Heteroatom-Substituted Bicyclo[1.1.1]pentanes

Helena Pickford

Jesus College
University of Oxford

Doctor of Philosophy

Trinity Term 2022

Thesis dedicated to my parents

Jo and Chris Pickford

I. Acknowledgements

Ed, thank you for welcoming me into the EAA group and for all the support and opportunities you have given me over the last four years. It has been a huge learning experience, and I do not think I ever realised quite how far I would come. The EAA group has been a great environment to develop as a chemist and has enabled my confidence to grow. I am looking forward to celebrating in EAA style with mint chocolate martinis!

I am proud to have had the support and funding from the SBM CDT, Jesus College, EPSRC and industrial partners.

My industrial supervisor Russell, thank you for supporting me with such enthusiasm! Your positivity and advice have been essential to my projects and personal development. James, thank you for your contributions to the aziridine and Giese projects and your partnership on early BCP projects within the group. Jim, thank you for being an excellent college advisor and for your reassurance. Attending High Table was an absolute highlight!

To those who taught and inspired my passion for Chemistry along the way, thank you to Prof. Jeremy Robertson, Dr Paul Roberts, Mrs Kingston and Mrs Vaughan.

Beth, we made it! I don't know how we would have gotten through the last few years without each other, a continual supply of earl grey tea and spontaneous kitchen dancing. You have been a source of daily laughter and support, and I am extremely glad we ended up sitting next to each other on our first day. Jeremy, as much as I complained about the suboptimal milk temperature of the coffee and, in fact, my dislike of coffee, I miss the daily lab Horsebox trips! As one of the original Best Chemistry Pals, I am very grateful for all you taught me. Ali, another BCP original, it has been great to have another cycling buddy in the group, and I wish you all the best on your adventures in California! Nils, thank you for entertaining me whilst thesis writing and for pre 6 am conversations! Ryan thank you for all your assistance with the BCB compounds and for always asking the good questions. PJ, you are just priceless, don't change.

Thanks to every member who has been involved in the small rings team for insightful discussions – Jeremy, Beth, Ali, Marie, Ryan, Nils, Marius, Dimitri, Carlos, and all those who joined for shorter periods along the way. F9 and the entire EAA group, past and present, it has been a delight to work alongside and share ideas with you all. I wish you all the best. ps. I am sorry I broke so many B24 swan neck adaptors. A special mention to all those who helped proofread this thesis.

Amber and Kirsten, thank you for everything you have taught me about X-ray crystallography and for answering my countless questions so patiently.

To the OUWLRC squads of 21' and 22', and coaches Nic and Tina, you've made juggling the schedule and the trials of being a student-athlete not only somehow possible but also tremendous fun! I have great pride in being a part of such a determined and supportive team of women. Thank you to JCBC for re-starting my rowing journey, even after I said *'never ever again'*.

Thank you to everyone who keeps the CRL running. In particular to the catering staff, the tea and coffee trolley over lockdown was a favourite!

A very special thank you to my family. In particular to my parents, thank you for all your generosity and support over the years, and well done for putting up with me!

II. Declaration

The experimental work presented in this thesis was completed at the Chemistry Research Laboratory, Department of Chemistry, University of Oxford between Hilary Term 2018 and Trinity Term 2022.

The following individuals are credited for their contributions:

Dr Jeremy Nugent prepared α-iodoaziridines **2w** – **2ab**, BCP iodides **4aa1**, **4ab1** and **4ac1**, radical acceptor **6u** and sulfinate salts **18b-S**, **18j-S** and **18l-S**

Ms Bethany Shire prepared BCP iodides **4i1** and **4k1**.

Mr Frank Nightingale prepared BCP iodide **4ad1.**

Mr Nils Frank prepared TCHep precursor **30**.

Mr Ryan McNamee synthesised of BCBs precursors **31a – 31d** and assisted in the characterisation of cyclobutyl halides **31a-I – 31d-I.**

Dr Tarn Johnson prepared sulfinate salts **18d-S**, **18e-S**, **18g-S**, **18i-S**, **23a-S**, **25c-S**, **25e-S**, **25h-S** and **25j-S**.

Dr Amber Thompson and Dr Kirsten Christensen assisted with X-ray crystallography.

Helena D. Pickford

May 2022

III. Abbreviations

ABB	Azabicyclo[1.1.1]butane
Ac	Acyl
acac	Acetylacetonate
AIBN	Azobisisobutyronitrile
An.	Anhydrous
App.	Apparent
Aq.	Aqueous
Ar	Aryl
Atm.	Atmosphere
ATRA	Atom Transfer Radical Addition
BCB	Bicyclo[1.1.0]butane
BCHep	Bicyclo[3.1.1]heptane
BCP	Bicyclo[1.1.1]pentane
BCPA	Bicyclo[1.1.1]penylamine
BDE	Bond Dissociation Energy
Bn	Benzyl
Br.	Broad
BTMG	2-*t*-Butyl-1,1,3,3-tetramethylguanidine
Bu	Butyl
Cat.	Catalyst
Cbz	Benzyloxycarbonyl
CI	Chemical Ionisation
Conc.	Concentration
CY	Cytochrome
d	Doublet
DBAD	Di-*t*-butyl-diazene-1,2-dicarboxylate
DBH	1,3-Dibromo-5,5-dimethylhydantoin
DCE	1,2-Dichloroethane
DEAD	Diethyl azodicarboxylate
Decomp.	Decomposition
DG	Directing Group
DIBAL	Di-*iso*-butyl Aluminium Hydride
DID	2,2-Diiododimedone
DIH	1,3-Di-iodo-5,5-dimethylhydantoin
DMF	Dimethylformamide
dppp	1,3-Bis(diphenylphosphino) propane
dr	Diasteromeric ratio
ee	Enantiomeric excess
EDA	Electron-donor-acceptor
EI	Electron Ionisation
ESI	Electrospray Ionisation
Et	Ethyl
Equiv.	Equivalents
fac-	Facial
Fc	Ferrocene
FDA	Food and Drug Administration
FT	Fourier Transform
FVP	Flash vacuum pyrolysis
glyme	1,2-Dimethoxyethane
h	hour

HAT	Hydrogen Atom Transfer
HATU	Hexafluorophosphate Azabenzotriazole Tetramethyl Uronium
HE	Hantzsch Ester
Het	Hetero-
HRMS	High Resolution Mass Spectrometry
i-	*iso-*
IR	Infra-Red Spectrometry
LA	Lewis Acid
LAH	$LiAlH_4$
LED	Light Emitting Diode
LCT	Liquid Chromatography
LG	Leaving Group
LPA	Lysophosphatidic Acid
LRMS	Low Resolution Mass Spectrometry
m-	*meta-*
m	Multiplet
Me	Methyl
MEK	MAPK ERK Kinase
Min.	Minutes
m.p.	Melting Point
Ms	Mesyl
MS	Molecular Sieves
MTBE	Methyl *t*-Butyl Ether
m/z	Mass to Charge Ratio
n-	*normal-*
NBS	*N*-Bromosuccinamide
NBrSacc	*N*-Bromosaccharin
NHIP	*N*-Hydroxyphthalimide
NIS	*N*-Iodosuccinamide
NMR	Nuclear Magnetic Resonance
Ns	Nosyl
NSAID	Nonsteroidal Anti-Inflammatory Drug
o-	*ortho-*
Obsc.	Obscured
OC	Organocatalyst
p-	*para-*
pc	Phthalocyanine
PC	Photocatalyst
Pent	Pentyl
PG	Protecting Group
Ph	Phenyl
PPTS	Pyridinium *p*-Toluenesulfonate
Pr	Propyl
PTAB	PhNMe^{3+} Br^{3-}
Pyrm	Pyrimidine
Pyrz	Pyrizine
q	Quartet
quin.	Quintet
R	Generic Group/Substituent
Ref.	Reference
rt	Room Temperature
s	Singlet
SAR	Structure-Activity Relationship
Sat.	Saturated

s	Seconds
SET	Single Electron Transfer
SCE	Saturated Calomel Electrode
S_H2	Homolytic Substitution
SOMO	Singularly Occupied Molecular Orbital
sxt.	Sextet
t-	*tert*-
t	Triplet
TBAB	Tetra-*n*-Butylammonium Bromide
TBAP	Tetra-*n*-Butylammonium Perchlorate
TBHP	*t*-Butyl Hydroperoxide Solution
TCHep	Tricyclo[3,1,1]heptane
TCP	Tricyclo[1.1.1.0^{1,3}]pentane
TFA	Trifluoroacetic Acid
THF	Tetrahydrofuran
TOF	Time of Flight
Tol	Tolyl
TLC	Thin Layer Chromatography
TMEDA	Tetramethylethylenediamine
TTMSS	Tris(trimethylsilyl)silane
Ts	Tosyl
UV	Ultra Violet
X	Halide
3D	Three-Dimensional

IV. Contents

3. Functionalisation of BCP(A) Iodides 55

4. Sulfonyl Substituted BCPs 95

V. Abstract

The theme of this thesis is to explore novel methodologies to access useful heteroatom-substituted bicyclo[1.1.1]pentane (BCP) scaffolds. BCPs are utilised as non-classical bioisosteres and as a metabolically stable spacer unit in their own right within pharmaceutical and agrochemical industries, they have also found application in materials chemistry.

Firstly, we investigated the addition of nitrogen-centred radicals across the strained central bond of [1.1.1]propellane **1** as an efficient entry to *N,I*-disubstituted BCPs (Figure i). In an atom-transfer radical addition (ATRA) process, we demonstrated fragmentation of α-iodoaziridines **2** for the formal addition of *N,I* across **1** to give iodo-bicyclo[1.1.1]pentylamines (BCPAs) **3**. The developed methodology demonstrates good functional group tolerance and applicability to pharmaceutical analogues.

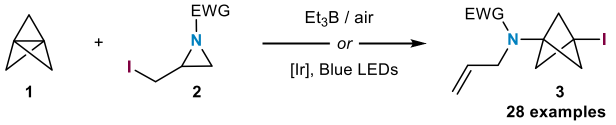


Figure i: α-Iodoaziridine fragmentation and ATRA reaction to achieve BCPA iodides.

Having discovered that BCPA iodides were significantly more challenging to functionalise than carbon-substituted BCPs, due to expulsion of the amine component from anionic BCPA intermediates, the development of a novel C–C bond formation tolerant of heteroatom-substituted BCP halides was required. Through investigation into the use of photocatalysis as a means to generate BCPA radical intermediates, we demonstrated that the resident iodide of BCP(A) iodide compounds could be functionalised through a photocatalysed silyl-mediated Giese reaction (Figure ii). This transformation enables access to challenging and desirable *N,C*-disubstituted BCPAs **4**, for example α-amino acid analogues. In combination, these two methodologies contribute a significant advancement to the field and provide access to aniline and *N*-*t*-butyl bioisosteres.

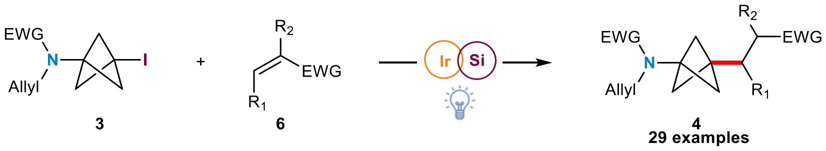


Figure ii: Photocatalysed Giese reaction of BCPA iodides.

Following a serendipitous result from the synthesis of BCPA iodides, we discovered that sulfonyl halides, generated *in situ* from readily accessible sulfinate salts **18-S**, add rapidly to [1.1.1]propellane **1** under mild conditions and in exceptional yields (Figure iii). This methodology represents the first synthesis of sulfonyl BCP iodides and bromides **18-X**.

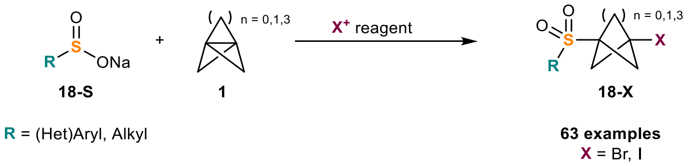


Figure iii: In situ generation of sulfonyl halides for the synthesis of sulfonyl BCP iodides

1.

Introduction

1.1 The Potential of Bioisosteres

1.1.1 Challenges Within the Pharmaceutical Industry

Bringing a new drug to market takes a pharmaceutical company between 10 – 15 years and costs \$1 – 2 billion dollars.[1] Thousands of potential compounds are steadily funnelled through the drug discovery bottleneck through this labour intensive process; consideration of Lipinski's rule of five or computer-aided drug-design modelling is often employed to streamline the process.[2, 3] Consequently, the pharmaceutical industry is at risk of restricting progress in discovering novel drug molecules due to accessing only a fraction of available chemical space.[4] A potential cause of lack of diversity stems from the uptake of quick and practical chemistry such as amide bond formations, S_NAr reactions and Suzuki cross-couplings, for example resulting in (hetero)arene rich compound screening libraries.[5] Therefore, research into new methodologies and new structural motifs is of increasing value in the search for effective drug candidates.

The pharmaceutical industry is beginning to address the need to explore a wider area of chemical space through a diversity orientated approach to drug discovery.[6] The use of bioisosteric replacements of certain functional groups offers a potential solution to this challenge. The widely accepted definition for a classical bioisostere was termed by Burger in 1991:[7]

> *"Compounds or groups that possess near-equal molecular shapes and volumes, approximately the same distribution of electrons, and which exhibit similar physicochemical properties…"*

However, consideration of 'nonclassical' bioisosteres allows for more freedom in structural, electronic and physicochemical properties compared to the parent analogues, and is perhaps more helpful to consider when aiming to increase diversity within the pharmaceutical industry.

1.1.2 Pharmaceutical Applications of Nonclassical Bioisosteres

Bioisosteric modification enables fine-tuning within structure-activity relationship (SAR) studies of new lead compounds. It is a powerful tool for the design of new drug candidates, agrochemicals and materials.[8-10] By surveying a broader range of steric and electronic properties, the degree of drug-like chemical space evaluated can be increased (Figure 1.1).[11, 12] A demonstration of this is the application of carboxylic acid alternatives, such as sulfonamides and isoxazoles, which offer altered pK_as and H-bond donor/acceptor properties.[13] Another example includes surrogates of ketones, esters or amides with increased steric bulk or modified lipophilicity, of which oxetanes have been of particular success.[14] Spiro and fused motifs have also demonstrated the importance of considering the conformational flexibility of target compounds.[15, 16] Similarly, replacement or arene groups with rigid 3D, sp^3 rich groups has proven beneficial for metabolic stability and solubility effects.[9, 17] Hence, it is considered that accessing novel bioisosteres will benefit the pharmaceutical and agrochemical industries by diversifying drug-like chemical space, while also enabling intellectual property advantages.

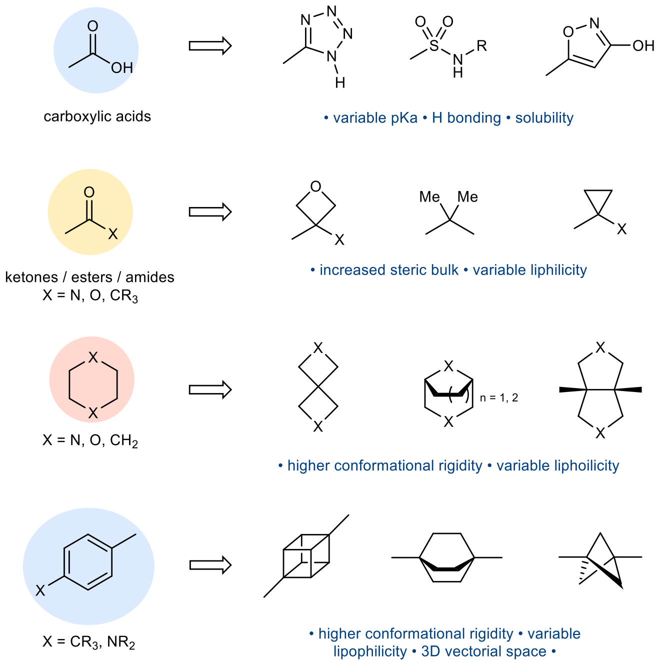


Figure 1.1. Examples of Nonclassical Bioisosteres.

1.2 Bicyclo[1.1.1]pentanes (BCPs)

1.2.1 Applications of BCPs

Bicyclo[1.1.1]pentanes (BCPs) are three-dimensional linkers that have been used as nonclassical bioisosteres of aryl,[10, 18] *t*-butyl,[19] and alkynyl[20] groups in medicinal chemistry (Figure 1.2, a). Although the difference in inter-substituent C–C distance between *p*-substituted arenes and a disubstituted BCP is greater than 1 Å,[21] BCPs possess a 180 ° substituent vector bond angle, meaning they are well proportioned to act as a linker in place of arenes and alkynyl groups (Figure 1.2, b). In addition, the mono-substituted BCP system can be used as an alternative to bulky *t*-butyl groups. The sp^3 rich BCP framework offers a new complement of pharmacokinetic properties for SAR studies, such as interrupted π-stacking interactions, improved lipophilicity, and increased metabolic half-life.[22] [23] Including three-dimensional aspects into drug design probes new vectors of chemical space, accessing new opportunities for identifying successful drug candidates.

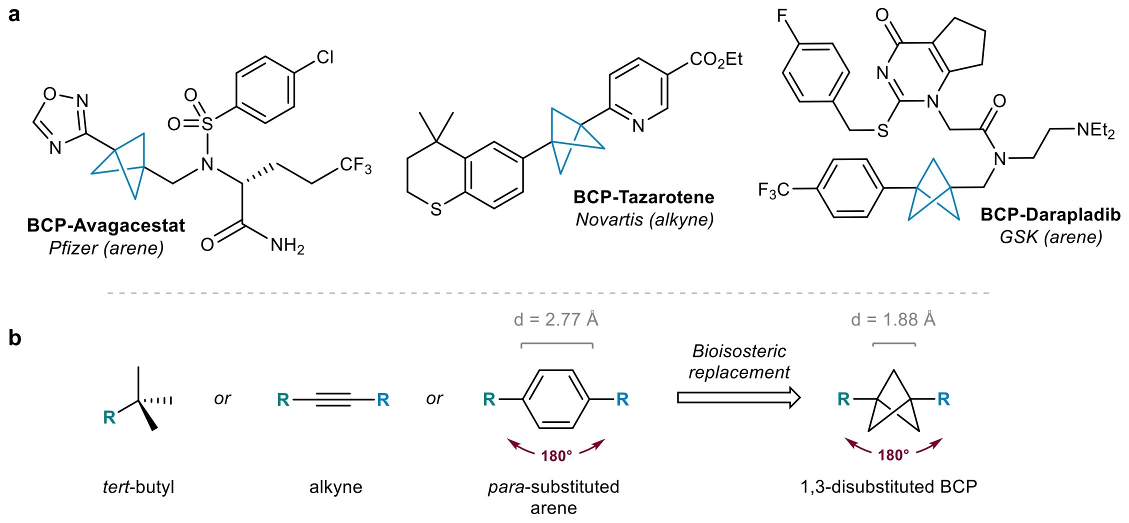


Figure 1.2: a. Bicyclo[1.1.1]pentanes in pharmaceuticals compound. b. Bicyclo[1.1.1]pentanes as surrogates for arenes, alkynes and t-butyl groups.

Complementing their emergence within the pharmaceutical industry, BCPs have found applications in materials and supramolecular chemistry fields (Figure 1.3).[24, 25] Examples include molecular rods,[26] molecular rotors,[27] liquid crystals,[28] FRET sensors,[29] and supramolecular assemblies.[30]

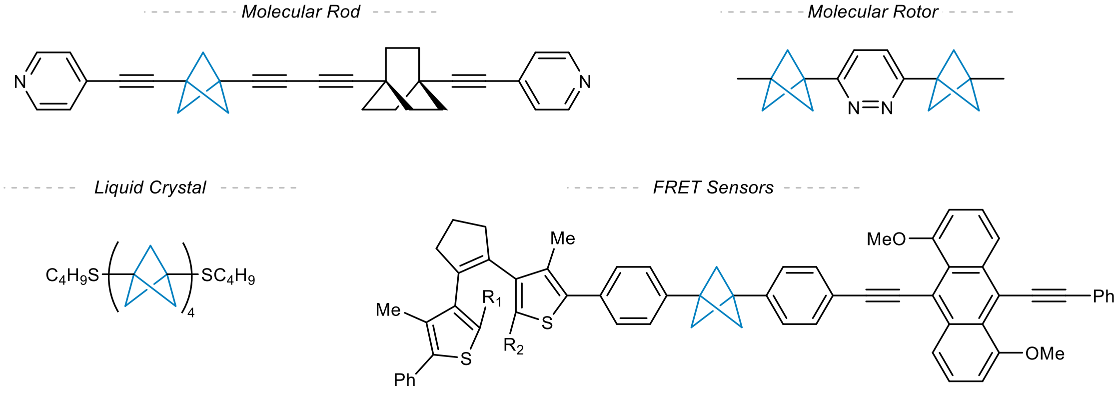


Figure 1.3: Applications of BCPs within materials chemistry.

Over the last five years, BCPs have seen a marked increase in popularity in both synthetic approaches and through their application (Figure 1.4). Therefore, novel methodologies to access BCPs are of interest to further develop the field.

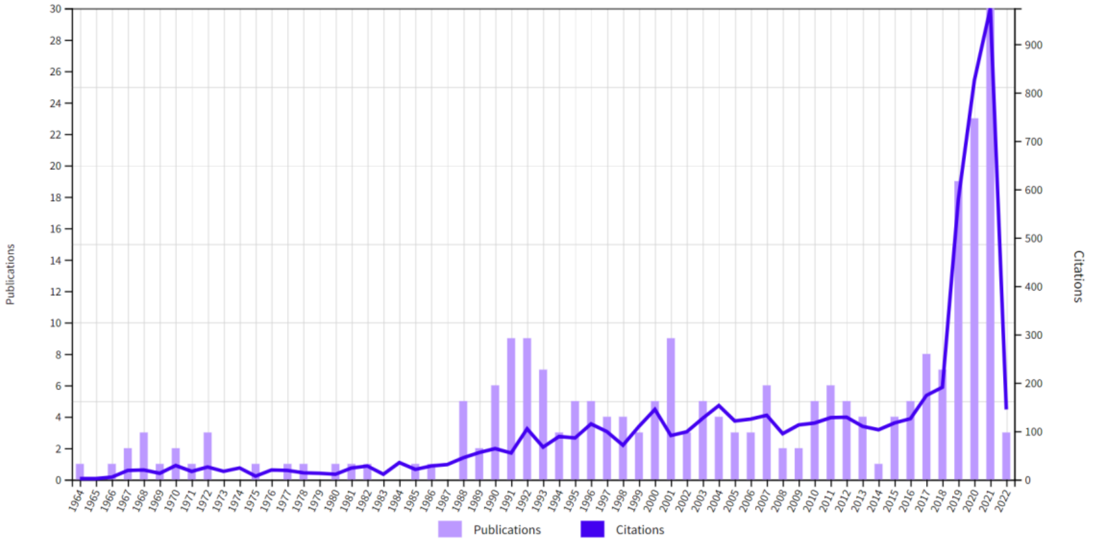


Figure 1.4: Citation Report for 'bicyclo[1.1.1]pentane'. Web of Science - Accessed 07.03.2022.

1.2.2 Synthesis of Bicyclo[1.1.1]pentanes

The first isolation of bicyclo[1.1.1]pentane was described by Wiberg in 1966 through intramolecular Wurtz reaction of dibromocyclobutane, albeit in a poor 1% yield due to elimination and thermal rearrangement products (Figure 1.5, path a).[31] Subsequent syntheses used mercury-sensitised photolysis to implement ring contraction of the bicyclo[2.1.1]pentanone (path b),[32] and cycloaddition of 1,4-pentadiene (path c).[33] Cyclopropanation of bicyclo[1.1.0]butane via diazomethane carbene insertion is another route to BCPs (path d).[34] Reaction across the central C–C bond of [1.1.1]propellane **1** has by far been the most utilised method to access BCPs with considerably milder reaction conditions (path e).[35]

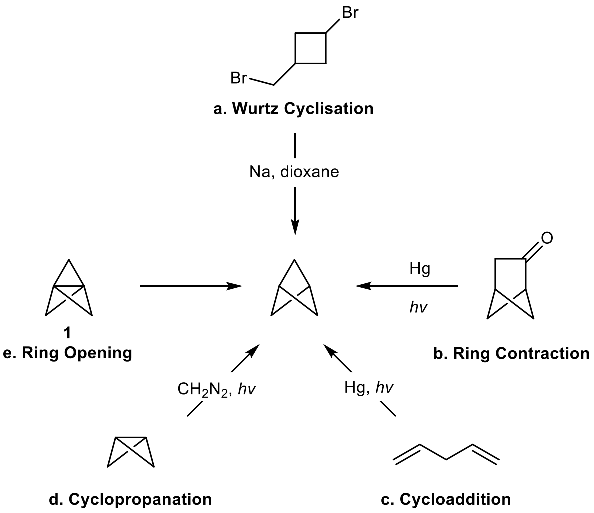


Figure 1.5: Early syntheses of bicyclo[1.1.1]pentanes.

1.2.3 [1.1.1]Propellane

In 1982 Wiberg reported the first synthesis of [1.1.1]propellane **1**, achieved by lithiation and cyclisation of the now commercially available bis(chloromethyl)dibromocyclopropane

(Figure 1.6, a).[35] The preferred synthesis of **1** remains essentially unchanged and has been optimised to >100 g scale and adapted to flow conditions.[36, 37] Alternative and less efficient preparations of **1** include carbene cyclisation of *exo*-cyclobutene structures[38] and ring closures of 1,3 disubstituted BCPs (Figure 1.6, b).[39-43] Once prepared, [1.1.1]propellane can be conveniently stored in dilute ethereal solutions (typically <1.0 M) at –20 °C for several months; however, neat solutions polymerize spontaneously above 0 °C.[35] Determination of the structure and dimensions of **1** was made possible by the use of low-temperature X-ray crystallography, [44] gas-phase measurements[45] and DFT calculations.[46]

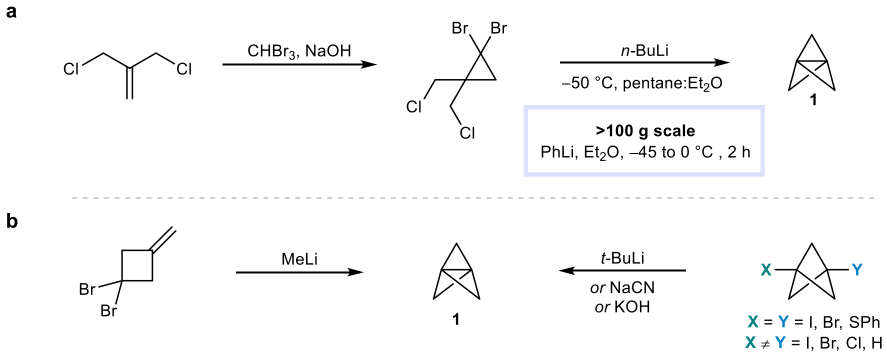


Figure 1.6: Syntheses of [1.1.1]propellane.

[1.1.1]propellane **1** has established itself as the reagent of choice to construct BCPs, owing to its susceptibility to undergo rapid reactions across the central C–C σ bond with nucleophiles, electrophiles and radicals (Figure 1.7).[46, 47]

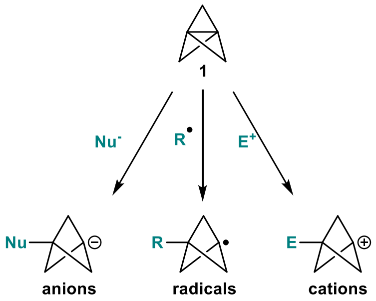


Figure 1.7. Reactivity of [1.1.1]propellane ***1****.*

The reaction of [1.1.1]propellane **1** with radicals is the most expansive research area for BCP synthesis to date, and this approach has successfully enabled the synthesis of both mono- and disubstituted BCPs (Figure 1.8, a).[48] The first reported example of radical addition to **1** obtained a BCP sulfide on reaction with thiophenol (Figure 1.8, b).[49] Following this initial isolation, further development included examples of aryl- and alkyl thiols, and disulfides.[50, 51] A principal example for the addition of carbon-centred radicals to **1** involves the homolysis of diacetyl under mercury irradiation to obtain diketyl BCP (Figure 1.8, b).[52] Sequential oxidation with sodium hypobromite achieved the di-carboxylic acid BCP, which is a key intermediate in the many syntheses of asymmetrically 1,3-disubstituted BCPs (see chapter 4 for examples). Further advancements in radical chemistry have since enabled the generation of carbon-centred radicals under much milder reaction conditions, forgoing the need for harsh irradiation.[47] A range of heteroatom-centred radicals have also undergone radical addition to **1** (Figure 1.8, c), while nitrogen- and sulfur-centred radicals will be covered in greater detail in the following chapters due to their direct link to this thesis (Chapters 2 and 4).

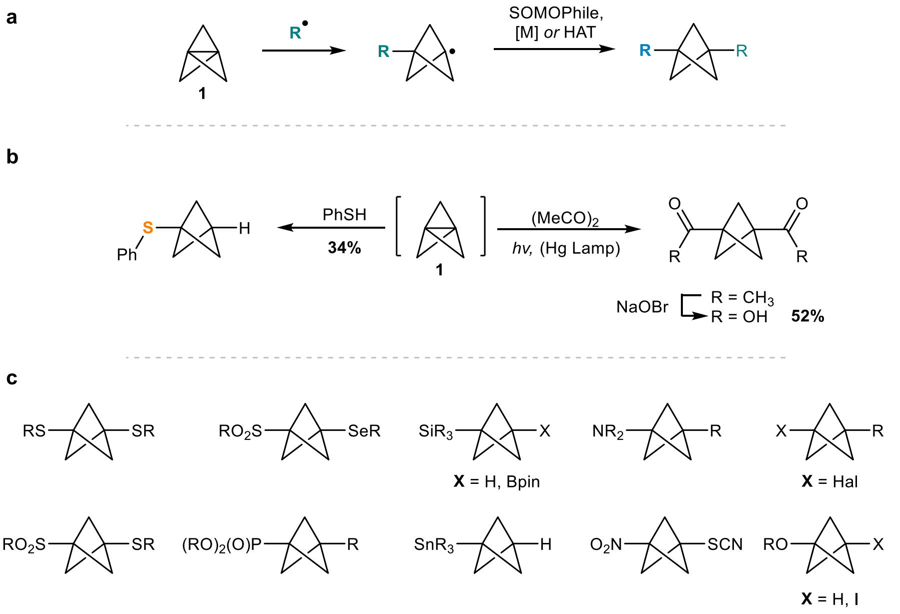


*Figure 1.8: a. Summary of reactivity of [1.1.1]propellane **1** with radicals. b. Early examples of radical addition to **1**, reported yields are from the bis(chloromethyl)dibromocyclopropane precursor. c. Addition of heteroatom radicals to **1**.*

The addition of nucleophilic reagents to [1.1.1]propellane **1** and subsequent reactions of the BCP anionic intermediate have enabled the synthesis of disubstituted BCPs (Figure 1.9, a). Seminal work in this area achieved the addition of aryl Grignard reagents to **1**, and the resulting BCP Grignard intermediate has been trapped with electrophiles (CO_2[41] or RCOCl[20, 53]), or reacted via transmetallation for cross-coupling ($ZnCl_2$ then Pd^{II} or Ni^{II})[20, 53] (Figure 1.9, b). The limitation of this approach lies in the use of high temperatures (up to 100 °C) in low flash point solvents, such as Et_2O, to achieve anionic addition to **1**, leading to the metallated BCP intermediate. Turbo-lithium amides have also demonstrated analogous additions of nucleophilic nitrogen centres to form terminal BCP amides (Figure 1.9, c).[37] This methodology has since been advanced to achieve 1,3-disubstituted-BCPAs through transmetallation with Cu^{I} to couple to activated electrophiles.[54] These selected examples highlight the current state of the art of nucleophilic additions to **1**.

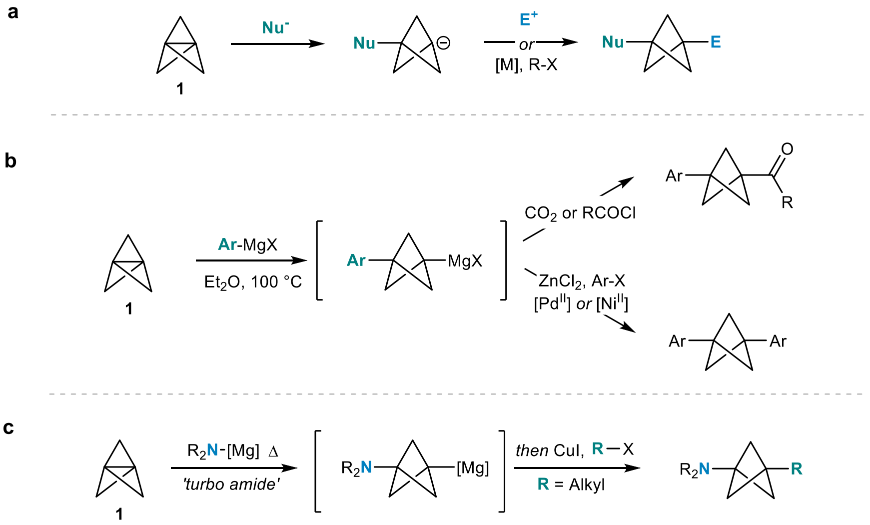


*Figure 1.9: a. Summary of reactivity of [1.1.1]propellane **1** with nucleophiles. b. Reaction of **1** with Grignard reagents. c. Reaction of **1** with lithium amides.*

The reaction of [1.1.1]propellane **1** with electrophiles leads to the generation of a cationic BCP intermediate that undergoes rapid rearrangement to give *exo*-methylene cyclobutane products (Figure 1.10).[41] This rearrangement typically outcompetes interception with nucleophiles. However, cations formed from halo-BCPs are less susceptible to rearrangement and could be trapped with strong nucleophiles.[41]

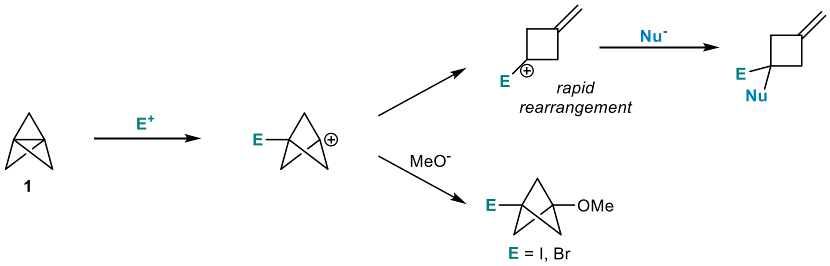


*Figure 1.10: Reaction of [1.1.1]propellane **1** with electrophiles.*

Similar rearrangements of [1.1.1]propellane **1** have been observed on heating to temperatures above 100 °C, or through the generation of carbene intermediates via flash vacuum pyrolysis (FVP) (Figure 1.11, a).[35] [55] Formation of cyclobutene products and higher oligomers have also been initiated by transition metal centres (Figure 1.11, b). Recently, such rearrangement of **1** to metalla-cyclobutylcarbene intermediates has been exploited by Ni^{II} catalysed cyclopropanation of alkenes to form methylenespiro[2.3]hexanes products (Figure 1.11, c).[56] A further example of the reactivity of **1** is the formation of allene and alkyne coupled methylene-cyclobutane products under Cu^{I} catalysis (Figure 1.11, d).[57]

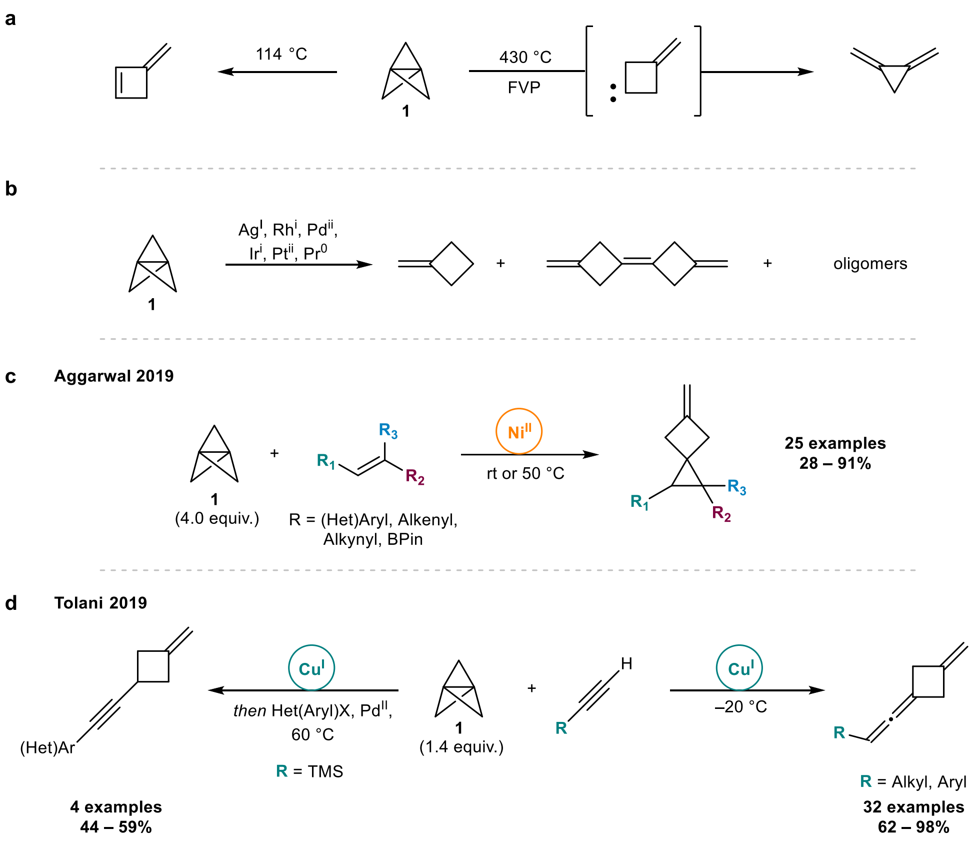


*Figure 1.11: Rearrangements of [1.1.1]propellane **1**.*

1.3 Thesis Aims

This thesis aims to explore novel methods to achieve heteroatom-disubstituted BCPs via the reaction of heteroatom-centred radicals with [1.1.1]propellane **1**, and then to exploit the conveniently installed halide for further functionalisation opportunities (Figure 1.12). At the start of this investigation, the methods available to access such disubstituted hetero-BCPs were limited in comparison to the better-studied carbon disubstituted BCPs. Novel synthetic developments in this field would enable further evaluation of the biological activities and pharmacokinetics of heteroatom-substituted BCPs as bioisosteres. Throughout the research, we aimed to employ practical, effective and mild reaction conditions to achieve the desired compounds while maintaining functional group tolerance, and for the chemistry to be amenable to multigram scale synthesis and pharmaceutical applications.

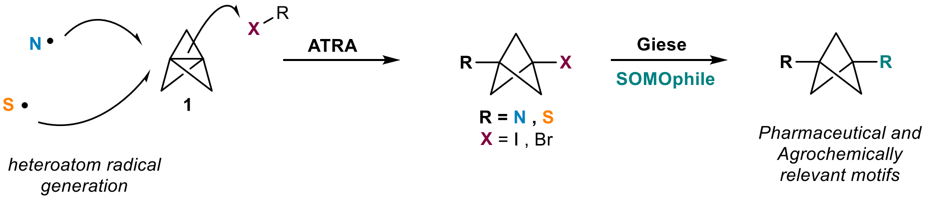


Figure 1.12: Project Overview, methods towards hetero disubstituted BCPs.

The results of this research are split across three chapters, each of which will be introduced in more detail in turn (Figure 1.13). Firstly, we investigate the use of an atom transfer radical addition (ATRA) reaction to obtain synthetically convenient nitrogen-substituted BCP iodides through the generation of nitrogen-centred radicals (Chapter 2). We then highlight the utility of these BCP halides through novel functionalisation methods for C–C bond formation to obtain *N,C*-disubstituted BCPs (Chapter 3). Finally, we develop a practical synthesis of sulfonyl BCP halides through the *in situ* generation of sulfonyl halides (Chapter 4).

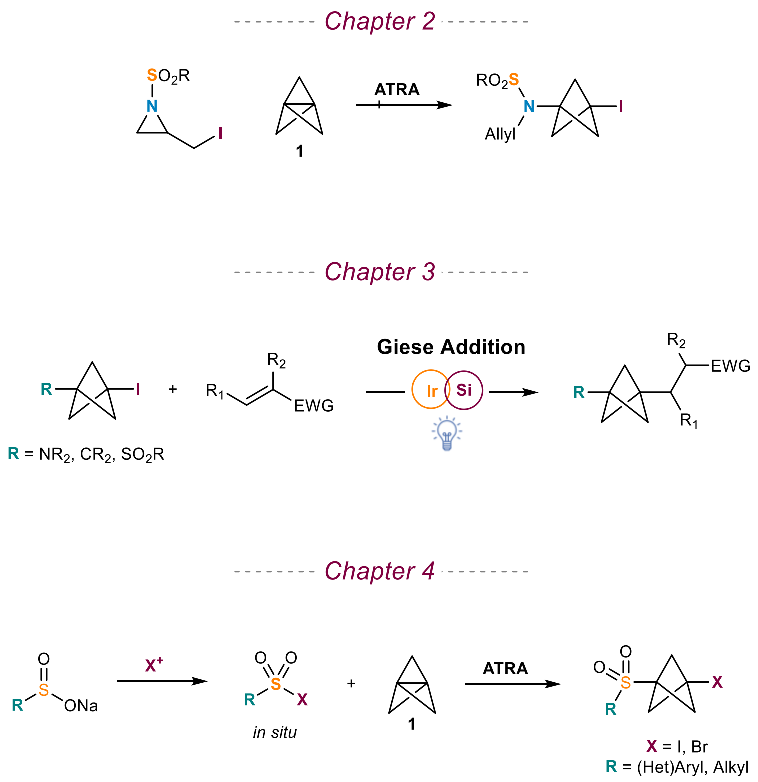


Figure 1.13: Thesis Chapters.

2.

Nitrogen-Substituted BCPs

2.1 Introduction

2.1.1 Bicyclo[1.1.1]pentylamines (BCPAs) as Bioisosteres

Bicyclo[1.1.1]pentyl amines (BCPAs) have the potential to be applied as nonclassical bioisosteres of *N*-*t*-butyl and aniline motifs, the latter of which is a pharmaceutical toxicophore. Cytochrome P_{450} (CYP_{450}) oxidation of anilines to form reactive quinone imine intermediates is a suspected cause of their hepatotoxicity and, as a result, their replacement with more metabolically stable sp^3 rich cage frameworks is of considerable interest (Figure 2.1, a).[58] Indeed, the Food and Drug Administration (FDA) withdrew numerous aniline containing drug compounds from the market for displaying undesirable side effects resulting from CYP_{450} oxidation (Figure 2.1, b); examples include the antidepressant Nefazodone which was rescinded in 2003 for causing severe cases of liver damage,[59] cancellation of the registration of the non-steroidal anti-inflammatory drug

(NSAID) Lumiracoxib in 2007 after concerns it may cause liver failure,[60] and similarly withdrawal of Amodiaquine from phase four malaria trials in 1998.[61] Drugs containing *N*-*t*-butyl groups have demonstrated similar susceptibility to hepatic metabolism; for instance, the biologically inactive oxidised by-products of Finasteride are observed to be readily excreted by the body (Figure 2.1, c).[62]

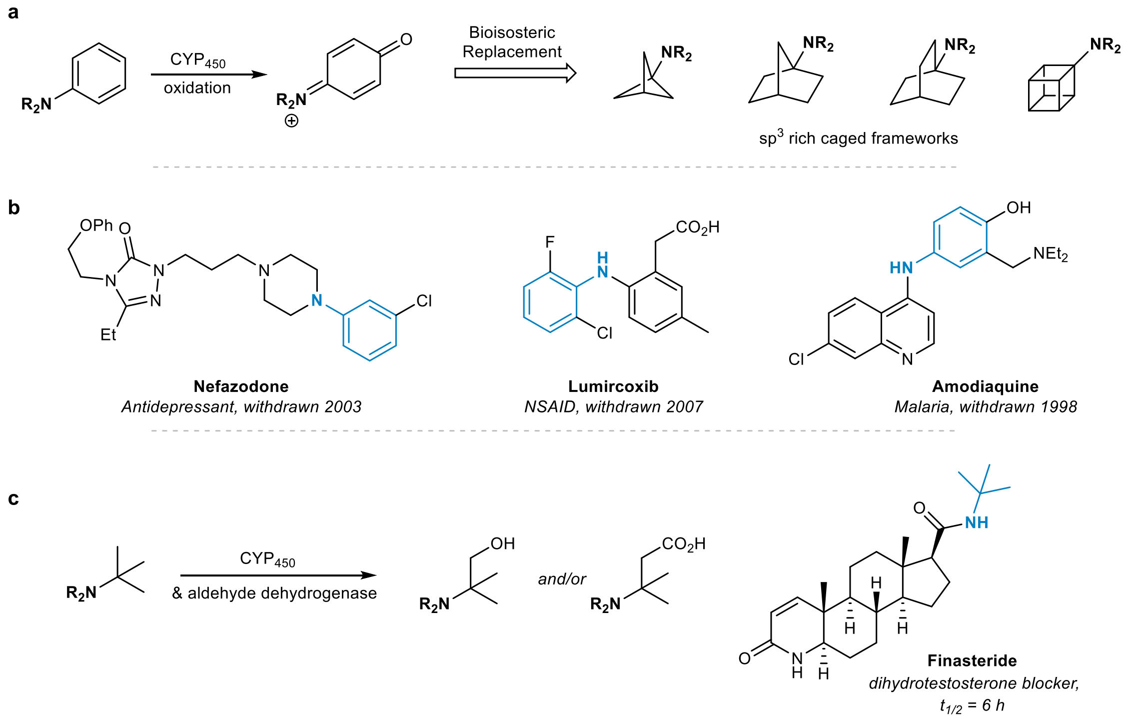


Figure 2.1: a. Proposed metabolism of anilines and their potential bioisosteric replacements, scheme adapted from 'Recent Advances and Outlook for the Isosteric Replacement of Anilines.'[58] b. Withdrawn aniline-containing drug compounds. c. Proposed metabolism of N-t-butyl groups.

sp^3 rich frameworks are increasingly included in structure-activity relationship (SAR) surveys to discover new lead compounds. In particular, the growing interest in BCPA derivatives can be monitored by their recent appearance in numerous patents and in drugs produced by pharmaceutical companies (e.g. Figure 2.2, a).[63-68] SAR investigations by The Upjohn Company highlighted BCPA derivative U-87947E of the fluoroquinolone ciprofloxacin, which can be used to treat severe bacterial infections such as pneumonia.[69]

The BCPA analogue displayed *in vitro* antibacterial activity against gram-positive and gram-negative aerobic bacteria (Figure 2.2, b). Notably, U-87947E proved to be significantly more active than ciprofloxacin against a resistant strain of *Staphylococcus aureus* owing to increased steric bulk and electronegativity of the bridgehead carbon atom.[70]

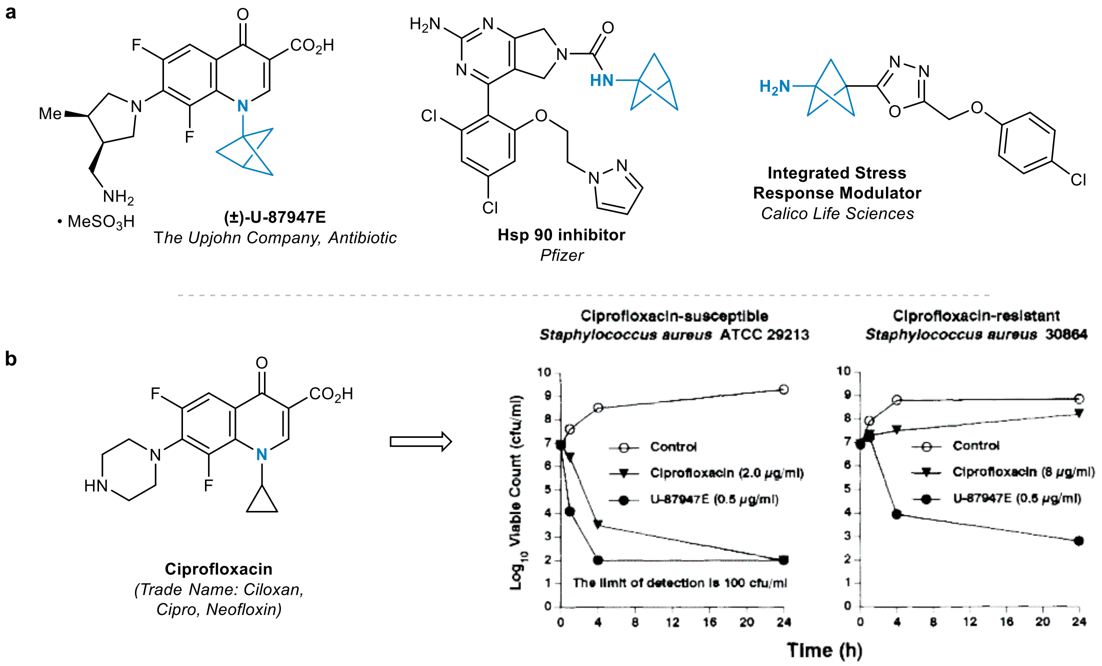


Figure 2.2: a. BCPAs in pharmaceutical lead compounds. b. Time-kill curves for U-87947E and Ciprofloxacin, figure from 'U-87947E, A Potent Quinolone Antibacterial Agent Incorporating a Bicyclo[1.1.1]pent-1yl (BCP) subunit.'[70]

In an attempt to broaden the available biological data for BCPA drug analogues, MacMillan and co-workers demonstrated that BCPA analogues of Indoprofen and Leflunomide displayed either equal or improved metabolic stability in rat and human liver microsomes (Figure 2.3).[71] These results show great promise for using BCPA templates in the pharmaceutical industry. In the future, we can expect to see an increase of these fragments being utilised, especially if novel methodologies are continuously developed to access BCPA motifs.

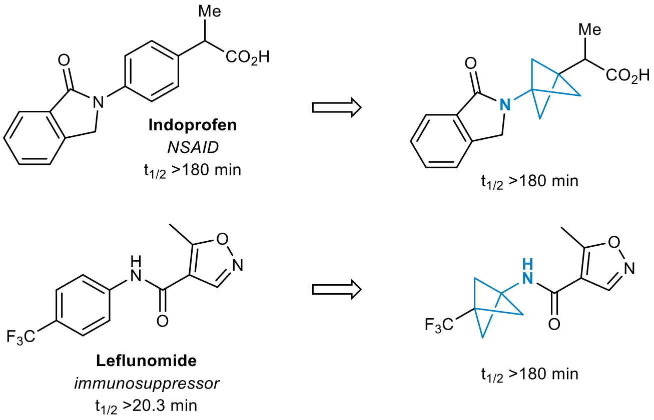


Figure 2.3: MacMillan and co-workers' metabolic stability studies of BCPA drug analogues.[71]

2.1.2 General Methodologies to Access BCPAs

Early routes towards 1,3-disubstituted BCPAs predominantly centred around multistep manipulations of BCP dicarboxylic acid derivatives or other pre-functionalised BCPs. However, following the popularisation of [1.1.1]propellane **1** as a 'strain-release' reagent in 2016 by Baran,[37] which saw the preparation of this versatile reagent on >100 g scale, the majority of proceeding publications capitalised on ring-opening reactions of **1** to access BCPAs (Figure 2.4). The synthesis of mono- and disubstituted BCPAs from **1** can be categorised into three distinct approaches: reaction of *N*-centred anions, *C*-centred radicals and *N*-centred radicals.

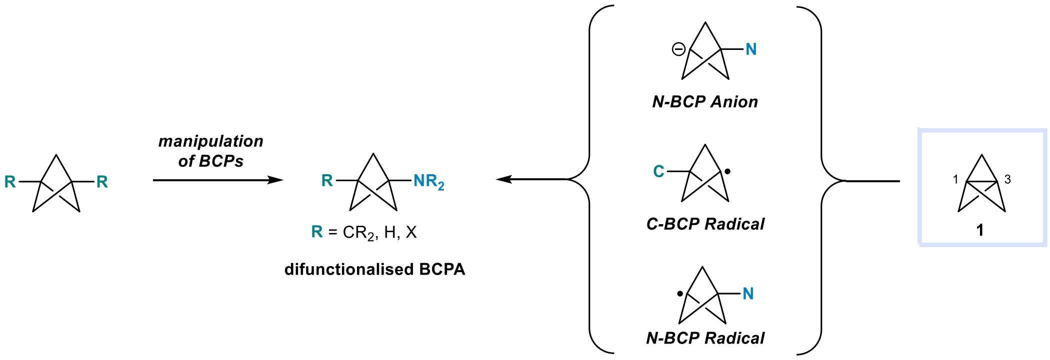


*Figure 2.4: Approaches towards difunctionalised BCPAs via [1.1.1]propellane **1**.*

2.1.3 Manipulation of BCP Derivatives

Early approaches towards mono- and disubstituted BCPAs involved multi-step routes using pre-formed BCP building blocks, typically derived from [1.1.1]propellane **1**. Of these, acyl nitrene rearrangements have proved the most successful and widely used entry to disubstituted BCPAs (Figure 2.5, a).[72-75] In addition, high-pressure reductions of BCP azides and hydrazines have been reported (Figure 2.5, b).[76, 77] A further example involves lithiation of BCP stannanes followed by quenching with a lithium alkoxyamine (Figure 2.5, c).[78] The formal alkoxide displacement on nitrogen by the lithiated BCP, is proposed to involve an S_N2-like process in a lithium aggregate complex, rather than via generation of a nitrene intermediate.[79] Unfortunately, the majority of these methods are restricted to accessing mono-substituted BCPAs, require multiple steps and/or are not suitable for scaled-up protocols.

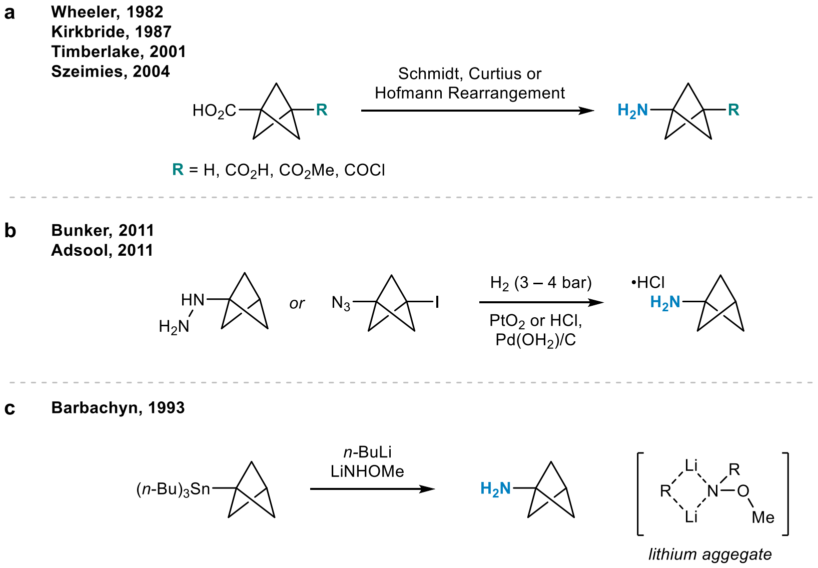


Figure 2.5: Early multi-step approaches towards BCPAs.

2.1.4 Reaction of Nitrogen-Centred Anions with [1.1.1]Propellane

Methodologies utilising the direct reaction of [1.1.1]propellane **1** with nitrogen-centred anions have given efficient access to both mono-substituted BCPAs and the more challenging 1,3-disubstituted-BCPAs. In 2016, Baran and co-workers demonstrated that through the generation of 'turbo-amides' with *i*Pr-MgCl•LiCl, *N*-centred anions could engage in 'strain-release' additions to **1** to access mono-substituted BCPAs bearing a wide variety of *N*-alkyl substituents (Figure 2.6).[37, 80] However, these processes require elevated temperatures (50 – 90 °C), restricting functional group tolerance. This methodology was later adapted to achieve 1,3-disubstituted BCPAs by Gleason through transmetallation of the metallated BCPA intermediate to a Cu^I catalyst that can be used to couple with activated electrophiles; however, this approach is limited to the use of alkyl amines.[54]

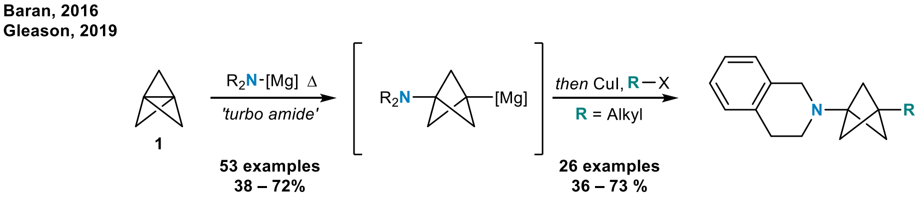


Figure 2.6: Reaction of N-centred anions with [1.1.1]propellane ***1****.*

2.1.5 Amination of BCP Radicals

Methodologies that involve adding *C*-centred radicals to [1.1.1]propellane **1** followed by amination of the resultant BCP radical intermediate have successfully achieved the sought after unsymmetrical disubstituted BCPAs. Primarily demonstrated by the Uchiyama group, Fe^{II} catalysis was used to generate acyl, (hetero)aryl or alkyl radical intermediates through oxidative de-nitrogenation (Figure 2.7, a).[81] Upon addition of this *C*-centred radical to **1**, the resultant BCP radical was trapped by diethyl azodicarboxylate (DEAD) as an *N*-centred SOMOphile to achieve BCP hydrazines in a multicomponent one-pot process. Reduction of the BCP hydrazine products to the free amine could then be achieved in two steps. In 2020, MacMillan and co-workers described a three-component metallaphotoredox methodology to achieve 'drug-like' BCPAs (Figure 2.7, b).[71] Primary, secondary and tertiary alkyl radicals were generated through photoredox-catalysed decarboxylation of activated alkyl carboxylic acids (alkyl bromides were also successful). The alkyl radical was trapped with **1** to give a BCP radical intermediate that can then be intercepted by a Cu^{II} catalyst for coupling to nucleophilic *N*-heterocycles. These methodologies provide tidy one-pot solutions toward the challenging synthesis of difunctionalised BCPAs.

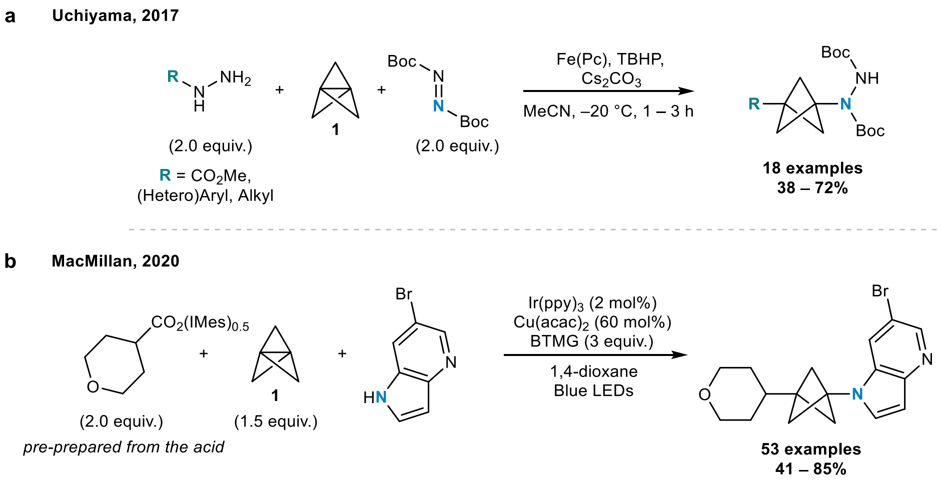


Figure 2.7: Three component reactions to make 1,3-difunctionalised BCPAs via C-substituted BCP radical intermediates. Fe(Pc) – Iron(II) phthalocyanine. TBHP – t-Butyl hydroperoxide. BTMG – 2-t-Butyl-1,1,3,3-tetramethylguanidine.

2.1.6 Reaction of Nitrogen-Centred Radicals with [1.1.1]Propellane

The reaction of [1.1.1]propellane **1** with electrophilic *N*-centred radicals is comparatively underexplored in comparison to the addition of *C*-centred radicals to **1**. Seminal work in the field by Wiberg in 1986 included a reaction of **1** with nitric oxide and carbon disulphide to give nitro-thiocyano BCPs (Figure 2.8, a).[82] The addition of *N*-radicals to **1** then remained unexplored until 2020, when Leonori and co-workers demonstrated a robust three-component construction of 1,3-disubstituted BCPAs. Photoredox-catalysed decarboxylation of the amidyl radical precursor for trapping with **1** and a third SOMOphile component (Figure 2.8, b).[83] Amide, sulfonamide and carbamate functionalities were well tolerated as the electron-withdrawing group on the nitrogen atom. However, this chemistry is restricted to halogen (Cl or Br only) or *S*-substituents at the C_3-position of the BCPA, and C–C bond formation was markedly absent. In 2021, following the completion of the work presented later in this chapter, an amidopyridylation of **1** was described by Hong and co-workers through light-promoted N–N bond cleavage (Figure 2.8, c).[84] The proposed reaction mechanism proceeds via a photoexcited electron-donor-acceptor (EDA) complex, generating an electrophilic sulfonamidyl radical through single-electron transfer (SET) that can then be intercepted by **1**. These procedures demonstrate that adding *N*-radicals to **1** is a particularly efficient entry to difunctionalised BCPAs; however, versatility at the C_3-BCP position remains somewhat limited.

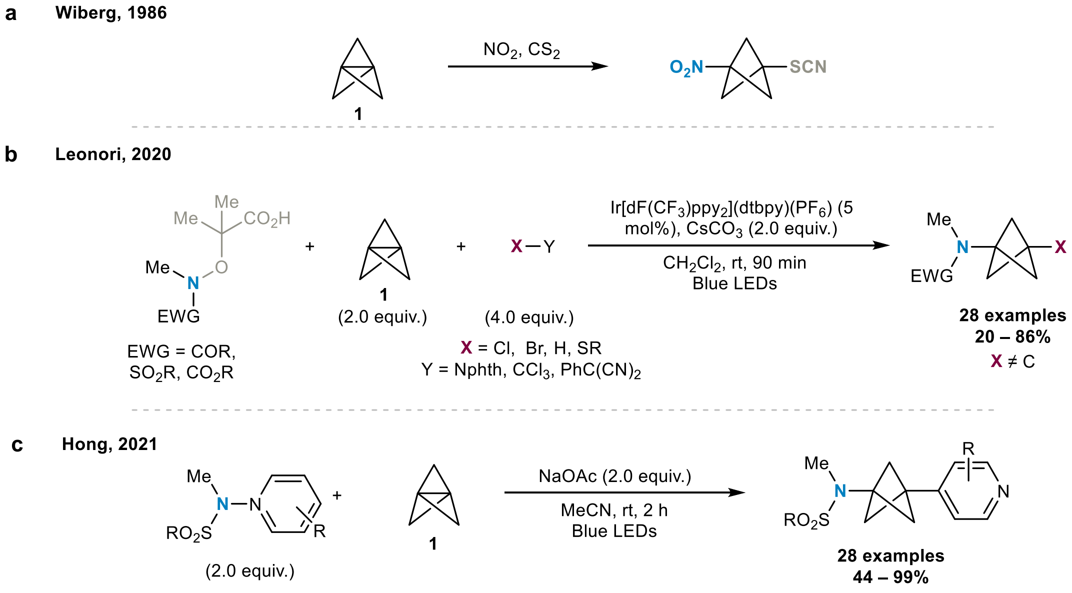
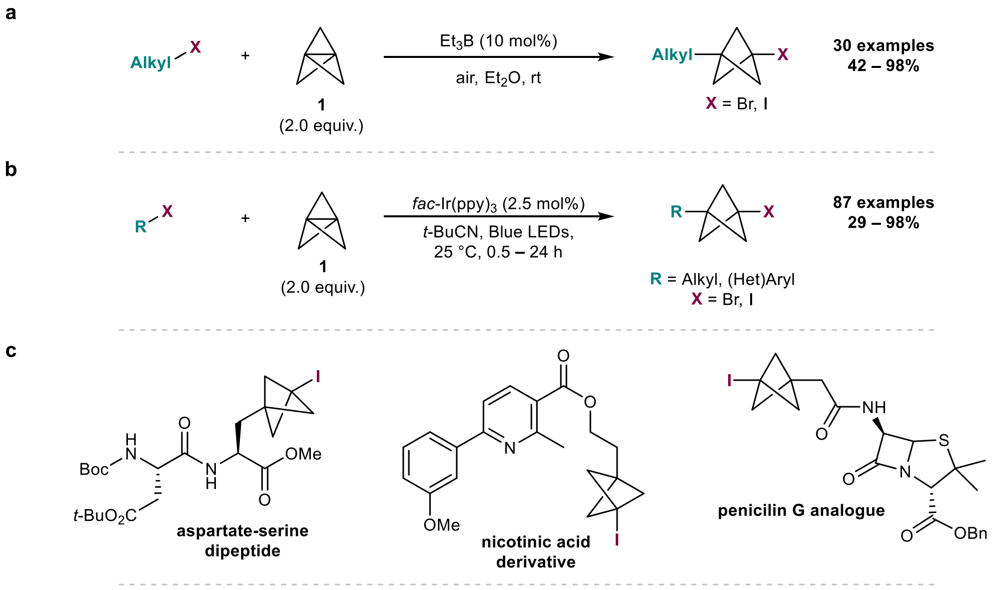


*Figure 2.8: Reaction of N-centred radicals with [1.1.1]propellane **1**.*

2.1.7 Previous Synthesis of BCPs in the EAA group

In previous work, we described the efficient synthesis of BCP halides through an atom transfer radical addition (ATRA) reaction of alkyl halides across the central bond of [1.1.1]propellane **1** using Et_3B/O_2 as an initiator (Figure 2.9, a).[85] Heteroaryl and aryl iodides were unreactive under these conditions, which led to the development of a complementary photoredox-catalysed ATRA methodology to access this class of substrates under very mild conditions (Figure 2.9, b).[86] These methods have been applied to pharmaceutically relevant substrates such as BCP derivatives of dipeptides, penicillin and nicotinic acid (Figure 2.9, c). The BCP halide products provide an excellent opportunity for further functionalisation, such as C–C bond formation; this will be discussed and explored in chapter 3. Photoredox catalysis can also be combined with hydrogen-atom transfer (HAT) cycles to generate monosubstituted BCPs bearing α-carbonyl chiral and quaternary centres (Figure 2.9, d).[87, 88] In the first instance, the photocatalyst/HAT cycle is used in conjugation with chiral enamine organocatalysis to achieve a direct asymmetric radical addition to **1**.



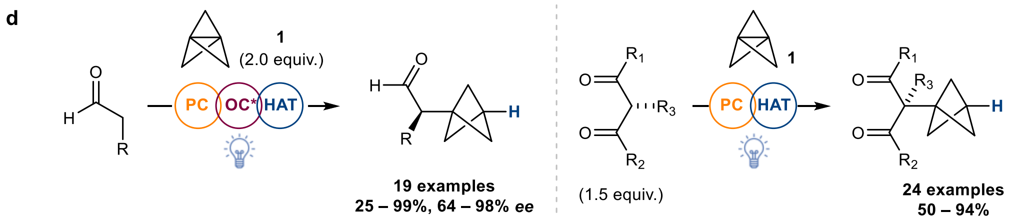


Figure 2.9: Et_3B/O_2 and photoredox-initiated ATRA reactions with [1.1.1]propellane ***1****. PC = Photocatalyst. OC = Organocatalyst.*

2.1.8 BCPA Halides

A BCPA halide was first reported in experiments carried out by Wiberg in the early 1990s to prove the formation of BCP cationic intermediates (Figure 2.10, a).[41, 89] In 2001, Timberlake and co-workers reported the same azido-BCP-iodide compound in 92% yield, following reaction of IN_3 with [1.1.1]propellane **1** (Figure 2.10, b).[90] Timberlake attempted $LiAlH_4$ (LAH) reductions to achieve the BCPA iodide with a free amine as a functional synthetic building block, however, this gave rearranged and ring-opened products. A borane reduction was supposedly successful; however, the authors note that *'analytical analyses were unsatisfactory'* but *'reduction [of the amine product] with LAH gave [the exo-methylene-cyclobutane] thus implying the correct structure'*. To our knowledge, there are no other reported syntheses of BCPA iodides in the literature. In fact, with the addition of the elegant work by Leonori *et al.* discussed in Section 2.1.6,[83] these publications constitute the only syntheses of BCPA halides altogether. This substrate class holds untapped potential for the synthesis of disubstituted BCPA bioisosteres.

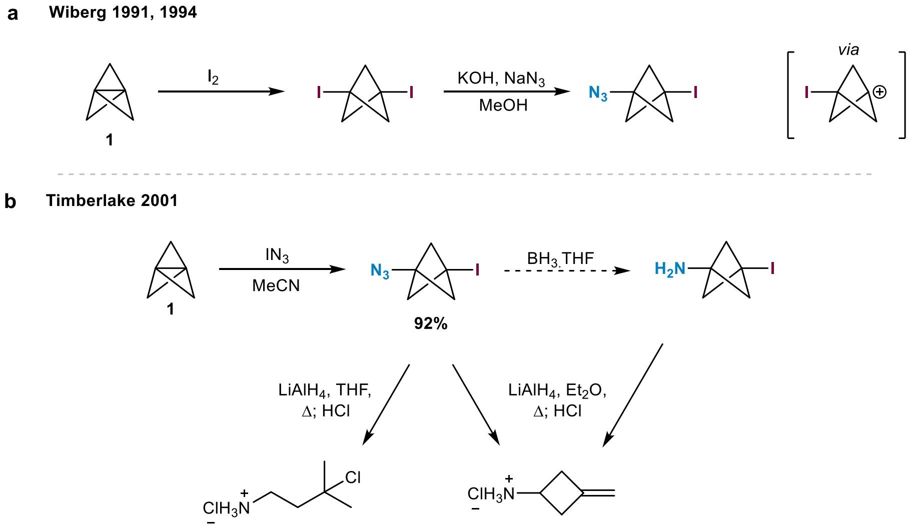


Figure 2.10: Synthesis of BCPA iodides.

2.1.9 Generation of Nitrogen Radicals

Based on our experience with ATRA reactions of *C*-centred radicals with [1.1.1]propellane **1** to form BCP halides, we anticipated applying this concept to *N*-centred radicals to provide analogous BCPA halides. Such a method would constitute an excellent opportunity to access 1,3-disubstituted BCPAs as *p*-substituted aniline bioisosteres. *N*-centred radicals are typically highly electrophilic based on their Pauling electronegativity values compared to that of carbon (χ_p (N) = 3.04 *vs* χ_p (C) = 2.55),[91] except iminyl radicals which demonstrate ambiphilic reactivity. Typically, these intermediates are generated from N–H, N–X, N–O or N–N bond cleavage, and are initiated by homolysis, SET or redox processes (Figure 2.11).

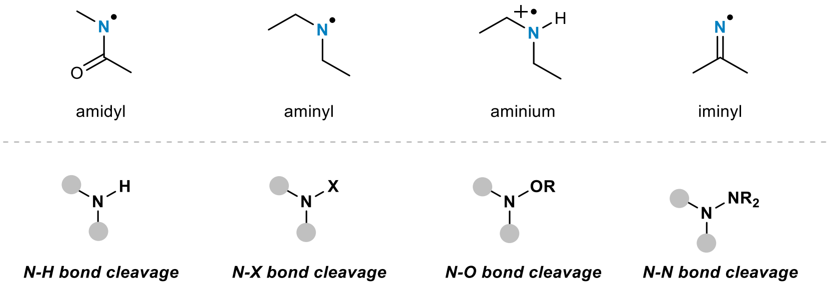


Figure 2.11: Classes of N-centred radicals and their generation.

Of these methods, N–I bond cleavage is the most appealing class of reagents to consider for ATRA reactivity across [1.1.1]propellane **1**. A selection of N–I reagents bearing electron-withdrawing groups are known to achieve one-pot additions across double bonds (Figure 2.12).[92]

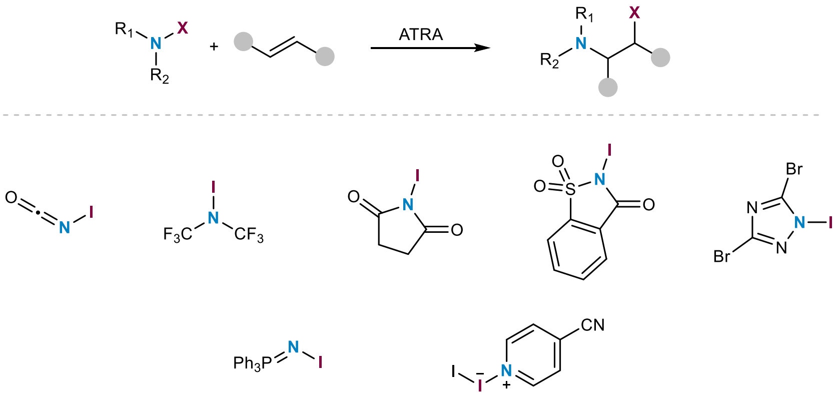


Figure 2.12: Examples of N–I reagents having undergone ATRA reaction with olefins.

Further evaluation of the literature identified that *N*-centred radicals could also be conveniently accessed by fragmentation of α-iodoaziridines. This system has been used for formal (3+2) cycloadditions to unactivated and electron-rich alkenes with stoichiometric Et_3B/O_2 (Figure 2.13).[93, 94]

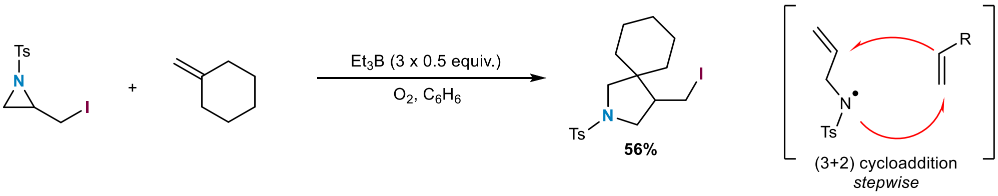


Figure 2.13: Iodoaziridine fragmentation with Et_3B/O_2 to generate N-centred radicals.

2.1.10 Chapter Aims

We questioned whether [1.1.1]propellane **1** could be a suitable radical acceptor for *N*-centred radicals generated from α-iodoaziridines. The resultant BCPA radical would be able to abstract an iodine atom from the starting halide in a chain propagation process, affording BCPA iodides in one step (Figure 2.14). The BCPA iodide products could enable entry to highly desirable 1,3-disubstituted BCPA motifs through lithiation, cross-coupling or further radical reactivity. In addition, the resulting *N*-substituents have the potential to be manipulated or cleaved entirely to give the free BCP amine. For example, the electron-withdrawing substituent on nitrogen could be an amide, carbamate or sulfonamide functionality, and the *N*-allyl chain could undergo olefin manipulations for example oxidation, de-allylation and cross-coupling.

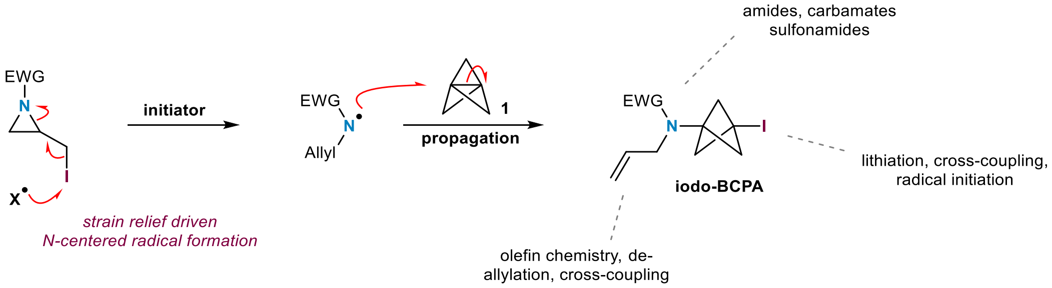


Figure 2.14: Proposed ATRA reaction of N-centred radicals with [1.1.1]propellane ***1****.*

2.2 Results and Discussion

2.2.1 Triethylborane-Initiated ATRA Reaction Optimisation

α-Iodoaziridine **2a** was selected to optimise the ATRA reaction with [1.1.1]propellane **1**. Triethylborane (Et_3B) was first trialled as a radical initiator for this process, based on the success of Taguchi,[93, 94] and our experience with addition of *C*-centred radicals to **1**.[85, 86] Encouragingly, iodo-BCP sulfonamide **3a** was obtained in 67% yield following the required C–N σ bond fragmentation and ATRA with 2.0 equiv. of **1** (Figure 2.15). BCP staffane oligomer **3a–S** resulting from a secondary addition to **1** was also formed in small quantities (6:1, **3a**:**3a-S**) and was inseparable from the desired mono addition product. In addition, products **3a–H** (20:1, **3a**:**3a-H**) and *N*-allylsulfonamide **5a** (17% yield) arising from premature HAT were also isolated. We considered two potential HAT sources: The α-*N* allylic H-atom of **5a** or **3a**, or the reaction solvent, as was found to be significant by Leonori and co-workers.[83] These undesired side products accounted for 28% yield loss of BCPA **3a**, and we endeavoured to improve the yield by minimising their formation.

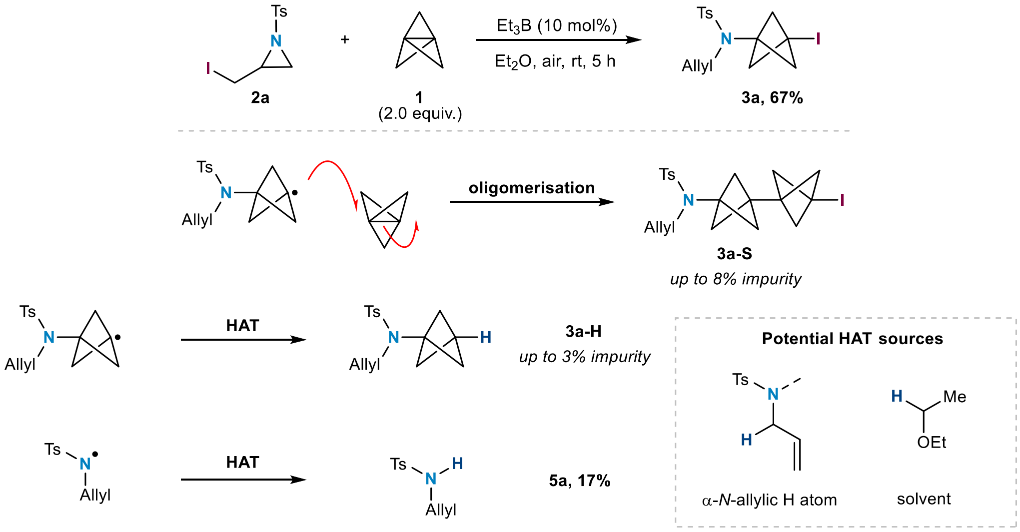
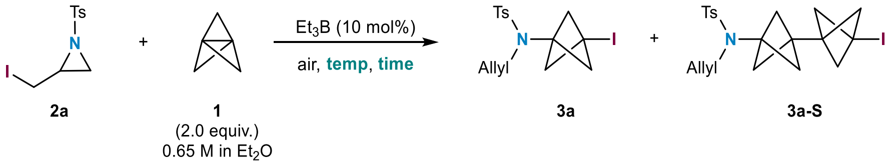


*Figure 2.15: Successful formation of BCPA iodide **3a** and the by-products of the reaction.*

2.2.1.1 Variation in temperature

Following our initial result of 67% yield of **3a** (Table 2.1, entry 1), the effect of temperature on the reaction was investigated.[1] The proportion of staffane product **3a-S** could be significantly reduced (from 6:1 to 20:1 of **3a**:**3a-S**) by lowering the reaction temperature, at a cost to the conversion of **2a** (entries 1 to 3). A prolonged reaction time was then required to achieve a comparable conversion of **2a** and yield of **3a** (entries 4 and 5).



Entry	*Temp. / °C*	*Time / h*	*Conversion of **2a** /%*	***3a**:**3a-S***	***3a** NMR Yield /% (isolated)^a*
1	20	5	100	6:1	67 (79)
2	0	5	91	11:1	63 (69)
3	–20	5	70	20:1	61 (68)
4	–20 to 5 after 2 h	16	100	13:1	70
5	0	16	64	20:1	36

*Table 2.1: Variation of temperature for the Et$_3$B-initiated ATRA reaction. ^{a} Yields of the isolated product are uncorrected for staffane impurity so are greater than the NMR yield when **3a**:**3a-S** is <20:1.*

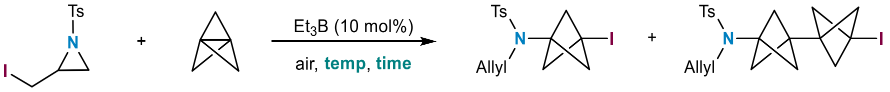
2.2.1.2 Variation of equivalents of [1.1.1]propellane

At room temperature, the proportion of staffane impurity **3a-S** could be further reduced by lowering the equivalents of **1** to 1.3 equiv. (Table 2.2, entries 1 and 2). Notably, under these conditions **3a** could be obtained in 71% yield. An inverted reaction stoichiometry, with **2a** in 1.5 equiv. excess was tested to reduce the influence of premature HAT on

---

[1] NMR yields were obtained by ^{1}H NMR analysis of the crude reaction mixture using mesitylene as an internal standard throughout this chapter. Isolated yields are uncorrected for staffane impurities.

depletion of the reaction yield by the formation of **5a** and to minimize oligomerisation. This was an effective change but resulted in a lower yield of **3a** (65% with respect to [1.1.1]propellane **1**) due to reduced conversion of the starting α-iodoaziridine **2a** (entry 3). Taking the improved result using just 1.3 equiv. of **1** (entry 2), reducing the temperature and increasing the duration of the reaction reduced the yield of **3a** significantly (23 – 47%, entries 4 and 5). The conditions of entry 2 were taken forward as the optimal result.



2a

1
(**XX** equiv.)
0.65 M in Et_2O

3a

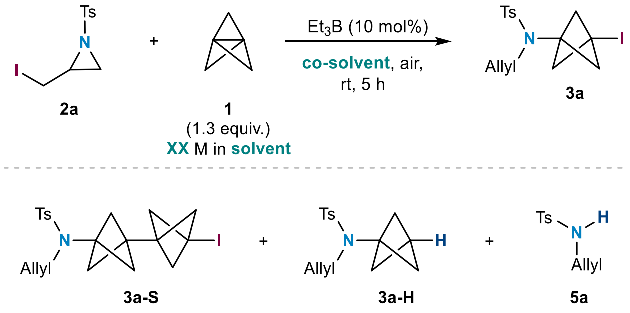
3a-S

Entry	***1** equiv.*	*Temp. / °C*	*Time / h*	*Conversion of **2a** /%*	***3a**:**3a-S***	***3a** NMR Yield /% (isolated)*[a]
1	2.0	20	5	100	6:1	67
2	1.3	20	5	100	17:1	71 (79)
3	1.0[b]	20	5	76[c]	>20:1	65[d]
4	1.3	0	16	59	>20:1	23
5	1.3	0 to 20 after 2 h	16	76	>20:1	47

*Table 2.2: Variation of equivalents of [1.1.1]propellane **1** for the Et_3B-initiated ATRA reaction.* [a] *Yields of the isolated product are uncorrected for staffane impurity.* [b] *1.5 equiv. of **2a**.* [c] *74% of **2a** remained unreacted, starting from 1.5 equiv. of **2a**.* [d] *Yield with respect to **1**.*

2.2.1.3 Solvent Effects

Two unwanted side products, **3a-H** and **5a**, resulting from HAT were observed during the reaction optimisation. The proportion of **3a-H** (<5% throughout the optimisation process) was insignificant compared to **5a** (up to 20%). Solvent effects were studied to probe the cause and reduce the proportion of these HAT products (Table 2.3). The addition of CH_2Cl_2 as a co-solvent improved the staffane formation ratio (from 17:1 to >20:1) and gave an admirable 72% yield of **3a**. Unfortunately, the formation of **5a** was not reduced (entries 1 and 2). Based on the studies by Leonori,[83] we hypothesized that Et_2O might serve as an H-atom source for premature capture of the *N*-centred radical. Preparation of **1** as a stock solution in CH_2Cl_2 instead of Et_2O (by deposition of [1.1.1]propellane **1** on a cold finger and dissolving the solid **1** in CH_2Cl_2, following distillation from Bu_2O)[2] was indeed effective in reducing the proportion of **5a** but gave no further benefit in yield due to reduced conversion of α-iodoaziridine **2a** (entry 3). The use CH_2Cl_2 co-solvent was retained as the optimal conditions for investigating the reaction scope.



Entry	*Solution of **1***	*Co-solvent*[a]	*Conversion of **2a** /%*	***3a**:**3a-S***	***3a**:**3a-H***	***5a** NMR Yield /%*	***3a** NMR Yield /% (isolated)*[b]
1	Et_2O, 0.65 M	-	100	17:1	>20:1	17	71 (79)
2	Et_2O, 0.80 M	CH_2Cl_2	100	>20:1	>20:1	16	72 (75)
3	CH_2Cl_2, 1.06 M	-	88	>20:1	>20:1	12	64

Table 2.3: Variation of solvent for the Et_3B-initiated ATRA reaction. [a]***2a** was prepared as a 1.0 M solution in the co-solvent.* [b]*Yields of the isolated products are uncorrected for staffane impurity.*

2.2.1.4 Reaction Monitoring

The progression of the ATRA reaction over time was monitored with [1.1.1]propellane **1** as the limiting reagent and α-iodoaziridine **2a** in 1.5 equiv. excess. Theoretically, this stoichiometry would reduce the negative impact on the yield due to premature HAT forming allyl sulfonamide **5a** (Figure 2.14). The time course study showed that the reaction

---

[2] Preparation of **1** in CH_2Cl_2 was carried out by Alistair Sterling.

rate reduced significantly after 2 h and that un-fragmented α-iodoaziridine remained unreacted after stirring for 5 h.

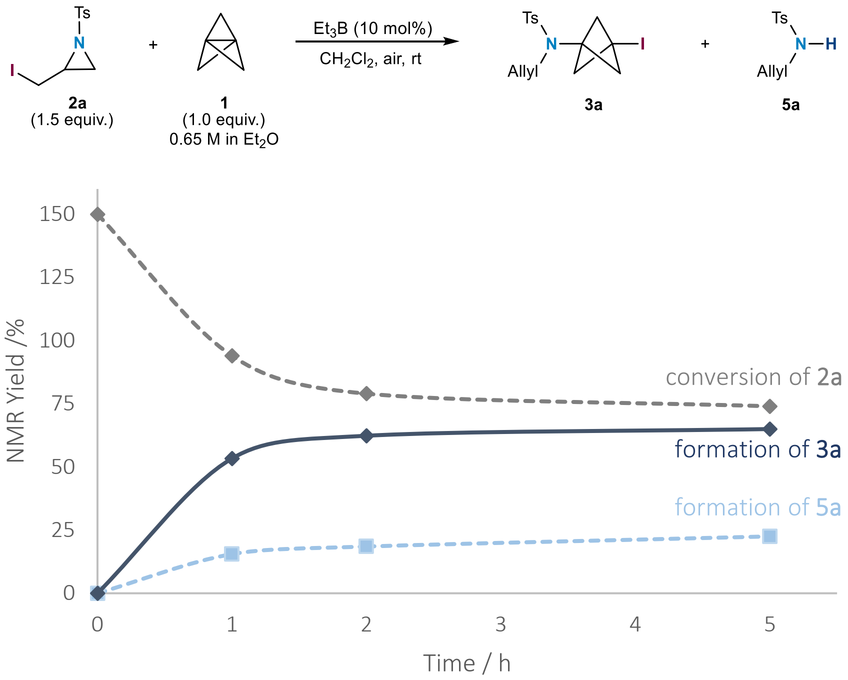
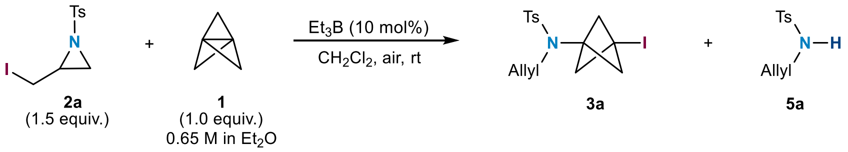


Figure 2.14: Reaction progress over time. [a] Remaining yield assumes 1.5 equiv. of ***2a*** *= 150% at t = 0 h.[b]* ***3a****:****3a-S*** *>20:1 for all.*

To improve the conversion of α-iodoaziridine **2a**, we investigated the addition of a second portion of Et_3B (10 mol%) at the 2 h mark. However, this led to no improvement in the yield of **3a** over our optimised conditions (Table 2.4).



Entry	*Et_3B equiv.*	*Remaining **2a** / %[a]*	***3a** NMR Yield /%[b]*	***5a** NMR Yield /%*
1	1 x 10 mol%	74	65	23
2	2 x 10 mol%[c]	59	67	25

*Table 2.4: Portionwise addition of Et_3B. [a] Remaining yield of **2a** assumes a maximum of 150% based on 1.5 equiv. of **2a**. [b] Ratio of **3a**:**3a-S** was >20:1 for all reactions. [c] Second portion of Et_3B was added after 2 h with an additional two syringes (100 µL) of air, 4 h total reaction time.*

2.2.2 Photocatalytic ATRA Reaction Optimisation

Photocatalysis is a powerful tool for radical initiation and has found broad application and advantages in organic synthesis.[95, 96] In our ongoing work at the time, we found success in using photoredox catalysis to enable ATRA reactions of *C*-centred radicals with [1.1.1]propellane **1** (see section 2.1.7).[86] Therefore, we aimed to test whether photocatalysis could be applied in the synthesis of BCPA iodides.

A photocatalyst can take part in either a redox cycle or an energy transfer process with a substrate. The general catalytic cycle for photoredox reactions proceeds as follows (Figure 2.15).[97] First, the ground state photocatalyst (PC) undergoes excitation to the triplet state upon irradiation with an appropriate wavelength of visible light (dependent on the catalyst λ_{max} absorption). The excited photocatalyst (PC*) can then undergo either reductive quenching with an electron donor (ED) or oxidative quenching with an electron acceptor (EA). In the case of reductive quenching, the reduced photocatalyst (PC^-) is oxidised back to its ground state by an EA. For oxidative quenching the reverse is true, the oxidised photocatalyst (PC^+) is reduced by an ED. The ground state catalyst is then able to undergo further catalytic cycles. Photoredox catalysis can be used in an overall redox neutral cycle concerning the substrate (when $ED^+ = EA$ or $EA^- = ED$), or a sacrificial or off-cycle oxidant/reductant can be used to achieve the sole oxidation or reduction of a substrate.

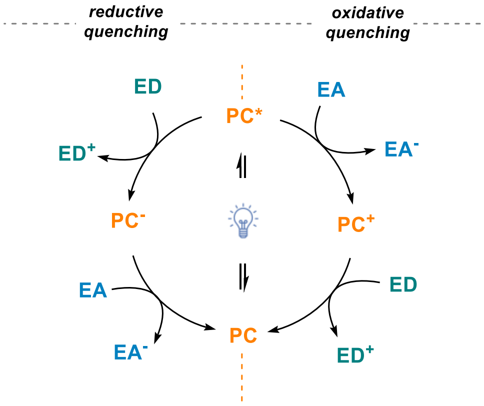


Figure 2.15: Photoredox catalytic cycle.[97]

Energy transfer photocatalysis is another mechanism of action for an excited photocatalyst (Figure 2.16).[98, 99] The ground state photocatalyst absorbs irradiated light and is excited to a singlet state (^{1*}PC); following inter-system crossing to the excited triplet state (^{3*}PC), the photocatalyst is quenched through a Dexter energy transfer process with the substrate that cannot absorb the irradiated light itself. The overall indirect photoexcitation of the substrate enables further reactivity to give the product.

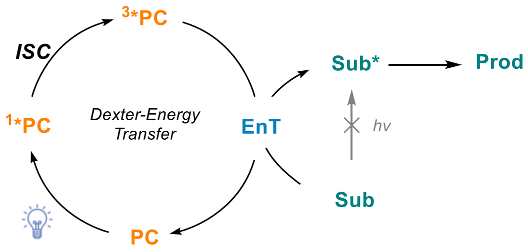
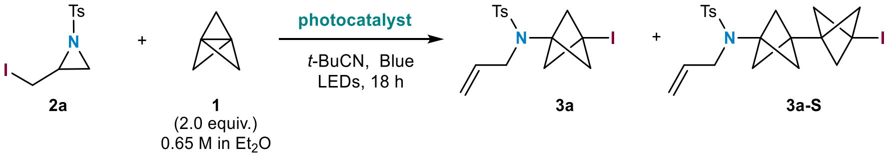


Figure 2.16: Dexter energy transfer mechanism for excited photocatalysts.[98, 99]

2.2.2.1 Variation of Photocatalyst

To our delight, multiple photocatalysts successfully formed BCPA iodide **3a** from α-iodoaziridine **2a** (Table 2.5). Generally, a higher proportion of staffane **3a-S** oligomer impurity was obtained compared to triethylborane initiation. Of the investigated photocatalysts, *fac*-Ir(ppy)$_3$ gave the best yield of **3a** at 64% with the lowest proportion of staffane formed (14:1 ratio of **3a** to **3a-S**), and this result was taken forward as a representative catalyst for a screen of reaction stoichiometries (entry 10). Notably, environmentally friendly organocatalysts PTH and 4-CzIPN gave comparable yields of 61% and 63% respectively (entries 2 and 9). No significant correlation was drawn between the reduction potential of the photocatalyst and yield of **3a** or consumption of α-iodoaziridine **2a**.



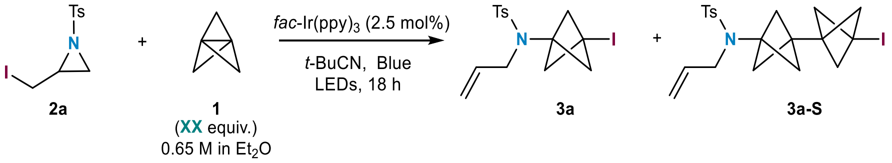
Entry	*Photocatalyst*[a]	*Reduction potential E_{red} (PC^{*}/PC^{+}) vs SCE*	*Conversion of **2a** /%*	***3a**:**3a-S***	***3a** NMR Yield /% (isolated)*[c]
1	Rhodamine B[b]	−1.31	45	17:1	26
2	4-CzIPN[b]	−1.04	89	11:1	58 (61)
3	$Ru(bpy)_3(PF_6)_2$	−0.81	0	20:1	4
4	$[Ir(dF(CF_3)ppy)_2(dtbpy)]PF_6$	−0.89	32	17:1	23
5	$[Ir(dtbbpy)(ppy)_2]PF_6$	−0.96	100	8:1	60
6	$[Ir(dF(CF_3)ppy)_2(bpy)]PF_6$	−1.00	96	11:1	61 (69)
7	$Ru(d(Me)bpy)_3(PF_6)_2$	−1.43	56	14:1	40
8	$Ir(4'\text{-}CF_3ppy)_3$	−1.70	96	13:1	59 (69)
9	PTH[b]	−2.10	-	17:1	(63)
10	*fac*-$Ir(ppy)_3$	−1.73	-	14:1	57 (64)
11	*fac*-$Ir(p\text{-}Fppy)_3$	−1.91	-	8:1	25 (20)

Table 2.5: Variation of photocatalyst for ATRA reaction. [a]2.5 mol% of photocatalyst.[b] 5 mol% of organophotocatalyst. PTH = 10-phenylphenothiazine. 4-CzIPN = 2,4,5,6-Tetrakis(9H-carbazol-9-yl) isophthalonitrile. [c] Yields of the isolated products are uncorrected for staffane impurity.

2.2.2.2 Variation of equivalents of [1.1.1]propellane

As expected, reducing the equivalents of [1.1.1]propellane **1** lowered the proportion of staffane **3a-S** impurity formed (20:1 *vs* 14:1), however, at a high cost to the yield of **3a** (Table 2.6, entries 2 to 6). Similarly, increasing the equivalents of **1** resulted in a higher proportion of staffane formation but with no additional benefit to the yield (entries 6 to

8). The use of 2.0 equiv. of **1** was maintained as the optimal reaction conditions (entry 6). Interestingly, in the absence of **1** only 10% of α-iodoaziridine **2a** fragmented to give the *N*-allylsulfonamide **5a** (entry 1), which appears to suggest that **1** is involved in reaction initiation. In addition, no dehalogenated (but non-fragmented) aziridine was observed.

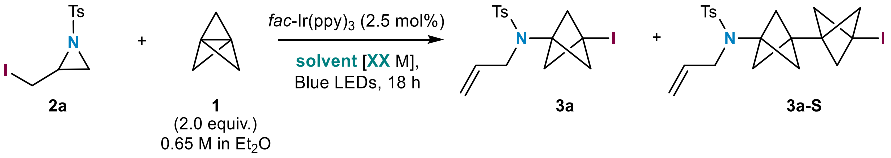


Entry	***1** equiv.*	*Conversion of **2a** /%*	***3a**:**3a-S***	***3a** NMR Yield /% (isolated)*[a]
1	0.0	10	-	0[b]
2	1.0	29	>20:1	(24)
3	1.3	63	20:1	31
4	1.5	-	20:1	(49)
5	1.8	81	13:1	42
6	2.0	78	14:1	57 (64)
7	2.5	82	10:1	57
8	3.0	91	8:1	64 (76)

*Table 2.6: Variation in equivalents of [1.1.1]propellane **1**. [a] Yields of the isolated products are uncorrected for staffane impurity. [b]10% yield of N-allyl sulfonamide **4a**, 90% yield of α-iodoaziridine **2a**.*

2.2.2.3 Solvent and Concentration

An investigation into solvent and concentration effects confirmed *t*-BuCN to be optimal for this transformation, superseding MeCN, which gave only a 31% yield (Table 2.7, entries 1 and 2). More polar solvents only returned trace amounts of product **3a** (entries 3 to 5). Dilution of the reaction improved the product to staffane ratio from 14:1 to >20:1, however, at the cost of a 11% yield loss (entries 2 and 6). Increasing the reaction concentration was slightly detrimental to the optimal result previously obtained (entry 7).

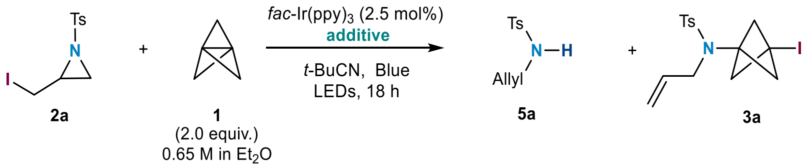


Entry	*Solvent*	*Concentration /M*	***3a**:**3a-S***	***3a** NMR Yield /% (isolated)*[a]
1	MeCN	0.10	17:1	31
2	*t*-BuCN	0.10	14:1	57 (64)
3	DMF	0.10	-	3
4	DMSO	0.10	-	2
5	MeOH	0.10	-	2
6	*t*-BuCN	0.08	>20:1	46 (53)
7	*t*-BuCN	0.18	13:1	54 (62)

Table 2.7: Solvent and concentration effect on the photocatalysed ATRA reaction. [a] Yields of the isolated products are uncorrected for staffane impurity.

2.2.2.4 Reaction Additives

Should a photoredox catalytic cycle be in operation, an efficient catalyst turnover event following an initial catalyst quenching would enable a high turn-over number and theoretically improve the yield of **3a**. Presuming an oxidative quenching pathway, the addition of external reductants was investigated (Table 2.8). However, tertiary alkyl amines were found to inhibit the desired ATRA reactivity, forming only *N*-allyl sulfonamide **5a** (entries 1 to 3). Sodium ascorbate was also trialed as a reductant and gave trace amounts of **3a** (entries 4 and 5). To probe whether I^- could be involved as a cation trap in a radical–polar crossover mechanism LiI was added (entry 5). However, no product **3a** was observed, yet a significant 55% NMR yield of diiodo BCP was observed on ^{1}H NMR analysis of the crude reaction mixture. Finally, the addition of the oxidant $K_2S_2O_8$ to probe a reductive quenching pathway resulted in only 24% of **3a** (entry 6).



Entry	Additive	**5a**:**3a**	**3a** NMR Yield /%
1	i-Pr_2NEt (1.0 equiv.)	100:1	0
2	NBu_3 (1.0 equiv.)	100:1	0
3	NEt_3 (1.0 equiv.)	100:1	0
4	Na-Ascorbate (2.0 equiv.), TBAB (0.1 equiv.)	8:1	trace[a]
5	LiI (1.0 equiv.)	100:1	0[b]
6	$K_2S_2O_8$ (2.0 equiv.)	-	26

Table 2.8: Addition of reductants for catalyst turnover and addition of LiI as a potential cation trap. [a]Diiodo-BCP and α-iodoaziridine ***2a*** *were also observed. [b]55% yield of diiodo-BCP observed.*

2.2.2.5 Photochemical Equipment and Setup

Photocatalysed reactions are sensitive to several variables in the reaction set-up:

- Wavelength – dependent on λ_{max} of the photocatalyst,
- Irradiation Intensity – affected by distance between the reaction mixture and the light source, power of the light source and solution transparency,
- Temperature – heat produced by the light source.

Three different reaction setups were assessed to probe these sensitivities of the ATRA reaction. The optimisation so far was carried out using reaction LED strips as in **set-up 2** (Table 2.9). Firstly, no significant change was noted between using an 18 W bulb in a PhotoRedOx box with a fan, and an LED strip (Table 2.9, entries 1 and 2). However, direct irradiation with a 50 W Kessil lamp gave a reduced 56% yield of **3a** (entry 3), presumably due to degradation of the α-iodoaziridine **2a** or product **3a** from an increased reaction temperature and a higher intensity of irradiation.

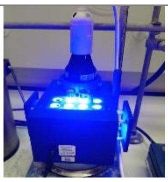
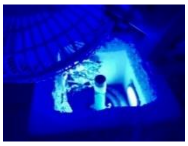
Entry	*Reaction Set Up*		***3a*** *NMR Yield /%*^{a}
1	Evoluchem™ 455 nm 18 W LED in PhotoRedOx box with a fan to regulate reaction temperature.		64
2	Tingkam® Waterproof 5M 5050 SMD RGB LED Strips. No fan for temperature regulation.		62
3	Kessil PR160L 456 nm 50 W clamped 5 cm from a vial, cooled with desk fan from above.		56

Table 2.9: Variation of reaction set-up conditions.

Having considered the results obtained from the optimisation of the reaction conditions, we pursued triethylborane initiation for evaluating the scope of the iodo-sulfamidation of [1.1.1]propellane **1**.

2.2.3 Substrate Synthesis

To investigate the iodoamination of [1.1.1]propellane **1** reaction scope, a selection of α-iodoaziridine substrates was prepared using a two-step procedure. α-Iodoaziridines **2** could be readily synthesised by iodination/aziridination of *N*-allyl sulfonamides **5**,[100-102] which could be obtained by sulfonylation of *N*-allylamine or allylation of tosylamine (Figure 2.17, a).[103-105] Alternatively, an Mitsunobu reaction of α-alcohol aziridines obtained from allyl alcohols could be used (Figure 2.17, b).[106, 107]

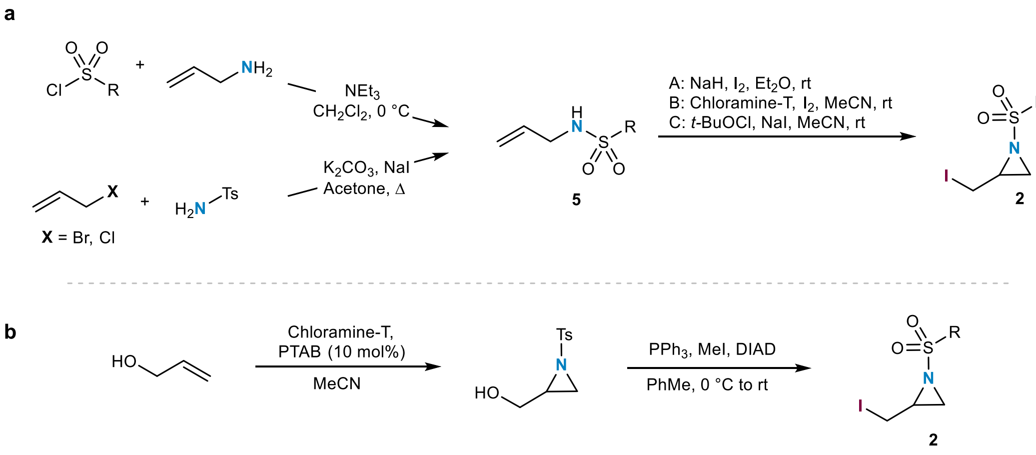


*Figure 2.17: General syntheses of sulfonamide-iodoaziridines **2**. PTAB = trimethylphenylammonium tribromide. DIAD = Diisopropyl azodicarboxylate.*

α-Iodoaziridines **2a** – **2k**, **2ac** and **2ad** were prepared bearing different aryl sulfonamide protecting groups (Figure 2.18).

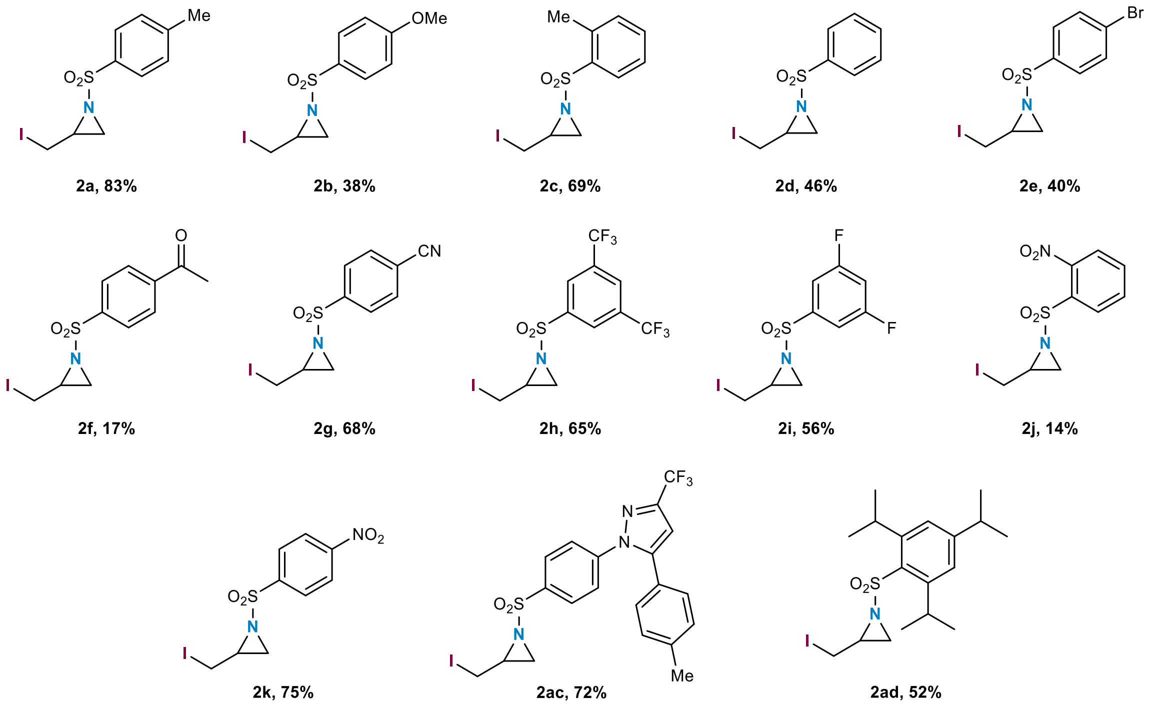
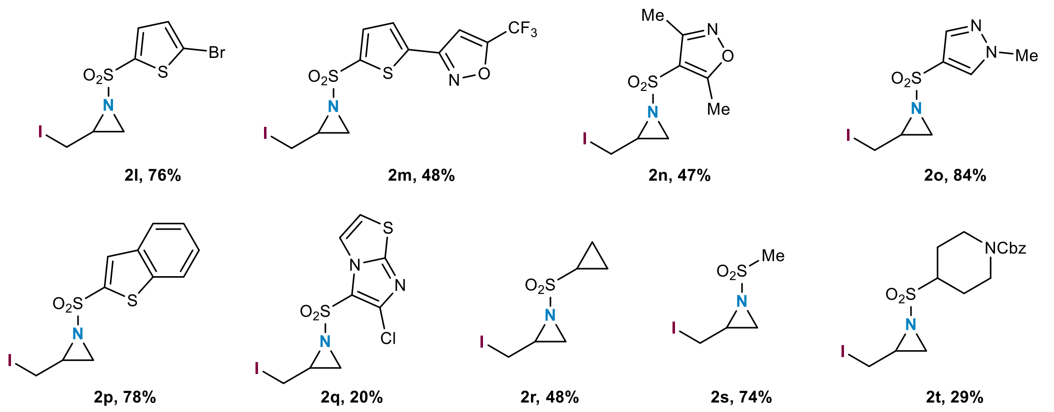


Figure 2.18: α-Iodoaziridines with aryl sulfonamide protecting groups. Reported yields are for the iodo-aziridination step only, please see supporting information for the yield of N-allyl sulfonamide formation.

Aziridines with heteroaryl **2l** – **2q** and alkyl sulfonamide **2r** – **2t** protecting groups were also synthesised successfully (Figure 2.19).

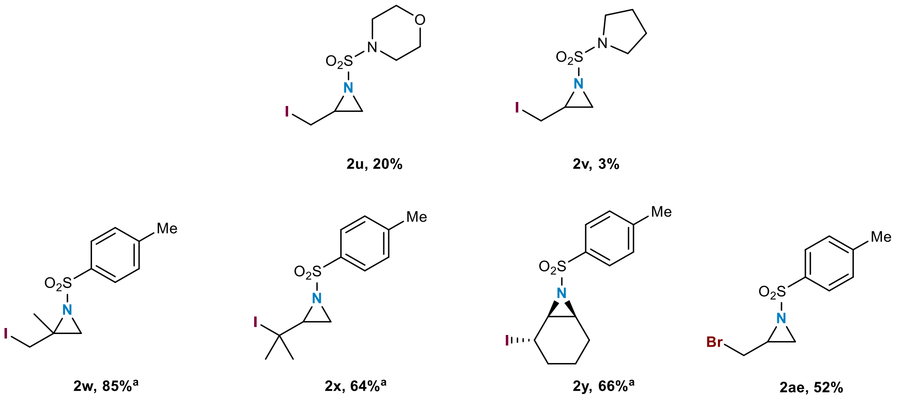


2l, 76% **2m, 48%** **2n, 47%** **2o, 84%**

2p, 78% **2q, 20%** **2r, 48%** **2s, 74%** **2t, 29%**

Figure 2.19: α-Iodoaziridines with heteroaryl and alkyl sulfonamide protecting groups. Reported yields are for the iodo-aziridination step only, please see supporting information for details of N-allyl sulfonamide formation.

