



**University of
Nottingham**

UK | CHINA | MALAYSIA

Investigation of Sulfur(VI) Chemistry

Priscilla Mendonça Matos

Thesis submitted to the University of Nottingham

for the degree of Doctor of Philosophy

March 2019

Acknowledgements

I would like to thank Professor Robert Stockman for giving me the opportunity to conduct my research in his laboratory over the last four years and for his guidance on the projects during my Ph.D. programme.

Secondly, I'd like to thank the post-doctoral researchers in both the Stockman Group and the Department of Chemistry that have offered advice along the way – Dr. Thomas Storr, Dr. Johnny Moore, Dr. Irene Georgiou, Dr. Ross Wilkie, Dr. Suresh Chidipudi and Dr. Matthew Palframan. I also would like to thank the University of Nottingham and all staff for the great facilities and the help throughout the years.

Extended thanks go to Professor Hon Wai Lam for allowing me to use his Chiral HPLC to analyse samples and Dr. Somnath Karad, Dr. Rebecca Ruscoe and Harley Green for their help.

Thanks goes as well to Dr. William Lewis and Dr. Stephen Argent for collecting X-ray crystal structure data. Further to this, I am grateful to Professor Roger Bayston and Dr. Katherine Belfield for collecting biological activity data on sulfoximine compounds (Biomaterials-Related Infection Group, University of Nottingham).

Many thanks go to the PhD and MChem students of the Stockman group over the last four years.

I am grateful for the support and funding from CAPES Foundation (Ministry of Education of Brazil) over the last four years.

I'd finally like to thank my family and friends both in the UK and Brazil for their support.

“Algo só é impossível até que alguém duvide e resolva provar ao contrário”

Albert Einstein

Table of Contents

1.0 Introduction to Sulfoximines.....	1
1.1 Sulfur Compounds	1
1.2 Introduction to Sulfoximines: Properties and Biological Activity.....	2
1.3 Medicinal Properties of Sulfoximines.....	3
1.4 Preparation of Sulfoximines.....	5
1.5 Sulfoxide Imination.....	6
1.5.1 With Azides	6
1.5.2 Metal Catalysed Iminations	7
1.5.3 Imination with <i>o</i> -Mesitylenesulfonyl Hydroxylamine.....	14
1.6 Sulfilimine Oxidation.....	15
1.6.1 Oxidation using KMnO ₄	16
1.6.2 Oxidation using <i>m</i> -CPBA	17
1.6.3 Oxidation using Ruthenium	18
1.6.4 Oxidation using Dioxiranes	18
1.6.5 Oxidation using H ₂ O ₂ / NaOH aqueous	19
1.7 Synthesis of Sulfoximines from Sulfides.....	20
1.7.1 Bull and Luisi's Synthesis of Sulfoximines.....	20
1.7.2 Reboul's Synthesis of Sulfoximines	21
1.7.3 Bull and Luisi's Flow Synthesis of Sulfoximines.....	22
1.7.4 Li's Synthesis of Sulfoximines	23
1.8 Sulfoximine Synthesis from Sulfonimidoyl Halides	24
1.8.1 Bolm's Synthesis of CF ₃ Sulfoximines.....	24
1.8.2 Sharpless's Synthesis of Sulfoximines	25
1.9 Sulfoximine Synthesis from Sulfonimides.....	26
1.9.1 Synthesis of Sulfoximines from Acyclic Sulfonimides	26
1.9.2 Synthesis of Sulfoximines from Cyclic Sulfonimides	27

2.0 Introduction to Sulfonimides	30
2.1 Synthesis and General Considerations	30
2.2 Synthesis of Acyclic Sulfonimides	31
2.2.1 Synthesis of Acyclic Sulfonimides <i>via</i> Sulfonimidoyl Halides	31
2.2.2 Synthesis of Acyclic Sulfonimides From Sulfinyl Hydroxylamines	35
2.2.3 Synthesis of Acyclic Sulfonimides from Sulfinamides Utilising Hypervalent Iodine Species	36
2.3 Synthesis of Cyclic Sulfonimides	41
2.3.1 Synthesis of Cyclic Sulfonimides <i>via</i> Sulfonimidoyl Chlorides	41
3.0 Results and Discussion: Racemic Sulfoximines	47
3.1 Chapter preview	47
3.2 Synthesis of Functionalised Sulfoximines <i>via</i> Sulfonimides	49
3.2.1 Synthesis of Sulfinyl Chlorides	49
3.2.2 Herrmann's Methodology	49
3.2.3 Vogel's Protocol	50
3.2.4 Fernandez's Method	50
3.2.5 Block's Procedure	51
3.3 Synthesis of Sulfinamides	52
3.4 Synthesis of Sulfonimides	55
3.5 Synthesis of Sulfoximines	60
3.6 Antibacterial Activity of Sulfoximines	68
3.7 Conclusions: Synthesis of Functionalised Sulfoximines <i>via</i> Sulfonimides	70
4.0 Results and Discussion: Enantioenriched Sulfoximines	71
4.1 Cyclic Sulfonimide to Sulfoximine Overview	71
4.2 Synthesis of Sulfinamides bearing Chiral Amino Alcohols	72
4.3 Cyclic Sulfonimide Synthesis	75
4.4 Synthesis of Enantioenriched Sulfoximines	80
4.5 Synthesis of NH-Sulfoximines	92

4.6 Mechanism of Deprotection.....	96
4.7 Synthesis of Racemic <i>NH</i> -Sulfoximines	102
4.8 Reaction of Cyclic Sulfonimides with Other Nucleophiles	104
4.9 Conclusions to Second Project and Future Work	107
5.0 Experimental: Racemic Sulfoximines.....	110
5.1 General Experimental and Procedures	110
6.0 Experimental: Enantioenriched Sulfoximines.....	178
6.1 General Experimental and Procedures	178
7.0 References	270

Abstract

This thesis focuses closely on the latest advancements in the synthesis of sulfur(VI) analogues, namely sulfonimides and sulfoximines. A detailed analysis of their applications and syntheses is reported into two sections: synthesis of racemic sulfoximines from acyclic sulfonimides, and secondly, the synthesis of enantioenriched *NH*-sulfoximines from cyclic sulfonimides.

The route towards the synthesis of racemic sulfoximine products starting from sulfinamides (sulfur(IV) species) that were converted into sulfonimides through a hypervalent iodine mediated oxidative alkoxylation reaction and explored in detail to allow modification of the core structure. Subjecting the acyclic sulfonimides to Grignard reaction conditions allowed a general method for C-S bond formation to be explored and adding a third point of diversity to the sulfoximine products.

The second part of the results and discussion closely follows the synthesis of cyclic sulfonimides and their subsequent conversion into sulfoximine products. Oxidative chlorination of sulfinamides followed by cyclisation allows access to cyclic sulfonimides. Structural diversity was investigated further through Grignard addition to these cyclic sulfonimide templates. Furthermore, the stereochemical outcome of all steps towards sulfoximines was carefully monitored by X-ray crystallography. Pleasingly, *NH*-sulfoximines were isolated using basic conditions under an oxygen atmosphere to cleave the phenylethanol moiety with no loss of stereochemical information at sulfur during this transformation giving free *NH*-sulfoximines with excellent enantiomeric excess.

Abbreviations

aq.	aqueous
ATR	ataxia telangiectasia and rad3 related
BocN ₃	<i>N</i> - <i>tert</i> -butyloxycarbonyl azide
°C	degrees celcius
CDK	cyclin-dependent kinase
CF ₃	trifluoromethyl
CYP24	human cytochrome hydroxylase enzyme
Δ	heat
d.r.	diastereomeric ratio
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
DIB	diacetoxyiodobenzene
DMDO	dimethyldioxirane
DMSO	dimethylsulfoxide
ee	enantiomeric excess
<i>epi</i>	epimer
h	hour(s)
HRMS	high resolution mass spectrometry
IC ₅₀	half maximal inhibitory concentration
<i>J</i>	coupling constant
MBC	minimum bactericidal concentration
<i>m</i> -CPBA	<i>meta</i> -chloroperbenzoic acid
M	molar
MIC	minimum inhibitory concentration

MSH	<i>o</i> -mesitylenesulfonyl hydroxylamine
MSO	methionine sulfoximine
MTBE	methyl <i>tert</i> -butyl ether
NCS	<i>N</i> -chlorosuccinimide
NMR	nuclear magnetic resonance spectroscopy
PhIO	iodosylbenzene
RLi	organolithium
RMgBr	organomagnesium bromide (Grignard reagent)
rt	room temperature
S _N 2	bimolecular nucleophilic substitution
TBAF	tetrabutylammonium fluoride
<i>t</i> -BuOCl	<i>tert</i> -butylhypochlorite
TcesN ₃	2,2,2-trichloroethoxysulfonyl azide
THF	tetrahydrofuran
TLC	thin layer chromatography
TMSCF ₃	trifluoromethyltrimethylsilane (Ruppert-Prakash reagent)
TMSN ₃	trimethylsilyl azide
<i>t</i> _r	residence time
UVA	ultraviolet A

1

Chapter One

Introduction

Synthesis of Sulfoximines

1.0 Introduction to Sulfoximines

1.1 Sulfur Compounds

Sulfur compounds are of particular interest due to their numerous applications across a wide range of chemistry. The chemical series include those of sulfur(II), sulfur(IV) and sulfur(VI); some key examples are highlighted just below in Figure 1.1.

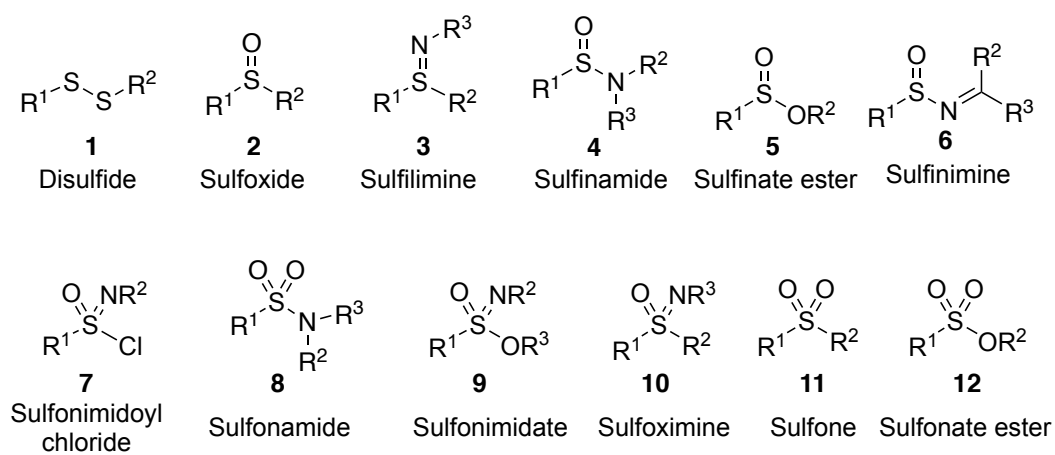


Figure 1.1. Interesting sulfur compounds.

As highlighted in Figure 1.1, many of these sulfur compounds contain a number of atoms or groups surrounding the central sulfur atom, and it is these individual features that leads to the different nomenclature associated with them. This report, will focus closely on sulfur(VI) compounds named sulfonimides (**9**) and sulfoximines (**10**). The introduction section will be divided into two subsections, the first focusing on sulfoximine synthesis, and the second half investigating the synthesis of both acyclic and cyclic sulfonimides.

1.2 Introduction to Sulfoximines: Properties and Biological Activity

The first reported synthesis and study of a sulfoximine was by Bentley and Whitehead in 1949,¹⁻³ methionine sulfoximine **13** (MSO), which was shown to exert interesting biological activity. The researchers tested the action of nitrogen trichloride on zein, the principle component of maize; upon careful analysis, they found methionine sulfoximine had formed as the product of this reaction. This caused toxic adverse effects when tested on rabbits (and also replicated in dogs). Ever since this seminal report, MSO has been subject of intense studies even today (Figure 1.2).⁴⁻⁶

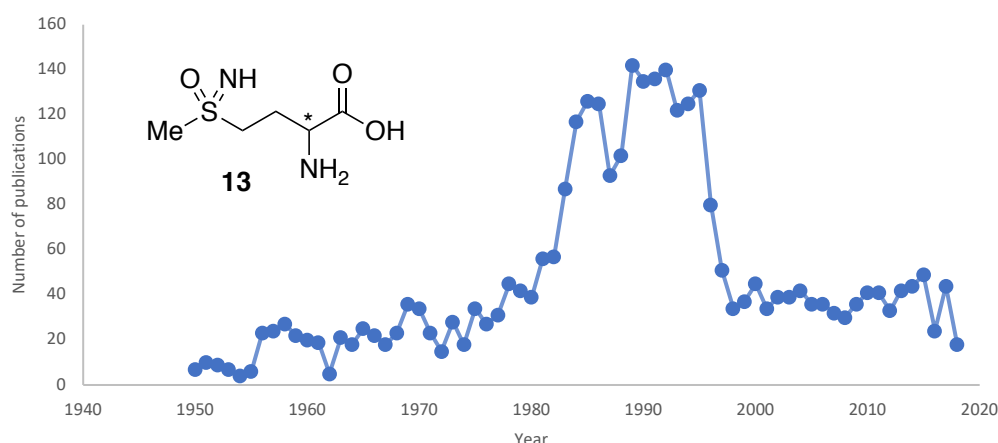


Figure 1.2. Above left: methionine sulfoximine (MSO) **13**. Above right: chart indicating number of scientific articles containing “methionine sulfoximine” since its discovery, determined using CAS SciFinder® search.

When sulfoximines contain two different sulfur-carbon bonds, the molecule has an asymmetric center and two possible enantiomers can exist (sulfoximine **14**, Figure 1.3). Moreover, the complexity of this compound class can be highlighted further by the oxygen and nitrogen atoms acting as hydrogen bond donors and acceptors.⁷ When the R³-substituent on the nitrogen atom is modified, the acidity of protons on the group R¹ bound to the sulfur atom can be tuned.⁸

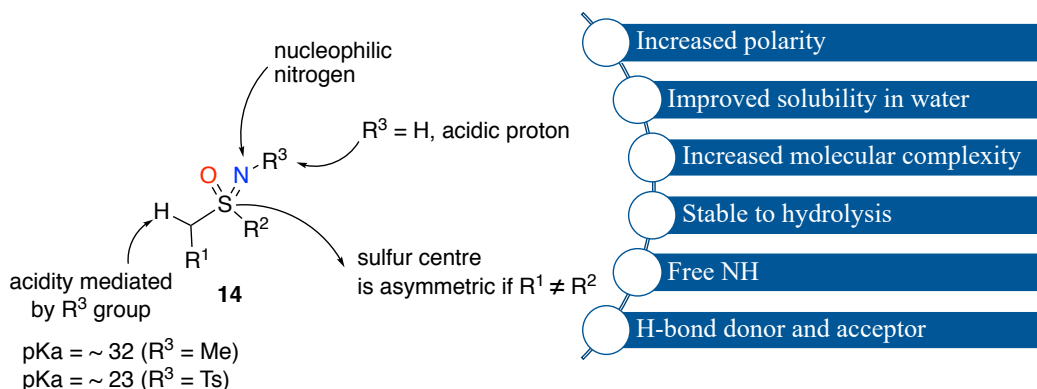


Figure 1.3. Various properties of sulfoximines compared to sulfones.

As shown in Figure 1.3, sulfoximines have been shown to be more soluble in water and alcoholic solvents than sulfones; these combined properties have led to chemists exploiting the sulfoximine moiety as useful ligands in asymmetric transformations.⁹

1.3 Medicinal Properties of Sulfoximines

The sulfoximine moiety has been incorporated in a variety of medicinal chemistry programs, providing an isosteric alternative to the more commonly employed sulfone group. This section covers some of the most intriguing cases in which the sulfoximine functional group has had a productive impact on drug discovery programs, for example, Posner and co-workers synthesised a library of hormone analogues **15** bearing the sulfoximine moiety, that in turn were found to inhibit hydroxylase enzymes (Figure 1.4).¹⁰ The sulfoximines were shown to be extremely potent inhibitors of specifically CYP24 (CYP24 is the human cytochrome hydroxylase enzyme, responsible for the oxidation of calcitriol, the metabolite of Vitamin D), with an IC_{50} value of 7.4 nM reported. Around the same time as these reporting's, the Bayer Pharmaceutical group have reported a variety of sulfoximines to be promising drug candidates. For example, sulfoximine **16** was shown to be selective towards cyclin-dependent kinases (CDK), acting as inhibitors

for potential application in cancer treatment (Figure 1.4).¹¹ Most recently, the same authors have reported a pan-CDK inhibitor **17** (BAY1000394) designed for the treatment of cancer. This sulfoximine derived pharmaceutical is currently active at nanomolar concentrations and is being investigated in phase 1 clinical trials.¹²

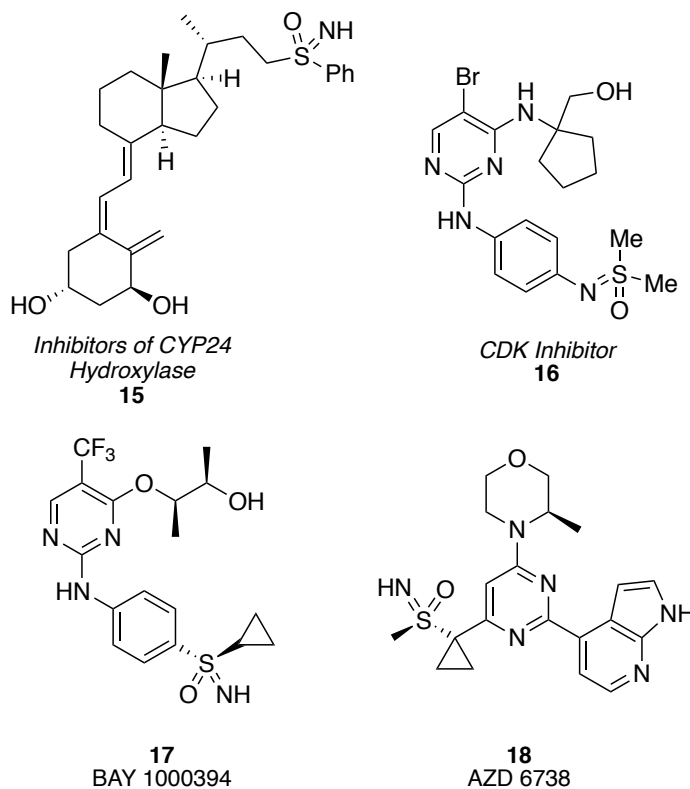


Figure 1.4. Examples of biologically relevant sulfoximine compounds.

AstraZeneca have introduced the sulfoximine moiety into their drug discovery program for the treatment of cancers in the search for an Ataxia-telangiectasia mutated and RAD-3 kinase (ATR) inhibitor. AZD-6738 **18**, a morpholino-pyrimidine with a sulfoximine moiety was shown to be highly active in the inhibition of their ATR target (Figure 1.4).¹³

The agrochemical industry has greatly benefitted from the introduction of the sulfoximine moiety. Dow AgroSciences and Syngenta have both marketed

successful agrochemicals, with either insecticidal (compounds **19** and **20**)^{14–16} or herbicidal activity (compound **21**, Figure 1.5).¹⁷

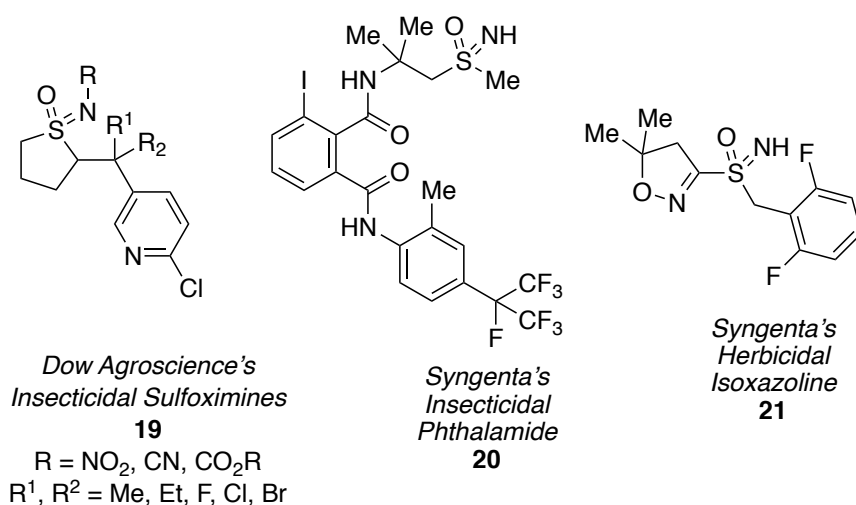
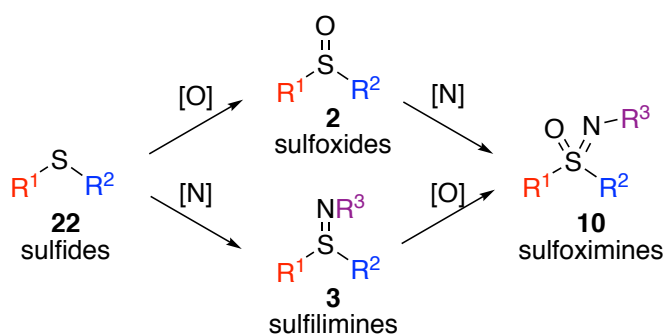


Figure 1.5. Popular agrochemicals from Dow AgroSciences and Syngenta.

1.4 Preparation of Sulfoximines

The synthesis of sulfoximines has drawn considerable interest from academic research groups and pharmaceutical companies alike, and as such, numerous methods exist for their synthesis and detailed reviews have been documented.^{12,13,18–20} The most commonly employed methods for sulfoximine **10** synthesis^{8,21,22} largely stem from either the imination of sulfoxides **2**,^{23–31} the oxidation of sulfilimines **3**^{32–34} or directly from sulfides **22**³⁵ by a dual oxidation/imation protocol (Scheme 1.1).

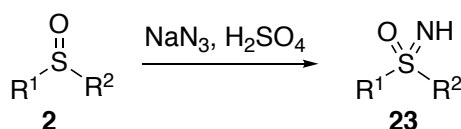


Scheme 1.1. Strategies for accessing sulfoximines.

1.5 Sulfoxide Imination

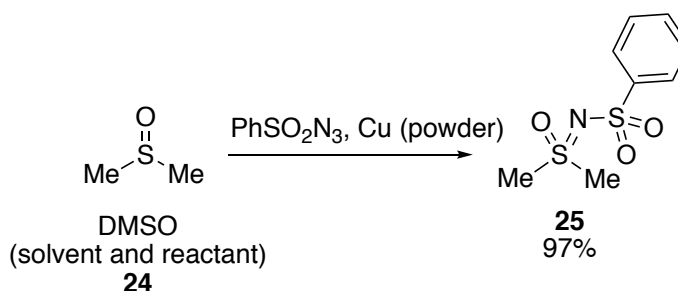
1.5.1 With Azides

One of the most prevalent examples in the literature for the synthesis of sulfoximines begins with the oxidative imination of sulfoxides **2**. The first reported synthesis utilised hydrazoic acid as the nitrogen transfer source (generated on combining sodium azide with concentrated sulfuric acid) (Scheme 1.2).^{36–40} Despite the dangers of using hydrazoic acid,⁴¹ it is one of the most common ways to access the important sulfoximine scaffold.



Scheme 1.2. Synthesis of sulfoximines from sulfoxides using hydrazoic acid.

Iminations of sulfoxides utilising benzenesulfonylazide and copper powder was first reported by Kwart in 1967 (Scheme 1.3).⁴² They showed that addition of copper powder effected the decomposition of the azide, and when conducted in DMSO **24**, the resultant *N*-sulfonylaryl sulfoximine **25** was isolated in 97% yield.

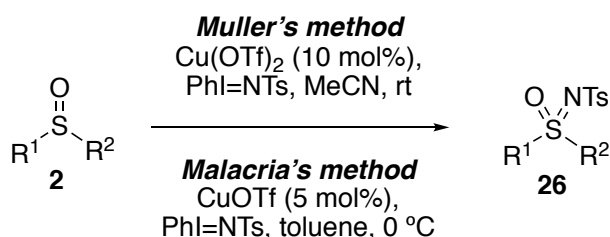


Scheme 1.3. Kwart's copper-catalysed decomposition of benzenesulfonyl azide, and its addition to DMSO **24**.

The use of azides in synthesis, especially in combination with acids, generate hydrazoic acid, which is known to be toxic and explosive and usually will be avoided if another alternative is available. To avoid such reagents, there has been a vast amount of interest in metal catalysed nitrene transfer reactions to sulfur compounds, especially sulfides and sulfoxides.

1.5.2 Metal Catalysed Iminations

Ever since the seminal work by Kwart and co-workers investigating metal-catalysed sulfoxide iminations,⁴² a plethora of publications have appeared over the last 50 years showing the popularity of such methods. Kwart's original paper focused on copper catalysed iminations; more recent developments in the field of copper catalysed iminations of sulfoxides have been reported by the groups of Müller⁴³ and Malacria.⁴⁴ Both research groups have successfully implemented either catalytic amounts of copper(I)/(II) triflate salts, in combination with phenyliminoiodinanes as the source of nitrogen, to affect the imination of sulfoxides **2** (Scheme 1.4).

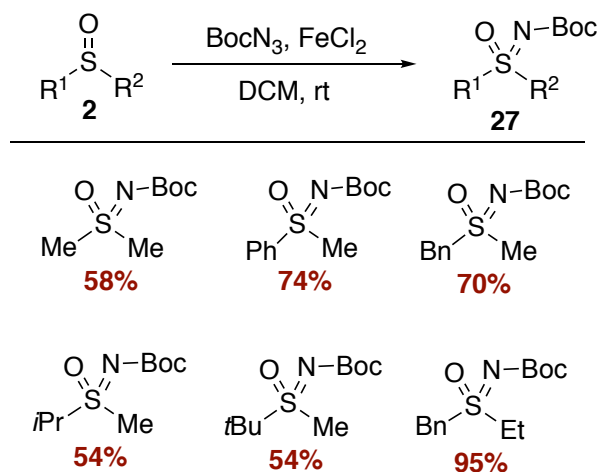


Scheme 1.4. Müller and Malacria's synthesis of *N*-tosyl sulfoximines **26** using catalytic copper salts and iminoiodinanes.

Other metals have been discovered that catalyse the same transformation – Bolm and co-workers have conducted a comparative study that evaluates which metal salts and nitrogen sources can be used on various sulfide and sulfoxide-based systems.⁴⁵ Looking at other key metal salts (in comparison to the

aforementioned copper catalysed iminations), iron,^{29,46} silver,⁴⁷ rhodium^{23,27} and ruthenium³⁰ are amongst the most popular systems to be studied.

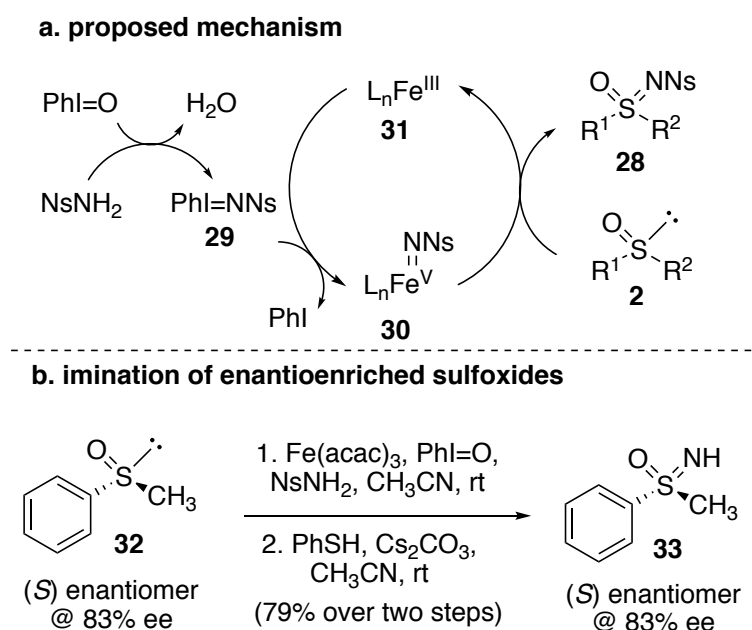
Iron(II) chloride was employed in substoichiometric amounts in the presence of *N*-*tert*-butyloxycarbonyl azide (BocN₃) to bring about the imidation of sulfoxides **2**.⁴⁶ Bach and co-workers utilised this method under relatively mild reaction conditions, with yields ranging from 10-95%. Enantioenriched sulfoxides gave the corresponding sulfoximines with retention of configuration. The authors postulated a mechanism that involves an intermediate Fe^{IV} complex as the reactive nitrene transfer reagent (Scheme 1.5).



Scheme 1.5. Bach's synthesis of *N*-*tert*-butyloxycarbonyl sulfoximines **27**.

In 2006, the Bolm group disclosed their findings on the iron catalysed iminations of sulfoxides. Compared to Bach's method, Bolm's technique utilises a catalytic iron(III) salt in combination with sulfonylamides and a hypervalent iodine source (instead of azide) as the nitrogen transfer source **29**. The reaction was found to tolerate modification at all three points on the sulfoximine core; generally, R¹ and R² were alkyl or aryl, while the sulfonamide nitrogen substituent could be tosyl-NH₂, nosyl-NH₂ and also SES-

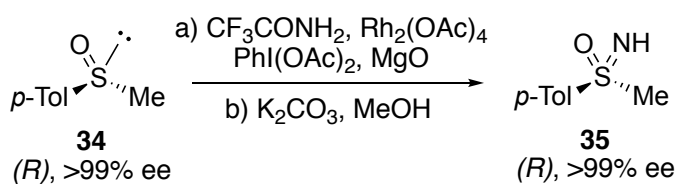
NH₂ amongst others (Scheme 1.6, a).²⁹ They showed in a single example that imination of an enantioenriched sulfoxide **32** proceeds with retention of configuration at the stereogenic sulfur centre (Scheme 1.6, b). A postulated mechanism is thought to have involved an iron-imido complex, formed itself through the reaction of the iron catalyst with PhI=NNs. This iron intermediate is then attacked by the sulfoxide to yield the desired sulfoximine species, along with regeneration of the iron(III) catalyst **31**.



Scheme 1.6. Bolm's iron(III) catalysed imination of sulfoxides **2**.

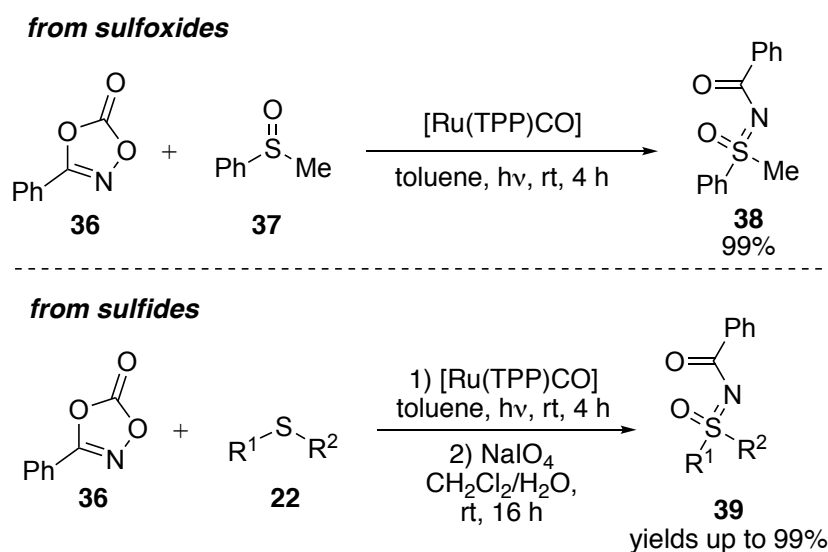
In 2004, Bolm and co-workers showed that rhodium could be utilised as a catalyst for the imination of sulfoxides.²⁷ The protocol reported utilises [Rh₂(OAc)₄] as catalyst with trifluoroacetamide or sulfonylamides in combination with iodobenzene diacetate and magnesium oxide. The authors show that the *N*-acyl bond can be cleaved under basic conditions to afford the desired *NH*-sulfoximines. On implementing an enantiopure sulfoxide **34** to the optimised reaction conditions, optical rotation data collected for the product **35**

revealed that the reaction had occurred with retention of configuration (Scheme 1.7).



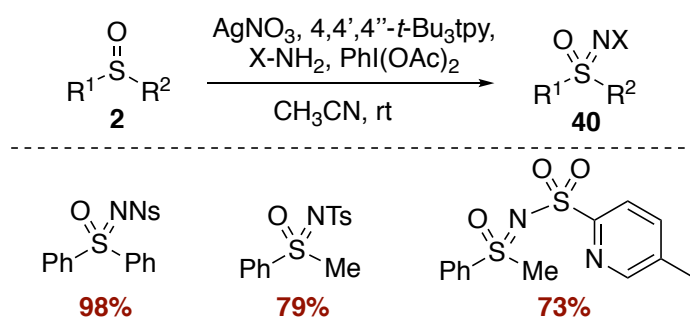
Scheme 1.7. Bolm's rhodium(II) acetate dimer catalysed imination.

Following on from their initial findings with rhodium catalysis, the same research group 10 years later disclosed their findings of a light-induced ruthenium-catalysed nitrene transfer to sulfoxides.³⁰ Light induced decarboxylation of 1,4,2-dioxazol-5-ones **36** in the presence of a ruthenium carbonyl porphyrin complex generated the active nitrene species; this allowed a broad range of *N*-acyl sulfoximines **39** to be accessed utilising relatively mild reaction conditions (Scheme 1.8). Interestingly, starting from sulfides **22**, a one pot protocol that proceeds firstly with an imination, followed by a sodium periodate-driven oxidation afforded the desired sulfoximines in yields up to 99%.



Scheme 1.8. Bolm's ruthenium(II)-catalysed imination of sulfoxides and sulfides.

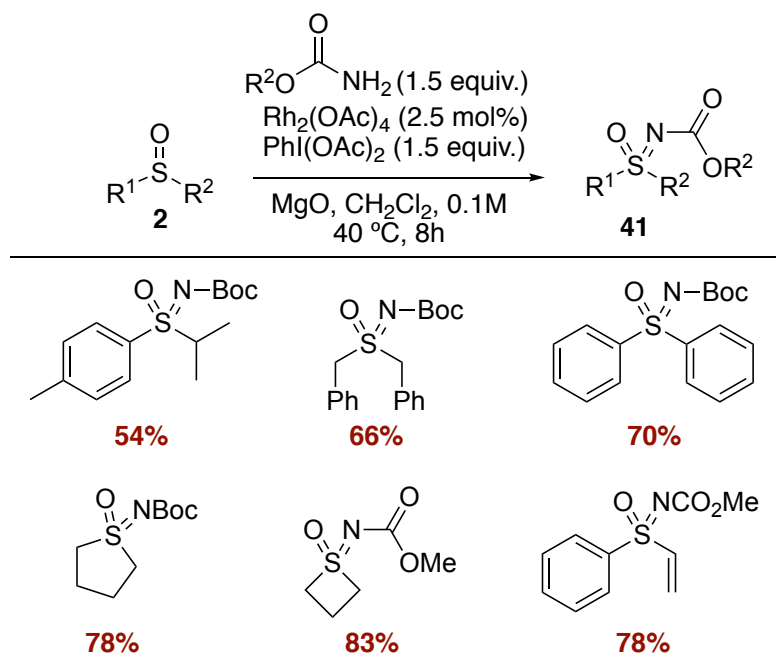
Silver was shown to be an excellent, cheaper alternative to some of the more expensive metals such as rhodium, used in these catalysis reactions (Scheme 1.9). Bolm's group showed that silver nitrate (8 mol% optimised catalyst loading), in the presence of an essential terpyridine ligand, allowed the imination of a range of sulfoxides in good to excellent yields. This procedure only required short reaction times whilst operating under mild reaction conditions (ambient temperature and desirable reaction solvents such as acetonitrile). In these examples with silver catalysis, the sulfonamide is combined with diacetoxyiodobenzene, presumably forming the iminoiodinane *in situ* as the nitrogen source.⁴⁷



Scheme 1.9. Bolm's silver catalysed synthesis of sulfoximines **40**.

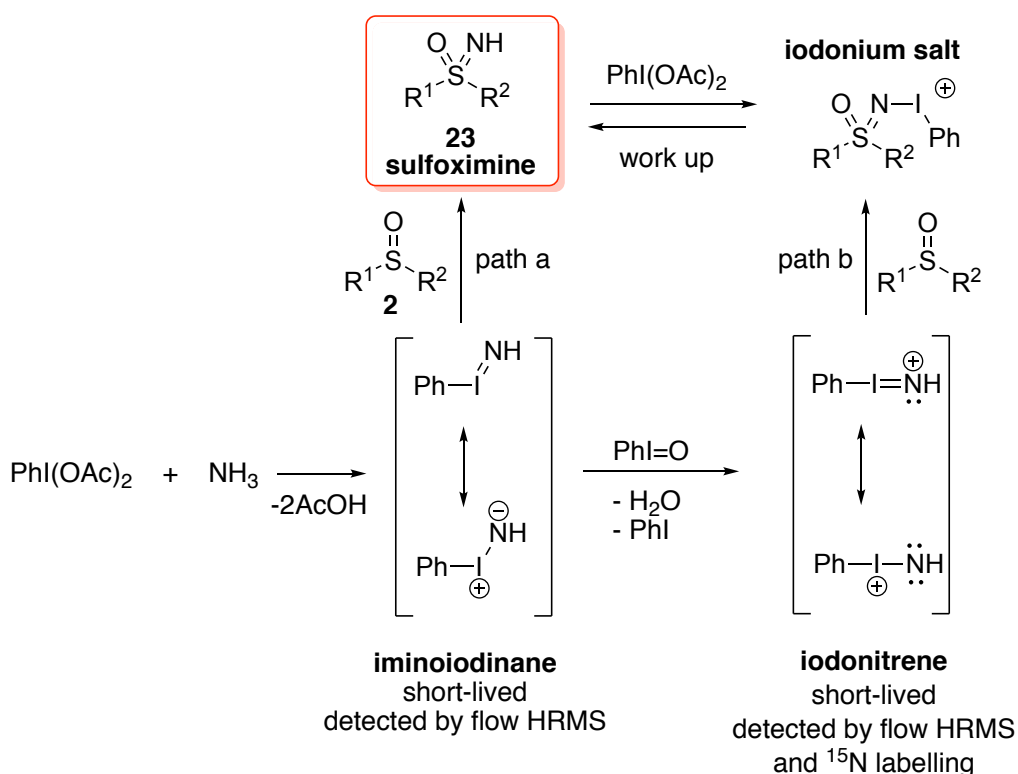
Of late, the interest in this field of organic synthesis has been developed further by the research groups of Luisi and Bull. Their collaborative research efforts have accumulated in a rhodium catalysed nitrene transfer of carbamates to sulfoxides **2** (Scheme 1.10). The authors have shown that utilising low catalyst loadings of $\text{Rh}_2(\text{OAc})_4$ (2.5 mol%), in conjugation with a hypervalent iodine reagent under mild reaction conditions, allowed the stereospecific imination of a range of sulfoxides in high yields. The substrate scope was broad, and for the first time, 4-membered thietane sulfoxides were iminated in good yields, providing new motifs for future medicinal chemistry programmes (Scheme 1.10).²³ The authors

showcase this rhodium catalysed method further by synthesising methionine sulfoximine **13** (Figure 1.2). Cleavage of the carbamate groups can be achieved, utilising acidic conditions to afford the NH-derived sulfoximines.



Scheme 1.10. Bull and Luisi's rhodium catalysed synthesis of *N*-acyl sulfoximines **41**.

The same research groups later showed a metal free, nitrogen transfer protocol to sulfoxides **2** affording desired sulfoximines **23**. The report shows how various ammonia sources can be incorporated with PhI(OAc)₂, allowing the formation of electrophilic nitrogen. Through detailed NMR and HRMS analysis studies on the reaction, the authors highlight a short lived electrophilic intermediate likely to be either an iminoiodinane or an iodonitrene (Scheme 1.11).²⁴

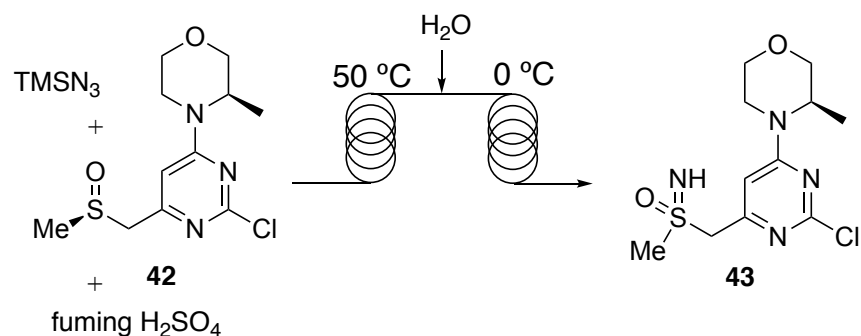


Scheme 1.11. Bull and Luisi's proposed mechanism for nitrogen transfer.

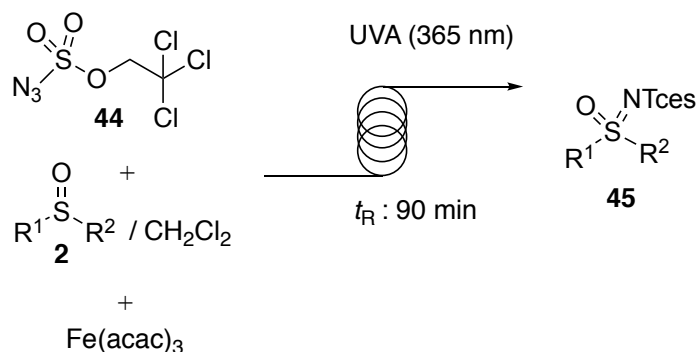
One of the current trends in organic synthesis, especially looking from an industrial chemists' point of view, is the deliverance of large quantities (gram to kilogram scale) of target molecules utilising flow chemistry. The synthesis of sulfoximines utilising a flow chemistry approach has been successfully reported by the groups of Kappe/Roberge⁴⁸ and Lebel⁴⁹, both reporting the imination of sulfoxides as a key step (Scheme 1.12). The aforementioned Kappe/Roberge protocol utilised classic imination conditions of sulfoxides - fuming sulfuric acid/ TMSN_3 , but in flow, to bring about the imination of a pharmaceutically relevant enantiopure sulfoxide **42**, of which sulfoximine **43** was furnished in good yield but racemises under the reaction conditions. Furthermore, sulfoximine **43** was trialled as an ATR kinase inhibitor. The latter protocol reported by Lebel and co-workers showcase a photochemical (UVA) continuous flow process for the imination of sulfoxides **2**, using trichloroethoxysulfonyl azide **44** as the nitrogen source, and catalytic iron(III)

acetylacetonate as catalyst. Their reported protocol afforded a range of aliphatic and aromatic sulfoximines **45** in good yields (a single example was increased to a gram scale without significant loss of yield), but the reaction times were shortened. The authors postulate that UVA light was necessary for activation of the $\text{Fe}(\text{acac})_3$, so that it reacted exclusively with TcesN_3 to form an intermediate capable of conducting the imination.

a) Roberge and Kappe's Methodology



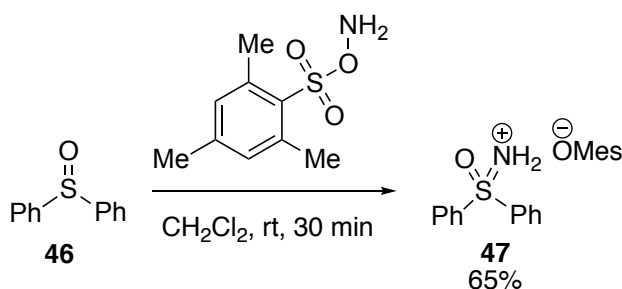
b) Lebel's Methodology



Scheme 1.12. a) Kappe and Roberge's flow synthesis of sulfoximines; b) Lebel's iron-catalysed flow synthesis imination of sulfoxides.

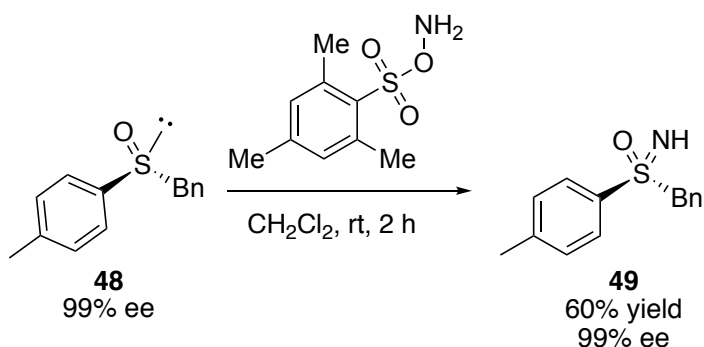
1.5.3 Imination with *o*-Mesitylenesulfonyl Hydroxylamine

The utilisation of *o*-mesitylenesulfonyl hydroxylamine (MSH) provided a breakthrough in the field of sulfoxide iminations in 1972 (Scheme 1.13) - research reported by Tamura and co-workers⁵⁰ showed that MSH was capable of iminating diphenylsulfoxide **46** into the corresponding sulfoximine salt **47** in 65% yield (Scheme 1.13).



Scheme 1.13. Tamura's MSH mediated imination of sulfoxides.

These exact reaction conditions were then utilised by Johnson and co-workers who found that enantiopure sulfoxide **48** could be iminated using MSH, occurring with retention of configuration at the sulfur (Scheme 1.14, enantiomeric excess was maintained at 99% during the imination process).⁵¹



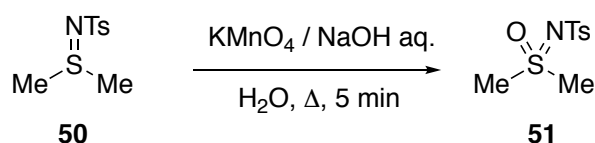
Scheme 1.14. Johnson's synthesis of NH-sulfoximine **49**.

1.6 Sulfilimine Oxidation

The oxidation of sulfilimines to sulfoximines has been studied in detail over the last 70 years – a broad range of oxidants have been successfully employed to perform the modification. Over 40 years ago, Gilchrist and Moody reviewed the transformation,⁵² and since this time, a number of new publications have arisen for this transformation but many of these new articles report slight modifications of originally discovered conditions.

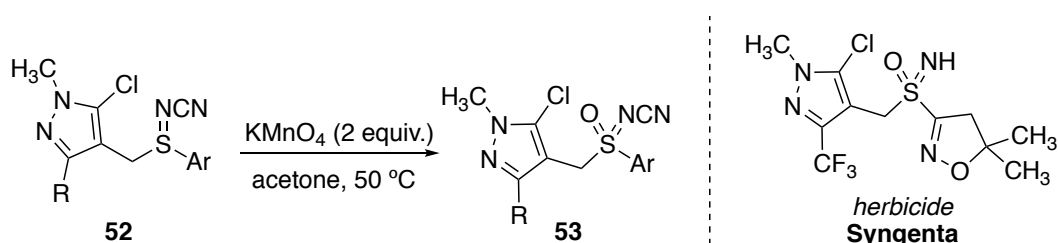
1.6.1 Oxidation using KMnO_4

In 1950, Bentley and Whitehead reported the oxidation of *N*-tosyl-dimethylsulfilimine **50** with either neutral or aqueous basic potassium permanganate (Scheme 1.15).⁵³ Prolonged exposure to permanganate was found to further oxidise the methyl group of the tosyl to the carboxylic acid.



Scheme 1.15. Bentley and Whitehead's oxidation of sulfilimine **50**.

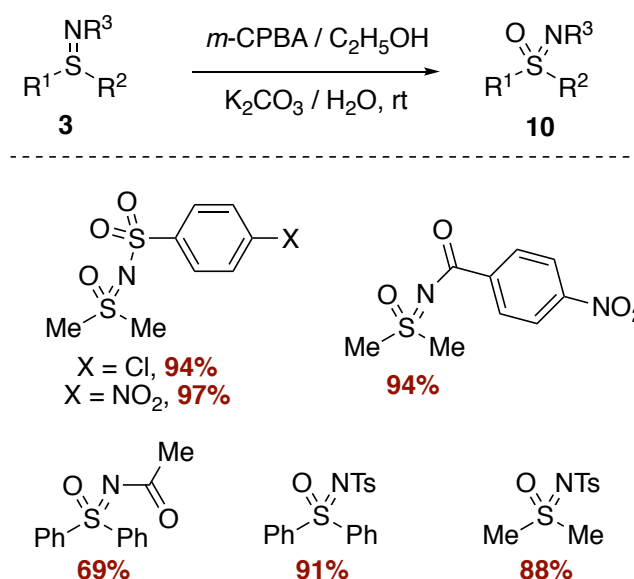
Most recently, Mancheno *et al.* have utilised potassium permanganate with wet acetone as reaction solvent for the oxidation of *N*-cyano-sulfilimines **52**.⁵⁴ They reported good yields for the transformation, and in comparison, to other oxidative systems trialled (*m*-CPBA/ NaHCO_3 in EtOH afforded the desired product, Oxone®/wet- Al_2O_3 / CH_2Cl_2 or H_2O_2 /AcOH led to decomposition), potassium permanganate gave the cleanest reaction with *N*-cyano-sulfilimines **52** (Scheme 1.16). The core aryl pyrazolylmethyl sulfoximine products **53** accessed with this methodology have been utilised in the synthesis of potential herbicides during trials conducted by Syngenta.¹⁷



Scheme 1.16. Bolm's KMnO_4 oxidation of *N*-cyano-sulfilimines **52** to *N*-cyano-sulfoximines **53**.

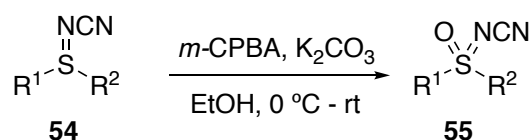
1.6.2 Oxidation using *m*-CPBA

Cram and co-workers were the first to report the oxidation of sulfilimines to sulfoximines utilising *m*-CPBA (in large excess), however yields were moderate, and the reaction drawbacks included the requirement for a huge excess of oxidant, and long reaction times.⁵⁵ The Swern research group some 10 years later reported a similar system that addressed the prior problems (Scheme 1.17). They reported that various *N*-aryl/acyl/sulfonyl sulfilimines **3** are oxidised to the corresponding sulfoximines **10** through *m*-chloroperoxybenzoate (generated by having *m*-CPBA converted into its anion under conditions in an EtOH/H₂O solvent mixture) attack at the electrophilic sulfur centre.⁵⁶



Scheme 1.17. Swern's *m*-CPBA catalysed oxidation of sulfilimines **3**.

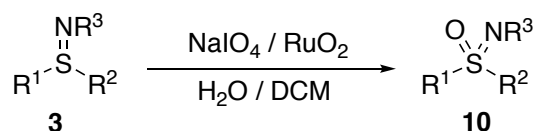
Most recently, Bolm and co-workers reported the synthesis of *N*-cyano sulfoximines **55** from *N*-cyano-substituted sulfilimines **54** utilising the conditions reported above by Swern and co-workers.^{33,57} The sulfilimine oxidation step afforded the sulfoximine products in good to excellent yields (60-96%). All of the examples were conducted on a gram scale showing the scale-up proficiency of their designed protocol (Scheme 1.18).



Scheme 1.18. Bolm's *m*-CPBA catalysed oxidation of sulfilimines **54**.

1.6.3 Oxidation using Ruthenium

In 1978, Veale *et al.* showed that ruthenium could be used to catalyse the oxidation of sulfilimines **3** (Scheme 1.19).⁵⁸ A combination of oxidant (sodium periodate worked best, but sodium hypochlorite was also feasible) and ruthenium dioxide was shown to form ruthenium tetroxide, capable of oxidising a range of sulfilimines in yields up to 95%. The authors report that oxidation of -acyl and -aryl sulfonyldimethylsulfilimines to the corresponding sulfoximines **10** is achievable in short reaction times (less than 15 minutes). The reaction could be self-monitored without analytical analysis; when the dichloromethane layer has a persistent yellow colour, no remaining sulfilimine is available for oxidation and thus the reaction is complete.

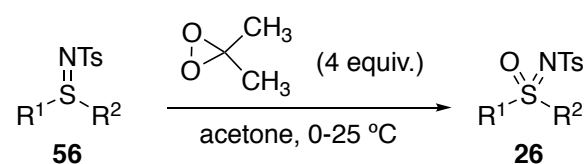


Scheme 1.19. Swern's ruthenium tetroxide oxidation of sulfilimines.

1.6.4 Oxidation using Dioxiranes

Over two decades ago, Curci, Colonna and co-workers discovered that electrophilic oxygen, in the form of dimethyldioxirane (DMDO), was a suitable oxygen transfer reagent for the formation of *N*-tosyl-sulfoximines **26** from *N*-tosyl-sulfilimines **56** (Scheme 1.20).⁵⁹ Isolated yields for the oxidation reaction were always above 90%; a single example on an enantioenriched sulfilimine (ca 80% ee) was oxidised, with no loss of enantiomeric excess and retention of configuration observed. The authors

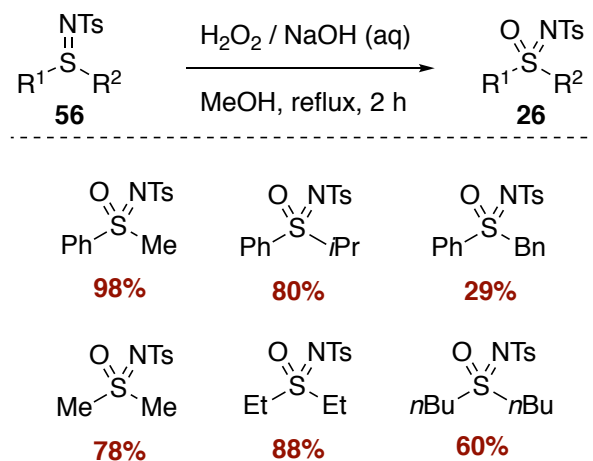
proposed mechanistically that the oxidation involves electrophilic oxygen transfer from DMDO to the lone electron-pair at the sulfilimine sulfur centre.



Scheme 1.20. Curci and Colonna's DMDO oxidation of sulfilimines **56**.

1.6.5 Oxidation using H_2O_2 / NaOH aqueous

In 1979, Johnson's group reported that sulfilimines (containing an *N*-sulfonyl substituent) could be readily oxidised in good yield to give *N*-(*p*-tolylsulfonyl)sulfoximines utilising alkaline hydrogen peroxide (Scheme 1.21). The authors attribute the success of this reaction to the nucleophilic oxidant reacting with a highly electrophilic sulfilimine sulfur atom, caused by the electronegative *N*-tosyl group.³²

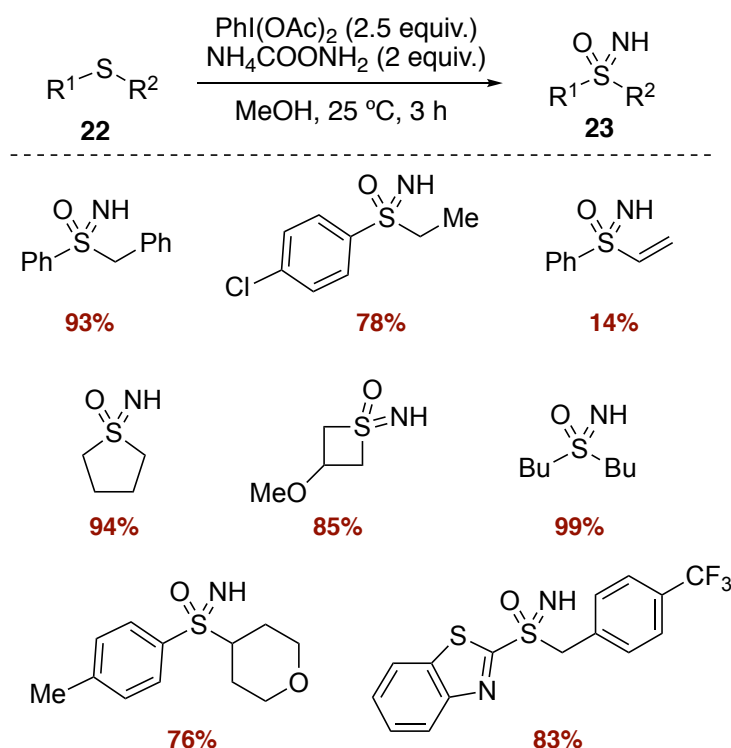


Scheme 1.21. Johnson's oxidation of sulfilimines with alkaline hydrogen peroxide.

1.7 Synthesis of Sulfoximines from Sulfides

1.7.1 Bull and Luisi's Synthesis of Sulfoximines

In 2017, the groups of Bull and Luisi reported a straightforward direct NH-transfer procedure that allowed sulfides **22** to be converted into sulfoximines **23** in one step.³⁵ The authors were hoping to access the sulfur(IV) species, sulfilimines, but instead observed that sulfoximines **23** were the major product (Scheme 1.22). This metal free approach utilised ammonium carbamate ($\text{NH}_2\text{COONH}_4$) (2.0 equiv) in the presence of $\text{PhI}(\text{OAc})_2$ (2.5 equiv) in MeOH, toluene or acetonitrile, at room temperature for a short reaction time. As shown in Scheme 1.22, the methodology tolerates a wide range of sulfides; incorporation of aryl, alkyl and cycloalkyl groups were all well tolerated. Reported yields were good to excellent, reaching up to 99% in some cases. Heterocyclic sulfides were also well incorporated, some of which incorporate medicinally desirable CF_3 /benzothiazole/tetrahydropyran moieties.

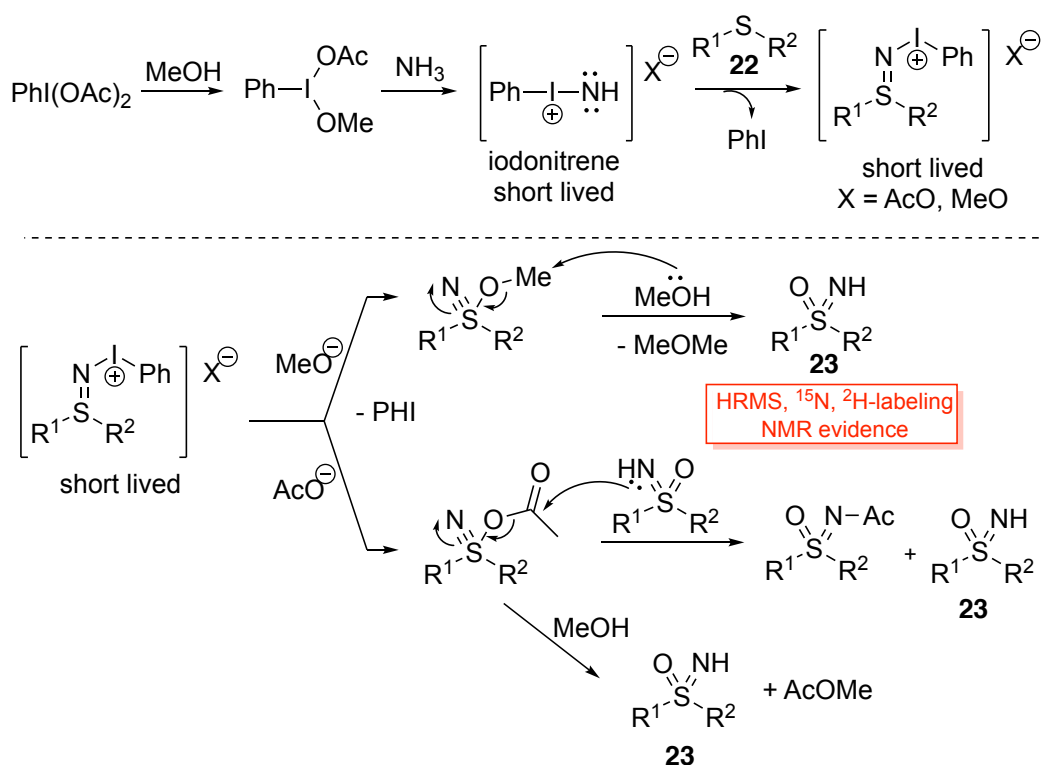


Scheme 1.22. Bull and Luisi's metal-free NH-transfer to sulfides.

The hypothesis of whether *N*- or *O*- transfer occurs first in this reaction was investigated; results from numerous control experiments show that *N*-transfer occurs first, followed by $\text{PhI}(\text{OAc})_2$ oxidation of the resulting sulfilimine to give the desired sulfoximine products (Scheme 1.22).

1.7.2 Reboul's Synthesis of Sulfoximines

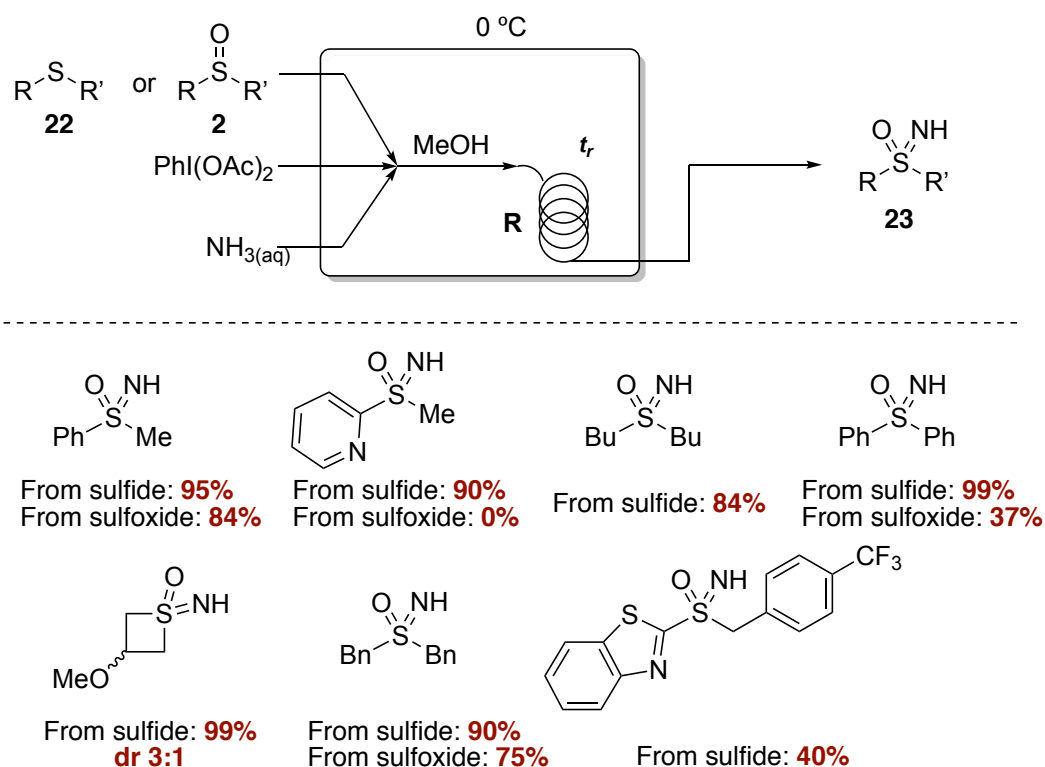
At the same time, research into the nitrogen transfer process to sulfides **22** was investigated by the Reboul group.⁶⁰ The group investigated the transformation of diphenyl sulfide into the corresponding sulfoximine, using $\text{PhI}(\text{OAc})_2$, ammonia (in methanol) or ammonium carbamate and water in acetonitrile. To investigate the exact mechanism of this transformation, the authors conducted extensive NMR studies on the crude reaction mixture (after 5 minutes), along with HRMS analysis, of which acetoxy- or methoxy-sulfanenitrile intermediates could be identified (Scheme 1.23). Further evidence for sulfanenitrile intermediate formation towards the final sulfoximine **23** was confirmed using ^{15}N NMR analysis. Reboul utilised $\text{AcO}^{15}\text{NH}_4$ as the ammonia source, and when the experiment was conducted at -30°C , the desired isotopically labelled sulfanenitrile intermediates, along with the ^{15}N -labelled sulfoximine were observed.



Scheme 1.23. Reboul's proposed mechanism for the *N,O*-transfer to sulfides **22**.

1.7.3 Bull and Luisi's Flow Synthesis of Sulfoximines

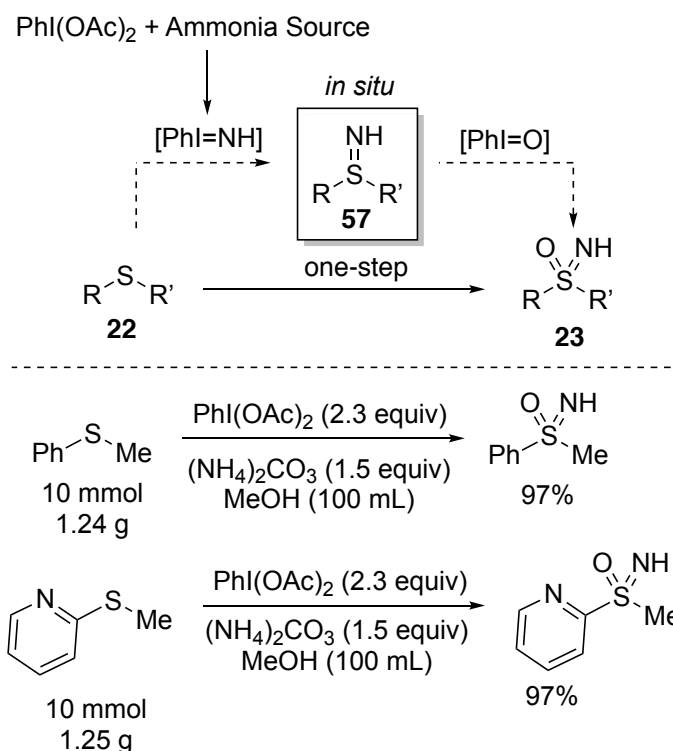
Luisi and co-workers subsequently showed that their earlier reported methodology could in turn be applied to flow chemistry. The authors show advantages over the original method, including the flow process using a more convenient stoichiometry for PhI(OAc)₂, with respect to batch conditions, and an aqueous solution of ammonia can be employed as the nitrogen source (optimised at two equivalents). The substrate scope for substituted sulfides **22** or sulfoxides **2** is broad, and the yields of *NH*-sulfoximines **23** remain very good to excellent (Scheme 1.24).⁶¹



Scheme 1.24. Luisi's flow protocol for the synthesis of sulfoximines from sulfides: *Reagents and conditions:* sulfide (0.2 M), $\text{PhI}(\text{OAc})_2$ (0.4 M), NH_3 (aq.) (0.4 M), 15 min residence time, MeOH, 0 °C (For sulfoxides (0.4 M), 30 min residence time).

1.7.4 Li's Synthesis of Sulfoximines

At the time of the reporting's of Bull and Luisi, Li and co-workers published their findings on the one-step synthesis of sulfoximines **23** from sulfides **22**.⁶² The authors report that again, $\text{PhI}(\text{OAc})_2$ proved optimum as oxidant with ammonium carbonate as the ammonia source. The solvent was shown to proceed under ambient conditions, and two examples could be scaled up to a gram scale (Scheme 1.25). Their method was specifically trialled on sulfides containing an aryl and alkyl moiety in nearly all examples, with only one dialkyl sulfide trialled (diethylsulfide as substrate generated the corresponding NH-sulfoximine in 98% yield).



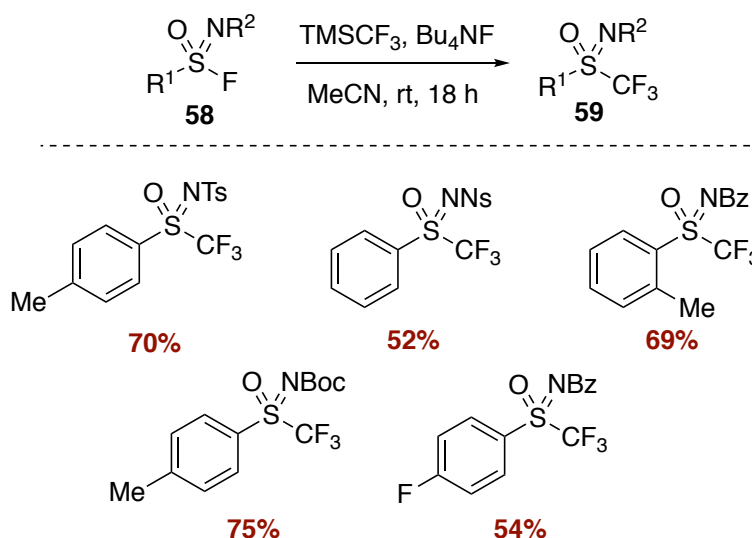
Scheme 1.25. Li's oxidative imination of sulfides using hypervalent iodine.

1.8 Sulfoximine Synthesis from Sulfonimidoyl Halides

1.8.1 Bolm's Synthesis of CF₃ Sulfoximines

In 2011, the Bolm research group reported the synthesis of *N*-Protected trifluoromethyl-substituted sulfoximines **59** by reacting sulfonimidoyl fluorides **58** with the Ruppert-Prakash reagent, in combination with TBAF under ambient reaction conditions. The method allowed access to a broad range of aryl-substituted sulfoximines in moderate to good yields (Scheme 1.26).⁶³ The sulfonimidoyl fluoride **58** starting materials were accessed using one of two routes; firstly, reacting sulfinyl chlorides with Chloramine T (yielding the sulfonimidoyl chloride), which is subsequently reacted with potassium fluoride and a sub-stoichiometric amount of 18-crown-6. The second route involves oxidising *N*-benzoyl and *N*-Boc sulfinamides with *t*-BuOCl, affording sulfonimidoyl chlorides which were then converted in to the fluoride derivatives using the KF/18-crown-6

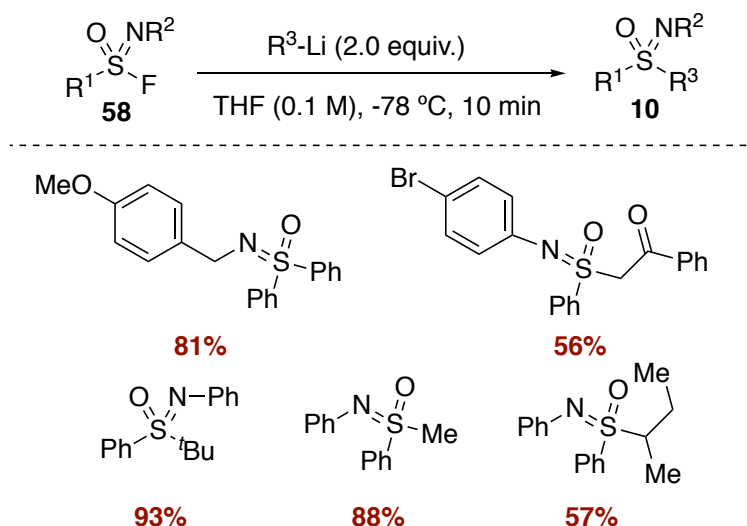
protocol. Interestingly, sulfonimidoyl chlorides failed when subjected to the same reaction conditions.



Scheme 1.26. Bolm's synthesis of trifluoromethyl sulfoximines from sulfonimidoyl fluorides using Ruppert-Prakash Reagent/TBAF combination.

1.8.2 Sharpless's Synthesis of Sulfoximines

The Sharpless group have shown that sulfonimidoyl fluorides **58** can be utilised as precursors for sulfoximines **10** through organolithium addition (Scheme 1.27).⁶⁴ Sharpless utilised his previously discovered SuFEx (sulfur fluoride exchange) click chemistry reaction to build the sulfonimidoyl fluorides **58** from thionyl tetrafluoride (SOF_4) gas.⁶⁵ The addition of organolithium reagents, both aryl and alkyl variants, were successfully incorporated in the reaction protocol – isolated reaction yields ranged from 56-93%. The authors report that THF was utilised to enhance the reactivity of the organolithium nucleophiles towards nucleophilic attack at the electrophilic sulfur centre,⁶⁶ and that 2 equivalents of organolithium reagent were necessary.



Scheme 1.27. Sharpless's synthesis of sulfoximines **10** from sulfonimidoyl fluorides **58**.

1.9 Sulfoximine Synthesis from Sulfonimides

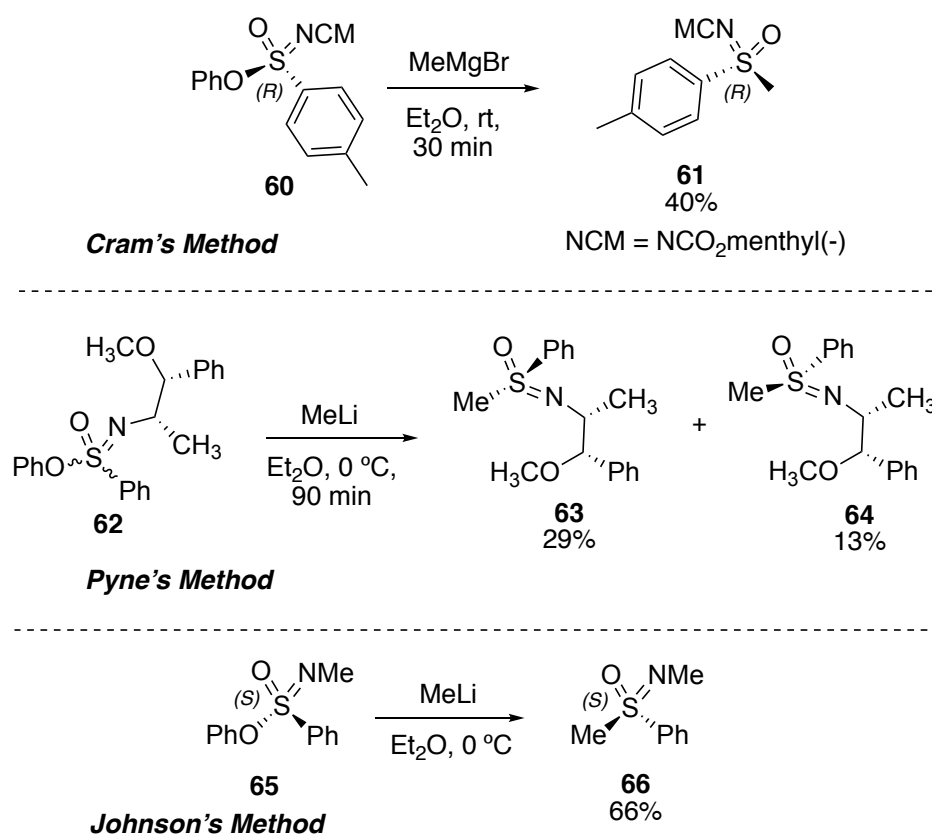
The use of sulfonimides as starting materials to access sulfoximines is a desirable transformation, and of recent times, has attracted attention. This section has been separated into two parts; the synthesis of sulfoximines from either acyclic sulfonimides (less common), and from cyclic sulfonimides (more popular).

1.9.1 Synthesis of Sulfoximines from Acyclic Sulfonimides

Cram, Johnson and Pyne's Sulfoximine Synthesis

The groups of Cram,⁶⁷ Johnson⁶⁸ and Pyne⁶⁹ independently reported that sulfonimides could be used as useful intermediates towards the synthesis of sulfoximines (Scheme 1.28). Although with just one limited example each, in which an acyclic sulfonimide in all cases is reacted with a methyl magnesium bromide or methyl lithium reagent, the protocols showed promise as potential alternatives to known sulfoximine syntheses. Whilst each of the authors did not expand substrate scope, the conditions reported show the potential of this

transformation to access a wide variety of sulfoximines, a valuable compound class that are becoming more prevalent in drug discovery programmes. Moreover, their individual methods benefit from using commercially available organometallic reagents.

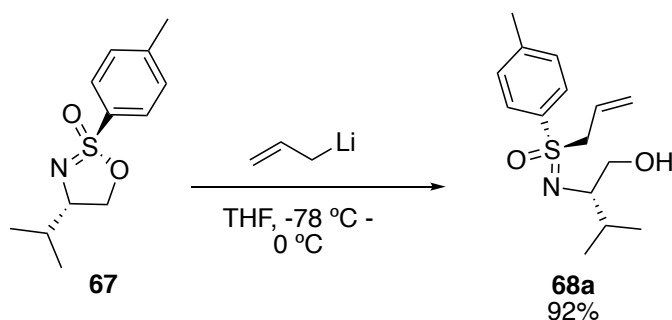


Scheme 1.28. Synthesis of sulfoximines from acyclic sulfonimides.

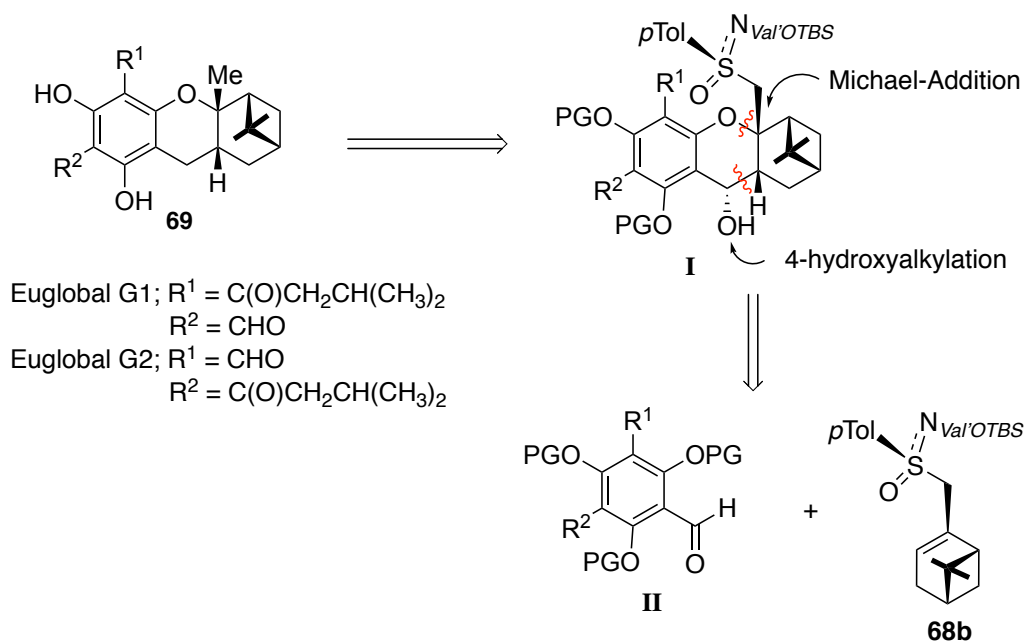
1.9.2 Synthesis of Sulfoximines from Cyclic Sulfonimides

The Reggelin group have found that cyclic sulfonimide variants **67** can be used to access enantioenriched 2-alkenylsulfoximines **68a** (Scheme 1.29, a).⁷⁰ These cyclic sulfonimides were envisaged as an alternative to the well-known menthyl-*p*-toluenesulfonates (used to access enantiopure sulfoxides, which can then in turn be iminated to give enantiopure sulfoximines).⁷¹ Reggelin showcased that alkenylsulfoximines such as **68b** could be used as a starting point in the total synthesis of natural products euglobal G1 and G2 **69** (Scheme 1.29, b).⁷²

a. Reggelin's synthesis of sulfoximines



b. Retrosynthetic analysis for Euglobal G1/G2

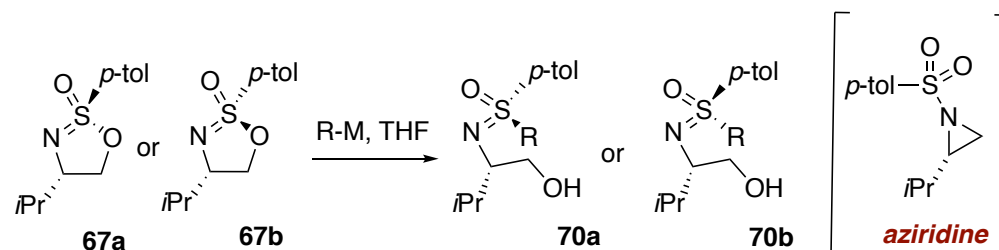
Scheme 1.29. a) Reggelin's synthesis of 2-alkenylsulfoximines **68a**. b)

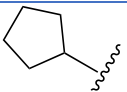
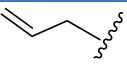
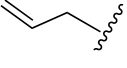
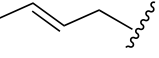
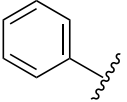
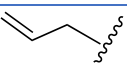
Reggelin's retrosynthesis of euglobal G1/G2.

In Reggelin's seminal work in 1992,⁷⁰ they advocated the use of an excess of organometallic reagent (2 equivalents) in their reaction, but the authors favoured the use of Grignard reagents due to their ease of preparation. Whilst a range of aryl, linear and branched alkyl, alkenyl and cycloalkyl organometallic reagents worked in the transformation, the authors reported that sterically cumbersome *tert*-butyl organomagnesium reagents failed in the transformation and did not lead to any isolated sulfoximine product (Table 1.1). Sulfoximines **70a/b** can be accessed

cleanly through organometallic attack on pure cyclic sulfonimidates with no observed racemisation.

Table 1.1. Synthesis of enantiomerically pure sulfoximines.



Starting Material	R (alkyl/aryl)	M (metal)	Yield (%)
67a	-CH ₃	Li	85
67b	-CH ₃	Li	90
67b	-CH ₃	MgI	quantitative
67b		MgBr	93
67b		MgBr	94
67b		MgBr	97
67b		Li	89
67b		MgBr	89
67b		MgBr	91
67b		MgBr / Cl	0 (aziridine side product isolated in 73%)
67a		Li	92

Chapter Two
Introduction
Synthesis of Sulfonimides

2.0 Introduction to Sulfonylimides

2.1 Synthesis and General Considerations

Sulfonylimides show great versatility, their structure can generally be modified at one or more of three possible key positions (Figure 2.1). The nitrogen atom attached to the sulfur centre shows the most variation; examples of different functional groups on the nitrogen include alkyl,⁷³ aromatic,⁷⁴ silyl or amide,⁷⁵ mesyl or tosyl,⁷⁶ nitrile,⁷⁷ phosphonate,⁷⁸ urea,⁷⁹ phosphorous oxychlorides,⁸⁰ triflate,⁸¹ hydrazines and halides.⁸² As shown in Figure 2.1, the other regions of the sulfonylimide motif that have received attention includes the S-O-R³ group, and the S-R¹ group substituent. For a number of acyclic sulfonylimides **71** currently reported, modifications to both R¹ and R³ have been limited to a few examples of aromatic and aliphatic functionalities. Cyclic variations of sulfonylimides **72** have been realized when R² and R³ are directly connected, usually through a short carbon chain that has been derived from chiral amino alcohols.

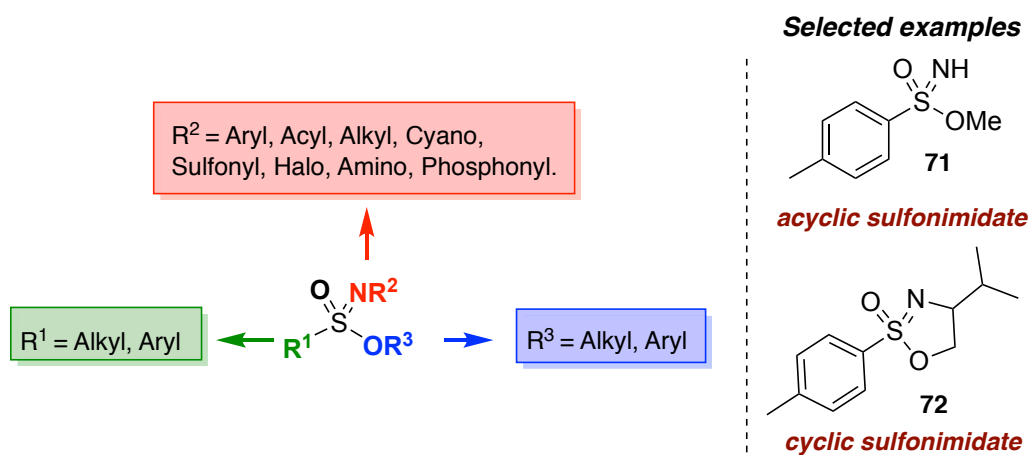
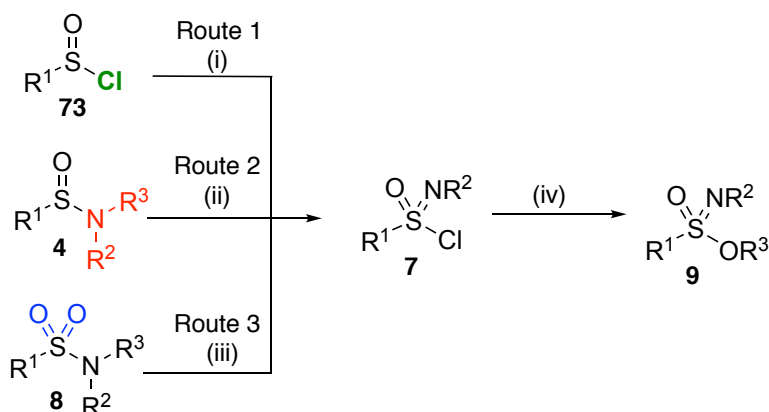


Figure 2.1. Sulfonylimide core structure: three sites for diversity.

2.2 Synthesis of Acyclic Sulfonimides

2.2.1 Synthesis of Acyclic Sulfonimides *via* Sulfonimidoyl Halides

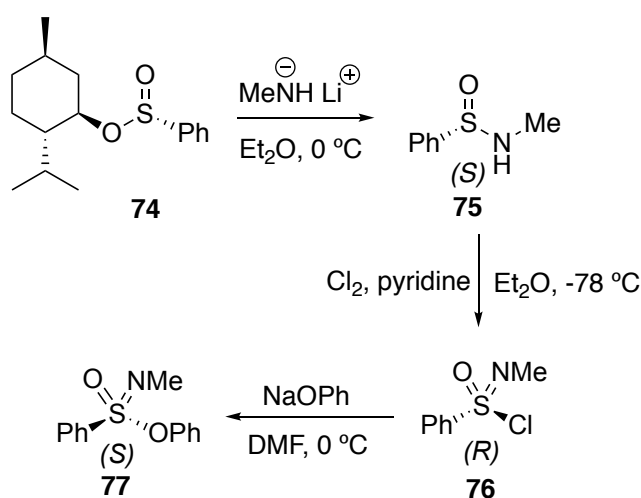
Most of the important early contributions towards the synthesis of sulfonimides **9** were developed from the esterification of alcohols with racemic sulfonimidoyl chlorides **7**. Levchenko *et al.* discovered that oxidation of arylsulfinyl chlorides **73** with sodium salts of *N*-chloroamides afforded sulfonimidoyl chloride **7** (route 1, Scheme 2.1). Subsequent substitution of **7** with an alcohol gave the desired sulfonimides **9**.^{83,84} The sulfonimides synthesised using route 1 contain either alkyl, acyl, aryl or dichlorophosphoryl moieties as the R¹ substituent.



Scheme 2.1. *Reagents and Conditions:* (i) ArNCINa; (ii) Cl₂, rt, 2 h or *t*-BuOCl, 0 °C, 1 h; (iii) Et₃N, Ph₃PCl₂, 30 min. (iv) R²OH, Et₃N, 0 °C, 2 h.

