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Gold-Catalysed Reactions of Nitrogen Containing Molecules

by

Nicolas Martin

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Abstract

In this thesis the development of several new gold-catalysed reactions are described. Two new strategies have been employed to access pyrroles by the cycloisomerisation of alkynyl aziridines, and the formation of α,β-unsaturated imides by the oxidation of ynamides has been developed.

A rare gold-mediated vinylidene rearrangement of brominated or silylated alkynes has been used to prepare brominated or silylated 2,4-substituted pyrroles regioselectively. The practical applicability of this process was limited by instability of products under the reaction conditions.

Cationic gold catalysis was used in a novel synthesis of 2,4- and 2,5-substituted pyrroles from alkynyl aziridines. The role of counterion in these processes was studied and shown to be important in determining reaction outcomes. A Ph_3PAuCl/AgOTs catalyst system, allows 2,5-substituted pyrroles to be regioselectively synthesised in an atom-economical manner in near quantitative yield. From the same aryl-substituted starting materials the 2,4-substituted pyrrole isomer were accessed preferentially when a Ph_3PAuCl/AgOTf catalytic system was employed. A reaction mechanism accounting for the reaction outcome was proposed on the basis of ^{13}C- and deuterium-labelling studies.

A new gold-catalysed synthesis of α,β-unsaturated imides was developed using a ynamide oxidation approach. Gold carbenoid intermediates can be formed regioselectively by action of a mild external oxidising agent, and were subsequently used in 1,2-insertion reactions.

Acknowledgments

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List of Abbreviations

Å	Ångström
Ac	Acetyl
Ar	aromatic
Bu	butyl
C	Celsius
δ	chemical shift
d	doublet
DMF	*N*,*N*-dimethylformamide
DMDO	dimethyldioxirane
DMP	Dess-Martin periodinane
DMSO	dimethylsulfoxide
dr	diastereomeric ratio
ee	enantiomeric excess
EI	electron impact
equiv.	equivalent
ESI	electronspray ionisation
Et	ethyl
FT-IR	Fourier transform infrared
g	gram(s)
h	hour(s)
HMBC	heteronuclear multiple bond correlation
HRMS	high resolution mass spectrometry

Hz	Hertz
I	*iso*
IR	infrared
J	coupling constant
L	litre
[M]	metal
m	multiplet
M	molar
*m*CPBA	*meta*-chloroperbenzoic acid
min	minute(s)
mol	moles
mp	melting point
Ms	methanesulfonyl
m/*z*	mass/charge
NIS	*N*-iodosuccinimide
n	normal
NBS	*N*-bromosuccinimide
NMR	nuclear magnetic resonance
o	ortho
p	para
Ph	phenyl
Phth	phthaloyl
PIDA	phenyliodine diacetate
ppm	part(s) per million

Pr	propyl
q	quartet
quint	quintuplet
rt	room temperature
s	singlet
sept	septuplet
T	temperature
t	*tert*
t	triplet
TES	triethylsilane
Tf	trifluoromethanesulfonyl
TBDMS	*tert*-butyldimethylsilane
THF	tetrahydrofuran
TOF	time of flight
Ts	toluenesulfonyl
UV	ultraviolet
v	frequency
Z	atomic number

Chapter 1: Introduction

1.1 Gold: A widely used metal

Gold has been used for millennia by mankind. It has long been employed as currency and in jewellery manufacturing and decoration thanks to its famous malleability and resistance to tarnish. It has been associated to numerous industrial processes where its properties to resist oxidation from air or moisture were also very useful. More importantly, gold's excellent chemical resistance and conductivity has made this metal a key component in electronics. Aerospatiale, among other high technology companies, has used gold for the preparation of highly efficient and reliable heat shields, semiconductors, connecting wires, switches and relay contacts indispensable in the 21st century. Dentistry and medicine[1,2] have also employed gold: Its non-allergenic, non-toxic characteristics were particularly prized for use in fillings or bridges for example, and gold-based anticancer,[3] antimicrobial[4] or antiarthritis[5] complexes have already successfully been developed.

But despite those numerous applications in a variety of fields, gold has been considered of low interest in organic chemistry for a long period of time. When other transition metals were already used in catalysis, gold was still commonly considered chemically inert and too expensive. In fact, rhodium and platinum, commonly used in catalysts, were for example 100% and 30% more expensive than gold in the beginning of August 2010 (Au: 1182 US$ per ounce, Rh: 2175, Pt: 1590).[6]

The huge increase in the development of homogeneous gold catalysed processes in the past decade has proved that chemists have finally realised the fantastic possibilities offered by the use of gold complexes in organic chemistry. The renunciation of mercury catalysis, due to the high toxicity of mercuric salts, has certainly helped to drive the interest of chemists on to its neighbour of the periodic table.

1.2 Gold homogeneous catalysis: Origin of reactivity

1.2.1 Relativistic effects

With the development of new processes using homogeneous gold catalysis, where all the reactive species of the reaction are in the same phase, a better understanding of the reactivity modes of gold complexes has emerged. Furthermore, relativistic effects have helped rationalize the observed reactivity of gold complexes.[7] Those effects account for the contraction of the s and p-orbitals of elements of the sixth period (mainly Ir, Pt, Au, Hg and Tl) and are more significant for gold than any other metal (Figure 1). The electrons of those orbitals are therefore closer to the nucleus and have greater ionization energies. A result of this is the expansion of the 5d and 4f-orbitals which are more shielded from the core.

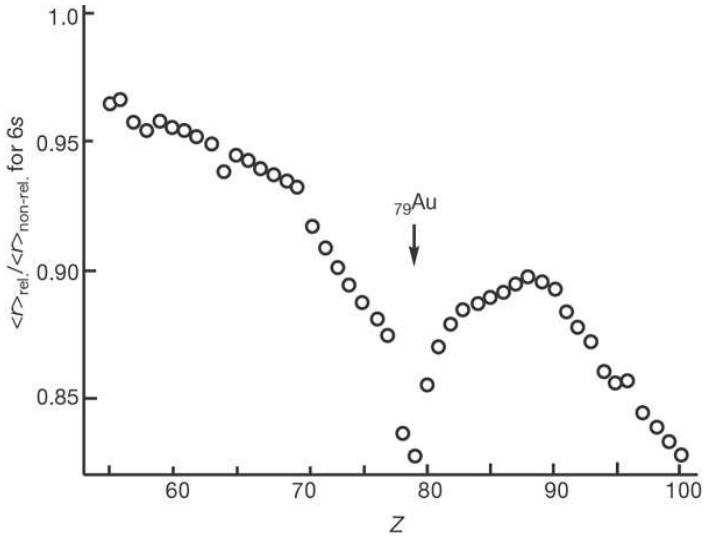

Figure 1: Calculated relativistic contraction of the 6s orbital (the relativistic and non-relativistic radii were dertermined computationally)[8]

One direct consequence of these relativistic effects is the reduction of the M-L (Metal-Ligand) bond length in gold complexes in comparison with its neighbours in the periodic table (Pt and Hg).[9] In other terms the Au-L bonds are strengthened. The electronegativity of the ligand is important and the relating effect will be, for example, more pronounced for a phosphine ligand than a bound chloride (Figure 2).[10]

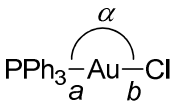

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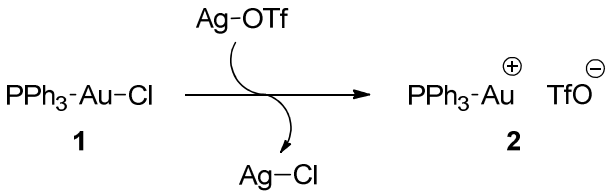
Figure 2: Structure of [AuCl(PPh$_3$)]. α = 179.6°, a = 2.235 Å, b = 2.279 Å

Furthermore, as illustrated in Figure 2, gold (I) LAuX compounds have a pronounced preference to form two coordinate linear complexes.[11] Frequently one of the ligands is abstracted in order to obtain reactive species of the type LAu^+, bearing an empty coordination site. To that respect silver salts are often used in an *in situ* ligand metathesis step prior to catalysis to replace chlorine by a weakly coordinated counterion (Scheme 1).



1 **2**

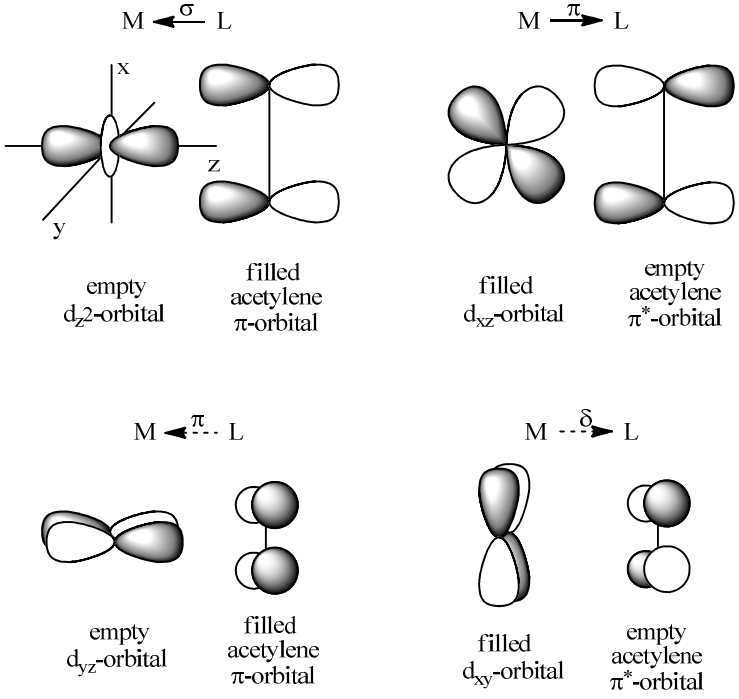
Scheme 1: Metathesis reaction between Ph$_3$PAuCl and AgOTf

Another consequence of the relativistic studies results is the Lewis acid character of gold (I) complexes. The large and diffuse d-orbitals of the gold atom renders it more susceptible to get involved in orbital rather than charge interactions.[12] Therefore, gold catalysts predominantly activate "soft" nucleophilic π-systems such as alkynes, alkenes and allenes. This very specific

affinity of gold compounds generally allows the use of a wide variety of functional groups, a quality particularly appreciated for transformations involving complex functionalized molecules and illustrated later in this chapter.

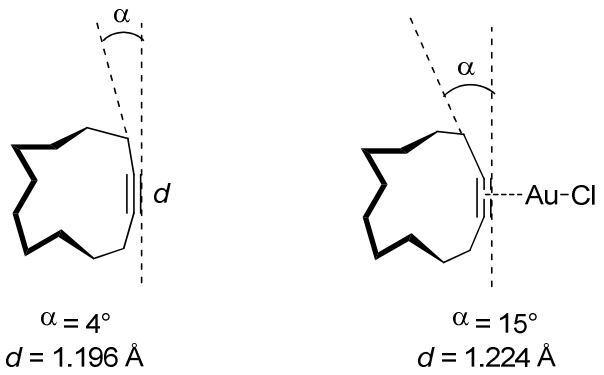
1.2.2 π-System activation

According to the Dewar-Chatt-Duncanson model (DCD),[13] upon complexation a π-system (alkyne or alkene) acts as a ligand to a transition metal complex and donates electron density through σ-bonding from its π-orbital to an empty metal d-orbital (Scheme 2). Back-donation occurs from a filled d-orbital of the metal into the empty π^* antibonding orbital of the ligand to create a π-interaction. Two more π and δ interactions are also involved in the interaction between the metal and an alkyne ligand, the δ interaction contributing only very weakly to the bonding because of poor overlap (dashed interactions represented in Scheme 2).



