Aziridinations of Tethered Allenes

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To begin, I'll thank Andy T
Though you'll always be Tiger to me
You're the first X-ray king
But bad luck you bring
When trying to watch a grand prix

Chris North you're the oldest I know
Team Naf I will never outgrow
You're the best at all sport
When French speaking contort
And you rescued me once from the road

Will Unsworth, you are a great dad
You introduced Kiri as 'Glad'
Former enemies we be
You threw water on me
Thank you for the fun times we've had

To my fellow fourth year Sarah O'
Getting ready, you can be quite slow
We'd a great Cali time
Your cooking's sublime
Just please don't stand near to a crow

To Kirifer Stevens, Hooray!
You so enjoy lexical play
And when we were betrothed
A tapestry you sewed
Do you remember our bigger day?

Big thanks go to Anthony Wu
Over time our companionship grew
Through labminton games
Taurospongin acclaims
And dancing the whole night through!

Alex, for journal resolver, Cheers!
Dan and Jamesy for nights on the beers
My fume-hood bud Jack
Games with Praful – run back!
Seb and Aurélie thanks in arrears

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Thanks to Bryony and Jessie and Lou
Graeme, Carly and Phil
Liz, Tom, Nicola and still
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Lastly I would like to thank James and my family and friends for their continuing love and support.

GCF (The Column King)

Abbreviations

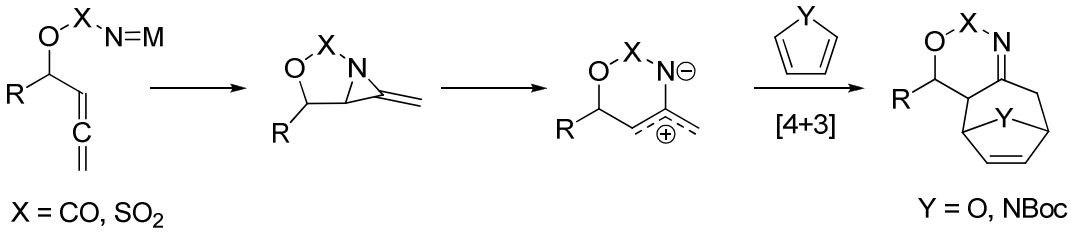
Ac	acetyl
AIBN	azobisisobutyronitrile
aq.	aqueous
Ar	aryl
Az	1,2,3-triazolyl
BHT	butylated hydroxytoluene
Bn	benzyl
Boc	*tert*-butoxycarbonyl
Bu	butyl
ca.	*circa*
cat.	catalytic
Cbz	carbobenzyloxy
CDI	*N,N'*-carbonyldiimidazole
CI	chemical ionisation
conc.	concentrated
COSY	correlation spectroscopy
Cp	cyclopentenyl
CSA	camphorsulfonic acid
d	day(s)
DBU	1,8-diazabicycloundec-7-ene
DCM	dichloromethane
DEAD	diethylazodicarboxylate
DEM	dimethylmalonate
DEPT	distortionless enhancement by polarisation transfer
DHP	2,3-dihydrofuran
DIAD	diisopropylazodicarboxylate
DIBAL	diisobutylaluminium hydride
DMA	*N,N'*-dimethylacetamide
DMAP	*N,N'*-dimethylaminopyridine
DMDO	dimethyldioxirane
DMF	*N,N'*-dimethylformamide
DMP	Dess–Martin periodinane
DMSO	dimethylsulfoxide
DPPA	diphenylphosphoryl azide
dr	diastereomeric ratio
E	electrophile
EAA	ethylacetoacetate
ee	enantiomeric excess
EI	electron impact ionisation
eq.	equivalents
ESI	electrospray ionisation
esp	tetramethyl-1,3-benzenedipropionic acid
Et	ethyl
FI	field ionisation
Fu	furyl
GCMS	gas chromatography mass spectrometry
Grubbs' II	Grubbs' second generation catalyst
h	hour(s)
Hal	halogen
HMBC	heteronuclear multiple-bond correlation
HMDS	hexamethyldisilazide
HMPA	hexamethylphosphoramide
HMQC	heteronuclear multiple-quantum correlation
HOMO	highest occupied molecular orbital
i-	*iso*
IPA	isopropyl alcohol
IR	infrared
J	coupling constant
LDA	lithium diisopropylamide
Lit.	literature value
LUMO	lowest unoccupied molecular orbital
M	molar

m-	meta
m-CPBA	*meta*-chloroperbenzoic acid
MA	methylene aziridine
Me	methyl
MEOX	methyl-2-oxazolidinone-4-carboxylate
min	minute(s)
m.p.	melting point
MS	molecular sieves
m/z	mass/charge ratio
n-	*normal*
NBSH	*o*-nitrobenzenesulfonylhydrazine
NMO	*N*-morpholine-*N*-oxide
nOe	nuclear Overhauser effect
NPSP	*N*-phenylselenylphthalimide
o-	*ortho*
oct	octanoate
p-	*para*
Ph	phenyl
Piv	pivaloyl
PMB	*para*-methoxybenzyl
PMHS	polymethylhydrosiloxane
ppm	parts per million
Pr	propyl
pyr	pyridine
quant.	quantitative
R_f	retention factor
r.t.	room temperature
s- or *sec*-	*secondary*
sat.	saturated
t- or *tert*-	*tertiary*
TBAF	tetra-*n*-butylammonium fluoride
TBDPS	*tert*-butyldiphenylsilyl
TBS	*tert*-butyldimethylsilyl
TBSP	1-[(4-*tert*-butylphenyl)sulfonyl]-2-pyrrolidinecarboxylate
TES	triethylsilyl
Tf	trifluoromethanesulfonyl
THF	tetrahydorfuran
TLC	thin layer chromatography
TMEDA	tetramethylethylenediamine
TMS	trimethylsilyl
TPAP	tetrapropylammonium perruthenate
Ts	*para*-toluenesulfonyl
Tces	2,2,2-trichloroethoxysulfonyl
UV	ultraviolet
v/v	volume/volume

1. Introduction

1.1 Amino-allyl cations for diversity oriented synthesis

The aziridination of carbamate and sulfamate tethered allenes *via* rhodium-nitrenoid cyclisation were expected to generate bicyclic methylene aziridines (MAs). It was anticipated that these strained compounds would undergo formal electrocyclic ring-opening to generate an amino-allyl cation intermediate[1] which could then be trapped by cycloaddition reactions (Scheme 1).

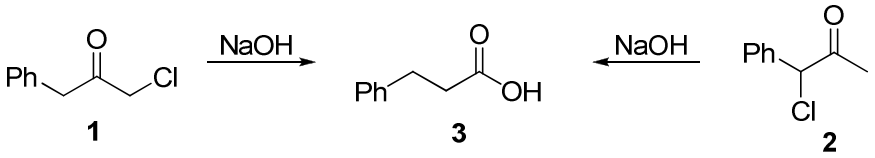


Scheme 1

The theme of this research project was to generate these tricycles and utilise them as constructive synthetic intermediates. They were predicted to undergo a wide range of reactions with potential application in diversity oriented synthesis.

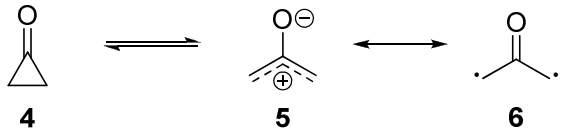
1.2 Oxy-allyls in synthesis

In 1951 Loftfield[2] proposed a mechanism for the Favorskii rearrangement of an α-chloro ketone involving formation of a cyclopropanone. It was believed that in order to account for the product distribution from isomeric α-chloro ketones **1** and **2** there had to be a symmetrical intermediate from which hydroxide attack could yield acid **3** from both starting materials (Scheme 2).



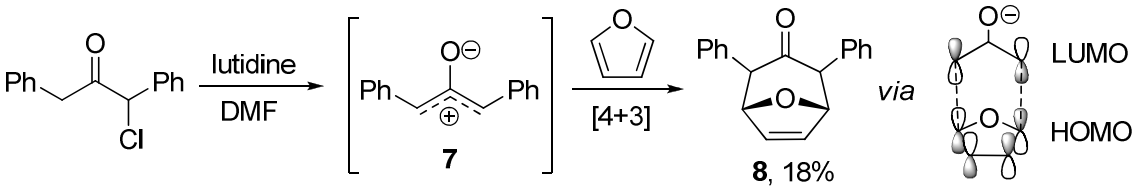
Scheme 2

In the same year Aston and Newkirk[3] proposed an oxy-allyl (2-oxy-allyl cation) as an alternative intermediate in the same reaction and it was Fort[4] in 1962 who provided evidence for their existence. It is now understood that oxy-allyl **5** and cyclopropanone **4** are converted rapidly by electrocyclic ring closure.[5, 6] Oxy-allyls can also be considered as resonance forms of diradical species **6**[7] (Scheme 3).



Scheme 3

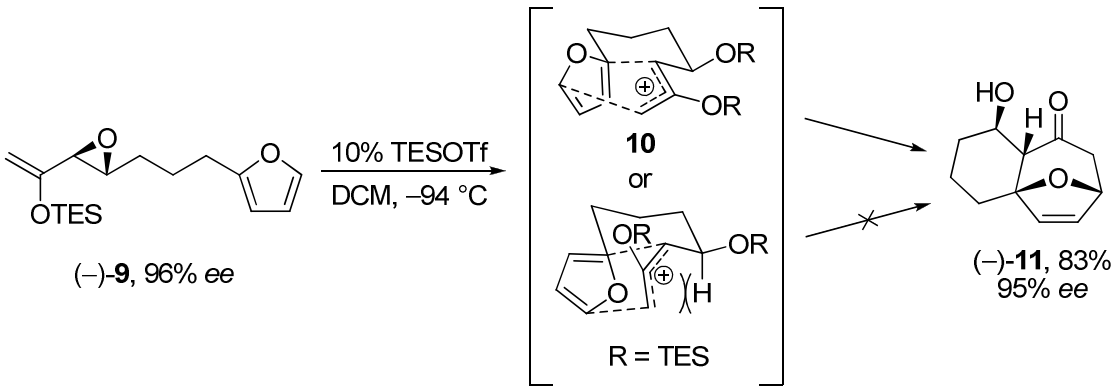
Fort went on to capture his 'Favorskii intermediate' **7** with furan in the first example of a [4+3] cycloaddition of an oxy-allyl to give bicycle **8**.[8] The favourable HOMO–LUMO overlap leads to 7-membered ring products exclusively (Scheme 4).



Scheme 4

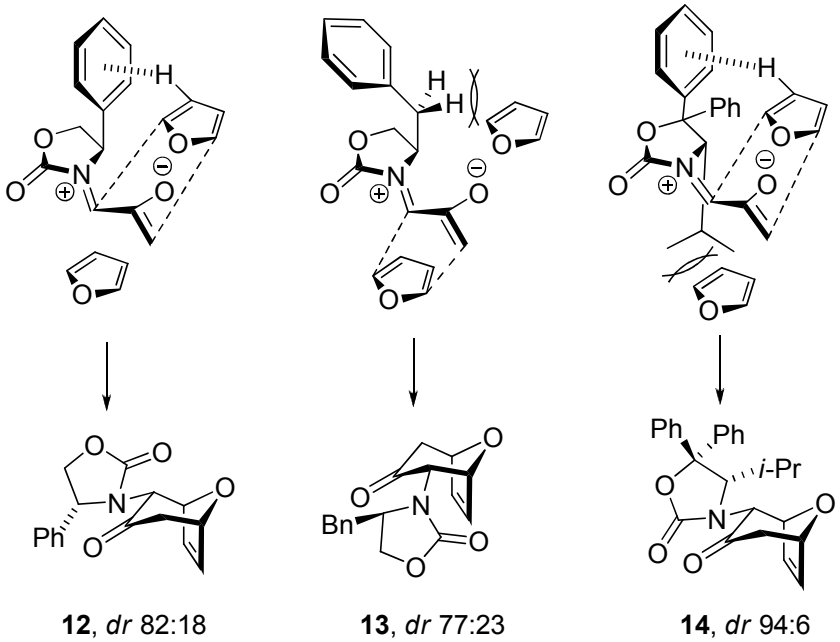
The generation of oxy-allyls and their cycloaddition reactions have become a valuable tool in organic synthesis.[9-11] The basic conditions of their synthesis from α-haloketones used in the Favorskii reaction are still commonly employed; other methods for oxy-allyl generation include reduction of dihaloketones,[12] activation of 2-siloxyacroleins with Lewis acids[13] and photochemical excitation of dienones.[14]

Cycloaddition reactions of oxy-allyls can be achieved intramolecularly with good diastereoselective control. Chiu *et al.*[15, 16] showed that chiral epoxy-enol silane **9** can undergo intramolecular [4+3] cycloaddition after oxy-allyl formation with a Lewis acid. Tricyclic product **11** was formed in very good yield *via* less-hindered W-type transition state **10**, giving rise to the high selectivity (Scheme 5).



Scheme 5

Hsung *et al.*[17, 18] have found that oxazolidinone chiral auxilaries can be used to control stereoselectivity in intermolecular oxy-allyl [4+3] cycloadditions. Computational studies, backed up with experimental evidence, suggest the factors effecting stereochemical control are different from those established for Diels-Alder reactions for a given auxilary.[19] A combination of steric repulsions and attractive CH–π interactions appear to determine the facial selectivity of furan attack to give [4+3] cycloaddition products **12**, **13**, and **14** in the ratios shown (Figure 1).

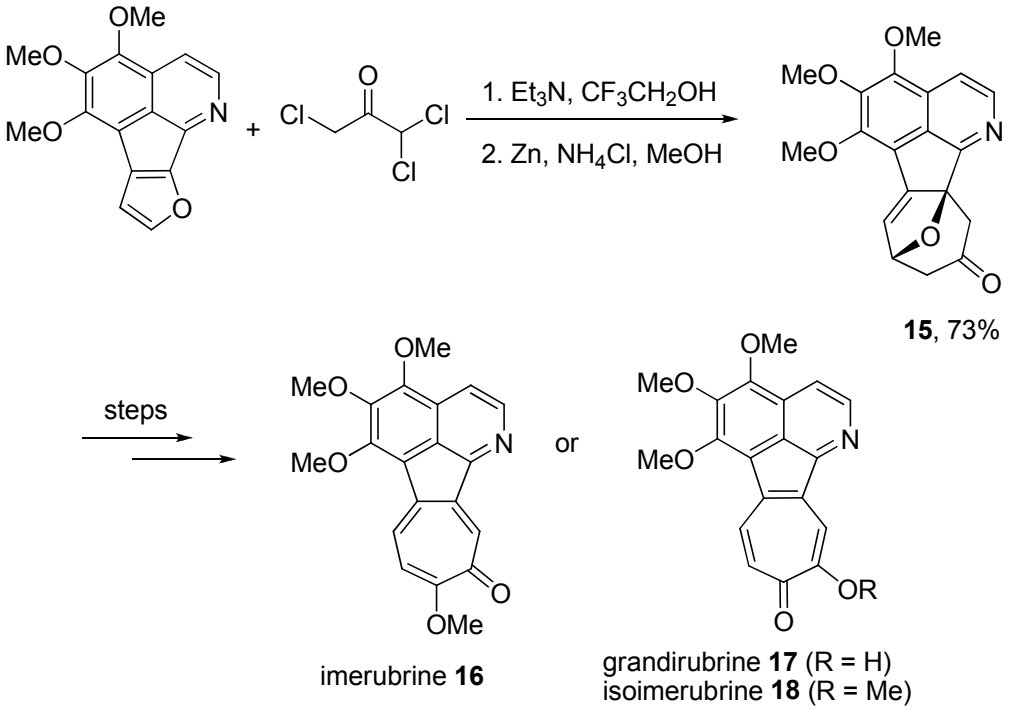


12, *dr* 82:18 **13**, *dr* 77:23 **14**, *dr* 94:6

Figure 1

Oxy-allyls have been used as intermediates in total synthesis as they can be readily converted into tropones. For example, Cha *et al.* [20] utilised the elimination of the oxygen

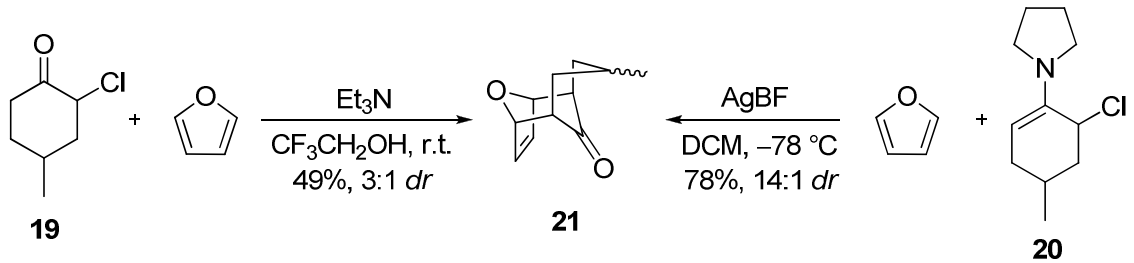
bridge from [4+3] adduct **15** in the short syntheses of tropoloisoquinoline alkaloids, imerubrine **16**, grandirubrine **17**, and isoimerubrine **18** (Scheme 6).



Scheme 6

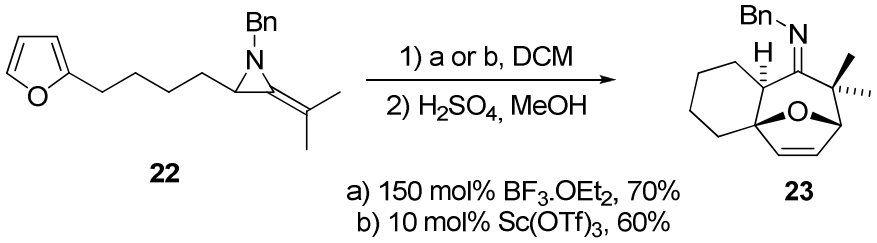
1.3 Amino-allyl cations in synthesis

The chemistry of 2-amino-allyl cations is less explored than that of their oxygen oxy-allyl analogues, however they have been shown to participate in similar [4+3] cycloadditions.[21, 22] A detailed study by Cha *et al.*[23, 24] showed that the synthesis of ketone **21** was achieved in higher yield when using amino-allyl cation precursor **20**, than oxy-allyl precursor **19**; higher diastereoselectivities were achieved since the reaction was able to be carried out at a lower temperature (Scheme 7).



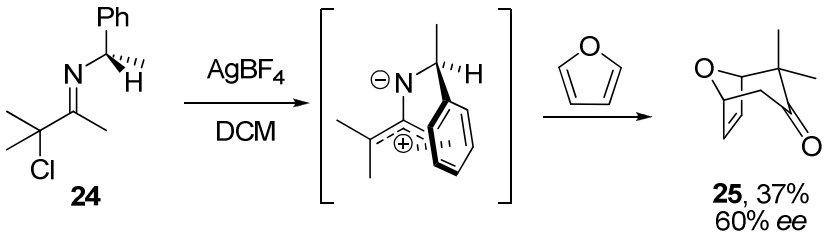
Scheme 7

The most common method for amino-allyl cation synthesis requires unstable α-chloro enamines and stoichiometric amounts of silver(I) salts. An improved generation was developed by Shipman *et al.*[1] whereby Lewis acid catalysed ring-opening of a methylene aziridine (MA) **22** revealed an amino-allyl cation, which was then trapped by a tethered diene to yield tetracycles, such as **23**, in good yield (Scheme 8). The use of the term 'methylene aziridine' is used here and throughout this thesis to denote any alkylidene aziridine.



Scheme 8

Asymmetric [4+3] cycloadditions of amino-allyl cations are yet to reach the levels of induction found for oxy-allyls.[25] Kende *et al.*[26] showed that by using a chiral α-chloro imine some asymmetric induction was possible in the [4+3] cycloaddition of amino-allyl cation precursor **24** to give bicycle **25** in moderate *ee*. The selectivity is believed to have arisen from attack of furan on the less-hindered *re* face, the *si* face being blocked by favourable π-interactions between the aromatic ring and the allyl cation (Scheme 9).

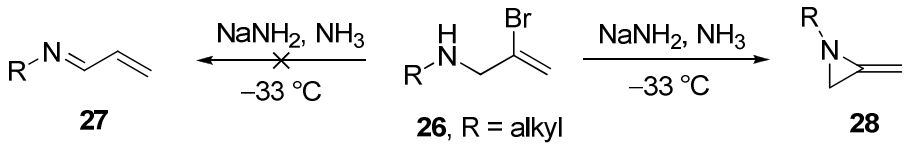


Scheme 9

1.4 Methylene aziridine synthesis

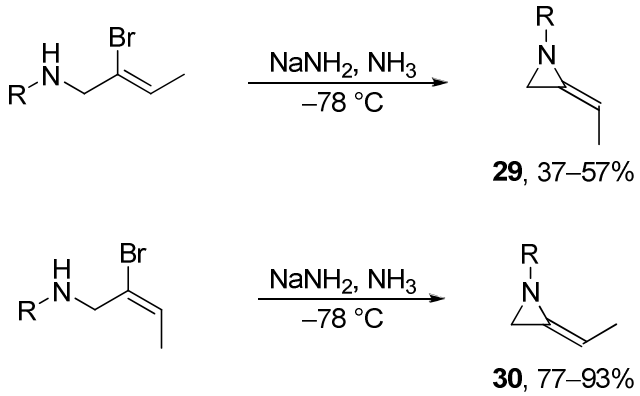
Current routes to MAs are not particularly diverse and there have been few developments since the first reported preparation in 1951 by Pollard and Parcell.[27] Originally the authors

believed that the reaction of *N*-(2-bromoallyl)alkylamines **26** with sodium amide in liquid ammonia gave *N*-allylidene-alkylamines **27**; it was discovered later, by a mixture of degradation studies and comparison of IR and ^{1}H NMR data by Bottini and Roberts,[28] that the products were MAs **28** (Scheme 10).



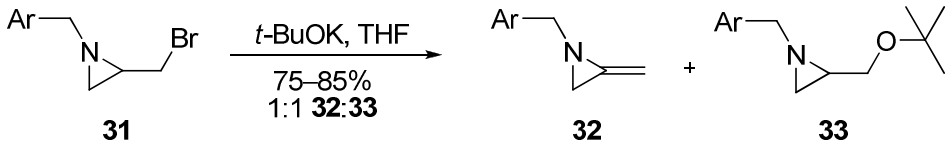
Scheme 10

This method has been refined slightly over time but still remains popular.[29] The reaction was thought to proceed *via* an elimination-addition mechanism,[30] however more recent studies by the Shipman group[31] reveal an inversion of the vinylic carbon atoms in the formation of MAs **29** and **30** (Scheme 11) and thus an internal S_N2 substitution at the vinylic centre has been suggested.



Scheme 11

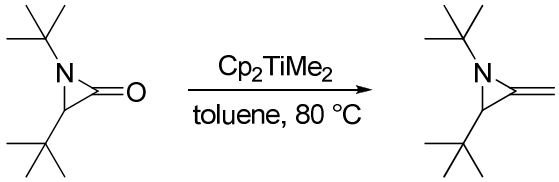
Alternative methods of MA synthesis are poor yielding or the products difficult to purify. De Kimpe *et al.*[32] showed that base induced dehydrobromination of 2-(bromomethyl)aziridines **31** yielded MAs **32**, but only as a 1:1 inseparable mixture with S_N2 products **33** (Scheme 12).



31 **32** **33**

Scheme 12

De Kimpe[33] also showed that the methylenation of 2-aziridinone **34**, using dimethyl titanocene, yielded MA **35** in moderate yield; however the sample was unable to be purified successfully and, due to the elevated temperatures required, other α-lactam precursors were not tolerated (Scheme 13).



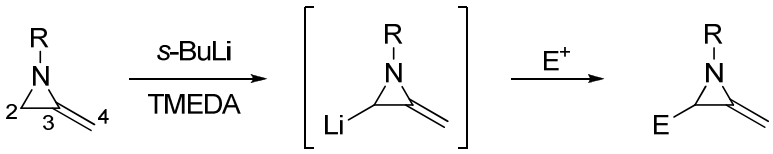
34 **35**, 56% crude

Scheme 13

The preparation of MAs by intermolecular aziridination of allenes has been reported in a single figure percentage yield[34] and MAs have been implicated as intermediates in the thermal addition of ethyl azidoformate to tetramethyl allene[35] and in the formation of a diazaspiro[2.2]pentane from 2-methylbuta-2,3-dienoate.[36] There are no known intramolecular transfers of nitrogen to an allene to give a MA.

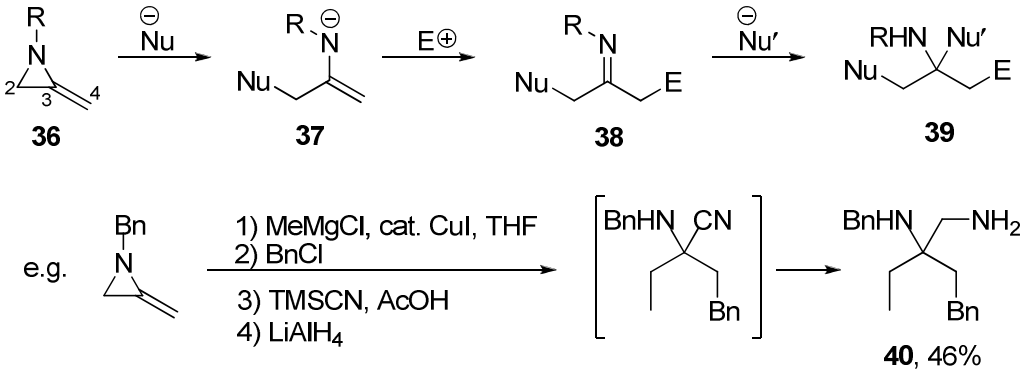
1.5 Methylene aziridine reactivity

Other than Hodgson's work[37, 38] on α-lithiated terminal aziridines, there is little precedent for the formation of aziridinyl anions by deprotonation of unactivated aziridines. By contrast, MAs readily produce aziridinyl anions by deprotonation, commonly using *s*-BuLi. The anions can be alkylated with a wide variety of electrophiles, suggesting that the neighbouring exocyclic double bond plays an important role in increasing the acidity of the C(2) hydrogens[39] (Scheme 14).



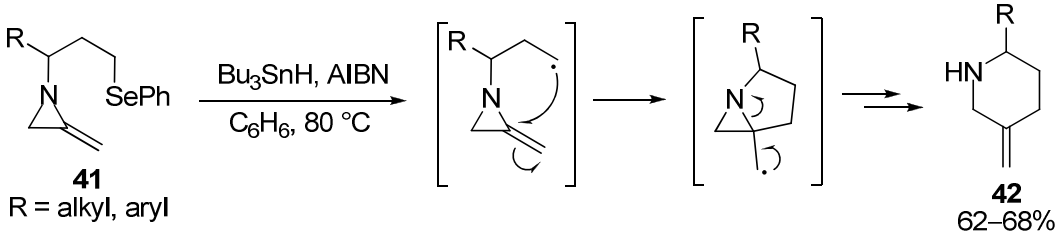
Scheme 14

The release of ring strain in aziridines provides a powerful thermodynamic driving force for chemical reactions. In comparison with simple aziridines, the greater angle strain, and therefore ring strain, of MAs renders them excellent substrates for ring-opening reactions. Shipman *et al.*[40-42] showed that nucleophilic ring opening of MAs **36** lead to enamines **37** which can be then be alkylated at C(4) to give imines **38**. A second nucleophile is then able to attack to yield multi-component reaction products **39**, such as diamine **40** (formed after *in situ* reduction of the nitrile) (Scheme 15).



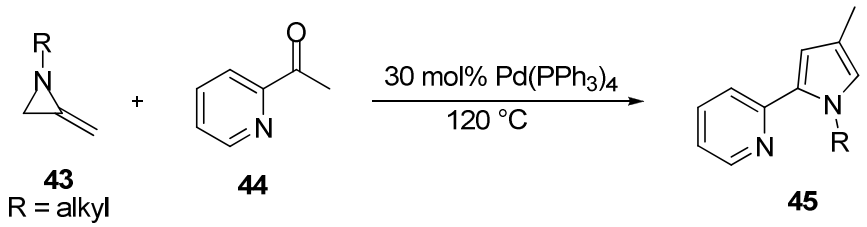
Scheme 15

In these reactions the ring-opening process occurs, unsurprisingly, at the allylic C(2) carbon. Shipman[43] also showed that the direct cleavage of the C(3)–N bond by carbon nucleophiles was possible *via* a pendant radical, such as the conversion of MAs **41** into piperidines **42** (Scheme 16).



Scheme 16

Furthemore, Yamamoto *et al.*[44, 45] showed that C(3)–N bond cleavage of MA **43** could occur *via* a Pd-catalysed insertion reaction with acetylpyridine **44** to yield pyrroles **45** (Scheme 17).



43
R = alkyl

44

45

Scheme 17

1.6 Intramolecular aziridinations

In the last ten years the area of intramolecular aziridinations of carbamate and sulfamate tethered alkenes has grown dramatically, originally as an off-shoot in the development of C–H aminations. Du Bois'[46] work in the area led to the preparation of vicinal amino alcohols from oxazolidinones *via* rhodium-nitrenoid insertion. Oxazolidinones **46** were prepared from readily accessible carbamates by reaction with a Rh(II) catalyst and a hypervalent iodine oxidant; MgO was added to scavenge acetic acid. This method was widely applicable, successfully cyclising substrates containing both benzylic and tertiary C–H centres in high yield (Scheme 18).

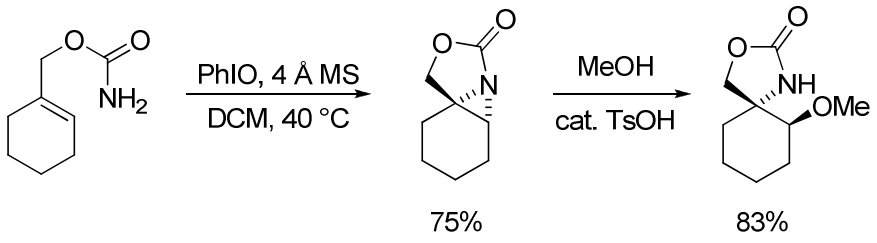


46
74–84%

Scheme 18

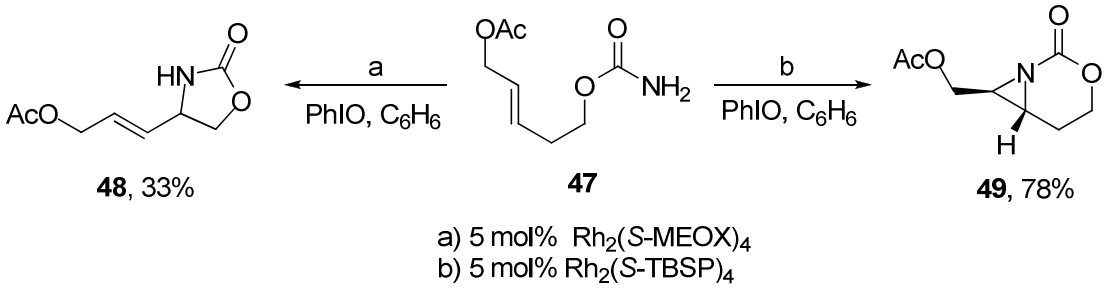
Padwa *et al.*[47] recognised that the intermediate rhodium-nitrenoid could undergo addition to a tethered olefin and it was found that cyclisations of simple allylic carbamates under Du Bois' conditions led to bicyclic aziridines in good yields. The reaction worked equally well without the metal in some cases, using iodosobenzene as an alternative oxidant. The

resultant aziridines were stable to silica but were rapidly opened by various nucleophiles (Scheme 19).



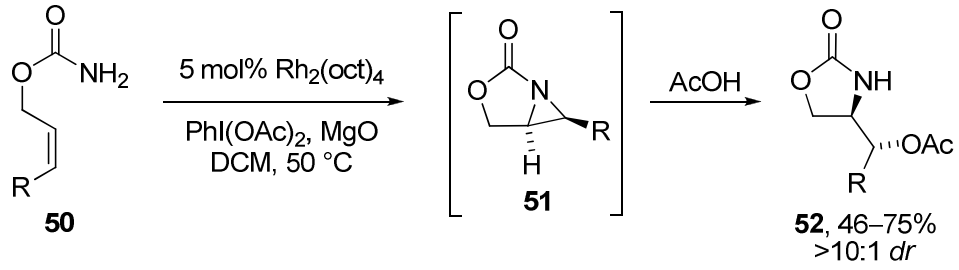
Scheme 19

Hayes *et al.*[48] extended this methodology further to include homoallylic carbamates, showing that by varying the rhodium catalyst, one could obtain either bicyclic aziridine **49** or oxazolidinone **48** from carbamate **47** (Scheme 20).



Scheme 20

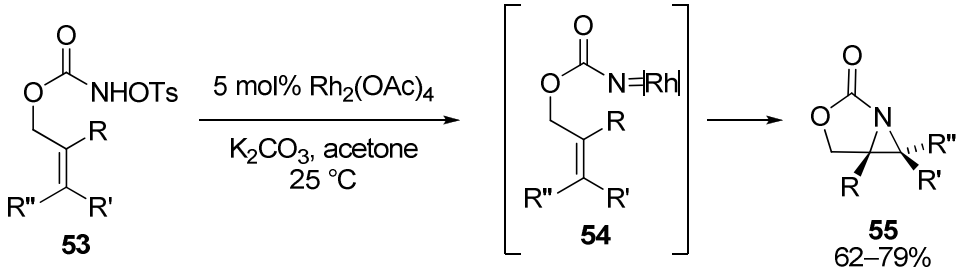
Interest in this area within the Robertson group[49] originated in a study of the diastereoselectivity of acetoxyamination reactions, whereby aziridines **51** (formed *in situ* from the rhodium-catalysed cyclisation of allylic carbamates **50**) were ring-opened by acetate released from the oxidant to yield oxazolidinones **52** (Scheme 21).



Scheme 21

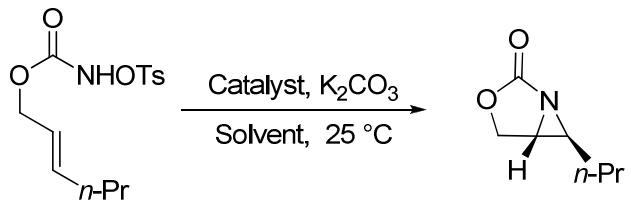
A wide range of olefin substitution patterns were tolerated and in the majority of cases the diasteroselectivity was greater than 10:1, implying a favoured S_N2 acetolysis of the exocyclic C–N bond. An asymmetric variant met limited success.

The requirement for hypervalent iodine reagents to oxidise the carbamate has drawbacks – iodobenzene is produced in stoichiometric amounts and by-products (e.g. acetic acid from $PhI(OAc)_2$) are generated that may interfere with the reaction. Lebel overcame this problem by using a pre-oxidised carbamate equivalent; in this variant, allylic *N*-tosyloxycarbamates **53** are decomposed by addition of Rh(II) to produce rhodium-nitrenoids **54**, which then undergo cyclisation to give bicyclic aziridines **55** in very good yields[50] (Scheme 22).



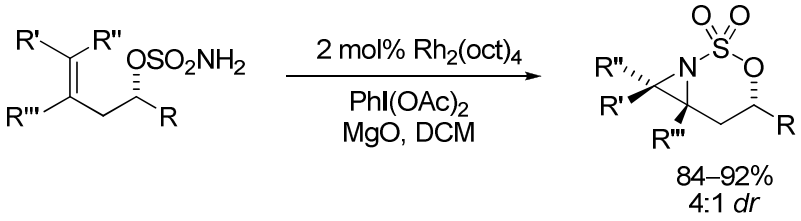
Scheme 22

Aziridination reactions of this type have also been carried out using copper catalysts. Both Fleming[51] and Lebel[52] have reported aziridinations of allylic *N*-tosyloxycarbamates with $(CF_3SO_3Cu)\cdot C_6H_6$ and $Cu(pyr)_4(OTf)_2$ respectively without significant erosion of yield (Scheme 23).



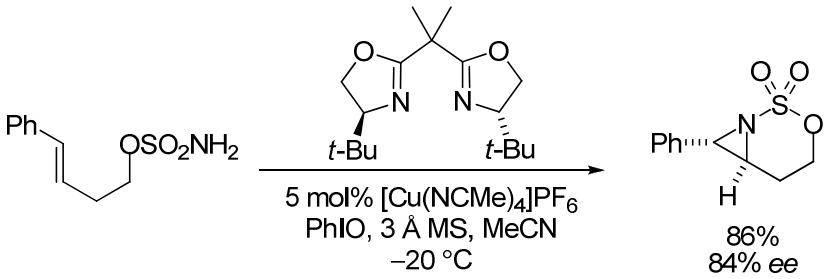
Scheme 23

Sulfamate esters have been shown to be a useful alternative to carbamates and *N*-tosyloxycarbamates in the synthesis of bicyclic aziridines. In an early study, Du Bois *et al.*[53] found that aziridination of homoallylic sulfamates occurred exclusively, with no evidence of competing C–H insertion reactions. Moderate diastereoselectivities were achieved when using chiral sulfamates and selectivities were greatly increased when bulkier substrates were used[54] (Scheme 24).



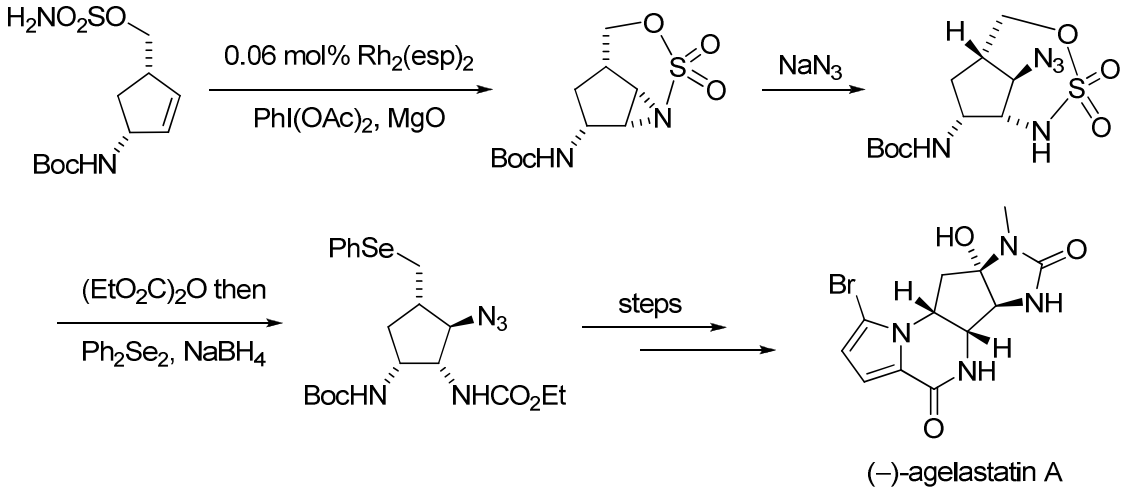
Scheme 24

Fruit and Müller[55] attempted to effect an asymmetric aziridination of sulfamate tethered alkenes, however only moderate *ee*s were accessible. Higher *ee*s were obtained by Dauban *et al.*[56] using a copper catalyst and a chiral bis(oxazoline) ligand (Scheme 25).



Scheme 25

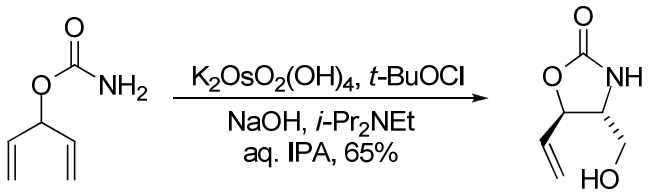
One of the advantages of sulfamate tethers is the diverse range of subsequent transformations that can be employed. The aziridine ring can be opened by a variety of nucleophiles to break the endocyclic C–N bond[57] and, following protection of the nitrogen, SO_3 can be eliminated[58] or displaced.[59] Du Bois *et al.*[60] utilised this in their synthesis of (–)-agelastatin A in 15% overall yield (Scheme 26).



Scheme 26

1.7 Previous work within the Robertson group

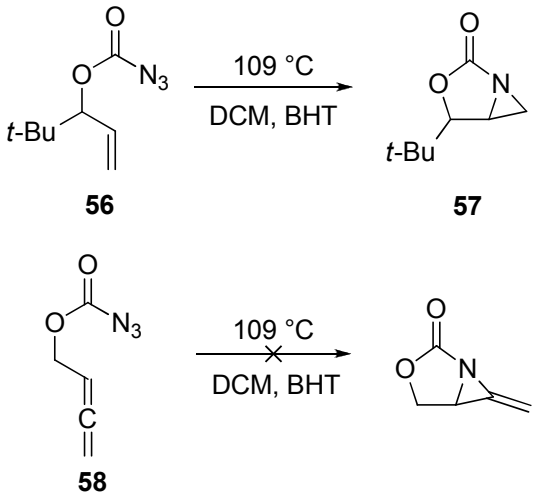
A key step of work within the Robertson group towards the synthesis of nagstatin[61] and sphingosine[62] included a tethered aminohydroxylation (TA)[63] of a 1,4-diene (Scheme 27).



Scheme 27

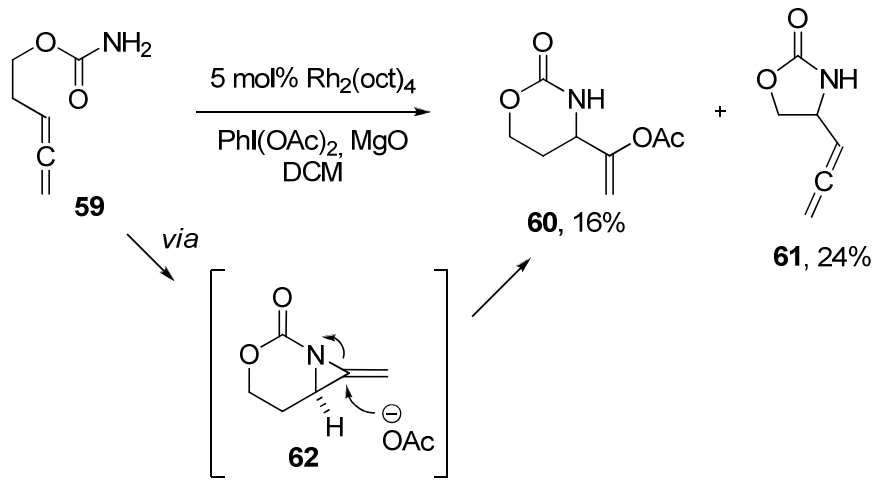
This represented a new substrate class for the TA reaction and the Robertson group developed the idea of applying an unprecedented intramolecular amination reaction to tethered 1,2-dienes.

Initially it was envisaged that cyclisation of an allene-tethered azidoformate would occur upon heating, since, following earlier work by Dreiding,[64] Bergmeier[65] had found that heating alkene-tethered azidoformate **56** afforded bicyclic aziridine **57**. Under the same conditions allene-tethered azidoformate **58** yielded a complex and inseparable mixture of products[66] (Scheme 28).



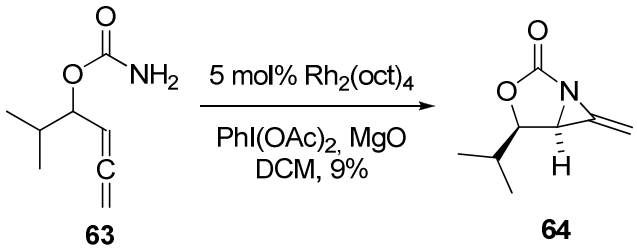
Scheme 28

Attention was thus turned to carbamate-tethered allenes, building on the earlier success of carbamate-tethered 1,4-dienes. Subjecting β-allenic carbamate **59** to Du Bois' cyclisation condtions[46] resulted in the formation of two isolable products, oxazinanone **60** and C–H insertion product **61**. It was hypothesised that **60** had been formed by direct S_N2 attack, from acetate released in the reaction, at the vinylic C–N bond of MA **62** (Scheme 29).



Scheme 29

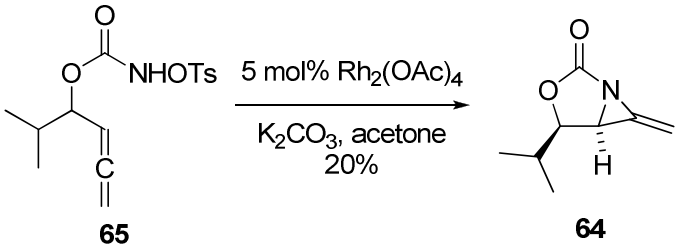
The shorter chain α-allenic carbamate **63** was not expected to undergo C–H insertion, thus increasing the likelihood of isolating a MA or subsequently derived product. A number of unidentified products were formed, however a small amount of MA **64** was tentatively identified (full characterisation was not possible) (Scheme 30).



63 **64**

Scheme 30

Since isolation of MA **64** had proven difficult, *N*-tosyloxycarbamate **65** was synthesised in order to apply Lebel's conditions[50] which do not require an external oxidant (thus removing potential nucleophilic by-products). MA **64** was isolated in a reproducible yield and sufficient pure material was produced to fully characterise using HMBC (^{1}H–^{13}C, ^{1}H–^{15}N) and nOe experiments[66] (Scheme 31).



65 **64**

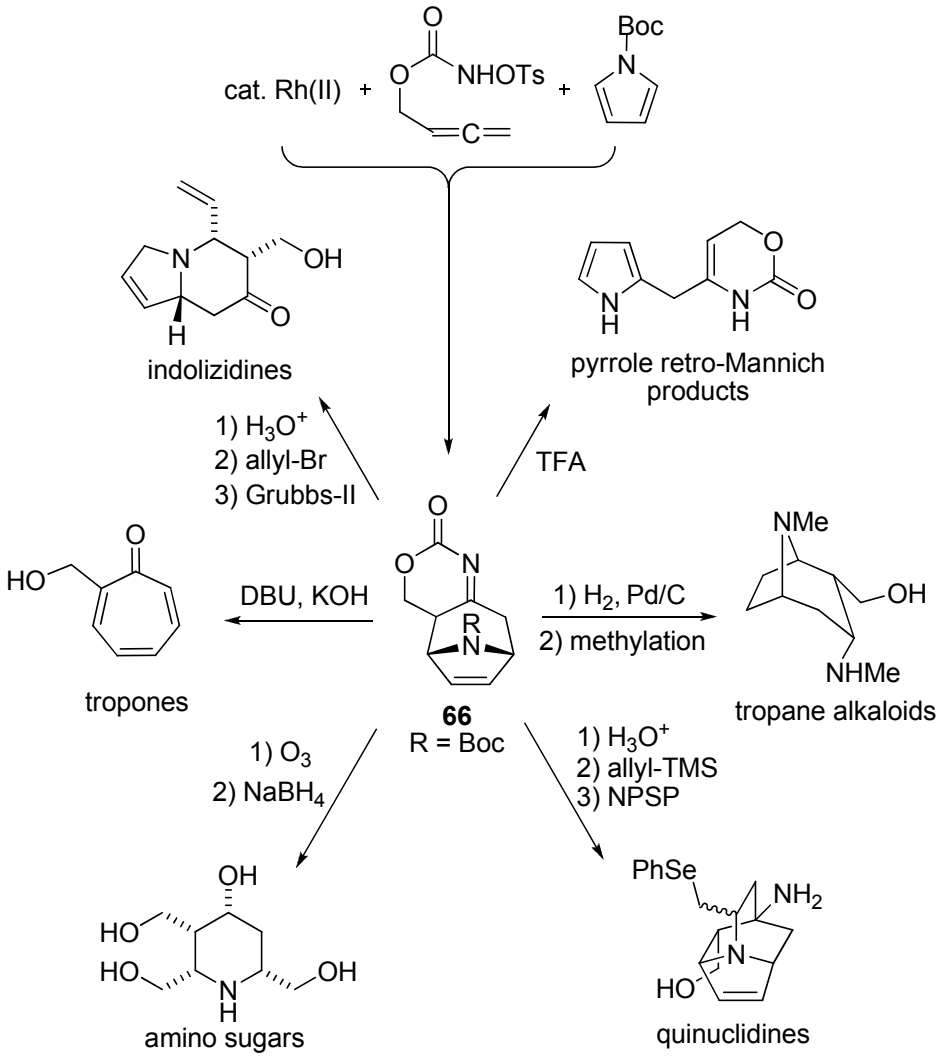
Scheme 31

Very few reactions were attempted to probe the reactivity of MA **64** due to the low quantities synthesised, however it was found to be surprisingly stable to both heat and acidic conditions on an NMR scale. Polymerisation was suspected after extended periods at 70 °C.[66]

1.8 Aims

Prior to the start of this project, only one MA had been produced; the initial aim therefore, was to explore the substrate scope of the *N*-tosyloxycarbamate cyclisation. Furthermore, by up-scaling the reaction, enough material should be available to undertake a detailed analysis of the reactivity of these unique compounds. Studies would then be directed

towards a [4+3] cycloaddition with a simple diene, such as *N*-Boc-pyrrole, to afford tricycle **66**, which could lead to a whole raft of synthetic opportunities (Scheme 32).



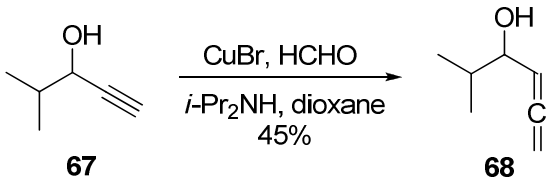
Scheme 32

With potential variation in tether length and substitution, type of diene and the possibility of nucleophilic trapping, a wide range of compounds were expected to be accessible in short sequences. In addition, this study would investigate the analogous reactions of sulfamate-tethered allenes to compare and contrast their reactivity.

2. Carbamate linked MAs

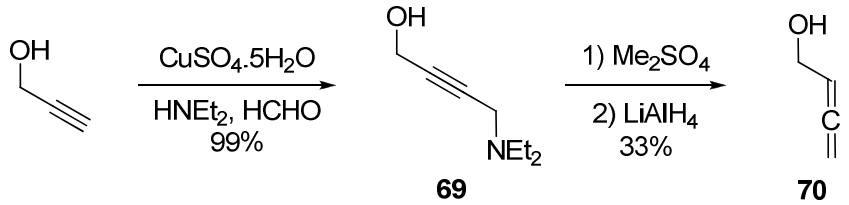
2.1 Synthesis of α-allenic *N*-tosyloxycarbamates

To test a range of *N*-tosyloxycarbamate substrates for intramolecular allene aziridinations a variety of precursor α-allenic alcohols were required.[50] Previous work within the group had established a synthesis of *iso*-propyl alcohol **68** *via* homologation[67] of propargylic alcohol **67** and this was successfully repeated (Scheme 33).



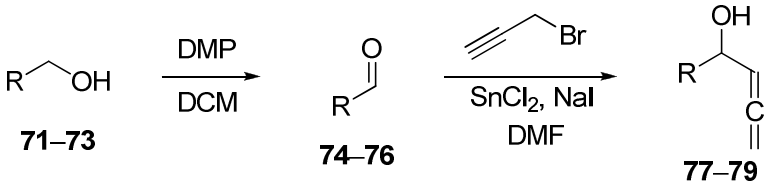
Scheme 33

Volatile unsubstituted α-allenic alcohol **70** was prepared in a related homologation of propargyl alcohol, *via* amine **69**[68] (Scheme 34).



Scheme 34

For more complex α-allenic substrates, allenation[69] of the appropriate aldehyde was found to be a versatile and substrate tolerant approach. DMP oxidation[70] of commercially available alcohols **71–73** to aldehydes **74–76**, followed by allenation with propargyl bromide, $SnCl_2$ and NaI in DMF, led to α-allenic alcohols **77–79** in moderate yields (Table 1).

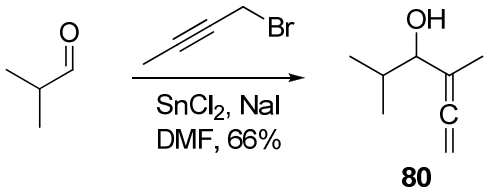


71–73 **74–76** **77–79**

R	**74–76**, yield (%)	**77–79**, yield (%)
CH_2Ph	81	57
$CH_2C_6H_4(p\text{-}NO_2)$	99	44
CH_2(1-Naphthyl)	88	61

Table 1

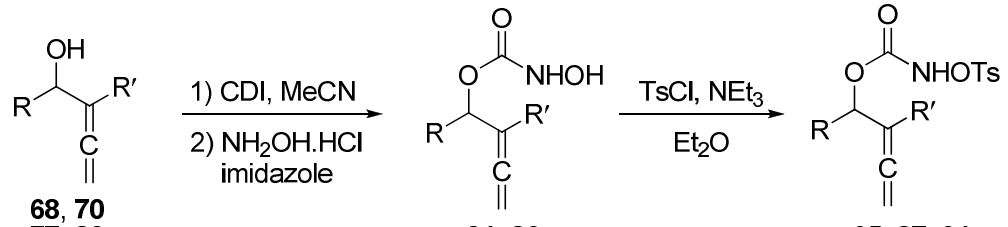
Finally, by substituting propargyl bromide for 1-bromobut-2-yne, internally disubstituted allene **80** was prepared from isobutyraldehyde (Scheme 35).



80

Scheme 35

Treatment of alcohols **68**, **70**, and **77–80** with CDI followed by hydroxylamine hydrochloride provided hydroxycarbamates **81–86**. These were then tosylated[50] under standard conditions to yield *N*-tosyloxycarbamates **65** and **87–91** (Table 2).



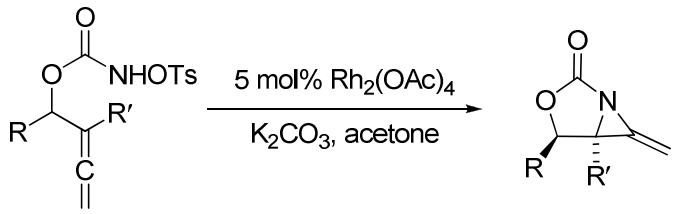
68, **70** **77–80** **81–86** **65, 87–91**

R	R′	Compound	Yield (%)	Compound	Yield (%)
H	H	**81**	56	**87**	70
i-Pr	H	**82**	66	**65**	92
i-Pr	Me	**83**	50	**88**	61
CH_2Ph	H	**84**	48	**89**	61
$CH_2C_6H_4p\text{-}NO_2$	H	**85**	40	**90**	46
CH_2(1-Naphthyl)	H	**86**	56	**91**	54

Table 2

2.2 Rh(II) cyclisations of α-allenic *N*-tosyloxycarbamates[71]

With *N*-tosyloxycarbamates **65** and **87–91** in hand the scope of the intramolecular allene aziridination reaction was tested. All reactions were carried out using Lebel's conditions[50] (Table 3).



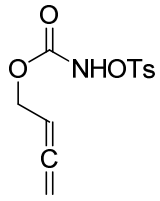
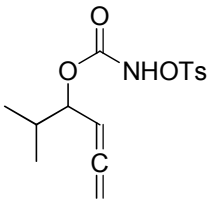
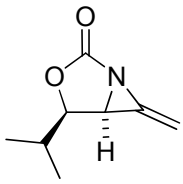
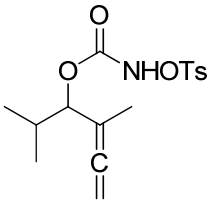
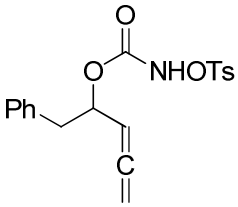
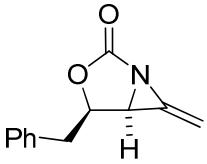
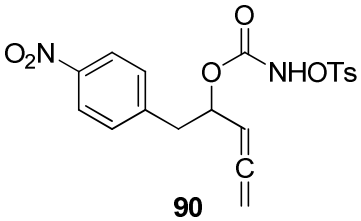
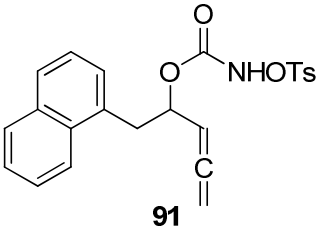
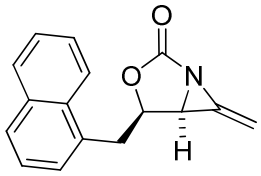
N-tosyloxycarbamate	Product	Yield (%)
 **87**	Decomposition only	–
 **65**	 **64**	27
 **88**	Decomposition only	–
 **89**	 **92**	7
 **90**	Evidence of product in the crude material but unable to purify	–
 **91**	 **93**	20

Table 3

Formation of MA **64** was achieved in an improved[66] and reproducible 27% yield, but no MA was isolated from the reaction of unsubstituted *N*-tosyloxycarbamate **87**. Furthermore, *N*-tosyloxycarbamate **88**, containing an internal methyl substituent, led to a mixture of unidentified products but no MA could be identified in the ^{1}H NMR spectrum of the crude material.

It was predicted that incorporation of a bulky side chain substituent would yield a crystalline MA, from which a single crystal could be grown, to unequivocally confirm the existence of this unique heterocyclic system. Phenyl substituted α-hydroxy allenes have been shown to be unstable[66] thus benzylic *N*-tosyloxycarbamates **89** and **90** were synthesised; the products of the cyclisation reaction could not be purified satisfactorily on silica or alumina and the isolated products quickly decomposed. An even bulkier 1-naphthylmethyl substituted *N*-tosyloxycarbamate **91** was therefore synthesised and gratifyingly crystalline MA **93** was afforded in 20% yield. A single crystal was grown which proved suitable for X-ray structural analysis (Figure 2, Appendix A).

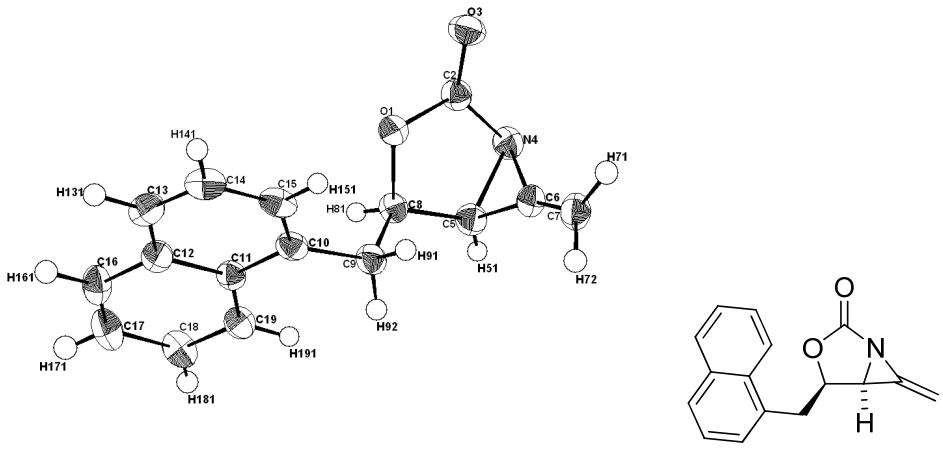
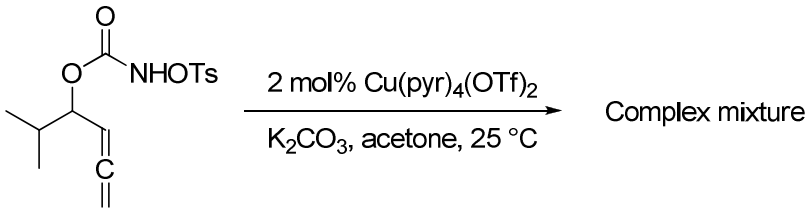


Figure 2

The naphthylmethyl substituent is *endo*-disposed, in accordance with the relative stereochemistry assigned by NMR to MA **64**[66] and, as expected, the nitrogen atom is highly pyramidalised, being 0.79 Å out of the C(2)–C(5)–C(6) plane (crystal numbering). The angle between the two rings was measured to be 108.7°; this significant angle strain should

facilitate ring-opening of the aziridine, ideal for the proposed amino-allyl cation cycloadditions.

Lebel *et al.*[52] demonstrated $Cu(pyr)_4(OTf)_2$ to be a relatively cheap (compared to rhodium) and efficient catalyst for intramolecular aziridinations of alkene tethered *N*-tosyloxcarbamates. The catalyst was readily synthesised[72] and an aziridination reaction was attempted on *N*-tosyloxycarbamate **65** as a test substrate. Under the reported conditions only a complex mixture of products was isolated (Scheme 36).

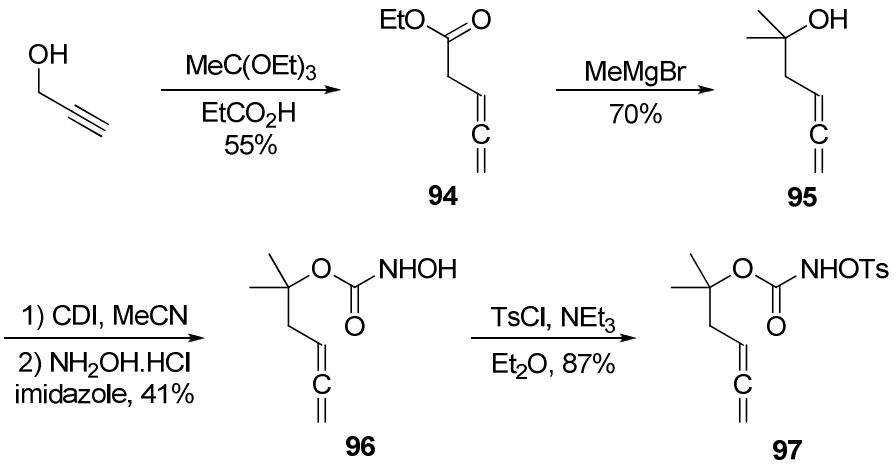


Scheme 36

After increasing the catalyst loading (5 mol%), analysis of the reaction mixture by TLC after 90 min showed that all starting material had been consumed, however no evidence of MA formation was found in the crude material by ^{1}H NMR analysis.

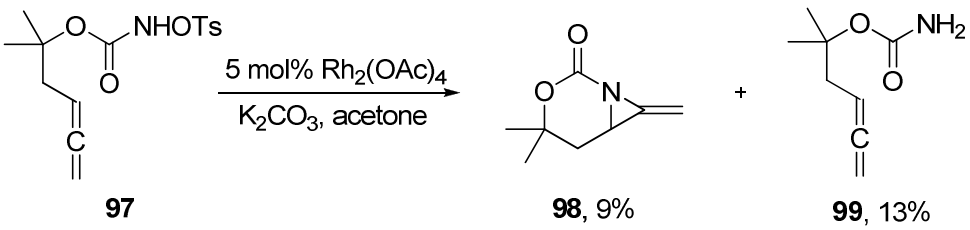
2.3 Extending the tether[71]

Tether extension to yield a six membered ring bicycle, rather than five, may afford a less strained and therefore more stable MA product. To this end, Johnson–Claisen rearrangement[73] of propargyl alcohol with triethylorthoacetate yielded β-allenic ester **94**. To discourage competing C–H insertion reactions in the cyclisation step, steric bulk was added by double alkylation to give dimethyl tertiary alcohol **95**. This was subsequently converted to cyclisation precursor **97** (Scheme 37).



Scheme 37

Upon subjecting *N*-tosyloxycarbamate **97** to rhodium cyclisation conditions, six-membered bicycle **98** formed in low yield, however competing de-tosylation to afford carbamate **99** was preferred (Scheme 38).



Scheme 38

The low yield could be accounted for by the less favourable kinetic conditions of 6-membered ring formation. For subsequent investigations α-allenic *N*-tosyloxycarbamates will be used.

Since the publication of these resultst, further work in the area of carbamate-linked MAs has been completed by Schomaker *et al.*[74a,b] who discovered that bicyclic MAs could be synthesised in moderate yields from terminally substituted α- and β-allenic carbamates.

2.4 Bicyclic MAs from an alternative route

Despite extensive NMR data[66] for MA **64**, and before X-ray crystal data for MA **93** had been acquired, studies were undertaken to synthesise a bicyclic MA independently in order to

provide unequivocal evidence for the structure of this unique heterocycle. The idea, based upon existing methodology,[50] was to create a substituted bicyclic aziridine with a pendant leaving group, which could then undergo elimination[32] to give bicyclic MA **100** (Figure 3).

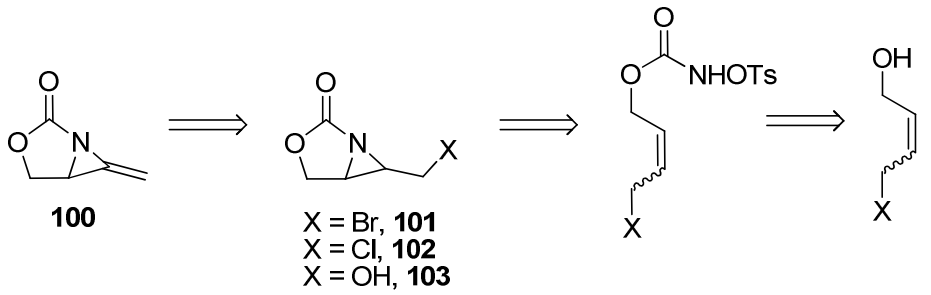
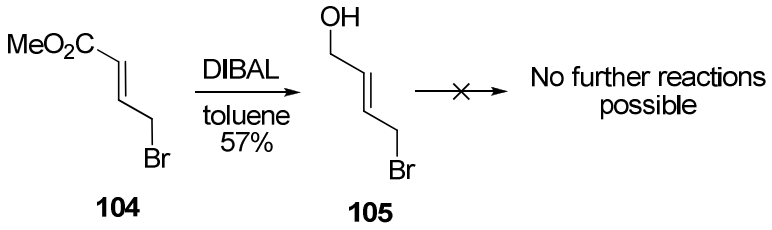


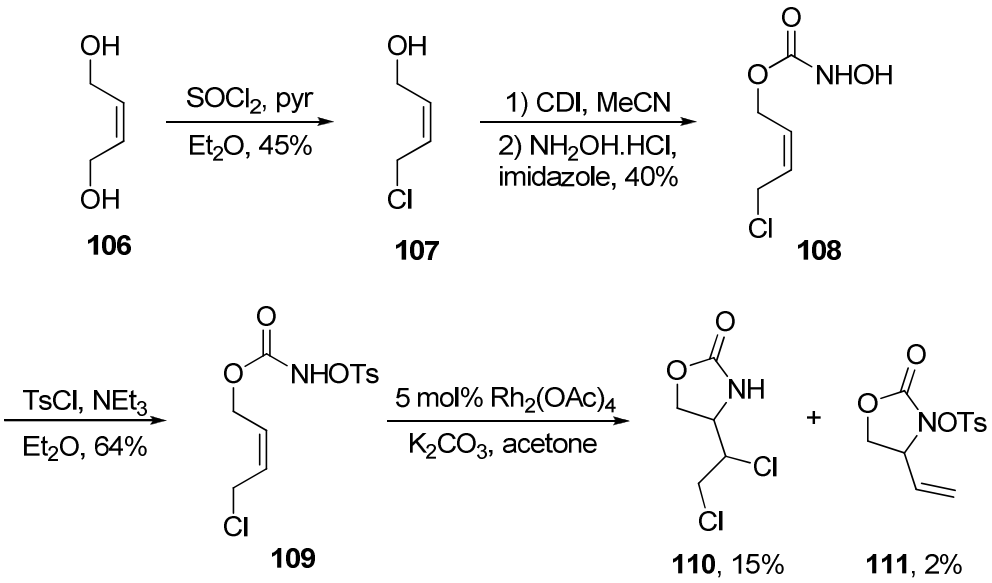
Figure 3

The synthesis of bromine substituted bicyclic aziridine **101** was envisaged by reduction and elaboration of commercially available ester **104**. Reduction with DIBAL afforded allylic bromide **105**, however this was extremely unstable and incompatible with subsequent steps (Scheme 39).



Scheme 39

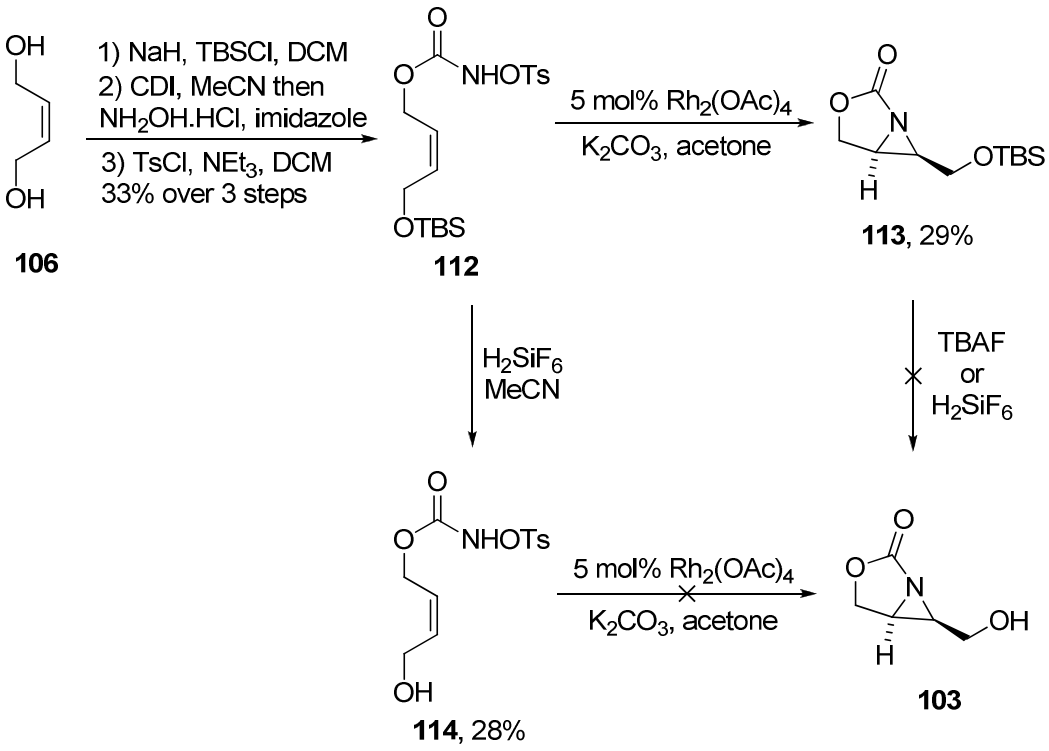
The corresponding chloride **107**, synthesised from diol **106**, proved to be more stable and formation of *N*-tosyloxycarbamate **109** *via* hydroxycarbamate **108** proceeded without difficulty. Aziridination employing Lebel's conditions[50] did not lead to the required bicycle however, only unproductive dichlorooxazolidinone **110**, and *N*-tosyloxyoxazolidinone **111** were able to be isolated (Scheme 40).



Scheme 40

Dichlorooxazolidinone **110** could have formed from successful aziridination followed by ring-opening with adventitious chloride, however *N*-tosyloxyoxazolidinone **111** isolation revealed an unwanted S_Ni' reaction had occurred before rhodium-nitrenoid formation.

Synthesis of hydroxyl substituted aziridine **103** followed by dehydration with Burgess' reagent[74c] or similar could also furnish a MA; in this case unwanted S_Ni' reactions, which hampered aziridine **102** formation, should not hinder the reaction. Mono-protection of diol **106** followed by *N*-tosyloxycarbamate formation and aziridination gave known aziridine **113**[49] from which hydroxyl deprotection was expected to give aziridine **103** (Scheme 41).



Scheme 41

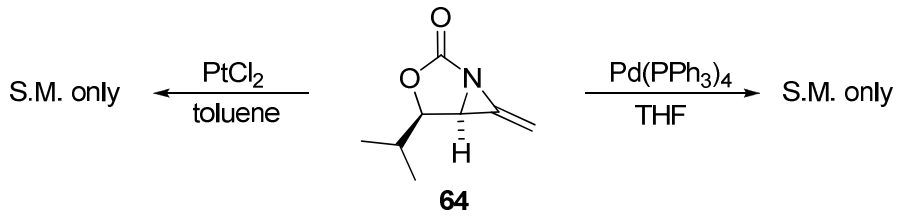
Attempts to remove the TBS group proved futile, with both TBAF, and less basic fluorosilicic acid, producing complex mixtures of products. A second approach involved deprotection before rhodium-catalysed cyclisation. Fluorosilicic acid deprotection conditions were applied to *N*-tosyloxycarbamate **112** to afford alcohol **114**, however, from the subsequent rhodium-catalysed cyclisation, no constructive products could be identified.

During the course of this investigation an X-ray crystal structure of MA **93** had unequivocally confirmed the existence of bicyclic MAs (Figure 2), hence this route was abandoned. It did however illustrate the difficulties involved in forming these species by simple manipulation of known methodologies.

2.5 Reactions of MA 64

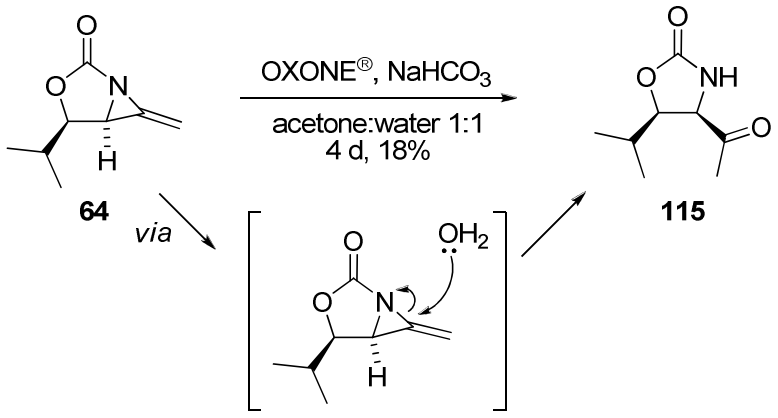
With an improved and reproducible yield of MA **64** the reaction was scaled up and a large quantity of material was synthesised to test the reactivity profile.

The first reactions attempted aimed to isomerise MA **64** with transition metals. Ibuka *et al.*[75] had found that $Pd(PPh_3)_4$ could be used to isomerise *cis*- and *trans*- aziridines whilst Fürstner *et al.*[76, 77] had showed that $PtCl_2$ could isomerise a variety of unsaturated systems. Treatment of MA **64** with 5 mol% Pd(0) at room temperature for 18 h appeared by TLC analysis to show no reaction. A further 5 mol% was thus added and the reaction heated to 45 °C and stirred overnight; TLC analysis now appeared to show a mixture of products, however upon column chromatography almost all the starting material was recovered. Similarly, prolonged periods of heating MA **64** with $PtCl_2$ led to the same result (Scheme 42).



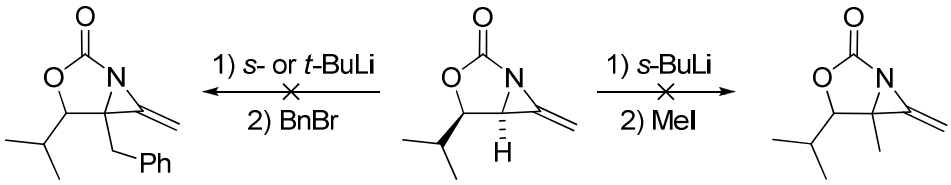
Scheme 42

Epoxidations of the double bond were attempted with both DMDO in acetone and *m*-CPBA, however only starting material was recovered; oxidation with DMDO generated *in situ* led to a mixture of products including interesting acetyl oxazolidinone **115**, which could be derived from the formal attack of water at the sp^2 centre. Rapid decomposition meant full characterisation was not possible (Scheme 43).



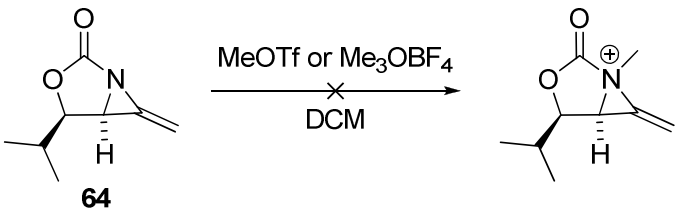
Scheme 43

Deprotonation at C(2) with *s*-BuLi,[1] with subsequent alkylation by both iodopropane and benzyl bromide, was attempted, but was unsuccessful. A similar result occurred with *t*-BuLi and benzyl bromide (Scheme 44).



Scheme 44

Kirby *et al*.[78] had shown that in cases of extreme twisting, amides undergo preferential methylation on nitrogen rather than oxygen; the highly pyramidalised nature of the nitrogen in MA **93** correlates with this localisation of the lone pair. Methylation of MA **64** was attempted with both MeOTf[79] and Me_3OBF_4[78] on preparative and NMR scales, however neither proved conclusive as to whether methylation had occured at nitrogen, oxygen or indeed at all (Scheme 45).

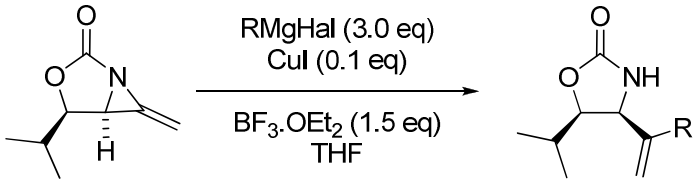


Scheme 45

2.6 S_NV reactions of MA 64[71]

Eis and Ganem[80] showed that aziridines could be alkylated with $BF_3.OEt_2$ and organocopper reagents to afford primary and secondary amines. It was expected that by applying this methodology to MA **64**, ring-opening would be preferred over carbamate carbonyl attack.

When MA **64** was treated with ethylmagnesium bromide, $BF_3.OEt_2$ and catalytic CuI, ring-opening occurred exclusively at the vinylic C(3)–N bond to give oxazolidinone **116**. This result was repeated with a variety of Grignard reagents (Table 4).



64 **116-119**

R (compound)	Et (**116**)	*i*-Pr (**117**)	*n*-Bu (**118**)	Ph (**119**)
Yield (%)	72	26	23	27

Table 4

The *cis*- geometry of the MA was retained, as confirmed by an X-ray crystal structure of oxazolidinone **118** (Figure 4, Appendix B).

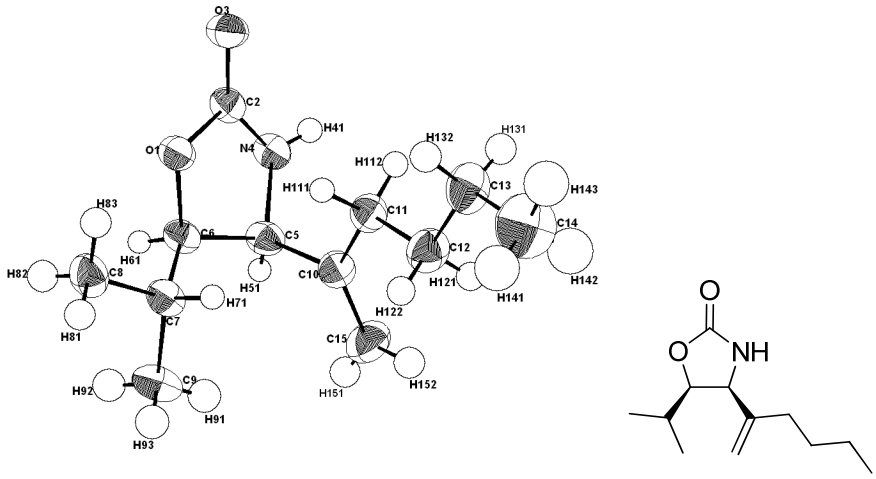
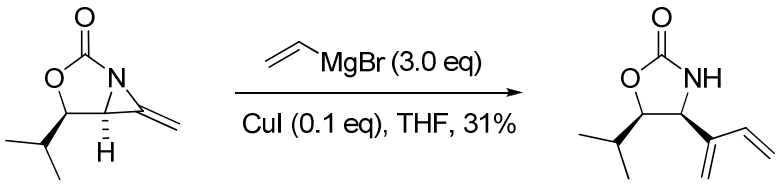


Figure 4

The structural information acquired for MA **93** can help to explain the regiochemical outcome; of the two C–N bonds in the aziridine, the C(5)–N bond (crystal numbering, Figure 2) is naturally antiperiplanar to the carbonyl bond (in **93**: (O=C)/(C–N) dihedral angle = 176°) whereas the C(6)–N bond is more closely orthogonal to the carbonyl (in **93**: (O=C)/(C–N) dihedral angle = 116°). In effect, cleavage by nucleophiles of the C(6)–N bond should be accompanied by delocalisation of the developing negative charge on nitrogen into the C=O π-system without significant conformational change. This interesting S_NV mode of reactivity is surprisingly common and has recently been reviewed by Narasaka *et al.*[81]

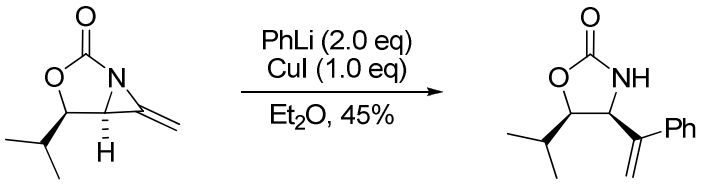
The ^{1}H NMR spectra of the crude products suggested the reactions proceeded more cleanly than the isolated yields implied. Initial optimisation, by omission of the Lewis acid raised the yield of butyl substituted oxazolidinone **118** from 23% to 32%, and a further oxazolidinone, potentially useful diene-tethered oxazolidinone **120**, was also synthesised in this manner (Scheme 46).



