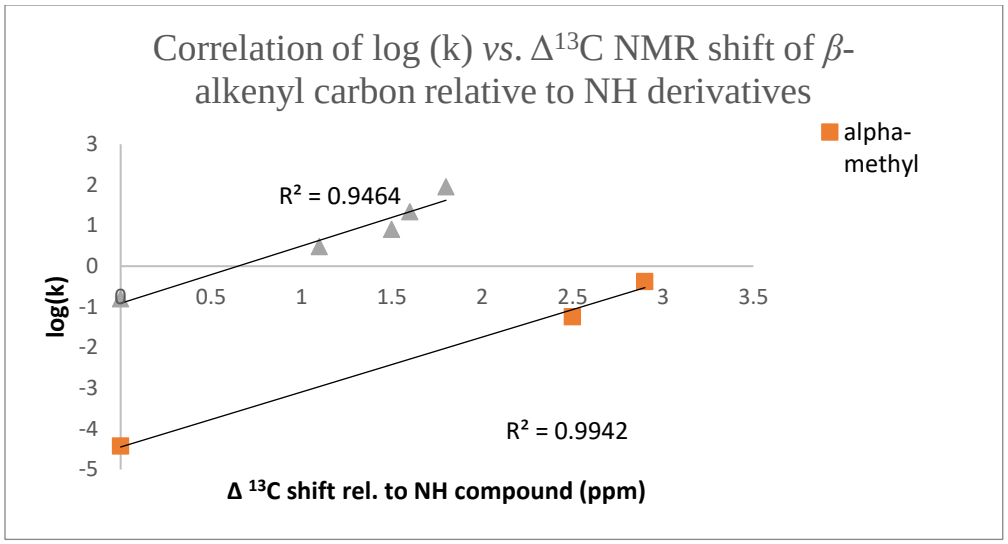


Figure 2-2 Correlation of log(k) versus Δ^{13}C NMR shift.

2.6 Summary and Future Work

In summary, we have shown that a variety of vinyl sulfonimidamides are available in a single step, and that the imidic *N*-H can be functionalised with a variety of different groups. These substrates have shown good reactivity with both lysine and cysteine derived nucleophiles, and the kinetic study of vinyl sulfonimidamides with glutathione demonstrated exceptional reactivity, compared with the corresponding acrylamide and sulfonamide analogues. The reactivities of these electrophiles have shown to be dependent on the imidic *N*-substituent and alkene substitution, and can be tuned to either above or below that of the corresponding acrylamides and sulfonamides. Given the wide range of reactivities that can be achieved and their modular assembly, we anticipate that vinyl sulfonimidamides should be of broad utility in medicinal and polymer applications. To further investigate the potential of vinyl sulfonimidamides in medicinal chemistry, more detailed biological assay studies could be done through collaboration with other research groups.

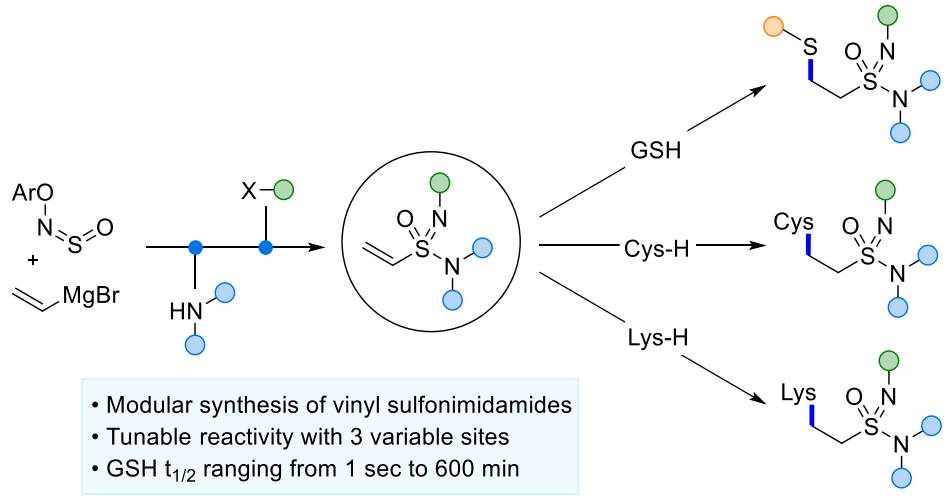
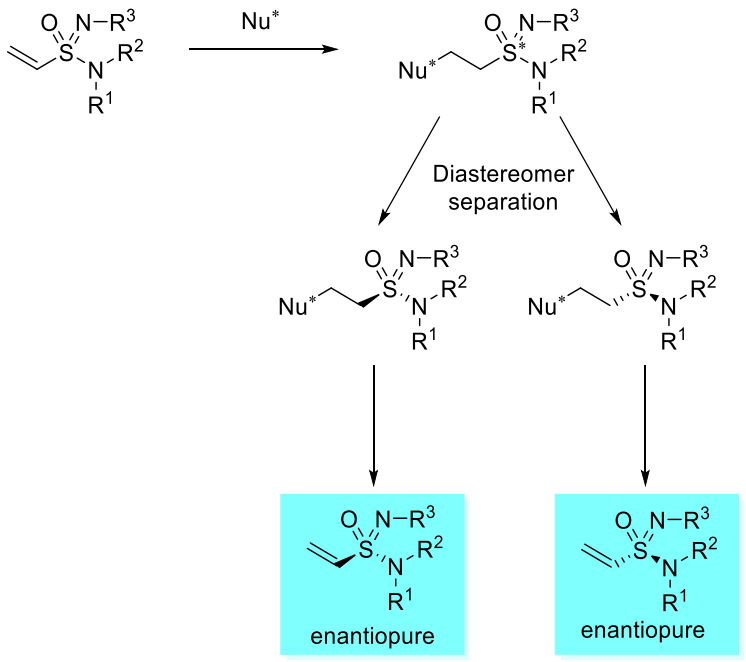


Figure 2-3 Summary of vinyl sulfonimidamides synthesis and reactivity.

One important feature of sulfonimidamides is their stereogenic sulfur center, but the synthetic strategy employed in this chapter only allows the access to a racemic mixture of products. The chirality of the vinyl sulfonimidamides may potentially affect their reactivities towards chiral nucleophiles, thus this would be an attractive area to explore further. However, to the best of our knowledge, only one literature example has reported access to enantiopure vinyl sulfonimidamides, which was achieved via chiral HPLC separation of racemic mixtures. The direct synthesis route to enantiomerically pure vinyl sulfonimidamides has yet been reported. This limitation may stem from the incompatibility of electrophilic vinyl moiety with many of the modern synthetic strategies commonly employed for enantioselective synthesis of sulfonimidamides. One possible way to access optically pure vinyl sulfonimidamide is through the addition of a chiral nucleophile to the vinyl group to generate two diastereomers which are separable, followed by elimination to the retain the enantiopure vinyl sulfonimidamides.



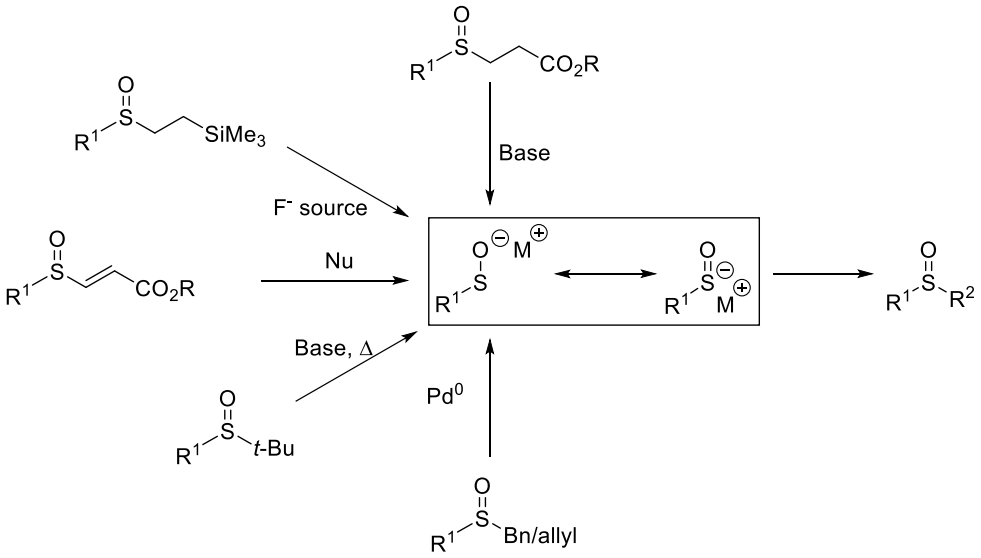
Scheme 2-14 Potential route for isolation of enantiopure vinyl sulfonimidamides.

Chapter 3 Access to Iminosulfamides through SuFEx Amination of Sulfuramidimidoyl Fluorides

3.1 The Elimination Strategy for Synthesising S(IV) and S(VI) Compounds

3.1.1 Synthesis of Sulfoxide through Sulfenate Anion

Sulfenate anions, the conjugate base of sulfenic acids, are useful intermediates for the synthesis of sulfoxides due to their exquisite S-nucleophilicity over the oxygen.[165] Although they have been known for over 60 years, sulfenic anions received limited attention until Schwan and co-workers re-visited their reactivity in 2004.[166] Due to the instability of sulfenic acids and their corresponding anions, they have to be generated and functionalised *in situ*.[166] Various strategies have been developed for the generation of sulfenate anions, and the most widely employed methods are retro-Michael reaction of β-sulfinyl ester[167] and fluoride induced fragmentation of 2-trimethylsilyethyl sulfoxides.[168] β-Sulfinyl acrylate ester,[169] *tert*-butyl sulfoxides,[170] benzyl sulfoxides[171]and allyl sulfoxides[172] could also be utilized to generate sulfenate anions (**Scheme 3-1**).

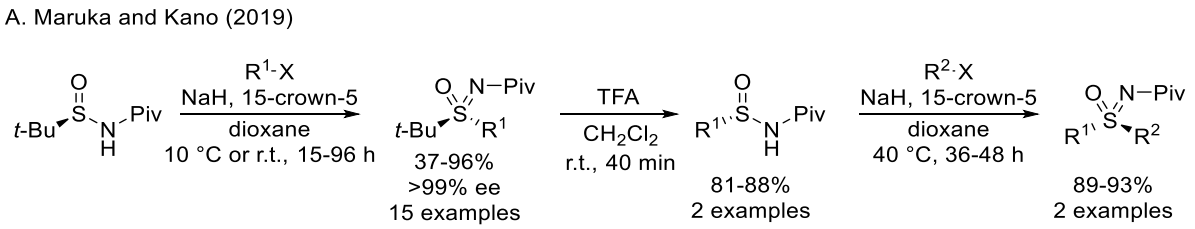


Scheme 3-1 Different methods for generating sulfenate anions.

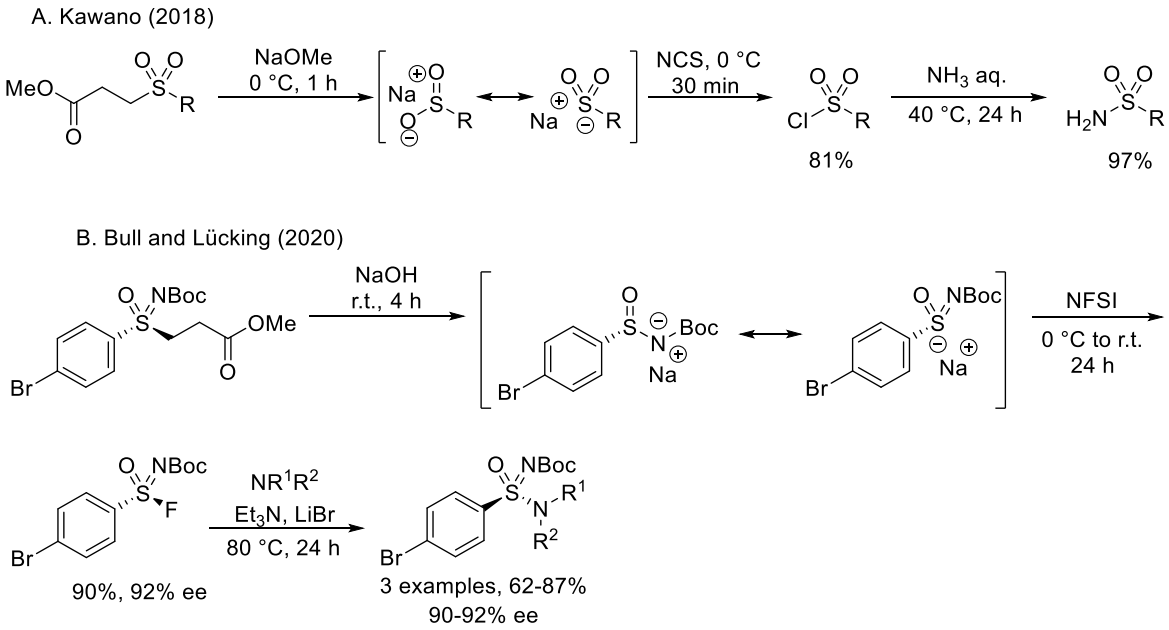
3.1.2 Synthesis of Sulfoximines, Sulfonamides, and Sulfonimidamides through Sulfinate Anion Intermediates

Similar strategy can also be applied to synthesise S(VI) compounds. For instance, Maruoka and Kano reported the asymmetric synthesis of chiral sulfoximines, through the deprotonation of sulfinamides, followed by sulfur-selective alkylation. Subsequent de-*tert*-butylation with TFA, followed by a second S-alkylation afford sulfoximine without loss of optical purity(**Scheme 3-2**).[173] Kawano and co-workers applied the retro-Michael chemistry on helicene-based β-sulfonyl esters, followed by chlorination with *N*-chlorosuccinimide and subsequent reaction with aqueous ammonia to form corresponding sulfonamides (**Scheme 3-3 A**).[174] Bull and Lücking applied a similar strategy on enantioenriched sulfoximine derivatives

to access sulfonimidoyl fluorides, followed by SuFEx reaction with Grignard reagents or amines to generate enantiopure sulfonimidamides (**Scheme 3-3 B**), with no racemisation observed.[90]



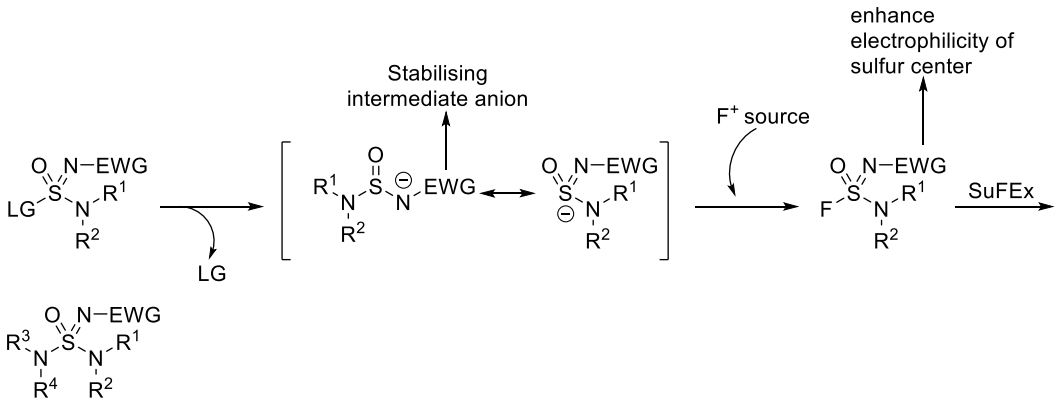
Scheme 3-2 Access to chiral sulfoximines through sulfur-selective alkylation.



Scheme 3-3 Synthesis of S(VI) compounds employing retro-Michael addition.

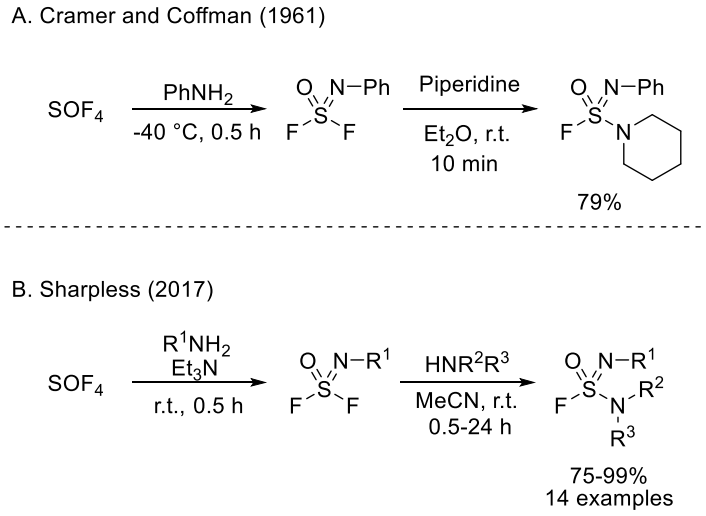
Although the above elimination strategy has been used on sulfones and sulfoximines to synthesise sulfonamide or sulfonimidamides, to the best of our knowledge, this strategy has yet been applied on sulfonimidamides. We envisioned that through the generation of aminosulfinamide anion, followed by fluorination we would access sulfuramidimidoyl fluorides (SAFs). Such SAFs were less explored due to their low reactivity, originating from their reduced electrophilicity at their sulfur center compared to other

S(VI) fluoride derivatives,[175] but still interesting because it could afford the rarely reported iminosulfamates or iminosulfamides through SuFEx reaction with oxygen or nitrogen nucleophiles.[129] As mentioned in chapter 2, the nitrogen substituent on sulfonimidamides demonstrated remarkable effect on their reactivity towards nucleophiles. We hypothesised that by introducing an electron-withdrawing group on the imidic substituent, the reactivity of SAFs would be enhanced significantly, which could enable access to the largely underexplored iminosulfamide motifs through mild SuFEx conditions (**Scheme 3-4**).



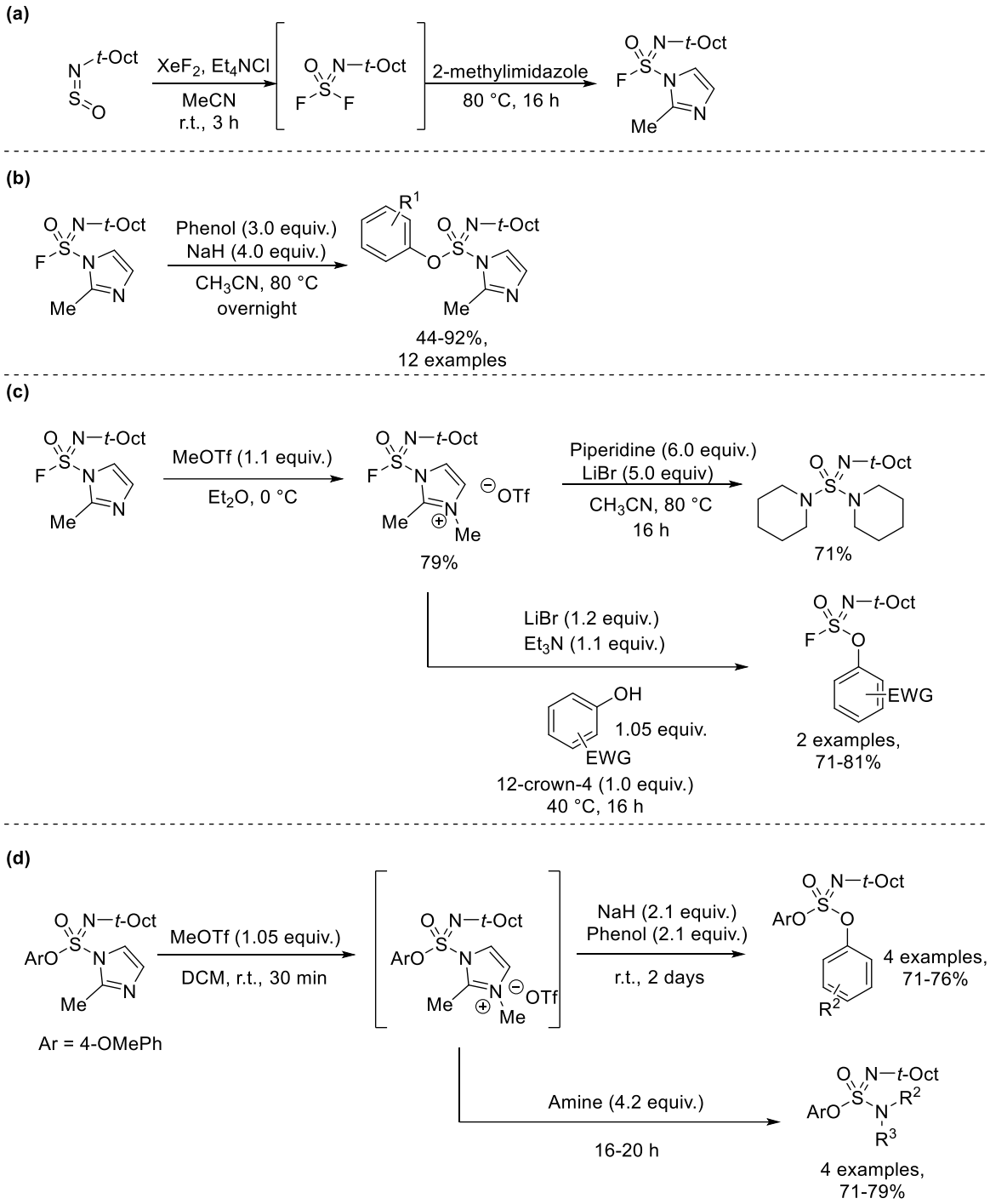
Scheme 3-4 Proposed synthetic route to iminosulfamides.

Such sulfuramidimidoyl fluoride (SAF) intermediates were first synthesised by Cramer and Coffman, by reacting phenyliminosulfur oxydifluoride with piperidine (**Scheme 3-5 A**).[176] Sharpless and co-workers in 2017 revisited and expanded the scope of this work with a wider selection of amine nucleophiles (**Scheme 3-5 B**).[177] The biggest limitation of these two methods is that the synthetic method involved the use of SOF_4, which is a non-commercially available and highly hazardous gas. Although they did not report any further SuFEx reaction on the SAFs, potentially due to the low reactivity of SAFs, Kelly and Sharpless in 2020 described the application of these S(VI) fluoride intermediates for inverse drug discovery. A thymidine-based SAF demonstrated covalent inhibition of poly(ADP-ribose) polymerase 1, and the weak electrophilicity of SAFs reduces potential off-target effect.[178]



Scheme 3-5 Synthesis of SAFs.

Miloserdov and Zuilhof in 2024 reported an alternative synthetic pathway to access SAF, through the reaction of *t*-OctNSO with XeF_2 and 2-methylimidazole (**Scheme 3-6 a**).[129] The resulting sulfuramidimodoyl fluoride underwent SuFEx reaction with phenol to form iminosulfamates (**Scheme 3-6 b**). The imidazole motif of iminosulfamates can also be converted to the imidazolium salt using MeOTf and undergoes substitution reaction with phenol or amine (**Scheme 3-6 c**). Additionally, they reported one example of iminosulfamide synthesis, by reacting the imidazolium salt of ImSF with piperidine (6.0 equiv.) and LiBr (5.0 equiv.) (**Scheme 3-6 c**). Because of the low reactivity of SAF, the reported SuFEx reactions required excess nucleophile and base under high temperature. The iminosulfamates synthesised can be treated with methyl triflate to generate imidazolium salt, which could *in-situ* react with amine of phenolate nucleophiles (**Scheme 3-6 d**).

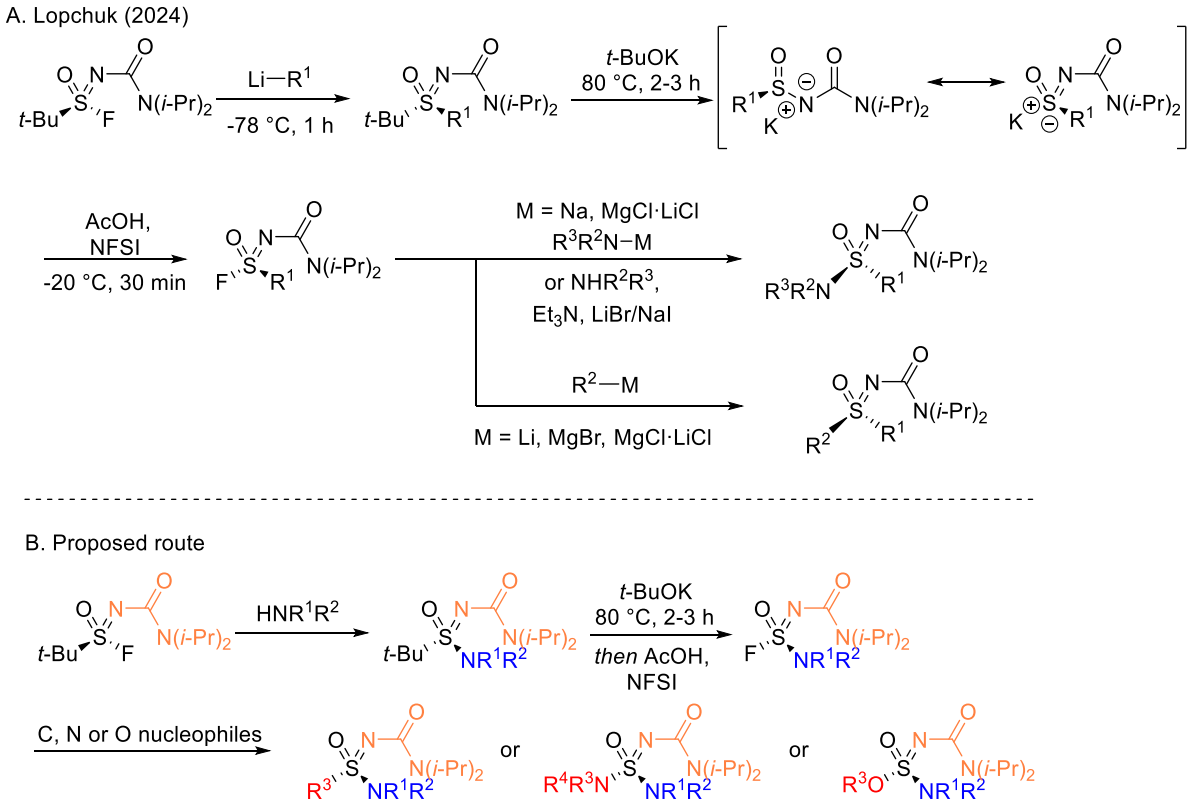


Scheme 3-6 SuFEx reaction of 2-methylimidazole-1-(*N*-tert-octyl)sulfonimidoyl Fluoride.

3.2 Synthesis of Sulfuramidimidoyl Fluorides

3.2.1 Employing *tert*-Butyl Group as the Leaving Group

In 2024, Lopchuk and co-workers reported the asymmetric synthesis of sulfoximines and sulfonimidamides, through an enantiopure bifunctional S(VI) reagent N,N-(diisopropylcarbamoyl)-2-methylpropane-2-sulfonimidoyl (*t*-BuSF) (**Scheme 3-7 A**).[92] We envisioned that by reacting *t*-BuSF with an amine, followed by de-*tert*-butylation and electrophilic fluorination, we could generate the desired SAFs, which would undergo SuFEx reaction to form enantiopure sulfonimidamides, iminosulfamides or iminosulfamates (**Scheme 3-7 B**).

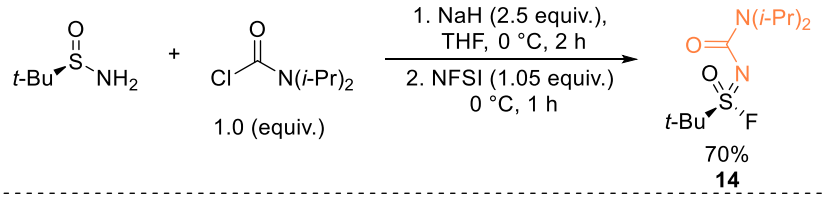


Scheme 3-7 (A) Lopchuk's strategy to access enantiopure sulfoximines and sulfonimidamides (B) Proposed synthetic route.

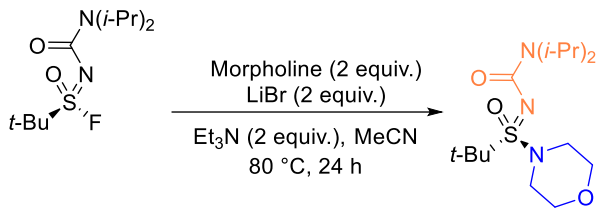
We initiated our investigation by synthesising *t*-BuSF employing the literature procedure,[92] using (*R*)-*t*-Bu sulfinamide as the enantiopure starting material. Applying the reaction conditions reported by Bull and Lücking[90] on *t*-BuSF using morpholine failed to generate the corresponding sulfonimidamide (**Scheme 3-8 B**), but sulfonimidamide **15** could be obtained in moderate yield (54%) by reacting *t*-BuSF with *N*-methyl-*p*-anisidine in the presence of NaHMDS (**Scheme 3-8 C**) (**for detailed evaluation, see Appendix**).

The subsequent de-*tert*-butylation was however unsuccessful. Applying the sulfoximine de-*tert*-butylation/*S*-fluorination procedure described by Lopchuk and co-workers[92] on sulfonimidamide **15** did not yield the desired S(VI) fluoride product, with 44% starting material recovered. Additionally, *N*-methyl-*p*-anisidine was isolated (37%), indicating potential decomposition of either an intermediate or final product. To determine whether decomposition occurred at the intermediate or product stage, we attempted to isolate the S(IV) intermediate by quenching the de-*tert*-butylation reaction with silica gel. The result obtained was similar to the initial attempt, suggesting that the S(IV) intermediate decomposed under the reaction conditions. De-*tert*-butylation using trifluoroacetic acid[179] was also not successful, with 80% starting material being recovered (**Scheme 3-8 D**).

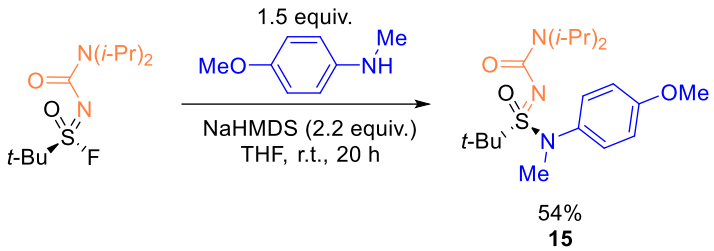
A.Synthesis of *t*-BuSF



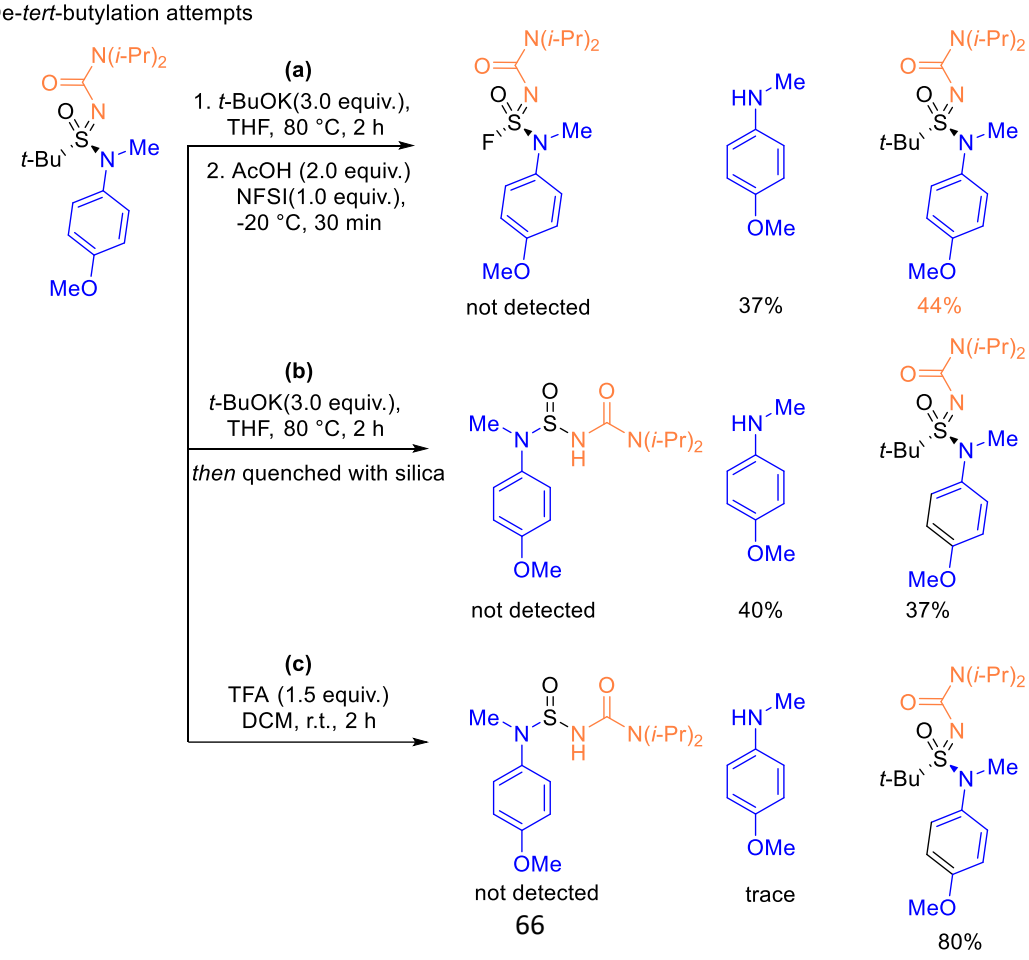
B.Condition reported by Bull and Lücking



C.Condition reported by Lopchuk and co-workers



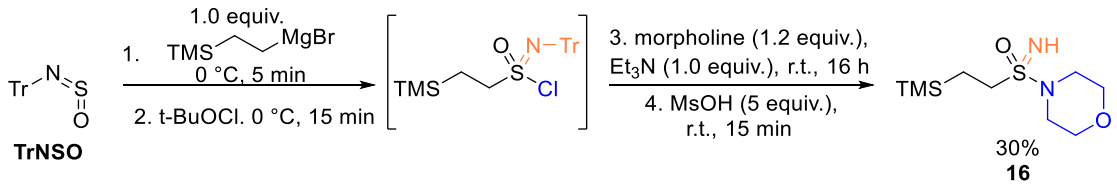
D. De-*tert*-butylation attempts



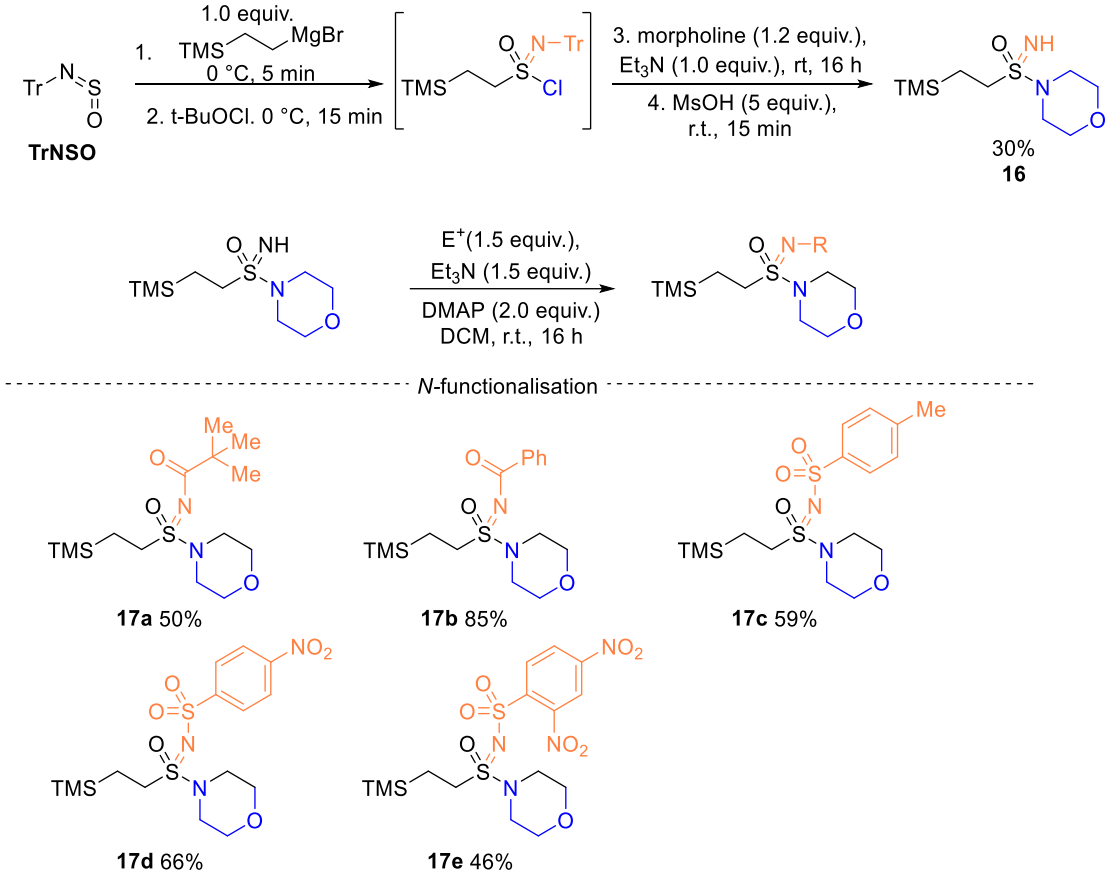
Scheme 3-8 (A) Synthesis of *t*-BuSF (B-C) SuFEx amination of *t*-BuSF (D) De-*tert*-butylation attempts.

3.2.2 Employing 2-Trimethylsilyethyl as the Leaving Group

We proposed that milder reaction conditions might prevent the observed decomposition, therefore the 2-trimethylsilyethyl group was selected as the leaving group for generating the aminosulfinamide anion intermediates. Sulfonimidamide **16** was prepared using the synthetic strategy developed by our group[79] employing 2-(trimethylsilyl)ethyl magnesium bromide with TrNSO (**Scheme 3-9**). Sulfonimidamide **16** was subsequently functionalised to install various electron withdrawing groups, including pivaloyl, benzoyl, tosyl, nosyl and 2,4-dinitrobenzenesulfonyl group (**Scheme 3-10**).



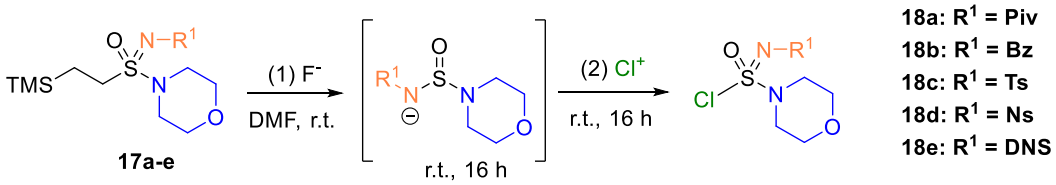
Scheme 3-9 Synthesis of trimethylethylsilyl sulfonimidamide 16.



Scheme 3-10 Installation of electron withdrawing group.

Following this, the sulfuramidimidoyl chlorides **18b-d** were obtained in moderate yield via a two-step process; removal of the 2-(trimethylsilyl)ethyl group using CsF, followed by oxidative chlorination with trichloroisocyanuric acid (TCCA). The highest yield obtained was 60% (**entry 9**), likely limited by the decomposition of intermediate anion during the extended reaction time (2 to 2.5 h) for the desilylation step. When TBAF or TBAF(*t*BuOH)$_4$ were used as the fluoride source, the desilylation completed within 10 minutes, but no (**entry 3**) or limited (**entry 8**) desired product was observed after the addition of TCCA. In addition, replacing the chlorinating reagent to *t*-BuOCl led to a significant decrease in product yield.

Table 3-1 Selected optimisation for synthesis of sulfuramidimidoyl chloride 18.



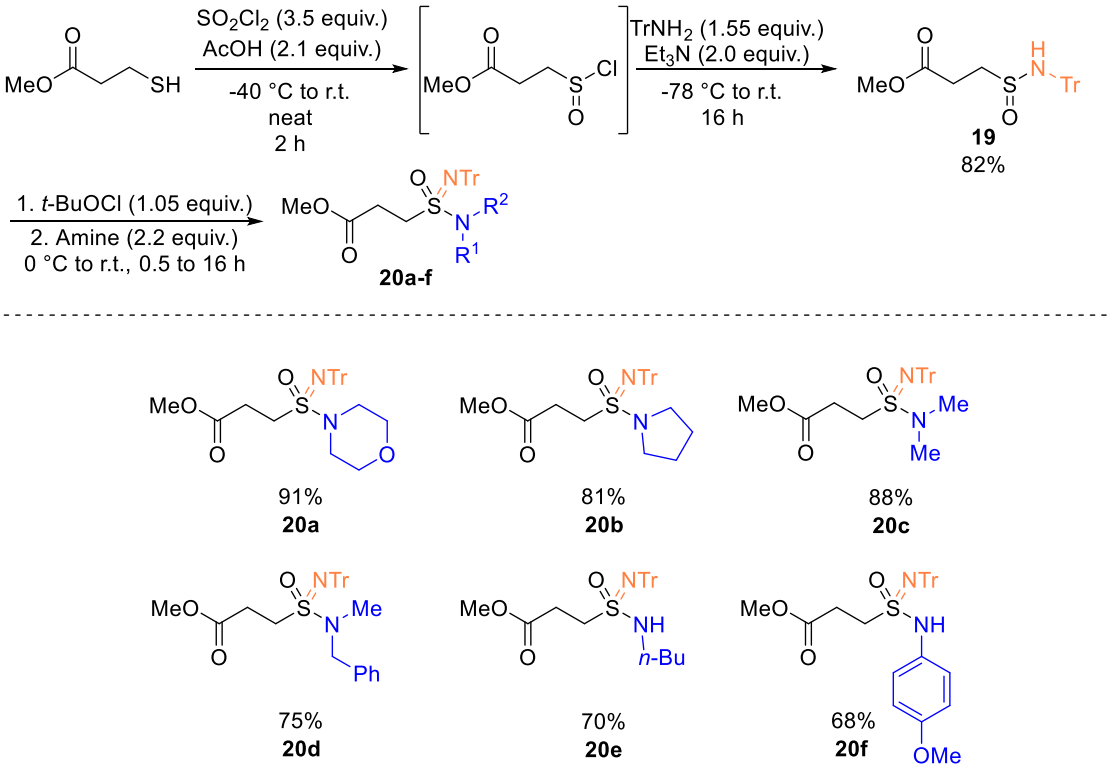
entry	Fluoride Soruce	Cl^+	R^1	Yield (**18**)
1	CsF (2.0 equiv.) 2 h	TCCA (0.5 equiv.)	Piv	n.d.
2	CsF (2.0 equiv.) 2 h	TCCA (0.5 equiv.)	Bz	50%
3	TBAF (1.1 equiv.) 10 min	TCCA (0.5 equiv.)	Bz	n.d.
4	CsF (2.0 equiv.) 2 h	TCCA (0.5 equiv.)	Ts	44%
5	CsF (2.0 equiv.) 2 h	TCCA (0.7 equiv.)	Ts	49%
6	CsF (2.0 equiv.) 2 h	*t*-BuOCl (1.5 equiv.)	Ts	13%
7	CsF (2.0 equiv.) 2 h	TCCA (0.7 equiv.)[a]	Ts	48%
8	TBAF(*t*-BuOH)$_4$ (1.1 equiv.) 10 min	TCCA (0.7 equiv.)[a]	Ts	11%
9	CsF (1.5 equiv.) 2 h	TCCA (0.7 equiv.)	Ns	60%
10	CsF (1.5 equiv.) 2 h	TCCA (0.7 equiv.)[a]	DNS	n.d.

[a] 2.5 h

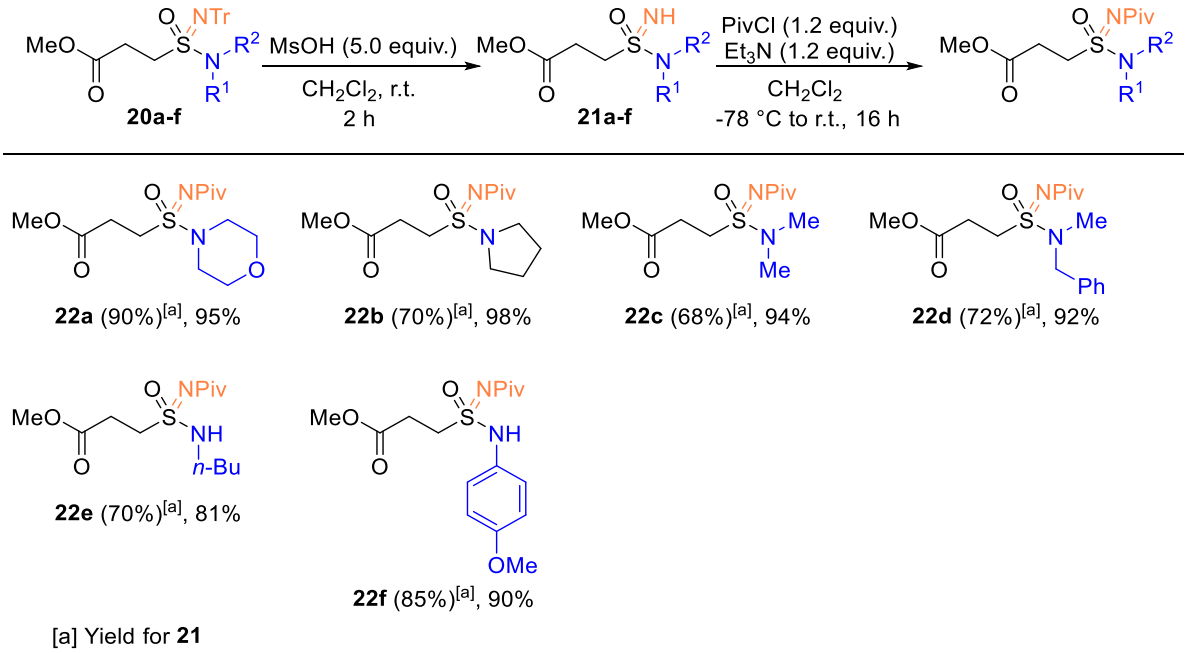
3.3.3 Employing Methyl Acrylate as the Leaving Group

Given that the yields of sulfuramidimidoyl chloride **18** remained unsatisfactory despite extensive condition screening (**for detailed screening, see Appendix**), we opted to use methyl acrylate as the leaving group to generate the aminosulfinamide anion. The precursor sulfinamide could be synthesised by reacting methyl 3-mercaptopropionate with SO_2Cl_2 and AcOH neat to form the sulfinyl chloride, which was subsequently treated with $TrNH_2$ to afford the desired sulfinamide **19.**[180] Reaction of **19** with *t*-BuOCl, followed by the

addition of a secondary or primary amine gave sulfonimidamides **20a-f** in good to excellent yield (68-91%) (**Scheme 3-11**). Cleavage of the trityl group was achieved using 5 equivalents of methanesulfonic acid to obtain *N*H-sulfonimidamides **21a-f**, in which the electron-withdrawing pivaloyl group was introduced to form **22a-f** (**Scheme 3-12**).



Scheme 3-11 Synthesis of *β*-ester sulfonimidamide 20.

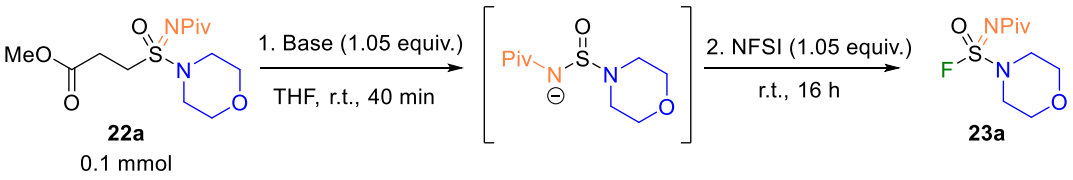


Scheme 3-12 Trityl cleavage and pivaloyl installation of sulfonimidamide 20.

We then initiated our investigation on the synthesis of SAFs using **22a** as model substrate. Initial attempts employed *t*-BuOK as base for the retro-Michael reaction, followed by addition of NFSI in a one-pot procedure, giving product **23a** in 31% yield (**entry 1**). Based on previous results, the presence of H_2O or *t*-BuOH hindered the reaction for synthesising sulfuramidimidoyl chloride **18**, and we thus hypothesised that using non-oxygen-centered bases would be preferred in this reaction. Substituting *t*-BuOK with KHMDS and increasing the equivalents of NFSI (**entry 4 and 5**) led to an improved yield (51% and 56%), and the choice of the metal counter ion had a significant impact on the reaction (**entry 2, 3 and 4**). Suspecting that decomposition of the intermediate aminosulfinamide anion contributed to the loss of product yield, we performed the retro-Michael addition at 0 °C (**entry 6**); however, this resulted in decreased yield (39%). As mentioned above, the choice of counter ion had pronounced effect. When NaHMDS was used together with 15-crown-5 as the additive (**entry 7, 52%**), a substantial improvement of reaction yield was observed. However, when 18-crown-6 was added as the additive along with KHMDS, the yield slightly decreased (**entry 8, 52%**). Changing the solvent of KHMDS from toluene to THF had a pronounced positive effect

(**entry 9, 68%**). By increasing the number of equivalents of KHMDS, the product yield was ultimately improved to 80% (**entry 10**).

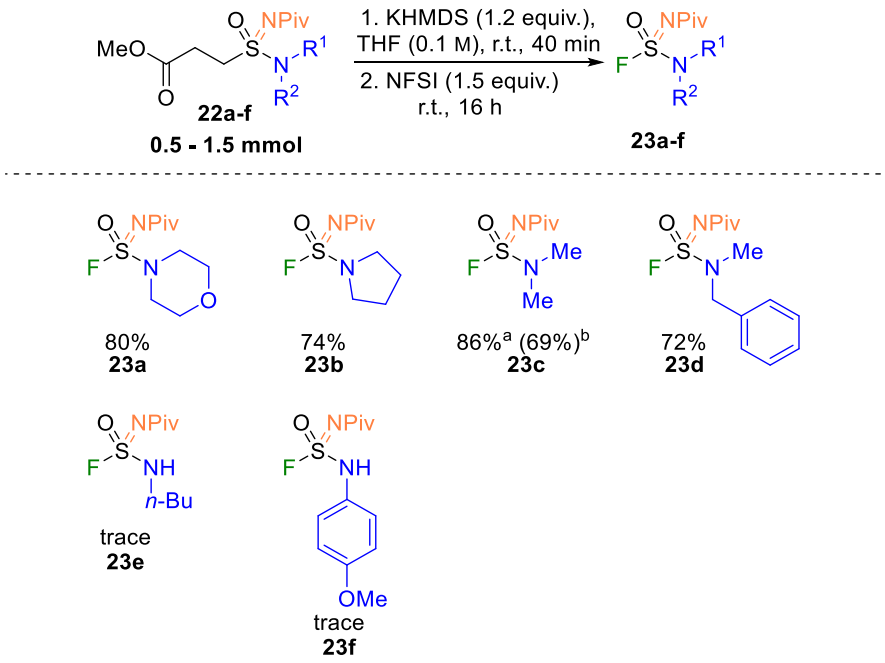
Table 3-2 Selected optimisation for synthesis of sulfuramidimidoyl fluoride 23.



entry	Base	Yield (**23a**)
1	*t*-BuOK	31%
2	LiHMDS[a]	n.d.
3	NaHMDS[a]	33%
4	KHMDS[b]	51%
5	KHMDS[b]	56%[c]
6	KHMDS[b,d]	39%[c]
7	NaHMDS[a,e]	52%[c]
8	KHMDS[b,f]	52%[c]
9	KHMDS[g]	68%[c]
10	KHMDS[g] (1.2 equiv.)	80%[c], (74%)[c,h]

[a] 1.0 mol solution in THF. [b] 0.5 mol solution in toluene [c] 1.5 equiv. NFSI
[d] Retro-Michael reaction performed at 0 °C [e] 15-Crown-5 (1.05 equiv.) as additive
[f] 18-Crown-6 (1.05 equiv.) as additive [g] 1.0 mol solution in THF
[h] Reaction performed at 3.0 mmol

Under the optimised conditions, sulfuramidimidoyl fluorides derivatives with both cyclic and acyclic secondary amines were synthesised in good yields (**23a-d**). However, derivatives bearing primary amines (**23e** and **23f**) failed to produce corresponding sulfuramidimidoyl fluorides, likely due to HF elimination in basic environment as described by Sharpless and co-workers.[177]

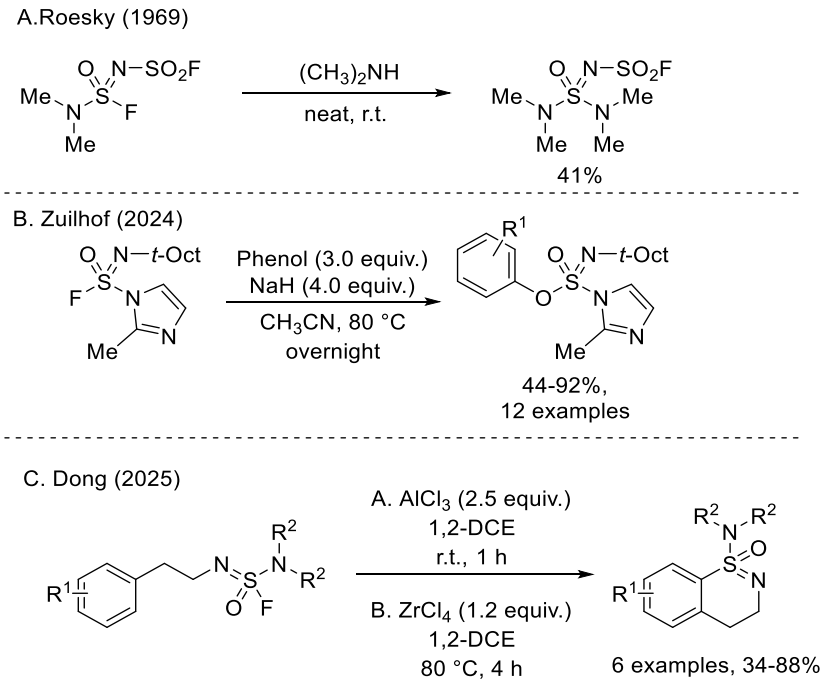


a 80% purity
b Yield calculated by quantative NMR spectroscopy

Scheme 3-13 Synthesis of sulfuramidimidoyl fluorides 23a-f.

3.3 Application of Sulfuramidimidoyl Fluorides in SuFEx Reactions

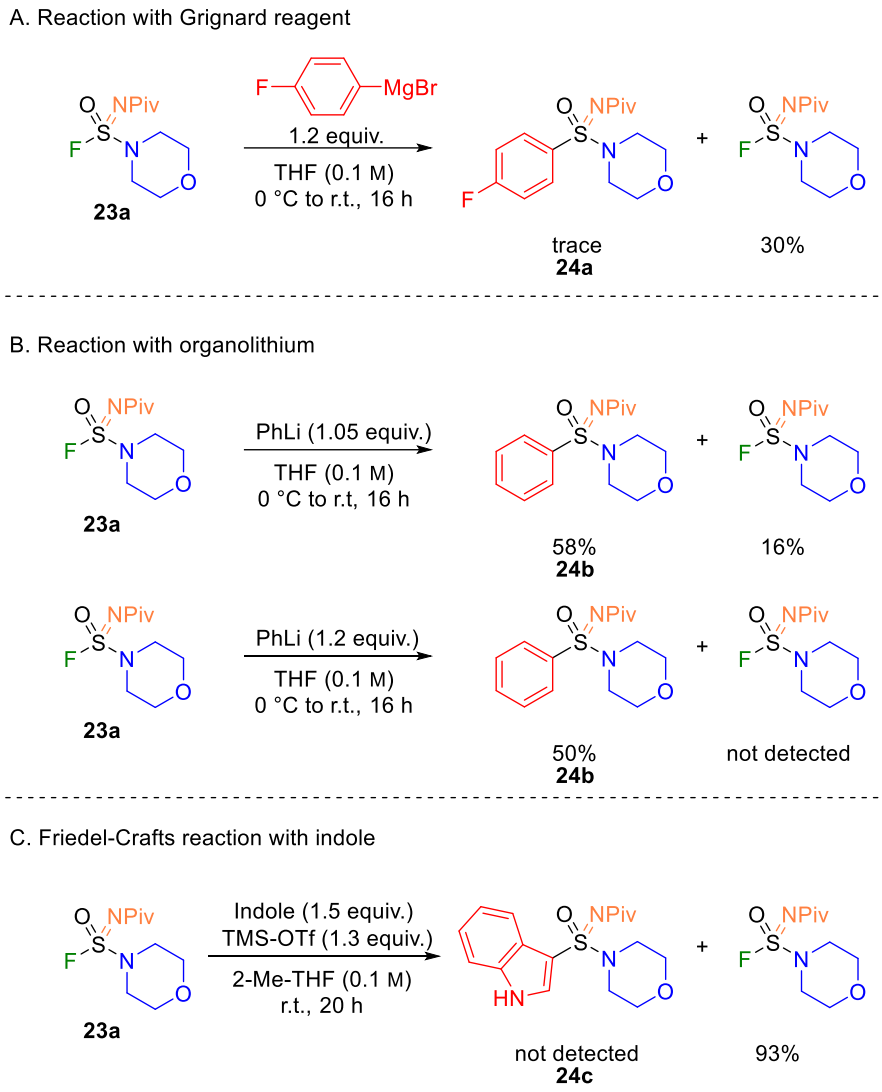
As discussed in chapter 1, the SuFEx reaction has emerged as a powerful tool for constructing various S(VI) compounds. Compared to sulfonyl fluorides, sulfonimidoyl fluorides and sulfamoyl fluorides, the reactivity of sulfuramidimidoyl fluorides remains underexplored due to their relatively low intrinsic reactivity,[175] with limited literature reported on the SuFEx reactivities of these S(VI) fluoride derivatives (**Scheme 3-14**).[129, 181, 182] With reliable access to sulfuramidimidoyl fluorides bearing different amine components, we commenced investigation into the SuFEx reactivities of these S(VI) fluoride derivatives.



Scheme 3-14 Reported SuFEx reaction of sulfuramidimidoyl fluorides.

3.3.1 Reaction of Sulfuramidimidoyl Fluorides with Carbon Nucleophiles

With sulfuramidimidoyl fluorides **23a** prepared on large scale (3 mmol), we initiated the investigation with the examination of their reactivity with organometallic reagents to access sulfonimidamides. Initial reactions with *p*-fluorophenylmagnesium bromide afforded only trace amounts of the desired product, with 30% starting material remaining (**Scheme 3-15 A**). Subsequent attempts using phenyllithium as nucleophile demonstrated significantly improved performance, yielding **24b** in moderate yield (58%) with 16% starting material recovered (**Scheme 3-15 B**). However, increasing the number of equivalents of organolithium led to a decrease in product yield, likely due to the instability of the pivaloyl group under the strongly basic and nucleophilic environment. Suspecting that **23a** was not stable under strongly basic condition, a Friedel-Crafts reaction with indole was attempted to avoid the use of strongly basic reagents. However, treating **23a** with TMS-OTf and indole[183] resulted in no desired product, with most of the starting material being recovered (**Scheme 3-15 C**).



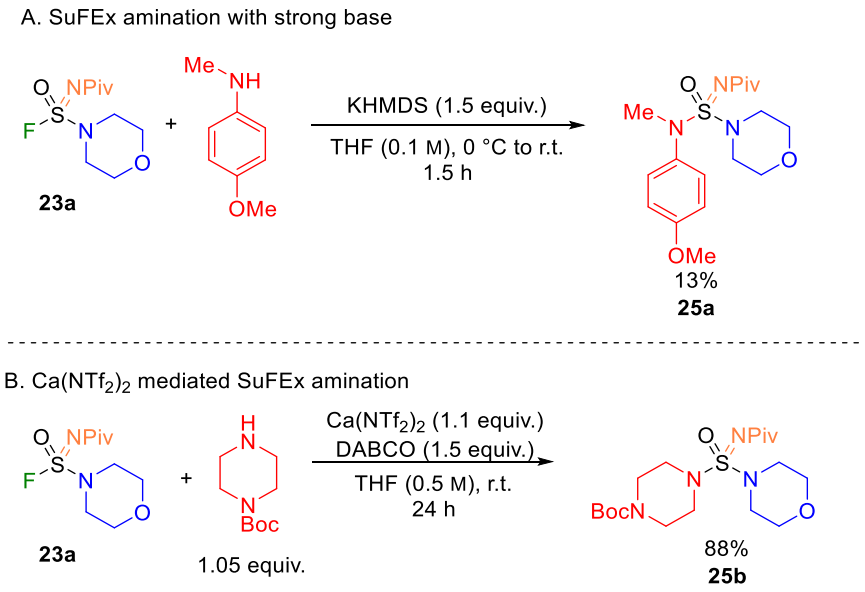
Scheme 3-15 Reaction of 23a with carbon nucleophiles.

3.3.2 Reaction of Sulfuramidimidoyl Fluorides with Nitrogen Nucleophiles

As mentioned in chapter 1, the synthesis of iminosulfamides is rarely reported in literature, and there are only two examples of SuFEx amination of sulfuramidimidoyl fluorides to access iminosulfamides, described by Roesky and co-workers in 1969 and Zuilhof and co-workers in 2024.[129, 182] As we had demonstrated that sulfuramidimidoyl fluorides **23** bearing different amine components could be readily

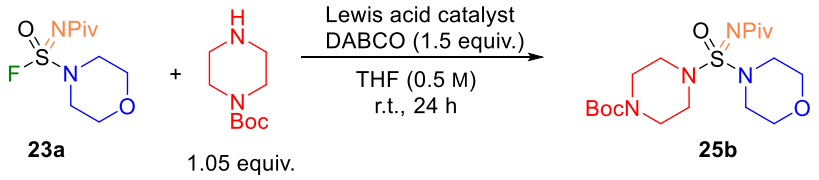
synthesised, we sought to investigate suitable conditions for SuFEx amination that would enable access to a broad range of iminosulfamides.

Initial attempts by reacting **23a** with 4-methoxy-*N*-methylaniline in the presence of KHMDS afforded iminosulfamide **25a** in low yield (13%) and full consumption of starting material (**Scheme 3-16 A**), likely due to the instability of starting material or product under the strong base conditions. Encouragingly, applying the $Ca(NTf_2)_2$ mediated SuFEx amination reported by Ball and co-workers,[24] iminosulfamide **25b** was synthesised in excellent yield (88%) (**Scheme 3-16 B**). Further investigation revealed that stoichiometric (1.1 equiv.) $Ca(NTf_2)_2$ was necessary for high yield. When 0.4 equivalents of $Ca(NTf_2)_2$ (**Table 3-3 entry 1**) were used, the yield dropped significantly (34%). Applying the conditions reported by Ball and co-workers[26] utilising sub-stoichiometric amounts of $Ca(NTf_2)_2$ (**entry 2 and 3**) provided decent yields (56% and 57%), but did not achieve full conversion of starting material. Switching the solvent to 2-MeTHF (**entry 4**) led to a slight drop in product yield (47%). We then examined the effect of different Lewis acid catalysts, and $Ca(NTf_2)_2$ remained the best-performing catalyst. Both $Ca(OTf)_2$ and $LiNTf_2$ (**entry 5 and 6**) gave low yields, while $Sc(OTf)_3$, $Cu(OTf)_2$ and $AlCl_3$ (**entry 7-9**) afforded no product, with most of the starting material recovered.



Scheme 3-16 SuFEx amination of 23a.

Table 3-3 Optimisation for Lewis acid catalysed SuFEx amination.

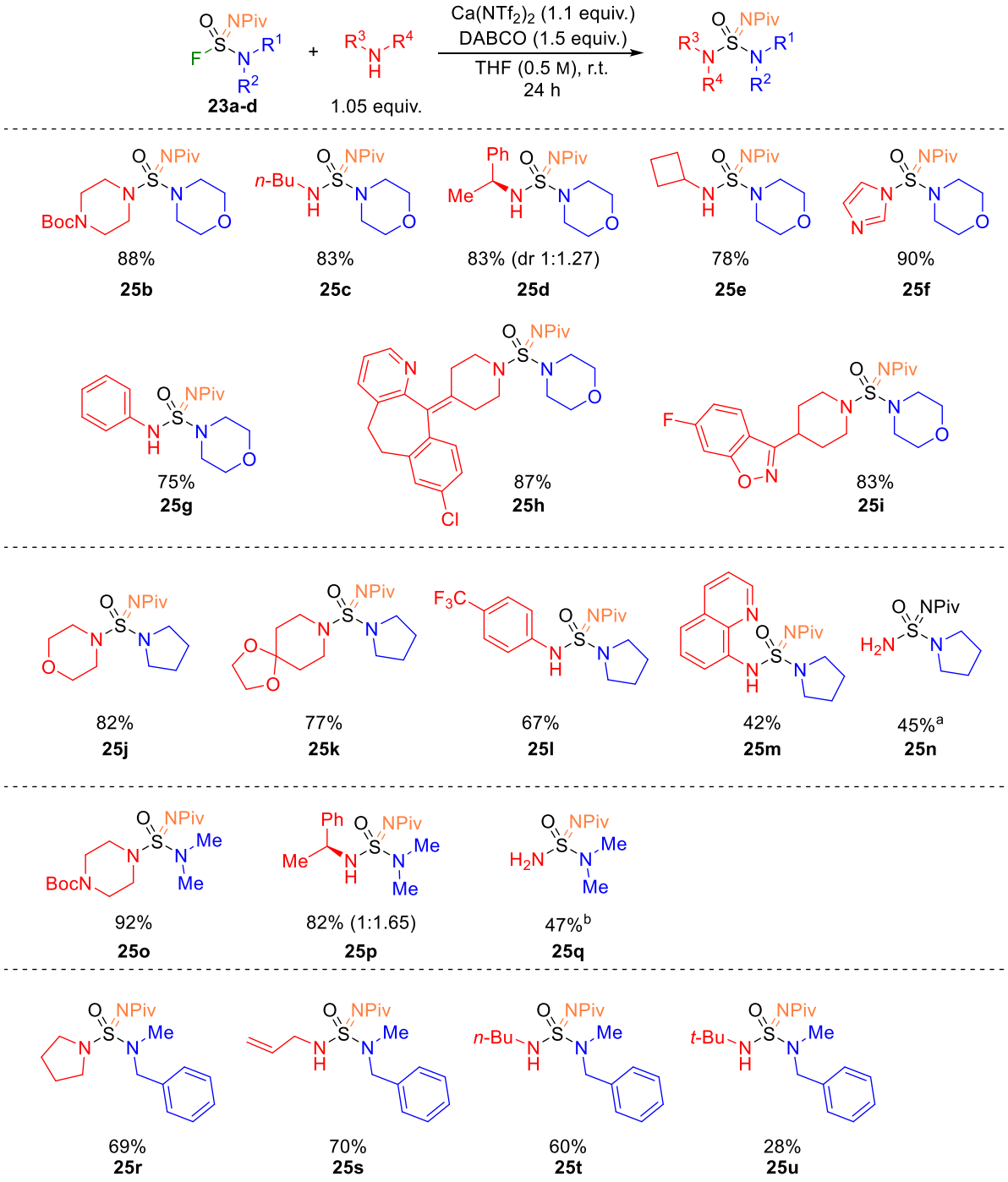


entry	Lewis acid catalyst	Yield (**25b**)
1	$Ca(NTf_2)_2$ (0.4 equiv.)	34%
2	$Ca(NTf_2)_2$ (0.4 equiv.)[a]	56%
3	$Ca(NTf_2)_2$ (0.4 equiv.)[b]	57%
4	$Ca(NTf_2)_2$ (0.4 equiv.)[c]	47%
5	$Ca(OTf)_2$ (1.1 equiv.)	34%
6	LiNTf (1.1 equiv.)	17%
7	$Sc(OTf)_3$ (1.1 equiv.)	n.d. (82%)[d]
8	$Cu(OTf)_2$ (1.1 equiv.)	n.d. (83%)[d]
9	$AlCl_3$ (1.1 equiv.)	n.d. (75%)[d]

[a] THF (0.375 M), TMDS (2.0 equiv.), 35 °C
[b] THF (0.375 M), TMDS (2.0 equiv.), 50 °C
[c] 2-MeTHF (0.375 M), TMDS (2.0 equiv.), 50 °C
[d] Starting material remaining

After obtaining the optimised reaction conditions, SuFEx amination with a large variety of amines was achieved. Primary and secondary amines reacted readily with **23a** to afford the corresponding iminosulfamides (**25b-f**) in good to excellent yields. Weak amine nucleophiles such as aniline (**25g**) also provided the product in good yield. Piperidine fragments from the drugs Loratadine (**25h**) and Risperidone (**25i**) were well tolerated in the reaction. The pyrrolidine and dimethylamine derived SAFs (**23b**,**23c**) showed comparable reactivity with the morpholine derived SAF **23a**. Electron deficient 4-(trifluoromethyl)aniline also reacted smoothly with **23b** to deliver iminosulfamide **25l** in good yield.

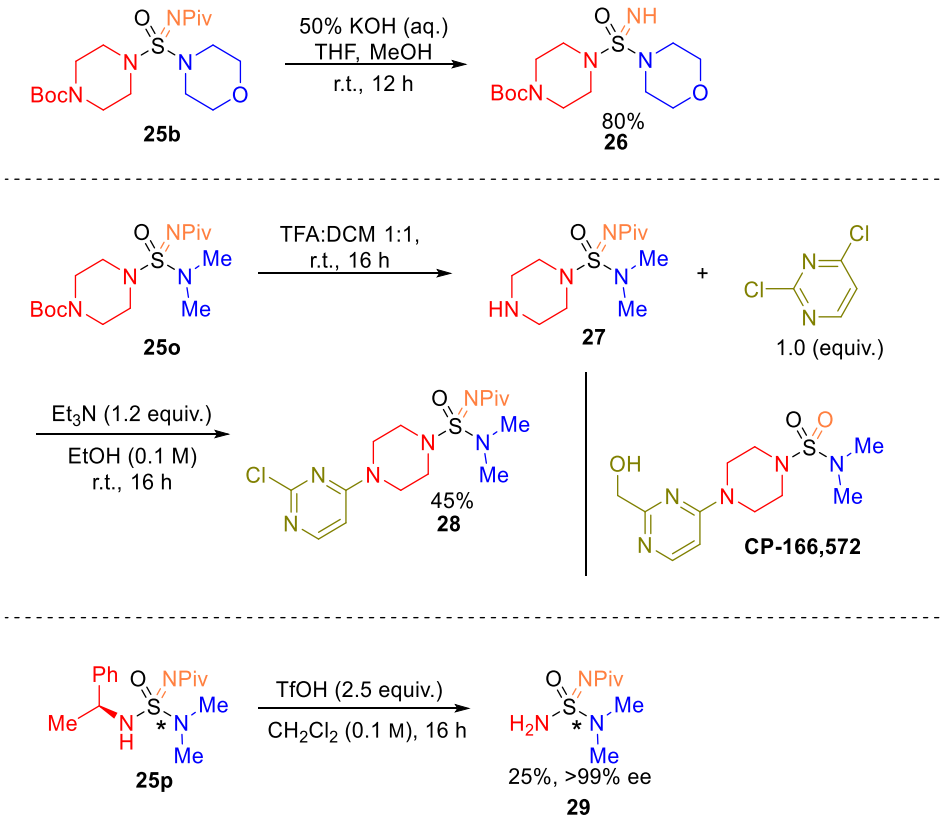
Ammonia in MeOH (**25n**) or THF (**25q**) could be used as nucleophile to generate iminosulfamides featuring primary amino groups. Benzylamine derived SAF **23d** underwent SuFEx amination with secondary and primary amines readily, although generally in lower yield compared to **23a-c**. Bulky *t*-butylamine was also compatible with the reaction, albeit in low yield. In general, the reaction demonstrated broad functional group compatibility (eg., halides, alkene), with good tolerance towards acid sensitive Boc and acetal protecting groups, as well as various heterocycles. Compare with the method reported by Zasukha and co-workers[128] (**Scheme 1-29 B**), the scope of the reaction described in this thesis is significantly broader. Notably, the initial amidic component was not limited to dimethylamine, allowing for greater structural diversity. Furthermore, no heterocyclic substrates were demonstrated in their study, and the reactions involving electron-deficient anilines required elevated temperatures (80 °C) to proceed. In contrast, the SuFEx reaction developed in this work exhibits enhanced robustness and functional tolerance under milder conditions.



Scheme 3-17 Substrate scope for iminosulfamide synthesis.

With a variety of iminosulfamides prepared, we moved on to investigate their derivatisation. The pivaloyl group of **25b** was readily cleaved under basic conditions to afford the *N*H-iminosulfamide **26**. The Boc

group from the amidic nitrogen of piperazine was removed under acidic condition to yield **27**, which underwent S_NAr reaction with 2,4-dichloropyrimidine in the presence of Et_3N to produce **28**, an analogue of SORD inhibitor CP-166572.[184] In addition, the diastereomers of both **25d** and **25p** were separated by flash column chromatography, and treatment of one of the diastereomers of **25p** with triflic acid afforded **29** with >99% ee, albeit obtained in low yield.

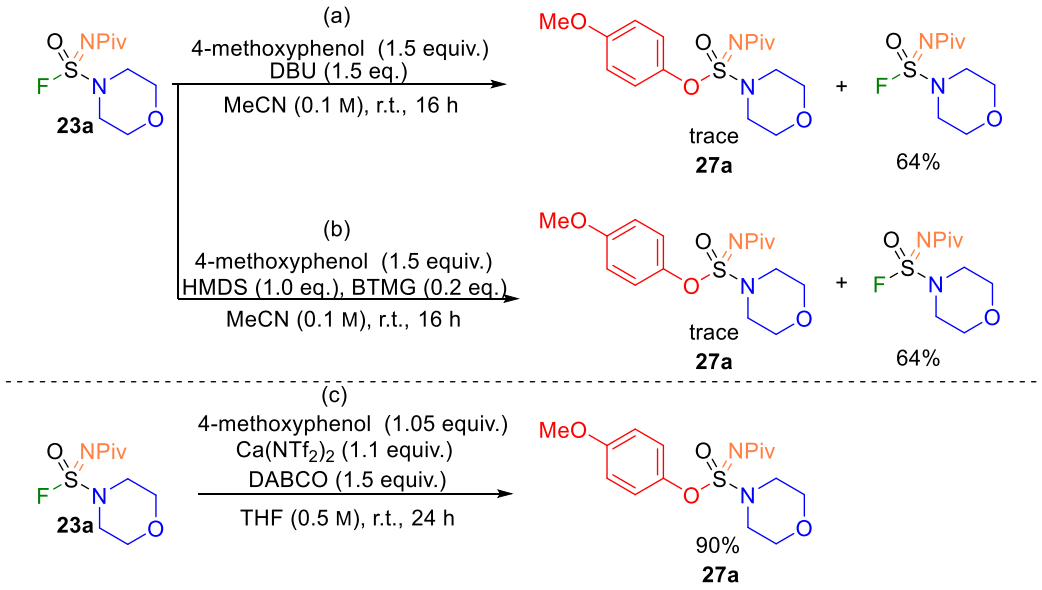


Scheme 3-18 Derivatisation of iminosulfamide 25.

3.3.3 Reaction of Sulfuramidimidoyl Fluorides with Oxygen Nucleophiles

As previously mentioned, Zuilhof and co-workers reported the reaction of sulfuramidimidoyl fluorides with phenol in 2024.[129] Due to the low reactivity of sulfuramidimidoyl fluorides, the reaction required excess phenol under a strongly basic environment at 80 °C. With the electron-withdrawing pivaloyl group installed,

we hypothesised that the SuFEx reactivity would be enhanced. Disappointingly, treating **23a** with 4-methoxyphenol in the presence of DBU[185] (A) or HMDS and BTMG[186] (B) (**Scheme 3-19 a and b**) produced only trace amount of iminosulfamates **27a**, with most of the starting materials remained unreacted. Encouragingly, applying the $Ca(NTf_2)_2$ catalysed system, using 4-methoxyphenol as nucleophile delivered product **27a** in excellent yield (90%) with full conversion of starting materials (**Scheme 3-19 c**).

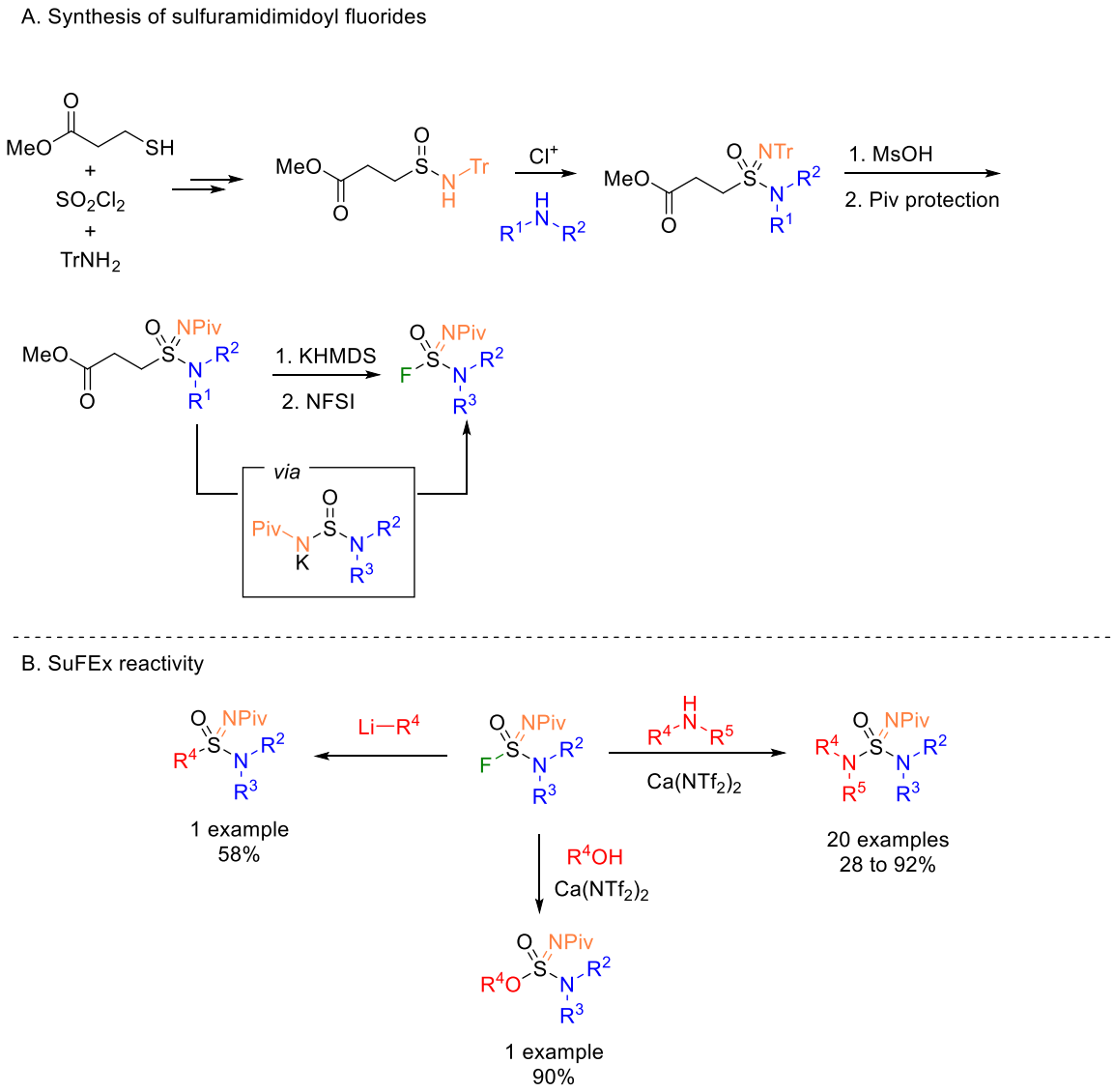


Scheme 3-19 SuFEx reaction of sulfuramidimidoyl fluoride with phenol.

3.4 Summary and Future Work

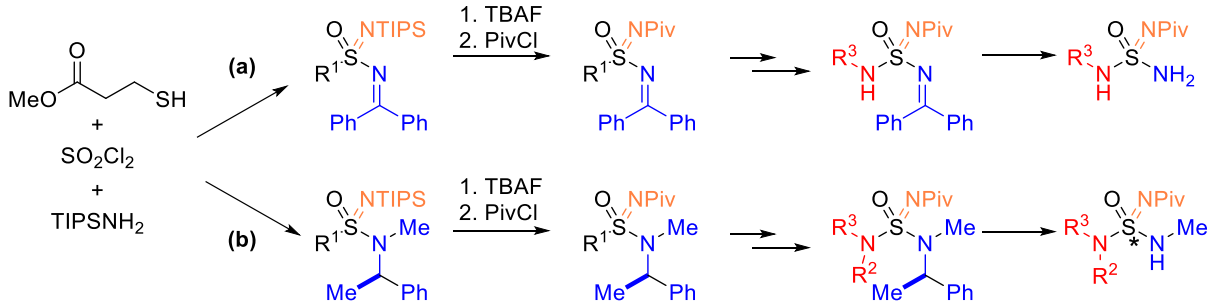
In summary, we have demonstrated that sulfuramidimidoyl fluorides could be synthesised readily through a general and practical approach, starting from easily accessible and commercially available starting materials. The synthesis of sulfuramidimidoyl fluorides involved a key elimination/fluorination process. The use of methyl acrylate as leaving group improved the yield. The presence of the electron withdrawing pivaloyl group enhanced the reactivity of the S(VI) fluoride, enabling subsequent SuFEx reactions of SAFs with amines to generate a wide variety of the iminosulfamides, which were previously considered synthetically challenging. Further derivatisations allowed access to analogues of bioactive sulfamide

molecule, as well as the first reported example of an enantiopure iminosulfamide. Additionally, SAFs also reacted with carbon or oxygen nucleophiles to produce sulfonimidamides and iminosulfamates in moderate to excellent yields.



Scheme 3-20 Summary of synthetic route towards sulfuramidimidoyl fluorides and subsequent SuFEx chemistry.

One limitation of this method was the instability of primary amine derived sulfuramidimidoyl fluorides. A potential strategy to overcome this is to employ masked secondary amines with cleavable functionality, namely *N*-methyl-*N*-(1-phenylethyl)amine or benzophenone imine, which could be converted into primary amine after the SuFEx reaction. However, the acid labile properties of these amines would require the change of $TrNH_2$ to $TIPSNH_2$ for the sulfonimidamides synthesis. This synthetic route would allow the access to iminosulfamides with two primary amines. In addition, early installation of enantiopure *N*-methyl-*N*-(1-phenylethyl)amine would produce diastereomeric sulfonimidamides, which could provide a promising route to access chiral iminosulfamides.

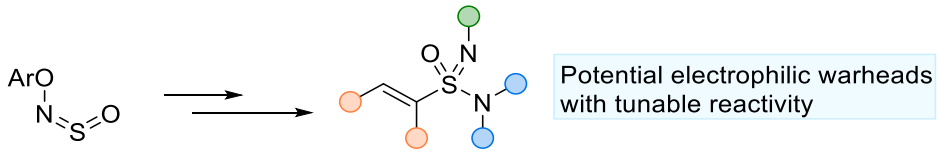


Scheme 3-21 Possible strategy to access (a) Iminosulfamides with two primary amines. (b) Enantiopure iminosulfamides.

Chapter 4 Conclusion and Future Work

Sulfonamides and sulfamides have been a pivotal class of compounds in medicinal chemistry and the agrochemical industry. However, the aza-analogue of these two compounds, named sulfonimidamides and iminosulfamides, despite having a potential advantages over sulfonamides and sulfamides, are rarely explored due to the lack of convenient and robust synthetic methods to prepare these molecules.

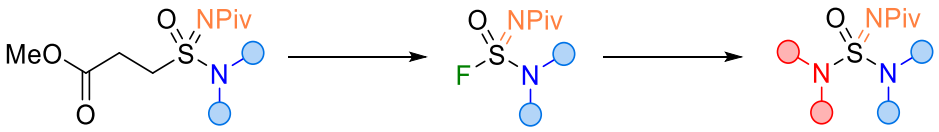
Although recently the synthesis of sulfonimidamides has been much further developed, they are yet to be found in an approved drug. The initial work in this thesis described a single step conversion of O-aryl-N-sulfinylhydroxylamines **BiPhONSO** into *N*-H vinyl sulfonimidamides, which could be easily functionalised to install different electron-withdrawing and donating groups on the imidic N-atom. This class of electrophilic fragments showed good reactivity with cysteine and lysine derived nucleophiles. Kinetic analysis of vinyl sulfonimidamides with glutathione showed that this reactivity is highly dependent on the imidic *N*-substituent. By tuning the imidic *N*-substituent, combined with variation of the alkene substitution pattern, reactivity above or below the corresponding acylamides or sulfonamides could be achieved. With the wide range of reactivities shown, vinyl sulfonimidamides should have broad utility in medicinal chemistry applications.



Scheme 4-1 Summary of Chapter 2.

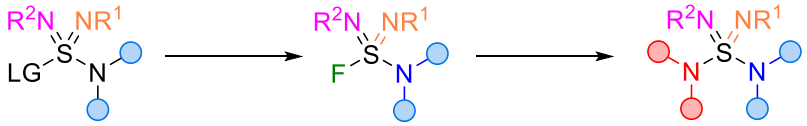
Compared with sulfonimidamides, iminosulfamides are far less explored, and the synthetic methods to access this class of compound are limited. The second half of this thesis demonstrated a general and practical approach for the synthesis of sulfuramidimidoyl fluorides, through an elimination/fluorination process. In this strategy, the first amine component was installed through a one-pot chlorination, amination

reaction, and used in combination with the later SuFEx amination gave access to a wide variety of iminosulfamides containing different amidic components. Further derivatisations allowed access to an analogue of a bioactive sulfamide molecule, as well as the first reported example of enantiopure iminosulfamides.



Scheme 4-2 Summary of Chapter 3.

As an extension of the above established chemistry, a similar strategy might be applied on sulfondiimine derivatives to generate sulfondiimidamidoyl fluorides, which could undergo SuFEx amination to form the tetra-nitrogen substituted diiminosulfamide. This class of compound possess two imidic substituents and could undergo various derivatisation reactions to give great structural diversity and fine-tuning of physiochemical properties, which could be interesting for synthetic or medicinal chemists to explore novel chemical space.



Scheme 4-3 Potential future work.

Chapter 5 Experimental Data and Procedures

5.1 General Considerations

Reactions were performed under an inert nitrogen atmosphere with anhydrous solvent unless otherwise stated. All glassware was oven dried at 200 °C and cooled to room temperature under positive pressure of nitrogen. Reactions were monitored by HPLC/TLC using aluminium backed silica plates. Plates were visualized under ultraviolet light (254 nm) and/or staining with $KMnO_4$. The cooling of reaction mixture to -78 °C was achieved using a dry ice-acetone bath.

Reagents were purchased from Sigma-Aldrich Chemical Co. Ltd., Fisher Scientific, Alfa Aesar, Acros Organics Ltd., Fluorochem Ltd., Fluka™ and were used as supplied. Grignard reagents and *n*-butyllithium were titrated against salicylaldehyde phenylhydrazone.[187]

Flash chromatography was carried out using Geduran® Si 60, 40-63 micron silica gel. 'Petrol' refers to the fraction of light petroleum ether with boiling point in the range of 40-60 °C.

^{1}H NMR spectra were obtained on Bruker AVIII400 (400 MHz), Bruker AVIIIHD 500 (500MHz) and Bruker NEO 600 spectrometer using the residual solvent as an internal standard. ^{13}C-NMR spectra were obtained on a Bruker AVIII 400 (101 MHz), Bruker AVIIIHD 500 (126 MHz) and Bruker NEO 600 (151 MHz) spectrometer using the residual solvent as an internal standard. ^{19}F-NMR spectra were obtained on a Bruker AVIII400 (376 MHz) or Bruker AVIIIHD 500 (476 MHz) spectrometer. Chemical shifts (δ) were reported in parts per million (ppm) with the multiplicities of the spectra reported as following: singlet (s); broad singlet (br. s); doublet (d); triplet (t); quartet (q); pentet (pent); sextet (sext); heptet (hept); multiplet (m); apparent (app.). Coupling constants (*J*) were given in Hertz (Hz) and rounded to the nearest 0.5 Hz.

Low resolution ESI mass spectra were recorded on a Waters LCT Premier spectrometer. High resolution mass spectrometry measurements were recorded on BioAccord LC-MS, performed on ACQUITY RDa mass spectrometer an ACQUITY I-Class PLUS UPLC System (Waters, Milford, MA, USA) coupled to an ACQUITY RDa mass spectrometer (Waters, Milford, MA, USA) equipped with an ESI probe or Bruker

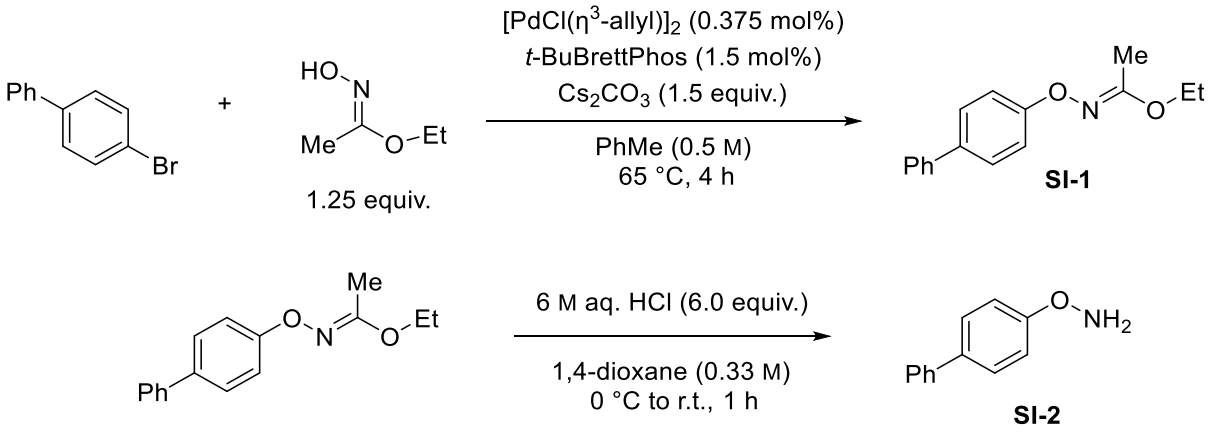
Daltronics MicroTOF (ESI) spectrometer by the internal service at Chemistry Research Laboratory, University of Oxford. Samples for mass spectra were prepared as 10 µg/mL solution in MeCN or MeOH (LRMS, HRMS-ESI, HRMS-LCMS).

Infrared spectra were recorded as thin films on a Bruker Tensor 27 FT-IR spectrometer.

Melting points were determined using a Stuart Scientific Melting Point Apparatus SMP1 and are reported uncorrected.

5.2 Chapter 2 Data

5.2.1 Preparation of BiPhONSO



***O*-([1,1'-biphenyl]-4-yl)hydroxylamine (SI-2)**

Procedures adapted from T. J. Maimone, S. L. Buchwald, *J. Am. Chem. Soc*. 2010, **132**, 9990-9991.[188]

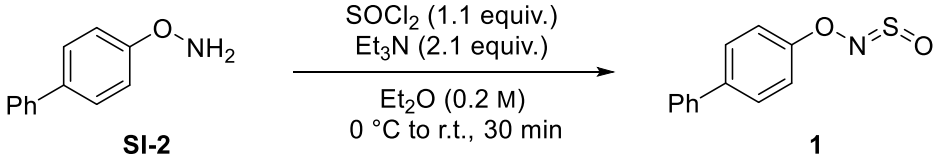
4-Bromobiphenyl (5.83 g, 25.0 mmol, 1.0 equiv.), [PdCl(η3-allyl)]$_2$ (34.3 mg, 0.094 mmol, 0.375 mol%), *t*-BuBrettPhos (182 mg, 0.375 mmol, 1.5 mol%) and Cs_2CO_3 (12.2 g, 37.5 mmol, 1.5 equiv.) were added to an oven dried round-bottomed flask. The flask was evacuated and back-filled with nitrogen three times. Anhydrous, degassed toluene (50 mL, 0.5 M) and ethyl acetohydroxamate (3.10 mL, 31.0 mmol, 1.25 equiv.) were added and the resultant solution was placed in a pre-heated sand bath at 65 °C and stirred for

4 hours. HPLC of the crude mixture showed complete conversion to product. The reaction mixture was then diluted with EtOAc, filtered through a short pad of silica and concentrated *in vacuo*. The crude mixture was used directly in the next reaction without further purification.

The flask containing the crude mixture was evacuated and back-filled with nitrogen three times and the crude mixture was dissolved in anhydrous, degassed 1,4-dioxane (75 mL, 0.33 M) and cooled to 0 °C. 6.0 M aqueous HCl (25 mL, 6 equiv.) was added dropwise. The resultant solution was stirred at 0 °C for 5 min then warmed to room temperature and stirred for 1 hour. The reaction mixture was diluted with Et_2O (250 mL) and transferred to a separating funnel. The organic layer was washed with 1 M aqueous NaOH (300 mL) and brine (250 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was purified by flash chromatography (*n*-hexane/EtOAc 4:1) to give the product as a white solid (3.94 g, 85% over 2 steps).

IR (thin film, ν_{max}/cm^{-1}) 3312, 3056, 3035, 1608, 1483, 1141, 833, 757, 688; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.59-7.54 (m, 2H, Ar-*H*), 7.54-7.51 (m, 2H, Ar-*H*), 7.45-7.38 (m, 2H, Ar-*H*), 7.35-7.28 (m, 1H, Ar-*H*), 7.24-7.19 (m, 2H, Ar-*H*), 5.89 (br. s, 2H, N*H*$_2$); $\boldsymbol{\delta_C}$ (100 MHz, $CDCl_3$) 161.0, 141.1, 134.4, 128.9, 128.1, 126.9, 126.8, 113.6; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 186.077; **HRMS** (ESI^+, *m/z* calculated for $[C_{12}H_{12}NO]^+$ 186.0913 ($[M+H]^+$), found 186.0914. Data is consistent with the literature.[188]

BiPhONSO (1)

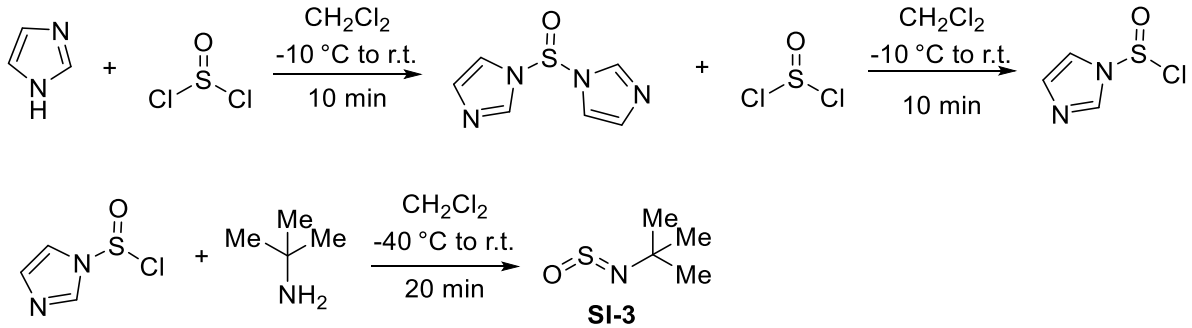


Procedure adapted from T. Q. Davies, M. J. Tilby, J. Ren, N. A. Parker, D. Skolc, A. Hall, F. Duarte, M. C. Willis., *J. Am. Chem. Soc*. **2020**, *142*, 15445-15453.[88]

O-([1,1'-biphenyl]-4-yl)hydroxylamine (1.85 g, 10.0 mmol, 1.0 equiv.) was added to an oven dried round-bottom flask and evacuated and back-filled with nitrogen three times. The hydroxylamine was dissolved in anhydrous, degassed Et_2O (50 mL, 0.20 M) and cooled to 0 °C. Anhydrous triethylamine (2.90 mL, 21.0 mmol, 2.1 equiv.) was added. Thionyl chloride (0.79 mL, 11.0 mmol, 1.1 equiv.) was added dropwise and the reaction mixture was stirred at 0 °C for 15 min, then warmed to room temperature and stirred for 15 min. The reaction mixture was filtered through Celite® and washed with Et_2O (100 mL). The solution was concentrated *in vacuo* to afford BiPhONSO **1** as a gold solid (2.09 g, 90%).

IR (thin film, ν_{max}/cm^{-1}) 1601, 1484, 1208, 1156, 1030, 902, 837, 760, 687; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.66-7.59 (m, 2H, Ar-*H*), 7.59-7.54 (m, 2H, Ar-*H*). 7.48-7.42 (m, 2H, Ar-*H*), 7.39-7.33 (m, 3H, Ar-*H*); $\boldsymbol{\delta_C}$ (100 MHz, $CDCl_3$) 158.2, 140.1, 138.4, 129.0, 128.5, 127.6, 127.1, 114.9; **LRMS** *m/z* (ESI^+) $[M+Na]^+$ 264.040; **HRMS** (ESI^-), *m/z* calculated for $[C_{12}H_8NO_2S]^-$ 230.0281 ($[M-H]^-$), found 230.0276. Data is consistent with the literature.[88]

5.2.2 Preparation of *tert*-Butyl N-sulfinylamine (SI-3)



Procedure adapted from Y. H. Kim, J. M. Shin., *Tetrahedron Lett*. **1985**, *26*, 3821-3824.[158]

Imidazole (1.36 g, 20.0 mmol, 2.0 equiv.) was added to an oven dried round-bottom flask and evacuated and back filled with nitrogen three times. The imidazole was dissolved in CH_2Cl_2 (20 mL) and cooled to -10 °C. Thionyl chloride (0.36 mL, 5.00 mmol, 0.5 equiv.) was added dropwise and stirred at room temperature for 10 min. The solution was filtered through a sinter into another oven dried round-bottom

flask under N_2, cooled to 10 °C and thionyl chloride (0.36 mL, 5.00 mmol, 0.5 equiv.) was added dropwise and stirred at room temperature for 10 min. The *N*-(Chlorosulfinyl)imidazole solution formed was added dropwise to a solution of *tert*-butylamine solution (1.05 mL, 10.0 mmol, 1.0 equiv.) in CH_2Cl_2 (10 mL) at -40 ℃ and stirred for 20 min at room temperature. The solution was filtered through Celite® and washed with CH_2Cl_2 (10 mL). Solvents were removed *in vacuo*, followed by distillation of the crude product (97°C, 1013 mbar) to afford *tert*-butyl *N*-sulfinylamine **SI-3** as a brown liquid (0.92 g, 63%).

IR (thin film, ν_{max}/cm^{-1}) 2953, 2927, 2870, 1466, 1199; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 1.52 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 64.1, 30.7. Data is consistent with the literature.[158]

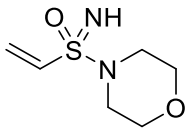
5.2.3 Preparation of Vinyl N-H Sulfonimidamides

General procedure A:

The method was adapted from Procedure adapted from T. Q. Davies, M. J. Tilby, J. Ren, N. A. Parker, D. Skolc, A. Hall, F. Duarte, M. C. Willis., *J. Am. Chem. Soc*. **2020**, *142*, 15445-15453.[88]

BiPhONSO **1** (34.7 mg, 0.15 mmol, 1.0 equiv.) was added to an oven-dried reaction tube. The reaction tube was evacuated and back-filled with nitrogen three times. Anhydrous THF (1.0 mL) was added, and the resulting solution was cooled to -78 °C. The organometallic reagent (1.0 equiv.) was added dropwise over 30 seconds, then the reaction mixture was stirred for 3 min at -78 °C before the amine (1.2 – 1.5 equiv.) was added. The reaction mixture was then transferred to an ice-water bath at 0 °C and stirred for 7 min. The reaction was filtered through a short pad of silica, washed with EtOAc (50 mL) and concentrated *in vacuo*. The crude mixture was purified by flash chromatography to afford the desired sulfonimidamide.

4-(Vinylsulfonimidoyl)morpholine (2a)

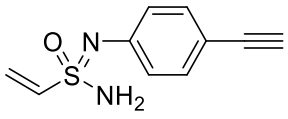


Prepared according to general procedure A, using BiPhONSO **1** (34.7 mg, 0.15 mmol, 1.0 equiv.), vinylmagnesium bromide (167 µL, 0.15 mmol, 0.90 M in THF, 1.0 equiv.) and morpholine (16 µL, 0.18 mmol, 1.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc/MeOH, 1:3:0 to 0:1:0 to 0:98:2), to afford sulfonimidamide **2a** as a pale-yellow oil (15.0 mg, 57%).

IR (thin film, ν_{max}/cm^{-1}) 3272, 1645, 1245, 1110, 1070, 973, 738; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 6.46 (dd, 1H, *J* = 10.0 Hz, 16.5 Hz, Alkenyl-*H*), 6.24 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.06 (d, 1H, *J* = 10.0 Hz, Alkenyl-H), 3.74-3.72 (t, 4H, *J* = 5.0 Hz, Alkyl-*H*), 3.13-3.11 (m, 4H, Alkyl-*H*), 2.38 (br. s, 1H, N*H*); $\boldsymbol{\delta_C}$ (100 MHz, $CDCl_3$) 132.3, 128.6, 66.5, 46.8; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 177.049; **HRMS** (ESI^+), *m/z* calculated for $[C_6H_{13}N_2O_2S]^+$ 177.0692 ($[M+H]^+$), found 177.0690. Data is consistent with literature.[88]

Note: When the reaction was performed on larger scale (0.5 mmol), the yield obtained is significantly lower (35%).

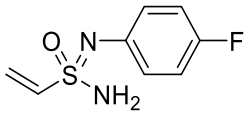
***N*'-(4-Ethynylphenyl)ethenesulfonimidamide (2b)**



Prepared according to general procedure A, using BiPhONSO **1** (34.7 mg, 0.15 mmol, 1.0 equiv.), vinylmagnesium bromide (167 µL, 0.15 mmol, 0.90 M in THF, 1.0 equiv.) and 4-ethynylaniline (26.4 mg, 0.23 mmol, 1.5 equiv.) Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 3:1 to 1:1), to afford sulfonimidamide **2b** as a pale brown oil (8.70 mg, 28%).

IR (thin film, ν_{max}/cm^{-1}) 3282, 2102, 1601, 1293, 1260, 1045, 967, 841; δ_H (400 MHz, $CDCl_3$) 7.40-7.36 (m, 2H, Ar-*H*), 7.12-7.04 (m, 2H, Ar-*H*), 6.72 (dd, 1H, *J* = 16.5 Hz, 9.5 Hz, Alkenyl-*H*), 6.37 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 5.97 (d, 1H, *J* = 9.5 Hz, Alkenyl-*H*), 4.77 (br.s, 2H, N*H*$_2$), 3.02 (s, 1H, Alkynyl-*H*); δ_C (100 MHz, $CDCl_3$) 142.7, 138.4, 133.3, 126.4, 122.8, 116.5, 83.9; 76.6; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 207.051; **HRMS** (ESI^+), *m/z* calculated for $[C_8H_{10}FN_2OS]^+$ 207.0587 ($[M+H]^+$), found 207.0588.

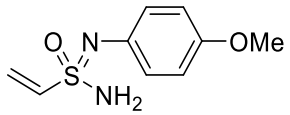
***N*-(4-Fluorophenyl)ethenesulfonimidamide (2c)**



Prepared according to general procedure A, using BiPhONSO **1** (34.7 mg, 0.15 mmol, 1.0 equiv.), vinylmagnesium bromide (167 µL, 0.15 mmol, 0.90 M in THF, 1.0 equiv.) and 4-fluoroaniline (21 µL, 0.23 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 3:1 to 1:1.5), to afford sulfonimidamide **2c** as a pale-yellow oil (7.50 mg, 25%).

IR (thin film, ν_{max}/cm^{-1}) 3219, 1500, 1301, 1213, 1045, 799; δ_H (500 MHz, $CDCl_3$) 7.13-7.03 (m, 2H, Ar-*H*), 6.98-6.88 (m, 2H, Ar-*H*), 6.67 (dd, 1H, *J* = 16.5 Hz, 9.5 Hz, Alkenyl-*H*), 6.27 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 5.91 (d, 1H, *J* = 9.5 Hz, Alkenyl-*H*), 4.71 (br. s, 2H, N*H*$_2$); δ_C (126 MHz, $CDCl_3$) 159.4 (d, $^1J_{CF}$ = 243.5 Hz), 138.1, 137.1 (d, $^4J_{CF}$ = 3.0 Hz), 126.3, 124.7(d, $^3J_{CF}$ = 10.0 Hz), 115.9 (d, $^2J_{CF}$ = 22.5 Hz); **^{19}F NMR** (470 MHz, $CDCl_3$) -119.8 (s); **LRMS** *m/z* (ESI^+) $[M+H]^+$ 201.019; **HRMS** (ESI^+), *m/z* calculated for $[C_8H_{10}FN_2OS]^+$ 201.0492 ($[M+H]^+$), found 201.0491.

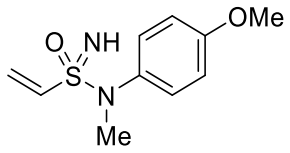
***N*'-(4-Methoxyphenyl)ethenesulfonimidamide (2d)**



Prepared according to general procedure A, using BiPhONSO **1** (34.7 mg, 0.15 mmol, 1.0 equiv.), vinylmagnesium bromide (167 µL, 0.15 mmol, 0.90 M in THF, 1.0 equiv.) and 4-methoxyaniline (27.7 mg, 0.23 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, CH_2Cl_2/EtOAc, 5:1 to 3:1 to 1:1), to afford sulfonimidamide **2d** as a pale brown oil (8.01 mg, 25%).

IR (thin film, ν_{max}/cm^{-1}) 3245, 1503, 1235, 1051, 1030, 834; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 7.12-7.04 (m, 2H, Ar-*H*), 6.83-6.76, (m, 2H, Ar-*H*), 6.67 (dd, 1H, *J* = 16.5 Hz, 9.5 Hz, Alkenyl-*H*), 6.24 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 5.88 (d, 1H, *J* = 9.5 Hz, Alkenyl-H_b), 4.93 (br. s, 2H, NH_2), 3.76 (s, 3H, OCH_3); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 156.8, 137.6, 132.7, 126.4, 125.1, 114.6, 55.6; **LRMS** *m/z* (ESI$^+$) $[M+H]^+$ 213.057; **HRMS** (ESI$^+$), *m/z* calculated for $[C_9H_{12}N_2O_2S]^+$ 213.0692 ($[M+H]^+$), found 213.0694.

***N*-(4-Methoxyphenyl)-*N*-methylethenesulfonimidamide (2e)**

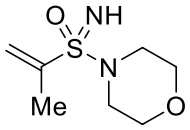


Prepared according to general procedure A, using BiPhONSO **1** (34.7 mg, 0.15 mmol, 1.0 equiv.), vinylmagnesium bromide (167 µL, 0.15 mmol, 0.90 M in THF, 1.0 equiv.) and 4-methoxy-*N*-methylaniline (30.9 mg, 0.23 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, CH_2Cl_2/EtOAc, 5:1 to 3:1 to 1:1), to afford sulfonimidamide **2e** as a pale-yellow oil (12.6 mg, 37%).

IR (thin film, ν_{max}/cm^{-1}) 3293, 3065, 3013, 2967, 2901, 1607, 1510, 1277, 1247, 1031, 863; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 7.20-7.17 (m, 2H, Ar-*H*), 6.87-6.84 (m, 2H, Ar-*H*), 6.55 (dd, 1H, *J* = 16.5 Hz, 10.0 Hz, Alkenyl-*H*), 6.20 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.00 (d, 1H, *J* = 10.0 Hz, Alkenyl-*H*), 3.80 (s, 3H, Alkyl-*H*), 3.20

(s, 3H, Alkyl-*H*), 2.55 (br. s, 1H, N*H*); **δ_C** (126 MHz, $CDCl_3$) 158.8, 135.7, 133.4, 128.5, 127.5, 114.4, 55.6, 39.7; **HRMS** (ESI^+), *m/z* calculated for $[C_{10}H_{15}N_2O_2S]^+$ 227.0849 ($[M+H]^+$), found 227.0850.

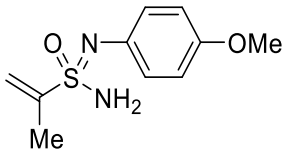
4-(Prop-1-en-2-ylsulfonimidoyl)morpholine (2f)



Prepared according to general procedure A, using BiPhONSO **1** (34.7 mg, 0.15 mmol, 1.0 equiv.), isopropenyl magnesium bromide (285 µL, 0.15 mmol, 0.53 M in THF, 1.0 equiv.) and morpholine (16 µL, 0.18 mmol, 1.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:3 to 0:1), to afford sulfonimidamide **2f** as a pale-yellow oil (16.2 mg, 57%).

IR (thin film, ν_{max}/cm^{-1}) 3268, 3084, 3018, 2967, 2920, 2855, 1452, 1254, 1101, 933, 642, 543; **δ_H** (400 MHz, $CDCl_3$) 5.98 (s, 1H, Alkenyl-*H*), 5.67 (s, 1H, Alkenyl-*H*), 3.71 (app. s, 4H, Alkyl-*H*), 3.17 (app. s, 4H, Alkyl-*H*), 2.32 (br. s, 1H, N*H*), 2.10 (s, 3H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$)143.1, 123.9, 67.0, 46.8, 19.0; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 191.059; **HRMS** (ESI^+), *m/z* calculated for $[C_7H_{15}N_2O_2S]^+$ 191.0849 ($[M+H]^+$), found 191.0848.

***N*'-(4-Methoxyphenyl)prop-1-ene-2-sulfonimidamide (2g)**

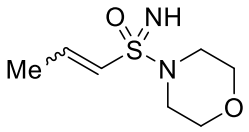


Prepared according to general procedure A, using BiPhONSO **1** (34.7 mg, 0.15 mmol, 1.0 equiv.), isopropenyl magnesium bromide (285 µL, 0.15 mmol, 0.53 M in THF, 1.0 equiv.) and 4-methoxyaniline

(27.7 mg, 0.23 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 3:1 to 1:1 to 1:3), to afford sulfonimidamide **2g** as a pale-yellow oil (19.0 mg, 56%).

IR (thin film, ν_{max}/cm^{-1}) 3256, 3064, 2922, 2835, 1599, 1504, 1234, 1106, 1043, 836, 742; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 7.08-7.05 (m, 2H, Ar-*H*), 6.81-6.78 (m, 2H, Ar-*H*), 6.08 (s, 1H, Alkenyl-*H*), 5.60 (s, 1H, Alkenyl-*H*), 4.67 (br. s, 2H, N*H*$_2$), 3.76 (s, 3H, Alkyl-*H*), 2.14 (s, 3H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 156.4, 145.4, 133.7, 124.4, 123.6, 114.5, 55.6, 17.5; **HRMS** (ESI^+), *m/z* calculated for $[C_7H_{15}N_2O_2S]^+$ 227.0849 ($[M+H]^+$), found 227.0848.

4-(Prop-1-en-1-ylsulfonimidoyl)morpholine (2h)

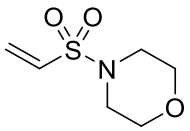


Prepared according to general procedure A, using BiPhONSO **1** (34.7 mg, 0.15 mmol, 1.0 equiv.), 1-propenyl magnesium bromide (300 µL, 0.15 mmol, 0.50 M in THF, 1.0 equiv.) and morpholine (16 µL, 0.18 mmol, 1.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:3 to 0:1), to afford sulfonimidamide **2h** as an inseparable 1:1 mixture of cis-trans isomers, as a pale-yellow oil (18.0 mg, 63%).

IR (thin film, ν_{max}/cm^{-1}) 3268, 3056, 3024, 2961, 2918, 2855, 1630, 1454, 1292, 1111, 1069, 1003, 930, 759, 708; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 6.76 (dq, 1H, *J* = 15.0 Hz, 7.0 Hz, *E* isomer, Alkenyl-*H*), 6.43 (dq, 1H, *J* = 11.0 Hz, 7.5 Hz, *Z* isomer, Alkenyl-*H*), 6.15 (dq, 1H, *J* = 15.0 Hz, 1.5 Hz, *E* isomer, Alkenyl-*H*), 6.07 (dq, 1H, *J* = 11.0 Hz, 1.5 Hz, *Z* isomer, Alkenyl-*H*), 3.75-3.71 (m, 8H, *Z* and *E* isomers, Alkyl-*H*$_2$), 3.18-3.16 (m, 4H, *Z* isomer, Alkyl-*H*), 3.10-3.08 (m, 4H, *E* isomer, Alkyl-*H*) 2.38 (br. s, 1H, *Z* isomer, N*H*), 2.29 (br. s, 1H, *E* isomer, N*H*), 2.16 (dd, 3H, *J* = 7.5 Hz, 1.5 Hz, *Z* isomer, Alkyl-*H*), 1.95 (dd, 3H, *J* = 7.0 Hz, 1.5 Hz, *E* isomer, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 143.7, 142.6, 124.9, 124.5, 66.8, 66.7, 47.04, 46.97, 17.4, 14.4; **HRMS** (ESI^+), *m/z* calculated for $[C_7H_{14}N_2O_2SNa]^+$ 213.0668 ($[M+Na]^+$), found 213.0667.

5.2.4 Synthesis of Vinyl Sulfonamide

4-(Vinylsulfonyl)morpholine (12)



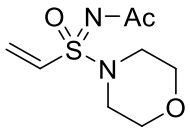
Procedure adapted from Ł. Woźniak, A. A. Rajkiewicz, L. Monsigny, A. Kajetanowicz, K. Grela. *Org. Lett*, **2020**, *22*, 4970-4973.[189]

Morpholine (172 µL, 2.00 mmol, 1.0 equiv.) and triethylamine (975 µL, 7.00 mmol, 3.5 equiv.) were added to an oven dried flask that had been evacuated and back-filled with nitrogen three times. Anhydrous CH_2Cl_2 (6.0 mL, 0.33 M) was added and the solution was cooled to 0 °C. 2-Chloroethanesulfonyl chloride (209 µL, 2.00 mmol, 1.0 equiv.) was added and the solution was stirred at 0 °C for 2 hours. The reaction mixture was diluted by $CHCl_3$ (10 mL), washed with brine (2 × 10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography (Petrol/EtOAc, 1:3 to 0:1), to afford the product **12** as a pale-yellow oil (263.2 mg, 74%).

IR (thin film, ν_{max}/cm^{-1}) 3105, 3058, 2985, 2899, 2864, 1456, 1349, 1261, 1161, 1115, 1075, 947, 763.1, 668; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 6.43 (dd, 1H, *J* = 16.5 Hz, 10.0 Hz, Alkenyl-*H*), 6.27 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.09 (d, *J* = 10.0 Hz, Alkenyl-*H*), 3.77-3.75 (m, 4H, Alkyl-*H*), 3.15-3.13 (m, 4H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 131.9, 129.7, 66.4, 45.8; **HRMS** (ESI^+), *m/z* calculated for $[C_7H_{15}N_2O_2S]^+$ 178.0532 ($[M+H]^+$), found 178.0534. Data is consistent with literature.[189]

5.2.5 *N*-functionalization of Sulfonimidamides

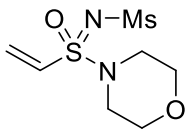
***N*-(Morpholino(oxo)(vinyl)-λ^6-sulfaneylidene)acetamide (3a)**



Sulfonimidamide **2a** (26.4 mg, 0.15 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (1.5 mL, 0.10 M) was added and the solution was cooled to 0 °C. Anhydrous triethylamine (31 µL, 0.23 mmol, 1.5 equiv.) was added to the solution, followed by the addition of acetyl chloride (16 µL, 0.23 mmol, 1.5 equiv.). The reaction mixture was warmed to room temperature and stirred for 4 hours. The crude mixture was filtered through Celite®, washed with EtOAc (30 mL) and concentrated *in vacuo.* Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:3 to 0:1), to afford the product **3a** as a colourless oil (18.3 mg, 56%).

IR (thin film, ν_{max}/cm^{-1}) 2970, 2921, 2900, 1643, 1363, 1243, 1112, 1074, 937, 843, 742; **δ_H** (400 MHz, $CDCl_3$) 6.57 (dd, 1H, *J* = 16.5 Hz, 9.5 Hz, Alkenyl-*H*), 6.40 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.20 (d, 1H, *J* = 9.5 Hz, Alkenyl-*H*), 3.77-3.75 (m, 4H, Alkyl-*H*), 3.25-3.15 (m, 4H, Alkyl-*H*), 2.12 (s, 3H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 178.4, 132.4, 130.4, 66.4, 45.6, 27.2; **LRMS** *m/z* (ESI$^+$) $[M+H]^+$ 219.072; **HRMS** (ESI$^+$), *m/z* calculated for $[C_8H_{15}N_2O_3S]^+$ 219.0798 ($[M+H]^+$), found 219.0798.

***N*-(Morpholino(oxo)(vinyl)-λ^6-sulfaneylidene)methanesulfonamide (3b)**

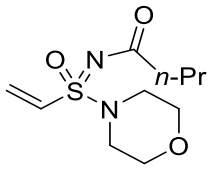


Sulfonimidamide **2a** (26.4 mg, 0.15 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (1.5 mL, 0.10 M) was added

and the solution was cooled to 0 °C. Anhydrous triethylamine (31 µL, 0.23 mmol, 1.5 equiv.) was added to the solution, followed by the addition of methanesulfonyl chloride (17 µL, 0.23 mmol, 1.5 equiv.). The reaction mixture was warmed to room temperature and stirred for 3 hours. The crude mixture was filtered through Celite®, washed with EtOAc (30 mL) and concentrated *in vacuo.* Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:1 to 1:3 to 0:1), to afford the product **3b** as a pale-yellow oil (26.7 mg, 70%).

IR (thin film, ν_{max}/cm^{-1}) 3055, 3020, 2922, 2859, 1304, 1259, 1145, 1101, 1071, 937, 801, 760; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 6.49 (dd, 1H, *J* = 16.5 Hz, 9.0 Hz, Alkenyl-*H*), 6.41 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.24 (d, 1H, *J* = 9.0 Hz, Alkenyl*H*), 3.77-3.75 (m, 4H, Alkyl-*H*), 3.36-3.17 (m, 4H, Alkyl-*H*), 3.14-3.09 (s, 3H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 132.1, 130.9, 66.2, 46.1, 45.0; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 255.067; **HRMS** (ESI^+), *m/z* calculated for $[C_8H_{15}N_2O_3S]^+$ 255.0472 ($[M+H]^+$), found 255.0465.

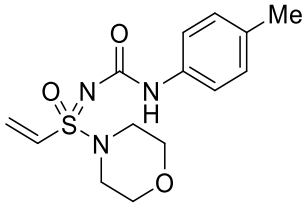
***N*-(Morpholino(oxo)(vinyl)-λ^6-sulfaneylidene)butyramide (3c)**



Sulfonimidamide **2a** (38.7 mg, 0.22 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (2.2 mL, 0.10 M) was added and the solution was cooled to 0 °C. Anhydrous triethylamine (46 µL, 0.33 mmol, 1.5 equiv.) was added to the solution, followed by the addition of butyryl chloride (34 µL, 0.33 mmol, 1.5 equiv.) The reaction mixture was warmed to room temperature and stirred for 4 hours. The crude mixture was filtered through Celite®, washed with EtOAc (30 mL) and concentrated *in vacuo.* Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:3 to 0:1), to afford the product **3c** as a colourless oil (40.0 mg, 73%).

IR (thin film, ν_{max}/cm^{-1}) 3102, 3054, 2964, 2928, 2863, 1644, 1455, 1245, 1199, 1073, 937, 847, 740; **δ_H** (400 MHz, $CDCl_3$) 6.57 (dd, 1H, *J* = 16.5 Hz, 9.5 Hz, Alkenyl-*H*), 6.40 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.19 (d, 1H, *J* = 9.5 Hz, Alkenyl-*H*), 3.80-3.70 (m, 4H, Alkyl-*H*), 3.25-3.16 (m, 4H, Alkyl-*H*), 2.34 (t, 2H, *J* = 7.5 Hz, Alkyl-*H*), 1.64 (sext., 2H, *J* = 7.5 Hz, Alkyl-*H*), 0.93 (t, 3H, J = 7.5 Hz, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 181.2, 132.6, 130.2, 66.4, 45.5, 42.0, 19.1, 13.9; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 247.075; **HRMS** (ESI^+), *m/z* calculated for $[C_{10}H_{19}N_2O_3S]^+$ 247.1110 ($[M+H]^+$), found 247.1111.

1-(Morpholino(oxo)(vinyl)-λ^6-sulfaneylidene)-3-(*p*-tolyl)urea (3d)

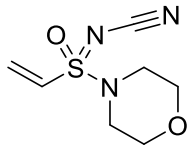


Sulfonimidamide **2a** (26.4 mg, 0.15 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (1.5 mL, 0.10 M) was added and the solution was cooled to 0 °C. Anhydrous triethylamine (21 µL, 0.15 mmol, 1.5 equiv.) was added to the solution, followed by the addition of *p*-tolyl isocyanate (30.0 mg, 0.23 mmol, 1.5 equiv.). The reaction mixture was warmed to room temperature and stirred for 20 hours. Saturated $NH_4Cl_{(aq)}$ (3 mL) was added and EtOAc (3 × 5 mL) was used for extraction. The organic layers were washed with brine (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 5:1 to 1:1 to 0:1), to afford the product **3d** as a pale-yellow oil (16.9 mg, 36%).

IR (thin film, ν_{max}/cm^{-1}) 3295, 3102, 3046, 2966, 2920, 2858, 1646, 1521, 1275, 1228, 1111, 941, 850, 820; **δ_H** (400 MHz, $CDCl_3$) 7.30 (d, 2H, *J* = 8.0 Hz, Ar-*H*), 7.07 (d, 2H, *J* = 8.5 Hz, Ar-*H*), 6.90 (br. s, 1H, N*H*), 6.66 (dd, 1H, *J* = 16.5Hz, 10.0 Hz, Alkenyl-*H*), 6.40 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.18 (d, 1H, *J* = 10.0 Hz, Alkenyl-*H*), 3.79-3.76 (m, 4H, Alkyl-*H*), 3.30-3.20 (m, 4H, Alkyl-*H*), 2.28 (s, 3H, Alkyl-*H*); **δ_C** (101

MHz, $CDCl_3$) 155.7, 136.3, 132.7 (2C), 129.7, 129.5, 119.0, 66.4, 45.8, 20.9; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 310.109; **HRMS** (ESI^+), *m/z* calculated for $[C_{14}H_{20}N_3O_3S]^+$ 310.1220 ($[M+H]^+$), found 310.1217.

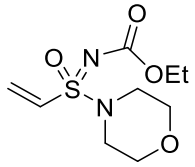
***N*-(Morpholino(oxo)(vinyl)-λ^6-sulfaneylidene)cyanamide (3e)**



Sulfonimidamide **2a** (35.2 mg, 0.20 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous CH_2Cl_2 (2.0 mL, 0.10 M) was added and the solution was cooled to 0 °C. Anhydrous triethylamine (42 µL, 0.30 mmol, 1.5 equiv.) was added to the solution, followed by the addition of cyanogen bromide (80 µL, 0.24 mmol, 3.0 M in CH_2Cl_2, 1.2 equiv.). The reaction mixture was warmed to room temperature and stirred for 16 hours. The crude mixture was quenched with saturated $NaHCO_{3\,(aq)}$ (10 mL) and extracted with dichloromethane (10 mL × 3). The combined organic layers were washed with brine (10 mL) and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:1 to 0:1), to afford the product **3e** as a colourless oil (4.4 mg, 11%).

IR (thin film, ν_{max}/cm^{-1}) 3057, 2984, 2921, 2860, 2205, 1455, 1259, 1201, 1111, 1073, 942, 844, 771, 647, 621; $\boldsymbol{\delta_H}$ (600 MHz, $CDCl_3$) 6.49-6.35 (m, 2H, SC*H*, Alkenyl-*H*), 6.30 (dd, 1H, *J* = 7.5 Hz, 1.5 Hz, Alkenyl-*H*), 3.82-3.71 (m, 4H, Alkyl-*H*), 3.24-3.14 (m, 4H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (151 MHz, $CDCl_3$) 133.4, 129.9, 110.2, 66.1, 46.2; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 202.061; **HRMS** (ESI^+), *m/z* calculated for $[C_9H_{17}N_2O_4S]^+$ 202.0645 ($[M+H]^+$), found 202.0646.

Ethyl (morpholino(oxo)(vinyl)-λ^6-sulfaneylidene)carbamate (3f)

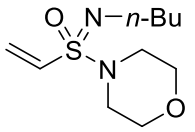


Procedure adapted from F. Izzo, M. Schäfer, P. Lienau, U. Ganzer, R. Stockman, U. Lücking. *Chem. Eur. J*. **2018**., *24*, 9295-9304.[156]

Sulfonimidamide **2a** (35.3 mg, 0.20 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (2.0 mL, 0.10 M) was added and the solution was cooled to 0 °C. Pyridine (29 µL, 0.36 mmol, 1.8 equiv.) was added to the solution, followed by the addition of ethyl chloroformate (29 µL, 0.30 mmol, 1.5 equiv.). The reaction mixture was warmed to room temperature and stirred for 16 hours. The crude mixture was filtered through Celite®, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:1 to 1:3), to afford the product **3f** as a pale-yellow oil (34.7 mg, 70%).

IR (thin film, ν_{max}/cm^{-1}) 3054, 2979, 2903, 2861, 1672, 1245, 1111, 1071, 1021, 938, 787, 695, 654; **δ_H** (400 MHz, $CDCl_3$) 6.49 (dd, 1H, *J* = 16.5 Hz, 9.5 Hz, Alkenyl-*H*), 6.37 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.17 (d, 1H, *J* = 9.5 Hz, Alkenyl-*H*), 4.10 (q, 2H, *J* = 7.5 Hz, Alkenyl-*H*), 3.75-3.73 (m, 4H, Alkyl-*H*), 3.27-3.15 (m, 4H, Alkyl-*H*), 1.25 (t, 3H, *J* = 7.5 Hz, Alkyl-*H*); **δ_C** (101 MHz) 157.3, 132.3, 130.2, 66.3, 62.2, 45.7, 14.4; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 249.054; **HRMS** (ESI^+), *m/z* calculated for $[C_9H_{17}N_2O_4S]^+$ 249.0904 ($[M+H]^+$), found 249.0904.

4-(*N*-Butylvinylsulfonimidoyl)morpholine (3g)

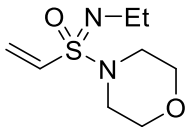


Procedure adapted from F. Izzo, M. Schäfer, P. Lienau, U. Ganzer, R. Stockman, U. Lücking. *Chem. Eur. J*. **2018**., *24*, 9295-9304.[156]

Sulfonimidamide **2a** (45.8 mg, 0.26 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous DMSO (1.3 mL, 0.2 M) and bromobutane (42 µL, 0.39 mmol, 1.5 equiv.) was added, followed by the addition of KHMDS (104 mg, 0.52 mmol, 2.0 equiv.). The solution was stirred at room temperature for 2 hours. H_2O (10 mL) and EtOAc (3 × 20 mL) were used for extraction and the organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:1 to 0:1), to afford the product **3g** as a pale-yellow oil (28.6 mg, 47%).

IR (thin film, ν_{max}/cm^{-1}) 3054, 2958, 2927, 2857, 1453, 1278, 1255, 1152, 1113, 1068, 931, 758, 653; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 6.40 (dd, 1H, *J* = 17.0 Hz, 10.0 Hz, Alkenyl-*H*), 6.16 (d, 1H, *J* = 17.0 Hz, Alkenyl-*H*), 5.97 (d, 1H, *J* = 10.0 Hz, Alkenyl-*H*), 3.78-3.65 (m, 4H, Alkyl-H), 3.24-2.89 (m, 6H, Alkyl-*H*), 1.58-1.46 (m, 2H, Alkyl-*H*), 1.42-1.29 (m, 2H, Alkyl-*H*), 0.89 (t, 3H, *J* = 7.5 Hz, Alkyl-H); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 132.5, 127.6, 66.6, 46.8, 41.5, 34.8, 20.5, 14.0; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 233.082; **HRMS** (ESI^+), *m/z* calculated for $[C_{10}H_{21}N_2O_2S]^+$ 233.1818 ($[M+H]^+$), found 233.1818.

4-(*N*-Ethylvinylsulfonimidoyl)morpholine (3h)

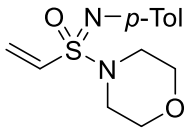


Procedure adapted from F. Izzo, M. Schäfer, P. Lienau, U. Ganzer, R. Stockman, U. Lücking. *Chem. Eur. J*. **2018**., *24*, 9295-9304.[156]

Sulfonimidamide **2a** (45.8 mg, 0.26 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous DMSO (1.3 mL, 0.20 M) and bromoethane (30 µL, 0.39 mmol, 1.5 equiv.) was added, followed by the addition of KHMDS (103.7 mg, 0.52 mmol, 2.0 equiv.). The solution was stirred at room temperature for 2 hours. H_2O (10 mL) and EtOAc (3 × 20 mL) were used for extraction and the organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:2 to 0:1), to afford the product **3h** as a pale-yellow oil (26.6 mg, 50%).

IR (thin film, ν_{max}/cm^{-1}) 3052, 2967, 2917, 2895, 2857, 1453, 1293, 1245, 1152, 1111, 1084, 927, 824, 756, 650; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 6.41 (dd, 1H, *J* = 17.0 Hz, 10.0 Hz, Alkenyl-*H*), 6.17 (d, 1H, *J* = 17.0 Hz, Alkenyl-*H*), 5.98 (d, 1H, *J* = 10.0 Hz, Alkenyl-*H*), 3.76-3.67 (m, 4H, Alkyl-*H*) 3.27-3.16 (m, 1H, Alkyl-*H*), 3.12-2.96 (m, 5H, Alkyl-*H*), 1.19 (3H, t, *J* = 7.0 Hz, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 132.4, 127.7, 66.6, 46.9, 36.6, 18.2; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 205.076; **HRMS** (ESI^+), *m/z* calculated for $[C_8H_{17}N_2O_2S]^+$ 205.1005 ($[M+H]^+$), found 205.1005.

4-(*N*-(*p*-Tolyl)vinylsulfonimidoyl)morpholine (3i)

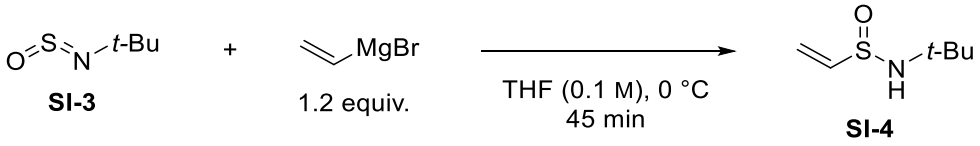


Procedure adapted from J. C. Vantourout, L. Li, E. B. Moll, S. Chabbra, K. Arrington, B. E. Bode, A. I. Llobet, J. A. Kowalski, M. G. Nilson, K. M. P. Wheelhouse, J. L. Woodard, S. Xie, D. Leitch, A. J. B. Watson. *ACS Catal*. **2018**, *8*, 9560–9566.[157]

Sulfonimidamide **2a** (44.1 mg, 0.25 mmol, 1.0 equiv.), *p*-tolylboronic acid (78.2 mg, 0.58 mmol, 2.3 equiv.), $Cu(MeCN)_4BF_4$ (11.8 mg, 0.038 mmol, 15 mol%) were added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous DMF (0.83 mL, 0.3 M) was added and the flask was changed to an oxygen environment. The reaction mixture was stirred at room temperature for 24 hours. H_2O (10 mL) was added to the vial for quenching the reaction and the flask was opened to air. The crude mixture was extracted with EtOAc (3 × 10 mL), the organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash chromatography (Petrol/EtOAc, 5:1, 2:1 to 1:1), to afford the product **3i** as a pale-yellow oil (27.9 mg, 42%).

IR (thin film, ν_{max}/cm^{-1}) 3052, 3022, 2965, 2917, 2893, 2856, 1609, 1506, 1452, 1379, 1310, 1257, 1225, 1112, 1074, 930, 822, 761, 654; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.06-7.01 (m, 4 H, Ar-*H*), 6.53 (dd. 1H, *J* = 16.5 Hz, 10.0 Hz, Alkenyl-*H*), 6.31 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.08 (d, 1H , *J* = 10.0 Hz, Alkenyl-*H*), 3.71-3.60 (m, 4H, Alkyl-*H*), 3.21-3.09 (m, 4H, Alkyl-*H*), 2.28 (s, 3H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 140.3, 132.8, 131.7, 129.7, 128.3, 123.5, 66.5, 46.6, 20.9; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 267.077; **HRMS** (ESI^+), *m/z* calculated for $[C_{13}H_{19}N_2O_2S]^+$ 267.1162 ($[M+H]^+$), found 267.1162.

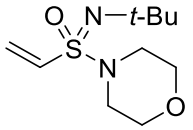
***N*-(*tert*-Butyl)ethenesulfinamide (SI-4)**



Sulfinylamine **SI-3** (238 mg, 2.00 mmol, 1.0 equiv.) was added to an oven dried flask and dissolved in anhydrous THF (2.0 mL, 0.10 M). The solution was quickly degassed and refilled with nitrogen three times. The solution was cooled to 0 °C and vinylmagnesium bromide (2.45 mL, 0.98 M, 2.40 mmol, 1.2 equiv.) was added dropwise. The solution was stirred at 0 °C for 45 min, quenched with silica, filtered through a short pad of silica and washed with EtOAc (30 mL). The crude mixture was concentrated *in vacuo* and purified using flash column chromatography (Petrol/EtOAc 1:1 to 1:3), to afford the product **SI-4** as a pale-yellow solid (86.2 mg, 29%).

m.p. 48-50 °C (EtOAc**); IR** (thin film, ν_{max}/cm^{-1}) 3146, 3053, 3012, 2969, 2921, 1735, 1605, 1367, 1235, 1054, 963, 806, 668; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 6.59 (dd, 1H, *J* = 16.5, 9.5 Hz, Alkenyl-*H*), 6.11 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 5.87 (d, 1H , *J* = 9.5 Hz, Alkenyl-*H*), 3.64 (br. s., 1H, N*H*), 1.33 (s, 9H, Alkenyl-*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 143.0, 122.3, 54.3, 31.1; **HRMS** (ESI$^+$), *m/z* calculated for $[C_6H_{14}NOS]^+$ 148.0791 ($[M+H]^+$), found 148.0790.

4-(*N*-(*tert*-Butyl)vinylsulfonimidoyl)morpholine (3j)

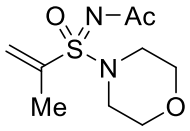


Sulfinamide **SI-4** (86.2 mg, 0.59 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. The sulfinamide **SI-4** was dissolved in anhydrous CH_2Cl_2 (5.9 mL, 1.0 M) and cooled to 0 °C. *tert*-Butyl hypochlorite (66 µL, 0.59 mmol, 1.0 equiv.) was added and the solution was stirred for 30 min. Anhydrous triethylamine (244 µL, 1.76 mmol, 3.0 equiv.)

and morpholine (61 µL, 0.70 mmol, 1.2 equiv.) were added and the solution was warmed to room temperature and stirred for 4 hours. The crude mixture was filtered through Celite®, washed with EtOAc (30 mL), concentrated *in vacuo* and purified using flash column chromatography (SiO_2, Petrol/EtOAc 1:1 to 1:3), to afford the product **3j** as a yellow oil (23.6 mg, 17%).

IR (thin film, ν_{max}/cm^{-1}) 3077, 3045, 2974, 2898, 2861, 1455, 1300, 1257, 1212, 1142, 930, 757, 651; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 6.37 (dd, 1H, *J* = 16.5, 10.0 Hz, Alkenyl-*H*), 6.05 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 5.87 (d, 1H, 10.0 Hz, Alkenyl-*H*), 3.76-3.69 (m, 4H, Alkyl-*H*), 3.08-3.06 (m, 4H, Alkyl-*H*), 1.35 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 133.7, 125.4, 66.8, 55.2, 47.5, 33.2; **HRMS** (ESI^+), *m/z* calculated for $[C_{10}H_{21}N_2O_2S]^+$ 233.1318 ($[M+H]^+$), found 231.1321.

***N*-(Morpholino(oxo)(prop-1-en-2-yl)-λ^6-sulfaneylidene)acetamide (4a)**

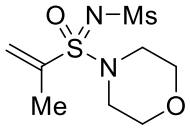


Sulfonimidamide **2f** (19.0 mg, 0.10 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (1.0 mL, 0.10 M) was added and the solution was cooled to 0 °C. Triethylamine (21 µL, 0.15 mmol, 1.5 equiv.) was added to solution, followed by the addition of acetyl chloride (11 µL, 0.15 mmol, 1.5 equiv.). The reaction mixture was warmed to room temperature and stirred for 2 hours. The crude mixture was filtered through Celite$^@$, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:3 to 0:1), to afford the product **4a** as a colourless oil (14.0 mg, 60%).

IR (thin film, ν_{max}/cm^{-1}) 3106, 2974, 2916, 2899, 2862, 1648, 1453, 1364, 1256, 1113, 1073, 1043, 940, 835, 737; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 6.18 (s, 1H, Alkenyl-*H*), 5.85 (s, 1H, Alkenyl-*H*), 3.76-3.74 (m, 4H, Alkyl-*H*), 3.27-3.24 (m, 4H, Alkyl-*H*), 2.12 (s, 3H, Alkyl-*H*), 2.07 (s, 3H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 178.7,

142.0, 126.4, 66.6, 45.5, 27.1, 17.0; **HRMS** (ESI$^+$), *m/z* calculated for $[C_9H_{17}N_2O_3S]^+$ 233.0954 ($[M+H]^+$), found 233.0945.

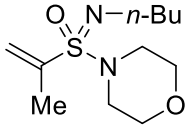
***N*-(Morpholino(oxo)(prop-1-en-2-yl)-λ^6-sulfaneylidene)methanesulfonamide (4b)**



Sulfonimidamide **2f** (30.4 mg, 0.16 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (1.6 mL, 0.10 M) was added and the solution was cooled to 0 °C. Anhydrous triethylamine (34 µL, 0.24 mmol, 1.5 equiv.) was added to solution, followed by the addition of methanesulfonyl chloride (19 µL, 0.24 mmol, 1.5 equiv.). The reaction mixture was warmed to room temperature and stirred for 2 hours. The crude mixture was filtered through Celite$^@$, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:1 to 1:3 to 0:1), to afford the product **4b** as a pale-yellow oil (39.0 mg, 91%).

IR (thin film, ν_{max}/cm^{-1}) 3106, 3018, 2967, 2926, 2862, 1452, 1306, 1258, 1207, 1146, 1109, 1084, 943, 802, 747; **δ_H** (400 MHz, $CDCl_3$) 6.20 (s, 1H, Alkenyl-*H*), 5.87 (s, 1H, Alkenyl-*H*), 3.81-3.72 (m, 4H, Alkyl-*H*), 3.38-3.24 (m, 4H, Alkyl-*H*), 3.12 (s, 3H, Alkyl-*H*), 2.12 (s, 3H, Alkyl-*H*); **δ_C** (100 MHz, $CDCl_3$) 141.9, 126.9, 66.4, 46.1, 44.9, 16.9; **HRMS** (ESI$^+$), *m/z* calculated for $[C_8H_{17}N_2O_4S_2]^+$ 269.0624 ($[M+H]^+$), found 269.0624.