Scheme 2: Qualitative orbital diagram representing interactions between alkyne ligand and gold

Gold complexes follow this DCD mode of interaction and the resulting activated C-C multiple bond in alkynes and also alkenes are lengthened and the geometry of the carbon atoms can be considered changed from trigonal planar (alkene) and linear (alkyne) to bent as spectroscopic data and isolated complexes confirm (Scheme 3).[14]



Scheme 3: Impact of the association of a gold complex on the geometry of cyclododecyne[14]

Nevertheless, a reluctance of the metal center to back-donate electrons to the π-system has been suggested by calculations.[15] Only approximately 25% of the interaction with the acetylene ligand model ($[Au^{+}(C_2H_2)]$) would be due to back-donation from the metal while the filled π-orbital of the C-C multiple bond would contribute to 64% of the bonding. Those results suggest the alkyne is impoverished in electron density and its carbons atoms are rendered more electrophilic. As a consequence, those gold-activated π-systems are suitable intermediates for attack by various nucleophiles.

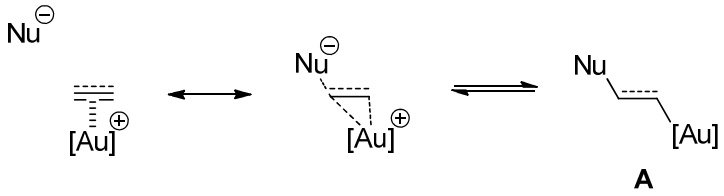
1.2.3 Nucleophilic addition

Despite calculations having shown ethylene binds more strongly than acetylene to a LAu^{+} fragment,[15] experimental results confer a preference of gold complexes to catalyse transformation of alkynes versus allenes and alkenes. This “alkynophilicity” is considered to

be driven by kinetics and reflects discrimination by the incoming nucleophile more than a better activation of the C-C triple bond versus other π-systems. Indeed as alkynes bear lower "highest occupied molecular orbital" (HOMO) and "lower unoccupied molecular orbital" (LUMO) than alkenes, it can be generally expected that LAu-alkyne complex should have a lower LUMO preferred for the addition of a nucleophile than the corresponding LAu-alkene one.[16]

Subsequently to the anti approach of a nucleophile, to the activated π -system, slippage of the metallic η^2 complex along the axis of the π-system-Au bond occurs (Scheme 4).[17]

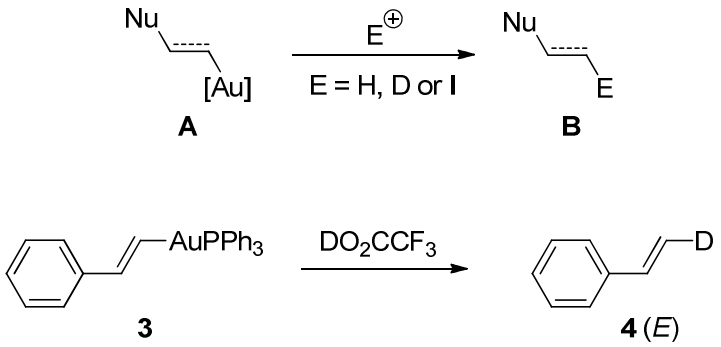
Redistribution of electron density leads to the formation of *trans*-η^1-complex **A** with new C-Au and C-Nu bonds.



Scheme 4: Redistribution of electron density upon nucleophilic attack on alkyne or alkene

At that stage the η^1-intermediate can undergo different transformations depending on the functionalities present in the substrate or in the reaction mixture.

The catalytic cycle can end with the regeneration of the catalyst through protodeauration or trapping by another appropriate electrophile like *N*-iodosuccinimide (NIS).[18] This process is completely stereospecific and deuteriated experiments from vinyl gold species **3** have proved the electrophile is positioned exactly where the gold was (Scheme 5).[19]



Scheme 5: Example of stereoselective deuterodeauration

On the other hand when the η^1-intermediate **A** is a vinylgold species, arising from an activated alkyne, more possibilities than regeneration of the catalyst are offered. This intermediate can be involved in further reactions or rearrangement due to the presence of the double bond.

The next sections of this chapter will introduce the main modes of reactivity possible with gold activated alkynes. It will concentrate on heterocycle formation and the synthetic potential offered by functional group migration during gold catalysed processes.

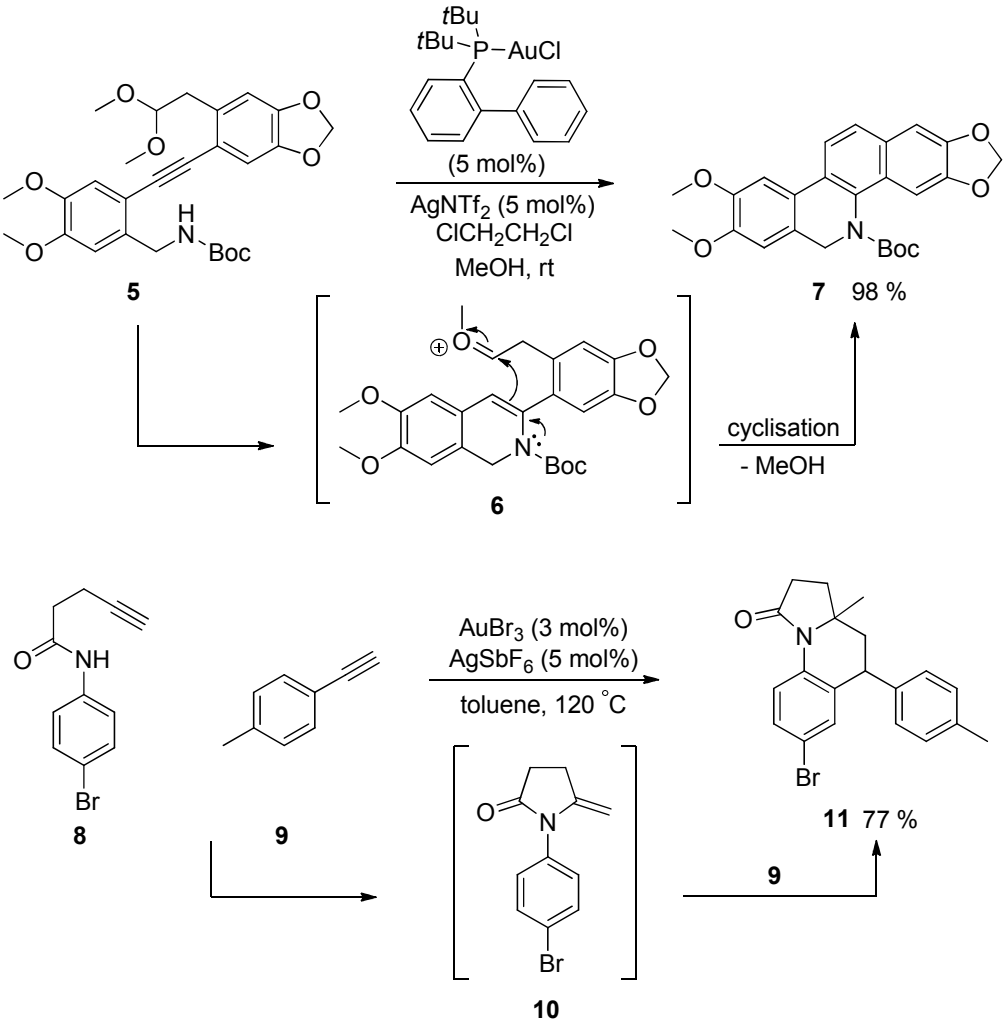
1.3 Selected recent examples of alkyne activation

Among C-C π systems, alkynes have been the most widely studied in gold catalysis. The use of alkynes allows more complex molecules to be obtained than when simple alkenes are employed, and alkynes are also more readily available than the similarly reactive allenes.

Many methods were recently developed in this area using heteroatom nucleophiles, mainly oxygen or nitrogen. Hydroamination, which describes the addition of a primary or secondary amine across an alkyne, was for example used in an efficient gold (I)-catalysed tandem reaction to access various tetracyclic heterocycles like **7** (Scheme 6).[20] These important precursors of benzo[c]phenanthridine alkaloids, a promising class of antitumor agents,[21] were

obtained from a 6-*endo* gold-mediated cyclisation followed by condensation under mild conditions.

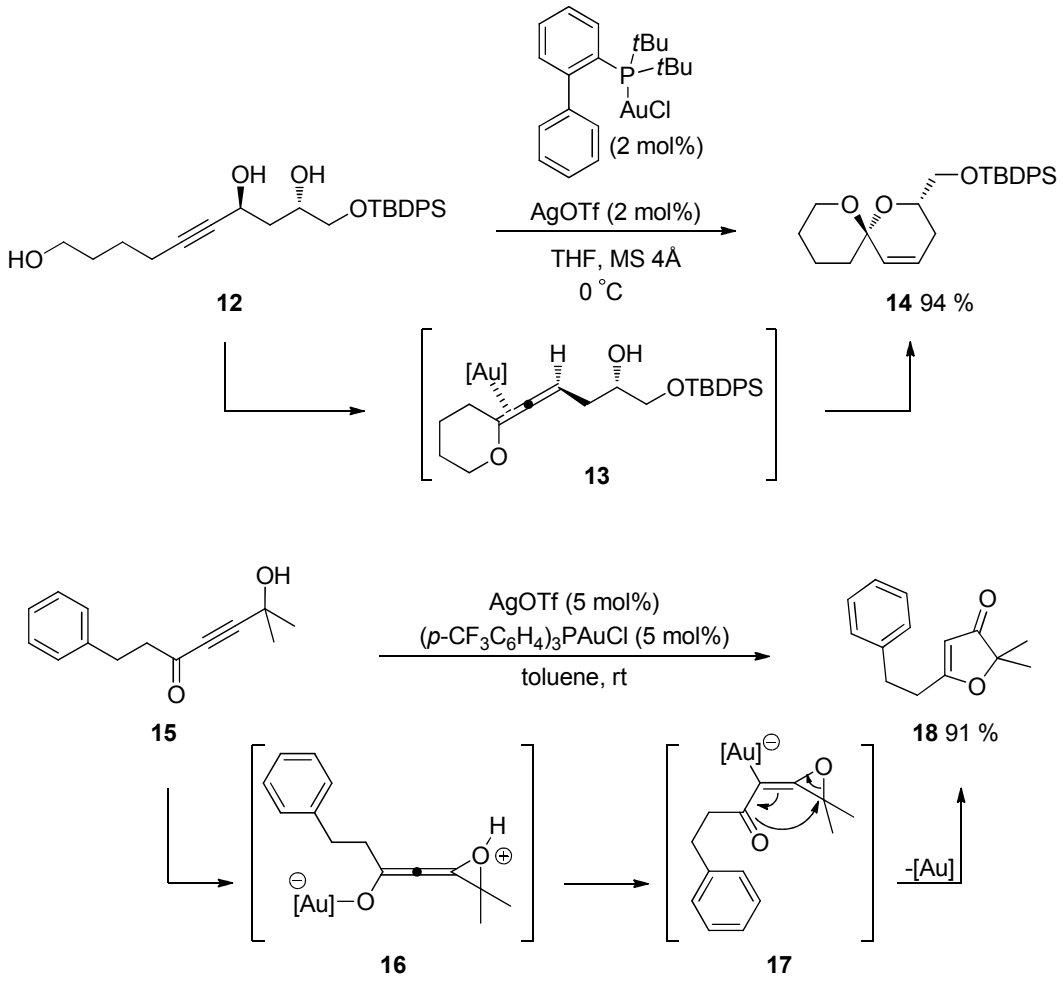
Another remarkable transformation in a one pot cascade manner this time was created to prepare highly functionalised pyrrolo[1,2-a]quinolin-1(2H)-ones (Scheme 6).[22] It was suggested that hydroamination was followed by a gold-catalysed hydroarylation of the starting arylamide **8** to give product **11** in good yield and good regioselectivity. The use of a combination of gold and silver salts was necessary to obtain total conversion of the starting material, and dramatic reduction of the yield was observed when lower temperatures were employed.