64 **120**

Scheme 46

Benzalacetone was used as a test substrate to examine a selection of organocuprate reactions. Investigations showed that using stoichiometric amounts of organocuprate (formed from CuI and the appropriate organolithium) led to an increase in the yield of nucleophilic alkylations. Transferring this methodology back to MA **64**, the reaction was not superior when using butyllithium, however with phenyllithium, oxazolidinone **119** was afforded in 45% yield, an increase of 18% (Scheme 47).



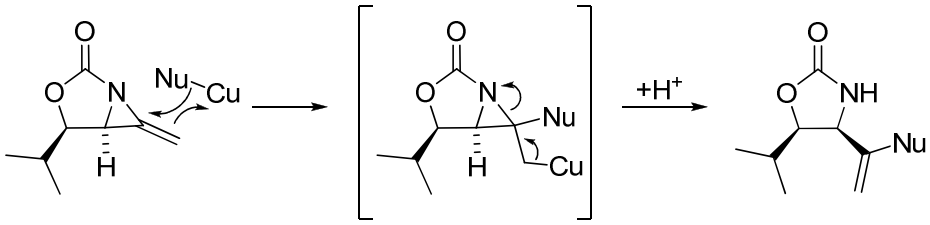
64 **119**

Scheme 47

2.7 Mechanistic study of S_NV reaction

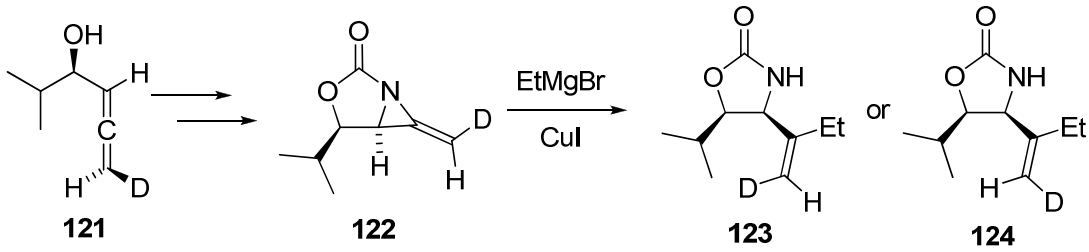
The X-ray structure of *cis*-oxazolidinone **118** (Figure 4) had shown that the configuration at C(2) was retained; however a true S_NV mechanism could only be confirmed if inversion at C(3) could be proven. Calculations based on the crystal structure of MA **93**, show that the C=C π* is concentrated on the internal carbon centre, thus an alternative

addition-elimination mechanism could also be envisaged. Addition of the nucleophile at the vinylic centre would lead to a localisation of charge at the external carbon in the transition state (which could be stabilised by copper), followed by ring-opening to give the *cis*-oxazolidinone. Furthermore *syn*- addition of Cu–Nu across the double bond could be considered the initial step (Scheme 48).



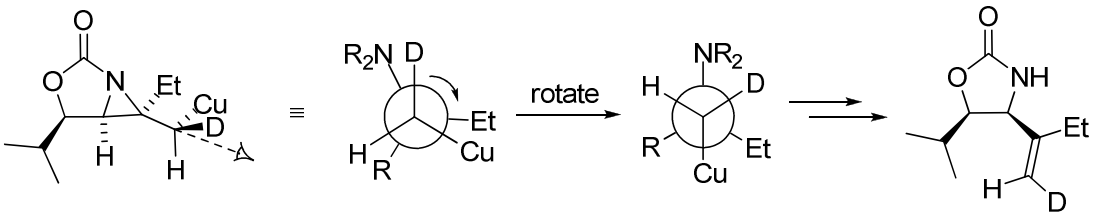
Scheme 48

Since the rhodium-catalysed cyclisation reaction was sensitive to the substitution pattern of the allene, deuterium labelling was the best option for tracking inversion. Deuterium-labelled allene **121** would be converted to MA **122**, which after organocuprate addition, would yield inversion product **123**, retention product **124** or a mixture of the two (Scheme 49).



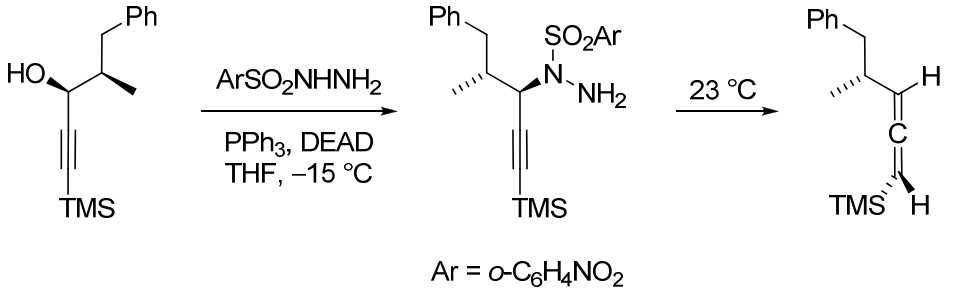
Scheme 49

If inversion product **123** is observed then direct S_NV is inferred, whilst other results implicate the alternative addition-elimination mechanism. If retention product **124** is formed exclusively, then rotation of the *syn*- Cu–Et adduct in the transition state could account for the observed stereochemistry (Scheme 50).



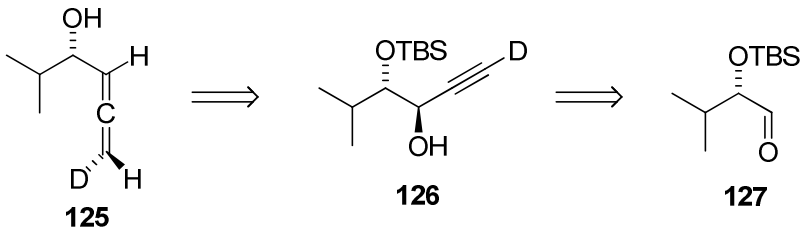
Scheme 50

A synthesis was therefore required of deuterium labelled α-hydroxy allene **121**. Myers and Zheng[82] had shown that allenes could be made stereospecifically from propargylic alcohols by a Mitsunobu reaction with *o*-nitrobenzenesulfonylhydrazine (NBSH) followed by spontaneous rearrangement (Scheme 51).



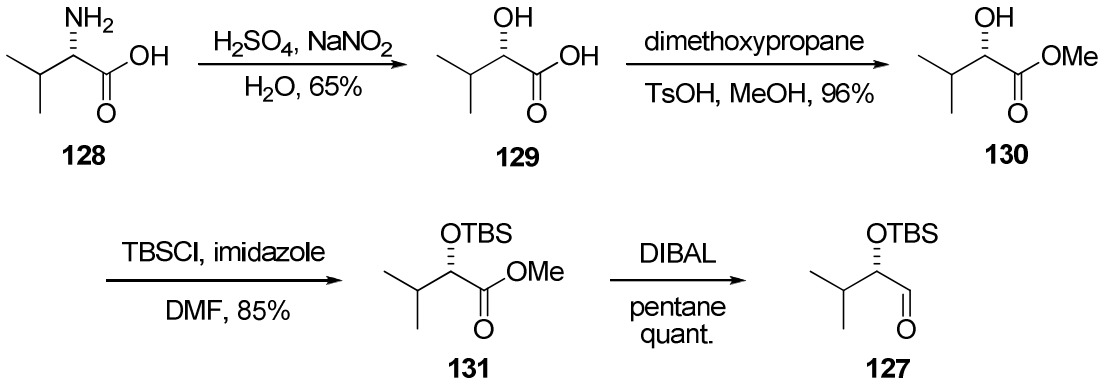
Scheme 51

Based on this precedent, retro-synthetic analysis for allene **125** suggested synthesis of propargyl alcohol **126** from a stereoselective addition into known[83] aldehyde **127** (Scheme 52).



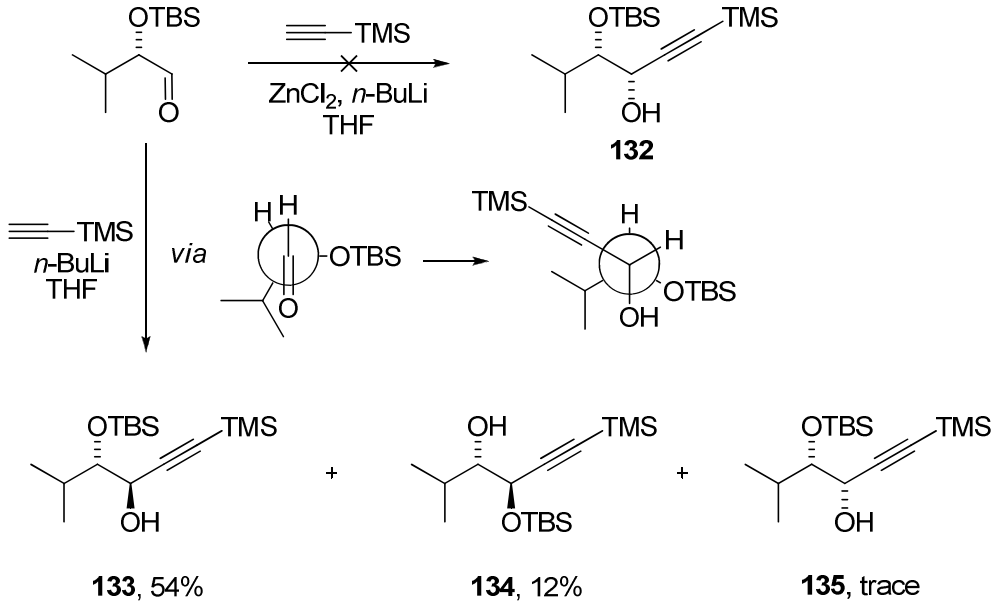
Scheme 52

Aldehyde **127** was synthesised from L-valine **128** following literature procedures. Diazotisation and double inversion gave hydroxy acid **129**[84] and esterification[85] followed by protection gave ester **131** which was subsequently reduced to aldehyde **127** with DIBAL[83] (Scheme 53).



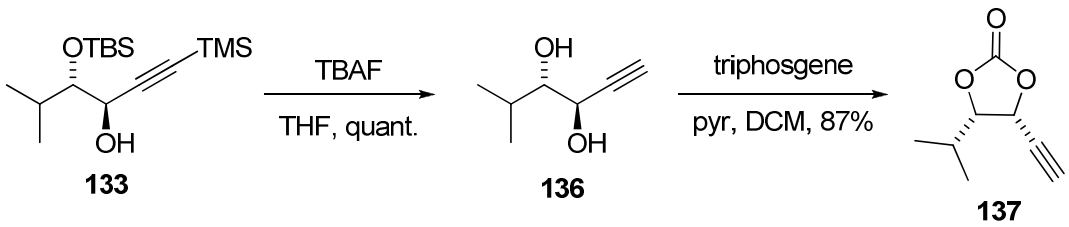
Scheme 53

Since deuterium should not affect the aziridination reaction, the stereoselectivity of alkyne addition to give the (*S*)- or (*R*)- alcohol was not important, so long as the diastereomers were separable. It was envisaged that TMS-acetylide addition followed by deprotection with *in situ* deuteration would be the best reaction sequence. Attempts were made to control the TMS-acetylide addition using Walsh's[86] zinc chelation control of α-silyoxy groups to give the *anti*-Felkin–Anh *syn*- product **132** (Scheme 54). The reaction appeared to consume the starting material but mass recovery was poor. An approach without a Lewis acid was therefore adopted to acquire the classic Felkin–Anh *anti*- result. Pleasingly separable *anti*-alcohol **133** was obtained, along with minor amounts of inseparable silicon-migrated alcohol **134** and *syn*- diastereomer **135** (Scheme 54).



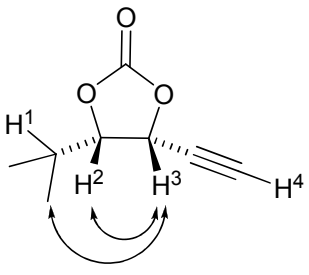
Scheme 54

In order to confirm the stereochemistry of alcohol **133** the silyl groups were removed with TBAF to give diol **136**, which was subsequently cyclised to afford carbonate **137** (Scheme 55).



Scheme 55

The coupling constant between the carbonate ring protons of 7.2 Hz did not define the relative stereochemistry, therefore an nOe experiment was run (Figure 5).

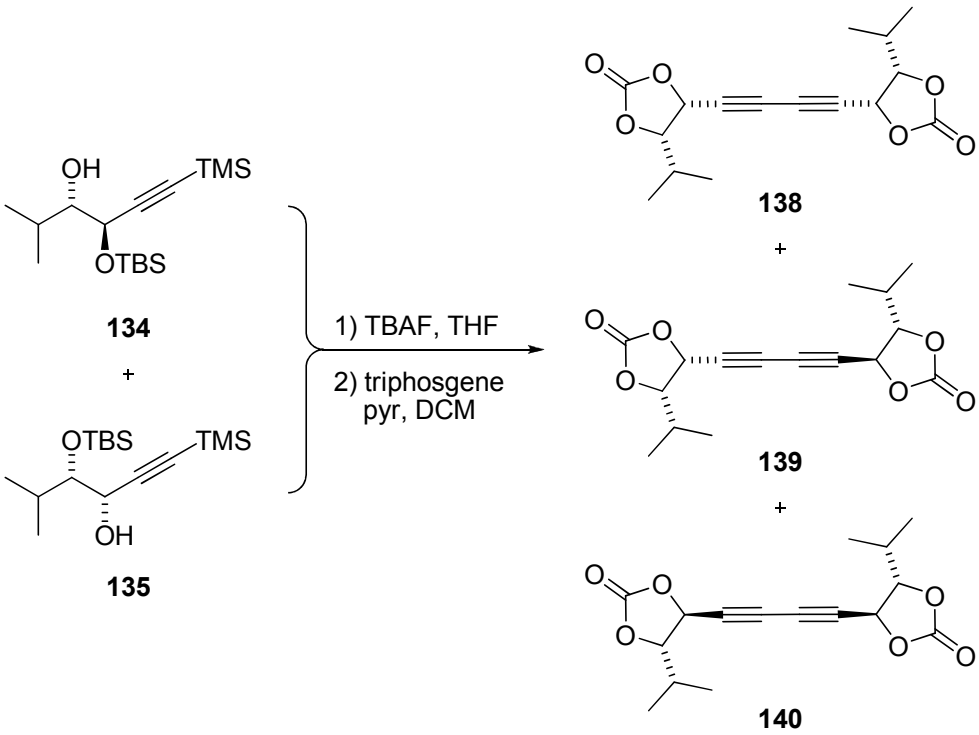


nOe correlations

Figure 5

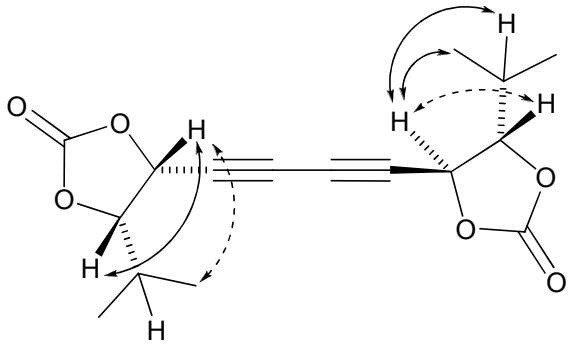
The structure was tentatively assigned as *cis*- since there were no nOe correlations between H^4 and H^2, however correlations were observed between H^3 and one of the methyl groups. There was a very strong nOe correlation between H^2 and H^3.

More conclusive evidence was desired, therefore the trace amount of *syn*- diastereomer **135** (present in a mixture with silicon-migrated alcohol **134**) from the aldehyde addition reaction was used to synthesise the alternative carbonate. Accordingly, TBAF removal of the silyl protecting groups led to a mixture of products which were treated directly with triphosgene in the prospect of forming separable carbonates. Surprisingly, a mixture of three separable dimers was formed in the reaction sequence, consisting of *cis-cis* dimer **138**, *cis-trans* dimer **139** and *trans-trans* dimer **140** (Scheme 56).



Scheme 56

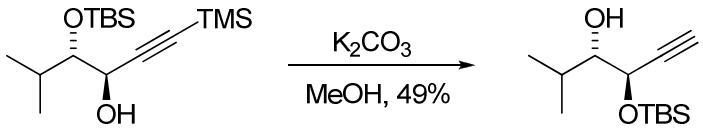
The coupling constants for the *cis-cis* dimer **138** matched exactly those of carbonate **137** and nOe experiments on all three compounds (Figure 6 shows *cis-trans* dimer **139**) confirmed that alcohol **133** had the expected Felkin–Anh *anti*- stereochemistry.



nOe correlations
dashed = weak

Figure 6

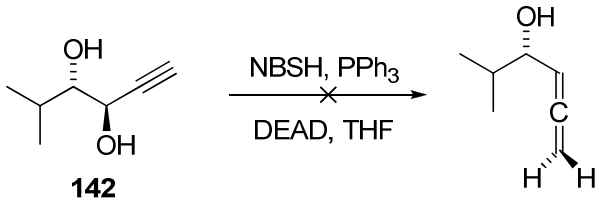
To synthesise deuterated alkyne **125**, desilylation of alcohol **133** with deuteration *in situ* was required using K_2CO_3 in deuterated methanol.[87] The principle was first tested with ordinary methanol, however migration of the TBS group could not be prevented under these conditions. Careful reaction monitoring by TLC confirmed that silyl migration occurred before TMS removal (Scheme 57).



133 **141**

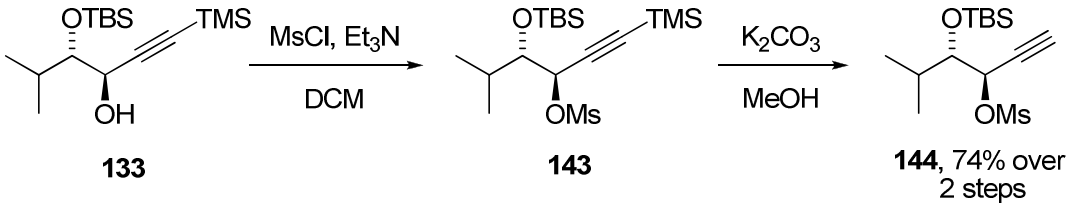
Scheme 57

A variety of other conditions were attempted to induce the required deprotection. Treatment with 1.0 M HCl in ether led only to recovered starting material, whereas reaction with controlled amounts of TBAF gave global deprotection. A small scale (10 mg) reaction with $AgNO_3$ and KCN[88] appeared to yield the desired product; however upon scaling up to a 50 mg scale, only the silyloxy-migrated product was isolated. Since alkyne deprotection had proven difficult, the Myers chemistry was attempted on fully deprotected diol **142**, but this led to an inseparable mixture of products (Scheme 58).



Scheme 58

Scale-up of the synthesis of alcohol **133** had been successful, therefore an alternative approach was to convert the hydroxyl into a leaving group and effect stereoselective conjugate reduction to yield required α-hydroxy allene **125**. Mesylation[89] of alcohol **133** followed by deprotection (non-deuterated methanol used for test reactions) with K_2CO_3 afforded desired mesylate **144** in good yield (Scheme 59).



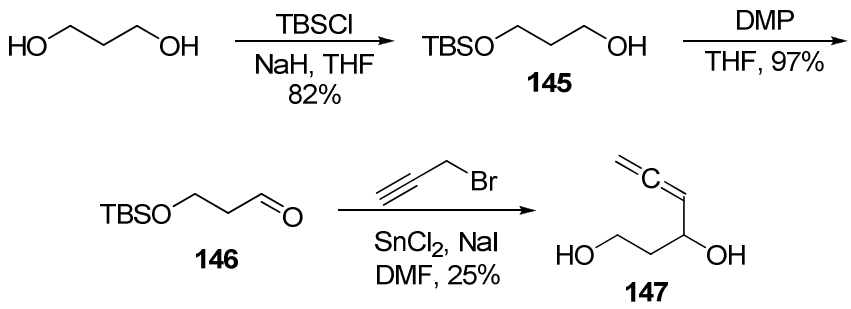
Scheme 59

A variety of conditions were employed to induce conjugate reduction; hydride addition with $LiAlH_4$[90] or $LiBEt_3H$ led to recovered starting material, whilst the inclusion of $Pd_2(dba)_3$[91] gave a mixture of unisolable products with both reductants. An interesting approach using CuCN, Bu_3SnH and butyllithium[92] led to butyl addition products only. Lastly, it was believed substitution with tosylhydrazine[93] could lead to a spontaneous rearrangement to the allene, however the molecule was too hindered for successful S_N2 displacement and starting material was recovered. This route was becoming unwieldy and due to time constraints, efforts were directed elsewhere.

2.8 *In situ* trapping of MAs by tethered hydroxyl groups

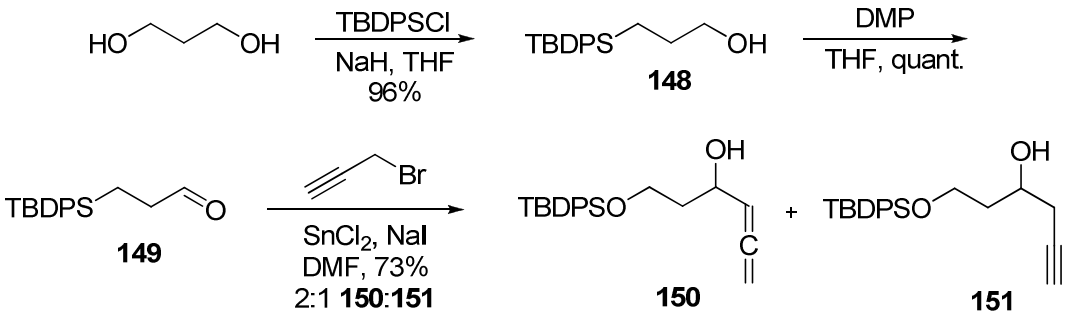
An investigation was carried out to examine whether a MA could be trapped *in situ* by a tethered hydroxyl during the rhodium-catalysed cyclisation, complementing results obtained elsewhere within the group for hydroxyl-tethered allylic carbamates.[49] Starting from

propan-1,3-diol, protection of one hydroxyl enabled oxidation of the other to yield aldehyde **146**. Allenation was attempted under the reaction conditions described previously, however TBS deprotection could not be avoided and only unproductive diol **147** was obtained (Scheme 60).



Scheme 60

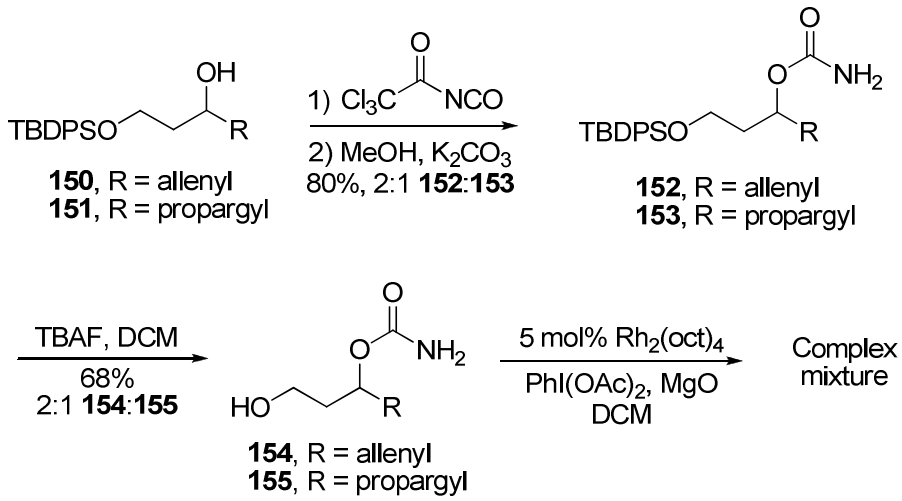
A bulkier silyl group was expected to survive the reaction conditions, thus a similar route was employed to afford TBDPS protected aldehyde **149**, which was allenated without alcohol deprotection. Propargyl side-product **151** could not be removed from required allene, however it was intended separation would be achieved at a later stage (Scheme 61).



Scheme 61

Formation of the hydroxycarbamate proved arduous, and therefore the route was switched to access carbamate **154** so that Du Bois' conditions for aziridination[46] could be utilised as an alternative. Removal of the TBDPS group gave alcohol **154**, however separation from the alkynyl by-product was still not possible. The mixture of carbamates **154** and **155** was

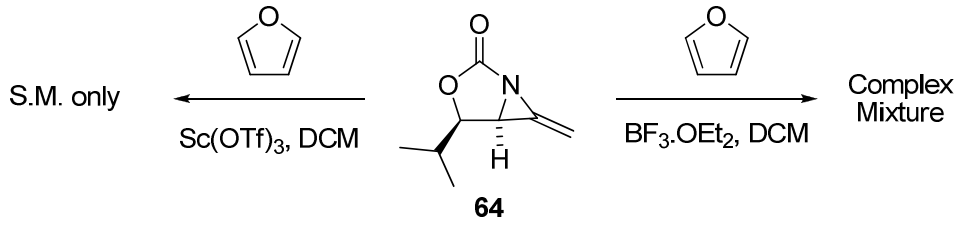
treated with rhodium octanoate under Du Bois' conditions but, after exhaustive purification, it became clear that the products were too numerous and minor to isolate (Scheme 62).



Scheme 62

2.9 *In situ* trapping of MAs by furan[71]

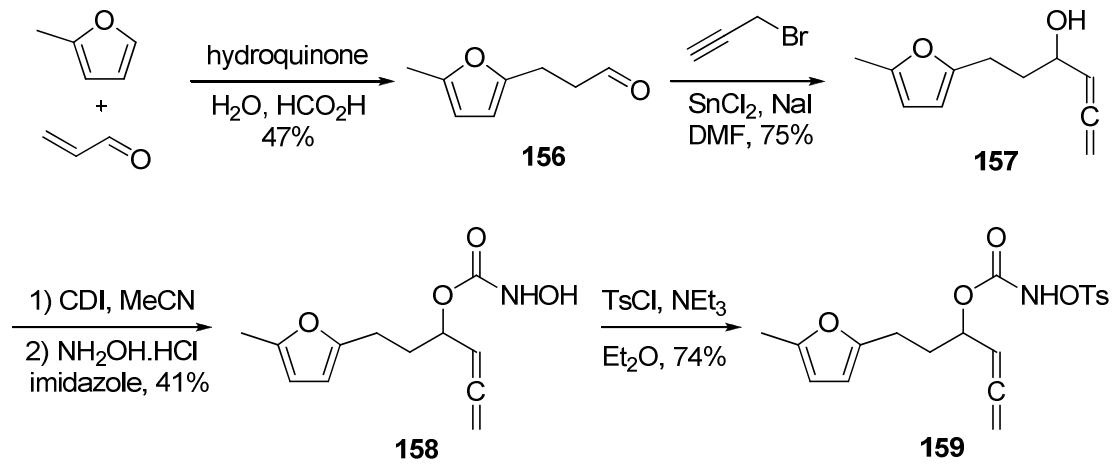
Returning to the aim of using MAs as precursors to amino-allyl cations for [4+3] cycloaddition reactions, MA **64** was treated with either $BF_3.OEt_2$ or $Sc(OTf)_3$ in the presence of excess furan. The reaction with $BF_3.OEt_2$ gave a complex mixture of products, whilst that with $Sc(OTf)_3$ merely returned starting material (Scheme 63).



Scheme 63

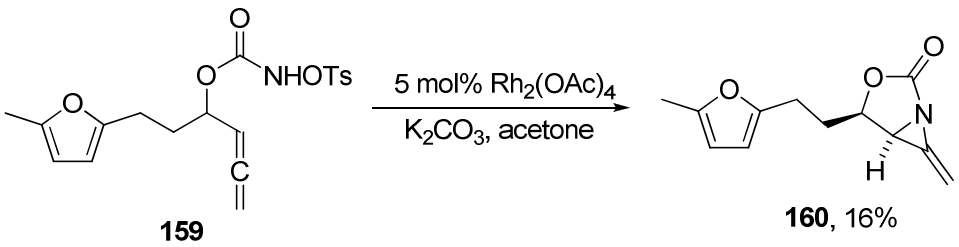
There appeared to be some evidence (from the ^1H NMR spectrum of the crude material) for cycloaddition in the $BF_3.OEt_2$ reaction, but side reactions were dominating due to the strength of the Lewis acid; it was thought that an intramolecular variant would undergo cycloaddition under milder reaction conditions. To this end, Michael addition[94] of 2-methyl-furan into acrolein gave aldehyde **156** which was subsequently allenated to yield

alcohol **157**. Hydroxycarbamate formation and tosylation afforded desired furan-tethered *N*-tosyloxycarbamate **159** (Scheme 64).



Scheme 64

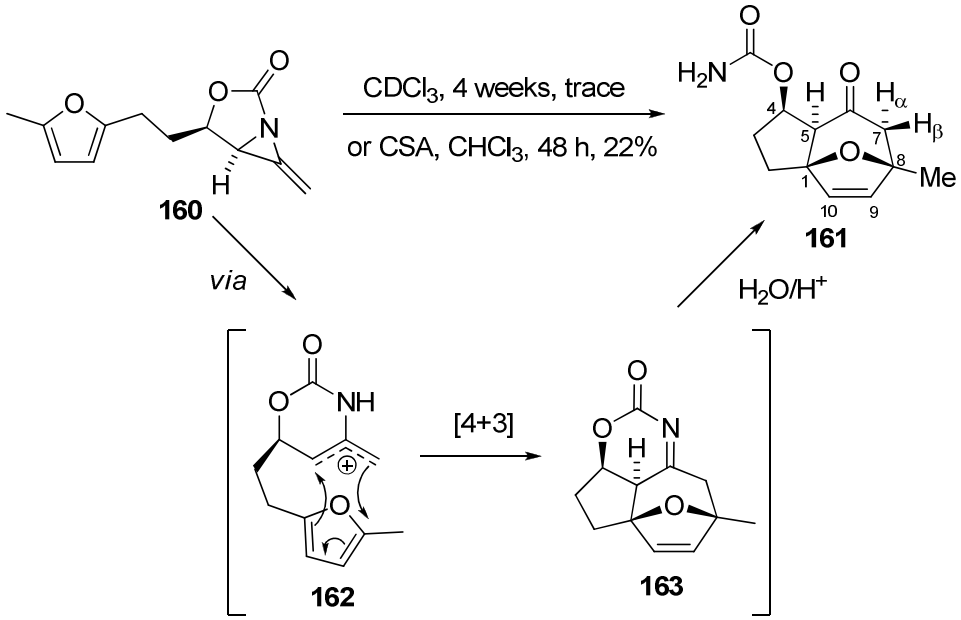
Reaction of *N*-tosyloxycarbamate **159** under Lebel's aziridination conditions led to formation of MA **160** in an unoptimised 16% yield, comparable to that obtained with simpler substrates (Scheme 65).



Scheme 65

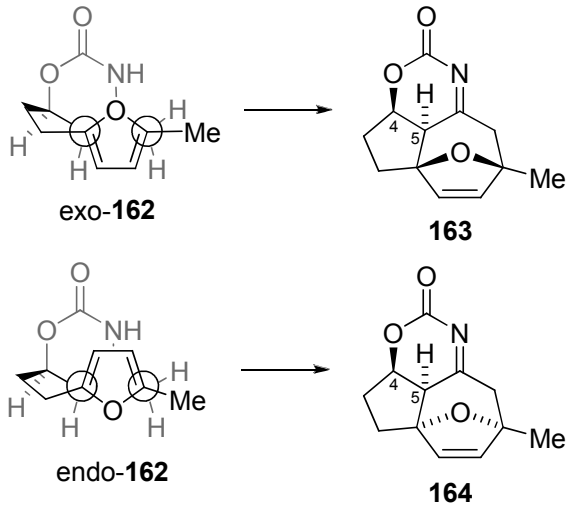
After leaving an NMR sample of MA **160** in $CDCl_3$ for 72 h, it became apparent that the molecule was not stable since the ^1H NMR spectrum appeared to show degradation of characteristic peaks. New peaks had appeared however and the sample was monitored by NMR every 3–4 days. After four weeks, ^1H NMR spectroscopy revealed that MA **160** was no longer present in the sample and an alternative compound had formed. Preparative TLC was employed to remove the impurities and carbamate **161** was recovered, presumably derived from hydrolysis of imine **163**. Freshly synthesised MA **160** was then dissolved in chloroform containing a small quantity of CSA and, once TLC analysis had shown the

complete consumption of starting material, a pure sample of carbamate **161** was isolated and characterised (Scheme 66).



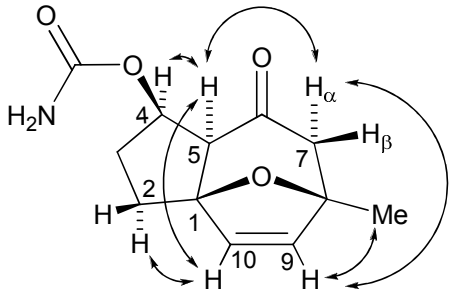
Scheme 66

The stereochemical assignment of tricycle **161** began by considering the two possible approaches of the furan to the amino-allyl cation to generate imine **163** and its diastereomer **164**. In both products there is a *cis*- relationship between H(4) and H(5) which would be carried forward to carbamate **161** (Scheme 67).



Scheme 67

A NOESY experiment (on carbamate **161**) allowed H(9) to be distinguished from H(10) by its correlation to H(7_α) and the methyl group. From this, correlation of H(10) to H(5) set the HC=CH bridge *syn*- to H(5) to complete the assignment (Figure 7).



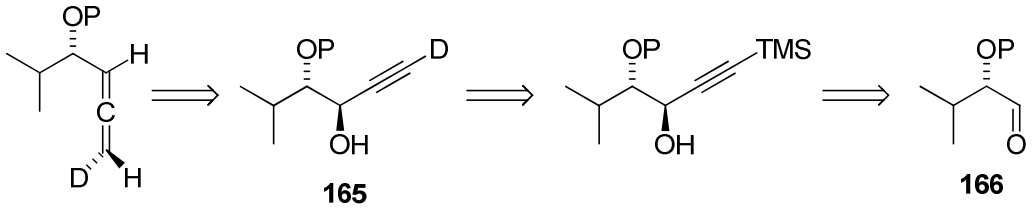
Important nOe correlations

Figure 7

This result proved that bicyclic MAs are able to ring-open to yield amino-allyl cations and undergo intramolecular [4+3] cycloadditions. Improved conversion and substrate scope was believed to be possible by utilising a sulfamate linker and efforts towards this are discussed in the next chapter.

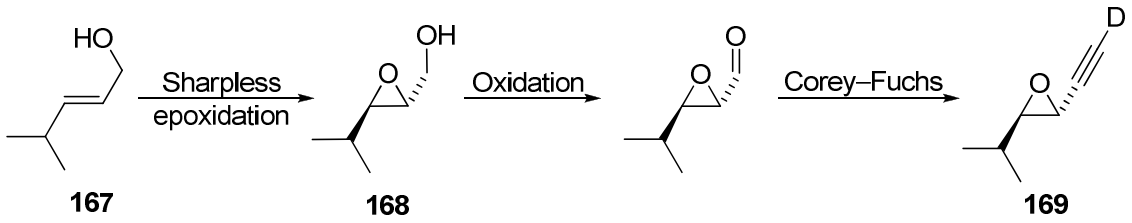
2.10 Future work

The formation of deuterated MA **122**, and the result of its copper-catalysed nucleophilic alkylation, should provide compelling evidence for the operation of an invertive S_NV mechanism or otherwise. Future work will focus on alternative methods of synthesising MA **122** precursor **121**. Simple substitution to a less migratory-prone protecting group, for example PMB or the bulkier TBDPS group, should lead to required deuterated alkyne **165**, from which the Myers[82] rearrangement chemistry could then be tested. This will, however, require re-evaluation of the stereoselectivity of the TMS-acetylide addition into aldehyde **166** (Scheme 68).



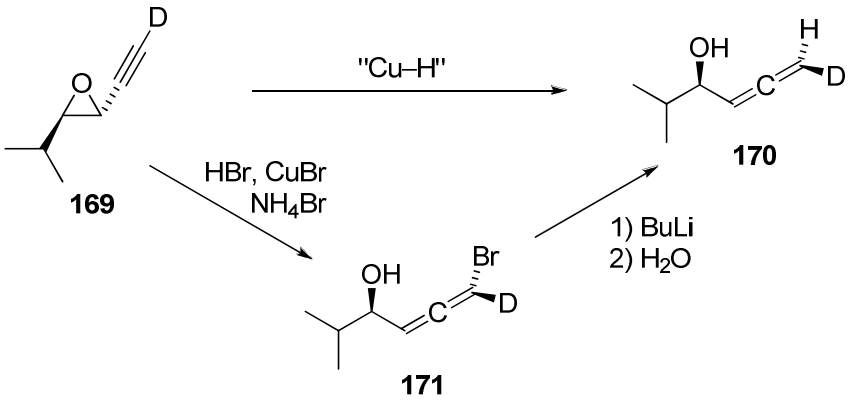
Scheme 68

An appealing alternative approach is envisaged based on work by Chemla *et al.*[95, 96] In this, formation of epoxide **168** would be achieved by Sharpless asymmetric epoxidation[97] of known[98] allylic alcohol **167**, which could then be transformed into alkyne **169** after oxidation and trapping of the Corey–Fuchs[99] product with D_2O (Scheme 69).



Scheme 69

Conjugate addition of copper hydride, for example, should then lead to alcohol **170** as a single diastereomer. Alternatively, use could be made of Chemla's[95] synthesis of bromallenols to give allene **171**. Lithiation and anion trapping *in situ* should also provide the desired substrate, however allenyl anion rearrangement would have to be avoided (Scheme 70).



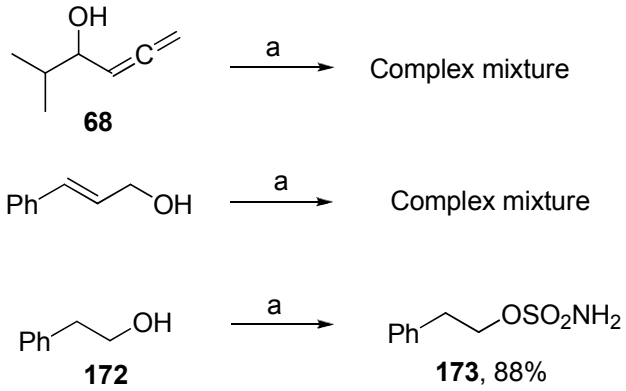
Scheme 70

3. Sulfamate linked MAs

3.1 Initial investigations

Du Bois[54] has shown that the intramolecular rhodium-nitrenoid aziridination of alkenes could be achieved with sulfamates as well as carbamates. This variant was tested to see if the intramolecular amination of allenes could be improved in both yield and substrate scope.

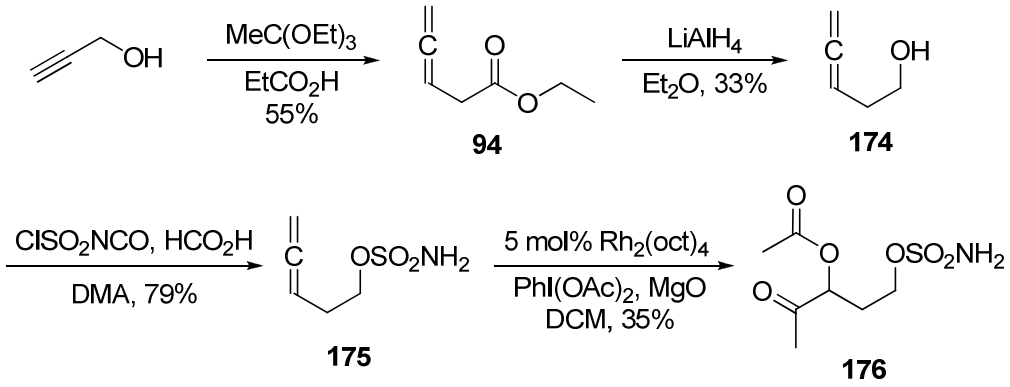
Sulfamate formation from α-hydroxyallene **68** failed using sulfamoyl chloride produced *in situ*[56] and indeed the lack of sulfamate product when the reaction was attempted with cinnamyl alcohol, showed that allylic alcohols cannot undergo sulfamate formation without decomposition. A test with phenylethanol **172** gave sulfamate **173** which proved that the methodology was sound, therefore β-allenic sulfamate substrates would be studied (Scheme 71).



a) $ClSO_2NCO$, HCO_2H, DMA

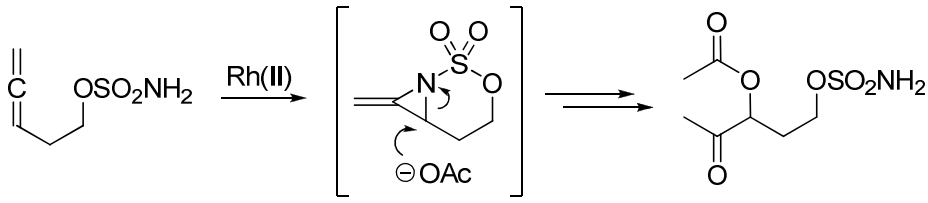
Scheme 71

Previously, a Johnson–Claisen rearrangement of propargyl alcohol had been used to synthesise β-allenic ester **94** (Scheme 37). Simple reduction to give alcohol **174** followed by sulfamate formation yielded unsubstituted β-allenic sulfamate **175**. Treatment under Du Bois' conditions ($Rh_2(oct)_4$, MgO and $PhI(OAc)_2$ in DCM) afforded acetoxysulfamoyl ketone **176** in moderate yield (Scheme 72).



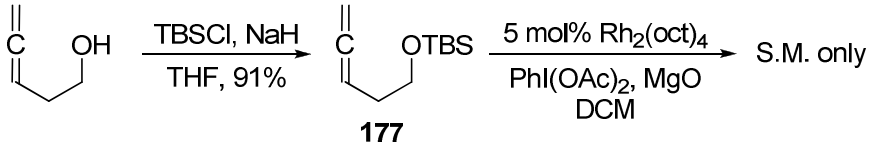
Scheme 72

It was envisaged that ketone **176** could form *via* the ring opening of a MA intermediate by acetate, followed by hydrolysis of the subsequent enamine (Scheme 73).



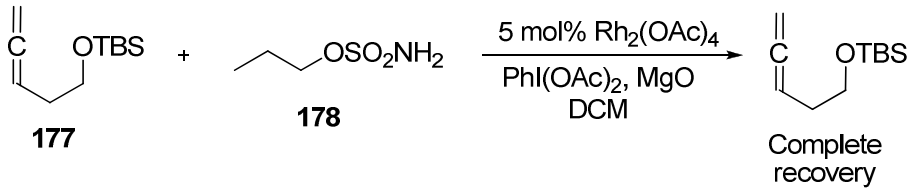
Scheme 73

A test reaction was run to either confirm the participation of the sulfamate group or discover that iodobenzene diacetate had oxidised the allene independently. In the reaction of protected alcohol **177** only starting material was recovered after a prolonged reaction time; thus it was concluded that the sulfamate group is implicated in the synthesis of ketone **176** (Scheme 74).



Scheme 74

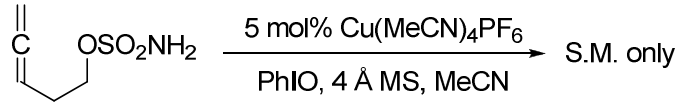
Production of ketone **176** by an intermolecular reaction was ruled out by treating a mixture of protected alcohol **177** and propylsulfamate **178** under the rhodium-nitrenoid cyclisation conditions; protected alcohol **177** was fully recovered (Scheme 75).



177 178

Scheme 75

Dauban *et al.*[57] had found that copper could also be used as a catalyst for the intramolecular sulfamate aziridination of tethered alkenes. Sulfamate **175** was subjected to the reported conditions, however even after extended reaction times, starting material was fully recovered (Scheme 76).



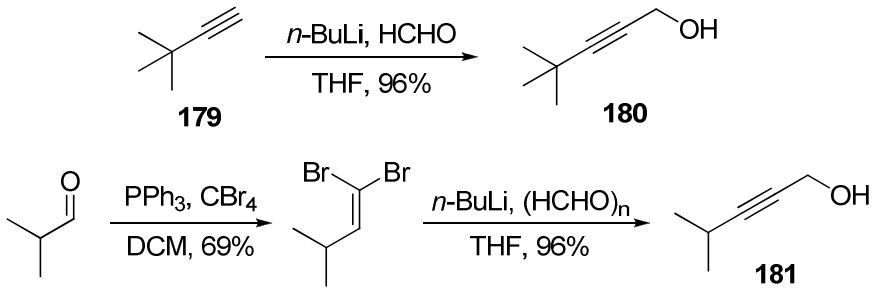
175

Scheme 76

Since the initial result of the rhodium cyclisation had proved promising, investigations continued to assay a range of β-allenic sulfamate substrates.

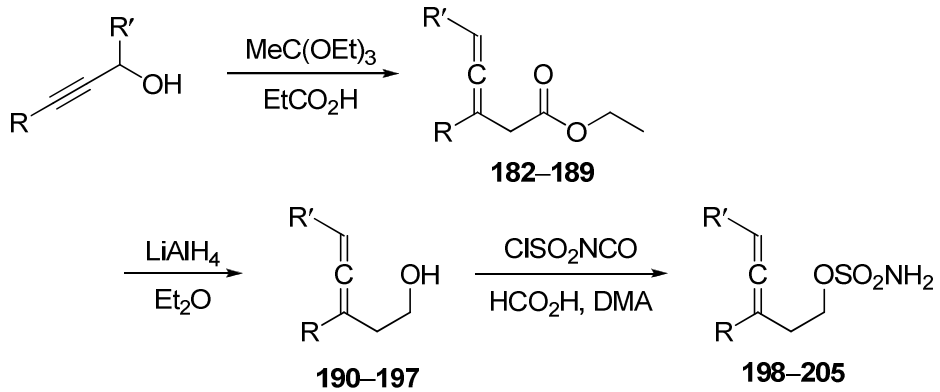
3.2 Synthesis of sulfamates

Based on a successful route to β-allenic esters from the Johnson–Claisen rearrangement of propargylic alcohols, a variety of β-allenic sulfamates were synthesised. Most of the starting propargylic alcohols were commercially available and others were synthesised using simple literature procedures; *tert*-butyl substituted alcohol **180** was prepared from the addition of lithiated alkyne **179** into paraformaldehyde,[100] whilst the Corey–Fuchs reaction of isobutyraldehyde, quenching with paraformaldehyde, yielded *iso*-propyl substituted alcohol **181**[101] (Scheme 77).



Scheme 77

From these and commercially available compounds, β-allenic sulfamates **198–205** were synthesised (Table 5).



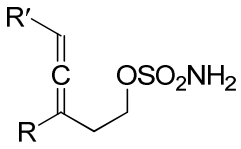
R	R′	Compound	Yield (%)	Compound	Yield (%)	Compound	Yield (%)
H	*i*-Pr	**182**	94	**190**	99	**198**	68
Me	H	**183**	42	**191**	93	**199**	82
n-Pr	H	**184**	39	**192**	76	**200**	70
i-Pr	H	**185**	60	**193**	98	**201**	85
t-Bu	H	**186**	42	**194**	93	**202**	82
Ph	H	**187**	24	**195**	75	**203**	55
TMS	H	**188**	49	**196**	98	**204**	52
Et	Me	**189**	80	**197**	99	**205**	82

Table 5

The yields of the Johnson–Claisen rearrangement were sometimes unsatisfactory, often due to volatility of the product. Higher yields were obtained in later syntheses by increasing the amount of orthoacetate from 3 eq. to 6–7 eq.. In the sulfamation step, use of fresh $ClSO_2NCO$ gave much higher yields.

3.3 Rh(II) cyclisations of sulfamates[102]

The rhodium-nitrenoid cyclisation was tested on sulfamates **198**–**205** using readily available $Rh_2(OAc)_4$ (Table 6).



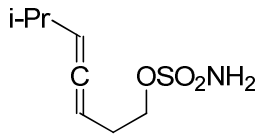
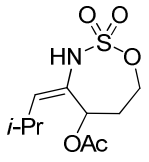
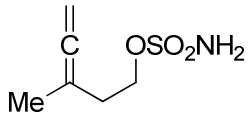
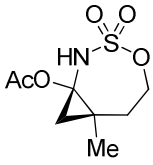
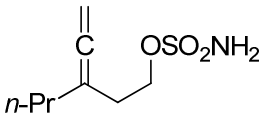
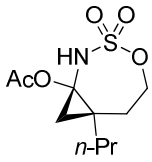
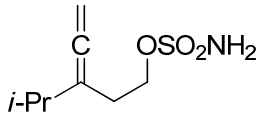
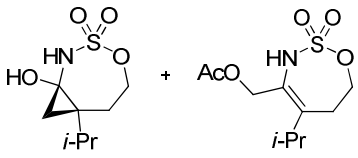
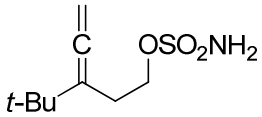
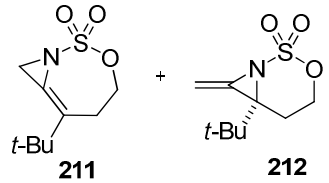
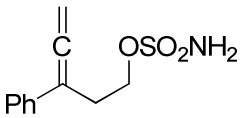
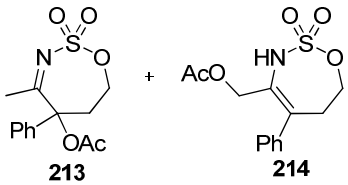
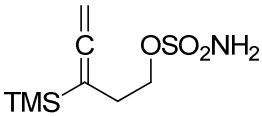
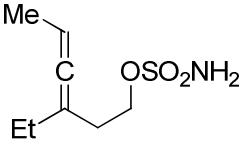
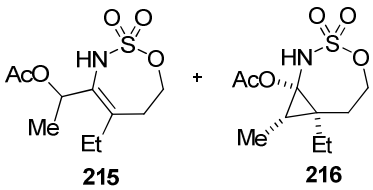
Sulfamate	Product(s)	Yield(s) (%)
 **198**	 **206**	52
 **199**	 **207**	50
 **200**	 **208**	40
 **201**	 **209** **210**	20 (**209**) and 12 (**210**)
 **202**	 **211** **212**	68 (**211**) and 12 (**212**)
 **203**	 **213** **214**	24 (**213**) and 5 (**214**)
 **204**	Decomposition	–
 **205**	 **215** **216**	28 (**215**) and 26 (**216**)

Table 6

Externally substituted sulfamate-tethered allene **198** appeared to react *via* a similar intermediate as for unsubstituted allene **175**, however in this case the enamine was more stable under the reaction conditions and was not hydrolysed during purification. The *E*-geometry was assigned courtesy of an X-ray crystal structure (Figure 8, Appendix C).

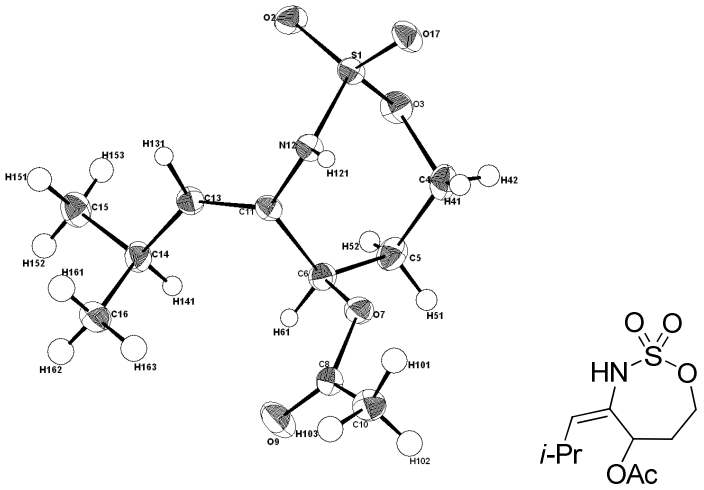
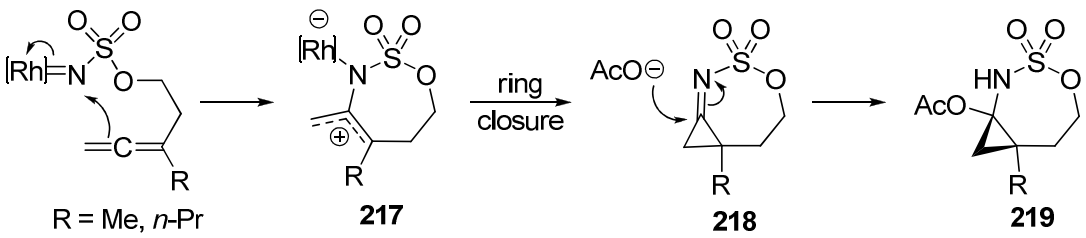


Figure 8

Since acetate attack occurred at the internal C–N bond in the reactions of sulfamates **175** and **198**, it was predicted that internal allene substituents would block attack, allowing the MA to be isolated. In fact, the reaction of primary alkyl substituted allenes **199** and **200** gave unexpected aminocyclopropane products **207** and **208** in moderate yields. The formation of these compounds is unlikely to have occurred *via* a MA and so amino-allyl cation **217** should be considered the correct intermediate. With an internal primary alkyl group, amino-allyl cation **217** has time to ring-close before acetate attack on imine **218** yields aminocyclopropane **219** (Scheme 78).



Scheme 78

The structure of aminocyclopropane **208** was confirmed by X-ray crystallography (Figure 9, Appendix D).

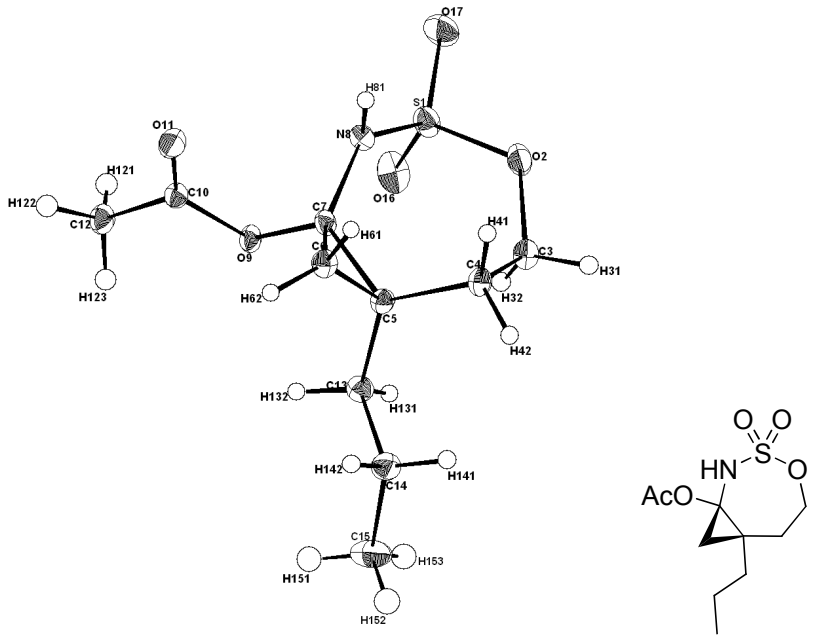
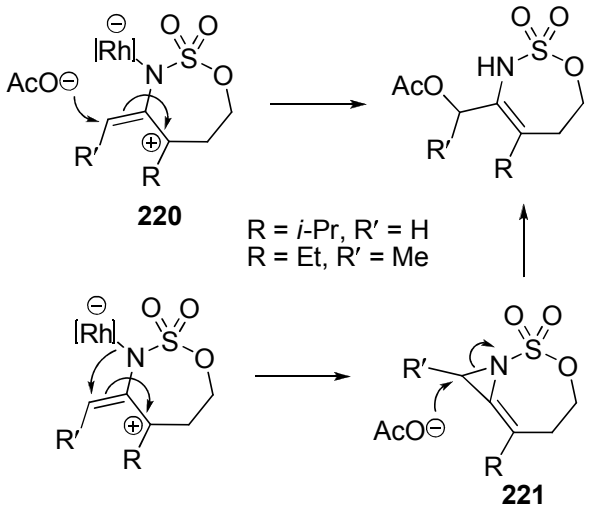


Figure 9

By slightly increasing the bulk of the substituents to *iso*-propyl allene **201** or trisubstituted allene **205**, a mixture of cyclic enamines and aminocyclopropanes was observed. Interestingly, the ester functionality of aminocyclopropane **209** was formally hydrolysed to yield a hemi-aminal during the reaction. The regiochemistry of acetate attack to yield cyclic enamines **210** and **215** is determined by steric factors; attack occurs at the less-hindered terminal end of amino-allyl cation **220** or *via* terminal ring-opening of *endo*-MA **221**. This compares with internally unsubstituted sulfamates **175** and **198** in which acetate attack occurs at the internal position or ring-opens an *exo*-MA, when steric hindrance is reduced (Scheme 79).



Scheme 79

The stereochemistry of aminocyclopropane **216** was assigned by nOe experiments and implicates a *trans*- geometry of amino-allyl cation intermediate **222**, this minimises steric interactions with the bulky rhodium species before disrotatory electrocyclic ring closure occurs (Figure 10).

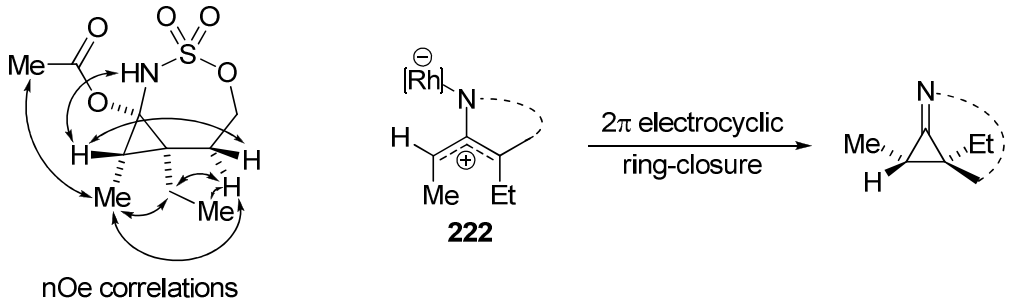
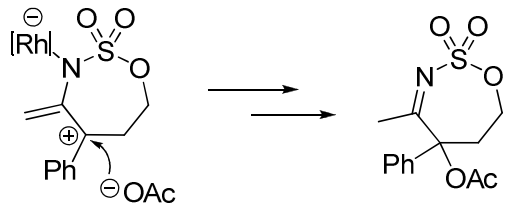


Figure 10

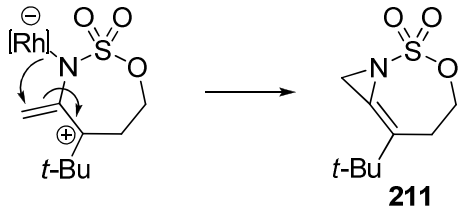
Phenyl substituted sulfamate **203** behaved in a similar manner to sulfamates **201** and **205**; however the majority of acetate attack occurred at the benzylic position of the amino-allyl cation (or ring opening of an *exo*-MA) to yield tautomerised cyclic imine **213** as the major product (Scheme 80).



213

Scheme 80

Two unprecedented MAs were obtained in very good overall yield when *tert*-butyl substituted allene **202** was used. In this substrate the steric bulk was too great to allow acetate attack at either end of the amino-allyl cation and ring-closure to form MAs **211** and **212** occurred as the final step. A *ca*. 5:1 preference for the *endo*-MA **211** resulted, in accordance with the findings for the less sterically hindered substrates (Scheme 81).



211

Scheme 81

Highly strained *endo*-MA **211** was isolated as a crystalline solid and a single crystal was grown allowing X-ray structure determination (Figure 11, Appendix E).

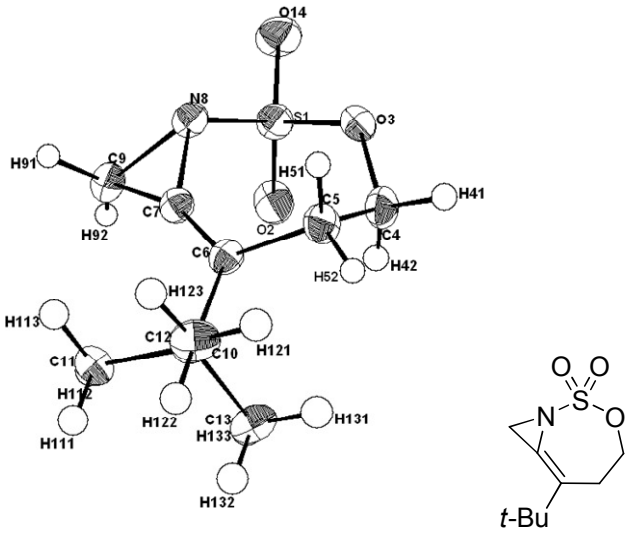
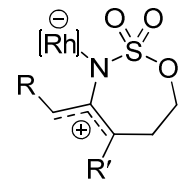


Figure 11

From the structure the C(6)–C(7)–C(9) (crystal numbering) bond angle was found to be unusually large at 157.5°. The crystal lattice was structurally interesting and refined in the $P2_1/c$ space group as well as the non-standard space group $P2_1/n$, details of which are discussed elsewhere.[103]

In light of this result, it was anticipated that the similar bulk of a TMS group would yield a MA which contained a handle for further reactions. However, the reaction of TMS substituted allene **204** under the cyclisation conditions led only to decomposition.

The results of the intramolecular rhodium-nitrenoid cyclisation of β-allenic sulfamates clearly depend upon the substitution pattern of the allene (Table 7).



Product(s)	Cyclic enamine	Cyclopropane	Cyclopropane + cyclic enamine	Methylene aziridine
R	Secondary alkyl	H	H or primary alkyl	H
R′	H	Primary alkyl	Secondary alkyl	Tertiary alkyl

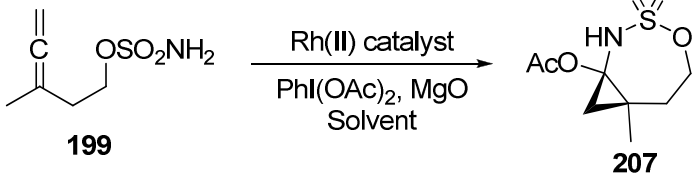
Table 7

External allene substituents led to cyclic enamines, whilst primary internal substituents gave aminocyclopropanes. Secondary alkyl internal substituents gave a mixture of both aminocyclopropanes and cyclic enamines, whilst tertiary internal groups gave MAs which were not attacked by acetate.

3.4 Further investigations

Du Bois was able to reduce catalyst loadings and increase the yields of aziridinations and C–H insertion reactions by using a new rhodium species, bis[rhodium(α,α,α′,α′-tetramethyl-1,3-benzenedipropionic acid)] more commonly called $Rh_2(esp)_2$.[104] Optimisation of the

rhodium-nitrenoid cyclisation of sulfamate tethered allenes began by using this new rhodium species in the cyclisation of sulfamate **199** (Table 8).



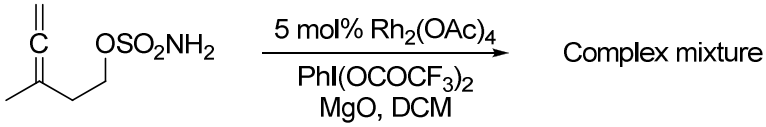
199 **207**

Entry	Catalyst	Catalyst loading (mol%)	Solvent	Yield (%)
1	$Rh_2(OAc)_4$	5	DCM	50
2	$Rh_2(OAc)_4$	1	DCM	47
3	$Rh_2(esp)_2$	5	DCM	50
4	$Rh_2(esp)_2$	5	Toluene	56
5	$Rh_2(esp)_2$	1	Toluene	65

Table 8

When compared to the original result (Entry 1), little drop off in yield was found by reducing the loading of $Rh_2(OAc)_4$, indicating good catalyst turnover. Direct substitution for $Rh_2(esp)_2$ led to no improvement, but by switching to a more hydrophobic solvent (not possible with $Rh_2(OAc)_4$) and reducing loadings, yields increased significantly.

It was predicted that by decreasing the nucleophilicity of the ligand released from the oxidant it may be possible to isolate non-acetate trapped products, however replacing $PhI(OAc)_2$ with $PhI(OCOCF_3)_2$ resulted in a complex mixture of products (Scheme 82).

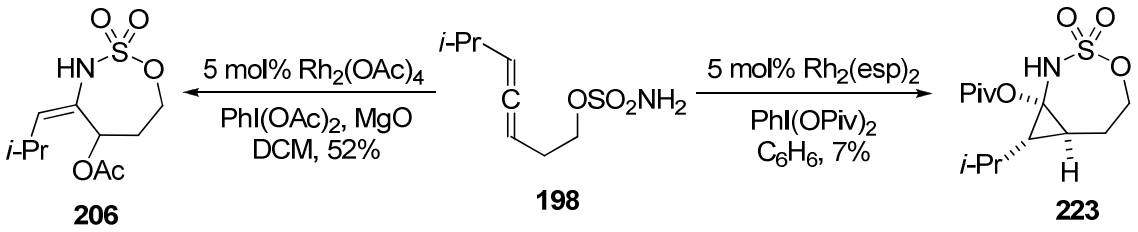


199

Scheme 82

Alternatively, increasing the steric bulk of the oxidant should reduce its ability to attack and increase the lifetime of the amino-allyl cation. Du Bois[105] found that $PhI(OPiv)_2$ could be used as an alternative oxidant for C–H insertion reactions of sulfamates, a reaction so successful that magnesium oxide was no longer required. When these conditions were

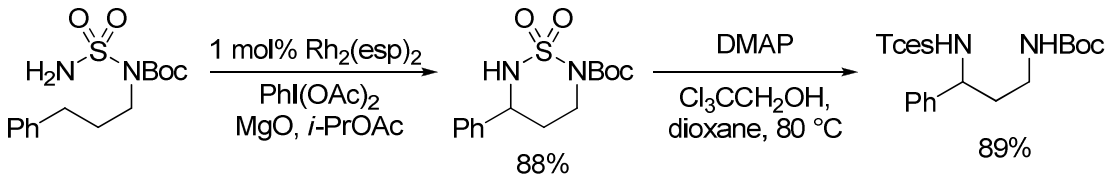
applied to the cyclisation of terminally substituted β-allenic sulfamate **198**, a change of product was observed; the original conditions gave cyclic enamine **206**, whilst the new conditions gave aminocyclopropane **223** (Scheme 83).



Scheme 83

Although the low yield and mass recovery indicates that other products were also forming in the reaction, this result supports the theory that amino-allyl cation intermediate **220** is directly attacked by acetate to yield cyclic enamines **210** and **215** rather than *via* MA **221** (Scheme 79). If MA **221** was an intermediate, then the analogous cyclisation of sulfamate **198** under the $Rh_2(esp)_2$ conditions could only yield a MA or cyclic enamine, not an aminocyclopropane (unless MA formation was reversible).

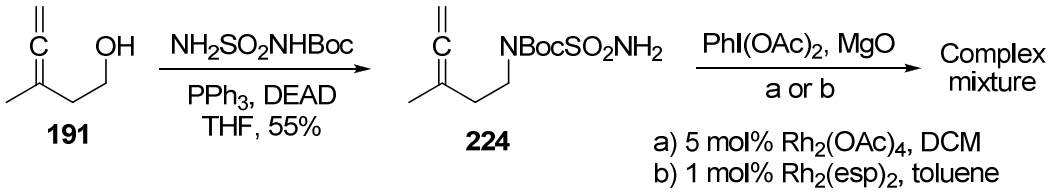
More recently, Du Bois[106] showed that sulfamides could also be used in C–H insertion reactions and intramolecular aziridinations of tethered alkenes. These were then easily manipulated to give 1,3-diamines (Scheme 84).



Scheme 84

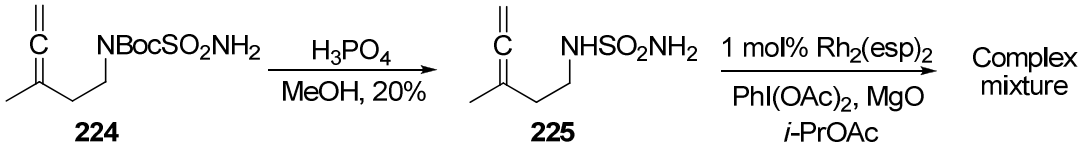
Based on this, it was predicted that an allene-tethered sulfamide could form aminocyclopropanes which could then be converted into cyclopropyl-diamines. Previously synthesised β-allenic alcohol **191** was reacted under Mitsunobu conditions[107] with *N*-Boc-sulfamide[108] to yield β-allenic sulfamide **224**; however attempted cyclisation

reactions under standard or optimised conditions led to mixtures of unidentified products (Scheme 85).



Scheme 85

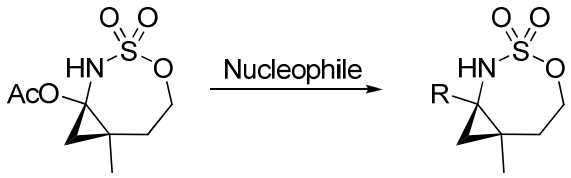
The ^{1}H NMR spectra of the crude products from these reactions were dominated by the *tert*-butyl proton signals from Boc residues in the reaction; it was therefore expected that a free sulfamate would allow more details of the reaction products to be observed. It was appreciated that a free N–H had caused degradation of $PhI(OAc)_2$ in similar reactions,[106] but sufficient quantities of isolable products may be obtainable to assist in the investigation. Deprotection of sulfamide tethered allene **224** was not possible with HCl but enough material from a phosphoric acid[109] mediated deprotection was obtained; however it was not possible to isolate any products from the rhodium-catalysed cyclisation of sulfamide **225** (Scheme 86).



Scheme 86

3.5 Reactions of aminocyclopropane 207[102]

If the mechanism of aminocyclopropane formation is correct (*via* cyclopropylimine **218**, Scheme 78) the elimination of AcOH would regenerate strained cyclopropylimine **218**, which could then be trapped by an external nucleophile. This was found to be a highly successful and versatile reaction (Table 9).



207 **226–232**

Reagents	R	Product	Yield (%)
$NaBH_4$, MeOH	OMe	**226**	23
$NaBH_4$, IPA	H	**227**	62
$LiAlH_4$, Et_2O	OH	**228**	76
NaOH, EtOH	OEt	**229**	82
EAA, NaH, THF	$CH(COMe)CO_2Et$	**230**	75
DEM, NaH, THF	$CH(CO_2Et)_2$	**231**	65
EtMgBr, THF	Et	**232**	69
Allyl-TMS, $BF_3.OEt_2$, DCM	–	–	–

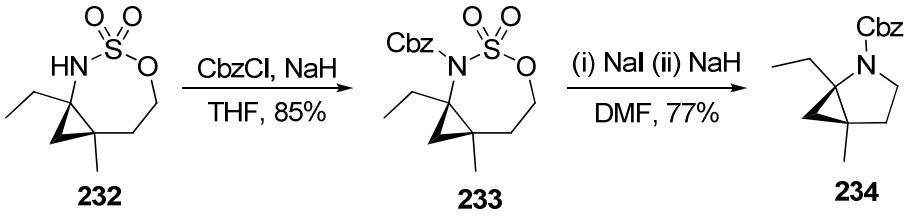
Table 9

Reaction with $NaBH_4$ under standard conditions[110] (MeOH as solvent) led to attack of the solvent upon the imine intermediate. By switiching to a more hindered solvent (IPA) it was possible to achieve hydride attack to afford aminocyclopropane **227** in good yield. Substitution for $LiAlH_4$[111] led to formal attack at the ester carbonyl to yield cyclopropyl hemi-aminal **228** in very good yield.

NaOH in ethanol led to the nucleophilic attack of ethoxide in excellent yield. Whilst reaction with stabilised enolates worked particularly well, with both ethyl acetoacetate and diethyl malonate producing new C–C bonds efficiently. Grignard[112] addition created a tertiary aminocyclopropane in good yield, however allylation with allyl-TMS[113] was not possible and starting material was fully recovered.

Du Bois *et al.*[114] had shown that cyclic Cbz-protected sulfamates could undergo oxidative cleavage to yield β-amino acids, whilst Dauban[57] and Gallagher[59] showed that ring opening of protected cyclic sulfamates was possible with a variety of nucleophiles. Blakey *et al.*[58] developed a similar two-step protocol for sulfur trioxide extrusion of oxathiazepanes to produce corresponding pyrrolidines and, after some optimisation of Cbz *N*- protection,

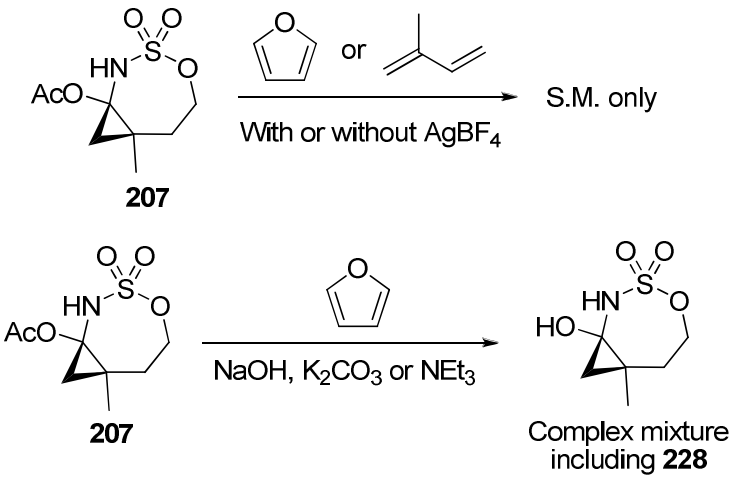
ethyl-substituted aminocyclopropane **233** was able to undergo the same ring-opening/ring-closing cascade to afford pyrrolidine **234** in very good yield (Scheme 87).



Scheme 87

If developments towards diversity oriented synthesis are found to be viable, this simple removal of the sulfamate linker will be a vital tool.

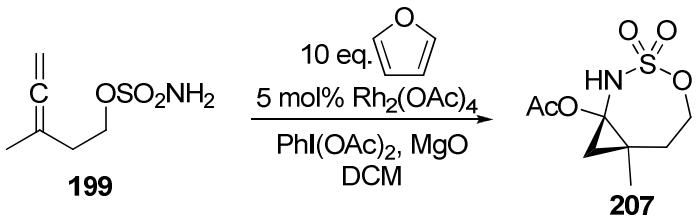
Since the loss of AcOH proved trivial under the conditions of the nucleophilic substitution reactions (Table 9), it was postulated that cyclopropylimine **218** could be in equilibrium with amino-allyl cation **217** and therefore [4+3] cycloadditions with dienes could be possible. Treatment of aminocyclopropane **207** with 10 eq. furan or isoprene led only to recovered starting materials, whilst the addition of NaOH, K_2CO_3 or NEt_3 to facilitate AcOH elimination led to the formation of complex product mixtures containing hemi-aminal **228**; the inclusion of $AgBF_4$[115] as a Lewis acid led only to recovered starting material (Scheme 88).



Scheme 88

A further experiment was conducted, in which furan was added to the rhodium cyclisation reaction of methyl substituted sulfamate **199**, in an attempt to trap the amino-allyl cation

217 *in situ*. Under standard reaction conditions plus 10 eq. furan, the now familiar cyclopropane **207** was the only product observed in the ^{1}H NMR spectrum of the crude material (Scheme 89).

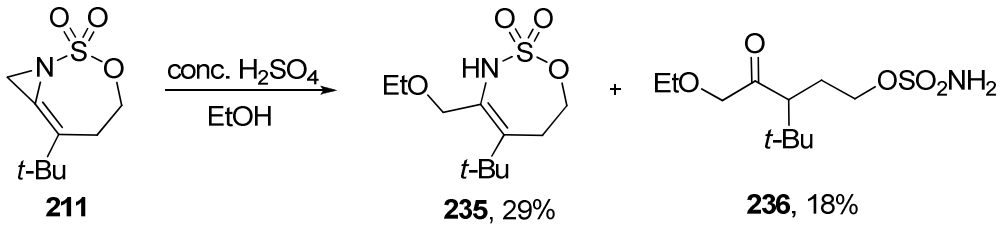


Scheme 89

During the course of this investigation, Blakey[116a] reported that the addition of external nucleophiles to rhodium-nitrenoid cyclisations of β-allenic sulfamates gave substituted aminocyclopropanes in good yields. In further work[116b] it was also shown that the addition of nitrones gave complex [3+3] annulation products.

3.6 Reactions of sulfamate linked MA 211[102]

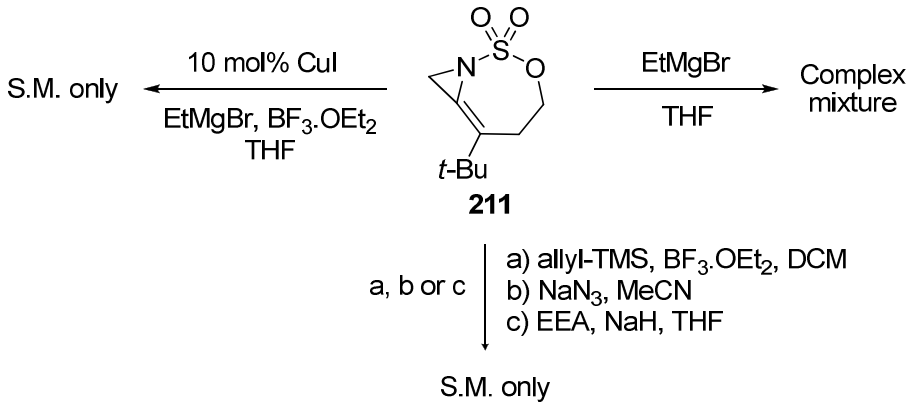
The reactivity of *endo*-MA **211** was also studied and this molecule proved to be surprisingly stable. Heating MA **211** at reflux in methanol led to no observable change, but, under strongly acidic conditions (conc. sulphuric acid in ethanol), acid-mediated ring-opening occurred at the terminal position to yield a mixture of cyclic enamine **235** and its hydrolysed analogue **236** (Scheme 90).



Scheme 90

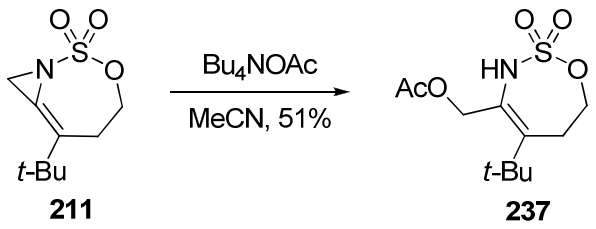
The conditions for ring-opening of carbamate-linked MA **64** were repeated with MA **211**, however no ring opened products (S_NV or otherwise) were observed and starting material was fully recovered. Grignard reagents in the absence of an additive led to a complex

mixture of products. Many other nucleophiles were unable to successfully open the aziridine ring, with allyl-TMS, sodium azide and the enolate of ethyl acetoacetate all yielding recovered starting material (Scheme 91).