Work reported by Johnson *et al.* in 1979 identified that route 2 could also be used to access sulfonimidoyl chlorides **7** through the oxidation of sulfinylamides **4** using either chlorine or *tert*-butyl hypochlorite as the oxidant (route 2, Scheme 2.1).^{85,86} Johnson and co-workers also reported that access to non-racemic sulfonimides **77** could be achieved when starting the synthesis from enantiopure (+)-(*S*)-*N*-methylbenzenesulfinamide **75** (Scheme 2.2). In a trial experiment, the group had observed that optically active sulfinamide **75** racemised on addition of hydrogen

chloride. To avoid racemisation during the chlorination step, the reaction was conducted at $-78\text{ }^{\circ}\text{C}$ and utilised pyridine as a hydrogen chloride scavenger.⁶⁸



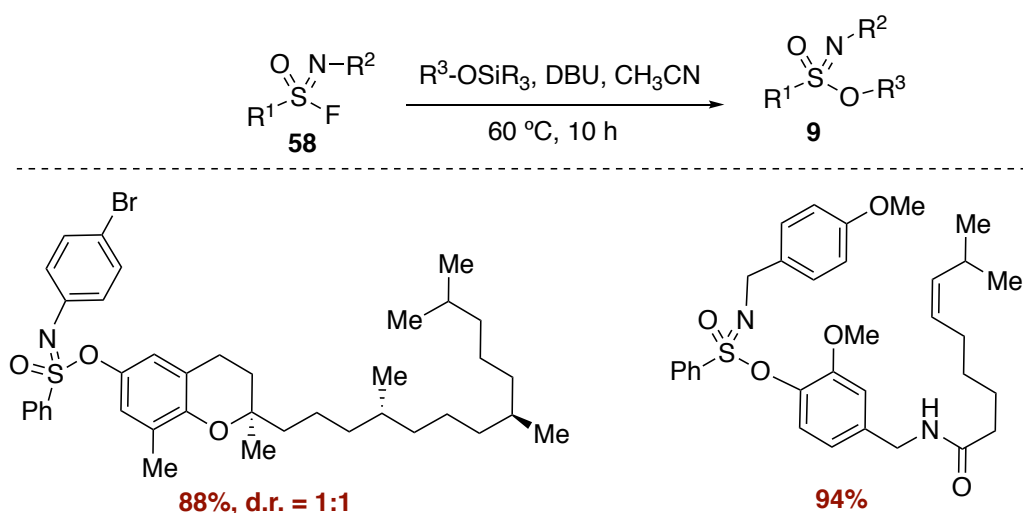
Scheme 2.2. Johnson's synthesis of sulfonimides **77**.

Roy and co-workers disclosed that sulfonamides **8** react with bulky halophosphoranes to undergo a rearrangement reaction to access the key sulfonimidoyl chlorides **7** (Scheme 2.1, route 3).⁷⁵ The same group also disclosed that the bromo-derivative of **7**, sulfonimidoyl bromide, could be isolated when Ph_3PBr_2 was used. The desired sulfonimides **9** could be isolated in yields of up to 78% after reacting sulfonimidoyl chloride **7** with a mixture of alcohol and triethylamine at $0\text{ }^{\circ}\text{C}$ for 2 hours.

In 2018, the synthesis of sulfonimides from sulfonimidoyl halides has received a recent resurgence in attention – this may be due to the sulfonimide being identified as a useful intermediate towards the synthesis of other sulfur(VI) containing molecules found in drug discovery programmes, such as sulfoximines and sulfonimidamides.

Nobel prize winner Barry Sharpless has recently expanded his click-chemistry concept towards sulfur-fluoride exchange chemistry or 'SuFEx' chemistry, and in

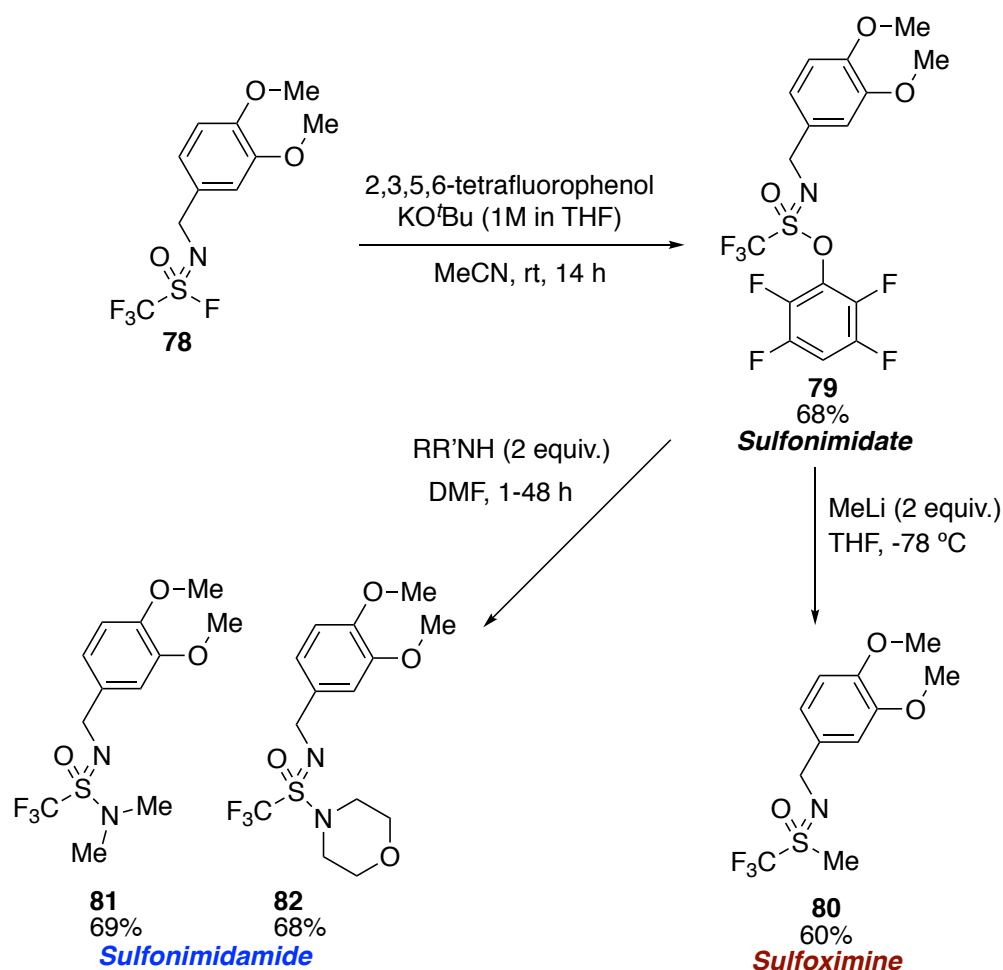
2018, reported the synthesis of sulfonimides **9** from sulfonimidoyl fluorides **58** (Scheme 2.3). As shown below, the authors advocate the use of sulfonimidoyl fluorides over the analogous chlorides due to the latter's lability to hydrolysis. Sharpless showed that through DBU-promoted formation of the S-O bond in the sulfonimide product, complex natural products containing a phenol motif including (+)- δ -tocopherol and capsaicin could successfully be incorporated in excellent yields.⁶⁴



Scheme 2.3. Sharpless's synthesis of sulfonimides from sulfonimidoyl fluorides.

Following on from Sharpless's use of sulfonimidoyl fluorides to access sulfonimides, a joint research article from Wright, Oehrich and co-workers also in 2018 led to the development of a bench stable sulfonimide **79** that can be easily scaled for medicinal chemistry programmes looking to access CF₃-derived sulfonimidamides **81/82** (Scheme 2.4).⁸⁷ The synthesis of sulfonimides was realised by reacting tetrafluorophenol and sulfonimidoyl fluoride **78** – a precursor that the same group previously reacted with amines directly to access sulfonimidamides. The authors show that their sulfonimide **79** had a few key advantages over its predecessor (sulfonimidoyl fluorides) for the synthesis of

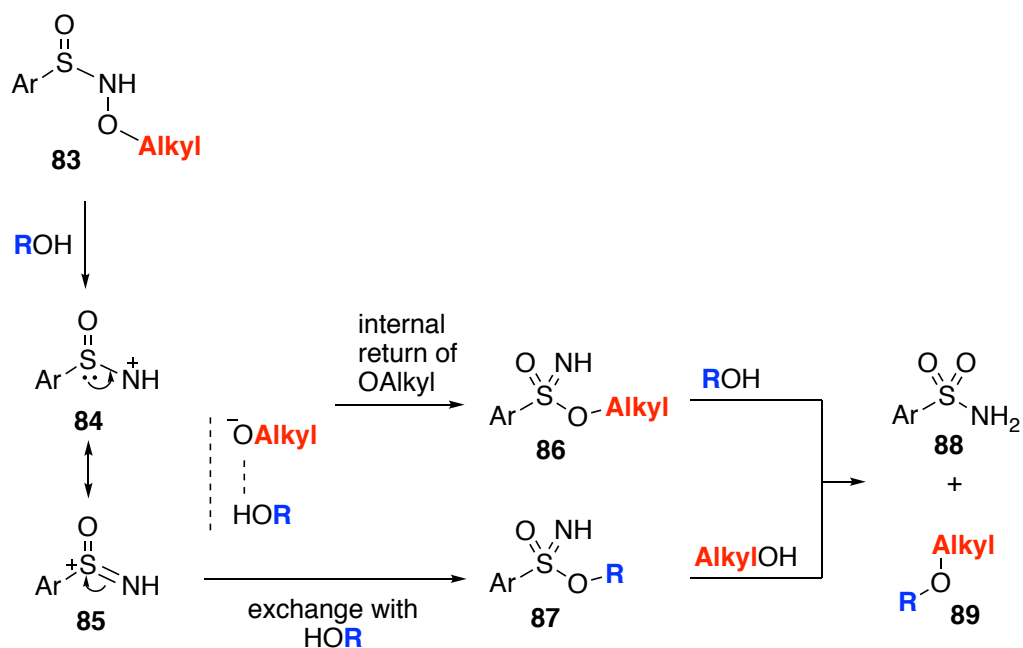
sulfonylimidamides; firstly, the sulfonylimidate reagent was found to be more reactive towards amines than sulfonylimidoyl fluorides. Secondly, during the sulfonylimidamide formation reactions, the authors report less unwanted sulfonylimide by-product was observed when the bench stable sulfonylimidate was utilised. The authors have shown a single example in which two equivalents of methyl lithium were reacted with the sulfonylimidate, affording the desired sulfoximine **80** in 60% yield (Scheme 2.4).



Scheme 2.4. Wright and Oehlrich's bench stable sulfonylimidate from sulfonylimidoyl fluorides, and further applications of sulfonylimidates.

2.2.2 Synthesis of Acyclic Sulfonimides From Sulfinyl Hydroxylamines

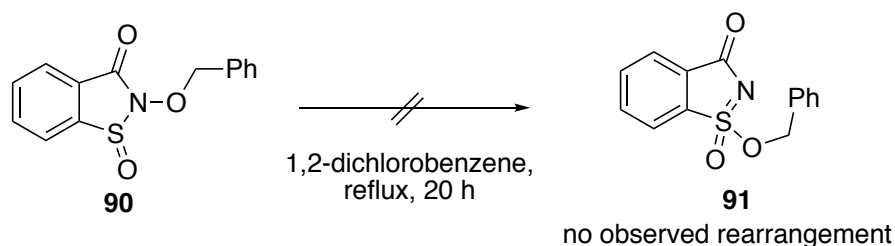
In 1973, Maricich *et al.* showed that sulfinyl hydroxylamines **83** undergo a rapid rearrangement to sulfonimides **86/87**, in which an alkoxy group migrates from the nitrogen to the sulfur atom.⁸⁸ The sulfonimides formed were unstable and were found to transfer their alkyl group to a range of alcohols when heated at 50 °C forming ethers **89** along with the corresponding sulfonamide **88** (Scheme 2.5).



Scheme 2.5. Proposed mechanism of alkyl transfer to alcohols.

The mechanism of the reaction was thought to proceed through a sulfonimide species **86** or **87**, that may have been formed through a dissociation process of the migrating alkoxy group and the solvent (ROH). Two possible sulfonimides were postulated that could transfer the alkyl substituent to the alcohol. They also believe that a delocalised nitrenium species **84**, stabilised by the sulfinyl electron pair is possible, and this was supported when cyclic *N*-acyl derivative **90** failed to rearrange after refluxing in *ortho*-dichlorobenzene for 20 hours, since the nitrenium ion from **90** would be destabilised by the *N*-acyl group (Scheme 2.6). No other

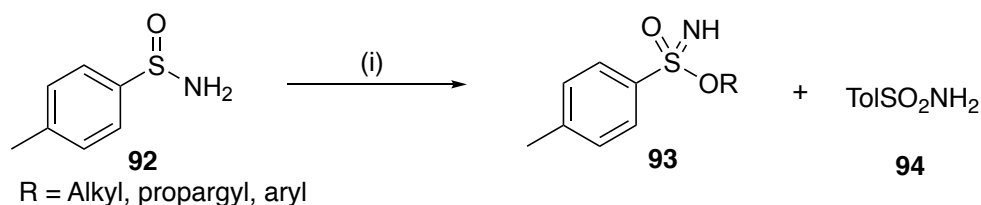
supporting information or experiments were provided by the authors to support this mechanism.



Scheme 2.6. No observed rearrangement was observed on heating *N*-acyl derived sulfinyl hydroxylamine **90**.

2.2.3 Synthesis of Acyclic Sulfonimides from Sulfonamides Utilising Hypervalent Iodine Species

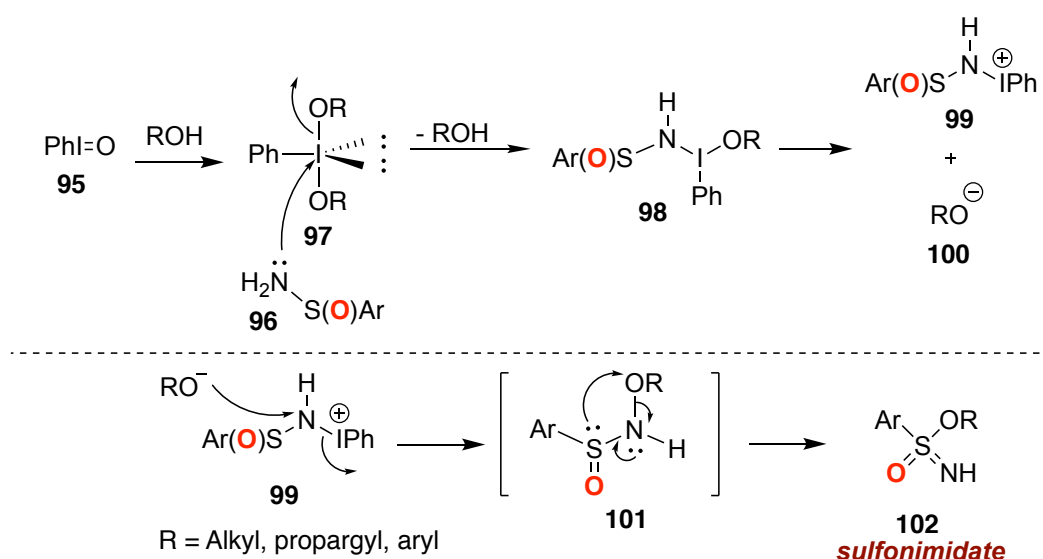
Malacria and co-workers reported that sulfonimides **93** could be formed from sulfonamides **92** in a one-pot procedure, utilising mild conditions, and allowed access to a broad range of sulfonimides in yields up to 95% (Scheme 2.7).⁷³



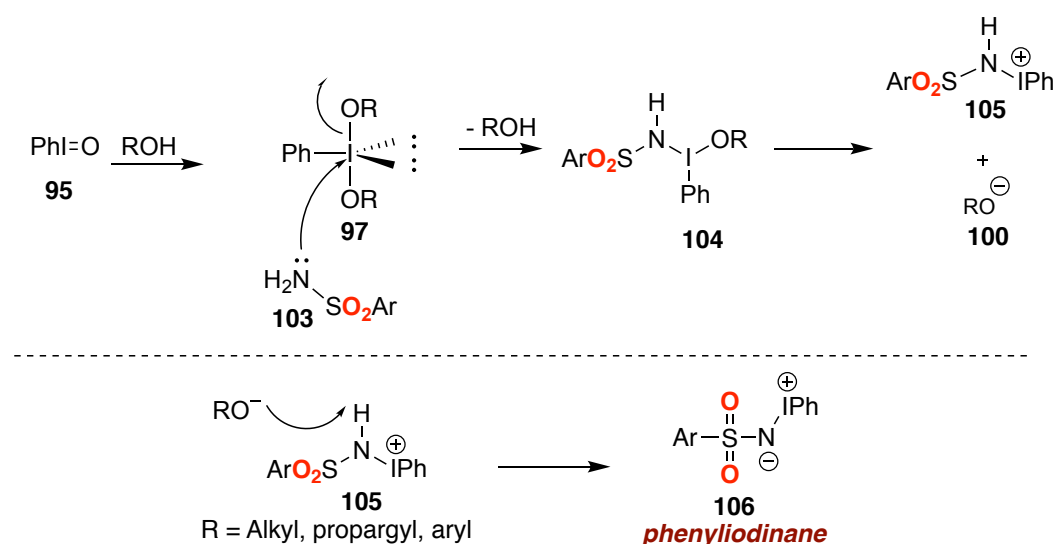
Scheme 2.7. Reagents and conditions: (i) PhI=O , ROH, MeCN, rt, 15 min.

Malacria's procedure built upon the initial reporting's of Maricich's sulfinyl hydroxylamines, in which they devised a way of oxidising the sulfonamide to form the key N-O bond, and minimised the amounts of unwanted sulfonamide **94** that was known to occur when oxidants such as *m*-CPBA were employed.⁸⁹ The use of a mild oxidising agent derived from iodine(III)⁹⁰ allowed the necessary N-O bond formation to proceed smoothly (Scheme 2.7). The proposed mechanism of this transformation is shown in Scheme 2.8. Initially, iodosylbenzene **95** is solvated in

the desired alcohol, and **97** is then attacked by the sulfinamide species **96**. The mechanism then postulates that this species can form a dissociated intermediate **99**, that in the presence of the remaining alkoxide anion **100**, can re-attack the nitrogen centre and expel the iodobenzene moiety to give the key sulfinyl hydroxylamine intermediate **101** first identified by Maricich (Scheme 2.5). This can then rapidly rearrange to yield the key sulfonylimidate product **102**.



Scheme 2.8. Malacria's proposed mechanism for the formation of sulfonylimidates.



Scheme 2.9. Malacria's proposed mechanism for the formation of phenyliodinanes **106**.

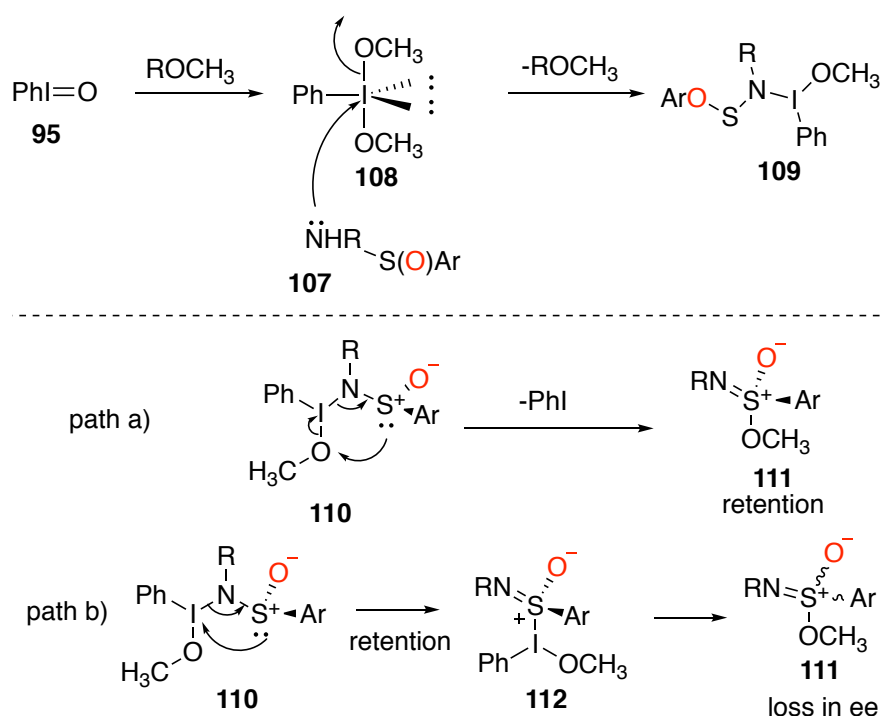
Malacria reasoned that the sulfinamides, containing only one S=O bond, gave the N-H proton in **99** a higher pK_a than the equivalent proton on sulfonamide **105** (that contains two S=O bonds, Scheme 2.9), and thus deprotonation of **99** would not occur and instead a nucleophilic attack gave the respective sulfonimides **102** as the main product (Scheme 2.8).

The scope of this reaction showed that primary alcohols work best; secondary alcohols such as isopropyl alcohol reacted slowly, whilst tertiary alcohols failed to work at all.

In 2004, Malacria and co-workers further extended this research by optimising the reaction conditions. Their findings showed the reaction proceeds well in acetonitrile.⁹¹ They also reported an asymmetric variation that showed the stereochemistry mainly occurred with retention of configuration at the sulfur centre in the product. This work allowed them to revisit the mechanism proposed in Scheme 2.8/2.9 above. To date, this is their most plausible mechanism; the sulfinamide contains an alkyl substituent along with a hydrogen on the nitrogen, and a rearrangement *via* a 6-electron transition state would allow access to sulfonimides with retention of stereochemistry (path a, Scheme 2.10).

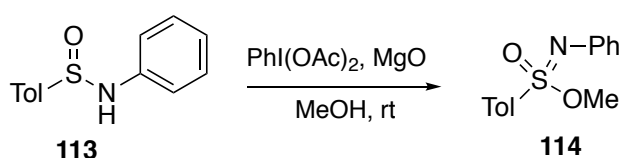
The Malacria group proposed that a competitive three-atom rearrangement, first reported by Reggelin *et al.* (Scheme 2.15, intermediate **124**),⁹² would afford a sulfonimidoyl iodonium species **112**. Previously, Reggelin reported that a sulfonimidoyl bromide variant **128** (Scheme 2.16), could be identified by NMR analysis and was shown to epimerise at $-20\text{ }^{\circ}\text{C}$. With this supporting information,

Malacria reasoned that his proposed iodonium species **112** could be responsible for the observed loss in enantiomeric excess (path b, Scheme 2.10).



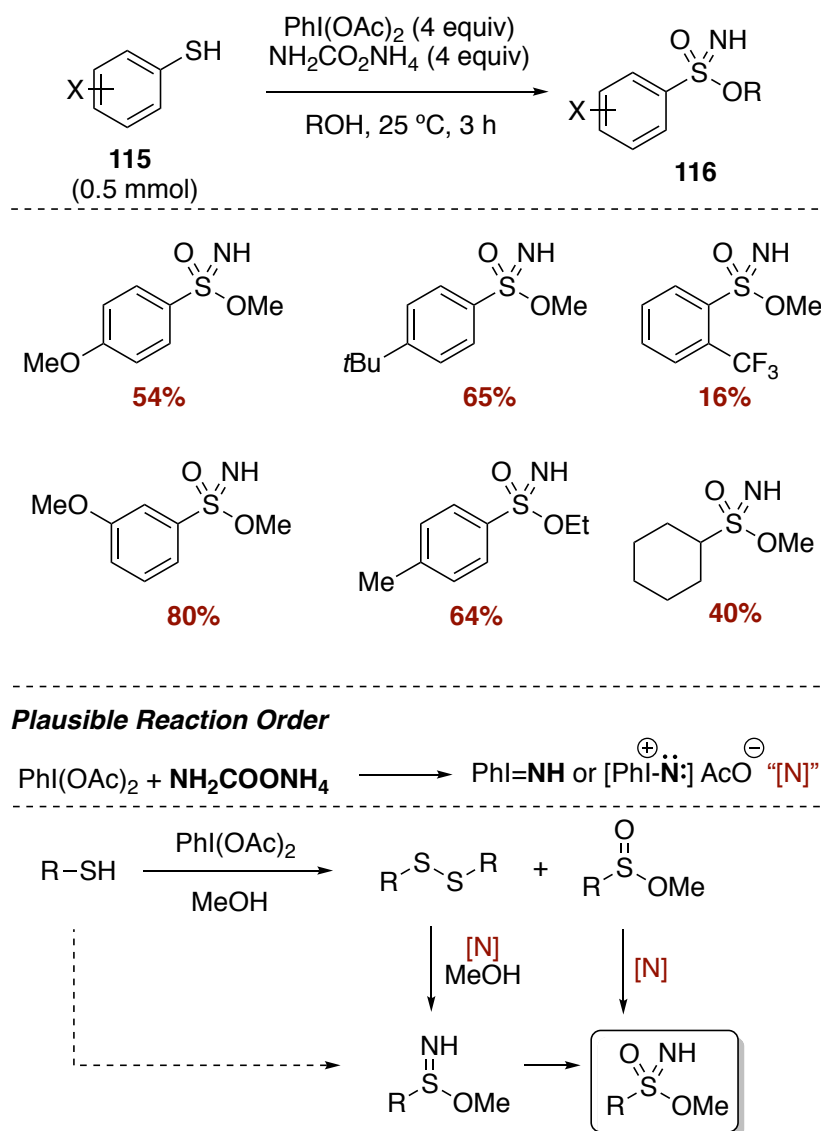
Scheme 2.10. Malacria's revised mechanism for the preparation of sulfonimides.

In 2006, Malacria showed that *N*-aryl sulfinamides **113** could also be utilised in the formation of sulfonimides **114** with their one-pot procedure utilising diacetoxyiodobenzene. With these examples, aryl derived sulfinamides required diacetoxyiodobenzene (DIB) and a mild base such as magnesium oxide to achieve high yields (Scheme 2.11).⁷⁴



Scheme 2.11. Malacria's synthesis of arylsulfonimides.

In 2018, Bull, Luisi and co-workers have most recently reported the synthesis of aryl thiols **115** into sulfonimides **116** utilising hypervalent iodine reagents and ammonium carbamate as nitrogen source (Scheme 2.12).⁹³ Using a 4-equivalent loading of ammonium carbamate forced the reaction to produce exclusively sulfonimide (at 1 equivalent of nitrogen source, sulfonamide was formed as the major reaction product). The reaction scope allowed a range of aryl thiols to participate in the reaction – substitution on the aromatic ring at *ortho*, *meta* and *para* with both electron withdrawing and donating substituents were well tolerated affording sulfonimides in good yields. In one case, a cycloalkylthiol was submitted to the optimised conditions, and the desired sulfonimide was isolated in moderate yield. Whilst the exact sequence of events to form the sulfonimide from thiol is unclear, the mechanism of Bull and Luisi's method was based on a range of control experiments that allowed the identification of disulfides and sulfinic acid esters during the reaction (Scheme 2.12).



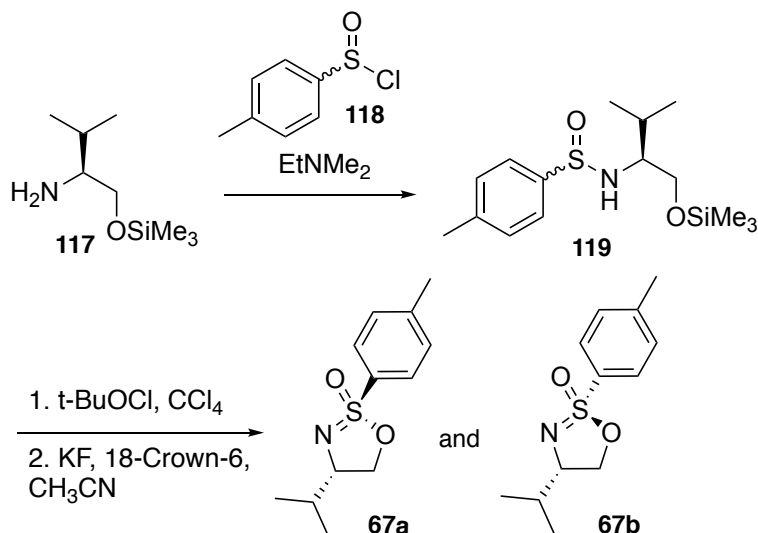
Scheme 2.12. Bull and Luisi's sulfonimide synthesis from aryl thiols **115**.

2.3 Synthesis of Cyclic Sulfonimides

2.3.1 Synthesis of Cyclic Sulfonimides *via* Sulfonimidoyl Chlorides

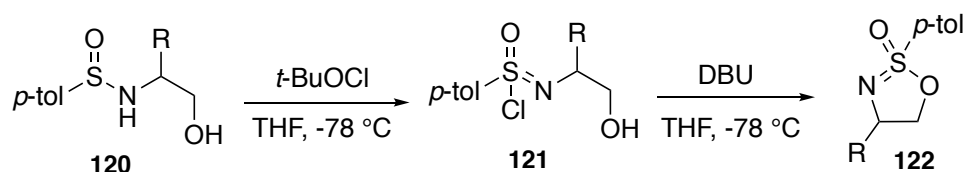
The research reported by the group of Reggelin has dominated this particular field of sulfur(VI) chemistry over the last 35 years. Reggelin's seminal work on the synthesis of cyclic sulfonimides in 1992 featured a one pot procedure, in which (*S*)-*O*-trimethylsilyl valinol **117** and *p*-toluenesulfinyl chloride **118** could be carried through to the desired sulfonimide products **67a** and **67b** without need of isolating

reaction intermediates (Scheme 2.13).⁷⁰ Reggeline utilised potassium fluoride to conduct the desilylation of the primary alcohol, thus allowing the cyclisation to occur.



Scheme 2.13. Reggeline's one-pot synthesis of cyclic sulfonimides.

In 1995, Reggeline followed up his seminal work by reporting an alternative route to access cyclic sulfonimides **122** (Scheme 2.14).⁹⁴ Sulfonamides **120** bearing chiral amino alcohols were identified as suitable starting materials that would be subjected to oxidative chlorination conditions to afford sulfonimidoyl chlorides **121** – a process that involves *tert*-butyl hypochlorite at low temperatures. The protocol reported shows the oxidation occurs after 30 minutes, and the addition of a bulky base such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in a one pot fashion facilitates the intramolecular attack of the pendant alcohol group to the sulfur centre. Reggeline importantly showed that the reaction must be carried out at low temperatures if the desired isomeric purity of the starting material is to be retained in the isolated product. X-ray analysis was utilised as a tool to confirm the absolute configuration of final cyclic sulfonimides obtained from (*R*)-valinol.

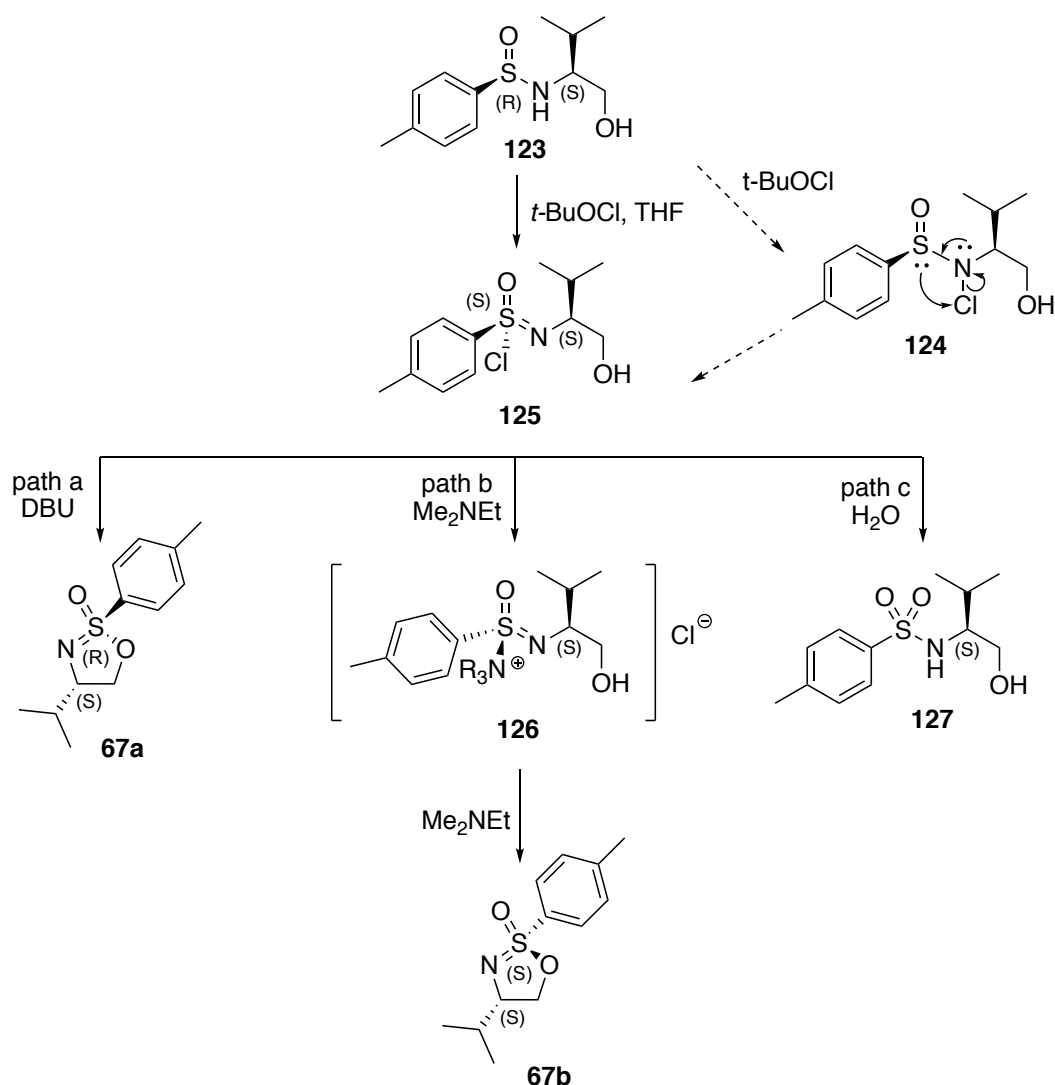


Entry	R subst.	Configuration @ S, @ C	Yield [%]	ds [%]	$[\alpha]_{\text{D}}^{20}$
1	<i>i</i> Pr	(<i>S</i> , <i>R</i>)	89	>98	+ 83.9
2	<i>i</i> Pr	(<i>R</i> , <i>R</i>)	92	96	− 56.6
3	Ph	(<i>S</i> , <i>R</i>)	91	>98	+ 127.4
4	Ph	(<i>R</i> , <i>R</i>)	92	98	− 126.7
5	<i>i</i> Bu	(<i>R</i> , <i>S</i>)	74	cyclisation without separation of diastereoisomers	− 105.7
6	<i>i</i> Bu	(<i>S</i> , <i>S</i>)	61		− 38.4
7	Me	(<i>R</i> , <i>S</i>)	69		− 76.4
8	Me	(<i>S</i> , <i>S</i>)	47		+ 58.7

Scheme 2.14. Reggeli's cyclic sulfonimide synthesis using DBU.

Over a decade ago, Reggeli shed light on the mechanism believed to be in operation during the synthesis of cyclic sulfonimides.⁹² He found through optimisation reactions that two particular pathways were in operation, depending on the base used, and the temperature of the reaction (Scheme 2.15). Oxidative cyclisation of an enantiomer of sulfonamide involved two key stereoselective steps; the first process is an oxidative chlorination reaction to afford sulfonimidoyl chloride intermediate **125**, that proceeds with proposed retention of stereochemistry at the sulfur. The mechanism of this chlorination was posited to firstly involve chlorination of the nitrogen, followed by rearrangement to give the sulfonimidoyl chloride, which was supported through NMR control experiments (integration of *meta*-aromatic signals to NH signal changed from 2:1 to 3.58:1 during the course of the chlorination reaction). The second step is a base-induced cyclisation. If the

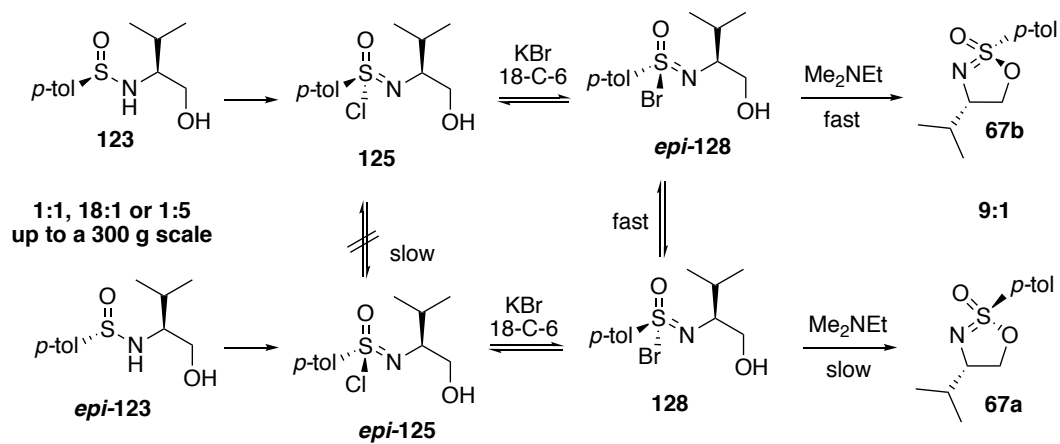
base used is bulky, for example, DBU, whilst conducted at low temperatures (-78°C), the chloride is displaced directly by the tethered alcohol in an $\text{S}_{\text{N}}2$ -like fashion, giving the product (path a, Scheme 2.15). However, when dimethylethylamine was used as a smaller, more nucleophilic base (path b), sulfonimide ammonium salt **126** would be generated as an intermediate, which in turn could undergo base-catalysed cyclisation to form sulfonimide **67b**. A third pathway was identified (path c), which shows that if the base used is not strong enough, such as pyridine or 2,6-lutidine, then hydrolysis of the intermediate sulfonimidoyl chloride was found.



Scheme 2.15. Oxidative chlorination of sulfonamides and cyclisation of the generated sulfonimidoyl chlorides to the target sulfonimides **67a** and **67b**.

This intricate procedure comes with a few drawbacks; firstly, the separation of diastereomeric sulfinamide starting materials is necessary, this is done by crystallisation to good effect, but moreover, a second recrystallisation is required to purify the cyclic sulfonimide product. During these recrystallisations, the authors disclose that for each sulfonimide shown above, a maximum yield of around 35% was achieved for each epimer.

In the same article, Reggelin later described the conversion of the sulfonimidoyl chlorides into sulfonimidoyl bromides using 1.2 equivalents of KBr and 5 mol% 18-crown-6 (Scheme 2.16). These species were initially thought to be labile, albeit invisible intermediates, yet NMR studies conducted at $-20\text{ }^{\circ}\text{C}$ showed <5% of a species that was not the chloride **125**, but potentially the bromide **128**. Through further NMR experiments at low temperature, they observed that starting from either a 1:1, 18:1 or 1:5 diastereomeric mixture of sulfinamides **123**, an enriched ratio of 9:1 was observed in favour of the final sulfonimide product **67b**. The catalyst loading was found to be crucial in maintaining the stereoselectivity and found that at catalyst loadings of 0.5 mol%, the selectivity halved to 4.6:1 in favour of the target sulfonimide **67b**. The reaction was impressively shown to be reproducible on a large scale (checked up to 300 g). They did not observe interconversion of the sulfonimidoyl chlorides species, yet after transhalogenation, fast interconversion between the epimers is observed (dynamic epimer differentiation, in which *epi*-**128** reacts 9-10 times faster than **128**).



Scheme 2.16. Formation of sulfonimidoyl bromides and their epimerisation and interconversion.

3

Chapter Three
Results and Discussions
Synthesis of Racemic Sulfoximines

3.0 Results and Discussion: Racemic Sulfoximines

3.1 Chapter preview:

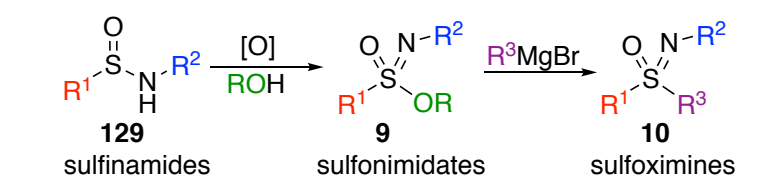
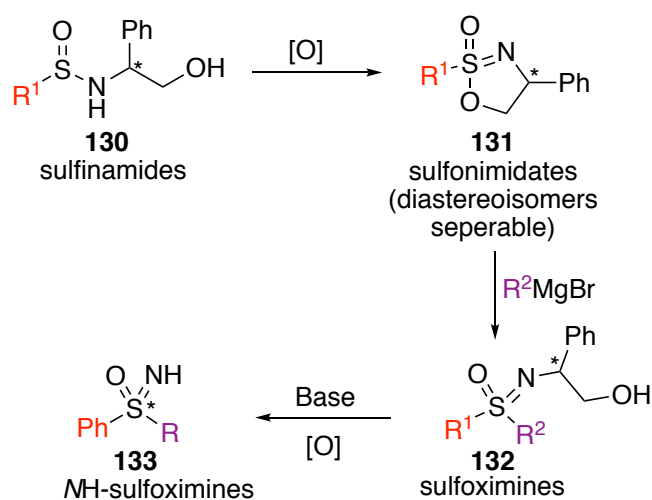
The work described in this chapter builds on the work on the synthesis of sulfur(IV) and sulfur(VI) derived organic compounds studied in the Stockman group over the last 20 years. The chapter will be divided into two parts, the first of which details the synthesis of functionalised sulfoximines **10** *via* sulfonimides **9** (Scheme 3.1, a) – this project aimed to fulfil:

- Synthesis of a broad range of sulfinamides **129** that allowed functionalisation at two key sites.
- Oxidative alkoxylation of sulfinamides with a broad range of alcohols (mediated by hypervalent iodine) – adding a third site of diversity.
- Synthesis of sulfoximines **10** through Grignard addition to sulfonimides.
- Application of sulfoximines in biological assays.

The second part of this chapter details the synthesis of enantioenriched NH-sulfoximines **133** utilising Grignard addition to cyclic sulfonimides **131** (Scheme 3.1, b). The chirality in this project will be installed from the starting materials, chiral amino alcohol derived sulfinamides. This second project aims to achieve:

- Synthesis of a range of chiral amino alcohol derived sulfinamides **130**.
- Conduct oxidative chlorination of sulfinamides followed by base catalysed (DBU) cyclisation to access cyclic sulfonimides **131** – without loss of stereochemical information.

- Grignard addition to diastereomeric cyclic sulfonimides to access sulfoximines **132**.
- *NH*-sulfoximines **133** can be accessed *via* base induced removal of the phenylethanol nitrogen group under an oxygen atmosphere (mechanistic data collected on Metler Toledo React IR15).
- Analysis of the enantiomeric excesses of the final *NH*-sulfoximines **133** through HPLC.

a) **Project 1**b) **Project 2**

Scheme 3.1. Overview of projects. (a) Synthesis of functionalised sulfoximines *via* sulfonimides. (b) Synthesis of enantioenriched *NH*-derived sulfoximines from cyclic sulfonimides.

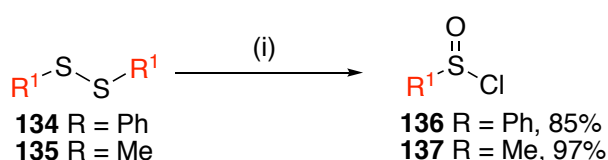
3.2 Synthesis of Functionalised Sulfoximines *via* Sulfonimides

3.2.1 Synthesis of Sulfinyl Chlorides

At the start of the project, the main aim was to access a range of sulfoximines that could be modified at three key positions around the central sulfur atom. At this point, one of the first requirements was to have the sulfur-carbon bond incorporate a broad range of functionalities. Sulfinyl chlorides would act as an excellent starting point for the projected route towards sulfoximines. The literature provided various protocols that would allow us entrance to a variety of sulfinyl chlorides containing methyl, phenyl, *tert*-butyl, allyl and even cyclopropyl substituents.

3.2.2 Herrmann's Methodology

The synthesis of sulfinyl chlorides allowing modification at R¹ was exemplified by Herrmann and co-workers in 1986 (Scheme 3.2).⁹⁵ Herrmann reported that disulfides could be reacted with acetic acid and sulfuryl chloride to generate the desired sulfinyl chlorides with acetyl chloride as reaction by-product. Pleasingly, it proved possible to replicate these conditions exactly, allowing the synthesis of both phenyl- **136** and methyl- **137** sulfinyl chlorides on scales up to 25 g (good scalability). The reaction was conducted initially at –20 °C, and slowly raised to 35 °C over a 6.5 hour period.



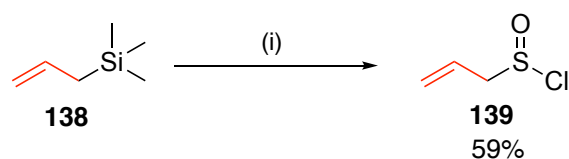
Scheme 3.2. *Reagents and conditions:* (i) acetic acid, sulfuryl chloride, –20 °C to rt to 35 °C, 6.5 h.

The reaction involves a simple work-up; evaporation of residual acetic acid and by-product acetyl chloride by distillation on a rotary evaporator affords the desired

sulfinyl chloride, usually isolated as a liquid. Herrmann's methodology worked effectively for the methyl and phenyl variants but did not function when trying to access the *tert*-butyl derivative **142** (0% yield). With this in mind, and to bolster the number of sulfinyl chlorides synthesised, other protocols were sought after to access the aforementioned *tert*-butyl and other sulfinyl chlorides.

3.2.3 Vogel's Protocol

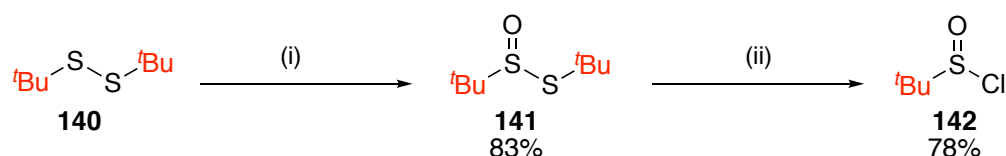
To access the allyl sulfinyl chloride variant, the method reported by Vogel and co-workers was utilised.⁹⁶ Vogel's protocol proceeded well - reacting allyltrimethylsilane **138** with two equivalents of thionyl chloride in the presence of 6 mol% aluminium trichloride afforded the desired allyl sulfinyl chloride **139** in 59% yield (Scheme 3.3).



Scheme 3.3. *Reagents and conditions:* (i) thionyl chloride (2 equiv.), aluminium trichloride (6 mol%), $-20\text{ }^{\circ}\text{C}$ to rt, 1 h.

3.2.4 Fernandez's Method

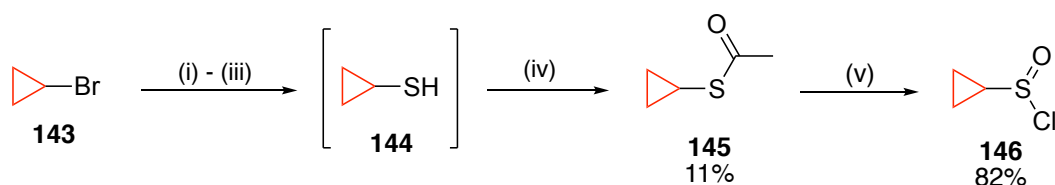
To access *tert*-butyl sulfinyl chloride **142**, the procedure reported by Fernandez and co-workers was employed.⁹⁷ *Tert*-butyldisulfide **140** was firstly oxidised to *tert*-butylthiosulfinate **141** in 83% yield using hydrogen peroxide (1.1 equivalents) and acetic acid (2 equivalents). Subsequently, *tert*-butylthiosulfinate **141** was reacted with one equivalent of sulfuryl chloride, and after gently removing volatiles, the desired *tert*-butyl sulfinyl chloride **142** product was obtained in 78% yield (Scheme 3.4).



Scheme 3.4. *Reagents and conditions:* (i) hydrogen peroxide (1.1 equiv.), acetic acid (2 equiv.), 0 °C – rt, 24 h; (ii) sulfonyl chloride (1 equiv.), dichloromethane, 0 °C – rt, 24 h.

3.2.5 Block's Procedure

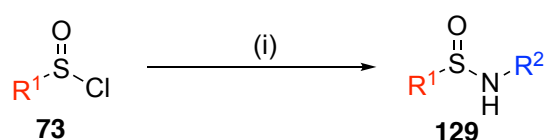
Cyclopropyl moieties have recently been incorporated in a number of biologically active molecules based on sulfur(VI) variants, and as such, a cyclopropyl sulfinyl chloride **146** would provide a suitable building block for the synthesis of cyclopropyl derived sulfonimides and sulfoximines in this project. The synthesis of cyclopropylsulfinyl chloride proved to be far lengthier with 3 operationally difficult steps to access the target compound. Following the methodology first reported by Block and co-workers, the synthesis was successfully replicated albeit in moderate yield (Scheme 3.5).⁹⁸ This protocol produced two incredibly volatile intermediates, undoubtedly the major issue when making cyclopropylsulfinyl chloride - firstly cyclopropanethiol **144** (only isolatable in a THF-ether solution due to its volatility), and secondly, *S*-cyclopropyl ethanethioate **145** – a foul smelling liquid that was isolated after evaporation under reduced pressure, yet proved volatile and may account for such a low yield to access this intermediate (11% yield).



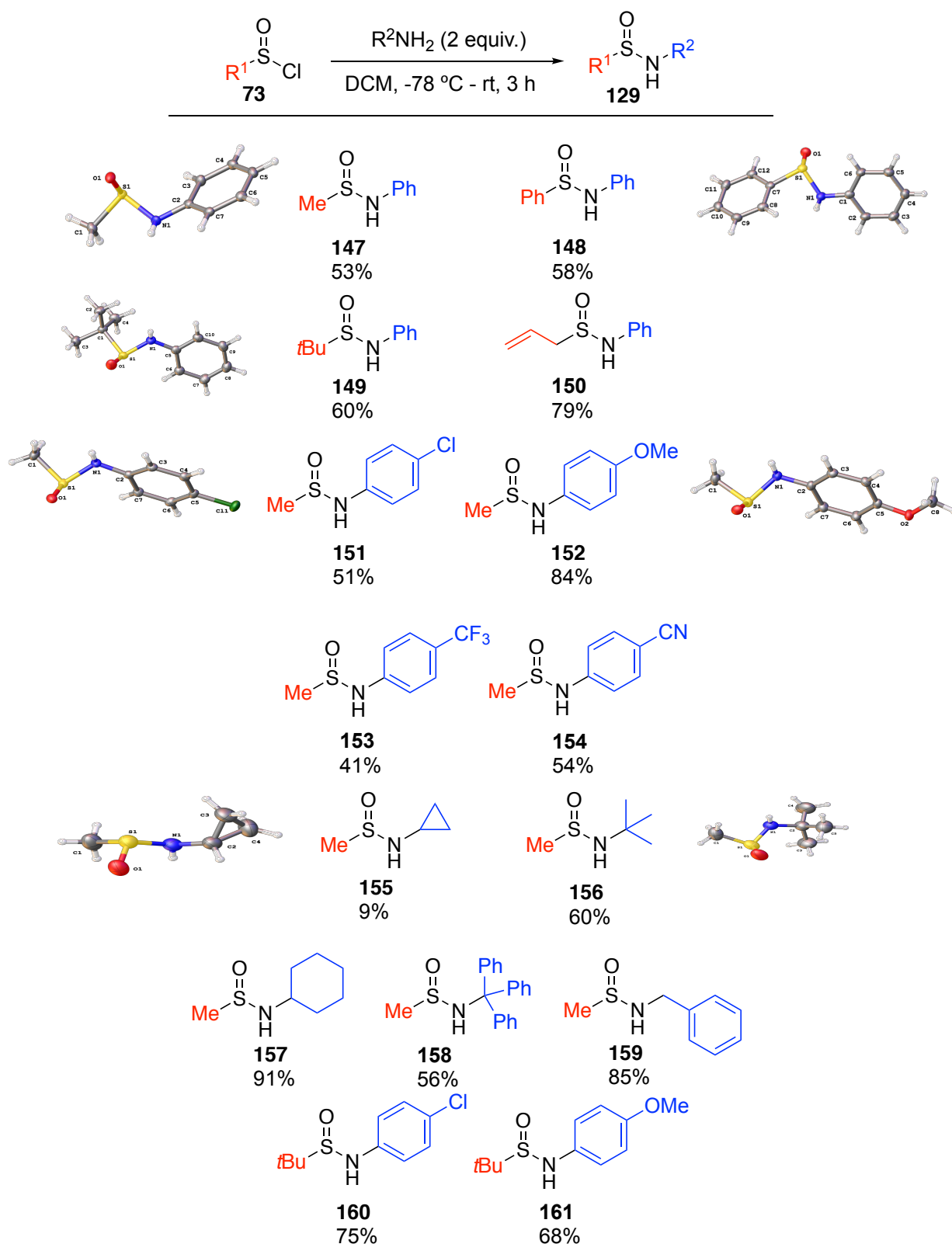
Scheme 3.5. *Reagents and conditions:* (i) Magnesium (1.8 equiv.), THF, 50 °C, 3 h; (ii) Sulfur-8 (1.5 equiv.), THF, 0-50 °C, 3 h; (iii) LiAlH₄ (1 equiv.), THF, 0 °C, 3 h then water; (iv) acetyl chloride (1.3 equiv.), sodium carbonate (4.1 equiv.), THF/Et₂O, rt, 18 h; (v) acetic anhydride (1 equiv.), sulfonyl chloride (2 equiv.), -10 °C to rt, 4 h.

3.3 Synthesis of Sulfinamides

With five sulfinyl chlorides to hand, the next step of the synthetic route was generating a library of sulfinamides **129** ready for oxidative cyclisation with iodosylbenzene to access sulfonimides. The sulfinamide could be modified at both R¹ and R² simply by changing the sulfinyl chloride **73** used and the amine reactant (Scheme 3.6). Optimised conditions found that reacting 2 equivalents of amine with one equivalent of sulfinyl chloride yielded the desired sulfinamides in yields ranging from 9% - 91% (Scheme 3.7). Initially, sulfinamides generated from methanesulfinyl chloride were studied – a range of amines were well tolerated, including cyclohexylamine, cyclopropylamine, *tert*-butylamine, benzylamine, *para*-substituted anilines and even bulky tritylamine.



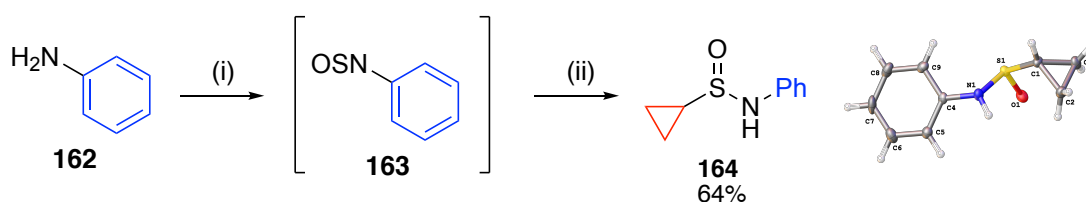
Scheme 3.6. *Reagents and conditions:* (i) R²NH₂ (2 equiv.), DCM, -78 °C - rt, 3 h



Scheme 3.7. Substrate scope for sulfinamide synthesis. Single crystal x-ray structures are shown adjacent to respective compounds.

As shown in Scheme 3.7 above, both phenyl, *tert*-butyl and allyl sulfinyl chloride were reacted with aniline and provided the target sulfinamides **148-150** in yields up to 79%. When *para*-substituted anilines were employed as amine source, both electron donating substituents, such as OMe (**152**), and electron withdrawing substituents such as CF₃ (**153**), CN (**154**) were all well incorporated. Pleasingly, sterically hindered amines such as *tert*-butyl amine and tritylamine gave the corresponding sulfinamides **156** and **158** in 60% and 56% respectively. Finally, cyclopropyl sulfinamide **155** could be accessed using cyclopropylamine, but due to volatility of the product, only 9% could be isolated. However, cyclohexylamine **157** gave the highest yield (91%) of all examples tested.

The hope was to employ cyclopropylsulfinyl chloride **146** formed in Scheme 3.5 to access sulfinamides containing a cyclopropyl substituent bound directly to the sulfur. However, due to such low yields obtained for cyclopropylsulfinyl chloride **146**, another approach to access the desired sulfinamide was utilised. Pal and co-workers have recently reported the direct synthesis of *N*-phenylcyclopropanesulfinamide **164** starting from thionyl chloride and aniline **162** (Scheme 3.8).⁹⁹ *N*-Thionylanilines **163** formed from the aforementioned reaction were then subjected to a Grignard reagent (cyclopropylmagnesium bromide), leading to the desired sulfinamide **164**. This transformation worked in good yield and allowed rapid access to the desired sulfinamide on a larger scale, starting from relatively cheap starting materials.

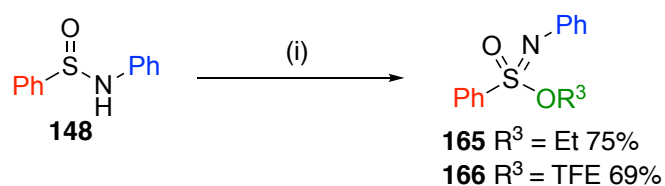


Scheme 3.8. *Reagents and conditions:* (i) thionyl chloride (1.3 equiv.), toluene, reflux, 2-3 h; (ii) cyclopropylmagnesium bromide (1.5 equiv.), THF, 0 °C - rt, 2 h.

With a broad range of sulfinamides in hand, the first step to accessing sulfoximines was complete. This library of sulfinamides would be converted into sulfonimides. After careful analysis of the literature, Malacria's hypervalent iodine mediated synthesis of sulfonimides from aryl sulfinamides proved significant to the project moving forwards (See introduction, section 2.2.3, page 36). With a range of sulfinamides to hand, the synthesis of various sulfonimide based substrates could be approached using Malacria's developed methodology.

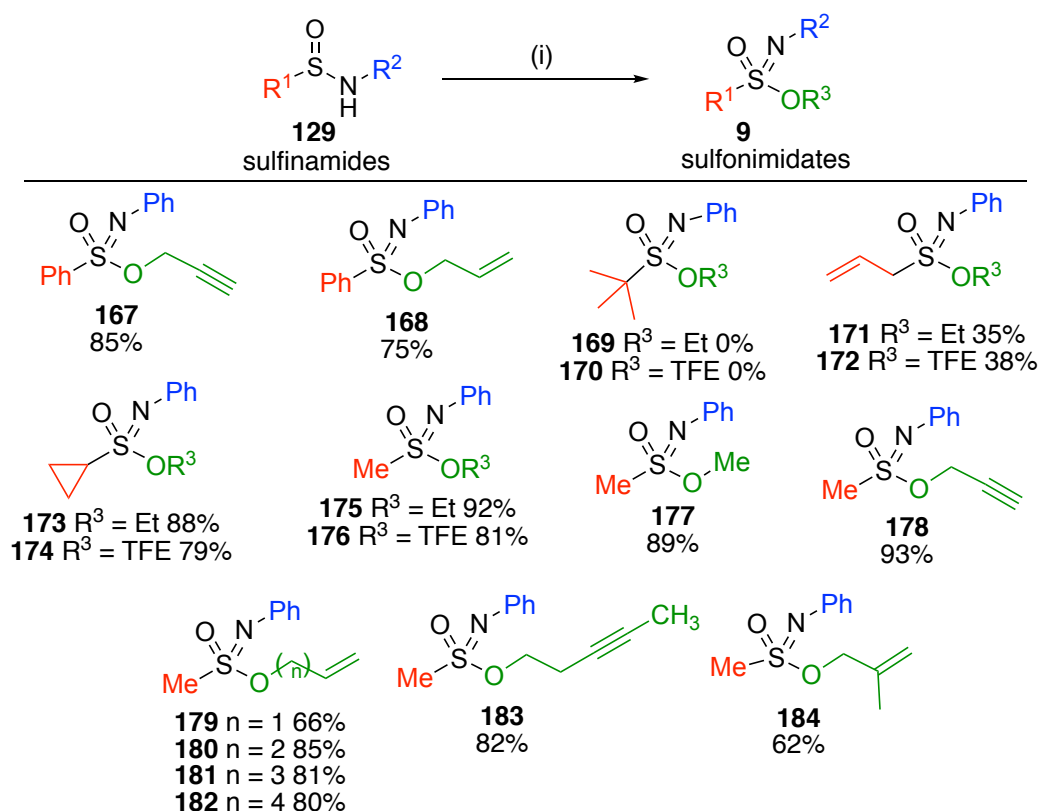
3.4 Synthesis of Sulfonimides

Initially, sulfonimide formation was performed *via* oxidation of the corresponding sulfinamides with iodosylbenzene in the presence of an excess of alcohol as solvent (Scheme 3.9).^{73,74,91} The oxidation of *N*-phenyl benzenesulfinamide **148** was trialled first under these conditions, and proceeded smoothly both in ethanol and trifluoroethanol to afford the desired sulfonimides **165** and **166** in good yields (75% and 69% respectively).



Scheme 3.9. *Reagents and conditions:* (i) PhIO (1 equiv.), R³OH, rt, 15 min.

Excited by these results, the substrate scope for the reaction was explored utilising these iodosylbenzene mediated conditions. Firstly, the alcohol functionality was varied - bond unsaturations are tolerated under these oxidising reaction conditions; this was confirmed by the formation of *O*-propargyl and *O*-allyl sulfonimides **167** and **168** (85% and 75% yields respectively, Scheme 3.10).



Scheme 3.10. Investigating the substrate scope of sulfonimide synthesis at R¹ and R³. *Reagents and conditions:* (i) Iodosylbenzene (1 equiv.), R³OH, rt, 15 min.

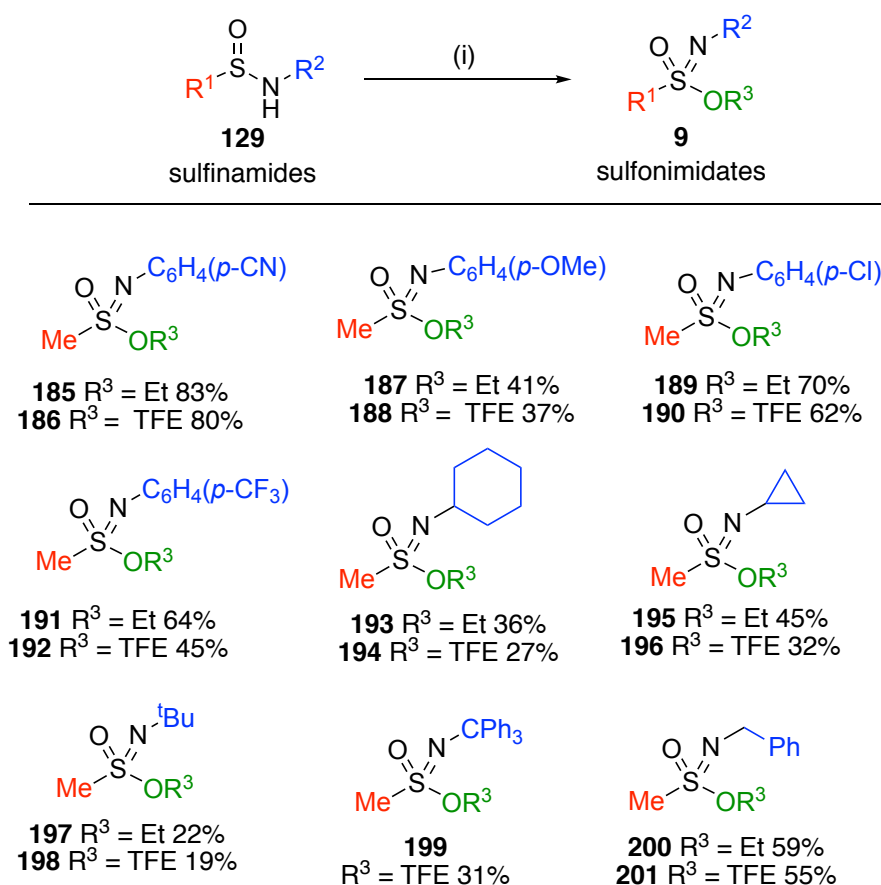
Previous studies in the literature for sulfonimide formation are limited almost exclusively to *S*-phenyl and *S*-tolyl substrates,^{73,74,91} and as such, further investigations into the scope of this transformation with regard to *S*-substitution became appealing. Unfortunately, the formation of the *S*-*t*Bu sulfonimides **169** or **170** failed under these conditions, presumably due to steric hindrance. When switching to the *S*-allyl functionality, sulfonimides **171** and **172** were isolated in

reduced yields of 35% and 38% respectively. Pleasingly, however, the medically relevant *S*-cyclopropyl derivatives **173** and **174** could be accessed in 88% and 79% yields, respectively.

For the purposes of many drug discovery programs, low molecular weight fragments are favoured so that screening compounds can be developed that populate “Lipinski space”.¹⁰⁰ Satisfyingly, the highest yields were obtained in the synthesis of *S*-methyl sulfonimides **175** and **176** (92% and 81% yields, Scheme 3.10). Consequently, *N*-phenyl methanesulfonamide **147** was selected as a test substrate to further investigate the scope of the reaction with regard to the alcohol component – a range of alkyl, alkenyl (linear and branched) and even alkynyl based alcohols proceeded well in the transformation (yields ranging between 62-93% for substrates **177-184**). As shown with all examples in both Scheme 3.10 and 3.11, in all cases, primary alcohols proceeded well. When either a secondary alcohol (*iso*-propanol) or tertiary alcohol (*tert*-butyl alcohol) were trialled as alcohol for the transformation, the desired sulfonimide was not observed. These outcomes are matched by Malacria’s research team who noted a similar result when *iso*-propanol led to a depleted yield of sulfonimide, whilst *tert*-butanol gave no sulfonimide product, but in fact sulfonamide.⁷³ The solvolysis of iodobenzene appears to be optimum when non-sterically demanding primary alcohols are utilised.

In their proposed role as an intermediate for sulfoximine synthesis, however, the “alkoxyl” substituent on the sulfonimide core would serve as a leaving group. Ethanol and trifluoroethanol were selected to screen the scope of sulfonimide formation with regard to *N*-substitution (Scheme 3.11). The effect of incorporating electron-rich and -poor *N*-aryl substituents was investigated.

Pleasingly, the *p*-cyano, -methoxy, -chloro and -trifluoromethyl sulfonimides **185-192** were obtained in yields ranging from 37-83%, with the lowest product yields found when the *p*-methoxy substituent was used. After investigating *N*-aryl modifications, *N*-alkyl modifications were trialled – cycloalkanes such as cyclohexyl **193/194** and cyclopropyl **195/196** gave moderate reaction yields (27-45%), whilst *N*-benzyl sulfonimide **200** and **201** were formed in improved yields of 59% and 55% respectively. Sterically demanding substituents such as *N*-*tert*-butyl **197/198** and *N*-trityl **199** were also afforded, indicating that bulky substituents are better tolerated on the nitrogen atom of the sulfonimide scaffold, rather than on the sulfur or the alcohol substituent (Scheme 3.11).



Scheme 3.11. Investigating substrate scope of sulfonimides at R². *Reagents and conditions:* (i) Iodosylbenzene (1 equiv.), R³OH, rt, 15 min.

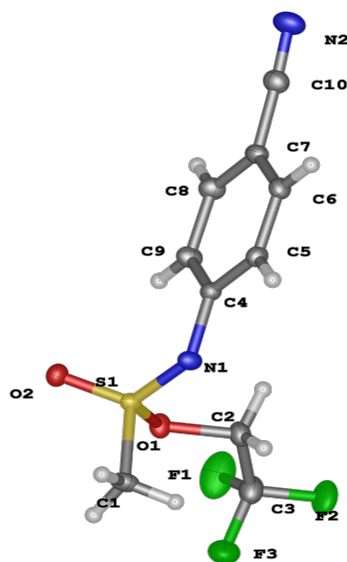


Figure 3.1. Single crystal X-ray analysis of 2,2,2-trifluoroethyl *N*-(4-cyanophenyl)methanesulfonimide **186**.

With a succinct analysis of reaction scope, the best yields for sulfonimide formation were obtained with *N*-aryl substrates. As such, *N*-phenyl sulfonimides **175** and **176** were selected as test substrates to probe sulfoximine formation by Grignard addition.

3.5 Synthesis of Sulfoximines

The conversion of sulfonimides into sulfoximines was initially optimised to find the best reaction conditions – investigations looked at two sulfonimides - **175** and its analogous trifluoroethyl **176** derivative (Table 3.1). Initially, the reaction was attempted using the conditions reported by Cram,⁶⁷ with the addition of 5 equivalents of Grignard reagent at 25 °C in diethyl ether as reaction solvent. Under these conditions, the desired product **202** was obtained in 52% yield.

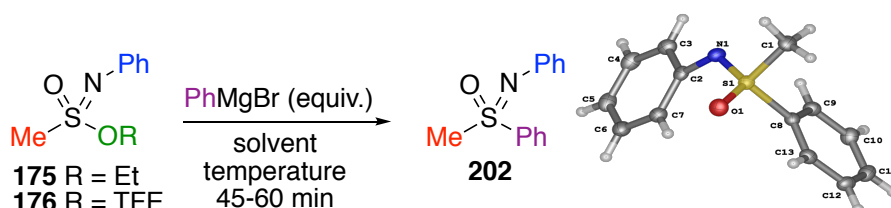


Table 3.1. Optimisation Study for Converting Sulfonimides into Sulfoximines.

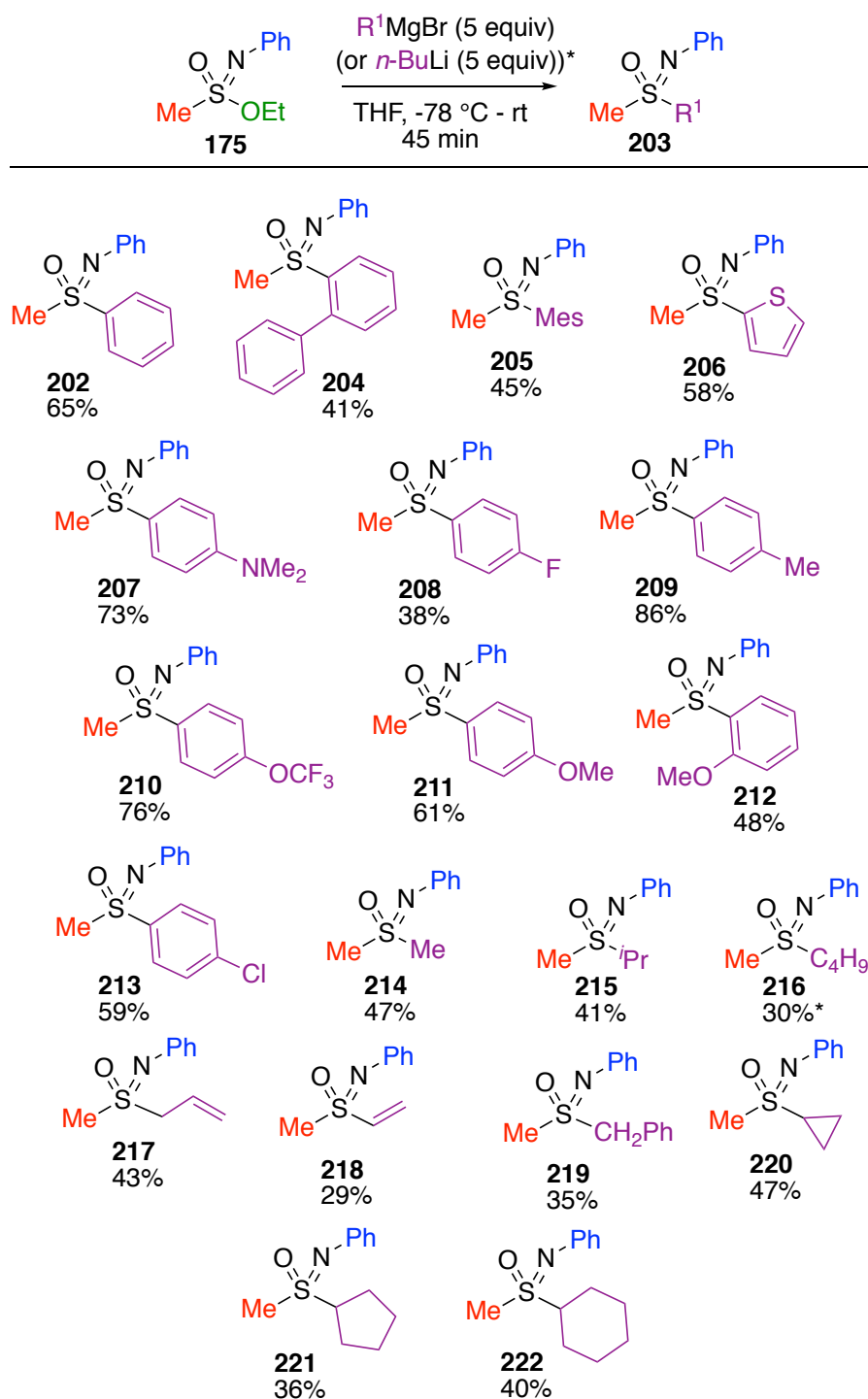
Entry	Starting Material	PhMgBr (equiv)	Solvent	Temp (°C)	Isolated Yield of 202 (%)
1	175	5	Et ₂ O	25	52
2	175	5	Et ₂ O	−78	55
3	175	5	toluene	−78	48
4	175	5	THF	−78	65
5	175	3	THF	−78	54
6	175	1	THF	−78	31
7	175	5	THF	−20	59
8	175	5	THF	0	41
9	176	5	THF	−78	42

Next the reaction was attempted at $-78\text{ }^{\circ}\text{C}$, again with 5 equivalents of Grignard reagent being employed. In this case, the desired sulfoximine **202** was obtained in a moderately improved 55% yield. Changing the reaction solvent to toluene caused a reduction in yield (48%). However, superior conditions were found when THF was employed (65%). Reducing the equivalents of organometallic to 3 and 1 equiv served to reduce the yields (54% and 31%, respectively) as did raising the reaction temperature to -20 or $0\text{ }^{\circ}\text{C}$ (59% and 41%, respectively). The trifluorethyl-derived sulfonimide **176** produced lower yields of sulfoximine than the ethyl derivative **175**. Confirmation of the final product was achieved through X-ray analysis after obtaining crystals of **202** (see experimental for X-ray data).

With the optimised conditions in hand, we set out to investigate the substrate scope of sulfoximine formation with respect to the organometallic component (Scheme 3.12). Firstly, aryl derived Grignard reagents were trialled in the transformation; after the success of phenylmagnesium bromide in the transformation (65% yield of the desired sulfoximine), sterically hindered aryl Grignard's such as biphenyl and mesityl led to an erosion in yield (41% and 45% yield respectively). Introduction of heteroaryl Grignards was also demonstrated to be possible with the 2-thienyl sulfoximine **206** being obtained in 58% yield.

The application of monosubstituted aryl Grignard reagents in the transformation was met with varying success. As shown in Scheme 3.12, *para*-tolyl magnesium bromide gave the best yield of 86% for the respective sulfoximine product. *Para*-methoxy and -dimethylamino aryl Grignards also provided good yields of 61% and 73% yield, whilst changing to a *para*-halide substituted aryl Grignard (*p*-F and *p*-Cl) gave lower yields of 38% and 59% yield respectively. Substitution at the *ortho*-

ring position (*o*-OMe) gave sulfoximine **212** in 48% yield. Changing to alkyl derived Grignard reagents gave access to sulfoximines in moderate to good yields – first of all, methylmagnesium chloride gave dimethylsulfoximine **214** in 47% yield.



Scheme 3.12. Synthesis of sulfoximines from sulfonimides.

Both allylmagnesium bromide and vinylmagnesium bromide afforded the respective sulfoximines **217** and **218** in 43% and 29% yield, whilst *iso*-propyl (41%), and benzyl (35%) based Grignards were tolerated in moderate yields as well. In one single case, the butyl sulfoximine **216** was accessed using *n*-butyllithium in a moderate yield of 30%.

There are a number of medicinally relevant sulfoximines in the literature that incorporate the cyclopropyl moiety bonded directly to the sulfur (see drug molecule AZD 6738 **223**, Figure 3.2). Pleasingly, a range of cycloalkyl Grignard reagents worked in the transformation – cyclopropyl (47%), cyclopentyl (36%) and cyclohexyl (40%) (Scheme 3.12, sulfoximines **220-222**).

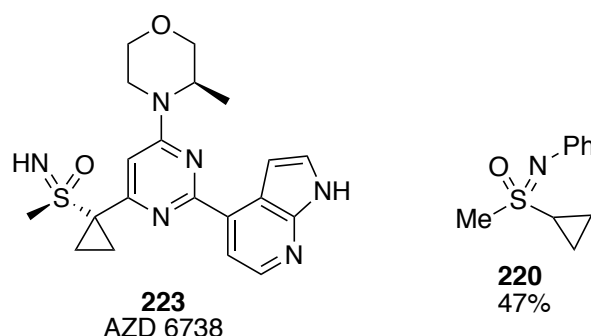
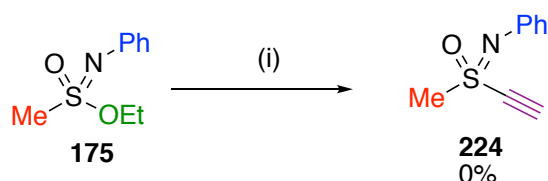


Figure 3.2. Drug molecule AZD 6738 and sulfoximine **220** synthesized in this work.

When substrate **175** was subjected to alkynyl magnesium bromide, the desired sulfoximine **224** was not obtained (Scheme 3.13). However, an interesting cyclic sulfoximine product **225** was obtained from the reaction in 29% yield (Figure 3.3). The structure of **225** was determined by NMR analysis along with single crystal X-ray analysis.



Scheme 3.13. Grignard addition to sulfonimide **175**. *Reagents and conditions:*

alkynyl magnesium bromide (5 equiv.), THF, -78 °C – rt, 45 min.

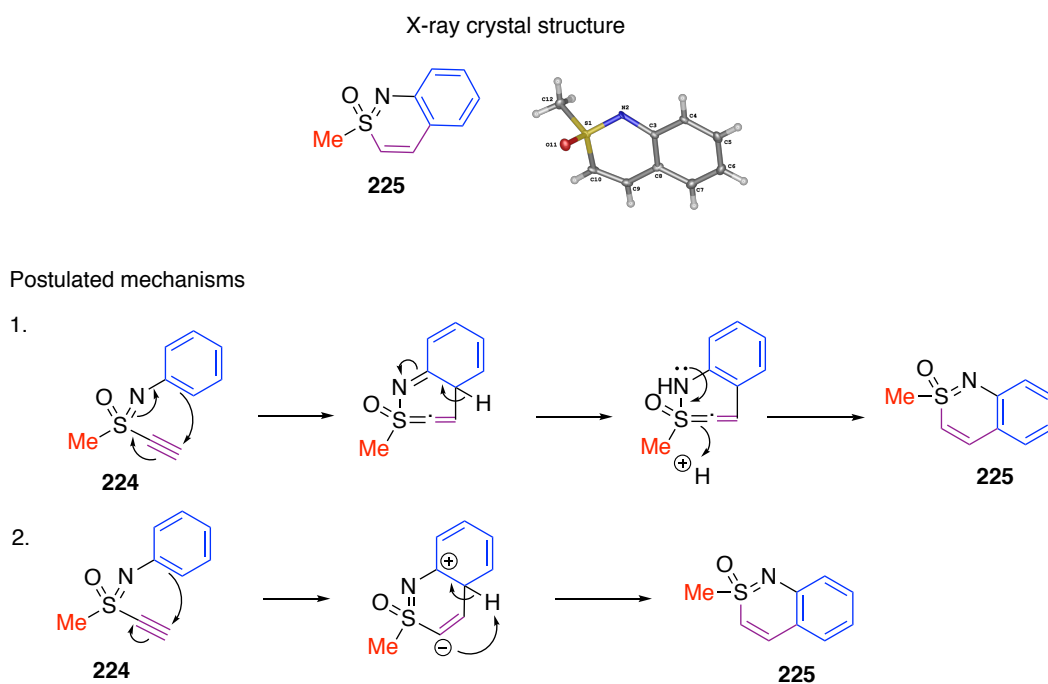


Figure 3.3. Above: Cyclic sulfoximine product **225** and its crystal structure. Below: Two postulated routes to access product **225** from alkynyl Grignard addition to sulfonimide **175**.

The reaction was repeatable; yields remained consistent on numerous replications of the reaction conditions. Attempts were made to elucidate why and how this product came to form. Investigations into other sulfonimides **187-200** reacting with this particular Grignard reagent were trialled (Table 3.2). Sulfonimides bearing a *para*-substituted aryl substituent on the nitrogen (entries 1-3), showed no sign of Grignard attack on the sulfur atom, and no sign of cyclic sulfoximine product **228**, with only starting material recovered after 45 minutes. When the

nitrogen substituent remained as phenyl but modifying the methyl-sulfur bond (to either allyl/cyclopropyl - entries 4 and 5), neither sulfoximine product was observed and only starting material recovered. Using either an *N*-benzyl or *N*-cyclohexyl sulfonimide (entries 6 and 7) did not yield any sulfoximine product from Grignard attack at the sulfur. Leaving any of these reactions for extended reaction times, along with raising the temperature of the reaction slowly, only afforded the corresponding unwanted sulfonamide products.

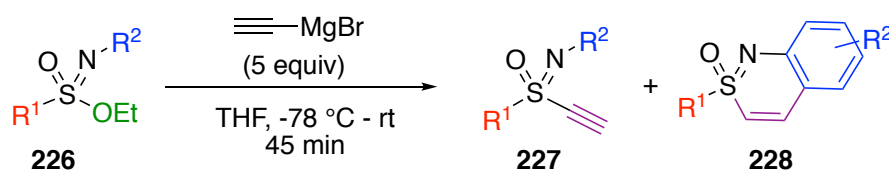
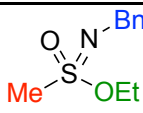
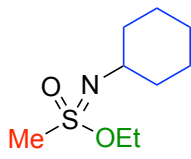
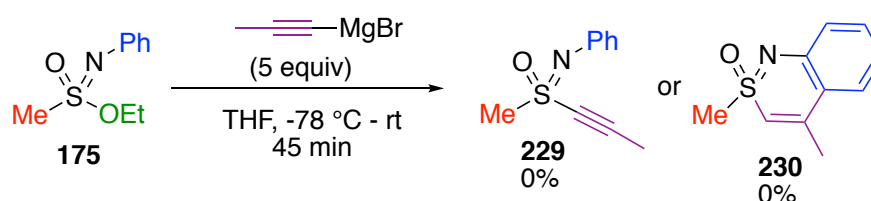


Table 3.2. Investigating substrate scope with alkynyl magnesium bromide.

Entry	Starting material	Yield of 227 (%)	Yield of 228 (%)
1	 187	0	0
2	 189	0	0
3	 191	0	0
4	 171	0	0
5	 173	0	0

6	 200	0	0
7	 193	0	0

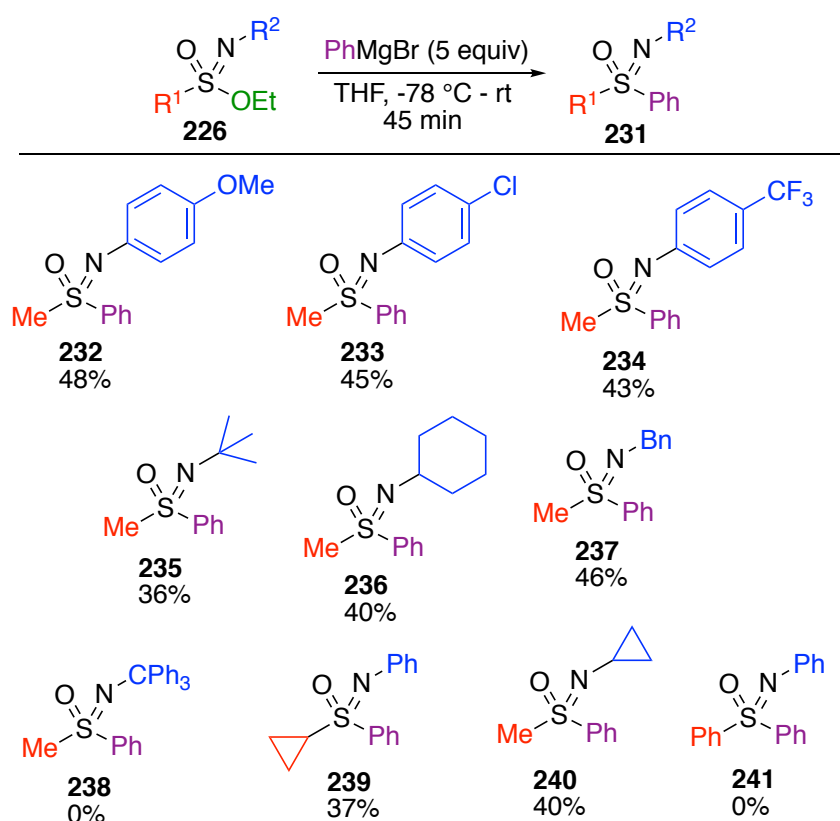
Switching to an alternative alkynyl Grignard reagent, 1-propynylmagnesium bromide, (Scheme 3.14), only afforded recovered starting material, with no sulfoximine product obtained. These experiments confirm that this unusual transformation is substrate specific for one example currently (Figure 3.3).



Scheme 3.14. Attempted sulfoximine synthesis from sulfonylimide **175** and 1-propynylmagnesium bromide.

Following on from these studies on substrate scope with respect to varying the organometallic species used, focus was next turned to modification of the sulfoximine at the nitrogen atom or the sulfur atom (Scheme 3.15). In this case, the optimised reaction conditions were utilised as in Scheme 3.12, only this time phenylmagnesium bromide was used as the Grignard reagent. Both electron-donating and -withdrawing groups were tolerated comparably on nitrogen-aryl derivatives; the *para*-methoxy, -chloro and -trifluoromethyl sulfoximines **232-234** were obtained in 43–48% yields. *N*-Alkyl substituents such as *tert*-butyl,

cyclohexyl, and benzyl performed well in the transformation, affording sulfoximines **235-237** in yields of 36%, 40% and 46% yield – however, when *N*-trityl sulfonimide was employed in the transformation, the desired sulfoximine **238** was not formed. In the case of incorporating cyclopropyl moieties on either the sulfur or nitrogen atom, both sulfonimides reacted well with phenylmagnesium bromide to afford the desired sulfoximines **239** and **240** in 37% and 40% yields respectively. When a phenyl substituent is on the sulfur atom, no desired sulfoximine **241** was observed.



Scheme 3.15. Synthesis of sulfoximines with alternating *N*- or *S*- substitution.

With a range of sulfoximines accessed using this methodology, and due to the medicinal properties of sulfoximines in drug discovery programs, a library of sulfoximines were screened for antibacterial activity in collaboration with the Biomaterials-Related Infection Group at University of Nottingham.

3.6 Antibacterial Activity of Sulfoximines

The work detailed in this section highlights the experiments captured by Dr. Katherine Belfield and Professor Roger Bayston at the Biomaterials-Related Infection Group, University of Nottingham. Novel sulfoximines (Figure 3.4) were screened for antibacterial activity by broth microdilution against a representative gram-positive and gram-negative organism. Results showed the novel sulfoximine compounds tested, none were able to inhibit bacterial growth at a concentration of 512 mg/L or less. Therefore, the only conclusions are that the MICs and MBCs against *S. aureus* and *E. coli* are greater than 512 mg/L for all compounds.