Scheme 6: Selected examples of gold-catalysed hydroamination of alkynes in cascade reactions

New advances in hydroalkoxylation reactions also led to the development of efficient methodologies (Scheme 7). Valuable spiroketals could be prepared in an expedient intramolecular hydroalkoxylation of functionalised monopropargylic triols.[23] The gold catalysed reaction is though to go through the formation of a cyclic alkoxyallene **13** which next underwent cyclisation into the spiroketal in excellent yield.

This type of transformation was also employed in the preparation of 3-(2*H*)-furanones, naturally occurring and biologically active moieties. The γ-hydroxyalkynone precursor **15** was engaged in a Michael addition of the hydroxyl group across the gold-activated triple bond. The proposed epoxide intermediate **17** would then cyclise to form heterocycle **18** in very good yield.

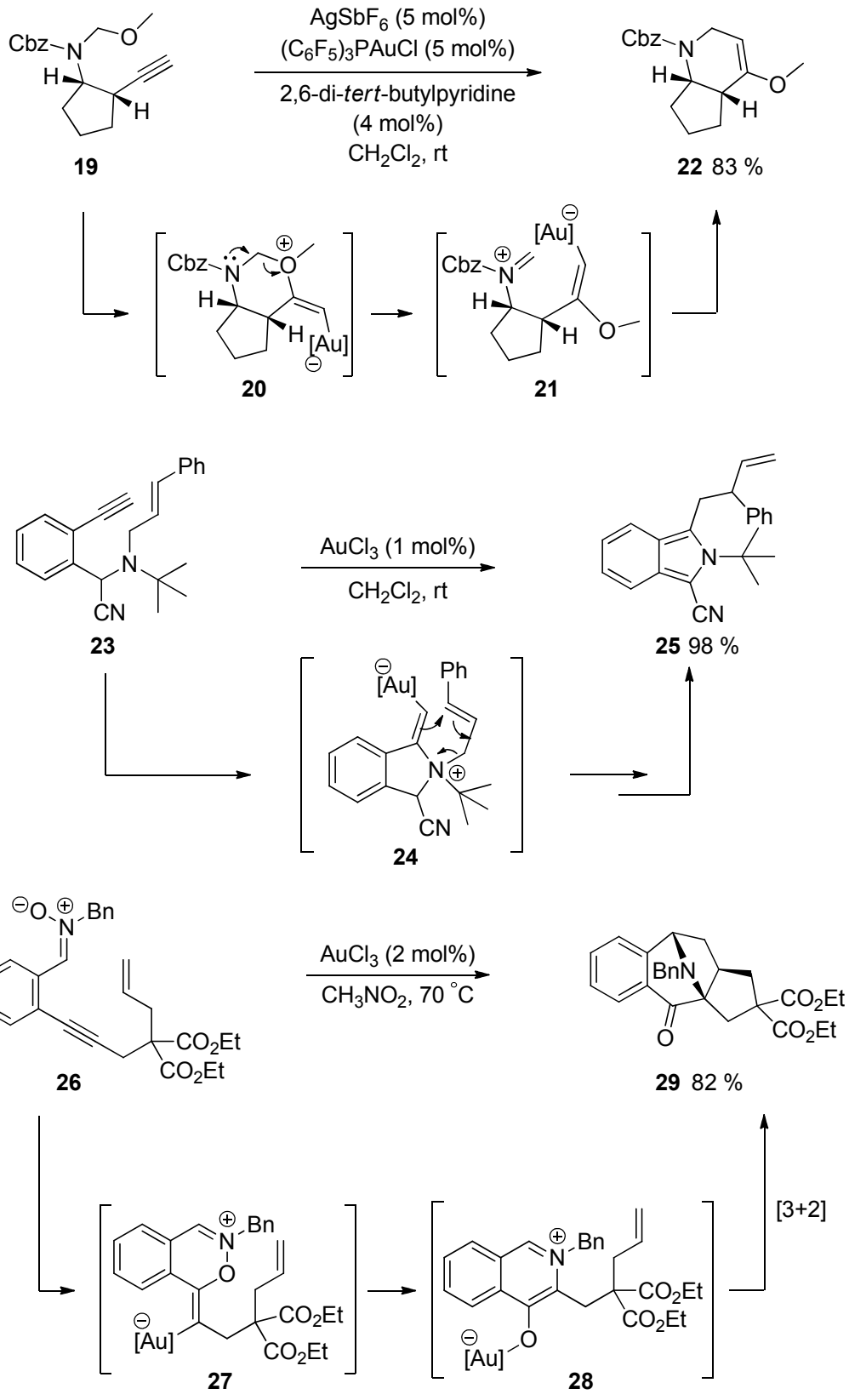


Scheme 7: Selected recent examples of gold catalysed hydroalkoxylation and hydration of alkynes

Substituted piperidines were expediently synthesised in a cationic gold (I) catalysed reaction of mixed N,O-acetals (Scheme 8).[24] 2,6-di-*tert*-butyl pyridine was employed as an additive to avoid in situ hydration of the enolether. The product of the reaction could eventually further react under acidic conditions to give the corresponding ketone.

In the case of allylic tertiary amine **23**, a five-*exo* nucleophilic addition occurred under gold activation conditions and rearrangement of the intermediate **24** delivered the corresponding cyanoindole **25** in excellent yield.[25]

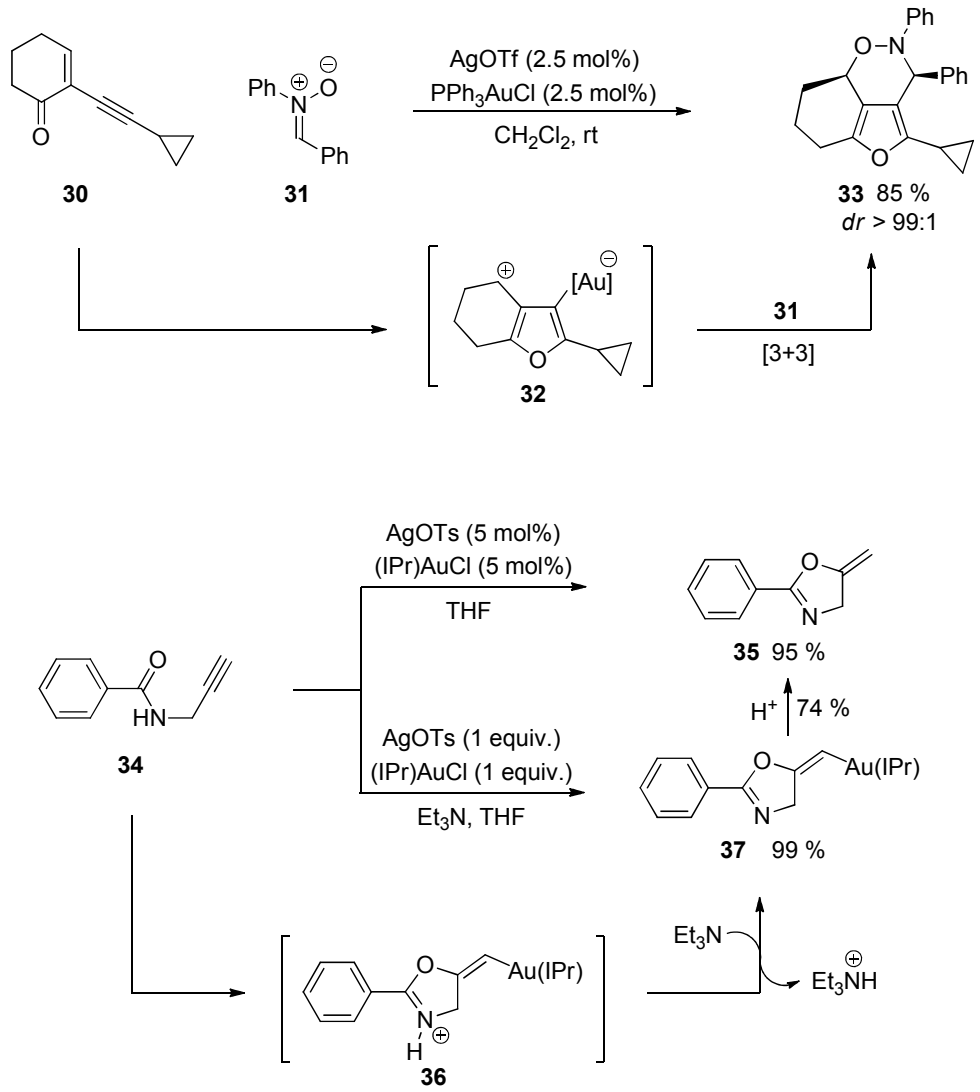
Reactions using nitrones could also be performed.[26] It was proposed that after addition of the nucleophile on the activated C-C triple bond, intermediate **27** rearranged to give 1,3-dipole **28**. Subsequent [3+2] cycloaddition between the alkene moiety and the dipole would then form the final seven-membered ring. Application of the same type of reactivity with other kinds of *N*-oxides will be developed and discussed in more details in chapter 5.