Sulfinamide-protected *N*-allyl compounds underwent iodoaziridination to form **2u** – **2v** (Figure 2.20). Additionally, we were able to incorporate substituents onto the aziridine alkyl backbone **2w** – **2y**, these substrates were prepared by Dr Jeremy Nugent. α-Bromoaziridine **2ae** was prepared according to a literature procedure via bromination of *N*-allyl tosylsulfonamide.[108]

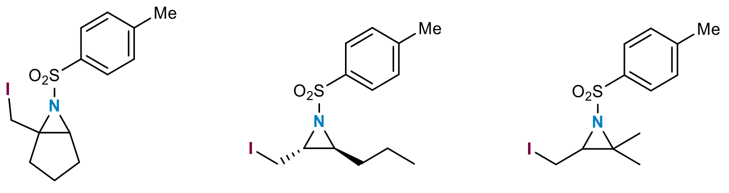


2u, 20% **2v, 3%**

2w, 85%[a] **2x, 64%**[a] **2y, 66%**[a] **2ae, 52%**

Figure 2.20: Sulfinamide-substituted aziridines, aziridines with various alkyl backbones and α-bromoaziridine. Reported yields are for the iodo-aziridination step only, please see supporting information for the yields of N-allyl sulfonamide formation. [a] *Prepared by Dr Jeremy Nugent.*

The following substrates **2z** – **2ab** were synthesised by Mitsunobu reactions of the corresponding α-alcohol aziridine (Figure 2.21).



2z, 66% **2aa, 70%** **2ab, 68%**

Figure 2.21: Substituted α-iodoaziridines prepared by Mitsunobu reactions. Reported yields are for the Mitsunobu step only, please see supporting information for more information.

The following *N*-allyl sulfonamides were either unreactive or underwent decomposition under aziridination conditions (Figure 2.22).

Figure 2.22: Allyl sulfonamides that were unsuccessful under general aziridination procedures.

2.2.4 Bicyclopentylation Scope

The scope of the bicyclopentylation reaction was evaluated under the optimised conditions with a wide range of α-iodoaziridines (Figures 2.23 – 2.25). High yields of aryl sulfonamide aziridines bearing electron-donating (**3a** – **c**, 61% – 75%), electron-neutral (**3d**, 75%) and electron-withdrawing (**3e** – **i**, 55 – 73%) substituents were obtained, however nosyl protecting groups were less successful (**3j** and **k**, 10 – 36%) (Figure 2.23). The reaction was equally efficient on a 6.50 mmol scale up with just 1.1 equiv. of **1** giving 67% of **3a**.

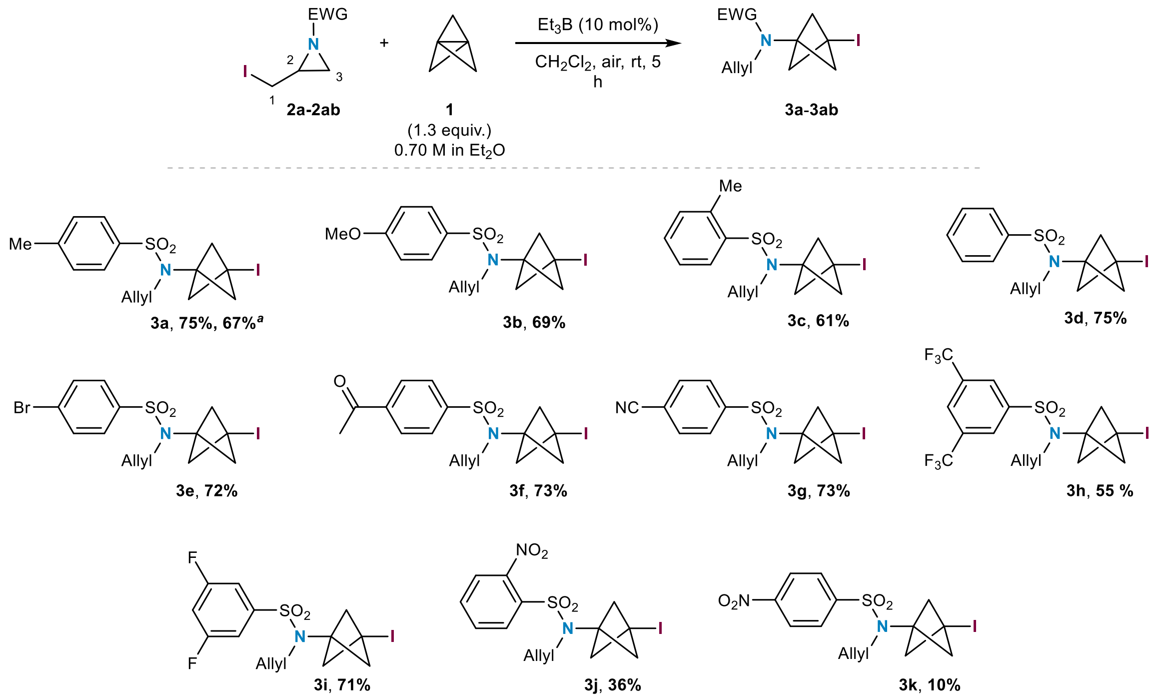


Figure 2.23: Scope of aryl sulfonamide BCPA iodides. [a] *2.19 g, 6.50 mmol of* ***2a****, 1.1 equiv. of* ***1****.*

Heterocyclic sulfonamide aziridines including thiophenes **3l** – **m**, oxazole **3n**, pyrazole **3o**, benzothiophene **3p** and imidazothiazole **3q** afforded the corresponding BCPA products in fair to very good yields (52 – 81%) (Figure 2.24). Aziridines featuring alkyl sulfonamide (**3r** – **t**, 37 – 66%) and sulfamide-substituted aziridines (**3u** – **3v**, 22 – 61%) were also accommodated.

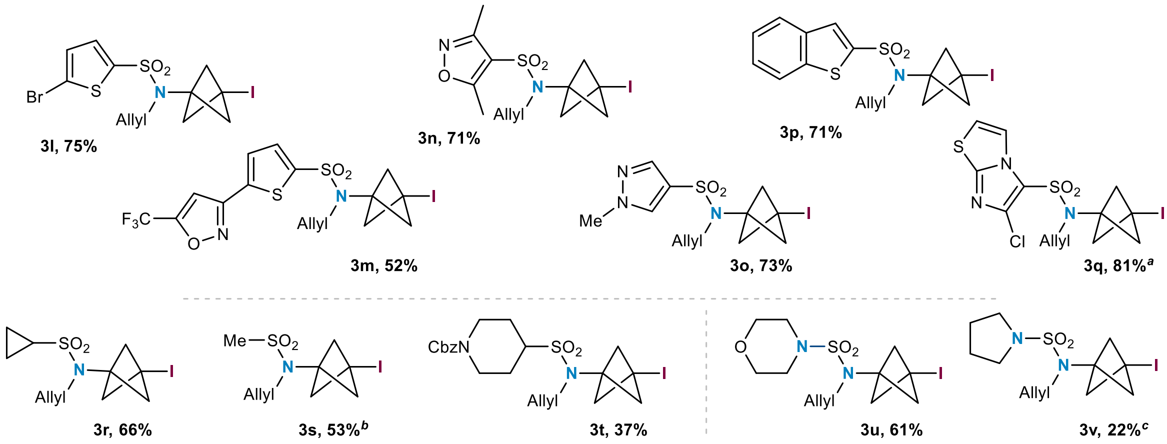


*Figure 2.24: Scope of heteroaryl and alkyl sulfonamides,and sulfamide BCPA iodides. [a] Isolated as an inseparable 7:1 mixture of the desired product to staffane **3q–S**; recorded yield is that of **3q**. [b] 1.6 equiv. of **1** used for complete conversion and to improve product purity. [c] 0.09 mmol scale.*

Substitution of the α-iodoaziridine alkyl backbone was well tolerated (Figure 2.26). We investigated aziridines featuring substituents at the 1-, 2- or 3- positions, including fused cyclopentane and cyclohexane aziridines (**3v** – **aa**, 30 – 73%). The reaction of a disubstituted aziridine under our optimised conditions gave a disappointing yield (**3ab** 4%). Finally, inclusion of the NSAID celecoxib BCPA iodide example demonstrates the potential of this chemistry to operate effectively in medicinal chemistry settings (**3ac**, 70%).

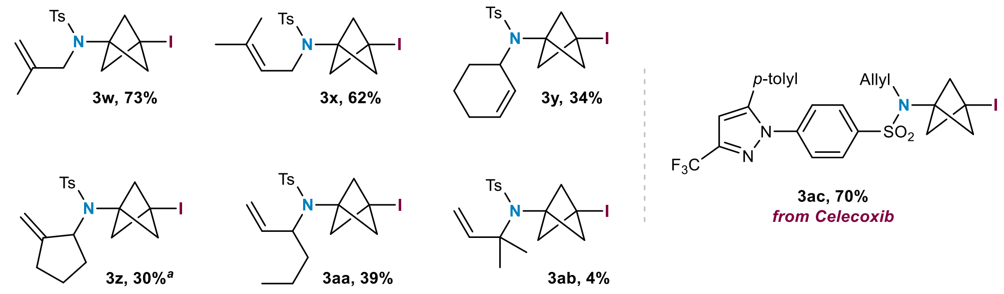


*Figure 2.26. Scope of α-iodoaziridine alkyl backbone substituents and application to a pharmaceutical example. [a] 1.6 equiv. of **1** was used for complete conversion.*

2.2.5 Unsuccessful α-Haloaziridine Substrates

Over the course of our substrate investigations, additional substrate classes were tested to broaden the reaction scope. Unfortunately, these examples were unsuccessful but are discussed below.

2.2.5.1 Sulfonamide α-Haloaziridine Substrates

The bulky triisopropyl aryl sulfonamide aziridine **2ad** was found to be unreactive under triethylborane and photoredox initiation methods (Figure 2.27, a). Interestingly, we considered the possibility of 1,5-HAT reactivity of the intermediary *N*-centred radical with the *o*-benzylic protons. However, this was not observed for either the triisopropyl substrate **2ad** or the *o*-tosyl aziridine **2c** (Figure 2.27, b). We next hoped to be able to apply our chemistry to α-bromo aziridine **2ae** to access the corresponding BCPA bromides, however, once more only unreacted starting material was recovered under our optimised reaction conditions.

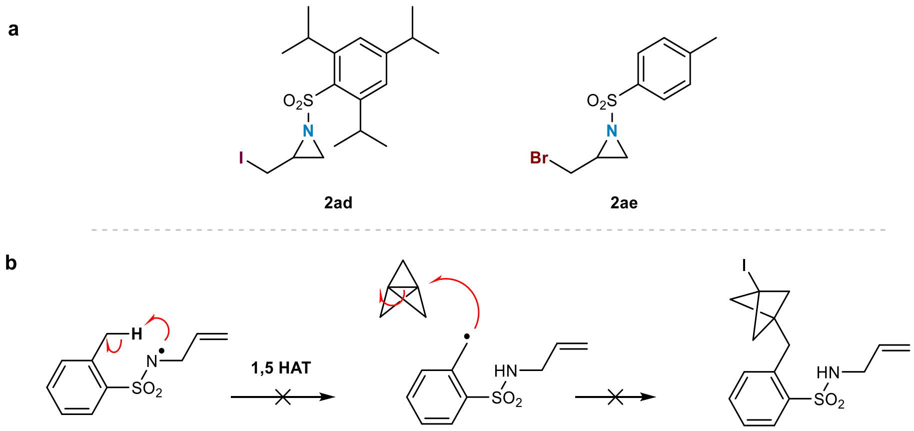


Figure 2.27: a. Unsuccessful α-haloaziridine substrates. b. Possible 1,5-HAT on o-alkyl benzylic substituents.

2.2.5.2 Amide and Carbamate α-Haloaziridines

We explored the potential for different electron-withdrawing substituents on the aziridine nitrogen to aid ring fragmentation and stability of the resulting electrophilic *N*-centred radical. Encouraged by the results of Leonori and co-workers,[83] where amidyl radicals were shown to add efficiently to [1.1.1]propellane **1**, we had hoped that amide and carbamate protecting groups would translate to our developed methodology.

The primary challenge lay in the synthesis of amide protected aziridines. *N*-Allyl amides and carbamates are known to undergo cyclisation of the carbonyl to form iodomethyl oxazolines under iodo-aziridination conditions (Figure 2.28, a).[101] Nevertheless, we tested whether **2af** could undergo C–O bond fragmentation to form an *N*-centred amidyl radical. Instead, we observed the direct ATRA product **3af** with [1.1.1]propellane **1** in an excellent 91% yield. Unfortunately, the synthesis of a carbamate-substituted aziridine was unsuccessful under multiple different reaction conditions (Figure 2.28, b).

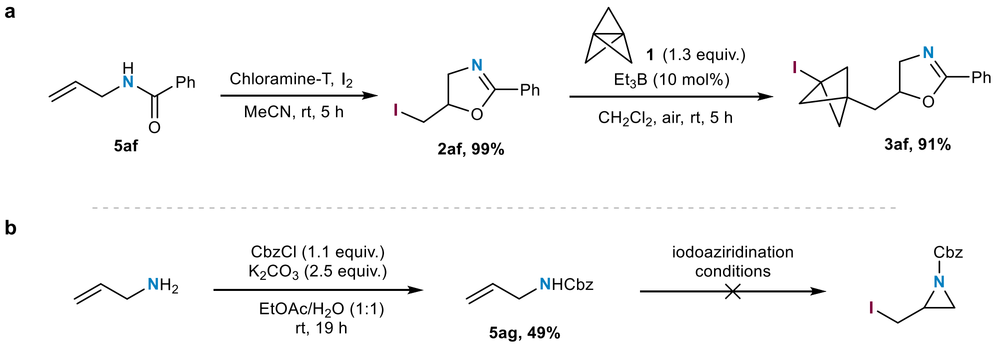


Figure 2.28: a. Oxazoline synthesis and attempted fragmentation. b. Investigation into carbamate protecting groups.

We managed to prepare the Cbz-protected aziridine **2ah** through an alternative route, albeit in a very low yield (Figure 2.29). Aziridination of methyl vinyl ketone with Chloramine-Cbz[109] gave **2ah-S** in good 83% yield on a 6.0 mmol scale.[110] However, reduction and subsequent Mitsunobu reaction to form α-iodoaziridine **2ah** was very low yielding likely due to the instability of the aziridine alcohol towards aza-Payne-type rearrangements. Unfortunately, iodo-aziridine **2ah** proved largely unreactive under both Et_3B and photoredox initiation. Unreacted starting material was returned and only trace amounts of BCPA iodide **3ah** were isolated (4%). Due to their challenging synthesis and limited reactivity, this class of substrates was no longer pursued.

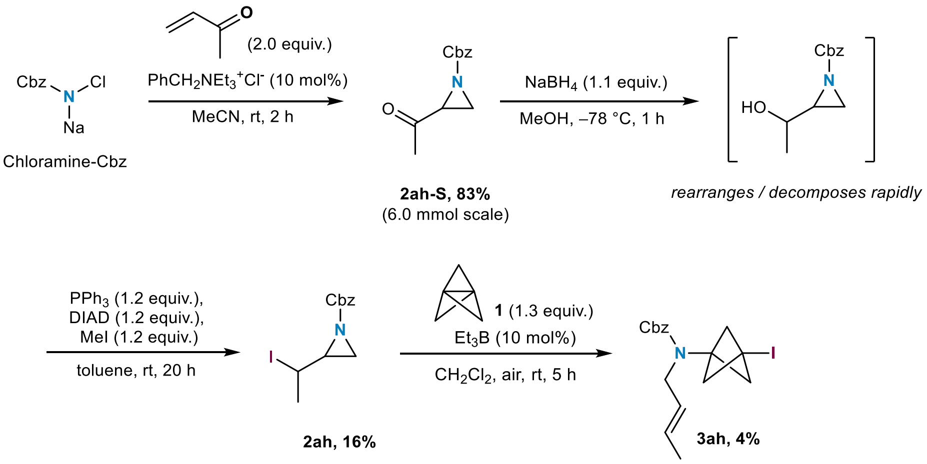


Figure 2.29: Synthesis of a Cbz-protected iodoaziridine and subsequent ATRA attempt.

2.2.5.3 Oxaphosphinane and Sulfinamide Aziridines

We next probed oxaphosphinane and sulfinamide aziridine electron-withdrawing groups. Oxaphosphinane iodoaziridine **2ai** was successfully prepared but unfortunately, this compound failed to undergo the desired fragmentation and addition to [1.1.1]propellane **1**, with only unreacted starting material returned (Figure 2.30, a). Attempted syntheses of a sulfinamide iodoaziridine were unsuccessful under our general iodoaziridination procedures (Figure 2.30, b).

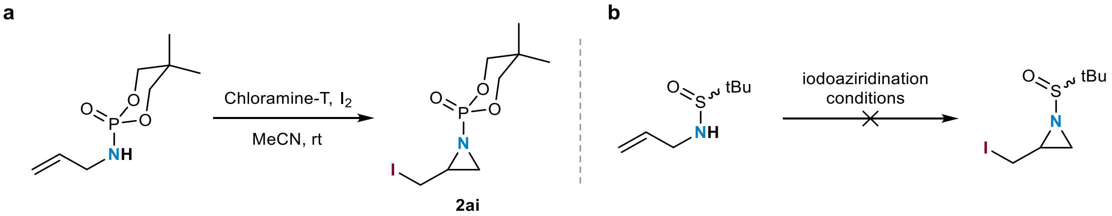


Figure 2.30: a. Oxaphosphinane iodoaziridine synthesis. b. Attempted sulfinamide iodoaziridine synthesis.

These failed results show the importance of a strong σ electron-withdrawing group on the aziridine to enable C–N bond fragmentation and enhance *N*-centred radical stability. However, increased electron deficiency of the *N*-protecting group causes reduced *N*-nucleophilicity for the initial iodoaziridine synthesis and promotes sulfone de-arylation decomposition pathways.

2.2.6 Mechanistic Discussion

The mechanism of the *N*-centred radical ATRA to [1.1.1]propellane **1** was considered under both triethylborane and photoredox conditions.

2.2.6.1 Triethylborane Initiation

The literature proposes that triethylborane initiates radical processes through an Et_3B / O_2 couple to generate ethyl and peroxide radicals, which can then engage in a radical propagation process (Figure 2.31).[111]

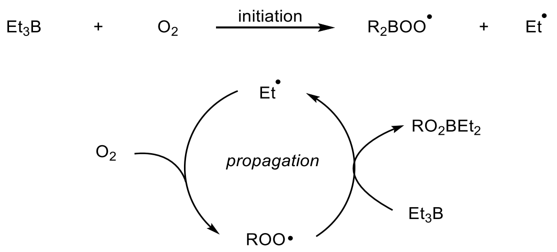


Figure 2.31: Proposed initiation mechanism for organoborane radicals.[111]

Following initiation by Et_3B / O_2, we propose an ATRA chain reaction mechanism (Figure 2.32). After iodine atom abstraction and C–N bond fragmentation of iodo-aziridine **2**, the resulting electrophilic *N*-centred radical **A** is trapped by [1.1.1]propellane **1**. The BCPA radical intermediate **B** can abstract iodine from the substrate in a propagation mechanism to give the desired BCPA iodide product **3** and reform the *N*-centred radical after ring fragmentation. While Et_3B is reported to initiate radicals from alkyl iodides and forming ethyl iodide, the ethyl radical could alternatively undergo addition to **1** to form a BCPA radical intermediate also capable of iodine atom abstraction from **2**. However, the ethyl BCP iodide presumably formed in such a process was never isolated.

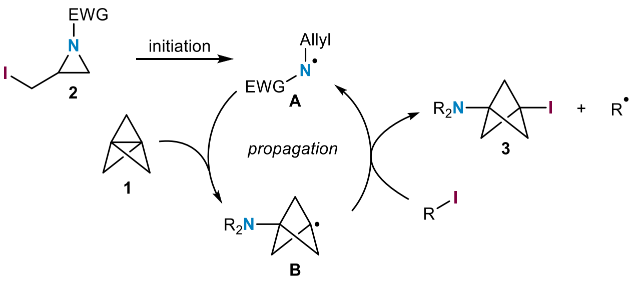


Figure 2.32: Aziridine fragmentation/ATRA mechanism.

As previously discussed in Section 2.2.1, both intermediates **A** and **B** can engage in HAT termination events, giving rise to unwanted side products **3a-H** and **5a** (Figure 2.33, a). H-atom sources could arise from the reaction solvent, as proposed by Leonori and co-workers,[83] or from the α-*N* allylic proton of the allyl sulfonamide. Alternatively, BCPA radical intermediate **B** can engage in oligomerisation with a second equivalent of **1** to form staffanes **3-S** that can be isolated as a minor contaminant (≥20:1 ratio of product to staffane in 89% of scope examples) (Figure 2.33, b).

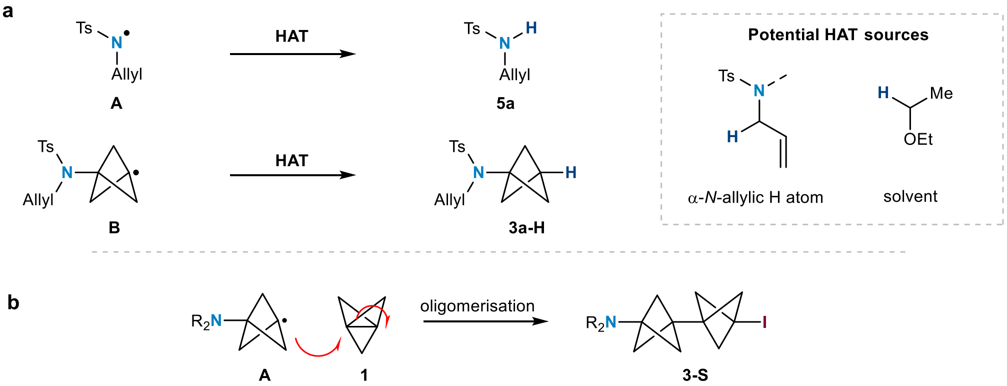


Figure 2.33: ATRA side products and their formation.

2.2.6.2 Photoredox-Catalysed Initiation

We were delighted that we could use photocatalysis initiation in addition to triethylborane for this reaction. Our previous work using photocatalysis for ATRA reactions with [1.1.1]propellane **1** proposed an oxidative quenching mechanism.[86] In this publication, isolation of reaction by-products resulting from oxidation of the BCP radical intermediate to give the BCP cation supported this mechanism. We considered the following hypothesis for the photoredox reaction of iodoaziridines (Figure 2.34). Initially, the excited-state photocatalyst could undergo oxidative quenching with iodoaziridine **2** to give an *N*-centred radical **A** following ring fragmentation. As with the triethylborane-initiation mechanism, this intermediate could form BCPA **3** in a propagation cycle following addition to **1** and subsequent iodine abstraction from the iodoaziridine substrate. A turn-over event is required to reduce the catalyst back to the neutral oxidation state. Under the reaction conditions, intermediate **B** could fulfil this role to give BCPA cation **C**. BCP cationic intermediates undergo rapid fragmentation to cyclobutene products and in this case, the nitrogen lone pair would further promote this fragmentation to give *exo*-cyclobutadiene **D**.[47, 86] Intermediate **D** can either lose a proton to give cyclobutene **E** or be trapped with iodide in a radical polar crossover mechanism to give cyclobutene **F**, which in turn could undergo elimination to give **E** or participate in further propagation events to form **G**. However, no by-products arising from formation of intermediate **D** could be isolated or observed in crude reaction mixtures.

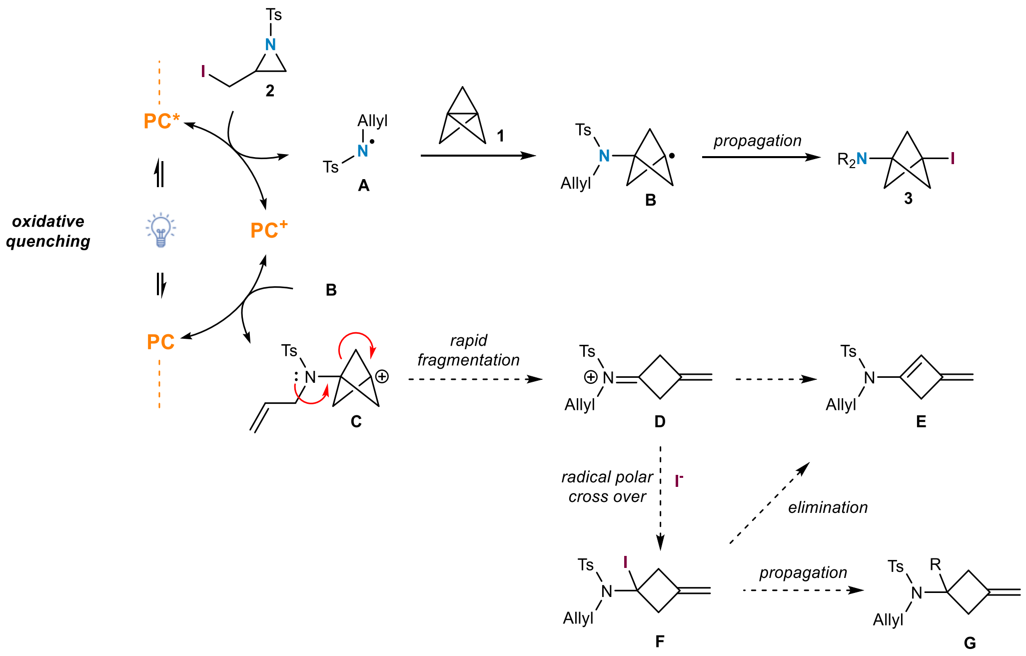


Figure 2.34: Hypothetical photoredox catalysis mechanism and possible by-products resulting from an oxidative catalyst turn-over event by the substrate.

Instead, we considered a photosensitisation mechanism where the excited-state photocatalyst undergoes a Dexter energy transfer process to the substrate to initiate the propagation cycle (see Section 2.2.2). In 2020, during the course of this work, Fodran and co-workers reported an aziridine fragmentation/(3+2) cycloaddition reaction, initially discovered by Kitagawa,[94] under photocatalytic conditions (Figure 2.35).[112] The authors elucidated a Dexter energy transfer mechanism for this process instead of a photoredox catalysed mechanism. Among the supporting evidence for their hypothesis, the reduction potential of aziridine **2a** was measured at $E_{1/2}$ = –1.88 V, which is more negative the reducing capabilities of the photocatalyst $E_{1/2}[{}^*\mathrm{Ir}^{\mathrm{III}}/\mathrm{Ir}^{\mathrm{IV}}]$ = –0.96 V *vs* SCE. Based on the absence of BCP oxidation by-products and the low reduction potential of α-iodoaziridines we conclude that a Dexter-energy transfer mechanism was likely to be in operation. The role of [1.1.1]propellane **1** with respect to redox processes of the photocatalyst in the reaction mechanism is unclear, however due to time constraints, further investigation was not carried out.

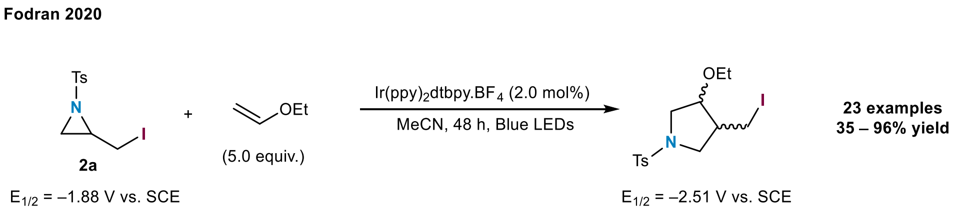


Figure 2.35: Photocatalysed Dexter Energy Transfer for an aziridine fragmentation/(3+2) cycloaddition reaction.

2.3 Conclusion

2.3.1 Conclusion

In conclusion, we have developed an efficient route to achieve highly desirable 1,3-disubstituted BCPAs **3**, through fragmentation of α-iodoaziridines **2** and subsequent ATRA reaction with [1.1.1]propellane **1** (Figure 2.36). These results mark a significant contribution to the field in accessing difunctionalised BCPAs with the resident iodide perfectly set up for further functionalisation. We endeavour to address this challenge in the following chapter, in order to exploit the utility of BCPA iodides for use as aniline bioisosteres.

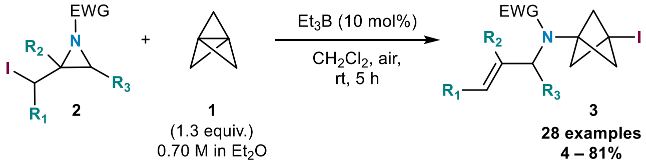


*Figure 2.36: N-centred radical ATRA reaction with [1.1.1]propellane **1**.*

The triethylborane-initiated aziridine fragmentation/ATRA methodology demonstrates good functional group tolerance for a range of sulfonamide protecting groups and aziridine substituents, including applications in more complex settings that are relevant to compounds found in the pharmaceutical industry. The limitations of this methodology are that we were unable to include alternative nitrogen protecting groups such as amides, carbamates, sulfinamides and phospinanes. The work presented in this chapter has been since been published in *J. Am. Chem. Soc.*[113]

Following the publication of these results, a novel halogen-bond mediated electrophilic activation of [1.1.1]propellane **1** was reported by Aïssa and co-workers to access *N,I*-disubstituted-BCPAs (Figure 2.37).[114] The methodology obtained a selection of *N*-heterocyclic and primary and secondary aniline BCP products. This complementary contribution to the field further highlights the importance and desirability of BCPA iodide compounds to the scientific community.

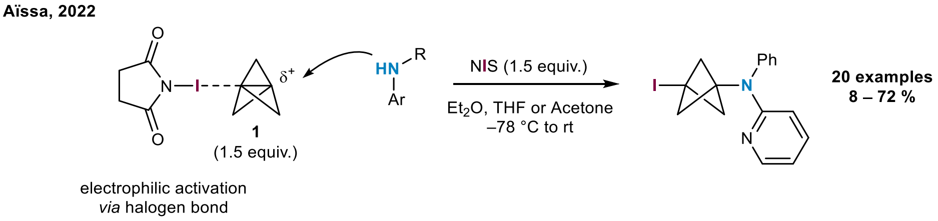


Figure 2.37: Synthesis of N-substituted BCPs through electrophilic activation.

3.

Functionalisation of BCP(A) Iodides

3.1 Introduction

3.1.1 Reactions of BCP Halides

Bicyclo[1.1.1]pentane (BCP) and bicyclo[1.1.1]pentylamine (BCPA) halides possess a handle for a diverse range of functionalisation opportunities and can be used for the generation of anionic, radical or cationic BCP intermediates (Figure 3.1). For example, electrophiles or transition metals can intercept BCP anionic intermediates for C–C bond formation (top). Similarly, BCP radical intermediates can be captured by SOMOphiles or transition metals for further functionalisation (middle). BCP cationic intermediates, however, are known to undergo rapid rearrangement to *exo*-methylene cyclobutenes (bottom).[41] Having established the methodology to synthesise BCPA iodides in the previous chapter, we sought to investigate derivatization methods to attain desirable 1,3-disubstituted BCP(A)s.

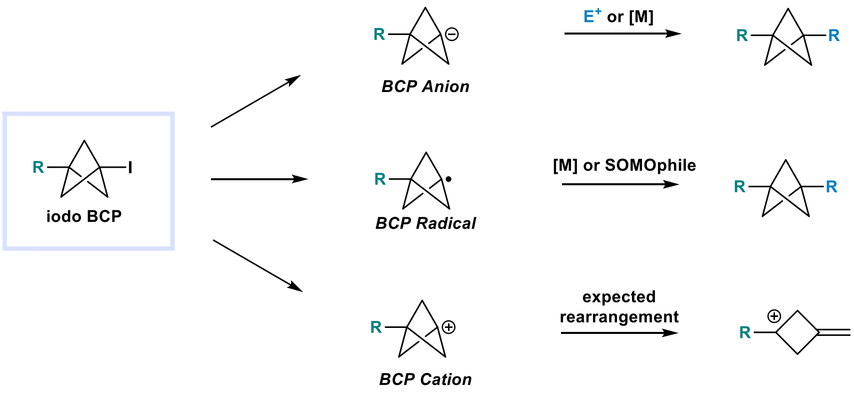


Figure 3.1: Diversification methods of BCP halides.

3.1.2 Functionalisation of Carbon-Substituted BCP Halides

Due to the limited number of preparations of BCPA halides, the majority of literature methods for the functionalisation of BCP halides focus on *C*-substituted BCP iodides. These compounds can undergo C–C bond formation following lithiation with *t*-BuLi and trapping with electrophiles such as acyl chlorides and CO_2 (Figure 3.2, a).[53] Direct palladium-catalysed cross-coupling of BCP iodides suffer from competing ring fragmentation (Figure 3.2, b);[115] to bypass these issues, BCP iodides can be lithiated before transmetalation and Negishi cross-coupling (Figure 3.2, c).[53] In 2020, our group reported a milder and more scalable iron-catalysed Kumada cross-coupling with readily available (hetero)aryl Grignard reagents (Figure 3.2, d).[115] However, alkyl and vinyl Grignard reagents were not tolerated. Finally, an isolated example of photo-induced copper catalysed alkynylation has also been described, albeit requiring 48 h reaction time (Figure 3.2, e).[116]

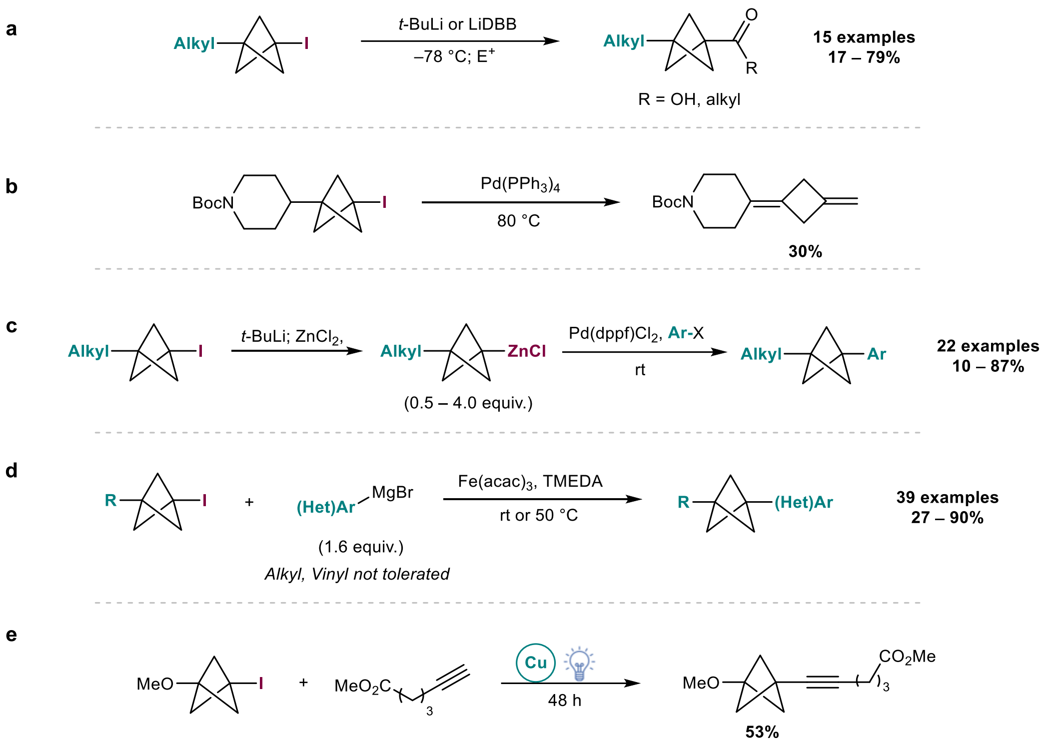


Figure 3.2: Functionalisation of BCP iodides.

3.1.3 Generation of BCP Radical Intermediates

C-substituted BCPs can undergo C–C bond formation via radical intermediates, predominantly through decarboxylative processes. For example, photoredox catalysis can initiate a decarboxylative Heck reaction from a BCP carboxylic acid (Figure 3.2, a),[117] and BCP redox-active esters can be decarboxylated in the presence of zinc and nickel to form BCP amino acids following addition into a chiral sulfinyl imine acceptor (Figure 3.2, b).[118] Both of these examples are isolated results within a general methodology but demonstrate the ability of BCP radical intermediates to be generated under photocatalysis and undergo C-C bond formation in respectable yields (54% and 55% respectively).

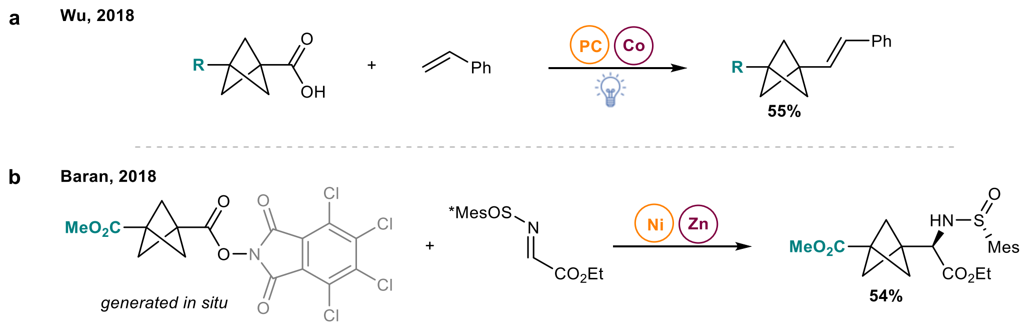


Figure 3.2: Isolated examples of decarboxylative photoredox functionalisation of BCPs.

3.1.4 Functionalisation of BCPA Halides

Compared to *C*-substituted BCP iodides, the reported methodology for the functionalisation of BCPA iodides to form *N,C*-disubstituted BCPAs is lacking. This is predominantly due to the absence of methodology to synthesis *N,C*-disubstituted BCPAs . Only BCPA iodides with azide or triazole *N*-substituents have been studied for C–C bond formation. These methods rely on toxic organotin reagents (Figure 3.3, a),[77] or require the radical acceptor as the reaction solvent using relatively harsh UV conditions and high temperatures (Figure 3.3, b).[119]

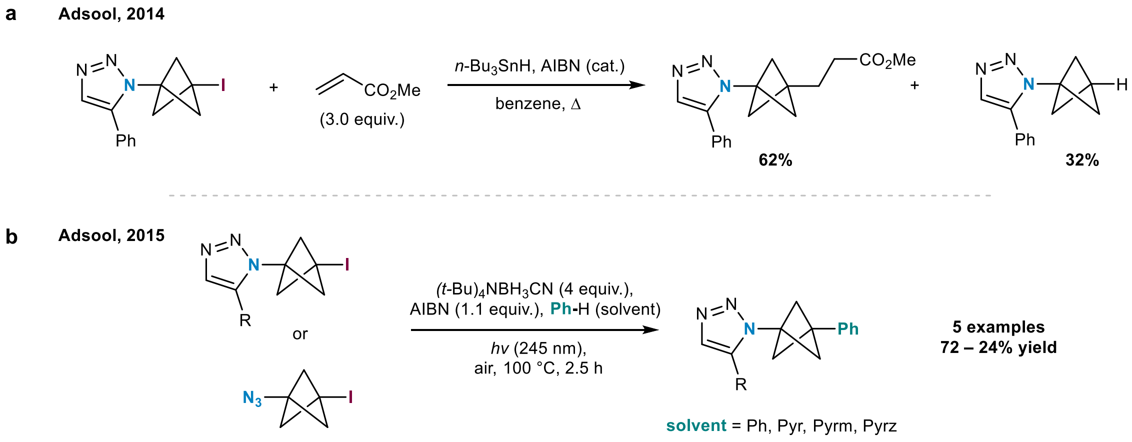


Figure 3.3: Functionalisation of BCPA iodides.

We questioned whether photoredox catalysis could offer a solution to this challenge. By utilising photocatalysis to generate a BCPA radical intermediate from the corresponding iodide under mild conditions, we could then achieve C–C bond formation in a Giese-type reaction.[120, 121] This would represent the first visible-light photocatalysed initiation of BCP radicals from BCP iodides, and it would also offer an alternative to the dominance of cross-coupling transformations in the literature.

3.1.5 Silyl Mediators in Photoredox Catalysis

Silane and silanol mediators have enabled the photocatalytic generation of radicals from alkyl and aryl halides with reduction potentials beyond the redox capabilities of common photocatalyst (Figure 3.4).[122] Recently, this method has been used to achieve trifluoromethylation (Figure 3.4, a),[123, 124] cross-coupling (Figure 3.4, b),[125] Giese reactions (Figure 3.4, c),[126] and Minisci reactions (Figure 3.4, d) of alkyl and aryl bromides.[127, 128] The use of iodides is less common compared to bromides; and only one example exists for the activation of tertiary alkyl iodide (*t*-BuI) in a silyl-mediated Minisci reaction (Figure 3.4, d).[128]

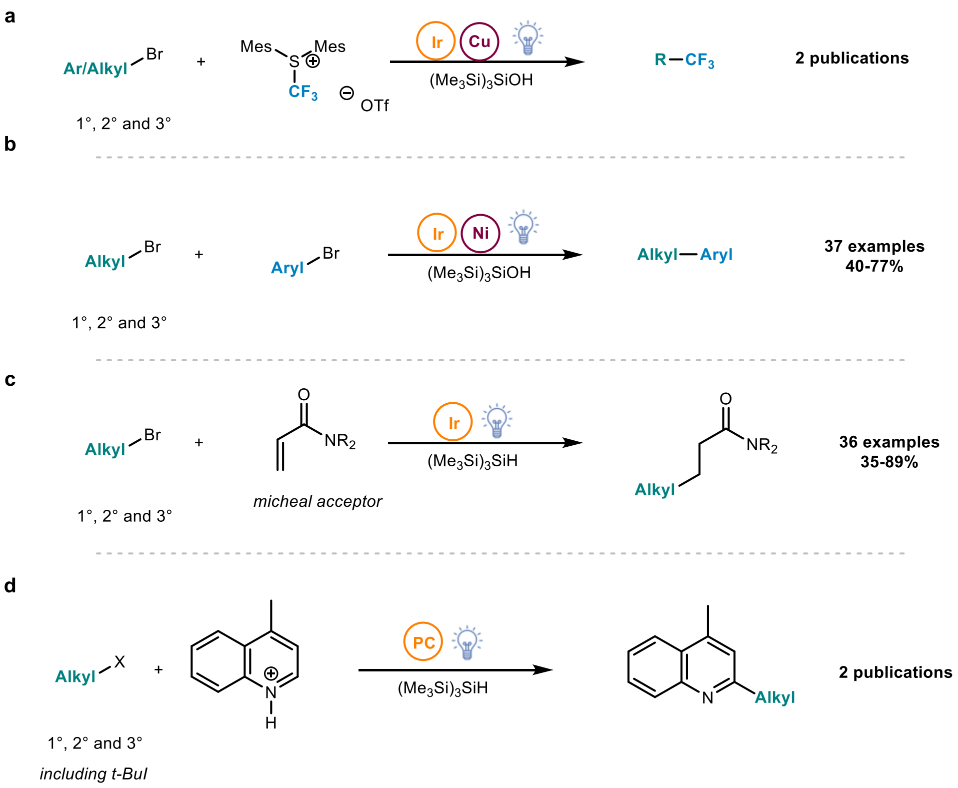


Figure 3.4: Silyl-mediated photoredox reactions of alkyl and aryl halides.

Si–X	*BDE / kcal mol^{-1}*
Me_3Si–Cl	113
Me_3Si–Br	96
Me_3Si–H	90
Me_3Si–I	77
t-(C_4H_9)–Br	63
t-(C_4H_9)–I	50

Figure 3.5: Si–X Bond Strengths.[125, 129, 130]

MacMillian speculated that the success of bromides in this chemistry is a result of irreversible halide abstraction due to the greater Si–Br bond strength compared to sp^3 C–Br (difference of 33 kcal mol^{-1}) (Figure 3.5).[125] By analogy an Si–I bond is stronger than the C–I bond of *t*-BuI by 27 kcal mol^{-1} and should be able to be employed in iodide atom abstraction with similar efficiency. Silanes are able to act as HAT agents in addition to an energy transfer mediator or X• scavenger. For C–C bond formation, fast HAT processes are unproductive due to premature radical termination. Therefore, the choice of silane can be crucial for controlling the rate of HAT vs the formation of new C–C bonds. The rates of HAT of different silanes and silane/thiol couples are typically reflective of the Si-H bond dissociation energies (Figure 3.6 and 3.7); the success of $(Me_3Si)_3SiH$ in C–C bond forming reactions compared to Bu_3SnH for example, has been attributed to the 5 kcal mol^{-1} difference in Sn–H vs Si–H bond strength.[131, 132 133]

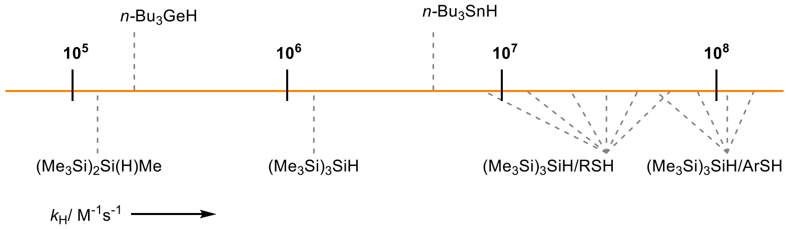


Figure 3.6: Rate constants of H-abstraction from Group 14 hydrides by primary alkyl radicals at 80 °C.[134]

Reductant	*BDE / kcal mol^{-1}*	*Availability*
$Bu_3Sn–H$	73.7	Commercial
$(Me_3Si)_3Si–H$	79.0	Commercial
$Et_3Ge–H$	82.3	Commercial
$(MeS)_3Si–H$	82.5	Ref. [129]
$Bu_3Ge–H$	82.6	Commercial
$(Me_3Si)_2MeSi–H$	82.9	Ref. [135]
$Ph_3Si–H$	84.0	Commercial
$(Me_3Si)Me_2Si–H$	85.3	Commercial
$(i PrS)_3Si–H$	85.6	Ref. [129]
$Et_3Si–H$	90.1	Commercial

Figure 3.7: Literature bond dissociation energies for commonly used reductants.[136-138] *Note: The synthesis of non-commercially available reductants is typically lengthy or unpleasant.*

3.1.6 Chapter Aims

This chapter aims to use BCPA iodides as precursors to *N,C*-disubstituted BCPAs, which can then be investigated as bioisosteres for *p*-substituted anilines (Figure 3.8). Our strategy was to first investigate the reported methods to generate BCPA anionic intermediates and their trapping with electrophiles or transition metals for cross-coupling, before investigating the formation and application of BCPA radical intermediates in novel C-C bond forming reactions.[120]

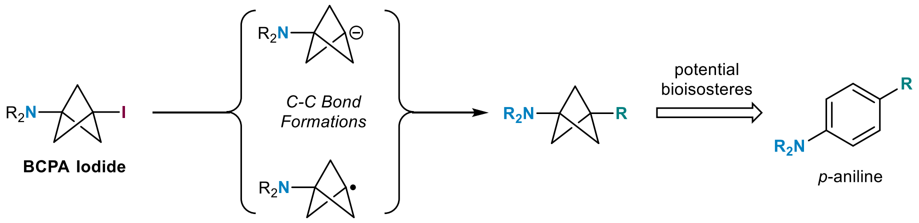


Figure 3.8: Methods to functionalise BCPA iodides.

3.2 Results and Discussion

3.2.1 Literature Methods to Functionalise BCPA Iodides

We commenced our investigation with methodologies previously published by our group that were successful with *C*-substituted BCPs. We first investigated the lithiation of BCPA iodide **3a** with *t*-BuLi with a view to transmetallate for Negishi cross-coupling, or electrophilic trapping.[85, 115] Unfortunately, even conducting the lithiation at –96 °C led to fragmentation of the BCPA carbanion intermediate to give *N*-allyl sulfonamide **5a**, presumably reforming [1.1.1]propellane **1**.

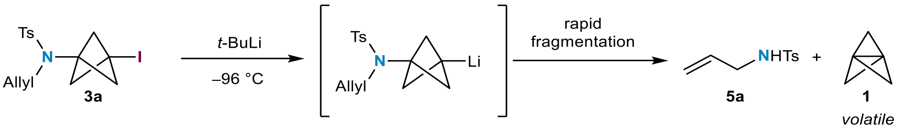


*Figure 3.9: Anionic fragmentation of BCPA iodide **3a**.*

Attempts to perform iron-catalysed Kumada cross-coupling of **3a** with aryl Grignard reagents also failed, only returning starting material when performed at room temperature or 50 °C (Figure 3.10).

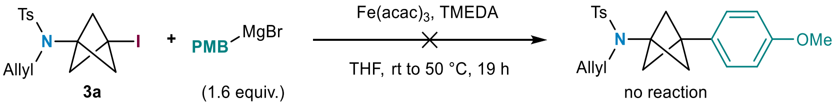


*Figure 3.10: Failed Kumada cross-coupling of BCPA iodide **3a**.*

3.2.2 Photochemical Reduction of BCPA Iodides

We observed that BCPA iodide **3a** becomes pale pink when standing in ambient light and questioned whether this was indicative of C–I homolysis and resulting iodine liberation. We aimed to exploit this decomposition pathway by attempting a photoinduced ATRA reaction of BCPA iodide **3a** with methyl acrylate **6b**. Unfortunately, attempts to promote this transformation using either white or blue LEDs were unsuccessful (Figure 3.11). The UV/Vis spectrum of BCPA iodide **3a** showed that only UV wavelengths <350 nm were absorbed by the substrate so homolysis of the BCPA C–I bond is likely to be inefficient under visible light (Figure 3.12). For safety reasons we opted to steer away from the use of UV wavelength light and attempted to instead promote radical initiation with Et_3B or a photocatalyst (PC = *fac*-Ir(ppy)$_3$, E_{red} $^*Ir^{III}/Ir^{II}$ = –1.7 V vs SCE[95] or PTH = 10-phenylphenothiazine, E_{red} $^*PC^{n}/PC^{n+1}$ = –2.1 V vs SCE[139]). However, no ATRA (or de-halogenated) products were obtained in these cases.

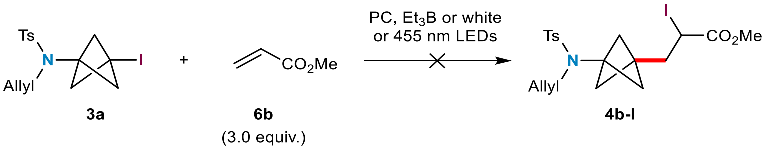


Figure 3.11: Attempted ATRA process with visible light, triethylborane, and photocatalysis.

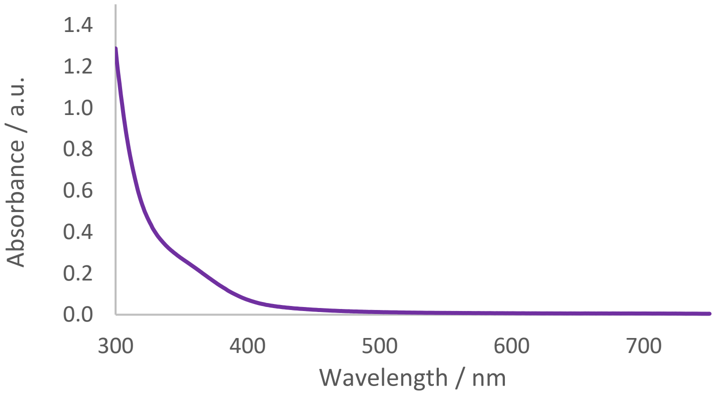


*Figure 3.12: UV/Vis Spectra of BCPA iodide **3a**.*

Photoredox catalysis can be used to effect single-electron reduction of C–I bonds via oxidative quenching of the photoexcited catalyst. We sought to implement a photoredox catalysed de-halogenation based on the work by Nguyen *et al.* (Figure 3.13).[140] A oxidative quenching mechanism of the photocatalyst is proposed, where either NBu_3/HCO_2H or NBu_3/Hantzsch Ester (HE) are used for catalyst turn-over and as an HAT source. Both variations of these conditions returned unreacted starting iodide **3a**.

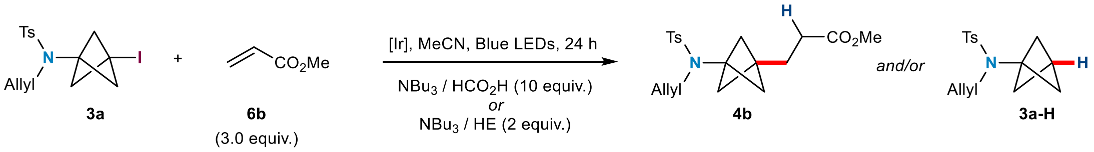
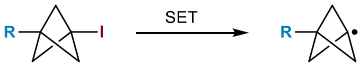


*Figure 3.13: Attempted photoredox catalysed dehalogenation of BCPA iodide **3a.** HE = Hantzsch Ester, diethyl 1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylate. [Ir] = fac-Ir(ppy)$_3$.*

We therefore considered the reduction potential of the BCPA iodide C–I bond to probe whether single-electron reduction was energetically feasible through an oxidative quenching method. Approximate figures for the reduction potentials of BCP halides are promising, based on the reported reduction potentials of mono- and di-halide BCP (–1.09 V to –0.64 V vs SCE) (Figure 3.14)[141] and the capabilities of common photoredox catalysts (–0.57 V to –2.19 V).[142]



R	$E_{1/2}$*Red vs SCE*
H	–1.09
F	–1.17
Cl	–0.84
Br	–0.74
I	–0.64

Figure 3.14: Literature data for reduction potentials of BCP iodides.[141]

A square wave voltammogram of BCPA iodide **3a** showed a reduction peak at –2.29 V vs SCE in MeCN (Figure 3.15, a), and no oxidative peak was observed in a scan in the positive direction (Figure 3.15, b). The cyclic voltammogram supports **3a** undergoing irreversible reduction at this potential (Figure 3.15, c and d). Notably, we observed degradation of the substrate over multiple scans, presumably a result of degradation or rearrangement through the generation of ionic and /or cationic BCPA intermediates. We cannot conclude that the reduction peak at –2.29 V is directly due to the C–I bond. Regardless, this potential is beyond the reduction capabilities of common photoredox catalysts and explains the lack of reactivity of BCP iodide **3a** under photoredox conditions thus far.

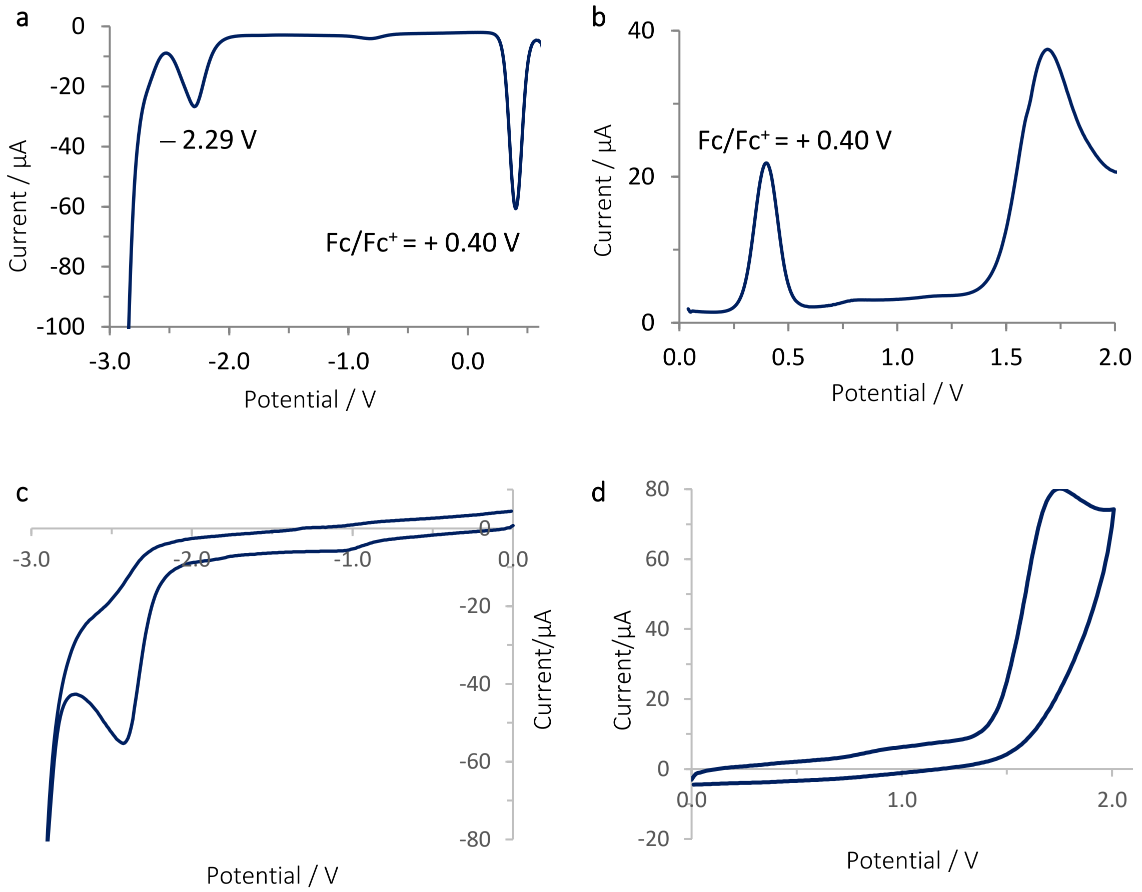


*Figure 3.15: Voltammograms of BCPA iodide **3a** in MeCN. a. Square Wave Reduction. b. Square Wave Oxidation. c. Reduction Cyclic Voltammogram (unreferenced). d. Oxidation Cyclic Voltammogram (unreferenced).*

3.2.3 Silanes as Iodide Scavengers

It was not until we attempted to de-halogenate BCPA iodide **3a** with $(Me_3Si)_3SiH$ that we could utilise photocatalysis to generate BCPA **3a-H** in 54% yield (Figure 3.16). We anticipated the role of the silane to not only be as a HAT reagent but also as a mediator between the BCPA halide and photocatalyst to enable generation of a BCPA radical intermediate by iodine atom abstraction.

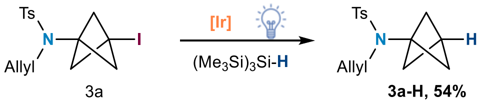


*Figure 3.16: Photocatalysed de-halogenation of BCPA iodide **3a**. [Ir] = fac-Ir(ppy)₃.*

With evidence that a direct radical initiation of the BCPA iodide was not feasible under direct photoredox catalysis, triethylborane initiation or visible light homolysis; we investigated the potential of a one-pot, three-component cascade ATRA reaction with iodoaziridine **2a**, [1.1.1]propellane **1** and methyl acrylate **6b** to achieve an *N,C*-difunctionalised BCP **4b**. The aim was to intercept the BCPA radical intermediate with a SOMOphile before it could abstract iodide from the iodoaziridine substrate or undergo HAT termination events. Unfortunately, with photoredox and triethylborane initiation protocols, BCPA iodide **3a** was obtained as the primary product (Figure 3.17, top). Inclusion of $(Me_3Si)_3SiH$ as a potential iodide scavenger resulted in premature HAT of the intermediate sulfamidyl radical to give *N*-allyl sulfonamide **5a** as the major product (Figure 3.17, middle). The desired Giese addition product **4b** was not observed until the addition of $(Me_3Si)_3SiH$ was delayed by 2 hours when **2a** was consumed. Under these conditions with Et_3B, an encouraging 13% yield of Giese addition product **4b** was obtained

(Figure 3.17, bottom). From here, we took a step back to implement a stepwise Giese reaction to address these challenges, before re-visiting a one-pot procedure.

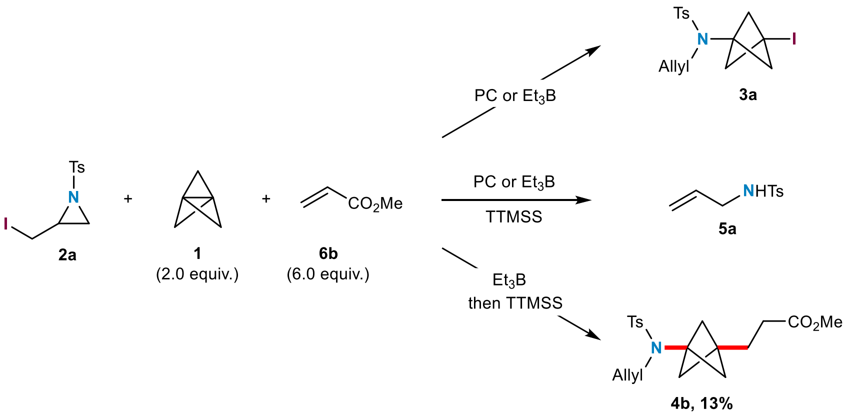
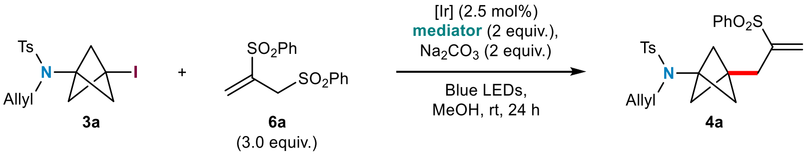


Figure 3.17: Three-component Giese reaction attempts.

3.2.4 Giese Reaction Optimisation – Allyl Sulfone Acceptor, Conditions A

Allyl sulfone **6a** was selected as an efficient radical acceptor for the Giese addition of BCPA iodide **3a**.[143] Initial attempts using Ir[(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$ with (Me$_3$Si)$_3$SiH (TTMSS) as a radical mediator delivered addition product **4a** in 16% yield, along with a significant amount of the de-iodination product **3a–H** (Table, 3.1, entry 1). This competing H-atom abstraction by the presumed BCPA radical intermediate could be reduced by using (Me$_3$Si)$_3$SiOH, which is proposed to act as a silyl radical source via silanolate oxidation / radical-Brook rearrangement.[123, 144] This led to a significant improvement in yield (38%, entry 2).

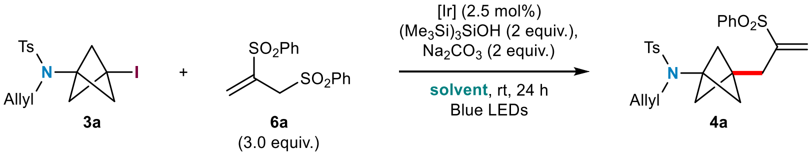


Entry	*Mediator*	***4a** NMR Yield /%[a]*
1	$(Me_3Si)_3SiH$	16
2	$(Me_3Si)_3SiOH$	38

Table 3.1: Giese Reaction Optimisation. [Ir] = Ir[(dF(CF_3)ppy)$_2$(dtbbpy)]PF_6. [a] NMR yield determined using mesitylene as internal standard throughout.

3.2.4.1 Variation of Solvent

The choice of solvent had a significant influence on the reaction yield, likely due to improved solubility of **6a** (Table 3.2). An extensive solvent screen confirmed that CH_2Cl_2 gave optimal yields of (**4a**, 60%) (entry 7). Notably, *t*-BuCN and DME gave good yields based on recovered starting material (entries 9 and 12), and these were further investigated in later optimisation.



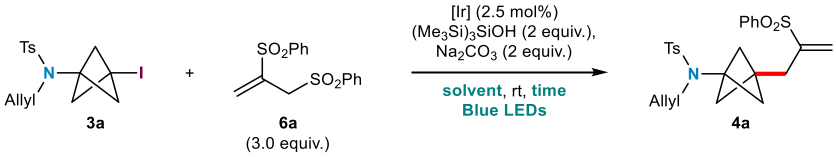
Entry	*Solvent*	*NMR Conversion of **3a** /%*	***4a** NMR Yield /% (isolated)*
1	MeOH	-	38
2	DMF	25	3
3	DMA	-	18
4	DCE	91	56
5	DMSO	16	1
6	TFE	72	37
7	CH_2Cl_2	86	(60)
8	MeCN	78	41
9	*t*-BuCN	58	42 (43)
10	MeOH	-	38
11	$PhCF_3$	79	33
12	DME	48	47 (37)

13	*EtOAc*	*14*	*23*
14	MeOH/H_2O (2:1)	56	42 (47)
15	1,4-dioxane/CH_2Cl_2 (8:2)	-	54 (58)
16	1,4-dioxane/H_2O/CH_2Cl_2 (4:4:2)	98	49
17	DCE/H_2O (2:1)	100	36

Table 3.2: Variation of reaction solvent. [Ir] = Ir[(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$.

3.2.4.2 Variation of reaction setup

A reduced yield was observed when using the more powerful 50 W LED '**set-up 3**' compared to the 18 W LED '**set-up 1**' (see section 2.2.2.5 for further information), presumably due to an increased substrate degradation rate (Table 3.3, entries 1 and 2). In addition, a longer reaction time gave a reduced yield of 50% (Table 3.3, entry 1 *vs* 2 and 3). Re-investigation of DME and *t*-BuCN as potential reaction solvents at this stage showed no improvement with longer reaction times (entries 4 and 5).

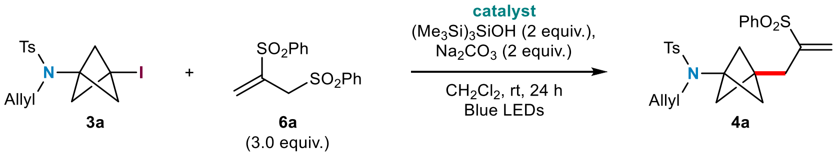


Entry	LED Set up	Time / h	Solvent	Conversion of 3a /%	4a NMR Yield /% (isolated)
1	18 W **Set-up 1**	24 h	CH_2Cl_2	86	(60)
2	50 W **Set-up 2**	24 h	CH_2Cl_2	91	48
3	18 W **Set-up 1**	48 h	CH_2Cl_2	90	50
4	18 W **Set-up 1**	48 h	DME	47	29
5	18 W **Set-up 1**	72 h	*t*-BuCN	98	63

Table 3.3: Variation of reaction set up and re-evaluation of promising solvents. [Ir] = Ir[(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$.

3.2.4.3 Variation of photocatalyst

Multiple catalysts were suitable for this transformation (Table 3.4); in particular, the organo-catalyst 4-CzIPN gave a comparable 56% yield to the optimal Ir[(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$ in 60% (entry 2 vs 7). No correlation between reaction yield and reduction or oxidation potential could be drawn (Figure 3.18).



Entry	*Catalyst*	*E$_{Ox}$*	*E$_{Red}$*	*Conversion of **3a** /%*	***4a** NMR Yield /% (isolated)*
1	Ir[(dF(CF$_3$)ppy)2(5,5'-d(CF$_3$)bpy)]PF$_6$	1.68	–0.69	81	41
2	Ir[(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$	1.21	–1.37	86	(60)
3	Ru(bpz)$_3$(PF$_6$)$_2$	1.45	–0.80	29	6
4	Rose Bengal [a,b]	0.81	–0.99	31	15
5	Ir(ppy)$_2$(dtbbpy)PF$_6$	0.66	–1.51	61	35
6	Ir[(dF(CF$_3$)ppy)$_2$(bpy)]PF$_6$	1.32	–1.37	-	55
7	4-CzIPN [a]	1.35	–1.21	-	56
8	Mes-[Acr]$^+$BF$_4$ [a]	2.08	–0.57	-	33
9	(-)-Riboflavin	1.50	–0.50	68	17
10	Ir[(dF(F)ppy)$_2$(d(CF$_3$)bpy)]PF$_6$	1.55	–0.83	-	56 (53)

Table 3.4: Investigation of photocatalysts. [a] 5 mol% of catalyst. [b] Green LEDs.

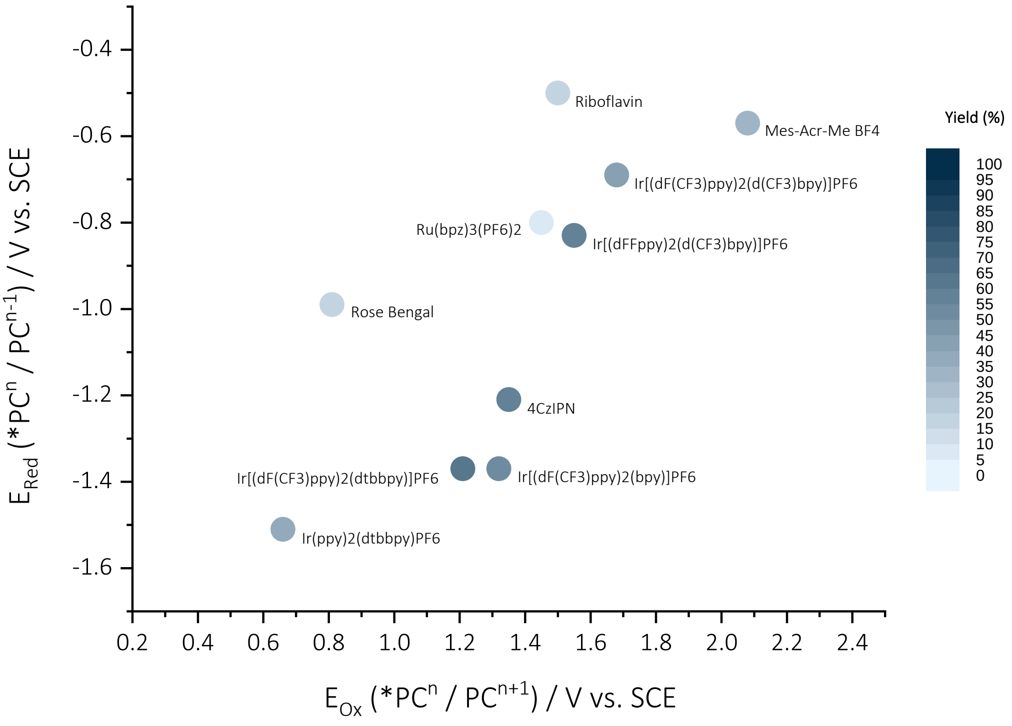
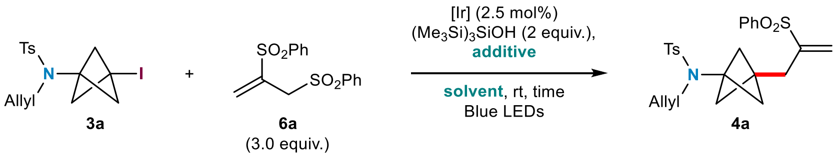


Figure 3.18: Temperature plot of reaction yield against redox potentials of the photocatalysts.

3.2.4.4 Base variation and Additives

Screening of inorganic and organic bases demonstrated Na_2CO_3 to be the optimal choice (Table 3.5, entries 1 to 7). The addition of NaI as a potential source of I^- for the initial reduction of the catalyst, as proposed mechanistically by ElMarrouni, did not benefit the yield of **4a** (entry 8).[126] Addition of phase transfer catalysts such as TBAI to increase solubility was not beneficial and resulted in diminished yields (entry 9).

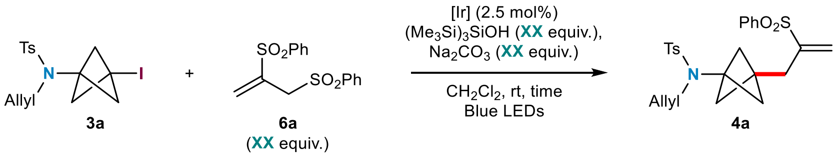


Entry	Base^a	Additive	Solvent	**4a** NMR Yield /% (isolated)
1	Na_2CO_3	-	MeOH	38
2	Cs_2CO_3	-	MeOH	6
3	K_4PO_3	-	MeOH	11
4	Na_2CO_3	-	1,4-Dioxane/CH_2Cl_2 (8:2)	54 (58)
5	Bu_4N^+ OH^-	-	1,4-Dioxane/CH_2Cl_2 (8:2)	12
6	Bu_4N^+ OAc^-	-	1,4-Dioxane/CH_2Cl_2 (8:2)	5
7	$Bu_4N^+(O)P(OBu)_2$^{b}	-	1,4-Dioxane/CH_2Cl_2 (8:2)	0
8	Na_2CO_3	NaI (2.0 equiv.)	1,4-Dioxane/CH_2Cl_2 (8:2)	51
9	Na_2CO_3	TBAI (2.5 equiv.)	1,4-Dioxane/CH_2Cl_2 (8:2)	1

Table 3.5: Screen of organic and inorganic bases, and addition of other additives. ^{a} *2.0 equiv. base.* ^{b} *$Bu_4N^+(O)P(OBu)_2$ was prepared according to known literature procedures.*[145] *[Ir] = Ir[(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$.*

3.2.4.5 Variation of Silane, Base and Acceptor Equivalents

Variation of the equivalents of silane, base and acceptor **6a** to try and control the proportion of undesired HAT revealed our initial ratio of 2:2:3 respectively to be optimal (Table 3.6, entry 2).

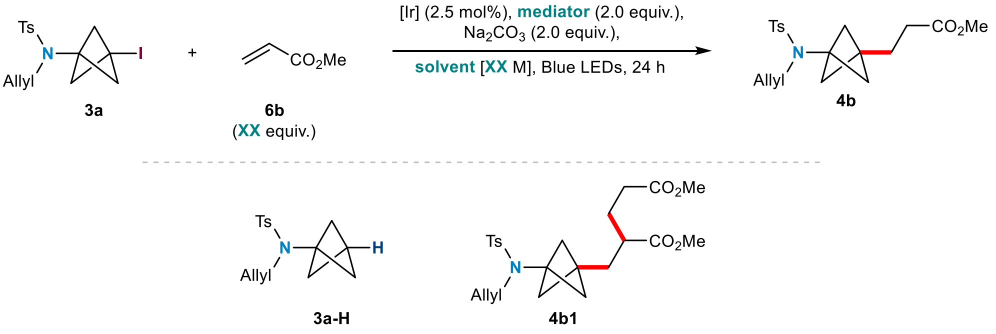


Entry	**6a** equiv.	$(TMS)_3SiOH$ equiv.	Na_2CO_3 equiv.	**4a** NMR Yield /% (isolated)
1	2.0	2.0	2.0	43
2	3.0	2.0	2.0	(60)
3	4.0	2.0	2.0	54 (50)
4	3.0	1.2	1.2	52 (47)
5	2.0	1.5	1.5	45 (44)

Table 3.6: Evaluation of reaction stoichiometry. [Ir] = Ir[(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$.

3.2.5 Giese Reaction Optimisation – Methyl Acrylate Acceptor, Conditions B

In stark comparison, when methyl acrylate **6b** was used as a radical acceptor with these optimised conditions, only 3% of Giese addition product **4b** was obtained. Even an increased loading of methyl acylate (6.0 equiv.), improved the yield of **4b** to just 9% (Table 3.7, entries 1 and 2). By returning to the use of $(Me_3Si)_3SiH$ as a mediator, we were pleased to restore the desired reactivity (48%, entry 3). An optimal 60% yield of **6b** was achieved by changing the reaction solvent to MeOH / H_2O (9:1) (entry 4). Alongside the formation of **6b**, a significant proportion of over-addition product **4b1** and premature HAT product **3a-H** were isolated, which negatively impacted the reaction yield. To reduce the formation of **3a-H**, Et_3GeH was tried as a mediator due to its stronger Ge–H bond (BDE = 82.3 $kcalmol^{-1}$) than the Si–H bond of $(Me_3Si)_3SiH$ (BDE = 79.0 $kcalmol^{-1}$, see section 3.1.5); while the amount of **3a-H** was reduced, a lower yield of **4b** was returned (entry 5). Dilution of the reaction and reduction of the equivalents of **6b** were trialled to minimised the formation of over-addition product **4b1**, however at a cost to the yield of desired Giese product **4b** (entries 6 to 8).



Entry	*6b* equiv.	*Mediator*	*Solvent*	*Conc. / M*	*3a-H NMR Yield /%*	*4b1 isolated /%*	*4b NMR Yield /% (isolated)*
1	3.0	$(Me_3Si)_3SiOH$	CH_2Cl_2	0.15	-	-	3
2	6.0	$(Me_3Si)_3SiOH$	CH_2Cl_2	0.15	41	-	9
3	6.0	$(Me_3Si)_3SiH$	CH_2Cl_2	0.15	24	22	(48)
4	6.0	$(Me_3Si)_3SiH$	$MeOH/H_2O^a$	0.15	23	27	(60)

5	6.0	Et_3GeH[b]	$MeOH/H_2O$[a]	0.15	7	-	35
6	6.0	$(Me_3Si)_3SiH$	$MeOH/H_2O$[a]	0.06	20	23	(52)
7	3.0	$(Me_3Si)_3SiH$	$MeOH/H_2O$[a]	0.15	35	-	44
8	4.0	$(Me_3Si)_3SiH$	$MeOH/H_2O$[a]	0.15	23	-	49

Table 3.7: Giese reaction optimsation with methyl acrylate acceptor. Reactions carried out using ***set-up 1****. [Ir] = Ir[(dF(CF_3)ppy)$_2$(dtbbpy)]PF_6. [a] MeOH:H_2O (9:1). [b] 1.0 equiv. of mediator.*

3.2.6 Control Reactions

The use of a silane mediator was essential for achieving the desired reactivity. Irradiation of BCP iodide **3a** with blue LEDs alone (Table 3.8, entry 1), or in the sole presence of the Ir photocatalyst (entry 2), only returned starting material. The addition of TEMPO as a radical trap yielded the same result, with no TEMPO adduct observed by ^{1}H NMR, mass spectrometry or LCMS, with or without the photocatalyst (entries 3 and 4). Only in the presence of a silyl mediator was the Giese product **4b** obtained (X = H, entry 5), albeit in reduced yield without the presence of the photocatalyst (22% compared to 60% with [Ir], entry 6). These results show that all reaction components are required for successful Giese addition.

Entry	Additives	**3a** NMR Yield /%	**4b** NMR Yield /%	**3a-H** NMR Yield /%
1	-	100	0	0
2	[Ir]	99	0	0
3	TEMPO[a]	94	0	0
4	TEMPO[a], [Ir][b]	100	0	0
5	$(Me_3Si)_3SiH$,[a] Na_2CO_3[a]	-	22 (X=H)	40
6	$(Me_3Si)_3SiH$,[a] Na_2CO_3[a], [Ir][b]	-	60 (X=H)	23

Table 3.8: Control experiments. [a] 2.0 equiv. [b] [Ir] = Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (2.5 mol%).

3.2.7 Substrate Scope

With two sets of reaction conditions in hand, the Giese methodology was applied to a range of radical acceptors (Figure 3.19, a and b).

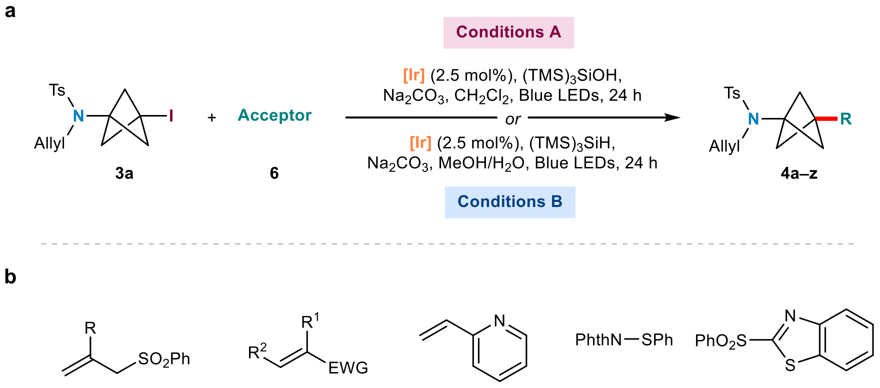


Figure 3.19: Optimised reaction conditions and radical acceptors used. [Ir] = Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6. Reaction were carried out on a 0.15 mmol scale.

Under Conditions A, addition to allylic sulfones bearing sulfonyl, ester and bromide substituents delivered the corresponding allyl-BCPA products **4a**, **4c** and **4d** following sulfone elimination (29 – 60%, Figure 3.20, a). *Ipso*-substitution of a benzothiazole sulfone gave the hetero-arylated BCPA **4e** in a modest 24% yield. Although lower yielding, isolation of this heteroarylated BCPA compliments the cross-coupling protocols reported for carbon-substituted BCP iodides (section 3.1.2). Trapping of the BCPA radical intermediate with *N*-(phenylthio)phthalimide delivered an *N,S*-disubstituted BCP (**4f**, 32%). Variation of the sulfonamide group on the BCPA iodide was also well-tolerated, including functionalisation of the anti-inflammatory agent Celecoxib (**4g** and **4h**, 50 – 53%, Figure 3.20, b). To our delight, *C*-substituted BCP iodides featuring ester, piperidine and pyridine functionalities performed comparatively well to give **4i** – **k** in 40 – 59% yield.

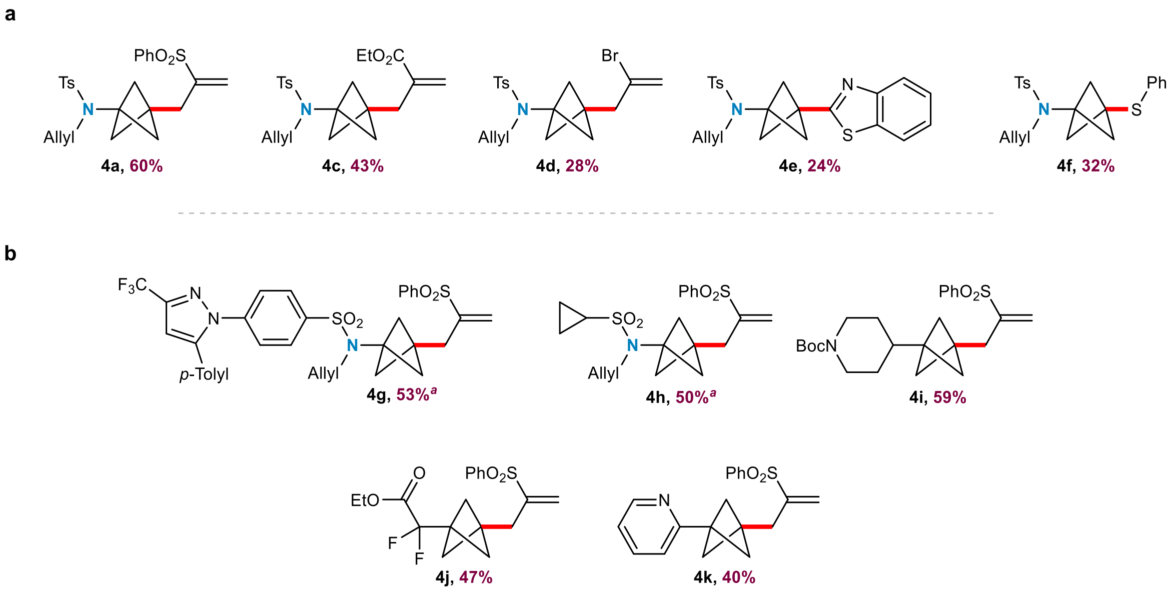


Figure 3.20: Scope of BCPA iodide functionalization. Red yields indicate Conditions A. Blue yields indicate Conditions B. [a] 0.13 mmol scale.

Acrylonitrile, acrylate and acrylamide acceptors (**4b**, **4l** – **o**, 42 – 60%) were more suited to reaction Conditions B with $(Me_3Si)_3SiH$ as a mediator (Figure 3.21). The Giese reaction demonstrated potential for larger scale applications, whereby a 1.0 mmol scale procedure returned **4b** in 50% yield. Additionally, the structure of **4l** was determined by single-crystal X-ray diffraction.[146] 2-Benzylidene malononitrile however, reacted poorly under these conditions but delivered **4o** in 57% yield under Conditions A. Vinyl sulfone, and 2-vinylpyridine radical acceptors were also successful, giving compounds (**4p**, 45%) and (**4q**, 34%). Vinyl boronic esters were also suitable radical acceptors for this chemistry, and the Giese additions products could be oxidised directly for ease of isolation (**4s** and **4t**, 29 – 31%).

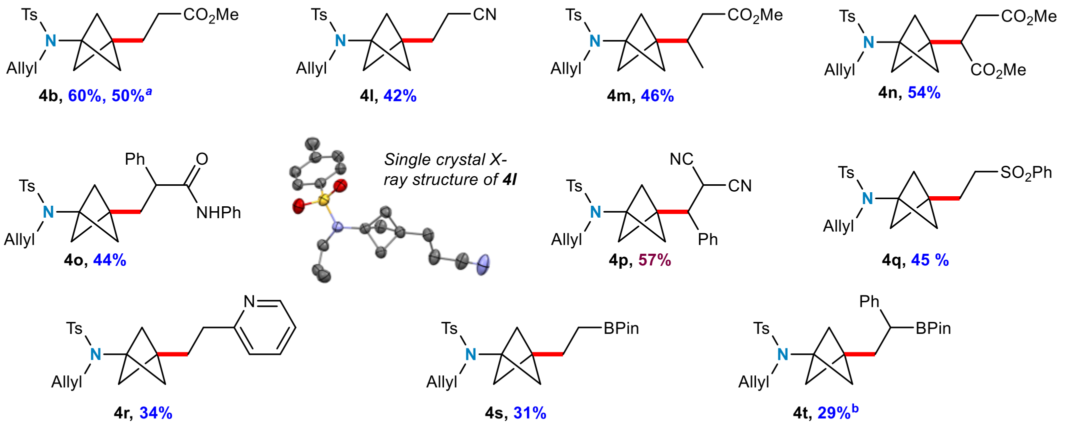


Figure 3.21. Scope of BCPA iodide functionalization. Red yields indicate Conditions A; blue yields indicate Conditions B. ^{a} 1.00 mmol scale. ^{b} The crude boronic ester was directly oxidized with H_2O_2/NaOH (aq.); the yield refers to the isolation of the corresponding alcohol.

Pharmaceutically-relevant BCPA α-amino acid analogues of 4-amino phenylalanine could be obtained on addition to dehydroalanine **6u**, indeed compound **4u** was isolated in a good 52% yield under reaction Conditions B (Figure 3.22, a). BCPA iodides bearing both electron deficient *p*-CN- (**4v**) and electron donating *p*-OMe- (**4w**) aryl substituents showed comparable reactivity (54% and 57% respectively). These mild reaction conditions also tolerated heteroaryl and alkyl sulfonamides giving BCPA phenylalanine derivatives **4x** and **4y** in 38% and 69%. Once more, this chemistry was applied smoothly to the photocatalytic functionalisation of *C*-substituted BCP iodides (**4z** – **ad**, 44 – 58%) (Figure 3.22, b). The exemplary functional group tolerance of this Giese methodology was further demonstrated by application to nicotinic acid derivative (**4ac**, 45%) and BCP-brequinar analogue (**4ad**, 53%). These previously unobtainable BCP(A) α-amino acid analogues demonstrate the power of this strategy to access pharmaceutically-relevant structures directly from BCP(A) iodides.

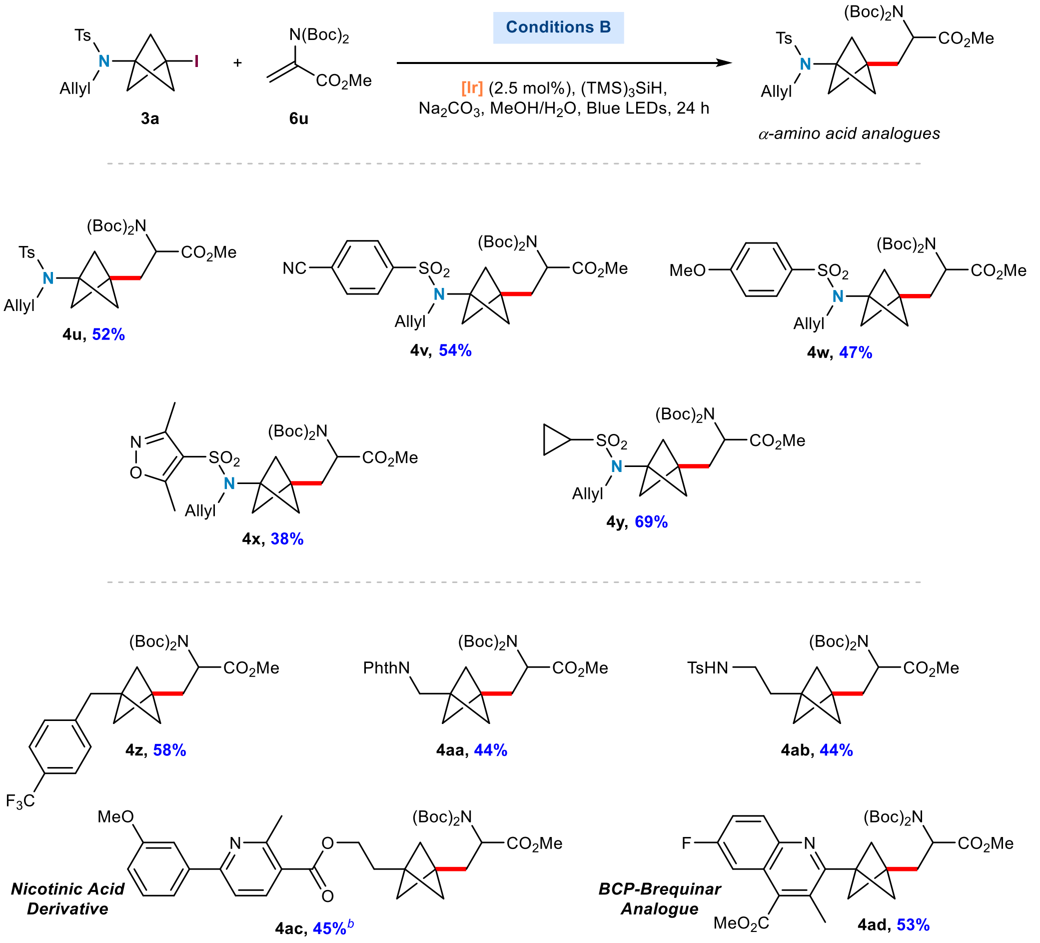


Figure 3.22: BCPA α-amino acid analogues.^{a} *0.13 mmol scale. [Ir] = Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$.*

3.2.8 Telescoped Reaction

Earlier in this thesis, photocatalysis was shown to achieve the formation of BCPA iodides **3** through aziridine fragmentation and addition to [1.1.1]propellane **1** (section 2.2.2). On reflection of our Giese conditions, we anticipated that a single photocatalyst could be used to promote all three steps in one pot – azridine fragmentation, ring opening of [1.1.1]propellane **1** and Giese addition (Figure 3.23, a). A telescoped procedure, where addition of $(Me_3Si)_3SiH$ was delayed until 24 h to prevent premature HAT events, led to the successful formation of product **4b** in 31% yield (average 55% per step, comparable to the individual steps 58%/60%). This results highlights the great potential of this chemistry to generate *C,N*-difunctionalised BCPAs directly from [1.1.1]propellane **1** in a multicomponent reaction. Notably, the organo-photocatalyst 4-CzIPN (5 mol%) gave a comparable 29% yield in this procedure. Similarly, the use of Et_3B in the first step, followed by the addition of an Ir catalyst and $(Me_3Si)_3SiH$ after just 2 h, resulted in a lower 21% yield of **4b** but reduced overall reaction time (26 h) (Figure 3.23, b). This method is an excellent candidate for application and scale up with photo-flow chemistry techniques.[147, 148]

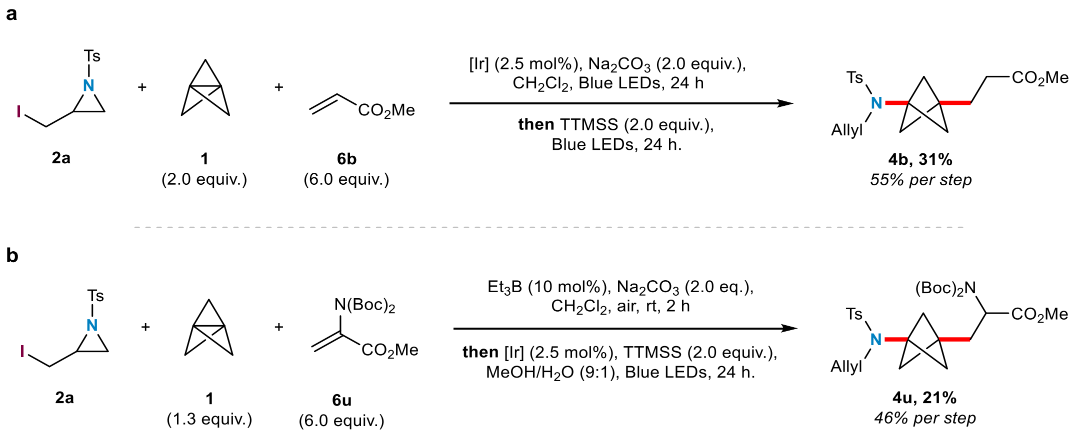


Figure 3.23: Telescoped reaction conditions using photocatalysis and/or triethylborane.

3.2.9 Mechanistic Studies

Literature studies have suggested that reaction with either silane mediator ($(Me_3Si)_3SiH$ or $(Me_3Si)_3SiOH$) requires the initial formation of a silyl radical in a reductive quenching process with the excited photocatalyst.[122-125] The resultant silyl radicals can abstract a halide atom from the substrate before engaging in further reaction pathways (Figure 3.24).

- *Conditions A:* In the case of $(Me_3Si)_3SiOH$ (Figure 3.24, conditions A), oxidation of the silanolate ion (generated on deprotonation of the silanol under basic conditions) by the redox-active excited triplet state of the iridium catalyst (E_{red}

Ir(III)*/Ir(II) = +1.21 V vs SCE in MeCN),[149, 150] followed by radical Brook rearrangement could give the silyl radical intermediate.

- *Conditions B:* With $(Me_3Si)_3SiH$ as a mediator (Figure 3.24, conditions B), it has been proposed that $(Me_3Si)_3Si^{\bullet}$ can be generated by direct oxidation of the silane ([E_{ox} $(Me_3Si)_3SiH/(Me_3Si)_3SiH^{\bullet+}$ = +0.73 V vs SCE in MeCN),[151] followed by deprotonation.

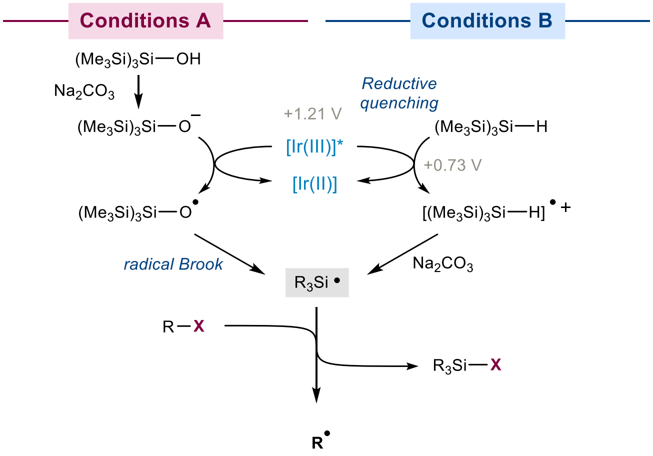


Figure 3.24: Proposed role of silane mediators in photoredox catalysis.

To probe these proposals a Stern−Volmer quenching study was conducted (Figure 3.25 and table 3.9). Both BCPA iodide **3a** (purple line) and $(Me_3Si)_3SiOH$ (red line) were found to be efficient quenchers of the excited photocatalyst. In contrast, $(Me_3Si)_3SiH$ was found to be a poor quencher (blue line). These results support that Conditions A proceeds (at least in part) according to the proposed mechanistic hypothesis (Figure 3.24). However, it opens the debate on the mechanism in the presence of $(Me_3Si)_3SiH$.

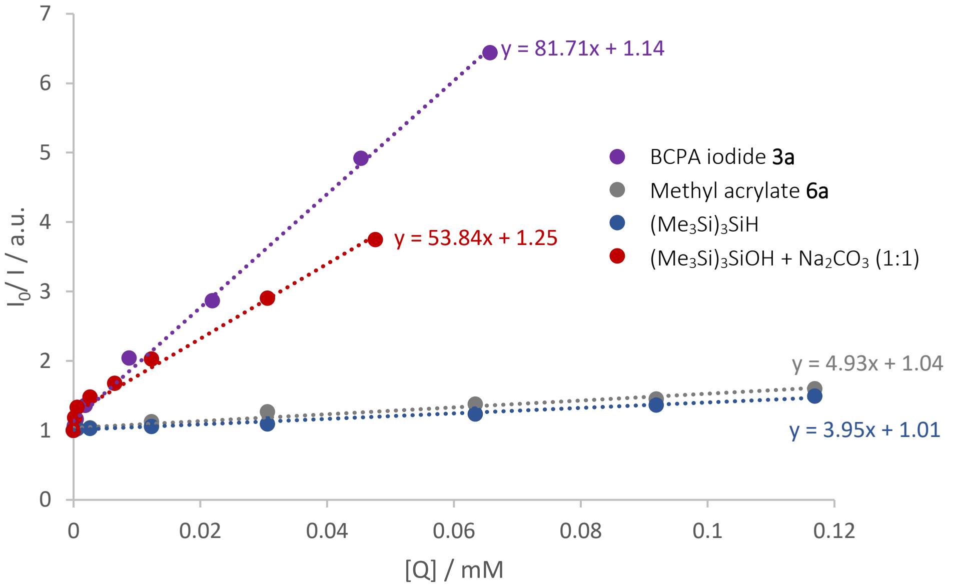


Figure 3.25: Stern-Volmer Plot of 0.38-0.50 M solutions of quenchers with a 5 µM solution of Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$. Intensities are corrected for increasing dilution.

Quenching constants were obtained using the Stern-Volmer relationship:

$$\frac{I_0}{I} = 1 + k_q\tau_0[quencher]$$

Quencher	*Quenching Constant/ M^{-1} s^{-1}*
BCPA iodide **3a**	3.55×10^7
Methyl acrylate **6a**	2.14×10^6
$(Me_3Si)_3SiH$	1.72×10^6
$(Me_3Si)_3SiOH + Na_2CO_3$	2.34×10^7

Table 3.9: Quenching constants of reaction components. Excited state lifetime of photocatalyst $\tau_0 = 2.3$ µs.[149]

Our earlier voltammetry experiments determined the reduction potential of **3a** to be −2.29 V vs SCE, which is beyond the reducing capabilities of most common photocatalysts (section 3.2.2). As a result, we believe an oxidative quenching pathway to be unlikely for the Giese reaction. Visible light alone may instigate C–I bond homolysis; however, the UV/Vis spectrum of the reaction components show no absorption at 455 nm, and suggest that initiation by this mode is unlikely to be promoted by Blue LEDs (Figure 3.26). While iodide ions have been proposed to quench the excited state photocatalysts (E^0 $I^-/I^\bullet$ = +1.35 V);[152] deliberate addition of excess sodium iodide to the Giese reaction delivered no yield improvement, and we do not believe that I^- would be involved in the reaction mechanism (see optimisation section 3.2.5.4).

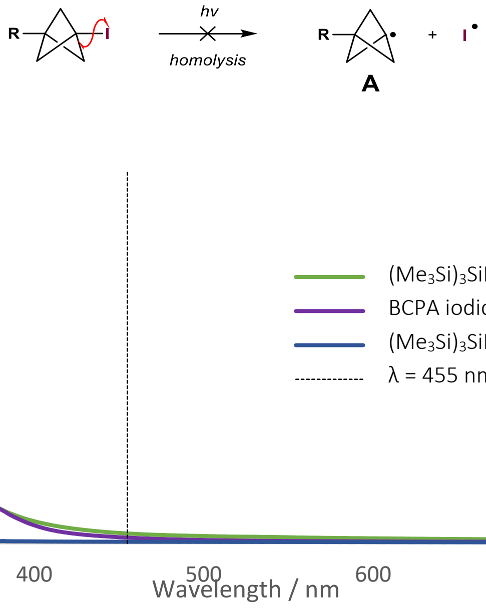


Figure 3.26: UV/Vis absorbance spectrum of reaction components and substrates.

Therefore, in the absence of $(Me_3Si)_3SiOH$ to act as an energy transfer mediator (conditions B), we propose a Dexter energy transfer mechanism between BCPA iodide **3a** and the iridium photocatalyst (Figure 3.27).[98] [99] The triplet T1 energy state of $Ir[(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (258 kJ mol^{-1})[149] is within the BDE range of a C–I bond (~213 kJ mol^{-1}), rendering homolysis to form intermediate **A** feasible by this mechanism.

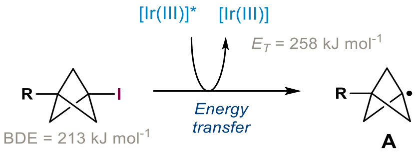


*Figure 3.27: Dexter Energy Transfer between photocatalyst and BCPA iodide **3a**.*

Having probed the mechanism by which BCPA radical intermediate **A** is formed under both conditions, we then proposed that this intermediate undergoes addition to the radical acceptor to give the EWG-stabilized radical **B** (or competing HAT to generate **C**) (Figure 3.28).

- *Conditions A:* For acceptors such as allyl sulfones which give intermediate radical **B**, this addition is slower than competing HAT when using $(Me_3Si)_3SiH$ as a mediator to give **C**, rationalizing the need for $(Me_3Si)_3SiOH$. Catalyst turnover is achieved by reduction of the eliminated sulfonyl radical to the sulfinate ion (E_{red} $PhSO_2^{\bullet}$ / $PhSO_2^{-}$ = +0.37 V vs SCE;[153] E_{ox} $Ir^{(II)}/Ir^{(III)}$ = +1.37 V vs SCE in MeCN).[149]

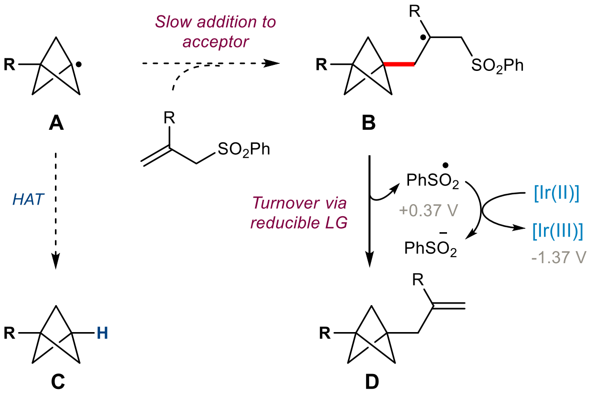


Figure 3.28: Proposed catalyst turnover for conditions A.

- *Conditions B:* Intermediate **B** may either engage in:
  1. Reduction by $Ir^{(II)}$ (E_{red} $^{\bullet}CH(CH_3)CO_2Et/^{-}CH(CH_3)CO_2Et$ = +0.66 V vs SCE in MeCN) as in Conditions A (Figure 3.29, path A).
  2. Or, HAT with $(Me_3Si)_3SiH$ to generate the Giese product, along with $(Me_3Si)_3Si^{\bullet}$, which propagates the reaction by iodine atom abstraction from the BCPA iodide (Figure 3.29, path B).

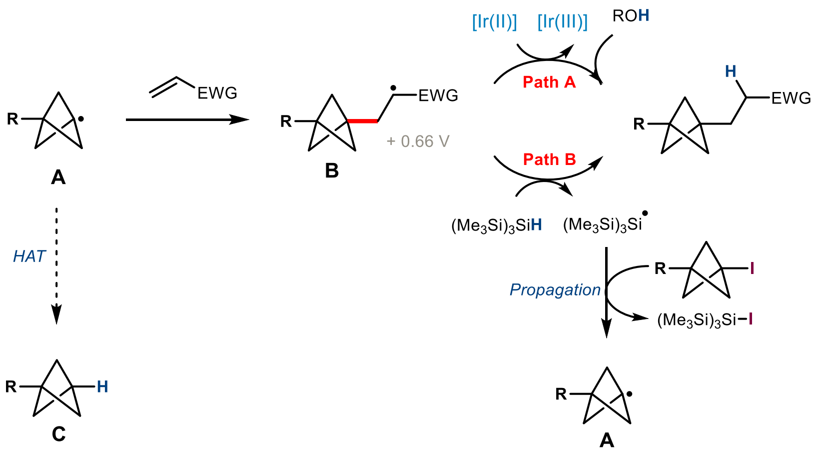
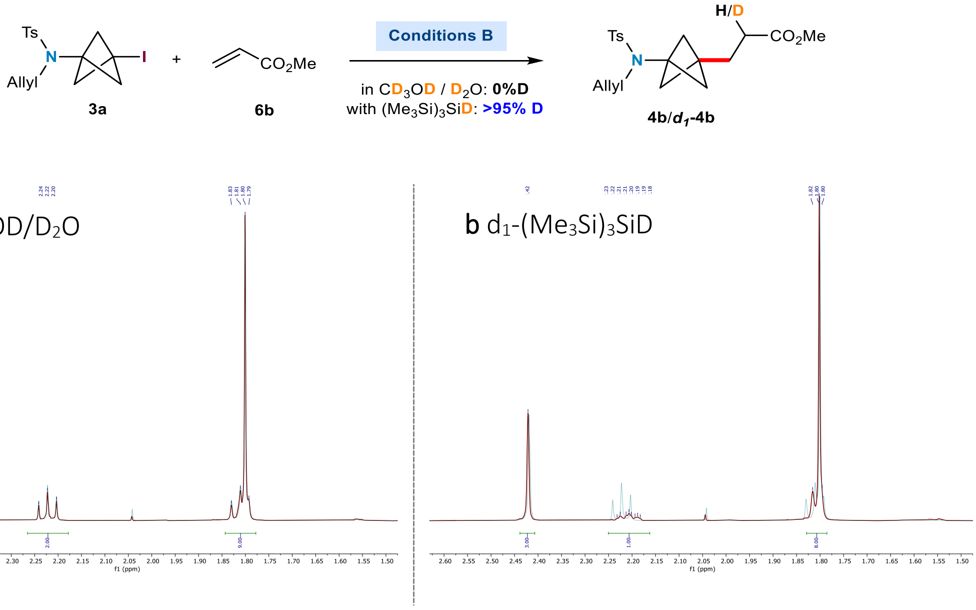


Figure 3.29: Proposed termination events of conditions B.

Deuteration studies were carried out to determine the fate of intermediate **B** (Figure 3.30). A catalyst turnover event and protonation of the resulting substrate anion (path A) or propagation through a HAT cycle was considered (path B). In contrast to the findings of ElMarrouni et al.,[126] in deuterated reaction solvent (CD_3OD/D_2O) no product deuteration was observed, implying that SET reduction of $Ir^{(II)}$ back to the ground state by the substrate does not occur (path A). We were delighted that $(Me_3Si)_3SiD$ could be obtained by reduction of $(Me_3Si)_3SiBr$ with $LiAlD_4$, and found that its use led to complete α-deuteration (>95%) of **d_1-4b**, strongly supporting the propagation pathway (path B).

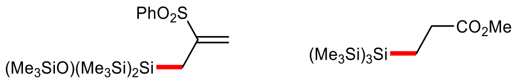


a d_4-MeOD/D_2O

b d_1-$(Me_3Si)_3SiD$

*Figure 3.30: ^{1}H NMR (400 MHz, $CDCl_3$) spectra. Primary spectra including integrals in maroon: d_4-MeOD/D_2O or $(Me_3Si)_3SiD$. Secondary spectra in teal: MeOH/H_2O and $(Me_3Si)_3SiH$. a. no deuterium incorporation with **4b** in d_4-MeOD/D_2O. b. > 95% deuterium incorporation of **d_1-4b** with d_1-$(Me_3Si)_3SiD$.*

Isolation of allyl sulfone **6a-S** and methyl acrylate **6b-Si** silane adducts provides supporting evidence for formation of silyl radical intermediates (Figure 3.31). Unreacted radical acceptors could be recovered from the reaction mixtures, so that these by-products were not a significant cause of loss in yield.



6a-Si **6b-Si**

Figure 3.31: Isolated silyl adducts.

To conclude the mechanistic discussion, the overall mechanisms for the Giese reaction is presented as follows (Figure 3.32).[113]

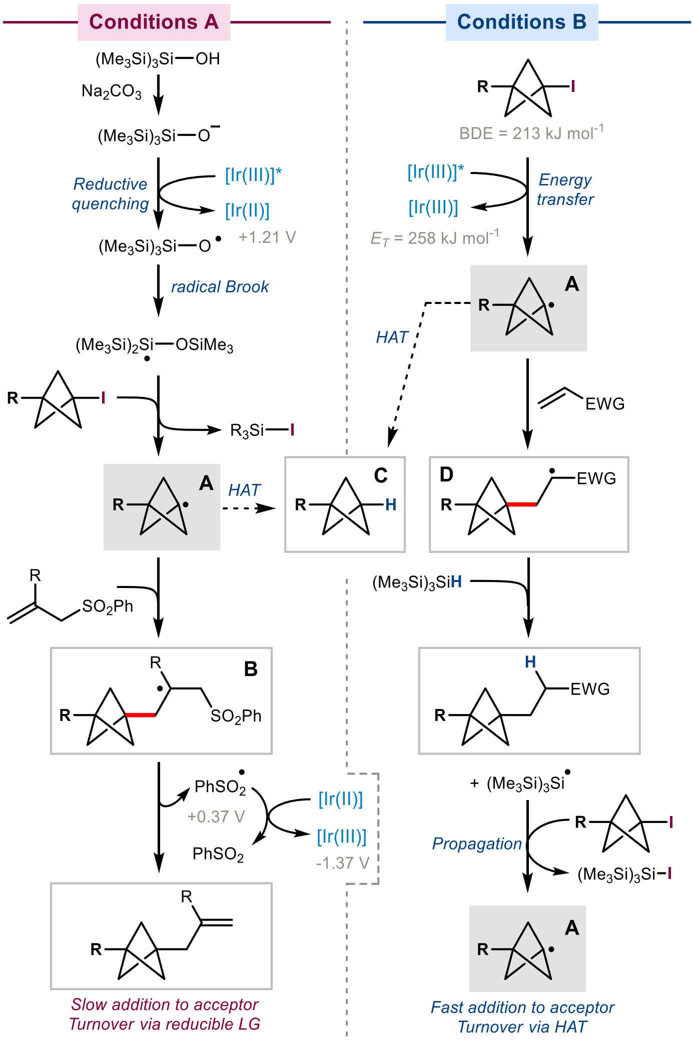


Figure 3.32. Proposed mechanism of Giese reaction of BCP(A) iodides under conditions A and conditions B.[113]

3.2.10 Unsuccessful Photoredox Functionalisations

3.2.10.1 Giese Acceptors

The following radical acceptors were either unsuccessful under both conditions A and B, or gave <10% yield (Figure 3.33).