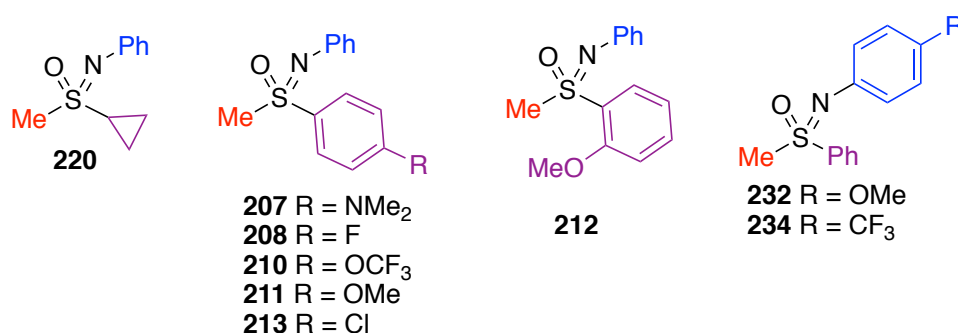


Figure 3.4. Sulfoximine molecules trialled.

Details of the method utilized by the Biomaterials-Related Infection Group include:

Broth Microdilution Method:

Method is in accordance with ISO 20776-1:2006

1. Prepare a 5×10^5 CFU/mL bacterial inoculum in Mueller-Hinton broth (MHB)
2. Add 100 μ L of sterile MHB to all rows in triplicate in 96-well plate
3. Add 100 μ L of compound stock solution (1024 mg/L) to the wells in the first column
4. Serially dilute 100 μ L along the columns leaving the last column free from the compound as control for positive bacterial growth
5. To all wells at 10 μ L of adjusted bacterial suspension
6. Incubate aerobically overnight at 37 °C.

7. After incubation, determine the Minimum Inhibitory Concentration (MIC) visually by examining wells for turbidity. The MIC is the lowest concentration which inhibits visual growth.
8. To determine the Minimum Bactericidal Concentration (MBC) spot plate 10 μ L from each clear well (ie no growth) onto blood agar.
9. Incubate blood agar plates overnight aerobically at 37 °C.

MBC is determined by the lowest concentration that has prevented growth. In conclusion, none of the nine compounds showed antimicrobial activity against *Staphylococcus aureus* or *Escherichia coli*.

3.7 Conclusions: Synthesis of Functionalised Sulfoximines *via* Sulfonimides

In conclusion, a general method for the synthesis of sulfoximines has been developed that proceeds *via* C–S bond formation.¹⁰¹ The sulfoximines generated have three points of diversity, allowing access to 3D space – it is envisaged that this method in the near future may be utilised in drug discovery programs to access the next generation of bioactive sulfoximines.

The procedure utilises the reaction of organometallic reagents with sulfonimides, a class of compounds that have not been widely employed as precursors to sulfoximines. Two key advantages of this transformation over other methods include utilising commercially available Grignard reagents and short reaction times. A few select Grignard reagents proved to be unreactive in this methodology however, namely alkynyl derived Grignard reagents, and in one example, provided access to an interesting cyclic sulfoximine product.

Moreover, to compliment this strategy towards sulfoximine synthesis, the scope of sulfonimide formation *via* the oxidation of sulfinamides has been greatly expanded and shown to include *S*-alkyl substrates for the first time. The inexpensive and ready availability of starting materials, namely anilines and disulfides for sulfinamide synthesis, was a benefit in generating a library of compounds.

Whilst a selection of the sulfoximines performed poorly in an antibacterial study, they may still prove to have applications as potent agrochemicals or in other areas of medicinal chemistry programmes, such as oncology.

4

Chapter Four

Results and Discussions

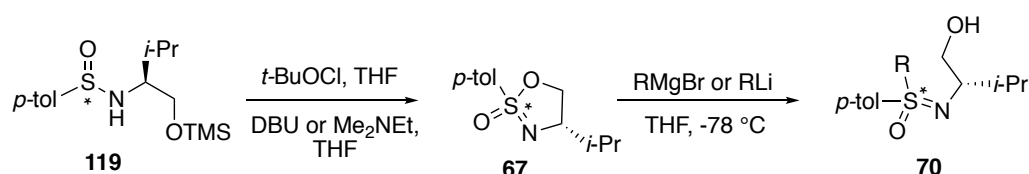
Synthesis of Enantioenriched Sulfoximines

4.0 Results and Discussion: Enantioenriched Sulfoximines

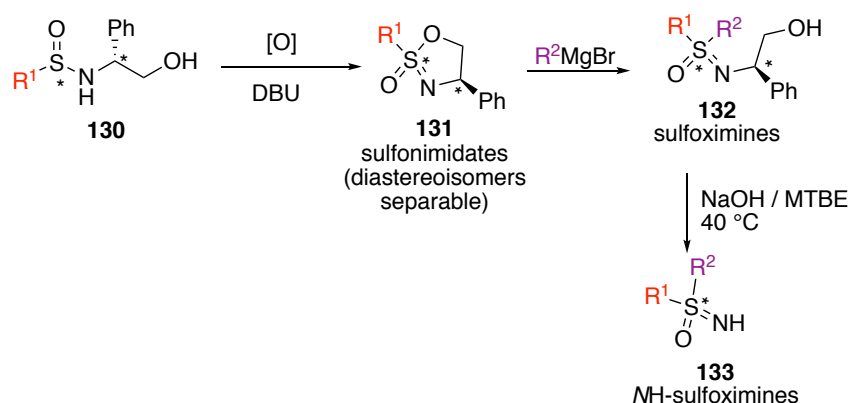
4.1 Cyclic Sulfonimide to Sulfoximine Overview

The synthesis of cyclic sulfonimides **67** was originally discovered by Reggeline and co-workers in 1992.⁷⁰ Their pioneering studies showed further applications of these cyclic sulfonimides – ring opening with organometallic reagents yielded sulfoximines **70** bearing an *N*-valinol moiety (Scheme 4.1, a). In a subsequent publication by the same research group, they reported cleavage of the *N*-valinol group on the sulfoximine core over three steps to access enantioenriched NH-sulfoximines (Scheme 4.10).¹⁰²

a) Reggeline's protocol



b) This work



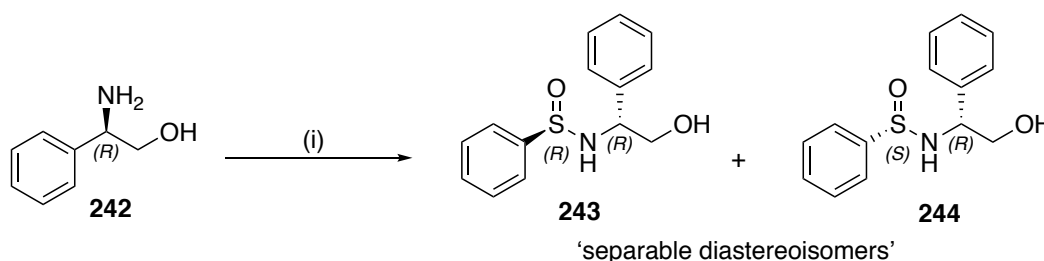
Scheme 4.1. Sulfoximine synthesis; (a) Reggeline's protocol. (b) this work.

The work conducted in this chapter proposes a new approach to cyclic sulfonimides **131**, and subsequent Grignard addition followed by base catalysed auxiliary removal to afford enantioenriched NH-sulfoximines **133** in a reduced

number of steps. To begin the project, sulfinamides **130** would prove to be a similar starting point, except (*R*)-phenylglycinol would be used instead of (*S*)-valinol (UV-active, ease of removal at a late stage, Scheme 4.1, b).

4.2 Synthesis of Sulfinamides bearing Chiral Amino Alcohols

To access a range of sulfinamides, the reaction between sulfinyl chlorides and chiral amino alcohols in dichloromethane at 0 °C was conducted. Subsequent addition of NaOH in MeOH selectively cleaved one of the sulfinyl groups to give the desired sulfinamide.¹⁰³ Diastereomers formed at this point could be separated using column chromatography, but also can be separated at later stages if necessary (for example the cyclic sulfonimides). The first sulfinamide that was accessed using this method was formed from phenylsulfinyl chloride and (*R*)-phenylglycinol **242**, affording separable diastereoisomers **243** and **244** in a combined 90% yield (Scheme 4.2).



Scheme 4.2. *Reagents and conditions:* (i) PhSOCl **136**, CH_2Cl_2 , Et_3N , 0 °C – rt, 3-4 h. (ii) NaOH/MeOH.

Sulfinamides **243** and **244** were successfully separated. Excitingly, sulfinamide **244** was crystallised by slow evaporation from dichloromethane, affording single crystals suitable for X-ray analysis (Figure 4.1).

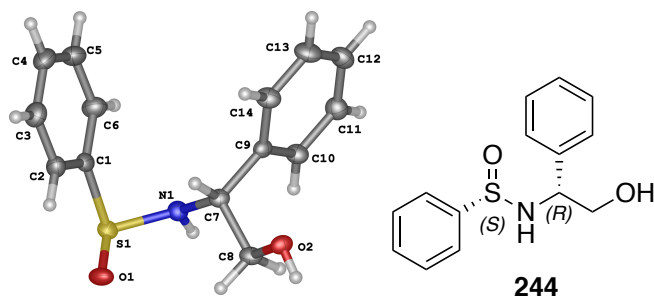
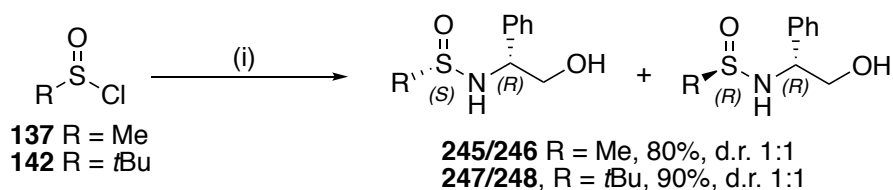


Figure 4.1. X-ray analysis of (*S*)-*N*-((*R*)-2-hydroxy-1-phenylethyl)benzenesulfonamide **244**.

Under these conditions an additional two sulfinamides were synthesised (Scheme 4.3). Modification at the sulfur atom was trialled first; introduction of methanesulfinyl chloride **137** and *tert*-butylsulfinyl chloride **142** in place of the phenylsulfinyl chloride **136** gave the corresponding methyl sulfinamides **245/246** (d.r. 1:1, 80%) and *tert*-butylsulfinamide **247/248** (d.r. 1:1, 90%) respectively (both diastereoisomers as a combined yield).



Scheme 4.3. Reagents and conditions: (i) (*R*)-phenylglycinol **242**, CH₂Cl₂, Et₃N, 0 °C – rt, 3-4 h. (ii) NaOH/MeOH.

Purification of both the methyl sulfinamides **245** and **246**, and *tert*-butyl sulfinamides **247** and **248**, in both cases the diastereomers were successfully separated. Excitingly, methyl derived sulfinamide **245** (*S,R*) was successfully crystallised by slow evaporation from dichloromethane, affording single crystals suitable for X-ray analysis (Figure 4.2). Moreover, *tert*-butylsulfinamide **247** crystallised by slow evaporation from ethyl acetate (Figure 4.3).

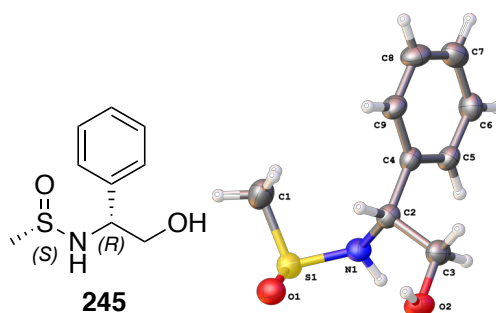


Figure 4.2. X-ray analysis of (*S*)-*N*-((*R*)-2-hydroxy-1-phenylethyl)methanesulfinamide **245**.

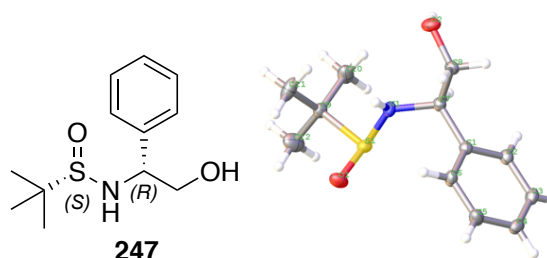
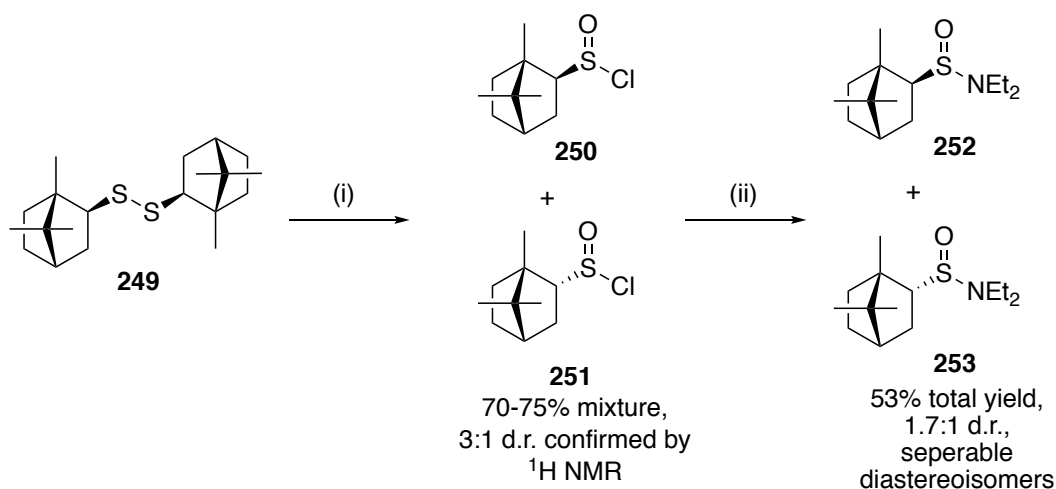


Figure 4.3. X-ray analysis of *N*-((*R*)-2-hydroxy-1-phenylethyl)-2-methylpropane-2-sulfinamide **247**.

The synthesis of diastereomeric sulfinyl chlorides would allow the formation of diastereomeric sulfinamide as starting material. The only reported synthesis of such sulfinyl chlorides was by Izmetev and co-workers in 2014 (Scheme 4.4),¹⁰⁴ in which isobornanesulfinyl chloride **250/251** was formed in a 3:1 diastereomeric ratio by reacting diisobornyl disulfide **249** with aqueous chlorine dioxide in dichloromethane. The authors only identify the compound through NMR analysis and show further evidence of its formation by reacting the sulfinyl chloride with diethylamine, affording the corresponding sulfinamides **252/253** in a 1.7:1 diastereomeric ratio.



Scheme 4.4. Izmetev's synthesis of diastereomeric sulfinyl chlorides. *Reagents*

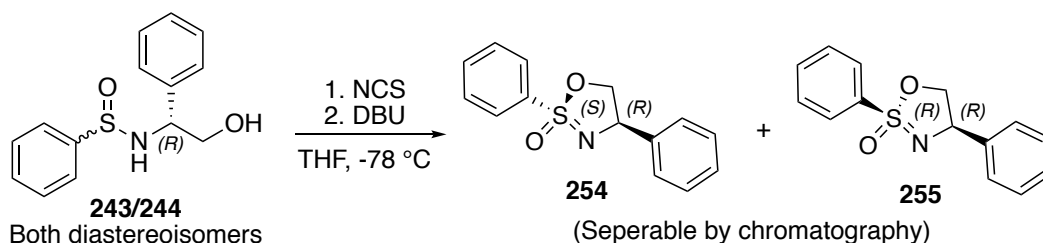
and conditions: (i) ClO_2 (aq), CH_2Cl_2 , rt, 0.5 h; (ii) Et_2NH , CH_2Cl_2 , rt.

Since Izmetev's methodology relies on the chiral substituent on the disulfide as the C-S bond substituent, and that this disulfide is not commercially available and has to be synthesised itself,¹⁰⁵ this methodology was not pursued as a route to access single diastereoisomers of sulfinamides.

4.3 Cyclic Sulfonimide Synthesis

With three sulfinamides to hand, the project moved onto the synthesis of cyclic sulfonimides. The Reggeli group have previously reported the oxidative chlorination of sulfinamides to sulfonimidoyl chlorides, followed by cyclisation to give cyclic sulfonimides. Their research group advocate the use of *tert*-butylhypochlorite for the oxidative chlorination step – a reagent that works well, but poses a number of safety risks due to its reactivity with sunlight and when coming into contact with rubber.¹⁰⁶ With this in mind, *N*-chlorosuccinimide was trialled instead of *tert*-butylhypochlorite (Scheme 4.5). Initially, one equivalent of NCS was trialled – cyclised product along with recovered starting material was

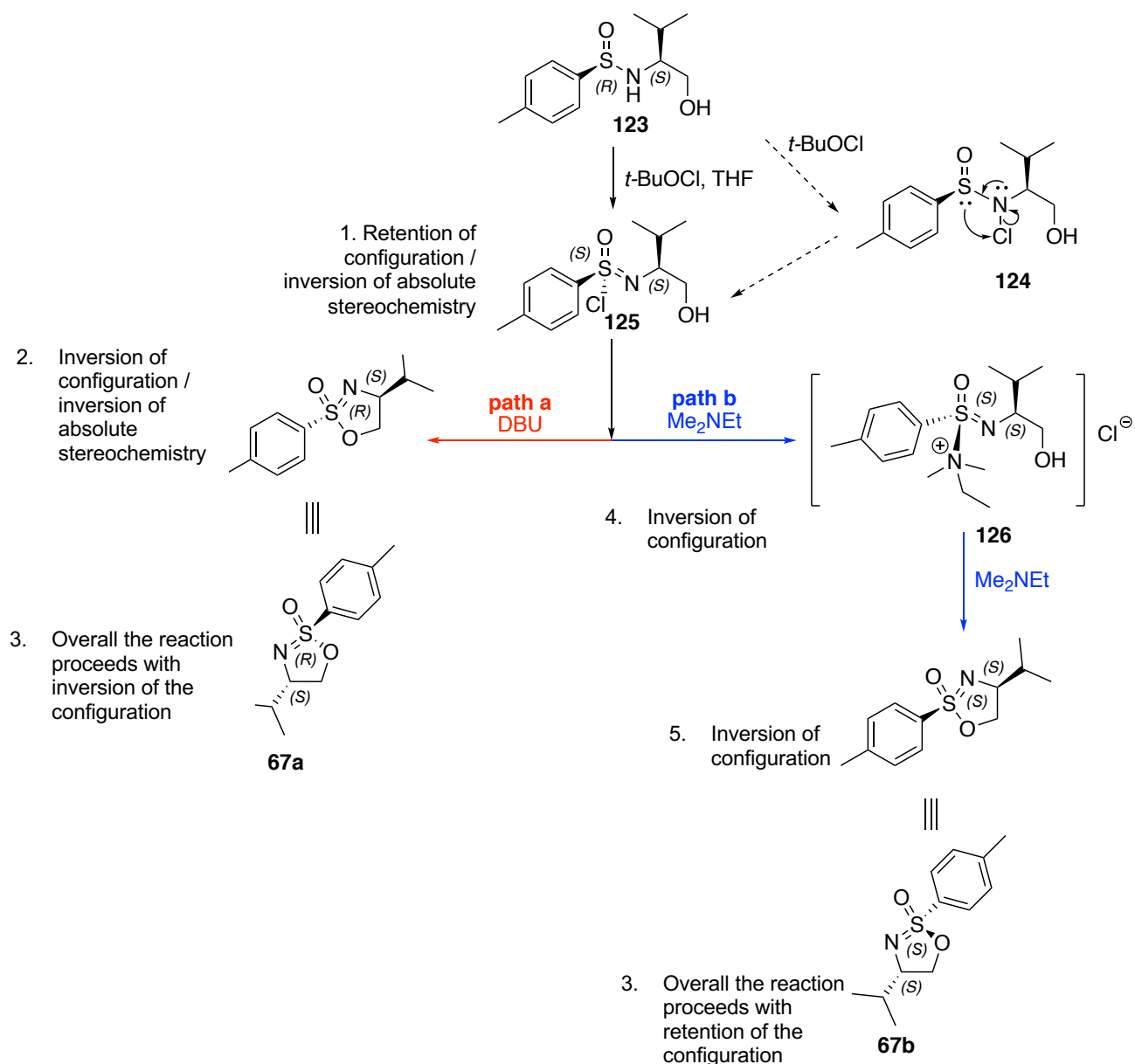
observed. Increasing to two equivalents of NCS gave an optimum product yield of 86% (d.r. 1:1) of **254/255**. Increasing to three equivalents was the limit of the reaction – both starting material **243/244** was consumed, but no product **254/255** was observed by TLC or mass spectrometry.



Scheme 4.5. Synthesis of 2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide **254/255**.

Tert-butylhypochlorite (made from *tert*-butanol, sodium hypochlorite and acetic acid)¹⁰⁷ was then trialled as an oxidant in the place of NCS. This proved to be a better alternative as the by-product is *tert*-butanol that can be easily removed under reduced pressure, compared to succinimide, providing a cleaner reaction and affording diastereomeric products **254/255** in 92% yield, 1:1 d.r.

Oxidative chlorination using either NCS or *tert*-butylhypochlorite provided the best option to maintain stereochemistry at the sulfur atom in the reaction. As previously described in the introduction (and shown below again, Scheme 4.6), Reggelin and co-workers conducted detailed experiments to elucidate the control during the oxidative chlorination-base cyclisation step.⁹² As shown in the scheme, judicious choice of base dictates the stereochemistry of the cyclic sulfonimide obtained.

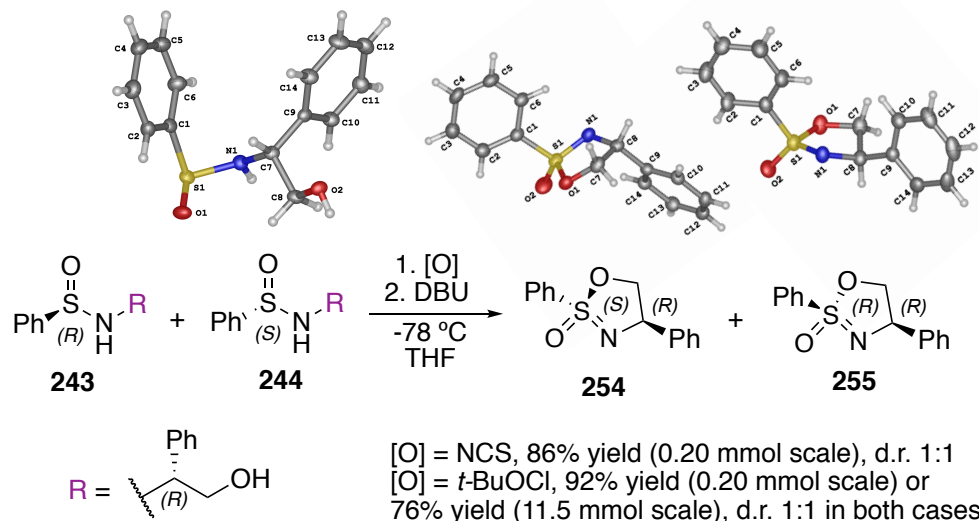


Scheme 4.6. Reggeli's oxidative chlorination-base cyclisation study.

As shown above in Scheme 4.6, DBU was used as the desired base (path a, Scheme 4.6). It was important to find more information about the stereochemical outcome of this cyclisation with the sulfinamides synthesised in this second project.

Taking single diastereomer sulfinamide **244** (of which a crystal structure was in hand, Scheme 4.7) and subjecting it to the reaction conditions, pleasingly sulfonimide **254** was obtained as a single product. The stereochemistry of **254**

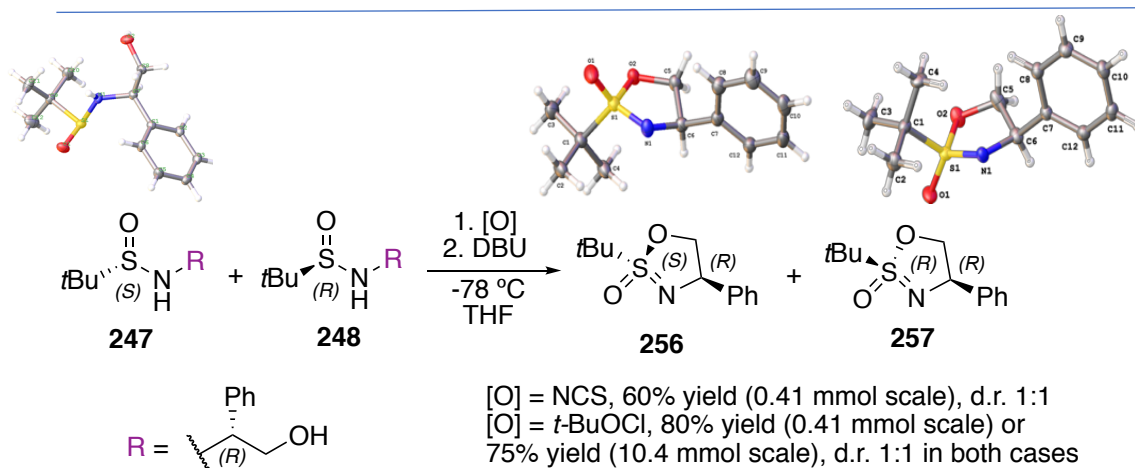
was confirmed by X-ray crystallography and matches with Reggelin's findings as shown in Scheme 4.6 - overall the reaction proceeds with inversion of the configuration when DBU is used as base.



Scheme 4.7. Initial study of cyclisation of cyclic phenylsulfonimide **254/255**.

After confirming the stereochemistry pattern, the most facile way to access cyclic sulfonimides **254/255** is to use a combination of both sulfinamide diastereoisomers **243/244** (1:1 diastereomeric ratio, difficult to separate chromatographically), and then separate the cyclic sulfonimide products **254/255** after the cyclisation has occurred.

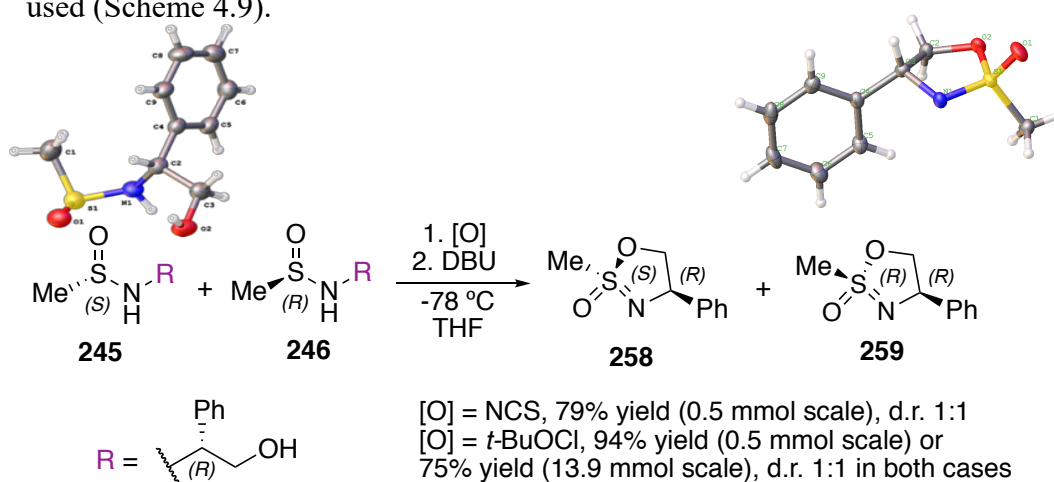
The aim was to synthesise a range of cyclic sulfonimides, allowing functionalisation at the sulfur centre. *Tert*-butyl sulfinamide **247** and **248** were firstly subjected to the oxidative chlorination-base cyclisation conditions (Scheme 4.8). In both cases, the isolated product yields for **256** and **257** were slightly lower than that obtained for the phenyl variant as described in Scheme 4.7, presumably due to steric hinderance of the cumbersome *tert*-butyl group. The absolute configuration of the products was determined by X-ray crystallography.



Scheme 4.8. Oxidative chlorination-base cyclisation of *tert*-butylsulfonamide **247** and **248**.

Taking single diastereomer sulfonamide **247** (of which a crystal structure was in hand, Scheme 4.8) and subjecting it to the reaction conditions, pleasingly sulfonimide **256** was obtained as a single product.

The final cyclic sulfonimides to be accessed are the methyl variants **258** and **259**. Subjecting methylsulfonamides **245** and **246** to standard oxidation-cyclisation conditions gave the respective cyclic sulfonimides. The yields for the methyl-derived cyclic sulfonimides were excellent when either NCS or *t*-BuOCl were used (Scheme 4.9).



Scheme 4.9. Oxidative chlorination-base cyclisation of methylsulfonamides **245** and **246**.

Taking single diastereomer sulfinamide **246** and subjecting it to the reaction conditions, pleasingly sulfonimide **259** was obtained as a single product.

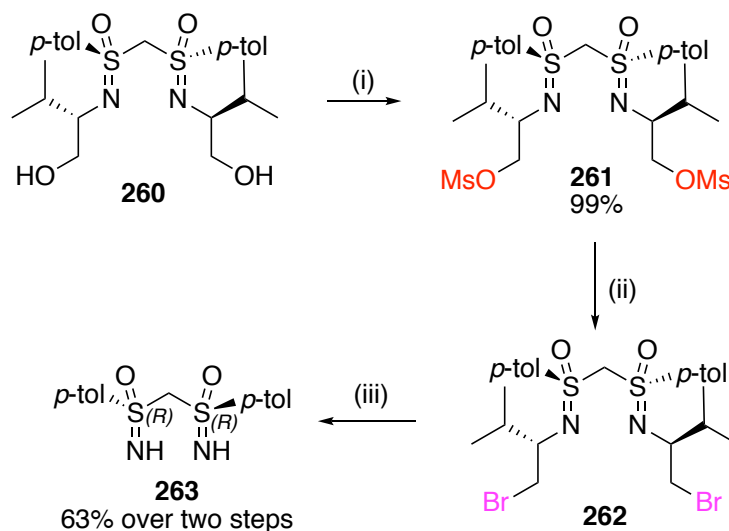
4.4 Synthesis of Enantioenriched Sulfoximines

The synthesis of single enantiomers of sulfoximines has been the aim of numerous medicinal chemistry programmes to access biologically relevant compounds over the last two decades.¹⁹ Reggelin has pioneered the ring opening of cyclic sulfonimides with either organolithium or Grignard reagents – under the optimised conditions, two equivalents of organometallic reagent are reacted in THF at –78 °C with the cyclic sulfonimides. One of the huge advantages of this method is that no side products, such as potential sulfonamides are formed, with exclusive formation of sulfoximine products. The success of the reaction protocol has been exemplified over numerous publications from the Reggelin Group.^{70,72,92,94,102,108}

The method suffers from limitations, some of which will be addressed in the coming sections of this second project. The first which will be addressed is the scope of the core sulfonimide employed – favoured by the Reggelin Group, *para*-tolyl-sulfur moiety is found in all publications, and that *N*-valinol is reported in most cases (a report in 1995 from the same group showed modification of the amino alcohol moiety used).⁹⁴

The work reported herein will focus on methyl-, *tert*-butyl- and phenyl- sulfur bonded sulfonimides to allow access to sulfoximines containing a range of C-S functionalities. A second limitation is the removal of the nitrogen substituent – in a single article, Reggelin accessed a bis-NH-sulfoximine **263** from its *N*-valinol precursor **260** over 3 steps (Scheme 4.10).¹⁰² This method has never been trialled on a *mono*-sulfoximine, and would provide medicinal chemists an approach to access the NH-sulfoximine compounds with the desired stereochemistry.

This project has devised a shorter, one step route that allows the cleavage of this *N*-substituent without loss of enantiomeric excess at the sulfur using cheap, commercially available reagents (see section 4.5).

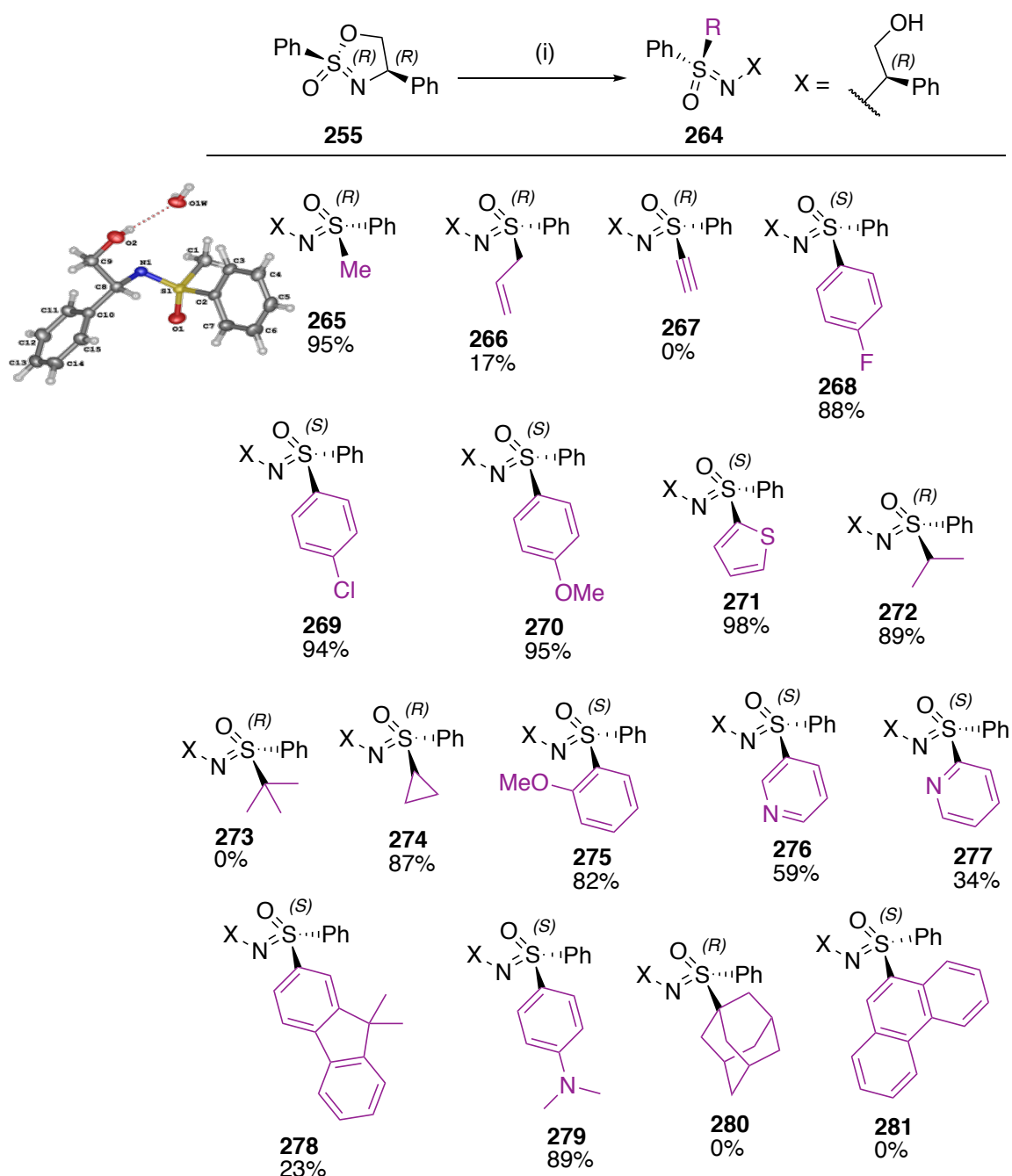


Scheme 4.10. Reggelin's deprotection of Bis-sulfoximine **260**. *Reagents and*

conditions: (i) MsCl, Et₃N; (ii) NH₄Br; (iii) Zn, I₂, DMF, 45 °C, 3 h.

With the optimised Grignard addition conditions reported by Reggelin, these were trialled on (*R*)-glycinol phenyl cyclic sulfonimide **255** (Scheme 4.11). The first Grignard reagent trialled was methyl magnesium bromide with template **255**. Pleasingly, the reaction proceeded smoothly with 2 equivalents of Grignard reagent in THF and afforded the desired sulfoximine **265** in 95% yield. Moreover, single crystals of **265** were obtained by slow evaporation from ethyl acetate that were suitable for X-ray crystallographic analysis - confirmation of the absolute stereochemistry of product **265** was realised as (*R*) at sulfur (Scheme 4.11, above left). Other sp³-based Grignard's were next trialled under the reaction conditions. Allyl magnesium bromide afforded sulfoximine **266** in a low yield of 17%, whilst *iso*-propyl magnesium bromide gave sulfoximine **272** in a vastly improved 89% yield. Cyclopropyl magnesium bromide fared similar, affording sulfoximine **274** in

87% yield. The sterically larger adamantylmagnesium bromide failed in the transformation, with no desired sulfoximine **280** observed. When using *tert*-butylmagnesium bromide, this Grignard proved to be unreactive as well, with no desired *tert*-butyl sulfoximine **273** formed.



Scheme 4.11. Grignard addition to cyclic sulfonimide **255**. *Reagents and conditions:* (i) RMgBr (2 equiv.), THF, $-78\text{ }^{\circ}\text{C}$ – rt. Above left; X-ray analysis of (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ 6-sulfanone **265**.

Changing the Grignard reagent to the *sp*-hybridised alkynylmagnesium bromide, unfortunately gave no sulfoximine product **267** – only unreacted starting material was observed initially, but on extended reaction times to drive the reaction forward, the rearranged aziridine product **282** was isolated (this was previously observed by Reggelin and co-workers but under different reaction conditions, Figure 4.4).⁷⁰

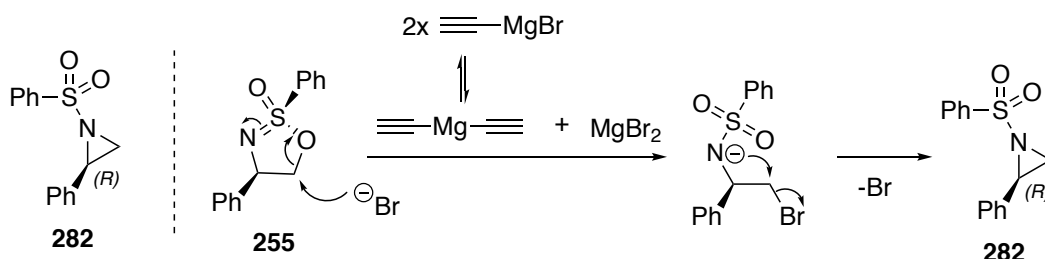


Figure 4.4. Structure of rearranged aziridine **282**.

The focus then moved towards aryl derived Grignard reagents; firstly, substitution at the *para*-position on the aromatic ring of the Grignard reagent was investigated. Halide substituents fluoro- and chloro- were well tolerated, with sulfoximines **268** (88%) and **269** (94%) forming in excellent yields. Addition of an electron donating methoxy- or dimethylamino- substituent at the *para*-position of the aryl Grignard provided excellent yields (**270** = 95%, **279** = 89%). Moving the methoxy substituent to the *ortho*-position gave sulfoximine **275** in a similar yield (82%) as that observed with its *para*-analogue **270**. Heteroaryl Grignard reagents such 2-thiophenyl, 2- and 3- pyridyl magnesium bromides gave good to excellent yields of the corresponding sulfoximines **271**, **276** and **277** (98%, 59% and 34% yield respectively). Finally, incorporation of the fluorescent, sterically bulky, 9,9-dimethyl-9*H*-fluorene moiety in sulfoximine **278** was successfully achieved in modest yield (23%), through the reaction of cyclic sulfonimide **255** and freshly prepared (9,9-dimethyl-9*H*-fluoren-2-yl)magnesium bromide.

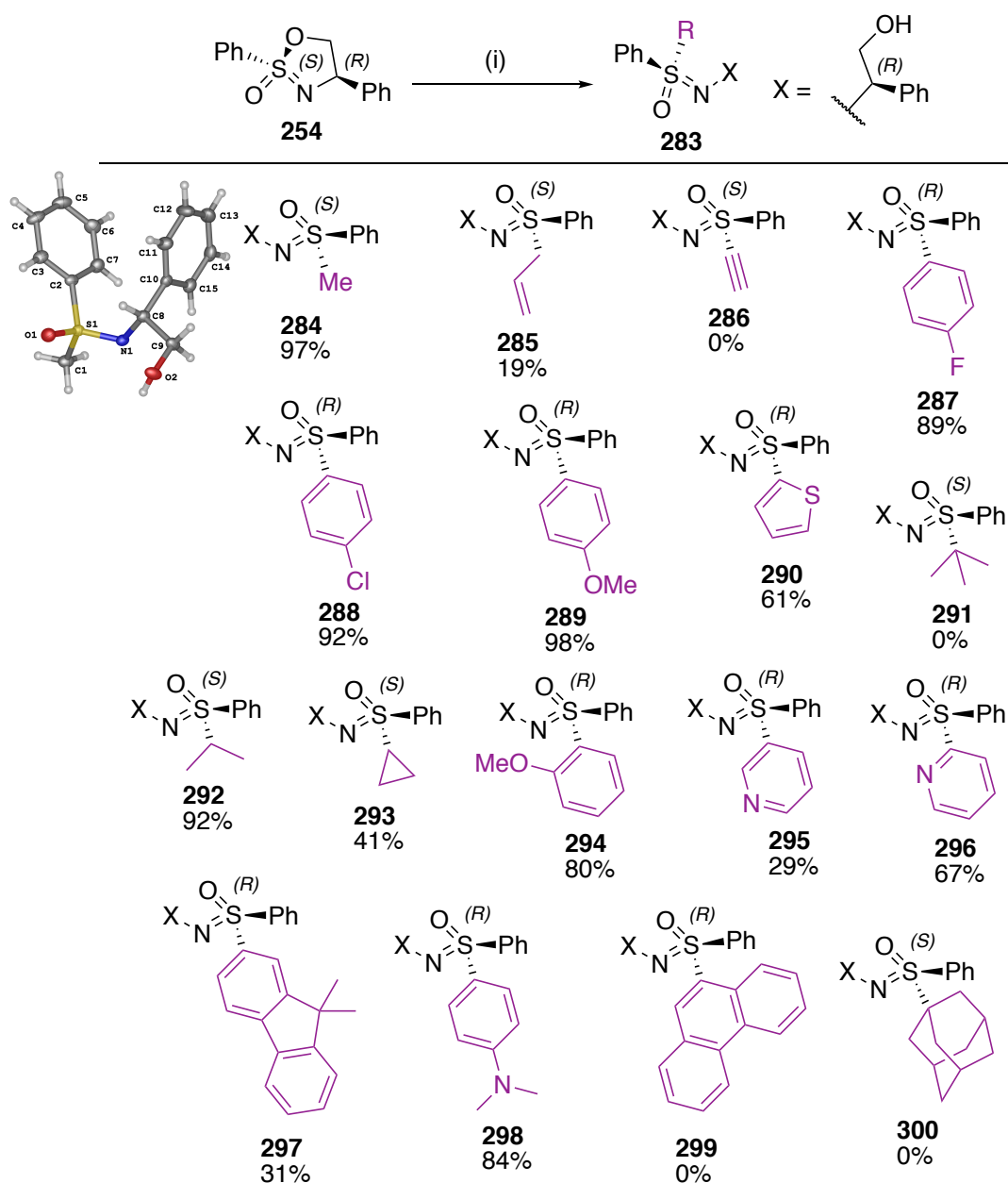
With a range of Grignard reagents successfully screened with template **255**, the focus was turned to the reaction of Grignard reagents with the other phenyl cyclic sulfonimide diastereoisomer **254** (Scheme 4.12).

Some of the best results were obtained when using *para*-substituted aryl Grignard reagents; *para*-fluoroaryl derived sulfoximine **287** was formed in excellent yield (89%), with its analogous chloro version **288** affording similarly high product yield (92%). Changing the *para*-substituent to a strongly electron donating one on the Grignard reagent used, either methoxy **289** (98% yield), or dimethylamino **298** (84% yield) performed well in the transformation. Moving the electron donating substituent to an *ortho*-position on the aryl ring of the Grignard reagent proved fruitful, affording the desired sulfoximine **294** in 80% yield.

Changing from aryl to heteroaryl Grignard reagents reacting with template **254** gave slightly lower product yields; 2-thiophenyl magnesium bromide afforded sulfoximine **290** in good yield (61%), and 2-pyridyl magnesium bromide afforded sulfoximine **296** in 67%. Moving the nitrogen atom round the aryl ring one position led to a moderate product yield of 29% for sulfoximine **295**.

Bulky Grignard reagents worked poorly in the transformation; none of the desired phenanthryl (**299**), adamantyl (**300**) and *tert*-butyl (**291**) sulfoximines were afforded, and in each case, only recovered starting material was observed.

Alkyl-based Grignard reagents such as methyl (**284** = 97%), allyl (**285** = 19%), cyclopropyl (**293** = 41%) and *iso*-propyl (**292** = 92%) were all incorporated. Pleasingly, single crystals of methyl derived sulfoximine **284** were grown by slow evaporation from ethyl acetate, confirming the absolute stereochemistry for the Grignard addition as (*S*) at the sulfur atom (Scheme 4.12, above left).



Scheme 4.12. Grignard addition to cyclic sulfonimide **254**. *Reagents and conditions:* (i) RMgBr (2 equiv.), THF, $-78\text{ }^{\circ}\text{C}$ – rt. Above left; X-ray analysis of (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ 6-sulfanone **284**.

In the case of *iso*-propyl derived sulfoximine **292**, potential rotamers were observed. A variable temperature (VT) ^1H NMR experiment was conducted on this sample and at elevated temperature, coalescence of the peaks was observed at 90 °C (Figure 4.5).

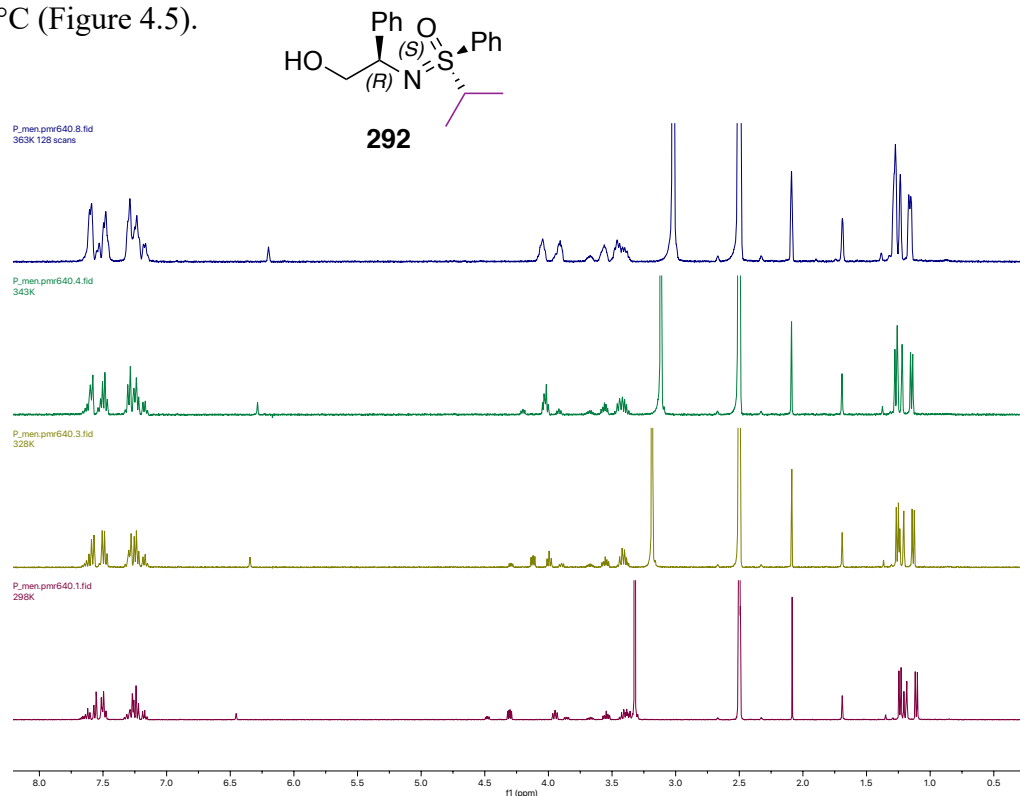
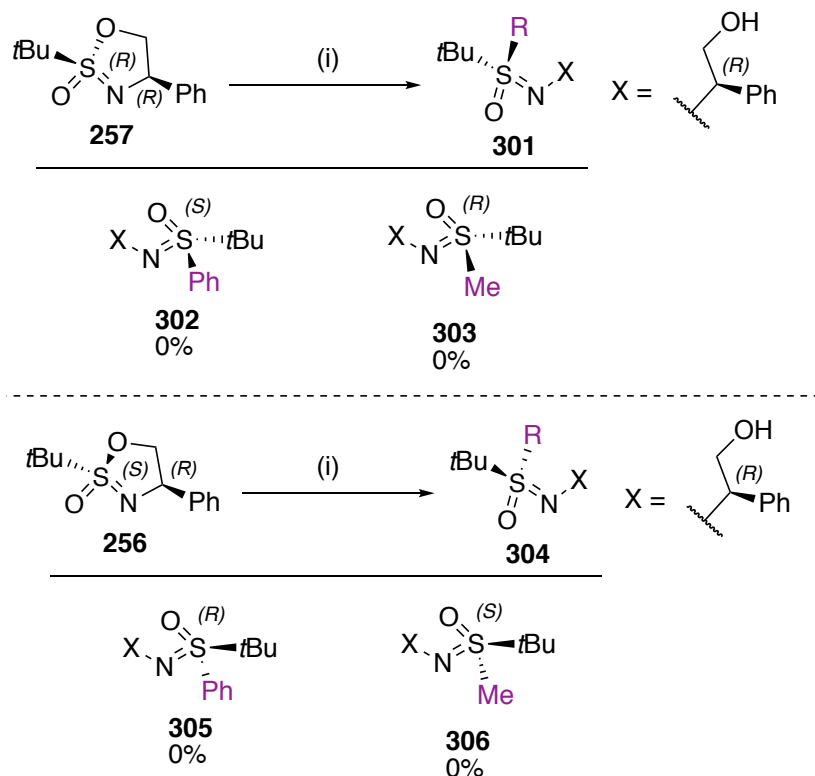


Figure 4.5. VT NMR study on *iso*-propyl derived sulfoximine **292**.

With two alternative cyclic sulfonimide templates available (methyl **258/259** and *tert*-butyl analogues **256/257**), a small library of Grignard reagents were tested to explore their substrate scope.

Tert-butyl analogue **256** and **257** were subjected to ring opening conditions with two Grignard reagents – phenyl and methyl magnesium bromide (Scheme 4.13). Unfortunately, sulfoximine products **302/305** derived from phenyl magnesium bromide attack, and sulfoximine products **303/306** from methyl magnesium bromide attack, were not observed. These results are unsurprising; steric bulk of

the *tert*-butyl group hindered Grignard attack on the acyclic variants described in chapter 3.0 – moreover, Reggelin and co-workers previously reported that *tert*-butyl derived Grignard's failed to react with their cyclic sulfonimides.⁷⁰

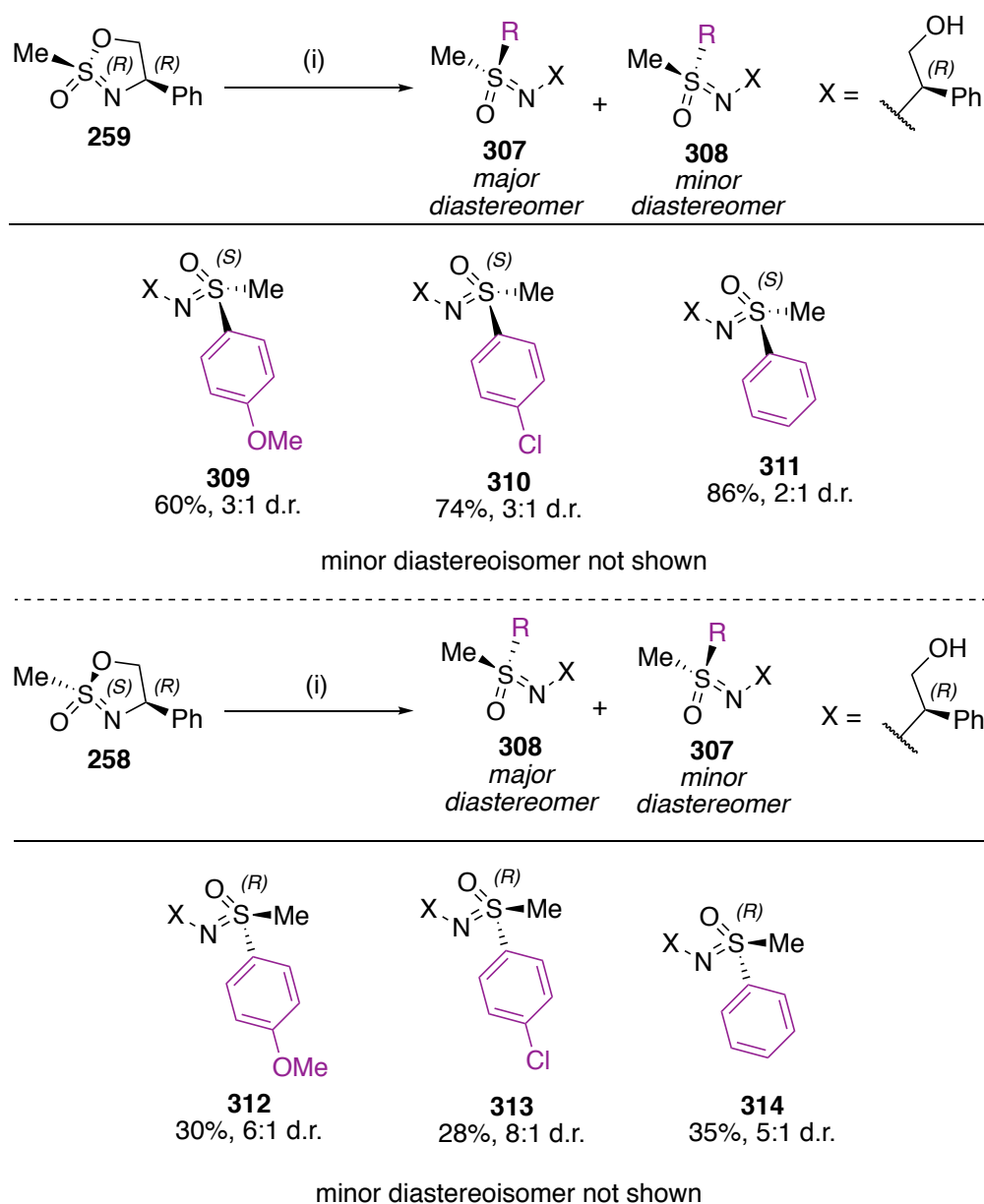


Scheme 4.13. Grignard addition to *tert*-butyl derived cyclic sulfonimide

257/256. *Reagents and conditions:* (i) RMgBr (2 equiv.), THF, $-78\text{ }^{\circ}\text{C}$ – rt.

Methyl derived sulfonimides **258** and **259** were reacted with three aryl derived Grignard reagents – a necessity to be aryl derived so that a UV tracer on the molecule would be present for detection on chiral HPLC. On Grignard addition to a single diastereoisomer sulfonimide **259**, a mixture of diastereomeric sulfoximines **307:308** was observed, with ratios ranging between 2:1-3:1 depending on substitution on the aryl Grignard used (ratios of major:minor sulfoximines is shown in Scheme 4.14). When the opposite methyl sulfonimide diastereoisomer **258** was utilised, both diastereomeric sulfoximine products were

observed, but the d.r. ratio was in favour of the major product **308** this time, with diastereomeric ratios ranging from 5:1-8:1.

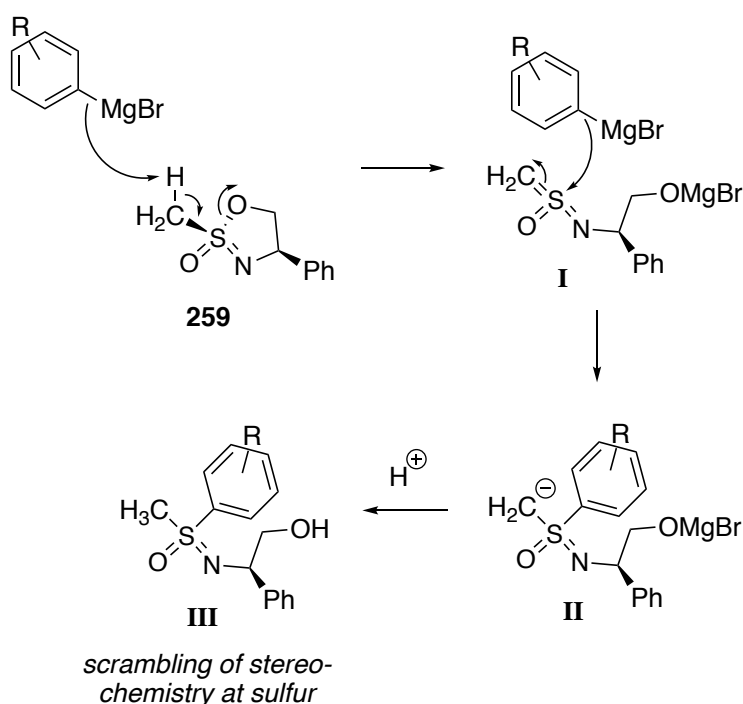


Scheme 4.14. Grignard addition to methyl derived cyclic sulfonimide **259/258**.

Reagents and conditions: (i) RMgBr (2 equiv.), THF, $-78\text{ }^{\circ}\text{C}$ – rt.

Unfortunately, this template proved extremely problematic with respect to retaining stereochemistry at the sulfur centre. During the reaction of either methyl sulfonimide diastereomers **258** or **259** with Grignard reagents it was possible to

see both diastereomer sulfoximine products **307** and **308** form – this had not previously been seen with other templates. A thought was that deprotonation of the methyl substituent on sulfonimide **258/259** caused ring opening of the sulfonimide, and subsequent attack by a second molecule of Grignard reagent affords the sulfoximine product (Scheme 4.15, mechanism shown for sulfonimide **259**). This postulated mechanism could explain why both diastereoisomeric sulfoximine products are observed from the methyl cyclic sulfonimide template.



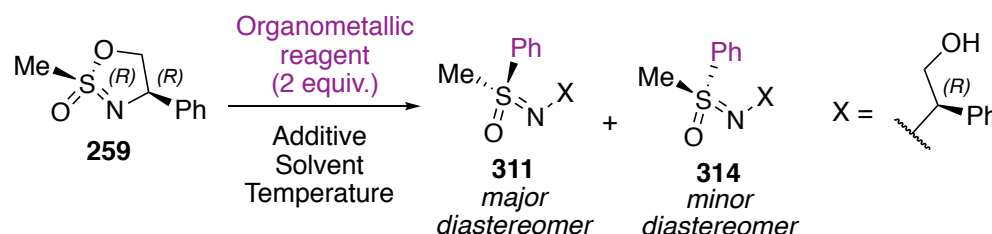
Scheme 4.15. Possible route to loss of stereochemistry at sulfur on methyl sulfonimide template **259**.

When conducting the reaction with one equivalent of Grignard reagent, both diastereoisomers of sulfoximine product form, along with remaining starting material. If the reaction temperature is held at $-78\text{ }^{\circ}\text{C}$ without allowing to warm to room temperature, the same result of both sulfoximines **307/308** is observed.

As a final attempt to investigate this loss of stereochemistry at sulfur in the methyl sulfonimide templates, a few variables were changed in the Grignard addition

reaction to probe this further. The first change was to add phenyl lithium instead of phenyl magnesium bromide to template **259** (Table 4.1, entry 1). This unfortunately proved unsuccessful, with only starting material recovered from the reaction.

Table 4.1. Reactivity study on methyl cyclic sulfonimide **259**.



Entry	Organometallic Reagent	Solvent	Additive	Temp (°C)	Reaction outcome
1	PhLi	THF	None	-78 to 25	Recovered starting material 259
2	PhMgBr	THF	Quench with CD ₃ OD	-78 to 25	 315
3	PhMgBr	THF	CeCl ₃	-78 to 25	No product
4	PhMgBr	THF	Yb(OTf) ₃	-78 to 25	No product

When the Grignard reaction was quenched with deuterated methanol (CD₃OD), and ¹H NMR analysis was conducted on the isolated product, the CH₃ singlet peak of sulfoximine **311** had decreased in integration, with a new triplet peak occurring next to it, indicating the formation of deuterated product **315** (Table 4.1, entry 2, and Figure 4.6). Both proton and carbon NMR spectra of **315** show this new triplet signal, indicating incorporation of one deuterium atom on the methyl group. HRMS analysis of deuterated-**315** confirmed its formation on quenching with CD₃OD.

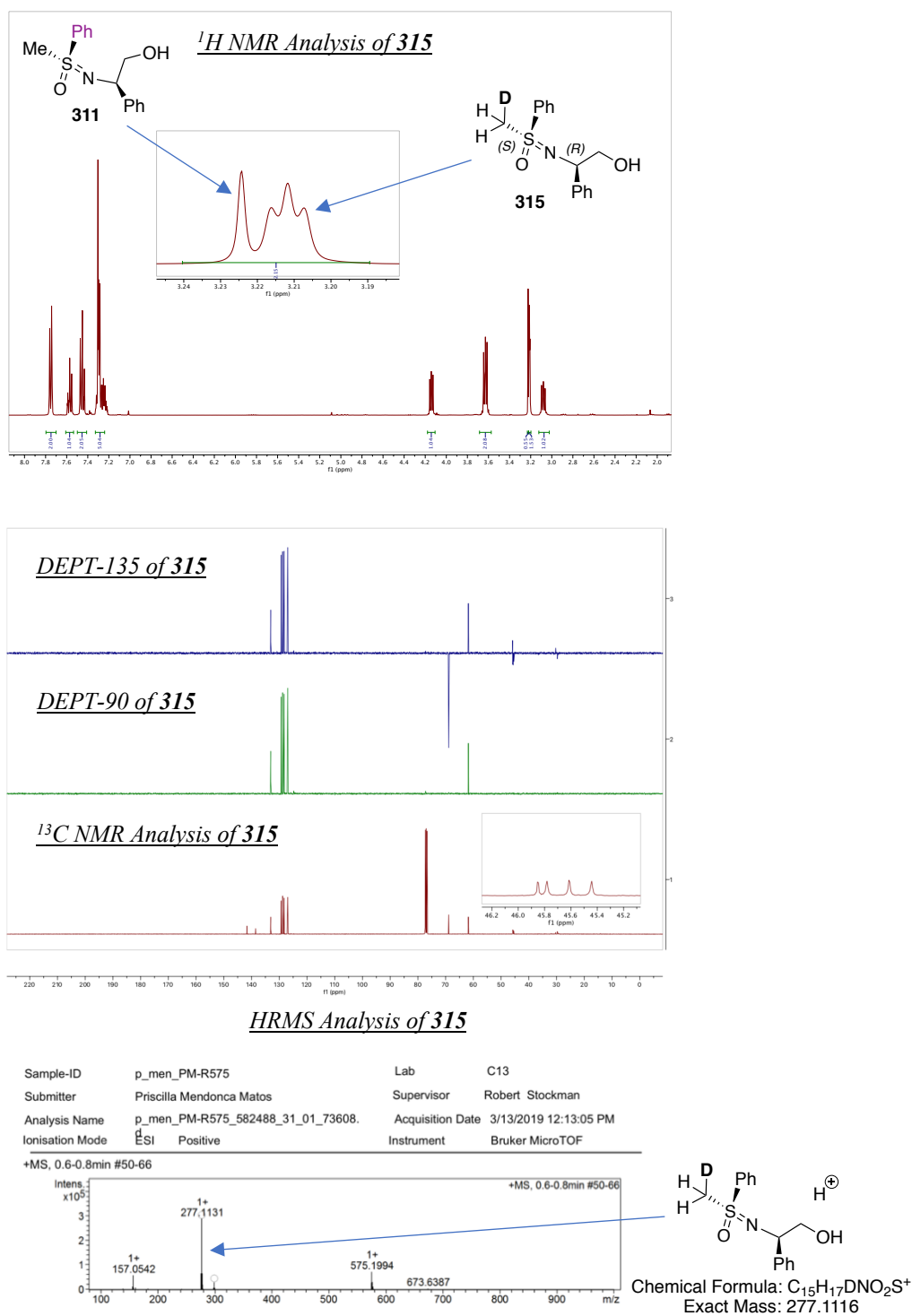


Figure 4.6. NMR analysis and mass spectra of deuterated-**315**.

Finally, addition of cerium(III) chloride or ytterbium(III) triflate as Lewis acids to enhance the nucleophilicity of the Grignard reagent (and thus reducing the

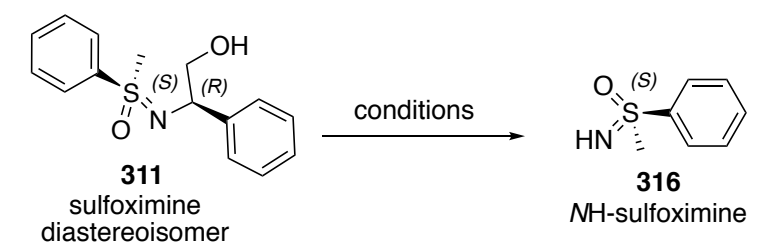
Grignard's basicity), unfortunately led to no sulfoximine product being isolated (Table 4.1, entry 3 and 4).

4.5 Synthesis of NH-Sulfoximines

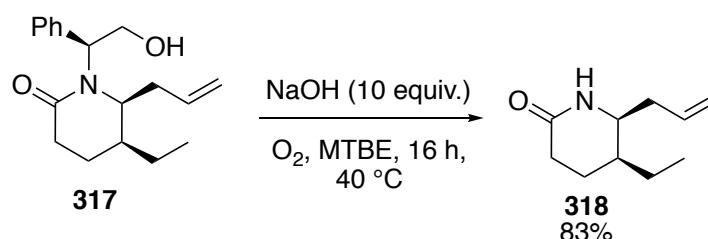
To remove the chiral auxiliary, a screen of reaction conditions was attempted to remove the phenylethanol moiety from the nitrogen in a single step. The results of this investigation are summarised in Table 4.2. Initially, acidic conditions using methanolic hydrochloric acid solution was trialled, but no product was isolated (entry 1). Hydrogenation conditions to remove the phenylethanol moiety were next trialled (entries 2-5) as the nitrogen-group resembled a benzyl group in structure. No product was observed with either palladium on carbon, nor palladium hydroxide, by changing the reaction solvent, pressure of hydrogen used, and even the reaction time. Reacting sulfoximine **311** with 1-chloroethylchloroformate could give a carbamate product (with loss of phenylethanol moiety), which upon treatment with methanol, would yield NH-sulfoximine **316**. Unfortunately, no desired NH-sulfoximine **316** was observed under these conditions. Replication of Reggeli's conditions to remove the phenylethanol moiety of sulfoximine **311** over 3 steps was trialled; the final step utilised DMF as reaction solvent, and this proved problematic to separate from the final NH-sulfoximine **316**, even though the desired product mass was observed by mass spectrometry (Entry 7). As a final attempt, oxygenated, base-catalysed conditions were trialled on sulfoximine **311** using a procedure first utilised by Escolano and co-workers to remove the phenylethanol moiety on phenylglycinol-derived lactams (Scheme 4.16).¹⁰⁹ This procedure made use of an excess of sodium hydroxide (10 equivalents), with methyl-*tert*-butyl ether as reaction solvent heated to 40 °C. For the first time, the desired (*S*)-NH-sulfoximine **316** was isolated cleanly in a pleasing 80% yield, and 98% enantiomeric excess (see Figure 4.8 for enantiomeric purity).

The use of oxygen was advocated by the original authors for their different substrate; this was found also to be the case for the removal of the phenylethanol group in sulfoximine **311**. Using 1 atm of oxygen, the reaction proceeded well, and in its absence, only traces of product were detected by TLC and ^1H NMR analysis of the crude reaction mixture (Entry 9).

Table 4.2. Optimisation study to cleave the phenylethanol group from the nitrogen atom of the sulfoximine.



Entry	Reagents	Solvents	Temp (°C)	Time (h)	Yield of 316 (%)
1	HCl in MeOH (1.25 M)	-	25	24	0
2	H ₂ (1 bar)/ Pd/C (10 mol%)	Ethyl Acetate	25	24	0
3	H ₂ (1 bar) / Pd/C (10 mol%)	Ethanol	25	72	0
4	H ₂ (1 bar) /Pd(OH) ₂	MeOH	25	24	0
5	H ₂ (40 bar) /Pd(OH) ₂	MeOH	25	20	0
6	1-chloroethylchloroformate	DCM then MeOH	-10 - reflux	3.5	0
7	a) Et ₃ N, MsCl b) NH ₄ Br c) Zn, I ₂	DCM, then THF:H ₂ O, then DMF	a) 0 b) 60 c) 45	a) 4 b) 6 c) 3	*Not isolatable from DMF (bp to high)
8	NaOH (10 eq.), O ₂ (1 atm.)	MTBE	40	16	80
9	NaOH (10 eq.), no oxygen	MTBE	40	24	trace



Scheme 4.16. Escolano's deprotection of glycinol derived substrate **317**.

^1H NMR analysis after purification of the *NH*-sulfoximine **316** showed clean removal of the phenylethanol moiety (comparative NMR between starting material and product shown below, signals for product in alignment with literature data for *NH*-sulfoximine **316** Figure 4.7).¹¹⁰

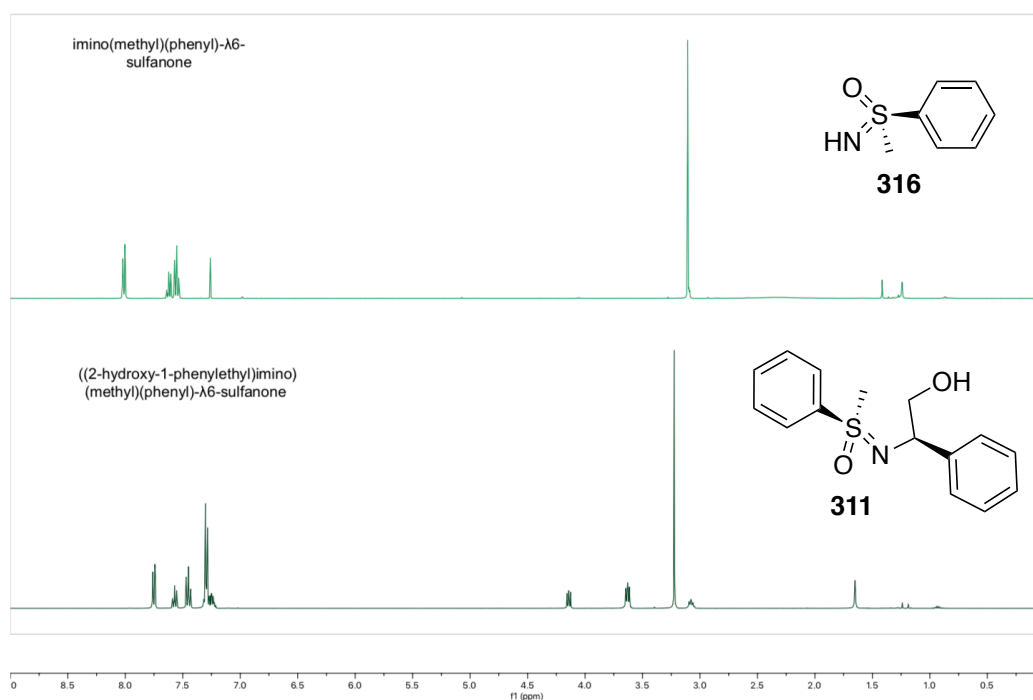
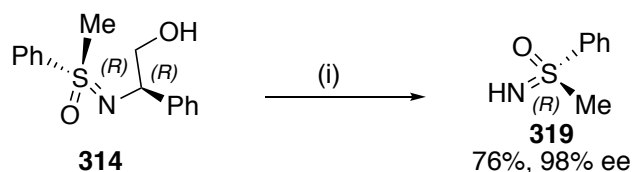


Figure 4.7. ^1H NMR analysis of *NH*-sulfoximine **316** and sulfoximine diastereomer **311**.

With optimised oxygenated basic conditions for the removal of the phenylethanol moiety in hand, the conditions were then replicated for the other diastereoisomer of sulfoximine **314** (Scheme 4.17). Pleasingly, the (*R*)-enantiomer of *NH*-sulfoximine **319** was isolated in 76% yield, 98% ee (see Figure 4.8 for enantiomeric excess determination by chiral HPLC analysis).



Scheme 4.17. Reagents and conditions: (i) NaOH (10 equiv.), MTBE, O₂ (1 atm.), 40 °C, 16 h.

Excitingly, HPLC analysis along with optical rotation data collected for each enantiomer proved no loss of stereochemical information at the sulfur was observed during the transformation (Figure 4.8).

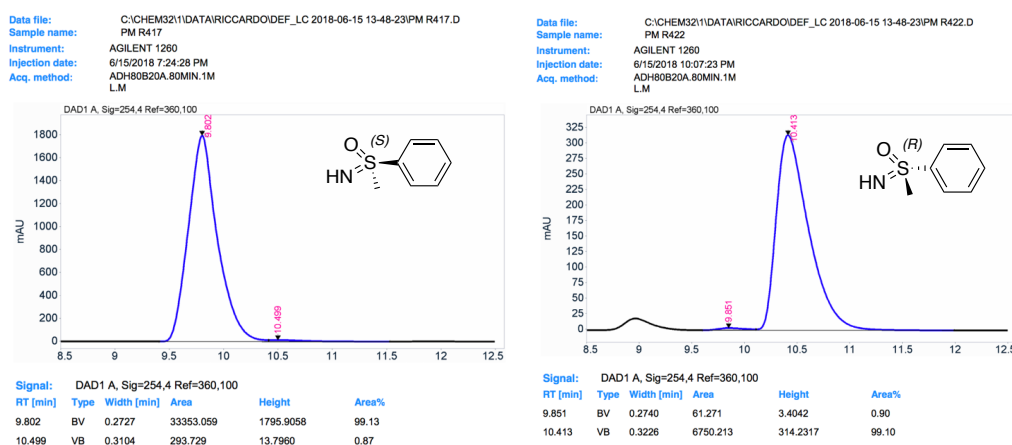
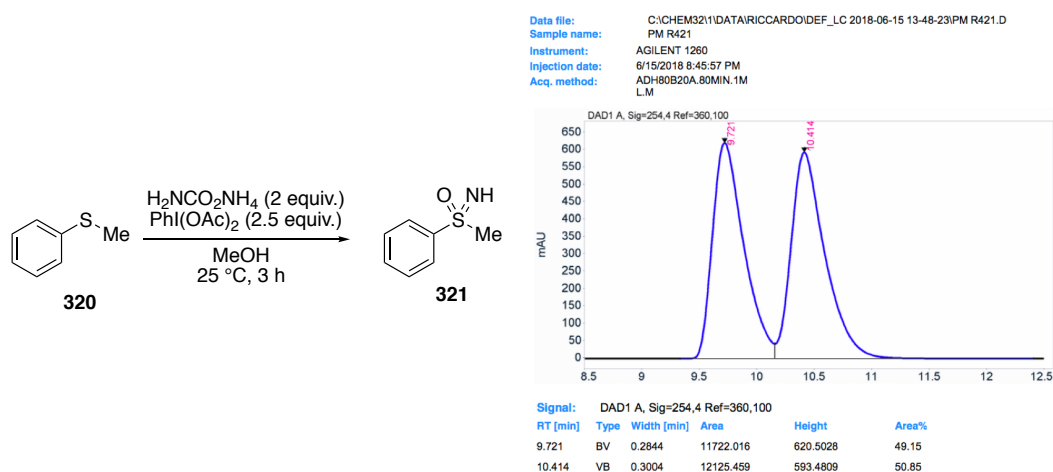


Figure 4.8. HPLC analysis of (*S*)-**316** (above left), (*R*)-**319** (above right). Data was collected on an Agilent HPLC instrument using a Chiracel ADH column (*iso*-hexane:*iso*-propanol, 80:20), flow rate: 1.0 ml/min, $\lambda = 254$ nm.

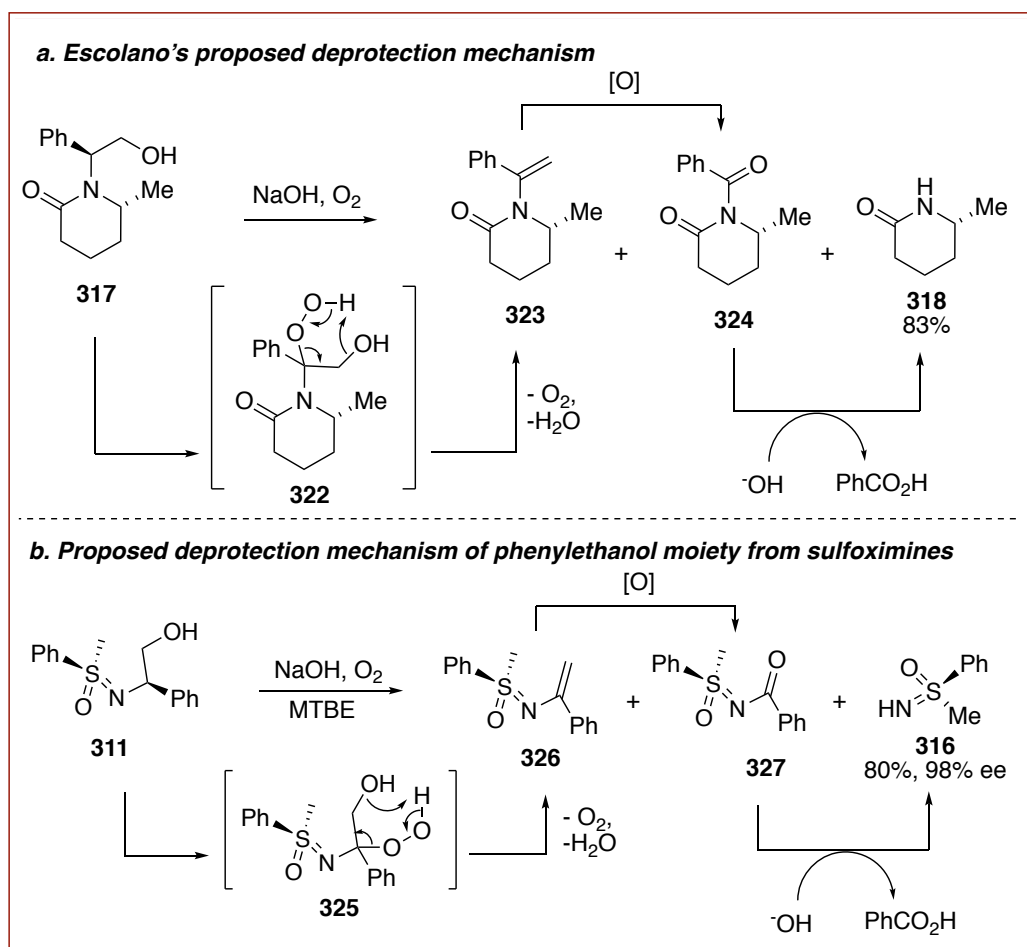
A racemic sample **321** was generated using the methodology reported by Bull and co-workers.³⁵ This protocol involved reacting phenylmethyl sulfide **320** with 2 equivalents of ammonium carbamate and 2.5 equivalents of diacetoxyiodobenzene (Scheme 4.18). The protocol allowed facile access to the desired racemic imino(methyl)(phenyl)- λ 6-sulfanone **321**. Pleasingly, this material separated under the HPLC conditions to provide a racemic HPLC trace, further corroborating the enantiomeric excesses described in Figure 4.8.



Scheme 4.18. Above left; formation of racemic *NH*-sulfoximine **321** using Bull's methodology. Above right; HPLC of racemic **321**, (Chiracel ADH column, *iso*-hexane:*iso*-propanol (80:20), flow rate: 1.0 ml/min, $\lambda = 254$ nm).

4.6 Mechanism of Deprotection

The proposed mechanism for the removal of the phenylethanol moiety described by Escolano is detailed in Scheme 4.19 below. To further build on this mechanism, it was decided to use react-IR data during a deprotection reaction to identify the plausible intermediates shown in Scheme 4.19 towards the formation of *NH*-sulfoximines. The analytical instrument used was a Metler Toledo React IR15, which would allow the analysis of key infra-red stretches during the reaction over time (Figure 4.9). A limitation of using this method is that the instrument can only measure in the range of 3000-650 cm^{-1} . This would mean that formation of the free *NH* signal (observed in standard IR analysis at 3200 cm^{-1} for **316**) would not be possible.



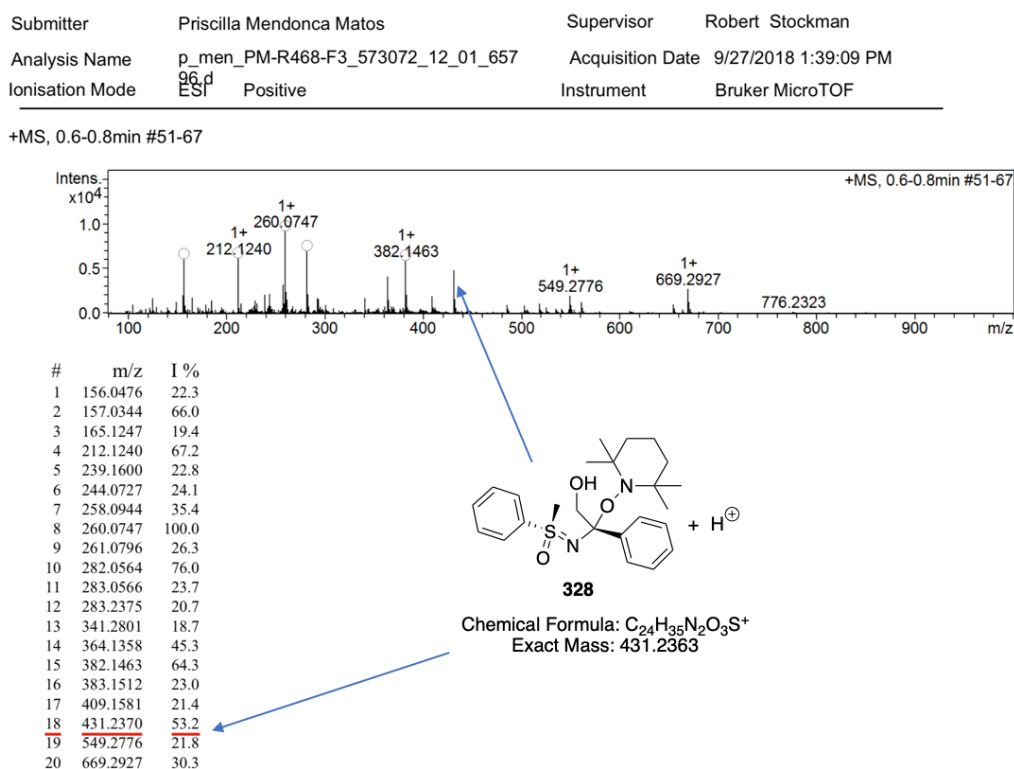
Scheme 4.19. a) Escolano's proposed deprotection of phenylethanol moiety from **317** to yield cleaved amine product **318**. b) Proposed deprotection mechanism of sulfoximine **311** to *N*H-sulfoximine **316**.

As shown below in Figure 4.9, the reaction progress of *N*H-sulfoximine formation could be monitored by carefully measuring IR absorbances over a time period of 9 hours. The most pronounced signal during the experiment was observed at 1602 cm^{-1} (C=O stretch), which gradually increases after 1 hour of reacting, up to the end of the 9-hour experiment. This stretch could provide evidence for potential amide intermediate **327** (Scheme 4.19) forming during the reaction. Sulfoximine **327** is a known literature compound, with an IR stretch observed at 1612 cm^{-1} (C=O),¹¹¹ whilst the stretch for benzoic acid is found at 1720 cm^{-1} (C=O).¹¹²

Table 4.3. Trapping experiment of radical intermediates with TEMPO.

	Entry	Equiv. of TEMPO	% yield of 328
	1	1.3	0
	2	1.0	0
	3	0.2	0

Varying the equivalents of TEMPO added into the reaction was explored; when 1.3 equivalents of TEMPO were employed, the radical trapped product **328** was identified only by HRMS analysis of the reaction mixture (Figure 4.10). Changing to lower amounts of TEMPO in the reaction gave no product by HRMS and ^1H NMR analysis (entries 2 and 3).

**Figure 4.10.** HRMS analysis of TEMPO trapping experiment of radical intermediate **328**.

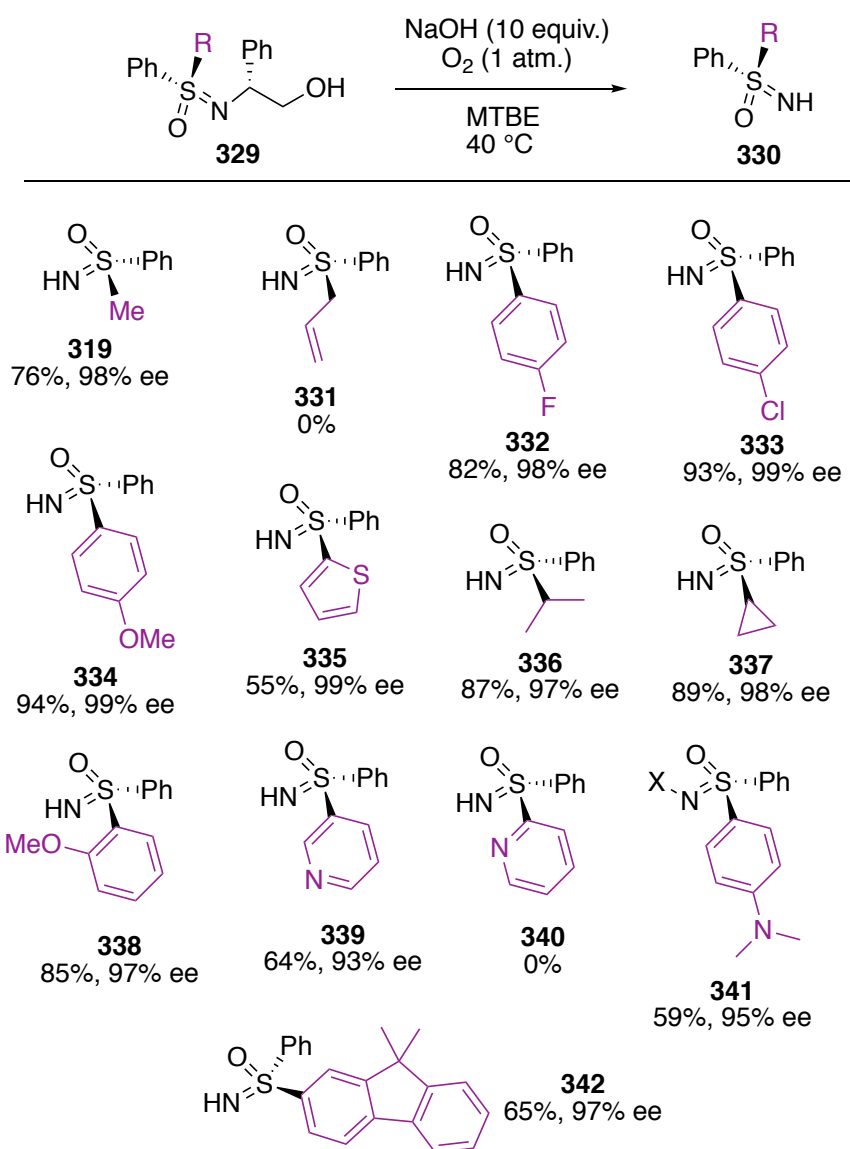
With the reaction mechanism investigated through control experiments, the focus returned to exploring the substrate scope for NH-sulfoximine formation (Scheme 4.20). Initially, the optimised conditions were trialled on other alkyl-sulfur derived sulfoximines (derived from cyclic sulfonimide **255**, see Scheme 4.11).

Initially, allyl NH-sulfoximine **331** failed in the reaction conditions. Undeterred by this result, *iso*-propyl **336** (87%, 97% ee) and cyclopropyl **337** (89%, 98% ee) were successfully formed under the reaction conditions. Enantiomeric purity in both examples had been maintained.