Scheme 8: Selected recent examples of gold-catalysed reactions between alkynes and nucleophiles

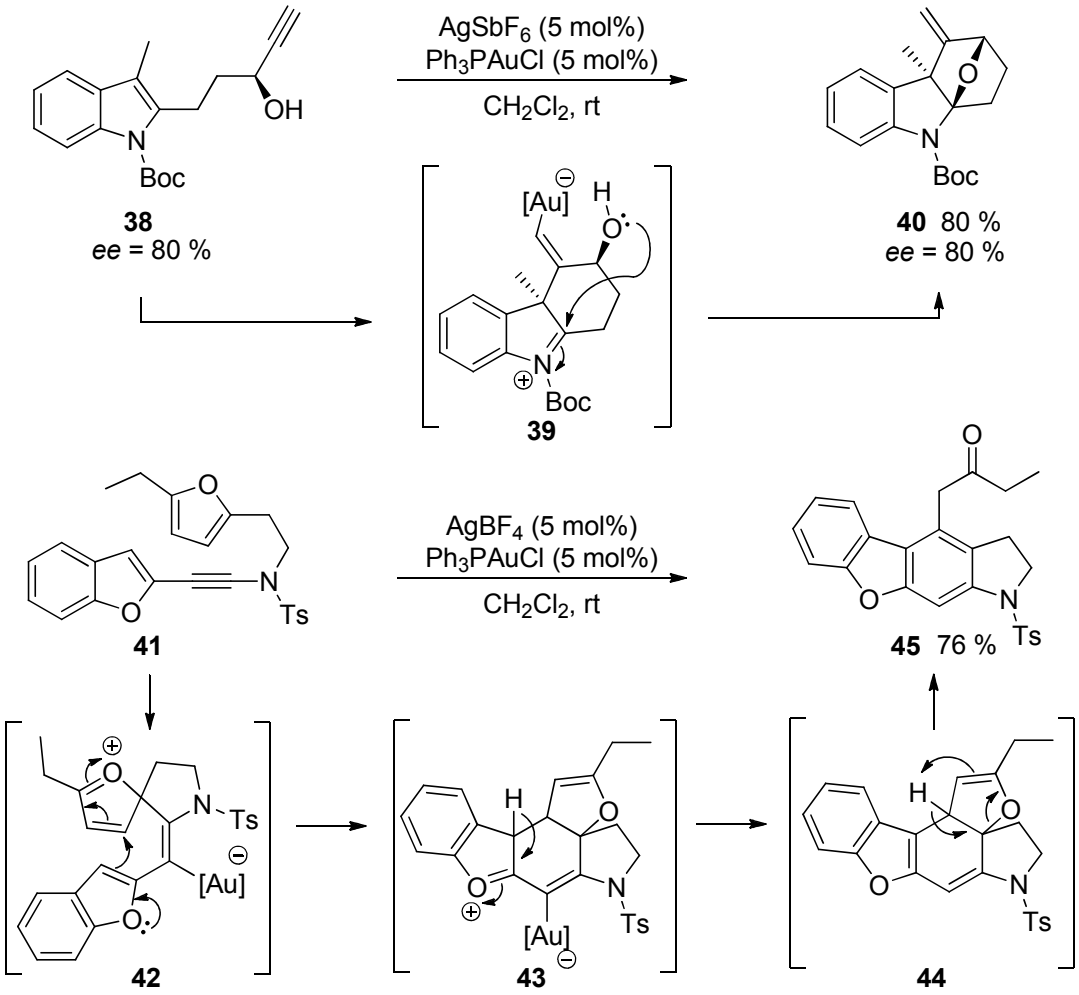
Reactions involving sp^2-hybridised heteroatom nucleophiles were also employed in novel methodologies (Scheme 9). For example highly substituted tricyclic furo[3,4-*d*][1,2]oxazines were accessed in high yield and diastereoselectivity.[27] This gold (I)-catalysed reaction proceeded through cyclisation of *α*,*β*-unsaturated ketone **30** to form intermediate **32** which was immediately trapped with a nitrone in a 1,3-dipolar [3+3] cycloaddition.

Amide derivatives also proved to be suitable reagent for these transformations. The already known simple formation of alkylidene oxazoline[28] **35** from propargyl carboxamide **34** recently attracted much attention again.[29] Indeed after running the reaction using one equivalent of gold catalyst in the presence of triethylamine, isolation and characterisation of the key vinyl gold intermediate **37** was possible. As expected the organogold compound could easily be transformed into the corresponding alkylidene oxazoline under acidic conditions.



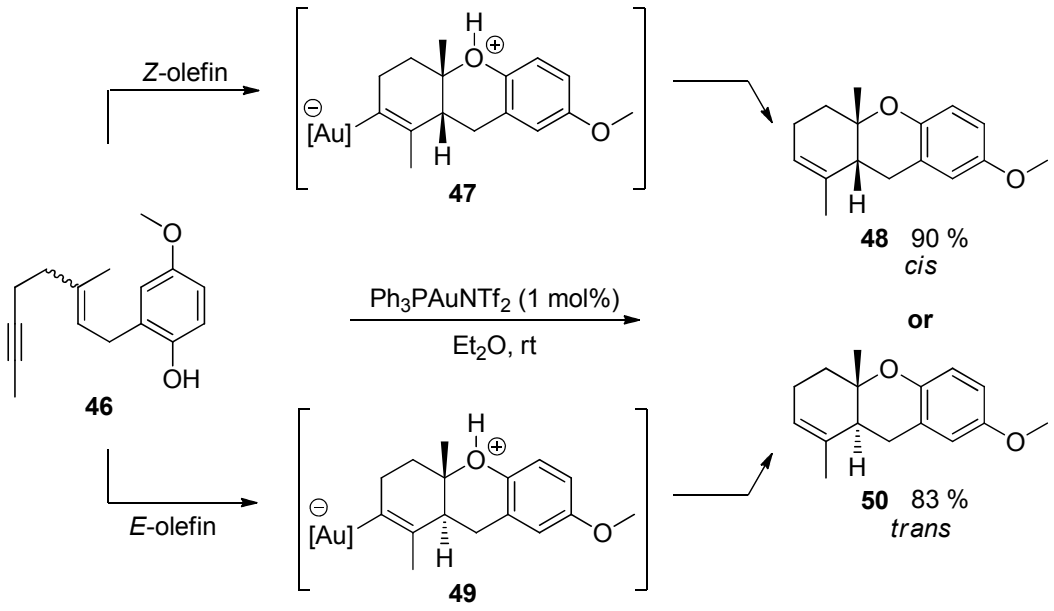
Scheme 9: Selected examples of gold-catalysed reaction involving sp^2-hybridised heteroatom nucleophiles

Heteroaryl functionalities like indoles were employed as carbon nucleophiles to form heterocyclic compounds. A recent reaction of alkynylindole **38** illustrated this in a diastereoselective 6-*exo*-*dig* cyclisation (Scheme 10).[30] The bridged tricyclic indoline product **40** was obtained in high yields with total retention of chirality at the secondary propargyl alcohol when the indole nitrogen bore an electron-withdrawing group. Furans were also used in a similar fashion to access polyheterocyclic compounds. Ynamide **41** endured a 6-*exo* cyclisation followed by a nucleophilic attack from the second furan moiety.[31] Protodeauration and aromatisation process by elimination of the furyl enol ether bridge delivering the final product **45**.



Scheme 10: Selected examples of gold-catalysed reaction of heteroaryls with alkynes

Recently, novel reactions concerning different types of enynes and the trapping of their organogold intermediates upon activation were developed to form heterocycles (Scheme 11). Tricyclic structure **48** was obtained employing 1,5-enynes in a 6-endo-dig intramolecular phenoxycyclisation.[32] High yields were reported under smooth reaction conditions using commercially available $Ph_3PAuNTf_2$. The importance of the geometry of the starting alkene was also highlighted as *E*-olefin gave *trans* product **50** and the *Z*-olefin furnished the *cis* isomer **48** only.



Scheme 11: Example of a 6-endo-dig intramolecular phenoxycyclisation

1.4 Functional group migration with alkyne activation

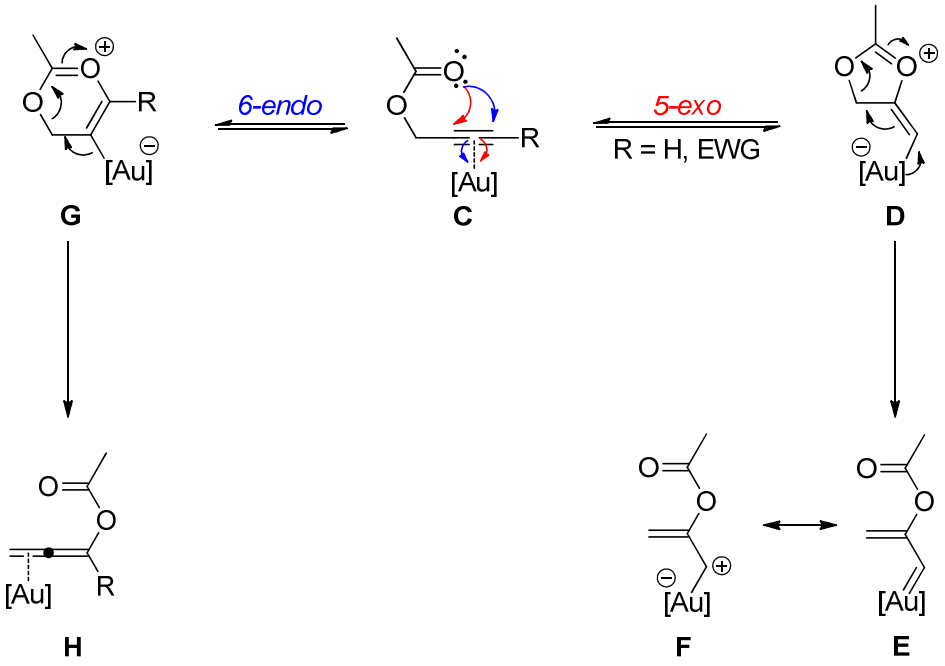
The examples presented in the previous section have illustrated the broad range of transformations possible in gold-catalysed processes to access heterocycles from alkynes. A large number of these reactions can also include migrations, such as 1,2-alkyl and aryl shifts, ring expansion or pinacol-type rearrangement among others, to achieve powerful new transformations.

1.4.1 1,2- and 1,3-ester migration of propargylic carboxylates

As mentioned previously, sp^2-hybridised nucleophiles have been used in gold-catalysed transformations. Among this class of compounds propargylic carboxylates **C** have represented a special case as two divergent initial transformations have been proposed (Scheme 12). A 1,2-ester migration would take place through a 5-*exo* nucleophilic attack to form species **E**. This carbenoid form can also be described as a metal-stabilised carbocation **F** by mesomeric resonance.

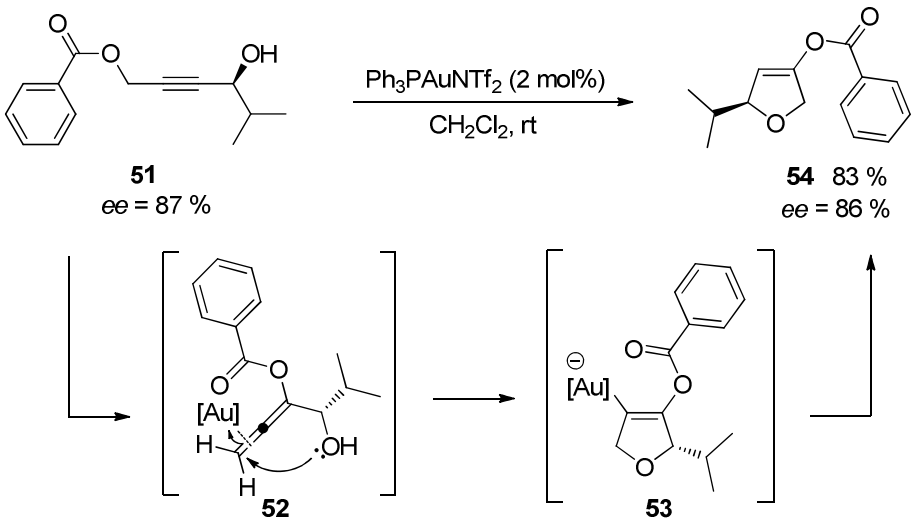
A 1,3-rearrangement forming **H** would be the result of a 6-*endo* attack pathway to access intermediate **G**.