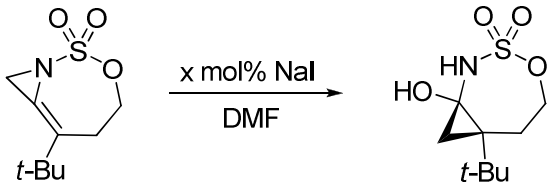
Scheme 91

Since cyclic enamines **210** and **215** were formed under rhodium cyclisation conditions with sulfamates **201** and **205** (Table 6), if the reaction proceeded *via* a MA intermediate (Scheme 79), it should be possible to open the aziridine ring of MA **211** under more forcing conditions. Whilst the reaction of MA **211** with 5 eq. AcOH in ethanol led to a similar acid-mediated ring-opening as with H_2SO_4 (Scheme 90), a basic acetate source could achieve the desired transformation. After some optimisation of solvent, it was found that tetrabutylammonium acetate could achieve ring-opening to afford cyclic enamine **237** in moderate yield (Scheme 92).



Scheme 92

In contrast to aminocyclopropane **207** (Scheme 87), treatment of MA **211** with NaI in DMF gave cyclopropyl hemi-aminal **238** as the only identifiable product. An investigation was then carried out to determine whether the process varied with NaI concentration (Table 10).

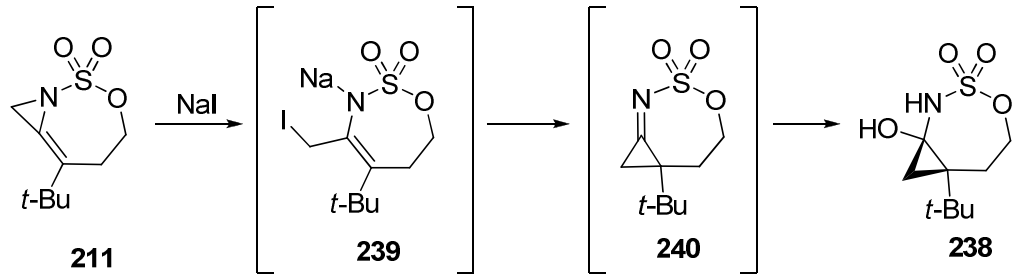


211 **238**

mol% NaI	Time (h)	Yield (%)
10	24	0
25	72	27
50	24	33
100	24	41
200	1	19

Table 10

The yield increased (at fixed time) and the reaction time decreased (at comparable conversion) with increasing relative quantities of NaI. At low loadings the reaction did not occur at all, whilst excess iodide decreased the yield by increasing the production of unwanted side products. A mechanism can be envisaged that initiates with iodide ring-opening of MA **211**, followed by ring-closure to iminocyclopropane **240** and trapping with water, to give cyclopropyl hemi-aminal **238** (Scheme 93).

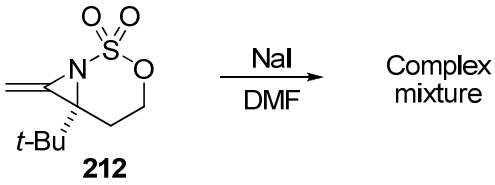


211 **239** **240** **238**

Scheme 93

Alternative mechanisms include iodide-mediated single electron transfer or induction by adventitious HI. The latter was ruled out by the reaction of MA **211** with 10 mol% aqueous HI in CD_3CN. Reaction monitoring by ^1H NMR revealed MA **211** to be unchanged after 24 h.

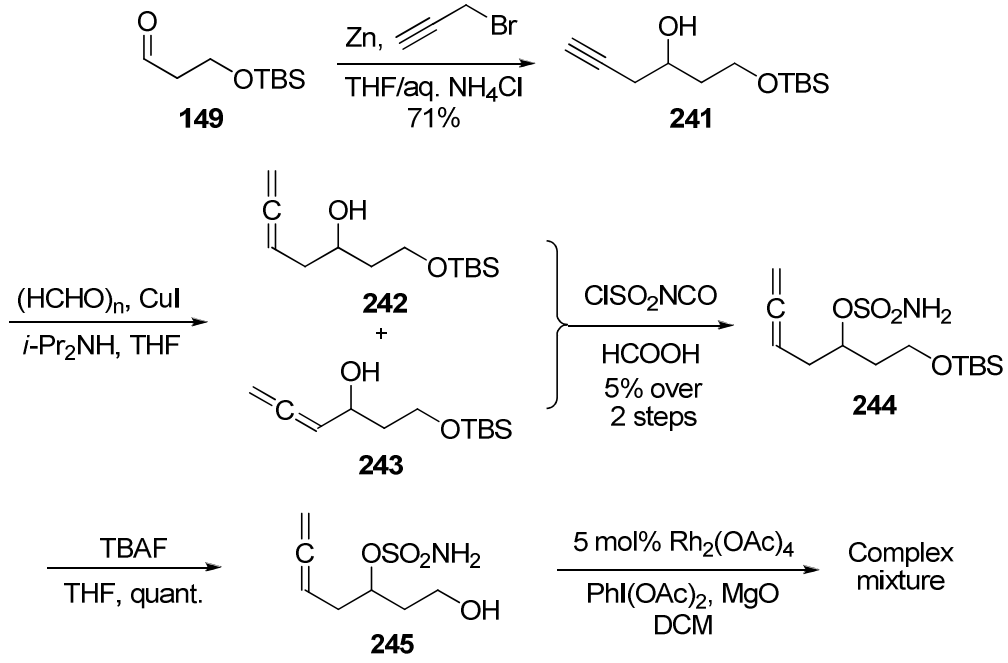
The reactivity of *exo*-MA **212** could not be fully assessed due to the instability of the compound; a test reaction with NaI in DMF led to a complex mixture of products (Scheme 94).



Scheme 94

3.7 *In situ* trapping of aminocyclopropanes by tethered hydroxyl groups

By tethering a nucleophile to a β-allenic sulfamate, creation of a polycyclic ring system may be possible either by acid cataylsis or spontaneously during rhodium-catalysed cyclisation. Initially (and prior to a full understanding of the sulfamate reactivity) chemistry developed in the carbamate series was tested. Aldehyde **149** (Scheme 61) was subjected to zinc-mediated alkyne addition[117] to give alcohol **241** in good yield. However homologation[118] gave an inseparable mixture of alcohols **242** and **243** (Scheme 95).



Scheme 95

Treatment of alcohols **242** and **243** under sulfamoylation conditions yielded desired sulfamate **244**, which was expected, since an earlier investigation had shown α-allenic alcohols were not able to undergo sulfamate formation (Scheme 71). The low yield was attributed to degradation of the α-allenic alcohol since there was ^{1}H NMR evidence of deprotection of the TBS group. On a large scale, a small quantity of desired sulfamate **244** was obtained and was readily deprotected with TBAF to yield alcohol **245**. However rhodium-catalysed cyclisation afforded no isolable products on such small scale.

As parallel results for nucleophilic substitution of aminocyclopropanes were obtained (Table 9), it was suggested that in order for hydroxyl cyclisation to occur onto the intermediate amino-allyl cation, the internal position of the allene should bear an alkyl group; therefore the hydroxyalkyl side chain should be at the internal position of the allene or at the terminal position with a further alkyl internal substituent (Figure 12).

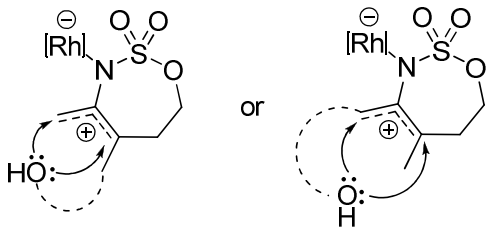
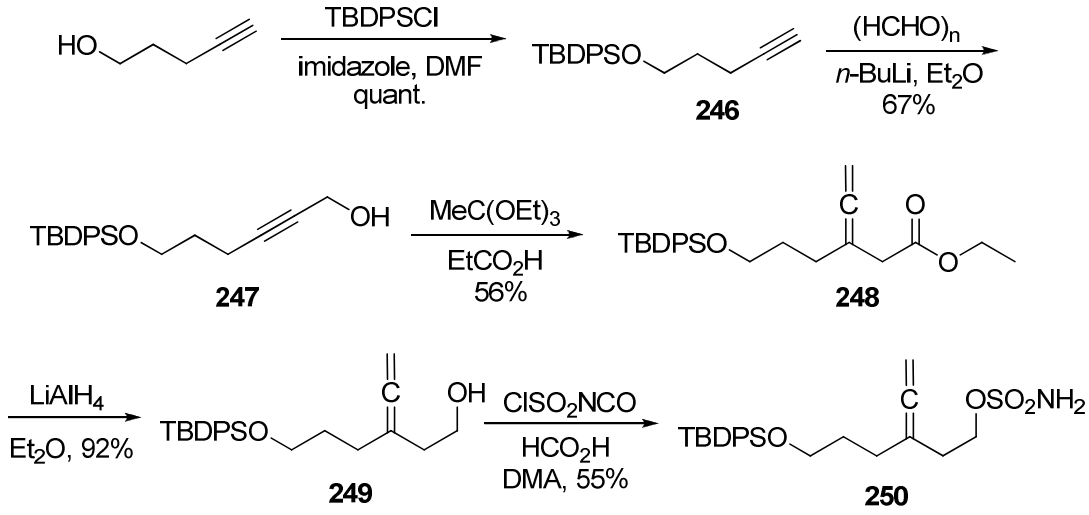


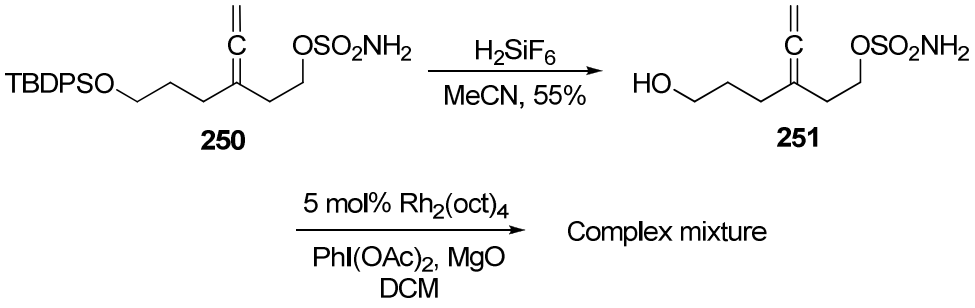
Figure 12

Since TBS had proven to be an unreliable during sulfamate formation, TBDPS was chosen as a better protecting group. Known alkyne[119] **246** was taken through to hydroxyl-protected sulfamate **250** without difficulty (Scheme 96).



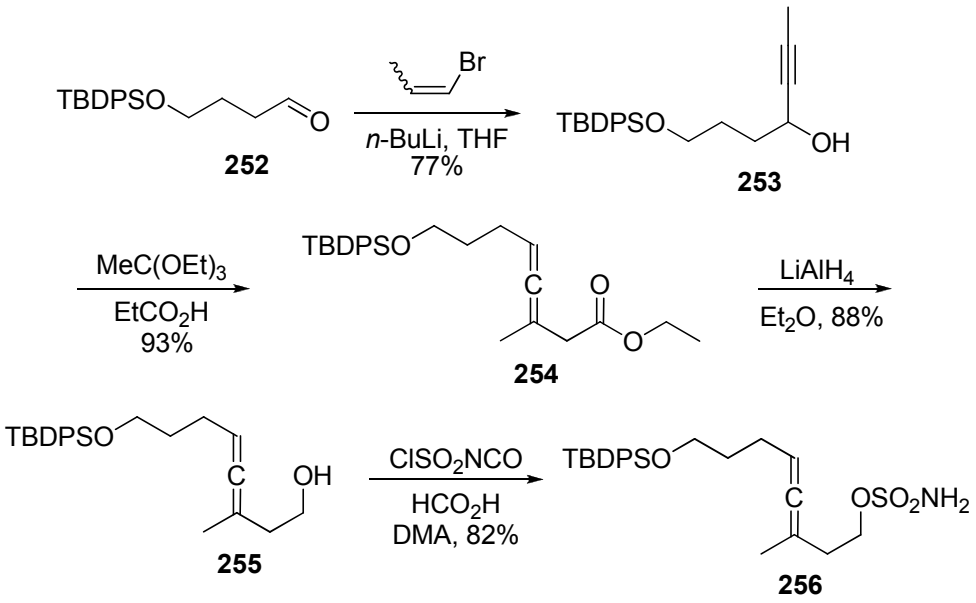
Scheme 96

Removal of the protecting group to afford alcohol **251** with TBAF proceeded in 41% yield, which was improved to 55% by switching to fluorosilicic acid. Treatment of sulfamate **251** under standard rhodium-catalysed cyclisation conditions led to a complex mixture of products, with the major product co-eluting with $Rh_2(OAc)_4$ upon column chromatography. Substitution for less polar $Rh_2(oct)_4$ allowed better chromatographic separation, however any constructive products were not identified (Scheme 97).



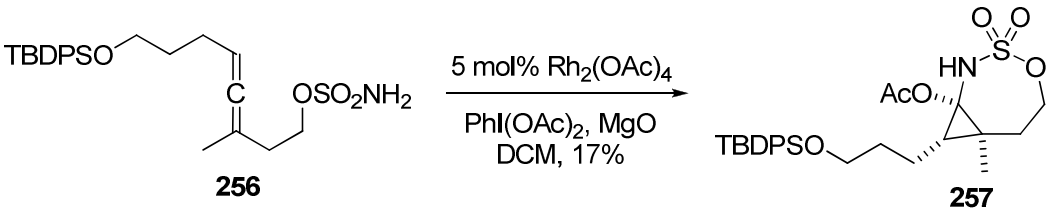
Scheme 97

For the alternative external hydroxyalkyl tether, known aldehyde[49] **252** was treated with propynyllithium[120] to give alcohol **253** which was subsequently transformed into sulfamate **256** in very good overall yield (Scheme 98).



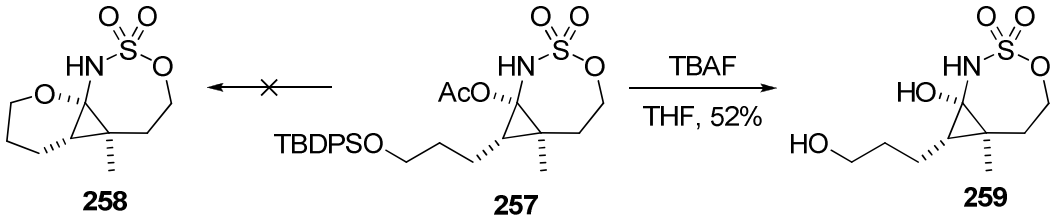
Scheme 98

Two possible routes were then considered; rhodium-catalysed cyclisation followed by deprotection, or deprotection followed by cyclisation. Since a mixture of aminocyclopropane **216** and cyclic enamine **215** was formed from sulfamate **205** it was decided to check the cyclisation first to gain an understanding of the product distribution. Cyclisation gave a reasonably cluttered ^{1}H NMR spectrum of the crude material, from which aminocyclopropane **257** was the only isolable product (Scheme 99).



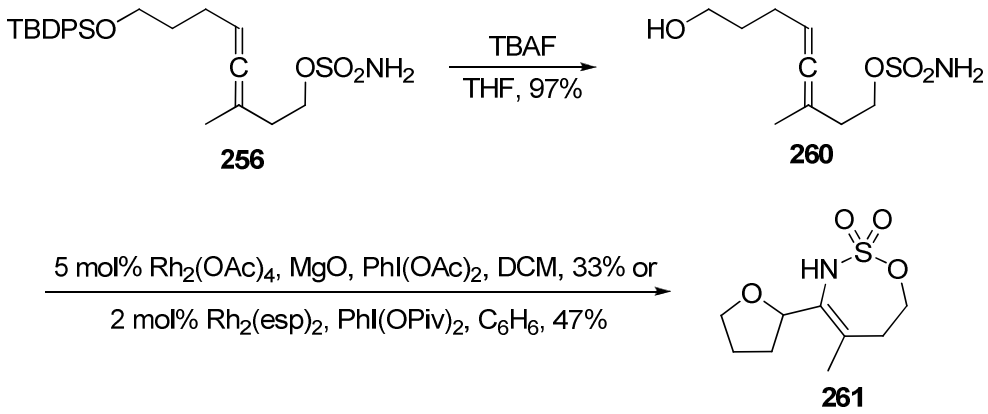
Scheme 99

It was predicted that upon deprotection and loss of acetate, the revealed hydroxyl should cyclise onto the cyclopropane to yield tricyclic product **258**; however the fluoride conditions tested led only to formal substitution with water to yield unproductive hemi-aminal **259** (Scheme 100).



Scheme 100

Attention was turned to the alternative, deprotection followed by cyclisation, route. Deprotection of sulfamate **256** proceeded in excellent yield to afford cyclisation precursor **260**; cyclisation under original conditions gave tetrahydrofuran derivative **261** in moderate yield, which was improved by switching to optimised $Rh_2(esp)_2$ conditions (Scheme 101).



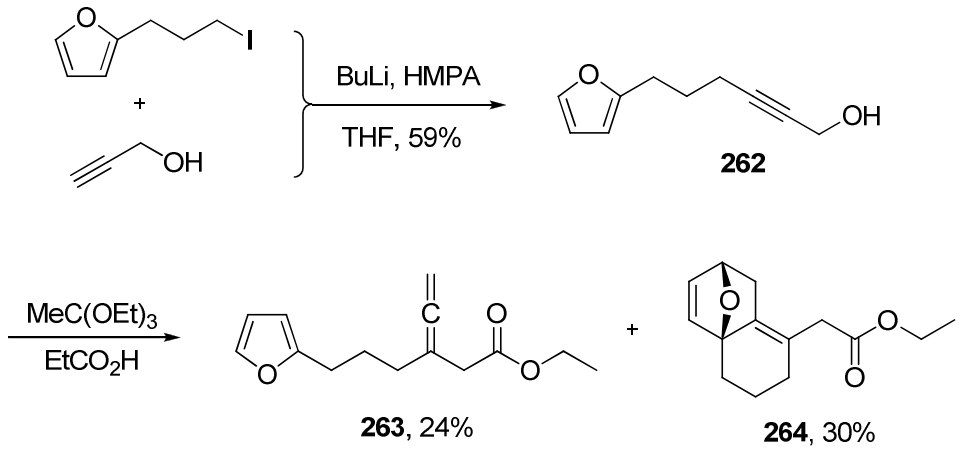
Scheme 101

This exciting result demonstrates that amino-allyl cation trapping is possible with internal nucleophiles in rhodium-nitrenoid sulfamate cyclisations and provides further evidence of an amino-allyl cation intermediate. With the sulfamate linker easy to remove, this double-cyclisation method could be utilised in diversity oriented syntheses, affording complex bicyclic systems from readily accessible acyclic precursors.

3.8 *In situ* trapping of aminocyclopropanes by diene cycloaddition

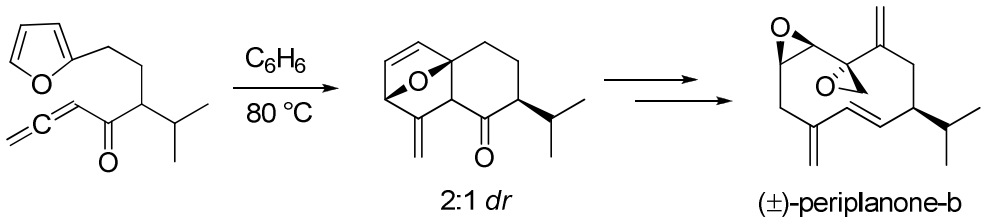
The results gathered to this point showed that the amino-allyl cation intermediate, formed from rhodium-nitrenoid cyclisation, has a finite lifetime and that it can be trapped by nucleophiles. Since it was not possible for sulfamate **199** to react *in situ* with external furan

during cyclisation (Scheme 89), it was proposed that a tethered furan may lead to successful cycloaddition by virtue of an increased effective concentration (*cf*. carbamate series). Coupling of propargyl alcohol with 2-(3-iodopropyl)furan afforded Johnson–Claisen precursor **262**; however the rearranged product underwent partial cycloaddition to afford tetracycle **264**, lowering the yield of desired ester **263** (Scheme 102).



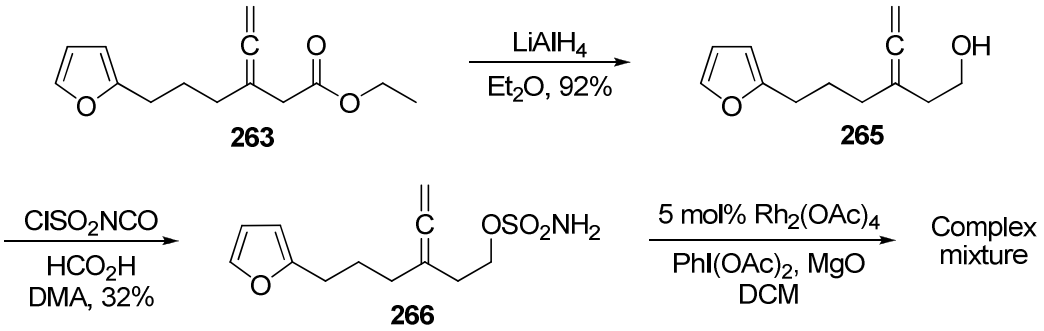
Scheme 102

This type of intramolecular allene-furan Diels–Alder reaction has precedent; for example, Cauwbergh and De Clercq utilised this as a key step in the synthesis of periplanone-b[121] (Scheme 103).



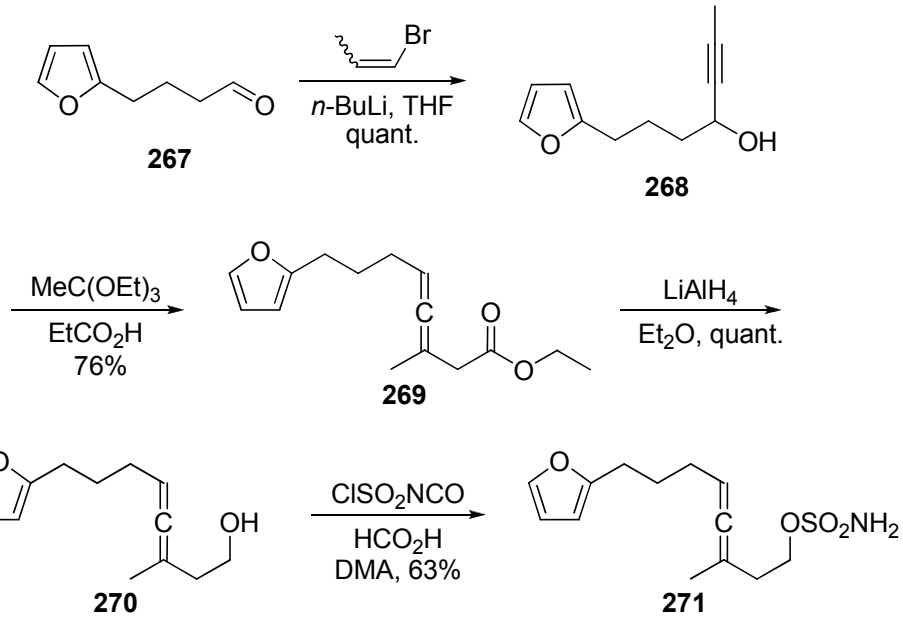
Scheme 103

The small amount of ester **263** formed from the Johnson–Claisen rearrangement was elaborated to sulfamate **266** using previously described conditions; however rhodium-catalysed cyclisation gave a mixture of unidentified products (Scheme 104).



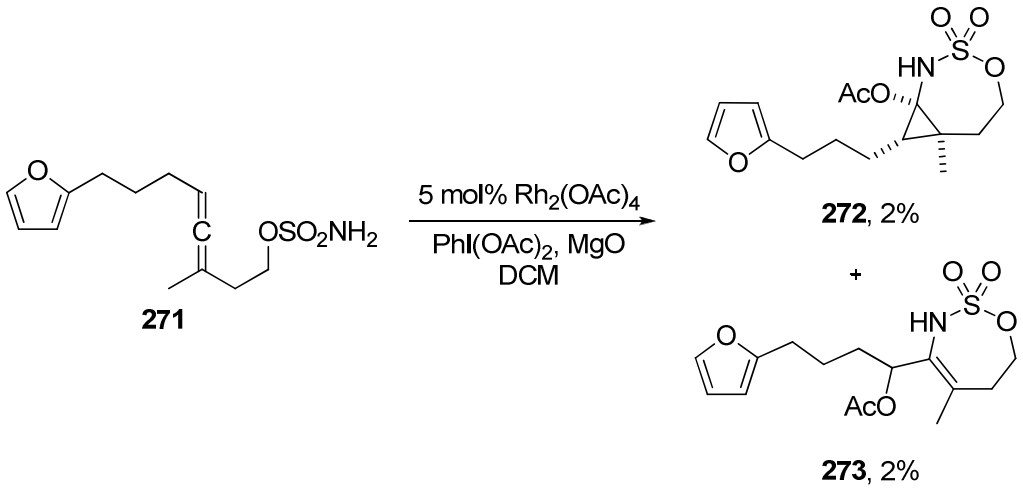
Scheme 104

Since dual-cyclisation success had been achieved for terminal hydroxyl-tethered sulfamate **260**, it was anticipated that a terminal furan tether may lead to the desired *in situ* cycloaddition. Cyclisation precursor **271** was synthesised in good overall yield from known[15] aldehyde **267** (Scheme 105).



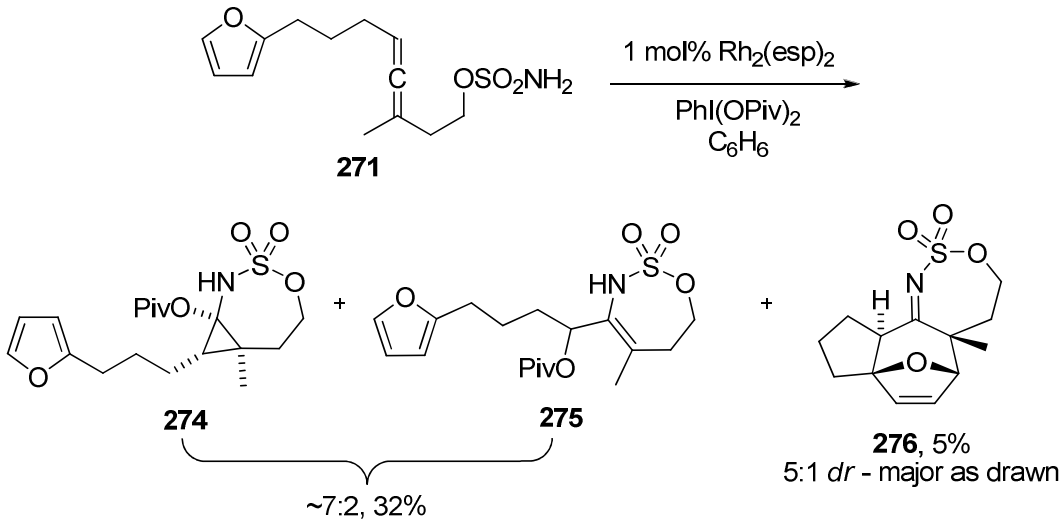
Scheme 105

Rhodium-nitrenoid cyclisation under standard conditions gave a complex mixture of products from which trace amounts of aminocyclopropane **272** and cyclic enamine **273** were isolated (Scheme 106).



Scheme 106

The optimised conditions for cyclisation were expected to increase the likelihood of cycloaddition by extending the lifetime of the amino-allyl cation intermediate. Reaction of sulfamate **271** afforded aminocyclopropane **274** and cyclic enamine **275** as a *ca*. 7:2 mixture, as well as a small quantity of desired tetracyclic imine **276** as a mixture of inseparable diastereomers (Scheme 107).



Scheme 107

The stereochemistry of tetracycle **276** was assigned by nOe experiments. The lack of correlation between H(10) and the methyl group alludes to a *trans*- geometry of the amino-allyl cation intermediate (*cf*. Figure 10), whereby the largest substitutents are *trans*- to one another in the transition state (Figure 13).

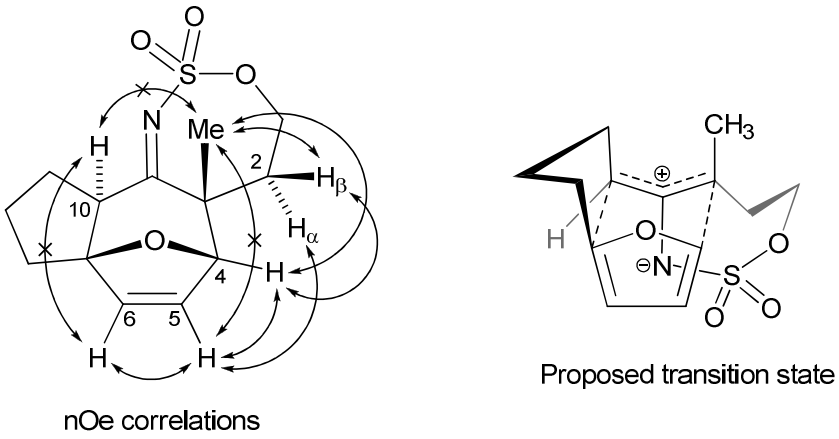
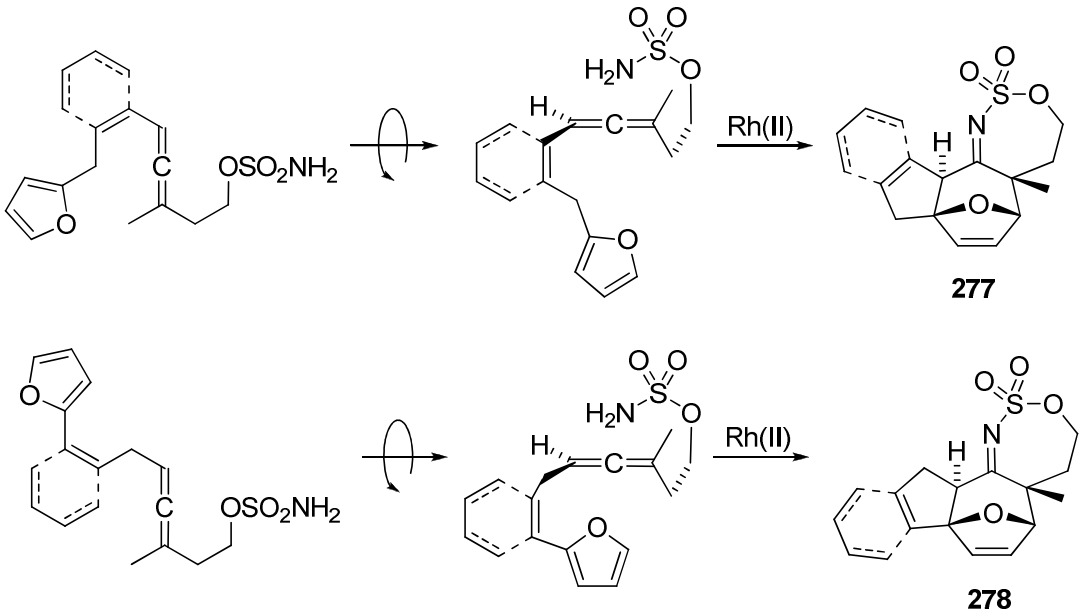


Figure 13

Correlation between H(4) and the methyl group and their correlations to H(2_β) implicate the oxygen-bridge stereochemistry shown. Neither H(10) and H(6) or H(5) and the methyl group show correlation to one another, however in the alternative structure, H(5) would not be able to correlate to either H(2_α) or H(2_β).

3.9 Future work

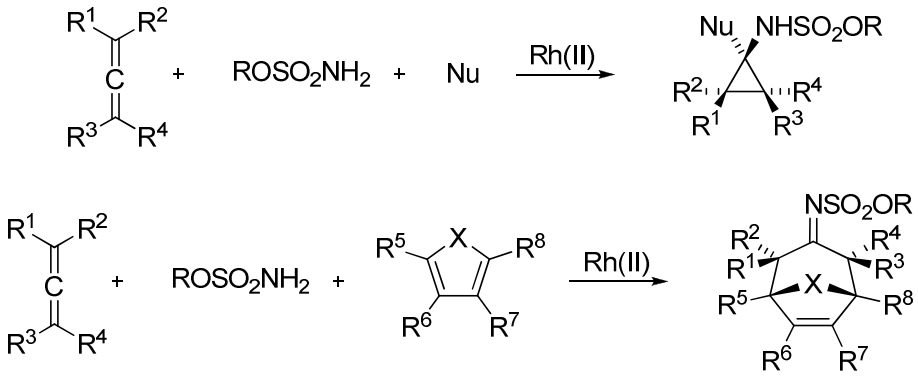
Since proof-of-principle has been established for the *in situ* [4+3] cycloaddition of furan-tethered allene **271**, it is postulated that by adding ridigity to the side chain, for example with a *cis*- olefin or phenyl group, the furan will be brought into closer proximity to the transient amino-allyl cation, reducing the entropic loss of the reaction. This should increase the chances of a cycloaddition reaction occurring before the amino-allyl cation is trapped by an external nucleophile. Since such substitution is possible at two positions along the chain to give polycyclic products **277** or **278**, there is plenty of scope for optimisation (Scheme 108).



Scheme 108

The use of other tethered dienes such as *N*-Boc-pyrrole and 1,3-butadiene could also lead to potentially useful products if the dual-cyclisation can be optimised.

The principal aim of future work will be to activate allenes by nitrenoids intermolecularly. Although preliminary studies were unsuccessful (Scheme 75), the knowledge gained since should give an insight into how this could be achieved, for example by adding more substituents to the allene or altering the rhodium catalyst. In this approach, the trapping of an amino-allyl cation will not be restricted to tethered nucleophiles and dienes, and thus a whole variety of tranformations could be accomplished in one multi-component step. This will then be truly useful in organic synthesis for producing complex molecules in a convergent fashion (Scheme 109).

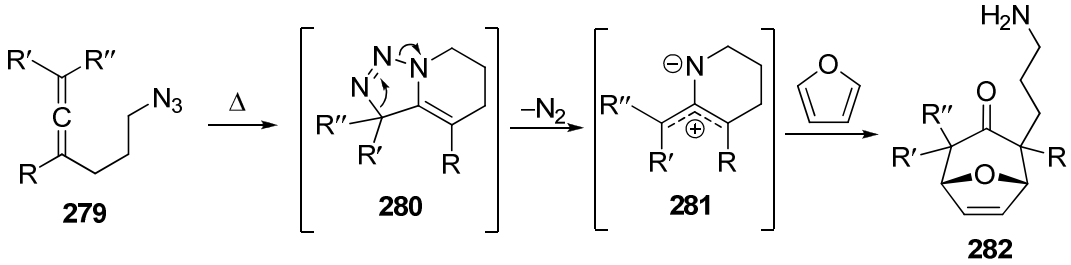

R1
R2
C
R3
R4
+
ROSO2NH2
+
Nu
Rh(II)
Nu
NHSO2OR
R2
R4
R1
R3
R1
R2
C
R3
R4
+
ROSO2NH2
+
R5
X
R8
R6
R7
Rh(II)
NSO2OR
R2
R4
R1
R3
X
R5
R8
R6
R7

Scheme 109

4. Azide tethered allenes

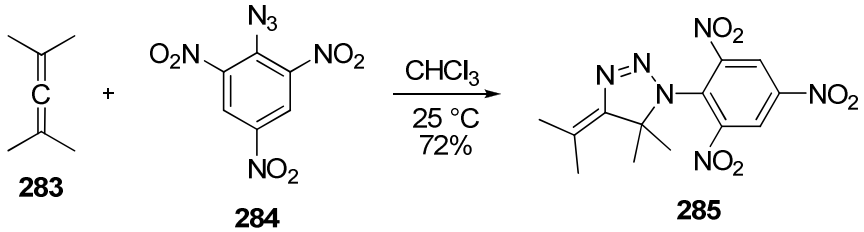
4.1 Introduction

Chapters 2 and 3 described how limited success was achieved in initiating [4+3] cycloadditions between carbamate and sulfamate linked amino-allyl cations. A third method for generating an amino-allyl cation was envisaged based on the thermally induced cycloaddition of allene-tethered azide **279**, followed by loss of N_2; this could then be trapped with furan to form cycloadduct **282** (following subsequent imine hydrolysis) (Scheme 110).



Scheme 110

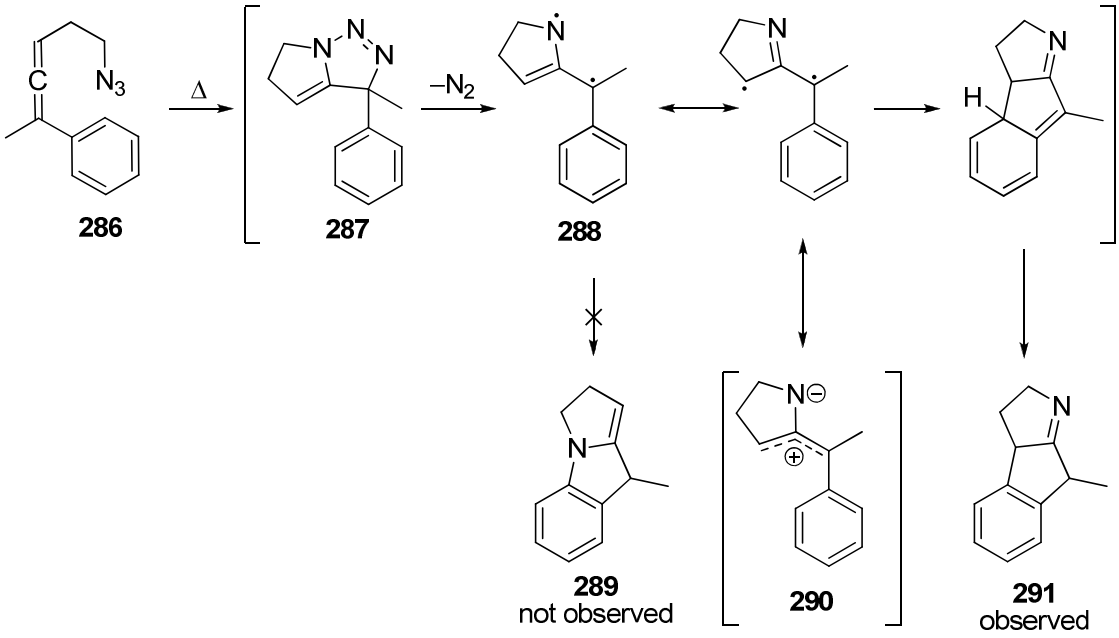
The intermolecular reactions of azides with alkynes has been extensively explored,[122, 123] however there is relatively little known about the reaction of azides with allenes. Bleiholder and Schecter were the first to report on such reactions,[35] mixing picryl azide **284** and excess tetramethylallene **283** to afford triazoline **285** in good yield (Scheme 111).



Scheme 111

Banert *et al*. extensively covered the rearrangements of 1-azidoallenes into 2-methylene-2*H*-azirines by photolysis,[124, 125] whilst Mukai *et al*.[126] introduced the cyclisation of azides onto tethered sulfonylallenes to form nitrogen-containing heterocycles. This work

has been greatly extended by Feldman *et al*.[127] who proposed that cyclisation of allene-tethered azides proceeds *via* an azatrimethylenemethane (ATMM) diyl species; the thermally-induced cyclisation of allene-tethered azide **286** affords triazoline **287**, which subsequently fragments to yield ATMM species **288**. Ring-closure occurs preferentially to afford imine **291** rather than indoline **289**, implying that amino-allyl cation canonical **290** contributes greatly to the overall electron distribution of the ATMM intermediate (Scheme 112).

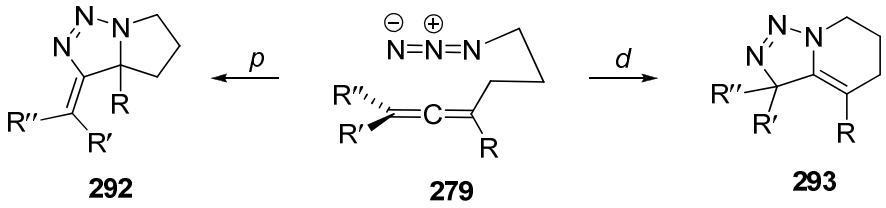


Scheme 112

In Mukai's and Feldman's examples of azide-tethered allene cycloadditions, electron withdrawing groups or allene-conjugated groups have been utilised to render the allene more reactive to the initial [3+2] cycloaddition. By contrast, alkyl substituents may stabilise an amino-allyl cation intermediate which could then react in further cycloadditions. A selection of allene-tethered azides were therefore synthesised, initially to isolate the cycloadducts and gain knowledge of their chemistry.

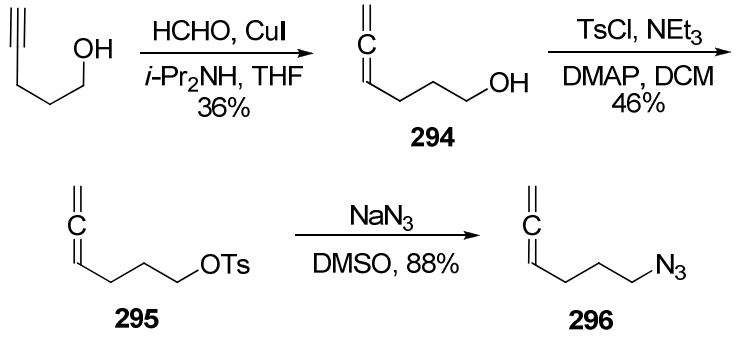
4.2 Synthesis of azide-tethered allenes

Initial work in the area focused on γ-allenic azides **279**, the [3+2] cycloaddition of which could occur at either the proximal (*p*) or distal (*d*) double bond of the allene. By varying the substitution pattern around the allene both cycloaddition products **292** and **293** may be possible (Scheme 113).



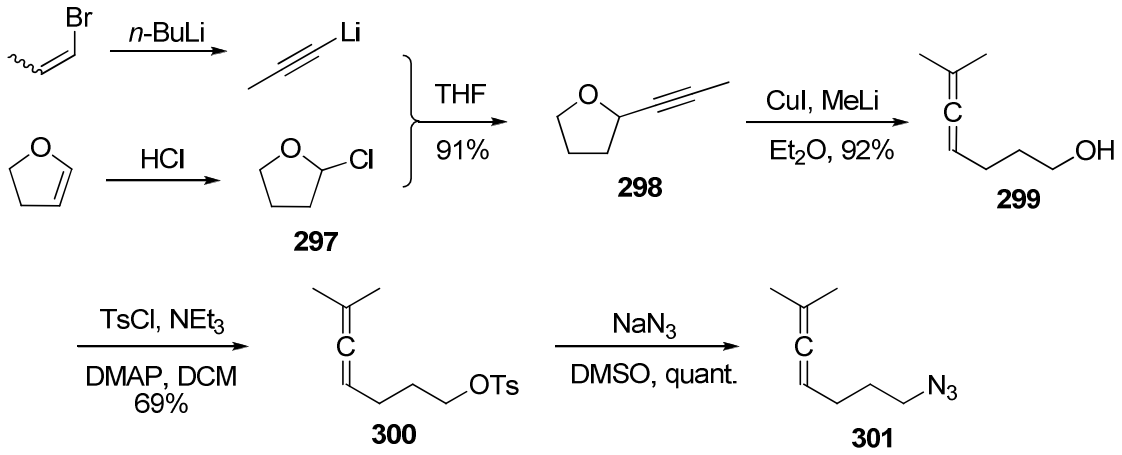
Scheme 113

Unsubstituted allene **296** was synthesised in three steps from pent-4-yn-1-ol. Homologation, as described previously,[118] gave alcohol **294** which was then tosylated,[128] before S_N2 displacement with sodium azide to afford allene **296** (Scheme 114). The low yield of the initial steps can be attributed to the high volatility of the starting materials and products.



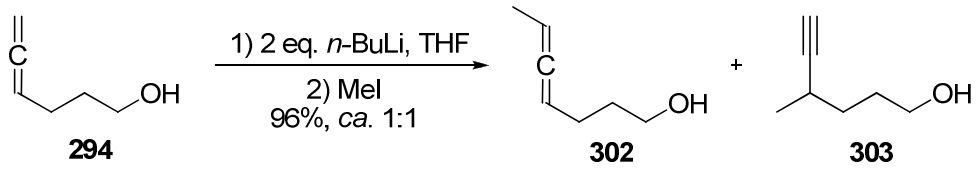
Scheme 114

Terminally di-substituted allene **301** was synthesised in four steps from readily available starting materials in good overall yield. Addition of prop-1-ynyllithium to chloro-THF **297** gave alkyne **298**, and conjugate addition of methyl copper afforded alcohol **299**. Tosylation gave known[129] allene **300** which was then converted into azide **301** by nucleophilc substitution (Scheme 115).



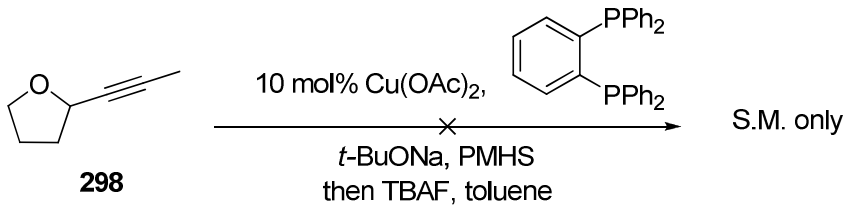
Scheme 115

The synthesis of a terminally mono-substituted allene proved more problematic. Walkup and Kim[130] reported the synthesis of allene **302** by double deprotonation and alkylation of γ-allenic alcohol **294**; however in our hands this provided an inseparable mixture of allenic and propargylic products **302** and **303** (Scheme 116).



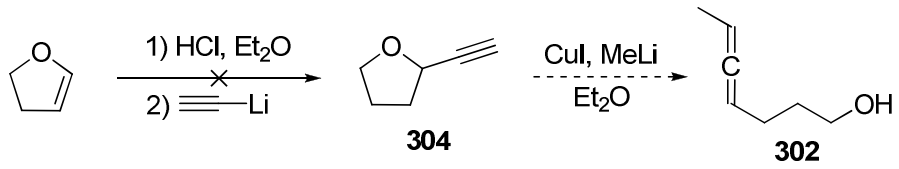
Scheme 116

Alternatively, copper-catalysed conjugate addition into alkyne **298**, similar to that in the synthesis of alcohol **298**, could be utilised. Krause *et al.*[131] developed a conjugate hydride addition into alkyne-tethered epoxides, although the same methodology could not be transferred to THF **298** (Scheme 117).



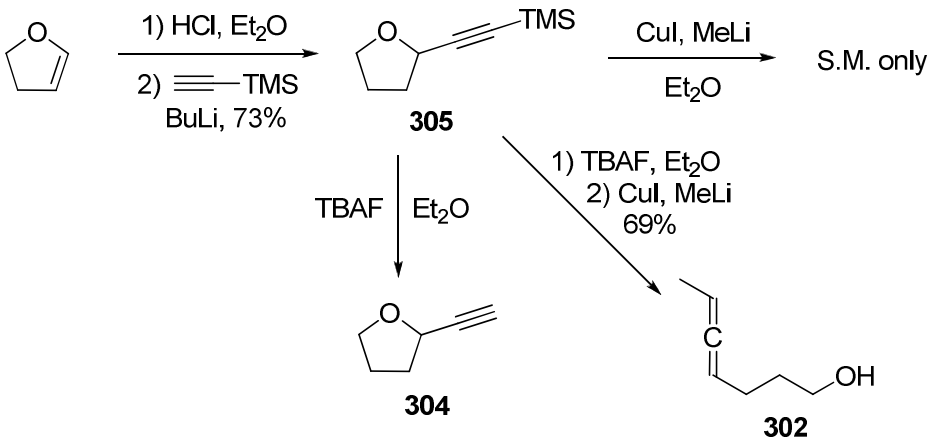
Scheme 117

Since hydride addition was unsuccessful, conjugate methyl addition into alkyne **304** could give the desired compound as an alternative; however the volatility of alkyne **304** produced from DHP prevented further experimentation (Scheme 118).



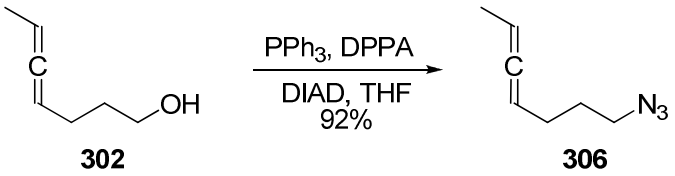
Scheme 118

By contrast, addition of TMS-acetylide to afford less volatile THF derivative **305** was achieved in good yield. Subsequent conjugate methyl addition gave only starting material and, whilst the ^{1}H NMR spectrum of the crude material looked promising, mass recovery of volatile THF **304** from alkyne **305** deprotection was predictably low. A tandem reaction was thus devised whereby a short work-up after silyl group removal was followed by immediate conjugate addition into alkyne **304** to afford alcohol **302** in good yield (Scheme 119).



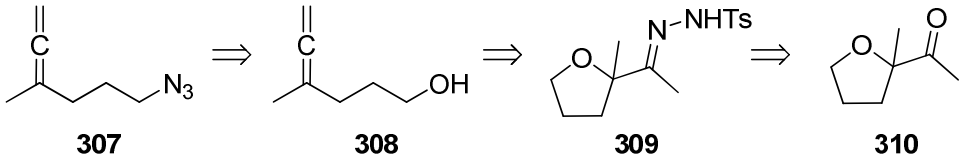
Scheme 119

An improved single-step route from alcohol **302** to azide **306** *via* a Mitsunobu reaction[132] was then attempted and proceeded in excellent yield (Scheme 120).



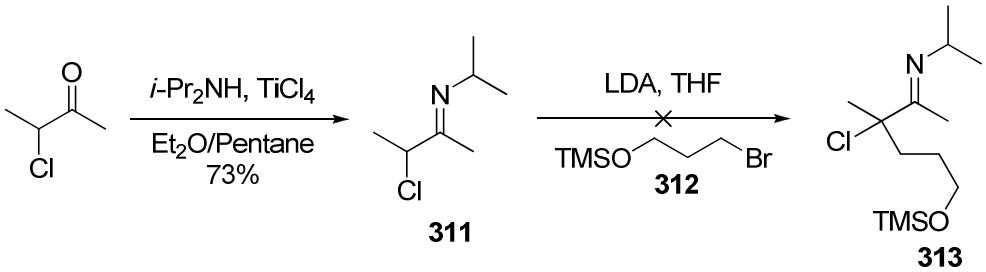
Scheme 120

The final substrate to be prepared was internally substituted azide **307**. Foster and Agosta[133] had shown that internally substituted γ-allenic alcohol **308** could be synthesised *via* a Shapiro type reaction of tosylhydrazone **309**, readily produced from ketone **310** (Scheme 121).



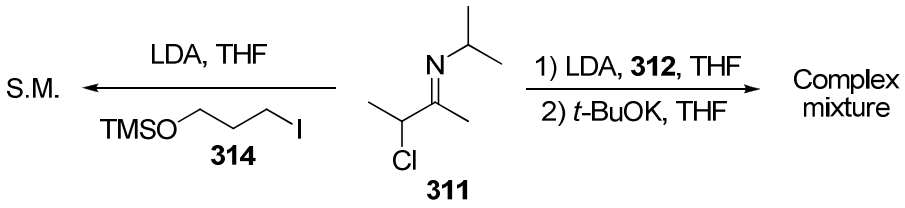
Scheme 121

De Kimpe *et al.*[134] developed a synthesis of ketone **310** from α-chloro imine **311** *via* enamine formation, alkylation and cyclisation. Following their route, treatment of 3-chlorobutan-2-one with diisopropylamine and $TiCl_4$ gave imine **311**[135] in good yield, however attempts to alkylate with bromide **312**[136] to give cyclisation precursor **313** were unsuccessful (Scheme 122).



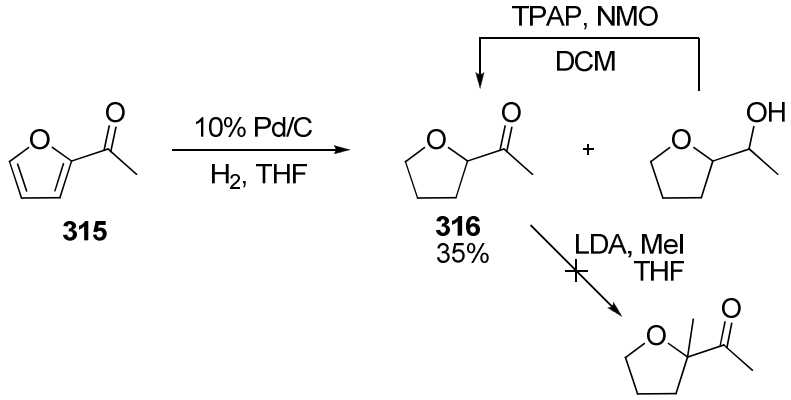
Scheme 122

Switching the electrophile from bromide to iodide **314** led to recovered starting material, whilst taking the crude reaction mixture onwards to the cyclisation step led to a complex mixture of products (Scheme 123).



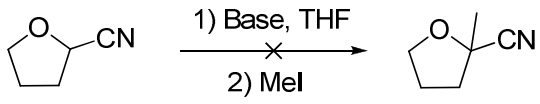
Scheme 123

An alternative route was devised *via* hydrogenation of furyl-ketone **315**. A variety of catalysts and reaction times were tested but over-reduction could not be fully avoided and the crude mixture had to be reoxidised with TPAP[137] to give ketone **316**. Attempts to alkylate[138] at the tertiary centre proved ineffective (Scheme 124).



Scheme 124

Alkylation of known[139] nitrile **317** to give THF derivative **318** followed by methyllithium addition, could also afford desired ketone **310**. Many alkylation conditions were attempted but all led to either recovered starting material or to a complex mixture of products, most likely due to the instability of the carbanion (Table 11).

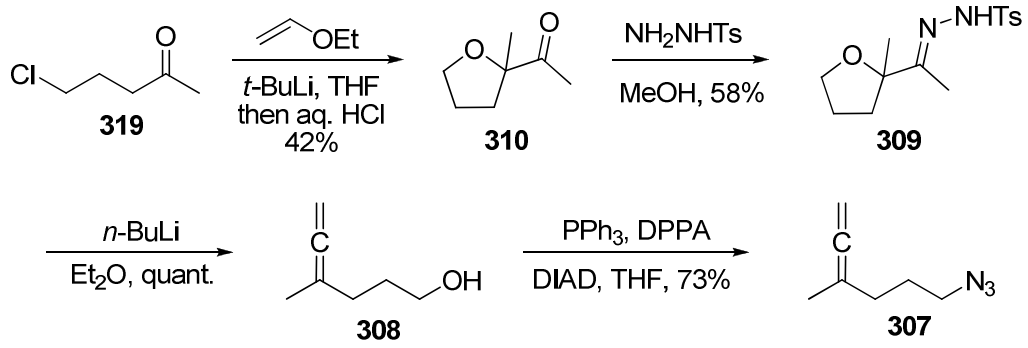


317 **318**

Entry	Base	Result
1	LiHMDS	Complex mixture
2	NaHMDS	Complex mixture
3	LDA	Complex mixture
4	*n*-BuLi	Complex mixture
5	NaH	Recovered S.M.

Table 11

A direct route to ketone **310** was finally accomplished by adding lithiated ethyl vinyl ether into chloroketone **319** followed by *in situ* cyclisation. Foster and Agosta's procedure[133] afforded alcohol **308**, *via* tosylhydrazone **309**, which was subsequently transformed into azide **307** (Scheme 125).



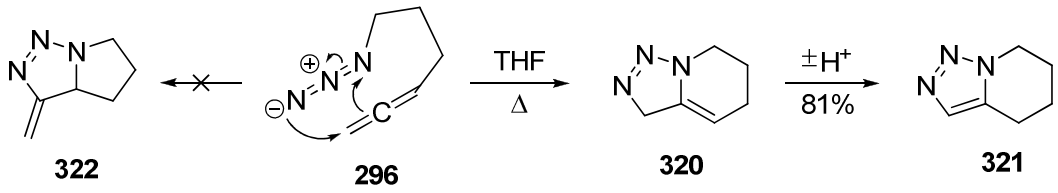
Scheme 125

With a selection of γ-allenic azides in hand, the thermally-induced [3+2] cycloadditions were then tested.

4.3 Cycloadditions

The first experiments were conducted on unsubstituted azide **296**, which was dissolved in d_8-toluene in an NMR tube, heated in an oil bath and the reaction monitored by ^{1}H NMR. After 2 h at 70 °C, signals corresponding to azide **296** had begun to diminish and new peaks began to appear, and after 24 h the starting material had been consumed and a single product had formed. The product was not isolable on this scale, therefore a

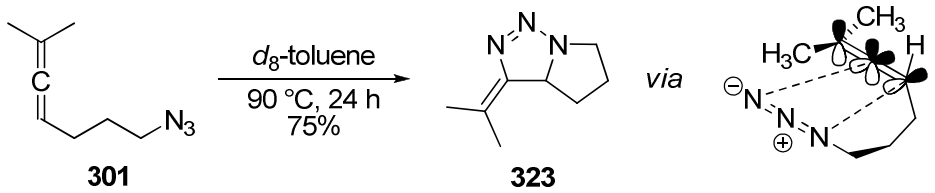
preparative reaction was run, in which azide **296** was heated at reflux in THF for 24 h, and bicyclic triazole **321** was observed (Scheme 126).



Scheme 126

Triazole **321**, formed by tautomerisation of intermediate **320** *in situ*, was isolated in good yield and characterised by comparison with material prepared by an analogous alkyne/azide cycloaddition.[140] Attack occurred exclusively on the distal double bond of the allene to give a [5,6]-bicycle; the alternative proximal cycloaddition product **322** was not observed.

A similar reaction was carried out by heating terminally di-substituted allene **301** in d_8-toluene and monitoring by ^{1}H NMR. In this case no reaction was apparent when the solution was heated to 70 °C for 24 h and so the reaction mixture was heated to 90 °C whereby clean conversion to triazoline **323** was observed after 24 h. The product was stable and able to be purified by column chromatography without aromatisation (Scheme 127).

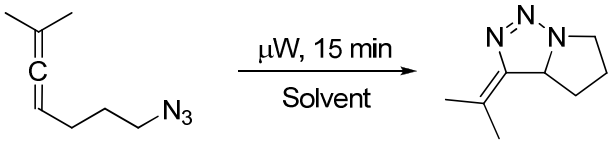


Scheme 127

The introduction of methyl substituents diverted the cycloaddition from the distal double bond to the proximal double bond of the allene. This mode of attack appears to be more hindered on simplistic plane-of-attack grounds, however compression of the geminal methyl groups is avoided. It is conceivable that similar formation of unsubstituted triazoline

322 (Scheme 126) is favourable but reversible and that reaction is driven by the formation of the thermodynamically favoured aromatic triazole **321**.

An investigation commenced to find out whether the reaction of azide **301** could be accelerated under microwave conditions. The reactions were carried out for 15 min and the values stated are isolated yields of triazoline **323** after column chromatography (Table 12).



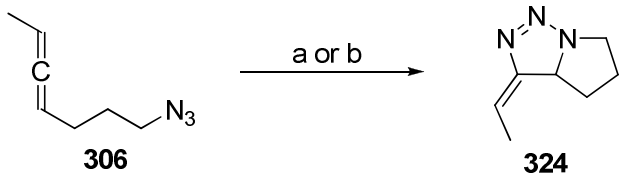
301 **323**

Solvent	Temperature (°C)	Yield (%)
MeCN	160	66
MeOH	160	53
DMSO	140	70
Water	160	–

Table 12

It was found that DMSO was the best solvent in terms of conversion and rate of reaction; the reaction could be carried out at lower temperature, reducing the likelihood of competing thermal decomposition (in MeCN or MeOH there was little conversion after 15 min at 140 °C). Acetonitrile proved to be the solvent of choice however, since the recovery of the products was aided by straightforward removal of the solvent *in vacuo*. Only starting material was recovered when the reaction was attempted in water.[141]

Terminally mono-substituted allene **306** was predicted to cyclise onto the proximal double bond primarily, however the stability of the resultant triazoline was unknown. After heating in d_8-toluene for 4 h at 80 °C it became apparent that a higher temperature would be required to induce cyclisation and, after increasing the temperature to 90 °C, triazoline **324** was isolated after heating for 24 h (Scheme 128).



a) d_8-toluene, 90 °C, 24 h, 11%
b) MeCN, μW, 140 °C, 25 min, 25%

Scheme 128

The ^{1}H NMR spectrum of the crude material was quite complex, implying the presence of a range of products which could account for the low reaction yield. The reaction was optimised in the microwave, however even at lower temperatures, 25% yield was the best that could be achieved. The stereochemistry of the product, determined by nOe experiments, can be rationalised by considering approach of the azide from the less sterically hindered face of the allene (Figure 14).

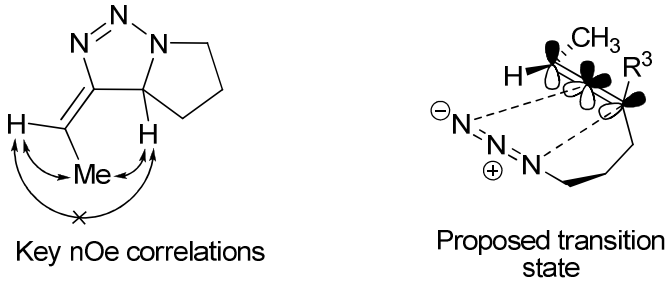
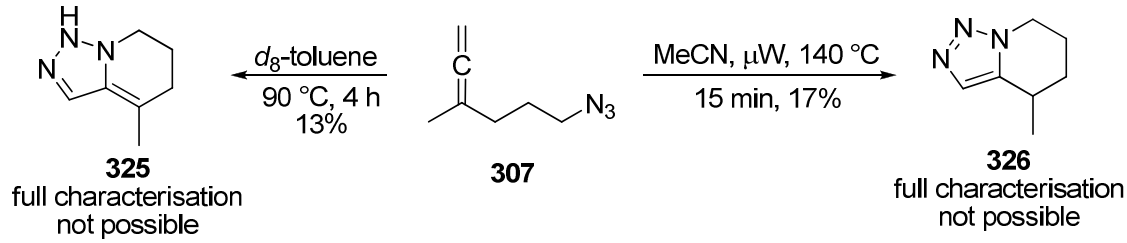


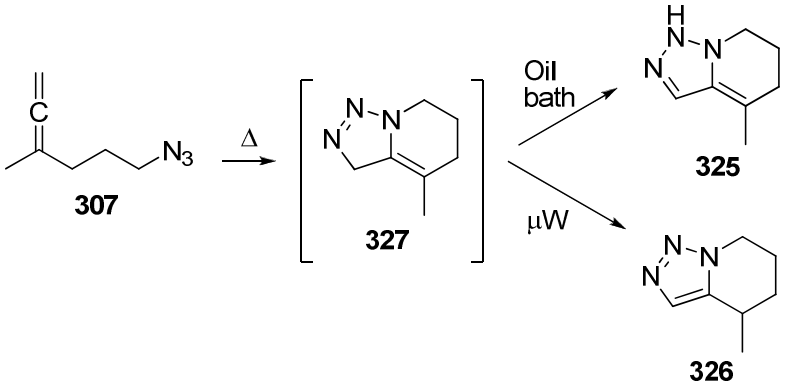
Figure 14

The products from the cycloaddition reaction of internally-substituted azide **307** were the most difficult to isolate and characterise. Upon heating allene **307** at 90 °C in toluene for 4 h, TLC analysis showed complete consumption of starting material. The ^{1}H and ^{13}C NMR spectra of the only isolable product (see experimental) was consistent with bicycle **325**, although full characterisation was hindered by decomposition of the product. Interestingly, by switching to microwave heating, triazole **326** was isolated albeit on a small scale and, once more, only NMR data was able to be attained before decomposition (Scheme 129).



Scheme 129

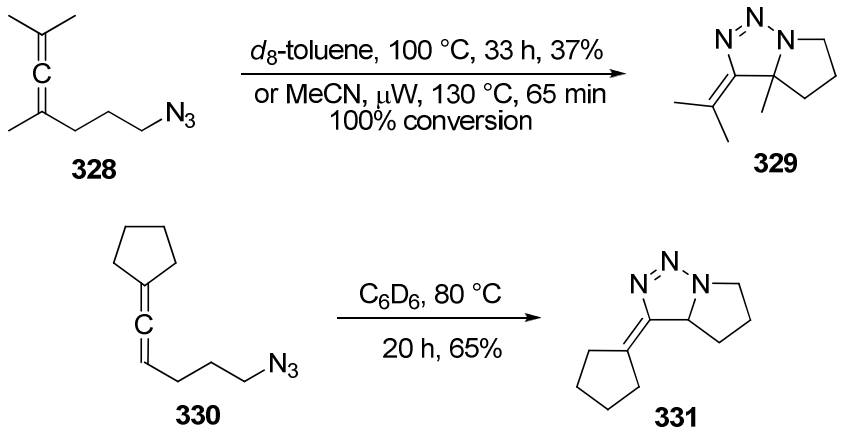
This work has subsequently been continued by others within the Robertson group, where it was found that heating azide **307** in d_8-toluene at 100 °C for 18 h resulted in complete conversion to bicycle **325**.[142] It appears that cyclisation occurs, as expected, on the less-hindered distal double bond to give triazoline **327** which can then form isomers **325** or **326** depending on the conditions (Scheme 130).



Scheme 130

4.4 Further work within the Robertson group[142, 143]

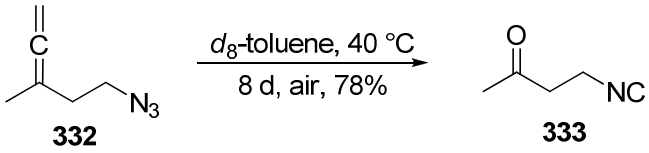
Further work has been completed within the area of azide-tethered allenes. To complete the γ-allenic series, tetra-substituted allene **328** was synthesised and, as predicted, cycloaddition occurred at the proximal double bond to yield triazoline **329** under both conventional and microwave heating conditions (Scheme 131). It was also possible to cyclise cyclopentyl-allene **330** to yield tricyclic triazoline **331**.



328 329 330 331

Scheme 131

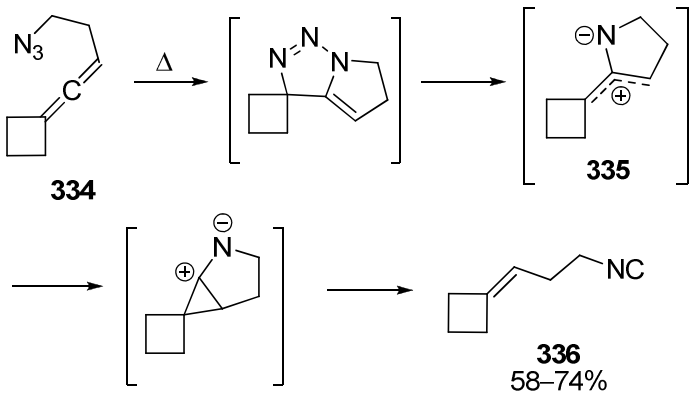
Work has also been undertaken to test β-allenic azides, where distal allene cycloaddition was predicted to occur preferentially. Interestingly, the only products isolated were isonitriles, such as **333**, under conventional or microwave heating (Scheme 132).



332 333

Scheme 132

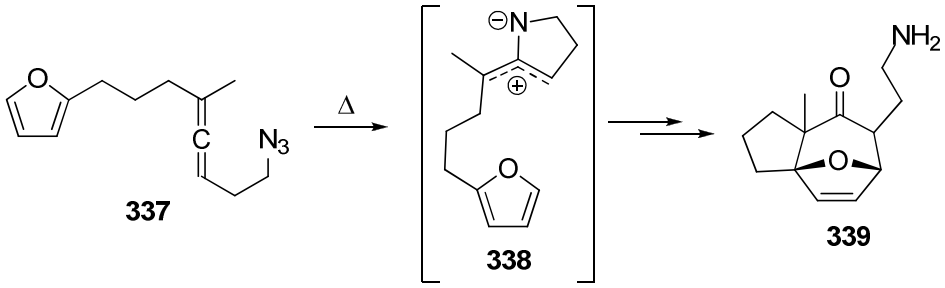
Further investigations allowed isonitrile **336** to be isolated (after vigorous drying and degassing) from strained azide **334**, thought to arise *via* amino-allyl cation intermediate **335** (Scheme 133).



334 335 336
58–74%

Scheme 133

Future work in the area is focussed on the cyclisation of furan-tethered allene **337**. It is anticipated that amino-allyl cation **338** can be trapped before isonitrile formation, to yield tetracycle **339** after imine hydrolysis (Scheme 134).

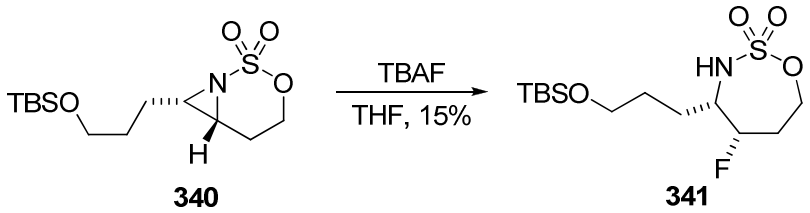


Scheme 134

5. Fluorinations of sulfamate linked aziridines

5.1 Introduction

During an undergraduate project within the group, investigating the tandem Rh(II) catalysed aziridination-cyclisation reactions of homoallylic sulfamates, an interesting pattern of reactivity was uncovered. Bicyclic aziridine **340** was treated with TBAF with the intention of deprotecting the hydroxyl and initiating aziridine ring-opening. The researcher was surprised to find a single diastereomer of fluoro-oxathiazepane **341** as the only isolable product[144] (Scheme 135).



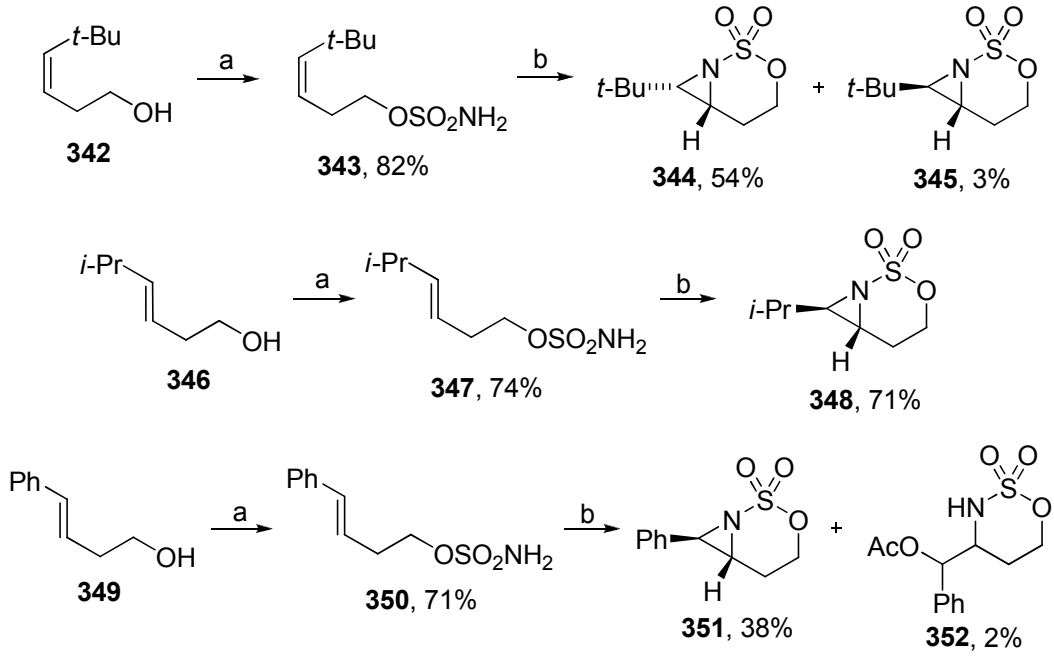
340 **341**

Scheme 135

Since fluoride ions are usually highly selective for silyl groups, fluoro-oxathiazepane formation was unexpected but of significant interest. Despite the discovery of very few fluorine-containing natural products,[145] there has been a growing interest in the synthesis of highly functionalised fluorinated molecules, such as amino acids, due to their effective and increasingly extensive use as pharmaceutical agents.[146] There has long been evidence for the ring opening of aziridines with fluoride sources,[147-149] as well as cleavage of the C–O bond of sulfamates,[150-152] however only Burton has utilised the ring-opening of bicyclic sulfamate-linked aziridines with fluoride.[153, 154] Given the stereospecificity of the reaction of aziridine **340**, it was felt that the result was worthy of further investigation as a potentially stereoselective route to highly substituted fluorinated amines.

5.2 Substrate synthesis

A number of different substrates were synthesised to explore the scope and selectivity of the reaction. Known[155-157] homoallylic alcohols **342**, **346** and **349** were transformed into sulfamates in good yields and cyclised under Du Bois' conditions[53] to afford desired aziridines **344**, **348** and **351** (Scheme 136).



342 **343**, 82% **344**, 54% **345**, 3%

346 **347**, 74% **348**, 71%

349 **350**, 71% **351**, 38% **352**, 2%

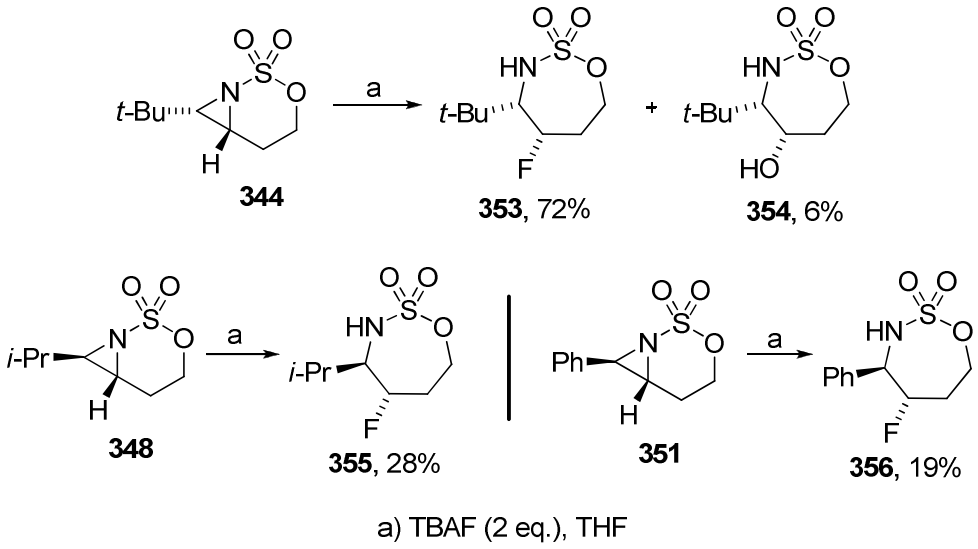
(a) $ClSO_2NCO$, HCO_2H, DMA; (b) 5 mol% $Rh_2(OAc)_4$, $PhI(OAc)_2$, MgO, DCM

Scheme 136

With (*Z*)-sulfamate **343** there was some minor diastereomer **345** formed, however the two oxathiazepanes were separable by column chromatography. Similarly, the unique electronic demands of the phenyl-substituted sulfamate **350** led to some unwanted acetate ring-opening to afford cyclic sulfamate **352**. Assignment of stereochemistry was achieved by comparison of data with compounds synthesised elsewhere.[144]

5.3 Fluorinations of sulfamate-linked aziridines

The original conditions[144] for ring opening of aziridine **340** were then tested on these substrates (Scheme 137).



Scheme 137

The reaction with *tert*-butyl substituted aziridine **344** proceeded in very good yield, however some hydrolysed product **354** was also isolated. By contrast, the yields of the products from the two *trans*-substituted aziridines, fluoro-oxathiazepanes **355** and **356**, were lower, a result found elsewhere within the group for other *trans*- aziridine substrates.[144] The relative stereochemistry of the products were determined by comparison of coupling constants and by X-ray crystal analysis of *tert*-butyl substituted aziridine **353** (Figure 15, Appendix F).

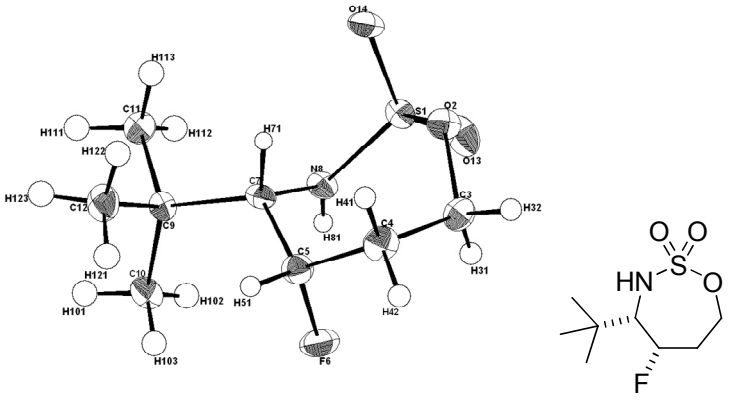
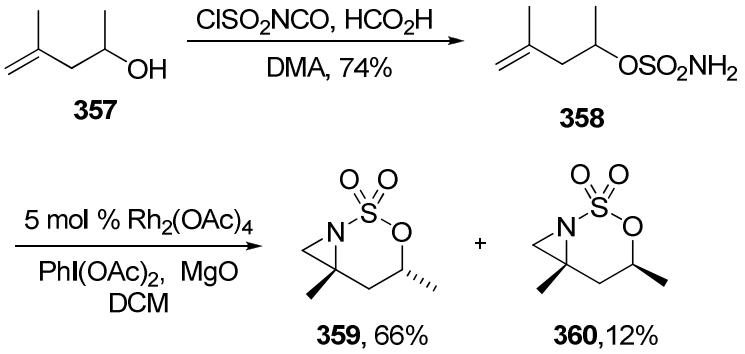


Figure 15

If these reactions are stereospecific then fluorination of a diasteromeric pair of aziridines should give different diastereomeric products. To this end, di-substituted sulfamate **358** was synthesised from known[158] alcohol **357** and, pleasingly, a pair of separable diastereomers were formed in the rhodium cyclisation reaction (Scheme 138).



Scheme 138

The relative stereochemistry of isomers **359** and **360** were assigned by comparison of nOe correlations (Figure 16).

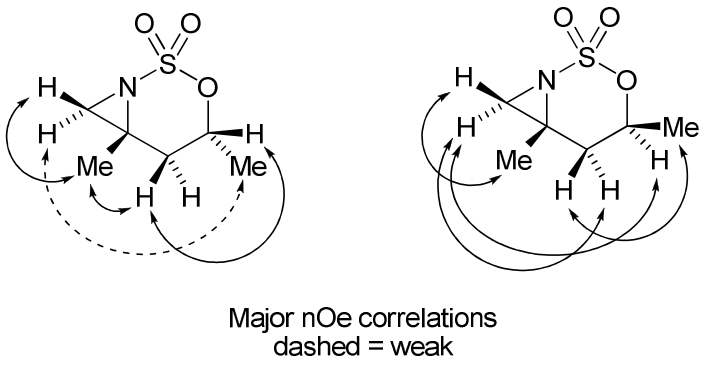
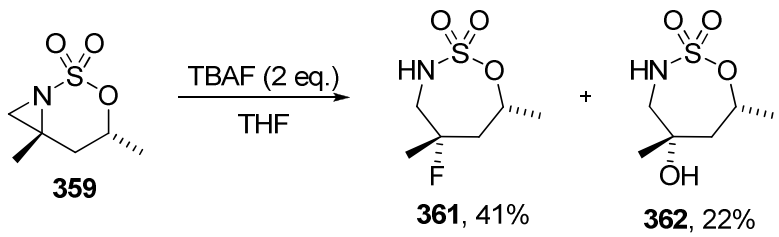


Figure 16

Fluorination of the major aziridine **359** was successful under standard conditions to afford fluoro-oxathiazepane **361** *via* S_N2 substitution at the tertiary carbon centre; it appears the inherent bias for internal C–N cleavage of bicyclic sulfamate-linked aziridines overrides the high steric constraints. Ring-opening by adventitious water from the TBAF solution led to some formation of side-product **362** (Scheme 139).