Some of the best results using this protocol were obtained with substituted aryl-sulfur derived sulfoximines (**332-334**, **338-341**). In all *para*-substituted cases, including fluorine, chlorine, methoxy and dimethylamino, all reactions proceeded smoothly affording yields ranging between 59-94% yield. In all cases, enantiomeric excesses were excellent. *Ortho*-methoxy substituted **338** was formed in comparative yield to its *para*-analogue **334** (**338** = 85%, **334** = 94%), whilst enantiomeric excess remained high at 97%.

Heteroaryl sulfoximines including thiophenyl **335** (55%, 99% ee) and 3-pyridyl **339** (64%, 93% ee) also performed well under the reaction conditions, however, 2-pyridyl NH-sulfoximine **340** failed to form under the reaction conditions.

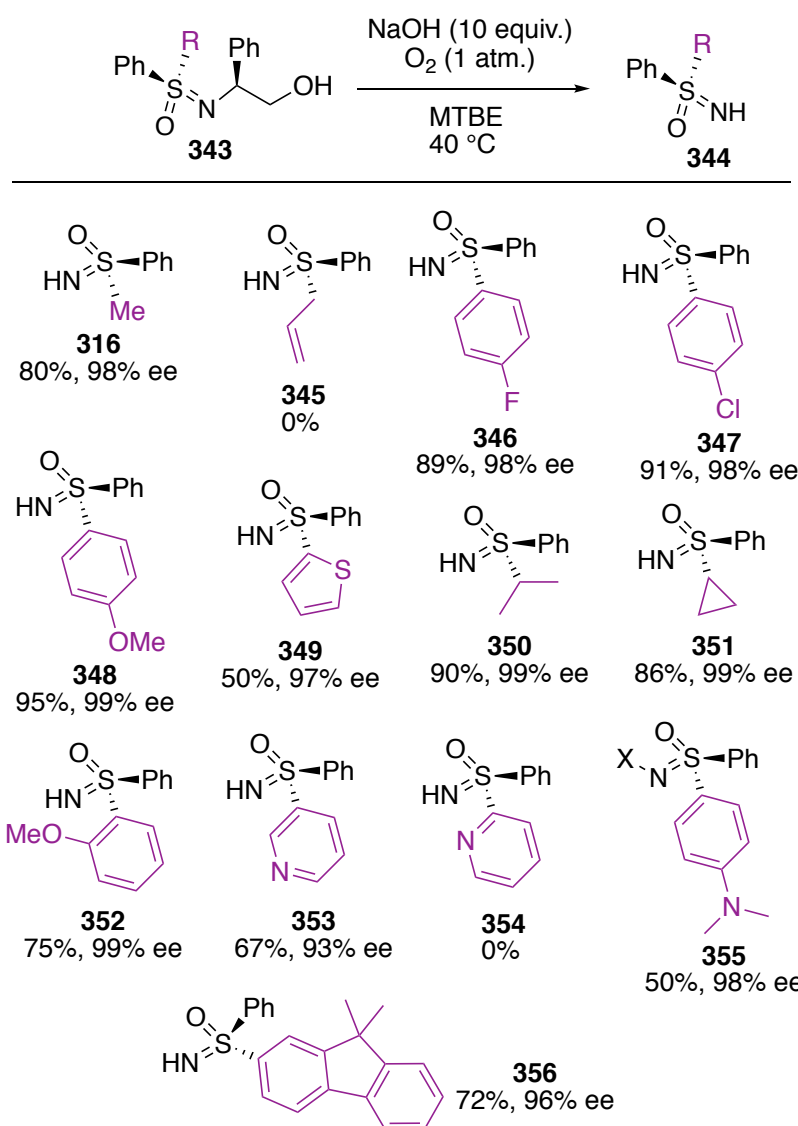
Sterically cumbersome aryl-sulfur sulfoximines also worked in the transformation, for example, fluorenyl-sulfur sulfoximine **342** in 65% yield, 97% ee.



Scheme 4.20. Investigating substrate scope of phenylethanol deprotection on **329**.

With the success of the deprotection reaction working on template **329**, and that stereochemistry at sulfur was maintained with NH-sulfoximines afforded in excellent enantiomeric excess, the reaction conditions were tested on the opposite sulfoximine diastereomers **343** (Scheme 4.21). In all cases, the opposite enantiomers to those obtained in Scheme 4.20 were observed, in good to excellent yields and enantiomeric excesses. Both allyl **345** and 2-pyridyl **354** NH-sulfoximines failed to form again. Some of the best results came from *para*-substituted aryl NH-sulfoximines, for example **346** (89%, 98% ee), **347** (91%, 98%

ee), and **348** (95%, 99% ee). Alkyl substituents were well tolerated, for example, *iso*-propyl **350** (90%, 99% ee) and cyclopropyl **351** (86%, 99% ee) *NH*-sulfoximines were stand out examples. Heterocyclic containing *NH*-sulfoximines such as thiophenyl **349** and 3-pyridyl **353** formed in good yields and maintained excellent enantiomeric purity at sulfur.

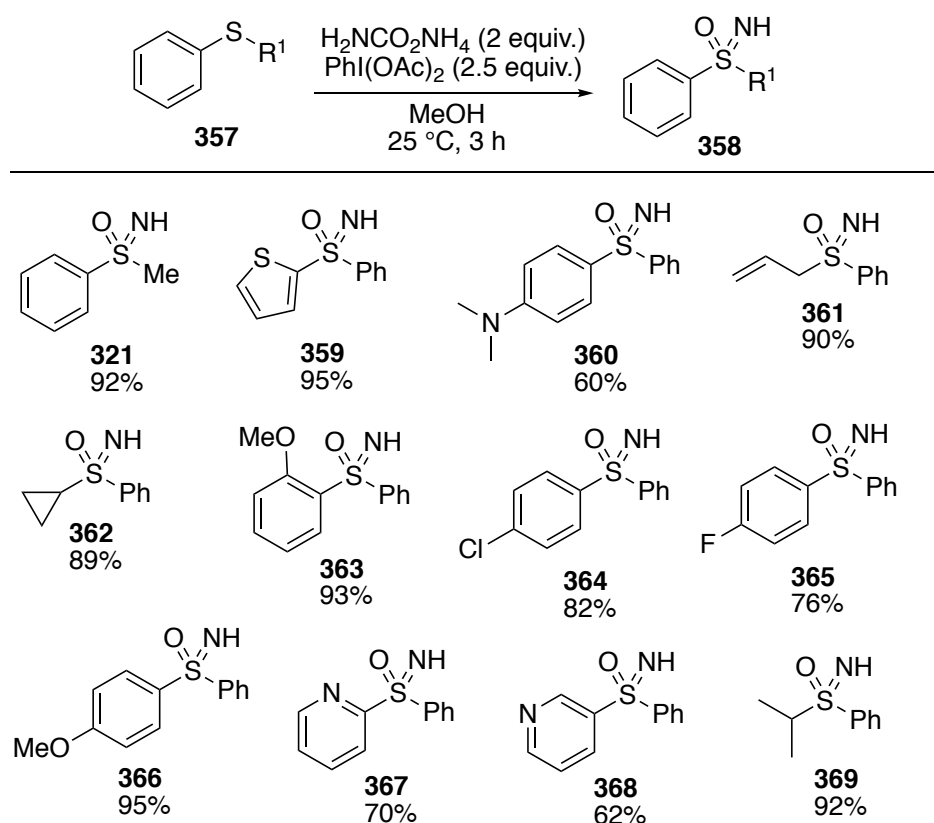


Scheme 4.21. Investigating substrate scope of the phenylethanol deprotection.

4.7 Synthesis of Racemic *NH*-Sulfoximines

To confirm enantiomeric excess data in section 4.5, it was important to collect racemic samples for comparative purposes. As shown briefly in Scheme 4.18,

Bull's methodology was employed to synthesise racemic imino(methyl)(phenyl)- λ 6-sulfanone **321** in 92% yield. The conditions involved reacting 1 equivalent of sulfide with 2 equivalents of ammonium carbamate, 2.5 equivalents of diacetoxyiodobenzene, in methanol at room temperature. Based on this initial result, the scope of the reaction was explored on a range of sulfides (Scheme 4.22). Thiophenyl-derived NH-sulfoximine **359** was formed in 95% yield, whilst nitrogen containing heterocyclic variants were formed in good yields, such as 2-pyridyl **367** (70%) and 3-pyridyl **368** (62%) sulfoximines. Substitution on the aromatic ring either *para* (-NMe₂ (**360**) = 60%, -Cl (**364**) = 82%, -F (**365**) = 76%, -OMe (**366**) = 95%) or *ortho* (-OMe **363** = 93%) was well tolerated in all cases. Both -allyl, cyclopropyl and *iso*-propyl sulfides provided racemic sulfoximines (**361**, **362** and **369**) in yields ranging from 89-92%. HPLC traces for racemic sulfoximines can be found in the experimental section.

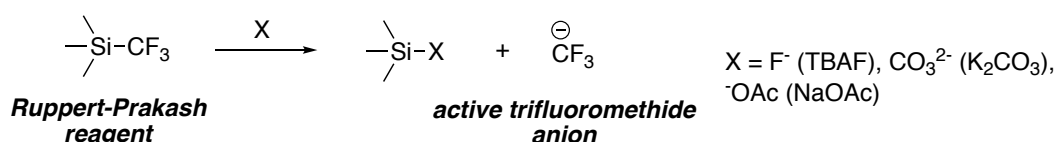


Scheme 4.22. Synthesis of NH-sulfoximines using Bull's protocol.

In a single case, a racemic fluorenyl derived *N*H-sulfoximine was prepared by mixing the two sulfoximines **342** and **356**.

4.8 Reaction of Cyclic Sulfonimides with Other Nucleophiles

With the reaction of Grignard reagents proving to be successful, other nucleophilic reagents were trialled to briefly investigate their reactivity as well. The first reagent trialled was the Ruppert-Prakash reagent (TMSCF₃, Table 4.4). The activation of the Ruppert-Prakash reagent was trialled with three reagents (Scheme 4.23, TBAF, K₂CO₃ and NaOAc).



Scheme 4.23. Activation of Ruppert-Prakash reagent.

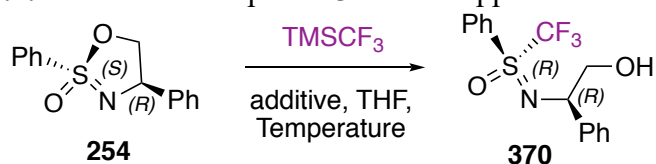
Firstly, tetrabutylammonium fluoride was used at room temperature with THF as reaction solvent on diastereomer template **254** (entry 1, Table 4.4).^{113,114} The product isolated was not CF₃ addition to the sulfur centre to give the desired sulfoximine **370**, but instead, fluoride presumably from the TBAF attacks at the carbon atom to give fluorosulfonamide product **371** in 40% yield.

The second additive trialled was sodium acetate to activate the Ruppert-Prakash reagent.¹¹⁵ Interestingly, the acetate anion appears to have attacked the carbon atom rather than the sulfur atom in template **254**, in a similar way to the fluoride anion from TBAF, to ring open the cyclic sulfonimide to give acetate sulfonamide **372** in 52% yield.

In a final attempt to get CF₃ addition at the sulfur atom, potassium carbonate was employed as activator.¹¹⁶ Following the literature conditions reported by Prakash

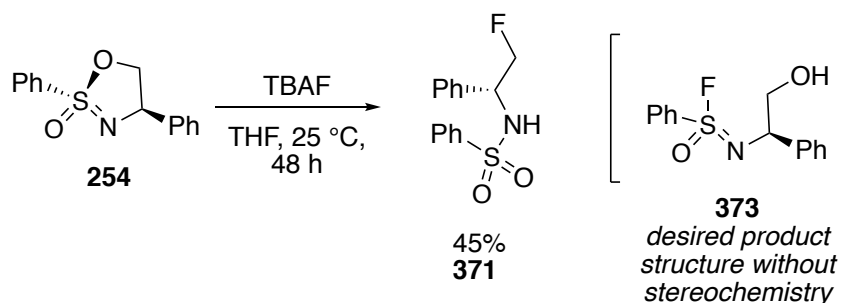
and co-workers, the reaction did not provide any of the desired product, with the starting material quantitatively recovered.

Table 4.4. Reaction of template **254** with Ruppert-Prakash reagent.



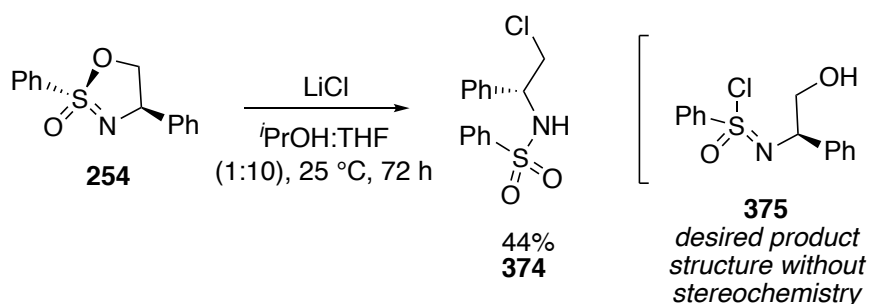
Entry	Additive	Temperature	Solvent	Yield of Product
1	TBAF	0 - 25	THF	40% 371
2	NaOAc	25	DMF	52% 372
3	K ₂ CO ₃	25	DMF	Recovered starting material

When the reaction was conducted in the presence of TBAF only, desired sulfonimidoyl fluoride **373** was not observed. Instead, β -fluorinated sulfonamide **371** was isolated in 45% yield (Scheme 4.24). Reacting sulfonimide **255** under the same conditions gave the same sulfonamide product **371**.



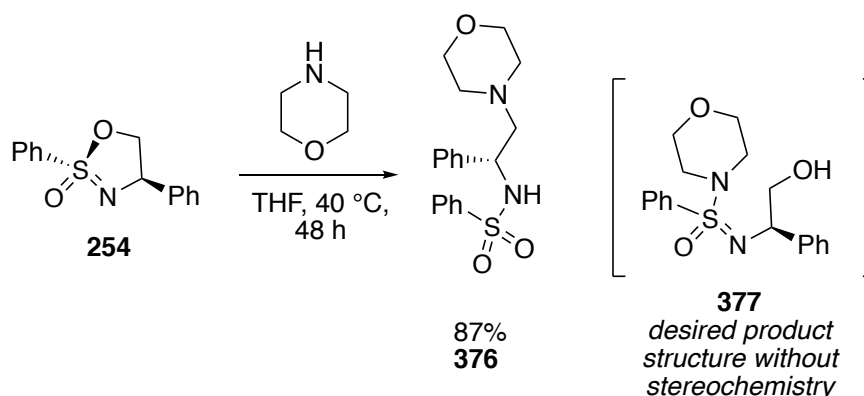
Scheme 4.24. Reaction of diastereomer **254** with tetrabutylammonium fluoride.

The reaction of phenyl cyclic diastereomer **254** was also reacted with lithium chloride. Utilising a mixture of *iso*-propanol:THF as reaction solvent at room temperature, chloride was found to have attacked at the carbon atom ring opening the sulfonimide to afford chloro-sulfonamide product **374** in 44% yield (Scheme 4.25). This same product was identified by NMR analysis when the other template **255** was utilised.



Scheme 4.25. Reaction of diastereomer **254** with lithium chloride.

Reaction of diastereomer **254** with an amine source, in this case morpholine, with attack at the sulfur centre would yield sulfonimidamide **377** (Scheme 4.26). When two equivalents of morpholine was reacted in THF with diastereomer template **254**, sulfonamide product **376** was obtained in 87% yield. Again, sulfonamide **376** was also observed by NMR analysis when using the other cyclic sulfonimide diastereomer **255**.



Scheme 4.26. Reaction of diastereomer **254** with morpholine.

To summarise, when trialling other nucleophiles that were not organometallic reagents, attack at the carbon rather than sulfur resulted in sulfonamides as the main reaction product.

4.9 Conclusions to Second Project and Future Work

The second research project shows the synthesis of cyclic sulfonimide templates as precursors for enantioenriched *NH*-sulfoximine synthesis. Accessing cyclic sulfonimides was realised through an oxidative chlorination-base catalysed cyclisation, using either *tert*-butyl hypochlorite or *N*-chlorosuccinimide and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as base. The stereochemistry of this transformation was monitored by obtaining X-ray crystals of both diastereomers of sulfinamide starting materials, then subjecting individually, each sulfinamide diastereomer to the oxidative conditions. The absolute stereochemistry of each cyclic sulfonimide in the case of the phenyl derivatives was confirmed by X-ray crystallography.

The most successful sulfonimide template was that with a phenyl-sulfur substituent. Both diastereomers **254** and **255** of this template reacted cleanly and efficiently with a range of Grignard reagents to introduce further functionalities at the sulfur atom. The stereochemistry of these Grignard reactions on each diastereomer template was confirmed by X-ray crystallographic analysis, corroborating with findings previously reported by the Reggeli group. Reaction yields for Grignard addition ranged from 17-98% yield, depending on substitution around the central sulfur atom.

To access enantioenriched *NH*-sulfoximines, the phenylethanol group on the nitrogen atom was successfully removed using an excess of sodium hydroxide and an oxygen atmosphere. Pleasingly, the reaction conditions were relatively mild, and limited stereochemical information was lost. This is the first reporting of this reaction to access *NH*-sulfoximines, an important moiety found in a number of chiral pharmaceuticals. The reaction yields for this final step were good to excellent (up to 95% yield), and enantiomeric excesses for *NH*-sulfoximines were good to excellent, from each diastereoisomer tested. Furthermore, computational studies with Professor Andy Teale (University of Nottingham) are ongoing to fully understand this reactivity pattern.

Finally, reaction of the template with alternative nucleophiles that were not of organometallic nature failed to attack the sulfur centre of the cyclic sulfonimide core **254** or **255**. Instead, attack at the carbon of the cyclic sulfonimide was observed with nucleophile examples including TMS-CF₃ (Ruppert reagent), LiCl or morpholine, favouring the sulfonamide products **371-372**, **374** and **376**.

With respect to future work, preliminary results obtained when hypervalent iodine species are used instead of oxidative chlorination reagents for the formation of cyclic sulfonimides **254/255** has shown promising results. Using acetonitrile as reaction solvent to allow the tethered alcohol on the sulfinamide substrates to react has been important. The desired cyclic sulfonimide products have been detected by both HRMS and NMR analysis, but further work will be needed in the future to investigate if the stereochemistry at sulfur is maintained.

5

Chapter Five *Experimental* *Synthesis of Racemic Sulfoximines*

5.0 Experimental: Racemic Sulfoximines

5.1 General Experimental and Procedures

Unless otherwise stated, all reagents were purchased from commercial sources and used without additional purification. Tetrahydrofuran was freshly distilled under argon from the sodium anion of benzophenone. All other anhydrous solvents were purchased or obtained from in house solvent purification towers. Water was deionised prior to use. All reactions were conducted in flame-dried glassware under an inert atmosphere of nitrogen or argon. Petroleum ethers refers to the fraction in the boiling range 40-60 °C. Brine is a saturated aqueous solution of sodium chloride in distilled water. Solvent(s) evaporation was performed under reduced pressure using a rotary evaporator with water bath temperature of 30 °C unless stated otherwise.

Thin layer chromatography was performed on Merck silica gel 60 F254 and visualised by UV lamp, aqueous alkaline potassium permanganate or cerium molybdate. Column chromatography was performed on silica gel Fluka 60. ¹H and ¹³C NMR spectral data were recorded using a Bruker DPX400, Bruker AV400 and Bruker AV(III)400 and Bruker AV500 spectrometer. Chemical shifts in ¹H NMR and ¹³C are quoted in ppm in reference to tetramethylsilane as an internal standard and/ or in reference to chloroform (7.26 ppm, 77.0 ppm), methanol (3.35 ppm, 49.3) and acetone (2.04, 29.8 ppm). Coupling constant (J) values are given in Hertz. Infrared spectral data were recorded using a Perkin-Elmer 1600 FTIR spectrometer. Optical rotation data were recorded using an ADP440 polarimeter. Mass spectrometry data were recorded using the open access Bruker MicroTOF spectrometer. Melting points were taken using Stuart Scientific SMP20 melting point apparatus.

Crystallography experiments were run at the University of Nottingham, on either an Atlas diffractometer or a Titan S2 diffractometer by Dr William Lewis or Dr. Stephen Argent.

The names of compounds were generated using Cambridgesoft ChemDraw® software.

General Procedure for Accessing Acyclic Sulfoximines

General Procedure: Preparation of sulfinyl chloride (GP1)

The corresponding disulfide (1 eq., 23-100 mmol) and acetic acid (2 eq., 46-200 mmol) were mixed and cooled to -20 °C. Sulfuryl chloride (3.1 eq., 71-310 mmol) was added dropwise with stirring over a period of 30 min. The reaction mixture was then stirred for 3 h at -20 °C and then allowed to warm to room temperature over a period of about 2 h. Evolution of SO₂ and HCl was observed during this time. The mixture was warmed to 35 °C for 1 h. The resulting acetyl chloride was evaporated under reduced pressure, providing the desired product as a liquid which was used without further purification.

General Procedure: Preparation of sulfinamide (GP2)

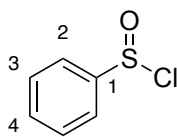
Sulfinyl chloride (1 eq., 0.56-60.8 mmol) in CH₂Cl₂ (3 M) was added dropwise to a solution of the corresponding amine (2 eq., 1.12-121.7 mmol) in CH₂Cl₂ (1M) at -78 °C. The mixture was then warmed to rt and stirred for 3 h. The solution was filtered and the filtrate was washed with water and then dried (MgSO₄), and concentrated under reduced pressure. The crude product was purified by flash column chromatography utilising a mixture of petroleum ether: ethyl acetate as eluent.

General Procedure: Preparation of sulfonimide (GP3)

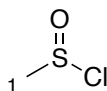
Iodosylbenzene (1 eq., 0.42-1.89 mmol) was added at room temperature to a solution of sulfinamide (1 eq., 0.42-1.89 mmol) in the relevant alcohol (2-5 mL). After completion of the reaction as monitored by TLC and mass spectrometry (ranging from 15 min to 1 h), the excess alcohol was removed under reduced pressure. The crude mixture was purified by flash chromatography utilising a mixture of petroleum ether:ethyl acetate or pentane/petroleum ether:diethyl ether as eluent.

General Procedure: Preparation of sulfoximine (GP4)

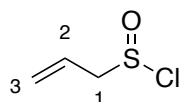
Sulfonimide (1 eq., 0.1-0.32 mmol) was dissolved in THF (2-6 mL) and cooled to -78 °C. The corresponding Grignard reagent or alkyl lithium reagent (5 eq., 0.5-1.59 mmol, 1.0-3.0 M in THF) was added dropwise, and then the reaction was brought to room temperature over 45 minutes. Upon completion as judged by TLC analysis, the reaction was quenched with saturated aqueous ammonium chloride (10 mL). Extraction of the product with diethyl ether (3 x 20 mL), followed by drying the combined organic layers (MgSO₄) and evaporation of organic solvents under reduced pressure afforded the crude sulfoximine. The sulfoximine products were purified by flash chromatography utilising a mixture of petroleum ether:ethyl acetate or pentane/petroleum ether:diethyl ether as eluent.

(±)-Benzenesulfinic chloride (136)⁹⁵

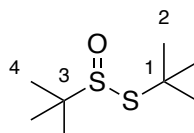
Following GP1, benzenesulfinic chloride (**136**) was prepared from diphenyl disulfide **134** (5.00 g, 23.0 mmol), sulfuryl chloride (9.58 g, 71.0 mmol) and acetic acid (2.75 g, 46.0 mmol), affording the desired compound as a pale yellow liquid (6.22 g, 85%); IR ν_{max} (cm^{-1}): 3066, 3005, 2927, 2854, 1476, 1327, 1147, 1092, 1035; ^1H NMR (400 MHz, CDCl_3) δ 7.92-7.89 (2H, m, H-2 or H-3), 7.68-7.56 (3H, m, H-3,4 or H-2,4); ^{13}C NMR (101 MHz, CDCl_3) δ 148.7 (C-1), 133.8 (C-4), 129.6 (C-2 or C-3), 123.8 (C-3 or C-2); HRMS calculated for $[\text{C}_7\text{H}_9\text{O}_2\text{S}]$ (compound was dissolved in MeOH and analysed as the corresponding methyl ester) $[\text{M} + \text{H}]^+$ 157.0318, found 157.0323.

(±)-Methanesulfinic chloride (137)⁹⁵

Following GP1, methanesulfinic chloride (**137**) was prepared from dimethyl disulfide **135** (9.42 g, 100 mmol), sulfuryl chloride (41.8 g, 310 mmol) and acetic acid (12.0 g, 200 mmol), affording the desired compound as a pale yellow liquid (19.1 g, 97%); IR ν_{max} (cm^{-1}): 2924, 2533, 1651, 1404, 1304, 1214, 1046, 953, 813, 747, 703; ^1H NMR (400 MHz, CDCl_3) δ 3.38 (3H, s, H-1); ^{13}C NMR (101 MHz, CDCl_3) δ 52.5 (C-1).

(±)-Prop-2-ene-1-sulfinic chloride (139)⁹⁶

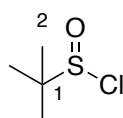
Allyltrimethylsilane **138** (4.00 mL, 25.2 mmol) was added dropwise to a vigorously stirred solution of thionyl chloride (3.67 mL, 50.3 mmol) and AlCl₃ (0.201 g, 1.51 mmol) at -20 °C under an atmosphere of N₂, over 30 min. The solution was then brought to room temperature, and stirred for a further 20 min (full conversion into sulfinyl chloride was confirmed by ¹H NMR). The product was concentrated under reduced pressure to afford the compound as a pale yellow liquid (1.85 g, 59%); IR ν_{max} (cm⁻¹): 2920, 1635, 1421, 1394, 1248, 1054, 1032, 988, 896, 838, 675, 607, 523; ¹H NMR (400 MHz, CDCl₃) δ 6.05-5.87 (1H, m, H-2), 5.66-5.44 (2H, m, H-3), 4.08 (2H, d, J = 7.5 Hz, H-1); ¹³C NMR (101 MHz, CDCl₃) δ 126.6 (C-3), 124.2 (C-2), 68.3 (C-1).

(±)-S-(*tert*-Butyl)-2-methylpropane-2-sulfinothioate (141)⁹⁷

Hydrogen peroxide (10.0 mL, 97.0 mmol, 30% aqueous solution) was added slowly to a solution of di-*tert*-butyl disulfide **140** (17.0 mL, 88.0 mmol) in glacial acetic acid (88.0 mL) at 0 °C. After addition, the reaction was warmed slowly to room temperature and stirred for 16 h. The reaction was quenched by adding ice/water (100 mL), and the mixture was extracted with CH₂Cl₂ (2 × 20 mL). The organic layer was washed with saturated aq. NaHCO₃ solution (20 mL), water (20 mL), dried (MgSO₄), filtered and concentrated under reduced pressure. The product was afforded as a colourless oil (14.1 g, 83%); IR ν_{max} (cm⁻¹): 2959, 2925, 1467, 1363, 1160, 1069, 1034, 565, 511, 463; ¹H NMR (400 MHz, CDCl₃) δ 1.56 (9H, s, H-4),

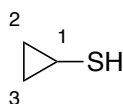
1.38 (9H, s, H-2); ^{13}C NMR (101 MHz, CDCl_3) δ 59.6 (C-3), 48.8 (C-1), 32.5 (C-4), 24.4 (C-2); HRMS calculated for $[\text{C}_8\text{H}_{19}\text{OS}_2]$ $[\text{M} + \text{H}]^+$ 195.0872, found 195.0873; / $[\text{C}_8\text{H}_{18}\text{OS}_2\text{Na}]$ $[\text{M} + \text{Na}]^+$ 217.0691, found 217.0692.

(±)-2-Methylpropane-2-sulfinic chloride (142)⁹⁷



S-(*tert*-butyl) 2-Methylpropane-2-sulfinothioate (**141**) (14.1 g, 72.7 mmol) was dissolved in CH_2Cl_2 (100 mL), and the solution was cooled to 0 °C. A solution of sulfuryl chloride (9.81 g, 72.7 mmol) in CH_2Cl_2 (100 mL) was added dropwise. After the addition was complete, the reaction mixture was stirred for 1 h, during which time the temperature was allowed to rise slowly to room temperature. The volatiles were removed under reduced pressure without heating to give the title compound as a yellow liquid and in good purity, with no further purification necessary (15.9 g, 78%); IR ν_{max} (cm^{-1}): 2965, 2924, 2853, 1456, 1365, 1310, 1214, 1181, 1160, 1110, 1059, 1017, 752, 667, 634, 565, 485; ^1H NMR (400 MHz, CDCl_3) δ 1.41 (9H, s, H-2); ^{13}C NMR (101 MHz, CDCl_3) δ 64.5 (C-1), 22.6 (C-2); HRMS calculated for $[\text{C}_5\text{H}_{13}\text{O}_2\text{S}_1]$ (compound was dissolved in MeOH and analysed as the corresponding methyl ester) $[\text{M} + \text{H}]^+$ 137.0631, found 137.0632.

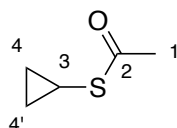
Cyclopropanethiol (144)⁹⁸



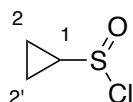
Cyclopropylmagnesium bromide was prepared by slow addition of cyclopropyl bromide **143** (14.2 g, 117 mmol) in THF (48.0 mL) to magnesium (2.69 g, 111 mmol) suspended in THF (6.00 mL) at 0 °C. The solution was then warmed to 50 °C for 3 h and then cooled to 0 °C, at which time S_8 (2.92 g, 91.2 mmol) was added

in small portions. Once addition was complete, the mixture was heated to 50 °C for 3 h and then cooled to 0 °C. Solid LiAlH₄ (2.39 g, 62.9 mmol) was added in portions and the solution was heated at reflux for 0.5 h. To the chilled (0 °C) solution were added (**SLOWLY!**) H₂O (35.0 mL), 5% aqueous H₂SO₄ (24.0 mL) and ether (60.0 mL). The layers were separated, the aqueous layer was extracted with ether (60.0 mL), and the combined ether extracts were washed with 5% aqueous H₂SO₄ (1 × 24.0 mL), 5% aqueous Na₂CO₃ (10 × 18.0 mL), saturated NH₄Cl (1 × 24.0 mL) and brine, dried over MgSO₄ and filtered affording an ether/THF solution of cyclopropanethiol.

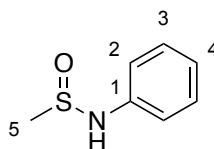
S-Cyclopropyl ethanethioate (145)⁹⁸



To an ether/THF solution of cyclopropanethiol (**144**) (from 117 mmol of cyclopropyl bromide) was added oven-dried Na₂CO₃ (51.0 g, 480 mmol) and acetyl chloride (11.5 g, 147 mmol). The solution was stirred vigorously at room temperature for 18 h. The mixture was filtered through Celite® and concentrated under reduced pressure. Distillation of the residue afforded the product as a colourless, foul-smelling liquid (1.48 g, 11%); b.p. 42 °C, 20 mm Hg; IR ν_{max} (cm⁻¹): 2936, 2843, 1754, 1731, 1681, 1283, 1052, 1013; ¹H NMR (400 MHz, CDCl₃) δ 2.30 (3H, s, H-1), 2.12 (1H, tt, J = 8.0, 4.5 Hz, H-3), 1.10-1.00 (2H, m, H-4_a and H-4'_a), 0.64 – 0.50 (2H, m, H-4_b or H-4'_b); ¹³C NMR (101 MHz, CDCl₃) δ 198.1 (C-2), 30.4 (C-1), 10.6 (C-3), 7.4 (C-4, C-4').

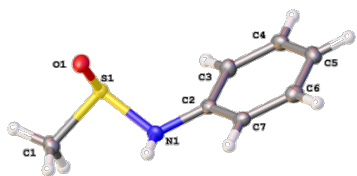
(±)-Cyclopropanesulfinic chloride (146)⁹⁸

A stirred solution of *S*-cyclopropyl thioacetate (**145**) (0.920 g, 7.95 mmol) and acetic anhydride (0.81 g, 7.95 mmol) was cooled to -10 °C. Sulfuryl chloride (2.15 g, 15.9 mmol) was added dropwise over a period of 45 min, and the solution was stirred for 45 min more at this temperature. The flask was then fitted with distillation apparatus, and the acetyl chloride was removed under reduced pressure followed by cyclopropanesulfinyl chloride (0.806 g, 82%), bp: 28-29 °C, 1 mm Hg; IR ν_{max} (cm⁻¹): 2931, 2847, 1619, 1511, 1420, 1366, 1318, 1257, 1159, 1067, 1026, 883, 820, 782, 686, 632, 608, 580, 542, 527, 480, 423; ¹H NMR (400 MHz, CDCl₃) δ 3.12-2.87 (1H, m, H-1), 1.57-1.47 (1H, m, H-2 or H-2'), 1.33-1.13 (3H, m, H-2 and H-2'); ¹³C NMR (101 MHz, CDCl₃) δ 41.1 (C-1), 8.6 (C-2 or C-2'), 4.6 (C-2 or C-2').

(±)-*N*-Phenylmethanesulfinamide (147)¹¹⁷

Following GP2, *N*-phenylmethanesulfinamide (**147**) was prepared from methanesulfinic chloride (**137**) (6.00 g, 60.8 mmol) and aniline (11.3 g, 121.7 mmol). The crude mixture was purified by flash chromatography (1:1 petroleum ether/diethyl ether) to afford the title compound as a pale yellow solid (5.06 g, 53%); m.p. 85-86 °C, lit. 87°C;¹¹⁷ IR ν_{max} (cm⁻¹): 3171, 2000, 1621, 1490, 1401, 1301, 1227, 1715, 1150, 1050, 975, 879, 840, 749, 691, 502; ¹H NMR (400 MHz, CDCl₃) 7.28 (2H, dd, *J* = 9.0, 7.0 Hz, H-3), 7.11-7.02 (3H, m, H-2,4), 6.97 (1H, s, NH), 2.85 (3H, s, H-5); ¹³C NMR (101 MHz, CDCl₃) 141.1 (C-1), 129.6 (C-3),

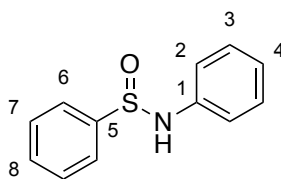
123.2 (C-4), 118.5 (C-2), 42.2 (C-5); HRMS calculated for $[C_7H_{10}NOS] [M + H]^+$ 156.0478, found 156.0478 / $[C_7H_9NOSNa] [M + Na]^+$ 178.0297, found 178.0298.



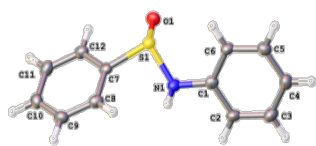
X-ray crystal structure of *N*-phenylmethanesulfinamide C_7H_9NOS $M_w = 155.21$;

$T = 120(2)$ K; $\lambda = 1.54184$ Å; orthorhombic; $P2_1/n$ space group; $a = 6.0087(2)$ Å, $b = 7.3575(3)$ Å, $c = 16.9078(6)$ Å; $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 90^\circ$; $V = 747.48(5)$ Å³; $Z = 4$; $D = 1.379$ g/cm³; $R_1 = 0.0275$, $wR_2 = 0.0723$ (all data), $GoF = 1.049$; CCDC: 1837492.

(±)-*N*-Phenylbenzenesulfinamide (148)¹¹⁸

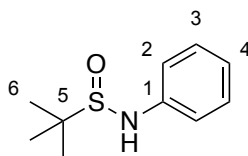


Following GP2, *N*-phenylbenzenesulfinamide (**148**) was prepared from benzenesulfinic chloride (**136**) (6.22 g, 38.7 mmol) and aniline (7.21 g, 77.4 mmol). The crude mixture was purified by flash chromatography (9:1 petroleum ether/ethyl acetate) to afford the title compound as a pale white solid (4.93 g, 58%); m.p. 110–112 °C, lit. 113 °C;¹¹⁸ IR $\nu_{\max}$ (cm⁻¹): 3184, 3042, 1589, 1496, 1473, 1443, 1404, 1279, 1229, 1176, 1088, 1053, 1023, 994, 876, 820, 743, 658, 633, 612, 504, 453; ¹H NMR (400 MHz, CDCl₃) δ 7.93–7.82 (2H, m, H-6), 7.66–7.58 (3H, m, H-7,8), 7.42–7.32 (2H, m, H-2), 7.25–7.11 (3H, m, H-3,4), 6.63 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 144.6 (C-5), 140.8 (C-1), 131.5 (C-8), 129.6 (C-3), 129.2 (C-7), 125.7 (C-6), 123.7 (C-4), 119.0 (C-2); HRMS calculated for $[C_{12}H_{12}NOS] [M + H]^+$ 218.0634, found 218.0641 / $[C_{12}H_{11}NOSNa] [M + Na]^+$ 240.0454, found 240.0457.

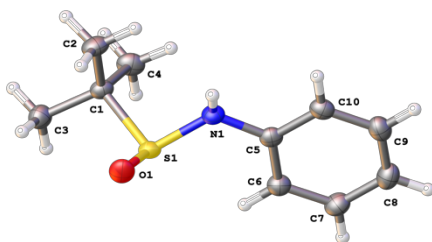


X-ray crystal structure of *N*-phenylbenzenesulfinamide $C_{12}H_{11}NOS$ Mw = 217.28; T = 120(2) K; $\lambda = 1.54184$ Å; Monoclinic; $P2_1/n$ space group; $a = 12.3690(5)$ Å, $b = 15.5248(5)$ Å, $c = 5.55474(17)$ Å; $\alpha = 90^\circ$, $\beta = 101.153(4)^\circ$, $\gamma = 90^\circ$; $V = 1046.51(6)$ Å³; $Z = 4$; $D = 1.379$ g/cm³; $R_1 = 0.0620$, $wR_2 = 0.1497$ (all data), GoF = 1.053; CCDC: 1837493.

(±)-2-Methyl-*N*-phenylpropane-2-sulfinamide (149)^{118,119,120}



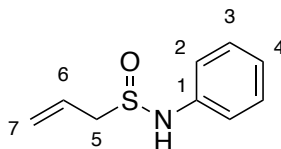
Following GP2, 2-methyl-*N*-phenylpropane-2-sulfinamide (**149**) was prepared from 2-methylpropane-2-sulfinic chloride (**142**) (5.00 g, 35.6 mmol) and aniline (6.62 g, 71.1 mmol). The crude mixture was purified by flash chromatography (1:1 petrol/ethyl acetate) to afford the title compound as a white solid (4.23 g, 60%); m.p. 102-104 °C, lit. 103-104 °C;¹¹⁸ IR $\nu_{\max}$ (cm⁻¹): 3184, 2958, 1598, 1494, 1473, 1389, 1360, 1280, 1134, 1056, 1029, 874, 748, 692, 611, 560, 505; ¹H NMR (400 MHz, CDCl₃) δ 7.31-7.24 (2H, m, H-2 or 3), 7.07-6.98 (3H, m, H-2,4 or H-3,4), 5.57 (1H, s, NH), 1.35 (9H, s, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 142.2 (C-1), 129.5 (C-2 or C-3), 123.0 (C-4), 118.4 (C-2 or C-3), 56.6 (C-5), 22.6 (C-6); HRMS calculated for [C₁₀H₁₆NOS] [M + H]⁺ 198.0947, found 198.0947 / [C₁₀H₁₅NOSNa] [M + Na]⁺ 220.0767, found 220.0767.



X-ray crystal structure of 2-methyl-*N*-phenylpropane-2-sulfinamide $C_{10}H_{15}NOS$ Mw = 197.29; T = 120(2) K; $\lambda = 1.54184$ Å; Monoclinic; $P2_1/c$ space group; $a =$

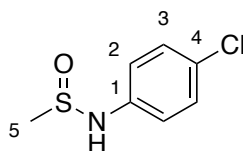
10.32845(14) Å, $b = 20.5078(2)$ Å, $c = 10.35372(12)$ Å; $\alpha = 90^\circ$, $\beta = 103.5675(13)$, $\gamma = 90^\circ$; $V = 2131.86(5)$ Å³; $Z = 8$; $D = 1.229$ g/cm³; $R_1 = 0.0426$, $wR_2 = 0.1206$ (all data), $GoF = 1.097$; CCDC: 1837494.

(±)-*N*-Phenylprop-2-ene-1-sulfinamide (150)



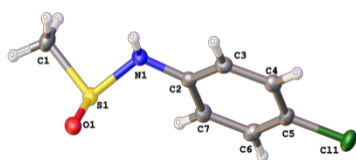
Following GP2, *N*-phenylprop-2-ene-1-sulfinamide (**150**) was prepared from prop-2-ene-1-sulfinic chloride (**139**) (0.800 g, 6.42 mmol) and aniline (1.20 g, 12.8 mmol). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.930 g, 79%); IR $\nu_{\max}$ (cm⁻¹): 3152, 1598, 1494, 1412, 1396, 1280, 1047, 991, 690, 614, 594, 568; ¹H NMR (400 MHz, CDCl₃) δ 7.51-7.32 (1H, m, NH), 7.24-7.15 (2H, m, H-2 or H-3), 7.07-6.94 (3H, m, H-2,4 or H-3,4), 6.00-5.79 (1H, m, H-6), 5.47-5.31 (2H, m, H-7), 3.80 (1H, ddt, $J = 13.0, 7.5, 1.0$ Hz, H-5), 3.63 (1H, dd, $J = 13.0, 7.5$ Hz, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 141.3 (C-1), 129.4 (C-2 or C-3), 126.0 (C-6), 123.8 (C-7), 123.0 (C-4), 118.3 (C-2 or C-3), 59.2 (C-5); HRMS calculated for [C₉H₁₂NOS] [M + H]⁺ 182.0634, found 182.0628 / [C₉H₁₁NOSNa] [M + Na]⁺ 204.0454, found 204.0451.

(±)-*N*-(4-Chlorophenyl)methanesulfinamide (151)¹²¹



Following GP2, *N*-(4-chlorophenyl)methanesulfinamide (**151**) was prepared from methanesulfinic chloride (**137**) (3.00 g, 30.4 mmol) and 4-chloroaniline (7.76 g, 60.8 mmol). The crude mixture was purified by flash chromatography (1:1

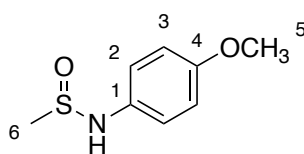
petroleum ether/ethyl acetate) to afford the title compound as a white solid (2.95 g, 51%); m.p. 73-75 °C; lit. 73-74 °C;¹²¹ IR ν_{max} (cm⁻¹): 3143, 3047, 2918, 2841, 1490, 1297, 1238, 1062, 1046, 1008, 972, 885, 853, 706, 516; ¹H NMR (400 MHz, CDCl₃) δ 7.48 (1H, s, NH), 7.17 (2H, d, J = 9.0 Hz, H-2 or H-3), 6.92 (2H, d, J = 9.0 Hz, H-2 or H-3), 2.84 (3H, s, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 139.7 (C-1 or C-4), 129.5 (C-2 or C-3), 128.4 (C-1 or C-4), 119.6 (C-2 or C-3), 42.3 (C-5); HRMS calculated for [C₇H₉NOS³⁵Cl] [M + H]⁺ 190.0088, found 190.0083 / [C₇H₈NOS³⁵ClNa] [M + Na]⁺ 211.9907, found 211.9903.



X-ray crystal structure of *N*-(4-chlorophenyl)methanesulfinamide C₇H₈ClNOS
Mw = 189.65; T = 120(2) K; λ = 1.54184 Å;

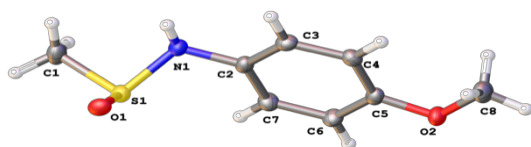
orthorhombic; Pbc_a space group; a = 12.661(2) Å, b = 6.2568(10) Å, c = 21.107(3) Å; α = 90°, β = 90°, γ = 90°; V = 1672.0(5) Å³; Z = 8; D = 1.507 g/cm³; R₁ = 0.0410, wR₂ = 0.1139 (all data), GoF = 1.047; CCDC: 1837500.

(±)-*N*-(4-Methoxyphenyl)methanesulfinamide (152**)**¹²²



Following GP2, *N*-(4-methoxyphenyl)methanesulfinamide (**152**) was prepared from methanesulfinic chloride (**137**) (3.00 g, 30.4 mmol) and *p*-anisidine (7.50 g, 60.9 mmol). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate to 9.5:0.5 dichloromethane/methanol) to afford the title compound as an off-white solid (4.77 g, 84%); m.p. 106-107 °C, lit. 107-108 °C;¹²² IR ν_{max} (cm⁻¹): 3162, 2924, 2834, 1607, 1593, 1507, 1440, 1300, 1281,

1240, 1117, 1031, 971, 887, 826, 760, 700; ^1H NMR (400 MHz, CDCl_3) δ 7.03 (2H, d, $J = 7.0$ Hz, H-2 or H-3), 6.81 (2H, d, $J = 7.0$ Hz, H-2 or H-3), 6.49 (1H, s, NH), 3.77 (3H, s, H-5), 2.76 (3H, s, H-6); ^{13}C NMR (101 MHz, CDCl_3) δ 156.7 (C-1 or C-4), 133.3 (C-1 or C-4), 122.5 (C-2 or C-3), 114.8 (C-2 or C-3), 55.6 (C-5), 42.2 (C-6); HRMS calculated for $[\text{C}_8\text{H}_{12}\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 186.0583, found 186.0581 / $[\text{C}_8\text{H}_{11}\text{NO}_2\text{SNa}]$ $[\text{M} + \text{Na}]^+$ 208.0403, found 208.0400.

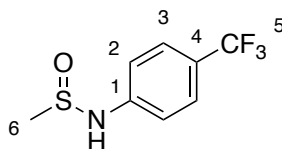


X-ray crystal structure of *N*-(4-methoxyphenyl)methanesulfinamide

$\text{C}_8\text{H}_{11}\text{NO}_2\text{S}$ Mw = 185.24; T =

120(2) K; $\lambda = 1.54184$ Å; Monoclinic; $\text{P2}_1/\text{c}$ space group; $a = 7.1297(10)$ Å, $b = 8.7567(12)$ Å, $c = 14.1017(18)$ Å; $\alpha = 90^\circ$, $\beta = 91.383(12)^\circ$, $\gamma = 90^\circ$; $V = 880.1(2)$ Å³; $Z = 4$; $D = 1.398$ g/cm³; $R_1 = 0.0353$, $wR_2 = 0.0946$ (all data), GoF = 1.070; CCDC: 1837496.

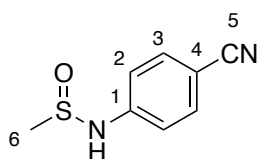
(±)-*N*-(4-(Trifluoromethyl)phenyl)methanesulfinamide (153)



Following GP2, *N*-(4-(trifluoromethyl)phenyl)methanesulfinamide (**153**) was prepared from methanesulfinic chloride (**137**) (0.234 g, 2.38 mmol) and 4-(trifluoromethyl)aniline (0.770 g, 4.75 mmol). The crude mixture was purified by flash chromatography (1:1 petrol/ethyl acetate to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a white solid (0.216 g, 41%); m.p. 114-117 °C; IR ν_{max} (cm⁻¹): 3170, 2376, 1616, 1519, 1472, 1410, 1112, 1083, 1061, 838, 789; ^1H NMR (400 MHz, CD_3OD) δ 7.58 (2H, d, $J = 8.0$ Hz, H-2 or H-3), 7.22 (2H, d, $J = 8.0$ Hz, H-2 or H-3), 2.89 (3H, s, H-6), (NH not

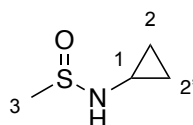
observed); ^{13}C NMR (101 MHz, CD_3OD) δ 146.9 (C-1), 127.8 (q, $J = 4.0$ Hz, C-3), 125.8 (q, $J = 270$ Hz, C-5), 125.2 (q, $J = 32.5$ Hz, C-4), 117.9 (C-2), 41.5 (C-6); ^{19}F NMR (376 MHz, CD_3OD) δ -63.4; HRMS calculated for $[\text{C}_8\text{H}_9\text{NOSF}_3] [\text{M} + \text{H}]^+$ 224.0351, found 224.0356 / $[\text{C}_8\text{H}_8\text{NOSF}_3\text{Na}] [\text{M} + \text{Na}]^+$ 246.0171, found 246.0171.

($\pm$)-*N*-(4-Cyanophenyl)methanesulfinamide (154**)**



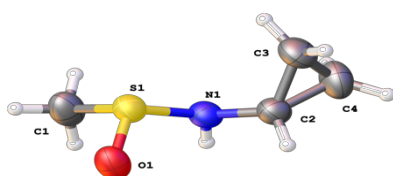
Following GP2, *N*-(4-Cyanophenyl)methanesulfinamide (**154**) was prepared from methanesulfinic chloride (**137**) (2.00 g, 20.3 mmol) and 4-aminobenzonitrile (4.82 g, 40.6 mmol). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a yellow solid (1.98 g, 54%); m.p. 135-138 °C; ^1H NMR (400 MHz, CD_3OD) δ 7.68-7.61 (2H, m, H-2 or H-3), 7.24-7.18 (2H, m, H-2 or H-3), 2.91 (3H, s, H-6), (NH not observed); ^{13}C NMR (101 MHz, CD_3OD) δ 147.9 (C-1), 134.9 (C-2 or C-3), 119.9 (C-4), 117.8 (C-2 or C-3), 105.7 (C-5), 41.5 (C-6); HRMS calculated for $[\text{C}_8\text{H}_9\text{N}_2\text{OS}] [\text{M} + \text{H}]^+$ 181.0430, found 181.0432 / $[\text{C}_8\text{H}_8\text{N}_2\text{OSNa}] [\text{M} + \text{Na}]^+$ 203.0250, found 203.0251.

($\pm$)-*N*-Cyclopropylmethanesulfinamide (155**)**



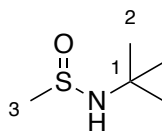
Following GP2, *N*-cyclopropylmethanesulfinamide (**155**) was prepared from methanesulfinic chloride (**137**) (3.00 g, 30.4 mmol) and cyclopropylamine (3.48 g,

60.9 mmol). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.310 g, 9%); IR ν_{max} (cm^{-1}): 2965, 2921, 2853, 1703, 1651, 1305, 1145, 1045, 965, 787, 536; ^1H NMR (400 MHz, CDCl_3) δ 4.55 (1H, s, NH), 2.78-2.69 (1H, m, H-1), 2.59 (3H, s, H-3), 0.70-0.64 (2H, m, H-2_a and H-2'_a), 0.61-0.53 (2H, m, H-2_b and H-2'_b); ^{13}C NMR (101 MHz, CDCl_3) δ 41.7 (C-3), 24.1 (C-1), 8.3 (C-2 or C-2'), 6.2 (C-2 or C-2'); HRMS calculated for $[\text{C}_4\text{H}_{10}\text{NOS}]$ $[\text{M} + \text{H}]^+$ 120.0478, found 120.0481 / $[\text{C}_4\text{H}_9\text{NOSNa}]$ $[\text{M} + \text{Na}]^+$ 142.0297, found 142.0303.



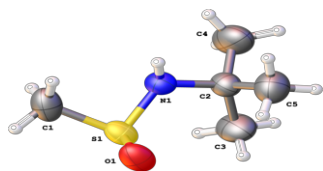
X-ray crystal structure of *N*-cyclopropylmethanesulfinamide $\text{C}_4\text{H}_9\text{NOS}$ $M_w = 119.18$; $T = 120(2)$ K; $\lambda = 1.54184$ Å; Monoclinic; $P2_1/c$ space group; $a = 9.6787(4)$ Å, $b = 6.5804(2)$ Å, $c = 10.7622(4)$ Å; $\alpha = 90^\circ$, $\beta = 115.444(5)$, $\gamma = 90^\circ$; $V = 618.95(4)$ Å³; $Z = 4$; $D = 1.279$ g/cm³; $R_1 = 0.0342$, $wR_2 = 0.1081$ (all data), GoF = 1.124; CCDC: 1837495.

(±)-*N*-(*tert*-butyl)Methanesulfinamide (156**)**¹²³



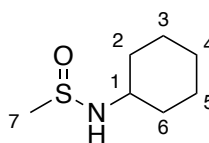
Following GP2, *N*-(*tert*-butyl)methanesulfinamide (**156**) was prepared from methanesulfinic chloride (**137**) (3.00 g, 30.4 mmol) and *tert*-butylamine (4.45 g, 60.9 mmol). The crude mixture was purified by flash chromatography (1:1 petrol/ethyl acetate to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a colourless oil (2.50 g, 60%); IR ν_{max} (cm^{-1}): 3410, 3186, 2969, 2935, 2919, 1644, 1542, 1428, 1413, 1305, 1226, 1140, 1032, 948, 858; ^1H NMR (400 MHz, CDCl_3) δ 3.97 (1H, s, NH), 2.50 (3H, s, H-3), 1.20 (9H, s, H-2); ^{13}C NMR (101 MHz, CDCl_3) δ 53.8 (C-1), 43.9 (C-3), 30.9 (C-2); HRMS calculated for

[C₅H₁₄NOS] [M + H]⁺ 136.0791, found 136.0783 / [C₅H₁₃NOSNa] [M + Na]⁺ 158.0610, found 158.0605.

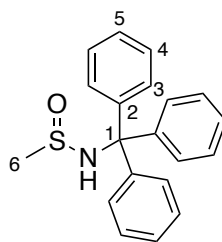


X-ray crystal structure of *N*-(*tert*-butyl)methanesulfinamide C₅H₁₃NOS Mw = 135.22; T = 120(2) K; λ = 1.54184 Å; Monoclinic; P2₁ space group; a = 9.6839(3) Å, b = 7.3888(3) Å, c = 11.5131(4) Å; α = 90°, β = 103.909 (3), γ = 90°; V = 799.64(5) Å³; Z = 4; D = 1.123 g/cm³; R₁ = 0.0443, wR₂ = 0.1255 (all data), GoF = 1.168; CCDC: 1837497.

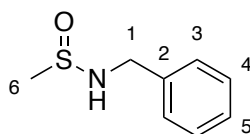
(±)-*N*-Cyclohexylmethanesulfinamide (157**)**¹²⁴



Following GP2, *N*-cyclohexylmethanesulfinamide (**157**) was prepared from methanesulfinic chloride (**137**) (3.00 g, 30.4 mmol) and cyclohexylamine (6.04 g, 60.9 mmol). The crude mixture was purified by flash chromatography (1:1 petrol/ethyl acetate to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a colourless oil (4.49 g, 91%); IR ν_{max} (cm⁻¹): 3409, 3173, 2925, 2852, 1649, 1449, 1411, 1366, 1046, 964, 890, 864, 698; ¹H NMR (400 MHz, CDCl₃) δ 3.77 (1H, d, J = 5.5 Hz, NH), 3.31-3.11 (1H, m, H-1), 2.58 (3H, s, H-7), 2.04-1.87 (2H, m, H-Cy), 1.78-1.63 (2H, m, H-Cy), 1.62-1.53 (1H, m, H-Cy), 1.40-1.22 (3H, m, H-Cy), 1.22-1.07 (2H, m, H-Cy); ¹³C NMR (101 MHz, CDCl₃) δ 53.3 (C-1), 43.0 (C-7), 35.4 (Cy), 34.2 (Cy), 25.5 (Cy), 24.9 (Cy), 24.7 (Cy); HRMS calculated for [C₇H₁₆NOS] [M + H]⁺ 162.0947, found 162.0946 / [C₇H₁₅NOSNa] [M + Na]⁺ 184.0767, found 184.0773.

(±)-*N*-Tritylmethanesulfinamide (158)

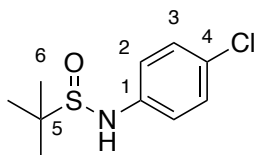
Following GP2, *N*-tritylmethanesulfinamide (**158**) was prepared from methanesulfinic chloride (**137**) (0.0550 g, 0.560 mmol) and tritylamine (0.291 g, 1.12 mmol). The crude mixture was purified by flash chromatography (1:1 petrol/ethyl acetate to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a colourless oil (0.101 g, 56%); IR ν_{max} (cm^{-1}): 3182, 3057, 2360, 1492, 1446, 1408, 1043, 981, 757, 731, 700; ^1H NMR (400 MHz, CDCl_3) δ 7.35-7.27 (15H, m, H-3,4,5), 4.97 (1H, s, NH), 2.59 (3H, s, H-6); ^{13}C NMR (101 MHz, CDCl_3) δ 144.9 (C-2), 129.2 (C-3 or C-4), 128.2 (C-3 or C-4), 127.5 (C-5), 73.0 (C-1), 44.3 (C-6); HRMS calculated for $[\text{C}_{20}\text{H}_{20}\text{NOS}]$ $[\text{M} + \text{H}]^+$ 322.1260, found 322.1257 / $[\text{C}_{20}\text{H}_{19}\text{NOSNa}]$ $[\text{M} + \text{Na}]^+$ 344.1080, found 344.1078.

(±)-*N*-Benzylmethanesulfinamide (159)

Following GP2, *N*-benzylmethanesulfinamide (**159**) was prepared from methanesulfinic chloride (**137**) (3.00 g, 30.4 mmol) and benzylamine (6.52 g, 60.9 mmol). The crude mixture was purified by flash chromatography (1:1 petrol/ethyl acetate) to afford the title compound as a colourless oil (4.40 g, 85%); IR ν_{max} (cm^{-1}): 3172, 3028, 1494, 1453, 1046, 1023, 749, 732, 696; ^1H NMR (400 MHz, CDCl_3) δ 7.62-6.88 (5H, m, Ar), 4.50 (1H, t, $J = 6.0$ Hz, NH), 4.39-4.06 (2H, m, H-1), 2.64 (3H, s, H-6); ^{13}C NMR (101 MHz, CDCl_3) δ 138.1 (C-2), 128.7 (C-3 or C-4), 128.2

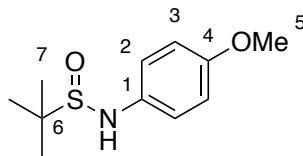
(C-3 or C-4), 127.7 (C-5), 46.0 (C-1), 41.8 (C-6); HRMS calculated for $[\text{C}_8\text{H}_{12}\text{NOS}] [\text{M} + \text{H}]^+$ 170.0634, found 170.0634 / $[\text{C}_8\text{H}_{11}\text{NOSNa}] [\text{M} + \text{Na}]^+$ 192.0454, found 192.0457.

(±)-*N*-(4-Chlorophenyl)-2-methylpropane-2-sulfinamide (160)



Following GP2, *N*-(4-chlorophenyl)-2-methylpropane-2-sulfinamide (**160**) was prepared from 2-methylpropane-2-sulfinic chloride (**142**) (5.00 g, 35.6 mmol) and 4-chloro aniline (9.07 g, 71.1 mmol). The crude mixture was purified by flash chromatography (1:1 pentane/diethyl ether to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a white solid (6.15 g, 75%); m.p. 120-123 °C; IR ν_{max} (cm^{-1}): 3227, 2964, 1619, 1489, 1376, 1335, 1090, 1028, 871, 822, 725, 607; ^1H NMR (400 MHz, CDCl_3) δ 7.22-7.14 (2H, m, H-2 or H-3), 6.96-6.89 (2H, m, H-2 or H-3), 5.78 (1H, s, NH), 1.31 (9H, s, H-6); ^{13}C NMR (101 MHz, CDCl_3) δ 141.0 (C-1 or C-4), 129.4 (C-2 or C-3), 128.1 (C-1 or C-4), 119.6 (C-2 or C-3), 56.9 (C-5), 22.6 (C-6); HRMS calculated for $[\text{C}_{10}\text{H}_{15}\text{NOS}^{35}\text{Cl}] [\text{M} + \text{H}]^+$ 232.0557, found 232.0552 / $[\text{C}_{10}\text{H}_{14}\text{NOS}^{35}\text{ClNa}] [\text{M} + \text{Na}]^+$ 254.0377, found 254.0372.

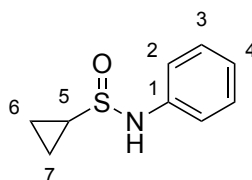
(±)-*N*-(4-Methoxyphenyl)-2-methylpropane-2-sulfinamide (161)¹²⁵



Following GP2, *N*-(4-methoxyphenyl)-2-methylpropane-2-sulfinamide (**161**) was prepared from 2-methylpropane-2-sulfinic chloride (**142**) (5.00 g, 35.6 mmol) and *p*-anisidine (8.76 g, 71.1 mmol). The crude mixture was purified by flash chromatography (1:1 pentane/diethyl ether to 9.5:0.5 dichloromethane/methanol)

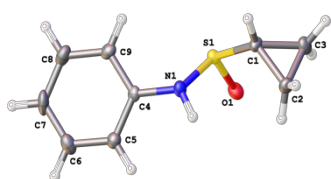
to afford the title compound as a white solid (5.50 g, 68%) m.p. 110-112 °C; lit. 110 °C;¹²⁵ IR ν_{max} (cm⁻¹): 3194, 2953, 2833, 1593, 1507, 1459, 1276, 1241, 1145, 1053, 883, 824, 759; ¹H NMR (400 MHz, CDCl₃) δ 7.03-6.94 (2H, m, H-2 or H-3), 6.85-6.78 (2H, m, H-2 or H-3), 5.20 (1H, s, NH), 3.77 (3H, s, H-5), 1.32 (9H, s, H-7); ¹³C NMR (101 MHz, CDCl₃) δ 156.4 (C-4), 135.0 (C-1), 121.6 (C-2 or C-3), 114.8 (C-2 or C-3), 56.4 (C-6), 55.7 (C-5), 22.6 (C-7); HRMS calculated for [C₁₁H₁₈NO₂S] [M + H]⁺ 228.1053, found 228.1053 / [C₁₁H₁₇NO₂SNa] [M + Na]⁺ 250.0872, found 250.0871.

(±)-*N*-Phenylcyclopropanesulfinamide (164)⁹⁹



To a stirred solution of aniline (0.500 g, 5.37 mmol) in anhydrous toluene (2.50 mL) at 25 °C was added a solution of thionyl chloride (0.830 g, 6.98 mmol) in anhydrous toluene (2.50 mL). This suspension was heated to reflux for 2-3 h under N₂ atmosphere, whereupon a clear solution was observed. All volatiles were removed under reduced pressure to afford the crude *N*-thionylaniline, which was dissolved in anhydrous THF (2.50 mL). To this solution was added at 0 °C cyclopropylmagnesium bromide solution in Et₂O (8.05 mL, 8.05 mmol, 1 M) under N₂ atmosphere. The reaction mixture was stirred at 0 °C for 1 h, and then at rt for 1 h, under N₂ atmosphere. The mixture was quenched by sat. aq NH₄Cl (12.5 mL) and extracted with EtOAc (3 × 35 mL). The combined organic layers were dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (4:1 petroleum ether/ethyl acetate) to afford the desired sulfinamide as a white solid (0.620 g, 64%); m.p. 85-87 °C, lit. 84-

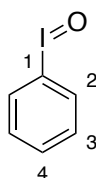
86 °C;⁹⁹ IR ν_{max} (cm⁻¹): 3183, 3170, 1598, 1495, 1481, 1280, 1228, 1189, 1067, 1026, 878, 692, 644, 613; ¹H NMR (400 MHz, CDCl₃) δ 7.31-7.26 (2H, m, H-2 or H-3), 7.09-7.02 (3H, m, H-2,4 or H-3,4), 5.93 (1H, s, NH), 2.37 (1H, tt, J = 8.0, 5.0 Hz, H-5), 1.42-1.31 (1H, m, H-6 or H-7); 1.00-0.82 (3H, m, H-6,7); ¹³C NMR (101 MHz, CDCl₃) δ 141.2 (C-1), 129.5 (C-2 or C-3), 123.1 (C-4), 118.4 (C-2 or C-3), 31.2 (C-5), 3.49 (C-6 or C-7), -0.57 (C-6 or C-7); HRMS calculated for [C₉H₁₂NOS] [M + H]⁺ 182.0634, found 182.0633 / [C₉H₁₁NOSNa] [M + Na]⁺ 204.0454, found 204.0453.



X-ray crystal structure of compound *N*-phenylcyclopropanesulfinamide C₉H₁₁NOS Mw = 181.25; T = 120(2) K; λ = 1.54184 Å; orthorhombic;

Pca2₁/n space group; a = 9.3636(5) Å, b = 11.2097(5) Å, c = 8.4946(4) Å; α = 90°, β = 90°, γ = 90°; V = 891.62(7) Å³; Z = 4; D = 1.350 g/cm³; R₁ = 0.0488, wR₂ = 0.1264 (all data), GoF = 1.025; CCDC: 1837498.

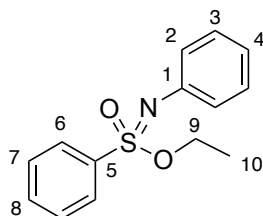
Iodosylbenzene (95)¹²⁶



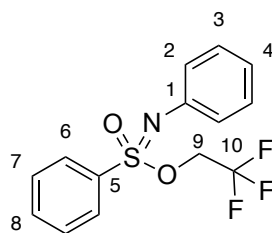
(Diacetoxyiodo)benzene (2.50 g, 7.76 mmol) was dispersed in aqueous NaOH (15% w/w, 19 mL) and stirred for 2 h at rt. The reaction was then filtered and the solid was washed with H₂O (2 × 30 mL), CHCl₃ (30 mL) and dried overnight *in vacuo*. The product was obtained as a pale yellow solid (1.60 g, 93%); m.p. 205-206 °C, lit. 210 °C;¹²⁶ IR ν_{max} (cm⁻¹): 2364, 2236, 2174, 2035, 1434, 734, 689, 488, 445; ¹H NMR (400 MHz, CD₃OD) 8.08-8.03 (2H, m, H-2), 7.63-7.50 (3H, m, H-3,4); ¹³C NMR (101 MHz, CD₃OD) 133.3 (C-4), 132.2 (C-2 or C-3), 132.0 (C-3 or

C-2), 122.5 (C-1); HRMS calculated for $[\text{C}_6\text{H}_6\text{IO}]$ $[\text{M} + \text{H}]^+$ 220.9458, found 220.9450.

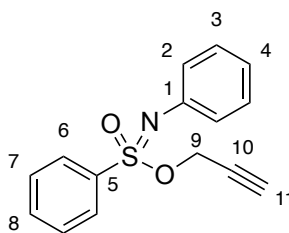
(±)-Ethyl *N*-phenylbenzenesulfonimide (165**)**⁷⁴



Following GP3, ethyl *N*-phenylbenzenesulfonimide (**165**) was prepared from sulfinamide **148** (0.105 g, 0.485 mmol), iodosylbenzene (0.107 g, 0.485 mmol) and ethanol (2 mL). The crude mixture was purified by flash chromatography (4:1 petroleum ether/diethyl ether) to afford the title compound as a yellow oil (0.0944 g, 75%); IR ν_{max} (cm^{-1}): 2980, 1594, 1488, 1446, 1319, 1302, 1233, 1174, 1145, 1112, 1057, 998, 896, 783, 751, 687, 628, 588, 570, 546; ^1H NMR (400 MHz, CDCl_3) δ 8.16-8.07 (2H, m, H-6 or H-7), 7.68-7.62 (1H, m, H-8), 7.61-7.54 (2H, m, H-6 or H-7), 7.33-7.24 (4H, m, H-2, 3), 7.05 (1H, tt, $J = 7.5, 1.5$ Hz, H-4), 4.11-4.03 (2H, m, H-9), 1.25 (3H, t, $J = 7.0$ Hz, H-10); ^{13}C NMR (101 MHz, CDCl_3) δ 142.5 (C-1), 137.6 (C-5), 133.2 (C-8), 129.2 (C-6 or C-7 or C-2 or C-3), 129.1 (C-6 or C-7 or C-2 or C-3), 127.9 (C-6 or C-7 or C-2 or C-3), 123.6 (C-6 or C-7 or C-2 or C-3), 122.6 (C-4), 66.4 (C-9), 14.7 (C-10); HRMS calculated for $[\text{C}_{14}\text{H}_{16}\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 262.0896, found 262.0901 / $[\text{C}_{14}\text{H}_{15}\text{NO}_2\text{SNa}]$ $[\text{M} + \text{Na}]^+$ 284.0716, found 284.0712.

(±)-2,2,2-Trifluoroethyl *N*-phenylbenzenesulfonimide (166)⁷⁴

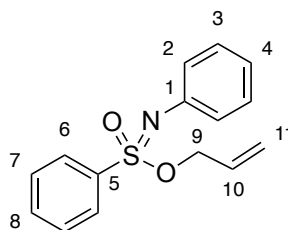
Following GP3, 2,2,2-trifluoroethyl *N*-phenylbenzenesulfonimide (**166**) was prepared from sulfinamide **148** (0.163 g, 0.750 mmol), iodosylbenzene (0.165 g, 0.750 mmol) and 2,2,2-trifluoroethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/diethyl ether) to afford the title compound as a dark brown oil (0.162 g, 69%); IR ν_{max} (cm⁻¹): 3224, 3042, 2434, 1521, 1476, 1423, 1334, 1192, 1017, 1192, 1017, 928, 909, 849, 660, 626; ¹H NMR (400 MHz, CDCl₃) δ 8.16-7.83 (2H, m, H-6), 7.68-7.53 (1H, m, H-8), 7.53-7.43 (2H, m, H-7), 7.25-7.18 (2H, m, H-3), 7.19-7.12 (2H, m, H-2), 7.04-6.94 (1H, m, H-4), 4.15 (2H, q, J = 8.0 Hz, H-9); ¹³C NMR (101 MHz, CDCl₃) δ 140.9 (C-1), 136.4 (C-5), 134.1 (C-8), 129.42 (C-7), 129.41 (C-3), 128.0 (C-6), 123.9 (C-2), 123.7 (C-4), 122.2 (q, J = 276 Hz, C-10), 65.0 (q, J = 38.0 Hz, C-9); ¹⁹F NMR (376 MHz, CDCl₃) δ -73.5; HRMS calculated for [C₁₄H₁₃F₃NO₂S] [M + H]⁺ 316.0614, found 316.0620.

(±)-Prop-2-yn-1-yl *N*-phenylbenzenesulfonimide (167)

Following GP3, prop-2-yn-1-yl *N*-phenylbenzenesulfonimide (**167**) was prepared from sulfinamide **148** (0.163 g, 0.750 mmol), iodosylbenzene (0.165 g, 0.750

mmol) and propargyl alcohol (2 mL). The crude mixture was purified by flash chromatography (7:3 pentane/ethyl acetate) to afford the title compound as a yellow oil (0.172 g, 85%); IR ν_{max} (cm^{-1}): 3307, 3066, 3009, 2133, 1596, 1493, 1448, 1334, 1306, 1240, 1177, 1114, 1060, 1024, 981, 922, 629; ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$) δ 8.16 (2H, d, $J = 7.5$ Hz, H-6), 7.78 (1H, t, $J = 7.5$ Hz, H-8), 7.70 (2H, t, $J = 7.5$ Hz, H-7), 7.28 (2H, t, $J = 7.5$ Hz, H-3), 7.22 (2H, d, $J = 7.5$ Hz, H-2), 7.03 (1H, t, $J = 7.5$ Hz, H-4), 4.74 (2H, d, $J = 2.5$ Hz, H-9), 3.03 (1H, t, $J = 2.5$ Hz, H-11); ^{13}C NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$) δ 143.0 (C-1), 138.3 (C-5), 134.6 (C-8), 130.2 (C-2), 129.9 (C-7), 128.8 (C-6), 124.5 (C-3), 123.6 (C-4), 78.5 (C-10), 77.2 (C-11), 58.4 (C-9); HRMS calculated for $[\text{C}_{15}\text{H}_{14}\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 272.0740, found 272.0737.

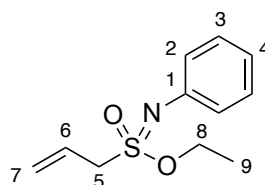
(±)-Allyl N-phenylbenzenesulfonimide (168)



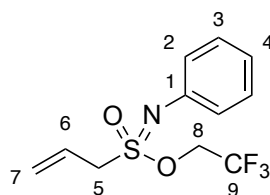
Following GP3, allyl N-phenylbenzenesulfonimide (**168**) was prepared from sulfonamide **148** (0.163 g, 0.750 mmol), iodosylbenzene (0.165 g, 0.750 mmol) and 2-propen-1-ol (2 mL). The crude mixture was purified by flash chromatography (9:1 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.153 g, 75%); IR ν_{max} (cm^{-1}): 3066, 3009, 1596, 1493, 1448, 1422, 1323, 1305, 1240, 1113, 1059, 965, 937, 909, 628; ^1H NMR (400 MHz, CDCl_3) δ 8.13 (2H, d, $J = 8.0$ Hz, H-6), 7.66 (1H, t, $J = 8.0$ Hz, H-8), 7.58 (2H, t, $J = 8.0$ Hz, H-7), 7.27 (2H, t, $J = 7.5$ Hz, H-3), 7.26 (2H, d, $J = 7.5$ Hz, H-2), 7.05 (1H, t, $J = 7.5$ Hz, H-4), 5.86-5.68 (1H, m, H-10), 5.32-5.16 (2H, m, H-11), 4.50 (2H, d, $J = 6.0$ Hz, H-9); ^{13}C NMR (101 MHz, CDCl_3) δ 142.3 (C-1), 137.7 (C-5), 133.4 (C-8), 130.8 (C-

10), 129.3 (C-7), 129.2 (C-2), 128.0 (C-6), 123.8 (C-3), 122.9 (C-4), 119.9 (C-11), 70.7 (C-9); HRMS calculated for $[C_{15}H_{15}NO_2SNa]$ $[M + Na]^+$ 296.0716, found 296.0707.

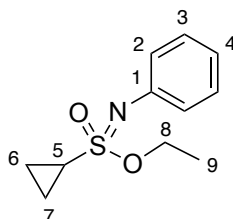
(±)-Ethyl *N*-phenylprop-2-ene-1-sulfonimide (171)



Following GP3, ethyl *N*-phenylprop-2-ene-1-sulfonimide (**171**) was prepared from sulfinamide **150** (0.0842 g, 0.465 mmol), iodosylbenzene (0.102 g, 0.465 mmol) and ethanol (2 mL). The crude mixture was purified by flash chromatography (7:3 pentane/ether) to afford the title compound as an orange oil (0.0369 g, 35%); IR $\nu_{\max}$ (cm⁻¹): 2982, 1639, 1594, 1574, 1488, 1309, 1270, 1235, 1064, 996, 935, 891, 805, 756, 694, 652, 545, 513, 480; ¹H NMR (400 MHz, CDCl₃) δ 7.29-7.16 (2H, m, H-2 or H-3), 7.14-7.06 (2H, m, H-2 or H-3), 7.04-6.94 (1H, m, H-4), 6.00 (1H, ddt, J = 17.5, 10.0, 7.0 Hz, H-6), 5.61-5.38 (2H, m, H-7), 4.25 (2H, q, J = 7.0 Hz, H-8), 4.03-3.91 (2H, m, H-5), 1.34 (3H, t, J = 7.0 Hz, H-9); ¹³C NMR (101 MHz, CDCl₃) δ 142.9 (C-4), 129.2 (C-2 or C-3), 125.1 (C-6), 124.4 (C-7), 123.5 (C-2 or C-3), 122.6 (C-4), 66.4 (C-8), 56.9 (C-5), 15.2 (C-9); HRMS calculated for $[C_{11}H_{16}NO_2S]$ $[M + H]^+$ 226.0896, found 226.0900 / $[C_{11}H_{15}NO_2SNa]$ $[M + Na]^+$ 248.0716, found 248.0720.

(±)-2,2,2-Trifluoroethyl *N*-phenylprop-2-ene-1-sulfonimide (172)

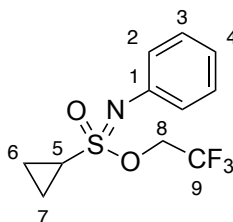
Following GP3, 2,2,2-trifluoroethyl *N*-phenylprop-2-ene-1-sulfonimide (**172**) was prepared from sulfinamide **150** (0.134 g, 0.739 mmol), iodosylbenzene (0.163 g, 0.739 mmol) and 2,2,2-trifluoroethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 pentane/diethyl ether) to afford the title compound as a yellow oil (0.0797 g, 38%); IR ν_{max} (cm⁻¹): 2966, 2939, 1594, 1490, 1323, 1275, 1166, 1032, 959, 757; ¹H NMR (400 MHz, CDCl₃) δ 7.30-7.21 (2H, m, H-2 or H-3), 7.13-6.99 (3H, m, H-2,4 or H-3,4), 6.00 (1H, ddt, J = 17.0, 10.0, 7.0 Hz, H-6), 5.62-5.34 (2H, m, H-7), 4.45 (2H, q, J = 8.0 Hz, H-8), 4.08 (2H, ddt, J = 7.0, 2.0, 1.0 Hz, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 141.2 (C-1), 129.4 (C-2 or C-3), 125.6 (C-7), 124.1 (C-6), 123.74 (C-2 or C-3), 123.68 (C-4), 122.5 (q, J = 278 Hz, C-9), 65.4 (q, J = 37.0 Hz, C-8), 58.1 (C-5); ¹⁹F NMR (376 MHz, CDCl₃) δ -73.7; HRMS calculated for [C₁₁H₁₃F₃NO₂S] [M+H]⁺ 280.0614, found 280.0606 / [C₁₁H₁₂F₃NO₂SNa] [M + Na]⁺ 302.0433, found 302.0436.

(±)-Ethyl *N*-phenylcyclopropanesulfonimide (173)

Following GP3, ethyl *N*-phenylcyclopropanesulfonimide (**173**) was prepared from sulfinamide **164** (0.125 g, 0.690 mmol), iodosylbenzene (0.152 g, 0.690 mmol) and ethanol (2 mL). The crude mixture was purified by flash chromatography (4:1 petroleum ether/diethyl ether) to afford the title compound as

a dark yellow oil (0.136 g, 88%); IR $\nu_{\max}$ (cm⁻¹): 2981, 1594, 1489, 1309, 1227, 1189, 1073, 1055, 1004, 886, 825, 778, 756, 694; ¹H NMR (400 MHz, CDCl₃) δ 7.28-7.17 (2H, m, H-2 or H-3), 7.13-7.07 (2H, m, H-2 or H-3), 7.03-6.91 (1H, m, H-4), 4.31-4.18 (2H, m, H-8), 2.66 (1H, tt, J = 8.0, 5.0 Hz, H-5), 1.45-1.30 (5H, m, H-9, H-6 or H-7), 1.18-1.00 (2H, m, H-6 or H-7); ¹³C NMR (101 MHz, CDCl₃) δ 142.8 (C-1), 129.1 (C-2 or C-3), 123.4 (C-2 or C-3), 122.4 (C-4), 66.1 (C-8), 30.0 (C-5), 15.2 (C-9), 6.5 (C-6 or C-7), 5.4 (C-6 or C-7); HRMS calculated for [C₁₁H₁₆NO₂S] [M+H]⁺ 226.0896, found 226.0896 / [C₁₁H₁₅NO₂SNa] [M + Na]⁺ 248.0716, found 248.0713.

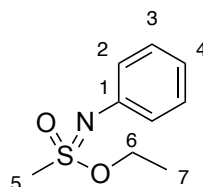
(±)-2,2,2-Trifluoroethyl *N*-phenylcyclopanesulfonimide (174)



Following GP3, 2,2,2-trifluoroethyl *N*-phenylcyclopanesulfonimide (**174**) was prepared from sulfinamide **164** (0.0936 g, 0.517 mmol), iodosylbenzene (0.114 g, 0.517 mmol), and 2,2,2-trifluoroethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 pentane/diethyl ether) to afford the title compound as a yellow oil (0.114 g, 79%); IR $\nu_{\max}$ (cm⁻¹): 3022, 2964, 1595, 1490, 1321, 1273, 1230, 1162, 1080, 1032, 849, 756, 704, 588; ¹H NMR (400 MHz, CDCl₃) δ 7.25 (2H, t, J = 7.5 Hz, H-3), 7.09 (2H, d, J = 7.5 Hz, H-2), 7.04 (1H, t, J = 7.5 Hz, H-4), 4.60-4.31 (2H, m, H-8), 2.75 (1H, tt, J = 8.0, 4.5 Hz, H-5), 1.54-1.30 (2H, m, H-6 or H-7), 1.28-1.10 (2H, m, H-6 or H-7); ¹³C NMR (101 MHz, CDCl₃) δ 141.2 (C-1), 129.3 (C-3), 123.6 (C-2), 123.4 (C-4), 122.6 (q, J = 278 Hz, C-9), 65.1 (q, J = 37.0 Hz, C-8), 30.8 (C-5), 7.1 (C-6 or C-7), 5.9 (C-6 or C-7); ¹⁹F NMR (376

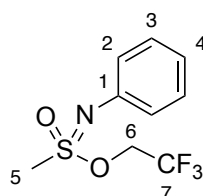
MHz, CDCl₃) δ -73.7; HRMS calculated for [C₁₁H₁₃NO₂SF₃] [M + H]⁺ 280.0614, found 280.0618 / [C₁₁H₁₂NO₂SF₃Na] [M + Na]⁺ 302.0433, found 302.0430.

(±)-Ethyl *N*-phenylmethanesulfonimide (175)



Following GP3, ethyl *N*-phenylmethanesulfonimide (**175**) was prepared from sulfinamide **147** (0.116 g, 0.750 mmol), iodosylbenzene (0.165 g, 0.750 mmol) and ethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/diethyl ether) to afford the title compound as a yellow oil (0.137 g, 92%); IR ν_{max} (cm⁻¹): 3042, 2412, 1521, 1476, 1239, 1017, 928, 909, 849, 660, 626; ¹H NMR (400 MHz, CDCl₃) δ 7.24 (2H, t, *J* = 7.5 Hz, H-3), 7.09 (2H, d, *J* = 7.5 Hz, H-2), 7.00 (1H, t, *J* = 7.5 Hz, H-4), 4.25 (2H, q, *J* = 7.0 Hz, H-6), 3.16 (3H, s, H-5), 1.37 (3H, t, *J* = 7.0 Hz, H-7); ¹³C NMR (101 MHz, CDCl₃) δ 142.8 (C-1), 129.3 (C-3), 123.4 (C-2), 122.6 (C-4), 66.0 (C-6), 39.8 (C-5), 15.2 (C-7); HRMS calculated for [C₉H₁₄NO₂S] [M + H]⁺ 200.0740, found 200.0749.

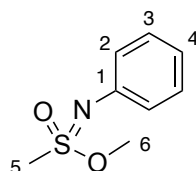
(±)-2,2,2-Trifluoroethyl *N*-phenylmethanesulfonimide (176)



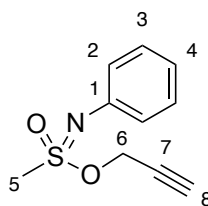
Following GP3, 2,2,2-trifluoroethyl *N*-phenylmethanesulfonimide (**176**) was prepared from sulfinamide **147** (0.116 g, 0.750 mmol), iodosylbenzene (0.165 g, 0.750 mmol) and 2,2,2-trifluoroethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/diethyl ether) to afford the title

compound as a black oil (0.154 g, 81%); IR ν_{max} (cm^{-1}): 3042, 2412, 1522, 1423, 1239, 928, 909, 849, 660, 626; ^1H NMR (400 MHz, CDCl_3) δ 7.30-7.17 (2H, m, H-3), 7.14-6.94 (3H, m, H-2,4), 4.50-4.36 (2H, m, H-6), 3.26 (3H, s, H-5); ^{13}C NMR (101 MHz, CDCl_3) δ 141.2 (C-1), 129.4 (C-3), 123.8 (C-4), 123.7 (C-2), 122.6 (q, $J = 276$ Hz, C-7), 65.0 (q, $J = 37.0$ Hz, C-6), 41.1 (C-5); ^{19}F (377 MHz, CDCl_3) δ -73.6; HRMS calculated for $[\text{C}_9\text{H}_{11}\text{F}_3\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 254.0457, found 254.0458.

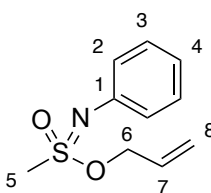
(±)-Methyl *N*-phenylmethanesulfonimide (177)



Following GP3, methyl *N*-phenylmethanesulfonimide (**177**) was prepared from sulfonamide **147** (0.116 g, 0.750 mmol), iodosylbenzene (0.165 g, 0.750 mmol) and methanol (2 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/diethyl ether) to afford the title compound as a brown oil (0.124 g, 89%); IR ν_{max} (cm^{-1}): 3042, 2685, 2412, 2035, 2253, 1522, 1476, 1423, 1265, 1239, 906, 849, 660, 651, 626; ^1H NMR (400 MHz, CDCl_3) δ 7.25 (2H, t, $J = 7.5$ Hz, H-3), 7.09 (2H, d, $J = 7.5$ Hz, H-2), 7.01 (1H, t, $J = 7.5$ Hz, H-4), 3.87 (3H, s, H-6), 3.16 (3H, s, H-5); ^{13}C NMR (101 MHz, CDCl_3) δ 142.5 (C-1), 129.3 (C-3), 123.5 (C-2), 122.9 (C-4), 55.8 (C-6), 38.9 (C-5); HRMS calculated for $[\text{C}_8\text{H}_{12}\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 186.0583, found 186.0597.

(±)-Prop-2-yn-1-yl *N*-phenylmethanesulfonimide (178)

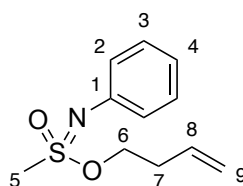
Following GP3, prop-2-yn-1-yl *N*-phenylmethanesulfonimide (**178**) was prepared from sulfinamide **147** (0.116 g, 0.750 mmol), iodosylbenzene (0.165 g, 0.750 mmol) and propargyl alcohol (2 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/diethyl ether) to afford the title compound as a pale yellow oil (0.146 g, 93%); IR ν_{max} (cm⁻¹): 3306, 3009, 1596, 1491, 1334, 1316, 1241, 993, 921, 641; ¹H NMR (400 MHz, (CD₃)₂CO) δ 7.21 (2H, t, J = 7.5 Hz, H-3), 7.05 (2H, d, J = 7.5 Hz, H-2), 6.97 (1H, t, J = 7.5 Hz, H-4), 4.89 (2H, d, J = 2.5 Hz, H-6), 3.34 (3H, s, H-5), 3.27 (1H, t, J = 2.5 Hz, H-8); ¹³C NMR (101 MHz, (CD₃)₂CO) δ 143.6 (C-1), 129.8 (C-3), 124.2 (C-2), 123.2 (C-4), 78.7 (C-8), 78.0 (C-7), 58.2 (C-6), 41.3 (C-5); HRMS calculated for [C₁₀H₁₂NO₂S] [M + H]⁺ 210.0583, found 210.0580.