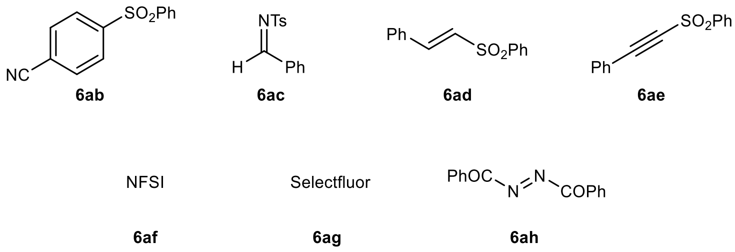


Figure 3.33: Unsuccessful Giese reaction acceptors.

3.2.10.2 Minisci Reaction

To complement our developed methodology, we hoped to achieve (hetero)arylation of BCPA iodides through a similar silyl-mediated photoredox initiation. Minisci reactions of alkyl halides have been reported, and we tested two sets of conditions to try and achieve this class of compound (Figure 3.34). The first set of conditions attempted includes one example of a tertiary iodide *t*-BuI in the reported scope, however, this set-up only returned starting BCPA iodide **3a** (Figure 3.34, a).[128] The second conditions trialed gave (**3a-H**) as the dominant product however, trace amounts of the desired Minisci product could be observed by LCMS (Figure 3.34, b).[127]

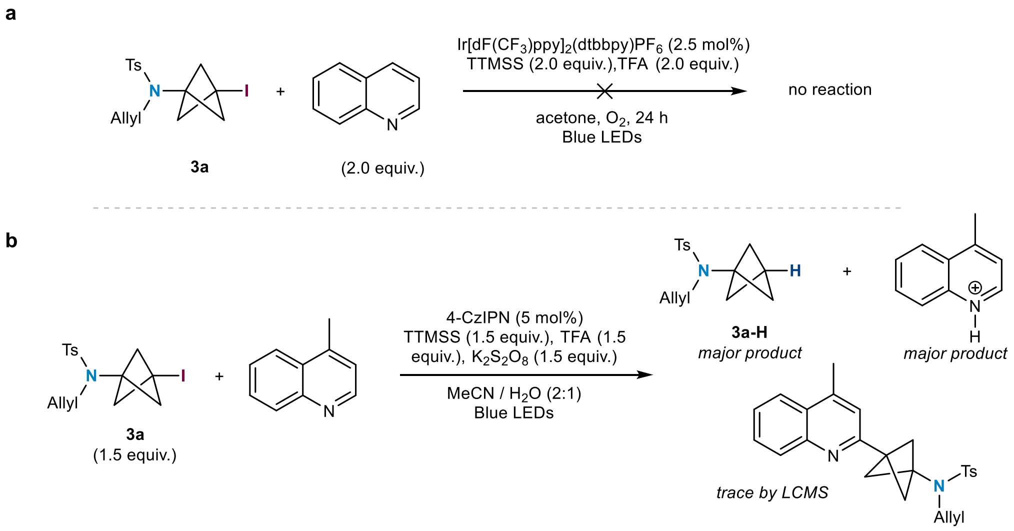


Figure 3.34: Attempted Minisci reactions conditions.

3.2.10.3 Metallaphotoredox Cross-Coupling

Ir/Ni metallaphotoredox-catalysed cross-couplings have been achieved between alkyl and aryl bromides using silane mediators.[154] While there is a single reported example of a BCP bromide described to undergo this chemistry in a patent,[155] there is limited precedent for this process using tertiary alkyl iodides in general. Our attempt at this transformation with BCPA iodide **3a** thus far only resulted in premature HAT of the BCPA radical intermediate to give **3a-H** as the primary product (Figure 3.35).

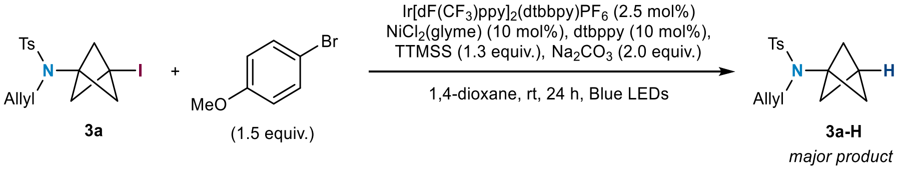


*Figure 3.35: Attempted metallaphotoredox-catalysed cross-coupling of BCP iodide **3a**.*

3.2.10.4 Fluorination

Finally, Selectfluor has been shown to give tertiary alkyl fluorides from the corresponding iodides, however these conditions resulted only in the decomposition of BCPA iodide **3a** (Figure 3.36).[156]

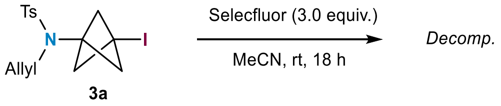


*Figure 3.36: Attempted fluorination of BCPA iodide **3a**.*

3.2.11 Further Transformations

Having established methods to access 1,3-disubstituted BCPAs over the first two chapters, we investigated a selection of further transformations of these compounds.

3.2.11.1 Manipulation of *N*-Substituents

The ability to cleave either the *N*-allyl or sulfonyl substituents from the nitrogen atom was of the highest priority. Detosylation of BCPA iodide **3a** (Mg/MeOH) resulted in C–I bond reduction and fragmentation of the intermediate BCPA carbanion to give **5a** in quantitative yield (Figure 3.37, right). However, detosylation could be successfully achieved on compound **4b** via sonication with Mg/MeOH, which to our delight gave amine **7** in 64% yield (Figure 3.37, left).

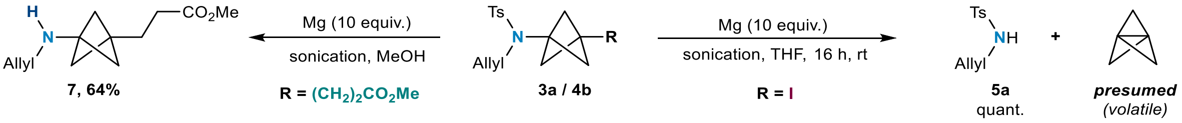


Figure 3.37: De-tosylation of BCPA.

Attempted de-allylation of the BCPA **3a** with $Pd^{2+}/NaBH(OAc)_3$ gave cyclobutene rearranged compound **8** (Figure 3.38, right). Pleasingly, the use of milder conditions allowed the formation of BCPA **9** in 72% yield with $Pd(PPh_3)_4$ as catalyst and 1,3-dimethylbarbituric acid as nucleophile (Figure 3.38, left).[157]

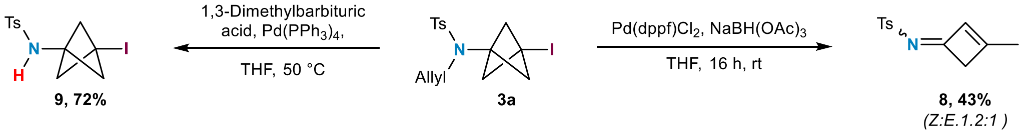


*Figure 3.38: De-tosylation of BCPA iodide **3a**.*

3.2.11.2 Additional manipulations

Further product manipulations were tested to demonstrate access to other potentially useful derivatives. De-iodination of **3a** was carried out under silyl-mediated photocatalytic conditions (**3a-H**, 54%). The *N*-allyl group could undergo classic olefin manipulations such as oxidation to the epoxide **10** (oxone/KBr, 71%),[57] aldehyde **11** (O_3, 71%) or BCP glycine analogue **12** ($RuCl_3/NaIO_4$, 34%) (Figure 3.39). Finally, cross-metathesis with methyl acrylate gave **13** (Grubbs II, 72%).

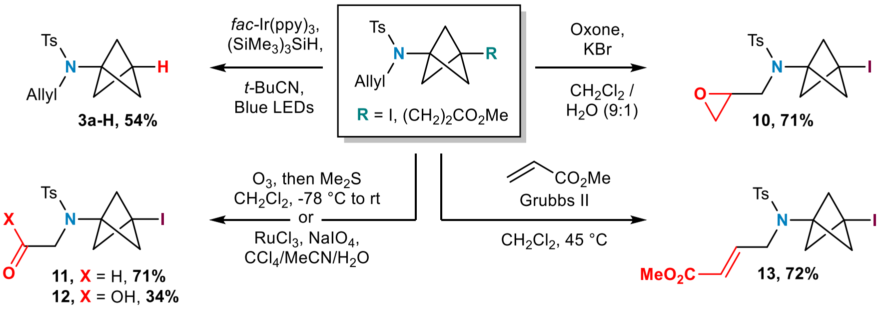


Figure 3.39. Further transformations.

In addition, we investigated a hydroboration / Suzuki cross-coupling across the *N*-allyl group (Figure 3.40).[158, 159] First attempts at this transformation with 2-bromopyridine as the coupling partner gave **14** in 28% yield (Figure 3.40). Under these conditions, we also isolated an equivalent cross-coupled product in which the ester was reduced to alcohol **15** in 20% yield. Therefore, we effected $LiAlH_4$ reduction of ester **4b** to give alcohol **16** in 88% yield prior to hydroboration and Suzuki cross-coupling. However, this gave only a slightly improved yield of **15** in 33% yield. Due to time constraints, this chemistry has not been further investigated.

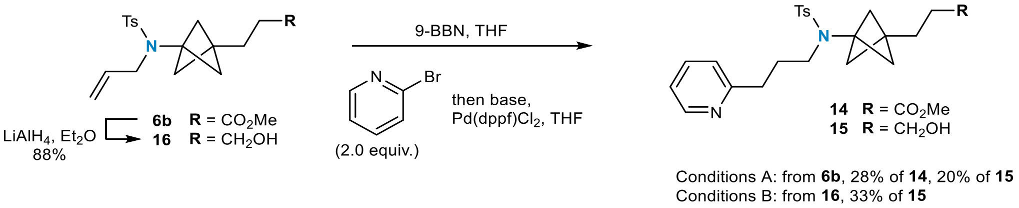


*Figure 3.40: Hydroboration / Suzuki reaction of BCPA **6b**. See supporting information in differences in reaction conditions.*

Finally, we hypothesised that we could generate a BCPA cationic intermediate from the BCPA iodide with the addition of a silver salt (Figure 3.41). On the generation of a BCPA cation intermediate, we expected a rapid rearrangement to occur, accelerated by the nitrogen lone pair to give an iminium cyclobutadiene intermediate. We had hoped that an appended alcohol nucleophile could intercept this intermediate to give exciting oxa-azaspiro[3.4]octane products. To test this hypothesis with reduction of BCPA aldehyde **12** to give alcohol **17** was carried out; unfortunately, treating compound **12** with $AgSbF_4$ lead only to decomposition of the BCPA iodide.

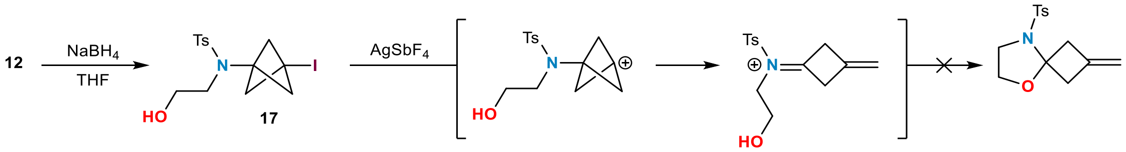


Figure 3.41: Proposed cationic generation, fragmentation and interception.

3.3 Conclusion

3.3.1 Conclusion

In summary, BCPA iodides are significantly more challenging to functionalise than carbon-substituted BCPs, owing to the excellent leaving group ability of the nitrogen substituent (Figure 3.42). Additionally, we found that the generation of BCPA radical intermediates for C–C bond formation using both previously reported methodology and photoredox catalysis was unsuccessful.

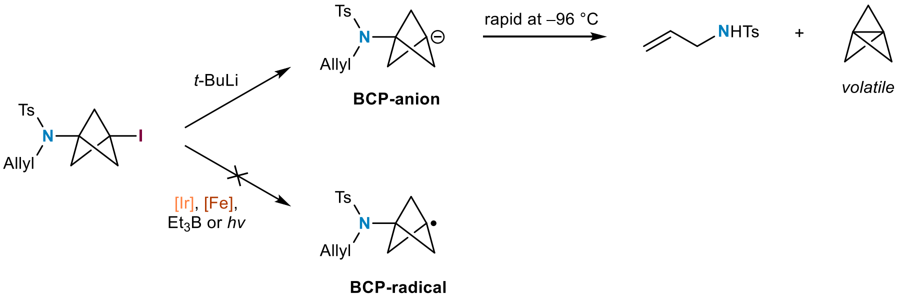


Figure 3.42: Summary of failed BCPA iodide functionalisations.

By using silane mediators, photocatalysed radical functionalization of BCPA iodides could be used to prepare 1,3-*N*,*C*-disubstituted BCPs, Thus opening a new route to valuable aniline bioisosteres (Figure 3.43). This chemistry displays high functional group tolerance, affording unobtainable products by novel methods, including application to the synthesis of BCPA amino acid and drug analogues, which highlights the potential utility of this methodology for the pharmaceutical industry.

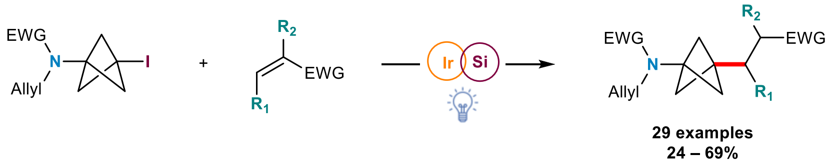


Figure 3.43: Silyl-mediated Photocatalysed Giese reaction.

An exciting progression of this work would be through application of our three-component telescoped procedure to photo-flow chemistry. In theory, this would enable precise control over addition timings of reagents and enable high throughput synthesis in improved yield.

4.

Sulfonyl Substituted BCPs

4.1 Introduction

4.1.1 A Serendipitous Discovery of Tosyl BCP Iodide

In Chapter 2, the fragmentation / ATRA reaction of α-iodo aziridines with [1.1.1]propellane **1** was demonstrated. In exploring the scope of the substituents on the aziridine ring, we unexpectedly discovered that the 3-phenyl substituted aziridine **2aj** underwent C–C bond fragmentation to form a stabilised α-amino benzylic radical instead of the previously observed C–N bond fragmentation (Figure 4.1). Following this C–C bond fragmentation, we propose the loss of a sulfonyl radical which then underwent ATRA with **1** to give tosyl BCP iodide **18a-I** in 42% yield, as confirmed by X-ray crystallography. Following this serendipitous discovery, we considered the desirability and accessibility of such sulfonyl BCP halides.

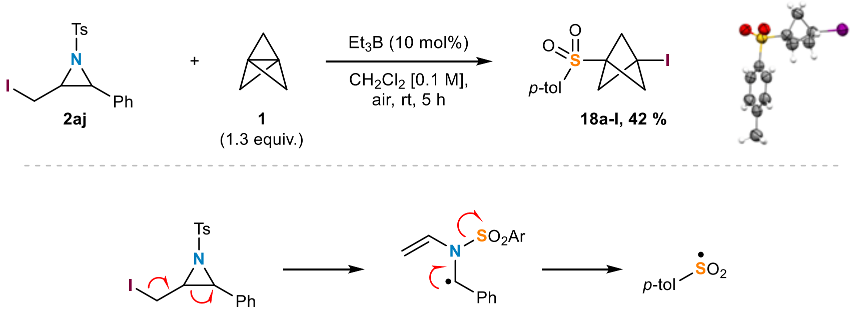
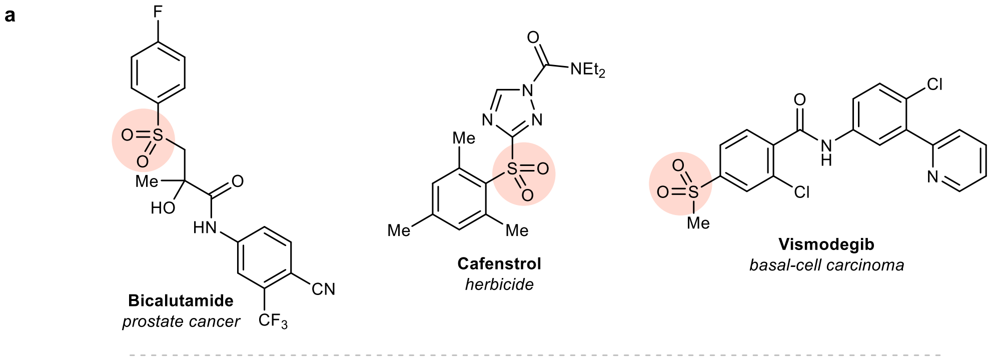


Figure 4.1: Formation of tosyl BCP iodide through aziridine C–C bond fragmentation.

4.1.2 Application of Aryl Sulfones

Sulfonyl motifs are abundant in pharmaceuticals and agrochemical compounds (Figure 4.2, a).[160, 161] To our knowledge, there are no comparative studies of ‘drug-like’ sulfonyl BCP compounds, and BCP sulfones have only appeared in three patents.[162-164] Preparation of the mesyl BCPA analogue of the NSAID Acetaminophen (paracetamol), required five steps from the unsymmetrically disubstituted methyl ester-BCP-carboxylic acid (Figure 4.2, b).[163] This key intermediate necessitates a four step synthesis from **1** and is a common intermediate for the synthesis of BCP sulfones (section 4.1.3).[165] Efficient methodologies to construct disubstituted BCP sulfones are rare compared to carbon-, nitrogen- and sulfide derivatives; therefore, an efficient methodology to obtain disubstituted sulfonyl BCPs would considerably advance the field.[166-168]



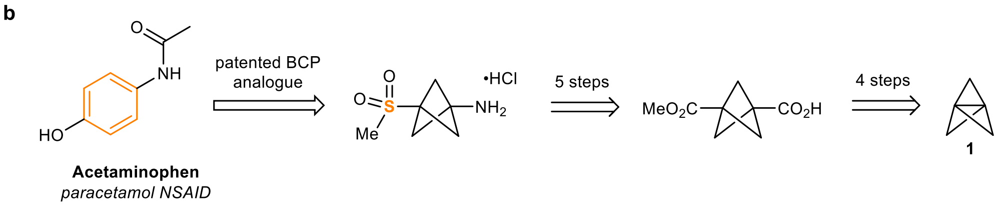


Figure 4.2: a. Aryl sulfones in pharmaceutical and agrochemical compounds. b. Synthesis of the patented BCP analogue of Acetaminophen.

4.1.3 Synthesis of Sulfonyl BCPs

Oxidation of BCP sulfides is one successful strategy to access sulfonyl BCPs, where the precursors can be obtained in one or more steps from [1.1.1]propellane **1** (Figure 4.3). For terminal sulfonyl BCPs, oxidation with *m*-CPBA of the aryl and alkyl sulfide BCPs has been reported.[49, 51] Oxidation of BCP sulfides can also be achieved with H_2O_2 or potassium peroxymonosulfate sulfate.[163, 169]

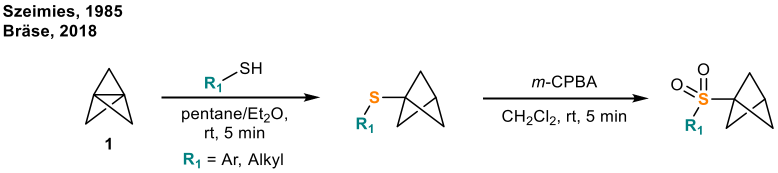


Figure 4.3: Synthesis of mono-substituted BCP sulfones.

Compared to the concise synthesis of mono-substituted sulfonyl BCPs, the formation of disubstituted sulfonyl BCPs requires pre-installation of the C_3-substituent early in the synthesis, via the methyl ester-BCP-carboxylic acid, as described in two patents released in 2021 (Figure 4.4). Methyl ester-BCP-carboxylic acid is a crucial intermediate for such compounds. In the synthesis of a potential menin inhibitor, a silver-mediated decarboxylative C–S cross-coupling and oxidation converted the carboxylic acid into the required aryl sulfone (Figure 4.4, a).[162] Similarly, a mesyl BCP carboxylic acid building block was employed in the synthesis of an lysophosphatidic acid (LPA) receptor antagonist. The synthesis of this BCP fragment was not described but presumably could be obtained from the same methyl ester-BCP-carboxylic acid (Figure 4.4, b).[164] One example of a photocatalysed decarboxylative sulfonylation of a BCP redox-active ester (*N*-hydroxyphthalimide (NHPI)) has also been reported by Li and co-workers in 2020, although in low yield due to steric constraints (Figure 4.4, c).[170]

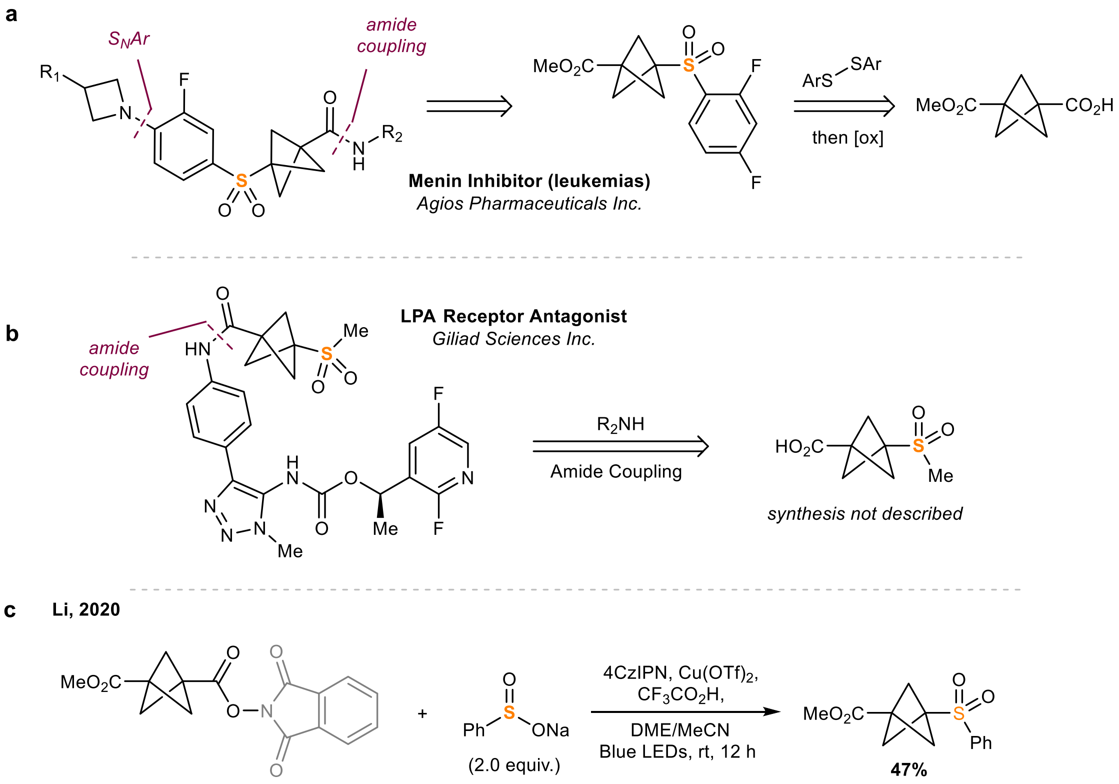


Figure 4.4: a. Retrosynthesis of a patented menin inhibitor. b. Retrosynthesis of a patented LPA receptor antagonist. c. Decarboxylative sulfonylation of BCP redox-active ester.

BCP sulfinate salts are convenient bench-stable building blocks that can be used to access sulfonyl-, sulfonamide- and sulfoxide BCPs following reaction with electrophiles (such as MeI, NFSI, H_2NOSO_3H), S_NAr reactions, and copper-catalysed cross-coupling (with aryl bromides) (Figure 4.5, a).[171-173] The mono-substituted BCP sulfinate can be prepared on greater than 60 mmol scale in three steps from **1** via elimination of the methyl propanoate sulfone (Figure 4.5, b).[172] Synthesis of disubstituted BCP sulfinates, however, required up to ten step manipulations via Barton esters (Figure 4.5, c).[171]

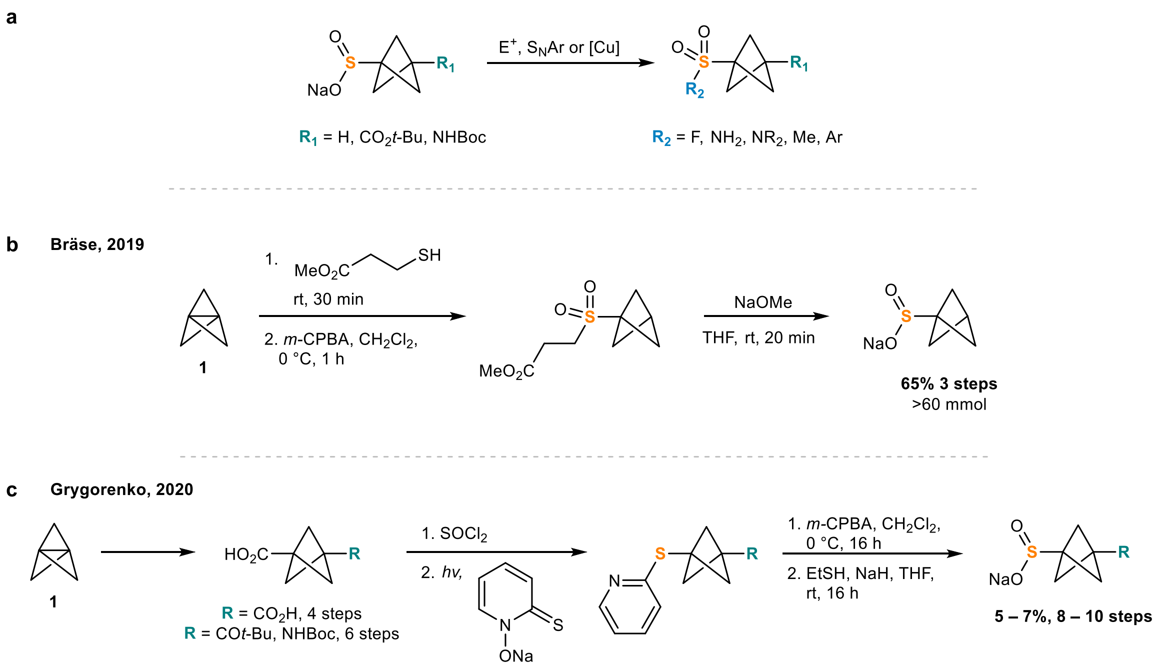


Figure 4.5: a. General manipulations of BCP sulfinate salts to achieve BCP sulfones and sulfonamides. b. Synthesis of a mono-substituted BCP sulfinate. c. Synthesis of disubstituted BCP sulfinates.

The direct addition of sulfonyl radicals across the central bond of [1.1.1]propellane **1** is limited to only a few examples. Methylsulfonyl- and sulfuryl chloride have undergone ATRA addition to **1** under UV irradiation (Figure 4.6, a);[174] this early example reported by Zeifrov et al. in 1990 suffers from poor yields and uncontrolled reactivity, generating staffanes (n = 2) and other products. The resultant BCP chlorides, so far, are not synthetically useful, being inert to reductions with Bn_3SnH under photochemical and thermal conditions.[175] A single example by MacMillan and co-workers demonstrated the metallo-photocatalysed homolysis of PhO_2S–SPh, which after addition to **1** to generate a sulfonyl BCP radical, underwent a Cu-catalysed amination (Figure 4.6, b).[71] Two publications released in 2020 by Zhu and co-workers generated thioether- and selenoether BCP sulfones through mild heating or irradiation with Blue LEDs to affect S–S bond cleavage (Figure 4.6, c).[176, 177] The same group later reported a photocatalysed energy transfer S–O bond homolysis to achieve a carbo-sulfonylation of **1** (Figure 4.6, d).[178] Finally, Wu and co-workers reported an organophotocatalysed sulfonyl alkynylation and allylation of **1** (Figure 4.6, e).[179] The disadvantage of these methods is the lack of sulfone variety achieved and pre-requisites of the substrate.

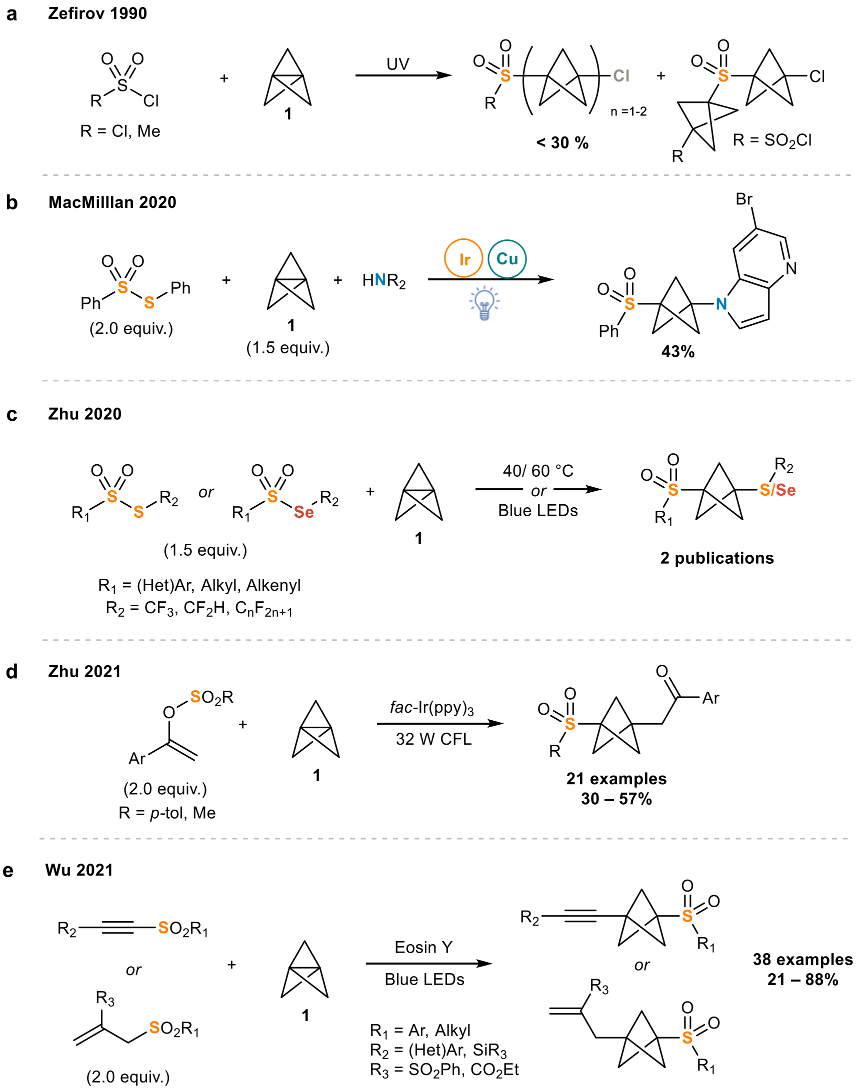


*Figure 4.6: Synthesis of sulfonyl BCPs through direct addition to [1.1.1]propellane **1**.*

Overall, there is limited convenient and general methodology available to access disubstituted sulfonyl BCPs. However, we anticipated that an improved synthesis of sulfonyl BCP halides (as discovered in section 4.1.1) could provide an elegant solution to this problem. We therefore considered other, streamlined methods to generate sulfonyl radicals for the addition to **1** to generate sulfonyl BCP halides.

4.1.4 Generation of Sulfonyl Radicals

A survey of sulfonyl radical precursors identified S–X bond cleavage (when X = Hal, S, Se or N) as a prominent reagent class for homolysis (Figure 4.7).[180] Likewise, allyl sulfones, tetrazole sulfones, and sulfonyl cyanides are similarly engineered substrates that promote efficient S–C bond cleavage to access sulfonyl radicals.

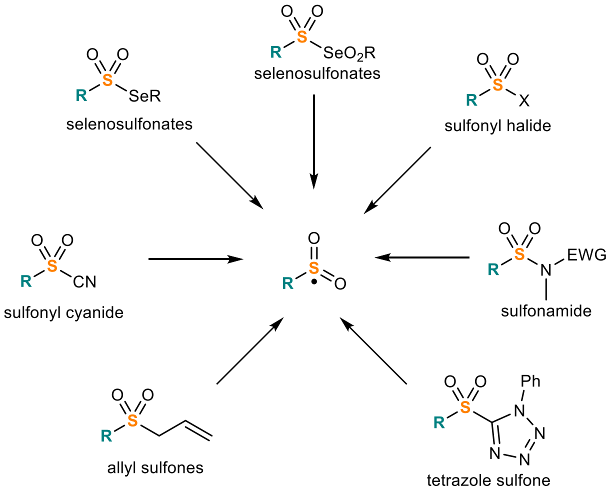


Figure 4.7: Sulfonyl radical precursors.

Of these, sulfonyl iodides and bromides appeared to be the most attractive due to the close analogy to our previous studies on ATRA reactions with alkyl-, (hetero)aryl- and aziridine halides with [1.1.1]propellane **1**.[85, 113, 181] Sulfonyl halides are not routinely isolated due to their instability to de-sulfonylation and elimination pathways, particularly with electron-deficient or alkyl substituents (Figure 4.8, a). Sulfonyl bromides and iodides can be easily homolysed via photolysis or thermolysis, while sulfonyl chlorides generally require radical initiators or transition metal catalysts (Figure 4.8, b).[180] Notably, catalysis with Pd", Rh^{I,} and Ir^{I} often results in desulfonylation.[180]

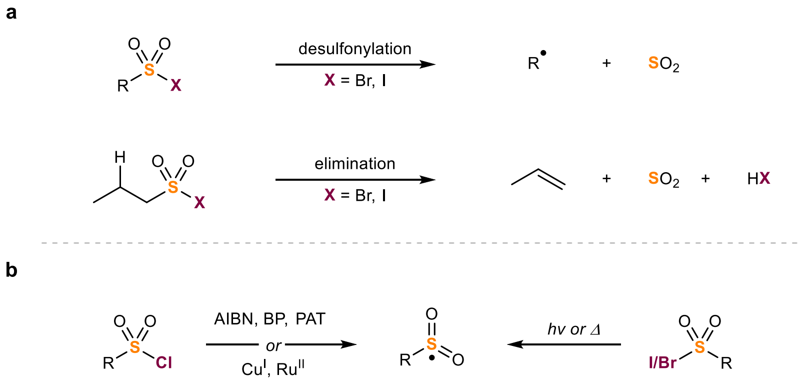


Figure 4.8: a. General decomposition pathways of sulfonyl halides. b. Generation of sulfonyl radicals from sulfonyl halides. AIBN = Azobisisobutyronitrile, PAT = phenylazotriphenylmethane and BP = benzoyl peroxide.

4.1.5 Preparation of Sulfonyl Bromide and Iodides Reagents

Sulfonyl halides, when isolated, are most readily accessed by halogenation of sulfinate salts with electrophilic halogenating reagents (Figure 4.9, a). Cleavage of sulfonyl hydrazides is also a common approach with nucleophilic halogenating agents in combination with an oxidant (Figure 4.9, b).[182-184] In addition, sulfonyl bromides have been obtained through the oxidation/halogenation of thiols and disulfides (Figure 4.9, c and d);[185, 186] or the reduction/oxidation of sulfonyl chlorides (Figure 4.9, e).[187] While this is not an exhaustive analysis, as these reagents are often formed *in situ*, a comprehensive survey would go beyond the scope of this thesis.

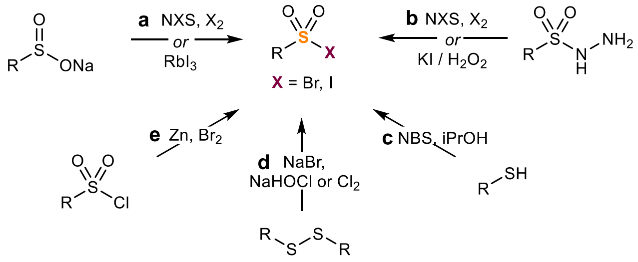


Figure 4.9: Overview of sulfonyl halides synthesis.

4.1.6 ATRA Reaction of Sulfonyl Bromides and Iodides

Sulfonyl halides can engage in atom transfer radical addition (ATRA) reactions with electron-deficient and unactivated alkenes, allenes and alkynes (Figure 4.10).[188-192] Often, the β-halide sulfones formed are subjected to basic elimination conditions to form vinyl sulfones through the elimination of HBr or HI. Typically, sulfonyl iodides employ Cu^I and Cu^{II} catalysts for effective reaction across double bonds,[193, 194] but visible light homolysis of the S–I bond can also achieve this transformation.[195] The analogous sulfonyl bromides necessitate the use of radical initiators such as AIBN and/or high temperatures or UV light.[196, 197] The most successful sulfone substituents tolerated in ATRA reactions are simple mono-substituted aryl groups. However, rare examples of heteroaryl and alkyl substituents are also reported. In 1980, Lui commented on the challenging inherent instability of alkyl sulfonyl halides:

> *"Alkyl sulfonyl iodides were so unstable that they should be generated and allowed to react in situ. Both methanesulfonyl and 1-butanesulfonyl iodides and their adducts with alkenes decomposed instantly when exposed to daylight."* [193, [3]]

---

[3] On analysis of the experimental procedure, the alkyl sulfonyl halides were isolated in dilute solution and after drying for 3-4 hours in a refrigerator were used in solution for the ATRA step.

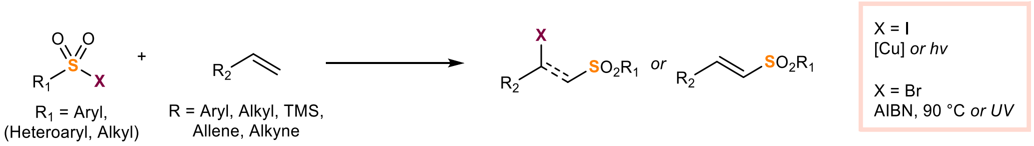


Figure 4.10: ATRA reaction of pre-formed sulfonyl halides.

Sulfinate salts have been employed in ATRA transformations via *in situ* formation of sulfonyl halides (Figure 4.11). Electrophilic halogenating agents used for this transformation are exclusively NXS[189, 198] or X_2[188, 191] reagents, and both β-iodo- and β-bromo sulfones can be formed in this manner (X = Br or I). However, the less reactive sulfonyl bromides required heating up to 80 °C for successful addition. The use of nucleophilic halides (NaI or KI, no bromides reported) requires the addition of an oxidant such as ceric ammonium nitrate (CAN)[199] or $PhI(OAc)_2$[200] for the same transformation. As is the case for isolated sulfonyl halides, aryl sulfinate salts are most frequently reported with minimal application to hetero(aryl) or alkyl substituents.

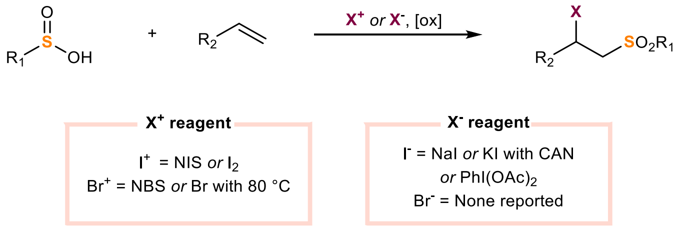


Figure 4.11: Generation of sulfonyl halides in situ from sulfinate salts for ARTA reactions.

Beyond these general considerations, the first iodo-sulfonylation of π-bonds from sulfonyl chlorides was reported by Li and co-workers in 2021 (Figure 4.12).[201] Proposed to proceed via the formation of a surfactant-EDA-complex (electron-donor-acceptor), this is a unique solution to achieve ATRA of sulfonyl halides. However, once again, applications with alkyl sulfones are absent.

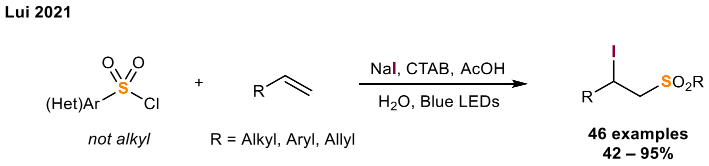


Figure 4.12: Iodo-sulfonylation of olefins direct from sulfonyl chlorides. CTAB = cetyltrimethylammoniumbromide.

We recognised that sulfonyl halides reagents would be an excellent starting point for the development of an efficient and potentially catalyst- or iniator-free difunctionalisation of the central bond of [1.1.1]propellane **1**.

4.1.7 Chapter Aims

We sought to utilise the homolytic cleavage of weak S–X σ bonds to rapidly construct novel halide BCP sulfones through ATRA reaction with [1.1.1]propellane **1** (Figure 4.13). As with our previous work, the BCP halide could then provide an excellent handle for C–C bond formation (see chapter 3), and we hoped to demonstrate that this methodology can be used to access 1,3-difunctionalised BCP sulfones.

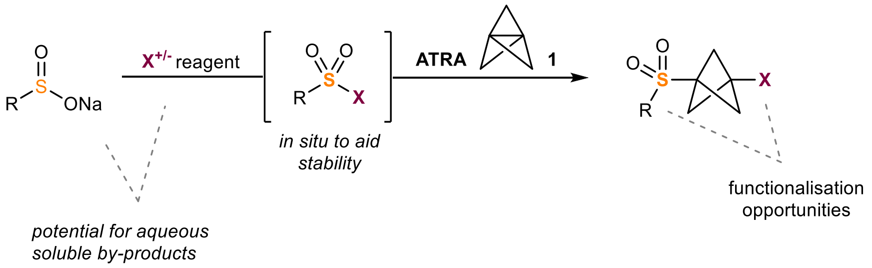


*Figure 4.13: Proposed ATRA reaction of sulfonyl halides with **1**.*

We envisaged the formation of sulfonyl halide intermediates *in situ* from readily accessible sulfinate salts to reduce decomposition pathways, and we aimed to develop conditions amenable to heteroaryl and alkyl substituents. The development of a practical method was of paramount importance to have the greatest appeal to industry and to improve the current state of the art for sulfonyl halide reagents. We hoped to minimise purification steps through high yields, optimal stoichiometry, formation of aqueous soluble by-products and minimal use of catalysts or initiators.

4.2 Results and Discussion

4.2.1 Proof of Concept

Following the isolation of tosyl BCP iodide **18a-I** from aziridine fragmentation, we set out to synthesise tosyl iodide **19a-I** to test conditions for an ATRA reaction with [1.1.1]propellane **1**. Tosyl iodide **19a-I** could be prepared as a crystalline yellow solid in 95% yield from the corresponding sulfinate salt **18a-S** with molecular iodine in EtOH/H_2O (Figure 4.14). To our delight, our initial attempt to effect an ATRA reaction with **1** turned the yellow solution of **19a-I** colourless instantly on the addition of **1**, and the white precipitate of **18a-I** precipitated out of the solution. The sulfonyl BCP halide **18a-I** was obtained in excellent purity, and the reaction could be carried out on a 1 gram scale in 88% yield.

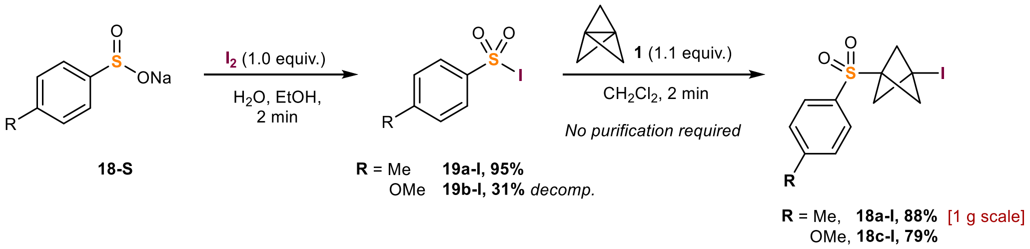
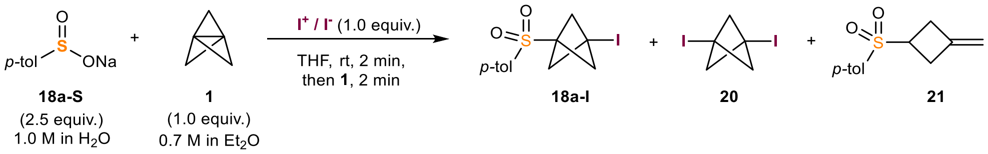


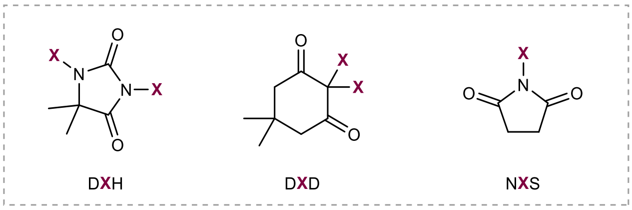
*Figure 4.14: Proof of concept for the ATRA reaction of sulfonyl iodides with [1.1.1]propellane **1**.*

Before starting reaction optimisation, we tested an electron-rich sulfinate salt in the reaction (*p*-OMe), **18b-S**, and discovered that the sulfonyl iodide **19b-I** decomposed on concentration or standing in light (approx. 31% yield). However, the use of the sulfonyl halide in dilute solution enabled the smooth formation of BCP iodide **18a-I** in a 79% yield. This result highlighted the importance of the formation of sulfonyl halide intermediates *in* *situ* to access a broader range of substrates. Encouraged by these results, we set out to optimise the reaction.

4.2.2 Sulfonyl BCP Iodide Optimisation

We commenced our investigation by considering commercially available I^- and I^+ sources to generate a tosyliodide **19a-I** from the corresponding sulfinate salt **18a-S** *in situ* before engaging in ATRA with [1.1.1]propellane to give sulfonyl BCP iodides **18a-I** (Table 4.1). Electrophilic I^+ sources proved promising; however contrary to the previous stepwise procedure, the use of I_2 returned a poor 7% yield of **18a-I** (entry 1). Presumably, this is caused by the decomposition of intermediate sulfonyl iodide by I^- generated *in situ*, and then the direct reaction of I_2 with **1** to form di-iodinated BCP **20**. The use of *N*-iodosuccinimide (NIS) gave an improved 41% yield of **18a-I** (entry 2), which was increased to 49% with the use of ICl (entry 3), and then drastically improved to 78% by the use of 1,3-diiodo-5,5-dimethylhydantoin (DIH) (entry 4). Other iodinating agents such as IPy_2BF_4 (Barluenga's reagent) and 2,2-diiododimedone (DID) did not improve the reaction yield and suffered from the generation of rearrangement product **21** (entries 5 – 7, MeCN was used to improve solubility). In contrast, I^- reagents such as NaI gave no reaction in either THF or water (entries 8 and 9).





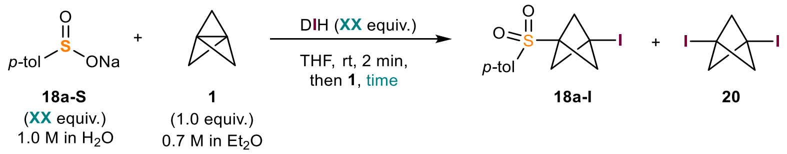
Entry	$I^{+/-}$ source	Solvent	**18a-I** NMR Yield /%	**20** NMR Yield /%	**21** NMR Yield /%
1	I_2	THF	7	18	0
2	NIS	THF	41	9	0
3	ICl^a	-	49	0	16
4	DIH	THF	78	13	0
5	IPy_2BF_4	THF	9	24	0
6	IPy_2BF_4	MeCN	2	2	52
7	DID	THF	31	6	27
8	NaI	THF	0	0	0
9	NaI	H_2O	0	0	0

*Table 4.1: I^+ and I^- sources for the formation of sulfonyl BCP iodides. **1** was prepared as a [0.70 M] stock solution in Et_2O throughout. ^{a} [1.0 M in CH_2Cl_2]. NIS = N-Iodosuccinimide. DIH = 1,3-Diiodo-5,5-dimethylhydantoin. DID = 2,2-diiododimedone.*

4.2.2.1 Reaction Stoichiometry

The relative stoichiometry of the reagents was investigated (Table 4.2). As a control, the reaction was carried out without the sulfinate salt **18a-S**, and an 18% yield of di-iodinated BCP **20** was obtained (entry 1). We aimed to reduce this by-product formation by using a minimal amount of iodinating agent. Increasing the equivalents of sulfinate salt from 1.00 to 3.00 equivalents improved the yield of **18a-I** up to 87% (entries 2 – 6). DIH possesses two N–I bonds, and we therefore tested halving the equivalents of the iodinating agent

(0.5 equiv.) with respect to **1** (1.0 equiv.), however a near halving of the reaction yield of BCP iodide **18a-I** resulted (38%, entry 7). This appears to imply that only one iodine atom of DIH is sufficiently labile to react under these conditions. Delaying the addition of [1.1.1]propellane **1** to 15 min instead of 2 min gave no significant change in reaction yield, indicating that the sulfonyl iodide **19a-I** was formed entirely within 2 min and was stable in solution for at least 15 min (entries 4 and 8). Use of 2.5 equiv. was preferred to limit wasted reagent and was taken forward for a solvent screen.

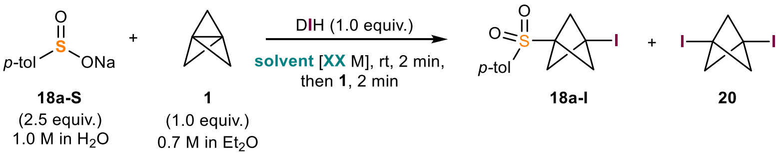


Entry.	***18a-S*** *equiv.*	*DIH equiv.*	*Time / min*	***18a-I*** *NMR Yield /%*	***20*** *NMR Yield /%*
1	0.00	1.0	2	0	18
2	1.00	1.0	2	35	29
3	1.50	1.0	2	58	34
4	2.00	1.0	2	73	22
5	2.50	1.0	2	78	13
6	3.00	1.0	2	87	12
7	2.50	0.5	2	38	10
8	2.00	1.0	15	71	29

Table 4.2: Investigation of reaction stiochiometry.

4.2.2.2 Solvent effects

Changing the solvent had a significant influence on the reaction yield (Table 4.3). Both THF and MeCN were found to be less well suited to this reaction (entries 1-3). They were surpassed by more suitable solvents Et_2O, CH_2Cl_2 and even H_2O, which all gave the desired sulfonyl BCP iodide **18a-I** in near quantitative yield (99% average, entries 4-6). DIH was poorly soluble in all of these solvents, however, the use of MeOH to solubilise DIH actually led to a lower yield, and a higher proportion of BCP di-iodide **20** (entry 7). Et_2O was carried forward as the solvent of choice to maintain consistency with the [1.1.1]propellane **1** stock solution (0.70 M in Et_2O throughout).

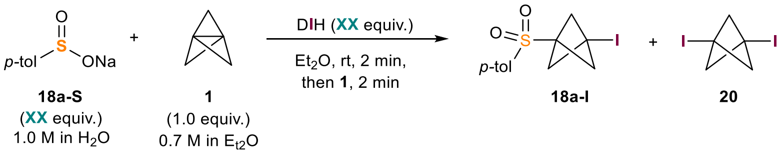


Entry	*Solvent*	*Conc. of DIH /M*	***18a-I** NMR Yield /%*	***20** NMR Yield /%*
1	THF	1.0	78	13
2	THF	0.25	54	38
3	MeCN	1.0	74	19
4	Et_2O	1.0	100	1
5	H_2O	1.0	99	1
6	CH_2Cl_2	1.0	100	0
7	MeOH	1.0	83	12

*Table 4.3: Solvent effects on the formation of **18a-I**.*

4.2.2.3 Secondary Stoichiometry Screen

Having optimised the reaction solvent, we endeavoured to minimise the equivalents of sulfinate salt **18a-S** required to achieve quantitative yield (Table 4.4). While reducing the equivalents of sulfinate salt **18a-S** from 2.5 to 1.5, an excellent yield of sulfonyl BCP iodide **18a-I** was maintained, only dropping by 10 % (entries 1-3). However, consequently, the di-BCP di-iodide **20** impurity increased by a comparable amount. **20** is similar in polarity to **18a-I** and could be separated by careful column chromatography; however, we aimed to minimise the formation of **20** to avoid unnecessary purification steps. Maintaining the optimal 2.5:1 ratio of sulfinate **18a-S**: DIH but with reduced equivalents with respect to [1.1.1]propellane **1** reduced the formation of **20** to just 1%, however, the reaction yield suffered as a result (entries 4 and 5). Therefore, we continued with 2.5 equiv. of the sulfinate salt (entry 1).

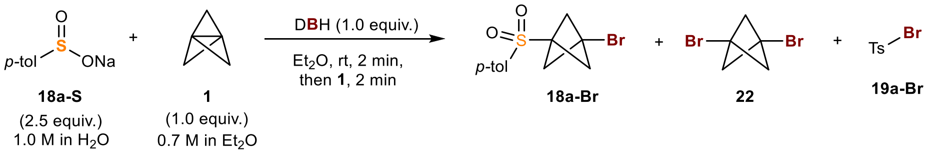


Entry	***18a-S** equiv.*	*DIH equiv.*	***18a-I** NMR Yield /%*	***20** NMR Yield /%*
1	2.50	1.00	100	1
2	2.00	1.00	98	4
3	1.50	1.00	90	7
4	2.00	0.80	77	1
5	1.50	0.60	73	1
6	1.00	0.40	51	1

Table 4.4: Re-evaluation of reaction stoichiometry.

4.2.3 Sulfonyl BCP Bromide Optimisation

We sought to apply the developed conditions to the synthesis of sulfonyl BCP bromide **18a-Br** with the analogous electrophilic brominating agent 1,3-dibromo-5,5-dimethylhydantoin (DBH) (Table 4.5). In contrast to the reactivity of sulfonyl iodides, in a reaction time of 2 min, only a 9% yield of BCP bromide **18a-Br** was obtained (entry 1). Tosylbromide **19a-Br** was detected in the crude reaction mixture, and increasing the reaction time to 18 h led to complete conversion of **19a-Br**, obtaining **18a-Br** in quantitative yield (entries 1 – 4).

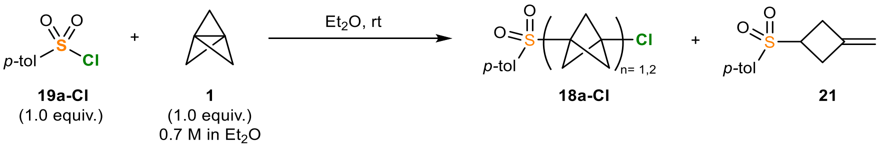


Entry	*Time*	***18a-Br** NMR Yield /% (isolated)*	***19a-Br** NMR Yield /%*
1	2 min	9	77
2	3 h	54	38
3	6 h	69	4
4	18 h	102 (100)	0

*Table 4.5: Optimisation for the formation of sulfonyl BCP bromide **18a-Br**.*

4.2.4 Sulfonyl BCP Chlorides

The ATRA reaction with tosyl chloride **19a-Cl** and **1** was also tested under similar conditions (Table 4.6). Sulfonyl BCP chloride **18a-Cl** could be obtained, albeit in low yield. Higher proportions of staffane and rearranged by-product **21** were formed (entries 1 – 4).



Entry	*Time*	***18a-Cl**, (n = 1) NMR Yield /%*	***18a-Cl**, (n = 2) NMR Yield /%*	***21** NMR Yield /%*
1	2 min	0	0	7
2	3 h	14	9	59
3	6 h	14	9	-
4	18 h	29	-	39

*Table 4.6: Reaction of [1.1.1]propellane **1** with sulfonyl chlorides.*

^{1}H NMR monitoring the progress of the halo-sulfonylation of [1.1.1]propellane **1** over time showed that the addition of sulfonyl bromides required over 6 h and was complete after

18 h reaction time (Figure 4.15) in comparison to the near-instant reaction of sulfonyl iodides. As expected, sulfonyl chlorides reacted significantly slower.

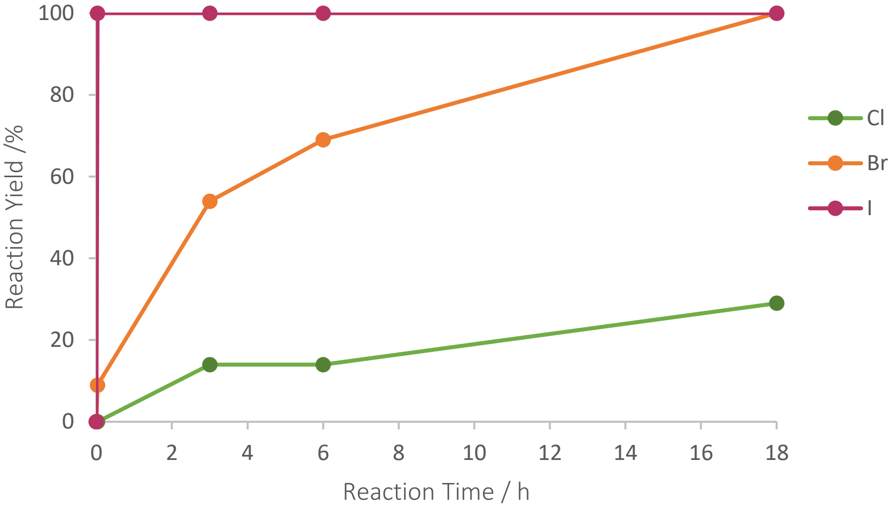
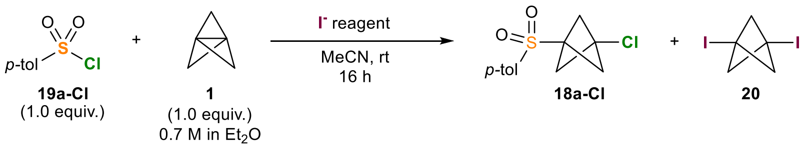


Figure 4.15: Reaction progression for the formation of sulfonyl BCP halides ***18a*** *from the corresponding sulfinate salt/sulfonyl halide under optimised conditions.*

Sulfinate salts are easily accessed by the reduction of sulfonyl chlorides, and we considered whether a substitution-type reaction of sulfonyl chlorides could be used to obtain sulfonyl halides directly.[202] Unfortunately, our attempts to implement this led to the significant formation of di-iodo BCP diiodide **20** and were not pursued further (Table 4.7).

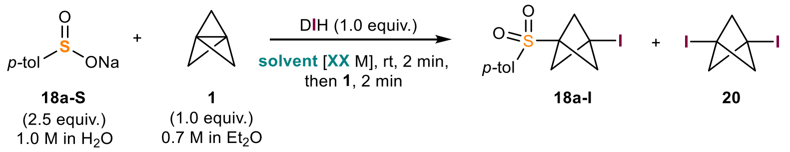


Entry	*I⁻ source*	*Equiv.*	*Additive*	*19a-Cl NMR Yield /%*	*18a-Cl NMR Yield /%*	*20 NMR Yield /%*
1	KI	1.0	-	-	7	43
2	KI	2.0	-	-	4	26
3	NIS	1.0	-	97	0	12
4	NaI	2.0	DMAP[a]	85	1	7

Table 4.7: Attempted formation of sulfonyl BCP iodides from sulfonyl chlorides. [a] *10 mol%.*

4.2.5 Instability of Sulfonyl Iodides

Over the course of the reaction, the generated sulfonyl iodide **19a-I** precipitated out of the reaction solution in Et_2O as a yellow solid. We anticipated that for electron-deficient and alkyl substrates, the stability of the sulfonyl iodide would improve if it were in solution at this stage (by dilution or use of more polar solvents). Therefore, we used a suboptimal set of reaction conditions (2.0 equiv. of **18a-S**) to investigate the effect of the concentration of the solvent on the reaction outcome (Table 4.8). Dilution of the reaction from 1.00 M to 0.25 M improved the yield of **18a-I** from 74% to 89% (entries 1 and 2). MTBE ($(CH_3)_3COCH_3$) is a more attractive solvent than Et_2O for industrial scale-up due to its higher flash point; however, its use was not productive (entry 3). Switching to CH_2Cl_2 maintained an excellent yield of 89% and further reduced the formation of BCP di-iodide **20** (entry 4).

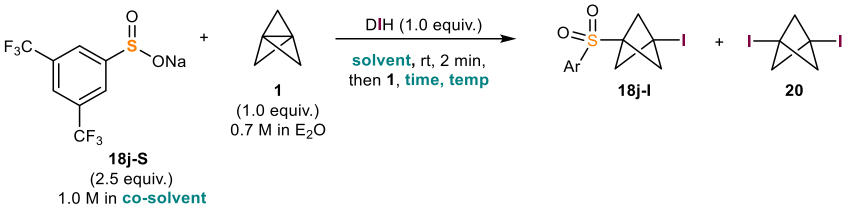


Entry	*Solvent*	*Conc. of DIH / M*	***18a-I** NMR Yield /%*	***20** NMR Yield /%*
1	Et_2O	1.00	74	1
2	Et_2O	0.25	89	2
3	MTBE	0.25	7	14
4	CH_2Cl_2	0.25	89	<1

Table 4.8: Solvent and concentration effect on reaction yield.

4.2.5.1 Electron deficient substrates

On application of the optimal conditions to an electron-deficient sulfinate **18j-S** (3,5-dCF_3PhSO_2Na), a significantly reduced yield of 23% of **18j-I** was observed, presumably due to the instability of the intermediate sulfonyl iodide to de-sulfonylation and formation of iodine (Table 4.9, entry 1). A reduced temperature of –5 °C, with CH_2Cl_2 as the solvent, slightly improved the yield to 31% (entries 2 and 3). Dilution of the reaction at this temperature ensured the intermediate sulfonyl iodide was fully dissolved and gave a 47% yield of **18j-I** (entry 4). Cooling to –40 °C gave an optimal 69% yield of **18j-I**: preparation of sodium sulfinate **18j-S** with DMF co-solvent (rather than water) was required to prevent freezing, with the reaction warmed to room temperature over 30 mins to ensure complete conversion (entry 5). Reducing the temperature to –78 °C required IPA or MeOH as the co-solvent, which led to significantly reduced yields (entries 6 and 7).



Entry	*Co-solvent*	*Solvent*	*Conc. of DIH/ M*	*Temp/ °C*	*Time/ min*	***18j-I** NMR Yield /%*	***20** NMR Yield /%*
1	H_2O	Et_2O	1.00	25	2	23	21
2	H_2O	Et_2O	1.00	–5	2	24	25
3	H_2O	CH_2Cl_2	1.00	–5	2	31	9
4	H_2O	CH_2Cl_2	0.25	–5	2	47	5
5	DMF	CH_2Cl_2	0.25	–40	30	69	0
6	IPA	CH_2Cl_2	0.25	–78	30	40	6
7	MeOH	CH_2Cl_2	0.25	–78	30	16	2

*Tabel 4.9: Optimisation with an electron-deficient sulfinate salt **18j-S**.*

We concluded the optimisation for sulfonyl BCP iodides with the following conditions (Figure 4.16).

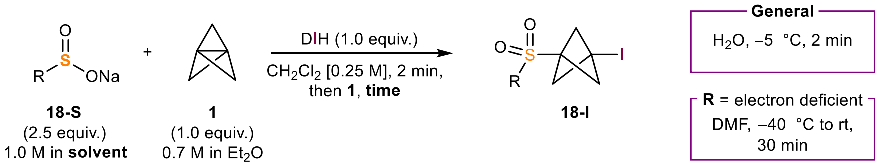
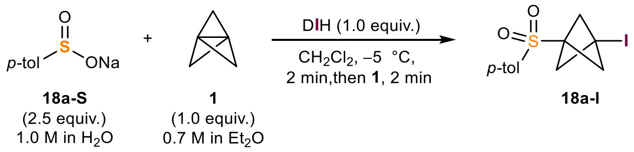


*Figure 4.16: Optimised conditions for sulfonyl BCP iodide formation. [1.1.1]propellane **1** was prepared as a [0.70 M] solution in Et_2O.*

4.2.6 Control Reactions

To gain insight into the initiation process, we carried out several control experiments (Table 4.10). Firstly, carrying out the iodo-sulfonylation of [1.1.1]propellane **1** in the dark led to no formation of tosyl iodide **19a-I** or BCP iodide **18a-I** (entry 1). Secondly, the addition of TEMPO as a radical inhibitor completely shut down the desired reactivity (entry 2). Analysis by LCMS or ^{1}H NMR observed no TEMPO-tosyl adducts. These results indicate that ambient light is necessary to initiate a radical process on this time scale. The omission of [1.1.1]propellane **1** led to the formation of sulfone dimer (entry 3). These observations are consistent with a radical mechanism.



Entry	*Variation*	*Result*
1	Dark	No reaction
2	TEMPO (3.0 equiv.)	No reaction
3	Omission of **1**	Ts-Ts major product

Table 4.10: Control experiments.

4.2.7 Substrate Synthesis

Sulfinate salts can be readily achieved from feedstock chemicals, for example, by reduction of sulfonyl chlorides or oxidation of thiols (Figure 4.17).[173] In addition, cleavage of weak S-S or S-C bonds can be employed. Sulfinate salts can also be isolated or prepared *in situ* by the addition of organometallic nucleophiles to 'SO$_2$ surrogates'.[203]

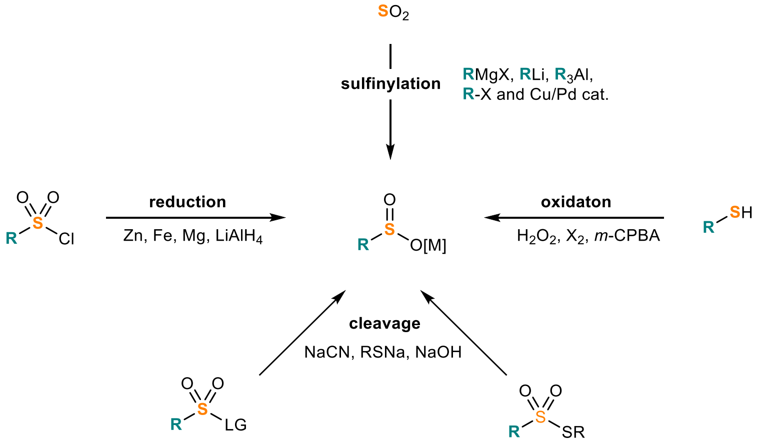


Figure 4.17: Methods to prepare sulfinate salts. LG = leaving group.

The majority of the sodium sulfinate salts for the scope herein were prepared by reduction of sulfonyl chlorides with sodium sulfite and sodium bicarbonate (Figure 4.18).[204] Sulfinates salts denoted with an '[a]' were prepared by Dr J. Nugent and substrates denoted with a '[b]' were available within our department and prepared by Dr T. C. Johnson.

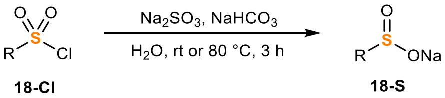


Figure 4.18: Methods to prepare sulfinate salts.

The following aryl sodium sulfinates **18-S** were prepared from the corresponding sulfonyl chlorides (Figure 4.19).

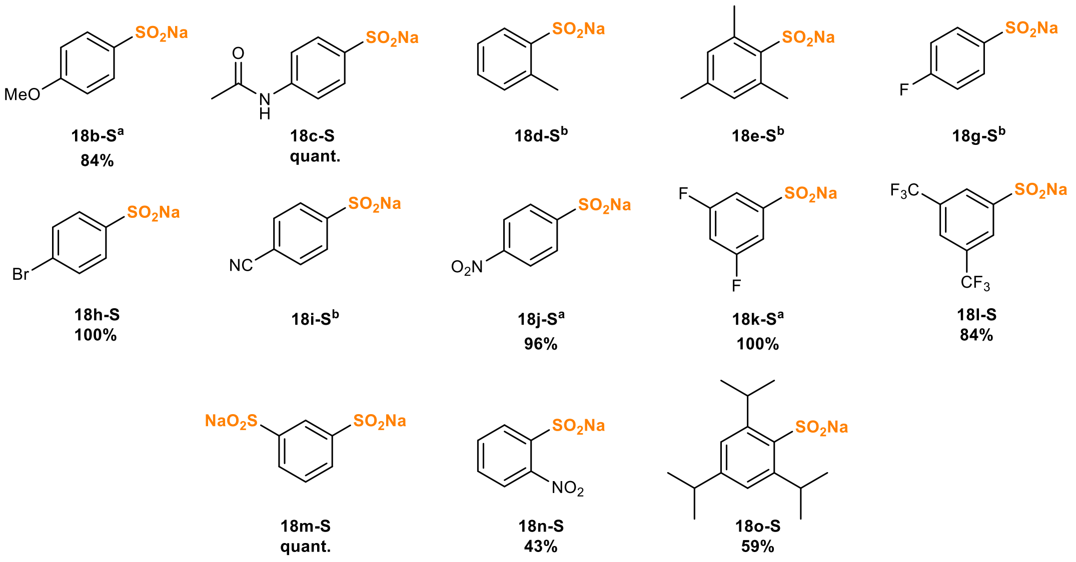

18b-S[a] 84%
18c-S quant.
18d-S[b]
18e-S[b]
18g-S[b]
18h-S 100%
18i-S[b]
18j-S[a] 96%
18k-S[a] 100%
18l-S 84%
18m-S quant.
18n-S 43%
18o-S 59%

Figure 4.19: Sulfinate salts prepared by reduction of sulfonyl chlorides. [a] Prepared by Dr J. Nugent. [b] Available within our department and prepared by Dr T. C. Johnson.[204, 205]

Heteroaryl sulfinate salts **23-S** were prepared using this method (Figure 4.20). Sulfinate **23h-S** was prepared according to a modified literature procedure.[206]

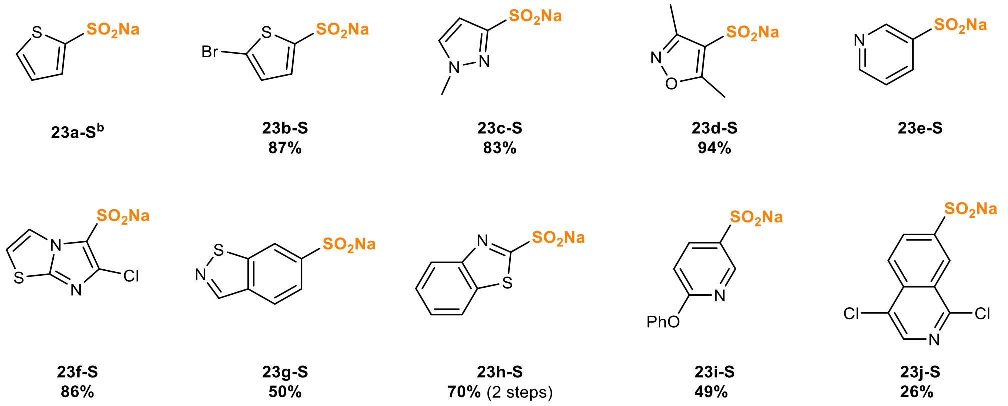
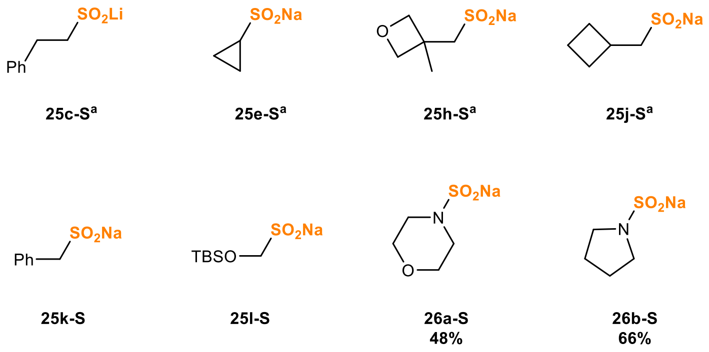

23a-S[b]
23b-S 87%
23c-S 83%
23d-S 94%
23e-S
23f-S 86%
23g-S 50%
23h-S 70% (2 steps)
23i-S 49%
23j-S 26%

Figure 4.20: Heteroaryl sulfinate salts prepared by reduction of sulfonyl chlorides. [a] Available within our department and prepared by Dr T. C. Johnson.[204, 205]

A selection of alkyl sulfinate salts **25-S** were obtained for this chemistry (Figure 4.21). Benzyl sulfinate **25k-S** [207] and the sulfinate salt of TBS-rongalite **25l-S** [208] were prepared according to literature procedures. In addition, morpholine **26a-S** and pyrrolidine **26b-S** sulfinates could be prepared.

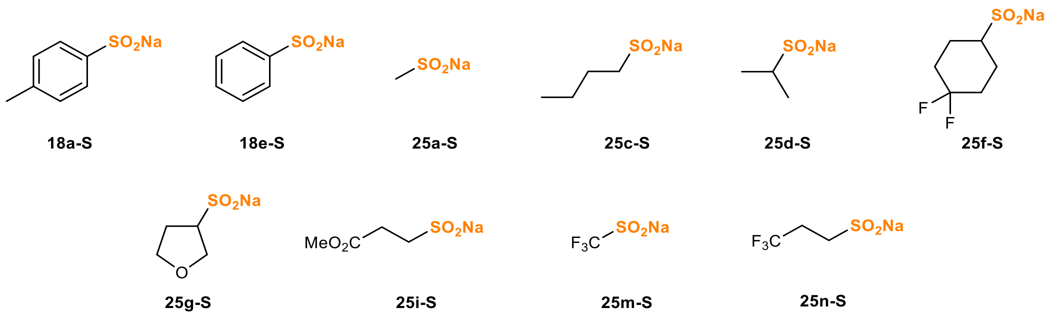


25c-S[a] **25e-S**[a] **25h-S**[a] **25j-S**[a]

25k-S **25l-S** **26a-S** **48%** **26b-S** **66%**

Figure 4.21: Alkyl, morpholine and pyrrolidine sulfinate salts obtained. [a] *Available within our department and prepared by Dr T. C. Johnson.*[204, 205]

A wide variety of sodium and/ or zinc sulfinate salts are commercially available, and a selection was chosen to evaluate the scope (Figure 4.22). As part of a collaboration project between Sigma-Aldrich and the Baran lab, a selection of Diversinates^{TM} sulfinate salts are available for purchase for use in late-stage functionalisation projects.[209]



18a-S **18e-S** **25a-S** **25c-S** **25d-S** **25f-S**

25g-S **25i-S** **25m-S** **25n-S**

Figure 4.22: Commercially available sodium sulfinate salts used in this project.

4.2.8 Hetero(Aryl) Sulfonyl BCP Halides Scope

The scope of the reaction was evaluated at –5 °C for the BCP iodides and room temperature for the corresponding BCP bromides (Figure 4.23). Sulfinates bearing *p*-electron-donating Me- **18a**, OMe- **18b** substituents gave the corresponding sulfone BCP halides (X = I and Br) in nearly quantitative yields (99–100%). Lower yields were obtained with acetamide **18c**, even on cooling to –40 °C, presumably due to the amide nucleophilicity (43% and 46% for the iodide and bromide respectively). Incorporating an *o*-substituent gave a slightly reduced yield for the *o*-tosyl BCP iodide (**18d-I**, 88%). Interestingly, synthesis of the corresponding BCP bromide gave a significantly reduced yield (**18d-Br**, 33%) due to competing bromination of the benzylic position. The bulky mesityl sulfinate **18e** benefitted from cooling to –40 °C for the iodide (66%) but did not suffer under bromination conditions, giving the BCP bromide in 88% yield. The use of an electron neutral arene substituent gave **18f** in 96% and quantitative yield for the BCP iodide and bromide respectively. As expected, electron-deficient arenes required reduced reaction temperatures of –40 °C to prevent rapid desulfonylation (**18g-I** to **18m-I**, except **18h-I**). Generally, the corresponding sulfonyl bromides were sufficiently stable at room temperature and achieved excellent reaction profiles with **1** (**18g-Br** to **18m-Br**). Mildly electron-withdrawing *p*-F and *p*-Br substituents afforded good to excellent yields for both halides (**18g** and **18h**, 50–100%). Similar results were obtained with stronger electron-withdrawing *p*-CN and *p*-NO_2 groups (**18i** and **18j**, 54 – 90% yield). *Meta*-electron withdrawing substituents were well tolerated, with 3,5-dF **18k** and 3,5-dCF_3 **18l** arenes achieving both BCP halides in 69 – 100% yield. Finally, the bis-sulfinate was used successfully to deliver bis-BCP sulfone iodide **18m-I** in 26% yield, and bromide **18m-Br** in 92% yield.

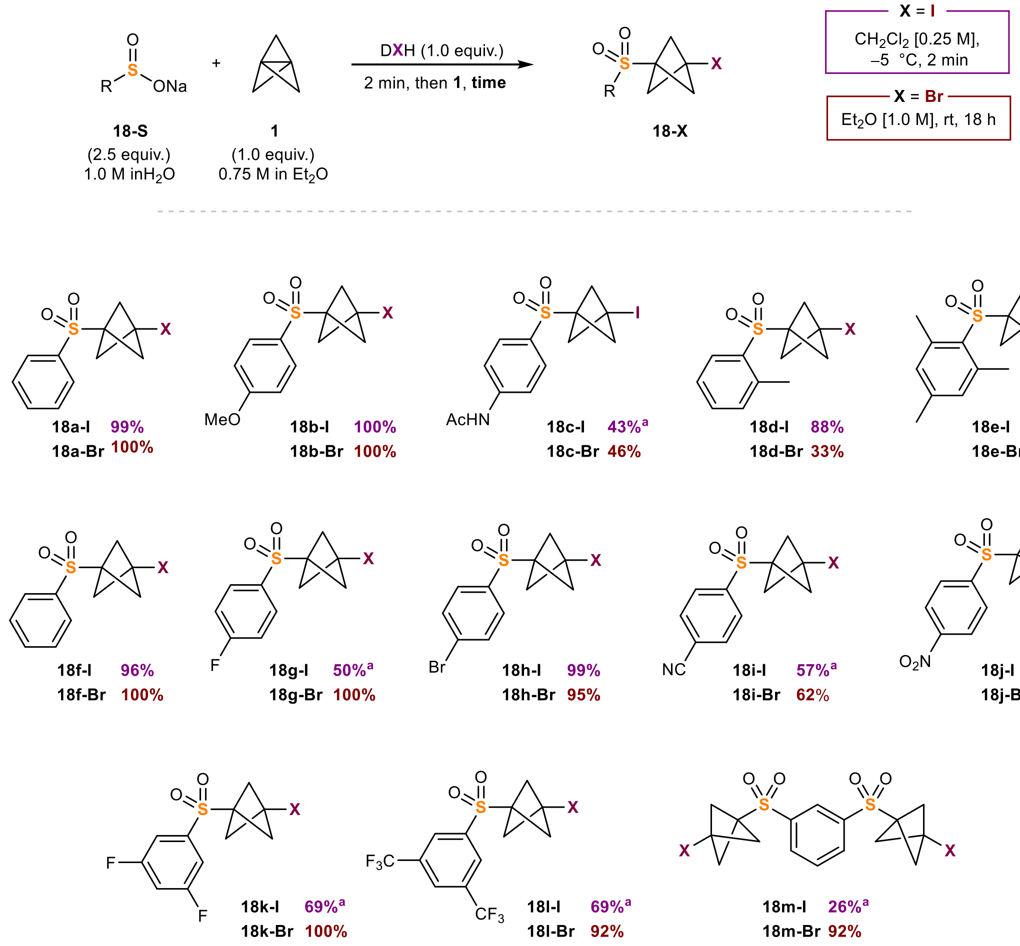


Figure 4.23: Aryl Sulfonyl BCP Halide Scope. [a] Reaction carried out at –40 °C for 30 min, sulfinate prepared as a solution 1.0 M in DMF (see Figure 4.14).

Heteroaryl sulfonyl halides excelled under our developed protocol (Figure 4.24). Electron-rich 5-membered rings such as thiophene **23a**, bromo-thiophene **23b** and pyrazole **23** performed best, with yields ranging from 91 – 100% for both the iodide and bromide products. A limitation of this chemistry was observed with substrates containing nucleophilic nitrogen atoms such as oxazole **23d** and pyridyl **23e**, presumably due to competing reactivity addition to the sulfonyl halide. These substrates give low to no product yields for the BCP iodides (0 – 19%) and reduced yields of the BCP bromides (24 and 67%).

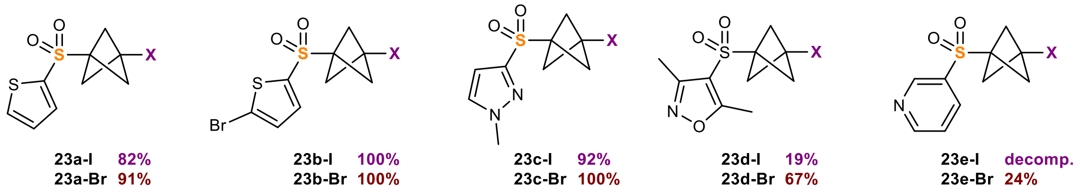


Figure 4.24: Heteroaryl substituted BCP sulfonyl halides. Reaction conditions as in Figure 4.23.

4.2.9 Pharmaceutical and Agrochemical Examples

The triazole rice herbicide Cafenstrole was an ideal substrate for bioisosteric replacement of the mesityl sulfone with a BCP motif (Figure 4.25, a and b).[210] Synthesis of the cafenstrol BCP sulfonyl halide **24a** could conceivably allow access to analogous substrates where X = H, Me, or CF_3 as potential mimics of the mesityl group. SAR analysis of cafenstrole derivatives found an increased bulk and lipophilicity of the sulfone substituent such as 2-adamantyl- (P*f* (3D7) IC_{50} = 0.008 μM) and cyclohexyl (IC_{50} = 0.028 μM) demonstrated increased potency compared to the parent mesityl compound (IC_{50} = 0.164 μM).[211] These results demonstrate the appeal of developing a practical methodology for constructing sp^3 rich sulfone analogues.

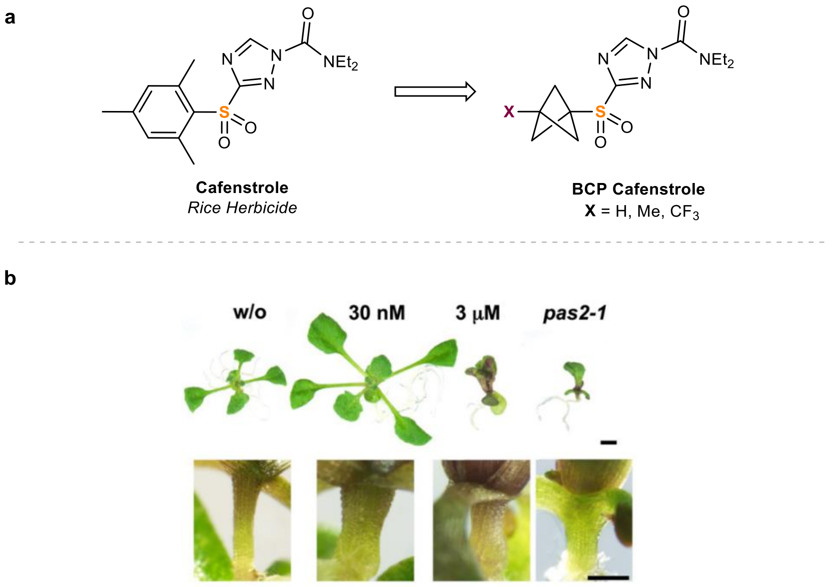


Figure 4.25: a. Tiazole herbicide Carenstrole. b. Figure taken from PLOS Biology [210] – "12-d-old wild-type seedlings grown in the absence (w/o) or presence of cafenstrole 30 nM or 3mM). pas2-1 [mutant] grown in the absence of cafenstrole is shown for comparison."

The sulfinate salt of cafenstrole **24a-S** could be synthesised from the commercially available triazole-thiol **24a-S$_3$** (Figure 4.26). Benzylation and amidation were implemented in a one-pot procedure to form the carbamoyl triazole **24a-S$_2$** in 78% yield over two steps.[211] The sulfonyl chloride **24a-S$_1$** could be obtained by reaction with NCS in AcOH in 35% yield. We speculated that the reduced yield came from a sodium bicarbonate aqueous workup recommended in the literature, causing the premature formation of the sulfonate salt and loss in the aqueous phase. Reduction of sulfonyl chloride **24a-S$_1$** with sodium sulfite and sodium bicarbonate was effective, affording **24a-S** in 67% yield. To our delight, the sulfinate salt underwent efficient halo-bicyclopentylation to give **24a-I** and **24a-Br** in 55% and 59% yields, respectively. Functionalisation of the cafenstrole BCP halides through de-halogenation or radical trifluoromethylation would access potential mesityl surrogates, but due to time constraints development of these methods was not investigated.[212]

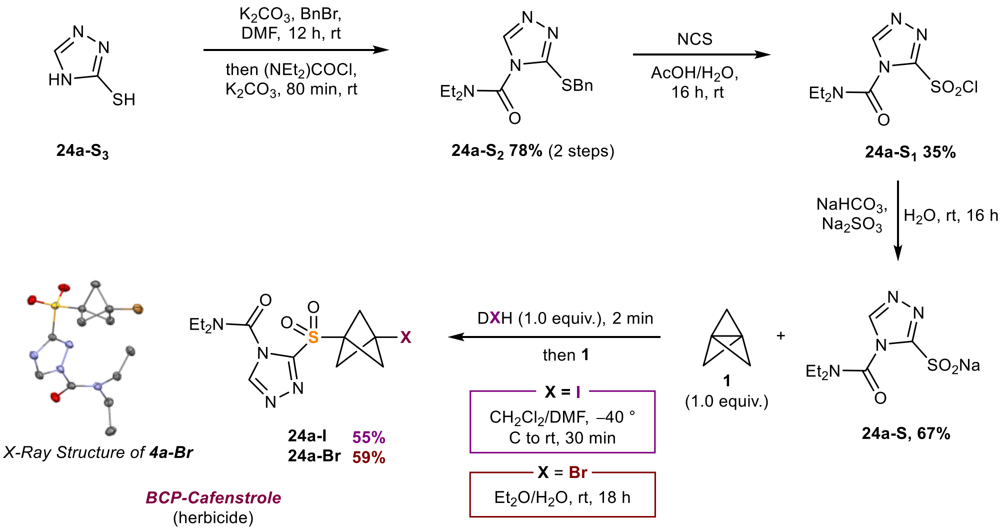
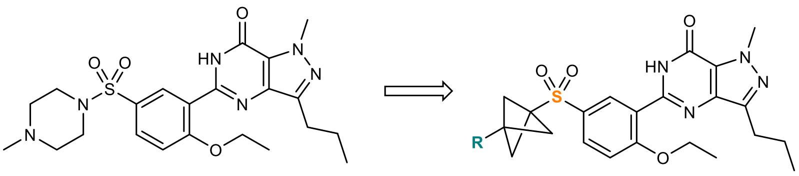


Figure 4.26: Synthesis of Cafenstrole sulfinate derivative.

Next, we considered the synthesis of a BCP derivative of the Pfizer drug Sildenafil (Figure 4.27).



Sildenafil
Viagra

BCP Sildenafil Analogue
R = H, Me, CF_3

Figure 4.27: BCP Derivative of Sildenafil.

Chlorosulfonic acid could be employed to effectively synthesise the aryl sulfonyl chloride **24b-S1**, which was manipulated to the sulfinate salt **24b-S** in high yield (Figure 4.28).[213] We were concerned about the potential nucleophilicity of the pyrazolopyrimidinone motif, however under standard conditions Sildenafil BCP iodide **24b-I** and bromide **24b-Br** analogues were isolated in a very good 84% and 83% yield, respectively. The nitrogen lone pairs were presumably sufficiently non-nucleophilic to not compete for sulfonylation of the *in situ* generated sulfonyl halide.

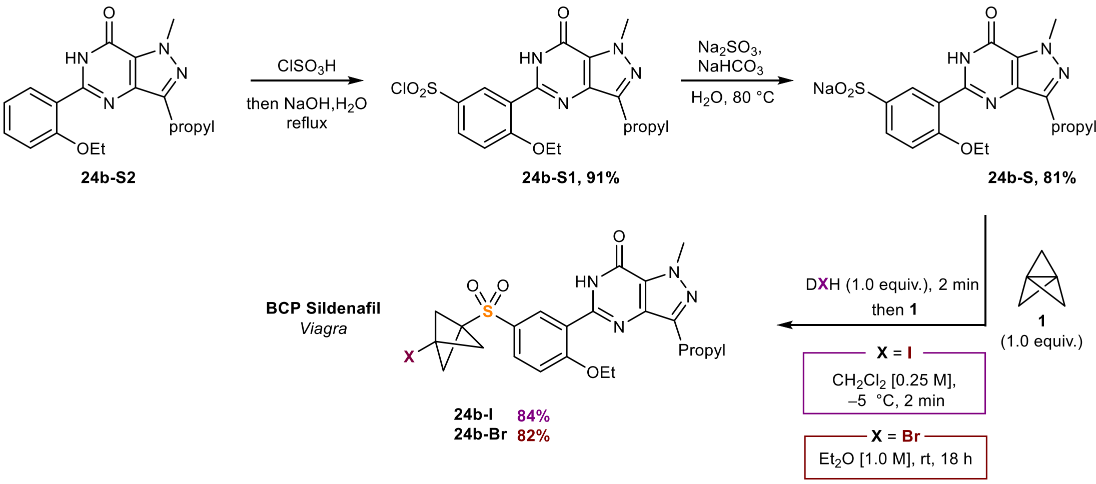


Figure 4.28: Synthesis of BCP Sildenafil derivatives.

4.2.10 Alkyl Sulfonyl BCP Halides Optimisation

The reaction of methoxypropanoate sulfinate **25i-S** under standard halo-bicyclopentylation conditions returned the sulfonylated hydantoin reagent **27** as a significant product (Figure 4.29). The lack of de-sulfonylation was highly encouraging, and we therefore considered methods to reduce the nucleophilicity of the halogenating agent to improve selectivity for the formation of the BCP ATRA product.

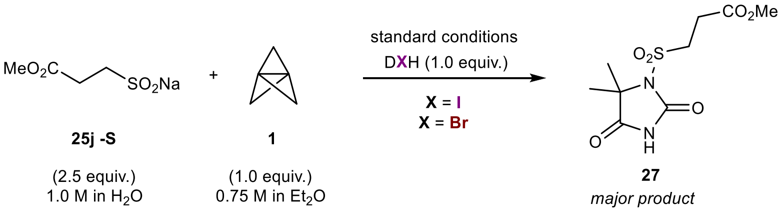
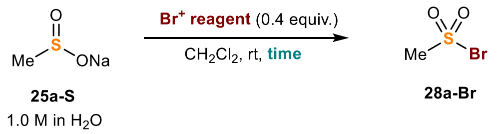


Figure 4.29: Sulfonylation of hydantoin halogenating agent.

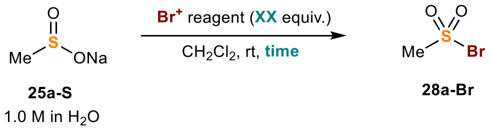
We commenced this investigation with alkyl sulfonyl bromides. From our experience with the aryl and heteroaryl substrates, we anticipated the alkyl sulfonyl bromides to be more stable and easier to handle. Commercially available sodium methanesulfinate **25a-S** was selected for reaction optimisation. The optimisation was approached stepwise to confirm efficient conversion to the mesyl bromide **28a-Br** before addressing the reactivity of the mesyl bromide with [1.1.1]propellane **1**. First, we considered different brominating agents, present in a substoichiometric amount (0.4 equiv.) to ensure complete consumption, therefore preventing di-bromination of **1** later in the ATRA optimisation (Table 4.11). Bromine was found to be the superior brominating agent, giving mesyl bromide **28a-Br** in 27% yield within a 2 minute reaction time (entry 1). PTAB ($PhNMe_3^+Br_3^-$) gave a similarly promising result and was retained as a backup (entry 2). All other brominating reagents screened were less successful in the reaction (entries 3–7). Leaving the reaction for 18 h resulted in a 0% yield of mesyl bromide due to decomposition overnight (entry 8).



Entry	*Br^+ Reagent*	*Time*	***28a-Br** NMR yield /%*
1	Br_2	2 min	27
2	PTAB ($PhNMe_3^+$ Br_3^-)	2 min	26
3	TBAB ($Bu_4N^+Br^-$)	2 min	0
4	DBH	2 min	19
5	$PyrH^+Br_3^-$	2 min	9
6	$Bu_4N^+Br_3^-$	2 min	4
7	NBrSac	2 min	0
8	Br_2	18 h	0

*Table 4.11: Optimisation for the formation of mesylbromide **28a-Br**. NBrSac = N-Bromosaccharin was prepared according to literature procedure.*[214]

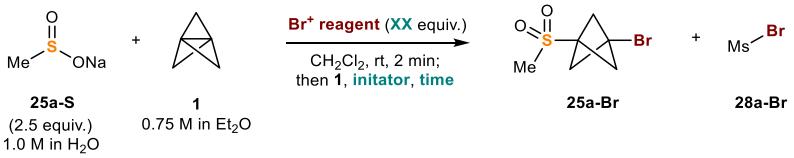
Increasing the equivalents of bromine (from 0.4 to 0.8 equiv.) with respect to the sulfinate salt **25a-S** gave an improved 63% yield of mesyl bromide **28a-Br** (Table 4.12, entries 1 and 2). However, re-evaluation of PTAB as a brominating agent with this new stoichiometry did not offer further improvements (entry 3). Promisingly, no degradation of mesyl bromide **28a-Br** was observed between a 2 min and 15 min reaction time (entries 3 and 4).



Entry	Br⁺ Source	Equiv.	Time	**28a-Br** NMR yield /%
1	Br_2	0.4	2 min	27
2	Br_2	0.8	2 min	63
3	PTAB	0.8	2 min	59
4	PTAB	0.8	15 min	59

*Table 4.12: Improved reaction stoichiometry for the formation of mesylbromide **28a-Br**.*

These conditions were taken forward to prepare mesyl bromide **28a-Br** *in situ* prior to reaction with [1.1.1]propellane **1** (Table 4.13). Unfortunately, stirring the pre-formed mesyl bromide **28a-Br** with **1** resulted in no sulfonyl BCP bromide **25a-Br** (entry 1). Only after the addition of triethylborane as a radical initiator did we obtain **25a-Br** in 30% yield (entry 2). Modification of the reaction stoichiometry to include 2.0 equiv. of Br_2 increased the yield to 76% in only 30 min reaction time (entry 3), and a 2 hour reaction time was later found to be optimal (96%, entries 5 – 7). Compared to our earlier findings, PTAB was not a suitable reagent in the presence of **1**, suffering from a complex mixture of decomposition products (entry 4). During these optimisation reactions, the potential di-brominated BCP side product was not observed.

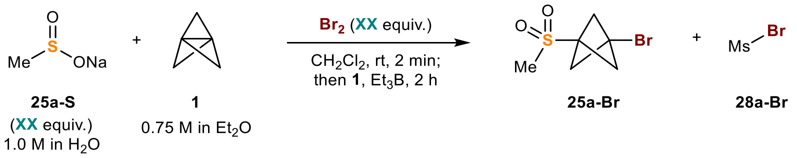


Entry	Br⁺ reagent	Br⁺ equiv.	Initiator[a]	Time	**25a-Br** NMR Yield /% (isolated)	**28a-Br** NMR Yield /%
1	Br_2	1.0	-	18 h	0	0
2	Br_2	1.0	Et_3B	18 h	30	-
3	Br_2	2.0	Et_3B	30 min	76	39

4	PTAB	2.0	Et_3B	30 min	17	40
5	Br_2	2.0	Et_3B	1 h	81	50
6	Br_2	2.0	Et_3B	2 h	94 (96)	51
7	Br_2	2.0	Et_3B	2.5 h	94	36

*Table 4.13: Optimisation for bromo-sulfonylation of [1.1.1]propellane. [a] Et_3B in 10 mol%. nr = not recorded. [1.1.1]propellane **1** was prepared as a 0.70 M solution in Et_2O.*

The current best conditions isolated 96% of BCP bromide **25a-Br** along with 51% of undesired mesyl bromide **28a-Br** (Table 4.14, entry 6). We endeavoured to make final adjustments to the reaction stoichiometry to improve the reaction efficiency and minimise the purification requirements. Proportional reduction of the amount of Br_2 and **25a-S** with respect to **1** (1.6 : 2.0: 1.0 equiv.) gave a slightly worse 86% yield of **25a-Br**, but did reduce the formation of unreacted mesyl bromide **28a-Br** to just 6% (entry 2). Gratifyingly, the use of 1.8 equiv. of Br_2 gave a near quantitative yield of **25a-Br** (entry 3), and these conditions were pursued to evaluate the scope of alkyl sulfonyl bromides.

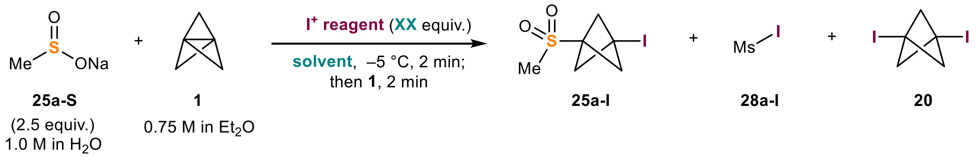


Entry	***25a-S** equiv.*	*Br_2 Equiv.*	***25a-Br** NMR Yield /% (isolated)*	***28a-Br** NMR Yield /%*
1	2.5	2.0	94 (96)	51
2	2.0	1.6	86 (86)	6
3	2.0	1.8	99 (98)	-

Table 4.14: Final adjustments to reaction stoichiometry.

Having achieved bromo-sulfonylation of [1.1.1]propellane **1** in excellent yield, we set out to apply these modified reaction conditions to an iodo-sulfonylation procedure (Table 4.15). However, comparable use of iodine as an X^+ source resulted in only a 28% yield of

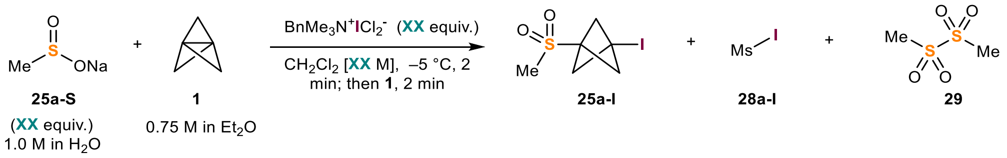
25a-I and a considerable 50% yield of di-iodinated BCP **20** (entry 1). Happily, an alternative source of I^+ – $BnMe_3NICl_2$ – was found to be an excellent iodinating agent for this transformation.[215] Sulfonyl BCP iodide **25a-I** was isolated in 92% yield in just 2 min (entry 2). An additional benefit was the minimal formation of **20** (2%). However, a significant proportion of unreacted mesyl iodide **28a-I** was observed on analysis of the crude ^1H NMR reaction mixture (109%, decomposition amount unknown), indicating the amount of iodinating agent and sulfinate salt should be reduced to prevent waste of reagents.



No.	I^+ source	I^+ equiv.	Solvent	**25a-I** NMR Yield /% (isolated)	**28a-I** NMR Yield /% [a]	**20** NMR Yield /%
1	I_2	1.0	Et_2O	28	-	50
2	$BnMe_3N^+ICl_2^-$	2.5	CH_2Cl_2	83 (92)	109	2

Table 4.15: Iodinating agents for iodo-sulfonylation of [1.1.1]propellane ***1****.* [a] *NMR Yield of mesyliodide is out of 250% based on reaction stoichiometry.*

The reaction efficiency was improved by using 1.4 equiv. of $BnMe_3N^+ICl_2^-$ and just 2.0 equiv. of sulfinate salt, obtaining BCP iodide **25a-I** in an excellent 100% yield (Table 4.16, entries 1 –5). In contrast to electron-deficient (hetero)aryl sulfonyl iodides, dilution of the reaction led to a reduced 39% yield of **25a-I** and the formation of disulfone **29** (entry 6). The conditions outlined in entry 4 were taken forward to evaluate the scope of alkyl sulfonyl BCP iodides.



Entry	$BnMe_3N^+ICl_2^-$ equiv.	*25a-S* equiv.	Conc. / M	*25a-I* NMR Yield /% (isolated)	*28a-I* NMR Yield /% [a]	*29* NMR Yield /%
1	2.5	2.5	1.0	83 (92)	109	7
2	1.8	2.5	1.0	71	57	0
3	1.4	2.5	1.0	102	24	0
4	1.4	2.0	1.0	102 (100)	27	2
5	1.4	1.5	1.0	77	35	7
6	1.4	2.0	0.25	39	24	23

*Table 4.16: Adjustment of reaction stoichiometry. The yield of di-iodinated BCP **20** was <2 % for all entries.*

4.2.11 Alkyl Sulfonyl BCP Halides Scope

We explored the alkyl substituent scope with an improved set of conditions for the synthesis of alkyl sulfonyl BCP halides in hand (Figure 4.30). Primary alkyl substituents, including methyl **25a** and butyl **25b** groups, gave good to excellent yields for both bromide and iodide compounds (64 – 98%). Phenylethyl sulfone **25c** gave the BCP iodide in an excellent 98% yield; however, under bromination conditions, a complex mixture was returned, presumably due to bromination of the benzylic position as seen in the *o*-Ts example in section 4.2.8 (Figure 4.23). Secondary alkyl substituents such as cyclopropyl **25d**, di-isopropyl **25e** and dF-cyclohexyl **25f**, were also well tolerated under these conditions (67 – 100% yield), somewhat surprisingly due to their increased potential for the elimination of HBr or HI. Tetrahydrofuran example **25g** performed admirably under these conditions, and was isolated in 71% and 96% yields for the iodide and bromide, respectively. Oxetane substituents were well tolerated **25h** to form the BCP iodide (100%), however, a reduced yield was obtained for the bromide (50%). Finally, methyl-propanoate ester BCP derivative **25i** was synthesised as the iodide (39%) and bromide (73%). These compounds are of particular significance as halide-substituted BCP sulfinate precursors, an improvement to the synthesis of mono-substituted BCP sulfinates by Bräse.[172]

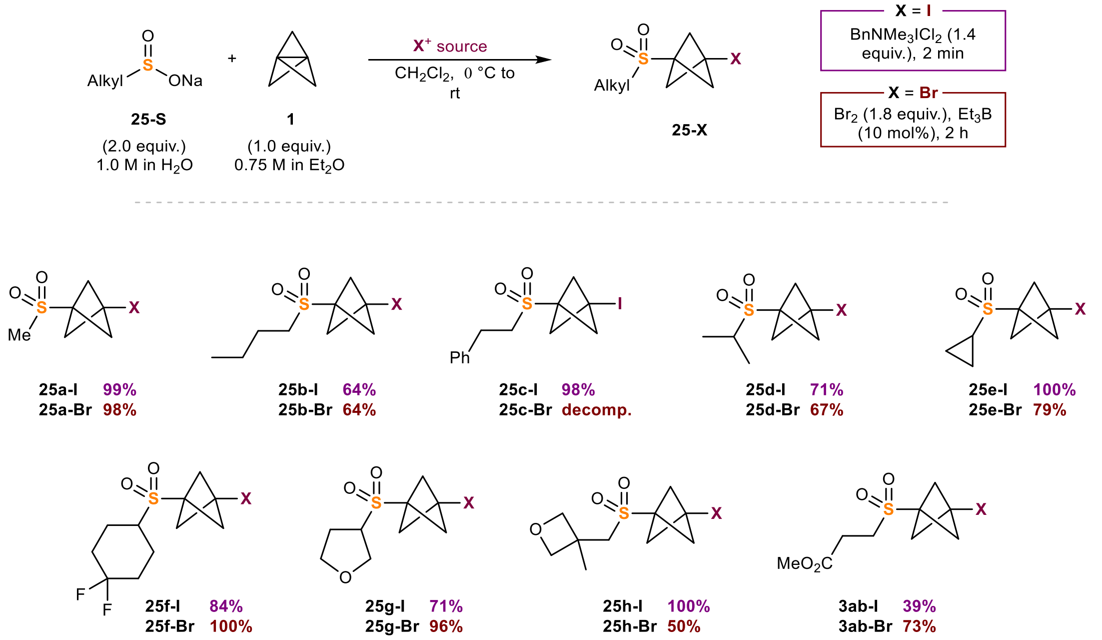


Figure 4.30: Alkyl sulfonyl BCP halides scope.

4.2.12 Strain Release Reagents

To highlight the breadth of this methodology, we investigated the use of alternative ‘strain release reagents’ such as bicyclo[1.1.0]butanes (BCBs) and tricyclo[3.1.1]heptane (TCHep) **30**. Our group's ongoing and unpublished work has demonstrated TCHep **30** as a powerful and convenient reagent to access *meta*-substituted arene bioisosteres (Figure 4.31).[216]

The ATRA reaction of sulfonyl halides translated smoothly to this system to give sulfonyl bicyclo[3.1.1]heptane halide products (**30a-I**, 87%) and (**30a-Br**, 100%) in excellent yields.

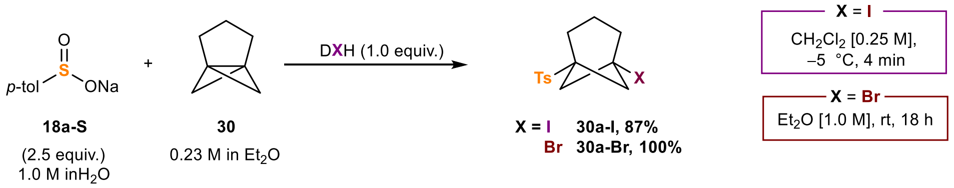


*Figure 4.31: Synthesis of sulfonyl bicyclo[3.1.1]heptane halides. TCHep **30** prepared by N. Frank.*

Encouraged by this success, we turned our attention to BCB reagents. Radical intermediates (α-amino and alkyl) have been shown to add to exclusively mono-substituted BCBs bearing electron-withdrawing substituents (boronates,[217] sulfones,[218, 219] as well as sulfoxides and esters) under photocatalysed conditions, visible light homolysis or Ti^{III} catalysis (Figure 4.32).[220]

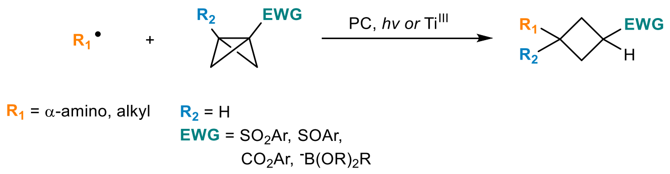


Figure 4.32: Summary of radical additions to BCB reagents.

We were delighted to find that the ATRA reaction of *in situ* generated sulfonyl halides with BCBs was successful, albeit Et_3B initiation was required to form both the iodide and bromide cyclobutyl sulfones **31** (Figure 4.33). Tosyliodide underwent effective ATRA addition to mono-substituted BCBs bearing amide (**31a-I**, 80%, 2.5:1 dr), aryl sulfone (**31b-I**, 66%, 2.1:1 dr) and alkyl sulfone (**31c-I**, 28%, >20:1 dr) substituents. Future investigation into reaction duration could be used to improve the reaction yields for less electron deficient BCB **31c**. Pleasingly, tosylbromide also underwent addition to BCB **31a** and the formation of the sulfonyl cyclobutyl bromide **31a-Br** was achieved in 72% yield, 2.3:1 dr. Apart from the di-iodination of BCB sulfones with elemental I_2[177] and mono-bromination with NBS,[178] this work represents some of the first bromination and iodination of BCB motifs. We tested disubstituted amide BCB **31d** under these conditions and successfully achieved an excellent yield of iodo-sulfonylated product (**31d-I**, 94%, 3.3:1 dr). This represents the first radical addition to disubstituted BCBs.

At the time of writing, the major diastereisomer of **31a-I** was provisionally assigned as the *syn*-addition product, from NOESY correlations of the cyclobutyl protons. However, NOSEY correlations of **31b-I**, **31c-I** and **31d-I** were inconclusive, they have been tentatively assigned as the same diastereisomer based on ^{1}H NMR shift and coupling patterns of the cyclobutyl CH_2 protons. Further structural determination by X-Ray crystallography would support assignment.

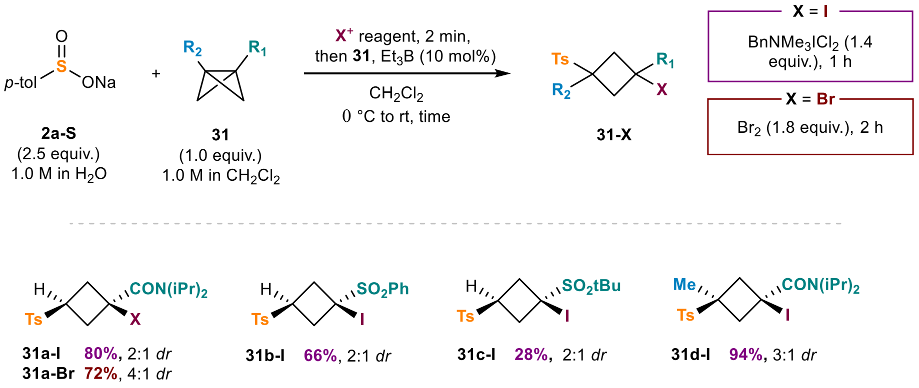


*Figure 4.33: ATRA reaction of BCB reagents. BCB substrates **31a – 31d** prepared by R. McNamee.*[221]

Halo-cyclobutane products offer a convenient handle for further functionalisation, as discussed for the BCP analogues. However, this compound class presents a unique opportunity to re-form BCB compounds following deprotonation/cyclisation of the acidic α-sulfone position (Figure 4.34). Interestingly, the use of NaOMe for this process resulted in the isolation of MeOH adduct **32** in 93% yield, >20:1 dr. The single diastereoisomer isolated presumes that this reaction proceeded via a BCB intermediate. We anticipate that the use of an organometallic base would circumvent this issue and enable the desired BCB formation **33**, however this was not attempted due to time constraints.[222]

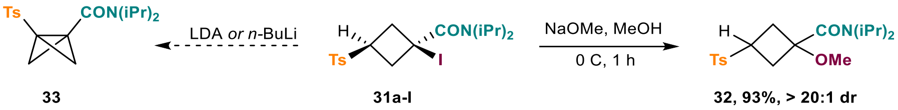


Figure 4.34: Attempted deprotonation/cyclisation conditions for the reformation of BCB compounds.