Scheme 139

The stereochemistry of fluoro-oxathiazepane **361** was unequivocally confirmed by X-ray crystallography (Figure 17).

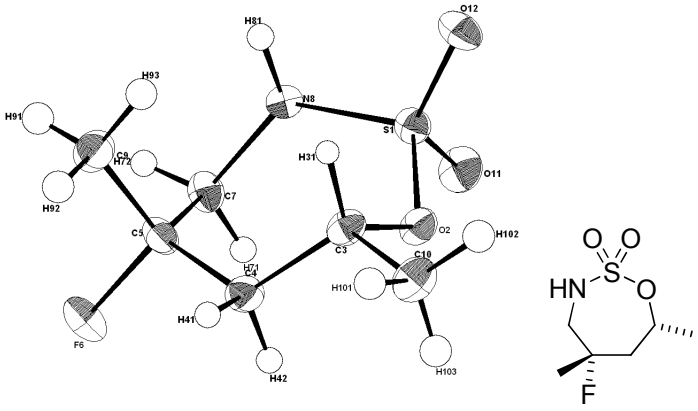
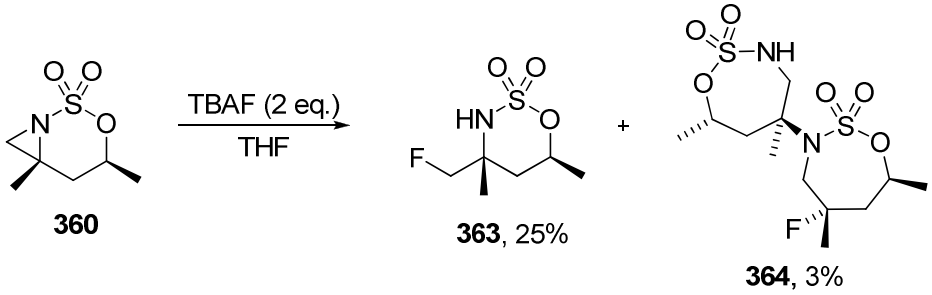


Figure 17

If the product from the ring opening of minor *syn*- diastereomer **360** was found to be spectroscopically different from fluoro-oxathiazepane **361**, then the reaction will have been shown to be stereospecific and S_N2 like. In the event, reaction of aziridine **360** under standard fluorination conditions led to two isolated products, primary fluoride **363** and curious bicycle **364** (Scheme 140).



360

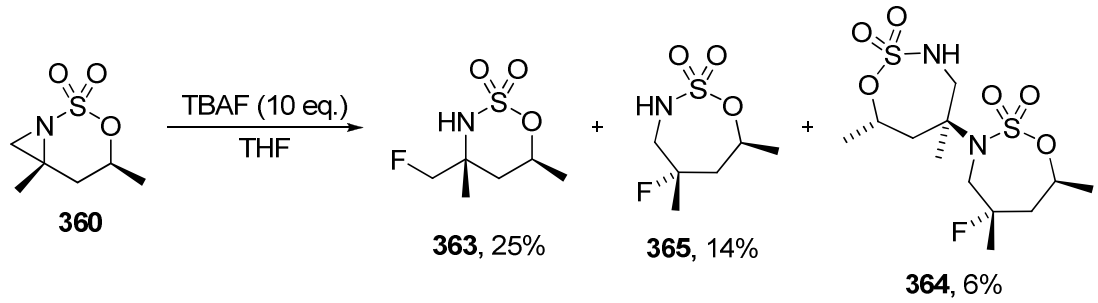
363, 25%

364, 3%

Scheme 140

The major product is a rare example of terminal ring-opening of such aziridines, the other known examples being minor side products in more strained systems,[60, 153] however the target of obtaining a comparable fluoro-oxathiazepane had not been achieved. Since bicycle **364** was presumably formed by ring-opening of a nitrogen anion formed *in situ*, it was predicted that an increase in TBAF concentration should favour formation of the

desired product. Upon increasing to 10 eq. TBAF, a mixture of all three fluorides was produced (Scheme 141).

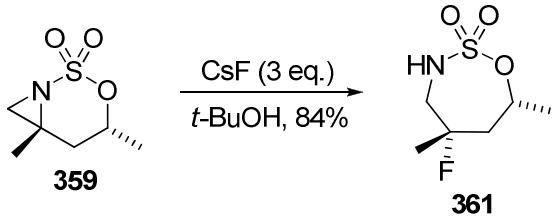


Scheme 141

The NMR data for fluoro-oxathiazepane **365** was notably different from fluoro-oxathiazepane **361**, for example δ_H ($CDCl_3$) of the OC**H** proton signal was 4.67 ppm in **361** compared to 4.93 ppm in **365**. This result provides compelling evidence that a stereospecific S_N2 mechanism is in operation in these reactions.

5.4 Optimisation

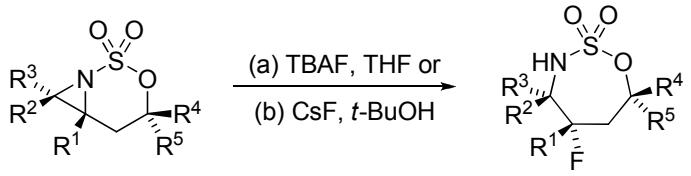
It was predicted that the yields of fluoride ring-openings could be increased by changing the fluoride source. Inspired by a report from Kim *et al.*,[159] in which nucleophilic fluorinations with alkali metal fluorides were performed efficiently in *tert*-alcohol solvents, a method was developed using CsF in *t*-butanol. A test reaction was carried out on aziridine **359**, whereby CsF was dissolved by heating to 80 °C, before cooling to 40 °C and a solution of aziridine **359** added. The yield of fluoro-oxathiazepane **361** more than doubled and hydrolysed product **362** was no longer observed (Scheme 142).



Scheme 142

In addition, it was found that the aqueous work up procedures used in the original conditions were problematic due to the difficulty of extracting the hydrophilic product; a more effective approach was to remove the solvent *in vacuo* and purify the residue by dry-load column chromatography.

When combined with results obtained elsewhere within the group[144] it was determined that *cis*- aziridines are superior to *trans*- aziridines in the fluorination reaction. Increasing the bulk of the substrates led, in general, to an increase in yield which can be accounted for by a release of strain in the transition state. The optimised conditions led to an increase in yield in all attempted examples and, with various eliminations of the sulfamate linker available, a successful method for the production of fluorinated amines has been established (Table 13).



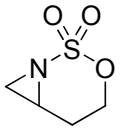
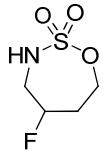
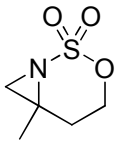
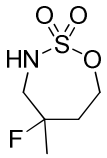
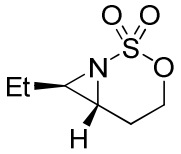
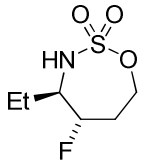
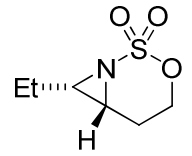
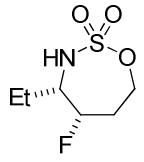
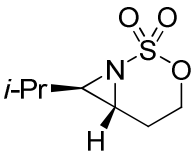
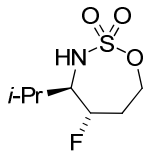
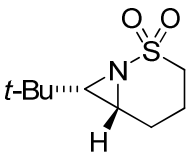
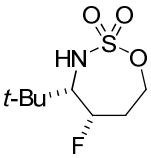
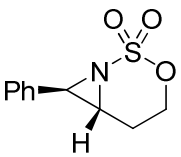
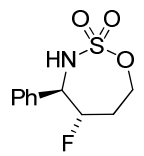
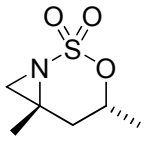
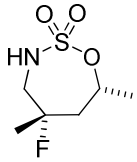
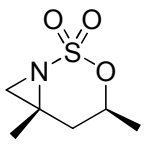
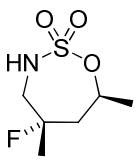
Aziridine	Fluoro-oxathiazepane	Yield – a (%)	Yield – b (%)
		25	46
		13	16
		43	82
		35	72
		28	51
		72	Not attempted
		19	Not attempted
		41	84
		14 (10 eq. TBAF)	Not attempted

Table 13

6. Experimental

6.1 General experimental techniques

Chromatographic techniques: Thin layer chromatography was performed on Merck DC-Alufolien 60 F_{254} 0.22 mm precoated plates. Product spots were visualised by the quenching of UV fluorescence (v_{max} = 254 nm) then stained and heated using 5% $KMnO_4$ in 5% aq. NaOH solution, 5% anisaldehyde in ethanol or 5% phosphomolydbic acid in ethanol. Retention factors are reported with the solvent system used in parentheses. Flash column chromatography was carried out on silica gel (ICN Silica 32–63 60 Å) with the solvent system in parentheses; graduated solvent systems are indicated with an arrow.

Melting points: Melting points were recorded on a Griffin melting point apparatus and are uncorrected.

Infra-red spectra: Infra-red spectra were recorded on a Bruker Tensor 27 Fourier Transform spectrometer as a thin film between sodium chloride plates or directly onto a diamond ATR module. Absorption maxima (λ_{max}) are described as s (strong), m (medium), w (weak), or br (broad) and are quoted in wavenumbers (cm^{-1}).

NMR Spectra: Proton (^1H), and Carbon (^{13}C) NMR spectra were recorded on a Bruker AV 400 (400/100 MHz) or Bruker AV 500 (500/125 MHz) spectrometer. Chemical shifts (δ_H or δ_C) are quoted in parts per million (ppm) downfield of tetramethylsilane, with residual protonated solvent as the internal standard. Assignments were made on the basis of chemical shifts, coupling constants, DEPT-135, COSY, HMQC, HMBC, NOESY data and comparison with spectra of related compounds. Resonances are described as s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), sxt (sextet), sept (septet), oct (octet), non (nonet), dec (dectet), m (multiplet), app. (apparent) or br (broad). Coupling constants (*J*) are given in Hz. H and H′ refer to diastereotopic protons attached to the same carbon and imply no particular stereochemistry. Fluorine (^{19}F) NMR spectra were recorded on a Bruker

AV 400 (376.5 MHz) or Bruker AV 500 (470.4 MHz) spectrometer. Chemical shifts (δ_F) are reported in parts per million (ppm).

Mass spectra: Low resolution mass spectra were recorded by the author on a Walters Micormass GCT spectrometer with an Aglient 6890N GC (CI). High resolution mass spectra were recorded either using the GCT spectrometer by the author, or using a Bruker Daltronics microTOF spectrometer (ESI) by Robin Procter or James McCullagh. Values are calculated to four decimal places from the molecular formula. *m/z* values are reported with their percentage abundance and, where known, the relevant fragment ion in parentheses. Peaks with a relative intensity less than 10% are not recorded.

Polarimetry: Optical rotations were recorded using a Perkin–Elmer 241 polarimeter at a wavelength of 589 nm and are quoted in units of 10^{-1} deg cm^{-2} g^{-1}. Concentrations are quoted in g/100 mL.

X-ray crystallography: Single crystal X-ray crystallography was performed by the author or Andrew Tyrrell. A single crystal was mounted on a glass fibre using perfluoropolyether oil and cooled rapidly to 150K in a stream of cold N_2 using an Oxford CRYOSTREAM unit. Diffraction data were measure using an Enraf-Nonius KappaCCD diffractometer (graphite-monochromated MoK_α radiation, λ = 0.71073 Å). Intensity data were processed using the DENZO-SMN package.[160] Structures were solved using the direct-methods program SIR92 which located all non-hydrogen atoms.[161] Subsequent full-matrix least-squares refinement was carried out using the CRYSTALS program suite.[162] Coordinates and anisotropic thermal parameters of all non-hydrogen atoms were refined.

Solvents and reagents: Solvents and commercially available reagents were dried and purified before use, as appropriate. Ether, DCM, THF, pentane and toluene were obtained dry and oxygen free from Grubbs solvent dispenser units. Acetonitrile, pyridine DMF and triethylamine were distilled from CaH_2 under reduced pressure and stored over 4 Å MS or

KOH. 'Petrol' refers to the fraction of light petroleum ether boiling in the range 30–40 °C. 'Brine' refers to a saturated aqueous solution of NaCl.

Reaction: All non-aqueous reactions were carried out in oven-dried glassware under an inert atmosophere of argon where appropriate.

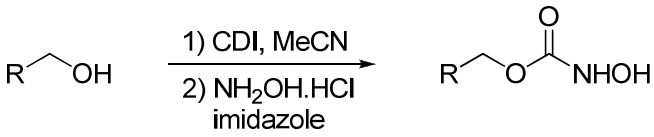
6.2 General experimental procedures

General procedure A: Oxidation with DMP[70]



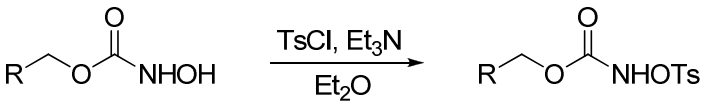
To a stirred solution of alcohol (1 eq.) in DCM (30 mL/mmol) at 0 °C was added DMP (1.2 eq.) and stirring continued until TLC analysis revealed the consumption of the starting material. The mixture was then concentrated *in vacuo* to give the crude product.

General procedure B: Synthesis of *N*-hydroxycarbamates[50]



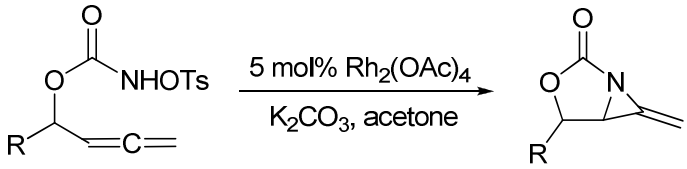
N,N'-Carbonyl diimidazole (1.5 eq.) was added to a stirred solution of alcohol (1 eq.) in acetonitrile (5 mL/mmol). Once TLC analysis had showed full consumption of the starting material, imidazole (4.0 eq.) and hydroxylamine hydrochloride (5.0 eq.) were added and stirring continued until TLC analysis showed conversion of the intermediate to be complete. The solvent was removed *in vacuo* and the residue partitioned between 1.0 M aq. HCl and ether. The phases were separated and the aqueous phase extracted twice with ether. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to give the crude product.

General procedure C: Synthesis of *N*-tosyloxycarbamates[50]



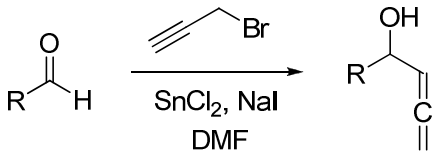
To a solution of *N*-hydroxycarbamate (1.0 eq.) in ether (10 mL/mmol) at 0 °C was added toluenesulfonylchloride (1.1 eq.). Triethylamine (1.02 eq.) was added dropwise and the resulting white suspension stirred at r.t. for 18 h. The reaction mixture was then diluted and washed successively with water and brine, dried over $MgSO_4$ and concentrated *in vacuo* to give the crude product.

General procedure D: Cyclisation of *N*-tosyloxycarbamates[50]



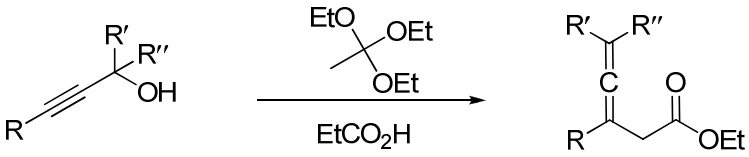
To a stirred solution of *N*-tosyloxycarbamate (1.0 eq.) in degassed acetone (8 mL/mmol) at 25 °C was added $Rh_2(OAc)_4$ (0.05 eq.) and K_2CO_3 (7.0 eq.). The reaction mixture was stirred vigorously for 18 h before diluted with DCM, filtered through Celite® and concentrated *in vacuo* to give the crude product.

General procedure E: Synthesis of α-hydroxy allenes[69]



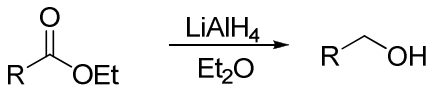
A suspension of $SnCl_2$ (1.2 eq.), NaI (1.2 eq.) and propargyl bromide (1.4 eq.) in DMF (2 mL/mmol) was stirred at room temperature for 1 h. The reaction mixture was cooled to 0 °C before addition of aldehyde (1.0 eq.) and stirring continued for 16 h. The reaction was quenched with water, allowed to warm to r.t. and extracted with ether. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to give the crude product.

General procedure F: Synthesis of β-allenyl ethyl-esters[163]



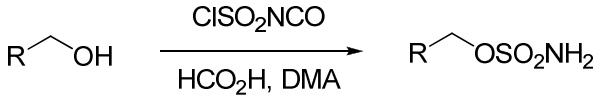
To a round bottom flask fitted with a side arm distillation apparatus, was added propargylic alcohol (1.0 eq.), propionic acid (0.05 eq.) and triethylorthoacetate (3-7 eq.). The reaction mixture was heated with stirring to 145 °C and once the distillation of ethanol had subsided, heated for a further hour. The reaction mixture was allowed to cool to r.t. and diluted with ether. 1.0 M aq. HCl was added and the product extracted with ether. The combined organic extracts were washed with sat. aq. $NaHCO_3$ solution and brine, dried over $MgSO_4$ and concentrated *in vacuo* to give the crude product.

General procedure G: Reduction of esters to alcohols



To a stirred solution of ester (1.0 eq.) in ether (10 mL/mmol) was added portionwise $LiAlH_4$ (2.0 eq.) at 0 °C. After 30 min, the reaction was quenched with water and filtered through Celite®. The cake was washed with ether and the combined organic extracts dried over $MgSO_4$ and concentrated *in vacuo* to give the crude product.

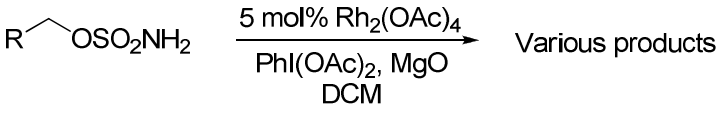
General procedure H: Synthesis of sulfamate esters[56]



Formic acid (2.0 eq) was added dropwise to chlorosulfonylisocyanate (2.0 eq.) at 0 °C with rapid stirring. Once gas evolution had subsided, the resulting mixture was allowed to warm to r.t. and stirred for 18 h. The reaction was recooled to 0 °C and DMA (0.5 mL/mmol) was added. After stirring for 5 min a solution of alcohol (1.0 eq.) in DMA (0.5 mL/mmol) was added dropwise *via* canula. Once TLC analysis showed consumption of starting material,

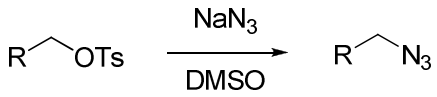
the reaction was diluted with ether and quenched with brine. The mixture was poured onto ether and water, separated, and the aqueous layer extracted with ether. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to give the crude product.

General procedure I: Cyclisation of sulfamate esters[54]



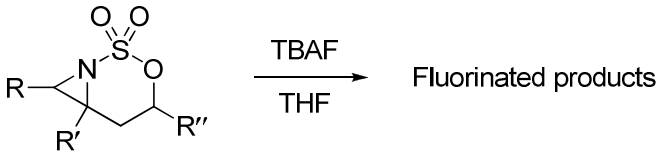
To a stirred solution of sulfamate (1.0 eq.) in DCM (10 mL/mmol) was added MgO (2.3 eq.), $PhI(OAc)_2$ (1.3 eq.) and $Rh_2(OAc)_4$ (0.05 eq.). After 18 h, the reaction mixture was filtered through Celite® and the cake washed with DCM. The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo* to give the crude product.

General procedure J: Synthesis of organic azides[140]



To a stirred solution of tosylate (1.0 eq.) in DMSO (3 mL/mmol) was added NaN_3 (1.1 eq.). After 48 h the solution was extracted with petrol. The combined petrol extracts were washed three times with brine, dried over Na_2SO_4 and concentrated *in vacuo* to give the crude product.

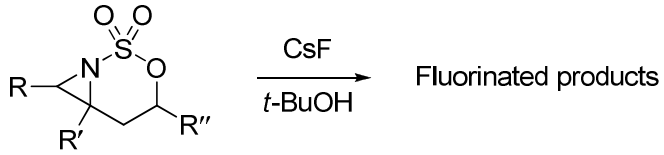
General procedure K: Fluorination of aziridines (Method A)



To a stirred solution of aziridine (1.0 eq.) in THF (5 mL/mmol) was added tetrabutylammonium fluoride (2.0 eq. of a 1.0 M solution in THF). Once TLC analysis showed consumption of starting material, the reaction was quenched with water. The

mixture was extracted with ethyl acetate and the combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to give the crude product.

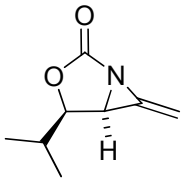
General procedure L: Fluorination of aziridines (Method B)[159]



CsF (3 eq.) was dissolved in *t*-BuOH (10 mL/mmol) at 80 °C. The solution was then cooled to 40 °C before addition of aziridine (1.0 eq.) in *t*-BuOH (5 mL/mmol) *via* canula. Once TLC analysis showed consumption of starting material, silica was added and the solvent removed *in vacuo* to give the dry-load crude material.

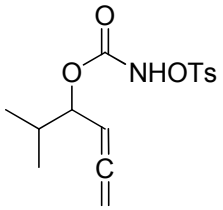
6.3 Experimental procedures

4-Isopropyl-6-methylene-3-oxa-1-azabicyclo[3.1.0]hexan-2-one[66] (64)



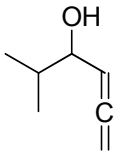
The reaction of *N*-tosyloxycarbamate **65** according to general procedure D and purification by column chromatography (2:1 petrol:ether) afforded the title compound (119 mg, 27%) as a yellow oil; R_f 0.30 (1:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 1.03 (3H, d, *J* 7.0, C**H**$_3$), 1.08 (3H, d, *J* 6.4, C**H**$_3$), 1.77–1.86 (1H, m, Me_2C**H**), 3.64 (1H, d, *J* 5.6, NC**H**), 4.36 (1H, dd, *J* 9.5, 5.6, OC**H**), 5.18 (1H, d, *J* 3.2, =C**H**H′), 5.39 (1H, app. dt, *J* 3.2, 1.0, =CH**H′**); δ_C (100 MHz, $CDCl_3$) 17.5 (**C**H_3), 19.7 (**C**H_3), 32.1 (Me_2**C**H), 43.7 (N**C**H), 83.7 (O**C**H), 91.4 (=**C**H_2), 130.2 (H_2C=**C**), 162.8 (O=**C**).

2-Methylhexa-4,5-dien-3-yl tosyloxycarbamate[66] (65)



The reaction of hydroxycarbamate **82** according to general procedure C and purification by column chromatography (10:1 petrol:ether → 1:2 petrol:ether) afforded the title compound (6.72 g, 92%) as a white solid; R_f 0.07 (5:1 petrol:ether); m.p. 48–51 °C; δ_H (400 MHz, $CDCl_3$) 0.81 (3H, d, *J* 6.8, C**H**$_3$), 0.84 (3H, d, *J* 6.8, C**H**$_3$), 1.75–1.84 (1H, m, Me_2C**H**), 2.45 (3H, s, ArC**H**$_3$), 4.76–4.78 (2H, m, =C**H**$_2$), 4.85–4.94 (2H, m, =C**H**, overlays OC**H**), 7.35 (2H, d, *J* 8.2, Ar**H**), 7.87 (2H, d, *J* 8.2, Ar**H**) 8.08 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 17.7 (**C**H$_3$), 17.9 (**C**H$_3$), 21.8 (Ar**C**H$_3$), 32.2 (Me_2**C**H), 76.9 (=**C**H$_2$), 80.1 (O**C**H), 88.0 (=**C**H), 129.6 (Ar), 129.7 (Ar), 130.3 (Ar), 146.1 (Ar), 155.1 (O=**C**), 208.9 (=**C**=).

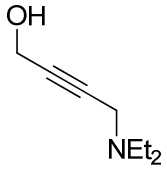
2-Methylhexa-4,5-dien-3-ol[164] (68)



To a round bottom flask containing CuBr (3.90 g, 27.2 mmol) and paraformaldehyde (4.34 g, 130.4 mmol) was added diisopropylamine (9.86 mL, 97.8 mmol), 4-methylpent-1-yn-3-ol (8.00 g, 81.5 mmol) and 1,4-dioxane (100 mL). The reaction mixture was stirred and heated at 120 °C for 2 hr, then allowed to cool and concentrated *in vacuo*. The residue was dissolved in ether (100 mL), filtered and concentrated *in vacuo*. The crude mixture was purified by column chromatography (10:1 petrol:ether) affording the title compound (4.10 g, 45%) as a colourless oil; R_f 0.35 (2:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 0.94 (3H, d, *J* 6.4, C**H**$_3$), 0.95 (3H, d, *J* 6.4, C**H**$_3$), 1.72–1.81 (1H, m, Me_2C**H**), 1.83 (1H, br s, OH), 3.94 (1H, br s, HOC**H**), 4.85 (2H, dd, *J* 6.6, 2.4, =C**H**$_2$), 5.22 (1H, app. q, *J* 6.6, =C**H**); δ_C (100 MHz,

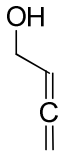
$CDCl_3$) 17.8 (**C**H_3), 18.0 (**C**H_3), 34.2 (Me**C**H), 74.6 (**C**OH), 77.2 (=**C**H_2), 93.0 (=**C**H), 207.3 (=**C**=).

4-(Diethylamino)but-2-yn-1-ol[68] (69)



To a round bottomed flask charged with diethylamine (12.4 mL, 120 mmol) and distilled water (4 mL) with the pH adjusted to 8.5 with conc. H_2SO_4, was added formaldehyde (11.9 mL of a 37% v/v aq. solution, 160 mmol) followed by propargyl alcohol (2.93 mL, 50.7 mmol) and an aq. solution of $CuSO_4.5H_2O$ (390 mg, 1.6 mmol). The pH was adjusted to 8.0 with conc. H_2SO_4 and the reaction was heated with stirring to 80 °C. After 2 h the reaction mixture was cooled and conc. aq. NH_3 solution was added (50 mL). The mixture was extracted with ether (3 x 100 mL) and the combined organic extracts were dried over $MgSO_4$. Concentration *in vacuo* afforded the title compound (6.80 g, 99%) as a yellow oil which was used without further purification; δ_H (400 MHz, $CDCl_3$) 1.04 (6H, t, *J* 7.2, $N(CH_2C\mathbf{H_3})_2$), 2.53 (4H, q, *J* 7.2, $N(C\mathbf{H_2}CH_3)_2$), 3.42 (2H, t, *J* 1.9, ≡CC$\mathbf{H_2}$N), 4.23 (2H, t, *J* 1.9, HOC$\mathbf{H_2}$); δ_C (100 MHz, $CDCl_3$) 12.2 (**C**H_3), 40.7 (≡C**C**H_2N), 47.0 ($H_3C\mathbf{C}H_2N$), 50.5 (HO**C**H_2), 79.5 ($HOCH_2\mathbf{C}$≡), 83.7 ($NCH_2\mathbf{C}$≡).

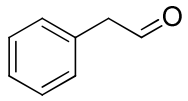
Buta-2,3-dien-1-ol[68] (70)



Dimethyl sulphate (4.89 mL, 51.7 mmol) was added dropwise to a vigorously stirred solution of alcohol **69** (6.00 g, 44.2 mmol) in ether (100 mL). The mixture was heated at reflux for 2 h and allowed to cool before the addition of a suspension of $LiAlH_4$ (3.35 g, 88.4 mmol) in ether (50 mL) was added *via* a pressure equalising dropping funnel. The solution

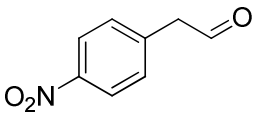
was heated at reflux for 4 h before cooling in an ice bath. The reaction was quenched with water (5 mL) before the addition of 1.0 M aq. HCl (20 mL). The organic layer was separated and the aqueous layer extracted with ether (2 x 40 mL). The combined organic extracts were dried over $MgSO_4$ and concentration *in vacuo* gave the title compound (1.00 g, 33%) as a volatile, colourless oil; R_f (2:1 ether:petrol) 0.44; δ_H (400 MHz, $CDCl_3$) 4.15 (2H, app. quin., *J* 3.0, HOC**H₂**), 4.86 (2H, dt, *J* 6.3, 3.0, =C**H₂**), 5.35 (1H, app. quin, *J* 6.3, =C**H**); δ_C (100 MHz, $CDCl_3$) 60.2 (HO**C**H), 77.0 (=**C**H_2), 90.9 (=**C**H), 207.8 (=**C**=).

2-Phenylacetaldehyde[165] (74)



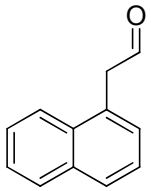
The reaction of 2-phenylethanol according to general procedure A and purification by column chromatography (10:1 petrol:ether) afforded the title compound (802 mg, 81%) as a colourless oil; R_f 0.21 (10:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 3.71 (2H, d, *J* 2.4, PhC**H₂**), 7.23–7.25 (2H, m, Ph**H**), 7.31–3.34 (1H, m, Ph**H**), 7.37–7.41 (3H, m, Ph**H**), 9.77 (1H, t, *J* 2.4, O=C**H**); δ_C (100 MHz, $CDCl_3$) 50.6 (Ph**C**H_2), 128.3 (Ar), 129.0 (Ar), 129.6 (Ar), 131.8 (Ar), 199.5 (O=**C**).

2-(4-Nitrophenyl)acetaldehyde[166] (75)



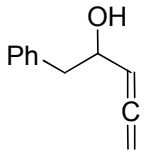
The reaction of 2-(4-nitrophenyl)ethanol according to general procedure A and purification by column chromatography (ether) afforded the title compound (2.0 g, quant.) as a colourless oil; R_f 0.37 (ether); δ_H (400 MHz, $CDCl_3$) 3.88 (2H, d, *J* 1.5, ArC**H₂**), 7.41 (2H, d, *J* 8.8, Ar**H**), 8.23 (2H, d, *J* 8.8, Ar**H**), 9.82 (1H, t, *J* 1.5, O=C**H**); δ_C (100 MHz, $CDCl_3$) 50.0 (**C**H_2), 124.1 (Ar), 130.6 (Ar), 139.3 (Ar), 147.3 (Ar), 197.4 (O=**C**).

2-(Naphthalen-1-yl)acetaldehyde[167] (76)



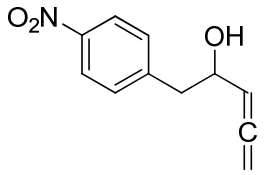
The reaction of 2-(naphthalen-1-yl)ethanol according to general procedure A and purification by column chromatography (10:1 petrol:ether) afforded the title compound (1.48 g, 88%) as a white solid; m.p. 29–33 °C; R_f 0.20 (5:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 4.12 (2H, d, *J* 2.4, ArC**H**$_2$), 7.42–7.59 (4H, m, Ar**H**), 7.85–7.93 (3H, m, Ar**H**), 9.80 (1H, t, *J* 2.4, O=C**H**); δ_C (100 MHz, $CDCl_3$) 48.4 (Ar**C**H$_2$), 123.6 (Ar), 125.7 (Ar), 126.1 (Ar), 126.7 (Ar), 128.4 (Ar), 128.4 (Ar), 128.5 (Ar), 128.9 (Ar), 132.3 (Ar), 133.9 (Ar), 199.7 (O=**C**).

1-Phenylpenta-3,4-dien-2-ol[168] (77)



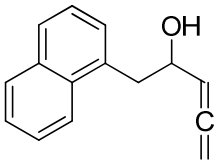
The reaction of aldehyde **74** according to general procedure E and purification by column chromatography (5:1 petrol:ether) afforded the title compound (76 mg, 57%) as a colourless oil; R_f 0.15 (5:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 1.84 (1H, br s, O**H**), 2.88 (1H, dd, *J* 13.6, 7.6, PhC**H**H′), 2.94 (1H, dd, *J* 13.6, 5.4, PhCH**H′**), 4.40–4.46 (1H, m, OC**H**), 4.85–4.88 (2H, m, =C**H**$_2$), 5.32 (1H, app. q, *J* 6.7, =C**H**), 7.24–7.27 (3H, m, Ph**H**), 7.32–7.35 (2H, m, Ph**H**); δ_C (100 MHz, $CDCl_3$) 43.9 (Ph**C**H$_2$), 70.2 (O**C**H), 77.9 (=**C**H$_2$), 94.1 (=**C**H), 126.6 (Ar), 128.5 (Ar), 129.6 (Ar), 137.7 (Ar), 206.9 (=**C**=).

1-(4-Nitrophenyl)penta-3,4-dien-2-ol (78)



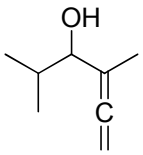
The reaction of aldehyde **75** according to general procedure E and purification by column chromatography (2:1 petrol:ether) afforded the title compound (1.09 g, 44%) as a colourless oil; R_f 0.29 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3395br, 3086s, 1956s, 1713s, 1601s, 1518s, 1346s; δ_H (400 MHz, $CDCl_3$) 2.97 (1H, dd, *J* 13.6, 7.3, ArC**H**H′), 3.03 (1H, dd, *J* 13.6, 5.3, ArCH**H′**), 4.44–4.50 (1H, m, OC**H**), 4.89 (2H, app. ddd, *J* 6.7, 2.4, 1.3, =C**H**$_2$), 5.30 (1H, app. q, *J* 6.7, =C**H**), 7.42 (2H, d, *J* 8.7, Ar**H**), 8.17 (2H, d, *J* 8.7, Ar**H**); δ_C (100 MHz, $CDCl_3$) 43.4 (Ar**C**H$_2$), 69.8 (O**C**H), 78.5 (=**C**H$_2$), 93.9 (=C**H**), 123.5 (Ar), 130.5 (Ar), 145.8 (Ar), 146.8 (Ar), 206.9 (=**C**=); Accurate mass (FI): Found 205.0729: $C_{11}H_{11}NO_3$ (M) requires 205.0739.

1-(Naphthalen-1-yl)penta-3,4-dien-2-ol (79)



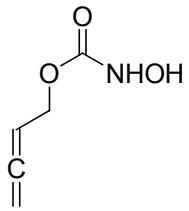
The reaction of aldehyde **76** according to general procedure E and purification by column chromatography (15:1 petrol:ethyl acetate) afforded the title compound (901 mg, 61%) as a colourless oil; R_f 0.18 (5:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3383br, 3061s, 2931s, 1955s, 1597s, 1510s, 1396s; δ_H (400 MHz, $CDCl_3$) 1.85 (1H, br s, O**H**), 3.31 (1H, dd, *J* 14.0, 8.0, ArC**H**H′), 3.43 (1H, dd, *J* 14.0, 5.2, ArCH**H′**), 4.56–4.63 (1H, m, OC**H**), 4.86–4.96 (2H, m, =C**H**$_2$), 5.39 (1H, app. q, *J* 6.6, =C**H**); 7.40–7.47 (2H, m, Ar**H**), 7.49–7.57 (2H, m, Ar**H**), 7.79 (1H, d, *J* 7.8, Ar**H**), 7.87–7.90 (1H, m, Ar**H**), 8.08 (1H, d, *J* 8.3, Ar**H**); δ_C (100 MHz, $CDCl_3$) 41.1 (Ar**C**H$_2$), 69.5 (O**C**H), 78.0 (=**C**H$_2$), 94.4 (=C**H**), 123.8 (Ar), 125.5 (Ar), 125.7 (Ar), 126.1 (Ar), 127.5 (Ar), 127.9 (Ar), 128.9 (Ar), 132.2 (Ar), 133.8 (Ar), 134.0 (Ar), 206.9 (=**C**=); Accurate mass (ESI$^+$): Found 233.0934: $C_{15}H_{14}NaO$ (MNa^+) requires 233.0937.

2,4-Dimethylhexa-4,5-dien-3-ol[169] (80)



A suspension of $SnCl_2$ (3.67 g, 19.3 mmol), NaI (2.89 g, 19.3 mmol) and 1-bromobut-2-yne (1.34, 15.2 mmol) in DMF (40 mL) was stirred at room temperature for 1 h. The reaction mixture was then cooled to 0 °C before the addition of isobutyraldehyde (1.0 mL, 13.8 mmol) and stirring continued for 16 h. The reaction was quenched with water (100 mL), allowed to warm to r.t. and extracted with ether (3 × 100 mL). The combined organic extracts were washed with brine (80 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (15:1 petrol:ether) afforded the title compound (1.15g, 66%) as a colourless oil; R_f 0.31 (5:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 0.94 (6H, dd, *J* 6.8, 4.6, HC(C**H**$_3$)$_2$), 1.70 (3H, t, *J* 3.2, =CC**H**$_3$), 1.82 (1H, app. oct, *J* 6.4, Me_2C**H**), 3.75–3.78, (1H, m, HOC**H**), 4.77–4.80 (2H, m, =C**H**$_2$); δ_C (100 MHz, $CDCl_3$) 14.3 (=C**C**H$_3$), 16.9 (**C**H$_3$), 19.5 (**C**H$_3$), 31.3 (Me_2**C**H), 76.4 (=**C**H$_2$), 77.7 (O**C**H), 101.2 (OC**C**=), 205.4 (=**C**=).

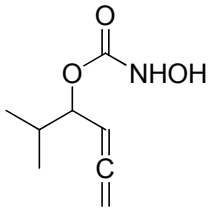
Buta-2,3-dienyl hydroxycarbamate (81)



The reaction of alcohol **70** according to general procedure B and purification by column chromatography (1:1 petrol:ether) afforded the title compound (52 mg, 56%) as a colourless oil; R_f 0.44 (ether); ν_{max}/cm^{-1} (thin film) 3301br, 2960s, 1958s, 1722s, 1493s, 1350s, 1270m, 1116s; δ_H (400 MHz, $CDCl_3$) 4.64 (2H, dt, *J* 7.1, 2.3, OC**H**$_2$), 4.86 (2H, dt, *J* 6.6, 2.3, =C**H**$_2$), 5.30 (1H, app. quin, *J* 6.9, =C**H**) 7.56 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$)

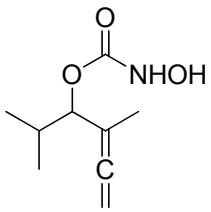
63.9 (O**C**H_2), 76.8 (=**C**H_2), 86.0 (=**C**H), 159.1 (O=**C**), 209.9 (=**C**=); Accurate mass (ESI^+): Found 152.0317: $C_5H_7NNaO_3$ (MNa^+) requires 152.0318.

2-Methylhexa-4,5-dien-3-yl hydroxycarbamate[66] (82)



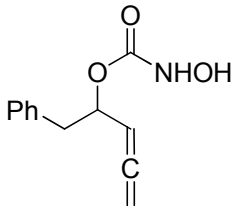
The reaction of alcohol **68** according to general procedure B and purification by column chromatography (5:1 petrol:ether) afforded the title compound (2.99 g, 66%) as a colourless oil; R_f 0.06 (3:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 0.94 (6H, d, *J* 6.8, C**H**$_3$), 1.93 (1H, app. oct, *J* 6.8, Me_2C**H**), 4.80-4.89 (2H, m, =C**H**$_2$), 5.00–5.05 (1H, m, OC**H**), 5.13 (1H, app. q, *J* 6.8, =C**H**); δ_C (100 MHz, $CDCl_3$) 17.9 (**C**H_3), 18.0 (**C**H_3), 32.4 (Me_2**C**H), 76.9 (=**C**H_2), 78.8 (O**C**H), 88.6 (=**C**H), 159.1 (O=**C**), 208.9 (=**C**=).

2,4-Dimethylhexa-4,5-dien-3-yl hydroxycarbamate (83)



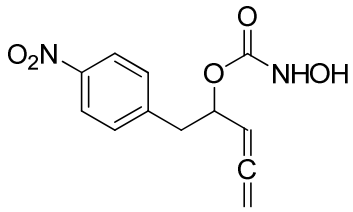
The reaction of alcohol **80** according to general procedure B and purification by column chromatography (2:1 → 1:1 petrol:ether) afforded the title compound (430 mg, 50%) as a colourless oil; R_f 0.20 (1:1 petrol:ether); v_{max}/cm^{-1} (thin film) 33132br, 2965s, 1961s, 1722s, 1470s, 1261s, 1109s; δ_H (500 MHz, $CDCl_3$) 0.93 (3H, d, *J* 6.8, CHC**H**$_3$), 0.95 (3H, d, *J* 6.8, CHC**H**$_3$), 1.62–1.71 (3H, m, =CC**H**$_3$), 1.96 (1H, app. oct, *J* 6.9, Me_2C**H**), 4.71–4.78 (2H, m, C=C**H**$_2$), 4.90 (1H, d, *J* 7.2, OC**H**), 7.20 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 14.6 (=C**C**H_3), 17.1 (**C**H_3), 19.0 (**C**H_3), 30.3 (Me_2**C**H), 75.8 (=**C**H_2), 81.9 (O**C**H), 97.0 (OC**C**=), 159.1 (O=**C**), 207.1 (=**C**=); Accurate mass (ESI^+): Found 208.0942: $C_9H_{15}NNaO_3$ (MNa^+) requires 208.0944.

1-Phenylpenta-3,4-dien-2-yl hydroxycarbamate (84)



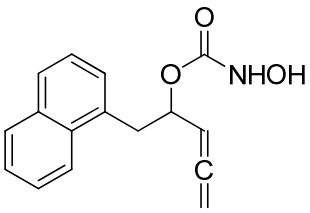
The reaction of alcohol **77** according to general procedure B and purification by column chromatography (2:1 petrol:ether) afforded the title compound (152 mg, 48%) as a colourless oil; R_f 0.13 (1:1 petrol:ether); v_{max}/cm^{-1} (thin film) 3300br, 3088w, 3064w, 3030s, 2925s, 1957s, 1721s, 1604w, 1499s, 1455s; δ_H (400 MHz, $CDCl_3$) 3.04-3.07 (2H, m, PhC**H₂**), 4.81–4.91 (2H, m, =C**H₂**), 5.26 (1H, app. q, *J* 6.7, =C**H**), 5.44–5.50 (1H, m, OC**H**), 5.99 (1H, br s, N**H**) 7.20–7.32 (5H, m, Ph**H**); δ_C (125 MHz, $CDCl_3$) 40.5 (Ph**C**H_2), 74.2 (O**C**H), 77.8 (=**C**H_2), 90.1 (=**C**H), 126.6 (Ar), 128.4 (Ar), 129.5 (Ar), 136.5 (Ar), 158.5 (O=**C**), 206.9 (=**C**=); Accurate mass – Not found.

1-(4-Nitrophenyl)penta-3,4-dien-2-yl hydroxycarbamate (85)



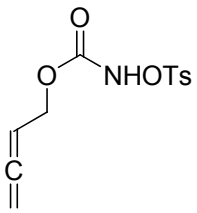
The reaction of alcohol **78** according to general procedure B and purification by column chromatography (1:1 petrol:ether) afforded the title compound (346 mg, 40%) as a colourless oil; R_f 0.16 (1:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 3.10 (2H, d, *J* 6.7, ArC**H₂**), 4.83–4.93 (2H, m, =C**H₂**), 5.25 (1H, app. q, *J* 6.6, =C**H**), 5.44–5.50 (1H, m, OC**H**), 6.95 (1H, br s, N**H**), 7.38 (2H, d, *J* 8.7, Ar**H**), 8.14 (2H, d, *J* 8.7, Ar**H**); δ_C (100 MHz, $CDCl_3$) 40.2 (Ar**C**H_2), 71.9 (O**C**H), 78.3 (=**C**H_2), 89.7 (=C**H**), 123.5 (Ar), 130.4 (Ar), 144.4 (Ar), 146.9 (Ar), 158.3 (O=**C**), 208.5 (=**C**=); Accurate mass (ESI^+): Found 287.0638: $C_{12}H_{12}N_2NaO_5$ (MNa^+) requires 287.0638.

1-(Naphthalen-1-yl)penta-3,4-dien-2-yl hydroxycarbamate (86)



The reaction of alcohol **79** according to general procedure B and purification by column chromatography (2:1 → 1:1 petrol:ether) afforded the title compound (414 mg, 56%) as a colourless oil; R_f 0.15 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3289br, 3048w, 2975s, 1957s, 1721s, 1597s, 1456s, 1261s; δ_H (500 MHz, $CDCl_3$) 1.83 (1H, br s, O**H**), 3.37 (1H, dd, *J* 14.2, 6.5, ArC**H**H′), 3.54 (1H, dd, *J* 14.2, 7.3, ArCH**H′**), 4.77 (1H, ddd, *J* 11.4, 6.6, 2.0, =C**H**H′), 4.86 (1H, ddd, *J* 11.4, 6.6, 2.2, =CH**H′**), 5.30 (1H, app. q, *J* 6.6, =C**H**), 5.58–5.64 (1H, m, OC**H**), 6.80 (1H, br s, N**H**), 7.34 (1H, d, *J* 6.2, Ar**H**), 7.39 (1H, app. t, *J* 7.0, Ar**H**), 7.47–7.50 (1H, m, Ar**H**), 7.54 (1H, ddd, *J* 8.4, 7.0, 1.6), 7.75 (1H, d, *J* 8.2, Ar**H**), 7.85 (1H, d, *J* 8.0, Ar**H**), 8.11 (1H, d, *J* 8.4, Ar**H**); δ_C (125 MHz, $CDCl_3$) 37.7 (Ar**C**H_2), 73.9 (O**C**H), 77.9 (=**C**H_2), 90.3 (=**C**H), 123.7 (Ar), 125.3 (Ar), 125.6 (Ar), 126.1 (Ar), 127.6 (Ar), 127.9 (Ar), 128.8 (Ar), 132.2 (Ar), 132.6 (Ar), 133.8 (Ar), 158.5 (O=**C**), 208.4 (=**C**=); Accurate mass (ESI^+): Found 292.0943: $C_{16}H_{15}NNaO_3$ (MNa^+) requires 292.0944.

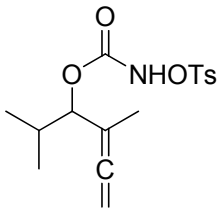
Buta-2,3-dienyl tosyloxycarbamate (87)



The reaction of hydroxycarbamate **81** according to general procedure C and purification by column chromatography (5:1 petrol:ether → 2:1 petrol:ether) afforded the title compound (522 mg, 70%) as a colourless oil; R_f 0.39 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3233br, 2958s, 1958s, 1744s, 1597s, 1455s, 1382m, 1341m, 1309s, 1234m; δ_H (400 MHz, $CDCl_3$) 2.47 (3H, s, ArC**H$_3$**), 4.50 (2H, dt, *J* 7.2, 2.3, OC**H$_2$**), 4.84 (2H, dt, *J* 6.6, 2.3, =C**H$_2$**), 5.10

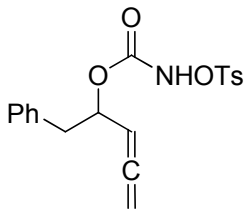
(1H, app. quin, *J* 6.9, =C**H**), 7.37 (2H, d, *J* 8.3, Ar**H**), 7.88 (2H, d, *J* 8.3, Ar**H**), 8.03 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 21.8 (Ar**C**H_3), 64.7 (O**C**H_2), 77.0 (=**C**H_2), 85.4 (=**C**H), 129.6 (Ar), 129.8 (Ar), 130.2 (Ar), 146.2 (Ar), 155.2 (O=**C**), 210.0 (=**C**=); Accurate mass (ESI^+): Found 282.0429: $C_{12}H_{12}NO_5S$ (MH^+) requires 282.0442.

2,4-Dimethylhexa-4,5-dien-3-yl tosyloxycarbamate (88)



The reaction of hydroxycarbamate **83** according to general procedure C and purification by column chromatography (4:1 petrol:ether) afforded the title compound (530 mg, 61%) as a colourless oli; R_f 0.34 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3282br, 2968s, 1961s, 1739s, 1598s, 1462s, 1381s, 1325s, 1238s; δ_H (400 MHz, $CDCl_3$) 0.79 (3H, d, *J* 6.7, CHC**H$_3$**), 0.83 (3H, d, *J* 6.7, CHC**H$_3$**), 1.54 (3H, t, *J* 3.2, =CC**H$_3$**), 1.87 (1H, dsept, *J* 8.0, 6.7, Me_2C**H**), 4.64–4.72 (2H, m, =C**H$_2$**), 4.76 (1H, d, *J* 8.0, OC**H**), 7.36 (2H, d, *J* 8.5, Ar**H**), 7.88 (2H, d, *J* 8.5, Ar**H**); δ_C (100 MHz, $CDCl_3$) 14.2 (=C**C**H_3), 17.8 (**C**H_3), 18.8 (**C**H_3), 21.8 (Ar**C**H_3), 30.1 (Me_2**C**H), 75.8 (=**C**H_2), 83.3 (O**C**H), 96.3 (OC**C**=), 129.6 (Ar), 129.7 (Ar), 130.3 (Ar), 146.1 (Ar), 155.2 (O=**C**), 207.1 (=**C**=); Accurate mass (ESI^+): Found 362.1036: $C_{16}H_{21}NNaO_5S$ (MNa^+) requires 362.1033.

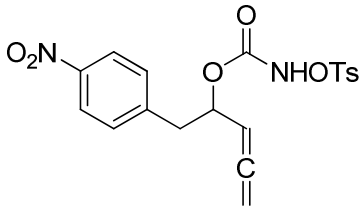
1-Phenylpenta-3,4-dien-2-yl tosyloxycarbamate (89)



The reaction of hydroxycarbamate **84** according to general procedure C and purification by column chromatography (5:1 petrol:ether → 2:1 petrol:ether) afforded the title compound (195 mg, 61%) as a viscous, colourless oil; R_f 0.22 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film)

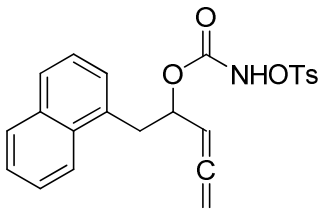
3287s, 3065w, 3031w, 2326s, 2871s, 1957s, 1739s, 1597s. 1496s, 1455s; δ_H (500 MHz, $CDCl_3$) 2.45 (3H, s, C**H**$_3$), 2.87 (2H, d, *J* 6.8, PhC**H**$_2$), 4.82 (1H, ddd, *J* 11.5, 6.5, 1.9, =C**H**H′), 4.87 (1H, ddd, *J* 11.5, 6.8, 2.0, =CH**H′**), 5.01 (1H, app. q, *J* 6.7, =C**H**), 5.25–5.30 (1H, m, OC**H**), 7.11–7.14 (2H, m, Ph**H**), 7.23–7.31 (3H, m, Ph**H**), 7.33 (2H, d, *J* 8.2, Ar**H**), 7.76 (1H, br s, N**H**) 7.84 (2H, d, *J* 8.2, Ar**H**); δ_C (125 MHz, $CDCl_3$) 21.8 (**C**H$_3$), 40.2 (Ph**C**H$_2$), 75.5 (O**C**H), 77.8 (=**C**H$_2$), 89.4 (=**C**H), 126.7 (Ar), 128.3 (Ar), 129.1 (Ar), 129.5 (Ar), 129.7 (Ar), 130.3 (Ar), 136.0 (Ar) 146.0 (Ar), 154.5 (O=**C**), 208.5 (=**C**=); Accurate mass (ESI$^+$): Found 396.0878: $C_{19}H_{19}NNaO_5S$ (MNa$^+$) requires 396.0876.

1-(4-Nitrophenyl)penta-3,4-dien-2-yl tosyloxycarbamate (90)



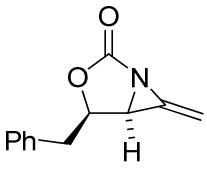
The reaction of hydroxycarbamate **85** according to general procedure C and purification by column chromatography (2:1 petrol:ether → 1:1 petrol:ether) afforded the title compound (278 mg, 46%) as a viscous, colourless oil; R_f 0.23 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3298br, 3052s, 1957s, 1770s, 1599s, 1520s, 1391s 1347s; δ_H (500 MHz, $CDCl_3$) 2.46 (3H, s, ArC**H**$_3$), 3.02 (2H, d, *J* 6.6, ArC**H**$_2$), 4.82–4.90 (2H, m, =C**H**$_2$), 5.07 (1H, app. q, *J* 6.6, =C**H**), 5.32–5.37 (1H, m, OC**H**), 7.33 (2H, d, *J* 8.7, Ar**H**), 7.35 (2H, d, *J* 8.2, Ar**H**), 7.66 (1H, br s, N**H**), 7.85 (2H, d, *J* 8.2, Ar**H**), 8.14 (2H, d, *J* 8.7, Ar**H**); δ_C (125 MHz, $CDCl_3$) 22.3 (Ar**C**H$_3$) 40.5 (Ar**C**H$_2$), 74.7 (O**C**H), 78.3 (=**C**H$_2$), 89.1 (=**C**H), 123.6 (Ar), 129.5 (Ar), 129.8 (Ar), 130.3 (Ar), 130.4 (Ar), 143.8 (Ar), 146.3 (Ar), 147.0 (Ar), 154.5 (O=**C**), 208.6 (=**C**=); Accurate mass (ESI$^+$): Found 441.0717: $C_{19}H_{18}N_2NaO_7S$ (MNa$^+$) requires 441.0727.

1-(Naphthalen-1-yl)penta-3,4-dien-2-yl tosyloxycarbamate (91)



The reaction of hydroxycarbamate **86** according to general procedure C and purification by column chromatography (4:1 petrol:ether) afforded the title compound (457 mg, 54%) as a colourless oli; R_f 0.36 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3288br, 3067s, 2976s, 1957s, 1738s, 1597s, 1511s, 1449s, 1382s; δ_H (500 MHz, $CDCl_3$) 2.38 (3H, s, ArC**H**$_3$), 3.26 (1H, dd, *J* 14.2, 6.3, ArC**H**H′), 3.36 (1H, dd, *J* 14.2, 7.4, ArCH**H′**), 4.74 (1H, ddd, *J* 11.5, 6.8, 2.0, =C**H**H′), 4.83 (1H, ddd, *J* 11.5, 6.8, 1.9, =CH**H′**), 5.08 (1H, app. q, *J* 6.8, =C**H**), 5.40–5.45 (1H, m, OC**H**), 7.23–7.31 (4H, m, Ar**H**), 7.40 (1H, dd, *J* 8.2, 7.1, Ar**H**), 7.49–7.56 (2H, m, Ar**H**), 7.74 (1H, br s, N**H**), 7.77–7.79 (3H, m, Ar**H**), 7.87–7.89 (1H, m, Ar**H**), 7.97 (1H, d, *J* 8.2, Ar**H**); δ_C (125 MHz, $CDCl_3$) 21.7 (Ar**C**H$_3$), 37.4 (Ar**C**H$_2$), 75.0 (O**C**H), 77.9 (=**C**H$_2$), 89.6 (=C**H**), 123.5 (Ar), 125.3 (Ar), 125.7 (Ar), 126.2 (Ar), 127.4 (Ar), 128.1 (Ar), 128.8 (Ar), 129.5 (Ar), 129.6 (Ar), 130.2 (Ar), 132.0 (Ar), 132.2 (Ar), 133.8 (Ar), 146.1 (Ar), 154.5 (O=**C**), 208.5 (=**C**=); Accurate mass (ESI^+): Found 446.1033: $C_{23}H_{21}NNaO_5S$ (MNa^+) requires 446.1033.

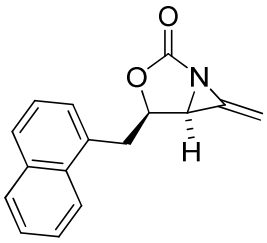
4-Benzyl-6-methylene-3-oxa-1-azabicyclo[3.1.0]hexan-2-one (92)



The reaction of *N*-tosyloxycarbamate **89** according to general procedure D and purification by column chromatography (2:1 petrol:ether) afforded the title compound (7 mg, 7%) as a yellow oil; R_f 0.24 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3029m, 2926s, 1716s, 1602m, 1496s; δ_H (500 MHz, $CDCl_3$) 2.91 (1H, dd, *J* 13.7, 7.2, PhC**H**H′), 3.18 (1H, dd, *J* 13.7, 6.5, PhCH**H′**), 3.54 (1H, dt, *J* 5.5, 1.0, NC**H**), 4.96 (1H, app. td, *J* 6.8, 5.5, OC**H**), 5.26 (1H, d, *J*

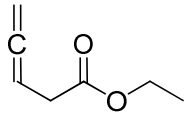
3.3, =C**H**H′), 5.46 (1H, dd, *J* 3.3, 1.0, =CH**H′**), 7.23–7.38 (5H, m, Ph**H**); δ_C (125 MHz, $CDCl_3$) 38.8 (Ph**C**H_2), 44.0 (N**C**H), 78.5 (O**C**H), 91.9 (=**C**H_2), 127.5 (Ar), 129.0 (Ar), 129.1 (Ar), 130.2 (H_2C=**C**), 162.5 (O=**C**); Accurate mass (ESI^+) - Not found.

6-Methylene-4-(naphthalen-1-ylmethyl)-3-oxa-1-azabicyclo[3.1.0]hexan-2-one (93)



The reaction of *N*-tosyloxycarbamate **91** according to general procedure D and purification by column chromatography (4:1 petrol:ether) afforded the title compound (11 mg, 20%) as a pale yellow, crystalline solid; R_f (2:1 petrol:ether) 0.24; m.p. 82–84 °C; ν_{max}/cm^{-1} (thin film) 3049s, 1791s, 1597s, 1511s, 1396s, 1175s; δ_H (500 MHz, $CDCl_3$) 3.47 (1H, dd, *J* 14.1, 8.1, ArC**H**H′), 3.48 (1H, dt, *J* 5.5, 1.0, NC**H**) 3.74 (1H, dd, *J* 14.1, 5.8, ArCH**H′**), 5.16–5.20 (1H, m, OC**H**), 5.27 (1H, d, *J* 3.3, =C**H**H′), 5.49 (1H, dt, *J* 3.3, 1.0, =CH**H′**), 7.39 (1H, d, *J* 7.0, Ar**H**), 7.46 (1H, dd, *J* 8.2, 6.9, Ar**H**), 7.53–7.57 (1H, m, Ar**H**), 7.58–7.62 (1H, m, Ar**H**), 7.84 (1H, d, *J* 8.2, Ar**H**), 7.92 (1H, d, *J* 8.1, Ar**H**), 8.00 (1H, d, *J* 8.2, Ar**H**); δ_H (500 MHz, $CDCl_3$) 35.6 (OCH**C**H_2), 44.1 (N**C**H), 77.6 (O**C**H), 92.0 (=**C**H_2), 122.9 (Ar), 125.6 (Ar), 126.1 (Ar), 126.7 (Ar), 127.6 (Ar), 128.4 (Ar), 129.1 (Ar), 130.3 and 130.5 (H_2C=**C** and Ar), 131.7 (Ar), 134.0 (Ar), 162.5 (O=**C**); Accurate mass (ESI^+) - Not found; For X-Ray crystal data see appendix A.

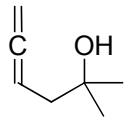
Ethyl penta-3,4-dienoate[73] (94)



The reaction of propargyl alcohol according to general procedure F and purification by reduced pressure distillation (60 °C, 18 mmHg, Lit.[73] 65 °C, 21 mmHg) afforded the title compound (6.94 g, 55%) as a colourless oil; δ_H (400 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.2, C**H$_3$**),

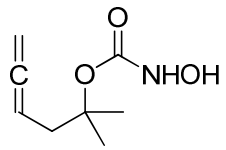
3.04 (2H, dt, *J* 7.4, 3.0, O=CC**H$_2$**), 4.16 (2H, q, *J* 7.2, OC**H$_2$**), 4.76 (2H, app. dt, *J* 6.8, 3.0, =C**H$_2$**), 5.27 (1H, tt, *J* 7.4, 6.8, =C**H**); δ_C (100 MHz, $CDCl_3$) 14.2 (**C**H$_3$), 34.2 (O=C**C**H$_2$), 60.8 (O**C**H$_2$), 75.8 (=**C**H$_2$), 83.5 (=**C**H), 171.4 (O=**C**), 209.3 (=**C**=).

2-Methylhexa-4,5-dien-2-ol[73] (95)



To a two-necked round bottom flask fitted with a reflux condenser and pressure equalising dropping funnel, was added methyl magnesium bromide (38.7 mL of a 3.0 M solution in ether, 116 mmol) and ether (12 mL) at 0 °C. Ester **94** (5.85 g, 46.4 mmol) was dissolved in anhydrous ether (15 mL) and added dropwise over 1 h. The reaction mixture was stirred at reflux for 2 h, cooled to 0 °C and quenched with sat. aq. NH_4Cl solution (100 mL). The resultant mixture was extracted with ether (3 × 20 mL). The solvent was removed by distillation at atmospheric pressure (38–40 °C) and the residue distilled at reduced pressure (62 °C, 25 mmHg, Lit.[73] 80 °C, 21 mmHg) to afford the title compound (3.64 g, 70%) as a colourless oil; R_f 0.21 (2:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 1.24 (6H, s, C**H$_3$**), 2.18 (2H, dt, *J* 7.9, 2.4, HOCC**H$_2$**), 4.69 (2H, dt, *J* 6.7, 2.4, =C**H$_2$**), 5.14 (1H, tt, *J* 7.9, 6.7, =C**H**); δ_C (100 MHz, $CDCl_3$) 28.9 (**C**H$_3$), 43.0 (HOC**C**H$_2$), 70.9 (HO**C**), 74.1 (=**C**H$_2$), 85.4 (=**C**H), 210.0 (=**C**=).

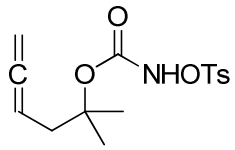
2-Methylhexa-4,5-dien-2-yl hydroxycarbamate[66] (96)



The reaction of alcohol **95** according to general procedure B and purification by column chromatography (2:1 petrol:ether) afforded the title compound (1.26 g, 41%) as a colourless oil; R_f 0.14 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3312br, 2980s, 2936s, 1957s, 1717s, 1473m 1386s, 1371s; δ_H (400 MHz, $CDCl_3$) 1.48 (6H, s, C**H$_3$**), 2.48–2.50 (2H, m,

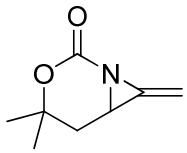
=CHC**H₂**), 4.66–4.69 (2H, m, =C**H₂**), 5.05 (1H, app. quin, *J* 7.7, =C**H**) 7.16 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 25.8 (**C**H_3), 40.1 (=CH**C**H_2), 74.2 (=**C**H_2), 83.6 (Me_2**C**), 84.8 (=**C**H), 158.6 (O=**C**), 210.1 (=**C**=); Accurate mass (ESI^+): Found 194.0791: $C_8H_{13}NNaO_3$ (MNa^+) requires 194.0788.

2-Methylhexa-4,5-dien-2-yl tosyloxycarbamate (97)



The reaction of hydroxycarbamate **96** according to general procedure C and purification by column chromatography (4:1 petrol:ether → 1:1 petrol:ether) afforded the title compound (1.32 g, 87%) as a viscous, colourless oil; R_f 0.19 (1:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 1.31 (6H, s, C**H₃**), 2.31 (2H, dt, *J* 7.8, 2.5 =CHC**H₂**), 4.67 (2H, dt, *J* 6.6, 2.5, =C**H₂**), 4.79–4.86 (1H, m, =C**H**), 7.37 (2H, d, *J* 8.2, Ar**H**) 7.73 (1H, br s, N**H**), 7.88 (2H, d, *J* 8.2, Ar**H**); δ_C (100 MHz, $CDCl_3$) 27.8 (Ar**C**H_3), 25.8 (**C**H_3), 39.7 (=CH**C**H_2), 74.4 (=**C**H_2), 84.4 (=**C**H), 85.4 (**C**Me_2), 129.6 (Ar), 129.7 (Ar), 130.4 (Ar), 146.0 (Ar), 153.9 (O=**C**), 210.1 (=**C**=); Accurate mass (ESI^+): Found 348.0874: $C_{15}H_{19}NNaO_5S$ (MNa^+) requires 348.0876.

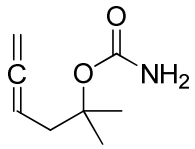
4,4-Dimethyl-7-methylene-3-oxa-1-azabicyclo[4.1.0]heptan-2-one (98)



The reaction of *N*-tosyloxycarbamate **97** according to general procedure D and purification by column chromatography (1:1 petrol:ethyl acetate) afforded the title compound (42 mg, 9%) as a yellow oil; R_f (1:1 petrol:ether) 0.17; v_{max}/cm^{-1} (thin film) 3288br, 2982s, 2936s, 1956s, 1722s, 1492m, 1348m, 1275s, 1215w; δ_H (500 MHz, $CDCl_3$) 1.43 (3H, s, C**H₃**), 1.47 (1H, dd, *J* 14.3, 9.1, OCCH**H′**), 1.62 (3H, s, C**H₃**), 2.23 (1H, dd, *J* 14.3, 6.5, OCC**H**H′), 3.38 (1H, dd, *J* 9.1, 6.5 NC**H**), 4.97 (1H, d, *J* 2.9, =CH**H′**), 5.15 (1H, d, *J* 2.9, =C**H**H′); δ_C (125

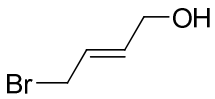
MHz, $CDCl_3$) 25.3 (**C**H_3), 29.3 (**C**H_3), 34.1 (OC**C**H_2), 37.5 (N**C**H), 84.8 (O**C**Me_2), 85.8 (=**C**H_2), 134.4 (H_2C=**C**), 155.5 (O=**C**) Accurate mass (FI^+): Found 153.0789: $C_8H_{11}NO_2$ (MH^+) requires 153.0790.

2-Methylhexa-4,5-dien-2-yl carbamate[66] (99)



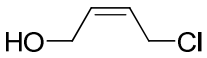
Formed as a by-product in the reaction of **97** according to general procedure D. Purification by column chromatography (1:1 petrol:ethyl acetate) afforded the title compound (61 mg, 13%) as a yellow oil; R_f (1:1 petrol:ether) 0.31; δ_H (400 MHz, $CDCl_3$) 1.45 (6H, s, C**H**$_3$), 2.48 (2H, dt, *J* 7.9, 2.5, =CHC**H**$_2$), 4.61 (2H, br s, N**H**$_2$), 4.67 (2H, dt, *J* 6.7, 2.5, =C**H**$_2$), 5.04–5.12 (1H, dt, *J* 7.9, 6.7, =C**H**); δ_C (100 MHz, $CDCl_3$) 25.9 (**C**H_3), 40.1 (=CH**C**H_2), 74.0 (=**C**H_2), 81.3 (**C**Me_2), 85.1 (=**C**H), 156.2 (O=**C**), 210.0 (=**C**=).

(*E*)-4-Bromobut-2-en-1-ol[170] (105)



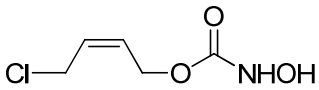
To a stirred solution of methyl 4-bromocrotonate (2.51 g, 14.0 mmol) in toluene (40 mL) was added dropwise DIBAL (35.0 mL of a 1.0 M solution in toluene, 35 mmol) at –78 °C. After 30 min 50% aq. acetic acid (10 mL) was added and the resulting mixture allowed to warm to r.t.. The insoluble material was removed by filtration through Celite® and the cake washed with ether (20 mL). The filtrate was washed with sat. aq. $NaHCO_3$, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (5:1 petrol:ether) afforded the title compound (1.21 g, 57%) as a colourless oil; R_f 0.22 (2:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 3.41 (1H, s, O**H**), 3.97 (2H, d, *J* 6.3, BrC**H**$_2$), 4.18 (2H, d, *J* 3.8, HOC**H**$_2$), 5.92–5.95 (2H, m, =C**H**); δ_C (100 MHz, $CDCl_3$) 32.0 (Br**C**H_2), 62.3, (HO**C**H_2), 127.4 (=**C**H), 133.9 (=**C**H).

(*Z*)-4-Chlorobut-2-en-1-ol[171] (107)



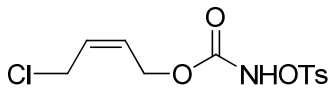
2-Butene-1,4-diol (3.00 g, 34.0 mmol) was dissolved in anhydrous diethyl ether in a two-necked round bottomed flask equipped with a reflux condenser and a pressure equalising addition funnel. Pyridine (2.99 ml, 37.3 mmol) was added and the reaction mixture cooled to 0 ºC before dropwise addition of thionyl chloride (2.73 ml, 37.3 mmol). The reaction mixture was allowed to warm to r.t. and stirred for 18 h, after which was poured on to ice water (20 mL) and extracted with ether (3 × 20 ml). The combined organic extracts were washed successively with sat. aq. $NaHCO_3$ solution (20 mL) and brine (15 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (2:1 petrol:ether) afforded the title compound (1.63 g, 45%) as a colourless oil; R_f 0.14 (2:1 petrol:ether); δ_H (200 MHz, $CDCl_3$) 4.13 (2H, d, *J* 6.8, ClC**H**$_2$), 4.30 (2H, d, *J* 5.1, HOC**H**$_2$), 5.76–5.84 (2H, m, **H**C=C**H**).

(*Z*)-4-Chlorobut-2-enyl hydroxycarbamate (108)



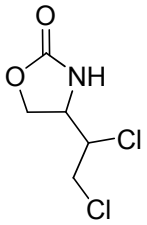
The reaction of alcohol **107** according to general procedure B and purification by column chromatography (1:1 petrol:ethyl acetate) afforded the title compound (942 mg, 40%) as a colourless oil; R_f 0.17 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3300br, 2962s, 1722s, 1471s, 4665s, 1263s, 1121s; δ_H (400 MHz, $CDCl_3$) 4.14 (2H, d, *J* 7.8, ClC**H**$_2$), 4.75 (2H, d, *J* 6.8, OC**H**$_2$), 5.70–5.77 (1H, m, OCH_2C**H**), 5.84–5.91 (1H, m, $ClCH_2$C**H**) 7.60 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 38.6 (Cl**C**H$_2$), 61.9 (O**C**H$_2$), 127.3 (OCH_2**C**H), 130.4 ($ClCH_2$**C**H), 159.0 (O=**C**); Accurate mass (ESI$^+$): Found 188.0085: $C_5H_8{}^{35}ClNNaO_3$ (MNa^+) requires 188.0085.

(*Z*)-4-Chlorobut-2-enyl tosyloxycarbamate (109)



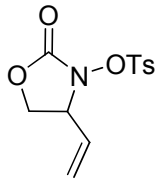
The reaction of hydroxycarbamate **108** according to general procedure C and purification by column chromatography (2:1 petrol:ether → 1:1 petrol:ether) afforded the title compound (1.10 g, 64%) as a white solid; R_f 0.21 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3541s, 3287s, 2960m, 1747s, 1597s, 1455s, 1384s, 1322s, 1296s; δ_H (400 MHz, $CDCl_3$) 2.47 (3H, s, ArC**H**$_3$), 4.04 (2H, d, *J* 7.8, ClC**H**$_2$), 4.61 (2H, d, *J* 7.0, OC**H**$_2$), 5.52 (1H, dt, *J* 10.9, 7.0, OCH_2C**H**), 5.83 (1H, dt, *J* 10.9, 7.8, $ClCH_2$C**H**) 7.37 (2H, d, *J* 8.2, Ar**H**), 7.87 (2H, d, *J* 8.2, Ar**H**), 8.07 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 21.8 (Ar**C**H$_3$), 38.4 (Cl**C**H$_2$), 61.5 (O**C**H), 126.4 (OCH_2**C**H), 129.6 (Ar), 129.9 (Ar), 130.1 (Ar), 130.7 ($ClCH_2$**C**H), 146.3 (Ar), 155.2 (O=**C**); Accurate mass (ESI^+): Found 342.0174: $C_{12}H_{14}{}^{35}ClNNaO_5S$ (MNa^+) requires 342.0173.

4-(1,2-Dichloroethyl)oxazolidin-2-one (110)



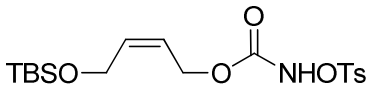
The reaction of *N*-tosyloxycarbamate **109** according to general procedure D and purification by column chromatography (3:1 petrol:ethyl acetate) afforded the title compound (17 mg, 15%) as a yellow oil; R_f (1:1 petrol:ether) 0.15; δ_H (500 MHz, $CDCl_3$) 3.76 (1H, dd, *J* 11.9, 8.7, ClCH**H′**), 3.82 (1H, dd, *J* 11.9, 5.2 ClC**H**H′), 4.07 (1H, ddd, *J* 8.7, 5.2, 4.2, ClC**H**), 4.37 (1H, dd, *J* 8.8, 4.2, OCH**H′**), 4.47 (1H, dt, *J* 8.8, 4.2, NC**H**), 4.58 (1H, app. t, *J* 8.8, OC**H**H′), 7.00 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 43.9 (Cl**C**H$_2$), 53.7 (N**C**H), 61.7 (Cl**C**H), 67.4 (O**C**H$_2$), 159.8 (O=**C**); *m/z* (GCMS, Cl^+) 203 (16%), 201 (MNH_4^+, 21), 184 (MH^+, 12), 133 (10), 131 (20), 116 (16), 114 (100); Accurate mass: Found 203.0166: $C_5H_{11}N_2O_2{}^{35}Cl^{37}Cl$ (MNH_4^+) requires 203.0168.

2-Oxo-4-vinyloxazolidin-3-yl 4-methylbenzenesulfonate (111)



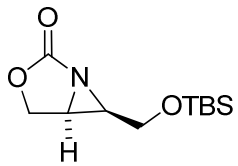
The reaction of *N*-tosyloxycarbamate **109** according to general procedure D and purification by column chromatography (3:1 petrol:ethyl acetate) afforded the title compound (3 mg, 2%) as a yellow oil; R_f (1:1 petrol:ether) 0.22; ν_{max}/cm^{-1} (thin film) 3197s, 3067s, 1762s, 1598m, 1435s, 1387s; δ_H (500 MHz, $CDCl_3$) 2.47 (3H, s, ArC**H**$_3$) 4.07 (1H, dd, *J* 8.4, 6.8, OCH**H′**), 4.39–4.48 (2H, m, OC**H**H′ overlays NC**H**), 5.41–5.47 (2H, m, =C**H**$_2$), 5.77–5.84 (1H, m, =C**H**), 7.37 (2H, d, *J* 8.2, Ar**H**), 7.90 (2H, d, *J* 8.2, Ar**H**); δ_C (125 MHz, $CDCl_3$) 21.9 (**C**H$_3$), 63.7 (N**C**H), 66.2 (O**C**H$_2$), 123.3 (=**C**H$_2$), 129.7 (Ar), 129.8 (Ar), 130.6 (Ar), 130.7 (=**C**H), 146.4 (Ar), 156.2 (O=**C**); Accurate mass (ESI^+): Found 306.0402: $C_{12}H_{13}NNaO_5S$ (MNa^+) requires 306.0407.

(Z)-4-(t*ert*-Butyldimethylsilyloxy)but-2-enyl tosyloxycarbamate[49] (112)



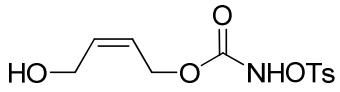
The reaction of hydroxycarbamate **367** according to general procedure C and purification by column chromatography (3:1 petrol:ether → 1:1 petrol:ether) afforded the title compound (2.11 g, 72%) as a white solid; R_f 0.24 (1:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 0.06 (6H, s, Si(C**H**$_3$)$_2$), 0.89 (9H, s, C(C**H**$_3$)$_3$), 2.47 (3H, s, ArC**H**$_3$), 4.20 (2H, d, *J* 5.8, SiOC**H**$_2$), 4.60 (2H, d, *J* 6.8, SOC**H**$_2$), 5.30–5.37 (1H, m, =C**H**), 5.66–5.73 (1H, m, =C**H′**), 7.36 (2H, d, *J* 8.2, Ar**H**), 7.88 (2H, d, *J* 8.2, Ar**H**), 7.95 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) –5.3 (Si(**C**H$_3$)$_2$), 18.2 (Si**C**Me$_3$), 21.8 (Ar**C**H$_3$), 25.9 (C(**C**H$_3$)$_3$), 59.5 (O**C**H$_2$), 62.8 (O**C**H$_2$), 122.8 (=**C**), 129.6 (Ar), 129.8 (Ar), 130.3 (Ar), 134.7 (=**C**), 146.2 (Ar), 155.3 (O=**C**).

6-((*tert*-Butyldimethylsilyloxy)methyl)-3-oxa-1-azabicyclo[3.1.0]hexan-2-one[49] (113)



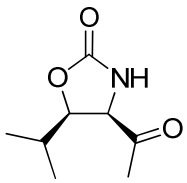
The reaction of *N*-tosyloxycarbamate **112** according to general procedure D and purification by column chromatography (3:1 petrol:ethyl acetate) afforded the title compound (170 mg, 29%) as a yellow oil; R_f (1:1 petrol:ether) 0.24; δ_H (400 MHz, $CDCl_3$) 0.14 (3H, s, SiC**H**$_3$), 0.15 (3H, s, SiC**H**$_3$), 0.96 (9H, s, C(C**H**$_3$)$_3$), 2.99 (1H, dt, *J* 7.0, 5.6, SiOCH$_2$C**H**), 3.32 (1H, ddd, *J* 6.1, 5.6, 2.2, COCH$_2$C**H**), 3.81 (1H, dd, *J* 11.9, 7.0, SiOC**H**H′), 4.06 (1H, dd, *J* 11.9, 5.6, SiOCH**H′**), 4.46 (1H, dd, *J* 9.9, 2.2, COC**H**H′), 4.61 (1H, dd, *J* 9.9, 6.1, COCH**H′**).

(*Z*)-4-Hydroxybut-2-enyl tosyloxycarbamate (114)



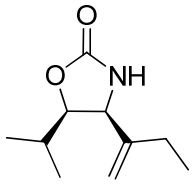
To a plastic beaker was added *N*-tosyloxycarbamate **112** (300 mg, 0.734 mmol) and acetonitrile (7 mL). The mixture was stirred at 0 °C and flurosilicic acid (0.106 mL of a 20% aq. solution, 0.147 mmol) was added. After 1 h the reaction was poured onto sat. aq. $NaHCO_3$ solution (5 mL) and extracted with ether (3 × 10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (50:1 ether:methanol) afforded the title compound (63 mg, 28%) as a white solid; R_f (1:1 petrol:ether) 0.28; ν_{max}/cm^{-1} (thin film) 3297br, 2932s, 1739s, 1597m, 1397s, 1242m; δ_H (500 MHz, MeOD) 2.49 (3H, s, ArC**H**$_3$), 4.13 (2H, d, *J* 5.8, HOC**H**$_2$), 4.59 (2H, d, *J* 6.8, COC**H**$_2$), 5.41–5.46 (1H, m, =C**H**), 5.73–5.78 (1H, m, =C**H′**), 7.47 (2H, d, *J* 8.1, Ar**H**), 7.85 (2H, d, *J* 8.1, Ar**H**); δ_C (125 MHz, MeOD) 21.7 (Ar**C**H$_3$), 58.6 (O**C**H$_2$), 62.9 (O**C**H$_2$), 125.3 (=**C**H), 129.8 (Ar), 130.7 (Ar), 132.2 (Ar), 135.3 (=**C**H), 147.5 (Ar), 158.0 (O=**C**); Accurate mass (ESI$^+$): Found 324.0510: $C_{12}H_{15}NNaO_6S$ (MNa$^+$) requires 324.0512.