(±)-Allyl *N*-phenylmethanesulfonimide (179)

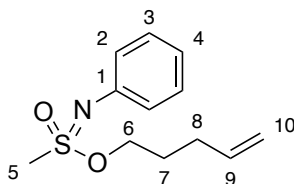
Following GP3, allyl *N*-phenylmethanesulfonimide (**179**) was prepared from sulfinamide **147** (0.116 g, 0.750 mmol), iodosylbenzene (0.165 g, 0.750 mmol) and 2-propen-1-ol (2 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/diethyl ether) to afford the title compound as a yellow oil (0.104 g, 66%); IR ν_{max} (cm⁻¹): 3445, 1646, 1597, 1491, 1451, 1332, 1314, 1273, 1240, 1156, 1074, 939, 907; ¹H NMR (400 MHz, CDCl₃) δ 7.24 (2H, d, J = 7.5 Hz,

H-3), 7.10 (2H, d, $J = 7.5$ Hz, H-2), 7.01 (1H, t, $J = 7.5$ Hz, H-4), 5.94 (1H, ddt, $J = 17.0, 10.0, 6.0$ Hz, H-7), 5.41 (1H, ddd, $J = 17.0, 3.0, 1.5$ Hz, H-8), 5.32 (1H, ddd, $J = 10.0, 3.0, 1.5$ Hz, H-8), 4.67 (2H, dt, $J = 6.0, 1.5$ Hz, H-6), 3.18 (3H, s, H-5); ^{13}C NMR (101 MHz, CDCl_3) δ 142.5 (C-1), 131.1 (C-7), 129.3 (C-3), 123.5 (C-2), 122.9 (C-4), 120.5 (C-8), 70.4 (C-6), 40.5 (C-5); HRMS calculated for $[\text{C}_{10}\text{H}_{14}\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 212.0740, found 212.0744.

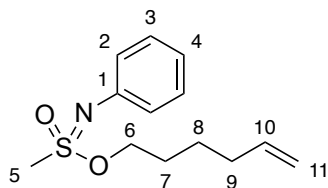
(±)-But-3-en-1-yl *N*-phenylmethanesulfonimide (180**)**



Following GP3, but-3-en-1-yl *N*-phenylmethanesulfonimide (**180**) was prepared from sulfinamide **147** (0.116 g, 0.750 mmol), iodosylbenzene (0.165 g, 0.750 mmol) and 3-buten-1-ol (2 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/diethyl ether) to afford the title compound as a violet oil (0.143 g, 85%); IR ν_{max} (cm^{-1}): 2984, 1643, 1596, 1491, 1332, 1313, 1273, 1240, 1075, 946, 886; ^1H NMR (400 MHz, CDCl_3) δ 7.24 (2H, t, $J = 7.5$ Hz, H-3), 7.09 (2H, d, $J = 7.5$ Hz, H-2), 7.00 (1H, t, $J = 7.5$ Hz, H-4), 5.76 (1H, ddt, $J = 17.0, 10.0, 7.0$ Hz, H-8), 5.22-5.01 (2H, m, H-9), 4.20 (2H, t, $J = 7.0$ Hz, H-6), 3.16 (3H, s, H-5), 2.46 (2H, qq, $J = 7.0, 1.0$ Hz, H-7); ^{13}C NMR (101 MHz, CDCl_3) δ 142.6 (C-1), 133.0 (C-8), 129.3 (C-3), 123.5 (C-2), 122.8 (C-4), 118.4 (C-9), 68.9 (C-6), 39.8 (C-5), 33.7 (C-7); HRMS calculated for $[\text{C}_{11}\text{H}_{16}\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 226.0896, found 226.0890.

(±)-Pent-4-en-1-yl *N*-phenylmethanesulfonimide (181)

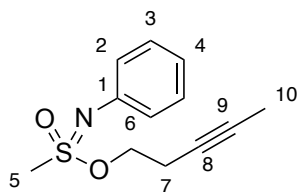
Following GP3, pent-4-en-1-yl *N*-phenylmethanesulfonimide (**181**) was prepared from sulfinamide **147** (0.116 g, 0.750 mmol), iodosylbenzene (0.165 g, 0.750 mmol) and 4-penten-1-ol (2 mL). The crude mixture was purified by flash chromatography (9:1 petroleum ether/ ethyl acetate) to afford the title compound as a dark orange oil (0.145 g, 81%); IR ν_{max} (cm⁻¹): 3006, 1641, 1596, 1491, 1332, 1313, 1240, 1074, 956, 908, 820; ¹H NMR (400 MHz, CDCl₃) δ 7.24 (2H, t, J = 7.5 Hz, H-3), 7.09 (2H, d, J = 7.5 Hz, H-2), 7.00 (1H, t, J = 7.5 Hz, H-4), 5.75 (1H, ddt, J = 17.0, 10.0, 7.0 Hz, H-9), 5.08-4.97 (2H, m, H-10), 4.17 (2H, t, J = 7.0 Hz, H-6), 3.16 (3H, s, H-5), 2.20-2.10 (2H, m, H-8), 1.86-1.76 (2H, m, H-7); ¹³C NMR (101 MHz, CDCl₃) δ 142.7 (C-1), 137.0 (C-9), 129.3 (C-3), 123.4 (C-2), 122.8 (C-4), 116.0 (C-10), 69.2 (C-6), 39.7 (C-5), 29.7 (C-8), 28.4 (C-7); HRMS calculated for [C₁₂H₁₈NO₂S] [M + H]⁺ 240.1053, found 240.1060.

(±)-Hex-5-en-1-yl *N*-phenylmethanesulfonimide (182)

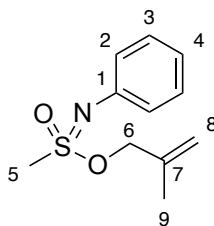
Following GP3, hex-5-en-1-yl *N*-phenylmethanesulfonimide (**182**) was prepared from sulfinamide **147** (0.116 g, 0.750 mmol), iodosylbenzene (0.165 g, 0.750 mmol) and 5-hexen-1-ol (2 mL). The crude mixture was purified by flash chromatography (9:1 petroleum ether/ ethyl acetate) to afford the title compound

as a ruby red oil (0.152 g, 80%); IR $\nu_{\max}$ (cm^{-1}): 2928, 2360, 1640, 1491, 1332, 1313, 1240, 1074, 909; ^1H NMR (400 MHz, CDCl_3) δ 7.24 (2H, t, $J = 7.5$ Hz, H-3), 7.09 (2H, d, $J = 7.5$ Hz, H-2), 7.00 (1H, t, $J = 7.5$ Hz, H-4), 5.75 (1H, ddt, $J = 17.0, 10.0, 7.0$ Hz, H-10), 5.07-4.87 (2H, m, H-11), 4.17 (2H, t, $J = 7.0$ Hz, H-6), 3.16 (3H, s, H-5), 2.05 (2H, q, $J = 7.0$ Hz, H-9), 1.79-1.62 (2H, m, H-8), 1.54-1.36 (2H, m, H-7); ^{13}C NMR (101 MHz, CDCl_3) δ 142.8 (C-1), 138.1 (C-10), 129.3 (C-3), 123.4 (C-2), 122.7 (C-4), 115.3 (C-11), 69.8 (C-6), 39.7 (C-5), 33.2 (C-9), 28.7 (C-8), 24.9 (C-7); HRMS calculated for $[\text{C}_{13}\text{H}_{19}\text{NO}_2\text{SNa}]$ $[\text{M} + \text{Na}]^+$ 276.1029, found 276.1024.

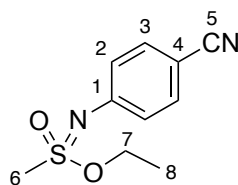
($\pm$)-Pent-3-yn-1-yl *N*-phenylmethanesulfonimide (183**)**



Following GP3, pent-3-yn-1-yl *N*-phenylmethanesulfonimide (**183**) was prepared from sulfinamide **147** (0.116 g, 0.750 mmol), iodosylbenzene (0.165 g, 0.750 mmol) and 3-pentyn-1-ol (2 mL). The crude mixture was purified by flash chromatography (9:1 petroleum ether/ ethyl acetate) to afford the title compound as a yellow oil (0.145 g, 82%); IR $\nu_{\max}$ (cm^{-1}): 2959, 1601, 1490, 1332, 1314, 1239, 1076, 967, 909; ^1H NMR (400 MHz, CDCl_3) δ 7.24 (2H, t, $J = 7.5$ Hz, H-3), 7.10 (2H, d, $J = 7.5$ Hz, H-2), 7.01 (1H, t, $J = 7.5$ Hz, H-4), 4.21 (2H, t, $J = 7.0$ Hz, H-6), 3.20 (3H, s, H-5), 2.54 (2H, tq, $J = 7.0, 2.5$ Hz, H-7), 1.76 (3H, t, $J = 2.5$ Hz, H-10); ^{13}C NMR (126 MHz, CDCl_3) δ 142.5 (C-1), 129.3 (C-3), 123.5 (C-2), 122.9 (C-4), 78.4 (C-8 or C-9), 74.0 (C-8 or C-9), 68.0 (C-6), 40.0 (C-5), 20.2 (C-7), 3.6 (C-10); HRMS calculated for $[\text{C}_{12}\text{H}_{15}\text{NO}_2\text{SNa}]$ $[\text{M} + \text{Na}]^+$ 260.0716, found 260.0712.

(±)-2-Methylallyl *N*-phenylmethanesulfonimide (184)

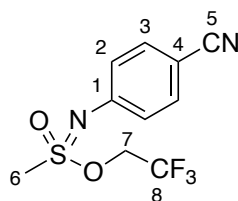
Following GP3, 2-methylallyl *N*-phenylmethanesulfonimide (**184**) was prepared from sulfinamide **147** (0.116 g, 0.750 mmol), iodosylbenzene (0.165 g, 0.750 mmol) and 2-methyl-2-propen-1-ol (2 mL). The crude mixture was purified by flash chromatography (9:1 petroleum ether/ ethyl acetate) to afford the title compound as a yellow oil (0.105 g, 62%); IR ν_{max} (cm⁻¹): 3042, 2412, 1710, 1521, 1476, 1434, 1334, 1239, 1017, 928, 849, 660, 626; ¹H NMR (400 MHz, CDCl₃) δ 7.24 (2H, t, J = 7.5 Hz, H-3), 7.10 (2H, d, J = 7.5 Hz, H-2), 7.00 (1H, t, J = 7.5 Hz, H-4), 5.08 (1H, s, H-8), 5.01 (1H, s, H-8), 4.57 (2H, s, H-6), 3.18 (3H, s, H-5), 1.78 (3H, s, H-9); ¹³C NMR (101 MHz, CDCl₃) δ 142.6 (C-1), 138.9 (C-7), 129.3 (C-3), 123.5 (C-2), 122.9 (C-4), 115.7 (C-8), 73.4 (C-6), 40.3 (C-5), 19.5 (C-9); HRMS calculated for [C₁₁H₁₆NO₂S] [M + H]⁺ 226.0896, found 226.0887.

(±)-Ethyl *N*-(4-cyanophenyl)methanesulfonimide (185)

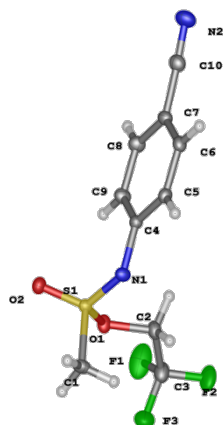
Following GP3, ethyl *N*-(4-cyanophenyl)methanesulfonimide (**185**) was prepared from sulfinamide **154** (1.54 g, 8.58 mmol), iodosylbenzene (1.89 g, 8.58 mmol), and ethanol (20 mL). The crude mixture was purified by flash chromatography (1:1 pentane/ether) to afford the title compound as a yellow oil (1.60 g, 83%); IR ν_{max} (cm⁻¹): 2983, 2936, 2221, 1600, 1499, 1331, 1303, 1271, 1239, 1174, 1108, 1057, 1002, 973, 889, 840, 802, 718, 548, 512, 459; ¹H NMR

(400 MHz, CDCl_3) δ 7.54-7.42 (2H, m, H-2 or H-3), 7.15-7.04 (2H, m, H-2 or H-3), 4.31-4.19 (2H, m, H-7), 3.20 (3H, s, H-6), 1.38 (3H, t, $J = 7.0$ Hz, H-8); ^{13}C NMR (101 MHz, CDCl_3) δ 147.9 (C-1), 133.4 (C-2 or C-3), 123.5 (C-2 or C-3), 119.5 (C-4), 105.2 (C-5), 66.9 (C-7), 40.4 (C-6), 15.1 (C-8); HRMS calculated for $[\text{C}_{10}\text{H}_{13}\text{N}_2\text{O}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 225.0692, found 225.0696 / $[\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_2\text{SNa}]$ $[\text{M} + \text{Na}]^+$ 247.0512, found 247.0515.

($\pm$)-2,2,2-Trifluoroethyl *N*-(4-cyanophenyl)methanesulfonimide (186**)**

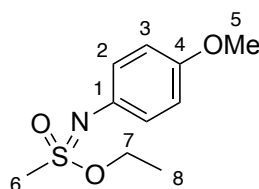


Following GP3, 2,2,2-trifluoroethyl *N*-(4-cyanophenyl)methanesulfonimide (**186**) was prepared from sulfinamide **154** (0.335 g, 1.86 mmol), iodosylbenzene (0.409 g, 1.86 mmol), and 2,2,2-trifluoroethanol (4 mL). The crude mixture was purified by flash chromatography (1:1 pentane/ether) to afford the title compound as a yellow oil (0.412 g, 80%); IR ν_{max} (cm^{-1}): 3018, 2934, 2224, 1600, 1498, 1417, 1333, 1310, 1270, 1250, 1167, 1069, 1028, 977, 959, 847, 836, 795, 738, 690, 648, 568, 550, 505, 475, 454, 413; ^1H NMR (400 MHz, CDCl_3) δ 7.66-7.49 (2H, m, H-2 or H-3), 7.24-7.11 (2H, m, H-2 or H-3), 4.57-4.43 (2H, m, H-7), 3.35 (3H, s, H-6); ^{13}C NMR (101 MHz, CDCl_3) δ 146.0 (C-1), 133.5 (C-2 or C-3), 124.1 (C-2 or C-3), 122.3 (q, $J = 278$ Hz, C-8), 119.2 (C-4), 106.7 (C-5), 65.4 (q, $J = 37.5$ Hz, C-7), 41.5 (C-6); ^{19}F NMR (376 MHz, CDCl_3) δ -73.57; HRMS calculated for $[\text{C}_{10}\text{H}_8\text{F}_3\text{N}_2\text{O}_2\text{S}]$ $[\text{M} - \text{H}]^+$ 277.0264, found 277.0255.

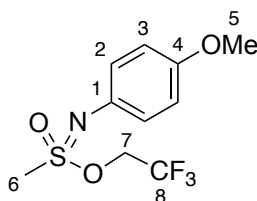


X-ray crystal structure of 2,2,2-trifluoroethyl *N*-(4-cyanophenyl)methanesulfonimide $\text{C}_{10}\text{H}_9\text{N}_2\text{O}_2\text{F}_3\text{S}$ $M_w = 278.25$ $T = 120(2)$ K; $\lambda = 1.54184$ Å; monoclinic; $P 2_1/c$ space group; $a = 8.67784(19)$ Å, $b = 14.1628(3)$ Å, $c = 9.7885(2)$ Å; $\alpha = 90(2)^\circ$, $\beta = 99.299(2)^\circ$, $\gamma = 90(2)^\circ$; $V = 1187.22(5)$ Å³; $Z = 4$; $D = 1.557$ g/cm³; $R_1 = 0.0287$, $wR_2 = 0.0746$ (all data), $\text{GoF} = 1.041$.

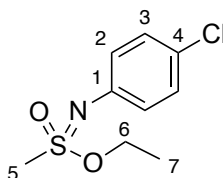
(±)-Ethyl *N*-(4-methoxyphenyl)methanesulfonimide (187**)**



Following GP3, ethyl *N*-(4-methoxyphenyl)methanesulfonimide (**187**) was prepared from sulfinamide **152** (0.350 g, 1.89 mmol), iodosylbenzene (0.416 g, 1.89 mmol), and ethanol (5 mL). The crude mixture was purified by flash chromatography (1:1 pentane/diethyl ether) to afford the title compound as a red oil (0.178 g, 41%); IR ν_{max} (cm⁻¹): 2981, 2935, 2907, 2834, 1502, 1463, 1441, 1313, 1271, 1231, 1179, 1154, 1104, 1069, 1031, 1005, 970, 890, 832, 810, 724, 690, 639, 570, 521, 496; ¹H NMR (400 MHz, CDCl₃) δ 7.01 (2H, d, $J = 9.0$ Hz, H-2 or H-3), 6.78 (2H, d, $J = 9.0$ Hz, H-2 or H-3), 4.21 (2H, q, $J = 7.0$ Hz, H-7), 3.75 (3H, s, H-5), 3.12 (3H, s, H-6), 1.34 (3H, t, $J = 7.0$ Hz, H-8); ¹³C NMR (101 MHz, CDCl₃) δ 155.4 (C-4), 135.7 (C-1), 124.3 (C-2 or C-3), 114.5 (C-2 or C-3), 65.8 (C-7), 55.6 (C-5), 39.5 (C-6), 15.2 (C-8); HRMS calculated for [C₁₀H₁₆NO₃S] [M + H]⁺ 230.0845, found 230.0842 / [C₁₀H₁₅NO₃SNa] [M + Na]⁺ 252.0665, found 252.0664.

(±)-2,2,2-Trifluoroethyl- *N*-(4-methoxyphenyl)methanesulfonimide (188)

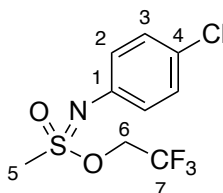
Following GP3, 2,2,2-trifluoroethyl- *N*-(4-methoxyphenyl)methanesulfonimide (**188**) was prepared from sulfinamide **152** (0.117 g, 0.630 mmol), iodosylbenzene (0.138 g, 0.630 mmol), and 2,2,2-trifluoroethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 pentane/diethyl ether) to afford the title compound as a dark yellow oil (0.0664 g, 37%); IR ν_{max} (cm⁻¹): 3020, 2937, 2839, 1504, 1465, 1443, 1407, 1324, 1276, 1236, 1163, 1080, 1030, 960, 833, 791, 724, 644, 559; ¹H NMR (400 MHz, CDCl₃) δ 7.05-6.97 (2H, m, H-2 or H-3), 6.88-6.76 (2H, m, H-2 or H-3), 4.50-4.36 (2H, m, H-7), 3.77 (3H, s, H-5), 3.26 (3H, s, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 156.1 (C-4), 134.0 (C-1), 124.6 (C-2 or C-3), 122.6 (q, J = 278 Hz, C-8), 114.7 (C-2 or C-3), 64.9 (q, J = 37.0 Hz, C-7), 55.6 (C-5), 40.9 (C-6); ¹⁹F NMR (376 MHz, CDCl₃) δ -73.7; HRMS calculated for [C₁₀H₁₃F₃NO₃S] [M + H]⁺ 284.0563, found 284.0566 / [C₁₀H₁₂F₃NO₃SNa] [M + Na]⁺ 306.0382, found 306.0390.

(±)-Ethyl *N*-(4-chlorophenyl)methanesulfonimide (189)

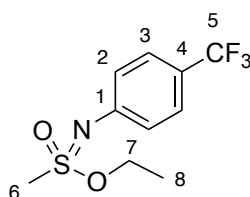
Following GP3, ethyl *N*-(4-chlorophenyl)methanesulfonimide (**189**) was prepared from sulfinamide **151** (0.125 g, 0.662 mmol), iodosylbenzene (0.146 g, 0.662 mmol), and ethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 pentane/ether) to afford the title compound as a yellow oil

(0.109 g, 70%); IR ν_{max} (cm^{-1}): 2981, 2936, 1588, 1486, 1329, 1305, 1233, 1173, 1154, 1092, 1063, 1005, 971, 889, 830, 799, 780, 714, 699, 650, 624, 554, 537, 487, 457; ^1H NMR (400 MHz, CDCl_3) δ 7.19 (2H, d, $J = 8.5$ Hz, H-2 or H-3), 7.01 (2H, d, $J = 8.5$ Hz, H-2 or H-3), 4.23 (2H, q, $J = 7.0$ Hz, H-6), 3.16 (3H, s, H-5), 1.36 (3H, t, $J = 7.0$ Hz, H-7); ^{13}C NMR (101 MHz, CDCl_3) δ 141.5 (C-1), 129.2 (C-2 or C-3), 127.8 (C-4), 124.6 (C-2 or C-3), 66.4 (C-6), 40.0 (C-5), 15.2 (C-7); HRMS calculated for $[\text{C}_9\text{H}_{13}\text{NO}_2\text{S}^{35}\text{Cl}]$ $[\text{M} + \text{H}]^+$ 234.0350, found 234.0343 / $[\text{C}_9\text{H}_{12}\text{NO}_2\text{S}^{35}\text{ClNa}]$ $[\text{M} + \text{Na}]^+$ 256.0169, found 256.0163.

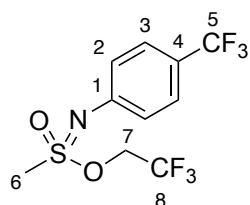
($\pm$)-2,2,2-Trifluoroethyl *N*-(4-chlorophenyl)methanesulfonimide (190**)**



Following GP3, 2,2,2-trifluoroethyl *N*-(4-chlorophenyl)methanesulfonimide (**190**) was prepared from sulfinamide **151** (0.0979 g, 0.518 mmol), iodosylbenzene (0.114 g, 0.518 mmol), and 2,2,2-trifluoroethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a dark yellow oil (0.0919 g, 62%); IR ν_{max} (cm^{-1}): 3024, 2941, 1608, 1487, 1455, 1405, 1319, 1277, 1236, 1163, 1094, 1073, 1031, 959, 831, 795, 777, 715, 642, 565, 543, 474; ^1H NMR (400 MHz, CDCl_3) δ 7.26-7.17 (2H, m, H-2 or H-3), 7.05-6.99 (2H, m, H-2 or H-3), 4.51-4.36 (2H, m, H-6), 3.28 (3H, s, H-5); ^{13}C NMR (101 MHz, CDCl_3) δ 139.8 (C-1), 129.4 (C-2 or C-3), 129.0 (C-4), 124.9 (C-2 or C-3), 122.5 (q, $J = 276$ Hz, C-7), 65.1 (q, $J = 37.0$ Hz, C-6), 41.1 (C-5); ^{19}F NMR (376 MHz, CDCl_3) δ -73.6; HRMS calculated for $[\text{C}_9\text{H}_8^{35}\text{ClF}_3\text{NO}_2\text{S}]$ $[\text{M} - \text{H}]^+$ 285.9922, found 285.9919.

(±)-Ethyl *N*-(4-(trifluoromethyl)phenyl)methanesulfonimide (191)

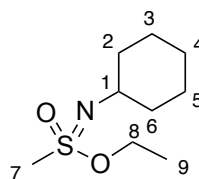
Following GP3, Ethyl *N*-(4-(trifluoromethyl)phenyl)methanesulfonimide (**191**) was prepared from sulfinamide **153** (0.0942 g, 0.422 mmol), iodosylbenzene (0.0929 g, 0.422 mmol), and ethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 pentane/diethyl ether) to afford the title compound as a yellow oil (0.0722 g, 64%); IR ν_{max} (cm⁻¹): 1614, 1515, 1321, 1281, 1239, 1157, 1108, 1054, 1013, 972, 897, 844, 804, 741, 710, 618, 594, 520; ¹H NMR (400 MHz, CDCl₃) δ 7.48 (2H, d, J = 8.0 Hz, H-2 or H-3), 7.16 (2H, d, J = 8.0 Hz, H-2 or H-3), 4.31-4.19 (2H, m, H-7), 3.19 (3H, s, H-6), 1.38 (3H, t, J = 7.0 Hz, H-8); ¹³C NMR (101 MHz, CDCl₃) δ 146.4 (C-1), 126.4 (q, J = 4.0 Hz, C-3), 124.6 (q, J = 270 Hz, C-5), 124.4 (q, J = 32.5 Hz, C-4), 123.1 (C-2), 66.6 (C-7), 40.2 (C-6), 15.1 (C-8); HRMS calculated for [C₁₀H₁₃F₃NO₂S] [M + H]⁺ 268.0614, found 268.0614 / [C₁₀H₁₂F₃NO₂SNa] [M + Na]⁺ 290.0433, found 290.0430.

(±)-2,2,2-Trifluoroethyl *N*-(4-(trifluoromethyl)phenyl)methanesulfonimide (192)

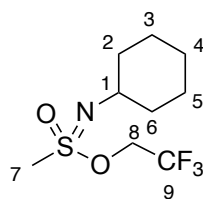
Following GP3, 2,2,2-trifluoroethyl *N*-(4-(trifluoromethyl)phenyl)methanesulfonimide (**192**) was prepared from sulfinamide **153** (0.0986 g, 0.442 mmol), iodosylbenzene (0.0972 g, 0.442 mmol),

and 2,2,2-trifluoroethanol (2 mL). The crude mixture was purified by flash chromatography (7:3 to 1:1 pentane/diethyl ether) to afford the title compound as a yellow oil (0.0643 g, 45%); IR ν_{max} (cm^{-1}): 2362, 2343, 1613, 1577, 1311, 1278, 1160, 1106, 1058, 960, 843, 789, 711, 637; ^1H NMR (400 MHz, CDCl_3) δ 7.51 (2H, d, $J = 8.0$ Hz, H-2 or H-3), 7.17 (2H, d, $J = 8.0$ Hz, H-2 or H-3), 4.61-4.36 (2H, m, H-7), 3.32 (3H, s, H-6); ^{13}C NMR (126 MHz, CDCl_3) δ 144.7 (C-1), 126.6 (q, $J = 4.0$ Hz, C-3), 125.5 (q, $J = 33.0$ Hz, C-4), 124.4 (q, $J = 270$ Hz, C-5), 123.7, 122.4 (q, $J = 276$ Hz, C-8), 65.2 (q, $J = 37.5$ Hz, C-7), 41.3 (C-6); ^{19}F NMR (376 MHz, CDCl_3) δ -62.1 (F-5), -73.6 (F-8).

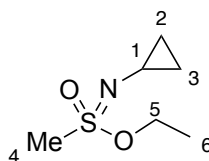
(±)-Ethyl *N*-cyclohexylmethanesulfonimide (193**)**



Following GP3, ethyl *N*-cyclohexylmethanesulfonimide (**193**) was prepared from sulfonamide **157** (0.292 g, 1.81 mmol), iodosylbenzene (0.399 g, 1.81 mmol), and ethanol (5 mL). The crude mixture was purified by flash chromatography (1:1 pentane/diethyl ether) to afford the title compound as a yellow oil (0.134 g, 36%); IR ν_{max} (cm^{-1}): 2926, 2852, 1447, 1320, 1272, 1156, 1145, 1091, 1010, 978, 887, 793, 705, 571, 520; ^1H NMR (400 MHz, CDCl_3) δ 4.16-4.04 (2H, m, H-8), 3.46-3.24 (1H, m, H-1), 2.98 (3H, s, H-7), 1.98-1.77 (2H, m, Cy), 1.74-1.67 (2H, m, Cy), 1.63-1.51 (1H, m, Cy), 1.34 (3H, t, $J = 7.0$ Hz, H-9), 1.30-1.08 (5H, m, Cy); ^{13}C NMR (101 MHz, CDCl_3) δ 64.9 (C-8), 53.1 (C-1), 40.1 (C-7), 36.7 (Cy), 36.4 (Cy), 25.7 (Cy), 25.42 (Cy), 25.37 (Cy), 15.3 (Cy); HRMS calculated for $[\text{C}_9\text{H}_{20}\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 206.1209, found 206.1208 / $[\text{C}_9\text{H}_{19}\text{NO}_2\text{SNa}]$ $[\text{M} + \text{Na}]^+$ 228.1029, found 228.1022.

(±)-2,2,2-Trifluoroethyl *N*-cyclohexylmethanesulfonimide (194)

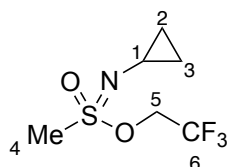
Following GP3, 2,2,2-trifluoroethyl *N*-cyclohexylmethanesulfonimide (**194**) was prepared from sulfinamide **157** (0.100 g, 0.621 mmol), iodosylbenzene (0.137 g, 0.621 mmol), and 2,2,2-trifluoroethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 pentane/diethyl ether) to afford the title compound as a colourless oil (0.0433 g, 27%); IR ν_{max} (cm⁻¹): 2929, 2855, 1450, 1276, 1159, 1036, 981, 960, 889, 703, 634; ¹H NMR (400 MHz, CDCl₃) δ 4.43-4.29 (2H, m, H-8), 3.44-3.28 (1H, m, H-1), 3.08 (3H, s, H-7), 1.90-1.76 (2H, m, Cy), 1.75-1.67 (2H, m, Cy), 1.60-1.53 (1H, m, Cy), 1.39-1.06 (5H, m, Cy); ¹³C NMR (101 MHz, CDCl₃) δ 122.9 (q, J = 278 Hz, C-9), 64.6 (q, J = 37.0 Hz, C-8), 53.4 (C-1), 41.2 (C-7), 36.2 (Cy), 35.9 (Cy), 25.6 (Cy), 25.14 (Cy), 25.11 (Cy); ¹⁹F NMR (376 MHz, CDCl₃) δ -73.8; HRMS calculated for [C₉H₁₇NO₂SF₃] [M + H]⁺ 260.0927, found 260.0922 / [C₉H₁₆NO₂SF₃Na] [M + Na]⁺ 282.0746, found 282.0738.

(±)-Ethyl *N*-cyclopropylmethanesulfonimide (195)

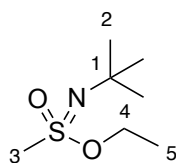
Following GP3, ethyl *N*-cyclopropylmethanesulfonimide (**195**) was prepared from sulfinamide **155** (0.126 g, 1.05 mmol), iodosylbenzene (0.232 g, 1.05 mmol), and ethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/diethyl ether) to afford the title compound as a colourless oil (0.0769 g, 45%); IR ν_{max} (cm⁻¹): 3087, 2985, 2928, 2852, 1447, 1416, 1355, 1283,

1203, 1174, 1085, 1012, 981, 966, 888, 790, 741, 701, 552, 515, 482; ^1H NMR (400 MHz, CDCl_3) δ 4.15 (2H, q, $J = 7.0$ Hz, H-5), 2.98 (3H, s, H-4), 2.68-2.53 (1H, m, H-1), 1.37 (3H, t, $J = 7.0$ Hz, H-6), 0.67-0.48 (3H, m, H-2,3), 0.50-0.34 (1H, m, H-2 or H-3); ^{13}C NMR (101 MHz, CDCl_3) δ 64.8 (C-5), 39.0 (C-4), 25.9 (C-1), 15.3 (C-6), 6.7 (C-2 or C-3), 6.6 (C-2 or C-3); HRMS calculated for $[\text{C}_6\text{H}_{14}\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 164.0740, found 164.0739 / $[\text{C}_6\text{H}_{13}\text{NO}_2\text{SNa}]$ $[\text{M} + \text{Na}]^+$ 186.0559, found 186.0557.

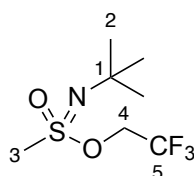
(±)-2,2,2-Trifluoroethyl *N*-cyclopropylmethanesulfonimide (196)



Following GP3, 2,2,2-trifluoroethyl *N*-cyclopropylmethanesulfonimide (**196**) was prepared from sulfinamide **155** (0.123 g, 1.03 mmol), iodosylbenzene (0.228 g, 1.03 mmol), and 2,2,2-trifluoroethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/diethyl ether) to afford the title compound as a colourless oil (0.0721 g, 32%); IR ν_{max} (cm^{-1}): 3012, 1487, 1451, 1409, 1359, 1278, 1207, 1160, 1105, 1039, 984, 959, 932, 911, 847, 786, 741, 700, 635, 558, 521, 503, 484; ^1H NMR (400 MHz, CDCl_3) δ 4.40 (2H, q, $J = 8.0$ Hz, H-5), 3.08 (3H, s, H-4), 2.69-2.59 (1H, m, H-1), 0.66-0.52 (3H, m, H-2,3), 0.52-0.42 (1H, m, H-2 or H-3); ^{13}C NMR (101 MHz, CDCl_3) δ 122.8 (q, $J = 279$ Hz, C-6), 64.3 (q, $J = 37.0$ Hz, C-5), 40.3 (C-4), 25.7 (C-1), 6.7 (C-2 or C-3), 6.6 (C-2 or C-3); ^{19}F NMR (376 MHz, CDCl_3) δ -73.9; HRMS calculated for $[\text{C}_6\text{H}_{11}\text{F}_3\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 218.0457, found 218.0465 / $[\text{C}_6\text{H}_{10}\text{F}_3\text{NO}_2\text{SNa}]$ $[\text{M} + \text{Na}]^+$ 240.0277, found 240.0272.

(±)-Ethyl *N*-*tert*-butylmethanesulfonimide (197)

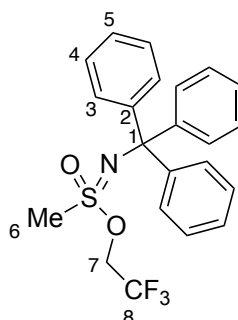
Following GP3, ethyl *N*-*tert*-butylmethanesulfonimide (**197**) was prepared from sulfinamide **156** (0.124 g, 0.919 mmol), iodosylbenzene (0.202 g, 0.919 mmol), and ethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/diethyl ether) to afford the title compound as a colourless oil (0.0354 g, 22%); IR ν_{max} (cm^{-1}): 2969, 1387, 1361, 1288, 1210, 1135, 1099, 1056, 1012, 977, 888, 784, 717, 671, 544, 523, 482, 469, 421; ^1H NMR (400 MHz, CDCl_3) δ 4.16-4.06 (2H, m, H-4), 2.96 (3H, s, H-3), 1.36 (3H, t, $J = 7.0$ Hz, H-5), 1.32 (9H, s, H-2); ^{13}C NMR (101 MHz, CDCl_3) δ 65.4 (C-4), 55.5 (C-1), 41.7 (C-3), 32.7 (C-2), 15.3 (C-5); HRMS calculated for $[\text{C}_7\text{H}_{18}\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 180.1053, found 180.1056 / $[\text{C}_7\text{H}_{17}\text{NO}_2\text{SNa}]$ $[\text{M} + \text{Na}]^+$ 202.0872, found 202.0861.

(±)-2,2,2-Trifluoroethyl *N*-*tert*-butylmethanesulfonimide (198)

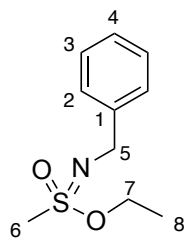
Following GP3, 2,2,2-trifluoroethyl *N*-*tert*-butylmethanesulfonimide (**198**) was prepared from sulfinamide **156** (0.122 g, 0.902 mmol), iodosylbenzene (0.198 g, 0.902 mmol), and 2,2,2-trifluoroethanol (2 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/diethyl ether) to afford the title compound as a colourless oil (0.0407 g, 19%); IR ν_{max} (cm^{-1}): 2974, 1459, 1403, 1365, 1315, 1281, 1212, 1166, 1042, 981, 963, 906, 849, 783, 728, 648, 633, 568, 557, 521, 422; ^1H NMR (400 MHz, CDCl_3) δ 4.36 (2H, q, $J = 8.5$ Hz, H-4), 3.05

(3H, s, H-3), 1.32 (9H, s, H-2); ^{13}C NMR (101 MHz, CDCl_3) δ 123.0 (q, $J = 278$ Hz, C-5), 65.0 (q, $J = 37.0$ Hz, C-4), 56.4 (C-1), 42.7 (C-3), 32.5 (C-2); ^{19}F NMR (376 MHz, CDCl_3) δ -73.7; HRMS calculated for $[\text{C}_7\text{H}_{15}\text{F}_3\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 234.0770, found 234.0770 / $[\text{C}_7\text{H}_{14}\text{F}_3\text{NO}_2\text{SNa}]$ $[\text{M} + \text{Na}]^+$ 256.0590, found 256.0595.

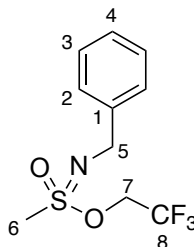
($\pm$)-2,2,2-Trifluoroethyl *N*-tritylmethanesulfonimide (199**)**



Following GP3, 2,2,2-trifluoroethyl *N*-tritylmethanesulfonimide (**199**) was prepared from sulfinamide **158** (0.142 g, 0.442 mmol), iodosylbenzene (0.0971 g, 0.442 mmol), and 2,2,2-trifluoroethanol (2 mL). The crude mixture was purified by flash chromatography (9:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0578 g, 31%); IR ν_{max} (cm^{-1}): 3058, 3032, 1595, 1490, 1447, 1403, 1335, 1319, 1280, 1164, 1084, 1043, 988, 959, 897, 849, 783, 748, 701, 633, 591, 561; ^1H NMR (400 MHz, CDCl_3) δ 7.52-7.47 (6H, m, Ar), 7.36-7.24 (9H, m, Ar), 3.70 (1H, dq, $J = 13.0, 8.5$ Hz, H-7), 3.38 (1H, dq, $J = 13.0, 8.5$ Hz, H-7), 3.27 (3H, s, H-6); ^{13}C NMR (101 MHz, CDCl_3) δ 146.9 (C-2), 128.9 (C-3 or C-4), 127.8 (C-3 or C-4), 126.9 (C-5), 122.7 (q, $J = 278.0$, C-8), 72.9 (C-1), 64.2 (q, $J = 36.5$ Hz, C-7), 43.8 (C-6). ^{19}F NMR (376 MHz, CDCl_3) δ -73.9; HRMS calculated for $[\text{C}_{22}\text{H}_{20}\text{F}_3\text{NO}_2\text{SNa}]$ $[\text{M} + \text{Na}]^+$ 442.1059, found 442.1066.

(±)-Ethyl *N*-benzylmethanesulfonimide (200**)**

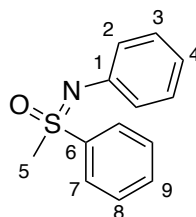
Following GP3, ethyl *N*-benzylmethanesulfonimide (**200**) was prepared from sulfinamide **159** (0.250 g, 1.48 mmol), iodosylbenzene (0.325 g, 1.48 mmol), and ethanol (4 mL). The crude mixture was purified by flash chromatography (1:1 pentane/diethyl ether) to afford the title compound as a yellow oil (0.186 g, 59%); IR ν_{max} (cm⁻¹): 3027, 2981, 2903, 2848, 1494, 1452, 1411, 1387, 1358, 1274, 1234, 1152, 1014, 986, 892, 785, 734, 697, 572, 523, 498, 478; ¹H NMR (400 MHz, CDCl₃) δ 7.44-7.36 (2H, m, H-2 or H-3), 7.37-7.31 (2H, m, H-2 or H-3), 7.25 (1H, t, J = 7.0 Hz, H-4), 4.45-4.21 (2H, m, H-5), 4.14-4.00 (2H, m, H-7), 3.06 (3H, s, H-6), 1.31 (3H, t, J = 7.0 Hz, H-8); ¹³C NMR (101 MHz, CDCl₃) δ 140.8 (C-1), 128.5 (C-2 or C-3), 127.7 (C-2 or C-3), 126.9 (C-4), 65.1 (C-7), 46.6 (C-5), 39.7 (C-6), 15.2 (C-8); HRMS calculated for [C₁₀H₁₆NO₂S] [M + H]⁺ 214.0896, found 214.0895 / [C₁₀H₁₅NO₂SNa] [M + Na]⁺ 236.0716, found 236.0713.

(±)-2,2,2-Trifluoroethyl *N*-benzylmethanesulfonimide (201**)**

Following GP3, 2,2,2-trifluoroethyl *N*-benzylmethanesulfonimide (**201**) was prepared from sulfinamide **159** (0.115 g, 0.680 mmol), iodosylbenzene (0.150 g, 0.680 mmol) and 2,2,2-trifluoroethanol (2 mL). The crude mixture was purified by

flash chromatography (7:3 to 1:1 pentane/diethyl ether) to afford the title compound as a colourless oil (0.100 g, 55%); IR ν_{max} (cm^{-1}): 3029, 1514, 1274, 1159, 1039, 988, 959, 780, 732, 697; ^1H NMR (400 MHz, CDCl_3) δ 7.29-7.22 (4H, m, H-2,3), 7.19-7.13 (1H, m, H-4), 4.32-4.13 (2H, m, H-5), 4.18-4.05 (2H, m, H-7), 3.05 (3H, s, H-6); ^{13}C NMR (101 MHz, CDCl_3) δ 139.9 (C-1), 128.6 (C-2 or C-3), 127.7 (C-2 or C-3), 127.2 (C-4), 122.7 (q, $J = 278$ Hz, C-8), 64.4 (q, $J = 37.0$ Hz, C-7), 46.4 (C-5), 40.8 (C-6); ^{19}F NMR (376 MHz, CDCl_3) δ -73.9; HRMS calculated for $[\text{C}_{10}\text{H}_{13}\text{NO}_2\text{SF}_3] [\text{M} + \text{H}]^+$ 268.0614, found 268.0610 / $[\text{C}_{10}\text{H}_{12}\text{NO}_2\text{SF}_3\text{Na}] [\text{M} + \text{Na}]^+$ 290.0433, found 290.0431.

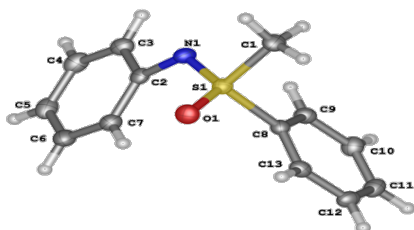
($\pm$)-Methyl(phenyl)(phenylimino)- λ^6 -sulfanone (202**)¹²⁷**



Following GP4, methyl(phenyl)(phenylimino)- λ^6 -sulfanone (**202**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0486 g, 0.244 mmol) dissolved in THF (2 mL) and phenylmagnesium bromide (1.22 mL, 1.22 mmol, 1M). The crude mixture was purified by flash chromatography (8:2 petroleum ether/ethyl acetate) to afford the title compound as an orange oil (0.0366 g, 65%); IR ν_{max} (cm^{-1}): 3055, 3013, 2952, 1593, 1572, 1484, 1444, 1406, 1317, 1286, 1263, 1198, 1176, 1092, 1071, 1038, 1016, 994, 967, 788, 754, 741, 688, 618, 591, 529, 509, 496; ^1H NMR (400 MHz, CDCl_3) δ 7.98 (2H, d, $J = 7.0$ Hz, H-7 or H-8), 7.67-7.45 (3H, m, H-7,9 or H-8,9), 7.12 (2H, dd, $J = 8.5, 7.5$ Hz, H-2 or H-3), 7.01 (2H, d, $J = 7.5$ Hz, H-2 or H-3), 6.87 (1H, t, $J = 7.5$ Hz, H-4), 3.24 (3H, s, H-5); ^{13}C NMR (101 MHz, CDCl_3) δ 145.1 (C-1), 139.6 (C-6), 133.3 (C-9), 129.7 (C-7 or C-8), 129.1 (C-2 or

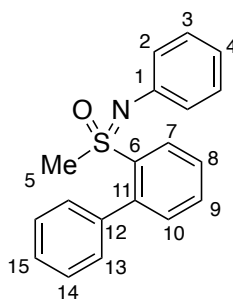
C-3), 128.8 (C-7 or C-8), 123.4 (C-2 or C-3), 121.8 (C-4), 46.2 (C-5); HRMS calculated for $[C_{13}H_{14}NOS] [M + H]^+$ 232.0791, found 232.0791 / $[C_{13}H_{13}NOSNa] [M + Na]^+$ 254.0610, found 254.0607.

X-ray crystal structure of methyl(phenyl)(phenylimino)- λ^6 -sulfanone $C_{13}H_{13}NOS$



Mw = 231.30 T = 120(2) K; λ = 1.54184 Å; triclinic; P-1 space group; a = 9.0644(2) Å, b = 11.1524(3) Å, c = 12.0031(4) Å; α = 88.750(2)°, β = 84.848(2)°, γ = 72.002(2)°; V = 1149.33 (6) Å³; Z = 4; D = 1.337 g/cm³; R₁ = 0.0406, wR₂ = 0.1015 (all data), GoF = 1.122; CCDC: 1837499.

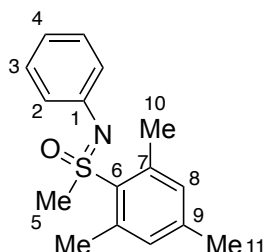
(±)- [1,1'-Biphenyl]-2-yl(methyl)(phenylimino)- λ^6 -sulfanone (204)



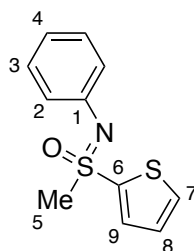
Following GP4, [1,1'-biphenyl]-2-yl(methyl)(phenylimino)- λ^6 -sulfanone (**204**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0479 g, 0.241 mmol) dissolved in THF (2 mL) and 2-biphenylmagnesium bromide (1.20 mL, 1.20 mmol, 1M). The crude mixture was purified by flash chromatography (9:1 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0305 g, 41%); IR $\nu_{\max}$ (cm⁻¹): 3055, 3027, 2922, 2851, 1719, 1676, 1594, 1487, 1461, 1315, 1292, 1267, 1197, 1126, 1074, 1049, 1032, 1017, 960, 890, 756, 698, 617, 510; ¹H NMR (400 MHz, CDCl₃) δ 8.46-8.27 (1H, m, H-7 or H-8 or H-9 or H-10), 7.63-7.50 (2H, m, H-7 or H-8 or H-9 or H-10), 7.46-7.36 (3H, m, H-13, 15 or H-14, 15), 7.33-7.25 (3H, m, H-7 or H-8 or H-9 or H-10 and H-13 or H-14), 7.19-7.10

(2H, m, H-2 or H-3), 6.97-6.91 (2H, m, H-2 or H-3), 6.90-6.83 (1H, m, H-4), 2.88 (3H, s, H-5); ^{13}C NMR (101 MHz, CDCl_3) δ 145.2 (C-1), 141.9 (C-6), 139.0 (C-11 or C-12), 138.3 (C-11 or C-12), 133.1 (C-13 or C-14), 132.7 (C-7 or C-8 or C-9 or C-10), 130.8 (C-7 or C-8 or C-9 or C-10), 129.7 (C-7 or C-8 or C-9 or C-10), 129.1 (C-2 or C-3), 128.4 (C-15), 128.1 (C-7 or C-8 or C-9 or C-10), 127.8 (C-13 or C-14), 122.9 (C-2 or C-3), 121.6 (C-4), 44.9 (C-5); HRMS calculated for $[\text{C}_{19}\text{H}_{18}\text{NOS}]$ $[\text{M} + \text{H}]^+$ 308.1104, found 308.1109 / $[\text{C}_{19}\text{H}_{17}\text{NOSNa}]$ $[\text{M} + \text{Na}]^+$ 330.0923, found 330.0925.

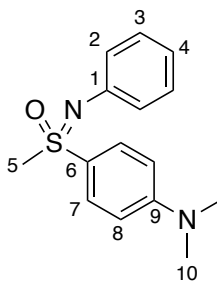
($\pm$)-Mesityl(methyl)(phenylimino)- λ^6 -sulfanone (205**)**



Following GP4, mesityl(methyl)(phenylimino)- λ^6 -sulfanone (**205**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0315 g, 0.158 mmol) dissolved in THF (2 mL) and 2-mesitylmagnesium bromide (0.791 mL, 0.791 mmol, 1M). The crude mixture was purified by flash chromatography (8:2 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0196 g, 45%); IR ν_{max} (cm^{-1}): 2966, 2931, 2872, 1595, 1487, 1450, 1401, 1316, 1291, 1266, 1202, 1059, 1041, 1033, 995, 966, 852, 754, 706, 621, 608, 592, 550, 495, 476, 456, 434; ^1H NMR (400 MHz, CDCl_3) δ 7.15-7.08 (2H, m, Ar), 6.97-6.91 (4H, m, Ar), 6.88-6.83 (1H, m, H-4), 3.28 (3H, s, H-5), 2.69 (6H, s, H-10), 2.27 (3H, s, H-11); ^{13}C NMR (101 MHz, CDCl_3) δ 145.7 (C-1), 142.8 (C-9), 140.3 (C-7), 133.7 (C-6), 132.9 (C-8), 129.1 (C-2 or C-3), 122.0 (C-2 or C-3), 121.4 (C-4), 45.9 (C-5), 23.4 (C-10), 21.0 (C-11); HRMS calculated for $[\text{C}_{16}\text{H}_{20}\text{NOS}]$ $[\text{M} + \text{H}]^+$ 274.1260, found 274.1264 / $[\text{C}_{16}\text{H}_{19}\text{NOSNa}]$ $[\text{M} + \text{Na}]^+$ 296.1080, found 296.1080.

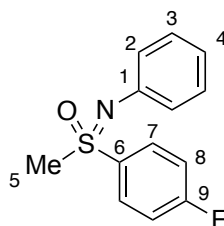
(±)-Methyl(phenylimino)(thiophen-2-yl)-λ⁶-sulfanone (206)

Following GP4, methyl(phenylimino)(thiophen-2-yl)-λ⁶-sulfanone (**206**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0421 g, 0.211 mmol) dissolved in THF (4 mL) and 2-thienylmagnesium bromide (1.06 mL, 1.06 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0292 g, 58%); IR ν_{max} (cm⁻¹): 2923, 1594, 1486, 1400, 1319, 1291, 1268, 1201, 1154, 1093, 1044, 1004, 779, 764, 724, 694, 595, 535, 509, 492, 476; ¹H NMR (400 MHz, CDCl₃) δ 7.70-7.61 (2H, m, H-8,9), 7.18-7.13 (2H, m, H-2 or H-3), 7.11-7.03 (3H, m, H-7 and H-2 or H-3), 6.98-6.88 (1H, m, H-4), 3.38 (3H, s, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 144.6 (C-1), 140.9 (C-6), 134.4 (C-8 or C-9), 134.2 (C-8 or C-9), 129.1 (C-2 or C-3), 128.2 (C-7), 123.6 (C-2 or C-3), 122.4 (C-4), 48.2 (C-5); HRMS calculated for [C₁₁H₁₂NOS₂] [M + H]⁺ 238.0355, found 238.0355 / [C₁₁H₁₁NOS₂Na] [M + Na]⁺ 260.0174, found 260.0171.

(±)-(4-(Dimethylamino)phenyl)(methyl)(phenylimino)-λ⁶-sulfanone (207)

Following GP4, (4-(dimethylamino)phenyl)(methyl)(phenylimino)- λ^6 -sulfanone (**207**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0545 g, 0.274 mmol) dissolved in THF (5 mL) and 4-(*N,N*-dimethyl)anilinemagnesium bromide (1.37 mL, 1.37 mmol, 1M). The crude mixture was purified by flash chromatography (6:4 petroleum ether/ethyl acetate) to afford the title compound as an off white oil (0.0546 g, 73%); IR ν_{max} (cm⁻¹): 2923, 2860, 2818, 1591, 1513, 1485, 1444, 1367, 1286, 1263, 1191, 1036, 1016, 957, 817, 785, 695, 509; ¹H NMR (400 MHz, CDCl₃) δ 7.80-7.70 (2H, m, H-7 or H-8), 7.16-7.07 (2H, m, H-2 or H-3), 7.05-6.98 (2H, m, H-2 or H-3), 6.87-6.81 (1H, m, H-4), 6.70-6.63 (2H, m, H-7 or H-8), 3.20 (3H, s, H-5), 3.01 (6H, s, H-10); ¹³C NMR (101 MHz, CDCl₃) δ 153.2 (C-9), 145.8 (C-1), 130.4 (C-7 or C-8), 129.0 (C-2 or C-3), 123.7 (C-6), 123.3 (C-2 or C-3), 121.2 (C-4), 111.5 (C-7 or C-8), 46.9 (C-5), 40.2 (C-10); HRMS calculated for [C₁₅H₁₉N₂OS] [M + H]⁺ 275.1213, found 275.1217 / [C₁₅H₁₈N₂OSNa] [M + Na]⁺ 297.1032, found 297.1024.

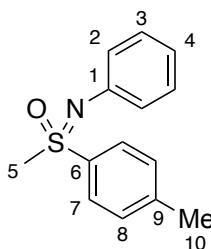
(±)-(4-Fluorophenyl)(methyl)(phenylimino)- λ^6 -sulfanone (208)



Following GP4, (4-fluorophenyl)(methyl)(phenylimino)- λ^6 -sulfanone (**208**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0468 g, 0.235 mmol) dissolved in THF (4 mL) and 4-fluorophenylmagnesium bromide (1.18 mL, 1.18 mmol, 1M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a dark yellow oil (0.0224 g, 38%); IR ν_{max} (cm⁻¹): 2922, 2844, 1586, 1486, 1401, 1284, 1263, 1200,

1154, 1092, 1034, 1011, 961, 838, 815, 779, 763, 718, 695, 627, 602, 590, 576, 545, 518, 501, 450; ^1H NMR (400 MHz, CDCl_3) δ 8.04-7.92 (2H, m, H-7), 7.23-7.17 (2H, m, H-8), 7.16-7.10 (2H, m, H-2 or H-3), 7.03-6.97 (2H, m, H-2 or H-3), 6.92-6.84 (1H, m, H-4), 3.24 (3H, s, H-5); ^{13}C NMR (101 MHz, CDCl_3) δ 165.7 (d, $J = 255$ Hz, C-9), 144.8 (C-1), 135.4 (d, $J = 3.0$ Hz, C-6), 131.6 (d, $J = 9.5$ Hz, C-7), 129.2 (C-2 or C-3), 123.4 (C-2 or C-3), 122.1 (C-4), 117.0 (d, $J = 23.0$ Hz, C-8), 46.4 (C-5); ^{19}F NMR (376 MHz, CDCl_3) δ -104.6; HRMS calculated for $[\text{C}_{13}\text{H}_{13}\text{FNOS}] [\text{M} + \text{H}]^+$ 250.0696, found 250.0690 / $[\text{C}_{13}\text{H}_{12}\text{FNOSNa}] [\text{M} + \text{Na}]^+$ 272.0516, found 272.0505.

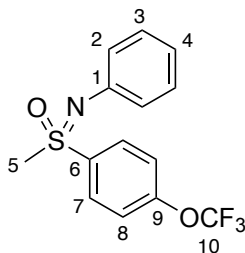
(±)-Methyl(phenylimino)(p-tolyl)-λ6-sulfanone (209)¹²⁷



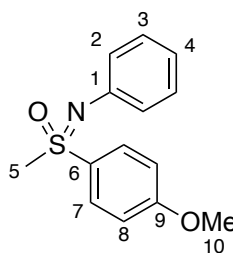
Following GP4, methyl(phenylimino)(p-tolyl)-λ6-sulfanone (**209**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0486 g, 0.244 mmol) dissolved in THF (5 mL) and *p*-tolylmagnesium bromide (1.22 mL, 1.22 mmol, 1M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a red oil (0.0514 g, 86%); IR ν_{max} (cm^{-1}): 3054, 3026, 2924, 1594, 1572, 1486, 1400, 1287, 1264, 1197, 1074, 1038, 1012, 958, 759, 694, 506; ^1H NMR (400 MHz, CDCl_3) δ 7.85 (2H, d, $J = 8.0$ Hz, H-7 or H-8), 7.31 (2H, d, $J = 8.0$ Hz, H-7 or H-8), 7.16-7.07 (2H, m, H-2 or H-3), 7.03-6.99 (2H, m, H-2 or H-3), 6.90-6.82 (1H, m, H-4), 3.22 (3H, s, H-5), 2.40 (3H, s, H-10); ^{13}C NMR (101 MHz, CDCl_3) δ 145.2 (C-1), 144.2 (C-9), 136.4 (C-6), 130.3 (C-7 or C-8), 129.1 (C-7 or C-8 or C-2 or C-3), 128.8 (C-7 or C-8 or C-2 or C-3),

123.4 (C-2 or C-3), 121.7 (C-4), 46.3 (C-5), 21.7 (C-10); HRMS calculated for $[C_{14}H_{16}NOS] [M + H]^+$ 246.0947, found 246.0950 / $[C_{14}H_{15}NOSNa] [M + Na]^+$ 268.0767, found 268.0768.

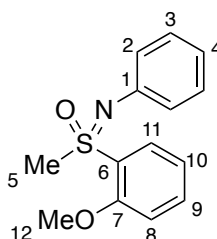
(±)-Methyl(phenylimino)(4-(trifluoromethoxy)phenyl)-λ6-sulfanone (210)



Following GP4, methyl(phenylimino)(4-(trifluoromethoxy)phenyl)-λ6-sulfanone (**210**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0456 g, 0.229 mmol) dissolved in THF (5 mL) and 4-(trifluoromethyl)phenylmagnesium bromide (1.15 mL, 1.15 mmol, 1M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a dark yellow oil (0.0546 g, 76%); IR $\nu_{\max}$ (cm⁻¹): 3058, 3029, 2928, 1588, 1485, 1404, 1289, 1251, 1199, 1165, 1094, 1040, 1012, 996, 969, 922, 855, 809, 780, 756, 731, 694, 672, 664, 591, 555, 527, 504, 457; ¹H NMR (400 MHz, CDCl₃) δ 8.07-7.95 (2H, m, H-7 or H-8), 7.40-7.30 (2H, m, H-7 or H-8), 7.21-7.09 (2H, m, H-2 or H-3), 7.05-6.97 (2H, m, H-2 or H-3), 6.95-6.86 (1H, m, H-4), 3.25 (3H, s, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 152.8 (q, J = 2.0 Hz, C-9), 144.6 (C-1), 137.8 (C-6), 131.0 (C-7 or C-8), 129.2 (C-2 or C-3), 123.4 (C-2 or C-3), 122.2 (C-4), 121.4 (C-7 or C-8), 120.3 (q, J = 260 Hz, C-10), 46.2 (C-5); ¹⁹F NMR (376 MHz, CDCl₃) δ -57.7; HRMS calculated for $[C_{14}H_{13}F_3NO_2S] [M + H]^+$ 316.0614, found 316.0617 / $[C_{14}H_{12}F_3NO_2SNa] [M + Na]^+$ 338.0433, found 338.0432.

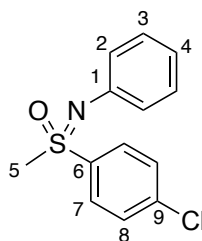
(±)-(4-Methoxyphenyl)(methyl)(phenylimino)-λ⁶-sulfanone (211)¹²⁷

Following GP4, (4-methoxyphenyl)(methyl)(phenylimino)-λ⁶-sulfanone (**211**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0451 g, 0.227 mmol) dissolved in THF (5 mL) and 4-methoxyphenylmagnesium bromide (1.13 mL, 1.13 mmol, 1M). The crude mixture was purified by flash chromatography (6:4 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0361 g, 61%); IR ν_{max} (cm⁻¹): 3011, 2927, 2838, 1591, 1576, 1484, 1440, 1409, 1286, 1256, 1197, 1173, 1093, 1036, 1018, 967, 895, 834, 803, 760, 695, 624, 591, 526, 511, 449; ¹H NMR (400 MHz, CDCl₃) δ 7.93-7.85 (2H, m, H-7 or H-8), 7.16-7.09 (2H, m, H-2 or H-3), 7.03-6.99 (2H, m, H-2 or H-3), 6.99-6.95 (2H, m, H-7 or H-8), 6.87 (1H, tt, *J* = 7.0, 1.0 Hz, H-4), 3.84 (3H, s, H-10), 3.23 (3H, s, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 163.6 (C-9), 145.1 (C-1), 130.9 (C-7 or C-8), 130.5 (C-6), 129.1 (C-2 or C-3), 123.4 (C-2 or C-3), 121.7 (C-4), 114.9 (C-7 or C-8), 55.8 (C-10), 46.5 (C-5); HRMS calculated for [C₁₄H₁₆NO₂S] [M + H]⁺ 262.0896, found 262.0910 / [C₁₄H₁₅NO₂SNa] [M + Na]⁺ 284.0716, found 284.0731.

(±)-(2-Methoxyphenyl)(methyl)(phenylimino)-λ⁶-sulfanone (212)¹²⁸

Following GP4, (2-methoxyphenyl)(methyl)(phenylimino)- λ^6 -sulfanone (**212**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0523 g, 0.263 mmol) dissolved in THF (2 mL) and 2-methoxyphenylmagnesium bromide (1.31 mL, 1.31 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0329 g, 48%); IR ν_{max} (cm⁻¹): 3012, 2932, 2839, 1589, 1477, 1433, 1315, 1276, 1245, 1195, 1133, 1070, 1044, 1016, 995, 960, 800, 756, 695, 592, 525, 492, 418; ¹H NMR (400 MHz, CDCl₃) δ 8.02 (1H, dd, *J* = 8.0, 2.0 Hz, OMeAr), 7.51 (1H, ddd, *J* = 8.5, 7.5, 2.0 Hz, OMeAr), 7.14-7.02 (3H, m, OMeAr/H-2 or H-3), 7.01-6.94 (3H, m, OMeAr/H-2 or H-3), 6.89-6.80 (1H, m, H-4), 3.94 (3H, s, H-12), 3.40 (3H, s, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 157.1 (C-7), 145.4 (C-1), 135.2 (OMeAr), 132.2 (OMeAr), 128.9 (C-2 or C-3), 126.6 (C-6), 123.5 (C-2 or C-3), 121.8 (C-4), 120.8 (OMeAr), 112.5 (OMeAr), 56.3 (C-12), 44.0 (C-5); HRMS calculated for [C₁₄H₁₆NO₂S] [M + H]⁺ 262.0896, found 262.0893 / [C₁₄H₁₅NO₂SNa] [M + Na]⁺ 284.0716, found 284.0713.

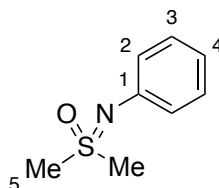
(±)-(4-Chlorophenyl)(methyl)(phenylimino)- λ^6 -sulfanone (213**)**¹²⁷



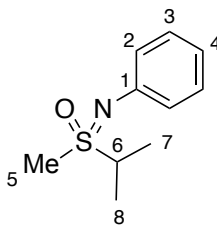
Following GP4, (4-chlorophenyl)(methyl)(phenylimino)- λ^6 -sulfanone (**213**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0245 g, 0.123 mmol) dissolved in THF (2 mL) and 4-chlorophenylmagnesium bromide (0.615 mL, 0.615 mmol, 1M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as pale yellow oil

(0.0192 g, 59%); IR ν_{max} (cm^{-1}): 3079, 3057, 3015, 2925, 1594, 1572, 1485, 1392, 1288, 1265, 1202, 1084, 1040, 1021, 996, 968, 829, 781, 765, 731, 694, 620, 590, 557, 505, 472, 438; ^1H NMR (400 MHz, CDCl_3) δ 7.91 (2H, d, $J = 8.5$ Hz, H-7 or H-8), 7.50 (2H, d, $J = 8.5$ Hz, H-7 or H-8), 7.17-7.10 (2H, m, H-2 or H-3), 7.05-6.96 (2H, m, H-2 or H-3), 6.92-6.87 (1H, m, H-4), 3.24 (3H, s, H-5); ^{13}C NMR (101 MHz, CDCl_3) δ 144.7 (C-1), 140.1 (C-9 or C-6), 138.1 (C-9 or C-6), 130.3 (C-7 or C-8), 130.0 (C-7 or C-8), 129.2 (C-2 or C-3), 123.4 (C-2 or C-3), 122.1 (C-4), 46.3 (C-5); HRMS calculated for $[\text{C}_{13}\text{H}_{13}\text{NOS}^{35}\text{Cl}]$ $[\text{M} + \text{H}]^+$ 266.0401, found 266.0398 / $[\text{C}_{13}\text{H}_{12}\text{NOS}^{35}\text{ClNa}]$ $[\text{M} + \text{Na}]^+$ 288.0220, found 288.0217.

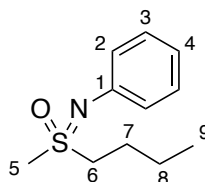
($\pm$)-Dimethyl(phenylimino)- λ^6 -sulfanone (214**)¹²⁹**



Following GP4, dimethyl(phenylimino)- λ^6 -sulfanone (**214**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0531 g, 0.267 mmol) dissolved in THF (5 mL) and methylmagnesium bromide (0.446 mL, 1.33 mmol, 3M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a dark yellow oil (0.0213 g, 47%); IR ν_{max} (cm^{-1}): 3013, 2925, 1591, 1571, 1484, 1416, 1326, 1284, 1261, 1192, 1050, 1025, 934, 758, 697, 675, 584, 476, 419; ^1H NMR (400 MHz, CDCl_3) 7.29-7.19 (2H, m, H-2 or H-3), 7.08 (2H, dt, $J = 7.5, 1.0$ Hz, H-2 or H-3), 7.03-6.97 (1H, m, H-4), 3.15 (6H, s, H-5); ^{13}C NMR (101 MHz, CDCl_3) δ 145.2 (C-1), 129.4 (C-2 or C-3), 123.6 (C-2 or C-3), 122.4 (C-4), 42.2 (C-5); HRMS calculated for $[\text{C}_8\text{H}_{12}\text{NOS}]$ $[\text{M} + \text{H}]^+$ 170.0634, found 170.0634 / $[\text{C}_8\text{H}_{11}\text{NOSNa}]$ $[\text{M} + \text{Na}]^+$ 192.0454, found 192.0453.

(±)-Isopropyl(methyl)(phenylimino)-λ⁶-sulfanone (215)

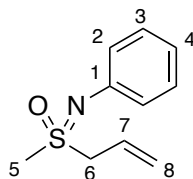
Following GP4, isopropyl(methyl)(phenylimino)-λ⁶-sulfanone (**215**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0513 g, 0.258 mmol) dissolved in THF (5 mL) and isopropylmagnesium bromide (1.29 mL, 1.29 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a dark yellow oil (0.0207 g, 41%); IR ν_{max} (cm⁻¹): 2973, 2932, 2872, 1592, 1570, 1484, 1286, 1262, 1186, 1065, 1034, 1017, 995, 935, 780, 756, 696, 520, 495; ¹H NMR (400 MHz, CDCl₃) 7.25-7.13 (2H, m, H-2 or H-3), 7.14-7.06 (2H, m, H-2 or H-3), 7.02-6.87 (1H, m, H-4), 3.39 (1H, hept, *J* = 7.0 Hz, H-6), 2.91 (3H, s, H-5), 1.51 (3H, d, *J* = 7.0 Hz, H-7 or H-8), 1.47 (3H, d, *J* = 7.0 Hz, H-7 or H-8); ¹³C NMR (101 MHz, CDCl₃) δ 145.7 (C-1), 129.3 (C-2 or C-3), 123.6 (C-2 or C-3), 121.9 (C-4), 55.4 (C-6), 35.0 (C-5), 16.7 (C-7 or C-8), 16.6 (C-7 or C-8); HRMS calculated for [C₁₀H₁₆NOS] [M + H]⁺ 198.0947, found 198.0947 / [C₁₀H₁₅NOSNa] [M + Na]⁺ 220.0767, found 220.0762.

(±)-Butyl(methyl)(phenylimino)-λ⁶-sulfanone (216)

Following GP4, butyl(methyl)(phenylimino)-λ⁶-sulfanone (**216**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0216 g, 0.109 mmol) dissolved in THF (3 mL) and *n*-butyllithium (0.217 mL, 0.542 mmol, 2.5M). The crude

mixture was purified by flash chromatography (8:2 petroleum ether/ethyl acetate) to afford the title compound as a dark yellow oil (0.0069 g, 30%); IR $\nu_{\max}$ (cm⁻¹): 3052, 2959, 2930, 2873, 1593, 1574, 1486, 1288, 1264, 1177, 1081, 1039, 1018, 915, 755, 696, 582, 518, 483; ¹H NMR (400 MHz, CDCl₃) δ 7.25-7.19 (2H, m, H-2 or H-3), 7.11-7.06 (2H, m, H-2 or H-3), 7.00-6.94 (1H, m, H-4), 3.30-3.16 (2H, m, H-6), 3.03 (3H, s, H-5), 2.01-1.81 (2H, m, H-7), 1.57-1.31 (2H, m, H-8), 0.96 (3H, t, J = 7.5 Hz, H-9); ¹³C NMR (101 MHz, CDCl₃) δ 145.3 (C-1), 129.3 (C-2 or C-3), 123.6 (C-2 or C-3), 122.2 (C-4), 54.6 (C-6), 39.3 (C-5), 25.6 (C-7), 21.8 (C-8), 13.7 (C-9); HRMS calculated for [C₁₁H₁₈NOS] [M + H]⁺ 212.1104, found 212.1113 / [C₁₁H₁₇NOSNa] [M + Na]⁺ 234.0923, found 234.0919.

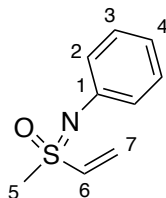
(±)-Allyl(methyl)(phenylimino)- λ^6 -sulfanone (217)



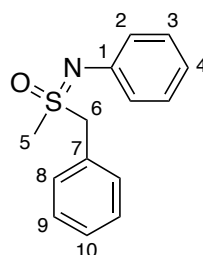
Following GP4, allyl(methyl)(phenylimino)- λ^6 -sulfanone (**217**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0567 g, 0.285 mmol) dissolved in THF (2 mL) and allylmagnesium bromide (1.42 mL, 1.42 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0238 g, 43%); IR $\nu_{\max}$ (cm⁻¹): 2955, 2920, 2850, 1593, 1486, 1289, 1266, 1181, 1040, 1019, 995, 972, 939, 758, 696, 628, 583, 495, 480; ¹H NMR (400 MHz, CDCl₃) δ 7.25-7.21 (2H, m, H-2 or H-3), 7.12-7.07 (2H, m, H-2 or H-3), 7.02-6.95 (1H, m, H-4), 5.98 (1H, ddt, J = 17.5, 10.0, 7.5 Hz, H-7), 5.48 (1H, dd, J = 10.0, 1.0 Hz, H-8), 5.43 (1H, dq, J = 17.0, 1.0 Hz, H-8), 3.95 (2H, d, J = 7.5 Hz, H-6), 3.01 (3H, s, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 145.2 (C-1), 129.4 (C-2 or C-3), 126.7 (C-7), 124.3 (C-8), 123.7 (C-2 or

C-3), 122.4 (C-4), 58.3 (C-6), 38.7 (C-5); HRMS calculated for $[C_{10}H_{14}NOS]$ $[M + H]^+$ 196.0791, found 196.0790 / $[C_{10}H_{13}NOSNa]$ $[M + Na]^+$ 218.0610, found 218.0610.

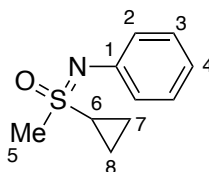
(±)-Methyl(phenylimino)(vinyl)-λ⁶-sulfanone (218)



Following GP4, methyl(phenylimino)(vinyl)-λ⁶-sulfanone (**218**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0528 g, 0.265 mmol) dissolved in THF (2 mL) and vinylmagnesium bromide (1.33 mL, 1.33 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0141 g, 29%); IR $\nu_{\max}$ (cm⁻¹): 3005, 2921, 2848, 1593, 1518, 1486, 1290, 1266, 1195, 1044, 1018, 972, 793, 758, 696; ¹H NMR (400 MHz, CDCl₃) δ 7.20 (2H, dd, J = 8.5, 7.5 Hz, H-3), 7.07-7.02 (2H, m, H-2), 6.96 (1H, t, J = 7.5 Hz, H-4), 6.67 (1H, dd, J = 16.5, 9.5 Hz, H-6), 6.49 (1H, d, J = 16.5 Hz, H-7), 6.20 (1H, d, J = 9.5 Hz, H-7), 3.14 (3H, s, H-5); ¹³C NMR (126 MHz, CDCl₃) δ 144.9 (C-1), 137.3 (C-6), 131.1 (C-7), 129.2 (C-2 or C-3), 123.5 (C-2 or C-3), 122.2 (C-4), 43.3 (C-5); HRMS calculated for $[C_9H_{12}NOS]$ $[M + H]^+$ 182.0634, found 182.0634 / $[C_9H_{11}NOSNa]$ $[M + Na]^+$ 204.0454, found 204.0451.

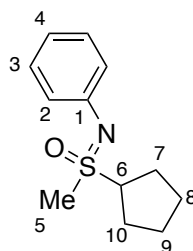
(±)-Benzyl(methyl)(phenylimino)-λ⁶-sulfanone (219)

Following GP4, benzyl(methyl)(phenylimino)-λ⁶-sulfanone (**219**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0562 g, 0.282 mmol) dissolved in THF (5 mL) and benzylmagnesium bromide (1.41 mL, 1.41 mmol, 1M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0244 g, 35%); IR ν_{max} (cm⁻¹): 3058, 3027, 2923, 1590, 1571, 1484, 1454, 1409, 1287, 1264, 1204, 1175, 1073, 1039, 1018, 995, 970, 780, 756, 696, 663, 576, 499, 464; ¹H NMR (400 MHz, CDCl₃) δ 7.45-7.36 (5H, m, H-8, 9, 10), 7.33-7.27 (2H, m, H-2 or H-3), 7.19-7.13 (2H, m, H-2 or H-3), 7.02 (1H, tt, J = 7.5, 1.0 Hz, H-4), 4.62-4.36 (2H, m, H-6), 2.88 (3H, s, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 145.4 (C-1), 130.9 (C-8 or C-9), 129.5 (C-7), 129.4 (C-8 or C-9 or C-2 or C-3), 129.2 (C-8 or C-9 or C-2 or C-3), 129.1 (C-10), 123.6 (C-2 or C-3), 122.2 (C-4), 60.1 (C-6), 38.9 (C-5); HRMS calculated for [C₁₄H₁₆NOS] [M + H]⁺ 246.0947, found 246.0946 / [C₁₄H₁₅NOSNa] [M + Na]⁺ 268.0767, found 268.0767.

(±)-Cyclopropyl(methyl)(phenylimino)-λ⁶-sulfanone (220)

Following GP4, cyclopropyl(methyl)(phenylimino)- λ^6 -sulfanone (**220**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0473 g, 0.238 mmol) dissolved in THF (2 mL) and cyclopropylmagnesium bromide (1.19 mL, 1.19 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0217 g, 47%); IR ν_{max} (cm⁻¹): 3014, 2918, 2849, 1592, 1484, 1408, 1287, 1264, 1198, 1182, 1069, 1045, 1017, 888, 827, 780, 757, 695, 673, 662, 647, 588, 508, 477; ¹H NMR (400 MHz, CDCl₃) δ 7.25-7.16 (2H, m, H-2 or H-3), 7.11-7.05 (2H, m, H-2 or H-3), 7.02-6.92 (1H, m, H-4), 3.09 (3H, s, H-5), 2.55 (1H, tt, *J* = 8.0, 4.5 Hz, H-6), 1.45-1.36 (1H, m, H-7 or H-8), 1.27-1.17 (1H, m, H-7 or H-8), 1.15-0.97 (2H, m, H-7 or H-8); ¹³C NMR (101 MHz, CDCl₃) δ 145.3 (C-1), 129.2 (C-2 or C-3), 123.7 (C-2 or C-3), 122.1 (C-4), 41.1 (C-5), 31.6 (C-6), 5.7 (C-7 or C-8), 4.9 (C-7 or C-8); HRMS calculated for [C₁₀H₁₄NOS] [M + H]⁺ 196.0791, found 196.0793 / [C₁₀H₁₃NOSNa] [M + Na]⁺ 218.0610, found 218.0611.

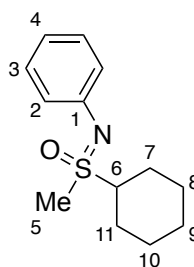
(±)-Cyclopentyl(methyl)(phenylimino)- λ^6 -sulfanone (221**)**



Following GP4, cyclopentyl(methyl)(phenylimino)- λ^6 -sulfanone (**221**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0403 g, 0.202 mmol) dissolved in THF (4 mL) and cyclopentylmagnesium chloride (0.506 mL, 1.01 mmol, 2M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0161 g, 36%); IR ν_{max} (cm⁻¹): 2964, 2888, 2870, 1593, 1486, 1445, 1408, 1289, 1263,

1191, 1126, 1070, 1045, 1020, 968, 951, 780, 756, 696, 567, 535, 504, 474; ^1H NMR (400 MHz, CDCl_3) δ 7.27-7.18 (2H, m, H-2 or H-3), 7.14-7.07 (2H, m, H-2 or H-3), 7.01-6.90 (1H, m, H-4), 3.81-3.57 (1H, m, H-6), 2.98 (3H, s, H-5), 2.32-2.02 (4H, m, Cy), 1.88-1.80 (2H, m, Cy), 1.76-1.65 (2H, m, Cy); ^{13}C NMR (101 MHz, CDCl_3) δ 145.8 (C-1), 129.2 (C-2 or C-3), 123.8 (C-2 or C-3), 122.0 (C-4), 64.4 (C-6), 37.3 (C-5), 27.8 (Cy), 27.6 (Cy), 26.12 (Cy), 26.10 (Cy); HRMS calculated for $[\text{C}_{12}\text{H}_{18}\text{NOS}] [\text{M} + \text{H}]^+$ 224.1104, found 224.1103 / $[\text{C}_{12}\text{H}_{17}\text{NOSNa}] [\text{M} + \text{Na}]^+$ 246.0923, found 246.0917.

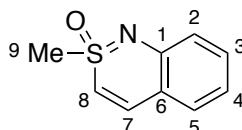
($\pm$)-Cyclohexyl(methyl)(phenylimino)- λ^6 -sulfanone (222**)**



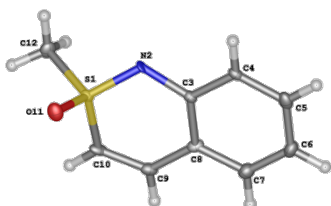
Following GP4, cyclohexyl(methyl)(phenylimino)- λ^6 -sulfanone (**222**) was prepared from ethyl *N*-phenylmethanesulfonimidate (**175**) (0.0397 g, 0.199 mmol) dissolved in THF (4 mL) and cyclohexylmagnesium chloride (0.499 mL, 0.997 mmol, 2M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0189 g, 40%); IR ν_{max} (cm^{-1}): 2931, 2856, 1593, 1485, 1450, 1411, 1287, 1263, 1220, 1185, 1130, 1049, 1018, 994, 944, 892, 857, 783, 755, 696, 619, 596, 534, 483, 450, 422; ^1H NMR (400 MHz, CDCl_3) δ 7.26-7.17 (2H, m, H-2 or H-3), 7.14-7.07 (2H, m, H-2 or H-3), 7.01-6.91 (1H, m, H-4), 3.25-3.06 (1H, m, H-6), 2.92 (3H, s, H-5), 2.40-2.33 (2H, m, Cy), 2.00-1.95 (2H, m, Cy), 1.79-1.73 (1H, m, Cy), 1.61-1.53 (2H, m, Cy), 1.37-1.29 (2H, m, Cy), 1.24-1.19 (1H, m, Cy); ^{13}C NMR (101 MHz, CDCl_3) δ 145.5 (C-1), 129.3 (C-2 or C-3), 123.6 (C-2 or C-3), 122.0 (C-4),

63.4 (C-6), 35.5 (C-5), 26.52 (Cy), 26.50 (Cy), 25.61 (Cy), 25.59 (Cy), 25.3 (Cy); HRMS calculated for $[C_{13}H_{20}NOS] [M + H]^+$ 238.1260, found 238.1272 / $[C_{13}H_{19}NOSNa] [M + Na]^+$ 260.1080, found 260.1089.

(±)-2-Methyl-2λ⁴-benzo[*c*][1,2]thiazine 2-oxide (225)



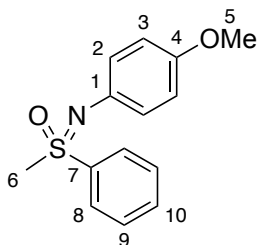
Following GP4, 2-Methyl-2λ⁴-benzo[*c*][1,2]thiazine 2-oxide (**225**) was prepared from ethyl *N*-phenylmethanesulfonimidate **175** (0.0509 g, 0.255 mmol) dissolved in THF (5 mL) and ethynylmagnesium bromide (2.55 mL, 1.27 mmol, 0.5 M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0133 g, 29%); IR $\nu_{\max}$ (cm⁻¹): 3066, 3009, 2923, 2865, 2844, 1609, 1589, 1536, 1469, 1436, 1417, 1363, 1338, 1296, 1190, 1150, 1134, 1111, 1054, 1032, 997, 962, 800, 773, 746, 726, 699, 650, 577, 562, 494, 466, 414; ¹H NMR (400 MHz, CDCl₃) δ 7.64 (1H, d, J = 10.0 Hz, H-7), 7.41 (1H, ddd, J = 8.5, 7.0, 1.5 Hz, H-3), 7.31 (1H, dd, J = 8.5, 1.5 Hz, H-5), 7.21 (1H, d, J = 8.5 Hz, H-2), 7.05-6.93 (1H, m, H-4), 6.56 (1H, d, J = 10.0 Hz, H-8), 3.42 (3H, s, H-9); ¹³C NMR (101 MHz, CDCl₃) δ 145.3 (C-1), 140.1 (C-7), 132.4 (C-3), 129.9 (C-5), 123.7 (C-2), 120.2 (C-4), 116.7 (C-6), 108.4 (C-8), 47.2 (C-9); HRMS calculated for $[C_9H_{10}NOS] [M + H]^+$ 180.0478, found 180.0474 / $[C_9H_9NOSNa] [M + Na]^+$ 202.0297, found 202.0293.



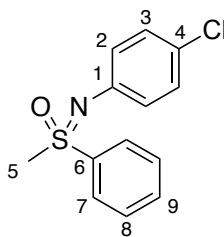
X-ray crystal structure of 2-Methyl-2λ⁴-benzo[*c*][1,2]thiazine 2-oxide C_9H_9NOS Mw = 179.23
T = 120(2) K; λ = 1.54184 Å; monoclinic; Pc space group; a = 8.6439(5) Å, b = 5.9186(3) Å, c = 8.3712(5) Å; α = 90°, β = 106.686(6)°, γ = 90°.

$\gamma = 90^\circ$; $V = 410.24 (4) \text{ \AA}^3$; $Z = 2$; $D = 1.451 \text{ g/cm}^3$; $R_1 = 0.0919$, $wR_2 = 0.22090$ (all data), $\text{GoF} = 1.240$.

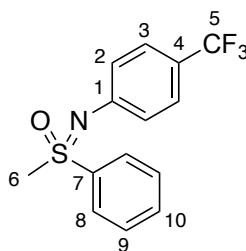
(±)-((4-Methoxyphenyl)imino)(methyl)(phenyl)- λ^6 -sulfanone (232)¹²⁷



Following GP4, ((4-methoxyphenyl)imino)(methyl)(phenyl)- λ^6 -sulfanone (**232**) was prepared from ethyl *N*-(4-methoxyphenyl)methanesulfonimidate (**187**) (0.0507 g, 0.221 mmol) dissolved in THF (2 mL) and phenylmagnesium bromide (1.11 mL, 1.11 mmol, 1M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a brown oil (0.0279 g, 48%); IR ν_{max} (cm^{-1}): 3000, 2928, 2832, 1500, 1475, 1463, 1443, 1406, 1260, 1233, 1180, 1092, 1039, 1019, 967, 831, 809, 785, 742, 709, 687, 639, 571, 516; ^1H NMR (400 MHz, CDCl_3) δ 8.18-7.84 (2H, m, H-8 or H-9), 7.61-7.52 (1H, m, H-10), 7.53-7.48 (2H, m, H-8 or H-9), 6.95 (2H, d, $J = 9.0$ Hz, H-2 or H-3), 6.68 (2H, d, $J = 9.0$ Hz, H-2 or H-3), 3.68 (3H, s, H-5), 3.20 (3H, s, H-6); ^{13}C NMR (101 MHz, CDCl_3) δ 154.9 (C-4), 139.6 (C-7), 138.0 (C-1), 133.2 (C-10), 129.6 (C-8 or C-9), 128.8 (C-8 or C-9), 124.4 (C-2 or C-3), 114.4 (C-2 or C-3), 55.5 (C-5), 45.8 (C-6); HRMS calculated for $[\text{C}_{14}\text{H}_{16}\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 262.0896, found 262.0897 / $[\text{C}_{14}\text{H}_{15}\text{NO}_2\text{SNa}]$ $[\text{M} + \text{Na}]^+$ 284.0716, found 284.0718.

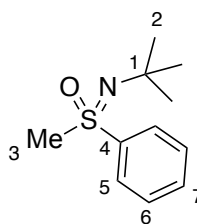
(±)-((4-Chlorophenyl)imino)(methyl)(phenyl)-λ⁶-sulfanone (233)¹²⁷

Following GP4, ((4-chlorophenyl)imino)(methyl)(phenyl)-λ⁶-sulfanone (**233**) was prepared from ethyl *N*-(4-chlorophenyl)methanesulfonimidate (**189**) (0.0653 g, 0.280 mmol) dissolved in THF (5 mL) and phenylmagnesium bromide (1.40 mL, 1.40 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0337 g, 45%); IR ν_{max} (cm⁻¹): 3062, 3024, 3004, 2923, 2851, 1588, 1486, 1445, 1404, 1377, 1287, 1257, 1204, 1174, 1032, 1019, 998, 970, 831, 788, 777, 743, 687, 651, 625, 542, 502, 457, 443, 412; ¹H NMR (400 MHz, CDCl₃) δ 8.00-7.89 (2H, m, H-7 or H-8), 7.67-7.57 (1H, m, H-9), 7.56-7.45 (2H, m, H-7 or H-8), 7.07 (2H, d, *J* = 9.0 Hz, H-2 or H-3), 6.93 (2H, d, *J* = 9.0 Hz, H-2 or H-3), 3.24 (3H, s, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 143.8 (C-1), 139.1 (C-6), 133.6 (C-9), 129.8 (C-7 or C-8), 129.1 (C-7 or C-8 or C-2 or C-3), 128.7 (C-7 or C-8 or C-2 or C-3), 126.9 (C-4), 124.6 (C-2 or C-3), 46.2 (C-5); HRMS calculated for [C₁₃H₁₃³⁵ClNOS] [M + H]⁺ 266.0401, found 266.0389 / [C₁₃H₁₂³⁵ClNOSNa] [M + Na]⁺ 288.0220, found 288.0210.

(±)-Methyl(phenyl)((4-(trifluoromethyl)phenyl)imino)-λ⁶-sulfanone (234)¹²⁷

Following GP4, methyl(phenyl)((4-(trifluoromethyl)phenyl)imino)- λ^6 -sulfanone (**234**) was prepared from ethyl *N*-(4-(trifluoromethyl)phenyl)methanesulfonimidate (**191**) (0.0545 g, 0.204 mmol) dissolved in THF (5 mL) and phenylmagnesium bromide (1.02 mL, 1.02 mmol, 1M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0263 g, 43%); IR ν_{max} (cm⁻¹): 3062, 2927, 1610, 1511, 1475, 1445, 1412, 1321, 1297, 1272, 1205, 1183, 1157, 1105, 1093, 1066, 1029, 1017, 997, 970, 841, 785, 743, 686, 640, 616, 592, 534, 502; ¹H NMR (400 MHz, CDCl₃) δ 8.17-7.90 (2H, m, H-8 or H-9), 7.67-7.60 (1H, m, H-10), 7.58-7.53 (2H, m, H-8 or H-9), 7.35 (2H, d, *J* = 8.0 Hz, H-3), 7.05 (2H, d, *J* = 8.0 Hz, H-2), 3.27 (3H, s, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 148.8 (C-1), 139.0 (C-7), 133.7 (C-10), 129.9 (C-8 or C-9), 128.6 (C-8 or C-9), 126.3 (q, *J* = 4.0 Hz, C-3), 124.7 (q, *J* = 270 Hz, C-5), 123.4 (q, *J* = 32.5 Hz, C-4), 122.9 (C-2), 46.5 (C-6); ¹⁹F NMR (376 MHz, CDCl₃) δ -61.7; HRMS calculated for [C₁₄H₁₃F₃NOS] [M + H]⁺ 300.0664, found 300.0663 / [C₁₄H₁₂F₃NOSNa] [M + Na]⁺ 322.0484, found 322.0483.