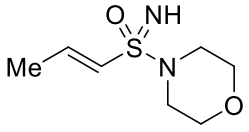
4-(*N*-Butylprop-1-en-2-ylsulfonimidoyl)morpholine (4c)



Sulfonimidamide **2f** (38.0 mg, 0.20 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous DMSO (2 mL, 0.10 M) and bromobutane (32 µL, 0.30 mmol, 1.5 equiv.) were added, followed by the addition of KHMDS (79.8 mg, 0.40 mmol, 2.0 equiv.). The reaction mixture was stirred for 2 hours at room temperature. H_2O (15 mL) and EtOAc (3 × 15 mL) were used for extraction and the organic layer was washed with brine (15 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 3:1 to 1:1 to 1:3), to afforded the product **4c** as a pale-yellow oil (37.5 mg, 76%).

IR (thin film, ν_{max}/cm^{-1}) 2958, 2928, 2856, 1635, 1452, 1361, 1294, 1275, 1144, 1113, 745; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 5.91 (q, 1H, *J* = 1.0 Hz, Alkenyl-*H*), 5.61 (q, 1H, *J* = 1.5 Hz, Alkenyl-*H*), 3.73-3.70 (m, 4H, Alkyl-*H*), 3.19-3.06 (m, 5H, Alkyl-*H*), 2.98-2.91 (m, 1H, Alkyl-*H*), 2.08 (dd, 3H, *J* = 1.5 Hz, 1.0 Hz, Alkyl-*H*), 1.57-1.49 (m, 2H, Alkyl-*H*), 1.42-1.33 (m, 2H, Alkyl-*H*), 0.91 (t, 3H, 7.5 Hz, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 143.0, 122.9, 67.0, 47.0, 41.9, 35.0, 20.6, 19.2, 14.0; **HRMS** (ESI^+), *m/z* calculated for $[C_{11}H_{23}N_2O_2S]^+$ 247.1475 ($[M+H]^+$), found 247.1474.

(*E*)-4-(Prop-1-en-1-ylsulfonimidoyl)morpholine ((*E*)-2h)

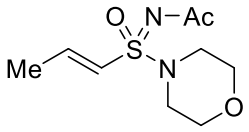


Sulfonimidamide **2h** (16.4 mg, 0.197 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. The sulfonimidamide was dissolved in

anhydrous DMSO (2.0 mL, 0.99 M). KHMDS (47.1 mg, 0.394 mmol, 2.0 equiv.) was added and the solution was stirred at room temperature for 2 hours. H_2O (10 mL) and EtOAc (3 × 20 mL) were used for extraction and the organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:3 to 0:1), to afford the product (*E*)-**2h** as a pale-yellow oil (23.5 mg, 60%).

IR (thin film, ν_{max}/cm^{-1}) 3285, 3056, 3024, 2985, 2975, 2862, 1642, 1455, 1294, 1261, 1115, 1071, 1011, 933, 805, 710; δ_H (400 MHz, $CDCl_3$) 6.77 (dq, 1H, *J* = 15.0 Hz, 7.0 Hz, Alkenyl-*H*), 6.16 (dq, 1H, *J* = 15.0 Hz, 1.5 Hz, Alkenyl-*H*), 3.75-3.70 (m, 4H, Alkyl-*H*), 3.11-3.09 (m, 4H, Alkyl-*H*), 2.28 (br. s, 1H, N*H*), 1.96 (dd, 3H, *J* = 7.0 Hz, 1.5 Hz, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 143.5, 125.1, 66.7, 47.1, 17.4; **HRMS** (ESI^+), *m/z* calculated for $[C_7H_{15}N_2O_2S]^+$ 191.0849 ($[M+H]^+$), found 191.0855.

(*E*)-*N*-(Morpholino(oxo)(prop-1-en-1-yl)-λ^6-sulfaneylidene)acetamide (4d)

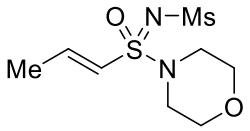


Sulfonimidamide (*E*)-**2h** (11.4 mg, 0.06 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (0.6 mL, 0.10 M) was added and the solution was cooled to 0 °C. Anhydrous triethylamine (12 µL, 0.09 mmol, 1.5 equiv.) was added to solution, followed by the addition of acetyl chloride (6 µL, 0.09 mmol, 1.5 equiv.). The reaction mixture was warmed to room temperature and stirred for 2 hours. The crude mixture was filtered through Celite$^@$, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:1 to 1:3 to 0:1), to afford the product **4d** as a pale-yellow oil (9.7 mg, 72%).

IR (thin film, ν_{max}/cm^{-1}) 3048, 3030, 2987, 2976, 2900, 2863, 1644, 1455, 1440, 1364, 1256, 1113, 1074, 936, 845, 732; δ_H (500 MHz, $CDCl_3$) 6.94 (dq, 1H, *J* = 15.0 Hz, 7.0 Hz, Alkenyl-*H*), 6.28 (dq, 1H, *J* = 15.0

Hz, 1.5 Hz, Alkenyl-*H*), 3.77-3.75 (m, 4H, Alkyl-*H*), 3.19-3.17 (m, 4H, Alkyl-*H*), 2.11 (s, 3H, Alkyl-*H*), 2.00 (dd, 3H, *J* = 7.0 Hz, 1.5 Hz, Alkyl-*H*); **δ_C** (126 MHz, $CDCl_3$) 178.4, 145.7, 125.0, 66.4, 45.5, 27.2, 17.7; **HRMS** (ESI^+, *m/z* calculated for $[C_9H_{17}N_2O_3S]^+$ 233.0954 ($[M+H]^+$), found 233.0952.

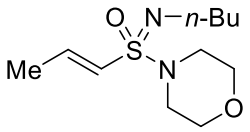
(*E*)-*N*-(Morpholino(oxo)(prop-1-en-1-yl)-λ^6-sulfaneylidene)methanesulfonamide (4e)



Sulfonimidamide (*E*)-**2h** (11.4 mg, 0.06 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (0.6 mL, 0.10 M) was added and the solution was cooled to 0 °C. Anhydrous triethylamine (12 µL, 0.09 mmol, 1.5 equiv.) was added to solution, followed by the addition of methanesulfonyl chloride (7 µL, 0.09 mmol, 1.5 equiv.). The reaction mixture was warmed to room temperature and stirred for 2 hours. The crude mixture was filtered through Celite$^{@}$, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:1 to 1:3 to 0:1), to afford the product **4e** as a pale-yellow oil (13.8 mg, 86%).

IR (thin film, ν_{max}/cm^{-1}) 3058, 3030, 2978, 2960, 2918, 2864, 1629, 1456, 1311, 1261, 1149, 1113, 940, 801, 732, 635; **δ_H** (500 MHz, $CDCl_3$) 6.96 (dq, 1H, *J* = 15.0 Hz, 7.0 Hz, Alkenyl-*H*), 6.18 (dq, 1H, *J* = 15.0 Hz, 1.5 Hz, Alkenyl-*H*), 3.82-3.75 (m, 4H, Alkyl-*H*), 3.32-3.16 (m, 4H, Alkyl-*H*), 3.12 (s, 3H, Alkyl-*H*), 2.02 (dd, 3H, *J* = 7.0 Hz, 1.5 Hz, Alkyl-*H*); **δ_C** (126 MHz, $CDCl_3$) 146.5, 124.7, 66.2, 46.1, 44.9, 17.7; **HRMS** (ESI^+), *m/z* calculated for $[C_8H_{16}N_2O_4S_2Na]^+$ 291.0444 ($[M+H]^+$), found 291.0442.

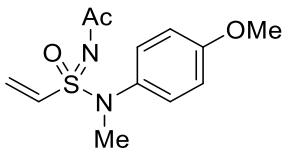
(*E*)-4-(*N*-Butylprop-1-en-1-ylsulfonimidoyl)morpholine (4f)



Sulfonimidamide (*E*)-**2h** (8.2 mg, 0.043 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous DMSO (0.5 mL, 0.10 M) and *n*-bromobutane (7 µL, 0.065 mmol, 1.5 equiv.) were added, followed by the addition of KHMDS (17.2mg, 0.086 mmol, 2.0 equiv.). The reaction mixture was stirred for 2 hours at room temperature. H_2O (15 mL) and EtOAc (3 × 15 mL) were used for extraction and the organic layer was washed with brine (15 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 3:1 to 1:1 to 1:3), to afford the product **4f** as a pale-yellow oil (8.7 mg, 82%).

IR (thin film, ν_{max}/cm^{-1}) 3054, 3021, 2959, 2917, 2896, 2858, 1645, 1454, 1273, 1257, 1122, 1152, 1115, 932, 818, 702; δ_H (400 MHz, $CDCl_3$) 6.71 (dq, 1H, *J* = 15.0 Hz, 7.0 Hz, Alkenyl-*H*), 6.14 (dq, 1H, *J* = 1.5 Hz, Alkenyl-*H*), 3.78-3.69 (m, 4H, Alkyl-*H*), 3.20-3.13 (m, 1H, Alkyl-*H*), 3.10-2.97 (m, 4H, Alkyl-*H*), 2.96-2.90 (m, 1H, Alkyl-*H*), 1.93 (dd, 3H, *J* = 7.0 Hz, 1.5 Hz, Alkyl-*H*), 1.54-1.49 (m, 2H, Alkyl-*H*), 1.42-1.33 (m, 2H, Alkyl-*H*), 0.91 (t, 3H, 7.5 Hz, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 142.3, 125.3, 66.7, 46.9, 41.6, 39.4, 20.6, 17.3, 14.0; **HRMS** (ESI^+), *m/z* calculated for $[C_{11}H_{23}N_2O_2S]^+$ 247.1475 ($[M+H]^+$), found 247.1468.

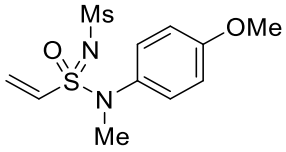
***N*-(((4-Methoxyphenyl)(methyl)amino)(oxo)(vinyl)-λ^6-sulfaneylidene)acetamide (5a)**



Sulfonimidamide **2e** (19.3 mg, 0.085 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (0.85 mL, 0.10 M) was added and the solution was cooled to 0 °C. Anhydrous triethylamine (18 µL, 0.128 mmol, 1.5 equiv.) was added, followed by the addition of acetyl chloride (9 µL, 0.128 mmol, 1.5 equiv.), The reaction mixture was warmed to room temperature and stirred for 5 hours. The crude mixture was filtered through Celite@, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, CH_2Cl_2/EtOAc, 5:1 to 3:1 to 1:1), to afford the product **5a** as a pale-yellow oil (8.9 mg, 39%).

IR (thin film, ν_{max}/cm^{-1}) 3081, 3072. 3059, 3022, 2997, 2952, 2903, 2894, 1653, 1510, 1364, 1249, 1058, 876, 795, 669; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 7.29-7.26 (m, 2H, Ar-*H*), 6.88-6.85 (m, 2H, Ar-*H*), 6.76 (dd, 1H, *J* = 16.5 Hz, 10.0 Hz, Alkenyl-*H*), 6.33 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.09 (d, 1H, *J* = 10.0 Hz, Alkenyl-*H*), 3.80 (s, 3H, Alkyl-*H*), 3.23 (s, 3H, Alkyl-*H*), 2.03 (s, 3H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 178.3, 159.5, 133.5, 133.3, 129.6, 129.4, 114.6, 55.6, 39.0, 27.2; **HRMS** (ESI^+), *m/z* calculated for $[C_{12}H_{17}N_2O_3S]^+$ 269.0954 ($[M+H]^+$), found 269.0943.

***N*-(((4-Methoxyphenyl)(methyl)amino)(oxo)(vinyl)-λ^6-sulfaneylidene)methanesulfonamide (5b)**

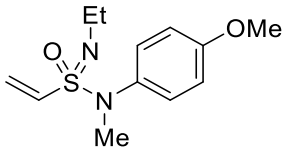


Sulfonimidamide **2e** (19.3 mg, 0.085 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (0.85 mL, 0.10 M) was added and the solution was cooled to 0 °C. Anhydrous triethylamine (18 µL, 0.128 mmol, 1.5 equiv.) was added to the solution, followed by the addition of methanesulfonyl chloride (10 µL, 0.128 mmol, 1.5 equiv.). The reaction mixture was warmed to room temperature and stirred for 2 hours. The crude mixture was filtered through Celite@, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification was carried

out using flash column chromatography (SiO_2, CH_2Cl_2/EtOAc, 7:1 to 5:1 to 3:1), to afford the product **5b** as a pale-yellow oil (13.2 mg, 51%).

IR (thin film, ν_{max}/cm^{-1}) 3130, 3105, 3067, 3058, 2944, 2906,1607, 1511, 1314, 1252,883, 807; δ_H (500 MHz, $CDCl_3$) 7.33-7.30 (m, 2H, Ar-*H*), 6.91-6.87 (m, 2H, Ar-*H*), 6.60 (dd, 1H, *J* = 16.5 Hz, 10.0 Hz, Alkenyl-*H*), 6.33 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.14 (d, 1H, *J* = 10.0 Hz, Alkenyl-*H*), 3.81 (s, 3H, Alkyl-*H*), 3.66 (s, 3H, Alkyl-*H*), 3.13 (s, 3H, Alkyl-*H*); δ_C (126 MHz, $CDCl_3$) 159.8, 133.3, 132.5, 129.8, 129.6, 114.8, 55.6, 45.0, 40.0; **HRMS** (ESI^+), *m/z* calculated for $[C_{11}H_{16}N_2O_4S_2Na]^+$ 327.0444 ($[M+Na]^+$), found 327.0443.

***N*'-Ethyl-*N*-(4-methoxyphenyl)-*N*-methylethenesulfonimidamide (5c)**

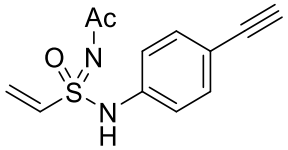


Sulfonimidamide **2e** (22.6 mg, 0.10 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous DMSO (1.0 mL, 0.10 M) and bromoethane (11 µL, 0.15 mmol, 1.5 equiv.) were added, followed by the addition of KHMDS (40.0 mg, 0.2 mmol, 2.0 equiv.). The reaction mixture was stirred for 2 hours at room temperature. H_2O (15 mL) and EtOAc (3 × 15 mL) were used for extraction and the organic layer was washed with brine (15 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, CH_2Cl_2/EtOAc, 7:1 to 5:1 to 3:1), afforded the product **5c** as a pale-yellow oil (11 mg, 43%).

IR (thin film, ν_{max}/cm^{-1}) 3056, 6013, 2965, 2933, 2920, 2860, 1510, 1300, 1248, 1108, 1008, 862, 745, 657; δ_H (400 MHz, $CDCl_3$) 7.19-7.15 (m, 2H, Ar-*H*), 6.87-6.83 (m, 2H, Ar-*H*), 6.56 (dd, 1H, *J* = 16.5 Hz, 10.0 Hz, Alkenyl-*H*), 6.11 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 5.92 (d, 1H, *J* = 10.0 Hz, Alkenyl-*H*), 3.79 (s, 3H,

Alkyl-*H*), 3.36 (dq, 1H, *J* = 12.5, 7.5 Hz, Alkyl-*H*), 3.15 (s, 3H, Alkyl-*H*), 3.15-3.07 (m, 1H, Alkyl-*H*), 1.22 (t, 3H, *J* = 7.5 Hz, Alkyl-*H*); **δ_C** (100 MHz, $CDCl_3$) 158.4, 136.4, 133.7, 128.1, 126.4, 114.3, 55.6, 39.5, 36.9, 18.1; **HRMS** (ESI^+), *m/z* calculated for $[C_{12}H_{19}N_2O_2S]^+$ 255.1162 ($[M+H]^+$), found 255.1156.

***N*-(*N*-(4-Ethynylphenyl)vinylsulfonimidoyl)acetamide (6a)**

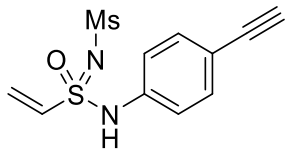


Sulfonimidamide **2c** (31.8 mg, 0.15 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (1.5 mL, 0.10 M) was added and the solution was cooled to 0 °C. Pyridine (18 µL, 0.23 mmol, 1.5 equiv.) was added to the solution, followed by the addition of acetyl chloride (12 µL, 0.17 mmol, 1.1 equiv.). The reaction mixture was warmed to room temperature and stirred for 20 hours. The crude mixture was filtered through Celite®, washed with EtOAc (30 mL) and concentrated in *vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 2:1 to 1:1), to afford the product **6a** as a pale-yellow oil (9.5 mg, 26%).

Note: This compound is not stable and decomposes gradually at room temperature, therefore a clean NMR spectrum was not able to be obtained.

IR (thin film, ν_{max}/cm^{-1}) 3283, 3102, 3087, 3063, 2923, 2847, 2103, 1691, 1627, 1603, 1503, 1366, 1271, 1219, 1176, 1107, 972, 838, 654; **δ_H** (400 MHz, $CDCl_3$) 7.45-7.40 (m, 2H, Ar-*H*), 7.15-7.11 (m, 2H, Ar-*H*), 6.67 (dd, 1H, *J* = 16.5 Hz, 10.0 Hz, Alkenyl-*H*), 6.31 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.03 (d, 1H, *J* = 10.0 Hz, Alkenyl-*H*), 3.07 (s, 1H, Alkyl-*H*), 2.17 (s, 3H, Alkyl-*H*); **δ_C** (100 MHz, $CDCl_3$) 179.5, 137.1, 134.1, 133.5, 129.2, 121.9, 119.1, 83.0, 77.8, 27.2; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 249.066; **HRMS** (ESI^+), *m/z* calculated for $[C_{12}H_{13}N_2O_2S]^+$ 249.0692 ($[M+H]^+$), found 249.0694.

***N*-(*N*-(4-Ethynylphenyl)vinylsulfonimidoyl)methanesulfonamide (6b)**

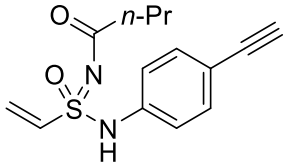


Sulfonimidamide **2c** (31.8 mg, 0.15 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (1.5 mL, 0.10 M) was added and the solution was cooled to 0 °C. Triethylamine (23 µL, 0.23 mmol, 1.5 equiv.) was added to the solution, followed by the addition of methanesulfonyl chloride (13 µL, 0.17 mmol, 1.1 equiv.). The reaction mixture was warmed to room temperature and stirred for 20 hours. The crude mixture was filtered through Celite®, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc/MeOH, 1:1:0 to 1:3:0 to 0:1:0 to 0:96:4), afforded the product **6b** as a pale-yellow oil (24.7 mg, 58%).

Note: This compound is not stable and decomposes rapidly at room temperature within hours, therefore a clean NMR spectrum was not able to be obtained.

IR (thin film, ν_{max}/cm^{-1}) 3279, 3104, 3055, 3041, 2934, 2359, 1601, 1502, 1289, 1259, 1095, 971, 839, 750, 661; $\boldsymbol{\delta_H}$ (600 MHz, $CDCl_3$) 7.29 (d, 2H, *J* = 8.5 Hz, Ar-*H*), 6.99 (d, 2H, *J* = 8.5 Hz, Ar-*H*), 6.57 (dd, 1H, *J* = 16.5 Hz, 9.5 Hz, Alkenyl-*H*), 6.17 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 5.85 (d, 1H, *J* = 9.5 Hz, Alkenyl-*H*), 3.54 (br s. 1H, N*H*), 3.04 (s, 3H, Alkyl-*H*), 3.04 (s, 1H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (151 MHz, $CDCl_3$) 142.8, 137.0, 133.2, 127.7, 122.3, 116.2, 83.7, 79.7, 43.5; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 285.035; **HRMS** (ESI^+), *m/z* calculated for$[C_{11}H_{11}N_2O_3S_2]^-$ 283.0206 ($[M-H]^-$), found 283.0212.

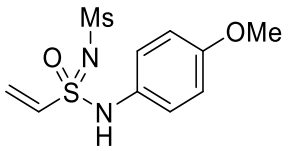
***N*-(*N*-(4-Ethynylphenyl)vinylsulfonimidoyl)butyramide (6c)**



Sulfonimidamide **2c** (26.8 mg, 0.13 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (1.3 mL, 0.10 M) was added and the solution was cooled to 0 °C. Pyridine (17 µL, 0.21 mmol, 1.6 equiv.) was added to the solution, followed by the addition of butyryl chloride (15 µL, 0.14 mmol, 1.1 equiv.). The reaction mixture was warmed to room temperature and stirred for 20 hours. The crude mixture was filtered through Celite®, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification was carried out using flash column chromatography (Petrol/EtOAc, 2:1 to 1:1), to afford the product **6c** as a pale-yellow oil (10.0 mg, 28%).

IR (thin film, ν_{max}/cm^{-1}) 3286, 3107, 3104, 3089, 2964, 2929, 2873, 2109, 1624, 1605, 1506, 1308, 1201, 1094, 1017, 838, 640; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.45-7.42 (m, 2H, Ar-*H*), 7.16-7.12 (m, 2H, Ar-*H*), 6.66 (dd, 1H, *J* = 16.5 Hz, 10.0 Hz, Alkenyl-*H*), 6.31 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.04 (d, 1*H*, *J* = 10.0 Hz, Alkenyl-*H*), 3.07 (s, 1H, Alkyl-*H*), 2.39 (t, 2H, *J* = 7.5 Hz, Alkyl-*H*), 1.68 (sext, 2H, 7.5 Hz, Alkyl-*H*), 0.95 (t, 3H, *J* = 7.5 Hz, Alkyl-*H*); $\boldsymbol{\delta_C}$ (100 MHz, $CDCl_3$) 182.3, 136.5, 134.0, 133.6, 129.4, 121.9, 119.5, 82.9, 77.9, 42.0, 19.0, 13.8; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 277.078; **HRMS** (ESI^+), *m/z* calculated for $[C_{14}H_{16}N_2O_2S]^-$ 275.0860 ($[M-H]^-$), found 275.0857.

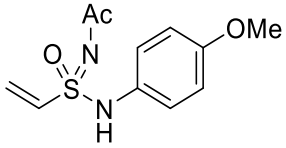
***N*-(*N*-(4-Methoxyphenyl)vinylsulfonimidoyl)methanesulfonamide (6d)**



Sulfonimidamide **2d** (40.3 mg, 0.190 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (1.9 mL, 0.1 M) was added and the solution was cooled to 0 °C. Sodium hydride (9.1 mg, 60% dispersion in mineral oil, 0.228 mmol, 1.2 equiv.) was added to solution, followed by the addition of methanesulfonyl chloride (16 µL, 0.209 mmol, 1.1 equiv.). The reaction was stirred for 15 min and warmed to room temperature and stirred for 18 hours. The crude mixture was filtered through Celite[@], washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, CH_2Cl_2/EtOAc 5:1 to 3:1 to 1:1), to afford the product **6d** as a pale-yellow oil (9.1 mg, 17%).

IR (thin film, ν_{max}/cm^{-1}) 3191, 3082, 3062, 3025, 2952, 2936, 2838, 1606, 1509, 1297, 1251, 1141, 1095, 1030, 971, 830, 805, 766; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.21-7.17 (m, 2H, Ar-*H*), 6.88-6.82 (m, 2H, Ar-*H*), 6.72 (dd, 1H, *J* = 16.5 Hz, 10.0 Hz, Alkenyl-*H*), 6.25 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 6.08 (d, 1H, *J* = 10.0 Hz, Alkenyl-*H*); 3.79 (s, 3H, Alkyl-*H*), 3.22 (s, 3H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (100 MHz, $CDCl_3$) 159.0, 135.0, 130.3, 127.2, 127.0, 114.9, 55.6, 44.8; **LRMS** *m/z* (ESI^+) $[M-H]^-$ 289.0; **HRMS** (ESI^+), *m/z* calculated for $[C_{10}H_{15}N_2O_4S_2]^+$ 291.0468 ($[M+H]^+$), found 291.0467.

***N*-(*N*-(4-Methoxyphenyl)vinylsulfonimidoyl)acetamide (6e)**

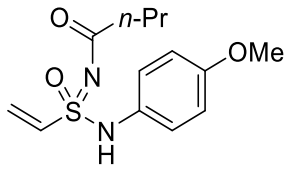


Sulfonimidamide **2d** (18.2 mg, 0.085 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (0.85 mL, 0.10 M) was added and the solution was cooled to 0 °C. Pyridine (10 µL, 0.128 mmol, 1.5 equiv.) was added to solution, followed by the addition of acetyl chloride (7 µL, 0.094 mmol, 1.1 equiv.). The reaction mixture was warmed to room temperature and stirred for 3 hours. The crude mixture was filtered through Celite[@], washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification was carried out using flash column

chromatography (SiO_2, CH_2Cl_2/EtOAc, 5:1 to 3:1 to 1:1), to afford the product **6e** as a pale-yellow oil (7.3 mg, 34%).

IR (thin film, ν_{max}/cm^{-1}) 3430, 3033, 2918, 2849, 1655, 1510, 1281, 1026, 1000, 826, 765; δ_H (500 MHz, $CDCl_3$) 8.67 (br. s, 1H, N*H*), 7.17-7.14 (m, 2H, Ar-*H*), 6.86-6.83 (m, 2H, Ar-*H*), 6.69 (dd, 1H, *J* = 16.5, 10.0 Hz, Alkenyl-*H*), 6.20 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 5.99 (d, 1H, *J* = 10.0 Hz, Alkenyl-*H*), 3.78 (s, 3H, Alkyl-*H*), 2.18 (s, 3H, Alkyl-*H*); δ_C (126 MHz, $CDCl_3$) 180.0, 158.5, 133.6, 129.3, 127.5, 126.2, 114.8, 55.6, 27.2; **HRMS** (ESI^+), *m/z* calculated for $[C_{11}H_{15}N_2O_3S]^+$ 255.0798 ($[M+H]^+$), found 255.0793.

***N*-(*N*-(4-Methoxyphenyl)vinylsulfonimidoyl)butyramide (6f)**

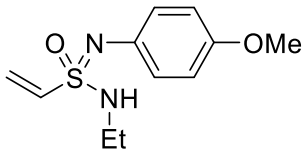


Sulfonimidamide **2d** (31.8 mg, 0.150 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (1.5 mL, 0.10 M) was added and the solution was cooled to 0 °C. Pyridine (18 µL, 0.225 mmol, 1.5 equiv.) was added to solution, followed by the addition of butyryl chloride (17 µL, 0.165 mmol, 1.1 equiv.). The reaction mixture was warmed to room temperature and stirred for 3 hours. The crude mixture was filtered through Celite[@], washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 5:1 to 1:1), to afford the product **6f** as a pale-yellow oil (12.7 mg, 30%).

IR (thin film, ν_{max}/cm^{-1}) 3107, 3066, 3055, 2959, 2933, 2872, 2837, 1606, 1508, 1463, 1362, 1247, 1202, 1095, 1032, 835 ; δ_H (400 MHz, $CDCl_3$) 7.17-7.12 (m, 2H, Ar-H), 6.86-6.82 (m, 2H, Ar-H), 6.68 (dd, 1H, *J* = 16.5 Hz, 10.0 Hz, Alkenyl-*H*), 6.19 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 5.96 (d, 1H, *J* = 10.0 Hz, Alkenyl-*H*), 3.78 (s, 3H, Alkyl-*H*), 2.38 (t, 2H, *J* = 7.5 Hz, Alkyl-*H*), 1.68 (sext, 2H, *J* = 7.5 Hz, Alkyl-*H*), 0.95 (t, 3H, *J* = 7.5 Hz, Alkyl-*H*); δ_C (100 MHz, $CDCl_3$) 182.8, 163.2, 147.5, 133.7, 129.0, 126.1, 114.8, 55.6, 42.0,

19.1, 13.9; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 283.092, $[M+Na]^+$ 305.071; **HRMS** (ESI^+), *m/z* calculated for $[C_{13}H_{19}N_2O_3S_2Na]^+$ 305.0930 ($[M+Na]^+$), found 305.0930.

***N*-Ethyl-*N*'-(4-methoxyphenyl)ethenesulfonimidamide (6g)**



Sulfonimidamide **2d** (45.6 mg, 0.215 mmol, 1.0 equiv.) was added to an oven dried flask and the reaction flask was evacuated and back-filled with nitrogen three times. Anhydrous DMSO (2.15 mL, 0.10 M) and bromoethane (18 µL, 0.237 mmol, 1.1 equiv.) was added, followed by the addition of KHMDS (51.5 mg, 0.258 mmol, 1.2 equiv.). The solution was stirred at room temperature for 2 hours. H_2O (15 mL) and EtOAc (3 × 15 mL) were used for extraction and the organic layer was washed with brine (15 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash chromatography (SiO_2, CH_2Cl_2/EtOAc, 7:1 to 5:1 to 3:1), to afford the product **6g** as a pale-yellow oil (7.8 mg, 19%)

IR (thin film, ν_{max}/cm^{-1}) 3289, 3106, 3060, 2980, 2935, 1509, 1246,1156, 1064, 1031, 897, 834 ; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 7.16-7.13 (m, 2H, Ar-*H*), 6.89-6.85 (m, 2H, Ar-*H*), 6.61 (dd, 1H, *J* = 16.5 Hz, 10.0 Hz, Alkenyl-*H*), 6.19 (d, 1H, *J* = 16.5 Hz, Alkenyl-*H*), 5.94 (d, 1H, *J* = 10.0 Hz, Alkenyl-*H*), 3.80 (s, 3H, Alkyl-*H*), 3.60 (q, 2H, *J* = 7.0 Hz, Alkyl-*H*), 1.07 (t, 3H, *J* = 7.0 Hz, Alkyl-*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 159.2, 135.3, 133.0, 130.4, 126.5, 114.5, 55.6, 46.7, 14.7; **HRMS** (ESI^+), *m/z* calculated for $[C_{11}H_{17}N_2O_2S]^+$ 241.1005 ($[M+H]^+$), found 241.0999.

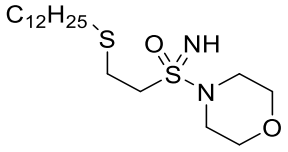
5.2.6 Conjugate Addition with Dodecanethiol

General procedure B:

The method was adapted from C.H. Wu, J. H. Sheu, C. Y. Chen, Y. C. Chien, S. C. Chen, C. H. Pan, C. Y. Huang. *USPTO*, **2016**, US2016009642A1.[190]

The sulfonimidamide or acrylamide (0.10 mmol, 1.0 equiv.) was added to an oven-dried reaction flask. The flask was evacuated and back-filled with nitrogen three times. Anhydrous THF (1.0 mL) and the solution was cooled to 0 °C. Anhydrous triethylamine (3 µL, 0.02 mmol, 0.2 equiv.) was added to the solution, followed by the addition of 1-dodecanethiol (24 µL, 0.10 mmol, 1.0 equiv.). The reaction flask was warmed to room temperature and stirred for 20 hours. The crude mixture was quenched with saturated $NH_4Cl_{(aq)}$ (3.0 mL), extracted with EtOAc (3 × 5.0 mL), washed with brine (5.0 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification was carried out using flash column chromatography to afford pure product.

4-(2-(Dodecylthio)ethylsulfonimidoyl)morpholine (7a)

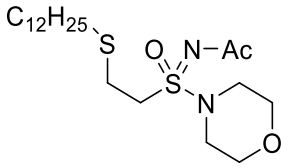


Prepared according to general procedure B, using sulfonimidamide **2a** (17.6 mg, 0.10 mmol, 1.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 3:1 to 1:3 to 0:1), to afford the product **7a** as a white solid (6.0 mg, 16%).

m.p. 57-59 °C ($CDCl_3$) ; **IR** (thin film, ν_{max}/cm^{-1}) 3264, 2954, 2923, 2835, 1455, 1282, 1245, 1112, 1068, 935, 743, 691; δ_H (400 MHz, $CDCl_3$) 3.74-3.72 (m, 4H, Alkyl-*H*), 3.33-3.24 (m, 4H, Alkyl-H_2), 3.21-3.15 (m, 1H, Alkyl-*H*), 3.05-2.91 (m, 3H, Alkyl-*H*), 2.54 (t, 2H, Alkyl-*H*), 2.17 (s, 1H, N*H*), 1.63-1.52 (m, 2H, Alkyl-*H*), 1.39-1.32 (m, 2H, Alkyl-*H*), 1.30-1.19 (m, 16H, Alkyl-*H*), 0.89-0.84 (m, 3H, Alkyl-*H*); δ_C (101

MHz, $CDCl_3$) 67.0, 49.1, 46.9, 32.6, 32.0, 29.8, 29.74, 29.70, 29.63, 29.61, 29.5, 29.3, 28.9, 25.5, 22.8, 14.2; **HRMS** (ESI^+), *m/z* calculated for $[C_{18}H_{39}N_2O_2S_2]^+$ 379.2447 ($[M+H]^+$), found 379.2446.

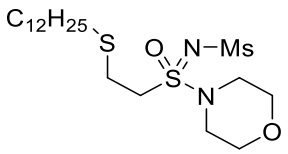
***N*-((2-(Dodecylthio)ethyl)(morpholino)(oxo)- λ^6-sulfaneylidene)acetamide (7b)**



Prepared according to general procedure B, using sulfonimidamide **3a** (21.8 mg, 0.10 mmol, 1.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 3:1 to 1:1 to 1:3), to afford the product **7b** as a colourless oil (7.6 mg, 18%).

IR (thin film, ν_{max}/cm^{-1}) 2954, 2923, 2853, 1644, 1456, 1361, 1256, 1235, 1114, 1071, 938, 832; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 3.81-3.72 (m, 4H, Alkyl-*H*), 3.56-3.48 (m, 1H, Alkyl-*H*), 3.38-3.25 (m, 5H, Alkyl-*H*), 2.94-2.82 (m, 2H, Alkyl-*H*), 2.55 (t, 2H, *J* = 7.5 Hz, Alkyl-*H*), 2.10 (s, 3H, Alkyl-*H*), 1.62-1.55 (m, 2H, Alkyl-*H*), 1.39-1.34 (m, 2H, Alkyl-*H*), 1.32-1.20 (m, 16H, Alkyl-*H*), 0.89-0.86 (m, 3H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 179.0, 66.6, 51.7, 46.1, 32.6, 32.1, 29.78, 29.77, 29.73, 29.65, 29.54, 29.48, 29.3, 28.9, 27.0, 24.6, 22.8, 14.3; **LRMS** *m/z* (ESI^+) $[M+Na]^+$ 443.2; **HRMS** (ESI^+), *m/z* calculated for $[C_{20}H_{41}N_2O_3S_2]^+$ 421.2553 ($[M+H]^+$), found 421.2554.

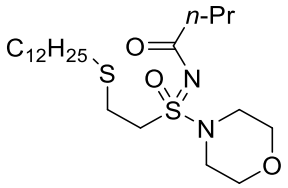
***N*-((2-(Dodecylthio)ethyl)(morpholino)(oxo)-λ^6-sulfaneylidene)methanesulfonamide (7c)**



Prepared according to general procedure B, using sulfonimidamide **3b** (25.4 mg, 0.10 mmol, 1.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 3:1 to 1:1 to 1:3), to afford the product **7c** as a white solid (38.4 mg, 84%).

m.p. 31-33 °C ($CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2924, 2853, 1456, 1309, 1242, 1147, 1111, 1081, 944, 798, 699; **δ_H** (400 MHz, $CDCl_3$) 3.84-3.73 (m, 4H, Alkyl-*H*), 3.52-3.41 (m, 3H, Alkyl-*H*), 3.36-3.22 (m, 3*H*, 2Alkyl-*H*), 3.10 (s, 3H, Alkyl-*H*), 2.94-2.85 (m, 2H, Alkyl-*H*), 2.58-2.50 (m, 2H, Alkyl-*H*), 1.63-1.52 (m, 2H, Alkyl-*H*), 1.40-1.32 (m, 2H, Alkyl-*H*), 1.30-1.18 (m, 16H, Alkyl-H_6), 0.90-0.83 (m, 3H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 66.4, 53.0, 46.5, 44.8, 32.7, 32.0, 29.73, 29.70, 29.67, 29.6, 29.5, 29.4, 29.3, 28.9, 24.5, 22.8, 14.2; **LRMS** *m/z* (ESI$^-$) $[M-H]^-$ 455.1; **HRMS** (ESI$^+$), *m/z* calculated for $[C_{19}H_{41}N_2O_4S_3]^+$ 457.2223 ($[M+H]^+$), found 457.2222.

***N*-((2-(Dodecylthio)ethyl)(morpholino)(oxo)-λ^6-sulfaneylidene)butyramide (7d)**

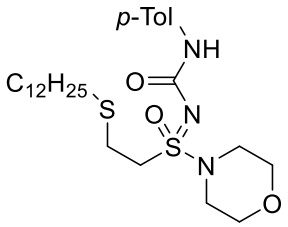


Prepared according to general procedure B, using sulfonimidamide **3c** (24.6 mg, 0.10 mmol, 1.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 5:1 to 3:1 to 1:1), to afford the product **7d** as a colourless oil (12.1 mg, 27%).

IR (thin film, ν_{max}/cm^{-1}) 2958, 2924, 2854, 1643, 1457, 1258, 1235, 1198, 1114, 937, 850, 723; **δ_H** (400 MHz, $CDCl_3$) 3.79-3.73 (m, 4H, Alkyl-*H*), 3.57-3.48 (m, 1H, Alkyl-*H*), 3.36-3.25 (m, 5H, Alkyl-*H*), 2.92-

2.82 (m, 2H, Alkyl-*H*), 2.54 (t, 2H, 7.4 Hz, Alkyl-*H*), 2.31 (t, 2H. 7.4 Hz, Alkyl-*H*), 1.68-1.54 (m, 4H, Alkyl-*H*), 1.41-1.33 (m, 2H, Alkyl-*H*), 1.32-1.22 (m, 16H, Alkyl-*H*), 0.94 (t, 3H, 7.4 Hz, Alkyl-*H*), 0.87 (t, 3H, 6.7 Hz, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 181.7, 66.6, 51.8, 46.1, 41.9, 32.5, 32.0, 29.78, 29.76, 29.7, 29.6, 29.53, 29.47, 29.3, 28.9, 24.6, 22.8, 19.2, 14.3, 14.0; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 449.243; **HRMS** (ESI^+), *m/z* calculated for $[C_{22}H_{45}N_2O_3S_2]^+$ 449.2866 ($[M+H]^+$), found 449.2864.

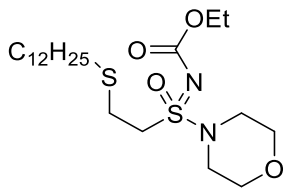
1-((2-(Dodecylthio)ethyl)(morpholino)(oxo)-λ^6-sulfaneylidene)-3-(*p*-tolyl)urea (7e)



Prepared according to general procedure B, using sulfonimidamide **3d** (30.9 mg, 0.10 mmol, 1.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 5:1 to 3:1), to afford the product **7e** as a white solid (38.4 mg, 75%).

m.p. 87-89 °C (CH_2Cl_2); **IR** (thin film, ν_{max}/cm^{-1}) 3334, 3076, 3035, 2954, 2920, 2853, 1632, 1594, 1454, 1406, 1288, 1236, 1116, 950, 854, 726, 638; **δ_H** (400 MHz, $CDCl_3$) 7.30 (d, 2H, *J* = 8.0 Hz, Ar-*H*), 7.07 (d, 2H, *J* = 8.0 Hz, Ar-*H*), 6.87 (br. s, 1H, N*H*), 3.80-3.72 (m, 4H, Alkyl-*H*), 3.62-3.53 (m, 1H, Alkyl-*H*), 3.43-3.23 (m, 5H, Alkyl-*H*), 2.97-2.86 (m, 2H, Alkyl-*H*), 2.55 (t, 2H, 7.4 Hz, Alkyl-*H*), 2.28 (s, 3H, Alkyl-*H*), 1.63-1.54 (m, 2H, Alkyl-*H*), 1.41-1.33 (m, 2H, Alkyl-*H*), 1.31-1.20 (m, 16H, Alkyl-*H*), 0.88 (t, 3H, 6.7 Hz, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 156.0, 136.3, 132.7, 129.5, 119.0, 66.6, 51.9, 46.3, 32.5, 32.0, 29.8, 29.73, 29.69, 29.6, 29.5, 29.4, 29.3, 28.9, 24.7, 22.8, 20.9, 14.2; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 512.234; **HRMS** (ESI^+), *m/z* calculated for $[C_{26}H_{46}N_3O_3S_2]^+$ 512.2975 ($[M+H]^+$), found 512.2971.

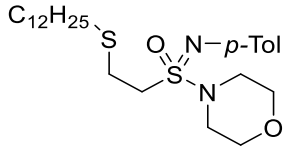
Ethyl ((2-(dodecylthio)ethyl)(morpholino)(oxo)-λ^6-sulfaneylidene)carbamate (7f)



Prepared according to general procedure B, using sulfonimidamide **3f** (24.8 mg, 0.10 mmol, 1.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 3:1 to 1:1 to 1:3), to afford the product **7f** as a colourless oil (11.7 mg, 26%).

IR (thin film, ν_{max}/cm^{-1}) 2955, 2924, 2853, 1670, 1456, 1254, 1114, 1019, 940, 890; **δ_H** (400 MHz, $CDCl_3$) 4.18-4.07 (m, 2H, Alkyl-*H*), 3.80-3.70 (m, 4H, Alkyl-*H*), 3.52-3.43 (m, 1H, Alkyl-*H*), 3.41-3.31 (m, 4H, Alkyl-*H*), 3.31-3.21 (m, 1H, Alkyl-*H*), 2.98-2.83 (2H, Alkyl-*H*), 2.53 (t, 2H, *J* = 7.5 Hz, Alkyl-*H*), 1.62-1.52 (m, 2H, Alkyl-*H*), 1.41-1.32 (m, 2H, Alkyl-*H*), 1.32-1.18 (m, 19H, Alkyl-*H*), 0.91-0.83 (m, 3H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 157.6, 66.6, 62.3, 52.3, 46.3, 32.7, 32.0, 29.8, 29.73, 29.71, 29.64, 29.58, 29.5, 29.3, 28.9, 24.6, 22.8, 14.5, 14.3; **LRMS** *m/z* (ESI$^+$) $[M+Na]^+$ 473.2; **HRMS** (ESI$^+$), *m/z* calculated for $[C_{21}H_{43}N_2O_4S_2]^+$ 451.2659 ($[M+H]^+$), found 451.2658.

4-(2-(Dodecylthio)-*N*-(*p*-tolyl)ethylsulfonimidoyl)morpholine (7g)

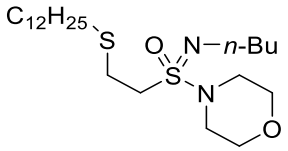


Prepared according to general procedure B, using sulfonimidamide **3i** (26.6 mg, 0.10 mmol, 1.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 5:1 to 3:1 to 1:1), to afford the product **7g** as a colourless oil (3.3 mg, 7%).

IR (thin film, ν_{max}/cm^{-1}) 3075, 3027, 2923, 2853, 1610, 1507, 1310, 1259, 1208, 1113, 1044, 931, 822, 785, 637; **δ_H** (400 MHz, $CDCl_3$) 7.03-6.94 (m, 4H, Ar-*H*) 3.69-3.54 (m, 4H, Alkyl-*H*), 3.41-3.23 (m, 5H, NCH_2,

Alkyl-*H*), 3.18-3.10 (m, 1H, Alkyl-*H*), 3.09-2.94 (m, 2H, Alkyl-*H*), 2.57 (t, 2H, *J* = 7.4 Hz, Alkyl-*H*), 1.65-1.56 (m, 2H, Alkyl-*H*), 1.42-1.34 (m, 2H, Alkyl-*H*), 1.31-1.20 (m, 16H, Alkyl-*H*), 0.88 (t, 3H, *J* = 6.7 Hz, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 141.0, 131.6, 129.8, 123.3, 66.8, 51.5, 46.7, 32.6, 32.1, 29.81, 29.79, 29.75, 29.68, 29.67, 29.5, 29.4, 29.0, 25.4, 22.8, 20.9, 14.3; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 469.238; **HRMS** (ESI^+), *m/z* calculated for $[C_{25}H_{45}N_2O_2S_2]^+$ 469.2917 ($[M+H]^+$), found 469.2916.

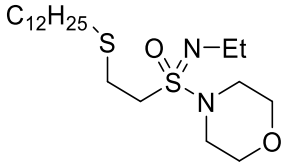
4-(*N*-Butyl-2-(dodecylthio)ethylsulfonimidoyl)morpholine (7h)



Prepared according to general procedure B, using sulfonimidamide **3g** (23.2 mg, 0.10 mmol, 1.0 equiv.). Purification was carried out using flash chromatography (SiO_2, Petrol/EtOAc, 4:1 to 1:1), to afford the product **7h** as a colourless oil (32.2 mg, 74%).

IR (thin film, ν_{max}/cm^{-1}) 2956, 2924, 2854, 1455, 1362, 1330, 1295, 1281, 152, 936, 757, 630; **δ_H** (400 MHz, $CDCl_3$) 3.77-3.68 (m, 4H, Alkyl-*H*), 3.26-3.14 (m, 5H, Alkyl-*H*), 3.31-3.21 (m, 1H, Alkyl-*H*), 3.00-2.81 (4H, Alkyl-*H*), 2.55-2.51 (m, 2H, Alkyl-*H*), 1.61-1.52 (m, 2H, Alkyl-*H*), 1.51-1.44 (m, 2H, Alkyl-*H*), 1.40-1.32 (m, 4H, Alkyl-*H*), 1.30-1.21 (m, 16H, Alkyl-*H*), 0.93-0.85 (m, 6H, Alkyl-*H*; **δ_C** (101 MHz, $CDCl_3$) 67.0, 49.7, 46.8, 41.6, 34.8, 32.5, 32.1, 29.78, 29.76, 29.74, 29.72, 29.65, 29.5, 29.3, 29.0, 25.4, 22.8, 20.5, 14.3, 14.0; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 435.211; **HRMS** (ESI^+), *m/z* calculated for $[C_{22}H_{47}N_2O_2S_2]^+$ 435.3073 ($[M+H]^+$), found 435.3081.

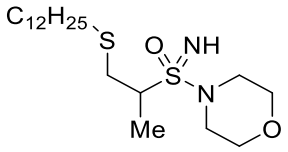
4-(2-(Dodecylthio)-*N*-ethylethylsulfonimidoyl)morpholine (7i)



Prepared according to general procedure B, using sulfonimidamide **3h** (20.4 mg, 0.10 mmol, 1.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 5:1 to 3:1 to 1:1), to afford the product **7i** as a colourless oil (30.5 mg, 75%).

IR (thin film, ν_{max}/cm^{-1}) 2956, 2924, 2853, 1453, 1295, 1251, 1155, 1114, 1068, 934, 757, 686; **δ_H** (400 MHz, $CDCl_3$) 3.77-3.67 (m, 4H, Alkyl-*H*), 3.27-3.15 (m, 5H, Alkyl-*H*), 3.15-3.07 (m, 1H, Alkyl-*H*), 3.00-2.84 (m, 4H, Alkyl-*H*), 2.55-2.48 (m, 2H, Alkyl-*H*), 1.62-1.51 (m, 2H, Alkyl-*H*), 1.39-1.30 (m, 2H, Alkyl-*H*), 1.30-1.20 (m, 16H, Alkyl-*H*), 1.14 (t, 3H, J = 7.2 Hz, Alkyl-*H*) 0.90-0.81 (m, 3H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 66.9, 49.6, 46.8, 36.7, 32.5, 32.0, 29.8, 29.73, 29.72, 29.70, 29.6, 29.5, 29.3, 28.9, 25.3, 22.8, 18.1, 14.2; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 407.225; **HRMS** (ESI^+), *m/z* calculated for $[C_{20}H_{43}N_2O_2S_2]^+$ 407.2760 ($[M+H]^+$), found 407.2755.

4-(1-(Dodecylthio)propan-2-ylsulfonimidoyl)morpholine (7j)



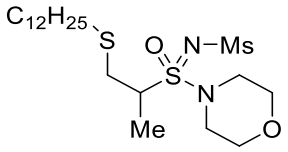
Prepared according to general procedure B, using sulfonimidamide **2f** (19.0 mg, 0.10 mmol, 1.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 3:1 to 1:1 to 1:3), to afford the product **7j** as a colourless oil (0.7 mg, 2%).

IR (thin film, ν_{max}/cm^{-1}) 3277, 2923, 2853, 1652, 1455, 1362, 1256, 1114, 1068, 986, 943, 718, 676; **δ_H** (400 MHz, $CDCl_3$) 3.74-3.66 (m, 4H, Alkyl-*H*), 3.40-3.35 (m, 4H, Alkyl-*H*), 3.25-3.14 (m, 2H, Alkyl-*H*),

2.63-2.47 (m, 3H, Alkyl-*H*), 2.17 (br. s, 1H, N*H*), 1.62-1.53 (m, 2H, Alkyl-*H*), 1.49-1.44 (m, 3H, Alkyl-*H*), 1.39-1.32 (m, 2H, Alkyl-*H*), 1.31-1.20 (m, 16H, Alkyl-*H*), 0.91-0.84 (m, 3H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 67.5, 58.3, 47.3, 33.8, 33.2, 32.1, 29.80, 29.78, 29.74, 29.70, 29.67, 29.5, 29.4, 29.0, 22.8, 14.3, 13.8; **HRMS** (ESI^+), *m/z* calculated for $[C_{19}H_{41}N_2O_2S_2]^+$ 393.2604 ($[M+H]^+$), found 393.2621.

Note: The product was isolated as a mixture of diastereomers where the dr was not determined due to the overlap of the signals.

***N*-((1-(Dodecylthio)propan-2-yl)(morpholino)(oxo)-λ^6-sulfaneylidene)methanesulfonamide (7k)**

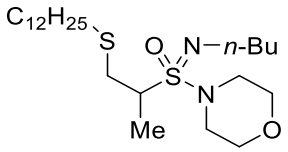


Prepared according to general procedure B, using sulfonimidamide **4b** (26.8 mg, 0.10 mmol, 1.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 3:1 to 1:1 to 1:3), to afford the product **7k** as a colourless oil (2.8 mg, 6%).

IR (thin film, ν_{max}/cm^{-1}) 2954, 2923, 2853, 1457, 1311, 1258, 1147, 1112, 1075, 951, 800, 739; **δ_H** (400 MHz, $CDCl_3$) 3.85-3.69 (m, 4H, Alkyl-*H*), 3.55-3.35 (m, 4H, Alkyl-*H*), 3.32-3.21 (m, 1H, Alkyl-*H*), 3.18-3.07 (m, 4H, Alkyl-*H*), 2.63-2.45 (m, 3H, Alkyl-*H*), 1.62-1.44 (m, 5H, Alkyl-*H*), 1.44-1.31 (m, 2H, Alkyl-*H*), 1.31-1.20 (m, 16H, Alkyl-*H*), 0.90-0.83 (m, 3H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 66.6, 66.5, 61.3, 60.4, 47.4, 47.1, 44.9, 44.8, 33.24, 33.21, 32.3, 32.0, 31.9, 29.74, 29.72, 29.68, 29.6, 29.5, 29.4, 29.3, 28.9, 22.8, 14.2, 13.6, 12.5; **HRMS** (ESI^+), *m/z* calculated for $[C_{20}H_{42}N_2O_4S_3Na]^+$ 493.2199 ($[M+Na]^+$), found 493.2199.

Note: The product was isolated as a mixture of diastereomers where the dr was not determined due to the overlap of the signals.

4-(*N*-Butyl-1-(dodecylthio)propan-2-ylsulfonimidoyl)morpholine (7l)

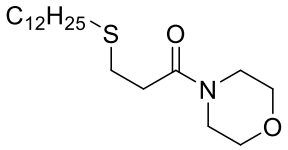


Prepared according to general procedure B, using sulfonimidamide **4c** (23.3 mg, 0.10 mmol, 1.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 7:1 to 3:1 to 1:1), to afford the product **7l** as a colourless oil (1.3 mg, 3%).

IR (thin film, ν_{max}/cm^{-1}) 2956, 2924, 2853, 1456, 1374, 1297, 1212, 1149, 1068, 943, 733; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 3.74-3.64 (m, 4H, Alkyl-*H*), 3.37-3.24 (m, 5H, Alkyl-*H*), 3.21-3.12 (m, 1H, Alkyl-*H*), 3.12-3.03 (dt, 1H, *J* = 12.1 Hz, 6.8 Hz, Alkyl-*H*), 2.88-2.77 (dt, 1H, *J* = 12.1 Hz, 6.8 Hz, Alkyl-*H*), 2.59-2.45 (m, 3H, Alkyl-*H*), 1.61-1.52 (m, 2H, Alkyl-*H*), 1.52-1.44 (m, 2H, Alkyl-*H*) 1.41-1.31 (m, 7H, Alkyl-*H*), 1.31-1.21 (m, 16H, Alkyl-*H*), 0.93-0.83 (m, 6H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 67.4, 58.5, 47.1, 41.8, 34.9, 33.7, 33.0, 32.1, 29.79, 29.77, 29.74, 29.70, 29.66, 29.5, 29.4, 29.0, 22.8, 20.5, 14.3, 14.1, 13.5; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 449.214; **HRMS** (ESI^+), *m/z* calculated for $[C_{23}H_{49}N_2O_2S_2]^+$ 449.3230 ($[M+H]^+$), found 449.3223.

Note: The product was isolated as a mixture of diastereomers where the dr was not determined due to the overlap of the signals.

3-(Dodecylthio)-1-morpholinopropan-1-one (7m)



Prepared according to general procedure B, using 4-acryloylmorpholine **8** (13 µL, 0.10 mmol, 1.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 3:1 to 1:1 to 0:1), to afford the product **7m** as a colourless oil (2.1 mg, 6%).

IR (thin film, ν_{max}/cm^{-1}) 2923, 2852, 1650, 1433, 1299, 1208, 1116, 1026, 911, 852; **δ_H** (400 MHz, $CDCl_3$) 3.71-3.65 (m, 4H, Alkyl-*H*), 3.60-3.64 (m, 2H, Alkyl-*H*), 3.49-3.45 (m, 2H, Alkyl-*H*), 2.85-2.80 (m, 2H, Alkyl-*H*), 2.61-2.57 (m, 2H, Alkyl-*H*), 2.56-2.52 (m, 2H, Alkyl-*H*), 1.62-1.56 (m, 2H, Alkyl-*H*), 1.39-1.33 (m, 2H, Alkyl-*H*), 1.29-1.23 (m, 16H, Alkyl-*H*), 0.88 (t, 3H, *J* = 7.0 Hz, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 162.0, 67.0, 66.8, 42.2, 33.7, 32.8, 32.1, 29.83, 29.81, 29.76, 29.7, 29.5, 29.4, 29.1, 27.6, 22.8, 14.3; **LRMS** *m/z* (ESI^+) $[M+H]^+$ 344.195; **HRMS** (ESI^+), *m/z* calculated for $[C_{19}H_{38}NO_2S]^+$ 344.2618 ($[M+H]^+$), found 344.2614.

5.2.7 Procedure for Competition Reaction with 1-Dodecanethiol

The respective sulfonimidamide (0.10 mmol, 1.0 equiv.) was added to an oven-dried reaction flask. The flask was evacuated and back-filled with nitrogen three times. 4-Acryloylmorpholine **8** (13 µL, 0.10 mmol, 1.0 equiv.) was added and the mixture was dissolved in anhydrous THF (1.0 mL) and the solution was cooled to 0 °C. Anhydrous triethylamine (3 µL, 0.02 mmol, 0.2 equiv.) was added to the solution, followed by the addition of 1-dodecanethiol (24 µL, 0.10 mmol, 1.0 equiv.). The reaction flask was warmed to room temperature and stirred for 20 hours. The crude mixture was quenched with $NH_4Cl_{(aq)}$ (3.0 mL), extracted with EtOAc (3 × 5.0 mL), washed with brine (5.0 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography to afford the products with matching analytical data to those reported above.

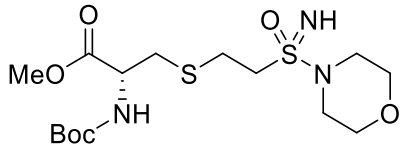
5.2.8 Procedure for Conjugate Addition Reactions with Amino Acids

General procedure C:

Method adapted from H. Chen, R. Huang, Z. Li, W. Zhu, J. Chen, Y. Zhan, B. Jiang. *Org. Biomol. Chem.*, **2017**, 15, 7339-7345.[191]

The respective sulfonimidamide (1.0 equiv.) was added to an oven dried reaction flask. The flask was evacuated and back-filled with nitrogen three times. Anhydrous MeCN (0.1 M) was added, followed by the addition of anhydrous triethylamine (0.2 - 2.0 equiv.) and amino acid (1.0 equiv.). The reaction mixture was stirred at room temperature for 16 hours. The crude mixture was quenched with $NaHCO_3$(aq), extracted with EtOAc, washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography to afford the product.

Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(2-(morpholine-4-sulfonimidoyl)ethyl)-*L*-cysteinate (9a)



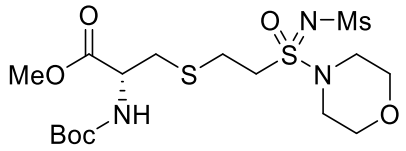
9a

Prepared according to general procedure C, using sulfonimidamide **2a** (15.8 mg, 0.09 mmol, 1.0 equiv.), anhydrous triethylamine (12.5 µL, 0.09 mmol, 1.0 equiv.), Boc-Cys-OMe (21.1 mg, 0.09 mmol, 1.0 equiv.) and MeCN (0.9 mL). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:3 to 0:1), to afford the product **9a** as a colourless oil (20 mg, 54%, mixture of diastereomers).

IR (thin film, ν_{max}/cm^{-1}) 3320, 3282, 2978, 1747, 1713, 1519, 1367, 1248, 1169, 1114, 939, 738; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 5.37 (d, 1H, *J* = 7.9 Hz, Boc-N*H*), 4.55 (br. s, 1H, Alkyl-*H*), 3.79 (s, 3H, Alkyl-*H*), 3.74 (t, 4H, *J* = 4.6 Hz, Alkyl-*H*), 3.32-3.25 (m, 4H, Alkyl-*H*), 3.19 (ddd, 1H, *J* = 14.1 Hz, 7.1 Hz, 3.9 Hz, Alkyl-*H*), 3.05-2.95 (m, 5H, Alkyl-*H*), 2.16 (br. s, 1H, N*H*), 1.45 (s, 9 H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 171.4, 155.3, 80.5, 67.0, 66.7, 53.5, 52.9, 48.98, 48.96, 47.0, 46.9, 35.19, 35.16, 28.4, 26.28, 26.25; **HRMS** (ESI^+, *m/z* calculated for $[C_{15}H_{30}N_3O_6S_2]^+$ 412.1571 ($[M+H]^+$), found 412.1571.

Note: The product was isolated as a mixture of diastereomers where the dr was not determined due to the overlap of the signals.

Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(2-(*N*-(methylsulfonyl)morpholine-4-sulfonimidoyl)ethyl)-*L*-cysteinate (9b)



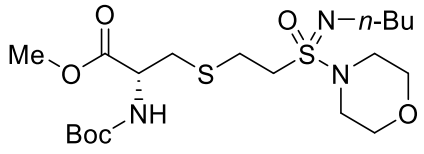
9b

Prepared according to general procedure C, using sulfonimidamide **3b** (25.4 mg, 0.10 mmol, 1.0 equiv.), anhydrous triethylamine (14 µL, 0.10 mmol, 1.0 equiv.), Boc-Cys-OMe (23.5 mg, 0.10 mmol, 1.0 equiv.) and MeCN (1.0 mL). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:1 to 1:3 to 0:1), to afford the product **9b** as a colourless oil (36.6 mg, 89%, mixture of diastereomers).

IR (thin film, ν_{max}/cm^{-1}) 3380, 2981, 1747, 1713, 1517, 1367, 1247, 1149, 1112, 951, 737; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 5.41-5.26 (m, 1H, Boc-N*H*), 4.57-4.41 (m, 1H,Alkyl-*H*), 3.82-3.74 (m, 7H, Alkyl-*H*), 3.46-3.25 (m, 6H, Alkyl-*H*), 3.08 (s, 3H, Alkyl-*H*), 3.05-3.00 (m, 1 H, Alkyl-*H*), 2.97-2.89 (m, 3 H, Alkyl-*H*), 1.43 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 171.2, 155.2, 80.6, 66.3, 53.5, 53.4, 52.9, 52.7, 52.6, 46.4, 44.8. 35.2, 28.4, 25.2, 25.0; **HRMS** (ESI^+), *m/z* calculated for $[C_{16}H_{32}N_3O_8S_3]^+$ 490.1346 ($[M+H]^+$), found 490.1338.

Note: The product was isolated as a mixture of diastereomers where the dr was not determined due to the overlap of the signals.

Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(2-(*N*-butylmorpholine-4-sulfonimidoyl)ethyl)-*L*-cysteinate (9c)



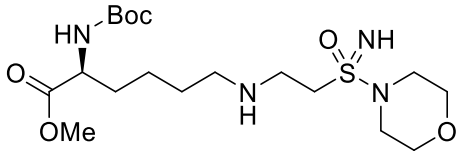
9c

Prepared according to general procedure C, using sulfonimidamide **3g** (18.6 mg, 0.08 mmol, 1.0 equiv.), anhydrous triethylamine (11.1 µL, 0.08 mmol, 1.0 equiv.), Boc-Cys-OMe (18.8 mg, 0.08 mmol, 1.0 equiv.) and MeCN (0.8 mL). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:1 to 1:3 to 0:1), to afford the product **9c** as a colourless oil (32.2 mg, 86%, mixture of diastereomers).

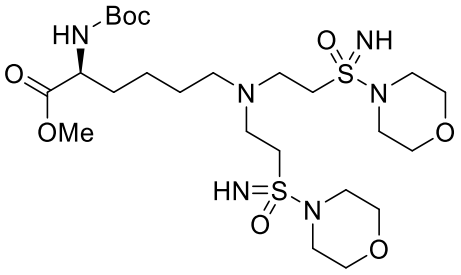
IR (thin film, ν_{max}/cm^{-1}) 3344, 2958, 1749, 1716, 1517, 1455, 1364, 1255, 1167, 1068, 937, 736; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 5.43-5.37 (m, 1H, , Boc-N*H*), 4.56-4.52 (m, 1H,Alkyl-*H*), 3.77 (s, 3H, Alkyl-*H*), 3.76-3.69 (m, 4H, Alkyl-*H*), 3.25-3.14 (m, 5H, Alkyl-*H*), 3.08-2.89 (m, 6H, Alkyl-*H*), 2.86-2.81 (m, 1H, Alkyl-*H*), 1.50-1.46 (m, 2H, Alkyl-*H*), 1.44 (s, 9H, Alkyl-*H*), 1.38-1.31 (m, 2H, Alkyl-*H*), 0.89 (t, 3H, J = 7.3 Hz, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 171.4, 155.3, 80.0, 66.9, 53.49, 53.45, 52.8, 49.5, 49.4, 46.7, 41.6, 35.2, 35.1, 34.8, 34.7, 28.4, 26.21, 26.18, 20.5, 14.0; **HRMS** (ESI^+), *m/z* calculated for $[C_{19}H_{38}N_3O_6S_2]^+$ 468.2197 ($[M+H]^+$), found 468.2206.

Note: The product was isolated as a mixture of diastereomers where the dr was not determined due to the overlap of the signals.

Methyl N^2-(*tert*-butoxycarbonyl)-N^6-(2-(morpholine-4-sulfonimidoyl)ethyl)-*L*-lysinate (10a) & methyl N^2-(*tert*-butoxycarbonyl)-N^6,N^6-bis(2-(morpholine-4-sulfonimidoyl)ethyl)-*L*-lysinate (10aa)



10a



10aa

Prepared according to general procedure C, using sulfonimidamide **2a** (15.8 mg, 0.09 mmol, 1.0 equiv.), anhydrous triethylamine (25 µL, 0.18 mmol, 2.0 equiv.), Boc-Lys-OMe·HCl (26.7 mg, 0.09 mmol, 1.0 equiv.) and MeCN (0.9 mL). Purification was carried out using flash column chromatography (SiO_2, CH_2Cl_2/MeOH, 50:1 to 20:1 to 10:1), to afford the product **10a** as a colourless oil (20.8 mg, 53%, mixture of diastereomers) and **10aa** as a colourless oil (7.2 mg, 13%, mixture of diastereomers).

10a IR (thin film, ν_{max}/cm^{-1}) 3220, 2980, 1743, 1712, 1521, 1368, 1250, 1168, 1048, 940; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 5.17-5.10 (m, 1H, Boc-N*H*), 4.30-4.25 (m, 1H, Alkyl-*H*), 3.91-3.73 (m, 8 H, Alkyl-*H*), 3.47 (s, 1H, Alkyl-*H*), 3.40-3.33 (m, 1H, Alkyl-*H*), 3.30-3.26 (m, 3H, Alkyl-*H*), 3.25-3.19 (m, 1H, Alkyl-*H*), 3.11-2.96 (m, 1H, Alkyl-*H*), 2.87-2.67 (m, 2H, Alkyl-*H*), 1.81-1.77 (m, 1H, Alkyl-*H*), 1.69-1.57 (m, 3H, Alkyl-*H*), 1.43-1.39 (m, 12 H, Alkyl-*H*), 1.27-1.19 (m, 1H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 173.4, 155.5, 80.2, 67.7, 66.9, 53.5, 53.3, 52.5, 52.4, 49.1, 49.0, 47.5, 46.9, 46.3, 44.4, 43.8, 32.6, 29.8, 29.5, 29.1, 28.5, 23.0; **HRMS** (ESI^+), *m/z* calculated for $[C_{18}H_{36}N_4O_6SNa]^+$ 459.2248 ($[M+Na]^+$), found 459.2251.

Note: The product was isolated as a mixture of diastereomers where the dr was not determined due to the overlap of the signals.

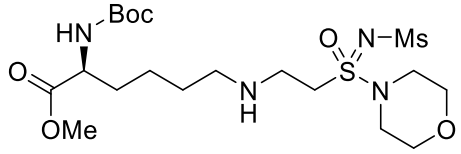
Note: Two NH proton signal was not identified due to the overlap of signals

10aa IR (thin film, ν_{max}/cm^{-1}) 3303, 2979, 1742, 1713, 1522, 1455, 1393, 1250, 1114, 1047, 939; δ_H (500 MHz, $CDCl_3$) 5.15-5.08 (m, 1H, BocN*H*), 4.28 (d, 1H, *J* = 7.4 Hz, Alkyl-*H*), 3.77-3.67 (m, 11H, Alkyl-*H*), 3.33-3.23 (m, 6H, Alkyl-*H*), 3.18-2.97 (m, 5H, Alkyl-*H*), 2.95-2.87 (m, 2H, Alkyl-*H*), 2.52-2.44 (m, 4H, Alkyl-*H*), 2.30 (br. s, 1H, Alkyl-*H*), 1.80 (br. s, 2H, Alkyl-*H*), 1.66-1.61 (m, 1H, Alkyl-*H*), 1.55-1.48 (m, 2H, Alkyl-*H*), 1.44 (s, 9H, Alkyl-*H*), 1.37-1.31 (m, 1H, Alkyl-*H*), 1.25-1.24 (m, 2H, Alkyl-*H*); δ_C (126 MHz, $CDCl_3$) 173.4, 155.6, 80.1, 67.1, 67.05, 67.05, 66.97, 53.83, 53.75, 53.7, 53.5, 53.4, 52.6, 52.4, 50.8, 47.9, 47.91, 47.89, 47.87, 46.86, 46.85, 45.9, 45.6, 43.3, 32.7, 32.1, 29.8, 28.5, 26.8, 23.1 ; **HRMS** (ESI^+, *m/z* calculated for $[C_{24}H_{49}N_6O_8S_2]^+$ 613.3048 ($[M+H]^+$), found 613.3069.

Note: The product was isolated as a mixture of diastereomers where the dr was not determined due to the overlap of the signals.

Note: One NH proton signal was not identified due to the overlap of signals

Methyl N^2-(*tert*-butoxycarbonyl)-N^6-(2-(*N*-(methylsulfonyl)morpholine-4-sulfonimidoyl)ethyl)-*L*-lysinate (10b)



10b

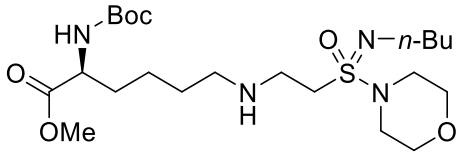
Prepared according to general procedure C, using sulfonimidamide **3b** (25.4 mg, 0.10 mmol, 1.0 equiv.), anhydrous triethylamine (28 µL, 0.20 mmol, 2.0 equiv.), Boc-Lys-OMe.HCl (29.7 mg, 0.10 mmol, 1.0 equiv.) and MeCN (1.0mL). Purification was carried out using flash column chromatography (SiO_2, CH_2Cl_2/MeOH, 50:1 to 20:1 to 10:1), to afford the product **10b** as a colourless oil (50.4 mg, 98%, mixture of diastereomers).

IR (thin film, ν_{max}/cm^{-1}) 3351, 3334, 2979, 1742, 1709, 1521, 1456, 1304, 1250, 1164, 1111, 945, 736; **δ_H** (500 MHz, $CDCl_3$) 5.15-5.10 (m, 1H, BocN*H*), 4.29-4.24 (m, 1H, Alkyl-*H*), 3.82-3.73 (m, 4H, Alkyl-*H*), 3.71 (s, 3H, Alkyl-*H*), 3.46-3.28 (m, 5H, Alkyl-*H*), 3.26-3.19 (m, 1H, Alkyl-*H*), 3.11-3.04 (m, 5H, Alkyl-*H*), 2.58 (t, 2H, *J* = 7.0 Hz, Alkyl-*H*), 1.82-1.73 (m, 1H, Alkyl-*H*), 1.66-1.57 (m, 1H, Alkyl-*H*), 1.53-1.30 (m, 14H, Alkyl-*H*); **δ_C** (126 MHz, $CDCl_3$) 173.3, 155.5, 80.0, 66.3, 53.3, 52.6, 52.5, 52.4, 49.3, 46.3, 44.8, 43.1, 32.6, 29.5, 28.4, 23.1; **HRMS** (ESI^+), *m/z* calculated for $[C_{19}H_{39}N_4O_8S_2]^+$ 515.2204 ($[M+H]^+$), found 515.2205.

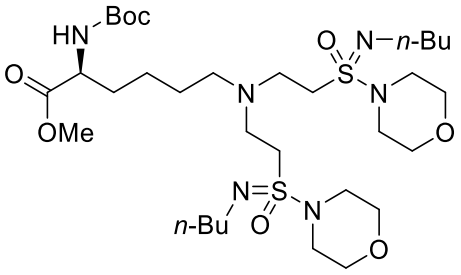
Note: The product was isolated as a mixture of diastereomers where the dr was not determined due to the overlap of the signals.

Note: One NH proton was not identified due to the overlap of signals

Methyl N^2-(*tert*-butoxycarbonyl)-N^6-(2-(*N*-butylmorpholine-4-sulfonimidoyl)ethyl)-*L*-lysinate (10c) & methyl N^2-(*tert*-butoxycarbonyl)-N^6,N^6-bis(2-(*N*-butylmorpholine-4-sulfonimidoyl)ethyl)-*L*-lysinate (10cc)



10c



10cc

Prepared according to general procedure C, using sulfonimidamide **3g** (18.6 mg, 0.08 mmol, 1.0 equiv.), anhydrous triethylamine (22.3 µL, 0.16 mmol, 2.0 equiv.), Boc-Lys-OMe.HCl (23.7 mg, 0.08 mmol, 1.0 equiv.) and MeCN (0.8 mL). Purification was carried out using flash column chromatography (SiO_2,

CH_2Cl_2/MeOH, 50:1 to 20:1 to 10:1), to afford the product **10c** as a colourless oil (13.4 mg, 34%, mixture of diastereomers) and **10cc** as a colourless oil (11.6 mg, 20%, mixture of diastereomers).

10c IR (thin film, ν_{max}/cm^{-1}) 3368, 3344, 2957, 2936, 1746, 1714, 1520, 1456, 1392, 1298, 1257, 1169, 940, 738; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 5.11-5.08 (m, 1H, BocN*H*), 4.28 (d, 1H, *J* = 7.4 Hz, Alkyl-*H*), 3.77-3.69 (m, 7H, Alkyl-*H*), 3.49 (br. s, 1H, Alkyl-*H*), 3.30-3.17 (m, 6H, Alkyl-*H*), 3.10-3.04 (m, 1H, Alkyl-*H*), 2.92-2.68 (m, 4H, Alkyl-*H*), 1.81 (br. s, 1H, Alkyl-*H*), 1.68-1.61 (m, 3H, Alkyl-*H*), 1.50-1.31 (m, 16 H, Alkyl-*H*), 0.91 (t, 3H, *J* = 7.3 Hz, Alkyl-*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 173.3, 155.6, 80.1, 66.8, 53.3, 52.5, 48.6, 46.8 46.7, 43.4, 41.3, 34.71, 34.69, 32.6, 28.5, 23.0, 20.5, 14.0; **HRMS** (ESI^+), *m/z* calculated for $[C_{22}H_{45}N_4O_6S]^+$ 493.3054 ($[M+H]^+$), found 493.3056.

Note: The product was isolated as a mixture of diastereomers where the dr was not determined due to the overlap of the signals.

Note: One NH proton was not identified due to the overlap of signals.

10cc IR (thin film, ν_{max}/cm^{-1}) 3368, 2958, 1746, 1714, 1519, 1455, 1336, 1274, 1154, 1069, 938, 737; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 5.08 (d, 1H, *J* = 8.4 Hz, BocN*H*), 4.28 (d, 1H, *J* = 6.6 Hz, Alkyl-*H*), 3.77-3.70 (m, 11H, Alkyl-*H*), 3.24-3.15 (m, 8H, Alkyl-*H*), 3.08-2.98 (m, 6H, Alkyl-*H*), 2.89-2.81 (m, 4H, Alkyl-*H*), 2.44 (br. s, 2H, Alkyl-*H*), 1.77 (br. s, 4H, Alkyl-*H*), 1.51-1.45 (m, 6H, Alkyl-*H*), 1.44 (s, 9H, Alkyl-*H*), 1.39-1.31 (m, 6H, Alkyl-*H*), 0.92-0.88 (m, 6H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 173.4, 155.5, 80.0, 66.9, 53.7, 53.5, 52.4, 47.7, 47.6, 46.8, 46.1, 46.0, 41.6, 34.8, 32.8, 28.5, 23.1, 20.5, 14.0; **HRMS** (ESI^+), *m/z* calculated for $[C_{32}H_{65}N_6O_8S_2]^+$ 725.4300 ($[M+H]^+$), found 725.4305.

Note: The product was isolated as a mixture of diastereomers where the dr was not determined due to the overlap of the signals.

5.2.9 Procedure for Competition Reactions of Lys- and Cys-derivatives

The respective sulfonimidamide (0.1 mmol, 1.0 equiv.) was added to an oven dried reaction flask. The flask was evacuated and back-filled with nitrogen three times. Anhydrous CH_3CN (0.7 mL) was added, followed by the addition of anhydrous triethylamine (0.1 mmol, 1.0 equiv.). Boc-Lys-OMe (0.1 mmol, 1.0 equiv.) and Boc-Cys-OMe (0.1 mmol, 1.0 equiv.) were dissolved in anhydrous CH_3CN (0.3 mL) and added to the solution containing sulfonimidamide. The reaction mixture was stirred at room temperature for 16 hours. The crude mixture was quenched with $NaHCO_3$(aq) (3.0 mL), extracted with EtOAc (3 x 5 mL), washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, CH_2Cl_2/MeOH, 50:1 to 20:1 to 10:1), to afford the products with matching analytical data to those reported above.

5.2.10 Procedure for Determination of Half-life for the Conjugate Addition of Glutathione

General procedure D:

The rate determination reaction was conducted using nuclear magnetic resonance (NMR) spectroscopy. ^1H NMR spectra were obtained on a Bruker AVIIIHD 500 (500MHz) using 5 mm NMR tubes at 20 °C. The spectra were recorded using zg60 pulse program with a spectral width of 10000 Hz and a relaxation time of 1 second. Due to the extremely fast reaction rate of some reactive substrates, for majority of the substates, each acquisition consisted of 1 scan with an increasing interval time from 0 second to 120 seconds for a total elapsed time of 2 hours. Consumption of starting material was determined by monitoring the disappearance of alkene proton signals (6.0 to 6.5 ppm) relative to a sodium acetate internal standard.

Reaction was conducted in a mixture of buffer solution and deuterated DMSO (Buffer:$(CD_3)_2SO$ = 2:1). A relatively high $(CD_3)_2SO$ ratio was employed due to the insolubility of less polar substrates in the buffer solution.

Buffer solution containing 0.0648 mol/L disodium hydrogen phosphate and 0.0153 mol/L potassium dihydrogen phosphate at pH 7.3[10] was prepared using deuterium oxide and stored at 20 °C. The prepared buffer solution had a shelf life of one month. The stock solution of sodium acetate (0.1 M) was prepared using the buffer solution. Glutathione stock solution (0.1 M) was freshly prepared before each experiment, stored under argon and used within 20 minutes to minimise the effect of background oxidation of glutathione. The sulfonimidamide was dissolved in $(CD_3)_2SO$ to form a stock solution (0.1 M).

The procedure for the kinetic study was as follows: sulfonimidamide stock solution (100 μL, 0.1 M in $(CD_3)_2SO$, 0.01 mmol, 1.0 equiv.) and sodium acetate solution (100 μL, 0.01 mmol, 1.0 equiv.) were added sequentially to the NMR tube. $(CD_3)_2SO$ (0.3 mL) and buffer solution were added (0.5 mL) to give an overall volume of 0.8 mL. Locking and shimming of the reaction mixture was performed, and a spectrum was obtained to check the concentration of electrophile before the addition of corresponding amount of glutathione solution (0.01 mmol, 1.0 equiv., 0.1 mL) such that the acquisition could be started right after the addition of glutathione.

For the majority of substrates, the half-life was determined using second order kinetics with 1.0 equivalents of glutathione used as the nucleophile. The consumption of starting material was measured and plotted as the inverse against time. The half-life was calculated through the equation obtained from the best-fitted line. An example plot is shown below for compound **2a** (**Figure S1**).

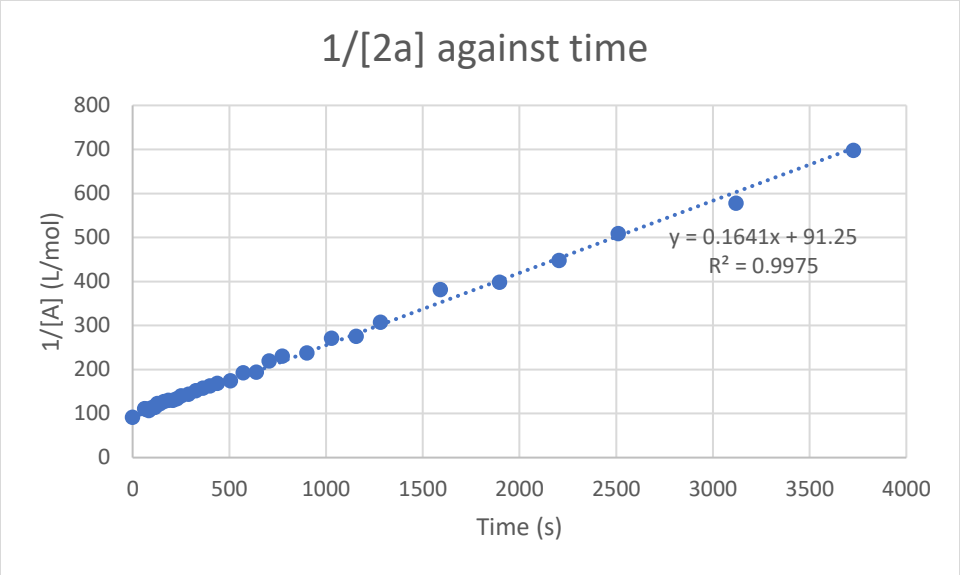


Figure S1: 1/[2a] against time

For substrates with much lower reactivity, such as **2f** and *E*-**2h**, half-life was calculated through pseudo-first order kinetic using excess glutathione (6.0 equiv.). The concentration of starting material was plotted as natural log and the half-life was calculated through the best-fitted line obtained. An example plot is shown below for compound **2f** (**Figure S2**).

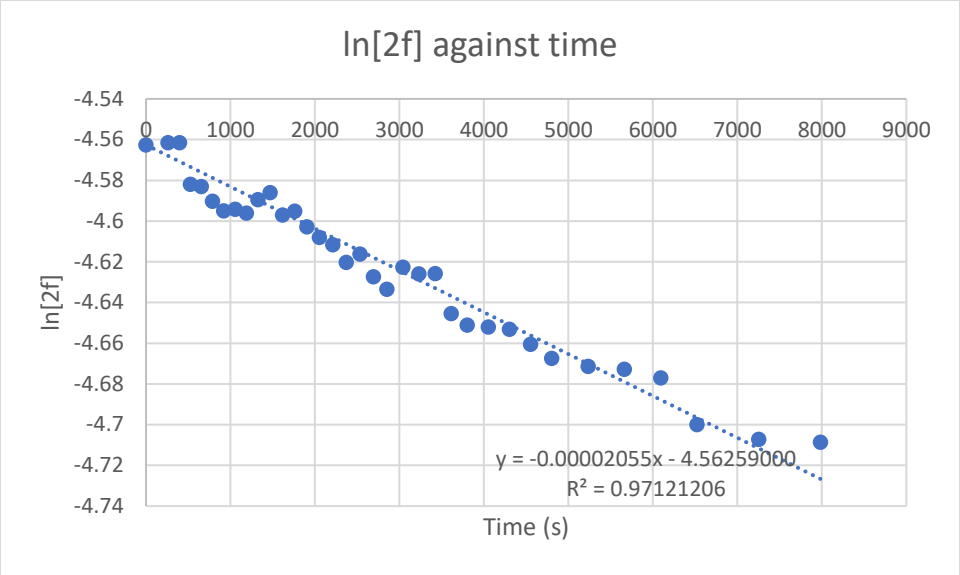
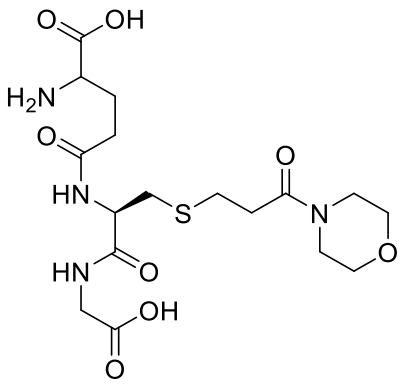


Figure S2: ln[2f] against time

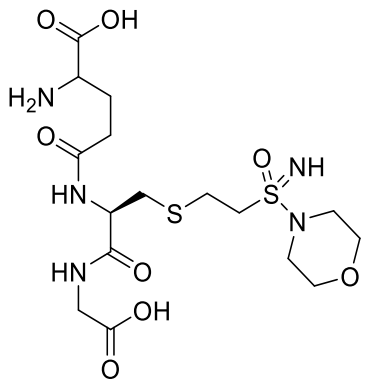
4-Acryloylmorpholine-GSH adduct (13a)



Prepared according to general procedure D, using 4-acryloylmorpholine **8**, except that each acquisition consisted of 4 scans with a relaxation time of 50 seconds, 1200 seconds interval time and the total elapsed time was 6 hours. The half-life was calculated using the data within the first 3.5 hours. The half-life calculated from two separate experiments were 13923 seconds and 14259 seconds respectively, with an averaged value of 14091 seconds.

HRMS (ESI^+), *m/z* calculated for $[C_{17}H_{27}N_4O_8SD_2]^+$ 451.1826 ($[M-H+2D]^+$), found 451.1824.

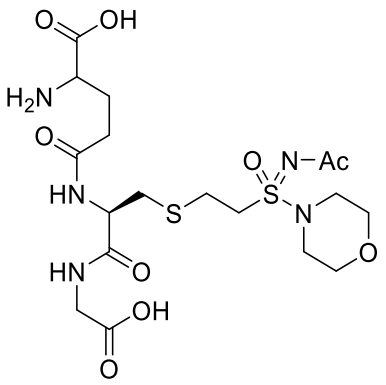
Sulfonimidamide-GSH Adduct (13b)



Prepared according to general procedure D, using 4-(vinylsulfonimidoyl)morpholine **2a**. The half-life calculated from three experiments were 584 seconds, 588 seconds and 556 seconds respectively, the average half-life calculated was 576 seconds (standard deviation 17 seconds).

δ_H (500 MHz, D_2O) 4.64 (dd, 1H, *J* = 8.5 Hz, 5.2Hz, Alkyl-*H*)), 3.98 (s, 2H, Alkyl-*H*), 3.85-3.77 (m, 5H, Alkyl-*H*), 3.49-3.41 (m, 2H, Alkyl-*H*), 3.38-3.28 (m, 4H, Alkyl-*H*), 3.16(dd, 0.44H (diastereomer A), *J* = 5.2 Hz, 1.8 Hz, Alkyl-H_a), 3.13 (dd, 0.57H, (diastereomer B), *J* = 5.3 Hz, 1.9 Hz, Alkyl-*H*) 3.05-2.91 (m, 3H, Alkyl-*H*), 2.55 (m, 2H, Alkyl-*H*), 2.18 (m, 2H, Alkyl-*H*); **δ_C** (126 MHz, $CDCl_3$) 174.8, 173.7, 173.6, 172.4, 66.5, 53.9, 52.94, 52.88, 49.2, 49.1, 46.1, 41.7, 33.02, 32.96, 31.2, 26.0, 24.84, 24.76; **HRMS** (ESI^+), *m/z* calculated for $[C_{16}H_{28}N_5O_8S_2D]^+$ 485.1593 ($[M+D]^+$), found 485.1594.

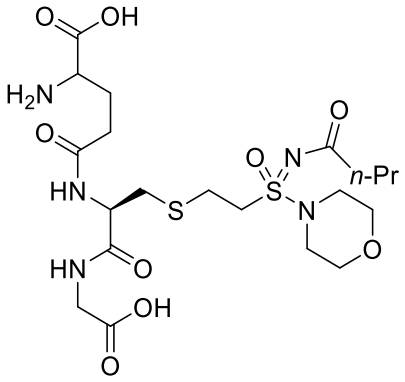
Sulfonimidamide-GSH Adduct (13c)



Prepared according to general procedure D, using *N*-(morpholino(oxo)(vinyl)-λ^6-sulfaneylidene)acetamide **3a**. The half-life calculated from two experiments were 1.06 second and 0.96 second respectively, the average half-life calculated was 1.01 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{18}H_{32}N_5O_9S_2]^+$ 526.1636 ($[M+H]^+$), found 526.1639.

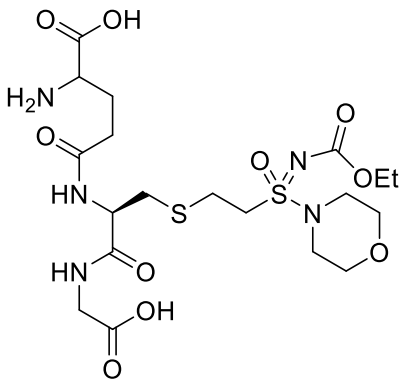
Sulfonimidamide-GSH Adduct (13d)



Prepared according to general procedure D, using *N*-(morpholino(oxo)(vinyl)-λ^6-sulfaneylidene)butyramide **3b**. The half-life calculated from two experiments were 8.36 seconds and 11.4 seconds respectively, the average half-life calculated was 9.88 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{20}H_{34}N_5O_9S_2D_2]^+$ 556.2075 ($[M-H+2D]^+$), found 556.2079.

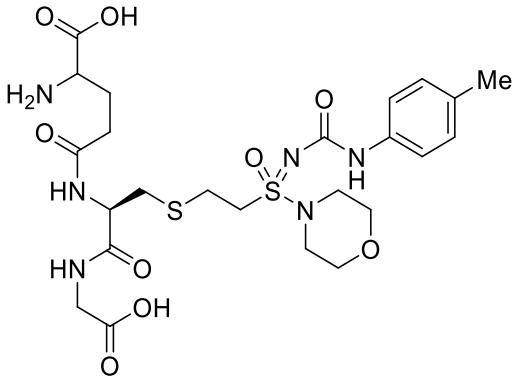
Sulfonimidamide-GSH Adduct (13e)



Prepared according to general procedure D, using ethyl (morpholino(oxo)(vinyl)-λ^6-sulfaneylidene)carbamate **3c**. The half-life calculated from two experiments were 3.95 seconds and 4.48 seconds respectively, the average half-life calculated was 4.22 seconds.

HRMS (ESI^+), *m/z* calculated for $[C_{19}H_{32}N_5O_{10}S_2D_2]^+$ 558.1867 ($[M-H+2D]^+$), found 558.1866.

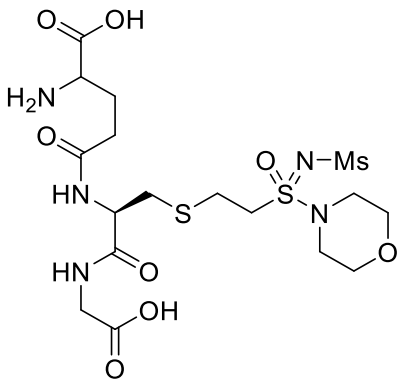
Sulfonimidamide-GSH Adduct (13f)



Prepared according to general procedure D, using 1-(morpholino(oxo)(vinyl)-λ^6-sulfaneylidene)-3-(p-tolyl)urea **3d**. The half-life calculated from two experiments were 26.5 seconds and 31.0 seconds respectively, the average half-life calculated was 28.8 seconds.

HRMS (ESI^+), *m/z* calculated for $[C_{24}H_{35}N_6O_9S_2D_2]^+$ 619.2184 ($[M-H+2D]^+$), found 619.2191.

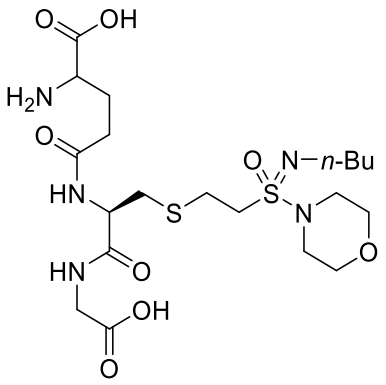
Sulfonimidamide-GSH Adduct (13g)



Prepared according to general procedure D, using *N*-(morpholino(oxo)(vinyl)-λ^6-sulfaneylidene)butyramide **3e**. The reaction was too fast to accurately determine the half-life.

HRMS (ESI$^+$), *m/z* calculated for $[C_{17}H_{31}N_5O_{10}S_3D]^+$ 563.1369 ($[M+D]^+$), found 563.1361.

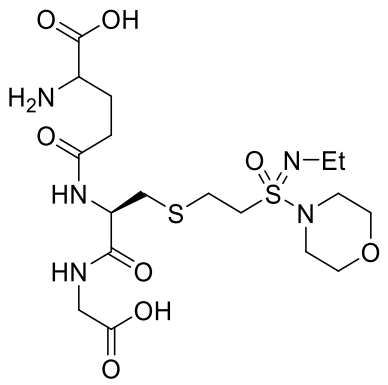
Sulfonimidamide-GSH Adduct (13h)



Prepared according to general procedure D, using 4-(*N*-butylvinylsulfonimidoyl)morpholine **3g**. The half-life calculated from three experiments were 167 seconds ,172 seconds and 148 seconds respectively, the average half-life calculated was 162 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{20}H_{38}N_5O_8S_2]^+$ 540.2156 ($[M+H]^+$), found 540.2160.

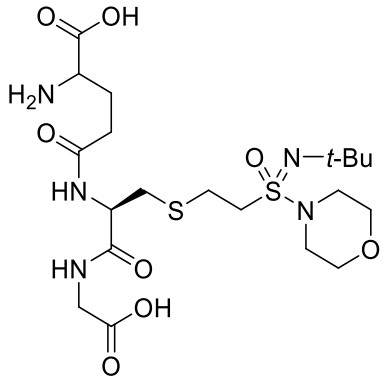
Sulfonimidamide-GSH Adduct (13i)



Prepared according to general procedure D, using 4-(*N*-ethylvinylsulfonimidoyl)morpholine **3h**. The half-life calculated from two experiments were 146 seconds and 176 seconds respectively, the average half-life calculated was 161 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{18}H_{32}N_5O_8S_2D_2]^+$ 514.1969 ($[M-H+2D]^+$), found 514.1959.

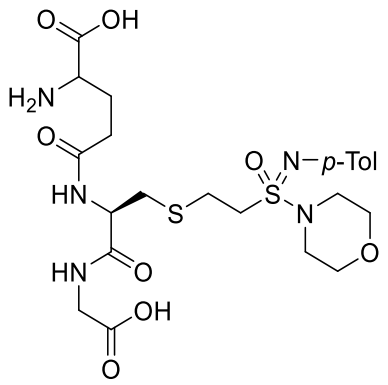
Sulfonimidamide-GSH Adduct (13j)



Prepared according to general procedure D, using 4-(*N*-(tert-butyl)vinylsulfonimidoyl)morpholine **3i**. The half-life calculated from two experiments were 415 seconds and 391 seconds respectively, the average half-life calculated was 403 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{20}H_{37}N_5O_8S_2Na]^+$ 562.1976 ($[M+Na]^+$), found 562.1977.

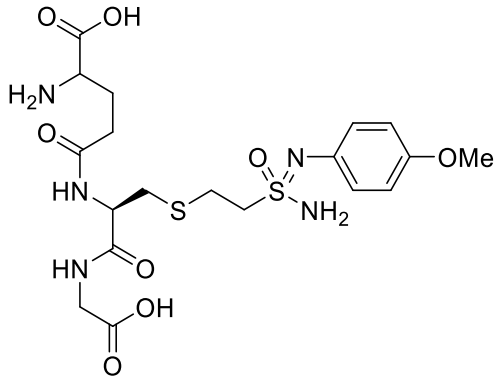
Sulfonimidamide-GSH Adduct (13k)



Prepared according to general procedure D, using 4-(*N*-(*p*-tolyl)vinylsulfonimidoyl)morpholine **3j**. The half-life calculated from two experiments were 501 seconds and 562 seconds respectively, the average half-life calculated was 532 seconds.

HRMS (ESI^+), *m/z* calculated for $[C_{23}H_{34}N_5O_8S_2D_2]^+$ 576.2125 ($[M-H+2D]^+$), found 576.2116.

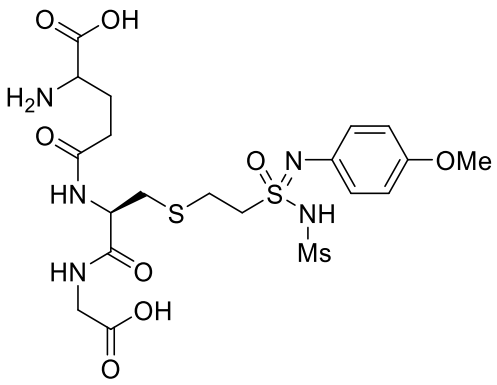
Sulfonimidamide-GSH Adduct (13l)



Prepared according to general procedure D, using *N*'-(4-methoxyphenyl)ethenesulfonimidamide **2d**. The half-life calculated from two experiments were 1006 seconds and 1123 seconds respectively, the average half-life calculated was 1065 seconds.

HRMS (ESI^+), *m/z* calculated for $[C_{19}H_{29}N_5O_8S_2D]^+$ 521.1593 ($[M+D]^+$), found 521.1600.

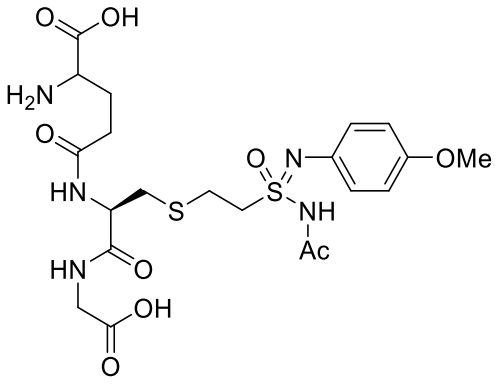
Sulfonimidamide-GSH Adduct (13m)



Prepared according to general procedure D, using *N*-(*N*-(4-methoxyphenyl)vinylsulfonimidoyl)methanesulfonamide **6a**. The half-life calculated from two experiments were 284 seconds and 264 seconds respectively, the average half-life calculated was 274 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{20}H_{31}N_5O_{10}S_3D]^+$ 599.1369 ($[M+D]^+$), found 599.1369.

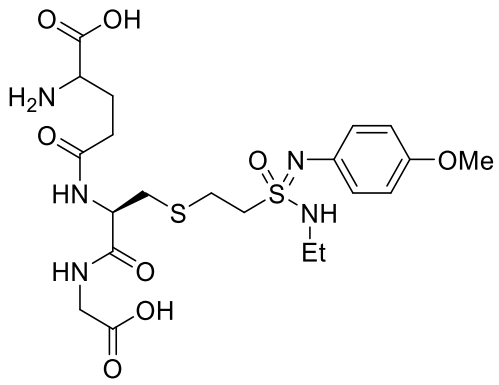
Sulfonimidamide-GSH Adduct (13n)



Prepared according to general procedure D, using *N*-(*N*-(4-methoxyphenyl)vinylsulfonimidoyl)acetamide **6b**. The half-life calculated from two experiments were 72.7 seconds and 90.7 seconds respectively, the average half-life calculated was 81.7 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{21}H_{31}N_5O_9S_2D]^+$ 563.1699 ($[M+D]^+$), found 563.1717.

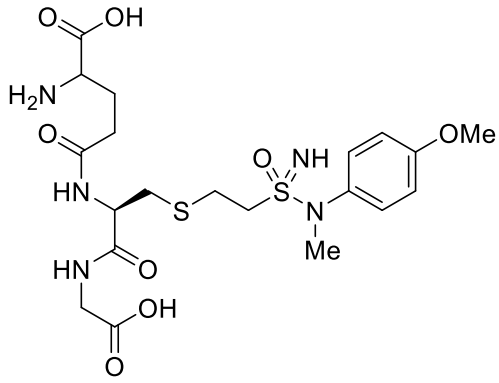
Sulfonimidamide-GSH Adduct (13o)



Prepared according to general procedure D, using *N*-ethyl-*N*'-(4-methoxyphenyl)ethenesulfonimidamide **6d**. The half-life calculated from two experiments were 827 seconds and 860 seconds respectively, the average half-life calculated was 842 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{21}H_{33}N_5O_8S_2D]^+$ 549.1906 ($[M+D]^+$), found 549.1913.

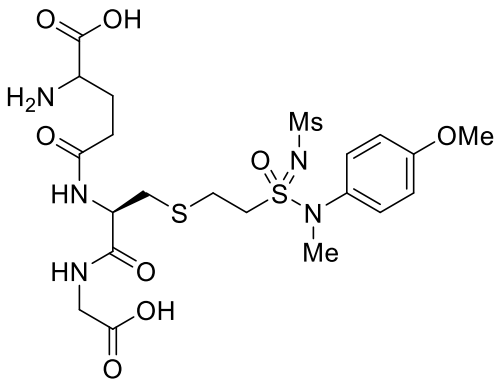
Sulfonimidamide-GSH Adduct (13p)



Prepared according to general procedure D, using *N*-(4-methoxyphenyl)-*N*-methylethenesulfonimidamide **2e**. Decomposition was observed when the substrate **2e** was added into the buffer-DMSO mixture thus the half-life of the conjugate addition could not be determined.

HRMS (ESI$^+$) not found.

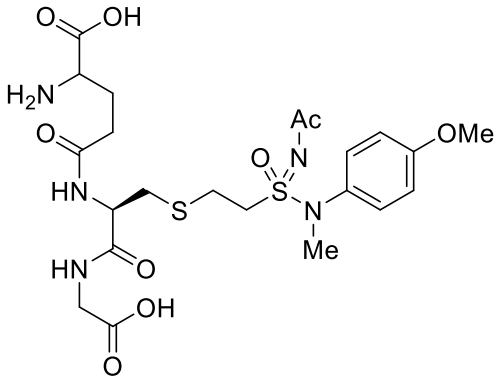
Sulfonimidamide-GSH Adduct (13q)



Prepared according to general procedure D, using *N*-(((4-methoxyphenyl)(methyl)amino)(oxo)(vinyl)-λ^6-sulfaneylidene)methanesulfonamide **5a**. The reaction was too fast to accurately determine the half-life.

HRMS (ESI$^+$), *m/z* calculated for $[C_{21}H_{31}N_5O_{10}S_3D_2K]^+$ 652.1147 ($[M-2H+2D+K]^+$, found 652.1146.

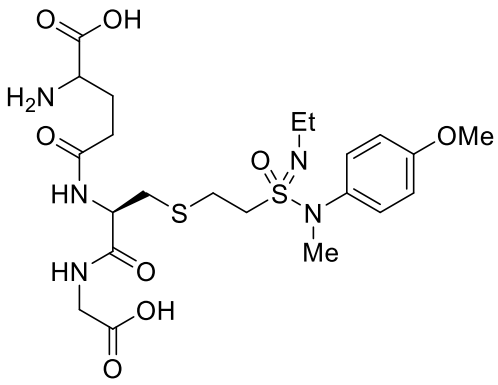
Sulfonimidamide-GSH Adduct (13r)



Prepared according to general procedure D, using *N*-(((4-methoxyphenyl)(methyl)amino)(oxo)(vinyl)-λ^6-sulfaneylidene)acetamide **5b**. The half-life calculated from two experiments were 3.46 seconds and 2.93 seconds respectively, the average half-life calculated was 3.20 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{22}H_{34}N_5O_9S_2]^+$ 576.1793 ($[M+H]^+$), found 576.1797.

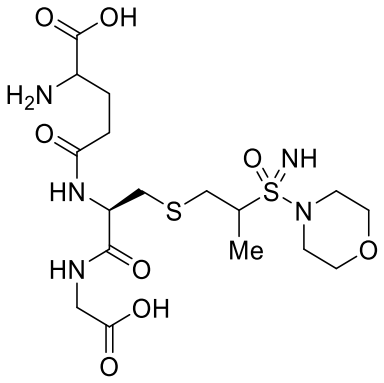
Sulfonimidamide-GSH Adduct (13s)



Prepared according to general procedure D, using *N'*-ethyl-*N*-(4-methoxyphenyl)-*N*-methylethenesulfonimidamide **5c**. The half-life calculated from two experiments were 192 seconds and 200 seconds respectively, the average half-life calculated was 196 seconds.

HRMS (ESI^+), *m/z* calculated for $[C_{22}H_{33}N_5O_8S_2D_2Na]^+$ 586.1945 ($[M-H+2D+Na]^+$), found 586.1942.

Sulfonimidamide-GSH Adduct (13t)

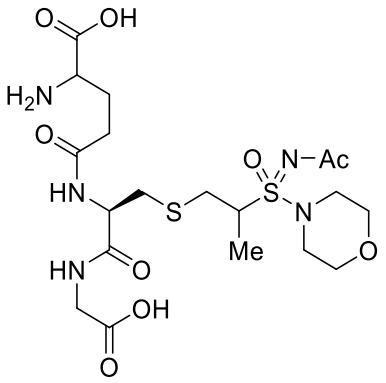


Prepared according to general procedure D, using 4-(prop-1-en-2-ylsulfonimidoyl)morpholine **2f** except that 6 equiv. of glutathione was used, and the half-life was determined using pseudo-first-order kinetics.

The half-life calculated from two experiments were 33095 seconds and 38650 seconds respectively, the average half-life calculated was 35873 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{17}H_{31}N_5O_8S_2D]^+$ 499.1750 ($[M+D]^+$), found 499.1741.

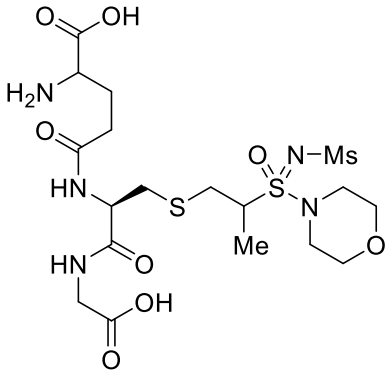
Sulfonimidamide-GSH Adduct (13u)



Prepared according to general procedure D, using *N*-(morpholino(oxo)(prop-1-en-2-yl)-λ^6-sulfaneylidene)acetamide **4a**. The half-life calculated from two experiments were 4738 seconds and 4621 seconds respectively, the average half-life calculated was 4680 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{19}H_{33}N_5O_9S_2D]^+$ 541.1855 ($[M+D]^+$), found 541.1853.

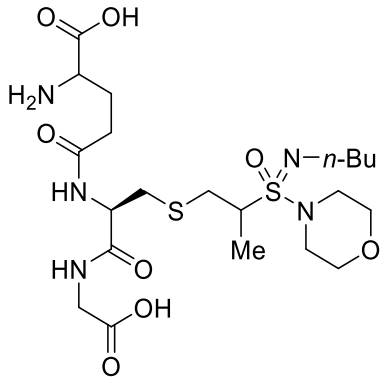
Sulfonimidamide-GSH Adduct (13v)



Prepared according to general procedure D, using *N*-(morpholino(oxo)(prop-1-en-2-yl)-λ^6-sulfaneylidene)methanesulfonamide **4b**. The half-life calculated from two experiments were 230 seconds and 268 seconds respectively, the average half-life calculated was 249 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{18}H_{34}N_5O_{10}S_3]^+$ 576.1462 ($[M+H]^+$), found 576.1463.

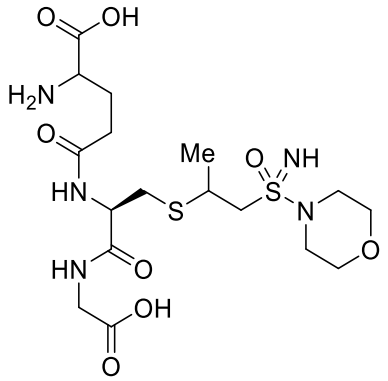
Sulfonimidamide-GSH Adduct (13w)



Prepared according to general procedure D, using 4-(*N*-butylprop-1-en-2-ylsulfonimidoyl)morpholine **4c**. The half-life calculated from two experiments were 11143 seconds and 10902 seconds respectively, the average half-life calculated was 11023 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{21}H_{40}N_5O_8S_2]^+$ 554.2313 ($[M+H]^+$), found 554.2318.

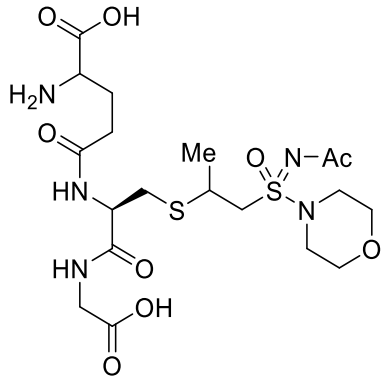
Sulfonimidamide-GSH Adduct (13x)



Prepared according to general procedure D, using (*E*)-4-(prop-1-en-1-ylsulfonimidoyl)morpholine **trans-2h** except that 6 equiv. of glutathione was used, and the half-life was determined using pseudo-first-order kinetics. The half-life calculated from two experiments were 16989 seconds and 15768 seconds respectively, the average half-life calculated was 16379 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{17}H_{31}N_5O_8S_2D]^+$ 499.1750 ($[M+D]^+$), found 499.1754.

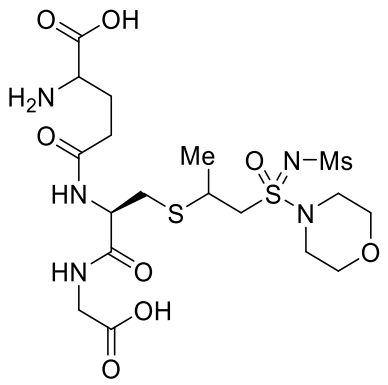
Sulfonimidamide-GSH Adduct (13y)



Prepared according to general procedure D, using (*E*)-*N*-(morpholino(oxo)(prop-1-en-1-yl)-λ^6-sulfaneylidene)acetamide **4d**. The half-life calculated from two experiments were 1450 seconds and 1647 seconds respectively, the average half-life calculated was 1549 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{19}H_{33}N_5O_9S_2D]^+$ 541.1855 ($[M+D]^+$), found 541.1862.

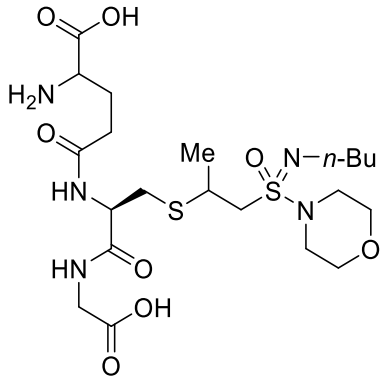
Sulfonimidamide-GSH Adduct (13z)



Prepared according to general procedure D, using (*E*)-*N*-(morpholino(oxo)(prop-1-en-1-yl)-λ^6-sulfaneylidene)methanesulfonamide **4e**. The half-life calculated from two experiments were 221 seconds and 215 seconds respectively, the average half-life calculated was 218 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{18}H_{32}N_5O_{10}S_3DNa]^+$ 599.1345 ($[M+D+Na]^+$), found 599.1347.

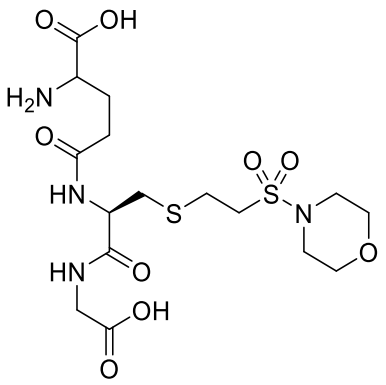
Sulfonimidamide-GSH Adduct (13aa)



Prepared according to general procedure D, using (*E*)-4-(*N*-butylprop-1-en-1-ylsulfonimidoyl)morpholine **4f**. The half-life calculated from two experiments were 9016 seconds and 9598 seconds respectively, the average half-life calculated was 9307 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{21}H_{37}N_5O_8S_2D_2Na]^+$ 578.2258 ($[M-H+2D+Na]^+$), found 578.2257.

Sulfonamide-GSH Adduct (13ab)



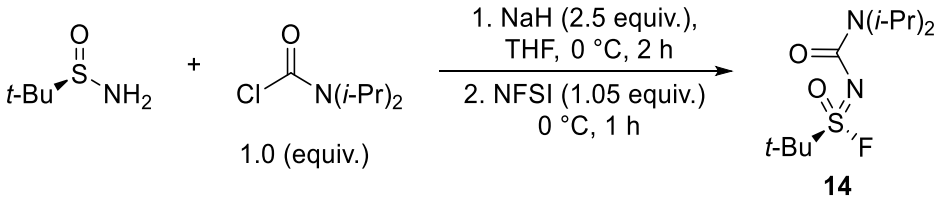
Prepared according to general procedure D, using 4-(vinylsulfonyl)morpholine **12**. The half-life calculated from two experiments were 230 second and 246 second respectively, the average half-life calculated was 238 seconds.

HRMS (ESI$^+$), *m/z* calculated for $[C_{16}H_{29}N_4O_9S_2]^+$ 485.1371 ($[M+H]^+$), found 485.1369.

5.3 Chapter 3 Data

5.3.1 Synthesis of (*S*)-*t*-BuSF

***t*-BuSF (14)**



Procedures adapted from S. Teng, Z.P. Shultz, C. Shan, L. Wojtas, J. M. Lopchuk, *Nat. Chem*. 2024, **16**, 183-192.[92]

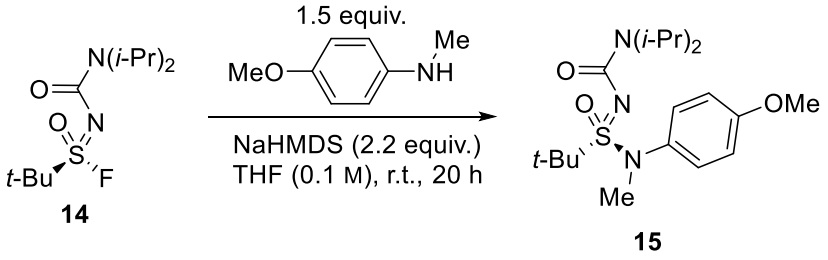
(*R*)-*t*-Bu sulfinamide (363.6 mg, 3 mmol, 1.0 equiv.), was added to an oven-dried round-bottom flask and the flask was evacuated and back-filled with nitrogen three times. The sulfinamide was dissolved in anhydrous, degassed THF (30 mL, 0.1 M) and cooled to 0 °C. NaH (300 mg, 7.5 mmol, 2.5 equiv.) was added portion-wise (3 portions), and the resultant solution was stirred at 0 °C for 20 minutes. DIPC-CCl

was added and the solution was stirred at 0 °C for 1.5 hour, followed by the addition of NFSI and the reaction mixture was stirred for an additional 1 hour at 0 °C. The crude mixture was then diluted with 10% EtOAc in hexanes (30 mL) then filtered through celite while rinsing with 10% EtOAc in hexanes. The organic layer was washed water (20 mL) and with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (SiO_2, Petrol/EtOAc, 7:1 to 5:1) to give the product **14** as white solid (609 mg, 76%).

IR (thin film, ν_{max}/cm^{-1})2993, 1652, 1430, 1298, 1217, 1151, 1043, 715; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 3.99 (s, 1H, alkyl-*H*), 3.82 (s, 1 H, Alkyl-*H*), 1.54 (s, 9H, alkyl-*H*), 1.29-1.12 (m, 12 H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 153.7, 62.7 (*J* = 11.5 Hz), 47.7, 45.7, 29.7, 24.5, 21.2, 20.5, 20.4; **HRMS** (ESI^+), *m/z* calculated for $[C_{11}H_{24}FN_2O_2S]^+$ 267.1537 ($[M+H]^+$), found 267.1536. Specific rotation [α] = +77.8 (c 1.00, $CHCl_3$, 25 °C). Data is consistent with the literature.[92]

5.3.2 SuFEx Amination of (*S*)-*t*-BuSF

(*S*)-*N*'-(Diisopropylcarbamoyl)-*N*-(4-methoxyphenyl)-*N*,2-dimethylpropane-2-sulfonimidamide (15)



t-BuSF **14** (39.9 mg, 0.15 mmol, 1.0 equiv.) and 4-methoxy-*N*-methylaniline (30.9 mg, 0.225 mmol, 1.5 equiv.) were added to an oven-dried reaction tube. The flask was evacuated and back-filled with nitrogen three times and dissolved in anhydrous, degassed THF (1.5 mL, 0.1 M) at 0 °C. NaHMDS (330 µL, 0.33 mmol, 1.0 M in THF, 2.2 equiv.) was added dropwise to the solution, and the reaction mixture was warmed to room temperature and stirred for 20 hours. The crude mixture was filtered through a short pad of silica, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification was carried out using flash column

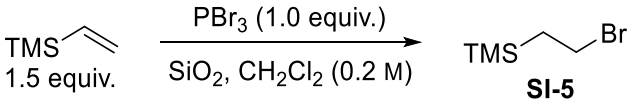
chromatography (SiO_2, Petrol/EtOAc, 5:1 to 3:1), to afford the product **15** as a pale-yellow solid (31.1 mg, 54%).

m.p. 124-126 °C ($CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3078, 2991, 1621, 1510, 1321, 1248, 1091, 892; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.56 (d, 2H, *J* = 9.0 Hz, Ar-*H*), 6.84 (d, 2H, *J* = 9.0 Hz, Ar-*H*), 4.03 (br. s, 2 H, alkyl-*H*), 3.78 (s, 3H, Alkyl-*H*), 3.28 (s, 3H, Alkyl-*H*), 1.47 (s, 9H, Alkyl-*H*), 1.27-1.21 (m, 12H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 158.6 (2C), 136.9, 130.8, 114.2, 64.4, 55.5, 45.1, 43.4, 25.0, 21.6, 21.1, 20.8; **HRMS** (ESI^+), *m/z* calculated for $[C_{19}H_{33}N_3O_3SNa]^+$ 406.2135 ($[M+Na]^+$), found 406.2139.

Note: Stereochemistry of the compound was yet to be determined.

5.3.3 Synthesis of Trimethylethylsilyl Sulfonimidamide 16

5.3.3.1 Preparation of (2-bromoethyl)trimethylsilane (SI-5)



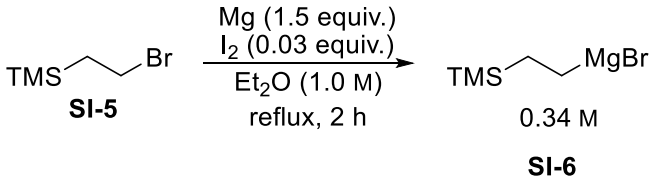
Procedures adapted from T. K. Tran, Q. Bricaud, M. Oçafrain, P. Blanchard, J. Roncali, S. Lenfant, S. Godey, D. Vuillaume, D. Rondeau, *Chem. Eur. J*., 2011, **17**, 5628-5640.[192]

Silica gel (4.67 g) was added to an oven-dried round-bottom flask. The flask was evacuated and back-filled with nitrogen three times and anhydrous, degassed CH_2Cl_2 (50 mL, 0.2 M) was added, followed by the addition of vinyltrimethylsilane (1.47 mL, 10 mmol, 1.5 equiv.). The reaction mixture was cooled to -10 °C, and a solution of phosphorus tribromide (627 µL, 6.67 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (8 mL) was added dropwise. The resultant solution was stirred at -10 °C for 10 minutes, then warmed to room temperature and stirred for an additional 30 minutes. The crude mixture was filtered, washed with saturated Na_2CO_3 (aq.) (50 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give **SI-5** as a pale-yellow oil (1.20 g, 66%).

IR (thin film, ν_{max}/cm^{-1}) 2927, 1751, 1461, 1246, 1030, 700, 650; δ_H (400 MHz, $CDCl_3$) 3.59-3.54 (m, 2H, alkyl-*H*), 1.40-1.35 (m, 2H, Alkyl-*H*), 0.04 (s, 9H, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 32.1, 24.1, -1.65; **HRMS** not detected. Data is consistent with the literature.[192]

Note: **SI-5** slowly decomposes at room temperature, thus is used immediately after synthesis.

5.3.3.2 Preparation of (2-(trimethylsilyl)ethyl)magnesium bromide (SI-6)

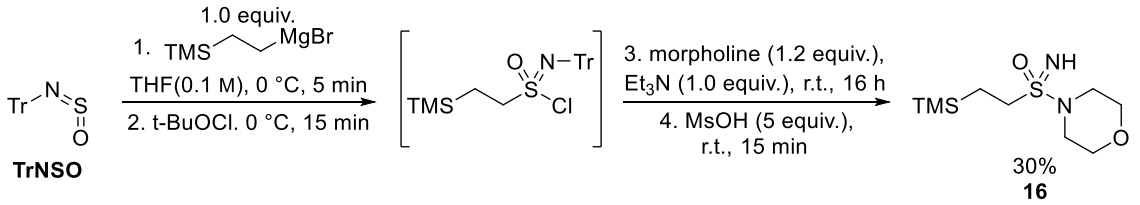


Procedures adapted from W. Zhao, J. Zhang, B. Chen, W. Shu, *Nat Commun.*, 2023, **14**, 2938.[193]

Magnesium turning (240.6 mg, 9.9 mmol, 1.5 equiv.) was added to an oven-dried two-necked round bottom flask connected to water condenser. The flask was evacuated and back-filled with nitrogen three times, followed by the addition of iodine (50.3 mg, 0.198 mmol, 0.03 equiv.). A solution of (2-bromoethyl)trimethylsilane (1.20 g , 6.60 mmol, 1.0 equiv.) in Et_2O (6.6 mL, 1.0 M) was added dropwise, and the resultant solution was refluxed for 2 hours. The concentration of resultant Grignard reagent was determined by titrating against salicylaldehyde phenylhydrazone.

5.3.3.3 Preparation of trimethylethylsilyl sulfonimidamide (16) through TrNSO

4-(2-(Trimethylsilyl)ethylsulfonimidoyl)morpholine (16)



Procedures adapted from T. Q. Davies, A. Hall, M. C. Willis, *Angew. Chem. Int. Ed.* 2017, **56**, 14937.-14941.[79]

TrNSO (519.2 mg, 1.7 mmol, 1.0 equiv.) was added to an oven-dried round-bottom flask. The flask was evacuated and back-filled with nitrogen three times. followed by addition of degassed THF (17 mL, 0.10 M) and then cooled to 0 °C. (2-(Trimethylsilyl)ethyl)magnesium bromide (5 mL, 1.7 mmol ,0.34 M in Et_2O, 1.0 equiv.) was added dropwise and the reaction mixture was stirred for 5 minutes. *tert*-Butyl hypochlorite (203 µL, 1.79 mmol, 1.05 equiv.) was added and the solution was stirred for 15 minutes. Anhydrous triethylamine (237 µL, 1.7 mmol, 1.0 equiv.) and morpholine (176 µL, 2.04 mmol, 1.2 equiv.) were added and the solution was warmed to room temperature and stirred for 16 hours. Methanesulfonic acid (550 µL, 8.5 mmol, 5.0 equiv.) was added and the solution was stirred vigorously for 15 minutes at room temperature before dilution with CH_2Cl_2 (30 mL). The crude was quenched with $NaHCO_3$(aq) (30 mL), extracted with CH_2Cl_2 (3 × 20 mL), washed with brine (100 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 1:1 to 0:1) to afford the product **16** as a pale-yellow oil (127.7 mg, 30%).

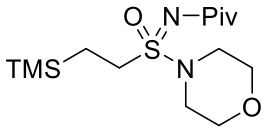
IR (thin film, ν_{max}/cm^{-1}) 3281, 2956, 1614, 1454, 1294, 1114, 938, 892, 739; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 3.74-3.72 (m, 4H, Alkyl-*H*), 3.35-3.28 (m, 4H, Alkyl-*H*), 2.96-2.85 (m, 2 H, Alkyl-*H*), 1.16-0.98 (m, 2H, Alkyl-*H*), 0.06 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 67.2, 47.1, 45.7, 10.4, -1.8; **HRMS** (ESI^+), *m/z* calculated for $[C_9H_{23}N_2O_2SSi]^+$ 251.1244 ($[M+H]^+$), found 251.1253.

5.3.3.4 *N*-functionalisation of sulfonimidamide 16

General procedure E

Sulfonimidamide **16** (1.0 equiv.) was added to an oven-dried round-bottom flask. The flask was evacuated and back-filled with nitrogen three times. The sulfonimidamide **16** was dissolved in CH_2Cl_2 (0.1 M), followed by the addition of Et_3N (1.5 equiv.), 4-dimethylaminopyridine (0.2 equiv.) and electrophile (1.5 equiv.). The solution was stirred at room temperature for 16 hours. The crude mixture was quenched with NH_4Cl (aq.), extracted with EtOAc, washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc) to afford the desired product.

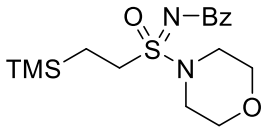
***N*-(Morpholino(oxo)(2-(trimethylsilyl)ethyl-λ6-sulfaneylidene)pivalamide (17a)**



Prepared according to **General procedure E**, using sulfonimidamide **16** (125 mg, 0.5 mmol, 1.0 equiv.), Et_3N (105 µL, 0.75 mmol, 1.5 equiv.), 4-dimethylaminopyridine (12.2 mg, 0.1 mmol, 0.2 equiv.) and pivaloyl chloride (91.8 µL, 0.75 mmol, 1.5 equiv.). Purification was carried out using flash chromatography (SiO_2, Petrol/EtOAc, 4:1 to 2:1), to afford sulfonimidamide **17a** as a white solid (83.6 mg, 50%).

m.p. 84-86 °C (EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 2957, 1639, 1547, 1297, 1193, 937, 845; δ_H (400 MHz, $CDCl_3$) 3.74-3.71 (m, 4H, Alkyl-*H*), 3.33-3.22 (m, 4H, Alkyl-*H*), 3.20-3.03 (m, 2H, Alkyl-*H*), 1.17 (s, 9H, Alkyl-*H*), 1.02-0.87 (m, 2H, Alkyl-*H*), 0.05 (s, 9H, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 187.4, 66.7, 48.4, 46.2, 41.6, 27.9, 9.4, -1.8; **HRMS** (ESI^+), *m/z* calculated for $[C_{14}H_{31}N_2O_3SSi]^+$ 335.1819 ($[M+H]^+$), found 335.1824.

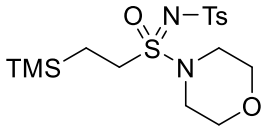
***N*-(Morpholino(oxo)(2-(trimethylsilyl)ethyl)-λ6-sulfaneylidene)benzamide (17b)**



Prepared according to **General procedure E**, using sulfonimidamide **16** (125 mg, 0.5 mmol, 1.0 equiv.), Et_3N (105 µL, 0.75 mmol, 1.5 equiv.), 4-dimethylaminopyridine (12.2 mg, 0.1 mmol, 0.2 equiv.) and benzoyl chloride (87 µL, 0.75 mmol, 1.5 equiv.). Purification was carried out using flash chromatography (SiO_2, Petrol/EtOAc, 7:1 to 5:1 to 3:1), to afford sulfonimidamide **17b** as a pale-yellow solid (151 mg, 85%).

m.p. 62-64 °C (EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 3089, 2956, 1633, 1451, 1314, 1289, 1259, 1116, 944, 840, 716, 654; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 8.13-8.11 (m, 2H, Ar-*H*), 7.52-7.48 (m, 1H, Ar-*H*), 7.42-7.38 (m, 2H, Ar-*H*), 3.83-3.74 (m, 4H, Alkyl-*H*), 3.45-3.34 (m, 5H, Alkyl-*H*), 3.26-3.18 (m, 1H, Alkyl-*H*), 1.15-0.98 (m, 2H, Alkyl-*H*), 0.10 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 173.1, 135.8, 132.2, 129.6, 128.2, 66.8, 48.8, 46.4, 9.5, -1.8; **HRMS** (ESI^+), *m/z* calculated for $[C_{16}H_{27}N_2O_3SSi]^+$ 355.1506 ($[M+H]^+$), found 355.1521.

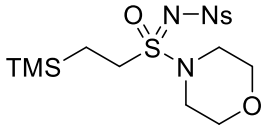
4-Methyl-*N*-(morpholino(oxo)(2-(trimethylsilyl)ethyl)-λ6-sulfaneylidene)benzenesulfonamide (17c)



Prepared according to **General procedure E**, using sulfonimidamide **16** (125 mg, 0.5 mmol, 1.0 equiv.), Et_3N (105 µL, 0.75 mmol, 1.5 equiv.), 4-dimethylaminopyridine (12.2 mg, 0.1 mmol, 0.2 equiv.) and *p*-toluenesulfonyl chloride (143.0 mg, 0.75 mmol, 1.5 equiv.). Purification was carried out using flash chromatography (SiO_2, Petrol/EtOAc, 4:1 to 2:1), to afford sulfonimidamide **17c** as a pale-yellow solid (119.4 mg, 59%).

m.p. 78-80 °C (EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 3031, 2974, 1600, 1454, 1318, 1249, 1156, 1090, 957, 863, 752, 673; δ_H (400 MHz, $CDCl_3$) 7.88-7.85 (m, 2H, Ar-*H*), 7.29-7.26 (m, 2H, Ar-*H*), 3.81-3.72 (m, 4H, Alkyl-*H*), 3.50-3.32 (m, 4H, Alkyl-*H*), 3.16-2.99 (m, 2H, Alkyl-*H*), 2.41 (s, 3H, Alkyl-*H*), 1.03-0.83 (m, 2H, Alkyl-*H*), 0.04 (s, 9H, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 143.0, 140.8, 129.4, 126.9, 66.5, 50.2, 46.6, 21.7, 9.2, -1.8; **HRMS** (ESI$^+$), *m/z* calculated for $[C_{16}H_{28}N_2O_4S_2SiNa]^+$ 427.1152 ([M+Na]$^+$), found 427.1152.

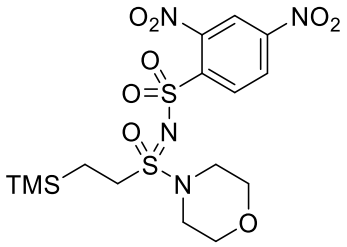
***N*-(Morpholino(oxo)(2-(trimethylsilyl)ethyl)-λ6-sulfaneylidene)-4-nitrobenzenesulfonamide (17d)**



Prepared according to **General procedure E**, using sulfonimidamide **16** (125 mg, 0.5 mmol, 1.0 equiv.), Et_3N (105 µL, 0.75 mmol, 1.5 equiv.), 4-dimethylaminopyridine (12.2 mg, 0.1 mmol, 0.2 equiv.) and 4-nitrobenzenesulfonyl chloride (166.2 mg, 0.75 mmol, 1.5 equiv.). Purification was carried out using flash chromatography (SiO_2, Petrol/EtOAc, 4:1 to 2:1), to afford sulfonimidamide **17d** as a pale-yellow solid (143.7 mg, 66%).

m.p. 108-110 °C (EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 3108, 2954, 1607, 1531, 1352, 1305, 1251, 1093, 949, 858, 747, 686; δ_H (400 MHz, $CDCl_3$) 8.35-8.32 (m, 2H, Ar-*H*), 8.17-8.14 (m, 2H, Ar-*H*), 3.87-3.77 (m, 4H, Alkyl-*H*), 3.53-3.35 (m, 4H, Alkyl-*H*), 3.19-3.03 (m, 2H, Alkyl-*H*), 0.97-0.86 (m, 2H, Alkyl-*H*), 0.06 (s, 9H, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 149.9, 149.1, 128.3, 124.1, 66.5, 50.6, 46.6, 9.2, -1.8; **HRMS** (ESI$^+$), *m/z* calculated for $[C_{15}H_{25}N_3O_6S_2SiNa]^+$ 458.0846 ([M+Na]$^+$), found 458.0840.

***N*-(Morpholino(oxo)(2-(trimethylsilyl)ethyl)-λ6-sulfaneylidene)-2,4-dinitrobenzenesulfonamide (17e)**

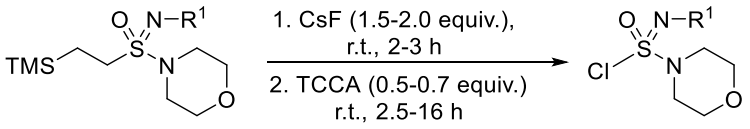


Prepared according to **General procedure E**, using sulfonimidamide **16** (55.1 mg, 0.22 mmol, 1.0 equiv.), Et_3N (46.0 µL, 0.33 mmol, 1.5 equiv.), 4-dimethylaminopyridine (5.4 mg, 0.044 mmol, 0.2 equiv.) and 4-2,4-dinitrobenzenesulfonyl chloride (88.0 mg, 0.33 mmol, 1.5 equiv.). Purification was carried out using flash chromatography (SiO_2, Petrol/EtOAc, 4:1 to 2:1), to afford sulfonimidamide **17e** as a pale-yellow solid (48.6 mg, 46%).

m.p. 136-138 °C (EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 3107, 2951, 1611, 1538, 1348, 1305, 1254, 1091, 950, 843, 755, 676; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 8.49-8.38 (m, 2H, Ar-*H*), 8.40-8.38 (m, 1H, Ar-*H*), 3.85-3.76 (m, 4H, Alkyl-*H*), 3.52-3.34 (m, 4H, Alkyl-*H*), 3.25-3.09 (m, 2H, Alkyl-*H*), 1.06-0.87 (m, 2H, Alkyl-*H*), 0.08 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 149.5, 148.1, 141.4, 131.8, 126.1, 119.4, 66.3, 50.6, 46.4, 9.0, -2.0; **HRMS** (ESI^+), *m/z* calculated for $[C_{15}H_{24}N_4O_8S_2SiK]^+$ 519.0437 ($[M+K]^+$), found 519.0427.

5.3.4 Desilylation-chlorination of Sulfonimidamide 17

General procedure F

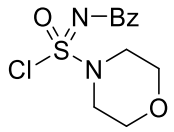


Sulfonimidamide **17** (0.1 mmol, 1.0 equiv.) and anhydrous CsF (0.15-0.2 mmol, 1.5-2.0 equiv.) was added to an oven-dried reaction tube. The reaction tube was evacuated and back-filled with nitrogen three times. Anhydrous DMF (1.0 mL, 0.1 M) was added, and the solution was stirred for 2-3 hours at room temperature

before a solution of trichloroisocyanuric acid (0.05-0.07 mmol, 0.5-0.7 equiv.) in anhydrous DMF (0.1 mL) was added dropwise. The reaction mixture was stirred at room temperature for 2.5-16 hours. The crude mixture was evaporated to dryness under a gentle stream of nitrogen and purified using flash column chromatography (SiO_2, Petrol/EtOAc) to afford the desired product.

Note: CsF was dried before the reaction by heating at 100 °C for 2 h *in vacuo*.

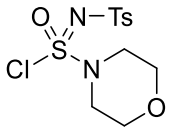
***N*-Benzoylmorpholine-4-sulfonimidoyl chloride (18b)**



Prepared according to **General procedure F**, using sulfonimidamide **17b** (35.5 mg, 0.1 mmol, 1.0 equiv.), CsF (30.4 mg, 0.2 mmol, 2.0 equiv.) and trichloroisocyanuric acid (11.6 mg, 0.05 mmol, 0.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 7:1 to 5:1 to 3:1), to afford sulfuramidimidoyl chloride **18b** as a colourless oil (14.4 mg, 50%).

IR (thin film, ν_{max}/cm^{-1}) 3061, 2916, 1661, 1451, 1270, 1109, 978, 802, 708; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 8.11-8.08 (m, 2H, Ar-*H*), 7.58-7.54 (m, 1H, Ar-*H*), 7.45-7.41 (m, 2H, Ar-*H*), 3.86-3.84 (m, 4H, Alkyl-*H*), 3.67-3.58 (m, 4H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 170.1, 134.1, 133.3, 130.0, 128.5, 65.8, 47.0; **HRMS** (ESI^+), *m/z* calculated for $[C_{11}H_{14}N_2O_3SCl]^+$ 289.0408 ($[M+H]^+$), found 289.0410.

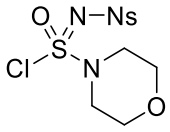
***N*-Tosylmorpholine-4-sulfonimidoyl chloride (18c)**



Prepared according to **General procedure F**, using sulfonimidamide **17c** (40.4 mg, 0.1 mmol, 1.0 equiv.), CsF (30.4 mg, 0.2 mmol, 2.0 equiv.) and trichloroisocyanuric acid (16.3 mg, 0.07 mmol, 0.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 5:1 to 3:1 to 2:1), to afford sulfuramidimidoyl chloride **18c** as a colourless oil (16.7 mg, 49%).

IR (thin film, ν_{max}/cm^{-1}) 3061, 2916, 1661, 1451, 1270, 1109, 978, 802, 708; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.90-7.87 (m, 2H, Ar-*H*), 7.35-7.32 (m, 2H, Ar-*H*), 3.88-3.78 (m, 4H, Alkyl-*H*), 3.42-3.26 (m, 4H, Alkyl-*H*), 2.44 (s, 4H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 144.5, 138.5, 129.8, 127.4, 65.2, 47.4, 21.8; **HRMS** (ESI^+), *m/z* calculated for $[C_{11}H_{16}N_2O_4S_2Cl]^+$ 339.0235 ($[M+H]^+$), found 339.0235.

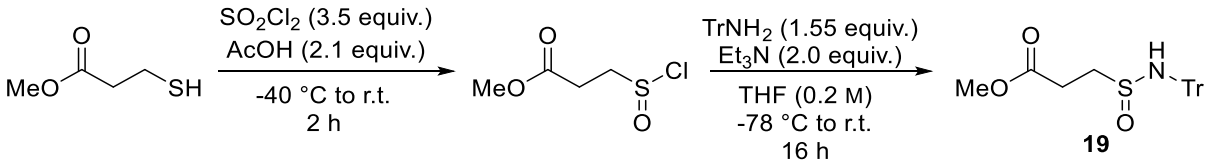
***N*-((4-Nitrophenyl)sulfonyl)morpholine-4-sulfonimidoyl chloride (18d)**



Prepared according to **General procedure F**, using sulfonimidamide **17d** (43.6 mg, 0.1 mmol, 1.0 equiv.), CsF (22.8 mg, 0.15 mmol, 1.5 equiv.) and trichloroisocyanuric acid (16.3 mg, 0.07 mmol, 0.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc, 5:1 to 1:1 to 2:1), to afford sulfuramidimidoyl chloride 1**8d** as a white solid (16.7 mg, 49%).

m.p. 132-134 °C (decompose) ($CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3112, 2954, 1534, 1456, 1353, 1314, 1174, 1108, 953, 767, 609; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 8.40-8.36 (m, 2H, Ar-*H*), 8.21-8.17 (m, 2H, Ar-*H*), 3.92-3.82 (m, 4H, Alkyl-*H*), 3.46-3.29 (m, 4H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 150.4, 146.7, 128.7, 124.3, 65.0, 47.3; **HRMS** (ESI^+), *m/z* calculated for $[C_{10}H_{12}N_3O_6S_2Na]^+$ 391.9748 ($[M+Na]^+$), found 391.9741.

5.3.5 Synthesis of Sulfinamide Precursor 19



Procedure adapted from M. Jabczun, V. Nosek, J. Míšek, *Org. Biomol. Chem*., 2023, **21**, 2950-2954.[180]

Methyl 3-mercaptopropionate (2.77 mL, 25 mmol, 1.0 equiv.) and acetic acid (3.00 mL, 52.5 mmol, 2.1 equiv.) were added in an oven-dried round-bottom flask purged with nitrogen. The reaction mixture was cooled to -40 °C and sulfuryl chloride (7.07 mL, 35 mmol, 3.5 equiv.) was added dropwise. The reaction mixture was warmed to room temperature and stir for two hours. The volatiles were evaporated *in vacuo* and the crude residue was dissolved in anhydrous, degassed THF (40 mL). The resulting solution was added dropwise to a solution of triphenylmethylamine (10.0 g, 38.75 mmol, 1.55 equiv.) and Et_3N (6.97 mL, 50 mmol, 2 equiv.) in anhydrous, degassed THF (85 mL, 0.2 M) at -78 °C. The reaction mixture was warmed to room temperature and stirred for 16 hours. The crude mixture was diluted with CH_2Cl_2 (200 mL) and washed with saturated $NaHCO_3$(aq.) (200 mL). The aqueous phase was extracted with CH_2Cl_2 (150 mL × 2), and the combined organic layer was washed with brine (400 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 3:1 to 2:1 to 1:1), to afford the product **19** as a white solid (8.07 g, 82%).