The type of cyclisation in the initial step was shown to be dependent on the nature of the substrate, with terminal or electron-withdrawing substituted alkynes favouring the formation of the carbenoid species **F**, mesomeric form of **E**. On the other hand internal alkynes would react preferentially to give allene intermediate **H**.



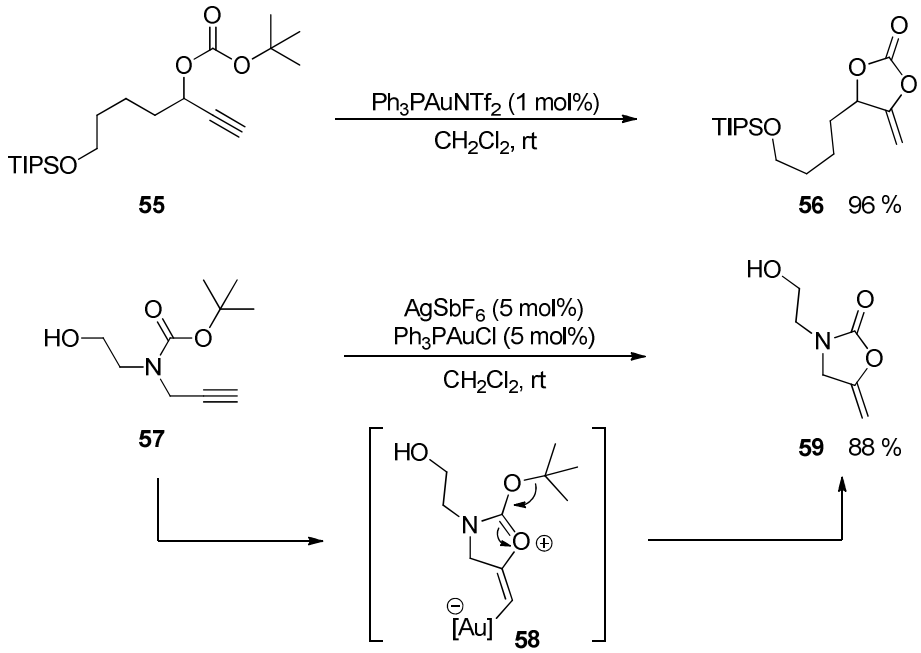
Scheme 12: Evolution of gold-activated propargyl acetates

This latter case was for example described in a cascade gold(I)-catalysed synthesis of 2,5-dihydrofurans from readily available butynediol monobenzoates (Scheme 13).[33] Activation of the triple bond by the gold complex was proposed to promote the nucleophilic attack of the benzoate moiety to form **52** through a 1,3-migration of the ester. Subsequent activation of the allene by the catalyst allowed nucleophilic attack of the alcohol causing formation of the vinyl-gold species **53**. Protonation finally ended the reaction and the final product was released. A good yield of 2,5-dihydrofuran **54** was obtained and excellent retention of the stereochemical information from the starting material was observed.



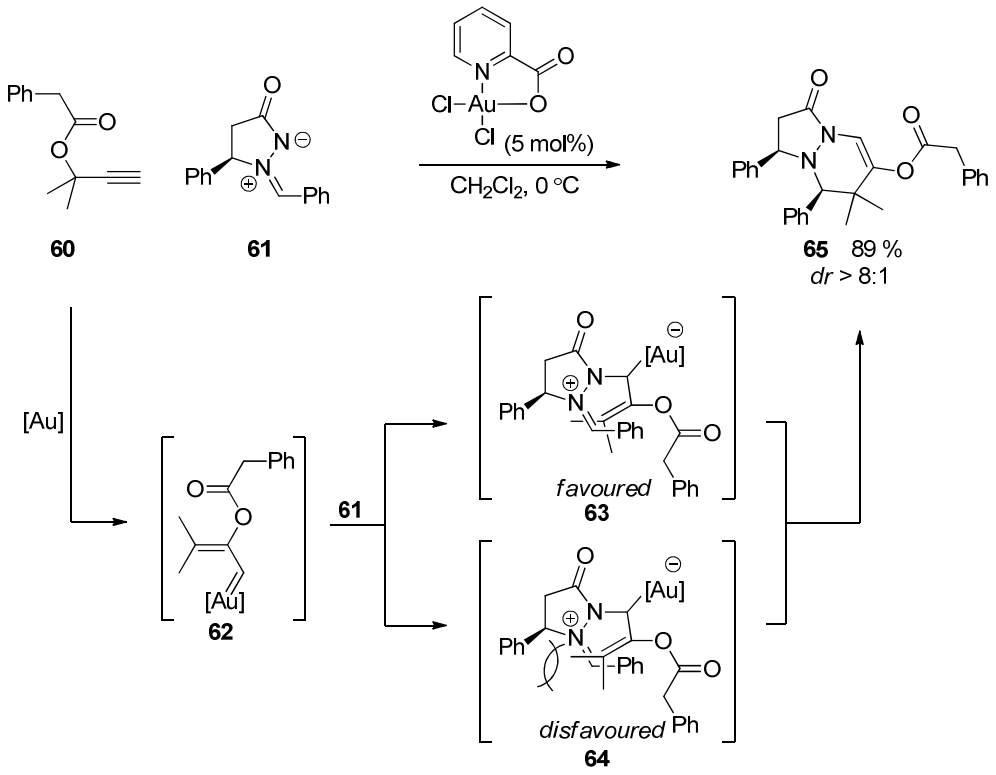
Scheme 13: Gold-catalysed 2,5-dihydrofuran formation involving a 1,3-benzoate migration

However it was found that some analogues were unable to undergo the same π-acid-induced rearrangement. *tert*-Butyl carbonate **55** led to the formation of isolable 1,3-dioxolan-2-one **56**[34] and carbamate **57** gave oxazolidinone **59**[35] by elimination of isobutene and subsequent protonation from intermediate **58** (Scheme 14).



Scheme 14: Gold-catalysed formation of 1,3-dioxolan-2-ones or oxazolidinones

The carbenoid pathway, involving a gold-catalysed 1,2-acyloxy migration, was also used in recent transformations (Scheme 15). Notably, the first reported trapping of a rearranged propargylic ester with a 1,3-dipole was performed under mild conditions to access bicyclic structures.[36] The cycloaddition of carbenoid species **62** with chiral azomethine imine **61** led to high yields of product **65** in good distereomeric ratios at 0 °C. The diastereoselectivity observed was rationalised by minimisation of unfavourable steric interactions in the ring closing transition state and led to the preferred *cis* product.

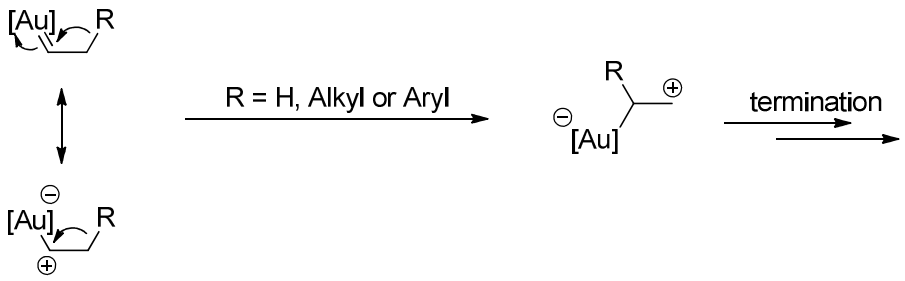


Scheme 15: Example of gold-catalysed 1,2-migration of propargylic esters

1.4.2 1,2-migration onto a gold carbenoid

Formation of carbenoid intermediates has been evoked in gold-catalysed processes and the use of such species in reactions was described in the previous section.

One way to take advantage of such very reactive functionality is to incorporate, in the molecular structure, a moiety capable of migrating to an adjacent gold carbenoid center thus providing a means to terminate the reaction (Scheme 16). Hydrogen, aryls and alkyls have all been shown to be suitable substituents for 1,2-shifts and their migrating aptitude to gold carbenoids generally followed the order H > aryl > alkyl, as is observed for free carbenes.[37]

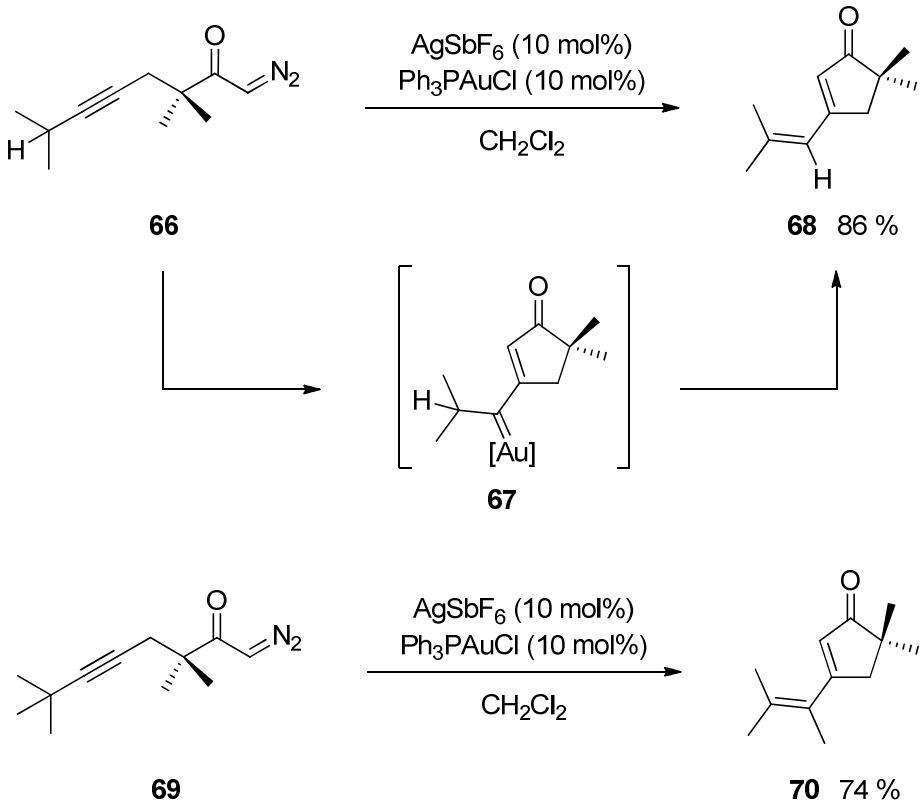


Scheme 16: 1,2-migration step to a gold carbenoid center

Due to the fact that 1,2-hydrogen shift is usually favoured, 1,2-alkyl and aryl migration are only found in gold-catalysed reactions where no hydrogen could compete.