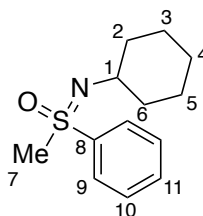
(±)-(tert-Butylimino)(methyl)(phenyl)- λ^6 -sulfanone (235)



Following GP4, (*tert*-butylimino)(methyl)(phenyl)- λ^6 -sulfanone (**235**) was prepared from ethyl *N-tert*-butylmethanesulfonimidate (**197**) (0.0272 g, 0.152 mmol) dissolved in THF (2 mL) and phenylmagnesium bromide (0.759 mL, 0.759 mmol, 1M). The crude mixture was purified by flash chromatography (1:1

petroleum ether/ethyl acetate) to afford the title compound as a pale yellow oil (0.0115 g, 36%); IR ν_{max} (cm^{-1}): 2964, 2923, 2863, 1443, 1405, 1386, 1359, 1243, 1201, 1123, 1077, 1067, 968, 851, 777, 740, 706, 689, 560, 533, 472, 453, 405; ^1H NMR (400 MHz, CDCl_3) δ 8.00-7.93 (2H, m, H-5 or H-6), 7.58-7.47 (3H, m, H-5,7 or H-6,7), 3.02 (3H, s, H-3), 1.20 (9H, s, H-2); ^{13}C NMR (101 MHz, CDCl_3) δ 145.2 (C-4), 132.2 (C-7), 129.2 (C-5 or C-6), 128.1 (C-5 or C-6), 55.3 (C-1), 48.6 (C-3), 33.2 (C-2); HRMS calculated for $[\text{C}_{11}\text{H}_{18}\text{NOS}]$ $[\text{M} + \text{H}]^+$ 212.1104, found 212.1093.

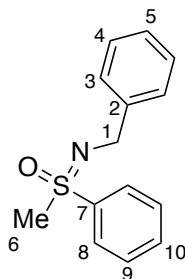
($\pm$)-(Cyclohexylimino)(methyl)(phenyl)- λ^6 -sulfanone (236**)¹³⁰**



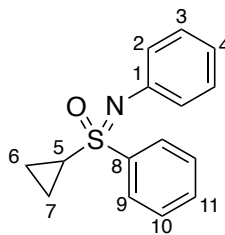
Following GP4, (cyclohexylimino)(methyl)(phenyl)- λ^6 -sulfanone (**236**) was prepared from ethyl *N*-cyclohexylmethanesulfonimidate (**193**) (0.0652 g, 0.318 mmol) dissolved in THF (4 mL) and phenylmagnesium bromide (1.59 mL, 1.59 mmol 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0301 g, 40%); IR ν_{max} (cm^{-1}): 2924, 2850, 1444, 1407, 1365, 1317, 1244, 1224, 1128, 1084, 1068, 972, 888, 791, 742, 689, 568, 533, 519, 482, 460; ^1H NMR (400 MHz, CDCl_3) δ 7.92 (2H, d, $J = 7.0$ Hz, H-9 or H-10), 7.64-7.55 (1H, m, H-11), 7.56-7.51 (2H, m, H-9 or H-10), 3.05 (3H, s, H-7), 2.85 (1H, tt, $J = 10.5, 4.0$ Hz, H-1), 1.90-1.84 (1H, m, Cy), 1.72-1.59 (3H, m, Cy), 1.50-1.00 (6H, m, Cy); ^{13}C NMR (101 MHz, CDCl_3) δ 141.0 (C-8), 132.8 (C-11), 129.4 (C-9 or C-10), 128.8 (C-9 or C-10), 54.3 (C-1), 45.9 (C-7), 37.8 (Cy), 36.6 (Cy), 25.7 (Cy), 25.6 (Cy),

25.4 (Cy); HRMS calculated for $[C_{13}H_{20}NOS]$ $[M + H]^+$ 238.1260, found 238.1261 / $[C_{13}H_{19}NOSNa]$ $[M + Na]^+$ 260.1080, found 260.1076.

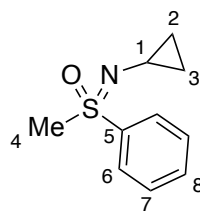
(±)-(Benzylimino)(methyl)(phenyl)-λ6-sulfanone (237)¹³¹



Following GP4, (Benzylimino)(methyl)(phenyl)-λ6-sulfanone (**237**) was prepared from ethyl *N*-benzylmethanesulfonimidate (**200**) (0.0674 g, 0.316 mmol) dissolved in THF (6 mL) and phenylmagnesium bromide (1.58 mL, 1.58 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ ethyl acetate) to afford the title compound as a colourless oil (0.0359 g, 46%); IR $\nu_{\max}$ (cm⁻¹): 3084, 3060, 3025, 2926, 1494, 1444, 1407, 1254, 1222, 1198, 1132, 1084, 1069, 1031, 978, 779, 740, 689, 591, 538, 510, 482; ¹H NMR (400 MHz, CDCl₃) δ 8.02-7.86 (2H, m, H-8 or H-9), 7.65-7.59 (1H, m, H-10), 7.60-7.52 (2H, m, H-8 or H-9), 7.40-7.33 (2H, m, H-3 or H-4), 7.31-7.27 (2H, m, H-3 or H-4), 7.25-7.15 (1H, m, H-5), 4.21 (1H, d, J = 14.0 Hz, H-1), 3.98 (1H, d, J = 14.0 Hz, H-1), 3.14 (3H, s, H-6); ¹³C NMR (101 MHz, CDCl₃) δ 141.3 (C-2), 139.6 (C-7), 133.1 (C-10), 129.6 (C-8 or C-9), 128.8 (C-8 or C-9), 128.4 (C-3 or C-4), 127.8 (C-3 or C-4), 126.7 (C-5), 47.5 (C-1), 45.5 (C-6); HRMS calculated for $[C_{14}H_{16}NOS]$ $[M + H]^+$ 246.0947, found 246.0952 / $[C_{14}H_{15}NOSNa]$ $[M + Na]^+$ 268.0767, found 268.0764.

(±)-Cyclopropyl(phenyl)(phenylimino)-λ⁶-sulfanone (239)

Following GP4, cyclopropyl(phenyl)(phenylimino)-λ⁶-sulfanone (**239**) was prepared from ethyl *N*-phenylcyclopropanesulfonimide (**173**) (0.0524 g, 0.233 mmol) dissolved in THF (4 mL) and phenylmagnesium bromide (1.16 mL, 1.16 mmol, 1M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0221 g, 37%); IR ν_{max} (cm⁻¹): 3055, 3014, 2920, 1595, 1485, 1445, 1291, 1266, 1202, 1185, 1094, 1069, 1043, 1013, 994, 885, 823, 775, 755, 721, 671, 585, 552, 527; ¹H NMR (400 MHz, CDCl₃) δ 8.05-7.83 (2H, m, H-2,3 or H-9,10), 7.62-7.53 (1H, m, H-4 or H-11), 7.54-7.45 (2H, m, H-2,3 or H-9,10), 7.14-7.07 (2H, m, H-2,3 or H-9,10), 7.06-6.99 (2H, m, H-2,3 or H-9,10), 6.85 (1H, tt, $J = 7.0, 1.5$ Hz, H-4 or H-11), 2.72 (1H, tt, $J = 8.0, 5.0$ Hz, H-5), 1.67-1.50 (1H, m, H-6 or H-7), 1.27-1.09 (2H, m, H-6 or H-7), 1.02-0.83 (1H, m, H-6 or H-7); ¹³C NMR (101 MHz, CDCl₃) δ 144.9 (C-1 or C-8), 139.7 (C-1 or C-8), 133.1 (C-4 or C-11), 129.5 (C-2 or C-3 or C-9 or C-10), 129.0 (C-2 or C-3 or C-9 or C-10), 128.9 (C-2 or C-3 or C-9 or C-10), 123.5 (C-2 or C-3 or C-9 or C-10), 121.7 (C-4 or C-11), 34.4 (C-5), 6.7 (C-6 or C-7), 5.3 (C-6 or C-7); HRMS calculated for [C₁₅H₁₆NOS] [M + H]⁺ 258.0947, found 258.0947 / [C₁₅H₁₅NOSNa] [M + Na]⁺ 280.0767, found 280.0763.

(±)-(Cyclopropylimino)(methyl)(phenyl)-λ6-sulfanone (240)

Following GP4, (cyclopropylimino)(methyl)(phenyl)-λ6-sulfanone (**240**) was prepared ethyl *N*-cyclopropylmethanesulfonimidate (**195**) (0.0166 g, 0.102 mmol) dissolved in THF (2 mL) and phenylmagnesium bromide (0.509 mL, 0.509 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ ethyl acetate) to afford the title compound as a colourless oil (0.0080 g, 40%); IR ν_{max} (cm⁻¹): 3083, 3063, 3003, 2925, 1581, 1476, 1445, 1408, 1351, 1319, 1245, 1193, 1156, 1095, 1057, 1014, 975, 954, 923, 806, 742, 689, 520; ¹H NMR (400 MHz, CDCl₃) δ 8.01-7.90 (2H, m, H-6 or H-7), 7.70-7.51 (3H, m, H-6,8 or H-7,8), 3.09 (3H, s, H-4), 2.45-2.32 (1H, m, H-1), 0.63-0.55 (1H, m, H-2 or H-3), 0.54-0.45 (1H, m, H-2 or H-3), 0.45-0.37 (2H, m, H-2 or H-3); ¹³C NMR (101 MHz, CDCl₃) δ 140.1 (C-5), 133.1 (C-8), 129.5 (C-6 or C-7), 128.7 (C-6 or C-7), 45.1 (C-4), 26.3 (C-1), 7.1 (C-2 or C-3), 6.3 (C-2 or C-3); HRMS calculated for [C₁₀H₁₄NOS] [M + H]⁺ 196.0791, found 196.0808 / [C₁₀H₁₃NOSNa] [M + Na]⁺ 218.0610, found 218.0615.

6

Chapter Six
Experimental
Synthesis of Enantioenriched
Sulfoximines

6.0 Experimental: Enantioenriched Sulfoximines

6.1 General Experimental and Procedures

Preparation of Sulfinyl Chlorides (GP1) (Methyl and Phenyl derivatives)

The corresponding disulfide (1 equiv., 23-100 mmol) and acetic acid (2 eq., 46-200 mmol) were mixed and cooled to -20 °C. Sulfuryl chloride (3.1 eq., 71-310 mmol) was added dropwise with stirring over a period of 30 min. The reaction mixture was then stirred for 3 h at -20 °C and then allowed to warm to room temperature over a period of about 2 h. Evolution of SO₂ and HCl was observed during this time. The mixture was warmed to 35 °C for 1 h. The resulting acetyl chloride was evaporated under reduced pressure, providing the desired product as a liquid which was used without further purification.

Preparation of Sulfinamides (GP5)

A mixture of Et₃N (3.0 equiv.) and amino alcohol (1.0 equiv.) in CH₂Cl₂ (0.5 M) was added dropwise over 5 min to a stirred mixture of sulfinyl chloride (2.2 equiv.) in CH₂Cl₂ (0.5 M) at 0 °C. The mixture was stirred at 0 °C for 1 h and then brought to rt for a further 3-4 h (reaction completion was monitored by TLC, 1:1 petroleum ether/ethyl acetate). The mixture was quenched with sat. aq. NaHCO₃ (5 mL) and extracted with CH₂Cl₂ (3 × 30 mL). The combined organic layers were dried (MgSO₄), filtered and concentrated under reduced pressure. The residue was dissolved in MeOH (0.1 M) and cooled to 0 °C. A 1 M solution of NaOH in MeOH (1.05 equiv. of base) was added dropwise over 5 min, and the reaction was stirred for a further 5 min (reaction completion was monitored by TLC, 1:1 petroleum ether/ethyl acetate for disappearance of the *bis*-protected substrate). After

completion, the solvent was removed under reduced pressure. Addition of sat. aq. NaHCO_3 solution (5 mL), followed by extraction of the product using CH_2Cl_2 (3 x 30 mL). The combined organic phase was dried (MgSO_4), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography.

Preparation of Cyclic Sulfonimides (GP6)

To the solution of sulfonamide in THF (0.2 M) at $-78\text{ }^\circ\text{C}$ was added oxidant (*N*-chlorosuccinimide (2.0 equiv.) or *t*BuOCl (1.1 equiv.). After stirring at this temperature for 30 min, 1,8-diazabicyclo(5.4.0)undec-7-ene (2 equiv.) was added and the mixture was stirred for another 15 min. The reaction is quenched with sat. aq. NH_4Cl , the aqueous layer is extracted with Et_2O (3 x 5 mL) and the combined organic layers were dried (MgSO_4), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography.

Preparation of Sulfoximines (GP7)

To a solution of sulfonimide in dry THF (0.3 M) at $-78\text{ }^\circ\text{C}$, 2 equiv. of the corresponding Grignard reagent were added. After 5 min, the reaction mixture was allowed to reach $0\text{ }^\circ\text{C}$ and then rt and the reaction was stirred for another 45 min at this temperature. The reaction was quenched with saturated NH_4Cl solution (2 mL) and the aqueous layer was extracted with Et_2O (3 x 5 mL) and the combined organic layers were dried (MgSO_4), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography.

Cleavage of Phenyl Ethanol Group (GP8)

Freshly ground NaOH (10 equiv.) was added to a solution of sulfoximine (1 equiv.) in MTBE (0.1 M). The round bottomed flask was equipped with two balloons containing O₂ and the mixture was warmed at 40 °C for 16 h. The reaction was monitored by TLC and after completion, H₂O (5 mL) was added and the aqueous phase was extracted with CH₂Cl₂ (3 × 10 mL). The combined organic phases were dried with MgSO₄ and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography.

Preparation of Racemic Sulfoximines (GP9)

The sulfide (1 equiv.), (diacetoxyiodo)benzene (2.5 eq.) and ammonium carbamate (2.0 equiv.) were added to a round bottom flask containing a stirrer bar. MeOH (0.5 M) was added and the reaction was stirred at 25 °C for 3 h. The solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography.

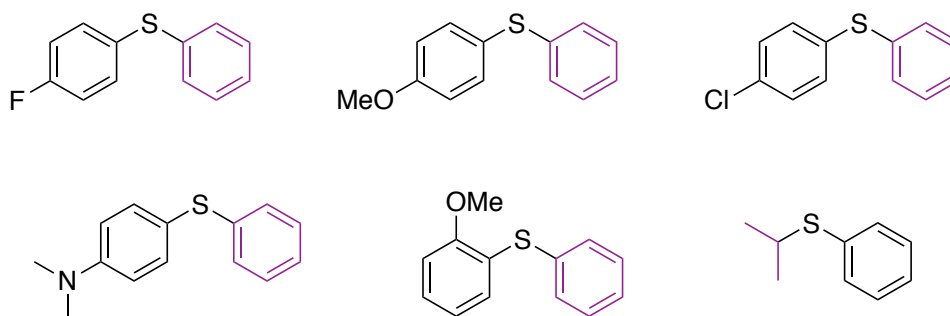
Preparation of Sulfides I (GP10)

For a solid disulfide: A schlenk tube with a magnetic stirring bar was charged with aniline (1 equiv.) and disulfide (1 equiv.). The tube was evacuated and backfilled three times with dry nitrogen. Acetonitrile was added by syringe, followed by L-ascorbic acid (0.5 equiv.) dissolved in DMSO (0.1 mL).

For liquid disulfide: A 10-mL schlenk tube with a magnetic stirring bar was charged with aniline (0.2 mmol). The tube was evacuated and backfilled with dry nitrogen (this operation was repeated three times). Acetonitrile (1 mL) was added by

syringe, followed by disulfide (0.2 mmol or 0.4 mmol) and L-ascorbic acid (0.5 equiv.) dissolved in DMSO (0.1 mL).

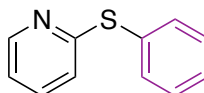
The mixture was then stirred vigorously for 1 minute before *t*-BuONO (0.3 mmol), was added *via* syringe. After the resulting mixture was stirred at 20 °C for 4 hours, the solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography.



Note: Disulfide fragment is shown above in purple. All compounds above are known in the literature.^{132,133,134,135}

Preparation of Sulfides II (GP11)

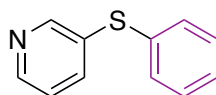
A suspension of a heteroaryl halide (1 equiv.) and thiol (1.2 equiv.) in H₂O (0.2 M) was added to a round bottom flask and stirred at 100 °C for 8 h. After completion of the reaction (as indicated by TLC), the product was extracted with EtOAc (3x), and the combined organic extracts were dried (Na₂SO₄). The solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography.



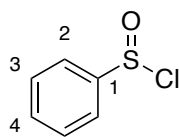
Note: Thiol fragment is shown above in purple. The compound above is known in the literature.¹³⁶

Preparation of Sulfides III (GP12)

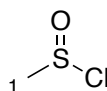
A mixture of thiol (1 equiv.), aryl halide (1.2 equiv.), CuI (5 mol%), DABCO (10 mol%), K₂CO₃ (2 equiv.) and DME (0.2 M) were added to an oven dried sealed tube equipped with a stirring bar under nitrogen. The reaction was heated for 12 h at 120 °C. After being cooled to rt, the mixture was diluted with EtOAc and washed with sat. aqueous NaCl solution (3 ×). The organic phase was dried with anhydrous Na₂SO₄, filtered and the solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography.



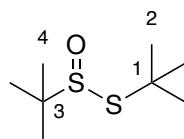
Note: Thiol fragment is shown above in purple. The compound above is known in the literature.¹³⁷

(±)-Benzenesulfinic chloride (136)⁹⁵

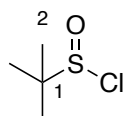
Following GP1, benzenesulfinic chloride (**136**) was prepared from diphenyl disulfide **134** (5.00 g, 23.0 mmol), sulfuryl chloride (9.58 g, 71.0 mmol) and acetic acid (2.75 g, 46.0 mmol), affording the desired compound as a pale yellow liquid (6.22 g, 85%); IR ν_{max} (cm^{-1}): 3066, 3005, 2927, 2854, 1476, 1327, 1147, 1092, 1035; ^1H NMR (400 MHz, CDCl_3) δ 7.92-7.89 (2H, m, H-2 or H-3), 7.68-7.56 (3H, m, H-3,4 or H-2,4); ^{13}C NMR (101 MHz, CDCl_3) δ 148.7 (C-1), 133.8 (C-4), 129.6 (C-2 or C-3), 123.8 (C-2 or C-3); HRMS calculated for $[\text{C}_7\text{H}_9\text{O}_2\text{S}]$ (compound was dissolved in MeOH and analysed as the corresponding methyl ester) $[\text{M} + \text{H}]^+$ 157.0318, found 157.0323.

(±)-Methanesulfinic chloride (137)⁹⁵

Following GP1, methanesulfinic chloride (**137**) was prepared from dimethyl disulfide **135** (9.42 g, 100 mmol), sulfuryl chloride (41.8 g, 310 mmol) and acetic acid (12.0 g, 200 mmol), affording the desired compound as a pale yellow liquid (19.1 g, 97%); IR ν_{max} (cm^{-1}): 2924, 2533, 1651, 1404, 1304, 1214, 1046, 953, 813, 747, 703; ^1H NMR (400 MHz, CDCl_3) δ 3.38 (3H, s, H-1); ^{13}C NMR (101 MHz, CDCl_3) δ 52.5 (C-1).

(±)-*S*-(*tert*-butyl)-2-Methylpropane-2-sulfinothioate (141**)**⁹⁷

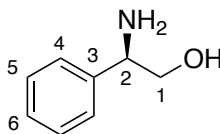
Hydrogen peroxide (10.0 mL, 97.0 mmol, 30% aqueous solution) was added slowly to a solution of di-*tert*-butyl disulfide **140** (17.0 mL, 88.0 mmol) in glacial acetic acid (88.0 mL) at 0 °C. After addition, the reaction was warmed slowly to room temperature and stirred for 16 h. The reaction was quenched by adding ice/water (100 mL), and the mixture was extracted with CH₂Cl₂ (2 × 20 mL). The organic layer was washed with saturated aq. NaHCO₃ solution (20 mL), water (20 mL), dried (MgSO₄), filtered and concentrated under reduced pressure. The product was afforded as a colourless oil (14.1 g, 83%); IR ν_{max} (cm⁻¹): 2959, 2925, 1467, 1363, 1160, 1069, 1034, 565, 511, 463; ¹H NMR (400 MHz, CDCl₃) δ 1.56 (9H, s, H-4), 1.38 (9H, s, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 59.6 (C-3), 48.8 (C-1), 32.5 (C-4), 24.4 (C-2); HRMS calculated for [C₈H₁₉OS₂] [M + H]⁺ 195.0872, found 195.0873; / [C₈H₁₈OS₂Na] [M + Na]⁺ 217.0691, found 217.0692.

(±)-2-Methylpropane-2-sulfinic chloride (142**)**⁹⁷

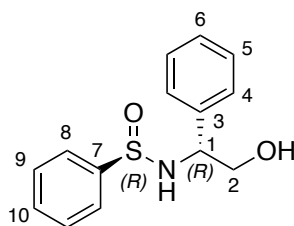
S-(*tert*-butyl) 2-Methylpropane-2-sulfinothioate (**141**) (14.1 g, 72.7 mmol) was dissolved in CH₂Cl₂ (100 mL), and the solution was cooled to 0 °C. A solution of sulfuryl chloride (9.81 g, 72.7 mmol) in CH₂Cl₂ (100 mL) was added dropwise. After the addition was complete, the reaction mixture was stirred for 1 h, during which time the temperature was allowed to rise slowly to room temperature. The volatiles were removed under reduced pressure without heating to give the title

compound as a yellow liquid and in good purity, with no further purification necessary (15.9 g, 78%); IR ν_{max} (cm⁻¹): 2965, 2924, 2853, 1456, 1365, 1310, 1214, 1181, 1160, 1110, 1059, 1017, 752, 667, 634, 565, 485; ¹H NMR (400 MHz, CDCl₃) δ 1.41 (9H, s, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 64.5 (C-1), 22.6 (C-2); HRMS calculated for [C₅H₁₃O₂S₁] (compound was dissolved in MeOH and analysed as the corresponding methyl ester) [M + H]⁺ 137.0631, found 137.0632.

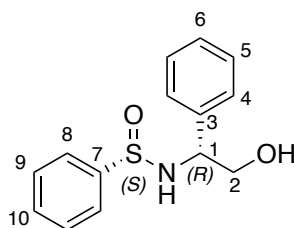
(*R*)-2-Amino-2-phenylethan-1-ol (242)¹³⁸



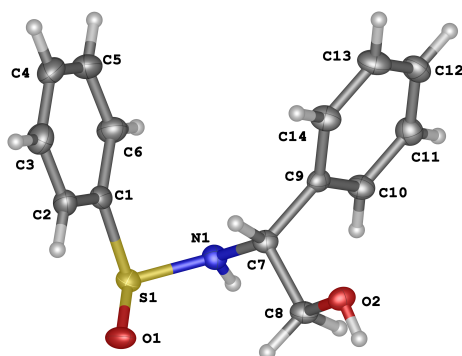
Lithium aluminium hydride (4.90 g, 129 mmol, 1.95 eq.) was suspended in dry THF (200 mL) under argon at 0 °C. Solid (*R*)-2-phenylglycine (10.0 g, 66.15 mmol) was added in small portions. The mixture was stirred at 0 °C for 1 h, then slowly heated to reflux at 80 °C for 16 h. The reaction was cooled to 0 °C and then a saturated potassium carbonate solution (75 mL) was added very slowly to the mixture. The mixture was filtered, and the solvents were removed from the filtrate under reduced pressure. The crude yellow solid was recrystallised from hot toluene to yield a white crystalline solid (7.62 g, 84%); m.p. 77-79 °C, lit. 76-78 °C;¹³⁸ IR ν_{max} (cm⁻¹): 3327, 3115, 3028, 2893, 2833, 1597, 1495, 1450, 1392, 1357, 1317, 1298, 1209, 1063, 1044, 1027, 979, 933, 866, 794, 765, 751, 703, 618, 586, 554, 491, 425; ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.26 (5H, m, Ar), 4.05 (1H, dd, *J* = 8.5, 4.5 Hz, H-2), 3.74 (1H, dd, *J* = 10.5, 4.5 Hz, H-1), 3.55 (1H, dd, *J* = 10.5, 8.5 Hz, H-1), 1.92 (2H, s, NH₂), (OH not observed); ¹³C NMR (101 MHz, CDCl₃) δ 142.9 (C-3), 128.8 (C-4 or C-5), 127.7 (C-6), 126.6 (C-4 or C-5), 68.2 (C-1), 57.5 (C-2); HRMS calculated for [C₈H₁₂NO] [M + H]⁺ 138.0913, found 138.0923 / [C₈H₁₁NONa] [M + Na]⁺ 160.0733, found 160.0732.

(*R*)-*N*-((*R*)-2-Hydroxy-1-phenylethyl)benzenesulfinamide (243**)**

Following GP5, (*R*)-*N*-((*R*)-2-hydroxy-1-phenylethyl)benzenesulfinamide (**243**) was prepared from (*R*)-phenylglycinol **242** (5.5 g, 40.1 mmol), phenyl sulfinyl chloride **136** (14.2 g, 88.2 mmol) and Et₃N (12.2 g, 120.3 mmol). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a colourless oil (combined yield for both diastereomers, 9.42 g, 90%); $[\alpha]_{\text{D}}^{28}$ -136.41 (c 0.660 CHCl₃); IR ν_{max} (cm⁻¹): 3272, 3060, 3029, 2919, 2871, 1652, 1603, 1582, 1493, 1475, 1453, 1342, 1085, 1044, 998, 923, 749, 698, 561, 504, 449; ¹H NMR (400 MHz, CDCl₃) δ 7.70-7.65 (2H, m, H-8 or H-9), 7.47 (3H, dd, J = 5.5, 2.0 Hz, H-8, 10 or H-9,10), 7.43-7.36 (4H, m, H-4,5), 7.35-7.30 (1H, m, H-6), 5.05 (1H, d, J = 5.5 Hz, NH), 4.68 (1H, ddd, J = 9.0, 5.5, 4.0 Hz, H-1), 3.90 (1H, dt, J = 11.5, 4.0 Hz, H-2), 3.80 (1H, s, OH), 3.72-3.63 (1H, m, H-2); ¹³C NMR (101 MHz, CDCl₃) δ 144.8 (C-7), 138.8 (C-3), 131.3 (C-10), 129.1 (Ar), 128.9 (Ar), 128.3 (C-6), 127.6 (Ar), 125.7 (Ar), 67.3 (C-2), 61.7 (C-1); HRMS calculated for [C₁₄H₁₆NO₂S] [M + H]⁺ 262.0896, found 262.0904 / [C₁₄H₁₅NO₂SNa] [M + Na]⁺ 284.0716, found 284.0723.

(*S*)-*N*-((*R*)-2-Hydroxy-1-phenylethyl)benzenesulfinamide (244**)**

Following GP5, (*S*)-*N*-((*R*)-2-hydroxy-1-phenylethyl)benzenesulfinamide (**244**) was prepared from (*R*)-phenylglycinol **242** (5.5 g, 40.1 mmol), phenyl sulfinyl chloride **136** (14.2 g, 88.2 mmol) and Et₃N (12.2 g, 120.3 mmol). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a colourless oil (combined yield for both diastereomers, 9.42 g, 90%); [α]_D²⁸ -215.02 (c 0.620 CHCl₃); IR ν_{max} (cm⁻¹): 3277, 3180, 3058, 3029, 2912, 2886, 1600, 1584, 1494, 1475, 1444, 1334, 1306, 1236, 1195, 1186, 1154, 1083, 1071, 1039, 1021, 996, 989, 924, 914, 875, 750, 694; ¹H NMR (400 MHz, CDCl₃) δ 7.70-7.66 (2H, m, H-8 or H-9), 7.52-7.46 (3H, m, H-8, 10 or H-9, 10), 7.31-7.26 (3H, m, H-4, 6 or H-5, 6), 7.10-7.04 (2H, m, H-4 or H-5), 5.04 (1H, d, *J* = 8.5 Hz, NH), 4.18 (1H, td, *J* = 8.5, 3.5 Hz, H-1), 3.82-3.68 (2H, m, H-2), 1.73 (1H, s, OH); ¹³C NMR (101 MHz, CDCl₃) δ 141.8 (C-7), 138.9 (C-3), 131.4 (C-10), 129.1 (Ar), 128.9 (Ar), 128.0 (C-6), 126.68 (Ar), 126.65 (Ar), 66.4 (C-2), 59.8 (C-1); HRMS calculated for [C₁₄H₁₆NO₂S] [M + H]⁺ 262.0896, found 262.0902 / [C₁₄H₁₅NO₂SNa] [M + Na]⁺



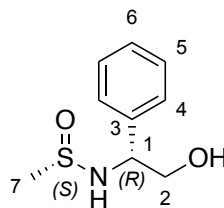
284.0716, found 284.0723.

X-ray crystal structure of (*S*)-*N*-((*R*)-2-hydroxy-1-phenylethyl)benzenesulfinamide C₁₄H₁₅NO₂S Mw = 261.33; T = 120(2) K; λ = 1.54184 Å; orthorhombic; P2₁/n space

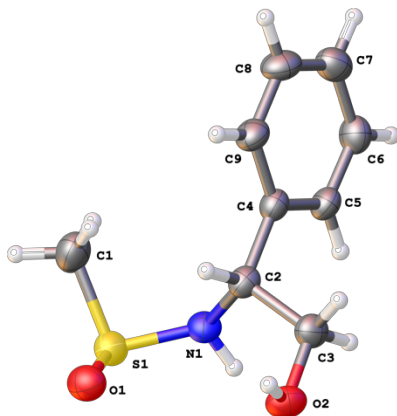
group; a = 5.1446(4) Å, b = 13.9660(12) Å, c = 18.3542(16) Å; α = 90°, β = 90°, γ

$= 90^\circ$; $V = 1318.8(16) \text{ \AA}^3$; $Z = 4$; $D = 1.316 \text{ g/cm}^3$; $R_1 = 0.0421$, $wR_2 = 0.0936$ (all data), $\text{GoF} = 1.070$.

(*S*)-*N*-((*R*)-2-Hydroxy-1-phenylethyl)methanesulfinamide (245**)**



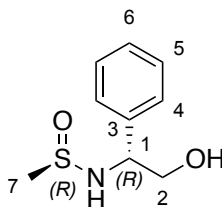
Following GP5, (*S*)-*N*-((*R*)-2-hydroxy-1-phenylethyl)methanesulfinamide **245** was prepared from (*R*)-phenylglycinol **242** (3.23 g, 23.6 mmol), sulfinyl chloride **137** (5.11 g, 51.9 mmol) and Et_3N (7.16 g, 70.7 mmol). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a colourless oil (combined yield for both diastereoisomers, 3.77 g, 80%); $[\alpha]_{\text{D}}^{20} -84.11$ (c 2.13 CHCl_3); IR ν_{max} (cm^{-1}): 3247, 3202, 2919, 2868, 2353, 1651, 1494, 1453, 1041, 1024, 785, 700; ^1H NMR (400 MHz, CDCl_3) δ 7.38–7.27 (5H, m, Ar), 5.04 (1H, d, $J = 5.5$ Hz, NH), 4.76 (1H, ddd, $J = 8.5, 5.5, 4.0$ Hz, H-1), 3.86 (1H, dd, $J = 12.0, 4.0$ Hz, H-2), 3.66 (1H, dd, $J = 12.0, 8.5$ Hz, H-2), 2.51 (3H, s, H-7), (OH not observed); ^{13}C NMR (101 MHz, CDCl_3) δ 139.8 (C-3), 129.0 (C-4 or C-5), 128.2 (C-6), 127.1 (C-4 or C-5), 66.8 (C-2), 56.5 (C-1), 40.7 (C-7); HRMS calculated for $[\text{C}_9\text{H}_{14}\text{NO}_2\text{S}] [\text{M} + \text{H}]^+$ 200.0740, found 200.0736 / $[\text{C}_9\text{H}_{13}\text{NO}_2\text{SNa}] [\text{M} + \text{Na}]^+$ 222.0559, found 222.0563.



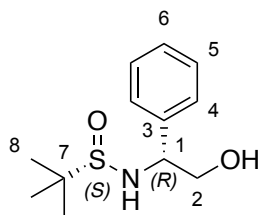
X-ray crystal structure of (*S*)-*N*-((*R*)-2-hydroxy-1-phenylethyl)methanesulfinamide $\text{C}_9\text{H}_{13}\text{NO}_2\text{S}$ $M_w = 199.26$; $T = 120(2) \text{ K}$; $\lambda = 1.54184 \text{ \AA}$; monoclinic; $P2_1/n$ space group; $a = 11.6171(5) \text{ \AA}$, $b = 7.3962(3) \text{ \AA}$, $c = 11.7096(6) \text{ \AA}$; $\alpha = 90^\circ$, $\beta =$

94.740°, $\gamma = 90^\circ$; $V = 1002.67(8) \text{ \AA}^3$; $Z = 4$; $D = 1.320 \text{ g/cm}^3$; $R_1 = 0.0528$, $wR_2 = 0.1363$ (all data), $\text{GoF} = 1.092$.

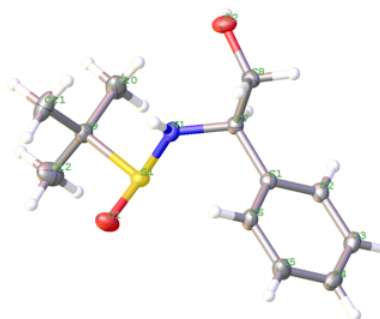
(*R*)-*N*-((*R*)-2-Hydroxy-1-phenylethyl)methanesulfinamide (246**)**



Following GP5, (*R*)-*N*-((*R*)-2-hydroxy-1-phenylethyl)methanesulfinamide (**246**) was prepared from (*R*)-phenylglycinol **242** (3.23 g, 23.6 mmol), methanesulfinyl chloride **137** (5.11 g, 51.9 mmol) and Et_3N (7.16 g, 70.7 mmol). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a colourless oil (combined yield for both diastereoisomers, 3.77 g, 80%); $[\alpha]_{\text{D}}^{25} -49.38$ (c 0.955 CHCl_3); IR ν_{max} (cm^{-1}): 3230, 2920, 2899, 2871, 2088, 1651, 1602, 1493, 1453, 1023, 960, 757, 699; ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.31 (5H, m, Ar), 5.24 (1H, t, $J = 4.5$ Hz, NH), 4.54 (1H, ddd, $J = 8.5, 4.5, 3.5$ Hz, H-1), 3.87 (1H, dd, $J = 12.0, 3.5$ Hz, H-2), 3.69-3.60 (1H, m, H-2), 2.73 (3H, s, H-7), (OH not observed); ^{13}C NMR (101 MHz, CDCl_3) δ 138.7 (C-3), 128.8 (C-4 or C-5), 128.2 (C-6), 127.4 (C-4 or C-5), 67.3 (C-2), 61.8 (C-1), 42.7 (C-7); HRMS calculated for $[\text{C}_9\text{H}_{14}\text{NO}_2\text{S}]$ $[\text{M} + \text{H}]^+$ 200.0740, found 200.0749 / $[\text{C}_9\text{H}_{13}\text{NO}_2\text{SNa}]$ $[\text{M} + \text{Na}]^+$ 222.0559, found 222.0571.

(*S*)-*N*-((*R*)-2-hydroxy-1-phenylethyl)-2-methylpropane-2-sulfinamide (247**)**

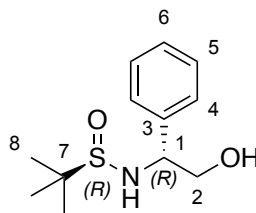
Following GP5, (*S*)-*N*-((*R*)-2-hydroxy-1-phenylethyl)-2-methylpropane-2-sulfinamide **247** was prepared from (*R*)-phenylglycinol **242** (3.21 g, 23.4 mmol), *tert*-butylsulfinyl chloride **142** (7.25 g, 51.5 mmol) and Et₃N (7.11 g, 70.3 mmol). The crude mixture was purified by flash chromatography (1:1 pentane/diethyl ether to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a colourless oil (combined yield for both diastereomers 5.09 g, 90%); IR ν_{max} (cm⁻¹): 3274, 2952, 2924, 2867, 2106, 1659, 1602, 1493, 1453, 1363, 1180, 1027, 931, 757, 699, 679, 636, 598, 531; [α]_D²¹ 85.25 (c 0.290 CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.41-7.30 (5H, m, Ar), 4.56 (1H, dt, *J* = 7.0, 5.5 Hz, H-1), 4.02 (1H, d, *J* = 5.5 Hz, NH), 3.93 (2H, t, *J* = 6.0 Hz, H-2), 2.79 (1H, s, OH), 1.25 (9H, s, H-8); ¹³C NMR (101 MHz, CDCl₃) δ 139.3 (C-3), 128.9 (C-4 or C-5), 128.2 (C-6), 127.5 (C-4 or C-5), 66.3 (C-2), 60.2 (C-1), 56.5 (C-7), 22.8 (C-8); HRMS calculated for [C₁₂H₂₀NO₂S] [M + H]⁺ 242.1209, found 242.1212 / [C₁₂H₁₉NO₂SNa] [M + Na]⁺ 264.1029, found 264.1033.



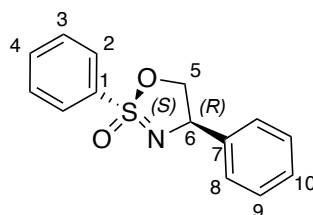
X-ray crystal structure of (*S*)-*N*-((*R*)-2-hydroxy-1-phenylethyl)-2-methylpropane-2-sulfinamide

C₁₂H₁₉NO₂S Mw = 241.34; T = 120(2) K; λ = 1.54184 Å; orthorhombic; P2₁2₁2₁ space group; a = 6.22440(10) Å, b = 11.1272(2) Å, c =

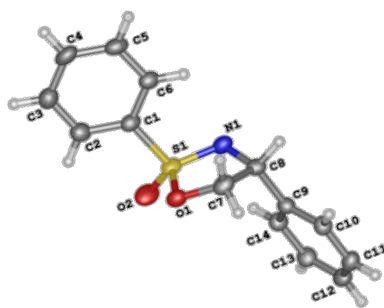
19.2804(4) Å; α = 90°, β = 90°, γ = 90°; V = 1335.36(4) Å³; Z = 4; D = 1.201 g/cm³; R₁ = 0.0252, wR₂ = 0.0630 (all data), GoF = 1.035.

(*R*)-*N*-((*R*)-2-Hydroxy-1-phenylethyl)-2-methylpropane-2-sulfinamide**(248)**¹³⁹

Following GP5, (*R*)-*N*-((*R*)-2-hydroxy-1-phenylethyl)-2-methylpropane-2-sulfinamide **248** was prepared from (*R*)-phenylglycinol **242** (3.21 g, 23.4 mmol), *tert*-butylsulfinyl chloride **142** (7.25 g, 51.5 mmol) and Et₃N (7.11 g, 70.3 mmol). The crude mixture was purified by flash chromatography (1:1 pentane/diethyl ether to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a colourless oil (combined yield for both diastereomers 5.09 g, 90%); [α]_D¹⁹ 22.18 (c 0.755 CHCl₃); IR ν_{max} (cm⁻¹): 3241, 2954, 2925, 2867, 1453, 1390, 1363, 1181, 1027, 931, 757, 699, 637, 596, 532; ¹H NMR (400 MHz, CDCl₃) δ 7.39-7.29 (5H, m, Ar), 4.51 (1H, dt, J = 7.0, 5.5 Hz, H-1), 4.26 (1H, d, J = 5.5 Hz, NH), 3.93-3.81 (2H, m, H-2), 3.40 (1H, s, OH), 1.22 (9H, s, H-8); ¹³C NMR (101 MHz, CDCl₃) δ 139.4 (C-3), 128.8 (C-4 or C-5), 128.0 (C-5), 127.5 (C-4 or C-5), 66.3 (C-2), 60.2 (C-1), 56.5 (C-7), 22.8 (C-8); HRMS calculated for [C₁₂H₂₀NO₂S] [M + H]⁺ 242.1209, found 242.1216 / [C₁₂H₁₉NO₂SNa] [M + Na]⁺ 264.1029, found 264.1034.

(2*S*,4*R*)-2,4-Diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (254)

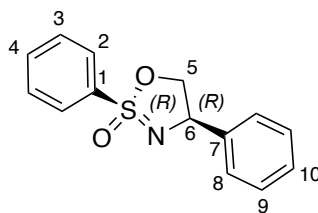
Following GP6, (2*S*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide **254** was prepared from sulfinamide **243/244** (3.01 g, 11.5 mmol), *t*BuOCl (1.37 g, 12.7 mmol) and DBU (3.50 g, 23.0 mmol). The crude mixture was purified by flash chromatography (9:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (combined yield for both diastereoisomers, 2.25 g, 76%); $[\alpha]_D^{29}$ 106.00 (c 0.490 CHCl₃); IR $\nu_{\max}$ (cm⁻¹): 3062, 2912, 1602, 1582, 1492, 1474, 1446, 1329, 1272, 1215, 1130, 1094, 1072, 1031, 978, 937, 901, 834, 810, 741, 719, 699, 685, 638, 616, 590, 535, 490; ¹H NMR (400 MHz, CDCl₃) δ 8.00-7.94 (2H, m, H-2 or H-3), 7.64 (1H, ddt, *J* = 8.5, 7.0, 1.5 Hz, H-4), 7.59-7.51 (4H, m, H-2 or H-3 and H-8 or H-9), 7.43-7.37 (2H, m, H-8 or H-9), 7.36-7.30 (1H, m, H-10), 5.29 (1H, dd, *J* = 7.5, 7.0 Hz, H-6), 4.66 (1H, dd, *J* = 7.5, 7.0 Hz, H-5), 4.18 (1H, dd, *J* = 7.5, 7.5 Hz, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 140.0 (C-7), 139.4 (C-1), 133.6 (C-4), 129.4 (C-2 or C-3), 128.8 (C-2 or C-3), 128.2 (C-10), 127.8 (C-8 or C-9), 126.5 (C-8 or C-9), 76.5 (C-5), 69.5 (C-6); HRMS calculated for [C₁₄H₁₄NO₂S] [M + H]⁺ 260.0740, found 260.0763 / [C₁₄H₁₃NO₂SNa] [M + Na]⁺ 282.0559, found



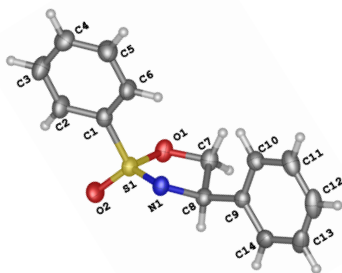
282.0570. X-ray crystal structure of (2*S*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide

C₁₄H₁₃NO₂S Mw = 259.31; T = 120(2) K; λ = 1.54184 Å; monoclinic; P2₁/n space group; a = 5.8528(3) Å, b = 7.5096(4) Å, c = 14.0649(6) Å; α = 90°, β = 91.222(4)°, γ = 90°; V = 618.05(5)

Å³; Z = 2; D = 1.393 g/cm³; R₁ = 0.0362, wR₂ = 0.0895 (all data), GoF = 1.060.

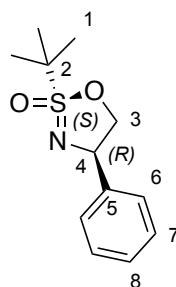
(2*R*,4*R*)-2,4-Diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (255)

Following GP6, (2*R*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide **255** was prepared from sulfinamide **243/244** (3.01 g, 11.5 mmol), *t*BuOCl (1.37 g, 12.7 mmol) and DBU (3.50 g, 23.0 mmol). The crude mixture was purified by flash chromatography (9:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (combined yield for both diastereoisomers, 2.25 g, 76%); $[\alpha]_D^{28}$ 93.0 (c 0.35 CHCl₃); IR $\nu_{\max}$ (cm⁻¹): 3061, 2884, 1493, 1447, 1291, 1261, 1118, 1070, 1024, 980, 949, 906, 836, 742, 723, 699, 684, 634, 618, 591, 530, 519, 487; ¹H NMR (400 MHz, CDCl₃) δ 8.08-8.01 (2H, m, H-2 or H-3), 7.70-7.63 (1H, m, H-4), 7.59-7.52 (2H, m, H-2 or H-3), 7.51-7.46 (2H, m, H-8 or H-9), 7.41 (2H, ddd, *J* = 7.5, 7.0, 1.5 Hz, H-8 or H-9), 7.37-7.31 (1H, m, H-10), 5.51 (1H, dd, *J* = 9.0, 6.5 Hz, H-6), 4.98 (1H, dd, *J* = 8.0, 6.5 Hz, H-5), 3.99 (1H, dd, *J* = 9.0, 8.0 Hz, H-5); ¹³C NMR (101 MHz, CDCl₃) δ 140.2 (C-7), 138.0 (C-1), 134.2 (C-4), 129.4 (C-2 or C-3), 129.3 (C-2 or C-3), 129.0 (C-8 or C-9), 128.2 (C-10), 126.3 (C-8 or C-9), 78.1 (C-5), 67.2 (C-6); HRMS calculated for [C₁₄H₁₄NO₂S] [M + H]⁺ 260.0740, found 260.0758 / [C₁₄H₁₃NO₂SNa] [M + Na]⁺ 282.0559, found 282.0565.

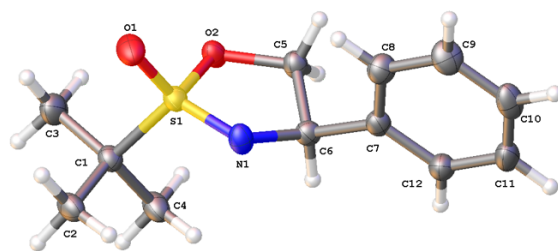


X-ray crystal structure of (2*R*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide C₁₄H₁₃NO₂S
 Mw = 259.31; T = 120(2) K; λ = 1.54184 Å;
 trigonal; P2₁/n space group; a = 13.3192(4) Å, b = 13.3192(4) Å, c = 6.0701(3) Å; α = 90°, β = 90°, γ = 120°; V = 932.57(8) Å³; Z = 3; D = 1.385 g/cm³;

R₁ = 0.0401, wR₂ = 0.1016 (all data), GoF = 1.072.

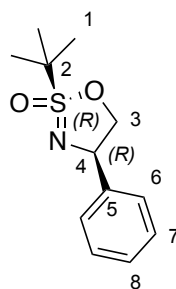
(2*S*,4*R*)-2-(*tert*-Butyl)-4-phenyl-4,5-dihydro-1,2λ⁶,3-oxathiazole 2-oxide (256)

Following GP6, (2*S*,4*R*)-2-(*tert*-Butyl)-4-phenyl-4,5-dihydro-1,2λ⁶,3-oxathiazole 2-oxide (**256**) was prepared from sulfinamide **247/248** (2.51 g, 10.4 mmol), *t*BuOCl (1.24 g, 11.4 mmol) and DBU (3.16 g, 20.8 mmol). The crude mixture was purified by flash chromatography (8:2 pentane/diethyl ether) to afford the title compound as a colourless oil (combined yield for both diastereoisomers, 1.85 g, 75%); $[\alpha]_D^{20}$ -61.31 (c 0.244 CHCl₃); IR $\nu_{\max}$ (cm⁻¹): 3063, 3029, 2971, 2923, 1731, 1478, 1304, 1265, 1126, 1031, 757, 700; ¹H NMR (400 MHz, CDCl₃) δ 7.50-7.44 (2H, m, H-6 or H-7), 7.40-7.30 (3H, m, H-6, 8 or H-7, 8), 5.06 (1H, dd, *J* = 7.5, 7.5 Hz, H-4), 4.58 (1H, dd, *J* = 7.5, 7.5 Hz, H-3), 4.04 (1H, dd, *J* = 9.5, 7.5 Hz H-3), 1.57 (9H, s, H-1); ¹³C NMR (101 MHz, CDCl₃) δ 140.2 (C-5), 128.8 (C-6 or C-7), 128.2 (C-8), 126.6 (C-6 or C-7), 76.5 (C-3), 70.2 (C-4), 63.7 (C-2), 25.0 (C-1); HRMS calculated for [C₁₂H₁₈NO₂S] [M + H]⁺ 240.1053, found 240.1053 / [C₁₂H₁₇NO₂SNa] [M + Na]⁺ 262.0872, found 262.0870.

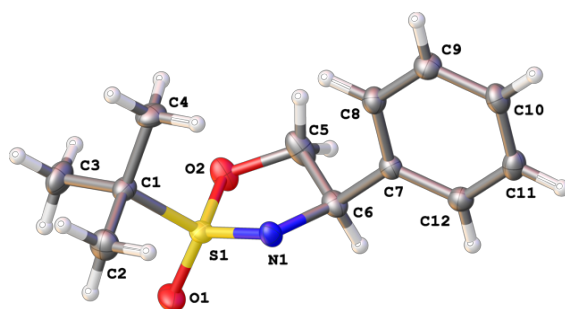


X-ray crystal structure of
(2*S*,4*R*)-2-(*tert*-Butyl)-4-phenyl-
4,5-dihydro-1,2λ⁶,3-oxathiazole
2-oxide C₁₂H₁₇NO₂S Mw =

239.32; T = 120(2) K; λ = 1.54184 Å; monoclinic; P2₁/n space group; a = 6.02621(19) Å, b = 23.1524(8) Å, c = 8.7719(3) Å; α = 90°, β = 94.755(3)°, γ = 90°; V = 1219.65(7) Å³; Z = 4; D = 1.303 g/cm³; R₁ = 0.0331, wR₂ = 0.0845 (all data), GoF = 1.064.

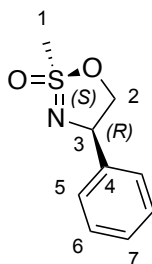
(2*R*,4*R*)-2-(*tert*-butyl)-4-phenyl-4,5-dihydro-1,2λ⁶,3-oxathiazole 2-oxide (257)

Following GP6, (2*R*,4*R*)-2-(*tert*-butyl)-4-phenyl-4,5-dihydro-1,2λ⁶,3-oxathiazole 2-oxide (**257**) was prepared from sulfinamide **247/248** (2.51 g, 10.4 mmol), *t*BuOCl (1.24 g, 11.4 mmol) and DBU (3.16 g, 20.8 mmol). The crude mixture was purified by flash chromatography (8:2 pentane/diethyl ether) to afford the title compound as a colourless oil (combined yield for both diastereoisomers, 1.85 g, 75%); $[\alpha]_D^{19}$ -32.60 (c 1.198 CHCl₃); IR $\nu_{\max}$ (cm⁻¹): 2981, 2936, 2868, 1477, 1455, 1365, 1256, 1057, 1032, 747, 700, 670; ¹H NMR (400 MHz, CDCl₃) δ 7.44-7.29 (5H, m, Ar), 5.43-5.35 (1H, m, H-4), 4.93 (1H, dd, *J* = 7.0, 7.0 Hz, H-3), 3.77 (1H, dd, *J* = 9.0, 7.0 Hz, H-3), 1.59 (9H, s, H-1); ¹³C NMR (101 MHz, CDCl₃) δ 140.3 (C-5), 128.8 (C-6 or C-7), 128.1 (C-8), 126.3 (C-6 or C-7), 79.6 (C-3), 66.8 (C-4), 62.3 (C-2), 25.5 (C-1); HRMS calculated for [C₁₂H₁₈NO₂S] [M + H]⁺ 240.1053, found 240.1051 / [C₁₂H₁₇NO₂SNa] [M + Na]⁺ 262.0872, found 262.0870.

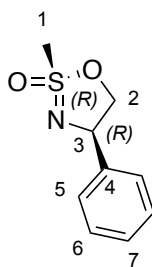


X-ray crystal structure of (2*R*,4*R*)-
(*tert*-butyl)-4-phenyl-4,5-dihydro-
1,2λ⁶,3-oxathiazole 2-oxide
C₁₂H₁₇NO₂S Mw = 239.32; T =
120(2) K; λ = 1.54184 Å;

monoclinic; P2₁/n space group; a = 11.0954(7) Å, b = 5.8622(4) Å, c = 18.8002(13) Å; α = 90°, β = 98.417°, γ = 90°; V = 1209.66(14) Å³; Z = 4; D = 1.314 g/cm³; R₁ = 0.0520, wR₂ = 0.1387 (all data), GoF = 1.060.

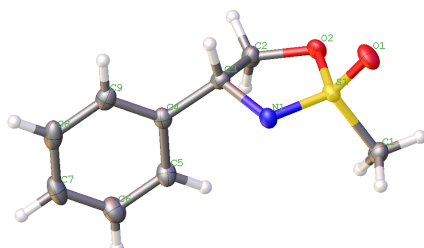
(2*S*,4*R*)-2-Methyl-4-phenyl-4,5-dihydro-1,2λ⁶,3-oxathiazole 2-oxide (258)

Following GP6, (2*S*,4*R*)-2-methyl-4-phenyl-4,5-dihydro-1,2λ⁶,3-oxathiazole 2-oxide (**258**) was prepared from sulfinamide **245/246** (2.78 g, 13.9 mmol), *t*BuOCl (1.67 g, 15.3 mmol) and DBU (4.25 g, 27.9 mmol). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (combined yield for both diastereoisomers, 2.06 g, 75%); $[\alpha]_{\text{D}}^{25}$ -62.74 (c 0.755 CHCl₃); IR ν_{max} (cm⁻¹): 3289, 3063, 2927, 1706, 1454, 1319, 1277, 1147, 1074, 977, 927, 785, 700, 517; ¹H NMR (400 MHz, CDCl₃) δ 7.48-7.44 (2H, m, H-5 or H-6), 7.39-7.29 (3H, m, H-5, 7 or H-6, 7), 4.99 (1H, dd, *J* = 9.0, 6.5 Hz, H-3), 4.59 (1H, dd, *J* = 7.5, 6.5 Hz, H-2), 3.96 (1H, dd, *J* = 9.0, 7.5 Hz, H-2), 3.22 (3H, s, H-1); ¹³C NMR (101 MHz, CDCl₃) δ 138.8 (C-4), 128.9 (C-5 or C-6), 128.4 (C-7), 126.6 (C-5 or C-6), 76.0 (C-2), 68.1 (C-3), 40.6 (C-1); HRMS calculated for [C₉H₁₂NO₂S] [M + H]⁺ 198.0583, found 198.0586 / [C₉H₁₁NO₂SNa] [M + Na]⁺ 220.0403, found 220.0399.

(2*R*,4*R*)-2-Methyl-4-phenyl-4,5-dihydro-1,2λ⁶,3-oxathiazole 2-oxide (259)

Following GP6, (2*R*,4*R*)-2-methyl-4-phenyl-4,5-dihydro-1,2λ⁶,3-oxathiazole 2-oxide (**259**) was prepared from sulfinamide **245/246** (2.78 g, 13.9 mmol), *t*BuOCl (1.67 g, 15.3 mmol) and DBU (4.25 g, 27.9 mmol). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (combined yield for both diastereoisomers, 2.06 g, 75%); $[\alpha]_D^{20}$ 17.66 (c 3.255 CHCl₃); IR $\nu_{\max}$ (cm⁻¹): 3285, 3028, 2935, 1454, 1322, 1147, 963, 772, 701, 587, 515; ¹H NMR (400 MHz, CDCl₃) δ 7.41-7.29 (5H, m, Ar), 5.34 (1H, dd, *J* = 6.0, 6.0 Hz, H-3), 4.85 (1H, dd, *J* = 7.0, 6.0 Hz, H-2), 4.27 (1H, dd, *J* = 7.0, 6.0 Hz, H-2), 3.25 (3H, s, H-1); ¹³C NMR (101 MHz, CDCl₃) δ 140.8 (C-4), 128.9 (C-5 or C-6), 128.1 (C-7), 126.0 (C-5 or C-6), 77.5 (C-2), 67.4 (C-3), 42.4 (C-1); HRMS calculated for [C₉H₁₂NO₂S] [M + H]⁺ 198.0583, found

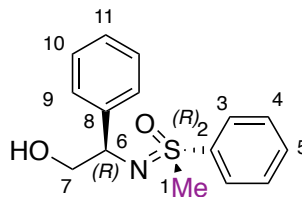
198.0595.



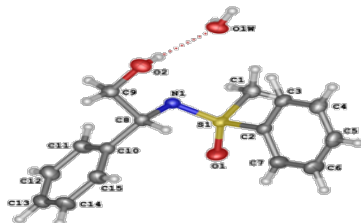
X-ray crystal structure of ((2*R*,4*R*)-2-methyl-4-phenyl-4,5-dihydro-1,2λ⁶,3-oxathiazole 2-oxide C₉H₁₂NO₂S Mw = 198.26; T = 120(2)

K; λ = 1.54184 Å; monoclinic; I2 space group; a = 9.4562(3) Å, b = 5.3529(2) Å, c = 19.3334(6) Å; α = 90°, β = 100.579(3)°, γ = 90°; V = 961.99(6) Å³; Z = 4; D = 1.369 g/cm³; R₁ = 0.0456, wR₂ = 0.1172 (all data), GoF = 1.055.

(*R*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ^6 -sulfanone (265)



Following GP7, (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ^6 -sulfanone (**265**) was prepared from (2*R*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**255**) (0.146 g, 0.563 mmol) dissolved in THF (5 mL) and methylmagnesium bromide (0.376 mL, 1.13 mmol, 3M). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.147 g, 95%); IR ν_{max} (cm⁻¹): 3411, 3059, 3024, 2925, 2865, 1600, 1581, 1445, 1404, 1349, 1309, 1230, 1132, 1086, 1067, 1032, 1012, 997, 854, 785, 745, 700, 690, 636, 562, 525; ¹H NMR (400 MHz, CDCl₃) δ 8.05-8.01 (2H, m, H-3 or H-4), 7.70-7.64 (1H, m, H-5), 7.63-7.58 (2H, m, H-3 or H-4), 7.48-7.43 (2H, m, H-9 or H-10), 7.39-7.32 (2H, m, H-9 or H-10), 7.31-7.25 (1H, m, H-11), 4.41 (1H, dd, J = 8.0, 4.5 Hz, H-6), 3.70 (1H, ddd, J = 10.5, 8.5, 4.5 Hz, H-7), 3.65-3.57 (1H, m, H-7), 3.05 (3H, s, H-1), 2.72 (1H, dd, J = 10.5, 4.5 Hz, OH); ¹³C NMR (101 MHz, CDCl₃) δ 142.4 (C-8), 139.8 (C-2), 133.3 (C-5), 129.5 (C-3 or C-4), 128.5 (C-3 or C-4 or C-9 or C-10), 128.4 (C-3 or C-4 or C-9 or C-10), 127.4 (C-11), 127.1 (C-9 or C-10), 69.1 (C-7), 60.9 (C-6), 44.5 (C-1); HRMS calculated for [C₁₅H₁₈NO₂S] [M + H]⁺ 276.1053, found 276.1068 / [C₁₅H₁₇NO₂SNa] [M + Na]⁺ 298.0872, found 298.0872.



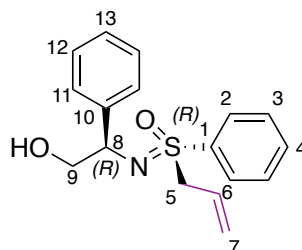
X-ray crystal structure of (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ^6 -sulfanone

C₁₅H₁₇NO₂S · H₂O Mw = 293.37; T = 120(2) K; λ =

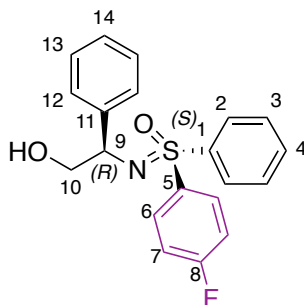
1.54184 Å; trigonal; P3₁/n space group; a = 14.5653(6) Å, b = 14.5653(6) Å, c =

6.3425(3) Å; $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 120^\circ$; $V = 1165.28(11)$ Å³; $Z = 3$; $D = 1.254$ g/cm³; $R_1 = 0.0320$, $wR_2 = 0.0767$ (all data), $GoF = 1.058$.

(*R*)-Allyl(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)-λ⁶-sulfanone (266)

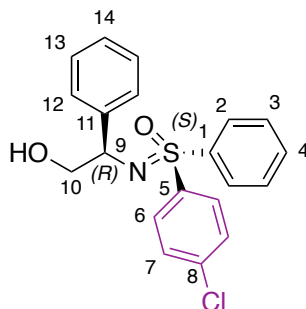


Following GP7, (*R*)-allyl(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)-λ⁶-sulfanone (**266**) was prepared from (2*R*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**255**) (0.135 g, 0.519 mmol) dissolved in THF (5 mL) and allylmagnesium bromide (1.04 mL, 1.04 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0261 g, 17%); IR $\nu_{\max}$ (cm⁻¹): 3438, 3060, 3026, 2920, 2863, 1445, 1421, 1392, 1349, 1240, 1130, 1067, 1032, 997, 932, 872, 854, 816, 791, 750, 689, 636, 608, 523; ¹H NMR (400 MHz, CDCl₃) δ 8.04-7.95 (2H, m, H-2 or H-3), 7.70-7.64 (1H, m, H-4), 7.63-7.56 (2H, m, H-2 or H-3), 7.49-7.43 (2H, m, H-11 or H-12), 7.40-7.33 (2H, m, H-11 or H-12), 7.30 (1H, t, $J = 1.5$ Hz, H-13), 5.62 (1H, ddt, $J = 17.0, 10.0, 7.5$ Hz, H-6), 5.19 (1H, dd, $J = 10.0, 1.0$ Hz, H-7), 4.95 (1H, dd, $J = 17.0, 1.5$ Hz, H-7), 4.51 (1H, dd, $J = 8.5, 4.5$ Hz, H-8), 4.02-3.83 (2H, m, H-5), 3.75-3.61 (2H, m, H-9), (OH not observed); ¹³C NMR (101 MHz, CDCl₃) δ 142.3 (C-10), 136.8 (C-1), 133.5 (C-4), 129.5 (C-2 or C-3), 129.2 (C-2 or C-3), 128.5 (C-11 or C-12), 127.5 (C-13), 127.1 (C-11 or C-12), 125.6 (C-6), 124.3 (C-7), 69.1 (C-9), 60.8 (C-8), 60.4 (C-5); HRMS calculated for [C₁₇H₂₀NO₂S] [M + H]⁺ 302.1209, found 302.1216 / [C₁₇H₁₉NO₂SNa] [M + Na]⁺ 324.1029, found 324.1034.

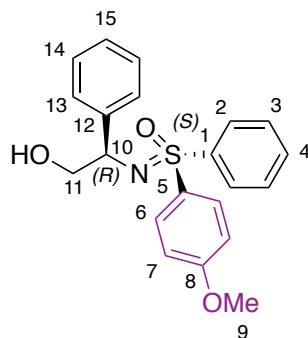
(*S*)-(4-Fluorophenyl)(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (268)

Following GP7, (*S*)-(4-fluorophenyl)(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (**268**) was prepared from (2*R*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**255**) (0.114 g, 0.439 mmol) dissolved in THF (5 mL) and 4-fluorophenylmagnesium bromide (0.878 mL, 0.878 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.137 g, 88%); IR ν_{max} (cm⁻¹): 3478, 3063, 2918, 2868, 1586, 1489, 1446, 1400, 1349, 1234, 1135, 1093, 1062, 1025, 997, 909, 836, 818, 753, 730, 700, 686, 644, 578, 556, 541; ¹H NMR (400 MHz, CDCl₃) δ 8.11 (2H, d, *J* = 7.5 Hz, H-2), 7.81-7.73 (2H, m, H-6), 7.59-7.49 (3H, m, H-3,4), 7.44 (2H, d, *J* = 7.5 Hz, H-12), 7.36 (2H, t, *J* = 7.5 Hz, H-13), 7.30 (1H, dd, *J* = 7.5, 5.5 Hz, H-14), 7.09-7.01 (2H, m, H-7), 4.35-4.29 (1H, m, H-9), 3.70 (2H, d, *J* = 6.5 Hz, H-10), 3.02 (1H, s, OH); ¹³C NMR (101 MHz, CDCl₃) δ 165.3 (d, *J* = 255 Hz, C-8), 142.0 (C-11), 140.7 (C-1), 135.7 (d, *J* = 3.0 Hz, C-5), 133.0 (C-4), 131.8 (d, *J* = 9.5 Hz, C-6), 129.4 (C-3), 128.5 (C-2 or C-13), 128.4 (C-2 or C-13), 127.4 (C-14), 127.1 (C-12), 116.6 (d, *J* = 22.5 Hz, C-7), 69.2 (C-10), 61.9 (C-9); ¹⁹F NMR (376 MHz, CDCl₃) δ -105.48; HRMS calculated for [C₂₀H₁₉FNO₂S] [M + H]⁺ 356.1115, found 356.1133 / [C₂₀H₁₈FNO₂SNa] [M + Na]⁺ 378.0934, found 378.0936.

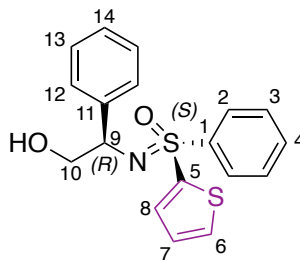
(*S*)-(4-Chlorophenyl)((*R*)-2-hydroxy-1-phenylethylimino)(phenyl)- λ^6 -sulfanone (269**)**



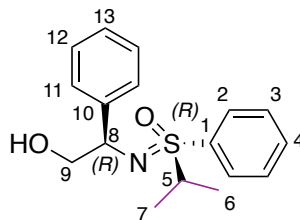
Following GP7, (*S*)-(4-chlorophenyl)((*R*)-2-hydroxy-1-phenylethylimino)(phenyl)- λ^6 -sulfanone (**269**) was prepared from (2*R*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**255**) (0.117 g, 0.452 mmol) dissolved in THF (5 mL) and 4-chlorophenylmagnesium bromide (0.904 mL, 0.904 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.158 g, 94%); IR ν_{max} (cm⁻¹): 3514, 3257, 3062, 2924, 2868, 1573, 1491, 1473, 1446, 1391, 1330, 1307, 1241, 1137, 1307, 1241, 1137, 1085, 1067, 1012, 908, 825, 746, 723, 699, 686, 601, 589, 558, 539, 493, 459; ¹H NMR (400 MHz, CDCl₃) δ 8.13-8.09 (2H, m, H-2 or H-3), 7.71-7.67 (2H, m, H-6 or H-7), 7.61-7.56 (1H, m, H-4), 7.55-7.51 (2H, m, H-2 or H-3), 7.46-7.42 (2H, m, H-12 or H-13), 7.39-7.33 (4H, m, H-6, 12 or 13; or H-7, 12 or 13), 7.32-7.27 (1H, m, H-14), 4.32 (1H, dd, *J* = 7.5, 5.0 Hz, H-9), 3.70 (2H, d, *J* = 7.5 Hz, H-10), (OH not observed); ¹³C NMR (101 MHz, CDCl₃) δ 141.9 (C-11), 140.5 (C-8), 139.4 (C-1), 138.4 (C-5), 133.1 (C-4), 130.5 (C-6 or C-7), 129.6 (Ar), 129.4 (Ar), 128.51 (Ar), 128.46 (Ar), 127.4 (C-14), 127.1 (C-12 or C-13), 69.3 (C-10), 61.9 (C-9); HRMS calculated for [C₂₀H₁₉³⁵ClNO₂S] [M + H]⁺ 372.0820, found 372.0830 / [C₂₀H₁₈³⁵ClNO₂SNa] [M + Na]⁺ 394.0639, found 394.0638.

(*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(4-methoxyphenyl)(phenyl)- λ^6 -sulfanone (270)

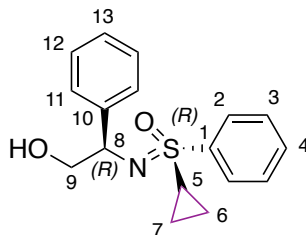
Following GP7, (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(4-methoxyphenyl)(phenyl)- λ^6 -sulfanone (**270**) was prepared from (2*R*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**255**) (0.125 g, 0.481 mmol) dissolved in THF (5 mL) and 4-methoxyphenylmagnesium bromide (1.92 mL, 0.962 mmol, 0.5M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.168 g, 95%); IR ν_{max} (cm⁻¹): 3488, 3061, 2941, 2867, 1591, 1577, 1493, 1445, 1409, 1351, 1307, 1255, 1238, 1132, 1094, 1063, 1023, 909, 832, 801, 729, 701, 686, 647, 579, 548; ¹H NMR (400 MHz, CDCl₃) δ 8.13-8.08 (2H, m, H-2 or H-3), 7.73-7.68 (2H, m, H-6), 7.55-7.45 (5H, m, H-2, 4 or H-3,4 and H-13 or H-14), 7.40-7.34 (2H, m, H-13 or H-14), 7.32-7.27 (1H, m, H-15), 6.89-6.84 (2H, m, H-7), 4.34 (1H, dd, J = 8.0, 4.5 Hz, H-10), 3.81 (3H, s, H-9), 3.73-3.64 (2H, m, H-11) 3.15 (1H, s, OH); ¹³C NMR (101 MHz, CDCl₃) δ 163.1 (C-8), 142.3 (C-1 or C-12), 141.5 (C-1 or C-12), 132.6 (C-4), 131.2 (C-6), 130.7 (C-5), 129.2 (C-2 or C-3 or C-13 or C-14), 128.4 (C-2 or C-3 or C-13 or C-14), 128.2 (C-2 or C-3 or C-13 or C-14), 127.2 (C-15), 127.1 (C-2 or C-3 or C-13 or C-14), 114.6 (C-7), 69.3 (C-11), 61.9 (C-10), 55.7 (C-9); HRMS calculated for [C₂₁H₂₂NO₃S] [M + H]⁺ 368.1315, found 368.1341 / [C₂₁H₂₁NO₃SNa] [M + Na]⁺ 390.1134, found 390.1118.

(*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)(thiophen-2-yl)- λ^6 -sulfanone (271)

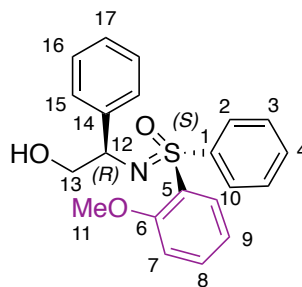
Following GP7, (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)(thiophen-2-yl)- λ^6 -sulfanone (**271**) was prepared from (*2R,4R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**255**) (0.0687 g, 0.265 mmol) dissolved in THF (3 mL) and 2-thienylmagnesium bromide (0.530 mL, 0.530 mmol, 1M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0892 g, 98%); IR ν_{max} (cm⁻¹): 3507, 3085, 3063, 2921, 2869, 1492, 1475, 1446, 1399, 1341, 1306, 1250, 1224, 1137, 1095, 1063, 1032, 1010, 855, 817, 752, 726, 701, 686, 654, 593, 566, 548, 535; ¹H NMR (400 MHz, CDCl₃) δ 8.19-8.14 (2H, m, H-2 or H-3), 7.60-7.52 (4H, m, H-2,4 or H-3, 4 and H-7 or H-8), 7.50-7.46 (2H, m, H-12 or H-13), 7.41-7.36 (2H, m, H-12 or H-13), 7.35 (1H, dd, *J* = 4.0, 1.5 Hz, H-7 or H-8), 7.33-7.29 (1H, m, H-14), 6.98 (1H, dd, *J* = 5.0, 4.0 Hz, H-6), 4.55 (1H, dd, *J* = 8.5, 4.0 Hz, H-9), 3.79-3.65 (2H, m, H-10), 3.00 (1H, s, OH); ¹³C NMR (101 MHz, CDCl₃) δ 142.1 (C-11), 141.7 (C-1 or C-5), 141.6 (C-1 or C-5), 134.3 (C-7 or C-8), 134.0 (C-7 or C-8), 133.0 (C-4), 129.3 (C-2 or C-3), 128.5 (C-12 or C-13), 128.2 (C-2 or C-3), 128.1 (C-6), 127.3 (C-14), 127.1 (C-12 or C-13), 69.3 (C-10), 62.1 (C-9); HRMS calculated for [C₁₈H₁₈NO₂S₂] [M + H]⁺ 344.0773, found 344.0782 / [C₁₈H₁₇NO₂S₂Na] [M + Na]⁺ 366.0593, found 366.0594.

(*R*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(isopropyl)(phenyl)- λ^6 -sulfanone (272)

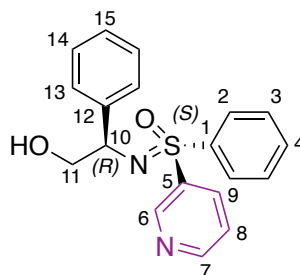
Following GP7, (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(isopropyl)(phenyl)- λ^6 -sulfanone (**272**) was prepared from (2*R*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**255**) (0.0955 g, 0.368 mmol) dissolved in THF (5 mL) and isopropylmagnesium chloride (0.737 mL, 0.737 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0997 g, 89%); IR ν_{max} (cm⁻¹): 3447, 3059, 2924, 2867, 1467, 1445, 1385, 1364, 1349, 1224, 1129, 1066, 815, 755, 717, 672, 564; ¹H NMR (400 MHz, CDCl₃) δ 7.93-7.88 (2H, m, H-2 or H-3), 7.66-7.61 (1H, m, H-4), 7.57 (2H, ddt, *J* = 8.5, 6.5, 1.5 Hz, H-2 or H-3), 7.42-7.37 (2H, m, H-11 or H-12), 7.33-7.27 (2H, m, H-11 or H-12), 7.25-7.19 (1H, m, H-13), 4.34 (1H, dd, *J* = 8.0, 4.5 Hz, H-8), 3.65 (1H, ddd, *J* = 10.5, 8.5, 4.5 Hz, H-9), 3.57 (1H, ddd, *J* = 10.5, 8.0, 4.0 Hz, H-9), 3.40 (1H, hept, *J* = 7.0 Hz, H-5), 2.70 (1H, dd, *J* = 9.0, 4.0 Hz, OH), 1.36 (3H, d, *J* = 7.0 Hz, H-6 or H-7), 1.13 (3H, d, *J* = 7.0 Hz, H-6 or H-7); ¹³C NMR (101 MHz, CDCl₃) δ 143.0 (C-10), 135.9 (C-1), 133.1 (C-4), 130.3 (C-2 or C-3), 129.2 (C-2 or C-3), 128.3 (C-11 or C-12), 127.2 (C-13), 127.1 (C-11 or C-12), 69.3 (C-9), 60.3 (C-8), 55.9 (C-5), 16.7 (C-6 or C-7), 16.3 (C-6 or C-7); HRMS calculated for [C₁₇H₂₂NO₂S] [M + H]⁺ 304.1366, found 304.1379 / [C₁₇H₂₁NO₂SNa] [M + Na]⁺ 326.1185, found 326.1179.

(*R*)-Cyclopropyl(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (274)

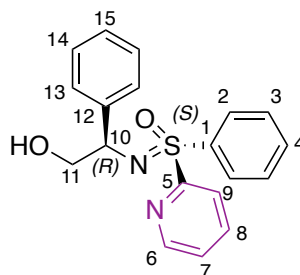
Following GP7, (*R*)-cyclopropyl(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (**274**) was prepared from (2*R*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**255**) (0.172 g, 0.663 mmol) dissolved in THF (5 mL) and cyclopropylmagnesium bromide (1.33 mL, 1.33 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.174 g, 87%); IR ν_{max} (cm⁻¹): 3241, 3060, 2867, 2245, 1491, 1477, 1445, 1349, 1234, 1185, 1130, 1086, 1064, 1036, 997, 907, 884, 856, 825, 755, 726, 699, 665, 645, 635, 556, 532; ¹H NMR (400 MHz, CDCl₃) δ 8.02-7.94 (2H, m, H-2 or H-3), 7.66-7.61 (1H, m, H-4), 7.60-7.54 (2H, m, H-2 or H-3), 7.50-7.45 (2H, m, H-11 or H-12), 7.38-7.32 (2H, m, H-11 or H-12), 7.30-7.23 (1H, m, H-13), 4.55 (1H, dd, J = 8.5, 4.5 Hz, H-8), 3.68 (1H, dd, J = 10.5, 4.5 Hz, H-9), 3.60 (1H, dd, J = 10.5, 8.5 Hz, H-9), 2.92 (1H, s, OH), 2.28-2.20 (1H, m, H-5), 1.55 (1H, dtt, J = 8.5, 4.0, 1.5 Hz, H-6 or H-7), 1.04-0.94 (2H, m, H-6 or H-7), 0.81-0.70 (1H, m, H-6 or H-7); ¹³C NMR (101 MHz, CDCl₃) δ 142.9 (C-10), 139.8 (C-1), 132.9 (C-4), 129.3 (C-2 or C-3), 128.4 (C-2 or C-3 or C-11 or C-12), 128.3 (C-2 or C-3 or C-11 or C-12), 127.2 (C-13), 127.1 (C-11 or C-12), 69.1 (C-9), 60.5 (C-8), 32.2 (C-5), 6.56 (C-6 or C-7), 5.56 (C-6 or C-7); HRMS calculated for [C₁₇H₂₀NO₂S] [M + H]⁺ 302.1209, found 302.1211 / [C₁₇H₁₉NO₂SNa] [M + Na]⁺ 324.1029, found 324.1040.

(S)-(((R)-2-Hydroxy-1-phenylethyl)imino)(2-methoxyphenyl)(phenyl)- λ^6 -sulfanone (275)

Following GP7, (S)-(((R)-2-hydroxy-1-phenylethyl)imino)(2-methoxyphenyl)(phenyl)- λ^6 -sulfanone (**275**) was prepared from (2R,4R)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**255**) (0.205 g, 0.791 mmol) dissolved in THF (5 mL) and 2-methoxyphenylmagnesium bromide (1.58 mL, 1.58 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.238 g, 82%); IR ν_{max} (cm⁻¹): 3488, 3060, 3025, 2937, 2918, 2865, 2840, 1588, 1476, 1464, 1446, 1433, 1391, 1353, 1278, 1250, 1131, 1057, 1020, 909, 858, 821, 800, 754, 735, 700, 686, 647, 591, 556, 539; ¹H NMR (400 MHz, CDCl₃) δ 8.23-8.15 (3H, m, H-2, 4 or H-3,4), 7.59-7.53 (1H, m, H-ArOMe), 7.52-7.48 (2H, m, H-2 or H-3), 7.47-7.44 (1H, m, H-ArOMe), 7.40-7.36 (2H, m, H-15 or H-16), 7.33-7.28 (2H, m, H-15 or H-16), 7.25-7.20 (1H, m, H-17), 7.09 (1H, td, J = 8.0, 1.0 Hz, H-ArOMe), 6.68 (1H, dd, J = 8.0, 1.0 Hz, H-ArOMe), 4.24 (1H, dd, J = 9.0, 4.0 Hz, H-12), 3.72-3.57 (2H, m, H-13), 3.22 (3H, s, H-11), 3.18 (1H, dd, J = 10.5, 3.0 Hz, OH); ¹³C NMR (101 MHz, CDCl₃) δ 156.8 (C-6), 142.3 (C-14), 140.3 (C-1), 135.1 (Ar-OMe), 132.62 (Ar-OMe or C-4), 132.55 (Ar-OMe or C-4), 129.6 (C-2 or C-3), 128.5 (C-2 or C-3), 128.0 (C-15 or C-16), 127.0 (C-15 or C-16), 126.8 (C-17), 126.0 (C-5), 120.7 (Ar-OMe), 111.8 (Ar-OMe), 69.0 (C-13), 62.2 (C-12), 54.8 (C-11); HRMS calculated for [C₂₁H₂₂NO₃S] [M + H]⁺ 368.1315, found 368.1324 / [C₂₁H₂₁NO₃SNa] [M + Na]⁺ 390.1134, found 390.1136.

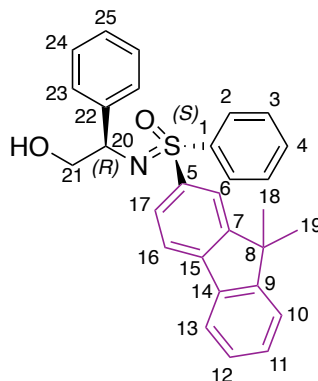
(*S*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(phenyl)(pyridin-3-yl)- λ^6 -sulfanone (276)

Following GP7, (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)(pyridin-3-yl)- λ^6 -sulfanone (**276**) was prepared from (2*R*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**255**) (0.101 g, 0.388 mmol) dissolved in THF (5 mL) and 3-pyridylmagnesium bromide (0.776 mL, 0.776 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 to 1:9 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0777 g, 59%); IR ν_{max} (cm⁻¹): 3366, 3060, 2918, 2868, 1571, 1463, 1446, 1413, 1246, 1193, 1141, 1119, 1065, 1022, 997, 909, 856, 805, 734, 687, 620, 593, 557, 535; ¹H NMR (400 MHz, CDCl₃) δ 8.94 (1H, d, J = 2.5 Hz, H-py), 8.66 (1H, dd, J = 5.0, 1.5 Hz, H-py), 8.16-8.09 (2H, m, H-2 or H-3), 8.00 (1H, dt, J = 8.0, 2.0 Hz, H-py), 7.62-7.57 (1H, m, H-4), 7.54 (2H, dd, J = 8.5, 6.5 Hz, H-2 or H-3), 7.43-7.39 (2H, m, H-13 or H-14), 7.36-7.31 (2H, m, H-13 or H-14), 7.29 (1H, dd, J = 4.5, 3.0 Hz, H-15), 7.26 (1H, d, J = 7.5 Hz, H-py), 4.35 (1H, t, J = 6.0 Hz, H-10), 3.77-3.66 (2H, m, H-11), 2.98 (1H, s, OH); ¹³C NMR (101 MHz, CDCl₃) δ 153.0 (py-Ar), 149.9 (py-Ar), 141.6 (C-12), 140.1 (C-1), 136.8 (C-5), 136.7 (py-Ar), 133.3 (C-4), 129.5 (C-2 or C-3), 128.53 (C-2 or C-3 or C-13 or C-14), 128.52 (C-2 or C-3 or C-13 or C-14), 127.5 (C-15), 127.0 (C-13 or C-14), 123.8 (py-Ar), 69.1 (C-11), 61.7 (C-10); HRMS calculated for [C₁₉H₁₉N₂O₂S] [M + H]⁺ 339.1162, found 339.1176 / [C₁₉H₁₈N₂O₂SNa] [M + Na]⁺ 361.0981, found 361.0980.

(*S*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(phenyl)(pyridin-2-yl)- λ^6 -sulfanone (277)

Following GP7, (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)(pyridin-2-yl)- λ^6 -sulfanone (**277**) was prepared from (2*R*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**255**) (0.152 g, 0.586 mmol) dissolved in THF (5 mL) and 2-pyridylmagnesium bromide (1.17 mL, 1.17 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 to 1:9 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0673 g, 34%); IR ν_{max} (cm⁻¹): 3424, 3059, 3027, 2922, 2856, 1732, 1600, 1575, 1562, 1491, 1475, 1447, 1423, 1240, 1143, 1115, 1064, 1040, 990, 932, 857, 818, 756, 739, 700, 686, 589, 555; ¹H NMR (400 MHz, CDCl₃) δ 8.53 (1H, d, *J* = 5.0 Hz, H-py), 8.24-8.19 (2H, m, H-2 or H-3), 8.15 (1H, d, *J* = 8.0 Hz, H-py), 7.82 (1H, td, *J* = 8.0, 4.0 Hz, H-py), 7.64-7.58 (1H, m, H-4), 7.55 (2H, td, *J* = 7.5, 2.0 Hz, H-2 or H-3), 7.38 (2H, d, *J* = 8.0 Hz, H-13 or H-14), 7.36-7.32 (1H, m, H-py), 7.30-7.26 (2H, m, H-13 or H-14), 7.25-7.19 (1H, m, H-15), 4.38 (1H, dd, *J* = 8.5, 4.5 Hz, H-10), 3.79-3.66 (2H, m, H-11), 3.21 (1H, dd, *J* = 9.5, 4.0 Hz, OH); ¹³C NMR (101 MHz, CDCl₃) δ 158.3 (C-5), 150.4 (C-py), 141.7 (C-12), 138.2 (C-1), 137.8 (C-py), 133.3 (C-4), 129.8 (C-2 or C-3), 129.1 (C-2 or C-3), 128.3 (C-13 or C-14), 127.2 (C-13 or C-14), 127.1 (C-15), 126.2 (C-py), 124.2 (C-py), 69.2 (C-11), 61.8 (C-10); HRMS calculated for [C₁₉H₁₉N₂O₂S] [M + H]⁺ 339.1162, found 339.1180 / [C₁₉H₁₈N₂O₂SNa] [M + Na]⁺ 361.0981, found 361.0965.

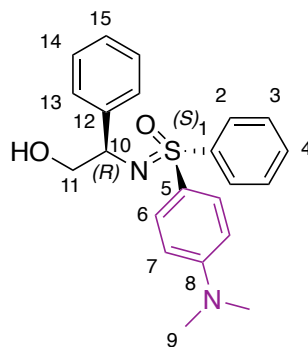
(*S*)-(9,9-Dimethyl-9*H*-fluoren-2-yl)((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (278**)**



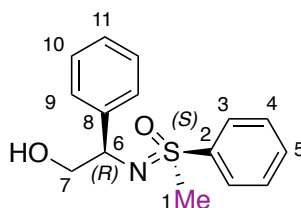
Following GP7, (*S*)-(9,9-dimethyl-9*H*-fluoren-2-yl)((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (**278**) was prepared from (2*R*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**255**) (0.134 g, 0.518 mmol) dissolved in THF (5 mL) and (9,9-dimethyl-9*H*-fluoren-2-yl)magnesium bromide (1.04 mL, 1.04 mmol, 1M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0548 g, 23%) IR ν_{max} (cm⁻¹): 3490, 3061, 3027, 2961, 2923, 2866, 1600, 1471, 1445, 1405, 1361, 1305, 1289, 1237, 1136, 1097, 1062, 1026, 999, 933, 908, 840, 756, 736, 726, 701, 686, 659, 637, 618, 580, 567, 543, 479, 447, 411; ¹H NMR (400 MHz, CDCl₃) δ 8.21-8.16 (2H, m, H-2 or H-3), 7.82-7.67 (4H, m, Ar), 7.59-7.51 (3H, m, H-2, 4 or H-3,4), 7.50-7.47 (2H, m, Ar), 7.45-7.35 (5H, m, Ar), 7.33-7.28 (1H, m, Ar), 4.40 (1H, dd, *J* = 7.5, 4.5 Hz, H-20), 3.77-3.67 (2H, m, H-21), 3.13-2.94 (1H, m, OH), 1.40 (3H, s, H-18 or H-19), 1.29 (3H, s, H-18 or H-19); ¹³C NMR (101 MHz, CDCl₃) δ 154.7 (C-7 or C-9), 154.6 (C-7 or C-9), 144.0 (C-22), 142.4 (C-5 or C-14 or C-15), 141.4 (C-1), 137.8 (C-5 or C-14 or C-15), 137.3 (C-5 or C-14 or C-15), 132.7 (C-4), 129.3 (C-2 or C-3), 129.0 (Ar), 128.7 (C-25), 128.5 (C-2 or C-3), 128.3 (C-23 or C-24), 127.4 (Ar), 127.3 (Ar), 127.1 (C-23 or C-24), 123.5 (Ar), 122.9 (Ar), 121.1 (Ar), 120.6 (Ar), 69.4 (C-21), 61.8 (C-20), 47.2 (C-8), 26.9 (C-18 or C-19), 26.7 (C-18 or C-19); HRMS calculated for

$[\text{C}_{29}\text{H}_{28}\text{NO}_2\text{S}] [\text{M} + \text{H}]^+$ 454.1835, found 454.1856 / $[\text{C}_{29}\text{H}_{27}\text{NO}_2\text{SNa}] [\text{M} + \text{Na}]^+$ 476.1655, found 476.1651.