4-Acetyl-5-isopropyloxazolidin-2-one (115)



To a stirred solution of MA **64** (20 mg, 0.13 mmol) in 1:1 acetone:water (2 mL) was added $NaHCO_3$ (78 mg, 0.93 mmol). The reaction mixture was cooled to 0 °C before addition of OXONE® (160 mg, 0.26 mmol). After 4 d the reaction mixture was poured onto water (2 mL), extracted with chloroform (3 × 5 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (1:1 petrol:ether) afforded to title compound (4 mg, 18%) as a yellow oil; R_f 0.22 (1:1 petrol:ether); δ_H (500 MHz, $CDCl_3$) 1.08 (3H, d, *J* 6.8, CHC**H**$_3$), 1.10 (3H, d, *J* 6.8, CHC**H**$_3$), 1.81 (1H, septd, *J* 6.8, 6.0, C**H**$(CH_3)_2$), 2.42 (3H, s, O=CC**H**$_3$), 4.48 (1H, dd, *J* 6.0, 5.2, OC**H**), 4.59 (1H, d, *J* 5.2, NC**H**); δ_C (125 MHz, $CDCl_3$) 16.5 (CH**C**H_3), 16.9 (CH**C**H_3), 26.5 (O=C**C**H_3), 32.1 (OCH**C**H), 80.8 (N**C**H), 83.1 (O**C**H), 153.5 (O**C**=O), 204.2 (CH_3**C**=O); Further characterisation not possible due to decomposition.

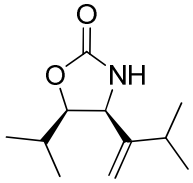
4-(But-1-en-2-yl)-5-isopropyloxazolidin-2-one (116)



To a pear shaped flask was added CuI (1 mg, 0.005 mmol) and THF (1 mL). The resulting suspension was stirred and cooled to −40 °C before addition of ethylmagnesium bromide (0.29 mL of a 1.0 M solution in THF, 0.29 mmol). After 10 min $BF_3.OEt_2$ (0.018 mL, 0.147 mmol) was added followed by a solution of MA **64** (15 mg, 0.098 mmol) in THF (0.5 mL) *via* canula. The mixture was allowed to warm slowly to 0 °C over 1 h and was quenched with sat. aq. NH_4Cl solution (1 mL). The mixture was warmed to r.t. and extracted with ether (3 × 5 mL). The combined organic extracts were washed with brine (5 mL), dried over $MgSO_4$

and concentrated *in vacuo*. Purification by column chromatography afforded the title compound (13 mg, 72%) as a yellow oil; R_f 0.25 (ether); ν_{max}/cm^{-1} (thin film) 3236br, 2964s, 1745s, 1480m, 1417s, 1216s; δ_H (500 MHz, $CDCl_3$) 0.90 (3H, d, *J* 6.6, CHC**H$_3$**), 1.07 (3H, d, *J* 6.6, CHC**H$_3$**), 1.10 (3H, t, *J* 7.3, =CCH$_2$C**H$_3$**), 1.81 (1H, dsept, *J* 9.2, 6.6, OCHC**H**), 2.02–2.18 (2H, m, =CC**H$_2$**), 4.24 (1H, dd, *J* 9.2, 7.0, OC**H**), 4.30 (1H, d, *J* 7.0, NC**H**), 5.08 (2H, d, *J* 7.2, =C**H$_2$**), 5.21 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 11.8 (=CCH$_2$**C**H$_3$), 19.1 (CH**C**H$_3$), 19.1 (CH**C**H$_3$), 24.1 (=C**C**H$_2$), 61.6 (N**C**H), 85.8 (O**C**H), 114.3 (=**C**H$_2$), 146.7 (H$_2$C=**C**), 159.6 (O=**C**); Accurate mass (ESI$^+$): Found 206.1151: $C_{10}H_{17}NNaO_2$ (MNa$^+$) requires 206.1151.

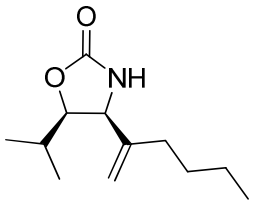
5-Isopropyl-4-(3-methylbut-1-en-2-yl)oxazolidin-2-one (117)



To a pear shaped flask was added CuI (3.1 mg, 0.016 mmol) and THF (1.5 mL). The resulting suspension was stirred and cooled to –40 °C before addition of *iso*-propylmagnesium chloride (0.49 mL of a 2.0 M solution in THF, 0.98 mmol). After 10 min $BF_3.OEt_2$ (0.03 mL, 0.24 mmol) was added followed by a solution of MA **64** (25 mg, 0.16 mmol) in THF (0.5 mL) *via* canula. The mixture was allowed to warm slowly to 0 °C over 1 h and was quenched with sat. aq. NH_4Cl solution (2 mL) before warming to r.t. and extracted with ether (3 × 10 mL). The combined organic extracts were washed with brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (2:1 → 1:1 petrol:ether) afforded the title compound (8 mg, 26%) as a colourless oil; R_f 0.20 (ether); ν_{max}/cm^{-1} (thin film) 3205br, 3124m, 2958s, 2871w, 1767s, 1736s, 1461m, 1405m, 1374s; δ_H (500 MHz, $CDCl_3$) 0.90 (3H, d, *J* 6.6, OCHCHC**H$_3$**), 1.06 (3H, d, *J* 6.6, OCHCHC**H$_3$**), 1.10 (3H, d, *J* 6.7, =CCHC**H$_3$**), 1.13 (3H, d, *J* 6.7, =CCHC**H$_3$**), 1.85 (1H, app. oct, *J* 6.6, OCHC**H**), 2.20–2.26 (1H, m, =CC**H**(CH$_3$)$_2$), 4.31–4.35 (2H, m, OC**H** overlays NC**H**), 4.98 (1H, br s, N**H**) 5.14 (1H, s, =C**H**H′), 5.17 (1H, s, =CH**H′**); δ_C (125

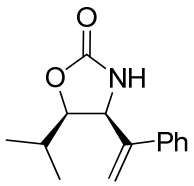
MHz, $CDCl_3$) 18.4 (OCHCH**C**H_3), 19.3 (OCHCH**C**H_3), 22.8 (=CCH**C**H_3), 23.4 (=CCH**C**H_3), 28.6 (OCH**C**H), 31.2 (=C**C**HMe_2), 60.5 (N**C**H), 85.6 (O**C**H), 112.6 (=**C**H_2) 151.9 (H_2C=**C**), 159.3 (O=**C**); Accurate mass (ESI^+): Found 220.1305: $C_{11}H_{19}NNaO_2$ (MNa^+) requires 220.1308.

4-(Hex-1-en-2-yl)-5-isopropyloxazolidin-2-one (118)



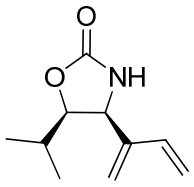
To a pear shaped flask was added CuI (2.7 mg, 0.014 mmol) and THF (1.5 mL). The resulting suspension was stirred and cooled to –40 °C before addition of butylmagnesium chloride (0.22 mL of a 2.0 M solution in THF, 0.430 mmol). After 10 min $BF_3.OEt_2$ (0.027 mL, 0.216 mmol) was added followed by a solution of MA **64** (22 mg, 0.144 mmol) in THF (0.5 mL) *via* canula. The mixture was allowed to warm slowly to 0 °C over 1 h and was then quenched with sat. aq. NH_4Cl solution (2 mL). The mixture was warmed to r.t., extracted with ether (3 × 10 mL) and the combined organic extracts washed with brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (1:1 petrol:ether → ether) afforded the title compound (7 mg, 23%) as a colourless oil; R_f 0.20 (ether); δ_H (500 MHz, $CDCl_3$) 0.90 (3H, d, *J* 6.5, CHC**H$_3$**), 0.93 (3H, t, *J* 7.3, CH_2C**H$_3$**), 1.07 (3H, d, *J* 6.5, CHC**H$_3$**), 1.36 (2H, app. sxt, *J* 7.6, =CCH_2CH_2C**H$_2$**), 1.45–1.51 (2H, m, =CCH_2C**H$_2$**), 1.84 (1H, dsept, *J* 8.8, 6.5, OCHC**H**), 1.99–2.12 (2H, m, =CC**H$_2$**), 4.23–4.29 (2H, m, OC**H** overlays NC**H**), 4.96 (1H, br s, N**H**), 5.07–5.09 (2H, m, =C**H$_2$**); δ_C (125 MHz, $CDCl_3$) 11.8 (=C$CH_2CH_2CH_2$**C**H_3), 19.1 (OCHCH**C**H_3), 19.1 (OCHCH**C**H_3), 22.5 (=CCH_2CH_2**C**H_2), 28.2 (OCH**C**H), 30.2 (=CCH_2**C**H_2), 31.2 (=C**C**H_2), 61.6 (N**C**H), 85.8 (O**C**H), 114.9 (=**C**H_2), 145.4 (H_2C=**C**), 159.4 (O=**C**); Accurate mass (ESI^+): Found 234.1469: $C_{12}H_{21}NNaO_2$ (MNa^+) requires 234.1465; For X-Ray crystal data see appendix B.

5-Isopropyl-4-(1-phenylvinyl)oxazolidin-2-one (119)



To a stirred solution of CuI (35 mg, 0.183 mmol) in ether (1 mL) at 0 °C was added PhLi (0.21 mL of a 1.8 M solution in dibutylether, 0.37 mmol) dropwise. After 90 min a solution of MA **64** (28 mg, 0.183 mmol) in ether (0.5 mL) was added *via* canula and stirring continued for a further 30 min. The reaction was quenched with sat. aq. NH_4Cl solution (5 mL), allowed to warm to r.t. and extracted with ether (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (1:1 petrol:ether) afforded the title compound (19 mg, 45%) as a yellow oil; R_f 0.27 (ether); ν_{max}/cm^{-1} (thin film) 3277br, 2941s, 1751s, 1461m, 1389s; δ_H (500 MHz, $CDCl_3$) 0.60 (3H, d, *J* 6.6, C**H**$_3$), 1.00 (3H, d, *J* 6.6, C**H**$_3$) 1.81 (1H, dsept, *J* 7.5, 6.6, OCHC**H**), 4.41 (1H, app. t, *J* 7.5, OC**H**), 4.95 (1H, d, *J* 7.5, NC**H**), 5.44 (1H, d, *J* 1.3, =C**H**$_2$), 5.60 (1H, s, =C**H**$_2$), 5.81 (1H, br s, N**H**) 7.32–7.37 (5H, m, Ar**H**); δ_C (125 MHz, $CDCl_3$) 17.9 (**C**H$_3$), 19.5 (**C**H$_3$), 28.5 (OCH**C**H), 58.4 (N**C**H), 85.6 (O**C**H), 116.7 (=**C**H$_2$), 126.2 (Ar), 128.3 (Ar), 128.9 (Ar), 139.6 (Ar), 144.5 (H_2C=**C**), 159.8 (O=**C**); Accurate mass (ESI^+): Found 254.1156: $C_{14}H_{17}NNaO_2$ (MNa^+) requires 254.1151.

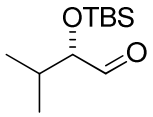
4-(Buta-1,3-dien-2-yl)-5-isopropyloxazolidin-2-one (120)



To a pear shaped flask was added CuI (6.0 mg, 0.030 mmol) and THF (2 mL). The resulting suspension was stirred and cooled to –30 °C before addition of vinylmagnesium bromide (1.18 mL of a 1.0 M solution in THF, 1.18 mmol). After 10 min a solution of MA **64** (90 mg, 0.59 mmol) in THF (1 mL) was added *via* canula. The mixture was allowed to warm

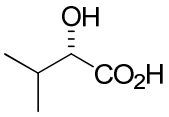
slowly to 0 °C over 1 h and was then quenched with sat. aq. NH_4Cl solution (3 mL) and stirring continued for 30 min. The mixture was warmed to r.t. and extracted with ether (3 × 20 mL). The combined organic extracts were washed with brine (15 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (1:1 petrol:ether → ether) afforded the title compound (33 mg, 31%) as a crystalline solid; R_f 0.18 (ether); m.p. 78–81 °C; ν_{max}/cm^{-1} (thin film) 3266br, 2362m, 1745s, 1403m, 1249s; δ_H (500 MHz, $CDCl_3$) 0.90 (3H, d, *J* 6.8, C**H**$_3$), 1.01 (3H, d, *J* 6.8, C**H**$_3$) 1.90 (1H, app. oct, *J* 6.8, OCHC**H**), 4.45 (1H, dd, *J* 8.0, 6.8, OC**H**), 4.65 (1H, d, *J* 8.0, NC**H**), 5.13 (1H, br s, N**H**), 5.19 (1H, d, *J* 11.3, HC=C**H**H′), 5.29 (1H, s, NCHC=C**H**H′), 5.31 (1H, d, *J* 17.5, HC=CH**H′**), 5.43 (1H, s, NCHC=CH**H′**), 6.38 (1H, dd, *J* 17.5, 11.3, H_2C=C**H**); δ_C (125 MHz, $CDCl_3$) 17.8 (**C**H_3), 19.8 (**C**H_3), 28.4 (OCH**C**H), 57.1 (N**C**H), 84.8 (O**C**H), 115.5 (HC=**C**H_2), 117.9 (NCHC=**C**H_2), 135.9 (H_2C=**C**H), 141.9 (NCH**C**=CH_2), 159.3 (O=**C**); Accurate mass (ESI$^+$): Found 204.0997: $C_{10}H_{15}NNaO_2$ (MNa^+) requires 204.0995.

(*S*)-2-(*tert*-Butyldimethylsilyloxy)-3-methylbutanal[83] (127)



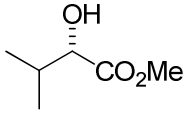
Synthesised according to a literature procedure.

(*S*)-2-Hydroxy-3-methylbutanoic acid[84] (129)



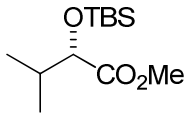
Synthesised according to a literature procedure.

(*S*)-Methyl 2-hydroxy-3-methylbutanoate[85] (130)



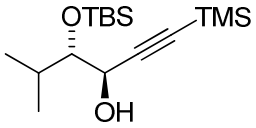
Synthesised according to a literature procedure.

(*S*)-Methyl 2-(*tert*-butyldimethylsilyloxy)-3-methylbutanoate[83] (131)



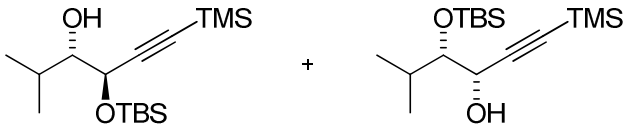
Synthesised according to a literature procedure.

(3*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-5-methyl-1-(trimethylsilyl)hex-1-yn-3-ol (133)



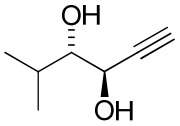
n-Butyllithium (3.74 mL of a 1.6 M solution in hexanes, 5.99 mmol) was added dropwise to a stirred solution of trimethylsilylacetylene (0.84 mL, 6.0 mL) in THF (10 mL) at –78 °C. After 1 h, the solution was warmed to 0 °C before recooling to –78 °C and a solution of aldehyde **127** (1.18 g, 5.45 mmol) in THF (5 mL) added *via* canula. After stirring for 1 h, the solution was warmed to r.t. and quenched with sat. aq. NH_4Cl solution (10 mL). The mixture was extracted with ether (3 × 50 mL) and the combined organic extracts washed with brine (30 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (50:1 petrol:ether) afforded the title compound (930 mg, 54%) as a colourless oil; R_f 0.10 (50:1 petrol:ether); $[\alpha]_D^{25}$ –16.9 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} (thin film) 3444br, 2959s, 2858s, 2172m, 1472s, 1387m; δ_H (400 MHz, $CDCl_3$) 0.11 (3H, s, Si(C**H**$_3$)), 0.13 (3H, s, Si(C**H**$_3$)), 0.17 (9H, s, Si(C**H**$_3$)$_3$), 0.94 (9H, s, SiC(C**H**$_3$)$_3$), 0.96 (6H, d, *J* 6.4, CH(C**H**$_3$)$_2$), 1.99 (1H, dsept, *J* 6.4, 5.4, C**H**(CH$_3$)$_2$), 2.14 (1H, d, *J* 6.0, O**H**), 3.51 (1H, dd, *J* 5.4, 4.0, SiOC**H**), 4.35 (1H, dd, *J* 6.0, 4.0, HOC**H**); δ_C (100 MHz, $CDCl_3$) –4.2 (Si**C**H$_3$), –4.1 (Si**C**H$_3$), –0.2 (Si(**C**H$_3$)$_3$), 18.2 (CH**C**H$_3$), 18.3 (Si**C**(CH$_3$)$_3$), 19.8 (CH**C**H$_3$), 26.0 (SiC(**C**H$_3$)$_3$), 30.9 (**C**H(CH$_3$)$_2$), 65.9 (HO**C**H), 79.5 (SiO**C**H), 91.3 (≡**C**), 104.4 (≡**C**); Accurate mass (ESI$^+$): Found 337.1982: $C_{16}H_{34}NaO_2Si_2$ (MNa$^+$) requires 337.1990.

(3*S*,4*R*)-4-(*tert*-Butyldimethylsilyloxy)-2-methyl-6-(trimethylsilyl)hex-5-yn-3-ol (134) and (3*S*,4*S*)-4-(*tert*-butyldimethylsilyloxy)-5-methyl-1-(trimethylsilyl)hex-1-yn-3-ol (135)



Formed as side products in the reaction of aldehyde **127** to alcohol **133**. Purification by column chromatography (50:1 petrol:ether) afforded the title compound **134** (201 mg, 12%) with trace amounts of title compound **135** as a colourless oil; R_f 0.14 (50:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3473br, 2959s, 2172s, 1471s, 1389m, 1362m; δ_H (500 MHz, $CDCl_3$) (**134** only) 0.14 (3H, s, Si(C**H**$_3$)), 0.17 (9H, s, Si(C**H**$_3$)$_3$), 0.17 (3H, s, Si(C**H**$_3$)), 0.91 (9H, s, SiC(C**H**$_3$)$_3$), 0.96 (3H, d, *J* 6.8, CHC**H**$_3$), 0.99 (3H, d, *J* 6.8, CHC**H**$_3$), 1.93 (1H, app. oct, *J* 6.8, C**H**(CH$_3$)$_2$), 2.40 (1H, d, *J* 3.1, O**H**), 3.28 (1H, ddd, *J* 6.8, 5.1, 3.1, HOC**H**), 4.38 (1H, d, *J* 5.1, SiOC**H**); δ_C (125 MHz, $CDCl_3$) (**134** only) –5.1 (Si**C**H$_3$), –4.4 (Si**C**H$_3$), –0.2 (Si(**C**H$_3$)$_3$), 17.6 (CH**C**H$_3$), 18.2 (Si**C**(CH$_3$)$_3$), 19.1 (CH**C**H$_3$), 25.8 (SiC(**C**H$_3$)$_3$), 29.6 (**C**H(CH$_3$)$_2$), 65.9 (SiO**C**H), 78.8 (HO**C**H), 91.2 (≡**C**), 104.0 (≡**C**); Accurate mass (ESI$^+$): Found 337.1982: $C_{16}H_{34}NaO_2Si_2$ (MNa$^+$) requires 337.1990.

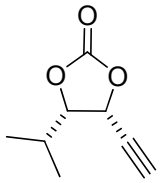
(3*R*,4*S*)-5-Methylhex-1-yne-3,4-diol (136)



To a stirred solution of alcohol **133** (212 mg, 0.67 mmol) in THF (2 mL) was added TBAF (1.41 mL of a 1.0 M solution in THF, 1.41 mmol). After 30 min the reaction was quenched with water (3 mL) and extracted with ether (3 × 10 mL). The combined organic extracts washed were with brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (1:1 petrol:ether) afforded the title compound (87 mg, quant.) as a colourless oil; R_f 0.21 (1:1 petrol:ether); $[\alpha]_D^{25}$ –9.4 (*c* 0.5 in $CHCl_3$); ν_{max}/cm^{-1} (thin film) 3326br, 3293br, 2962s, 2875m, 2120m, 1634w, 1472s, 1386s; δ_H (400 MHz, $CDCl_3$) 0.92

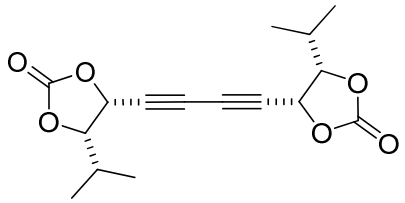
(3H, d, *J* 6.8 CHC**H**$_3$), 1.06 (3H, d, *J* 6.8, CHC**H**$_3$), 1.84 (1H, dsept, *J* 8.6, 6.8, C**H**$(CH_3)_2$), 2.18 (1H, br s, O**H**), 2.49 (1H, d, *J* 2.1, ≡C**H**), 3.00 (1H, br s, O**H**), 3.33 (1H, dd, *J* 8.6, 3.5, $(CH_3)_2$CHC**H**OH), 4.46 (1H, dd, *J* 3.5, 2.1, ≡CC**H**OH); δ_C (100 MHz, $CDCl_3$) 18.6 (CH**C**H$_3$), 18.9 (CH**C**H$_3$), 31.2 (**C**H$(CH_3)_2$), 64.5 (≡C**C**HOH), 74.7 (≡**C**H), 79.3 $(CH_3)_2$CH**C**HOH), 81.3 (≡**C**); *m/z* (GCMS, Cl^+) 149 (100%), 131 (22), 129 (10, MH^+), 128 (10), 87 (33); Accurate mass: Found 129.0911: $C_7H_{13}O_2$ (MH^+) requires 129.0916.

(4*R*,5*S*)-4-Ethynyl-5-isopropyl-1,3-dioxolan-2-one (137)



To a stirred solution of triphosgene (90 mg, 0.30 mmol) and pyridine (0.5 mL) in DCM (2 mL) was added diol **136** (41 mg, 0.32 mmol) at 0 °C. After 1.5 h the reaction was quenched with quenched with sat. aq. NH_4Cl solution (2 mL). The mixture was extracted with DCM (3 × 5 mL) and the combined organic extracts washed successively with sat. aq. $NaHCO_3$ solution (5 mL) and brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound (40 mg, 87%) as a colourless oil without the need for further purification; R_f 0.21 (4:1 petrol:ether); $[\alpha]_D^{25}$ +14.8 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} (thin film) 2969s, 2128m, 1802s, 1471m, 1397m, 1349s; δ_H (400 MHz, $CDCl_3$) 1.00 (3H, d, *J* 6.6 CHC**H**$_3$), 1.15 (3H, d, *J* 6.6, CHC**H**$_3$), 2.28 (1H, dsept, *J* 9.0, 6.6, C**H**$(CH_3)_2$), 2.78 (1H, d, *J* 2.1, ≡C**H**), 4.29 (1H, dd, *J* 9.0, 7.2, $(CH_3)_2$CHC**H**OC), 5.29 (1H, dd, *J* 7.2, 2.1, ≡CC**H**OC); δ_C (100 MHz, $CDCl_3$) 17.8 (CH**C**H$_3$), 18.6 (CH**C**H$_3$), 29.5 (**C**H$(CH_3)_2$), 69.6 (≡C**C**HOC), 74.6 (≡**C**), 79.7 (≡**C**H), 83.8 ($(CH_3)_2$CH**C**HOC), 153.6 (O=**C**); Accurate mass (ESI^+): Found 177.0523: $C_8H_{10}NaO_3$ (MNa^+) requires 177.0522.

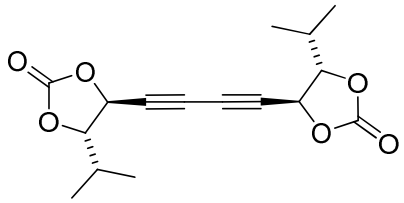
(4*S*,4′*S*,5*R*,5′*R*)-5,5′-(Buta-1,3-diyne-1,4-diyl)bis(4-isopropyl-1,3-dioxolan-2-one) (138)



To a mixture of alcohols **134** and **135** (206 mg, 0.65 mmol) in THF (5 mL) was added TBAF (1.37 mL of a 1.0 M solution in THF, 1.37 mmol) and the reaction stirred at r.t. for 1 h. The reaction was quenched with water (2 mL) and extracted with ether (3 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to afford a mixture of inseparable products.

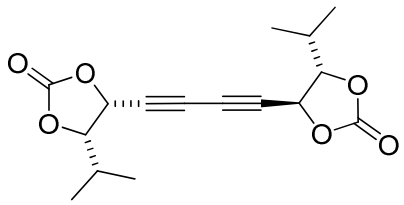
To a stirred solution of triphosgene (52 mg, 0.18 mmol) and pyridine (0.2 mL) in DCM (1 mL) was added the crude material (24 mg) in DCM (5 mL) at 0 °C. After 1.5 h the reaction was quenched with quenched with sat. aq. NH_4Cl solution (1 mL). The mixture was extracted with DCM (3 × 5 mL) and the combined organic extracts washed successively with sat. aq. $NaHCO_3$ solution (5 mL) and brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (2:1 → 1:1 petrol:ether) afforded the title compound (2 mg, trace) as a colourless oil; R_f 0.27 (1:1 petrol:ether); δ_H (500 MHz, $CDCl_3$) 1.02 (3H, d, *J* 6.6 CHC**H**$_3$), 1.17 (3H, d, *J* 6.6, CHC**H**$_3$), 2.24 (1H, dsept, *J* 9.2, 6.6, C**H**$(CH_3)_2$), 4.32 (1H, dd, *J* 9.2, 7.2, $(CH_3)_2$CHC**H**OC), 5.37 (1H, d, *J* 7.2, ≡CC**H**OC); δ_C (125 MHz, $CDCl_3$) 17.8 (CH**C**H$_3$), 18.7 (CH**C**H$_3$), 29.7 (**C**H$(CH_3)_2$), 69.8 (≡C**C**HOC), 72.3 (≡**C**), 73.6 (≡**C**), 83.9 ($(CH_3)_2$CH**C**HOC), 153.1 (O=**C**); Accurate mass (ESI^+): Found 329.0989: $C_{16}H_{18}NaO_6$ (MNa^+) requires 329.0996.

(4*S*,4′*S*,5*S*,5′*S*)-5,5′-(Buta-1,3-diyne-1,4-diyl)bis(4-isopropyl-1,3-dioxolan-2-one) (139)



Formed in the reaction of **134** and **135**. Purification by column chromatography (2:1 petrol:ether) afforded the title compound (3 mg, trace) as a colourless oil; R_f 0.16 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 2969s, 2140m, 1805s, 1469s, 1365s; δ_H (500 MHz, $CDCl_3$) 1.04 (3H, d, *J* 6.7 CHC**H**$_3$), 1.07 (3H, d, *J* 6.7, CHC**H**$_3$), 2.24 (1H, app. oct, *J* 6.7, C**H**$(CH_3)_2$), 4.36 (1H, app. t, *J* 6.7, $(CH_3)_2$CHC**H**OC), 4.99 (1H, d, *J* 6.6, ≡CC**H**OC); δ_C (125 MHz, $CDCl_3$) 16.8 (CH**C**H_3), 17.3 (CH**C**H_3), 31.7 (**C**H$(CH_3)_2$), 68.7 (≡C**C**HOC), 72.2 (≡**C**), 74.7 (≡**C**), 86.3 ($(CH_3)_2$CH**C**HOC), 152.8 (O=**C**); Accurate mass (ESI^+): Found 329.0991: $C_{16}H_{18}NaO_6$ (MNa^+) requires 329.0996.

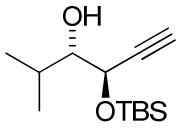
(4*S*,4′*S*,5*R*,5′*S*)-5,5′-(Buta-1,3-diyne-1,4-diyl)bis(4-isopropyl-1,3-dioxolan-2-one) (140)



Formed in the reaction of **134** and **135**. Purification by column chromatography (2:1 petrol:ether) afforded the title compound (2 mg, trace) as a colourless oil; R_f 0.22 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 2969s, 2143m, 1803s, 1469s, 1348s; δ_H (500 MHz, $CDCl_3$) 1.02 (3H, d, *J* 6.6 CHC**H**$_3$), 1.04 (3H, d, *J* 6.8 CHC**H**$_3$), 1.08 (3H, d, *J* 6.8, CHC**H**$_3$), 1.16 (3H, d, *J* 6.6, CHC**H**$_3$), 2.00 (1H, app. oct *J* 6.8, C**H**$(CH_3)_2$), 2.22 (1H, dsept, *J* 9.1, 6.6, C**H**$(CH_3)_2$), 4.32 (1H, dd, *J* 9.1, 7.2, $(CH_3)_2$CHC**H**OC), 4.37 (1H, app. t, *J* 6.8, $(CH_3)_2$CHC**H**OC), 4.99 (1H, d, *J* 6.8, ≡CC**H**OC), 5.37 (1H, d, *J* 7.2, ≡CC**H**OC); δ_C (125 MHz, $CDCl_3$) 16.8 (CH**C**H_3), 17.3 (CH**C**H_3), 17.8 (CH**C**H_3), 18.6 (CH**C**H_3), 29.8 (**C**H$(CH_3)_2$), 31.7 (**C**H$(CH_3)_2$), 68.8 (≡C**C**HOC), 69.8 (≡C**C**HOC), 72.3 (≡**C**), 72.6 (≡**C**), 73.5 (≡**C**), 74.4

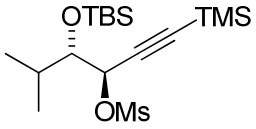
(≡**C**), 83.9 ((CH$_3$)$_2$CH**C**HOC), 86.2 ((CH$_3$)$_2$CH**C**HOC), 152.8 (O=**C**) 153.1 (O=**C**); Accurate mass (ESI$^+$): Found 329.0984: $C_{16}H_{18}NaO_6$ (MNa$^+$) requires 329.0996.

(3*S*,4*R*)-4-(*tert*-Butyldimethylsilyloxy)-2-methylhex-5-yn-3-ol (141)



To a solution of alcohol **133** (135 mg, 0.43 mmol) in MeOH (5 mL) was added K_2CO_3 (178 mg, 1.28 mmol). After 2 h the reaction was quenched with 0.1 M aq. HCl solution (10 mL) and extracted with ether (3 × 30 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (10:1 petrol:ether) afforded the title compound (68 mg, 49%) as a colourless oil; R_f 0.23 (10:1 petrol:ether); $[\alpha]_D^{25}$ –30.3 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} (thin film) 3311br, 2957s, 2930s, 2886m, 2858s, 2115m, 1472s; δ_H (400 MHz, $CDCl_3$) 0.15 (3H, s, Si(C**H$_3$**)), 0.18 (3H, s, Si(C**H$_3$**)), 0.92–0.94 (12H, s, SiC(C**H$_3$**)$_3$ overlays CHC**H$_3$**), 1.03 (3H, d, *J* 6.8, CHC**H$_3$**), 1.93 (1H, app. oct, *J* 6.8, C**H**(CH$_3$)$_2$), 2.43 (1H, d, *J* 2.2, ≡C**H**), 2.51 (1H, d, *J* 2.7, O**H**), 3.28 (1H, ddd, *J* 6.8, 4.4, 2.7, HOC**H**), 4.42 (1H, dd, *J* 4.4, 2.2, SiOC**H**); δ_C (100 MHz, $CDCl_3$) –4.8 (Si**C**H$_3$), –4.1 (Si**C**H$_3$), 18.6 (CH**C**H$_3$), 18.7 (Si**C**(CH$_3$)$_3$), 19.2 (CH**C**H$_3$), 26.1 (SiC(**C**H$_3$)$_3$), 30.1 (**C**H(CH$_3$)$_2$), 65.6 (SiO**C**H), 74.5 (≡**C**H), 79.6 (HO**C**H), 82.3 (≡**C**); Accurate mass (ESI$^+$): Found 265.1593: $C_{13}H_{26}NaO_2Si$ (MNa$^+$) requires 265.1594.

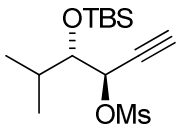
(3*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-5-methyl-1-(trimethylsilyl)hex-1-yn-3-yl methanesulfonate (143)



To a stirred solution of alcohol **133** (208 mg, 0.66 mmol) and triethylamine (0.10 mL, 0.72 mmol) in DCM (8 mL) was added methanesulfonyl chloride (0.06 mL, 0.72 mmol) at 0 °C. After 1 h the reaction was quenched with sat. aq. NH_4Cl solution (5 mL) and extracted with

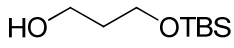
DCM (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the crude material which was taken on without purification.

(3*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-5-methylhex-1-yn-3-yl methanesulfonate (144)



To a solution of alcohol **143** (259 mg, 0.66 mmol) in MeOH (8 mL) was added K_2CO_3 (297 mg, 2.14 mmol). After 2 h the reaction was quenched with 0.1 M aq. HCl solution (10 mL) and extracted with ether (3 × 30 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (10:1 petrol:ether) afforded the title compound (157 mg, 74% over 2 steps) as a colourless oil; R_f 0.19 (10:1 petrol:ether); $[\alpha]_D^{25}$ –41.6 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} (thin film) 3277w, 2959s, 2931s, 2858s, 2125m, 1738m, 1473s, 1364s; δ_H (500 MHz, $CDCl_3$) 0.10 (3H, s, SiC**H**$_3$), 0.15 (3H, s, SiC**H**$_3$), 0.94 (9H, s, SiC(C**H**$_3$)$_3$), 0.97 (3H, d, *J* 6.8, CHC**H**$_3$), 1.00 (3H, d, *J* 6.8, CHC**H**$_3$), 1.99 (1H, app. oct, *J* 6.8, C**H**$(CH_3)_2$), 2.69 (1H, d, *J* 1.6, ≡C**H**), 3.14 (3H, s, SC**H**$_3$), 3.66 (1H, dd, *J* 6.8, 2.6, SiOC**H**), 5.20 (1H, dd, *J* 2.6, 1.6, SOC**H**); δ_C (125 MHz, $CDCl_3$) –4.3 (Si**C**H_3), –4.0 (Si**C**H_3), 18.3 (Si**C**$(CH_3)_3$), 18.4 (CH**C**H_3), 19.4 (CH**C**H_3), 26.0 (SiC(**C**$H_3)_3$), 31.6 (**C**$H(CH_3)_2$), 39.5 (S**C**H_3), 73.9 (SO**C**H), 77.5 (≡**C**), 78.3 (≡**C**), 78.9 (SiO**C**H); Accurate mass (ESI^+): Found 343.1371: $C_{14}H_{28}NaO_4SSi$ (MNa^+) requires 343.1370.

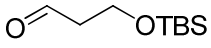
3-(*tert*-Butyldimethylsilyloxy)propan-1-ol[172] (145)



To a stirred suspension of NaH (1.09 g of a 60% suspension in mineral oil, 27.3 mmol) in THF (60 mL) was added 1,3-propandiol (2.0 mL, 27.7 mmol). After 45 min *tert*-butylchlorodimethylsilane (4.11 g, 27.3 mmol) was added and stirring continued for 1 h.

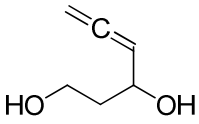
The mixture was diluted with ether (200 mL), washed sequentially with 10% aq. K_2CO_3 (2 × 100 mL) and brine (2 × 100 mL) and dried over Na_2SO_4. Concentration *in vacuo* afforded the title compound (4.31 g, 82%) as a colourless oil without the need for further purification; δ_H (400 MHz, $CDCl_3$) 0.03 (6H, s, Si(C**H$_3$**)$_2$), 0.85 (9H, s, C(C**H$_3$**)$_3$), 1.72 (2H, app. quin. *J* 5.7, OCH$_2$C**H$_2$**), 3.71–3.74 (2H, m, SiOC**H$_2$**), 3.77 (2H, d, *J* 5.7, HOC**H$_2$**); δ_C (100 MHz, $CDCl_3$) –5.6 (Si(**C**H$_3$)$_2$), 18.1 (Si**C**Me$_3$), 25.7 (C(**C**H$_3$)$_3$), 34.3 (OCH$_2$**C**H$_2$), 61.7 (SiO**C**H$_2$), 62.4 (HO**C**H$_2$).

3-(*tert*-Butyldimethylsilyloxy)propanal[173] (146)



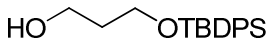
The reaction of alcohol **145** according to general procedure A and purification by column chromatography (10:1 petrol:ether) afforded the title compound (115 mg, 97%) as a colourless oil; δ_H (400 MHz, $CDCl_3$) 0.07 (6H, s, Si(C**H$_3$**)$_2$), 0.88 (9H, s, C(C**H$_3$**)$_3$), 2.60 (2H, dt, *J* 6.1, 1.9, O=CHC**H$_2$**), 3.99 (2H, t, *J* 6.1, SiOC**H$_2$**), 9.80 (1H, t, *J* 1.9, O=C**H**); δ_C (100 MHz, $CDCl_3$) –5.5 (Si(**C**H$_3$)$_2$), 18.2 (Si**C**Me$_3$), 25.8 (C(**C**H$_3$)$_3$), 46.5 (O=CH**C**H$_2$), 57.4 (SiO**C**H$_2$), 202.1 (O=**C**H).

Hexa-4,5-diene-1,3-diol (147)



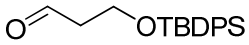
The reaction of aldehyde **146** according to general procedure E and purification by column chromatography (ethyl acetate) afforded the title compound (30 mg, 25%) as a colourless oil; δ_H (500 MHz, $CDCl_3$) 1.66 (1H, br s, O**H**), 1.79–1.91 (2H, m, HOCH$_2$C**H$_2$**), 2.31 (1H, br s, O**H**), 3.83–3.91 (2H, m, HOC**H$_2$**), 4.44–4.45 (1H, m, HOC**H**), 4.90 (2H, dt, *J* 6.8, 2.5, =C**H$_2$**), 5.31 (1H, app. q, *J* 6.8, =C**H**); δ_C (125 MHz, $CDCl_3$) 38.6 (HOCH$_2$**C**H$_2$), 61.1 (HO**C**H$_2$), 69.3 (HO**C**H), 78.0 (=**C**H$_2$), 94.6 (=**C**H), 206.8 (=**C**=).

3-(*tert*-Butyldiphenylsilyloxy)propan-1-ol[174] (148)



To a stirred suspension of NaH (221 mg of a 60% suspension in mineral oil, 5.53 mmol) in THF (10 mL) was added 1,3-propandiol (0.40 mL, 5.53 mmol). After 30 min *tert*-butylchlorodimethylsilane (1.44 mL, 5.53 mmol) was added and stirring continued for 16 h. The mixture was diluted with ethyl acetate (100 mL), washed sequentially with water (3 × 50 mL) and brine (50 mL), dried over Na_2SO_4 and concentration *in vacuo*. Purification by column chromatography (2:1 petrol:ether) afforded the title compound (1.67 g, 96%) as a colourless oil; R_f 0.15 (2:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, C(C**H$_3$**)$_3$), 1.83 (2H, app. quin, *J* 5.7, HOCH$_2$C**H$_2$**), 2.44 (1H, t, *J* 5.7, O**H**), 3.84–3.88 (4H, m, HOC**H$_2$** overlays SiOC**H$_2$**), 7.39–7.48 (6H, m, Ph**H**), 7.70 (4H, dd, *J* 7.8, 1.4, Ph**H**).

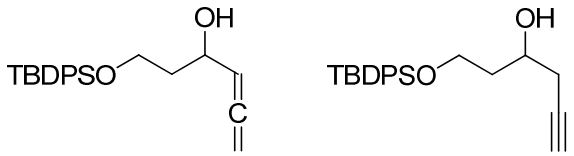
3-(*tert*-Butyldiphenylsilyloxy)propanal[175] (149)



The reaction of alcohol **148** according to general procedure A and purification by column chromatography (4:1 petrol:ether) afforded the title compound (109 mg, 97%) as a colourless oil; R_f 0.40 (10:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 1.06 (9H, s, C(C**H$_3$**)$_3$), 2.63 (2H, dt, *J* 6.0, 2.3, O=CHC**H$_2$**), 4.04 (2H, t, *J* 6.0, SiOC**H$_2$**), 7.39–7.48 (6H, m, Ph**H**), 7.68 (4H, dd, *J* 7.8, 1.5, Ph**H**) 9.84 (1H, t, *J* 2.3, O=C**H**); δ_C (100 MHz, $CDCl_3$) 19.1 (Si**C**Me$_3$), 26.7 (C(**C**H$_3$)$_3$), 46.4 (O=CH**C**H$_2$), 58.3 (SiO**C**H$_2$), 127.8 (Ar), 129.8 (Ar), 133.2 (Ar), 135.5 (Ar), 201.9 (O=**C**H).

1-(*tert*-Butyldiphenylsilyloxy)hexa-4,5-dien-3-ol (150) and

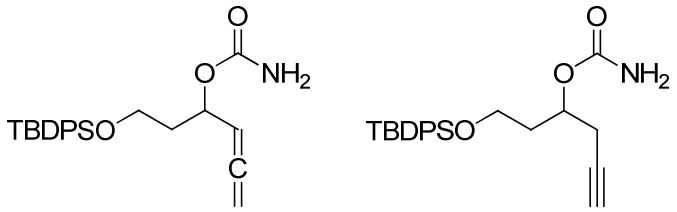
1-(*tert*-Butyldiphenylsilyloxy)hex-5-yn-3-ol (151)



The reaction of aldehyde **149** according to general procedure E and purification by column chromatography (4:1 petrol:ether) afforded the title compounds (116 mg, 69%) as a 2:1 inseparable mixture as a yellow oil; R_f 0.16 (5:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, C(C**H**$_3$)$_3$, allenyl and alkynyl), 1.81–1.88 (2H, m, HOCH$_2$C**H**$_2$, allenyl and alkynyl), 2.04 (1H, t, *J* 2.6, ≡C**H**, alkynyl) 2.44 (2H, app. dt, *J* 6.4, 2.6, ≡CC**H**$_2$, alkynyl), 3.17 (1H, d, *J* 3.5, O**H**, allenyl), 3.45 (1H, d, *J* 3.0, O**H**, alkynyl), 3.82–3.96 (2H, m, SiOC**H**$_2$, allenyl and alyknyl), 4.07–4.13 (1H, m, HOC**H**, alkynyl), 4.50–4.56 (1H, m, HOC**H**, allenyl), 4.87 (2H, app. dt, *J* 6.6, 2.0, =C**H**$_2$, allenyl), 5.30 (1H, app. q, *J* 6.6, =C**H**, allenyl) 7.39–7.48 (6H, m, Ph**H**, allenyl and alkynyl), 7.68–7.71 (4H, m, Ph**H** allenyl and alkynyl); δ_C (100 MHz, $CDCl_3$) allenyl only, 19.1 (Si**C**Me$_3$), 26.8 (C(**C**H$_3$)$_3$), 38.6 (HOCH$_2$**C**H$_2$), 62.5 (SiO**C**H$_2$), 68.9 (HO**C**H), 81.0 (=**C**H$_2$), 94.5 (=**C**H), 127.8 (Ar), 129.9 (Ar), 132.9 (Ar), 135.6 (Ar), 207.1 (=**C**=); Accurate mass (ESI$^+$): Found 375.1748: $C_{22}H_{28}NaO_2Si$ (MNa$^+$) requires 375.1751.

1-(*tert*-Butyldiphenylsilyloxy)hexa-4,5-dien-3-yl carbamate (152) and

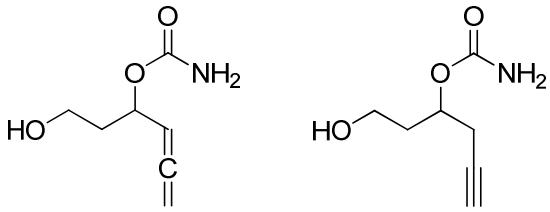
1-(*tert*-Butyldiphenylsilyloxy)hex-5-yn-3-yl carbamate (153)



To a stirred solution of a *ca*. 2:1 mixture of alcohols **150** and **151** (455 mg, 1.29 mmol) in DCM (4 mL) was added trichloroacetyl isocyanate (0.18 mL, 1.55 mmol) dropwise at 0 °C. After 1 h, TLC showed consumption of starting materials to be complete and the mixture was concentrated *in vacuo*. The residue was diluted with methanol (3 mL) and K_2CO_3 (538

mg, 3.87 mmol) in water (1 mL) was added at 0 °C. After 4 h the solvent was removed *in vacuo* and the residue was extracted with DCM (3 × 50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (1:1 petrol:ether) afforded the title compounds (500 mg, 98%) as a *ca*. 2:1 inseparable mixture; R_f 0.12 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3310br, 2957s, 2930s, 2857s, 1957m, 1719s, 1590m, 1472m; δ_H (500 MHz, $CDCl_3$) 1.06 (9H, s, C(C**H**$_3$)$_3$, allenyl and alkynyl), 1.93–1.99 (2H, m, COCH$_2$C**H**$_2$, allenyl and alkynyl), 2.01 (1H, t, *J* 2.7, ≡C**H**, alkynyl) 2.50 (1H, ddd, *J* 17.0, 4.7, 2.7, ≡CC**H**H′, alkynyl), 2.66 (1H, ddd, *J* 17.0, 5.8, 2.7, ≡CCH**H′**, alkynyl), 3.72–3.76 (2H, m, SiOC**H**$_2$, allenyl and alkynyl), 4.61 (2H, br s, N**H**$_2$, allenyl), 4.64 (2H, br s, N**H**$_2$, alkynyl), 4.81–4.88 (2H, m, =C**H**$_2$, allenyl), 5.02–5.07 (1H, m, COC**H**, alkynyl), 5.30 (1H, app. q, *J* 6.5, =C**H**, allenyl), 5.73–5.41 (1H, m, COC**H**, allenyl), 7.37–7.45 (6H, m, Ph**H**, allenyl and alkynyl), 7.66–7.69 (4H, m, Ph**H** allenyl and alkynyl); δ_C (125 MHz, $CDCl_3$) allenyl only, 19.1 (Si**C**Me$_3$), 26.8 (C(**C**H$_3$)$_3$), 36.9 (COCH$_2$**C**H$_2$), 59.9 (SiO**C**H$_2$), 69.5 (CO**C**H), 79.8 (=**C**H$_2$), 91.1 (=**C**H), 127.6 (Ar), 129.6 (Ar), 133.6 (Ar), 135.6 (Ar), 156.1 (O=**C**), 208.1 (=**C**=); Accurate mass (ESI$^+$): Found 418.1803: $C_{23}H_{29}NNaO_3Si$ (MNa$^+$) requires 418.1809.

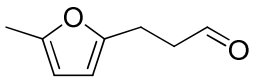
1-Hydroxyhexa-4,5-dien-3-yl carbamate (154) and 1-Hydroxyhex-5-yn-3-yl carbamate (155)



To a stirred solution of a *ca*. 2:1 mixture of carbamates **152** and **153** (500 mg, 1.26 mmol) in THF (20 mL) was added TBAF (1.58 mL of a 1.0 M solution in THF, 1.58 mmol) at 0 °C. After 1 h the reaction was quenched with water (30 mL) and extracted with ethyl acetate (3 × 40 mL). The combined organic extracts were washed with brine (40 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (ether) afforded the title compounds (120 mg, 61 %) as a *ca*. 2:1 inseparable mixture; R_f 0.38 (ethyl

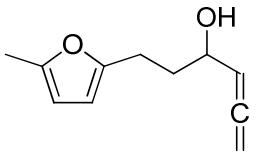
acetate); ν_{max}/cm^{-1} (thin film) 3351br, 2956s, 1957m, 1700s, 1607m, 1514w, 1391s, 1325s; δ_H (500 MHz, $CDCl_3$) 1.80–1.88 (2H, m, $COCH_2C\mathbf{H_2}$, allenyl and alkynyl), 2.04 (1H, dd, *J* 4.7, 1.9, ≡C**H**, alkynyl), 2.44–2.56 (2H, m, ≡C$C\mathbf{H_2}$, alkynyl), 3.65–3.74 (2H, m, HOC$\mathbf{H_2}$, allenyl and alyknyl), 4.07–4.13 (1H, m, COC**H**, alkynyl), 4.76 (2H, br s, N$\mathbf{H_2}$, allenyl), 4.80 (2H, br s, N$\mathbf{H_2}$, alkynyl), 4.90 (2H, ddd, *J* 6.6, 4.4, 2.4, =C$\mathbf{H_2}$, allenyl), 5.30 (1H, app. q, *J* 6.6, =C**H**, allenyl) 5.37–5.42 (1H, m, COC**H**, allenyl); δ_C (125 MHz, $CDCl_3$) allenyl only, 37.4 ($COCH_2\mathbf{C}H_2$), 58.4 (HO**C**H_2), 69.9 (CO**C**H), 77.9 (=**C**H_2), 91.1 (=**C**H), 156.9 (O=**C**), 208.1 (=**C**=); Accurate mass (ESI^+): Found 180.0632: $C_7H_{11}NNaO_3$ (MNa^+) requires 180.0631.

3-(5-Methylfuran-2-yl)propanal[176] (156)



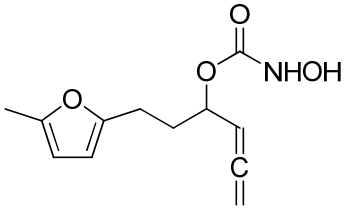
Acrolein (3.47 mL, 52.0 mmol), hydroquinone (100 mg), water (4.5 mL) and 2-methylfuran (5.13 mL, 57.0 mmol) were stirred in a round bottomed flask at 0 °C. Glacial acetic acid (7.5 mL) was added and stirring continued for 3 h before ether (25 mL) was added and the mixture warmed to r.t.. The layers were separated and the organic fragment washed successively with sat. aq. $NaHCO_3$ solution (2 × 10 mL) and brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (10:1 petrol:ether → 5:1 petrol:ether) afforded the title compound (3.35 g, 47%) as a yellow oil; R_f 0.32 (5:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 2.24 (3H, s, FuC$\mathbf{H_3}$), 2.75–2.79 (2H, m, OCHC$\mathbf{H_2}$), 2.93 (2H, t, *J* 7.3, FuC$\mathbf{H_2}$), 5.84–5.59 (2H, m, Fu**H**), 9.82 (1H, t, *J* 1.4, O=C**H**); δ_C (100 MHz, $CDCl_3$) 13.4 (Fu**C**H_3), 20.8 (Fu**C**H_2), 42.0 (OCH**C**H_2), 106.0 (Fu), 106.1 (Fu), 150.8 (Fu), 151.9 (Fu), 201.3 (O=**C**).

1-(5-Methylfuran-2-yl)hexa-4,5-dien-3-ol (157)



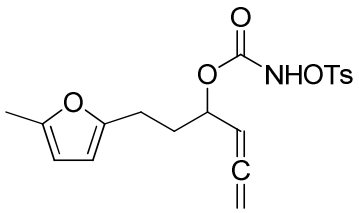
The reaction of aldehyde **156** according to general procedure E and purification by column chromatography (7:1 petrol:ether) afforded the title compound as a colourless oil (1.45 g, 75%); R_f 0.25 (5:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3380br, 3104w, 2985w, 2945s, 1223s, 2857w, 1956s, 1618s, 1571s, 1448m, 1219s; δ_H (400 MHz, $CDCl_3$) 1.87–1.93 (2H, m, HOCHC**H$_2$**), 2.26 (3H, s, FuC**H$_3$**), 2.72 (2H, app. dt, *J* 7.7, 4.0, FuC**H$_2$**), 4.20–4.26 (1H, m, HOC**H**), 4.89 (2H, dd, *J* 6.5, 2.2, =C**H$_2$**), 5.28 (1H, app. q, *J* 6.5, =C**H**), 5.84–5.88 (2H, m, Fu**H**); δ_C (100 MHz, $CDCl_3$) 13.5 (Fu**C**H$_3$), 24.1 (Fu**C**H$_2$), 35.7 (HOCH$_2$**C**H$_2$), 68.8 (HO**C**H), 77.7 (=**C**H$_2$), 94.5 (=**C**H), 105.6 (Fu), 105.8 (Fu), 150.4 (Fu), 153.5 (Fu), 207.0 (=**C**=); Accurate mass (ESI^+): Found 201.0893: $C_{11}H_{14}NaO_2$ (MNa^+) requires 201.0886.

1-(5-Methylfuran-2-yl)hexa-4,5-dien-3-yl hydroxycarbamate (158)



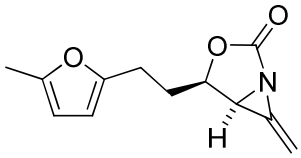
The reaction of alcohol **157** according to general procedure B and purification by column chromatography (2:1 petrol:ether) afforded the title compound (505 mg, 38%) as a colourless oil; R_f 0.26 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3302br, 2924s, 1958s, 1723s, 1571s, 1451s, 1262s, 1114s; δ_H (500 MHz, $CDCl_3$) 2.00–2.06 (2H, m, OCHC**H$_2$**), 2.25 (3H, s, FuC**H$_3$**), 2.66 (2H, app. dt, *J* 7.6, 3.5, FuC**H$_2$**), 4.90 (2H, dd, *J* 6.2, 4.6, =C**H$_2$**), 5.24–5.28 (2H, m, =C**H** overlays OC**H**), 5.84–5.88 (2H, m, Fu**H**) 7.19 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 13.3 (Fu**C**H$_3$), 23.9 (Fu**C**H$_2$), 32.5 (OCH**C**H$_2$), 73.3 (O**C**H), 77.7 (=**C**H$_2$), 90.3 (=**C**H), 105.8 (Fu), 105.9 (Fu), 150.6 (Fu), 152.7 (Fu), 158.5 (O=**C**), 208.5 (=**C**=); Accurate mass (ESI^+): Found 260.0893: $C_{12}H_{15}NNaO_4$ (MNa^+) requires 206.0895.

1-(5-Methylfuran-2-yl)hexa-4,5-dien-3-yl tosyloxycarbamate (159)



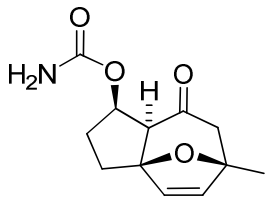
The reaction of hydroxycarbamate **158** according to general procedure C and purification by column chromatography (5:1 petrol:ether → 2:1 petrol:ether) afforded the title compound (690 mg, 74%) as a colourless oil; R_f 0.23 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3285br, 3070s, 2924s, 1957s, 1739s, 1597s, 1571s, 1452s, 1382s; δ_H (400 MHz, $CDCl_3$) 1.82–1.91 (2H, m, OCHC**H**$_2$), 2.25 (3H, s, FuC**H**$_3$), 2.43 (ArC**H**$_3$), 2.66 (2H, dd, *J* 9.2, 6.4, FuC**H**$_2$), 4.82–4.89 (2H, m, =C**H**$_2$), 5.01–5.11 (2H, m, =C**H** overlays OC**H**), 5.80–5.83 (2H, m, Fu**H**) 7.36 (2H, d, *J* 8.6, Ar**H**), 7.87 (1H, br s, N**H**), 7.89 (2H, d, *J* 8.6, Ar**H**); δ_C (100 MHz, $CDCl_3$) 13.5 (Fu**C**H$_3$), 21.7 (Ar**C**H$_3$), 23.7 (Fu**C**H$_2$), 32.3 (OCH**C**H$_2$), 74.5 (HO**C**H), 77.8 (=**C**H$_2$), 89.6 (=**C**H), 105.9 (Fu), 105.9 (Fu), 129.6 (Ar), 129.7 (Ar), 130.3 (Ar), 146.2 (Ar), 150.6 (Fu), 152.4 (Fu), 154.8 (O=**C**), 208.6 (=**C**=); Accurate mass (ESI$^+$): Found 414.0987: $C_{19}H_{21}NNaO_6S$ (MNa$^+$) requires 414.0982.

6-Methylene-4-(2-(5-methylfuran-2-yl)ethyl)-3-oxa-1-azabicyclo[3.1.0]hexan-2-one (160)



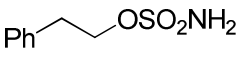
The reaction of *N*-tosyloxycarbamate **159** according to general procedure D and purification by column chromatography (4:1 petrol:ether) afforded the title compound (33 mg, 16%) as a yellow oil. Characterisation was not possible due to rearrangement to carbamate **161**.

6-Methyl-8-oxo-2,3,6,7,8,8a-hexahydro-1*H*-3a,6-epoxyazulen-1-yl carbamate (161)



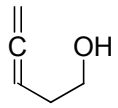
To a stirred solution of MA **160** (33 mg, 0.15 mmol) in chloroform (3 mL) was added CSA (2 crystals). After 48 h the solvent was removed *in vacuo* and purification by column chromatography (1:1 petrol:ethyl acetate → ethyl acetate) afforded the title compound (7 mg, 22%) as a colourless oil; R_f (ethyl acetate) 0.29; ν_{max}/cm^{-1} (thin film) 3356br, 2970s, 1712s, 1610s, 1395s, 1337s; δ_H (500 MHz, C_6D_6) 1.40–1.45 (1H, m, OCC**H**H′), 1.99–2.08 (2H, m, OCCH**H′** overlays OCHC**H**H′), 2.11–2.16 (1H, m, OCHCH**H′**), 2.20 (1H, d, *J* 7.9, O=CC**H**), 2.28 (1H, d, *J* 17.2, O=C**H**H′), 2.40 (1H, d, *J* 17.2, O=CH**H′**), 3.76 (2H, br s, N**H₂**), 5.59 (1H, d, *J* 5.7, MeCCH=C**H**), 5.62 (1H, d, *J* 5.7, MeCC**H**) 5.66 (1H, ddd, *J* 9.5, 7.9, 3.2, OC**H**); δ_C (125 MHz, $CDCl_3$) 24.0 (**C**H_3), 32.1 (OC**C**H_2), 32.8 (OCH**C**H_2), 50.1 (O=C**C**H_2), 60.0 (O=C**C**), 75.9 (O**C**H), 83.0 (Me**C**) 92.5 (MeCO**C**),134.9 (MeC**C**H=), 138.0 (MeCC=**C**H), 155.8 (O=**C**ON), 205.9 (O=**C**); Accurate mass (ESI^+): Found 260.0889: $C_{12}H_{15}NNaO_4$ (MNa^+) requires 260.0893.

Phenethyl sulfamate[177] (173)



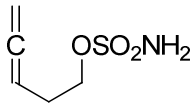
The reaction of 2-phenylethanol according to general procedure H and purification by column chromatography (1:1 petrol:ether) afforded the title compound (147 mg, 88%) as a colourless oil; R_f 0.33 (2:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 3.05 (2H, t, *J* 7.0, PhC**H₂**), 4.40 (2H, t, *J* 7.0, OC**H₂**), 7.24–7.36 (5H, m, Ar**H**); δ_C (100 MHz, $CDCl_3$) 35.2 (Ph**C**H_2), 71.5 (O**C**H_2), 127.0 (Ar), 128.7 (Ar), 129.0 (Ar), 136.5 (Ar).

Penta-3,4-dien-1-ol[178] (174)



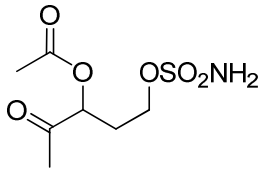
To a stirred solution of ester **94** (300 mg, 2.37 mmol) in ether (30 mL) at 0 °C was added $LiAlH_4$ (268 mg, 7.13 mmol). After 90 min the reaction was quenched with water (20 mL) and extracted with ether (3 × 30 mL). The combined organic extracts were washed with brine (30 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound (120 mg, 60%) as a pale yellow, volatile oil which required no further purification; R_f 0.27 (2:1 petrol:ether); δ_H (500 MHz, $CDCl_3$) 1.56 (1H, br s, O**H**), 2.26–2.31 (2H, m, $HOCH_2C\mathbf{H_2}$-), 3.73 (2H, app. q, *J* 6.0, $HOC\mathbf{H_2}$), 4.74 (2H, dt, *J* 6.8, 3.2 $=C\mathbf{H_2}$), 5.14 (1H, app. quin, *J* 6.8, =C**H**); δ_C (125 MHz, $CDCl_3$) 31.4 ($HOCH_2\mathbf{C}H_2$), 61.8 ($HO\mathbf{C}H_2$), 75.2 ($=\mathbf{C}H_2$), 86.4 (=**C**H), 209.0 (=**C**=).

Penta-3,4-dienyl sulfamate (175)



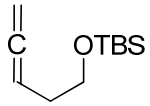
The reaction of alcohol **174** according to general procedure H and purification by column chromatography (1:1 petrol:ether) afforded the title compound (91 mg, 79%) as a colourless oil; R_f 0.20 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3287br, 1957s, 1557s, 1467w, 1427w, 1180s; δ_H (400 MHz, $CDCl_3$) 2.42–2.49 (2H, m, $OCH_2C\mathbf{H_2}$), 4.26 (2H, t, *J* 6.7, $OC\mathbf{H_2}$), 4.76 (2H, dt, *J* 6.7, 3.2 $=C\mathbf{H_2}$), 5.11–5.16 (1H, m, =C**H**); δ_C (100 MHz, $CDCl_3$) 27.7 ($OCH_2\mathbf{C}H_2$), 70.2 ($O\mathbf{C}H_2$), 76.1 ($=\mathbf{C}H_2$), 85.0 (=**C**H), 209.1 (=**C**=); Accurate mass (ESI^-): Found 162.0223: $C_5H_8NO_3S$ $(M-H)^-$ requires 162.0230.

4-Oxo-1-(sulfamoyloxy)pentan-3-yl acetate (176)



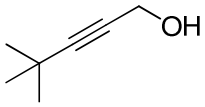
The reaction of sulfamate **175** according to general procedure I and purification by column chromatography (ether) afforded the title compound (63 mg, 35%) as a colourless oil; R_f 0.14 (ether); ν_{max}/cm^{-1} (thin film) 36277br, 1726br, 1564s, 1374s, 1244s; δ_H (400 MHz, $CDCl_3$) 2.19 (3H, s, HCC(=O)C**H$_3$**), 2.21 (3H, s, OC(=O)C**H$_3$**), 2.26–2.34 (2H, m, OCHC**H$_2$**), 4.22–4.33 (2H, m, SOC**H$_2$**), 5.19 (1H, dd, *J* 8.3, 4.2, OC**H**); δ_C (100 MHz, $CDCl_3$) 20.5 (CHC(=O)**C**H$_3$), 26.1 (OC(=O)**C**H$_3$), 29.5 (OCH**C**H$_2$), 66.3 (SO**C**H$_2$), 74.8 (O**C**H), 170.7 (O**C**=O), 205.3 (H$_3$C**C**=O); Accurate mass (ESI$^+$): Found 262.0354: $C_7H_{13}NNaO_6S$ (MNa^+) requires 262.0356.

***tert*-Butyldimethyl(penta-3,4-dienyloxy)silane[179] (177)**



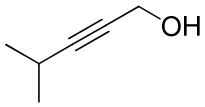
To a stirred suspension of NaH (171 mg of a 60% suspension in mineral oil, 4.30 mmol) in THF (15 mL) was added a solution of alcohol **174** (360 mg, 4.30 mmol) in THF (5 mL) *via* canula. After 45 min *tert*-butylchlorodimethylsilane (648 mg, 4.30 mmol) was added and stirring continued for 1 h. The mixture was diluted with ether (50 mL), washed sequentially with 10% aq. K_2CO_3 (2 × 20 mL) and brine (2 × 20 mL) and dried over Na_2SO_4. Concentration *in vacuo* afforded the title compound (780 mg, 91%) as a colourless oil without the need for further purification; δ_H (500 MHz, $CDCl_3$) 0.07 (6H, s, Si(C**H$_3$**)$_2$), 0.90 (9H, s, C(C**H$_3$**)$_3$), 2.23 (2H, dtt, *J* 6.9, 6.6, 2.8, OCH$_2$C**H$_2$**), 3.68 (2H, t, *J* 6.6, OC**H$_2$**), 4.66 (2H, dt, *J* 6.9, 2.8 =C**H$_2$**), 5.12 (1H, app. quin, *J* 6.9, =C**H**); δ_C (125 MHz, $CDCl_3$) –5.3 (Si(**C**H$_3$)$_2$), 18.3 (Si**C**Me$_3$), 25.9 (C(**C**H$_3$)$_3$), 32.0 (OCH$_2$**C**H$_2$), 62.8 (O**C**H$_2$), 74.5 (=**C**H$_2$), 86.6 (=**C**H), 209.0 (=**C**=).

4,4-Dimethylpent-2-yn-1-ol[100] (180)



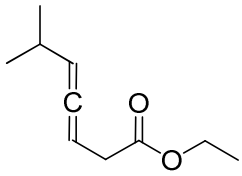
Synthesised according to a literature procedure.

4-Methylpent-2-yn-1-ol[101] (181)



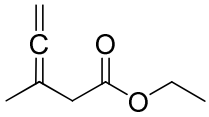
Synthesised according to a literature procedure.

Ethyl 6-methylhepta-3,4-dienoate (182)



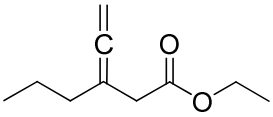
The reaction of 2-methylbut-3-yn-2-ol according to general procedure F and purification by column chromatography (20:1 petrol:ether) afforded the title compound (3.04 g, 94%) as a colourless oil; R_f 0.42 (5:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 2963s, 2871m, 1964m, 1740s, 1446m, 1367s, 1331s; δ_H (400 MHz, $CDCl_3$) 1.00 (3H, d, *J* 6.8, CHC**H$_3$**), 1.00 (3H, d, *J* 6.8, CHC**H$_3$**), 1.26 (3H, t, *J* 7.2, CHC**H$_3$**), 2.30 (1H, septdd, *J* 6.8, 5.7, 3.0, $(CH_3)_2$C**H**), 3.01 (2H, dd, *J* 7.2, 2.8, O=CC**H$_2$**), 4.15 (2H, q, *J* 7.2, OC**H$_2$**), 5.20 (1H, ddt, *J* 6.4, 5.7, 2.8, =C**H**CH), 5.24–5.30 (1H, tdd, *J* 7.2, 6.4, 3.0, =C**H**CH_2); δ_C (100 MHz, $CDCl_3$) 14.0 (CH_2**C**H_3), 22.3 (CH**C**H_3), 22.4 (CH**C**H_3), 27.8 (CH_3**C**H), 35.2 (O=C**C**H_2), 60.7 (O**C**H_2), 85.3 (=**C**HCH_2), 99.6 (=**C**HCH), 171.6 (O=**C**), 203.5 (=**C**=); Accurate mass (ESI^+): Found 191.1035: $C_{10}H_{16}NaO_2$ (MNa^+) requires 191.1043.

Ethyl 3-methylpenta-3,4-dienoate (183)



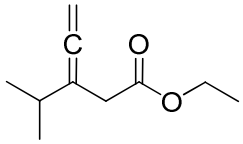
The reaction of but-2-yn-1-ol according to general procedure F and purification by column chromatography (10:1 petrol:ethyl acetate) afforded the title compound (4.41 g, 52%) as a colourless oil; R_f 0.52 (5:1 petrol:ethyl acetate); v_{max}/cm^{-1} (thin film) 2984m, 1965m, 1734s, 1437m, 1367s, 1331s, 1245s, 1160s; δ_H (400 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.2, $OCH_2C\mathbf{H_3}$), 1.77 (3H, t, *J* 3.2, $=CC\mathbf{H_3}$), 2.98 (2H, t, *J* 2.4, $=CC\mathbf{H_2}$), 4.16 (2H, q, *J* 7.2, $OC\mathbf{H_2}$), 4.65–4.68 (2H, m, $=C\mathbf{H_2}$); δ_C (100 MHz, $CDCl_3$) 14.3 ($OCH_2\mathbf{C}H_3$), 18.4 ($=C\mathbf{C}H_3$), 39.8 ($=C\mathbf{C}H_2$), 60.7 ($O\mathbf{C}H_2$), 74.5 ($=\mathbf{C}H_2$), 92.6 (=**C**), 171.1 (O=**C**), 207.5 (=**C**=); *m/z* (GCMS, Cl^+) 158 (MNH_4^+, 32%), 141 (MH^+, 100); Accurate mass: Found 141.0922: $C_8H_{13}O_2$ (MH^+) requires 141.0916.

Ethyl 3-vinylidenehexanoate (184)



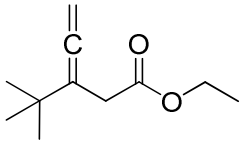
The reaction of hex-2-yn-1-ol according to general procedure F and purification by column chromatography (30:1 petrol:ether) afforded the title compound (1.31 g, 39%) as a colourless oil; R_f 0.38 (5:1 petrol:ether); v_{max}/cm^{-1} (thin film) 2962s, 1961m, 1739s, 1366m, 1158s; δ_H (400 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.4 $CH_2CH_2C\mathbf{H_3}$), 1.26 (3H, t, *J* 7.2, $OCH_2C\mathbf{H_3}$), 1.46 (2H, app. sxt, *J* 7.4, $=CCH_2C\mathbf{H_2}$), 1.97–2.02 (2H, m, $=CC\mathbf{H_2}CH_2$), 2.98 (2H, t, *J* 2.5, $=CC\mathbf{H_2}C(=O)$), 4.16 (2H, q, *J* 7.2, $OC\mathbf{H_2}$), 4.74 (2H, tt, *J* 3.4, 2.5,$=C\mathbf{H_2}$); δ_C (100 MHz, $CDCl_3$) 13.7 ($CH_2CH_2\mathbf{C}H_3$), 14.2 ($OCH_2\mathbf{C}H_3$), 20.5 ($=CCH_2\mathbf{C}H_2$), 33.7 ($=C\mathbf{C}H_2CH_2$), 38.7 ($=C\mathbf{C}H_2C(=O)$), 60.6 ($O\mathbf{C}H_2$), 75.9 ($=\mathbf{C}H_2$), 97.2 (=**C**), 171.3 (O=**C**), 207.0 (=**C**=); *m/z* (GCMS, Cl^+) 186 (MNH_4^+, 66%), 169 (MH^+, 100), 168 (15), 123 (13), 111 (22); Accurate mass: Found 186.1485: $C_{10}H_{20}NO_2$ (MNH_4^+) requires 186.1494.

Ethyl 3-isopopylpenta-3,4-dienoate (185)



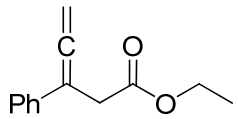
The reaction of alcohol **181** according to general procedure F and purification by column chromatography (10:1 petrol:ether) afforded the title compound (1.91 g, 60%) as a colourless oil; R_f 0.19 (10:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 2964s, 1958s, 1735s, 1464m, 1366m, 1243m, 1152s; δ_H (400 MHz, $CDCl_3$) 1.04 (6H, d, *J* 7.0, $CH(C\mathbf{H_3})_2$), 1.26 (3H, t, *J* 7.2, $OCH_2C\mathbf{H_3}$), 2.17–2.25 (1H, m, =CC**H**), 3.00 (2H, t, *J* 2.6, =$CC\mathbf{H_2}$), 4.15 (2H, q, *J* 7.2, $OC\mathbf{H_2}$), 4.78 (2H, app. q, *J* 2.6, =$C\mathbf{H_2}$); δ_C (100 MHz, $CDCl_3$) 14.3 ($OCH_2\mathbf{C}H_3$), 21.4 ($CH(\mathbf{C}H_3)_2$), 30.1 (=C**C**H), 37.3 (=$C\mathbf{C}H_2$), 60.6 ($O\mathbf{C}H_2$), 77.1 (=$\mathbf{C}H_2$), 103.6 (=**C**), 171.5 (O=**C**), 206.0 (=**C**=); *m/z* (GCMS, Cl^+) 186 (MNH_4^+, 79%), 169 (MH^+, 100) 168 (30), 125 (25), 123 (38), 111 (23); Accurate mass: Found 169.1226: $C_{10}H_{17}O_2$ (MH^+) requires 169.1229.

Ethyl 3-*tert*-butylpenta-3,4-dienoate[178] (186)



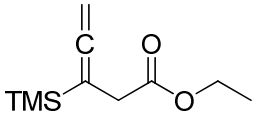
The reaction of alcohol **180** according to general procedure F and purification by column chromatography (20:1 petrol:ethyl acetate) afforded the title compound (2.96 g, 42%) as a colourless oil; R_f 0.21 (20:1 petrol:ethyl acetate); δ_H (400 MHz, $CDCl_3$) 1.05 (9H, s, $(C\mathbf{H_3})_3$), 1.21 (3H, t, *J* 7.1, $CH_2C\mathbf{H_3}$), 2.97 (2H, t, *J* 2.7, =$CC\mathbf{H_2}$), 4.13 (2H, q, *J* 7.1, $OC\mathbf{H_2}$), 4.73 (2H, t, *J* 2.7,=$C\mathbf{H_2}$); δ_C (100 MHz, $CDCl_3$) 14.2 ($CH_2\mathbf{C}H_3$), 28.9 ($C(\mathbf{C}H_3)_3$, 33.1 ($\mathbf{C}(CH_3)_3$), 34.8 (=$C\mathbf{C}H_2$), 60.6 ($O\mathbf{C}H_2$), 77.1 (=$\mathbf{C}H_2$), 106.2 (=**C**), 171.9 (O=**C**), 205.6 (=**C**=).

Ethyl 3-phenylpenta-3,4-dienoate (187)



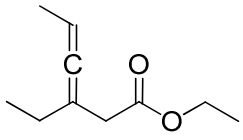
The reaction of 3-phenylprop-2-yn-1-ol according to general procedure F and purification by column chromatography (20:1 petrol:ethyl acetate) afforded the title compound (1.18 g, 24%) as a colourless oil; R_f 0.42 (10:1 petrol:ethyl acetate); ν_{max}/cm^{-1} (thin film) 2981s, 1944s, 1735s, 1597m, 1495s, 1452s, 1420m, 1387w, 1366m; δ_H (400 MHz, $CDCl_3$) 1.23 (3H, t, *J* 7.0, $OCH_2C\mathbf{H_3}$), 3.46 (2H, t, *J* 2.4, $=CC\mathbf{H_2}$), 4.16 (2H, q, *J* 7.0, $OC\mathbf{H_2}$), 5.16 (2H, t, *J* 2.4, $=C\mathbf{H_2}$), 7.21 (1H, t, *J* 7.3, Ar**H**), 7.32 (2H, t, *J* 7.3, Ar**H**), 7.37 (2H, d, *J* 7.3, Ar**H**); δ_C (100 MHz, $CDCl_3$) 14.2 ($OCH_2\mathbf{C}H_3$), 36.8 ($=C\mathbf{C}H_2$), 60.9 ($O\mathbf{C}H_2$), 78.6 ($=\mathbf{C}H_2$), 99.3 (=**C**), 125.7 (Ar), 126.9 (Ar), 128.3 (Ar), 135.1 (Ar), 171.1 (O=**C**), 209.7 (=**C**=); *m/z* (GCMS, Cl^+) 220 (MNH_4^+, 28%), 204 (16), 203 (MH^+, 100), 202 (19), 174 (31), 157 (38), 129 (36); Accurate mass: Found 220.1332: $C_{13}H_{18}NO_2$ (MNH_4^+) requires 220.1338.

Ethyl 3-(trimethylsilyl)penta-3,4-dienoate[178] (188)



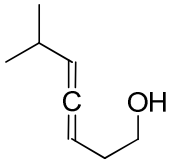
The reaction of 3-(trimethylsilyl)prop-2-yn-1-ol according to general procedure H and purification by column chromatography (50:1 petrol:ether) afforded the title compound (1.89 g, 49%) as a colourless oil; R_f 0.46 (10:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 0.00 (9H, s, $Si(C\mathbf{H_3})_3$), 1.11 (3H, t, *J* 7.1, $OCH_2C\mathbf{H_3}$), 2.86 (2H, t, *J* 2.6, $=CC\mathbf{H_2}$), 4.02 (2H, q, *J* 7.1, $OC\mathbf{H_2}$), 4.32 (2H, t, *J* 2.6, $=C\mathbf{H_2}$); δ_C (100 MHz, $CDCl_3$) 0.0 ($Si(\mathbf{C}H_3)_3$), 15.8 ($OCH_2\mathbf{C}H_3$), 37.3 ($=C\mathbf{C}H_2$), 62.3 ($O\mathbf{C}H_2$), 71.2 ($=\mathbf{C}H_2$), 90.4 (=**C**), 173.4 (O=**C**), 211.8 (=**C**=).

Ethyl 3-ethylhexa-3,4-dienoate (189)



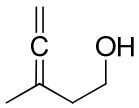
The reaction of 3-hexyn-2-ol according to general procedure F and purification by column chromatography (30:1 petrol:ether) afforded the title compound (3.74 g, 80%) as a colourless oil; R_f 0.18 (30:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 2930s, 2909m, 1970s, 1733s, 1460s, 1444s, 1410s; δ_H (400 MHz, $CDCl_3$) 1.00 (3H, t, *J* 7.3 $CCH_2C\mathbf{H_3}$), 1.26 (3H, t, *J* 7.1, $OCH_2C\mathbf{H_3}$), 1.65 (3H, d, *J* 6.8, $=CHC\mathbf{H_3}$), 2.01 (1H, qd, *J* 7.3, 3.5, $=CC\mathbf{H_2}CH_3$), 2.96 (2H, d, *J* 2.3, $O=CC\mathbf{H_2}$), 4.14 (2H, q, *J* 7.1, $OC\mathbf{H_2}$), 5.14–5.20 (1H, m, $=C\mathbf{H}$); δ_C (100 MHz, $CDCl_3$) 12.1 ($CCH_2\mathbf{C}H_3$), 14.2 ($OCH_2\mathbf{C}H_3$), 14.6 ($=CH\mathbf{C}H_3$), 25.4 ($=C\mathbf{C}H_2CH_3$), 39.3 ($O=C\mathbf{C}H_2$), 60.5 ($O\mathbf{C}H_2$), 87.6 ($=\mathbf{C}H$), 99.2 ($=\mathbf{C}$), 171.6 ($O=\mathbf{C}$), 202.6 ($=\mathbf{C}=$); *m/z* (GCMS, Cl^+) 186 (MNH_4^+, 10%), 170 (11), 169 (MH^+, 100); Accurate mass: Found 186.1500: $C_{10}H_{20}NO_2$ (MNH_4^+) requires 186.1494.

6-Methylhepta-3,4-dien-1-ol (190)



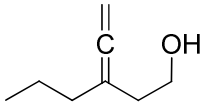
The reduction of ester **182** according to general procedure G afforded the title compound (1.90 g, 99%) as a colourless oil; R_f 0.21 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3356br, 2396s, 2903s, 1961s, 1466s, 1382m, 1300s; δ_H (400 MHz, $CDCl_3$) 0.99 (3H, d, *J* 6.8, $CHC\mathbf{H_3}$), 1.01 (3H, d, *J* 6.8, $CHC\mathbf{H_3}$), 1.84–1.90 (1H, m, $(CH_3)_2C\mathbf{H}$), 2.22–2.30 (2H, m, $=CHC\mathbf{H_2}$), 3.69 (2H, app. q, *J* 5.8, $OC\mathbf{H_2}$), 5.12–5.18 (2H, m, $\mathbf{H}C=C\mathbf{H}$); δ_C (100 MHz, $CDCl_3$) 22.4 ($CH\mathbf{C}H_3$), 22.5 ($CH\mathbf{C}H_3$), 27.9 ($CH_3\mathbf{C}H$), 32.4 ($=C\mathbf{C}H_2$), 62.1 ($O\mathbf{C}H_2$), 88.4 ($=\mathbf{C}HCH_2$), 99.1 ($=\mathbf{C}HCH$), 203.0 ($=\mathbf{C}=$); *m/z* (GCMS, Cl^+) 144 (MNH_4^+, 31%), 127 (MH^+, 100), 125 (53), 111 (82), 109 (26), 95 (33); Accurate mass: Found 144.1386: C_8H_8NO (MNH_4^+) requires 144.1388.

3-Methylpenta-3,4-dien-1-ol (191)



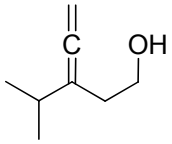
The reduction of ester **183** according to general procedure G afforded the title compound (2.96 g, 94%) as a colourless oil; R_f 0.14 (2:1 petrol:ether); v_{max}/cm^{-1} (thin film) 3338br, 2981m, 2921s, 1960s, 1427s, 1371m, 1268w, 1188w, 1149m; δ_H (400 MHz, $CDCl_3$) 1.72 (3H, t, *J* 3.1, C**H$_3$**), 2.51 (2H, tt, *J* 6.1, 3.1, =CC**H$_2$**), 3.75 (2H, t, *J* 6.1, OC**H$_2$**), 4.68 (2H, app. sxt, *J* 3.1, =C**H$_2$**); δ_C (100 MHz, $CDCl_3$) 18.8 (**C**H$_3$), 36.6 (=C**C**H$_2$), 60.6 (O**C**H$_2$), 74.8 (=**C**H$_2$), 95.5 (=**C**), 206.1 (=**C**=); *m/z* (GCMS, Cl^+) 116 (MNH_4^+, 12%), 99 (MH^+, 32), 97 (29), 83 (100), 81 (19); Accurate mass: Found 116.1071: $C_6H_{14}NO_2$ (MNH_4^+) requires 116.1075.