4.2.13 Unsuccessful Sulfinate Salt Substrates

4.2.13.1 Sulfinate Salts

The following sulfinate salts were unsuccessful under our reaction conditions and reasonable modifications (Figure 4.35). Typical limitations included de-sulfonylation of the sulfonyl halide intermediate (even at low temperature), significant formation of di-iodinated BCP **20** or purification challenges.

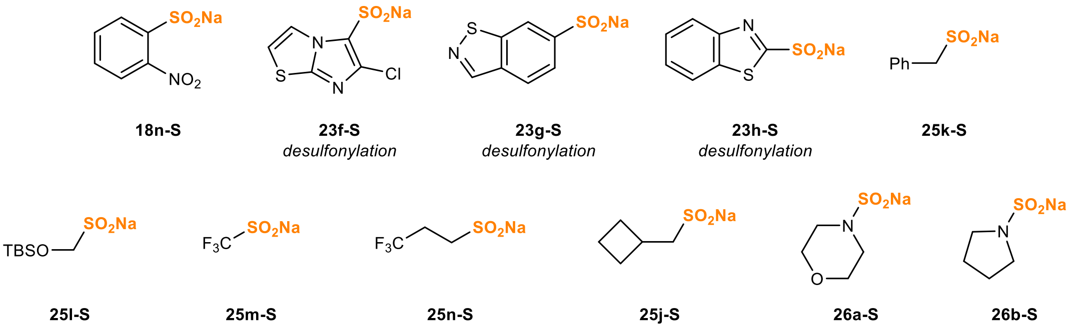
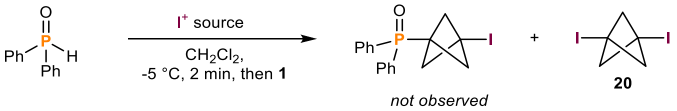


Figure 4.35: Unsuccessful sulfinate salts.

4.2.13.2 Phosphinic Iodides

Phosphinic iodides were identified as potentially analogous reagents to sulfonyl halides; these reagents have only been proposed intermediates and never isolated. Attempts to implement this chemistry were not promising, and we did not further pursue this reagent class (Table 4.17).[223]



Entry	*I$^+$ source*	*I$^+$ equiv.*	*Ph$_3$P(O)H equiv.*	***20** NMR yield /%*
1	DIH	1.0	2.0	39
2	BzMe$_3$N$^+$ICl$_2^-$	1.4	1.0	30

Table 4.17: Attempted formation of phosphinic iodides.

4.2.14 Functionalisation of sulfonyl BCP Halides

To demonstrate the utility of sulfonyl BCP halides, we sought to address the functionalisation of these substrates. Attempted lithiation of BCP halide **18a-I** was unsuccessful; as with BCPA halides, rapid fragmentation was observed with the presumed formation of volatile [1.1.1]propellane **1** (Figure 4.36, a). Additionally, attempted insertion of freshly prepared Rieke Zinc at 50 °C returned unreacted BCP bromide **18a-Br** and fragmented the BCP iodide **18a-I** (Figure 4.36, b).

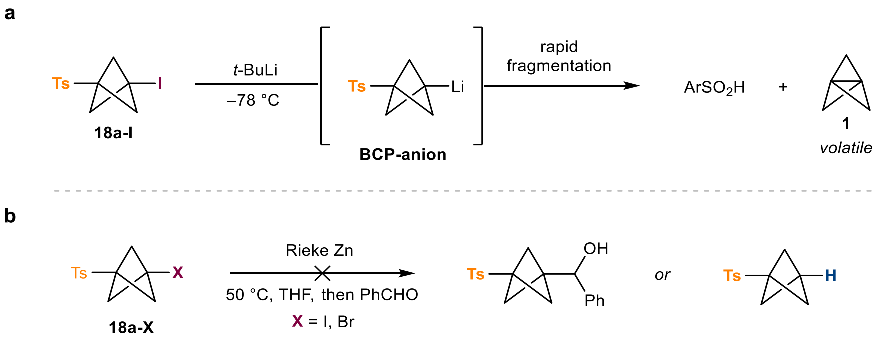


Figure 4.36: Attempted lithiation and zinc insertion of sulfonyl BCP halides ***18a-X****.*

Attempted iron-catalysed Kumada cross-coupling of sulfonyl BCP iodide **18a-I** with *p*-OMePhMgBr resulted in predominant homo-coupling of the aryl Grignard, unreacted starting material and minor amounts of rearrangement products (Figure 4.37).[115]

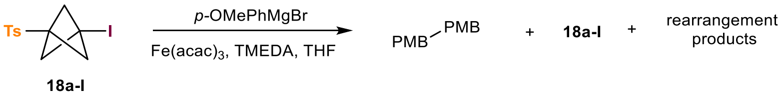


Figure 4.37: Attempted Kumada cross-coupling of sulfonyl BCP iodide ***18a-I****.*

In contrast to these attempts, the use of our previously developed Giese reaction conditions for the functionalisation of iodo BCPAs (Chapter 3) was far more successful. Sulfonyl BCP iodide **18a-I** underwent efficient Giese addition with de-hydroaniline **6u** to give BCP α-amino acid analogue **34** in 76% yield (Figure 4.38).[113] Unfortunately, the corresponding BCP bromide **18a-Br** was unreactive under these conditions. From our previous mechanistic investigations in (Chapter 3, Section 3.2.10), these conditions (conditions B) involve initiation by Dexter-energy transfer between the Ir photocatalyst and the BCP(A) iodide. We hypothesised that the energy transfer between the Ir-photocatalyst and the BCP bromide was inefficient by comparison. We therefore tested conditions which involve $(Me_3Si)_3SiOH$ as a mediator between the BCP halide and Ir photocatalyst (conditions A). Under these conditions with malononitrile acceptor **6p**, we observed <10 % NMR yield of Giese addition product **35**, along with unreacted bromide **18a-Br**. Future investigations could improve this reaction through inversion of the reaction stoichiometry, for example using the BCP bromide in excess.

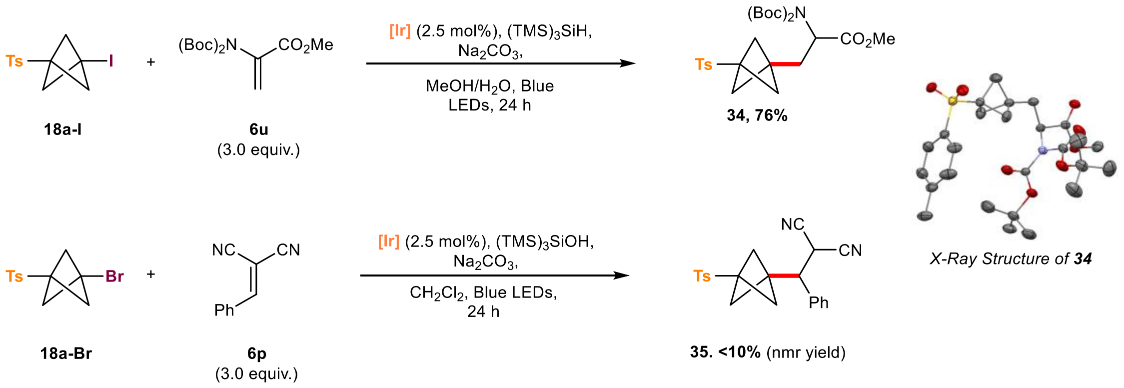


Figure 4.38: Photocatalysed Giese Reaction of sulfonyl BCP halides. [Ir] = Ir[(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$.

Following this, methyl propanoate ester BCP derivative **25i-Br** was converted to the corresponding difunctionalised BCP sulfinate (**36**, 80%) (Figure 4.39). BCP sulfinates have been utilised in the formation of sulfonamides, sulfone and sulfoxides; these transformations were not carried out on **36** due to time restraints but are precedented on the mono-substituted BCP sulfinate.[172] Notably, this represents a considerably shorter 2-step synthesis of difunctionalised BCP sulfinates from [1.1.1]propellane **1** compared to the multistep approaches (8-10 steps) discussed in section 4.1.3.

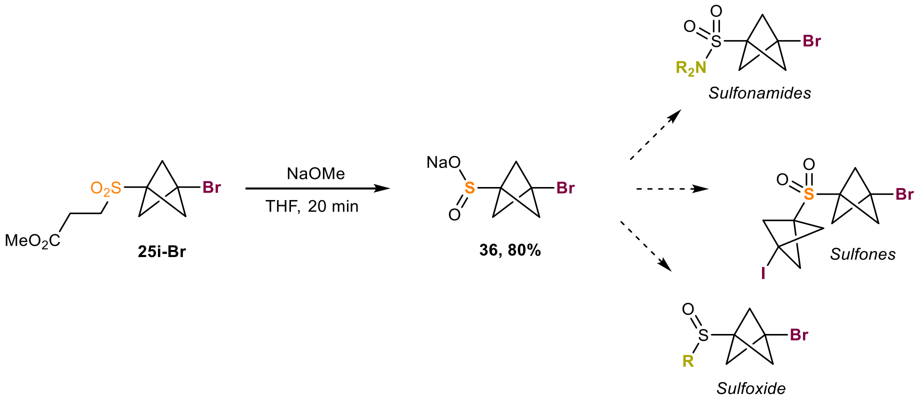


Figure 4.39: Formation of bromide BCP sulfinate.

4.2.15 Synthesis of Sulfonyl Halides from Grignard Reagents

Aryl Grignard reagent can add to DABSO as an SO_2 surrogate to generate sulfinate salts *in situ* before engaging in further reactivity.[203] We recognised that this would be an attractive one-pot method to generate sulfonyl BCP halides (Figure 4.40). Attempts at this four-component, one-pot synthesis of sulfonyl BCP halides gave sulfonyl BCP iodide **18a-I** in a 32% yield by ^{1}H NMR, along with 20% of BCP di-iodide **20**. No improvement was observed when an organic phase wash to remove DABCO was included. The formation of $MgBr_2$ or $Mg(OH)_2$ salts in the first step could be a cause of reduced product formation, and we chose not to pursue this method further as yields were inferior to the stepwise approach. Nonetheless, the possibility of a one-pot conversion of Grignards to BCP sulfonyl halides using this chemistry remains very attractive.

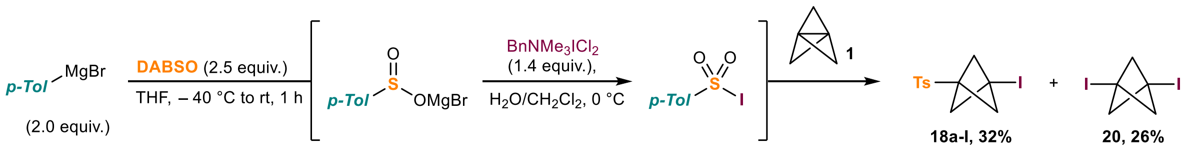


Figure 4.40: Attempted four-component, one-pot synthesis of sulfonyl BCP halides from readily available Grignard reagents.

4.3. Conclusions and Future Work

4.3.1 Conclusions

In this chapter, we have developed an efficient and versatile methodology to construct sulfonyl BCP bromides and iodides (Figure 4.41). A wide range of substituents were tolerated under the reaction conditions. In particular, the range of heteroaryl and alkyl examples represents a positive advancement in the functional group tolerance of sulfonyl halide reagents in the literature. The use of sulfonyl BCP halides as precursors for *para*-disubstituted arene bioisosteres has been demonstrated through Giese C–C bond formation and application to pharmaceutical and agrochemical examples.

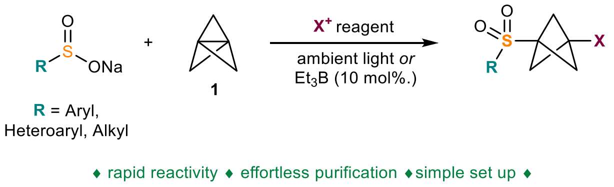


Figure 4.41: Summary of sulfonyl BCP halides.

The reaction protocol is rapid and simple to execute, forgoing the need for anhydrous solvents and inert reaction conditions. Minimal purification steps were required, and re-crystallisation could be used effectively. The ATRA reaction could be carried out initiator-free in ambient light, or assisted with substoichiometric amounts of Et_3B for more challenging substrates, or to achieve faster reaction times.

4.3.2 Future Work

Several areas could be targeted for improvement and further investigations.

4.3.2.1 Functionalisation of sulfonyl BCP Bromides

This methodology accesses an extensive collection of BCP bromide substrates, and the functionalisation of these building blocks would be an asset to this chemistry. We have been able to form trace Giese addition products from BCP bromides under photocatalysed conditions, however further investigations to develop this reactivity are currently being investigated by our industrial collaborators.

4.3.2.2 Strain release reagents

Application of sulfonyl halide reagents to other strained systems such as azabicyclo[1.1.1]butane (ABB) to form azetidine products would be equally attractive (Figure 4.42, a).[224] The addition of tosyl chloride to ABB proceeds at 87% in 18 h at room temperature to give 3-chloro-1-tosylazetidine; [224] it would be of interest to determine the regioselectivity of a similar reaction with tosyl iodide and bromide. Addition to housane would further demonstrate the generality of our reaction protocol to form halo-cyclopentane products (Figure 4.42, b). [37]

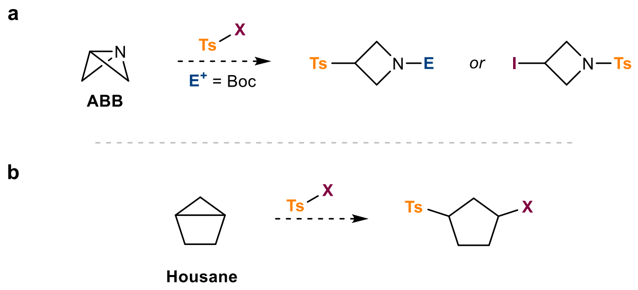


Figure 4.42: a. ABB as a strain release reagent to form azetidines. b. ATRA reaction with Houseane.

4.3.2.3 Pharmaceutical Derivatives

Synthesis of additional pharmaceutical BCP derivatives, such as sunscreen agent Ensulizole (Figure 4.41), and the comparative biological testing and analysis of pharmacokinetic properties with the parent compound would provide data on applications of sulfonyl BCP bioisosteres within the industry.

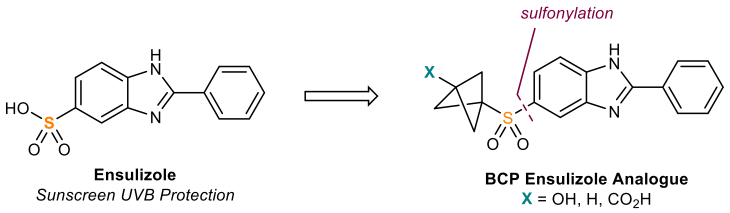


Figure 4.43: Possible sulfonyl BCP analogue of Ensulizole.

4.3.2.4 Sulfoniminoyl Halides

Aryl sulfoximine motifs can be identified in pharmaceutical compounds such as Ronicibib (Figure 4.42, a).[225] Oxidation of BCP sulfides has proven to be the only reported strategy to synthesise sulfoximine BCPs to date (Figure 4.44, b).[226] This approach requires prior synthesis of the BCP sulfide and is only applicable to mono-functionalised BCPs.

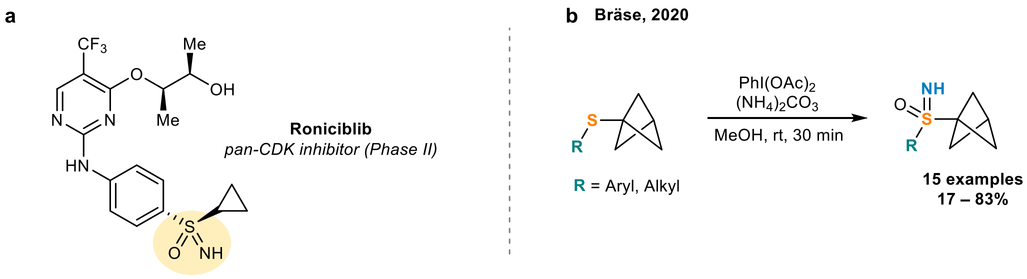


Figure 4.44: Sulfoximine motifs in pharmaceuticals and current syntheses of sulfoximine BCPs.

We questioned whether sulfonimidoyl halides could be implemented to achieve ATRA chemistry with [1.1.1]propellane **1**. Sulfonimidoyl chlorides have been prepared *in situ* from sulfinamide (salts) with NCS, Cl_2 or *t*-BuOCl to generate sulfonimidoyl amides following nucleophilic addition, for example (Figure 4.45, path a). There is only one reported example of a sulfonimidoyl chloride undergoing an addition across a double bond, in this case, under Lewis acid catalysis (path b).[227] Typically, these conditions are instead used for the generation of benzothiacenes.[227] In contrast, the generation of sulfonimidoyl iodide or bromide intermediates are, to our knowledge, unknown.

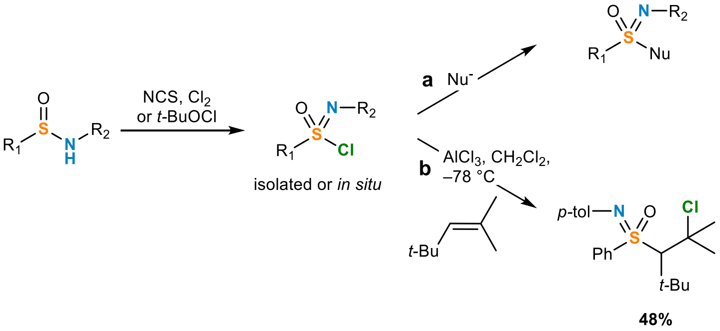


Figure 4.45: Formation and reactivity of sulfonimidoyl chlorides.

Our initial attempt at this chemistry did not return the desired sulfoximine BCP halide product **37**. Promisingly, the free sulfoximine rearranged *exo*-cyclobutene product **38** was isolated in 27% yield, in addition to sulfinamide **39** (Figure 4.46, a). Further investigations into this transformation, starting with sulfinamide reagents such as **39**, could be carried out (Figure 4.44, b). If successful, this would represent a significant contribution to the sulfoximine BCP field and a novel application of sulfonimidoyl halide reagents.

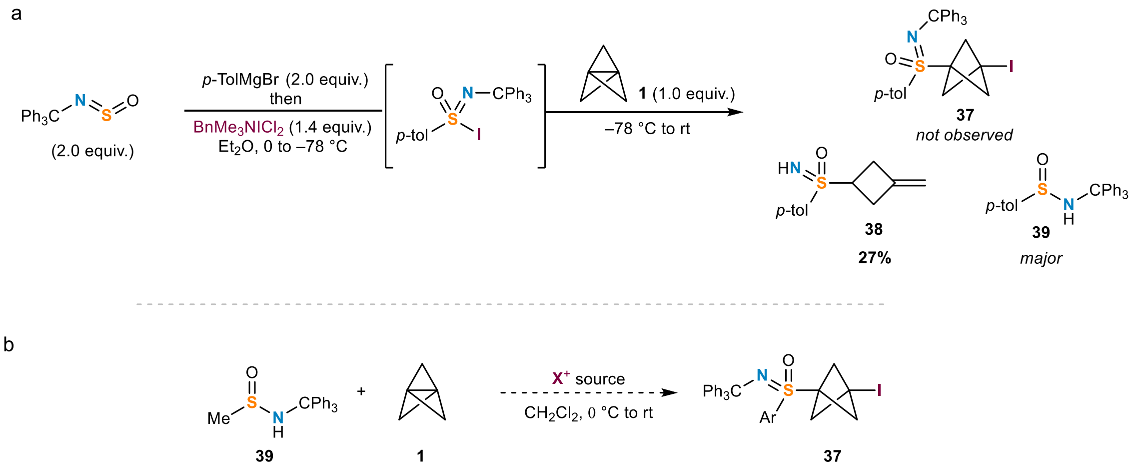


Figure 4.46: Sulfonimidoyl halide reagents for ATRA reactions.

5.

Conclusions and Future Work

5.1 Conclusions

The resurgence of [1.1.1]propellane **1** as a readily accessible and versatile reagent has increased interest in the synthesis and application of bicyclo[1.1.1]pentane motifs. As a result, the demonstration of BCP units as sp^3 rich bioisosteres in pharmaceutical settings, as well as their application in materials chemistry, has seen an enormous rise in popularity. At the time of starting this work, methods available to achieve nitrogen- and sulfone-based BCP motifs were far less well established than those accessing carbon- or sulfide substituted BCPs. Our demonstration of the ability of these heteroatom-radicals to add across the central bond of **1** to form heteroatom-substituted BCPs halides therefore represents a significant contribution to the field.

An efficient route to achieve desirable 1,3-disubstituted BCPAs through fragmentation of α-iodoaziridines and subsequent radical ATRA with [1.1.1]propellane **1** was developed (Chapter 1, Figure 5.1). The limitation of this work is the restriction of the aziridine electron-withdrawing substituent to mainly sulfonamides, although the scope of the sulfonamide substituent is very broad. The resultant halide incorporated onto the BCP is an asset to this methodology for further C–C bond formation.

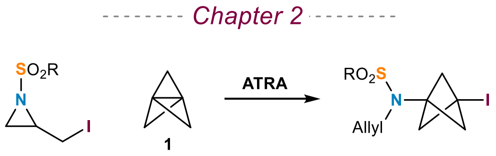


Figure 5.1: Synthesis of N,I BCPs through aziridine fragmentation.

Heteroatom-substituted BCP halides are significantly more challenging to functionalise than carbon-substituted BCPs, due to rapid retro-ATRA or anionic expulsion processes resulting in loss of the heteroatom substituent and reformation of [1.1.1]propellane **1**. To overcome this challenge, we developed a silyl-mediated photocatalysed Giese reaction to ffect the C–C bond formation of BCP iodides with a broad range of radical acceptors (Chapter 3, Figure 5.2). This methodology improves previous radical-based functionalisation of BCP halides, which typically require harmful UV radiation of toxic stannane reagents, and has received positive reviews on its applicability from our industrial collaborators. The functionalisation of BCP bromides, however, remains an unsolved challenge.

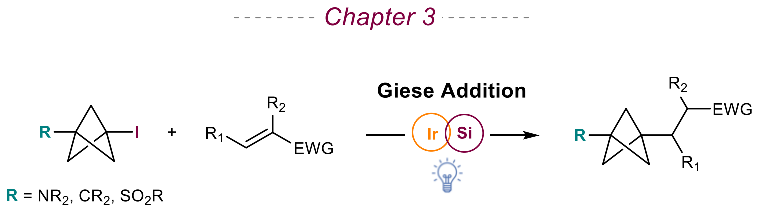


Figure 5.2: Giese functionalisation of BCP(A) halides.

Following an opportune discovery in our work on the fragmentation of α-iodoazirines, we developed a methodology to achieve sulfonyl BCP halides (Chapter 4, Figure 5.3). Sulfonyl BCP halides are limited to a couple of BCP chloride examples in the literature, and the synthesis of sulfonyl BCP bromides and iodides was unprecedented. The convenient and efficient method we developed for the *in situ* generation of sulfonyl halides has enhanced the generality of these reagents by tolerance of heteroaryl and alkyl substituents. Furthermore, we demonstrated the application of these reagents to pharmaceutical and agrochemical examples and the addition to other strained systems.

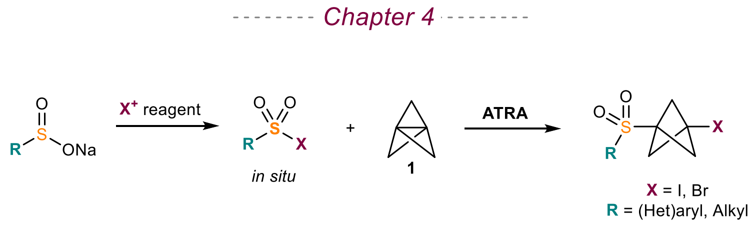


Figure 5.3: Sulfonyl halide reagents for the practical synthesis of sulfonyl BCP halides.

In combination, these methods have enabled the synthesis of heteroatom-difunctionalised bicyclo[1.1.1]pentanes, which have the potential to be applied as non-classical bioisosteres of *para*-substituted arenes, alkynes and *tert*-butyl groups.

5.2 Future Work

Since the beginning of this thesis work, the number of novel methods to synthesise *N*-substituted BCPs has increased dramatically, and this area of research has arguably become saturated. One of the most significant opportunities for further development lies in the modification of the Giese chemistry to include the functionalisation of BCP bromides (Figure 5.4, a). A second natural progression for the photocatalysed Giese reaction would be to re-visit metallaphotoredox methods to obtain cross-coupled products (Figure 5.4, b). The benefit of these improvements would be the tolerance of heteroatom-substituted BCPs by circumventing retro ATRA reactivity or rearrangements observed with lithiation or direct transition-metal catalysed processes.

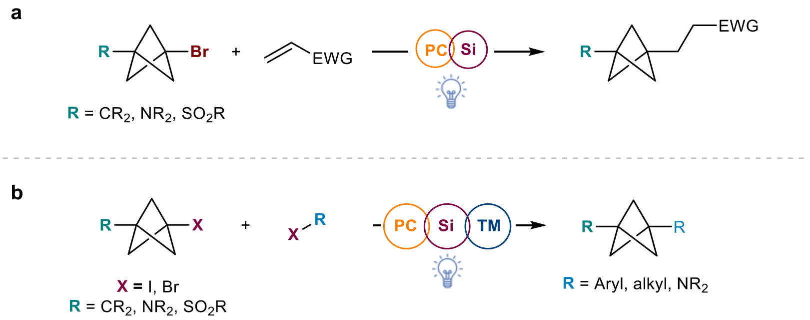


Figure 5.4: a. Radical functionalisation of BCP Bromides. b. Metallaphotoredox catalysed cross-coupling of BCP halides.

Finally, obtaining biological activity data and a survey of the pharmacokinetic properties of drug-like heteroatom-substituted BCP and BCHep derivatives, in comparison to their parent compounds, would provide evidence to support these motifs as bioisosteres. Ongoing work within our group is investigating the use of [3.1.1]propellane **30** as a convenient reagent to prepare *meta*-substituted arene bioisosteres, to great success

(Figure 5.5).[216] Including BCHep biological analogues would help establish the re-discovered reagent.

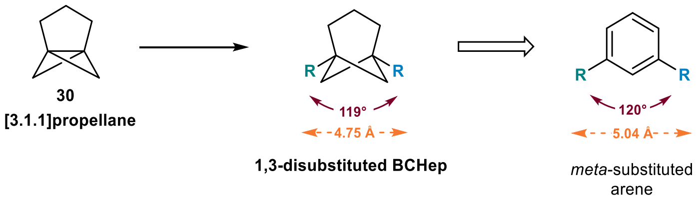


Figure 5.5: Reactivity of [3.1.1]propellane **30** *and its application as meta-substituted arene bioisosteres.*

Of particular interest would be targets containing sulfonyl (and sulfide) BCP or BCHep structures, as there is currently no biological or pharmacokinetic data avaliable for these motifs (Figure 5.6). The sulfonyl halide ATRA procedure developed in chapter 4 could be used to synthesise potential targets effectively. For example, a BCHep derivative of the *meta*-phenyl group in Lifitegrast, an active ingredient in eye drops, would be a compound of interest. Following the ATRA reaction of mesyl iodide with [3.1.1]propellane **30**, a subsequent Giese reaction with a dehydroanaline acceptor would provide access to the amide coupling partner of Lifitegrast. Building on our work towards the synthesis of the BCP derivatives of Cafenstrole **24a** and Sildenafil **24b**, if we could effect de-halogenation or radical trifluoromethylation, this would be a potential piperazine and mesityl surrogates for testing.[212] Additionally, a synthetic route to BCP-Eletriptan could be envisaged through S_N2 reaction of the BCP sulfinate salt obtained on a multigram scale by Bräse and co-workers.[172]

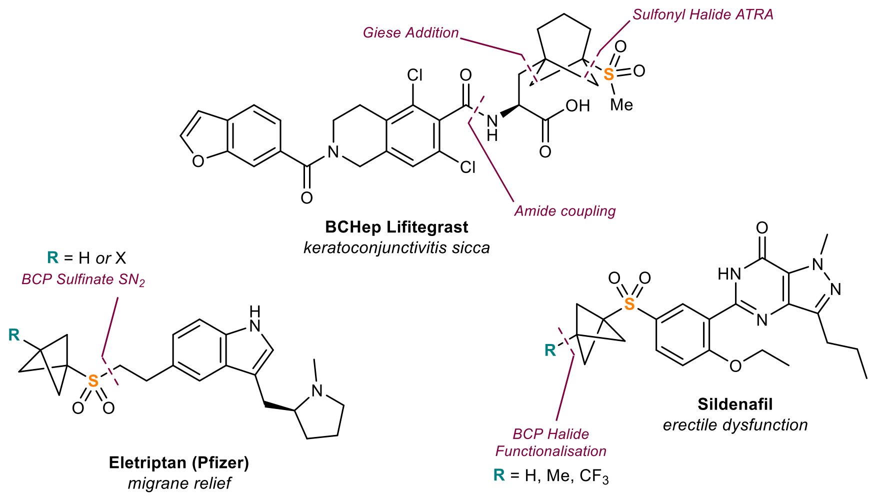


Figure 5.6: Potential BCP and BCPHep biological targets.

The interest in the synthesis and reactivity of propellanes and the bicyclic structures they can obtain is at an all-time high within chemical communities. The surge of novel methodologies in the last decade has led to a saturated field. Novel syntheses of heteroatom-substituted BCPs are still on the rise and, as a result, we can expect to see an increase in uptake of these compounds in the coming years.

6.

References

1. Sun, D.; Gao, W.; Hu, H.; Zhou, S., Why 90% of clinical drug development fails and how to improve it? *Acta. Pharm. Sin. B,* **2022**, *in press*, doi:10.1016/j.apsb.2022.1002.1002.

2. Sliwoski, G.; Kothiwale, S.; Meiler, J.; Lowe, E. W., Computational Methods in Drug Discovery. *Pharmacol. Rev.,* **2014**, *66*, 334-395.

3. Benet, L. Z.; Hosey, C. M.; Ursu, O.; Oprea, T. I., BDDCS, the Rule of 5 and drugability. *Adv. Drug Delivery Rev.,* **2016**, *101*, 89-98.

4. Doak, B. C.; Kihlberg, J., Drug discovery beyond the rule of 5 - Opportunities and challenges. *Expert Opinion on Drug Discovery,* **2017**, *12*, 115-119.

5. Brown, D. G.; Boström, J., Analysis of Past and Present Synthetic Methodologies on Medicinal Chemistry: Where Have All the New Reactions Gone? *J. Med. Chem.,* **2016**, *59*, 4443-4458.

6. Galloway, W. R. J. D.; Isidro-Llobet, A.; Spring, D. R., Diversity-oriented synthesis as a tool for the discovery of novel biologically active small molecules. *Nat. Commun.,* **2010**, *1*, 1-13.

7. Burger, A., Isosterism and bioisosterism in drug design. *Prog. Drug Res.,* **1991**, *37*, 287-371.

8. Meanwell, N. A., Improving Drug Design: An Update on Recent Applications of Efficiency Metrics, Strategies for Replacing Problematic Elements, and Compounds in Nontraditional Drug Space. *Chem. Res. Toxicol.,* **2016**, *29*, 564-616.

9. Mykhailiuk, P. K., Saturated bioisosteres of benzene: where to go next? *Org. Biomol. Chem.,* **2019**, *17*, 2839-2849.

10. Stepan, A. F.; Subramanyam, C.; Efremov, I. V.; Dutra, J. K.; O'Sullivan, T. J.*, et al.*, Application of the bicyclo[1.1.1]pentane motif as a nonclassical phenyl ring bioisostere in the design of a potent and orally active gamma-secretase inhibitor. *J. Med. Chem.,* **2012**, *55*, 3414-3434.

11. Meanwell, N. A., Synopsis of some recent tactical application of bioisosteres in drug design. *J. Med. Chem.,* **2011**, *54*, 2529-2591.

12. Smith, B. A useful overview of biososteres is avaliable as an online resource from the Baran Lab - Bioisosteres v2 - Recent Trends and Tactics, **2020**, https://baranlab.org/wp-content/uploads/2020/11/Bioisosteres-v2-Recent-Trends-and-Tacticsf.pdf.

13. Ballatore, C.; Huryn, D. M.; Smith, A. B., Carboxylic Acid (Bio)Isosteres in Drug Design. *ChemMedChem,* **2013**, *8*, 385-395.

14. Bull, J. A.; Croft, R. A.; Davis, O. A.; Doran, R.; Morgan, K. F., Oxetanes: Recent Advances in Synthesis, Reactivity, and Medicinal Chemistry. *Chem. Rev.,* **2016**, *116*, 12150-12233.

15. Reilly, S. W.; Puentes, L. N.; Wilson, K.; Hsieh, C.-J.; Weng, C.-C.; Makvandi, M.; Mach, R. H., Examination of Diazaspiro Cores as Piperazine Bioisosteres in the Olaparib Framework Shows Reduced DNA Damage and Cytotoxicity. *J. Med. Chem.,* **2018**, *61*, 5367-5379.

16. Singh, S. B.; Kaelin, D. E.; Wu, J.; Miesel, L.; Tan, C. M.*, et al.*, Oxabicyclooctane-Linked Novel Bacterial Topoisomerase Inhibitors as Broad Spectrum Antibacterial Agents. *ACS Med. Chem. Lett.,* **2014**, *5*, 609-614.

17. Subbaiah, M. A. M.; Meanwell, N. A., Bioisosteres of the Phenyl Ring: Recent Strategic Applications in Lead Optimization and Drug Design. *J. Med. Chem.,* **2021**, *64*, 14046-14128.

18. Measom, N. D.; Down, K. D.; Hirst, D. J.; Jamieson, C.; Manas, E. S.; Patel, V. K.; Somers, D. O., Investigation of a Bicyclo[1.1.1]pentane as a Phenyl Replacement within an LpPLA2 Inhibitor. *ACS Med. Chem. Lett.,* **2017**, *8*, 43-48.

19. Westphal, M. V.; Wolfstadter, B. T.; Plancher, J. M.; Gatfield, J.; Carreira, E. M., Evaluation of *tert*-butyl isosteres: case studies of physicochemical and pharmacokinetic properties, efficacies, and activities. *ChemMedChem,* **2015**, *10*, 461-469.

20. Makarov, I. S.; Brocklehurst, C. E.; Karaghiosoff, K.; Koch, G.; Knochel, P., Synthesis of Bicyclo[1.1.1]pentane Bioisosteres of Internal Alkynes and *para*-Disubstituted Benzenes from [1.1.1]Propellane. *Angew. Chem. Int. Ed.,* **2017**, *56*, 12774-12777.

21. Tse, E. G.; Houston, S. D.; Williams, C. M.; Savage, G. P.; Rendina, L. M.*, et al.*, Nonclassical Phenyl Bioisosteres as Effective Replacements in a Series of Novel Open-Source Antimalarials. *J. Med. Chem.,* **2020**, *63*, 11585-11601.

22. Lovering, F.; Bikker, J.; Humblet, C., Escape from flatland: increasing saturation as an approach to improving clinical success. *J. Med. Chem.,* **2009**, *52*, 6752-6756.

23. Mykhailiuk, P. K., Saturated Bioisosteres of Benzene: Where to go Next? *Organic & Biomolecular Chemistry,* **2019**, *17*, 2839-2849.

24. Levin, M. D.; Kaszynski, P.; Michl, J., Bicyclo[1.1.1]pentanes, [n]Staffanes, [1.1.1]Propellanes, and Tricyclo[2.1.0.0^{2,5}]pentanes. *Chem. Rev.,* **2000**, *100*, 169-234.

25. Locke, G. M.; Bernhard, S. S. R.; Senge, M. O., Nonconjugated Hydrocarbons as Rigid-Linear Motifs: Isosteres for Material Sciences and Bioorganic and Medicinal Chemistry. *Chem. Eur. J.,* **2019**, *25*, 4590-4647.

26. Kaleta, J.; Bastien, G.; Císařová, I.; Batail, P.; Michl, J., Molecular Rods: Facile Desymmetrization of 1,4-Diethynylbicyclo[2.2.2]octane. *Eur. J. Org. Chem.,* **2018**, *2018*, 5137-5142.

27. Dron, P. I.; Zhao, K.; Kaleta, J.; Shen, Y.; Wen, J.; Shoemaker, R. K.; Rogers, C. T.; Michl, J., Bulk Inclusions of Pyridazine-Based Molecular Rotors in Tris(*o*-phenylenedioxy)cyclotriphosphazene (TPP). *Adv. Funct. Mater.,* **2016**, *26*, 5718-5732.

28. De Meijere, A.; Messner, M.; Vill, V., Liquid Crystalline Bicyclo[1.1.1]pentane Derivatives. *Molecular Crystals and Liquid Crystals Science and Technology. Section A. Molecular Crystals and Liquid Crystals,* **2006**, *257*, 161-167.

29. De Meijere, A.; Zhao, L.; Belov, V. N.; Bossi, M.; Noltemeyer, M.; Hell, S. W., 1,3-bicyclo[1.1.1]pentanediyl: the shortest rigid linear connector of phenylated photochromic units and a 1,5-dimethoxy-9,10-di(phenylethynyl)anthracene fluorophore. *Chem. Eur. J.,* **2007**, *13*, 2503-2516.

30. Cotton, F. A.; Daniels, L. M.; Lin, C.; Murillo, C. A.; Yu, S.-Y., Supramolecular squares with Rh_2^{4+} corners. *J. Chem. Soc. Dalton Trans.,* **2001**, (*5)*, 502-504.

31. Wiberg, K. B.; Connor, D. S., Bicyclo[1.1.1]pentanes. *J. Am. Chem. Soc.,* **1966**, *88*, 4437-4441.

32. Meinwald, J.; Szkrybalo, W.; Dimmel, D. R., Bicyclo[1.1.1]pentane from mercury sensitized and unsensitized gas phase photolyses of bicyclo[2.1.1]hexan-2-one. *Tetrahedron Lett.,* **1967**, *8*, 731-733.

33. Srinivasan, R.; Carlough, K. H., Mercury($^3P_1$) photosensitized internal cycloaddition reactions in 1,4-, 1,5-, and 1,6-dienes. *J. Am. Chem. Soc.,* **1967**, *89*, 4932-4936.

34. Wiberg, K. B.; Lampman, G. M.; Ciula, R. P.; Connor, D. S.; Schertler, P.; Lavanish, J., Bicyclo[1.1.0]butane. *Tetrahedron,* **1965**, *21*, 2749-2769.

35. Wiberg, K. B.; Walker, F. H., [1.1.1]Propellane. *J. Am. Chem. Soc.,* **1982**, *104*, 5239-5240.

36. Pinchman, J. R.; Bunker, K. D.; Bio, M. M.; Breen, C.; Clausen, A. M.; Fang, Y.; Li, H.; Sheeran, J. W., Continuous flow processes for making bicyclic compounds, **2019**, WO 2019051038 A1.

37. Gianatassio, R.; Lopchuk, J. M.; Wang, J.; Pan, C.; Malins, L. R.*, et al.*, Strain-release amination. *Science,* **2016**, *351*, 241-246.

38. Belzner, J. G., Brigitte; Polborn, Kurt; Schmid, Wolfgang; Semmler, Klaus; Szeimies, Guenter, Syntheses of [1.1.1]propellanes. *Chem. Ber.,* **1989**, *122*, 1509-1529.

39. Wiberg, K. B.; Waddell, S. T., Formation and reactions of 1-lithiobicyclo[1.1.1]pentane. *Tetrahedron Lett.,* **1988**, *29*, 289-292.

40. Della, E. W.; Taylor, D. K.; Tsanaktsidis, J., Unusual bridgehead reactivity: Formation of [1.1.1]Propellane by 1,3-dehydrobromination of 1-bromobicyclo[1.1.1]Pentane. *Tetrahedron Lett.,* **1990**, *31*, 5219-5220.

41. Wiberg, K. B.; Mcmurdie, N., Formation and Reactions of Bicyclo[1.1.1]pentyl-1 Cations. *J. Am. Chem. Soc.,* **1994**, *116*, 11990-11998.

42. Hamrock, S. J.; Michl, J., 2,2-Dichloro[1.1.1]propellane. *J. Org. Chem.,* **1992**, *57*, 5027-5031.

43. Della, E. W.; Taylor, D. K., Synthesis of Some Bridgehead-Bridgehead-Disubstituted Bicyclo[1.1.1]pentanes. *J. Org. Chem.,* **1994**, *59*, 2986-2996.

44. Seiler, P., The Crystal Structure of [1.1.1]Propellane at 138 K. *Helv. Chim. Acta.,* **1990**, *73*, 1574-1585.

45. Hedberg, L.; Hedberg, K., The Molecular Structure of Gaseous [1.1.1]Propellane: An Electron-Diffraction Investigation. *J. Am. Chem. Soc.,* **1985**, *107*, 7257-7260.

46. Sterling, A. J.; Dürr, A. B.; Smith, R. C.; Anderson, E. A.; Duarte, F., Rationalizing the diverse reactivity of [1.1.1]propellane through σ–π-delocalization. *Chem. Sci.,* **2020**, *11*, 4895-4903.

47. Justin M. Lopchuk; Phil S. Baran; Helena D. Pickford; Bethany R. Shire; Anderson, E. A. [1.1.1]Propellane, *e-EROS*, **2020**, doi: 10.1002/047084289X.rn02055.pub2.

48. Wiberg, K. B.; Waddell, S. T.; Laidig, K., [1.1.1]propellane: reaction with free radicals. *Tetrahedron Lett.,* **1986**, *27*, 1553-1556.

49. Semmler, K.; Szeimies, G.; Belzner, J., Tetracyclo[5.1.0.0^{1,6}.0^{2,7}]octane, a [1.1.1]propellane derivative, and a new route to the parent hydrocarbon. *J. Am. Chem. Soc.,* **1985**, *107*, 6410-6411.

50. Bär, R. M.; Heinrich, G.; Nieger, M.; Fuhr, O.; Bräse, S., Insertion of [1.1.1]propellane into aromatic disulfides. *Beilstein J. Org. Chem.,* **2019**, *15*, 1172-1180.

51. Bär, R. M.; Kirschner, S.; Nieger, M.; Bräse, S., Alkyl and Aryl Thiol Addition to [1.1.1]Propellane: Scope and Limitations of a Fast Conjugation Reaction. *Eur. J. Org. Chem.,* 2018, *24*, 1373-1382.

52. Kaszynski, P.; Michl, J., A practical photochemical synthesis of bicyclo[1.1.1]pentane-1,3-dicarboxylic acid. *J. Org. Chem.,* 1988, *53*, 4593-4594.

53. Messner, M.; Kozhushkov, S. I.; De Meijere, A., Nickel- and Palladium-Catalyzed Cross-Coupling Reactions at the Bridgehead of Bicyclo[1.1.1]pentane Derivatives - A Convenient Access to Liquid Crystalline Compounds Containing Bicyclo[1.1.1]pentane Moieties. *Eur. J. Org. Chem.,* 2000, *2000*, 1137-1155.

54. Hughes, J. M. E.; Scarlata, D. A.; Chen, A. C.; Burch, J. D.; Gleason, J. L., Aminoalkylation of [1.1.1]Propellane Enables Direct Access to High-Value 3-Alkylbicyclo[1.1.1]pentan-1-amines. *Org. Lett.,* 2019, *21*, 6800-6804.

55. Belzner, J.; Szeimies, G., Thermal rearrangement of some [1.1.1]propellanes. *Tetrahedron Lett.,* 1986, *27*, 5839-5842.

56. Yu, S.; Noble, A.; Bedford, R. B.; Aggarwal, V. K., Methylenespiro[2.3]hexanes via Nickel-Catalyzed Cyclopropanations with [1.1.1]Propellane. *J. Am. Chem. Soc.,* 2019, *141*, 20325-20334.

57. Lasányi, D.; Tolnai, G. L., Copper-Catalyzed Ring Opening of [1.1.1]Propellane with Alkynes: Synthesis of Exocyclic Allenic Cyclobutanes. *Org. Lett.,* 2019, *21*, 10057-10062.

58. Sodano, T. M.; Combee, L. A.; Stephenson, C. R. J., Recent Advances and Outlook for the Isosteric Replacement of Anilines. *ACS Med. Chem. Lett.,* 2020, *11*, 1785-1788.

59. Amit S. Kalgutkar; Alfin D. N. Vaz; Mary E. Lame; Kirk R. Henne; John Soglia*, et al.*, Bioactivation of the nontricyclic antidepressant nefazodone to a reactive quinone-imine species in human liver microsomes and recombinant cytochrome P450. *Drug Metab. Dispo.,* 2005, *33*, 243-253.

60. Hughes, T. B.; Swamidass, S. J., Deep Learning to Predict the Formation of Quinone Species in Drug Metabolism. *Chem. Res. Toxicol.,* 2017, *30*, 642-656.

61. Naisbitt, D. J.; Williams, D. P.; O'Neill, P. M.; Maggs, J. L.; Willock, D. J.; Pirmohamed, M.; Park, B. K., Metabolism-Dependent Neutrophil Cytotoxicity of Amodiaquine: A Comparison with Pyronaridine and Related Antimalarial Drugs. *Chem. Res. Toxicol.,* 1998, *11*, 1586-1595.

62. Barnes-Seeman, D.; Jain, M.; Bell, L.; Ferreira, S.; Cohen, S.; Chen, X.-H.; Amin, J.; Snodgrass, B.; Hatsis, P., Metabolically Stable *tert*-Butyl Replacement. *ACS Med. Chem. Lett.,* 2013, *4*, 514-516.

63. Rogers, M.; Kirby, R.; Shomi, G.; Matsuo, T.; Kobayashi, S.; Kanazawa, J.; Yamaoka, N.; Torizuka, M.; Suzawa, K., Heterocyclic Sulfonamide Derivates and Pharmaceutical Uses Thereof, **2020**, WO 2020008206 A1.

64. Bunker, K. D.; Guo, C.; Grier, M. C.; Hopkins, C. D.; Pinchman, J. R.; Slee, D. H.; Huang, Q.; Kahraman, M., Bicyclic Compounds, **2016**, US 20160075654 A1.

65. Bartels, B.; Cook, X. A. F.; Ratni, H.; Reutlinger, M.; Vifian, W., Pyrimidine Derivatives, **2018**, WO 2019101984 A1.

66. Bartels, B.; Cook, X. A. F.; Ratni, H.; Reutlinger, M.; Vifian, W., Triazolo-Azepine Derivatives, **2018**, WO 2019121434 A1.

67. Kung, P.; Meng, J. J., 2-Amino Pyrimidine Compounds as Potent HSP-90 Inhibitors, **2009**, WO 2010018481 A1.

68. Carmela Sidrauski; Marina Pliushchev; Jennifer M. Frost; Black, L. A.; Xiangdong Xu*, et al.*, Modulators of the integrated stress pathway, **2017**, WO 2017193030 A1.

69. Mokrushina, G. A.; Charushin, V. N.; Chupakhin, O. N., Relationship between structure and antibacterial activity in the fluoroquinoloe series of compounds. *Pharma. Chem. J.,* **1995**, *29*, 590-606.

70. Barbachyn, M. R.; Hutchinson, D. K.; Toops, D. S.; Reid, R. J.; Zurenko, G. E.; Yagi, B. H.; Schaadt, R. D.; Allison, J. W., U-87947E, A Potent Quinolone Antibacterial Agent Incorporating a Bicyclo[1.1.1]pent-1yl (BCP) subunit. *Bioorg. Med. Chem. Lett.,* **1993**, *13*, 611-616.

71. Zhang, X.; Smith, R. T.; Le, C.; McCarver, S. J.; Shireman, B. T.; Carruthers, N. I.; MacMillan, D. W. C., Copper-mediated synthesis of drug-like bicyclopentanes. *Nature,* **2020**, *580*, 220-226.

72. Applequist, D. E.; Renken, T. L.; Wheeler, J. W., Polar substituent effects in 1,3-disubstituted bicyclo[1.1.1]pentanes. *J. Org. Chem.,* **1982**, *47*, 4985-4995.

73. Della, E. W.; Kasum, B.; Kirkbride, K. P., Properties of bridgehead-substituted polycycloalkanes. Synthesis and NMR analysis of nitrogen-15-labeled 1-aminobicycloalkanes and their hydrochlorides. *J. Am. Chem. Soc.,* **1987**, *109*, 2746-2749.

74. Hossain, M. T.; Timberlake, J. W., Synthesis of Bisbicyclo[1.1.1]pentyldiazene. The Smallest Bridgehead Diazene. *J. Org. Chem.,* **2001**, *66*, 6282-6285.

75. Pätzel, M.; Sanktjohanser, M.; Doss, A.; Henklein, P.; Szeimies, G., 3-Aminobicyclo[1.1.1]pentane-1-carboxylic Acid Derivatives: Synthesis and Incorporation into Peptides. *E. J. Org. Chem. ,* **2004**, *2004*, 493-498.

76. Bunker, K. D.; Sach, N. W.; Huang, Q.; Richardson, P. F., Scalable Synthesis of 1-Bicyclo[1.1.1]pentylamine via a Hydrohydrazination Reaction. *Org. Lett.,* **2011**, *13*, 4746-4748.

77. Goh, Y. L.; Tam, E. K. W.; Bernardo, P. H.; Cheong, C. B.; Johannes, C. W.; William, A. D.; Adsool, V. A., A New Route to Bicyclo[1.1.1]pentan-1-amine from 1-Azido-3-iodobicyclo[1.1.1]pentane. *Org. Lett.,* **2014**, *16*, 1884-1887.

78. Toops, D. S.; Barbachyn, M. R., Efficient Synthesis of 1-(Trialkylstannyl)- and 1-(Triarylstannyl) bicyclo[1.1.1]pentanes. *J. Org. Chem.,* **1993**, *58*, 6505-6508.

79. Beak, P.; Basha, A.; Kokko, B.; Loo, D., The geometry of displacements at nonstereogenic atoms: the formal displacement of alkoxide from alkoxyamines by organolithium reagents. *J. Am. Chem. Soc. ,* **1986**, *108*, 6016-6023.

80. Lopchuk, J. M.; Fjelbye, K.; Kawamata, Y.; Malins, L. R.; Pan, C. M.*, et al.*, Strain-Release Heteroatom Functionalization: Development, Scope, and Stereospecificity. *J. Am. Chem. Soc.,* **2017**, *139*, 3209-3226.

81. Kanazawa, J.; Maeda, K.; Uchiyama, M., Radical Multicomponent Carboamination of [1.1.1]Propellane. *J. Am. Chem. Soc.,* **2017**, *139*, 17791-17794.

82. Wiberg, K. B.; Waddell, S. T., Reactions of [1.1.1]Propellane. *J. Am. Chem. Soc.,* **1990**, *112*, 2194-2216.

83. Kim, J. H.; Ruffoni, A.; Al-Faiyz, Y. S. S.; Sheikh, N. S.; Leonori, D., Divergent Strain-Release Amino-Functionalization of [1.1.1]Propellane with Electrophilic Nitrogen-Radicals. *Angew. Chem. Int. Ed.,* **2020**, *59*, 8225-8231.

84. Shin, S.; Lee, S.; Choi, W.; Kim, N.; Hong, S., Visible-Light-Induced 1,3-Aminopyridylation of [1.1.1]Propellane wit *N*-Aminopyridinium Salts. *Angew. Chem. Int. Ed.,* **2021**, *60*, 7873-7879.

85. Caputo, D. F. J.; Arroniz, C.; Durr, A. B.; Mousseau, J. J.; Stepan, A. F.; Mansfield, S. J.; Anderson, E. A., Synthesis and applications of highly functionalized 1-halo-3-substituted bicyclo[1.1.1]pentanes. *Chem. Sci.,* **2018**, *9*, 5295-5300.

86. Nugent, J.; Arroniz, C.; Shire, B. R.; Sterling, A. J.; Pickford, H. D.*, et al.*, A General Route to Bicyclo[1.1.1]pentanes through Photoredox Catalysis. *ACS Catal.,* **2019**, *9*, 9568-9574.

87. Wong, M. L. J.; Sterling, A. J.; Mousseau, J. J.; Duarte, F.; Anderson, E. A., Direct catalytic asymmetric synthesis of α-chiral bicyclo[1.1.1]pentanes. *Nat. Commun.,* **2021**, *12,*

88. Nugent, J.; Sterling, A. J.; Frank, N.; Mousseau, J. J.; Anderson, E. A., Synthesis of alpha-Quaternary Bicyclo[1.1.1]pentanes through Synergistic Organophotoredox and Hydrogen Atom Transfer Catalysis. *Org. Lett.,* **2021**, *23*, 8628-8633.

89. Wiberg, K. B.; Mcmurdie, N., Formation of [1.1.1]propellane by nucleophilic attack on 1,3-diiodobicyclo[1.1.1]pentane. Unrearranged carbocation intermediates in the reaction of [1.1.1]propellane with electrophiles. *J. Am. Chem. Soc.,* **1991**, *113*, 8995-8996.

90. Hossain, M. T.; Timberlake, J. W., Rearrangements in the Reduction of 3-Iodobicyclo[1.1.1]pentyl Azide with Lithium Aluminum Hydride: Mechanistic Evidence of Intermediates. *J. Org. Chem.,* **2001**, *66*, 4409-4412.

91. Parsaee, F.; Senarathna, M. C.; Kannangara, P. B.; Alexander, S. N.; Arche, P. D. E.; Welin, E. R., Radical philicity and its role in selective organic transformations. *Nat. Rev. Chem.,* **2021**, *5*, 486-499.

92. Troll, T., 1-Iodo-n-Heteroatom-Functionalized Alkanes (n ≥2) with Both Functions Formed Simultaneously.1st ed., Sci. Synth., **2007**, *35*.

93. Kitagawa, O.; Miyaji, S.; Yamada, Y.; Fujiwara, H.; Taguchi, T., Iodine Atom Transfer [3 + 2] Cycloaddition Reaction with Electron-Rich Alkenes Using N-Tosyliodoaziridine Derivatives as Novel Azahomoallyl Radical Precursors. *J. Org. Chem.,* **2003**, *68*, 3184-3189.

94. Kitagawa, O.; Yamada, Y.; Fujiwara, H.; Taguchi, T., Iodoaziridine Derivatives as Novel Azahomoallyl Radical Precursors for [3+2] Cycloaddition Reactions with Alkenes. *Angew. Chem. Int. Ed.,* **2001**, *40*, 3865-3867.

95. Prier, C. K.; Rankic, D. A.; MacMillan, D. W., Visible light photoredox catalysis with transition metal complexes: applications in organic synthesis. *Chem. Rev.,* **2013**, *113*, 5322-5363.

96. Shaw, M. H.; Twilton, J.; Macmillan, D. W. C., Photoredox Catalysis in Organic Chemistry. *J. Org. Chem.,* **2016**, *81*, 6898-6926.

97. Romero, N. A.; Nicewicz, D. A., Organic Photoredox Catalysis. *Chem. Rev.,* **2016**, *116*, 10075-10166.

98. Strieth-Kalthoff, F.; Glorius, F., Triplet Energy Transfer Photocatalysis: Unlocking the Next Level. *Chem.,* **2020**, *6*, 1888-1903.

99. Strieth-Kalthoff, F.; James, M. J.; Teders, M.; Pitzer, L.; Glorius, F., Energy transfer catalysis mediated by visible light: principles, applications, directions. *Chem. Soc. Rev.,* **2018**, *47*, 7190-7202.

100. Kitagawa, O.; Suzuki, T.; Taguchi, T., NaH-mediated Iodoaziridination Reaction of N-Aliylic Tosylamides. *Tetrahedron Lett.,* **1997**, *38*, 8371-8374.

101. Morino, Y.; Hidaka, I.; Oderaotoshi, Y.; Komatsu, M.; Minakata, S., Electrophilic cyclization of N-alkenylamides using a chloramine-T/I_2 system. *Tetrahedron,* **2006**, *62*, 12247-12251.

102. Minakata, S.; Morino, Y.; Oderaotoshi, Y.; Komatsu, M., Practical and Convenient Synthesis of N-Heterocycles: Stereoselective Cyclization of N-Alkenylamides with *t*-BuOI under Neutral Conditions. *Org. Lett.,* **2006**, *8*, 3335-3337.

103. Welin, E. R.; Warkentin, A. A.; Conrad, J. C.; Macmillan, D. W. C., Enantioselective α-Alkylation of Aldehydes by Photoredox Organocatalysis: Rapid Access to Pharmacophore Fragments from β-Cyanoaldehydes. *Angew. Chem. Int. Ed.,* 2015, *54*, 9668-9672.

104. Aubineau, T.; Cossy, J., Chemoselective alkynylation of N-sulfonylamides versus amides and carbamates - synthesis of tetrahydropyrazines. *Chem. Commun.,* 2013, *49*, 3303-3305.

105. Johnson, J. A.; Petersen, B. M.; Kormos, A.; Echeverría, E.; Chen, Y.-S.; Zhang, J., A New Approach to Non-Coordinating Anions: Lewis Acid Enhancement of Porphyrin Metal Centers in a Zwitterionic Metal–Organic Framework. *J. Am. Chem. Soc.,* 2016, *138*, 10293-10298.

106. Vedejs, E.; Naidu, B. N.; Klapars, A.; Warner, D. L.; Li, V.-S.; Na, Y.; Kohn, H., Synthetic Enantiopure Aziridinomitosenes: Preparation, Reactivity, and DNA Alkylation Studies. *J. Am. Chem. Soc.,* 2003, *125*, 15796-15806.

107. Jeong, J. U.; Tao, B.; Sagasser, I.; Henniges, H.; Sharpless, K. B., Bromine-Catalyzed Aziridination of Olefins. A Rare Example of Atom-Transfer Redox Catalysis by a Main Group Element. *J. Am. Chem. Soc.,* 1998, *120*, 6844-6845.

108. Gensler, W. J., The Benzenesulfonyl Derivatives of 1-Amino-2,3-dibromopropane and 2-Amino-1,3-dibromopropane. *J. Am. Chem. Soc.,* 1948, *70*, 1843-1846.

109. Greene, A. E.; Le Drian, C.; Crabbe, P., Conversion of carbalkoxymethyl groups to.gamma.-oxocrotonate derivatives. *J. Org. Chem.,* 1980, *45*, 2713-2715.

110. Minakata, S.; Murakami, Y.; Tsuruoka, R.; Kitanaka, S.; Komatsu, M., Catalytic aziridination of electron-deficient olefins with an *N*-chloro-*N*-sodio carbamate and application of this novel method to asymmetric synthesis. *Chem. Commun.,* 2008, (*47)*, 6363-6365.

111. Ollivier, C.; Renaud, P., Organoboranes as a Source of Radicals. *Chem. Rev.,* 2001, *101*, 3415–3434.

112. Fodran, P.; Wallentin, C.-J., Harnessing Energy-Transfer in *N*-Centered Radical-Mediated Synthesis of Pyrrolidines. *Eur. J. Org. Chem.,* 2020, *2020*, 3213-3218.

113. Pickford, H. D.; Nugent, J.; Owen, B.; Mousseau, J. J.; Smith, R. C.; Anderson, E. A., Twofold Radical-Based Synthesis of *N*,*C*-Difunctionalized Bicyclo[1.1.1]pentanes. *J. Am. Chem. Soc.,* 2021, *143*, 9729-9736.

114. S. Livesley; A. J. Sterling; C. M. Robertson; W. R. F. Goundry; J. A. Morris; F. Duarte; Aissa, C., Electrophilic Activation of [1.1.1]Propellane for the Synthesis of Nitrogen-Substituted Bicyclo[1.1.1]pentanes. *Angew. Chem. Int. Ed.,* 2022, *61*, e202111291.

115. Nugent, J.; Shire, B.; Caputo, D.; Pickford, H.; Nightingale, F.; Houlsby, I.; Mousseau, J.; Anderson, E. A., Synthesis of All-carbon Disubstituted Bicyclo[1.1.1]pentanes by Iron-Catalyzed Kumada Cross-Coupling. *Angew. Chem. Int. Ed.,* 2020, *59*, 11866-11870.

116. Hazra, A.; Lee, M. T.; Chiu, J. F.; Lalic, G., Photoinduced Copper-Catalyzed Coupling of Terminal Alkynes and Alkyl Iodides. *Angew. Chem. Int. Ed.,* **2018**, *57*, 5492-5496.

117. Cao, H.; Jiang, H.; Feng, H.; Kwan, J. M. C.; Liu, X.; Wu, J., Photo-induced Decarboxylative Heck-Type Coupling of Unactivated Aliphatic Acids and Terminal Alkenes in the Absence of Sacrificial Hydrogen Acceptors. *J. Am. Chem. Soc.,* **2018**, *140*, 16360-16367.

118. Ni, S.; Garrido-Castro, A. F.; Merchant, R. R.; de Gruyter, J. N.; Schmitt, D. C.*, et al.*, A General Amino Acid Synthesis Enabled by Innate Radical Cross-Coupling. *Angew. Chem. Int. Ed.,* **2018**, *57*, 14560-14565.

119. Thirumoorthi, N. T.; Jia Shen, C.; Adsool, V. A., Expedient synthesis of 3-phenylbicyclo[1.1.1]pentan-1-amine via metal-free homolytic aromatic alkylation of benzene. *Chem. Commun.,* **2015**, *51*, 3139-3142.

120. Kanegusuku, A. L. G.; Roizen, J. L., Recent Advances in Photoredox-Mediated Radical Conjugate Addition Reactions: An Expanding Toolkit for the Giese Reaction. *Angew. Chem. Int. Ed.,* **2021**, *60*, 21116-21149.

121. Ye, S.; Xiang, T.; Li, X.; Wu, J., Metal-catalyzed radical-type transformation of unactivated alkyl halides with C–C bond formation under photoinduced conditions. *Org. Chem. Front.,* **2019**, *6*, 2183-2199.

122. Li, J.-S.; Wu, J., Recent Developments in the Photo-Mediated Generation of Silyl Radicals and Their Application in Organic Synthesis. *ChemPhotoChem,* **2018**, *2*, 839-846.

123. Le, C.; Chen, T. Q.; Liang, T.; Zhang, P.; MacMillan, D. W. C., A radical approach to the copper oxidative addition problem: Trifluoromethylation of bromoarenes. *Science,* **2018**, *360*, 1010–1014.

124. Kornfilt, D. J. P.; MacMillan, D. W. C., Copper-Catalyzed Trifluoromethylation of Alkyl Bromides. *J. Am. Chem. Soc.,* **2019**, *141*, 6853-6858.

125. Zhang, P.; Le, C. C.; MacMillan, D. W., Silyl Radical Activation of Alkyl Halides in Metallaphotoredox Catalysis: A Unique Pathway for Cross-Electrophile Coupling. *J. Am. Chem. Soc.,* **2016**, *138*, 8084-8087.

126. ElMarrouni, A.; Ritts, C. B.; Balsells, J., Silyl-mediated photoredox-catalyzed Giese reaction: addition of non-activated alkyl bromides. *Chem. Sci.,* **2018**, *9*, 6639-6646.

127. Perkins, J. J.; Schubert, J. W.; Streckfuss, E. C.; Balsells, J.; Elmarrouni, A., Photoredox Catalysis for Silyl-Mediated C-H Alkylation of Heterocycles with Non-Activated Alkyl Bromides. *E. J. Org. Chem.,* **2020**, *2020*, 1515-1522.

128. Dong, J.; Lyu, X.; Wang, Z.; Wang, X.; Song, H.; Liu, Y.; Wang, Q., Visible-light-mediated Minisci C-H alkylation of heteroarenes with unactivated alkyl halides using O2 as an oxidant. *Chem. Sci.,* **2019**, *10*, 976-982.

129. Lambert, J. B.; W. J. Schulz, J.; McConnell, J. A.; Schilfld, W., The First Silylenium Ions in Solution. *J. Am. Chem. Soc.,* **1988**, *110*, 2201-2210.

130. Kerr, J. A., Bond Dissociation Energies by Kinetic Methods. *Chem. Rev.,* **1966**, *66*, 465-500.

131. Chatgilialoglu, C.; Ferreri, C.; Landais, Y.; Timokhin, V. I., Thirty Years of $(TMS)_3SiH$: A Milestone in Radical-Based Synthetic Chemistry. *Chem. Rev.,* **2018**, *118*, 6516-6572.

132. Chatgilialoglu, C., Structural and Chemical Properties of Silyl Radicals. *Chem. Rev.,* **1995**, *95*, 1229-1251.

133. Chatgilialoglu, C., Organosilanes as radical based reducing agents in synthesis. *Acc. Chem. Res.,* **1992**, *25*, 188-194.

134. Chatgilialoglu, C., $(Me_3Si)_3SiH$: twenty years after its discovery as a radical-based reducing agent. *Chem. Eur. J. ,* **2008**, *14*, 2310-2320.

135. Iwamoto, T.; Okita, J.; Kabuto, C.; Kira, M., Sila-metalation Route to Hydrido(trialkylsilyl)silyllithiums. *J. Am. Chem. Soc.,* **2002**, *124*, 11604-11605.

136. Chatgilialoglu, C.; M.Guerra; Guerrini, A.; Seconi, G., A Study on the Reducing Abilities of Tris(alkylthio)silanes. *J. Org. Chem.,* **1992**, *57*, 2427-2433.

137. Chatgilialoglu, C.; Guerrini, A.; Lucarini, M., The Me_3Si Substituent Effect on the Reactivity of Silanes. Structural Correlations between Silyl Radicals and Their Parent Silanes. *J. Org. Chem.,* **1992**, *57*, 3405-3409.

138. Ballestri, M.; Chatgilialoglu, C.; Guerra, M.; Guerrini, A.; Lucarini, M.; Seconi, G., Organosilanes as radical-based reducing agents with low hydrogen donating abilities. *J. Chem. Soc. Perkin Trans.,* **1993**, *2*, 421-425.

139. Discekici, E. H.; Treat, N. J.; Poelma, S. O.; Mattson, K. M.; Hudson, Z. M.; Luo, Y.; Hawker, C. J.; Read de Alaniz, J., A highly reducing metal-free photoredox catalyst: design and application in radical dehalogenations. *Chem. Commun.,* **2015**, *51*, 11705-11708.

140. Nguyen, J. D.; D'Amato, E. M.; Narayanam, J. M.; Stephenson, C. R., Engaging unactivated alkyl, alkenyl and aryl iodides in visible-light-mediated free radical reactions. *Nat. Chem.,* **2012**, *4*, 854-859.

141. Adcock, W.; Clark, C. I.; Houmam, A.; Krstic, A. R.; Pinson, J.; Savéant, J.-M.; Taylor, D. K.; Taylor, J. F., Dissociative Electron Transfer to Dihaloalkanes. Electrochemical Reduction of 1,3-Dihaloadamantanes, l,4-Dihalobicyclo[2.2.2]octanes, and 1,3-Dihalobicyclo[1.1.1] pentanes. *J. Am. Chem. Soc.,* **1994**, *116*, 4653-4659.

142. DiRocco, D. Electrochemical Series of Photocatalysts and Common Organic Compounds, **2014**, https://macmillan.princeton.edu/wp-content/uploads/Merck-Photocatalysis-Chart.pdf.

143. Liu, H.; Ge, L.; Wang, D. X.; Chen, N.; Feng, C., Photoredox-Coupled F-Nucleophilic Addition: Allylation of gem-Difluoroalkenes. *Angew. Chem. Int. Ed.,* **2019**, *58*, 3918-3922.

144. Lucarini, M.; Marchesi, E.; Pedulli, G. F.; Chatgilialoglu, C., Homolytic Reactivity of Group 14 Organometallic Hydrides toward Nitroxides. *J. Org. Chem.,* **1998**, *63*, 1687-1693.

145. Nguyen, S. T.; Zhu, Q.; Knowles, R. R., PCET-Enabled Olefin Hydroamidation Reactions with N-Alkyl Amides. *ACS Catal.,* **2019**, *9*, 4502-4507.

146. Low temperature single crystal X-ray diffraction data were collected using a Rigaku Oxford SuperNova diffractometer. Raw frame data were reduced using CrysAlisPro and the structures were solved using 'Superflip' [L. Palatinus and G. Chapuis, J. Appl. Cryst., **2007**, *40*, 786-790. before refinement with CRYSTALS [(a) P. Parois, R.I. Cooper and A.L. Thompson Chem. Cent. J., 2015, 9:30. (b) R. I. Cooper, A. L. Thompson and D. J. Watkin, J. Appl. Cryst. **2010**, *43*, 1100-1107. Full refinement details are given in the Supporting Information.,

147. González-Esguevillas, M.; Fernández, D. F.; Rincón, J. A.; Barberis, M.; De Frutos, O.; Mateos, C.; García-Cerrada, S.; Agejas, J.; Macmillan, D. W. C., Rapid Optimization of Photoredox Reactions for Continuous-Flow Systems Using Microscale Batch Technology. *ACS Cent. Sci.,* **2021**, *7*, 1126-1134.

148. Fukuyama, T.; Kawamoto, T.; Kobayashi, M.; Ryu, I., Flow Giese reaction using cyanoborohydride as a radical mediator. *Beilstein J. Org. Chem.,* **2013**, *9*, 1791-1796.

149. M. S. Lowry; J. I. Goldsmith; J. D. Slinker; R. Rohl; R. A. Pascal, J.; G. G. Malliaras; Bernhard, S., Single-Layer Electroluminescent Devices and Photoinduced Hydrogen Production from an Ionic Iridium(III) Complex. *Chem. Mater.,* **2005**, *17*, 5712-5719.

150. The oxidation potential for $(Me_3Si)_3SiOH/(Me_3Si)_3SiOH^{\bullet+}$ has been measured at + 1.54 V vs SCE in MeCN. The silanolate ion is likely to be signifcantly lower; see reference 155.,

151. Zhu, J.; Cui, W. C.; Wang, S.; Yao, Z. J., Radical Hydrosilylation of Alkynes Catalyzed by Eosin Y and Thiol under Visible Light Irradiation. *Org. Lett.,* **2018**, *20*, 3174-3178.

152. D. A. Armstronga; R. E. Huie; S. Lymar; W. H. Koppenol; G. Merényi; P. Neta; D. M. Stanbury; Steenken, S.; Wardman, P., Standard electrode potentials involving radicals in aqueous solution: inorganic radicals. *BioInorg. React. Mech.,* **2013**, *9*, 59–61.

153. Meyer, A. U.; Jäger, S.; Prasad Hari, D.; König, B., Visible Light-Mediated Metal-Free Synthesis of Vinyl Sulfones from Aryl Sulfinates. *Adv. Synth. Catal.,* **2015**, *357*, 2050-2054.

154. Smith, R. T.; Zhang, X.; Rincon, J. A.; Agejas, J.; Mateos, C.; Barberis, M.; Garcia-Cerrada, S.; de Frutos, O.; MacMillan, D. W. C., Metallaphotoredox-Catalyzed Cross-Electrophile Csp^3-Csp^3 Coupling of Aliphatic Bromides. *J. Am. Chem. Soc.,* **2018**, *140*, 17433-17438.

155. Simov, V.; Kaplan, W. P.; Acton, J. J.; Ardolino, M. J.; Chen, J. L.*, et al.*, *N*-Heteroaryl Indazole Derivatives as LRRK2 Inhibitors, Pharmaceutical Compositions, and uses thereof. , **2020**, WO 2020092136 A1.

156. Chen, H.; Liu, Z.; Lv, Y.; Tan, X.; Shen, H.; Yu, H. Z.; Li, C., Selective Radical Fluorination of Tertiary Alkyl Halides at Room Temperature. *Angew. Chem. Int. Ed.,* **2017**, *56*, 15411-15415.

157. Moradei, S. M. L. d.; Therrien, E., Acyl inhibitors and uses thereof, **2019**, WO 2020097408 A1.

158. Mikagi, A.; Tokairin, D.; Usuki, T., Suzuki-Miyaura cross-coupling reaction of monohalopyridines and l-aspartic acid derivative. *Tetrahedron Lett.,* **2018**, *59*, 4602-4605.

159. Deforest, J. C.; Samame, R. A.; Suryn, G.; Burtea, A.; Rychnovsky, S. D., Second-Generation Synthesis of (+)-Fastigiatine Inspired by Conformational Studies. *J. Org. Chem.,* **2018**, *83*, 8914-8925.

160. Scott, K. A.; Njardarson, J. T., Analysis of US FDA-Approved Drugs Containing Sulfur Atoms. *Top. Curr. Chem.,* **2018**, *376*,

161. Devendar, P.; Yang, G.-F., Sulfur-Containing Agrochemicals. *Top. Curr. Chem.,* **2017**, *375*,

162. Liu, T.; Zhou, S.; Wang, S.; Zhang, M.; Xu, F.; Zhou, H.; Aguilar, A.; Huang, L., Preparation of piperidine derivatives as menin inhibitors and methods of use for treating cancer, **2021**, WO2021207310 A1.

163. Bunker, K. D.; Guo, C.; Grier, M. C.; Hopkins, C. D.; Pinchman, J. R.; Slee, D. H.; Huang, Q.; Kahraman, M., Preparation of bicyclic compounds as analgesics, **2015**, US 20160075654.

164. Bestvater, B. P.; Du, Z.; Farand, J.; Kaplan, J. A.; Tang, D. T.*, et al.*, Preparation of triazole compounds as LPA receptor antagonists useful in treatment of LPAR1-mediated diseases, **2021**, WO 2021247217 A1.

165. Ripenko, V.; Vysochyn, D.; Klymov, I.; Zhersh, S.; Mykhailiuk, P. K., Large-Scale Synthesis and Modifications of Bicyclo[1.1.1]pentane-1,3-dicarboxylic Acid (BCP). *J. Org. Chem.,* **2021**, *86*, 14061-14068.

166. Dilmac, A. M.; Spuling, E.; De Meijere, A.; Brase, S., Propellanes-From a Chemical Curiosity to "Explosive" Materials and Natural Products. *Angew. Chem. Int. Ed.,* **2017**, *56*, 5684-5718.

167. Kanazawa, J.; Uchiyama, M., Recent Advances in the Synthetic Chemistry of Bicyclo[1.1.1]pentane. *Synlett,* **2019**, *30*, 1-11.

168. He, F.-S.; Xie, S.; Yao, Y.; Wu, J., Recent advances in the applications of [1.1.1]-propellane in organic synthesis. *Chinese Chem. Lett.,* **2020**, *31*, 3065-3072.

169. Bunz, U.; Polborn, K.; Wagner, H. U.; Szeimies, G., Bridgehead-Coupled Bicyclo(1.1.1)pentanes: Synthesis and Structure. *Chem. Ber.,* **1988**, *121*, 1785-1790.

170. He, J.; Chen, G.; Zhang, B.; Li, Y.; Chen, J.-R.; Xiao, W.-J.; Liu, F.; Li, C., Catalytic Decarboxylative Radical Sulfonylation. *Chem.,* **2020**, *6*, 1149-1159.

171. Kokhan, S. O.; Valter, Y. B.; Tymtsunik, A. V.; Komarov, I. V.; Grygorenko, O. O., 3-Carboxy-3-Aminobicyclo[1.1.1]pentane-Derived Sulfonamides and Sulfonyl Fluorides - Advanced Bifunctional Reagents for Organic Synthesis and Drug Discovery. *Eur. J. Org. Chem.,* **2020**, *2020*, 2210-2216.

172. Bär, R. M.; Gross, P. J.; Nieger, M.; Bräse, S., Sodium Bicyclo[1.1.1]pentanesulfinate: A Bench-Stable Precursor for Bicyclo[1.1.1]pentylsulfones and Bicyclo-[1.1.1]pentanesulfonamides. *Eur. J. Org. Chem.,* **2020**, *26*, 4242-4245.

173. Liang, S.; Hofman, K.; Friedrich, M.; Manolikakes, G., Recent Advances in the Synthesis and Direct Application of Sulfinate Salts. *Eur. J. Org. Chem.,* **2020**, *2020*, 4664-4676.

174. Sadovaya, N. K.; Blokhin, A. V.; Surmina, L. S.; Tyurekhodzhaeva, M. A.; Koz'min, A. S.; Zefirov, N. S., Unusual reaction of [1.1.1]propellane with sulfonyl chlorides and sulfuryl chloride. *Russ. Chem. Bull.,* **1990**, *39*, 2451-2452.

175. Kaszynski, P.; McMurdie, N. D.; Michl, J., Synthesis of Doubly Bridgehead Substituted Bicyclo[1.1.1]pentanes. Radical Transformations of Bridgehead Halides and Carboxylic Acids. *J. Org. Chem.,* **1991**, *56*, 307-316.

176. Wu, Z.; Xu, Y.; Liu, J.; Wu, X.; Zhu, C., A practical access to fluoroalkylthio(seleno)-functionalized bicyclo[1.1.1]pentanes. *Sci. China Chem.,* **2020**, *63*, 1025–1029.

177. Wu, Z.; Xu, Y.; Wu, X.; Zhu, C., Synthesis of selenoether and thioether functionalized bicyclo[1.1.1]pentanes. *Tetrahedron,* **2020**, *76*, 131692.

178. Wei, Y.; Chen, Z.; Zhu, C.; Wu, Z.; Xu, Y.; Wu, X., Radical Carbosulfonylation of Propellane: Synthesis of Sulfonyl β-Keto-bicyclo[1,1,1]pentanes. *Synthesis,* **2021**, *53*, 3325-3332.

179. Wu, Z.; Xu, Y.; Zhang, H.; Wu, X.; Zhu, C., Radical-mediated sulfonyl alkynylation, allylation, and cyanation of propellane. *Chem. Commun.,* **2021**, *57*, 6066-6069.

180. Bertrand, M. P., Recent Progress in the use of Sulfonyl Radicals in Organic Syntheis. A Review. *Org. Prep. Proced. Int.,* **1994**, *26*, 257-290.

181. Nugent, J.; Arroniz, C.; Shire, B. R.; Sterling, A. J.; Pickford, H. D*., et al.*, A General Route to Bicyclo[1.1.1]pentanes through Photoredox Catalysis. **2019**,

182. Zeng, X.; Zhou, C., Iodosulfonylation of Alkynes under Ultrasound Irradiation. *Synthesis,* **2021**, *53*, 4614-4620.

183. Chen, R.; Xu, S.; Shen, F.; Xu, C.; Wang, K.; Wang, Z.; Liu, L., Facile Synthesis of Sulfonyl Chlorides/Bromides from Sulfonyl Hydrazides. *Molecules,* **2021**, *26*, 5551.

184. Poshkus, A. C.; Herweh, J. E.; Magnotta, F. A., The Synthesis of Aromatic Sulfonyl Bromides from Sulfonylhydrazides. *J. Org. Chem.,* **1963**, *28*, 2766-2769.

185. Silva-Cuevas, C.; Perez-Arrieta, C.; Polindara-García, L. A.; Lujan-Montelongo, J. A., Sulfonyl halide synthesis by thiol oxyhalogenation using NBS/NCS – *i*-PrOH. *Tetrahedron Lett.,* **2017**, *58*, 2244-2247.

186. Kirihara, M.; Odagiri, T.; Asawa, T., Method for the preparation of sulfonyl bromide compound, **2017**, JP2015-178765.

187. Sieber, G., Über die Spaltung von Tetrahydrofuran mit Methansulfobromid. *Justus Liebigs Ann. Chem.,* **1960**, *631*, 180-184.

188. Zhang, N.; Yang, D.; Wei, W.; Yuan, L.; Caob, Y.; Wang, H., Metal-free iodine-mediated synthesis of vinyl sulfones at room temperature using water as solvent. *RSC Adv.,* **2015**, *5*, 37013-37017.

189. Wolff, R. R.; Basava, V.; Giuliano, R. M.; Boyko, W. J.; Schauble, J. H., Iodosulfonation of alkenes with benzenesulfinic acid N-iodosuccinimide Facile preparation of α,β-unsaturated sulfones. *Can. J. Chem.,* **2006**, *84*, 667-675.

190. Katsuhiko, I.; Toshifumi, K.; Shin-ichi, S.; Hideki, K.; Hiroshi, K., Convenient Methods for the Preparation of Vinylic and Allylic Sulfones from Alkenes. *Chem. Lett.,* **1986**, *3*, 289-292.

191. Harwood, L. M.; Julia, M.; Thuillier, G. L., Organic synthesis with sulfones. XVII. The anti-Markovnikov halosulfonylation of olefins via an ionic path, and a new method of preparing benzensulfonyl iodide. *Tetrahedron,* **1980**, *36*, 2483-2487.

192. Truce, W. E.; Wolf, G. C., Adducts of sulfonyl iodides with acetylenes. *J. Org. Chem.,* **1971**, *36*, 1727-1732.

193. Liu, L. K.; Chi, Y.; Jen, K.-Y., Copper-catalyzed additions of sulfonyl iodides to simple and cyclic alkenes. *J. Org. Chem.,* **1980**, *45*, 406-410.

194. Lu, N.; Zhang, Z.; Ma, N.; Wu, C.; Zhang, G.; Liu, Q.; Liu, T., Copper-Catalyzed Difunctionalization of Allenes with Sulfonyl Iodides Leading to (*E*)-α-Iodomethyl Vinylsulfones. *Org. Lett.,* **2018**, *20*, 4318-4322.

195. Edwards, G. L.; Walker, K. A., para-toluenesulfonyl iodide as a convenient, mild reagent for the preparation of functionalised cyclic ethers. *Tetrahedron Lett.,* **1992**, *33*, 1779-1782.

196. Block, E.; Aslam, M., Organosulfur compounds in organic synthesis. 1. Bromomethanesulfonyl bromide in organic synthesis. Formation and base-induced reactions of alpha, beta.-unsaturated halomethyl sulfones. *J. Am. Chem. Soc.,* **1983**, *105*, 6164-6165.

197. Kang, S.-K.; Seo, H.-W.; Ha, Y.-H., Highly Regioselective and Stereoselective Radical Addition of *p*-TsBr to Substituted Terminal Allenes and Their Nucleophilic Substitutions: Synthesis of α,β-Unsaturated Sulfones. *Synthesis,* **2001**, *2001*, 1321-1326.

198. Wei, W.; Liu, X.; Yang, D.; Dong, R.; Cui, Y.; Yuan, F.; Wang, H., Direct difunctionalization of alkenes with sulfinic acids and NBS leading to β-bromo sulfones. *Tetrahedron Lett.,* **2015**, *56*, 1808-1811.

199. Nair, V.; Augustine, A.; Suja, T. D., CAN Mediated Reaction of Aryl Sulfinates with Alkenes and Alkynes: Synthesis of Vinyl Sulfones, β-Iodovinyl Sulfones and Acetylenic Sulfones. *Synthesis,* **2002**, *15*, 2259-2265.

200. Katrun, P.; Chiampanichayakul, S.; Korworapan, K.; Pohmakotr, M.; Reutrakul, V.; Jaipetch, T.; Kuhakarn, C., PhI$(OAc)_2$/KI-Mediated Reaction of Aryl Sulfinates with Alkenes, Alkynes, and α,β-Unsaturated Carbonyl Compounds: Synthesis of Vinyl Sulfones and β-Iodovinyl Sulfones. *Eur. J. Org. Chem.,* **2010**, *2010*, 5633-5641.

201. Lin, L.; Yang, Z.; Liu, J.; Wang, J.; Zheng, J.*, et al.*, Visible-light-induced surfactant-promoted sulfonylation of alkenes and alkynes with sulfonyl chloride by the formation of an EDA-complex with NaI in water at room temperature. *Green Chem.,* **2021**, *23*, 5467-5473.

202. Zheng, Y.; Qing, F.-L.; Huang, Y.; Xu, X.-H., Tunable and Practical Synthesis of Thiosulfonates and Disulfides from Sulfonyl Chlorides in the Presence of Tetrabutylammonium Iodide. *Adv. Synth. Catal.,* **2016**, *358*, 3477-3481.

203. Emmett, E. J.; Willis, M. C., The Development and Application of Sulfur Dioxide Surrogates in Synthetic Organic Chemistry. *Asian J. Org. Chem.,* **2015**, *4*, 602-611.

204. Li, Y.; Li, X.; Li, X.; Shi, D., Highly E-Selective Synthesis of α-Fluoro-β-arylalkenyl Sulfones from gem-Difluoroalkenes with Sodium Sulfinates. *J. Org. Chem.,* **2021**, *86*, 6983-6993.

205. Johnson, T. C.; Elbert, L., B.; Farley, A. J. M.; Gorman, T. W.; Genicot, C.*, et al.*, Direct sulfonylation of anilines mediated by visible light. *Chem. Sci.,* **2018**, *9*, 629-633.

206. Zálešák, F.; Kováč, O.; Lachetová, E.; Šť'Astná, N.; Pospíšil, J., Unified Approach to Benzo[*d*]thiazol-2-yl-Sulfonamides. *J. Am. Chem. Soc.,* **2021**, *86*, 11291-11309.

207. Gualandi, A.; Mazzarella, D.; Ortega-Martínez, A.; Mengozzi, L.; Calcinelli, F.*, et al.*, Photocatalytic Radical Alkylation of Electrophilic Olefins by Benzylic and Alkylic Zinc-Sulfinates. *ACS Catal.,* **2017**, *7*, 5357-5362.

208. Kim, D.-K.; Um, H.-S.; Park, H.; Kim, S.; Choi, J.; Lee, C., Silyloxymethanesulfinate as a sulfoxylate equivalent for the modular synthesis of sulfones and sulfonyl derivatives. *Chem. Sci.,* **2020**, *11*, 13071-13078.

209. Sigma-Aldrich, Diversinates™: Any-Stage Functionalization of (Hetero)aromatic Scaffolds, https://www.sigmaaldrich.com/GB/en/technical-documents/technical-article/chemistry-and-synthesis/ch-functionalization/baran-diversinates.

210. Nobusawa, T.; Okushima, Y.; Nagata, N.; Kojima, M.; Sakakibara, H.; Umeda, M., Synthesis of Very-Long-Chain Fatty Acids in the Epidermis Controls Plant Organ Growth by Restricting Cell Proliferation. *PLoS Biology,* **2013**, *11*, e1001531.

211. Mcconville, M.; Fernández, J.; Angulo-Barturen, Í.; Bahamontes-Rosa, N.; Ballell-Pages, L*., et al.*, Carbamoyl Triazoles, Known Serine Protease Inhibitors, Are a Potent New Class of Antimalarials. *J. Med. Chem.,* **2015**, *58*, 6448-6455.

212. Xiao, H.; Zhang, Z.; Fang, Y.; Zhu, L.; Li, C., Radical trifluoromethylation. *Chem. Soc. Rev.,* **2021**, *50*, 6308-6319.

213. Flores Toque, H. A.; Priviero, F. B. M.; Teixeira, C. E.; Perissutti, E.; Fiorino, F*., et al.*, Synthesis and Pharmacological Evaluations of Sildenafil Analogues for Treatment of Erectile Dysfunction. *J. Med. Chem.,* **2008**, *51*, 2807-2815.

214. Song, L.; Zhang, L.; Luo, S.; Cheng, J.-P., Visible-Light Promoted Catalyst-Free Imidation of Arenes and Heteroarenes. *Chem. Eur. J.,* **2014**, *20*, 14231-14234.

215. ACS Green Chemistry, Iodination Venn-Diagram, https://reagents.acsgcipr.org/reagent-guides/iodination/venn-diagram.

216. Frank, N.; Nugent, J.; Shire, B.; Pickford, H.;. Rabe. P.; Sterling, A.; Zarganes-Tzitzikas, T.; Grimes, T.; Thompson, A.; Smith, R.; Schofield, C.; Brennan, P.; Duarte, F.; Anderson, E. Synthesis of meta-substituted arene bioisosteres from [3.1.1]propellane, *pre-print*, **2022**, 10.26434/chemrxiv-2022-6k9sl.

217. Silvi, M.; Aggarwal, V. K., Radical Addition to Strained σ-Bonds Enables the Stereocontrolled Synthesis of Cyclobutyl Boronic Esters. *J. Am. Chem. Soc.,* **2019**, *141*, 9511-9515.

218. Pratt, C. J.; Aycock, R. A.; King, M. D.; Jui, N. T., Radical α-C–H Cyclobutylation of Aniline Derivatives. *Synlett,* **2020**, *31*, 51-54.

219. Ernouf, G.; Chirkin, E.; Rhyman, L.; Ramasami, P.; Cintrat, J. C., Photochemical Strain-Release-Driven Cyclobutylation of C(sp^3)-Centered Radicals. *Angew. Chem. Int. Ed.,* **2020**, *59*, 2618-2622.

220. Wu, X.; Hao, W.; Ye, K.-Y.; Jiang, B.; Pombar, G.; Song, Z.; Lin, S., Ti-Catalyzed Radical Alkylation of Secondary and Tertiary Alkyl Chlorides Using Michael Acceptors. *J. Am. Chem. Soc.,* **2018**, *140*, 14836-14843.

221. Mcnamee, R. E.; Haugland, M. M.; Nugent, J.; Chan, R.; Christensen, K. E.; Anderson, E. A., Synthesis of 1,3-disubstituted bicyclo[1.1.0]butanes *via* directed bridgehead functionalization. *Chem. Sci.,* **2021**, *12*, 7480-7485.

222. Jung, M.; Lindsay, V. N. G., One-Pot Synthesis of Strain-Release Reagents from Methyl Sulfones. *J. Am. Chem. Soc.,* **2022**, *144*, 4764-4769.

223. Kawaguchi, S.-I.; Ogawa, A., Highly Selective Hydroiodation of Alkynes Using an Iodine−Hydrophosphine Binary System. *Org. Lett.,* 2010, *12*, 1893-1895.

224. Andresini, M.; Degennaro, L.; Luisi, R., The renaissance of strained 1-azabicyclo[1.1.0]butanes as useful reagents for the synthesis of functionalized azetidines. *Org. Biomol. Chem.,* 2020, *18*, 5798-5810.

225. Siemeister, G.; Lucking, U.; Wengner, A. M.; Lienau, P.; Steinke, W.; Schatz, C.; Mumberg, D.; Ziegelbauer, K., BAY 1000394, a novel cyclin-dependent kinase inhibitor, with potent antitumor activity in mono- and in combination treatment upon oral application. *Mol. Cancer. Ther.,* 2012, *11*, 2265-2273.

226. Bär, R. M.; Langer, L.; Nieger, M.; Bräse, S., Bicyclo[1.1.1]pentyl Sulfoximines: Synthesis and Functionalizations. *Adv. Synth. Catal.,* 2020, *362*, 1356-1361.

227. Harmata, M., 4-Methyl-*N*-phenylbenzene Sulfonimidoyl Chloride. *EROS,* 2003, doi: 10.1002/047084289x.rn00015.

S.

Supporting Information

S1.

General Experimental Details

S1.1 Experimental Considerations

NMR Spectroscopy

^{1}H, ^{13}C, ^{19}F, ^{29}Si and ^{31}P NMR spectra were recorded on Bruker AV400 or Bruker AVII500 spectrometers using TOPSPIN software, with the deuterated solvent acting as the internal deuterium lock. ^{1}H NMR spectra were recorded at 400, 500 or 600 MHz, ^{13}C NMR spectra were recorded at 101 or 126 MHz with ^{1}H decoupling, and ^{19}F NMR spectra were recorded at 376 or 470 MHz. Assignments were determined either on the basis of unambiguous chemical shift/coupling patterns, or from 2D COSY, HMBC, HSQC and/or NOESY experiments. Peak multiplicities are defined as: s = singlet, d = doublet, t = triplet, q = quartet, quin. = quintet, hept. = septet, m = multiplet, br. = broad, app. = apparent, obsc. = obscured. Coupling constants (*J*) are reported to the nearest 0.1 Hz. ^{1}H NMR yields were calculated using mesitylene as an internal standard.

Infrared Spectroscopy

Infrared spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer with the sample being prepared as a thin film on a diamond ATR module. Absorption maxima (ν_{max}) are quoted in wavenumbers (cm^{-1}).

Mass Spectrometry

Low resolution mass spectra were recorded on a Micromass LCT Premier Open Access using electrospray ionization (ESI). High resolution mass spectra (HRMS) was determined under conditions of ESI, EI and CI on a Bruker MicroTOF. High resolution values are calculated to 4 decimal places from the molecular formula, and all values are within a tolerance of 5 ppm.

Melting Points

Melting points were obtained using a Griffin melting point apparatus and are uncorrected.

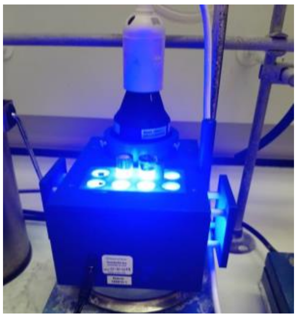
Reagents, solvents and techniques

All reagents were used directly as supplied. Solvents were either used as commercially supplied, or as purified by standard techniques. Anhydrous Et_2O, MeCN, CH_2Cl_2, THF, DMF and toluene were obtained from solvent dispenser units having been passed through an activated alumina column under argon. Unless otherwise stated, non-aqueous reactions were performed using flame-dried glassware under Nitrogen atmosphere.

Reactions were monitored by thin layer chromatography (TLC) on pre-coated aluminium-backed plates (Merck Kieselgel 60 with fluorescent indicator (UV254). Spots were visualized by quenching of UV fluorescence or by staining with potassium permanganate, vanillin, ninhydrin and PMA. Retention factors are reported with the solvent system. Column chromatography was performed on silica gel obtained from Merck (Silica gel Si 60, 0.040-0.063 mm) under a positive pressure of Nitrogen, using the stated solvent system.

Photochemical Equipment and Setup

The Blue LED lamps used for this work were either:

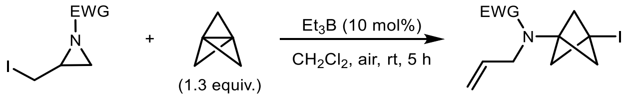
Set-up 1	Evoluchem™ 455 nm 18 W LED or Kessil PR160L 456 nm placed in an Evoluchem™ PhotoRedOx box. Set up used for all Giese reaction optimisation and scope examples.	
Set-up 2	Tingkam® Waterproof 5M 5050 SMD RGB Led Strips fixed to the inside of a crystallisation dish (left). Set up used in optimisation.	
Set-up 3	50 W Kessil PR160L 456 nm was clamped 5 cm from a vial, cooled with desk fan from above. A polystyrene box lined with foil was used to shield the light. Set up used for 1.0 mmol scale reaction.	

S2.

Chapter 2 Experimental Data

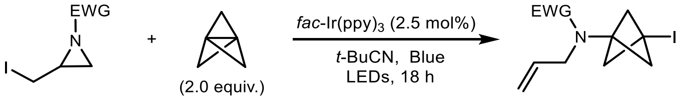
S2.1 General Experimental Procedures

General Procedure 1 - Et_3B initiated ATRA synthesis of BCPA iodides



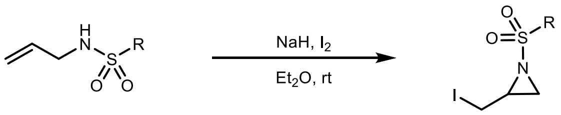
A flame dried vial was charged with α-iodoaziridine (1.0 equiv.) and sealed with a septum under air. The α-iodoaziridine was dissolved in CH_2Cl_2 (0.10 M, from solvent Winchester) and then [1.1.1]propellane **1** (0.60 – 1.00 M in Et_2O, 1.3 equiv.) was added. Et_3B (1.0 M in hexanes, 10 mol%) was added in one portion with the syringe needle tip in the solution, followed by syringes of air (100 µL × 2) directly into the solution. The vial was capped and sealed with parafilm and stirred vigorously at room temperature for 5 h protected from light. The reaction mixture was concentrated *in vacuo* and purified by column chromatography in the specified eluent system to afford the desired BCPA iodide.

General Procedure 12 - Photoredox initiated ATRA synthesis of BCPA iodides



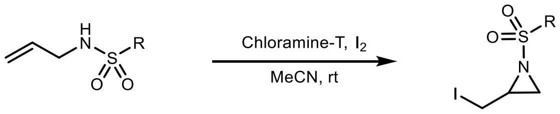
A flame dried vial was charged with α-iodoaziridine (1.0 equiv.) and *fac*-Ir(ppy)$_3$ (2.5 mol%). The vial was then equipped with a PTFE septum, evacuated and placed under an Ar atmosphere. *t*-BuCN (0.10 M) and [1.1.1]propellane **1** (0.60 – 0.85 M in E_2O, 2.0 equiv.) were added sequentially. The solution was degassed by freeze-pump-thaw cycles (× 3), vacuum was only applied while the reaction was frozen due to volatility of [1.1.1]propellane **1**), and then the mixture was irradiated with blue LEDs for 18 h (**set-up 1**). The reaction mixture was concentrated *in vacuo* and purified by column chromatography in the specified eluent system to afford the desired BCPA iodide.

General Procedure 3 – Iodoaziridination with NaH and Iodine



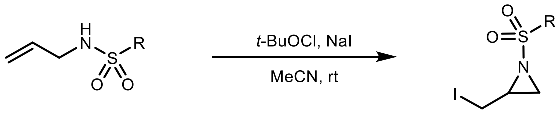
According to a modified literature procedure.[1] NaH (1.1 – 1.2 equiv.) was added portionwise to a solution of *N*-allyl-sulfonamide (1.0 equiv.) in anhydrous Et_2O (0.2 M) at room temperature. The mixture was stirred for 20 min and then iodine (3.0 equiv.) was added and stirring was continued for the specified duration protected from light. The mixture was poured into $Na_2S_2O_3$ (sat. aq.) and extracted with EtOAc (× 3), washed with brine, dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography in the specified eluent system gave the desired α-iodoaziridine.

General Procedure 4 – Iodoaziridination with Chloramine-T and Iodine



According to a modified literature procedure.[2] To a flame dried flask under Ar and protected from light was added *N*-allyl sulfonamide (1.0 equiv.) in anhydrous MeCN (0.17 M). Chloramine-T.3H_2O (1.0 equiv.) and iodine (1.0 equiv.) were added sequentially and the reaction mixture was stirred at room temperature, protected from light, for the specified duration. The reaction was quenched by addition of $Na_2S_2O_3$ (sat. aq.) and extracted with EtOAc (× 3). The combined organic phases were washed with brine, dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography in the specified eluent system gave the desired α-iodoaziridine.

General Procedure 5 – Iodoaziridination with *t*-BuOCl and NaI



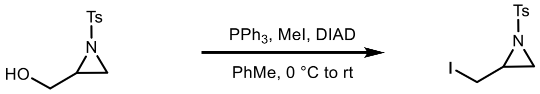
According to a modified literature procedure.[3] To a flame dried flask under Ar and protected from light was added *N*-allyl sulfonamide (1.0 equiv.) in anhydrous MeCN (0.17 M). NaI (1.2 equiv.) and *t*-BuOCl (1.2 equiv.) were then added sequentially and the reaction mixture was stirred at room temperature for the specified duration. The reaction mixture was quenched by addition of $Na_2S_2O_3$ (sat. aq.) and extracted with EtOAc (× 3). The combined organic phases were washed with brine, dried (Mg_2SO_4), filtered and concentrated *in vacuo*, shielded from light. Purification by column chromatography in the specified eluent system gave the desired α-iodoaziridine.

t-Butyl hypochlorite, t-BuOCl:

According to a modified literature procedure.[4, 5] NaOCl.5H_2O (8.93 g, 0.12 mol) was dissolved in H_2O (150 mL, 0.8 M) in a 1 L round bottom flask and then cooled to 0 °C. A mixture of *tert*-butyl alcohol (11.1 mL, 0.12 mol) and acetic acid (7.3 mL, 0.12 mol) was added in one portion to the bleach solution and stirred vigorously for 5 min. The biphasic mixture was separated and the yellow organic layer was washed with Na_2CO_3 (10% aq., 50 mL), H_2O (50 mL), and then dried (Na_2SO_4) and filtered. *t*-Butyl hypochlorite was obtained as a yellow liquid and was used without further purification.

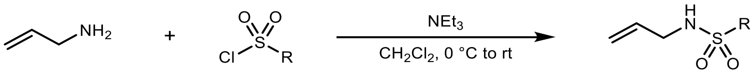
Note: t-Butyl hypochlorite was stored over Na_2SO_4 in an amber vial in the freezer for 3 weeks.

General Procedure 6 – Iodination of Aziridine alcohols with PPh_3, DIAD and MeI



According to a modified literature procedure.[6] To a flame dried flask under Ar and protected from light was added PPh_3 (1.2 equiv.) and anhydrous toluene (0.18 M). The solution was cooled to 0 °C and di-isopropylazodicarboxylate (DIAD) (1.2 equiv.) was added slowly. A solution of aziridinyl alcohol (1.0 equiv.) in anhydrous toluene (0.15 M) was then added to the mixture, followed by dropwise addition of MeI (1.2 equiv.). The reaction mixture was stirred at room temperature for 16 h, then quenched by addition of $Na_2S_2O_3$ (sat. aq.). The aqueous phase was extracted with EtOAc (× 3), then the combined organic phases were washed with brine, dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography in the specified eluent system gave the desired α-iodoaziridine.

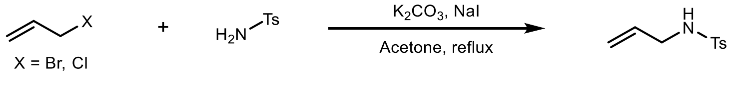
General Procedure 7 – Sulfonylation of *N*-allyl amines



A: *According to a modified literature procedure.*[7] NEt_3 (2.0 equiv.) was added to a solution of *N*-allyl amine (1.5 equiv.) in CH_2Cl_2 (0.2 M) at 0 °C. The sulfonyl chloride (1.0 equiv.) was added portionwise and the mixture was stirred for the specified duration at room temperature. The reaction mixture was poured onto HCl (1 N aq.) and extracted with CH_2Cl_2 (× 3). The combined organic phases were then washed with H_2O, brine, then dried (Mg_2SO_4), filtered and concentrated *in vacuo* to give the *N*-allyl sulfonamide. No further purification was required unless specified.

B: *According to a modified literature procedure.*[8] NEt_3 (1.0 – 1.1 equiv.) was added to a solution of *N*-allyl amine (1.1 equiv.) in CH_2Cl_2 (1.2 M) at 0 °C. The sulfonyl chloride (1.0 equiv.) was added portionwise and the mixture was stirred for the specified duration at room temperature. The mixture was then poured into $NaHCO_3$ (sat. aq.) and extracted with CH_2Cl_2 (× 3). The combined organic phases were washed with brine, dried (Mg_2SO_4), filtered and concentrated *in vacuo* to give the *N*-allyl-sulfonamide. No further purification was required unless specified.

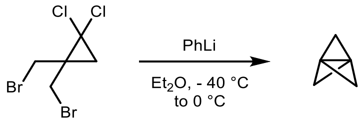
General Procedure 8 – *N*-Alkylation of Sulfonamides



According to a modified literature procedure.[9] *p*-Toluenesulfonamide (1.1 – 2.0 equiv.), K_2CO_3 (1.1 – 2.0 equiv.) and KI/NaI (if added, 10 mol%) were dissolved in reagent grade acetone (1.0 M). The alkyl halide (1.0 equiv.) was added and the reaction mixture was heated to reflux for the specified duration. The reaction mixture was cooled, then poured onto H_2O and extracted with EtOAc (× 3). The combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography in the specified eluent system gave the desired *N*-allyl sulfonamide.

S2.2 BCPA Iodides

Tricyclo[1.1.1.0^{1,3}]pentane, [1.1.1]propellane, 1



According to a modified literature procedure.[10] PhLi (1.9 M in Bu$_2$O, 100 mL, 190 mmol) was added to a solution of 1,1-dibromo – 2,2-bis(chloromethyl)-cyclopropane (28.2 g, 95.0 mmol) in Et$_2$O (60 mL, 3.2 M) in a 500 mL flask at –40 °C. The mixture was then stirred at 0 °C for 2 h to give a yellow/brown suspension. A rotary evaporator was cleaned with acetone and Et$_2$O, then dried under vacuum and flushed with Ar (× 3). The reaction mixture was distilled under reduced pressure using the rotary evaporator, maintaining a steady drip of [1.1.1]propellane solution (water bath 25 °C, condenser and trap –78 °C, 200 mbar → 50 mbar). Once the distillation was complete, the system was flushed with Ar and the distilled solution was transferred to a flame dried AcroSeal™ bottle with septum under Ar at –78 °C. The remaining residue was quenched with MeOH/acetone.

Total Volume = 62.0 mL (0.85 M in Et$_2$O), 56% yield.

The concentration of [1.1.1]propellane solution varied between 0.60 M and 1.00 M.

^{1}H NMR (400 MHz, CDCl$_3$) δ 1.94 (6H, s).

Spectroscopic data in agreement with that reported previously.[11]

Concentration and yield: Determined by ^{1}H NMR spectroscopy using a sample of stock solution (200 µL), DCE (50 µL) and CDCl$_3$ in NMR tube. An average NMR integral ratio of three samples was used.

2.47 (DCE, 3.7 ppm, 4H) : 1.00 ([1.1.1]propellane, 1.94 ppm, 6H)

(2.47/4) : (1.00/6) = 0.616 : 0.167

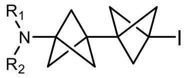
(50 µL x 1.253 g mL^{-1})/98.96 mg mol^{-1} = 0.63 mmol

(0.63 mmol/(0.616/0.167))/0.2 mL = 0.85 M

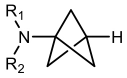
(0.85 M × 66.05 g mol^{-1} × 62.0 mL)/1000 = 3.48 g

(3.48 g/6.27 g) × 100 = 56% yield

Staffane 3-S and H-atom transfer 3-H impurities



3-S

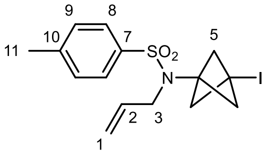


3-H

≥ 20:1 in 89% of examples

BCPA Iodides were isolated with small amounts of the corresponding staffane **3-S** and H-atom abstraction **3-H** impurities. The ratio of these impurities are calculated from ^{1}H NMR integrals and is reported with each compound where the ratio is <20:1. The characteristic ^{1}H NMR peaks of these impurites are also reported. Isolated yields are uncorrected for these impurities. The ratios of **3**:**3-S** and **3**:**3-H** are ≥20:1 in 25/28 examples. The three examples where these impurities are <20:1 is when a higher proportion of **1** was required to achieve better conversion of α-iodoaziridine.

N-Allyl-*N*-(6-iodobicyclo[1.1.1]pentan-4-yl)-*N*-methylbenzenesulfonamide, 3a



α-Iodoaziridine **2a** (51 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9) gave BCPA iodide **3a** (46 mg, 0.11 mmol, 75%) as a colourless oil. Recrystallization from Et_2O/pentane gave the BCPA iodide as a white crystalline solid.

Multigram scale *(note: 1.1 equiv. of* ***1****)*: α-Iodoaziridine **2a** (2.19 g, 6.50 mmol), [1.1.1]propellane **1** (0.61 M in Et_2O, 11.7 mL, 7.15 mmol), Et_3B (1.0 M in hexanes, 6.50 mL, 10 mol%) in CH_2Cl_2 (6.50 mL) was subjected to **general procedure 1** in a 50 mL flame-dried round bottomed flask. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9) gave BCPA iodide **3a** (1.76 g, 4.36 mmol, 67%) as a colourless oil.

R_f 0.41 (Et_2O/pentane, 1:4) [UV, vanillin].

m.p. 67 – 71 °C.

IR ν_{max}/cm^{-1} (film) 2920, 1345, 1195, 1158, 1090, 877, 831, 812, 660.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.65 (2H, m, H8), 7.31 – 7.28 (2H, m, H9), 5.79 (1H, ddt, *J* = 17.1, 10.2, 5.7 Hz, H2), 5.23 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.16 (H, app. dq, *J* = 10.2, 1.4 Hz, H1), 3.89 (2H, app. dt, *J* = 5.7, 1.6 Hz, H3), 2.43 (3H, s, H11), 2.40 (6H, s, H5).

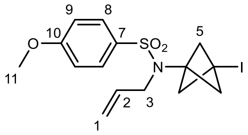
^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8, 137.9, 134.7, 129.9, 127.3, 117.8, 62.2, 56.1, 50.5, 21.7, –0.1.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{15}H_{18}O_2NINaS$ requires 425.9995; found 425.9992.

Characteristic data for staffane **3a-S** *and H-atom abstraction product* **3a-H***:*

^{1}H NMR (400 MHz, CDCl$_3$) δ 2.13 (6H, s, **3a-S**), 1.96 (6H, s, **3a-H**), 1.82 (6H, s, **3a-S**).

N-Allyl-*N*-(6-iodobicyclo[1.1.1]pentan-4-yl)-*p*-methoxybenzenesulfonamide, 3b



α-Iodoaziridine **2b** (53 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et$_2$O, 0.24 mL, 0.20 mmol), Et$_3$B (1.0 M in hexanes, 15 µL, 10 mol%) in CH$_2$Cl$_2$ (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO$_2$, Et$_2$O/pentane, 1:9 → 1:4) gave BCPA iodide **3b** (44 mg, 0.10 mmol, 69%) as a colourless oil.

0.45 mmol scale: α-Iodoaziridine **2b** (159 mg, 0.45 mmol), [1.1.1]propellane **1** (0.70 M in Et$_2$O, 0.84 mL, 0.59 mmol), Et$_3$B (1.0 M in hexanes, 45 µL, 10 mol%) in CH$_2$Cl$_2$ (0.45 mL) was subjected to **general procedure 1** in a 10 mL vial. Purification by column chromatography (SiO$_2$, Et$_2$O/pentane, 1:9 → 1:4) gave BCPA iodide **3b** (127 mg, 0.30 mmol, 67%) as a colourless oil. The product was isolated as an inseparable mixture of **3b**:**3b-S**:**3b-H**, 1:0.04:0.09 as determined by ^{1}H NMR spectroscopy.

R$_f$ 0.27 (Et$_2$O/pentane, 1:4) [UV, vanillin].

IR ν_{max}/cm^{-1} (film) 1579, 1497, 1343, 1257, 1194, 1153, 1091, 1022, 876, 827.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.74 – 7.70 (2H, m, H8), 6.99 – 6.94 (2H, m, H7), 5.79 (1H, ddt, *J* = 17.2, 10.2, 5.7 Hz, H2), 5.23 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.16 (1H, app. dq, *J* = 10.2, 1.5 Hz, H1), 3.89 – 3.87 (2H, m, H3), 3.88 (3H, s, H11), 2.40 (6H, s, H5).

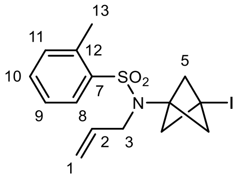
^{13}C NMR (101 MHz, CDCl$_3$) δ 163.1, 134.8, 132.5, 129.4, 117.8, 114.4, 62.3, 56.1, 55.8, 50.4, –0.1.