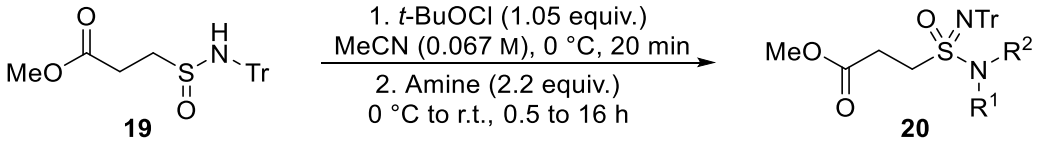
Note: The sulfinamide **19** has poor solubility and might crystallised in the column under low solvent polarity. Alternatively, the crude mixture can be purified by washing with Et_2O or Petrol/EtOAc 10:1 to remove most of the impurity.

m.p. 132-134 °C (EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 3246, 3058, 2953, 1738, 1492, 1362, 1259, 1112, 1066, 953, 736, 701, 634; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.34-7.26 (m, 15H, Ar-*H*), 5.60 (br.s, 1H, N-*H*), 3.64 (s, 3H, Alkyl-*H*), 3.16-3.09 (m, 1H, Alkyl-*H*), 3.01-2.96 (m, 1H, Alkyl-*H*), 2.89-2.83 (m, 1H, Alkyl-*H*), 2.66-2.58

(m, 1H, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 172.8, 144.9, 129.4, 128.2, 127.5, 73.2, 52.3, 50.8, 27.2; **HRMS** (ESI^+), *m/z* calculated for $[C_{23}H_{23}NO_3SNa]^+$ 416.1291 ($[M+Na]^+$), found 416.1291.

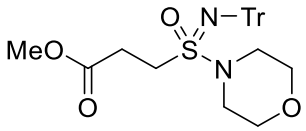
5.3.6 Synthesis of *β*-ester Sulfonimidamide 20

General procedure G



Sulfinamide **19** (1.0 equiv.) was added to an oven-dried round-bottom flask and the reaction flask was evacuated and back-filled with nitrogen three times. The sulfinamide **19** was dissolved in anhydrous MeCN (0.067 M) and cooled to 0 °C. *tert*-Butyl hypochlorite (1.05 equiv.) was added and the solution was stirred for 20 min, followed by the addition of amine (2.2 equiv.) and the solution was warmed to room temperature and stirred for 0.5 to 16 hours. The crude mixture was diluted with EtOAc, quenched with saturated NH_4Cl(aq.), and the aqueous layer was extracted with EtOAc two times. The combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc) to afford the desired product.

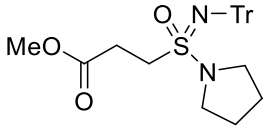
Methyl 3-(*N*-tritylmorpholine-4-sulfonimidoyl)propanoate (20a)



Prepared according to **General procedure G**, using sulfinamide **19** (1.97g, 5.0 mmol, 1.0 equiv.), *tert*-butyl hypochlorite (595 µL, 5.25 mmol, 1.05 equiv.) and morpholine (962 µL, 11 mmol, 2.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 4:1 to 2:1 to 1:1) to afford the desired product **20a** as a colourless oil (2.18 g, 91%).

m.p. 128-130 °C (EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 3057, 2957, 1739, 1595, 1447, 1295, 1067, 931, 703, 642; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.53-7.51 (m, 6H, Ar-*H*), 7.36-7.28 (m, 9H, Ar-*H*), 3.80 (s, 3H, Alkyl-*H*), 3.65-3.59 (m, 1H, Alkyl-*H*), 3.32-3.26 (m, 2H, Alkyl-*H*), 3.25-3.04 (m, 5H, Alkyl-*H*), 3.04-2.89 (m, 4H, Alkyl-*H*) ; $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 171.6, 147.7, 129.1, 127.3, 126.4, 71.5, 66.0, 52.2, 46.9, 46.0, 28.6; **HRMS** (ESI^+), *m/z* calculated for $[C_{27}H_{31}N_2O_4S]^+$ 479.1999 ($[M+H]^+$), found 479.1988.

Methyl 3-(*N*-tritylpyrrolidine-1-sulfonimidoyl)propanoate (20b)

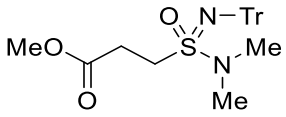


Prepared according to **General procedure G**, using sulfinamide **19** (1.97g, 3.0 mmol, 1.0 equiv.), *tert*-butyl hypochlorite (357 µL, 3.15 mmol, 1.05 equiv.) and pyrrolidine (469 µL, 6.6 mmol, 2.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 3:1 to 1:1) to afford the desired product **20b** as a white solid (1.11 g, 81%).

m.p. 64-66 °C (EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 3057, 2951, 1739, 1490, 1275, 1165, 1008, 755, 702, 634; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.49-7.45 (m, 6H, Ar-*H*), 7.26-7.22 (m, 6H, Ar-*H*), 7.19-7.15 (m, 3H, Ar-*H*), 3.70 (s, 3H, Alkyl-*H*), 3.64-3.57 (m, 1H, Alkyl-*H*), 3.27-3.20 (m, 1H, Alkyl-*H*), 3.07-2.99 (m, 1H, Alkyl-*H*),

2.93-2.72 (m, 5H, Alkyl-*H*), 1.48-1.41 (m, 4H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 172.0, 148.1, 129.3, 127.3, 126.3, 71.5, 52.2, 48.5, 47.5, 28.9, 25.6; **HRMS** (ESI^+), *m/z* calculated for $[C_{27}H_{30}N_2O_3SNa]^+$ 485.1869 ($[M+Na]^+$), found 485.1877.

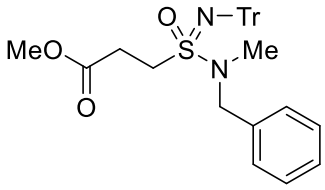
Methyl 3-(*N*,*N*-dimethyl-*N*'-tritylsulfamidimidoyl)propanoate (20c)



Prepared according to **General procedure G**, using sulfinamide **19** (787 mg, 2.0 mmol, 1.0 equiv.), *tert*-butyl hypochlorite (238 µL, 2.1 mmol, 1.05 equiv.) and dimethylamine (2.2 mL, 4.4 mmol, 2.0 M in THF, 2.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 7:1 to 4:1) to afford the desired product **20c** as a colourless oil (768.4 mg, 88%).

m.p. 106-108 °C (EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 3055, 2942, 1738, 1596, 1490, 1276, 1164, 958, 756, 702, 671, 633; **δ_H** (400 MHz, $CDCl_3$) 7.48-7.45 (m, 6H, Ar-*H*), 7.26-7.22 (m, 6H, Ar-*H*), 7.19-7.15 (m, 3H, Ar-*H*), 3.70 (s, 3H, Alkyl-*H*), 3.57-3.51 (m, 1H, Alkyl-*H*), 3.24-3.18 (m, 1H, Alkyl-*H*), 3.07-2.98 (m, 1H, Alkyl-*H*), 2.91-2.84 (m, 1H, Alkyl-*H*), 2.31 (s, 6H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 171.9, 147.9, 129.2, 127.3, 126.3, 71.5, 52.3, 48.8, 37.2, 28.8; **HRMS** (ESI^+), *m/z* calculated for $[C_{25}H_{28}N_2O_3SNa]^+$ 459.1713 ($[M+Na]^+$), found 459.1712.

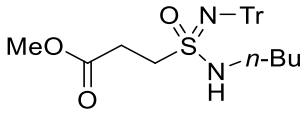
Methyl 3-(*N*-benzyl-*N*-methyl-*N*'-tritylsulfamidimidoyl)propanoate (20d)



Prepared according to **General procedure G**, using sulfinamide **19** (787 mg, 2.0 mmol, 1.0 equiv.), *tert*-butyl hypochlorite (238 µL, 2.1 mmol, 1.05 equiv.) and *N*-benzylmethylamine (568 µL, 4.4 mmol, 2.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 8:1 to 5:1) to afford the desired product **20d** as a colourless oil (769.0 mg, 75%).

IR (thin film, ν_{max}/cm^{-1}) 3085, 2951, 1739, 1596, 1491, 1276, 1167, 909, 701, 634; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 7.49-7.46 (m, 6H, Ar-*H*), 7.27-7.24 (m, 9H, Ar-*H*), 7.21-7.17 (m, 3H, Ar-*H*), 7.04-7.02 (m, 2H, Ar-*H*), 3.85-3.71 (m, 2H, Alkyl-*H*), 3.68 (s, 3H, Alkyl-*H*), 3.63-3.54 (m, 1H, Alkyl-*H*), 3.10-3.04 (m, 2H, Alkyl-*H*), 2.96-2.87 (m, 1H, Alkyl-*H*), 2.29 (s, 3H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 171.8, 147.9, 136.9, 129.3, 128.8, 128.6, 127.6, 127.4, 126.4, 71.7, 53.9, 52.2, 50.5, 34.6, 29.1; **HRMS** (ESI^+), *m/z* calculated for $[C_{31}H_{32}N_2O_3SNa]^+$ 535.2026 ($[M+Na]^+$), found 535.2028.

Methyl 3-(*N*-butyl-*N*'-tritylsulfamidimidoyl)propanoate (20e)

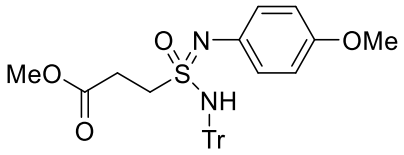


Prepared according to **General procedure G**, using sulfinamide **19** (197 mg, 0.5 mmol, 1.0 equiv.), *tert*-butyl hypochlorite (59 µL, 0.525 mmol, 1.05 equiv.) and *n*-butylamine (109 µL, 1.1 mmol, 2.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 8:1 to 5:1) to afford the desired product **20e** as a white solid (162.6 mg, 70%).

m.p. 88-90 °C (EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 3033, 2953, 1738, 1490, 1275, 1164, 913, 771, 702, 672; **δ_H** (500 MHz, $CDCl_3$) 7.51-7.49 (m, 6H, Ar-*H*), 7.28-7.24 (m, 6H, Ar-*H*), 7.21-7.17 (m, 3H, Ar-*H*), 3.71 (s, 3H, Alkyl-*H*), 3.47-3.35 (m, 2H, Alkyl-*H*), 3.00-2.93 (m, 3H, Alkyl-*H*), 2.54-2.47(m, 2H, N-*H*, Alkyl-*H*), 1.11-0.99 (m, 4H, Alkyl-*H*), 0.78 (t, 3H, *J* = 7.0 Hz, Alkyl-*H*); **δ_C** (126 MHz, $CDCl_3$) 171.7, 147.9, 128.9, 127.5, 126.4, 71.5, 52.4, 52.1, 43.6, 31.7, 29.6, 19.8, 13.7; **HRMS** (ESI^+), *m/z* calculated for $[C_{27}H_{33}N_2O_3S]^+$ 465.2206 ($[M+H]^+$), found 465.2198.

Note: Trace inseparable impurities containing trityl group is observed in ^{13}C NMR spectrum.

Methyl 3-(*N*-(4-methoxyphenyl)-*N*'-tritylsulfamidimidoyl)propanoate (20f)



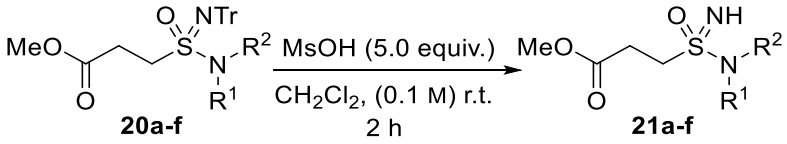
Prepared according to **General procedure G**, using sulfinamide **19** (197 mg, 0.5 mmol, 1.0 equiv.), *tert*-butyl hypochlorite (59 µL, 0.525 mmol, 1.05 equiv.) and *p*-anisidine (135 mg, 1.1 mmol, 2.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 3:1) to afford the desired product **20f** as a brown solid (175.0 mg, 68%).

m.p. 130-132 °C (Decompose) (EtOAc); **IR** (thin film, ν_{max}/cm^{-1}) 3287, 3055, 2949, 1738, 1508, 1446, 1262, 1141, 1033, 705, 631; **δ_H** (400 MHz, $CDCl_3$) 7.51-7.48 (m, 6H, Ar-*H*), 7.29-7.24 (m, 6H, Ar-*H*), 7.22-7.18 (m, 3H, Ar-*H*), 6.80-6.72 (m, 4H, Ar-*H*), 5.29 (br. s, 1H, N-*H*), 3.75 (s, 3H, Alkyl-*H*), 3.68 (s, 3H, Alkyl-*H*), 3.39-3.20 (m, 2H, Alkyl-*H*), 3.05-2.90 (m, 2H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 171.4, 156.4, 146.9, 132.2, 129.0, 127.7, 126.7, 123.3, 114.3, 72.0, 55.5, 52.2, 51.3, 29.8; **HRMS** (ESI^+), *m/z* calculated for $[C_{30}H_{30}N_2O_4SNa]^+$ 537.1819 ($[M+Na]^+$), found 537.1815.

Note: Trace inseparable impurities is observed in the NMR spectrum.

5.3.7 Trityl deprotection of Sulfonimidamide 20

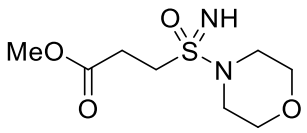
General procedure H



The method was adapted from T. Q. Davies, A. Hall, M. C. Willis, *Angew. Chem. Int. Ed.* 2017, **56**, 14937.[79]

Sulfonimidamide **20a-f** was added to an oven-dried round-bottom flask. The reaction flask was evacuated and back-filled with nitrogen three times. CH_2Cl_2 (0.1 M) was added, followed by the addition of methanesulfonic acid (5.0 equiv.). The reaction mixture was stirred for 2 hours at room temperature before diluted with CH_2Cl_2. The solution was washed with saturated $NaHCO_3$ (aq.), extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (SiO_2, Petrol/EtOAc) to afford the desired *N*-H sulfonimidamide **21a-f**.

Methyl 3-(morpholine-4-sulfonimidoyl)propanoate (21a)

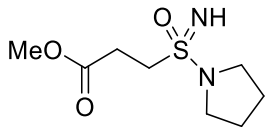


Prepared according to **General procedure H**, using sulfonimidamide **20a** (1.43 g, 3 mmol, 1.0 equiv.) and methanesulfonic acid (974 µL, 15 mmol, 5.0 equiv.). Purification was carried out using flash column

chromatography (SiO_2, Petrol/EtOAc 1:3 to 0:1) to afford the desired product **21a** as a colourless oil (638.0 mg, 90%).

IR (thin film, ν_{max}/cm^{-1}) 3284, 2981, 1736, 1456, 1381, 1257, 1111, 937, 733, 678, 636; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 3.75-3.72 (m, 7H, Alkyl-*H*), 3.33-3.23 (m, 5H, Alkyl-*H*), 3.20-3.13 (m, 1H, Alkyl-*H*), 2.92-2.88 (m, 2H, Alkyl-*H*), 2.15 (br. s, 1H, N-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 171.5, 67.0, 52.4, 46.8, 44.2, 28.5; **HRMS** (ESI^+), *m/z* calculated for $[C_8H_{16}N_2O_4SK]^+$ 275.0462 ($[M+K]^+$), found 275.0466.

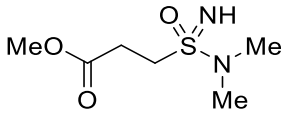
Methyl 3-(pyrrolidine-1-sulfonimidoyl)propanoate (21b)



Prepared according to **General procedure H**, using sulfonimidamide **20b** (925.2 mg, 2.0 mmol, 1.0 equiv.) and methanesulfonic acid (649 µL, 10 mmol, 5.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 1:3 to 0:1) to afford the desired product **21b** as a colourless oil (308 mg, 70%).

IR (thin film, ν_{max}/cm^{-1}) 3291, 2955, 1736, 1438, 1363, 1242, 1107, 1058, 1006, 757, 637; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 3.71 (s, 3H, Alkyl-*H*), 3.38-3.28 (m, 5H, Alkyl-*H*), 3.28-3.20 (m, 1H, Alkyl-*H*), 2.94-2.83 (m, 2H, Alkyl-*H*), 2.43 (br.s, 1H, N-*H*), 1.92-1.90 (m, 4H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 171.7, 52.3, 48.5, 44.8, 28.8, 26.0; **HRMS** (ESI^+), *m/z* calculated for $[C_8H_{17}N_2O_3S]^+$ 221.0954 ($[M+H]^+$), found 221.0948.

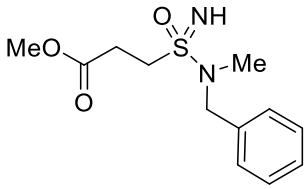
Methyl 3-(*N*,*N*-dimethylsulfamidimidoyl)propanoate (21c)



Prepared according to **General procedure H**, using sulfonimidamide **20c** (655 mg, 1.5 mmol, 1.0 equiv.) and methanesulfonic acid (649 µL, 10 mmol, 5.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 1:3 to 0:1) to afford the desired product **21c** as a colourless oil (198.1 mg, 68%).

IR (thin film, ν_{max}/cm^{-1}) 3289, 2954, 1736, 1439, 1364, 1246, 1109, 1017, 943, 712, 660; δ_H (400 MHz, $CDCl_3$) 3.72 (s, 3H, Alkyl-*H*), 3.33-3.15 (m, 2H, Alkyl-*H*), 2.92-2.86 (m, 8H, Alkyl-*H*), 2.13 (br. s, 1H, N-*H*); δ_C (101 MHz, $CDCl_3$) 171.6, 52.4, 43.6, 38.5, 28.6; **HRMS** (ESI^+), *m/z* calculated for $[C_6H_{15}N_2O_3S]^+$ 195.0798 ($[M+H]^+$), found 195.0793.

Methyl 3-(*N*-benzyl-*N*-methylsulfamidimidoyl)propanoate (21d)

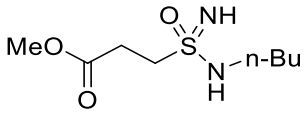


Prepared according to **General procedure H**, using sulfonimidamide **20d** (769 mg, 1.5 mmol, 1.0 equiv.) and methanesulfonic acid (487 µL, 7.5 mmol, 5.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 2:1 to 1:2) to afford the desired product **21d** as a colourless oil (292.0 mg, 72%).

IR (thin film, ν_{max}/cm^{-1}) 3302, 2961, 1738, 1445, 1382, 1259, 1102, 1031, 933, 759, 699, 638; δ_H (400 MHz, $CDCl_3$) 7.38-7.28 (m, 5H, Ar-*H*), 4.42-4.33 (m, 2H, Alkyl-*H*), 3.73(s, 3H, Alkyl-*H*), 3.43-3.22 (m, 2H, Alkyl-*H*), 2.95-2.91 (m, 2H, Alkyl-*H*), 2.80 (s, 3H, Alkyl-*H*), 2.15 (br. s, 1H, N-*H*); δ_C (101 MHz, $CDCl_3$)

171.5, 136.6, 128.9, 128.2, 128.0, 54.7, 52.4, 45.6, 35.3, 28.8; **HRMS** (ESI^+), *m/z* calculated for $[C_8H_{16}N_2O_4SK]^+$ 275.0462 ($[M+K]^+$), found 275.0466.

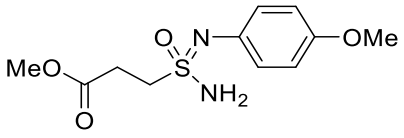
Methyl 3-(*N*-butylsulfamidimidoyl)propanoate (21e)



Prepared according to **General procedure H**, using sulfonimidamide **20e** (139.4 mg, 0.3 mmol, 1.0 equiv.) and methanesulfonic acid (97 µL, 1.5 mmol, 5.0 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 1:1 to 1:3 to 0:1) to afford the desired product **21e** as a colourless oil (46.7 mg, 70%).

IR (thin film, ν_{max}/cm^{-1}) 3280, 2958, 1736, 1438, 1364, 1238, 1107, 1024, 900, 734, 634; $\boldsymbol{\delta_H}$ (400 MHz, CD_3CN) 3.65 (s, 3H, Alkyl-*H*), 3.29-3.17 (m, 2H, Alkyl-*H*), 2.99-2.95 (m, 2H, Alkyl-*H*), 2.74-2.71 (m, 2H, Alkyl-*H*), 1.50-1.30 (m, 4H, Alkyl-*H*), 0.91 (t, 3H, *J* = 7.5 Hz, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 172.4, 52.5, 48.7, 44.1, 33.1, 30.0, 20.5, 13.9; **HRMS** (ESI^+), *m/z* calculated for $[C_8H_{18}N_2O_3SNa]^+$ 245.0930 ($[M+Na]^+$), found 245.0926.

Methyl 3-(*N*-(4-methoxyphenyl)sulfamidimidoyl)propanoate (21f)



Prepared according to **General procedure H**, using sulfonimidamide **20f** (154.4 mg, 0.3 mmol, 1.0 equiv.) and methanesulfonic acid (97 µL, 1.5 mmol, 5.0 equiv.). Purification was carried out using flash column

chromatography (SiO_2, Petrol/EtOAc 3:1 to 1:1 to 1:3) to afford the desired product **21f** as a brown solid (46.7 mg, 85%).

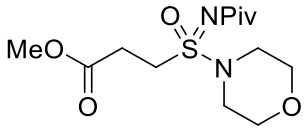
m.p. 100-102 °C ($CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3260, 3002, 2953, 1735, 1504, 1440, 1366, 1235, 1106, 1053, 835, 706; δ_H (400 MHz, $CDCl_3$) 7.08 (d, 2H, *J* = 9.0 Hz, Ar-*H*), 6.81 (d, 2H, *J* = 9.0 Hz, Ar-*H*), 4.76 (br. s, 2H, N*H*$_2$), 3.77 (s, 3H, Alkyl-*H*), 3.71 (s, 3H, Alkyl-*H*), 3.53-3.48 (m, 2H, Alkyl-*H*), 2.92 (t, 2H, *J* = 7.0 Hz, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 171.5, 156.4, 133.9, 124.7, 114.7, 55.6, 52.4, 50.4, 29.5; **HRMS** (ESI^+), *m/z* calculated for $[C_{11}H_{17}N_2O_4S]^+$ 273.0904 ($[M+H]^+$), found 273.0901.

5.3.8 Pivaloyl Protection of Sulfonimidamide 21

General procedure I

Sulfonimidamide **21a-f** was added to an oven-dried round-bottom flask. The reaction flask was evacuated and back-filled with nitrogen three times. DCM (0.1 M) was added, followed by the addition of Et_3N (1.2 equiv.), 4-Dimethylaminopyridine (0.2 equiv.) and trimethylacetyl chloride (1.2 equiv.). The reaction mixture was stirred for 16 hours at room temperature before diluted with CH_2Cl_2. The solution was washed with saturated NH_4Cl (aq.), extracted with EtOAc, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (SiO_2, Petrol/EtOAc) to afford the desired *N*-Piv sulfonimidamide **22a-f**.

Methyl 3-(*N*-pivaloylmorpholine-4-sulfonimidoyl)propanoate (22a)

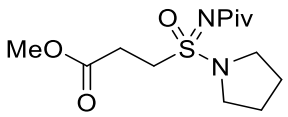


Prepared according to **General procedure I**, using sulfonimidamide **21a** (708.9 mg, 3 mmol, 1.0 equiv.) Et_3N (502 µL, 3.6 mmol, 1.2 equiv.), 4-Dimethylaminopyridine (73.3mg ,0.6 mmol, 0.2 equiv.) and

trimethylacetyl chloride (441 µL, 3.6 mmol, 1.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 3:1 to 1:1) to afford the desired product **22a** as a colourless oil (913.2 mg, 95%).

IR (thin film, ν_{max}/cm^{-1}) 2969, 1743, 1638, 1480, 1365, 1240, 1114, 1070, 938, 852, 736, 647; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 3.74-3.66 (m, 7H, Alkyl-*H*), 3.59-3.43 (m, 2H, Alkyl-*H*), 3.27-3.25 (m, 4H, Alkyl-*H*), 2.82-2.78 (m, 2H, Alkyl-*H*), 1.15 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 187.3, 171.0, 66.5, 52.5, 47.0, 46.1, 41.7, 27.8, 27.7; **HRMS** (ESI^+), *m/z* calculated for $[C_{13}H_{24}N_2O_5SK]^+$ 359.1038 ($[M+K]^+$), found 359.1021.

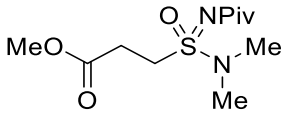
Methyl 3-(*N*-pivaloylpyrrolidine-1-sulfonimidoyl)propanoate (22b)



Prepared according to **General procedure I**, using sulfonimidamide **21b** (220.3 mg, 1 mmol, 1.0 equiv.) Et_3N (167 µL, 1.2 mmol, 1.2 equiv.), 4-Dimethylaminopyridine (24.4 mg ,0.2 mmol, 0.2 equiv.) and trimethylacetyl chloride (147 µL, 1.2 mmol, 1.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 2:1) to afford the desired product **22b** as a colourless oil (298.3 mg, 98%).

IR (thin film, ν_{max}/cm^{-1}) 2954, 1741, 1634, 1438, 1363, 1233, 1185, 1060, 846, 743; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 3.72 (s, 3H, Alkyl-*H*), 3.63-3.52 (m, 2H, Alkyl-*H*), 3.47-3.42 (m, 2H, Alkyl-*H*), 3.30-3.26 (m, 2H, Alkyl-*H*), 2.85-2.76 (m, 2H, Alkyl-*H*), 1.96-1.91 (m, 4H, Alkyl-*H*), 1.18 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 187.2, 171.0, 52.3, 48.0, 47.8, 41.5, 27.9, 27.7, 25.8; **HRMS** (ESI^+), *m/z* calculated for $[C_{13}H_{25}N_2O_4S]^+$ 305.1530 ($[M+H]^+$), found 305.1517.

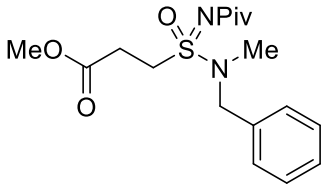
Methyl 3-(*N*,*N*-dimethyl-*N*'-pivaloylsulfamidimidoyl)propanoate (22c)



Prepared according to **General procedure I**, using sulfonimidamide **21c** (194.2 mg, 1 mmol, 1.0 equiv.), Et_3N (167 µL, 1.2 mmol, 1.2 equiv.), 4-Dimethylaminopyridine (24.4 mg ,0.2 mmol, 0.2 equiv.) and trimethylacetyl chloride (147 µL, 1.2 mmol, 1.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 4:1 to 2:1) to afford the desired product **22c** as a colourless oil (261.7 mg, 94%).

IR (thin film, ν_{max}/cm^{-1}) 2952, 1742, 1647, 1478, 1364, 1228, 1174, 1036, 946, 852, 771, 642; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 3.73 (s, 3H, Alkyl-*H*), 3.59-3.40 (m, 2H, Alkyl-*H*), 2.87 (s, 6H, Alkyl-*H*), 2.83-2.80 (m, 2H, Alkyl-*H*), 1.18 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 187.4, 170.1, 52.3, 46.8, 41.5, 37.5, 27.8, 27.6; **HRMS** (ESI^+), *m/z* calculated for $[C_{11}H_{22}N_2O_4SNa]^+$ 301.1193 ($[M+Na]^+$), found 301.1179.

Methyl 3-(*N*-benzyl-*N*-methyl-*N*'-pivaloylsulfamidimidoyl)propanoate (22d)

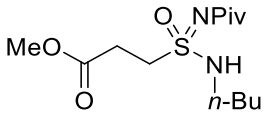


Prepared according to **General procedure I**, using sulfonimidamide **21d** (270.3 mg, 1 mmol, 1.0 equiv.), Et_3N (167 µL, 1.2 mmol, 1.2 equiv.), 4-Dimethylaminopyridine (24.4 mg ,0.2 mmol, 0.2 equiv.) and trimethylacetyl chloride (147 µL, 1.2 mmol, 1.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 7:1 to 5:1) to afford the desired product **22c** as a colourless oil (326.1 mg, 92%).

IR (thin film, ν_{max}/cm^{-1}) 3030, 2953, 1742, 1637, 1479, 1364, 1290, 1238, 1176, 1032, 936, 852, 771; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.38-7.31 (m, 5H, Ar-*H*), 4.59 (d, 1H, *J* = 14.5 Hz, Alkyl-*H*), 4.21 (d, 1H, *J* = 14.5 Hz,

Alkyl-*H*), 3.72 (s, 3H, Alkyl-*H*), 3.68-3.44 (m, 2H, Alkyl-*H*), 2.89-2.85 (m, 2H, Alkyl-*H*), 2.73(s, 3H, Alkyl-*H*), 1.19 (s, 9H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 187.4, 171.0, 136.0, 128.9, 128.6, 128.1, 53.9, 52.5, 47.7, 41.7, 34.4, 28.0, 27.8; **HRMS** (ESI^+), *m/z* calculated for $[C_{17}H_{26}N_2O_4SNa]^+$ 377.1506 ($[M+Na]^+$), found 377.1508.

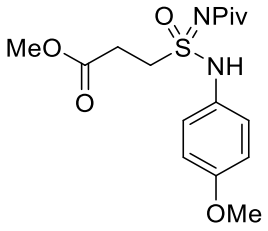
Methyl 3-(*N*-butyl-*N*'-pivaloylsulfamidimidoyl)propanoate (22e)



Prepared according to **General procedure I**, using sulfonimidamide **21e** (44.5 mg, 0.2 mmol, 1.0 equiv.), Et_3N (33 µL, 0.24 mmol, 1.2 equiv.), 4-Dimethylaminopyridine (4.9 mg, 0.04 mmol, 0.2 equiv.) and trimethylacetyl chloride (29 µL, 0.24 mmol, 1.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 3:1) to afford the desired product **22e** as a colourless oil (49.6 mg, 81%).

IR (thin film, ν_{max}/cm^{-1}) 3236, 2958, 1742, 1614, 1479, 1363, 1299, 1194, 1032, 937, 853, 773, 638; **δ_H** (400 MHz, CD_3CN) 5.95 (br. s, 1H, N-*H*), 3.69(s, 3H, Alkyl-*H*), 3.62-3.58 (m, 2H, Alkyl-*H*), 3.13-3.04 (m, 2H, Alkyl-*H*), 2.75-2.72 (m, 2H, Alkyl-*H*), 1.58-1.51 (m, 2H, Alkyl-*H*), 1.43-1.33 (m, 2H, Alkyl-*H*), 1.15 (s, 9H, Alkyl-*H*), 0.94 (t, 3H, *J* = 7.3 Hz, Alkyl-*H*); **δ_C** (101 MHz, CD_3CN) 187.2, 171.3, 52.3, 47.9, 42.0, 41.5, 32.3, 28.7, 27.6, 20.1, 13.5; **HRMS** (ESI^+), *m/z* calculated for $[C_{13}H_{26}N_2O_4SNa]^+$ 329.1506 ($[M+Na]^+$), found 329.1506.

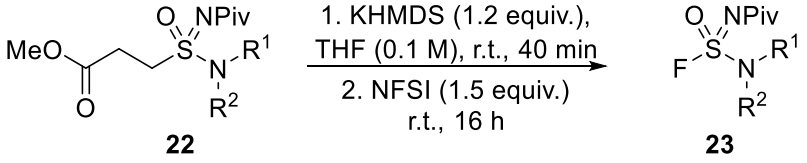
Methyl 3-(*N*-(4-methoxyphenyl)-*N*'-pivaloylsulfamidimidoyl)propanoate (22f)



Prepared according to **General procedure I**, using sulfonimidamide **21f** (54.5 mg, 0.2 mmol, 1.0 equiv.), Et_3N (33 µL, 0.24 mmol, 1.2 equiv.), 4-Dimethylaminopyridine (4.9 mg, 0.04 mmol, 0.2 equiv.) and trimethylacetyl chloride (29 µL, 0.24 mmol, 1.2 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 2:1) to afford the desired product **22f** as a brown oil (64.2 mg, 90%).

IR (thin film, ν_{max}/cm^{-1}) 3221, 3039, 2956, 1742, 1610, 1509, 1479, 1364, 1290, 1250, 1181, 1033, 847, 770; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.22-7.20 (m, 2H, Ar-*H*), 6.91-6.88 (m, 2H, Ar-*H*), 3.80 (s, 3H, Alkyl-*H*), 3.70 (s, 3H, Alkyl-*H*), 3.57-3.47 (m, 2H, Alkyl-*H*), 2.81-2.78 (m, 2H, Alkyl-*H*), 1.22 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 188.4, 170.5, 158.7, 127.5, 126.2, 115.1, 55.7, 52.5, 47.0, 41.9, 28.1, 27.7; **HRMS** (ESI^+), *m/z* calculated for $[C_{16}H_{25}N_2O_5S]^+$ 357.1479 ($[M+H]^+$), found 357.1467.

5.3.9 Synthesis of Sulfuramidimidoyl Fluoride (SAFs) 23

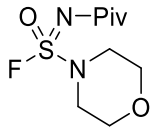


General procedure J

Sulfonimidamide **22a-d** (1.0 equiv.) was added to an oven-dried reaction flask. The flask was evacuated and back-filled with nitrogen three times. Anhydrous and degassed THF (1.0 mL, 0.1 M) was added, followed by the addition of KHMDS (1.0 M in THF, 1.2 equiv.) and the solution was stirred for 40 minutes at room temperature. *N*-Fluorobenzenesulfonimide (1.5 equiv.) was dissolved in minimum amount of

anhydrous, degassed THF and added dropwise to the reaction mixture. The resultant solution was stirred at room temperature for 16 hours. The crude mixture was filtered through Celite®, washed with EtOAc, concentrated in *vacuo* and purified using flash column chromatography (SiO_2, Petrol/EtOAc) to afford the desired product.

***N*-Pivaloylmorpholine-4-sulfonimidoyl fluoride (23a)**

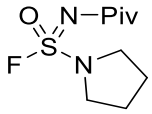


Prepared according to **General procedure J**, using sulfonimidamide **22a** (32.0 mg, 0.1 mmol, 1.0 equiv.), KHMDS (120 µL, 0.12 mmol, 1.0 M in THF, 1.2 equiv.), and *N*-Fluorobenzenesulfonimide (47.3 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 7:1 to 5:1 to 3:1) to afford the desired product **23a** as a colourless oil (20.2 mg, 80%).

IR (thin film, ν_{max}/cm^{-1}) 2978, 1684, 1481, 1338, 1285, 1192, 1012, 851, 736, 637; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 3.81-3.79 (m, 4H, Alkyl-*H*), 3.51-3.47 (m, 4H, Alkyl-*H*), 1.19 (s, 9H, Alkyl-*H*); **^{19}F NMR** (376 MHz, $CDCl_3$) 46.4; $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 183.8, 65.8, 46.8, 42.3 (d, $^4J_{CF}$ = 2.0 Hz), 27.3; **HRMS** (ESI^+), *m/z* calculated for $[C_9H_{18}FN_2O_3SNa]^+$ 291.0576 ($[M+Na]^+$), found 291.0584.

Notes: When the reaction was performed on larger scale (0.5 mmol and 3.0 mmol), the yield obtained was 78% and 74% respectively.

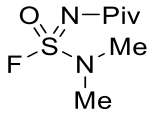
***N*-Pivaloylpyrrolidine-1-sulfonimidoyl fluoride (23b)**



Prepared according to **General procedure J**, using sulfonimidamide **22b** (304.4 mg, 1.0 mmol, 1.0 equiv.), KHMDS (1.2 mL, 1.2 mmol, 1.0 M in THF, 1.2 equiv.), and *N*-Fluorobenzenesulfonimide (473.0 mg, 1.5 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 7:1 to 5:1) to afford the desired product **23b** as a colourless oil (175 mg, 74%).

IR (thin film, ν_{max}/cm^{-1}) 2974, 1677, 1479, 1320, 1282, 1185, 1098, 846, 700, 621; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 3.57-3.51 (m, 4H, Alkyl-*H*), 2.04-2.01 (m, 4H, Alkyl-*H*), 1.19 (s, 9H, Alkyl-*H*); **^{19}F NMR** (376 MHz, $CDCl_3$) 46.4 (p, J = 3.5 Hz); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 184.0, 49.27, 49.26, 27.3, 25.7; **HRMS** (ESI^+), *m/z* calculated for $[C_9H_{17}FN_2O_2SNa]^+$ 259.0887 ($[M+Na]^+$), found 259.0890.

***N*,*N*-Dimethyl-*N*'-pivaloylsulfuramidimidoyl fluoride (23c)**

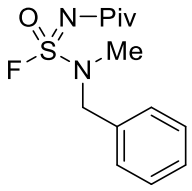


Prepared according to **General procedure J**, using sulfonimidamide **23c** (278.4 mg, 1.0 mmol, 1.0 equiv.), KHMDS (1.2 mL, 1.2 mmol, 1.0 M in THF, 1.2 equiv.), and *N*-Fluorobenzenesulfonimide (473.0 mg, 1.5 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 9:1 to 7:1 to 5:1) to afford the desired product **23c** as a colourless oil (181.4 mg, 86%, 80% purity).

IR (thin film, ν_{max}/cm^{-1}) 2973, 1679, 1479, 1324, 1279, 1168, 1053, 967, 850, 737, 694; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 3.07 (d, 6H, $^4J_{CF}$ = 3.0 Hz Alkyl-*H*), 1.20 (s, 9H, Alkyl-*H*); **^{19}F NMR** (376 MHz, $CDCl_3$) 44.0 (hept, J = 3.0 Hz); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 184.0, 42.2, 38.5, 27.3; **HRMS** (ESI^+), *m/z* calculated for $[C_7H_{15}FN_2O_2SNa]^+$ 233.0730 ($[M+Na]^+$), found 233.0719.

Note: *N*,*N*-dimethylbenzenesulfonamide was found as a side product which is inseparable with **23c**.

***N*-Benzyl-*N*-methyl-*N*'-pivaloylsulfuramidimidoyl fluoride (23d)**

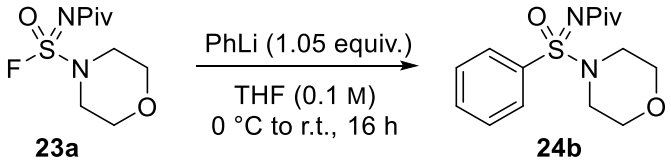


Prepared according to **General procedure J**, using sulfonimidamide **23d** (248.1 mg, 0.7 mmol, 1.0 equiv.), KHMDS (840 µL, 0.84 mmol, 1.0 M in THF, 1.2 equiv.), and *N*-Fluorobenzenesulfonimide (331.1 mg, 0.84 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 15:1 to 12:1 to 10:1) to afford the desired product **23d** as a colourless oil (144.3 mg, 72%).

IR (thin film, ν_{max}/cm^{-1}) 3034, 2974, 1678, 1479, 1320, 1280, 1176, 1053, 983, 850, 734, 697; δ_H (400 MHz, $CDCl_3$) 7.43-7.34 (m, 5H, Ar-*H*), 4.62-4.50 (m, 2H, Alkyl-*H*), 2.92 (d, 3H, *J* = 3.0 Hz, Alkyl-*H*), 1.21 (s, 9H, Alkyl-*H*); **^{19}F NMR** (376 MHz, $CDCl_3$) 51.1-51.0 (m); δ_C (101 MHz, $CDCl_3$) 184.0, 133.8 (d, $^4J_{CF}$ = 2.0 Hz), 129.2, 128.8, 128.6, 54.9 (d, $^3J_{CF}$ = 1.5 Hz), 42.3(d, $^4J_{CF}$ = 2.0 Hz), 35.0 (d, $^3J_{CF}$ = 1.5 Hz), 27.4; **HRMS** (ESI^+), *m/z* calculated for $[C_{13}H_{19}FN_2O_2SNa]^+$ 309.1043 ($[M+Na]^+$), found 309.1056.

5.3.10 SuFEx Reaction of 23a with Carbon Nucleophiles

***N*-((4-Fluorophenyl)(morpholino)(oxo)-λ^6-sulfaneylidene)pivalamide (24b)**



23a **24b**

Sulfuramidimidoyl fluorides **23a** (25.2 mg, 0.1 mmol, 1.0 equiv.) was added to an oven-dried reaction tube. The reaction tube was evacuated and back-filled with nitrogen three times. Anhydrous, degassed THF (1.0 mL, 0.1 M) was added, and the resultant solution was cooled to 0 °C. Phenyllithium (58 µL, 0.105 mmol,

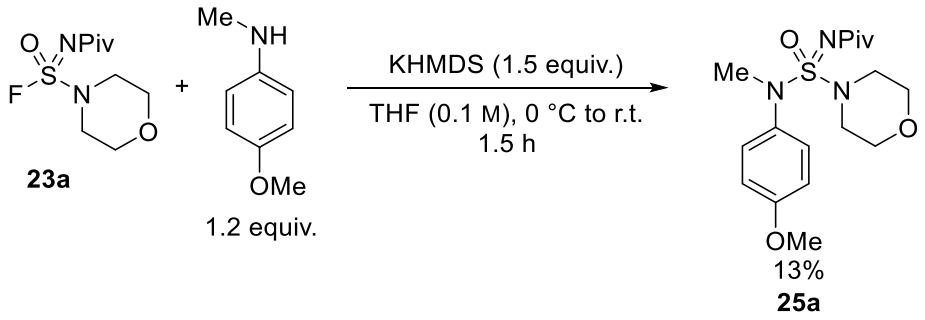
1.8 M in Et_2O, 1.05 equiv.) was added dropwise, and the reaction mixture was stirred at 0 °C for 1 hour, then warmed to room temperature for stir for additional 15 hours. The reaction was quenched with 2-propanol, concentrated *in vacuo* and purified by flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 3:1 to 1:1) to afford the desired product **24b** as a colourless oil (18 mg, 58%).

IR (thin film, ν_{max}/cm^{-1}) 3067, 2971, 1649, 1478, 1363, 1291, 1192, 1034, 940, 851, 729, 690; **δ_H** (500 MHz, $CDCl_3$) 7.85-7.83 (m, 2H, Ar-*H*), 7.64-7.61 (m, 1H, Ar-*H*), 7.57-7.54 (m, 2H, Ar-*H*), 3.74 (t, 4H, *J* = 4.5 Hz, Alkyl-*H*), 3.16-3.11 (m, 4H, Alkyl-*H*), 1.24 (s, 9H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 186.8, 136.0, 133.3, 129.4, 127.9, 66.3, 45.7, 42.1, 27.8; **HRMS** (ESI^+, *m/z* calculated for $[C_{15}H_{23}N_2O_3S]^+$ 311.1424 $[M+H]^+$), found 311.1432.

5.3.11 SuFEx Reaction of 23a with Nitrogen Nucleophile

5.3.11.1 SuFEx Amination with Strong Base

_N_-(((4-Methoxyphenyl)(methyl)amino)(morpholino)(oxo)-λ^6-sulfaneylidene)pivalamide (25a)

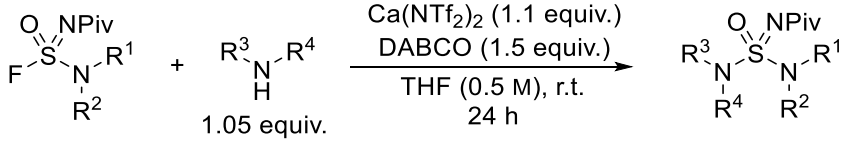


N-Methyl-*p*-anisidine (16.5 mg, 0.12 mmol, 1.2 equiv.) was added to an oven-dried reaction tube. The reaction tube was evacuated and back-filled with nitrogen three times. Anhydrous, degassed THF (1.0 mL, 0.1 M) was added, and the resultant solution was cooled to 0 °C. KHMDS (150 µL, 0.1 mmol, 1.0 M in THF, 1.5 equiv.) was added dropwise and the solution was stirred for 15 minutes at 0 °C. A solution of sulfuramidimidoyl fluorides **23a** (25.2 mg, 0.1 mmol, 1.0 equiv.) in anhydrous THF (0.1 mL) was added

dropwise to the reaction mixture, and the resultant was warmed to room temperature and stirred for 1.5 hour. The reaction was quenched with silica gel, concentrated *in vacuo* and purified by flash column chromatography (SiO_2, CH_2Cl_2/EtOAc 10:1 to 8:1 to 6:1) to afford the desired product **25a** as a pale-brown oil (4.8 mg, 13%).

IR (thin film, ν_{max}/cm^{-1}) 3038, 2971, 1636, 1501, 1249, 1193, 1074, 1033, 944, 852, 733, 650; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.34-7.31 (m, 2H, Ar-*H*), 6.90-6.86 (m, 2H, Ar-*H*), 3.81 (s, 3H, Alkyl-*H*), 3.68-3.65 (m, 4H, Alkyl-*H*), 3.30-3.24 (m, 7H, Alkyl-*H*), 1.13 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 186.3, 159.2, 134.6, 129.2, 114.5, 66.4, 55.6, 46.4, 41.8, 40.6, 27.9; **HRMS** (ESI^+, *m/z* calculated for $[C_{17}H_{28}N_3O_4S]^+$ 370.1795 $[M+H]^+$), found 370.1796.

5.3.11.2 SuFEx amination mediated by $Ca(NTf_2)_2$



23a-d **25b-u**

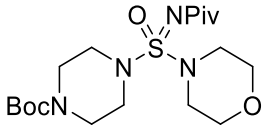
General procedure K

Procedures adapted from S. Mahapatra, C. P. Woroch, T. W. Butler, S. N. Carneiro, S. C. Kwan, S. R. Khasnavis, J. Gu, J. K. Dutra, B. C. Vetelino, J. Bellenger, C. W. am Ende and N. D. Ball, *Org. Lett*., 2020, **22**, 4389-4394.[24]

Sulfuramidimidoyl fluorides **23** (0.1 mmol, 1.0 equiv.), amine (1.05 equiv., if solid), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.) was added to an oven-dried reaction tube. The reaction tube was evacuated and back-filled with nitrogen three times. Anhydrous, THF (0.2 mL, 0.5 M) was added, followed by the addition of amine (1.05 equiv., if liquid). The reaction mixture was stirred at room temperature for 24 hours, then diluted with EtOAc (2 mL). The organic layer was washed

with saturated NH_4Cl (aq.) (3 mL), extracted with EtOAc (2 × 3 mL), washed with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (SiO_2, Petrol/EtOAc) to afford the desired product **25b-u**.

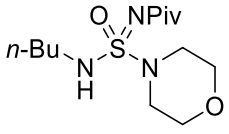
***tert*-Butyl 4-(*N*-pivaloylmorpholine-4-sulfonimidoyl)piperazine-1-carboxylate (25b)**



Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23a** (25.2 mg, 0.1 mmol, 1.0 equiv.), 1-Boc-piperazine (19.6 mg, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 2:1) to afford the desired product **25b** as a colourless oil (36.8 mg, 88%).

IR (thin film, ν_{max}/cm^{-1}) 2974, 1697, 1636, 1420, 1248, 1169, 1073, 1033, 932, 854, 731, 700; **δ_H** (400 MHz, $CDCl_3$) 3.78-3.69 (m, 4H, Alkyl-*H*), 3.55-3.42 (m, 4H, Alkyl-*H*), 3.34-3.24 (m, 8H, Alkyl-*H*), 1.46 (s, 9H, Alkyl-*H*), 1.18 (s, 9H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 186.5, 154.4, 80.6, 66.4, 46.32, 46.26, 46.2, 41.9, 28.5, 27.9; **HRMS** (ESI^+, *m/z* calculated for $[C_{18}H_{34}N_4O_5SNa]^+$ 441.2142 $[M+Na]^+$), found 441.2149.

***N*-((Butylamino)(morpholino)(oxo)-λ^6-sulfaneylidene)pivalamide (25c)**

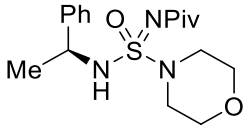


Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23a** (25.2 mg, 0.1 mmol, 1.0 equiv.), *n*-butylamine (10 µL, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.)

and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 3:1) to afford the desired product **25c** as a colourless oil (25.4 mg, 83%).

IR (thin film, ν_{max}/cm^{-1}) 3220, 2959, 1606, 1456, 1259, 1208, 1115, 1073, 939, 850, 781, 615; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 8.02 (Br. s, 1H, N-*H*), 3.80-3.68 (m, 4H, Alkyl-*H*), 3.22-3.03 (m, 6H, Alkyl-*H*), 1.60-1.53 (m, 2H, Alkyl-*H*), 1.43-1.33 (m, 2H, Alkyl-*H*), 1.18 (s, 9H, Alkyl-*H*), 0.92 (t, 3H, *J* = 7.5 Hz, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 186.9, 66.2, 46.0, 41.9, 41.4, 31.8, 27.9, 20.1, 13.7; **HRMS** (ESI^+, *m/z* calculated for $[C_{13}H_{27}N_3O_3SNa]^+$ 328.1665 $[M+Na]^+$), found 328.1669.

***N*-(Morpholino(oxo)(((*S*)-1-phenylethyl)amino)-λ^6-sulfaneylidene)pivalamide (25d, 25d')**



Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23a** (25.2 mg, 0.1 mmol, 1.0 equiv.), (S)-(-)-1-Phenylethylamine (13 µL, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 9:1 to 7:1 to 5:1) to afford the desired product **25d** (12.8 mg, 36%) and **25d'** as white solid (16.5 mg, 47%), (d.r. = 1:1.27). (Sulfur stereochemistry of these two compounds remains unknown)

Disastereomer A **(25d)** (Sulfur stereochemistry unknown)

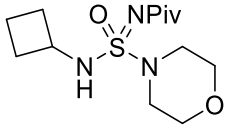
m.p. 98-100 °C ($CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3213, 3031, 2971, 1604, 1456, 1300, 1259, 1205, 1114, 1074, 940, 848, 764, 702, 627; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 8.71 (d, 1H, *J* = 7.0 Hz, N-*H*), 7.37-7.27 (m, 5H, Ar-*H*), 4.70-4.63 (m, 1H, Alkyl-*H*), 3.37-3.15 (m, 4H, Alkyl-*H*), 2.92-2.78 (m, 4H, Alkyl-*H*), 1.58 (d, 3H, *J* = 7.0 Hz, Alkyl-*H*), 1.19 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 186.9, 143.0, 128.9, 128.0, 126.5, 65.6,

52.6, 45.8, 42.0, 27.9, 24.5; **HRMS** (ESI$^+$, *m/z* calculated for $[C_{17}H_{27}N_3O_3SNa]^+$ 376.1665 $[M+Na]^+$), found 376.1667.

Diastereomer B **(25d')** (Sulfur stereochemistry unknown)

m.p. 136-138 °C ($CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3168, 3034, 2972, 1631, 1455, 1295, 1253, 1193, 1109, 1067, 963, 847, 764, 700, 629; δ_H (400 MHz, $CDCl_3$) 8.35 (d, 1H, *J* = 6.0 Hz N-*H*), 7.36-7.35 (m, 4H, Ar-*H*), 7.31-7.25 (m, 1H, Ar-*H*), 4.72-4.66 (m, 1H, Ar-*H*), 3.78-3.72 (m, 4H, Alkyl-*H*), 3.32-3.11 (m, 4H, Alkyl-*H*), 1.55 (d, 3H, *J* = 7.0 Hz, Alkyl-*H*), 1.16 (s, 9H, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 186.8, 142.4, 128.9, 127.9, 126.3, 66.2, 52.7, 46.1, 41.9, 27.9, 23.6; **HRMS** (ESI$^+$, *m/z* **HRMS** (ESI$^+$, *m/z* calculated for $[C_{17}H_{27}N_3O_3SNa]^+$ 376.1665 $[M+Na]^+$), found 376.1664.

***N*-((Cyclobutylamino)(morpholino)(oxo)-λ^6-sulfaneylidene)pivalamide (25e)**

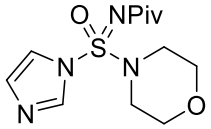


Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23a** (25.2 mg, 0.1 mmol, 1.0 equiv.), cyclobutylamine (9.0 µL, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 3:1) to afford the desired product **25e** as a colourless oil (23.7 mg, 78%).

IR (thin film, ν_{max}/cm^{-1}) 3219, 2954, 1606, 1455, 1258, 1204, 1115, 1072, 940, 850, 790, 616; δ_H (400 MHz, $CDCl_3$) 8.26 (d, 1H, *J* = 7.5 Hz, N-*H*), 3.99-3.93 (m, 1H, Alkyl-*H*), 3.73-3.71 (m, 4H, Alkyl-*H*), 3.10-3.07 (m, 4H, Alkyl-*H*), 2.39-2.25 (m, 2H, Alkyl-*H*), 2.12-1.92 (m, 2H, Alkyl-*H*), 1.78-1.60 (m, 2H, Alkyl-*H*),

1.17 (s, 9H, Alkyl-*H*); **δC** (101 MHz, $CDCl_3$) 186.9, 66.2, 46.7, 46.0, 41.9, 32.2, 31.9, 27.9, 15.3; **HRMS** (ESI^+, *m/z* calculated for $[C_{13}H_{27}N_3O_3SNa]^+$ 328.1665 $[M+Na]^+$), found 328.1669.

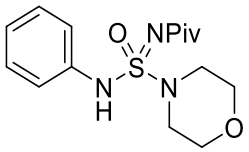
***N*-((1*H*-Imidazol-1-yl)(morpholino)(oxo)-λ⁶-sulfaneylidene)pivalamide (25f)**



Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23a** (25.2 mg, 0.1 mmol, 1.0 equiv.), imidazole (7.1 mg, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 3:1 to 1:2) to afford the desired product **25f** as a white solid (27.0 mg, 90%).

m.p. 115-117 °C ($CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3122, 2972, 1726, 1671, 1454, 1261, 1144, 1045, 943, 844, 731, 616; **δH** (400 MHz, $CDCl_3$) 7.91 (app. s, 1H, Ar-*H*), 7.21 (app. S, 1H, Ar-*H*), 7.14 (app. s, Ar-*H*), 3.76-3.74 (m, 4H, Alkyl-*H*), 3.30-3.19 (m, 4H, Alkyl-*H*), 1.21 (s, 9H, Alkyl-*H*); **δC** (101 MHz, $CDCl_3$) 184.7, 137.1, 131.1, 117.5, 65.8, 46.1, 42.4, 27.4; **HRMS** (ESI^+, *m/z* calculated for $[C_{12}H_{20}N_4O_3SNa]^+$ 323.1148 $[M+Na]^+$), found 323.1142.

***N*-(Morpholino(oxo)(phenylamino)-λ⁶-sulfaneylidene)pivalamide (25g)**

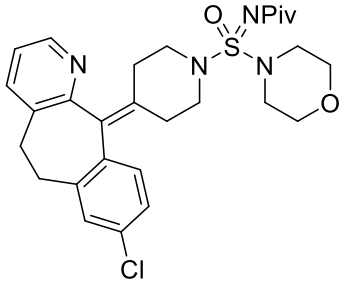


Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23a** (25.2 mg, 0.1 mmol, 1.0 equiv.), aniline (10 µL, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and

DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 3:1) to afford the desired product **25g** as a colourless oil (24.4 mg, 75%).

IR (thin film, ν_{max}/cm^{-1}) 3296, 3035, 2965, 1602, 1479, 1259, 1193, 1114, 1031, 940, 835, 752, 620; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.35-7.31 (m, 2H, Ar-*H*), 7.23-7.20 (m, 2H, Ar-*H*), 7.18-7.14 (m, 1H, Ar-*H*), 3.69-3.60 (m, 4H, Alkyl-*H*), 3.20-3.17 (m, 4H, Alkyl-*H*), 1.24 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 187.0, 136.0, 129.6, 125.2, 121.0, 66.0, 45.9, 42.1, 27.9; **HRMS** (ESI^+, *m/z* calculated for $[C_{12}H_{20}N_4O_3SNa]^+$ 323.1148 $[M+Na]^+$), found 323.1142.

***N*-((4-(8-Chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidin-1-yl)(morpholino)(oxo)-λ^6-sulfaneylidene)pivalamide (25h)**



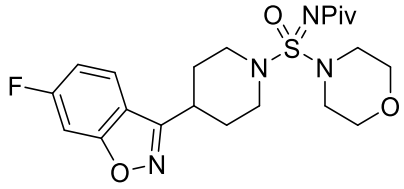
Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23a** (25.2 mg, 0.1 mmol, 1.0 equiv.), Desloratadine (32.6 mg, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 3:1 to 1:1 to 1:3) to afford the desired product **25g** as a colourless oil (24.4 mg, 75%).

m.p. 78-80 °C ($CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3094, 3050, 2922, 1727, 1635, 1478, 1258, 1193, 1115, 1031, 984, 847, 731, 622; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 8.39-8.37 (m, 1H, Ar-*H*), 7.47-7.44 (m, 1H, Ar-*H*), 7.16-7.07 (m, 4H, Ar-*H*), 3.73-3.67 (m, 4H, Alkyl-*H*), 3.65-3.51 (m, 2H, Alkyl-*H*), 3.41-3.23 (m, 6H, Alkyl-*H*), 3.17-3.01 (m, 2H, Alkyl-*H*), 2.85-2.76 (m, 2H, Alkyl-*H*), 2.55-2.51 (m, 2H, Alkyl-*H*), 2.47-2.41 (m, 3H,

Alkyl-*H*), 1.15 (s, 9H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 186.6, 156.5, 156.4, 146.5, 139.73, 139.67, 138.21, 138.15, 137.5, 137.3, 136.2, 136.1, 134.8, 133.79, 133.75, 133.3, 130.4, 129.2, 129.1, 126.33, 126.30, 122.7, 122.6, 66.4, 47.3, 47.2, 47.1, 46.3, 41.8, 31.63, 31.60, 31.57, 31.54, 30.6, 30.4, 29.8, 27.9; **HRMS** (ESI^+, *m/z* calculated for $[C_{28}H_{36}ClN_4O_3S]^+$ 543.2191 $[M+H]^+$), found 543.2191.

Note: Additional 13 peaks observed in ^{13}C NMR, due to presence of rotamers.

_N_-((4-(6-Fluorobenzo[*d*]isoxazol-3-yl)piperidin-1-yl)(morpholino)(oxo)-λ^6-sulfaneylidene)pivalamide (25i)

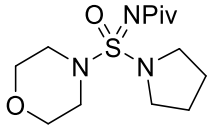


Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23a** (25.2 mg, 0.1 mmol, 1.0 equiv.), 6-Fluoro-3-(4-piperidinyl)benzisoxazole (23.1 mg, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 3:1) to afford the desired product **25g** as a colourless oil (24.4 mg, 75%).

m.p. 135-137 °C ($CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3060, 2923, 1725, 1631, 1447, 1244, 1196, 1115, 925, 851, 731, 612; **δ_H** (400 MHz, $CDCl_3$) 7.70-7.66 (m, 1H, Ar-*H*), 7.25-7.22 (m, 1H, Ar-*H*), 7.09-7.04 (m, 1H, Ar-*H*), 3.98-3.81 (m, 2H, Alkyl-*H*), 3.77-3.69 (m, 4H, Alkyl-*H*), 3.38-3.18 (m, 6H, Alkyl-*H*), 3.05-2.99 (m, 1H, Alkyl-*H*), 2.19-2.09 (m, 3H, Alkyl-*H*), 2.06-1.98 (m, 1H, Alkyl-*H*), 1.19 (s, 9H, Alkyl-*H*); **^{19}F NMR** (376 MHz, $CDCl_3$) -108.9 (m); **δ_C** (101 MHz, $CDCl_3$) 186.6, 164.3 (d, $^1J_{CF}$ = 250 Hz), 164.0 (d, $^3J_{CF}$ = 13.5 Hz), 160.3, 122.4 (d, $^3J_{CF}$ = 11.0 Hz), 117.1, 112.8 (d, $^2J_{CF}$ = 27.0 Hz), 97.6 (d, $^2J_{CF}$ = 27.0 Hz), 66.4, 46.5,

46.1, 45.8, 41.8, 33.7, 30.2, 29.7, 27.9; **HRMS** (ESI^+, *m/z* calculated for $[C_{28}H_{36}ClN_4O_3S]^+$ 543.2191 $[M+H]^+$), found 543.2191.

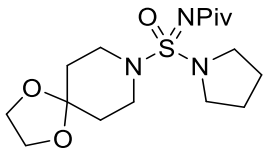
***N*-(Morpholino(oxo)(pyrrolidin-1-yl)-λ^6-sulfaneylidene)pivalamide (25j)**



Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23b** (23.6 mg, 0.1 mmol, 1.0 equiv.), morpholine (9 µL, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 4:1 to 2:1) to afford the desired product **25j** as a colourless oil (24.9 mg, 82%).

IR (thin film, ν_{max}/cm^{-1}) 2968, 1631, 1456, 1296, 1193, 1115, 1072, 1012, 940, 844, 704, 622; δ_H (400 MHz, $CDCl_3$) 3.72-3.69 (m, 4H, Alkyl-*H*), 3.44-3.38 (m, 2H, Alkyl-*H*), 3.32-3.3.20 (m, 6H, Alkyl-*H*), 1.93-1.90 (m, 4H, Alkyl-*H*), 1.16 (s, 9H, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 186.6, 66.5, 48.4, 46.2, 41.6, 29.8, 28.0, 27.9, 25.8; **HRMS** (ESI^+, *m/z* calculated for $[C_{13}H_{26}N_3O_3S]^+$ 304.1689 $[M+H]^+$), found 304.1689.

***N*-(Oxo(pyrrolidin-1-yl)(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-λ^6-sulfaneylidene)pivalamide (25k)**

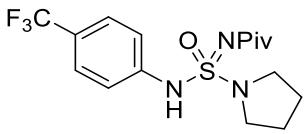


Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23b** (23.6 mg, 0.1 mmol, 1.0 equiv.), 1,4-Dioxa-8-azaspiro[4.5]decane (15.0 mg, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash

column chromatography (SiO_2, Petrol/EtOAc 4:1 to 2:1) to afford the desired product **25k** as a colourless oil (27.7 mg, 77%).

IR (thin film, ν_{max}/cm^{-1}) 2967, 1632, 1477, 1296, 1228, 1194, 1144, 1045, 941, 846, 731, 616; **δ_H** (400 MHz, $CDCl_3$) 3.94 (app. s, 4H, Alkyl-*H*), 3.44-3.38 (m, 6H, Alkyl-*H*), 3.28-3.21 (m, 2H, Alkyl-*H*), 1.94-1.85 (m, 4H, Alkyl-*H*), 1.80-1.71 (m, 4H, Alkyl-*H*), 1.16 (s, 9H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 186.3, 106.5, 64.5, 48.3, 44.4, 41.6, 34.8, 28.0, 25.8; **HRMS** (ESI^+, *m/z* calculated for $[C_{16}H_{30}N_3O_4S]^+$ 360.1952 $[M+H]^+$), found 360.1954.

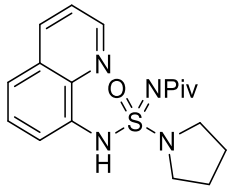
***N*-(Oxo(pyrrolidin-1-yl)((4-(trifluoromethyl)phenyl)amino)-λ^6-sulfaneylidene)pivalamide (25l)**



Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23b** (23.6 mg, 0.1 mmol, 1.0 equiv.), 4-(trifluoromethyl)aniline (13 µL, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 7:1 to 5:1) to afford the desired product **25l** as a pale-yellow oil (25.3 mg, 67%).

IR (thin film, ν_{max}/cm^{-1}) 3193, 3033, 2974, 1617, 1458, 1324, 1186, 1115, 1070, 211, 839, 782, 659; **δ_H** (500 MHz, $CDCl_3$) 7.57 (d, 2H, *J* = 8.5 Hz, Ar-*H*), 7.28 (d, 2H, *J* = 8.5 Hz, Ar-*H*), 3.36-3.23 (m, 4H, Alkyl-*H*), 1.92-1.89 (m, 4H, Alkyl-*H*), 1.23 (s, 9H, Alkyl-*H*); **^{19}F NMR** (476 MHz, $CDCl_3$) -62.2; **δ_C** (126 MHz, $CDCl_3$) 186.9, 140.0, 126.8 (q, $^3J_{CF}$ = 4.0 Hz), 126.3 ($^2J_{CF}$ = 32.5 Hz), 124.2 ($^1J_{CF}$ = 271.5 Hz), 119.8, 48.4, 42.0, 27.8, 27.4, 25.8; **HRMS** (ESI^+, *m/z* calculated for $[C_{16}H_{23}F_3N_3O_2S]^+$ 378.1458 $[M+H]^+$), found 378.1465.

***N*-(Oxo(pyrrolidin-1-yl)(quinolin-8-ylamino)-λ^6-sulfaneylidene)pivalamide (25m)**

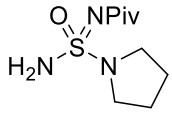


Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23b** (23.6 mg, 0.1 mmol, 1.0 equiv.), 8-Aminoquinoline (15.1mg, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 3:1 to 1:1) to afford the desired product **25m** as a brown oil (15.1 mg, 42%).

IR (thin film, ν_{max}/cm^{-1}) 3164, 3060, 2970, 1606, 1459, 1358, 1297, 1256, 1174, 1137, 1072, 989, 856, 786, 619; δ_H (400 MHz, $CDCl_3$) 11.1 (br. s, N-*H*), 8.77 (d, 1H, *J* = 2.5 Hz, Ar-*H*), 8.06 (d, 1H, *J* = 8.5 Hz, Ar-*H*), 8.01 (d, 1H, *J* = 2.5 Hz, Ar-*H*), 7.77 (dd, 1H, *J* = 8.0 Hz, 1.5 Hz) 7.67-7.63 (m, 1H, Ar-*H*), 7.56-7.53 (m, 1H, Ar-*H*), 3.40-3.27 (m, 4H, Alkyl-*H*), 1.90-1.87 (m, 4H, Alkyl-*H*), 1.24 (s, 9H, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 186.8, 145.5, 145.3, 130.7, 129.3, 128.8, 128.2, 127.6, 127.5, 125.1, 48.5, 41.9, 27.8, 25.8; **HRMS** (ESI^+, *m/z* calculated for $[C_{18}H_{25}N_4O_2S]^+$ 361.1693 $[M+H]^+$), found 361.1696.

Note: Trace amount of grease at 29.8 ppm was found in the NMR spectrum, but compound **25m** slowly decomposes at room temperature, thus a clean ^{13}C NMR spectrum was not obtained.

***N*-(Amino(oxo)(pyrrolidin-1-yl)-λ^6-sulfaneylidene)pivalamide (25n)**

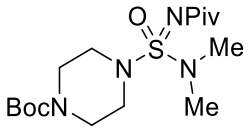


Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23b** (23.6 mg, 0.1 mmol, 1.0 equiv.), ammonia (15 µL, 0.105 mmol, 7N in MeOH, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1

equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 3:1 to 1:1) to afford the desired product **25m** as a brown oil (10.5 mg, 45%).

IR (thin film, ν_{max}/cm^{-1}) 3174, 2987, 1651, 1468, 1349, 1191, 1134, 1056, 840, 790, 615; **δ_H** (400 MHz, $CDCl_3$) 5.87 (br. s, 2H, N-*H*), 3.34-3.31 (m, 4H, Alkyl-*H*), 1.94-1.91 (m, 4H, Alkyl-*H*), 1.19 (s, 9H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 187.7, 48.2, 41.7, 27.8, 25.8; **HRMS** (ESI^+, *m/z* calculated for $[C_{18}H_{25}N_4O_2S]^+$ 361.1693 $[M+H]^+$), found 361.1696.

***tert*-Butyl 4-(*N*,*N*-dimethyl-*N*'-pivaloylsulfamidimidoyl)piperazine-1-carboxylate (25o)**

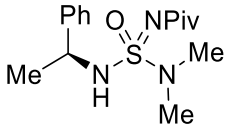


Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23c** (26.3 mg, 0.1 mmol, 80% purity, 1.0 equiv.), 1-Boc-piperazine (19.6 mg, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 2:1) to afford the desired product **25o** as a colourless oil (34.6 mg, 92%).

IR (thin film, ν_{max}/cm^{-1}) 2974, 1697, 1636, 1419, 1248, 1174, 1127, 1032, 934, 853, 724, 656; **δ_H** (400 MHz, $CDCl_3$) 3.49 (app. s, 4H, Alkyl-*H*), 3.30-3.25 (m, 4H, Alkyl-*H*), 2.87 (s, 6H, Alkyl-*H*), 1.46 (s, 9H, Alkyl-*H*), 1.19 (s, 9H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 186.5, 154.5, 80.5, 46.0, 41.8, 38.0, 28.5, 28.0; **HRMS** (ESI^+, *m/z* calculated for $[C_{16}H_{33}N_4O_5S]^+$ 377.2217 $[M+H]^+$), found 377.2212.

Note: One of the ^{13}C NMR signal was not observed due to the presence of rotamer.

***N*-((Dimethylamino)(oxo)(((*S*)-1-phenylethyl)amino)-λ^6-sulfaneylidene)pivalamide (25p, 25p')**



Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23c** (26.3 mg, 0.1 mmol, 80% purity, 1.0 equiv.), (S)-(-)-1-Phenylethylamine (13 µL, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 10:1 to 9:1 to 8:1) to afford the desired product **25p** (9.7 mg, 31%) and **25p'** as colourless oil (18.1 mg, 58%, 80% purity), (d.r. = 1:1.65). (Sulfur stereochemistry of these two compounds remains unknown)

Disastereomer A **(25p)** (Sulfur stereochemistry unknown)

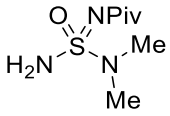
IR (thin film, ν_{max}/cm^{-1}) 3210, 3020, 2934, 1724, 1606, 1479, 1313, 1281, 1206, 1102, 1033, 887, 764, 703, 657; δ_H (400 MHz, $CDCl_3$) 8.46 (d, 1H, *J* = 7.0 Hz, N-*H*), 7.36-7.31 (m, 4H, Ar-*H*), 7.29-7.25 (m, 1H, Ar-*H*), 4.67-4.60 (m, 1H, Alkyl-*H*), 2.48 (s, 6H, Alkyl-*H*), 1.58 (d, 3H, *J* = 7.0 Hz, Alkyl-*H*), 1.18 (s, 9H, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 187.0, 142.8, 128.8, 127.8, 126.4, 52.6, 41.9, 37.5, 27.9, 24.5; **HRMS** (ESI$^+$, *m/z* calculated for $[C_{15}H_{25}N_3O_2SNa]^+$ 334.1560 $[M+Na]^+$), found 334.1543.

Diastereomer B **(25p')** (Sulfur stereochemistry unknown)

IR (thin film, ν_{max}/cm^{-1}) 3172, 3022, 2924, 1733, 1608, 1453, 1308, 1266, 1215, 1030, 950, 833, 786, 703, 640; δ_H (400 MHz, $CDCl_3$) 8.19 (d, 1H, *J* = 7.0 Hz N-*H*), 7.36-7.31 (m, 4H, Ar-*H*), 7.28-7.24 (m, 1H, Ar-*H*), 4.70-4.63 (m, 1H, Alkyl-*H*), 2.78 (s, 6H, Alkyl-*H*), 1.54 (d, 3H, *J* = 7.0 Hz, Alkyl-*H*), 1.16 (s, 9H, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 186.8, 142.7, 128.8, 127.8, 126.3, 52.6, 41.8, 37.9, 27.9, 23.4; **HRMS** (ESI$^+$, *m/z* **HRMS** (ESI$^+$, *m/z* calculated for $[C_{15}H_{25}N_3O_2SNa]^+$ 334.1560 $[M+Na]^+$), found 334.1557.

Note: Impurity *N*,*N*-dimethylbenzenesulfonamide from **23c** was inseparable with **25p'.**

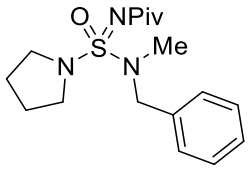
***N*-(Amino(dimethylamino)(oxo)-λ^6-sulfaneylidene)pivalamide (25q)**



Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23c** (26.3 mg, 0.1 mmol, 80% purity, 1.0 equiv.), ammonia (210 µL, 0.105 mmol, 0.5 N in THF, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 3:1) to afford the desired product **25q** as a white solid (9.7 mg, 47%).

mp 84-86 °C ($CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3241, 2979, 1612, 1479, 1306, 1244, 1046, 947, 845, 791, 733, 695; **δ_H** (400 MHz, $CDCl_3$) 5.99 (br. s, 2H, N-*H*), 2.81 (s, 6H, Alkyl-*H*), 1.20 (s, 9H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 187.7, 41.9, 37.9, 27.8; **HRMS** (ESI$^+$, *m/z* calculated for $[C_7H_{17}N_3O_2SNa]^+$ 230.0934 $[M+Na]^+$), found 230.0929.

***N*-((Benzyl(methyl)amino)(oxo)(pyrrolidin-1-yl)-λ^6-sulfaneylidene)pivalamide (25r)**

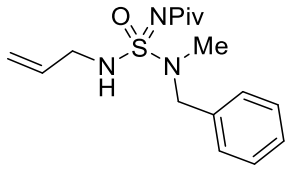


Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23d** (28.6 mg, 0.1 mmol, 1.0 equiv.), pyrrolidine (9 µL, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 3:1) to afford the desired product **25r** as a colourless oil (23.3 mg, 69%).

IR (thin film, ν_{max}/cm^{-1}) 3039, 2974, 1616, 1468, 1352, 1196, 1136, 1059, 950, 845, 789, 617; **δ_H** (400 MHz, $CDCl_3$) 7.36-7.27 (m, 5H, Ar-*H*), 4.58 (d, 1H, *J* = 14.5 Hz, Alkyl-*H*), 4.26 (d, 1H, *J* = 14.7 Hz, Alkyl-*H*),

3.47-3.31 (m, 4H, Alkyl-*H*), 2.67 (s, 3H, Alkyl-*H*), 1.93-1.91 (m, 4H, Alkyl-*H*), 1.21 (s, 9H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 186.5, 136.9, 128.7, 128.5, 127.8, 54.6, 48.2, 41.5, 34.3, 28.1, 25.8; **HRMS** (ESI^+, *m/z* calculated for $[C_{17}H_{27}N_3O_2SNa]^+$ 360.1716 $[M+Na]^+$), found 360.1714.

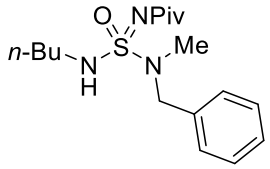
***N*-((Allylamino)(benzyl(methyl)amino)(oxo)-λ⁶-sulfaneylidene)pivalamide (25s)**



Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23d** (28.6 mg, 0.1 mmol, 1.0 equiv.), allylamine (8 µL, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 12:1 to 10:1) to afford the desired product **25s** as a colourless oil (22.6 mg, 70%).

IR (thin film, ν_{max}/cm^{-1}) 3233, 3031, 2967, 1605, 1478, 1392, 1305, 1246, 1208, 1117, 1032, 987, 853, 714; **δ_H** (400 MHz, $CDCl_3$) 7.86 (br.s, 1H, N-*H*), 7.38-7.28 (m, 5H, Ar-*H*), 5.93-5.83 (m, 1H, Alkenyl-*H*), 5.33-5.18 (m, 2H, Alkenyl-*H*), 4.43-4.23 (m, 2H, Alkyl-*H*), 3.85-3.68 (m, 2H, Alkyl-*H*), 2.63 (s, 3H, Alkyl-*H*), 1.19 (s, 9H, Alkyl-*H*); **δ_C** (101 MHz, $CDCl_3$) 186.9, 135.9, 133.1, 128.8, 128.6, 128.1, 118.1, 54.2, 44.1, 41.8, 34.3, 27.9; **HRMS** (ESI^+, *m/z* calculated for $[C_{17}H_{27}N_3O_2SNa]^+$ 360.1716 $[M+Na]^+$), found 360.1714.

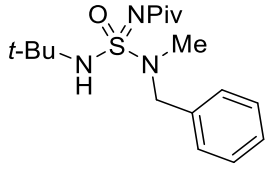
***N*-((Benzyl(methyl)amino)(butylamino)(oxo)-λ^6-sulfaneylidene)pivalamide (25t)**



Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23d** (28.6 mg, 0.1 mmol, 1.0 equiv.), *n*-butylamine (10 µL, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column chromatography (SiO_2, Petrol/EtOAc 15:1 to 13:1) to afford the desired product **25t** as a colourless oil (20.4 mg, 60%).

IR (thin film, ν_{max}/cm^{-1}) 3172, 3036, 2965, 1605, 1466, 1350, 1191, 1056, 988, 841, 741, 616; δ_H (400 MHz, $CDCl_3$) 7.85 (t, 1H, *J* = 6.0 Hz, N-*H*), 7.38-7.28 (m, 5H, Ar-*H*), 4.34-4.20 (m, 2H, Alkyl-*H*), 3.27-3.02 (m, 2H, Alkyl-*H*), 2.60 (s, 3H, Alkyl-*H*), 1.62-1.35 (m, 4H, Alkyl-*H*), 1.19 (s, 9H, Alkyl-*H*), 0.92 (t, 3H, *J* = 7.5 Hz, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 186.9, 136.0, 128.8, 128.6, 128.0, 54.2, 41.8, 41.4, 32.2, 31.7, 27.9, 20.1, 13.8; **HRMS** (ESI^+, *m/z* calculated for $[C_{17}H_{30}N_3O_2S]^+$ 340.2053 $[M+H]^+$), found 340.2054.

***N*-((Benzyl(methyl)amino)(tert-butylamino)(oxo)-λ^6-sulfaneylidene)pivalamide (25u)**



Prepared according to **General procedure K**, using sulfuramidimidoyl fluorides **23d** (28.6 mg, 0.1 mmol, 1.0 equiv.), *tert*-butylamine (11 µL, 0.105 mmol, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.). Purification was carried out using flash column

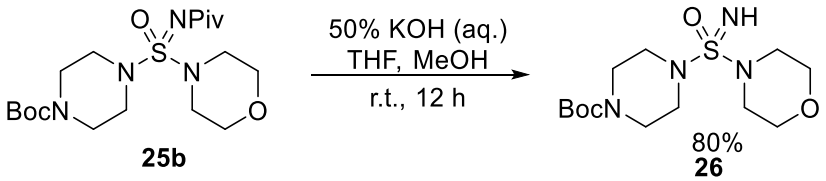
chromatography (SiO_2, Petrol/EtOAc 17:1 to 15:1) to afford the desired product **25u** as a colourless oil (9.5 mg, 28%).

IR (thin film, ν_{max}/cm^{-1}) 3213, 3064, 2971, 1601, 1479, 1311, 1274, 1209, 982, 829, 767, 610; δ_H (400 MHz, $CDCl_3$) 8.47 (br.s, 1H, N-*H*), 7.36-7.28 (m, 5H, Ar-*H*), 4.39-4.18 (m, 2H, Alkyl-*H*), 1.42 (s, 9H, Alkyl-*H*), 1.18 (s, 9H, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 186.6, 135.9, 128.8, 128.7, 128.0, 55.8, 54.2, 41.8, 34.3, 30.5, 28.0; HRMS (ESI^+, *m/z* calculated for $[C_{17}H_{30}N_3O_2S]^+$ 340.2053 $[M+H]^+$), found 340.2050.

5.3.12 Derivatisation of Iminosulfamides

5.3.12.1 Deprotection of Pivaloyl Group

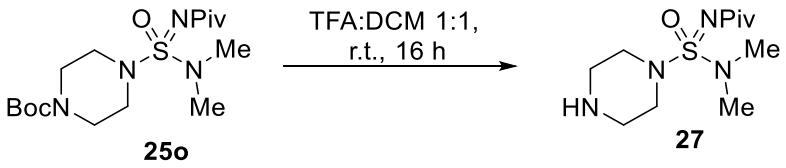
Procedure adapted from Y. Aota, T. Kano and K. Maruoka, *Angew. Chem. Int. Ed.*, 2019, **58**, 17661-17665.[173]



Iminosulfamide **25b** (41.9 mg, 0.1 mmol) was dissolved in THF (1 mL) and MeOH (1 mL). 50% KOH (aq.) (0.5 mL) was added to the solution and the reaction mixture was stirred for 12 hours at room temperature. The crude mixture was diluted with CH_2Cl_2 (5 mL), washed with brine (5 mL), extracted with CH_2Cl_2 (3×5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (SiO_2, Petrol/EtOAc 1:1 to 1:3 to 0:1) to afford the desired product **26** as a white solid. (26.8 mg, 80%)

m.p. 86-88 °C ($CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3282, 2975, 1694, 1420, 1249, 1115, 926, 721; δ_H (500 MHz, $CDCl_3$) 3.72-3.70 (m, 4H, Alkyl-*H*), 3.48-3.46 (m, 4H, Alkyl-*H*), 3.25-3.23 (m, 8H, Alkyl-*H*), 2.45 (br.s, 1H, N-*H*), 1.45 (s, 9H, Alkyl-*H*); δ_C (126 MHz, $CDCl_3$) 154.5, 80.5, 66.6, 47.1, 46.8, 28.5; **HRMS** (ESI^+, *m/z* calculated for $[C_{13}H_{27}N_4O_4S]^+$ 335.1748 $[M+H]^+$), found 335.1751.

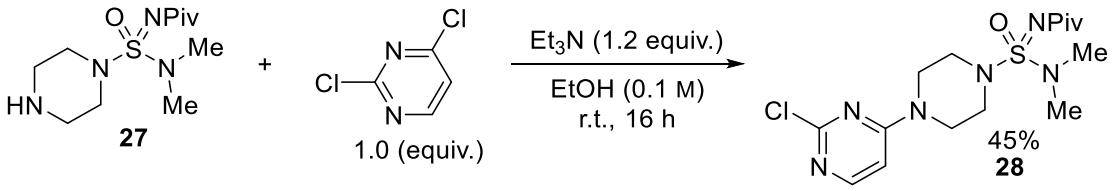
5.3.12.2 Deprotection of Boc Group



Procedure adapted from J. C. Verheijen, K. Yu, L. Toral-Barza, I. Hollander and A. Zask, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 375-379.[194]

Iminosulfamide **25o** (33.8 mg, 0.09 mmol) was dissolved in DCM (0.9 mL). TFA (0.9 mL) was added to the solution and the reaction mixture was stirred for 16 hours at room temperature. The crude mixture was diluted with CH_2Cl_2 (5 mL), quenched with saturated $NaHCO_3$, extracted with CH_2Cl_2 (3×5 mL), washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was used directly in the next reaction without further purification.

5.3.12.3 SnAr



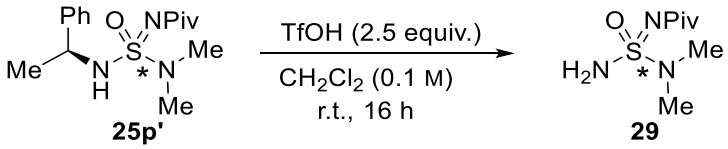
Procedure adapted from Z. Zhang, Z. Guo, X. Xu, D. Cao, H. Yang, Y. Li, Q. Shi, Z. Du, X. Guo, X. Wang, D. Chen, Y. Zhang, L. Chen, K. Zhou, J. Li, M. Geng, X. Huang and B. Xiong, *J. Med. Chem.*, 2021, **64**, 16650-16674. [195]

The crude mixture was dissolved in EtOH (0.9 mL, 0.1M). Et_3N (15 µL, 0.108 mmol, 1.2 equiv.) was added, followed by the addition of 2,4-Dichloropyrimidine (13.4 mg, 0.09 mmol, 1.0 equiv.). The solution was stirred 16 hours at room temperature. The crude mixture was diluted with EtOAc (5 mL), washed with saturated NH_4Cl (aq.) (5 mL), extracted with EtOAc (3×5 mL), and concentrated *in vacuo*. The crude

mixture was purified by flash column chromatography (SiO_2, Petrol/EtOAc 1:1 to 1:3) to afford the desired product **28** as a colourless oil. (15.8 mg, 45%)

IR (thin film, ν_{max}/cm^{-1}) 3099, 2966, 1632, 1586, 1355, 1236, 1172, 977, 852, 694; δ_H (400 MHz, $CDCl_3$) 8.08 (d, 1H, *J* = 6 Hz, Ar-*H*), 6.41 (d, 1H, *J* = 6 Hz, Ar-*H*), 3.77-3.70 (m, 4H, Alkyl-*H*), 3.44-3.32 (m, 4H, Alkyl-*H*), 2.89 (s, 6H, Alkyl-*H*), 1.18 (s, 9H, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 186.6, 162.6, 161.0, 157.9, 101.5, 45.6, 43.7, 41.8, 38.1, 27.9; **HRMS** (ESI^+, *m/z* calculated for $[C_{13}H_{27}N_4O_4S]^+$ 335.1748 $[M+H]^+$), found 335.1751.

5.3.12.4 Benzyl deprotection

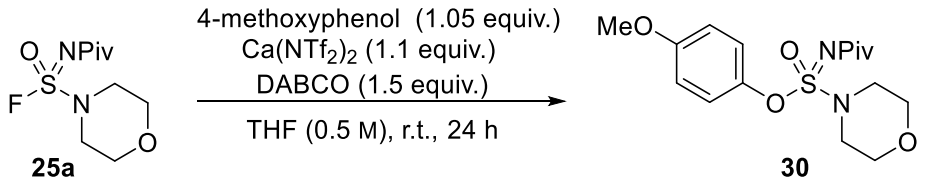


Iminosulfamide **25p'** (18.1mg, 0.058 mmol, 80% purity, 1.0 equiv.) was dissolved in DCM (0.46 mL). Triflic acid (10 µL, 0.116 mmol, 2.0 equiv.) was added to the solution and the reaction mixture was stirred for 16 hours at room temperature. The crude mixture was diluted with CH_2Cl_2 (3 mL), quenched with saturated $NaHCO_3$, extracted with CH_2Cl_2 (3×5 mL), washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (SiO_2, Petrol/EtOAc 5:1 to 3:1) to afford the desired product **29** as a white solid. (3.0 mg, 25%)

m.p. 84-86 °C ($CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3305, 2956, 1613, 1477, 1318, 1249, 1089, 946, 848, 782, 694; δ_H (400 MHz, $CDCl_3$) 5.98 (br. s, 2H, N-*H*), 2.81 (s, 6H, Alkyl-*H*), 1.20 (s, 9H, Alkyl-*H*); δ_C (101 MHz, $CDCl_3$) 187.7, 41.9, 37.9, 27.8; **HRMS** (ESI^+, *m/z* calculated for $[C_7H_{17}N_3O_2SK]^+$ 246.0673 $[M+K]^+$), found 246.0662; Enantiomeric excess: >99% e.e.;

HPLC conditions: Column: Daicel Chiralpak IA column; Solvent n-hexane/IPA (95:5); flow rate:1 mLmin^{-1}, 25 °C, UV detection wavelength: 222 nm, retention time: 11.737 min.

5.3.13 SuFEx Reaction with Oxygen Nucleophiles



Sulfuramidimidoyl fluorides **23** (0.1 mmol, 1.0 equiv.), 4-methoxyphenol (13.0 mg, 1.05 equiv.), $Ca(NTf_2)_2$ (66.0 mg, 0.11 mmol, 1.1 equiv.) and DABCO (16.8 mg, 0.15 mmol, 1.5 equiv.) was added to an oven-dried reaction tube. The reaction tube was evacuated and back-filled with nitrogen three times. Anhydrous, THF (0.2 mL, 0.5 M) was added, and the reaction mixture was stirred at room temperature for 24 hours. The crude mixture was diluted with EtOAc (2 mL), washed with saturated NH_4Cl (aq.) (3 mL), extracted with EtOAc (2 × 3 mL), washed with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (SiO_2, Petrol/EtOAc) to afford the desired product **30** as a colourless oil (32.1 mg, 90%).

IR (thin film, ν_{max}/cm^{-1}) 3056, 2967, 1663, 1502, 1282, 1145, 1004, 848, 788, 638; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$)), 7.22 (d, 2H, *J* = 9.0 Hz, Ar-*H*), 6.88 (d, 2H, *J* = 9.0 Hz, Ar-*H*), 3.80 (s, 3H, Alkyl-*H*), 3.77-3.74 (m, 4H, Alkyl-*H*), 3.49-3.35 (m, 4H, Alkyl-*H*), 1.15 (s, 9H, Alkyl-*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 185.7, 158.5, 143.1, 123.6, 114.6, 66.1, 55.8, 47.0, 42.1, 27.6; **HRMS** (ESI^+, *m/z* calculated for $[C_{16}H_{25}N_2O_5S]^+$ 357.1479 $[M+H]^+$), found 357.1485.

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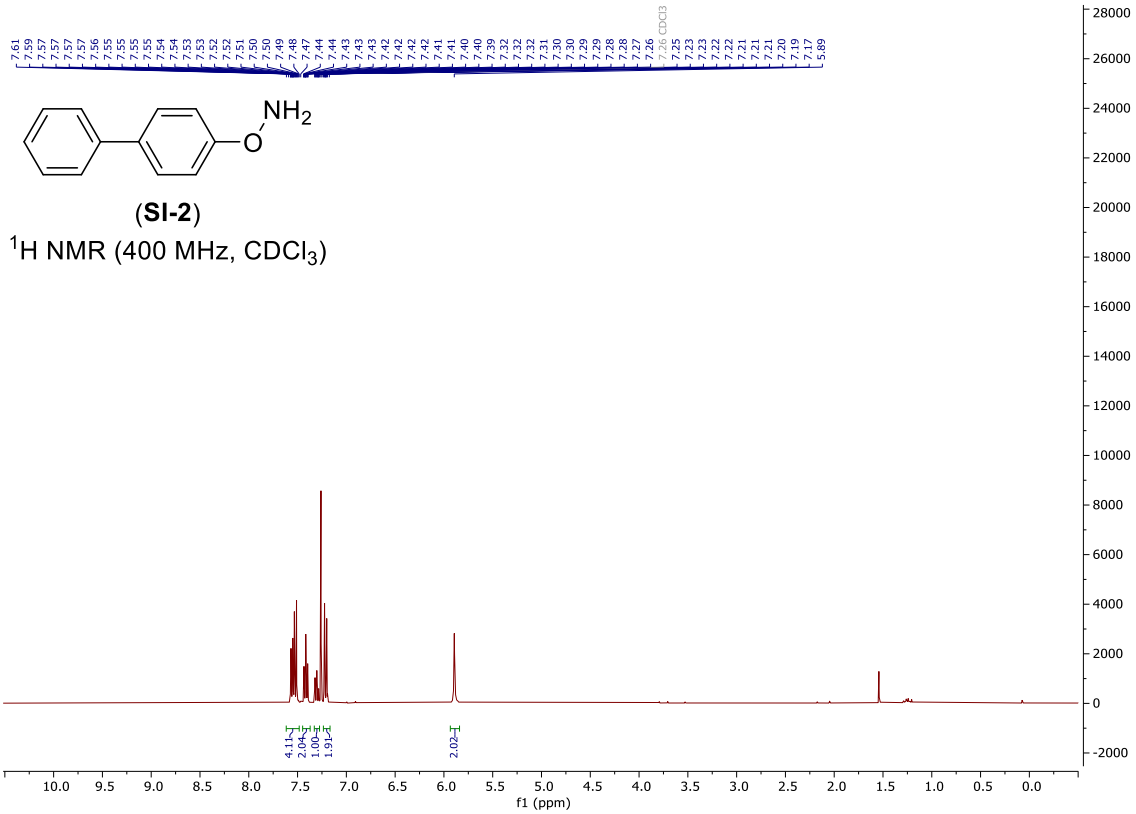
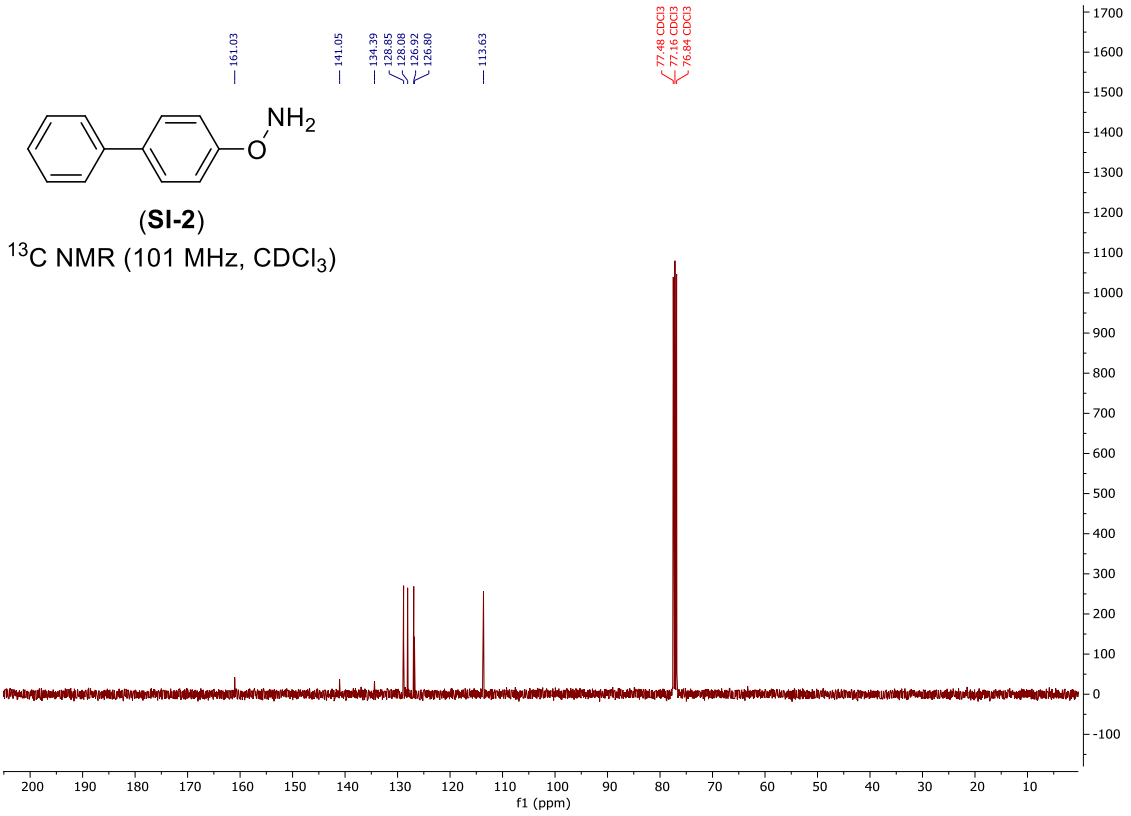
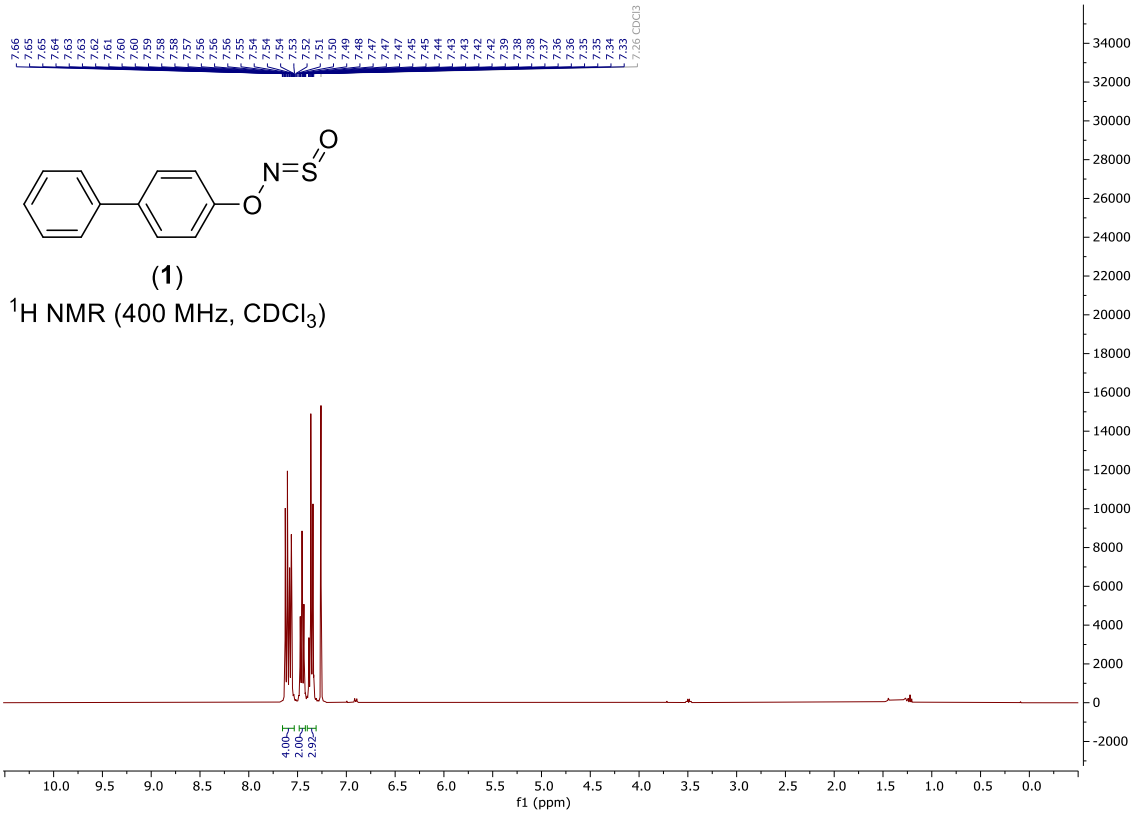
NMR Spectra

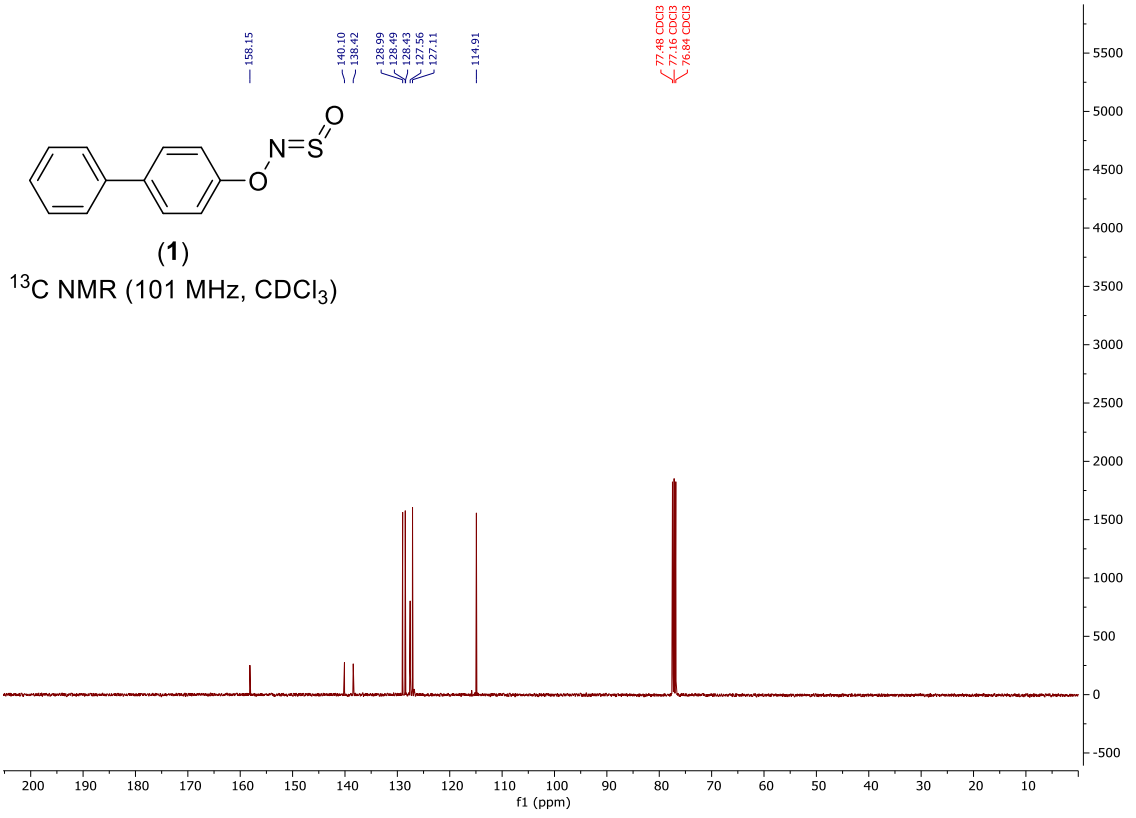
***O*-([1,1'-biphenyl]-4-yl)hydroxylamine (SI-2), BiPhONH2**



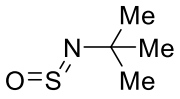

161.03
141.05
134.39
128.85
128.08
126.92
126.80
113.63
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
NH2
O
(SI-2)
13C NMR (101 MHz, CDCl3)
f1 (ppm)

(([1,1'-Biphenyl]-4-yloxy)imino)-lλ^4-sulfanone, BiPhONSO (1)





(*tert*-Butylimino)-λ^4-sulfanone(SI-3)



(**SI-3**)

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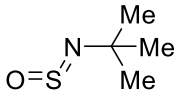
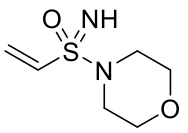


(**SI-3**)

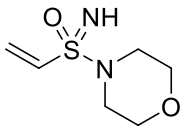
^{13}C NMR (126 MHz, CDCl3)

4-(Vinylsulfonimidoyl)morpholine (2a)



(**2a**)

^{1}H NMR (400 MHz, $CDCl_3$)



(**2a**)

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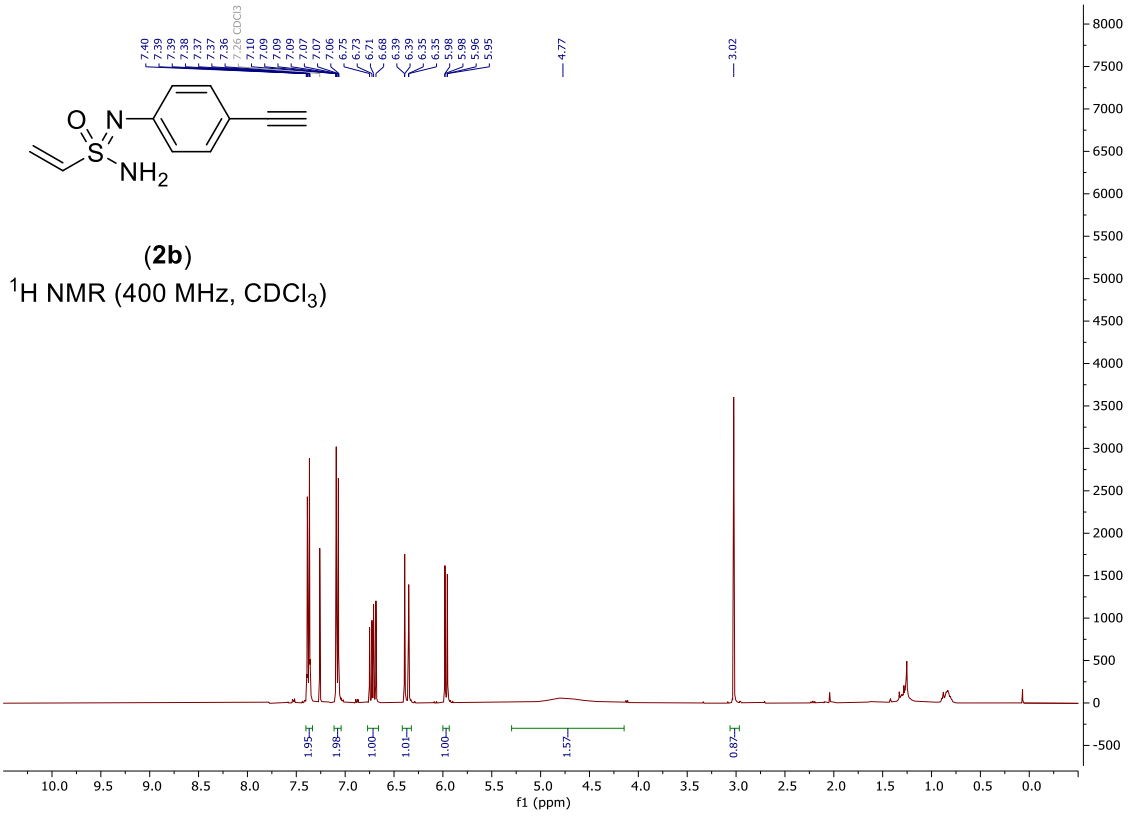
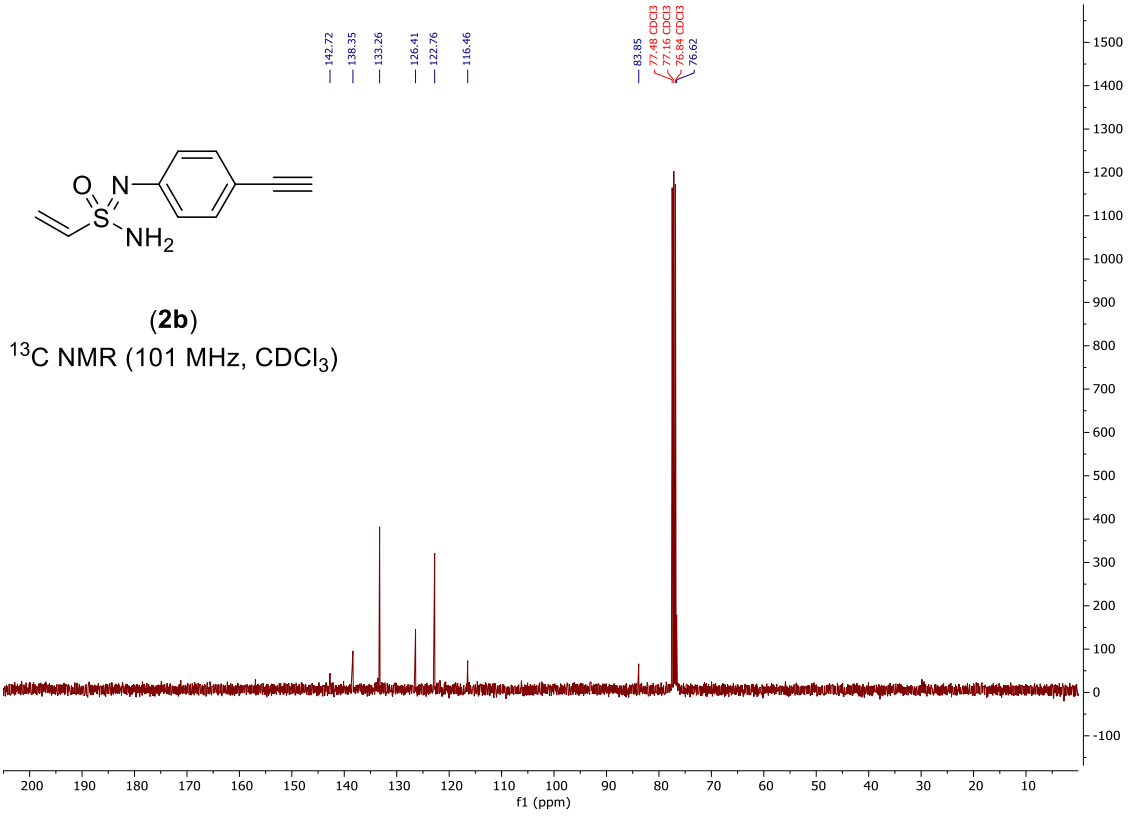
N'-(4-Ethynylphenyl)ethenesulfonimidamide (2b)



(**2b**)

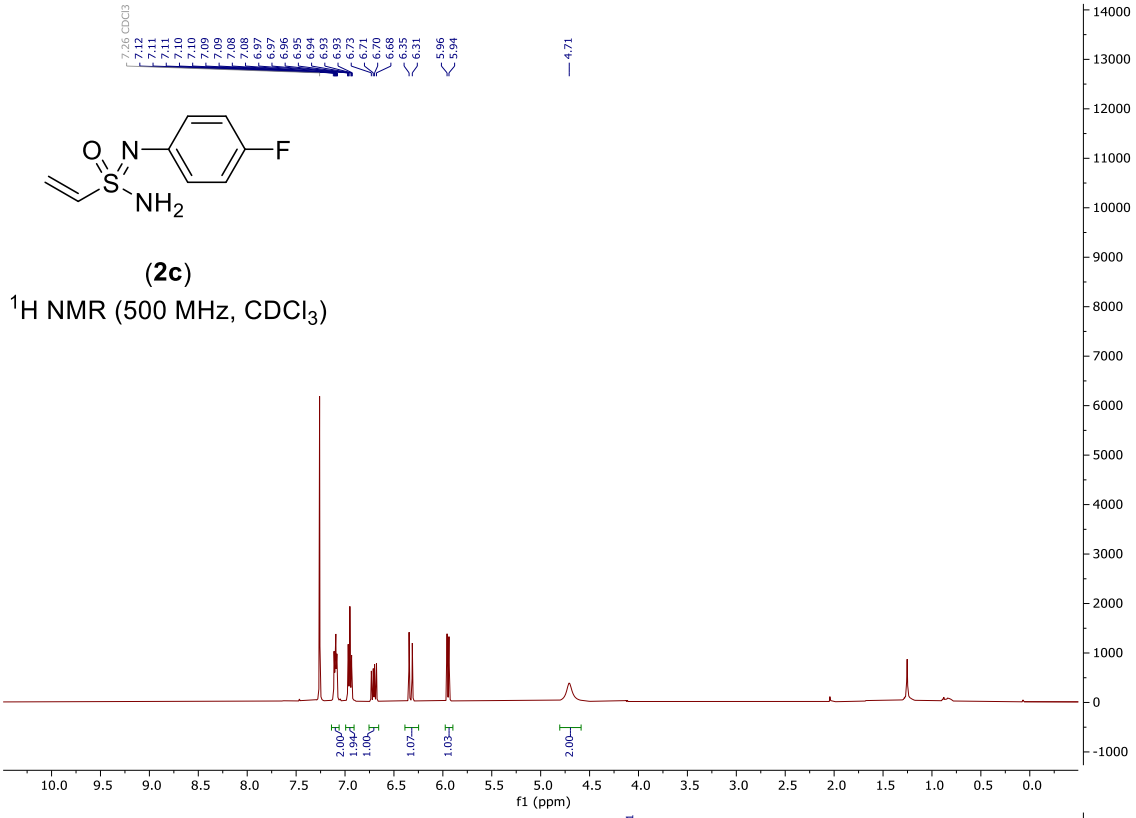
^{1}H NMR (400 MHz, $CDCl_3$)



(**2b**)

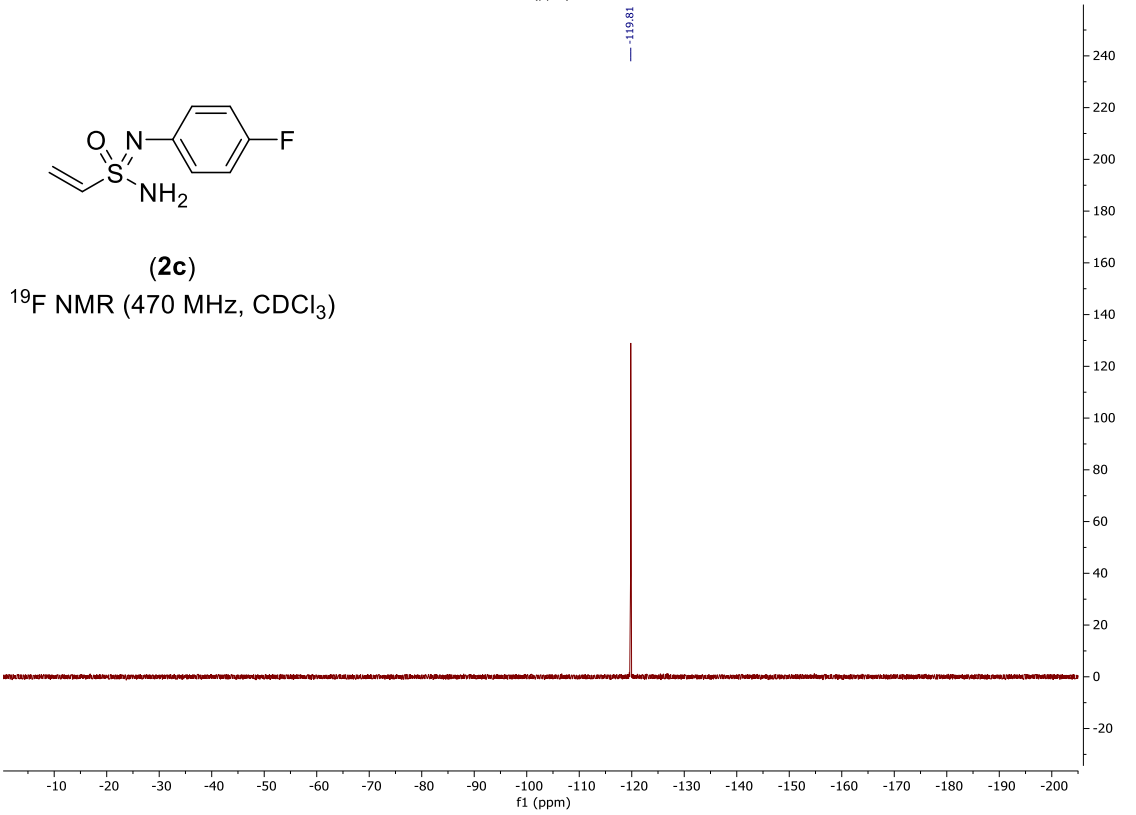
^{13}C NMR (101 MHz, $CDCl_3$)

N-(4-Fluorophenyl)ethenesulfonimidamide (2c)



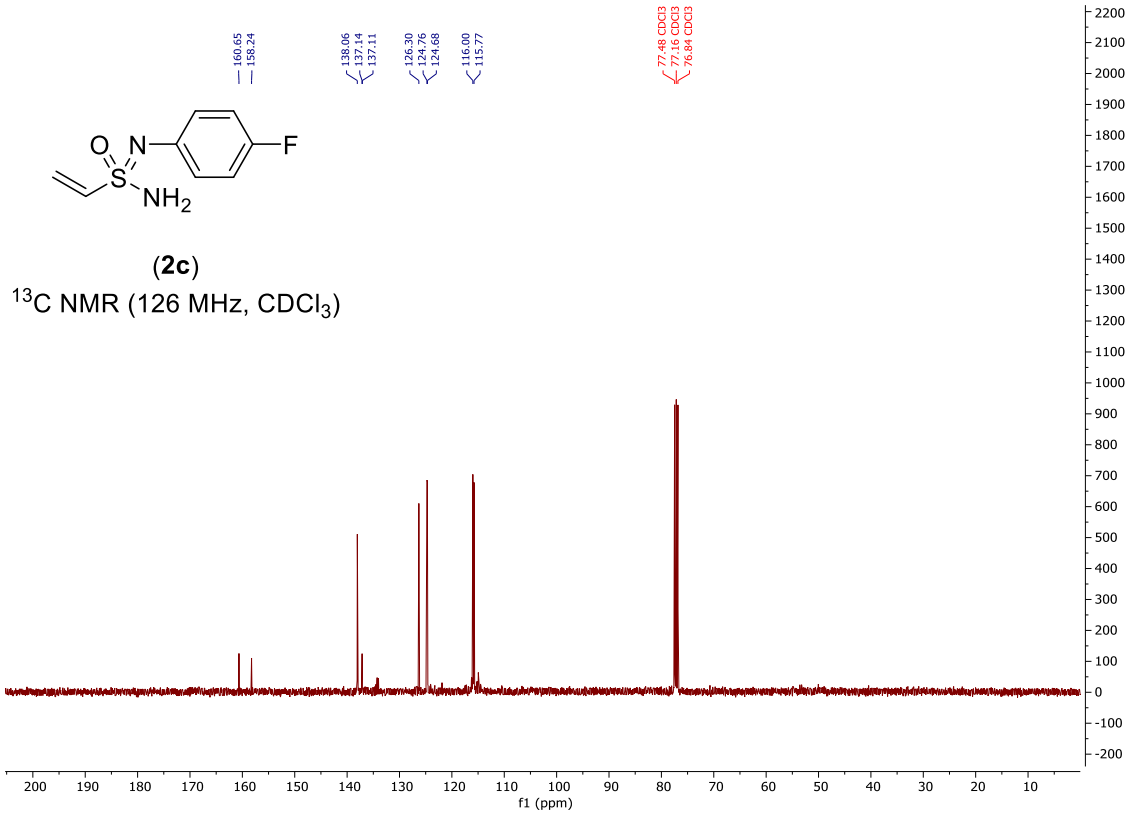
(**2c**)

^{1}H NMR (500 MHz, $CDCl_3$)



(**2c**)

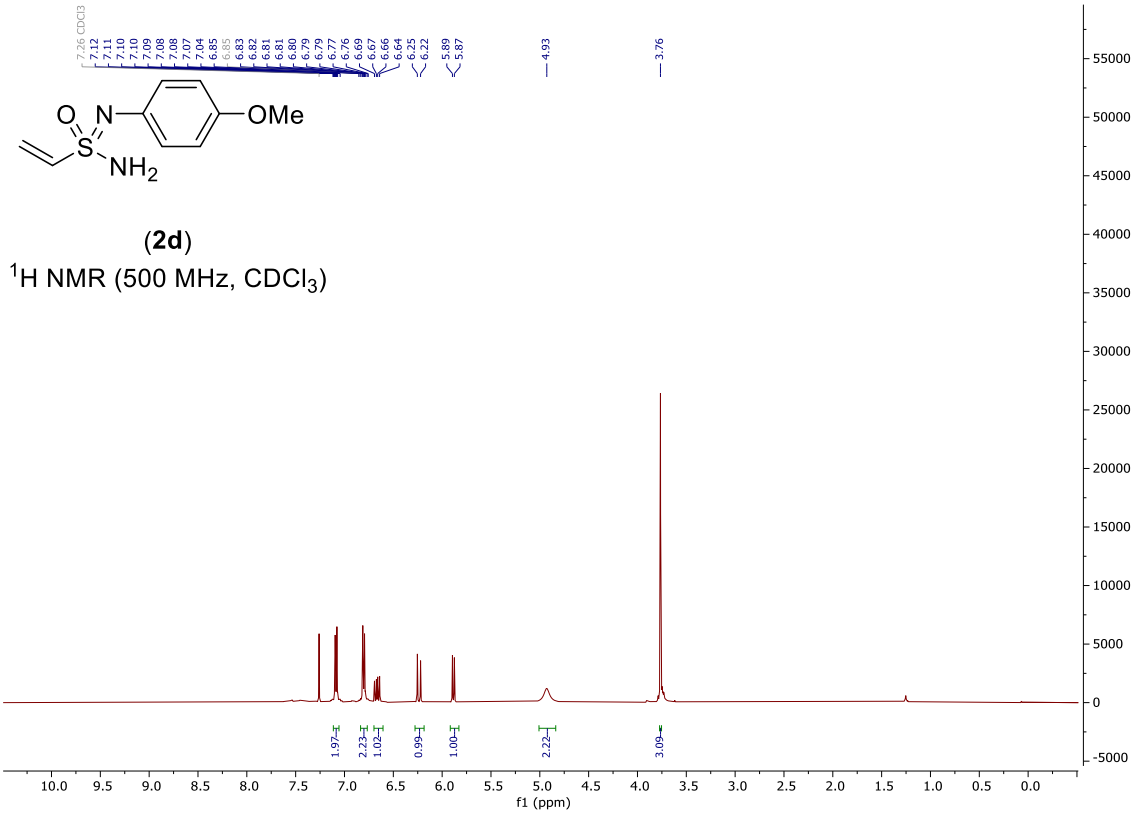
^{19}F NMR (470 MHz, $CDCl_3$)



(**2c**)

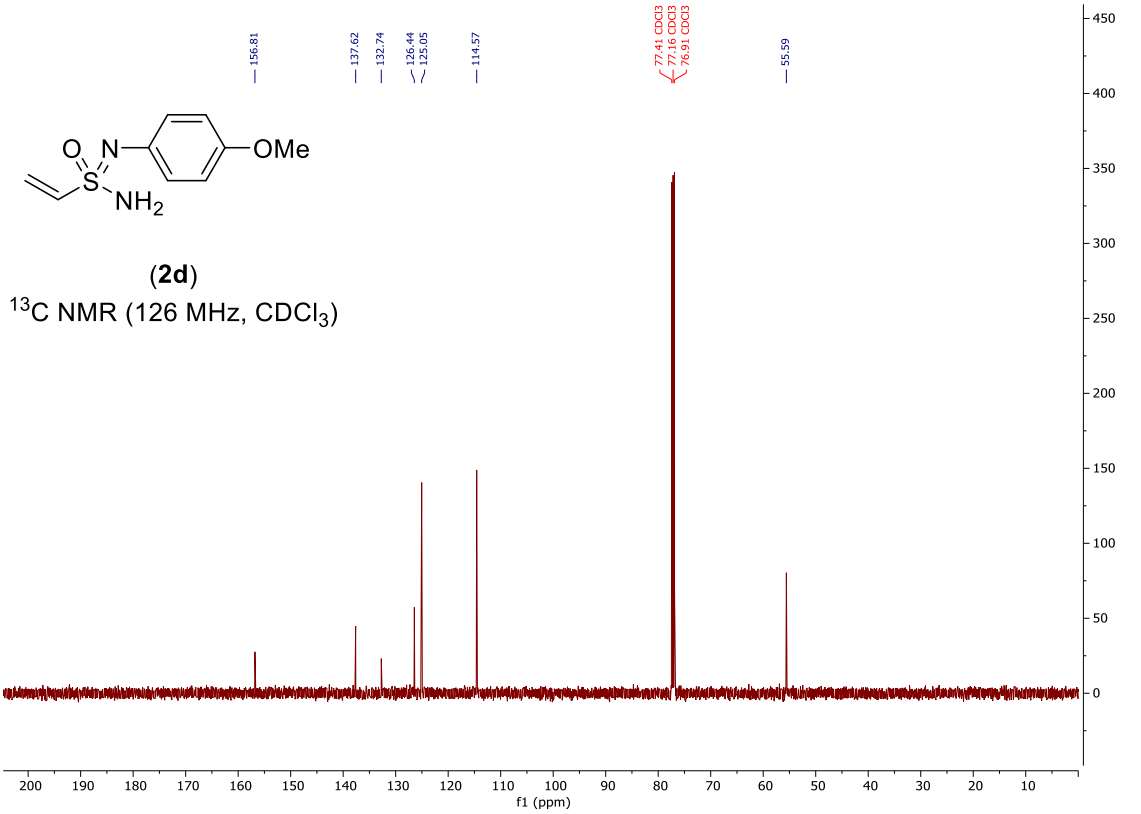
^{13}C NMR (126 MHz, $CDCl_3$)

N'-(4-Methoxyphenyl)ethenesulfonimidamide (2d)



(**2d**)

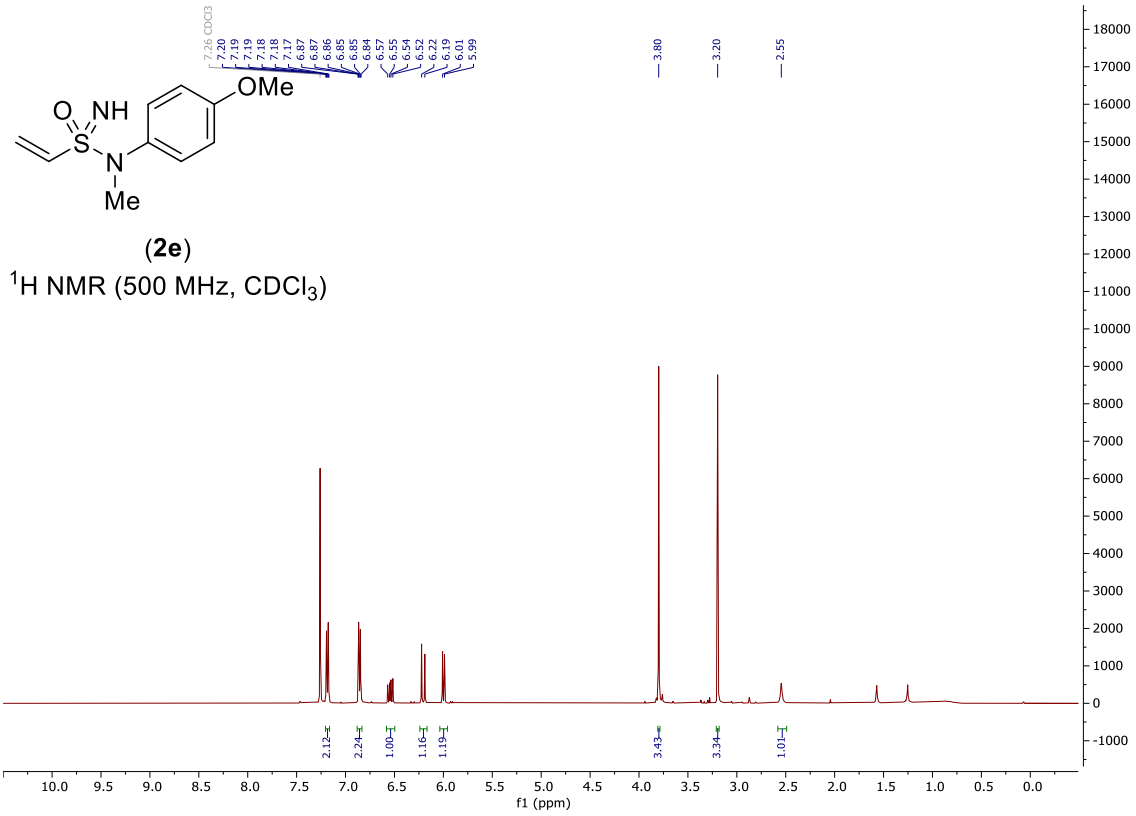
^{1}H NMR (500 MHz, $CDCl_3$)



(**2d**)

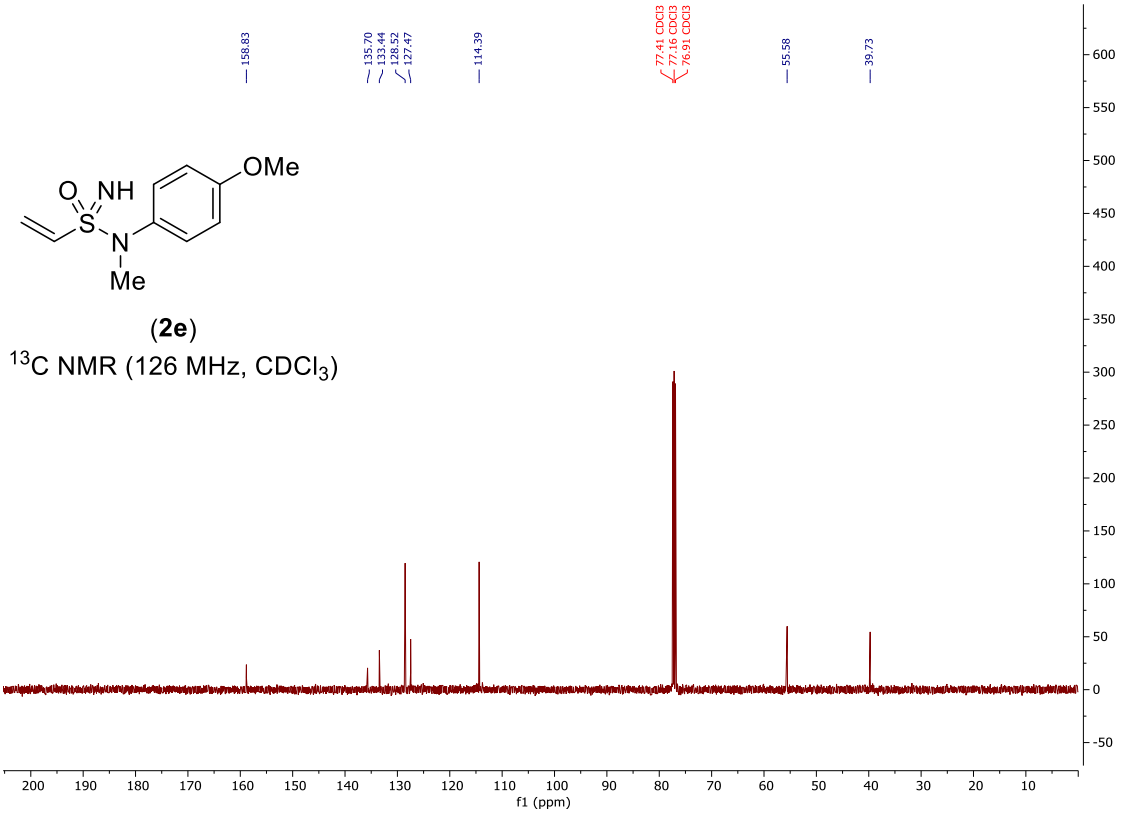
^{13}C NMR (126 MHz, $CDCl_3$)

_N_-(4-Methoxyphenyl)-_N_-methylethenesulfonimidamide (2e)



(**2e**)

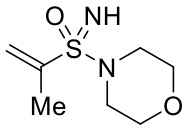
^{1}H NMR (500 MHz, $CDCl_3$)



(**2e**)

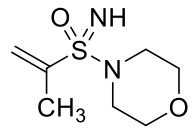
^{13}C NMR (126 MHz, $CDCl_3$)

4-(Prop-1-en-2-ylsulfonimidoyl)morpholine (2f)



(**2f**)

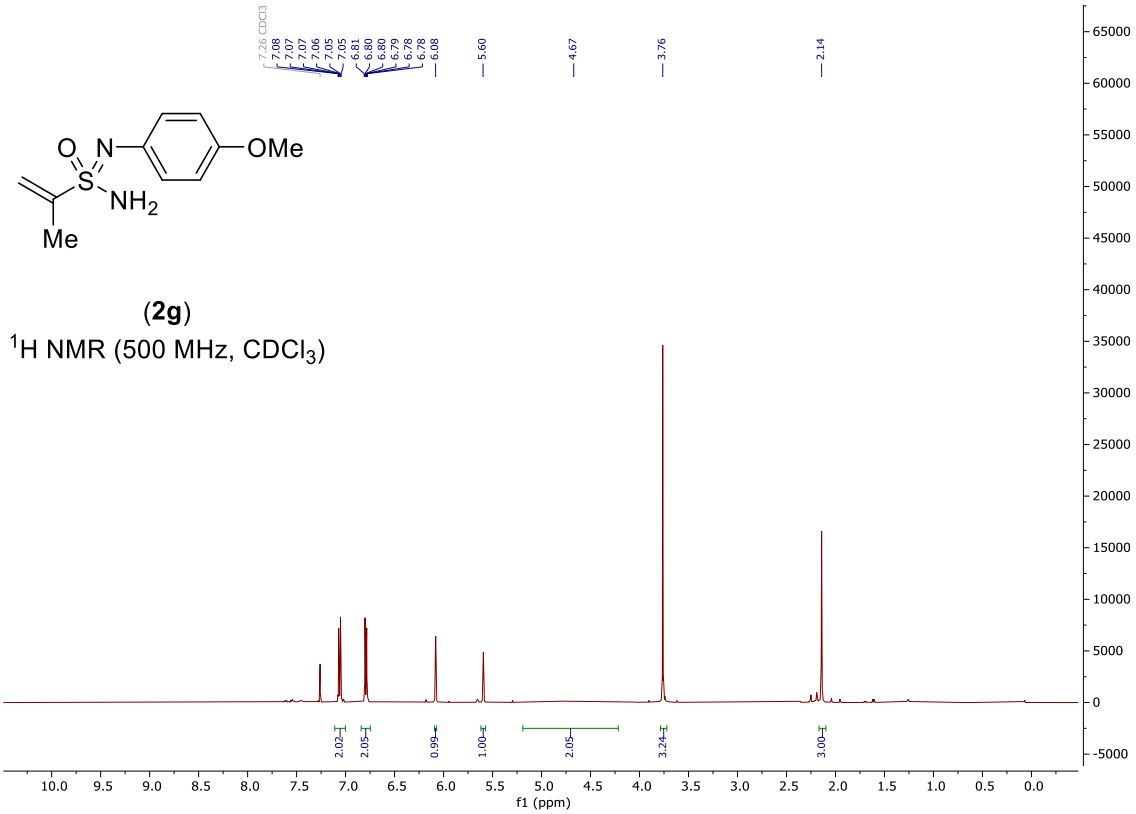
^{1}H NMR (400 MHz, $CDCl_3$)



(**2f**)

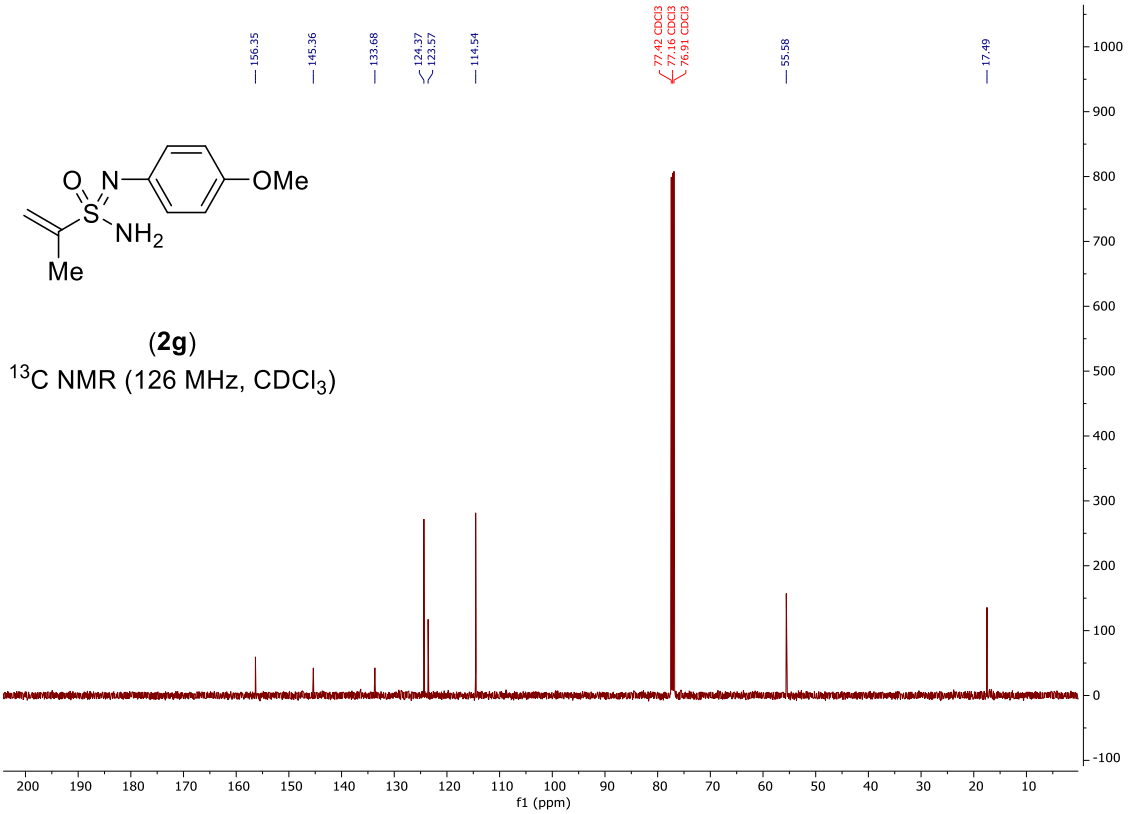
^{13}C NMR (101 MHz, $CDCl_3$)

_N_'-(4-Methoxyphenyl)prop-1-ene-2-sulfonimidamide (2g)



(**2g**)

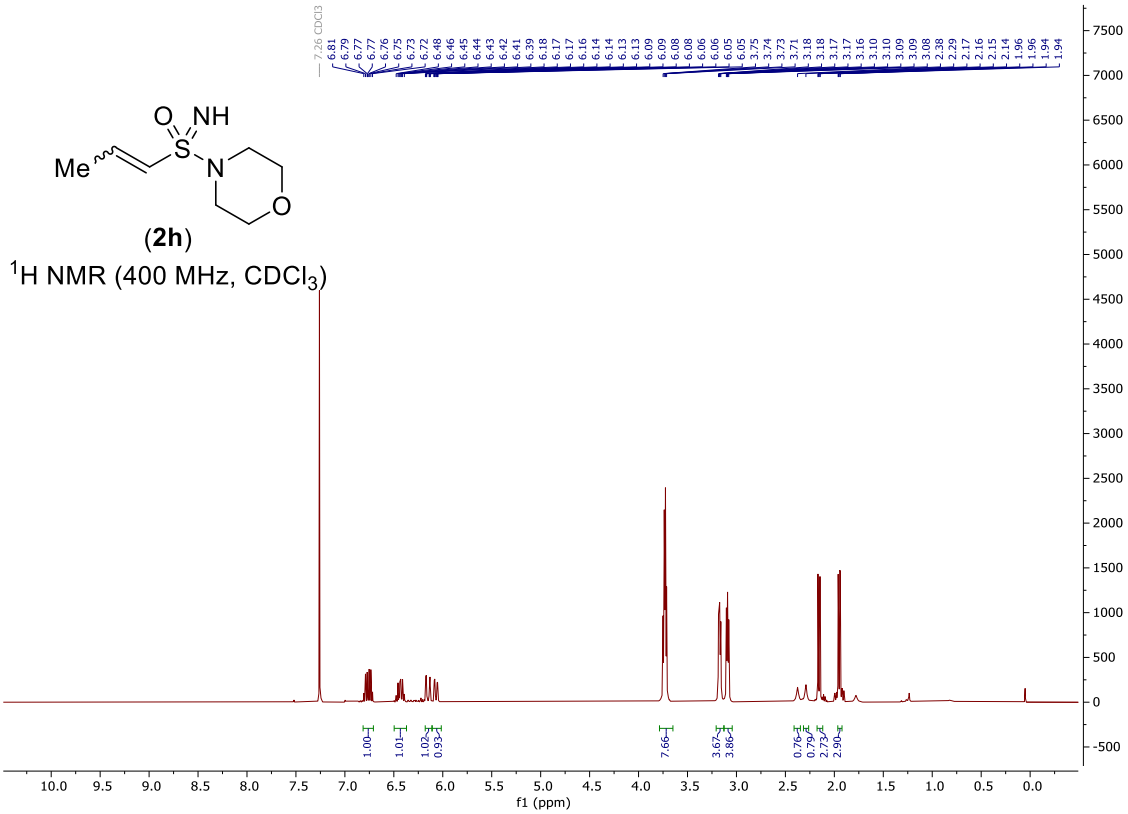
^{1}H NMR (500 MHz, $CDCl_3$)