3-Vinylidenehexan-1-ol (192)



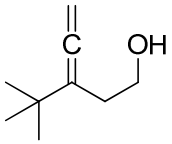
The reduction of ester **184** according to general procedure G and purification by column chromatography (2:1 petrol:ether) afforded the title compound (644 mg, 76%) as a colourless oil; R_f 0.18 (2:1 petrol:ether); v_{max}/cm^{-1} (thin film) 3356br, 2959s, 1956s, 1455m, 1046s; δ_H (500 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.4 C**H$_3$**), 1.47 (2H, app. sxt, *J* 7.4, =CCH$_2$C**H$_2$**CH$_3$), 1.93–1.97 (2H, m, =CC**H$_2$**CH$_2$CH$_3$), 2.22 (2H, tt, *J* 6.1, 3.2, =CC**H$_2$**CH$_2$OH)), 3.76 (2H, t, *J* 6.1, OC**H$_2$**), 4.75 (2H, app. quin, *J* 3.2, =C**H$_2$**); δ_C (125 MHz, $CDCl_3$) 13.7 (**C**H$_3$), 20.6 (=CCH$_2$**C**H$_2$), 34.3 (=C**C**H$_2$CH$_2$), 35.3 (=C**C**H$_2$CH$_2$O), 60.7 (O**C**H$_2$), 76.2 (=**C**H$_2$), 100.1 (=**C**), 205.5 (=**C**=); *m/z* (GCMS, Cl^+) 144 (MNH_4^+, 10%), 127 (MH^+, 100), 125 (88), 124 (23), 97 (42), 95 (24), 84 (19); Accurate mass: Found 127.1121: $C_8H_{15}O$ (MH^+) requires 127.1123.

3-Isopropylpenta-3,4-dien-1-ol (193)



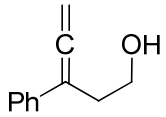
The reduction of ester **185** according to general procedure G and purification by column chromatography (5:1 petrol:ethyl acetate) afforded the title compound (1.37 g, 98%) as a colourless oil; R_f 0.26 (2:1 petrol:ethyl acetate); ν_{max}/cm^{-1} (thin film) 3336br, 2961s, 1952s, 1464m, 1383s, 1240m, 1042s; δ_H (400 MHz, $CDCl_3$) 1.04 (6H, d, *J* 6.8, CH(C**H**$_3$)$_2$), 2.08–2.16 (1H, m, =CC**H**), 2.21–2.26 (2H, m, =CC**H**$_2$), 3.75 (2H, t, *J* 6.1, OC**H**$_2$), 4.79 (2H, dt, *J* 3.3, 2.6, =C**H**$_2$); δ_C (100 MHz, $CDCl_3$) 21.5 (CH(**C**H$_3$)$_2$), 30.8 (=C**C**H), 33.4 (=C**C**H$_2$), 61.0 (O**C**H$_2$), 77.5 (=**C**H$_2$), 106.7 (=**C**), 204.3 (=**C**=); *m/z* (GCMS, Cl^+) 144 (MNH_4^+, 31%), 127 (MH^+, 100), 125 (20), 111 (95), 109 (78), 83 (41); Accurate mass: Found 144.1382: $C_8H_{18}NO$ (MNH_4^+) requires 144.1388.

3-*tert*-Butylpenta-3,4-dien-1-ol[180] (194)



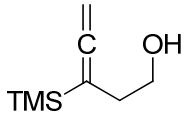
The reduction of ester **186** according to general procedure G and purification by column chromatography (2:1 petrol:ether) afforded the title compound (2.10 g, 93%) as a colourless oil; R_f 0.18 (5:1 petrol:ethyl acetate); δ_H (400 MHz, $CDCl_3$) 1.06 (9H, s, (C**H**$_3$)$_3$), 1.86 (1H, br s, O**H**), 2.23 (2H, tt, *J* 6.3, 3.7, =CC**H**$_2$), 3.75 (2H, t, *J* 6.3, HOC**H**$_2$), 4.78 (2H, t, *J* 3.7,=C**H**$_2$); δ_C (100 MHz, $CDCl_3$) 29.0 (C(**C**H$_3$)$_3$, 29.9 (=C**C**H$_2$), 32.9 (**C**(CH$_3$)$_3$), 61.5 (HO**C**H$_2$), 77.6 (=**C**H$_2$), 109.6 (=**C**), 203.7 (=**C**=).

3-Phenylpenta-3,4-dien-1-ol (195)



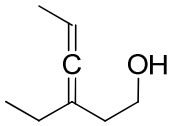
The reduction of ester **187** according to general procedure G and purification by column chromatography (2:1 petrol:ether) afforded the title compound (692 mg, 75%) as a colourless oil; R_f 0.18 (2:1 petrol:ether); v_{max}/cm^{-1} (thin film) 3345br, 2884s, 1940s, 1596m, 1493s, 1451s, 1421m, 1385m; δ_H (400 MHz, $CDCl_3$) 2.71 (2H, app. sept, *J* 3.3, =CC**H$_2$**), 3.88 (2H, t, *J* 6.4, OC**H$_2$**), 5.15 (2H, t, *J* 3.3, =C**H$_2$**), 7.22 (1H, t, *J* 7.4, Ar**H**), 7.30–7.35 (2H, m, Ar**H**), 7.41 (2H, d, *J* 7.7, Ar**H**); δ_C (100 MHz, $CDCl_3$) 32.8 (=C**C**H$_2$), 61.0 (O**C**H$_2$), 78.9 (=**C**H$_2$), 101.9 (=**C**), 125.9 (Ar), 127.0 (Ar), 128.5 (Ar), 135.7 (Ar), 208.3 (=**C**=); *m/z* (GCMS, Cl^+) 161 (MH^+, 100%), 159 (53), 158 (26), 148 (55), 143 (31), 131 (28), 117 (22), 115 (21); Accurate mass: Found 161.0972: $C_{11}H_{13}O$ (MH^+) requires 161.0966.

3-(Trimethylsilyl)penta-3,4-dien-1-ol (196)



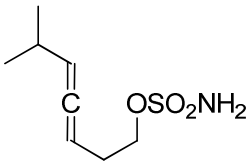
The reduction of ester **188** according to general procedure G and purification by column chromatography (3:1 petrol:ether) afforded the title compound (1.28 g, 98%) as a colourless oil; R_f 0.28 (2:1 petrol:ether); v_{max}/cm^{-1} (thin film) 3339br, 2956s, 1927s, 1745m, 1405m, 1248s, 1041s; δ_H (400 MHz, $CDCl_3$) 0.00 (9H, s, Si(C**H$_3$**)$_3$), 2.11 (2H, app. sept, *J* 3.1, =CC**H$_2$**), 3.66 (2H, t, *J* 6.1, OC**H$_2$**), 4.30 (2H, t, *J* 3.1, =C**H$_2$**); δ_C (100 MHz, $CDCl_3$) 0.0 (Si(**C**H$_3$)$_3$), 33.6 (=C**C**H$_2$), 64.0 (O**C**H$_2$), 71.2 (=**C**H$_2$), 93.4 (=**C**), 209.7 (=**C**=); *m/z* (GCMS, Cl^+) 157 (MH^+, 100%), 141 (22), 103 (18), 90 (94); Accurate mass: Found 157.1042: $C_8H_{17}OSi$ (MH^+) requires 157.1049.

3-Ethylhexa-3,4-dien-1-ol (197)



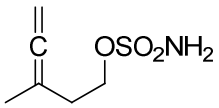
The reduction of ester **189** according to general procedure G afforded the title compound (1.39 g, 99%) as a colourless oil without the need for purification; R_f 0.29 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3345br, 2966s, 1961s, 1458s, 1372s; δ_H (400 MHz, $CDCl_3$) 1.00 (3H, td, *J* 7.3, 1.0 $CH_2C\mathbf{H_3}$), 1.66 (3H, d, *J* 6.8, =CHC$\mathbf{H_3}$), 1.80 (1H, br s, O**H**), 1.92–1.98 (2H, m, =CC$\mathbf{H_2}CH_3$), 2.21 (2H, br t, *J* 6.1, $OCH_2C\mathbf{H_2}$), 3.72 (2H, td, *J* 6.1, 1.1, OC$\mathbf{H_2}$), 5.15–5.22 (1H, m, =C**H**); δ_C (100 MHz, $CDCl_3$) 12.2 ($CH_2\mathbf{C}H_3$), 15.0 (=CH$\mathbf{C}H_3$), 25.8 (=C$\mathbf{C}H_2CH_3$), 35.8 ($OCH_2\mathbf{C}H_2$), 60.9 (O$\mathbf{C}H_2$), 87.9 (=**C**H), 102.4 (=**C**), 201.0 (=**C**=); *m/z* (GCMS, Cl^+) 144 (MNH_4^+, 12%), 127 (MH^+, 100), 109 (58), 98 (49), 81 (10); Accurate mass: Found 127.1118: $C_8H_{15}O$ (MH^+) requires 127.1123.

6-Methylhepta-3,4-dienyl sulfamate (198)



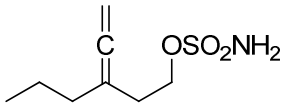
The reaction of alcohol **190** according to general procedure H and purification by column chromatography (1:1 petrol:ether) afforded the title compound (1.98 g, 68%) as a colourless oil; R_f 0.17 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3288br, 2961s, 2869m, 1962s, 1557m, 1466m, 1364s, 1182s; δ_H (400 MHz, $CDCl_3$) 1.01 (6H, d, *J* 6.8, C$\mathbf{H_3}$), 2.30 (1H, septdd, *J* 6.8, 5.7, 3.0, $(CH_3)_2C\mathbf{H}$), 2.45 (2H, m, app. dq, *J* 6.8, 2.9, =CHC$\mathbf{H_2}$), 4.25 (2H, t, *J* 6.8, OC$\mathbf{H_2}$), 4.99 (2H, br s, N$\mathbf{H_2}$), 5.14 (1H, dq, *J* 6.4, 2.9, =C**H**CH_2), 5.22 (1H, ddt, *J* 6.4, 5.7, 3.0, =C**H**CH); δ_C (100 MHz, $CDCl_3$) 22.4 (CH$\mathbf{C}H_3$), 22.4 (CH$\mathbf{C}H_3$), 27.7 ($CH_3\mathbf{C}H$), 28.6 (=C$\mathbf{C}H_2$), 70.5 (O$\mathbf{C}H_2$), 86.8 (=**C**HCH_2), 99.9 (=**C**HCH), 203.2 (=**C**=); Accurate mass (ESI^-): Found 204.0694: $C_8H_{14}NO_3S$ $(M–H)^-$ requires 204.0700.

3-Methylpenta-3,4-dienyl sulfamate (199)



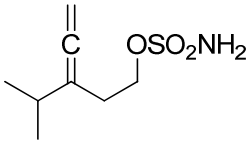
The reaction of alcohol **191** according to general procedure H and purification by column chromatography (1:1 petrol:ether) afforded the title compound (1.81 g, 68%) as a white crystalline solid, R_f 0.22 (1:1 petrol:ether); m.p. 32–35 °C; ν_{max}/cm^{-1} (thin film) 3390br, 3100w, 2932m, 2904m, 2861m, 1960s, 1558s, 1361s; δ_H (400 MHz, $CDCl_3$) 1.73 (3H, t, *J* 3.2, C**H$_3$**), 2.39 (2H, tt, *J* 6.9, 3.2, =CC**H$_2$**), 4.30 (2H, t, *J* 6.9, OC**H$_2$**), 4.69 (2H, app. sxt, *J* 3.2, =C**H$_2$**), 4.82 (2H, br s, N**H$_2$**); δ_C (100 MHz, $CDCl_3$) 18.9 (**C**H$_3$), 32.3 (=C**C**H$_2$), 69.3 (O**C**H$_2$), 75.6 (=**C**H$_2$), 94.0 (=**C**), 206.1 (=**C**=); Accurate mass (FI): Found 177.0456: $C_6H_{11}NO_3S$ (M) requires 177.0460.

3-Vinylidenehexyl sulfamate (200)



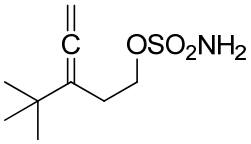
The reaction of alcohol **192** according to general procedure H and purification by column chromatography (2:1 petrol:ether) afforded the title compound (732 mg, 70%) as a colourless oil; R_f 0.17 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3288br, 2960m, 1958s, 1557m, 1366s, 1183s; δ_H (400 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.4 C**H$_3$**), 1.46 (2H, app. sxt, *J* 7.4, =CCH$_2$C**H$_2$**CH$_3$), 1.92–1.98 (2H, m, =CC**H$_2$**CH$_2$CH$_3$), 2.36–2.41 (2H, m, =CC**H$_2$**CH$_2$O), 4.30 (2H, t, *J* 7.1, OC**H$_2$**), 4.76 (2H, app. quin, *J* 3.4, =C**H$_2$**) 4.88 (2H, br s, N**H$_2$**); δ_C (100 MHz, $CDCl_3$) 13.7 (**C**H$_3$), 20.6 (=CCH$_2$**C**H$_2$), 30.9 (=C**C**H$_2$CH$_2$O), 34.4 (=C**C**H$_2$CH$_2$), 69.5 (O**C**H$_2$), 77.0 (=**C**H$_2$), 98.5 (=**C**), 205.5 (=**C**=); Accurate mass (ESI^-): Found 204.0701: $C_8H_{14}NO_3S$ $(M–H)^-$ requires 204.0700.

3-Isopropylpenta-3,4-dienyl sulfamate (201)



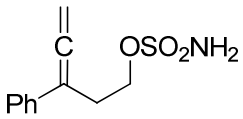
The reaction of alcohol **193** according to general procedure H and purification by column chromatography (4:1 petrol:ethyl acetate) afforded the title compound (1.54 g, 85%) as a colourless oil; R_f 0.39 (1:1 petrol:ethyl acetate); ν_{max}/cm^{-1} (thin film) 3394br, 3291br, 2964s, 1953s, 1553m, 1465s, 1361s, 1175s; δ_H (400 MHz, $CDCl_3$) 1.04 (6H, d, *J* 6.8, CH(C**H**$_3$)$_2$), 2.09–2.18 (1H, m, =CC**H**), 2.42 (2H, app. sept, *J* 3.5, =CC**H**$_2$), 4.29 (2H, t, *J* 7.2, OC**H**$_2$), 4.80 (2H, dt, *J* 3.5, 2.6, =C**H**$_2$), 4.86 (2H, br s, N**H**$_2$); δ_C (100 MHz, $CDCl_3$) 21.3 (CH(**C**H$_3$)$_2$), 29.1 (=C**C**H$_2$), 30.7 (=C**C**H), 69.8 (O**C**H$_2$), 78.3 (=**C**H$_2$), 104.9 (=**C**), 204.3 (=**C**=); Accurate mass (ESI^-): Found 204.0697: $C_8H_{14}NO_3S$ $(M–H)^-$ requires 204.0700.

3-*tert*-Butylpenta-3,4-dienyl sulfamate (202)



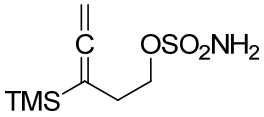
The reaction of alcohol **194** according to general procedure H and purification by column chromatography (4:1 petrol:ether) afforded the title compound (2.14 g, 82%) as a white solid; R_f 0.12 (4:1 petrol:ether); m.p. 55–58 °C; ν_{max}/cm^{-1} (thin film) 3265br, 2961s, 1950m, 1462s, 1364s, 1179s; δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, (C**H**$_3$)$_3$), 2.42 (2H, app. sept, *J* 3.5, =CC**H**$_2$), 4.29 (2H, t, *J* 7.4, SOC**H**$_2$), 4.79–4.82 (3H, m, =C**H**$_2$ overlays N**H**$_2$); δ_C (100 MHz, $CDCl_3$) 25.7 (=C**C**H$_2$), 28.9 (C(**C**H$_3$)$_3$, 32.9 (**C**(CH$_3$)$_3$), 70.2 (SO**C**H$_2$), 78.4 (=**C**H$_2$), 107.6 (=**C**), 203.8 (=**C**=); Accurate mass (ESI^+): Found 242.0812: $C_9H_{17}NNaO_3S$ (MNa^+) requires 242.0821.

3-Phenylpenta-3,4-dienyl sulfamate (203)



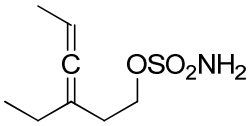
The reaction of alcohol **195** according to general procedure H and purification by column chromatography (2:1 petrol:ether) afforded the title compound (538 mg, 55%) as a white crystalline solid, R_f 0.25 (1:1 petrol:ether); m.p. 98–102 °C; ν_{max}/cm^{-1} (thin film) 3354br, 3261s, 1945s, 1557m, 1492m, 1453s, 1349s; δ_H (400 MHz, $CDCl_3$) 2.89 (2H, tt, *J* 7.1, 3.3, =CC**H$_2$**), 4.41 (2H, t, *J* 7.1, OC**H$_2$**), 4.73 (2H, br s, N**H$_2$**) 5.18 (2H, t, *J* 3.3, =C**H$_2$**), 7.23 (1H, t, *J* 7.0, Ar**H**), 7.32–7.39 (4H, m, Ar**H**); δ_C (100 MHz, $CDCl_3$) 28.8 (=C**C**H$_2$), 69.4 (O**C**H$_2$), 79.7 (=**C**H$_2$), 100.4 (=**C**), 125.8 (Ar), 127.2 (Ar), 128.6 (Ar), 135.1 (Ar), 208.2 (=**C**=); Accurate mass (ESI^+): Found 262.0508: $C_{11}H_{13}NNaO_3S$ (MNa^+) requires 262.0508.

3-(Trimethylsilyl)penta-3,4-dienyl sulfamate (204)



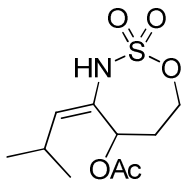
The reaction of alcohol **196** according to general procedure H and purification by column chromatography (3:1 petrol:ether) afforded the title compound (692 mg, 52%) as a white crystalline solid, R_f 0.32 (1:1 petrol:ether); m.p. 56–58 °C; ν_{max}/cm^{-1} (thin film) 3365s, 3274s, 2954s, 1926s, 1559m, 1468m, 1379m, 1348s, 1248s, 1174s; δ_H (400 MHz, $CDCl_3$) 0.00 (9H, s, Si(C**H$_3$**)$_3$), 2.27 (2H, tt, *J* 7.5, 3.3, =CC**H$_2$**), 4.20 (2H, t, *J* 7.5, OC**H$_2$**), 4.32 (2H, t, *J* 3.3, =C**H$_2$**) 4.65 (2H, br s, N**H$_2$**); δ_C (100 MHz, $CDCl_3$) 0.0 (Si(**C**H$_3$)$_3$, 29.4 (=C**C**H$_2$), 72.2 (O**C**H$_2$), 79.1 (=**C**H$_2$), 91.8 (=**C**), 210.3 (=**C**=); Accurate mass (ESI^-): Found 234.0624: $C_8H_{16}NO_3SSi$ $(M–H)^-$ requires 234.0626.

3-Ethylhexa-3,4-dienyl sulfamate (205)



The reaction of alcohol **197** according to general procedure H and purification by column chromatography (2:1 petrol:ether) afforded the title compound (1.32 g, 82%) as a white crystalline solid; R_f 0.26 (2:1 petrol:ether); m.p. 44–46 °C; ν_{max}/cm^{-1} (thin film) 3370br, 3280s, 2963s, 2908m, 1965s, 1552s, 1207s, 1173s; δ_H (400 MHz, $CDCl_3$) 1.00 (3H, t, *J* 7.3, $CH_2C\mathbf{H_3}$), 1.66 (3H, d, *J* 7.0, =CHC$\mathbf{H_3}$), 1.97 (1H, qd, *J* 7.3, 3.3, =CC$\mathbf{H_2}CH_3$), 2.37–2.42 (2H, m, $OCH_2C\mathbf{H_2}$), 4.29 (2H, t, *J* 7.1, OC$\mathbf{H_2}$), 4.74 (2H, br s, N$\mathbf{H_2}$), 5.15–5.24 (1H, m, =C**H**); δ_C (100 MHz, $CDCl_3$) 12.1 ($CH_2\mathbf{C}H_3$), 14.9 (=CH$\mathbf{C}H_3$), 25.9 (=C$\mathbf{C}H_2CH_3$), 31.5 ($OCH_2\mathbf{C}H_2$), 69.8 (O$\mathbf{C}H_2$), 88.7 (=**C**H), 100.6 (=**C**), 201.2 (=**C**=); Accurate mass (ESI^-): Found 204.0703: $C_8H_{14}NO_3S$ $(M–H)^-$ requires 204.0700.

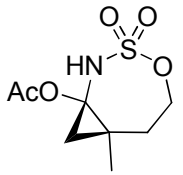
(4*E*)-4-(2-Methylpropylidene)-2,2-dioxido-1,2,3-oxathiazepan-5-yl acetate (206)



The reaction of sulfamate **198** according to general procedure I and purification by column chromatography (2:1 petrol:ether) afforded the title compound (382 mg, 52%) as a white crystalline solid; R_f 0.52 (ether); m.p. 85–87 °C; ν_{max}/cm^{-1} (thin film) 3272br, 2965s, 2872w, 1743s, 1467s, 1418s, 1375s; δ_H (400 MHz, $CDCl_3$) 1.04 (3H, d, *J* 6.6 CHC$\mathbf{H_3}$), 1.05 (3H, d, *J* 6.7, CHC$\mathbf{H_3}$), 2.10–2.16 (1H, m, $SOCH_2CH\mathbf{H'}$), 2.13 (3H, s, O=C$\mathbf{C}H_3$), 2.20 (1H, dt, *J* 11.6, 3.3, $SOCH_2C\mathbf{H}H'$), 2.59–2.68 (1H, m, $H_3CC\mathbf{H}$), 4.25 (1H, dt, *J* 12.3, 3.3, SOCH**H'**), 4.64 (1H, dt, *J* 12.3, 1.3, SOC**H**H′), 5.77 (1H, d, *J* 10.5, C=C**H**), 5.92 (1H, t, *J* 3.3, OC**H**), 6.28 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 21.1 (O=C$\mathbf{C}H_3$), 22.4 (CH$\mathbf{C}H_3$), 22.6 (CH$\mathbf{C}H_3$), 27.1 ($H_3C\mathbf{C}H$), 34.7 ($SOCH_2\mathbf{C}H_2$), 65.1 (SO$\mathbf{C}H_2$), 66.7 (O=COC**H**), 125.6 (NC=**C**H), 143.0

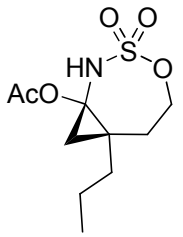
(N**C**), 169.3 (O=**C**); Accurate mass (ESI$^+$): Found 286.0719: $C_{10}H_{17}NNaO_5S$ (MNa^+) requires 286.0720; For X-Ray crystal data see appendix C.

7-Methyl-3,3-dioxido-4-oxa-3-thia-2-azabicyclo[5.1.0]oct-1-yl acetate (207)



The reaction of sulfamate **199** according to general procedure I and purification by column chromatography (2:1 petrol:ether) afforded the title compound (477 mg, 50%) as a white crystalline solid; R_f 0.21 (2:1 petrol:ether); m.p. 87–91 °C; ν_{max}/cm^{-1} (thin film) 3303br, 2973s, 2922s, 2865m, 1741m, 1455m, 1423s, 1345s; δ_H (400 MHz, $CDCl_3$) 1.03 (1H, d, *J* 6.6, NCC**H**H′), 1.35 (3H, s, NCCC**H$_3$**), 1.38 (1H, d, *J* 6.6, NCCH**H′**), 1.93 (1H, ddd, *J* 16.0, 12.0, 2.0, OCH_2C**H**H′), 2.10 (3H, s, O=CC**H$_3$**), 2.29 (1H, dd, *J* 16.0, 4.6, OCH_2CH**H′**), 4.26 (1H, ddd, *J* 12.0, 4.6, 2.0, OC**H**H′), 4.67 (1H, app. t, *J* 12.0, OCH**H′**), 6.75 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 17.7 (NCC**C**H$_3$), 21.2 (O=C**C**H$_3$), 27.6 (NC**C**), 31.1 (NC**C**H$_2$), 38.7 (OCH_2**C**H$_2$), 69.2 (O**C**H$_2$), 77.2 (N**C**), 171.6 (O=**C**); Accurate mass (ESI$^+$): Found 258.0407: $C_8H_{13}NNaO_5S$ (MNa^+) requires 258.0407.

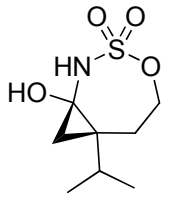
3,3-Dioxido-7-propyl-4-oxa-3-thia-2-azabicyclo[5.1.0]oct-1-yl acetate (208)



The reaction of sulfamate **200** according to general procedure I and purification by column chromatography (1:1 petrol:ether) afforded the title compound (167 mg, 40%) as a white crystalline solid; R_f 0.42 (ether); m.p. 76–79 °C; ν_{max}/cm^{-1} (thin film) 3260br, 2962s, 1740s, 1510m, 1363m, 1211s; δ_H (400 MHz, $CDCl_3$) 0.95 (3H, t, *J* 7.3 CH_2C**H$_3$**), 1.02 (1H, d, *J* 6.6, NCC**H**H′), 1.34 (1H, d, *J* 6.6, NCCH**H′**), 1.30–1.48 (2H, m, CCH**H′**CH_2CH_3 overlays

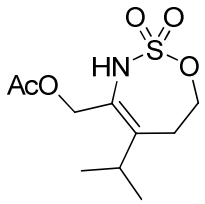
$CCH_2CH\mathbf{H'}CH_3$), 1.52–1.63 (1H, m, $CCH_2C\mathbf{H}H'CH_3$), 1.70 (1H, ddd, *J* 11.1, 4.3, 3.0, $CC\mathbf{H}H'CH_2CH_3$), 1.80 (1H, dd, *J* 16.0, 11.8, $OCH_2C\mathbf{H}H'$), 2.11 (3H, s, $O{=}CC\mathbf{H_3}$), 2.42 (1H, dd, *J* 16.0, 4.8, $OCH_2CH\mathbf{H'}$), 4.24 (1H, ddd, *J* 12.0, 4.8, 2.0, $OC\mathbf{H}H'$), 4.64 (1H, app. t, *J* 12.0, $OCH\mathbf{H'}$), 6.72 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 14.2 ($CH_2\mathbf{C}H_3$), 19.8 ($CH_3\mathbf{C}H_2$), 21.2 ($O{=}C\mathbf{C}H_3$), 30.2 ($NC\mathbf{C}H_2$), 31.7 (NC**C**), 32.4 ($CH_3CH_2\mathbf{C}H_2$), 35.4 ($OCH_2\mathbf{C}H_2$), 69.5 (N**C**), 69.6 ($O\mathbf{C}H_2$), 171.6 (O=**C**); Accurate mass (FI): Found 263.0820: $C_{10}H_{17}NO_5S$ (M) requires 263.0827; For X-Ray crystal data see appendix D.

7-(1-Methylethyl)-4-oxa-3-thia-2-azabicyclo[5.1.0]octan-1-ol 3,3-dioxide (209)



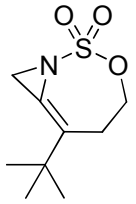
The reaction of sulfamate **201** according to general procedure I and purification by column chromatography (20:1 DCM:ethyl acetate) afforded the title compound (184 mg, 20%) as a white crystalline solid; R_f 0.20 (2:1 petrol:ethyl acetate); m.p. 165–167 °C; v_{max}/cm^{-1} (thin film) 3455s, 3211br, 2958m, 1466w, 1416s, 1366s, 1321m, 1262s, 1202s, 1169s; δ_H (400 MHz, $CDCl_3$) 0.88 (1H, d, *J* 5.7, $NCC\mathbf{H}H'$), 0.92 (1H, d, *J* 5.7, $NCCH\mathbf{H'}$), 1.01 (3H, d, *J* 7.0, $CHC\mathbf{H_3}$), 1.14 (3H, d, *J* 7.0, $CHC\mathbf{H_3}$), 1.68 (1H, ddd, *J* 16.5, 11.6, 2.0, $OCH_2C\mathbf{H}H'$), 1.79 (1H, sept, *J* 7.0, NCCC**H**), 2.48 (1H, dd, *J* 16.5, 4.6, $OCH_2CH\mathbf{H'}$), 3.62 (1H, br s, O**H**), 4.25 (1H, ddd, *J* 12.3, 4.6, 2.0, $OC\mathbf{H}H'$), 4.69 (1H, dd, *J* 12.3, 11.6, $OCH\mathbf{H'}$), 6.05 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 19.5 ($\mathbf{C}H_3$), 20.5 ($\mathbf{C}H_3$), 30.5 ($NC\mathbf{C}H_2$), 31.0 (NCC**C**H), 32.0 ($OCH_2\mathbf{C}H_2$), 37.8 (NC**C**), 70.6 ($O\mathbf{C}H_2$), 71.6 (N**C**); Accurate mass (ESI^+): Found 244.0612: $C_8H_{15}NNaO_4S$ (MNa^+) requires 244.0614.

(5-(1-Methyl)-2,2-dioxido-6,7-dihydro-3H-1,2,3-oxathiazepin-4-yl)methyl acetate (210)



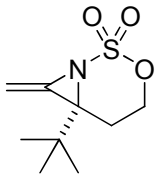
The reaction of sulfamate **201** according to general procedure I and purification by column chromatography (20:1 DCM:ethyl acetate) afforded the title compound (137 mg, 12%) as a white crystalline solid; R_f 0.24 (2:1 petrol:ethyl acetate); ν_{max}/cm^{-1} (thin film) 3284br, 2965s, 1736s, 1440m, 1364s, 1172s; δ_H (400 MHz, $CDCl_3$) 1.02 (6H, d, *J* 6.8, CH(C**H**$_3$)$_2$), 2.09 (3H, s, O=CC**H**$_3$), 2.56–2.59 (2H, m, SOCH$_2$C**H**$_2$), 2.96 (1H, sept, *J* 6.8, C**H**(CH$_3$)$_2$), 4.33–4.36 (2H, m, SOC**H**$_2$), 4.68 (2H, s, COC**H**$_2$), 6.39 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 20.1 (CH(**C**H$_3$)$_2$, 20.8 (**C**H$_3$), 27.8 (OCH$_2$**C**H$_2$), 30.2 (**C**H(CH$_3$)$_2$), 62.2 (CO**C**H$_2$), 70.8 (SO**C**H$_2$), 125.8 (NC=**C**), 142.6 (N**C**), 171.4 (O=**C**); Accurate mass (ESI$^-$): Found 262.0748: $C_{10}H_{16}NO_5S$ $(M–H)^-$ requires 262.0755.

6-(1,1-Dimethylethyl)-3-oxa-2-thia-1-azabicyclo[5.1.0]oct-6-ene 2,2-dioxide (211)



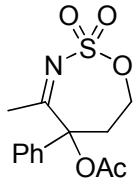
The reaction of sulfamate **202** according to general procedure I and purification by column chromatography (4:1 petrol:ether) afforded the title compound (160 mg, 68%) as a white crystalline solid; R_f 0.26 (2:1 petrol:ether); m.p. 58–61 °C; ν_{max}/cm^{-1} (thin film) 3075m, 2968s, 1468m, 1359s, 1296w, 1261w, 1183s; δ_H (500 MHz, CD_2Cl_2, 228K) 1.11 (9H, s, (C**H**$_3$)$_3$), 2.39 (1H, d, *J* 14.3, OCH$_2$CH**H′**), 2.90 (1H, app. t, *J* 14.3, OCH$_2$C**H**H′), 3.45 (1H, br s, NCH**H′**), 3.53 (1H, br s, NC**H**H′), 4.48–4.57 (2H, m, OC**H**$_2$); δ_C (100 MHz, $CDCl_3$) 27.9 (C(**C**H$_3$)$_3$, 28.0 (=C**C**H$_2$), 35.3 (**C**(CH$_3$)$_3$), 40.2 (N**C**H$_2$), 75.3 (O**C**H$_2$), 114.9 (NC=**C**), 126.4 (N**C**=C); Accurate mass (ESI$^+$): Found 240.0670: $C_9H_{15}NNaO_3S$ (MNa^+) requires 240.0665; For X-Ray crystal data see appendix E.

6-(1,1-Dimethylethyl)-7-methylidene-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-dioxide (212)



The reaction of sulfamate **202** according to general procedure I and purification by column chromatography (4:1 petrol:ether) afforded the title compound (31 mg, 13%) as a side product; R_f 0.11 (2:1 petrol:ether); v_{max}/cm^{-1} (thin film) 2972s, 2875m, 1626s, 1468s, 1371s, 1244m, 1187s; δ_H (500 MHz, $CDCl_3$) 1.06 (9H, s, (C**H**$_3$)$_3$), 2.11 (1H, dt, *J* 15.2, 3.4 OCH_2CH**H′**), 2.49 (1H, ddd, 15.2, 10.8, 5.3, OCH_2C**H**H′), 4.36 (1H, ddd, *J* 12.0, 10.8, 3.4, OCH**H′**), 4.43 (1H, ddd, *J* 12.0, 5.3, 3.4, OC**H**H′), 5.04 (1H, d, *J* 2.8, =CH**H′**), 5.36 (1H, d, *J* 2.8, =C**H**H′); δ_C (125 MHz, $CDCl_3$) 21.3 (OCH_2**C**H_2), 25.5 (C(**C**H_3)$_3$, 34.9 (**C**(CH_3)$_3$), 66.7 (OCH_2CH_2**C**), 67.3 (O**C**H_2), 90.0 (=**C**H_2), 133.2 (N**C**=CH_2); Accurate mass (ESI$^+$): Found 240.0661: $C_9H_{15}NNaO_3S$ (MNa^+) requires 240.0665.

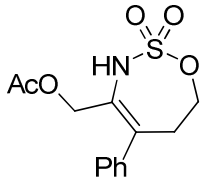
4-Methyl-2,2-dioxido-5-phenyl-6,7-dihydro-5H-1,2,3-oxathiazepin-5-yl acetate (213)



The reaction of sulfamate **203** according to general procedure I and purification by column chromatography (2:1 petrol:ether) afforded the title compound (135 mg, 24%) as a white crystalline solid; R_f 0.32 (ether); m.p. 114–118 ℃; v_{max}/cm^{-1} 3068s, 1745s, 1638s, 1448m, 1368s, 1258w, 1234s, 1180s; δ_H (500 MHz, $CDCl_3$) 2.07 (1H, ddd, *J* 14.8, 4.1, 1.1, OCH_2C**H**H′), 2.20 (3H, s, O=CC**H**$_3$), 2.24 (3H, s, N=CC**H**$_3$), 3.43–3.51 (1H, m, OC**H**H′), 4.06–4.15 (1H, m, OCH_2CH**H′**), 4.30 (1H, dd, *J* 11.0, 5.9, OCH**H′**), 7.37 (2H, dd, *J* 7.7, 1.9, Ar**H**), 7.45–7.48 (3H, m, Ar**H**); δ_C (100 MHz, $CDCl_3$) 21.3 (O=C**C**H_3), 25.2 (N=C**C**H_3), 36.7 (OCH_2**C**H_2), 65.2 (O**C**H_2), 88.4 (O**C**), 125.9 (Ar), 129.3 (Ar), 129.8 (Ar), 133.6 (Ar), 169.8

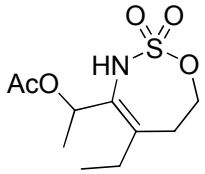
(O=**C**), 181.4 (N=**C**); Accurate mass (ESI$^+$): Found 320.0558: $C_{13}H_{15}NNaO_5S$ (MNa^+) requires 320.0563.

(2,2-Dioxido-5-phenyl-6,7-dihydro-3H-1,2,3-oxathiazepin-4-yl)methyl acetate (214)



The reaction of sulfamate **203** according to general procedure I and purification by column chromatography (2:1 petrol:ether) afforded the title compound (26 mg, 5%) as a yellow solid; R_f 0.49 (ether); δ_H (400 MHz, $CDCl_3$) 2.11 (3H, s, C**H$_3$**), 3.00 (2H, app. t, *J* 5.0, $SOCH_2C\mathbf{H_2}$), 4.51 (2H, app. tt, *J* 3.5, 1.5 $SOC\mathbf{H_2}$), 4.55 (2H, s, $COC\mathbf{H_2}$), 7.20–7.22 (2H, m, Ar**H**), 7.34–7.41 (3H, m, Ar**H**); δ_C (100 MHz, $CDCl_3$) 20.8 (**C**H_3), 36.4 ($SOCH_2\mathbf{C}H_2$), 63.1 ($CO\mathbf{C}H_2$), 70.5 ($SO\mathbf{C}H_2$), 128.0 (Ar), 128.3 (Ar), 128.6 (NC=**C**), 128.8 (Ar), 135.9 (Ar), 139.4 (N**C**), 171.4 (O=**C**); Accurate mass (ESI$^+$): Found 320.0560: $C_{13}H_{15}NNaO_5S$ (MNa^+) requires 320.0563.

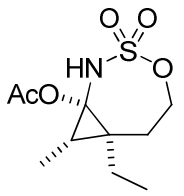
1-(5-Ethyl-2,2-dioxido-6,7-dihydro-3*H*-1,2,3-oxathiazepin-4-yl)ethyl acetate (215)



The reaction of sulfamate **205** according to general procedure I and purification by column chromatography (2:1 petrol:ether) afforded the title compound (180 mg, 28%) as a white solid; R_f 0.30 (ether); v_{max}/cm^{-1} (thin film) 3281br, 2975s, 2259s, 1734s, 1371s; δ_H (500 MHz, $CDCl_3$) 1.04 (3H, t, *J* 7.6, $CH_2C\mathbf{H_3}$), 1.40 (3H, d, *J* 6.7, $OCHC\mathbf{H_3}$), 2.05 (3H, s, $O{=}CC\mathbf{H_3}$), 2.13–2.19 (1H, m, $CH_3C\mathbf{H}H'$), 2.25–2.32 (1H, m, $CH_3CH\mathbf{H'}$), 2.48 (1H, ddd, *J* 16.2, 6.8, 1.7, $OCH_2C\mathbf{H}H'$), 2.74 (1H, ddd, *J* 16.2, 8.4, 2.7, $OCH_2CH\mathbf{H'}$), 4.34–4.42 (2H, m, $SOC\mathbf{H_2}$), 5.74 (1H, q, *J* 6.7, O**CH**), 6.23 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 12.3

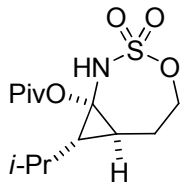
($CH_2\mathbf{C}H_3$), 18.4 ($OCH\mathbf{C}H_3$), 21.1 ($O{=}C\mathbf{C}H_3$), 26.9 ($CH_3\mathbf{C}H_2$), 33.7 ($OCH_2\mathbf{C}H_2$), 36.4 (O**C**H), 70.5 ($SO\mathbf{C}H_2$), 128.6 (NC=**C**), 136.2 (N**C**), 169.9 (O=**C**); Accurate mass (ESI^+): Found 286.0717: $C_{10}H_{17}NNaO_5S$ (MNa^+) requires 286.0720.

7-Ethyl-8-methyl-3,3-dioxido-4-oxa-3-thia-2-azabicyclo[5.1.0]oct-1-yl acetate (216)



The reaction of sulfamate **205** according to general procedure I and purification by column chromatography (2:1 petrol:ether) afforded the title compound (170 mg, 26%) as a white crystalline solid; R_f 0.42 (ether); m.p. 101–104 °C; ν_{max}/cm^{-1} (thin film) 3299br, 2975s, 1741s, 1411s, 1357s, 1256m, 1189s; δ_H (500 MHz, $CDCl_3$) 0.99 (3H, d, *J* 6.5, CHC**H**$_3$), 1.00 (3H, t, *J* 7.6 $CH_2C\mathbf{H}_3$), 1.40 (1H, q, *J* 6.5, NCC**H**), 1.50–1.58 (1H, m, NCCCH**H′**), 1.65–1.75 (2H, m, $OCH_2CH\mathbf{H'}$ overlays NCCC**H**H′), 2.13 (3H, s, O=CC**H**$_3$), 2.50 (1H, dd, *J* 16.2, 4.6, $OCH_2C\mathbf{H}$H′), 4.23 (1H, ddd, *J* 12.0, 4.6, 2.0, OC**H**H′), 4.63 (1H, app. t, *J* 12.0, OCH**H′**), 6.64 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 8.1 ($CH\mathbf{C}H_3$), 10.2 ($CH_2\mathbf{C}H_3$), 18.4 ($CH_3\mathbf{C}H_2$), 20.9 ($O{=}C\mathbf{C}H_3$), 33.2 (NC**C**), 33.4 (NC**C**H), 36.0 ($OCH_2\mathbf{C}H_2$), 69.2 ($O\mathbf{C}H_2$), 71.8 (N**C**), 171.5 (O=**C**); Accurate mass (ESI^+): Found 286.0716: $C_{10}H_{17}NNaO_5S$ (MNa^+) requires 286.0720.

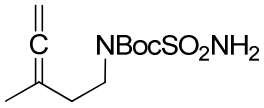
8-Isopropyl-3,3-dioxido-4-oxa-3-thia-2-azabicyclo[5.1.0]oct-1-yl pivalate (223)



To a stirred solution of sulfamate **198** (57 mg, 0.28 mmol) in benzene (4 mL) was added $Rh_2(esp)_2$ (10 mg, 0.014 mmol) and $PhI(OPiv)_2$ (142 mg, 0.35 mmol). After 20 h MgO (20 mg) was added and the reaction mixture filtered through Celite®. Concentration *in*

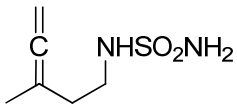
vacuo followed by purification by column chromatography (2:1 petrol:ether) afforded the title compound (6 mg, 7%) as a colourless oil; R_f 0.27 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3374br, 2961s, 2927s, 1728s, 1462s; δ_H (500 MHz, $CDCl_3$) 0.97 (3H, d, *J* 6.1, CHC**H**$_3$), 1.01 (3H, d, *J* 6.3, CHC**H**$_3$), 1.11–1.16 (2H, m, C**H**$(CH_3)_2$ overlays C**H**$CH(CH_3)_2$), 1.22 (9H, C(C**H**$_3)_3$), 1.36–1.40 (1H, m, NCC**H**$(CH)CH_2$), 1.76 (1H, dddd, *J* 16.2, 12.0, 9.5, 2.4, OCH_2C**H**H′) 2.51 (1H, dddd, *J* 16.2, 6.9, 4.4, 0.8, OCH_2CH**H′**), 4.28 (1H, ddd, *J* 12.0, 4.4, 2.4, OC**H**H′), 4.62 (1H, app. t, *J* 12.0, OCH**H′**), 6.77 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 22.4 (CH**C**H_3), 22.5 (CH**C**H_3), 26.8 (C(**C**$H_3)_3$), 27.3 (**C**$H(CH_3)_2$), 27.4 (NC**C**$H(CH)CH_2$), 32.0 (OCH_2**C**H_2), 38.8 (**C**$(CH_3)_3$), 45.0 (**C**$HCH(CH_3)_2$), 71.1 (N**C**), 71.4 (O**C**H_2), 179.3 (O=**C**); Accurate mass (ESI^+): Found 328.1191: $C_{13}H_{23}NNaO_5S$ (MNa^+) requires 328.1189.

***tert*-Butyl 3-methylpenta-3,4-dienyl(sulfamoyl)carbamate (224)**



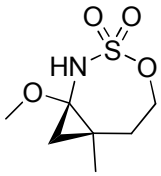
To a solution of alcohol **191** (417 mg, 4.25 mmol), *tert*-butylsulfamoylcarbamate[108] (1.00 g, 5.10 mmol) and triphenylphosphine (1.34 g, 5.10 mmol) in THF (30 mL) at 0 ℃ was added diethyl azodicarboxylate (0.99 mL, 5.10 mmol). After 4 h, TLC analysis showed the reaction to be complete. The solvent was removed *in vacuo* and purification by column chromatography (6:1 petrol:ethyl acetate) afforded the title compound (646 mg, 55%) as a white crystalline solid; R_f 0.18 (6:1 petrol:ether); m.p. 49–52 ℃; ν_{max}/cm^{-1} (thin film) 3361br, 3269br, 2982s, 1956s, 1705s, 1554m, 1452s, 1368s; δ_H (500 MHz, $CDCl_3$) 1.54 (9H, s, C(C**H**$_3)_3$), 1.74 (3H, t, *J* 3.1, =CC**H**$_3$), 2.28 (2H, tt, *J* 7.2, 2.7, =CC**H**$_2$), 3.82 (2H, app. q, *J* 7.2, NC**H**$_2$), 4.61 (2H, qt, *J* 3.1, 2.7, =C**H**$_2$), 5.25 (2H, br s, N**H**$_2$); δ_C (125 MHz, $CDCl_3$) 18.5 (=C**C**H_3), 28.0 C(**C**$H_3)_3$, 35.6 (=C**C**H_2), 45.6 (N**C**H_2), 74.3 (=**C**H_2), 84.3 (O**C**), 95.1 (=**C**), 152.2 (O=**C**), 206.8 (=**C**=); Accurate mass (ESI^-): Found 275.1070: $C_{11}H_{19}N_2O_4S$ $(M–H)^-$ requires 275.1071.

3-Methylpenta-3,4-dienyl sulfamide (225)



To a solution of sulfamide **224** (267mg, 0.97 mmol) in methanol (3 mL) was added conc. H_3PO_4 (3 mL). After 20 h the reaction was poured on to 2.0 M aq. NaOH solution (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (1:2 petrol:ether) afforded the title compound (35 mg, 20%) as a colourless oil; R_f 0.31 (ether); ν_{max}/cm^{-1} (thin film) 3285br, 2981s, 1960s, 1715s, 1559s, 1428s, 1332s; δ_H (500 MHz, $CDCl_3$) 1.72 (3H, t, *J* 3.3, =CC**H$_3$**), 2.25 (2H, app. sept, *J* 3.3, =CC**H$_2$**), 3.28 (2H, t, *J* 6.5, NC**H$_2$**), 4.44 (1H, br s, N**H**), 4.50 (2H, br s, N**H$_2$**), 4.72 (2H, sxt, *J* 3.3, =C**H$_2$**); δ_C (125 MHz, $CDCl_3$) 18.7 (=C**C**H$_3$), 29.7 (=C**C**H$_2$), 41.2 (N**C**H$_2$), 75.4 (=**C**H$_2$), 95.5 (=**C**), 205.9 (=**C**=); Accurate mass (ESI^-): Found 175.0544: $C_6H_{11}N_2O_2S$ $(M–H)^-$ requires 175.0547.

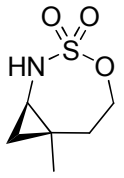
1-(Methoxy)-7-methyl-4-oxa-3-thia-2-azabicyclo[5.1.0]octane 3,3-dioxide (226)



To a stirred solution of cyclopropane **207** (20 mg, 0.085 mmol) in methanol (2 mL) was added $NaBH_4$ (3 mg, 0.26 mmol) at room temperature. After 2 h the reaction was quenched with water (5mL) and extracted with DCM (3 × 30 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo* to afford the title compound (4 mg, 23%) as a white solid, R_f 0.31 (1:1 petrol:ethyl acetate); ν_{max}/cm^{-1} (thin film) 3308br, 2975s, 2916s, 1451m, 1409s, 1369s; δ_H (500 MHz, $CDCl_3$) 0.88 (1H, d, *J* 5.4, NCC**H**H′), 0.92 (1H, d, *J* 5.4, NCCH**H′**), 1.32 (3H, s, NCCC**H$_3$**), 1.87 (1H, ddd, *J* 16.4, 11.8, 1.8, OCH$_2$C**H**H′), 2.30 (1H, dd, *J* 16.4, 4.7, OCH$_2$CH**H′**), 3.38 (3H, s, OC**H$_3$**), 4.22 (1H, ddd, *J* 11.8, 4.7, 1.8, SOC**H**H′), 4.65 (1H, app. t, *J* 11.8, SOCH**H′**), 5.96 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$)

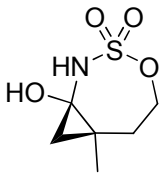
17.9 (NCC**C**H_3), 28.9 (NC**C**H_2), 31.3 (NC**C**), 39.2 (OCH_2**C**H_2), 53.3 (O**C**H_3), 69.2 (SO**C**H_2), 73.5 (N**C**); Accurate mass (ESI^+): Found 230.0455: $C_7H_{13}NNaO_4S$ (MNa^+) requires 230.0457.

7-Methyl-4-oxa-3-thia-2-azabicyclo[5.1.0]octane 3,3-dioxide (227)



To a stirred solution of cyclopropane **207** (78 mg, 0.33 mmol) in IPA (2 mL) was added $NaBH_4$ (50 mg, 1.32 mmol) at 0 ℃ and the reaction mixture was allowed to warm to r.t. After 20 h the reaction was quenched with water (5 mL) and extracted with DCM (3 × 20 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (4:1 petrol:ethyl acetate) afforded the title compound as a white solid (36 mg, 62%); R_f 0.28 (2:1 petrol:ethyl acetate); v_{max}/cm^{-1} (thin film) 3300br, 2961s, 1338s, 1163s; δ_H (500 MHz, $CDCl_3$) 0.83 (1H, dd, *J* 5.5, 3.7, NCHC**H**H′), 0.93 (1H, dd, *J* 7.3, 5.5, NCCH**H′**), 1.17 (3H, s, NCHCC**H**$_3$), 2.00 (1H, ddd, *J* 16.2, 11.2, 1.4, OCH_2C**H**H′), 2.21 (1H, dd, *J* 16.2, 4.7, OCH_2CH**H′**), 2.45 (1H, ddd, *J* 7.3, 3.7, 2.0, NC**H**), 4.20 (1H, ddd, *J* 12.3, 4.7, 1.4, OC**H**H′), 4.69 (1H, app. t, *J* 11.7, OCH**H′**), 5.16 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 22.2 (NCHC**C**H_3), 24.2 (NCH**C**), 24.7 (NCH**C**H_2), 34.9 (N**C**H), 37.8 (OCH_2**C**H_2), 69.8 (O**C**H_2); *m/z* (GCMS, CI^+) 195 (MNH_4^+, 100%); Accurate mass: Found 195.0795: $C_6H_{15}NO_3S$ (MNH_4^+) requires 195.0803.

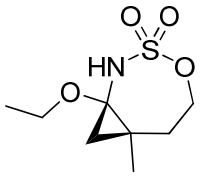
7-Methyl-4-oxa-3-thia-2-azabicyclo[5.1.0]octan-1-ol 3,3-dioxide (228)



Cyclopropane **207** (45 mg, 0.19 mmol) was dissolved in diethyl ether (6 mL) at r.t., $LiAlH_4$ (21 mg, 0.57 mmol) was added and the reaction stirred for 1 h. The reaction was quenched

with water (10 mL) and acidified with 1.0 M aq. HCl (5 mL). The mixture was extracted with ether (3 x 20mL) and the combined organic extracts washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (3:1 petrol:ethyl acetate) afforded the title compound (28 mg, 76%) as a white solid; R_f 0.34 (2:1 petrol:ethyl acetate); m.p. 89–92 °C; ν_{max}/cm^{-1} (thin film) 3259br, 2961s, 1710w, 1421s, 1266s; δ_H (400 MHz, $CDCl_3$) 0.99 (1H, d, *J* 6.6, NCC**H**H′), 1.06 (1H, d, *J* 6.6, NCCH**H′**), 1.30 (3H, s, NCCC**H$_3$**), 1.86 (1H, ddd, *J* 16.2, 11.6, 1.5, OCH_2C**H**H′), 2.26 (1H, dd, *J* 16.2, 4.6, OCH_2CH**H′**), 3.72 (1H, br s, O**H**), 4.25 (1H, ddd, *J* 11.8, 4.6, 1.5, OC**H**H′), 4.63 (1H, app. t, *J* 11.8, OCH**H′**), 6.14 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 17.2 (NCC**C**H$_3$), 29.2 (NC**C**), 29.4 (NC**C**H$_2$), 38.7 (OCH_2**C**H$_2$), 68.5 (N**C**), 69.8 (O**C**H$_2$); Accurate mass (ESI^+): Found 216.0300: $C_6H_{11}NNaO_4S$ (MNa^+) requires 216.0301.

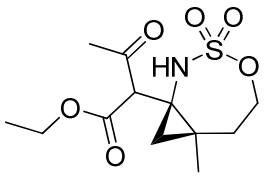
1-(Ethyloxy)-7-methyl-4-oxa-3-thia-2-azabicyclo[5.1.0]octane 3,3-dioxide (229)



To a stirred solution of cyclopropane **207** (43 mg, 0.183 mmol) in ethanol (15 mL) was added sodium hydroxide (146 mg, 3.66 mmol) at room temperature after 30 min TLC analysis showed the reaction to be complete. The residue was diluted with water (20mL), acidified with 1.0 M aq. HCl (5 mL) and extracted with DCM (3 × 30mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo.* Purification by column chromatography (2:1 petrol:ethyl acetate) afforded the title compound (33 mg, 82%) as a white crystalline solid, R_f 0.15 (2:1 petrol:ethyl acetate); m.p. 123–126 °C; ν_{max}/cm^{-1} (thin film) 3708br, 2981s, 2844m, 1417m, 1370s, 1213m, 1166m; δ_H (400 MHz, $CDCl_3$) 0.89 (1H, d, *J* 5.7, NCC**H**H′), 0.92 (1H, d, *J* 5.7, NCCH**H′**), 1.23 (3H, t, *J* 7.0, OCH_2C**H$_3$**), 1.32 (3H, s, NCCC**H$_3$**), 1.87 (1H, ddd, *J* 16.2, 11.0, 2.0, OCH_2C**H**H′), 2.29 (1H, ddd, *J* 16.2, 5.0, 1.1, OCH_2CH**H′**), 3.41 (1H, dq, *J* 9.0, 7.0, COC**H**H′), 3.84 (1H, dq, *J* 9.0, 7.0, COCH**H′**), 4.21 (1H, ddd, *J* 12.1, 5.0, 2.0, SOC**H**H′), 4.64 (1H, ddd, *J* 12.1, 11.0, 1.1, SOCH**H′**), 5.93

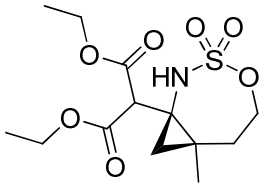
(1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 15.1 ($OCH_2\mathbf{C}H_3$), 18.0 ($NCC\mathbf{C}H_3$), 29.2 ($NC\mathbf{C}H_2$), 30.9 (NC**C**), 39.1 ($OCH_2\mathbf{C}H_2$), 61.9 ($CO\mathbf{C}H_2$), 69.2 ($SO\mathbf{C}H_2$), 72.8 (N**C**); Accurate mass (ESI^+): Found 244.0615: $C_8H_{15}NNaO_4S$ (MNa^+) requires 244.0614.

Ethyl-2-(7-methyl-3,3-dioxido-4-oxa-3-thia-2-azabicyclo[5.1.0]oct-1-yl)-3-oxobutanoate (230)



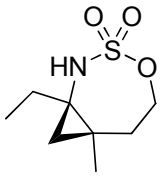
To a stirred solution of ethyl acetoacetate (28 mg, 0.21 mmol) in THF (2 mL) was added NaH (9 mg of a 60% suspension in mineral oil, 0.21 mmol) at 0 °C. After 15 min cyclopropane **207** (30 mg, 0.105 mmol) was added and the solution was allowed to warm to r.t. and stirred for 18 h. The reaction was quenched with water (2 mL), acidified with 1.0 M aq. HCl (0.5 mL) and extracted with ether (3 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (1:1 petrol:ether) afforded the title compound (26 mg, 77%) as a mixture of inseparable diatereomers A and B (A:B 2.4:1); R_f 0.16 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3301br, 2983s, 1716s, 1619m, 1414s, 1178s; δ_H (400 MHz, $CDCl_3$) 0.69 (1H, d, *J* 6.9, NCCH**H′** A), 0.88 (1H, d, *J* 6.6, NCCH**H′** B), 1.29 (3H, s, NCCC**H$_3$** B), 1.29 (3H, s, NCCC**H$_3$** A), 1.30 (3H, t, *J* 7.1, $OCH_2C\mathbf{H_3}$, B), 1.31 (3H, t, *J* 7.1, $OCH_2C\mathbf{H_3}$, A), 1.47 (1H, d, *J* 6.6, NCC**H**H′ B), 1.74 (1H, d, *J* 6.9, NCC**H**H′ A), 2.06–2.13 (1H, m, $SOCH_2CH$**H′** A & B), 2.29 (3H, d, *J* 1.0, O=CC**H$_3$** A), 2.33 (3H, d, *J* 1.0, O=CC**H$_3$** B), 2.41 (1H, app. dd, *J* 16.4, 8.7, $SOCH_2C\mathbf{H}$H′ A & B), 3.26 (1H, d, *J* 1.0, NCC**H** A), 3.64 (1H, br s, NCC**H** B), 4.07–4.15 (1H, m, SOCH**H′** A &B), 4.19–4.28 (2H, m, OC**H$_2$** A & B), 4.33–4.38 (1H, m, SOC**H**H′ A &B), 6.08 (1H, br s, N**H** B), 6.12 (1H, br s, N**H** A); δ_C (100 MHz, $CDCl_3$, A only) 13.9 ($OCH_2\mathbf{C}H_3$), 22.0 ($NCC\mathbf{C}H_3$), 24.9 ($NC\mathbf{C}H_2$), 28.7 (NC**C**), 29.4 ($O{=}C\mathbf{C}H_3$), 37.1 ($SOCH_2\mathbf{C}H_2$), 41.9 (N**C**), 62.1 ($O{=}CO\mathbf{C}H_2$), 63.5 (NC**C**H), 67.2 ($SO\mathbf{C}H_2$), 168.6 (O=**C**O), 202.43 (O=**C**); Accurate mass (ESI^+): Found 328.0822: $C_{12}H_{19}NNaO_6S$ (MNa^+) requires 328.0825.

Diethyl-(7-methyl-3,3-dioxido-4-oxa-3-thia-2-azabicyclo[5.1.0]oct-1-yl) malonate (231)



To a stirred solution of diethyl malonate (37 mg, 0.23 mmol) in THF (2 mL) was added NaH (9 mg of a 60% suspension in mineral oil, 0.23 mmol) at 0 ℃. After 15 min cyclopropane **207** (27 mg, 0.115 mmol) was added and the solution was allowed to warm to r.t. and stirred for 18 h. The reaction was quenched with water (2 mL), acidified with 1.0 M aq. HCl (0.5 mL) and extracted with ether (3 x 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (2:1 petrol:ether) afforded the title compound (25 mg, 65%) as a colourless oil; R_f 0.20 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3313br, 2984s, 1729s, 1391s, 1369s, 1313s, 1238s, 1175s; δ_H (500 MHz, $CDCl_3$) 0.71 (1H, d, *J* 6.3, NCCH**H′**), 1.30 (6H, td, *J* 7.1, 5.1, $OCH_2C\mathbf{H_3}$), 1.36 (1H, app. s, NCC**H**H′), 1.37 (3H, s, $NCCC\mathbf{H_3}$), 2.11 (1H, ddd, *J* 16.2, 8.8, 1.3, $SOCH_2CH\mathbf{H'}$), 2.43 (1H, ddd, *J* 16.2, 7.6, 1.1 $SOCH_2C\mathbf{H}H'$), 3.24 (1H, s, NCC**H**), 4.12 (1H, ddd, *J* 12.3, 7.6, 1.3, SOCH**H′**), 4.19–4.42 (2H, m, COC**H**H′), 4.26–4.31 (2H, m, COC**H**H′), 4.43 (1H, ddd, *J* 12.3, 8.8, 1.1, SOC**H**H′), 6.24 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 13.8 ($CH_2\mathbf{C}H_3$), 21.5 ($NCC\mathbf{C}H_3$), 27.2 ($NC\mathbf{C}H_2$), 29.4 (NC**C**), 38.5 ($SOCH_2\mathbf{C}H_2$), 41.9 (N**C**), 56.1 (NC**C**H), 61.8 ($CO\mathbf{C}H_2$), 67.7 ($SO\mathbf{C}H_2$), 167.1 (O=**C**), 168.7 (O=**C**); Accurate mass (ESI^+): Found 358.0925: $C_{13}H_{21}NNaO_7S$ (MNa^+) requires 358.0931.

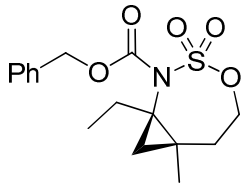
1-Ethyl-7-methyl-4-oxa-3-thia-2-azabicyclo[5.1.0]octane 3,3-dioxide (232)



To a stirred solution of cyclopropane **207** (70 mg, 0.30 mmol) in THF (10 mL) was added ethylmagnesium bromide (0.90 mL of a 1.0 M solution in THF, 0.90 mmol) at 0 ℃. The

reaction was allowed to warm to r.t. and stirring continued for 20 h. The reaction was quenched with sat. aq. NH_4Cl solution (10 mL) and extracted with ether (3 × 20 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (5:1 petrol:ethyl acetate) afforded the title compound (42 mg, 69%) as a white crystalline solid; R_f 0.48 (2:1 petrol:ethyl acetate); m.p. 86–88 °C; ν_{max}/cm^{-1} (thin film) 3299br, 2962s, 1421s, 1332s, 1164s, 1105m; δ_H (500 MHz, $CDCl_3$) 0.57 (1H, d, *J* 5.5, NCC**H**H′), 0.80 (1H, dd, *J* 5.5, 1.9, NCCH**H′**), 0.94–1.01 (1H, m, CH_3C**H**H′), 1.04 (3H, t, *J* 6.9, CH_2C**H_3**), 1.24 (3H, s, NCCC**H_3**), 2.03 (1H, ddd, *J* 16.1, 11.0, 1.6, OCH_2C**H**H′), 2.27 (1H, dd, *J* 16.1, 4.7, OCH_2CH**H′**), 2.34–2.42 (1H, m, CH_3CH**H′**), 4.19 (1H, ddd, *J* 12.0, 4.7, 1.6, SOC**H**H′), 4.57 (1H, dd, *J* 12.0, 11.0, SOCH**H′**), 5.13 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 10.0 (CH_2**C**H_3), 19.3 (NCC**C**H_3), 25.7 (CH_3**C**H_2), 29.3 (NC**C**), 29.8 (NC**C**H_2), 40.5 (OCH_2**C**H_2), 44.0 (N**C**), 69.0 (SO**C**H_2); Accurate mass (ESI^+): Found 228.0667: $C_8H_{15}NNaO_3S$ (MNa^+) requires 228.0665.

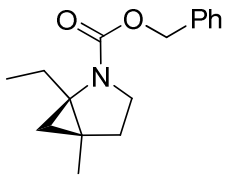
Benzyl-1-ethyl-7-methyl-4-oxa-3-thia-2-azabicyclo[5.1.0]octane-2-carboxylate-3,3-dioxide (233)



To a stirred solution of cyclopropane **232** (131 mg, 0.63 mmol) in THF (5 mL) at 0 °C was added NaH (76 mg of a 60% suspension in mineral oil, 1.91 mmol). After 45 min benzyl chloroformate (0.16 mL, 1.91 mmol) was added and the reaction allowed to warm to r.t. over 18 h. The reaction was quenched with water (10 mL) and extracted with ether (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (2:1 petrol:ether) afforded the title compound (177 mg, 83%) as a colourless oil; R_f 0.19 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3065s, 3032s,

2971s, 1733s, 1497m, 1455s; δ_H (500 MHz, $CDCl_3$) 0.91 (1H, d, *J* 6.6, NCC**H**H′), 1.05 (3H, t, *J* 7.4, $CH_2C\mathbf{H_3}$), 1.10 (1H, d, *J* 6.6, NCCH**H′**), 1.27 (3H, s, $NCCC\mathbf{H_3}$), 1.68 (1H, app. quin, *J* 7.4 $CH_3C\mathbf{H}$H′), 1.86 (1H, app. quin, *J* 7.4 CH_3CH**H′**), 2.00 (1H, ddd, *J* 15.0, 13.3, 6.1, $SOCH_2C\mathbf{H}$H′), 2.13 (1H, dd, *J* 15.0, 4.0, $SOCH_2CH$**H′**), 4.50 (1H, ddd, *J* 13.3, 11.2, 4.0, SOC**H**H′), 4.59 (1H, dd, *J* 11.2, 6.1, SOCH**H′**), 5.28 (1H, d, *J* 12.5, PhC**H**H′), 5.33 (1H, d, *J* 12.5, PhCH**H′**), 7.33–7.43 (5H, m, Ar**H**); δ_C (125 MHz, $CDCl_3$) 10.4 ($CH_2\mathbf{C}H_3$), 17.8 ($NCC\mathbf{C}H_3$), 24.8 (NC**C**), 27.0 ($CH_3\mathbf{C}H_2$), 30.2 ($NC\mathbf{C}H_2$), 35.5 ($SOCH_2\mathbf{C}H_2$), 48.4 (N**C**), 68.9 ($PH\mathbf{C}H_2$), 71.0 ($SO\mathbf{C}H_2$), 127.9 (Ar), 128.3 (Ar), 128.6 (Ar), 134.9 (Ar), 152.7 (O=**C**); Accurate mass (ESI^+): Found 362.1037: $C_{16}H_{21}NNaO_5S$ (MNa^+) requires 362.1033.

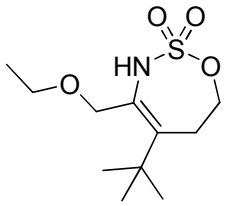
Benzyl 1-ethyl-5-methyl-2-azabicyclo[3.1.0]hexane-2-carboxylate (234)



To a stirred solution of sulfamate **233** (39 mg, 0.115 mmol) in DMF (1 mL) was added NaI (26 mg, 0.172 mmol) and the reaction mixture was heated to 60 °C for 2h. The reaction was cooled to r.t. before the addition of NaH (14 mg of a 60% suspension in mineral oil, 0.345 mmol) and stirring continued for 3 h. The reaction was quenched with water (2 mL) and 1.0 M aq. HCl (0.1 mL) and extracted with ether (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (4:1 petrol:ether) afforded the title compound (23 mg, 77%) as a colourless oil; R_f 0.29 (4:1 petrol:ether); v_{max}/cm^{-1} (thin film) 3063m, 3033m, 2966s, 2874s, 1705s, 1497m, 1455s; δ_H (500 MHz, DMSO-d_6, 363K) 0.55 (1H, d, *J* 4.7, NCC**H**H′), 0.76 (1H, d, *J* 4.7, NCCH**H′**), 1.05 (3H, t, *J* 7.4, $CH_2C\mathbf{H_3}$), 1.14 (1H, app. quin, *J* 7.4 $CH_3C\mathbf{H}$H′), 1.19 (3H, s, $NCCC\mathbf{H_3}$), 1.83–1.89 (1H, m, $NCH_2C\mathbf{H}$H′), 1.95–2.00 (1H, m, NCH_2CH**H′**), 2.56 (1H, app. quin, *J* 7.4 CH_3CH**H′**), 3.25–3.31 (1H, m, NC**H**H′), 4.59 (1H, ddd, *J* 10.9, 9.9, 5.4, NCH**H′**), 5.08 (1H, d, *J* 12.8, PhC**H**H′), 5.11 (1H, d, *J* 12.8, PhCH**H′**), 7.31–7.39 (5H, m, Ar**H**); δ_C (125 MHz, DMSO-d_6, 363K) 10.9 ($CH_2\mathbf{C}H_3$), 18.7 ($NCC\mathbf{C}H_3$), 23.1 ($CH_3\mathbf{C}H_2$), 27.0

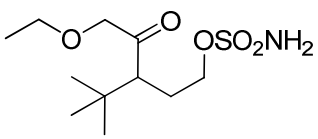
(NC**C**H_2), 28.5 (NC**C**), 33.1 (NCH_2**C**H_2), 47.9 (N**C**H_2), 51.1 (N**C**), 66.2 (PH**C**H_2), 127.8 (Ar), 128.1 (Ar), 128.8 (Ar), 137.8 (Ar), 153.9 (O=**C**); Accurate mass (ESI$^+$): Found 282.1466: $C_{16}H_{21}NNaO_2$ (MNa^+) requires 282.1465.

5-*tert*-Butyl-4-(ethoxymethyl)-6,7-dihydro-3*H*-1,2,3-oxathiazepine 2,2-dioxide (235)



To a solution of MA **211** (57 mg, 0.26 mmol) in ethanol (2 mL) was carefully added conc. sulfuric acid (0.3 mL) dropwise and the reaction was stirred for 48 h. The reaction was neutralised with 2.0 M aq. NaOH solution (5 mL) and extracted with ether (3 × 20 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (3:1 petrol:ether → ether) afforded the title compound (20 mg, 29%) as a colourless oil; R_f 0.29 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3291br, 2971s, 2875m, 1643w, 1394s, 1353s; δ_H (500 MHz, $CDCl_3$) 1.18 (9H, s, C(C**H**$_3$)$_3$), 1.23 (3H, t, *J* 6.9, CH_2C**H**$_3$), 2.74 (2H, t, *J* 4.8, SOCH_2C**H**$_2$), 3.53 (2H, q, *J* 6.9, CH_3C**H**$_2$), 4.28 (1H, s, NCC**H**$_2$), 4.37 (2H, t, *J* 4.8, SOC**H**$_2$), 6.71 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 15.1 (CH_2**C**H_3), 30.4 (C(**C**H_3)$_3$), 31.3 (SOCH_2**C**H_2), 36.0 (**C**(CH_3)$_3$), 66.5 (CH_3**C**H_2), 68.4 (NC**C**H_2), 71.9 (SO**C**H_2), 128.3 (NC=**C**), 138.6 (N**C**); Accurate mass (ESI$^+$): Found 286.1089: $C_{11}H_{21}NNaO_4S$ (MNa^+) requires 286.1083.

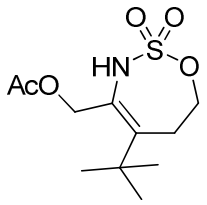
3-*tert*-Butyl-5-ethoxy-4-oxopentyl sulfamate (236)



Side product from the treatment of MA **211** with sulfuric acid. Purification by column chromatography (3:1 petrol:ether → ether) afforded the title compound (13 mg, 18%) as a colourless oil; R_f 0.19 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3285br, 2965s, 1720s, 1474s,

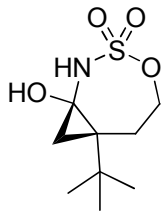
1368s; δ_H (500 MHz, $CDCl_3$) 0.97 (9H, s, C(C**H$_3$**)$_3$), 1.26 (3H, t, *J* 7.1, CH_2C**H$_3$**), 1.89 (1H, dddd, *J* 14.4, 7.1, 5.0, 2.3, SOCH_2C**H**H′), 2.20 (1H, dddd, *J* 14.4, 11.4, 6.9, 4.7, SOCH_2CH**H′**), 2.61 (1H, dd, *J* 11.4, 2.3, O=CC**H**), 3.59 (1H, dq, *J* 9.3, 7.1, COC**H**H′), 3.64 (1H, dq, *J* 9.3, 7.1, COCH**H′**), 4.12–4.18 (2H, m, SOC**H$_2$**), 4.17 (2H, s, O=CC**H$_2$**), 5.06 (2H, br s, N**H$_2$**); δ_C (125 MHz, $CDCl_3$) 14.9 (CH_2**C**H_3), 27.5 (SOCH_2**C**H_2), 27.7 (C(**C**H_3)$_3$), 33.6 (**C**(CH_3)$_3$), 53.2 (O=C**C**H), 67.2 (CH_3**C**H_2), 70.0 (SO**C**H_2), 78.0 (O=C**C**H_2), 211.6 (O=**C**); Accurate mass (ESI^+): Found 304.1194: $C_{11}H_{23}NNaO_5S$ (MNa^+) requires 304.1189.

8-(3-{[*tert*-Butyl(diphenyl)silyl]oxy}propyl)-7-methyl-3,3-dioxido-4-oxa-3-thia-2-azabicyclo[5.1.0]oct-1-yl acetate (237)



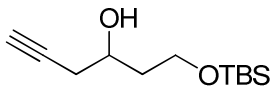
To a stirred solution of MA **211** (29 mg, 0.13 mmol) in acetonitrile (4 mL) at r.t. was added tetrabutylammonium acetate (80 mg, 0.27 mmol). After 2 h the solvent was removed *in vacuo* and the residue partitioned between ether (20 mL) and water (15 mL). The organic layer was separated, dried over $MgSO_4$ and concentrated *in vacuo* to give the title compound (19 mg, 51%) as a colourless oil without the need for purification; R_f 0.22 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3279br, 2963s, 1732s, 1372s; δ_H (400 MHz, $CDCl_3$) 1.23 (9H, s, C(C**H$_3$**)$_3$), 2.11 (3H, s, O=CC**H$_3$**), 2.72 (2H, t, *J* 4.8, SOCH_2C**H$_2$**), 4.35 (2H, t, *J* 4.8, SOC**H$_2$**), 4.84 (1H, s, NCC**H$_2$**), 6.49 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 20.9 (O=C**C**H_3), 30.1 (C(**C**H_3)$_3$), 32.0 (SOCH_2**C**H_2), 36.6 (**C**(CH_3)$_3$), 63.7 (NC**C**H_2), 71.1 (SO**C**H_2), 126.8 (NC=**C**), 144.7 (N**C**), 171.4 (O=**C**); Accurate mass (ESI^+): Found 300.0885: $C_{11}H_{19}NNaO_5S$ (MNa^+) requires 300.0876.

7-(1,1-Dimethylethyl)-4-oxa-3-thia-2-azabicyclo[5.1.0]octan-1-ol 3,3-dioxide (238)



To a stirred solution of MA **211** (47 mg, 0.21 mmol) in DMF (1.5 mL) was added NaI (32 mg, 0.21 mmol) at r.t. After 20 h the reaction was quenched with sat. aq. NH_4Cl solution (5 mL) and extracted with ether (3 × 20 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purifiaction by column chromatography (2:1 petrol:ether) afforded the title compound (20 mg, 41%) as a white crystalline solid; R_f 0.12 (2:1 petrol:ethyl acetate); m.p. 129–132 °C; ν_{max}/cm^{-1} (thin film) 3460s, 3180br, 2958s, 1457s, 1265s, 1144s; δ_H (400 MHz, $CDCl_3$) 0.75 (1H, d, *J* 6.2, NCC**H**H′), 1.12 (9H, s, C(C**H**$_3$)$_3$), 1.47 (1H, d, *J* 6.2, NCCH**H′**), 1.67 (1H, ddd, *J* 17.0, 11.2, 1.6, OCH_2C**H**H′), 2.69 (1H, dd, *J* 17.0, 5.3, OCH_2CH**H′**), 3.61 (1H, br s, O**H**), 4.27 (1H, ddd, *J* 12.3, 5.3, 1.6, OC**H**H′), 4.76 (1H, app. t, *J* 11.8, OCH**H′**), 6.05 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) 26.7 (NC**C**H$_2$), 29.8 (C(**C**H$_3$)$_3$), 34.1 (**C**(CH$_3$)$_3$), 36.3 (OCH_2**C**H$_2$), 40.1 (NC**C**), 71.1 (O**C**H$_2$), 71.8 (N**C**); Accurate mass (ESI^+): Found 258.0769: $C_9H_{17}NNaO_4S$ (MNa^+) requires 258.0770.

1-(*tert*-Butyldimethylsilyloxy)hex-5-yn-3-ol (241)

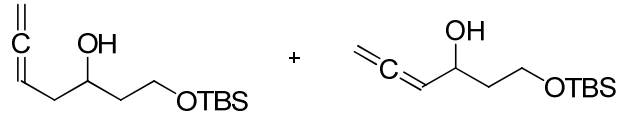


To a stirred solution of aldehyde **149** (2.66g, 14.1 mmol) in THF (125 mL) was added propargyl bromide (4.71 mL, 42.3 mmol) and activated zinc powder (2.76 g, 42.3 mmol) at 10 °C followed by dropwise addition of sat. aq. NH_4Cl solution (25 mL). The mixture was allowed to warm to r.t. and stirring continued for 2 h. The mixture was then filtered through Celite® and washed with DCM (100 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (5:1 petrol:ether) afforded the title compound

(2.95g, 71%) as a colourless oil; R_f 0.22 (5:1 petrol:ether); v_{max}/cm^{-1} (thin film) 3314br, 2930s, 2858s, 2131w, 1472s, 1362m, 1256s; δ_H (500 MHz, $CDCl_3$) 0.09 (6H, s, Si(C**H$_3$**)$_2$), 0.91 (9H, s, SiC(C**H$_3$**)$_3$), 1.73–1.87 (2H, m, SiOCH$_2$C**H$_2$**), 2.04 (1H, t, *J* 2.7, ≡C**H**), 2.41 (2H, app. ddq, *J* 16.7, 6.0, 2.7, ≡CC**H$_2$**), 3.58 (1H, d, *J* 2.8, O**H**), 3.82–3.87 (1H, m, SiOCH**H′**), 3.91–3.95 (1H, m, SiOC**H**H′), 3.99–4.04 (1H, m, HOC**H**); δ_C (125 MHz, $CDCl_3$) –5.6 (Si(**C**H$_3$)$_2$), 20.4 (Si**C**(CH$_3$)$_3$), 25.8 (SiC(**C**H$_3$)$_3$), 27.0 (≡C**C**H$_2$), 37.1 (SiOCH$_2$**C**H$_2$), 62.3 (SiO**C**H$_2$), 70.2 (≡**C**H), 70.4 (HO**C**H), 81.1 (≡**C**CH$_2$); Accurate mass (ESI$^+$): Found 251.1434: $C_{12}H_{24}NaO_2Si$ (MNa^+) requires 251.1438.

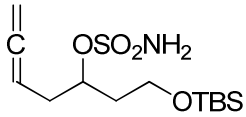
1-(*tert*-Butyldimethylsilyloxy)hepta-5,6-dien-3-ol (242) and

1-(*tert*-Butyldimethylsilyloxy)hexa-4,5-dien-3-ol (243)



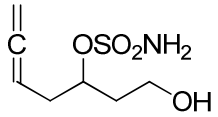
To a stirred soultion of alcohol **241** (2.26 g, 9.90 mmol) in THF (100 mL) was added diisopropylamine (2.78 mL, 19.8 mmol) and paraformaldehyde (744 mg, 24.8 mmol) before the portionwise addition of CuI (942 mg, 4.95 mmol). The reaction mixture was heated at reflux for 16 h before cooling, filtration through Celite® and concentration *in vacuo*. The residue was partitioned between water (30 mL) and ether (50 mL) before acidification with 1.0 M aq. HCl (10 mL). The layers were separated and the aqueous phase extracted with ether (2 × 50 mL) before the combined organic extracts were washed successively with water (50 mL) and brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The title compounds were taken on without further purification.

1-(*tert*-Butyldimethylsilyloxy)hepta-5,6-dien-3-yl sulfamate (244)



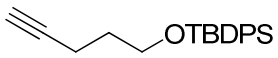
The reaction of alcohols **242** and **243** according to general procedure H and purification by column chromatography (2:1 petrol:ether) afforded the title compound (55 mg, 5% over 2 steps) as a colourless oil; R_f 0.19 (2:1 petrol:ether); δ_H (500 MHz, $CDCl_3$) 0.08 (6H, s, Si(C**H**$_3$)$_2$), 0.91 (9H, s, SiC(C**H**$_3$)$_3$), 1.90–1.94 (2H, m, SiOCH$_2$C**H**$_2$), 2.49–2.54 (2H, m, =CHC**H**$_2$), 3.78 (2H, t, *J* 5.7, SiOC**H**$_2$), 4.73 (2H, dt, *J* 6.6, 2.7, =C**H**$_2$), 4.84 (1H, app. quin, *J* 5.8, SOC**H**), 4.86 (2H, br s, N**H**$_2$), 5.13 (1H, app. quin, *J* 7.1, =C**H**); δ_C (125 MHz, $CDCl_3$) –5.3 (Si(**C**H$_3$)$_2$), 18.2 (Si**C**(CH$_3$)$_3$), 25.8 (SiC(**C**H$_3$)$_3$), 34.1 (=CH**C**H$_2$), 36.2 (SiOCH$_2$**C**H$_2$), 58.2 (SiO**C**H$_2$), 75.2 (=**C**H$_2$), 80.8 (SO**C**H), 84.5 (=**C**H), 209.8 (=**C**=); Accurate mass (ESI$^+$): Found 344.1312: $C_{13}H_{27}NNaO_4SSi$ (MNa$^+$) requires 344.1322.