HRMS (ESI$^+$) $[M + H]^+$ $C_{15}H_{19}O_3NIS$, requires 420.0125; found 420.0123.

Characteristic data for staffane **3b-S** *and H-atom abstraction product* **3b-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.82 (6H, s, **3b-S**), 1.96 (6H, s, **3b-H**), 2.13 (6H, s, **3b-S**).

N-Allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)-2-methylbenzenesulfonamide, 3c



α-Iodoaziridine **2c** (51 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 0:1 → 1:9) gave BCPA iodide **3c** (37 mg, 0.11 mmol, 61%) as a colourless oil.

R$_f$ 0.67 (Et_2O/pentane, 1:4) [UV, Vanillin].

IR ν_{max}/cm^{-1} (film) 2975, 2918, 1329, 1251, 1195, 1158, 877, 825, 760.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (1H, dd, *J* = 7.9, 1.5 Hz, H8), 7.46 (1H, app. td, *J* = 7.5, 1.5 Hz, H9), 7.36 – 7.26 (2H, m, H10, H11), 5.88 (1H, ddt, *J* = 17.2, 10.2, 5.8 Hz, H2), 5.27 (1H, app. dq, *J* = 17.2, 1.5 Hz, H1), 5.20 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 3.96 (2H, app. dt, *J* = 5.8, 1.5 Hz, H3), 2.56 (3H, s, H13), 2.38 (6H, s, H5).

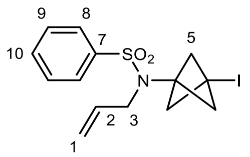
^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0, 137.9, 134.9, 133.1, 132.7, 129.7, 126.3, 118.1, 62.3, 55.9, 50.4, 20.3, –0.2.

HRMS (ESI$^+$) $[M + Na]^+$ $C_{15}H_{18}O_2NINaS$, requires 425.9995; found 425.9997.

Characteristic data for staffane 3c-S *and H-atom abstraction product* 3c-H*:*

^{1}H NMR (400 MHz, CDCl$_3$) δ 2.11 (6H, s, **3c-S**), 1.94 (6H, s, **3c-H**), 1.80 (6H, s, **3c-S**).

N-Allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)benzenesulfonamide, 3d



α-Iodoaziridine **2d** (48 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et$_2$O, 0.24 mL, 0.20 mmol), Et$_3$B (1.0 M in hexanes, 15 µL, 10 mol%) in CH$_2$Cl$_2$ (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO$_2$, Et$_2$O/pentane, 0:1 → 1:9) gave BCPA iodide **3d** (44 mg, 0.11 mmol, 75%) as a colourless oil.

R$_f$ 0.38 (Et$_2$O/pentane, 1:4) [UV, vanillin].

IR ν_{max}/cm^{-1} (film) 1446, 1346, 1195, 1159, 1090, 876, 827, 735, 719, 689.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.82 – 7.77 (2H, m, H8), 7.61 – 7.55 (1H, m, H10), 7.53 – 7.49 (2H, m, H9), 5.79 (1H, ddt, *J* = 17.1, 10.2, 5.7 Hz, H2), 5.24 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.17 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 3.91 (2H, app. dt, *J* = 5.7, 1.6 Hz, H3), 2.40 (6H, s, H5).

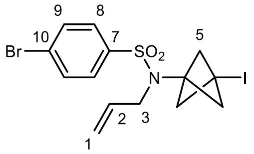
^{13}C NMR (101 MHz, CDCl$_3$) δ 141.0, 134.6, 132.9, 129.3, 127.3, 118.0, 62.3, 56.0, 50.5, –0.3.

HRMS (ESI$^+$) [M + Na]$^+$ C$_{14}$H$_{16}$O$_2$NINaS, requires 411.9839; found 411.9839.

Characteristic data for staffane 3d-S *and H-atom abstraction product* 3d-H*:*

^{1}H NMR (400 MHz, CDCl$_3$) δ 2.13 (6H, s, **3d-S**), 1.97 (6H, s, **3d-H**), 1.82 (6H, s, **3d-S**).

N-Allyl-*p*-bromo-*N*-(6-iodobicyclo[1.1.1]pentan–4-yl)benzenesulfonamide, 3e



α-Iodoaziridine **2e** (54 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9 → 1:4) gave BCPA iodide **3e** (51 mg, 0.11 mmol, 72%) as a white solid.

R_f 0.53 (Et_2O/pentane, 1:4) [UV, vanillin].

m.p. 85 – 86 °C.

IR ν_{max}/cm^{-1} (film) 1350, 1196, 1160, 1089, 1009, 878, 821, 739, 610.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 – 7.62 (4H, m, H8, H9), 5.77 (1H, ddt, *J* = 15.7, 10.2, 5.7 Hz, H2), 5.24 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.19 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 3.89 (2H, app. dt, *J* = 5.7, 1.6 Hz, H3), 2.42 (6H, s, H5).

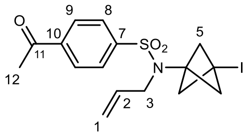
^{13}C NMR (126 MHz, $CDCl_3$) δ 140.1, 134.3, 132.6, 128.8, 127.9, 118.2, 62.3, 56.0, 50.6, –0.7.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{14}H_{15}O_2N^{79}BrINaS$, requires 489.8944; found 489.8945.

Characteristic data for staffane **3e-S** *and H-atom abstraction product* **3e-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.14 (6H, s, **3e-S**), 1.98 (6H, s, **3e-H**), 1.83 (6H, s, **3e-S**).

N-Allyl-*N*-(6-iodobicyclo[1.1.1]pentan-4-yl)-*p*-methoxybenzenesulfonamide, 3f



α-Iodoaziridine **3f** (53 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 μL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9 → 1:4) gave BCPA iodide **3f** (41 mg, 0.10 mmol, 64%) as a colourless oil.

R$_f$ 0.47 (EtOAc/pentane, 1:4) [UV, Vanillin].

IR ν_{max}/cm^{-1} (film) 2979, 1690, 1397, 1351, 1257, 1196, 1161, 1093, 878, 782, 637.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.02 (2H, m, H), 7.92 – 7.85 (2H, m, 1H), 5.78 (1H, ddtd, *J* = 16.9, 10.2, 5.7, 0.9 Hz, H2), 5.29 – 5.19 (1H, m, H1), 5.23 – 5.14 (1H, m, H1), 3.94 – 3.90 (2H, m, H3), 2.66 (3H, d, *J* = 0.9 Hz, H12), 2.42 (6H, d, *J* = 0.9 Hz, H5).

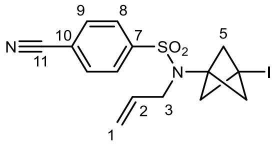
^{13}C NMR (101 MHz, $CDCl_3$) δ 196.7, 144.9, 140.2, 134.2, 129.1, 127.5, 118.3, 62.2, 55.9, 50.6, 27.0, –0.8.

HRMS (ESI$^+$) Not found.

Characteristic data for staffane **3f-S** *and H-atom abstraction product* **3f-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (6H, s, **3f-S**), 1.98 (6H, s, **3f-H**), 1.83 (6H, s, **3f-S**).

N-Allyl-4-cyano-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)benzenesulfonamide, 3g



α-Iodoaziridine **2g** (52 mg, 0.15 mmol), [1.1.1]propellane **1** (0.75 M in Et_2O, 0.27 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:19 → 1:4) gave BCPA iodide **3g** (46 mg, 0.11 mmol, 73%) as a pale-yellow oil.

0.45 mmol scale: α-Iodoaziridine **2g** (157 mg, 0.45 mmol), [1.1.1]propellane **1** (0.70 M in Et_2O, 0.84 mL, 0.59 mmol), Et_3B (1.0 M in hexanes, 45 µL, 10 mol%) in CH_2Cl_2 (0.45 mL) was subjected to **general procedure 1** in a 10 mL vial. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:19 → 1:4) gave BCPA iodide **3g** (130 mg, 0.31 mmol, 70%).

R_f 0.32 (Et_2O/pentane, 1:4).

IR ν_{max}/cm^{-1} (film) 2920, 2361, 2233, 1353, 1197, 1181, 1161, 1089, 880, 830, 634.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 – 7.89 (2H, m, ArH), 7.83 – 7.79 (2H, m, ArH), 5.76 (1H, ddt, *J* = 17.1, 10.2, 5.7 Hz, H2), 5.29 – 5.17 (2H, m, H1), 3.92 (2H, dt, *J* = 5.7, 1.6 Hz, H3), 2.43 (6H, s, H5).

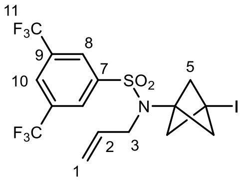
^{13}C NMR (126 MHz, $CDCl_3$) δ 145.4, 134.0, 133.2, 128.0, 118.7, 117.4, 116.8, 62.3, 55.9, 50.8, –1.1.

HRMS ($ESI^{+/-}$, APCI) Not found.

Characteristic data for staffane **3g-S** *and H-atom abstraction product* **3g-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.14 (6H, s, **3g-S**), 1.99 (6H, s, **3g-H**), 1.85 (6H, s, **3g-S**).

N-Allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)-3,5-bis(trifluoromethyl)benzenesulfonamide, 3h



α-Iodoaziridine **2h** (69 mg of a 90% pure sample, 0.14 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 0:1 → 1:19) gave BCPA iodide **3h** (39 mg, 0.077 mmol, 55%) as a white solid.

R_f 0.64 (Et_2O/pentane, 1:19).

m.p. 51 – 53 °C.

IR ν_{max}/cm^{-1} (film) 2360, 2341, 1360, 1280, 1182, 1162, 1143, 1110.

^{1}H NMR (400 MHz, $CDCl_3$) 8.23 (2H, br. s, H8), 8.08 (1H, br. s, H10), 5.74 (1H ddt, *J* = 17.2, 10.2, 5.8 Hz, H2), 5.30 – 5.21 (1H, m, H1), 5.25 – 5.18 (1H, m, H1), 3.94 (2H, app. dt, *J* = 5.8, 1.5 Hz, H3), 2.46 (6H, s, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9, 133.5, 133.2 (q, $^2J_{CF3}$ = 34.5 Hz), 127.5 (q, $^1J_{CF3}$ = 4.1 Hz), 126.5 – 126.2 (m), 122.5 (q, $^1J_{CF3}$ = 273.4 Hz), 119.0, 62.2, 55.9, 50.7, –1.6.

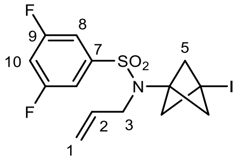
^{19}F NMR (377 MHz, $CDCl_3$) δ –62.97.

HRMS (ESI$^{+/-}$, APCI) Not found.

Characteristic data for staffane **3h-S** *and H-atom abstraction product* **3h-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16 (6H, s, **3h-S**), 2.02 (6H, s, **3h-H**), 1.88 (6H, s, **3h-S**).

N-Allyl–3,5-difluoro-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)benzenesulfonamide*,* 3i



α-Iodoaziridine **2i** (54 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 0:1 → 1:19) gave BCPA iodide **3i** (45 mg, 0.11 mmol, 71%) as a colourless oil.

R$_f$ 0.43 (Et_2O/pentane, 1:19).

IR ν_{max}/cm^{-1} (film) 1605, 1439, 1358, 1298, 1197, 1158, 1126, 989, 878, 671, 619.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (2H, app. ddd, *J* = 5.3, 2.3, 1.2 Hz, H8), 7.03 (1H, tt, *J* = 8.5, 2.3 Hz, H10), 5.78 (1H, ddt, *J* = 17.1, 10.2, 5.7 Hz, H2), 5.30 – 5.17 (2H, m, H1), 3.90 (2H, app. dt, *J* = 5.7, 1.6 Hz, H3), 2.45 (6H, s, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9 (dd, $^{1,3}J_{CF}$ = 255.0, 11.6 Hz), 144.3 (app. t, $^3J_{CF}$ = 8.1 Hz), 134.0, 118.5, 110.8 (dd, $^{2,4}J_{CF}$ = 19.8, 8.4 Hz), 108.5 (app. t, $^2J_{CF}$ = 25.0 Hz), 62.2, 55.8, 50.7, –1.1.

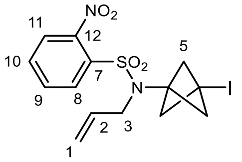
^{19}F NMR (377 MHz, $CDCl_3$) δ –105.22.

HRMS (ESI$^{+/-}$, APCI) Not found.

Characteristic data for staffane 3i-S *and H-atom abstraction product* 3i-H*:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.15 (6H, s, **3i-S**), 2.01 (6H, s, **3i-H**), 1.86 (6H, s, **3i-S**).

N-Allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)-2-nitrobenzenesulfonamide, 3j



α-Iodoaziridine **2j** (55 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9 → 1:4) gave BCPA iodide **3j** (24 mg, 0.054 mmol, 36%) as a white solid.

R_f 0.42 (Et_2O/pentane, 2:3).

m.p. 87 °C.

IR ν_{max}/cm^{-1} (film) 2919, 1542, 1354, 1198, 1163, 1125, 881, 629.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.01 (1H, m, ArH), 7.74 – 7.63 (3H, m, ArH), 5.86 (1H, ddt, *J* = 17.2, 10.2, 5.8 Hz, H2), 5.29 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.21 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 3.95 (2H, dt, *J* = 5.8, 1.6 Hz, H3), 2.38 (6H, s, H2).

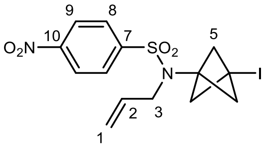
^{13}C NMR (126 MHz, $CDCl_3$) δ 148.1, 134.6, 134.3, 134.1, 132.1, 131.1, 124.5, 118.4, 62.1, 55.6, 51.3, –0.8.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{14}H_{15}O_4N_2INaS$, requires 456.9689; found 456.9689.

Characteristic data for staffane **3j-S** *and H-atom abstraction product* **3j-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.11 (6H, s, **3j-S**), 1.94 (6H, s, **3j-H**), 1.79 (6H, s, **3j-S**).

N-Allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)-4-nitrobenzenesulfonamide, 3k



α-Iodoaziridine **2k** (65 mg of an 85% pure sample, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.30 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9) gave BCPA iodide **3k** (7 mg, 0.02 mmol, 10%) as a colourless oil.

R$_f$ 0.69 (Et_2O/pentane, 1:4).

IR ν_{max}/cm^{-1} (film) 2920, 2361, 15330, 1350, 1311, 1198, 1163, 1090, 880, 736, 614.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 – 8.25 (2H, m, H8), 7.96 – 7.88 (2H, m, H9), 5.70 (1H, ddt, *J* = 17.1, 10.2, 5.7 Hz, H2), 5.22 – 5.12 (2H, m, H1), 3.87 (2H, app. dt, *J* = 5.7, 1.6 Hz, H3), 2.38 (6H, s, H5).

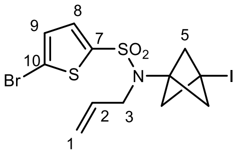
^{13}C NMR (151 MHz, $CDCl_3$) δ 150.2, 146.9, 133.8, 128.5, 124.6, 118.7, 62.3, 55.9, 50.7, –1.4.

HRMS (ESI$^{+/-}$, APCI) Not found.

Characteristic data for staffane **3k-S** *and H-atom abstraction product* **3k-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08 (6H, s, **3k-S**), 1.94 (6H, s, **3k-H**), 1.79 (6H, s, **3k-S**).

N-Allyl-5-bromo-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)thiophene-2-sulfonamide, 3l



α-Iodoaziridine **2l** (61 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 0:1 → 1:9) gave BCPA iodide **3l** (53 mg, 0.11 mmol, 75%) as a white solid.

R_f 0.56 (Et_2O/pentane, 1:4)

m.p. 44°C.

IR ν_{max}/cm^{-1} (film) 2919, 1403, 1357, 11996, 1157, 879, 670, 607.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (1H, d, *J* = 3.9 Hz, H8), 7.06 (1H, d, *J* = 3.9 Hz, H9), 5.79 (1H, ddt, *J* = 17.2, 10.2, 5.7 Hz, H2), 5.26 (1H, app. dq, *J* = 17.2, 1.5 Hz, H1), 5.20 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 3.85 (2H, app. dt, *J* = 5.8, 1.6 Hz, H3), 2.49 (6H, s, H5).

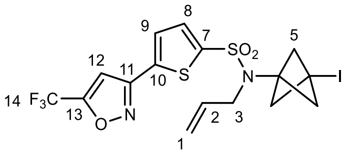
^{13}C NMR (126 MHz, $CDCl_3$) δ 142.3, 133.9, 132.6, 130.4, 120.1, 118.4, 62.2, 56.0, 50.6, –0.8.

HRMS (ESI$^+$) $[M + H]^+$ $C_{12}H_{13}O_2N^{79}BrIS_2$, requires 473.8689; found 473.8689.

Characteristic data for staffane **3l-S** *and H-atom abstraction product* **3l-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16 (6H, s, **3l-S**), 2.05 (6H, s, **3l-H**), 1.91 (6H, s, **3l-S**).

N-Allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)-5-(5-(trifluoromethyl)isoxazole-3-yl)thiophene-2-sulfonamide, 3m



α-Iodoaziridine **2m** (70 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9 → 3:7) gave BCPA iodide **3m** (41 mg, 0.078 mmol, 52%) as a colourless oil.

R$_f$ 0.18 (Et_2O/pentane, 1:4).

IR ν_{max}/cm^{-1} (film) 2981, 2360, 2341, 1315, 1291, 1196, 1157, 312.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (1H, d, *J* = 3.9 Hz, ArH), 7.45 (1H, d, *J* = 3.9 Hz, ArH), 6.98 (1H, q, J_{CF3} = 0.9 Hz, H12), 5.82 (1H, ddt, *J* = 17.1, 10.2, 5.8 Hz, H2), 5.28 (1H, app. dq, *J* = 17.1, 1.6 Hz, H1), 5.22 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 3.91 (2H, app. dt, *J* = 5.8, 1.6 Hz, H3), 2.51 (6H, s, H5).

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.2 (q, $^2J_{CF3}$ = 43.1 Hz), 156.8, 134.7, 133.8, 132.5, 128.1, 118.7 (q, $^1J_{CF3}$ = 270.7 Hz), 118.5, 103.6 (q, $^3J_{CF3}$ = 2.3 Hz), 62.2, 56.0, 53.3, 50.7, –1.0.

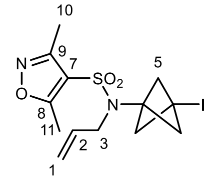
^{19}F NMR (377 MHz, $CDCl_3$) δ –64.17.

HRMS (ESI$^+$) [M + H]$^+$ $C_{16}H_{15}F_3O_3N_2IS_2$, requires 530.9515; found 531.3502.

Characteristic data for staffane **3m-S** *and H-atom abstraction product* **3m-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16 (6H, s, **3m-S**), 2.08 (6H, s, **3m-H**), 1.93 (6H, s, **3m-S**).

N-Allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)-3,5-dimethylisoxazole-4-sulfonamide, 3n



α-Iodoaziridine **2n** (51 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 0:1 → 1:19) gave BCPA iodide **3n** (44 mg, 0.11 mmol, 71%) as a colourless oil.

R$_f$ 0.52 (Et_2O/pentane, 1:4).

IR ν_{max}/cm^{-1} (film) 2981, 1593, 1338, 1178, 1119, 913, 745.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82 (1H, ddt, *J* = 17.2, 10.3, 5.7 Hz, H2), 5.29 – 5.18 (2H, m, H1), 3.92 (2H, dt, *J* = 5.8, 1.5 Hz, H3), 2.63 (3H, s, H11), 2.45 (6H, s, H5), 2.34 (3H, s, H10).

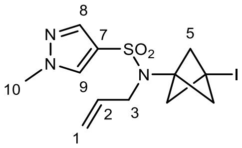
^{13}C NMR (126 MHz, $CDCl_3$) δ 173.5, 157.5, 134.3, 118.5, 117.3, 62.1, 55.7, 50.4, 13.0, 11.0, –1.1.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{13}H_{18}O_3N_2IS$, requires 409.0077; found 409.0076.

Characteristic data for staffane 3n-S *and H-atom abstraction product* 3n-H*:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.15 (6H, s, **3n-S**), 2.00 (6H, s, **3n-H**), 1.86 (6H, s, **3n-S**).

N-Allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)-1-methyl-1H-pyrazole-4-sulfonamide, 3o



α-Iodoaziridine **2o** (49 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 3:7) gave BCPA iodide **3o** (43 mg, 0.11 mmol, 73%) as a colourless oil.

R$_f$ 0.22 (EtOAc/pentane, 3:7).

IR ν_{max}/cm^{-1} (film) 2920, 1523, 1347, 1195, 1157, 1118, 877, 826, 658, 633, 614.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (1H, s, H9), 7.68 (1H, s, H8), 5.81 (1H, ddt, *J* = 17.2, 10.3, 5.7 Hz, H2), 5.25 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.18 (1H, app. dq, *J* = 10.3, 1.5 Hz, H1), 3.95 (3H, s, H10), 3.82 (2H, app. dt, *J* = 5.7, 1.6 Hz, H3), 2.47 (6H, s, H5).

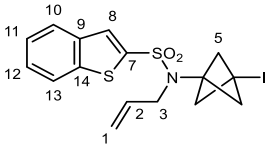
^{13}C NMR (126 MHz, $CDCl_3$) δ 138.5, 134.3, 131.8, 123.1, 118.0, 62.2, 56.1, 50.3, 39.8, – 0.4.

HRMS (ESI$^+$) [M + H]$^+$ $C_{12}H_{17}O_2N_3IS$, requires 394.0081; found 394.0081.

Characteristic data for staffane **3o-S** *and H-atom abstraction product* **3o-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16 (6H, s, **3o-S**), 2.03 (6H, s, **3o-H**), 1.88 (6H, s, **3o-S**).

N-Allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)benzo[*b*]thiophene-2-sulfonamide, 3p



α-Iodoaziridine **2p** (57 mg of a 94% pure sample, 0.14 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9 → 1:4) gave BCPA iodide **3p** (45 mg, 0.10 mmol, 71%) as a white solid.

R$_f$ 0.23 (Et_2O/pentane, 1:1) [UV, vanillin].

m.p. 67 °C.

IR ν_{max}/cm^{-1} (film) 2360, 1504, 1355, 1249, 1195, 1152, 1022, 879, 622.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.85 (2H, m, H10, H13), 7.85 – 7.83 (1H, m, H8), 7.53 – 7.45 (2H, m, H11, H12), 5.84 (1H, ddt, *J* = 17.1, 10.2, 5.7 Hz, H2), 5.28 (1H, app. dq, *J* = 17.0, 1.5 Hz, H1), 5.19 (1H, app. dq, *J* = 10.3, 1.4 Hz, H1), 3.92 (2H, app. dt, *J* = 5.7, 1.6 Hz, H3), 2.51 (6H, s, H5).

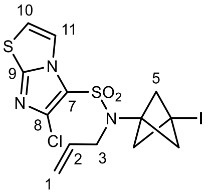
^{13}C NMR (101 MHz, $CDCl_3$) δ 141.7, 141.4, 137.5, 134.2, 129.7, 127.6, 125.8, 125.8, 122.9, 118.2, 62.3, 56.0, 50.7, –0.6.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{16}H_{16}O_2NINaS_2$, requires 436.9559; found 467.9558.

Characteristic data for staffane 3p-S *and H-atom abstraction product* 3p-H*:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.15 (6H, s, **3p-S**), 2.07 (6H, s, **3p-H**), 1.93 (6H, s, **3p-S**).

N-Allyl-6-chloro-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)-6H-4l4-imidazo[2,1-b]thiazole-5-sulfonamide, 3q



α-Iodoaziridine **2q** (95 mg of a 43% pure sample,* 0.13 mmol), [1.1.1]propellane **1** (0.73 M in Et_2O, 0.54 mL, 0.39 mmol), Et_3B (1.0 M in hexanes, 30 µL, 10 mol%) in CH_2Cl_2 (0.30 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9 → 1:3, then EtOAc/pentane, 1:4) gave BCPA iodide **3q** (49 mg, 0.10

mmol, 81%) as white crystalline solid. The product was isolated as an inseparable mixture of **3q**:**3q-S**:**3q-H**, 1:0.09:0.11 as determined by ^{1}H NMR spectroscopy.

*Note: The impurity in the α-iodoaziridine **2q** was characterized as 4-(iodomethyl)-1,2-thiazetidine 1,1-dioxide **2q1** (**2q**:**2q1**, 43:57) and was anticipated to be reactive under the reaction conditions. The amount of reagents used was calculated according to a total of 0.30 mmol of iodides **2q** (0.13 mmol) and **2q1** (0.17 mmol). BCP iodide **3q1** was then easily separated from the desired compound.*

R$_f$ 0.51 (EtOAc/pentane, 3:7).

m.p. 144 °C.

IR ν_{max}/cm^{-1} (film) 2919, 1456, 1437, 1351, 1321, 1271, 1251, 1197, 1178, 1137, 880, 831, 730, 622.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.93 (1H, d, *J* = 4.5 Hz, H11), 7.10 (1H, d, *J* = 4.5 Hz, H10), 5.84 (1H, ddt, *J* = 17.1, 10.3, 5.5 Hz, H2), 5.26 (1H, dtd, *J* = 17.1, 1.7, 1.0 Hz, H1), 5.20 (1H, app. dq, *J* = 10.3, 1.4 Hz, H1), 4.08 (1H, app. dt, *J* = 5.5, 1.7 Hz, H3), 2.39 (6H, s, H5).

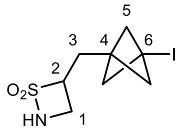
^{13}C NMR (126 MHz, CDCl$_3$) δ 149.7, 137.1, 134.4, 120.5, 120.2, 118.0, 114.7, 62.0, 55.6, 51.5, –1.2.

HRMS (ESI$^+$) [M + H]$^+$ $C_{13}H_{14}O_2N_3ClIS_2$, requires 469.9255; found 469.9254.

Characteristic data for staffane **3q-S** *and H-atom abstraction product* **3q-H***:*

^{1}H NMR (400 MHz, CDCl$_3$) δ 2.12 (6H, s, **3q-S**), 1.93 (6H, s, **3q-H**), 1.80 (6H, s, **3q-S**).

4-(3-Iodobicyclo[1.1.1]pentan-1-yl)isothiazolidine 1,1-dioxide, 3q1



Alkyl iodide **2q1** (95 mg of a 57 % pure sample, 0.17 mmol) was subjected to the above conditions. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:4) gave BCP iodide **3q1** (32 mg, 0.10 mmol, 61%) as a white crystalline solid.

R_f 0.12 (EtOAc/pentane, 3:7).

m.p. 116 °C.

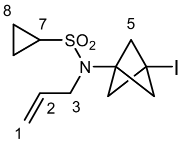
IR ν_{max}/cm^{-1} (film) 3276 (br.), 2914, 1400, 1335, 1182, 1029, 981, 843, 800.

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.74 (1H, dddd, *J* = 9.1, 8.2, 6.2, 3.9 Hz, H2), 4.49 (1H, br. s, NH), 3.72 (1H, dt, *J* = 12.0, 6.2 Hz, H1), 3.32 (1H, dt, *J* = 12.0, 8.2 Hz, H1), 2.31 (6H, s, H5), 2.15 (1H, dd, *J* = 15.0, 9.1 Hz, H3), 1.91 (1H, dd, *J* = 15.0, 3.9 Hz, H3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 82.4, 60.9, 48.6, 44.7, 36.1, 5.7.

HRMS ($ESI^{+/-}$, APCI) Not found.

N-Allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)cyclopropanesulfonamide, 3r



α-Iodoaziridine **2r** (43 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:4 → 3:7) gave BCPA iodide **3r** (35 mg, 0.10 mmol, 66%) as a white solid.

R$_f$ 0.52 (Et_2O/pentane, 3:7).

m.p. 76 – 78 °C.

IR ν_{max}/cm^{-1} (film) 2919, 1310, 1307, 1195, 1148, 1040, 876, 833, 703.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 (1H, ddt, *J* = 17.2, 10.2, 5.8 Hz, H2), 5.26 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.19 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 3.87 (2H, app. dt, *J* = 5.8, 1.6 Hz, H3), 2.54 (6H, s, H5), 2.33 – 2.26 (1H, m, H7), 1.20 – 1.14 (2H, m, H8), 1.02 – 0.96 (2H, m, H8).

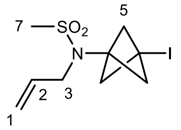
^{13}C NMR (101 MHz, $CDCl_3$) δ 134.8, 118.0, 62.7, 56.1, 50.5, 31.1, 5.9, – 0.4.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{11}H_{16}O_2NINaS$, requires 375.9839; found 375.9839.

Characteristic data for staffane **3r-S** *and H-atom abstraction product* **3r-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.18 (6H, s, **3r-S**), 2.10 (6H, s, **3r-H**), 1.95 (6H, s, **3r-S**).

N-Allyl-*N*-(6-iodobicyclo[1.1.1]pentan-4-yl)methanesulfonamide, 3s



α-Iodoaziridine **2s** (39 mg, 0.15 mmol), [1.1.1]propellane **1** (1.00 M in Et_2O, 0.24 mL, 0.24 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9 → 1:4) gave BCPA iodide **3s** (26 mg, 0.080 mmol, 53%) as a white solid.

R$_f$ 0.13 (Et_2O/pentane, 1:4).

m.p. 66 – 68 °C.

IR ν_{max}/cm^{-1} (film) 1338, 1253, 1196, 1151, 876, 830.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (1H, ddt, *J* = 17.1, 10.2, 5.9 Hz, H2), 5.28 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.22 (1H, app. dq, *J* = 10.3, 1.3 Hz, H1), 3.84 (2H, app. dt, *J* = 5.9, 1.5 Hz, H3), 2.55 (6H, s, H5), 2.87 (3H, s, H7).

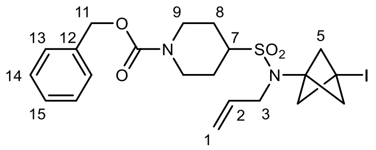
^{13}C NMR (126 MHz, $CDCl_3$) δ 134.1, 118.5, 62.3, 56.0, 50.2, 41.1, – 0.8.

HRMS ($ESI^{+/-}$, APCI) Not found.

Characteristic data for staffane **3s-S** *and H-atom abstraction product* **3s-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.19 (6H, s, **3s-S**), 2.11 (6H, s, **3s-H**), 1.97 (6H, s, **3s-S**).

Benzyl 4-(*N*-allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)sulfamoyl)piperidine – 1-carboxylate, 3t



α-Iodoaziridine **2t** (70 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 1:4) gave BCPA iodide **3t** (30 mg, 0.056 mmol, 37%) as a colourless oil.

R_f 0.58 (EtOAc/pentane, 1:4).

IR ν_{max}/cm^{-1} (film) 2920, 1695, 1433, 1331, 1279, 1260, 1215, 1196, 1145, 1119, 877, 732, 613.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.28 (5H, m, ArH), 5.82 (1H, ddt, *J* = 17.1, 10.2, 5.9 Hz, H2), 5.24 (1H, app. dq, *J* = 17.1, 1.4 Hz, H1), 5.20 (1H, app. dq, *J* = 10.2, 1.2 Hz, H1), 5.13

(2H, s, H11), 4.33 (2H, br. s, H9), 3.83 (2H, d, *J* = 5.9 Hz, H3), 2.94 (1H, tt, *J* = 11.7, 3.6 Hz, H7), 2.78 (2H, br. s, H9), 2.53 (6H, s, H5), 2.04 – 1.93 (2H, m, H8), 1.81 – 1.65 (2H, m, H8).

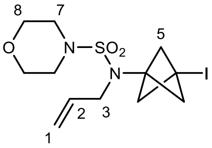
^{13}C NMR (101 MHz, $CDCl_3$) δ 155.1, 136.6, 135.0, 128.7, 128.3, 128.2, 118.3, 67.6, 62.6, 60.6, 56.3, 51.0, 43.0, 26.0, –0.8.

HRMS (ESI^+) $[M + Na]^+$ $C_{21}H_{27}O_4N_2INaS$, requires 553.0628; found 553.0628.

Characteristic data for staffane **3t-S** *and H-atom abstraction product* **3t-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.18 (6H, s, **3t-S**), 2.08 (6H, s, **3t-H**), 1.94 (6H, s, **3t-S**).

N-Allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)morpholine-4-sulfonamide, 3u



α-Iodoaziridine **2u** (50 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:4 → 1:3) gave BCPA iodide **3u** (36 mg, 0.092 mmol, 61%) as a colourless oil.

R_f 0.17 (Et_2O/pentane, 1:4).

IR ν_{max}/cm^{-1} (film) 2919, 2858, 1342, 1260, 1195, 1154, 1115, 935, 877.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (1H, ddt, *J* = 17.2, 10.3, 5.9 Hz, H2), 5.24 (1H, app. dt, *J* = 17.3, 1.6 Hz, H1), 5.20 (1H, app. dq, *J* = 10.1, 1.3 Hz, H1), 3.83 (2H, app. dt, *J* = 5.9, 1.5 Hz, H3), 3.75- 3.68 (4H, m, H8), 3.17 – 3.11 (4H, m, H7), 2.52 (6H, s, H5).

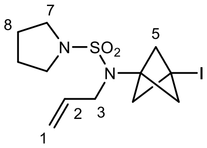
^{13}C NMR (101 MHz, $CDCl_3$) δ 134.6, 118.1, 66.4, 62.3, 56.3, 51.2, 46.1, –0.4.

HRMS (ESI$^+$) [M + H]$^+$ $C_{12}H_{20}O_3N_2IS$, requires 399.0234; found 399.0233.

Characteristic data for staffane **3u-S** *and H-atom abstraction product* **3u-H***:*

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 2.18 (6H, s, **3u-S**), 2.08 (6H, s, **3u-H**), 1.93 (6H, s, **3u-S**).

N-Allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)pyrrolidine-1-sulfonamide, 3v



α-Iodoaziridine **2v** (28 mg, 0.09 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.14 mL, 0.11 mmol), Et_3B (1.0 M in hexanes, 9 µL, 10 mol%) in CH_2Cl_2 (0.1 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9 → 1:4) gave BCPA iodide **3v** (7 mg, 0.02 mmol, 22%) as a colourless oil.

R$_f$ 0.56 (Et_2O/pentane, 3:7).

IR ν_{max}/cm^{-1} (film) 2977, 1330, 1193, 1150, 1010, 876, 826, 617.

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 5.84 (1H, ddt, *J* = 17.1, 10.2, 5.9 Hz, H2), 5.23 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.16 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 3.82 (2H, dt, *J* = 5.9, 1.5 Hz, H3), 3.28 – 3.20 (4H, m, H7), 2.51 (6H, s, H5), 1.94 – 1.86 (4H, m, H8).

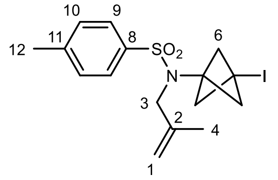
^{13}**C NMR** (101 MHz, $CDCl_3$) δ 135.0, 117.6, 62.2, 56.4, 50.8, 47.9, 25.8, 0.1.

HRMS (ESI$^+$) [M + H]$^+$ $C_{12}H_{20}O_2N_2IS$, requires 383.0285; found 383.0285.

Characteristic data for staffane **3v-S** *and H-atom abstraction product* **3v-H***:*

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 2.18 (6H, s, **3v-S**), 2.06 (6H, s, **3v-S**), 2.01 (6H, s, **3v-H**).

N-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-methyl-*N*-(2-methylallyl)benzenesulfonamide, 3w



α-Iodoaziridine **2w** (53 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 2:98 → 1:9) gave BCPA iodide **3w** (46 mg, 0.11 mmol, 73%) as a white solid.

R_f 0.58 (Et_2O/pentane, 1:4).

m.p 72 – 74 °C.

IR ν_{max}/cm^{-1} (film) 2919, 1345, 1195, 1159, 1093, 877, 668.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.62 (2H, m, H9), 7.33 – 7.26 (2H, m, H10), 4.97- 4.88 (2H, m, H1), 3.82 (2H, br. s, H3), 2.43 (3H, s, H12), 2.38 (6H, s, H6), 1.77 (3H, s, H4).

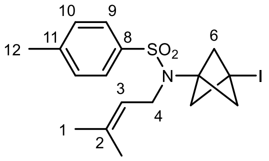
^{13}C NMR (126 MHz, $CDCl_3$) δ 143.7, 141.7, 138.0, 129.9, 127.2, 113.3, 62.1, 56.1, 54.0, 21.7, 19.8, –0.3

HRMS (ESI^+) $[M + H]^+$ $C_{16}H_{21}O_2NIS$, requires 418.0332; found 418.0332.

Characteristic data for staffane **3w-S** *and H-atom abstraction product* **3w-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.12 (6H, s, **3w-S**), 1.94 (6H, s, **3w-H**), 1.80 (6H, s, **3w-S**).

N-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-methyl-*N*-(3-methylbut-2-en-1-yl)benzenesulfonamide, 3x



α-Iodoaziridine **2x** (55 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9) gave BCPA iodide **3x** (40 mg, 0.093 mmol, 62%) as a white solid.

R_f 0.46 (Et_2O/pentane, 1:4).

m.p. 58 °C.

IR ν_{max}/cm^{-1} (film) 2919, 2360, 1345, 1193, 1158, 1091, 878, 667.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.62 (2H, m, H9), 7.32 – 7.25 (2H, m, H10), 5.09 (1H, app. tquin., *J* = 6.6, 1.4 Hz, H3), 3.91 – 3.84 (2H, m, H4), 2.43 (3H, s, H12), 2.38 (6H, s, H6), 1.68 (3H, d, *J* = 1.4 Hz, H1), 1.64 (3H, d, *J* = 1.4 Hz, H1).

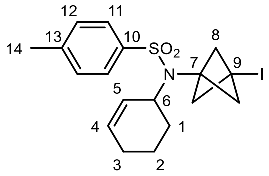
^{13}C NMR (126 MHz, $CDCl_3$) δ 143.6, 138.1, 135.4, 129.8, 127.3, 121.1, 62.3, 55.9, 46.1, 25.9, 21.7, 18.0, 0.1.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{17}H_{22}O_2NINaS$, requires 454.0308; found 454.0305.

Characteristic data for staffane **3x-S** *and H-atom abstraction product* **3x-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.14 (6H, s, **3x-S**), 1.95 (6H, s, **3x-H**), 1.80 (6H, s, **3x-S**).

N-(Cyclohex-2-en-1-yl)-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)-4-methylbenzenesulfonamide, **3y**



α-Iodoaziridine **2y** (57 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9) gave BCPA iodide **3y** (23 mg, 0.051 mmol, 34%) as a colourless oil.

R_f 0.37 (Et_2O/pentane, 1:9).

IR ν_{max}/cm^{-1} (film) 2922, 2360, 1327, 1191, 1159, 1093, 992, 666.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 – 7.65 (2H, m, H11), 7.29 (2H, br. d, *J* = 8.1 Hz, H12), 5.73 (1H, app. dt, *J* = 10.2, 3.5 Hz, H5), 5.35 (1H, app. dp, *J* = 10.2, 2.1 Hz, H4), 4.68 (1H, app. ddp, *J* = 11.3, 5.9, 3.0 Hz, H6), 2.53 (6H, s, H8), 2.43 (3H, s, H14), 2.01 – 1.91 (3H, m, H3, H1), 1.87 – 1.78 (1H, m, H2), 1.78 – 1.66 (1H, m, H1), 1.67 – 1.54 (1H, m, H2).

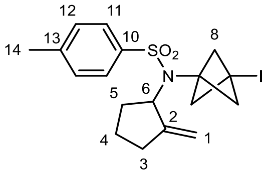
^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 138.9, 130.8, 129.8, 129.0, 127.2, 64.2, 56.6, 54.7, 29.5, 24.5, 22.6, 21.7, 0.5.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{18}H_{22}O_2NINaS$, requires 466.0308; found 466.0310.

Characteristic data for staffane **3y-S** *and H-atom abstraction product* **3y-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.14 (6H, s, **3y-S**), 2.10 (6H, s, **3y-H**), 2.04 (6H, s, **3y-S**).

N-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-methyl-N-(2-methylenecyclopentyl)-benzenesulfonamide, 3z



α-Iodoaziridine **2z** (57 mg, 0.15 mmol), [1.1.1]propellane **1** (0.73 M in Et_2O, 0.33 mL, 0.24 mmol), Et_3B (1.0 M in Hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.20 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9) gave BCPA iodide **3z** (20 mg, 0.045 mmol, 30%) as a colourless oil. The product was isolated as an inseparable mixture of **3z**:**3z-S**:**3z-H**, 1:0.04:0.06 as determined by ^{1}H NMR spectroscopy.

R$_f$ 0.58 (Et_2O/pentane, 1:4)

IR v_{max}/cm^{-1} (film) 2971, 1337, 1304, 1189, 1163, 1092, 814, 665.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 – 7.68 (2H, m, H11), 7.32 – 7.27 (2H, m, H12), 5.00 (1H, app. q, *J* = 2.6 Hz, H1), 4.85 (1H, app. q, *J* = 2.6 Hz, H1), 4.78 (1H, app. ddq, *J* = 10.9, 8.4, 2.9 Hz, H6), 2.52 (6H, s, H8), 2.43 (3H, s, H14), 2.40 – 2.34 (1H, m, H3), 2.33 – 2.23 (1H, m, H3), 1.94 – 1.87 (1H, m, H5), 1.81 – 1.75 (1H, m, H4), 1.72 – 1.65 (1H, m, H5), 1.53 – 1.39 (1H, m, H4).

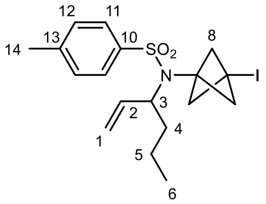
^{13}C NMR (126 MHz, $CDCl_3$) δ 149.1, 143.6, 138.6, 129.8, 127.3, 108.6, 64.2, 62.3, 55.0, 31.3, 31.2, 22.7, 21.7, 0.8.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{18}H_{22}O_2NINaS$, requires 466.0308; found 466.0310.

Characteristic data for staffane **3z-S** *and H-atom abstraction product* **3z-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (6H, s, **3z-S**), 2.08 (6H, s, **3z-H**), 1.94 (6H, s, **3z-S**).

N-(Hex-1-en-3-yl)-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)-4-methylbenzenesulfonamide, 3aa



α-Iodoaziridine **2aa** (57 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9 → 1:4) gave BCPA iodide **3aa** (26 mg, 0.05 mmol, 39%) as a colourless oil. The product was isolated as an inseparable mixture of **3aa**:**3aa-S**:**3aa-H**, 1:0.06:0.03 as determined by ^{1}H NMR spectroscopy.

R$_f$ 0.71 (Et_2O/pentane, 15:75).

IR ν_{max}/cm^{-1} (film) 2959, 1342, 1196, 1179, 1092, 908, 731, 665.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 – 7.65 (2H, m, H11), 7.31 – 7.25 (2H, m, H12), 5.84 – 5.75 (1H, m, H2), 5.17 – 5.10 (2H, m, H1), 4.51 (1H, dddt, *J* = 8.7, 7.4, 5.9, 1.7 Hz, H3), 2.50 – 2.44 (6H, m, H8), 2.43 (3H, s, H14), 1.74 – 1.56 (2H, m, H4), 1.43 – 1.32 (2H, m, H5), 0.93 (3H, t, *J* = 7.4 Hz, H6).

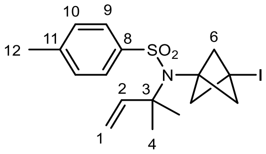
^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 139.0, 138.1, 129.7, 127.4, 117.5, 63.9, 61.0, 54.8, 35.3, 21.7, 20.0, 14.0, 0.4.

HRMS (ESI$^+$) $[M + Na]^+$ $C_{18}H_{24}O_2NINaS$, requires 468.0465; found 468.0464.

Characteristic data for staffane **3aa-S** *and H-atom abstraction product* **3aa-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.12 (6H, s, **3aa-S**), 2.05 – 2.03 (6H, m, **3aa-H**), 1.92 – 1.86 (6H, s, **3aa-S**).

N-(3-Iodobicyclo[1.1.1]pentan-1-yl) – 4-methyl-*N*-(2-methylbut-3-en-2-yl)benzenesulfonamide, 3ab



α-Iodoaziridine **2ab** (55 mg, 0.15 mmol), [1.1.1]propellane **1** (0.80 M in Et_2O, 0.24 mL, 0.20 mmol), Et_3B (1.0 M in Hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 0:1 → 1:9) gave BCPA iodide **3ab** (3 mg, 0.007 mmol, 4%) as a colourless oil.

R_f 0.61 (Et_2O/pentane, 1:4)

IR ν_{max}/cm^{-1} (film) 2981, 2361, 2342, 1738, 1380, 1231, 1161, 954, 665.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 – 7.64 (2H, m, H9), 7.30 – 7.25 (2H, obsc. m, H10), 5.99 (1H, dd, *J* = 17.6, 10.7 Hz, H2), 5.06 (1H, d, *J* = 17.6 Hz, H1), 4.99 (1H, d, *J* = 10.7 Hz, H1), 2.68 (6H, s, H6), 2.42 (3H, s, H12), 1.49 (6H, s, H4).

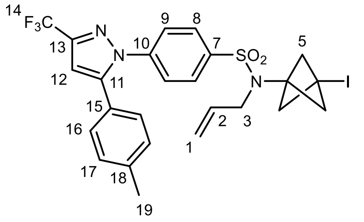
^{13}C NMR (126 MHz, $CDCl_3$) δ 146.5, 143.2, 141.5, 129.7, 126.8, 111.8, 65.8, 64.7, 57.8, 28.2, 21.6, 1.0.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{17}H_{22}O_2NINaS$, requires 454.0308; found 454.0308.

Characteristic data for staffane product **3ab-S***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29 (6H, s, **3ab-S**), 2.21 (6H, s, **3ab-S**).

N-Allyl-*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)-4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide, 3ac



α-Iodoaziridine **2ac** (82 mg, 0.15 mmol), [1.1.1]propellane **1** (0.73 M in Et_2O, 0.27 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:19 → 1:9) gave BCPA iodide **3ac** (64 mg, 0.11 mmol, 70%) as a white solid.

R_f 0.42 (Et_2O/pentane, 1:4).

m.p. 103 °C.

IR ν_{max}/cm^{-1} (film) 2361, 1472, 1352, 1237, 1161, 1136, 1096, 976, 827, 760.

^{1}H NMR (500 MHz, $CDCl_3$) 7.85 – 7.69 (2H, m, H8), 7.50 – 7.43 (2H, m, H9), 7.18 (2H, d, *J* = 8.2 Hz, 16), 7.09 (2H, d, *J* = 8.2 Hz, H17), 6.75 (1H, s, H12), 5.76 (1H, app. ddt, *J* = 17.2, 10.2, 5.8 Hz, H2), 5.24 (1H, app. dq, *J* = 17.2, 1.4 Hz, H1), 5.18 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 3.89 (2H, app. dt, *J* = 5.8, 1.6 Hz, H3), 2.39 (6H, s, H5), 1.55 (3H, s, H19).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.5, 144.4 (q, $^2J_{CF3}$ = 38.6 Hz), 142.7, 140.4, 140.1, 134.2, 129.9, 128.9, 128.3, 125.8, 125.8, 121.2 (q, $^1J_{CF3}$ = 269.4 Hz), 118.3, 106.5 (q, $^3J_{CF3}$ = 2.1 Hz), 62.2, 55.9, 50.6, 21.5, –0.8.

^{19}F NMR (377 MHz, $CDCl_3$) δ –62.4.

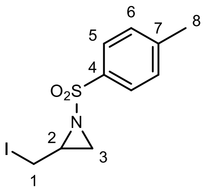
HRMS (ESI$^+$) $[M + H]^+$ $C_{25}H_{24}O_2N_3F_3IS$, requires 614.0581; found 614.0576.

Characteristic data for staffane **3ac-S** *and H-atom abstraction product* **3ac-H***:*

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (6H, s, **3ac-S**), 1.96 (6H, s, **3ac-H**), 1.82 (6H, s, **3ac-S**).

S2.3 α-Iodoaziridines

2-(Iodomethyl)-3-tosylaziridine, 2a



NaH (247 mg, 6.18 mmol), *N*-allyl sulfonamide **5a** (1.30 g, 6.13 mmol) and iodine (4.66 g, 18.4 mmol) in Et_2O (31 mL) were subjected to the conditions of **general procedure 5** for 4 h. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9) gave α-iodoaziridine **2a** (1.71 g, 5.09 mmol, 83%) as a pale-yellow oil. Slow recrystallization (Et_2O/pentane at –5 °C) gave **2a** as colourless crystals.

R_f 0.46 (EtOAc/pentane, 1:4) [UV, $KMnO_4$].

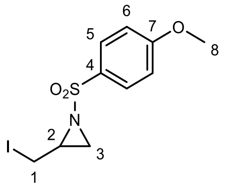
m.p. 45 °C (Et_2O) [lit.[12] 45 – 47 °C].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.82 (2H, m, H5), 7.39 – 7.32 (2H, m, H6), 3.13 – 3.01 (2H, m, H1, H2), 2.84 – 2.82 (1H, m, H3), 2.45 – 2.45 (3H, m, H8), 2.17 – 2.16 (1H, m, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1, 134.7, 129.9, 128.4, 41.2, 36.3, 21.8, 2.4.

Data in agreement with that reported previously.[1]

2-(Iodomethyl)-3-((*p*-methoxyphenyl)sulfonyl)aziridine, 2b



NaH (280 mg, 7.00 mmol), *N*-allyl sulfonamide **5b** (1.32 g, 5.83 mmol) and iodine (4.43 g, 17.5 mmol) in Et_2O (29 mL) were subjected to the conditions of **general procedure 5** for 20 h. Purification by column chromatography (SiO_2, EtOAc/pentane, 3:7) gave α-iodoaziridine **2b** (645 mg, 2.66 mmol, 38%) as a colourless oil.

R$_f$ 0.65 (EtOAc/pentane, 3:7) [UV, $KMnO_4$].

IR ν_{max}/cm^{-1} (film) 1595, 1498, 1325, 1259, 1151, 1091, 834, 805, 721, 696.

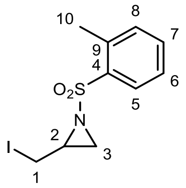
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.85 (2H, m, H5), 7.06 – 6.97 (2H, m, H6), 3.89 (3H, s, H8), 3.10 – 3.02 (3H, m, H1, H2), 2.84 – 2.81 (1H, m, H3), 2.17 – 2.15 (1H, m, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1, 130.7, 129.2, 114.5, 55.9, 41.2, 36.2, 2.5.

HRMS (ESI$^+$) [M + H]$^+$ $C_{10}H_{13}O_3NIS$ requires 353.9655; found 353.9659.

Data in agreement with that reported previously.[12]

2-(Iodomethyl)-1-(*o*-tolylsulfonyl)aziridine, 2c



Chloramine-T.3H_2O (565 mg, 2.0 mmol), *N*-allyl sulfonamide **5c** (930 mg, 2.0 mmol) and iodine (504 mg, 2.0 mmol) in MeCN (12 mL) were submitted to **General Procedure 4** for 16 h. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9 → 3:17) gave α-iodoaziridine **2c** (466 mg, 1.38 mmol, 69%) as an off white solid.

R$_f$ 0.57 (Et_2O/pentane, 3:7) [UV, $KMnO_4$].

m.p. 38 – 41 °C.

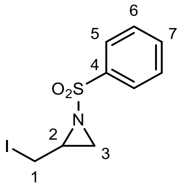
IR ν_{max}/cm^{-1} (film) 2981, 2360, 1320, 1160, 932, 871, 719, 607.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (1H, dd, *J* = 7.9, 1.4 Hz, ArH), 7.52 (1H, td, *J* = 7.5, 1.4 Hz, ArH), 7.40 – 7.29 (2H, m, ArH), 3.13 – 3.03 (3H, m, H1, H2), 2.95 – 2.89 (1H, m, H3), 2.81 (3H, s, H10), 2.20 (1H, dd, *J* = 3.0, 1.0 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 136.3, 134.1, 132.9, 129.8, 126.3, 41.1, 36.4, 21.0, 2.6.

HRMS (ESI$^+$) [M + H]$^+$ $C_{10}H_{13}O_2NIS$, requires 337.9706; found 337.9707.

2-(Iodomethyl)-3-(phenylsulfonyl)aziridine, 2d



Chloramine-T.3H_2O (1.35 g, 4.8 mmol), *N*-allyl sulfonamide **5d** (790 mg, 4.0 mmol), iodine (1.22 g, 4.8 mmol) in MeCN (20 mL) were subjected to **General Procedure 4** for 16 h. Purification by column chromatography (SiO_2, Et_2O/pentane, 3:7 → 1:1) gave α-iodoaziridine **2d** (600 mg, 1.86 mmol, 46%) as a white solid.

R_f 0.38 (EtOAc/pentane, 1:4) [UV, $KMnO_4$].

m.p. 61 – 62 °C [lit.[12] 60 – 68 °C].

IR ν_{max}/cm^{-1} (film) 1446, 1318, 1159, 1104, 919, 878, 732, 685.

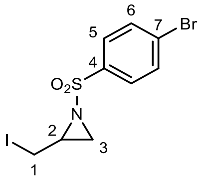
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.94 (2H, m, H5), 7.70 – 7.63 (1H, m, H7), 7.61 – 7.53 (2H, m, H6), 3.17 – 3.01 (3H, m, H2, H1), 2.92 – 2.84 (1H, m, H3), 2.21 – 2.19 (1H, m, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8, 134.0, 129.3, 128.4, 41.3, 36.4, 2.2.

HRMS (ESI$^+$) [M + Na]$^+$ $C_9H_{10}INO_2SNa$ requires 345.9369; found 345.9370.

Data in agreement with that reported previously.[12]

N-((*p*-Bromophenyl)sulfonyl)-2-(iodomethyl)aziridine, 2e



NaH (435 mg, 10.8 mmol), *N*-allyl sulfonamide **5e** (2.45 g, 8.90 mmol) and iodine (6.84 g, 26.9 mmol) in Et_2O (45 mL) were subjected to the conditions of **general procedure 5** for 19 h. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 1:4), and then recrystallisation (E_2O at –5 °C) gave α-iodoaziridine **2e** (1.44 g, 4.32 mmol, 40%) as orange crystals.

R_f 0.75 (EtOAc/pentane, 3:7) [UV, $KMnO_4$].

m.p. 85 – 87 °C (Et_2O) [lit.[12] 84 – 86 °C].

IR ν_{max}/cm^{-1} (film) 1574, 1325, 1157, 1089, 1068, 868, 749.

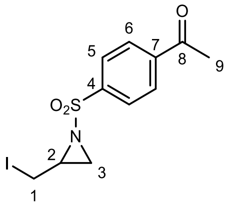
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.81 (2H, m, H5), 7.73 – 7.69 (2H, m, H6), 3.16 – 3.02 (3H, m, H1, H2), 2.88 (1H, d, *J* = 6.8 Hz, H3), 2.22 (1H, d, *J* = 3.9 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 136.9, 132.6, 130.0, 129.3, 41.6, 36.5, 2.1.

HRMS (ESI$^+$) $[M + H]^+$ $C_9H_{10}O_2N^{79}BrIS$ requires 401.8655; found 401.8656.

Data in agreement with that reported previously.[12]

1-(4-((2-(Iodomethyl)aziridine-1-yl)sulfonyl)phenyl)ethan-1-one, 2f



Chloramine-T.3H_2O (1.16 mg, 4.12 mmol), *N*-allyl sulfonamide **5f** (820 mg, 3.43 mmol) and iodine (1.05 g, 4.12 mmol) in MeCN (17 mL) were submitted to **General Procedure 4** for 16 h. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:4 → 3:7) gave α-iodoaziridine **2f** (217 mg, 0.59 mmol, 17%) as a white solid.

R$_f$ 0.33 (EtOAc/pentane, 3:7) [UV, $KMnO_4$].

m.p. 68 – 69 °C.

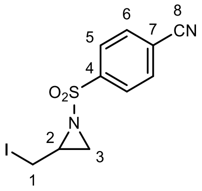
IR ν_{max}/cm^{-1} (film) 1689, 1398, 1328, 1296, 1161, 1092, 691, 643.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 – 8.02 (4H, m, H5, H6), 3.26 – 2.99 (3H, m, H1, H2), 2.92 (1H, d, *J* = 6.6 Hz, H2), 2.66 (3H, s, H9), 2.24 (1H, d, *J* = 4.2 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 196.8, 141.6, 141.1, 129.3, 129.0, 128.8, 127.6, 41.7, 36.6, 27.1, 10.3, 2.0.

HRMS (ESI$^+$) Not found.

4-((2-(Iodomethyl)aziridine-1-yl)sulfonyl)benzonitrile, 2g



Chloramine-T.3H_2O (533 mg, 1.89 mmol), *N*-allyl sulfonamide **5g** (424 mg, 1.89 mmol), iodine (480 mg, 1.89 mmol) in MeCN (11 mL) were subjected to **General Procedure 4** for 17 h. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:4 → 3:7) gave α-iodoaziridine **2g** (449 mg, 1.29 mmol, 68%) as a white solid.

R$_f$ 0.40 (Et_2O/pentane, 2:3) [UV, $KMnO_4$].

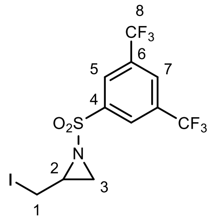
m.p. 75 – 77 °C [lit.[12] 59 – 60 °C].

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.08 (2H, m, H5), 7.90 – 7.84 (2H, m, H6), 3.22 – 3.11 (2H, m, H1, H2), 3.06 – 2.94 (2H, m, H1, H3), 2.32 – 2.25 (1H, m, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.1, 133.0, 129.2, 117.8, 117.3, 42.1, 36.8, 1.8.

Data in agreement with that reported previously.[12]

1-((3,5-Bis(trifluoromethyl)phenyl)sulfonyl)-2-(iodomethyl)aziridine, 2h



Chloramine-T.3H_2O (1.35 g, 4.8 mmol), *N*-allyl sulfonamide **5h** (1.33 g, 4.0 mmol) and iodine (1.22 g, 4.8 mmol) in MeCN (20 mL) were submitted to **General Procedure 4** for 16 h. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9) gave α-iodoaziridine **2h** (1.20 g, 2.61 mmol, 65%) as a colourless oil. Product was isolated as 90 % pure, as determined by ^{1}H NMR spectroscopy.

R_f 0.50 (Et_2O/pentane, 3:7) [UV, $KMnO_4$].

m.p. 37 – 38 °C.

IR ν_{max}/cm^{-1} (film) 1361, 1344, 1318, 1162, 1137, 1111, 697, 681.

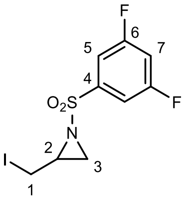
1H NMR (500 MHz, $CDCl_3$) δ 8.45 (2H, dq, *J* = 1.7, 0.6 Hz, H5), 8.15 (1H, app. tp, *J* = 1.5, 0.7 Hz, H7), 3.29 – 3.21 (1H, m, H2), 3.17 – 3.23 (1H, m, H1), 3.04 (1H, d, *J* = 7.1 Hz, H3), 2.98 (1H, dd, *J* = 10.4, 7.9 Hz, H1), 2.35 (1H, dd, *J* = 4.2, 0.7 Hz, H3).

^{13}C NMR (126 MHz, CDCl$_3$) δ 140.8, 133.2 (q, $^{2}J_{CF3}$ = 34.7 Hz), 128.9 (q, $^{3}J_{CF3}$ = 3.8 Hz), 127.6 (hept., $^{3}J_{CF3}$ = 3.6 Hz), 122.5 (q, $^{1}J_{CF3}$ = 273.4 Hz), 42.7, 37.1, 1.5.

^{19}F NMR (377 MHz, CDCl$_3$) δ – 63.0.

HRMS (ESI$^+$) [M + H]$^+$ $C_{11}H_9O_2NF_6IS$ requires 459.9297; found 459.9296.

1-((3,5-Difluorophenyl)sulfonyl)-2-(iodomethyl)aziridine, 2i



Chloramine-T.3H$_2$O (1.35 g, 4.8 mmol), *N*-allyl sulfonamide **5i** (930 mg, 4.0 mmol) and iodine (1.22 g, 4.8 mmol) in MeCN (20 mL) were submitted to **General Procedure 4** for 4 h. Purification by column chromatography (SiO$_2$, Et$_2$O/pentane 1:9) gave α-iodoaziridine **2i** (800 mg, 2.23 mmol, 56%) as an off white solid.

R$_f$ 0.40 (Et$_2$O/pentane, 3:7).

m.p. 100 – 103 °C.

IR ν_{max}/cm^{-1} (film) 3090, 2361, 1605, 1443, 1336, 1301, 1158, 1128, 990, 866, 700, 624.

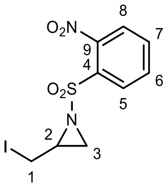
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.58 – 7.47 (2H, m, H5), 7.11 (1H, tt, *J* = 8.4, 2.3 Hz, H7), 3.22 – 3.09 (2H, m, H1, H2), 3.10 – 3.00 (1H, m, H1), 2.93 (1H, d, *J* = 6.7 Hz, H3), 2.27 (1H, d, *J* = 4.0 Hz, H3).

^{13}C NMR (101 MHz, CDCl$_3$) δ 162.9 (dd, $^{1,3}J_{CF}$ = 255.1, 11.5 Hz), 141.0, 112.2 (dd, $^{2,4}J_{CF}$ = 20.0, 8.6 Hz), 109.7 (t, $^{2}J_{CF}$ = 25.0 Hz), 42.0, 36.8, 1.7.

^{19}F NMR (377 MHz, CDCl$_3$) δ –105.2.

HRMS (ESI$^+$) [M + H]$^+$ $C_9H_9O_2NF_2IS$ requires 359.9361; found 359.9363.

2-(Iodomethyl)-1-((2-nitrophenyl)sulfonyl)aziridine, 2j



Chloramine-T.3H_2O (510 mg, 1.81 mmol), *N*-allyl sulfonamide **5j** (437 mg, 1.81 mmol, iodine (459 mg, 1.81 mmol) in MeCN (11 mL) were submitted to **General Procedure 4** for 20 h. Purification by column chromatography (SiO_2, Et_2O/pentane 3:7) gave α-iodoaziridine **2j** (91 mg, 0.24 mmol, 14%) as an off white solid. Product was isolated as 90 % pure, as determined by ^1H NMR spectroscopy.

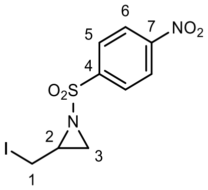
R$_f$ 0.31 (Et_2O/pentane, 3:2) [UV, $KMnO_4$].

^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (ddd, *J* = 6.8, 3.0, 1.7 Hz, H8), 7.84 – 7.73 (3H, m, H7, H6, H5), 3.43 – 3.31 (2H, m, H2, H1), 3.12 – 3.06 (1H, m, H3), 3.08 – 2.97 (1H, m, H1), 2.39 (1H, d, *J* = 3.3 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 148.8, 134.8, 132.4, 132.0, 131.6, 124.7, 42.9, 38.2, 2.2.

Data in agreement with that reported previously.[13]

2-(Iodomethyl)-1-((4-nitrophenyl)sulfonyl)aziridine, 2k



t-BuOCl (0.39 mL, 3.48 mmol), NaI (534 mg, 3.56 mmol) and *N*-allyl sulfonamide **5k** (701 mg, 2.90 mmol) in MeCN (18 mL) were subjected to **General Procedure 5** for 19 h. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9) gave α-iodoaziridine **2k**

(803 mg, 2.18 mmol, 75%) as an off white solid. Product was isolated as 85 % pure, as determined by ^{1}H NMR spectroscopy.

R$_f$ 0.47 (EtOAc/pentane, 1:4) [UV, $KMnO_4$].

m.p. 94 °C.

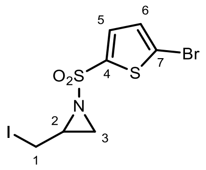
IR ν_{max}/cm^{-1} (film) 1530, 1350, 1311, 1164, 1090, 856, 752, 742, 694.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 – 8.38 (2H, m, H6), 8.23 – 8.15 (2H, m, H5), 3.27 – 3.11 (2H, m, H1, H2), 3.07 – 2.96 (2H, m, H2, H3), 2.30 (1H, d, *J* = 4.2 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 129.9, 129.7, 124.5, 42.3, 36.9, 1.8.

HRMS (ESI$^+$) $[M + H]^+$ $C_9H_9O_4N_2IS$ requires 368.9408; found 368.9402.

1-((5-Bromothiophen-2-yl)sulfonyl)-2-(iodomethyl)aziridine, 2l



Chloramine-T.3H_2O (1.28 g, 4.56 mmol), *N*-allyl sulfonamide **5l** (1.28 g, 4.56 mmol) and iodine (1.16 g, 4.56 mmol) in MeCN (27 mL) were subjected to **General Procedure 4** for 8 h. Purification by column chromatography (SiO_2, Et_2O/pentane 5:17) gave α-iodoaziridine **2l** (1.41 g, 3.46 mmol, 76%) as a yellow solid.

R$_f$ 0.24 (Et_2O/pentane, 1:4) [UV, $KMnO_4$].

m.p. 45 °C.

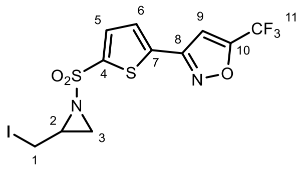
IR ν_{max}/cm^{-1} (film) 1400, 1330, 1155, 970, 914, 745, 702.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (1H, d, *J* = 4.0 Hz, H5/6), 7.12 (1H, d, *J* = 4.0 Hz, H5/6), 3.18 – 3.07 (3H, m, H1, H2), 2.92 – 2.85 (1H, m, H3), 2.27 (1H, d, *J* = 3.0 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 134.8, 130.7, 122.5, 42.1, 37.0, 1.8.

HRMS (ESI$^+$) $[M + H]^+$ $C_7H_8O_2N^{79}BrIS_2$, requires 407.8219; found 407.8220.

3-(5-((2-(Iodomethyl)aziridine-1-yl)sulfonyl)thiophen-2-yl)-5-(trifluoromethyl)isoxazole, 2m



Chloramine-T.3H_2O (368 mg, 1.31 mmol), *N*-allyl sulfonamide **5m** (444 mg, 1.31 mmol) and iodine (332 mg, 1.31 mmol) in MeCN (9 mL) were subjected to **General Procedure 4** for 20 h. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 1:4) gave α-iodoaziridine **2m** (291 mg, 0.63 mmol, 48%) as a white solid.

R$_f$ 0.68 (EtOAc/pentane, 1:4) [UV, $KMnO_4$].

m.p. 91 °C.

IR ν_{max}/cm^{-1} (film) 1552, 1335, 1315, 1187, 1157, 708, 619.

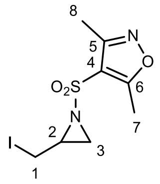
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (1H, d, *J* = 4.0 Hz, H5/6), 7.51 (1H, d, *J* = 4.0 Hz, H5/6), 6.99 (1H, q, J_{CF3} = 1.0 Hz, H9), 3.23 – 3.16 (1H, m, H2), 3.15 – 3.10 (2H, m, H1), 2.98 – 2.94 (1H, m, H3), 2.33 (1H, dd, *J* = 4.2, 0.8 Hz, H3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.3 (q, $^2J_{CF3}$ = 43.2 Hz), 156.8, 140.5, 136.7, 134.7, 128.2, 117.6 (q, $^1J_{CF3}$ = 270.8 Hz), 103.7 (q, $^3J_{CF3}$ = 2.2 Hz), 42.4, 37.1, 1.7.

^{19}F NMR (377 MHz, $CDCl_3$) δ –64.15.

HRMS (ESI$^+$) $[M + H]^+$ $C_{11}H_9O_3N_2F_3IS_2$ requires 464.9046; found 464.9047.

4-((2-(Iodomethyl)aziridine-1-yl)sulfonyl)-3,5-dimethylisoxazole, 2n



Chloramine-T.3H_2O (2.12 mg, 7.5 mmol), *N*-allyl sulfonamide **5n** (1.63 g, 7.5 mmol) and iodine (1.89 g, 7.5 mmol) in MeCN (9 mL) were subjected to **General Procedure 4** for 16 h. Purification by column chromatography (SiO_2, Et_2O/pentane 1:9) gave α-iodoaziridine **2n** (1.21 g, 3.54 mmol, 47%) as a white solid.

R$_f$ 0.33 (Et_2O/pentane, 2:3) [UV].

m.p. 45 – 46 °C.

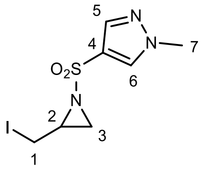
IR ν_{max}/cm^{-1} (film) 3658, 2981, 2888, 1594, 1406, 1373, 1328, 1186, 1121, 914, 745, 708, 647.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.23 (1H, dd, *J* = 10.2, 4.8 Hz, H1), 3.10 – 3.00 (1H, m, H2), 2.97 (1H, d, *J* = 10.2 Hz, H1), 2.97 – 2.92 (1H, m, H3), 2.67 (3H, s, H7), 2.50 (3H, s, H8), 2.29 (1H, d, *J* = 4.1 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.5, 158.5, 115.0, 41.6, 36.2, 13.0, 11.1, 2.1.

HRMS (ESI$^+$) [M + H]$^+$ $C_8H_{12}O_3N_2IS$, requires 342.9608; found 342.9609.

4-((2-(Iodomethyl)aziridine-1-yl)sulfonyl)-1-methyl-1H-pyrazole, 3o



Chloramine-T.3H_2O (664 mg, 2.35 mmol), *N*-allyl sulfonamide **5o** (473 mg, 2.35 mmol) and iodine (592 mg, 2.35 mmol) in MeCN (14 mL) were subjected to **General Procedure 4** for

19 h. Purification by column chromatography (SiO_2, EtOAc/pentane 3:7) gave α-iodoaziridine **2o** (647 mg, 1.98 mmol, 84%) as a colourless oil.

R$_f$ 0.33 (EtOAc/pentane, 1:1) [UV, $KMnO_4$].

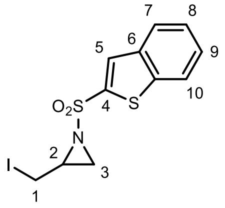
IR ν_{max}/cm^{-1} (film) 1524, 1319, 1156, 1119, 869, 713, 621.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (1H, s, H5), 7.86 (1H, s, H6), 3.97 (3H, s, H7), 3.14 – 3.07 (2H, m, H1), 3.10 – 2.99 (1H, m, H2), 2.81 (1H, d, *J* = 6.5 Hz, H3), 2.20 (1H, d, *J* = 4.1 Hz, H3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 139.8, 133.1, 119.7, 41.4, 39.9, 36.3, 2.4.

HRMS (ESI$^+$) [M + Na]$^+$ $C_7H_{10}O_2N_3INaS$, requires 349.9431; found 349.9432.

1-(Benzo[b]thiophen-2-ylsulfonyl)-2-(iodomethyl)aziridine, 2p



Chloramine-T.3H_2O (282 mg, 1.00 mmol), *N*-allyl sulfonamide **5p** (253 mg, 1.00 mmol), iodine (253 mg, 1.00 mmol) in MeCN (6 mL) were subjected to **General Procedure 4** for 16 h. Purification by column chromatography (SiO_2, Et_2O/pentane 1:9) gave α-iodoaziridine **4p** (297 mg, 0.78 mmol, 78%) as a white solid. Product was isolated as 90 % pure, as determined by ^{1}H NMR spectroscopy.

R$_f$ 0.73 (Et_2O/pentane, 4:6) [UV, $KMnO_4$]

m.p. 79 – 81 °C.

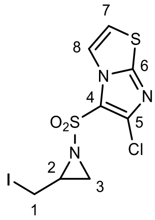
IR ν_{max}/cm^{-1} (film) 2360, 2342, 1504, 1332, 1152, 1022, 1000, 869, 700.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (1H, s, H5), 7.97 – 7.87 (2H, m, H7, H10), 7.58 – 7.44 (2H, m, H8, H9), 3.26 – 3.14 (2H, m, H1, H2), 3.11 – 3.01 (1H, m, H1), 2.99 – 2.90 (1H, m, H3), 2.33 – 2.22 (1H, m, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.8, 137.7, 137.5, 131.8, 128.0, 126.2, 125.8, 122.9, 42.0, 36.9, 1.9.

HRMS (ESI$^+$) $[M + Na]^+$ $C_{11}H_{10}O_2INNaS$, requires 401.9095; found 401.9090.

6-Chloro-5-((2-(iodomethyl)aziridine-1-yl)sulfonyl)imidazo[2,1-b]thiazole, 2q



Chloramine-T.3H_2O (432 mg, 1.53 mmol), *N*-allyl sulfonamide **5q** (424 mg, 1.53 mmol), iodine (385 mg, 1.53 mmol) in MeCN (10 mL) were subjected to **General Procedure 4** for 24 h. Purification by column chromatography (SiO_2, EtOAc/pentane 1:9 → 1:4) gave α-iodoaziridine **2q** (125 mg, 0.31 mmol, 20%) as a pale yellow oil. Product was isolated as 43% pure by ^{1}H NMR spectroscopy, where the impurity was identified as 4-(iodomethyl)-1,2-thiazetidine 1,1-dioxide **2q1.**

R_f 0.51 (EtOAc/pentane, 2:3) [UV, $KMnO_4$].

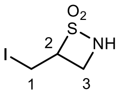
IR ν_{max}/cm^{-1} (film) 3265, 3119, 2361, 1455, 1438, 1343, 1274, 1257, 1184, 1144, 731, 636.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (1H, d, *J* = 4.5 Hz, H7/8), 7.13 (1H, d, *J* = 4.5 Hz, H7/8), 3.21 – 3.12 (2H, m, H1, H2), 3.09 – 3.03 (1H, m, H3), 3.01 – 2.90 (1H, m, H1), 2.34 (1H, dd, *J* = 4.2, 0.8 Hz, H3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.1, 140.4, 120.6, 116.7, 114.9, 41.6, 37.1, 1.9.

HRMS (ESI^+) $[M + H]^+$ $C_8H_8O_2N_3ClIS_2$, requires 403.8786; found 403.8787.

*4-(iodomethyl) – 1,2-thiazetidine 1,1-dioxide, **2q1***

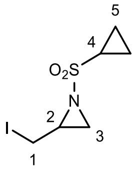


^{1}H NMR (500 MHz, $CDCl_3$) δ 4.87 (1H, app. dtd, *J* = 8.9, 6.5, 4.4 Hz, H2), 4.62 (1H, br. s, NH), 3.92 (1H, ddd, *J* = 12.4, 7.8, 6.5 Hz, H3), 3.51 (1H, dd, *J* = 10.4, 4.4 Hz, H1), 3.51 – 3.41 (1H, m, H3), 3.35 (1H, dd, *J* = 10.4, 8.9 Hz, H1).

^{13}C NMR (126 MHz, $CDCl_3$) δ 81.1, 49.0, 2.9.

HRMS (ESI^+) Not found.

1-(Cyclopropylsulfonyl)-2-(iodomethyl)aziridine, 2r



Chloramine-T.3H_2O (1.35 g, 4.8 mmol), *N*-allyl sulfonamide **5r** (647 mg, 4.0 mmol), iodine (1.22 g, 4.8 mmol) in MeCN (20 mL) were subjected to **General Procedure 4** for 19 h. Purification by column chromatography (SiO_2, Et_2O/pentane 1:9 → 1:4) gave α-iodoaziridine **2r** (550 mg, 1.92 mmol, 48%) as a white solid.

R_f 0.60 (Et_2O/pentane, 3:7) [$KMnO_4$].

m.p. 74 – 76°C.

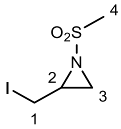
IR ν_{max}/cm^{-1} (film) 2360, 2342, 1342, 1310, 1196, 1149, 877, 834.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.21 (1H, dd, *J* = 10.4, 6.0 Hz, H1), 3.14 (1H, dd, *J* = 10.4, 7.4 Hz, H1), 3.07 – 2.96 (1H, m, H2), 2.80 (1H, d, *J* = 6.7 Hz, H3), 2.65 (1H, tt, *J* = 8.1, 4.8 Hz, H4), 2.22 (1H, d, *J* = 4.1 Hz, H3), 1.34 – 1.23 (2H, m, H5), 1.19 – 1.07 (2H, m, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 40.8, 35.7, 29.5, 6.3, 5.8, 3.0.

HRMS (ESI$^+$) $[M + Na]^+$ $C_6H_{10}O_2NINaS$, requires 309.9369; found 309.9370.

2-(Iodomethyl)-3-(methylsulfonyl)aziridine, 2s



NaH (207 mg, 5.17 mmol), *N*-allyl sulfonamide **5s** (5.12 g, 3.79 mmol), iodine (3.90 g, 15.4 mmol) in Et_2O (26 mL) were subjected to **General Procedure 3** for 4 h. Purification by column chromatography (SiO_2, EtOAc/pentane 1:4) gave α-iodoaziridine **2s** (984 mg, 3.83 mmol, 74%) as an orange solid.

R$_f$ 0.45 (EtOAc/pentane, 3:7) [$KMnO_4$].

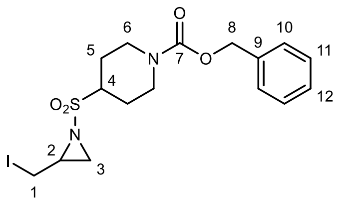
m.p. 51 ° C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.29 – 3.21 (1H, m, H1), 3.18 (3H, s, H4), 3.13 – 3.05 (2H, m, H1, H2), 2.87 – 2.84 (1H, m, H3), 2.25 – 2.23 (1H, m, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 41.4, 40.3, 35.8, 2.8.

Data in agreement with that reported previously.[14]

Benzyl 4-((2-(iodomethyl)aziridin-1-yl)sulfonyl)piperidine-1-carboxylate, 2t



Chloramine-T.3H_2O (282 mg, 1.00 mmol), *N*-allyl sulfonamide **5t** (338 mg, 1.00 mmol), iodine (253 mg, 1.00. mmol) in MeCN (6 mL) were subjected to **General Procedure 4** for 19 h. Purification by column chromatography (SiO_2, EtOAc/pentane 3:7) gave α-iodoaziridine **2t** (133 mg, 0.29 mmol, 29%) as a colourless oil.

R_f 0.23 (EtOAc/pentane, 2:3) [UV, PMA].

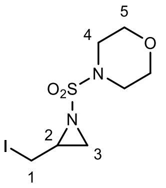
IR ν_{max}/cm^{-1} (film) 2980, 2360, 2342, 1697, 1431, 1318, 1279, 1217, 1119, 699.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.29 (5H, m, H10 – 12), 5.14 (2H, s, H8), 4.36 (2H, br. s, H6), 3.33 (1H, tt, *J* = 11.9, 3.7 Hz, H4), 3.23 – 3.10 (2H, m, H1), 3.12 – 3.01 (1H, m, H2), 2.85 (1H, d, *J* = 6.6 Hz, H3), 2.85 (2H, obsc. br. s, H6), 2.33 (1H, br. d, *J* = 13.3 Hz, H5), 2.23 (1H, d, *J* = 4.2 Hz, H3), 2.23 (1H, obsc. m, H5), 1.96 – 1.78 (2H, m, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.1, 136.6, 128.7, 128.3, 128.2, 67.6, 59.4, 43.0, 42.8, 40.5, 36.1, 26.2, 25.2, 3.0.

HRMS (ESI$^+$) $[M + Na]^+$ $C_{16}H_{21}O_4N_2INaS$ requires 487.0159; found 487.0158.

4-((2-(Iodomethyl)aziridin-1-yl)sulfonyl)morpholine, 2u



Chloramine-T.3H_2O (564 mg, 2.0 mmol), *N*-allyl sulfonamide **5u** (659 mg, 2.0 mmol), iodine (505 mg, 2.0 mmol) in MeCN (12 mL) were subjected to **General Procedure 4** for 19 h.

Purification by column chromatography (SiO_2, Et_2O/pentane 4:6 → 9:11) gave α-iodoaziridine **2u** (135 mg, 0.41 mmol, 20%) as a colourless oil.

R$_f$ 0.51 (Et_2O/pentane, 6:4) [$KMnO_4$].

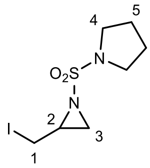
IR ν_{max}/cm^{-1} (film) 2981, 2889, 1382, 1348, 1262, 1162, 1113, 319, 744.

^{1}H NMR (400 MHz, $CDCl_3$) 3.44 – 3.33 (4H, m, H4, H5), 3.22 (1H, dd, *J* = 10.4, 6.5 Hz, H1), 3.10 (1H, dd, *J* = 10.4, 6.7 Hz, H1), 2.97 (1H, app. qd, *J* = 6.7, 4.1 Hz, H2), 2.72 (1H, d, *J* = 6.7 Hz, H3), 2.18 (1H, d, *J* = 4.2 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 66.3, 46.9, 40.2, 36.7, 2.9.

HRMS (ESI$^+$) [M + H]$^+$ $C_7H_{14}O_3N_2IS$ requires 332.9764; found 332.9765.

1-((2-(Iodomethyl)aziridin-1-yl)sulfonyl)pyrrolidine, 2v



t-BuOCl (0.47 mL, 4.16 mmol), NaI (624 mg, 4.16 mmol) and *N*-allyl sulfonamide **5v** (659 mg, 3.47 mmol) in MeCN (20 mL) were subjected to **General Procedure 5** for 24 h. Purification by column chromatography (SiO_2, Et_2O/pentane 1:9 → 3:7) gave α-iodoaziridine **2v** (31 mg, 0.10 mmol, 3%) as a pale-yellow oil.

R$_f$ 0.43 (Et_2O/pentane, 3:7) [$KMnO_4$].

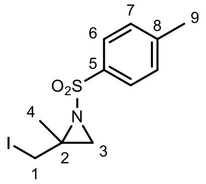
IR ν_{max}/cm^{-1} (film) 2981, 2888, 1382, 1344, 1251, 1239, 1156, 1078, 946.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.56 – 3.43 (4H, m, H4), 3.20 – 3.09 (2H, m, H1, H2), 3.02 – 2.95 (1H, m, H1), 2.73 (1H, d, *J* = 6.7 Hz, H3), 2.14 (1H, d, *J* = 4.0 Hz, H3), 2.04 – 1.93 (4H, m, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 48.9, 40.2, 36.3, 25.9, 3.7.

HRMS (ESI$^+$) $[M + H]^+$ $C_7H_{14}O_2N_2IS$ requires 316.9815; found 316.9815.

2-(Iodomethyl)-2-methyl-1-tosylaziridine, 2w



Chloramine-T.3H_2O (1.35 g, 4.80 mmol), *N*-allyl sulfonamide **5w** (1.13 g, 4.00 mmol), iodine (1.22 g, 4.80 mmol) in anhydrous MeCN (20 mL) were subjected to **General Procedure 4** for 19 h. Purification by column chromatography (SiO_2, Et_2O/pentane 1:9 → 1:4) gave α-iodoaziridine **2w** (1.20 g, 3.42 mmol, 85%) as an off white solid.

R_f 0.61 (Et_2O/pentane, 3:7) [UV, $KMnO_4$].

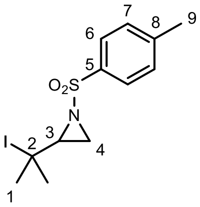
m.p. 73 – 74 °C [lit.[14] 76 °C]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (2H, d, *J* = 8.2 Hz, H6), 7.33 (2H, d, *J* = 8.2 Hz, H7), 3.36 – 3.29 (2H, m, H1), 2.77 (1H, d, *J* = 0.9 Hz, H3), 2.44 (3H, s, H9), 2.40 (1H, s, H3), 1.82 (3H, s, H4).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.4, 137.4, 129.7, 127.7, 49.8, 43.0, 21.8, 18.6, 12.1.

Data in agreement with that reported previously.[14]

2-(2-Iodopropan-2-yl)-1-tosylaziridine, 2x



According to a modified literature procedure.[14] *t*-BuOK (672 mg, 6.00 mmol) was added to a solution of *N*-allyl sulfonamide **5x** (957 mg, 4.00 mmol) in anhydrous toluene (20 mL). The reaction was stirred for 30 min at room temperature and then iodine (3.05 g, 12.0 mmol) was added and stirring was continued for 15 min. The reaction mixture was quenched by addition of $Na_2S_2O_3$ (sat. aq., 10 mL) and extracted with Et_2O (40 mL × 3). The combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo.* Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9) gave α-iodoaziridine **2x** (920 mg, 2.56 mmol, 64%) as a white solid.

R_f 0.48 (Et_2O/pentane, 1:3) [UV].

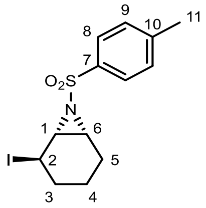
m.p. 61 – 62 °C [lit.[14] 63 °C].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.79 (2H, m, H6), 7.38 – 7.31 (2H, m, H7), 3.22 (1H, dd, *J* = 7.0, 4.5 Hz, H3), 2.71 (1H, dd, *J* = 7.0, 0.9 Hz, H4), 2.44 (3H, s, H9), 2.33 (1H, dd, *J* = 4.5, 0.9 Hz, H4), 1.76 (3H, s, H1), 1.70 (3H, s, H1).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1, 134.7, 130.0, 128.6, 51.4, 40.6, 35.5, 32.9, 31.7, 21.9.

Data in agreement with that reported previously.[15]

Trans-2-Iodo-7-tosyl-7-azabicyclo[4.1.0]heptane, 2y



According to a modified literature procedure.[14] *t*-BuOK (336 mg, 3.00 mmol) was added to a solution of *N*-allyl sulfonamide **5y** (502 mg, 2.00 mmol) in anhydrous toluene (10 mL). The reaction was stirred for 30 min at room temperature and then iodine (1.52 g, 6.00 mmol) was added and stirring was continued for 1 h. The reaction mixture was quenched by addition of $Na_2S_2O_3$ (sat. aq., 10 mL) and extracted with Et_2O (20 mL × 3). The combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo.* Purification by column chromatography (SiO_2, Et_2O/pentane, 1:4) gave α-iodoaziridine **2y** (500 mg, 1.30 mmol, 66%) as a white solid.

R_f 0.50 (Et_2O/pentane, 3:7) [UV, $KMnO_4$].

m.p. 58 – 60 °C [lit.[14] 63 °C].

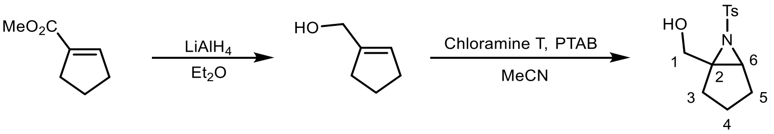
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.77 (2H, m, H8), 7.38 – 7.33 (2H, m, H9), 4.45 (1H, td, *J* = 4.4, 1.6 Hz, H2), 3.46 (1H, ddd, *J* = 6.8, 1.6, 0.8 Hz, H1), 3.09 (1H, ddd, *J* = 6.8, 5.7, 1.1 Hz, H6), 2.45 (3H, s, H11), 2.04 – 1.89 (1H, m, H5), 1.88 – 1.76 (2H, m, H3, H5), 1.76 – 1.66 (1H, m, H3), 1.64 – 1.50 (1H, m, H4), 1.46 – 1.34 (1H, m, H4).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 135.2, 129.9, 127.9, 46.2, 40.2, 29.9, 24.9, 21.8, 21.5, 17.7.

Data in agreement with that reported previously.[14]

1-(Iodomethyl)-6-tosyl-6-azabicyclo[3.1.0]hexane, 2z

*(6-Tosyl-6-azabicyclo[3.1.0]hexan-1-yl)methanol, **2z₁**, Steps 1 & 2:*



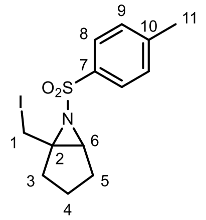
$LiAlH_4$ (4.0 M in Et_2O, 2.0 mL, 7.90 mmol) was added dropwise to a solution of methyl cyclopent-1-ene-1-carboxylate (1.00 g, 7.90 mmol) in anhydrous Et_2O (20 mL) at 0 °C. The reaction mixture was stirred for 3 h at 0 °C then quenched by addition of H_2O (0.3 mL), NaOH (15% aq., 0.3 mL), and then H_2O (0.9 mL). The phases were separated and the aqueous phase was extracted with Et_2O (30 mL × 2). The combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo*. The crude product was used directly in the next step.

According to a modified literature procedure.[16] The crude allylic alcohol (7.90 mmol) was diluted in anhydrous MeCN (40 mL) at room temperature. Chloramine-T.3H_2O (1.98 g, 8.70 mmol) and trimethylphenylammonium tribromide (PTAB) (300 mg, 0.80 mmol) were added sequentially and the reaction mixture was stirred for 16 h at room temperature. The mixture was poured onto H_2O (50 mL) and extracted with EtOAc (50 mL × 3), the combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:4 → 1:1) gave α-aziridinyl alcohol **2z₁** (950 mg, 3.60 mmol, 45%, 2 steps) as a colourless oil.

R_f 0.15 (EtOAc/pentane, 3:7).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.77 (2H, m, ArH), 7.36 – 7.28 (2H, m, ArH), 4.95 (1H, br. s, OH), 4.38 (1H, dd, *J* = 13.5, 4.3 Hz, H1), 4.16 (1H, dd, *J* = 13.5, 10.4 Hz, H1), 3.51 (1H, d, *J* = 2.2 Hz, H6), 3.05 (1H, dd, *J* = 10.4, 4.3 Hz, OH), 2.43 (3H, s, CH_3), 2.37 (1H, dd, *J* = 13.3, 7.9 Hz, CH_2), 1.86 – 1.77 (1H, m, CH_2), 1.72 – 1.56 (3H, m, CH_2), 1.44 – 1.31 (1H, m, CH_2).

*1-(Iodomethyl)-6-tosyl-6-azabicyclo[3.1.0]hexane, **2z**, Step 3:*



DIAD (0.84 mL, 4.00 mmol), PPh_3 (1.05 g, 4.00 mmol), MeI (0.26 mL, 4.00 mmol) and α-aziridinyl alcohol **2z₁** (900 mg, 3.37 mmol) in toluene (40 mL) were submitted to **General Procedure 6** for 16 h. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:4) gave α-iodoaziridine **2z** (1.50 g, 5.90 mmol, 66%) as an off white solid.

R$_f$ 0.21 (EtOAc/pentane, 1:19) [UV].

m.p. 98 – 100 °C.

IR ν_{max}/cm^{-1} (film) 2957, 2925, 2361, 2341, 1598, 1319, 1155.

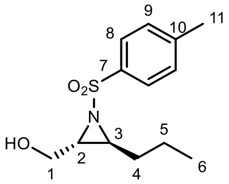
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (2H, d, *J* = 8.3 Hz, H8), 7.30 (2H, d, *J* = 8.3 Hz, H9), 4.18 (1H, d, *J* = 10.6 Hz, H1), 3.84 (1H, d, *J* = 10.6, Hz, H1), 3.41 (1H, d, *J* = 2.2 Hz, H6), 2.43 (3H, s, H11), 2.16 – 2.03 (2H, m, H3), 1.83 – 1.58 (3H, m, H4, H5), 1.52 – 1.40 (1H, m, H4).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.1, 138.0, 129.7, 127.3, 61.2, 54.5, 32.2, 28.1, 21.8, 20.5, 2.3.

HRMS (ESI$^+$) [M + H]$^+$ $C_{13}H_{17}O_2NIS$, requires 378.0019; found 378.0021.

trans-2-(Iodomethyl)-3-propyl-1-tosylaziridine, 2aa

trans-3-Propyl-1-tosylaziridin-2-yl)methanol, ***2aa1*** *Step 1:*



According to a modified literature procedure.[16] Chloramine-T.3H_2O (2.25 g, 9.90 mmol) was added to a solution of *trans*-2-hexanol (1.1 mL, 9.00 mmol) in anhydrous MeCN (45 mL) in a flame dried flask at room temperature. PTAB (339 mg, 0.90 mmol) was added and the reaction mixture was stirred for 16 h at room temperature. The reaction mixture was poured into H_2O (40 mL) and extracted with EtOAc (50 mL × 3). The combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:1 → 7:3) gave α-aziridinyl alcohol **2aa1** (1.60 g, 5.90 mmol, 66%) as a colourless oil.

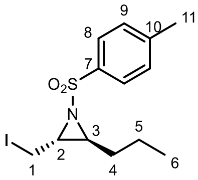
R_f 0.33 (Et_2O/pentane, 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.78 (2H, m, H8), 7.40 – 7.25 (2H, m, H9), 4.10 (1H, ddd, *J* = 13.2, 9.3, 2.6 Hz, H1), 3.98 – 3.80 (1H, m, H1), 3.02 – 2.88 (2H, m, H2, H3), 2.65 (1H, dd, *J* = 9.3, 5.1 Hz, OH), 2.45 (3H, s, H11), 1.69 – 1.48 (2H, m, H4), 1.29 (2H, app. dq, *J* = 14.5, 7.5 Hz, H5), 0.87 (t, *J* = 7.2 Hz, H6).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.4, 137.4, 129.8, 127.5, 61.1, 51.9, 46.4, 32.4, 21.8, 20.5, 13.7.

Data in agreement with that reported previously.[16]

*Trans-2-(Iodomethyl)-3-propyl-1-tosylaziridine, **2aa**, step 2:*



DIAD (0.76 mL, 3.60 mmol), PPh_3 (943 mg, 3.60 mmol), MeI (0.23 mL, 3.60 mmol) and α-aziridinyl alcohol **2aa1** (807 mg, 3.00 mmol) in anhydrous toluene (40 mL) were submitted to **General Procedure 6** for 16 h. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:19 → 1:9) gave α-iodoaziridine **2aa** (800 mg, 2.11 mmol, 70%) as a yellow oil.

R_f 0.33 (Et_2O/pentane, 1:17).

m.p. 42 °C.

IR ν_{max}/cm^{-1} (film) 2960, 2929, 2872, 2360, 2341, 1597, 1457, 1430, 1321, 1156, 920, 694.

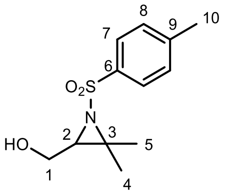
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.82 (2H, m, H9), 7.34 – 7.30 (2H, m, H8), 3.46 – 3.35 (2H, m, H1), 3.04 (1H, ddd, *J* = 9.0, 5.5, 4.3 Hz, H2), 2.74 (1H, ddd, *J* = 7.3, 6.0, 4.3 Hz, H3), 2.44 (3H, s, H11), 1.79 – 1.60 (2H, m, H4), 1.45 – 1.34 (2H, m, H5), 0.92 (3H, t, *J* = 7.4 Hz, H6).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.4, 137.5, 129.7, 127.7, 51.6, 49.8, 31.9, 21.8, 20.8, 13.9, 1.8.

HRMS (ESI$^-$) [M - H]$^-$ $C_{13}H_{17}O_2NIS$ requires 378.0019; found 378.0021.

3-(Iodomethyl)-2,2-dimethyl-1-tosylaziridine, 2ab

(3,3-Dimethyl-1-tosylaziridin-2-yl)methanol, ***2ab1****, Step 1:*



According to a modified literature procedure.[16] Chloramine-T.3H_2O (2.25 g, 9.90 mmol) was added to a solution of 3-methylbut – 2-en – 1-ol (1.1 mL, 9.00 mmol) in anhydrous MeCN (45 mL) in a flame dried flask at room temperature. PTAB (339 mg, 0.90 mmol) was added and the reaction mixture was stirred for 16 h at room temperature. The reaction mixture was poured into H_2O (30 mL) and extracted with EtOAc (50 mL × 3). The combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:1) gave α-aziridinyl alcohol **2ab1** (1.50 g, 5.90 mmol, 66%) as a white solid.

R_f 0.22 (EtOAc/pentane, 1:1).

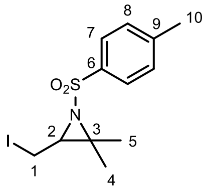
m.p. 60 – 65 °C [lit.[16] 63 – 64 °C].

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.74 (2H, m, H7), 7.39 – 7.25 (2H, m, H8), 3.74 (1H, ddd, *J* = 11.9, 7.6, 5.1 Hz, H1), 3.51 (1H, ddd, *J* = 11.9, 7.3, 4.8 Hz, H1), 3.13 (1H, dd, *J* = 7.3, 5.1 Hz, H2), 2.43 (3H, s, H10), 1.73 (3H, s, H4/5), 1.33 (3H, s, H4/5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.1, 138.0, 129.8, 127.5, 60.5, 52.5, 52.1, 21.7, 21.5, 21.3.

Data in agreement with that reported previously.[16]

*3-(Iodomethyl)-2,2-dimethyl-1-tosylaziridine, **2ab**, Step 2:*



DIAD (0.76 mL, 3.60 mmol), PPh_3 (943 mg, 3.60 mmol), MeI (0.23 mL, 3.60 mmol) and α-aziridinyl alcohol **2ab1** (766 mg, 3.00 mmol) in toluene (40 mL) were submitted to **General Procedure 6** for 16 h. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:19) gave α-iodoaziridine **2ab** (750 mg, 2.05 mmol, 68%) as a white solid.

R_f 0.38 (EtOAc/pentane, 1:9).

m.p. 86 – 88 °C.

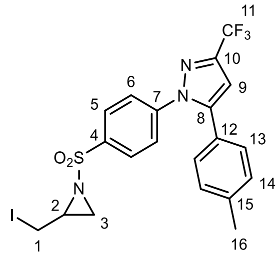
IR ν_{max}/cm^{-1} (film) 2967, 2926, 2359, 2343, 1558, 1458, 1322, 1156.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.80 (2H, m, H7), 7.34 – 7.27 (2H, m, H8), 3.28 (1H, dd, *J* = 8.0, 6.6 Hz, H1), 3.09 (1H, dd, *J* = 10.3, 6.6 Hz, H1), 2.95 (1H, dd, *J* = 10.3, 8.0 Hz, H2), 2.43 (3H, s, H10), 1.73 (3H, s, H4/5), 1.32 (3H, s, H4/5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.1, 138.2, 129.6, 127.8, 54.1, 52.7, 21.7, 21.2, 20.4, 0.1.

HRMS (ESI$^+$) $[M + H]^+$ $C_{12}H_{17}O_2NIS$ requires 366.0019; found 366.0020.

1-(4-((2-(Iodomethyl)aziridine-1-yl)sulfonyl)phenyl)-5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazole, 2ac



Chloramine-T.3H_2O (107 mg, 0.38 mmol), *N*-allyl sulfonamide **5ac** (135 mg, 0.32 mmol), iodine (97 mg, 0.38 mmol) in MeCN (2.5 mL) were subjected to **General Procedure 4** for 19 h. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:4 → 1:3) gave α-iodoaziridine **4ac** (125 mg, 0.23 mmol, 72%) as a white solid.

R_f 0.40 (Et_2O/pentane, 3:7).

m.p. 92 °C.

IR ν_{max}/cm^{-1} (film) 1498, 1333, 1237, 1162, 1135, 1096, 975, 746, 636.

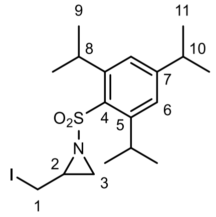
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.93 (2H, m, H5), 7.55 – 7.50 (2H, m, H6), 7.21 – 7.16 (2H, m, H14), 7.14 – 7.09 (2H, m, H13), 6.74 (1H, q, $^3J_{CF3}$ = 0.5 Hz, H9), 3.16 – 3.08 (2H, m, H1), 3.06 – 2.99 (1H, m, H2), 2.93 – 2.89 (1H, m, H3), 2.39 (3H, s, H16), 2.28 – 2.22 (1H, m, H3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.5, 144.4 (q, $^2J_{CF3}$ = 38.6 Hz), 143.7, 140.0, 137.0, 123.0, 129.6, 129.0, 125.9, 125.5, 121.2 (q, $^1J_{CF3}$ = 269.3 Hz), 106.7 (q, $^3J_{CF3}$ = 2.0 Hz), 41.9, 36.5, 21.5, 2.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ –62.5.

HRMS (ESI$^+$) $[M + H]^+$ $C_{20}H_{18}O_2N_3IS$ requires 548.0111; found 548.0111.

2-(Iodomethyl)-1-((2,4,6-triisopropylphenyl)sulfonyl)aziridine, 2ad



Chloramine-T.3H_2O (1.13 g, 4.00 mmol), *N*-allyl sulfonamide **5ad** (1.29 g, 4.00 mmol), iodine (1.01 g, 4.00 mmol) in MeCN (24 mL) were subjected to **General Procedure 4** for 19 h. Purification by column chromatography (SiO_2, Et_2O/pentane 1:19 → 1:9) gave α-iodoaziridine **2ad** (939 mg, 2.09 mmol, 52%) as an off white solid.

R_f 0.44 (Et_2O/pentane, 1:9).

m.p. 55 – 57 °C.

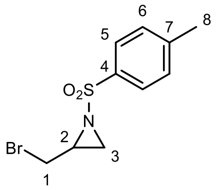
IR ν_{max}/cm^{-1} (film) 2960, 2361, 1600, 1460, 1320, 1162, 1154, 939, 697.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (2H, s, H6), 4.32 (2H, hept., *J* = 6.8 Hz, H8), 3.13 – 3.04 (3H, m, H1, H2), 2.97 – 2.85 (2H, m, H3, H10), 2.17 (1H, dd, *J* = 2.5, 1.2 Hz, H3), 1.28 (6H, d, *J* = 6.8 Hz, H9), 1.28 (6H, d, *J* = 6.7 Hz, H9), 1.25 (6H, d, *J* = 6.9 Hz, H11).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 151.4, 131.2, 124.0, 40.7, 35.7, 34.4, 29.9, 25.1, 25.0, 23.7, 2.8.

HRMS (ESI$^+$) $[M + H]^+$ $C_{18}H_{29}O_2NIS$ requires 450.0958; found 450.0955.

2-(Bromomethyl)-1-tosylaziridine, 2ae



According to a modified literature procedure.[17] A solution of bromine (0.10 mL, 2.00 mmol) in $CHCl_3$ (2 mL) was added dropwise to a solution of *N*-allyl-sulfonamide **5a** (422 mg, 2.00 mmol) in $CHCl_3$ (4 mL) at 0 °C. The mixture was stirred for 10 min and then left to stand at 0 °C for 1 h and then concentrated *in vacuo* at room temperature. The residue was re-diluted in EtOH (5 mL) and NaOH (0.1 N in EtOH, 25 mL, 2.50 mmol) was added at room temperature and the mixture was stirred for 15 min. The mixture was poured into $Na_2S_2O_3$ (sat. aq., 10 mL) and extracted with CH_2Cl_2 (10 mL × 3), washed with brine (20 mL), dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9) gave α-bromoaziridine **2ae** (237 g, 1.04 mmol, 52%) as a pale orange oil.

R_f 0.29 (Et_2O/pentane, 1:9) [UV, PMA].

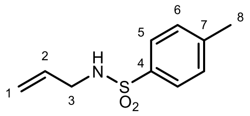
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* = 8.4 Hz, H5), 7.35 (2H, d, *J* = 8.0 Hz, H6), 3.33 – 3.23 (2H, m, H1), 3.13- 3.05 (1H, m, H2), 2.81 (1H, d, *J* = 6.8 Hz, H3), 2.45 (3H, s, H8), 2.23 (1H, d, *J* = 4.2 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1, 134.6, 129.9, 128.4, 40.0, 34.4, 30.7, 21.8.

Data in agreement with that reported previously.[18]

S2.4 *N*-Allyl Sulfonamides

N-Allyl-N-methylbenzenesulfonamide, 5a



NEt$_3$ (2.8 mL, 20.0 mmol), *N*-allyl amine (1.1 mL, 15.0 mmol) and 4-methylbenzenesulfonyl chloride (1.91 g, 10.0 mmol) in CH$_2$Cl$_2$ (50 mL) were subjected to the conditions of **general procedure 9A** for 90 min. *N*-Allyl-sulfonamide **5a** (2.20 g, 10.4 mmol, quant.) was obtained as a white solid.

R$_f$ 0.63 (EtOAc/pentane, 3:7) [UV, KMnO$_4$].

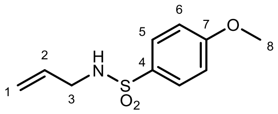
m.p. 59 – 60 °C [lit.[8] 63 °C].

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.77 – 7.74 (2H, m, H5), 7.34 – 7.29 (2H, m, H6), 5.72 (1H, ddt, *J* = 17.1, 10.2, 5.8 Hz, H2), 5.17 (1H, dtd, *J* = 17.1, 1.7, 1.1 Hz, H1), 5.10 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 4.44 (1H, br. s, NH), 3.61 – 3.57 (2H, m, H3), 2.43 (3H, s, H8).

^{13}C NMR (101 MHz, CDCl$_3$) δ 143.7, 137.2, 133.2, 129.9, 127.3, 117.9, 45.9, 21.7.

Data in agreement with that reported previously.[8]

N-Allyl-N-methoxybenzenesulfonamide, 5b



NEt$_3$ (1.40 mL, 10.00 mmol), *N*-allyl amine (0.56 mL, 7.50 mmol) and 4-methoxybenzenesulfonyl chloride (1.03 g, 5.00 mmol) in CH$_2$Cl$_2$ (25 mL) were subjected to the conditions of **general procedure 9A** for 2 h. *N*-Allyl-sulfonamide **5b** (966 mg, 4.38 mmol, 88%) was obtained as a pale-yellow oil.

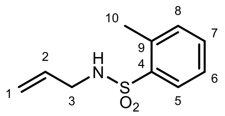
R$_f$ 0.49 (EtOAc/pentane, 3:7) [UV, $KMnO_4$].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.76 (2H, m, H5), 7.02 – 6.94 (2H, m, H6), 5.72 (1H, ddt, *J* = 17.1, 10.2, 5.8 Hz, H2), 5.16 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.10 (1H, app. dq, *J* = 10.3, 1.3 Hz, H1), 4.44 (1H, br. t, *J* = 6.1 Hz, NH), 3.87 (3H, s, H8), 3.58 (2H, app. tt, *J* = 6.0, 1.5 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 133.2, 131.7, 129.4, 117.8, 114.4, 55.8, 45.9.

Data in agreement with that reported previously.[19]

N-Allyl-2-methylbenzenesulfonamide, 5c



NEt_3 (0. 56 mL, 4.00 mmol), *N*-allyl amine (0.23 mL, 3.00 mmol) and *o*-tosyl chloride (0.29 mL, 2.00 mmol, 97% purity) in CH_2Cl_2 (10.0 mL) were subjected to the conditions of **general procedure 9A** for 2 h. *N*-Allyl-sulfonamide **5c** (534 mg, 2.52 mmol, quant.) was obtained as a colourless oil.

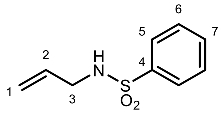
R$_f$ 0.32 (Et_2O/pentane, 3:7) [UV, $KMnO_4$].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (1H, dd, *J* = 8.2, 1.4 Hz, H5), 7.47 (1H, td, *J* = 7.5, 1.4 Hz, H7), 7.35 – 7.29 (2H, m, H8, H6), 5.72 (1H, ddt, *J* = 17.1, 10.3, 6.0 Hz, H2), 5.17 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.11 (1H, app. dq, *J* = 10.3, 1.3 Hz, H1), 4.45 (1H, br. s, NH), 3.59 (2H, tt, *J* = 6.0, 1.5 Hz, H3), 2.66 (3H, s, H10).

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.0, 137.2, 133.2, 133.0, 132.7, 129.7, 126.3, 118.0, 45.8, 20.5.

Data in agreement with that reported previously.[20]

N-Allylbenzenesulfonamide, 5d



NEt_3 (2.8 mL, 20.0 mmol), *N*-allyl amine (1.4 mL, 15.0 mmol) and 2-benzenesulfonyl chloride (1.3 mL, 10.0 mmol) in CH_2Cl_2 (50 mL) were subjected to the conditions of **general procedure 9A** for 10 min. *N-Allyl*-sulfonamide **5d** (2.20 g, 11.2 mmol, quant.) was obtained as a colourless oil.

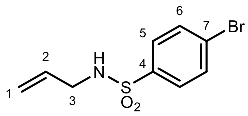
R$_f$ 0.30 (Et_2O/pentane, 1:1) [UV, $KMnO_4$].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.86 (2H, m, H5), 7.60 – 7.56 (1H, m, H7), 7.54 – 7.49 (2H, m, H6), 5.71 (1H, ddt, *J* = 17.1, 10.2, 5.8 Hz, H2), 5.15 (1H, app. dq, *J* = 17.1, 1.6 Hz, H1), 5.08 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 4.84 (1H, br. t, *J* = 6.4 Hz, NH), 3.59 (1H, app. tt, *J* = 6.0, 1.5 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.1, 133.0, 132.8, 129.2, 127.2, 117.8, 45.9.

Data in agreement with that reported previously.[21, 22]

N-Allyl-*N*-bromobenzenesulfonamide, 5e



NEt_3 (1.38 mL, 9.90 mmol), *N*-allyl amine (0.74 mL, 9.90 mmol) and 4-bromobenzenesulfonyl chloride (2.30 g, 9.00 mmol) in CH_2Cl_2 (36 mL) were subjected to the conditions of **general procedure 9B** for 18 h. *N-Allyl*-sulfonamide **5e** (2.45 g, 8.91 mmol, 99%) as an off white solid.

R$_f$ 0.55 (EtOAc/pentane, 3:7) [UV, $KMnO_4$].

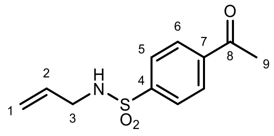
m.p. 57 – 58 °C [lit[23] 58 – 60 °C].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.70 (2H, m, H6), 7.70 – 7.62 (2H, m, H5), 5.72 (1H, ddt, *J* = 17.1, 10.2, 5.8 Hz, H2), 5.17 (1H, app. dq, *J* = 17.2, 1.5 Hz, H1), 5.12 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 4.60 (1H, br. s, NH), 3.62 (2H, d, *J* = 5.8 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.3, 132.9, 132.6, 128.8, 127.8, 118.2, 45.9.