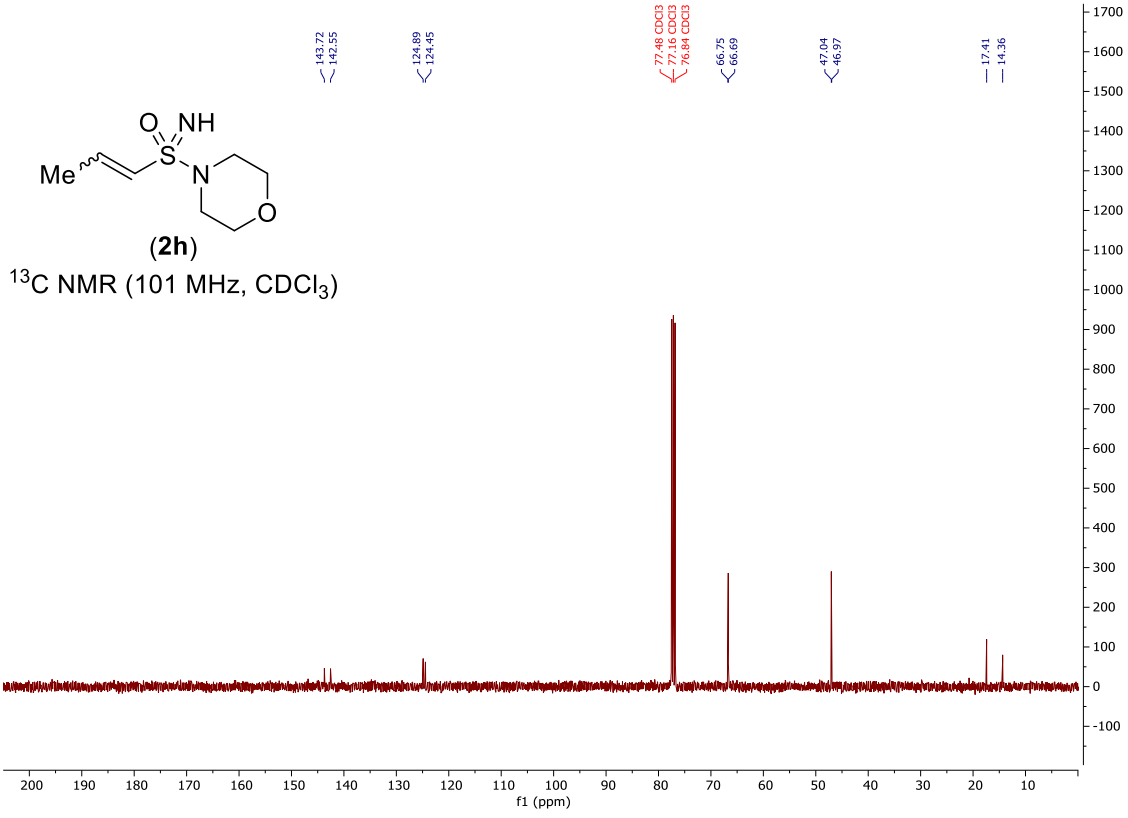


(**2g**)

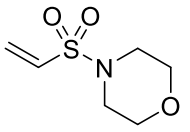
^{13}C NMR (126 MHz, $CDCl_3$)

4-(Prop-1-en-1-ylsulfonimidoyl)morpholine (2h)



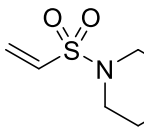


4-(Vinylsulfonyl)morpholine (12)



(**12**)

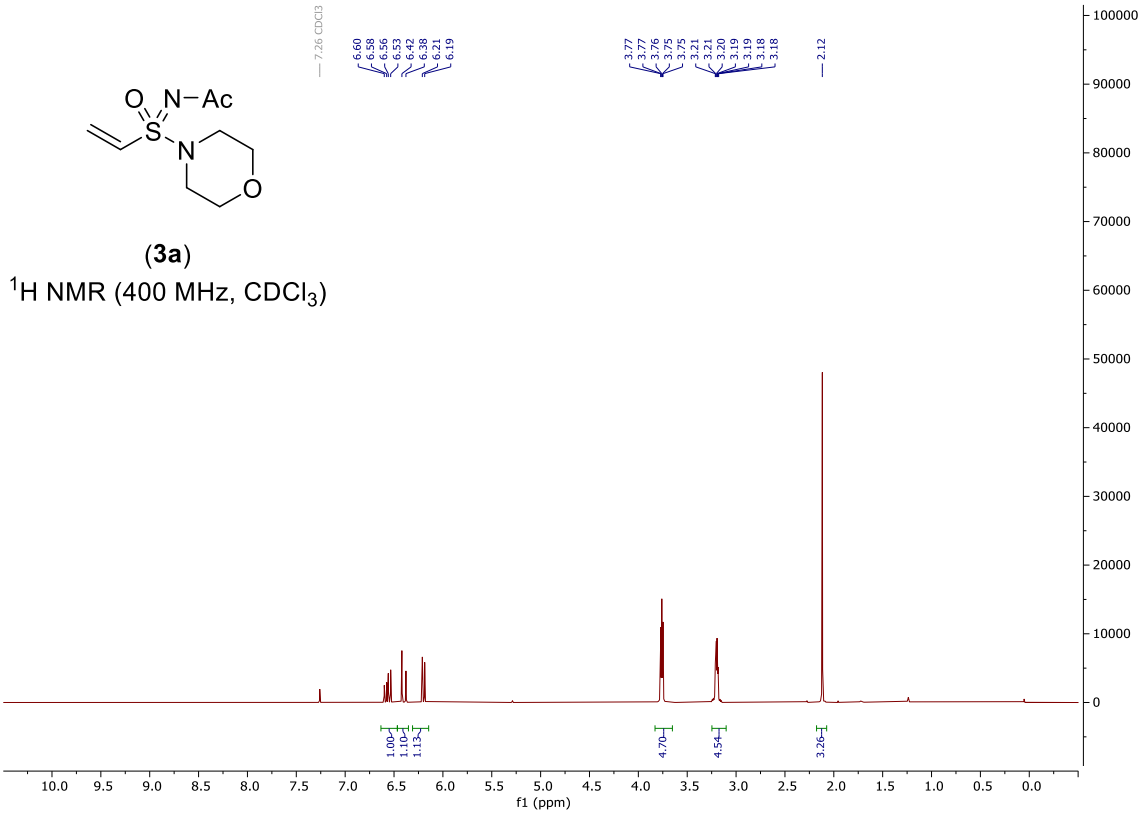
^{1}H NMR (500 MHz, $CDCl_3$)

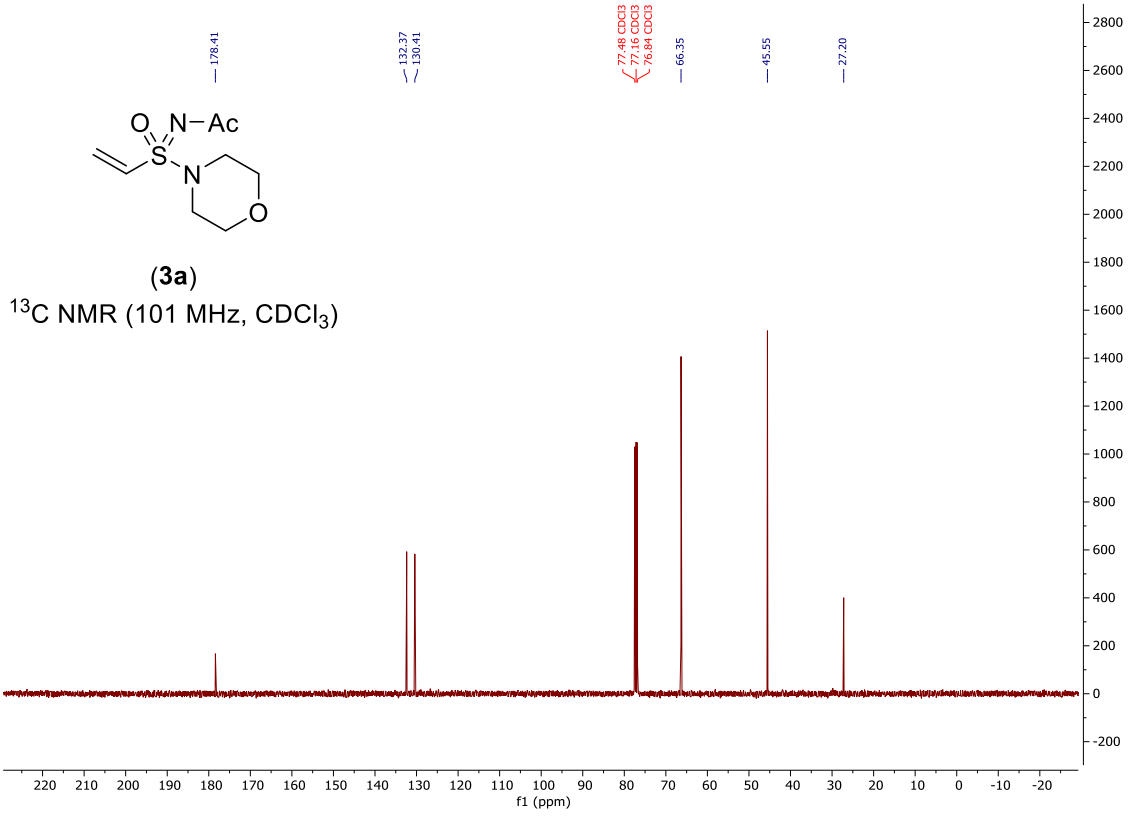


(**12**)

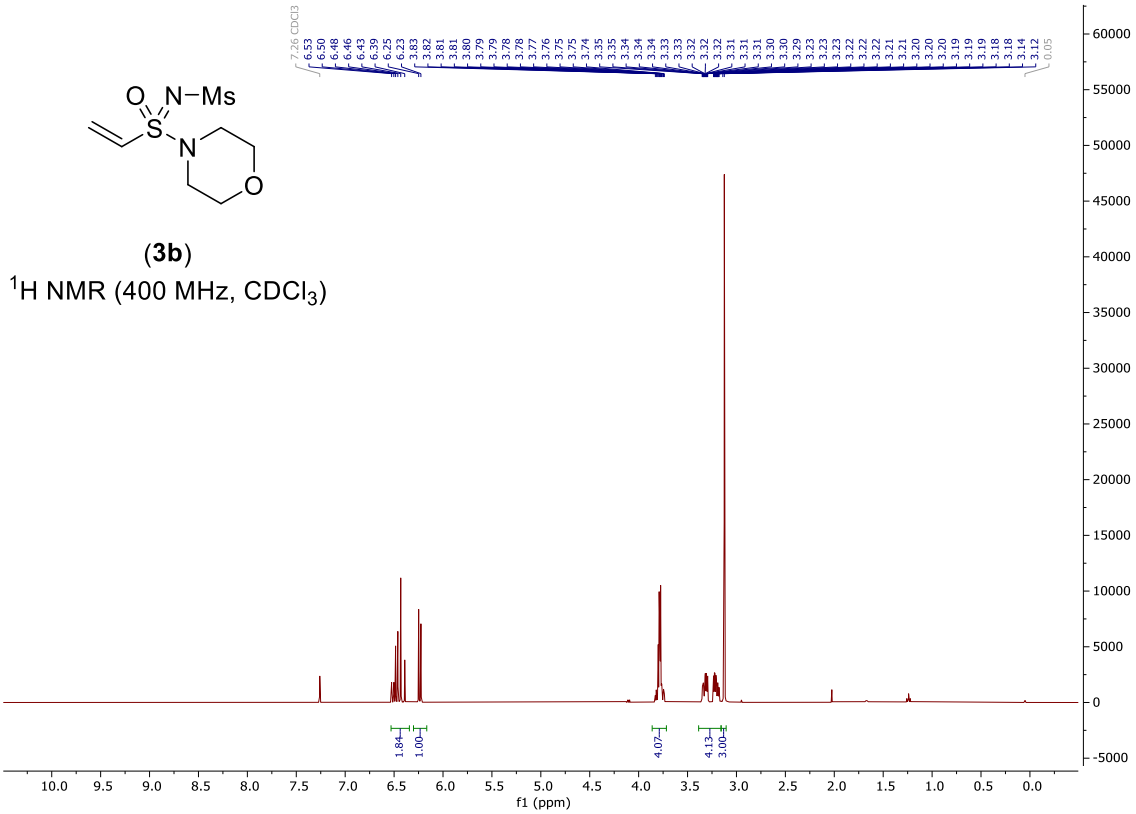
^{13}C NMR (126 MHz, $CDCl_3$)

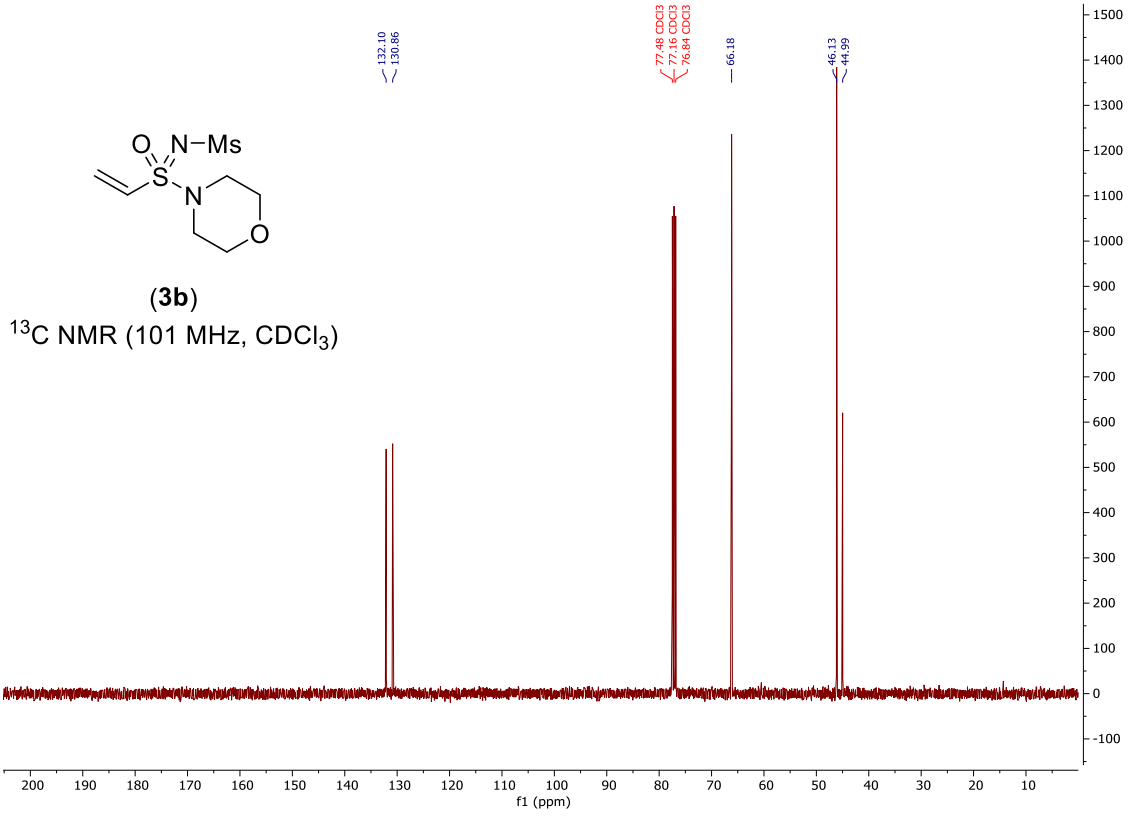
_N_-(Morpholino(oxo)(vinyl)-λ^6-sulfaneylidene)acetamide (3a)



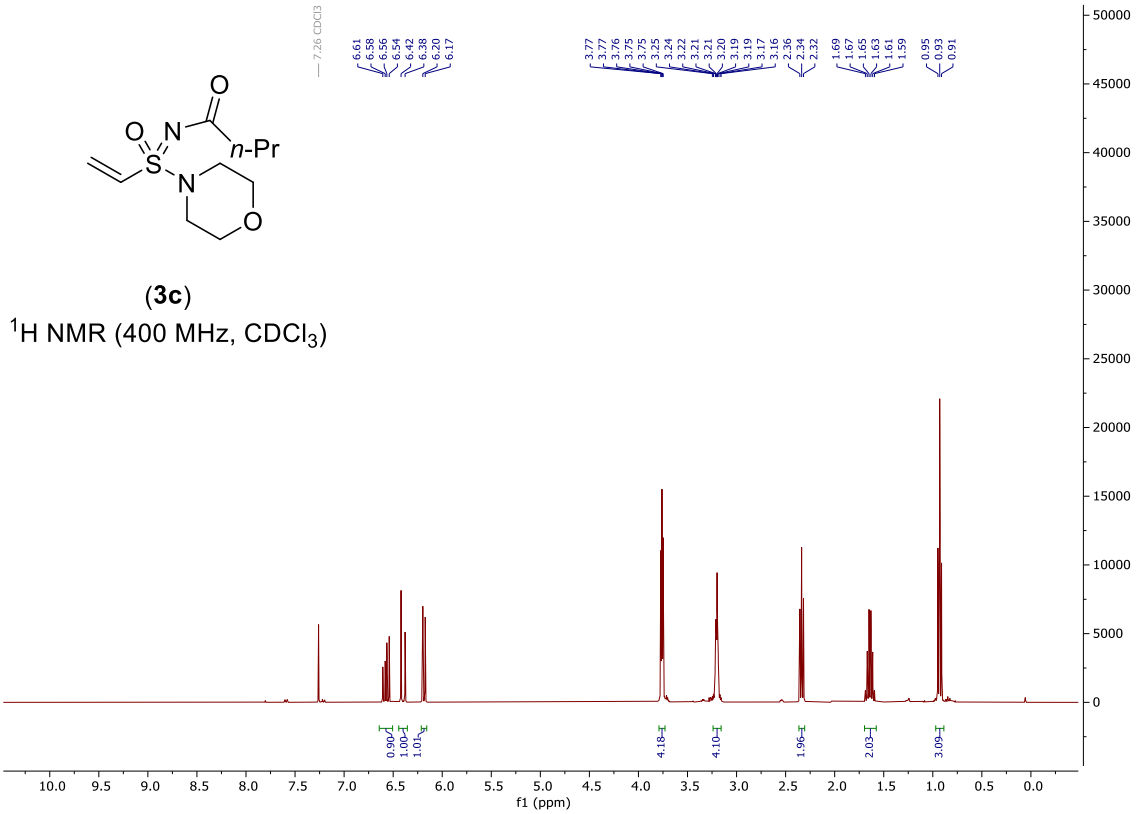


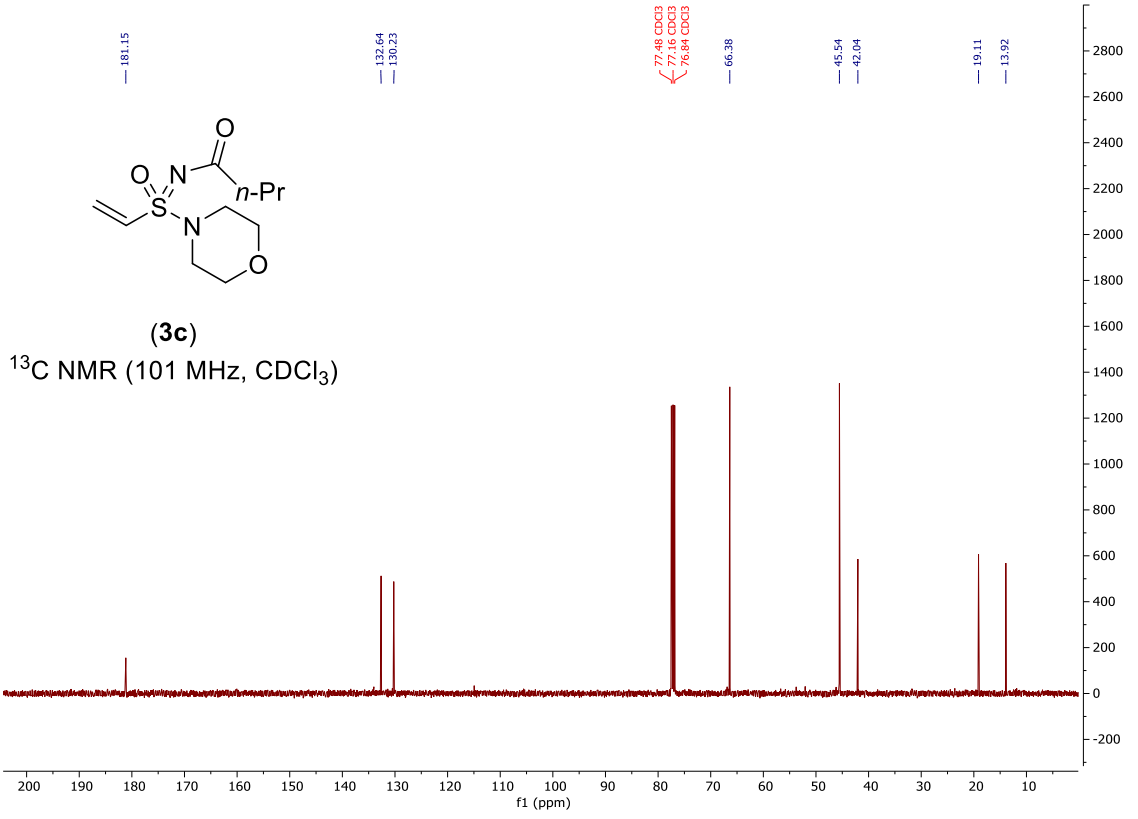
_N_-(Morpholino(oxo)(vinyl)- λ^6-sulfaneylidene)methanesulfonamide (3b)



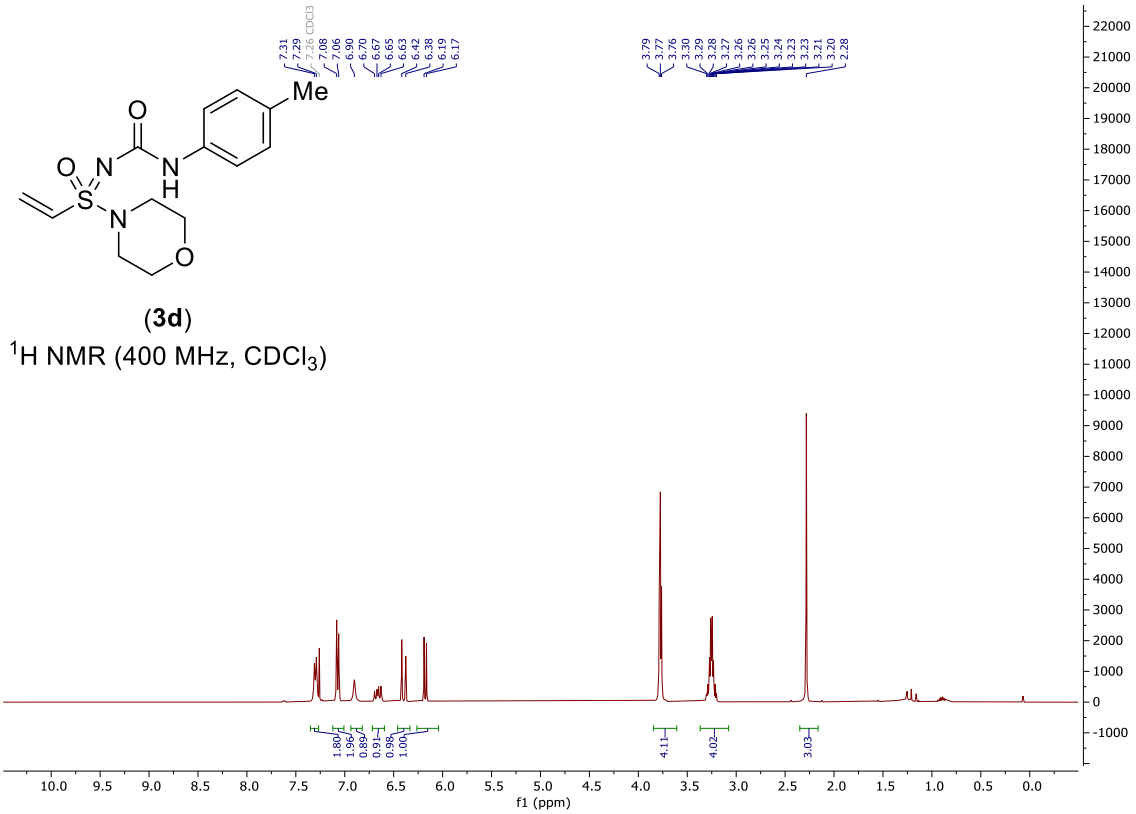


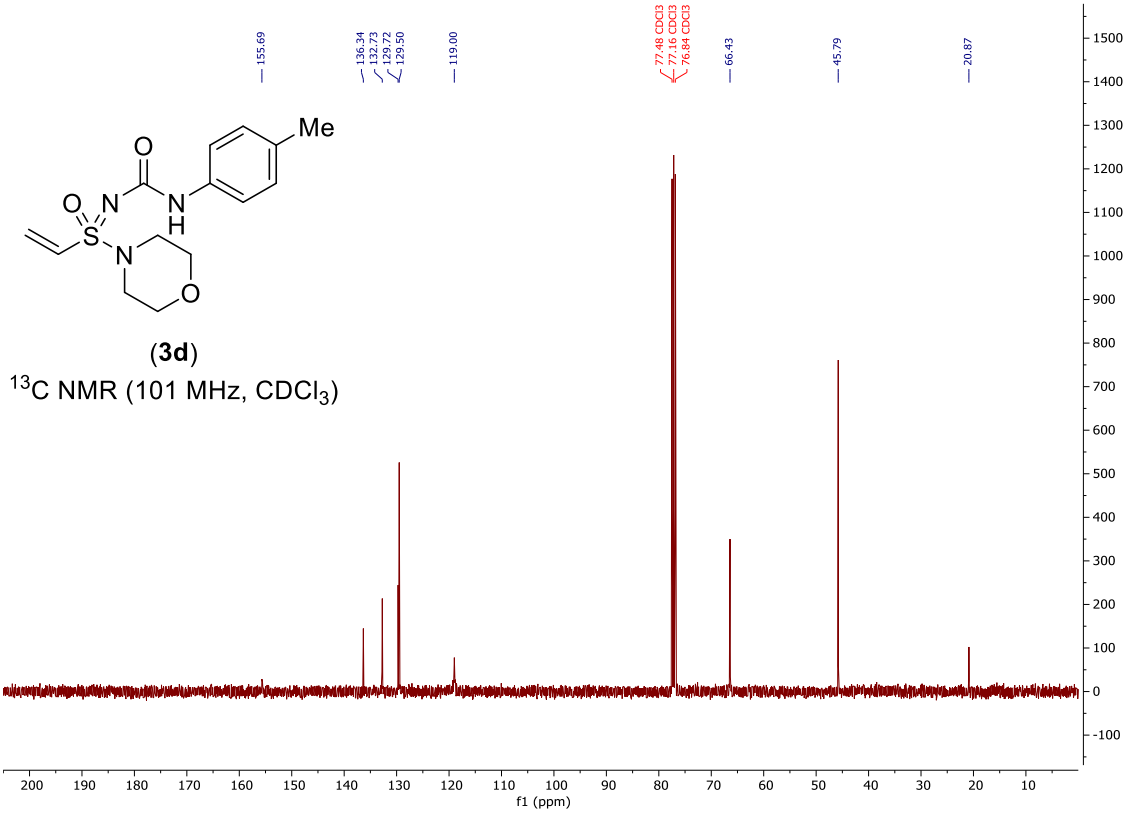
_N_-(Morpholino(oxo)(vinyl)-λ^6-sulfaneylidene)butyramide (3c)



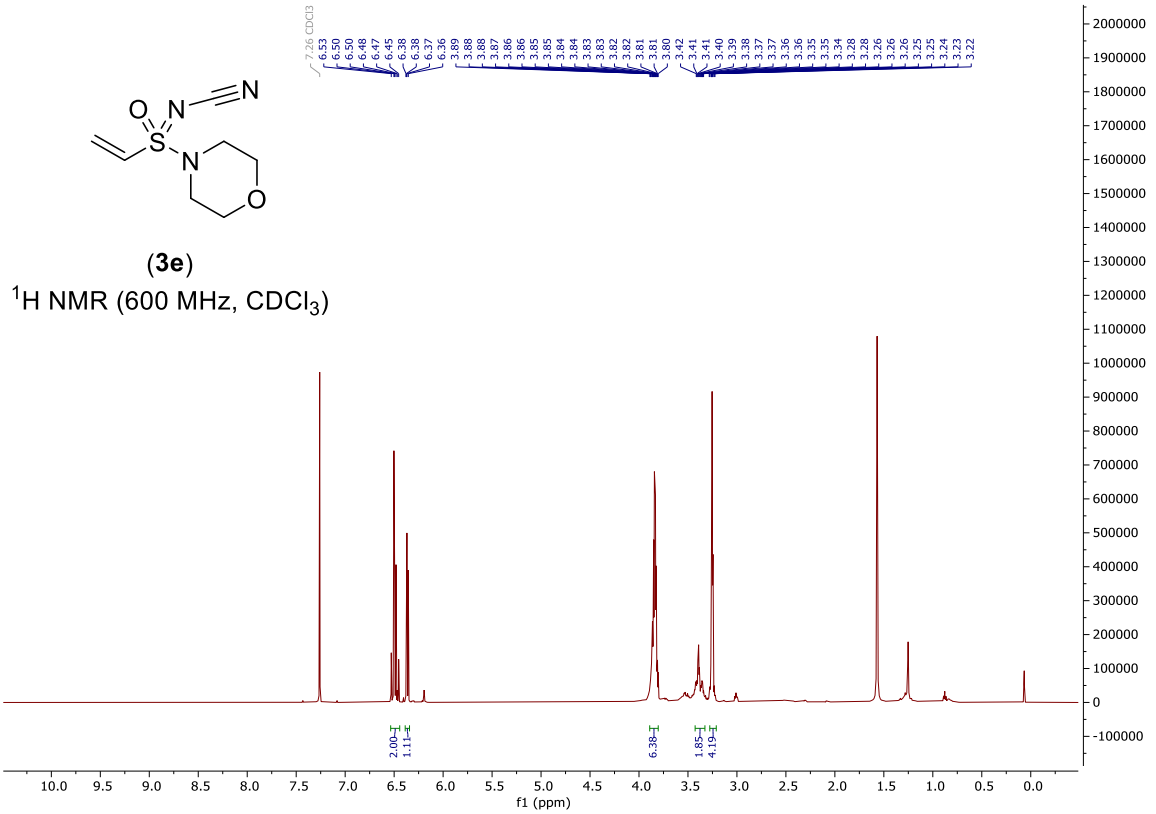


1-(Morpholino(oxo)(vinyl)- λ^6-sulfaneylidene)-3-(*p*-tolyl)urea (3d)



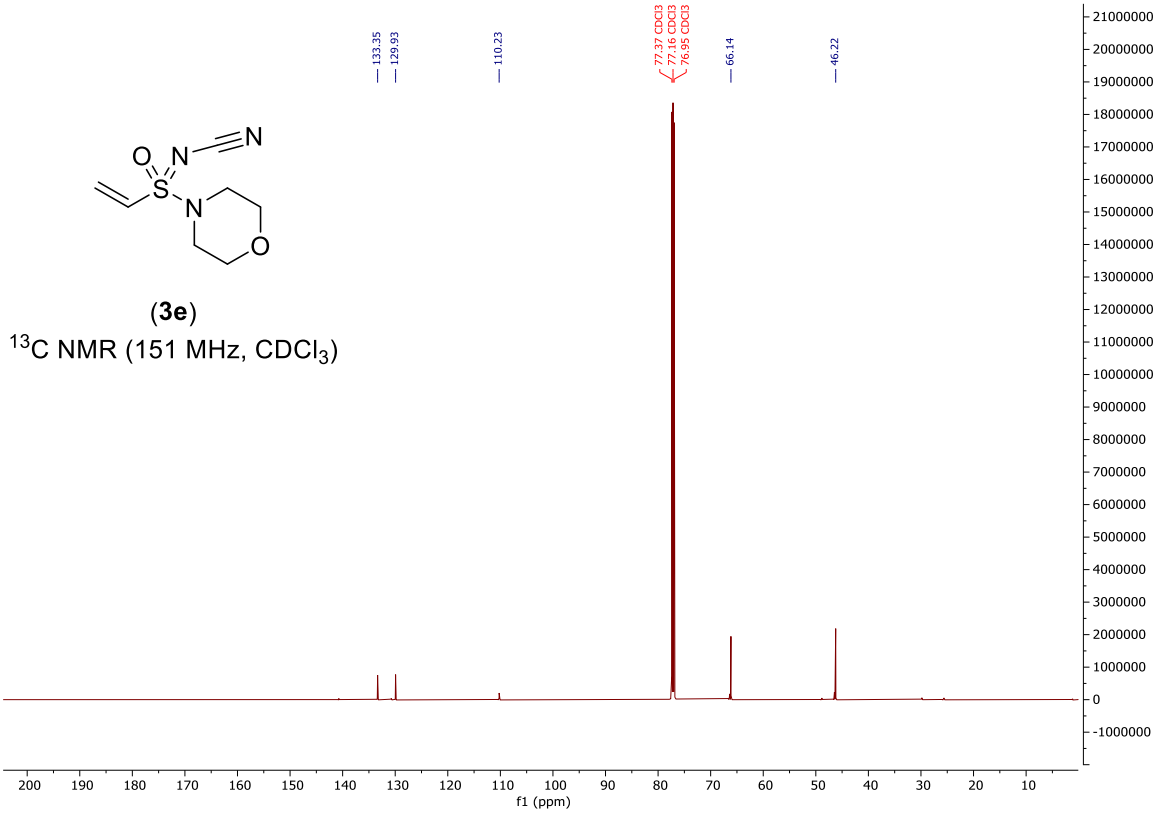


N-(morpholino(oxo)(vinyl)- λ^6-sulfaneylidene)cyanamide (3e)



(**3e**)

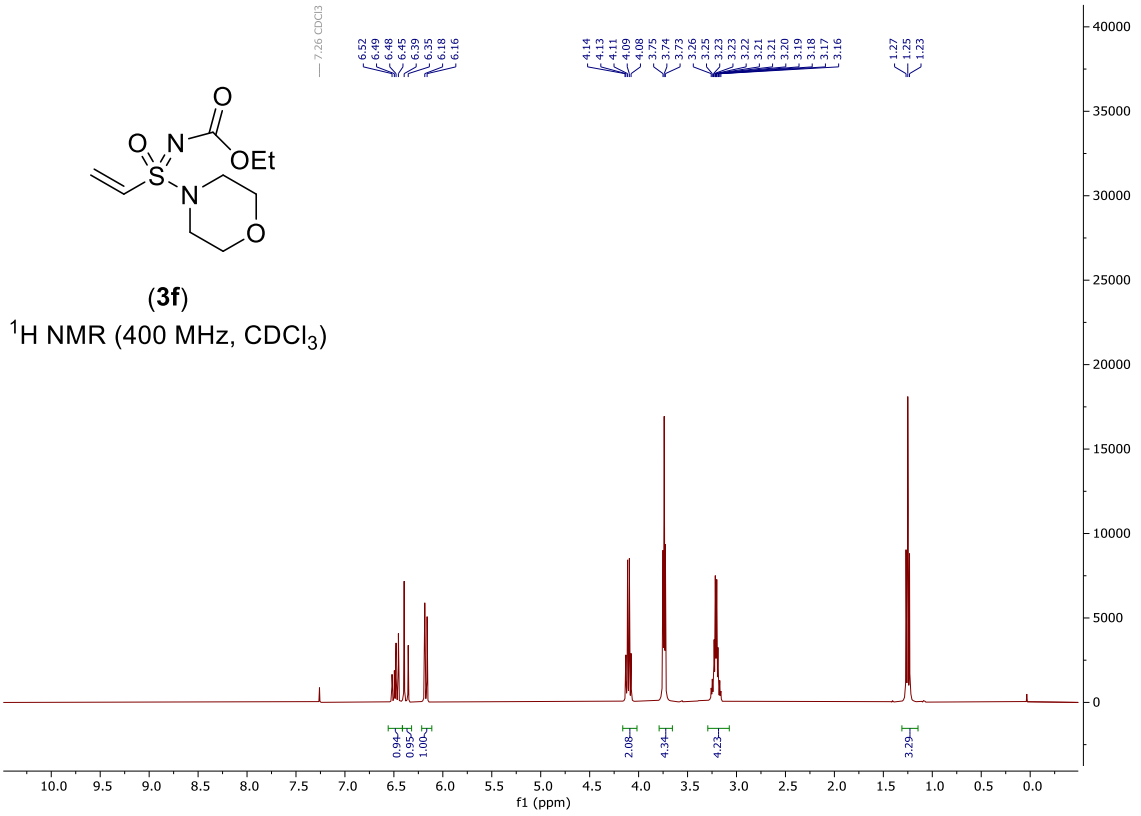
^{1}H NMR (600 MHz, $CDCl_3$)



(**3e**)

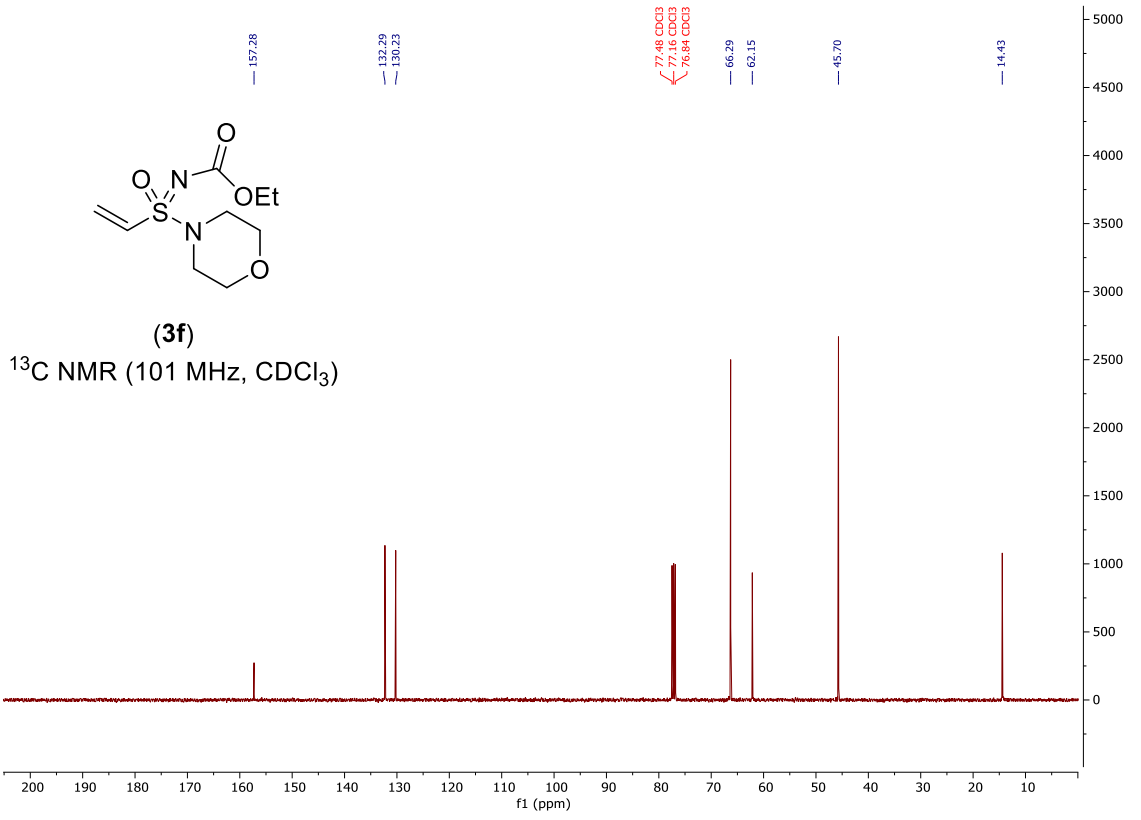
^{13}C NMR (151 MHz, $CDCl_3$)

Ethyl (morpholino(oxo)(vinyl)- λ^6-sulfaneylidene)carbamate (3f)



(**3f**)

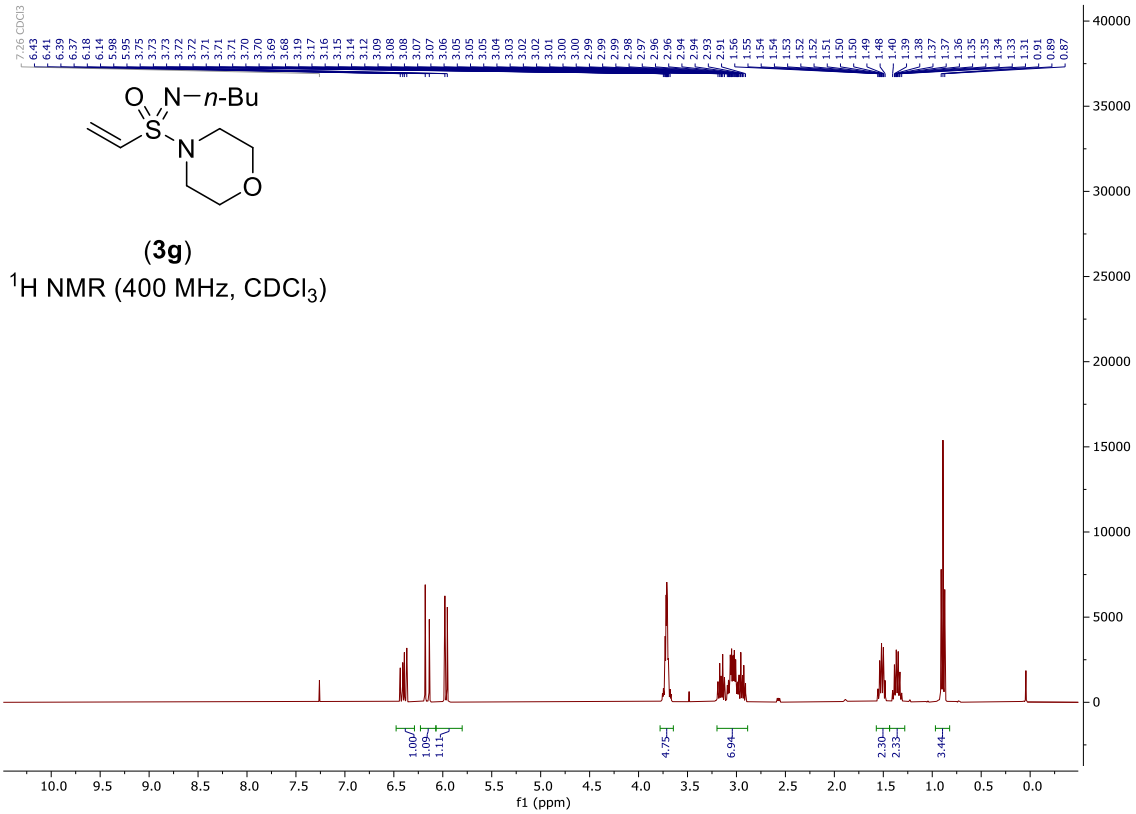
^{1}H NMR (400 MHz, $CDCl_3$)



(**3f**)

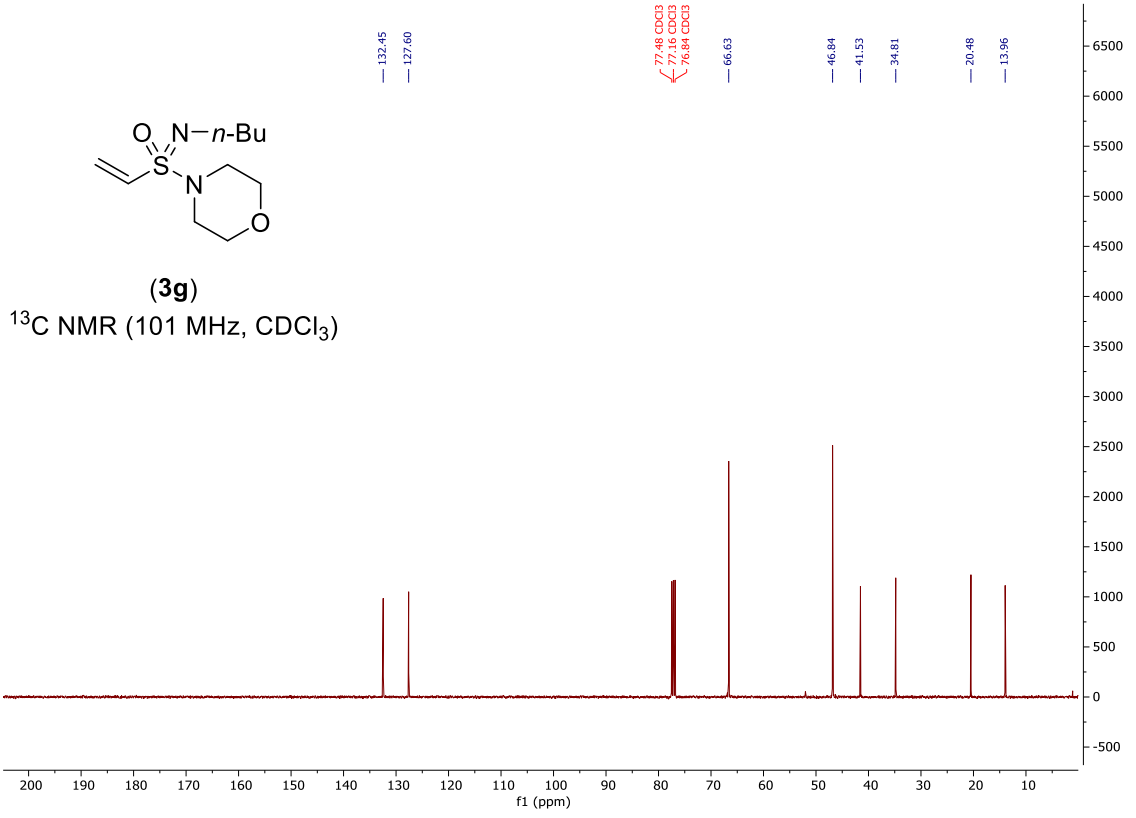
^{13}C NMR (101 MHz, $CDCl_3$)

4-(*N*-Butylvinylsulfonimidoyl)morpholine (3g)



(**3g**)

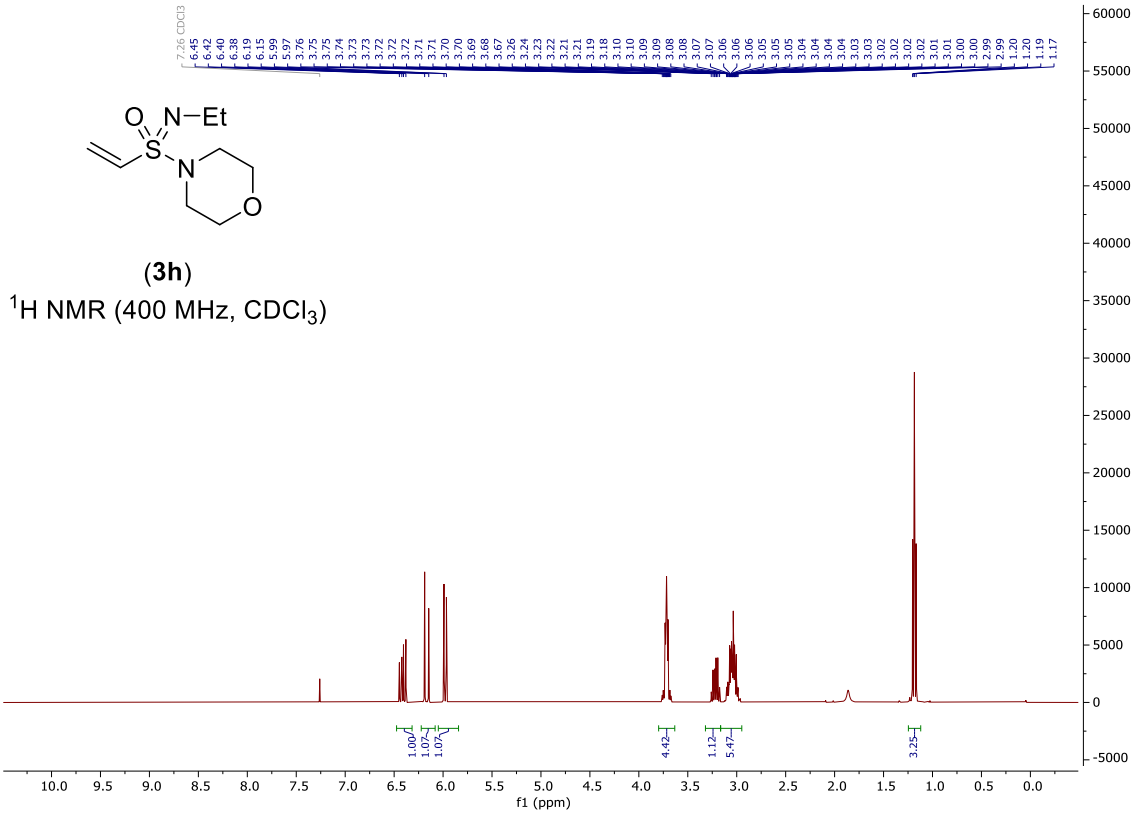
^{1}H NMR (400 MHz, $CDCl_3$)



(**3g**)

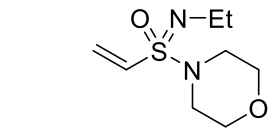
^{13}C NMR (101 MHz, $CDCl_3$)

4-(*N*-Ethylvinylsulfonimidoyl)morpholine (3h)



(**3h**)

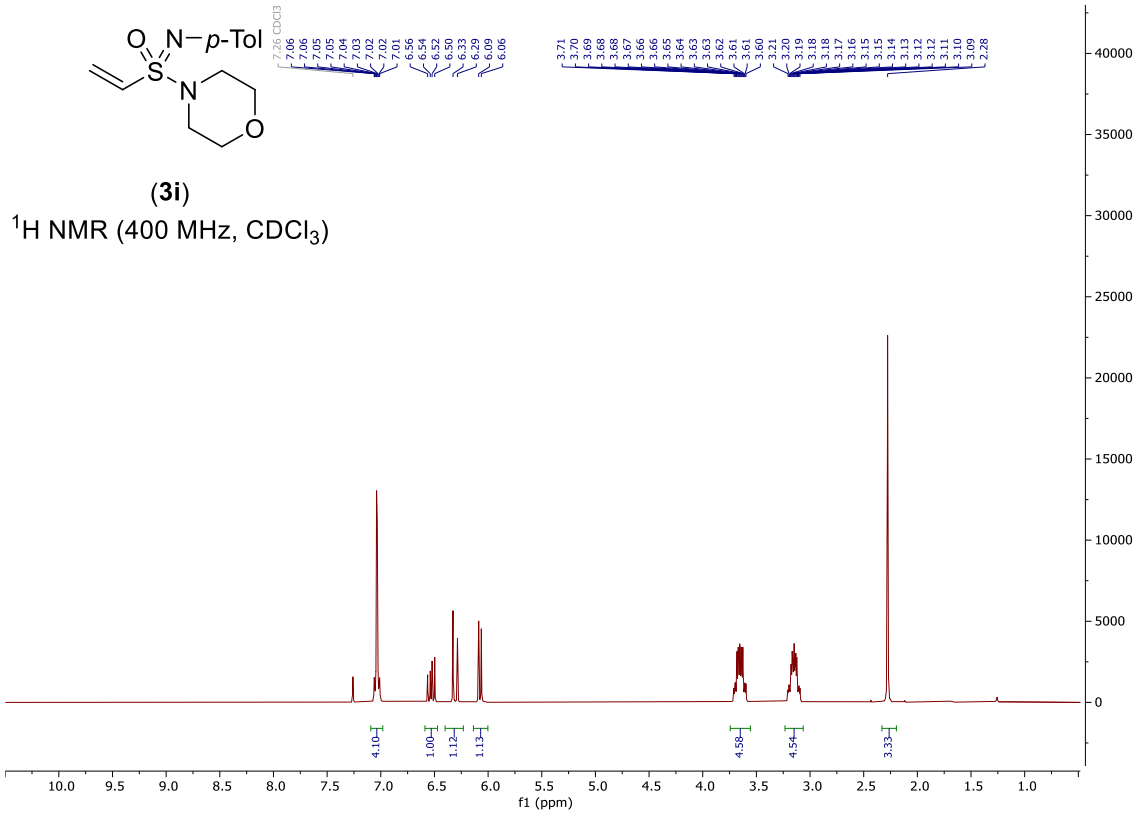
^{1}H NMR (400 MHz, $CDCl_3$)



(**3h**)

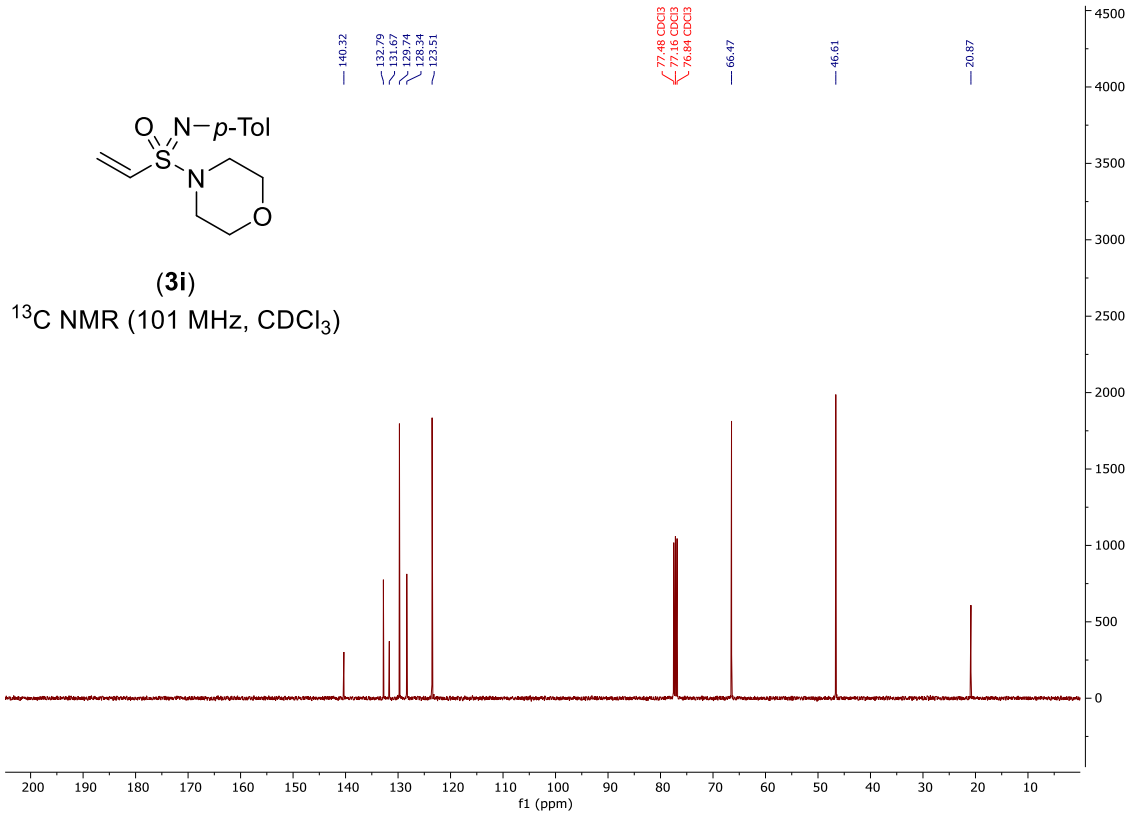
^{13}C NMR (101 MHz, $CDCl_3$)

4-(*N*-(*p*-Tolyl)vinylsulfonimidoyl)morpholine (3i)



(**3i**)

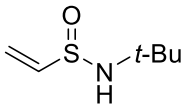
^{1}H NMR (400 MHz, $CDCl_3$)



(**3i**)

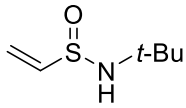
^{13}C NMR (101 MHz, $CDCl_3$)

N-(*tert*-Butyl)ethenesulfinamide (SI-4)



(**SI-4**)

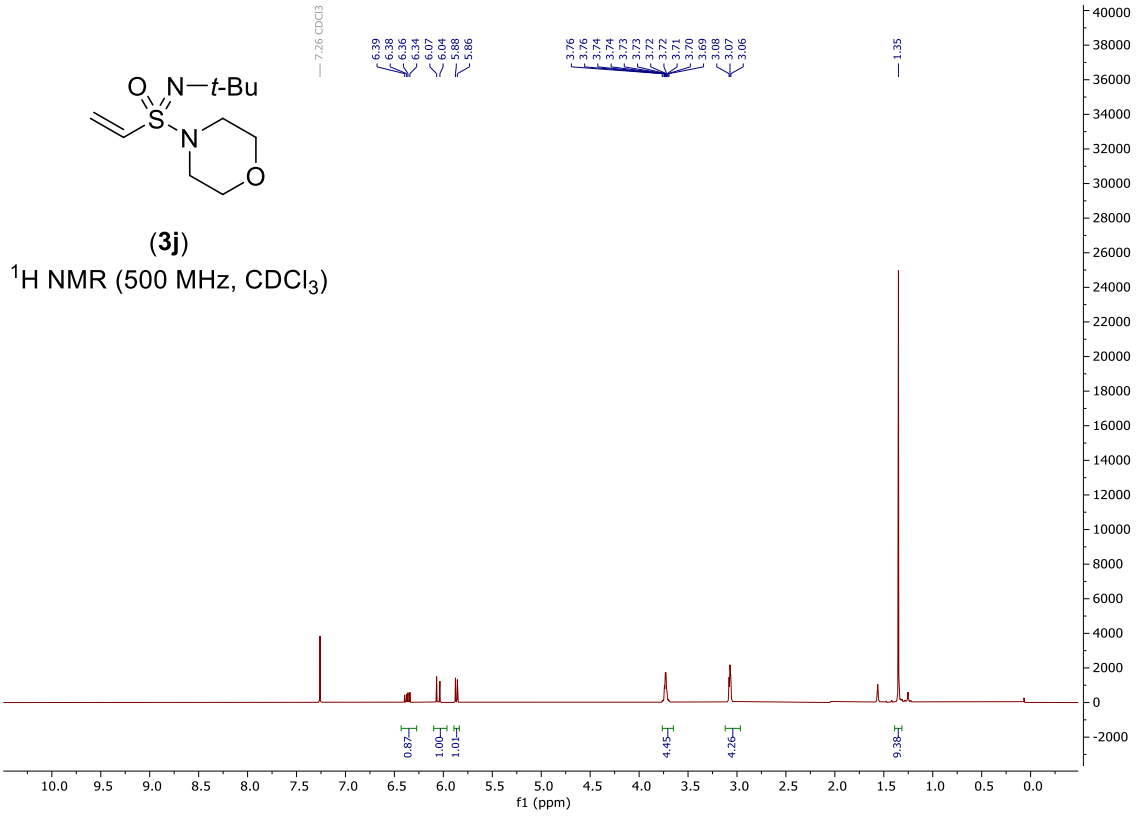
^{1}H NMR (500 MHz, $CDCl_3$)

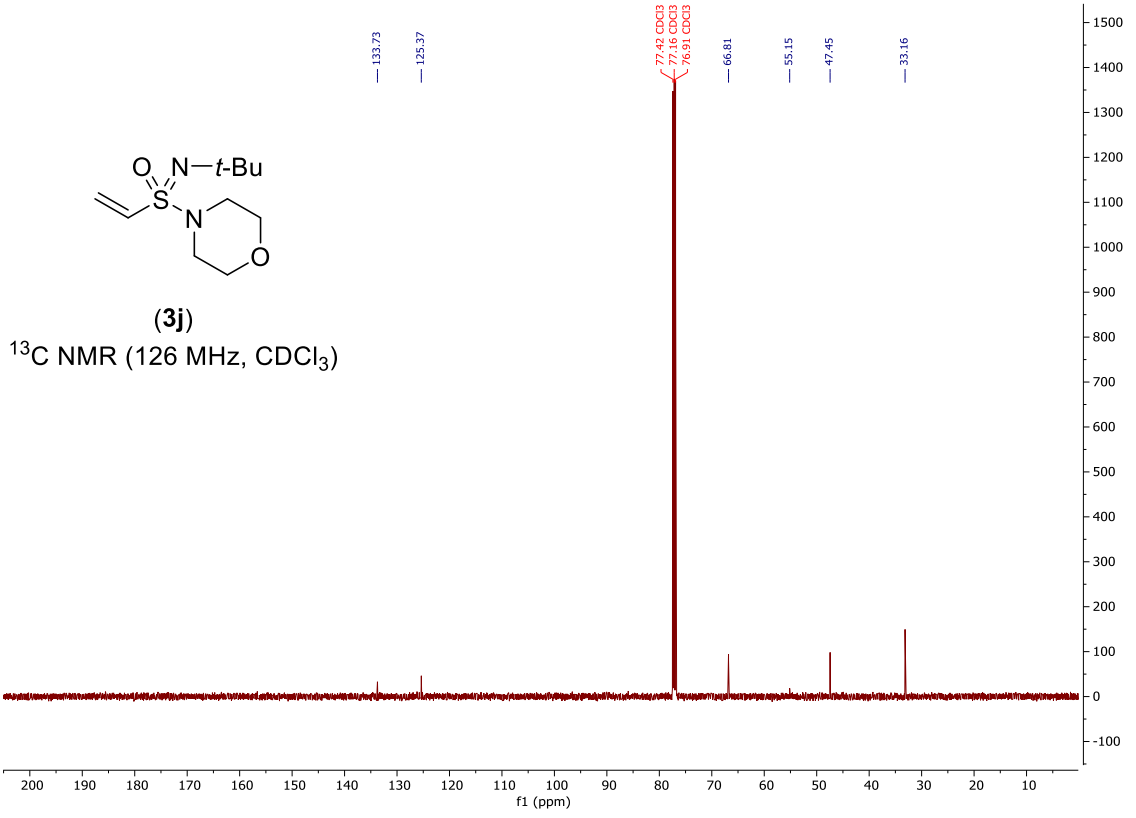


(**SI-4**)

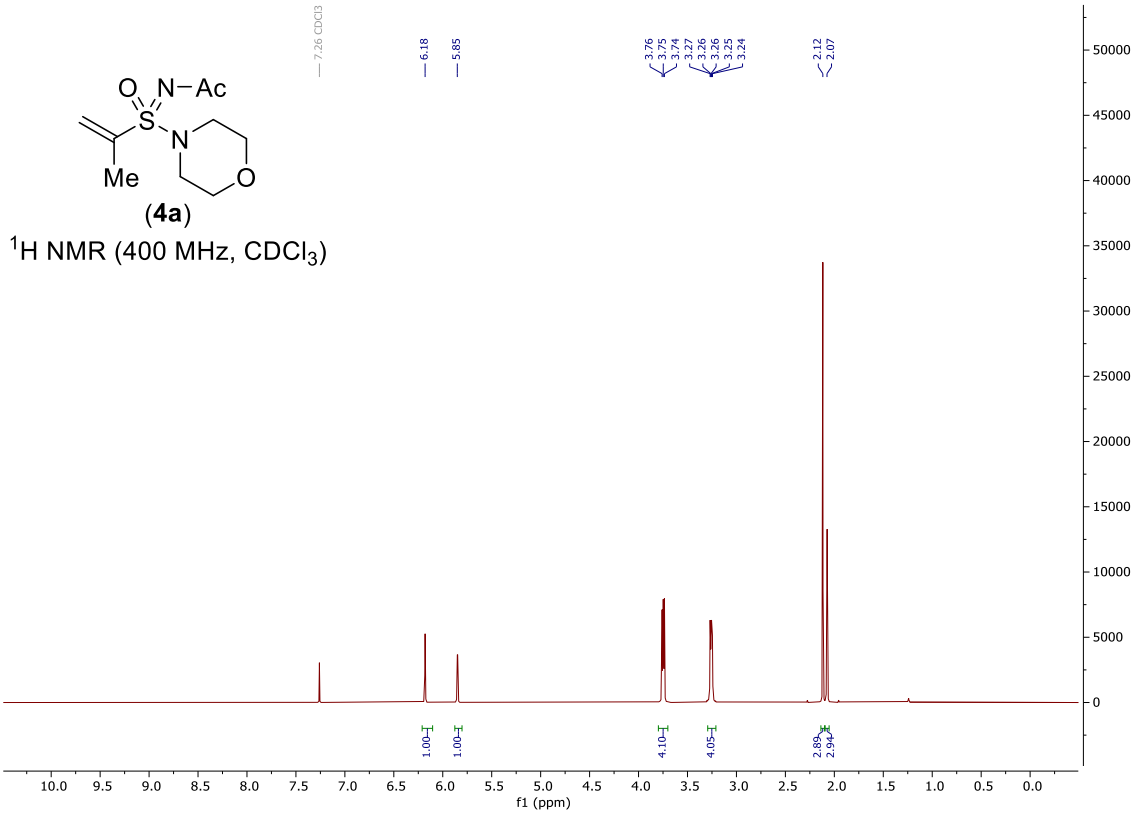
^{13}C NMR (126 MHz, $CDCl_3$)

4-(*N*-(*tert*-Butyl)vinylsulfonimidoyl)morpholine (3j)



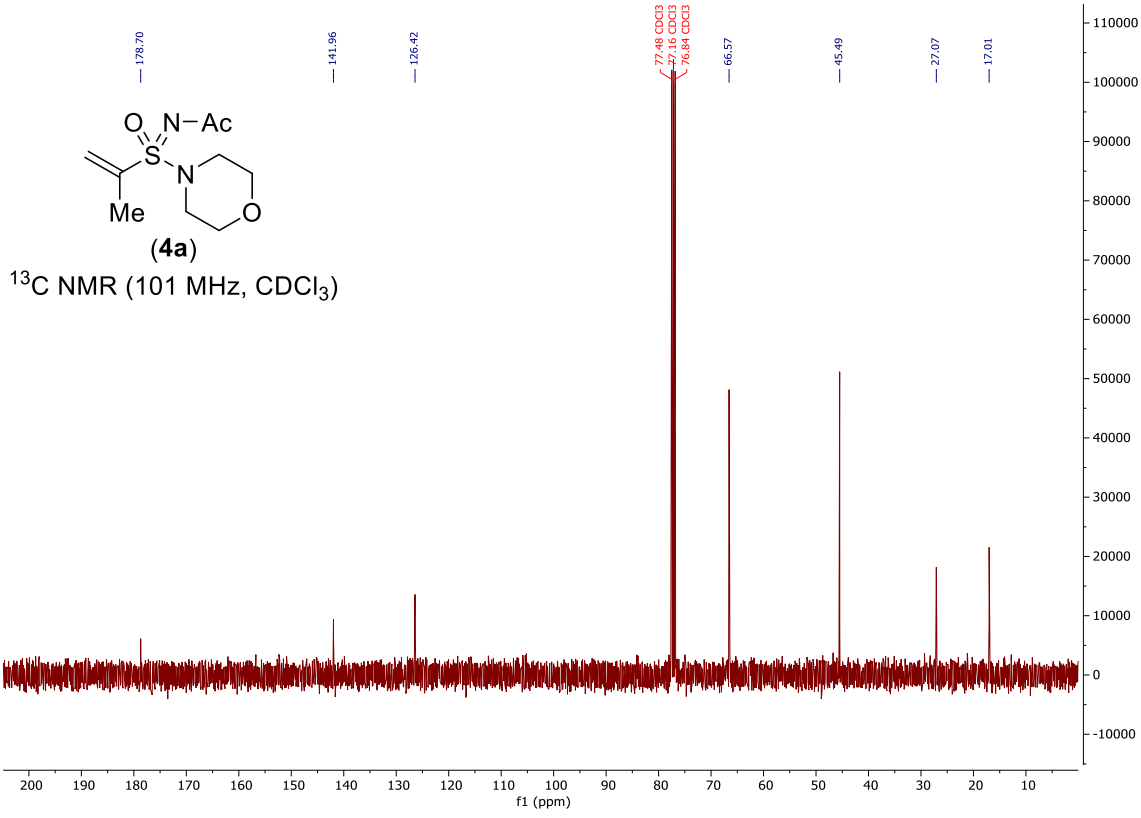


_N_-(morpholino(oxo)(prop-1-en-2-yl)-λ6-sulfaneylidene)acetamide (4a)



(**4a**)

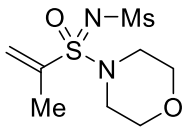
^{1}H NMR (400 MHz, $CDCl_3$)



(**4a**)

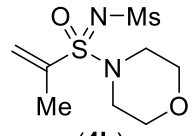
^{13}C NMR (101 MHz, $CDCl_3$)

_N_-(morpholino(oxo)(prop-1-en-2-yl)-λ6-sulfaneylidene)methanesulfonamide (4b)



(**4b**)

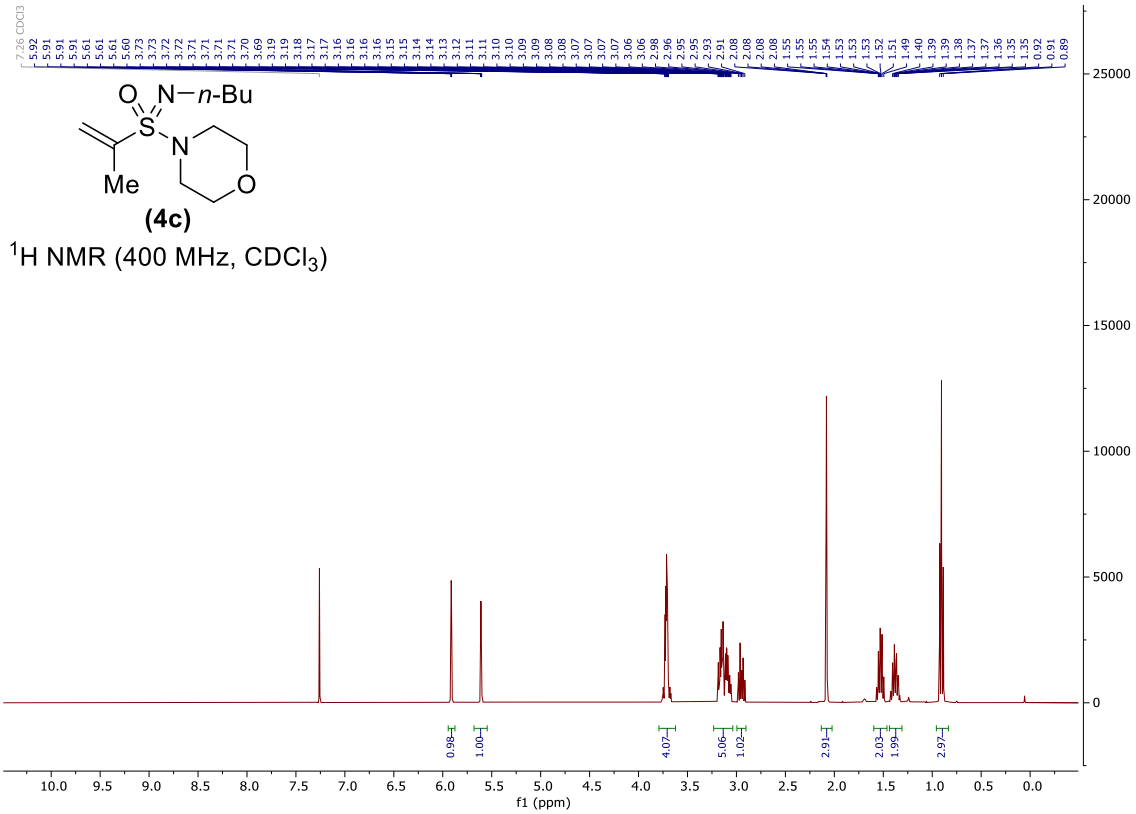
^{1}H NMR (400 MHz, $CDCl_3$)

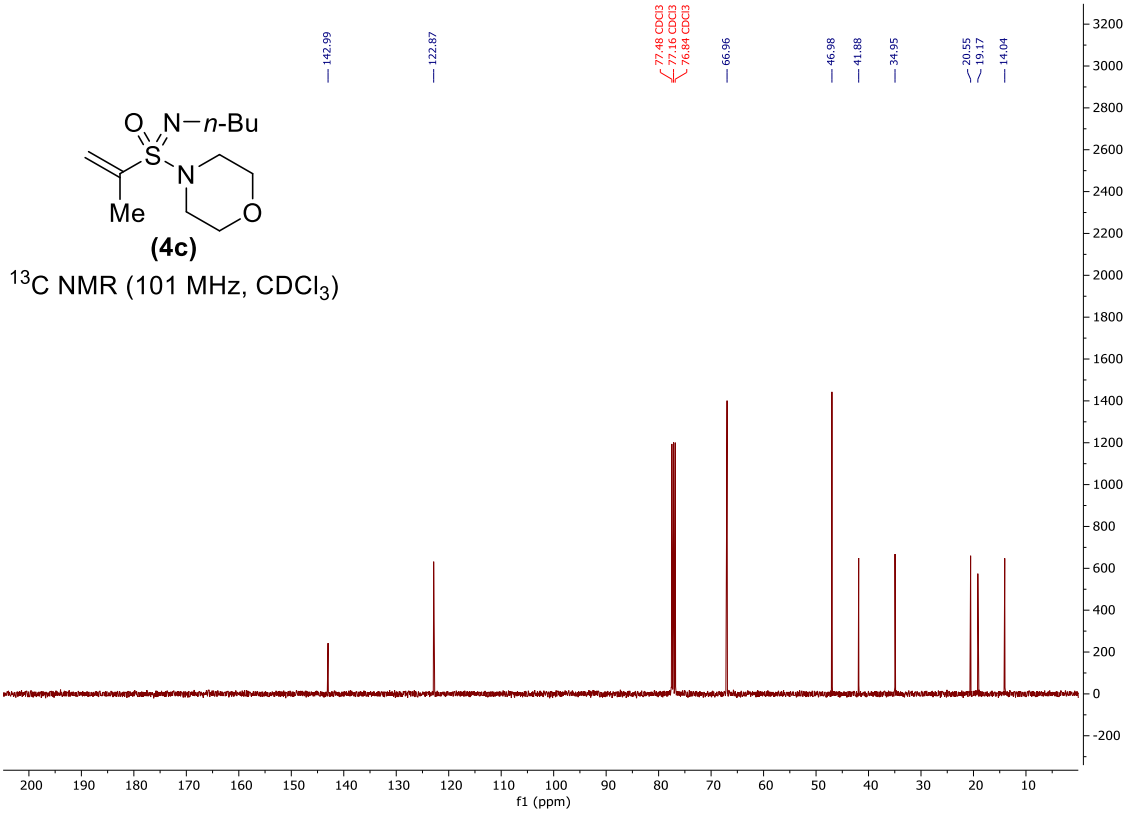


(**4b**)

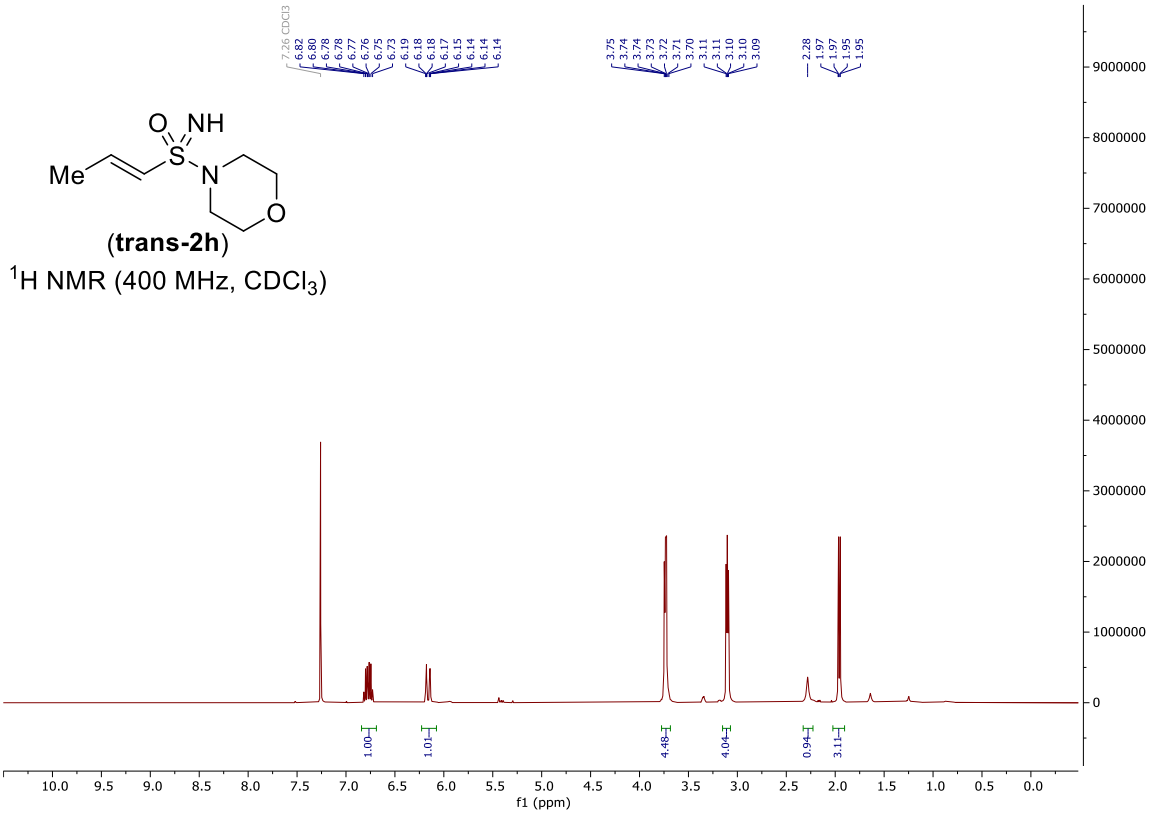
^{13}C NMR (101 MHz, $CDCl_3$)

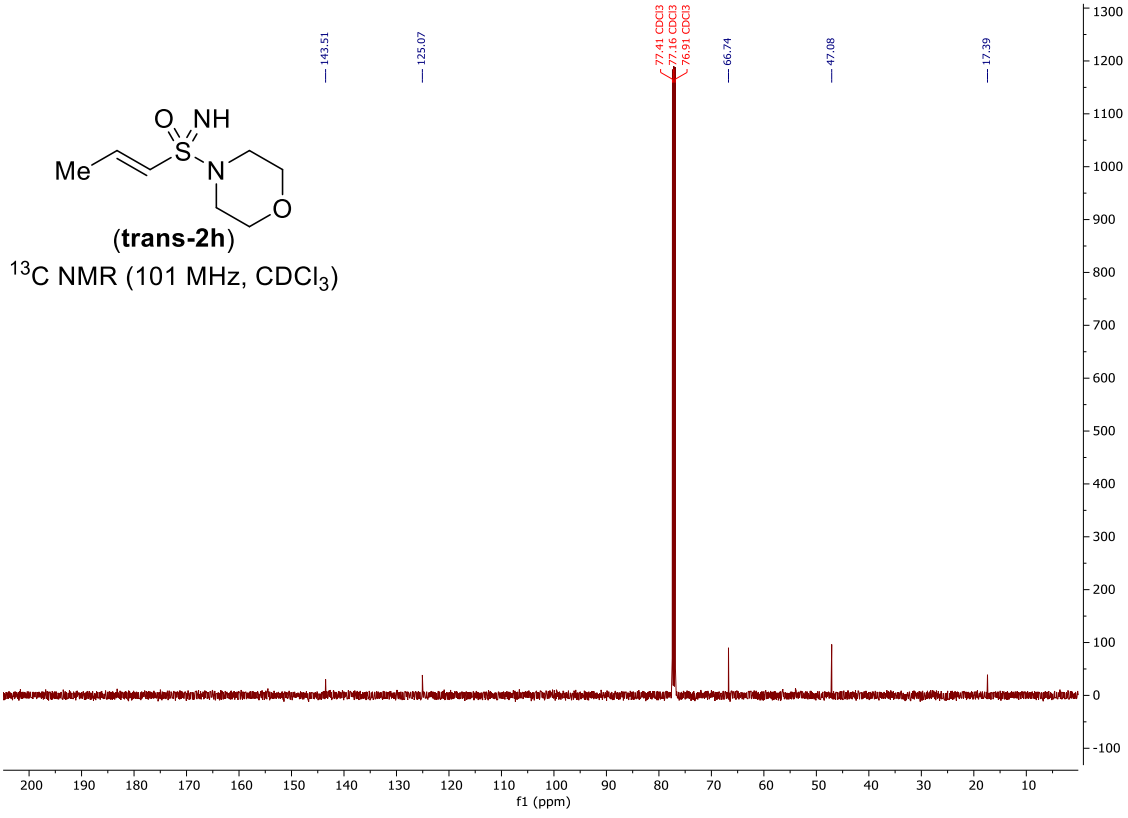
4-(*N*-butylprop-1-en-2-ylsulfonimidoyl)morpholine (4c)



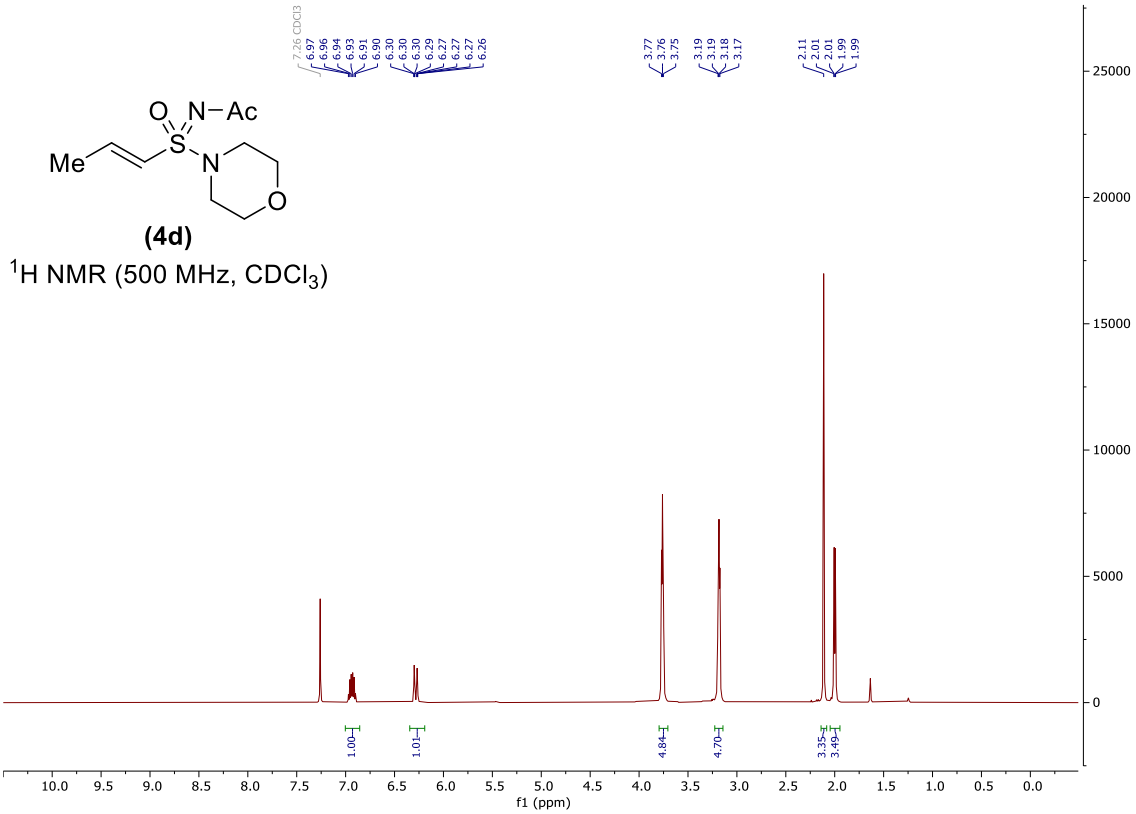


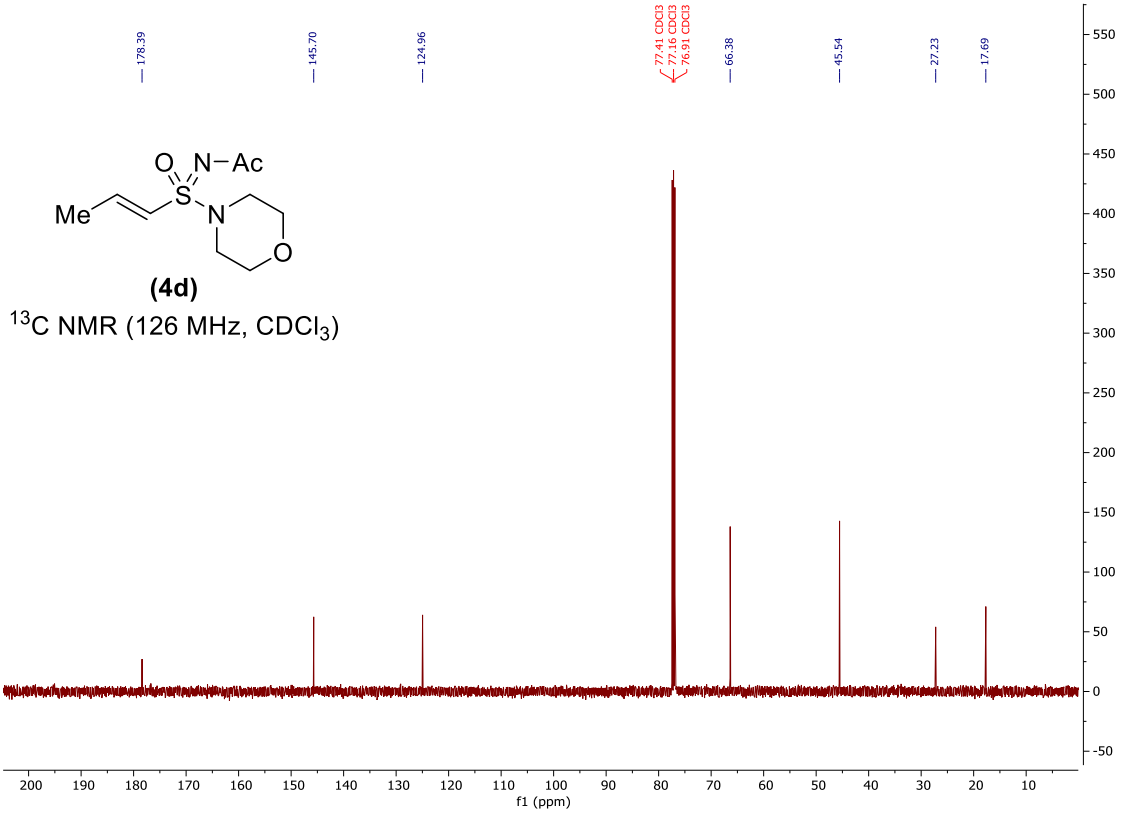
(*E*)-4-(prop-1-en-1-ylsulfonimidoyl)morpholine (trans-2h)



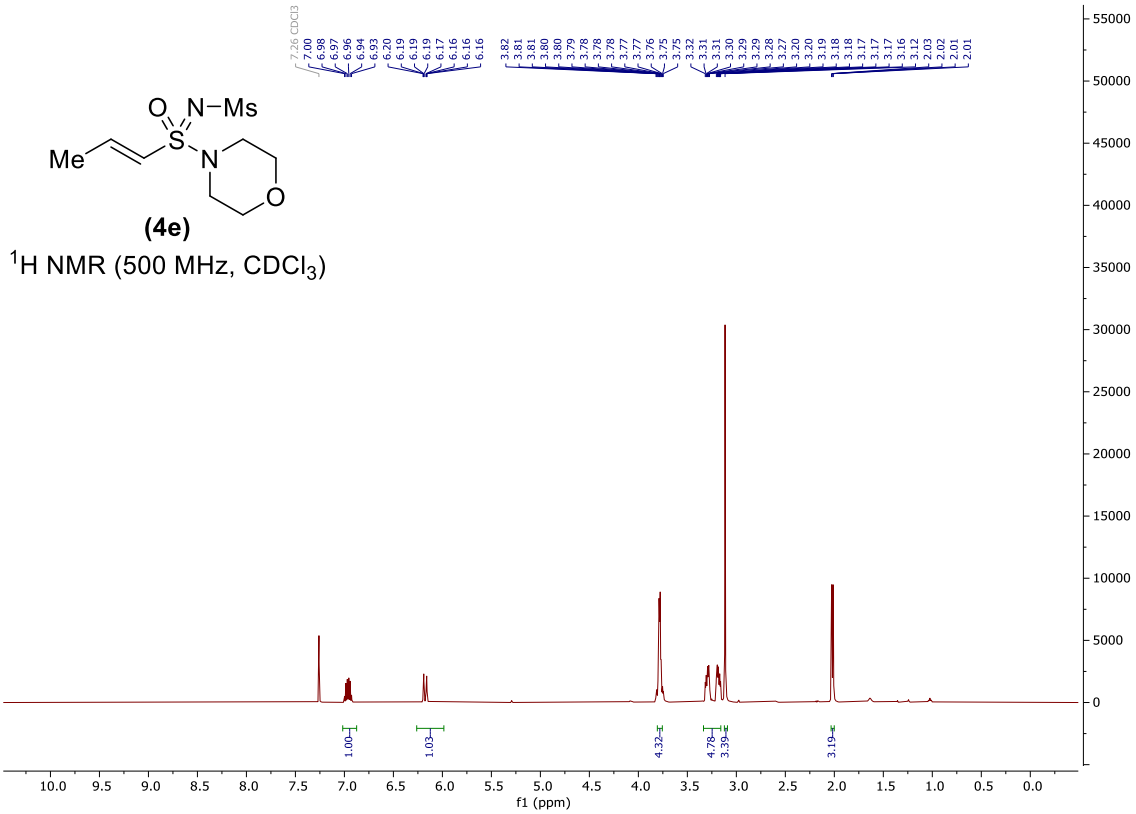


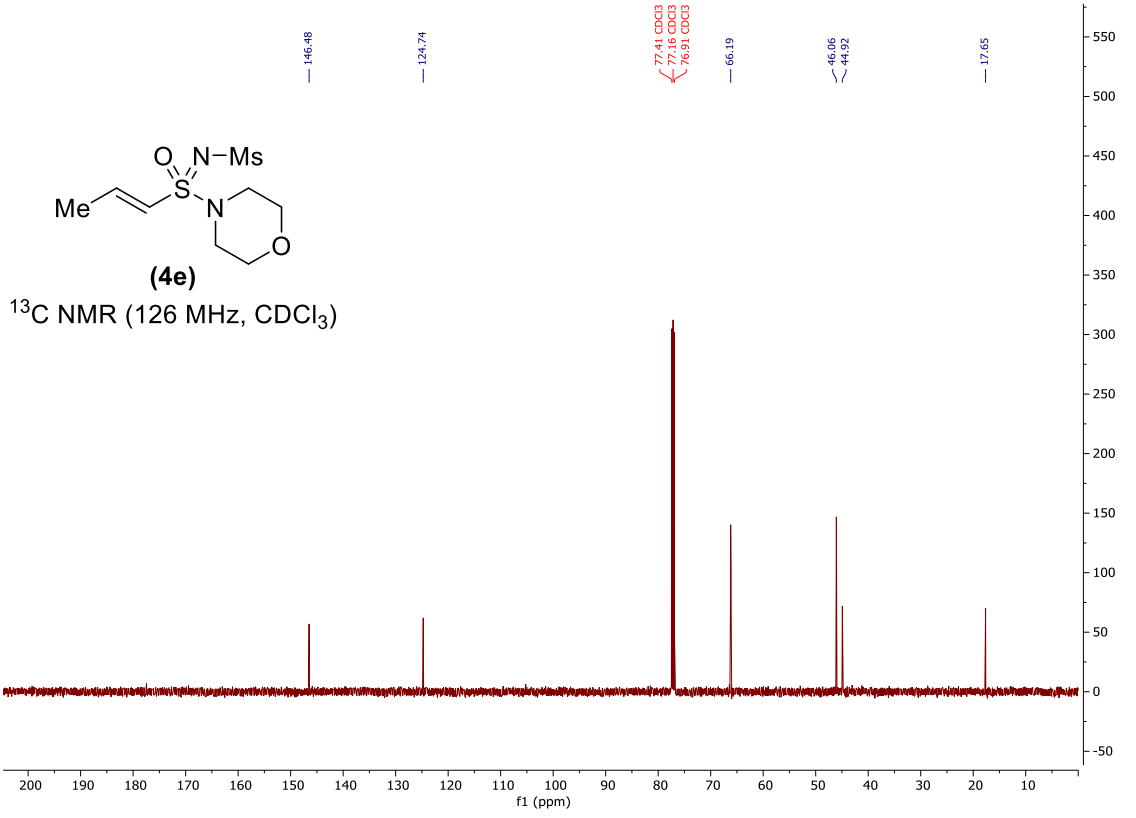
(*E*)-*N*-(morpholino(oxo)(prop-1-en-1-yl)-λ6-sulfaneylidene)acetamide (4d)



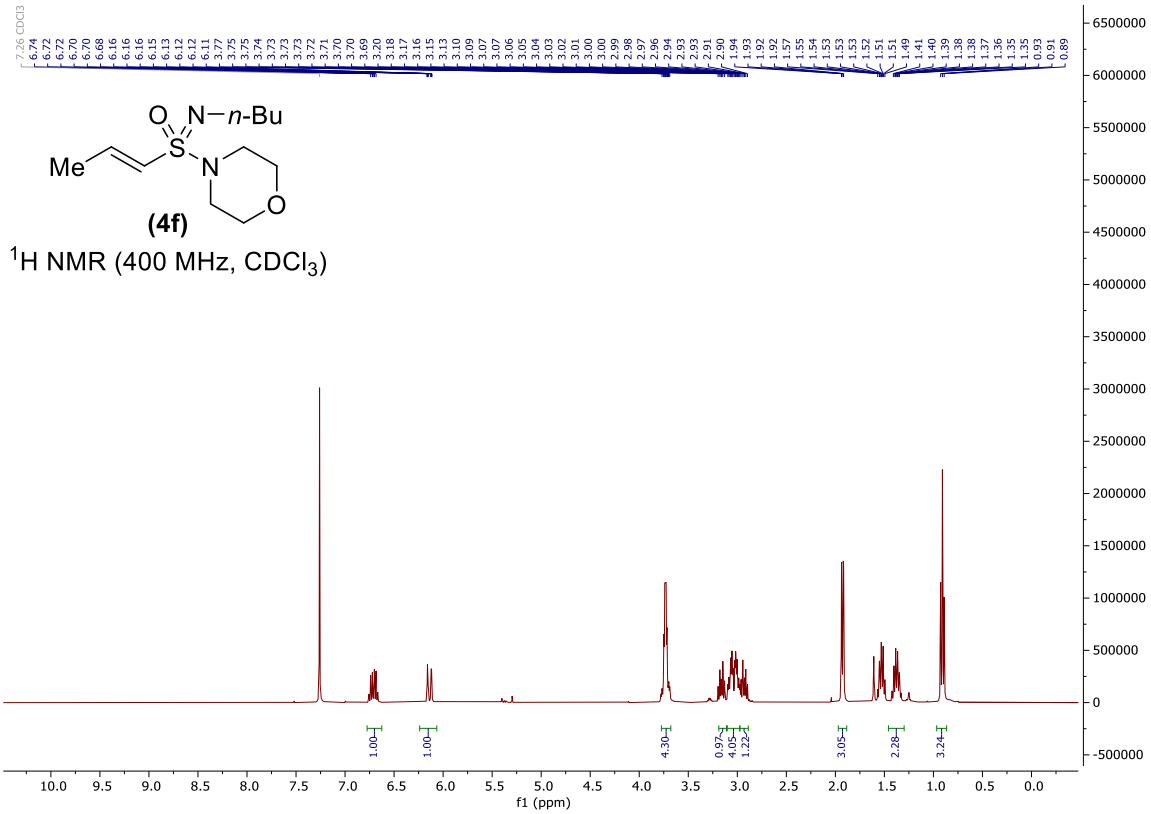


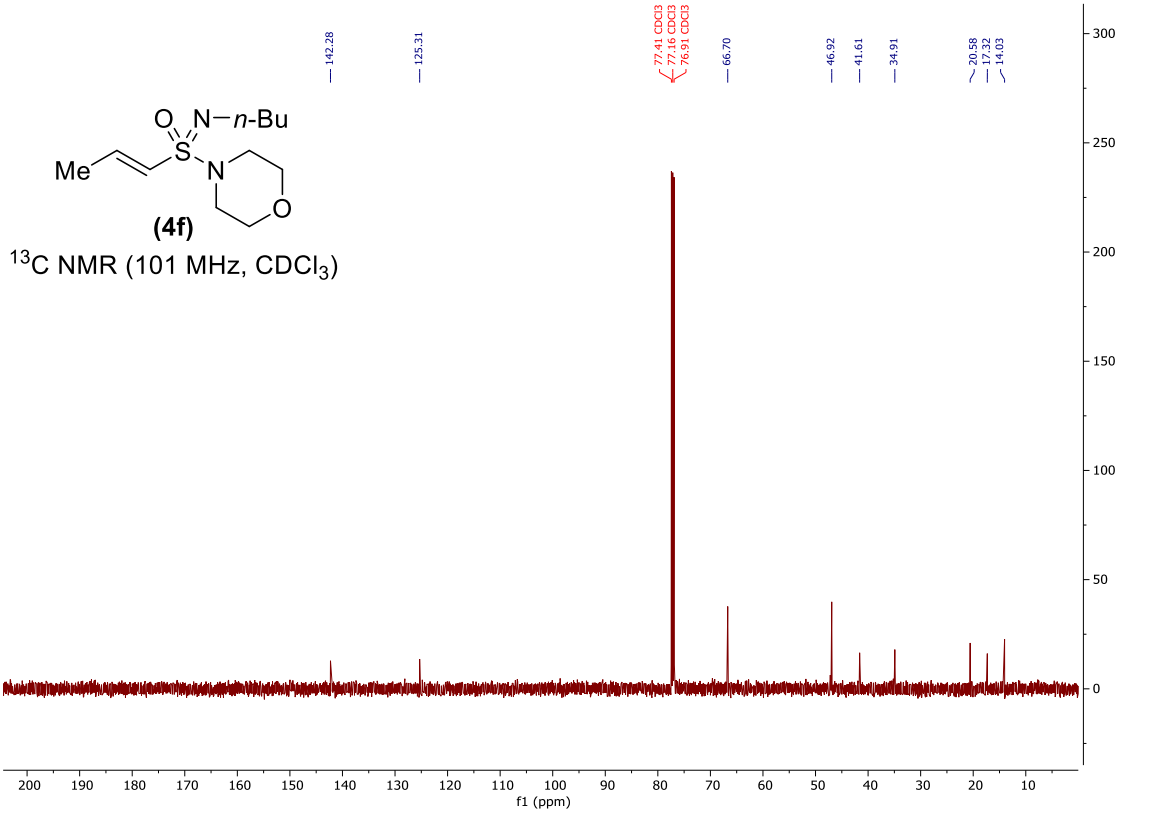
(*E*)-*N*-(morpholino(oxo)(prop-1-en-1-yl)-λ6-sulfaneylidene)methanesulfonamide (4e)



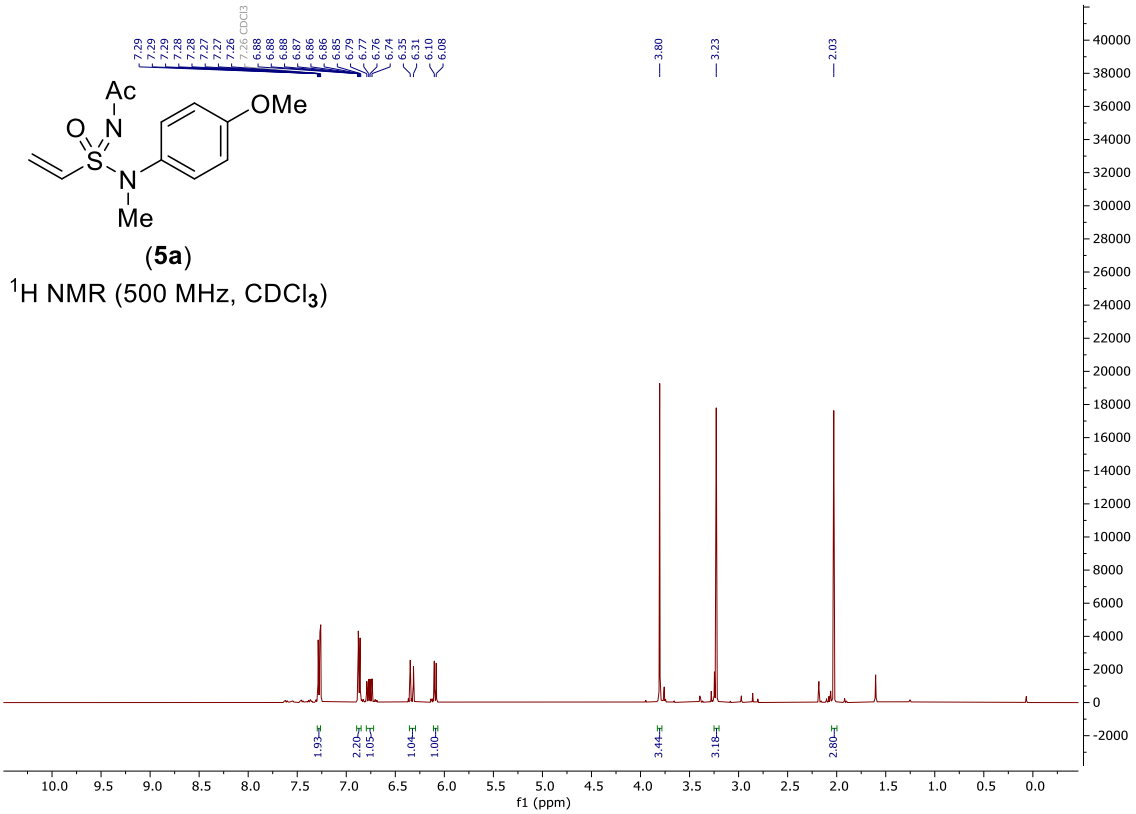


(*E*)-4-(*N*-butylprop-1-en-1-ylsulfonimidoyl)morpholine (4f)



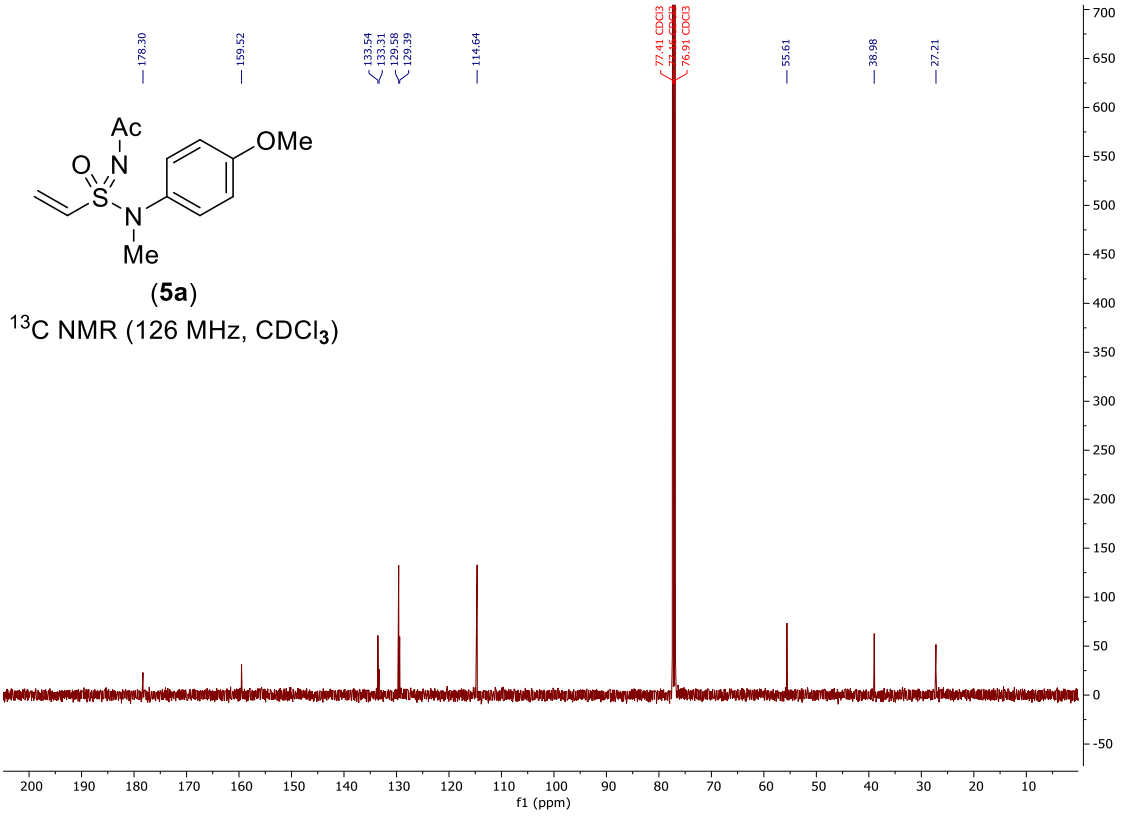


_N_-(((4-methoxyphenyl)(methyl)amino)(oxo)(vinyl)-λ6-sulfaneylidene)acetamide (5a)



(**5a**)

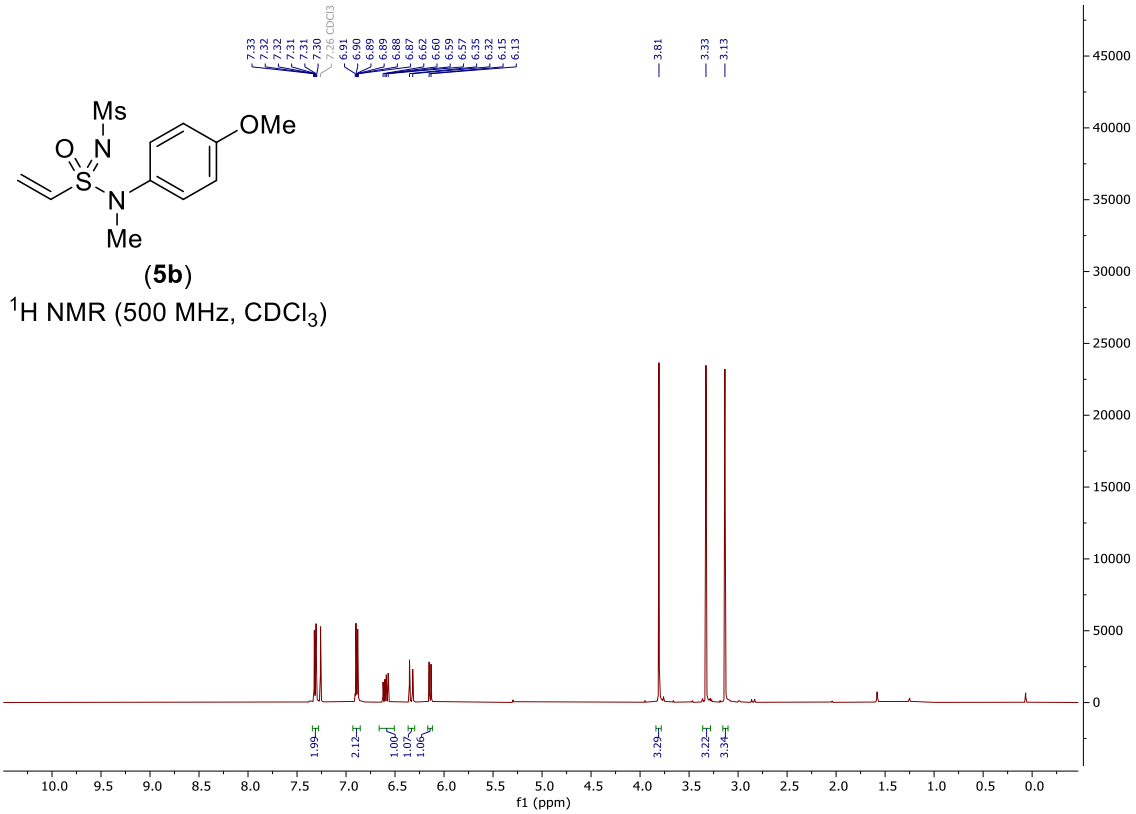
^{1}H NMR (500 MHz, $CDCl_3$)

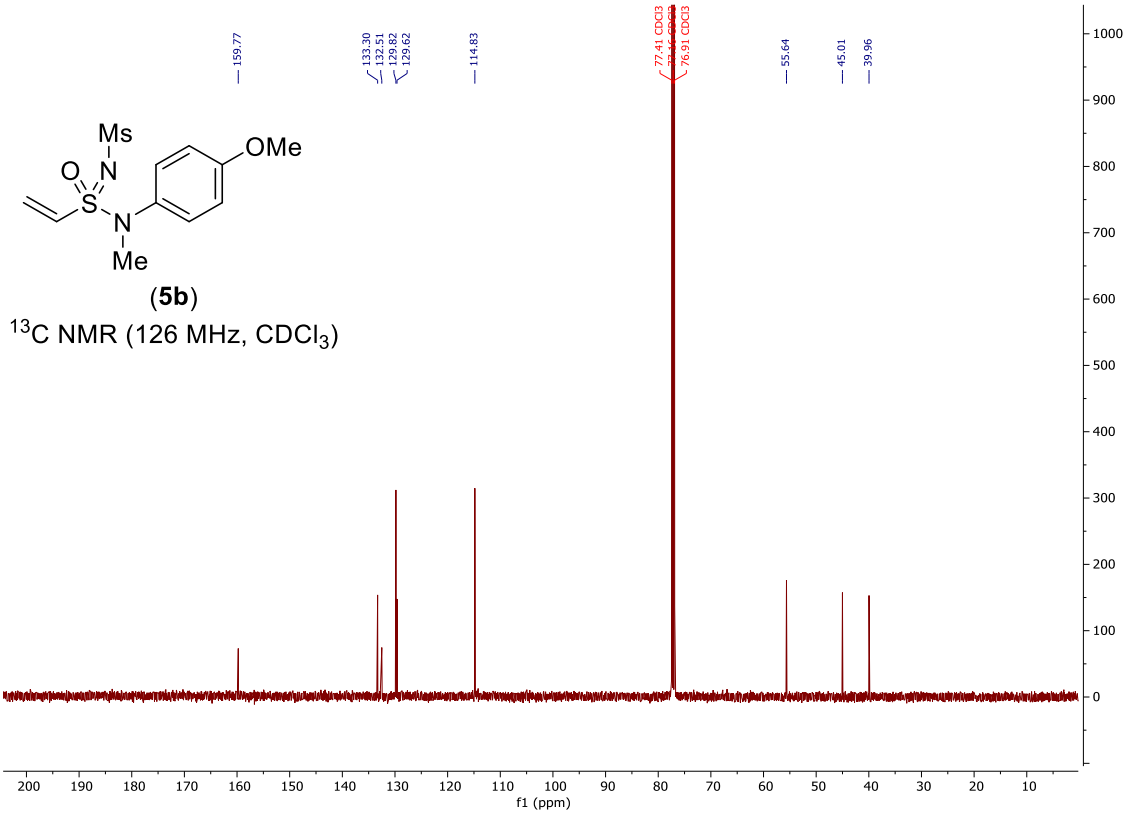


(**5a**)

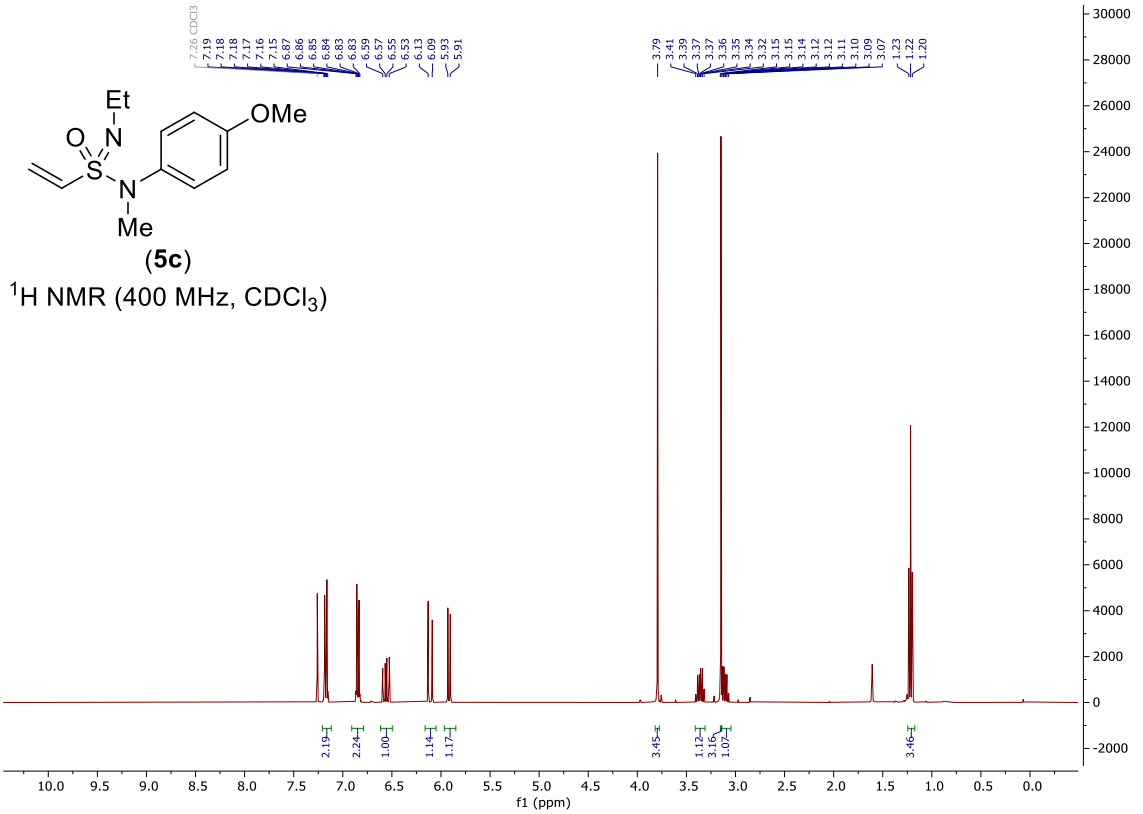
^{13}C NMR (126 MHz, $CDCl_3$)

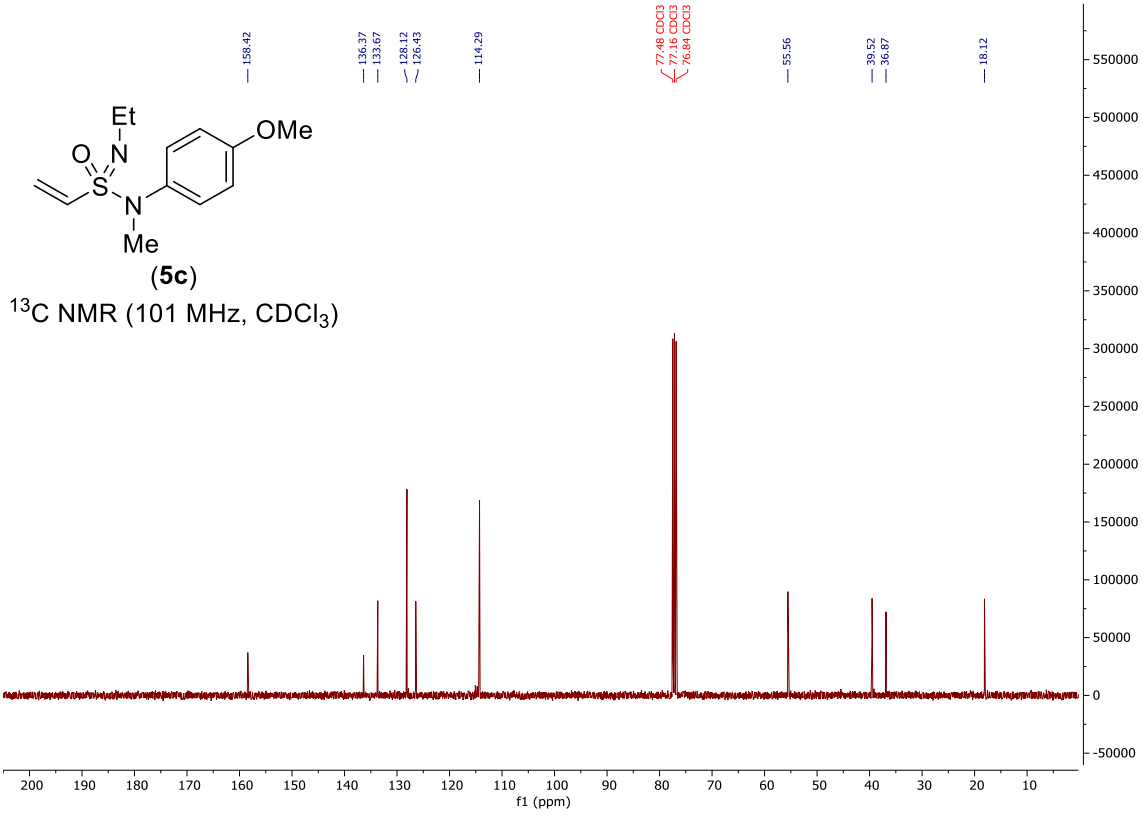
***N*-(((4-methoxyphenyl)(methyl)amino)(oxo)(vinyl)-λ6-sulfaneylidene)methanesulfonamide (5b)**



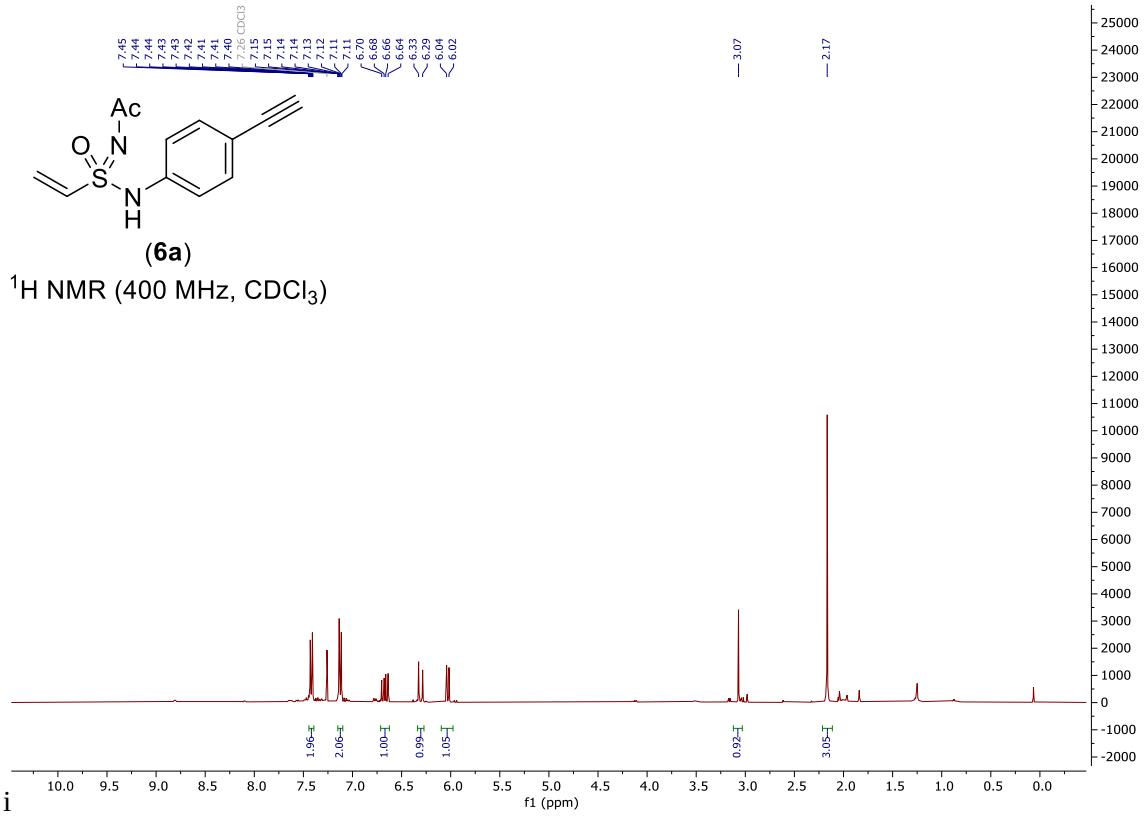


_N'_-ethyl-_N_-(4-methoxyphenyl)-N-methylethenesulfonimidamide (5c)

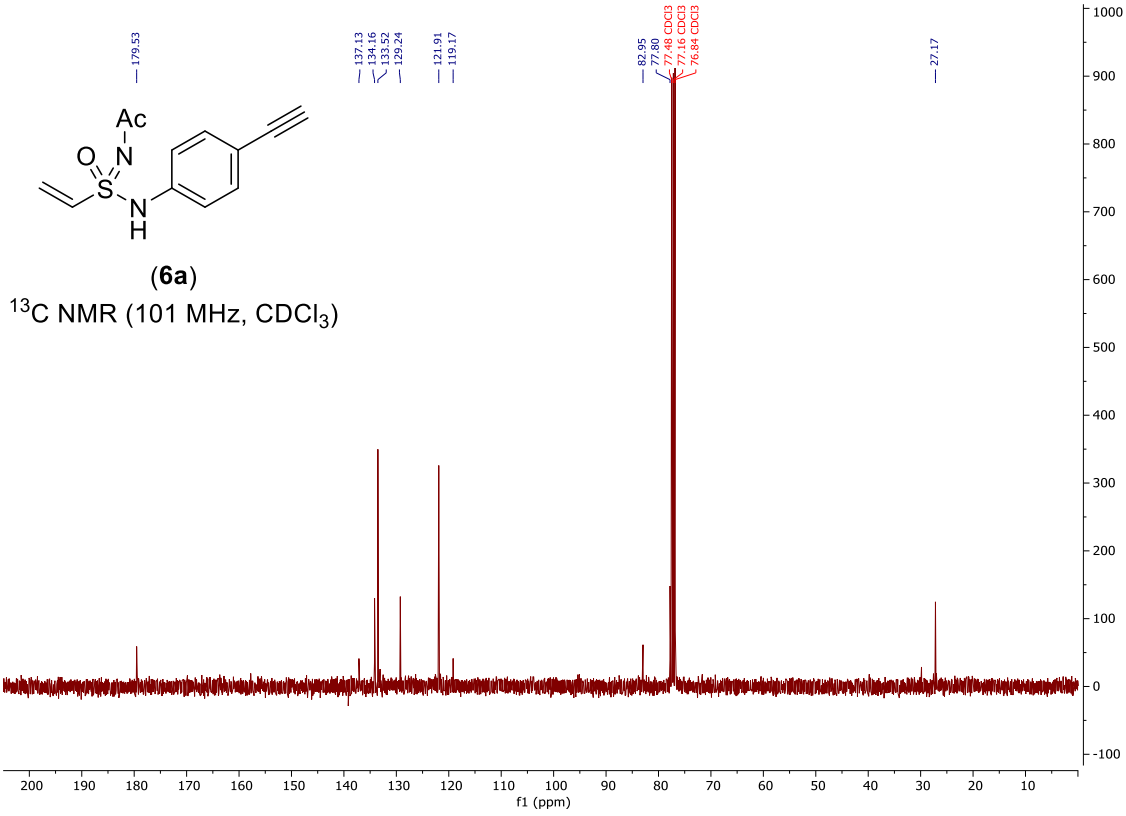




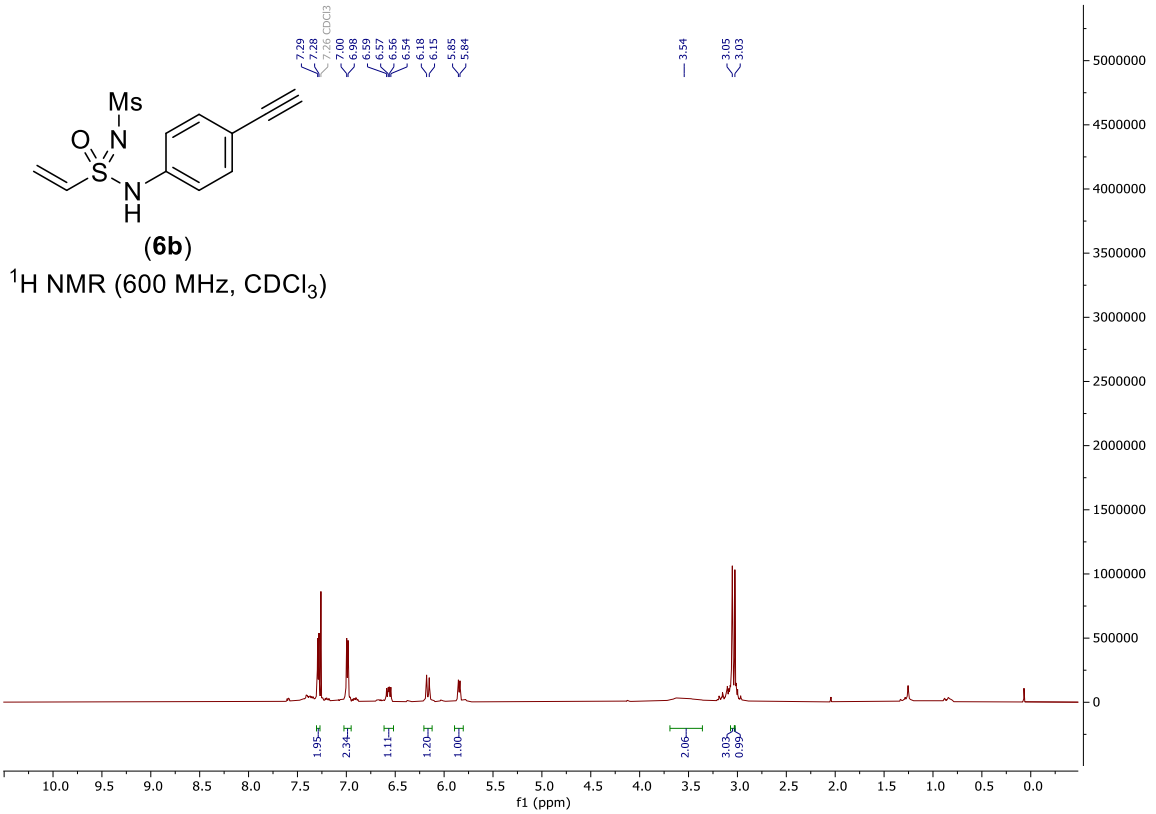
_N_-(_N_-(4-Ethynylphenyl)vinylsulfonimidoyl)acetamide (6a)

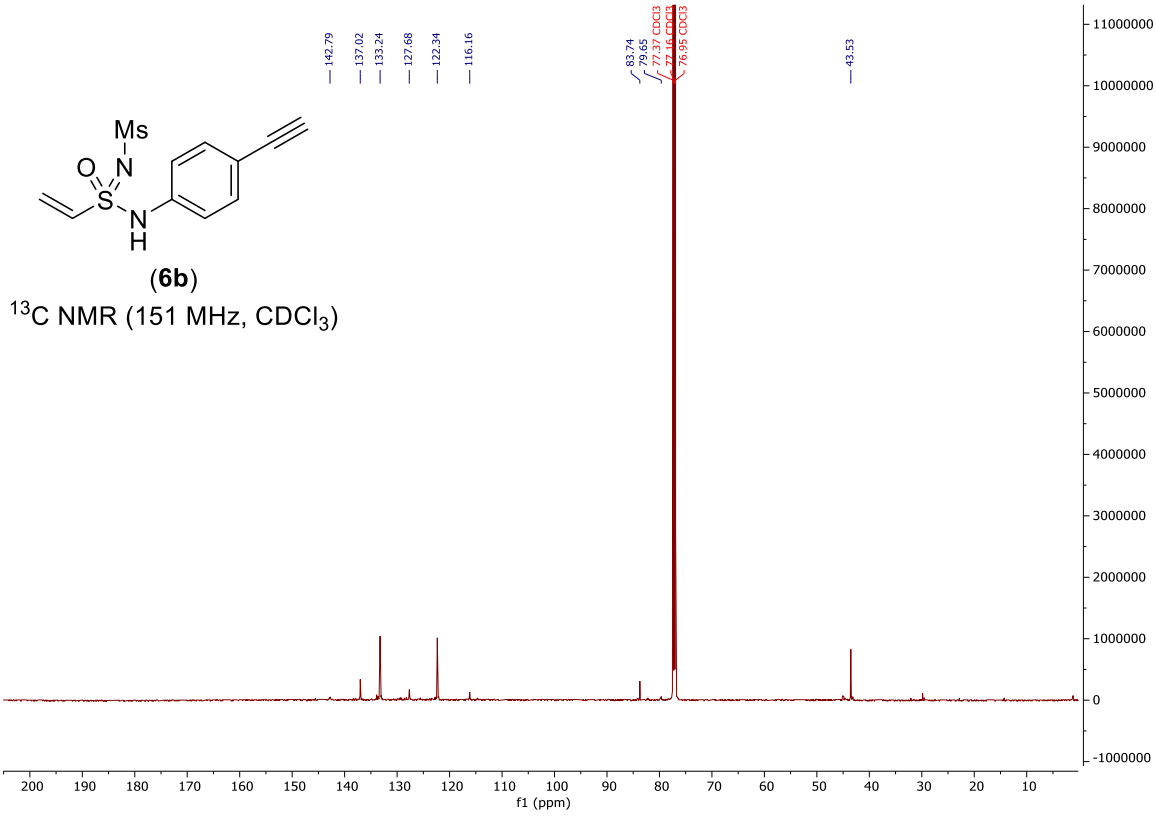


i

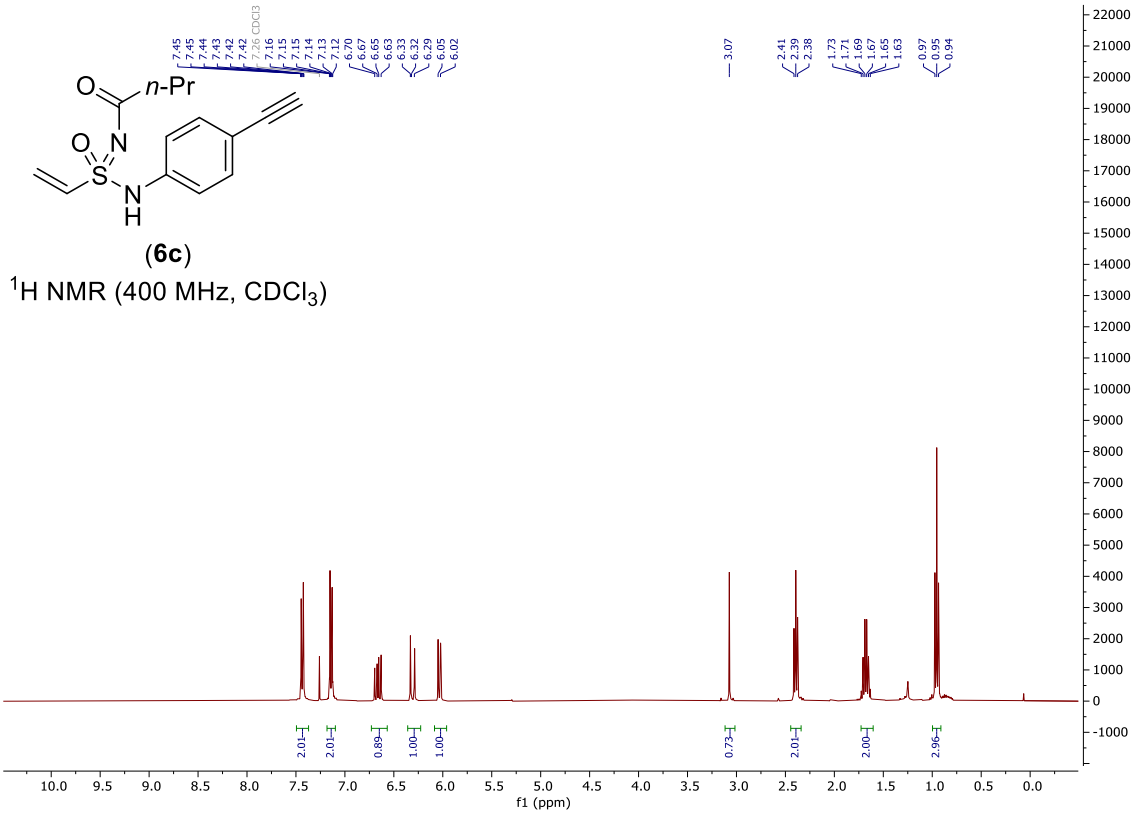


_N_-(_N_-(4-Ethynylphenyl)vinylsulfonimidoyl)methanesulfonamide (6b)



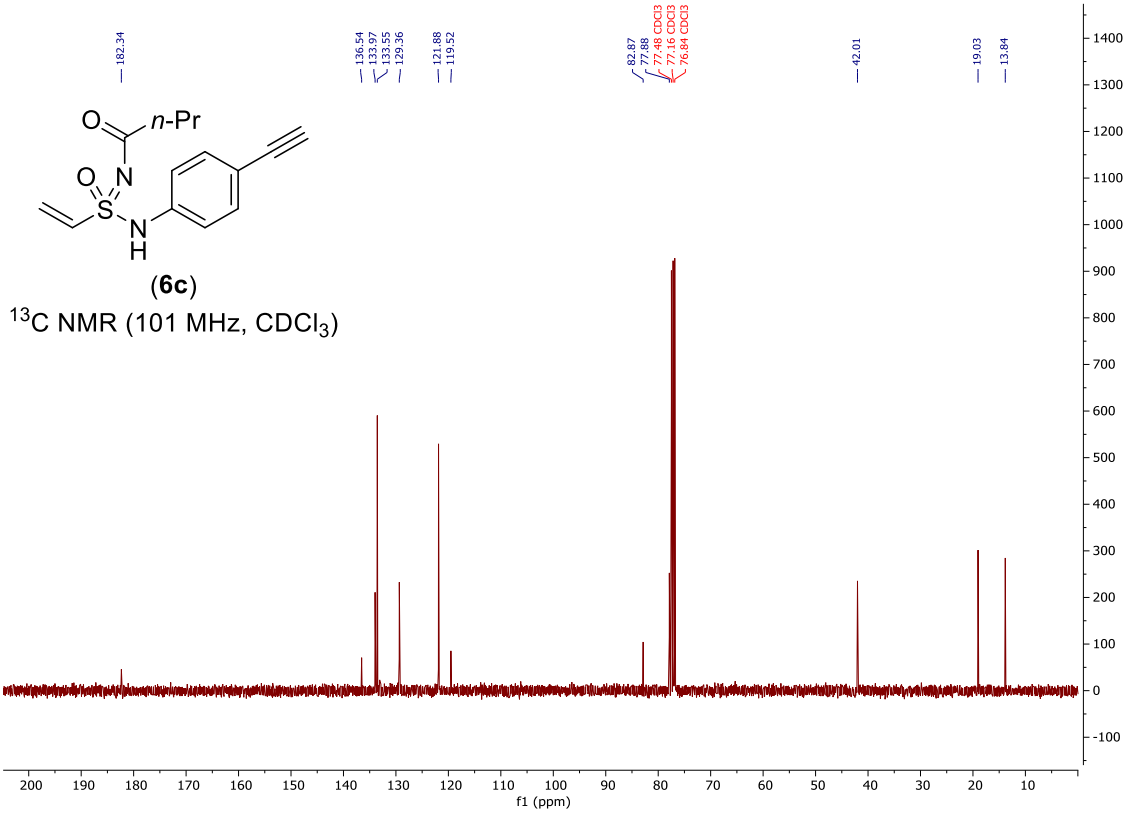


_N_-(_N_-(4-Ethynylphenyl)vinylsulfonimidoyl)butyramide (6c)



(**6c**)

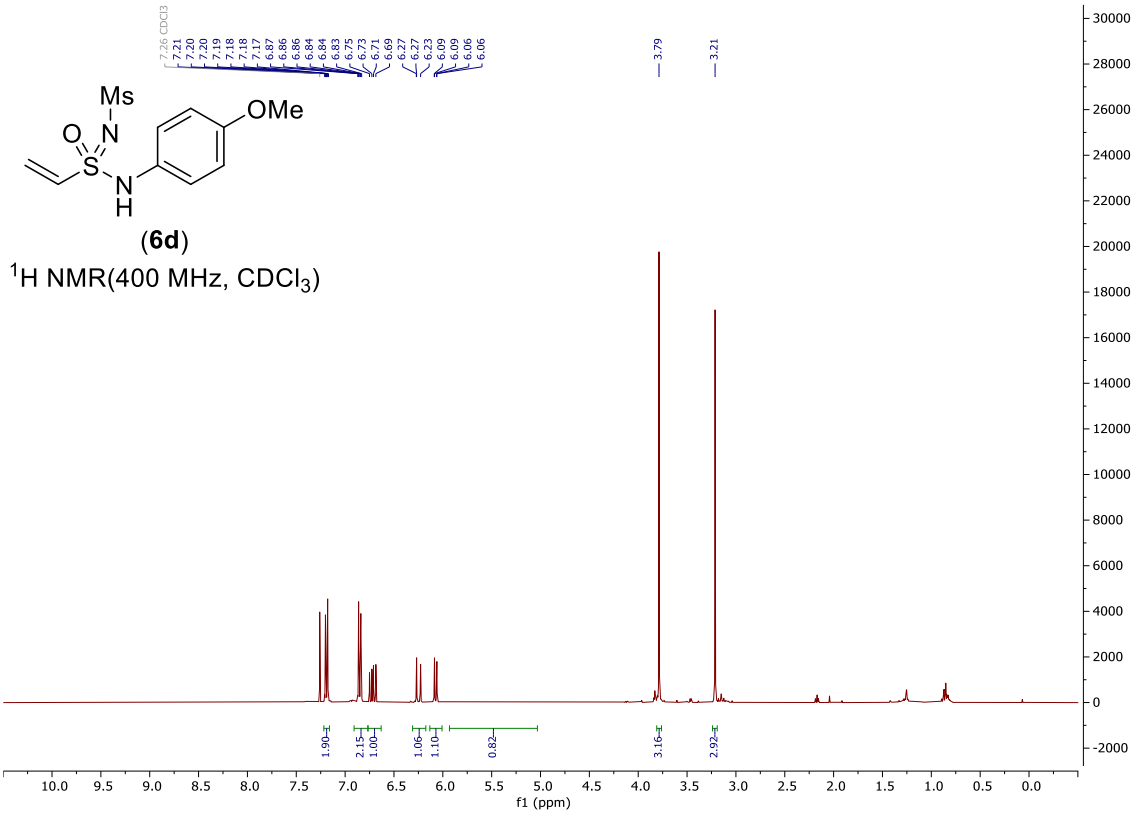
^{1}H NMR (400 MHz, $CDCl_3$)