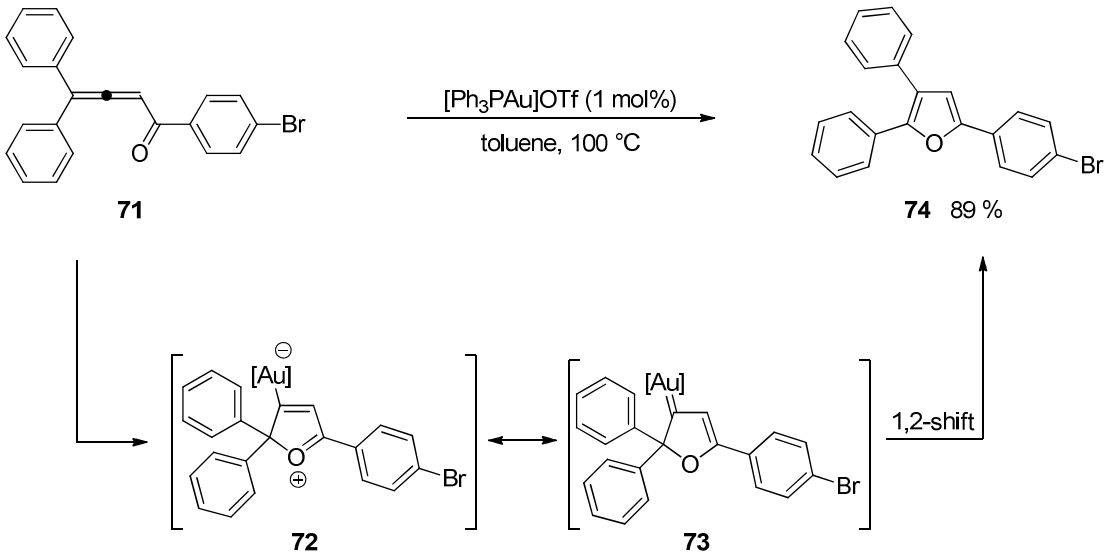
An example of this preference for a 1,2-hydrogen versus 1,2-alkyl shift was particularly well illustrated in a gold(I)-catalysed synthesis of diene **68** (Scheme 17).[38] In the case of *iso*-propyl-substituted alkyne **66**, the carbenoid intermediate **67** from diazo decomposition was shown to rearrange solely into diene **68** through a 1,2-hydrogen shift. In the absence of a

hydrogen, when *tert*-butyl-substituted alkyne **69** was submitted to the same reaction conditions, a 1,2-methyl shift occurred to form diene **70** in good yield.



Scheme 17: Example of a favoured 1,2-hydrogen migration versus 1,2-methyl migration

Cases involving a 1,2-aryl shift are very rare. Examples where this process can be proposed were described in the gold-catalysed preparation of furans from allenyl ketones (Scheme 18).[39] In this reaction nucleophilic attack of the lone pair of ketone **71** onto the allene would form cyclic oxonium **72**. A subsequent 1,2-phenyl shift would occur to give product **74** after demetallation.

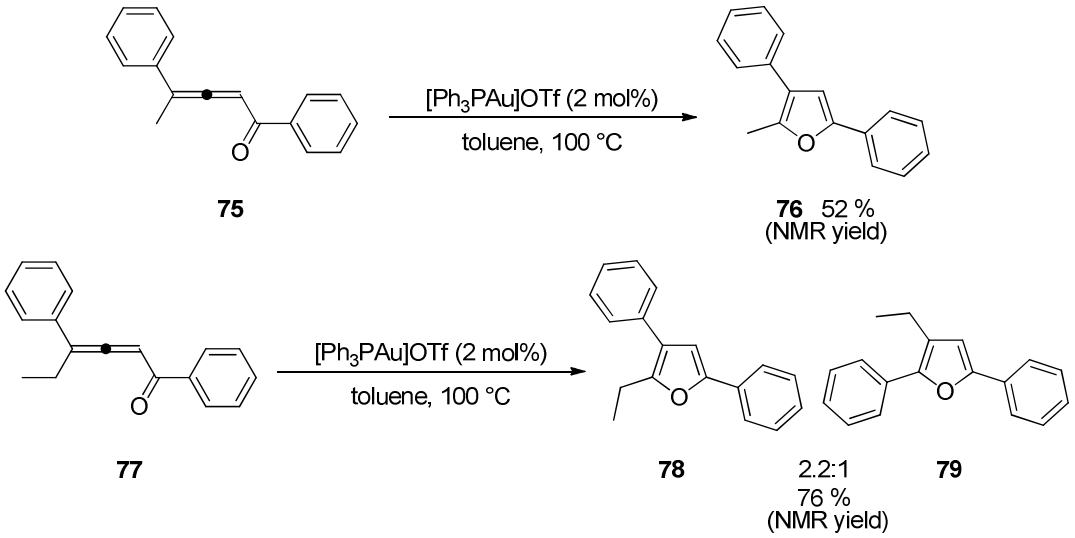


Scheme 18: Proposed 1,2-phenyl shift in the gold-catalysed formation of furan 74 from allenyl ketone 71

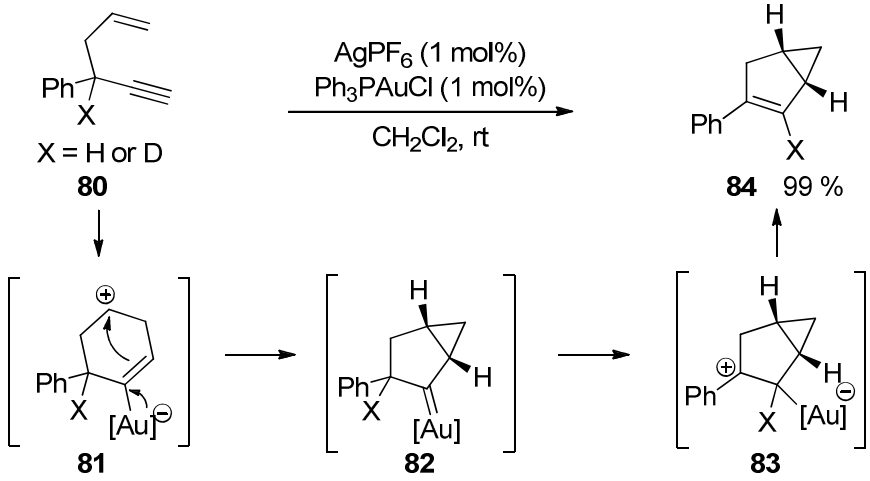
It was also shown that allenyl ketones bearing an alkyl and a phenyl substituent, instead of two phenyl groups like in substrate **71**, gave 1,2-phenyl migration products (Scheme 19). Compound **75** bearing a methyl group was transformed into furan **76** under gold catalysis, and allenyl ketone **77** with an ethyl substituent formed compound **78** as major product under similar conditions. The formation of a second furan **79** in this last case was a surprising result as it revealed that the 1,2-shift of the ethyl moiety competed with migration of the phenyl group. As a result it was suggested that this furan synthesis was probably more likely to involve a cationic, pathway although a carbene intermediate was not ruled out.

1,2-Hydrogen migration were more commonly reported in gold-catalysed processes. An isomerisation of 1,5-enynes was for example described (Scheme 20).[40] After a gold-catalysed 6-endo type cyclisation of compound **80**, formation of carbenoid intermediate **82** and closure of the cyclopropane ring were proposed. 1,2-Shift of a hydrogen or deuterium to the

carbenoid was shown to take precedence over a phenyl group migration and led to the formation of the corresponding bicyclic product **84**.



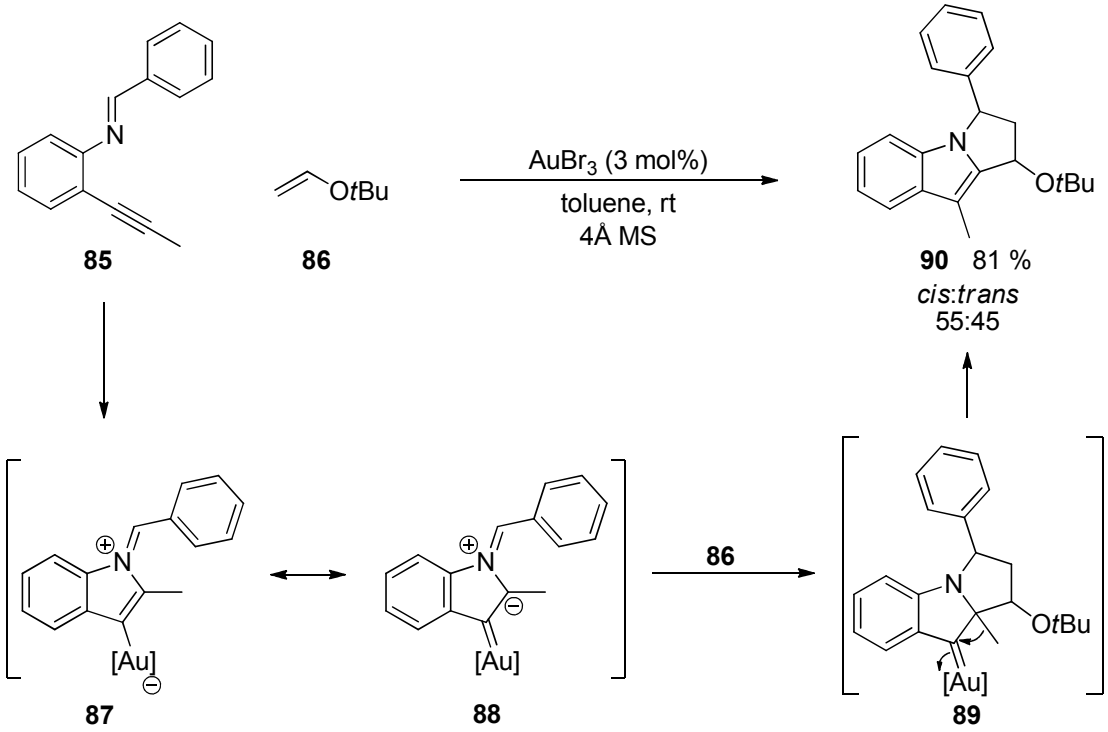
Scheme 19: 1,2-Phenyl and ethyl migration in gold-catalysed formation of furans from allenyl ketones



Scheme 20: 1,2-Hydrogen or deuterium shift in 1,5-enyne isomerisation

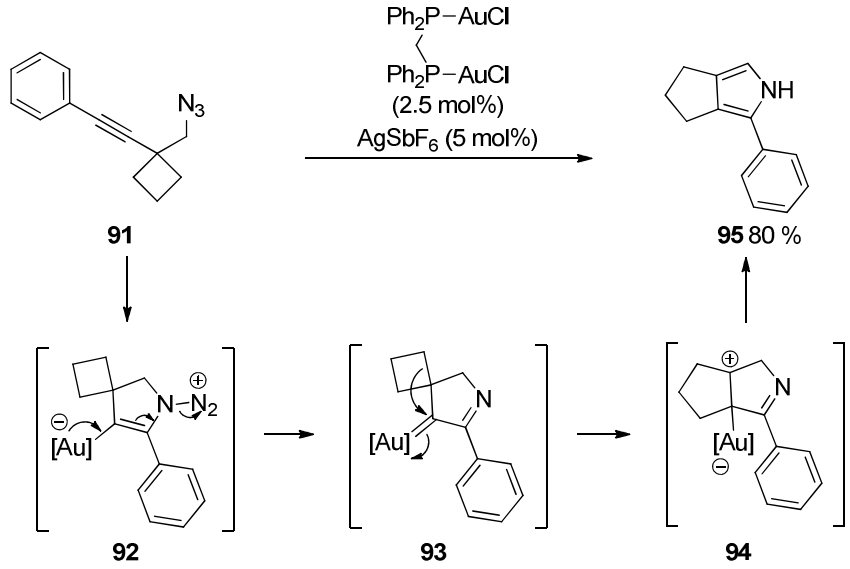
A combination of 1,2-alkyl migration with [3+2] cycloaddition was developed for the synthesis of tricyclic indole derivatives (Scheme 21).[41] In this sequence, π-acid activation of the alkyne moiety by $AuBr_3$ induced nucleophilic attack of the lone pair of imine **85**. The

resulting intermediate evolved to a fused polycyclic structure through a [3+2] cycloaddition between the 1,3-dipole **87** and the electron-rich vinyl ether present in the reaction mixture. Finally a 1,2-methyl shift to the adjacent metal "carbenoid" center followed by demetalation gave the reported indole product **90** in good yield.