Data in agreement with that reported previously.[24]

4-Acetyl-*N*-allylbenzenesulfonamide, 5f



NEt_3 (1.40 mL, 10.0 mmol), *N*-allyl amine (0.57 mL, 7.50 mmol) and 4-acetylbenzenesulfonyl chloride (1.10 g, 5.00 mmol) in CH_2Cl_2 (25 mL) were subjected to the conditions of **general procedure 9A** for 90 min. *N*-Allyl-sulfonamide **5f** (820 mg, 3.43 mmol, 67%) was obtained as a white solid.

R$_f$ 0.22 (EtOAc/pentane, 3:7) [UV, KMnO4].

m.p. 102 °C

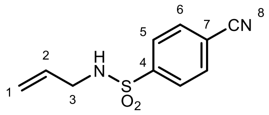
IR ν_{max}/cm^{-1} (film) 3272, 1687, 1398, 1359, 1158, 1111, 940, 643.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.04 (2H, m, H), 8.00 – 7.93 (2H, m, H), 5.71 (1H, ddt, *J* = 17.1, 10.2, 5.8 Hz, H2), 5.17 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.13 – 5.09 (1H, m, H1), 4.69 (1H, br. s, NH), 3.64 (2H, app. tt, *J* = 6.0, 1.6 Hz, H3), 2.66 (3H, s, H9).

^{13}C NMR (101 MHz, $CDCl_3$) δ 196.9, 144.2, 140.2, 132.8, 129.1, 127.5, 118.2, 46.0, 27.0.

HRMS (ESI^+) $[M + Na]^+$ $C_{11}H_{13}O_3NNaS$ requires 262.0508; found 262.0510.

N-Allyl-4-cyanobenzenesulfonamide, 5g



NEt_3 (0.56 mL, 4.00 mmol), *N*-allyl amine (0.23 mL, 3.00 mmol) and 4-cyanobenzenesulfonyl chloride (403 mg, 2.00 mmol) in CH_2Cl_2 (10 mL) were subjected to the conditions of **general procedure 9A** for 2 h. *N*-Allyl-sulfonamide **5g** (424 mg, 1.80 mmol, 95%) was obtained as a white solid.

R$_f$ 0.10 (Et_2O/pentane, 3:7) [UV, $KMnO_4$].

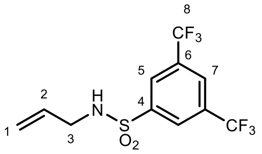
m.p. 83 °C [lit.[25] 81.5 – 82 °C].

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.94 (2H, m, H5), 7.88 – 7.78 (2H, m, H6), 5.71 (1H, ddt, *J* = 17.1, 10.2, 5.9 Hz, H2), 5.23 – 5.10 (2H, m, H1), 4.58 (1H, t, *J* = 6.5 Hz, NH), 3.67 (2H, app. tt, *J* = 6.0, 1.5 Hz, H3)

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 133.1, 132.6, 127.9, 118.5, 117.4, 116.7, 46.0.

Data in agreement with that reported previously.[25]

N-Allyl-3,5-bis(trifluoromethyl)benzenesulfonamide, 5h



NEt_3 (2.8 mL, 20.0 mmol), *N*-allyl amine (1.4 mL, 15.0 mmol) and 3,5-bis(trifluoromethyl)-benzenesulfonyl chloride (3.13 g, 10.0 mmol) in CH_2Cl_2 (50 mL) were subjected to the conditions of **general procedure 9A** for 1 h. *N*-Allyl-sulfonamide **5h** (3.30 g, 10.0 mmol, 100%) was obtained as a white solid.

R_f 0.50 (Et_2O/pentane, 3:7) [UV, $KMnO_4$].

m.p. 77 °C.

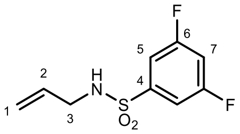
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (2H, app. dp, J = 1.7, 0.6 Hz, H5), 8.08 (1H, tq, J = 1.6, 0.8 Hz, H7), 5.71 (1H, ddt, J = 17.1, 10.2, 6.0 Hz, H2), 5.25 – 5.11 (2H, m, H1), 4.76 (1H, br. t, J = 6.2 Hz, NH), 3.72 (2H, app. tt, J = 6.0, 1.5 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 133.1 (q, $^2J_{CF3}$ = 34.3 Hz), 132.4, 127.6 (q, $^3J_{CF3}$ = 4.0 Hz), 126.4 (hept., $^3J_{CF3}$ = 3.7 Hz), 122.6 (q, $^1J_{CF3}$ = 273.4 Hz), 118.7, 46.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ –62.98.

Data in agreement with that reported previously.[26]

N-Allyl-3,5-difluorobenzenesulfonamide, 5i



NEt_3 (2.8 mL, 20.0 mmol), *N*-allyl amine (1.4 mL, 15.0 mmol) and 3,5-difluorobenzenesulfonyl chloride (2.13 g, 10.0 mmol) in CH_2Cl_2 (50 mL) were subjected to the conditions of **general procedure 9A** for 4 h. *N*-Allyl-sulfonamide **5i** (2.30 g, 9.96 mmol, 99%) was obtained as an off-white solid.

R_f 0.32 (Et_2O/pentane, 3:7) [UV, $KMnO_4$].

m.p. 66 °C.

IR ν_{max}/cm^{-1} (film) 1606, 1439, 1326, 1311, 1300, 1151, 1128, 987, 669.

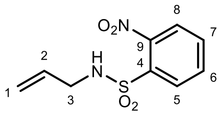
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.35 (2H, m, H5), 7.03 (1H, tt, *J* = 8.4, 2.3 Hz, H7), 5.74 (1H, ddt, *J* = 17.2, 10.3, 5.8 Hz, H2), 5.25 – 5.11 (2H, m, H1), 4.64 (1H, br. s, NH), 3.67 (2H, tt, *J* = 6.0, 1.5 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0 (dd, $^{1,3}J_{CF}$ = 254.7, 11.5 Hz), 132.6, 118.4, 110.8 (d, $^{2,4}J_{CF}$ = 19.8, 8.4 Hz), 110.8 (d, $^{3}J_{CF}$ = 11.4 Hz), 108.5 (t, $^{2}J_{CF}$ = 25.1 Hz), 46.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ –105.53.

HRMS (ESI$^+$) [M + H]$^+$ $C_9H_8O_2NF_2S$ requires 232.0249; found 232.0243.

N-Allyl-*N*-(*o*-nitrobenzene)sulfonamide, 5j



NEt_3 (0.38 mL, 2.73 mmol), *N*-allyl amine (0.23 mL, 3.00 mmol) and 2-nitrobenzenesulfonyl chloride (605 mg, 2.73 mmol) in CH_2Cl_2 (2.3 mL) were subjected to the conditions of **general procedure 9B** for 90 min. *N*-Allyl sulfonamide **5j** (590 mg, 2.43 mmol, 89%) was obtained as an off white solid.

R_f 0.43 (EtOAc/pentane, 3:7) [UV, $KMnO_4$].

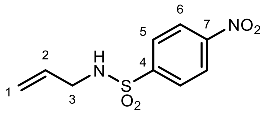
m.p. 64 – 65 °C. [lit.[27] 74 – 75 °C]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 – 8.09 (1H, m, ArH), 7.89 – 7.86 (1H, m, ArH), 7.79 – 7.70 (2H, m, ArH), 5.74 (1H, ddt, *J* = 17.1, 10.2, 5.8 Hz, H2), 5.38 (1H, br. t, *J* = 5.0 Hz, NH), 5.21 (1H, dtd, *J* = 17.1, 1.6, 1.0 Hz, H1), 5.11 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 3.77 (2H, app. tt, *J* = 6.0, 1.5 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 148.2, 134.2, 133.7, 133.0, 132.6, 131.2, 125.5, 118.3, 46.4.

Data in agreement with that reported previously.[28]

N-Allyl-*N*-(*p*-nitrobenzene)sulfonamide, 5k



According to a modified literature procedure.[13] *N*-Allyl amine (0.80 mL, 10.4 mmol) was added dropwise to a solution of 4-nitrobenzenesulfonyl chloride (2.21 g, 10.0 mmol) and K_2CO_3 (1.41 g, 10.1 mmol) in CH_2Cl_2 (12.0 mL). The mixture was stirred at room temperature for 2.5 h and then H_2O (5 mL) was added. The biphasic mixture was poured into $NaHCO_3$ (sat. aq. 10 mL) and extracted with CH_2Cl_2 (10 mL × 3). The organic phases were combined, washed with brine (50 mL), dried (Mg_2SO_4), filtered and concentrated *in vacuo.* Recrystallisation by dissolving the crude residue in a minimal amount of hot EtOAc, followed by slow addition of pentane, gave *N*-allyl sulfonamide **5k** (1.68 g, 6.30 mmol, 63%) as pale-yellow crystals.

R_f 0.58 (EtOAc/pentane, 3:7) [UV, $KMnO_4$].

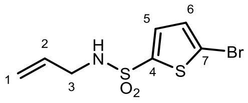
m.p. 104 – 106 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 – 8.35 (2H, m, H5), 8.08 – 8.04 (2H, m, H6), 5.72 (1H, ddt, *J* = 17.1, 10.2, 5.8 Hz, H2), 5.21 – 5.13 (2H, m, H1), 4.61 (1H, br. t, *J* = 5.7 Hz, NH), 3.70 (1H, app. tt, *J* = 6.0, 1.5 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 150.3, 146.3, 132.5, 128.5, 124.6, 118.6, 46.0.

Data in agreement with that reported previously.[19]

N-Allyl-5-bromothiophene-2-sulfonamide, 5l



NEt_3 (1.4 mL, 10.0 mmol), *N*-allyl amine (0.56 mL, 7.50 mmol) and 5-bromothiophene-2-sulfonyl chloride (1.31 g, 5.00 mmol) in CH_2Cl_2 (25 mL) were subjected to the conditions of **general procedure 9A** for 1 h. *N*-Allyl-sulfonamide **5l** (1.33 g, 4.70 mmol, 95%) was obtained as an orange solid.

R$_f$ 0.46 (Et_2O/pentane, 2:3) [UV, $KMnO_4$].

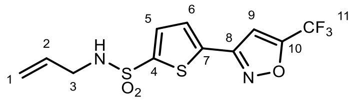
m.p. 45 – 46 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (1H, d, *J* = 4.0 Hz, H5/6), 7.07 (1H, d, *J* = 3.9 Hz, H5/6), 5.77 (1H, ddt, *J* = 17.1, 10.2, 5.8 Hz, H2), 5.23 (1H, app. dq, *J* = 17.2, 1.5 Hz, H1), 5.17 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 4.63 (1H, br. t, *J* = 5.9 Hz, NH), 3.69 (2H, app. tt, *J* = 6.0, 1.5 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 141.9, 132.6, 132.5, 130.5, 120.1, 118.4, 46.1.

Data in agreement with that reported previously.[29]

N-Allyl-5-(5-(trifluoromethyl)isoxazole-3-yl)thiophene-2-sulfonamide, 5m



NEt_3 (0.44 mL, 3.14 mmol), *N*-allyl amine (0.18 mL, 2.40 mmol) and 5-(5-(trifluoromethyl)isoxazole-3-yl)thiophene-2-sulfonyl chloride (500 mg, 1.57 mmol) in CH_2Cl_2 (8 mL) were subjected to the conditions of **general procedure 9A** for 90 min. *N*-Allyl-sulfonamide **5m** (436 mg, 1.29 mmol, 82%) was obtained as an off white solid.

R$_f$ 0.56 (EtOAc/pentane, 3:7).

m.p. 114 – 115 °C [lit.[30] 124 – 127 °C].

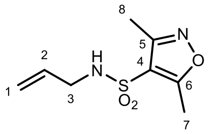
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (1H, d, *J* = 3.9 Hz, H5/6), 7.46 (1H, d, *J* = 3.9 Hz, H5/6), 6.97 (1H, q, *J* = 0.9 Hz, H9), 5.79 (1H, ddt, *J* = 17.1, 10.2, 5.9 Hz, H2), 5.24 (1H, dtd, *J* = 17.1, 1.6, 1.0 Hz, H1), 5.17 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 4.66 (1H, t, *J* = 6.1 Hz, NH), 3.75 (2H, app. tt, *J* = 5.9, 1.6 Hz, H3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.14 (q, $^2J_{CF3}$ = 43.0 Hz), 156.9, 144.2, 134.7, 132.5, 132.4, 128.3, 118.5, 117.6 (q, $^1J_{CF3}$ = 270.7 Hz), 103.6 (q, $^3J_{CF3}$ = 2.0 Hz), 46.2.

^{19}F NMR (377 MHz, $CDCl_3$) δ –64.20.

Data in agreement with that reported previously.[30]

N-Allyl-3,5-dimethylisoxazole-4-sulfonamide, 5n



NEt_3 (2.10 mL, 15.0 mmol), *N*-allyl amine (0.84 mL, 22.5 mmol) and 3,5-dimethylisoxazole-4-sulfonyl chloride (1.47g, 7.50 mmol) in CH_2Cl_2 (38 mL) were subjected to the conditions of **general procedure 9a** for 1 h. *N*-Allyl-sulfonamide **5n** (1.64 g, 7.50 mmol, 100%) was obtained as a colourless oil.

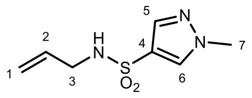
R$_f$ 0.28 (Et_2O/pentane, 2:3) [PMA].

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.75 (1H, ddt, *J* = 17.2, 10.2, 5.9 Hz, H2), 5.21 (1H, app. dq, *J* = 17.2, 1.5 Hz, H1), 5.18 – 5.12 (1H, m, H1), 4.76 (1H, br. s, NH), 3.63 (2H, app. tt, *J* = 6.0, 1.5 Hz, H3), 2.63 (3H, s, H7), 2.41 (3H, s, H8).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 157.7, 132.7, 118.4, 116.3, 45.5, 12.8, 11.0.

Data in agreement with that reported previously.[30]

N-Allyl-1-methyl-1H-pyrazole-4-sulfonamide, 5o



NEt_3 (0.77 mL, 5.54 mmol), *N*-allyl amine (0.31 mL, 4.16 mmol) and 1-methyl-1H-pyrazole-4-sulfonyl chloride (500 mg, 2.77 mmol) in CH_2Cl_2 (14 mL) were subjected to the conditions of **general procedure 9A** for 75 min. *N*-Allyl-sulfonamide **5o** (473 mg, 2.35 mmol, 85%) was obtained as an off-white solid.

R$_f$ 0.17 (EtOAc/pentane, 1:1) [UV, $KMnO_4$].

m.p. 81 – 85 °C.

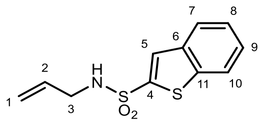
IR ν_{max}/cm^{-1} (film) 3275, 3128, 1525, 1321, 1155, 1120, 706, 659.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.77 (1H, s, H6), 7.76 (1H, d, *J* = 0.7 Hz, H5), 5.79 (1H, ddt, *J* = 17.1, 10.3, 5.8 Hz, H2), 5.22 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.16 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 4.44 (1H, br. s, NH), 3.95 (3H, s, H7), 3.64 (2H, s, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.7, 133.1, 132.0, 122.6, 118.1, 45.9, 39.7.

HRMS (ESI^+) $[M+H]^+$ $C_7H_{12}O_2N_3S$, requires 202.0645; found 202.0648.

N-Allylbenzo[b]thiophene-2-sulfonamide, 5p



NEt_3 (0.56 mL, 4.00 mmol), *N*-allyl amine (0.23 mL, 3.00 mmol) and benzo[b]thiophene – 2-sulfonyl chloride (464 mg, 2.00 mmol) in CH_2Cl_2 (10 mL) were subjected to the conditions of **general procedure 9A** for 1 h. *N*-Allyl-sulfonamide **5p** (503 mg, 1.99 mmol, 99%) was obtained as an off white solid.

R$_f$ 0.39 (Et_2O/pentane, 2:3) [UV, $KMnO_4$].

m.p. 64 – 66 °C.

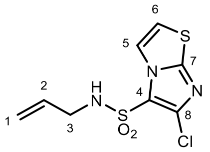
IR ν_{max}/cm^{-1} (film) 3286, 1505, 1425, 1328, 1152, 1070, 1022, 997, 750, 624.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.84 (3H, m, ArH), 7.54 – 7.42 (2H, m, ArH), 5.79 (1H, ddt, *J* = 17.1, 10.2, 5.9 Hz, H2), 5.28 – 5.18 (1H, m, H1), 5.14 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 4.59 (1H, br. t, NH), 3.74 (2H, app. tt, *J* = 6.0, 1.5 Hz, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 141.9, 141.0, 137.8, 132.7, 129.6, 127.5, 125.8, 125.7, 122.9, 118.3, 46.2.

HRMS (ESI^+) $[M + H]^+$ $C_{11}H_{12}O_2NS_2$ requires 254.0304; found 254.0305.

N-Allyl-6-chloroimidazo[2,1-b]thiazole-5-sulfonamide, 5q



NEt$_3$ (0.54 mL, 3.88 mmol), *N*-allyl amine (0.22 mL, 2.91 mmol) and 6-chloroimidazo[2,1-b]thiazole – 5-sulfonyl chloride (500 mg, 1.94 mmol) in CH$_2$Cl$_2$ (10 mL) were subjected to the conditions of **general procedure 9A** for 1.5 h. *N*-Allyl-sulfonamide **5q** (430 mg, 1.55 mmol, 82%) was obtained as a colourless oil.

R$_f$ 0.53 (EtOAc/pentane, 3:7) [UV, KMnO$_4$].

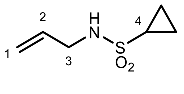
IR ν_{max}/cm^{-1} (film) 3287, 3122, 2360, 1458, 1437, 1345, 1272, 1249, 1272, 1249, 1178, 1141, 620.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.92 (1H, d, *J* = 4.5 Hz, H5/6), 7.06 (1H, d, *J* = 4.5 Hz, H5/6), 5.74 (1H, ddt, *J* = 17.1, 10.2, 6.0 Hz, H2), 5.23- 5.13 (1H, app. dq, *J* = 17.1, 1.2 Hz, H1), 5.10 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 5.00 (1H, br. t, *J* = 5.7 Hz, NH), 3.69 (2H, app. tt, *J* = 6.0, 1.5 Hz, H3).

^{13}C NMR (126 MHz, CDCl$_3$) δ 149.7, 137.2, 132.5, 120.5, 119.3, 118.5, 114.5, 46.0.

HRMS (ESI$^-$) [M - H]$^-$ C$_8$H$_7$O$_2$N$_3$ClS$_2$, requires 275.9674; found 275.9672.

N-Allylcyclopropanesulfonamide, 5r



NEt$_3$ (2.8 mL, 20.0 mmol), *N*-allyl amine (1.4 mL, 15.0 mmol) and cyclopropanesulfonyl chloride (1.0 mL, 10.0 mmol) in CH$_2$Cl$_2$ (50 mL) were subjected to the conditions of **general**

procedure 9A for 3 h. *N*-Allyl-sulfonamide **5r** (1.80 g, 11.2 mmol, quant.) was obtained as a yellow oil.

R$_f$ 0.17 (EtOAc/pentane, 1:4) [KMnO$_4$].

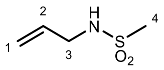
IR ν_{max}/cm^{-1} (film) 3282, 1422, 1323, 1302, 1143, 1067, 923, 704.

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.96 – 5.85 (1H, m, H2), 5.35 – 5.27 (1H, m, H1), 5.21 (1H, d, *J* = 10.3 Hz, H1), 4.29 (1H, br. s, NH), 3.80 (2H, br. t, *J* = 6.1, Hz, H3), 2.48 – 2.37 (1H, m, H4), 1.23 – 1.12 (2H, m, H5), 1.04-0.97 (2H, m, H5).

^{13}C NMR (101 MHz, CDCl$_3$) δ 134.0, 117.6, 46.0, 30.6, 5.6.

HRMS (ESI$^+$) [M +H]$^+$ $C_6H_{12}O_2NS$, requires 162.0583; found 162.0583.

N-Allylmethanesulfonamide, 5s



NEt$_3$ (0.85 mL, 6.12 mmol), *N*-allyl amine (0.59 mL, 6.73 mmol) and methanesulfonyl chloride (0.47 mL, 6.12 mmol) in CH$_2$Cl$_2$ (60 mL) were subjected to the conditions of **general procedure 9B** for 90 min. *N*-Allyl-sulfonamide **5s** (691 mg, 5.14 mmol, 84%) was obtained as a pale-orange oil.

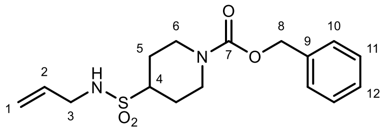
R$_f$ 0.21 (EtOAc/pentane, 3:7) [KMnO$_4$].

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.87 (1H, ddt, *J* = 17.1, 10.2, 5.8 Hz, H2), 5.31 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.24 – 5.20 (1H, m, H1), 4.51 (1H, br. s, NH), 3.80 – 3.75 (2H, m, H3), 2.97 (3H, s, H4).

^{13}C NMR (101 MHz, CDCl$_3$) δ 133.6, 118.0, 45.8, 41.2.

Data in agreement with that reported previously.[31]

Benzyl 4-(*N*-allylsulfamoyl)piperidine-1-carboxylate, 5t



NEt_3 (0.43 mL, 3.08 mmol), *N*-allyl amine (0.17 mL, 2.31 mmol) and benzyl 4-(chlorosulfonyl)piperidine-1-carboxylate (489 mg, 1.54 mmol) in CH_2Cl_2 (7.8 mL) were subjected to the conditions of **general procedure 9A** for 2 h. *N*-Allyl-sulfonamide **5t** (359 mg, 1.06 mmol, 69%) was obtained as a colourless oil.

R$_f$ 0.18 (Et_2O/pentane, 7:13) [UV, $KMnO_4$].

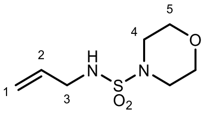
IR ν_{max}/cm^{-1} (film) 3265 (br.), 1684, 1473, 1433, 1317, 1279, 1217, 1138, 1080, 1016, 699.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.28 (5H, m, ArH), 5.86 (1H, ddt, *J* = 17.2, 10.2, 5.8 Hz, H2), 5.28 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.20 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 5.13 (2H, s, H8), 4.34 (2H, br. s, H6), 4.21 (1H, t, *J* = 6.2 Hz, NH), 3.75 (2H, app. tt, *J* = 6.0, 1.5 Hz, H3), 3.02 (1H, tt, *J* = 11.9, 3.7 Hz, H4), 2.80 (2H, br. s, H6), 2.12 (2H, br. d, *J* = 12.9 Hz, H5), 1.73 (2H, app. qd, *J* = 12.4, 4.6 Hz, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.1, 136.6, 134.0, 128.7, 128.3, 128.1, 117.9, 67.5, 60.0, 46.3, 43.0, 26.0.

HRMS (ESI$^+$) $[M + H]^+$ $C_{13}H_{33}O_2NS$, requires 361.1197; found 361.1193.

N-Allylmorpholine-4-sulfonamide, 5u



NEt_3 (2.79 mL, 20.0 mmol), *N*-allyl amine (1.13 mL, 15.0 mmol) and morpholine – 4-sulfonyl chloride (1.85 g, 10.0 mmol) in CH_2Cl_2 (50 mL) were subjected to the conditions of **general procedure 9A** for 20 h. *N*-Allyl-sulfonamide **5u** (1.39 g, 6.70 mmol, 67%) was obtained as a white solid.

R$_f$ 0.14 (Et_2O/pentane, 2:3) [$KMnO_4$].

m.p 28 °C.

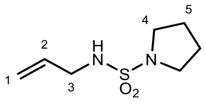
IR ν_{max}/cm^{-1} (film) 3290 (br.), 2860, 1454, 1325, 1295, 1262, 1152, 1112, 1072, 938, 845, 723.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 – 5.79 (1H, m, H2), 5.28 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.21 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 4.22 (1H, br. s, NH), 3.77 – 3.73 (4H, m, H4), 3.75 – 3.66 (2H, m, H3), 3.23 – 3.18 (4H, m, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 133.7, 117.9, 66.4, 46.4, 46.3.

HRMS (ESI$^+$) [M + H]$^+$ $C_7H_{15}O_3N_2S$, requires 207.0798; found 207.0800.

N-Allylpyrrolidine-1-sulfonamide, 5v



NEt_3 (3.36 mL, 24.0 mmol), *N*-allyl amine (1.34 mL, 18.0 mmol) and pyrrolidine – 1-sulfonyl chloride (2.04 g, 12.0 mmol) in CH_2Cl_2 (60 mL) were subjected to the conditions of **general procedure 9A** for 2 h. *N*-Allyl-sulfonamide **5v** (2.68 g, 14.0 mmol, 78%) was obtained as a yellow oil.

R$_f$ 0.28 (EtOAc/pentane, 3:7) [$KMnO_4$].

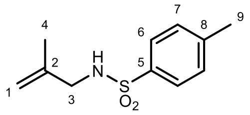
IR ν_{max}/cm^{-1} (film) 3289, 2978, 2879, 1428, 1315, 1144, 1064, 1005, 920.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87 (1H, ddt, *J* = 17.1, 10.2, 5.8 Hz, H2), 5.26 (1H, app. dq, *J* = 17.1, 1.6 Hz, H1), 5.17 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 4.32 (1H, br. s, NH), 3.68 (2H, d, *J* = 5.8 Hz, H3), 3.33 – 3.26 (4H, m, H4), 1.96 – 1.87 (4H, m, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 134.0, 117.4, 48.2, 46.2, 25.7.

HRMS (ESI^+) $[M + H]^+$ $C_7H_{15}O_2N_2S$, requires 191.0849; found 191.0850.

4-Methyl-*N*-(2-methylallyl)benzenesulfonamide, 5w



p-Toluenesulfonamide (7.0 g, 40 mmol), NaI (300 mg, 2.0 mmol), K_2CO_3 (6.0 g, 40 mmol) and 3-chloro – 2-methyl propene (2.0 mL, 20 mmol) in acetone (20 mL) were subjected to **general procedure 10** for 32 h. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 3:7) gave *N*-allyl sulfonamide **5w** (3.0 g, 13 mmol, 67%) as a yellow oil.

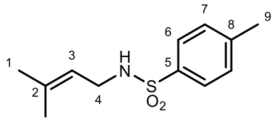
R_f 0.42 (Et_2O/pentane, 1:4) [$KMnO_4$].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.71 (2H, m, H6), 7.30 (2H, d, J = 7.8 Hz, H7), 4.89 – 4.86 (1H, m, H1), 4.86 – 4.82 (1H, m, H1), 4.58 (1H, s, NH), 3.48 (2H, d, *J* = 6.4 Hz, H3), 2.43 (3H, s, H9), 1.68 (3H, s, H4).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 140.6, 137.1, 129.8, 127.3, 112.9, 49.2, 21.7, 20.2.

Data in agreement with that reported previously.[32]

4-Methyl-*N*-(3-methylbut-2-en-1-yl)benzenesulfonamide, 5x



p-Toluenesulfonamide (3.80 g, 22.0 mmol), K_2CO_3 (3.10 g, 22.0 mmol) and prenyl bromide (2.3 mL, 20.0 mmol) in acetone (20 mL) were subjected to the conditions of **general procedure 10** for 32 h. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 3:7) gave *N*-allyl sulfonamide **5x** (2.50 g, 10.4 mmol, 52%) as a white solid.

R$_f$ 0.42 (EtOAc/pentane, 3:7) [$KMnO_4$].

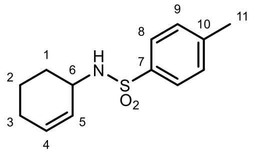
m.p. 52 °C [lit.[33] 54 – 55 °C].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.71 (2H, m, H6), 7.35 – 7.27 (2H, m, H7), 5.08 – 5.01 (1H, m, H3), 4.25 (1H, br. s, NH), 3.53 (2H, t, *J* = 6.4 Hz, H4), 2.43 (3H, s, H9), 1.63 (3H, s, H1), 1.54 (3H, s, H1).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5, 137.8, 137.2, 129.8, 127.3, 119.0, 41.2, 25.7, 21.7, 17.9.

Data in agreement with that reported previously.[33]

N-(Cyclohex-4-en-6-yl)-*p*-methylbenzenesulfonamide, 5y



Bromocyclohexene (1.30 mL, 11.0 mmol) and TBAI (734 mg, 2.0 mmol) were added to a mixture of *p*-toluenesulfonamide (1.70 g, 10.0 mmol) and K_2CO_3 (2.07 g, 15.0 mmol) in acetone (50 mL) at room temperature under air. The mixture was heated to reflux for 20 h, then cooled to room temperature and poured onto H_2O (10 mL). The aqueous phase was extracted with EtOAc (10 mL × 3), the combined organic layers were dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 1:4) gave *N*-allyl sulfonamide **5y** (1.80 g, 7.20 mmol, 72%) as a white solid.

R$_f$ 0.30 (EtOAc/pentane, 1:4) [$KMnO_4$].

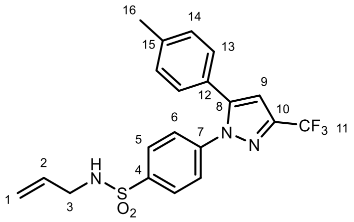
m.p. 100 – 103 °C [lit.[34] 102 – 104 °C].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.75 (2H, m, H8), 7.31 – 7.27 (2H, m, H9), 5.77 – 5.71 (1H, m, H4), 5.33 (1H, app. ddt, *J* = 10.0, 4.0, 2.2 Hz, H5), 4.71 (1H, br. s, NH), 3.79 (1H, m, H6), 2.42 – 2.41 (3H, m, H11), 1.95 – 1.87 (2H, m, H3), 1.78 – 1.69 (1H, m, H1), 1.64 – 1.48 (3H, m, H1, H2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.3, 138.4, 131.6, 129.8, 127.1, 127.1, 49.1, 30.3, 24.6, 21.6, 19.4.

Data in agreement with that reported previously.[34]

N-Allyl-4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide, 5ac



Celecoxib (250 mg, 0.66 mmol), K_2CO_3 (91 mg, 1.31 mmol), KI (11 mg, 0.066 mmol) and allyl bromide (60 µL, 0.66 mmol) in MeCN (2.19 mL) were subjected to the conditions of **General Procedure 8** for 45 h. Purification by flash column chromatography (SiO_2, Et_2O/pentane, 1:9 → 1:1) gave *N*-allyl sulfonamide **5ac** (133 mg, 0.32 mmol, 48%) as a white solid.

R_f 0.46 (Et_2O/pentane, 3:7).

m.p. 142 °C.

IR ν_{max}/cm^{-1} (film) 2981, 2360, 1472, 1237, 1161, 1138, 1097, 733.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 – 7.82 (2H, m, H5), 7.49 – 7.45 (2H, m, H6), 7.20 – 7.15 (2H, m, H14), 7.12 – 7.07 (2H, m, H13), 6.75 (1H, s, H9), 5.71 (1H, ddt, *J* = 17.1, 10.2, 5.8 Hz, H2), 5.17 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.12 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 4.43 (1H, t, *J* = 6.2 Hz, NH), 3.62 (2H, tt, *J* = 6.1, 1.5 Hz, H3), 2.38 (3H, s, H16).

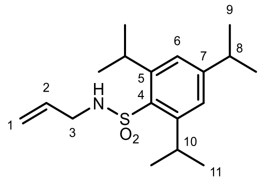
^{13}C NMR (126 MHz, $CDCl_3$) δ 145.4, 144.3 (q, $^2J_{CF3}$ = 38.8 Hz), 142.7, 140.0, 139.7, 132.8, 129.9, 128.9, 128.3, 125.8, 125.8, 121.2 (q, $^1J_{CF3}$ = 269 Hz), 118.3, 106.5 (q, $^3J_{CF3}$ = 2.1 Hz), 46.0, 21.5.

^{19}F NMR (377 MHz, $CDCl_3$) δ –62.5.

HRMS (ESI$^+$) $[M + H]^+$ $C_{20}H_{17}O_2N_3F_3S$, requires 420.0999, found 420.0986.

Compound is known but no data previously reported.[35]

N-Allyl-2,4,6-triisopropylbenzenesulfonamide, 5ad



NEt_3 (2.79 mL, 20.0 mmol), *N*-allyl amine (1.13 mL, 15.0 mmol) and 2,4,6-triisopropylbenzenesulfonyl chloride (3.03 g, 10.0 mmol) in CH_2Cl_2 (50 mL) were subjected to the conditions of **general procedure 9A** for 1 h. Purification by silica plug (Et_2O/pentane, 1:9) gave *N*-allyl sulfonamide **5ad** (3.15 g, 9.73 mmol, 97%) as a white solid.

R$_f$ 0.39 (Et_2O/pentane, 1:4).

m.p. 108 °C.

IR ν_{max}/cm^{-1} (film) 2981, 2887, 2363, 1384, 1253, 1151, 1072, 955.

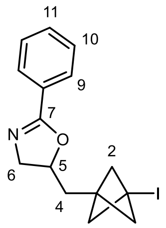
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (2H, s, H6), 5.77 (1H, ddt, *J* = 17.2, 10.3, 6.0 Hz, H2), 5.19 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.12 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 4.34 (1H, br. t, *J* = 6.1 Hz, NH), 4.15 (2H, hept., *J* = 6.8 Hz, H10), 3.60 (2H, tt, *J* = 6.1, 1.5 Hz, H3), 2.90 (1H, hept., *J* = 6.9 Hz, H8), 1.27 (12H, d, *J* = 6.8 Hz, H11), 1.26 (6H, d, *J* = 6.9 Hz, H9).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 150.5, 133.4, 132.3, 124.0, 118.0, 45.7, 34.3, 29.8, 25.0, 23.7.

HRMS (ESI$^+$) $[M + H]^+$ $C_{18}H_{30}O_2NS$, requires 324.1992; found 324.1992.

S2.5 Miscellaneous

5-((3-Iodobicyclo[1.1.1]pentan-1-yl)methyl)-2-phenyl-4,5-dihydrooxazole, 3af



Iodomethyl oxazoline **2af**[2] (43 mg, 0.15 mmol), [1.1.1]propellane **1** (0.71 M in Et_2O, 0.27 mL, 0.20 mmol), Et_3B (1.0 M in hexanes, 15 µL, 10 mol%) in CH_2Cl_2 (0.15 mL) was subjected to **general procedure 1**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:4 → 7:13) gave BCP iodide **3af** (47 mg, 0.14 mmol, 91%) as a colourless oil.

R_f 0.18 (Et_2O/pentane, 2:3).

IR ν_{max}/cm^{-1} (film) 2989, 2913, 1649, 1449, 1352, 1314, 1176, 1063, 839, 694.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.88 (2H, m, H9), 7.51 – 7.45 (1H, m, H11), 7.44 – 7.38 (2H, m, H10), 4.68 (1H, dddd, *J* = 9.6, 8.5, 7.4, 4.5 Hz, H5), 4.12 (1H, dd, *J* = 14.6, 9.6 Hz, H6), 3.61 (1H, dd, *J* = 14.6, 7.4 Hz, H6), 2.35 (6H, s, H2), 1.98 (1H, dd, *J* = 14.6, 8.5 Hz, H4), 1.85 (1H, dd, *J* = 14.6, 4.5 Hz, H4).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.9, 131.5, 128.5, 128.2, 127.9, 78.0, 61.3, 60.3, 45.8, 37.8, 7.0.

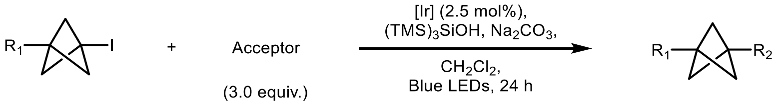
HRMS (ESI$^+$) [M + H]$^+$ $C_{15}H_{17}ONI$, requires 354.0349; found 354.0349.

S3.

Chapter 3 Experimental Data

S3.1 General Experimental Procedures

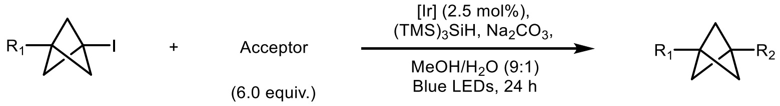
General Procedure 9 – Photoredox catalysed Giese reaction, Conditions A



A flame dried vial was charged with BCP(A) iodide (1.0 equiv.), radical acceptor (if solid, 3.0 equiv.), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (2.5 mol%), anhydrous Na_2CO_3 (2.0 equiv.) and $(Me_3Si)_3SiOH$ (2.0 equiv.). The vial was then fitted with a PTFE septum, evacuated, and placed under an Ar atmosphere. The solids were dissolved in CH_2Cl_2 (0.15 M) and then the radical acceptor (if liquid, 3.0 equiv.) was added. The vial was degassed by freeze-pump-thaw cycles (× 3), sonicated for 10 seconds, and then irradiated with blue LEDs for 24 h with rapid stirring (**set-up 1**). The reaction mixture was poured onto H_2O and extracted with CH_2Cl_2 (× 3). The combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography in the specified eluent system gave the desired Giese addition product.

Note: Silane by-products could be removed by either a slow, or second, purification by column chromatography. EtOAc often gave better results than Et_2O when used as the more polar solvent in the eluent system.

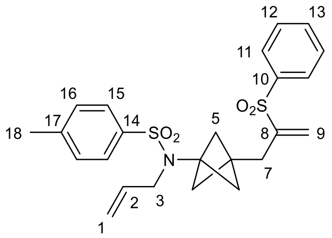
General Procedure 10 – Photoredox catalysed Giese reaction, Conditions A



A flame dried vial was charged with BCP(A) iodide (1.0 equiv.), radical acceptor (if solid, 6.0 equiv.), $Ir[dF(CF)_3ppy]_2(dtbbpy)PF_6$ (2.5 mol%) and anhydrous Na_2CO_3 (2.0 equiv.). The vial was then fitted with a PTFE septum, evacuated, and placed under an Ar atmosphere. The solids were dissolved in $MeOH/H_2O$ (9:1, 0.15 M), then $(Me_3Si)_3SiH$ (2.0 equiv.) and the radical acceptor (if liquid, 6.0 equiv.) were added. The vial was then degassed by freeze-pump-thaw cycles (× 3), sonicated for 10 seconds, and then irradiated with Blue LEDs for 24 h with rapid stirring (**set-up 1**). The reaction mixture was poured onto H_2O and extracted with CH_2Cl_2 (× 3). The combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography in the specified eluent system gave the desired Giese addition product.

S3.2 Giese Addition Products

N-Allyl-*p*-methyl-*N*-(6-(7-(phenylsulfonyl)allyl)bicyclo[1.1.1]pentan-4-yl)benzenesulfonamide, 4a



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6a** (145 mg, 0.45 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiOH$ (79 mg, 0.3 mmol) in CH_2Cl_2 (1.0 mL) was subjected to **General Procedure 9**. Purification by column chromatography (SiO_2, Et_2O/pentane, 3:7 → 1:1) gave the title compound **4a** (41 mg, 0.090 mmol, 60%) as a clear oil.

R_f 0.18 (Et_2O/pentane, 2:3) [UV, Vanillin].

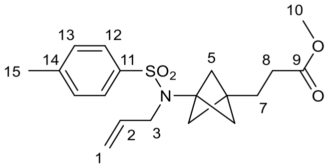
IR ν_{max}/cm^{-1} (film) 2981, 2884, 1736, 1598, 1382, 1347, 1246, 1158, 1091, 954, 814.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.81 (2H, m, ArH), 7.68 – 7.60 (4H, m, ArH), 7.57 – 7.50 (3H, m, ArH), 7.29 – 7.26 (2H, m, ArH), 6.39 (1H, d, *J* = 0.6 Hz, H9), 5.76 (1H, ddt, *J* = 17.2, 10.2, 5.7 Hz, H2), 5.73 – 5.67 (1H, m, H9), 5.19 (1H, app. dq, *J* = 17.1, 1.6 Hz, H1), 5.11 (1H, app. dq, *J* = 10.3, 1.4 Hz, H1), 3.85 (2H, app. dt, *J* = 5.6, 1.6 Hz, H3), 2.47 (2H, s, H7), 2.43 (3H, s, H18), 1.75 (6H, s, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 147.9, 143.3, 138.8, 138.5, 135.1, 133.7, 129.7, 129.3, 128.6, 127.2, 125.5, 117.2, 53.6, 50.9, 50.1, 35.2, 29.9, 21.7.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{24}H_{27}O_4NNaS_2$ requires 480.1273; found 480.1274.

Methyl 7-(6-((*N*-allyl-*p*-methylphenyl)sulfonamido)bicyclo[1.1.1]pentan-4-yl)propanoate, 4b



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6b** (81 µL, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na$_2$CO$_3$ (32 mg, 0.30 mmol), (Me$_3$Si)$_3$SiH (93 µL, 0.30 mmol) in MeOH/H$_2$O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO$_2$, Et$_2$O/pentane, 3:7 → 2:3) gave the title compound **4b** (32 mg, 0.09 mmol, 60%) as a colourless oil. *Over addition product **4b1** (18 mg, 0.04 mmol, 27%) was also isolated as a colourless oil.*

1.0 mmol scale: BCPA iodide **3a** (183 mg, 1.00 mmol), radical acceptor **6b** (0.54 mL, 6.00 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (28 mg, 2.5 mol%), Na$_2$CO$_3$ (213 mg, 2.00 mmol), (Me$_3$Si)$_3$SiH (0.62 mL, 2.00 mmol) in MeOH/H$_2$O (9:1, 6.67 mL) was subjected to **General Procedure 10** using a 21 mL vial and Blue LED **set-up 1** with Kessil lamp. Purification by column chromatography (SiO$_2$, Et$_2$O/pentane, 3:7 → 2:3) gave the title compound **4b** (183 mg, 0.50 mmol, 50%) as a clear oil. *Over addition product **4b1** (105 mg, 0.23 mmol, 23%) was also isolated as a colourless oil.*

Telescope: α-Iodoaziridine **2a** (51 mg, 0.15 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (2.5 mg, 2.5 mol%), Na$_2$CO$_3$ (32 mg, 0.30 mmol) were added to a flame dried vial with PTFE septa. The solids were dissolved in anhydrous CH$_2$Cl$_2$ (1.5 mL) and then methyl acrylate **6b** (81 µL, 0.90 mmol) and [1.1.1]propellane **1** (0.75 M in Et$_2$O, 0.40 mL, 0.30 mmol) were added. The vial was degassed by freeze-pump-thaw (× 3, *vacuum* only applied while frozen due to volatility of **1** and **6b**) and then the reaction mixture was irradiated with Blue LEDs, set-up

1, for 16 h. $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) was then added and the mixture was irradiated for a further 24 h. The reaction mixture was filtered and concentrated *in vacuo* to give **4b** (^{1}H NMR yield, 31%).

R$_f$ 0.38 (Et_2O/pentane, 1:1) [UV, vanillin].

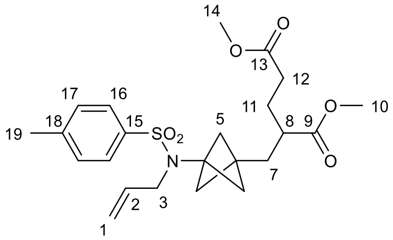
IR ν_{max}/cm^{-1} (film) 2980, 2915, 1737, 1437, 1346, 1245, 1159, 1092, 838.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.67 (2H, m, H12), 7.31 – 7.27 (2H, m, H13), 5.81 (1H, ddt, *J* = 17.2, 10.3, 5.6 Hz, H2), 5.24 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.14 (1H, app. dq, *J* = 10.3, 1.5 Hz, H1), 3.91 (2H, dt, *J* = 5.6, 1.6 Hz, H3), 3.64 (3H, s, H10), 2.42 (3H, s, H15), 2.26 (2H, t, *J* = 7.2 Hz, H8), 1.81 (2H, t, *J* = 7.1 Hz, H7), 1.80 (6H, s, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 143.2, 138.7, 135.3, 129.6, 127.3, 117.2, 53.1, 51.7, 50.7, 50.1, 36.0, 31.6, 25.2, 21.7.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{19}H_{25}O_4NNaS$, requires 386.1396; found 386.1395.

*Dimethyl-2-((3-((N-allyl-4-methylphenyl)sulfonamido)bicyclo[1.1.1]pentan-1-yl)methyl)pentanedioate, **4b1***



R$_f$ 0.63 (EtOAc/pentane, 2:3) [UV, vanillin].

IR ν_{max}/cm^{-1} (film) 2952, 1734, 1437, 1345, 1244, 1158, 1092, 837.

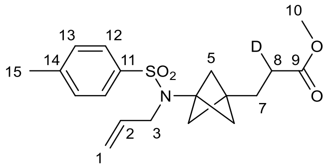
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.64 (2H, m, H16), 7.30 – 7.22 (2H, m, H17), 5.87 – 5.72 (1H, m, H2), 5.27 – 5.16 (1H, m, H1), 5.12 (1H, app. dq, *J* = 10.3, 1.5 Hz, H1), 3.88 (2H, app.

dt, *J* = 5.6, 1.4 Hz, H3), 3.65 (3H, s, OMe), 3.63 (3H, m, OMe), 2.42 (3H, s, H19), 2.34 (1H, dq, *J* = 8.9, 4.6 Hz, H8), 2.31 – 2.22 (2H, m, H12), 1.95 – 1.83 (2H, m, H7, H11), 1.87 – 1.73 (7H, m, H5, H11), 1.60 (1H, dd, *J* = 14.4, 4.5 Hz, H7).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.8, 173.3, 143.2, 138.6, 135.3, 129.6, 127.3, 117.2, 53.6, 52.8, 51.8, 50.7, 50.1, 43.0, 35.3, 32.5, 31.6, 27.9, 21.6.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{23}H_{31}O_6NNaS$, requires 472.1788; found 472.1764.

Methyl 3-(3-((N-allyl-4-methylphenyl)sulfonamido)bicyclo[1.1.1]pentan-1-yl)propanoate – 2-d, ***d$_1$-4b***



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6b** (81 µL, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF_6 (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiD$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, Et_2O/pentane, 3:7 → 2:3) gave the title compound **d$_1$-4b** (17 mg, 0.047 mmol, 30%) as a colourless oil.

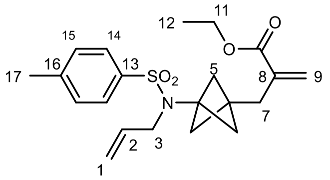
IR ν_{max}/cm^{-1} (film) 2914, 1736, 1346, 1244, 1182, 1159, 1092, 838, 661.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.64 (2H, m, H12), 7.30 – 7.24 (2H, m, H13), 5.81 (1H, ddt, *J* = 17.2, 10.3, 5.6 Hz, H2), 5.23 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.13 (1H, app. dq, *J* = 10.3, 1.5 Hz, H1), 3.90 (2H, app. dt, *J* = 5.6, 1.7 Hz, H3), 3.64 (3H, s, H10), 2.42 (3H, s, H15), 2.20 (0.88H, ddt, *J* = 7.5, 4.4, 2.6 Hz, H8), 1.84 – 1.77 (2H, m, H7), 1.80 (6H, s, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 143.2, 138.7, 135.3, 129.6, 127.3, 117.2, 53.1, 51.7, 50.7, 50.1, 35.9, 31.3, 25.2, 21.7.

HRMS (ESI$^+$) $[M + Na]^+$ $C_{19}H_{24}DO_4NNaS$, requires 387.1459; found 387.1459.

Ethyl-2-((3-((*N*-allyl-4-methylphenyl)sulfonamido)bicyclo[1.1.1]pentan-1-yl)methyl)acrylate, 4c



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6c** (142 mg, 0.45 mmol), $Ir[dF(CF)_3ppy]_2(dtbbpy)PF_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiOH$ (79 mg, 0.30 mmol) in CH_2Cl_2 (1.0 mL) was subjected to **General Procedure 9**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:19 → 1:4) gave the title compound **4c** (25 mg, 0.064 mmol, 43%) as a colourless oil.

R_f 0.37 (EtOAc/pentane, 1:9).

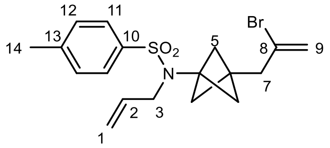
IR ν_{max}/cm^{-1} (film) 2982, 1716, 1276, 1261, 1158, 764, 750.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.63 (2H, m, H14), 7.30 – 7.22 (2H, m, H15), 6.13 (1H, d, *J* = 1.6 Hz, H9), 5.80 (1H, ddt, *J* = 17.2, 10.3, 5.6 Hz, H2), 5.44 (1H, dt, *J* = 1.6, 0.9 Hz, H9), 5.21 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.11 (1H, app. dq, *J* = 10.3, 1.6 Hz, H1), 4.16 (2H, q, *J* = 7.1 Hz, H11), 3.88 (2H, dt, *J* = 5.6, 1.6 Hz, H3), 2.50 (2H, d, *J* = 0.9 Hz, H7), 2.41 (3H, s, H17), 1.79 (6H, s, H5), 1.27 (3H, t, *J* = 7.1 Hz, H12).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 143.2, 138.7, 138.1, 135.3, 129.6, 127.3, 126.4, 117.1, 60.8, 53.5, 50.9, 50.1, 35.8, 32.9, 21.6, 14.3.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{21}H_{27}O_4NNaS$, requires 412.1550; found 412.1558.

N-Allyl-*N*-(3-(2-bromoallyl)bicyclo[1.1.1]pentan-1-yl)-4-methylbenzenesulfonamide, 4d



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6d** (118 mg, 0.45 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiOH$ (79 mg, 0.30 mmol) in CH_2Cl_2 (1.0 mL) was subjected to **General Procedure 9**. Purification by column chromatography (SiO_2, EtOAc/pentane, 3:97) gave the title compound **4d** (17 mg, 0.043 mmol, 28%) as a colourless oil.

R$_f$ 0.61 (EtOAc/pentane, 1:9) [UV, Vanillin].

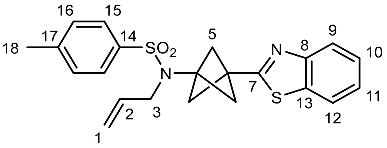
IR ν_{max}/cm^{-1} (film) 2981, 1629, 1345, 1244, 1183, 1158, 1092, 912, 733, 661.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.66 (2H, m, H11), 7.32 – 7.24 (2H, m, H12), 5.82 (1H, ddt, *J* = 17.1, 10.3, 5.6 Hz, H2), 5.49 (1H, dt, *J* = 1.7, 0.9 Hz, H9), 5.40 (1H, d, *J* = 1.7 Hz, H9) 5.24 (1H, app. dq, *J* = 17.1, 1.6 Hz, H1), 5.14 (1H, app. dq, *J* = 10.3, 1.5 Hz, H1), 3.91 (2H, app. dt, *J* = 5.6, 1.6 Hz, H3), 2.64 (2H, d, *J* = 0.9 Hz, H7), 2.42 (3H, s, H14), 1.94 (6H, s, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2, 138.7, 135.3, 130.5, 129.7, 127.3, 118.4, 117.2, 53.9, 51.1, 50.1, 42.3, 35.1, 21.7.

HRMS (ESI$^+$) [M + H]$^+$ $C_{18}H_{23}O_2N^{79}BrS$, requires 396.0627; found 396.0628.

N-Allyl-*N*-(3-(benzo[d]thiazol-2-yl)bicyclo[1.1.1]pentan-1-yl)-4-methylbenzenesulfonamide, 4e



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6e** (124 mg, 0.45 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiOH$ (79 mg, 0.30 mmol) in CH_2Cl_2 (1.0 mL) was subjected to **General Procedure 9**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:19 → 1:4) gave the title compound **4e** (15 mg, 0.037 mmol, 24%) as a colourless oil.

R$_f$ 0.44 (EtOAc/pentane, 1:4) [UV, $KMnO_4$].

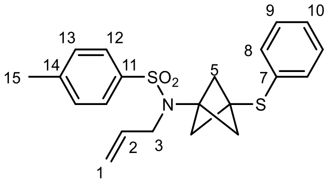
IR ν_{max}/cm^{-1} (film) 2981, 1438, 1345, 1246, 1159, 1091, 844, 761, 661.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (1H, ddd, *J* = 8.3, 1.3, 0.7 Hz, H9/12), 7.82 (1H, ddd, *J* = 8.0, 1.3, 0.7 Hz, H9/12), 7.76 – 7.72 (2H, m, H15), 7.45 (1H, ddd, *J* = 8.3, 7.2, 1.3 Hz, H10/11), 7.35 (1H, ddd, *J* = 8.0, 7.2, 1.3 Hz, H10/11), 7.33 – 7.29 (2H, m, H16), 5.87 (1H, ddt, *J* = 17.2, 10.2, 5.7 Hz, H2), 5.30 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.20 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 4.01 (2H, app. dt, *J* = 5.7, 1.6 Hz, H3), 2.48 (6H, s, H5), 2.43 (3H, s, H18).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 153.6, 143.6, 138.4, 135.5, 135.0, 129.9, 127.4, 126.4, 125.3, 123.1, 121.7, 117.8, 56.6, 51.2, 50.3, 37.0, 21.7.

HRMS (ESI$^+$) [M + H]$^+$ $C_{22}H_{23}O_2N_2S_2$, requires 411.1195; found 411.1189.

N-Allyl-4-methyl-*N*-(3-(phenylthio)bicyclo[1.1.1]pentan-1-yl)benzenesulfonamide, 4f



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6f** (115 mg, 0.45 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiOH$ (79 mg, 0.30 mmol) in CH_2Cl_2 (1.0 mL) was subjected to **General Procedure 9**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 1:98) gave the title compound **4f** (18 mg, 0.047 mmol, 32%) as a colourless oil.

R$_f$ 0.36 (EtOAc/pentane, 1:19).

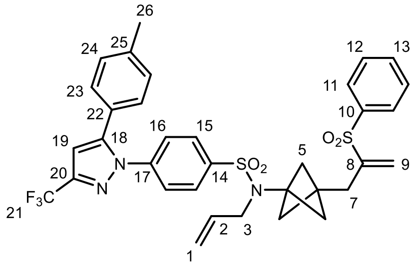
IR ν_{max}/cm^{-1} (film) 2917, 1345, 1207, 1181, 1159, 1091, 909, 731.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.63 (2H, m, H12), 7.41 – 7.37 (2H, m, ArH), 7.31 – 7.27 (5H, m, ArH, H13), 5.77 (1H, ddt, *J* = 17.2, 10.2, 5.6 Hz, H2), 5.21 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.12 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 3.87 (2H, app. dt, *J* = 5.6, 1.6 Hz, H3), 2.42 (3H, s, H15), 2.07 (6H, s, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5, 138.2, 134.9, 133.9, 133.3, 129.8, 129.1, 128.1, 127.3, 117.5, 56.8, 51.8, 50.3, 39.5, 21.7.

HRMS (ESI$^+$) $[M + Na]^+$ $C_{21}H_{23}O_2NNaS_2$, requires 408.1062; found 408.1063.

N-Allyl-*N*-(3-(2-(phenylsulfonyl)allyl)bicyclo[1.1.1]pentan-1-yl)-4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide, 4g



BCPA iodide **3ad** (75 mg, 0.12 mmol), radical acceptor **6a** (118 mg, 0.37 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (3.4 mg, 2.5 mol%), Na_2CO_3 (26 mg, 0.24 mmol), $(Me_3Si)_3SiOH$ (64 mg, 0.24 mmol) in CH_2Cl_2 (0.81 mL) was subjected to **General Procedure 9**. Purification by column chromatography (SiO_2, EtOAc/pentane, 3:17 → 3:7) gave the title compound **4g** (43 mg, 0.064 mmol, 53%) as a colourless oil.

R$_f$ 0.32 (EtOAc/pentane, 2:3) [UV, Vanillin].

IR ν_{max}/cm^{-1} (film) 2916, 1472, 1305, 1237, 1160, 1141, 1097, 976, 838, 732.

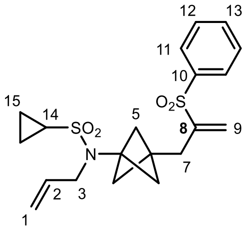
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 – 7.80 (2H, m, H11), 7.78 – 7.71 (2H, m, H15), 7.66 – 7.58 (1H, m, H13), 7.57 – 7.49 (2H, m, H12), 7.47 – 7.41 (2H, m, H16), 7.20 – 7.14 (2H, m, H24), 7.12 – 7.06 (2H, m, H23), 6.75 (1H, d, *J* = 0.6 Hz, H19), 6.39 (1H, d, *J* = 0.7 Hz, H9), 5.79 – 5.68 (1H, m, H2), 5.69 (1H, app. q, *J* = 1.1 Hz, H9), 5.18 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.12 (1H, app. dq, *J* = 10.1, 1.3 Hz, H1), 3.85 (2H, app. dt, *J* = 5.6, 1.6 Hz, H3), 2.47 (2H, d, J = 1.1 Hz, H7), 2.38 (3H, s, H26), 1.74 (6H, s, H5).

^{13}C NMR (126 MHz, $CDCl_3$) δ 147.8, 145.4, 144.2 (q, $^2J_{CF3}$ = 38.6 Hz), 142.4, 140.9, 140.0, 138.7, 134.6, 133.8, 129.9, 129.4, 128.9, 128.6, 128.2, 125.8, 125.6, 125.5, 121.2 (q, $^1J_{CF3}$ = 269.0 Hz), 117.7, 106.4 (q, $^3J_{CF3}$ = 2.3 Hz), 53.6, 50.8, 50.2, 35.3, 29.9, 21.5.

^{19}F NMR (377 MHz, $CDCl_3$) δ –62.4.

HRMS (ESI$^+$) [M + H]$^+$ $C_{34}H_{33}F_3N_2O_4S_2$ requires 668.1859; found 668.1855.

N-Allyl-*N*-(3-(2-(phenylsulfonyl)allyl)bicyclo[1.1.1]pentan-1-yl)cyclopropanesulfonamide, 4h



BCPA iodide **3s** (41 mg, 0.12 mmol), radical acceptor **6a** (112 mg, 0.36 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (3.3 mg, 2.5 mol%), Na_2CO_3 (25 mg, 0.24 mmol), $(Me_3Si)_3SiOH$ (61 mg, 0.24 mmol) in CH_2Cl_2 (0.78 mL) was subjected to **General Procedure 9**. Purification by column chromatography (SiO_2, EtOAc/pentane, 3:17 → 3:7) gave the product containing acceptor **6a** as a significant impurity, which could be partially triturated out as a white solid with Et_2O/pentane. The title compound **4h** was therefore isolated as an inseparable mixture of **4h**:**6a**, 1.8:1 (total 34 mg, calculated 0.061 mmol, 50%) as determined by ^{1}H NMR spectroscopy.

R$_f$ 0.32 (EtOAc/pentane, 2:3) [UV, Vanillin].

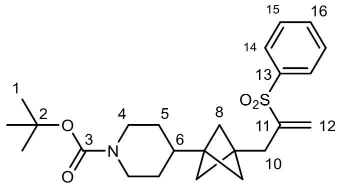
IR ν_{max}/cm^{-1} (film) 2981, 1473, 1448, 1383, 1340, 1306, 1249, 1147, 1081, 955.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.47 (5H, obsc. m, ArH), 6.42 (1H, d, *J* = 0.8 Hz, H9), 5.82 (1H, ddt, *J* = 17.2, 10.3, 5.7 Hz, H2), 5.75 (1H, d, *J* = 0.8 Hz, H9), 5.22 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.14 (1H, app. dq, *J* = 10.3, 1.5 Hz, H1), 3.84 (2H, dt, *J* = 5.6, 1.5 Hz, H3), 2.54 (2H, s, H7), 2.28 (1H, tt, *J* = 8.0, 4.9 Hz, H14), 1.89 (6H, s, H5), 1.17 – 1.11 (2H, m, H15), 0.97-0.91 (2H, m, H15).

^{13}C NMR (101 MHz, $CDCl_3$) δ 148.0, 138.8, 135.2, 133.8, 129.4, 128.6, 125.6, 117.4, 54.0, 50.9, 50.1, 35.1, 31.1, 30.0, 5.7.

HRMS (ESI^+) $[M + H]^+$ $C_{20}H_{26}NO_4S_2$ requires 408.1298; found 408.1296.

t-Butyl 4-(3-(2-(phenylsulfonyl)allyl)bicyclo[1.1.1]pentan-1-yl)piperidine-1-carboxylate, 4i



BCP iodide **4i1** (57 mg, 0.15 mmol), radical acceptor **6a** (145 mg, 0.45 mmol), $Ir[dF(CF)_3ppy]_2(dtbbpy)PF_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiOH$ (79 mg, 0.30 mmol) in CH_2Cl_2 (1.0 mL) was subjected to **General Procedure 9**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:19 → 1:4) gave the title compound **4i** (38 mg, 0.09 mmol, 59%) as a colourless oil.

R_f 0.23 (Et_2O/pentane, 1:4).

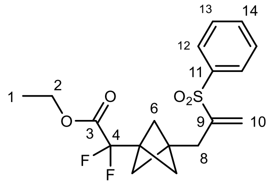
IR ν_{max}/cm^{-1} (film) 2965, 1687, 1424, 1306, 1236, 1174, 1144, 912, 732.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.83 (2H, m, H14), 7.67 – 7.58 (1H, m, H16), 7.58 – 7.49 (2H, m, H15), 6.41 (1H, s, H12), 5.78 – 5.73 (1H, m, H12), 4.12 – 4.02 (2H, m, H4), 2.59 (2H, td, *J* = 13.0, 2.7 Hz, H4), 2.46 (2H, d, *J* = 1.1 Hz, H10), 1.50 – 1.46 (1H, m, H6), 1.46 – 1.41 (2H, obsc. m, H5), 1.44 (9H, s, H1), 1.33 (6H, s, H8), 0.97 (2H, app. qd, *J* = 12.7, 4.4 Hz, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.0, 148.3, 139.0, 133.6, 129.3, 128.7, 124.8, 79.4, 48.3, 43.9, 42.9, 37.3, 36.5, 31.8, 28.6, 28.5.

HRMS (ESI^+) $[M + Na]^+$ $C_{24}H_{33}O_4NNaS$, requires 454.2023; found 454.2020.

Ethyl 2,2-difluoro-2-(3-(2-(phenylsulfonyl)allyl)bicyclo[1.1.1]pentan-1-yl)acetate, 4j



BCP iodide **4j1** (47 mg, 0.15 mmol), radical acceptor **6a** (145 mg, 0.45 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na$_2$CO$_3$ (32 mg, 0.30 mmol), (Me$_3$Si)$_3$SiOH (79 mg, 0.30 mmol) in CH$_2$Cl$_2$ (1.0 mL) was subjected to **General Procedure 9**. Purification by column chromatography (SiO$_2$, EtOAc/pentane, 1:9 → 3:17) gave the title compound **4j** (26 mg, 0.070 mmol, 47%) as a white solid.

R$_f$ 0.65 (EtOAc/pentane, 1:4) [UV, PMA].

m.p. 53 – 54 °C.

IR ν_{max}/cm^{-1} (film) 2982, 1764, 1448, 1305, 1156, 1143, 1094, 1082, 750.

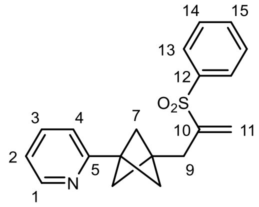
^{1}H NMR (500 MHz, CDCl$_3$) δ 7.90 – 7.83 (2H, m, H12), 7.69 – 7.60 (1H, m, H14), 7.59 – 7.52 (1H, m, H13), 6.43 (1H, d, *J* = 0.5 Hz, H10), 5.75 (1H, app. q, *J* = 1.0 Hz, H10), 4.30 (2H, q, *J* = 7.2 Hz, H2), 2.52 (2H, d, *J* = 1.0 Hz, H8), 1.70 (6H, s, H6), 1.33 (3H, t, *J* = 7.2 Hz, H1).

^{13}C NMR (126 MHz, CDCl$_3$) δ 163.3 (t, $^2J_{CF2}$ = 33.1 Hz), 147.5, 138.7, 133.8, 129.4, 128.6, 125.5, 111.9 (t, $^1J_{CF2}$ = 249.7 Hz), 62.8, 49.0, 38.5 (t, $^2J_{CF2}$ = 31.4Hz), 38.2, 31.4, 14.3.

^{19}F NMR (377 MHz, CDCl$_3$) δ –111.4.

HRMS (ESI$^+$) [M + Na]$^+$ C$_{18}$H$_{20}$O$_4$F$_2$NaS, requires 393.0943; found 393.0943.

2-(3-(2-(Phenylsulfonyl)allyl)bicyclo[1.1.1]pentan-1-yl)pyridine, 4k



BCP iodide **4k1** (41 mg, 0.15 mmol), radical acceptor **6a** (145 mg, 0.45 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiOH$ (79 mg, 0.30 mmol) in CH_2Cl_2 (1.0 mL) was subjected to **General Procedure 9**. Purification by column chromatography (SiO_2, Et_2O/pentane, 3:7 → 4:1) gave the title compound **4k** (20 mg, 0.06 mmol, 40%) as a colourless oil.

R$_f$ 0.20 (Et_2O/pentane, 3:2) [UV, $KMnO_4$].

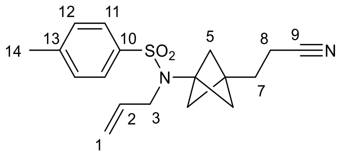
IR ν_{max}/cm^{-1} (film) 2969, 1589, 1475, 1447, 1304, 1141, 1080, 748, 691.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (1H, ddd, *J* = 4.9, 1.8, 1.0 Hz, H1), 7.93 – 7.84 (2H, m, H13), 7.66 – 7.59 (1H, m, H3), 7.61 – 7.49 (3H, m, H14, H15), 7.16 – 7.07 (2H, m, H2,H4), 6.47 (1H, d, *J* = 0.5 Hz, H11), 5.85 (1H, app. q, *J* = 1.1 Hz, H11), 2.59 (2H, d, *J* = 1.1 Hz, H9), 1.91 (6H, s, H7).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.3, 149.4, 148.0, 138.8, 136.3, 133.7, 129.3, 128.7, 125.0, 121.7, 120.7, 52.1, 42.7, 37.6, 31.4.

HRMS (ESI$^+$) [M + H]$^+$ $C_{19}H_{20}O_2NS$, requires 326.1209; found 326.1208.

N-Allyl-*N*-(6-(8-cyanoethyl)bicyclo[1.1.1]pentan-4-yl)-*p*-methylbenzenesulfonamide, 4l



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6l** (59 µL, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, Et_2O/pentane, 3:7) gave the title compound

4l (23 mg, 0.07 mmol, 46%) as an off white solid.

R$_f$ 0.21 (Et_2O/pentane, 2:3) [UV, vanillin].

m.p. 104 °C.

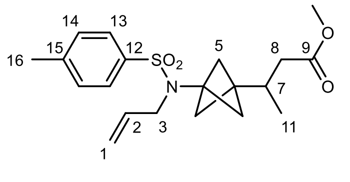
IR ν_{max}/cm^{-1} (film) 2920, 2853, 2247, 1341, 1244, 1183, 1159, 1092, 839.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.67 (2H, m, H11), 7.31 – 7.27 (2H, m, H12), 5.81 (1H, ddt, *J* = 17.2, 10.2, 5.6 Hz, H2), 5.24 (1H, app. dq, *J* = 17.1, 1.6 Hz, H1), 5.14 (1H, app. dq, *J* = 10.3, 1.5 Hz, H1), 3.91 (2H, app. dt, *J* = 5.6, 1.6 Hz, H3), 2.42 (3H, s, H14), 2.26 (2H, t, *J* = 7.2 Hz, H8), 1.92 (6H, s, H5), 1.85 (2H, t, *J* = 7.1 Hz, H7).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 138.5, 135.2, 129.7, 127.3, 119.5, 117.3, 53.3 50.8, 50.1, 35.5, 26.0, 21.7, 15.0.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{18}H_{22}O_2N_2NaS$, requires 353.1294; found 353.1296.

Methyl 7-(6-((*N*-allyl-*p*-methylphenyl)sulfonamido)bicyclo[1.1.1]pentan-4-yl)butanoate, 4m



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6m** (100 µL, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**.

Purification by column chromatography (SiO_2, Et_2O/pentane, 1:4 → 2:3) gave the title compound **4m** (28 mg, 0.07 mmol, 46%) as a colourless oil.

R

R_f 0.46 (Et_2O/pentane, 1:1) [UV, vanillin].

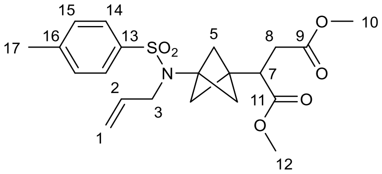
IR ν_{max}/cm^{-1} (film) 2961, 2919, 1736, 1345, 1245, 1158, 1092, 837, 813, 661.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.65 (2H, m, H13), 7.31 – 7.24 (2H, obsc. m, H14), 5.82 (1H, ddt, *J* = 17.1, 10.3, 5.6 Hz, H2), 5.23 (1H, app. dq, *J* = 17.1, 1.6 Hz, H1), 5.13 (1H, app. dq, *J* = 10.1, 1.4 Hz, H1), 3.91 (2H, app. dt, *J* = 5.6, 1.6 Hz, H3), 3.64 (3H, s, H10), 2.42 (3H, s, H16), 2.22 (2H, obsc. dd, *J* = 14.5, 6.1 Hz, H8), 2.16 (1H, obsc. dt, *J* = 13.6, 6.5 Hz, H7), 2.01 (1H, dd, *J* = 14.4, 7.7 Hz, H8), 1.77 (6H, s, H5), 0.84 (3H, dd, *J* = 6.8, 1.0 Hz, H11).

^{13}C NMR (400 MHz, $CDCl_3$) δ 173.4, 143.2, 138.7, 135.4, 129.6, 127.3, 117.2, 51.6, 51.3, 50.5, 50.1, 40.3, 38.8, 29.8, 21.7, 17.0.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{20}H_{27}O_4NNaS$, requires 400.1553; found 400.1552.

Dimethyl 2-(3-((*N*-allyl-4-methylphenyl)sulfonamido)bicyclo[1.1.1]pentan-1-yl)succinate, 4n



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6n** (113 µL, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF_6 (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:19 → 1:4) gave the title compound **4n** (34 mg, 0.09 mmol, 54%) as colourless oil.

R$_f$ 0.52 (Et_2O/pentane, 1:4) [UV, Vanillin].

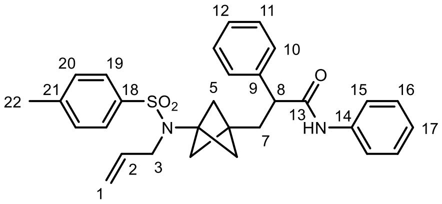
IR ν_{max}/cm^{-1} (film) 2981, 2360, 1736, 1437, 1345, 1247, 1159, 1092.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.65 (2H, m, H14), 7.29 – 7.26 (2H, m, H15), 5.80 (1H, ddt, *J* = 17.2, 10.2, 5.6 Hz, H2), 5.22 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.13 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 3.89 (2H, app. dt, *J* = 5.6, 1.6 Hz, H3), 3.67 (3H, s, OMe), 3.65 (3H, s, OMe), 3.03 (1H, dd, *J* = 9.8, 5.0 Hz, H7), 2.67 (1H, dd, *J* = 16.9, 9.8 Hz, H8), 2.42 (3H, s, H17), 2.32 (1H, dd, *J* = 16.9, 5.0 Hz, H8), 1.87 (6H, s, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 172.1, 143.4, 138.5, 135.1, 129.7, 127.3, 117.4, 52.8, 52.0, 52.0, 50.5, 50.1, 41.3, 36.4, 33.6, 21.7.

HRMS (ESI$^+$) $[M + H]^+$ $C_{21}H_{28}O_6NS$, requires 422.1632; found 422.1629

3-(3-((*N*-Allyl-4-methylphenyl)sulfonamido)bicyclo[1.1.1]pentan-1-yl)-*N*,2-diphenylpropanamide, 4o



BCPA iodide **3a** (61 mg, 0.15 mmol), *N*,2-diphenylacrylamide **6o** (155 mg, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9) gave the title compound **4o** (33 mg, 0.066 mmol, 44%) as a colourless oil.

R$_f$ 0.28 (EtOAc/pentane, 1:4).

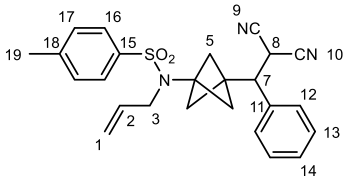
IR ν_{max}/cm^{-1} (film) 3344, 2980, 1665, 1599, 1538, 1441, 1242, 1155, 1091, 732, 696.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.58 (2H, m, ArH), 7.42 – 7.35 (2H, m, ArH), 7.38 – 7.22 (6H, obsc. m, ArH), 7.24 – 7.17 (2H, m, ArH), 7.14 – 7.03 (2H, m, ArH), 5.76 (1H, ddt, *J* = 17.2, 10.3, 5.6 Hz, H2), 5.17 (1H, app. dq, *J* = 17.1, 1.6 Hz, H1), 5.08 (1H, app. dq, *J* = 10.3, 1.4 Hz, H1), 3.84 (2H, app. dt, *J* = 5.6, 1.6 Hz, H3), 3.42 (1H, t, *J* = 7.5 Hz, NH), 2.52 (1H, dd, *J* = 14.5, 7.5 Hz, H8), 2.40 (3H, s, H22), 2.00 (1H, dd, *J* = 14.5, 7.5 Hz, H7), 1.81 – 1.66 (6H, m, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 143.2, 139.4, 138.5, 137.9, 135.2, 129.6, 129.2, 129.1, 128.0, 127.9, 127.3, 124.5, 119.9, 117.2, 53.7, 52.7, 50.8, 50.1, 35.5, 33.2, 21.6.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{30}H_{32}O_3N_2NaS$ requires 523.2026; found 523.2026.

N-Allyl-*N*-(3-(2,2-dicyano-1-phenylethyl)bicyclo[1.1.1]pentan-1-yl)-4-methylbenzenesulfonamide, 4p



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6p** (69 mg, 0.45 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiOH$ (79 mg, 0.30 mmol) in CH_2Cl_2 (1.0 mL) was subjected to **General Procedure 9**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9 → 7:13) gave the title compound **4p** (37 mg, 0.09 mmol, 57%) as a white solid. Recrystallisation from Et_2O/pentane gave the title compound as colourless crystals.

R$_f$ 0.25 (Et_2O/pentane, 2:3).

m.p. 138 °C.

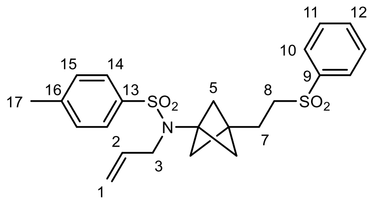
IR ν_{max}/cm^{-1} (film) 2981, 1663, 1342, 1342, 1248, 1184, 1158, 1092, 842, 707.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.62 (2H, m, H16), 7.42 – 7.34 (3H, m, ArH), 7.31 – 7.24 (2H, m, H17), 7.24 – 7.17 (2H, m, ArH), 5.77 (1H, ddt, *J* = 17.2, 10.2, 5.6 Hz, H2), 5.21 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.13 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 3.90 (1H, d, *J* = 7.0 Hz, H8), 3.88 (2H, dt, *J* = 5.6, 1.6 Hz, H3), 3.41 (1H, d, *J* = 7.0 Hz, H7), 2.42 (3H, s, H19), 2.12 – 2.01 (6H, m, H5).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.6, 138.2, 135.3, 134.9, 129.8, 129.4, 129.1, 127.8, 127.2, 117.6, 112.2, 111.9, 53.5, 51.5, 50.1, 46.7, 38.1, 26.9, 21.7.

HRMS (ESI$^-$) [M - H]$^-$ $C_{25}H_{24}O_2N_3S$, requires 430.1595; found 430.1588.

N-Allyl-4-methyl-*N*-(3-(2-(phenylsulfonyl)ethyl)bicyclo[1.1.1]pentan-1-yl)benzenesulfonamide, 4q



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6q** (151 mg, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF_6 (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:4 → 3:7) gave the title compound **4q** (30 mg, 0.07 mmol, 45%) as colourless oil.

R$_f$ 0.47 (EtOAc/pentane, 1:4) [Vanillin].

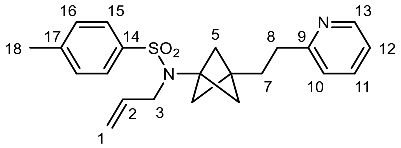
IR ν_{max}/cm^{-1} (film) 2916, 1342, 1307, 1290, 1245, 1148, 1088, 731.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.85 (2H, m, H10), 7.67 – 7.63 (3H, m, H14, H12), 7.60 – 7.54 (2H, m, H11), 7.28 – 7.24 (2H, m, H15), 5.78 (1H, ddt, *J* = 17.1, 10.2, 5.6 Hz, H2), 5.20 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.11 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 3.88 (2H, app. dt, *J* = 5.7, 1.6 Hz, H3), 2.97 – 2.89 (2H, m, H8), 2.41 (3H, s, H17), 1.96 – 1.86 (2H, m, H7), 1.79 (6H, s, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 139.1, 138.5, 135.2, 134.0, 129.7, 129.5, 128.2, 127.3, 117.3, 54.0, 53.2, 50.9, 50.1, 34.8, 23.3, 21.6.

HRMS (ESI$^+$) $[M + Na]^+$ $C_{23}H_{27}O_4NNaS_2$ requires 468.1274, found 468.1273.

N-Allyl-4-methyl-*N*-(3-(2-(pyridin – 2-yl)ethyl)bicyclo[1.1.1]pentan-1-yl)benzenesulfonamide, 4r



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6r** (98 µL, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF_6 (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, EtOAc/pentane, 3:7 → 7:13) gave the title compound **4r** (19 mg, 0.50 mmol, 34%) as colourless oil.

R$_f$ 0.38 (EtOAc/pentane, 1:4) [UV, $KMnO_4$].

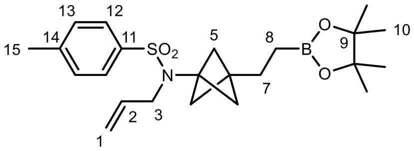
IR ν_{max}/cm^{-1} (film) 2957, 2361, 1245, 1161, 1067, 842.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (1H, ddd, *J* = 4.9, 1.9, 1.1 Hz, H13), 7.63 – 7.58 (2H, m, H15), 7.49 (1H, td, *J* = 7.7, 1.9 Hz, H11/12), 7.22 – 7.17 (2H, m, H16), 7.12 – 7.06 (2H, m, H10, H11/12), 5.74 (1H, ddt, *J* = 17.2, 10.2, 5.6 Hz, H2), 5.15 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.05 (1H, app. dq, *J* = 10.1, 1.4 Hz, H1), 3.82 (2H, dt, *J* = 5.6, 1.6 Hz, H3), 2.65 – 2.57 (2H, m, H8), 2.35 (3H, s, H18), 1.89 – 1.80 (2H, m, H7), 1.72 (6H, s, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6, 149.3, 143.2, 138.7, 136.5, 135.4, 129.6, 127.4, 122.8, 121.2, 117.1, 53.3, 50.8, 50.1, 36.5, 35.8, 29.8, 21.6.

HRMS (ESI$^{+/-}$) not found.

N-Allyl-4-methyl-*N*-(3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)bicyclo[1.1.1]pentan-1-yl)benzenesulfonamide, 4s



BCPA iodide **3a** (61 mg, 0.15 mmol), vinylboronic acid pinacol ester **6s** (153 µL, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:19 → 1:9) gave the title compound **4s** (20 mg, 0.046 mmol, 31 %) as a colourless oil.

R$_f$ 0.52 (EtOAc/pentane, 1:9).

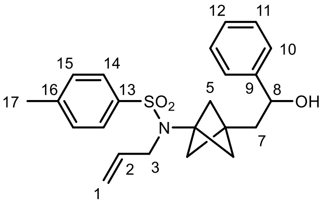
IR ν_{max}/cm^{-1} (film) 1978, 1373, 1322, 1242, 1158, 1144, 1092, 837, 660.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.65 (2H, m, H12), 7.29 – 7.22 (2H, m, H13), 5.82 (1H, ddt, *J* = 17.1, 10.2, 5.6 Hz, H2), 5.23 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.12 (1H, app. dq, *J* = 10.2, 1.4 Hz, 1H), 3.91 (2H, dt, *J* = 5.7, 1.6 Hz, H3), 2.41 (3H, s, H15), 1.75 (6H, s, H5), 1.61 – 1.51 (2H, m, H7), 1.21 (12H, s, H10), 0.71-0.61 (2H, m, H8).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.1, 135.5, 129.6, 127.4, 117.0, 83.2, 54.4, 52.7, 50.7, 50.1, 42.1, 38.0, 25.0, 24.3, 21.6.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{23}H_{34}O_4NBNaS$ requires 454.2196; found 454.2191.

N-Allyl-*N*-(3-(2-hydroxy-2-phenylethyl)bicyclo[1.1.1]pentan-1-yl)-4-methylbenzenesulfonamide, 4t



BCPA iodide **3a** (61 mg, 0.15 mmol), 1-phenylvinylboronic acid pinacol ester **6t** (183 µL, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF_6 (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. The crude reaction mixture was diluted in THF/Et_2O (1:1, 5 mL) and cooled to 0 °C. NaOH (2 M aq., 6 mL) and H_2O_2 (30% aq., 3 mL) were added dropwise and the reaction mixture was stirred for 16 h, then diluted with H_2O (10 mL) and EtOAc (10 mL). The phases were separated and the aquesous phase was extracted with EtOAc (10 mL × 2). The combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:4 → 1:1) gave the title compound **4t** (17 mg, 0.043 mmol, 29%) as a colourless oil.

R$_f$ 0.23 (EtOAc/pentane, 1:4).

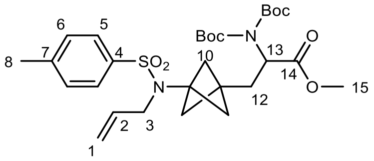
IR ν_{max}/cm^{-1} (film) 3516 (br.), 2913, 1339, 1241, 1156, 1092, 838, 813, 702, 661.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (2H, d, *J* = 8.3 Hz, H14), 7.37 – 7.22 (7H, obsc. m, ArH), 5.80 (1H, ddt, *J* = 17.2, 10.3, 5.6 Hz, H2), 5.21 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.11 (1H, dq, *J* = 10.2, 1.4 Hz, H1), 4.61 (1H, dd, *J* = 8.2, 5.1 Hz, H8), 3.88 (2H, app. dt, *J* = 5.6, 1.6 Hz, H3), 2.42 (3H, s, H17), 2.00 (1H, dd, *J* = 14.6, 8.2 Hz, H7), 1.90 (1H, dd, *J* = 14.6, 5.1 Hz, H7), 1.83 (6H, s, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.5, 143.2, 138.7, 135.3, 129.6, 128.7, 127.9, 127.3, 126.0, 117.1, 73.5, 54.1, 51.1, 50.1, 38.8, 34.5, 21.6.

HRMS (ESI$^+$) Not found.

Methyl 3-(3-((*N*-allyl-4-methylphenyl)sulfonamido)bicyclo[1.1.1]pentan-1-yl)-2-(bis(*tert*-butoxycarbonyl)amino)propanoate, 4u



BCPA iodide **3a** (61 mg, 0.15 mmol), radical acceptor **6u** (271 mg, 0.90 mmol), $Ir[dF(CF)_3ppy]_2(dtbbpy)PF_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in $MeOH/H_2O$ (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:19 → 1:4) gave the title compound **4u** (45 mg, 0.08 mmol, 52%) as a colourless oil.

R$_f$ 0.55 (EtOAc/pentane, 1:4) [UV, Ninhydrin].

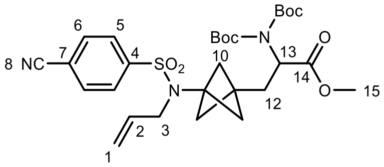
IR ν_{max}/cm^{-1} (film) 2980, 1746, 1700, 1367, 1353, 1276, 1246, 1159, 1129, 842.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.64 (2H, m, H5), 7.29 – 7.23 (2H, m, H6), 5.80 (1H, ddt, *J* = 17.2, 10.2, 5.5 Hz, H2), 5.22 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.11 (1H, app. dq, *J* = 10.2, 1.5 Hz, H1), 4.81 (1H, dd, *J* = 9.7, 4.6 Hz, H13), 3.89 (1H, app. dt, *J* = 6.0, 1.7 Hz, H3), 3.68 (3H, s, H15), 2.41 (3H, s, H8), 2.34 (1H, dd, *J* = 15.2, 4.6 Hz, H12), 2.09 (1H, dd, *J* = 15.2, 9.7 Hz, H12), 1.85 (6H, s, H10), 1.48 (18H, s, Boc).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 152.1, 143.2, 138.7, 135.3, 129.6, 127.3, 117.1, 83.3, 56.7, 53.9, 52.5, 50.8, 50.0, 34.5, 30.1, 28.2, 21.7.

HRMS (ESI^+) $[M + Na]^+$ $C_{29}H_{42}O_8N_2NaS$, requires 601.2554; found 601.2552.

Methyl 3-(3-((*N*-allyl-4-cyanophenyl)sulfonamido)bicyclo[1.1.1]pentan-1-yl)-2-(bis(*tert*-butoxycarbonyl)amino)propanoate, 4v



BCPA iodide **3g** (62 mg, 0.15 mmol), radical acceptor **6u** (271 mg, 0.90 mmol), $Ir[dF(CF)_3ppy]_2(dtbbpy)PF_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:17) gave the title compound **4v** (48 mg, 0.81 mmol, 54%) as a colourless oil.

R_f 0.30 (EtOAc/pentane, 1:4) [UV, Ninhydrin].

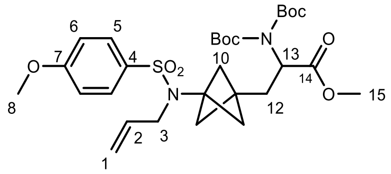
IR ν_{max}/cm^{-1} (film) 2980, 2360, 1745, 1700, 1367, 1242, 1161, 1130, 842.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 – 7.87 (2H, m, ArH), 7.82 – 7.74 (2H, m, ArH), 5.77 (1H, ddt, *J* = 17.2, 10.2, 5.6 Hz, H2), 5.22 (1H, app. dq, *J* = 17.2, 1.5 Hz, H1), 5.16 (1H, app. dq, *J* = 10.2, 1.3 Hz, H1), 4.81 (1H, dd, *J* = 9.5, 4.6 Hz, H13), 3.92 (2H, app. dt, *J* = 5.6, 1.6 Hz, H3), 3.69 (3H, s, H15), 2.37 (1H, dd, *J* = 15.3, 4.6 Hz, H12), 2.09 (1H, dd, *J* = 15.3, 9.5 Hz, H12), 1.88 (6H, s, H10), 1.48 (18H, s, Boc).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 152.1, 146.0, 134.4, 132.9, 127.9, 117.9, 117.5, 116.2, 83.4, 56.5, 54.0, 52.5, 50.8, 50.2, 34.7, 30.0, 28.2.

HRMS (ESI$^+$) $[M + Na]^+$ $C_{29}H_{39}O_8N_3NaS$, requires 612.2350; found 612.2358.

Methyl-3-(3-((*N*-allyl-4-methoxyphenyl)sulfonamido)bicyclo[1.1.1]pentan-1-yl)-2-(bis(*tert*-butoxycarbonyl)amino)propanoate, 4w



BCPA iodide **3b** (63 mg, 0.15 mmol), radical acceptor **6u** (271 mg, 0.90 mmol), $Ir[dF(CF)_3ppy]_2(dtbbpy)PF_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 1:3) gave the title compound **4w** (42 mg, 0.07 mmol, 47%) as a colourless oil.

R$_f$ 0.30 (EtOAc/pentane, 1:4) [Ninhydrin].

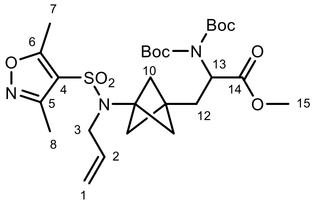
IR ν_{max}/cm^{-1} (film) 2980, 2360, 1746, 1700, 1367, 1351, 1258, 1155, 1130, 835.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.68 (2H, m, H), 6.97 – 6.89 (2H, m, H), 5.80 (1H, ddt, *J* = 17.1, 10.2, 5.6 Hz, H2), 5.21 (1H, app. dq, *J* = 17.1, 1.6 Hz, H1), 5.11 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 4.82 (1H, dd, *J* = 9.6, 4.7 Hz, H13), 3.88 (2H, app. dt, *J* = 5.5, 1.6 Hz, H3), 3.86 (3H, s, H8), 3.68 (3H, s, H15), 2.34 (1H, dd, *J* = 15.2, 4.7 Hz, H12), 2.09 (1H, dd, *J* = 15.2, 9.6 Hz, H12), 1.85 (6H, s, H10), 1.48 (18H, s, Boc).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 162.7, 152.1, 135.3, 133.3, 129.4, 117.1, 114.1, 83.3, 56.7, 55.7, 53.9, 52.4, 50.8, 50.0, 34.5, 30.1, 28.2.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{29}H_{42}O_9N_2NaS$, requires 617.2503; found 617.2495.

Methyl 3-(3-((*N*-allyl-3,5-dimethylisoxazole)-4-sulfonamido)bicyclo[1.1.1]pentan-1-yl)-2-(bis(*tert*-butoxycarbonyl)amino)propanoate, 4x



BCPA iodide **3n** (61 mg, 0.15 mmol), radical acceptor **6u** (271 mg, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 3:17) gave the title compound **4x** (34 mg, 0.058 mmol, 38%) as a colourless oil.

R$_f$ 0.37 (EtOAc/pentane, 1:4) [Ninhydrin].

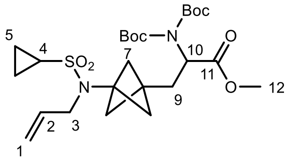
IR ν_{max}/cm^{-1} (film) 2980, 2360, 1747, 1700, 1596, 1368, 1341, 1243, 1341, 1243, 1177, 1129, 840.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (1H, ddt, *J* = 17.1, 10.2, 5.6 Hz, H2), 5.24 (1H, app. dq, *J* = 17.1, 1.5 Hz, H1), 5.17 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 4.84 (1H, dd, *J* = 9.7, 4.6 Hz, H13), 3.69 (3H, s, H15), 2.61 (3H, s, H7), 2.40 – 2.34 (1H, obsc. dd , *J* = 15.3, 4.6 Hz, H12), 2.33 (3H, s, H8), 2.12 (1H, dd, *J* = 15.3, 9.7 Hz, H12), 1.88 (6H, s, H10), 1.49 (18H, s, Boc).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 171.2, 157.6, 152.1, 134.8, 117.9, 117.7, 83.4, 56.6, 53.8, 52.5, 50.5, 50.0, 34.8, 29.9, 28.2, 12.9, 11.0.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{27}H_{41}O_9N_3NaS$, requires 606.2456; found 606.2427.

Methyl-3-(3-(*N*-allylcyclopropanesulfonamido)bicyclo[1.1.1]pentan-1-yl)-2-(bis(*tert*-butoxycarbonyl)amino)propanoate, 4y



BCPA iodide **3s** (53 mg, 0.15 mmol), radical acceptor **6u** (271 mg, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na$_2$CO$_3$ (32 mg, 0.30 mmol), (Me$_3$Si)$_3$SiH (93 µL, 0.30 mmol) in MeOH/H$_2$O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO$_2$, EtOAc/pentane, 1:9 → 3:17) gave the title compound **4y** (55 mg, 0.10 mmol, 69%) as a colourless oil.

R$_f$ 0.33 (EtOAc/pentane, 1:4) [Ninhydrin].

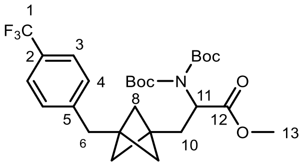
IR ν_{max}/cm^{-1} (film) 2980, 2360, 1746, 1699, 1367, 1343, 1247, 1235, 1148, 1129, 842.

^{1}H NMR (500 MHz, CDCl$_3$) δ 5.85 (1H, ddt, *J* = 17.1, 10.2, 5.7 Hz, H2), 5.24 (1H, app. dq, *J* = 17.1, 1.6 Hz, H1), 5.14 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 4.89 (1H, dd, *J* = 9.6, 4.7 Hz, H10), 3.87 (2H, app. dt, *J* = 5.7, 1.6 Hz, H3), 3.70 (3H, s, H12), 2.41 (1H, dd, *J* = 15.2, 4.7 Hz, H9), 2.31 (1H, tt, *J* = 8.1, 4.9 Hz, H4), 2.15 (1H, dd, *J* = 15.2, 9.6 Hz, H9), 1.99 (6H, s, H7), 1.50 (18H, s, Boc), 1.20 – 1.13 (2H, m, H5), 0.98-0.90 (2H, m, H5).

^{13}C NMR (126 MHz, CDCl$_3$) δ 171.3, 152.2, 135.4, 117.2, 83.4, 56.7, 54.3, 52.5, 50.8, 50.1, 34.3, 31.1, 30.1, 28.2, 5.7.

HRMS (ESI$^+$) [M + Na]$^+$ C$_{25}$H$_{40}$O$_8$N$_2$NaS, requires 551.2398; found 551.2394.

Methyl-2-(bis(*tert*-butoxycarbonyl)amino)-3-(3-(4-(trifluoromethyl)benzyl)bicyclo[1.1.1]pentan-1-yl)propanoate, 4z



BCP iodide **4z1** (53 mg, 0.15 mmol), radical acceptor **6u** (271 mg, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na$_2$CO$_3$ (32 mg, 0.30 mmol), (Me$_3$Si)$_3$SiH (93 µL, 0.30 mmol) in MeOH/H$_2$O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO$_2$, EtOAc/pentane, 1:19) gave the title compound **4z** (46 mg, 0.087 mmol, 58%) as a colourless oil.

R$_f$ 0.58 (EtOAc/pentane, 1:9) [Ninhydrin].

IR ν_{max}/cm^{-1} (film) 2980, 2361, 1748, 1700, 1368, 1325, 1162, 1127, 1067.

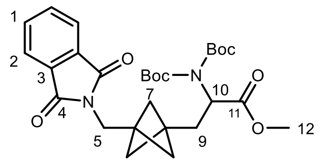
^{1}H NMR (500 MHz, CDCl$_3$) δ 7.54 – 7.47 (2H, d, *J* = 7.9 Hz, H3), 7.16 (2H, d, *J* = 7.9 Hz, H4), 4.86 (1H, dd, *J* = 10.1, 4.5 Hz, H11), 3.67 (3H, s, H13), 2.77 (2H, s, H6), 2.25 (1H, dd, *J* = 15.1, 4.5 Hz, H10), 2.07 (1H, dd, *J* = 15.1, 10.1 Hz, H10), 1.47 (6H, s, H8), 1.42 (18H, s, Boc).

^{13}C NMR (126 MHz, CDCl$_3$) δ 171.6, 152.0, 143.9, 129.3, 128.3 (q, $^2J_{CF3}$ = 32.1 Hz), 125.2 (q, $^3J_{CF3}$ = 3.8 Hz), 124.6 (q, $^1J_{CF3}$ = 271.7 Hz), 83.1, 56.7, 52.4, 50.8, 40.0, 39.2, 38.4, 31.9, 28.1.

^{19}F NMR (377 MHz, CDCl$_3$) δ –62.3.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{27}H_{36}O_6NF_3Na$, requires 550.2387; found 550.2387.

Methyl-2-(bis(*tert*-butoxycarbonyl)amino)-3-(3-((1,3-dioxoisoindolin-2-yl)methyl)bicyclo[1.1.1]pentan-1-yl)propanoate, 4aa



BCPA iodide **4aa1** (53 mg, 0.15 mmol), radical acceptor **6u** (271 mg, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:19) gave the title compound **4aa** (35 mg, 0.066 mmol, 44%) as a colourless oil.

R$_f$ 0.45 (EtOAc/pentane, 1:4).

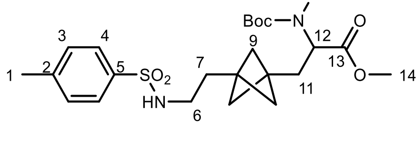
IR ν_{max}/cm^{-1} (film) 2975, 1747, 1716, 1392, 1367, 1129, 724.

^{1}H NMR (400 MHz, CDCl3) δ 7.83 (2H, dd, *J* = 5.5, 3.0 Hz, H2), 7.71 (2H, dd, *J* = 5.5, 3.0 Hz, H1), 4.86 (1H, dd, *J* = 9.7, 4.6 Hz, H10), 3.76 (2H, s, H5), 3.67 (3H, s, H12), 2.27 (1H, dd, *J* = 15.1, 4.6 Hz, H9), 2.05 (1H, dd, *J* = 15.1, 9.8 Hz, H9), 1.60 (6H, br. s, H7), 1.43 (18H, s, Boc).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 168.2, 152.1, 134.0, 132.3, 123.3, 83.1, 56.6, 52.4, 50.8, 39.4, 38.2, 37.9, 31.8, 28.1.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{28}H_{36}O_8N_2Na$, requires 551.2364; found 551.2363.

Methyl-2-(bis(*tert*-butoxycarbonyl)amino)-3-(3-(2-((4-methylphenyl)sulfonamido)ethyl)bicyclo[1.1.1]pentan-1-yl)propanoate, 4ab



BCP iodide **4ab1** (59 mg, 0.15 mmol), radical acceptor **6u** (271 mg, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$

(93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 1:4) gave the title compound **4ab** (37 mg, 0.065 mmol, 44%) as a colourless oil.

R_f (EtOAc/pentane, 1:4).

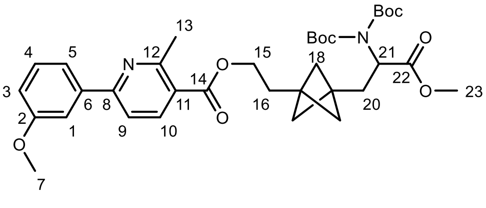
IR ν_{max}/cm^{-1} (film) 2979, 1745, 1699, 1368, 1261, 1233, 1161, 1130, 1094.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.69 (2H, m, H4), 7.31 (2H, d, J = 8.2 Hz, H3), 4.86 (1H, dd, J = 9.6, 4.7 Hz, H12), 4.18 (1H, br. s, NH), 3.69 (3H, s, H14), 2.90 (2H, td, J = 7.2, 6.2 Hz, H6), 2.43 (3H, s, H1), 2.27 (1H, dd, J = 15.1, 4.7 Hz, H11), 2.01 (1H, dd, J = 15.2, 9.6 Hz, H11), 1.58 (2H, t, J = 7.4 Hz, H7), 1.50 (6H, obsc. s, H9), 1.49 (18H, obsc. s, Boc).

^{13}C NMR (126 MHz, $CDCl_3$) δ 71.6, 152.1, 143.6, 137.0, 129.9, 127.2, 83.2, 56.6, 52.4, 51.2, 41.4, 38.1, 37.9, 31.8, 31.7, 28.2, 21.7.

HRMS (ESI$^-$) $[M - H]^-$ $C_{28}H_{41}O_8N_2S$, requires 565.2589; found 565.2588.

2-(3-(2-(Bis(*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)bicyclo[1.1.1]pentan-1-yl)ethyl 6-(3-methoxyphenyl)-2-methylnicotinate, 4ac



BCP iodide **4ac1** (62 mg, 0.13 mmol), radical acceptor **6u** (236 mg, 0.78 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF_6 (3.7 mg, 2.5 mol%), Na_2CO_3 (28 mg, 0.26 mmol), $(Me_3Si)_3SiH$ (81 µL, 0.26 mmol) in MeOH/H_2O (9:1, 0.87 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 1:4) gave the title compound **4ac** (37 mg, 0.058 mmol, 45%) as a colourless oil.

R$_f$ 0.31 (EtOAc/pentane, 1:4).

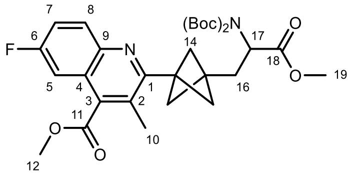
IR ν_{max}/cm^{-1} (film) 2972, 2361, 1747, 1721, 1585, 1381, 1368, 1258, 1155, 1130.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (1H, d, *J* = 8.2 Hz, H9/10), 7.64 (1H, dd, *J* = 2.6, 1.5 Hz, H1), 7.62 – 7.56 (2H, m, H5, H9/10), 7.38 (1H, t, *J* = 7.9 Hz, H4), 6.99 (1H, ddd, *J* = 8.2, 2.6, 1.0 Hz, H3), 4.90 (1H, dd, *J* = 9.8, 4.6 Hz, H21), 4.30 (2H, t, *J* = 6.7 Hz, H15), 3.89 (3H, s, OMe), 3.69 (3H, s, OMe), 2.90 (3H, s, H13), 2.30 (1H, dd, *J* = 15.1, 4.6 Hz, H20), 2.07 (1H, dd, *J* = 15.1, 9.8 Hz, H20), 1.92 (2H, t, *J* = 6.7 Hz, H16), 1.63 (6H, s, H18), 1.47 (18H, s, Boc).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 166.6, 160.2, 160.2, 159.0, 152.2, 140.0, 139.4, 129.9, 123.7, 119.8, 117.7, 115.7, 112.7, 83.1, 63.6, 56.6, 55.5, 52.3, 51.4, 38.2, 37.7, 31.8, 30.9, 28.2, 25.4.

HRMS (ESI$^+$) $[M + H]^+$ $C_{35}H_{47}O_9N_2$, requires 639.3276; found 639.3261.

Methyl-2-(3-(2-(bis(*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)bicyclo[1.1.1]pentan-1-yl)-6-fluoro-3-methylquinoline-4-carboxylate, 4ad



BCP iodide **4ad1** (62 mg, 0.15 mmol), radical acceptor **6u** (271 mg, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%), Na_2CO_3 (32 mg, 0.30 mmol), $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 1.0 mL) was subjected to **General Procedure 10**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 1:4) gave the title compound **4ad** (47 mg, 0.081 mmol, 53%) as an off white solid.

R$_f$ 0.24 (EtOAc/pentane, 1:4).

m.p. 97 – 99 °C.

IR ν_{max}/cm^{-1} (film) 2981, 2360, 1736, 1382, 1369, 1224, 1162, 1129, 955.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 – 7.99 (1H, m, H8), 7.39 (1H, ddd, *J* = 9.2, 8.1, 2.8 Hz, H7), 7.24 (1H, dd, *J* = 9.6, 2.8 Hz, H5), 5.02 (1H, dd, *J* = 9.7, 4.7 Hz, H17), 4.05 (3H, s, H12), 3.73 (3H, s, H19), 2.48 (3H, s, H10), 2.46 (1H, obsc. dd, *J* = 15.2, 4.7 Hz, H16), 2.23 (6H, s, H14), 2.21 (1H, obsc. dd, *J* = 15.2, 9.7 Hz, H16), 1.52 (18H, s, Boc).

^{13}C NMR (101 MHz, $CDCl_3$) δ 183.5, 171.6, 168.4, 160.9 (d, $^1J_{CF}$ = 248.0 Hz), 157.6 (d, $^4J_{CF}$ = 2.7 Hz), 152.2, 143.4, 132.2 (d, $^3J_{CF}$ = 10.0 Hz), 127.7, 124.1 (d, $^3J_{CF}$ = 10.4 Hz), 119.1 (d, $^2J_{CF}$ = 26.0 Hz), 107.8 (d, $^2J_{CF}$ = 23.4 Hz), 83.3, 56.6, 53.3, 52.8, 52.4, 44.6, 38.7, 31.8, 28.2, 17.3.

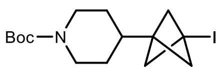
^{19}F NMR (377 MHz, $CDCl_3$) δ –112.44.

HRMS (ESI$^+$) $[M + H]^+$ $C_{31}H_{40}O_8N_2F$, requires 587.2763; found 587.2753.

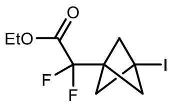
S3.3 BCP Iodides and Radical Acceptors

C-Substituted BCP Iodide Substrates

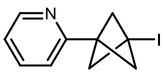
The following BCP Iodides **4i1**, **4j1**, **4k1**, **4z1**, **4aa1**, **4ab1**, **4ac1** and **4ad1** were prepared according to work previously published by our group.[36, 37]



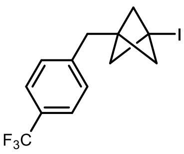
4i1



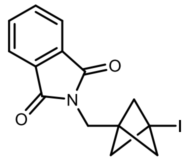
4j1



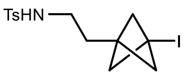
4k1



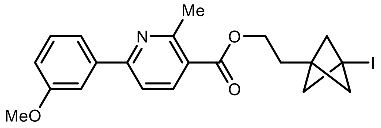
4z1



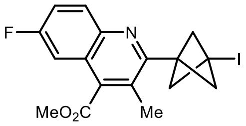
4aa1



4ab1



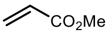
4ac1



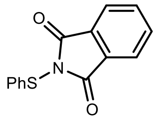
4ad1

Radical Acceptors

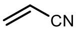
Radical acceptors **6b**, **6f** and **6l** – **6t** were obtained from commercial sources. Radical acceptors **6a**,[38] **6c**,[38] **6d**,[39] **6e**[40] and **6u**[41] were prepared according to literature procedures, which were modified where relevant.



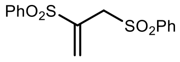
6b



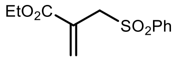
6f



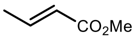
6l



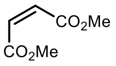
6a



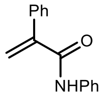
6c



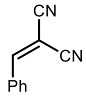
6m



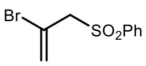
6n



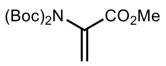
6o



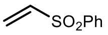
6p



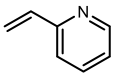
6d



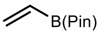
6u



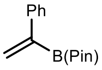
6q



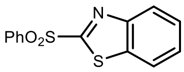
6r



6s



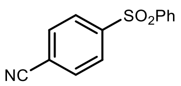
6t



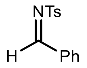
6e

Unsuccessful Radical Acceptors

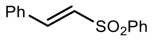
The following radical acceptors were either unsuccessful or gave <10% yield. **6ae**,[42] **6af**,[43] **6ag**,[44] and **6ah**[45] were prepared according to literature procedures. **6ai** and **6aj** were obtained from commercial sources.



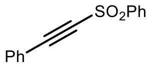
6ae



6af



6ag



6ah

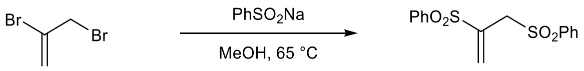
NFSI

6ai

Selectfluor

6aj

(Prop-1-ene-2,3-diyldisulfonyl)dibenzene, 6a



According to a modified literature procedure.[38] Sodium benzenesulfinate (4.62 g, 28.1 mmol) was added to a solution of 2,3-dibromoprop-1-ene (1.83 mL, 18.7 mmol) in anhydrous MeOH (38 mL) at room temperature. The reaction mixture was then heated to 65 °C for 2 h then left to cool and concentrated *in vacuo*. The reaction mixture was diluted with EtOAc (200 mL), washed with H_2O (100 mL), brine (100 mL) and then dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:4) and re-crystallisation from EtOAc/hexanes (1:1) gave the title compound (2.01 g, 8.23 mmol, 44%) as an off-white solid.

R_f 0.19 (EtOAc/pentane, 3:7) [UV, $KMnO_4$].

m.p. 121 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.73 (4H, m, Ar), 7.69 – 7.61 (2H, m, Ar), 7.55 – 7.48 (4H, m, Ar), 6.68 (1H, d, *J* = 1.2 Hz, H1), 6.52 (1H, app. q, *J* = 1.2 Hz, H1), 4.06 (2H, d, *J* = 1.2 Hz, H3).

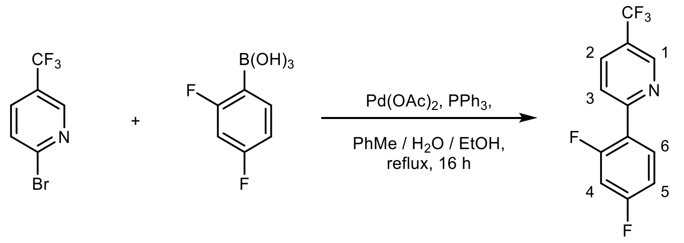
^{13}C NMR (101 MHz, $CDCl_3$) δ 139.7, 138.0, 134.5, 134.2, 131.3, 129.6, 129.5, 128.7, 128.6, 54.3.

Data in agreement with literature values.[46]

S3.4 Catalyst and Silanes

Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$

2-(2,4-Difluorophenyl)-5-(trifluoromethyl)pyridine, Step 1:



According to a modified literature procedure.[41] 2,4-difluorophenylboronic acid (3.68 g, 23.3 mmol), 2-bromo – 5-trifluoromethylpyridine (5.00 g, 22.1 mmol), potassium carbonate (9.17 g, 66.4 mmol), palladium acetate (148 mg, 0.66 mmol) and triphenylphosphine (349 mg, 1.33 mmol) were added to a three-necked 250 mL round bottomed flask. The flask was equipped with a condenser then evacuated and refilled with N_2 (× 3). Toluene (29 mL), H_2O (29 mL) and ethanol (6 mL) were then added and the reaction mixture was heated to reflux for 16 h. The flask was then cooled to room temperature and quenched with H_2O (100 mL). The organic phase was separated and then the aqueous phase was extracted with Et_2O (200 mL × 3). The combined organic phases were washed with brine (200 mL), dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, EtOAc/pentane 1:99 → 4:96) gave the title compound (4.89 g, 18.8 mmol, 85%) as a white solid.

R$_f$ 0.80 (EtOAc/pentane, 1:4).

m.p. 53 – 58 °C.