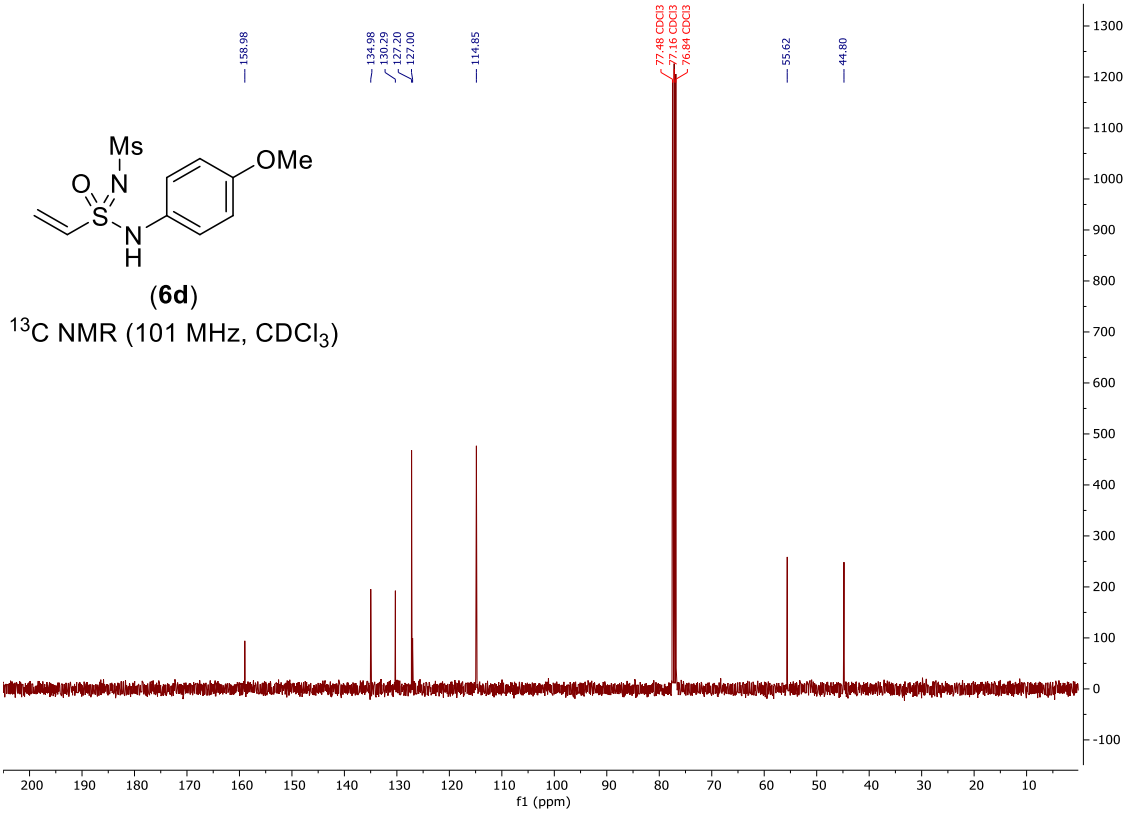


(**6c**)

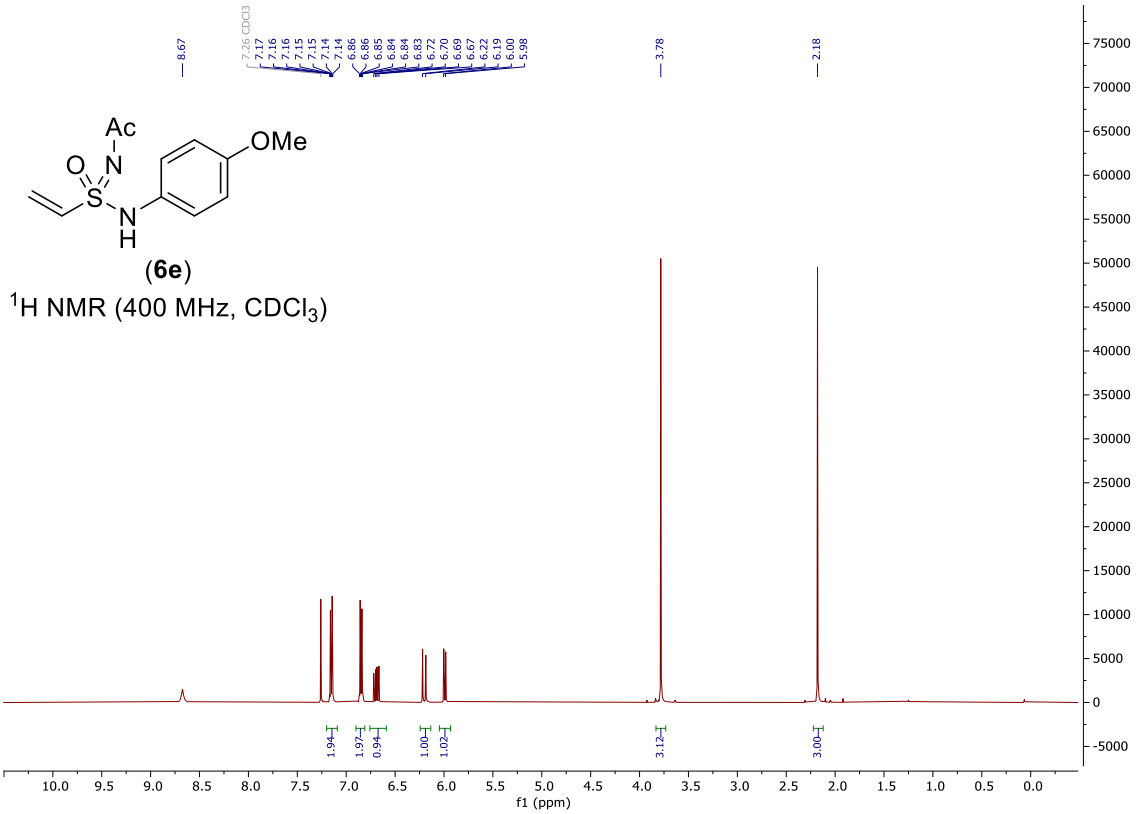
^{13}C NMR (101 MHz, $CDCl_3$)

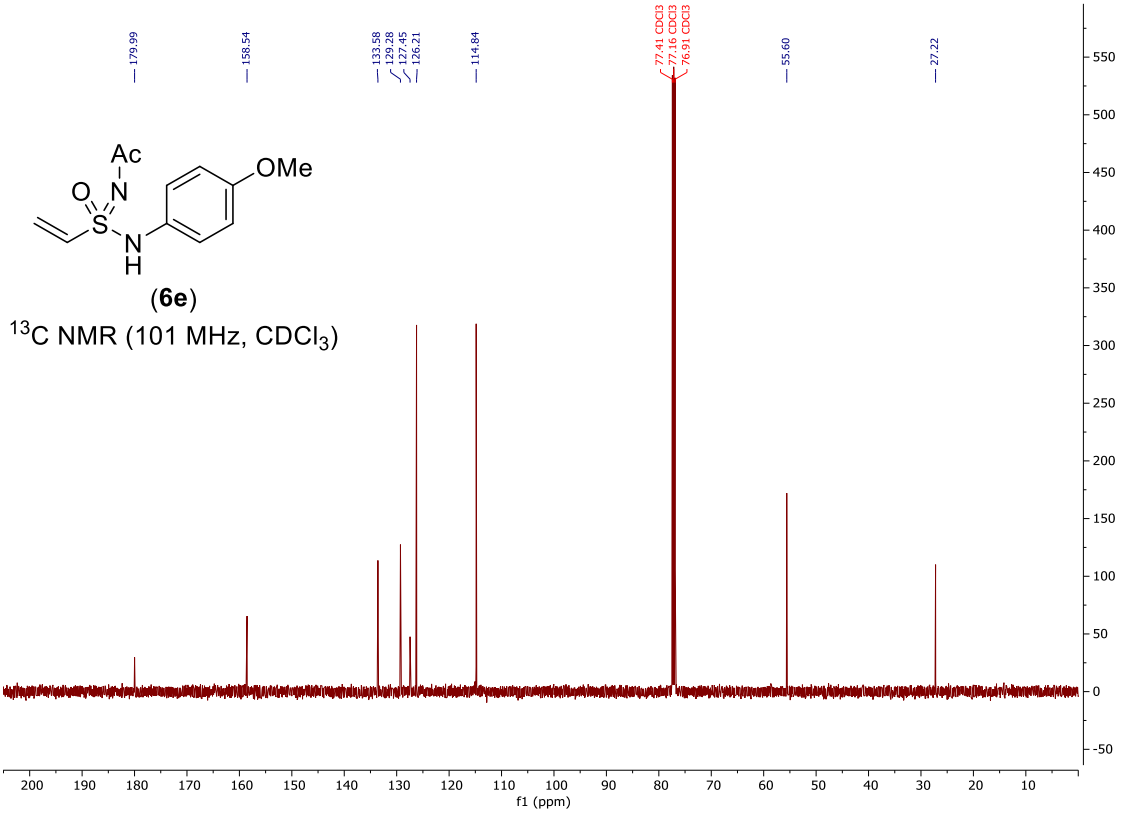
_N_-(_N_-(4-methoxyphenyl)vinylsulfonimidoyl)methanesulfonamide (6d)



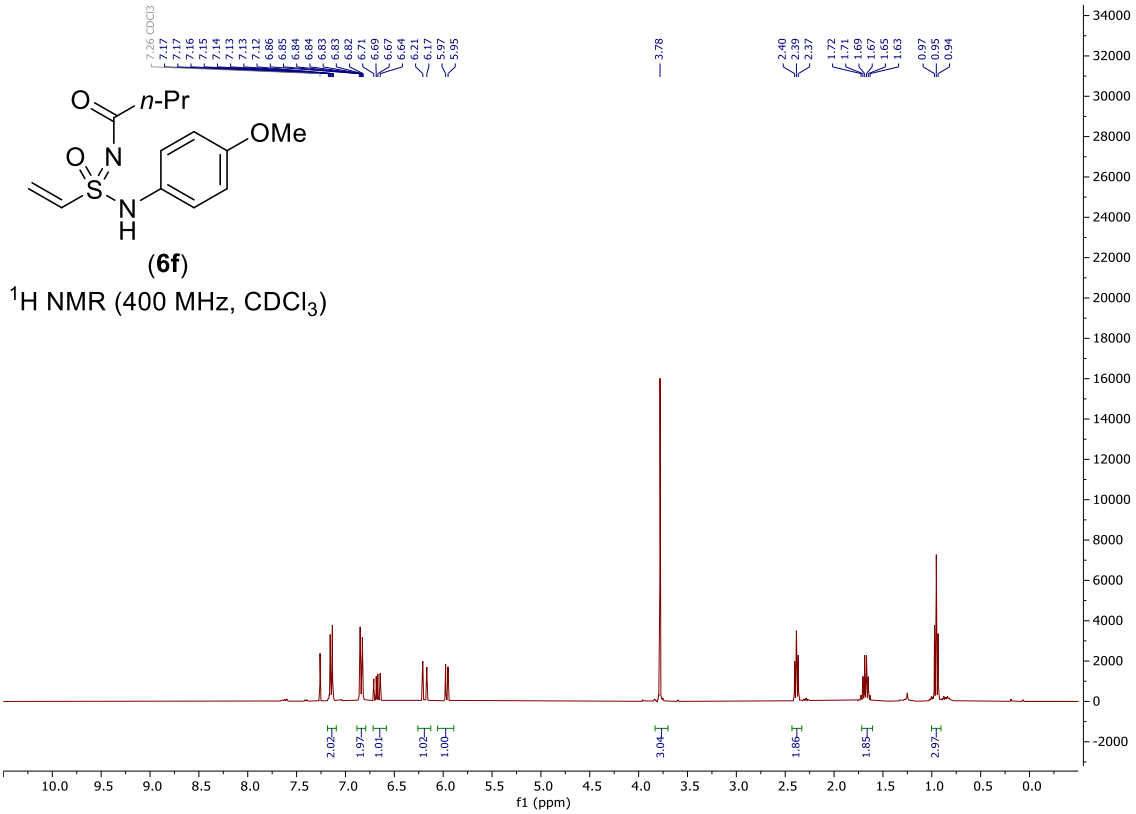


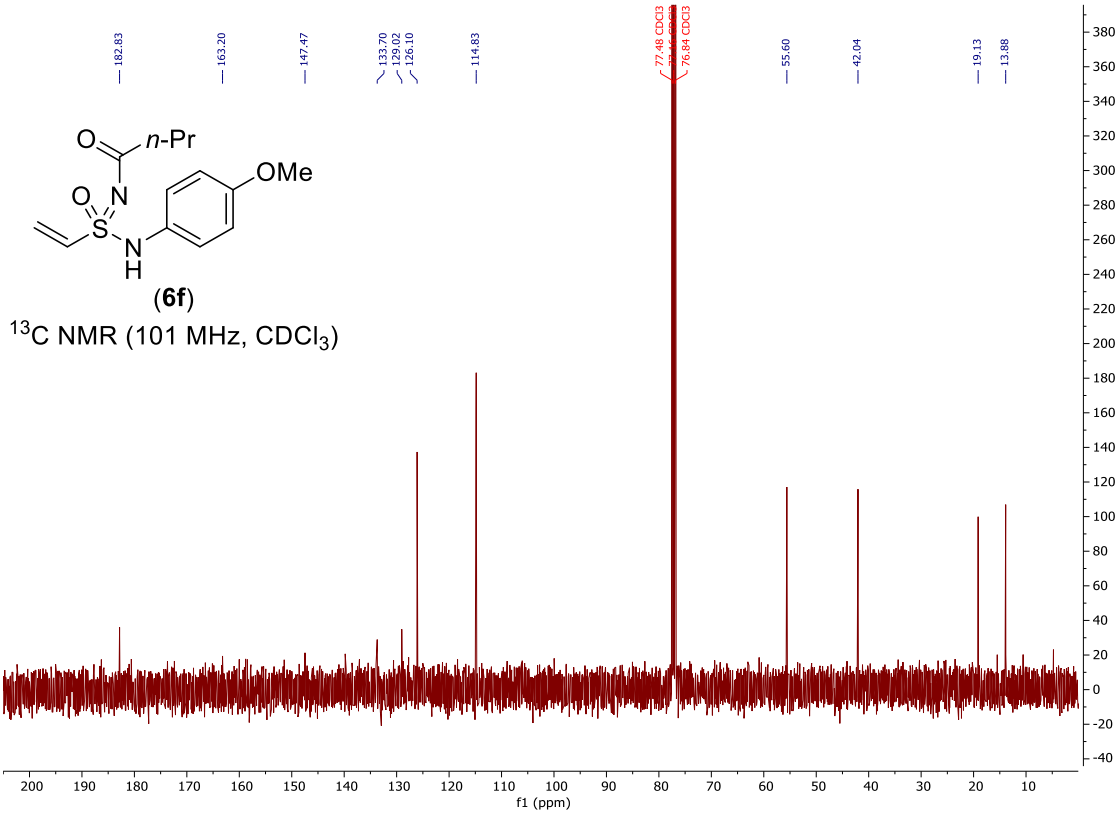
***N*-(*N*-(4-methoxyphenyl)vinylsulfonimidoyl)acetamide (6e)**



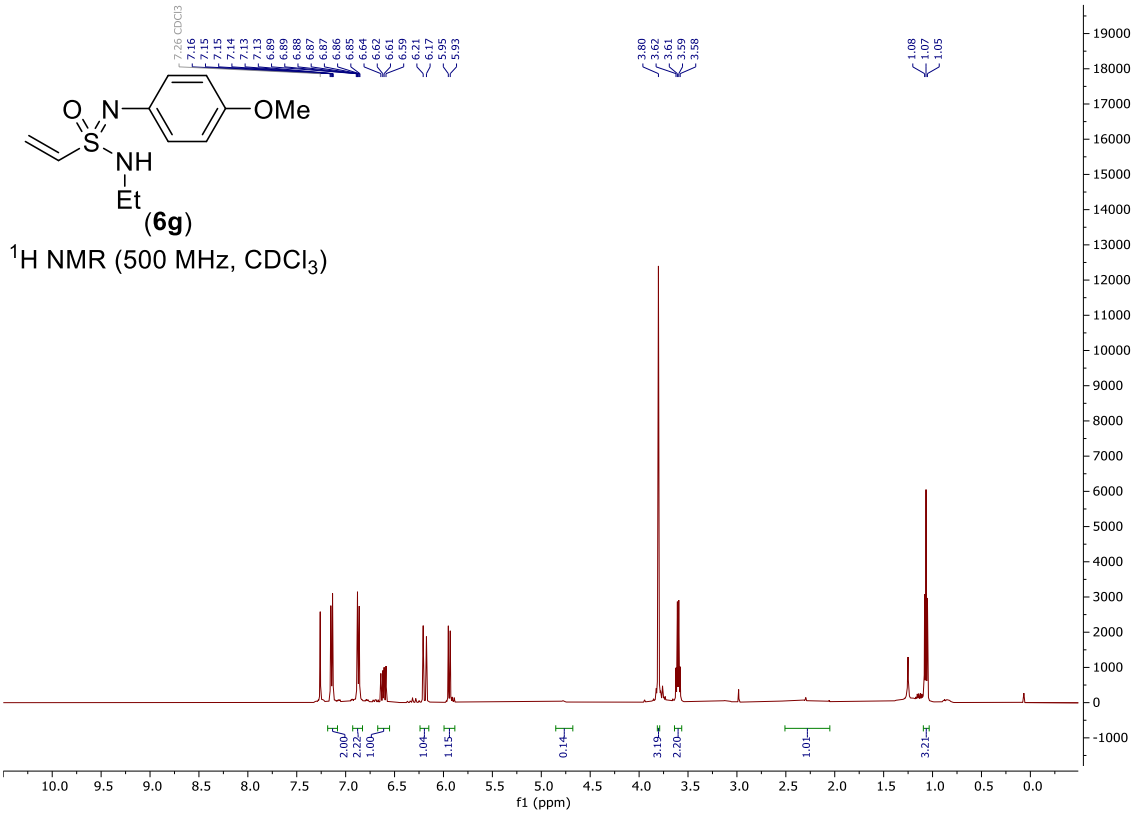


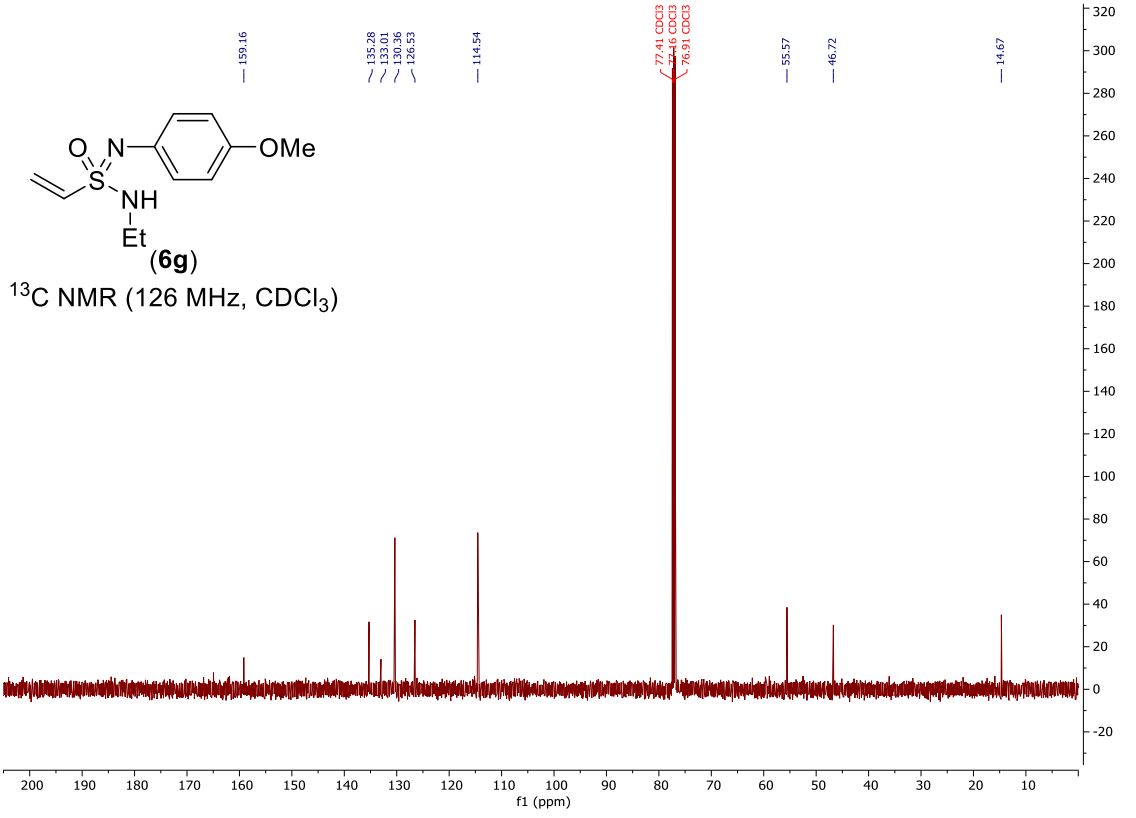
_N_-(_N_-(4-methoxyphenyl)vinylsulfonimidoyl)butyramide (6f)



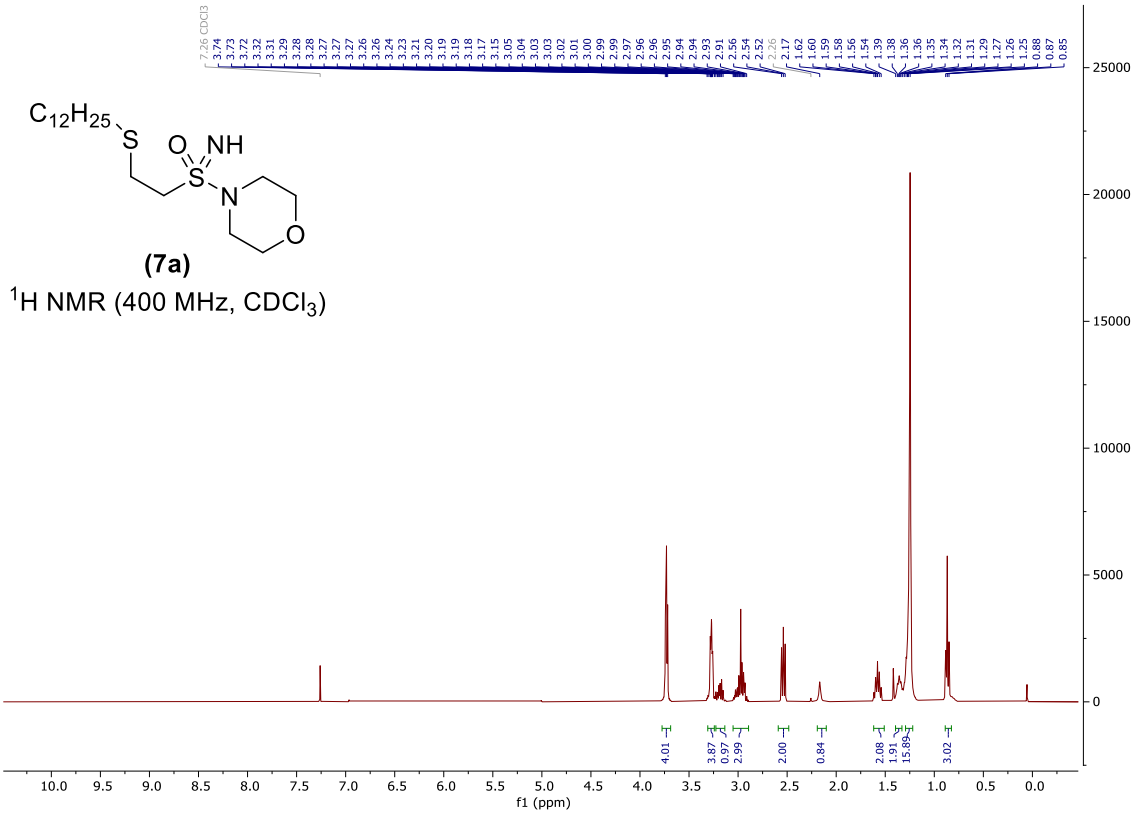


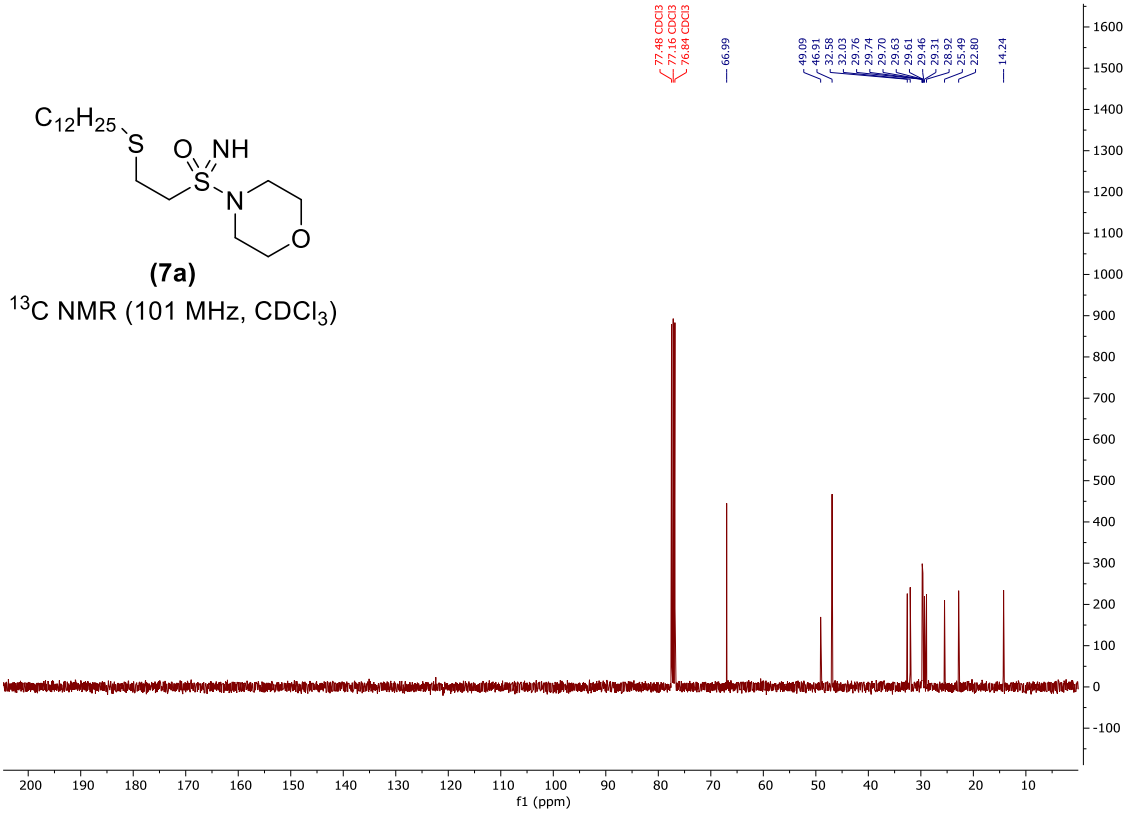
_N_-ethyl-_N_'-(4-methoxyphenyl)ethenesulfonimidamide (6g)



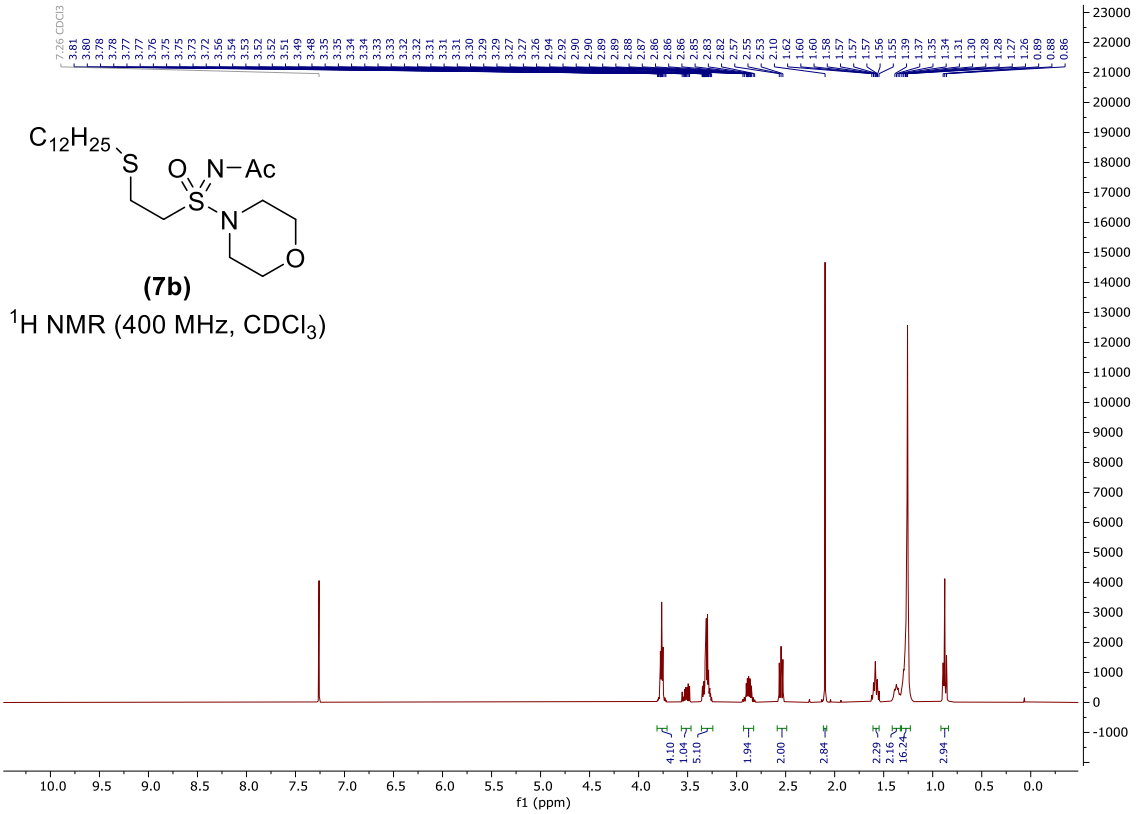


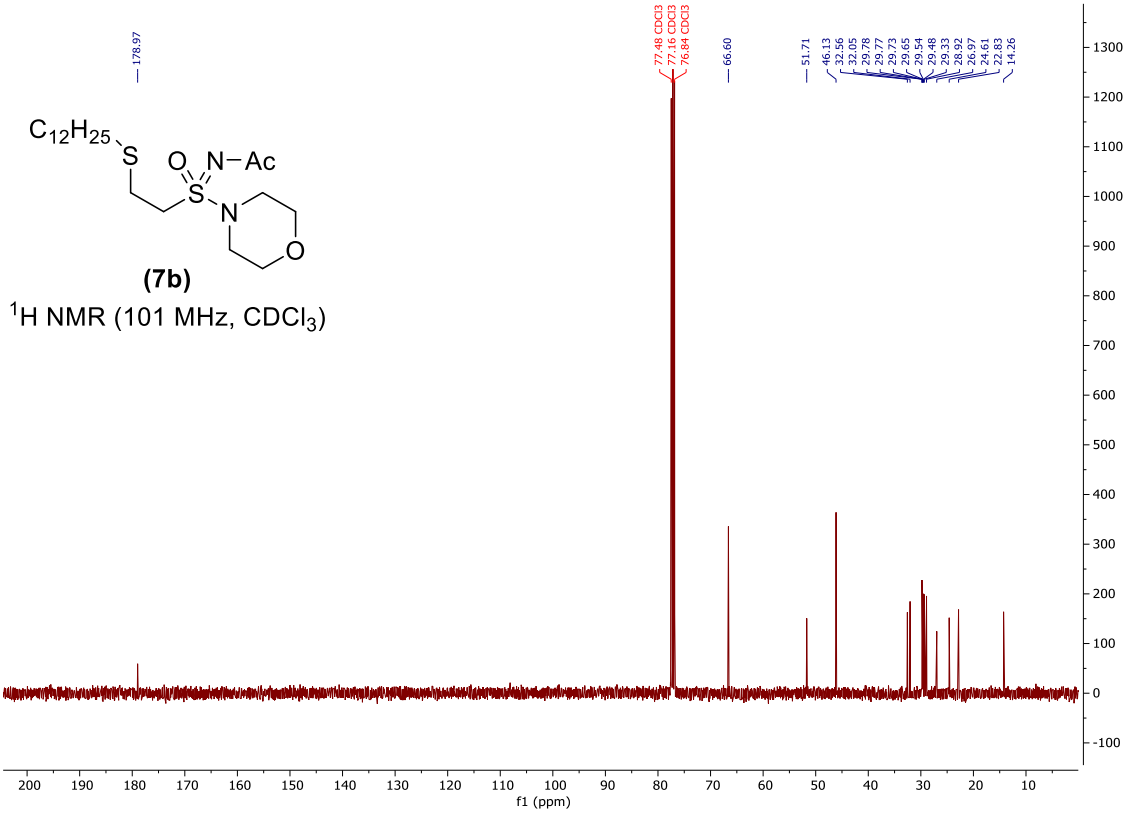
4-(2-(dodecylthio)ethylsulfonimidoyl)morpholine (7a)



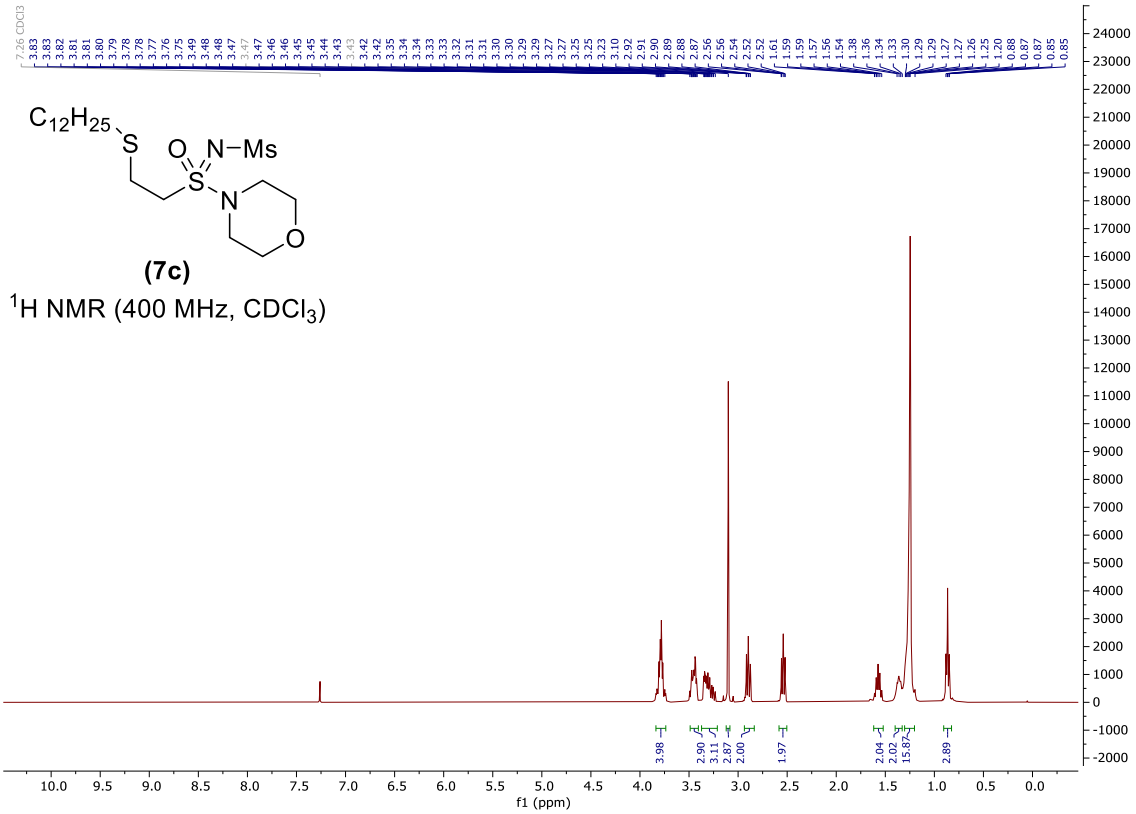


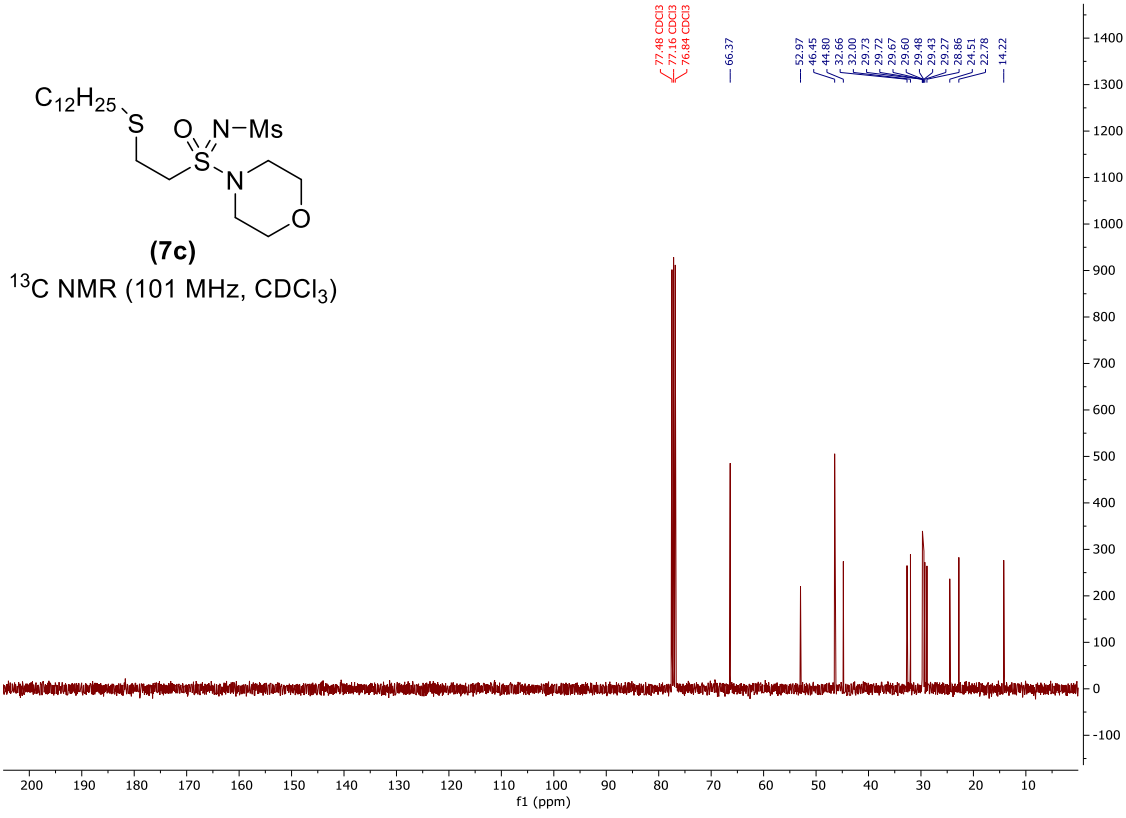
_N_-((2-(dodecylthio)ethyl)(morpholino)(oxo)- λ^6-sulfaneylidene)acetamide (7b)



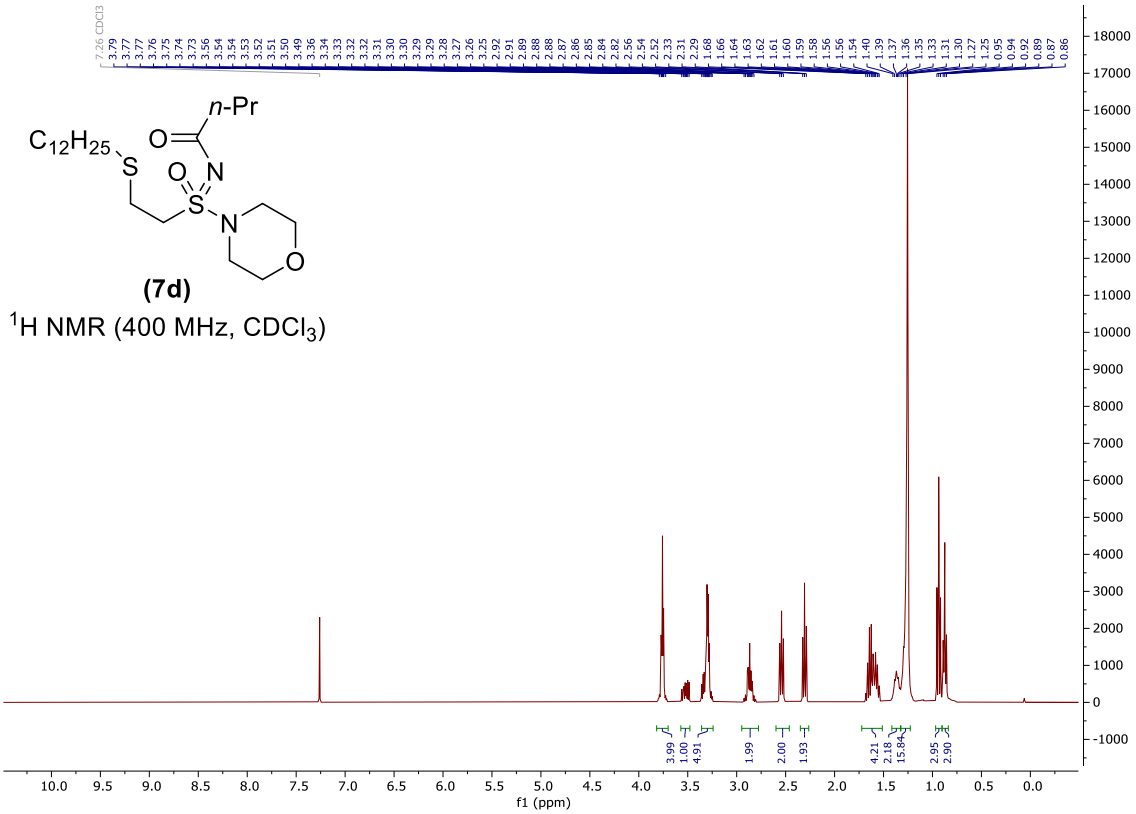


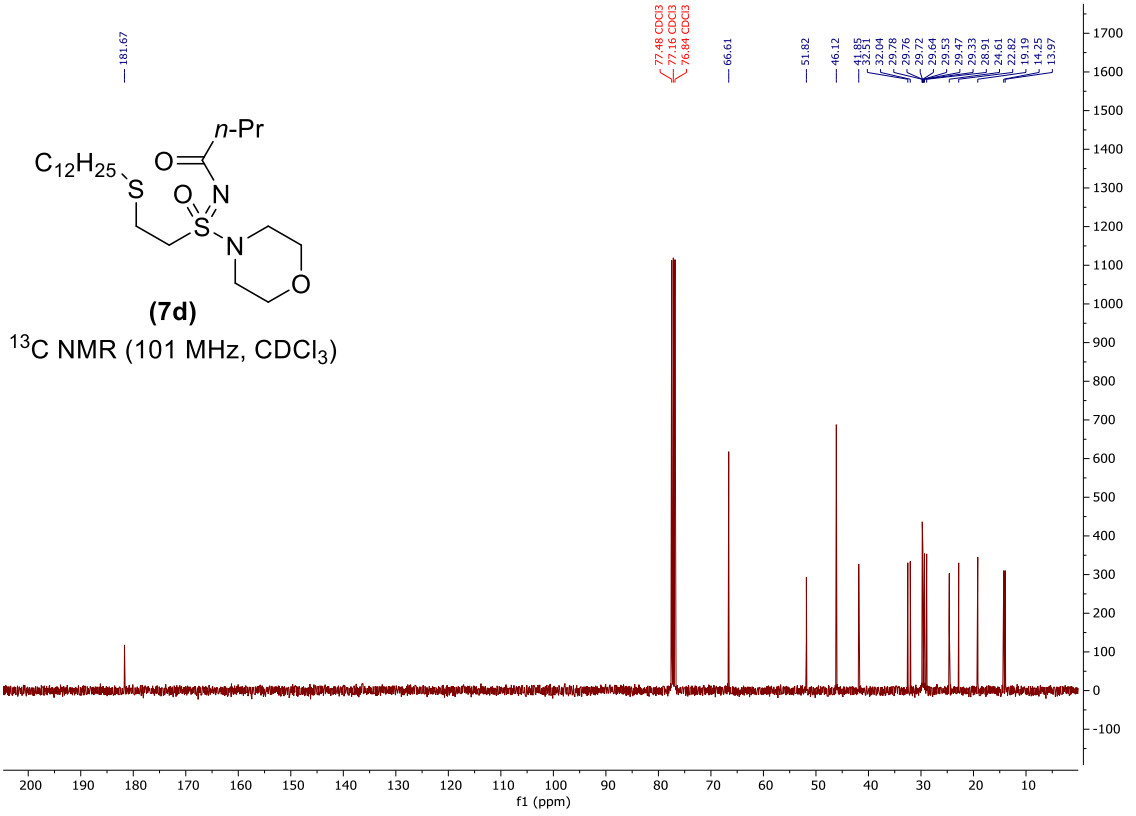
***N*-((2-(dodecylthio)ethyl)(morpholino)(oxo)- λ^6-sulfaneylidene)methanesulfonamide (7c)**



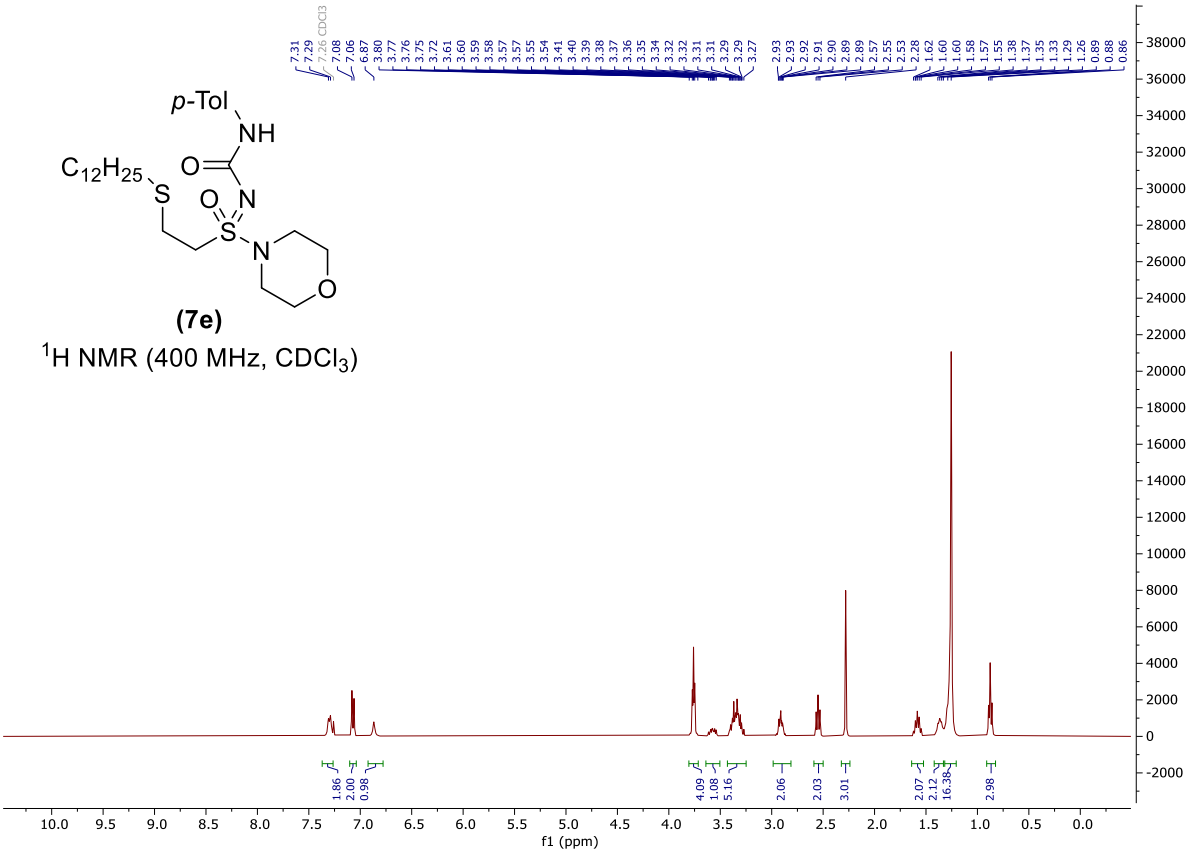


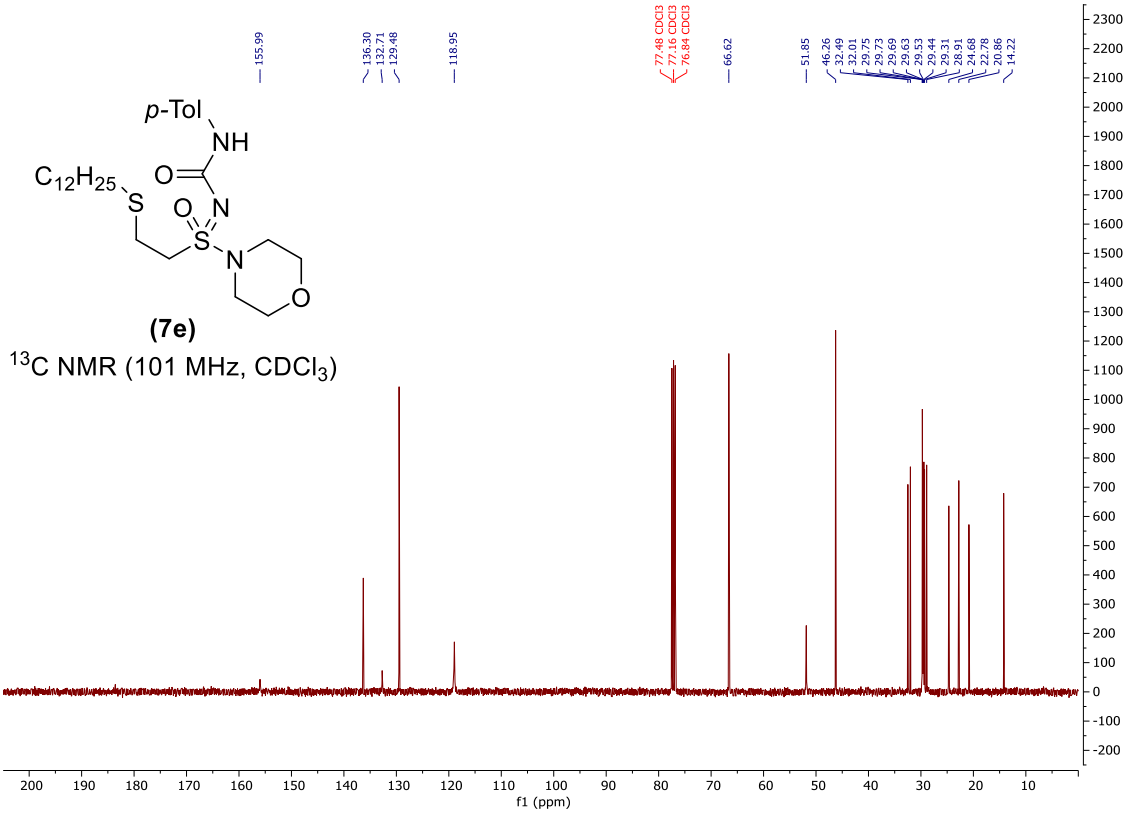
_N_-((2-(dodecylthio)ethyl)(morpholino)(oxo)-λ6-sulfaneylidene)butyramide (7d)



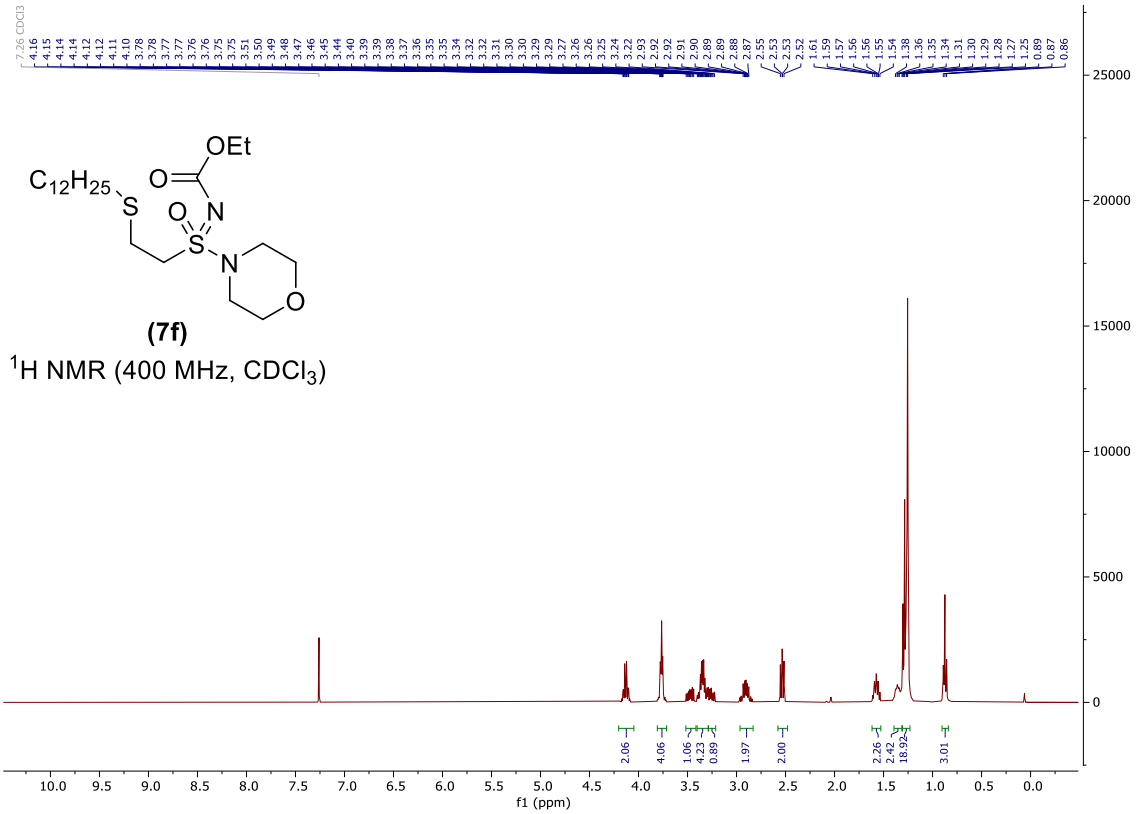


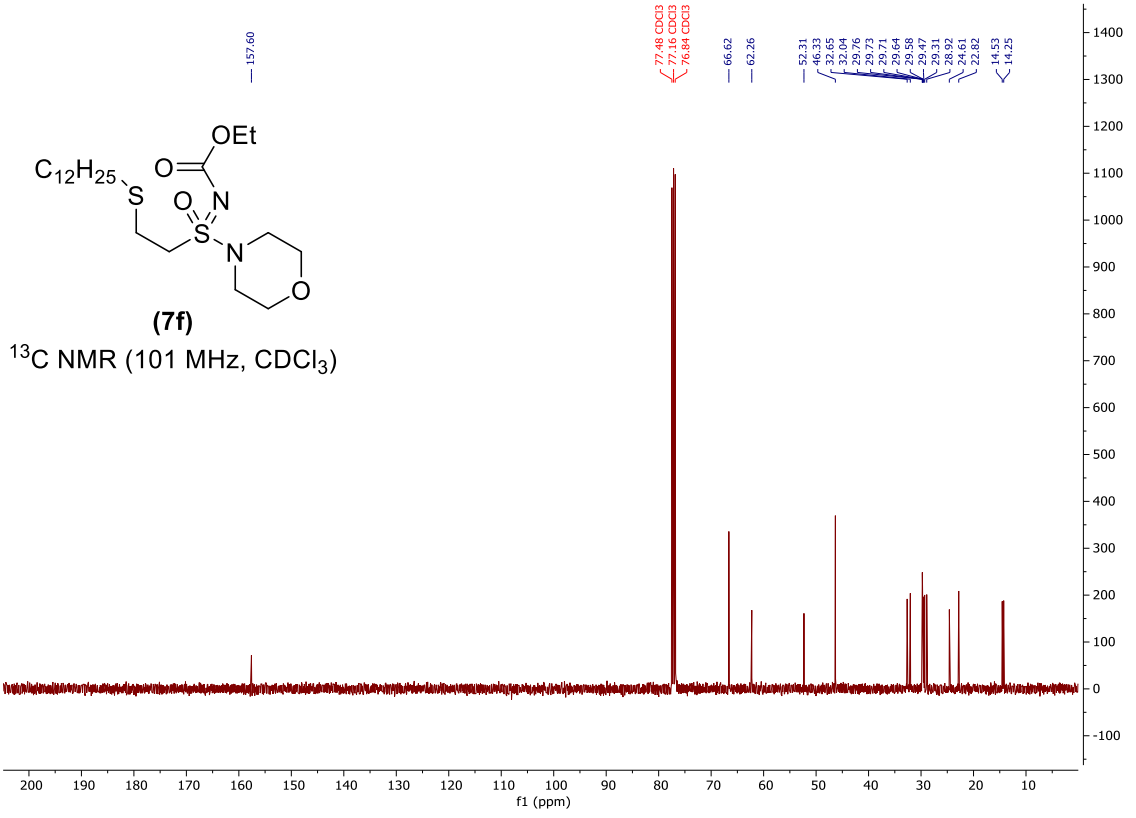
1-((2-(dodecylthio)ethyl)(morpholino)(oxo)-λ6-sulfaneylidene)-3-(p-tolyl)urea (7e)



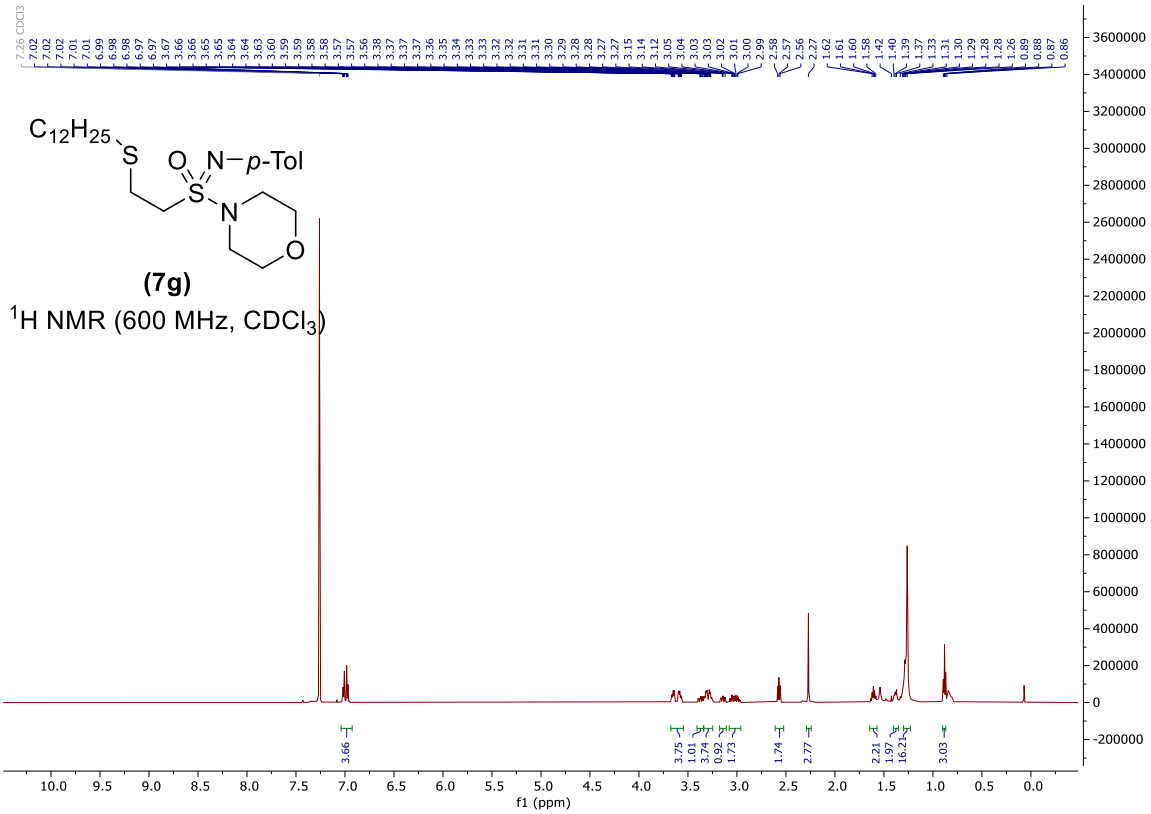


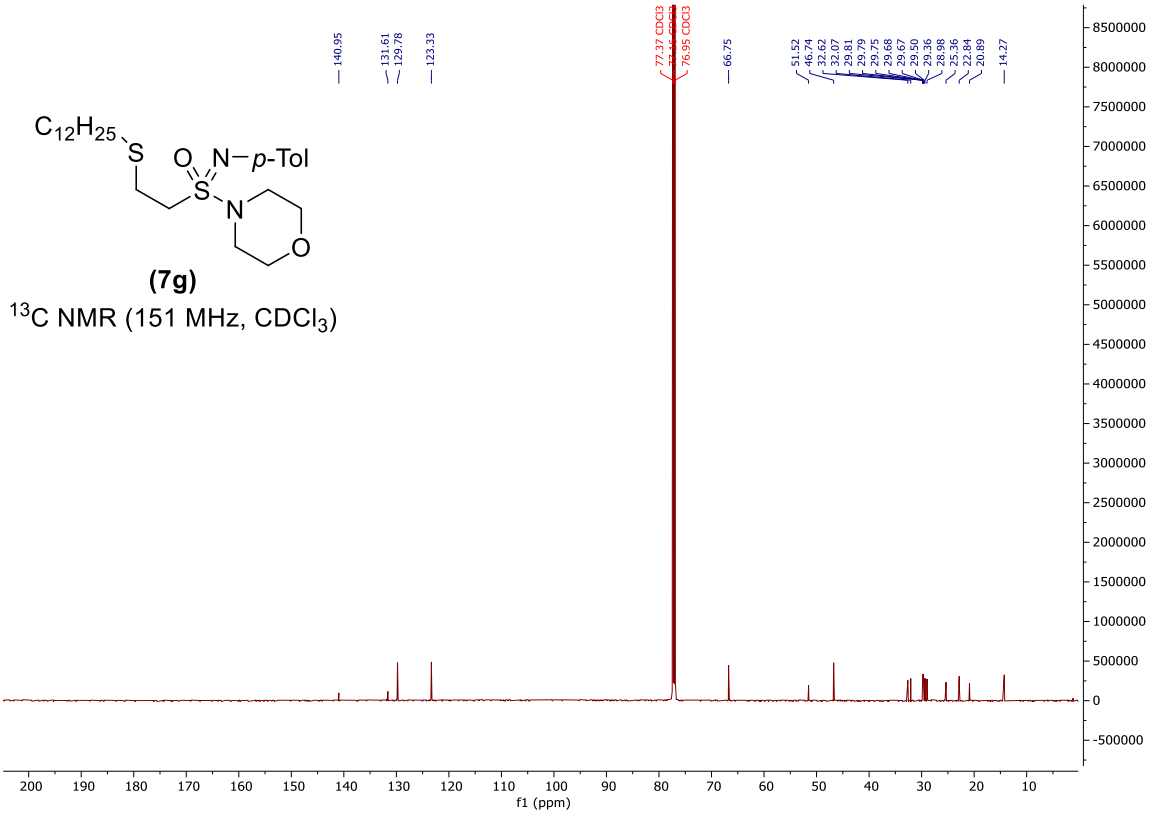
Ethyl ((2-(dodecylthio)ethyl)(morpholino)(oxo)- λ⁶-sulfaneylidene)carbamate (7f)



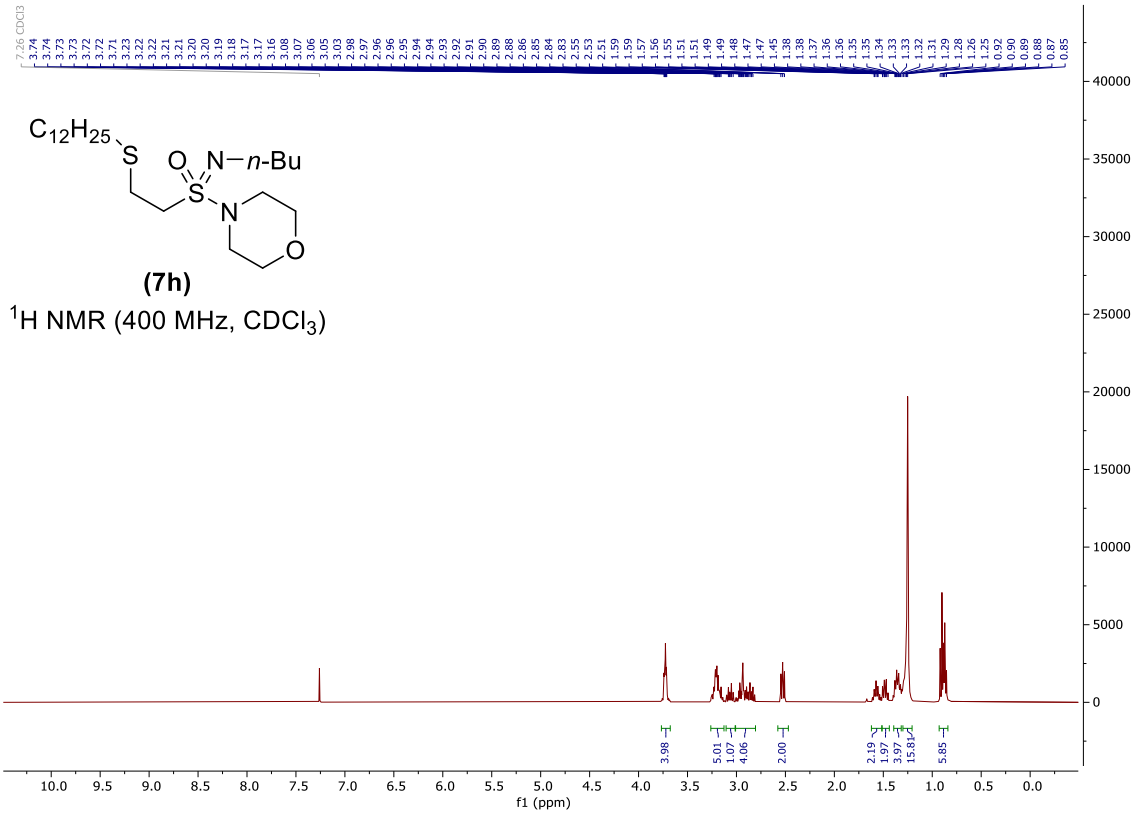


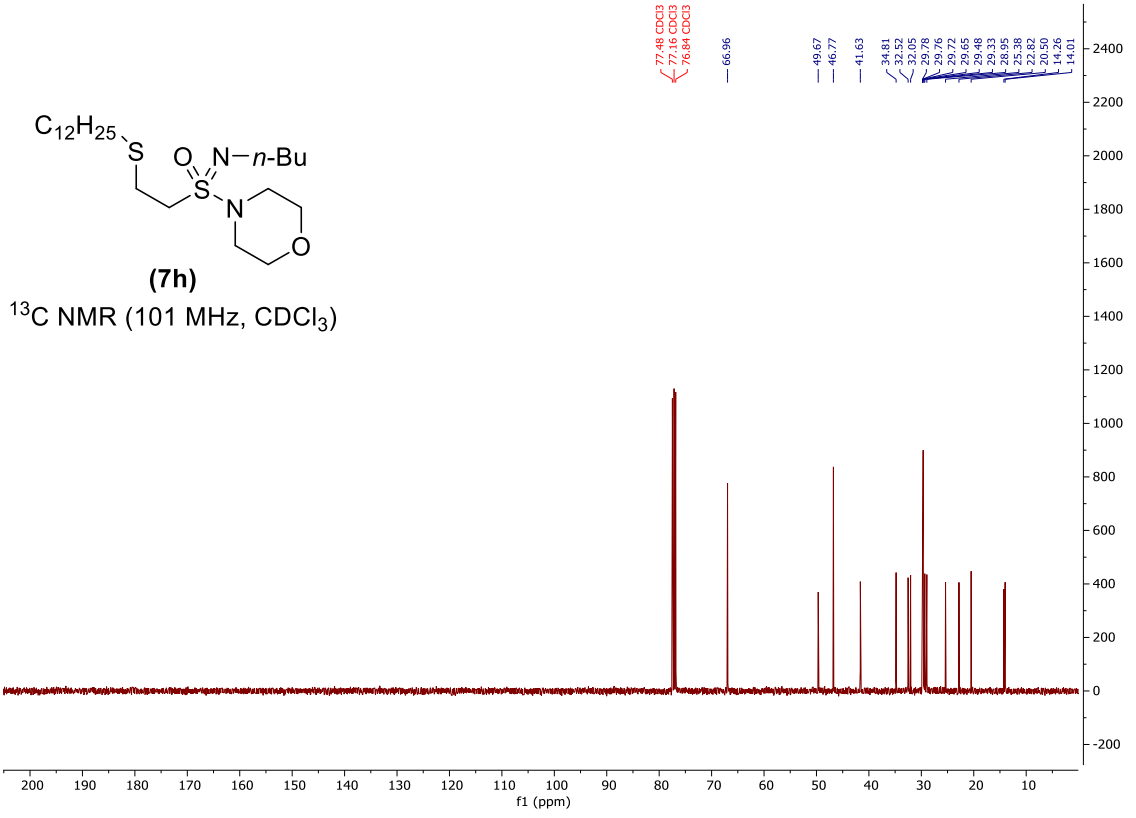
4-(2-(dodecylthio)-*N*-(p-tolyl)ethylsulfonimidoyl)morpholine (7g)



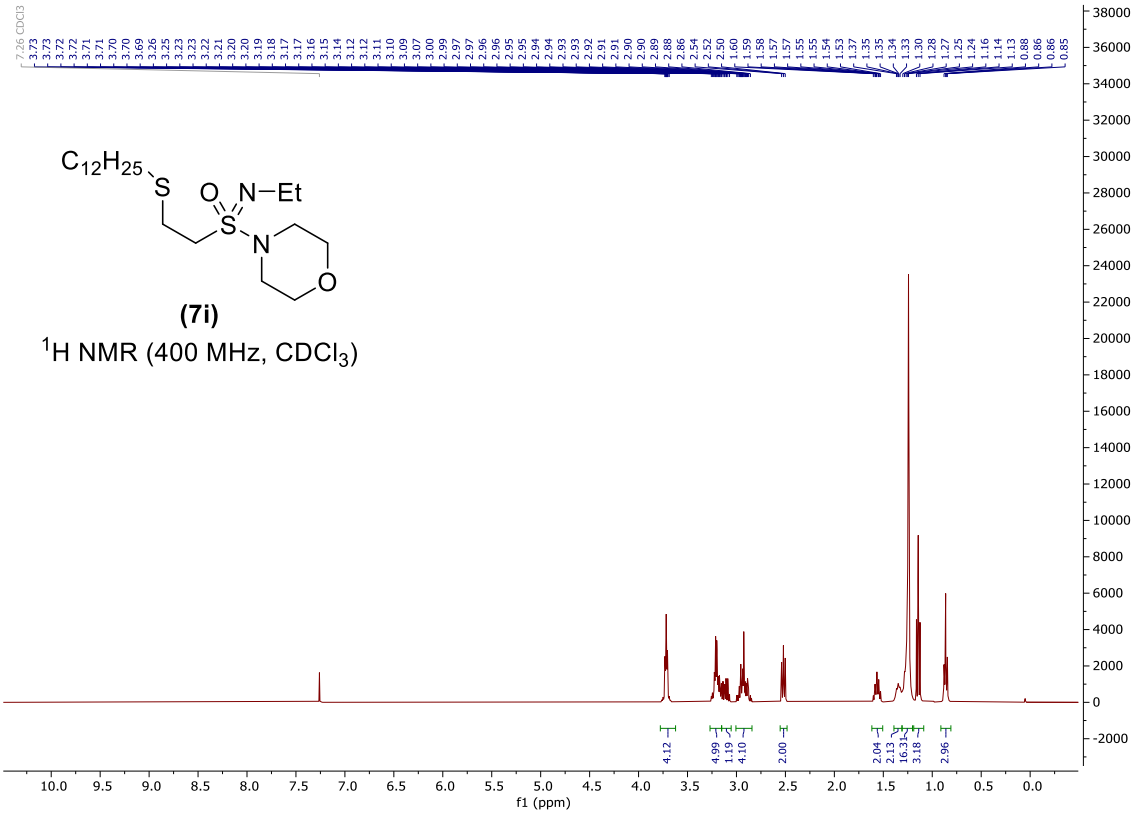


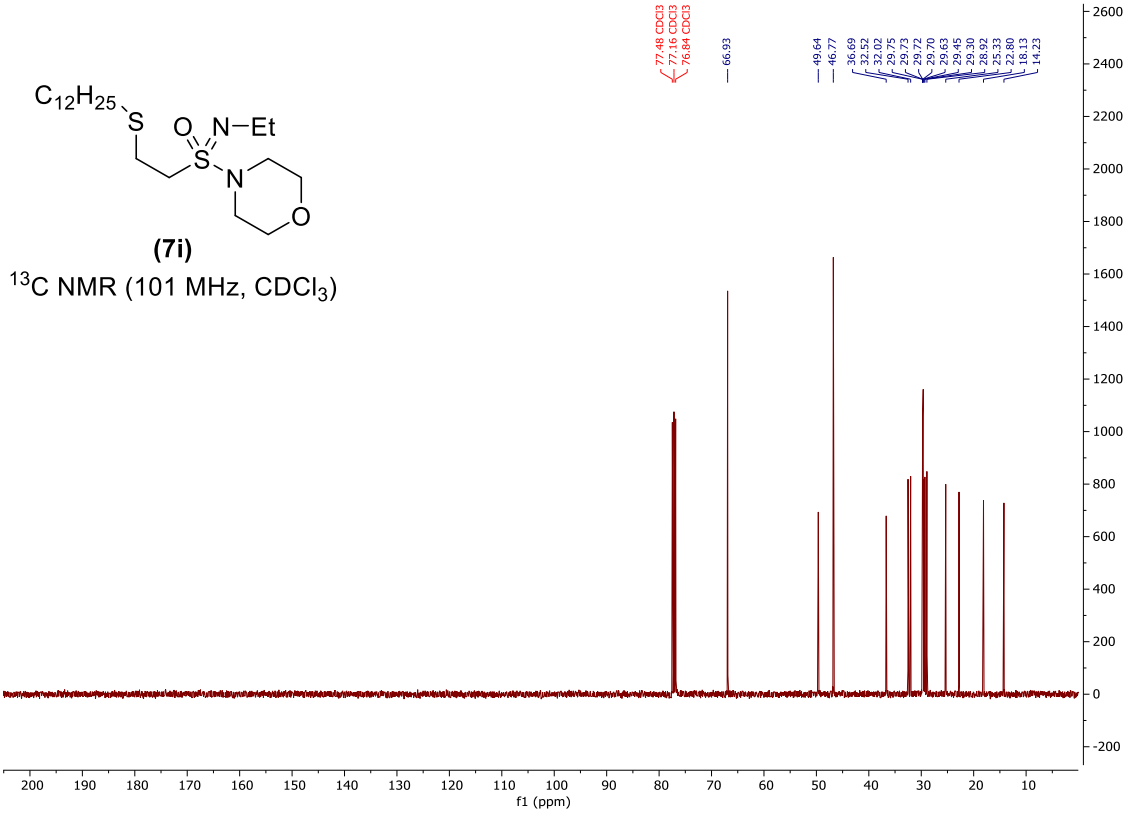
4-(*N*-butyl-2-(dodecylthio)ethylsulfonimidoyl)morpholine (7h)



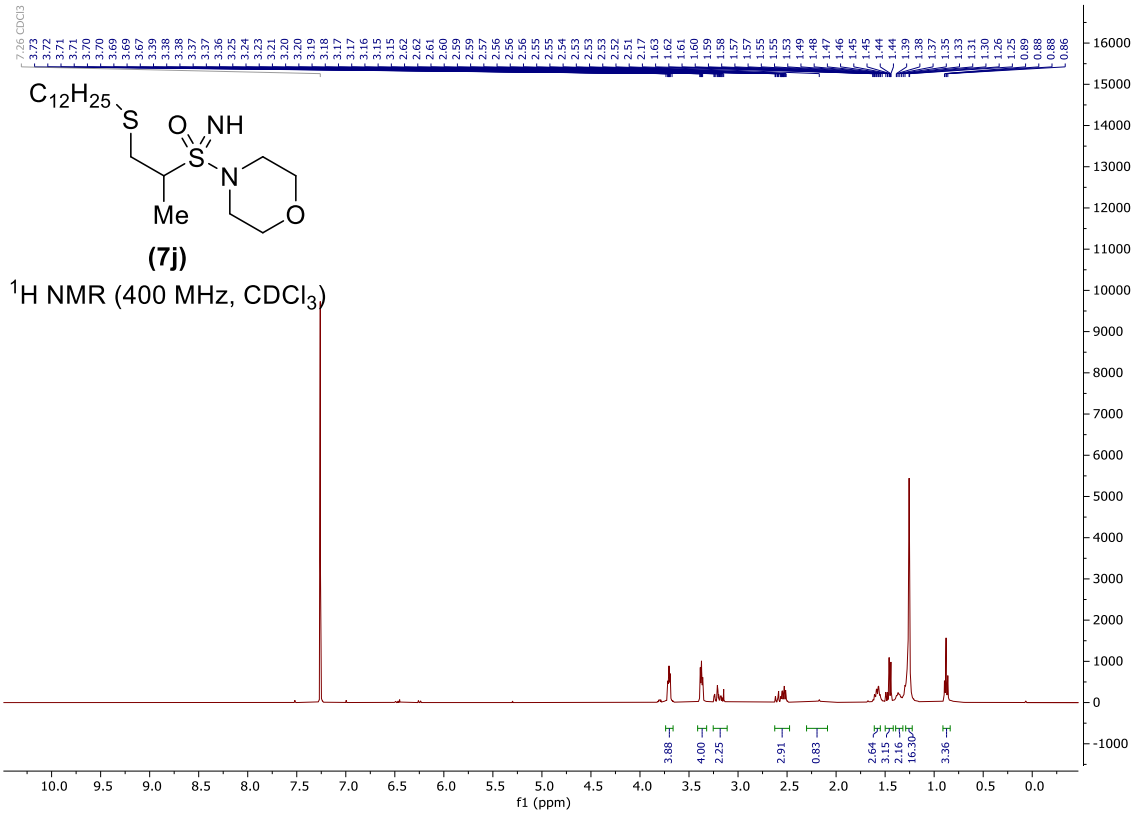


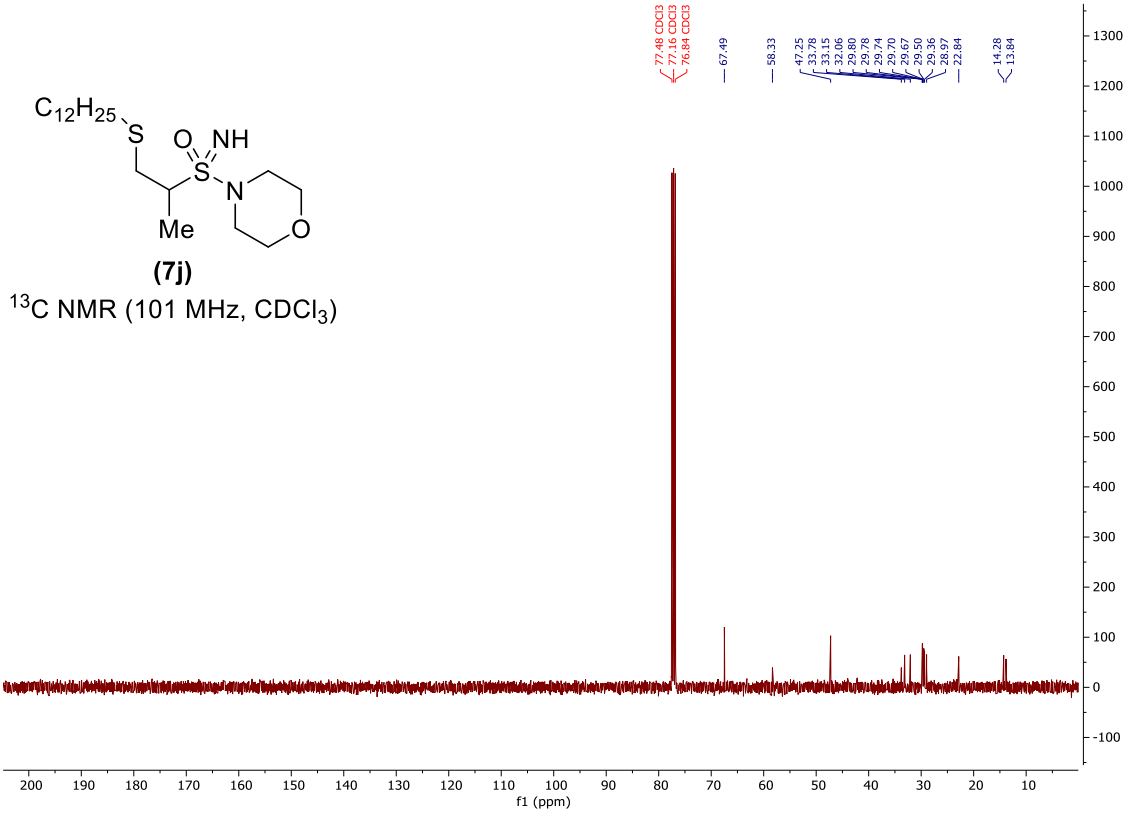
4-(2-(dodecylthio)-N-ethylethylsulfonimidoyl)morpholine (7i)



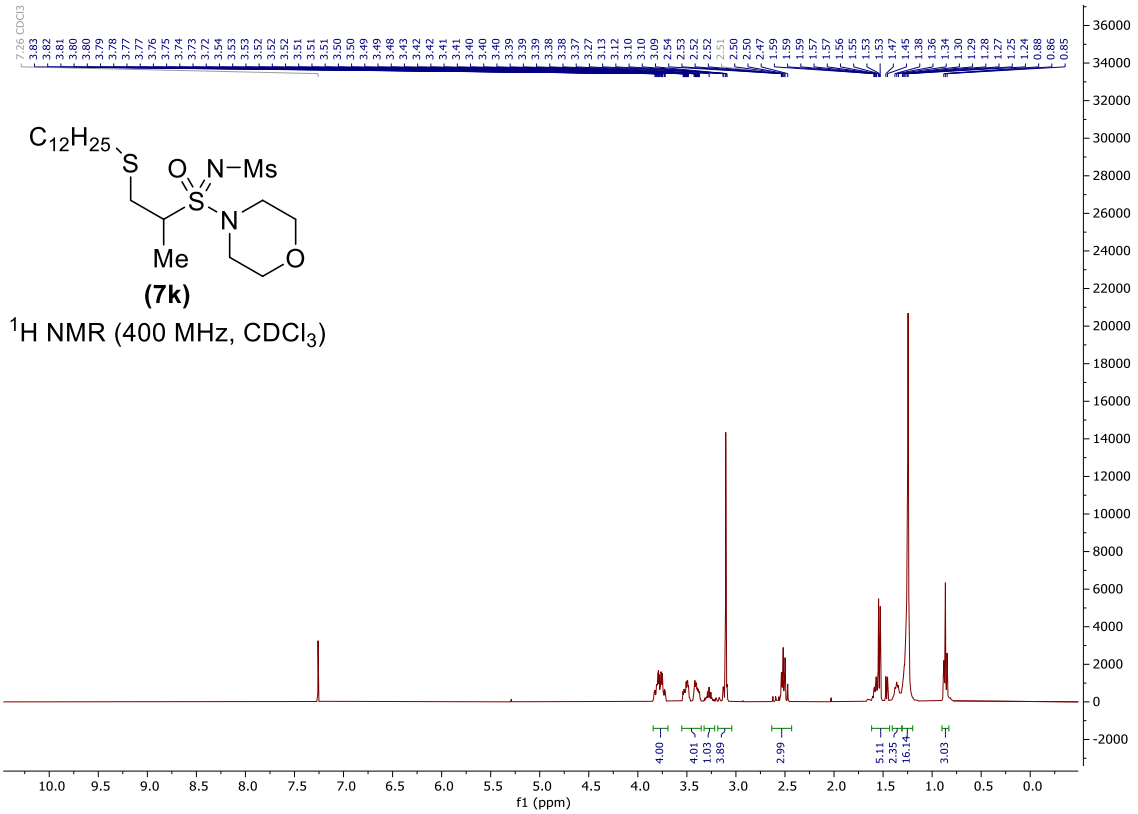


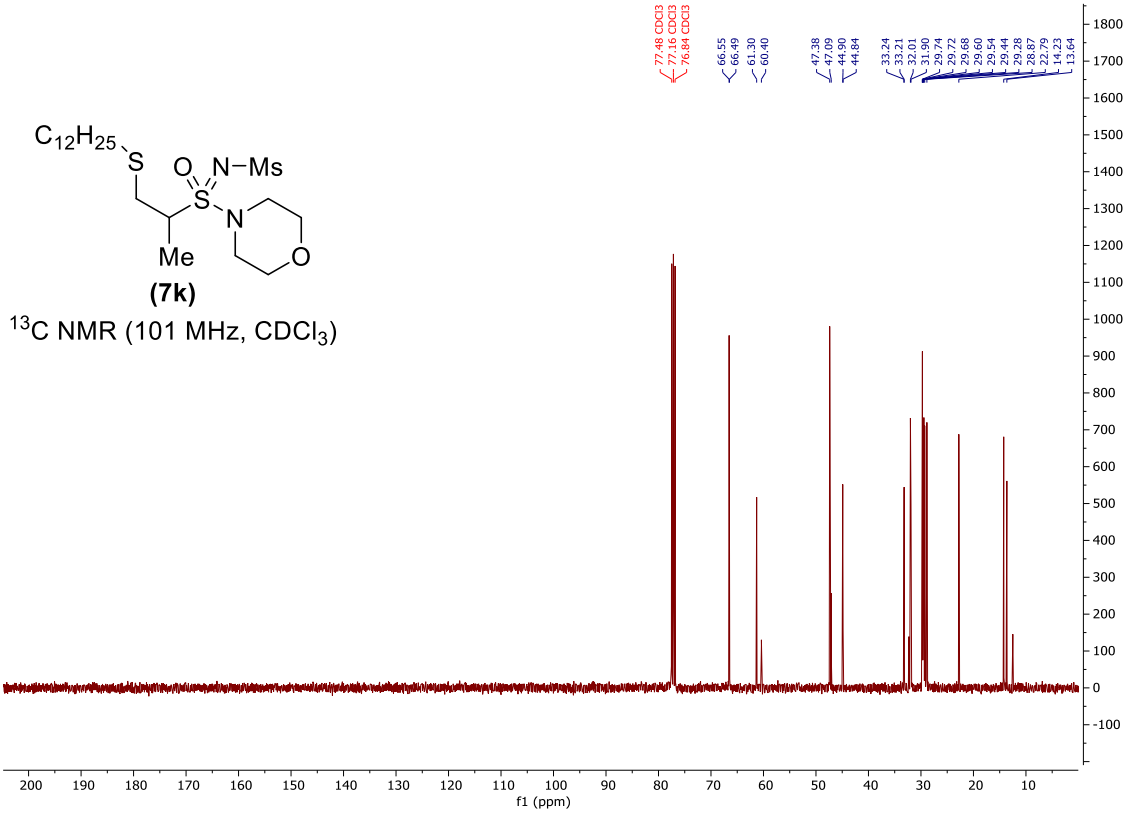
4-(1-(dodecylthio)propan-2-ylsulfonimidoyl)morpholine (7j)



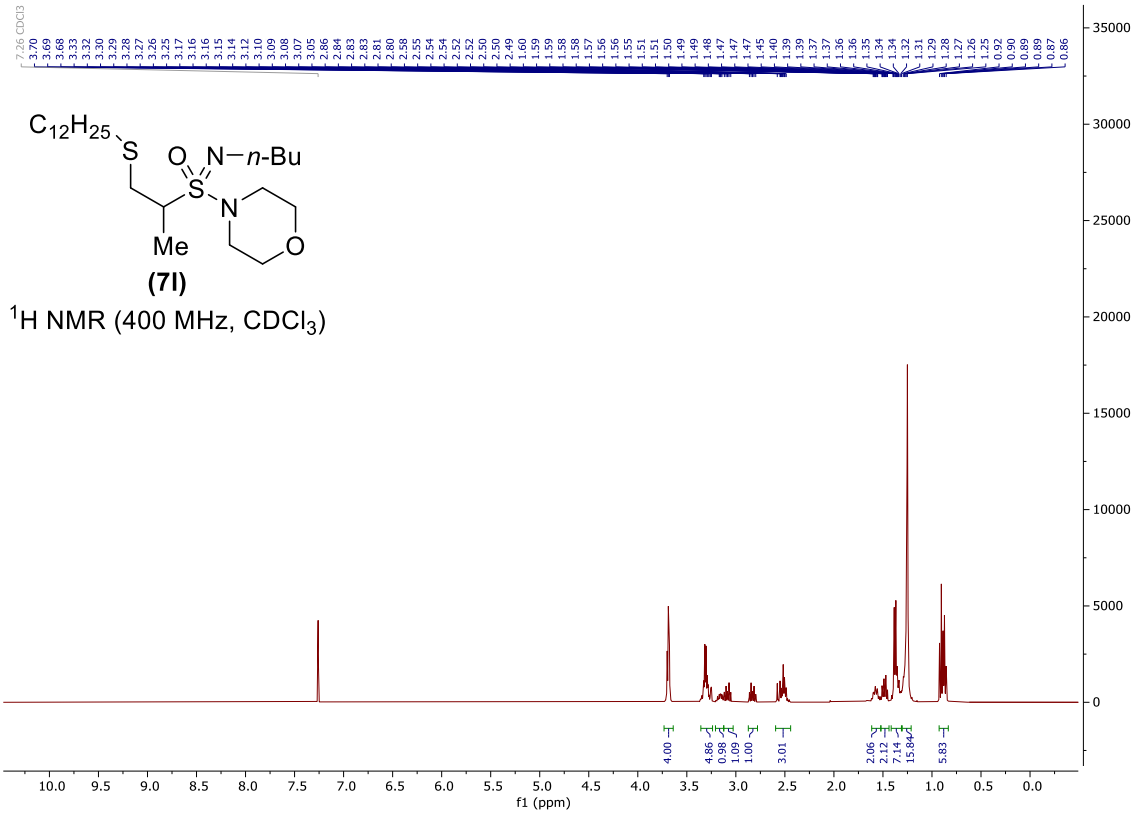


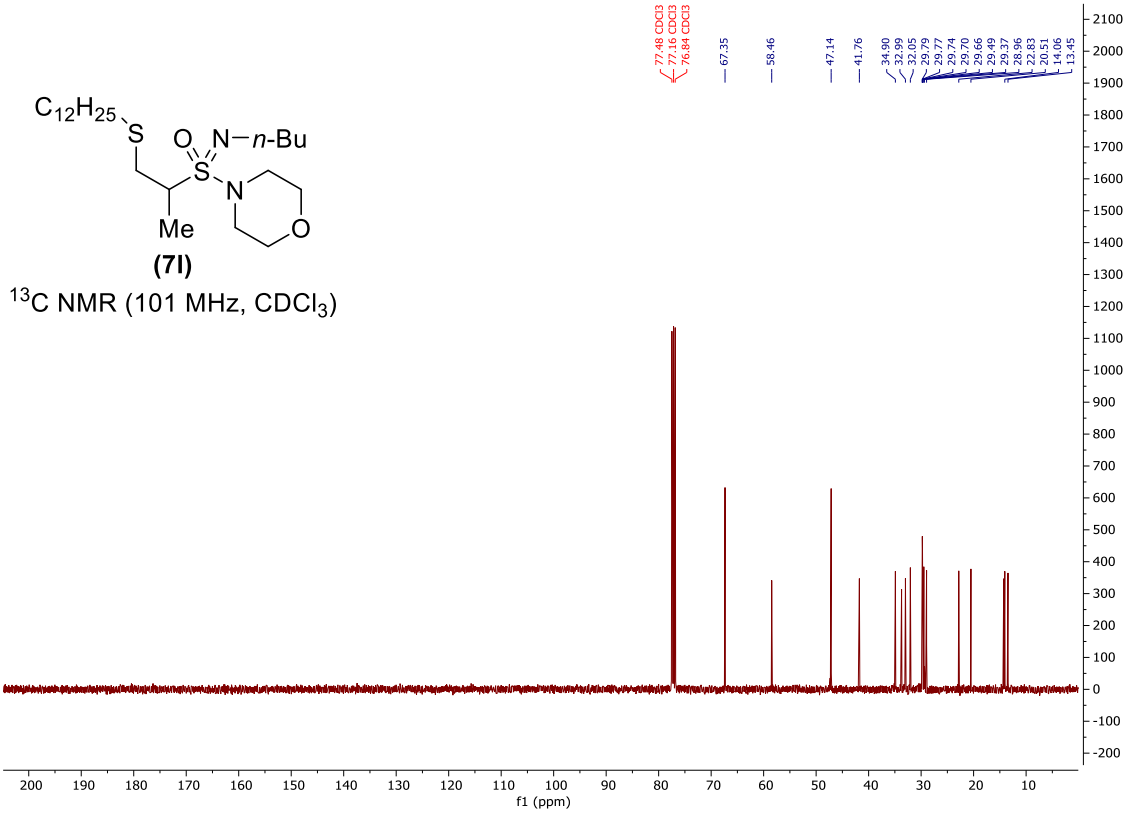
_N_-((1-(dodecylthio)propan-2-yl)(morpholino)(oxo)-λ6-sulfaneylidene)methanesulfonamide (7k)



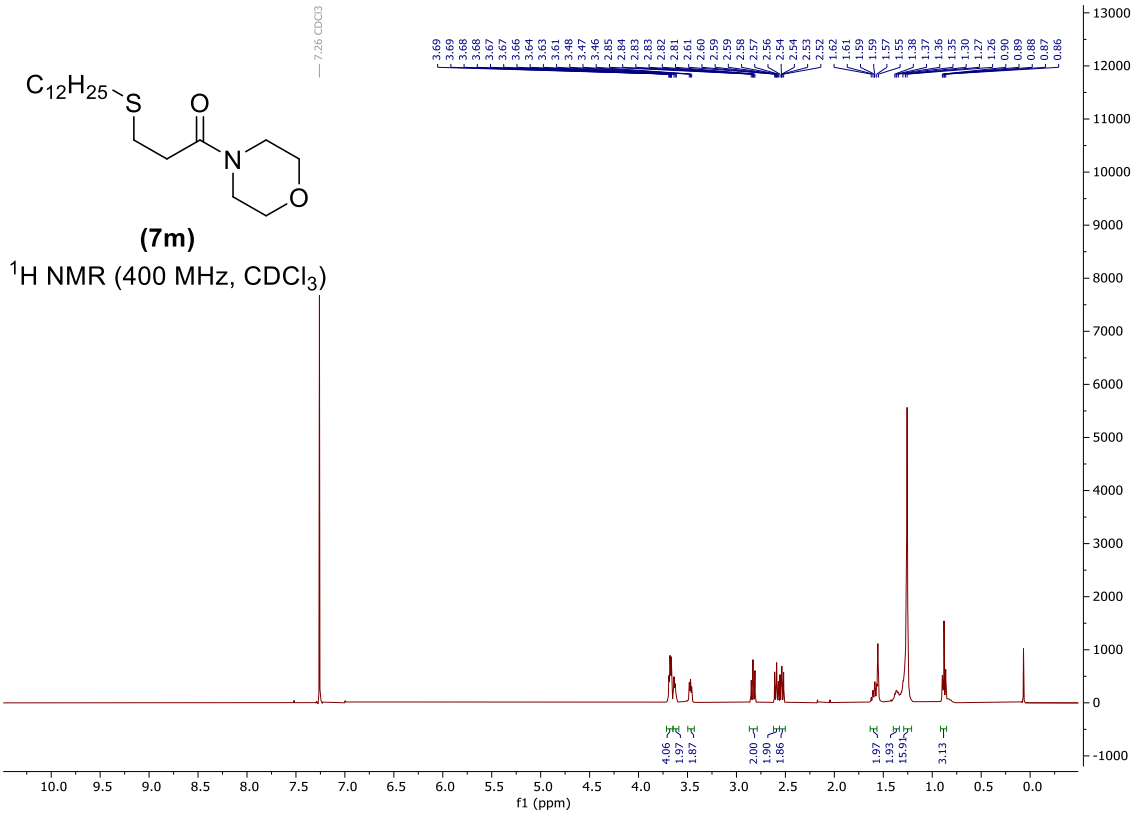


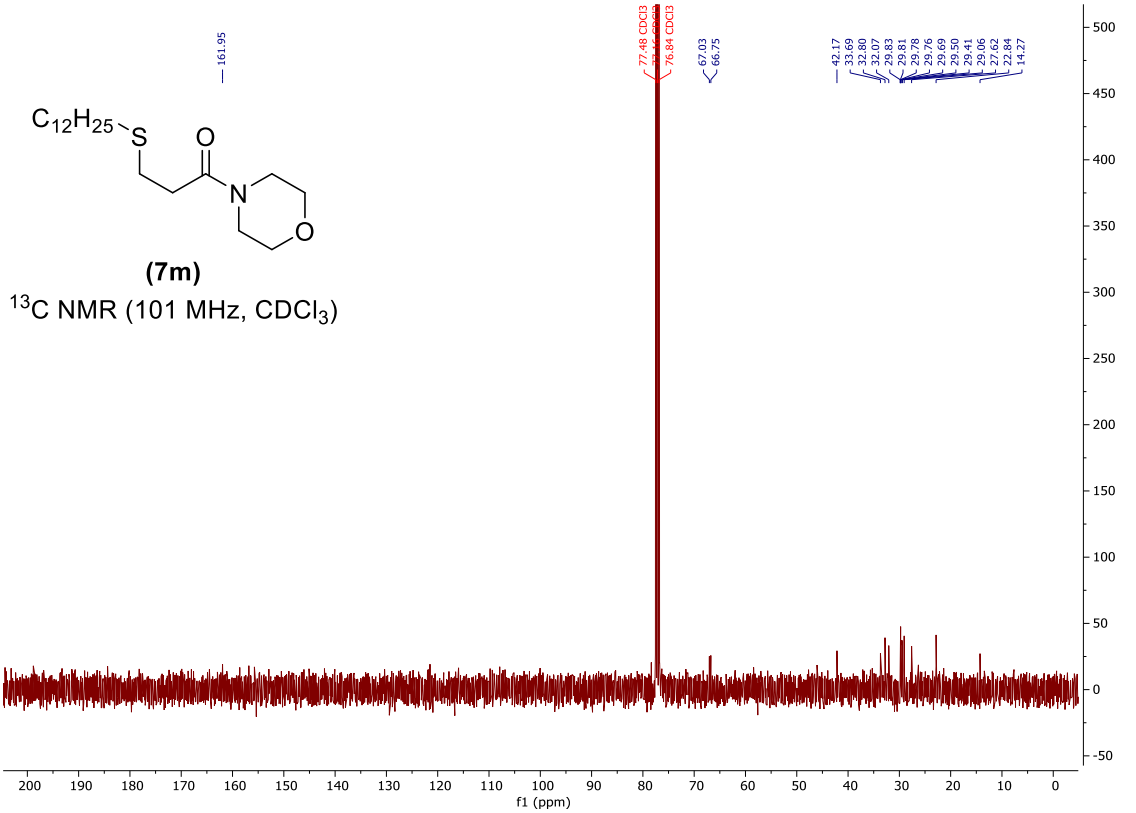
4-(*N*-butyl-1-(dodecylthio)propan-2-ylsulfonimidoyl)morpholine (7l)



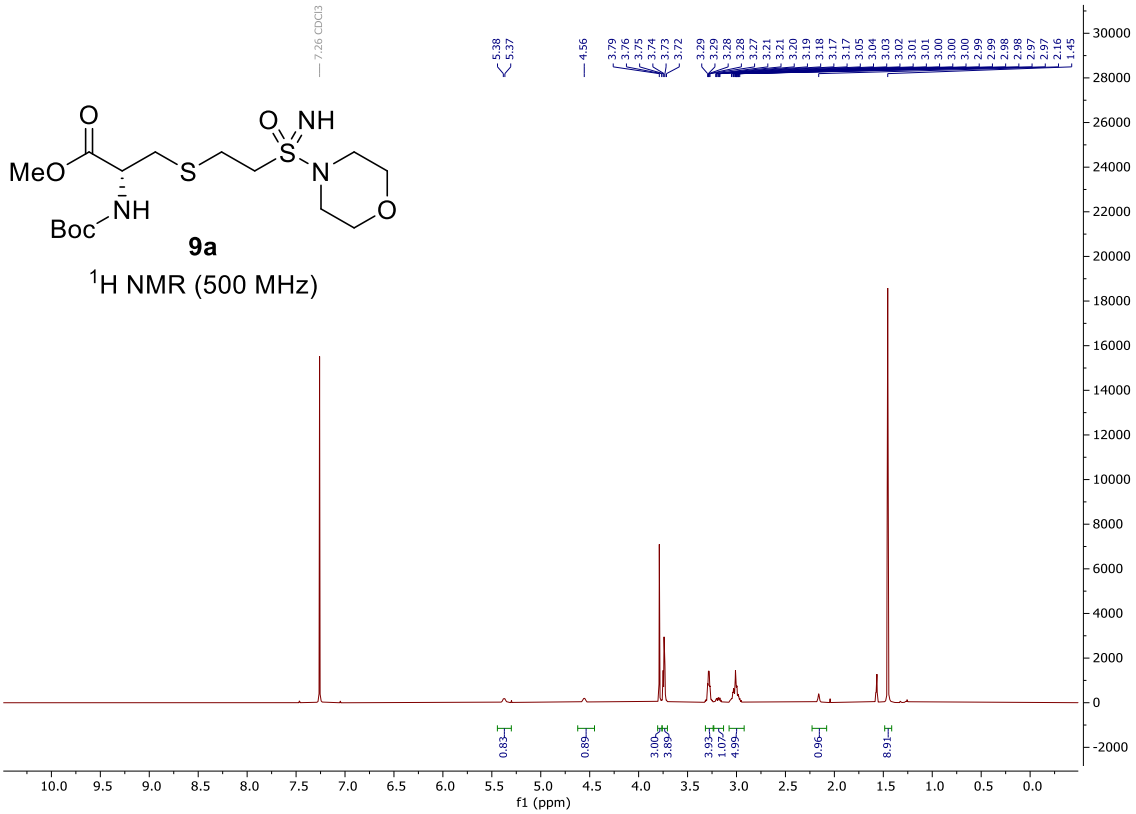


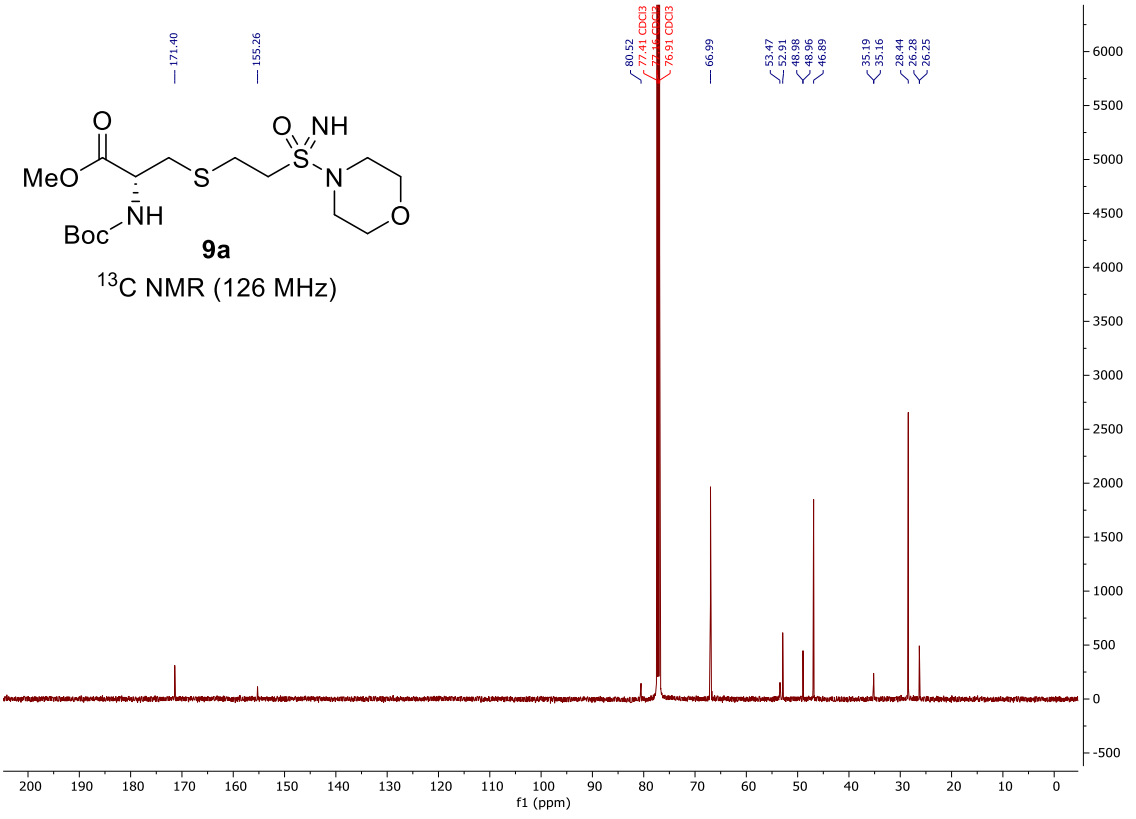
3-(dodecylthio)-1-morpholinopropan-1-one (7m)



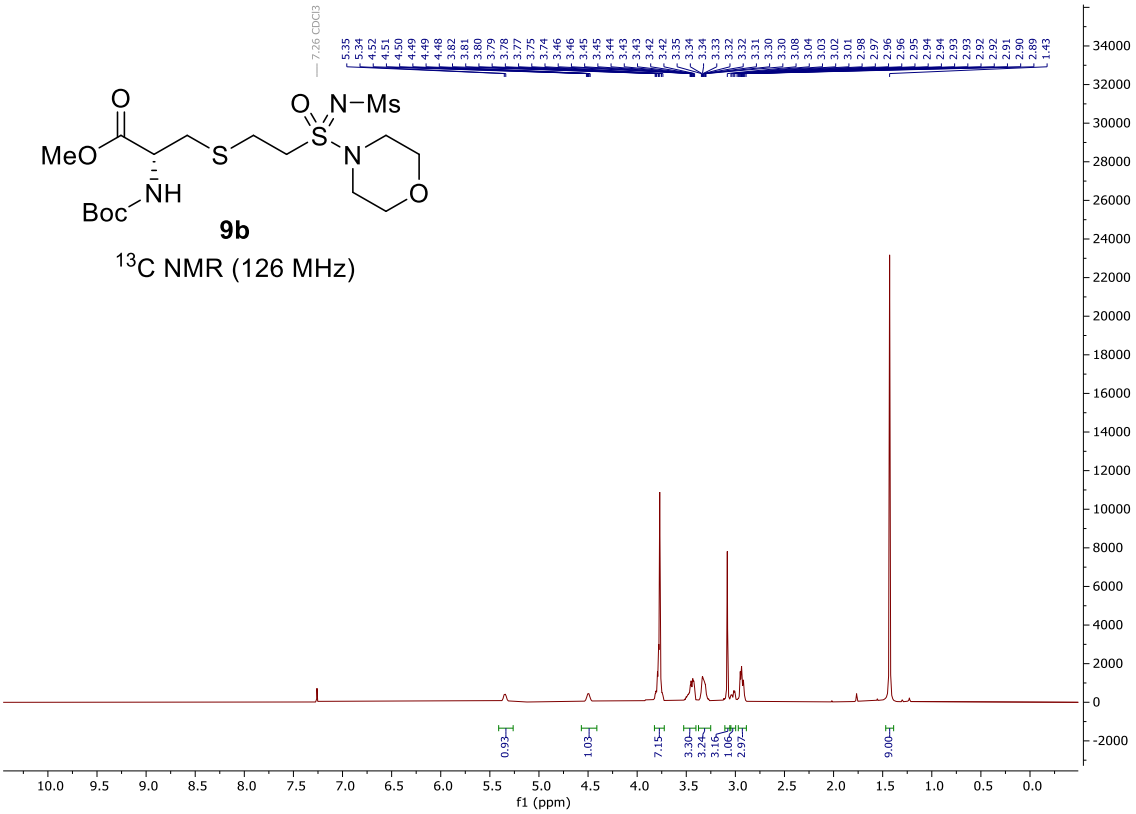


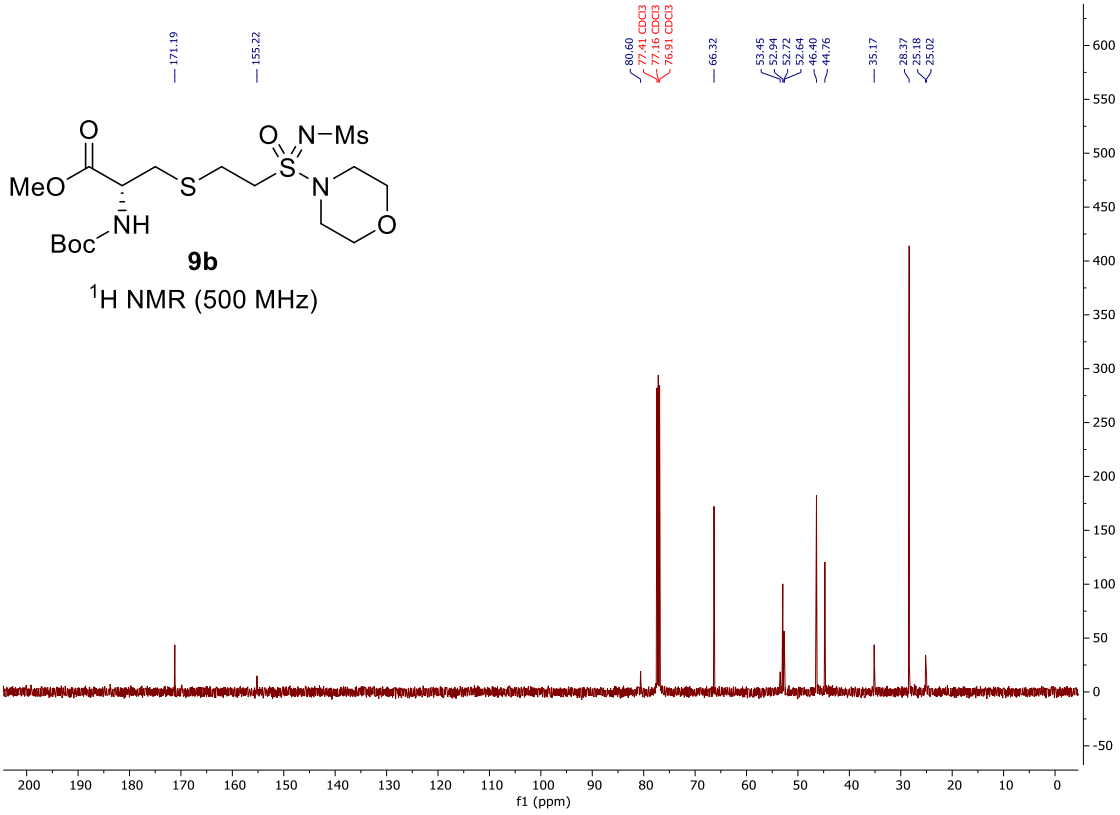
Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(2-(morpholine-4-sulfonimidoyl)ethyl)-*L*-cysteinate (9a)



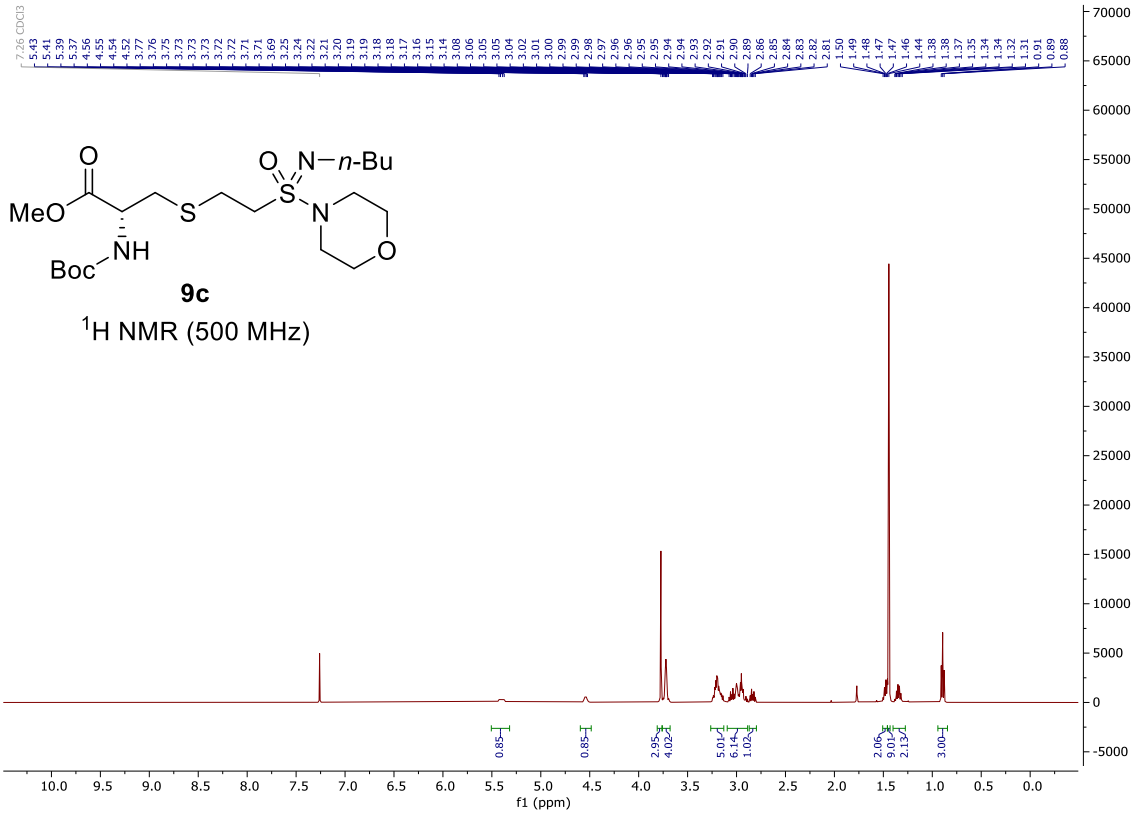


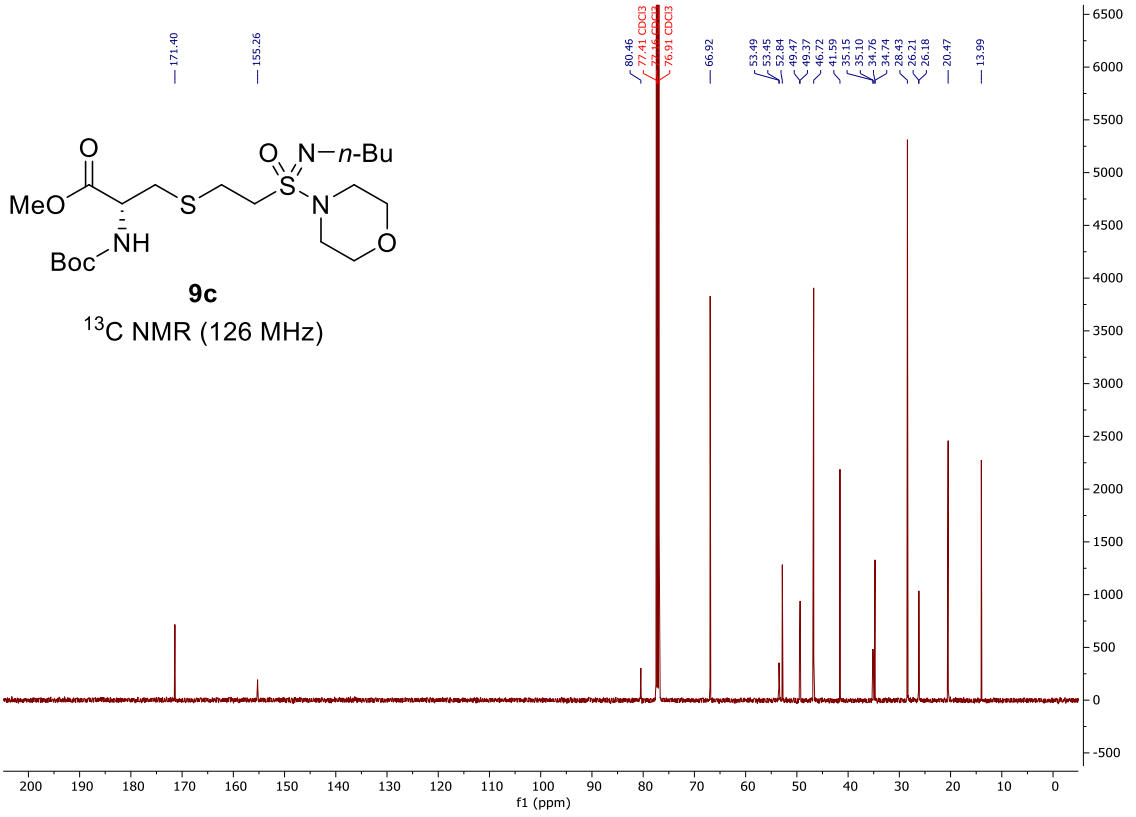
Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(2-(*N*-(methylsulfonyl)morpholine-4-sulfonimidoyl)ethyl)-*L*-cysteinate (9b)



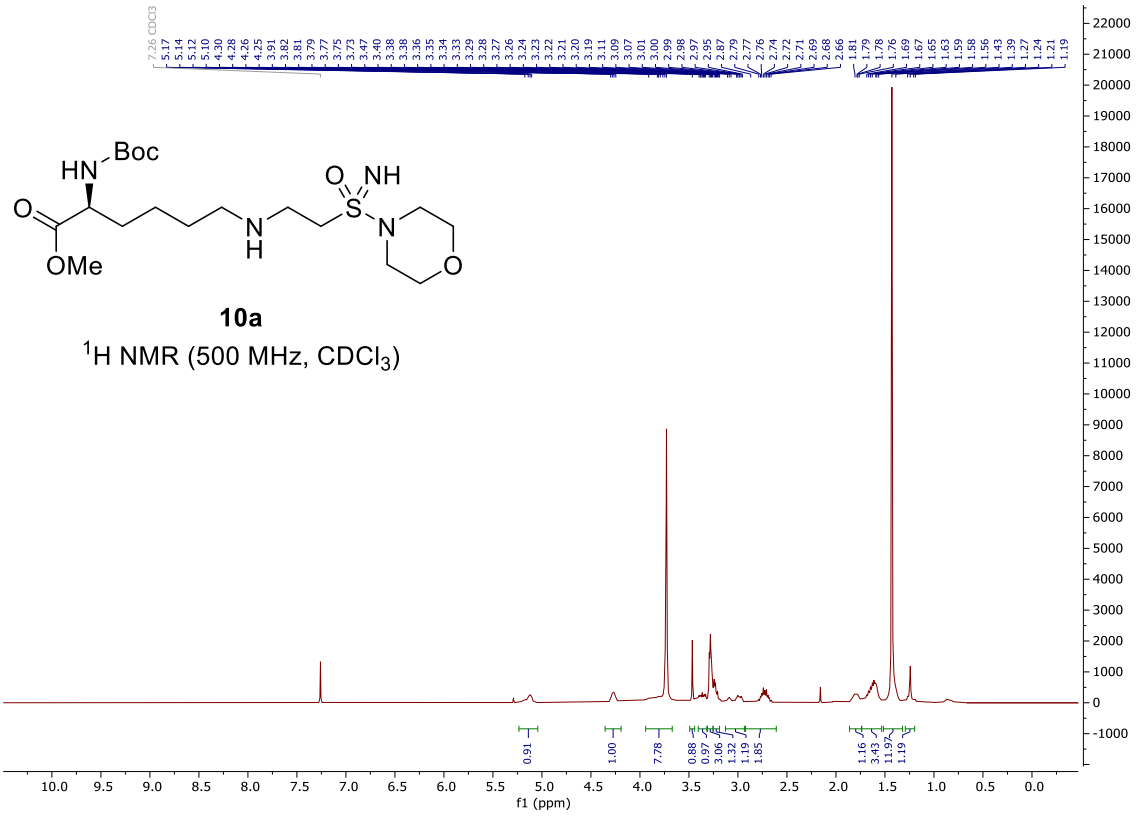


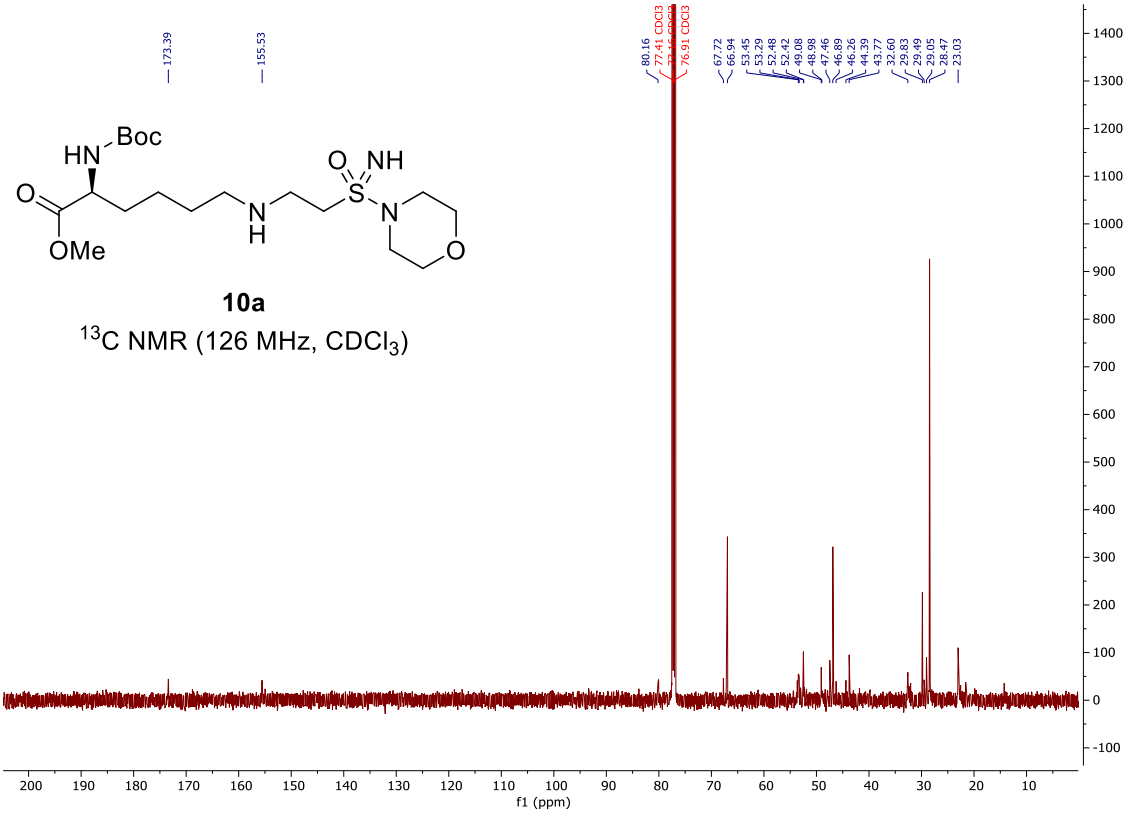
Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(2-(*N*-butylmorpholine-4-sulfonimidoyl)ethyl)-*L*-cysteinate (9c)



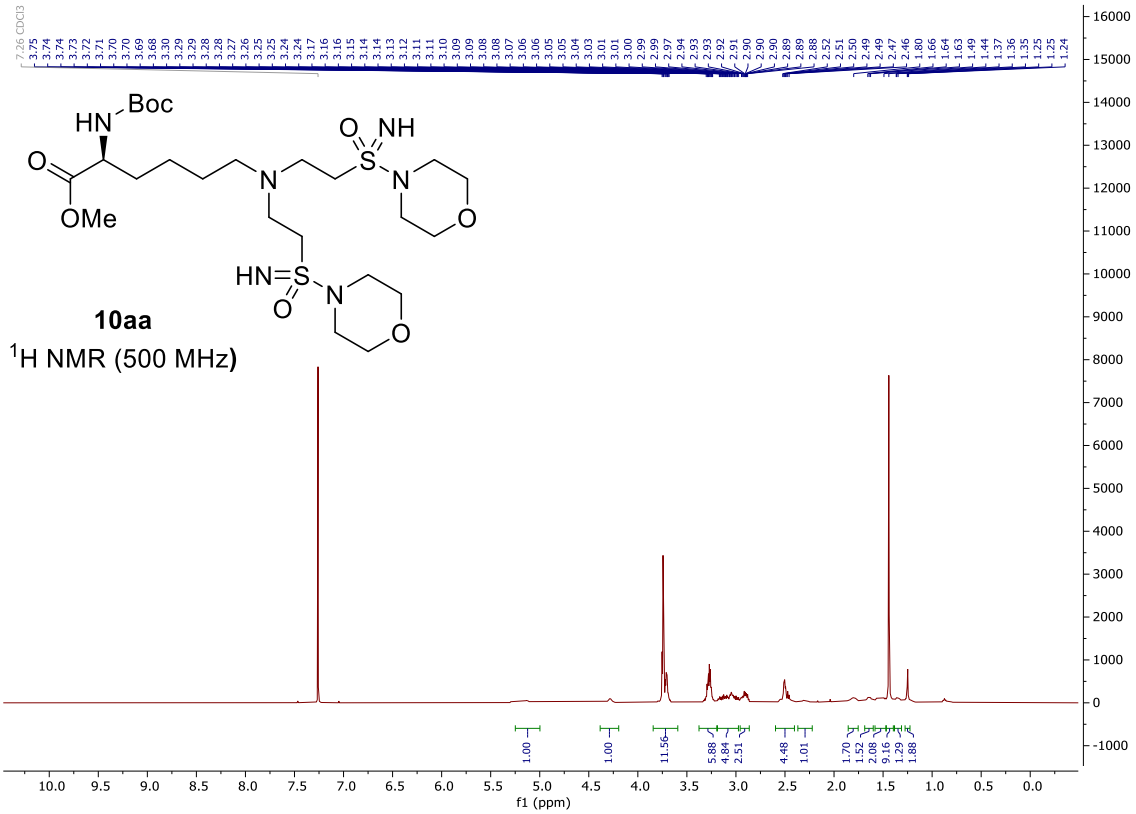


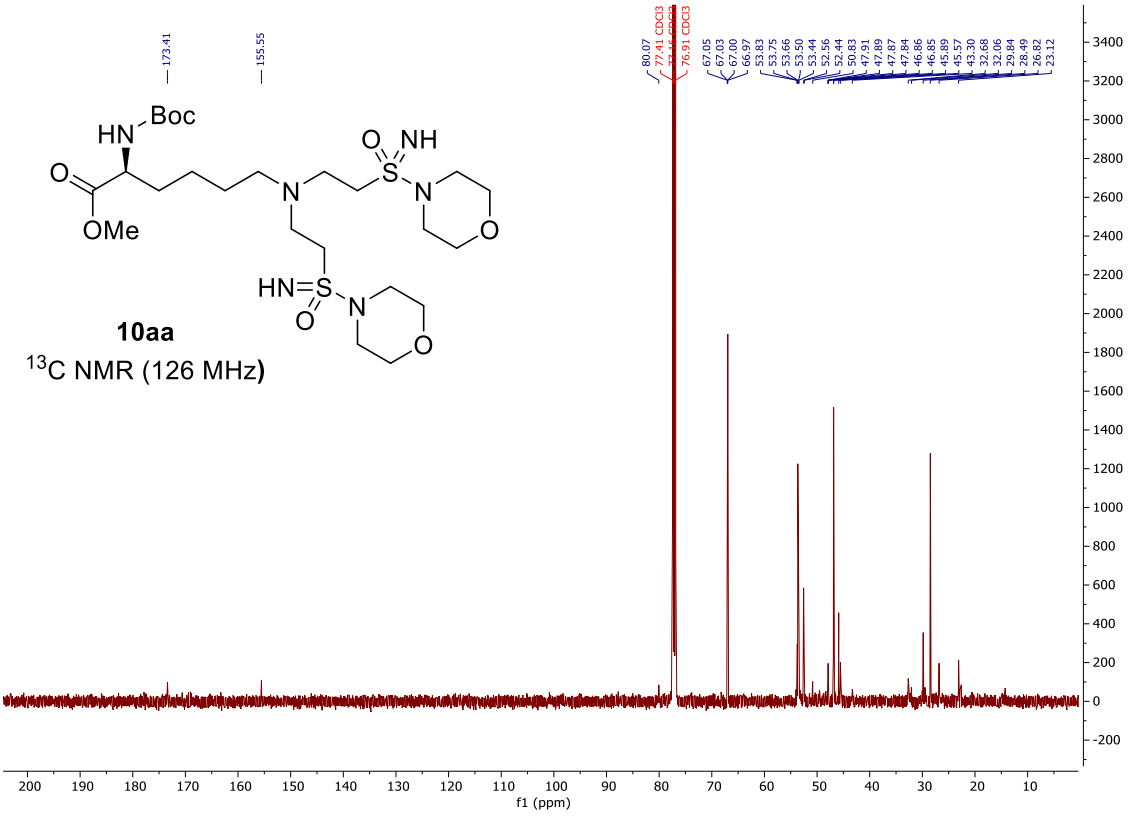
Methyl N^2-(tert-butoxycarbonyl)-N^6-(2-(morpholine-4-sulfonimidoyl)ethyl)-*L*-lysinate (10a)



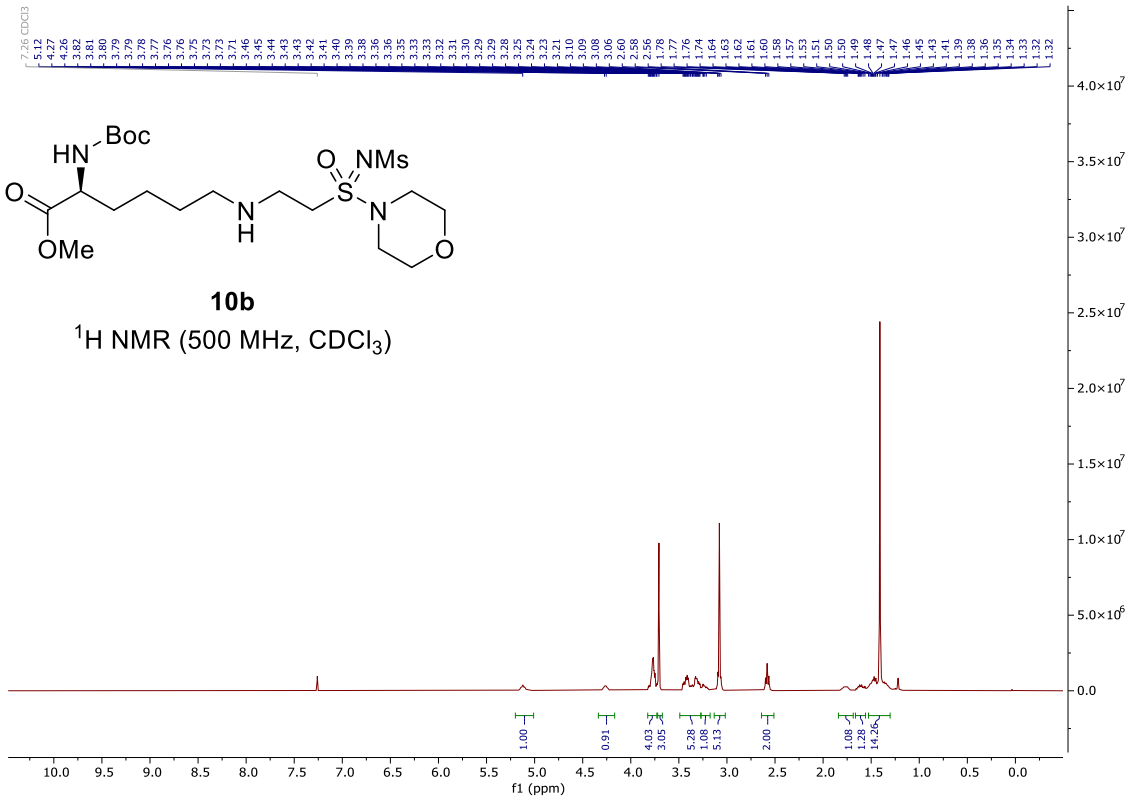


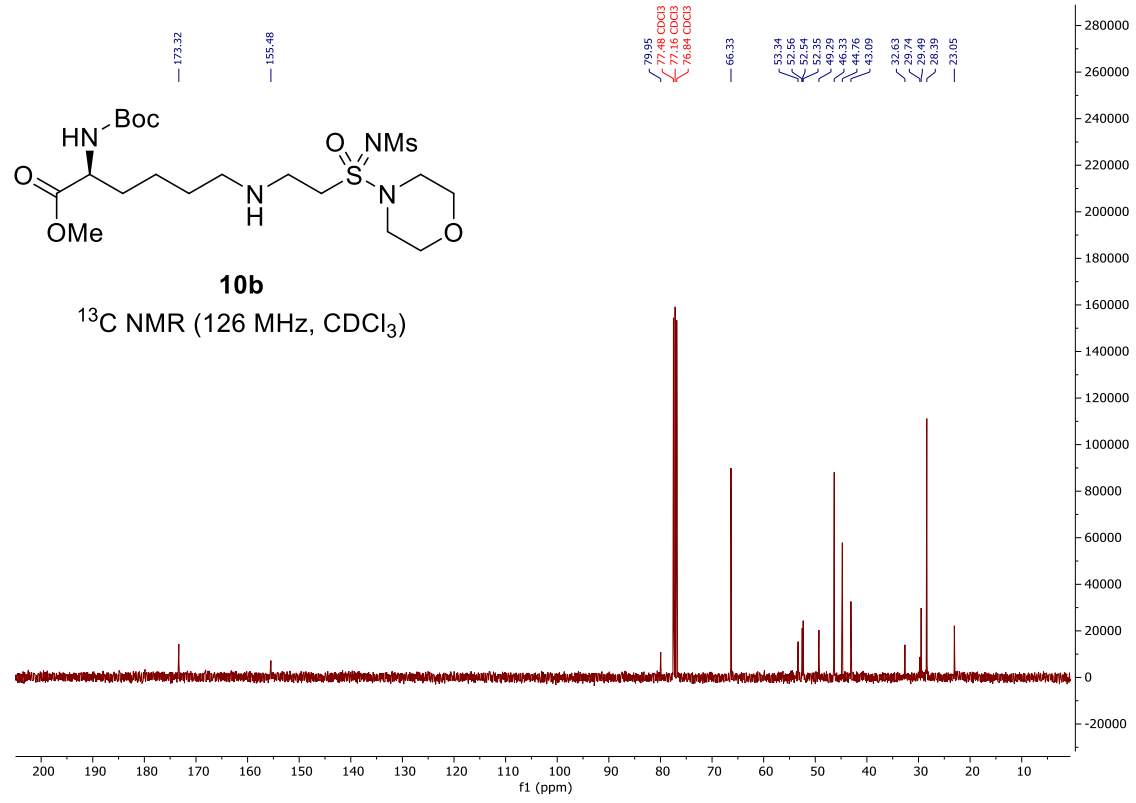
Methyl N^2-(*tert*-butoxycarbonyl)-N^6,N^6-bis(2-(morpholine-4-sulfonimidoyl)ethyl)-*L*-lysinate (10aa)



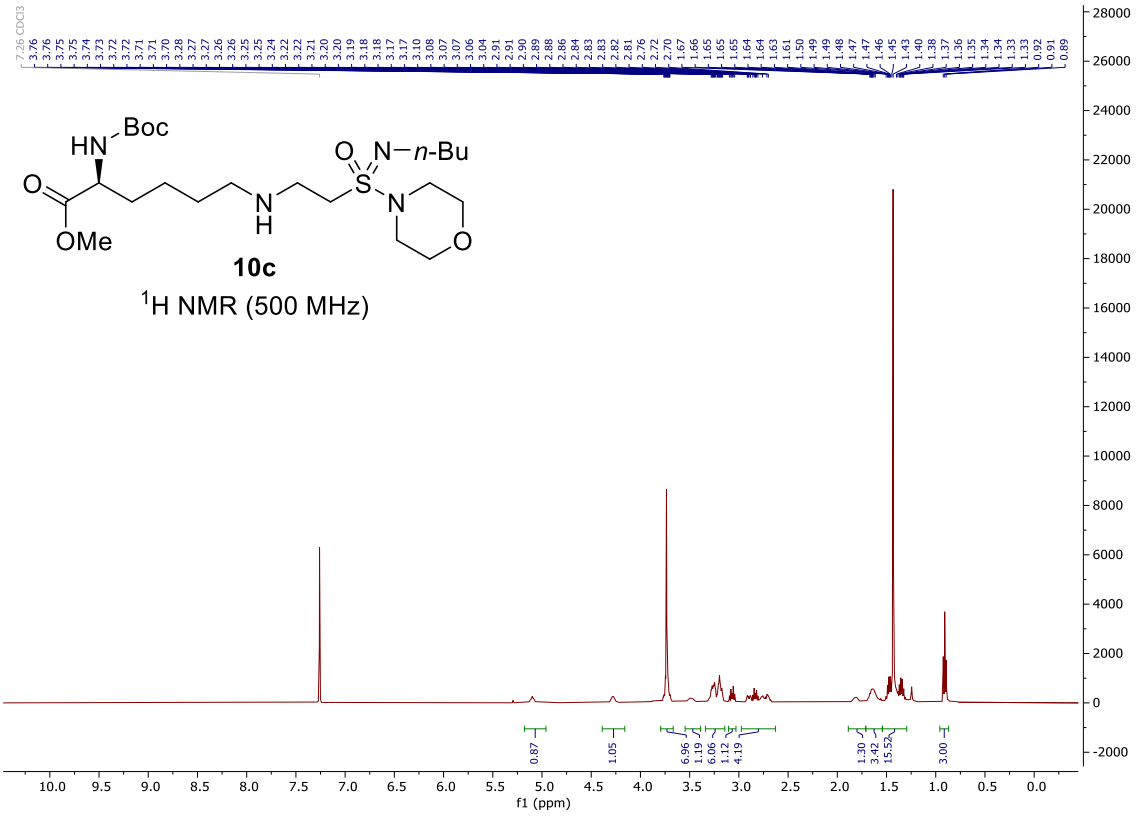


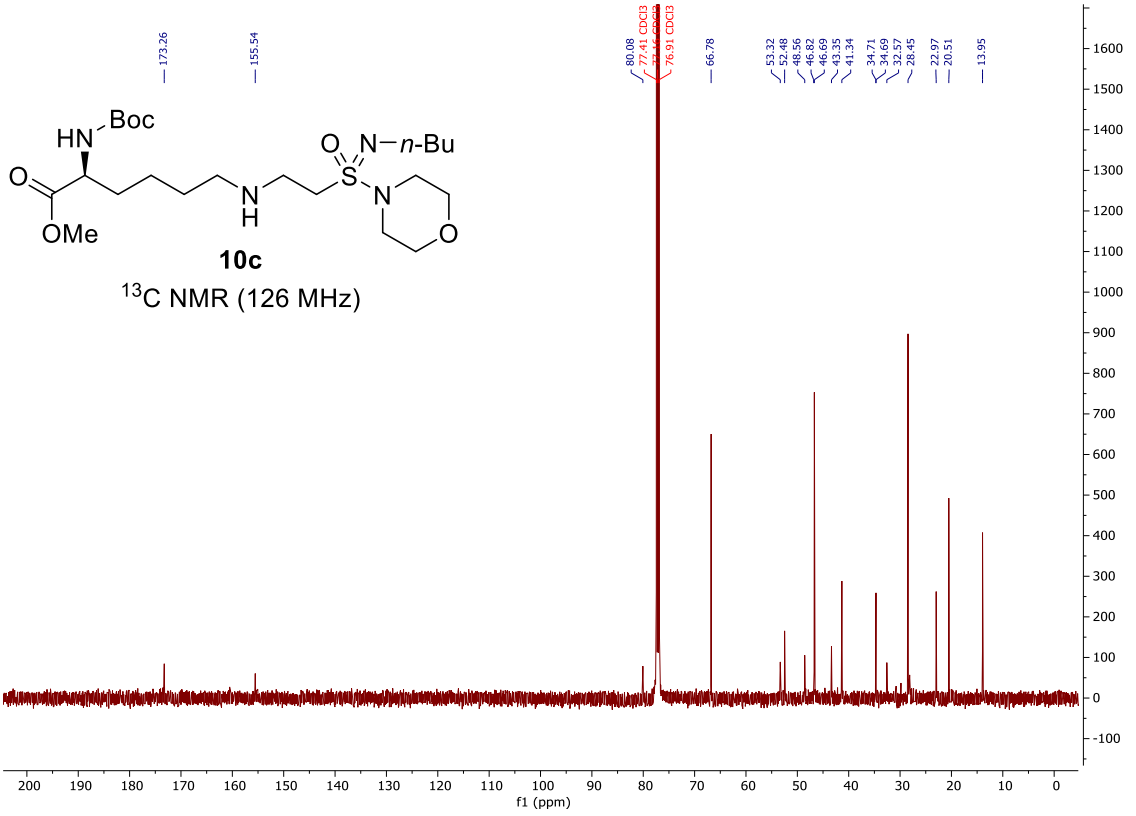
Methyl N^2-(*tert*-butoxycarbonyl)-N^6-(2-(*N*-(methylsulfonyl)morpholine-4-sulfonimidoyl)ethyl)-*L*-lysinate (10b)