Scheme 21: Combinaison of a 1,2-alkyl migration with a [3+2] cycloaddition

Another particularly effective 1,2-alkyl migration was reported in the case of a gold(I)-catalysed regioselective acetylenic Schmidt reaction of homopropargylic azides.[42] A mechanism involving gold(I) activation of alkyne toward nucleophilic addition was proposed. Loss of nitrogen gas formed species **93** and subsequent cyclobutane ring strain release occurred through 1,2-alkyl shift onto the carbenoid. Catalyst regeneration and tautomerisation gave the multiply substituted pyrrole **95** in good yield.

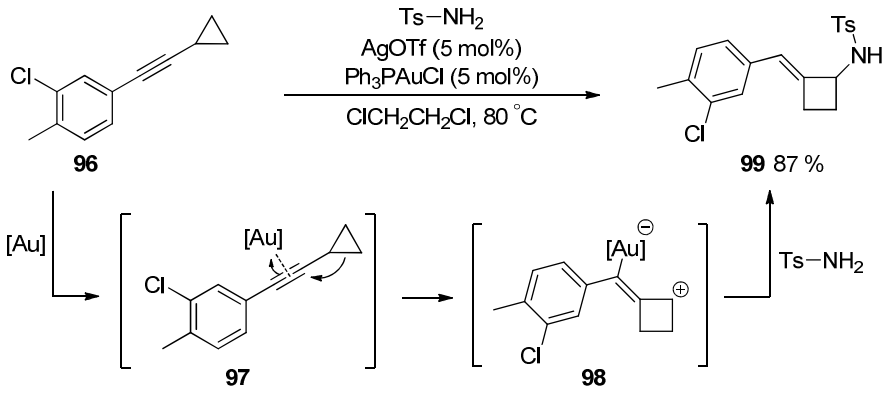


Scheme 22: An example of 1,2-migration to an adjacent gold carbenoid intermediate

1.4.3 1,2-alkyl shift to an adjacent carbocation

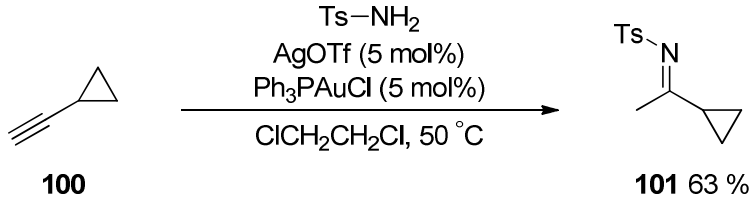
While the previous paragraph described 1,2-shifts to a carbenoid (metal-stabilised carbocation) intermediate, similar reorganisation was also recently used on carbocations formed by gold catalysed processes that are not directly connected to a metal.

Gold(I)-catalysed ring expansion of unactivated alkynylcyclopropanes was for example reported for the preparation of alkylidenecyclobutanamines (Scheme 23).[43] The positive charge developed on the alkyne by coordination of the gold fragment induced a 1,2-alkyl migration from the cyclopropane moiety. The resulting cyclobutane cationic intermediate **98** was further trapped by the sulfonamide present in the reaction mixture to give compound **99** in good yield.



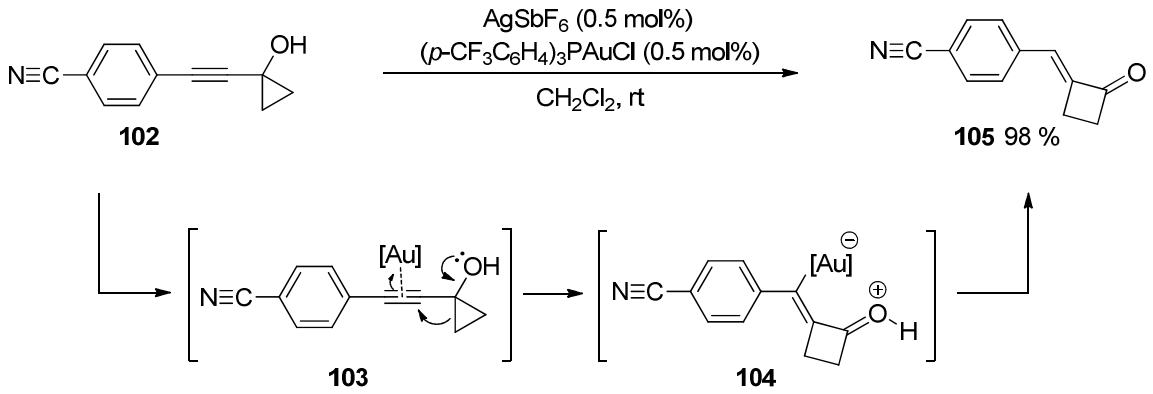
Scheme 23: Gold-catalysed ring expansion of alkynylcyclopropanes

These results showed that for substituted alkynylcyclopropanes, and under the reaction conditions reported, the ring expansion process was taking precedence to the competitive hydroamination reaction discussed previously in this chapter. On the other hand, when the reaction was conducted with terminal alkynylcyclopropane **100** the hydroamination process was this time favoured and imine **101** was formed instead of the cyclobutanamine (Scheme 24).



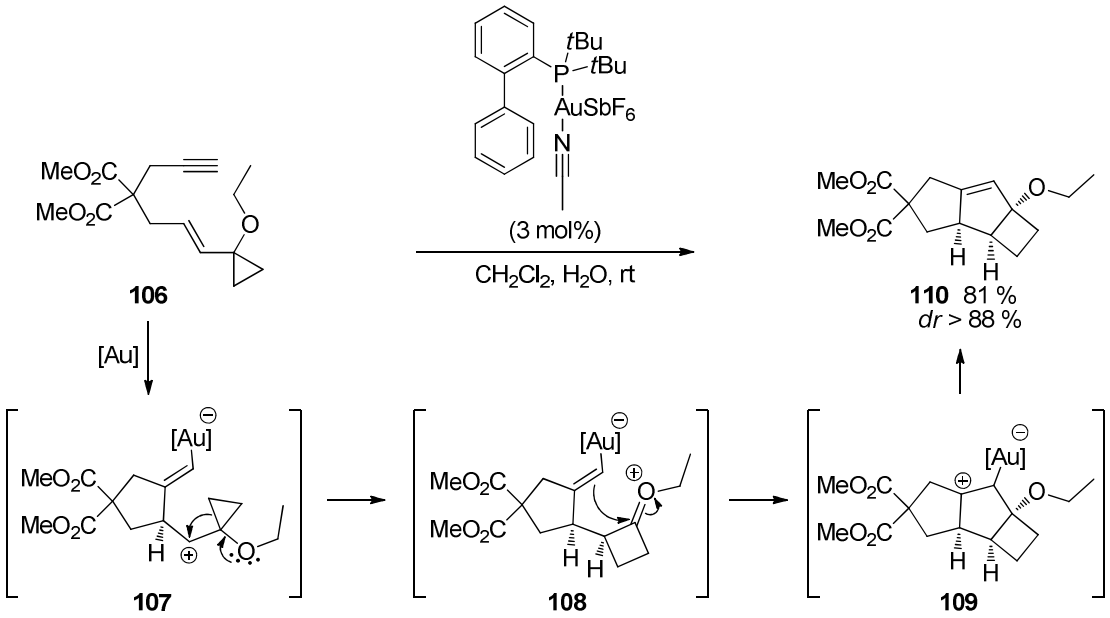
Scheme 24: Gold-catalysed hydroamination of terminal alkynylcyclopropane

Previous work in this area had already reported the formation of cyclobutanes but employing alkynylcyclopropanols as precursors (Scheme 25).[44] In that case 1,2-migration toward the alkyne was favoured by the presence of the alcohol functionality and cyclobutanone **105** was formed in good yields.



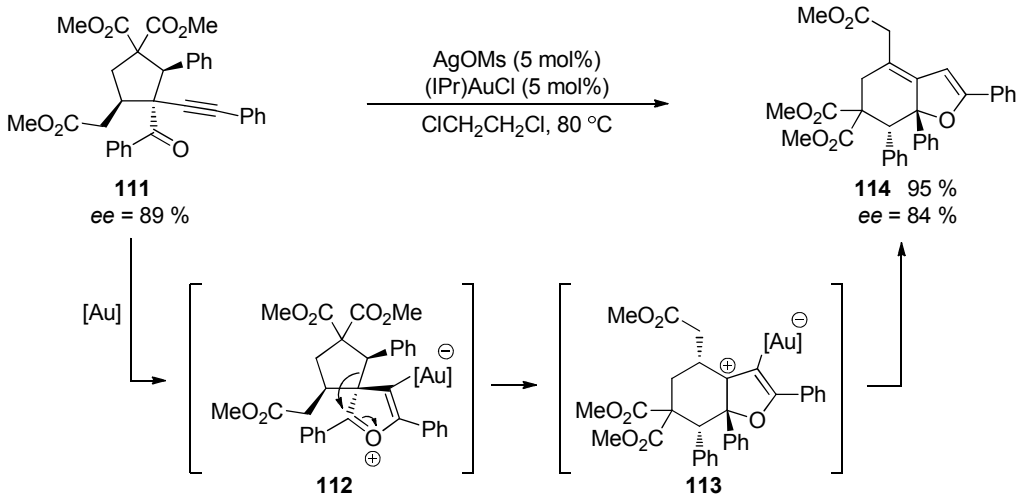
Scheme 25: Gold-catalysed ring expansion of alkynylcyclopropanols

Another example involving cycloisomerisation on enyne **106** this time allowed elegant access to complex tricyclic compound **110** (Scheme 26).[45] A 5-*exo* addition of the olefin on the activated alkyne was proposed to lead to carbocationic species **107**. A subsequent 1,2-alkyl shift formed cyclobutane intermediate **108** which suffered nucleophilic attack from the alkene moiety forming five-membered ring species **109**. This cascade reaction was ended by deauration and gave polycyclic product **110** in good yield.