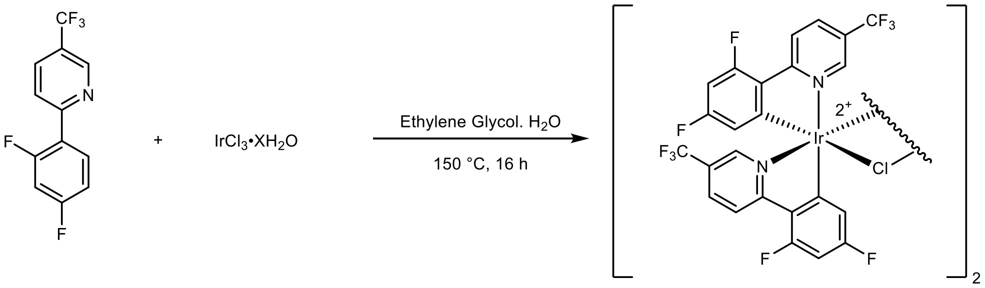
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (dq, *J* = 2.7, 0.9 Hz, H1), 8.10 (1H, app. td, *J* = 8.9, 6.6 Hz, H6), 8.02 – 7.95 (1H, m, H2), 7.91 (1H, ddt, *J* = 8.4, 2.0, 0.8 Hz, H3), 7.09 – 7.00 (1H, m, H5), 6.95 (1H, ddd, *J* = 11.3, 8.7, 2.5 Hz, H4).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1 (dd, $^{1,3}J_{CF}$ = 253.1, 12.4 Hz), 161.1 (dd, $^{1,3}J_{CF}$ = 253.8, 11.8 Hz), 155.9, 146.7 (q, $^3J_{CF3}$ = 4.1 Hz), 133.9 (q, $^3J_{CF3}$ = 3.6 Hz), 132.6 (dd, $^{3,3}J_{CF}$ = 9.8, 4.1 Hz), 125.3 (q, $^2J_{CF3}$ = 33.3 Hz), 123.8 (app. d, *J* = 10.8 Hz), 123.7 (q, $^1J_{CF3}$ = 272.3 Hz), 122.5 (dd, $^{2,4}J_{CF}$ = 11.3, 3.8 Hz), 112.4 (dd, $^{2,4}J_{CF}$ = 21.3, 3.6 Hz), 104.8 (dd, $^{2,2}J_{CF}$ = 26.9, 25.4 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ –62.40, –107.17 (app. t, *J* = 8.0 Hz), –112.06 (d, *J* = 9.3 Hz).

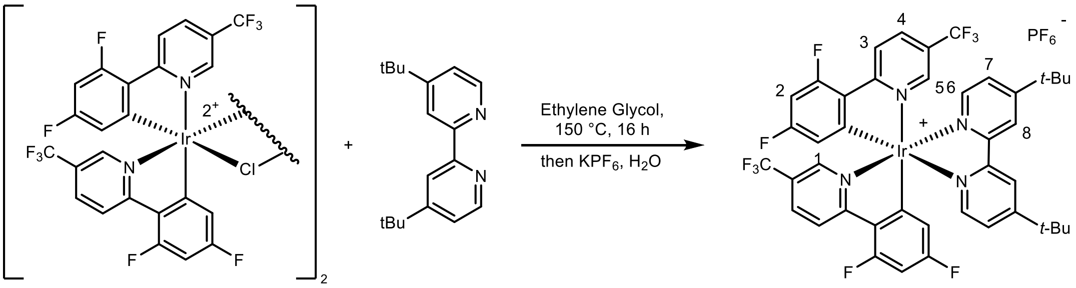
Data in agreement with literature values.[41]

[Ir(dF(CF$_3$)ppy)$_2$Cl]$_2$, Step 2:



According to a modified literature procedure.[41] Iridium(III) chloride hydrate (448 mg, 1.50 mmol) and 2-(2,4-difluorophenyl) – 5-(trifluoromethyl)pyridine (856 mg, 3.30 mmol) were added to a three-necked 100 mL round bottomed flask with a condenser, and then evacuated and refilled with N_2 (× 3). A mixture of rigorously degassed ethylene glycol (18 mL) and H_2O (6 mL) was then added. The reaction mixture was heated 150 °C for 16 h. The reaction mixture was then cooled to room temperature and the bright yellow precipitate formed was filtered under a blanket of N_2. The precipitate was washed with H_2O (150 mL) and then hexane (60 mL) and dried *via* high vacuum. The product was used immediately without further purification.

[Ir(dF(CF$_3$)ppy)$_2$(dtbpy)]PF$_6$, Step 3:



According to a modified literature procedure.[41] Crude [Ir(dF(CF$_3$)ppy)$_2$Cl]$_2$ (600 mg, 0.41 mmol) and 4,4′-di-*tert*-butyl – 2,2′-dipyridyl (268 mg, 1.00 mmol) were added to a three-necked 100 mL round bottomed flask equipped with a reflux condenser, and then evacuated and refilled with N$_2$ (× 3). Rigorously degassed ethylene glycol (28 mL) was then added *via* syringe. The reaction mixture was then heated to 150 °C for 16 h. The reaction mixture was then cooled to room temperature and then diluted with H$_2$O (150 mL) and hexane (150 mL). The aqueous phase was separated and then re-extracted with hexane (150 mL × 2). The combined aqueous phases were decanted into a 500 mL conical flask equipped with a stirrer bar. The flask was heated at 80 °C for 1 h to remove residual hexane. The flask was allowed to return to room temperature, and an aqueous solution of potassium hexafluorophosphate (4.40 g in 44 mL H$_2$O) was added with stirring, and a vibrant yellow precipitate was formed. The mixture was then allowed to stand at 0 °C for 1 h, before the precipitate was collected *via* vacuum filtration and then washed with H$_2$O (100 mL) and hexane (100 mL). The powdery solid was recrystalised from acetone and pentane to give the title compound (541 mg, 0.48 mmol, 32% over two steps) as a yellow solid.

m.p. >200 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 – 8.43 (4H, m), 8.03 (2H, d, *J* = 8.6 Hz), 7.87 (2H, d, *J* = 5.9 Hz), 7.60 (2H, dd, *J* = 5.9, 1.7 Hz), 7.41 (2H, s), 6.64 (2H, ddd, *J* = 12.4, 8.9, 2.3 Hz, H2), 5.63 (2H, dd, *J* = 8.1, 2.3 Hz, H1), 1.46 (18H, s, *t*-Bu).

^{19}F NMR (377 MHz, $CDCl_3$) δ –63.04 (6F, s), –72.27 (3F, s), –74.17 (3F, s), –101.95 (2F, dt, *J* = 12.5, 8.5 Hz), –105.95 (2F, td, *J* = 12.5, 3.4 Hz).

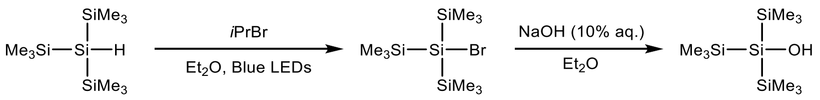
^{1}H NMR (500 MHz, d_6-Acetone) δ 8.92 (2H, app. d, *J* = 2.0 Hz, H5), 8.61 (2H, app. dd, *J* = 8.8, 2.6 Hz, H4), 8.39 (2H, app. dd, *J* = 8.8, 2.1 Hz, H3), 8.17 (2H, d, *J* = 5.9 Hz, H6), 7.81 (2H, dd, *J* = 5.9, 2.0 Hz, H7), 7.78 (2H, dt, *J* = 1.9, 0.9 Hz, H8), 6.85 (2H, ddd, *J* = 12.7, 9.3, 2.4 Hz, H2), 5.95 (2H, dd, *J* = 8.4, 2.4 Hz, H1), 1.43 (18H, s, *t*-Bu).

^{13}C NMR (126 MHz, d_6-Acetone) δ 168.8, 168.7, 165.5 (dd, $^{1,3}J_{CF}$ = 258.7, 12.7 Hz), 166.3, 163.3 (dd, $^{1,3}J_{CF}$ = 261.8, 13.3 Hz), 156.9, 156.6, 156.6, 152.0, 146.6 (q, $^3J_{CF3}$ = 4.7 Hz), 138.1 (q, $^3J_{CF3}$ = 3.7 Hz), 127.7 (dd, $^{3,3}J_{CF}$ = 4.6, 2.7 Hz), 127.0, 126.1 (q, $^2J_{CF3}$ = 34.7 Hz), 124.8 (d, $^2J_{CF}$ = 21.0 Hz), 123.5, 123.0 (q, $^1J_{CF3}$ = 271.9 Hz), 115.3 (dd, $^{2,4}J_{CF}$ = 17.9, 3.0 Hz), 100.1 (app. t, $^2J_{CF}$ = 27.0 Hz), 69.3, 36.6.

^{31}P NMR (202 MHz, d_6-Acetone) δ –144.27 (hept., *J* = 707.6 Hz).

Data in agreement with literature values.[47]

1,1,1,3,3,3-Hexamethyl-2-(trimethylsilyl)trisilan-2-ol, $(Me_3Si)_3SiOH$, Supersilanol



According to a literature procedure.[48] 2-bromopropane (2.3 mL, 25.0 mmol) was added dropwise to a solution of TMS_3SiH (3.6 mL, 12.5 mmol) in Et_2O (4.0 mL) under air in a 40 mL reaction vial. The reaction vial was capped under air and irradiated with blue LEDs for

12 hours. After irradiation, the reaction vial was slowly opened to allow for a slow gas evolution. After the gas evolution was complete, the organic solution was poured into a round-bottom flask containing NaOH (10% aq., 11.0 mL). More Et_2O was used to ensure complete transfer. This reaction mixture was stirred at room temperature under air for 24 h. Et_2O was then added and the organic layer was separated, dried and concentrated *in vacuo* to yield the crude silanol. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9 → 1:4) gave $(Me_3Si)_3SiOH$ as a colourless oil which was stored in the freezer.

$(Me_3Si)_3SiH$: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.15 (1H, s, SiH), 0.20 (27H, s, TMS).

$(Me_3Si)_3SiBr$: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 0.25 (27H, s, TMS).

IR ν_{max}/cm^{-1} (film) 3420 (br.), 2950, 2925, 2854, 2360, 1244, 836.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.18 (27H, s, TMS).

^{1}H NMR (400 MHz, CD_3CN) δ 1.80 (1H, s, OH), 0.15 (27H, s, TMS).

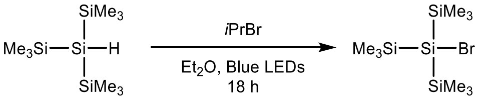
^{13}C NMR (101 MHz, CD_3CN) δ –0.21.

LRMS *m/z* (ESI$^+$) $[M - OH]^+$ 247.0.

Data in agreement with that reported previously.[48]

1,1,1,3,3,3-Hexamethyl-2-(trimethylsilyl)trisilane-2-d, *d₁*-$(Me_3Si)_3SiD$

2-Bromo-1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane, $(Me_3Si)_3SiBr$, Step 1:

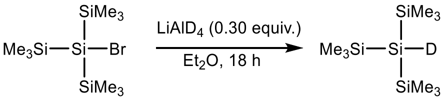


According *to a modified literature procedure.*[48] 2-bromopropane (09 mL, 6.00 mmol) was added dropwise to a solution of $(Me_3Si)_3SiH$ (1.54 mL, 5.00 mmol) in anhydrous Et_2O (1.60 mL) under air in a 20 mL reaction vial. The reaction vial was capped under air and irradiated with blue LEDs for 24 hours. After irradiation, the reaction vial was slowly opened to allow for a slow gas evolution. After the gas evolution was complete the mixture was concentrated *in vacuo* to give $(Me_3Si)_3SiBr$ (1.60g, 4.90 mmol, 98%) as a white solid. The product was of sufficient purity to use without further purification.

IR ν_{max}/cm^{-1} (film) 2981, 2888, 2361, 2341, 1387, 1251, 1152, 1073, 954.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.25 (27H, s, TMS).

1,1,1,3,3,3-Hexamethyl-2-(trimethylsilyl)trisilane-2-d, d_1-$(Me_3Si)_3SiD$, Step 2:



According to a modified literature procedure.[49] A solution of (trimethylsilyl) silane bromide (1.60 g, 4.90 mmol) in anhydrous Et_2O (2.75 mL) was added dropwise to a solution of lithium aluminium deuteride (63 mg, 1.5 mmol) in anhydrous ether (1.18 mL) under N_2. The reaction mixture was stirred at room temperature overnight and then quenched with dropwise addition of H_2O (1 mL) then HCl (1 M aq., 1 mL) at 0 °C then left to stir at room temperature for 15 min. The phases were separated and the aqueous phase was extracted with Et_2O (5 mL × 2). The combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo* to give deuteride of tris (trimethylsilyl) silane (1.08 g, 4.35 mmol, 89%) as a colourless oil and was used without further purification.

99.7% d-incorporation based on ^{1}H NMR.

92% purity (assuming $(Me_3Si)_2SiD_2$ as a by product).

Note: $(Me_3Si)_3SiBr$ was not reduced by $NaBD_4$.

IR v_{max}/cm^{-1} (film) 2981, 2888, 2361, 1382, 1251, 1152, 1073, 954.

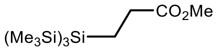
^{1}H NMR (500 MHz, $CDCl_3$) δ 0.19 (27H, s, TMS), satellites at (0.34, 0.04).

^{13}C NMR (126 MHz, $CDCl_3$) δ 2.0, –0.6.

^{29}Si NMR (99 MHz, $CDCl_3$) δ –12.3 (s), –22.6 (s).

$(Me_3Si)_3SiH$: **^{29}Si NMR** (99 MHz, $CDCl_3$) δ –11.28 (s), –11.47 (s).

Methyl 3-(1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-yl)propanoate, 6b-Si

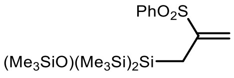


According to the procedure described for the synthesis **4b**, the silane adduct **6b-Si** could be isolated by colulmn chromatography. ^{1}H NMR yield of 40% with respect to $(Me_3Si)_3SiH$, 13% with respect to methyl acrylate **6b**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65 (3H, s, OMe), 2.36 – 2.30 (2H, m, CH_2), 1.12 – 1.16 (2H, m, CH_2), 0.16 (27H, s, Me_3Si).

Data in agreement with literature values.[50]

1,1,1-Trimethyl-3-(2-(phenylsulfonyl)allyl)-3,3-bis(trimethylsilyl)disiloxane, 6a-Si

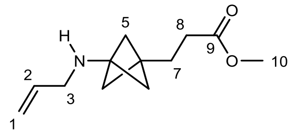


According to the procedure described for the synthesis **4a**, the silane adduct **6a-Si** could be isolated by column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.84 (2H, m, ArH), 7.66 – 7.57 (2H, m, ArH), 7.54 (1H, m, ArH), 6.20 (1H, s, $C=CH_2$), 5.55 (1H, app. q, *J* = 1.2 Hz, $C=CH_2$), 1.69 (2H, d, *J* = 1.3 Hz, CH_2), 0.18 (18 H, s, Me_3Si), 0.04 (9H, s, Me_3SiO).

S3.5 Further Functionalisations

Methyl 3-(3-(allylamino)bicyclo[1.1.1]pentan-1-yl)propanoate, 7



Mg turnings (17 mg, 0.70 mmol) were added to a solution of BCPA iodide **3a** (27 mg, 0.070 mmol) in MeOH (0.7 mL) and the reaction mixture was sonicated for 1 h. A second portion of Mg turnings (17 mg, 0.70 mmol) were added and sonication was continued until all the Mg had dissolved. The reaction mixture was quenched with NH_4Cl (sat. aq., 1 mL) then CH_2Cl_2 (5 mL) was added and the layers separated. The aqueous phase was extracted with CH_2Cl_2 (5 mL × 2) and then the combined organic layers were dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, EtOAc/pentane, 4:1 → 1:0) gave the title compound **7** (9 mg, 0.045 mmol, 64%) as a pale-yellow oil.

R_f 0.19 (EtOAc/pentane, 4:1).

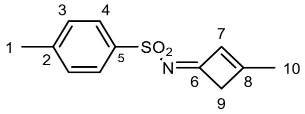
IR ν_{max}/cm^{-1} (film) 2965, 2910, 2868, 1738, 1672, 1437, 1249, 1194, 1175.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (1H, ddt, *J* = 17.2, 10.2, 5.9 Hz, H2), 5.16 (1H, app. dq, *J* = 17.2, 1.7 Hz, H1), 5.05 (1H, app. dq, *J* = 10.2, 1.5 Hz, H1), 3.66 (3H, s, H10), 3.21 (3H, dt, *J* = 5.9, 1.5 Hz, H3), 2.28 (2H, t, *J* = 7.6 Hz, H8), 1.86 (2H, t, *J* = 7.6 Hz, H7), 1.62 (6H, s, 10H), 1.59 (1H, br. s, NH).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 137.3, 115.5, 52.7, 51.7, 50.9, 48.6, 34.9, 31.9, 26.0.

HRMS (ESI^+) $[M + H]^+$ $C_{12}H_{20}O_2N$ requires 210.1489, found 210.1490.

(*Z,E*)-4-Methyl-*N*-(3-methylcyclobut-2-en-1-ylidene)benzenesulfonamide, 8



Pd(dppf)(Cl)$_2$ (3.8 mg, 10 mol%) and NaBH(OAc)$_4$ (16 mg, 0.080 mmol) were added sequentially to a solution of BCPA iodide **3a** (20 mg, 0.050 mmol) in anhydrous THF (0.4 mL) in a flame dried vial. The vial was capped and stirred at room temperature for 16 h, then quenched with NH$_4$Cl (sat. aq., 0.5 mL). The biphasic mixture was diluted with EtOAc (10 mL), separated and then the aqueous phase was extracted with further portions of EtOAc (10 mL × 2). The combined organic phases were dried (Mg$_2$SO$_4$), filtered and then concentrated *in vacuo*. Purification by column chromatography (SiO$_2$, EtOAc/pentane, 3:15 → 4:15) gave the title compound **8** (4 mg, 0.016 mmol, 32%, *Z:E*, 1.2:1) as a colourless oil.

R$_f$ 0.34 (EtOAc/pentane, 3:7).

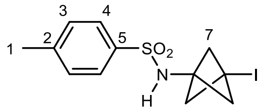
IR ν_{max}/cm^{-1} (film) 2981, 2360, 1657, 1574, 1320, 1159, 1089, 842.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.85 (3.6H, dd, *J* = 8.4, 2.6 Hz, H4), 7.35 – 7.28 (3.6H, m, H3), 6.57 (0.8H, qt, *J* = 1.4, 0.7 Hz, H7$_Z$), 6.00 (0.7H, app. dq, *J* = 2.1, 0.8 Hz, H7$_E$), 3.59 – 3.50 (1.7H, m, H9$_E$), 3.21 – 3.12 (2H, m, H9$_Z$), 2.43 (5.9H, s, H1), 2.26 (3H, app. q, *J* = 1.2 Hz, H10$_Z$), 2.24 (2.5H, app. q, *J* = 1.2 Hz, H10$_E$)

^{13}C NMR (101 MHz, CDCl$_3$) δ 133.1, 132.8, 129.8, 127.6, 46.5, 46.1, 21.7, 18.8, 18.8.

HRMS (ESI)$^+$ [M + H]$^+$ C$_{12}$H$_{14}$O$_2$NS requires 236.0740, found 236.0740.

N-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-methylbenzenesulfonamide, 9



According to a modified literature procedure.[51] BCPA iodide **3a** (40 mg, 0.10 mmol), 1,3-dimethylbarbituric acid (47 mg, 0.30 mmol) and Pd(PPh_3)$_3$ (35 mg, 0.030 mmol) were added to a vial and evacuated and purged with N_2 (× 3). Anhydrous THF (1.4 mL) was added and the vial was capped and stirred at 50 °C for 24 h. The reaction mixture was cooled to room temperature then H_2O (4 mL was added, and the biphasic mixture was extracted with EtOAc (5 mL × 3). The combined organic layers were dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 1:4) gave the title compound **9** (26 mg, 0.072 mmol, 72%). Recrystallisation (CH_2Cl_2/pentane) gave the product as off-white crystals.

R$_f$ 0.29 (EtOAc/pentane, 1:4) [UV, Ninhydrin].

m.p. 134 °C.

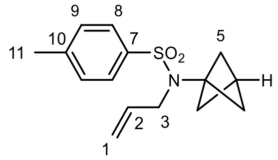
IR ν_{max}/cm^{-1} (film) 3253 (br.), 2980, 2361, 2342, 1325, 1191, 1160, 1093, 992.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.66 (2H, m, H4), 7.36 – 7.28 (2H, m, H3), 5.10 (1H, s, NH), 2.44 (3H, s, H1), 2.29 (6H, s, H7).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.2, 137.7, 130.0, 127.4, 61.9, 51.2, 21.7, –0.8.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{12}H_{14}O_2NINaS$ requires 385.9682; found 385.9682.

N-Allyl-*N*-(bicyclo[1.1.1]pentan-4-yl)-*p*-methylbenzenesulfonamide, 3a-H



BCPA iodide **3a** (74 mg, 0.18 mmol) and *fac*-Ir(ppy)$_3$ (3.0 mg, 2.5 mol%) were added to a flame dried vial, the vial was then evacuated and put under an Ar atmosphere. *tert*-BuCN (1.8 mL) and $(Me_3Si)_3SiH$ (72 µL, 0.23 mmol) were then added, and the solution was degassed by freeze-pump-thaw cycles (× 3). The stirred mixture was irradiated with blue LEDs for 1 h and then concentrated *in vacuo*. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:9) and slow recrystallization from pentane at –5 °C gave the title compound **3a-H** (28 mg, 0.10 mmol, 54%) as a white solid.

R$_f$ 0.30 (Et_2O/pentane, 1:9) [UV, vanillin].

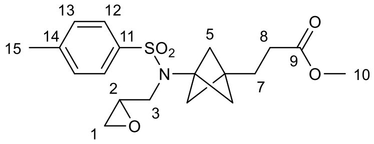
IR ν_{max}/cm^{-1} (film) 2950, 1343, 1243, 1158, 1092, 834.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.66 (2H, m, H8), 7.29 – 7.27 (2H, m, H9), 5.82 (1H, ddt, *J* = 17.2, 10.2, 5.6 Hz, H2), 5.24 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.13 (1H, app. dq, *J* = 10.2, 1.5 Hz, H1), 3.91 (2H, app. dt, *J* = 5.6, 1.6 Hz, H3), 2.42 (3H, s, H11), 2.33 (1H, s, H6), 1.96 (6H, s, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2, 138.7, 135.3, 129.6, 127.3, 117.1, 54.0, 53.2, 49.9, 23.8, 21.7.

HRMS (ESI)$^+$ [M + Na]$^+$ $C_{15}H_{19}O_2NNaS$, requires 300.1029; found 300.1030.

Methyl 6-(4-((*p*-methyl-*N*-(oxiran-2-ylmethyl)phenyl)sulfonamido)bicyclo[1.1.1]pentan-1-yl)propanoate, 10



According to a modified literature procedure.[52] KBr (50 mg, 0.42 mmol) was added to a solution of BCPA iodide **3a** (49 mg, 0.14 mmol) in CH_2Cl_2/H_2O (9:1, 0.82 mL) at room temperature. Then Oxone® (172 mg, 0.28 mmol) was added in one portion. The reaction mixture was stirred at room temperature for 22 h and then Na_2SO_3 (sat. aq., 3 mL) was added to the mixture. The aqueous phase was extracted with EtOAc (5 mL × 3), the combined organic phases were washed with brine (10 mL), dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, Et_2O/pentane, 1:4) gave epoxide **10** (37 mg, 0.10 mmol, 71%) as a colourless oil.

R_f 0.28 (Et_2O/pentane, 1:4) [UV, vanillin].

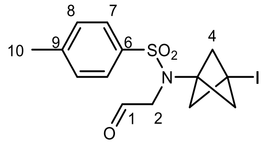
IR ν_{max}/cm^{-1} (film) 3649, 2981, 2883, 1737, 1351, 1246, 1160, 1091, 812.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.67 (2H, m, H12), 7.35 – 7.28 (2H, m, H13), 4.49 (1H, tt, *J* = 7.0, 5.8 Hz, H2), 3.84 (2H, app. dd, *J* = 5.9, 2.1 Hz, H3), 3.81 (1H, dd, *J* = 15.1, 7.0 Hz, H1), 3.44 (1H, dd, *J* = 15.1, 7.0 Hz, H1), 2.44 (3H, s, H15), 2.23 (2H, t, *J* = 7.5 Hz, H8), 1.86 – 1.77 (8H, m, H7, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 144.0, 137.2, 129.9, 127.7, 52.9, 52.7, 51.8, 51.1, 50.8, 35.7, 35.1, 31.5, 25.1, 21.7.

HRMS (ESI, APCI) Not Found.

N-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-methyl-*N*-(2-oxoethyl)benzenesulfonamide, 11



A solution of BCPA iodide **3a** (61 mg, 0.15 mmol) in anhydrous CH_2Cl_2 (2.0 mL) was cooled to –78 °C. A glass pipette O_3 bubbler was submerged into the flask and the exit tube was connected to a bubbler of $NaSO_3$ (sat. aq.). The reaction flask was purged with O_2 for 1 min, then O_3 for 10 min. The solution turned very pale blue and then the flask was purged with O_2 for 1 min. Me_2S (0.1 mL) was then added and the reaction stirred at room temperature overnight. The reaction mixture was poured onto H_2O (10 mL) and extracted with CH_2Cl_2 (5 mL × 3). The combined organic phases were washed with LiCl (5% aq., 5 mL × 3), dried (Mg_2SO_4), filtered and concentrated *in vacuo.* Purification by a column chromotography (SiO_2, EtOAc/pentane, 0:1 → 1:4) gave aldehyde **11** (43 mg, 0.11 mmol, 71%) as a colourless oil.

R_f 0.30 (EtOAc/pentane, 1:4).

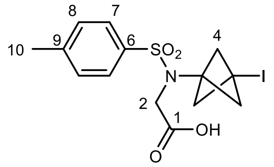
IR ν_{max}/cm^{-1} (film) 1734, 1349, 1199, 1159, 1094, 978, 885.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (1H, t, *J* = 1.3 Hz, H1), 7.73 – 7.66 (2H, m, H7), 7.37 – 7.29 (2H, m, H8), 3.97 (2H, d, *J* = 1.3 Hz, H2), 2.45 (3H, s, H10), 2.35 (6H, s, H4).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8, 144.6, 136.9, 130.1, 127.6, 61.6, 56.2, 56.0, 21.8, –1.4.

HRMS (ESI)$^+$ [M + H]$^+$ $C_{14}H_{17}O_3NIS$ requires 405.9965, found 405.9969.

N-(3-Iodobicyclo[1.1.1]pentan-1-yl)-*N*-tosylglycine, 12



According to a modified literature procedure.[53] $NaIO_4$ (160 mg, 0.75 mmol) was added to a solution of BCPA iodide **3a** (60.5 mg, 0.15 mmol) in CCl_4 (0.3 mL) and H_2O (0.45 mmol). A solution of $RuCl_3.3H_2O$ (2.0 mg, 0.0016 mmol) in MeCN (0.3 mL) was then added and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and H_2O (5 mL) and separated. The aqueous phase was extracted with CH_2Cl_2 (5 mL × 2) and the combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, CH_2Cl_2/MeOH, 93:7) gave the *N*-tosylglycine BCPA iodide **12** (23 mg, 0.055 mmol, 37%) as a white solid.

R_f 0.19 (CH_2Cl_2/MeOH, 9:1).

m.p. 116 – 120 °C

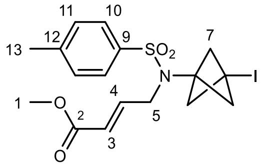
IR ν_{max}/cm^{-1} (film) 3452 (br.), 2360, 2342, 1597, 1597, 1260, 1199, 1156, 1092, 882, 745.

^{1}H NMR (400 MHz, *d*$_4$-MeOD) δ 7.76 (2H, br. d, *J* = 8.3 Hz, H7), 7.39 (2H, br. d, *J* = 8.3 Hz, H8), 3.85 (2H, s, H2), 2.44 (3H, s, H710), 2.35 (6H, s, H4).

^{13}C NMR (126 MHz, *d*$_4$-MeOD) δ 175.0, 145.3, 139.3, 130.8, 128.5, 62.9, 57.1, 50.8, 21.5, 0.3.

HRMS (ESI$^+$) $[M + H]^+$ $C_{14}H_{17}O_4NIS$ requires 421.9917; found 421.9918.

Methyl (*E*)-4-((*N*-(3-iodobicyclo[1.1.1]pentan-1-yl)-4-methylphenyl)sulfonamido)but-2-enoate, 13



According to a modified literature procedure.[54] Grubbs catalyst second generation (1.7 mg, 2 mol%) and BCPA iodide **3a** (40 mg, 0.10 mmol) were added to a flame dried vial. The vial was evacuated and refilled with Ar (× 3), then the solids were dissolved in degassed CH_2Cl_2 (1.0 mL) then methyl acrylate (45 µL, 0.50 mmol) was added. The vial was capped and stirred at 45 °C for 24 h. An additional portion of Grubbs catalyst second generation (1.7 mg, 2 mol%) was added and then the mixture was stired at 45 °C for a further 48 h. The reaction mixture was then cooled and concentrated *in vacuo*. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:19 → 3:17) gave the title compound **13** (33 mg, 0.072 mmol, 72%) as a pale-yellow oil.

R_f 0.43 (EtOAc/pentane, 1:4).

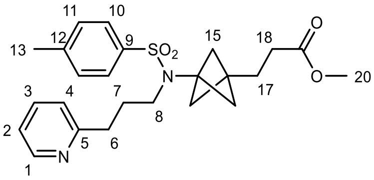
IR ν_{max}/cm^{-1} (film) 2980, 1722, 1347, 1277, 1197, 1172, 1091, 881, 666.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.62 (2H, m, H10), 7.35 – 7.27 (2H, m, H11), 6.85 (1H, dt, *J* = 15.6, 5.1 Hz, H4), 6.01 (1H, dt, *J* = 15.6, 1.9 Hz, H3), 4.02 (2H, dd, *J* = 5.1, 1.9 Hz, H5), 3.74 (3H, s, H1), 2.43 (3H, s, H13), 2.37 (6H, s, H7).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 144.2, 144.0, 137.5, 130.0, 127.3, 123.0, 62.0, 55.9, 53.0, 48.4, 21.7, –1.0.

HRMS (ESI$^+$) $[M + H]^+$ $C_{17}H_{21}NO_4IS$ requires 462.0230; found 462.0231.

Methyl-3-(3-((4-methyl-*N*-(3-(pyridine-2-yl)propyl)phenyl)sulfonamido)bicyclo[1.1.1]pentan-1-yl)propanoate, 14



According to a modified literature procedure.[55] Vials of THF and DMF were degassed by freeze-pump-thaw cycles (× 3). 9-BBN (0.5 M in THF, 0.3 mL, 0.15 mmol) was added to a solution of **6b** (36 mg, 0.10 mmol) in THF (0.17 mL) in a flame dried vial and stirred at room temperature for 19 h. Consumption of starting material was monitored by TLC. In a separate flame dried vial, Cs_2CO_3 (108 mg, 0.33 mmol), $AsPh_3$ (14 mg, 0.050 mmol), Pd(dppf)(Cl_2) (34 mg, 0.050 mmol) were added. The vial was evacuated and filled with N_2 (× 3). The solids were dissolved in DMF (1.0 mL), then 2-bromopyridine (14 µL, 0.15 mmol) was added and the mixture was stirred at room temperature for 15 min. The solution of hydroborated BCPA was then transferred with additional portions of DMF (0.1 mL × 2). The vial was capped and heated to 80 °C for 48 h. The reaction mixture was cooled to room temperature and diluted with EtOAc (5 mL) and LiCl (5% aq., 10 mL). The biphasic mixture was separated and the organic phase was washed with further portions of LiCl (5% aq., 10 mL × 2). The combined organic phases was dried (Mg_2SO_4), filtered and concentrated *in vacuo.* Purification by column chromatography (SiO_2, EtOAc/pentane, 3:7 → 3:2) gave the title compound **14** (12 mg, 0.027 mmol, 28%) as a pale-yellow oil. *Compound* ***15*** *(8.0 mg, 0.019 mmol, 20%) was also isolated on elution to EtOAc/pentane, 1:0.*

R$_f$ 0.14 (EtOAc/pentane, 2:3).

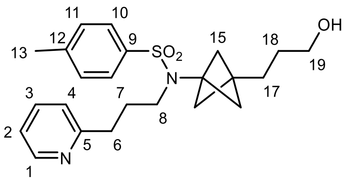
IR ν_{max}/cm^{-1} (film) 2972, 2914, 2873, 1736, 1592, 1343, 1249, 1158, 668.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (1H, ddd, *J* = 4.9, 1.9, 0.9 Hz, H1), 7.69 – 7.61 (2H, m, H10), 7.60 (1H, td, *J* = 7.6, 1.9 Hz, H3), 7.29 – 7.22 (2H, m, H11), 7.19 (1H, dt, *J* = 7.8, 1.2 Hz, H4), 7.11 (1H, ddd, *J* = 7.6, 4.9, 1.2 Hz, H2), 3.64 (3H, s, H20), 3.35 – 3.23 (2H, m, H8), 2.83 (2H, t, *J* = 7.6 Hz, H6), 2.41 (3H, s, H13), 2.21 (2H, dd, *J* = 8.0, 7.1 Hz, H18), 2.13 – 2.03 (2H, m, H7), 1.80 (2H, app. t, *J* = 7.6 Hz, H17), 1.75 (6H, s, H15).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 161.3, 149.4, 143.1, 138.7, 136.5, 129.6, 127.3, 123.1, 121.3, 53.0, 51.8, 50.6, 47.4, 35.7, 35.5, 31.6, 30.6, 25.2, 21.6.

HRMS (ESI^+) $[M + H]^+$ $C_{23}H_{29}N_2O_4S$ requires 443.1999; found 443.2001.

N-(3-(3-Hydroxypropyl)bicyclo[1.1.1]pentan-1-yl)-4-methyl-*N*-(3-(pyridine-2-yl)propyl)benzenesulfonamide, 15



According to a modified literature procedure.[56] 9-BBN (0.5 M in THF, 0.49 mL, 2.46 mmol) was added to a solution of BCPA **16** (42 mg, 1.23 mmol) in anhydrous THF (0.15 mL) in a flame dried vial cooled to 0 °C. The vial was capped and heated to 50 °C for 2.5 h. The reaction mixture was cooled to room temperature and then K_3PO_4 (3.0 M aq., 0.11 mL, 3.20 mmol) was added and the reaction mixture was stirred at room temperature for 30 min. In a separate flame dried vial, 2-bromopyridine (26 µL, 2.80 mmol) was added to a solution of $Pd(PPh_3)_4$ (7 mg, 5 mol%) in anhydrous THF (0.11 mL) and stirred for 15 min. The hydroborated BCPA was added and transferred with an additional portion of THF (0.1 mL × 3). The vial was capped and heated to 65 °C for 24 h. The reaction mixture was cooled to room temperature and quenched with H_2O_2 (30% aq., 0.2 mL) then diluted with EtOAc

(5 mL) and H_2O (5 mL). The biphasic mixture was separated and the aqueous phase was extracted with EtOAc (5 mL × 2). The combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo.* Purification by column chromatography (SiO_2, EtOAc/pentane, 7:3 → 9:1) gave the title compound **16** (15 mg, 0.036 mmol, 33%) as a pale-yellow oil. The product was inseparable from remaining catalyst, which is reflected in the aromatic region of the ^{1}H NMR.

R_f 0.35 (EtOAc) [UV, Vanillin].

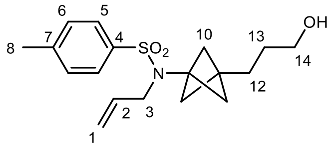
IR ν_{max}/cm^{-1} (film) 3346 (br.), 2968, 2916, 2872, 1594, 1342, 1246, 1158, 699.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.62 (8H, m, ArH), 7.57 – 7.52 (3H, m, ArH), 7.49 – 7.43 (6H, m, ArH), 7.28 (2H, d, *J* = 8.2 Hz, H11), 3.78 (2H, t, *J* = 5.6 Hz, H19), 3.59 (2H, t, *J* = 6.3 Hz, H8), 3.39 (2H, t, *J* = 6.3 Hz, H6), 2.66 (1H, s, OH), 2.42 (3H, s, H13), 1.80 (6H, s, H15), 1.79 – 1.72 (2H, m, H7), 1.60 – 1.42 (4H, m, H17, H18).

^{13}C NMR (151 MHz, $CDCl_3$) δ 143.4, 138.1, 133.0, 132.3, 132.2, 129.7, 128.7, 128.6, 127.2, 62.8, 58.6, 53.1, 50.5, 44.0, 36.3, 32.9, 30.2, 26.1, 21.6.

HRMS (ESI$^+$) $[M + H]^+$ $C_{23}H_{31}N_2O_3S$ requires 415.1977, found 415.2048.

N-Allyl-*N*-(3-(3-hydroxypropyl)bicyclo[1.1.1]pentan-1-yl)-4-methylbenzenesulfonamide, 16



BCPA **6b** (63 mg, 0.17 mmol) was dissolved in anhydrous Et_2O (1.7 mL) and cooled to 0 °C and then $LiAlH_4$ (4.0 M in THF, 0.03 mL, 0.13 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 30 min and then quenched *via* dropwise addition of Na_2SO_4 (sat. aq., 0.5 mL), then EtOAc (0.5 mL). The mixture was dried (Mg_2SO_4), filtered and concentrated *in vacuo* to give the title compound **15** (49 mg, 0.15 mmol, 88%). No purification was required.

R$_f$ 0.37 (EtOAc/pentane, 2:3) [UV, Vanillin].

IR ν_{max}/cm^{-1} (film) 3657, 2981, 2889, 1382, 1251, 1155, 1073, 955.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.65 (2H, m, H5), 7.30 – 7.24 (2H, m, H6), 5.82 (1H, ddt, *J* = 17.2, 10.2, 5.6 Hz, H2), 5.23 (1H, app. dq, *J* = 17.2, 1.6 Hz, H1), 5.13 (1H, app. dq, *J* = 10.2, 1.4 Hz, H1), 3.91 (2H, app. dt, *J* = 5.6, 1.6 Hz, H3), 3.59 (2H, t, *J* = 6.1 Hz, H14), 2.42 (3H, s, H8), 1.80 (6H, s, H10), 1.56 – 1.42 (4H, m, H12, H13).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2, 138.8, 135.4, 129.6, 127.4, 117.1, 62.9, 53.3, 50.8, 50.1, 36.4, 30.2, 26.1, 21.7.

HRMS (ESI$^+$) $[M + Na]^+$ $C_{18}H_{25}O_3NNaS$ requires 358.1447; found 358.1449.

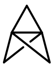
S4.

Chapter 4 Experimental Data

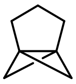
S4.1 General Experimental Procedures

Strain Release Reagents

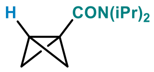
[1.1.1]Propellane **1** was prepared according to literature procedure (described in section S4.1).[57] TCH **30** was prepared by N. Frank[58] and BCBs **31a** – **31d** were prepared by R. McNamee.[59]



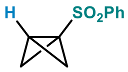
1



30



31a

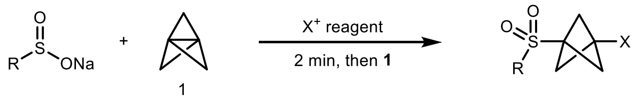


31b

31c

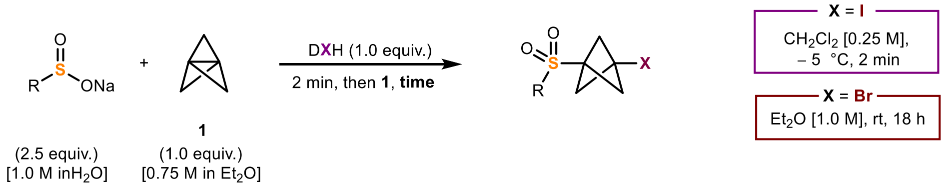
31d

General Procedure 11 – Sulfonyl BCP Halides from Sulfinate salts



All procedures were carried out under air, neither flame drying of glassware or use of anhydrous solvents were necessary. Purification of sulfonyl BCP halides with a short pad of silica was usually sufficient unless otherwise stated. Sulfonyl BCP halides were re-crystallised from CH_2Cl_2 / pentane at –18 °C to afford crystals of suitable quality for X-ray diffraction.

General Procedure 11.1 - Aryl Sulfonyl BCP Iodides R = (Het)Aryl and X = I



Diiodo-5,5-dimethylhydantoin (DIH) (78.4 mg, 0.20 mmol) was suspended in CH_2Cl_2 (0.80 mL) at –5 °C (ice / salt) in a 3 mL vial equipped with a stir bar and septum. A solution of sodium sulfinate salt in H_2O (0.50 mL, 0.50 mmol, 1.0 M) was added dropwise to the DIH suspension and the slurry turned pale-yellow. The mixture was stirred vigorously for 2 min. A solution of [1.1.1]propellane **1** (0.27 mL, 0.20 mmol of a 0.75 M solution in Et_2O) was added, a colour change from pale-yellow to white took place. The reaction mixture was stirred at –5 °C for 2 min and then vial was sonicated (5 s to ensure complete mixing). The reaction mixture was quenched at room temperature with $Na_2S_2O_3$ (sat. aq., 0.50 mL). The biphasic mixture was poured onto H_2O (2 mL), extracted with CH_2Cl_2 (3 × 2 mL), then the combined organic phases were concentrated *in vacuo*. The residue was purified by silica plug (wash with pentane, followed by collection with EtOAc/pentane, 2:3) to give the sulfonyl BCP iodide, unless stated otherwise.

General Procedure 11.2 - Modification at –40 ° C, R = electron-deficient and X = Br

A solution of sodium sulfinate salt in DMF (0.50 mL, 0.50 mmol, 1.0 M) was added dropwise to the suspension of DIH (78.4 mg, 0.20 mmol) in CH_2Cl_2 (0.80 mL) at –40 °C (MeCN / dry ice). The mixture was stirred vigorously for 2 min, then [1.1.1]propellane **1** (0.27 mL, 0.20 mmol of a 0.75 M solution in Et_2O) was added and the mixture was stirred at this temperature for 20 min. The reaction was sonicated (5 s) then stirred at 0 °C for 10 min. The reaction was quenched at room temperature with $Na_2S_2O_3$ (sat. aq., 0.50 mL) and the biphasic mixture was poured onto H_2O (2 mL) and extracted with CH_2Cl_2 (2 × 2 mL). The combined organic phases were washed with LiCl (5% aq., 5 × 2 mL) and concentrated *in vacuo*. The residue was purified by silica plug (wash with pentane, followed by collection with EtOAc/pentane, 2:3) to give the sulfonyl BCP iodide, unless stated otherwise.

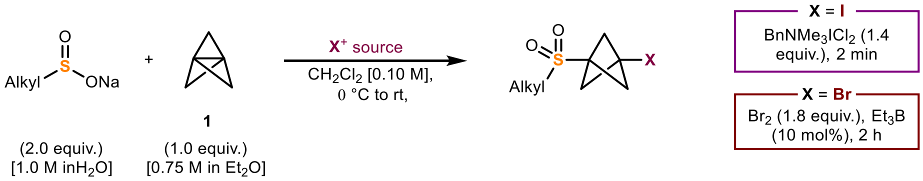
*Note: Lower reaction temperatures were required if the mixture containing the in-situ generated sulfonyl iodide turned dark orange/brown before addition of **1**. High yielding reactions typically remained pale yellow at this stage.*

General Procedure 11.3 - Aryl Sulfonyl BCP Bromides, *R = (Het)Aryl and X = Br*

Dibromo-5,5-dimethylhydantoin (DBH) (57.1 mg, 0.20 mmol) was suspended in Et_2O (0.20 mL, 1.0 M) at room temperature (21 °C) in a 3 mL vial equipped with a stir bar and septum. A solution of sodium sulfinate salt (0.50 mL, 0.50 mmol of a 1.0 M solution in H_2O) was added and the mixture was stirred for 2 min at room temperature. A solution of [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) was added. The vial was capped, wrapped in parafilm and stirred at room temperature for 18 h. The sulfonyl BCP bromide typically precipitated as a white solid overnight. The reaction mixture was quenched with $Na_2S_2O_3$ (sat. aq., 0.3 mL), extracted with CH_2Cl_2 (3 × 2 mL), then the combined organic phases were concentrated *in vacuo*. The residue was purified by silica plug (EtOAc/pentane, 2:3) to give the sulfonyl BCP bromide.

*Note: No colour changes were usually observed and a white precipitate (sulfonyl bromide) may from before addition of **1**.*

General Procedure 11.4 - Alkyl Sulfonyl BCP Iodides, *R = Alkyl and X = I*



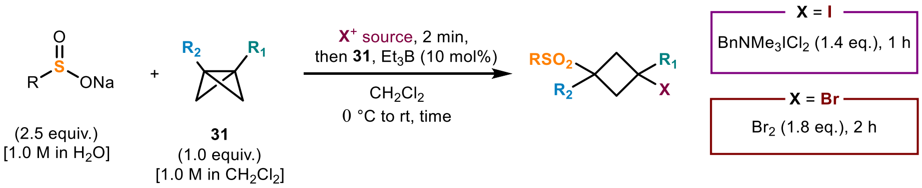
Benzyltrimethylammonium dichloroiodate (50.5 mg, 0.14 mmol) was suspended in CH_2Cl_2 (0.10 mL) in a 3 mL vial equipped with a stir bar and septum at –5 *°C*. A solution of sodium sulfinate salt (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O) was added and the mixture was stirred for 2 min. A solution of [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) was added. The reaction mixture was stirred at *–5 °C* for 2 min, then vial was sonicated (5 s) to ensure complete mixing. The reaction mixture was quenched at room temperature with $Na_2S_2O_3$ (sat. aq., 0.50 mL). The biphasic mixture was poured onto H_2O (1 mL), extracted with CH_2Cl_2 (3 × 2 mL), then the combined organic phases were concentrated *in vacuo*. The residue was purified by silica plug (EtOAc/pentane, 2:3) to give the sulfonyl BCP iodide.

General Procedure 11.5 - Alkyl Sulfonyl BCP Bromides, *R = Alkyl and X = Br*

A solution of sodium sulfinate salt (0.10 mL, 0.10 mmol of a 1.0 M solution in H_2O) was added to a 3 mL vial equipped with a stir bar and septum cooled to –5 °C. CH_2Cl_2 (0.10 mL) was added. A solution of Br_2 (0.18 mL, 0.18 mmol of a 1.0 M solution in CH_2Cl_2) was added and the mixture was stirred for 2 min, until disappearance of the bromine colour to a colourless solution. A solution of [1.1.1]propellane **1** (0.15

mL, 0.10 mmol of a 0.70 M solution in Et_2O) and then Et_3B (10 µL, 0.01 mmol, 1.0 M in hexanes) was added. The vial stirred at –5 °C for 2 min, then vial was sonicated (5 s) to ensure complete mixing. The vial was quenched at room temperature with $Na_2S_2O_3$ (sat. aq., 0.50 mL). The biphasic mixture was poured onto H_2O (1 mL), extracted with CH_2Cl_2 (3 × 2 mL), then the combined organic phases were concentrated *in vacuo*. The residue was purified by silica plug (EtOAc/pentane, 2:3) to give the sulfonyl BCP iodide.

General Procedure 11.6 - Sulfonyl BCB Iodides, *R = Aryl and X = I*

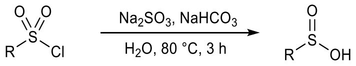


Benzyltrimethylammonium dichloroiodate (50.5 mg, 0.14 mmol) and CH_2Cl_2 (0.10 mL) was added to a 3 mL vial equipped with a stir bar and septum at –5 °C. A solution of sodium sulfinate salt (0.25 mL, 0.25 mmol of a 1.0 M solution in H_2O) was added and the mixture stirred for 2 min. A solution of BCB (0.10 mL, 0.10 mmol of a 1.0 M solution in Et_2O) and then Et_3B (10 µL, 0.01 mmol, 1.0 M in hexanes) was added. The vial was capped, sonicated (5 s) and then stirred at room temperature for 1 h. The reaction mixture was quenched with $Na_2S_2O_3$ (sat. aq., 0.50 mL). The biphasic mixture was poured onto H_2O (1 mL), extracted with CH_2Cl_2 (3 × 2 mL), then the combined organic phases were concentrated *in vacuo*. The residue was purified by silica plug (EtOAc/pentane, 2:3) to give the sulfonyl BCB iodide.

General Procedure 11.7 - Sulfonyl BCB Bromides, *R = Aryl and X = Br*

A solution of sodium sulfinate salt (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O) was added to a 3 mL vial equipped with a stir bar and septum at –5 °C. CH_2Cl_2 (0.10 mL) was added. A solution of Br_2 (0.18 mL, 0.18 mmol of a 1.0 M solution in CH_2Cl_2) was added and the mixture was stirred for 2 min, until disappearance of the bromine colour to a colourless solution. A solution of BCB (0.10 mL, 0.10 mmol of a 1.0 M solution in Et_2O) and then Et_3B (10 µL, 0.01 mmol, 1.0 M in hexanes) was added. The vial was capped, sonicated (5 s), and then stirred at room temperature for 2 h. The vial was quenched with $Na_2S_2O_3$ (sat. aq., 0.50 mL). The biphasic mixture was poured onto H_2O (1 mL), extracted with CH_2Cl_2 (3 × 2 mL), then the combined organic phases were concentrated *in vacuo*. The residue was purified by silica plug (EtOAc/pentane, 2:3) to give the sulfonyl BCB bromide.

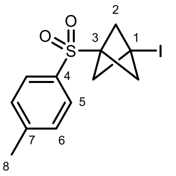
General Procedure 12 – Sulfinate salts from reduction of sulfonyl chlorides



According to a modified literature procedure.[60] Sulfonyl chloride (5.00 mmol) was added to a solution of sodium sulfite (1.26 g, 10.0 mmol) and sodium bicarbonate (840 mg, 10.0 mmol) in water (5.0 mL) and the suspension was heated at 80 °C for 4 h. After cooling to room temperature, the water was removed *in vacuo*. The resultant solid was stirred in EtOH (5 mL) for 30 min at 40 °C, then filtered and washed with EtOH (10 mL x 3). The combined ethanol washes were concentrated *in vacuo* to yield the sulfinate salt.

S4.2 Aryl Sulfonyl BCP Halides

1-Iodo-3-tosylbicyclo[1.1.1]pentane, 18a-I



A stock solution of sulfinate salt **18a-S** (213 mg, 1.20 mmol) in H_2O (1.20 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18a-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.1**. BCP iodide **18a-I** (68.8 mg, 0.20 mmol, 99%) was obtained as a white solid.

R$_f$ 0.74 (EtOAc/pentane, 1:9) [UV, Vanillin].

m.p. 188° C.

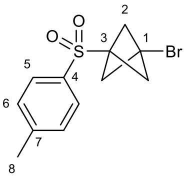
IR ν_{max}/cm^{-1} (film) 1594, 1314, 1302, 1290, 1166, 1136, 859, 811, 665.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.68 (2H, m, H5), 7.38 – 7.34 (2H, m, H6), 2.50 (6H, s, H2), 2.46 (3H, s, H8).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.4, 133.7, 130.2, 128.7, 59.3, 57.9, 21.8, 2.6.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{12}H_{13}O_2INaS$ requires 370.9573; found 370.9574.

1-Bromo-3-tosylbicyclo[1.1.1]pentane, 18a-Br



A stock solution of sulfinate salt **18a-S** (213 mg, 1.20 mmol) in H_2O (1.20 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18a-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. Purification by silica plug (EtOAc/pentane, 1:4) gave the BCP bromide **18a-Br** (60.4 mg, 0.20 mmol, 100%) as a white crystalline solid.

R_f 0.38 (EtOAc/pentane, 1:9) [UV, Vanillin].

m.p. 180 ° C.

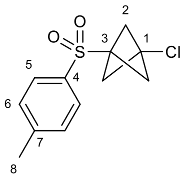
IR ν_{max}/cm^{-1} (film) 2970, 1379, 1160, 1128, 951, 817.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.68 (2H, m, H6), 7.40 – 7.32 (2H, m, H5), 2.46 (3H, s, H8), 2.44 (6H, s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.4, 133.9, 130.1, 128.6, 58.0, 52.6, 35.4, 21.8.

HRMS (ESI^+) $[M + Na]^+$ $C_{12}H_{13}O_2{}^{81}BrNaS$ requires 324.9691; found 324.9691.

1-Chloro-3-tosylbicyclo[1.1.1]pentane, 18a-Cl



[1.1.1]propellane **1** (0.27 mL, 0.20 mmol of a 0.75 M solution in Et_2O) was added to a solution of 4-methylbenzenesulfonyl chloride (38.0 mg, 0.20 mmol) in MeCN (0.2 mL) in a 3 mL vial under air. The vial was capped and stirred at room temperature for 16 h. Concentration *in vacuo* and purification by column chromatography (SiO_2, EtOAc/pentane, 0:1 → 1:9) gave BCP chloride **18a-Cl** (14.6 mg, 0.22 mmol, 29%) as a white crystalline solid.

R$_f$ 0.67 (EtOAc/pentane, 1:9).

IR ν_{max}/cm^{-1} (film) 2981, 1596, 1311, 1293, 1188, 1143, 811, 672.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.69 (2H, m, H5), 7.41 – 7.33 (2H, m, H6), 2.46 (3H, s, H8), 2.38 (6H, s, H2).

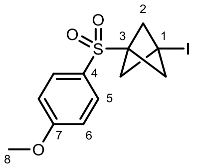
^{13}C NMR (101 MHz, $CDCl_3$) δ 145.4, 134.0, 130.1, 128.7, 57.2, 49.9, 48.6, 21.8.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{12}H_{13}O_2{}^{35}ClNaS$ requires 279.0217; found 279.0218.

Characteristic ^{1}H NMR data for Staffane of 18a-Cl (separable)

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (6H, s), 1.91 (6H, s).

1-Iodo-3-((4-methoxyphenyl)sulfonyl)bicyclo[1.1.1]pentane, 18b-I



A stock solution of sulfinate salt **18b-S** (126 mg, 0.60 mmol, contained 8% impurity) in H_2O (0.60 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18b-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.1**. BCP iodide **18b-I** (73.6 mg, 2.02 mmol, 101%) was obtained as a white solid.

R$_f$ 0.20 (EtOAc/pentane, 1:9).

m.p. 164 – 169 °C.

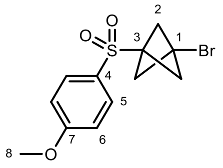
IR ν_{max}/cm^{-1} (film) 2981, 1593, 1492 1258, 1163, 1132, 803, 769, 669.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.72 (2H, m, H5), 7.06 – 6.98 (2H, d, *J* = 8.9 Hz, H6), 3.89 (3H, s, H8), 2.50 (6H, s, H2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 130.8, 128.1, 114.7, 59.3, 58.1, 55.9, 2.7.

HRMS (ESI^+) $[M + Na]^+$ $C_{12}H_{13}O_3INaS$ requires 386.9522; found 386.9521.

1-Bromo-3-((4-methoxyphenyl)sulfonyl)bicyclo[1.1.1]pentane, 18b-Br



A stock solution of sulfinate salt **18b-S** (126 mg, 0.60 mmol, contained 8% impurity) in H_2O (0.60 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18b-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. BCP bromide **18b-Br** (64.2 mg, 0.202 mmol, 101%) was obtained as a white solid.

R_f 0.20 (EtOAc/pentane, 1:9).

m.p. 149 °C.

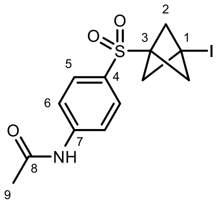
IR ν_{max}/cm^{-1} (film) 1595, 1495, 1307, 1259, 1177, 1138, 672.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 – 7.75 (2H, m, H5), 7.09 – 7.01 (2H, m, H6), 3.90 (3H, s, H8), 2.45 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 164.3, 130.8, 128.3, 114.7, 58.0, 55.9, 52.8, 35.5.

HRMS (ESI^+) $[M + H]^+$ $C_{12}H_{14}O_3{}^{79}BrS$ requires 316.9842; found 316.9841.

N-(4-((3-Iodobicyclo[1.1.1]pentan-1-yl)sulfonyl)phenyl)acetamide, 18c-I



A stock solution of sulfinate salt **18c-S** (133 mg, 0.60 mmol) in DMF (0.60 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18c-S** (0.50 mL, 0.50 mmol, 1.0 M in DMF), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.2** (–40 °C). BCP iodide **18c-I** (33.4 mg, 0.0854 mmol, 43%) was obtained as an off-white solid.

m.p. 136 °C.

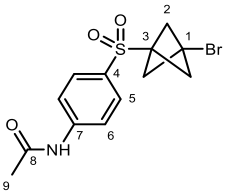
IR ν_{max}/cm^{-1} (film) 1675, 1591, 1532, 1402, 1322, 1309, 1169, 1134, 730.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 – 7.77 (2H, m, H5), 7.76 – 7.68 (2H, m, H6), 7.41 (1H, s, NH), 2.50 (6H, s, H2), 2.24 (3H, s, H9).

^{13}C NMR (151 MHz, $CDCl_3$) δ 168.6, 143.3, 131.3, 130.1, 119.5, 59.3, 58.0, 25.0, 2.4.

HRMS (ESI$^+$) [M + H]$^+$ $C_{13}H_{15}O_3INS$ requires 391.9808; found 391.9811.

N-(4-((3-Bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)phenyl)acetamide, 18c-Br



A stock solution of sulfinate salt **18c-S** (133 mg, 0.60 mmol) in H_2O (0.60 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18c-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. BCP bromide **18c-Br** (31.5 mg, 0.0915 mmol, 46%) was obtained as a white solid.

m.p. 217 °C.

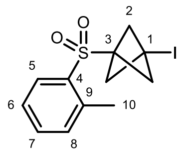
IR ν_{max}/cm^{-1} (film) 1680, 1591, 1531, 1322, 1184, 1140, 732.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 – 7.78 (2H, m, H5), 7.76 – 7.70 (2H, m, H6), 7.38 (1H, s, NH), 2.45 (6H, s, H2), 2.25 (3H, s, H9).

^{13}C NMR (151 MHz, $CDCl_3$) δ 168.6, 143.3, 131.5, 130.1, 119.5, 58.1, 52.7, 35.4, 25.0.

HRMS (APCI$^+$) [M + H]$^+$ $C_{13}H_{15}O_3{}^{79}BrNS^+$ requires 343.9951; found 343.9953.

1-Iodo-3-(o-tolylsulfonyl)bicyclo[1.1.1]pentane, 18d-I



A stock solution of sulfinate salt **18d-S** (107 mg, 0.601 mmol) in H_2O (0.60 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18d-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.1**. BCP iodide **18d-I** (61.0 mg, 0.175 mmol, 88%) was obtained as a yellow solid.

R$_f$ 0.53 (EtOAc/pentane, 1:9).

m.p. 130 °C.

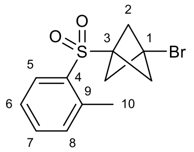
IR ν_{max}/cm^{-1} (film) 1303, 1292, 1203, 1162, 1139, 1122, 856, 689, 615.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91 (1H, dd, *J* = 7.9, 1.4 Hz, H5), 7.53 (1H, app. td, *J* = 7.5, 1.5 Hz, H7), 7.38 (1H, app. ddt, *J* = 7.9, 1.2, 0.6 Hz, H6), 7.36 – 7.32 (1H, m, H8), 2.64 (3H, s, H10), 2.54 (6H, s, H2).

^{13}C NMR (101 MHz, CDCl$_3$) δ 139.2, 135.0, 134.3, 133.0, 131.1, 127.0, 59.5, 58.3, 21.0, 2.3.

HRMS (ESI$^+$) [M + H]$^+$ $C_{12}H_{14}O_2IS$ requires 348.9754; found 348.9754.

1-Bromo-3-(o-tolylsulfonyl)bicyclo[1.1.1]pentane, 18d-Br



A stock solution of sulfinate salt **18d-S** (126 mg, 0.707 mmol) in H$_2$O (0.60 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18d-S** (0.50 mL, 0.50 mmol, 1.0 M in H$_2$O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et$_2$O) in Et$_2$O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. Purification by column chromatography (SiO$_2$, EtOAc/pentane, 1:9 → 1:4) gave BCP bromide **18d-Br** (19.6 mg, 0.0651 mmol, 33%) as a white solid.

R$_f$ 0.29 (EtOAc/pentane, 1:4)[UV].

m.p. 105 ° C.

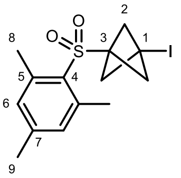
IR ν_{max}/cm^{-1} (film) 1473, 1305, 1181, 1168, 1147, 652.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.92 (1H, dd, *J* = 8.0, 1.4 Hz, H5), 7.54 (1H, td, *J* = 7.6, 1.4 Hz, H7), 7.38 (1H, ddq, *J* = 8.0, 1.2, 0.6 Hz, H8), 7.34 (1H, ddt, *J* = 7.6, 1.4, 0.6 Hz, H6), 2.65 (3H, s, H10), 2.49 (6H, s, H2)

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.2, 135.0, 134.3, 133.0, 131.1, 127.0, 59.5, 58.3, 21.0, 2.3.

HRMS (ESI$^{+/-}$, EI) Not found.

1-Iodo-3-(mesitylsulfonyl)bicyclo[1.1.1]pentane, 18e-I



A stock solution of sulfinate salt **18e-S** (124 mg, 0.601 mmol) in DMF (0.60 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18e-S** (0.50 mL, 0.50 mmol, 1.0 M in DMF), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.2** (–40 °C). BCP iodide **18e-I** (49.7 mg, 0.132 mmol, 66%) was obtained as an off-white solid.

R$_f$ 0.35 (EtOAc/pentane, 1:19).

m.p. 180 – 182 °C.

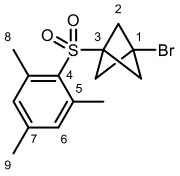
IR ν_{max}/cm^{-1} (film) 2976, 1602, 1310, 1193, 1165, 1132, 861, 658.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (2H, h, *J* = 0.7 Hz, H6), 2.59 – 2.58 (6H, m, H8), 2.57 (6H, s, H2), 2.31 – 2.30 (3H, m, H9).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 141.0, 132.4, 130.7, 59.4, 58.6, 23.4, 21.2, 2.5.

HRMS (ESI$^+$) [M + H]$^+$ $C_{14}H_{18}O_2IS^+$ requires 377.0067; found 377.0067.

1-Bromo-3-(mesitylsulfonyl)bicyclo[1.1.1]pentane, 18e-Br



A stock solution of sulfinate salt **18e-S** (124 mg, 0.6 mmol) in H_2O (0.60 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18e-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.34 mL, 0.20 mmol of a 0.59 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. BCP bromide **18e-Br** (53.6 mg, 0.163 mmol, 82%) was obtained as a white solid.

R$_f$ 0.35 (EtOAc/pentane, 1:19).

m.p. 82 °C.

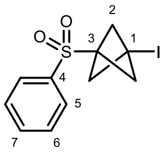
IR ν_{max}/cm^{-1} (film) 1357, 1311, 1167, 1139, 660.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 – 6.96 (2H, m, H6), 2.59 (6H, s, H8), 2.51 (6H, s, H2), 2.31 (3H, s, H9).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 141.0, 132.5, 130.8, 58.0, 53.2, 35.1, 23.4, 21.2.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{14}H_{17}O_2{}^{81}BrNaS$ requires 353.0004; found 353.0005.

1-Iodo-3-(phenylsulfonyl)bicyclo[1.1.1]pentane, 18f-I



A stock solution of sulfinate salt **18f-S** (98.4 mg, 0.599 mmol) in H_2O (0.60 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18f-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80

mL) were subjected to the conditions of **general procedure 11.1**. BCP iodide **18f-I** (64.4 mg, 0.193 mmol, 96%) was obtained as an off-white solid.

Note: The reaction *at 20 °C in Et$_2$O (0.20 mL) afforded BCP iodide* ***18f-I*** *in lower yield (56.6 mg, 0.169 mmol, 85%).*

R$_f$ 0.32 (EtOAc/pentane, 1:9).

m.p. 186° C.

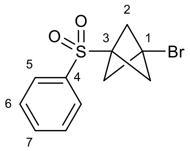
IR ν_{max}/cm^{-1} (film) 2972, 1450, 1305, 1291, 1201, 1168, 1140, 864, 721, 691, 610.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.88 – 7.81 (2H, m, H5), 7.73 – 7.64 (1H, m, H7), 7.63 – 7.54 (2H, m, H6), 2.51 (6H, s, H2).

^{13}C NMR (151 MHz, CDCl$_3$) δ 136.8, 134.3, 129.5, 128.7, 59.3, 57.9, 2.4.

HRMS (ESI$^{+/-}$, APCI) Not Found.

1-Bromo-3-(phenylsulfonyl)bicyclo[1.1.1]pentane, 18f-Br



A stock solution of sulfinate salt **18f-S** (196.8 mg, 1.20 mmol) in H$_2$O (1.20 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18f-S** (0.50 mL, 0.50 mmol, 1.0 M in H$_2$O), [1.1.1]propellane **1** (0.34 mL, 0.20 mmol of a 0.59 M solution in Et$_2$O) in Et$_2$O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. BCP bromide **18f-Br** (57.9 mg, 0.202 mmol, 100%) was obtained as a white solid.

R$_f$ 0.31 (EtOAc/pentane, 1:9).

m.p. 149 °C.

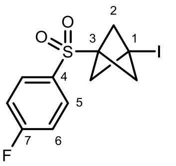
IR ν_{max}/cm^{-1} (film) 1449, 1307, 1291, 1205, 1180, 1147, 723, 616.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.88 – 7.83 (2H, m, H5), 7.72 – 7.66 (1H, m, H7), 7.61 – 7.57 (2H, m, H6), 2.46 (6H, s, H2).

^{13}C NMR (151 MHz, CDCl$_3$) δ 136.9, 134.3, 129.5, 128.7, 58.1, 52.6, 35.4.

HRMS (ESI+) Not found.

1-((4-Fluorophenyl)sulfonyl)-3-iodobicyclo[1.1.1]pentane, 18g-I



A stock solution of sulfinate salt **18g-S** (109 mg, 0.598 mmol) in DMF (0.60 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18g-S** (0.50 mL, 0.50 mmol, 1.0 M in DMF), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et$_2$O) in CH$_2$Cl$_2$ (0.80 mL) were subjected to the conditions of **general procedure 11.2** (–40 °C). BCP iodide **18g-I** (35.4 mg, 0.101 mmol, 50%) was obtained as a white solid.

R$_f$ 0.25 (EtOAc/pentane, 1:19).

m.p. 168 **–** 170 °C.

IR ν_{max}/cm^{-1} (film) 1593, 1314, 1293, 1170, 1137, 820.

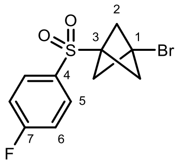
^{1}H NMR (600 MHz, CDCl$_3$) δ 7.89 – 7.83 (2H, m, H5), 7.29 – 7.23 (2H, m, H6), 2.51 (6H, s, H2).

^{13}C NMR (151 MHz, CDCl$_3$) δ 166.3 (d, $^{1}J_{CF}$ = 257.3 Hz), 132.8 (d, $^{4}J_{CF}$ = 3.3 Hz), 131.6 (d, $^{3}J_{CF}$ = 9.7 Hz), 117.0 (d, $^{2}J_{CF}$ = 22.5 Hz), 59.3, 58.0, 2.1.

^{19}F NMR (377 MHz, CDCl$_3$) δ –102.4

HRMS (ESI$^{+/-}$) Not found.

1-Bromo-3-((4-fluorophenyl)sulfonyl)bicyclo[1.1.1]pentane, 18g-Br



A stock solution of sulfinate salt **18g-S** (109 mg, 0.6 mmol) in H$_2$O (0.60 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18g-S** (0.50 mL, 0.50 mmol, 1.0 M in H$_2$O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et$_2$O) in Et$_2$O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. BCP bromide **18g-Br** (62.3 mg, 0.204 mmol, 102%) was obtained as a white solid.

R$_f$ 0.45 (EtOAc/pentane, 1:9).

m.p. 218 – 220 ° C.

IR ν_{max}/cm^{-1} (film) 2981, 1590, 1493, 1382, 1310, 1292, 1236, 1178, 1144, 1138, 870, 672.

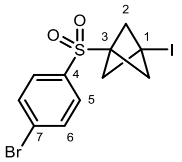
^{1}H NMR (600 MHz, CDCl$_3$) δ 7.90 – 7.84 (2H, m, H5), 7.31 – 7.23 (2H, m, H6), 2.46 (6H, s, H2).

^{13}C NMR (151 MHz, CDCl$_3$) δ 166.3 (d, $^{1}J_{CF}$ = 257.7 Hz), 133.0 (d, $^{3}J_{CF}$ = 3.2 Hz), 131.5 (d, $^{2}J_{CF}$ = 9.6 Hz), 117.0 (d, $^{2}J_{CF}$ = 22.8 Hz), 58.0, 52.7, 35.2.

^{19}F NMR (377 MHz, CDCl$_3$) δ –102.3.

HRMS (ESI^{+}) Not found.

1-((4-Bromophenyl)sulfonyl)–3-iodobicyclo[1.1.1]pentane, 18h-I



A stock solution of sulfinate salt **18h-S** (290 mg, 1.20 mmol) in H_2O (1.20 mL) was prepared, a drop of DMF was added to aid solubility of the sulfinate salt. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18h-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.1**. BCP iodide **18h-I** (81.4 mg, 1.97 mmol, 99%) was obtained as a white solid.

R$_f$ 0.32 (EtOAc/pentane, 1:17).

m.p. 230 ° C.

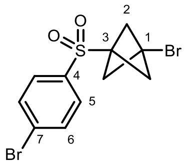
IR ν_{max}/cm^{-1} (film) 1574, 1311, 1278, 1202, 1168, 1136, 777.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 – 7.71 (2H, m, H5), 7.71 – 7.68 (2H, m, H6), 2.51 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 135.8, 132.9, 130.2, 129.9, 59.3, 57.9, 2.0.

HRMS (ESI$^{+/-}$) Not Found.

1-Bromo-3-((4-bromophenyl)sulfonyl)bicyclo[1.1.1]pentane, 18h-Br



A stock solution of sulfinate salt **18h-S** (145 mg, 0.597 mmol) in H_2O (0.60 mL) was prepared, a drop of DMF was added to aid solubility of the sulfinate salt. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18h-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. BCP iodide **18h-Br** (69.4 mg, 0.190 mmol, 95%) was obtained as a pale-yellow solid.

R_f 0.40 (EtOAc/pentane, 1:9).

m.p. 222 ° C.

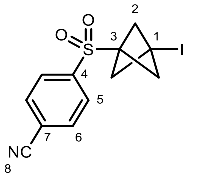
IR ν_{max}/cm^{-1} (film) 1574, 1387, 1312, 1180, 1141, 755, 644.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.67 (4H, m, H5, H6), 2.47 (6H, s, H2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 135.9, 132.9, 130.1, 129.9, 58.0, 52.6, 35.2.

HRMS (ESI$^{+/-}$) Not Found.

4-((3-Bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)benzonitrile, 18i-I



A stock solution of sulfinate salt **18i-S** (113mg, 0.597 mmol) in H_2O (0.60 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18i-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.34 mL, 0.20 mmol of a 0.59 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.1**. BCP iodide **18i-I** (40.6 mg, 0.113 mmol, 57%) was obtained as a white solid.

R_f 0.17 (EtOAc/pentane, 1:17).

m.p. 234 ° C.

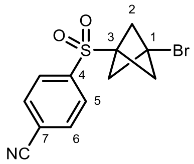
IR ν_{max}/cm^{-1} (film) 1311, 1293, 1201, 1168, 1135, 844.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 – 7.94 (2H, m, H5), 7.93 – 7.85 (2H, m, H6), 2.53 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 141.1, 133.3, 129.4, 118.2, 117.0, 59.3, 57.7, 1.4.

HRMS (ESI$^{+/-}$) Not found.

4-((3-Bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)benzonitrile, 18i-Br



A stock solution of sulfinate salt **18i-S** (113 mg, 0.60 mmol) in H_2O (0.60 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18i-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. BCP bromide **18i-Br** (38.5 mg, 0.123 mmol, 62%) was obtained as a white solid.

R$_f$ 0.10 (EtOAc/pentane, 1:17).

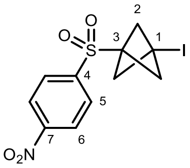
IR ν_{max}/cm^{-1} (film) 2981, 1583, 1465, 1311, 1275, 1204, 1184, 1141, 881.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 – 7.97 (2H, m, H5), 7.92 – 7.87 (2H, m, H6), 2.48 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 141.2, 133.3, 129.4, 118.3, 117.0, 58.1, 52.5, 34.9.

HRMS (ESI$^+$) Not found.

1-Iodo-3-((4-nitrophenyl)sulfonyl)bicyclo[1.1.1]pentane, 18j-I



A stock solution of sulfinate salt **18j-S** (140 mg, 0.60 mmol) in DMF (0.60 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18j-S** (0.50 mL, 0.50 mmol, 1.0 M in DMF), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.2** (–40 °C). Purification by column chromatography (SiO_2, EtOAc/pentane, 0:1→1:9) gave BCP iodide **18j-I** (40.8 mg, 0.108 mmol, 54%) as an off-white solid.

R$_f$ 0.57 (EtOAc/pentane, 1:9).

m.p. 240 °C.

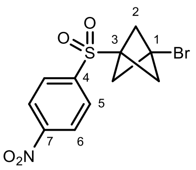
IR ν_{max}/cm^{-1} (film) 1385, 1166, 1151, 669.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 – 8.41 (2H, m, H6), 8.07 – 8.04 (2H, m, H5), 2.54 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 151.3, 142.6, 130.2, 124.7, 59.3, 57.7, 1.3.

HRMS (ESI$^{+/-}$, EI) Not found.

1-Bromo-3-((4-nitrophenyl)sulfonyl)bicyclo[1.1.1]pentane, 18j-Br



A stock solution of sulfinate salt **18j-S** (140 mg, 0.60 mmol) in H_2O (0.60 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18j-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. BCP bromide **18j-Br** (59.3 mg, 0.179 mmol, 90%) was obtained as a white solid.

R_f 0.57 (EtOAc/pentane, 1:9).

m.p. 221 ° C.

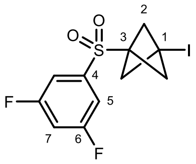
IR ν_{max}/cm^{-1} (film) 1759, 1538, 1352, 1308, 1205, 1181, 1143, 736, 669.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 – 8.40 (2H, m, H6), 8.11 – 8.03 (2H, m, H5), 2.50 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 151.3, 142.6, 130.2, 124.7, 58.1, 52.6, 34.9.

HRMS (ESI$^{+/-}$, APCI, EI) Not Found.

1-((3,5-Difluorophenyl)sulfonyl)-3-iodobicyclo[1.1.1]pentane, 18k-I



A stock solution of sulfinate salt **18k-S** (120 mg, 0.600 mmol) in DMF (0.60 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18k-S** (0.50 mL, 0.50 mmol, 1.0 M in DMF), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.2** (–40 °C). Purification by column chromatography (SiO_2, Et_2O/pentane, 2:98) gave BCP iodide **18k-I** (51.2 mg, 0.138 mmol, 69%) as a white solid.

R_f 0.45 (Et_2O/pentane, 2:98).

m.p. 180 ° C.

IR ν_{max}/cm^{-1} (film) 1592, 1534, 1403, 1371, 1362, 1191, 1171, 989, 781.

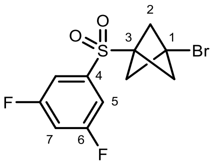
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 – 7.37 (2H, m, H5), 7.14 (1H, tt, J = 8.4, 2.4 Hz, H7), 2.55 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 163.1 (dd, $^{1,3}J_{CF}$ = 256.7, 11.4 Hz), 140.2 (t, $^3J_{CF}$ = 7.9 Hz), 112.3 (dd, $^{2,4}J_{CF}$ = 21.5, 6.5 Hz), 110.1 (t, $^2J_{CF}$ = 25.0 Hz), 59.3, 57.6, 1.4.

^{19}F NMR (377 MHz, $CDCl_3$) δ –104.3.

HRMS (ESI$^{+/-}$ / APCI) Not found.

1-Bromo-3-((3,5-difluorophenyl)sulfonyl)bicyclo[1.1.1]pentane, 18k-Br



A stock solution of sulfinate salt **18k-S** (120 mg, 0.60 mmol) in H_2O (0.60 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18k-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. BCP bromide **18k-Br** (64.9 mg, 0.202 mmol, 101%) was obtained as a white solid.

R$_f$ 0.73 (EtOAc/pentane, 1:9).

m.p. 163 °C.

IR ν_{max}/cm^{-1} (film) 1604, 1441, 1318, 1305, 1201, 1182, 1128, 986, 870, 676.

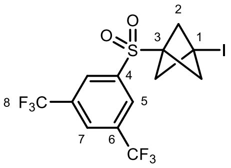
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 – 7.35 (2H, m, H5), 7.15 (1H, tt, J = 8.4, 2.3 Hz, H7), 2.50 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 163.1 (dd, $^{1,3}J_F$ = 256.7, 11.4 Hz), 140.3 (t, ^3J_F = 8.0 Hz), 112.3 (dd, $^{2,4}J_F$ = 21.8, 6.5 Hz), 110.1 (t, ^2J_F = 24.9 Hz), 58.1, 52.4, 34.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ –104.3.

HRMS (ESI$^+$ / APCI) Not found.

1-((3,5-Bis(trifluoromethyl)phenyl)sulfonyl)-3-iodobicyclo[1.1.1]pentane, 18l-I



A stock solution of sulfinate salt **18l-S** (205 mg, 0.60 mmol, contained 14% impurity) in DMF (0.60 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18l-S** (0.50 mL, 0.50 mmol, 1.0 M in DMF), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.2** (–41 °C). Purification by column chromatography (SiO_2, pentane) gave BCP iodide **18l-I** (64.5 mg, 0.137 mmol, 69%) as an off-white solid.

R$_f$ 0.75 (pentane).

m.p. 125 – 130° C.

IR ν_{max}/cm^{-1} (film) 2981, 1362, 1334, 1280, 1174, 1136, 1105, 647.

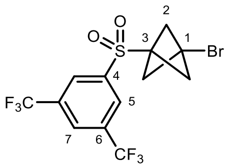
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (2H, app. dp, J = 1.7, 0.6 Hz, H5), 8.19 (1H, app. tp, J = 1.4, 0.7 Hz, H7), 2.56 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 139.9, 133.7 (q, $^2J_{CF3}$ = 34.9 Hz), 129.0 (q, $^3J_{CF3}$ = 3.7 Hz), 128.0 (p, $^3J_{CF3}$ = 3.7 Hz), 122.4 (q, $^1J_{CF3}$ = 273.6 Hz), 59.2, 57.7, 1.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ –62.9.

HRMS (ESI$^{+/-}$) Not found.

1-((3,5-Difluorophenyl)sulfonyl)-3-iodobicyclo[1.1.1]pentane, 18l-Br



A stock solution of sulfinate salt **18l-S** (205 mg, 0.60 mmol, contained 14% impurity) in H_2O (0.60 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18l-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. BCP bromide **18l-Br** (77.8 mg, 0.184 mmol, 92%) was obtained as a white solid.

R$_f$ 0.93 (EtOAc/pentane, 1:9).

m.p. 119 – 210 °C.

IR ν_{max}/cm^{-1} (film) 2981, 1279, 1267, 1282, 1138, 1107.

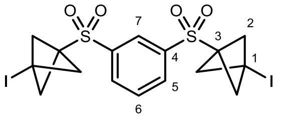
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31–8.30 (2H, m, H5), 8.20 (1H, tt, J = 1.5, 0.8 Hz, H7), 2.52 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 140.0, 133.7 (q, $^2J_{CF3}$ = 34.9 Hz), 129.6–128.7 (m), 128.0 (p, $^3J_{CF3}$ = 3.6 Hz), 122.4 (q, $^1J_{CF3}$ = 273.6 Hz), 58.1, 52.6, 34.7, 25.5.

^{19}F NMR (377 MHz, $CDCl_3$) δ –62.9.

HRMS (ESI$^{+/-}$, APCI) Not found.

1,3-Bis((3-bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)benzene, 18m-I



A stock solution of sulfinate salt **18m-S** (75.0 mg, 0.300 mmol) in DMF/H_2O (0.60 mL, 1:1) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18m-S** (0.50 mL, 0.25 mmol, 0.50 M in DMF/H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.2** (–40 °C). Purification by column chromatography (SiO_2, EtOAc/pentane, 1:19) gave BCP iodide **18m-I** (15.3 mg, 0.0259 mmol, 26%) as a yellow solid.

R_f 0.60 (EtOAc/pentane, 2:3).

m.p. 246 °C.

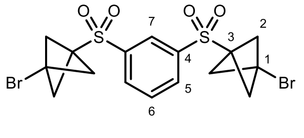
IR ν_{max}/cm^{-1} (film) 1537, 1384, 1353, 1308, 1169, 1149, 1137, 649.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (1H, dt, *J* = 1.8, 0.9 Hz, H7), 8.15 (2H, dd, *J* = 7.8, 1.8 Hz, H5), 7.83 (1H, td, *J* = 7.8, 0.5 Hz, H6), 2.53 (12H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 139.1, 133.9, 130.9, 128.9, 59.3, 57.8, 1.3.

HRMS (ESI$^{+/-}$, EI) Not found.

1,3-Bis((3-bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)benzene, 18m-Br



A stock solution of sulfinate salt **18m-S** (150 mg, 0.60 mmol) in H_2O (0.60 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18m-S** (0.25 mL, 0.25 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in Et_2O (0.20

mL) were subjected to the conditions of **general procedure 11.3**. Purification by silica plug (EtOAc/pentane, 1:4) gave BCP bromide **18m-Br** (45.6 mg, 0.0919 mmol, 92%) as a white solid.

R$_f$ 0.63 (EtOAc/pentane, 2:3).

m.p. 250 – 260 ° C.

IR ν_{max}/cm^{-1} (film) 1321, 1203, 1181, 1132, 800, 688, 637.

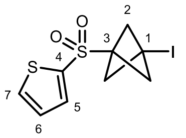
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.33 (1H, td, *J* = 1.8, 0.5 Hz, H7), 8.17 (2H, dd, *J* = 8.0, 1.8 Hz, H5), 7.85 (1H, td, *J* = 8.0 0.5 Hz, H6), 2.49 (12H, s, H2).

^{13}C NMR (101 MHz, CDCl$_3$) δ 139.2, 133.9, 131.0, 128.8, 58.1, 52.6, 34.9.

HRMS (ESI$^+$) Not found.

S4.3 Heteroaryl Sulfonyl BCP Halides

2-((3-Iodobicyclo[1.1.1]pentan-1-yl)sulfonyl)thiophene, 23a-I



A stock solution of sulfinate salt **23a**-**S** (102 mg, 0.599 mmol) in H_2O (0.60 mL) was prepared. DIH (39.2 mg, 0.10 mmol), sulfinate salt **23a-S** (0.25 mL, 0.25 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.59 M solution in Et_2O) in CH_2Cl_2 (0.40 mL) were subjected to the conditions of **general procedure 11.1**. BCP iodide **23a-I** (27.9 mg, 0.0820 mmol, 82%) was obtained as a white solid.

R_f 0.20 (EtOAc/pentane, 1:17).

m.p. 182 ° C.

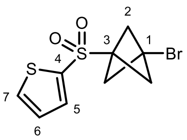
IR ν_{max}/cm^{-1} (film) 1400, 1305, 1199, 1167, 1128, 1017, 868, 856, 741, 616.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (1H, dd, *J* = 5.0, 1.3 Hz, H7), 7.65 (1H, dd, *J* = 3.8, 1.3 Hz, H5), 7.19 (1H, dd, *J* = 5.0, 3.8 Hz, H6), 2.56 (6H, s, H2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 137.5, 135.1, 135.0, 128.4, 59.4, 58.5, 1.8.

HRMS (ESI$^+$) $[M + H]^+$ $C_9H_{10}O_2IS_2^+$ requires 340.9161; found 340.9161.

2-((3-Bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)thiophene, 23a-Br



A stock solution of sulfinate salt **23a-S** (204 mg, 1.20 mmol) in H_2O (1.20 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **23a-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.34 mL, 0.20 mmol of a 0.59 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. BCP Bromide **23a-Br** (53.4 mg, 0.182 mmol, 91%) was obtained as an off-white solid.

R_f 0.20 (EtOAc/pentane, 1:17).

m.p. 160 °C.

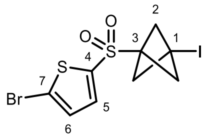
IR ν_{max}/cm^{-1} (film) 1401, 1344, 1202, 1181, 1133, 880, 742, 671, 618.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (1H, dd, *J* = 5.0, 1.3 Hz, H7), 7.67 (1H, dd, *J* = 3.8, 1.3 Hz, H5), 7.20 (1H, dd, *J* = 5.0, 3.8 Hz, H6), 2.51 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 137.7, 135.1, 135.0, 128.4, 58.2, 53.3, 35.0.

HRMS ($ESI^{+/-}$) Not found.

2-Bromo-5-((3-iodobicyclo[1.1.1]pentan-1-yl)sulfonyl)thiophene, 23b-I



A stock solution of sulfinate salt **23b-S** (376 mg, 1.20 mmol, contained 21% impurity) in H_2O (1.20 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **23b-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.1.** BCP iodide **23b-I** (82.8 mg, 0.198 mmol, 99%) was obtained as a pale-yellow solid.

R_f 0.29 (EtOAc/pentane, 1:17).

m.p. 169 °C.

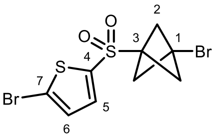
IR ν_{max}/cm^{-1} (film) 1399, 1316, 1201, 1164, 1129, 858, 678, 625.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 (1H, d, *J* = 4.0 Hz, H5), 7.16 (1H, d, *J* = 4.0 Hz, H6), 2.57 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 138.3, 135.3, 131.5, 123.4, 59.4, 58.4, 1.4.

HRMS (ESI$^+$) Not Found.

2-Bromo-5-((3-bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)thiophene, 23b-Br



A stock solution of sulfinate salt **23b-S** (376 mg, 1.20 mmol, contained 21% impurity) in H_2O (1.20 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **23b-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. BCP iodide **23b-Br** (74.7 mg, 0.201 mmol, 100%) was obtained as a pale-yellow solid.

R_f 0.28 (EtOAc/pentane, 1:17).

m.p. 174 ° C.

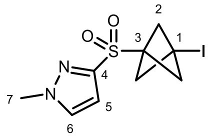
IR ν_{max}/cm^{-1} (film) 1399, 1316, 1204, 1177, 1136, 870, 679, 628.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (1H, d, *J* = 4.0 Hz, H5), 7.17 (1H, d, *J* = 4.0 Hz, H6), 2.53 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 138.4, 135.3, 131.5, 123.4, 58.2, 53.3, 34.8.

HRMS (ESI$^+$) Not Found.

3-((3-Iodobicyclo[1.1.1]pentan-1-yl)sulfonyl)-1-methyl-1H-pyrazole, 23c-I



A stock solution of sulfinate salt **23c-S** (131 mg, 0.545 mmol, contained 30% impurity) in H_2O (0.60 mL) was prepared. DIH (39.2 mg, 0.103 mmol), sulfinate salt **23c-S** (0.25 mL, 0.25 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) in CH_2Cl_2 (0.40 mL) were subjected to the conditions of **general procedure 11.1**. BCP iodide **23c-I** (32.8 mg, 0.970 mmol, 92%) was obtained as a pale-yellow solid.

R$_f$ 0.31(EtOAc/pentane, 2:3) [UV, PMA].

m.p. 182° C.

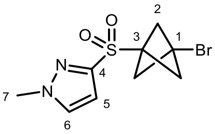
IR ν_{max}/cm^{-1} (film) 1521, 1308, 1201, 1169, 1141, 1111, 861, 706, 662.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (1H, m, H6), 7.75 (1H, d, *J* = 0.7 Hz, H5), 3.98 (3H, d, *J* = 0.4 Hz, H7), 2.55 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 139.9, 133.2, 119.3, 59.1, 58.5, 40.0, 2.3.

HRMS (ESI$^+$) [M + H]$^+$ $C_9H_{12}O_2N_2IS_2^+$ requires 338.9659; found 338.9659.

3-((3-Bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)-1-methyl-1H-pyrazole, 23c-Br



A stock solution of sulfinate salt **23c-S** (131 mg, 0.545 mmol, contained 30% impurity) in H_2O (0.60 mL) was prepared. DBH (28.6 mg, 0.100 mmol), sulfinate salt **23c-S** (0.25 mL, 0.25 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in

Et_2O) in Et_2O (0.10 mL) were subjected to the conditions of **general procedure 11.3**. Purification by silica plug (EtOAc/pentane 1:9 → 1:1) gave BCP Bromide **23c-Br** (31.2 mg, 0.107 mmol, 102%) was obtained as a white solid.

R_f 0.31(EtOAc/pentane, 2:3)[UV, PMA].

m.p. 145° C.

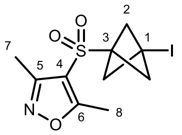
IR ν_{max}/cm^{-1} (film) 1522, 1388, 1310, 1175, 1113, 875, 667.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (1H, m, H6), 7.76 (1H, d, *J* = 0.7 Hz, H5), 3.98 (3H, d, *J* = 0.4 Hz, H3), 2.50 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 139.9, 133.2, 119.5, 57.9, 53.2, 40.0, 35.3.

HRMS (ESI$^+$) [M + H]$^+$ $C_9H_{12}O_2N_2{}^{79}BrS_2{}^+$ requires 290.9797; found 290.9797.

4-((3-Iodobicyclo[1.1.1]pentan-1-yl)sulfonyl)–3,5-dimethylisoxazole, 23d-I



A stock solution of sulfinate salt **23d-S** (220 mg, 1.201 mmol) in H_2O (1.20 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **23d-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.1.** BCP iodide **23d-I** (23.6 mg, 0.0668 mmol, 33%) was obtained as a white solid.

R_f 0.65 (EtOAc/pentane, 1:9).

m.p. 144 ° C.

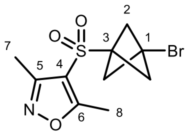
IR ν_{max}/cm^{-1} (film) 2342, 1586, 1408, 1315, 1271, 1183, 1101, 860, 669, 645.

^{1}H NMR (600 MHz, $CDCl_3$) δ 2.63 (3H, s, H8), 2.58 (6H, s, H2), 2.39 (3H, s, H7).

^{13}C NMR (151 MHz, $CDCl_3$) δ 175.8, 158.4, 113.3, 58.9, 12.8, 11.0, 1.3.

HRMS (ESI$^{+/-}$) Not Found.

4-((3-Bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)-3,5-dimethylisoxazole, 23d-Br



A stock solution of sulfinate salt **23d-S** (220 mg, 1.20 mmol) in H_2O (1.20 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **23d-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9) gave BCP bromide **23d-Br** (40.8 mg, 0.133 mmol, 67%) as a white solid.

R_f 0.63 (EtOAc/pentane, 1:9).

m.p. 138 – 140 ° C.

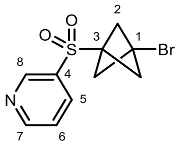
IR ν_{max}/cm^{-1} (film) 2981, 1576, 1407, 1379, 1317, 1271, 1191, 1183, 1166, 1103, 873, 689, 645.

^{1}H NMR (600 MHz, $CDCl_3$) δ 2.63 (3H, s, H7/8), 2.53 (6H, s, H2), 2.39 (3H, s, H7/8).

^{13}C NMR (151 MHz, $CDCl_3$) δ 175.8, 158.4, 113.5, 57.7, 53.5, 34.7, 12.8, 11.0.

HRMS (ESI$^{+/-}$) Not found.

3-((3-Bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)pyridine, 23e-Br



A stock solution of sulfinate salt **23e-S** (99.0 mg, 0.599 mmol) in H_2O (0.60 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **23e-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.70 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:4) gave BCP bromide **23e-S** (13.8 mg, 0.0479 mmol, 24%) was obtained as a white solid.

R$_f$ 0.26 (EtOAc/pentane, 1:4).

m.p. 150 ˚C.

IR ν_{max}/cm^{-1} (film) 1576, 1568, 1416, 1312, 1184, 1150, 703.

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.07 (1H, d, *J* = 2.4 Hz, H8), 8.92 (1H, dd, *J* = 4.9, 1.7 Hz, H7), 8.15 (1H, ddd, *J* = 8.1, 2.4, 1.7 Hz, H5), 7.55 (1H, app. ddd, *J* = 8.1, 4.9, 0.9 Hz, H6), 2.50 (6H, s, H2).

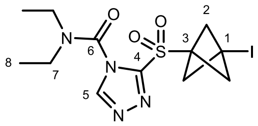
^{13}C NMR (151 MHz, $CDCl_3$) δ 154.9, 149.7, 136.4, 133.6, 124.1, 58.0, 52.9, 35.1.

HRMS (ESI$^+$) $[M + H]^+$ $C_{10}H_{11}O_2N^{81}BrS$ requires 289.9667; found 289.9668.

*Note: Attempts to prepare corresponding iodide **23e-I** under **general procedure 11.3** were unsuccessful.*

S4.4 Pharmaceutical and Agrochemical BCP Halides

N,N-Diethyl-3-((3-iodobicyclo[1.1.1]pentan-1-yl)sulfonyl)-4H-1,2,4-triazole-4-carboxamide, 24a-I



A stock solution of sulfinate salt **24a-S** (124 mg, 0.60 mmol) in DMF (0.60 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **24a-S** (0.50 mL, 0.50 mmol, 1.0 M in DMF), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.2** (–40 °C). Purification by column chromatography (SiO_2, EtOAc/pentane 1:9 → 1:4) gave BCP iodide **24a-I** (46.7 mg, 0.110 mmol, 55%) as a colourless oil.

R_f 0.67 (EtOAc/pentane, 3:7).

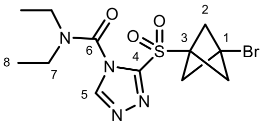
IR ν_{max}/cm^{-1} (film) 1718, 1387, 1337, 1201.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.90 (1H, s, H5), 3.68 – 3.50 (4H, m, H7), 2.70 (6H, s, H2), 1.31 (6H, t, *J* = 7.1 Hz, H8).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.6, 148.3, 147.6, 59.8, 57.1, 44.3, 14.2, 12.5, 1.6.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{12}H_{17}O_3N_4INaS$ requires 446.9958; found 446.9959.

3-((3-Bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)-N,N-diethyl-4H-1,2,4-triazole-4-carboxamide, 24a-Br



A stock solution of sulfinate salt **24a-S** (139 mg, 0.55 mmol) in H_2O (0.55 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **24a-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.34 mL, 0.20 mmol of a 0.59 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. Purification by column chromatography (SiO_2, EtOAc/pentane 1:9 → 1:4) gave BCP bromide **24a-Br** (44.7 mg, 0.119 mmol, 59%) as a white solid.

R$_f$ 0.28 (EtOAc/pentane, 1:4).

m.p. 111° C.

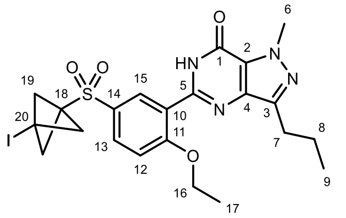
IR ν_{max}/cm^{-1} (film) 2981, 1713, 1338, 1203, 1183, 1138.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.91 (1H, s, H5), 3.74 – 3.48 (4H, br. m, H7), 2.66 (6H, s, H2), 1.32 (6H, t, *J* = 7.1 Hz, H8).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.7, 148.3, 147.7, 58.6, 51.9, 44.3, 34.9, 14.2, 12.5.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{12}H_{17}O_3N_4BrNaS$ requires 399.0097; found 399.0099.

5-(2-Ethoxy-5-((3-iodobicyclo[1.1.1]pentan-1-yl)sulfonyl)phenyl)-1-methyl-3-propyl-1,6-dihydro–7H-pyrazolo[4,3-d]pyrimidin–7-one, 24b-I



A stock solution of sulfinate salt **24b-S** (548 mg, 1.10 mmol) in H_2O (1.10 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **24b-S** (0.50 mL, 0.50 mmol, 1.0 M in DMF), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.2** (–40 °C). Purification by column chromatography (SiO_2, EtOAc/pentane 3:7 → 4:1) gave BCP iodide **24b-I** (95.5 mg, 0.168 mmol, 84%) as a white solid.

R$_f$ 0.43 (EtOAc/pentane, 1:1).

m.p. 220 °C.

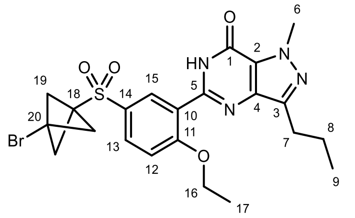
IR ν_{max}/cm^{-1} (film) 3322, 2960, 2361, 1698, 1320, 1170, 1140, 1030, 732, 619.

^{1}H NMR (600 MHz, $CDCl_3$) δ 10.75 (1H, s, NH), 8.90 (1H, d, *J* = 2.4 Hz, H15), 7.92 (1H, dd, *J* = 8.8, 2.4 Hz, H13), 7.19 (1H, d, *J* = 8.8 Hz, H12), 4.40 (2H, q, *J* = 7.0 Hz, H16), 4.28 (3H, s, H6), 2.94 (2H, t, *J* = 7.6 Hz, H7), 2.57 (6H, s, H19), 1.87 (2H, app. sxt., *J* = 7.4 Hz, H8), 1.66 (3H, t, *J* = 7.0 Hz, H17), 1.04 (3H, t, *J* = 7.4 Hz, H9).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.4, 153.7, 147.3, 146.2, 138.5, 132.4, 132.3, 130.0, 124.7, 121.7, 113.5, 66.5, 59.4, 58.0, 38.4, 27.9, 22.4, 14.7, 14.2, 2.3.

HRMS (ESI$^+$) $[M + H]^+$ $C_{22}H_{26}O_4IN_4S$ requires 569.0713; found 569.0711.

5-(5-((3-Bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)-2-ethoxyphenyl)-1-methyl-3-propyl- 1,6-dihydro–7H-pyrazolo[4,3-d]pyrimidin–7-one, 24b-Br



A stock solution of sulfinate salt **24b-S** (548 mg, 1.10 mmol) in H_2O (1.10 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **24b-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.34 mL, 0.20 mmol of a 0.59 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. Purification by column chromatography (SiO_2, EtOAc/pentane 1:9 → 1:4) gave BCP bromide **24b-Br** (78.9 mg, 0.152 mmol, 76%) as a white solid.

R_f 0.40 (EtOAc/pentane, 1:1).

m.p. 166 °C.

IR ν_{max}/cm^{-1} (film) 1774, 1724, 1701, 1180, 1145, 773.

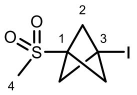
^{1}H NMR (600 MHz, $CDCl_3$) δ 10.78 (1H, s, NH), 8.89 (1H, d, *J* = 2.4 Hz, H15), 7.93 (1H, dd, *J* = 8.7, 2.5 Hz, H13), 7.19 (1H, d, *J* = 8.8 Hz, H12), 4.40 (2H, q, *J* = 7.0 Hz, H16), 4.28 (3H, s, H6), 2.94 (2H, t, *J* = 7.6 Hz, H7), 2.52 (6H, s, H19), 1.87 (2H, app. sxt., *J* = 7.4 Hz, H8), 1.66 (3H, t, *J* = 7.0 Hz, H17), 1.04 (3H, t, *J* = 7.4 Hz, H9).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.4, 153.7, 147.3, 146.2, 138.5, 132.4, 132.3, 130.1, 124.7, 121.8, 113.5, 66.4, 58.1, 52.8, 38.4, 35.4, 27.9, 22.4, 14.7, 14.2.

HRMS ($APCI^+$) $[M + H]^+$ $C_{22}H_{26}O_4BrN_4S$ requires 521.0853; found 521.0852.

S4.5 Alkyl Sulfonyl BCP Halides

1-Iodo-3-(methylsulfonyl)bicyclo[1.1.1]pentane, 25a-I



A stock solution of sulfinate salt **25a-S** (245 mg, 2.40 mmol) in H_2O (2.40 mL) was prepared. Benzyltrimethylammonium dichloroiodate (101 mg, 0.290 mmol), sulfinate salt **25a-S** (0.40 mL, 0.40 mmol of a 1.0 M solution in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.70 M solution in Et_2O) in CH_2Cl_2 (0.20 mL) were subjected to the conditions of **general procedure 11.4**. BCP iodide **25a-I** (54.7 mg, 0.201 mmol, 99%) was obtained as a white solid.

R$_f$ 0.30 (EtOAc/pentane, 3:7).

m.p. 182° C.

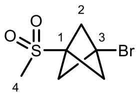
IR ν_{max}/cm^{-1} (film) 1296, 1188, 1167, 860, 838.

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.84 (3H, s, H4), 2.69 (6H, s, H2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 59.4, 57.2, 38.2, 1.2.

HRMS (ESI^{+}-) Not Found.

1-Bromo-3-(methylsulfonyl)bicyclo[1.1.1]pentane, 25a-Br



A stock solution of sulfinate salt **25a-S** (245 mg, 2.40 mmol) in H_2O (2.40 mL) was prepared. Sulfinate salt **25a-S** (0.40 mL, 0.40 mmol of a 1.0 M solution in H_2O), Br_2 (0.36 mL, 0.36 mmol of a 1.0 M solution in CH_2Cl_2), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.70

M solution in Et_2O) and Et_3B (20 µL, 0.02 mmol, 1.0 M in hexanes) in CH_2Cl_2 (0.20 mL) were subjected to the conditions of **general procedure 11.5**. BCP iodide **25a-Br** (44.6 mg, 0.198 mmol, 98%) was obtained as a white solid.

R$_f$ 0.39 (EtOAc/pentane, 3:7).

m.p. 125° C.

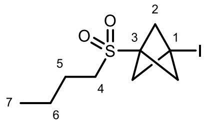
IR ν_{max}/cm^{-1} (film) 1359, 1308, 1178, 1162, 1133, 910, 876, 733.

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.87 (3H, s, H4), 2.64 (6H, s, H2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 58.2, 51.9, 38.6, 34.3.

HRMS (ESI$^+$) Not Found.

1-(Butylsulfonyl)-3-iodobicyclo[1.1.1]pentane, 25b-I



A stock solution of lithium sulfinate **25b-S** (25.6 mg, 0.209 mmol) in H_2O (0.20 mL) was prepared. Benzyltrimethylammonium dichloroiodate (50.5 mg, 0.145 mmol), lithium sulfinate **25a-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.4**. Purification by silica plug (pentane wash, followed by elution with EtOAc/pentane, 1:4) gave BCP iodide **25a-I** (20.0 mg, 0.0637 mmol, 64%) as a white solid.

R$_f$ 0.55 (EtOAc / Pentane, 1:4) [goofy].

m.p. 110 ° C.

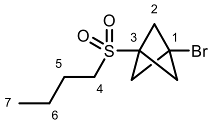
IR ν_{max}/cm^{-1} (film) 2980, 1318, 1290, 1269, 1203, 1165, 1119, 1100, 865, 623.

^{1}H NMR (600 MHz, $CDCl_3$) δ 2.96 – 2.88 (2H, m, H4), 2.64 (6H, s, H2), 1.88 – 1.77 (2H, m, H5), 1.47 (2H, sxt., *J* = 7.4 Hz, H6), 0.96 (3H, t, *J* = 7.4 Hz, H7).

^{13}C NMR (151 MHz, $CDCl_3$) δ 59.8, 56.8, 50.8, 23.5, 22.0, 13.7, 1.7.

HRMS (ESI$^{+/-}$) Not found.

1-Bromo-3-(butylsulfonyl)bicyclo[1.1.1]pentane, 25b-Br



A stock solution of lithium sulfinate **25b-S** (25.6 mg, 0.20 mmol) in H_2O (0.20 mL) was prepared. Lithium sulfinate **25b-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), Br_2 (0.18 mL, 0.18 mmol of a 1.0 M solution in CH_2Cl_2), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) and Et_3B (10 µL, 0.01 mmol, 1.0 M in hexanes) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.5**. BCP iodide **25b-Br** (17.0 mg, 0.0636 mmol, 64%) was obtained as a white solid.

R$_f$ 0.60 (EtOAc/pentane, 1:4) [goofy].

m.p. 97 ° C.

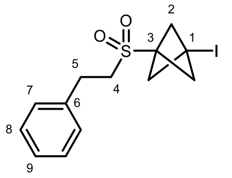
IR ν_{max}/cm^{-1} (film) 1319, 1173, 1100, 668.

^{1}H NMR (600 MHz, $CDCl_3$) δ 2.99 – 2.90 (2H, m, H4), 2.64 (6H, s, H2), 1.85 – 1.79 (2H, m, H5), 1.48 (2H, sxt, *J* = 7.4 Hz, H6), 0.97 (3H, t, *J* = 7.4 Hz, H7).

^{13}C NMR (151 MHz, $CDCl_3$) δ 58.5, 51.4, 51.1, 34.6, 23.6, 22.0, 13.7.

HRMS (ESI$^{+/-}$) Not found.

1-Iodo-3-(phenethylsulfonyl)bicyclo[1.1.1]pentane, 25c-I



A stock solution of sulfinate salt **25c-S** (38.4 mg, 0.200 mmol) in H_2O (0.20 mL) was prepared. Benzyltrimethylammonium dichloroiodate (50.5 mg, 0.145 mmol), sulfinate salt **25c-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.4**. Purification by silica plug (pentane wash, followed by elution with EtOAc/pentane, 1:4) gave BCP iodide **25c-I** (35.6 mg, 0.983 mmol, 98%) as a white solid.

R_f 0.70 (EtOAc/pentane, 1:4).

m.p. 151 ° C.

IR ν_{max}/cm^{-1} (film) 2981, 1303, 1291, 1262, 1164, 1151, 1115.

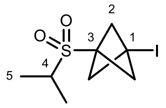
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.32 (2H, m, H8), 7.29 – 7.27 (1H, m, H9), 7.23 – 7.20 (2H, m, H7), 3.20–3.16 (2H, m, H4), 3.15–3.11 (2H, m, H5), 2.66 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 137.6, 129.2, 128.6, 127.4, 59.7, 56.9, 52.5, 27.5, 1.4.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{13}H_{15}O_2INaS$ requires 384.9730; found 384.9730.

Note: Attempts to prepare corresponding bromide ***25c-Br*** *under* ***general procedure 11.5*** *were unsuccessful.*

1-Iodo-3-(isopropylsulfonyl)bicyclo[1.1.1]pentane, 25d-I



A stock solution of sulfinate salt **25d-S** (32.5 mg, 0.250 mmol) in H_2O (0.25 mL) was prepared. Benzyltrimethylammonium dichloroiodate (50.5 mg, 0.145 mmol), sulfinate salt **25d-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.4**. Purification by silica plug (pentane wash, followed by elution with EtOAc/pentane, 1:4) gave BCP iodide **25d-I** (21.3 mg, 0.71 mmol, 71%) as a white solid.

R$_f$ 0.43 (EtOAc/pentane, 1:4).

m.p. 110 ° C.

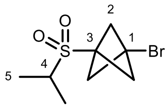
IR ν_{max}/cm^{-1} (film) 2979, 1300, 1288, 1204, 1161, 1116, 857, 686.

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.14 (1H, hept., *J* = 6.9 Hz, H4), 2.72 (6H, s, H2), 1.39 (6H, d, *J* = 6.9 Hz, H5).

^{13}C NMR (151 MHz, $CDCl_3$) δ 60.5, 56.0, 52.8, 15.8, 1.9.

HRMS (ESI$^{+/-}$) Not found.

1-Bromo-3-(isopropylsulfonyl)bicyclo[1.1.1]pentane, 25d-Br



A stock solution of sulfinate salt **25d-S** (32.5 mg, 0.25 mmol) in H_2O (0.25 mL) was prepared. Sulfinate salt **25d-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), Br_2 (0.18 mL, 0.18 mmol of a 1.0 M solution in CH_2Cl_2), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) and Et_3B (10 µL, 0.01 mmol, 1.0 M in hexanes) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.5**. BCP iodide **25d-Br** (17.0 mg, 0.0672 mmol, 67%) was obtained as a white solid.

R$_f$ 0.57 (EtOAc/pentane, 1:4) [goofy].

m.p. 105 ° C.

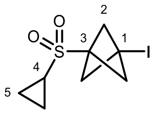
IR ν_{max}/cm^{-1} (film) 1283, 1210, 1173, 1160, 1108, 867.

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.16 (1H, hept., *J* = 6.9 Hz, H4), 2.67 (6H, s, H2), 1.40 (6H, d, *J* = 6.9 Hz, H5).

^{13}C NMR (151 MHz, $CDCl_3$) δ 59.2, 53.0, 50.6, 34.7, 15.8.

HRMS (ESI$^{+/-}$, APCI and EI) Not Found.

1-(Cyclopropylsulfonyl)-3-iodobicyclo[1.1.1]pentane, 25e-I



A stock solution of sulfinate salt **25e-S** (25.6 mg, 0.200 mmol) in H_2O (0.20 mL) was prepared. Benzyltrimethylammonium dichloroiodate (50.5 mg, 0.145 mmol)**,** sulfinate salt **25e-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.4**. BCP iodide **25e-I** (37.1 mg, 0.125 mmol, 118%, 100% NMR yield) was obtained as a white solid.

R$_f$ 0.33 (EtOAc/pentane, 1:4).

m.p. 145 ° C.

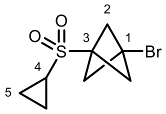
IR ν_{max}/cm^{-1} (film) 2980, 1315, 1292, 1167, 1143, 1123, 701, 610.

^{1}H NMR (600 MHz, $CDCl_3$) δ 2.70 (6H, s, H2), 2.30 (1H, tt, *J* = 7.9, 4.8 Hz, H4), 1.26 – 1.17 (2H, m, H5), 1.10 – 1.00 (2H, m, H5).

^{13}C NMR (151 MHz, $CDCl_3$) δ 59.8, 56.9, 27.2, 4.5, 2.2.

HRMS (ESI$^{+/-}$) Not found.

1-Bromo-3-(cyclopropylsulfonyl)bicyclo[1.1.1]pentane, 25e-Br



A stock solution of sulfinate salt **25e-S** (25.6 mg, 0.20 mmol) in H_2O (0.20 mL) was prepared. Sulfinate salt **25e-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), Br_2 (0.18 mL, 0.18 mmol of a 1.0 M solution in CH_2Cl_2), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) and Et_3B (10 µL, 0.01 mmol, 1.0 M in hexanes) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.5**. Purification by column chromatography (SiO_2, EtOAc/Pentane, 1:9 → 2:3) gave BCP Bromide **25e-Br** (19.8 mg, 0.788 mmol, 79%) as a white solid.