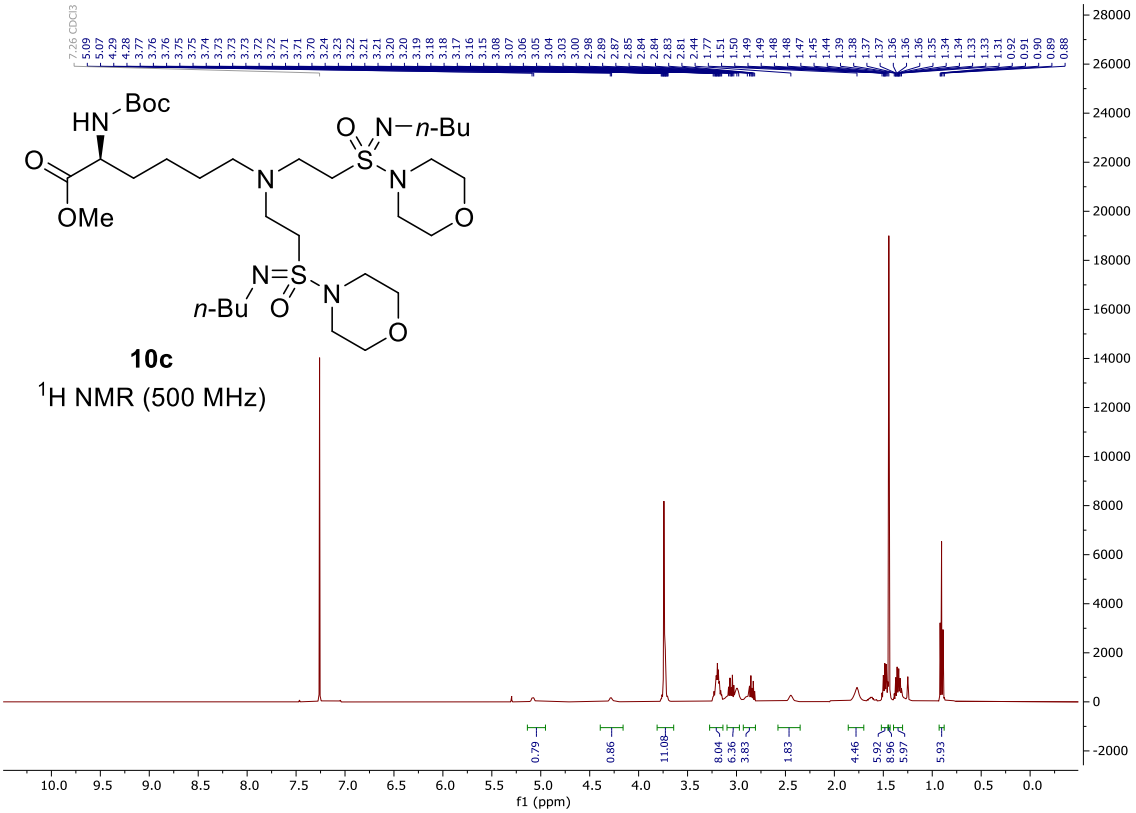


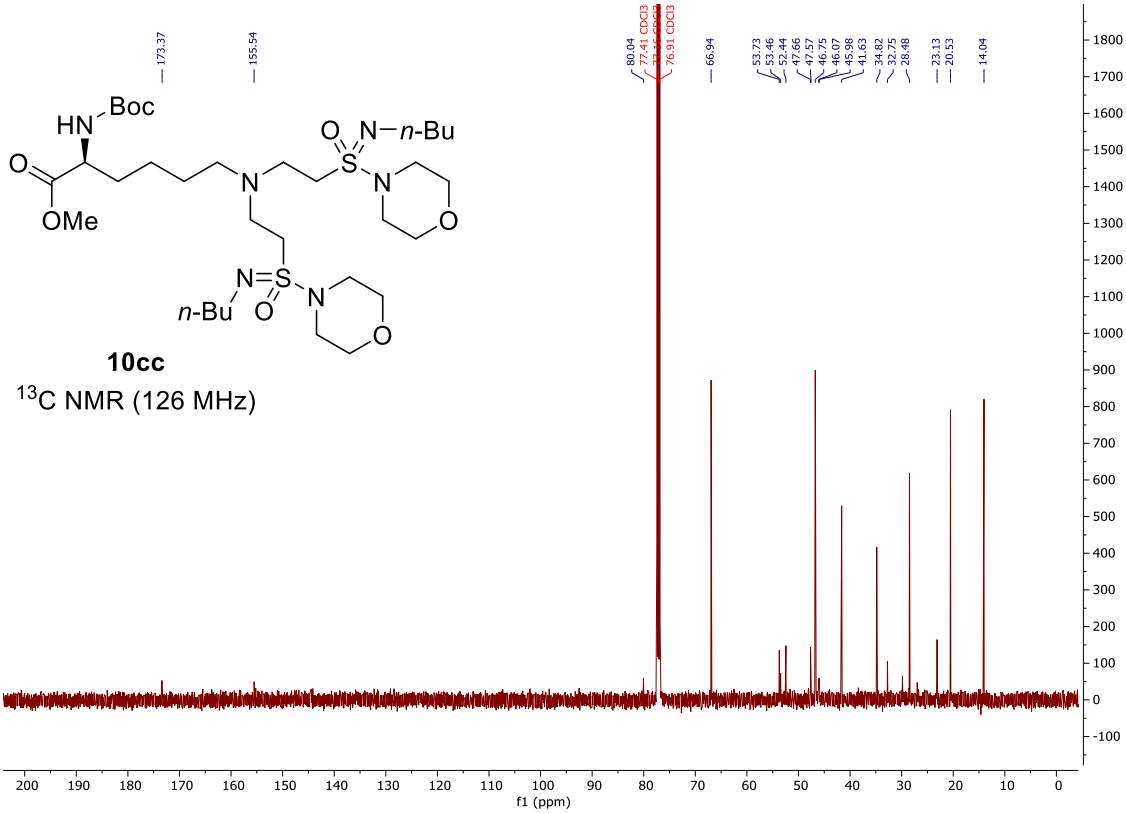
Methyl N^2-(tert-butoxycarbonyl)-N^6-(2-(N-butylmorpholine-4-sulfonimidoyl)ethyl)-L-lysinate (10c)



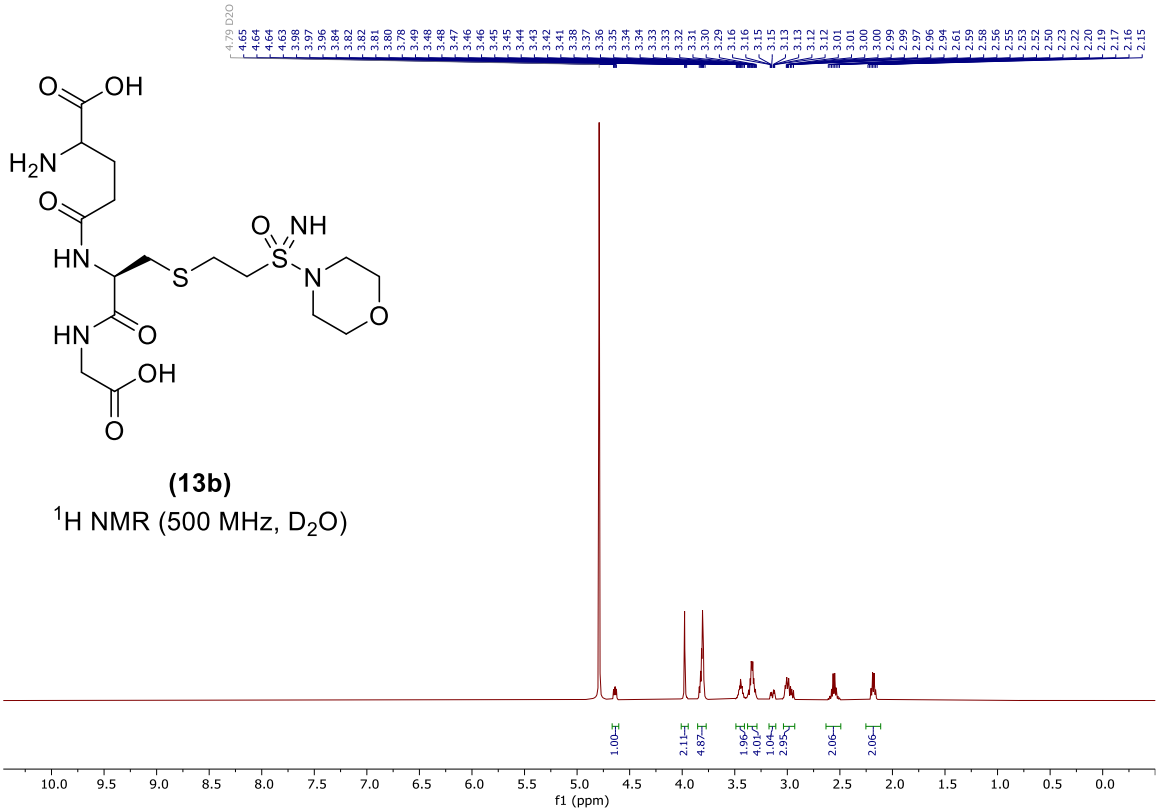


Methyl N^2-(tert-butoxycarbonyl)-N^6,N^6-bis(2-(N-butylmorpholine-4-sulfonimidoyl)ethyl)-L-lysinate (10cc)



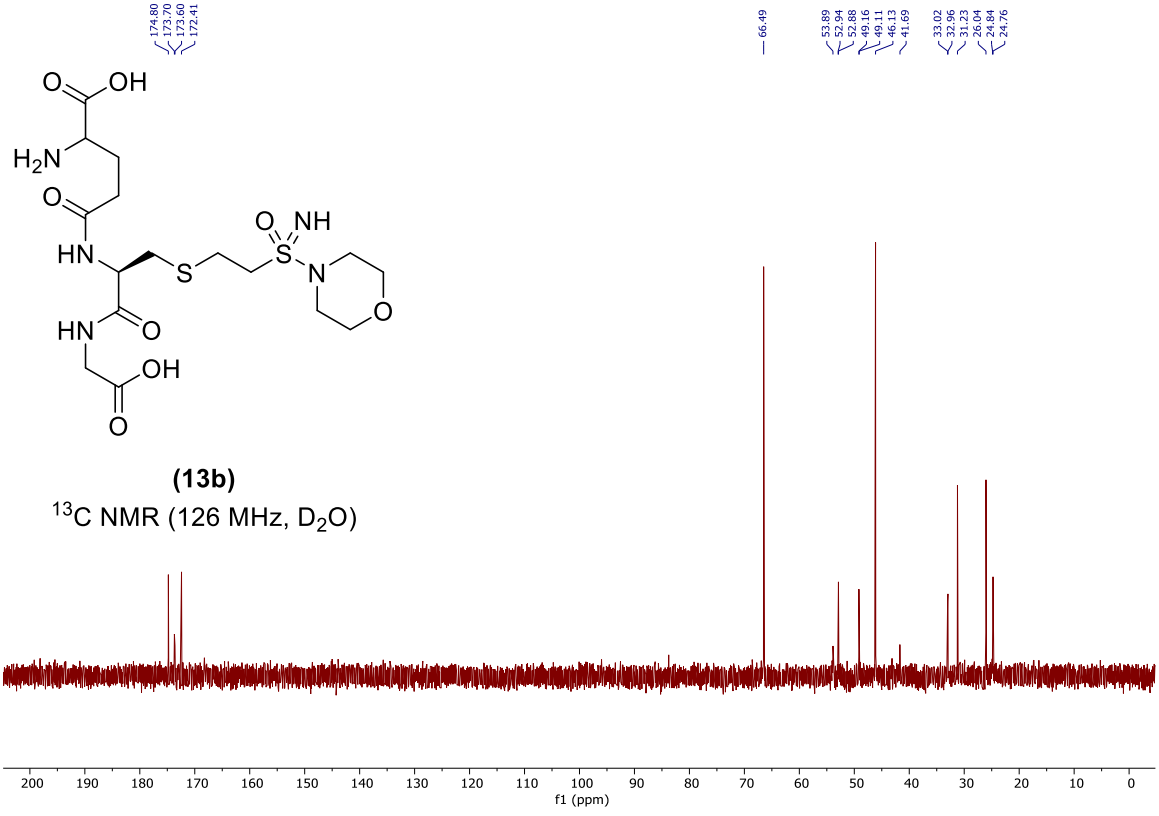


Sulfonimidamide-GSH Adduct (13b)



(13b)

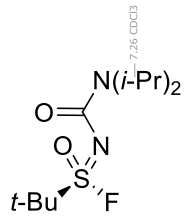
^{1}H NMR (500 MHz, D_2O)



(13b)

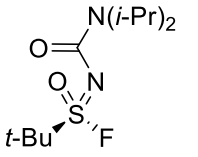
^{13}C NMR (126 MHz, D_2O)

***(S)*-t-BuSF, (14)**



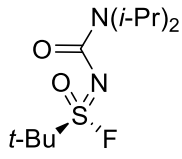
14

^{1}H NMR (400 MHz, $CDCl_3$)



14

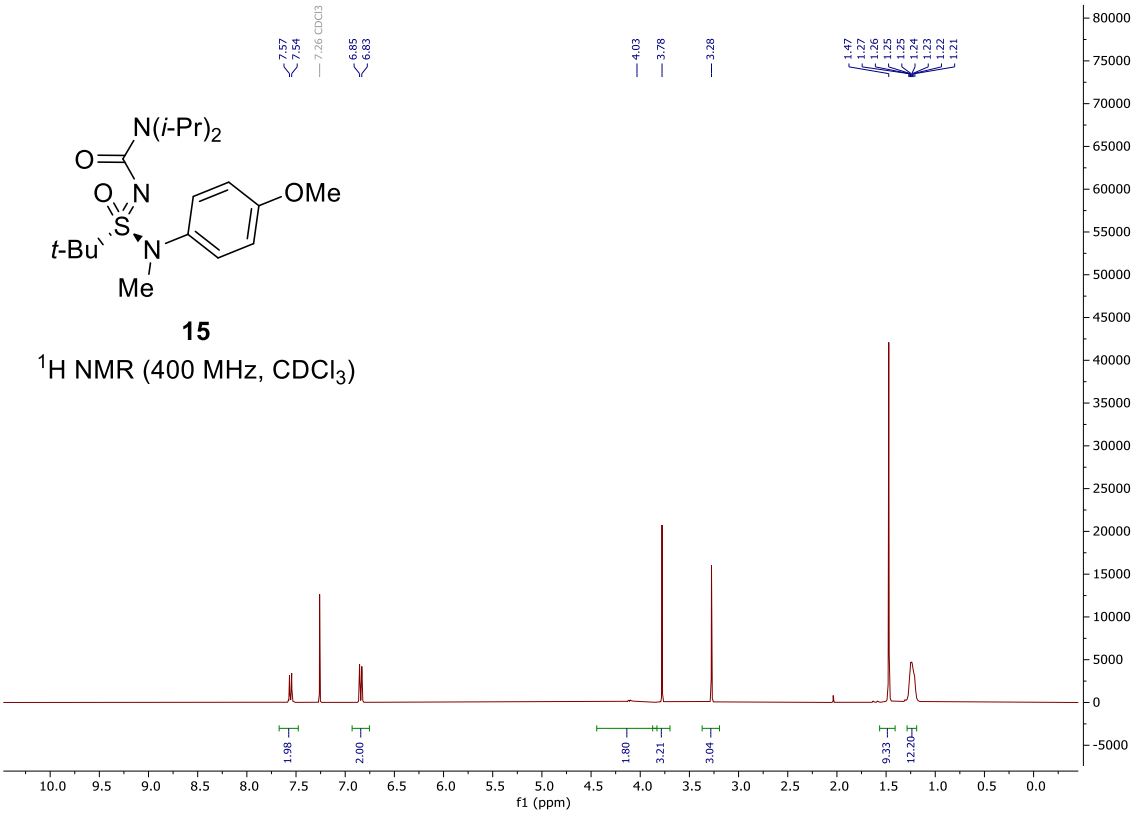
^{13}C NMR (101 MHz, $CDCl_3$)

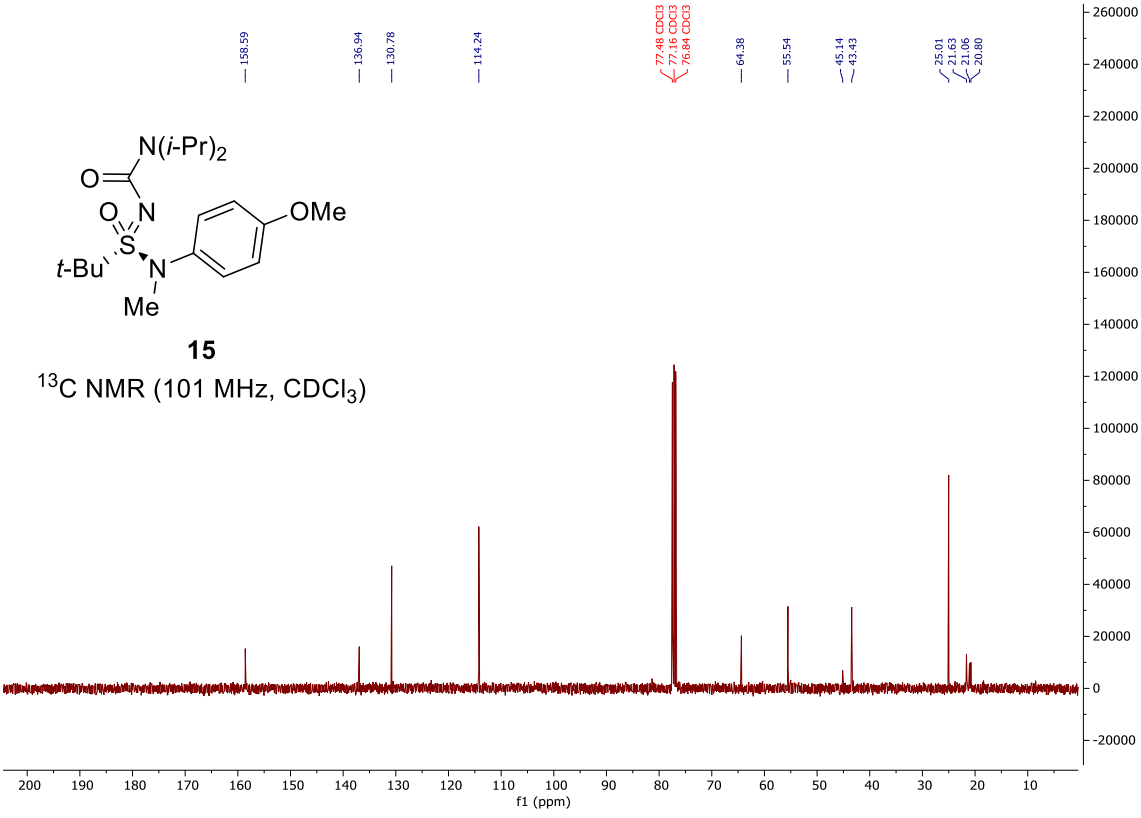


14

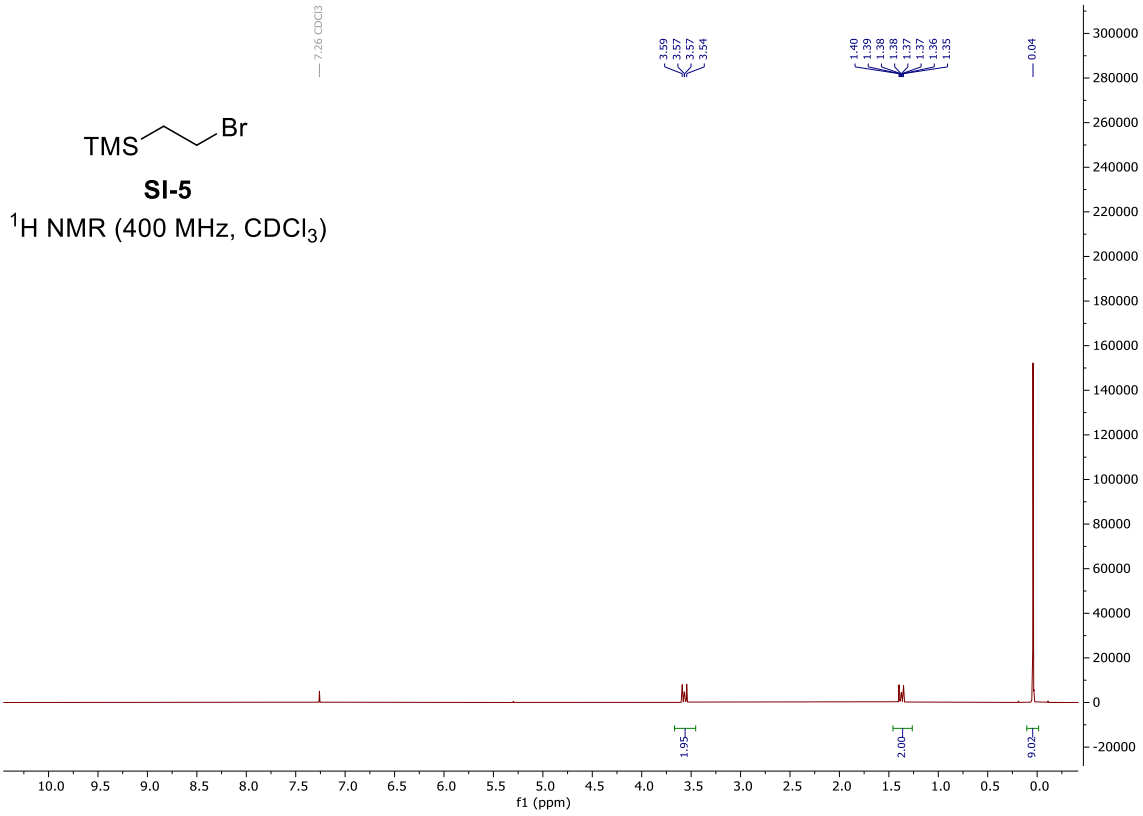
^{19}F NMR (377 MHz, $CDCl_3$)

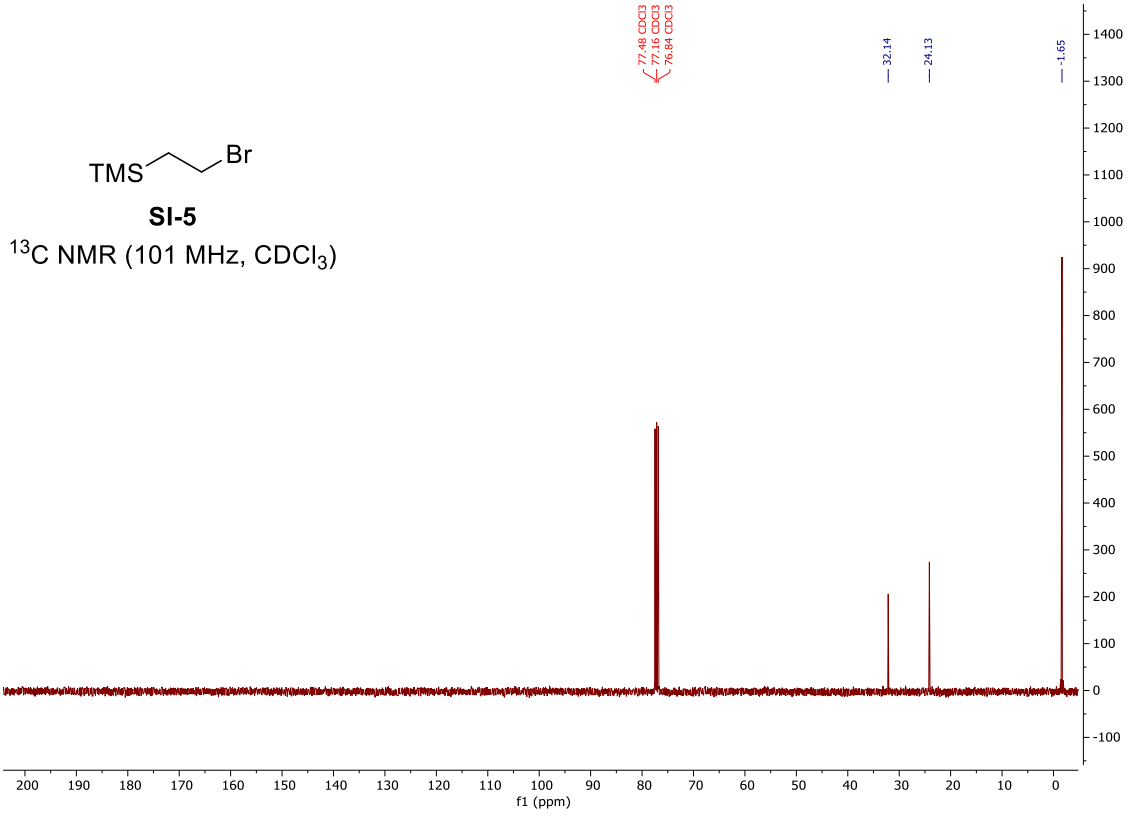
(*S*)-*N*'-(diisopropylcarbamoyl)-*N*-(4-methoxyphenyl)-*N*,2-dimethylpropane-2-sulfonimidamide (15)



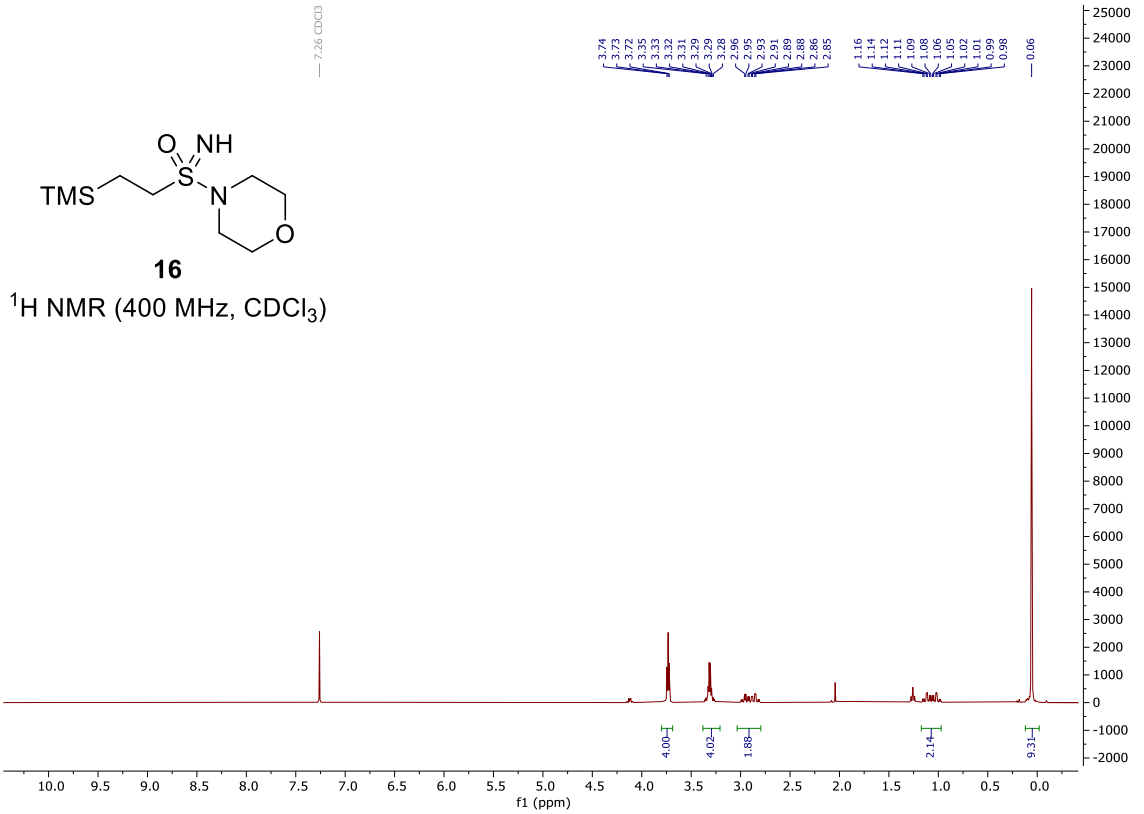


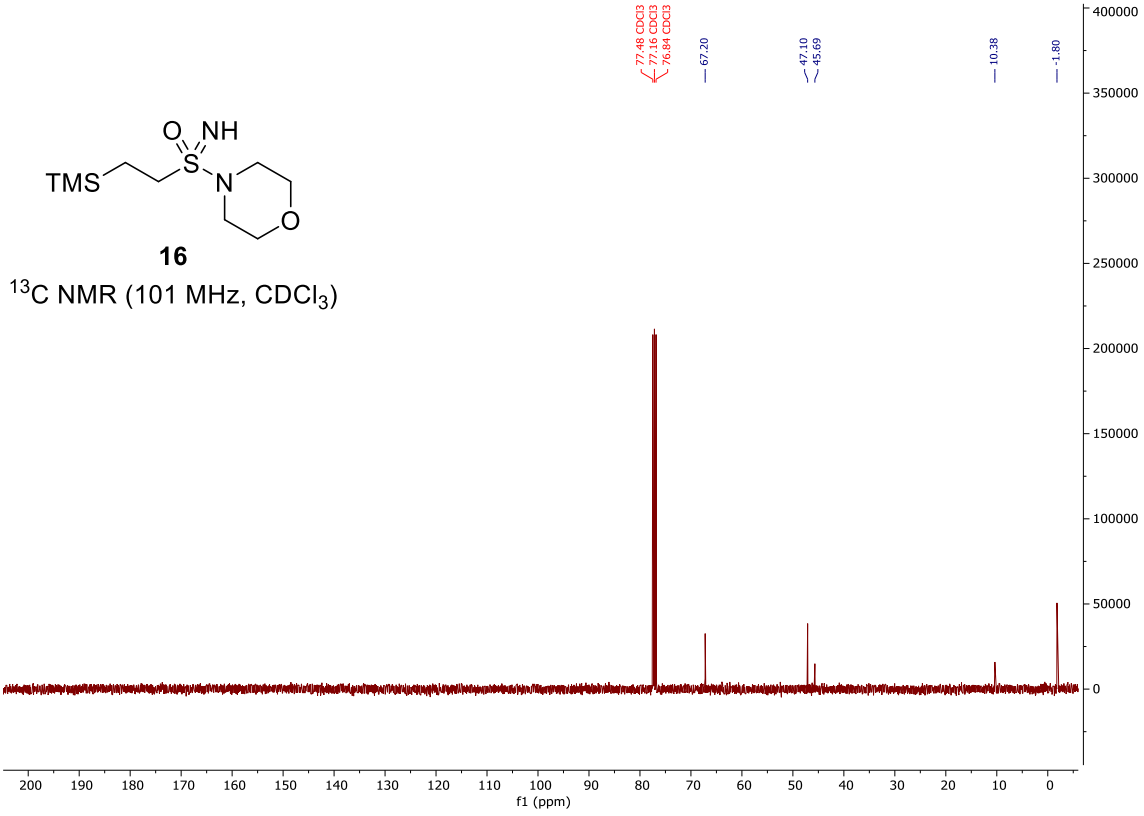
2-bromoethyl)trimethylsilane (SI-5)



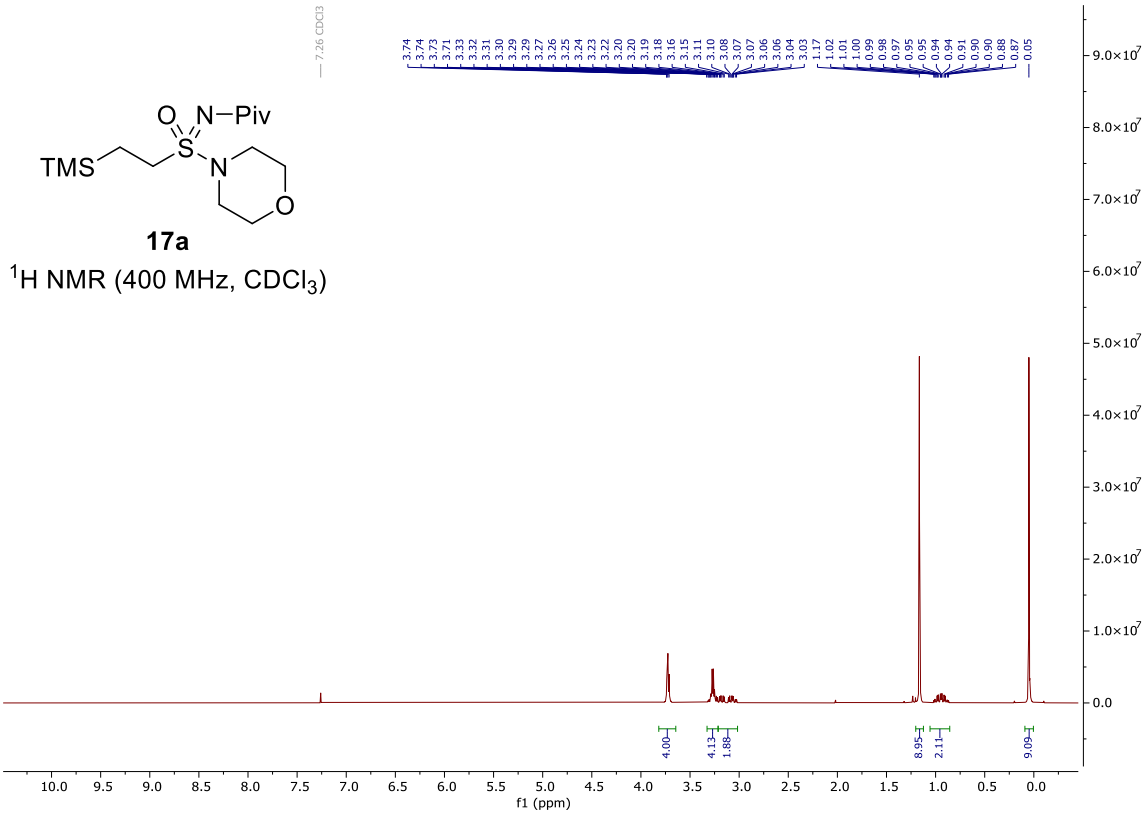


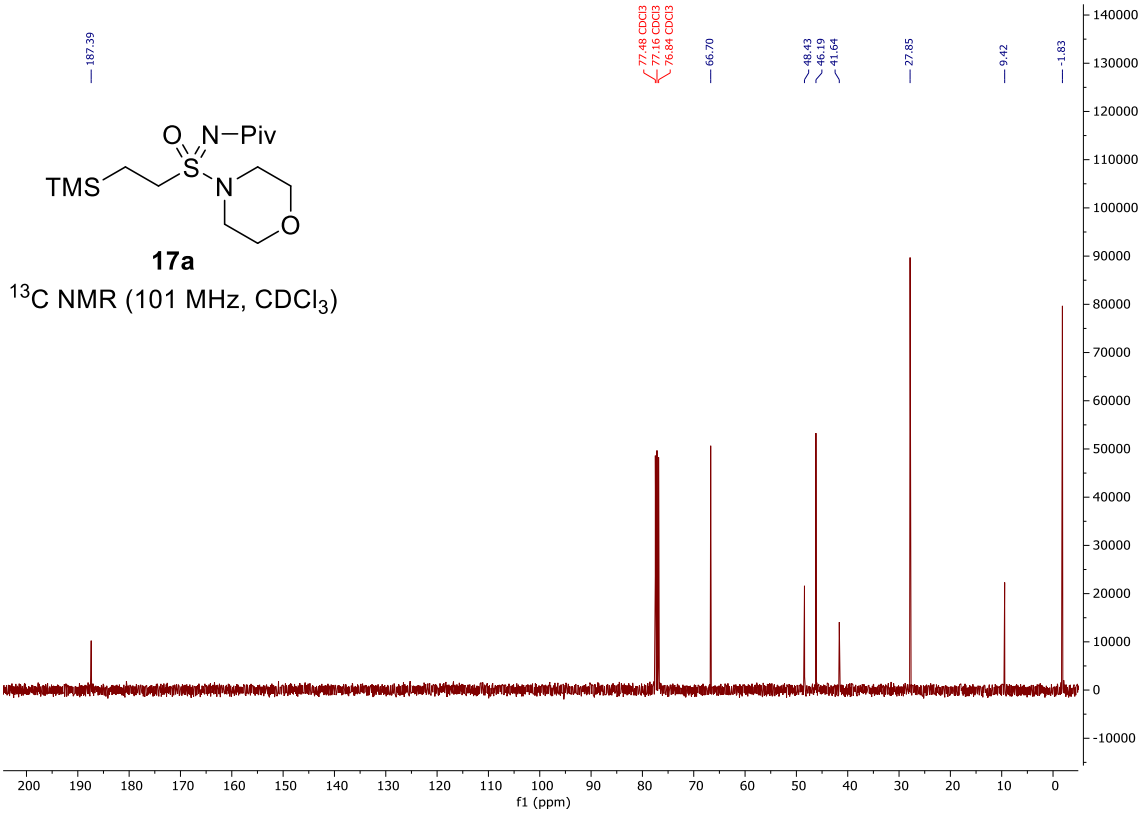
4-(2-(trimethylsilyl)ethylsulfonimidoyl)morpholine (16)



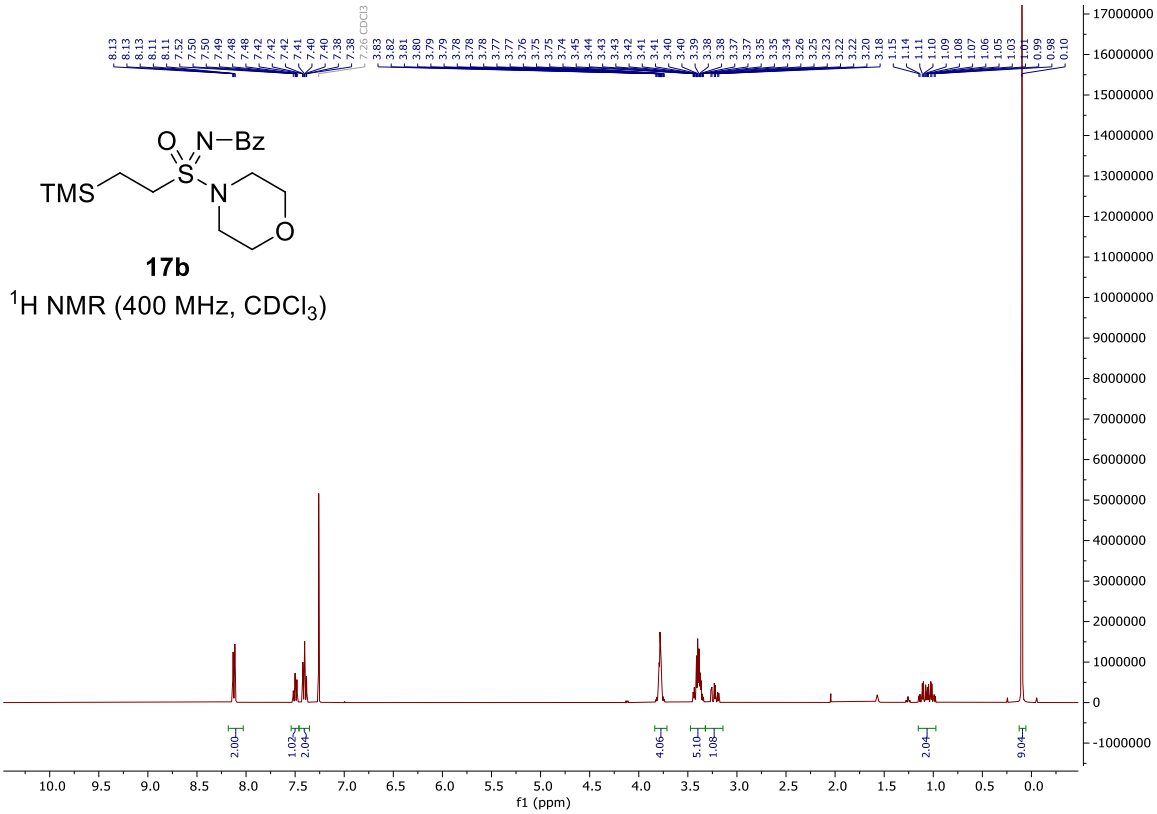


_N_-(morpholino(oxo)(2-(trimethylsilyl)ethyl)-λ6-sulfaneylidene)pivalamide (17a)



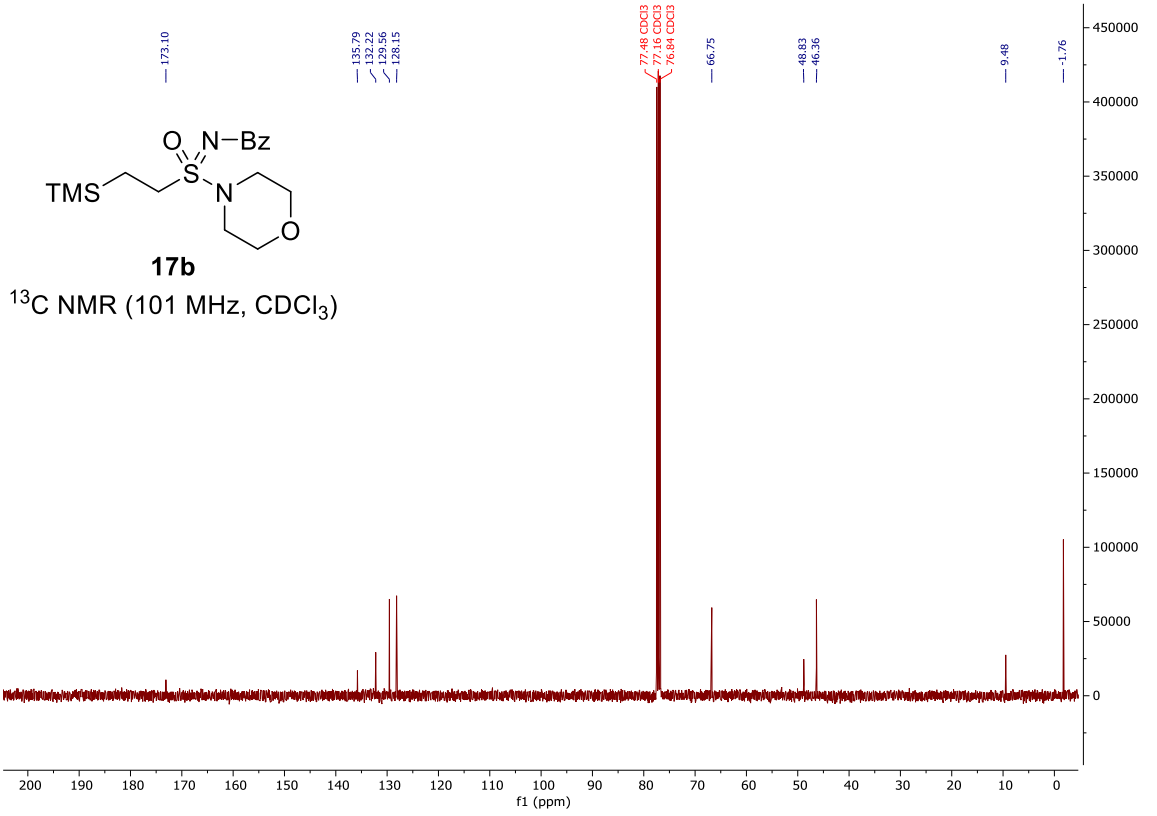


_N_-(morpholino(oxo)(2-(trimethylsilyl)ethyl)-λ6-sulfaneylidene)benzamide (17b)



17b

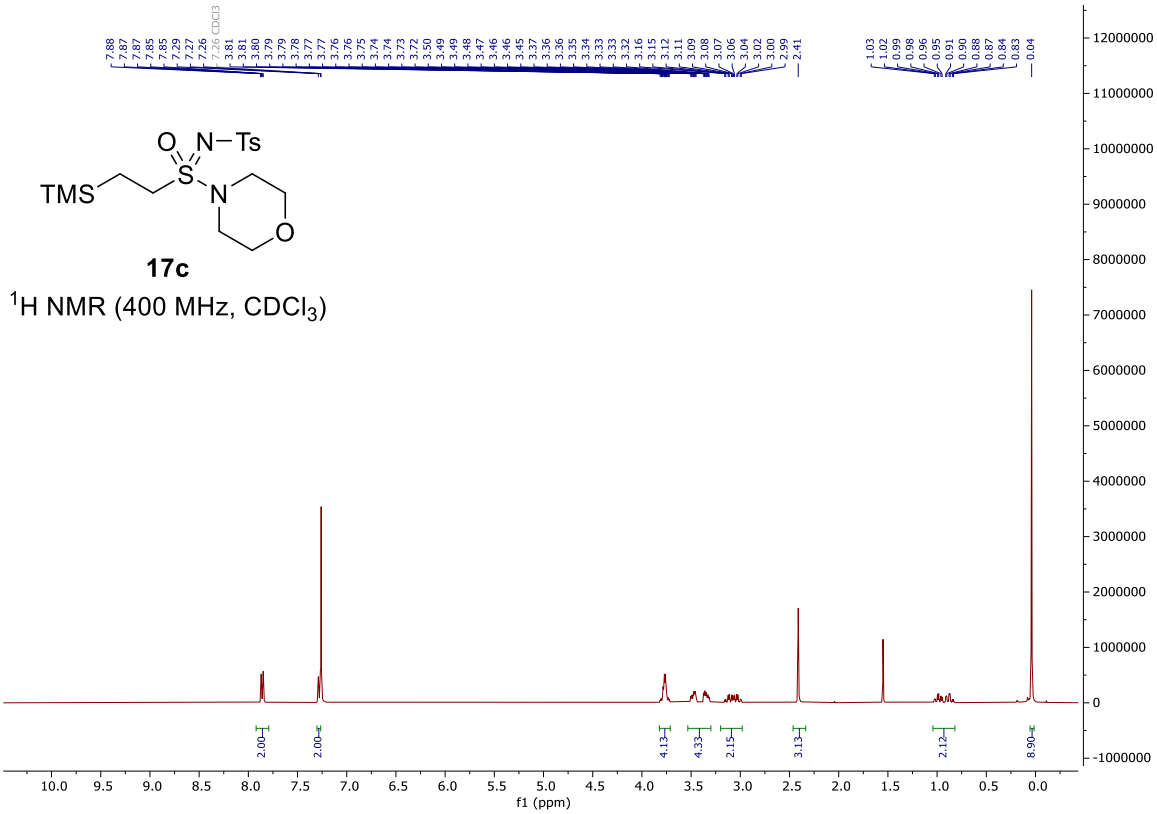
^{1}H NMR (400 MHz, $CDCl_3$)

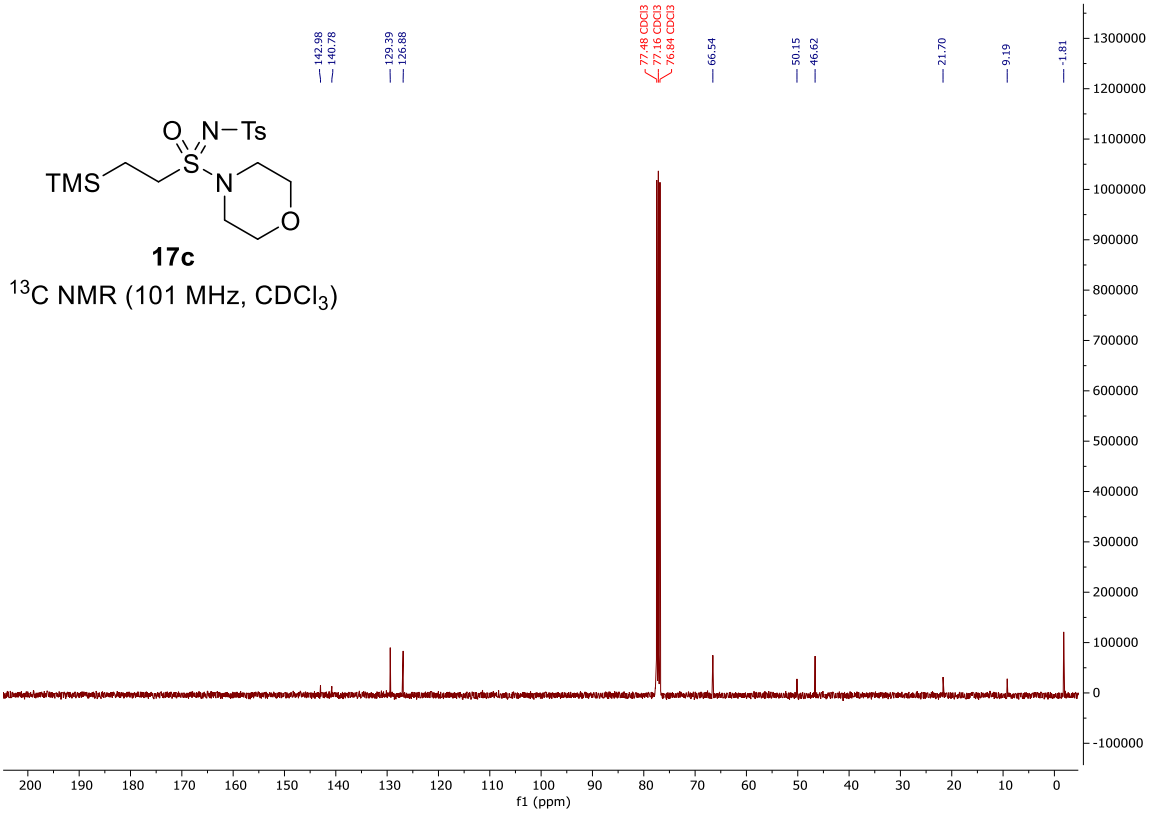


17b

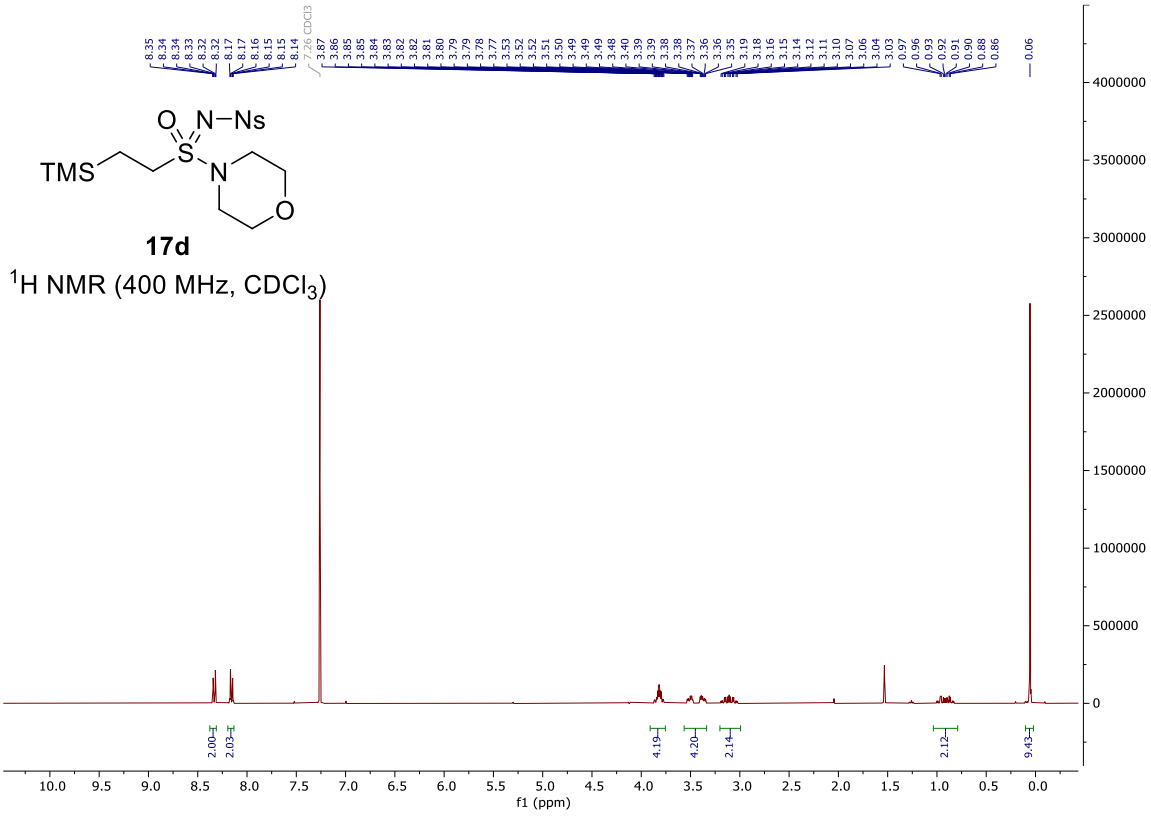
^{13}C NMR (101 MHz, $CDCl_3$)

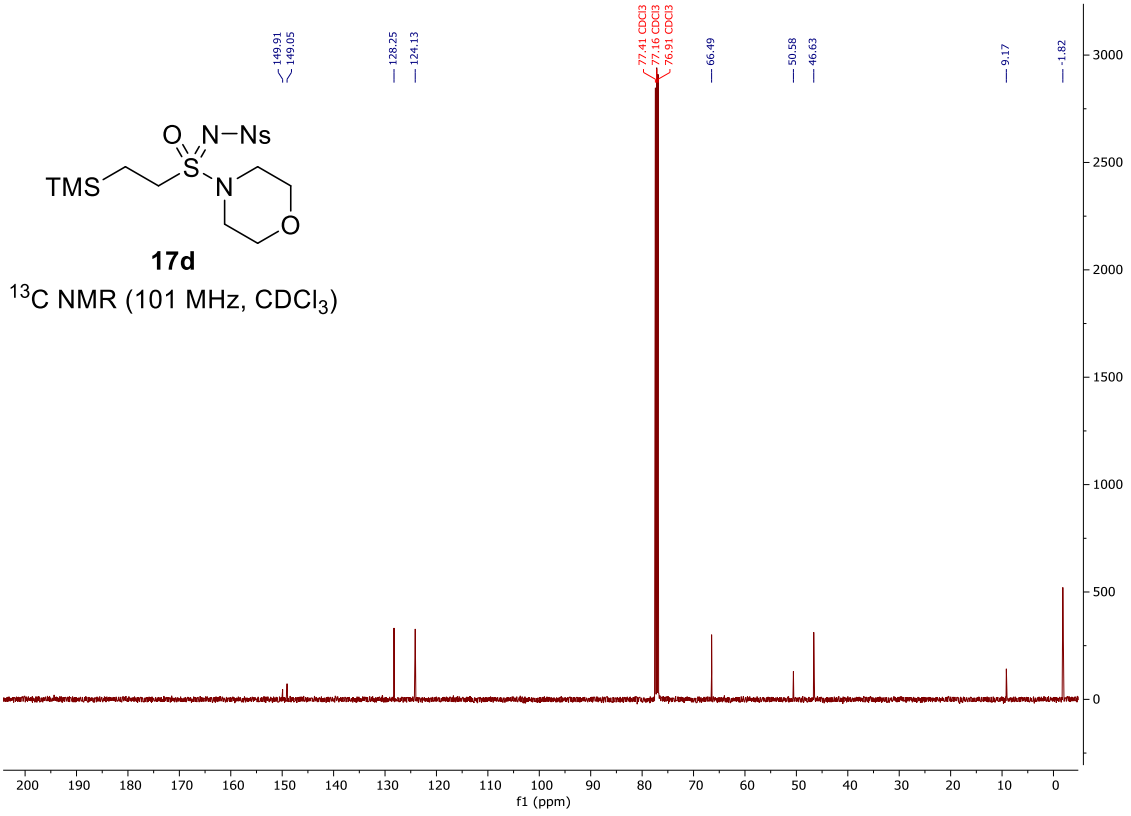
4-Methyl-*N*-(morpholino(oxo)(2-(trimethylsilyl)ethyl)-λ6-sulfaneylidene)benzenesulfonamide (17c)



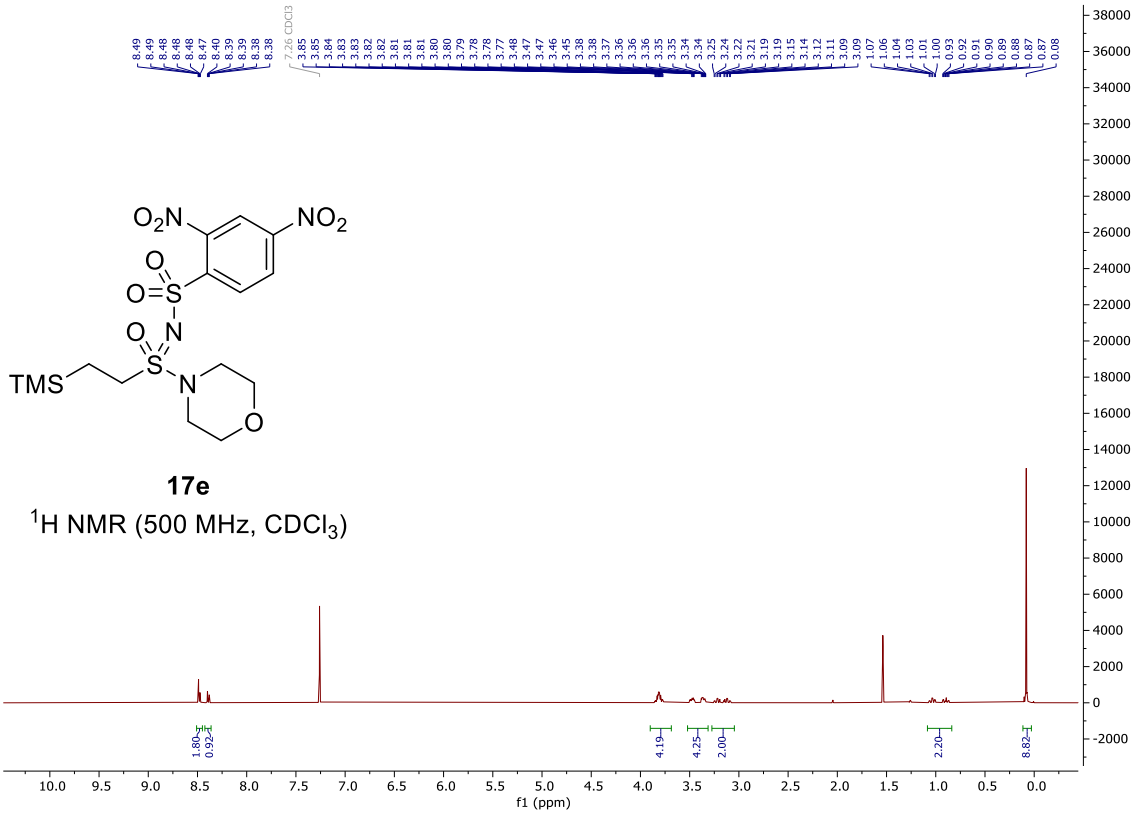


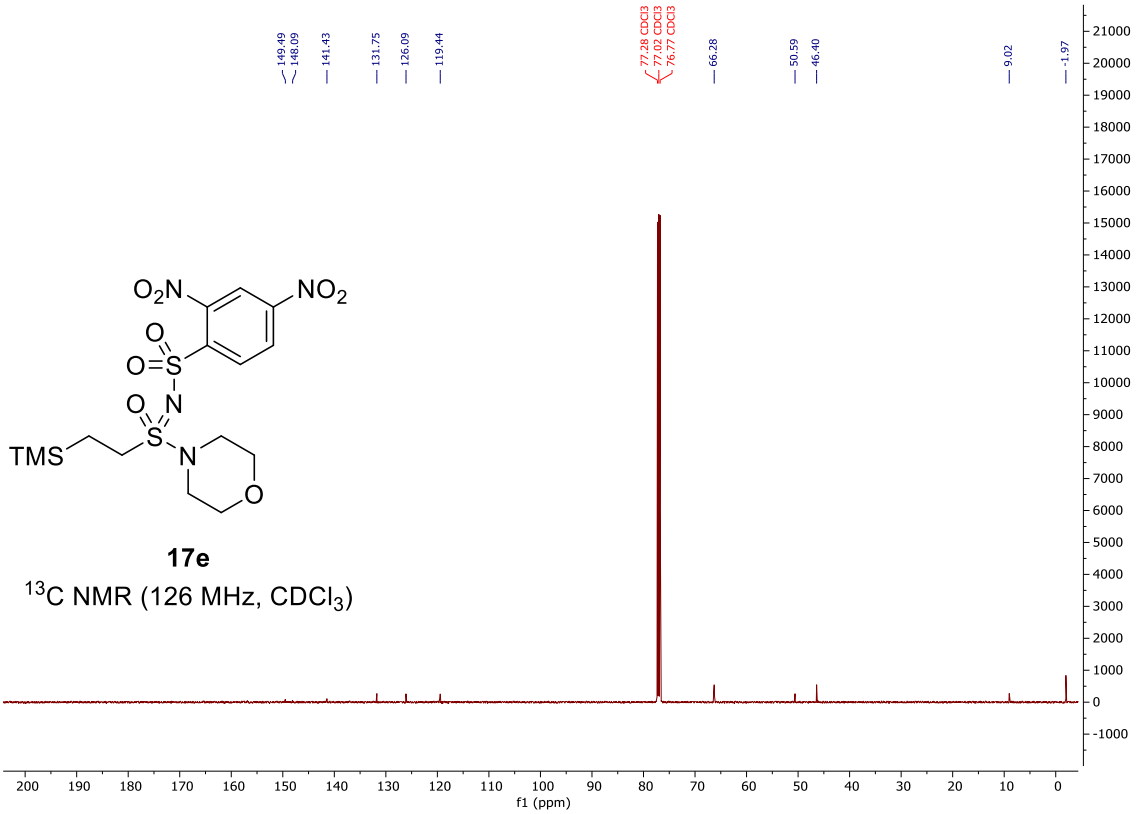
_N_-(morpholino(oxo)(2-(trimethylsilyl)ethyl)-λ6-sulfaneylidene)-4-nitrobenzenesulfonamide (17d)



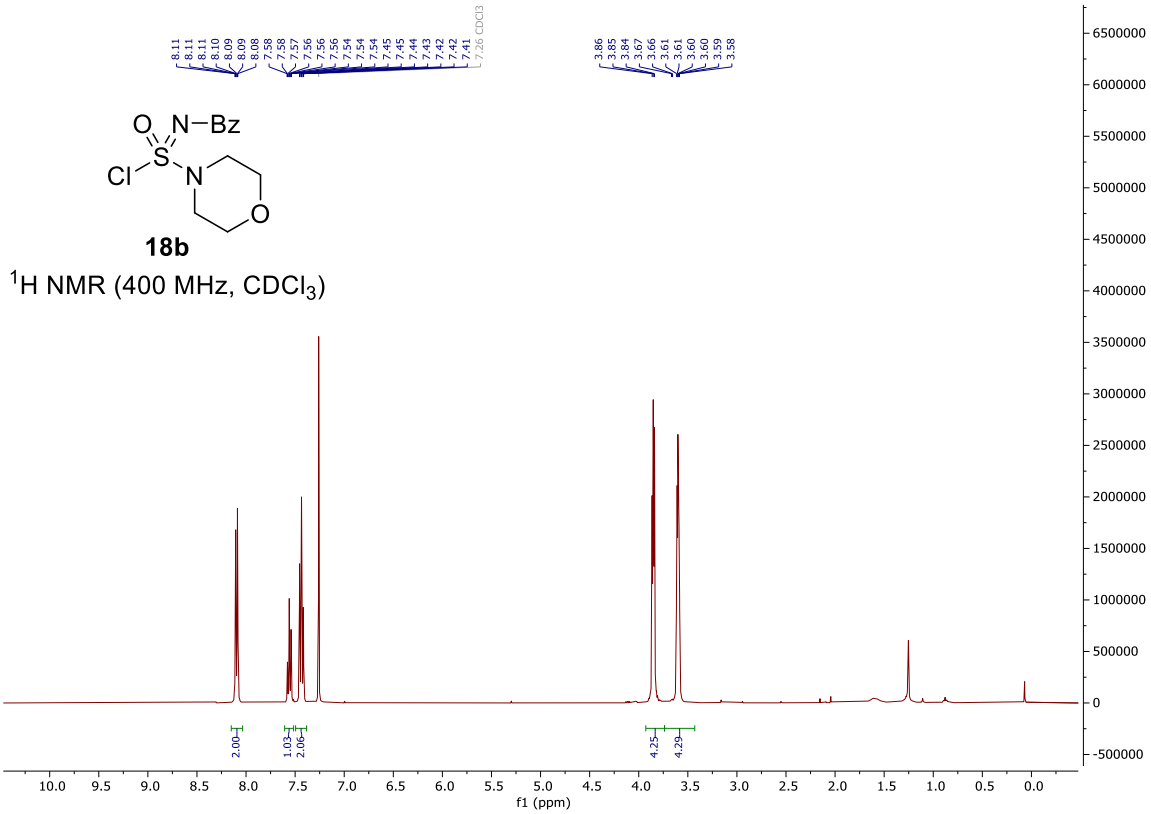


_N_-(morpholino(oxo)(2-(trimethylsilyl)ethyl)-λ6-sulfaneylidene)-2,4-dinitrobenzenesulfonamide (17e)

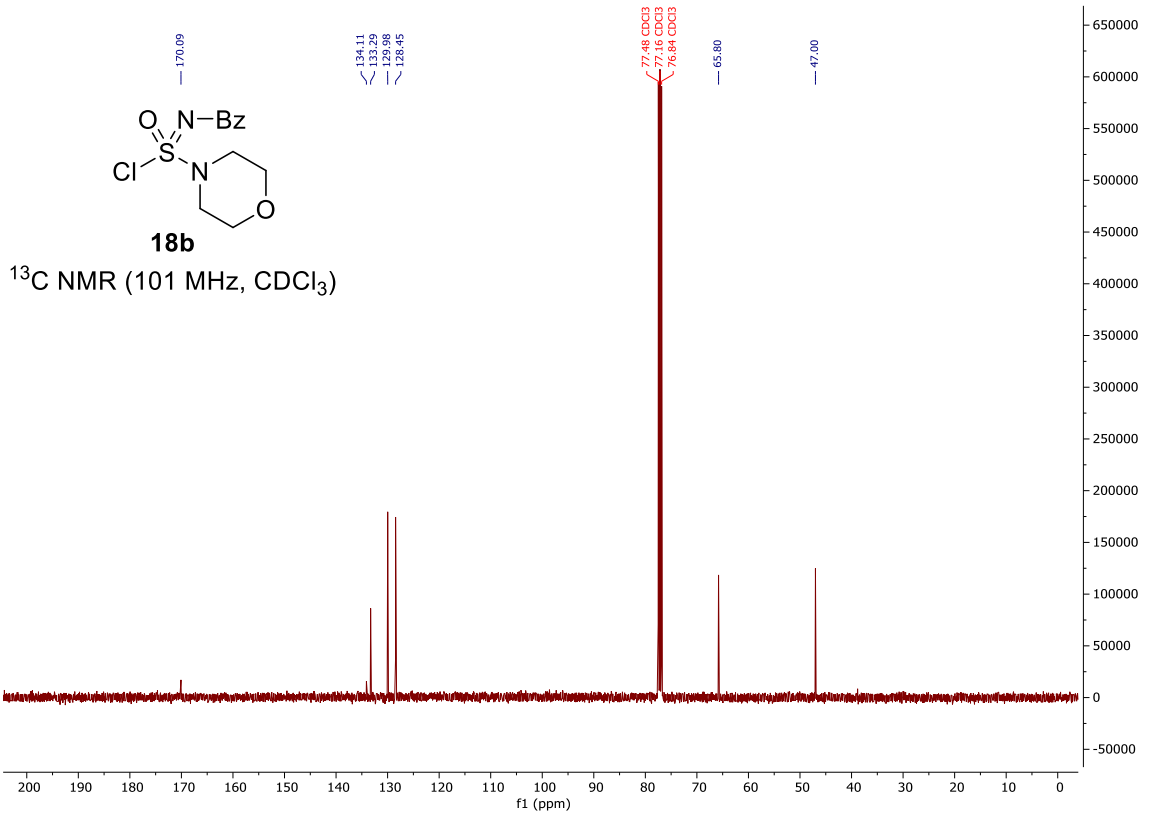




_N_-pivaloylmorpholine-4-sulfonimidoyl chloride (18b)

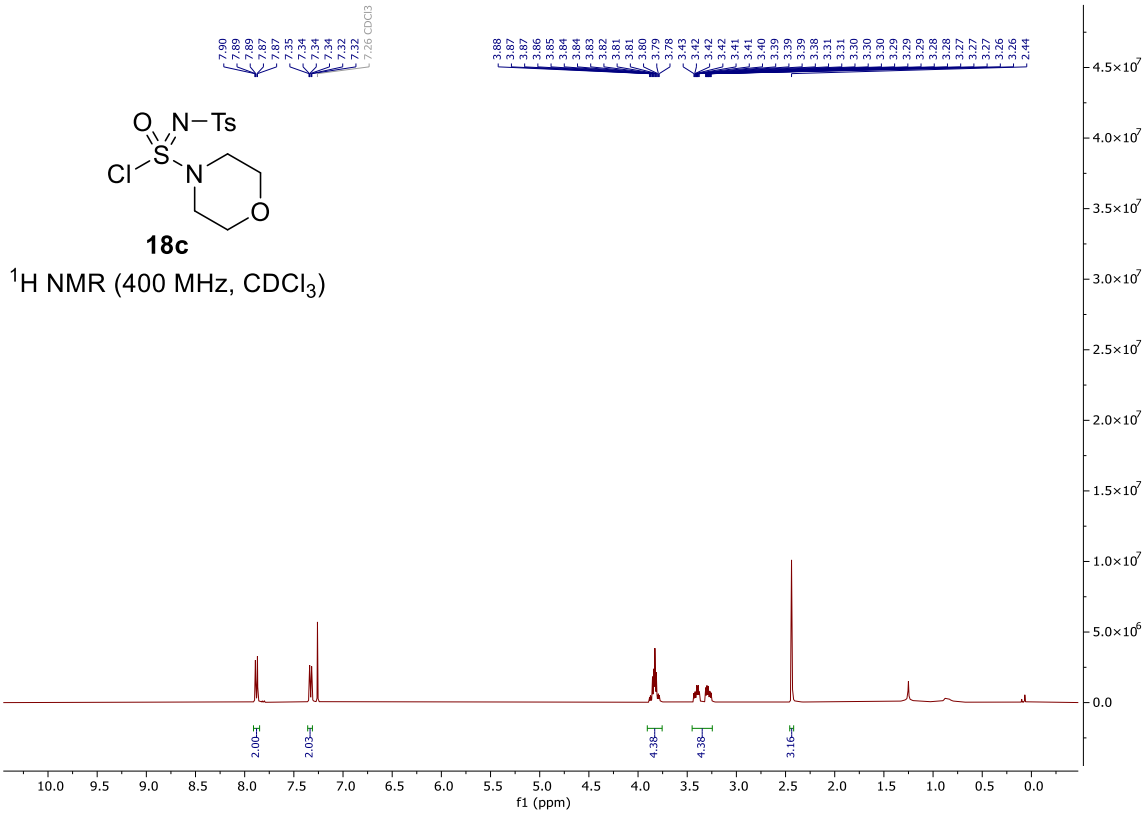


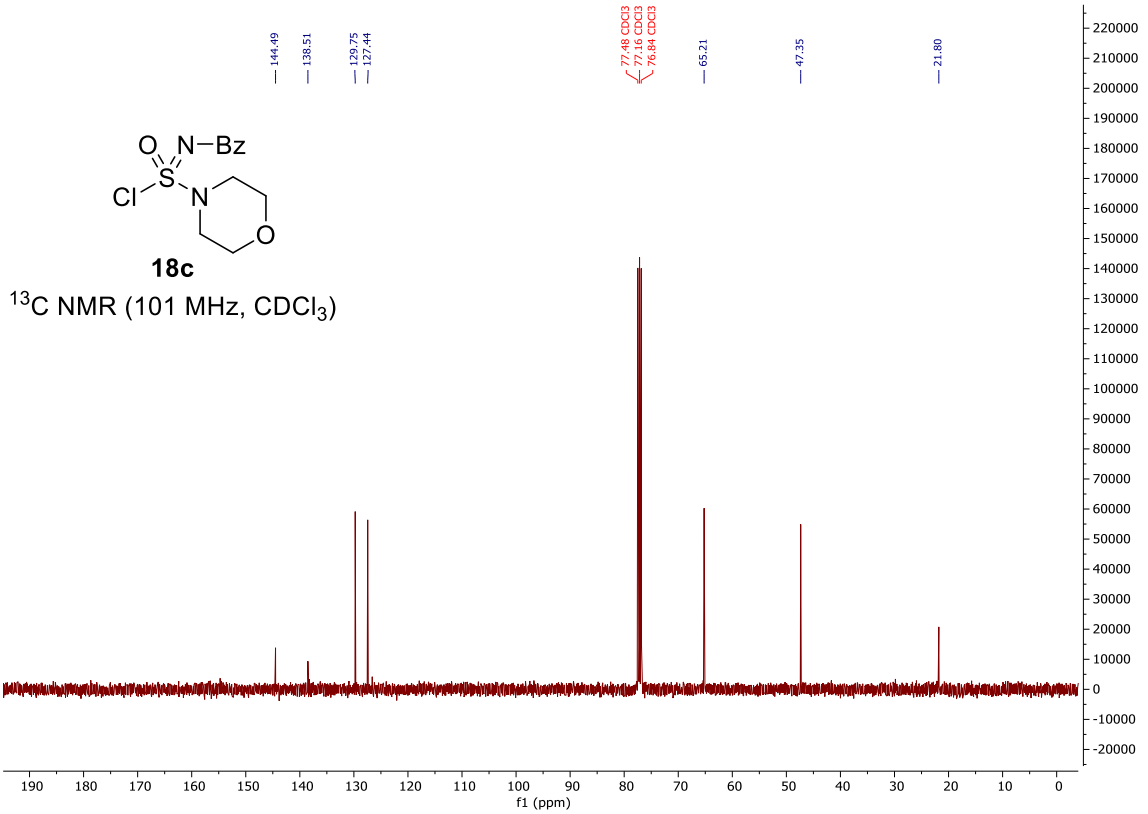
^{1}H NMR (400 MHz, $CDCl_3$)



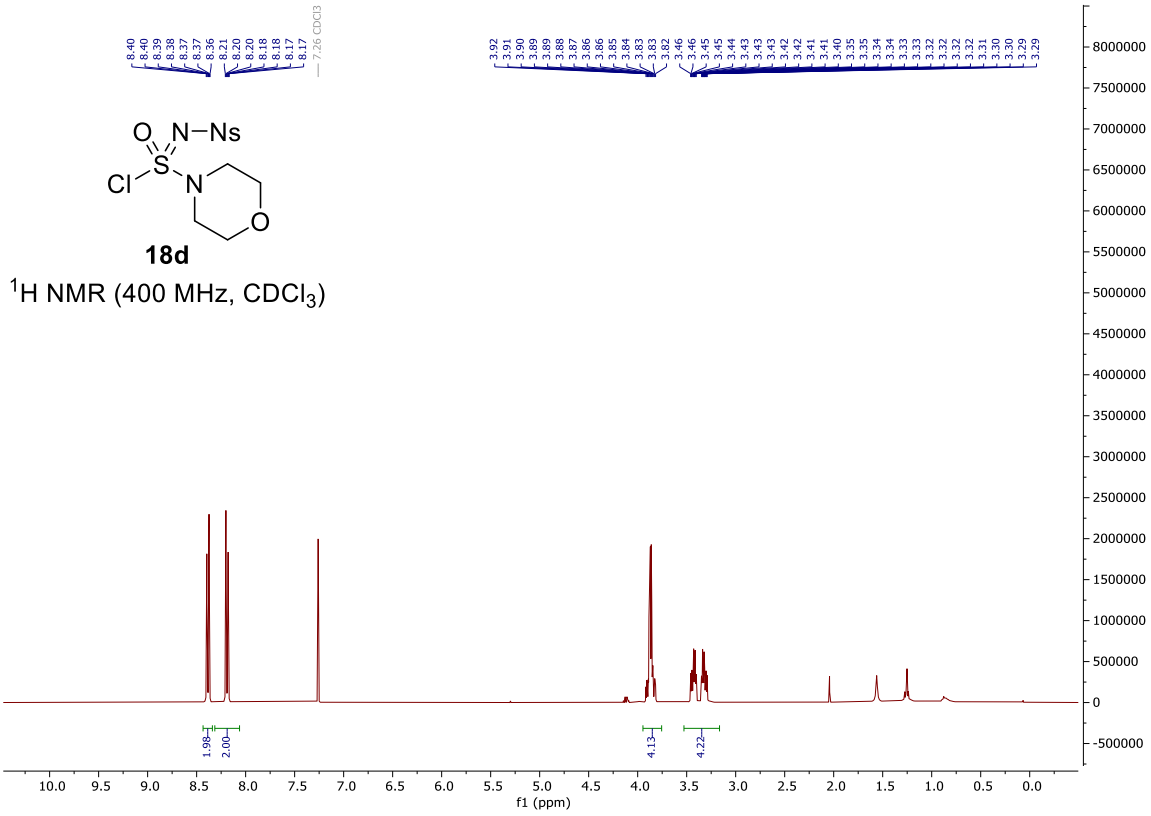
^{13}C NMR (101 MHz, $CDCl_3$)

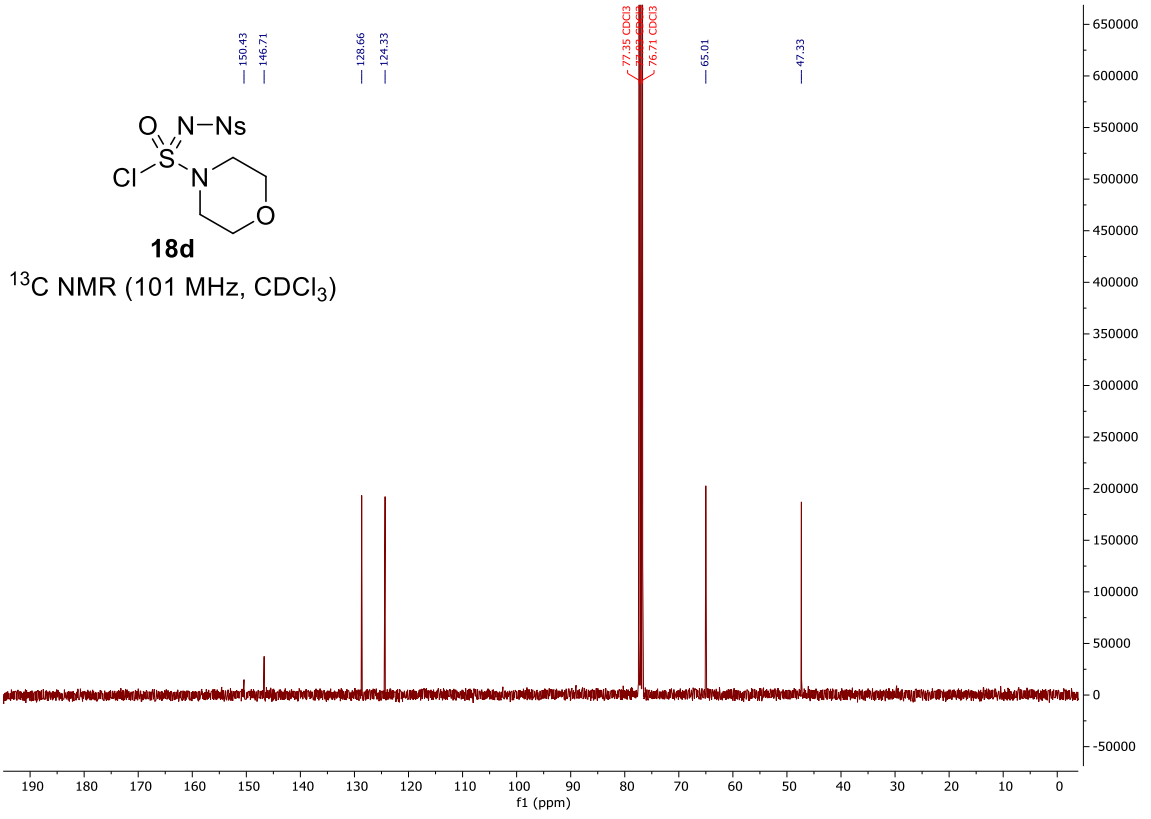
_N_-tosylmorpholine-4-sulfonimidoyl chloride (18c)



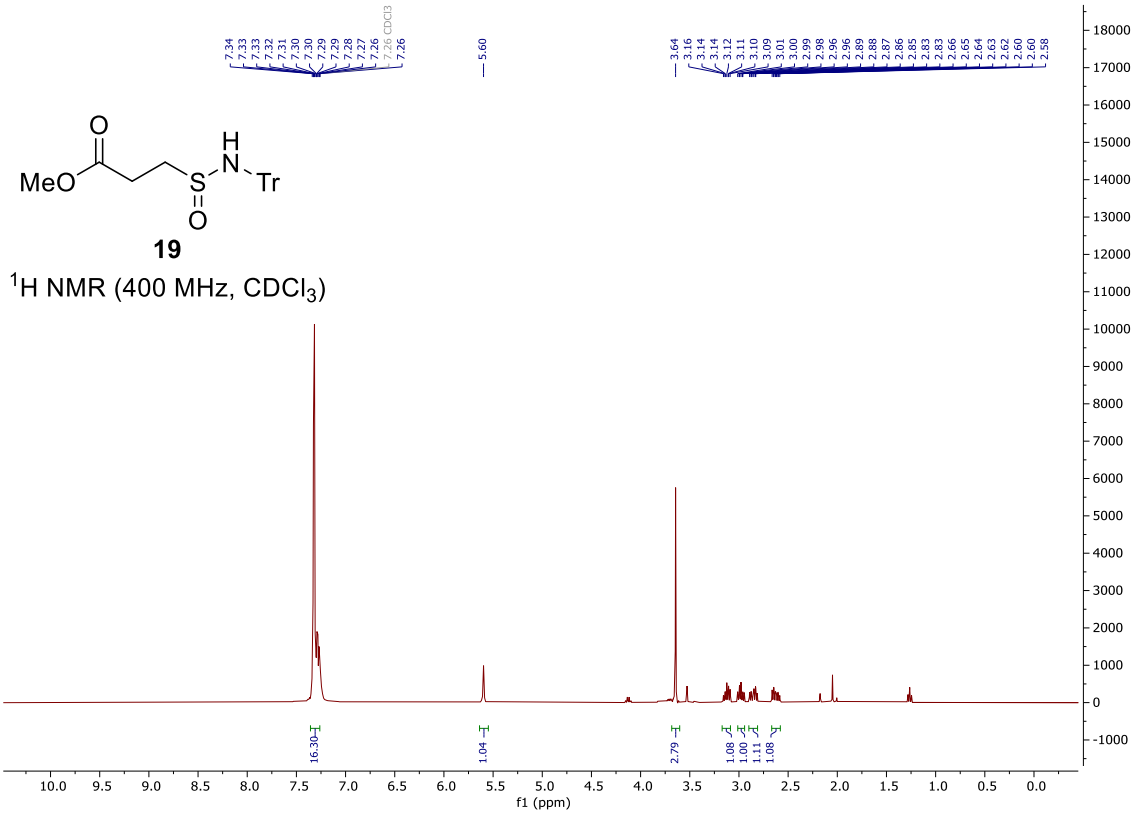


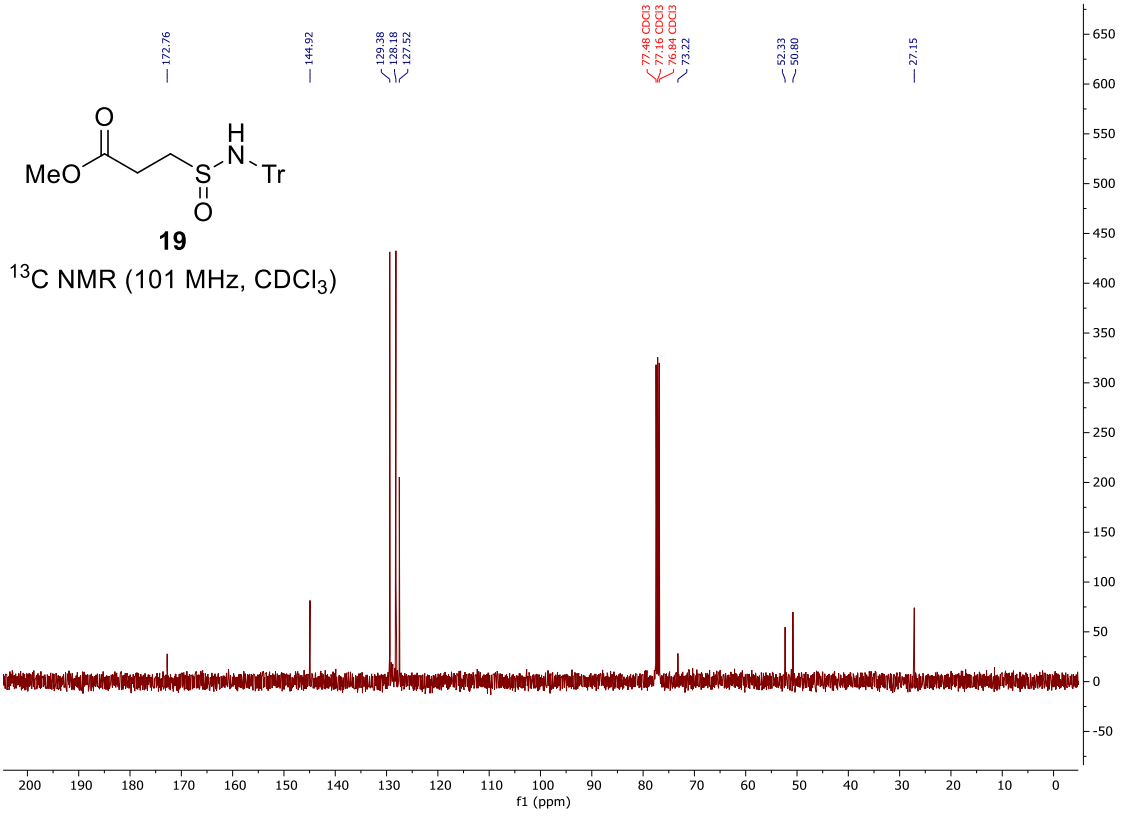
_N_-((4-nitrophenyl)sulfonyl)morpholine-4-sulfonimidoyl chloride (18d)



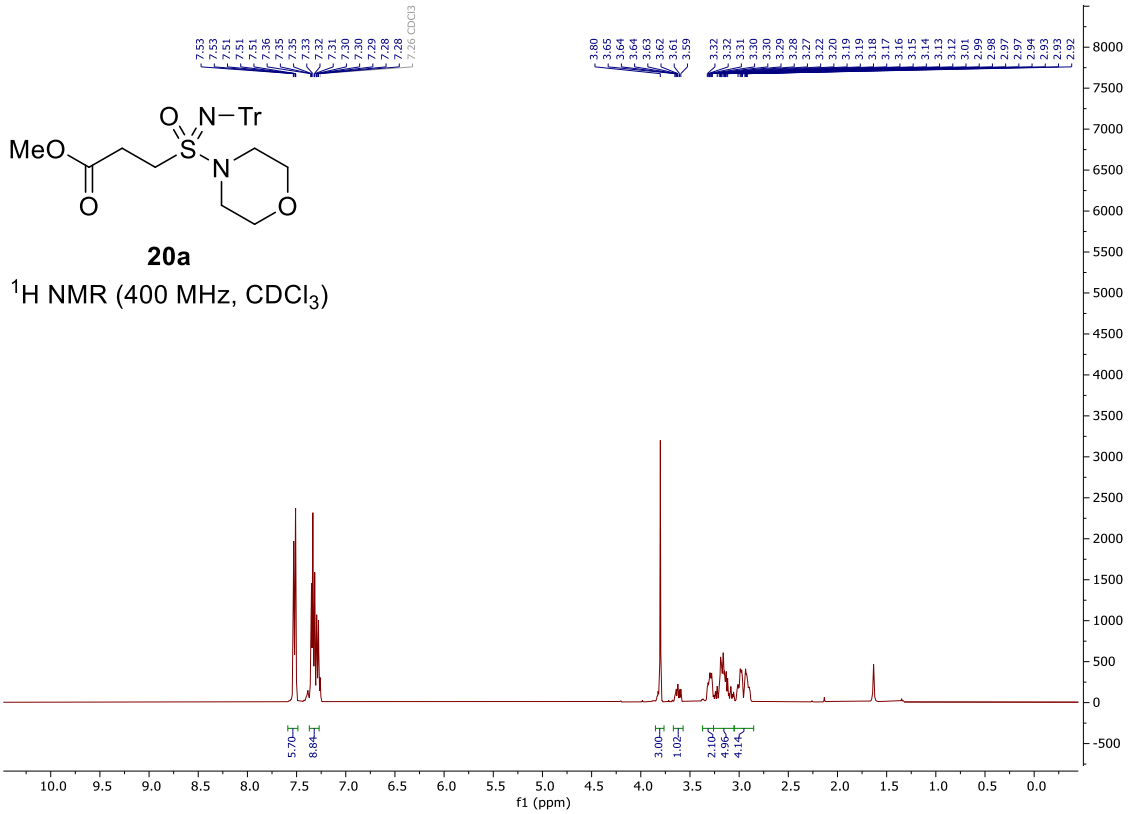


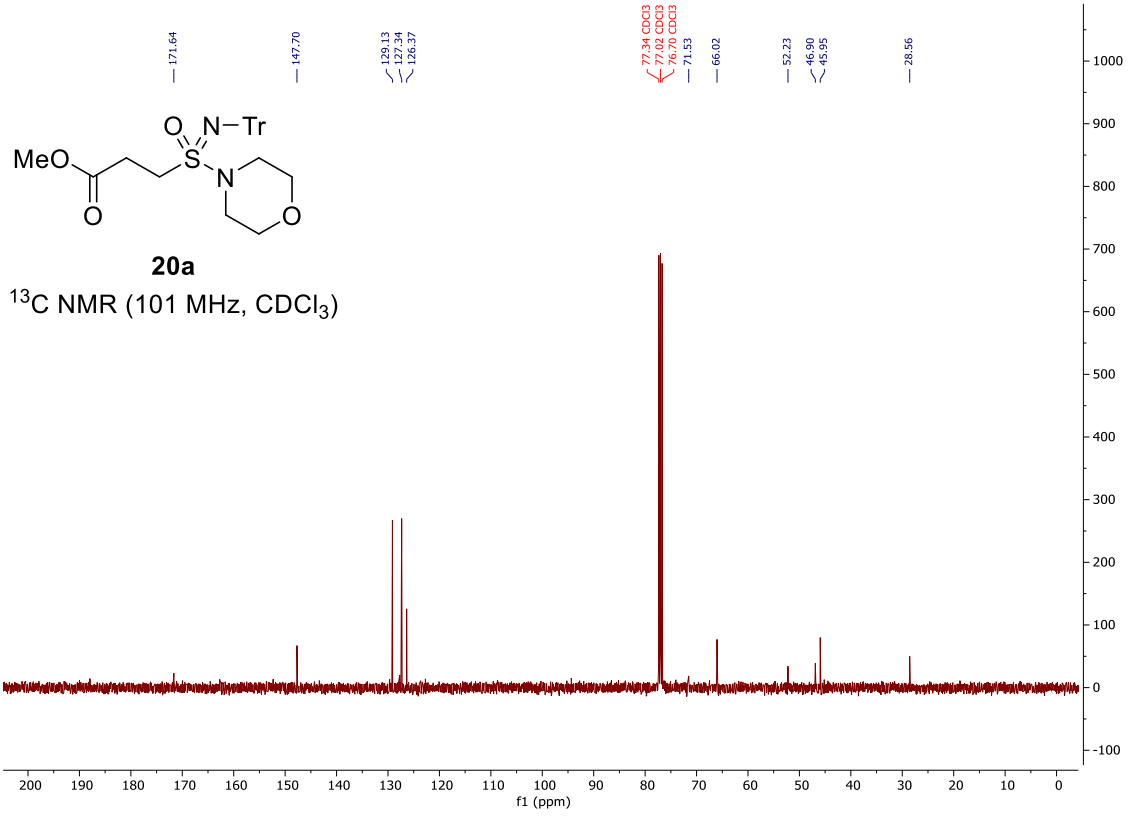
Methyl 3-((tritylamino)sulfinyl)propanoate (19)



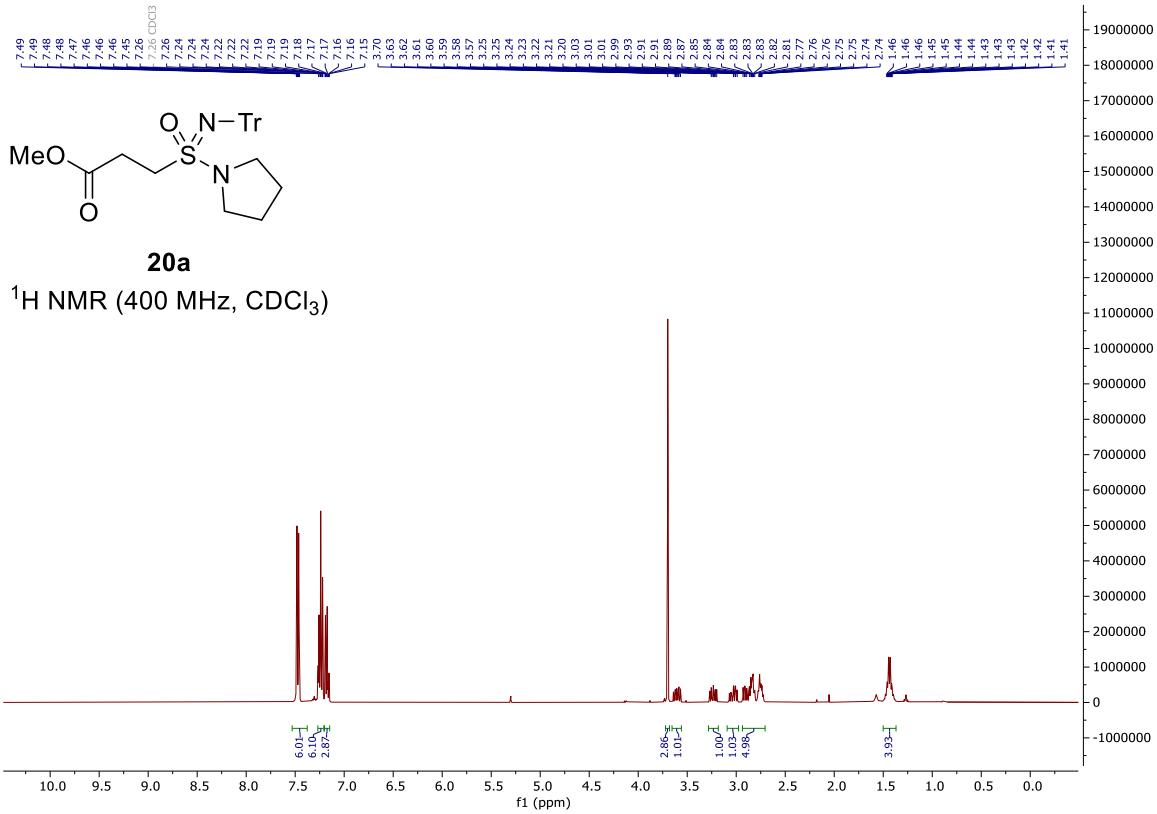


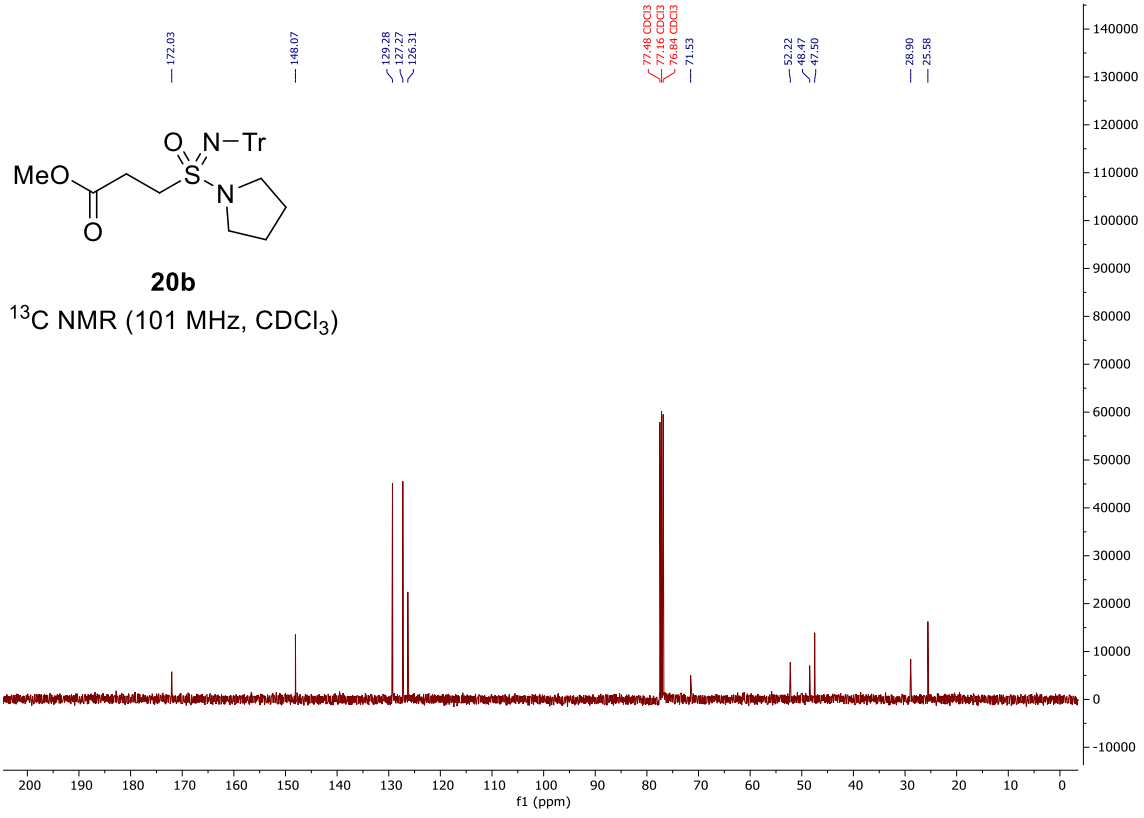
Methyl 3-(*N*-tritylmorpholine-4-sulfonimidoyl)propanoate (20a)



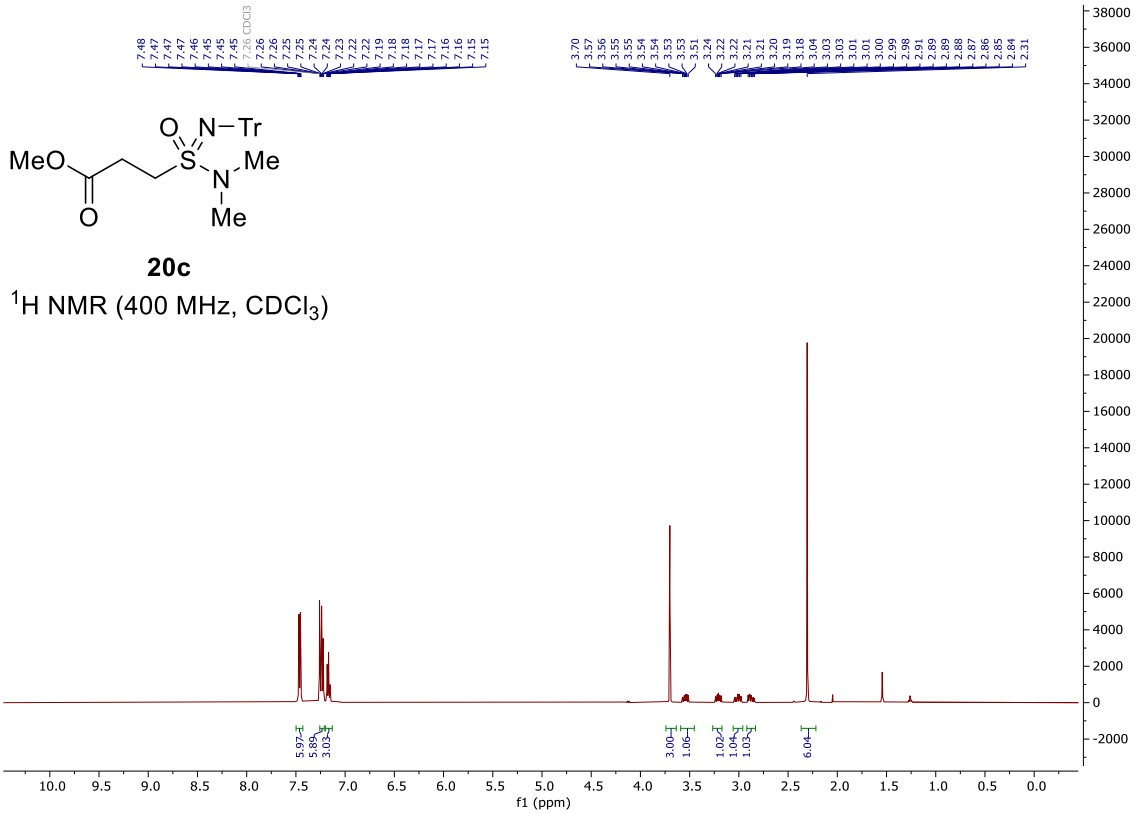


Methyl 3-(*N*-tritylpyrrolidine-1-sulfonimidoyl)propanoate (20b)



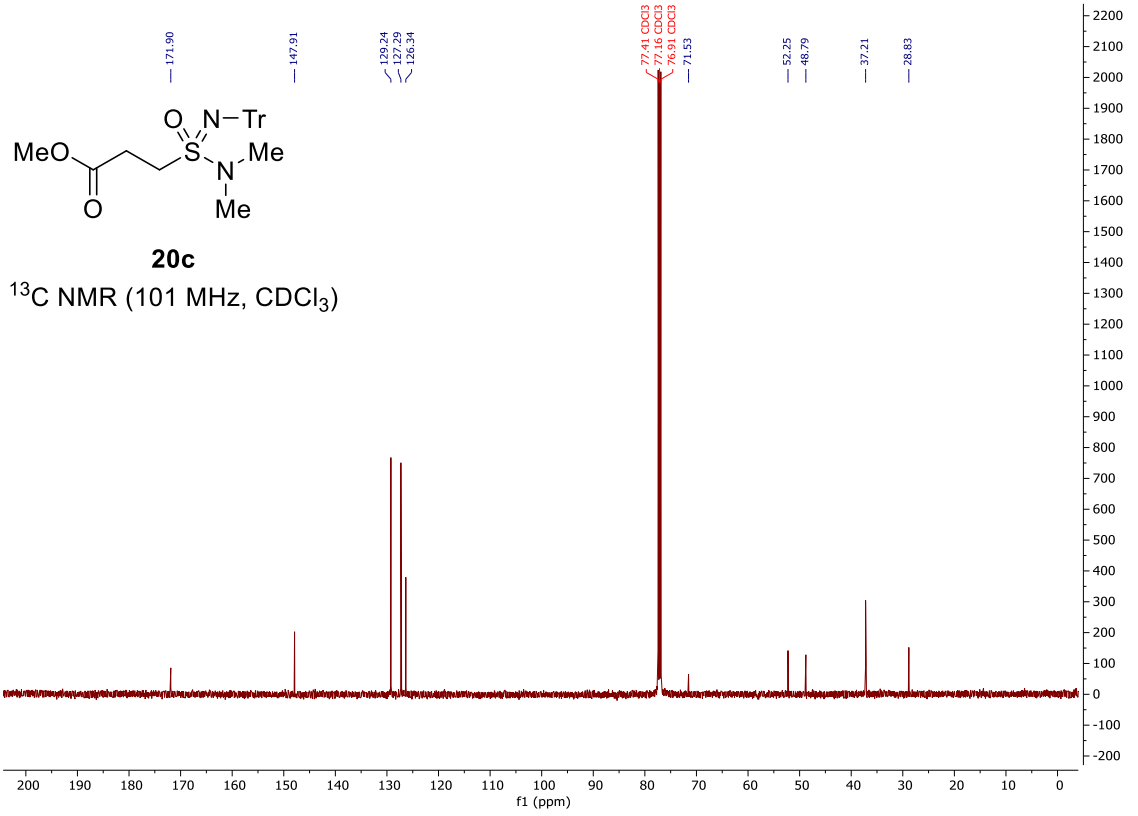


Methyl 3-(*N*,*N*-dimethyl-*N*'-tritylsulfamidimidoyl)propanoate (20c)



20c

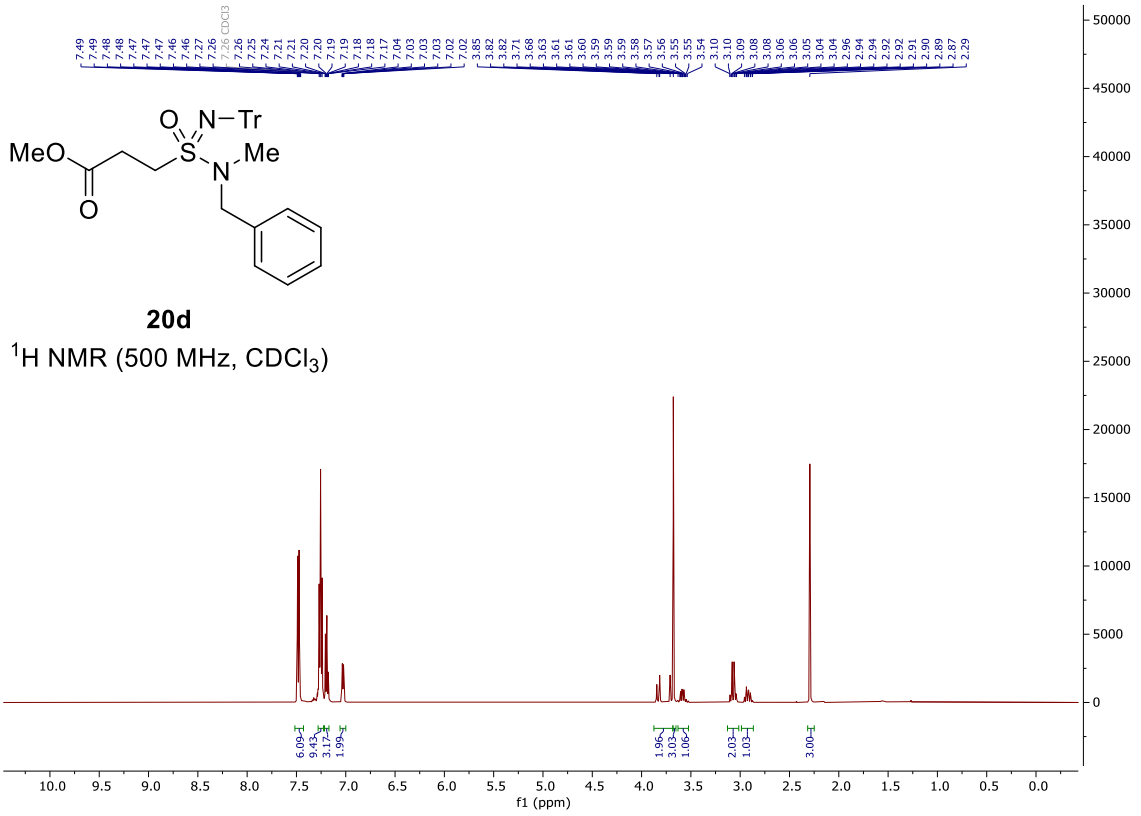
^{1}H NMR (400 MHz, $CDCl_3$)

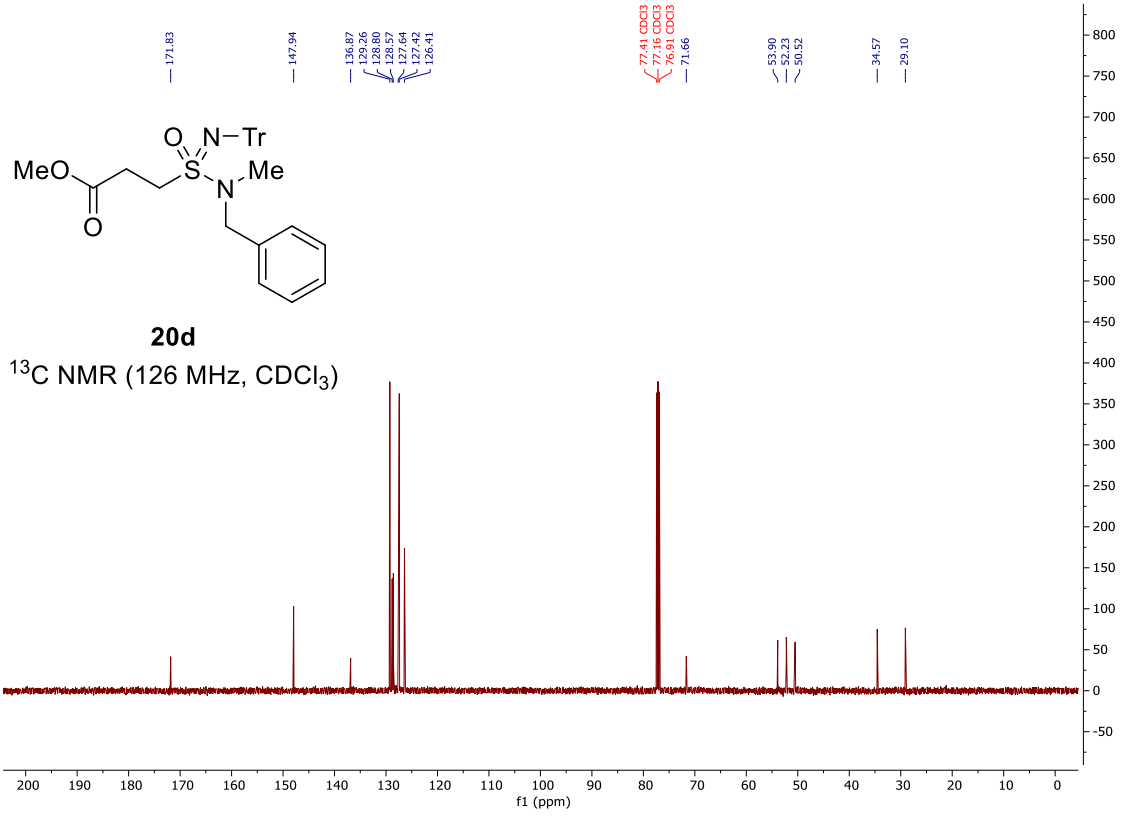


20c

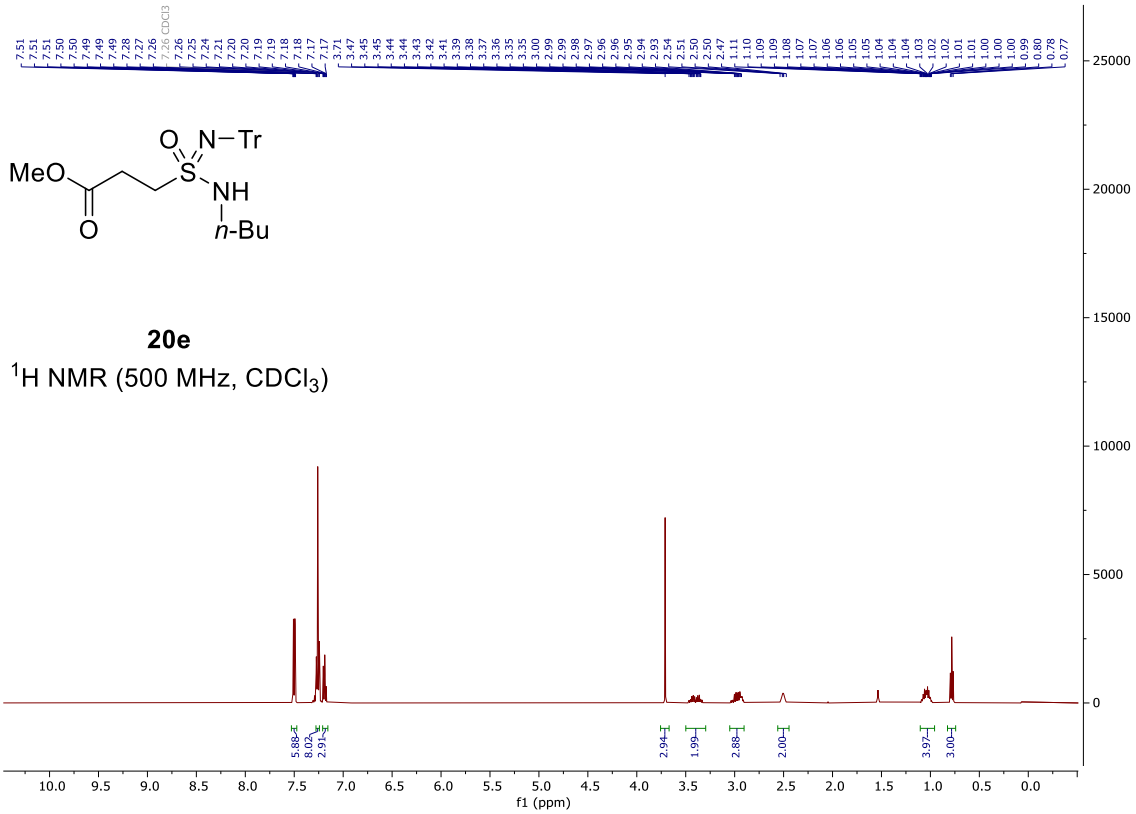
^{13}C NMR (101 MHz, $CDCl_3$)

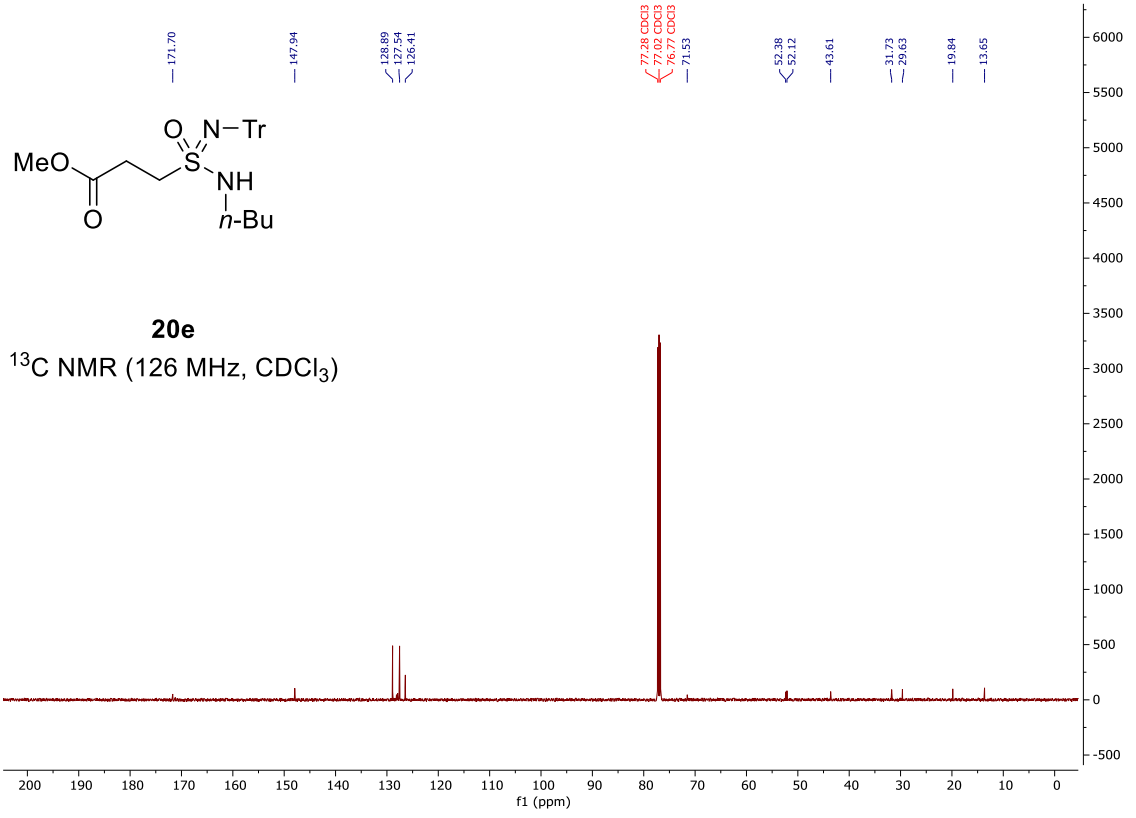
Methyl 3-(*N*-benzyl-*N*-methyl-*N*'-tritylsulfamidimidoyl)propanoate (20d)



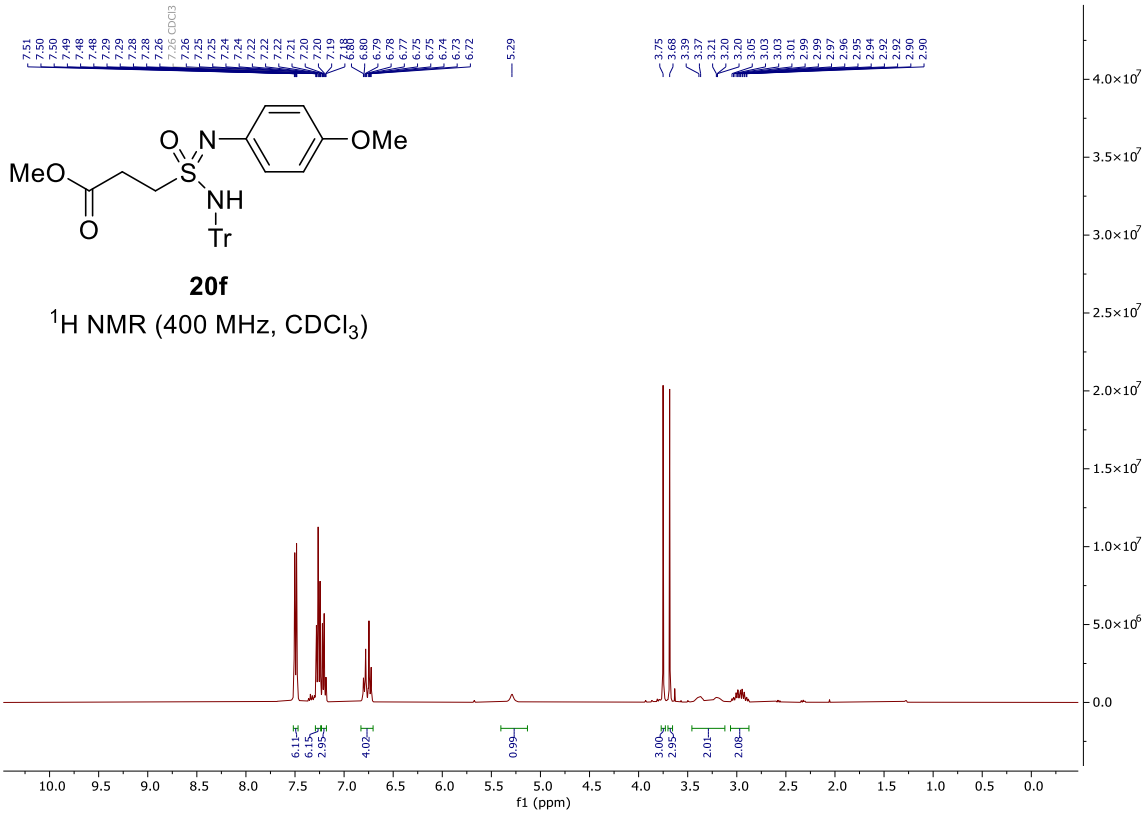


Methyl 3-(*N*-butyl-*N*'-tritylsulfamidimidoyl)propanoate (20e)



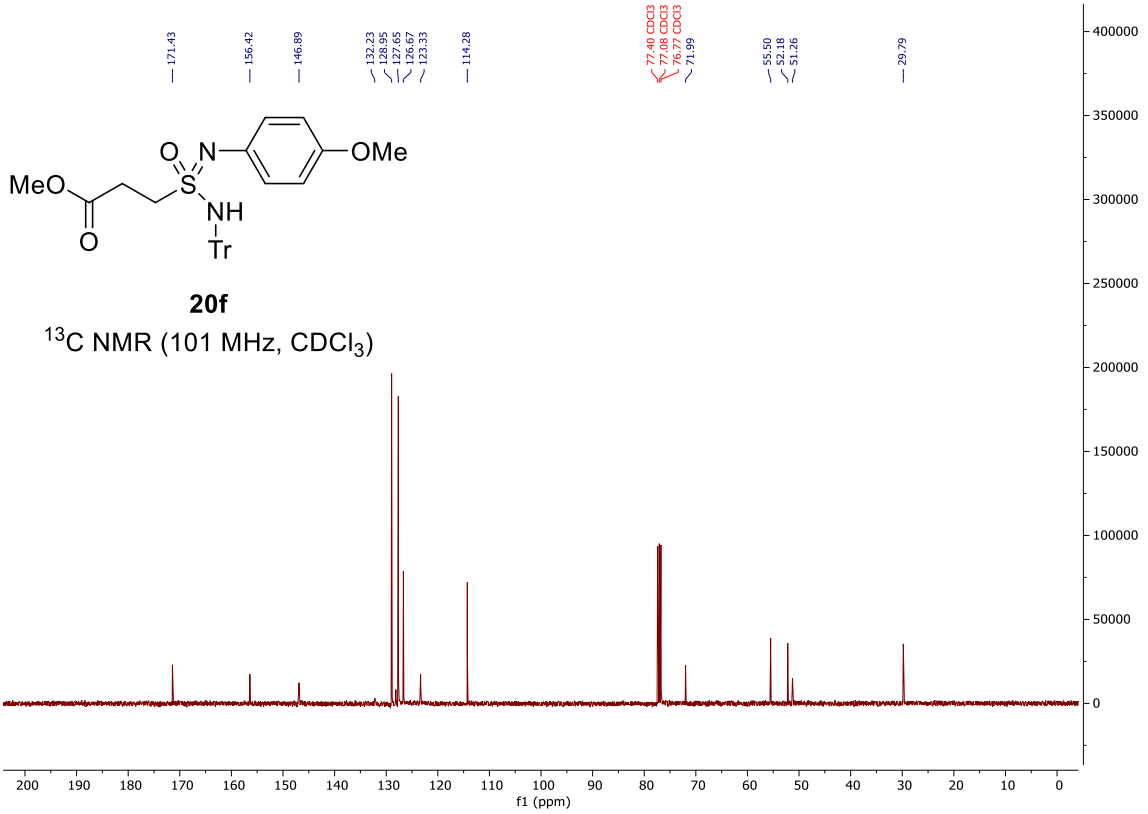


Methyl 3-(*N*-(4-methoxyphenyl)-*N*'-tritylsulfamidimidoyl)propanoate (20f)



20f

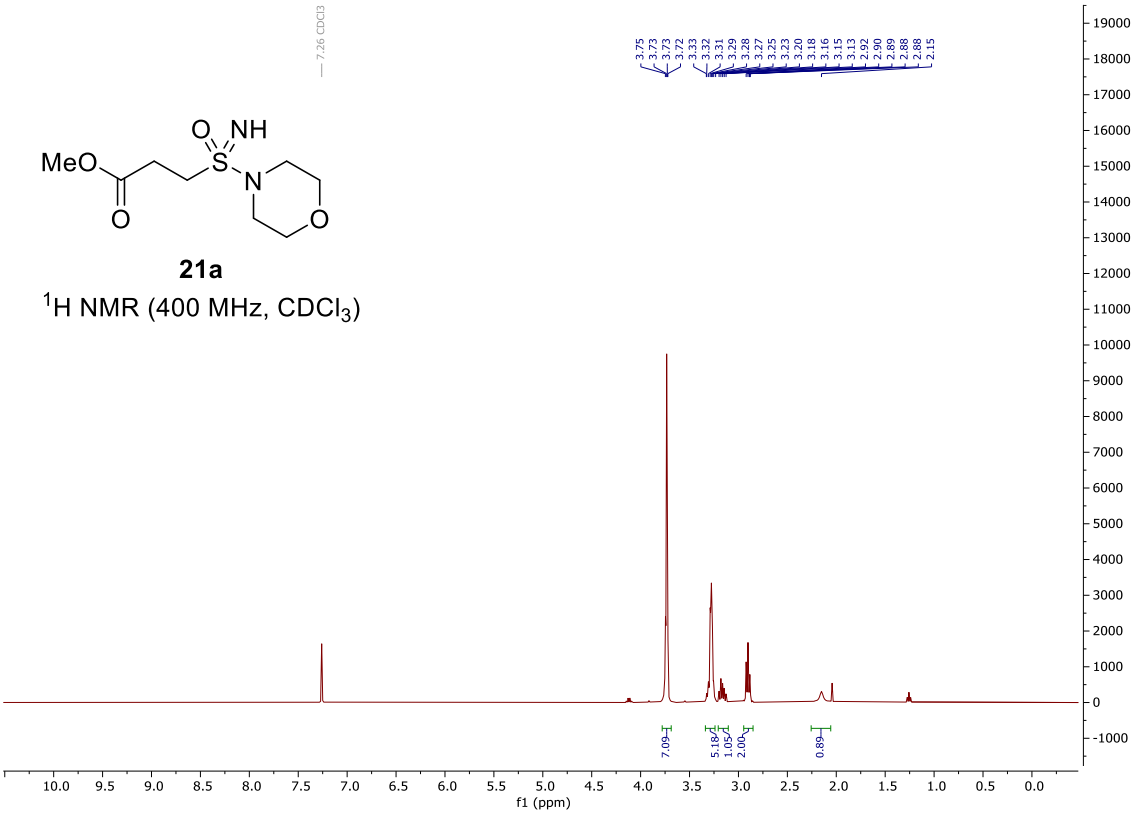
^{1}H NMR (400 MHz, $CDCl_3$)

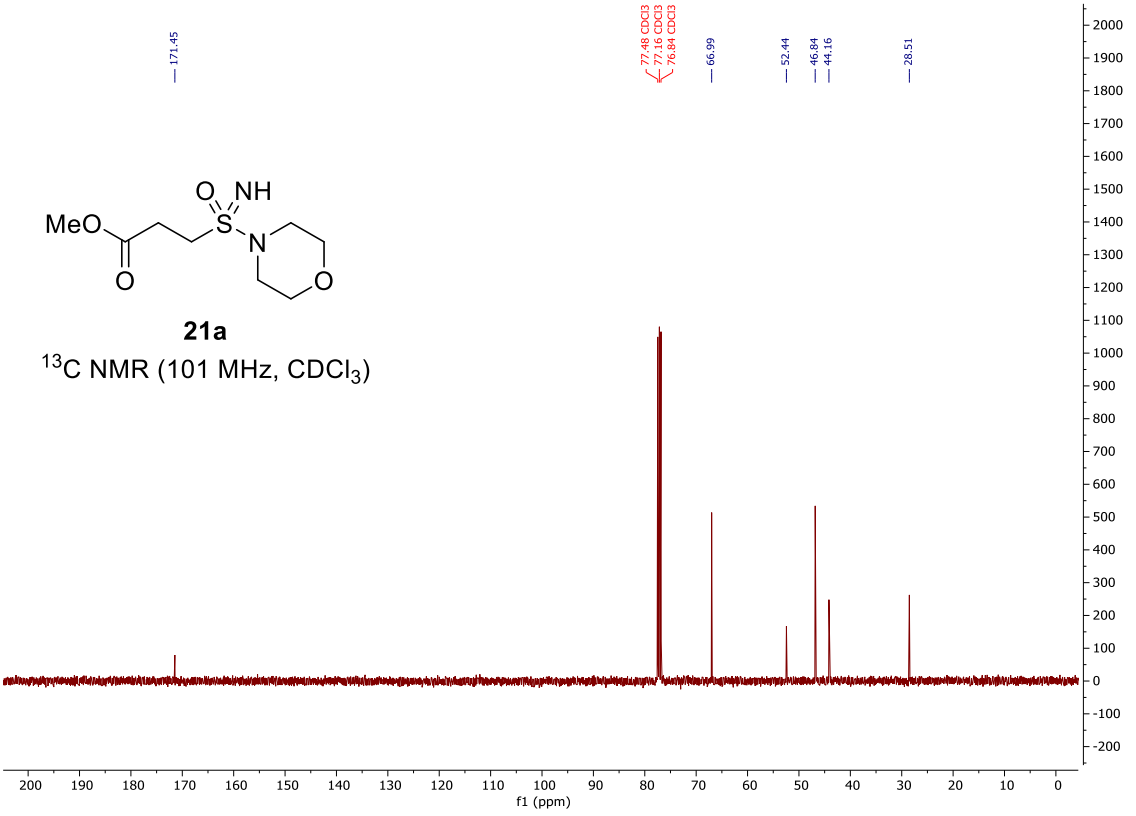


20f

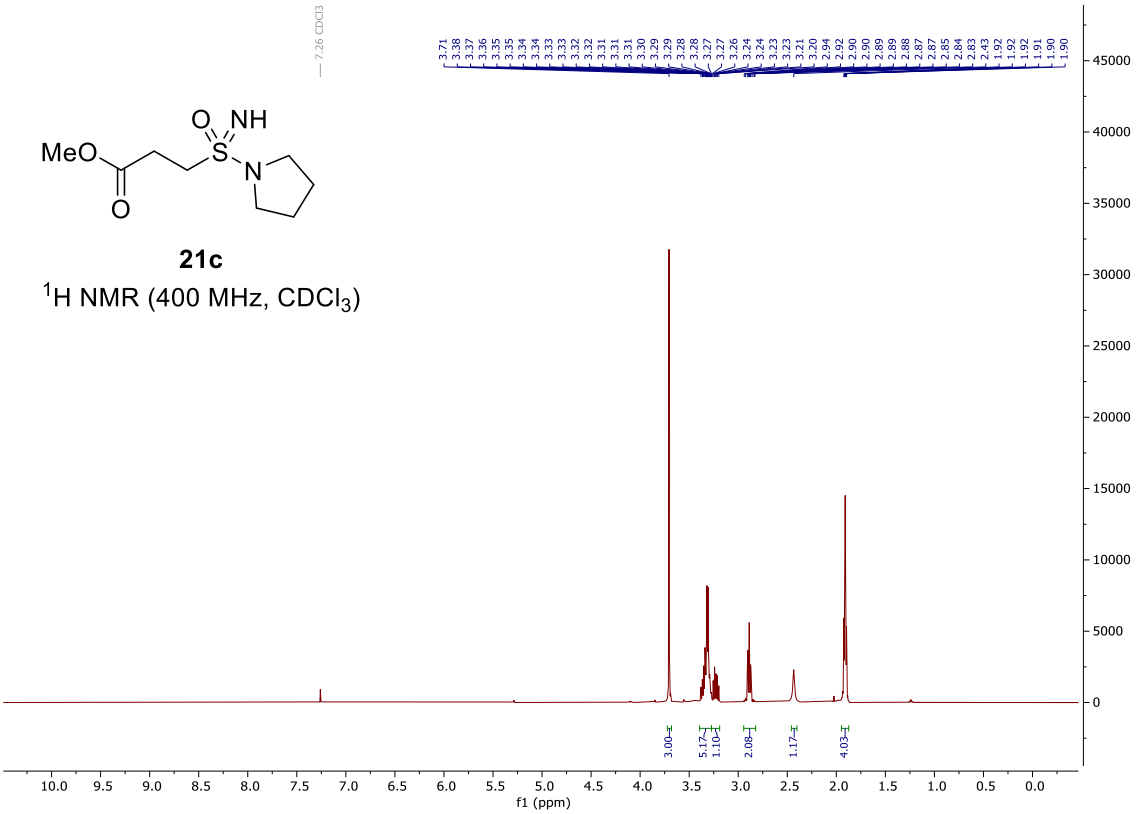
^{13}C NMR (101 MHz, $CDCl_3$)

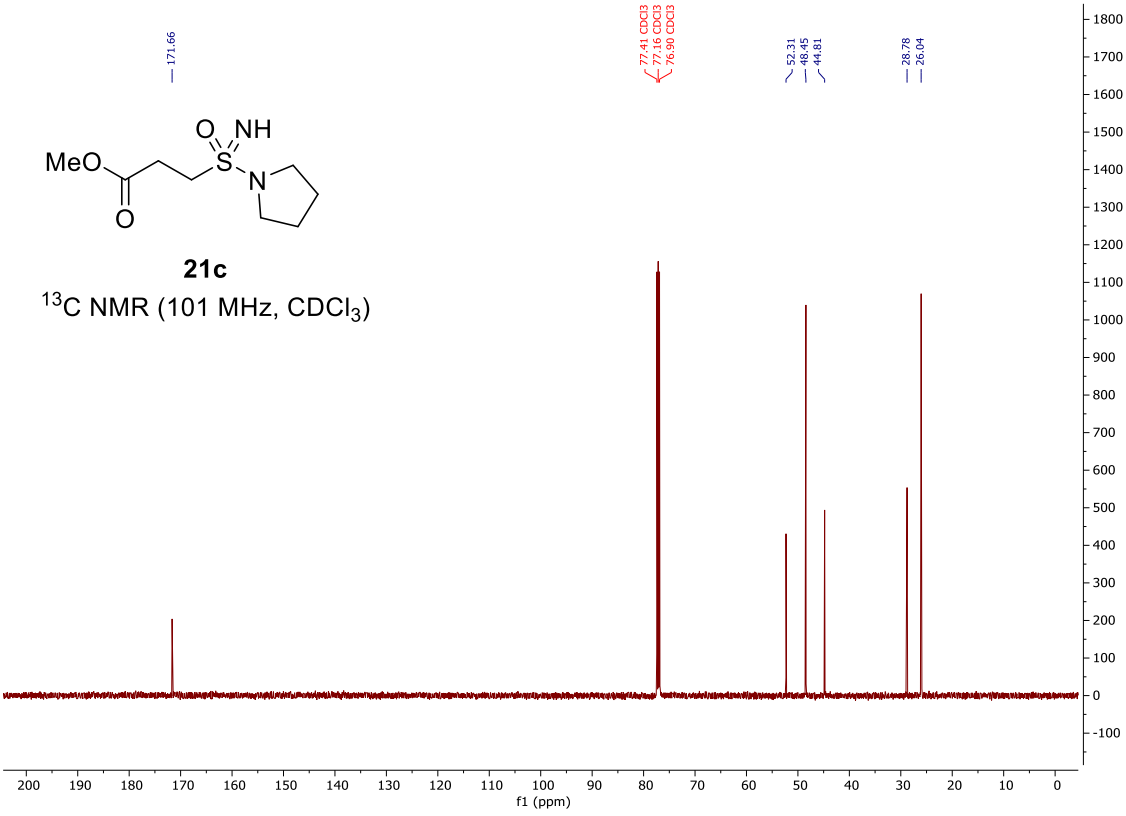
Methyl 3-(morpholine-4-sulfonimidoyl)propanoate (21a)



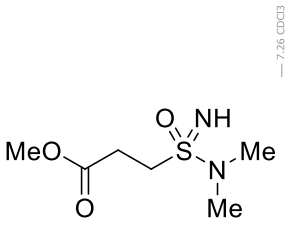


Methyl 3-(pyrrolidine-1-sulfonimidoyl)propanoate (21b)



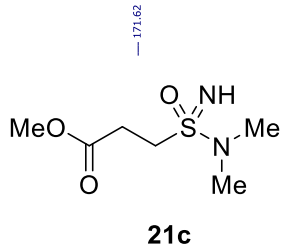


Methyl 3-(*N*,*N*-dimethylsulfamidimidoyl)propanoate (21c)



21c

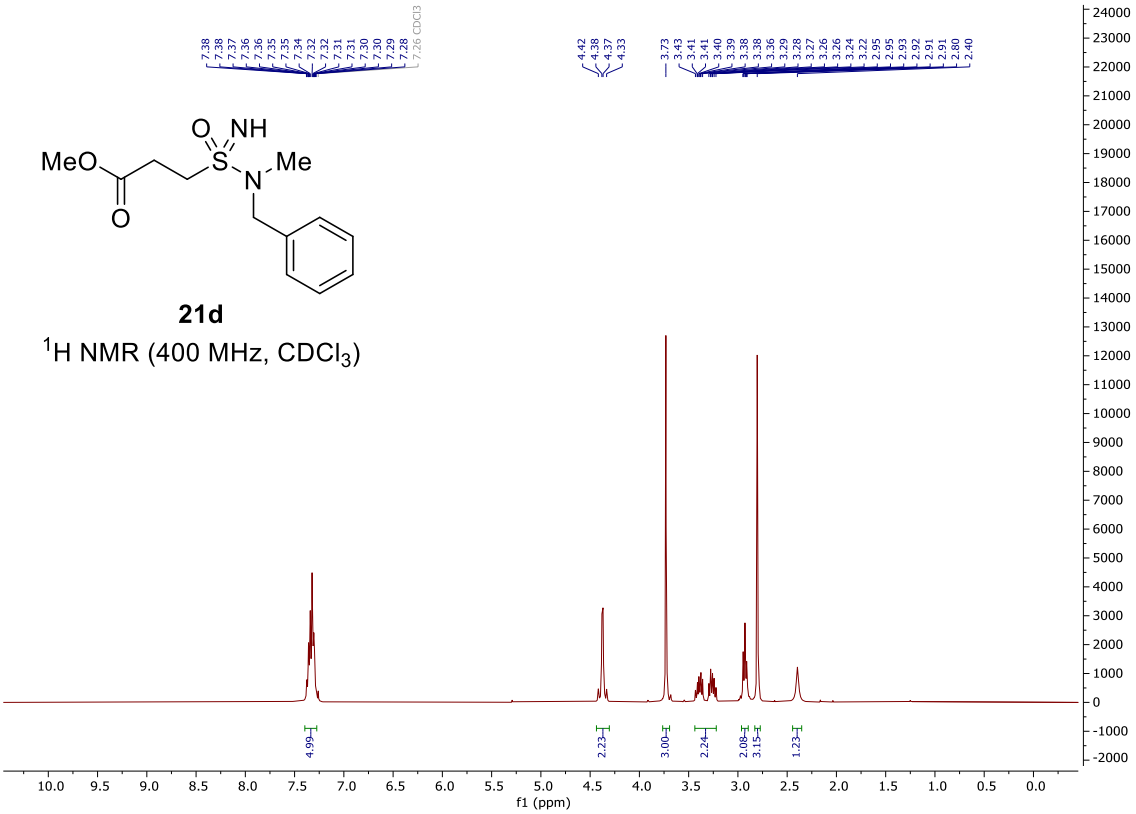
^{1}H NMR (400 MHz, $CDCl_3$)