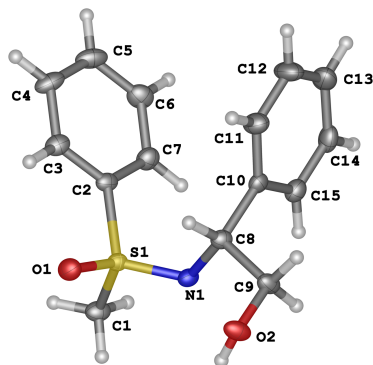
(*S*)-(4-(Dimethylamino)phenyl)((*R*)-2-hydroxy-1-phenylethylimino)(phenyl)- λ^6 -sulfanone (279**)**



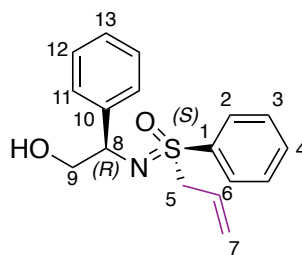
Following GP7, (*S*)-(4-(dimethylamino)phenyl)((*R*)-2-hydroxy-phenylethylimino)(phenyl)- λ^6 -sulfanone (**279**) was prepared from (*2R,4R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**255**) (0.166 g, 0.640 mmol) dissolved in THF (5 mL) and 4-(*N,N*-dimethyl)aniline magnesium bromide solution (1.28 mL, 1.28 mmol, 1M). The crude mixture was purified by flash chromatography (6:4 petroleum ether/ethyl acetate) to afford the title compound as a pale yellow oil (0.217 g, 89%); IR ν_{max} (cm^{-1}): 3482, 3060, 2913, 2864, 2246, 1591, 1491, 1444, 1368, 1230, 1200, 1126, 1092, 1064, 1026, 998, 943, 908, 815, 727, 687, 627, 577, 543; ^1H NMR (400 MHz, CDCl_3) δ 8.09 (2H, d, $J = 8.0$ Hz, H-2 or H-3), 7.62-7.56 (2H, m, H-6 or H-7), 7.54-7.50 (2H, m, H-13 or H-14), 7.49-7.45 (3H, m, H-2,4 or H-3,4), 7.42-7.35 (2H, m, H-13 or H-14), 7.33-7.27 (1H, m, H-15), 6.57 (2H, d, $J = 7.5$ Hz, H-6 or H-7), 4.42-4.35 (1H, m, H-10), 3.76-3.60 (2H, m, H-11), 3.32 (1H, s, OH), 2.98 (6H, s, H-9); ^{13}C NMR (101 MHz, CDCl_3) δ 152.9 (C-8), 142.6 (C-1 or C-12), 142.4 (C-1 or C-12), 132.0 (C-4), 130.8 (C-6 or C-7), 129.0 (C-2 or C-3), 128.3 (C-13 or C-14), 127.8 (C-2 or C-3), 127.1 (C-13 or C-14), 127.0 (C-15), 123.4 (C-5), 111.3 (C-6 or C-7), 69.4 (C-11), 61.7 (C-10), 40.0 (C-9); HRMS calculated for $[\text{C}_{22}\text{H}_{25}\text{N}_2\text{O}_2\text{S}] [\text{M} + \text{H}]^+$ 381.1631, found 381.1649 / $[\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_2\text{SNa}] [\text{M} + \text{Na}]^+$ 403.1451, found 403.1454.

(*S*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ^6 -sulfanone (284)

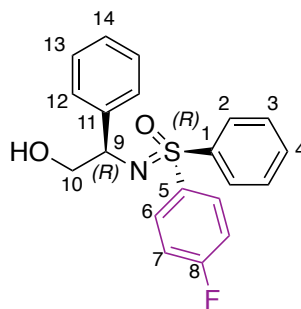
Following GP7, (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ^6 -sulfanone (**284**) was prepared from (*2S,4R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**254**) (0.0665 g, 0.256 mmol) dissolved in THF (5 mL) and methylmagnesium bromide (0.171 mL, 0.513 mmol, 3M). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0686 g, 97%); IR $\nu_{\max}$ (cm⁻¹): 3400, 3060, 3025, 3008, 2927, 2865, 1492, 1476, 1446, 1403, 1356, 1310, 1228, 1129, 1085, 1068, 1030, 978, 854, 785, 744, 701, 689, 530, 515; ¹H NMR (400 MHz, CDCl₃) δ 7.77-7.73 (2H, m, H-3 or H-4), 7.60-7.54 (1H, m, H-5), 7.49-7.42 (2H, m, H-3 or H-4), 7.31-7.28 (4H, m, H-9,10), 7.27-7.22 (1H, m, H-11), 4.14 (1H, dd, J = 7.0, 5.5 Hz, H-6), 3.65-3.61 (2H, m, H-7), 3.22 (3H, s, H-1), 3.08 (1H, t, J = 7.0 Hz, OH); ¹³C NMR (101 MHz, CDCl₃) δ 141.8 (C-8), 138.7 (C-2) 133.2 (C-5), 129.5 (C-3 or C-4), 128.9 (C-3 or C-4), 128.4 (C-9 or C-10), 127.2 (C-11), 127.1 (C-9 or C-10), 69.1 (C-7), 61.9 (C-6), 46.0 (C-1); HRMS calculated for [C₁₅H₁₈NO₂S] [M + H]⁺ 276.1053, found 276.1074 / [C₁₅H₁₇NO₂SNa] [M + Na]⁺ 298.0872, found



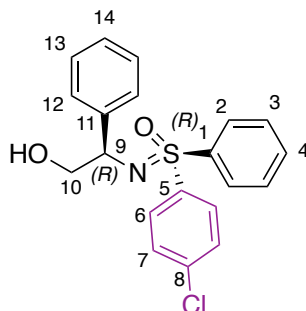
298.0881. X-ray crystal structure of (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ^6 -sulfanone C₁₅H₁₇NO₂S Mw = 275.35; T = 120(2) K; λ = 1.54184 Å; monoclinic; P2₁/n space group; a = 10.0075(5) Å, b = 10.2709(5) Å, c = 13.7357(7) Å; α = 90°, β = 96.642(5)°, γ = 90°; V = 1402.36(12) Å³; Z = 4; D = 1.304 g/cm³; R₁ = 0.0321, wR₂ = 0.0765 (all data), GoF = 1.049.

(*S*)-Allyl(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (285)

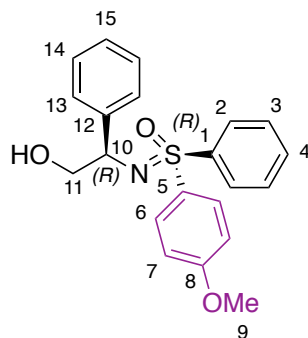
Following GP7, (*S*)-allyl(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (**285**) was prepared from (*2S,4R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**254**) (0.189 g, 0.729 mmol) dissolved in THF (5 mL) and allyl magnesium bromide (1.46 mL, 1.46 mmol, 1M). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0413 g, 19%) IR ν_{max} (cm⁻¹): 3498, 3083, 3061, 3027, 2920, 2867, 1638, 1615, 1601, 1582, 1492, 1476, 1445, 1421, 1394, 1355, 1227, 1124, 1066, 990, 931, 910, 819, 785, 749, 730, 688, 642, 618, 539, 510; ¹H NMR (400 MHz, CDCl₃) δ 7.69-7.64 (2H, m, H-2 or H-3), 7.59-7.53 (1H, m, H-4), 7.46-7.40 (2H, m, H-2 or H-3), 7.38-7.25 (5H, m, H-11,12,13), 5.87 (1H, ddt, J = 17.5, 10.0, 7.5 Hz, H-6), 5.31 (1H, dd, J = 10.0, 1.0 Hz, H-7), 5.11 (1H, dd, J = 17.0, 1.0 Hz, H-7), 4.21 (1H, dd, J = 8.0, 4.0 Hz, H-8), 4.05-3.92 (2H, m, H-5), 3.68-3.56 (2H, m, H-9), 3.12 (1H, dd, J = 10.0, 4.0 Hz, OH); ¹³C NMR (101 MHz, CDCl₃) δ 142.0 (C-10), 136.5 (C-1), 133.3 (C-4), 130.0 (C-2 or C-3), 129.2 (C-2 or C-3), 128.4 (C-11 or C-12), 127.2 (C-13), 127.1 (C-11 or C-12), 125.5 (C-6), 124.4 (C-7), 69.2 (C-9), 62.0 (C-5), 61.8 (C-8); HRMS calculated for [C₁₇H₂₀NO₂S] [M + H]⁺ 302.1209, found 302.1211 / [C₁₇H₁₉NO₂SNa] [M + Na]⁺ 324.1029, found 324.1033.

(*R*)-(4-Fluorophenyl)((*R*)-2-hydroxy-1-phenylethylimino)(phenyl)- λ 6-sulfanone (287**)**

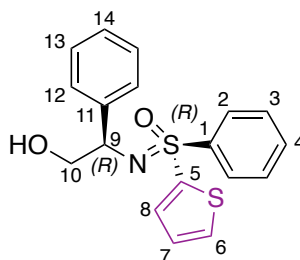
Following GP7, (*R*)-(4-fluorophenyl)((*R*)-2-hydroxy-1-phenylethylimino)(phenyl)- λ 6-sulfanone (**287**) was prepared from (2*S*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**254**) (0.129 g, 0.496 mmol) dissolved in THF (5 mL) and 4-fluorophenylmagnesium bromide (0.993 mL, 0.993 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.157 g, 89%); IR ν_{max} (cm⁻¹): 3483, 3063, 2925, 2869, 1587, 1489, 1446, 1401, 1351, 1306, 1289, 1234, 1137, 1094, 1064, 837, 819, 754, 732, 717, 701, 688, 666, 633, 582, 564, 542; ¹H NMR (400 MHz, CDCl₃) δ 8.16-8.10 (2H, m, H-6), 7.79-7.74 (2H, m, H-2 or H-3), 7.53-7.48 (1H, m, H-4), 7.45-7.40 (4H, m, H-2 or H-3 and H-12 or H-13), 7.38-7.34 (2H, m, H-12 or H-13), 7.32-7.28 (1H, m, H-14), 7.21-7.16 (2H, m, H-7), 4.34-4.28 (1H, m, H-9), 3.69 (2H, d, *J* = 7.0 Hz, H-10), 3.04 (1H, s, OH); ¹³C NMR (101 MHz, CDCl₃) δ 165.4 (d, *J* = 255 Hz, C-8), 142.0 (C-11), 139.6 (C-1), 136.8 (d, *J* = 3.0 Hz, C-5), 132.9 (C-4), 131.3 (d, *J* = 9.5 Hz, C-6), 129.4 (C-2 or C3), 129.0 (C-2 or C3), 128.5 (C-12 or C-13), 127.3 (C-14), 127.1 (C-12 or C-13), 116.5 (d, *J* = 23.0 Hz, C-7), 69.3 (C-10), 62.1 (C-9); ¹⁹F NMR (376 MHz, CDCl₃) δ -105.4; HRMS calculated for [C₂₀H₁₉FNO₂S] [M + H]⁺ 356.1115, found 356.1139 / [C₂₀H₁₈FNO₂SNa] [M + Na]⁺ 378.0934, found 378.0936.

(*R*)-(4-Chlorophenyl)((*R*)-2-hydroxy-1-phenylethylimino)(phenyl)- λ^6 -sulfanone (288)

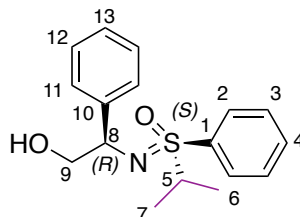
Following GP7, (*R*)-(4-chlorophenyl)((*R*)-2-hydroxy-1-phenylethylimino)(phenyl)- λ^6 -sulfanone (**288**) was prepared from (2*S*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**254**) (0.0858 g, 0.331 mmol) dissolved in THF (5 mL) and 4-chlorophenylmagnesium bromide (0.662 mL, 0.662 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a pale yellow oil (0.114 g, 92%); IR ν_{max} (cm⁻¹): 3449, 3062, 3027, 2918, 2869, 2246, 1600, 1574, 1491, 1472, 1445, 1392, 1241, 1137, 1086, 1065, 1027, 1012, 908, 819, 762, 746, 730, 687, 641, 612, 578, 554, 495; ¹H NMR (400 MHz, CDCl₃) δ 8.05 (2H, d, *J* = 7.0 Hz, H-2 or H-3), 7.77 (2H, d, *J* = 8.0 Hz, H-6 or H-7), 7.53-7.46 (3H, m, H-6,4 or H-7,4), 7.45-7.39 (4H, m, H-2 or H-3 or H-12 or H-13), 7.38-7.33 (2H, m, H-12 or H-13), 7.29 (1H, td, *J* = 7.0, 2.5 Hz, H-14), 4.32 (1H, t, *J* = 6.5 Hz, H-9), 3.70 (2H, d, *J* = 6.5 Hz, H-10), 3.04 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 142.0 (C-11), 139.5 (C-1 or C-5 or C-8), 139.42 (C-1 or C-5 or C-8), 139.36 (C-1 or C-5 or C-8), 132.9 (C-4 or C-14), 130.0 (Ar), 129.5 (Ar), 129.4 (Ar), 129.0 (Ar), 128.4 (Ar), 127.3 (C-4 or C-14), 127.0 (Ar), 69.3 (C-10), 62.0 (C-9); HRMS calculated for [C₂₀H₁₉³⁵ClNO₂S] [M + H]⁺ 372.0820, found 372.0833 / [C₂₀H₁₈³⁵ClNO₂SNa] [M + Na]⁺ 394.0639, found 394.0633.

(*R*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(4-methoxyphenyl)(phenyl)- λ^6 -sulfanone (289**)**

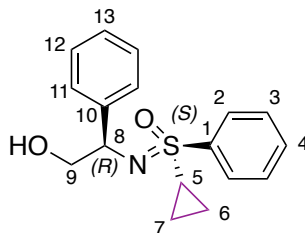
Following GP7, (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(4-methoxyphenyl)(phenyl)- λ^6 -sulfanone (**289**) was prepared from (2*S*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**254**) (0.0888 g, 0.342 mmol) dissolved in THF (5 mL) and 4-methoxyphenylmagnesium bromide (1.37 mL, 0.685 mmol, 0.5 M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.123 g, 98%); IR ν_{max} (cm⁻¹): 3488, 3061, 3026, 2941, 2868, 2840, 2245, 1591, 1493, 1444, 1411, 1393, 1352, 1308, 1255, 1238, 1131, 1108, 1063, 1024, 908, 832, 802, 753, 730, 701, 688, 666, 645, 627, 570, 551; ¹H NMR (400 MHz, CDCl₃) δ 8.07-8.02 (2H, m, H-6), 7.78-7.74 (2H, m, Ar), 7.44 (3H, dd, *J* = 8.0, 1.5 Hz, Ar), 7.39-7.32 (4H, m, Ar), 7.30-7.25 (1H, m, H-15), 7.00-6.95 (2H, m, H-7), 4.30 (1H, dd, *J* = 7.5, 5.0 Hz, H-10), 3.83 (3H, s, H-9), 3.72-3.66 (2H, m, H-11), 3.21 (1H, dd, *J* = 8.5, 5.0 Hz, OH); ¹³C NMR (101 MHz, CDCl₃) δ 163.2 (C-8), 142.2 (C-12), 140.2 (C-1), 132.4 (C-4), 132.0 (C-5), 130.6 (C-6), 129.2 (Ar), 128.7 (Ar), 128.3 (Ar), 127.1 (C-15), 127.0 (Ar), 114.4 (C-6), 69.2 (C-11), 61.9 (C-10), 55.6 (C-9); HRMS calculated for [C₂₁H₂₂NO₃S] [M + H]⁺ 368.1315, found 368.1327 / [C₂₁H₂₁NO₃SNa] [M + Na]⁺ 390.1134, found 390.1136.

(*R*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(phenyl)(thiophen-2-yl)- λ 6-sulfanone (290**)**

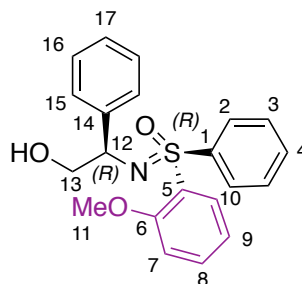
Following GP7, (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)(thiophen-2-yl)- λ 6-sulfanone (**290**) was prepared from (2*S*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**254**) (0.110 g, 0.424 mmol) dissolved in THF (5 mL) and 2-thienylmagnesium bromide (0.848 mL, 0.848 mmol, 1M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0889 g, 61%); IR ν_{max} (cm⁻¹): 3493, 3085, 3062, 3026, 2917, 2867, 1492, 1474, 1446, 1401, 1344, 1306, 1251, 1224, 1140, 1096, 1065, 1017, 929, 854, 818, 753, 727, 701, 687, 594, 566, 544; ¹H NMR (400 MHz, CDCl₃) δ 7.90-7.85 (2H, m, H-2 or H-3), 7.69-7.62 (2H, m, H-7, 8), 7.55-7.48 (1H, m, H-4), 7.46-7.39 (4H, m, H-2 or H3 or H-12 or H-13), 7.38-7.32 (2H, m, H-12 or H-13), 7.31-7.25 (1H, m, H-14), 7.09 (1H, dd, *J* = 5.0, 4.0 Hz, H-6), 4.34 (1H, dd, *J* = 8.0, 4.5 Hz, H-9), 3.76-3.63 (2H, m, H-10), 2.88 (1H, dd, *J* = 9.0, 4.5 Hz, OH); ¹³C NMR (101 MHz, CDCl₃) δ 142.9 (C-5), 141.8 (C-11), 140.2 (C-1), 134.3 (C-7 or C8), 133.8 (C-7 or C-8), 132.9 (C-4), 129.4 (Ar), 128.7 (Ar), 128.4 (Ar), 128.2 (C-6), 127.3 (C-14), 127.1 (Ar), 69.2 (C-10), 62.0 (C-9); HRMS calculated for [C₁₈H₁₈NO₂S₂] [M + H]⁺ 344.0773, found 344.0783 / [C₁₈H₁₇NO₂S₂Na] [M + Na]⁺ 366.0593, found 366.0583.

(*S*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(isopropyl)(phenyl)- λ^6 -sulfanone (292)

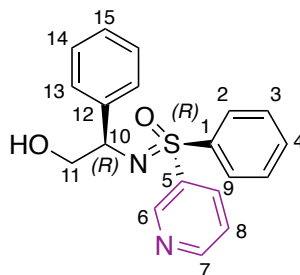
Following GP7, (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(isopropyl)(phenyl)- λ^6 -sulfanone (**292**) was prepared from (2*S*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**254**) (0.0970 g, 0.374 mmol) dissolved in THF (5 mL) and isopropylmagnesium chloride (0.748 mL, 0.748 mmol, 1M). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.104 g, 92%); IR ν_{max} (cm⁻¹): 3467, 3060, 2980, 2935, 2867, 1444, 1395, 1221, 1124, 1105, 1066, 991, 959, 934, 856, 821, 756, 717, 693, 671, 649, 630, 566, 545; ¹H NMR (400 MHz, CDCl₃) δ 7.67-7.63 (2H, m, H-2 or H-3), 7.59-7.54 (1H, m, H-4), 7.47-7.41 (2H, m, H-2 or H-3), 7.40-7.35 (2H, m, H-11 or H-12), 7.34-7.30 (2H, m, H-11 or H-12), 7.29-7.25 (1H, m, H-13), 4.19 (1H, dd, *J* = 8.5, 3.5 Hz, H-8), 3.63-3.52 (2H, m, H-9), 3.37 (1H, h, *J* = 6.5 Hz, H-5), 3.29 (1H, dd, *J* = 10.5, 3.0 Hz, OH), 1.41 (3H, d, *J* = 6.5 Hz, H-6 or H-7), 1.33 (3H, d, *J* = 6.5 Hz, H-6 or H-7); ¹³C NMR (101 MHz, CDCl₃) δ 142.2 (C-10), 135.1 (C-1), 133.1 (C-4), 130.5 (C-2 or C-3), 129.1 (C-2 or C-3), 128.7 (C-13), 128.2 (C-11 or C-12), 126.9 (C-11 or C-12), 69.4 (C-9), 61.6 (C-8), 56.7 (C-5), 16.6 (C-6 or C-7), 15.8 (C-6 or C-7); HRMS calculated for [C₁₇H₂₂NO₂S] [M + H]⁺ 304.1366, found 304.1374.

(*S*)-Cyclopropyl(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (293)

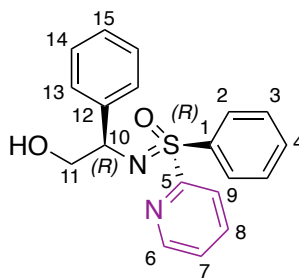
Following GP7, (*S*)-cyclopropyl(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (**293**) was prepared from (*2S,4R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**254**) (0.133 g, 0.511 mmol) dissolved in THF (5 mL) and cyclopropylmagnesium bromide (1.02 mL, 1.02 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 pentane/ether) to afford the title compound as a colourless oil (0.0637 g, 41%); IR ν_{max} (cm⁻¹): 3468, 3059, 3024, 2921, 2866, 1445, 1396, 1352, 1235, 1186, 1129, 1085, 1065, 1033, 885, 827, 756, 722, 700, 632, 566, 546; ¹H NMR (400 MHz, CDCl₃) δ 7.73-7.67 (2H, m, H-2 or H-3), 7.57-7.52 (1H, m, H-4), 7.43 (2H, dd, J = 8.5, 7.0 Hz, H-2 or H-3), 7.35-7.27 (4H, m, H-11,12), 7.26-7.21 (1H, m, H-13), 4.19 (1H, dd, J = 8.5, 4.0 Hz, H-8), 3.67-3.52 (2H, m, H-9), 3.07 (1H, dd, J = 10.0, 3.5 Hz, OH), 2.64 (1H, tt, J = 8.0, 5.0 Hz, H-5), 1.51 (1H, ddt, J = 10.0, 7.0, 5.0 Hz, H-6 or H-7), 1.27 (1H, ddt, J = 10.0, 7.0, 5.0 Hz, H-6 or H-7), 1.15 (1H, dtd, J = 9.0, 7.5, 5.0 Hz, H-6 or H-7), 0.92 (1H, dtd, J = 9.0, 7.5, 5.0 Hz, H-6 or H-7); ¹³C NMR (101 MHz, CDCl₃) δ 142.0 (C-10), 139.0 (C-1), 132.9 (C-4), 129.3 (Ar), 129.0 (Ar), 128.3 (Ar), 127.1 (C-13), 127.0 (C-11 or C-12), 69.1 (C-9), 61.6 (C-8), 33.6 (C-5), 6.94 (C-6 or C-7), 5.18 (C-6 or C-7); HRMS calculated for [C₁₇H₂₀NO₂S] [M + H]⁺ 302.1209, found 302.1210 / [C₁₇H₁₉NO₂SNa] [M + Na]⁺ 324.1029, found 324.1029.

(*R*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(2-methoxyphenyl)(phenyl)- λ 6-sulfanone (294**)**

Following GP7, (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(2-methoxyphenyl)(phenyl)- λ 6-sulfanone (**294**) was prepared from (2*S*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**254**) (0.193 g, 0.742 mmol) dissolved in THF (5 mL) and 2-methoxyphenylmagnesium bromide (1.48 mL, 1.48 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.217 g, 80%); IR ν_{max} (cm⁻¹): 3499, 3061, 3024, 2941, 2857, 1587, 1475, 1446, 1276, 1246, 1134, 1083, 1058, 1040, 1016, 909, 857, 802, 754, 732, 700, 688, 646, 600, 560, 541; ¹H NMR (400 MHz, CDCl₃) δ 8.27 (1H, dd, *J* = 8.0, 2.0 Hz, H-Ar-OMe), 8.01-7.95 (2H, m, H-2 or H-3), 7.56-7.48 (2H, m, H-Ar-OMe and H-4), 7.46-7.37 (4H, m, H-2 or H-3 and H-15 or H-16), 7.32-7.27 (2H, m, H-15 or H-16), 7.25-7.19 (1H, m, H-17), 7.12 (1H, ddd, *J* = 8.5, 7.5, 1.0 Hz, H-Ar-OMe), 6.91 (1H, dd, *J* = 8.5, 1.0 Hz, H-Ar-OMe), 4.23 (1H, t, *J* = 6.5 Hz, H-12), 3.70 (3H, s, H-11), 3.67-3.60 (2H, m, H-13), 3.31 (1H, s, OH); ¹³C NMR (101 MHz, CDCl₃) δ 156.7 (C-6), 142.4 (C-14), 140.1 (C-1), 135.1 (Ar-OMe), 132.5 (C-4), 131.9 (Ar-OMe), 129.3 (C-2 or C-3), 128.4 (C-2 or C-3 or C-15 or C-16), 128.2 (C-2 or C-3 or C-15 or C-16), 127.4 (C-5), 127.00 (C-15 or C-16), 126.97 (C-17), 120.8 (Ar-OMe), 112.7 (Ar-OMe), 69.1 (C-13), 61.4 (C-12), 55.7 (C-11); HRMS calculated for [C₂₁H₂₂NO₃S] [M + H]⁺ 368.1315, found 368.1326 / [C₂₁H₂₁NO₃SNa] [M + Na]⁺ 390.1134, found 390.1135.

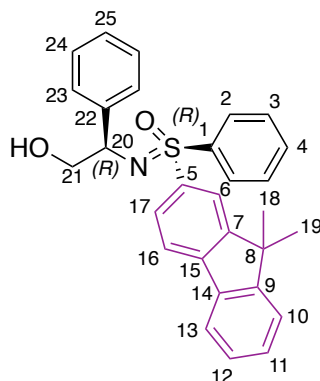
(*R*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(phenyl)(pyridin-3-yl)- λ 6-sulfanone (295**)**

Following GP7, (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)(pyridin-3-yl)- λ 6-sulfanone (**295**) was prepared from (2*S*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**254**) (0.153 g, 0.591 mmol) dissolved in THF (5 mL) and 3-pyridylmagnesium bromide (1.18 mL, 1.18 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 to 1:9 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0585 g, 29%); IR ν_{max} (cm⁻¹): 3422, 3059, 2919, 2867, 1571, 1491, 1446, 1414, 1248, 1193, 1142, 1066, 1021, 909, 856, 807, 738, 699, 688, 619, 594, 558, 536; ¹H NMR (400 MHz, CDCl₃) δ 9.32 (1H, dd, *J* = 2.5, 1.0 Hz, H-py), 8.77 (1H, dd, *J* = 5.0, 1.5 Hz, H-py), 8.36 (1H, dt, *J* = 8.0, 2.0 Hz, H-py), 7.79 (2H, dd, *J* = 8.5, 1.5 Hz, H-2 or H-3), 7.55-7.50 (1H, m, H-4), 7.48-7.40 (5H, m, H-2 or H-3 and H-13 or H-14 and H-py), 7.38-7.33 (2H, m, H-13 or H-14), 7.32-7.27 (1H, m, H-15), 4.33 (1H, t, *J* = 6.0 Hz, H-10), 3.70 (2H, d, *J* = 6.5 Hz, H-11), 2.97 (1H, s, OH); ¹³C NMR (101 MHz, CDCl₃) δ 153.2 (C-py), 149.7 (C-py), 141.8 (C-12), 139.0 (C-1), 137.7 (C-5), 136.2 (C-py), 133.3 (C-4), 129.6 (C-6 or C-7 or C-8 or C-9), 129.2 (C-2 or C-3), 128.5 (C-13 or C-14), 127.4 (C-15), 127.0 (C-2 or C-3 or C-13 or C-14), 123.7 (C-py), 69.2 (C-11), 62.1 (C-10); HRMS calculated for [C₁₉H₁₉N₂O₂S] [M + H]⁺ 339.1162, found 339.1172 / [C₁₉H₁₈N₂O₂SNa] [M + Na]⁺ 361.0981, found 361.0975.

(*R*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(phenyl)(pyridin-2-yl)- λ 6-sulfanone (296**)**

Following GP7, (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)(pyridin-2-yl)- λ 6-sulfanone (**296**) was prepared from (2*S*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**254**) (0.102 g, 0.394 mmol) dissolved in THF (5 mL) and 2-pyridylmagnesium bromide (0.788 mL, 0.788 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 to 1:9 petroleum ether/ethyl acetate) to afford the title compound as a yellow oil (0.0896 g, 67%); IR ν_{max} (cm⁻¹): 3397, 3059, 3027, 2921, 2865, 2244, 1601, 1576, 1562, 1446, 1424, 1352, 1243, 1145, 1114, 1081, 1066, 1032, 992, 909, 857, 818, 729, 700, 686, 645, 618, 595, 534; ¹H NMR (400 MHz, CDCl₃) δ 8.68 (1H, ddd, *J* = 4.5, 2.0, 1.0 Hz, H-py), 8.35 (1H, dt, *J* = 8.0, 1.0 Hz, H-py), 8.09-8.03 (2H, m, H-2 or H-3), 7.92 (1H, td, *J* = 8.0, 2.0 Hz, H-py), 7.57-7.51 (1H, m, H-4), 7.49-7.41 (5H, m, H-2 or H-3 and H-13 or H-14 and H-py), 7.34-7.27 (2H, m, H-13 or H-14), 7.25-7.20 (1H, m, H-15), 4.38 (1H, dd, *J* = 8.5, 4.0 Hz, H-10), 3.81-3.75 (1H, m, OH), 3.75-3.64 (2H, m, H-11); ¹³C NMR (101 MHz, CDCl₃) δ 158.6 (C-5), 150.3 (C-py), 142.1 (C-12), 138.5 (C-1), 138.4 (C-py), 133.2 (C-4), 129.6 (C-2 or C-3), 129.2 (C-13 or C-14 or C-2 or C-3), 128.4 (C-13 or C-14), 127.2 (C-15), 127.0 (C-13 or C-14 or C-2 or C-3), 126.7 (C-py), 124.8 (C-py), 69.6 (C-11), 61.3 (C-10); HRMS calculated for [C₁₉H₁₉N₂O₂S] [M + H]⁺ 339.1162, found 339.1174 / [C₁₉H₁₈N₂O₂SNa] [M + Na]⁺ 361.0981, found 361.0988.

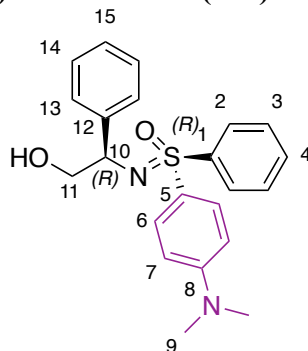
(*R*)-(9,9-Dimethyl-9*H*-fluoren-2-yl)(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ 6-sulfanone (297**)**



Following GP7, (*R*)-(9,9-dimethyl-9*H*-fluoren-2-yl)(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ 6-sulfanone (**297**) was prepared from (2*S*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**254**) (0.102 g, 0.393 mmol) dissolved in THF (5 mL) and (9,9-dimethyl-9*H*-fluoren-2-yl)magnesium bromide (0.786 mL, 0.786 mmol, 1M). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0559 g, 31%); IR ν_{max} (cm⁻¹): 3497, 3061, 3027, 2960, 2923, 2865, 1601, 1585, 1444, 1406, 1359, 1346, 1305, 1237, 1136, 1098, 1065, 1032, 1004, 908, 837, 781, 756, 735, 701, 688, 615, 588, 568, 542; ¹H NMR (400 MHz, CDCl₃) δ 8.17 (1H, d, *J* = 2.0 Hz, Ar), 8.12 (1H, dd, *J* = 8.0, 2.0 Hz, Ar), 7.87-7.81 (3H, m, Ar), 7.79-7.76 (1H, m, Ar), 7.52-7.47 (4H, m, Ar), 7.43 (1H, d, *J* = 2.0 Hz, Ar), 7.42-7.37 (5H, m, Ar), 7.34-7.29 (1H, m, Ar), 4.36 (1H, dd, *J* = 7.0, 5.0 Hz, H-20), 3.73 (2H, d, *J* = 7.0 Hz, H-21), 3.17 (1H, s, OH), 1.52 (6H, s, H-18 and H-19); ¹³C NMR (101 MHz, CDCl₃) δ 154.7 (C-7 or C-9), 154.5 (C-7 or C-9), 144.1 (C-5 or C-14 or C-15), 142.3 (C-22), 140.1 (C-5 or C-14 or C-15), 138.9 (C-1), 137.3 (C-5 or C-14 or C-15), 132.6 (Ar), 129.3 (C-2 or C-3 or C-23 or C-24), 129.03 (Ar), 129.00 (C-2 or C-3 or C-23 or C-24), 128.4 (C-2 or C-3 or C-23 or C-24), 128.2 (Ar), 127.5 (Ar), 127.3 (Ar), 127.1 (C-2 or C-3 or C-24 or C-25), 122.9 (Ar), 122.8 (Ar), 121.2 (Ar), 120.5 (Ar), 69.4 (C-21), 62.1 (C-20), 47.4 (C-8), 27.1

(C-18 or C-19), 26.9 (C-18 or C-19); HRMS calculated for $[\text{C}_{29}\text{H}_{28}\text{NO}_2\text{S}] [\text{M} + \text{H}]^+$ 454.1835, found 454.1852 / $[\text{C}_{29}\text{H}_{27}\text{NO}_2\text{SNa}] [\text{M} + \text{Na}]^+$ 476.1655, found 476.1654.

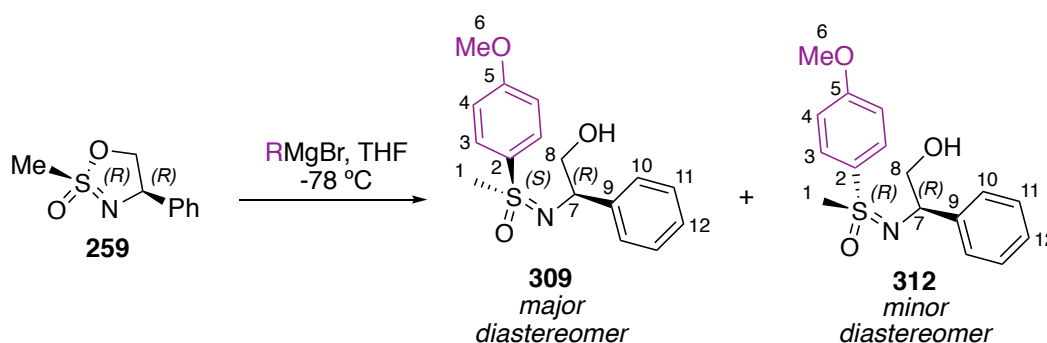
(*R*)-(4-(Dimethylamino)phenyl)((*R*)-2-hydroxy-1-phenylethylimino)(phenyl)- λ 6-sulfanone (298**)**



Following GP7, (*R*)-(4-(dimethylamino)phenyl)((*R*)-2-hydroxy-1-phenylethylimino)(phenyl)- λ 6-sulfanone (**298**) was prepared from (2*S*,4*R*)-2,4-diphenyl-4,5-dihydro-1,2,3-oxathiazole 2-oxide (**254**) (0.174 g, 0.669 mmol) dissolved in THF (5 mL) and 4-(*N,N*-dimethyl)aniline magnesium bromide (1.34 mL, 1.34 mmol, 1M). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a pale yellow oil (0.213 g, 84%); IR ν_{max} (cm^{-1}): 3481, 3059, 3026, 2912, 2863, 2245, 1591, 1513, 1444, 1368, 1228, 1121, 1096, 1064, 1035, 998, 943, 908, 858, 813, 752, 728, 701, 689, 656, 626, 562, 547; ^1H NMR (400 MHz, CDCl_3) δ 7.95-7.90 (2H, m, H-6 or H-7), 7.77-7.71 (2H, m, H-2 or H-3), 7.48-7.44 (2H, m, H-13 or H-14), 7.43-7.40 (1H, m, H-4), 7.38-7.32 (4H, m, H-2 or H-3 and H-13 or H-14), 7.31-7.25 (1H, m, H-15), 6.72-6.67 (2H, m, H-6 or H-7), 4.28 (1H, dd, $J = 8.0, 4.0$ Hz, H-10), 3.74-3.62 (2H, m, H-11), 3.28 (1H, dd, $J = 9.5, 3.5$ Hz, OH), 3.03 (6H, s, H-9); ^{13}C NMR (101 MHz, CDCl_3) δ 153.0 (C-8), 142.5 (C-12), 141.0 (C-1), 132.0 (C-4), 130.3 (C-6 or C-7), 129.1 (C-2 or C-3 or C-13 or C-14), 128.5 (C-2 or C-3), 128.3 (C-2 or C-3 or C-13 or C-14), 127.1 (C-13 or C-14), 127.0 (C-15), 125.3 (C-5), 111.3 (C-6 or C-7), 69.4 (C-11), 61.9 (C-10), 40.2 (C-9); HRMS calculated for

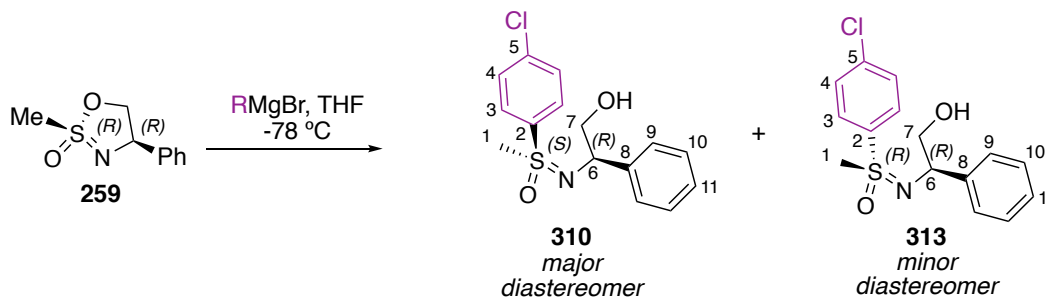
$[\text{C}_{22}\text{H}_{25}\text{N}_2\text{O}_2\text{S}] [\text{M} + \text{H}]^+ 381.1631$, found 381.1652 / $[\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_2\text{SNa}] [\text{M} + \text{Na}]^+ 403.1451$, found 403.1455 .

(*S*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(4-methoxyphenyl)(methyl)- λ^6 -sulfanone (309**)**



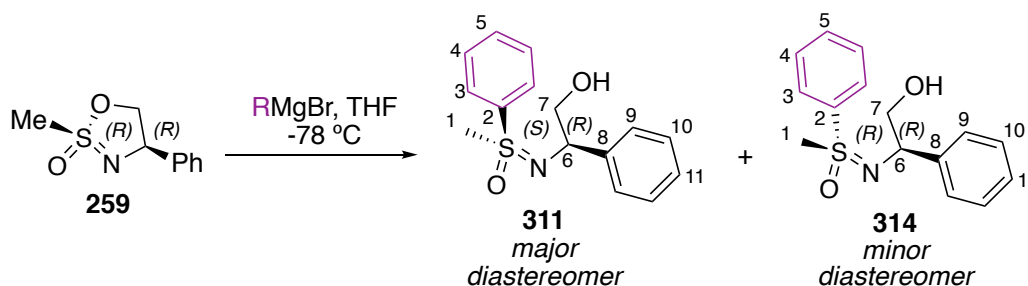
Following GP7, (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(4-methoxyphenyl)(methyl)- λ^6 -sulfanone (**309**) was prepared from (2*R*,4*R*)-2-methyl-4-phenyl-4,5-dihydro-1,2 λ^6 ,3-oxathiazole 2-oxide (**259**) (0.237 g, 1.20 mmol) dissolved in THF (5 mL) and 4-methoxyphenylmagnesium bromide (4.81 mL, 2.40 mmol, 0.5M). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.221 g, 60%); d.r.: 3:1 (**309-312**); IR ν_{max} (cm^{-1}): 3382, 3024, 2927, 2841, 1592, 1577, 1493, 1452, 1408, 1355, 1255, 1223, 1124, 1087, 1023, 980, 910, 834, 803, 759, 730, 701, 631, 535; ^1H NMR (400 MHz, CDCl_3) δ 7.69-7.63 (2H, m, H-3 or H-4), 7.33-7.23 (5H, m, Ar), 6.94-6.88 (2H, m, H-3 or H-4), 4.14 (1H, dd, $J = 7.5, 4.5$ Hz, H-7), 3.86 (3H, s, H-6), 3.65-3.58 (2H, m, H-8), 3.20 (3H, s, H-1), 3.14 (1H, dd, $J = 9.0, 4.5$ Hz, OH); ^{13}C NMR (101 MHz, CDCl_3) δ 163.5 (C-5), 142.0 (C-9), 131.1 (C-3 or C-4), 129.7 (C-2), 128.4 (C-10 or C-11), 127.2 (C-12), 127.1 (C-10 or C-11), 114.7 (C-3 or C-4), 69.1 (C-8), 61.9 (C-7), 55.8 (C-6), 46.3 (C-1); HRMS calculated for $[\text{C}_{16}\text{H}_{20}\text{NO}_3\text{S}] [\text{M} + \text{H}]^+ 306.1158$, found 306.1167 / $[\text{C}_{16}\text{H}_{19}\text{NO}_3\text{SNa}] [\text{M} + \text{Na}]^+ 328.0978$, found 328.0972 .

(*S*)-(4-Chlorophenyl)(((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)- λ^6 -sulfanone (310**)**

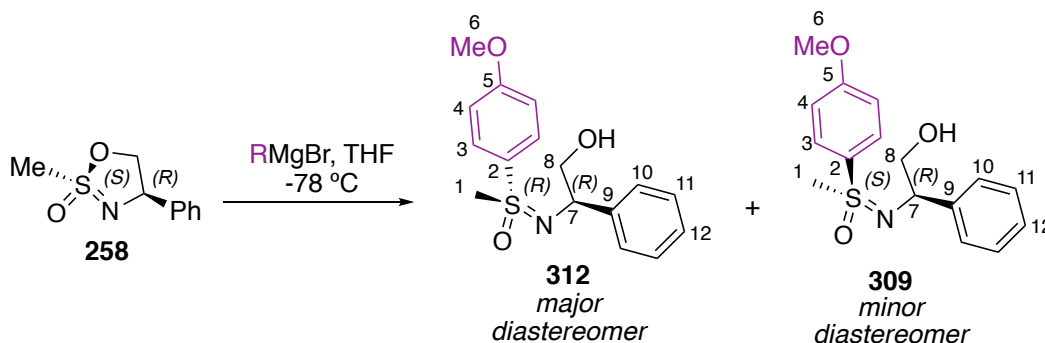


Following GP7, (*S*)-(4-chlorophenyl)(((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)- λ^6 -sulfanone (**310**) was prepared from (2*R*,4*R*)-2-methyl-4-phenyl-4,5-dihydro-1,2 λ^6 ,3-oxathiazole 2-oxide (**259**) (0.235 g, 1.19 mmol) dissolved in THF (5 mL) and 4-chlorophenylmagnesium bromide (2.38 mL, 2.38 mmol, 1M). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.271 g, 74%); d.r.: 3:1 (**310-313**); IR ν_{max} (cm⁻¹): 3362, 3084, 3062, 3025, 3006, 2927, 2867, 1573, 1492, 1472, 1452, 1433, 1392, 1357, 1318, 1230, 1133, 1084, 1009, 971, 829, 779, 759, 735, 701, 635, 559, 522, 463; ¹H NMR (400 MHz, CDCl₃) δ 7.69-7.63 (2H, m, H-3 or H-4), 7.43-7.38 (2H, m, H-3 or H-4), 7.31-7.27 (5H, m, H-9, H-10, H-11), 4.13 (1H, dd, *J* = 7.0, 5.5 Hz, H-6), 3.65-3.60 (2H, m, H-7), 3.21 (3H, s, H-1), 2.97 (1H, dd, *J* = 7.5, 6.0 Hz, OH); ¹³C NMR (101 MHz, CDCl₃) δ 141.4 (C-8), 139.8 (C-5), 137.3 (C-2), 130.3 (C-3 or C-4), 129.6 (C-3 or C-4), 128.3 (C-9 or C-10), 127.2 (C-11), 127.0 (C-9 or C-10), 68.8 (C-7), 61.7 (C-6), 45.9 (C-1); HRMS calculated for [C₁₅H₁₇³⁵ClNO₂S] [M + H]⁺ 310.0663, found 310.0662 / [C₁₅H₁₆³⁵ClNO₂SNa] [M + Na]⁺ 332.0482, found 332.0483.

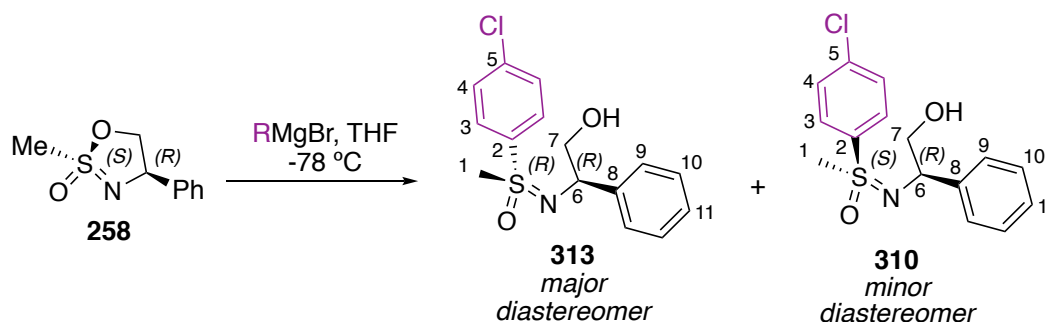
**(*S*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ^6 -sulfanone
(**311**)**



Following GP7, (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ^6 -sulfanone (**311**) was prepared from ((2*R*,4*R*)-2-methyl-4-phenyl-4,5-dihydro-1,2 λ^6 ,3-oxathiazole 2-oxide (**259**) (0.221 g, 1.12 mmol) dissolved in THF (5 mL) and phenylmagnesium bromide (2.24 mL, 2.24 mmol, 1M). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.264 g, 86%); d.r.: 2:1 (**311**-**314**). Major diastereoisomer **311** matches NMR data for sulfoximine **284**; IR ν_{max} (cm⁻¹): 3387, 3060, 3026, 2926, 2866, 1445, 1403, 1224, 1127, 1066, 1028, 910, 785, 742, 700, 689, 633, 528; ¹H NMR (400 MHz, CDCl₃) δ 7.77-7.73 (2H, m, H-3 or H-4), 7.60-7.54 (1H, m, H-5), 7.49-7.42 (2H, m, H-3 or H-4), 7.31-7.28 (4H, m, H-9,10), 7.27-7.22 (1H, m, H-11), 4.14 (1H, dd, *J* = 7.0, 5.5 Hz, H-6), 3.65-3.61 (2H, m, H-7), 3.22 (3H, s, H-1), 3.08 (1H, t, *J* = 7.0 Hz, OH); ¹³C NMR (101 MHz, CDCl₃) δ 141.8 (C-8), 138.7 (C-2) 133.2 (C-5), 129.5 (C-3 or C-4), 128.9 (C-3 or C-4), 128.4 (C-9 or C-10), 127.2 (C-11), 127.1 (C-9 or C-10), 69.1 (C-7), 61.9 (C-6), 46.0 (C-1); HRMS calculated for [C₁₅H₁₈NO₂S] [M + H]⁺ 276.1053, found 276.1055 / [C₁₅H₁₇NO₂SNa] [M + Na]⁺ 298.0872, found 298.0872.

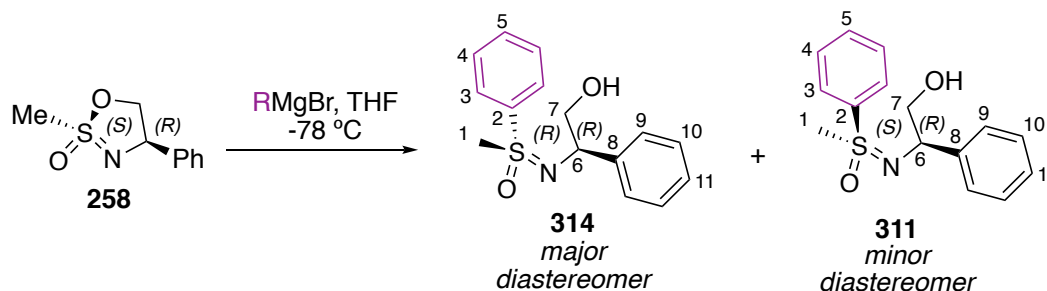
(*R*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(4-methoxyphenyl)(methyl)- λ^6 -sulfanone (312**)**

Following GP7, (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(4-methoxyphenyl)(methyl)- λ^6 -sulfanone (**312**) was prepared from (2*S*,4*R*)-2-methyl-4-phenyl-4,5-dihydro-1,2 λ^6 ,3-oxathiazole 2-oxide (**258**) (0.0459 g, 0.233 mmol) dissolved in THF (5 mL) and 4-methoxyphenylmagnesium bromide (0.931 mL, 0.465 mmol, 0.5M). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0216 g, 30%); d.r.: 6:1 (**312-309**); IR ν_{max} (cm⁻¹): 3424, 3060, 3024, 2927, 2841, 1592, 1577, 1494, 1452, 1408, 1308, 1254, 1223, 1176, 1124, 1087, 1065, 1022, 959, 833, 802, 757, 733, 700, 638, 532, 471; ¹H NMR (400 MHz, CDCl₃) δ 7.96-7.92 (2H, m, H-3 or H-4), 7.46-7.41 (2H, m, H-10 or H-11), 7.37-7.31 (2H, m, H-10 or H-11), 7.29-7.24 (1H, m, H-12), 7.09-7.02 (2H, m, H-3 or H-4), 4.38 (1H, dd, *J* = 8.5, 4.5 Hz, H-7), 3.90 (3H, s, H-6), 3.71-3.60 (2H, m, H-8), 3.04 (3H, s, H-1), (OH not observed); ¹³C NMR (101 MHz, CDCl₃) δ 163.5 (C-5), 142.6 (C-9), 130.8 (C-2), 130.6 (C-3 or C-4), 128.4 (C-10 or C-11), 127.3 (C-12), 127.1 (C-10 or C-11), 114.7 (C-3 or C-4), 69.0 (C-8), 60.8 (C-7), 55.8 (C-6), 44.7 (C-1); HRMS calculated for [C₁₆H₂₀NO₃S] [M + H]⁺ 306.1158, found 306.1179 / [C₁₆H₁₉NO₃SNa] [M + Na]⁺ 328.0978, found 328.0982.

(*R*)-(4-Chlorophenyl)((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)- λ^6 -sulfanone (313)

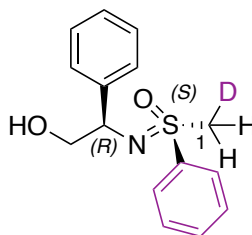
Following GP7, (*R*)-(4-chlorophenyl)((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)- λ^6 -sulfanone (**313**) was prepared from (2*S*,4*R*)-2-methyl-4-phenyl-4,5-dihydro-1,2λ⁶,3-oxathiazole 2-oxide (**258**) (0.163 g, 0.828 mmol) dissolved in THF (5 mL) and 4-chlorophenylmagnesium bromide (1.66 mL, 1.66 mmol, 1M). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0713 g, 28%); d.r.: 8:1 (**313**-**310**); IR ν_{max} (cm⁻¹): 3370, 3085, 3061, 3025, 2926, 2866, 1574, 1491, 1472, 1452, 1392, 1228, 1131, 1082, 1031, 1008, 966, 851, 828, 778, 758, 735, 700, 634, 558, 521, 461; ¹H NMR (400 MHz, CDCl₃) δ 7.99-7.93 (2H, m, H-3 or H-4), 7.60-7.55 (2H, m, H-3 or H-4), 7.45-7.40 (2H, m, H-9 or H-10), 7.38-7.33 (2H, m, H-9 or H-10), 7.30-7.27 (1H, m, H-11), 4.37 (1H, dd, *J* = 8.5, 4.5 Hz, H-6), 3.74-3.65 (2H, m, H-7), 3.05 (3H, s, H-1), 2.63 (1H, s, OH); ¹³C NMR (101 MHz, CDCl₃) δ 142.2 (C-8), 140.0 (C-5), 138.3 (C-2), 130.0 (C-3 or C-4), 129.8 (C-3 or C-4), 128.6 (C-9 or C-10), 127.5 (C-11), 127.1 (C-9 or C-10), 69.1 (C-7), 61.0 (C-6), 44.7 (C-1); HRMS calculated for [C₁₅H₁₇³⁵ClNO₂S] [M + H]⁺ 310.0663, found 310.0674 / [C₁₅H₁₆³⁵ClNO₂SNa] [M + Na]⁺ 332.0482, found 332.0483.

(*R*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ^6 -sulfanone (314)

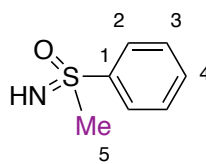


Following GP7, (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ^6 -sulfanone (**314**) was prepared from ((2*S*,4*R*)-2-methyl-4-phenyl-4,5-dihydro-1,2 λ^6 ,3-oxathiazole 2-oxide (**258**) (0.173 g, 0.877 mmol) dissolved in THF (5 mL) and phenylmagnesium bromide (1.75 mL, 1.75 mmol, 1M). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0850 g, 35%); d.r.: 5:1 (**314**-**311**). Major diastereoisomer **314** matches NMR data for sulfoximine **265**; IR ν_{max} (cm⁻¹): 3434, 3060, 3025, 2927, 2866, 1491, 1445, 1403, 1353, 1310, 1223, 1127, 1085, 1066, 1028, 977, 854, 784, 743, 700, 688, 633, 527, 516; ¹H NMR (400 MHz, CDCl₃) δ 8.05-8.01 (2H, m, H-3 or H-4), 7.70-7.64 (1H, m, H-5), 7.63-7.58 (2H, m, H-3 or H-4), 7.48-7.43 (2H, m, H-9 or H-10), 7.39-7.32 (2H, m, H-9 or H-10), 7.31-7.25 (1H, m, H-11), 4.41 (1H, dd, *J* = 8.0, 4.5 Hz, H-6), 3.70 (1H, ddd, *J* = 10.5, 8.5, 4.5 Hz, H-7), 3.65-3.57 (1H, m, H-7), 3.05 (3H, s, H-1), 2.72 (1H, dd, *J* = 10.5, 4.5 Hz, OH); ¹³C NMR (101 MHz, CDCl₃) δ 142.4 (C-8), 139.8 (C-2), 133.3 (C-5), 129.5 (C-3 or C-4), 128.5 (C-3 or C-4 or C-9 or C-10), 128.4 (C-3 or C-4 or C-9 or C-10), 127.4 (C-11), 127.1 (C-9 or C-10), 69.1 (C-7), 60.90 (C-6), 44.5 (C-1); HRMS calculated for [C₁₅H₁₈NO₂S] [M + H]⁺ 276.1053, found 276.1067 / [C₁₅H₁₇NO₂SNa] [M + Na]⁺ 298.0872, found 298.0887.

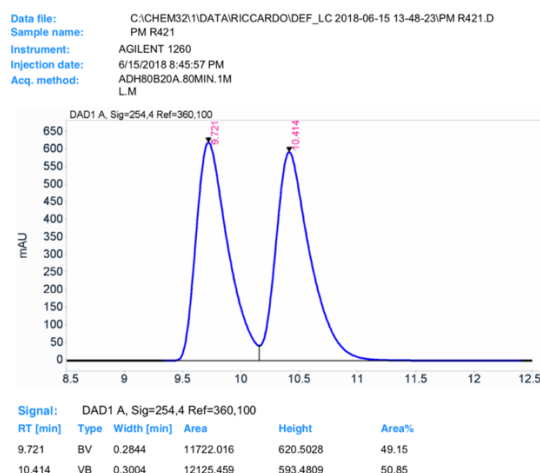
(*S*)-(((*R*)-2-Hydroxy-1-phenylethyl)imino)(methyl-*d*)(phenyl)- λ^6 -sulfanone (315)

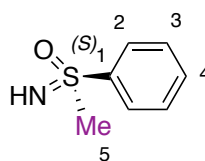


Following GP7, (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl-*d*)(phenyl)- λ^6 -sulfanone (**315**) was prepared from ((2*R*,4*R*)-2-methyl-4-phenyl-4,5-dihydro-1,2 λ^6 ,3-oxathiazole 2-oxide (**259**) (0.0619 g, 0.314 mmol) dissolved in THF (3 mL) and phenylmagnesium bromide (0.628 mL, 0.628 mmol, 1M). After completion, the reaction was quenched with CD₃OD. The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil; 3:1 ratio of deuterated-**315**:**311**; IR ν_{max} (cm⁻¹): 3392, 3060, 3025, 2925, 2865, 1492, 1476, 1446, 1392, 1357, 1222, 1128, 1084, 1068, 1028, 997, 746, 730, 701, 689, 633, 527, 516; ¹H NMR (400 MHz, CDCl₃) peaks match that found for **311** except; δ 3.21 (2H, t, J = 2.0 Hz, CH₂D); ¹³C NMR (101 MHz, CDCl₃) peaks match that found for **311** except; 45.8 (C-1) (t, J = 21.0 Hz); HRMS calculated for [C₁₅H₁₇DNO₂S] [M + H]⁺ 277.1116, found 277.1131 / [C₁₅H₁₆DNO₂SNa] [M + Na]⁺ 299.0935, found 299.0931.

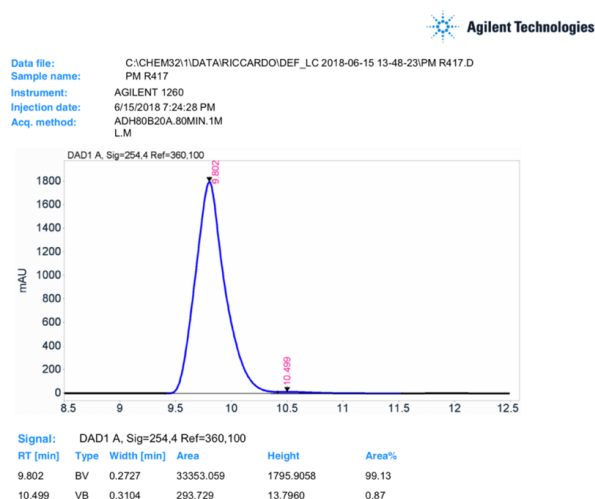
(±)-Imino(methyl)(phenyl)-λ⁶-sulfanone (321)¹¹⁰

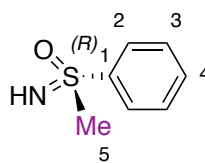
Following GP9, imino(methyl)(phenyl)-λ⁶-sulfanone (**321**) was prepared from methyl(phenyl)sulfane **320** (0.0427 g, 0.344 mmol), (diacetoxyiodo)benzene (0.277 g, 0.859 mmol) and ammonium carbamate (0.0537 g, 0.688 mmol) in methanol (0.7 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate to 9.5:0.5 DCM/MeOH) to afford the title compound as a colourless oil (0.0493 g, 92%); HPLC: Chiracel ADH, mobile phase: 80:20 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: 9.7 and 10.4 min, (49:51%); IR ν_{max} (cm⁻¹): 3258, 3061, 2926, 1710, 1582, 1445, 1409, 1320, 1215, 1095, 1008, 992, 951, 768, 740, 688, 523, 506; ¹H NMR (400 MHz, CDCl₃) δ 8.03-7.99 (2H, m, H-2 or H-3), 7.65-7.59 (1H, m, H-4), 7.58-7.52 (2H, m, H-2 or H-3), 3.11 (3H, s, H-5), 2.67 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 143.6 (C-1), 133.2 (C-4), 129.4 (C-2 or C-3), 127.8 (C-2 or C-3), 46.3 (C-5); HRMS calculated for [C₇H₁₀NOS] [M + H]⁺ 156.0478, found 156.0478 / [C₇H₉NOSNa] [M + Na]⁺ 178.0297, found 178.0294.



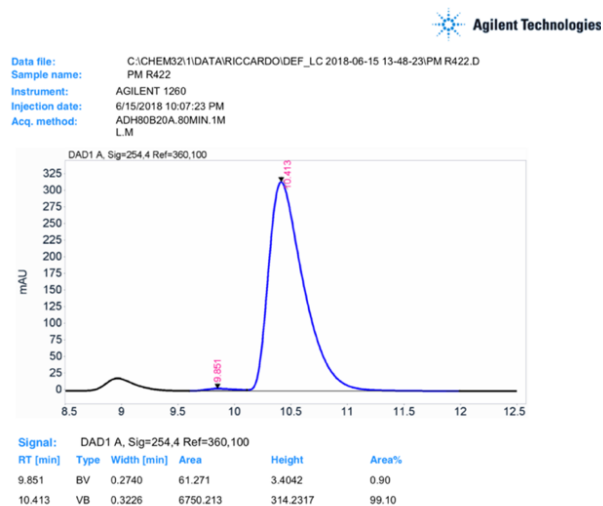
(*S*)-Imino(methyl)(phenyl)- λ^6 -sulfanone (316)¹⁴⁰

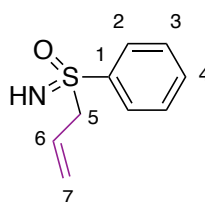
Following GP8, (*S*)-imino(methyl)(phenyl)- λ^6 -sulfanone (**316**) was prepared from (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ^6 -sulfanone (**284**) (0.0637 g, 0.231 mmol), NaOH (0.0925 g, 2.31 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate to 9.5:0.5 DCM/MeOH) to afford the title compound as colourless oil (0.0288 g, 80%); $[\alpha]_D^{23}$ 31.39 (c 0.075 CHCl₃); HPLC: Chiracel ADH, mobile phase: 80:20 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 9.8 min (99.1%), minor enantiomer = 10.5 min (0.9%), ee = 98%; IR $\nu_{\max}$ (cm⁻¹): 3263, 2924, 1476, 1445, 1409, 1320, 1215, 1096, 1028, 1009, 992, 767, 741, 688, 522, 506; ¹H NMR (400 MHz, CDCl₃) δ 8.03-7.99 (2H, m, H-2 or H-3), 7.65-7.59 (1H, m, H-4), 7.58-7.52 (2H, m, H-2 or H-3), 3.11 (3H, s, H-5), 2.67 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 143.6 (C-1), 133.2 (C-4), 129.4 (C-2 or C-3), 127.8 (C-2 or C-3), 46.3 (C-5); HRMS calculated for [C₇H₁₀NOS] [M + H]⁺ 156.0478, found 156.0479 / [C₇H₉NOSNa] [M + Na]⁺ 178.0297, found 178.0296.



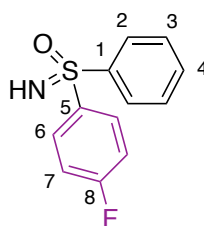
(*R*)-Imino(methyl)(phenyl)- λ^6 -sulfanone (319)¹⁴⁰

Following GP8, (*R*)-imino(methyl)(phenyl)- λ^6 -sulfanone (**319**) was prepared from (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(methyl)(phenyl)- λ^6 -sulfanone (**265**) (0.147 g, 0.534 mmol), NaOH (0.214 g, 5.34 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate to 9.5:0.5 DCM/MeOH) to afford the title compound as a colourless oil (0.0629 g, 76%); $[\alpha]_D^{29}$ -23.46 (c 0.31 CHCl₃); HPLC: Chiracel ADH, mobile phase: 80:20 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 10.4 min (99.1%), minor enantiomer = 9.9 min (0.9%), ee = 98%; IR $\nu_{\max}$ (cm⁻¹): 3265, 3060, 3017, 2926, 1707, 1645, 1582, 1476, 1445, 1409, 1320, 1215, 1095, 1029, 1008, 992, 950, 768, 739, 688, 523, 506; ¹H NMR (400 MHz, CDCl₃) δ 8.03-7.99 (2H, m, H-2 or H-3), 7.65-7.59 (1H, m, H-4), 7.58-7.52 (2H, m, H-2 or H-3), 3.11 (3H, s, H-5), 2.67 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 143.6 (C-1), 133.2 (C-4), 129.4 (C-2 or C-3), 127.8 (C-2 or C-3), 46.3 (C-5); HRMS calculated for [C₇H₁₀NOS] [M + H]⁺ 156.0478, found 156.0478 / [C₇H₉NOSNa] [M + Na]⁺ 178.0297, found 178.0294.

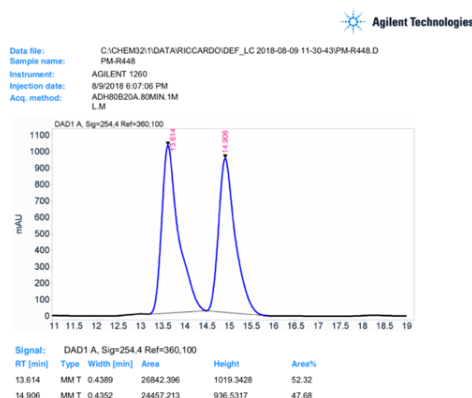


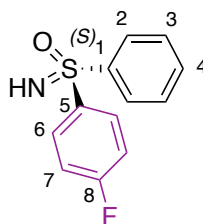
(±)-Allyl(imino)(phenyl)-λ⁶-sulfanone (361)⁶⁰

Following the procedure GP9, allyl(imino)(phenyl)-λ⁶-sulfanone (**361**) was prepared from allyl(phenyl)sulfane (0.500g, 3.33 mmol), (diacetoxyiodo)benzene (2.68 g, 8.32 mmol) and ammonium carbamate (0.520 g, 6.66 mmol) in methanol (7 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.545 g, 90%); IR ν_{max} (cm⁻¹): 3258, 1649, 1444, 1422, 1396, 1305, 1217, 1125, 1097, 1069, 983, 933, 868, 752, 688, 611, 507; ¹H NMR (400 MHz, CDCl₃) δ 7.97-7.92 (2H, m, H-2 or H-3), 7.64-7.58 (1H, m, H-4), 7.57-7.50 (2H, m, H-2 or H-3), 5.83 (1H, ddt, J = 17.5, 10.0, 7.5 Hz, H-6), 5.33 (1H, dt, J = 10.0, 1.0 Hz, H-7), 5.13 (1H, dq, J = 17.0, 1.5 Hz, H-7), 3.84 (2H, qdt, J = 13.5, 7.5, 1.0 Hz, H-5), (NH not observed); ¹³C NMR (101 MHz, CDCl₃) δ 141.0 (C-1), 133.3 (C-4), 129.1 (C-2 or C-3), 128.9 (C-2 or C-3), 125.5 (C-6), 124.5 (C-7), 62.6 (C-5); HRMS calculated for [C₉H₁₂NOS] [M + H]⁺ 182.0634, found 182.0635 / [C₉H₁₁NOSNa] [M + Na]⁺ 204.0454, found 204.0452.

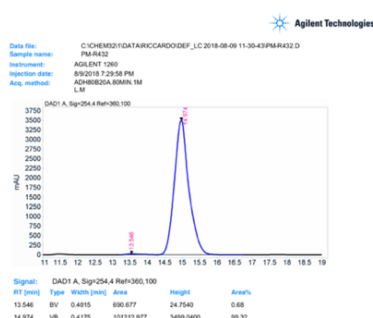
(±)-(4-Fluorophenyl)(imino)(phenyl)-λ⁶-sulfanone (365)

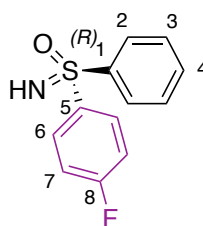
Following GP9, (4-fluorophenyl)(imino)(phenyl)-λ⁶-sulfanone (**365**) was prepared from (4-fluorophenyl)(phenyl)sulfane (0.579 g, 2.83 mmol), (diacetoxyiodo)benzene (2.28 g, 7.09 mmol) and ammonium carbamate (0.443 g, 5.67 mmol) in methanol (6 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.504 g, 76%); HPLC: Chiracel ADH, mobile phase: 80:20 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: 13.6 and 14.9 min (52:48); IR ν_{max} (cm⁻¹): 3267, 3098, 3063, 1586, 1488, 1445, 1401, 1226, 1154, 1129, 1093, 978, 837, 816, 754, 717, 702, 686, 643, 556, 534; ¹H NMR (400 MHz, CDCl₃) δ 8.08-8.04 (2H, m, H-6), 8.03-8.00 (2H, m, H-2 or H-3), 7.55-7.46 (3H, m, H-2,4 or H-3,4), 7.18-7.11 (2H, m, H-7), 3.05 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 165.3 (d, J = 255 Hz, C-8), 143.5 (C-1), 139.5 (d, J = 3.0 Hz, C-5), 132.8 (C-4), 130.9 (d, J = 9.0 Hz, C-6), 129.4 (C-2 or C-3), 127.9 (C-2 or C-3), 116.5 (d, J = 23.0 Hz, C-7); ¹⁹F NMR (376 MHz, CDCl₃) δ -105.8; HRMS calculated for [C₁₂H₁₁FNOS] [M + H]⁺ 236.0540, found 236.0540 / [C₁₂H₁₀FNOSNa] [M + Na]⁺ 258.0359, found 258.0357.



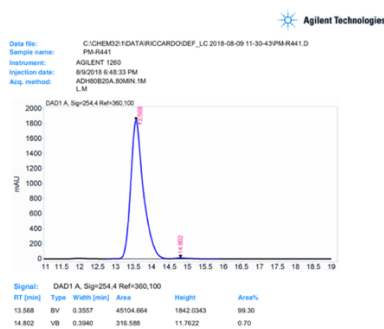
(*S*)-(4-Fluorophenyl)(imino)(phenyl)- λ^6 -sulfanone (332)

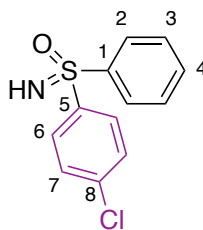
Following GP8, (*S*)-(4-fluorophenyl)(imino)(phenyl)- λ^6 -sulfanone (**332**) was prepared from (*S*)-(4-fluorophenyl)((*R*)-2-hydroxy-1-phenylethylimino)(phenyl)- λ^6 -sulfanone (**268**) (0.137 g, 0.387 mmol), NaOH (0.155 g, 3.87 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0747 g, 82%); $[\alpha]_D^{21}$ 7.36 (c 0.32 CHCl₃); HPLC: Chiracel ADH, mobile phase: 80:20 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 14.9 min (99.3%) minor enantiomer = 13.5 min (0.7%), ee = 98%; IR $\nu_{\max}$ (cm⁻¹): 3264, 3098, 3064, 1587, 1488, 1445, 1401, 1306, 1227, 1154, 1130, 1093, 1067, 977, 837, 817, 755, 717, 702, 687, 643, 643, 558, 534; ¹H NMR (400 MHz, CDCl₃) δ 8.08-8.04 (2H, m, H-6), 8.03-8.00 (2H, m, H-2 or H-3), 7.55-7.46 (3H, m, H-2,4 or H-3,4), 7.18-7.11 (2H, m, H-7), 3.05 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 165.3 (d, J = 255 Hz, C-8), 143.5 (C-1) 139.5 (d, J = 3.0 Hz, C-5), 132.8 (C-4), 130.9 (d, J = 9.0 Hz, C-6), 129.4 (C-2 or C-3), 127.9 (C-2 or C-3), 116.5 (d, J = 23.0 Hz, C-7); ¹⁹F NMR (376 MHz, CDCl₃) δ -105.8; HRMS calculated for [C₁₂H₁₁FNOS] [M + H]⁺ 236.0540, found 236.0540 / [C₁₂H₁₀FNOSNa] [M + Na]⁺ 258.0359, found 258.0356.



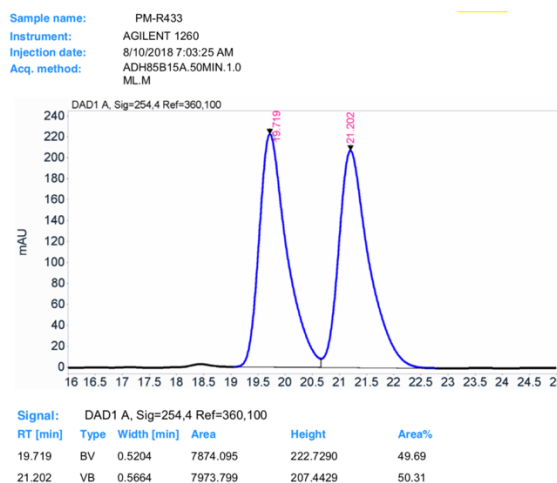
(*R*)-(4-Fluorophenyl)(imino)(phenyl)- λ^6 -sulfanone (346)

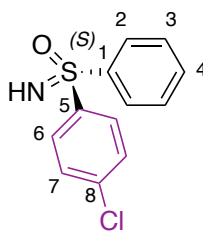
Following GP8, (*R*)-(4-fluorophenyl)(imino)(phenyl)- λ^6 -sulfanone (**346**) was prepared from (*R*)-(4-fluorophenyl)((*R*)-2-hydroxy-1-phenylethylimino)(phenyl)- λ^6 -sulfanone (**287**) (0.157 g, 0.442 mmol), NaOH (0.177 g, 4.42 mmol), dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0927 g, 89%); $[\alpha]_D^{21}$ 17.81 (c 0.14 CHCl₃); HPLC: Chiracel ADH, mobile phase: 80:20 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 13.5 min (99.3%), minor enantiomer = 14.8 min (0.7%), ee = 98%; IR $\nu_{\max}$ (cm⁻¹): 3256, 1618, 1875, 1489, 1445, 1401, 1229, 1155, 1130, 1094, 1066, 980, 838, 816, 755, 717, 702, 687, 643, 558, 535, 504; ¹H NMR (400 MHz, CDCl₃) δ 8.08-8.04 (2H, m, H-6), 8.03-8.00 (2H, m, H-2 or H-3), 7.55-7.46 (3H, m, H-2, 4 or H-3,4), 7.18-7.11 (2H, m, H-7), 3.05 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 165.4 (d, J = 255 Hz, C-8), 143.5 (C-1), 139.5 (d, J = 3.0 Hz, C-5), 132.9 (C-4), 130.9 (d, J = 9.5 Hz, C-6), 129.4 (C-2 or C-3), 128.0 (C-2 or C-3), 116.5 (d, J = 23.0 Hz, C-7); ¹⁹F NMR (376 MHz, CDCl₃) δ -105.8; HRMS calculated for [C₁₂H₁₁FNOS] [M + H]⁺ 236.0540, found 236.0546 / [C₁₂H₁₀FNOSNa] [M + Na]⁺ 258.0359, found 258.0360.



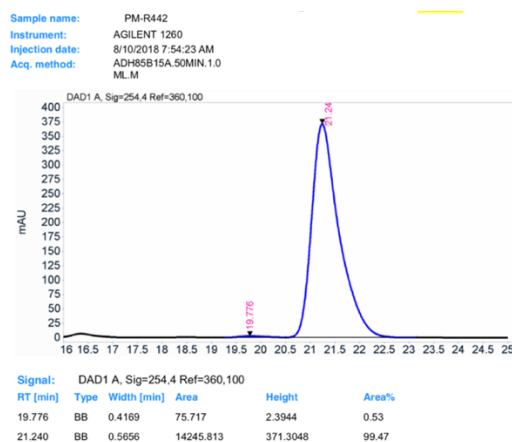
(±)-(4-Chlorophenyl)(imino)(phenyl)-λ⁶-sulfanone (364)¹⁴¹

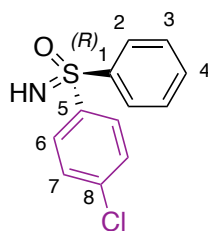
Following GP9, (4-chlorophenyl)(imino)(phenyl)-λ⁶-sulfanone (**364**) was prepared from (4-chlorophenyl)(phenyl)sulfane (0.735 g, 3.33 mmol), (diacetoxyiodo)benzene (2.68 g, 8.33 mmol) and ammonium carbamate (0.520 g, 6.66 mmol) in methanol (7 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as yellow oil (0.687 g, 82%); HPLC: Chiracel ADH, mobile phase: 85:15 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: 19.7 and 21.2 min (50:50); IR ν_{max} (cm⁻¹): 3261, 3085, 3065, 1576, 1473, 1445, 1391, 1333, 1231, 1160, 1130, 1093, 981, 827, 746, 712, 698, 686, 593, 545, 492; ¹H NMR δ 8.04-7.95 (4H, m, Ar), 7.56-7.42 (5H, m, Ar), 3.07 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 143.2 (C-1 or C-5 or C-8), 142.1 (C-1 or C-5 or C-8), 139.4 (C-1 or C-5 or C-8), 132.9 (C-4), 129.6 (Ar), 129.5 (Ar), 129.4 (Ar), 128.0 (Ar); HRMS calculated for [C₁₂H₁₁³⁵ClNOS] [M + H]⁺ 252.0244, found 252.0244 / [C₁₂H₁₀³⁵ClNOSNa] [M + Na]⁺ 274.0064, found 274.0063.



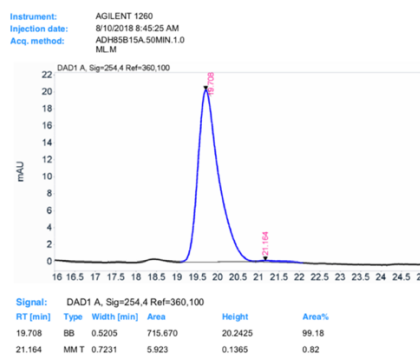
(*S*)-(4-Chlorophenyl)(imino)(phenyl)- λ^6 -sulfanone (333)

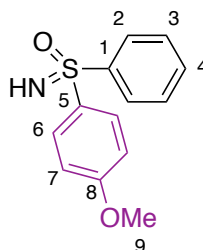
Following GP8, (*S*)-(4-chlorophenyl)(imino)(phenyl)- λ^6 -sulfanone (**333**) was prepared from (*S*)-(4-chlorophenyl)((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (**269**) (0.158 g, 0.424 mmol), NaOH (0.169 g, 4.24 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a pale yellow oil (0.0988 g, 93%); $[\alpha]_D^{21}$ 11.02 (c 0.49 CHCl₃); HPLC: Chiracel ADH, mobile phase: 85:15 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 21.2 min (99.5%), minor enantiomer = 19.8 min (0.5%), ee = 99%; IR ν_{max} (cm⁻¹): 3270, 1576, 1473, 1456, 1445, 1392, 1232, 1130, 1093, 975, 827, 746, 712, 697, 686, 594, 547, 493, 466; ¹H NMR δ 8.04-7.95 (4H, m, Ar), 7.56-7.42 (5H, m, Ar), 3.07 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 143.2 (C-1 or C-5 or C-8), 142.1 (C-1 or C-5 or C-8), 139.4 (C-1 or C-5 or C-8), 132.9 (C-4), 129.6 (Ar), 129.5 (Ar), 129.4 (Ar), 128.0 (Ar); HRMS calculated for [C₁₂H₁₁³⁵ClNOS] [M + H]⁺ 252.0244, found 252.0244 / [C₁₂H₁₀³⁵ClNOSNa] [M + Na]⁺ 274.0064, found 274.0063.



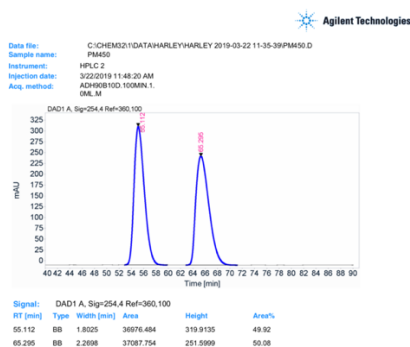
(*R*)-(4-Chlorophenyl)(imino)(phenyl)- λ^6 -sulfanone (347)

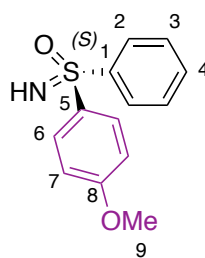
Following GP8, (*R*)-(4-chlorophenyl)(imino)(phenyl)- λ^6 -sulfanone (**347**) was prepared from (*R*)-(4-chlorophenyl)((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (**288**) (0.114 g 0.307 mmol), NaOH (0.123 g, 3.07 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a pale yellow oil (0.0705 g, 91%); $[\alpha]_D^{21}$ -11.77 (c 0.49 CHCl₃); HPLC: Chiracel ADH, mobile phase: 85:15 /isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 19.7 min (99.2%), minor enantiomer = 21.2 min (0.8%), ee = 98%; IR $\nu_{\max}$ (cm⁻¹): 3265, 1575, 1472, 1445, 1391, 1271, 1232, 1130, 1093, 1002, 979, 827, 746, 712, 687, 594, 545, 492, 450, 431; ¹H NMR δ 8.04-7.95 (4H, m, Ar), 7.56-7.42 (5H, m, Ar), 3.07 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 143.2 (C-1 or C-5 or C-8), 142.1 (C-1 or C-5 or C-8), 139.4 (C-1 or C-5 or C-8), 132.9 (C-4), 129.6 (Ar), 129.5 (Ar), 129.4 (Ar), 128.0 (Ar); HRMS calculated for [C₁₂H₁₁³⁵ClNOS] [M + H]⁺ 252.0244, found 252.0246 / [C₁₂H₁₀³⁵ClNOSNa] [M + Na]⁺ 274.0064, found 274.0063.



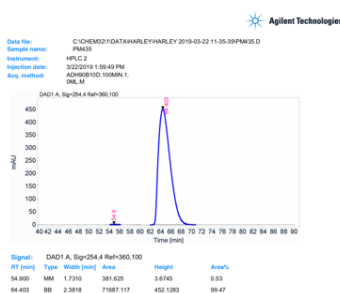
(±)-Imino(4-methoxyphenyl)(phenyl)-λ⁶-sulfanone (366)²⁵

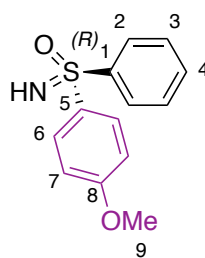
Following GP9, imino(4-methoxyphenyl)(phenyl)-λ⁶-sulfanone (**366**) was prepared from (4-methoxyphenyl)(phenyl)sulfane (0.829 g, 3.83 mmol), (diacetoxyiodo)benzene (3.08 g, 9.58 mmol) and ammonium carbamate (0.598 g, 7.66 mmol) in methanol (8 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.903 g, 95%); HPLC: Chiracel ADH, mobile phase: 90:10 isohexane/ethanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: 55.1 and 65.3 min (50:50); IR ν_{max} (cm⁻¹): 3264, 3060, 2839, 1591, 1577, 1493, 1460, 1443, 1410, 1308, 1255, 1223, 1174, 1126, 1094, 1021, 976, 833, 800, 755, 706, 688, 648, 626, 559, 541; ¹H NMR (400 MHz, CDCl₃) δ 8.03-7.99 (2H, m, H-2 or H-3), 7.98-7.95 (2H, m, H-6 or H-7), 7.53-7.42 (3H, m, H-2, 4 or H-3,4), 6.96-6.91 (2H, m, H-6 or H-7), 3.82 (3H, s, H-9), 2.98 (1H, s, OH); ¹³C NMR (101 MHz, CDCl₃) δ 163.1 (C-8), 144.3 (C-1), 134.9 (C-5), 132.4 (C-4), 130.3 (C-6 or C-7), 129.2 (C-2 or C-3), 127.7 (C-2 or C-3), 114.5 (C-6 or C-7), 55.7 (C-9); HRMS calculated for [C₁₃H₁₄NO₂S] [M + H]⁺ 248.0740, found 248.0743 / [C₁₃H₁₃NO₂SNa] [M + Na]⁺ 270.0559, found 270.0554.



(*S*)-Imino(4-methoxyphenyl)(phenyl)- λ^6 -sulfanone (334)

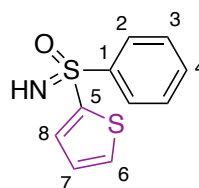
Following GP8, (*S*)-imino(4-methoxyphenyl)(phenyl)- λ^6 -sulfanone (**334**) was prepared from (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(4-methoxyphenyl)(phenyl)- λ^6 -sulfanone (**270**) (0.168 g, 0.457 mmol), NaOH (0.183 g, 4.57 mmol), dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.106 g, 94%); $[\alpha]_D^{21}$ -11.23 (c 0.635 CHCl₃); HPLC: Chiracel ADH, mobile phase: 90:10 isohexane/ethanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 64.4 min (99.5%), minor enantiomer = 54.9 min (0.5%), ee = 99%; IR $\nu_{\max}$ (cm⁻¹): 3272, 3062, 2839, 1592, 1577, 1493, 1444, 1410, 1308, 1256, 1225, 1174, 1127, 1094, 1022, 979, 833, 800, 756, 720, 706, 688, 665, 648, 626, 561, 542; ¹H NMR (400 MHz, CDCl₃) δ 8.03-7.99 (2H, m, H-2 or H-3), 7.98-7.95 (2H, m, H-6 or H-7), 7.53-7.42 (3H, m, H-2, 4 or H-3,4), 6.96-6.91 (2H, m, H-6 or H-7), 3.82 (3H, s, H-9), 2.98 (1H, s, OH); ¹³C NMR (101 MHz, CDCl₃) δ 163.1 (C-8), 144.3 (C-1), 134.9 (C-5), 132.4 (C-4), 130.3 (C-6 or C-7), 129.2 (C-2 or C-3), 127.7 (C-2 or C-3), 114.5 (C-6 or C-7), 55.7 (C-9); HRMS calculated for [C₁₃H₁₄NO₂S] [M + H]⁺ 248.0740, found 248.0749 / [C₁₃H₁₃NO₂SNa] [M + Na]⁺ 270.0559, found 270.0558.



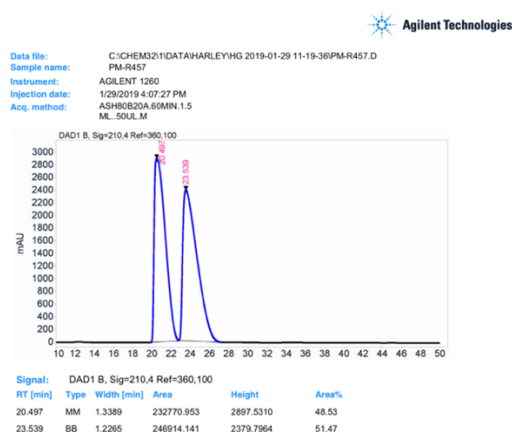
(*R*)-Imino(4-methoxyphenyl)(phenyl)-λ⁶-sulfanone (348)

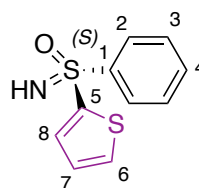
Following GP8, (*R*)-imino(4-methoxyphenyl)(phenyl)-λ⁶-sulfanone (**348**) was prepared from (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(4-methoxyphenyl)(phenyl)-λ⁶-sulfanone (**289**) (0.123 g, 0.335 mmol), NaOH (0.134 g, 3.35 mmol), dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0783 g, 95%); $[\alpha]_D^{21}$ 24.27 (c 0.1165 CHCl₃); HPLC: Chiracel ADH, mobile phase: 90:10 isohexane/ethanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 54.7 min (99.5%), minor enantiomer = 65.5 min (0.5%), ee = 99%; IR $\nu_{\max}$ (cm⁻¹): 3267, 3066, 2924, 2841, 1592, 1577, 1493, 1460, 1444, 1411, 1309, 1257, 1226, 1174, 1128, 1095, 1022, 981, 833, 800, 755, 720, 706, 688, 648, 627, 561, 542; ¹H NMR (400 MHz, CDCl₃) δ 8.03-7.99 (2H, m, H-2 or H-3), 7.98-7.95 (2H, m, H-6 or H-7), 7.53-7.42 (3H, m, H-2, 4 or H-3,4), 6.96-6.91 (2H, m, H-6 or H-7), 3.82 (3H, s, H-9), 2.98 (1H, s, OH); ¹³C NMR (101 MHz, CDCl₃) δ 163.1 (C-8), 144.3 (C-1), 134.9 (C-5), 132.4 (C-4), 130.3 (C-6 or C-7), 129.2 (C-2 or C-3), 127.7 (C-2 or C-3), 114.5 (C-6 or C-7), 55.7 (C-9); HRMS calculated for [C₁₃H₁₄NO₂S] [M + H]⁺ 248.0740, found 248.0748 / [C₁₃H₁₃NO₂SNa] [M + Na]⁺ 270.0559, found 270.0557.