R_f 0.39 (EtOAc / Pentane, 1:4) [goofy].

m.p. 140 – 144° C.

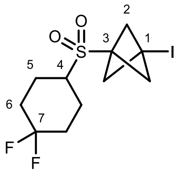
IR ν_{max}/cm^{-1} (film) 1315, 1289, 1206, 1178, 1126, 891.

^{1}H NMR (600 MHz, $CDCl_3$) δ 2.65 (6H, s, H2), 2.32 (1H, tt, *J* = 8.0, 4.8 Hz, H4), 1.25–1.20 (2H, m, H5), 1.08–1.04 (2H, m, H5).

^{13}C NMR (151 MHz, $CDCl_3$) δ 58.5, 51.4, 34.9, 27.5, 4.6.

HRMS (ESI$^{+/-}$, APCI and EI) Not Found.

1-((4,4-Difluorocyclohexyl)sulfonyl)-3-iodobicyclo[1.1.1]pentane, 25f-I



A stock solution of sulfinate salt **25f-S** (41.2 mg, 0.200 mmol) in H_2O (0.20 mL) was prepared. Benzyltrimethylammonium dichloroiodate (50.5 mg, 0.145 mmol), sulfinate salt **25f-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.4**. Purification by silica plug (pentane wash, followed by elution with EtOAc/pentane, 1:4) gave BCP iodide **25f-I** (31.4 mg, 0.0835 mmol, 84%) as a white solid.

R_f 0.46 (EtOAc/pentane, 1:4) [UV].

m.p. 165° C.

IR ν_{max}/cm^{-1} (film) 1301, 1205, 1162, 1100, 969, 741, 645.

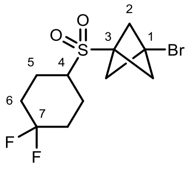
^{1}H NMR (600 MHz, $CDCl_3$) δ 2.98–2.90 (1H, m, H4), 2.73 (6H, s, H2), 2.34–2.25 (2H, m, H6), 2.24–2.18 (2H, m, H5), 2.03–1.93 (2H, m, H5), 1.86–1.72 (2H, m, H6).

^{13}C NMR (151 MHz, $CDCl_3$) δ 121.6 (dd, $^1J_{CF}$ = 242.8, 240.6 Hz), 60.4, 57.9 (d, $^4J_{CF}$ = 1.1 Hz), 56.3, 32.3 (dd,$^2J_{CF}$ = 25.9, 24.7 Hz), 22.4 (dd, $^3J_{CF}$ = 9.0, 1.4 Hz), 1.4.

^{19}F NMR (377 MHz, $CDCl_3$) δ –101.6 (d, J = 242.4 Hz), – 94.7 (d, J = 242.5 Hz).

HRMS (ESI^{+-}, APCI and EI) Not Found.

1-Bromo-3-((4,4-difluorocyclohexyl)sulfonyl)bicyclo[1.1.1]pentane, 25f-Br



A stock solution of sulfinate salt **25f-S** (41.2 mg, 0.200 mmol) in H_2O (0.20 mL) was prepared. Sulfinate salt **25f-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), Br_2 (0.18 mL, 0.18 mmol of a 1.0 M solution in CH_2Cl_2), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) and Et_3B (10 µL, 0.01 mmol, 1.0 M in hexanes) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.5**. BCP iodide **25f-Br** (35.4 mg, 0.108 mmol, 108%) was obtained as a white solid.

R$_f$ 0.50 (EtOAc/pentane, 1:4).

m.p. 163 – 164° C.

IR ν_{max}/cm^{-1} (film) 2981, 1379, 1301, 1171, 1102, 969, 879, 742.

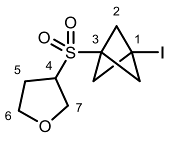
^{1}H NMR (600 MHz, $CDCl_3$) δ 3.00 – 2.92 (1H, m, H4), 2.68 (6H, s, H2), 2.35 – 2.25 (2H, m, H6), 2.25 – 2.18 (2H, m, H5), 2.04 – 1.94 (2H, m, H5), 1.86 – 1.73 (2H, m, H6).

^{13}C NMR (151 MHz, $CDCl_3$) δ 121.6 (dd, $^1J_{CF2}$ = 242.8, 240.6 Hz), 59.1, 58.2, 50.9, 34.4, 32.5–32.1 (m), 22.4 (dd, $^3J_{CF2}$ = 9.1, 1.5 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ –101.60 (d, J = 242.8 Hz), – 94.70 (d, J = 242.1 Hz).

HRMS (ESI$^{+/-}$, APCI) Not Found.

3-((3-Iodobicyclo[1.1.1]pentan-1-yl)sulfonyl)tetrahydrofuran, 25g-I



A stock solution of sulfinate salt **25g-S** (31.6 mg, 0.200 mmol) in H_2O (0.20 mL) was prepared. Benzyltrimethylammonium dichloroiodate (50.5 mg, 0.145 mmol)**,** sulfinate salt **25g-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.4**. Purification by silica plug (pentane wash, followed by elution with EtOAc/pentane, 1:4) gave BCP iodide **25g-I** (23.4 mg, 0.0713 mmol, 71%) as a white solid.

R$_f$ 0.13 (EtOAc/pentane, 1:4)[UV, goofy].

m.p. 139 – 142 ° C.

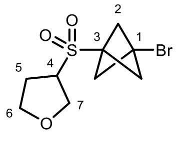
IR ν_{max}/cm^{-1} (film) 1292, 1272, 1206, 1165, 1117, 1083, 920, 870.

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.16 (1H, dd, *J* = 10.1, 5.4 Hz, H7), 4.03 (1H, dd, *J* = 10.1, 8.1 Hz, H7), 3.97 (1H, td, *J* = 8.2, 5.9 Hz, H6), 3.82 (1H, dt, *J* = 8.7, 6.8 Hz, H6), 3.65 (1H, ddt, *J* = 9.8, 8.1, 5.4 Hz, H4), 2.74–2.67 (6H, m, H2), 2.36 (1H, ddt, *J* = 13.4, 7.6, 6.0 Hz, H5), 2.26 (1H, dddd, *J* = 13.4, 9.8, 7.3, 5.9 Hz, H5).

^{13}C NMR (151 MHz, $CDCl_3$) δ 68.5, 67.2, 60.0, 59.9, 56.1, 27.4, 1.6.

HRMS (ESI$^{+/-}$, APCI and EI) Not Found.

3-((3-Bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)tetrahydrofuran, 25g-Br



A stock solution of sulfinate salt **25g-S** (31.6 mg, 1.20 mmol) in H_2O (0.20 mL) was prepared. Sulfinate salt **25g-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), Br_2 (0.18 mL, 0.18 mmol of a 1.0 M solution in CH_2Cl_2), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) and Et_3B (10 µL, 0.01 mmol, 1.0 M in hexanes) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.5**. BCP bromide **25g-Br** (26.9 mg, 0.0957 mmol, 96%) was obtained as a white solid.

R$_f$ 0.13 (EtOAc/pentane, 1:4) [goofy].

m.p. 115 – 118 °C.

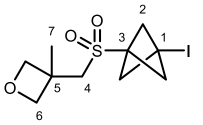
IR ν_{max}/cm^{-1} (film) 2981, 1382, 1312, 1174, 1081, 876, 668.

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.17 (1H, dd, *J* = 10.2, 5.5 Hz, H7), 4.04 (1H, dd, *J* = 10.2, 8.1 Hz, H7), 3.97 (1H, ddd, *J* = 8.8, 7.8, 6.0 Hz, H6), 3.83 (1H, dt, *J* = 8.8, 6.9 Hz, H6), 3.67 (1H, ddt, *J* = 9.8, 8.1, 5.5 Hz, H4), 2.68 – 2.63 (6H, m, H2), 2.37 (1H, ddt, *J* = 13.4, 7.6, 6.0 Hz, H5), 2.27 (1H, dddd, *J* = 13.4, 9.8, 7.3, 6.0 Hz, H5).

^{13}C NMR (151 MHz, $CDCl_3$) δ 68.5, 67.2, 60.3, 58.6, 50.7, 34.7, 27.5.

HRMS (ESI$^{+/-}$, APCI) Not found.

3-(((3-Iodobicyclo[1.1.1]pentan-1-yl)sulfonyl)methyl)-3-methyloxetane, 25h-I



A stock solution of sulfinate salt **25a-S** (17.2 mg, 0.100 mmol) in H_2O (0.10 mL) was prepared. Benzyltrimethylammonium dichloroiodate (25.3 mg, 0.0727 mmol), sulfinate salt **25a-S** (0.10 mL, 0.10 mmol of a 1.0 M solution in H_2O), [1.1.1]propellane **1** (0.08 mL, 50 µmol of a 0.70 M solution in Et_2O) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.4**. BCP iodide **25a-I** (17.3 mg, 0.0506 mmol, 101%) was obtained as a white solid.

R$_f$ 0.21 (EtOAc/pentane, 2:3).

m.p. 158 ° C.

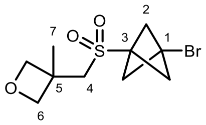
IR ν_{max}/cm^{-1} (film) 1292, 1272, 1206, 1165, 1117, 1083, 920, 870.

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.64 (2H, d, *J* = 6.4 Hz, H6), 4.46 (2H, d, *J* = 6.4 Hz, H6), 3.31 (2H, s, H4), 2.69 (6H, s, H2), 1.65 (3H, s, H7).

^{13}C NMR (151 MHz, $CDCl_3$) δ 82.4, 59.4, 57.9, 57.1, 37.8, 23.5, 1.2.

HRMS (EI$^+$) [M]$^+$ $C_{10}H_{15}O_3IS$ requires 341.9787; found 341.0202.

3-(((3-Bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)methyl)-3-methyloxetane, 25h-Br



A stock solution of sulfinate salt **25h-S** (34.4 mg, 0.20 mmol) in DMF:H_2O (1:2, 0.30 mL) was prepared. Sulfinate salt **25h-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), Br_2 (0.18 mL, 0.18 mmol of a 1.0 M solution in CH_2Cl_2), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) and Et_3B (10 µL, 0.01 mmol, 1.0 M in hexanes) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.5**. BCP iodide **25h-Br** (14.7 mg, 0.0498 mmol, 50%) was obtained as a white solid.

R$_f$ 0.27 (EtOAc/pentane, 1:4).

m.p. 125 – 128 °C.

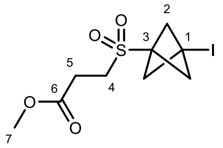
IR ν_{max}/cm^{-1} (film) 2957, 1303, 1284, 1177, 1122, 978.

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.64 (2H, d, *J* = 6.4 Hz, H6), 4.47 (2H, d, *J* = 6.4 Hz, H6), 3.33 (2H, s, H4), 2.64 (6H, s, H2), 1.66 (3H, s, H7).

^{13}C NMR (151 MHz, $CDCl_3$) δ 82.4, 58.1, 57.4, 52.6, 37.8, 34.5, 23.5.

HRMS (ESI$^+$) [M + H]$^+$ $C_{10}H_{16}O_3{}^{79}BrS$ requires 294.9998; found 294.9997.

Methyl 3-((3-iodobicyclo[1.1.1]pentan-1-yl)sulfonyl)propanoate, 25i-I



A stock solution of sulfinate salt **25i-S** (34.8 mg, 0.200 mmol) in H_2O (0.20 mL) was prepared. Benzyltrimethylammonium dichloroiodate (50.5 mg, 0.145 mmol), sulfinate salt **25i-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.4**. BCP iodide **25i-I** (13.3 mg, 0.0386 mmol, 39%) was obtained as a white solid.

R_f 0.30 (EtOAc/pentane, 1:4)[vanilin].

m.p. 115 °C.

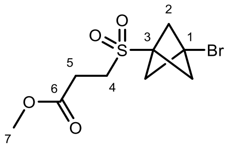
IR ν_{max}/cm^{-1} (film) 1738, 1311, 1203, 1167, 1120, 669.

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.74 (3H, s, H7), 3.26 (2H, t, *J* = 7.7 Hz, H4), 2.85 (2H, t, *J* = 7.7 Hz, H5), 2.70 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.8, 59.6, 56.8, 52.7, 31.1, 26.2, 1.2.

HRMS (ESI^+) $[M + Na]^+$ $C_9H_{13}O_4INaS$ requires 366.9471; found 366.9472.

Methyl 3-((3-bromobicyclo[1.1.1]pentan-1-yl)sulfonyl)propanoate, 25i-Br



A stock solution of sulfinate salt **25i-S** (34.8 mg, 0.20 mmol) in H_2O (0.20 mL) was prepared. Sulfinate salt **25b-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), Br_2 (0.18 mL, 0.18

mmol of a 1.0 M solution in CH_2Cl_2), [1.1.1]propellane **1** (0.15 mL, 0.10 mmol of a 0.70 M solution in Et_2O) and Et_3B (10 µL, 0.01 mmol, 1.0 M in hexanes) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 11.4**. BCP iodide **25b-Br** (21.5 mg, 0.0724 mmol, 73%) was obtained as a white solid.

R$_f$ 0.36 (EtOAc/pentane, 3:7) [Goofy].

IR ν_{max}/cm^{-1} (film) 2981, 1727, 1373, 1310, 1257, 1179, 1122.

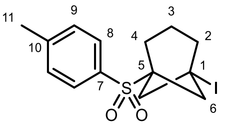
^{1}H NMR (600 MHz, $CDCl_3$) δ 3.75 (3H, s, H7), 3.30 (2H, t, *J* = 7.7 Hz, H4), 2.86 (2H, t, *J* = 7.7 Hz, H5), 2.65 (6H, s, H2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.8, 58.4, 52.7, 51.5, 46.5, 34.4, 26.2.

HRMS (ESI$^+$) $[M + H]^+$ $C_9H_{14}O_4{}^{79}BrS$ requires 296.9791; found 296.9788.

S4.6 Sulfonyl BCHep Halides

1-Iodo-5-tosylbicyclo[3.1.1]heptane, 30a-I



A stock solution of sulfinate salt **18a-S** (534 mg, 3.00 mmol) in H_2O (3.0 mL) was prepared. DIH (78.4 mg, 0.20 mmol), sulfinate salt **18a-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [3.1.1]propellane **30** (0.87 mL, 0.20 mmol of a 0.23 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.1**. Purification by silica plug (EtOAc/pentane, 1:4) gave sulfonyl BCHep iodide **30a-I** (65.4 mg, 0.174 mmol, 87%) as a white solid which could be recrystalised from CH_2Cl_2/pentane.

R_f 0.30 (EtOAc/pentane, 1:9).

m.p. 134 – 140 °C.

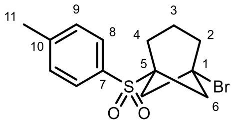
IR ν_{max}/cm^{-1} (film) 2954, 1596, 1310, 1300, 1290, 1150, 1108, 1079, 857, 816, 671.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.62 (2H, m, H8), 7.38 – 7.31 (2H, m, H9), 3.23 (2H, dt, *J* = 7.6, 3.8 Hz, H6), 2.52 – 2.44 (2H, m, H), 2.45 (3H, s, H11), 2.35 – 2.25 (2H, m, H6), 1.91 – 1.82 (4H, m, H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1, 132.6, 130.0, 129.3, 65.4, 46.2, 42.5, 26.7, 25.9, 21.8, 19.3.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{14}H_{17}O_2INaS$ requires 398.9886; found 398.9886.

1-Bromo-5-tosylbicyclo[3.1.1]heptane, 30a-Br



A stock solution of sulfinate salt **18a-S** (534 mg, 3.00 mmol) in H_2O (3.0 mL) was prepared. DBH (57.1 mg, 0.20 mmol), sulfinate salt **18a-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [3.1.1]propellane **30** (0.87 mL, 0.20 mmol of a 0.23 M solution in Et_2O) in Et_2O (0.20 mL) were subjected to the conditions of **general procedure 11.3**. BCP bromide **30a-Br** (81.7, 0.25 mmol, 125%, 100% NMR yield) was obtained as a white solid.

R_f 0.32 (EtOAc/pentane, 1:19).

m.p. 93 ° C.

IR ν_{max}/cm^{-1} (film) 1311, 1301, 1291, 1151, 1113, 1080, 671, 613.

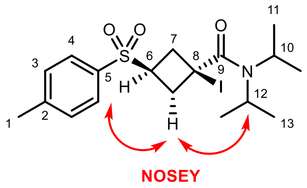
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.64 (2H, m, H8), 7.39 – 7.31 (2H, m, H9), 3.14 – 3.04 (2H, m, H6), 2.45 (3H, s, H11), 2.34 – 2.29 (2H, m, H4), 2.26 – 2.17 (2H, m, H6), 1.94 – 1.86 (2H, m, H3), 1.86 – 1.81 (2H, m, H2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1, 132.8, 130.0, 129.4, 62.4, 52.3, 44.5, 39.3, 26.0, 21.8, 18.7.

HRMS (ESI$^+$) $[M + Na]^+$ $C_{14}H_{17}O_2{}^{79}BrNaS$ requires 351.0025; found 351.0027.

S4.7 Sulfonyl BCB Halides

1-Iodo-N,N-diisopropyl-3-tosylcyclobutane-1-carboxamide, 31a-I



major diasterisomer

A stock solution of sulfinate salt **18a-S** (890 mg, 1.20 mmol) in H_2O (3.00 mL) was prepared. Benzyltrimethylammonium dichloroiodate (50.5 mg, 0.12 mmol)**,** sulfinate salt **18a-S** (0.20 mL, 0.20 mmol of a 1.0 M solution in H_2O), BCB **31a** (0.15 mL, 0.10 mmol of a 0.10 M solution in Et_2O) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 1.6**. BCP iodide **31a-I** (36.8 mg, 0.159 mmol, 80%, 2.5:1 dr) was obtained as a white solid.

R$_f$ 0.40 (EtOAc/pentane, 1:4) [UV].

IR ν_{max}/cm^{-1} (film) 2971, 1633, 1441, 1371, 1329, 1148, 1087, 732, 680.

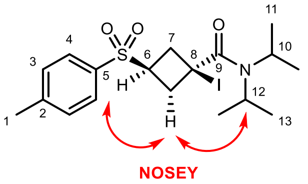
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 – 7.69 (2.4 H, m, H4, H4′), 7.39 – 7.32 (2.4H, m, H3, H3′), 4.11 (1H, tt, *J* = 9.5, 7.6 Hz, H6), 3.88 (0.4H, hept., *J* = 6.5 Hz, H12′), 3.77 (1H, hept., *J* = 6.6 Hz, H12), 3.70 (0.4H, pent., *J* = 8.6 Hz, H6′), 3.38 – 3.24 (1.4H, m, H10, H10′), 3.28 – 3.14 (2.8H, m, H7b, H7a′, 7b′), 2.56 (2H, br. s, H7a), 2.44 (4.2H, s, H1, H1′), 1.38 (6H, d, *J* = 6.8 Hz, H11), 1.35 (2.4H, d, *J* = 6.7 Hz, H11′), 1.26 – 1.20 (8.4, m, H13, H13′).

^{13}C NMR (151 MHz, $CDCl_3$) δ 169.1, 168.4, 145.3, 134.6, 134.4, 130.2, 128.5, 128.5, 55.1, 51.6, 51.0, 50.0, 46.9, 46.7, 40.8 (br.), 29.1, 21.9, 21.8, 19.9 (br.).

HRMS (ESI$^+$) $[M + H]^+$ $C_{18}H_{27}O_3NIS$ requires 464.0751; found 464.0748.

Numbers denoted with a prime in blue correspond to the minor diastereisomer. Diastereisomer ratio calculated from the analysis of the ^{1}H NMR of the crude sample.

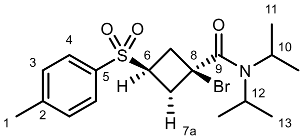
Recrystallisation from CH_2Cl_2/pentane at –20 °C gave a pure sample of the major diastereoisomer:



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (2H, br. d, *J* = 8.2 Hz, H4), 7.36 (2H, br. d, *J* = 8.5 Hz, H3), 4.12 (1H, tt, *J* = 9.3, 7.6 Hz, H6), 3.78 (1H, hept., *J* = 6.7 Hz, H12), 3.32 (1H, hept., *J* = 6.9 Hz, H10), 3.21 (2H, br. s, H7b), 2.56 (2H, br. s, H7a), 2.45 (3H, s, H1), 1.39 (6H, d, *J* = 6.9 Hz, H11), 1.24 (6H, d, *J* = 6.7 Hz, H13).

^{13}C NMR (151 MHz, $CDCl_3$) δ 169.1, 145.3, 134.7, 130.2, 128.5, 51.7, 50.0, 46.7, 40.9, 29.1, 21.8, 19.9.

1-Bromo-*N,N*-diisopropyl-3-tosylcyclobutane-1-carboxamide, 31a-Br



major diasterisomer
(tentative assignment)

A stock solution of sulfinate salt **18a-S** (890 mg, 1.20 mmol) in H_2O (3.00 mL) was prepared. Sulfinate salt **18a-S** (0.25 mL, 0.25 mmol of a 1.0 M solution in H_2O), Br_2 (0.18 mL, 0.18 mmol of a 1.0 M solution in CH_2Cl_2), BCB **31a** (18.1 mg, 0.2 mL, 0.10 mmol of a 0.50 M solution in CH_2Cl_2) and Et_3B (10 µL, 0.01 mmol, 1.0 M in hexanes) were subjected to the conditions of **general procedure 1.7**. Purification by column chromatography (SiO_2, EtOAc/pentane 1:19 → 1:4) gave bromide **31a-Br** (29.8 mg, 0.0718 mmol, 72%, 2.3:1 dr) as a white solid.

R$_f$ 0.39 (EtOAc/pentane, 1:4)[UV, ninhydrin].

m.p. 145 ° C.

IR v_{max}/cm^{-1} (film) 1632, 1593, 1339, 1149, 1076, 651.

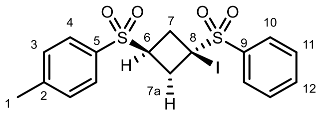
^{1}H NMR (600 MHz, CDCl$_3$) δ 7.78 – 7.72 (2.5H, m, H4, H4’), 7.39 – 7.33 (2.5H, m, H3, H3’), 4.07 (1H, pent., *J* = 8.5 Hz, H6), 3.95 (0.25H, hept., *J* = 6.6 Hz, H10’), 3.84 (1H, hept., *J* = 6.6 Hz, H12), 3.57 (0.25H, pent., *J* = 8.6 Hz, H6’), 3.39 – 3.30 (3.5H, m, H10, H12’, H7b), 3.29 – 3.22 (0.50H, m, H7b’), 3.17 (0.50H, dd, *J* = 13.3, 9.0 Hz, H7a’), 2.63 (2H, br. s, H7a), 2.45 (3.8H, s, H1), 1.39 (6H, d, *J* = 6.8 Hz, H11), 1.36 (1.5H, obsc. d, *J* = 6.6 Hz, H11’), 1.22 (7.5H, d, *J* = 6.6 Hz, H13, H13’).

^{13}C NMR (151 MHz, CDCl$_3$) δ 167.3, 166.7, 145.3, 134.6, 130.2, 128.5, 77.2, 53.1, 52.7, 51.5, 50.3, 49.5, 48.0, 46.9, 46.7, 38.6, 38.5, 21.8, 20.2, 20.1, 20.1, 20.0.

HRMS (ESI$^{+/-}$) Not found.

Numbers denoted with a prime in blue correspond to the minor diastereisomer. Diastereisomer ratio calculated from the analysis of the ^{1}H NMR of the crude sample. Assignment of the major diastereisomer was assigned based on comparison of 1H NMR to **31a-I**.

1-((3-Iodo-3-(phenylsulfonyl)cyclobutyl)sulfonyl)-4-methylbenzene, 31b-I



major diasterisomer
(tentative assignment)

A stock solution of sulfinate salt **18a-S** (890 mg, 1.20 mmol) in H$_2$O (3.00 mL) was prepared. Benzyltrimethylammonium dichloroiodate (50.5 mg, 0.14 mmol), sulfinate salt **18a-S** (0.25

mL, 0.25 mmol of a 1.0 M solution in H_2O), BCB **31b** (19.4 mg, 0.20 mL, 0.10 mmol of a 0.50 M solution in CH2Cl2), Et_3B (10 µL, 0.10 mmol of a 1.0 M solution in hexane) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 1.6**. Purification by column chromatography (SiO_2, EtOAc/ pentane 1:9 → 1:4) gave iodide **31b-I** (31.3 mg, 0.66 mmol, 66%, 2.1:1 dr) as a white solid.

R_f 0.19 (EtOAc/pentane, 1:4)[UV].

m.p. 137 ° C.

IR ν_{max}/cm^{-1} (film) 1384, 1317, 1148, 1085, 914, 687, 647.

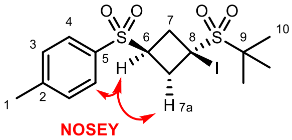
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 – 8.01 (0.6H, m, H10’), 8.00 – 7.96 (2H, m, H10), 7.77 – 7.70 (4.8H, m, H4, H4’, H12, H12’), 7.65 – 7.57 (2.6H, m, H11, H11’), 7.41 – 7.36 (2.6H, m, H3, H3’), 4.26 (0.6H, pent., *J* = 8.7 Hz, H6’), 4.09 (1H, tt, *J* = 9.6, 7.7 Hz, H6), 3.61 – 3.53 (2H, m, H7b), 3.49 – 3.42 (1.2H, m, H7a’), 3.41 – 3.34 (1.2H, m, H7b’), 2.57 – 2.50 (2H, m, H7a), 2.47 (3.6H, s, H1, H1’).

^{13}C NMR (151 MHz, $CDCl_3$) δ 145.7, 145.7, 135.1, 135.0, 134.2, 133.5, 131.6, 131.0, 130.4, 130.4, 129.4, 129.1, 128.6, 128.6, 55.7, 50.9, 42.4, 39.0, 39.0, 37.9, 21.9, 21.9.

HRMS (ESI$^+$) $[M + H]^+$ $C_{17}H_{18}O_4IS_2$ requires 476.9686; found 476.9686.

Numbers denoted with a prime in blue correspond to the minor diastereisomer. Diastereisomer ratio calculated from the analysis of the ^{1}H NMR of the crude sample. Assignment of the major diastereisomer was based on comparison of ^{1}H NMR data with **31a-I**.

1-((3-(*t*-Butylsulfonyl)-3-iodocyclobutyl)sulfonyl)-4-methylbenzene, 31c-I



Assumed diastereomer, tBu shows NOSEY to both 7a and 7b

A stock solution of sulfinate salt **18a-S** (890 mg, 1.20 mmol) in H_2O (3.00 mL) was prepared. Benzyltrimethylammonium dichloroiodate (50.5 mg, 0.14 mmol), sulfinate salt **18a-S** (0.25 mL, 0.25 mmol of a 1.0 M solution in H_2O), BCB **31c** (17.4 mg, 0.20 mL, 0.10 mmol of a 0.50 M solution in CH_2Cl_2), Et_3B (10 µL, 0.10 mmol of a 1.0 M solution in hexane) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 1.6**. The dr of the crude reaction mixture was 10:1. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 1:4) gave iodide **31c-I** (12.7 mg, 0.0279 mmol, 28%, 20:1 dr) as a white solid.

R_f 0.13 (EtOAc/pentane, 1:4).

m.p. 171 – 180 °C.

IR ν_{max}/cm^{-1} (film) 1596, 1320, 1395, 1148, 1114, 1086, 712, 695.

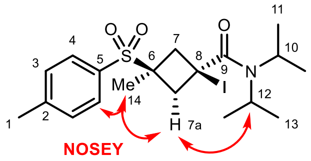
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (2H, d, J = 8.3 Hz, H4), 7.38 (2H, d, J = 8.0 Hz, H5), 4.21 (1H, tt, J = 9.7, 7.6 Hz, H6), 3.83 – 3.75 (2H, m, H7b), 2.61 (2H, ddt, J = 10.9, 7.6, 2.6 Hz, H7a), 2.46 (3H, s, H1), 1.62 (9H, s, H10).

^{13}C NMR (151 MHz, $CDCl_3$) δ 145.6, 134.3, 130.4, 128.6, 65.6, 52.1, 41.1, 36.1, 26.4, 21.9.

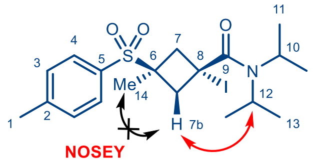
HRMS (ESI$^+$) [M + Na]$^+$ $C_{15}H_{21}O_4INaS_2^+$ requires 478.9818; found 478.9817.

Diastereisomer ratio calculated from the analysis of the ^{1}H NMR of the crude sample. Assignment of the major diastereisomer was based on comparison of ^{1}H NMR data with **31a-I**.

1-((3-Iodo-3-(phenylsulfonyl)cyclobutyl)sulfonyl)-4-methylbenzene, 31d-I



major diasteriosomer
(tentative assinment)



minor diasteriosomer

A stock solution of sulfinate salt **18a-S** (890 mg, 1.20 mmol) in H_2O (3.00 mL) was prepared. Benzyltrimethylammonium dichloroiodate (50.5 mg, 0.14 mmol)**,** sulfinate salt **18a-S** (0.25 mL, 0.25 mmol of a 1.0 M solution in H_2O), BCB **31d** (19.5 mg, 0.20 mL, 0.10 mmol of a 0.50 M solution in CH_2Cl_2), Et_3B (10 µL, 0.10 mmol of a 1.0 M solution in hexane) in CH_2Cl_2 (0.10 mL) were subjected to the conditions of **general procedure 1.6**. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 1:4) gave iodide **31d-I** (44.9 mg, 0.94 mmol, 94%, in 3.3:1 dr) as a white solid.

R$_f$ 0.31 (EtOAc/pentane, 1:4).

m.p. 144 – 146° C.

IR ν_{max}/cm^{-1} (film) 1634, 1596, 1416, 1372, 1329, 1301, 1138, 1081, 732, 647.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85 (0.7H, d, J = 8.4 Hz, H4’), 7.74 (2H, d, J = 8.6 Hz, H4), 7.43 (0.7H, d, J = 7.9 Hz, H3’), 7.34 (2H, d, J = 7.9 Hz, H3), 4.01 (1H, br. m, H7b), 3.87 (0.7H, hept., J = 6.5 Hz, H12’), 3.75 (1H, hept., J = 6.6 Hz, H12), 3.69 – 3.37 (2.3H, br. m, H7b, 7a’, 7b’), 3.33 (0.7H, hept. J = 6.9 Hz, H10’), 3.29 (1H, hept., J = 6.8 Hz, H10), 2.56 (2.3H, br. m, H7a, 7b’), 2.46 (2H, s, H1’), 2.43 (3H, s, H1), 1.90 (3H, s, H14), 1.37 (10.2H, d, J = 6.8 Hz, H11), 1.28 (2H, s, H14’), 1.25 (10.2H, d, J = 6.7 Hz, H13).

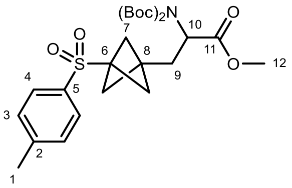
^{13}C NMR (151 MHz, $CDCl_3$) δ 169.6, 169.5, 145.3, 145.2, 132.0, 131.8, 131.7, 130.6, 130.2, 129.9, 59.8, 57.2, 51.0, 50.2, 46.9, 46.7, 46.6 (br.), 45.4 (br.), 23.5, 22.6, 21.8, 21.8, 21.1, 20.9, 20.2 (br.), 19.5 (br.).

HRMS (ESI$^+$) [M + H]$^+$ $C_{19}H_{29}O_3NIS^+$ requires 478.0907; found 478.0907.

Numbers denoted with a prime in blue correspond to the minor diastereoisomer. Diastereisomer ratio calculated from the analysis of the ^{1}H NMR of the crude sample. Tentative diastereoisomer assignment based on NOSEY correlations and comparison of ^{1}H NMR spectra of **31a-l**.

S4.8 Functionalisation Products

Methyl-2-(bis(tert-butoxycarbonyl)amino)-3-(3-tosylbicyclo[1.1.1]pentan-1-yl)propanoate, 34



According to a literature procedure.[57] A flame dried vial was charged with BCP iodide **18a-I** (52.1 mg, 0.15 mmol), methyl 2-(bis(tert-butoxycarbonyl)amino)acrylate (271 mg, 0.90 mmol), Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$ (4.2 mg, 2.5 mol%) and anhydrous Na_2CO_3 (32 mg, 0.30 mmol). The vial was then fitted with a PTFE septum, evacuated, and placed under an Ar atmosphere. The solids were dissolved in MeOH/H_2O (9:1, 1.0 mL, 0.15 M), then $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) was added. The vial was then degassed by freeze-pump-thaw cycles (× 3), sonicated for 10 seconds, and then irradiated with Blue LEDs for 24 h with rapid stirring. The reaction mixture was poured onto H_2O and extracted with CH_2Cl_2 (× 3). The combined organic phases were dried (Mg_2SO_4), filtered and concentrated in vacuo. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:19 → 1:4) gave the compound **34** (59.6 mg, 0.114 mmol, 76%) as a white foam.

R$_f$ 0.25 (EtOAc/pentane, 1:9).

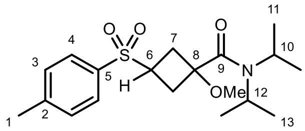
IR ν_{max}/cm^{-1} (film) 2981, 1747, 1700, 1368, 1312, 1149, 1128, 732, 667.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70 (2H, d, *J* = 8.1 Hz, H4), 7.32 (2H, d, *J* = 8.1 Hz, H3), 4.82 (1H, dd, *J* = 9.7, 4.7 Hz, H10), 3.67 (3H, s, H12), 2.43 (3H, s, H1), 2.35 (1H, dd, *J* = 15.3, 4.7 Hz, H9), 2.12 (1H, dd, *J* = 15.3, 9.7 Hz, H9), 1.95 – 1.88 (6H, m, H7), 1.43 (18H, s, Boc).

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.9, 152.0, 144.6, 134.1, 129.8, 128.8, 83.6, 56.0, 52.5, 51.6, 51.1, 37.5, 31.1, 28.1, 21.7.

HRMS (ESI^+) $[M + Na]^+$ $C_{26}H_{37}O_8NNaS$ requires 546.2132; found 546.2127.

N,N-Diisopropyl-1-methoxy-3-tosylcyclobutane-1-carboxamide, 32

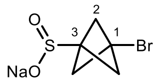


NaOMe (0.20 mL, 0.40 mmol, 0.5 M in MeOH) was added dropwise to a solution of **8a-I** (19.0 mg, 0.05 mmol) in anhydrous MeOH (0.5 mL) cooled to 0 °C. The reaction mixture was stirred for 1 h at 0 °C, then concentrated *in vacuo*. The residue was diluted with CH_2Cl_2 (5 mL) and washed with water (5 mL × 2), the organic phase was dried (Mg_2SO_4), filtered and concentrated *in vacuo* to give **32** (17.1 mg, 0.466 mmol, 93%, >20:1 dr) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (2H, d, *J* = 8.2 Hz, H4), 7.35 (2H, d, *J* = 8.2 Hz, H3), 4.41 (1H, t, *J* = 7.2 Hz, H6), 3.97 (1H, pent., *J* = 6.7 Hz, H12), 3.61 – 3.41 (2H, m, H7, H10), 3.38 (3H, s, OMe), 2.96 (1H, td, *J* = 9.7, 7.4 Hz, H7), 2.44 (3H, s, H1), 2.37 – 2.16 (1H, m, H7), 2.14 – 1.95 (1H, m, H7), 1.37 (6H, dd, *J* = 6.8, 2.8 Hz, H11), 1.14 (6H, dd, *J* = 6.8, 2.6 Hz, H13).

Awaiting additional NOSEY data for full assignment.

Sodium 3-bromobicyclo[1.1.1]pentane-1-sulfinate, 36



According to a modified literature procedure. [61] NaOMe (13 µL of a solution in MeOH) was added to a solution of sulfonyl BCP bromide **25i-Br** (14.8 mg, 0.05 mmol) in THF (0.5 mL). The reaction was stirred for 20 min at roomtemperature then concentrated *in vacuo* to give bromo-BCP sulfinate **36** (9.3 mg, 0.040 mmol, 80%) as a white solid.

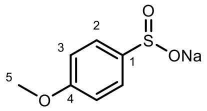
^{1}H NMR (400 MHz, MeOD) δ 2.67 (6H, s, H2).

HRMS (ESI$^+$) Not found.

Further reaction of **36** will be carried out to confirm its isolation.

S4.9 Sulfinate Salts

Sodium 4-methoxybenzenesulfinate, 18b-S



4-Methoxybenzenesulfonyl chloride (3.13 g, 10.0 mmol), sodium sulfite (2.52 g, 20.0 mmol) and sodium bicarbonate (1.68 g, 20.0 mmol) in water (10.0 mL, 1.0 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **18b-S** (2.53 g, 8.45 mmol, 84%) as a white solid. The product contained an 8% impurity by ^{1}H NMR ($ArSO_3H$).

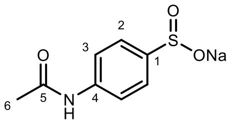
IR ν_{max}/cm^{-1} (film) 2522, 1593, 1493, 1248, 1084, 1012, 981.

^{1}H NMR (400 MHz, MeOD) δ 7.62 – 7.53 (2H, m, H2), 7.00 – 6.92 (2H, m, H3), 3.81 (3H, s, H5).

^{13}C NMR (101 MHz, MeOD) δ 162.2, 149.3, 126.7, 114.7, 55.8.

HRMS (ESI$^-$) [M - Na]$^-$ $C_7H_7O_3S$ requires 171.0121; found 171.0112.

Sodium 4-acetamidobenzenesulfinate, 18c-S



N-Acetylsulfinailyl chloride (1.17 g, 5.00 mmol), sodium sulfite (1.26 g, 10.0 mmol) and sodium bicarbonate (840 mg, 10.0 mmol) in water (5.0 mL, 1.0 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **18c-S** (1.49 g, 6.74 mmol, quant.) as a white solid.

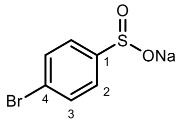
IR ν_{max}/cm^{-1} (film) 1654, 1600, 1394, 1190, 1134, 1051, 650.

^{1}H NMR (400 MHz, MeOD) δ 7.66 – 7.55 (4H, m, ArH), 2.13 (3H, s, H6).

^{13}C NMR (101 MHz, MeOD) δ 171.7, 152.6, 141.1, 125.9, 120.6, 23.9.

HRMS (ESI$^-$) [M - Na]$^-$ $C_8H_8O_3NS$ requires 198.0230; found 198.0220.

Sodium 4-bromobenzenesulfinate, 18h-S



4-Bromobenzenesulfonyl chloride (1.28 g, 5.00 mmol), sodium sulfite (1.26 g, 10.0 mmol) and sodium bicarbonate (840 mg, 10.0 mmol) in water (5.0 mL, 1.0 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **18h-S** (1.23 g, 5.08 mmol, 100%) as a white solid.

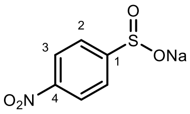
IR ν_{max}/cm^{-1} (film) 2437, 1569, 1469, 1048, 997, 975, 825, 725.

^{1}H NMR (400 MHz, MeOD) δ 7.56 (4H, app. d, *J* = 1.2 Hz, ArH).

^{13}C NMR (101 MHz, MeOD) δ 137.8, 132.5, 127.3, 122.9

HRMS (ESI$^-$) [M - Na]$^-$ $C_6H_4O_2{}^{79}BrS^-$ requires 218.9121; found 218.9115.

Sodium 4-nitrobenzenesulfinate, 18j-S



4-Nitrobenzenesulfonyl chloride (5.20 g, 23.5 mmol), sodium sulfite (6.00 g, 47.0 mmol) and sodium bicarbonate (4.00 mg, 47.0 mmol) in water (50 mL, 0.5 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **18j-S** (4.70 g, 22.6 mmol, 96%) as an orange solid. The product contained a 12% impurity by ^{1}H NMR ($ArSO_3H$).

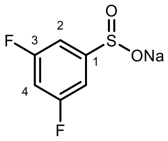
IR ν_{max}/cm^{-1} (film) 2361, 1517, 1354, 1040, 976, 853.

^{1}H NMR (400 MHz, MeOD) δ 8.34 – 8.25 (2H, m, H3), 7.89 – 7.83 (2H, m, H2).

^{13}C NMR (101 MHz, MeOD) δ 164.1, 128.4, 126.6, 124.7.

HRMS (ESI$^-$) [M - Na]$^-$ $C_6H_4O_4NS$ requires 185.9867; found 185.9858.

Sodium 3,5-difluorobenzenesulfinate, 18k-S



3,5-Difluorobenzenesulfonyl chloride (5.00 g, 23.5 mmol), sodium sulfite (6.00 g, 47.0 mmol) and sodium bicarbonate (4.00 mg, 47.0 mmol) in water (50 mL, 0.5 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **18k-S** (4.70 g, 23.5 mmol, 100%) as a white solid.

IR ν_{max}/cm^{-1} (film) 1604, 1432, 1283, 1124, 1003, 977, 677.

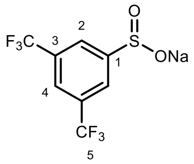
^{1}H NMR (400 MHz, MeOD) δ 7.25 – 7.18 (2H, m, H2), 6.93 (1H, tt, $^3J_{HF}$ = 8.9, 2.4 Hz, H4).

^{13}C NMR (101 MHz, MeOD) δ 164.37 (dd, $^{1,3}J_{CF}$ = 251.7, 10.9 Hz), 162.59 (t, $^3J_{CF}$ = 4.1 Hz), 108.40 – 107.97 (m), 105.25 (t, $^2J_{CF}$ = 26.3 Hz).

^{19}F NMR (377 MHz, MeOD) δ –110.8.

HRMS (ESI$^-$) [M - Na]$^-$ $C_6H_3O_2F_2S$ requires 176.9827; found 176.9818.

Sodium 3,5-bis(trifluoromethyl)benzenesulfinate, 18l-S



3,5-Bis(trifluoromethyl)benzenesulfonyl chloride (3.13 g, 10.0 mmol), sodium sulfite (2.52 g, 20.0 mmol) and sodium bicarbonate (1.68 g, 20.0 mmol) in water (10.0 mL, 1.0 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **18l-S** (2.53 g, 8.45 mmol, 84%) as a white solid. The product contained a 14% impurity by ^{1}H NMR ($ArSO_3H$).

IR ν_{max}/cm^{-1} (film) 2361, 2339, 1278, 1106.

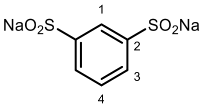
^{1}H NMR (600 MHz, MeOD) δ 8.19 (2H, qd, *J* = 1.1, 0.6 Hz, H2), 7.96 (1H, app. tp, *J* = 1.5, 0.7 Hz, H4).

^{13}C NMR (151 MHz, MeOD) δ 161.3, 132.8 (q, $^2J_{CF3}$ = 33.3 Hz), 126.3 (q, $^3J_{CF3}$ = 3.9 Hz), 124.8 (q, $^1J_{CF3}$ = 272.1 Hz), 123.8 (s, $^3J_{CF3}$ = 3.8 Hz).

^{19}F NMR (377 MHz, MeOD) δ –64.3.

HRMS (ESI$^-$) [M - Na]$^-$ $C_8H_3O_2F_6S$ requires 276.9763; found 276.9760.

Sodium benzene-1,3-disulfinate, 18m-S



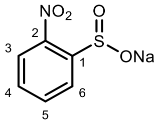
Benzene-1,3-disulfonyl dichloride (1.00 g, 3.65 mmol), sodium sulfite (1.84 g, 14.6 mmol) and sodium bicarbonate (1.23 g, 14.6 mmol) in H_2O (7.2 mL, 0.5 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **18m-S** (1.00 g, 4.00 mmol, quant.) as a white solid.

^{1}**H NMR** (400 MHz, MeOD) δ 7.98 (1H, td, *J* = 1.7, 0.6 Hz, H1), 7.70 (2H, dd, *J* = 7.6, 1.7 Hz, H3), 7.51 (1H, app. ddd, *J* = 7.8, 7.2, 0.6 Hz, H4).

^{13}**C NMR** (101 MHz, MeOD) δ 157.7, 129.7, 126.1, 121.6.

HRMS (ESI$^{+/-}$) Not found.

Sodium 2-nitrobenzenesulfinate, 18n-S



2-Nitrobenzenesulfonyl chloride (1.11 g, 5.00 mmol), sodium sulfite (1.26 g, 10.0 mmol) and sodium bicarbonate (840 mg, 10.0 mmol) in water (5.0 mL, 1.0 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **18n-S** (447 mg, 2.14 mmol, 43%) as an orange solid.

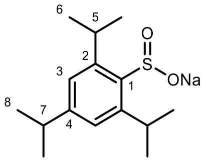
IR ν_{max}/cm^{-1} (film) 2550, 2361, 1537, 1372, 1206 (br.), 1143, 1027, 615.

^{1}**H NMR** (400 MHz, MeOD) δ 8.07 – 8.04 (1H, m, H3), 7.67 – 7.57 (3H, m, H4 – 6).

^{13}**C NMR** (101 MHz, MeOD) δ 158.6, 132.4, 130.5, 128.5, 124.4.

HRMS (ESI+/-) Not found.

Sodium 2,4,6-triisopropylbenzenesulfinate, 18o-S



2,4,6-Triisopropylbenzenesulfonyl chloride (1.50 g, 5.00 mmol), sodium sulfite (1.26 g, 10.0 mmol) and sodium bicarbonate (840 mg, 10.0 mmol) in water (5.0 mL, 1.0 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **18o-S** (890 mg, 2.96 mmol, 59%) as a white solid. The product contained a 45% impurity by ^{1}H NMR (ArsO$_3$H).

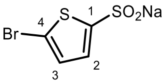
IR ν_{max}/cm^{-1} (film) 2960, 2159, 1210, 1188, 1089, 1051, 1019, 977, 684, 640.

^{1}H NMR (600 MHz, MeOD) δ 7.09 (2H, s, H3), 4.49 (2H, hept, *J* = 6.8 Hz, H5), 2.90 – 2.80 (1H, m, H7), 1.26 (6H, d, *J* = 6.9 Hz, H8), 1.23 (12H, obsc. d, *J* = 6.9 Hz, H6).

^{13}C NMR (151 MHz, MeOD) δ 150.9, 149.4, 139.9, 123.5, 35.3, 30.4, 25.2, 24.2.

HRMS (ESI$^-$) [M - Na]$^-$ $C_{15}H_{23}O_2S_1$ requires 267.1424; found 267.1422.

Sodium 5-bromothiophene-2-Sulfinate, 23b-S



5-Bromothiophene-2-sulfonyl chloride (1.31 g, 5.00 mmol), sodium sulfite (1.26 g, 10.0 mmol) and sodium bicarbonate (840 mg, 10.0 mmol) in H_2O (5.0 mL, 1.0 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **23b-S** (1.37 g, 5.53 mmol, 111%) as a pale-yellow solid. The product contained a 21% impurity by ^{1}H NMR (ArSO$_3$H) (87% calculated yield).

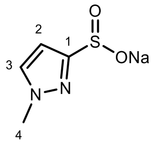
IR ν_{max}/cm^{-1} (film) 1404, 1199, 1062, 1049, 985, 956, 804, 656, 607.

^{1}H NMR (400 MHz, MeOD) δ 7.02 (1H, d, *J* = 3.8 Hz, H3), 7.00 (1H, d, *J* = 3.8 Hz, H2).

^{13}C NMR (151 MHz, MeOD) δ 165.0, 131.4, 126.6, 115.1.

HRMS (ESI$^-$) [M - Na]$^-$ $C_4H_2O_2{}^{79}BrS_2{}^-$ requires 224.8685; found 224.8681.

Sodium 1-methyl-1H-pyrazole-3-Sulfinate, 23c-S



1-Methyl-1H-pyrazole-3-sulfonyl chloride (661 mg, 3.66 mmol), sodium sulfite (920 mg, 7.32 mmol) and sodium bicarbonate (613 mg, 7.32 mmol) in H_2O (5.0 mL, 0.7 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **23c-S** (510 g, 3.04 mmol, 83%) as a white solid. The product contained a 25% impurity by ^{1}H NMR ($ArSO_3H$).

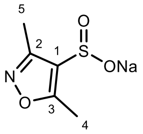
IR ν_{max}/cm^{-1} (film) 3391, 1510, 1230, 1113, 996, 968, 656, 638.

^{1}H NMR (400 MHz, MeOD) δ 7.64 (1H, br. s, H), 7.55 (1H, br. s, H), 3.88 (3H, s, H4).

^{13}C NMR (101 MHz, MeOD) δ 139.8, 137.4, 130.4, 38.9.

HRMS (ESI$^{-/+}$) Not found.

Sodium 3,5-dimethylisoxazole-4-Sulfinate, 23d-S



3,5-Dimethylisoxazole-4-sulfonyl chloride (978 mg, 5.00 mmol), sodium sulfite (1.26 g, 10.0 mmol) and sodium bicarbonate (840 mg, 10.0 mmol) in H_2O (5.0 mL, 1.0 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **23d-S** (868 mg, 4.74 mmol, 94%) as a white solid.

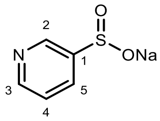
IR ν_{max}/cm^{-1} (film) 3378, 1601, 1407, 1357, 1248, 1036, 1018, 973, 682.

^{1}H NMR (400 MHz, MeOD) δ 2.50 (3H, s, H4/5), 2.38 (3H, s, H4/5).

^{13}C NMR (101 MHz, MeOD) δ 168.6, 159.3, 128.3, 11.4, 10.7.

HRMS (ESI$^-$) [M - Na]$^-$ $C_5H_6O_3NS$ requires 160.0063; found 160.0065.

Sodium pyridine-3-Sulfinate, 23e-S



Pyridine-3-sulfonyl chloride (1.77 g, 10.0 mmol), sodium sulfite (2.52 g, 10.0 mmol) and sodium bicarbonate (1.68 g, 10.0 mmol) in water (10.0 mL, 1.0 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **23e-S** (1.76 g, 10.7 mmol, quant.) as pale pink solid. The product contained a 5% impurity by ^{1}H NMR.

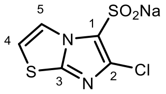
IR ν_{max}/cm^{-1} (film) 3281, 1696, 1412, 1049, 982, 706.

^{1}H NMR (400 MHz, MeOD) δ 8.76 (1H, dd, *J* = 2.1, 0.9 Hz, H2), 8.54 (1H, dd, *J* = 4.9, 1.6 Hz, H3), 8.10 – 8.04 (1H, m, H5), 7.50 (1H, ddd, *J* = 7.8, 4.9, 0.9 Hz, H4).

^{13}C NMR (101 MHz, MeOD) δ 153.4, 150.6, 147.1, 134.4, 125.3.

HRMS (ESI$^{+/-}$) Not found.

Sodium 6-chloroimidazo[2,1-b]thiazole-5-Sulfinate, 23f-S



6-Chloroimidazo[2,1-b]thiazole-5-sulfonyl chloride (500 mg, 1.95 mmol), sodium sulfite (492 mg, 3.91 mmol) and sodium bicarbonate (328 mg, 3.91 mmol) in H_2O (5.0 mL, 0.40 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **23f-S** (409 mg, 1.68 mmol, 86%) as a white solid.

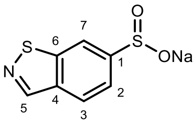
IR ν_{max}/cm^{-1} (film) 1454, 1235, 1210, 1165, 1011, 959, 657.

^{1}H NMR (400 MHz, MeOD) δ 7.64 (1H, s, H5), 7.55 (1H, s, H4).

^{13}C NMR (101 MHz, MeOD) δ 139.9, 138.4, 137.4, 131.5, 130.4, 49.0.

HRMS (ESI$^{+/-}$) Not found.

Sodium benzo[*d*]isothiazole-6-Sulfinate, 23g-S



Benzo[d]isothiazole-6-sulfonyl chloride (1.00 g, 4.28 mmol), sodium sulfite (1.08 g, 8.56 mmol) and sodium bicarbonate (719 mg, 8.56 mmol) in H_2O (4.3 mL, 1.0 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **23g-S** (475 mg, 2.15 mmol, 50%) as a white solid.

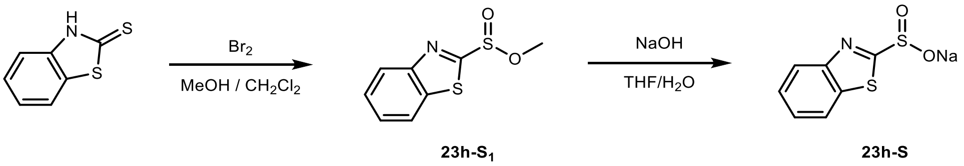
IR ν_{max}/cm^{-1} (film) 2160, 1220, 1195, 1144, 1128, 1056, 886, 814, 687, 663.

^{1}H NMR (600 MHz, MeOD) δ 9.35 (1H, s, H5), 8.54 (1H, dd, *J* = 1.7, 0.6 Hz, H7), 8.12 (1H, dd, *J* = 8.6, 0.6 Hz, H3), 8.01 (1H, dd, *J* = 8.6, 1.7 Hz, H2).

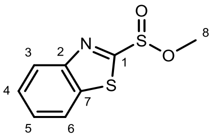
^{13}C NMR (151 MHz, MeOD) δ 159.2, 155.0, 144.2, 134.7, 125.6, 123.7, 121.3.

HRMS (ESI$^{+/-}$) Not Found.

Sodium Benzo[*d*]thiazole-2-Sulfinate, 23h-S



Step 1: Methyl benzo[d]thiazole-2-sulfinate, ***23h-S$_1$***



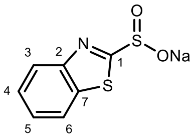
According to a modified literature procedure.[62] Sulfide (3.00 g, 18.0 mmol) was dissolved in dry CH_2Cl_2 (75 mL) and MeOH (75 mL) in a 500 ml conical flask. Bromine (2.31 mL, 45.0 mmol) was added dropwise and the reaction was stirred for 10 min. The reaction was quenched with sat. aq. $NaHCO_3$ (75 mL) and then extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with sat. aq. $Na_2S_2O_3$, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (SiO_2, EtOAc/ pentane, 1:9) to give the methyl sulfinate **23h-S$_1$** (3.26 g, 14.5 mmol, 81%) as an orange solid.

R$_f$ 0.56 (EtOAc/pentane, 1:9).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (1H, ddd, *J* = 8.1, 1.4, 0.7 Hz, H3/6), 8.01 (1H, ddd, *J* = 7.1, 1.4, 0.7 Hz, H3/6), 7.64 – 7.50 (2H, m, H4, H5), 3.74 (3H, s, H8).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.0, 153.8, 136.2, 127.3, 127.3, 125.1, 122.5, 51.5.

Step 2: Sodium benzo[d]thiazole-2-sulfinate, ***23h-S***

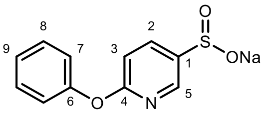


Methyl sulfinate **23h-S$_1$** was dissolved in THF (9.0 mL) and a solution of NaOH (2.0 M aq., 9.0 mL, 18.0 mmol) was added slowly at room temperature. The mixture was stirred for 10 min and checked for conversion of methyl ester by TLC. Addition of an additional portion of NaOH (2.0 M aq., 1.50 mL, 3 mmol) was added for complete conversion. The mixture was concentrated *in vacuo* and remaining H_2O was azeotroped with EtOH. The resulting pale-yellow solid was washed with Et_2O then dried under high vacuum overnight to give **23h-S** (3.42 g, 15.5 mmol, 86%, 2 steps).

^{1}H NMR (400 MHz, MeOD) δ 8.05 – 7.96 (2H, m, H3, H6), 7.52 (1H, ddd, *J* = 8.1, 7.2, 1.3 Hz, H4/5), 7.45 (1H, ddd, *J* = 7.9, 7.2, 1.3 Hz, H4/5).

^{13}C NMR (101 MHz, MeOD) δ 191.0, 154.7, 136.7, 127.4, 127.0, 124.2, 123.6.

Sodium 6-phenoxypyridine-3-Sulfinate, 23i-S



6-Phenoxypyridine-3-sulfonyl chloride (1.00 g, 3.71 mmol), sodium sulfite (934 mg, 7.42 mmol) and sodium bicarbonate (623 mg, 7.42 mmol) in H_2O (3.7 mL, 1.0 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **23h-S** (465 mg, 1.81 mmol, 49%) as a pale pink solid.

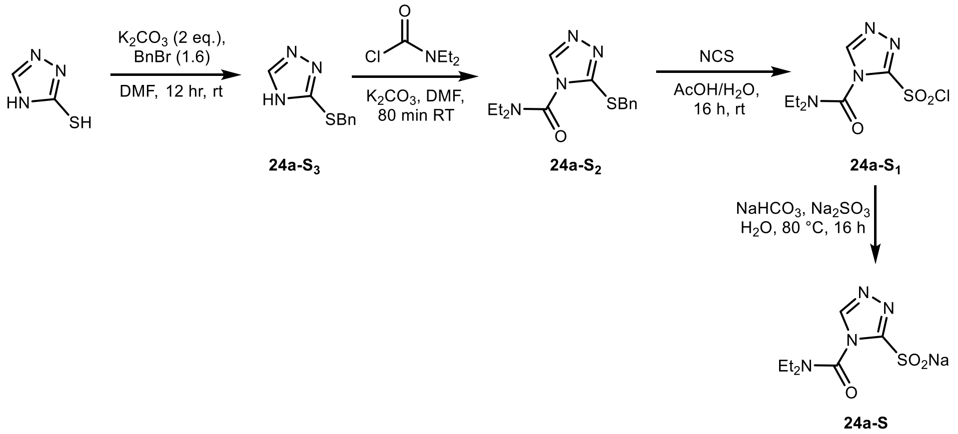
IR ν_{max}/cm^{-1} (film) 2981, 1583, 1492, 1465, 1366, 1276, 1214, 1199, 1050, 691, 629.

^{1}H NMR (600 MHz, MeOD) δ 8.53 (1H, dd, *J* = 2.5, 0.7 Hz, H5), 8.16 (1H, dd, *J* = 8.6, 2.5 Hz, H2), 7.46 – 7.40 (2H, m, H8), 7.24 (1H, tt, *J* = 7.2, 1.1 Hz, H9), 7.15 – 7.11 (2H, m, H7), 6.96 (1H, dd, *J* = 8.6, 0.7 Hz, H3).

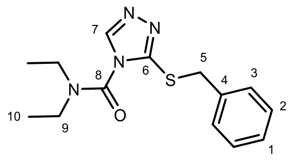
^{13}C NMR (151 MHz, MeOD) δ 165.8, 155.3, 146.4, 139.4, 138.0, 130.9, 126.2, 122.3, 111.9.

HRMS (ESI$^{+/-}$) Not found.

Sodium 4-(diethylcarbamoyl)-4H-1,2,4-triazole-3-Sulfinate, 24a-S



Step 1&2: 3-(Benzylthio)-N,N-diethyl-4H-1,2,4-triazole-4-carboxamide, ***24a-S$_2$***



According to a modified literature procedure.[63] K_2CO_3 (2.76 g, 20.0 mmol) then benzyl bromide (1.43 mL, 12.0 mmol) was added to a solution of 2,4-dihydro-18H-,2,4-triazole-3-thione (1.01 g, 10.0 mmol) in anhydrous DMF (10 mL). The reaction mixture was stirred at room temperature for 48 h. A further portion of K_2CO_3 (1.38 g, 10.0 mmol) was added, followed by diethylcarbamic chloride (1.89 mL, 15.0 mmol). The reaction mixture was stirred for 1 h, and then poured onto H_2O (20 mL) and extracted with EtOAc (15 mL × 2). The combined organic phases were washed with 10% aq. LiCl (10 mL × 3), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, pentane → EtOAc/pentane 1:9) gave **24a-S₂** (2.27 g, 7.83 mmol, 78%) as a white solid.

Note: The product contained di-benzylated impurity, a stepwise approach is recommended for ease of purification. Data for 3-(benzylthio)-4H-1,2,4-triazole-methane, ***24a-S₃.***[64]

R_f 0.39 (EtOAc/pentane, 1:4).

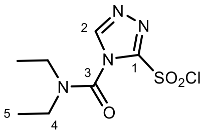
IR ν_{max}/cm^{-1} (film) 2361, 1693, 1429, 1269, 1252, 1207, 913, 862, 745.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (1H, s, H7), 7.42 – 7.38 (1H, m, ArH), 7.33 – 7.25 (4H, m, ArH), 4.38 (2H, s, H5), 3.56 (4H, br. s, H9), 1.25 (6H, t, *J* = 7.1 Hz, H10).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 147.5, 137.0, 128.9, 128.7, 127.6, 43.7, 36.2, 13.6.

HRMS (ESI^+) $[M + Na]^+$ $C_{14}H_{18}ON_4NaS$ requires 313.1094; found 313.1093.

Step 3: 4-(Diethylcarbamoyl)-4H-1,2,4-triazole-3-sulfonyl chloride, ***24a-S₁***



According to a modified literature procedure. NCS (5.34 g, 40.0 mmol) was added to a solution of 3-(benzylthio)-1-isopropyl-1H-1,2,4-triazole (2.27 g, 7.83 mmol) in AcOH (40 mL) and water (20 mL). The mixture was stirred for 2 h, then partitioned between EtOAc (200 mL) and water (200 mL). The organic layer was washed with sat. aq. $NaHCO_3$ (100 mL), brine (50 mL), dried ($MgSO_4$), filtered and evaporated. TBME (20 mL) was added to the residue, the solid filtered off and the filtrate evaporated. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9) gave the sulfonyl chloride **24a-S₁** (738 mg, 2.77 mmol, 35%) as a colourless oil.

R$_f$ 0.33 (EtOAc/pentane, 1:4).

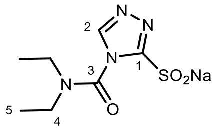
IR ν_{max}/cm^{-1} (film) 1723, 1678, 1399, 1265, 1167, 743, 611.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (1H, s, H2), 3.70 – 3.33 (4H, m, H4), 1.34 (6H, br. s, H5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 128.7, 128.4, 44.5, 12.4.

HRMS (ESI$^{+/-}$) Not found.

*Step 4: Sodium 4-(diethylcarbamoyl)-4H- 1,2,4-triazole-3-sulfinate, **24a-S***



4-(Diethylcarbamoyl)-4H-1,2,4-triazole-3-sulfonyl chloride **24a-S$_1$** (738 mg, 2.77 mmol), sodium sulfite (700 mg, 5.54 mmol) and sodium bicarbonate (467 mg, 5.54 mmol) in water (5.0 mL, 0.55 M) were subjected to the conditions of **general** procedure 12 at room temperature to give the sulfinate salt **24a-S** (470 mg, 1.85 mmol, 67%) as white solid.

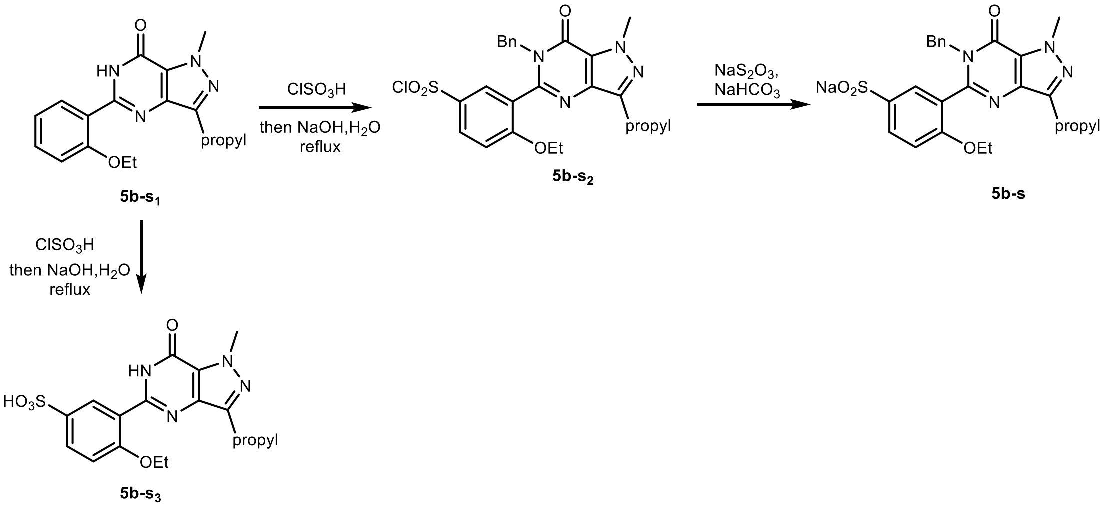
IR ν_{max}/cm^{-1} (film) 1703, 1435, 1273, 1056, 985.

^{1}H NMR (400 MHz, MeOD) δ 8.89 – 8.86 (1H, m, H2), 3.61 (4H, br. s, H4), 1.28 (6H, t, *J* = 7.1 Hz, H5).

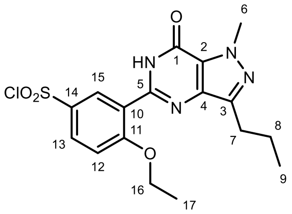
^{13}C NMR (151 MHz, MeOD) δ 175.4, 150.7, 148.2, 44.8 (br.), 14.2 (br.).

HRMS (ESI$^{+/-}$) Not found.

Sodium 4-ethoxy-3-(1-methyl–7-oxo-3-propyl-6,7-dihydro-1H-pyrazolo[4,3-d]pyrimidin-5-yl)benzenesulfinate, 24b-S



Step 1: 4-Ethoxy-3-(1-methyl-7-oxo-3-propyl-6,7-dihydro-1H-pyrazolo[4,3-d]pyrimidin-5-yl)benzenesulfonyl chloride, **24b-S$_2$**



According to a modified literature procedure.[65, 66] 5-(2-ethoxyphenyl)-1-methyl-3-propyl-1H pyrazolo[4,3-d]pyrimidin-7(6H)-one **24b-S$_1$** (1.00 g, 3.20 mmol) was added portionwise to neat chlorosulphonic acid (3.0 mL, 45.1 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 4 h. The reaction mixture was then cooled to 0 °C and $CHCl_3$ (2 mL) was added slowly to the reaction mixture. The reaction mixture was then added slowly to a stirred conical flask containing ice-water (5 mL). The phases were separated and the aqueous phase was extracted with $CHCl_3$:MeOH (9:1, 3 × 10 mL). The combined organic phases were washed with brine (30 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give sulfonyl chloride **24b-S$_2$** (1.12 g, 2.90 mmol, 91%) as a white solid.

R$_f$ 0.55 (EtOAc).

m.p. 145 – 148 °C [lit. 179 – 181 °C].[66]

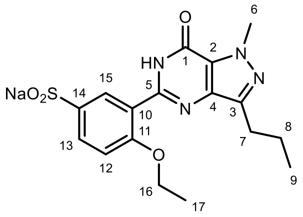
IR ν_{max}/cm^{-1} (film) 1683, 1596, 1376, 1177, 1155, 732.

^{1}H NMR (600 MHz, CDCl$_3$) δ 10.71 (1H, br. s, NH), 9.12 (1H, d, *J* = 2.6 Hz, H15), 8.11 (1H, dd, *J* = 9.0, 2.6 Hz, H13), 7.23 (1H, d, *J* = 9.0 Hz, H12), 4.44 (2H, q, *J* = 7.0 Hz, H16), 4.28 (3H, s, H6), 2.95 (2H, t, *J* = 7.6 Hz, H7), 1.87 (2H, app. sxt., *J* = 7.4 Hz, H8), 1.67 (3H, t, *J* = 7.0 Hz, H17), 1.04 (3H, t, *J* = 7.4 Hz, H9).

^{13}C NMR (151 MHz, CDCl$_3$) δ 161.0, 153.6, 147.4, 145.8, 138.3, 137.8, 131.2, 131.1, 124.7, 121.9, 113.7, 66.8, 38.4, 27.8, 22.5, 14.6, 14.2.

HRMS (ESI$^{+/-}$) not found.

Step 2: Sodium 4-ethoxy-3-(1-methyl-7-oxo-3-propyl-6,7-dihydro-1H-pyrazolo[4,3-d]pyrimidin – 5-yl)benzenesulfinate, **24b-S**



Sulfonyl chloride **24b-S$_2$** (1.11 g, 3.20 mmol), sodium sulfite (808 mg, 6.41 mmol) and sodium bicarbonate (538 mg, 6.41 mmol) in water (6.4 mL, 0.5 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **24b-S** (1.03 g, 2.59 mmol, 81%) as a white solid. The product contained a 25% impurity by ^{1}H NMR (ArSO$_3$H).

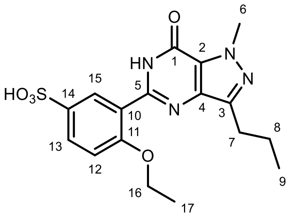
IR ν_{max}/cm^{-1} (film) 3414 (br.), 3285, 1705, 1581, 1537, 1206, 977, 776.

^{1}H NMR (600 MHz, MeOD) δ 8.37 (1H, d, *J* = 2.3 Hz, H15), 7.95 (1H, dd, *J* = 8.8, 2.3 Hz, H12/13), 7.21 (1H, d, *J* = 8.8 Hz, H12/13), 4.26 (2H, app. pentet, *J* = 7.0 Hz, H16), 4.23 (3H, s, H6), 2.88 (2H, t, *J* = 7.5 Hz, H7), 1.82 (2H, sxt., *J* = 7.4 Hz, H8), 1.47 (3H, app. td, *J* = 7.0, 2.8 Hz, H17), 1.00 (3H, t, *J* = 7.5 Hz, H9).

^{13}C NMR (151 MHz, MeOD) δ 159.3, 155.7, 150.6, 147.5, 139.7, 139.2, 131.2, 129.8, 125.8, 122.8, 113.4, 66.3, 38.4, 28.4, 23.5, 14.9, 14.2.

HRMS (ESI$^+$) [M + Na]$^+$ $C_{17}H_{20}O_4N_4NaS$ requires 399.1097; found 399.1098.

4-Ethoxy-3-(1-methyl-7-oxo-3-propyl-6,7-dihydro-1H-pyrazolo[4,3-d]pyrimidin-5-yl)benzenesulfonic acid, **24b-S$_3$**



A solution sulfonyl chloride **24b-S$_2$** (1.19 g, 2.90 mmol) in H_2O:EtOH (1:1, 20 mL) was heated to 100 °C for 18 h. The reaction mixture was then cooled to room temperature and concentrated *in vacuo* to give sulfonic acid **24b-S$_3$** (1.23 g, 3.15 mmol, 108%) as a white solid.

*Note: Compound was not required for the synthesis of **24b-S**.*

m.p. 235 °C [lit. 179 – 181 °C].[66]

IR ν_{max}/cm^{-1} (film) 3366 (br.), 1735, 1638, 1199, 1185, 1158, 1144, 1035

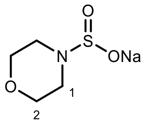
^{1}H NMR (400 MHz, DMSO-d$_6$) δ 7.86 (1H, d, *J* = 2.2 Hz, H15), 7.70 (1H, dd, *J* = 8.6, 2.2 Hz, H13), 7.11 (1H, d, *J* = 8.6 Hz, H12), 5.83 (1H, br. s, OH), 4.16 (3H, s, H6), 4.13 (2H, q, *J* = 7.0

Hz, H16), 2.79 (2H, t, *J* = 7.4 Hz, H7), 1.73 (2H, sxt., *J* = 7.4 Hz, H8), 1.32 (3H, t, *J* = 7.0 Hz, H17), 0.93 (3H, t, *J* = 7.4 Hz, H9).

^{13}C NMR (101 MHz, DMSO-d$_6$) δ 156.5, 153.5, 150.0, 144.3, 140.6, 136.4, 129.5, 128.1, 124.4, 120.6, 111.9, 64.3, 37.9, 27.2, 21.9, 14.5, 13.8.

HRMS (ESI$^+$) [M + H]$^+$ $C_{17}H_{21}O_5N_4S$ requires 393.1227; found 393.1227.

Sodium morpholine-4-Sulfinate, 26a-S



Morpholine-4-sulfonyl chloride (928 mg, 5.00 mmol), sodium sulfite (1.26 g, 10.0 mmol) and sodium bicarbonate (840 mg, 10.0 mmol) in H_2O (5.0 mL, 1.0 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **26a-S** (411.4 mg, 2.38 mmol, 48%) as a white solid. The product contained a 13% impurity by ^{1}H NMR.

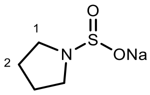
IR v_{max}/cm^{-1} (film) 3403, 2962, 2724, 1102, 1080, 871.

^{1}H NMR (400 MHz, MeOD) δ 3.93 – 3.86 (4H, m, H), 3.26 – 3.18 (4H, m, H).

^{13}C NMR (101 MHz, MeOD) δ 67.4, 65.0, 47.8, 44.7.

HRMS (ESI$^{+/-}$) Not found.

Sodium pyrrolidine-1-Sulfinate, 26b-S



Pyrrolidine-1-sulfonyl chloride (848 mg, 5.00 mmol), sodium sulfite (1.26 g, 10.0 mmol) and sodium bicarbonate (840 mg, 10.0 mmol) in H_2O (5.0 mL, 1.0 M) were subjected to the conditions of **general** procedure 12 to give the sulfinate salt **26b-S** (517 mg, 3.29 mmol, 66%) as a colourless solid. The product contained an 18% impurity by ^{1}H NMR.

IR ν_{max}/cm^{-1} (film) 3395, 1458, 1037, 669.

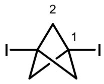
^{1}H NMR (400 MHz, MeOD) δ 3.30 – 3.22 (4H, m, H1), 2.04 – 1.97 (4H, m, H2).

^{13}C NMR (101 MHz, MeOD) δ 46.6, 25.1.

HRMS (ESI$^{+/-}$) Not found.

S4.10 Miscellaneous

1,3-Diiodobicyclo[1.1.1]pentane, 20



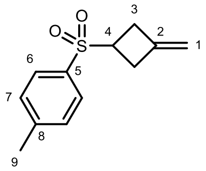
BCP di-iodide **20** was observed during reaction optimisation and ^{1}H NMR data is included here for reference.

^{1}H NMR (400 MHz, CDCl$_3$) δ 2.67 (6H, s, H2).

^{13}C NMR (101 MHz, CDCl$_3$) δ 68.1. 1.0.

Data in agreement with literature.[67]

1-Methyl-4-((3-methylenecyclobutyl)sulfonyl)benzene, 21

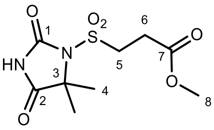


exo-methylene cyclobutane **21** was observed during reaction optimisation and ^{1}H NMR data is included here for reference.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.71 (2H, d, *J* = 8.3 Hz, H6), 7.40 – 7.32 (2H, m, H7), 4.85 (2H, tt, *J* = 2.8, 2.0 Hz, H1), 4.37 (1H, p, *J* = 6.8 Hz, H4), 2.96 (2H, dddd, *J* = 15.4, 6.8, 4.1, 2.0 Hz, H3), 2.73 – 2.61 (2H, m, H3), 2.46 (3H, s, H9).

^{13}C NMR (101 MHz, CDCl$_3$) δ 145.3, 129.9, 128.6, 125.1, 107.0, 63.5, 43.2, 43.2, 21.6.

Methyl 3-((5,5-dimethyl-2,4-dioxoimidazolidin-1-yl)sulfonyl)propanoate, 27



During the optimisation studies for the formation of alkyl sulfone BCP halides, compound **27** was isolated as a by-product. DIH (78.4 mg, 0.20 mmol), sulfinate salt **25i-S** (0.50 mL, 0.50 mmol, 1.0 M in H_2O), [1.1.1]propellane **1** (0.29 mL, 0.20 mmol of a 0.69 M solution in Et_2O) in CH_2Cl_2 (0.80 mL) were subjected to the conditions of **general procedure 11.1**

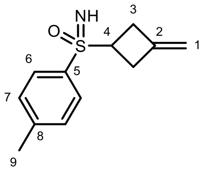
IR ν_{max}/cm^{-1} (film) 3422, 3307, 1741, 1655, 1382, 1366, 1194, 1167, 1129, 1052, 730.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (1H, s, NH), 3.83 (2H, t, *J* = 6.8 Hz, H5), 3.71 (3H, s, H8), 2.98 (t, *J* = 6.8 Hz, H6), 1.52 (6H, s, H4).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 170.5, 52.7, 49.9, 34.3, 27.9, 25.3.

HRMS (ESI$^+$) [M + Na]$^+$ $C_9H_{14}O_6N_2NaS$ requires 301.0465; found 301.0465.

Imino(3-methylenecyclobutyl)(p-tolyl)-l6-sulfanone, 39



A solution of *N*-Sulfinyltritylamine (TrNSO)[68] (61.0 mg, 0.20 mmol) in Et_2O (1.0 mL) was cooled to 0 °C. Tosyl magnesium bromide (0.40 mL, 0.20 mmol, 0.5 M in THF) was added and the reaction was stirred to 5 min. The suspension was then cooled to –78 °C and then benzyltrimethylammonium dichloroiodate (50.5 mg, 0.14 mmol) was added, stirred for 5 min, then [1.1.1]propellane **1** (0.15 mL, 0.10 mmol, 0.70 M solution in Et_2O) was added. The rection was stirred at 0 C to 30 min, then quenched at room temperature with $Na_2S_2O_3$

(sat. aq., 2 mL). The biphasic mixture was extracted with EtOAc (5 mL × 3), then the combined organic phases were dried (Mg_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, EtOAc/pentane, 1:9 → 1:0) gave methylene cyclobutane **39** (5.9 mg, 0.027 mmol, 27% contained minor impurities) as a yellow oil.

R_f 0.1 (EtOAc/pentane, 1:1)[Vanilin Red].

IR ν_{max}/cm^{-1} (film) 3333 (br.), 2981, 2361, 2341, 1382, 1254, 1151, 1071, 740, 668.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (2H, d, *J* = 8.0 Hz, H6), 7.20 – 7.12 (2H, m, H7), 4.71 (1H, dd, *J* = 7.1, 5.6 Hz, H4), 3.69 (2H, ddd, *J* = 6.7, 5.7, 3.6 Hz, H1), 2.34 (3H, s, H9), 2.18 (1H, s, NH), 1.89 – 1.82 (2H, m, H3), 1.75 – 1.64 (2H, m, H3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 141.9, 129.3, 125.9, 88.6, 74.5, 63.1, 36.2, 29.5, 21.3.

HRMS ($ESI^{+/-}$, APCI) Not Found.

S5.

Mechanistic Studies

S5.1 Voltammetry Experiments

Voltammetry measurements were made using an EmStat3 with a glassy carbon electrode as the working electrode, a platinum wire as counter electrode and a leak free Ag/AgCl (sat. KCl) reference electrode. Voltammograms were referenced to the Fc/Fc$^+$ (ferrocene) couple (0.400 V *vs* SCE) as an internal reference. Square wave voltammograms were acquired with a 5 mV step potential, 50 mV modulation amplitude and 5.0 Hz frequency. The supporting electrolyte, *tetra*-*n*-butylammonium hexafluorophosphate (Bu_4NPF_6, TBAP) was prepared as a 0.1 M solution in dry MeCN. Samples were measured at 0.01 M concentration.

S5.2 Photophysical Experiments

S6.2.1 UV/Vis absorption experiments

A quartz cuvette was charged with MeOH/H_2O (9:1, 2.5 mL) and the stock solution of substrate (0.50 – 1.00 mL) was added. UV-vis absorption spectra were measured using a Perkin Elmer Lambda 20 spectrometer at 20 ºC in the range of 300 – 750 nm (temperature controlled by a Perkin Elmer PTP-1 Peltier). Stock solutions of substrates were prepared as follows.

- 0.14 M solution of BCPA iodide **3a** (60.5 mg, 0.15 mmol) in MeOH/H_2O (9:1, 1.0 mL) and CH_2Cl_2 (0.1 mL).
- 0.30 M solution of $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 0.6 mL) and CH_2Cl_2 (0.4 mL).
- 2:1 solution of BCPA iodide **3a** (60.5 mg, 0.15 mmol) and $(Me_3Si)_3SiH$ (93 µL, 0.30 mmol) in MeOH/H_2O (9:1, 6.0 mL) and CH_2Cl_2 (0.4 mL).

S6.2.2 Stern-Volmer quenching experiments

Emission spectra were recorded at 20 °C using an Edinburgh Instruments FS5 spectrofluorimeter, equipped with a xenon arc lamp (400 nm excitation), an SC–20 thermostatic sample holder, and a Hamamatsu R13456 PMT detector measuring at 425 – 800 nm.

Preparation of stock solutions:

5.0 mM catalyst solution: Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF_6 (11.2 mg, 0.01 mmol) in degassed MeOH/H_2O (9:1, 2.0 mL).

Quencher solutions: Quencher solutions were prepared in pre-degassed solvent. CH_2Cl_2 was added to improve solubility.

- 0.38 M solution of BCPA iodide **3a** (201.5 mg, 0.50 mmol) in CH_2Cl_2 (0.4 mL) and MeOH/H_2O (9:1, 1.0 mL).
- 0.50 M solution of $(Me_3Si)_3SiH$ (154 µL, 0.50 mmol) in CH_2Cl_2 (0.4 mL) and MeOH/H_2O (9:1, 0.6 mL).
- 0.50 M solution of methyl acrylate **6b** (45 µL, 0.50 mmol) in MeOH/H_2O (9:1, 1.0 mL).
- 0.50 M solution of $(Me_3Si)_3SiH$ (66.0 mg, 0.25 mmol), Na_2CO_3 (26 mg, 0.25 mmol) in MeOH/H_2O (9:1, 0.5 mL).

A quartz cuvette (10 mm path length) was charged with 2.5 µL of a 5.0 mM stock solution of $Ir[dF(CF)_3ppy]_2(dtbbpy)PF_6$ dissolved in MeOH/H_2O (9:1). The catalyst solution was then diluted to 5.0 µM with degassed MeOH/H_2O (9:1, 2.5 mL) and then the cuvette was degassed by sparging with argon for 10 min. The appropriate volume of a 0.38 – 0.50 M solution of each quencher was added sequentially and the emission of the solution was measured. The cuvette was irradiated at 380 nm and the emission was scanned between 440 and 650 nm.

All emission intensities were corrected for increasing dilution of solution, according to the Beer-Lambert Law.

$$\text{Beer-Lambert Law:} \qquad A = \varepsilon l c$$

$$Corrected\ intensity = Measured\ intensity \times \frac{Actual\ volume\ mL}{Initial\ volume\ mL}$$

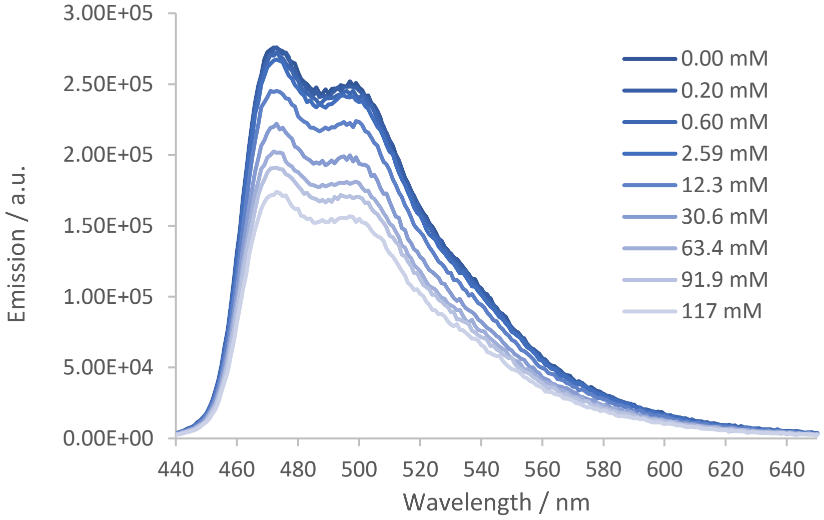


Figure S1: Fluorescence quenching titration for methyl acrylate ***6b*** *with a 5 µM solution of $Ir[dF(CF)_3ppy]_2(dtbbpy)PF_6$.*

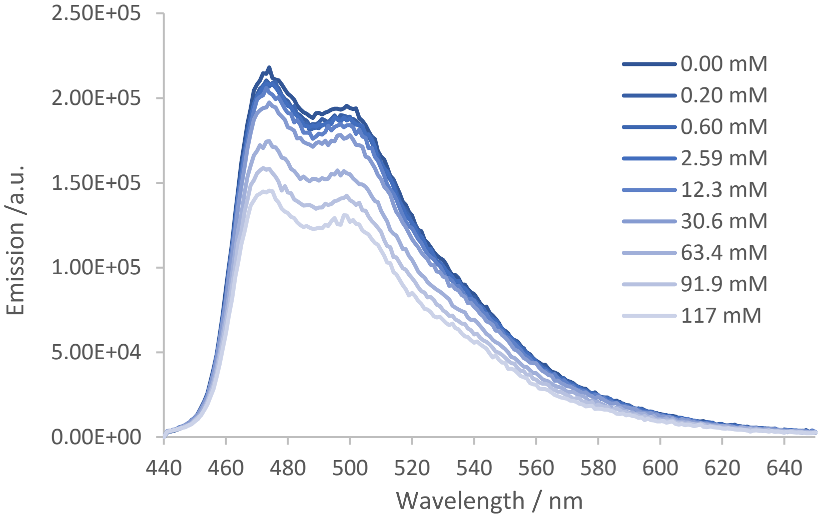


Figure S2: Fluorescence quenching titration for $(Me_3Si)_3SiH$ with a 5 µM solution of $Ir[dF(CF)_3ppy]_2(dtbbpy)PF_6$.

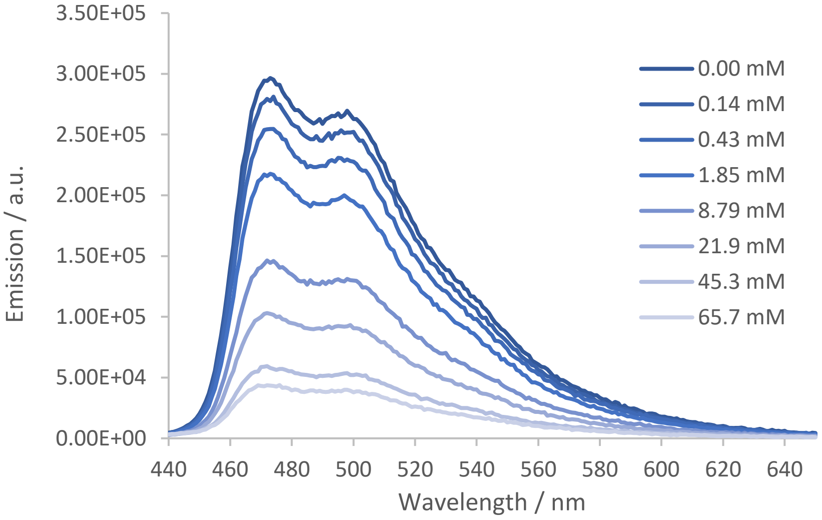


*Figure S3: Fluorescence quenching titration for BCPA iodide **3a** with a 5 µM solution of Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$.*

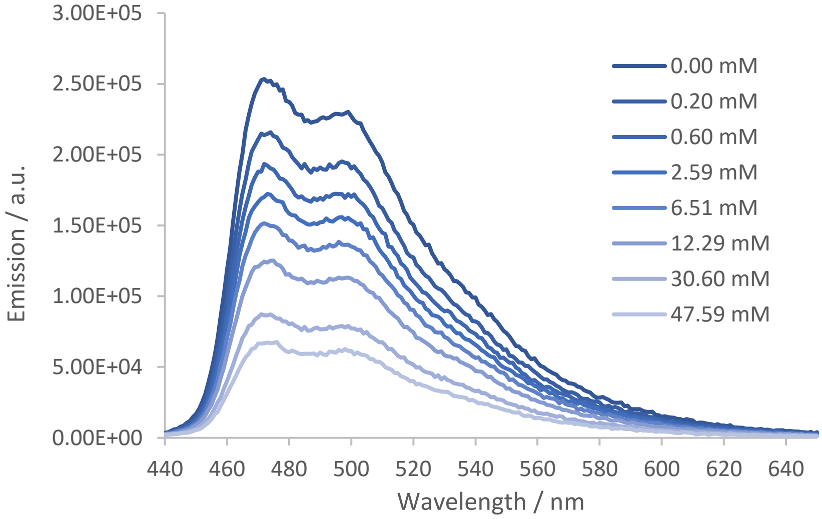


Figure S4: Fluorescence quenching titration for (Me$_3$Si)$_3$SiOH + Na$_2$CO$_3$ (1:1) with a 5 µM solution of Ir[dF(CF)$_3$ppy]$_2$(dtbbpy)PF$_6$. Note the stock solution contained undissolved base, it was sonicated for 5 min and only the solution was used for the quenching experiments.

S6.

X-Ray Crystallography

S6.1 X-Ray Crystal Structures

Low temperature single crystal X-ray diffraction data were collected using Oxford Diffraction (Rigaku) SuperNovae diffractometers at 150 K. These data were reduced using CrysAlisPro, solved using SuperFlip66 and the structures were refined using CRYSTALS. Further details about the refinements are documented in the CIF.

The crystallographic data for **4l** has been deposited with the CCDC as entry CCDC 2078089. The crystallographic data for compounds **24a-Br** and **34** is in the process of being finalised and uploaded to the CCDC.

N-Allyl-*N*-(6-(8-cyanoethyl)bicyclo[1.1.1]pentan-4-yl)-*p*-methylbenzenesulfonamide, 4l

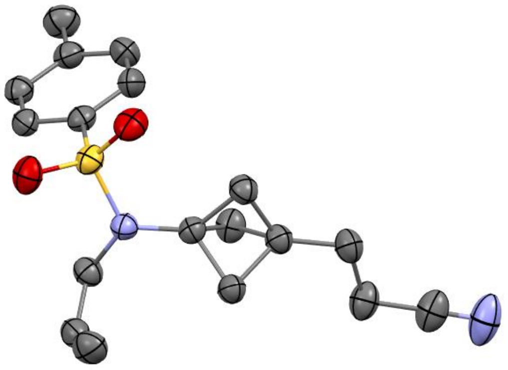


*Figure S7.1: Solid state structure of **4l**. Displacement ellipsoid plots are drawn at 50% probability. Hydrogen atoms are removed for clarity.*

CCDC Identification code	CCDC 2078089	
Empirical formula	$C_{18} H_{22} N_2 O_2 S_1$	
Formula Weight	330.45	
Temperature	150 K	
Wavelength	1.54184	
Crystal system	Monoclinic	
Space Group	P 21/c	
Unit cell dimensions	a = 11.7109(3) Å	α = 90°
	b = 17.3646(5) Å	β = 90.314(2)°
	c = 8.3512(2) Å	γ = 90°
Volume	1698.23(8) $Å^3$	
Z	4	
Density (calculated)	1.292 Mg/m^3	
Absorption coefficient	1.780 mm^{-1}	
F(000)	703.996	

Crystal size	0.01 x 0.03 x 0.20 mm^3
Theta range for data collection	4.554 to 77.226°
Index ranges	– 14<=h<=14, 0<=k<=21, 0<=l<=10
Reflections collected	9475
Independent reflections	3545 [R(int) = 0.0574]
Completeness to theta = 77.226°	98.3%
Absorption correction	Multi Scan
Max. and min. transmission	0.98 and 0.85
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3544 / 0 / 208
Goodness-of-fit on F2	0.9816
Final R indices [I>2sigma(I)]	R1 = 0.0406, wR2 = 0.0990
R indices (all data)	R1 = 0.0573, wR2 = 0.1116
Largest diff. peak and hole	0.42 and -0.43 e.Å^{-3}

Table S7.1: Crystal data and structure refinement for compound ***4l****.*

S7.

References

1. Kitagawa, O.; Suzuki, T.; Taguchi, T., NaH-mediated Iodoaziridination Reaction of *N*-Aliylic Tosylamides. *Tetrahedron Lett.,* **1997**, *38*, 8371-8374.

2. Morino, Y.; Hidaka, I.; Oderaotoshi, Y.; Komatsu, M.; Minakata, S., Electrophilic cyclization of *N*-alkenylamides using a chloramine-T/I_2 system. *Tetrahedron,* **2006**, *62*, 12247-12251.

3. Minakata, S.; Morino, Y.; Oderaotoshi, Y.; Komatsu, M., Practical and Convenient Synthesis of *N*-Heterocycles: Stereoselective Cyclization of *N*-Alkenylamides with *t*-BuOI under Neutral Conditions. *Org. Lett.,* **2006**, *8*, 3335-3337.

4. Gomez, J. E.; Guo, W.; Gaspa, S.; Kleij, A. W., Copper-Catalyzed Synthesis of gamma-Amino Acids Featuring Quaternary Stereocenters. *Angew. Chem. Int. Ed.,* **2017**, *56*, 15035-15038.

5. M. Mintz; C. Wallking; Ablin, L. A.; Baumgrten, H. E., *tert*-Butyl Hypochlorite. *Org. Synth.,* **1969**, *49*, 9.

6. Vedejs, E.; Naidu, B. N.; Klapars, A.; Warner, D. L.; Li, V.-S.; Na, Y.; Kohn, H., Synthetic Enantiopure Aziridinomitosenes: Preparation, Reactivity, and DNA Alkylation Studies. *J. Am. Chem. Soc.,* **2003**, *125*, 15796-15806.

7. Welin, E. R.; Warkentin, A. A.; Conrad, J. C.; Macmillan, D. W. C., Enantioselective α-Alkylation of Aldehydes by Photoredox Organocatalysis: Rapid Access to Pharmacophore Fragments from β-Cyanoaldehydes. *Angew. Chem. Int. Ed.,* **2015**, *54*, 9668-9672.

8. Aubineau, T.; Cossy, J., Chemoselective alkynylation of *N*-sulfonylamides versus amides and carbamates - synthesis of tetrahydropyrazines. *Chem. Comm.,* **2013**, *49*, 3303-3305.

9. Johnson, J. A.; Petersen, B. M.; Kormos, A.; Echeverría, E.; Chen, Y.-S.; Zhang, J., A New Approach to Non-Coordinating Anions: Lewis Acid Enhancement of Porphyrin Metal Centers in a Zwitterionic Metal–Organic Framework. *J. Am. Chem. Soc.,* **2016**, *138*, 10293-10298.

10. Gianatassio, R.; Lopchuk, J. M.; Wang, J.; Pan, C.; Malins, L. R.*, et al.*, Strain-release amination. *Science,* **2016**, *351*, 241.

11. Bunker, K. D.; Sach, N. W.; Huang, Q.; Richardson, P. F., Scalable Synthesis of 1-Bicyclo[1.1.1]pentylamine via a Hydrohydrazination Reaction. *Org. Lett.,* **2011**, *13*, 4746-4748.

12. Fodran, P.; Wallentin, C.-J., Harnessing Energy-Transfer in *N*-Centered Radical-Mediated Synthesis of Pyrrolidines. *Eur. J. Org. Chem.,* **2020**, *2020*, 3213-3218.

13. Takeda, Y.; Murakami, Y.; Ikeda, Y.; Minakata, S., Nucleophilic Ring-Opening of *N-o*-Nosylaziridines with *N*-Chloro-*N*-Sodiocarbamate: Facile Preparation of Differentially Protected Vicinal Diamines. *Asian J. Org. Chem.,* **2012**, *1*, 226-230.

14. Kitagawa, O.; Suzuki, T.; Taguchi, T., *t*-BuOK-Mediated Iodoaziridination Reaction of *N*-Allylic Tosylamide Derivatives. *J. Org. Chem.,* **1998**, *63*, 4842-4845.

15. Almansa, R.; Guijarro, D.; Yus, M., Triorganozincates as efficient nucleophiles for the diastereoselectiveaddition to *N*-(*tert*-butanesulfinyl)imines. *Tetrahedron Asymmetry,* **2009**, *19*, 603-606.

16. Jeong, J. U.; Tao, B.; Sagasser, I.; Henniges, H.; Sharpless, K. B., Bromine-Catalyzed Aziridination of Olefins. A Rare Example of Atom-Transfer Redox Catalysis by a Main Group Element. *J. Am. Chem. Soc.,* **1998**, *120*, 6844-6845.

17. Gensler, W. J., The Benzenesulfonyl Derivatives of 1-Amino-2,3-dibromopropane and 2-Amino-1,3-dibromopropane. *J. Am. Chem. Soc.,* **1948**, *70*, 1843-1846.

18. Tehrani, K. A.; NguyenVan, T.; Karikomi, M.; Rottiers, M.; Kimpe, N. D., Electron transfer induced ring opening of 2-(bromomethyl)aziridines by magnesium in methanol. *Tetrahedron,* **2002**, *58*, 7145-7152.

19. Zhang, X.; Cao, B.; Yu, S.; Zhang, X., Rhodium-catalyzed asymmetric hydroformylation of *N*-allylamides: highly enantioselective approach to beta2-amino aldehydes. *Angew. Chem. Int. Ed.,* **2010**, *49*, 4047-4050.

20. Tsui, G. C.; Menard, F.; Lautens, M., Regioselective Rhodium(I)-Catalyzed Hydroarylation of Protected Allylic Amines with Arylboronic Acids. *Org. Lett.,* **2010**, *12*, 2456-2459.

21. Luca, L. D.; Giacomelli, G., An Easy Microwave-Assisted Synthesis of Sulfonamides Directly from Sulfonic Acids. *J. Org. Chem.,* **2008**, *73*, 3967–3969.

22. Sarkar, D.; Ghosh, M. K.; Rout, N., PTAB mediated open air synthesis of sulfonamides, thiosulfonates and symmetrical disulfanes. *Tetrahedron Lett.,* **2018**, *59*, 2360-2364.

23. Li, X.; Pennington, J.; Stobaugh, J. F.; Schöneich, C., Synthesis of sulfonamide- and sulfonyl-phenylboronic acid-modified silica phases for boronate affinity chromatography at physiological pH. *Anal. Biochem.,* **2008**, *372*, 227-236.

24. Klapars, A.; Buchwald, S. L., Copper-Catalyzed Halogen Exchange in Aryl Halides: An Aromatic Finkelstein Reaction. *J. Am. Chem. Soc.,* **2002**, *124*, 14844–14845.

25. Gheorghe, A.; Quiclet-Sire, B.; Vila, X.; Zard, S. Z., Synthesis of substituted 3-arylpiperidines and 3-arylpyrrolidines by radical 1,4 and 1,2-aryl migrations. *Tetrahedron,* **2007**, *63*, 7187-7212.

26. Worthy, A. D.; Gagnon, M. M.; Dombrowski, M. T.; Tan, K. L., Regioselective Hydroformylation of Sulfonamides using a Scaffolding Ligand. *Org. Lett.,* **2009**, *11*, 2764-2767.

27. Beckwith, A. L. J.; Meijs, G. F., Iododediazoniation of arenediazonium salts accompanied by aryl radical ring closure. *J. Org. Chem.,* **1987**, *52*, 1922-1930.

28. Torres, Ò.; Roglans, A.; Pla-Quintana, A., An Enantioselective Cascade Cyclopropanation Reaction Catalyzed by Rhodium(I): Asymmetric Synthesis of Vinylcyclopropanes. *Adv. Synth. Cat.,* **2016**, *358*, 3512-3516.

29. Griffiths-Jones, C. M.; Hopkin, M. D.; Jönsson, D.; Ley, S. V.; Tapolczay, D. J.; Vickerstaffe, E.; Ladlow, M., Fully Automated Flow-Through Synthesis of Secondary Sulfonamides in a Binary Reactor System. *J. Comb. Chem.,* **2007**, *9*, 422-430.

30. Crespin, L. N. S.; Greb, A.; Blakemore, D. C.; Ley, S. V., Visible-Light-Mediated Annulation of Electron-Rich Alkenes and Nitrogen-Centered Radicals from *N*-Sulfonylallylamines: Construction of Chloromethylated Pyrrolidine Derivatives. *J. Org. Chem.,* **2017**, *82*, 13093-13108.

31. Sanchez-Cantalejo, F.; Priest, J. D.; Davies, P. W., A Gold Carbene Manifold to Prepare Fused gamma-Lactams by Oxidative Cyclisation of Ynamides. *Eur. J. Chem.,* **2018**, *24*, 17215-17219.

32. Suda, T.; Noguchi, K.; Tanaka, K., Rhodium-Catalyzed Asymmetric Formal Olefination or Cycloaddition: 1,3-Dicarbonyl Compounds Reacting with 1,6-Diynes or 1,6-Enynes. *Angew. Chem. Int. Ed.,* **2011**, *50*, 4475-4479.

33. Yamagishi, M.; Nishigai, K.; Hata, T.; Urabe, H., Nucleophilic Addition of Sulfonamides to Bromoacetylenes: Facile Preparation of Pyrroles. *Org. Lett.,* **2011**, *13*, 4873-4875.

34. Haubenreisser, S.; Niggemann, M., Calcium-Catalyzed Direct Amination of π-Activated Alcohols. *Adv. Synth. Cat.,* **2011**, *353*, 469-474.

35. Xu, X.; Zhang, K.; Li, P.; Yao, H.; Lin, A., [3 + 3] Cycloaddition of Azides with in Situ Formed Azaoxyallyl Cations To Synthesize 1,2,3,4-Tetrazines. *Org. Lett.,* **2018**, *20*, 1781-1784.

36. Nugent, J.; Arroniz, C.; Shire, B. R.; Sterling, A. J.; Pickford, H. D*., et al.*, A General Route to Bicyclo[1.1.1]pentanes through Photoredox Catalysis. *ACS Catal.,* **2019**, *9*, 9568-9574.

37. Nugent, J.; Shire, B.; Caputo, D.; Pickford, H.; Nightingale, F.; Houlsby, I.; Mousseau, J.; Anderson, E. A., Synthesis of All-carbon Disubstituted Bicyclo[1.1.1]pentanes by Iron-Catalyzed Kumada Cross-Coupling. *Angew. Chem. Int. Ed.,* **2020**, *59*, 11866-11870.

38. Zhang, M.-M.; Li, S.-H.; Tu, J.-L.; Min, Q.-Q.; Liu, F., Metal-free iminyl radical-mediated C–C single bond cleavage/functionalization of redox-active oxime esters. *Org. Chem. Front.,* **2020**, *7*, 622-627.

39. Pons, A.; Ivashkin, P.; Poisson, T.; Charette, A. B.; Pannecoucke, X.; Jubault, P., Catalytic Enantioselective Synthesis of Halocyclopropanes. *Chem. Eur. J.,* **2016**, *22*, 6239-6242.

40. Ramirez, N. P.; Lana-Villarreal, T.; Gonzalez-Gomez, J. C., Direct Decarboxylative Allylation and Arylation of Aliphatic Carboxylic Acids Using Flavin-Mediated Photoredox Catalysis. *Eur. J. Org. Chem.,* **2020**, *2020*, 1539-1550.

41. Rogova, T.; Gabriel, P.; Zavitsanou, S.; Leitch, J. A.; Duarte, F.; Dixon, D. J., Reverse Polarity Reductive Functionalization of Tertiary Amides via a Dual Iridium-Catalyzed Hydrosilylation and Single Electron Transfer Strategy. *ACS Catal.,* **2020**, *10*, 11438-11447.

42. Ulman, A.; Urankar, E., A novel synthesis of 4-[alkyl(aryl)sulfonyl]benzaldehydes: alkyl(aryl)sulfinate anion as a nucleophile in aromatic substitutions. *J. Org. Chem.,* **1989**, *54*, 4691-4692.

43. Chan, J. Z.; Yao, W.; Hastings, B. T.; Lok, C. K.; Wasa, M., Direct Mannich-Type Reactions Promoted by Frustrated Lewis Acid/Bronsted Base Catalysts. *Angew. Chem. Int. Ed.,* **2016**, *55*, 13877-13881.

44. Sun, K.; Lv, Y.; Zhu, Z.; Jiang, Y.; Qi, J.; Wu, H.; Zhang, Z.; Zhang, G.; Wang, X., A convenient access to β-iodo sulfone by the iodine-mediated iodosulfonylation of alkenes. *RSC Adv.,* **2015**, *5*, 50701-50704.

45. Nair, V.; Augustine, A.; Suja, T. D., CAN Mediated Reaction of Aryl Sulfinates with Alkenes and Alkynes: Synthesis of Vinyl Sulfones, β-Iodovinyl Sulfones and Acetylenic Sulfones. *Synthesis,* **2002**, *15*, 2259-2265.

46. Kamijo, S.; Kamijo, K.; Maruoka, K.; Murafuji, T., Aryl Ketone Catalyzed Radical Allylation of C(sp^3)-H Bonds under Photoirradiation. *Org. Lett.,* **2016**, *18*, 6516-6519.

47. Singh, A.; Teegardin, K.; Kelly, M.; Prasad, K. S.; Krishnan, S.; Weaver, J. D., Facile synthesis and complete characterization of homoleptic and heteroleptic cyclometalated Iridium(III) complexes for photocatalysis. *J. Organomet. Chem.,* **2015**, *776*, 51-59.

48. Le, C.; Chen, T. Q.; Liang, T.; Zhang, P.; MacMillan, D. W. C., A radical approach to the copper oxidative addition problem: Trifluoromethylation of bromoarenes. *Science,* **2018**, *360*, 1010–1014.

49. Ishido, R.; Kawashima, E.; Uchida, S., Production of optically active deuterated compound, **1998**, JPH 10298186 A.

50. Kopping, B.; Chatgilialoglu, C.; Zehnder, M.; Giese, B., Tris(trimethylsilyl)silane: an efficient hydrosilylating agent of alkenes and alkynes. *J. Org. Chem.,* **1992**, *57*, 3994-4000.

51. Moradei, S. M. L. d.; Therrien, E., Acyl inhibitors and uses thereof, **2019**, WO 2020097408 A1.

52. Moriyama, K.; Nakamura, Y.; Togo, H., Oxidative debenzylation of *N*-benzyl amides and *O*-benzyl ethers using alkali metal bromide. *Org. Lett.,* **2014**, *16*, 3812-3815.

53. Fraunhoffer, K. J.; White, M. C., Syn-1,2-Amino Alcohols via Diastereoselective Allylic C−H Amination. *J. Am. Chem. Soc.,* **2007**, *129*, 7274-7276.

54. Duffy, E. M.; Bhattacharjee, A.; Kanyo, Z. F.; Ippolito, J. A., Antimicrobials and methods of making and using same, **2017**, WO 2017193023 A1.

55. Deforest, J. C.; Samame, R. A.; Suryn, G.; Burtea, A.; Rychnovsky, S. D., Second-Generation Synthesis of (+)-Fastigiatine Inspired by Conformational Studies. *J. Org. Chem.,* **2018**, *83*, 8914-8925.

56. Mikagi, A.; Tokairin, D.; Usuki, T., Suzuki-Miyaura cross-coupling reaction of monohalopyridines and l-aspartic acid derivative. *Tetrahedron Lett.,* **2018**, *59*, 4602-4605.

57. Pickford, H. D.; Nugent, J.; Owen, B.; Mousseau, J. J.; Smith, R. C.; Anderson, E. A., Twofold Radical-Based Synthesis of *N,C*-Difunctionalized Bicyclo[1.1.1]pentanes. *J. Am. Chem. Soc.,* **2021**, *143*, 9729-9736.

58. Frank, N.; Nugent, J.; Shire, B.; Pickford, H.; Rabe, P.; Sterling, A.; Zarganes-Tzitzikas, T.; Thomas Grimes*, et al.*, Synthesis of meta-substituted arene bioisosteres from [3.1.1]propellane. **2022**,

59. Mcnamee, R. E.; Haugland, M. M.; Nugent, J.; Chan, R.; Christensen, K. E.; Anderson, E. A., Synthesis of 1,3-disubstituted bicyclo[1.1.0]butanes *via* directed bridgehead functionalization. *Chem. Sci.,* **2021**, *12*, 7480-7485.

60. Li, Y.; Li, X.; Li, X.; Shi, D., Highly E-Selective Synthesis of α-Fluoro-β-arylalkenyl Sulfones from gem-Difluoroalkenes with Sodium Sulfinates. *J. Org. Chem.,* **2021**, *86*, 6983-6993.

61. Bär, R. M.; Gross, P. J.; Nieger, M.; Bräse, S., Sodium Bicyclo[1.1.1]pentanesulfinate: A Bench-Stable Precursor for Bicyclo[1.1.1]pentylsulfones and Bicyclo-[1.1.1]pentanesulfonamides. *Eur. J. Org. Chem.,* **2020**, *26*, 4242-4245.

62. Zálešák, F.; Kováč, O.; Lachetová, E.; Šťastná, N.; Pospíšil, J., Unified Approach to Benzo[*d*]thiazol-2-yl-Sulfonamides. *J. Am. Chem. Soc.,* **2021**, *86*, 11291-11309.

63. Mcconville, M.; Fernández, J.; Angulo-Barturen, Í.; Bahamontes-Rosa, N.; Ballell-Pages, L., *et al.*, Carbamoyl Triazoles, Known Serine Protease Inhibitors, Are a Potent New Class of Antimalarials. *J. Med. Chem.,* **2015**, *58*, 6448-6455.

64. Eliazyan, K. A.; Shahbazyan, L. V.; Pivazyan, V. A.; Ghazaryan, E. A.; Yengoyan, A. P., Synthesis of novel 1,3-substituted 1H-[1,2,4]-triazole-3-thiol derivatives. *Heteroat. Chem.,* **2010**, *20*, 405-410.

65. Hudwekar, A. D.; Reddy, G. L.; Verma, P. K.; Gupta, S.; Vishwakarma, R. A.; Sawant, S. D., Transition Metal-free Single Step Approach for Arylated Pyrazolopyrimidinones and Quinazolinones Using Benzylamines/Benzylalcohols/Benzaldehydes. *ChemistrySelect,* **2017**, *2*, 4963-4968.

66. Flores Toque, H. A.; Priviero, F. B. M.; Teixeira, C. E.; Perissutti, E.; Fiorino, F.*, et al.*, Synthesis and Pharmacological Evaluations of Sildenafil Analogues for Treatment of Erectile Dysfunction. *J. Med. Chem.,* **2008**, *51*, 2807-2815.

67. Wiberg, K. B.; Waddell, S. T., Reactions of [1.1.1]Propellane. *J. Am. Chem. Soc.,* **1990**, *112*, 2194-2216.

68. Jung, M.; Lindsay, V. N. G., One-Pot Synthesis of Strain-Release Reagents from Methyl Sulfones. *J. Am. Chem. Soc.,* **2022**, *144*, 4764-4769.