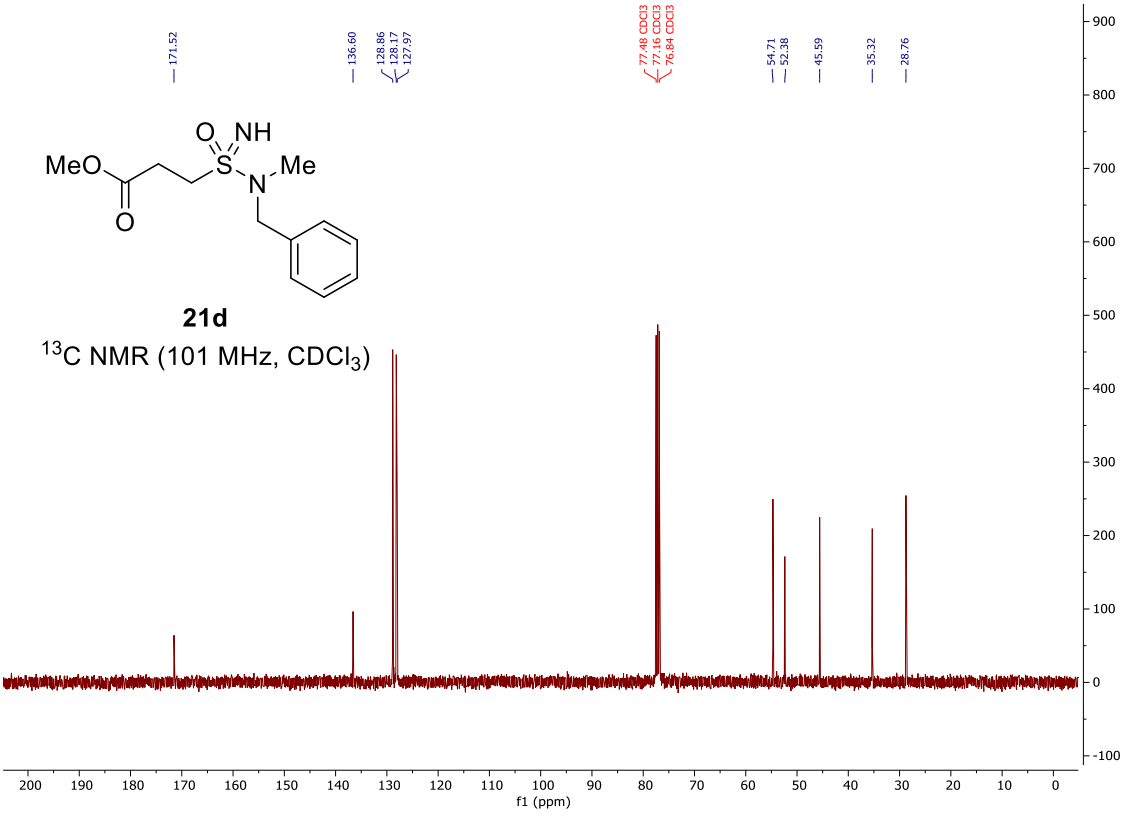


21c

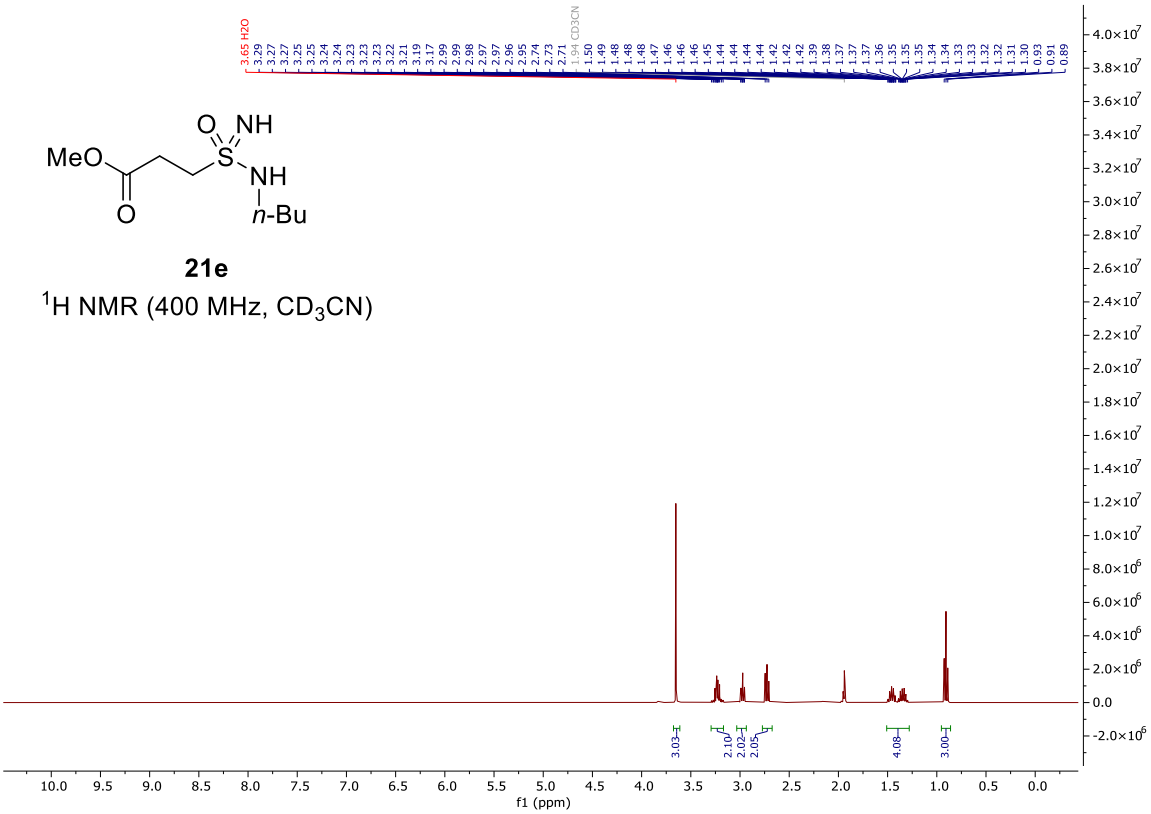
^{13}C NMR (101 MHz, $CDCl_3$)

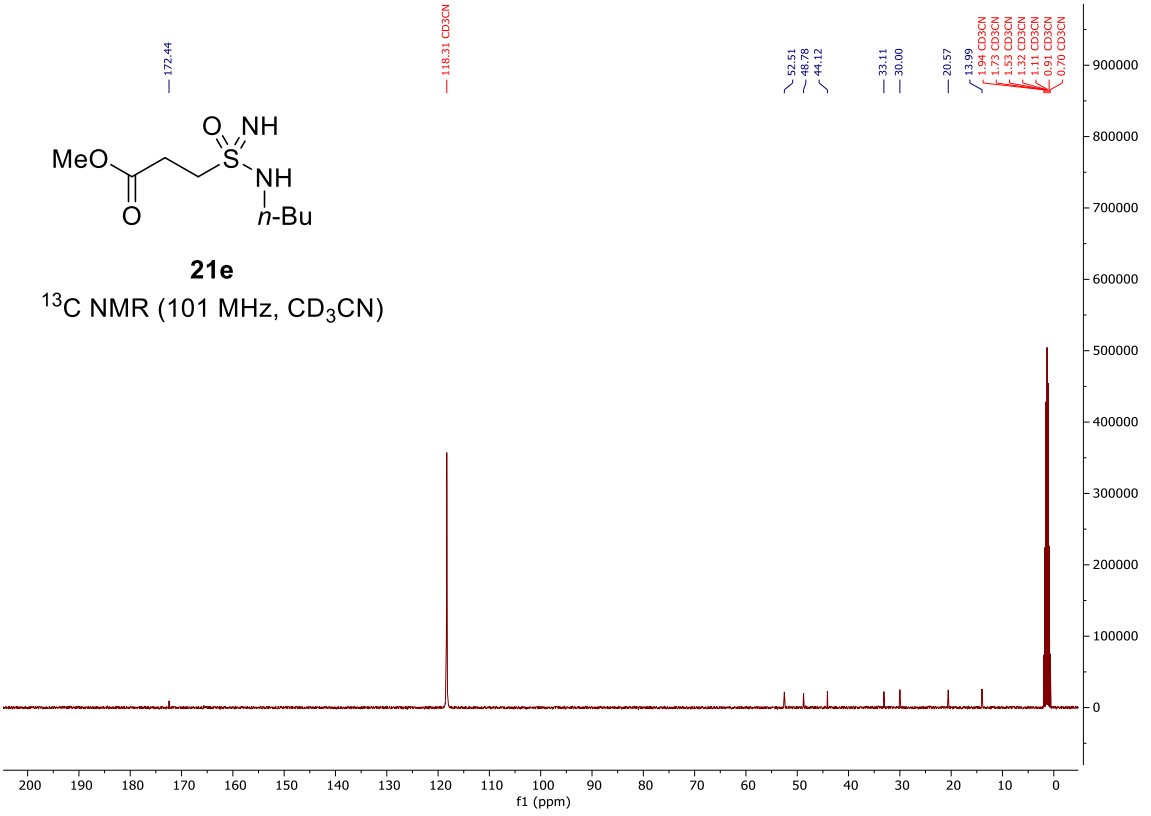
Methyl 3-(*N*-benzyl-*N*-methylsulfamidimidoyl)propanoate (21d)



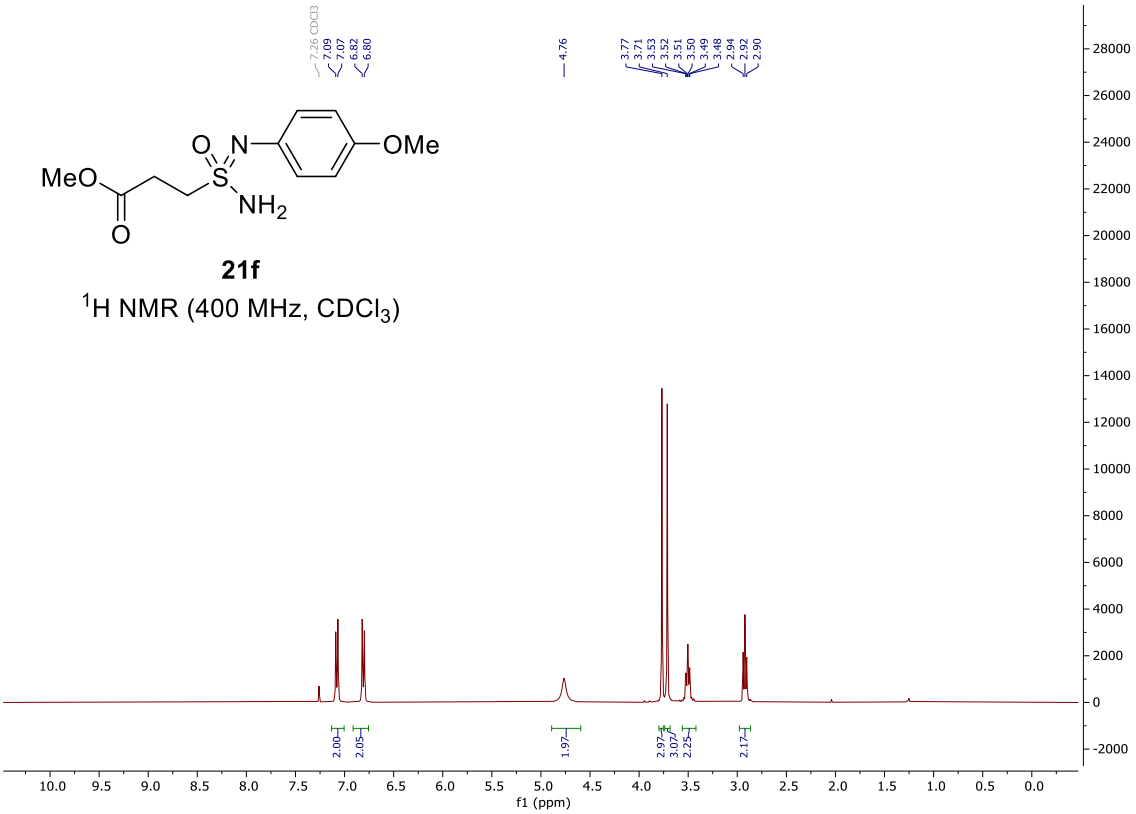


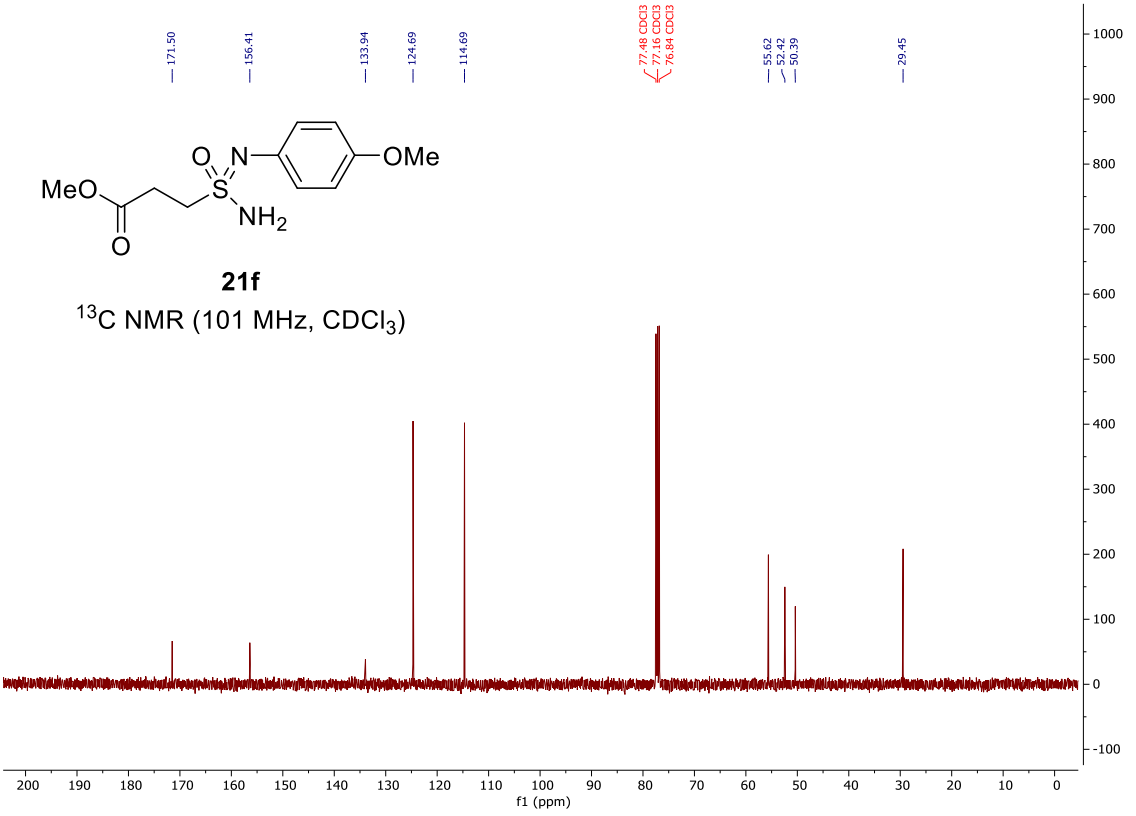
Methyl 3-(*N*-butylsulfamidimidoyl)propanoate (21e)



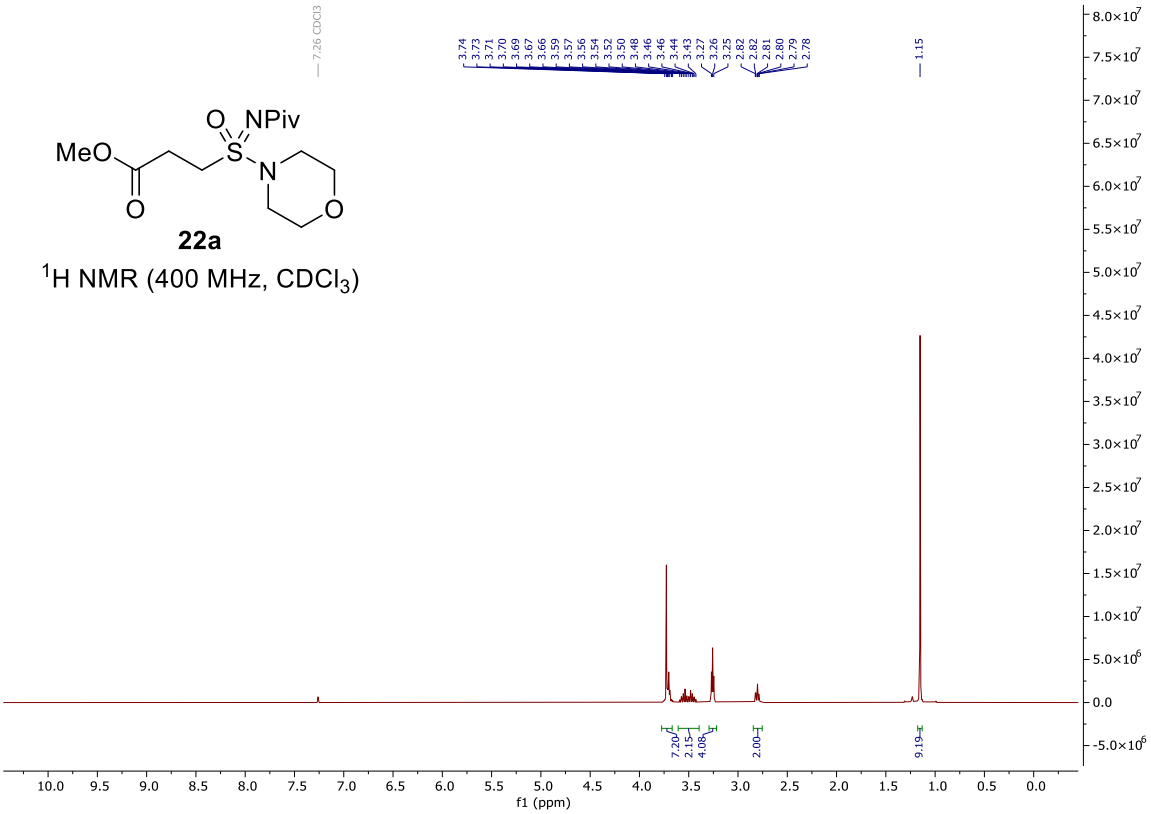


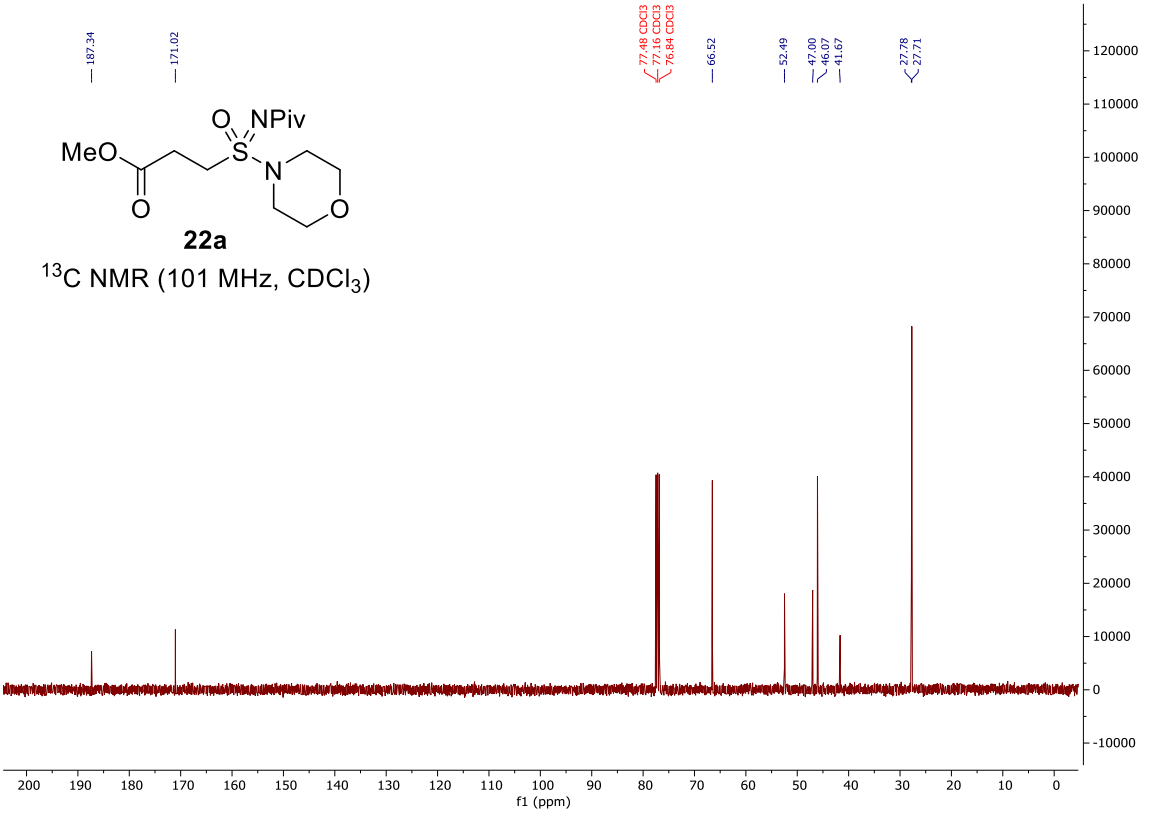
Methyl 3-(*N*-(4-methoxyphenyl)sulfamidimidoyl)propanoate (21f)



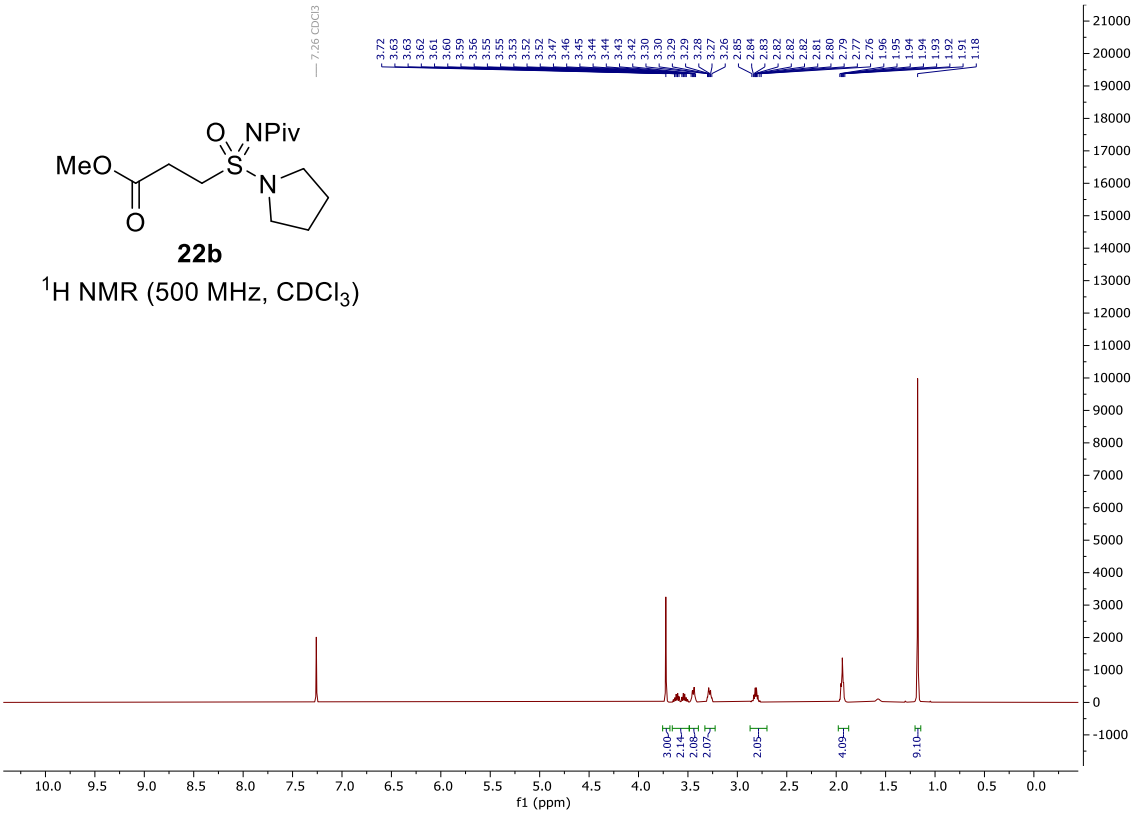


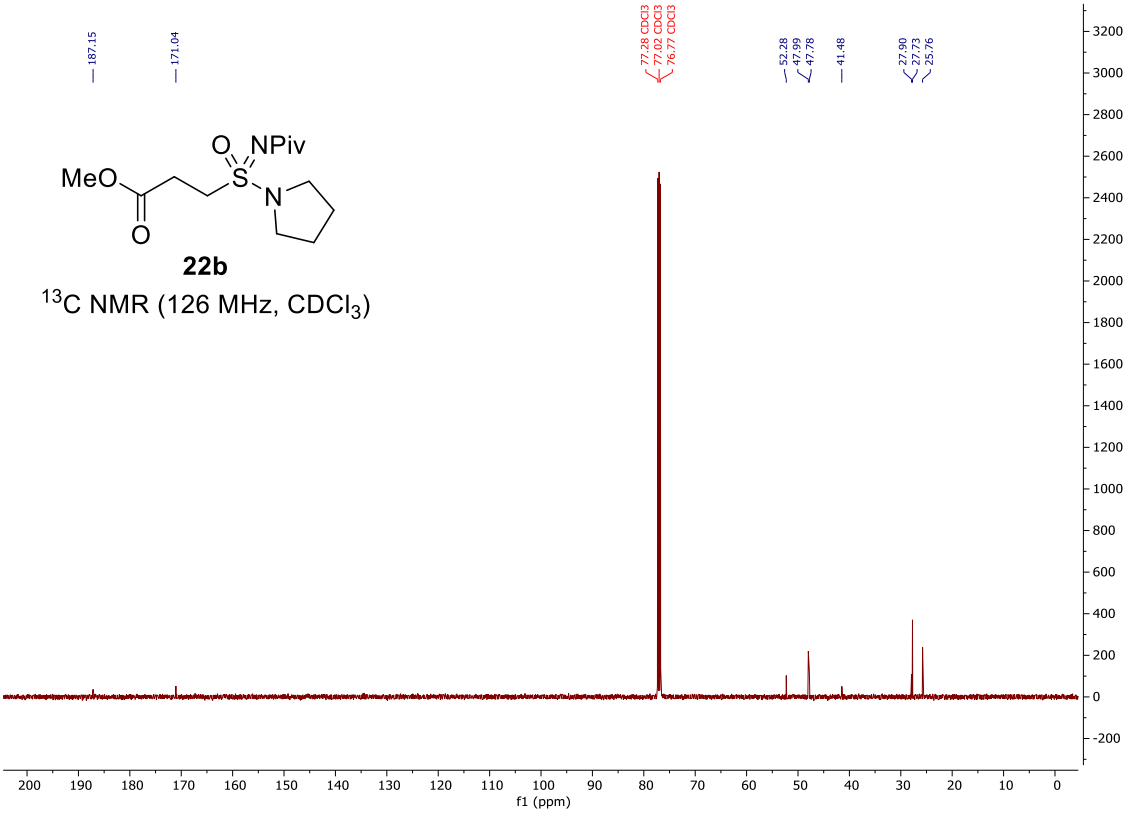
Methyl 3-(*N*-pivaloylmorpholine-4-sulfonimidoyl)propanoate (22a)



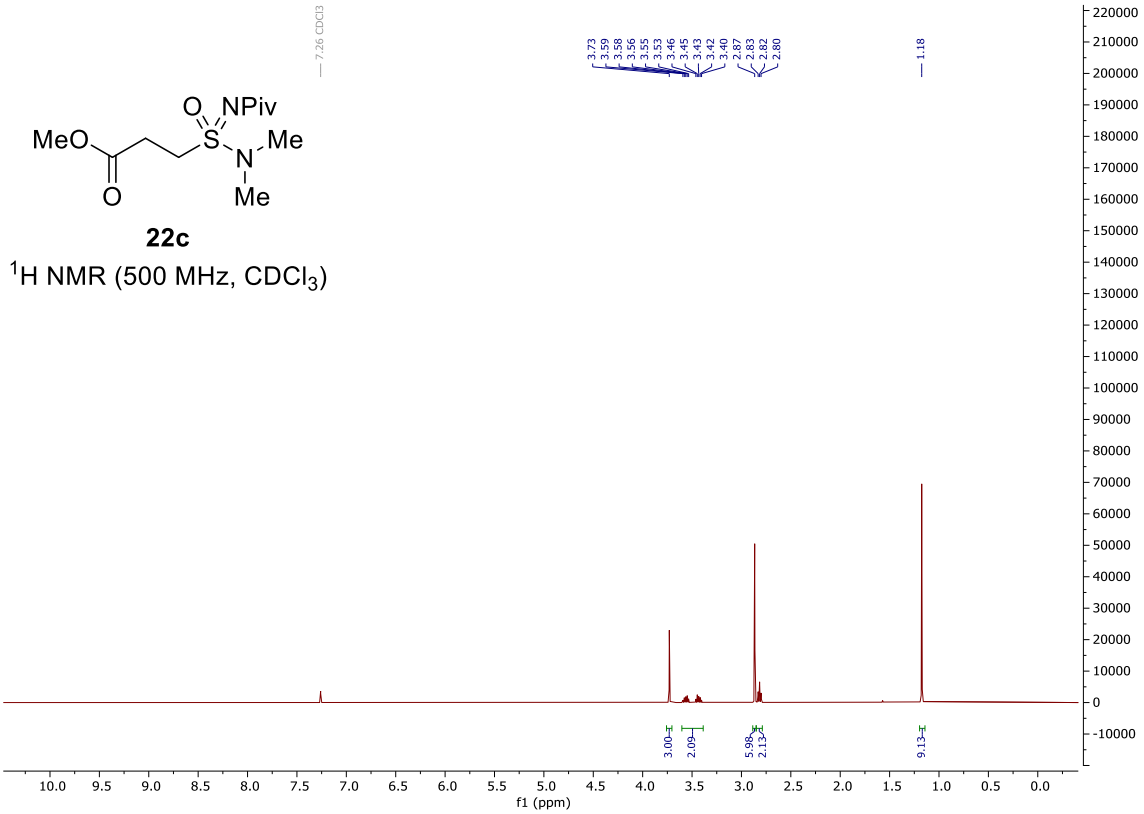


Methyl 3-(*N*-pivaloylpyrrolidine-1-sulfonimidoyl)propanoate (22b)



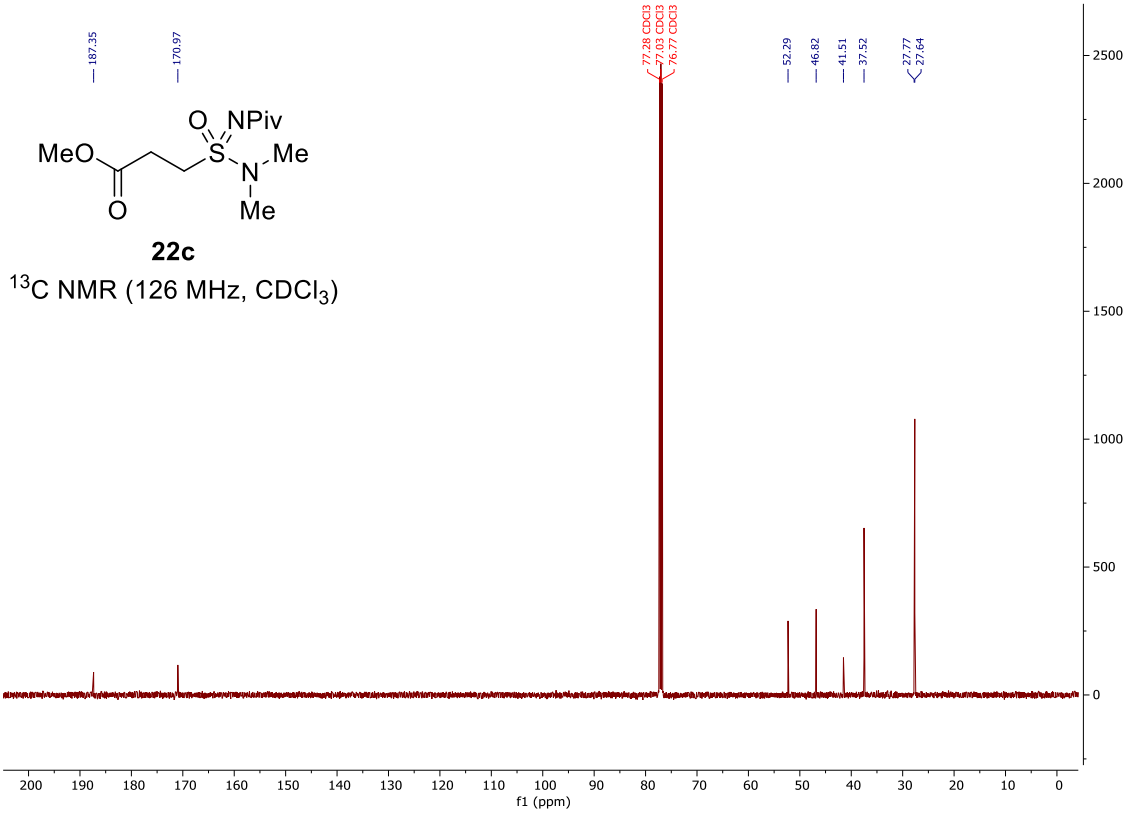


Methyl 3-(*N*,*N*-dimethyl-*N*'-pivaloylsulfamidimidoyl)propanoate (22c)



22c

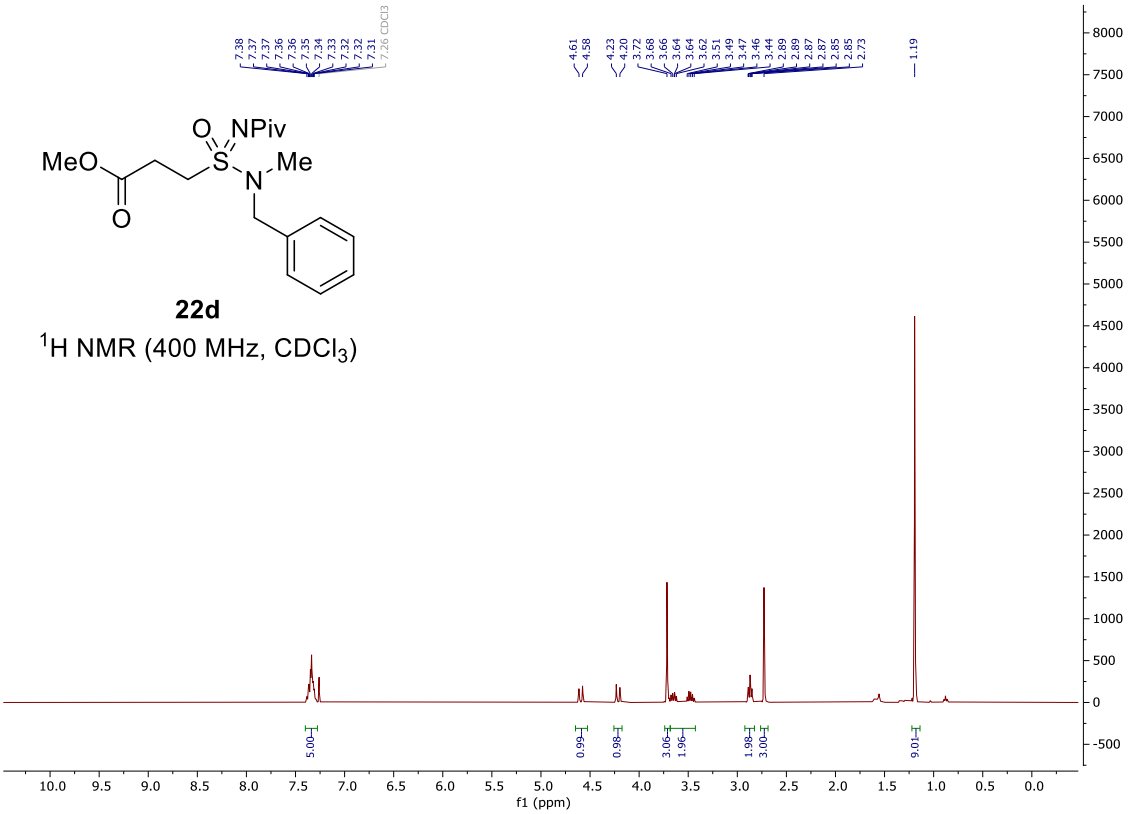
^{1}H NMR (500 MHz, $CDCl_3$)

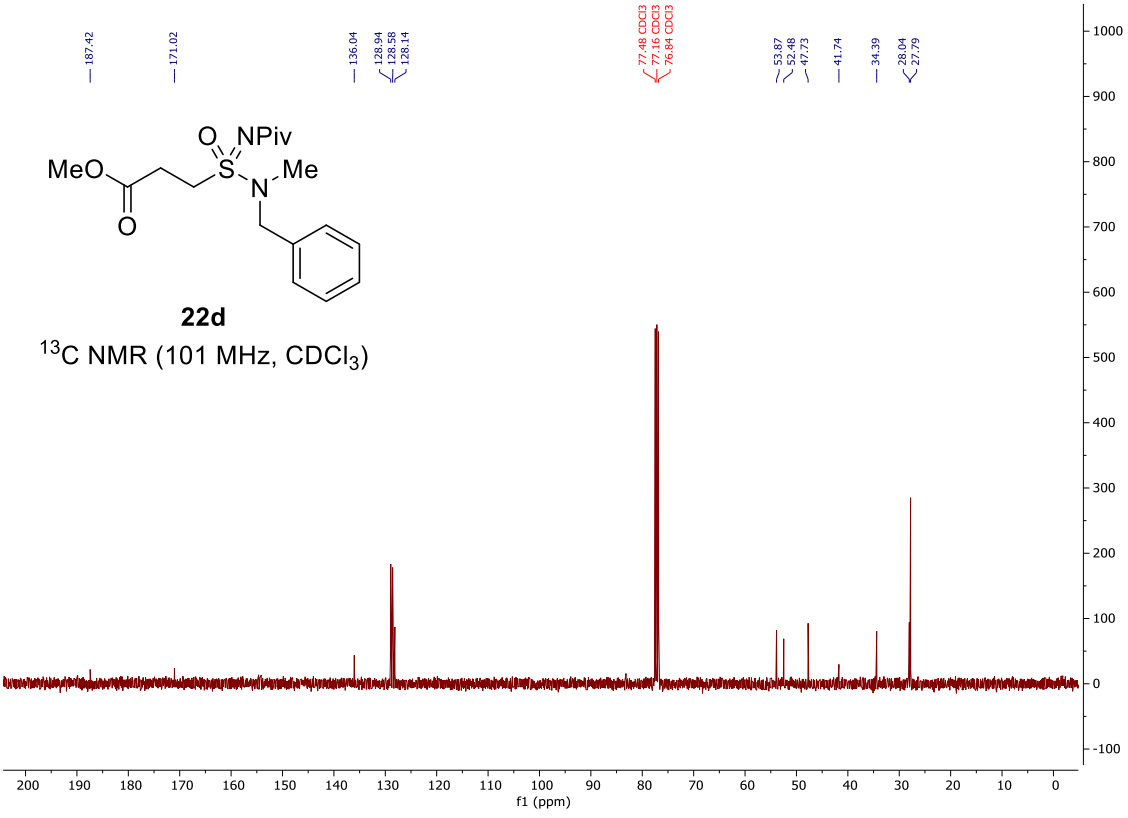


22c

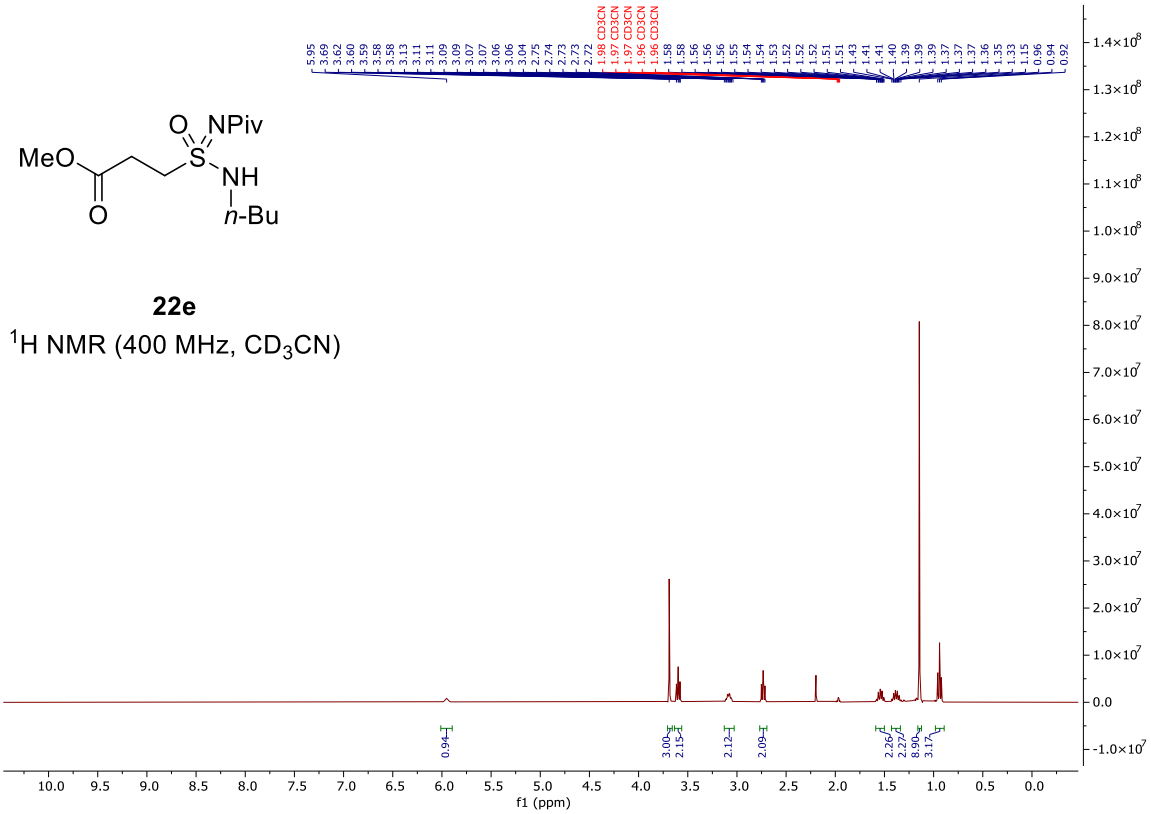
^{13}C NMR (126 MHz, $CDCl_3$)

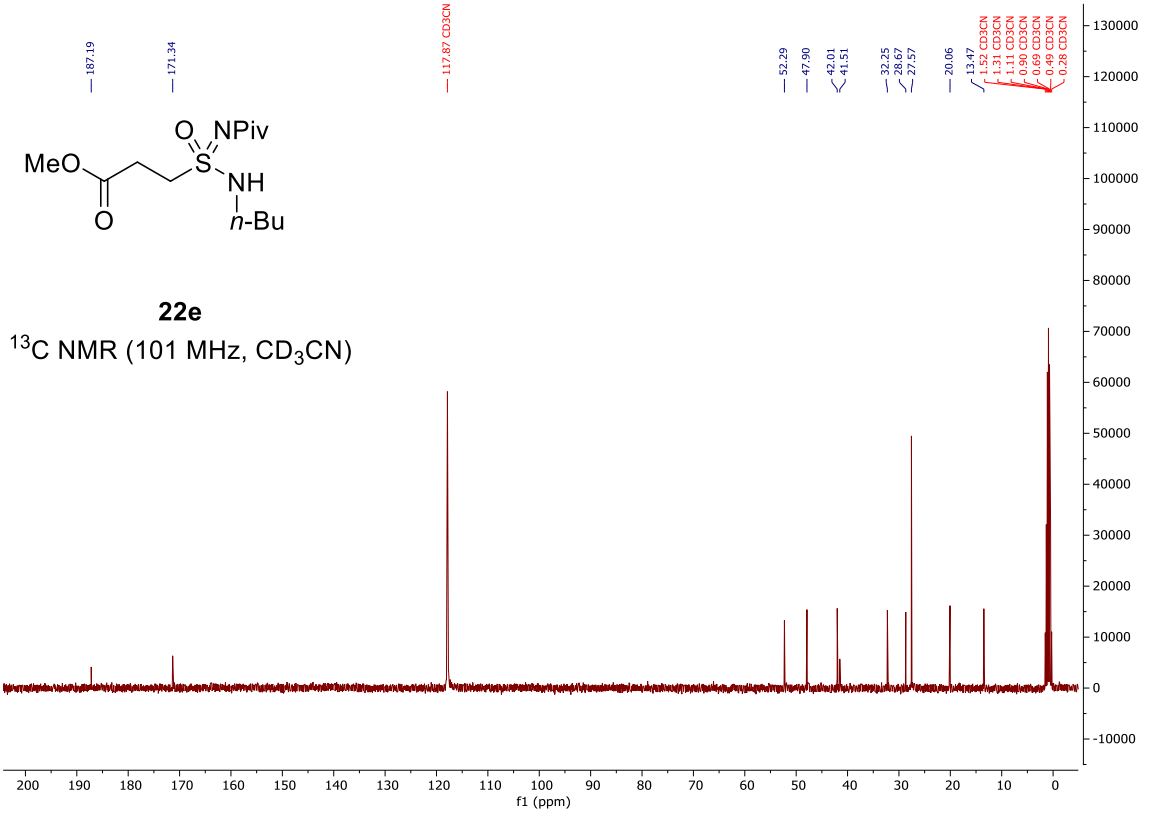
Methyl 3-(*N*-benzyl-*N*-methyl-*N*'-pivaloylsulfamidimidoyl)propanoate (22d)



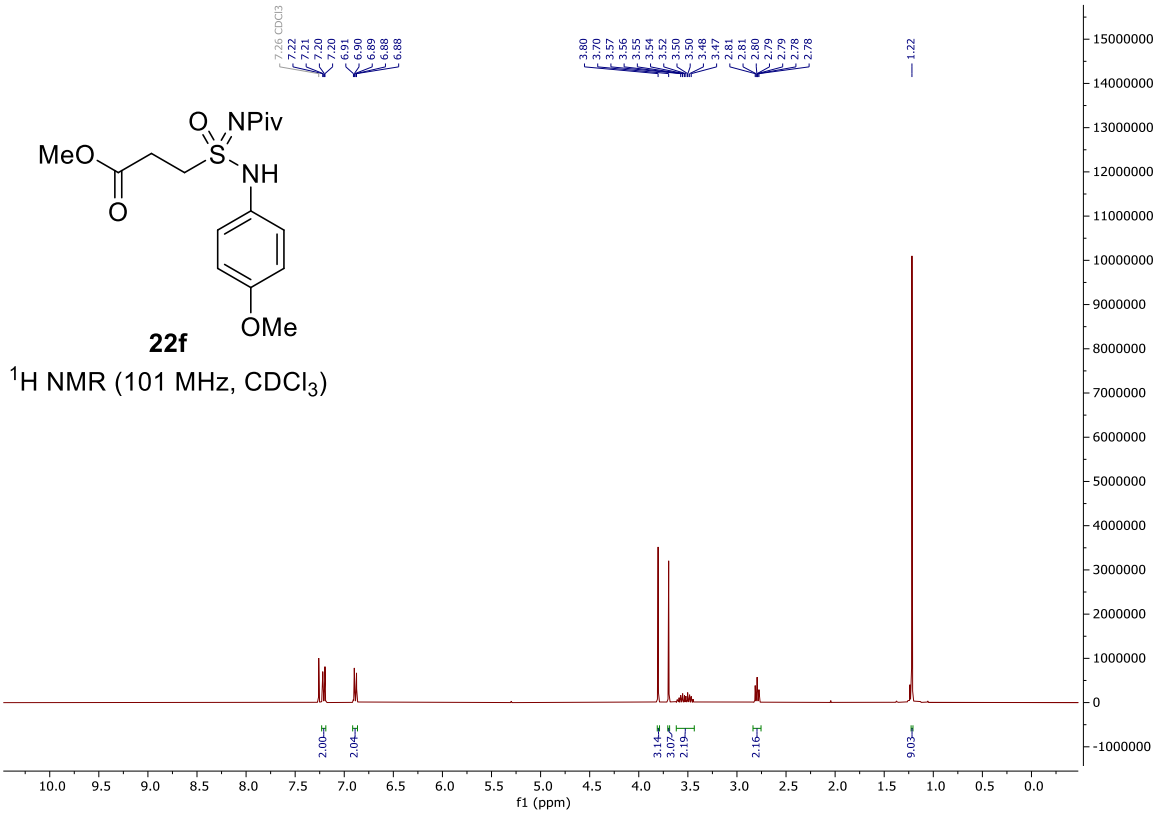


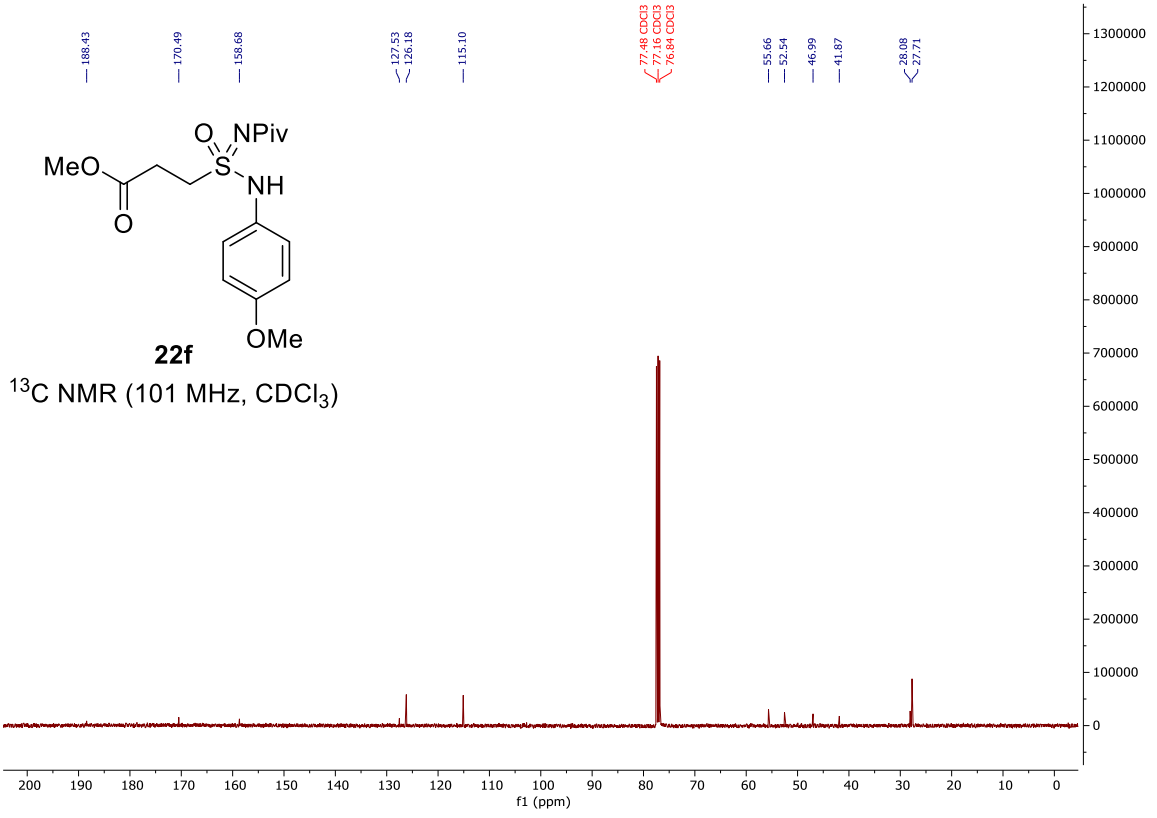
Methyl 3-(*N*-butyl-*N*'-pivaloylsulfamidimidoyl)propanoate (22e)



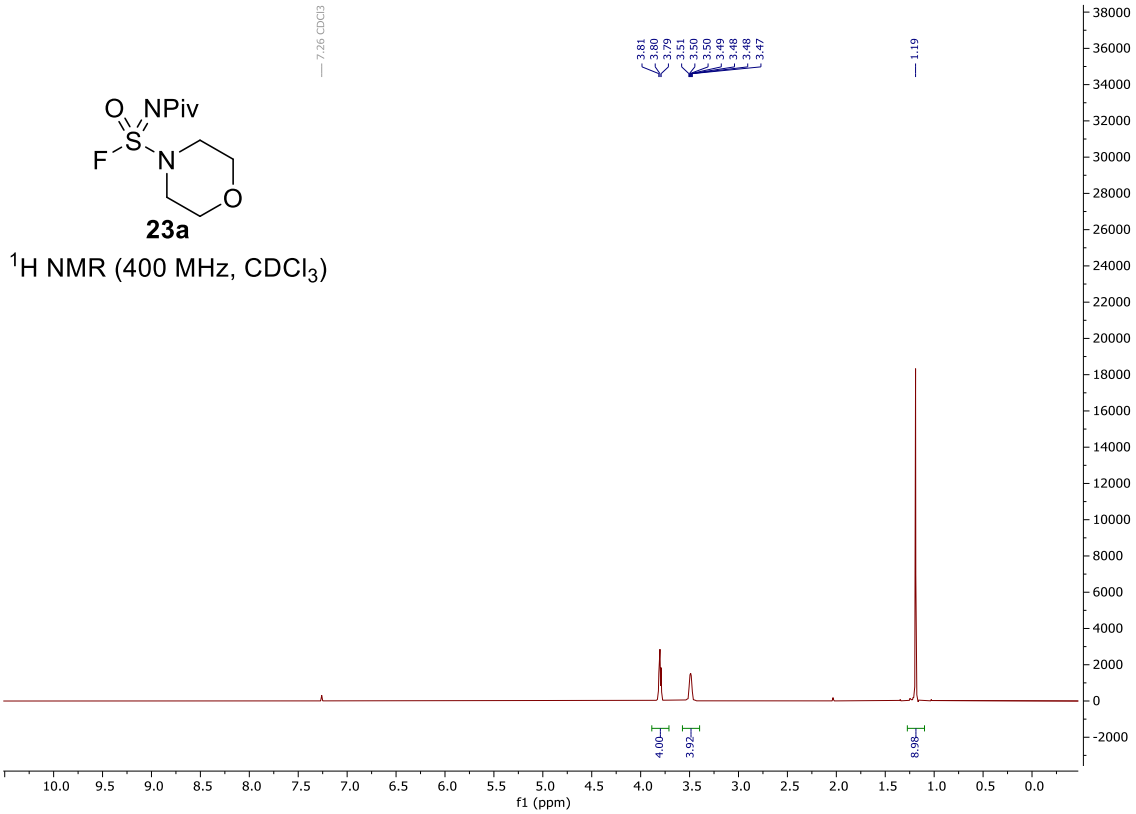


Methyl 3-(*N*-(4-methoxyphenyl)-*N*'-pivaloylsulfamidimidoyl)propanoate (22f)

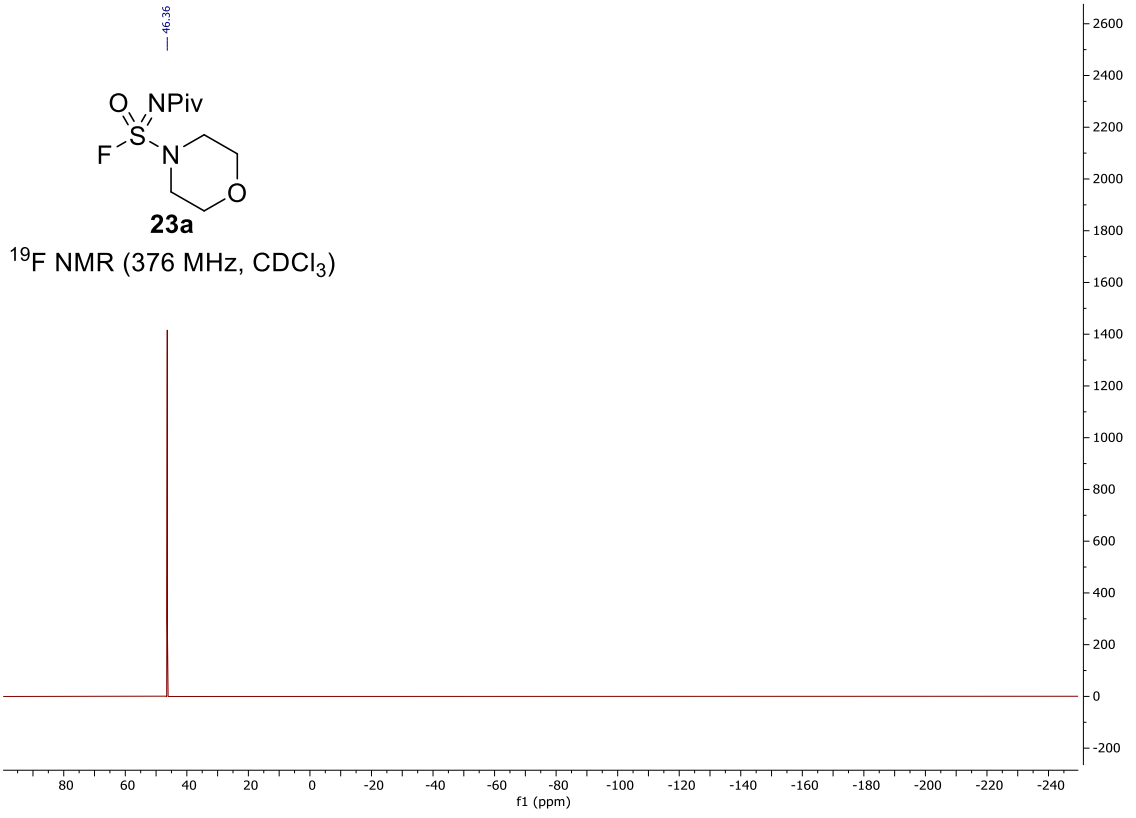




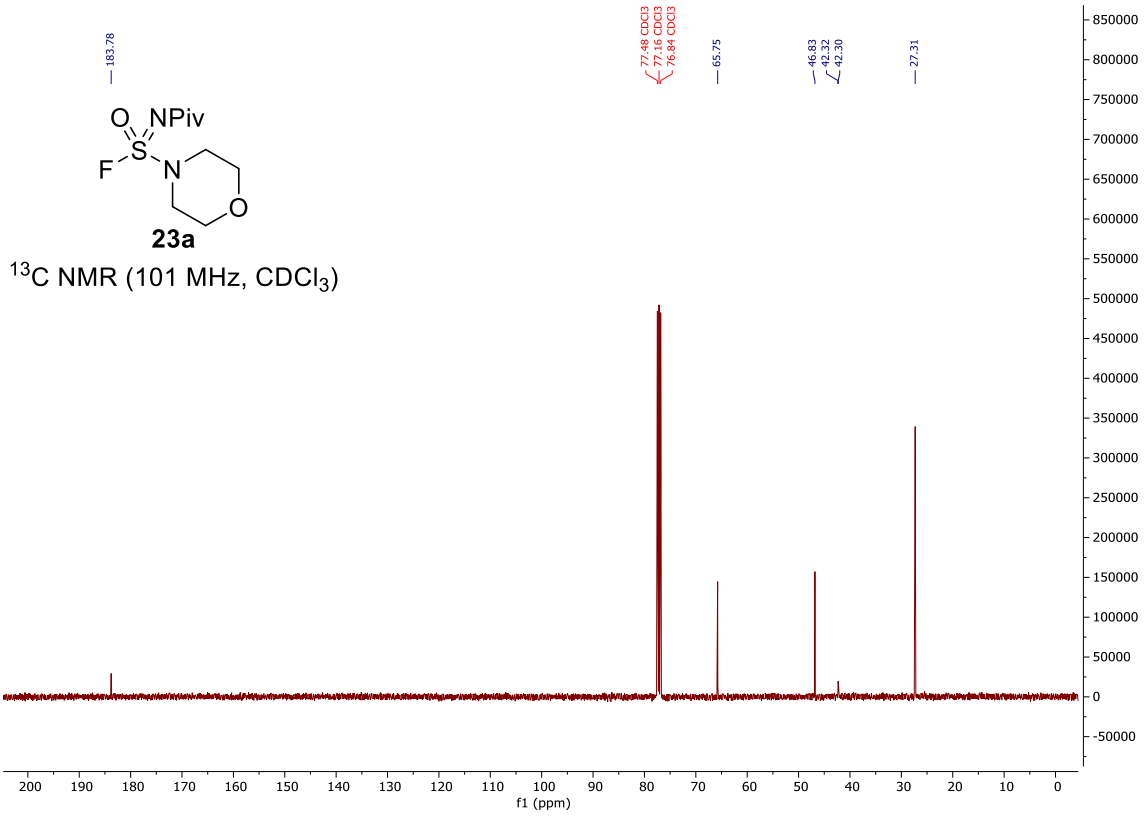
_N_-pivaloylmorpholine-4-sulfonimidoyl fluoride (23a)



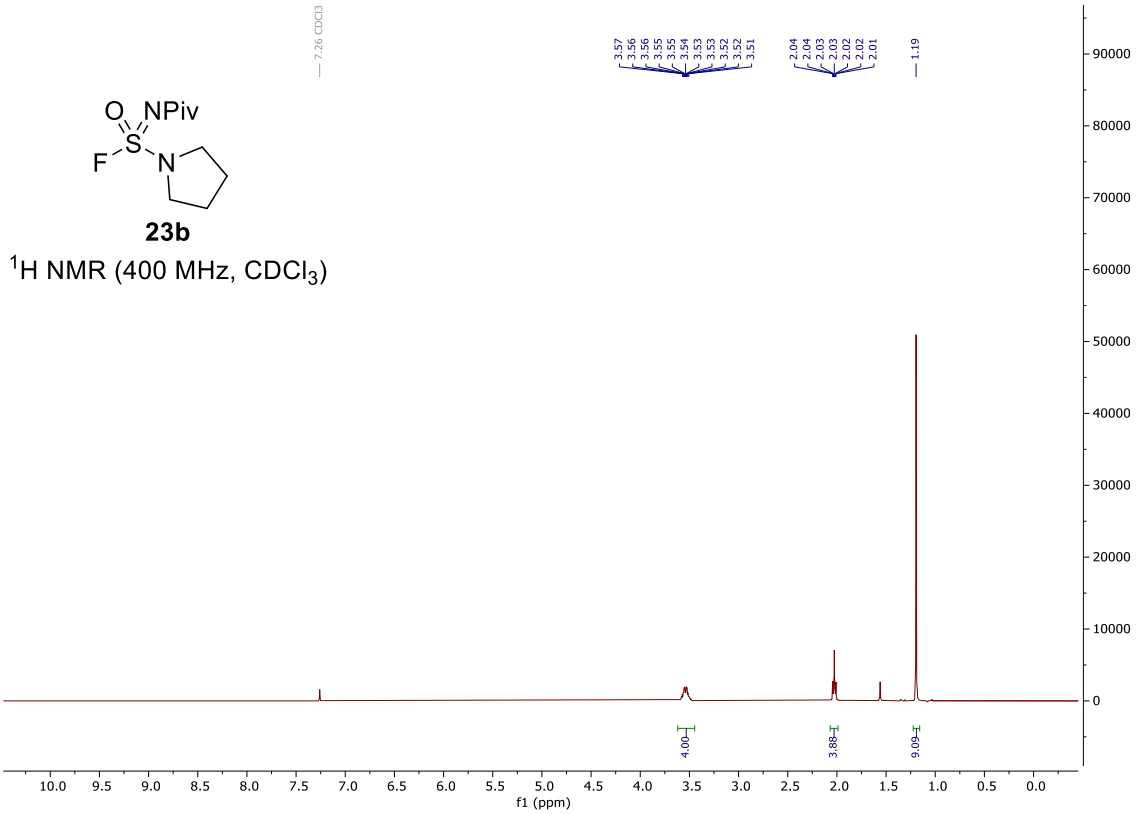
^{1}H NMR (400 MHz, $CDCl_3$)

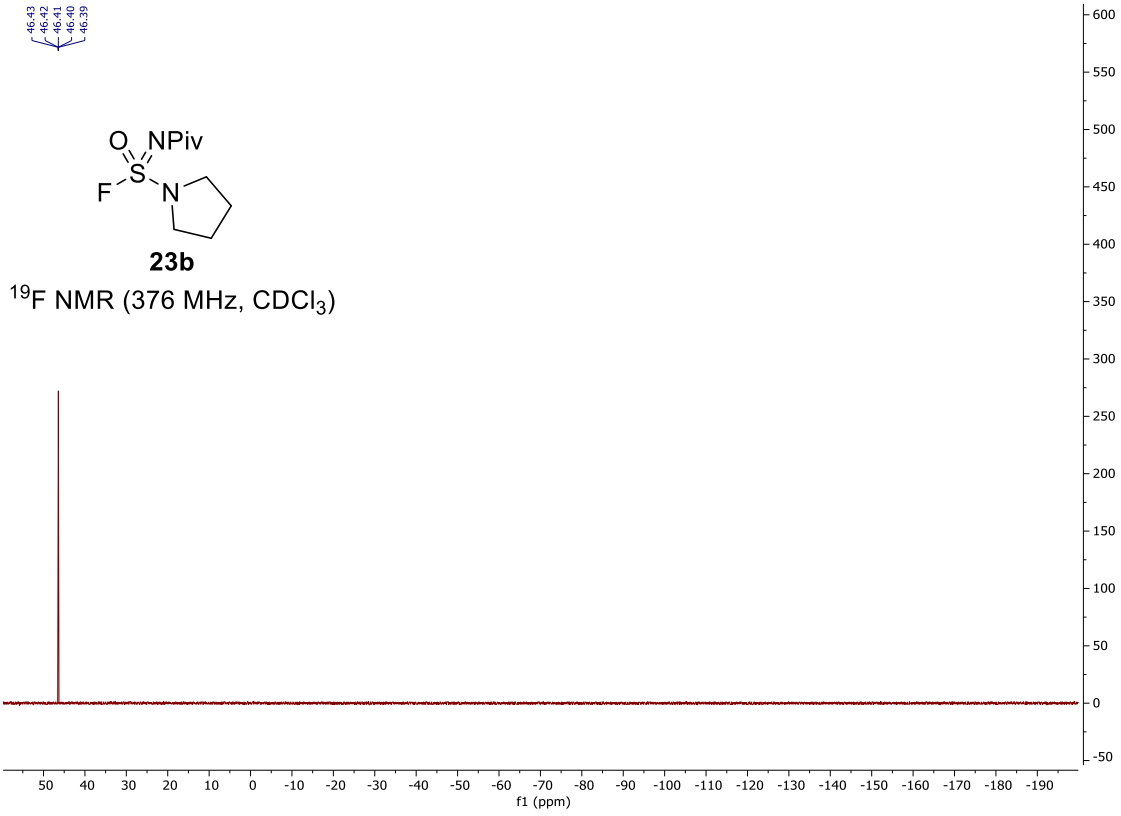


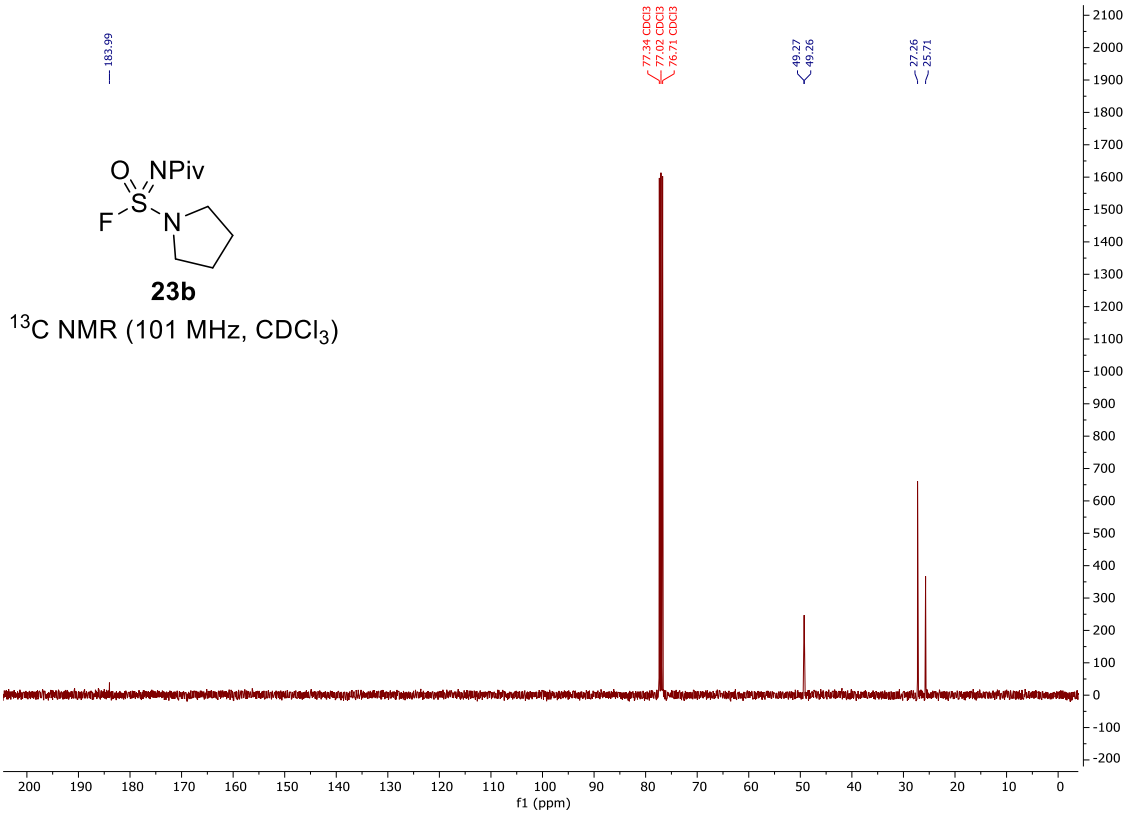
^{19}F NMR (376 MHz, $CDCl_3$)


183.78
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
65.75
46.83
42.32
42.30
27.31
O
NPiv
S
F
N
O
23a
13C NMR (101 MHz, CDCl3)
f1 (ppm)

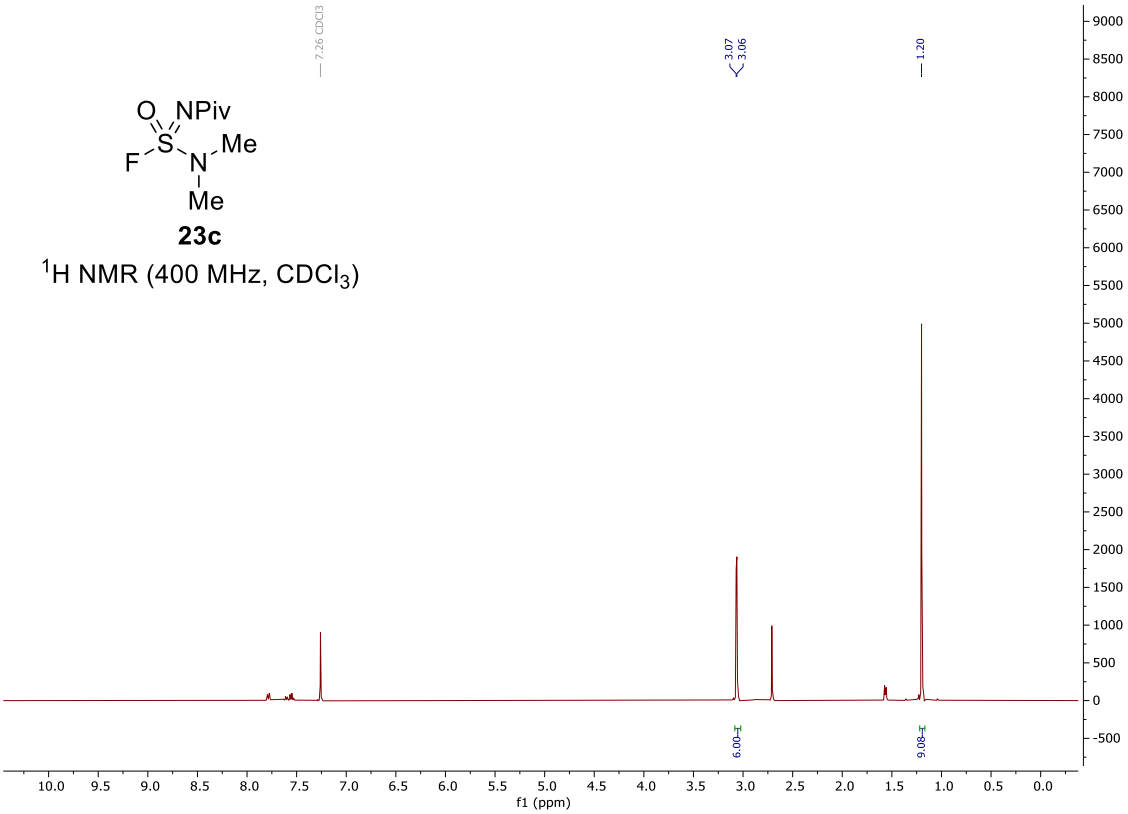
_N_-pivaloylpyrrolidine-1-sulfonimidoyl fluoride (23b)

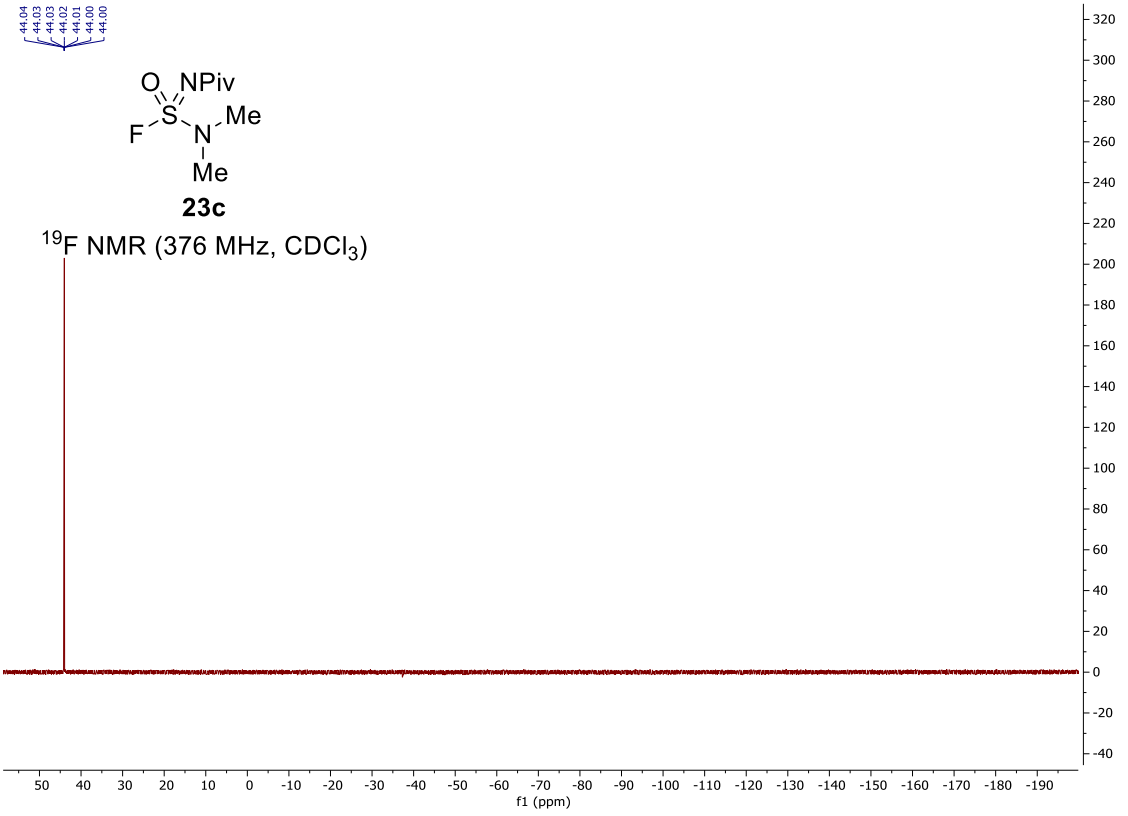


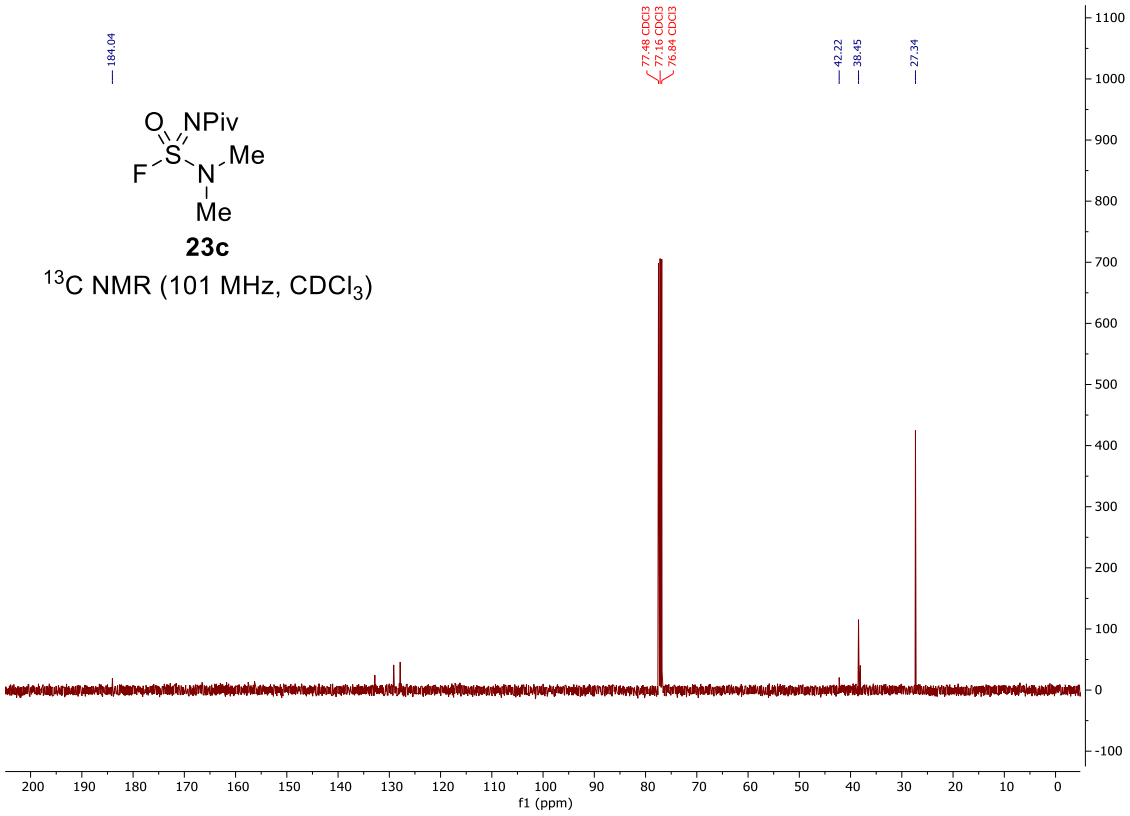



183.99
77.34 CDCl3
77.02 CDCl3
76.71 CDCl3
49.27
49.26
27.26
25.71
O
NPiv
S
F
N
23b
13C NMR (101 MHz, CDCl3)
f1 (ppm)

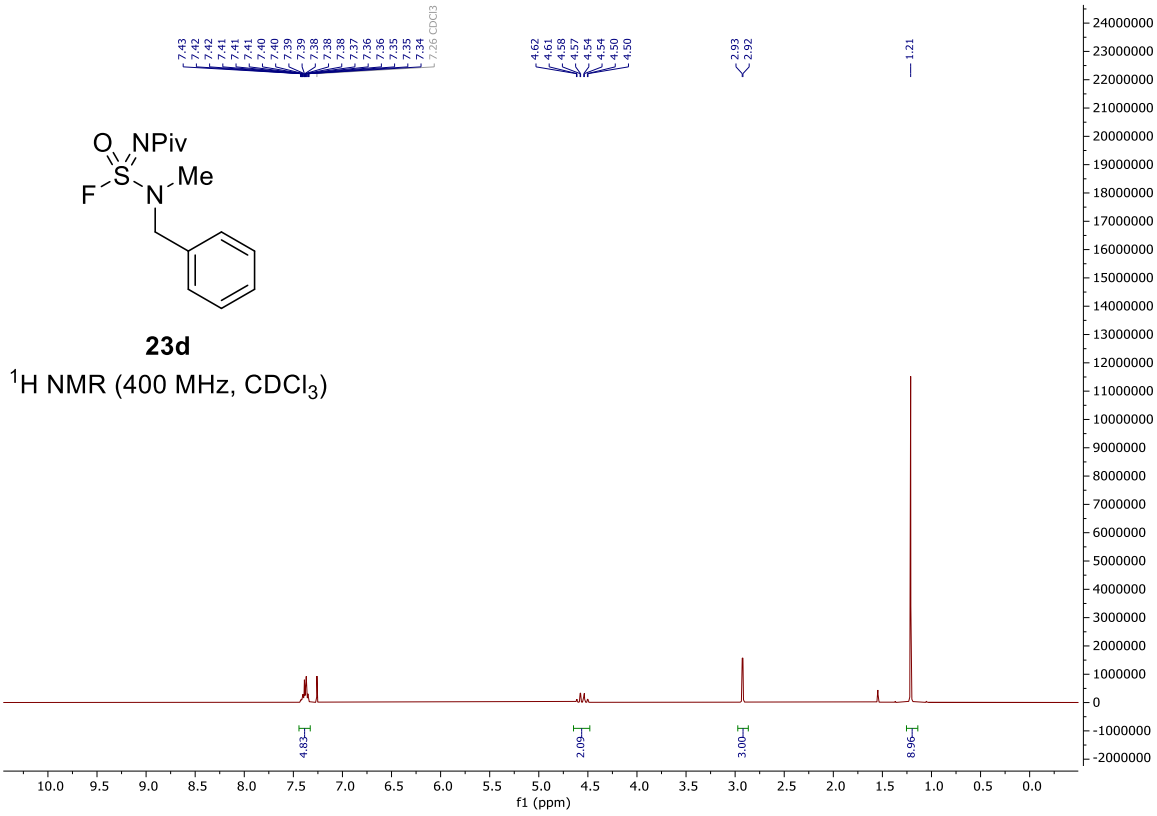
_N,N_-dimethyl-_N'_-pivaloylsulfuramidimidoyl fluoride (23c)





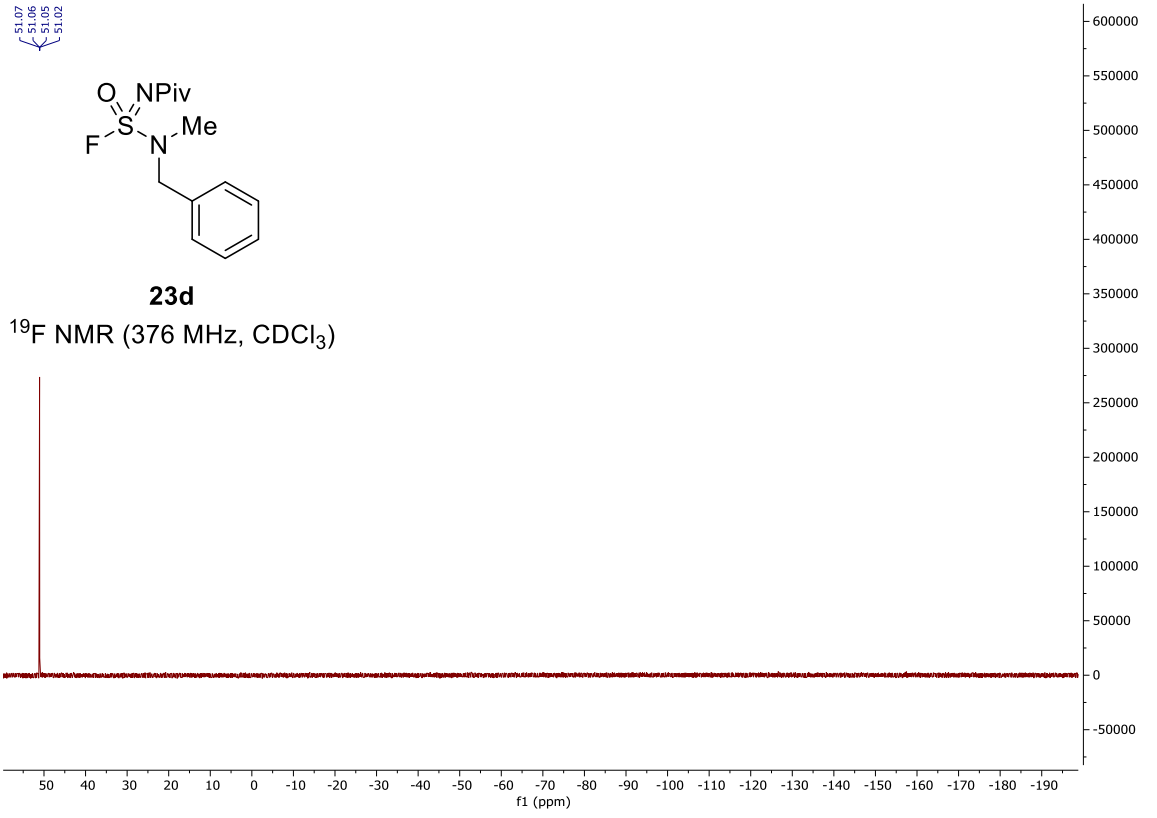

184.04
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
42.22
38.45
27.34
O
NPiv
S
F
N
Me
Me
23c
13C NMR (101 MHz, CDCl3)
f1 (ppm)

N-benzyl-*N*-methyl-*N*'-pivaloylsulfuramidimidoyl fluoride (23d)



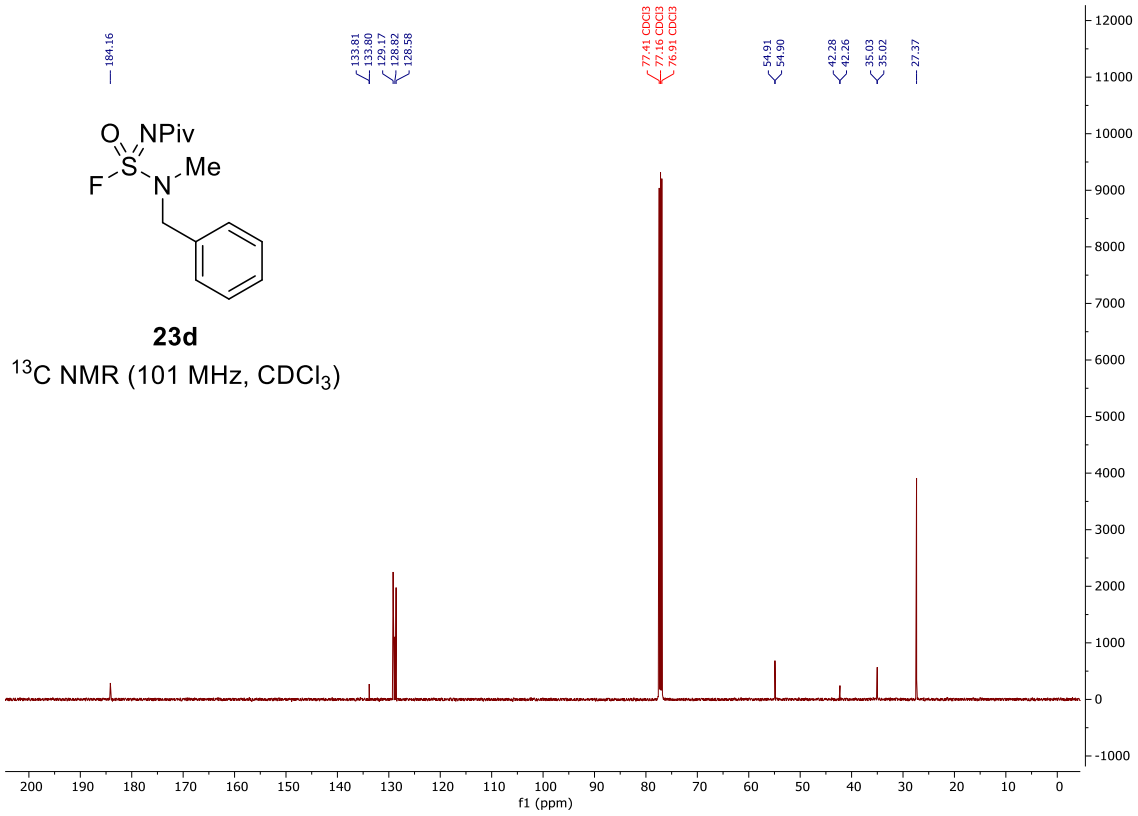
23d

^{1}H NMR (400 MHz, $CDCl_3$)



23d

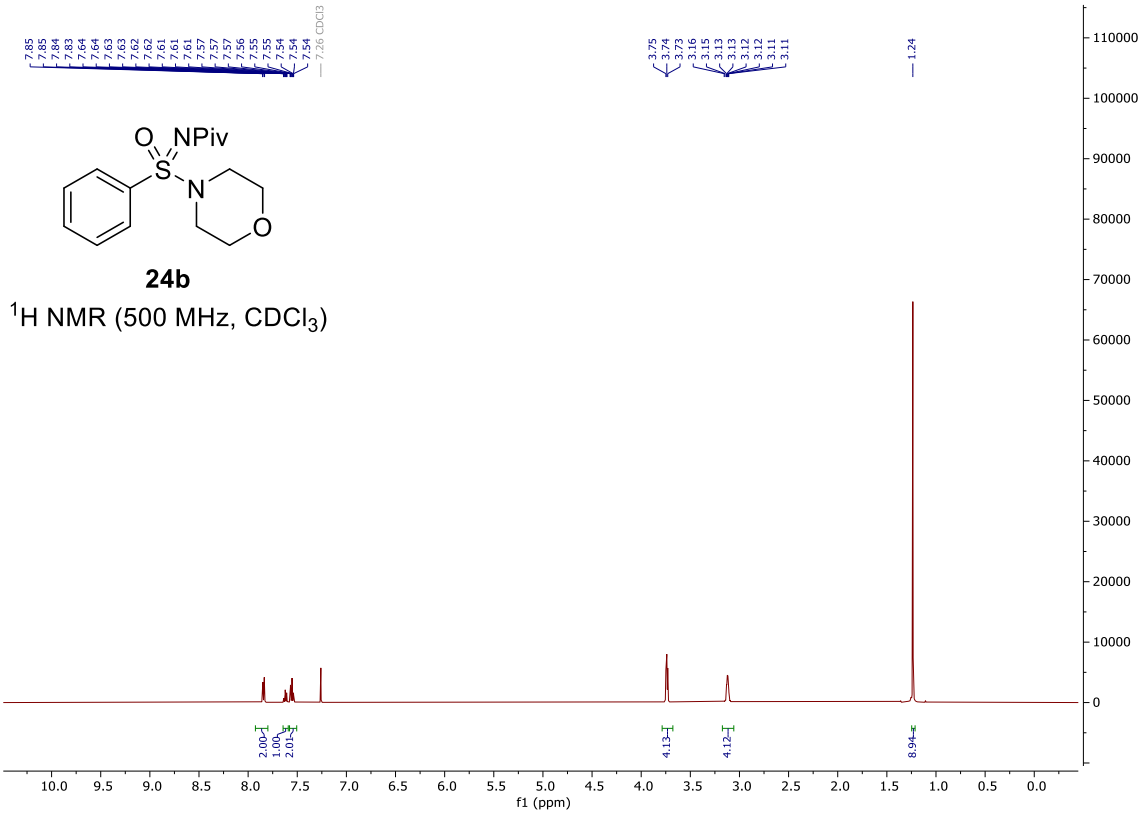
^{19}F NMR (376 MHz, $CDCl_3$)

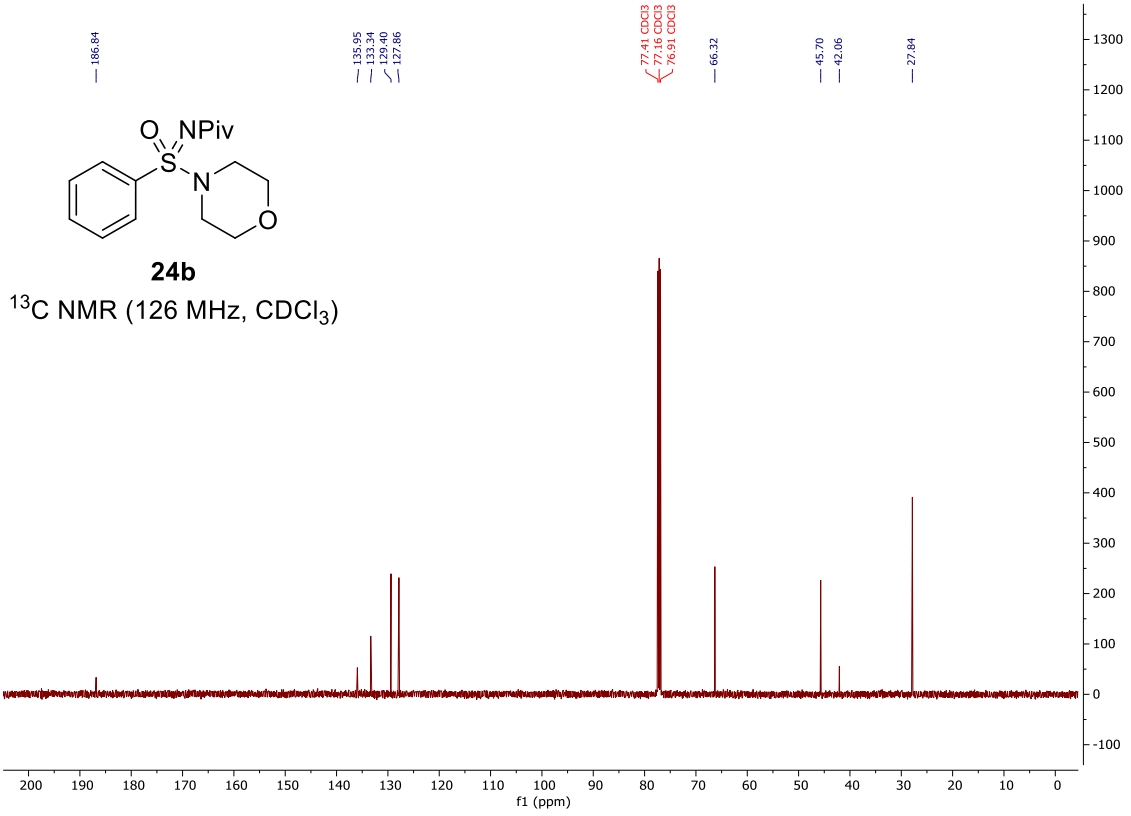


23d

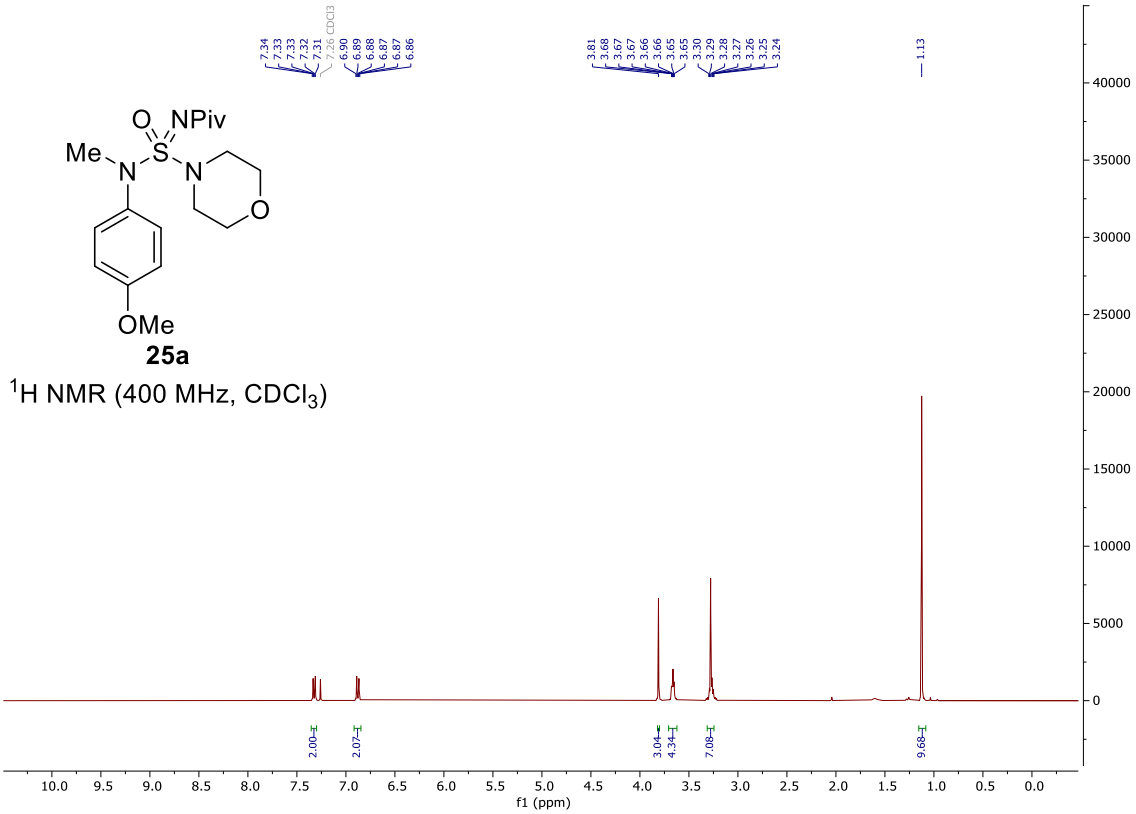
^{13}C NMR (101 MHz, $CDCl_3$)

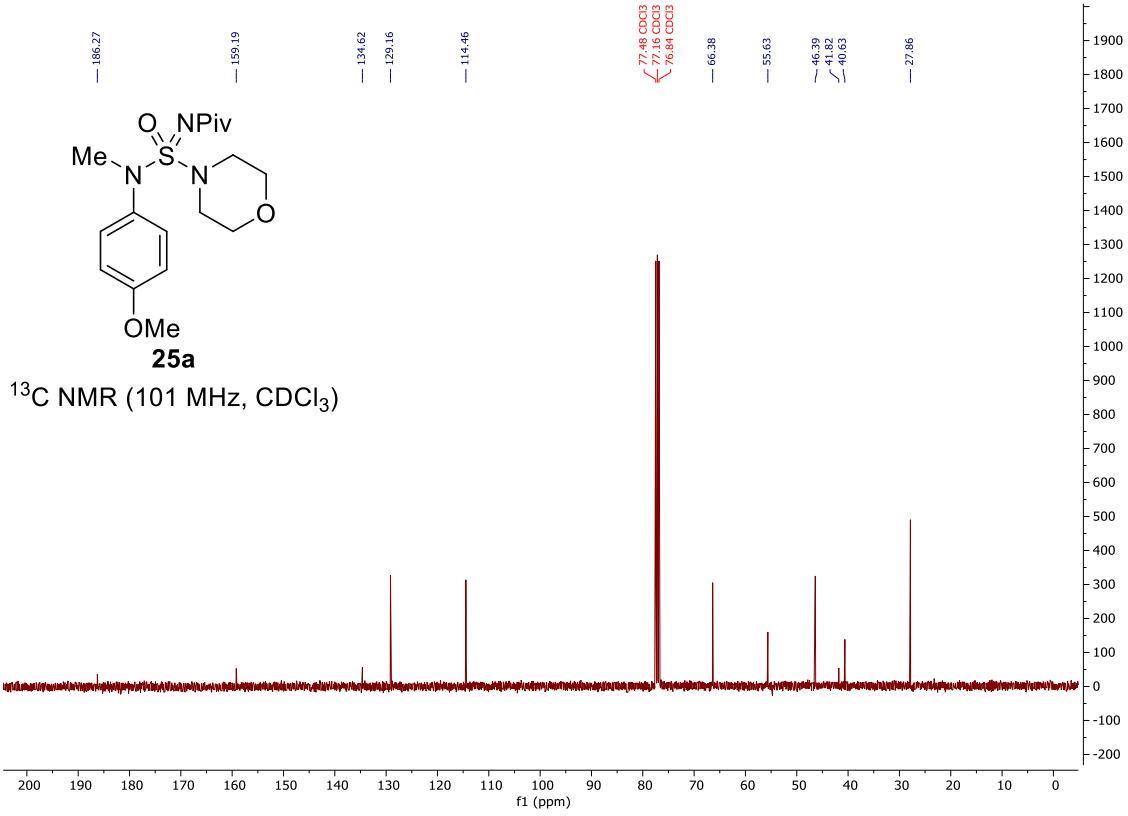
_N_-(morpholino(oxo)(phenyl)-λ6-sulfaneylidene)pivalamide (24b)



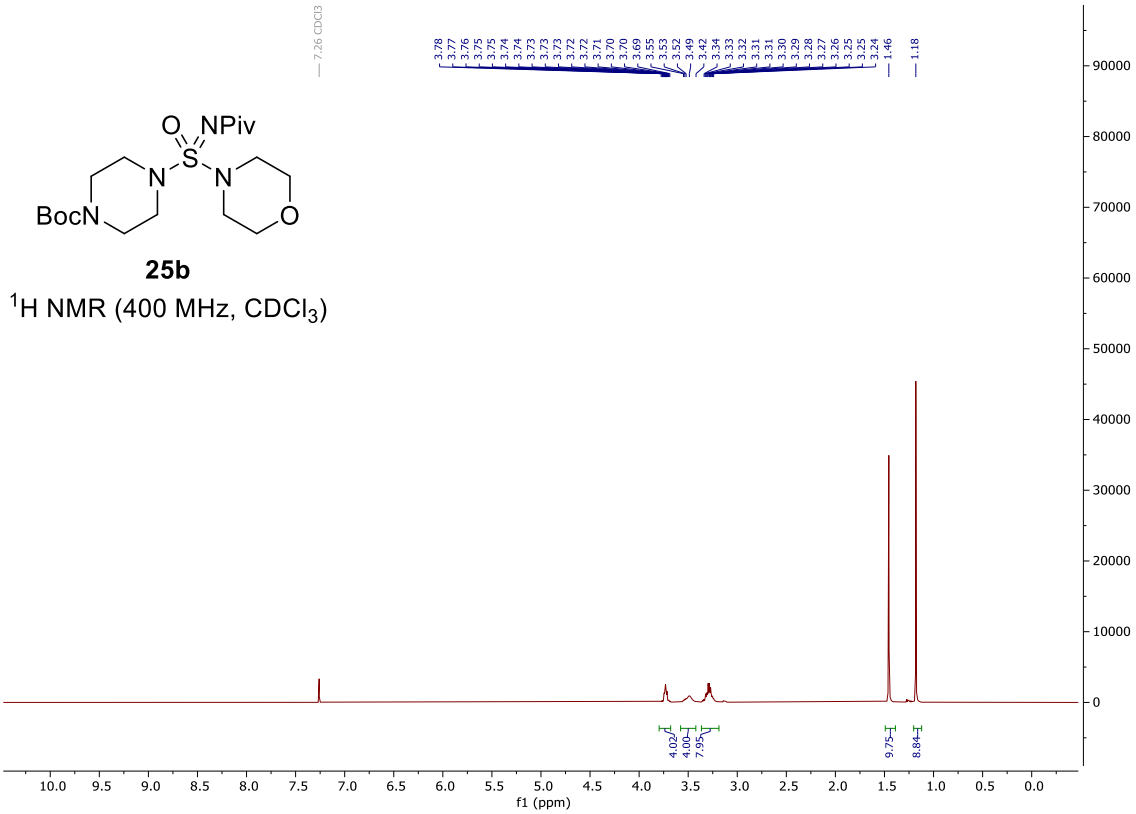


_N_-(((4-methoxyphenyl)(methyl)amino)(morpholino)(oxo)-λ6-sulfaneylidene)pivalamide (25a)



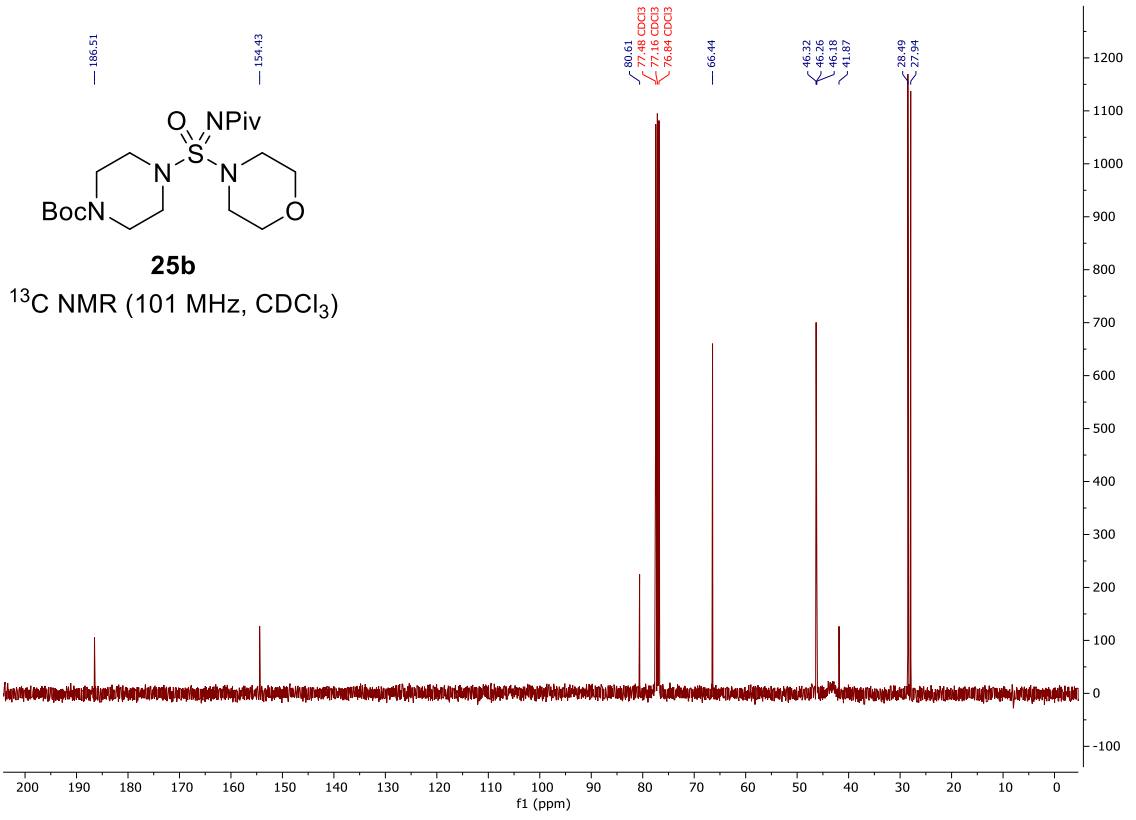


tert-Butyl 4-(_N_-pivaloylmorpholine-4-sulfonimidoyl)piperazine-1-carboxylate (25b)



25b

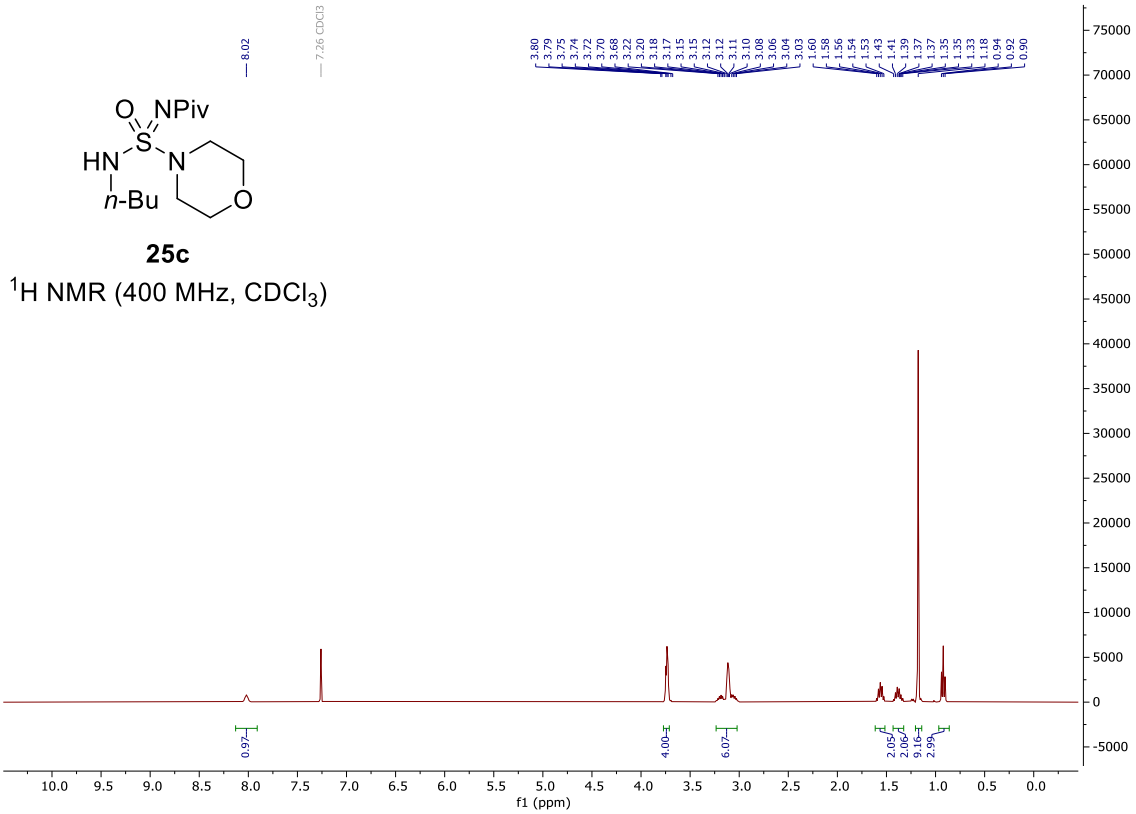
^{1}H NMR (400 MHz, $CDCl_3$)

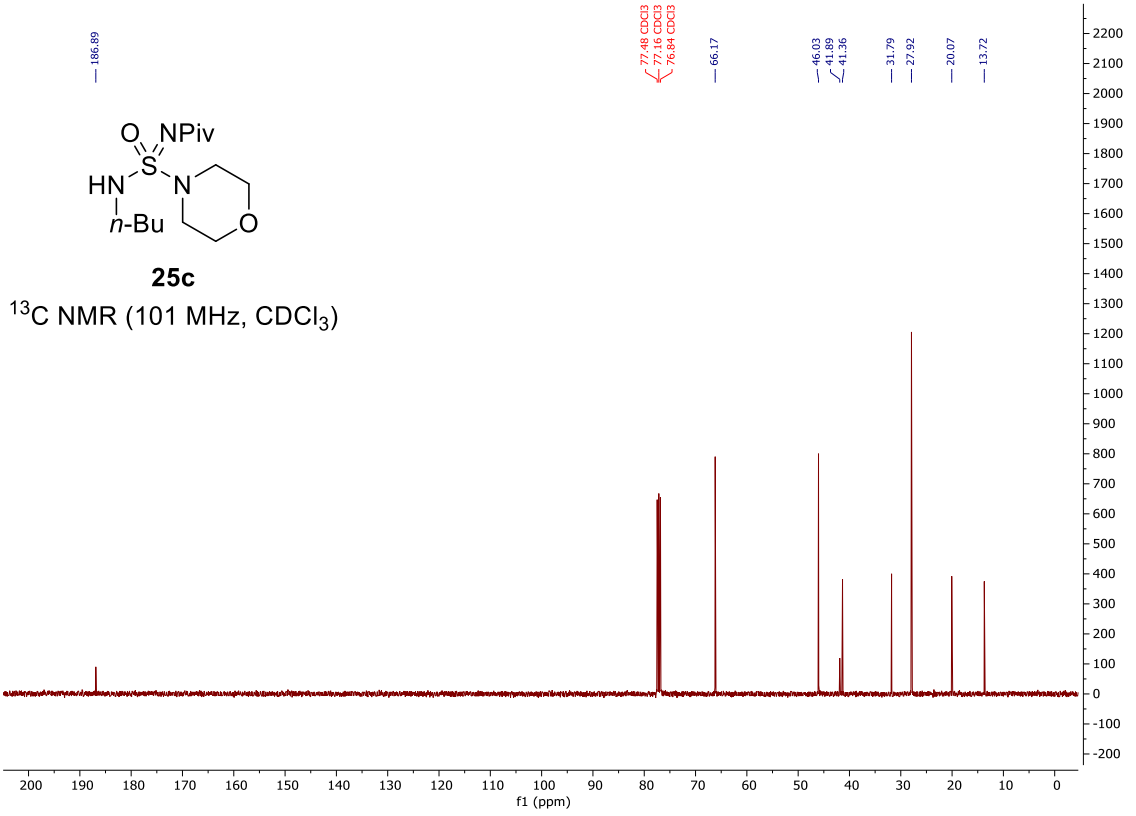


25b

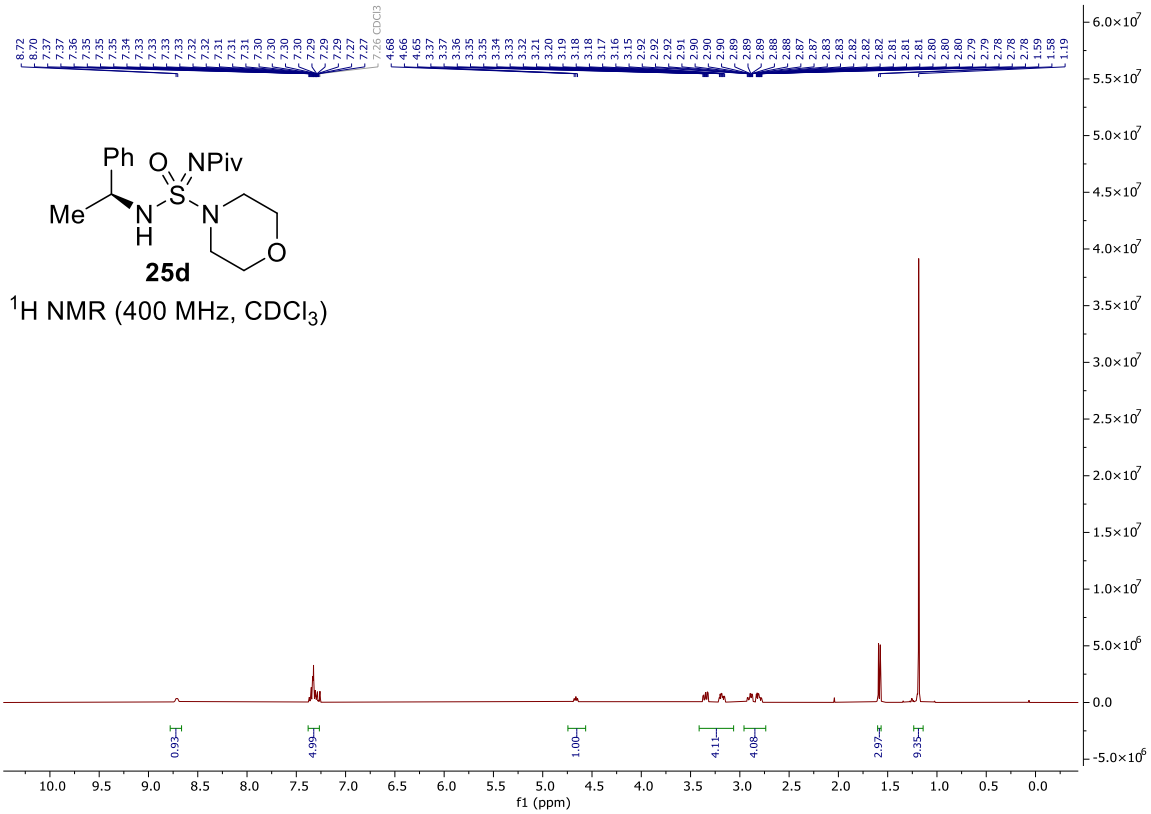
^{13}C NMR (101 MHz, $CDCl_3$)

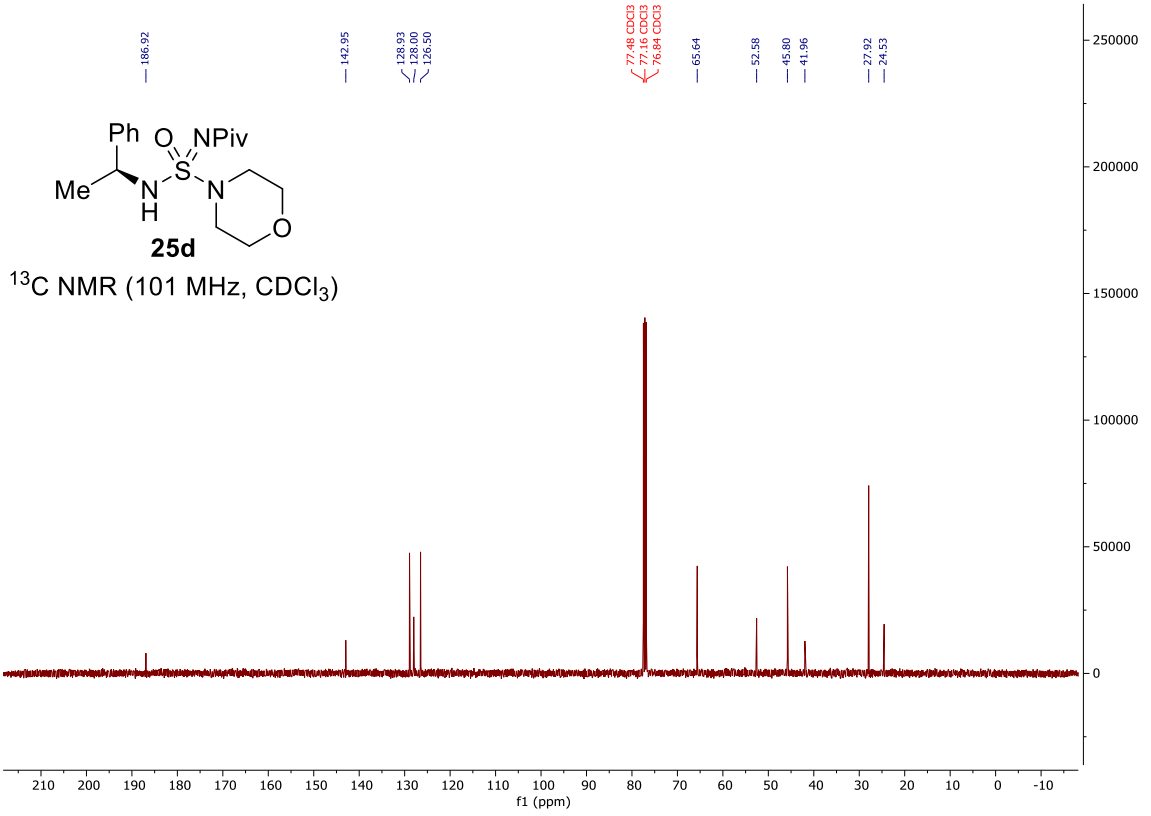
_N_-((butylamino)(morpholino)(oxo)-λ6-sulfaneylidene)pivalamide (25c)



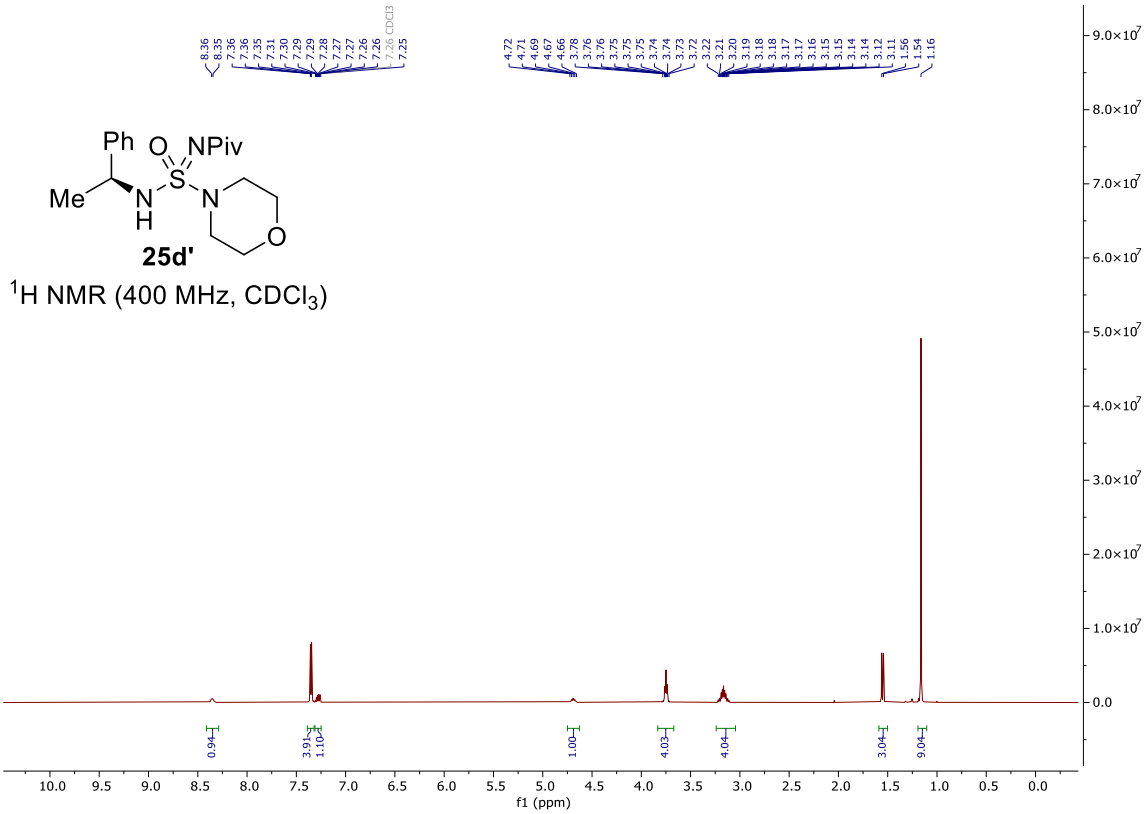


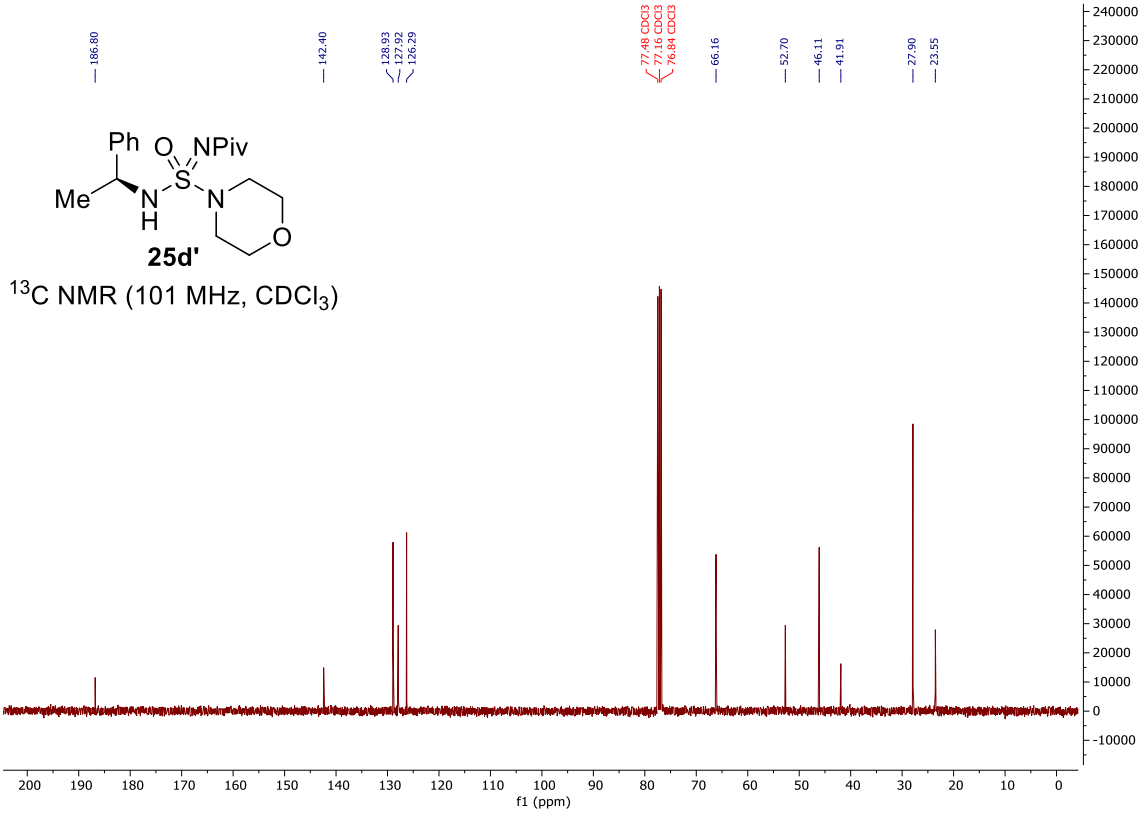
_N_-(morpholino(oxo)(((S)-1-phenylethyl)amino)-λ6-sulfaneylidene)pivalamide (25d)



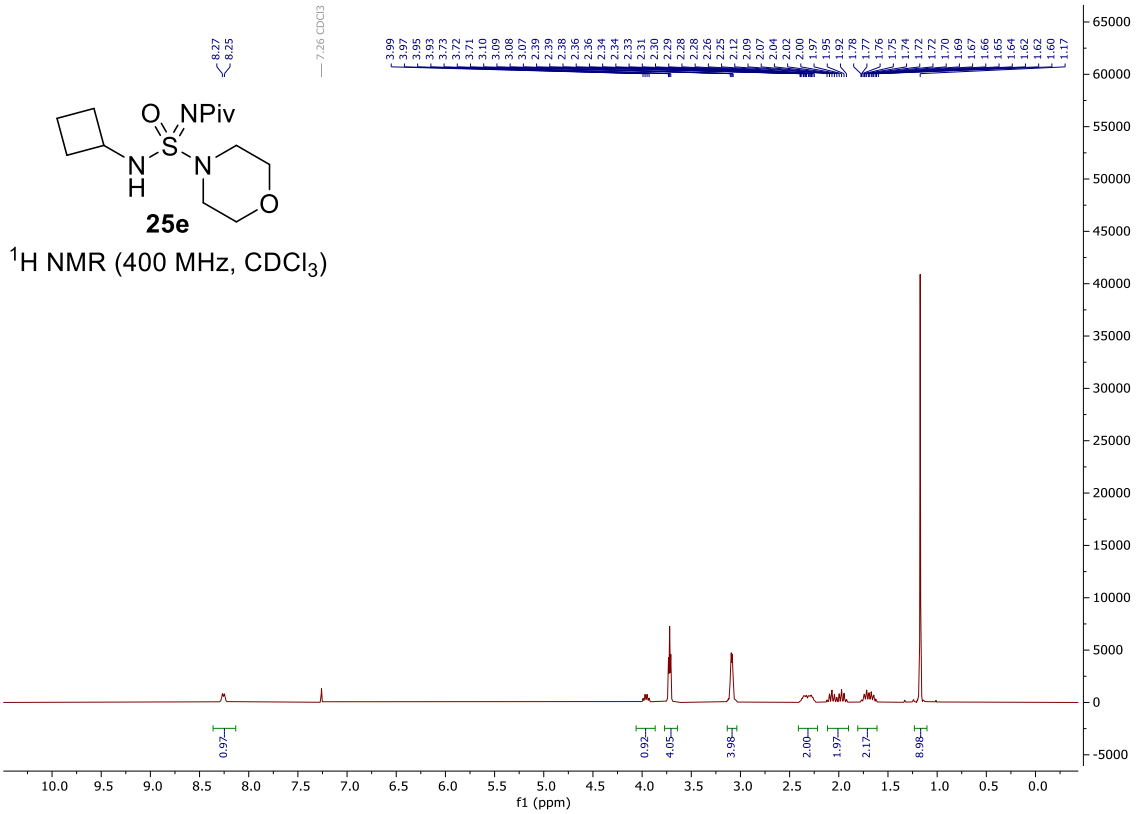


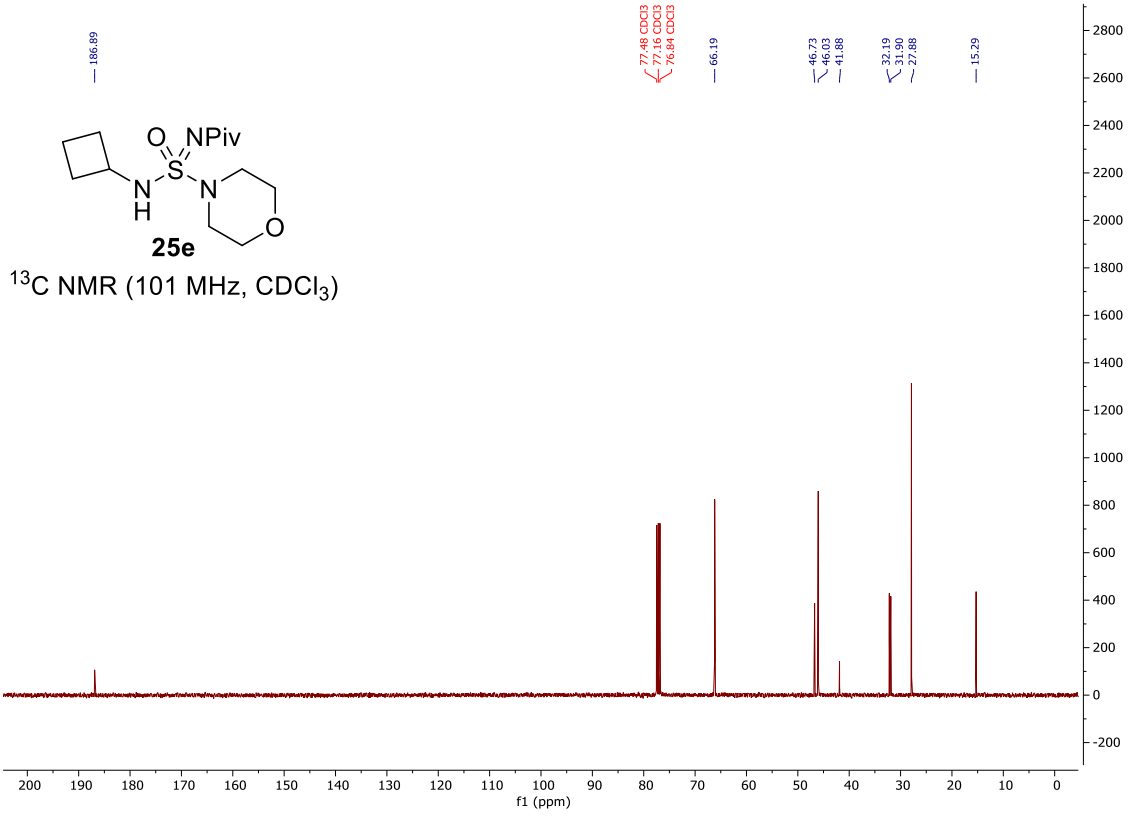
_N_-(morpholino(oxo)(((S)-1-phenylethyl)amino)-λ6-sulfaneylidene)pivalamide (25d')



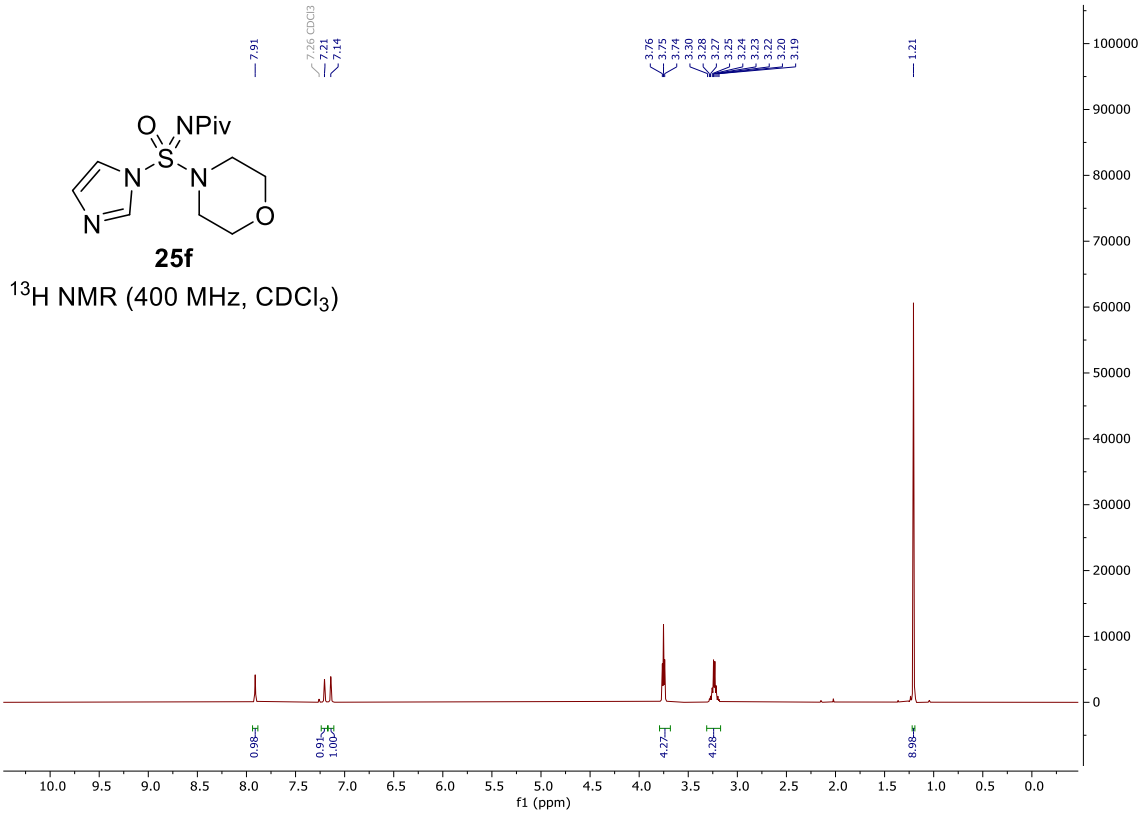


_N_-((cyclobutylamino)(morpholino)(oxo)-λ6-sulfaneylidene)pivalamide (25e)



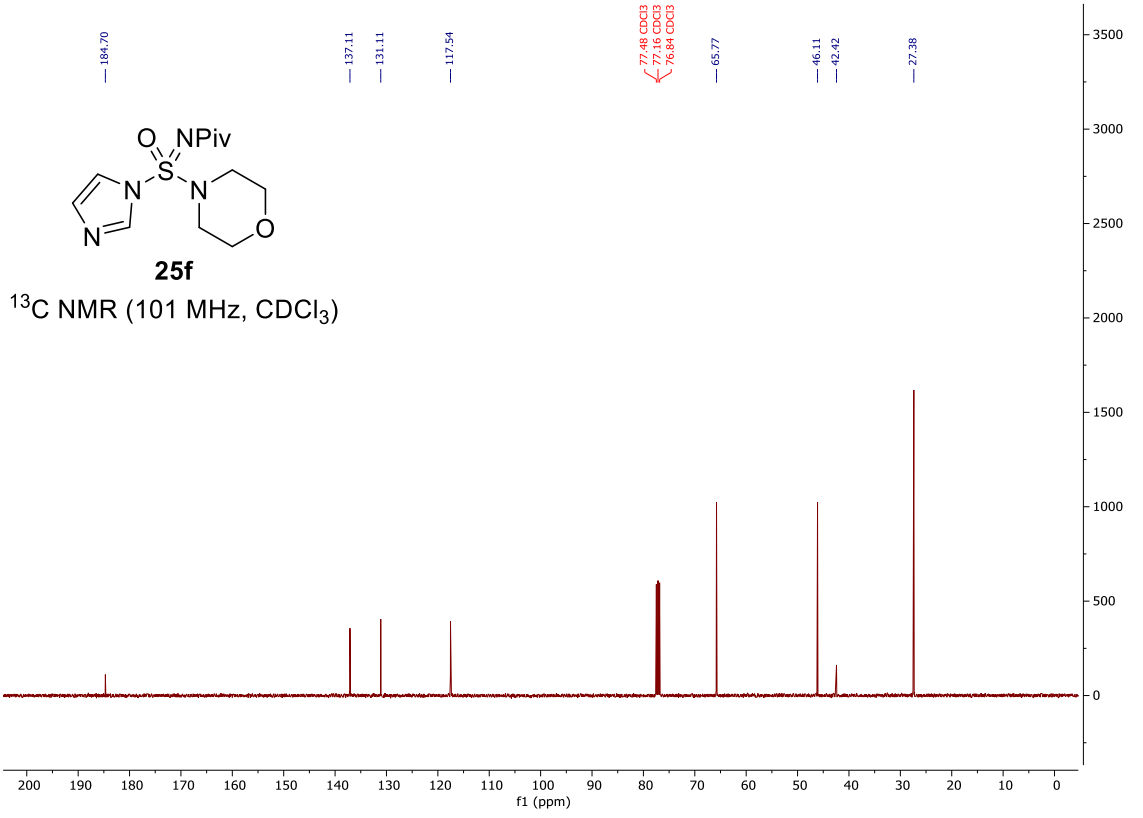


_N_-((1_H_-imidazol-1-yl)(morpholino)(oxo)-λ6-sulfaneylidene)pivalamide (25f)