1-Hydroxyhepta-5,6-dien-3-yl sulfamate (245)



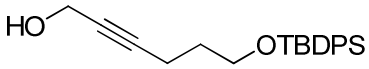
To a solution of sulfamate **244** (20 mg, 0.031 mmol) in THF (2 mL) was added TBAF (0.18 mL of a 1.0 M solution in THF). After 30 min the reaction was quenched with water (3 mL), extracted with ether (3 × 5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (1:1 petrol:ethyl acetate) afforded the title compound (13 mg, quant.) as a colourless oil; R_f 0.24 (1:1 petrol:ethyl acetate); ν_{max}/cm^{-1} (thin film) 3404br, 2956s, 2928s, 2856m, 1949w, 1464m,1259s; δ_H (500 MHz, $CDCl_3$) 1.88–2.00 (2H, m, HOCH$_2$C**H**$_2$), 2.49–2.53 (2H, m, =CHC**H**$_2$), 3.76–3.86 (2H, m, HOC**H**$_2$), 4.83–4.86 (2H, m, SOC**H**), 4.75 (1H, dt, *J* 6.8, 2.7, =C**H**$_2$), 5.13 (1H, app. quin, *J* 6.8, =C**H**) 5.21 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 34.2 (=CH**C**H$_2$), 36.2 (HOCH$_2$**C**H$_2$), 58.3 (HO**C**H$_2$), 75.3 (=**C**H$_2$), 80.5 (SO**C**H), 84.4 (=**C**H), 209.8 (=**C**=); Accurate mass (ESI$^+$): Found 230.0460: $C_7H_{13}NNaO_4S$ (MNa$^+$) requires 230.0457.

tert-Butyl(pent-4-ynyloxy)diphenylsilane[181] (246)



To a stirred solution of 4-pentyn-1-ol (1.25 mL, 13.4 mmol) in DMF (20 mL) was added imidazole (2.10 g, 29.5 mmol) and *tert*-butylchlorodiphenylsilane (3.83 mL, 14.7 mmol) at r.t.. After 5 h the reaction mixture was diluted with ether (50 mL) and sat. aq. NH_4Cl solution (30 mL), the layers were separated and the aqueous phase extracted with ether (3 × 50 mL). The combined organic extracts were washed with water (3 × 50 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the crude product (4.40 mg, quant.) as a colourless oil without the need for further purification; δ_H (400 MHz, $CDCl_3$) 1.08 (9H, s, $C(CH_3)_3$), 1.81 (2H, tt, *J* 7.0, 6.0, OCH_2CH_2), 1.94 (1H, t, *J* 2.6, ≡C**H**), 2.38 (2H, td, *J* 7.0, 2.6, ≡CCH_2), 3.78 (2H, t, *J* 6.0, OCH_2), 7.39–7.48 (6H, m, Ar**H**), 7.69–7.76 (4H, m, Ar**H**); δ_C (100 MHz, $CDCl_3$) 15.0 (≡CCH_2), 19.2 (Si**C**$(CH_3)_3$), 26.8 ($C(CH_3)_3$), 31.4 (OCH_2CH_2), 62.3 (OCH_2), 68.3 (≡**C**H), 84.3 (≡**C**), 127.6 (Ar), 129.6 (Ar), 133.8 (Ar), 135.6 (Ar).

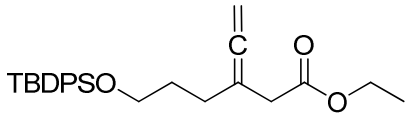
6-(_tert_-Butyldiphenylsilyloxy)hex-2-yn-1-ol[182] (247)



To a stirred solution of alkyne **246** (4.01 g, 12.4 mmol) in ether (80 mL) at –78 °C was added *n*-butyllithium (7.8 mL of a 1.6 M solution in hexanes, 12.4 mmol) dropwise. After 20 min the reaction was warmed to 0 °C before recooling and paraformaldehyde (4.0 g, 133.0 mmol) added. The mixture was then allowed to warm to r.t. and stirred for 18 h. The reaction was quenched with sat. aq. $NaHCO_3$ solution (30 mL) and extracted with ether (3 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (4:1 petrol:ether) afforded the title compound (2.91 g, 67%) as a colourless oil; δ_H (400 MHz, $CDCl_3$) 1.08 (9H, s, $C(CH_3)_3$), 1.78 (2H, tt, *J* 7.0, 6.0, $SiOCH_2CH_2$), 2.39 (2H, td, *J* 7.0, 2.0, ≡CCH_2), 3.76 (2H, t, *J* 6.0, $SiOCH_2$), 4.22 (2H, t, *J* 2.0, $HOCH_2$), 7.39–7.47 (6H, m, Ar**H**), 7.68–7.71 (4H, m, Ar**H**); δ_C (100 MHz, $CDCl_3$) 15.3 (≡CCH_2), 19.2 (Si**C**$(CH_3)_3$), 26.8 ($C(CH_3)_3$), 31.4

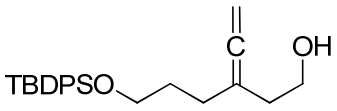
($OCH_2\mathbf{C}H_2$), 51.4 ($HO\mathbf{C}H_2$), 62.3 ($SiO\mathbf{C}H_2$), 78.5 (≡**C**), 86.1 (≡**C**), 127.6 (Ar), 129.6 (Ar), 133.8 (Ar), 135.6 (Ar).

Ethyl 6-(*tert*-butyldiphenylsilyloxy)-3-vinylidenehexanoate (248)



The reaction of alcohol **247** according to general procedure F and purification by column chromatography (10:1 petrol:ether) afforded the title compound (1.18 g, 56%) as a colourless oil; R_f 0.46 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3071m, 2932s, 1961s, 1737s, 1589m, 1427s, 1428s, 1390s; δ_H (400 MHz, $CDCl_3$) 1.05 (9H, s, $C(C\mathbf{H_3})_3$), 1.27 (3H, t, *J* 7.2, $OCH_2C\mathbf{H_3}$), 1.69–1.76 (2H, m, $=CCH_2C\mathbf{H_2}$), 2.09–2.16 (2H, m, $=CC\mathbf{H_2}CH_2$), 2.98 (2H, t, *J* 2.6, $O=CC\mathbf{H_2}$), 3.69 (2H, t, *J* 6.3, $SiOC\mathbf{H_2}$), 4.16 (2H, q, *J* 7.2, $COC\mathbf{H_2}$), 4.72 (2H, app. ddd, *J* 5.9, 3.4, 2.6, $=C\mathbf{H_2}$), 7.36–7.45 (6H, m, Ar**H**), 7.67 (4H, dd, *J* 7.8, 1.4, Ar**H**); δ_C (100 MHz, $CDCl_3$) 14.3 ($OCH_2\mathbf{C}H_3$), 19.2 ($Si\mathbf{C}(CH_3)_3$), 26.8 ($C(\mathbf{C}H_3)_3$), 27.9 ($SiOCH_2CH_2\mathbf{C}H_2$), 30.3 ($SiOCH_2\mathbf{C}H_2$), 38.9 ($O=C\mathbf{C}H_2$), 60.7 ($CO\mathbf{C}H_2$), 63.3 ($SiO\mathbf{C}H_2$), 76.4 ($=\mathbf{C}H_2$), 97.1 (=**C**), 127.6 (Ar), 129.5 (Ar), 134.0 (Ar), 135.6 (Ar), 171.2 (O=**C**), 206.3 (=**C**=); Accurate mass (ESI^+): Found 445.2176: $C_{26}H_{34}NaO_3Si$ (MNa^+) requires 445.2169.

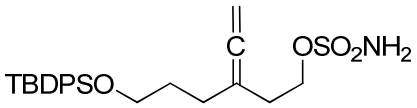
6-(*tert*-Butyldiphenylsilyloxy)-3-vinylidenehexan-1-ol (249)



The reduction of ester **248** according to general procedure G afforded the title compound (980 mg, 92%) as a colourless oil without the need for further purification; R_f 0.19 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3354br, 3070s, 2931s, 1956s, 1589s, 1472s, 1427s, 1389s, 1361s; δ_H (400 MHz, $CDCl_3$) 1.06 (9H, s, $C(C\mathbf{H_3})_3$), 1.72 (2H, tt, *J* 7.6, 6.3, $=CCH_2C\mathbf{H_2}$), 2.07 (2H, tt, *J* 7.6, 3.3, $=CC\mathbf{H_2}CH_2$), 2.21 (2H, tt, *J* 6.1, 3.3, $HOCH_2C\mathbf{H_2}$), 3.70 (2H, t, *J* 6.3, $SiOC\mathbf{H_2}$), 3.74 (2H, t, *J* 6.1, $HOC\mathbf{H_2}$), 4.73 (2H, quin, *J* 3.3, $=C\mathbf{H_2}$), 7.37–7.46

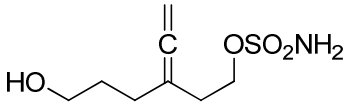
(6H, m, Ar**H**), 7.68 (4H, dd, *J* 6.8, 1.5, Ar**H**); δ_C (100 MHz, $CDCl_3$) 19.2 (Si**C**$(CH_3)_3$), 26.9 (C(**C**$H_3)_3$), 28.4 ($SiOCH_2CH_2$**C**H_2), 30.3 ($SiOCH_2$**C**H_2), 35.5 ($HOCH_2$**C**H_2), 60.7 (HO**C**H_2), 63.3 (SiO**C**H_2), 76.7 (=**C**H_2), 100.0 (=**C**), 127.6 (Ar), 129.5 (Ar), 134.0 (Ar), 135.6 (Ar), 205.3 (=**C**=); Accurate mass (ESI^+): Found 403.2059: $C_{24}H_{32}NaO_2Si$ (MNa^+) requires 403.2064.

6-(*tert*-Butyldiphenylsilyloxy)-3-vinylidenehexyl sulfamate (250)



The reduction of ester **249** according to general procedure H and purification by column chromatography (1:1 petrol:ether) afforded the title compound (323 mg, 76%) as a colourless oil; R_f 0.15 (2:1 petrol:ether); v_{max}/cm^{-1} (thin film) 3290br, 3071m, 2931s, 2858s, 1958s, 1558m, 1472s, 1428s, 1371s; δ_H (400 MHz, $CDCl_3$) 1.06 (9H, s, C(C**H$_3$**$)_3$), 1.67–1.74 (2H, m, $=CCH_2C$**H$_2$**), 2.07 (2H, tt, *J* 7.0, 3.3, $=CC$**H$_2$**CH_2), 2.37 (2H, tt, *J* 7.0, 3.3, $SOCH_2C$**H$_2$**), 3.70 (2H, t, *J* 6.2, SiOC**H$_2$**), 4.29 (2H, t, *J* 7.0, SOC**H$_2$**), 4.69 (2H, br s, N**H$_2$**), 4.73 (2H, quin, *J* 3.3, =C**H$_2$**), 7.37–7.46 (6H, m, Ar**H**), 7.67 (4H, dd, *J* 7.5, 1.4, Ar**H**); δ_C (100 MHz, $CDCl_3$) 19.2 (Si**C**$(CH_3)_3$), 26.9 (C(**C**$H_3)_3$), 28.4 ($SiOCH_2CH_2$**C**H_2), 30.2 ($SiOCH_2$**C**H_2), 31.1 ($SOCH_2$**C**H_2), 63.2 (SiO**C**H_2), 69.4 (SO**C**H_2), 77.5 (=**C**H_2), 98.4 (=**C**), 127.6 (Ar), 129.5 (Ar), 133.9 (Ar), 135.6 (Ar), 205.3 (=**C**=); Accurate mass (ESI^+): Found 458.1810: $C_{24}H_{32}NO_4SSi$ $(M-H)^-$ requires 458.1827.

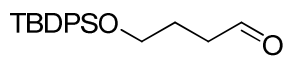
6-Hydroxy-3-vinylidenehexyl sulfamate (251)



To a stirred solution of sulfamate **250** (1.00 g, 2.18 mmol) in acetonitrile (20 mL) at 0 °C was added fluorosilicic acid (0.39 mL of a 25% aq. solution, 0.66 mmol). After 4 h the reaction was quenched with sat. aq. $NaHCO_3$ solution (20 mL) and extracted with ethyl

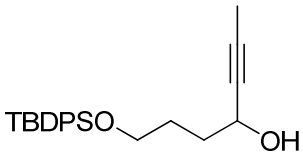
acetate (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (ether) afforded the title compound (264 mg, 55%) as a colourless oil; R_f 0.21 (ether); ν_{max}/cm^{-1} (thin film) 3344br, 2944s, 1958m, 1568m, 1366s, 1179s; δ_H (500 MHz, $CDCl_3$) 1.73 (2H, tt, *J* 7.3, 6.3, $HOCH_2C\mathbf{H_2}$), 2.10 (2H, tt, *J* 7.3, 3.3, $HOCH_2CH_2C\mathbf{H_2}$), 2.42 (2H, tt, *J* 6.6, 3.3 $SOCH_2C\mathbf{H_2}$), 3.70 (2H, t, *J* 6.3, $HOC\mathbf{H_2}$), 4.32 (2H, t, *J* 6.6, $SOC\mathbf{H_2}$), 4.79 (2H, quin, *J* 3.3, $=C\mathbf{H_2}$), 4.96 (2H, br s, $N\mathbf{H_2}$); δ_C (125 MHz, $CDCl_3$) 28.1 ($HOCH_2CH_2\mathbf{C}H_2$), 30.1 ($HOCH_2\mathbf{C}H_2$), 31.3 ($SOC\mathbf{C}H_2$), 62.1 ($HO\mathbf{C}H_2$), 69.4 ($SO\mathbf{C}H_2$), 77.5 ($=\mathbf{C}H_2$), 98.4 (=**C**), 205.5 (=**C**=); Accurate mass (ESI^+): Found 244.0612: $C_8H_{15}NNaO_4S$ (MNa^+) requires 458.1827.

4-(*tert*-Butyldiphenylsilyloxy)butanal[183] (252)



Synthesised according to a literature procedure.

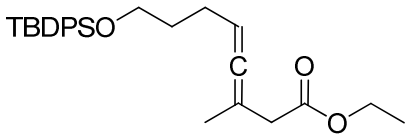
7-(*tert*-Butyldiphenylsilyloxy)hept-2-yn-4-ol (253)



To a stirred solution of 1-bromoprop-1-ene (1.08 mL, 12.6 mmol) in THF (50 mL) at –78 °C was added dropwise *n*-butyllithium (15.7 mL of a 1.6 M solution in hexanes, 25.2 mmol). After 2 h a solution of aldehyde **252** (3.93 g, 12.6 mmol) in THF (20 mL) was added *via* canula and after 1 h stirring at –78 °C the reaction mixture was allowed to warm to r.t.. The reaction was quenched with sat. aq. NH_4Cl solution (30 mL) and extracted with ether (3 × 70 mL). The combined organic extracts were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (5:1 → 2:1 petrol:ether) afforded the title compound (3.05 g, 77%) as a colourless oil; R_f 0.18 (5:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3386br, 3071s, 2857s, 2241m, 1589s, 1472s, 1427s; δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, $C(C\mathbf{H_3})_3$), 1.70–1.84 (4H, m, $SiOCH_2C\mathbf{H_2}$ overlays $SiOCH_2CH_2C\mathbf{H_2}$),

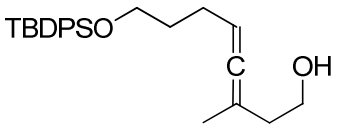
1.86 (3H, d, *J* 2.0, ≡CC**H$_3$**), 2.57 (1H, br s, O**H**), 3.69–3.73 (2H, m, SiOC**H$_2$**), 4.42 (1H, br s, HOC**H**), 7.39–7.47 (6H, m, Ar**H**), 7.68–7.71 (4H, m, Ar**H**); δ_C (100 MHz, $CDCl_3$) 3.6 (≡C**C**H$_3$), 19.1 (Si**C**(CH$_3$)$_3$, 26.8 (SiC(**C**H$_3$)$_3$, 28.3 (SiOCH$_2$**C**H$_2$), 35.2 (SiOCH$_2$CH$_2$**C**H$_2$), 62.5 (HO**C**H), 63.9 (SiO**C**H$_2$), 80.4 (≡**C**), 80.9 (≡**C**) 127.7 (Ar), 129.7 (Ar), 133.6 (Ar), 135.6 (Ar); Accurate mass (ESI$^+$): Found 389.1908: $C_{23}H_{30}NaO_2Si$ (MNa$^+$) requires 389.1907.

Ethyl 8-(*tert*-butyldiphenylsilyloxy)-3-methylocta-3,4-dienoate (254)



The reaction of alcohol **253** according to general procedure F afforded the title compound (4.10 g, 93%) as a colourless oil without the need for purification; R_f 0.30 (40:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3071s, 2932s, 1969m, 1737s, 1589s, 1472s, 1428s; δ_H (400 MHz, $CDCl_3$) 1.06 (9H, s, C(C**H$_3$**)$_3$), 1.25 (3H, t, *J* 7.1, COCH$_2$C**H$_3$**), 1.67 (2H, tt, *J* 7.3, 6.5, SiOCH$_2$C**H$_2$**), 1.72 (3H, d, *J* 2.5, =CC**H$_3$**), 2.09 (2H, app. q, *J* 7.3, =CHC**H$_2$**), 2.93 (2H, d, *J* 2.5, O=CC**H$_2$**), 3.70 (2H, t, *J* 6.5, OSiC**H$_2$**), 4.14 (2H, q, *J* 7.1, COC**H$_2$**), 5.12 (1H, app. oct, *J* 2.5, =C**H**), 7.37–7.43 (6H, m, Ar**H**), 7.68 (4H, dd, *J* 6.6, 0.8, Ar**H**); δ_C (100 MHz, $CDCl_3$) 14.2 (CH$_2$**C**H$_3$), 19.1 (=C**C**H$_3$), 19.2 (Si**C**(CH$_3$)$_3$), 25.1 (SiOCH$_2$CH$_2$**C**H$_2$), 26.9 (SiC(**C**H$_3$)$_3$), 31.7 (SiOCH$_2$**C**H$_2$), 40.5 (O=C**C**H$_2$), 60.5 (CH$_3$**C**H$_2$), 63.3 (SiO**C**H$_2$), 90.5 (=**C**H), 93.6 (=**C**), 127.6 (Ar), 129.5 (Ar), 134.0 (Ar), 135.6 (Ar) 171.3 (O=**C**), 202.8 (=**C**=); Accurate mass (ESI$^+$): Found 459.2326: $C_{27}H_{36}NaO_3Si$ (MNa$^+$) requires 459.2326.

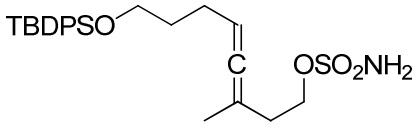
8-(*tert*-Butyldiphenylsilyloxy)-3-methylocta-3,4-dien-1-ol (255)



The reduction of ester **254** according to general procedure G and purification by column chromatography (3:1 petrol:ether) afforded the title compound (3.20 g, 88%) as a colourless oil; R_f 0.32 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3389br, 3030s, 2984s, 1948s,

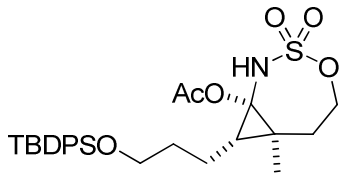
1618m, 1485s, 1462s, 1442s; δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, C(C**H**$_3$)$_3$), 1.65–1.72 (5H, m, SiOCH$_2$C**H**$_2$ overlays =CC**H**$_3$), 2.10 (2H, q, *J* 7.0, =CHC**H**$_2$), 2.18 (2H, td, *J* 6.0, 3.0, HOCH$_2$C**H**$_2$), 3.69–3.73 (4H, m, SiOC**H**$_2$ overlays HOC**H**$_2$), 5.12 (1H, app. oct, *J* 3.0, =C**H**) 7.37–7.45 (6H, m, Ar**H**), 7.65–7.71 (4H, m, Ar**H**); δ_C (100 MHz, $CDCl_3$) 19.2 (Si**C**(CH$_3$)$_3$, 19.5 (=C**C**H$_3$), 25.5 (SiOCH$_2$CH$_2$**C**H$_2$), 26.9 (SiC(**C**H$_3$)$_3$), 32.0 (SiOCH$_2$**C**H$_2$), 37.1 (HOCH$_2$**C**H$_2$), 60.7 (HO**C**H$_2$), 63.3 (SiO**C**H$_2$), 90.8 (=**C**H), 96.5 (=**C**), 127.6 (Ar), 129.5 (Ar), 134.0 (Ar), 135.6 (Ar), 201.1 (=**C**=); Accurate mass (ESI$^+$): Found 417.2221: $C_{25}H_{34}NaO_2Si$ (MNa$^+$) requires 417.2220.

8-(*tert*-Butyldiphenylsilyloxy)-3-methylocta-3,4-dienyl sulfamate (256)



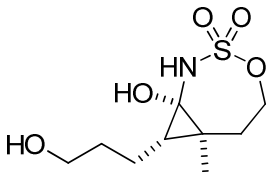
The reaction of alcohol **255** according to general procedure H and purification by column chromatography (2:1 petrol:ether) afforded the title compound (1.32 g, 82%) as a colourless oil; R_f 0.36 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3287br, 3071m, 2932s, 1965s, 1588s, 1558m, 1472s, 1428s, 1364s; δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, C(C**H**$_3$)$_3$), 1.68–1.73 (5H, m, SiOCH$_2$C**H**$_2$ overlays =CC**H**$_3$), 2.07 (2H, dt, *J* 7.3, 7.0, =CHC**H**$_2$), 2.35 (2H, td, *J* 6.6, 2.1, SOCH$_2$C**H**$_2$), 3.71 (2H, t, *J* 6.3, SiOC**H**$_2$), 4.25 (2H, t, *J* 6.6, SOC**H**$_2$), 4.78 (2H, br s, N**H**$_2$), 5.11–5.16 (1H, app. oct, *J* 3.0, =C**H**) 7.38–7.44 (6H, m, Ar**H**), 7.68 (4H, d, *J* 7.2, Ar**H**); δ_C (100 MHz, $CDCl_3$) 19.2 (Si**C**(CH$_3$)$_3$), 19.4 (=C**C**H$_3$), 25.2 (SiOCH$_2$CH$_2$**C**H$_2$), 26.9 (SiC(**C**H$_3$)$_3$), 31.7 (SiOCH$_2$**C**H$_2$), 32.9 (SOCH$_2$**C**H$_2$), 63.5 (SiO**C**H$_2$), 69.3 (SO**C**H$_2$), 91.5 (=**C**H), 95.1 (=**C**), 127.7 (Ar), 129.6 (Ar), 133.9 (Ar), 135.6 (Ar), 201.3 (=**C**=); Accurate mass (ESI$^+$): Found 496.1952: $C_{25}H_{35}NNaO_4SSi$ (MNa$^+$) requires 496.1948.

8-(3-{[*tert*-Butyl(diphenyl)silyl]oxy}propyl)-7-methyl-3,3-dioxido-4-oxa-3-thia-2-azabicyclo[5.1.0]oct-1-yl acetate (257)



The reaction of sulfamate **256** according to general procedure I and purification by column chromatography (2:1 petrol:ether) afforded the title compound (51 mg, 17%) as a colourless oil; R_f 0.30 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3292br, 2932s, 2858s, 1745s, 1471s, 1427s; δ_H (500 MHz, $CDCl_3$) 1.05 (9H, s, C(C**H**$_3$)$_3$), 1.17 (3H, s, NCCC**H**$_3$), 1.20–1.27 (2H, m, NCC**H** overlays $SiOCH_2CH_2CHH'$), 1.37–1.45 (1H, m, $SiOCH_2CH_2CHH'$), 1.55–1.65 (2H, m, $SiOCH_2CH_2$), 1.81 (1H, ddd, *J* 16.0, 11.4, 1.8, $SOCH_2CHH'$), 2.08 (3H, s, O=CC**H**$_3$), 2.19 (1H, dd, *J* 16.0, 4.4, $SOCH_2CHH'$), 3.57–3.69 (2H, m, $SiOCH_2$), 4.22 (1H, ddd, *J* 12.0, 4.4, 1.8, $SOCHH'$), 4.64 (1H, app. t, *J* 11.7, $SOCHH'$), 6.58 (1H, br s, N**H**) 7.36–7.44 (6H, m, Ar**H**), 7.64 (4H, dd, *J* 7.9, 1.3, Ar**H**); δ_C (125 MHz, $CDCl_3$) 12.4 (NCC**C**H_3), 19.2 (Si**C**$(CH_3)_3$), 20.1 ($SiOCH_2CH_2$**C**H_2), 20.8 (O=C**C**H_3), 26.9 (SiC(**C**$H_3)_3$), 28.8 (NC**C**), 31.5 ($SiOCH_2$**C**H_2), 38.4 (NC**C**H), 40.7 ($SOCH_2$**C**H_2), 63.4 (SiO**C**H_2), 69.0 (SO**C**H_2), 71.1 (N**C**), 127.6 (Ar), 129.6 (Ar), 133.8 (Ar), 135.5 (Ar), 171.4 (O=**C**); Accurate mass (ESI$^+$): Found 554.1987: $C_{27}H_{37}NNaO_6SSi$ (MNa^+) requires 554.2003.

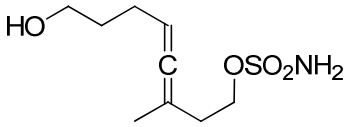
8-(3-Hydroxypropyl)-7-methyl-4-oxa-3-thia-2-azabicyclo[5.1.0]octan-1-ol 3,3-dioxide (259)



To a stirred solution of cyclopropane **257** (29 mg, 0.054 mmol) in THF (1 mL) at 0 °C was added dropwise tetrabutylammonium fluoride (65 µL of a 1.0 M solution in THF, 0.065 mmol). After 30 min the reaction was quenched with water (2 mL) and extracted with ethyl

acetate (3 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (ether) afforded the title compound (7 mg, 52%) as a colourless oil; R_f 0.19 (ether); ν_{max}/cm^{-1} (thin film) 3416br, 2918s, 2850m, 1552s, 1432m, 1413s; δ_H (500 MHz, $CDCl_3$) 0.99 (1H, dd, *J* 9.3, 4.6, NCC**H**), 1.17 (3H, s, NCCC**H$_3$**), 1.47–1.76 (5H, m, $SiOCH_2C\mathbf{H_2}$ overlays $SiOCH_2CH_2C\mathbf{H_2}$ and $CH_2O\mathbf{H}$), 1.89 (1H, dd, *J* 16.0, 12.0, $SOCH_2C\mathbf{H}H'$), 2.25 (1H, dd, *J* 16.0, 4.6, $SOCH_2CH\mathbf{H'}$), 3.70 (2H, t, *J* 5.0, $HOC\mathbf{H_2}$), 4.00 (1H, br s, NCO**H**), 4.24 (1H, ddd, *J* 12.0, 4.6, 1.7, SOC**H**H′), 4.63 (1H, app. t, *J* 12.0, SOCH**H′**), 6.23 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 12.4 (NCC**C**H$_3$), 18.9 ($SiOCH_2CH_2\mathbf{C}H_2$), 29.4 (NC**C**), 31.5 ($SiOCH_2\mathbf{C}H_2$), 37.4 (NC**C**H), 40.4 ($SOCH_2\mathbf{C}H_2$), 61.6 ($HO\mathbf{C}H_2$), 68.8 (N**C**), 69.6 ($SO\mathbf{C}H_2$); Accurate mass (ESI^+): Found 274.0719: $C_9H_{17}NNaO_{51}S$ (MNa^+) requires 274.0720.

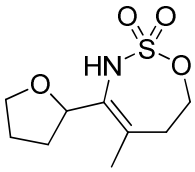
8-Hydroxy-3-methylocta-3,4-dienyl sulfamate (260)



To a stirred solution of sulfamate **256** (1.03 g, 2.18 mmol) in THF (35 mL) at 0 °C was added dropwise TBAF (2.4 mL of a 1.0 M solution in THF, 2.40 mmol). After 1 h the reaction was quenched with water (30 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (1:1 petrol:ethyl acetate) afforded the title compound (500 mg, 97%) as a colourless oil; R_f 0.17 (1:1 petrol:ethyl acetate); ν_{max}/cm^{-1} (thin film) 3356br, 2938s, 1966s, 1565s, 1443m, 1335s; δ_H (500 MHz, $CDCl_3$) 1.65–1.81 (2H, m, $HOCH_2C\mathbf{H_2}$ overlays 3H, d, *J* 3.0, =CC**H$_3$**), 2.03–2.09 (2H, m, =CHC**H$_2$**), 2.31 (1H, dtd, *J* 15.6, 6.4, 3.0, $SOCH_2C\mathbf{H}H'$), 2.43 (1H, dtd, *J* 15.6, 6.4, 3.0, $SOCH_2CH\mathbf{H'}$), 3.68–3.72 (2H, m, $HOC\mathbf{H_2}$), 4.28 (2H, td, *J* 6.4, 0.8, $SOC\mathbf{H_2}$), 5.15 (1H, app. oct, *J* 3.0, =C**H**), 5.50 (2H, br s, N**H$_2$**); δ_C (125 MHz, $CDCl_3$), 19.2 (=C**C**H$_3$), 24.8 ($HOCH_2CH_2\mathbf{C}H_2$), 31.1 ($HOCH_2\mathbf{C}H_2$), 33.0 ($SOCH_2\mathbf{C}H_2$), 62.1 ($HO\mathbf{C}H_2$), 68.6 ($SO\mathbf{C}H_2$), 91.1 (=**C**H), 95.5 (=**C**),

201.5 (=**C**=); Accurate mass (ESI$^+$): Found 258.0774: $C_9H_{17}NNaO_4S$ (MNa^+) requires 258.0770.

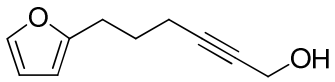
5-Methyl-4-(tetrahydrofuran-2-yl)-6,7-dihydro-3*H*-1,2,3-oxathiazepine 2,2-dioxide (261)



Method A: The reaction of sulfamate **260** according to general procedure I and purification by column chromatography (1:1 petrol:ether → ether) afforded the title compound (71 mg, 33%) as a colourless oil.

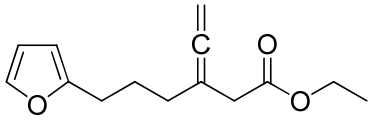
Method B: To a stirred solution of sulfamate **260** (140 mg, 0.59 mmol) in benzene (8 mL) was added $Rh_2(esp)_2$ (9 mg, 0.012 mmol) and $PhI(OPiv)_2$ (287 mg, 0.71 mmol). After 20 h MgO (50 mg) was added and the reaction mixture was filtered through Celite®. Concentration *in vacuo* followed by purification by column chromatography (1:1 petrol:ether → ether) afforded the title compound (65 mg, 47%) as a colourless oil; R_f 0.19 (ether); ν_{max}/cm^{-1} (thin film) 3287br, 2965s, 1715s, 1403s; δ_H (500 MHz, $CDCl_3$) 1.78 (3H, s, C**H$_3$**), 1.91–1.98 (2H, m, OCH_2C**H**H′ overlays OCH_2CH_2C**H**H′), 2.00–2.06 (1H, m, $COCH_2CH$**H′**), 2.07–2.11 (1H, m, $COCH_2CH_2CH$**H′**), 2.34 (1H, ddd, *J* 16.6, 6.7, 1.8, $SOCH_2C$**H**H′), 2.86 (1H, ddd, *J* 16.6, 9.1, 2.2, 1.7, $SOCH_2CH$**H′**), 3.82–3.87 (1H, m, COC**H**H′), 3.97 (1H, dt, *J* 8.0, 6.9, COC**H**H′), 4.39 (1H, ddd, *J* 11.7, 9.1, 1.8, SOC**H**H′), 4.46 (1H, ddd, *J* 11.7, 6.7, 2.2, SOCH**H′**), 4.62 (1H, dd, *J* 7.6, 7.2, COC**H**), 6.40 (1H, br s, N**H$_2$**); δ_C (125 MHz, $CDCl_3$), 19.4 (**C**H_3), 26.3 ($COCH_2$**C**H_2), 29.7 (OCH_2CH_2**C**H_2), 35.8 ($SOCH_2$**C**H_2), 69.1 (O**C**H_2), 70.2 (SO**C**H_2), 76.0 (O**C**H), 125.5 (NC**C**), 129.4 (N**C**); Accurate mass (ESI$^+$): Found 256.0610: $C_9H_{15}NNaO_4S$ (MNa^+) requires 256.0614.

6-(Furan-2-yl)hex-2-yn-1-ol (262)



To a stirred solution of propargyl alcohol (1.05 mL, 18.0 mmol) in HMPA (15mL) and THF (100 mL) at –78 °C was added dropwise *n*-butyllithium (22.4 mL of a 1.6 M solution in hexanes, 35.9 mmol). After 45 min 2-(3-iodopropyl)furan (2.12 g, 9.0 mmol) was added and the reaction mixture allowed to warm to r.t.. After 18 h the reaction was quenched with sat. aq. NH_4Cl solution (20 mL) and extracted with ether (3 × 100 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (4:1 petrol:ether) afforded the title compound (866 mg, 59%) as a colourless oil; R_f 0.18 (4:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3346br, 2937s, 2866s, 2287m, 2225s, 1596s, 1507s, 1430s; δ_H (400 MHz, $CDCl_3$) 1.86 (2H, tt, *J* 7.4, 7.0, $FuCH_2C\mathbf{H_2}$), 2.27 (2H, tt, *J* 7.0, 2.1, $FuCH_2CH_2C\mathbf{H_2}$), 2.74 (2H, t, *J* 7.4, $FuC\mathbf{H_2}$), 4.26 (2H, br s, $HOC\mathbf{H_2}$), 6.02 (1H, dd, *J* 3.1, 0.9, Fu**H**), 6.29 (1H, dd, *J* 3.1, 1.9, Fu**H**), 7.31 (1H, dd, *J* 1.9, 0.9, Fu**H**); δ_C (100 MHz, $CDCl_3$) 18.1 ($FuCH_2CH_2\mathbf{C}H_2$), 26.9 ($Fu\mathbf{C}H_2$), 30.0 ($FuCH_2\mathbf{C}H_2$), 51.3 ($HO\mathbf{C}H_2$), 78.9 (≡**C**), 85.7 (≡**C**), 105.2 (Fu), 110.1 (Fu), 141.0 (Fu), 155.2 (Fu); *m/z* (GCMS, Cl^+) 165 (MH^+, 100%), 164 (50), 147 (40), 135 (40), 119 (36), 94 (58), 81 (32); Accurate mass: Found 165.0915: $C_{10}H_{13}O_2$ (MH^+) requires 165.0916.

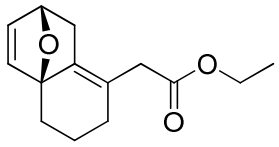
Ethyl 6-(furan-2-yl)-3-vinylidenehexanoate (263)



The reaction of alcohol **262** according to general procedure F and purification by column chromatography (50:1 → 4:1 petrol:ether) afforded the title compound (314 mg, 24%) as a colourless oil; R_f 0.42 (10:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 2982s, 2938s, 1961s, 1737s, 1596m, 1507s, 1445m, 1367s; δ_H (500 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.1, $OCH_2C\mathbf{H_3}$), 1.80 (2H, tt, *J* 7.6, 7.3, $FuCH_2C\mathbf{H_2}$), 2.07 (2H, tt, *J* 7.3, 3.4, $FuCH_2CH_2C\mathbf{H_2}$), 2.67 (2H, t, *J* 7.6, $FuC\mathbf{H_2}$), 2.99 (2H, t, *J* 2.7, $O{=}CC\mathbf{H_2}$), 4.16 (2H, q, *J* 7.1, $OC\mathbf{H_2}$), 4.78 (2H, tt, *J* 3.4, 2.7,

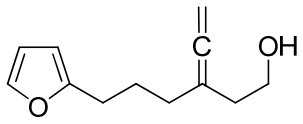
=C**H**$_2$), 5.99 (1H, dd, *J* 3.1, 0.8, Fu**H**), 6.28 (1H, dd, *J* 3.1, 1.9, Fu**H**), 7.30 (1H, dd, *J* 1.8, 0.9, Fu**H**); δ_C (125 MHz, $CDCl_3$) 14.2 ($OCH_2\mathbf{C}H_3$), 25.7 ($FuCH_2CH_2\mathbf{C}H_2$), 27.4 (Fu**C**H$_2$), 30.9 ($FuCH_2\mathbf{C}H_2$), 38.7 (O=C**C**H$_2$), 60.7 (O**C**H$_2$), 76.5 (=**C**H$_2$), 96.9 (=**C**), 104.8 (Fu), 110.0 (Fu), 140.8 (Fu), 155.9 (Fu), 171.2 (O=**C**), 206.9 (=**C**=); *m/z* (GCMS, Cl^+) 252 (MNH_4^+, 28%), 235 (MH^+, 90), 205 (100), 167 (72), 161 (38); Accurate mass: Found 235.1335: $C_{14}H_{19}O_3$ (MH^+) requires 235.1334.

Ethyl 1,5,6,7-tetrahydro-2*H*-2,4a-epoxynaphthalen-8-ylacetate (264)



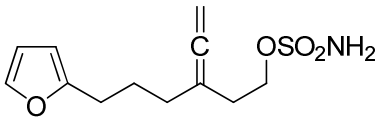
Formed as the side product in the reaction of alcohol **262** according to general procedure F and purification by column chromatography (2:1 petrol:ether) afforded the title compound (246 mg, 30%) as a colourless oil; R_f 0.19 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 2939s, 2865s, 2838m, 1734s, 1620m, 1601m, 1449s, 1366s; δ_H (500 MHz, $CDCl_3$) 1.24 (3H, t, *J* 7.1, C**H$_3$**), 1.69–1.80 (2H, m, OCC**H**H′ overlays $OCCH_2C\mathbf{H}H'$), 1.91 (1H, d, *J* 14.0, OCHC**H**H′), 1.99–2.04 (1H, m, OCCH**H′**), 2.11–2.14 (2H, m, $OCCH_2CH_2C\mathbf{H_2}$), 2.25–2.31 (1H, m, $OCCH_2CH\mathbf{H'}$), 2.46 (1H, ddd, *J* 14.0, 4.5, 2.2, OCHCH**H′**), 2.95 (2H, d, *J* 3.8, O=CC**H$_2$**), 4.11 (2H, q, *J* 7.1, OC**H$_2$**), 5.02 (1H, dd, *J* 4.5, 1.8, OC**H**), 6.28 (1H, d, *J* 5.7, OCC**H**), 6.35 (1H, ddd, *J* 5.7, 1.8, 1.0, OCHC**H**); δ_C (125 MHz, $CDCl_3$) 14.2 (**C**H$_3$), 20.8 (OC**C**H$_2$), 26.9 ($OCCH_2\mathbf{C}H_2$), 28.9 ($OCCH_2CH_2\mathbf{C}H_2$), 30.9 ($OCH\mathbf{C}H_2$), 40.1 (O=C**C**H$_2$), 60.5 (O**C**H$_2$), 77.4 (O**C**H), 85.9 (O**C**), 123.0 (=**C**$(CH_2)_2$), 133.6 (=**C**), 135.6 (OC**C**H), 135.7 (OCH**C**H), 171.3 (O=**C**); Accurate mass (ESI^+): Found 257.1149: $C_{14}H_{18}NaO_3$ (MNa^+) requires 257.1148.

6-(Furan-2-yl)-3-vinylidenehexan-1-ol (265)



The reduction of ester **263** according to general procedure G and purification by column chromatography (2:1 petrol:ether) afforded the title compound (220 mg, 92%) as a colourless oil; R_f 0.26 (2:1 petrol:ether); v_{max}/cm^{-1} (thin film) 3384br, 2940s, 1956s, 1596m, 1507s, 1433s; δ_H (500 MHz, $CDCl_3$) 1.80 (2H, tt, *J* 7.6, 7.1, $FuCH_2C\mathbf{H_2}$), 2.06 (2H, tt, *J* 7.1, 3.3, $FuCH_2CH_2C\mathbf{H_2}$), 2.22 (2H, tt, *J* 6.1, 3.3, $HOCH_2C\mathbf{H_2}$), 2.66 (2H, t, *J* 7.6, $FuC\mathbf{H_2}$), 3.75 (2H, t, *J* 6.1, $HOC\mathbf{H_2}$), 4.78 (2H, quin, *J* 3.3, $=C\mathbf{H_2}$), 5.99 (1H, dd, *J* 3.0, 0.6, Fu**H**), 6.28 (1H, dd, *J* 3.0, 1.8, Fu**H**), 7.30 (1H, dd, *J* 1.8, 0.6, Fu**H**); δ_C (125 MHz, $CDCl_3$) 25.8 ($FuCH_2\mathbf{C}H_2$), 27.4 ($Fu\mathbf{C}H_2$), 31.5 ($FuCH_2CH_2\mathbf{C}H_2$), 35.3 ($HOCH_2\mathbf{C}H_2$), 60.7 ($HO\mathbf{C}H_2$), 77.2 ($=\mathbf{C}H_2$), 99.7 (=**C**), 104.8 (Fu), 110.0 (Fu), 140.8 (Fu), 155.9 (Fu), 205.4 (=**C**=); *m/z* (GCMS, Cl^+) 193 (MH^+, 100%), 191 (55), 175 (30), 163 (70); Accurate mass: Found 193.1237: $C_{12}H_{17}O_2$ (MH^+) requires 193.1229.

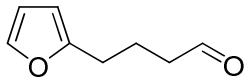
6-(Furan-2-yl)-3-vinylidenehexyl sulfamate (266)



The reaction of alcohol **265** according to general procedure H and purification by column chromatography (4:1 petrol:ethyl acetate) afforded the title compound (90 mg, 32%) as a colourless oil, R_f 0.21 (4:1 petrol:ethyl acetate); v_{max}/cm^{-1} (thin film) 3247br, 2964s, 1951m, 1561m, 1463s, 1363s, 1179s; δ_H (500 MHz, $CDCl_3$) 1.80 (2H, tt, *J* 7.4, 7.1, $FuCH_2C\mathbf{H_2}$), 2.02 (2H, tt, *J* 7.1, 3.3, $FuCH_2CH_2C\mathbf{H_2}$), 2.40 (2H, tt, *J* 6.9, 3.3, $SOCH_2C\mathbf{H_2}$), 2.66 (2H, t, *J* 7.4, $FuC\mathbf{H_2}$), 4.30 (2H, t, *J* 6.9, $SOC\mathbf{H_2}$), 4.79 (2H, quin, *J* 3.3, $=C\mathbf{H_2}$), 6.00 (1H, dd, *J* 3.1, 0.8, Fu**H**), 6.29 (1H, dd, *J* 3.1, 1.7, Fu**H**), 7.31 (1H, dd, *J* 1.7, 0.8, Fu**H**); δ_C (125 MHz, $CDCl_3$) 25.7 ($FuCH_2\mathbf{C}H_2$), 27.3 ($Fu\mathbf{C}H_2$), 31.0 ($SOCH_2\mathbf{C}H_2$), 31.5 ($FuCH_2CH_2\mathbf{C}H_2$), 69.3

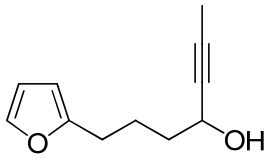
(SO**C**H_2), 77.5 (=**C**H_2), 98.2 (=**C**), 104.9 (Fu), 110.1 (Fu), 140.8 (Fu), 155.9 (Fu), 205.4 (=**C**=); Accurate mass (ESI^+): Found 294.0764: $C_{12}H_{17}NNaO_4S$ (MNa^+) requires 294.0770.

4-(Furan-2-yl)butanal[15] (267)



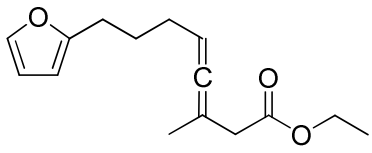
Synthesised according to a literature procedure.

7-(Furan-2-yl)hept-2-yn-4-ol (268)



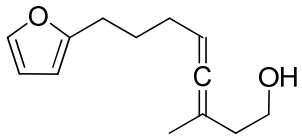
To a stirred solution of 1-bromoprop-1-ene (0.31 mL, 3.63 mmol) in THF (15 mL) at –78 °C was added dropwise *n*-butyllithium (4.54 mL of a 1.6 M solution in hexanes, 7.26 mmol). After 2 h a solution of aldehyde **267** (501 mg, 3.63 mmol) in THF (15 mL) was added *via* canula and after 1 h stirring at –78 °C the reaction mixture was allowed to warm to r.t.. The reaction was quenched with sat. aq. NH_4Cl solution (15 mL) and extracted with ether (3 × 20 mL). The combined organic extracts were washed with brine (15 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (2:1 petrol:ether) afforded the title compound (660 mg, quant.) as a colourless oil; R_f 0.24 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3404br, 2921s, 2222m, 1672s, 1596s, 1507s, 1440s; δ_H (400 MHz, $CDCl_3$) 1.69–1.75 (2H, m, FuCH_2C**H$_2$**), 1.77–1.84 (2H, m, FuCH_2CH_2C**H$_2$**), 1.85 (3H, d, *J* 2.0, ≡CC**H$_3$**), 2.64 (2H, t, *J* 7.4, FuC**H$_2$**), 4.34–4.28 (1H, m, HOC**H**), 6.00–6.01 (1H, m, Fu**H**), 6.28–6.29 (1H, m, Fu**H**), 7.30 (1H, d, *J* 1.0, Fu**H**); δ_C (100 MHz, $CDCl_3$) 3.5 (≡C**C**H_3), 23.7 (FuCH_2**C**H_2), 27.6 (Fu**C**H_2), 37.4 (FuCH_2CH_2**C**H_2), 62.4 (HO**C**H), 80.2 (≡**C**), 81.2 (≡**C**), 104.9 (Fu), 110.0 (Fu), 140.8 (Fu), 155.9 (Fu); Accurate mass (ESI^+): Found 201.0884: $C_{11}H_{14}NaO_2$ (MNa^+) requires 201.0886.

Ethyl 8-(furan-2-yl)-3-methylocta-3,4-dienoate (269)



The reaction of alcohol **268** according to general procedure F and purification by column chromatography (40:1 → 20:1 petrol:ether) afforded the title compound (527 mg, 76%) as a colourless oil; R_f 0.27 (30:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 2937s, 1973m, 1737s, 1596m, 1507m,1443m; δ_H (500 MHz, $CDCl_3$) 1.26 (3H, t, *J* 7.2, $OCH_2C\mathbf{H_3}$), 1.75 (2H, app. quin, *J* 7.3, $FuCH_2C\mathbf{H_2}$), 1.77 (3H, d, *J* 3.0, $=CC\mathbf{H_3}$), 2.03 (2H, q, 7.3, $FuCH_2CH_2C\mathbf{H_2}$), 2.66 (2H, t, *J* 7.6, $FuC\mathbf{H_2}$), 2.97 (2H, d, *J* 3.0, $O=CC\mathbf{H_2}$), 4.14 (2H, qd, *J* 7.2, 1.1, $CH_3C\mathbf{H_2}$), 5.11 (1H, app. dec, 3.0, =C**H**), 5.99 (1H, dd, *J* 3.0, 1.0, Fu**H**), 6.28 (1H, dd, *J* 3.0, 1.9, Fu**H**), 7.30 (1H, d, *J* 1.0, Fu**H**); δ_C (125 MHz, $CDCl_3$) 14.2 ($CH_2\mathbf{C}H_3$), 19.1 ($=C\mathbf{C}H_3$), 27.3 ($FuCH_2\mathbf{C}H_2$), 27.3 ($Fu\mathbf{C}H_2$), 28.2 ($FuCH_2CH_2\mathbf{C}H_2$), 40.5 ($O=C\mathbf{C}H_2$), 60.6 ($CH_3\mathbf{C}H_2$), 90.2 (=**C**H), 93.7 (=**C**), 104.8 (Fu), 110.0 (Fu), 140.7 (Fu), 156.1 (Fu), 171.3 (O=**C**), 202.9 (=**C**=); Accurate mass (ESI^+): Found 271.1306: $C_{15}H_{20}NaO_3$ (MNa^+) requires 271.1305.

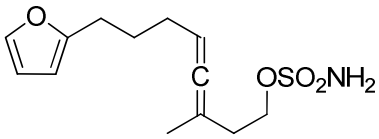
8-(Furan-2-yl)-3-methylocta-3,4-dien-1-ol (270)



The reduction of ester **269** according to general procedure G afforded the title compound (1.39 g, quant.) as a colourless oil without the need for purification; R_f 0.22 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3362br, 2934s, 1964s, 1596s, 1507s, 1441s; δ_H (500 MHz, $CDCl_3$) 1.72 (3H, d, *J* 3.0, $=CC\mathbf{H_3}$), 1.75 (2H, app. quin, *J* 7.4, $FuCH_2C\mathbf{H_2}$), 2.04 (2H, app. q, 7.1, $FuCH_2CH_2C\mathbf{H_2}$), 2.22 (2H, td, *J* 6.1, 3.0, $HOCH_2C\mathbf{H_2}$), 2.67 (2H, t, *J* 7.6, $FuC\mathbf{H_2}$), 3.73 (2H, t, *J* 6.1, $HOC\mathbf{H_2}$), 5.12 (1H, app. dec, 3.0, =C**H**), 5.99 (1H, dd, *J* 3.0, 1.0, Fu**H**), 6.28 (1H, dd, *J* 3.0, 1.9, Fu**H**), 7.29 (1H, d, *J* 1.0, Fu**H**); δ_C (125 MHz, $CDCl_3$) 19.4 ($=C\mathbf{C}H_3$), 27.3 ($FuCH_2\mathbf{C}H_2$), 27.5 ($Fu\mathbf{C}H_2$), 28.6 ($FuCH_2CH_2\mathbf{C}H_2$), 37.1 ($HOCH_2\mathbf{C}H_2$), 60.7 ($HO\mathbf{C}H_2$), 90.6

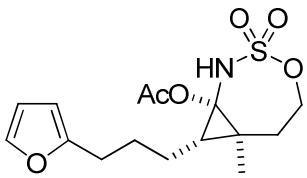
(=**C**H), 96.5 (=**C**), 104.8 (Fu), 110.0 (Fu), 140.7 (Fu), 156.0 (Fu), 201.3 (=**C**=); Accurate mass (ESI^+): Found 229.1203: $C_{13}H_{18}NaO_2$ (MNa^+) requires 229.1199.

8-(Furan-2-yl)-3-methylocta-3,4-dienyl sulfamate (271)



The reaction of alcohol **270** according to general procedure H and purification by column chromatography (2:1 petrol:ether) afforded the title compound (469 mg, 63%) as a colourless oil; R_f 0.31 (1:1 petrol:ether); v_{max}/cm^{-1} (thin film) 3290br, 2934s, 2859s, 1966s, 1595m, 1555m, 1507m, 1441s, 1367s; δ_H (500 MHz, $CDCl_3$) 1.73 (3H, d, *J* 3.0, =CC**H$_3$**), 1.75 (2H, app. quin, *J* 7.5, FuCH$_2$C**H$_2$**), 2.03 (2H, app. q, 7.5, FuCH$_2$CH$_2$C**H$_2$**), 2.39 (2H, td, *J* 7.0, 3.0, SOCH$_2$C**H$_2$**) 2.67 (2H, t, *J* 7.5, FuC**H$_2$**), 4.28 (2H, t, *J* 7.0, SOC**H$_2$**), 4.81 (2H, br s, N**H$_2$**), 5.14 (1H, app. dec, 3.0, =C**H**), 6.00 (1H, d, *J* 3.0, Fu**H**), 6.29 (1H, dd, *J* 3.0, 2.1, Fu**H**), 7.31 (1H, d, *J* 0.9, Fu**H**); δ_C (125 MHz, $CDCl_3$) 19.4 (=C**C**H$_3$), 27.3 (FuCH$_2$**C**H$_2$), 27.4 (Fu**C**H$_2$), 28.4 (FuCH$_2$CH$_2$**C**H$_2$), 32.9 (SOCH$_2$**C**H$_2$), 69.4 (SO**C**H$_2$), 91.3 (=**C**H), 95.0 (=**C**), 104.9 (Fu), 110.1 (Fu), 140.8 (Fu), 156.1 (Fu), 201.5 (=**C**=); Accurate mass (ESI^+): Found 284.0963: $C_{13}H_{18}NO_4S$ $(M–H)^–$ requires 284.0962.

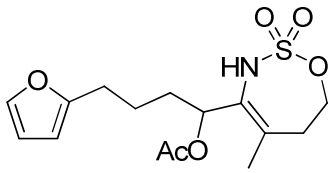
8-[3-(3-Furyl)propyl]-7-methyl-3,3-dioxido-4-oxa-3-thia-2-zabicyclo[5.1.0]oct-1-yl acetate (272)



The reaction of sulfamate **271** according to general procedure I and purification by column chromatography (2:1 → 1:1 petrol:ether) afforded the title compound (10 mg, 2%) as a colourless oil; R_f 0.26 (1:1 petrol:ether); v_{max}/cm^{-1} (thin film) 3299br, 2937s, 1746s, 1507m, 1369s; δ_H (500 MHz, $CDCl_3$) 1.11–1.16 (1H, m, FuCH$_2$CH$_2$C**H**H′), 1.17 (3H, s, NCCC**H$_3$**),

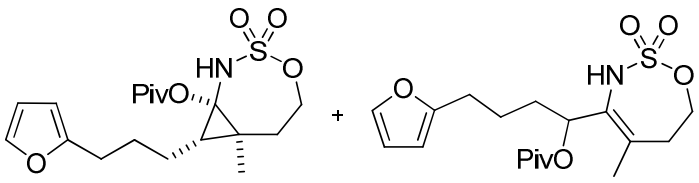
1.31 (1H, dd, *J* 8.3, 5.7, NCC**H**) 1.40 (1H, ddt, *J* 14.0, 9.9, 5.7, FuCH$_2$CH$_2$CH**H′**), 1.63–1.77 (2H, m, FuCH$_2$C**H$_2$**), 1.87 (1H, ddd, *J* 16.0, 12.0, 1.6, SOCH$_2$C**H**H′), 2.09 (3H, s, O=CC**H$_3$**), 2.26 (1H, ddd, *J* 16.0, 4.6, 0.4, SOCH$_2$CH**H′**), 2.62 (2H, t, *J* 7.4, FuC**H$_2$**), 4.24 (1H, ddd, *J* 12.0, 4.6, 2.0, SOC**H**H′), 4.65 (1H, app. t, *J* 12.0, SOCH**H′**), 5.98 (1H, dd, *J* 3.0, 0.7, Fu**H**), 6.28 (1H, dd, *J* 3.0, 1.8, Fu**H**), 6.65 (1H, br s, N**H**), 7.30 (1H, dd, *J* 1.8, 0.7, Fu**H**); δ_C (125 MHz, $CDCl_3$) 12.4 (NCC**C**H$_3$), 20.8 (O=C**C**H$_3$), 23.1 (FuCH$_2$CH$_2$**C**H$_2$), 27.2 (FuCH$_2$**C**H$_2$), 27.8 (Fu**C**H$_2$), 28.9 (NC**C**), 38.4 (NC**C**H), 40.7 (SOCH$_2$**C**H$_2$), 69.0 (SO**C**H$_2$), 71.1 (N**C**), 105.0 (Fu), 110.1 (Fu), 140.9 (Fu), 156.1 (Fu), 171.5 (O=**C**); Accurate mass (ESI$^+$): Found 366.0981: $C_{15}H_{21}NNaO_6S$ (MNa$^+$) requires 366.0982.

4-(3-Furyl)-1-(5-methyl-2,2-dioxido-6,7-dihydro-3*H*-1,2,3-oxathiazepin-4-yl)butyl acetate (273)



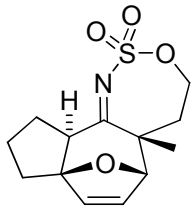
The reaction of sulfamate **271** according to general procedure I and purification by column chromatography (2:1 → 1:1 petrol:ether) afforded the title compound (8 mg, 2%) as a colourless oil; R_f 0.14 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3256br, 2935s, 2866m, 1713s, 1596m, 1507s, 1453s, 1409s; δ_H (500 MHz, $CDCl_3$) 1.65–1.79 (3H, m, FuCH$_2$C**H$_2$** overlays SOCH$_2$C**H**H′), 1.74 (3H, s, CC**H$_3$**), 2.05 (3H, s, O=CC**H$_3$**), 2.23–2.36 (2H, m, FuCH$_2$CH$_2$C**H$_2$**), 2.65 (2H, t, *J* 7.4, FuC**H$_2$**), 3.18 (1H, dtd, *J* 15.0, 6.1, 1.2, SOCH$_2$CH**H′**), 4.32–4.34 (2H, m, SOC**H$_2$**), 5.81 (1H, ddd, *J* 8.4, 7.4, 1.1, OC**H**), 6.00 (1H, dd, *J* 3.1, 0.8, Fu**H**), 6.28 (1H, dd, *J* 3.1, 1.8, Fu**H**), 6.44 (1H, br s, N**H**), 7.30 (1H, dd, *J* 1.8, 0.8, Fu**H**); δ_C (125 MHz, $CDCl_3$) 21.4 (O=C**C**H$_3$), 25.4 (C**C**H$_3$), 27.1 (FuCH$_2$CH$_2$**C**H$_2$), 27.4 (FuCH$_2$**C**H$_2$), 27.4 (Fu**C**H$_2$), 39.0 (SOCH$_2$**C**H$_2$), 65.6 (SO**C**H$_2$), 83.6 (O**C**H), 105.3 (Fu), 110.1 (Fu), 132.7 (NC=**C**), 136.7 (N**C**), 141.0 (Fu), 155.4 (Fu), 170.5 (O=**C**); Accurate mass (ESI$^+$): Found 366.0976: $C_{15}H_{21}NNaO_6S$ (MNa$^+$) requires 366.0982.

8-[3-(2-Furyl)propyl]-7-methyl-3,3-dioxido-4-oxa-3-thia-2-zabicyclo[5.1.0]oct-1-yl pivalate (274) and 4-(2-Furyl)-1-(5-methyl-2,2-dioxido-6,7-dihydro-3*H*-1,2,3-oxathiazepin-4-yl)butyl pivalate (275)



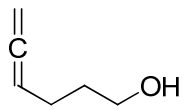
To a stirred solution of sulfamate **271** (468 mg, 1.64 mmol) in benzene (20 mL) was added $PhI(OPiv)_2$ (800 mg, 1.97 mmol) and $Rh_2(esp)_2$ (13 mg, 0.018 mmol). After 20 h MgO (100 mg) was added, the reaction mixture filtered through Celite® and the cake washed with DCM (100 mL). The extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (2:1 → 1:2 petrol:ether) afforded the title compounds (204 mg, 32%) as a *ca*. 7:2 inseparable mixture; R_f 0.20 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3278br, 2964s, 1735s, 1596w, 1507m, 1410s, 1178s; δ_H (400 MHz, $CDCl_3$) **274** only, 1.08–1.15 (1H, m, $FuCH_2CH_2CHH'$), 1.17 (3H, s, $NCCC\mathbf{H_3}$), 1.21 (9H, s, $C(C\mathbf{H_3})_3$), 1.29–1.41 (2H, m, NCC**H** overlays $FuCH_2CH_2CH\mathbf{H'}$), 1.64–1.80 (2H, m, $FuCH_2C\mathbf{H_2}$), 1.88 (1H, ddd, *J* 15.8, 11.6, 2.0, $SOCH_2CHH'$), 2.26 (1H, dd, *J* 15.8, 4.5, $SOCH_2CH\mathbf{H'}$), 2.55–2.69 (2H, m, $FuC\mathbf{H_2}$), 4.24 (1H, ddd, *J* 12.3, 4.5, 2.0, SOC**H**H′), 4.67 (1H, dd, *J* 12.3, 11.6, SOCH**H′**), 5.98 (1H, dd, *J* 3.2, 0.5, Fu**H**), 6.28 (1H, dd, *J* 3.2, 1.9, Fu**H**), 6.68 (1H, br s, N**H**), 7.33 (1H, d, *J* 1.9, Fu**H**); δ_C (100 MHz, $CDCl_3$) **274** only, 12.3 ($NCC\mathbf{C}H_3$), 22.8 ($FuCH_2CH_2\mathbf{C}H_2$), 27.2 ($C(\mathbf{C}H_3)_3$), 27.5 ($FuCH_2\mathbf{C}H_2$), 28.2 ($Fu\mathbf{C}H_2$), 28.9 (NC**C**), 38.3 (NC**C**H), 39.0 (O=C**C**), 40.7 ($SOCH_2\mathbf{C}H_2$), 69.0 ($SO\mathbf{C}H_2$), 70.6 (N**C**), 105.1 (Fu), 110.1 (Fu), 140.9 (Fu), 155.4 (Fu), 178.7 (O=**C**); Accurate mass – Not found.

5a-Methyl-4,5,5a,6,9,10,11,11a-octahydro-6,8a-epoxyazuleno[4,5-*d*]-[1,2,3]oxathiazepine 2,2-dioxide (276)



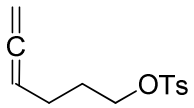
Formed in the reaction of sulfamate **271** to cyclopropane **274**. Purification by column chromatography (2:1 petrol:ethyl acetate) afforded the title compound (27 mg, 5%) as a 5:1 mixture of diasteromers; R_f 0.14 (1:2 petrol:ether); ν_{max}/cm^{-1} (thin film) 2962s, 1800m, 1725m, 1615s, 1446m, 1366s, 1178s; δ_H (500 MHz, C_6D_6) major diastereomer only, 0.31 (1H, dd, *J* 15.1, 4.6, $SOCH_2CHH'$), 1.33 (3H, s, CH_3), 1.38–1.43 (1H, m, $OCCHH'$), 1.58 (1H, ddd, *J* 14.2, 11.3, 6.1, $OCCH_2CHH'$), 1.70–1.77 (1H, m, $OCCHH'$), 1.82–1.90 (3H, m, $OCCH_2CHH'$ overlays $OCCH_2CH_2CH_2$), 1.94–2.01 (1H, m, $SOCH_2CHH'$), 2.32 (1H, dd, *J* 10.2, 9.9, N=CCH), 3.61 (1H, ddd, *J* 12.4, 11.6, 4.6, $SOCHH'$), 3.74 (1H, d, *J* 1.6, OCH), 3.96 (1H, dd, *J* 11.6, 6.6, $SOCHH'$), 5.63 (1H, dd, *J* 6.0, 1.6, =CH), 5.77 (1H, d, *J* 6.0, =CH); δ_C (125 MHz, C_6D_6) 21.5 (CH_3), 23.1 ($OCCH_2$), 31.1 ($OCCH_2CH_2CH_2$), 31.8 ($OCCH_2CH_2$), 32.6 ($SOCH_2CH_2$), 50.9 (N=CC), 54.7 (NCCH), 65.6 ($SOCH_2$), 86.8 (OCH), 93.5 (OC), 131.3 (=CH), 138.0 (=CH), 187.8 (N=C); Accurate mass (ESI^+): Found 306.0770: $C_{13}H_{17}NNaO_4S$ (MNa^+) requires 306.0770.

Hexa-4,5-dien-1-ol[184] (294)



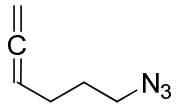
Synthesised according to a literature procedure.

Hexa-4,5-dienyl 4-methylbenzenesulfonate[128] (295)



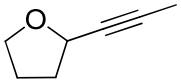
Synthesised according to a literature procedure.

6-azidohexa-1,2-diene (296)



The reaction of tosylate **295** according to general procedure J afforded the title compound (43 mg, 88%) as a colourless oil without the need for further purification; R_f 0.34 (50:1 petrol:ether); δ_H (500 MHz, $CDCl_3$) 1.74 (2H, app. quin *J* 7.0, $NCH_2C\mathbf{H_2}$), 2.08–2.13 (2H, m, $=CHC\mathbf{H_2}$), 3.33 (2H, t, *J* 7.0, $NC\mathbf{H_2}$), 4.72 (2H, dt. *J* 6.6, 3.3, $=C\mathbf{H_2}$), 5.11 (1H, app. quin, *J* 6.6, =C**H**); δ_C (125 MHz, $CDCl_3$) 25.1 ($=CH\mathbf{C}H_2$), 28.0 ($NCH_2\mathbf{C}H_2$), 50.7 (N**C**H), 75.4 ($=\mathbf{C}H_2$), 86.7 (=**C**H), 208.6 (=**C**=); *m/z* (GCMS, Cl^+) 124 (MH^+, 55%), 113 (30), 98 (38), 96 ($M-N_2$, 100), 94 (22); Accurate mass: Found 124.0880: $C_6H_{10}N_3$ (MH^+) requires 124.0875.

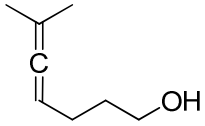
2-(Prop-1-ynyl)tetrahydrofuran[129] (298)



To a stirred solution of 1-bromoprop-1-ene (0.14 mL, 1.65 mmol) in THF (1 mL) at –78 °C was added dropwise *n*-butyllithium (2.27 mL of a 1.6 M solution in hexanes, 3.63 mmol). Meanwhile 2,3-dihydrofuran (0.13 mL, 1.65 mmol) was added dropwise to HCl (1.65 mL of a 1.0 M solution in ether, 1.65 mmol) at 0 °C and stirred for 30 mins. This was added to the reaction mixture *via* cannula and stirring continued at –78 °C for 2 h. The reaction mixture was warmed to r.t., quenched with sat. aq. NH_4Cl solution (3 mL) and extracted with ether (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (10:1 petrol:ether) afforded the title compound (165 mg, 91%) as a colourless oil; R_f 0.42 (2:1 petrol:ether); δ_H (400 MHz,

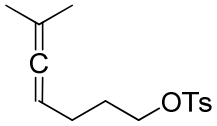
$CDCl_3$) 1.83 (3H, dd, *J* 2.0, 0.8. C**H$_3$**) 1.85–1.95 (2H, m, OCHC**H**H′, overlays OCH_2C**H**H′), 1.97–2.05 (1H, m, OCH_2CH**H′**), 2.07–2.15 (1H, m, OCHCH**H′**), 3.75–3.80 (1H, m, OC**H**H′), 3.91–3.96 (1H, m, OCH**H′**), 4.51–4.55 (1H, m, OC**H**); δ_C (100 MHz, $CDCl_3$) 3.6 (**C**H_3), 25.4 (OCH_2**C**H_2), 33.4 (OCH**C**H_2), 67.7 (O**C**H_2), 68.4 (O**C**H), 79.1 (≡**C**), 80.7 (≡**C**).

6-Methylhepta-4,5-dien-1-ol[129] (299)



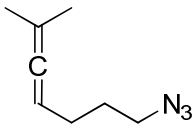
Synthesised according to a literature procedure.

6-Methylhepta-4,5-dienyl 4-methylbenzenesulfonate[129] (300)



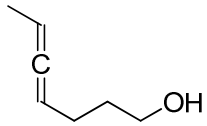
Synthesised according to a literature procedure.

7-Azido-2-methylhepta-2,3-diene (301)



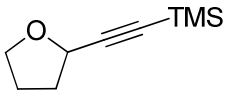
The reaction of tosylate **300** according to general procedure J afforded the title compound (641 mg, quant.) as a colourless oil without the need for further purification; R_f 0.28 (100:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 2937s, 2097s, 1969m, 1448s, 1363m, 1257m; δ_H (500 MHz, $CDCl_3$) 1.71 (2H, app. quin, *J* 7.1, NCH_2C**H$_2$**), 1.69 (3H, s, C**H$_3$**), 1.70 (3H, s, C**H$_3$**), 2.05 (2H, app. q, *J* 7.1, =CHC**H$_2$**), 3.32 (2H, t, *J* 7.1, NC**H$_2$**), 4.95 (1H, app. non, *J* 3.1, =C**H**); δ_C (125 MHz, $CDCl_3$) 20.7 (**C**H_3), 20.7 (**C**H_3), 26.0 (=CH**C**H_2), 28.1 (NCH_2**C**H_2), 50.8 (N**C**H_2), 87.4 (=**C**H), 95.8 (=**C**$(CH_3)_2$), 201.9 (=**C**=); *m/z* (GCMS, Cl^+) 152 (MH^+, 55%), 124 ($M(-N_2)H^+$, 100), 123 (62), 122 (55), 108 (31), 95 (28), 94 (26); Accurate mass: Found 152.1190: $C_8H_{14}N_3$ (MH^+) requires 152.1188.

Hepta-4,5-dien-1-ol[185] (302)



To a solution of silane **305** (404 mg, 2.40 mmol) in ether (15 mL) was added TBAF trihydrate (908 mg, 2.88 mmol) at 0 °C. After 30 mins, water (10 mL) was added and the reaction mixture extracted with ether (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to afford THF **304**, which was redissolved in ether (5 mL). Meanwhile, to a stirred suspension of CuI (548 mg, 2.88 mmol) in ether (10 mL) at −10 °C was added dropwise methyllithium (3.6 mL of a 1.6 M solution in ether, 5.76 mmol). After 10 min the solution of THF **304** was added *via* cannula and the reaction allowed to warm to r.t.. After 2 h the reaction was quenched with sat. aq. NH_4Cl solution (20 mL) and extracted with ether (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (2:1 petrol:ether) afforded the tilte compound (186 mg, 69%) as a colourless oil; R_f 0.21 (2:1 petrol:ether); δ_H (500 MHz, $CDCl_3$) 1.65 (3H, dd, *J* 5.2, 4.6, =CHC**H$_3$**), 1.66–1.72 (2H, m, $OCH_2C\mathbf{H_2}$), 2.05–2.09 (2H, m, =CHC**H$_2$**), 3.69 (2H, td, *J* 6.1, 5.0, OC**H$_2$**), 5.07 (2H, app. qt, *J* 5.2, 4.6, **H**C=C=C**H**); δ_C (125 MHz, $CDCl_3$) 14.5 (=C**C**H_3), 25.0 (=CH**C**H_2), 31.9 ($OCH_2\mathbf{C}H_2$), 62.4 (O**C**H_2), 86.0 (=**C**H), 89.6 (=**C**H), 204.7 (=**C**=).

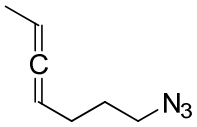
Trimethyl((tetrahydrofuran-2-yl)ethynyl)silane (305)



To a solution of trimethylsilyl acetylide (1.1 mL, 7.8 mmol) in THF (15 mL) was added *n*-butyllithium (4.8 mL of a 1.6 M solution in hexanes, 7.8 mmol) at −78 °C. The reaction mixture was allowed to warm to 0 °C over 1 h before recooling to −78 °C. Meanwhile 2,3-dihydrofuran (0.54 mL, 7.1 mmol) was added dropwise to HCl (7.1 mL of a 1.0 M solution in ether, 7.1 mmol) at 0 °C and stirred for 30 mins. This was added to the reaction mixture *via*

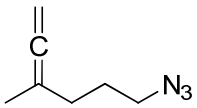
cannula and stirring continued at –78 °C for 2 h. The reaction mixture was warmed to r.t., quenched with sat. aq. NH_4Cl solution (10 mL) and extracted with ether (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (10:1 petrol:ether) afforded the title compound (874 mg, 73%) as a colourless oil; R_f 0.25 (10:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 2960s, 2874m, 2172s, 1459m, 1332m, 1250s; δ_H (400 MHz, $CDCl_3$) 0.10 (9H, s, $Si(C\mathbf{H_3})_3$), 1.85–1.93 (1H, m, $OCH_2C\mathbf{H}H'$), 1.95–2.08 (2H, m, $OCHC\mathbf{H}H'$, overlays $OCH_2CH\mathbf{H'}$), 2.11–2.19 (1H, m, $OCHCH\mathbf{H'}$), 3.78 (1H, ddd, *J* 8.0, 7.6, 5.8, $OC\mathbf{H}H'$), 3.95 (1H, app. td, *J* 7.6, 6.8, $OCH\mathbf{H'}$), 4.56 (1H, dd, *J* 6.7, 6.0, $OC\mathbf{H}$); δ_C (100 MHz, $CDCl_3$) –0.1 ($Si(\mathbf{C}H_3)_3$), 25.4 ($OCH_2\mathbf{C}H_2$), 33.3 ($OCH\mathbf{C}H_2$), 67.9 ($O\mathbf{C}H_2$), 68.5 ($O\mathbf{C}H$), 89.0 (≡**C**Si), 105.5 (≡**C**C); Accurate mass (ESI^+): Found 191.0862: $C_9H_{16}NaOSi$ (MNa^+) requires 191.0863.

7-azidohepta-2,3-diene (306)



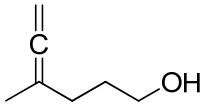
To a stirred solution of alcohol **302** (672 mg, 5.99 mmol) in THF (20 mL) at 0 °C was added sequentially triphenylphosphine (1.88 g, 7.19 mmol) and diisopropyl azodicarboxylate (1.41 mL, 7.19 mmol) and, after 5 mins, diphenylphosphoryl azide (1.67 mL). The reaction was allowed to warm to r.t. and after 2 h the solvent removed *in vacuo*. Purification by column chromatography (petrol → 100:1 petrol:ether) afforded the title compound (754 mg, 92%) as a colourless oil; R_f 0.36 (50:1 petrol:ether); ν_{max}/cm^{-1} (thin film); 2929s, 2097s, 1965s, 1442s, 1347s; δ_H (500 MHz, $CDCl_3$) 1.66 (3H, dd, *J* 7.0, 3.5, $C\mathbf{H_3}$), 1.72 (2H, app. quin *J* 7.0, $NCH_2C\mathbf{H_2}$), 2.08 (2H, app. qd, *J* 7.0, 2.8, $=CHC\mathbf{H_2}$), 3.32 (2H, t, *J* 7.0, $NC\mathbf{H_2}$), 5.02–5.06 (1H, m, =C**H**), 5.07–5.13 (1H, m, =C**H**); δ_C (125 MHz, $CDCl_3$) 14.5 ($\mathbf{C}H_3$), 25.7 ($=CH\mathbf{C}H_2$), 28.1 ($NCH_2\mathbf{C}H_2$), 50.7 (N**C**H), 86.4 (=**C**H), 86.9 (=**C**H), 204.9 (=**C**=); *m/z* (GCMS, Cl^+) 138 (MH^+, 50%), 127 (20), 110 (100); Accurate mass: Found 138.1026: $C_7H_{12}N_3$ (MH^+) requires 138.1031.

6-Azido-3-methylhexa-1,2-diene (307)



To a stirred solution of alcohol **308** (79 mg, 0.70 mmol) in THF (2 mL) at 0 °C was added sequentially triphenylphosphine (221 mg, 0.85 mmol) and diisopropyl azodicarboxylate (0.17 mL, 0.85 mmol) and, after 5 mins, diphenylphosphoryl azide (0.20 mL, 0.91 mmol). The reaction was allowed to warm to r.t. and after 2 h the solvent removed *in vacuo*. Purification by column chromatography (petrol) afforded the title compound (75 mg, 78%) as a colourless oil; R_f 0.49 (50:1 petrol:ether); ν_{max}/cm^{-1} (thin film); 2939s, 2171m, 2097s, 1960s, 1736m, 1591m, 1489s, 1451s; δ_H (500 MHz, $CDCl_3$) 1.70 (3H, t, *J* 3.3, C**H$_3$**), 1.75 (2H, app. quin *J* 6.9, NCH_2C**H$_2$**), 2.02 (2H, tt, *J* 6.9, 3.3, =CC**H$_2$**), 3.31 (2H, t, *J* 6.9, NC**H$_2$**), 4.64 (2H, app. sxt, *J* 3.3, =C**H$_2$**); δ_C (125 MHz, $CDCl_3$) 18.8 (**C**H_3), 26.6 (NCH_2**C**H_2), 30.2 (=C**C**H_2), 50.9 (N**C**H_2), 74.8 (=**C**H_2), 97.3 (=**C**), 205.9 (=**C**=); *m/z* (GCMS, Cl^+) 138 (MH^+, 100%), 112 (24), 110 (85), 84 (14); Accurate mass: Found 138.1031: $C_7H_{12}N_3$ (MH^+) requires 138.1031.

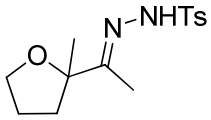
4-Methylhexa-4,5-dien-1-ol[133] (308)



To a stirred suspension of hydrazone **309** (158 mg, 0.53 mmol) in ether (1 mL) at 0 °C was added dropwise *n*-butyllithium (0.70 mL of a 1.6 M solution in hexanes) and the reaction allowed to warm to r.t.. After 30 min the reaction was quenched with water (2 mL) and extracted with ether (3 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (2:1 petrol:ether) afforded the tilt compound (81 mg, quant.) as a colourless oil; R_f 0.29 (1:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 1.71 (3H, t, *J* 3.2, C**H$_3$**), 1.73 (2H, tt *J* 7.2, 6.4, OCH_2C**H$_2$**), 2.01–2.06 (2H, m, =CC**H$_2$**), 3.69 (2H, t, *J* 6.4, OC**H$_2$**), 4.62 (2H, qt, *J* 3.2, 2.8, =C**H$_2$**); δ_C (100 MHz, $CDCl_3$)

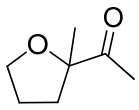
18.8 (**C**H_3), 22.3 (OCH_2**C**H_2), 30.4 (=C**C**H_2), 62.5 (O**C**H_2), 74.4 (=**C**H_2), 97.9 (=**C**), 206.0 (=**C**=).

(*E*)-4-Methyl-*N*′-(1-(2-methyltetrahydrofuran-2-yl)ethylidene)-benzenesulfonohydrazide[133] (309)



A stirred solution of ketone **310** (172 mg, 1.34 mmol) and tosylhydrazine (250 mg, 1.34 mmol) in MeOH (1.5 mL) was heated at reflux for 20 h. After cooling the solvent was removed *in vacuo* and purification by column chromatography (2:1 petrol:ethyl acetate) afforded the title compound (231 mg, 58%) as a white solid; R_f 0.14 (4:1 petrol:ethyl acetate); δ_H (400 MHz, $CDCl_3$) 1.25 (3H, s, CC**H**$_3$), 1.51–1.65 (3H, m, H_3CCC**H**H′ overlays OCH_2C**H**$_2$), 1.77 (3H, s, N=CC**H**$_3$), 2.36–2.43 (1H, m, H_3CCCH**H′**), 2.41 (3H, s, ArC**H**$_3$), 3.49–3.55 (1H, m, OC**H**H′), 3.82 (1H, td, *J* 8.0, 6.2, OCH**H′**), 7.29 (2H, d, *J* 8.3, Ar**H**), 7.82 (2H, d, *J* 8.3, Ar**H**); δ_C (100 MHz, $CDCl_3$) 11.0 (N=C**C**H_3), 21.6 (Ar**C**H_3), 24.6 (C**C**H_3), 25.5 (OCH_2**C**H_2), 34.5 (OC**C**H_2), 67.9 (O**C**H_2), 85.2 (O**C**), 128.0 (Ar), 129.4 (Ar), 135.3 (Ar), 144.0 (Ar), 159.8 (N=**C**).