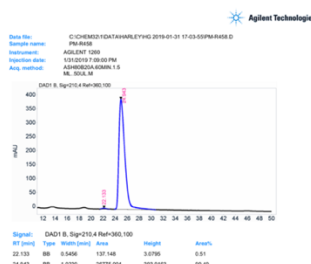
(±)-Imino(phenyl)(thiophen-2-yl)-λ⁶-sulfanone (359)

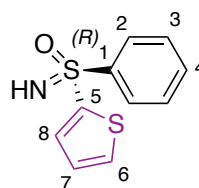
Following GP9, imino(phenyl)(thiophen-2-yl)-λ⁶-sulfanone (**359**) was prepared from 2-(phenylthio)thiophene (0.250 g, 1.30 mmol), (diacetoxyiodo)benzene (1.05 g, 3.25 mmol) and ammonium carbamate (0.203 g, 2.60 mmol) in methanol (3 mL). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.276 g, 95%); HPLC: Chiracel ASH, mobile phase: 80:20 isohexane/isopropanol, flow rate: 1.5 mL/min, $\lambda = 210$ nm, retention time: 20.5 and 23.5 min (49:51); IR ν_{max} (cm⁻¹): 3277, 3105, 3079, 1503, 1476, 1446, 1398, 1340, 1308, 1221, 1128, 1095, 1058, 1012, 963, 853, 756, 714, 683, 653, 579, 566, 532, 467; ¹H NMR (400 MHz, CDCl₃) δ 8.12-8.06 (2H, m, H-2 or H-3), 7.63 (1H, dd, $J = 4.0, 1.5$ Hz, H-6 or H-7 or H-8), 7.57 (1H, dd, $J = 5.0, 1.5$ Hz, H-6 or H-7 or H-8), 7.55-7.44 (3H, m, H-2,4 or H-3,4), 7.02 (1H, dd, $J = 5.0, 4.0$ Hz, H-6 or H-7 or H-8), 3.37 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 146.1 (C-5), 143.4 (C-1), 133.9 (C-6 or 7 or 8), 133.3 (C-6 or C-7 or C-8), 132.8 (C-6 or 7 or C-8), 129.2 (C-2 or C-3), 128.0 (C-4), 127.7 (C-2 or C-3); HRMS calculated for [C₁₀H₁₀NOS₂] [M + H]⁺ 224.0198, found 224.0199 / [C₁₀H₉NOS₂Na] [M + Na]⁺ 246.0018, found 246.0013.



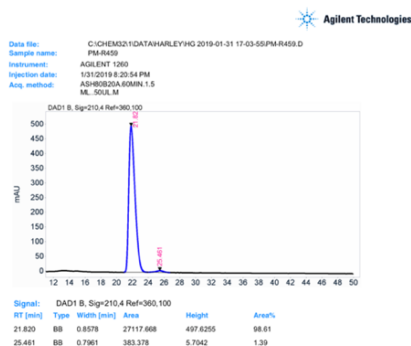
(*S*)-Imino(phenyl)(thiophen-2-yl)- λ^6 -sulfanone (335)

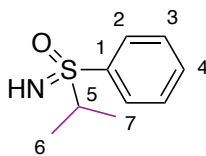
Following GP8, (*S*)-imino(phenyl)(thiophen-2-yl)- λ^6 -sulfanone (**335**) was prepared from (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)(thiophen-2-yl)- λ^6 -sulfanone (**271**) (0.0892 g, 0.260 mmol), NaOH (0.104 g, 2.60 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (6:4 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0318 g, 55%); $[\alpha]_D^{25}$ 140.35 (c 0.075 CHCl₃); HPLC: Chiracel ASH, mobile phase: 80:20 isohexane/isopropanol, flow rate: 1.5 mL/min, λ = 210 nm, retention time: major enantiomer = 24.9 min (99.5%), minor enantiomer = 22.1 min (0.5%), ee = 99%; IR $\nu_{\max}$ (cm⁻¹): 3263, 3088, 2922, 1445, 1401, 1342, 1236, 1127, 1094, 1060, 1014, 977, 853, 754, 715, 686, 654, 577, 563, 534; ¹H NMR (400 MHz, CDCl₃) δ 8.12-8.06 (2H, m, H-2 or H-3), 7.63 (1H, dd, J = 4.0, 1.5 Hz, H-6 or H-7 or H-8), 7.57 (1H, dd, J = 5.0, 1.5 Hz, H-6 or H-7 or H-8), 7.55-7.44 (3H, m, H-2,4 or H-3,4), 7.02 (1H, dd, J = 5.0, 4.0 Hz, H- H-6 or H-7 or H-8), 3.37 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 146.1 (C-5), 143.4 (C-1), 133.9 (C-6 or 7 or 8), 133.3 (C-6 or C-7 or C-8), 132.8 (C-6 or 7 or C-8), 129.2 (C-2 or C-3), 128.0 (C-4), 127.7 (C-2 or C-3); HRMS calculated for [C₁₀H₁₀NOS₂] [M + H]⁺ 224.0198, found 224.0205 / [C₁₀H₉NOS₂Na] [M + Na]⁺ 246.0018, found 246.0011.



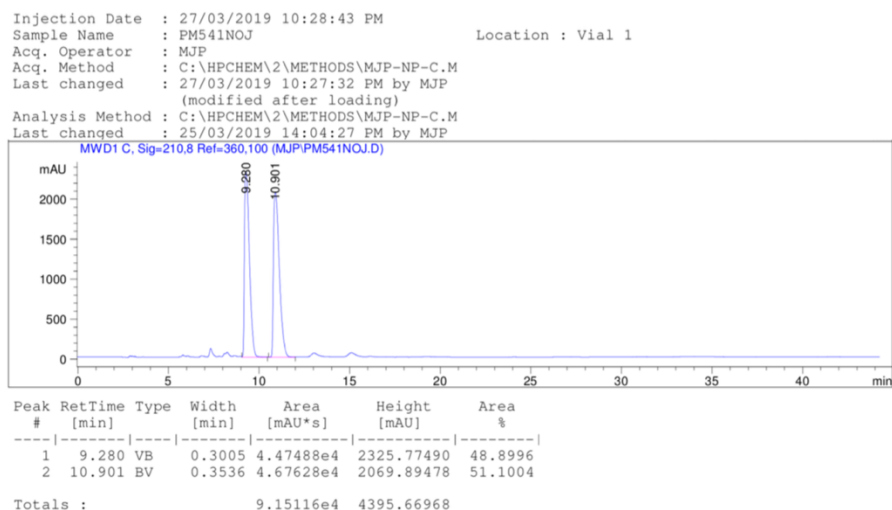
(*R*)-Imino(phenyl)(thiophen-2-yl)-λ⁶-sulfanone (349)

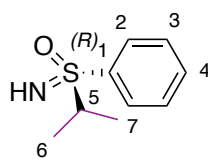
Following GP8, (*R*)-imino(phenyl)(thiophen-2-yl)-λ⁶-sulfanone (**349**) was prepared from (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)(thiophen-2-yl)-λ⁶-sulfanone (**290**) (0.0889 g, 0.259 mmol), NaOH (0.104 g, 2.59 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (6:4 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0287 g, 50%); $[\alpha]_D^{22}$ 70.93 (c 0.165 CHCl₃); HPLC: Chiracel ASH, mobile phase: 80:20 isohexane/isopropanol, flow rate: 1.5 mL/min, λ = 210 nm, retention time: major enantiomer = 21.8 min (98.6%), minor enantiomer = 25.5 min (1.4%), ee = 97%; IR $\nu_{\max}$ (cm⁻¹): 3280, 3104, 3080, 1502, 1492, 1476, 1446, 1399, 1341, 1223, 1128, 1095, 1059, 1013, 965, 853, 750, 714, 683, 671, 580, 564, 534; ¹H NMR (400 MHz, CDCl₃) δ 8.12-8.06 (2H, m, H-2 or H-3), 7.63 (1H, dd, *J* = 4.0, 1.5 Hz, H-6 or H-7 or H-8), 7.57 (1H, dd, *J* = 5.0, 1.5 Hz, H-6 or H-7 or H-8), 7.55-7.44 (3H, m, H-2,4 or H-3,4), 7.02 (1H, dd, *J* = 5.0, 4.0 Hz, H- H-6 or H-7 or H-8), 3.37 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 146.1 (C-5), 143.4 (C-1), 133.9 (C-6 or 7 or 8), 133.3 (C-6 or C-7 or C-8), 132.8 (C-6 or 7 or C-8), 129.2 (C-2 or C-3), 128.0 (C-4), 127.7 (C-2 or C-3); HRMS calculated for [C₁₀H₁₀NOS₂] [M + H]⁺ 224.0198, found 224.0215 / [C₁₀H₉NOS₂Na] [M + Na]⁺ 246.0018, found 246.0012.



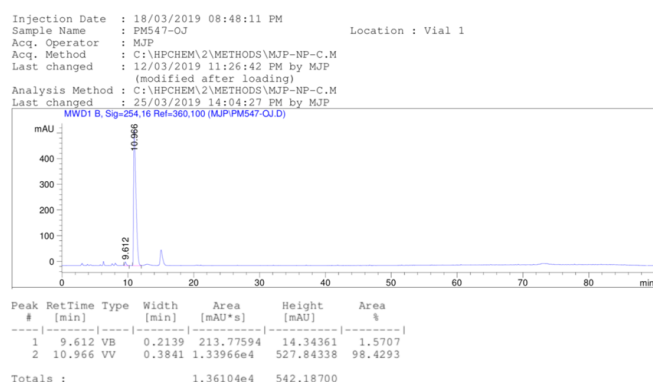
(±)-Imino(isopropyl)(phenyl)-λ⁶-sulfanone (369)¹⁴²

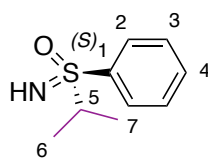
Following GP9, imino(isopropyl)(phenyl)-λ⁶-sulfanone (**369**) was prepared from isopropyl(phenyl)sulfane (0.477 g, 3.13 mmol), (diacetoxyiodo)benzene (2.52 g, 7.83 mmol) and ammonium carbamate (0.489 g, 6.26 mmol) in methanol (6.5 mL). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ether) to afford the title compound as a colourless oil (0.528 g, 92%); HPLC: Chiracel OJH, mobile phase: 85:15 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 210 nm, retention time: 9.28 and 10.9 min (49:51); IR ν_{max} (cm⁻¹): 3272, 3060, 2974, 2935, 1466, 1444, 1209, 1104, 1070, 1049, 971, 758, 714, 691, 649, 564, 548, 523, 435; ¹H NMR (400 MHz, CDCl₃) δ 7.97-7.90 (2H, m, H-2 or H-3), 7.65-7.58 (1H, m, H-4), 7.57-7.50 (2H, m, H-2 or H-3), 3.24 (1H, hept, *J* = 7.0 Hz, H-5), 2.61 (1H, s, NH), 1.31 (3H, d, *J* = 7.0 Hz, H-6 or H-7), 1.27 (3H, d, *J* = 7.0 Hz, H-6 or H-7); ¹³C NMR (101 MHz, CDCl₃) δ 139.9 (C-1), 133.1 (C-4), 129.5 (C-2 or C-3), 129.1 (C-2 or C-3), 56.6 (C-5), 16.5 (C-6 or C-7), 16.1 (C-6 or C-7); HRMS calculated for [C₉H₁₄NOS] [M + H]⁺ 184.0791, found 184.0781 / [C₉H₁₃NOSNa] [M + Na]⁺ 206.0610, found 206.0606.



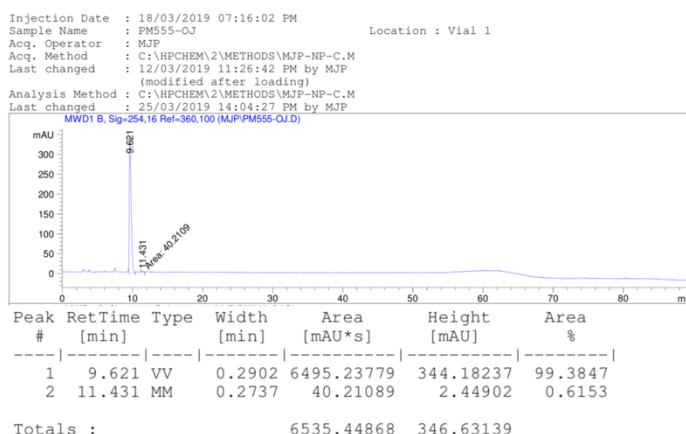
(*R*)-Imino(isopropyl)(phenyl)- λ^6 -sulfanone (336)

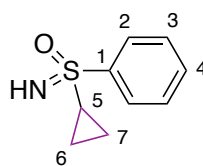
Following GP8, (*R*)-imino(isopropyl)(phenyl)- λ^6 -sulfanone (**336**) was prepared from (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(isopropyl)(phenyl)- λ^6 -sulfanone (**272**) (0.0997 g, 0.329 mmol), NaOH (0.131 g, 3.29 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate) to afford the title compound as colourless oil (0.0525 g, 87%); $[\alpha]_D^{22}$ -30.0 (c 0.60 CHCl₃); HPLC: Chiracel OJH, mobile phase: 85:15 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 10.9 min (98.4%), minor enantiomer = 9.62 min (1.6%), ee = 97%; IR $\nu_{\max}$ (cm⁻¹): 3263, 3060, 2974, 2933, 1466, 1444, 1384, 1365, 1209, 1125, 1103, 1070, 1049, 970, 878, 758, 714, 691, 648, 563, 547, 524, 449; ¹H NMR (400 MHz, CDCl₃) δ 7.97-7.90 (2H, m, H-2 or H-3), 7.65-7.58 (1H, m, H-4), 7.57-7.50 (2H, m, H-2 or H-3), 3.24 (1H, hept, *J* = 7.0 Hz, H-5), 2.61 (1H, s, NH), 1.31 (3H, d, *J* = 7.0 Hz, H-6 or H-7), 1.27 (3H, d, *J* = 7.0 Hz, H-6 or H-7); ¹³C NMR (101 MHz, CDCl₃) δ 139.9 (C-1), 133.1 (C-4), 129.5 (C-2 or C-3), 129.1 (C-2 or C-3), 56.6 (C-5), 16.5 (C-6 or C-7), 16.1 (C-6 or C-7); HRMS calculated for [C₉H₁₄NOS] [M + H]⁺ 184.0791, found 184.0802 / [C₉H₁₃NOSNa] [M + Na]⁺ 206.0610, found 206.0605.



(*S*)-Imino(isopropyl)(phenyl)- λ^6 -sulfanone (350)

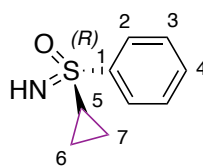
Following GP8, (*S*)-imino(isopropyl)(phenyl)- λ^6 -sulfanone (**350**) was prepared from (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(isopropyl)(phenyl)- λ^6 -sulfanone (**292**) (0.104 g, 0.343 mmol), NaOH (0.137 g, 3.43 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate) to afford the title compound as colourless oil (0.0563 g, 90%); $[\alpha]_D^{21}$ 17.7 (c 0.36 CHCl₃); HPLC: Chiracel OJH, Mobile phase: 85:15 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 9.62 min (99.4%), minor enantiomer = 11.4 min (0.6%), ee = 99%; IR $\nu_{\max}$ (cm⁻¹): 3266, 2972, 2929, 1466, 1444, 1384, 1259, 1211, 1104, 1070, 1050, 973, 758, 714, 691, 648, 564, 548, 524; ¹H NMR (400 MHz, CDCl₃) δ 7.97-7.90 (2H, m, H-2 or H-3), 7.65-7.58 (1H, m, H-4), 7.57-7.50 (2H, m, H-2 or H-3), 3.24 (1H, hept, *J* = 7.0 Hz, H-5), 2.61 (1H, s, NH), 1.31 (3H, d, *J* = 7.0 Hz, H-6 or H-7), 1.27 (3H, d, *J* = 7.0 Hz, H-6 or H-7); ¹³C NMR (101 MHz, CDCl₃) δ 139.9 (C-1), 133.1 (C-4), 129.5 (C-2 or C-3), 129.1 (C-2 or C-3), 56.6 (C-5), 16.5 (C-6 or C-7), 16.1 (C-6 or C-7); HRMS calculated for [C₉H₁₄NOS] [M + H]⁺ 184.0791, found 184.0799 / [C₉H₁₃NOSNa] [M + Na]⁺ 206.0610, found 206.0632.



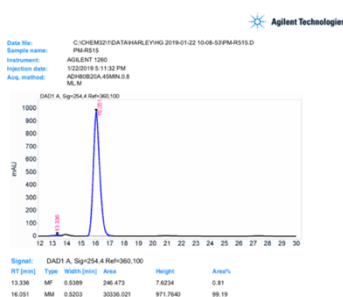
(±)-Cyclopropyl(imino)(phenyl)-λ⁶-sulfanone (362)¹⁴³

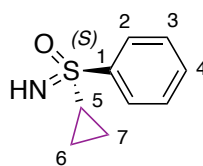
Following the procedure GP9, cyclopropyl(imino)(phenyl)-λ⁶-sulfanone (**362**) was prepared from cyclopropyl(phenyl)sulfane (0.500 g, 3.33 mmol), (diacetoxyiodo)benzene (2.68 g, 8.32 mmol) and ammonium carbamate (0.520 g, 6.66 mmol) in methanol (7 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.539 g, 89%); HPLC: Chiracel ADH, mobile phase: 80:20 isohexane/isopropanol, flow rate: 0.8 mL/min, λ = 254 nm, retention time: 13.3 and 16.0 min (50:50); IR ν_{max} (cm⁻¹): 3262, 3059, 3014, 1476, 1444, 1417, 1219, 1186, 1093, 1067, 1037, 975, 883, 826, 757, 689, 667, 560, 524; ¹H NMR (400 MHz, CDCl₃) δ 7.99-7.92 (2H, m, H-2 or H-3), 7.62-7.57 (1H, m, H-4), 7.56-7.50 (2H, m, H-2 or H-3), 2.69 (1H, s, NH), 2.59-2.49 (1H, m, H-5), 1.39 (1H, ddtd, J = 10.0, 6.5, 5.0, 1.5 Hz, H-6 or H-7), 1.18 (1H, ddtd, J = 10.0, 6.5, 5.0, 1.5 Hz, H-6 or H-7), 1.04 (1H, dddddd, J = 9.5, 8.0, 6.5, 5.0, 1.5 Hz, H-6 or H-7), 0.95-0.85 (1H, m, H-6 or H-7); ¹³C NMR (101 MHz, CDCl₃) δ 143.2 (C-1), 132.9 (C-4), 129.2 (C-2 or C-3), 128.0 (C-2 or C-3), 34.3 (C-5), 6.09 (C-6 or C-7), 5.72 (C-6 or C-7); HRMS calculated for [C₉H₁₂NOS] [M + H]⁺ 182.0634, found 182.0635 / [C₉H₁₁NOSNa] [M + Na]⁺ 204.0454, found 204.0456.

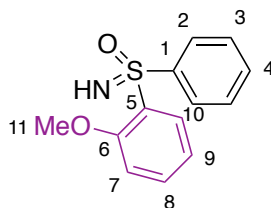


(*R*)-Cyclopropyl(imino)(phenyl)- λ^6 -sulfanone (337)¹⁴⁴

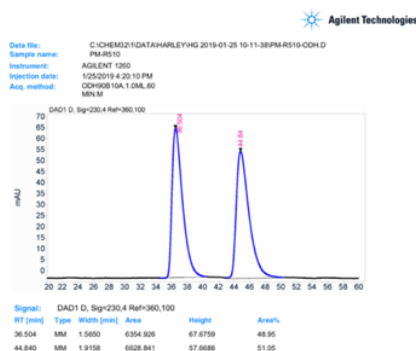
Following GP8, (*R*)-cyclopropyl(imino)(phenyl)- λ^6 -sulfanone (**337**) was prepared from (*R*)-cyclopropyl(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (**274**) (0.174 g, 0.577 mmol), NaOH (0.231 g, 5.77 mmol), dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0930 g, 89%); $[\alpha]_D^{22}$ 6.34 (c 2.24 CHCl₃); HPLC: Chiracel ADH, mobile phase: 80:20 isohexane/isopropanol, flow rate: 0.8 mL/min, λ = 254 nm, retention time: major enantiomer = 16.0 min (99.2%), minor enantiomer = 13.3 min (0.8%), ee = 98%; IR $\nu_{\max}$ (cm⁻¹): 3265, 3060, 3013, 1476, 1444, 1417, 1220, 1187, 1127, 1093, 1066, 1034, 976, 883, 826, 757, 716, 689, 669, 560, 524; ¹H NMR (400 MHz, CDCl₃) δ 7.99-7.92 (2H, m, H-2 or H-3), 7.62-7.57 (1H, m, H-4), 7.56-7.50 (2H, m, H-2 or H-3), 2.69 (1H, s, NH), 2.59-2.49 (1H, m, H-5), 1.39 (1H, ddtd, J = 10.0, 6.5, 5.0, 1.5 Hz, H-6 or H-7), 1.18 (1H, ddtd, J = 10.0, 6.5, 5.0, 1.5 Hz, H-6 or H-7), 1.04 (1H, dddddd, J = 9.5, 8.0, 6.5, 5.0, 1.5 Hz, H-6 or H-7), 0.95-0.85 (1H, m, H-6 or H-7); ¹³C NMR (101 MHz, CDCl₃) δ 143.2 (C-1), 132.9 (C-4), 129.2 (C-2 or C-3), 128.0 (C-2 or C-3), 34.3 (C-5), 6.09 (C-6 or C-7), 5.72 (C-6 or C-7); HRMS calculated for [C₉H₁₂NOS] [M + H]⁺ 182.0634, found 182.0642 / [C₉H₁₁NOSNa] [M + Na]⁺ 204.0454, found 204.0455.

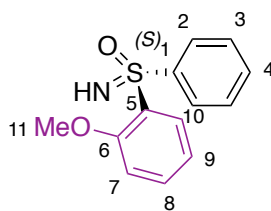


[illegible]

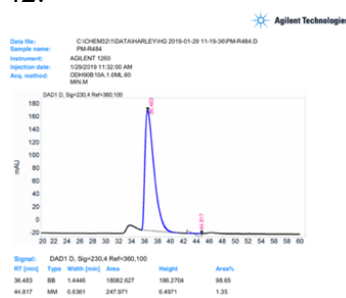
(±)-Imino(2-methoxyphenyl)(phenyl)-λ⁶-sulfanone (363)¹⁴¹

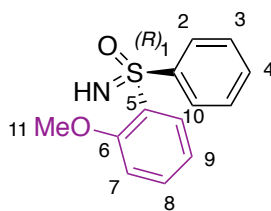
Following GP9, imino(2-methoxyphenyl)(phenyl)-λ⁶-sulfanone (**363**) was prepared from (2-methoxyphenyl)(phenyl)sulfane (0.746 g, 3.45 mmol), (diacetoxyiodo)benzene (2.78 g, 8.62 mmol) and ammonium carbamate (0.539 mmol, 6.90 mmol) in methanol (7 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.797 g, 93%); HPLC: Chiracel ODH, mobile phase: 90:10 isohexane/isopropanol, flow rate: 1.0 mL/min, $\lambda = 230$ nm, retention time: 36.5 and 44.8 min (49:51); IR ν_{max} (cm⁻¹): 3266, 3066, 2939, 2840, 1588, 1477, 1445, 1434, 1279, 1248, 1224, 1134, 1085, 1069, 1044, 1017, 973, 800, 756, 728, 712, 688, 569, 551, 530, 507; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (1H, dd, $J = 8.0, 1.5$ Hz, H-ArOMe), 8.05-8.01 (2H, m, H-2 or H-3), 7.55-7.50 (1H, m, H-ArOMe), 7.49-7.42 (3H, m, H-2,4 or H-3,4), 7.04 (1H, ddd, $J = 8.0, 7.5, 1.0$ Hz, H-ArOMe), 6.88 (1H, dd, $J = 8.0, 1.0$ Hz, H-ArOMe), 3.72 (3H, s, H-11), 3.01 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 156.8 (C-6), 142.6 (C-1), 134.7 (Ar-OMe), 132.5 (C-4), 131.2 (C-5), 129.4 (Ar-OMe), 128.7 (C-2 or C-3), 128.5 (C-2 or C-3), 120.5 (Ar-OMe), 112.7 (Ar-OMe), 55.9 (C-11); HRMS calculated for [C₁₃H₁₄NO₂S] [M + H]⁺ 248.0740, found 248.0749 / [C₁₃H₁₃NO₂SNa] [M + Na]⁺ 270.0559, found 270.0551.



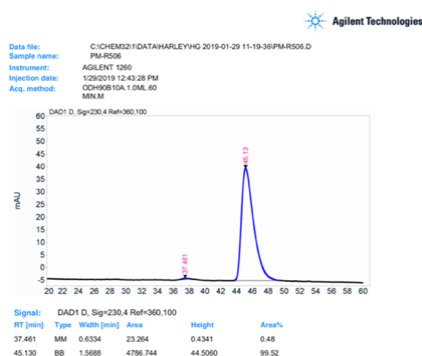
(*S*)-Imino(2-methoxyphenyl)(phenyl)- λ^6 -sulfanone (338)¹⁴⁵

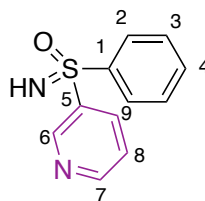
Following GP8, (*S*)-imino(2-methoxyphenyl)(phenyl)- λ^6 -sulfanone (**338**) was prepared from (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(2-methoxyphenyl)(phenyl)- λ^6 -sulfanone (**275**) (0.238 g, 0.648 mmol), NaOH (0.259 g, 6.48 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.137 g, 85%); $[\alpha]_D^{22}$ 22.95 (c 0.335 CHCl₃); HPLC: Chiracel ODH, mobile phase: 90:10 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 230 nm, retention time: major enantiomer = 36.5 min (98.7%), minor enantiomer = 44.8 min (1.3%), ee = 97%; IR $\nu_{\max}$ (cm⁻¹): 3265, 3064, 2938, 2839, 1588, 1477, 1445, 1433, 1279, 1248, 1224, 1134, 1085, 1069, 1043, 1017, 974, 800, 756, 729, 712, 688, 569, 551, 530; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (1H, dd, *J* = 8.0, 1.5 Hz, H-ArOMe), 8.05-8.01 (2H, m, H-2 or H-3), 7.55-7.50 (1H, m, H-ArOMe), 7.49-7.42 (3H, m, H-2,4 or H-3,4), 7.04 (1H, ddd, *J* = 8.0, 7.5, 1.0 Hz, H-ArOMe), 6.88 (1H, dd, *J* = 8.0, 1.0 Hz, H-ArOMe), 3.72 (3H, s, H-11), 3.01 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 156.8 (C-6), 142.6 (C-1), 134.7 (Ar-OMe), 132.5 (C-4), 131.2 (C-5), 129.4 (Ar-OMe), 128.7 (C-2 or C-3), 128.5 (C-2 or C-3), 120.5 (Ar-OMe), 112.7 (Ar-OMe), 55.9 (C-11); HRMS calculated for [C₁₃H₁₄NO₂S] [M + H]⁺ 248.0740, found 248.0742.



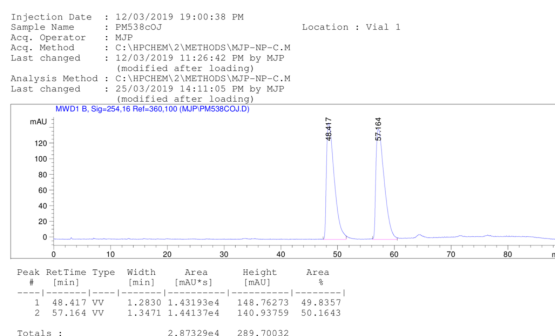
(*R*)-Imino(2-methoxyphenyl)(phenyl)- λ^6 -sulfanone (352)

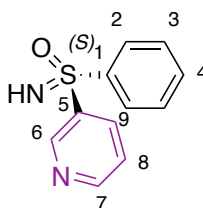
Following GP8, (*R*)-imino(2-methoxyphenyl)(phenyl)- λ^6 -sulfanone (**352**) was prepared from (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(2-methoxyphenyl)(phenyl)- λ^6 -sulfanone (**294**) (0.217 g, 0.591 mmol), NaOH (0.236 g, 5.91 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.109 g, 75%); $[\alpha]_D^{23}$ 59.5 (c 0.10 CHCl₃); HPLC: Chiracel ODH, mobile phase: 90:10 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 230 nm, retention time: major enantiomer = 45.1 min (99.5%), minor enantiomer = 37.5 min (0.5%), ee = 99%; IR $\nu_{\max}$ (cm⁻¹): 3277, 3063, 2925, 2849, 1589, 1477, 1434, 1279, 1248, 1226, 1134, 1085, 1018, 970, 800, 756, 713, 688, 570, 550, 532, 517, 429; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (1H, dd, J = 8.0, 1.5 Hz, H-ArOMe), 8.05-8.01 (2H, m, H-2 or H-3), 7.55-7.50 (1H, m, H-ArOMe), 7.49-7.42 (3H, m, H-2,4 or H-3,4), 7.04 (1H, ddd, J = 8.0, 7.5, 1.0 Hz, H-ArOMe), 6.88 (1H, dd, J = 8.0, 1.0 Hz, H-ArOMe), 3.72 (3H, s, H-11), 3.01 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 156.8 (C-6), 142.6 (C-1), 134.7 (Ar-OMe), 132.5 (C-4), 131.2 (C-5), 129.4 (Ar-OMe), 128.7 (C-2 or C-3), 128.5 (C-2 or C-3), 120.5 (Ar-OMe), 112.7 (Ar-OMe), 55.9 (C-11); HRMS calculated for [C₁₃H₁₄NO₂S] [M + H]⁺ 248.0740, found 248.0753.



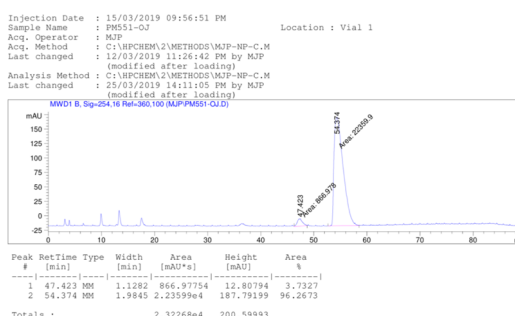
(±)-Imino(phenyl)(pyridin-3-yl)-λ⁶-sulfanone (368)

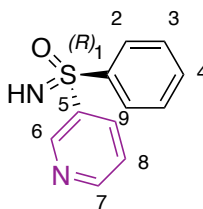
Following GP9, imino(phenyl)(pyridin-3-yl)-λ⁶-sulfanone (**368**) was prepared from 3-(phenylthio)pyridine (0.285 g, 1.52 mmol), (diacetoxyiodo)benzene (1.22 g, 3.80 mmol) and ammonium carbamate (0.237 g, 3.04 mmol) in methanol (3 mL). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ether to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a colourless oil (0.205 g, 62%); HPLC: Chiracel OJH, mobile phase: gradient 0-50 min, 85:15 – 50-70 min 75:25 isohexane/isopropanol, flow rate: 1.0 mL/min, $\lambda = 254$ nm, retention time: 48.4 and 57.2 min (50:50); IR ν_{max} (cm⁻¹): 3250, 3058, 1571, 1468, 1444, 1414, 1330, 1233, 1194, 1136, 1096, 1069, 975, 821, 734, 702, 686, 617, 572, 542, 462, 424; ¹H NMR (400 MHz, CDCl₃) δ 9.17 (1H, dd, $J = 2.5, 1.0$ Hz, H-py), 8.67 (1H, dd, $J = 5.0, 1.5$ Hz, H-py), 8.26 (1H, ddd, $J = 8.0, 2.5, 1.5$ Hz, H-py), 8.04-7.97 (2H, m, H-2 or H-3), 7.54-7.42 (3H, m, H-2,4 or H-3,4), 7.36 (1H, ddd, $J = 8.0, 5.0, 1.0$ Hz, H-py), 3.38 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 152.9 (C-py), 148.9 (C-py), 142.6 (C-1), 139.9 (C-5), 135.5 (C-py), 133.0 (C-4), 129.3 (C-2 or C-3), 127.9 (C-2 or C-3), 123.6 (C-py); HRMS calculated for [C₁₁H₁₁N₂OS] [M + H]⁺ 219.0587, found 219.0599 / [C₁₁H₁₀N₂OSNa] [M + Na]⁺ 241.0406, found 241.0399.



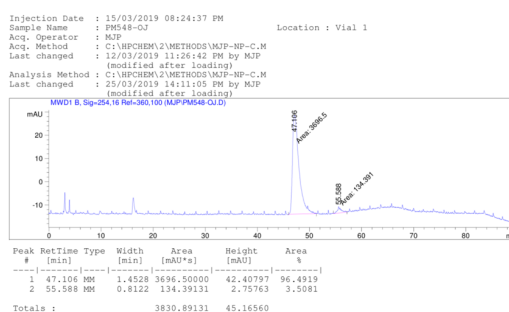
(*S*)-Imino(phenyl)(pyridin-3-yl)- λ^6 -sulfanone (339)

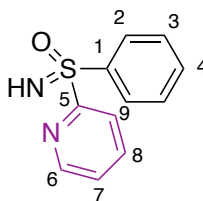
Following GP8, (*S*)-imino(phenyl)(pyridin-3-yl)- λ^6 -sulfanone (**339**) was prepared from (*S*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)(pyridin-3-yl)- λ^6 -sulfanone **276** (0.0777 g, 0.230 mmol), NaOH (0.0918 g, 2.30 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate to 100% ethyl acetate) to afford the title compound as a colourless oil (0.0319, 64%); $[\alpha]_D^{22}$ 7.88 (c 0.91 CHCl₃); HPLC: Chiracel OJH, mobile phase: gradient 0-50 min, 85:15 – 50-70 min 75:25 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 54.4 min (96.3%), minor enantiomer = 47.4 min (3.7%), ee = 93%; IR $\nu_{\max}$ (cm⁻¹): 3262, 3061, 2923, 1571, 1464, 1445, 1413, 1235, 1192, 1136, 1100, 982, 807, 759, 736, 702, 687, 618, 573, 545; ¹H NMR (400 MHz, CDCl₃) δ 9.17 (1H, dd, J = 2.5, 1.0 Hz, H-py), 8.67 (1H, dd, J = 5.0, 1.5 Hz, H-py), 8.26 (1H, ddd, J = 8.0, 2.5, 1.5 Hz, H-py), 8.04-7.97 (2H, m, H-2 or H-3), 7.54-7.42 (3H, m, H-2,4 or H-3,4), 7.36 (1H, ddd, J = 8.0, 5.0, 1.0 Hz, H-py), 3.38 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 152.9 (C-py), 148.9 (C-py), 142.6 (C-1), 139.9 (C-5), 135.5 (C-py), 133.0 (C-4), 129.3 (C-2 or C-3), 127.9 (C-2 or C-3), 123.6 (C-py); HRMS calculated for [C₁₁H₁₁N₂OS] [M + H]⁺ 219.0587, found 219.0600 / [C₁₁H₁₀N₂OSNa] [M + Na]⁺ 241.0406, found 241.0415.



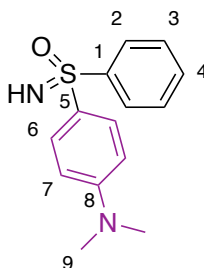
(*R*)-Imino(phenyl)(pyridin-3-yl)- λ 6-sulfanone (353)

Following GP8, (*R*)-imino(phenyl)(pyridin-3-yl)- λ 6-sulfanone (**353**) was prepared from (*R*)-(((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)(pyridin-3-yl)- λ 6-sulfanone (**295**) (0.0585 g, 0.173 mmol), NaOH (0.0691 g, 1.73 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ethyl acetate to 100% ethyl acetate) to afford the title compound as a colourless oil (0.0251 g, 67%); $[\alpha]_D^{21}$ 38.3 (c 0.215 CHCl₃); HPLC: Chiracel OJH, mobile phase: gradient 0-50 min, 85:15 – 50-70 min 75:25 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 47.1 min (96.5%), minor enantiomer = 55.6 min (3.5%), ee = 93%; IR $\nu_{\max}$ (cm⁻¹): 3264, 3060, 2922, 1572, 1464, 1445, 1414, 1319, 1236, 1193, 1137, 1100, 983, 807, 759, 736, 702, 687, 618, 574, 546; ¹H NMR (400 MHz, CDCl₃) δ 9.17 (1H, dd, *J* = 2.5, 1.0 Hz, H-py), 8.67 (1H, dd, *J* = 5.0, 1.5 Hz, H-py), 8.26 (1H, ddd, *J* = 8.0, 2.5, 1.5 Hz, H-py), 8.04-7.97 (2H, m, H-2 or H-3), 7.54-7.42 (3H, m, H-2,4 or H-3,4), 7.36 (1H, ddd, *J* = 8.0, 5.0, 1.0 Hz, H-py), 3.38 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 152.9 (C-py), 148.9 (C-py), 142.6 (C-1), 139.9 (C-5), 135.5 (C-py), 133.0 (C-4), 129.3 (C-2 or C-3), 127.9 (C-2 or C-3), 123.6 (C-py); HRMS calculated for [C₁₁H₁₁N₂OS] [M + H]⁺ 219.0587, found 219.0597.

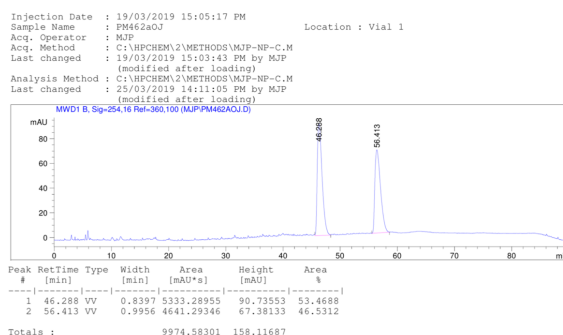


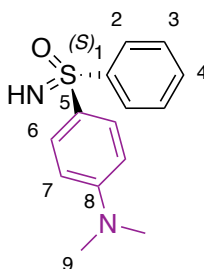
(±)-Imino(phenyl)(pyridin-2-yl)-λ⁶-sulfanone (367)¹⁴⁶

Following GP9, imino(phenyl)(pyridin-2-yl)-λ⁶-sulfanone (**367**) was prepared from 2-(phenylthio)pyridine (0.499 g, 2.66 mmol), (diacetoxyiodo)benzene (2.15 g, 6.66 mmol) and ammonium carbamate (0.416 g, 5.33 mmol) in methanol (5.5 mL). The crude mixture was purified by flash chromatography (4:6 petroleum ether/ether to 9.5:0.5 dichloromethane/methanol) to afford the title compound as a colourless oil (0.406 g, 70%); IR ν_{max} (cm⁻¹): 3262, 3059, 1575, 1475, 1446, 1423, 1229, 1135, 1117, 1105, 1086, 1066, 1043, 987, 969, 910, 776, 757, 729, 702, 686, 645, 616, 570, 543; ¹H NMR (400 MHz, CDCl₃) δ 8.54 (1H, ddd, J = 4.5, 1.5, 1.0 Hz, H-py), 8.12 (1H, dt, J = 8.0, 1.0 Hz, H-py), 8.07-8.02 (2H, m, H-2 or H-3), 7.78 (1H, td, J = 7.5, 1.5 Hz, H-py), 7.48-7.43 (1H, m, H-4), 7.42-7.37 (2H, m, H-2 or H-3), 7.31 (1H, ddd, J = 7.5, 4.5, 1.0 Hz, H-py), 3.37 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 160.1 (C-5), 150.0 (C-py), 140.5 (C-1), 138.0 (C-py), 133.0 (C-4), 128.90 (C-2 or C-3), 128.86 (C-2 or C-3), 126.3 (C-py), 122.2 (C-py); HRMS calculated for [C₁₁H₁₁N₂OS] [M + H]⁺ 219.0587, found 219.0604 / [C₁₁H₁₀N₂OSNa] [M + Na]⁺ 241.0406, found 241.0403.

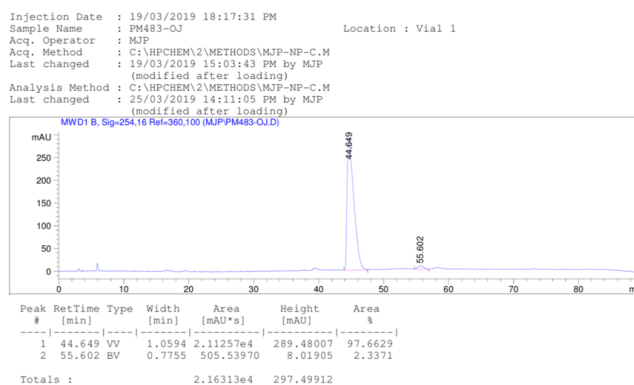
(±)-(4-(Dimethylamino)phenyl)(imino)(phenyl)-λ⁶-sulfanone (360)

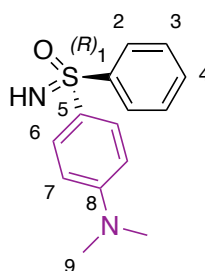
Following GP9, (4-(dimethylamino)phenyl)(imino)(phenyl)-λ⁶-sulfanone (**360**) was prepared from *N,N*-dimethyl-4-(phenylthio)aniline (0.396 g, 1.73 mmol), (diacetoxyiodo)benzene (1.39 g, 4.31 mmol) and ammonium carbamate (0.269 g, 3.45 mmol) in methanol (3.5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ ethyl acetate) to afford the title compound as a yellow oil (0.271 g, 60%); HPLC: Chiracel OJH, mobile phase: gradient 0-20 min, 80:20 – 20-60 min, 60:40 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: 46.3 and 56.4 min (53:47); IR ν_{max} (cm⁻¹): 3276, 2922, 2343, 1594, 1515, 1444, 1369, 1225, 1125, 1095, 1065, 1004, 976, 816, 754, 703, 689, 675, 628, 557, 536, 511; ¹H NMR (400 MHz, CDCl₃) δ 8.02-7.96 (2H, m, H-2 or H-3), 7.86-7.81 (2H, m, H6 or H-7), 7.45-7.38 (3H, m, H-2,4 or H-3,4), 6.66-6.61 (2H, m, H-6 or H-7), 2.99 (6H, s, H-9), 2.70 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 152.9 (C-8), 145.0 (C-1), 131.9 (C-4), 129.8 (C-6 or C-7), 129.0 (C-2 or C-3), 128.1 (C-5), 127.3 (C-2 or C-3), 111.2 (C-6 or C-7), 40.1 (C-9); HRMS calculated for [C₁₄H₁₇N₂OS] [M + H]⁺ 261.1056, found 261.1058 / [C₁₄H₁₆N₂OSNa] [M + Na]⁺ 283.0876, found 283.0888.



(*S*)-(4-(Dimethylamino)phenyl)(imino)(phenyl)- λ^6 -sulfanone (341)

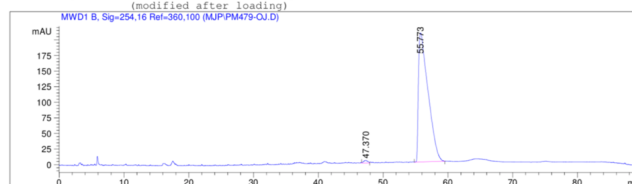
Following GP8, (*S*)-(4-(dimethylamino)phenyl)(imino)(phenyl)- λ^6 -sulfanone (**341**) was prepared from (*S*)-(4-(dimethylamino)phenyl)((*R*)-2-hydroxyphenylethylimino)(phenyl)- λ^6 -sulfanone (**279**) (0.217 g, 0.571 mmol), NaOH (0.228 g, 5.71 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a pale yellow oil (0.0881 g, 59%); $[\alpha]_D^{23}$ -14.93 (c 1.345 CHCl₃); HPLC: Chiracel OJH, mobile phase: gradient 0-20 min, 80:20 – 20-60 min, 60:40 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 44.6 min (97.7%), minor enantiomer = 55.6 min (2.3%), ee = 95%; IR $\nu_{\max}$ (cm⁻¹): 3332, 3252, 3061, 2912, 2817, 1589, 1552, 1514, 1476, 1444, 1369, 1222, 1121, 1092, 1068, 1002, 969, 818, 755, 688, 628, 549, 537; ¹H NMR (400 MHz, CDCl₃) δ 8.02-7.96 (2H, m, H-2 or H-3), 7.86-7.81 (2H, m, H-6 or H-7), 7.45-7.38 (3H, m, H-2,4 or H-3,4), 6.66-6.61 (2H, m, H-6 or H-7), 2.99 (6H, s, H-9), 2.70 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 152.9 (C-8), 145.0 (C-1), 131.9 (C-4), 129.8 (C-6 or C-7), 129.0 (C-2 or C-3), 128.1 (C-5), 127.3 (C-2 or C-3), 111.2 (C-6 or C-7), 40.1 (C-9); HRMS calculated for [C₁₄H₁₇N₂OS] [M + H]⁺ 261.1056, found 261.1063 / [C₁₄H₁₆N₂OSNa] [M + Na]⁺ 283.0876, found 283.0873.



(*R*)-(4-(Dimethylamino)phenyl)(imino)(phenyl)- λ^6 -sulfanone (355)

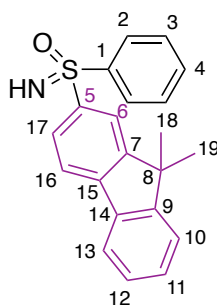
Following GP8, (*R*)-(4-(dimethylamino)phenyl)(imino)(phenyl)- λ^6 -sulfanone (**355**) was prepared from (*R*)-(4-(dimethylamino)phenyl)((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (**298**) (0.213 g, 0.560 mmol), NaOH (0.224 g, 5.60 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford the title compound as a pale yellow oil (0.0730 g, 50%); $[\alpha]_D^{23}$ 14.98 (c 1.045 CHCl₃); HPLC: Chiracel OJH, mobile phase: gradient 0-20 min, 80:20 – 20-60 min, 60:40 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 55.8 min (99.1%), minor enantiomer = 47.4 min (0.9%), ee = 98%; IR $\nu_{\max}$ (cm⁻¹): 3270, 2921, 2366, 1594, 1515, 1444, 1369, 1225, 1125, 1095, 1004, 977, 815, 769, 754, 703, 689, 629, 557, 536; ¹H NMR (400 MHz, CDCl₃) δ 8.02-7.96 (2H, m, H-2 or H-3), 7.86-7.81 (2H, m, H6 or H-7), 7.45-7.38 (3H, m, H-2,4 or H-3,4), 6.66-6.61 (2H, m, H-6 or H-7), 2.99 (6H, s, H-9), 2.70 (1H, s, NH); ¹³C NMR (101 MHz, CDCl₃) δ 152.9 (C-8), 145.0 (C-1), 131.9 (C-4), 129.8 (C-6 or C-7), 129.0 (C-2 or C-3), 128.1 (C-5), 127.3 (C-2 or C-3), 111.2 (C-6 or C-7), 40.1 (C-9); HRMS calculated for [C₁₄H₁₇N₂OS] [M + H]⁺ 261.1056, found 261.1060 / [C₁₄H₁₆N₂OSNa] [M + Na]⁺ 283.0876, found 283.0870.

Injection Date : 19/03/2019 16:42:36 PM Location : Vial 1
 Sample Name : PM479-OJ
 Acq. Operator : MJP
 Acq. Method : C:\HPCHEM\2\METHODS\MJP-NP-C.M
 Last changed : 19/03/2019 15:03:43 PM by MJP
 (modified after loading)
 Analysis Method : C:\HPCHEM\2\METHODS\MJP-NP-C.M
 Last changed : 25/03/2019 14:11:05 PM by MJP
 (modified after loading)



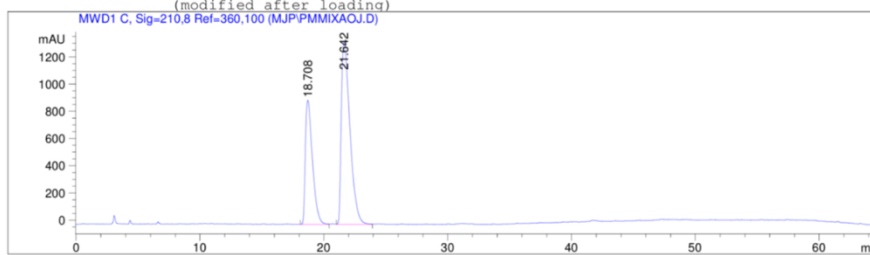
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	47.370	VV	0.5624	194.57408	4.16965	0.9035
2	55.773	VB	1.3962	2.13400e4	206.75011	99.0965

Totals : 2.15346e4 210.91975

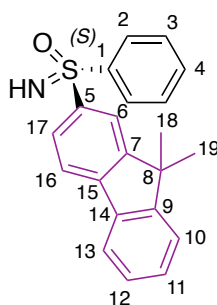
(±)-(9,9-Dimethyl-9*H*-fluoren-2-yl)(imino)(phenyl)-λ⁶-sulfanone

A combined mixture of enantiomers **342** and **356** was mixed to validate the racemic samples for HPLC analysis. HPLC: Chiracel OJH, mobile phase: 90:10 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 210 nm, retention time: 18.7 and 21.6 min (36:64).

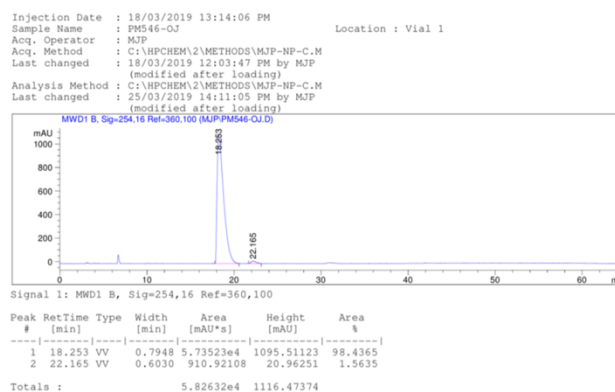
Injection Date : 18/03/2019 12:07:04 PM
 Sample Name : PMmixaOJ Location : Vial 1
 Acq. Operator : MJP
 Acq. Method : C:\HPCHEM\2\METHODS\MJP-NP-C.M
 Last changed : 18/03/2019 12:03:47 PM by MJP
 (modified after loading)
 Analysis Method : C:\HPCHEM\2\METHODS\MJP-NP-C.M
 Last changed : 25/03/2019 14:11:05 PM by MJP
 (modified after loading)

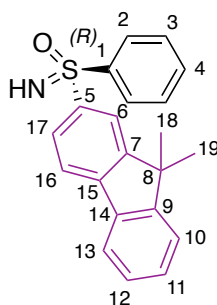


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.708	BV	0.6112	3.61868e4	911.48102	35.7198
2	21.642	VB	0.7404	6.51207e4	1346.19788	64.2802
Totals :				1.01308e5	2257.67889	

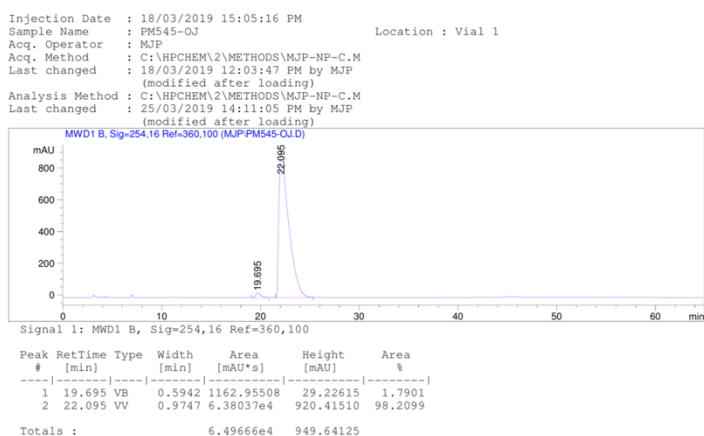
(*S*)-(9,9-Dimethyl-9*H*-fluoren-2-yl)(imino)(phenyl)- λ^6 -sulfanone (342)

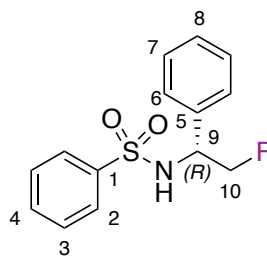
Following GP8, (*S*)-(9,9-dimethyl-9*H*-fluoren-2-yl)(imino)(phenyl)- λ^6 -sulfanone (**342**) was prepared from (*S*)-(9,9-dimethyl-9*H*-fluoren-2-yl)((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (**278**) (0.0548 g, 0.121 mmol), NaOH (0.0483 g, 1.21 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0263 g, 65%); $[\alpha]_D^{22}$ 3.89 (c 0.285 CHCl₃); HPLC: Chiracel OJH, mobile phase: 90:10 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 18.3 min (98.4%), minor enantiomer = 22.2 min (1.6%), ee = 97%; IR $\nu_{\max}$ (cm⁻¹): 3312, 3270, 3060, 2960, 2940, 1600, 1470, 1444, 1407, 1227, 1157, 1127, 1097, 1067, 1001, 908, 834, 782, 757, 736, 710, 687, 660, 616, 575, 560, 520; ¹H NMR (400 MHz, CDCl₃) δ 8.14-8.12 (1H, m, Ar), 8.10-8.06 (2H, m, Ar), 8.00 (1H, dd, *J* = 8.0, 2.0 Hz, Ar), 7.80-7.76 (1H, m, Ar), 7.75-7.72 (1H, m, Ar), 7.53-7.43 (4H, m, Ar), 7.41-7.33 (2H, m, Ar), 3.07 (1H, s, NH), 1.49 (6H, s, H-18, 19); ¹³C NMR (101 MHz, CDCl₃) δ 154.7 (Ar), 154.6 (Ar), 144.0 (Ar), 143.9 (Ar), 141.7 (Ar), 137.4 (Ar), 132.6 (Ar), 129.3 (Ar), 129.0 (Ar), 127.9 (Ar), 127.7 (Ar), 127.5 (Ar), 123.0 (Ar), 122.4 (Ar), 121.1 (Ar), 120.5 (Ar), 47.4 (C-8), 27.02 (C-18 or C-19), 26.98 (C-18 or C-19); HRMS calculated for [C₂₁H₂₀NOS] [M + H]⁺ 334.1260, found 334.1279 / [C₂₁H₁₉NOSNa] [M + Na]⁺ 356.1080, found 356.1077.



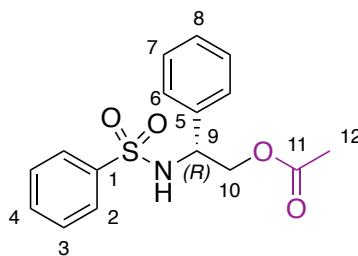
(*R*)-(9,9-Dimethyl-9*H*-fluoren-2-yl)(imino)(phenyl)- λ^6 -sulfanone (356)

Following GP8, (*R*)-(9,9-dimethyl-9*H*-fluoren-2-yl)(imino)(phenyl)- λ^6 -sulfanone (**356**) was prepared from (*R*)-(9,9-dimethyl-9*H*-fluoren-2-yl)((*R*)-2-hydroxy-1-phenylethyl)imino)(phenyl)- λ^6 -sulfanone (**297**) (0.0404 g, 0.0891 mmol), NaOH (0.0356 g, 0.891 mmol) dissolved in MTBE (5 mL). The crude mixture was purified by flash chromatography (7:3 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0215 g, 72%); $[\alpha]_D^{22}$ 26.6 (c 0.196 CHCl₃); HPLC: Chiracel OJH, mobile phase: 90:10 isohexane/isopropanol, flow rate: 1.0 mL/min, λ = 254 nm, retention time: major enantiomer = 22.1 min (98.2%), minor enantiomer = 19.7 min (1.8%), ee = 96%; IR $\nu_{\max}$ (cm⁻¹): 3294, 3063, 2960, 2923, 1470, 1444, 1407, 1228, 1134, 1097, 1068, 979, 835, 812, 782, 737, 709, 687, 660, 616, 576, 559, 519, 429; ¹H NMR (400 MHz, CDCl₃) δ 8.14–8.12 (1H, m, Ar), 8.10–8.06 (2H, m, Ar), 8.00 (1H, dd, *J* = 8.0, 2.0 Hz, Ar), 7.80–7.76 (1H, m, Ar), 7.75–7.72 (1H, m, Ar), 7.53–7.43 (4H, m, Ar), 7.41–7.33 (2H, m, Ar), 3.07 (1H, s, NH), 1.49 (6H, s, H-18, 19); ¹³C NMR (101 MHz, CDCl₃) δ 154.7 (Ar), 154.6 (Ar), 144.0 (Ar), 143.9 (Ar), 141.7 (Ar), 137.4 (Ar), 132.6 (Ar), 129.3 (Ar), 129.0 (Ar), 127.9 (Ar), 127.7 (Ar), 127.5 (Ar), 123.0 (Ar), 122.4 (Ar), 121.1 (Ar), 120.5 (Ar), 47.4 (C-8), 27.02 (C-18 or C-19), 26.98 (C-18 or C-19); HRMS calculated for [C₂₁H₂₀NOS] [M + H]⁺ 334.1260, found 334.1274.

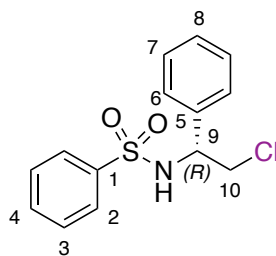


(*R*)-*N*-(2-Fluoro-1-phenylethyl)benzenesulfonamide (371)

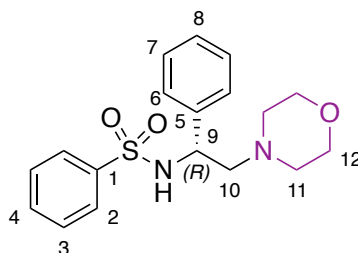
To a solution of sulfonimide **254** (0.0319 g, 0.123 mmol) in dry THF (2 mL), TBAF trihydrate (0.0776 g, 0.246 mmol) was added in portions. The reaction was stirred for 48 h at rt. The reaction was monitored by TLC, after completion, the solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography (8:2 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0155 g, 45%); IR ν_{max} (cm⁻¹): 3267, 2957, 1447, 1322, 1157, 1091, 1057, 1010, 965, 883, 753, 721, 688, 635, 590, 545; ¹H NMR (400 MHz, CDCl₃) δ 7.75-7.70 (2H, m, H-2 or H-3), 7.52-7.44 (1H, m, H-4), 7.37 (2H, dd, J = 8.5, 7.0 Hz, H-2 or H-3), 7.23-7.18 (3H, m, H-6, 8 or H-7,8), 7.12 (2H, td, J = 5.0, 4.5, 3.0 Hz, H-6 or H-7), 5.59 (1H, d, J = 7.0 Hz, NH), 4.69-4.61 (1H, m, H-9), 4.60-4.52 (1H, m, H-10), 4.50-4.41 (1H, m, H-10); ¹³C NMR (101 MHz, CDCl₃) δ 140.3 (C-1), 136.0 (d, J = 4.0 Hz, C-5), 132.7 (C-4), 129.0 (C-2 or C-3), 128.8 (C-6 or C-7), 128.4 (C-8), 127.2 (C-6 or C-7 or C-2 or C-3), 127.16 (C-6 or C-7 or C-2 or C-3), 84.9 (d, J = 178 Hz, C-10), 57.7 (d, J = 20.0 Hz, C-9); ¹⁹F NMR (376 MHz, CDCl₃) δ -183.1; HRMS calculated for [C₁₄H₁₅FNO₂S] [M + H]⁺ 280.0802, found 280.0802 / [C₁₄H₁₄FNO₂SNa] [M + Na]⁺ 302.0621, found 302.0621.

(R)-2-Phenyl-2-(phenylsulfonamido)ethyl acetate (372)

A solution of sulfonimide **254** (0.0501 g, 0.193 mmol) in anhydrous DMF (2 mL) was added anhydrous NaOAc (0.0317 g, 0.386 mmol) at rt. TMSCF₃ (0.145 mL, 0.290 mmol, 2M in THF) was added to the mixture after 5 min stirring. After sulfonimide was consumed as indicated by TLC, the resulting mixture was poured into water and extracted with DCM (3 ×). The combined organic phase was dried over anhydrous MgSO₄ and the solvent was removed under reduced pressure. The crude mixture was purified by flash chromatography (8:2 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0318 g, 52%); IR ν_{max} (cm⁻¹): 3270, 2255, 1734, 1447, 1431, 1384, 1325, 1230, 1160, 1091, 1042, 967, 907, 728, 699, 688, 648, 586, 546; ¹H NMR (400 MHz, CDCl₃) δ 7.76-7.72 (2H, m, H-2 or H-3), 7.52-7.47 (1H, m, H-4), 7.42-7.36 (2H, m, H-2 or H-3), 7.25-7.20 (3H, m, H-6,8 or H-7,8), 7.16-7.12 (2H, m, H-6 or H-7), 5.50 (1H, d, J = 7.0 Hz, NH), 4.69 (1H, td, J = 7.0, 4.5 Hz, H-9), 4.29-4.14 (2H, m, H-10), 1.96 (3H, s, H-12); ¹³C NMR (101 MHz, CDCl₃) δ 171.0 (C-11), 140.6 (C-1), 137.0 (C-5), 132.6 (C-4), 129.0 (C-2 or C-3), 128.8 (C-6 or C-7), 128.3 (C-8), 127.1 (C-2 or C-3 or C-6 or C-7), 126.9 (C-2 or C-3 or C-6 or C-7), 66.6 (C-10), 57.1 (C-9), 20.8 (C-12); HRMS calculated for [C₁₆H₁₈NO₄S] [M + H]⁺ 320.0951, found 320.0953 / [C₁₆H₁₇NO₄SNa] [M + Na]⁺ 342.0770, found 342.0754.

(*R*)-*N*-(2-Chloro-1-phenylethyl)benzenesulfonamide (374)¹⁴⁷

To a solution of sulfonimide **254** (0.0620 g, 0.239 mmol) in dry THF (2 mL), lithium chloride (0.0203 g, 0.478 mmol) dissolved in isopropyl alcohol (0.5 mL) was added dropwise. The reaction was stirred for 72 h at rt. The reaction was monitored by TLC, after completion, the solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography (8:2 petroleum ether/ethyl acetate) to afford the title compound as a pale yellow oil (0.0314 g, 44%); IR ν_{max} (cm⁻¹): 3270, 3064, 3032, 2957, 2922, 1447, 1425, 1324, 1157, 1091, 1070, 1032, 951, 909, 754, 721, 688, 616, 584, 547; ¹H NMR (400 MHz, CDCl₃) δ 7.79-7.73 (2H, m, H-2 or H-3), 7.57-7.51 (1H, m, H-4), 7.42 (2H, td, J = 7.5, 1.5 Hz, H-2 or H-3), 7.27-7.22 (3H, m, H-6, 8 or H-7,8), 7.16-7.11 (2H, m, H-6 or H-7), 5.38 (1H, d, J = 6.5 Hz, NH), 4.68-4.61 (1H, m, H-9), 3.75 (2H, dd, J = 6.0, 1.5 Hz, H-10); ¹³C NMR (101 MHz, CDCl₃) δ 140.0 (C-1), 137.1 (C-5), 132.8 (C-4), 129.0 (C-2 or C-3), 128.7 (C-6 or C-7), 128.4 (C-8), 127.1 (C-2 or C-3), 126.9 (C-6 or C-7), 58.4 (C-9), 48.0 (C-10); HRMS calculated for [C₁₄H₁₅³⁵ClNO₂S] [M + H]⁺ 296.0507, found 296.0501 / [C₁₄H₁₄³⁵ClNO₂SNa] [M + Na]⁺ 318.0326, found 318.1332.

(*R*)-*N*-(2-Morpholino-1-phenylethyl)benzenesulfonamide (376)

To a solution of sulfonimide **254** (0.0539 g, 0.208 mmol) in dry THF (3 mL), morpholine (0.0362 g, 0.416 mmol) was added. After 5 min, the reaction mixture was heated to 40 °C and stirred for 48 h at this temperature. The reaction was monitored by TLC, after completion, the solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography (8:2 petroleum ether/ethyl acetate) to afford the title compound as a colourless oil (0.0627 g, 87%); IR ν_{max} (cm⁻¹): 3240, 3064, 2946, 2855, 2815, 2252, 1511, 1494, 1447, 1397, 1327, 1157, 1115, 1092, 1067, 1008, 953, 910, 867, 754, 726, 689, 646, 596, 576, 550, 525, 455; ¹H NMR (400 MHz, CDCl₃) δ 7.72-7.68 (2H, m, H-2 or H-3), 7.50-7.45 (1H, m, H-4), 7.37 (2H, dd, J = 8.5, 7.0 Hz, H-2 or H-3), 7.23-7.16 (5H, m, H-6, 7, 8), 5.95 (1H, s, NH), 4.23 (1H, dd, J = 11.0, 4.5 Hz, H-9), 3.64-3.51 (4H, m, H-12), 2.47-2.31 (2H, m, H-10), 2.25 (4H, q, J = 4.5 Hz, H-11); ¹³C NMR (101 MHz, CDCl₃) δ 139.7 (C-1), 139.0 (C-5), 132.5 (C-4), 128.8 (C-2 or C-3), 128.4 (C-6 or C-7), 127.8 (C-8), 127.3 (C-2 or C-3), 127.1 (C-6 or C-7), 66.8 (C-12), 64.0 (C-10), 54.3 (C-9), 52.9 (C-11); HRMS calculated for [C₁₈H₂₃N₂O₃S] [M + H]⁺ 347.1424, found 347.1461 / [C₁₈H₂₂N₂O₃SNa] [M + Na]⁺ 369.1243, found 369.1242.

7.0 References

- 1 H. R. Bentley, E. E. McDermott, J. Pace, J. K. Whitehead and T. Moran, *Nature*, 1949, **163**, 675–676.
- 2 H. R. Bentley, E. E. McDermott, J. Pace, J. K. Whitehead and T. Moran, *Nature*, 1950, **165**, 150–151.
- 3 H. R. Bentley, E. E. McDermott and J. K. Whitehead, *Nature*, 1950, **165**, 735.
- 4 J. V. Andersen, L. F. McNair, A. Schousboe and H. S. Waagepetersen, *J. Neurosci. Res.*, 2017, **95**, 2207–2216.
- 5 W. S. A. Brusilow, *Neurosci. Lett.*, 2017, **647**, 165–167.
- 6 M. Feary, A. J. Racher, R. J. Young and C. M. Smales, *Biotechnol. Prog.*, 2017, **33**, 17–25.
- 7 W. L. Mock and J. T. Tsay, *J. Am. Chem. Soc.*, 1989, **111**, 4467–4472.
- 8 M. Reggelin and C. Zur, *Synthesis*, 2000, 1–64.
- 9 M. Frings, I. Thomé, I. Schiffers, F. Pan and C. Bolm, *Chem. Eur. J.*, 2014, **20**, 1691–1700.
- 10 M. Kahraman, S. Sinishtaj, P. M. Dolan, T. W. Kensler, S. Peleg, U. Saha, S. S. Chuang, G. Bernstein, B. Korczak and G. H. Posner, *J. Med. Chem.*, 2004, **47**, 6854–6863.
- 11 U. Lücking, M. Krüger, R. Jautelat, G. Siemeister. *Sulfoximine-substituted pyrimidines for use as CDK and/or VEGF inhibitors, the production thereof and their use as drugs*, WO 2005/037800 A1, 12th October 2004.
- 12 U. Lücking, R. Jautelat, M. Krüger, T. Brumby, P. Lienau, M. Schäfer, H. Briem, J. Schulze, A. Hillisch, A. Reichel, A. M. Wengner and G. Siemeister, *ChemMedChem*, 2013, **8**, 1067–1085.
- 13 K. M. Foote, J. W. M. Nissink, P. Turner. *Morpholino pyrimidines and their*

- use in therapy*, WO 2011/154737 A1, 9th June 2011.
- 14 J. X. Huang, Y. Zhu, R. B. Rogers, M. R. Loso, R. L. Hill, J. D. Thomas, T. Meade, J. M. Gifford, J. J. Demark and B. M. Nugent. *Use of N-substituted sulfoximines for control of invertebrate pests*, WO 2008/057130 A1, 9th February 2007.
- 15 A. Jeanguenat and A. C. O'Sullivan. *Novel Insecticides*, WO 2006/032462 A1, 20th September 2005.
- 16 C. Gnamm, A. Jeanguenat, A. C. Dutton, C. Grimm, D. P. Kloer and A. J. Crossthwaite, *Bioorganic Med. Chem. Lett.*, 2012, **22**, 3800–3806.
- 17 A. Plant, E. J. Boehmer, A. L. Peace. *Isoxazoline derivatives and their use as herbicides*, WO 2006/037945, 15th September 2005.
- 18 V. Bizet, R. Kowalczyk and C. Bolm, *Chem. Soc. Rev.*, 2014, **43**, 2426–2438.
- 19 U. Lücking, *Angew. Chem. Int. Ed.*, 2013, **52**, 9399–9408.
- 20 H. Okamura and C. Bolm, *Chem. Lett.*, 2004, **33**, 482–487.
- 21 V. Bizet, C. M. M. Hendriks and C. Bolm, *Chem. Soc. Rev.*, 2015, **44**, 3378–3390.
- 22 X. Shen and J. Hu, *Eur. J. Org. Chem.*, 2014, **2014**, 4437–4451.
- 23 M. Zenzola, R. Doran, R. Luisi and J. A. Bull, *J. Org. Chem.*, 2015, **80**, 6391–6399.
- 24 M. Zenzola, R. Doran, L. Degennaro, R. Luisi and J. A. Bull, *Angew. Chem. Int. Ed.*, 2016, **55**, 7203–7207.
- 25 T. Siu and A. K. Yudin, *Org. Lett.*, 2002, **4**, 1839–1842.
- 26 C. S. Tomooka and E. M. Carreira, *Helv. Chim. Acta*, 2002, **85**, 3773–3784.
- 27 C. Bolm and H. Okamura, *Org. Lett.*, 2004, **6**, 1305–1307.
- 28 J. Wang, M. Frings and C. Bolm, *Chem. Eur. J.*, 2014, **20**, 966–969.

- 29 O. G. Mancheño and C. Bolm, *Org. Lett.*, 2006, **8**, 2349–2352.
- 30 V. Bizet, L. Buglioni and C. Bolm, *Angew. Chem. Int. Ed.*, 2014, **53**, 5639–5642.
- 31 S. Schäfer and T. Wirth, *Angew. Chem. Int. Ed.*, 2010, **49**, 2786–2789.
- 32 C. R. Johnson and R. A. Kirchhoff, *J. Org. Chem.*, 1979, **44**, 2280.
- 33 O. G. Mancheño, O. Bistri and C. Bolm, *Org. Lett.*, 2007, **9**, 3809–3811.
- 34 H. Lebel, H. Piras and J. Bartholoméüs, *Angew. Chem. Int. Ed.*, 2014, **53**, 7300–7304.
- 35 A. Tota, M. Zenzola, S. J. Chawner, S. St John-Campbell, C. Carlucci, G. Romanazzi, L. Degennaro, J. A. Bull and R. Luisi, *Chem. Commun.*, 2017, **53**, 348–351.
- 36 J. K. Whitehead and H. R. Bentley, *J. Chem. Soc.*, 1952, **0**, 1572–1574.
- 37 C. R. Johnson, M. Haake and C. W. Schroeck, *J. Org. Chem.*, 1970, **92**, 6594–6598.
- 38 P. Stoss and G. Satzinger, *Angew. Chem.*, 1971, **83**, 83–84.
- 39 P. Stoss and G. Satzinger, *Angew. Chem. Int. Ed.*, 1971, **10**, 76.
- 40 R. H. Rynbrandt and D. P. Balgoyen, *J. Org. Chem.*, 1978, **43**, 1824–1825.
- 41 J. Wiss, C. Fleury, C. Heuberger, U. Onken and M. Glor, *Org. Process Res. Dev.*, 2007, **11**, 1096–1103.
- 42 H. Kwart and A. A. Kahn, *J. Am. Chem. Soc.*, 1967, **89**, 1950–1951.
- 43 J. F. K. Müller and P. Vogt, *Tetrahedron Lett.*, 1998, **39**, 4805–4806.
- 44 E. Lacôte, M. Amatore, L. Fensterbank and M. Malacria, *Synlett*, 2002, 116–118.
- 45 O. G. Mancheño and C. Bolm, *Chem. Eur. J.*, 2007, **13**, 6674–6681.
- 46 T. Bach and C. Körber, *Eur. J. Org. Chem.*, 1999, **1999**, 1033–1039.
- 47 G. Y. Cho and C. Bolm, *Org. Lett.*, 2005, **7**, 4983–4985.

- 48 B. Gutmann, P. Elsner, A. O’Kearney-McMullan, W. Goundry, D. M. Roberge and C. O. Kappe, *Org. Process Res. Dev.*, 2015, **19**, 1062–1067.
- 49 H. Lebel, H. Piras and M. Borduy, *ACS Catal.*, 2016, **6**, 1109–1112.
- 50 Y. Tamura, K. Sumoto, J. Minamikawa and M. Ikeda, *Tetrahedron Lett.*, 1972, **13**, 4137–4140.
- 51 C. R. Johnson, R. A. Kirchhoff and H. G. Corkins, *J. Org. Chem.*, 1974, **39**, 2458–2459.
- 52 T. L. Gilchrist and C. J. Moody, *Chem. Rev.*, 1977, **77**, 409–435.
- 53 H. R. Bentley and J. K. Whitehead, *J. Chem. Soc.*, 1950, **0**, 2081–2082.
- 54 O. G. Mancheño, J. Dallimore, A. Plant and C. Bolm, *Adv. Synth. Catal.*, 2010, **352**, 309–316.
- 55 D. R. Rayner, D. M. von Schriltz, J. Day and D. J. Cram, *J. Am. Chem. Soc.*, 1968, **90**, 2721–2723.
- 56 S. L. Huang and D. Swern, *J. Org. Chem.*, 1979, **44**, 2510–2513.
- 57 A. Pandey and C. Bolm, *Synthesis*, 2010, 2922–2925.
- 58 H. S. Veale, J. Levin and D. Swern, *Tetrahedron Lett.*, 1978, **19**, 503–506.
- 59 N. Gaggero, L. D’Accolti, S. Colonna and R. Curci, *Tetrahedron Lett.*, 1997, **38**, 5559–5562.
- 60 J. F. Lohier, T. Glachet, H. Marzag, A. C. Gaumont and V. Reboul, *Chem. Commun.*, 2017, **53**, 2064–2067.
- 61 L. Degennaro, A. Tota, S. De Angelis, M. Andresini, C. Cardellicchio, M. A. Capozzi, G. Romanazzi and R. Luisi, *Eur. J. Org. Chem.*, 2017, **2017**, 6486–6490.
- 62 Y. Xie, B. Zhou, S. Zhou, S. Zhou, W. Wei, J. Liu, Y. Zhan, D. Cheng, M. Chen, Y. Li, B. Wang, X. S. Xue and Z. Li, *ChemistrySelect*, 2017, **2**, 1620–1624.

- 63 R. Kowalczyk, A. J. F. Edmunds, R. G. Hall and C. Bolm, *Org. Lett.*, 2011, **13**, 768–771.
- 64 B. Gao, S. Li, P. Wu, J. E. Moses and K. B. Sharpless, *Angew. Chem. Int. Ed.*, 2018, **57**, 1939–1943.
- 65 S. Li, P. Wu, J. E. Moses and K. B. Sharpless, *Angew. Chem. Int. Ed.*, 2017, **56**, 2903–2908.
- 66 J. Clayden, *Organolithiums: Selectivity for Synthesis*, Elsevier Amsterdam, 2002.
- 67 M. R. Jones and D. J. Cram, *J. Am. Chem. Soc.*, 1974, **96**, 2183–2190.
- 68 C. R. Johnson, E. U. Jonsson and A. Wambsgans, *J. Org. Chem.*, 1979, **44**, 2061–2065.
- 69 S. G. Pyne, *J. Org. Chem.*, 1986, **51**, 81–87.
- 70 M. Reggelin and H. Weinberger, *Tetrahedron Lett.*, 1992, **33**, 6959–6962.
- 71 G. Solladié, *Synthesis*, 1981, 185–196.
- 72 M. Reggelin, M. Gerlach and M. Vogt, *Eur. J. Org. Chem.*, 1999, **1999**, 1011–1031.
- 73 D. Leca, L. Fensterbank, E. Lacôte and M. Malacria, *Org. Lett.*, 2002, **4**, 4093–4095.
- 74 A. Felim, A. Toussaint, C. R. Phillips, D. Leca, A. Vagstad, L. Fensterbank, E. Lacôte and M. Malacria, *Org. Lett.*, 2006, **8**, 337–339.
- 75 A. K. Roy, *J. Am. Chem. Soc.*, 1993, **115**, 2598–2603.
- 76 Y. Endo, K. Shudo and T. Okamoto, *J. Am. Chem. Soc.*, 1982, **104**, 6393–6397.
- 77 Pinchuk, A. M. *J. Gen. Chem. USSR*, 1967, **37**, 852–855.
- 78 Levchenko, E. S. *J. Gen. Chem. USSR*, 1963, **33**, 3315–3323.
- 79 Levchenko, E. S. *J. Gen. Chem. USSR*, 1962, **32**, 2585–2592.

- 80 V. I. Shevchenko and P. P. Kornuta, *Zhurnal Obs. khimii*, 1970, **40**, 551–553.
- 81 R. Koller, K. Stanek, D. Stolz, R. Aardoom, K. Niedermann and A. Togni, *Angew. Chem. Int. Ed.*, 2009, **48**, 4332–4336.
- 82 J. Iley, A. R. Bassindale and P. Patel, *J. Chem. Soc. Perkin Trans.*, 1984, 77–80.
- 83 E. S. Levchenko, L. N. Markovskii and A. V. Kirsanov, *Zhurnal Obs. khimii*, 1967, **3**, 1273–1282.
- 84 E. S. Levchenko, N. Y. Derkach and A. V. Kirsanov, *Zhurnal Obs. khimii*, 1960, **30**, 1971–1975.
- 85 C. R. Johnson, E. U. Jonsson and C. C. Bacon, *J. Org. Chem.*, 1979, **44**, 2055–2061.
- 86 C. R. Johnson and A. Wambsgans, *J. Org. Chem.*, 1979, **44**, 2278–2280.
- 87 M. Wright, C. Martínez-Lamenca, J. E. Leenaerts, P. E. Brennan, A. A. Trabanco and D. Oehlrich, *J. Org. Chem.*, 2018, **83**, 9510–9516.
- 88 T. J. Maricich, R. A. Jourdenais and T. A. Albright, *J. Am. Chem. Soc.*, 1973, **95**, 5831–5832.
- 89 F. A. Davis, P. Zhou and G. V. Reddy, *J. Org. Chem.*, 1994, **59**, 3243–3245.
- 90 P. J. Stang and V. V. Zhdankin, *Chem. Rev.*, 1996, **96**, 1123–1178.
- 91 D. Leca, K. Song, M. Amatore, L. Fensterbank, E. Lacôte and M. Malacria, *Chem. Eur. J.*, 2004, **10**, 906–916.
- 92 M. Reggelin and B. Junker, *Chem. Eur. J.*, 2001, **7**, 1232–1239.
- 93 A. Tota, S. St John-Campbell, E. L. Briggs, G. O. Estévez, M. Afonso, L. Degennaro, R. Luisi and J. A. Bull, *Org. Lett.*, 2018, **20**, 2599–2602.
- 94 M. Reggelin and R. Welcker, *Tetrahedron Lett.*, 1995, **36**, 5885–5886.
- 95 J.-H. Youn and R. Herrmann, *Tetrahedron Lett.*, 1986, **27**, 1493–1494.

- 96 J. Bai, B. K. Zambroń and P. Vogel, *Org. Lett.*, 2014, **16**, 604–607.
- 97 A. Chelouan, R. Recio, A. Alcudia, N. Khiar and I. Fernández, *Eur. J. Org. Chem.*, 2014, **2014**, 6935–6944.
- 98 E. Block, A. Schwan and D. A. Dixon, *J. Am. Chem. Soc.*, 1992, **114**, 3492–3499.
- 99 I. Sen, D. P. Kloer, R. G. Hall and S. Pal, *Synthesis*, 2013, **45**, 3018–3028.
- 100 C. A. Lipinski, F. Lombardo, B. W. Dominy and P. J. Feeney, *Adv. Drug. Deliv. Rev.*, 2001, **46**, 3–26.
- 101 P. M. Matos, W. Lewis, J. C. Moore and R. A. Stockman, *Org. Lett.*, 2018, **20**, 3674–3677.
- 102 M. Reggelin, C. Mehler and J. P. Kaiser, *Synlett*, 2012, **23**, 1095–1098.
- 103 E. M. McGarrigle, V. K. Aggarwal, A. Mumtaz, S. P. Fritz and M. Yar, *Eur. J. Org. Chem.*, 2011, **2011**, 3156–3164.
- 104 E. S. Izmetév, O. M. Lezina, O. N. Grebyonkina, S. A. Patov, S. A. Rubtsova and A. V. Kutchin, *Russ. Chem. Bull.*, 2014, **63**, 2067–2073.
- 105 E. S. Izmetév, D. V. Sudarikov, S. A. Rubtsova, P. A. Slepukhin and A. V. Kuchin, *Russ. J. Org. Chem.*, 2012, **48**, 184–192.
- 106 Y. Joyard, C. Papamicaël, P. Bohn and L. Bischoff, *Org. Lett.*, 2013, **15**, 2294–2297.
- 107 M. J. Mintz and C. Walling, *Org. Synth.*, 1969, **49**, 9.
- 108 M. Reggelin, H. Weinberger, M. Gerlach and R. Welcker, *J. Am. Chem. Soc.*, 1996, **118**, 4765–4777.
- 109 V. Semak, C. Escolano, C. Arróniz, J. Bosch and M. Amat, *Tetrahedron Asymmetry*, 2010, **21**, 2542–2549.
- 110 M. R. Yadav, R. K. Rit and A. K. Sahoo, *Chem. Eur. J.*, 2012, **18**, 5541–5545.

- 111 D. L. Priebbenow and C. Bolm, *Org. Lett.*, 2014, **16**, 1650–1652.
- 112 G. I. Nikishin, L. L. Sokova and N. I. Kapustina, *Russ. Chem. Bull.*, 2009, **58**, 303–308.
- 113 D. Enders and C. Herriger, *Eur. J. Org. Chem.*, 2007, **2007**, 1085–1090.
- 114 R. Krishnamurti, D. R. Bellew and G. K. S. Prakash, *J. Org. Chem.*, 1991, **56**, 984–989.
- 115 X. Liu, X. Xu, L. Pan, Q. Zhang and Q. Liu, *Org. Biomol. Chem.*, 2013, **11**, 6703–6706.
- 116 G. K. S. Prakash, C. Panja, H. Vaghoo, V. Surampudi, R. Kultyshev, M. Mandal, G. Rasul, T. Mathew and G. A. Olah, *J. Org. Chem.*, 2006, **71**, 6806–6813.
- 117 A. M. Piggott and P. Karuso, *Tetrahedron Lett.*, 2007, **48**, 7452–7455.
- 118 J. Wei and Z. Sun, *Org. Lett.*, 2015, **17**, 5396–5399.
- 119 X. Sun, X. Zhang, B. Zhang, W. Wang and Q. Zeng, *Acta Crystallogr. Sect. E Struct. Reports Online*, 2012, **68**, o1728.
- 120 M. Datta, A. J. Buglass and M. R. J. Elsegood, *Acta Crystallogr. Sect. E Struct. Reports Online*, 2009, **65**, o2034.
- 121 K. Okuma, T. Koike and H. Ohta, *J. Org. Chem.*, 1988, **53**, 4190–4193.
- 122 J.-B. Baundin, M.-G. Comménil, S. A. Julia, R. Lorne and L. Mauclaire, *Bull. Soc. Chim. Fr.*, 1996, **133**, 329–350.
- 123 J. Matsuo, D. Iida, K. Tatani and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, 2002, **75**, 223–234.
- 124 A. Kolbe and E. Wenschuh, *J. Mol. Struct.*, 1975, **28**, 359–369.
- 125 M. Datta, A. J. Buglass and M. R. J. Elsegood, *Acta Crystallogr. Sect. E Struct. Reports Online*, 2009, **65**, o2823.
- 126 L. I. Dixon, M. A. Carroll, T. J. Gregson, G. J. Ellames, R. W. Harrington

- and W. Clegg, *Eur. J. Org. Chem.*, 2013, **2013**, 2334–2345.
- 127 Y. Jiang, Y. You, W. Dong, Z. Peng, Y. Zhang and D. An, *J. Org. Chem.*, 2017, **82**, 5810–5818.
- 128 A. Correa and C. Bolm, *Adv. Synth. Catal.*, 2008, **350**, 391–394.
- 129 S. K. Aithagani, S. Dara, G. Munagala, H. Aruri, M. Yadav, S. Sharma, R. A. Vishwakarma and P. P. Singh, *Org. Lett.*, 2015, **17**, 5547–5549.
- 130 C. A. Dannenberg, V. Bizet and C. Bolm, *Synthesis*, 2015, **47**, 1951–1959.
- 131 C. M. M. Hendriks, R. A. Bohmann, M. Bohlem and C. Bolm, *Adv. Synth. Catal.*, 2014, **356**, 1847–1852.
- 132 M. J. Bu, G. P. Lu and C. Cai, *Synlett*, 2015, **26**, 1841–1846.
- 133 J. Yan, J. F. Poon, V. P. Singh, P. Gates and L. Engman, *Org. Lett.*, 2015, **17**, 6162–6165.
- 134 M. A. Fernández-Rodríguez and J. F. Hartwig, *J. Org. Chem.*, 2009, **74**, 1663–1672.
- 135 Y.-C. Wong, T. T. Jayanth and C.-H. Cheng, *Org. Lett.*, 2006, **8**, 5613–5616.
- 136 B. Sreedhar, P. S. Reddy and M. A. Reddy, *Synthesis*, 2009, 1732–1738.
- 137 A. M. Thomas, S. Asha, K. S. Sindhu and G. Anilkumar, *Tetrahedron Lett.*, 2015, **56**, 6560–6564.
- 138 S. E. Howson, L. E. N. Allan, N. P. Chmel, G. J. Clarkson, R. J. Deeth, A. D. Faulkner, D. H. Simpson and P. Scott, *Dalt. Trans.*, 2011, **40**, 10416–10433.
- 139 J. Park, Y. Lee, J. Kim and S. H. Cho, *Org. Lett.*, 2016, **18**, 1210–1213.
- 140 C. A. Dannenberg, L. Fritze, F. Krauskopf and C. Bolm, *Org. Biomol. Chem.*, 2017, **15**, 1086–1090.
- 141 N. Furukawa, K. Akutagawa and S. Oae, *Phosphorus Sulfur Relat. Elem.*, 1984, **20**, 1–14.

-
- 142 H. Yu, Z. Li and C. Bolm, *Angew. Chem. Int. Ed.*, 2018, **57**, 324–327.
- 143 A. Wimmer and B. König, *Adv. Synth. Catal.*, 2018, **360**, 3277–3285.
- 144 D. Zhang, G. Raabe, C. Bolm, M. Frings, H. Cheng, S. Dong and J. Wen, *J. Am. Chem. Soc.*, 2016, **138**, 2166–2169.
- 145 N. Furukawa, S. Oae, T. Numata, M. Moriyama and T. Yoshimura, *Tetrahedron*, 1976, **32**, 3003–3013.
- 146 J. Guilbaud, M. Labonde, A. Selmi, M. Kammoun, H. Cattey, N. Pirio, J. Roger and J. C. Hierso, *Catal. Commun.*, 2018, **111**, 52–58.
- 147 H. Terauchi and S. Takemura, *Chem. Pharm. Bull.*, 1975, **23**, 2410–2414.