25f

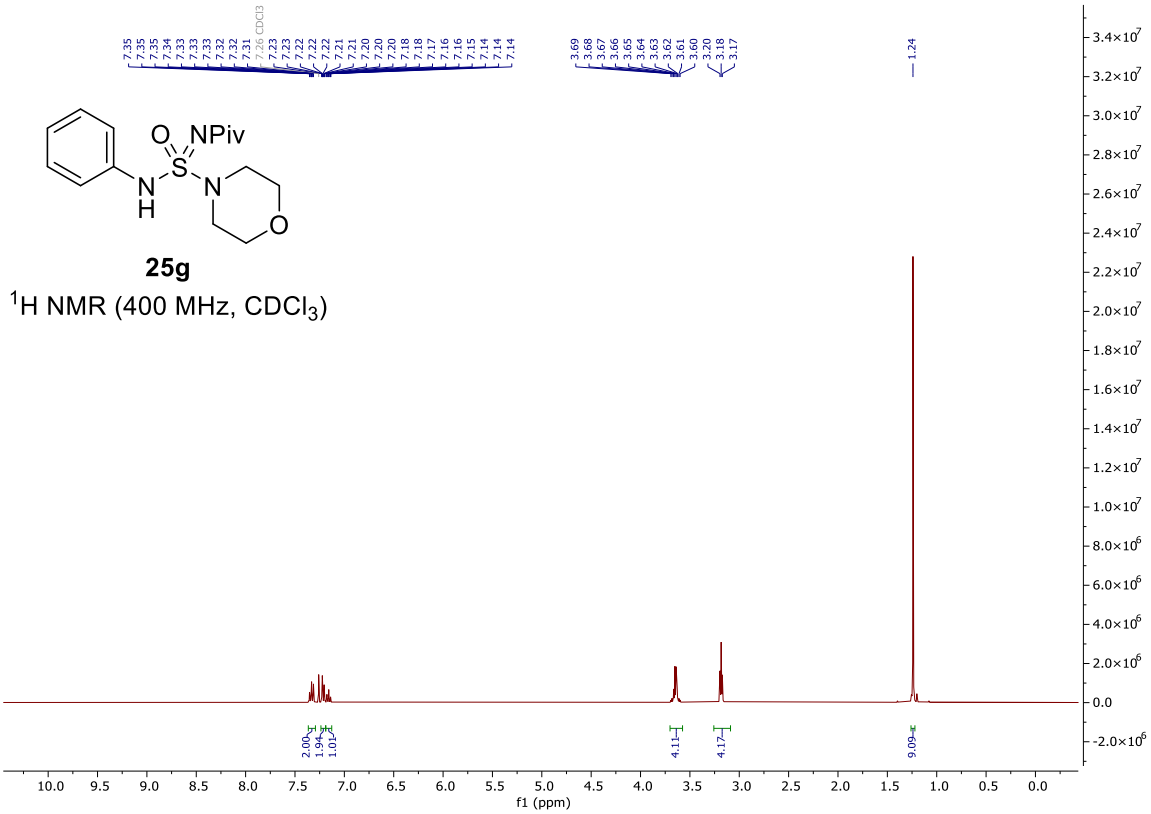
^{13}H NMR (400 MHz, $CDCl_3$)

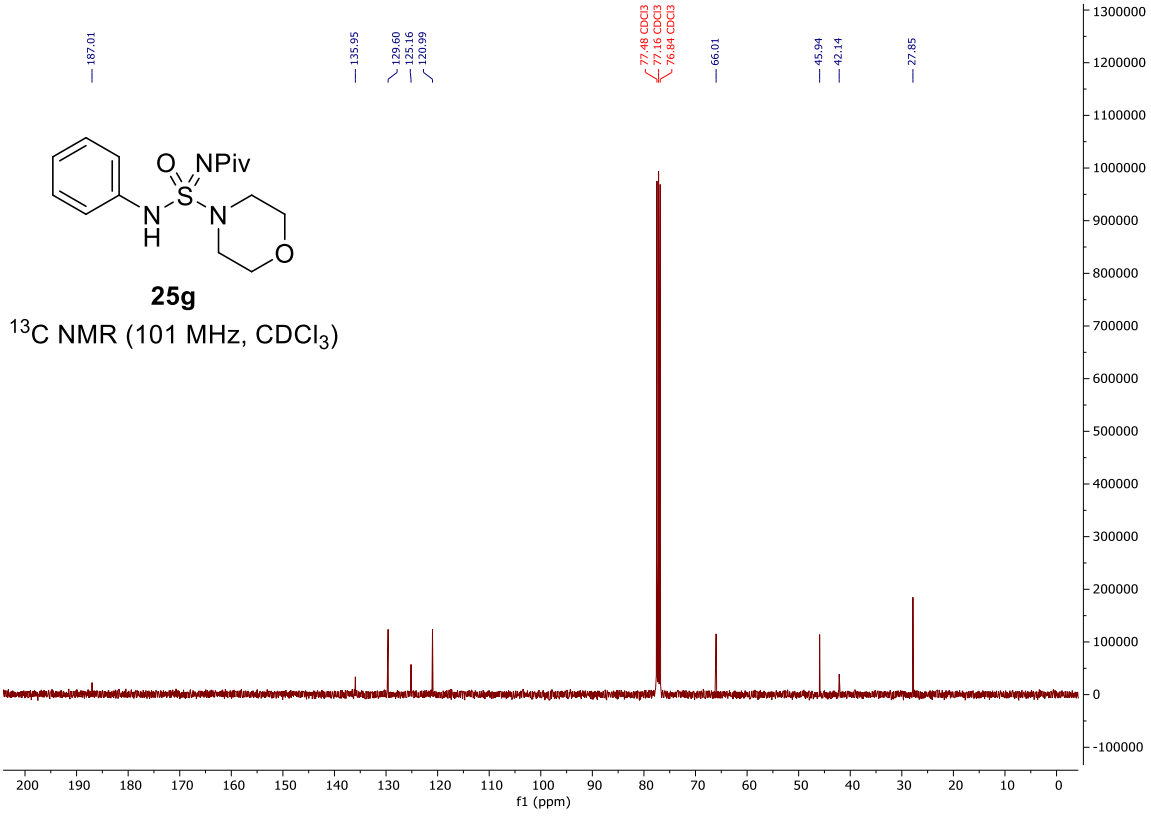


25f

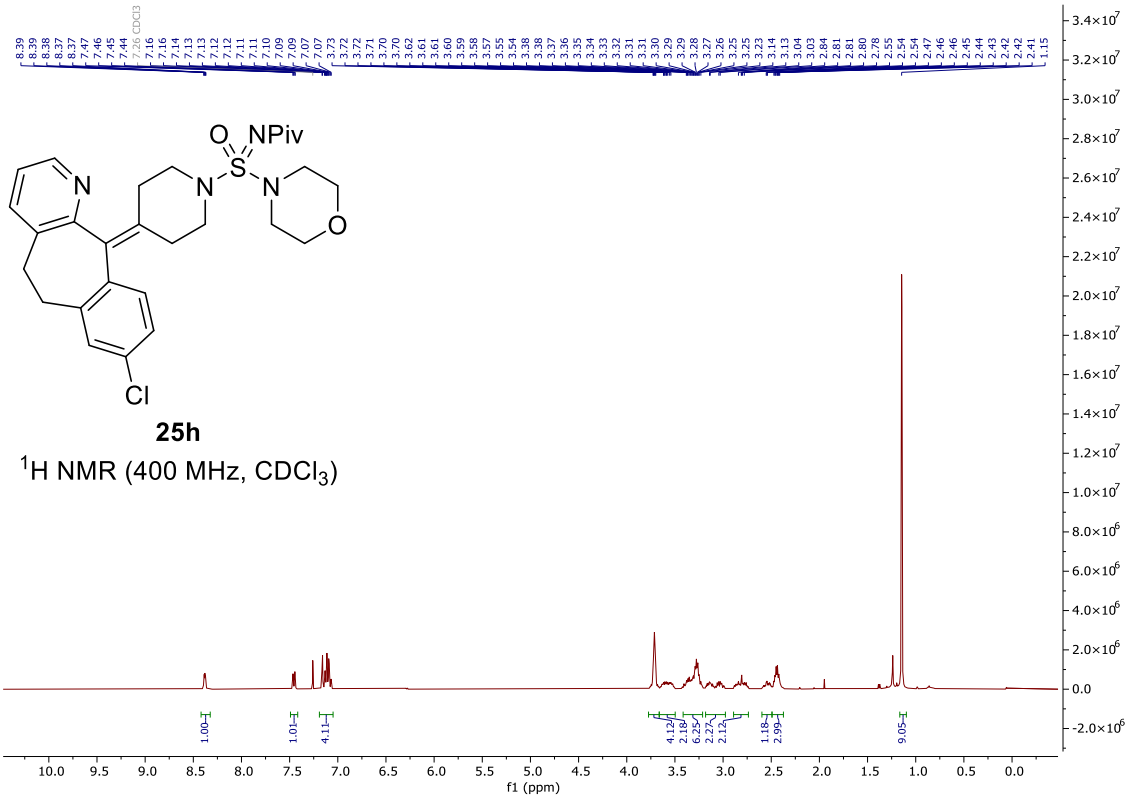
^{13}C NMR (101 MHz, $CDCl_3$)

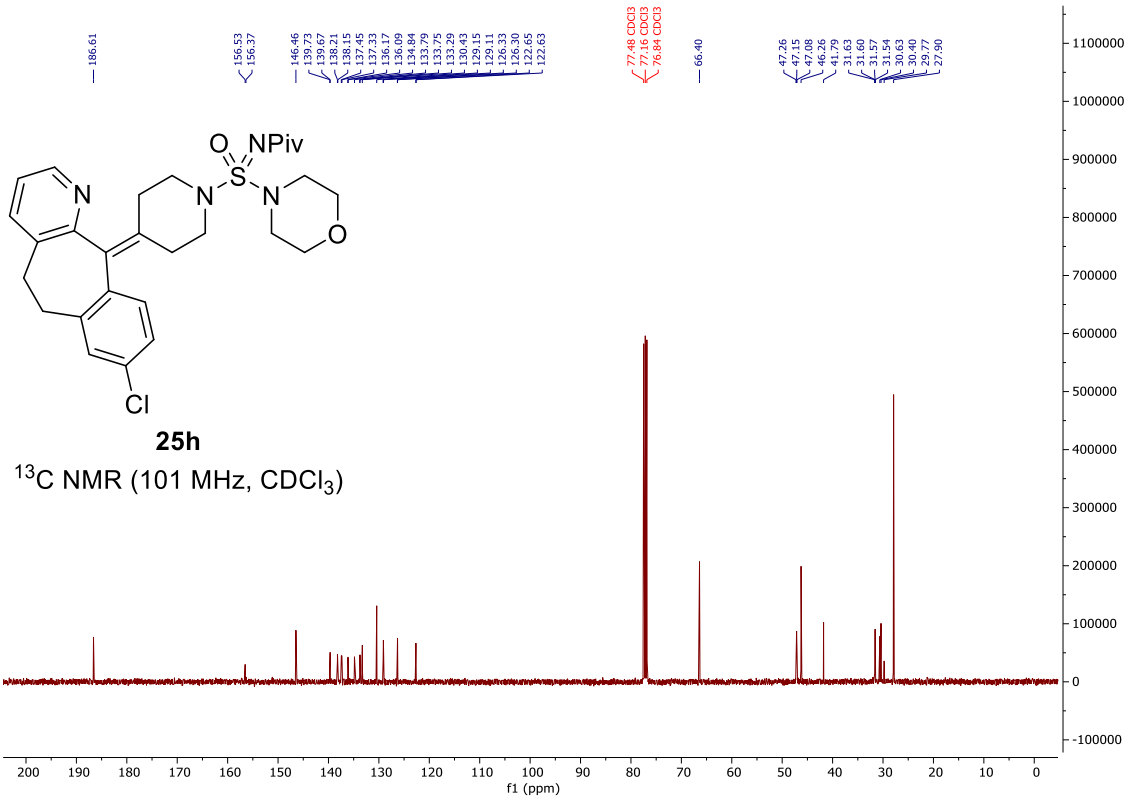
_N_-(morpholino(oxo)(phenylamino)-λ6-sulfaneylidene)pivalamide (25g)



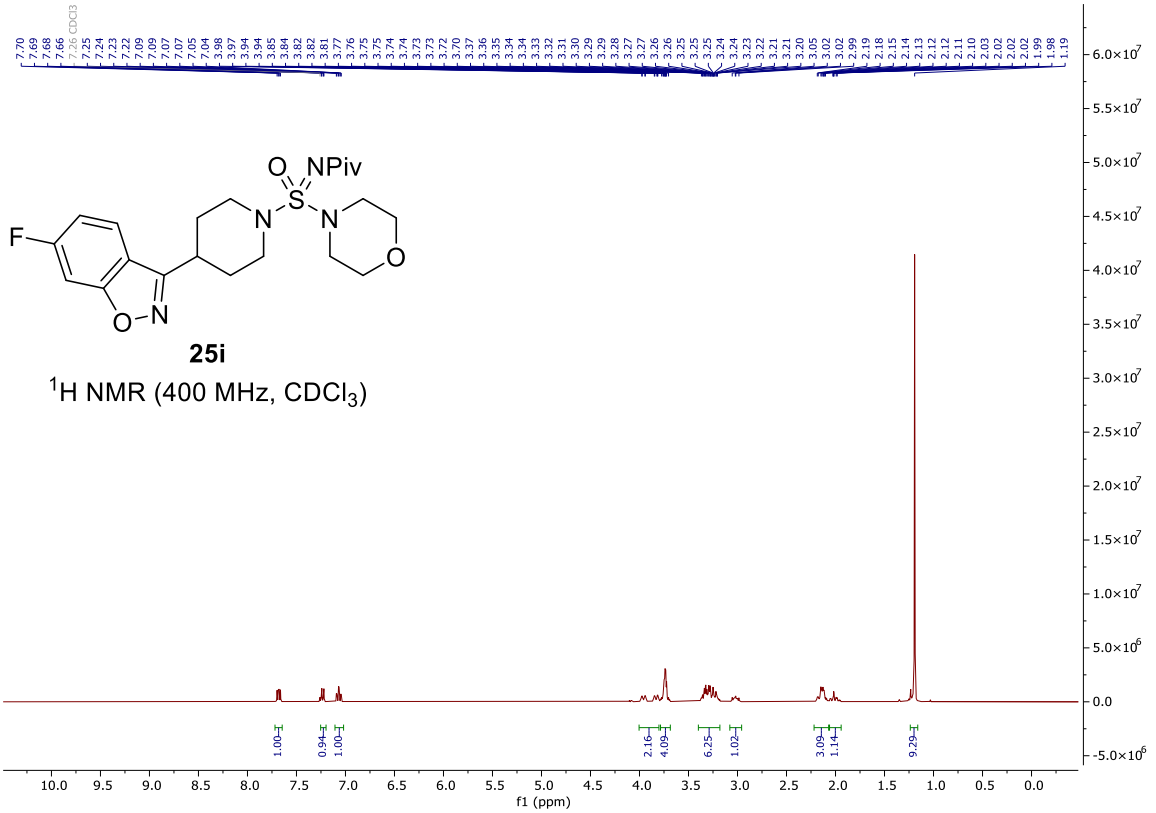


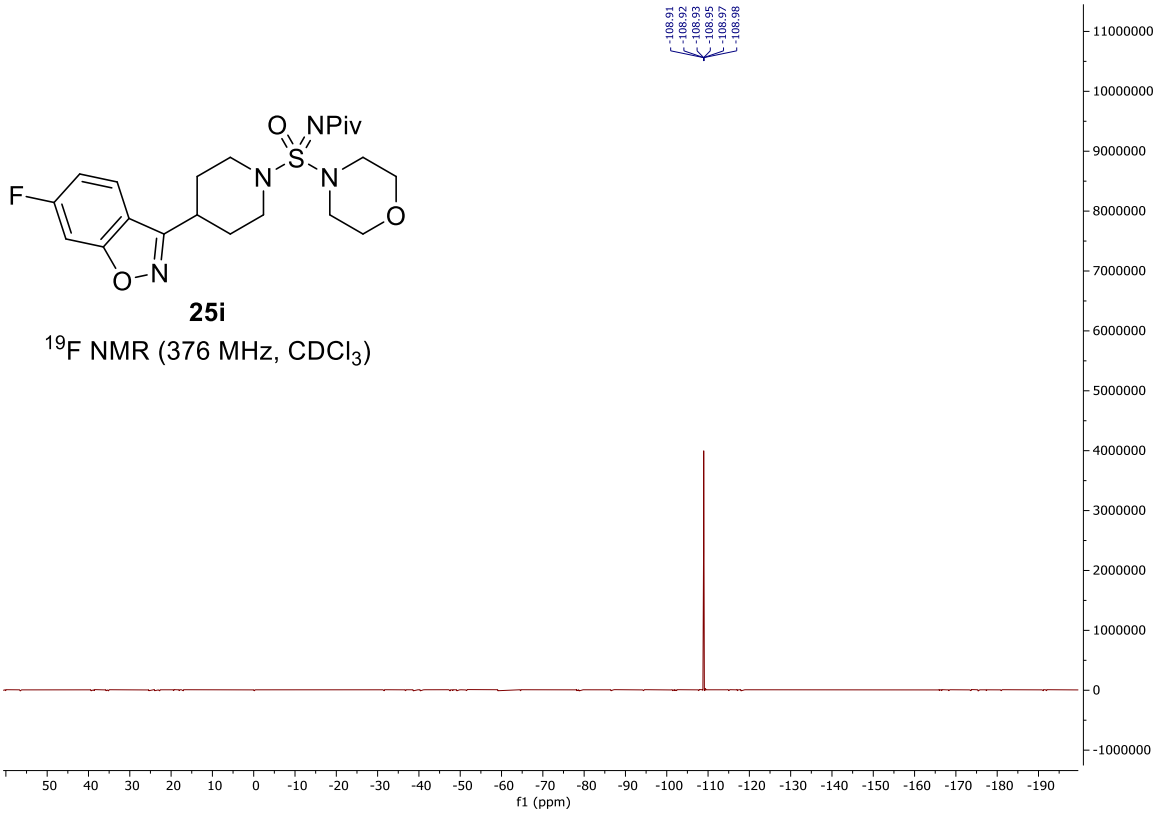
***N*-((4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)piperidin-1-yl)(morpholino)(oxo)-λ^6-sulfaneylidene)pivalamide (25h)**

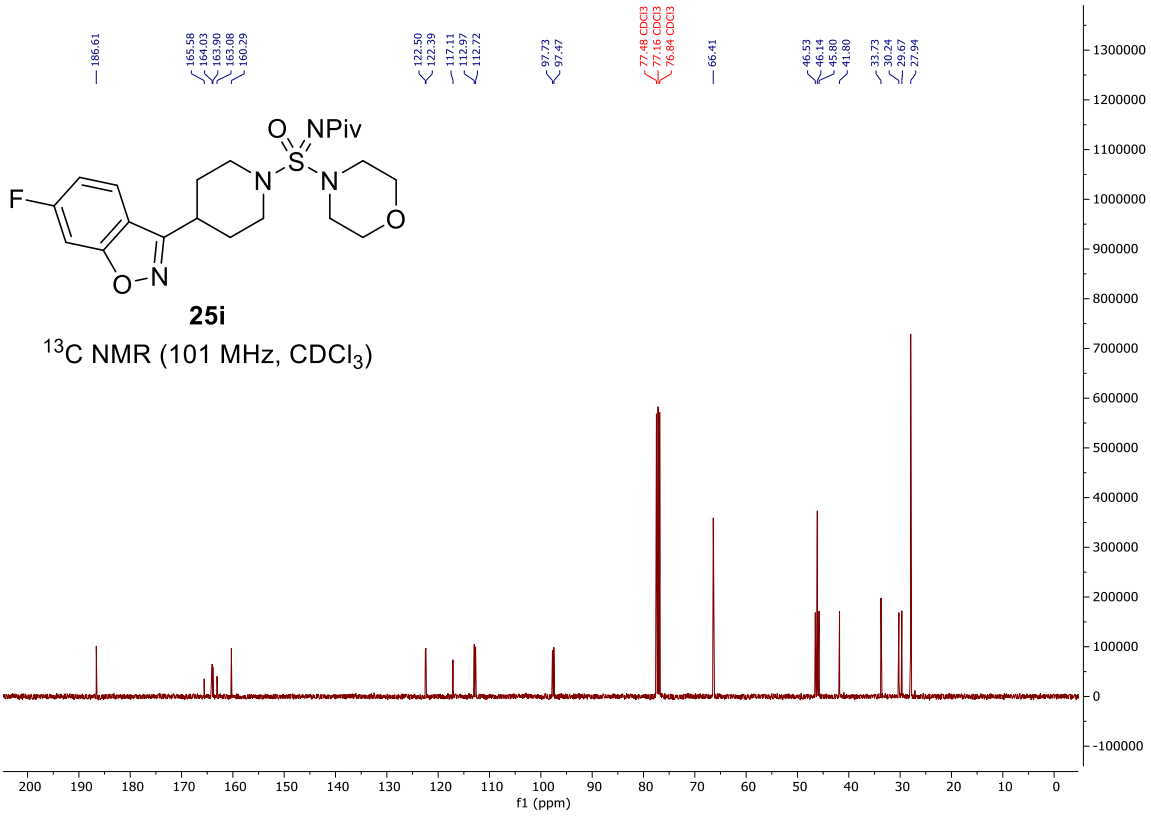




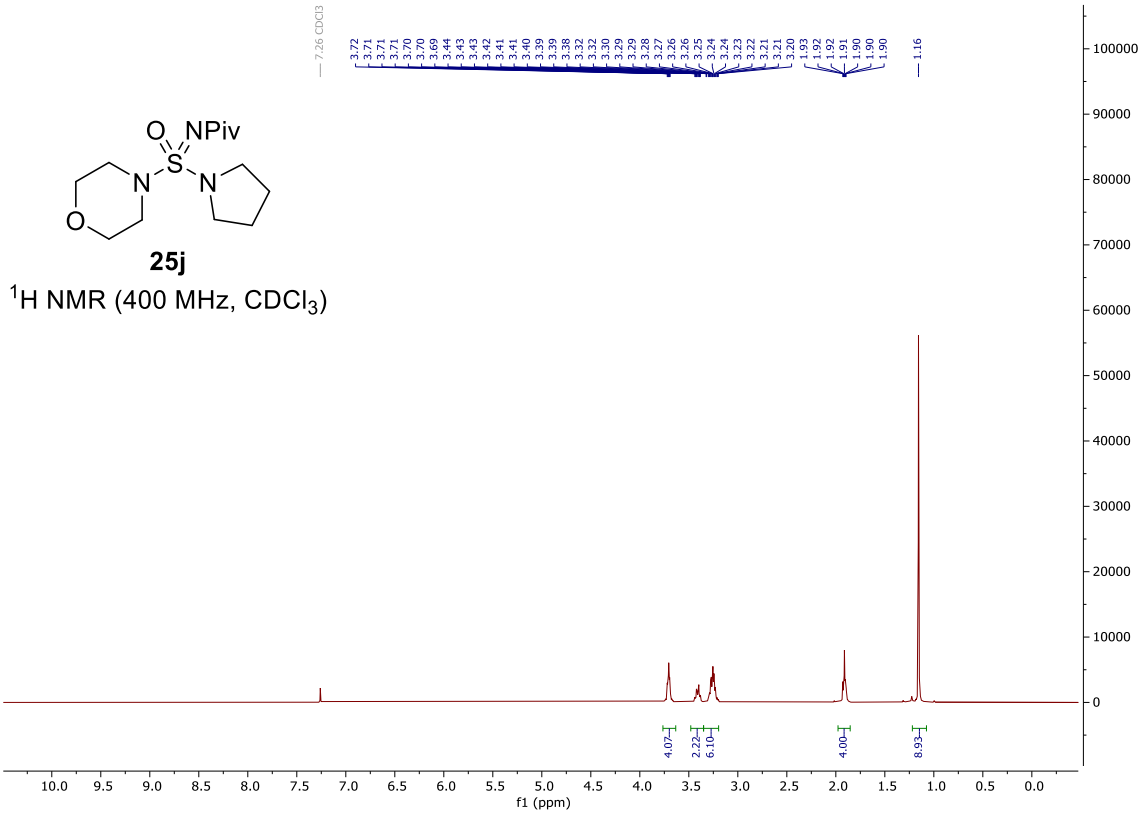
***N*-((4-(6-fluorobenzo[*d*]isoxazol-3-yl)piperidin-1-yl)(morpholino)(oxo)-λ6-sulfaneylidene)pivalamide (25i)**

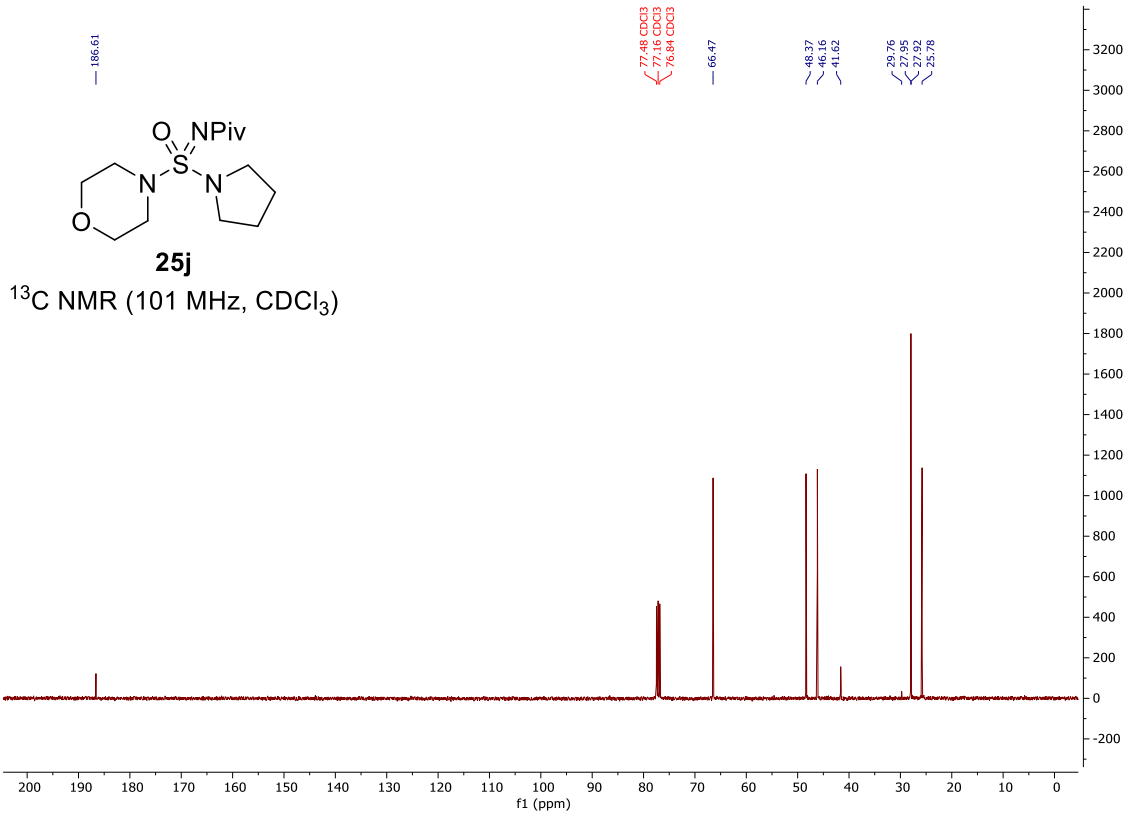




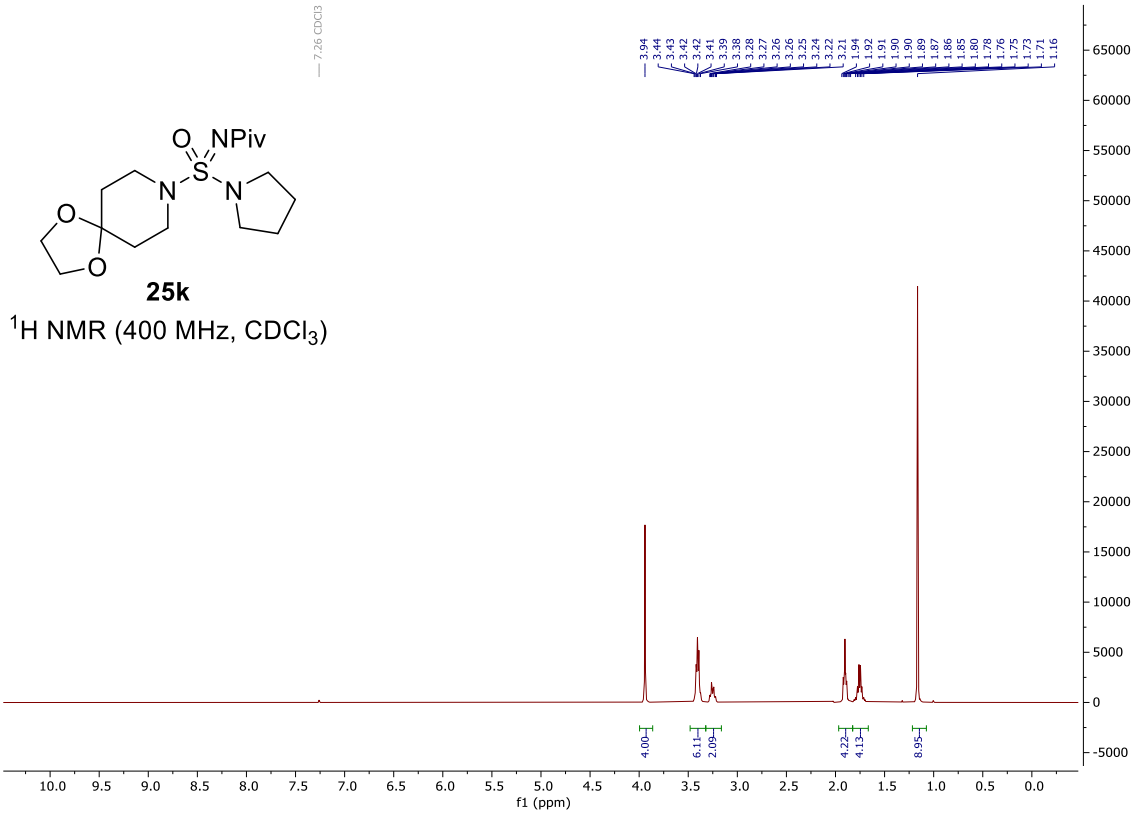

186.61
165.58
164.03
163.90
163.08
160.29
122.50
122.39
117.11
112.97
112.72
97.73
97.47
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
66.41
46.53
46.14
45.80
41.80
33.73
30.24
29.67
27.94
O
NPiv
S
N
N
O
F
O
N
25i
13C NMR (101 MHz, CDCl3)
f1 (ppm)

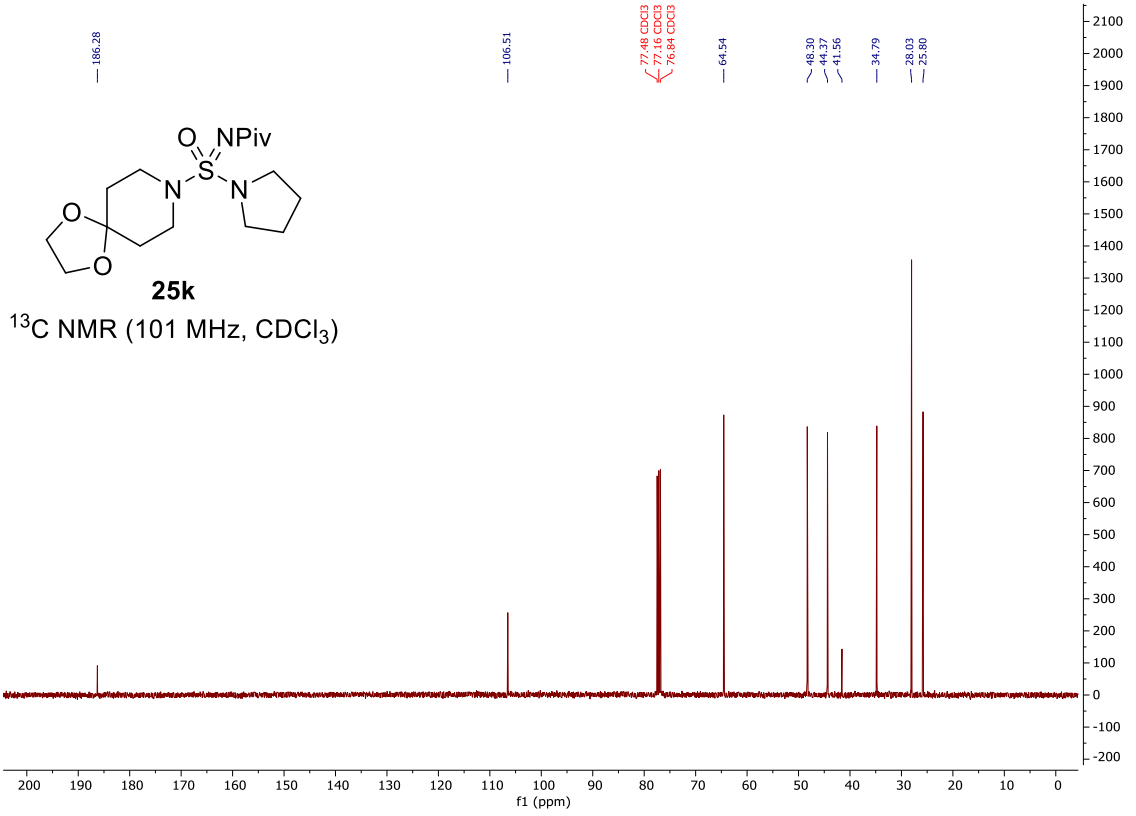
_N_-(morpholino(oxo)(pyrrolidin-1-yl)-λ6-sulfaneylidene)pivalamide (25j)



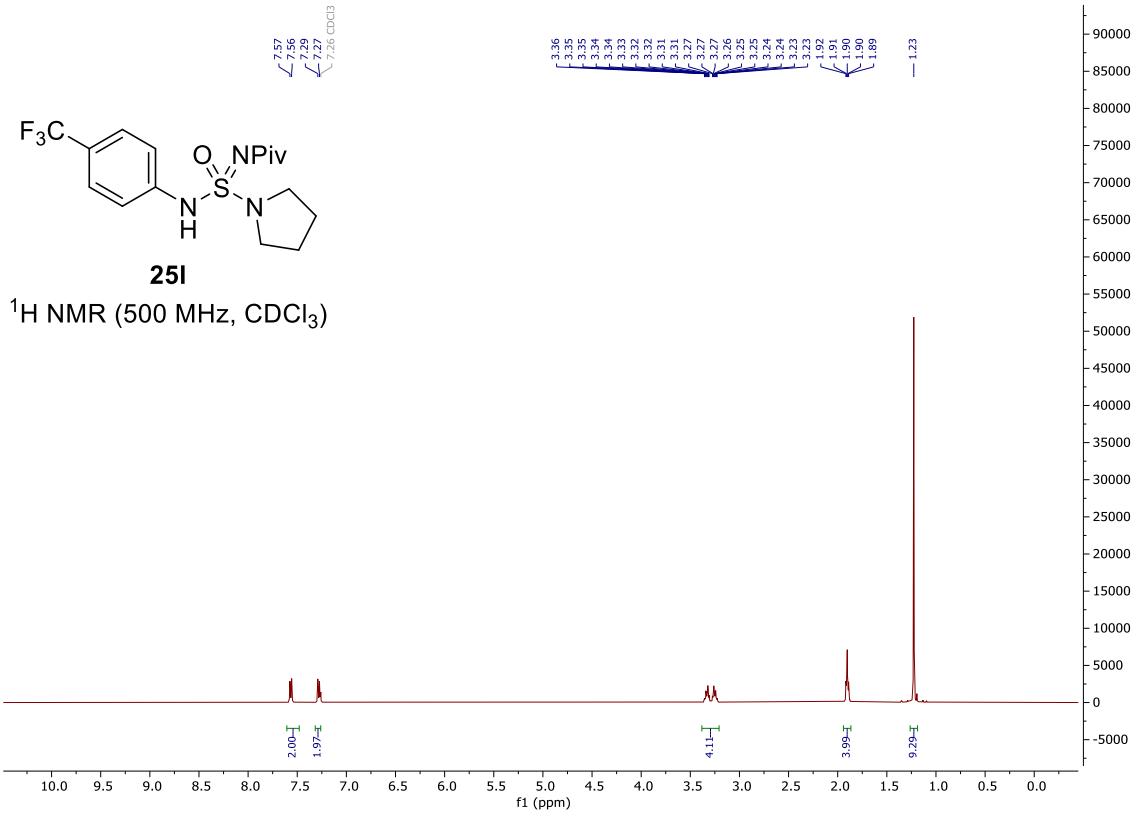


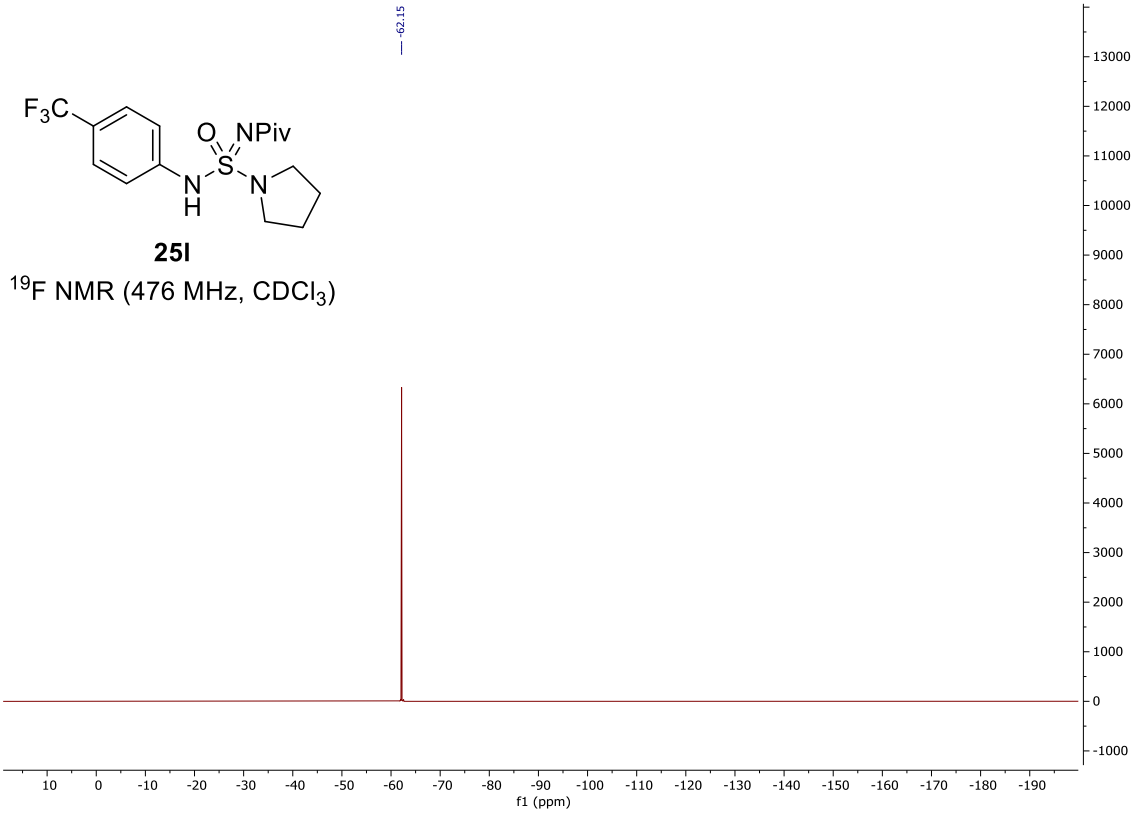
_N_-(oxo(pyrrolidin-1-yl)(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-λ6-sulfaneylidene)pivalamide (25k)

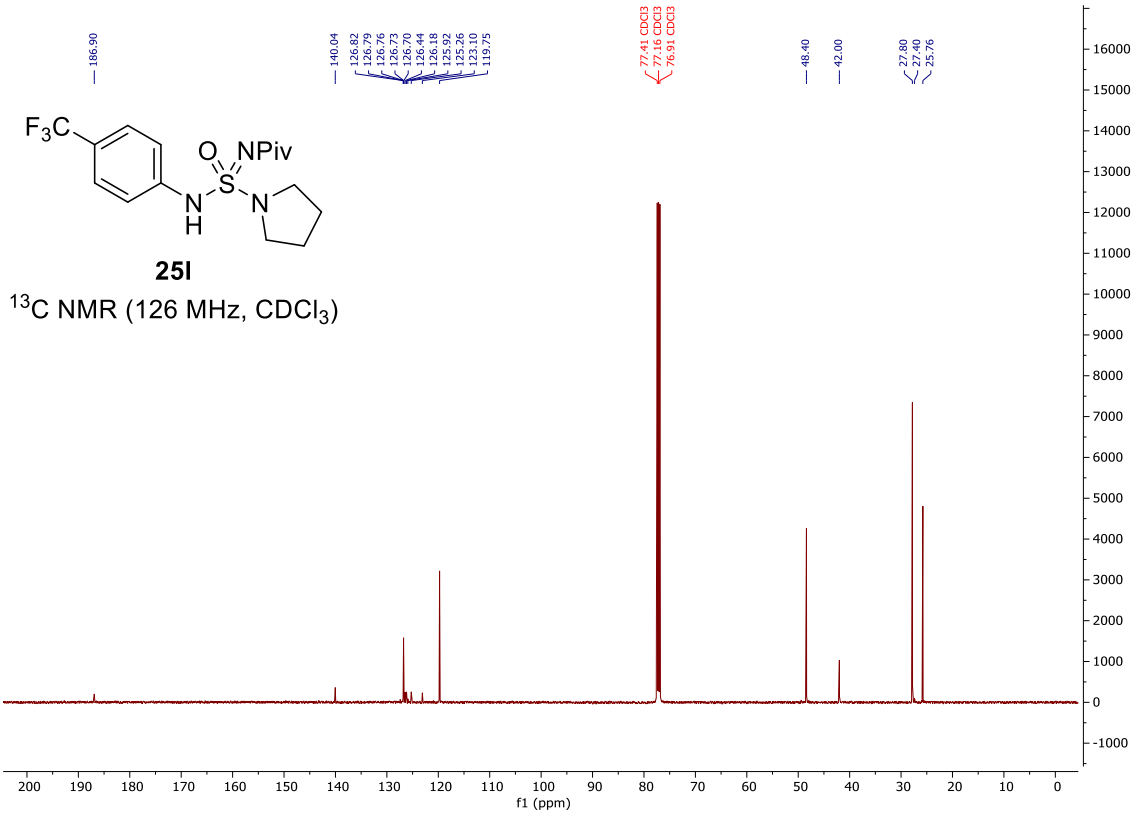




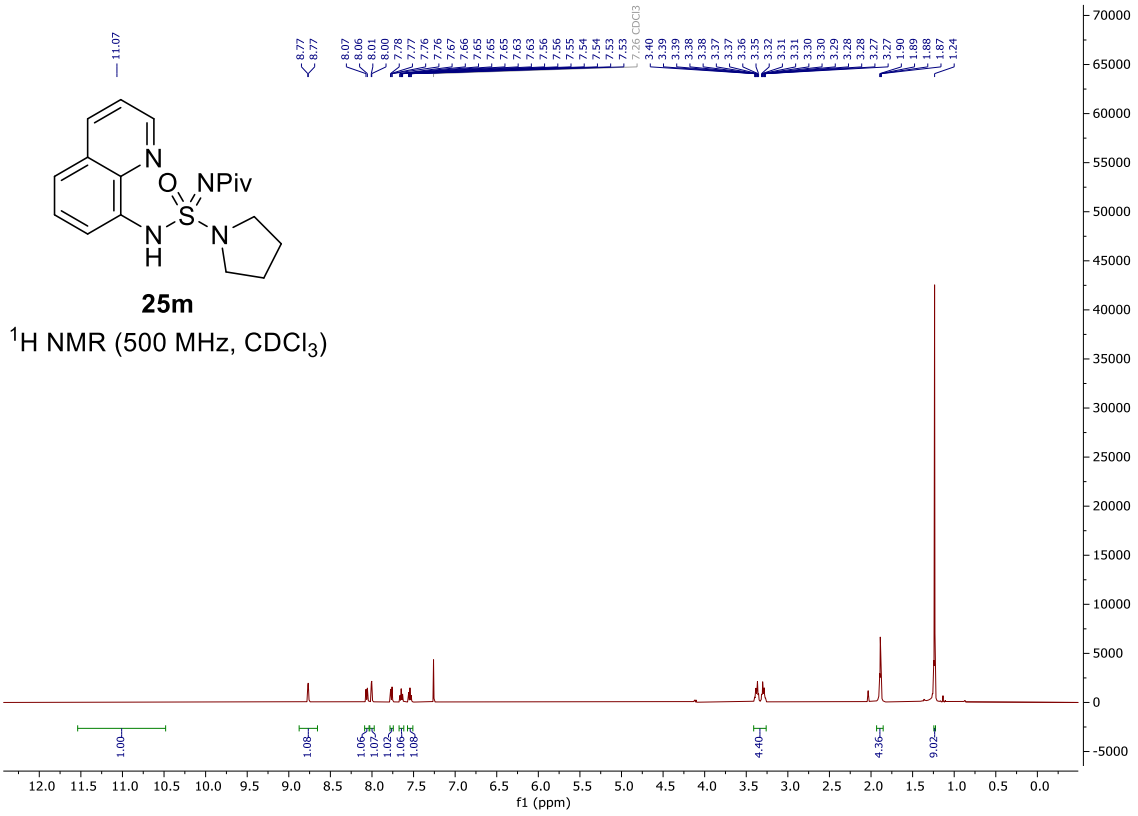
_N_-(oxo(pyrrolidin-1-yl)((4-(trifluoromethyl)phenyl)amino)-λ6-sulfaneylidene)pivalamide (25l)

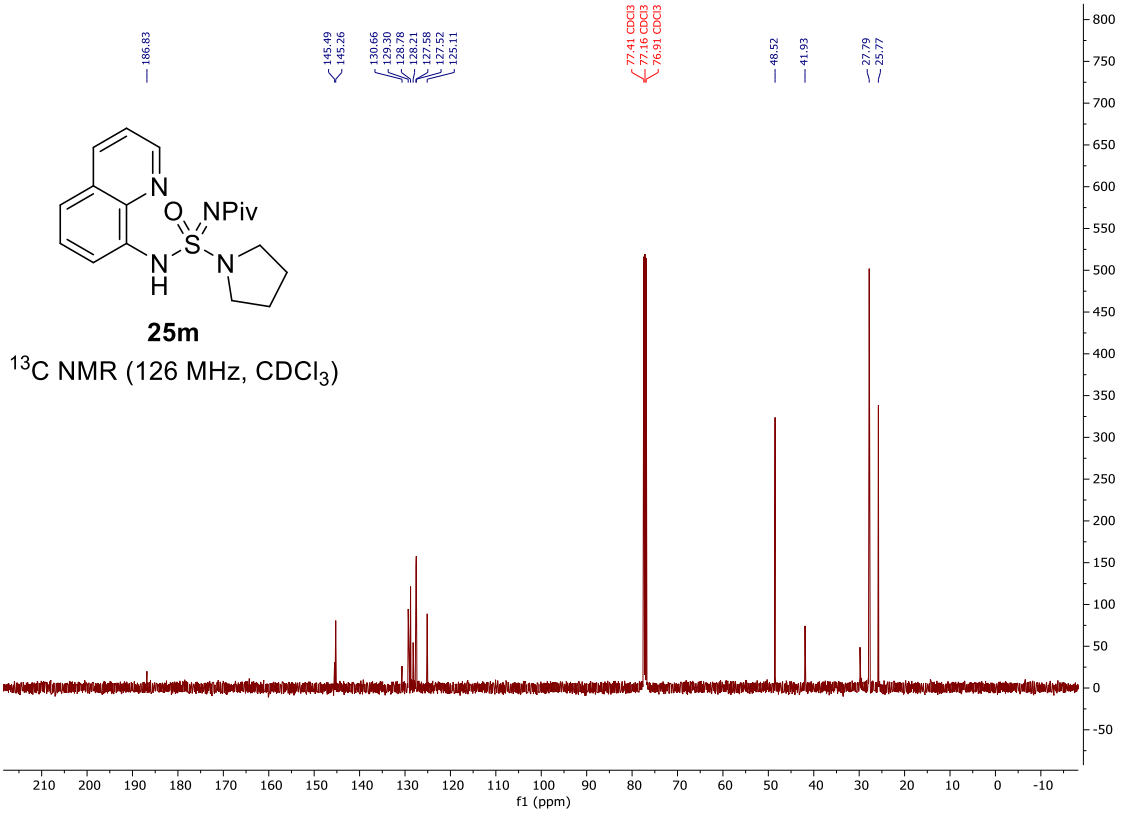




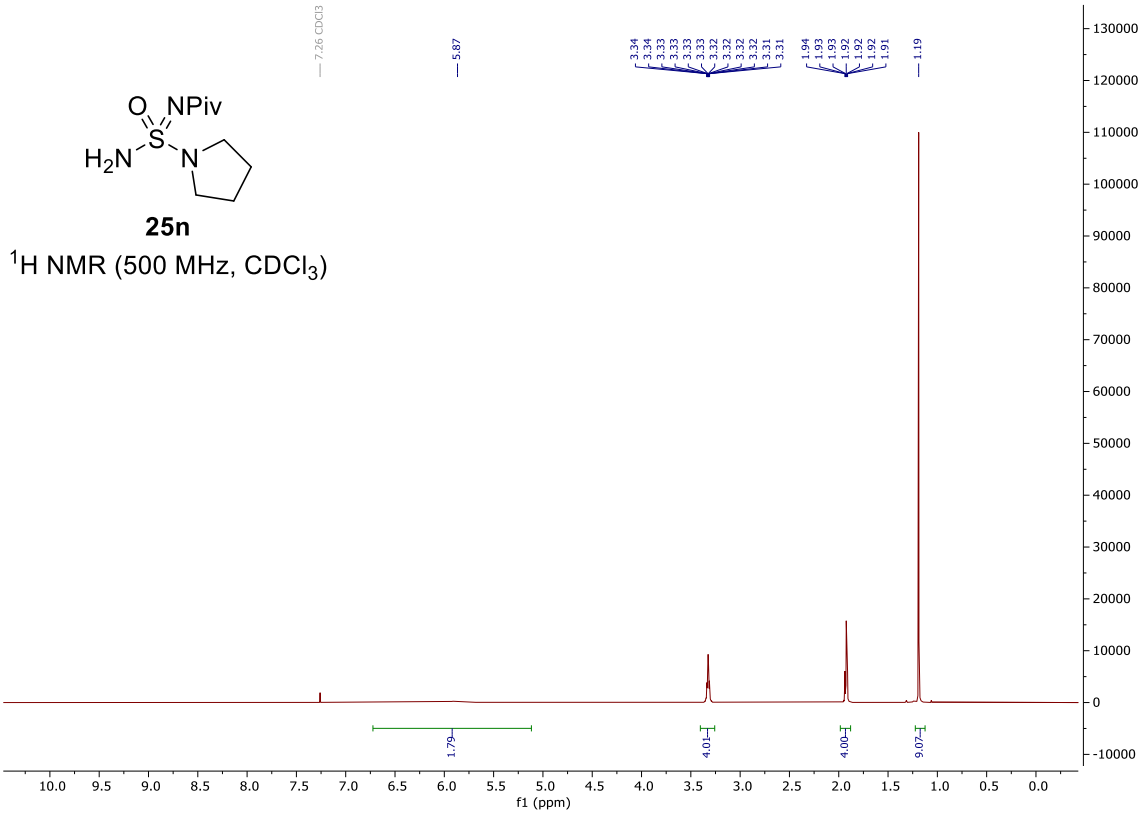

186.90
140.04
126.82
126.79
126.76
126.73
126.70
126.44
126.18
125.92
125.26
123.10
119.75
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
48.40
42.00
27.80
27.40
25.76
F3C
O
NPiv
S
N
H
N
25l
13C NMR (126 MHz, CDCl3)
f1 (ppm)

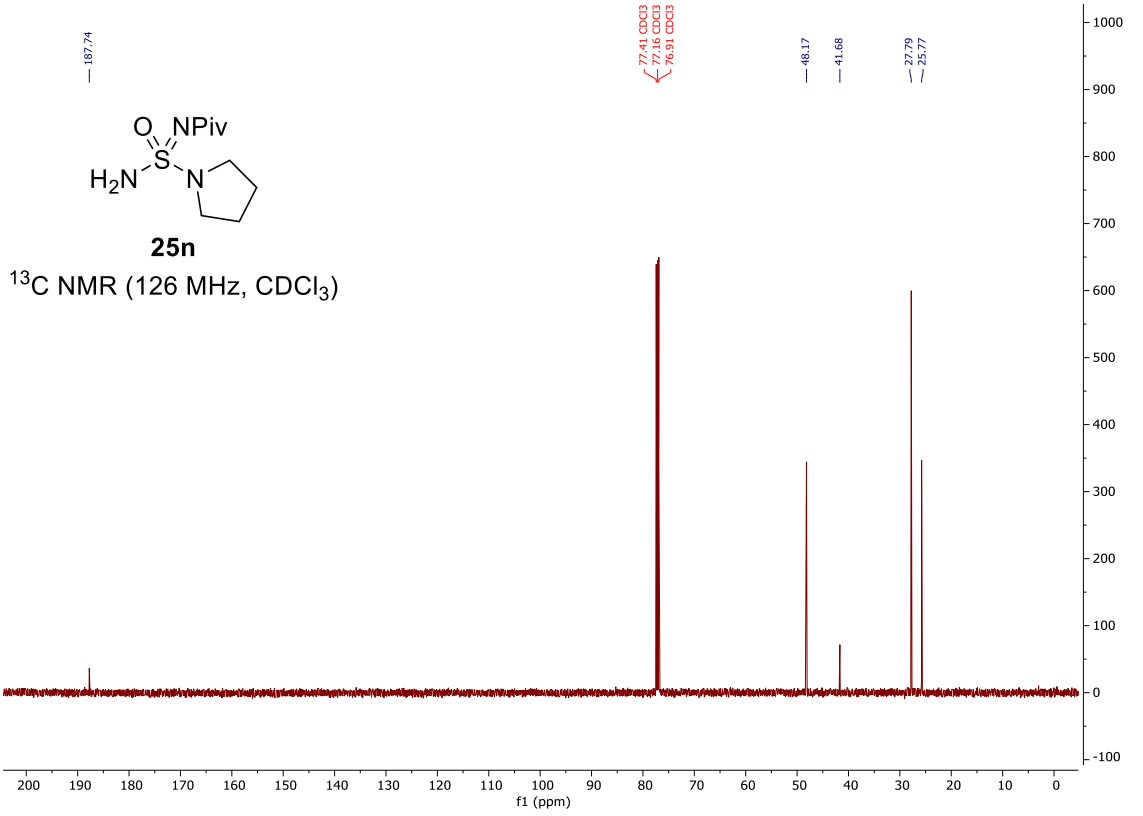
_N_-(oxo(pyrrolidin-1-yl)(quinolin-8-ylamino)-λ6-sulfaneylidene)pivalamide (25m)



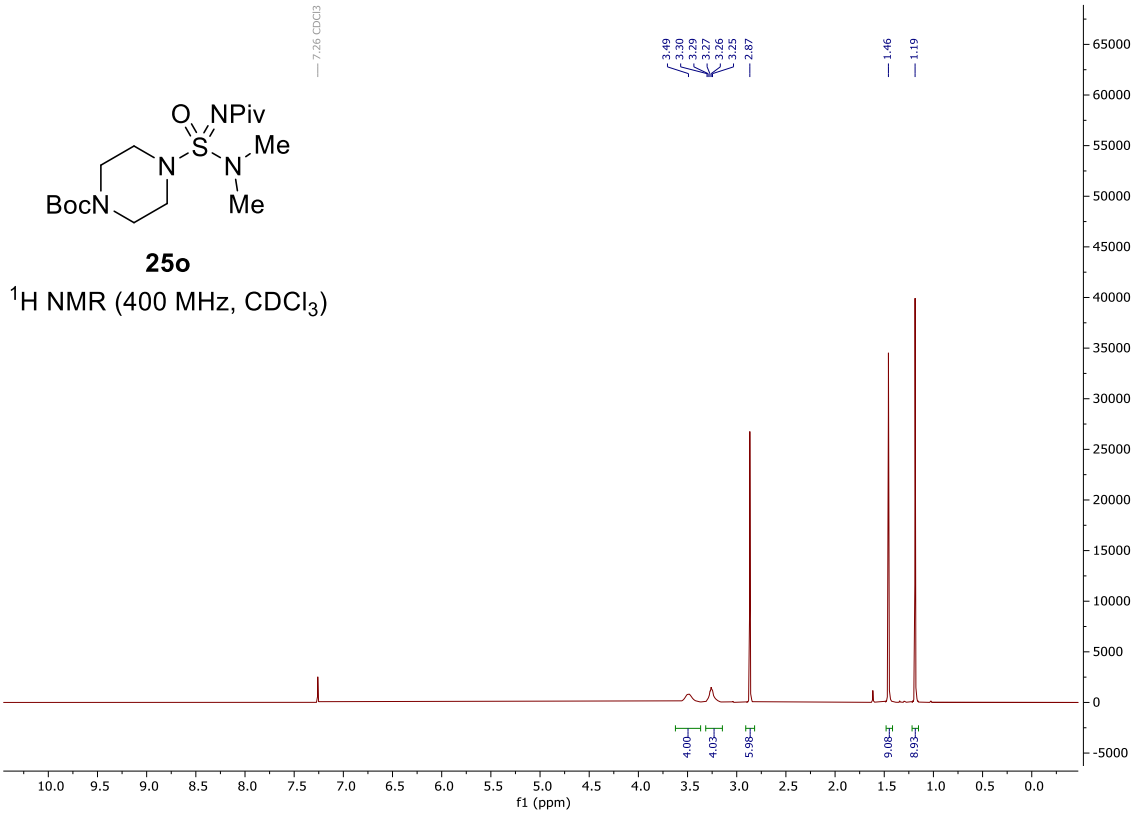


_N_-(amino(oxo)(pyrrolidin-1-yl)-λ6-sulfaneylidene)pivalamide (25n)



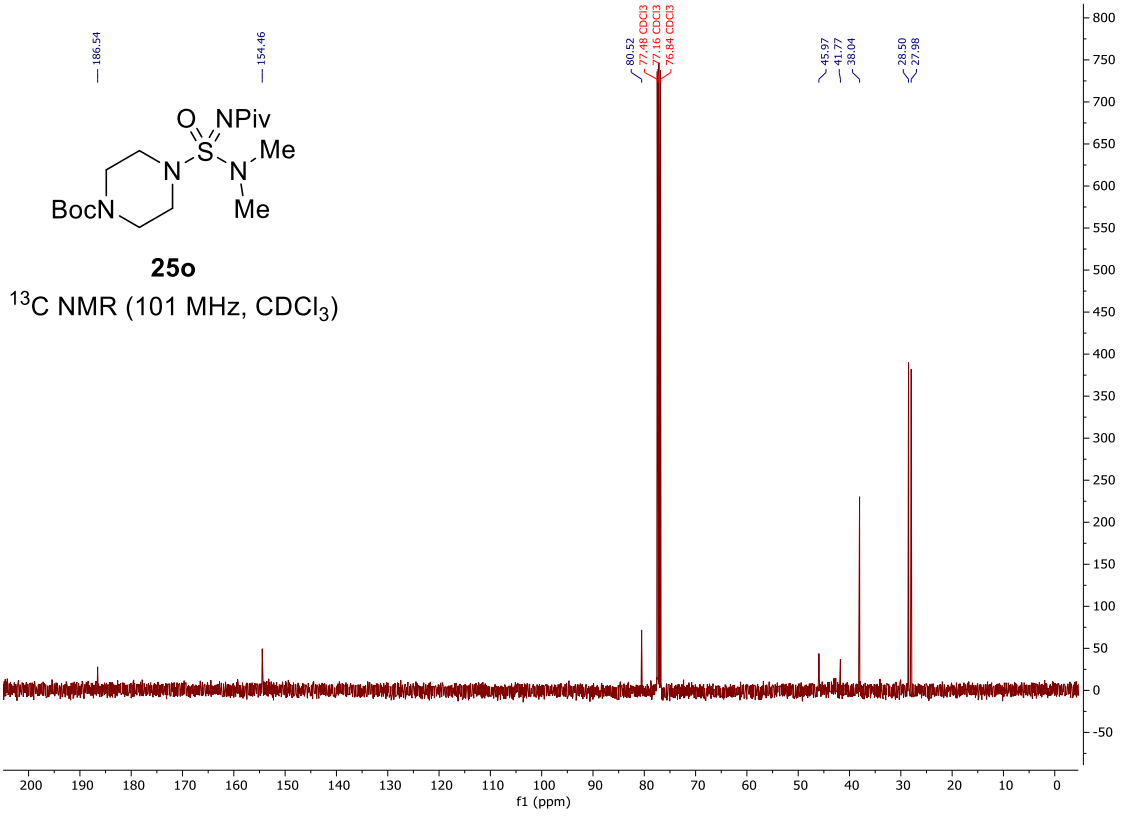


tert-Butyl 4-(_N_,_N_-dimethyl-_N_'-pivaloylsulfamidimidoyl)piperazine-1-carboxylate (25o)



25o

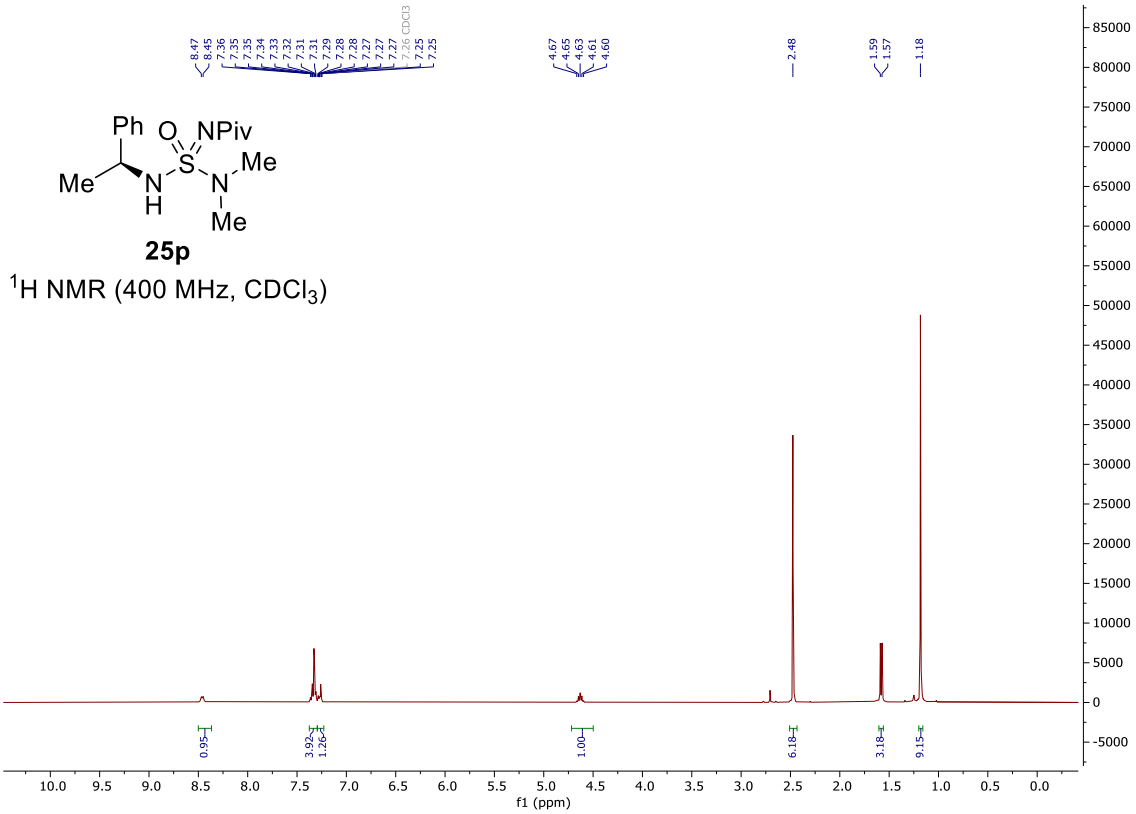
^{1}H NMR (400 MHz, $CDCl_3$)

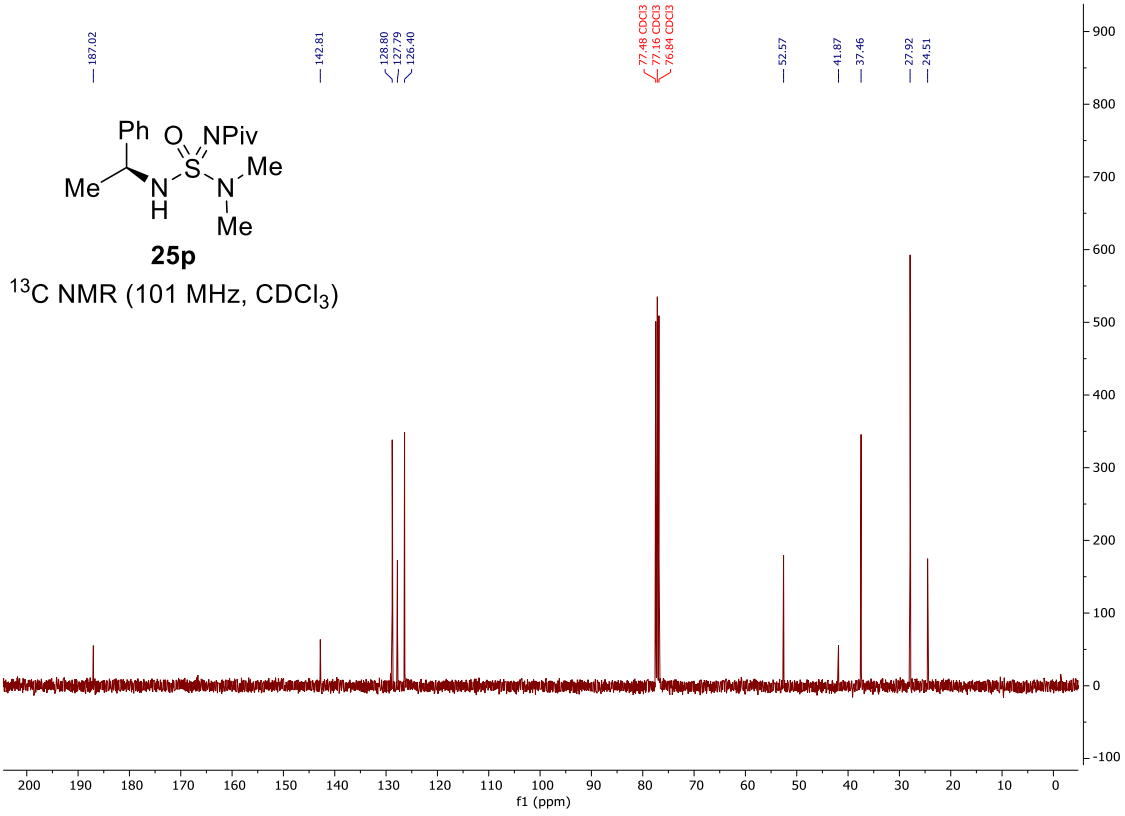


25o

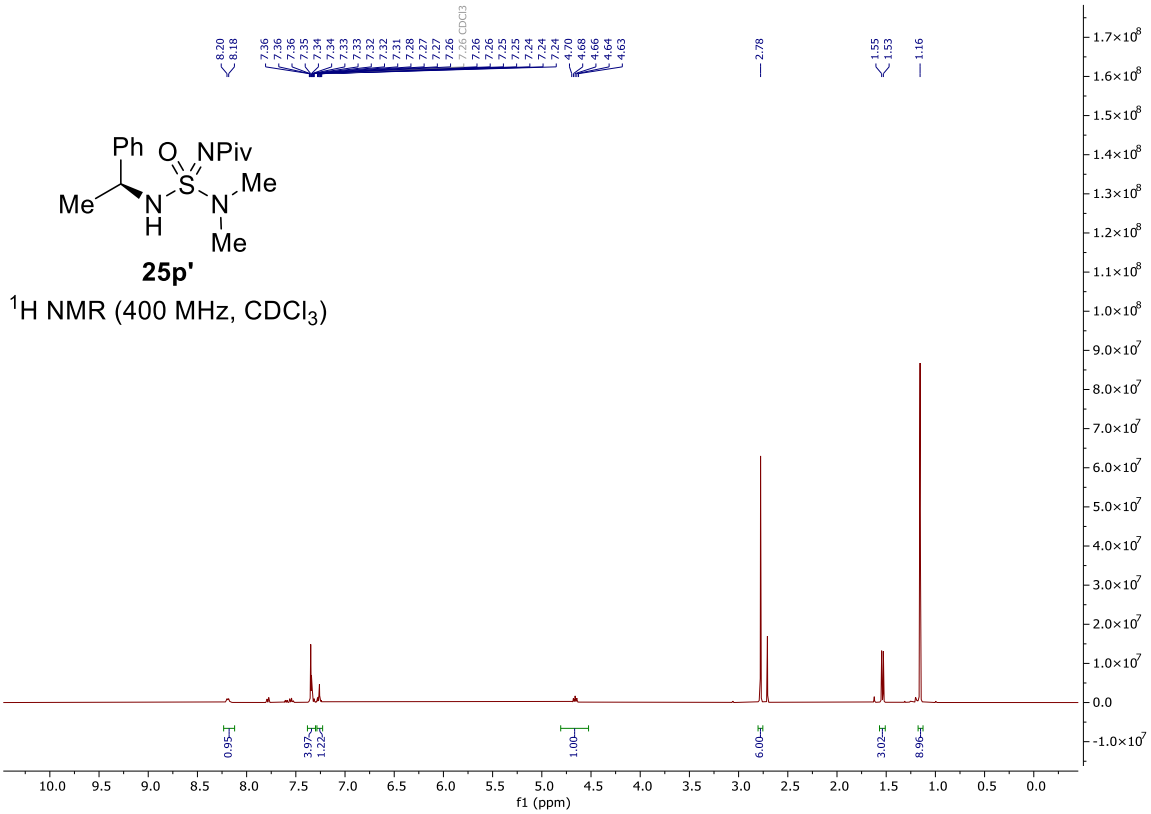
^{13}C NMR (101 MHz, $CDCl_3$)

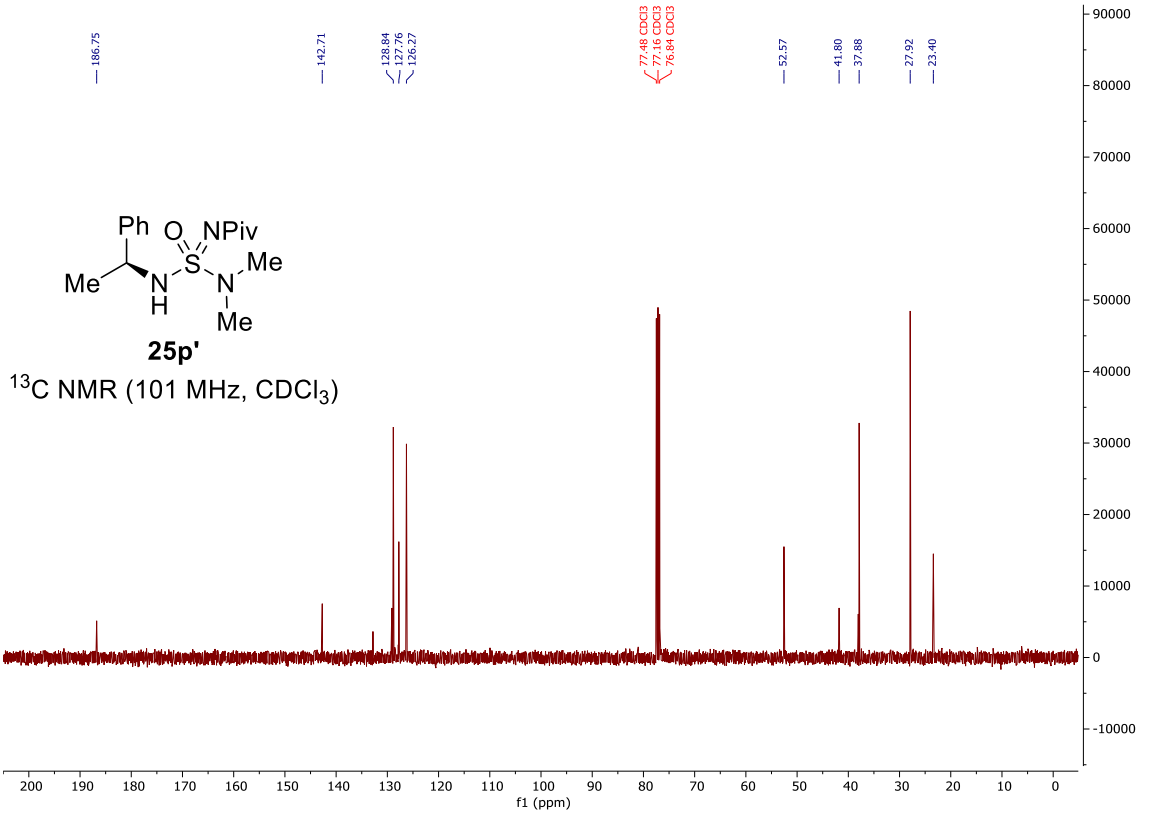
_N_-((dimethylamino)(oxo)(((_S_)-1-phenylethyl)amino)-λ6-sulfaneylidene)pivalamide (25p)



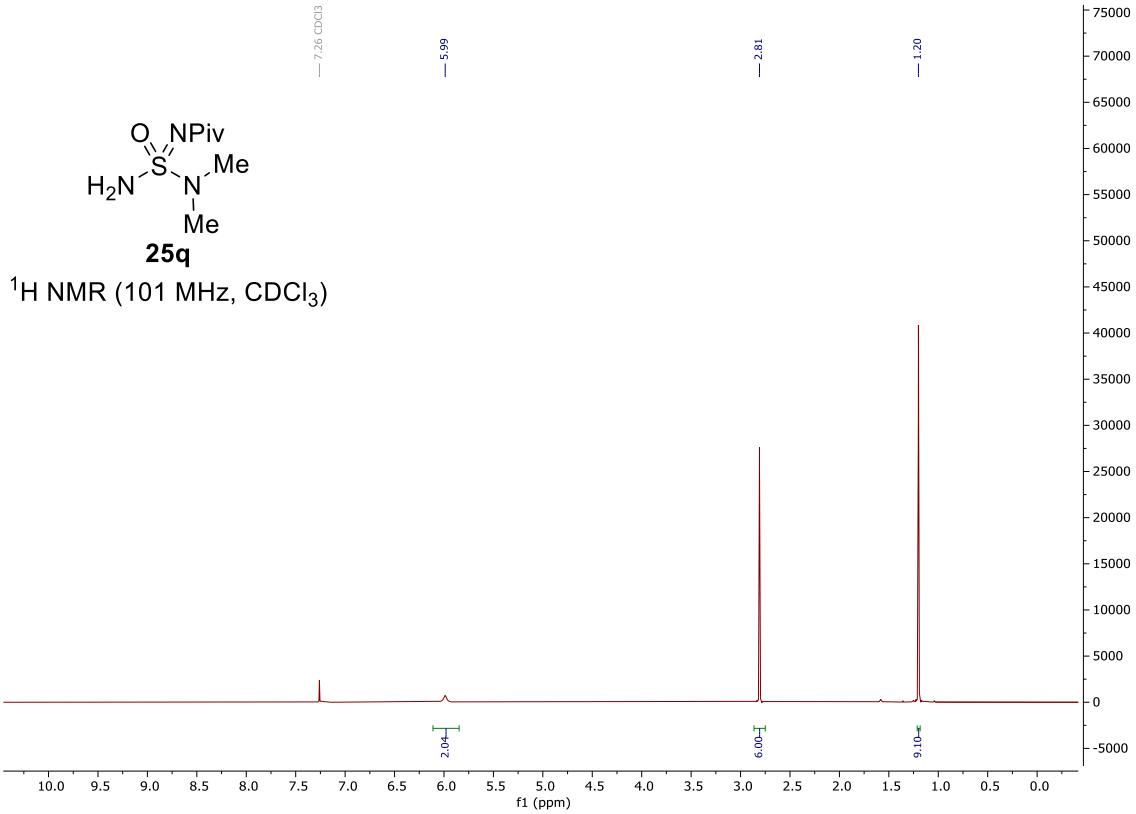


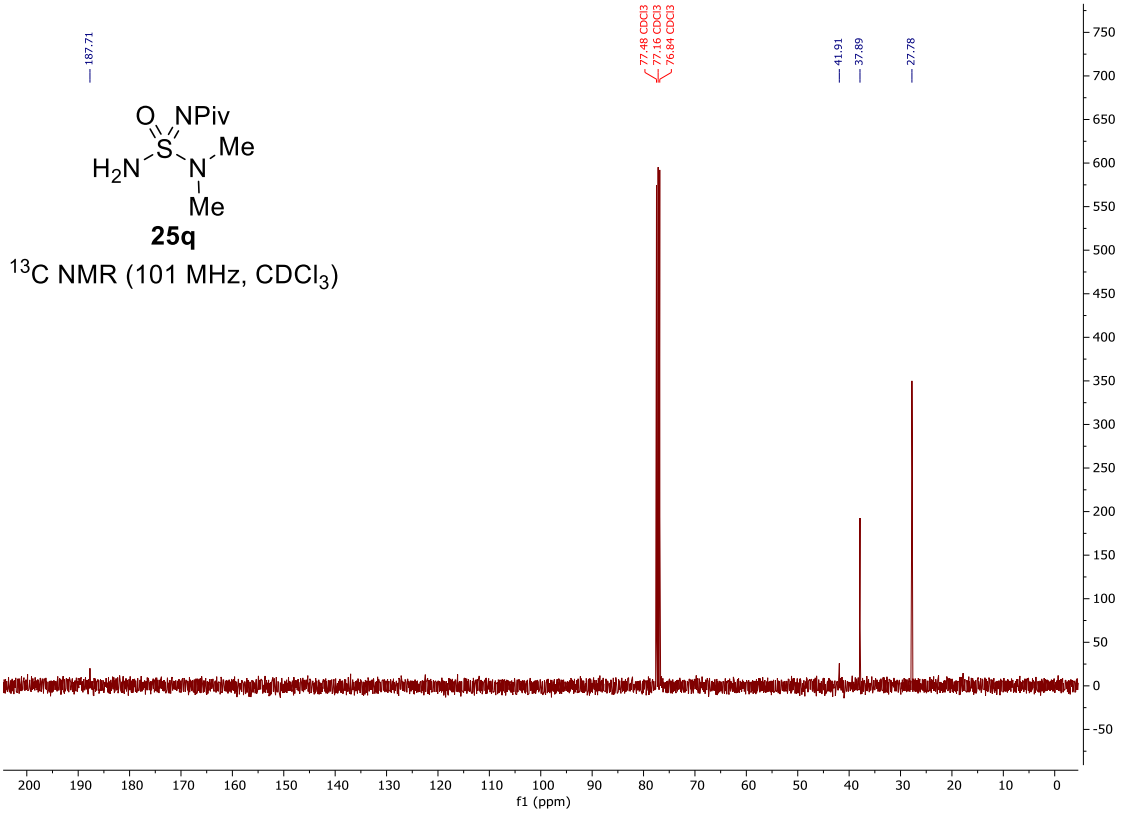
***N*-((dimethylamino)(oxo)(((*S*)-1-phenylethyl)amino)-λ6-sulfaneylidene)pivalamide (25p')**



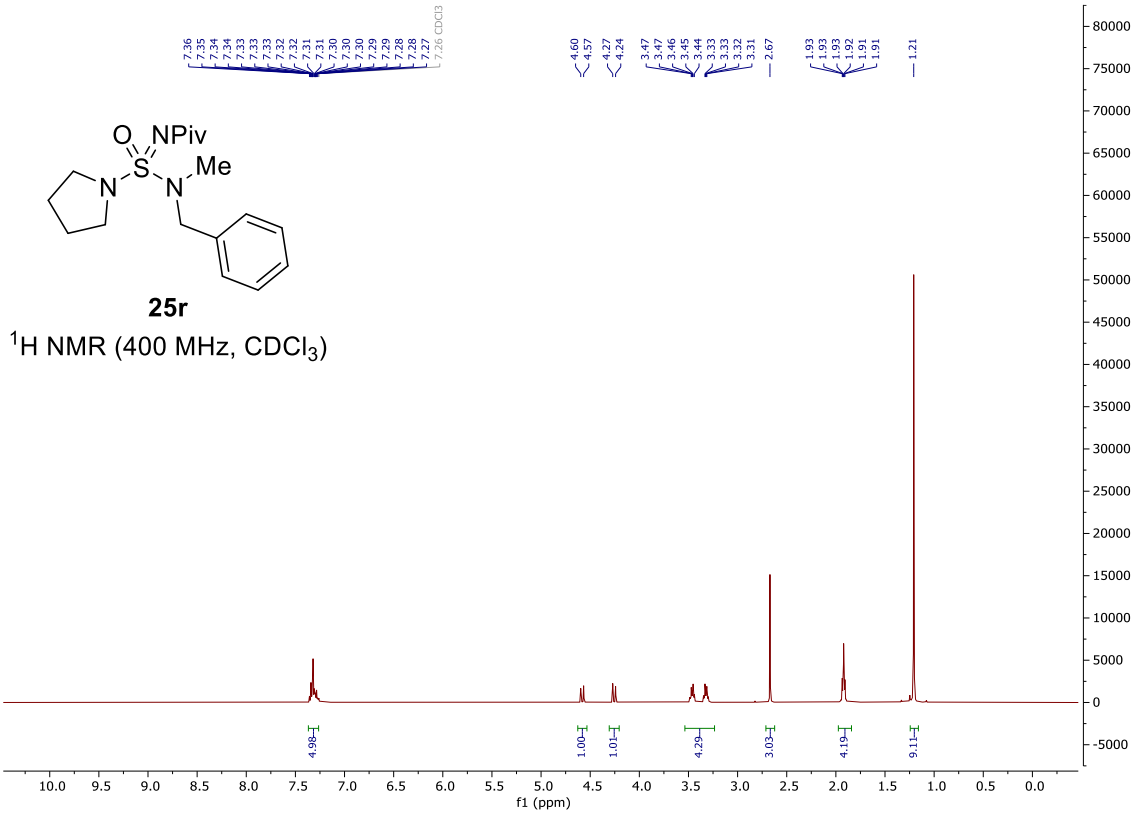


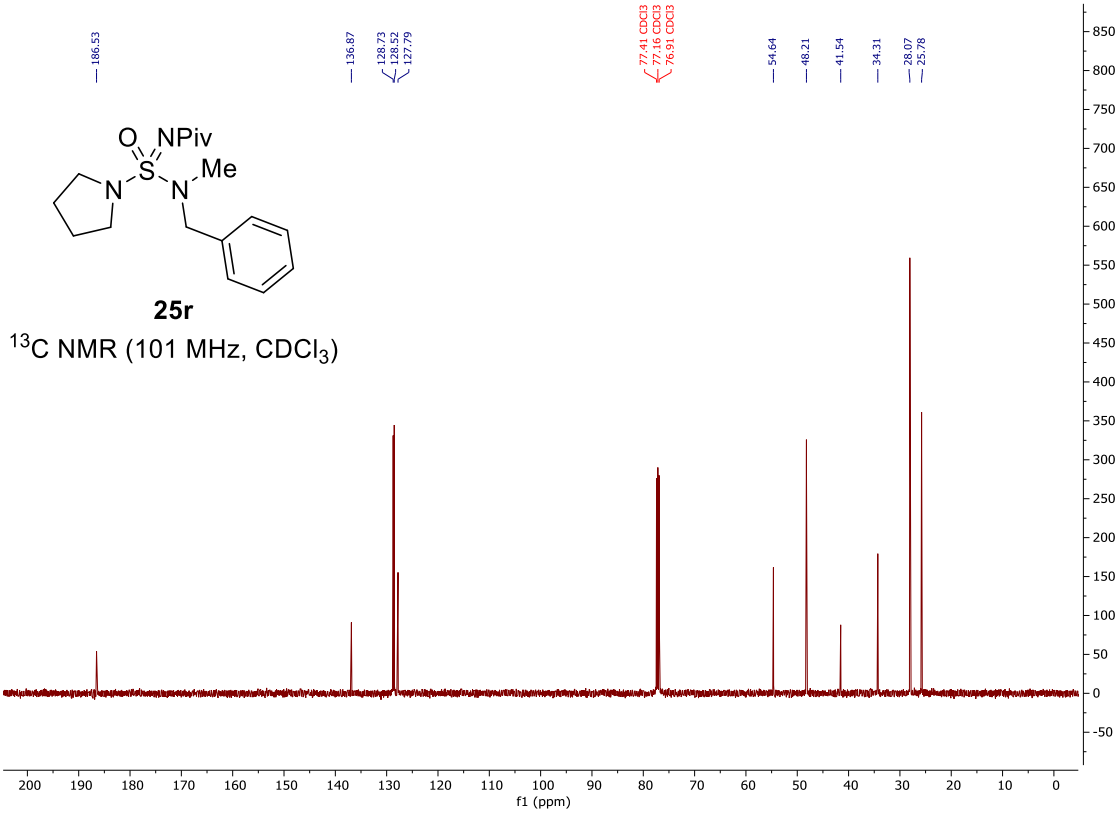
_N_-(amino(dimethylamino)(oxo)-λ6-sulfaneylidene)pivalamide (25q)



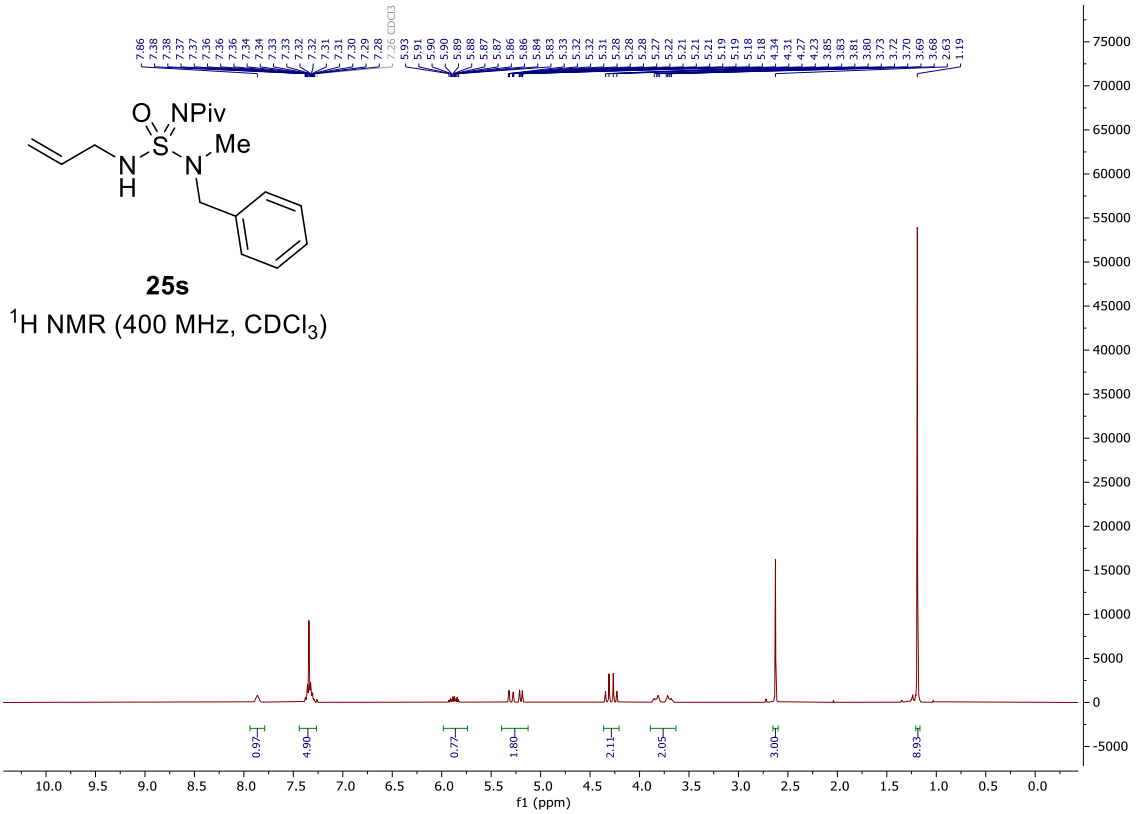


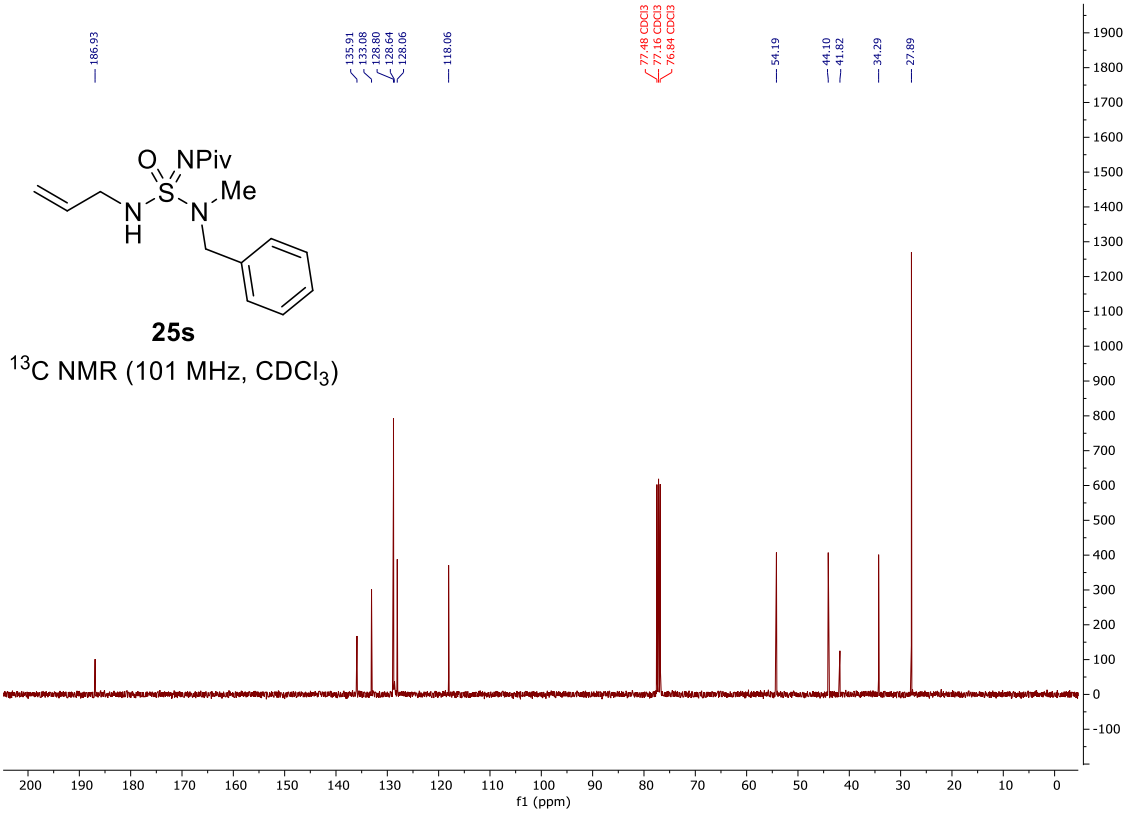
_N_-((benzyl(methyl)amino)(oxo)(pyrrolidin-1-yl)-λ6-sulfaneylidene)pivalamide (25r)



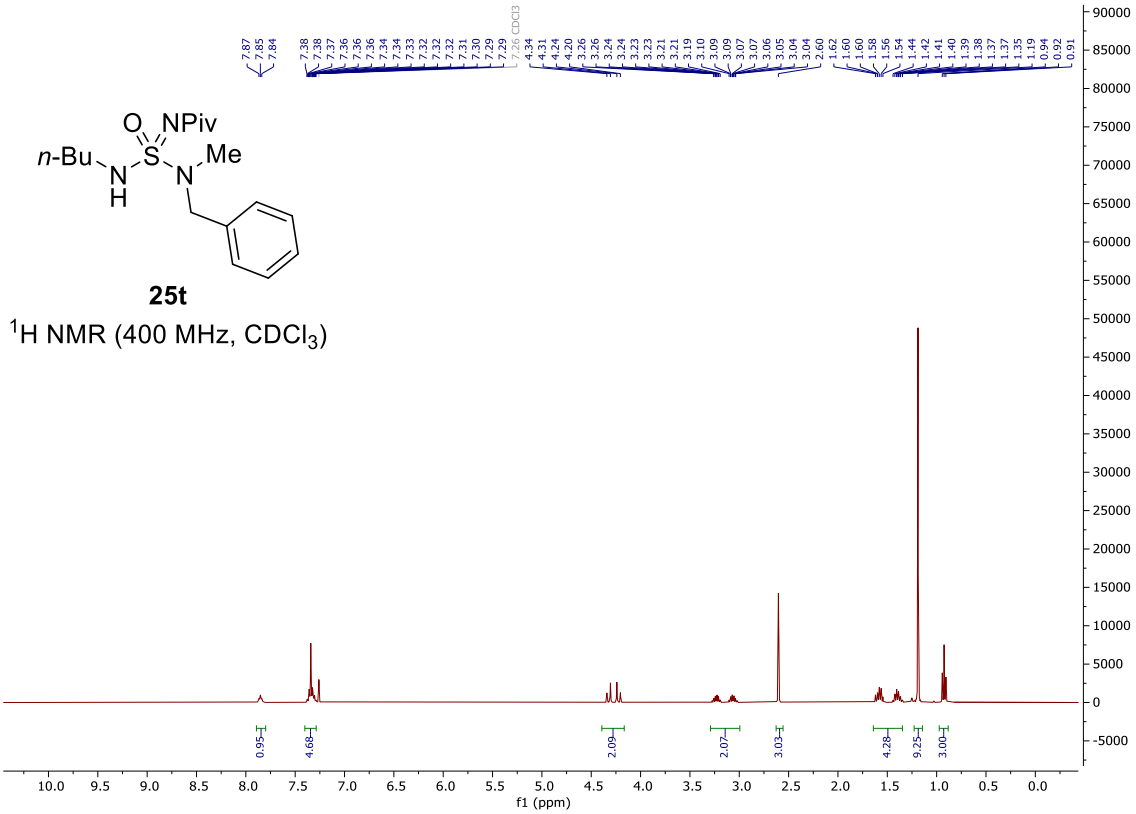


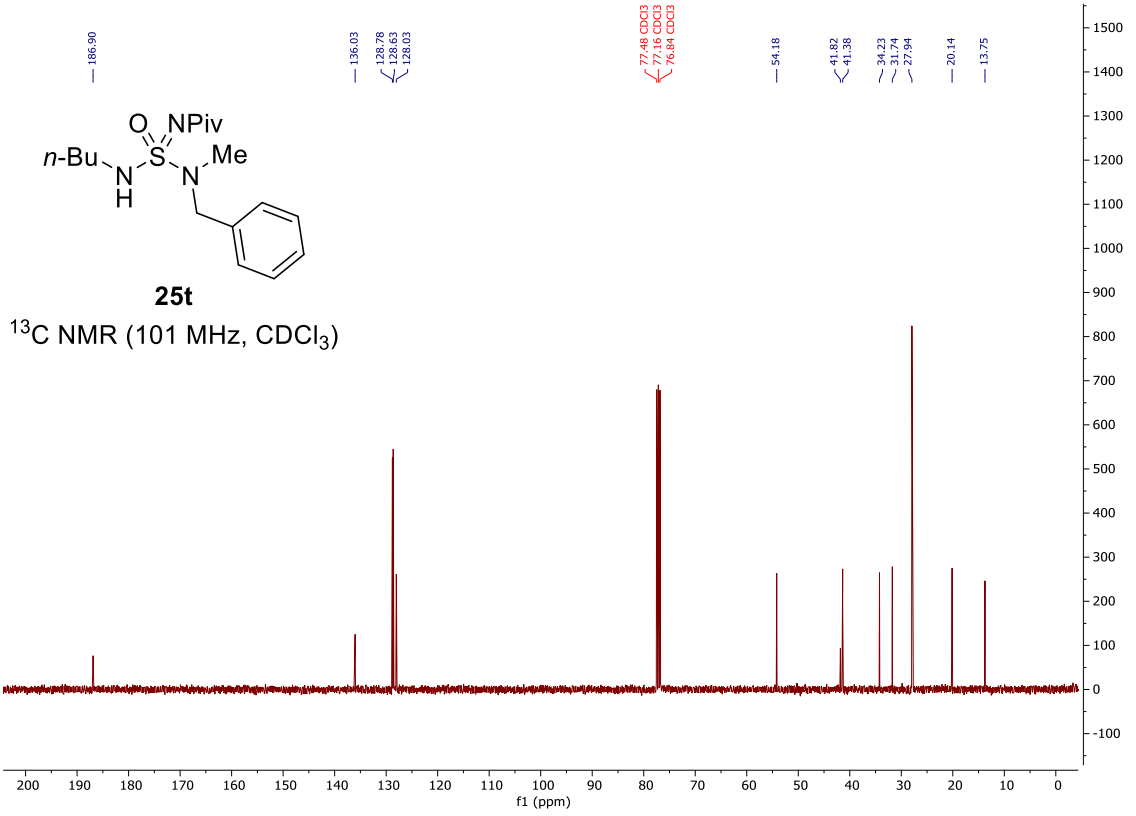
_N_-((allylamino)(benzyl(methyl)amino)(oxo)-λ6-sulfaneylidene)pivalamide (25s)



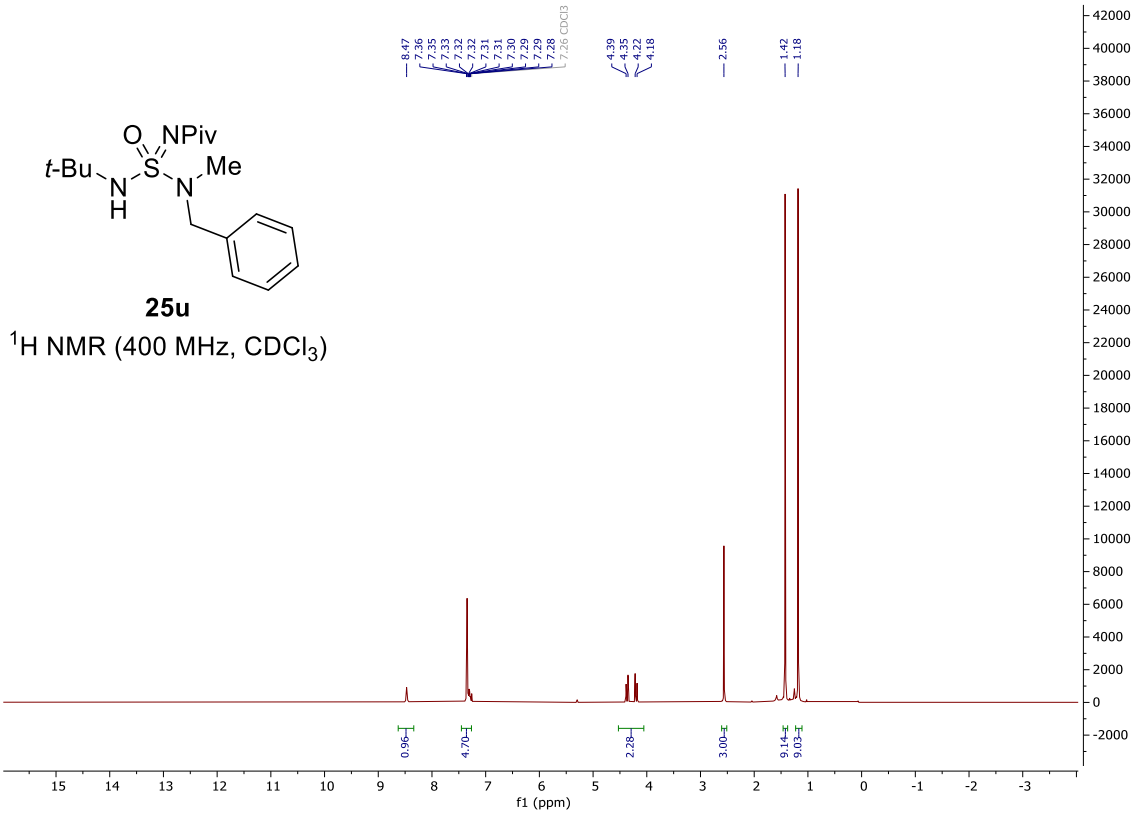


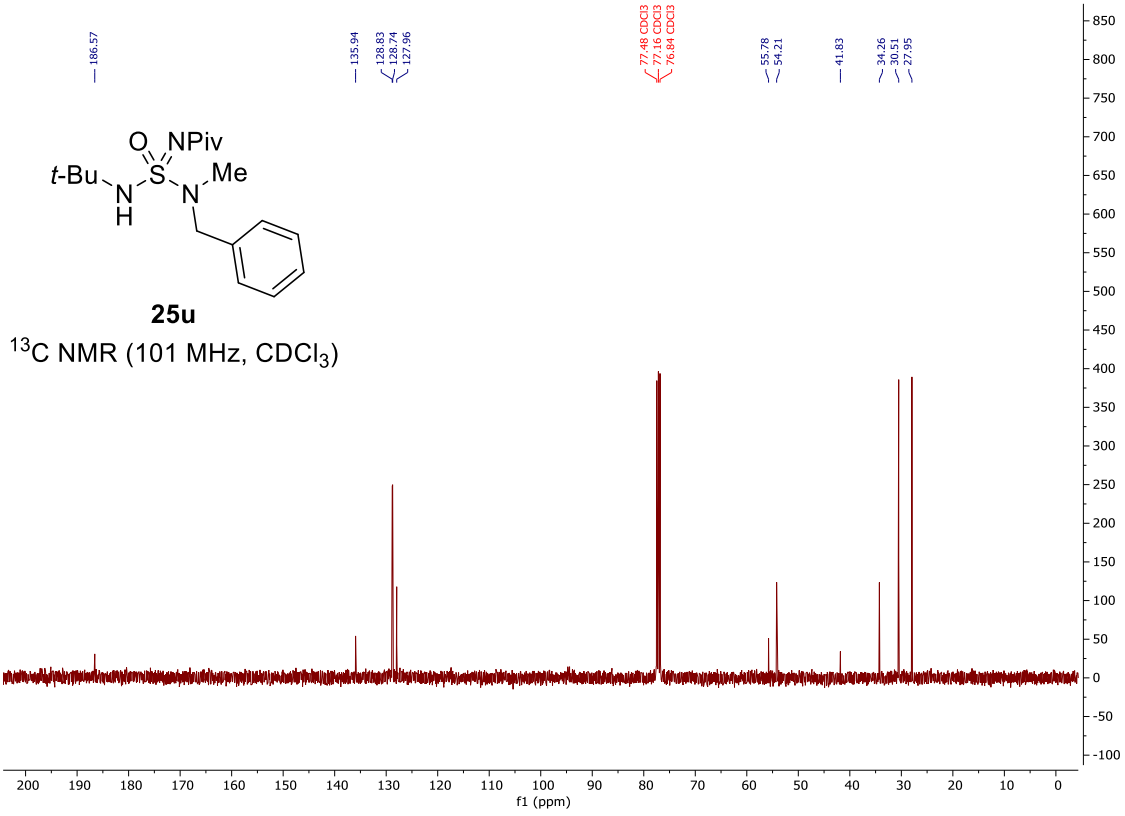
_N_-((benzyl(methyl)amino)(butylamino)(oxo)-λ6-sulfaneylidene)pivalamide (25t)



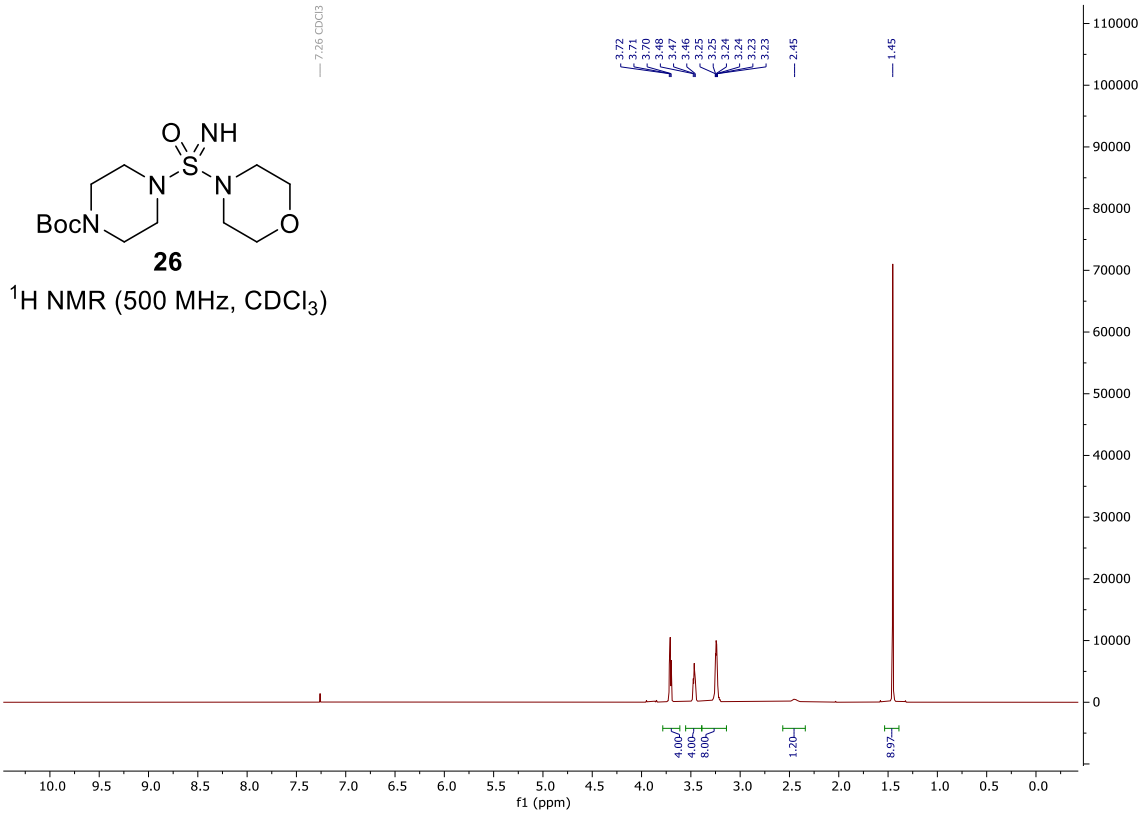


_N_-((benzyl(methyl)amino)(_tert_-butylamino)(oxo)-λ6-sulfaneylidene)pivalamide (25u)



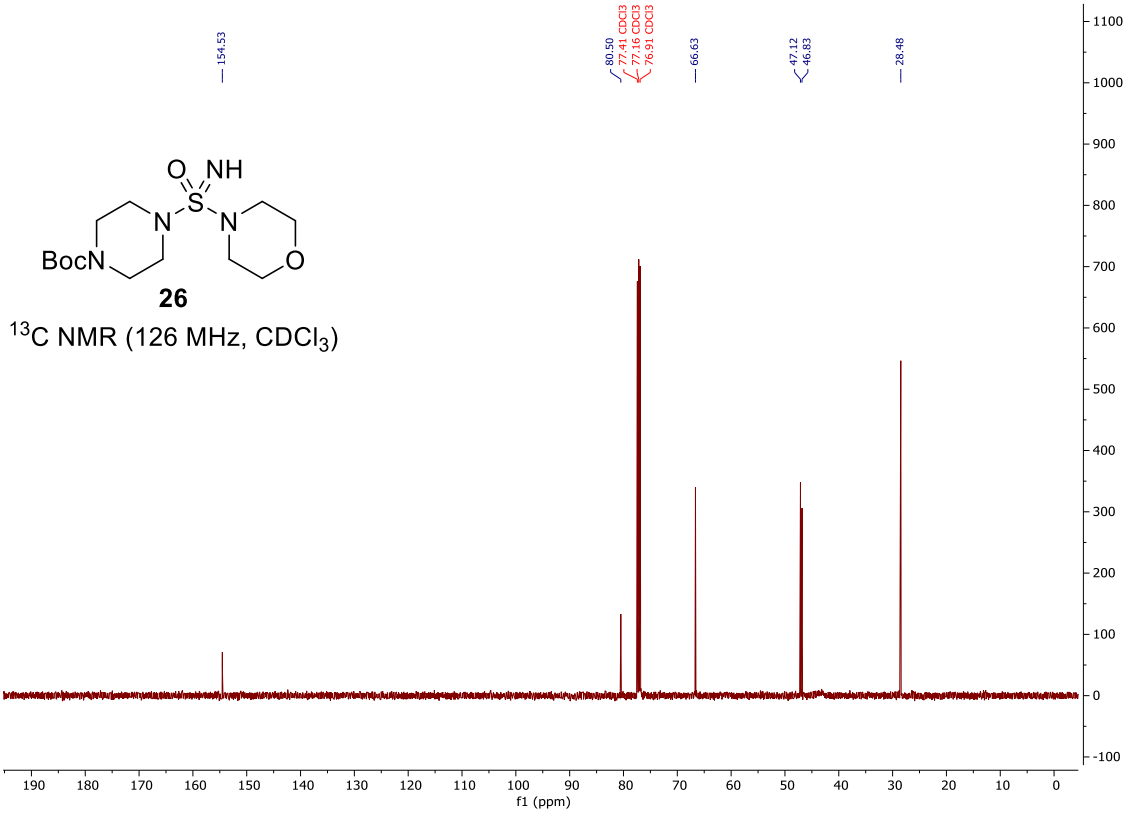


tert-Butyl 4-(morpholine-4-sulfonimidoyl)piperazine-1-carboxylate (26)



26

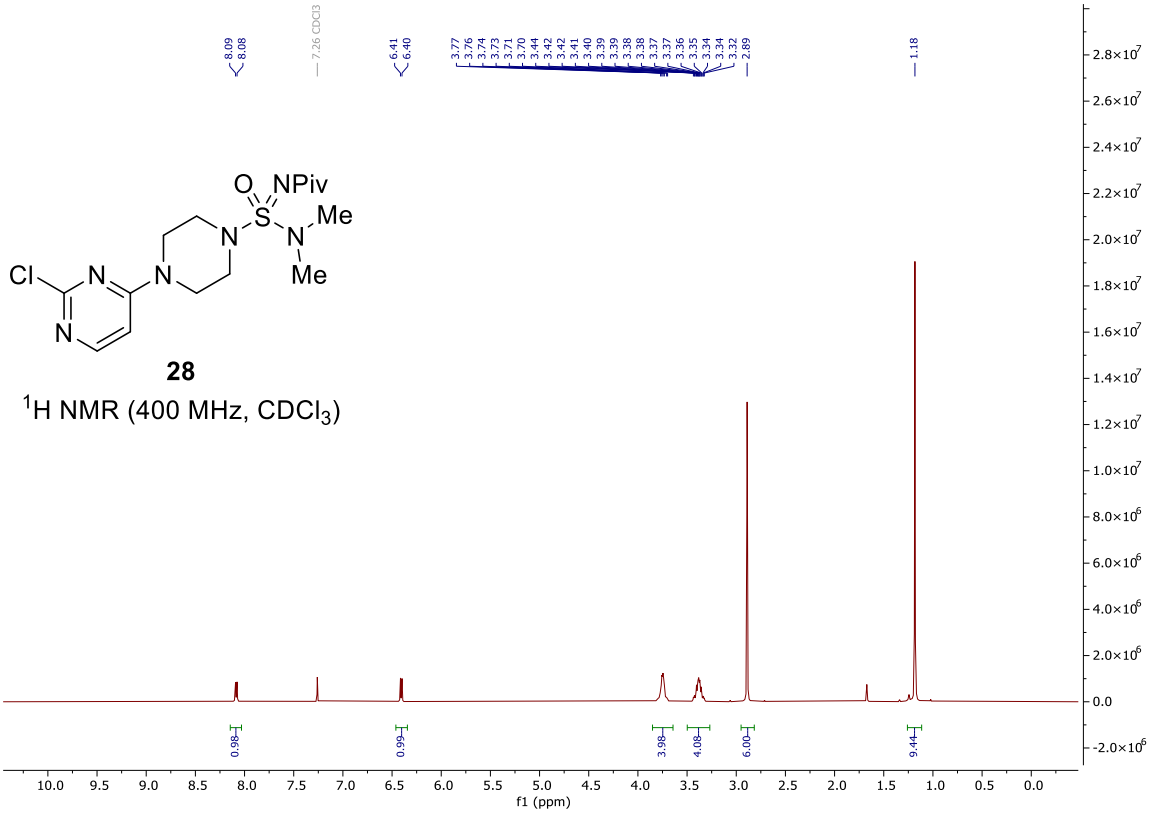
^{1}H NMR (500 MHz, $CDCl_3$)

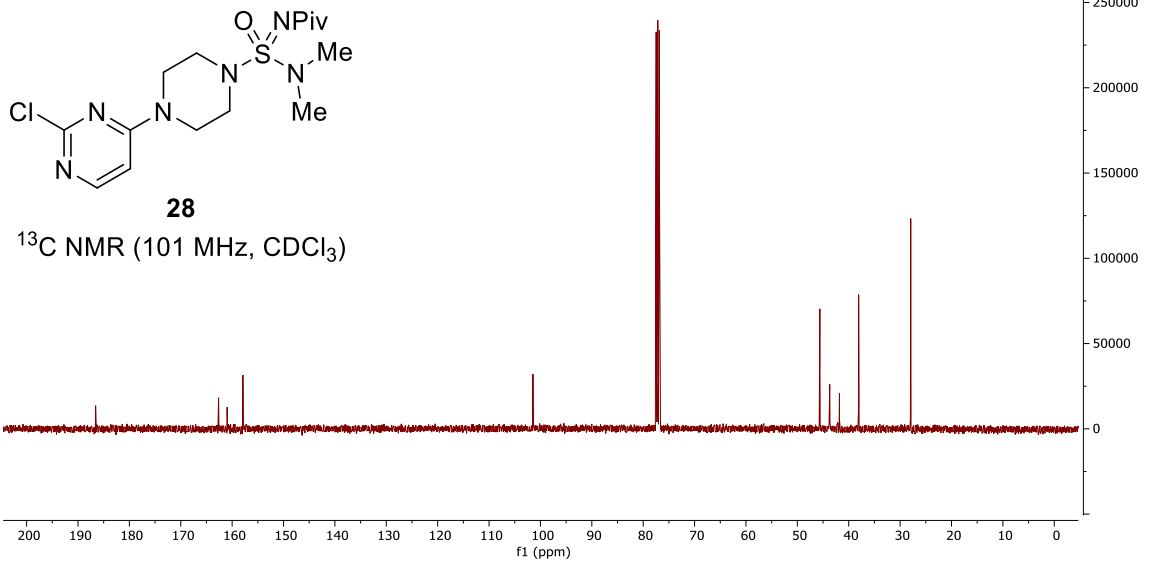


26

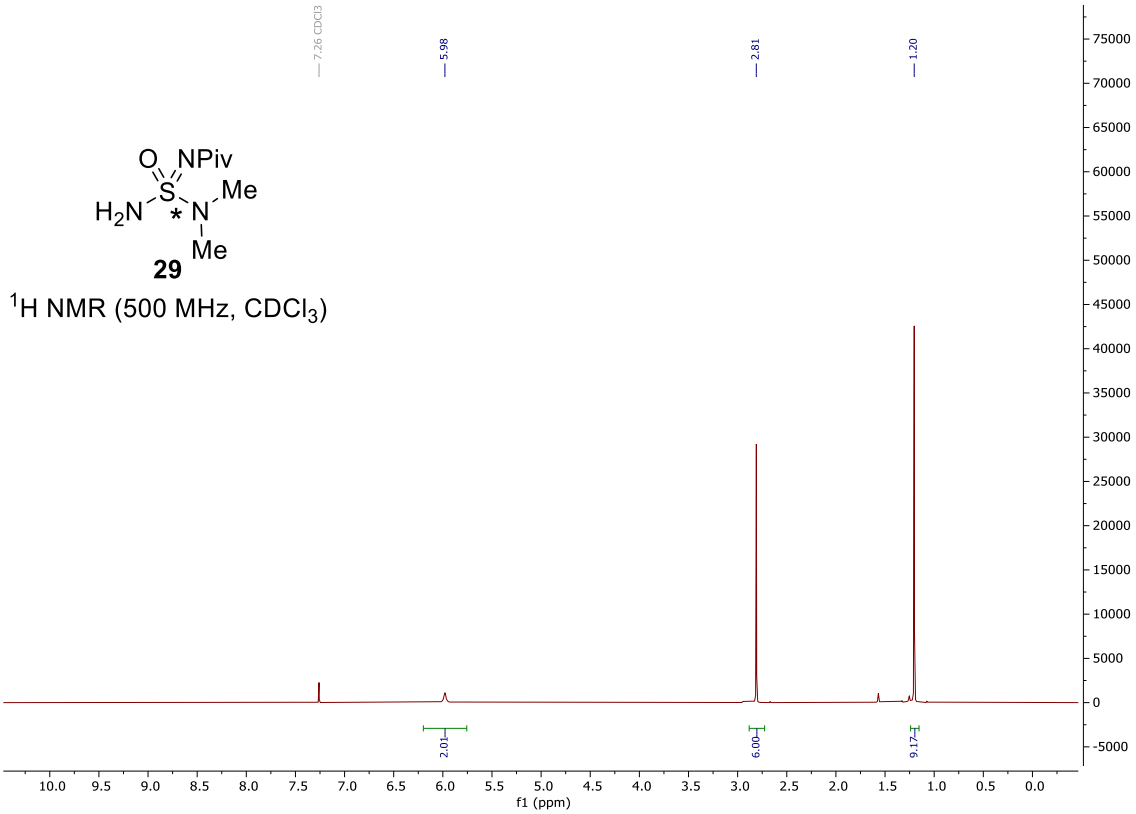
^{13}C NMR (126 MHz, $CDCl_3$)

_N_-((4-(2-chloropyrimidin-4-yl)piperazin-1-yl)(dimethylamino)(oxo)-lλ6-sulfaneylidene)pivalamide (28)

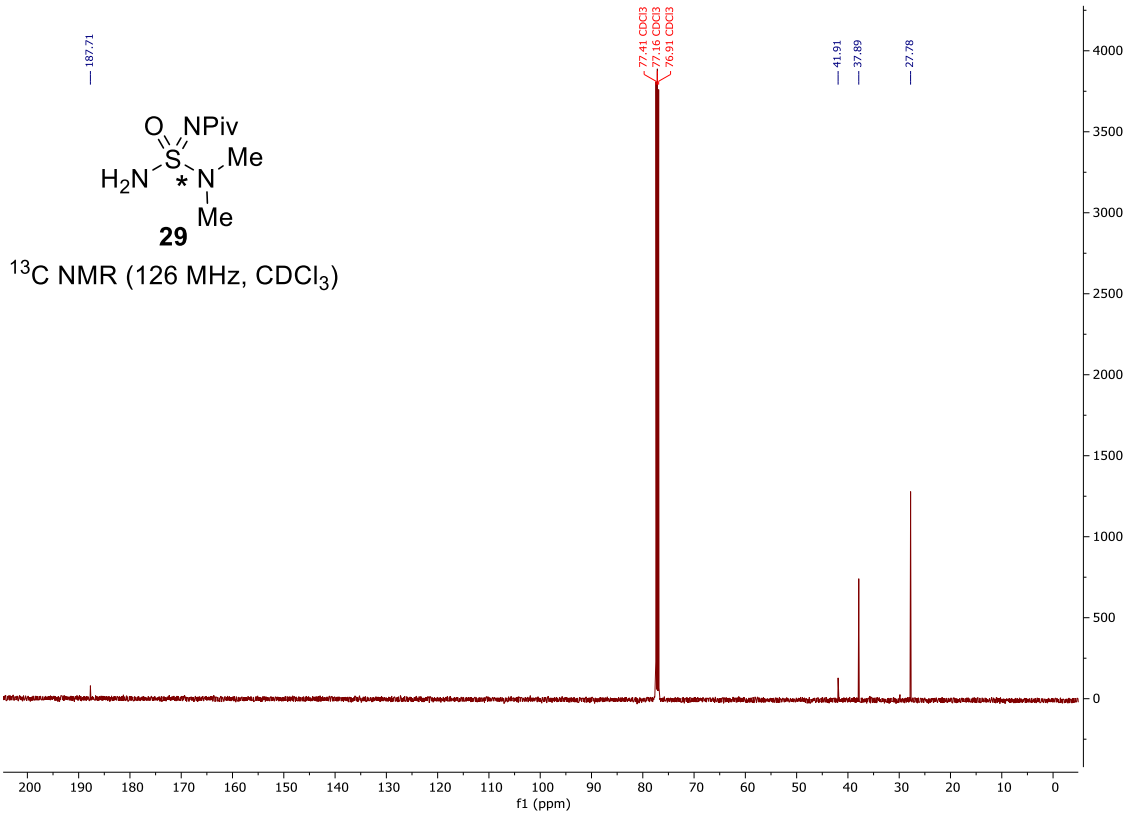




_N_-(amino(dimethylamino)(oxo)-λ6-sulfaneylidene)pivalamide

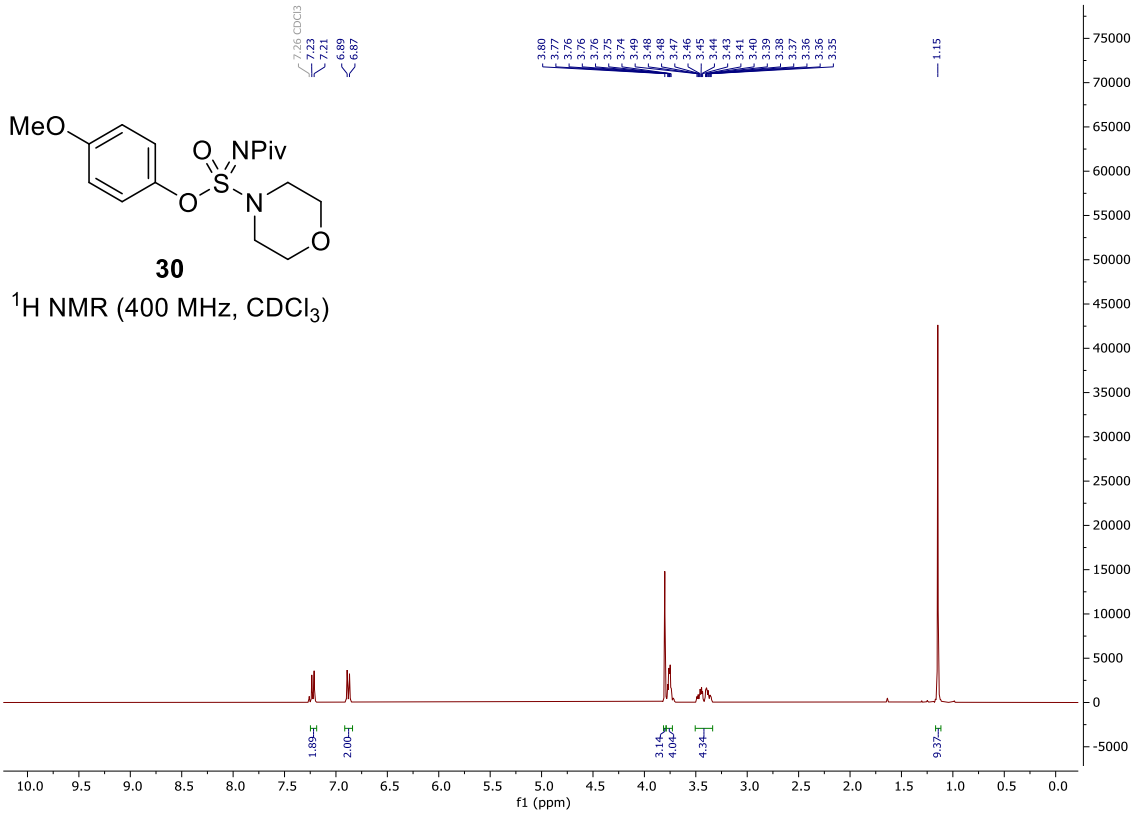


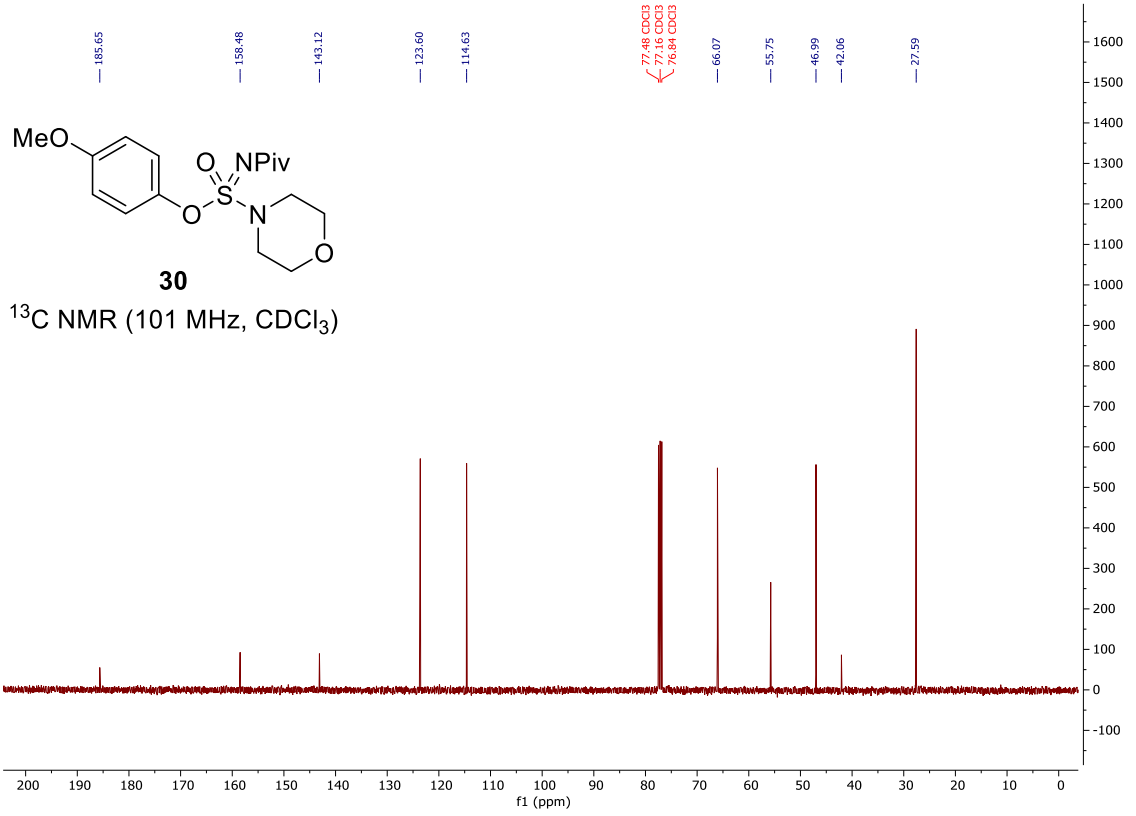
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

4-Methoxyphenyl *N*-pivaloylmorpholine-4-sulfonimidate (30)

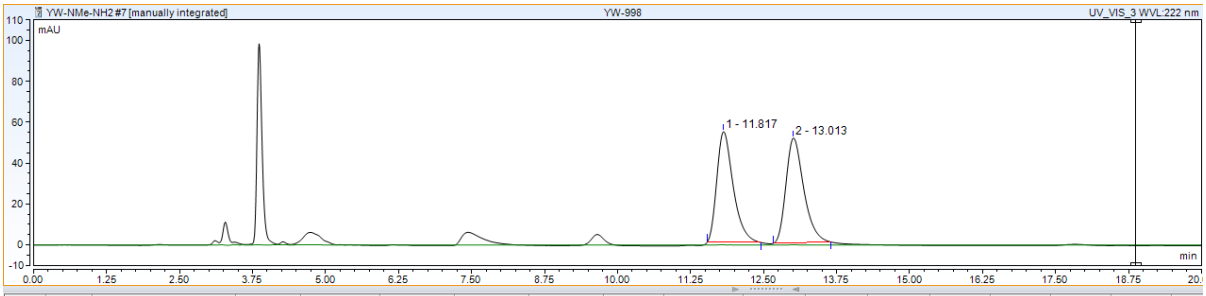




HPLC Chromatograms

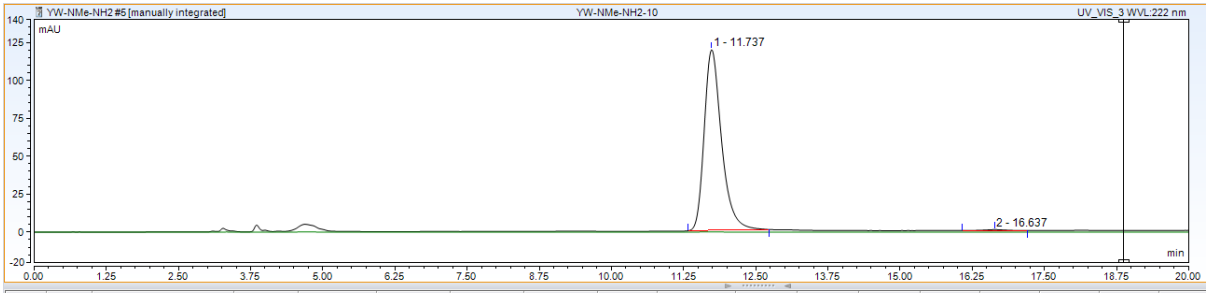
Column: Daicel Chiralpak IA column; Solvent n-hexane/IPA (95:5); flow rate:1 mLmin^{-1}, 25 °C, UV detection wavelength: 222 nm

Chromatogram for **25q: (*rac*)**



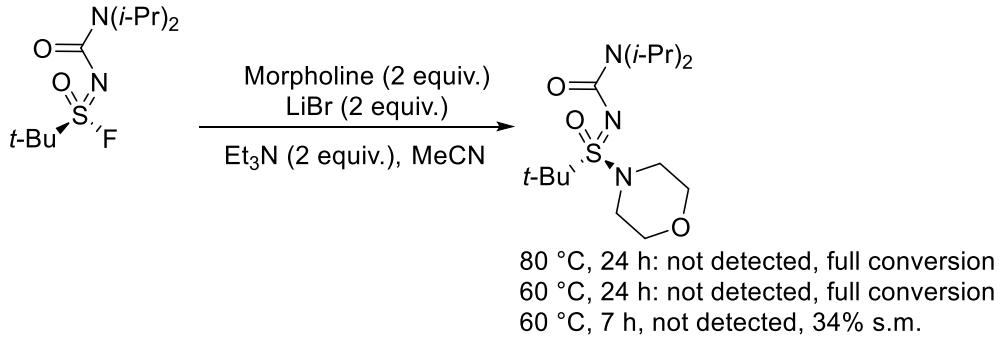
Peak No.	Peak Name	Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU	Type	Width (50%) min	Asym. EP	Resol. EP	Plates EP
1		11.817	n.a.	49.18	17.5072	53.98	BMB*	0.294	1.42	2.29	8925
2		13.013	n.a.	50.82	18.0890	51.26	BMB*	0.321	1.35	n.a.	9083
Maximum			0.0000	50.82	18.0890	53.98		0.321	1.42	2.29	9083
Minimum			0.0000	49.18	17.5072	51.26		0.294	1.35	2.29	8925
Sum			0.0000	100.00	35.5962	105.24					

Chromatogram for **25q'**

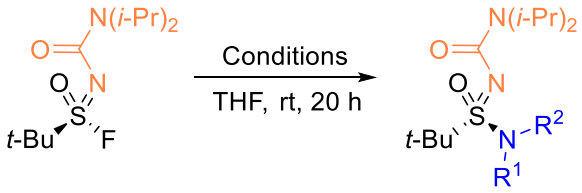


Peak No.	Peak Name	Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU	Type	Width (50%) min	Asym. EP	Resol. EP	Plates EP
1		11.737	n.a.	99.37	41.5083	119.16	BMB*	0.310	1.35	8.19	7943
2		16.637	n.a.	0.63	0.2630	0.61	M	0.396	1.03	n.a.	9795
Maximum			0.0000	99.37	41.5083	119.16		0.396	1.35	8.19	9795
Minimum			0.0000	0.63	0.2630	0.61		0.310	1.03	8.19	7943
Sum			0.0000	100.00	41.7712	119.77					

Appendix

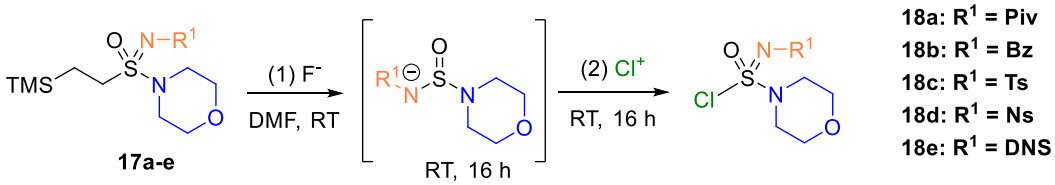


Appendix 1 Bull's condition for SuFEx amination with *t*-BuSF.



entry	Nucleophile	Base	Yield (**18**)
1	*N*-methyl-*p*-anisidine (1.0 equiv.)	NaHMDS (2.0 equiv.)	30%
2	*N*-methyl-*p*-anisidine (1.0 equiv.)	NaHMDS (3.0 equiv.)	30%
3	*N*-methyl-*p*-anisidine (1.0 equiv.)	NaHMDS (2.2 equiv.)	34%
4	*N*-methyl-*p*-anisidine (1.0 equiv.)	NaHMDS (1.8 equiv.)	32%
5	*N*-methyl-*p*-anisidine (1.2 equiv.)	NaHMDS (2.2 equiv.)	43%
6	*N*-methyl-*p*-anisidine (1.5 equiv.)	NaHMDS (2.2 equiv.)	54%
7	Morphoine (1.5 equiv.)	NaHMDS (2.2 equiv.)	n.d.

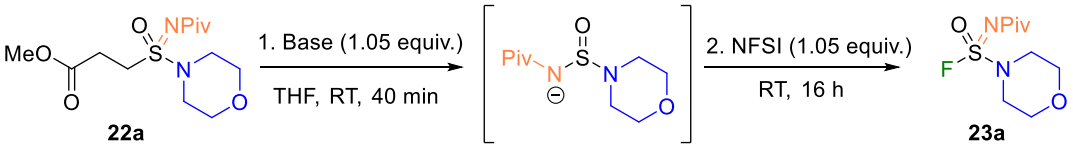
Appendix 2 SuFEx amination of *t*-BuSF with NaHMDS as base.



entry	Fluoride Soruce	Cl^+	R^1	Yield (**18**)
1	CsF (2.0 equiv.) 2 h	TCCA (0.5 equiv.)	Piv	n.d.
2	CsF (2.0 equiv.) 2 h	TCCA (0.5 equiv.)	Bz	50%
3	CsF (3.0 equiv.) 2 h	TCCA (0.5 equiv.)	Bz	48%[a]
4	TBAF (1.1 equiv.) 10 min	TCCA (0.5 equiv.)	Bz	n.d.
5	AgF (2.0 equiv.) 2 h	TCCA (0.5 equiv.)	Bz	n.d.
6	TMAF (1.1 equiv.) 10 min	TCCA (0.5 equiv.)	Bz	n.d.
7	KF (1.1 equiv.)[b] 2 h	TCCA (0.5 equiv.)	Bz	n.d.
8	CsF (1.2 equiv.)[c] 10 min	TCCA (0.5 equiv.)	Bz	n.d.
9	CsF (2.0 equiv.) 2 h	TCCA (0.5 equiv.)	Ts	44%
10	CsF (2.0 equiv.) 2 h	TCCA (0.7 equiv.)	Ts	49%
11	CsF (2.0 equiv.) 2 h	*t*-BuOCl (1.5 equiv.)	Ts	13%
12	CsF (2.0 equiv.) 2 h	TCCA (0.7 equiv.)[d]	Ts	48%
13	TBAF(*t*-BuOH)$_4$ (1.1 equiv.) 10 min	TCCA (0.7 equiv.)[d]	Ts	11%
14	CsF (1.5 equiv.) 2 h	TCCA (0.7 equiv.)[d]	Ns	60%
15	CsF (1.5 equiv.) 2 h	TCCA (0.7 equiv.)[d]	DNS	n.d.
16	CsF (2.0 equiv.) 2 h	Benzyl bromide (1.5 equiv.)	Ts	48%

[a] 1:1 mixture with SAFs [b] With 1.1 equiv. 18-Crown-6
[c] with 0.1 equiv. Schreiner's Catalyst [d] 2.5 h

Appendix 3 Condition screening for synthesis of sulfuramidimidoyl chloride.



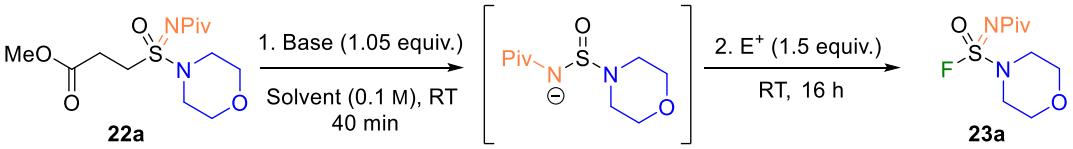
22a
0.1 mmol

23a

entry	Base	Yield (**23a**)
1	*t*-BuOK	31%
2	LiHMDS[a]	n.d.
3	NaHMDS[a]	33%
4	KHMDS[b]	51%
5	NaH	n.d.
6	Et_3N	n.d.
7	DBU	36%
8	KHMDS[b]	56%[c]
9	KHMDS[b,d]	39%[c]
10	NaHMDS[a,e]	52%[c]
11	KHMDS[b,f]	52%[c]
12	KHMDS[g]	68%[c]
13	KHMDS[g] (1.2 equiv.)	80%[c], (74%)[c,h]

[a] 1.0 mol solution in THF. [b] 0.5 mol solution in toluene [c] 1.5 equiv. NFSI
[d] Retro-Micahel reaction performed at 0 °C [e] 15-Crown-5 (1.05 equiv.) as additive
[f] 18-Crown-6 (1.05 equiv.) as additive [g] 1.0 mol solution in THF
[h] Reaction performed at 3.0 mmol

Appendix 4 Base screening for SAFs synthesis through retro-Michael reaction.



entry	Base	Solvent	Electrophile	Yield (**23a**)
1	KHMDS[a]	THF	1-Fluoropyridinium triflate	n.d.
2	KHMDS[a]	THF	TCCA[b]	16%[c]
3	DBU	MeCN	NFSI	33%
4	DBU	MeCN	Selectfluor	28%
5	DBU	MeCN	TCCA	20%
7	KHMDS[a]	Toluene	NFSI	51%
8	KHMDS[d] (1.2 equiv.)	THF[e]	NFSI	51%
9	KHMDS[d] (1.2 equiv.)	THF[f]	NFSI	53%

[a] 0.5 mol solution in toluene [b] 0.5 equiv. [c] sulfuramidimidoyl chloride
[d] 1.0 mol solution in THF [e] 0.2 M [e] 0.05 M

Appendix 5 Solvent and electrophile effect.