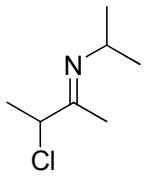
1-(2-Methyltetrahydrofuran-2-yl)ethanone[134] (310)



To a stirred solution of ethyl vinyl ether (0.19 mL, 1.94 mmol) in THF (2 mL) at –78 °C was added dropwise *t*-butyllithium (0.80 mL of a 1.7 M solution in pentane, 1.31 mmol). The resulting bright mixture was stirred for 30 min, allowed to warm to 0 °C for 10 min then recooled to –78 °C. After 15 min, 5-chloropentan-2-one (0.10 mL, 0.88 mmol) in THF (1 mL) was added *via* canula and the mixture was allowed to warm to r.t.. After 20 h the reaction was quenched with water (1 mL) and diluted with ether (5 mL). The mixture was acidified with aq. 1.0 M HCl (2 mL) and extracted with ether (3 × 5 mL). The combined organic

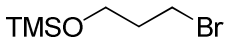
extracts were washed with brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (6:1 petrol:ether) afforded the title compound (47 mg, 42%) as a colourless oil; R_f 0.25 (4:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 1.33 (3H, s, CC**H**$_3$), 1.69 (1H, ddd, *J* 12.6, 8.3, 6.7, H_3CCC**H**H′), 1.77–1.87 (1H, m, OCH_2C**H**H′), 1.90–1.96 (1H, m, OCH_2CH**H′**), 2.22 (3H, s, O=CC**H**$_3$), 2.24 (1H, ddd, *J* 12.6, 8.0, 6.3, H_3CCCH**H′**), 3.84 (1H, dt, *J* 8.0, 7.0, OC**H**H′), 3.99 (1H, app. q, *J* 8.0, OCH**H′**); δ_C (100 MHz, $CDCl_3$) 23.5 (C**C**H$_3$), 24.8 (O=C**C**H$_3$), 25.8 (OCH_2**C**H$_2$), 34.8 (OC**C**H$_2$), 68.7 (O**C**H$_2$), 88.5 (O**C**), 213.5 (O=**C**).

(*Z*)-*N*-(3-chlorobutan-2-ylidene)propan-2-amine[186] (311)



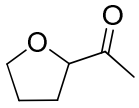
Synthesised according to a literature procedure.

(3-Bromopropoxy)trimethylsilane[187] (312)



Synthesised according to a literature procedure.

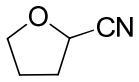
1-(Tetrahydrofuran-2-yl)ethanone[188] (316)



To a solution of 1-(furan-2-yl)ethanone (0.50 mL, 4.99 mmol) in THF (40 mL) was added 10% palladium on carbon (250 mg). This was rapidly stirred under an atmosphere of H_2 gas for 2 h before filtration through Celite® and concentration *in vacuo*. The crude material was dissovled in DCM (30 mL) and NMO (584 mg, 4.99 mmol) and 4 Å molecular sieves were added before the addition of TPAP (87 mg, 0.25 mmol). After 1 h the reaction was diluted with ether (30 mL) and filtered through neutral alumina. The filtrate was

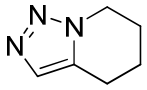
concentrated *in vacuo* and purification by column chromatography (10:1 petol:ether) afforded the title compound (200 mg, 35%) as a colourless oil; δ_H (200 MHz, $CDCl_3$) 1.94–2.06 (4H, m, OCHC**H$_2$** overlays OCH_2C**H$_2$**), 2.26 (3H, s, C**H$_3$**), 3.96–4.06 (2H, m, OC**H$_2$**), 4.37 (1H, dd, *J* 8.0, 6.3, OC**H**).

Tetrahydrofuran-2-carbonitrile[139] (317)



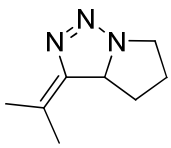
Synthesised according to a literature procedure.

4,5,6,7-Tetrahydro-[1,2,3]triazolo[1,5-a]pyridine[140] (321)



A stirred solution of azide **296** (21 mg, 0.17 mmol) in THF (3 mL) was heated at reflux for 24 h. The reaction was allowed to cool to r.t., concentrated *in vacuo* and purification by column chromatography (2:1 petrol:ether → ethyl acetate) afforded the title compound (17 mg, 81%) as a colourless oil; R_f 0.15 (ethyl acetate); ν_{max}/cm^{-1} (thin film) 2943s, 2866s, 1669m, 1638m, 1552s, 1463s, 1451s, 1238s; δ_H (500 MHz, $CDCl_3$) 1.89–1.94 (2H, m, NCH_2CH_2C**H$_2$**), 2.05–2.10 (2H, m, NCH_2C**H$_2$**), 2.84 (2H, t, *J* 6.5, NCC**H$_2$**), 4.38 (2H, t, *J* 6.2, NC**H$_2$**), 7.45 (1H, s, Az**H**); δ_C (125 MHz, $CDCl_3$) 20.2 (NCH_2CH_2**C**H_2), 20.2 (NC**C**H_2), 22.8 (NCH_2**C**H_2), 46.0 (N**C**H_2), 130.7 (Az), 133.2 (Az); Accurate mass (ESI^+): Found 146.0689: $C_6H_9N_3Na$ (MNa^+) requires 146.0689.

3-(Propan-2-ylidene)-3a,4,5,6-tetrahydro-3H-pyrrolo[1,2-c][1,2,3]triazole (323)

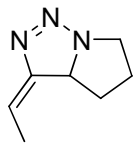


Method A: A stirred solution of azide **301** (16 mg, 0.11 mmol) in toluene (1 mL) was heated at 90 °C for 24 h. The reaction was allowed to cool to r.t. and purification by column

chromatography (2:1 petrol:ether) afforded the title compound (12 mg, 75%) as a colourless oil;

Method B: A solution of azide **301** (38 mg, 0.68 mmol) in acetonitrile (2 mL) was heated in a microwave for 15 min at 160 °C and after cooling the solvent was removed *in vacuo*. Purification by column chromatography (10:1 petrol:ethyl acetate) afforded the title compound (25 mg, 66%) as a colourless oil; R_f 0.24 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 2970s, 1684m, 1433s,1370s,1265m, 1174m, 1134s; δ_H (500 MHz, $CDCl_3$) 1.40–1.52 (2H, m, NCHCH**H′** overlays $NCHCH_2CH$**H′**), 1.72–1.77 (1H, m, $NCHCH_2C$**H**H′), 1.85 (3H, d, *J* 1.3, C**H**$_3$), 2.01–2.05 (1H, m, NCHC**H**H′), 2.17 (3H, d, *J* 1.6, C**H**$_3$), 3.31 (1H, ddd, *J* 12.0, 9.1, 6.5, NCH**H′**), 4.05–4.10 (1H, m, NC**H**H′), 4.16–4.19 (1H, m, NC**H**); δ_C (125 MHz, $CDCl_3$) 19.7 (**C**H_3), 21.4 (**C**H_3), 24.3 ($NCHCH_2$**C**H_2), 31.6 (NCH**C**H_2), 51.0 (N**C**H_2), 59.6 (N**C**H), 128.2 (NC=**C**), 155.9 (C=**C**N); *m/z* (GCMS, Cl^+) 152 (MH^+, 23%), 151 (18), 124 (33) 123 ($M–N_2$, 62), 122 (62), 108 (38), 95 (35), 94 (46),87 (36), 70 (100); Accurate mass: Found 152.1193: $C_8H_{14}N_3$ (MH^+) requires 152.1188.

(*E*)-3-Ethylidene-3a,4,5,6-tetrahydro-3H-pyrrolo[1,2-c][1,2,3]triazole (324)

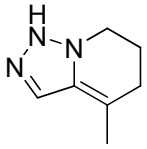


Method A: A solution of azide **306** (73 mg, 0.53 mmol) in toluene (2 mL) was heated to 90 °C and stirred for 20 h. The reaction mixture was cooled and the solvent removed *in vacuo*). Purification by column chromatography (2:1 petrol:ether) afforded the title compound (8 mg, 11%) as a colourless oil.

Method B: A solution of azide **306** (93 mg, 0.68 mmol) in acetonitrile (2 mL) was heated in a microwave for 25 min at 140 °C and after cooling the solvent was removed *in vacuo*. Purification by column chromatography (5:1 → 3:1 petrol:ether) afforded the title compound (23 mg, 25%) as a colourless oil; R_f 0.20 (5:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3045m,

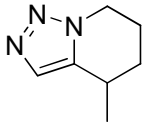
2969s, 2874s, 1720w, 1678w, 1590m, 1427s; δ_H (500 MHz, $CDCl_3$) 1.45–1.56 (2H, m, NCHCH**H′** overlays $NCHCH_2CH$**H′**), 1.75–1.82 (1H, m, $NCHCH_2C$**H**H′), 1.86 (3H, dd, *J* 7.4, 2.2, C$\mathbf{H_3}$), 2.05–2.13 (1H, m, NCHC**H**H′), 3.30–3.36 (1H, m, NC**H**H′), 4.08 (1H, ddd, *J* 11.7, 7.0, 3.3, NCH**H′**), 4.20–4.24 (1H, m, NC**H**), 6.30 (1H, qd, *J* 7.4, 3.0, =C**H**); δ_C (125 MHz, $CDCl_3$) 14.4 (**C**H_3), 24.5 ($NCHCH_2\mathbf{C}H_2$), 31.1 (NCH**C**H_2), 50.8 (N**C**H_2), 58.6 (N**C**H), 118.9 (NC=**C**H), 161.8 (N**C**=C); *m/z* (GCMS, Cl^+) 139 (MH^+, 100%), 138 (90), 111 (68), 110 (90); Accurate mass: Found 138.1029: $C_7H_{12}N_3$ (MH^+) requires 138.1031.

4-Methyl-1,5,6,7-tetrahydro-[1,2,3]triazolo[1,5-a]pyridine[142] (325)



A solution of azide **307** (15 mg, 0.11 mmol) in toluene (1 mL) was heated to 90 °C and stirred for 4 h. The reaction mixture was cooled and the solvent removed *in vacuo*. Purification by column chromatography (ether) afforded the title compound (2 mg, 13%) as a colourless oil; R_f 0.13 (ether); δ_H (500 MHz, $CDCl_3$) 1.65 (3H, s, C$\mathbf{H_3}$), 1.79–1.85 (1H, m, NC=CC**H**H′), 1.98–2.05 (1H, m, NCH_2C**H**H′), 2.31–2.40 (2H, m, NCH_2CH**H′** overlays NC=CCH**H′**), 4.19 (1H, ddd, *J* 13.4, 10.2, 5.0 NC**H**H′), 4.49 (1H, app. dt, *J* 13.4, 4.7, NCH**H′**), 7.63 (1H, s, N=C**H**), 9.12 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 19.4 ($NCH_2\mathbf{C}H_2$), 24.8 (**C**H_3), 31.7 (NC=C**C**H_2), 44.2 (N**C**H_2), 102.8 (NC=**C**), 132.2 (N=**C**), 136.0 (N**C**). Full characterisation not possible due to degredation.

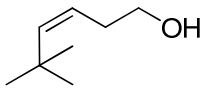
4-Methyl-4,5,6,7-tetrahydro-[1,2,3]triazolo[1,5-a]pyridine (326)



A solution of azide **307** (12 mg, 0.09 mmol) in acetonitrile (1 mL) was heated in the microwave at 140 °C for 15 min. After cooling, the solvent was removed *in vacuo*. Purification by column chromatography (ether) afforded the title compound (2 mg, 17%) as

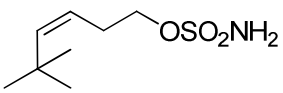
a colourless oil; R_f 0.22 (ether); δ_H (500 MHz, $CDCl_3$) 1.34 (3H, d, *J* 6.9, C**H**$_3$), 1.42–1.51 (1H, m, NCH_2CH_2CHH'), 1.94–2.04 (1H, m, NCH_2CHH'), 2.07–2.12 (1H, m, NCH_2CH_2CHH'), 2.16–2.23 (1H, m, NCH_2CHH'), 2.93–3.01 (1H, m, NCC**H**), 4.20 (1H, ddd, *J* 13.2, 10.9, 5.2 NC**H**H′), 4.52 (1H, ddd, *J* 13.2, 5.6, 3.3, NCH**H′**), 7.50 (1H, s, Ar**H**); δ_C (125 MHz, $CDCl_3$) 20.3 (**C**H_3), 21.8 (NCH_2**C**H_2), 27.3 (NC**C**H), 29.1 (NCH_2CH_2**C**H_2), 45.9 (N**C**H_2), 130.4 (Az), 138.9 (Az). Full characterisation not possible due to degredation.

(*Z*)-5,5-Dimethylhex-3-en-1-ol[155] (342)



To a stirred solution of (3-hydroxypropyl)triphenylphosphonium bromide (1.83 g, 4.56 mmol) in THF (20 mL) was added *n*-butyllithium (5.7 mL of a 1.6 M solution in hexanes, 9.12 mmol) at 0 °C. After 30 min the reaction was cooled to −78 °C and pivaldehyde (0.41 mL, 3.80 mmol) was added dropwise. After 2 h the reaction was allowed to warm to r.t. before sequential addition of ethanol (5 mL) and sat. aq. NH_4Cl solution (20 mL). The phases were separated and the aqueous phase extracted with ether (3 × 30 mL). The combined organic extracts were washed with brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (2:1 petrol:ether) afforded the title compound (111 mg, 23%) as a colourless oil; R_f 0.28 (2:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 1.13 (9H, s, (C**H**$_3$)$_3$), 2.46–2.51 (2H, m, =CHC**H**$_2$), 3.66 (2H, t, *J* 6.8, HOC**H**$_2$), 5.16 (1H, dt, *J* 12.2, 7.6, =C**H**CH_2), 5.49 (1H, dt, *J* 12.2, 1.8, =C**H**); δ_C (100 MHz, $CDCl_3$) 31.1 (C(**C**H_3)$_3$), 31.7 (=CH**C**H_2), 33.3 (**C**$(CH_3)_3$), 62.8 (HO**C**H_2), 123.8 (=**C**H), 142.9 (=**C**H).

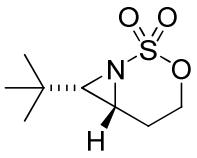
(*Z*)-5,5-dimethylhex-3-enyl sulfamate (343)



The reaction of alcohol **342** according to general procedure H and purification by column chromatography (2:1 petrol:ether) afforded the title compound (1.32 g, 82%) as a

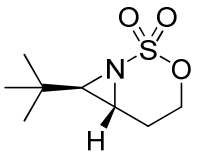
colourless oil; R_f 0.20 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3385br, 2958s, 1559s, 1467s, 1364s; δ_H (400 MHz, $CDCl_3$) 1.13 (9H, s, (C**H**$_3$)$_3$), 2.68 (2H, qd, *J* 7.0, 1.7, =CHC**H**$_2$), 4.22 (2H, t, *J* 7.0, SOC**H**$_2$), 4.71 (2H, br s, N**H**$_2$), 5.14 (1H, dt, *J* 12.0, 7.0, =C**H**CH$_2$), 5.51 (1H, dt, *J* 12.0, 1.7, =C**H**); δ_C (100 MHz, $CDCl_3$) 27.7 (=CH**C**H$_2$), 31.0 (C(**C**H$_3$)$_3$), 33.4 (**C**(CH$_3$)$_3$), 70.9 (SO**C**H$_2$), 121.4 (=**C**H), 143.5 (=**C**H); Accurate mass (ESI$^+$): Found 230.0826: $C_8H_{17}NNaO_3S$ (MNa^+) requires 230.0821.

7-*cis*-*tert*-Butyl-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-dioxide (344)



The reaction of sulfamate **343** according to general procedure I and purification by column chromatography (1:1 petrol:ether) afforded the title compound (83 mg, 54%) as a white crystalline solid; R_f 0.19 (1:1 petrol:ether); m.p. 110–114 °C; ν_{max}/cm^{-1} (thin film) 2958s, 2914m, 1474m, 1361s, 1173s; δ_H (500 MHz, $CDCl_3$) 1.26 (9H, s, (C**H**$_3$)$_3$), 2.08 (1H, dddd, *J* 14.8, 9.0, 3.5, 0.9, OCH$_2$CH**H′**), 2.50 (1H, dddd, 14.8, 13.4, 6.3, 6.0, OCH$_2$C**H**H′), 2.60 (1H, d, *J* 6.0, C**H**C(CH$_3$)$_3$), 3.34 (1H, dt, *J* 9.0, 6.0, OCH$_2$CH$_2$C**H**), 4.48 (1H, ddd, *J* 12.0, 6.3, 0.9, OCH**H′**), 4.88 (1H, ddd, *J* 13.4, 12.0, 3.5, OC**H**H′); δ_C (125 MHz, $CDCl_3$) 16.6 (OCH$_2$**C**H$_2$), 29.1 (C(**C**H$_3$)$_3$), 32.5 (**C**(CH$_3$)$_3$), 43.4 (H**C**C(CH$_3$)$_3$), 56.2 (OCH$_2$CH$_2$**C**H), 70.2 (O**C**H$_2$); Accurate mass (ESI$^+$): Found 228.0660: $C_8H_{15}NNaO_3S$ (MNa^+) requires 228.0665.

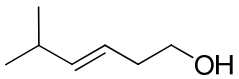
7-*trans*-*tert*-Butyl-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-dioxide (345)



Side product of the reaction of sulfamate **343** according to general procedure I. Purification by column chromatography afforded the title compound (5 mg, 3%) as a colourless oil; R_f 0.24 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 2963s, 1441m, 1362s, 1161s; δ_H (500 MHz,

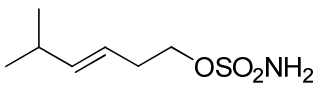
$CDCl_3$) 0.97 (9H, s, (C**H$_3$**)$_3$), 2.18 (1H, dddd, *J* 14.8, 7.9, 6.3, 2.5, OCH_2CH**H′**), 2.37 (1H, app. dq, 14.8, 6.3, OCH_2C**H**H′), 2.68 (1H, d, *J* 4.7, C**H**C$(CH_3)_3$), 3.14 (1H, ddd, *J* 6.9, 4.7, 2.5, OCH_2CH_2C**H**), 4.41 (1H, app. dt, *J* 12.0, 6.3, OCH**H′**), 4.68 (1H, ddd, *J* 12.0, 7.9, 5.7, OC**H**H′); δ_C (125 MHz, $CDCl_3$) 19.1 (OCH_2**C**H_2), 25.9 (C(**C**$H_3)_3$), 30.6 (**C**$(CH_3)_3$), 44.6 (H**C**C$(CH_3)_3$), 55.6 (OCH_2CH_2**C**H), 66.7 (O**C**H_2); Accurate mass (ESI^+): Found 228.0660: $C_8H_{15}NNaO_3S$ (MNa^+) requires 228.0665.

(*E*)-5-methylhex-3-en-1-ol[156] (346)



To a stirred solution of (3-hydroxypropyl)triphenylphosphonium bromide (1.63 g, 4.06 mmol) in ether (20 mL) was added *n*-butyllithium (5.08 mL of a 1.6 M solution in hexanes, 8.12 mmol) at 0 °C. After 30 min the reaction was cooled to –78 °C and pivaldehyde (0.41 mL, 3.80 mmol) was added dropwise. After 2 h the reaction was allowed to warm to r.t. before sequential addition of ethanol (5 mL) and sat. aq. NH_4Cl solution (20 mL). The phases were separated and the aqueous phase extracted with ether (3 × 30 mL). The combined organic extracts were washed with brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (10:1 petrol:ethyl acetate) afforded the title compound (256 mg, 55%) as a colourless oil; R_f 0.22 (10:1 petrol:ethyl acetate); δ_H (200 MHz, $CDCl_3$) 0.99 (6H, d, *J* 6.8, CH(C**H$_3$**)$_2$), 2.22–2.40 (3H, m, C**H**$(CH_3)_2$ overlays =CC**H$_2$**), 3.63 (2H, app. q, *J* 5.5, HOC**H$_2$**), 5.34 (1H, dtd, *J* 15.4, 6.8, 1.0, =C**H**), 5.55 (1H, ddt, *J* 15.4, 6.5, 1.0, =C**H**).

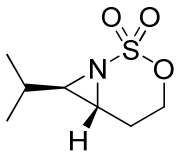
(*E*)-5-methylhex-3-enyl sulfamate (347)



The reaction of alcohol **346** according to general procedure H and purification by column chromatography (2:1 petrol:ether) afforded the title compound (245 mg, 74%) as a colourless oil; R_f 0.19 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3284br, 2958s, 1557s, 1466m,

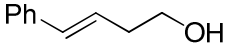
1359s, 1177s; δ_H (500 MHz, $CDCl_3$) 0.98 (6H, d, *J* 6.9, CH(C**H**$_3$)$_2$), 2.27 (1H, app. octd, *J* 6.9, 1.3, C**H**$(CH_3)_2$), 2.44 (2H, app. qt, *J* 6.9, 1.0 =CHC**H**$_2$), 4.21 (2H, t, *J* 6.9, SOC**H**$_2$), 4.75 (2H, br s, N**H**$_2$), 5.33 (1H, dtd, *J* 15.2, 6.9, 1.3, =C**H**), 5.56 (1H, ddt, *J* 15.2, 6.9, 1.0, =C**H**); δ_C (125 MHz, $CDCl_3$) 22.3 (CH(**C**$H_3)_2$), 31.0 (**C**$H(CH_3)_2$), 32.0 (=C**C**H_2), 71.1 (SO**C**H_2), 120.5 (=**C**H), 141.7 (=**C**H); Accurate mass (ESI^+): Found 192.0696: $C_7H_{14}NNaO_3S$ (MNa^+) requires 192.0700.

7-Isopropyl-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-dioxide (348)



The reaction of sulfamate **347** according to general procedure I and purification by column chromatography afforded the title compound (173 mg, 71%) as a colourless oil; R_f 0.17 (1:1 petrol:ether); v_{max}/cm^{-1} (thin film) 2965s, 1468w, 1363s, 1181s; δ_H (500 MHz, $CDCl_3$) 1.02 (3H, d, *J* 6.9 CHC**H**$_3$), 1.07 (3H, d, *J* 6.9, CHC**H**$_3$), 1.52–1.59 (1H, m, C**H**$(CH_3)_2$), 2.12 (1H, dddd, *J* 14.8, 7.3, 6.4, 2.5 OCH_2CH**H′**), 2.41 (1H, dtd, 14.8, 6.4, 5.7, OCH_2C**H**H′), 2.66 (1H, dd, *J* 7.6, 4.2, C**H**CH$(CH_3)_2$), 3.06 (1H, ddd, *J* 6.4, 4.2, 2.5, OCH_2CH_2C**H**), 4.39 (1H, app. dt, *J* 12.0, 6.4, OCH**H′**), 4.66 (1H, ddd, *J* 12.0, 7.3, 5.7, OC**H**H′); δ_C (125 MHz, $CDCl_3$) 18.7 (CH**C**H_3), 19.0 (CH**C**H_3), 19.1 (OCH_2**C**H_2), 30.3 (**C**$H(CH_3)_2$), 46.9 (OCH_2CH_2**C**H), 52.8 H**C**CH$(CH_3)_2$), 68.5 (O**C**H_2); Accurate mass (ESI^+): Found 214.0504: $C_7H_{13}NNaO_3S$ (MNa^+) requires 214.0508.

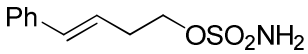
(*E*)-4-Phenylbut-3-en-1-ol[157] (349)



To a stirred solution of (3-hydroxypropyl)triphenylphosphonium bromide (1.78 g, 4.45 mmol) in ether (40 mL) was added *n*-butyllithium (5.2 mL of a 1.6 M solution in hexanes, 8.30 mmol) at 0 °C. After 30 min the reaction was cooled to −78 °C and benzaldehyde (0.30 mL, 2.97 mmol) was added dropwise. After 2 h the reaction was allowed to warm to

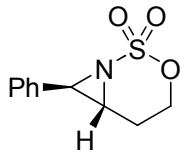
r.t. before sequential addition of ethanol (5 mL) and sat. aq. NH_4Cl solution (20 mL). The phases were separated and the aqueous phase extracted with ether (3 × 30 mL). The combined organic extracts were washed with brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (2:1 petrol:ether) afforded the title compound (100 mg, 23%) as a colourless oil; R_f 0.19 (2:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 2.50 (2H, dt, *J* 7.0, 6.0, =CC**H₂**), 3.77 (2H, app. q, *J* 6.0, HOC**H₂**), 6.22 (1H, dt, *J* 15.6, 7.0, =C**H**CH_2), 6.52 (1H, d, *J* 15.6, =C**H**Ph), 7.24 (1H, d, *J* 7.2, Ar**H**), 7.31 (2H, dd, *J* 7.6, 7.2, Ar**H**), 7.37 (2H, d, *J* 7.6, Ar**H**).

(*E*)-4-phenylbut-3-enyl sulfamate[189] (350)



The reaction of alcohol **349** according to general procedure H and purification by column chromatography (1:1 petrol:ether) afforded the title compound (105 mg, 71%) as a white solid; R_f 0.23 (1:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 2.68 (2H, app. qd, *J* 6.8, 1.4, =CC**H₂**), 4.33 (2H, t, *J* 6.8, SOC**H₂**), 4.72 (2H, br s, N**H₂**), 6.18 (1H, dt, *J* 15.9, 6.8, =C**H**CH_2), 6.53 (1H, d, *J* 15.9, =C**H**Ph), 7.23–7.26 (1H, m, Ar**H**), 7.30–7.37 (4H, m, Ar**H**); δ_C (100 MHz, $CDCl_3$) 29.7 (=C**C**H_2), 70.5 (SO**C**H_2), 123.9 (=**C**HCH_2), 126.1 (Ar), 127.6 (Ar), 128.6 (Ar), 133.4 (=**C**HPh), 136.8 (Ar).

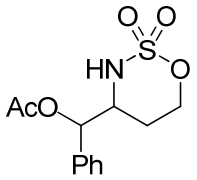
7-Phenyl-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-dioxide (351)



The reaction of sulfamate **350** according to general procedure I and purification by column chromatography (1:1 petrol:ether) afforded the title compound (49 mg, 38%) as a white solid; R_f 0.17 (1:1 petrol:ether); m.p. 111–114 °C; ν_{max}/cm^{-1} (thin film) 3021s, 2985w, 1498w, 1422m, 1363s, 1237w, 1182s; δ_H (500 MHz, $CDCl_3$) 2.41 (1H, dddd, *J* 15.1, 6.9, 6.3, 2.2. OCH_2CH**H′**), 2.51 (1H, app. dq, 15.1, 6.3, OCH_2C**H**H′), 3.27 (1H, ddd, *J* 6.5, 4.1,

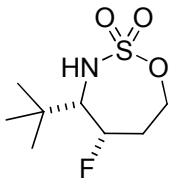
2.2, $OCH_2CH_2C\mathbf{H}$), 3.88 (1H, d, *J* 4.1, PhC**H**), 4.54 (1H, app. dt, *J* 12.0, 6.3, OCH**H′**), 4.78 (1H, ddd, *J* 12.0, 6.9, 5.7, OC**H**H′), 7.30–7.39 (5H, m, Ph**H**); δ_C (125 MHz, $CDCl_3$) 18.7 ($OCH_2\mathbf{C}H_2$), 47.7 (Ph**C**H), 50.4 ($OCH_2CH_2\mathbf{C}H$), 68.8 ($O\mathbf{C}H_2$), 126.3 (Ar), 128.8 (Ar), 128.8 (Ar), 134.1 (Ar); Accurate mass (ESI^+): Found 248.0351: $C_{10}H_{11}NNaO_3S$ (MNa^+) requires 248.0352.

(2,2-Dioxido-1,2,3-oxathiazinan-4-yl)(phenyl)methyl acetate (352)



Side product of the reaction of sulfamate **350** according to general procedure I. Purification by column chromatography (1:1 petrol:ether) afforded the title compound (3 mg, 2%) as a colourless oil; R_f 0.23 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3256m, 2945m, 1735s, 1423m, 1363s, 1235s, 1188s; δ_H (500 MHz, $CDCl_3$) 1.54 (1H, app. dq, *J* 14.5, 2.5, $SOCH_2CH\mathbf{H'}$), 1.85 (1H, dtd, 14.5, 12.9, 5.3, $SOCH_2C\mathbf{H}H'$), 2.17 (3H, s, $C\mathbf{H_3}$), 4.08–4.15 (1H, m, NC**H**), 4.37 (1H, br s, N**H**), 4.52 (1H, ddd, *J* 11.7, 5.3, 1.6, SOCH**H′**), 4.68 (1H, ddd, *J* 12.9, 11.7, 2.5, SOC**H**H′), 5.79 (1H, d, *J* 6.3, PhC**H**) 7.37–7.42 (5H, m, Ph**H**); δ_C (125 MHz, $CDCl_3$) 21.0 ($\mathbf{C}H_3$), 26.5 ($SOCH_2\mathbf{C}H_2$), 59.4 (N**C**H), 71.8 ($SO\mathbf{C}H_2$), 75.6 (Ph**C**H), 127.0 (Ar), 129.0 (Ar), 129.3 (Ar), 135.4 (Ar). 170.1 (O=**C**); Accurate mass (ESI^+): Found 308.0556: $C_{12}H_{15}NNaO_5S$ (MNa^+) requires 308.0563.

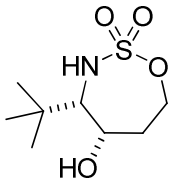
4-*tert*-Butyl-5-fluoro-1,2,3-oxathiazepane 2,2-dioxide (353)



The reaction of sulfamate **344** according to general procedure K and purification by column chromatography (1:1 petrol:ether) afforded the title compound (52 mg, 72%) as a white crystalline solid; R_f 0.26 (1:1 petrol:ether); m.p. 133–134 °C; ν_{max}/cm^{-1} (thin film) 2377br,

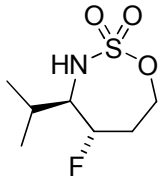
2969s, 2915m, 2878w, 1464m, 1349s, 1187s; δ_H (400 MHz, $CDCl_3$) 1.04 (9H, s, (C**H**$_3$)$_3$), 2.04–2.28 (2H, m, OCH$_2$C**H**$_2$), 3.14 (1H, dd, *J* 28.6, 11.0, NC**H**), 4.21 (1H, dt, *J* 13.4, 3.3, OCH**H′**), 4.61 (1H, ddd, *J* 13.4, 11.9, 2.5 OC**H**H′), 5.18 (1H, br s, N**H**), 5.19 (1H, dt, *J* 46.0, 3.3, FC**H**); δ_C (125 MHz, $CDCl_3$) 26.8 (C(**C**H$_3$)$_3$), 34.4 (**C**(CH$_3$)$_3$), 35.0 (d, *J* 21.9, OCH$_2$**C**H$_2$), 62.7 (d, *J* 16.2, N**C**H), 63.9 (O**C**H$_2$), 87.2 (d, *J* 174.5, F**C**H); δ_F (470.4 MHz, $CDCl_3$) –195.5; Accurate mass (ESI$^+$): Found 248.0723: $C_8H_{16}FNNaO_3S$ (MNa$^+$) requires 248.0727; For X-Ray crystal data see appendix F.

4-*tert*-Butyl-1,2,3-oxathiazepan-5-ol 2,2-dioxide (354)



Side product of the reaction of sulfamate **344** according to general procedure K. Purification by column chromatography (1:1 petrol:ether) afforded the title compound (4 mg, 6%) as a colourless oil; R_f 0.17 (1:1 petrol:ether); v_{max}/cm^{-1} (thin film) 3287br, 2962s, 2917s, 2849m, 11434m, 1355s, 1259s; δ_H (500 MHz, $CDCl_3$) 1.02 (9H, s, (C**H**$_3$)$_3$), 1.69 (1H, br s, O**H**), 1.87 (1H, dt, *J* 15.5, 3.4, SOCH$_2$CH**H′**), 2.14 (1H, ddt, 15.5, 12.9, 3.4, SOCH$_2$C**H**H′), 3.07 (1H, d, *J* 10.4, NC**H**), 4.15 (1H, dt, *J* 12.9, 3.4, OCH**H′**), 4.46 (1H, br m, HOC**H**), 4.67 (1H, app. t, *J* 12.9, OC**H**H′), 5.54 (1H, br d, *J* 10.4, N**H**); δ_C (125 MHz, $CDCl_3$) 27.1 (C(**C**H$_3$)$_3$), 34.6 (**C**(CH$_3$)$_3$), 37.9 (SOCH$_2$**C**H$_2$), 63.5 (N**C**H), 64.0 (SO**C**H$_2$), 65.0 (HO**C**H); Accurate mass (ESI$^+$): Found 246.0769: $C_8H_{17}NNaO_4S$ (MNa$^+$) requires 246.0770.

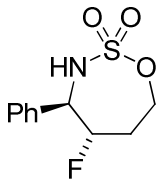
5-Fluoro-4-isopropyl-1,2,3-oxathiazepane 2,2-dioxide (355)



The reaction of sulfamate **348** according to general procedure K or L and purification by column chromatography (3:2 petrol:ethyl acetate) afforded the title compound (K = 23 mg,

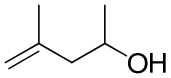
28%; L = 51%, 12 mg) as a white crystalline solid; R_f 0.34 (ether); m.p. 85–88 °C; ν_{max}/cm^{-1} (thin film) 3286br, 2967s, 1443s, 1353s, 1259m, 1177s; δ_H (400 MHz, $CDCl_3$) 0.95 (3H, d, *J* 6.8, CHC**H**$_3$), 1.06 (3H, d, *J* 7.1, CHC**H**$_3$), 2.19–2.31 (2H, m, C**H**$(CH_3)_2$ overlays OCH_2C**H**H′), 2.69 (1H, ddddd, *J* 17.2, 15.4, 6.1, 4.6, 1.3, OCH_2CH**H′**), 3.36 (1H, ddt, *J* 14.4, 9.6, 4.6, NC**H**), 4.29 (1H, ddt, *J* 13.2, 9.9, 1.3, OC**H**H′), 4.40 (1H, ddd, *J* 13.2, 5.0, 2.2, OCH**H′**), 4.59 (1H, dtd, *J* 46.0, 8.8, 4.6, FC**H**), 4.94 (1H, br d, *J* 9.6 N**H**); δ_C (100 MHz, $CDCl_3$) 15.8 (CH**C**H_3), 19.3 (CH**C**H_3), 27.2 (**C**H$(CH_3)_2$), 34.2 (d, *J* 24.0, OCH_2**C**H_2), 60.9 (d, *J* 25.6, N**C**H), 65.4 (d, *J* 9.6, O**C**H_2), 89.9 (d, *J* 178.9, F**C**H); δ_F (376.5 MHz, $CDCl_3$) –176.8; Accurate mass (ESI^+): Found 234.0570: $C_7H_{14}FNNaO_3S$ (MNa^+) requires 234.0571.

5-Fluoro-4-phenyl-1,2,3-oxathiazepane 2,2-dioxide (356)



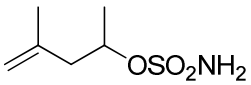
The reaction of sulfamate **351** according to general procedure K and purification by preparative TLC (ether) afforded the title compound (3 mg, 19%) as a white solid; R_f 0.41 (ether); ν_{max}/cm^{-1} (thin film) 3281br, 2920s, 2850m, 1496m, 1458m, 1357s, 1179s; δ_H (400 MHz, $CDCl_3$) 2.44–2.59 (2H, m, OCH_2C**H$_2$**), 4.46–4.49 (2H, m, OC**H$_2$**), 4.52 (1H, ddd, *J* 9.5, 7.9, 6.6, NC**H**), 4.93 (1H, dtd, *J* 45.7, 9.5, 4.7, FC**H**), 4.96 (1H, br s, N**H**), 7.37–7.45 (5H, m, Ar**H**); δ_C (125 MHz, $CDCl_3$) 34.8 (d, *J* 23.8, OCH_2**C**H_2), 59.6 (d, *J* 29.6, N**C**H), 66.6 (d, *J* 12.4, O**C**H_2), 91.8 (d, *J* 180.2, F**C**H), 127.1 (Ar), 129.0 (Ar), 129.1 (Ar), 136.4 (Ar); δ_F (470.4 MHz, $CDCl_3$) –170.7; Accurate mass (ESI^+): Found 268.0418: $C_{10}H_{12}FNNaO_3S$ (MNa^+) requires 268.0414.

4-Methylpent-4-en-2-ol[190] (357)



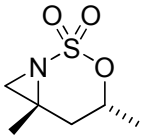
Synthesised according to a literature procedure.

4-Methylpent-4-en-2-yl sulfamate (358)



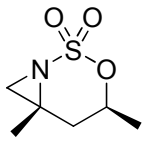
The reaction of sulfamate **357** according to general procedure H and purification by column chromatography (2:1 petrol:ether) afforded the title compound (328 mg, 74%) as a colourless oil; R_f 0.18 (2:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3377br, 3283br, 3079w, 2982m, 2983m, 1650s, 1558m, 1450m, 1355s, 1179s; δ_H (500 MHz, $CDCl_3$) 1.43 (3H, d, *J* 6.3, CHC**H$_3$**), 1.60 (3H, s, =CC**H$_3$**), 2.28 (1H, ddd, *J* 14.0, 6.4, 0.8, =CC**H**H′), 2.53 (1H, ddd, *J* 14.0, 6.9, 0.8, =CCH**H′**), 4.72 (2H, br s, N**H$_2$**), 4.82 (1H, br quin, *J* 0.8, =C**H**H′), 4.85 (2H, dt, *J* 6.9, 6.3, OC**H**), 4.89 (1H, br quin, *J* 1.6, =CH**H′**); δ_C (125 MHz, $CDCl_3$) 20.5 (CH**C**H$_3$), 22.5 (=C**C**H$_3$), 44.9 (=C**C**H$_2$), 79.5 (O**C**H$_2$), 114.4 (=**C**H$_2$), 140.7 (=**C**); Accurate mass (ESI$^+$): Found 178.0540: $C_6H_{12}NO_3S$ $(M–H)^-$ requires 178.0543.

***trans*-4,6-Dimethyl-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-dioxide (359)**



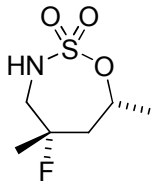
The reaction of sulfamate **358** according to general procedure I and purification by column chromatography (1:2 petrol:ether → ether) afforded the title compound (213 mg, 66%) as a colourless oil; R_f 0.27 (ether); ν_{max}/cm^{-1} (thin film) 2987m, 1448m, 1370s, 1346m, 1187s; δ_H (500 MHz, $CDCl_3$) 1.42 (3H, d, *J* 6.3, CHC**H$_3$**), 1.49 (3H, s, CC**H$_3$**), 2.05 (2H, d, *J* 7.5, OCHC**H$_2$**), 2.37 (1H, s, NC**H**H′), 2.50 (1H, s, NCH**H′**), 4.98 (1H, tq, *J* 7.5, 6.3, OC**H**); δ_C (125 MHz, $CDCl_3$) 21.2 (CH**C**H$_3$), 25.6 (C**C**H$_3$), 32.4 (OCH**C**H$_2$), 42.0 (N**C**H$_2$), 49.0 (N**C**), 78.1 (O**C**H); Accurate mass (ESI$^+$): Found 200.0355: $C_6H_{11}NNaO_3S$ (MNa^+) requires 200.0352.

cis-4,6-Dimethyl-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-dioxide (360)



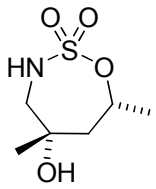
The reaction of sulfamate **358** according to general procedure K and purification by column chromatography (1:2 petrol:ether → ether) afforded the title compound (40 mg, 12%) as a colourless oil; R_f 0.19 (ether); ν_{max}/cm^{-1} (thin film) 2986m, 2933m, 1448m, 1361s, 1183s; δ_H (500 MHz, $CDCl_3$) 1.46 (3H, d, *J* 6.1 CHC**H**$_3$), 1.46 (3H, s, CC**H**$_3$), 2.24–2.30 (2H, m, OCHC**H**$_2$), 2.44 (1H, dd, *J* 2.0, 1.0, NC**H**H′), 2.93 (1H, d, *J* 2.0, NCH**H′**), 4.55 (1H, tq, *J* 11.1, 6.1, OC**H**); δ_C (125 MHz, $CDCl_3$) 21.4 (CH**C**H$_3$), 24.6 (C**C**H$_3$), 32.2 (OCH**C**H$_2$), 39.2 (N**C**H$_2$), 48.3 (N**C**), 76.1 (O**C**H); Accurate mass (ESI^+): Found 200.0355: $C_6H_{11}NNaO_3S$ (MNa^+) requires 200.0352.

5-Fluoro-*trans*-5,7-dimethyl-1,2,3-oxathiazepane 2,2-dioxide (361)



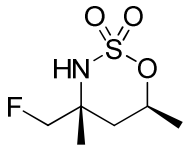
The reaction of sulfamate **359** according to general procedure K or L and purification by column chromatography (1:1 petrol:ether) afforded the title compound (K = 62 mg, 41%; L = 84%, 205 mg) as a white crystalline solid; R_f 0.23 (1:1 petrol:ether); m.p. 52–55 °C; ν_{max}/cm^{-1} (thin film) 3301br, 2987s, 1434m, 1352s, 1182s; δ_H (400 MHz, C_6D_6) 0.84 (3H, d, *J* 22.0, FCC**H**$_3$), 0.93 (3H, d, *J* 6.3, OCHC**H**$_3$), 1.39 (1H, dd, *J* 15.4, 7.3, OCHC**H**H′), 1.96 (1H, td, *J* 15.4, 6.6, OCHCH**H′**), 2.82 (1H, ddd, *J* 16.7, 15.4, 7.8, NC**H**H′), 3.07 (1H, dt, *J* 15.4, 6.6, NCH**H′**), 4.17–4.24 (1H, m, OC**H**), 4.34 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 21.9 (OCH**C**H$_3$), 24.6 (d, *J* 23.8, FC**C**H$_3$), 47.1 (d, *J* 25.8, OCH**C**H$_2$), 50.1 (d, *J* 31.5, N**C**H$_2$), 75.8 (d, *J* 10.5, O**C**H), 94.6 (d, *J* 172.6, F**C**); δ_F (376.5 MHz, $CDCl_3$) –137.4; Accurate mass (ESI^+): Found 220.0418: $C_6H_{12}FNNaO_3S$ (MNa^+) requires 220.0414; For X-Ray crystal data see appendix G.

***trans*-5,7-Dimethyl-1,2,3-oxathiazepan-5-ol 2,2-dioxide (362)**



Formed as a minor side product in reaction of sulfamate **359** according to general procedure K. Purification by preparative TLC (1:3 petrol:ethyl actetate) afforded the title compound (22%, 12 mg) as a colourless oil; R_f 0.17 (ether); ν_{max}/cm^{-1} (thin film) 3487br, 3309br, 2982m, 2917s, 2849m, 1455m, 1384s, 1177s; δ_H (500 MHz, $CDCl_3$) 1.37 (3H, s, HOCC**H**$_3$), 1.45 (3H, d, *J* 6.6, SOCHC**H**$_3$), 1.60 (1H, br s, O**H**), 1.97 (1H, dd, *J* 15.1, 1.6, SOCHC**H**H′), 2.16 (1H, ddd, *J* 15.1, 10.1, 0.6, SOCHCH**H′**), 3.13 (1H, ddd, *J* 15.1, 6.3, 1.2, NC**H**H′), 3.32 (1H, dd, *J* 15.1, 7.6, NCH**H′**), 4.69 (1H, dqd, *J* 10.1, 6.6, 1.6, SOC**H**), 4.84 (1H, br s, N**H**); δ_C (125 MHz, $CDCl_3$) 22.0 (SOCH**C**H$_3$), 26.4 (HOC**C**H$_3$), 49.8 (SOCH**C**H$_2$), 51.9 (N**C**H$_2$), 71.4 (HO**C**), 76.6 (O**C**H); Accurate mass (ESI^+): Found 218.0467: $C_6H_{13}NNaO_4S$ (MNa^+) requires 218.0457.

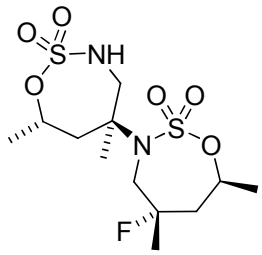
4-(Fluoromethyl)-*trans*-4,6-dimethyl-1,2,3-oxathiazinane 2,2-dioxide (363)



The reaction of sulfamate **360** according to general procedure K using 10 eq. TBAF and purification by column chromatography (1:1 petrol:ether) afforded the title compound (25%, 9 mg) as a colourless oil; R_f 0.33 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3273br, 2916s, 1423m, 1378m, 1353s, 1261w, 1181s; δ_H (500 MHz, $CDCl_3$) 1.37 (3H, dd, *J* 2.0, 1.0, NCC**H**$_3$), 1.47 (3H, d, *J* 6.3, OCHC**H**$_3$), 1.54 (1H, dddd, *J* 14.6, 12.0, 2.5, 1.0, OCHC**H**H′), 2.04 (1H, dt, *J* 14.6, 2.0, OCHCH**H′**), 4.19 (1H, br s, N**H**), 4.39 (1H, ddd, *J* 46.3, 9.8, 1.3, FC**H**H′), 4.87 (1H, dd, *J* 47.6, 9.8, FCH**H′**), 4.97 (1H, dqd, *J* 12.0, 6.3, 2.0, OC**H**); δ_C (125 MHz, $CDCl_3$) 21.1 (OCH**C**H$_3$), 26.4 (d, *J* 3.8, NC**C**H$_3$), 37.1 (d, *J* 1.9, OCH**C**H$_2$), 57.4 (d, *J*

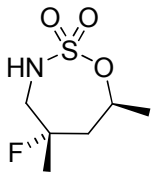
22.9, N**C**), 77.8 (d, *J* 10.5, O**C**H), 83.9 (d, *J* 174.5, F**C**H_2); δ_F (376.5 MHz, $CDCl_3$) –225.62; Accurate mass (ESI^-): Found: 196.0444 $C_6H_{11}FNO_3S$ $(M–H)^-$ requires 196.0449.

5-Fluoro-*trans*-*trans*-5,5′,7,7′-tetramethyl-3,5′-bi-1,2,3-oxathiazepan 2,2,2′,2′-tetraoxide (364)



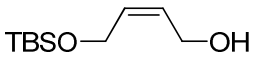
The reaction of sulfamate **360** according to general procedure K using 10 eq. TBAF and purification by column chromatography (1:1 petrol:ether) afforded the title compound (6%, 4 mg) as a colourless oil; R_f 0.12 (1:1 petrol:ether); v_{max}/cm^{-1} (thin film) 3265br, 2985s, 1427s, 1353s, 1242m, 1181s; δ_H (500 MHz, $CDCl_3$) 1.36 (3H, d, *J* 21.4, FCC**H**$_3$), 1.41–1.44 (9H, m, OCHC**H**$_3$ overlays OCHC**H**$_3$ and NCC**H**$_3$), 1.54–1.59 (1H, m, NCC**H**H′), 1.89 (1H, dd, *J* 15.0, 1.6, NCCH**H′**), 1.97–2.11 (2H, m, FCC**H**$_2$CH), 3.65 (1H, ddd, *J* 33.3, 16.2, 1.3, FCC**H**H′N), 3.84 (1H, d, *J* 16.0, HNC**H**H′), 3.90 (1H, ddd, *J* 16.2, 6.0, 1.6, FCCH**H′**N), 3.98 (1H, br s, N**H**), 4.19 (1H, d, *J* 16.0, HNCH**H′**), 4.83 (1H, app. quindd, *J* 6.5, 5.4, 1.4, FCCH_2C**H**), 5.01 (1H, app. sxtd, *J* 6.1, 1.4, NCCH_2C**H**); δ_C (125 MHz, $CDCl_3$) 21.2 (OCH**C**H_3), 21.2 (OCH**C**H_3), 25.1 (d, *J* 21.9, FC**C**H_3), 27.6 (NC**C**H_3), 40.3 (NC**C**H_2), 46.4 (d, *J* 23.8, FC**C**H_2), 53.5 (d, *J* 19.1, FC**C**H_2N), 54.5 (HN**C**H_2), 59.9 (N**C**), 74.5 (d, *J* 10.5, O**C**H), 77.8 (d, *J* 10.5, O**C**H), 95.0 (d, *J* 173.6, F**C**); δ_F (376.5 MHz, $CDCl_3$) –152.78; Accurate mass (ESI^+): Found 397.0860: $C_{12}H_{23}F_2N_2NaO_6S_2$ (MNa^+) requires 397.0874.

5-Fluoro-*cis*-5,7-dimethyl-1,2,3-oxathiazepane 2,2-dioxide (365)



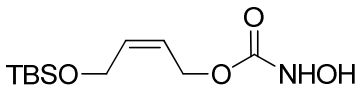
The reaction of sulfamate **360** according to general procedure K using 10 eq. TBAF and purification by column chromatography (1:1 petrol:ether) afforded the title compound (14%, 5 mg) as a colourless oil; R_f 0.22 (1:1 petrol:ether); ν_{max}/cm^{-1} (thin film) 3296br, 2985m, 2918s, 2849m, 1434s, 1384m, 1350s; δ_H (500 MHz, $CDCl_3$) 1.38 (3H, d, *J* 21.4, FCC**H$_3$**), 1.44 (3H, d, *J* 6.6, OCHC**H$_3$**), 2.02 (1H, ddd, *J* 39.7, 15.8, 10.7, OCHC**H**H′), 2.12 (1H, dddd, *J* 15.8, 12.9, 1.9, 1.1, OCHCH**H′**), 3.25 (1H, ddt, *J* 15.8, 6.9, 1.9, NC**H**H′), 3.47 (1H, ddd, *J* 32.2, 15.8, 11.0, NCH**H′**), 4.93 (1H, dqd, *J* 10.7, 6.6, 1.1, OC**H**), 5.14 (1H, br d, *J* 11.0 N**H**); δ_C (125 MHz, $CDCl_3$) 21.2 (OCH**C**H$_3$), 25.0 (d, *J* 21.9, FC**C**H$_3$), 46.8 (d, *J* 23.8, OCH**C**H$_2$), 49.3 (d, *J* 21.9, N**C**H$_2$), 73.8 (d, *J* 10.5, O**C**H), 93.5 (d, *J* 170.7, F**C**); δ_F (470.4 MHz, $CDCl_3$) −154.01; Accurate mass (ESI^-): Found: 196.0441 $C_6H_{11}FNO_3S$ $(M-H)^-$ requires 196.0449.

(Z)-4-(*tert*-Butyldimethylsilyloxy)but-2-en-1-ol[172] (366)



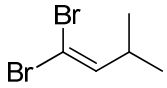
To a stirred suspension of NaH (960 mg of a 60% suspension in mineral oil, 24.0 mmol) in THF (60 mL) was added *cis*-but-2-ene-1,4-diol (2.14 g, 24.3 mmol). After 45 min *tert*-butylchlorodimethylsilane (3.62 g, 24.0 mmol) was added and stirring continued for 1 h. The mixture was diluted with ether (200 mL), washed sequentially with 10% aq. K_2CO_3 (2 × 100 mL) and brine (2 × 100 mL) and dried over Na_2SO_4. Concentration *in vacuo* afforded the title compound as a colourless oil (4.64 g, 99%) without the need for further purification; δ_H (400 MHz, $CDCl_3$) 0.09 (6H, s, Si(C**H$_3$**)$_2$), 0.91 (9H, s, C(C**H$_3$**)$_3$), 4.20 (2H, d, *J* 5.3, OC**H$_2$**), 4.26–4.27 (2H, m, OC**H$_2$**), 5.64–5.75 (2H, m, **H**C=C**H**); δ_C (100 MHz, $CDCl_3$) –5.3 (Si(**C**H$_3$)$_2$), 18.3 (Si**C**Me$_3$), 25.9 (C(**C**H$_3$)$_3$), 58.8 (O**C**H$_2$), 59.6 (O**C**H$_2$), 130.1 (=**C**H), 131.3 (=**C**H).

(*Z*)-4-(t*ert*-Butyldimethylsilyloxy)but-2-enyl hydroxycarbamate[49] (367)



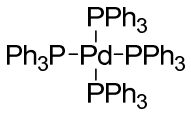
The reaction of alcohol **366** according to general procedure B and purification by column chromatography (2:1 petrol:ether) afforded the title compound (2.07 g, 46%) as a colourless oil; R_f 0.08 (2:1 petrol:ether); δ_H (400 MHz, $CDCl_3$) 0.08 (6H, s, Si(C**H**$_3$)$_2$), 0.90 (9H, s, C(C**H**$_3$)$_3$), 4.29 (2H, d, *J* 5.9, SiOC**H**$_2$), 4.72 (2H, d, *J* 6.7, COC**H**$_2$), 5.53–5.60 (1H, m, =C**H**), 5.72–5.78 (1H, m, =C**H**) 7.43 (1H, br s, N**H**); δ_C (100 MHz, $CDCl_3$) –5.3 (Si(**C**H$_3$)$_2$), 18.3 (Si**C**Me$_3$), 25.9 (C(**C**H$_3$)$_3$), 59.5 (O**C**H$_2$), 61.8 (O**C**H$_2$), 123.7 (=**C**), 134.4 (=**C**) 159.1 (O=**C**).

1,1-Dibromo-3-methylbut-1-ene[101] (368)



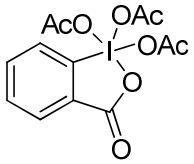
Synthesised according to a literature procedure.

Tetrakis(triphenylphosphine)palladium[191]



Palladium chloride (323 mg, 1.82 mmol) and triphenylphosphine (2.39 g, 9.11 mmol) were added to stirred DMF (25 mL) and heated to 140 °C for 1 h. The reaction was allowed to cool slowly to 80 °C, before addition of a 25% aq. solution of hydrazine hydrate (0.353 mL, 7.28 mmol) dropwise. The reaction was stirred for 30 min before being allowed to cool to r.t. The mixture was filtered and washed under a stream of nitrogen with degassed isopropylalcohol (2 × 5 mL) and hexane (2 × 5 mL) and dried *in vacuo* for 24 h to afford the product (1.81 g, 86%) as a bright yellow solid.

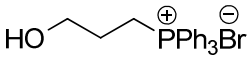
Dess-Martin periodinane[192]



To a three necked flask fitted with a mechanical stirrer and a reflux condenser was added $KBrO_3$ (30.3 g, 181 mmol) and 2.0 M aq. H_2SO_4 solution (280 mL). The solution was heated to 60 °C before 2-iodobenzoic acid (30.0 g, 121 mmol) was added portionwise over 30 min. Bromine gas was evolved and vented through a thiosulfate bubbler connected to an aspirator, and the temperature maintained for 2.5 h. The reaction mixture was cooled to 0 °C and the precipitate collected by vacuum filtration. The filter cake was washed thoroughly with water (150 mL), ethanol (2 × 30 mL) and water (150 mL) once more to afford an iodinane oxide intermediate.

Acetic acid (50 mL) and acetic anhydride (100 mL) were added to a round bottomed flask charged with iodinane oxide intermediate, and the mixture stirred at 85 °C until all solids had dissolved. The solution was then cooled to r.t. and stirring maintained for 24 h. The reaction mixture was then filtered and the precipitate washed with ether (2 × 20 mL) and dried *in vacuo* to afford the title compound (33.0 g, 65%) as a white solid.

(3-Hydroxypropyl)triphenylphosphonium bromide[193]



Synthesised according to a literature procedure.

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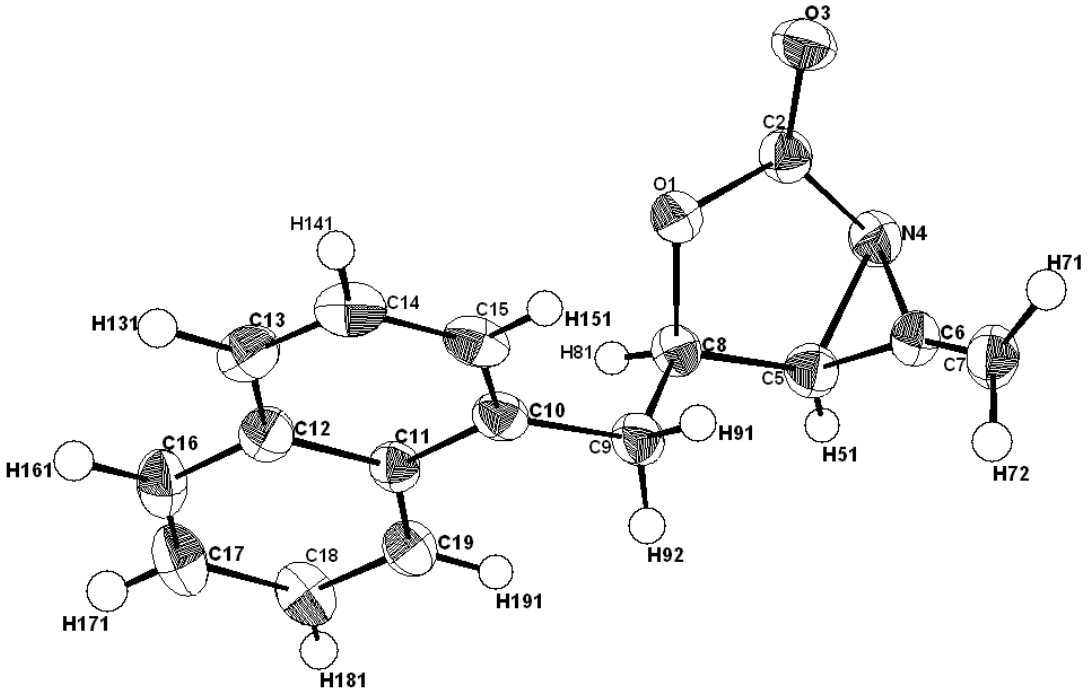
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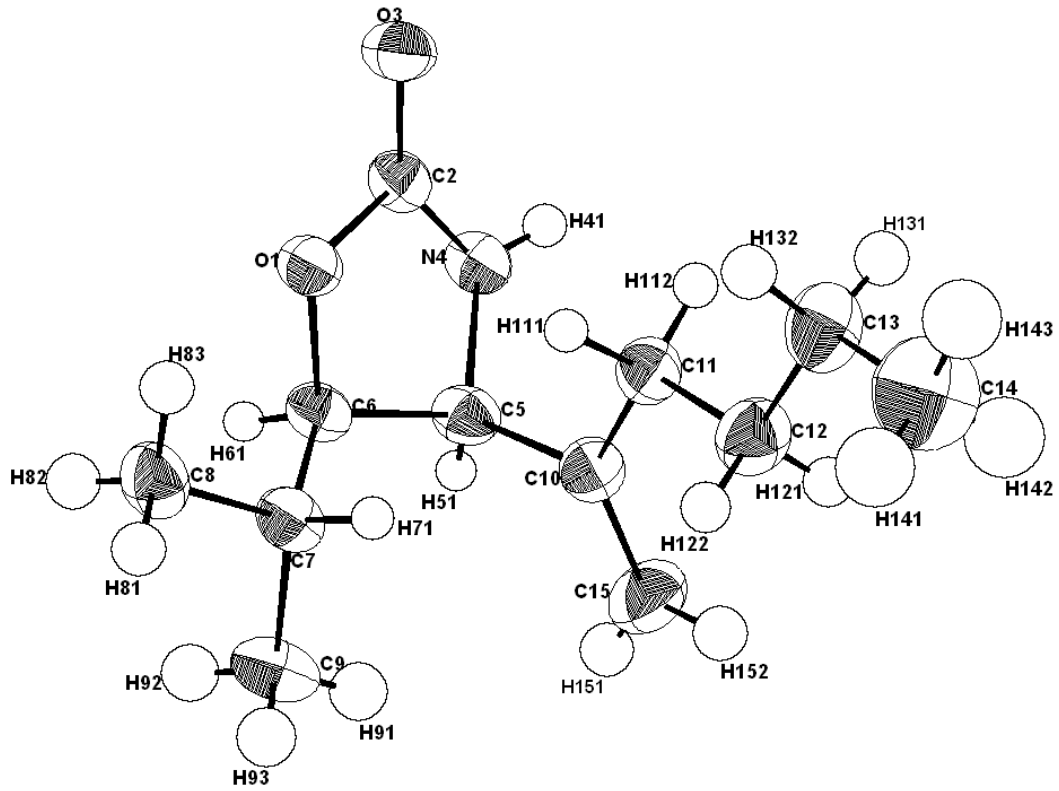
Appendices

Appendix A: Single crystal X-Ray diffraction report for MA 93



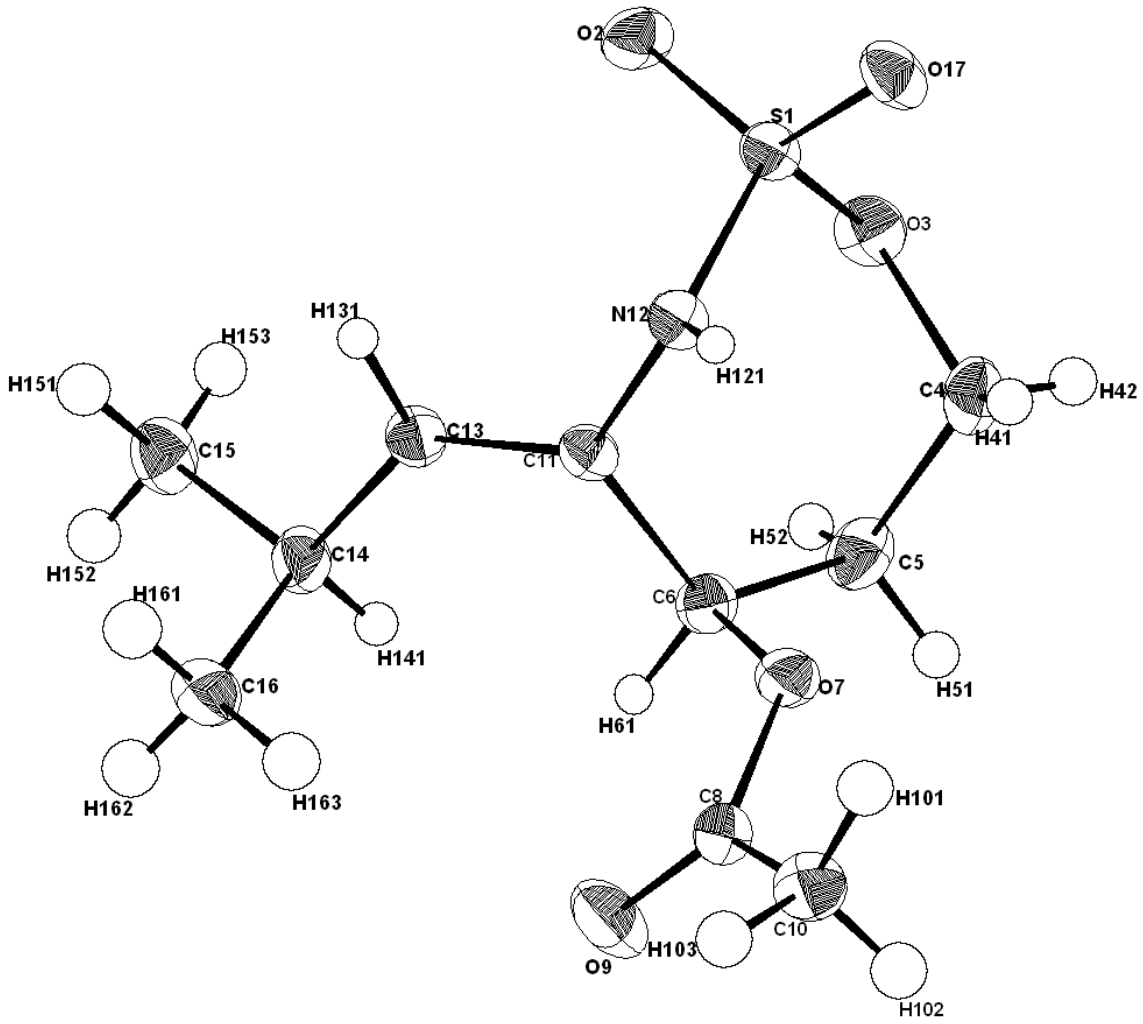
Chemical formula	C16 H13 N1 O2
Space group (Hermann-Mauguin)	P 1 21/n 1
a (Å)	11.8660(3)
b (Å)	9.5726(3)
c (Å)	12.1209(4)
α (°)	90
β (°)	115.3492(11)
γ (°)	90
Cell volume (Å^3)	1244.23(7)
R (I > 2σ(I))	0.0448
wR (I > 2σ(I))	0.1201

Appendix B: Single crystal X-Ray diffraction report for oxazolidinone 118



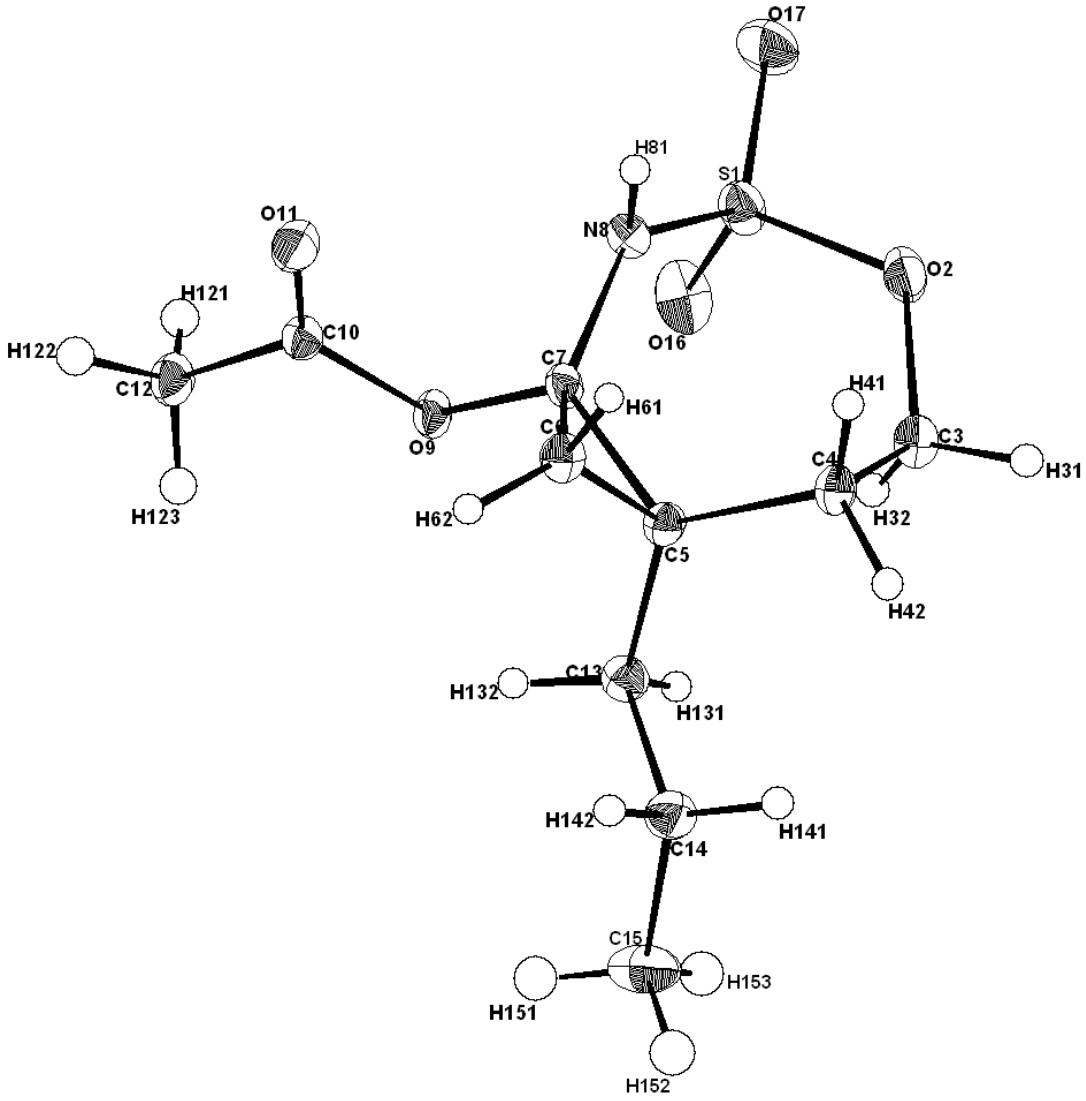
Chemical formula	C12 H21 N1 O2
Space group (Hermann-Mauguin)	P 1 21/a 1
a (Å)	8.3937(4)
b (Å)	11.5174(7)
c (Å)	13.4324(6)
α (°)	90
β (°)	100.112(3)
γ (°)	90
Cell volume (Å^3)	1278.39(11)
R (I > 2σ(I))	0.0528
wR (I > 2σ(I))	0.1422

Appendix C: Single crystal X-Ray diffraction report for cyclic enamine 206



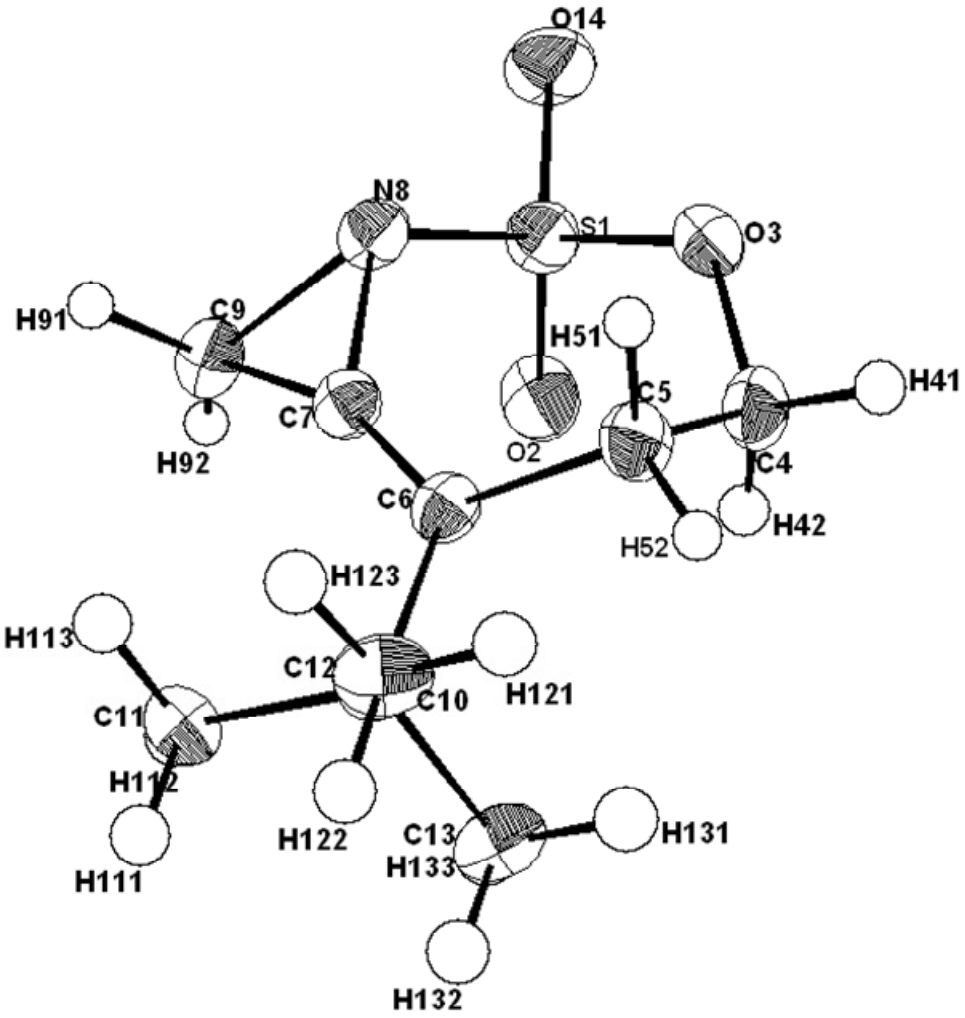
Chemical formula	C10 H17 N1 O5 S1
Space group (Hermann-Mauguin)	P 1 21/n 1
a (Å)	6.5055(2)
b (Å)	22.4224(6)
c (Å)	8.9905(3)
α (°)	90
β (°)	108.6921(10)
γ (°)	90
Cell volume (Å^3)	1242.26(7)
R (I > 2σ(I))	0.0391
wR (I > 2σ(I))	0.0864

Appendix D: Single crystal X-Ray diffraction report for aminocyclopropane 208



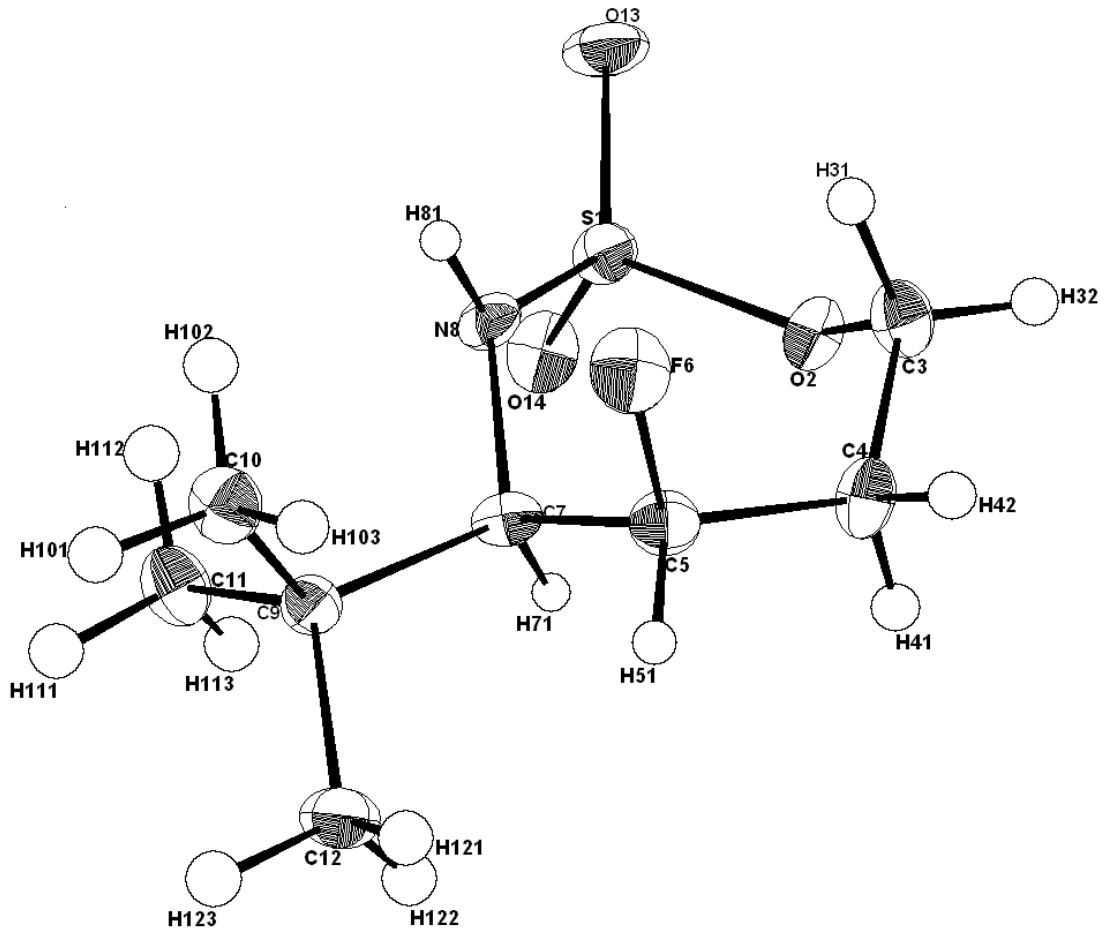
Chemical formula	C10 H17 N1 O5 S1
Space group (Hermann-Mauguin)	P –1
a (Å)	7.6562(2)
b (Å)	8.7683(2)
c (Å)	10.0293(2)
α (°)	77.2922(12)
β (°)	78.9430(12)
γ (°)	69.3572(10)
Cell volume (Å^3)	609.79(2)
R (I > 2σ(I))	0.0330
wR (I > 2σ(I))	0.0837

Appendix E: Single crystal X-Ray diffraction report for MA 211



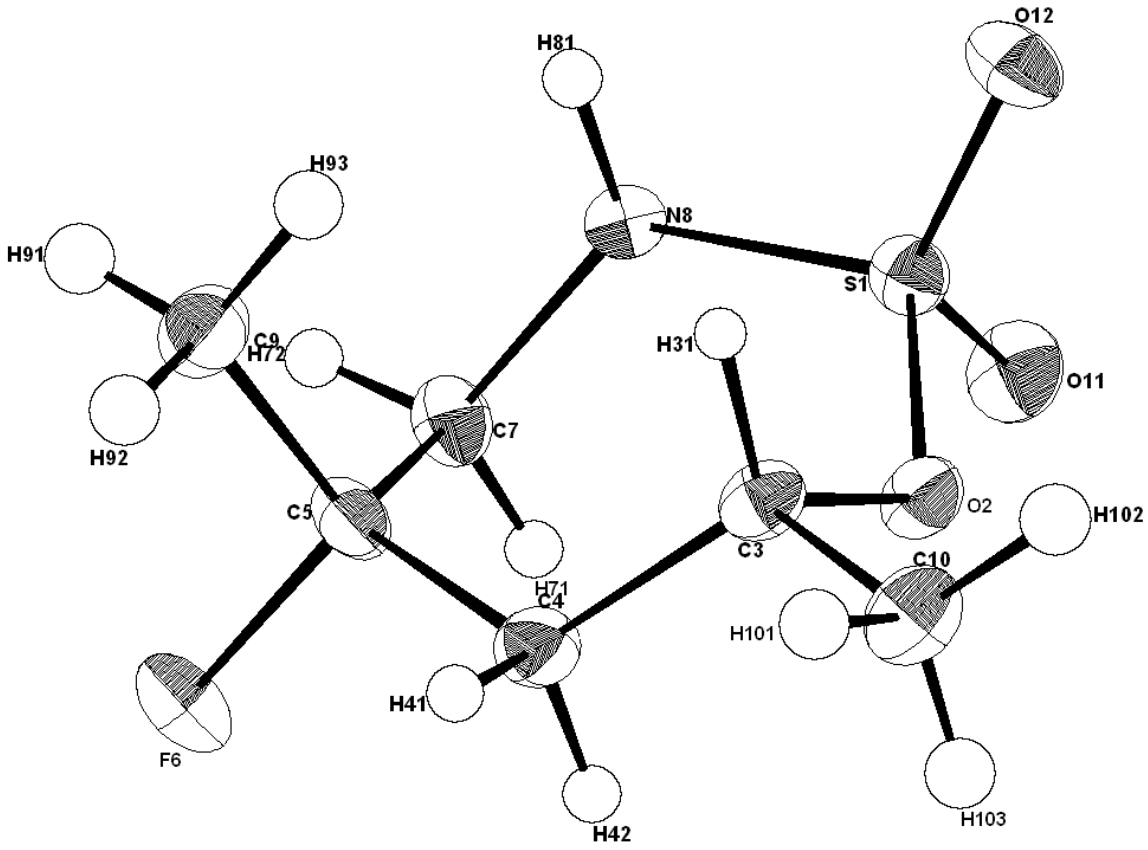
Chemical formula	C9 H15 N1 O3 S1
Space group (Hermann-Mauguin)	P 1 21/n 1
a (Å)	13.8593(3)
b (Å)	10.5242(2)
c (Å)	14.8044(4)
α (°)	90
β (°)	92.0014(7)
γ (°)	90
Cell volume (Å^3)	2158.02(9)
R (I > 2σ(I))	0.0428
wR (I > 2σ(I))	0.0998

Appendix F: Single crystal X-Ray diffraction report for oxathiazepane 353



Chemical formula	C8 H16 F1 N1 O3 S1
Space group (Hermann-Mauguin)	P 21 21 21
a (Å)	7.1809(2)
b (Å)	8.9341(3)
c (Å)	16.3768(6)
α (°)	90
β (°)	90
γ (°)	90
Cell volume ($Å^3$)	1050.65(6)
R (I > 2σ(I))	0.0380
wR (I > 2σ(I))	0.0731

Appendix G: Single crystal X-Ray diffraction report for oxathiazepane 361



Chemical formula	C6 H12 F1 N1 O3 S1
Space group (Hermann-Mauguin)	P 1 21/n 1
a (Å)	6.1029(2)
b (Å)	15.2815(4)
c (Å)	9.7626(3)
α (°)	90
β (°)	105.2081(10)
γ (°)	90
Cell volume (Å^3)	878.59(5)
R (I > 2σ(I))	0.0351
wR (I > 2σ(I))	0.0735