Scheme 26: Gold-catalysed cascade reaction of enyne 110

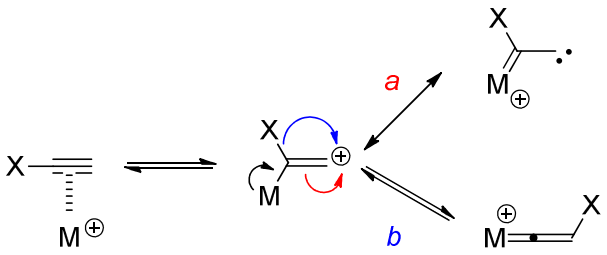
More recently the potential of regioselective and stereospecific 1,2-alkyl migration was highlighted in a cationic gold(I)-catalysed tandem reaction (Scheme 27).[46] An initial intramolecular attack of the carbonyl moiety to the activated alkyne was proposed. The spiro-bicyclic derivative would then undergo a 1,2-alkyl migration to give cationic intermediate **113**. Double bond formation followed by protodeauration would terminate the process and deliver the fused-bicyclic final structure in excellent yield and enantiomeric excess.



Scheme 27: Selected examples of 1,2-alkyl migration in gold catalysed processes

1.4.4 1,2-shifts to form gold vinylidene intermediates

Although well known for other metals, vinylidene intermediates were only lately discovered and very rarely used so far in gold-catalysed transformations. Their formation was shown to result from a 1,2-shift of a migrating group upon π-acid activation of a C-C triple bond (Scheme 28).[47]



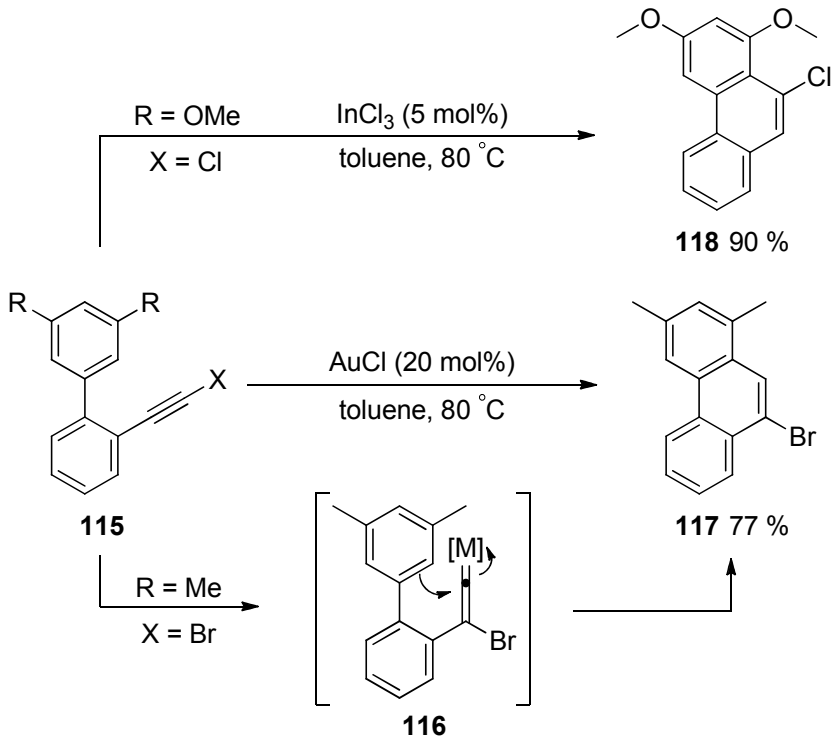
Scheme 28: Metal mediated vinylidene intermediate formation

Various alkyne substituents such as hydrogen, halogens[48], silanes or stannanes[49] proved suitable for the gold-catalysed rearrangement to take place. In the presence of a nucleophile the gold-vinylidene intermediate would evolve toward a vinyl-gold species through an attack on the carbon adjacent to the metal center. Termination of the gold-catalysed process would then occur in a similar manner to those described previously depending on the substrate.

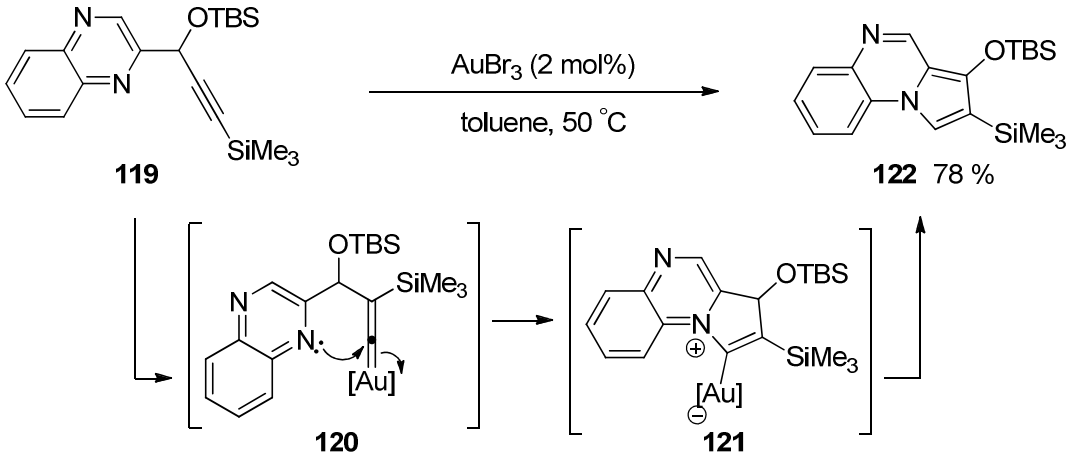
A gold(I)-mediated vinylidene rearrangement was for example proposed in a synthesis of 9-bromophenanthrene **117** (Scheme 29).[48] Under AuCl catalysis alkyne **115** would rearrange into intermediate **116**. A Friedel-Crafts type hydroarylation would then take place to give product **117** after protodemetallation.

The gold vinylidene rearrangement pathway was particularly interesting as it complemented another transformation where compound **118** was accessed by $InCl_3$ catalysis.

Another illustration of this transformation with a silicon substituent was given by a gold(III)-catalysed synthesis of polycyclic pyrroles (Scheme 30).[49] Here the vinylidene rearrangement was followed by nucleophilic attack from the lone pair of the nitrogen to give rise to zwitterion **121,** which upon protodeauration released the product in good yield.



Scheme 29: Gold vinylidene rearrangement in phenanthrene synthesis

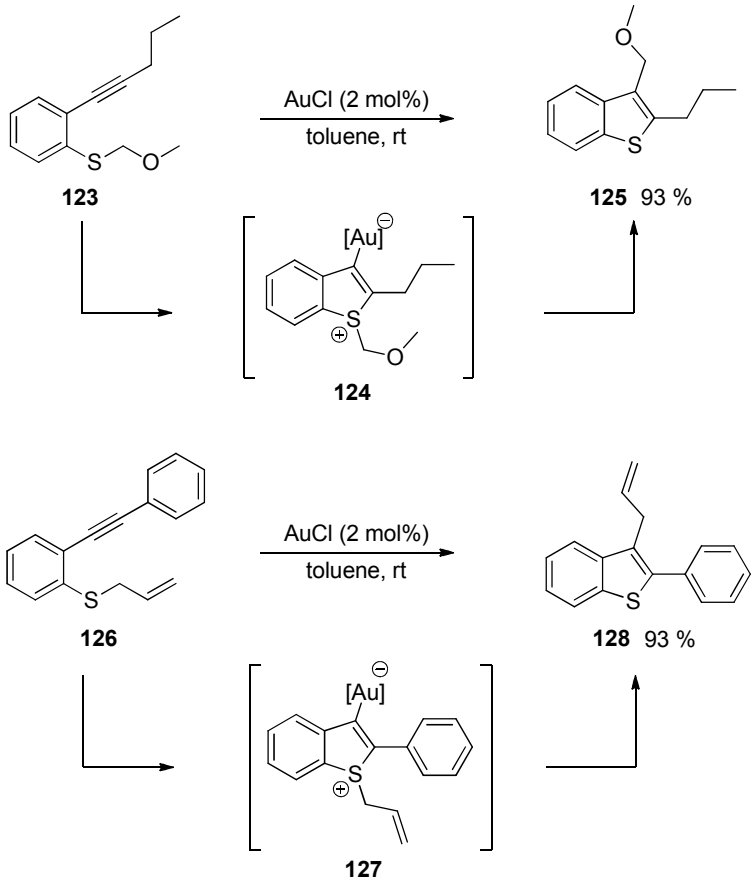


Scheme 30: Trimethylsilane 1,2-shift to form gold vinylidene intermediate

1.4.5 X → C shift reactions

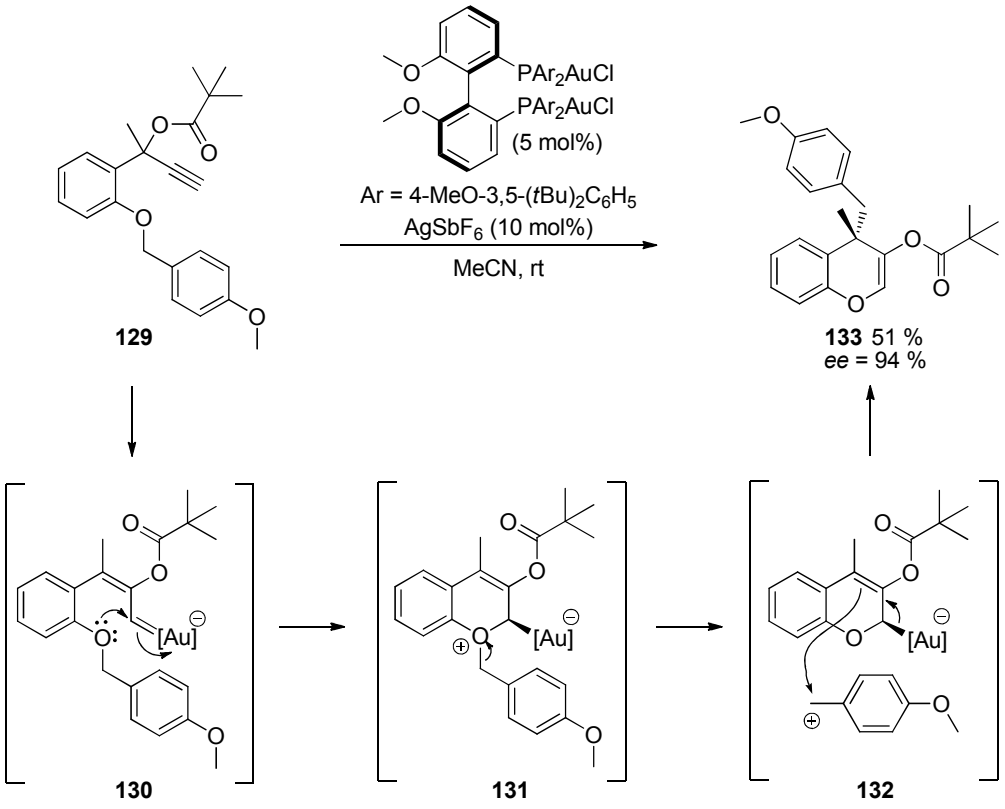
The migratory possibilities offered by the use of aprotic heteroatom nucleophiles, such as ethers, thioethers, amides or sulfonylanilines were also explored.[50] Unlike the widely used alcohols or amines which undergo deprotonation followed by protodemetallation after gold-catalysed nucleophilic attack on alkynes (see section 1.5), those reagents would lead to alternate outcomes.

As illustrated in Scheme 31 thioethers **123** and **126** were for example employed in a gold (I)-catalysed transformation wherein a cyclisation and a formal migration of the α-alkoxy alkyl,[51] or allyl sulfide substituent occurred.



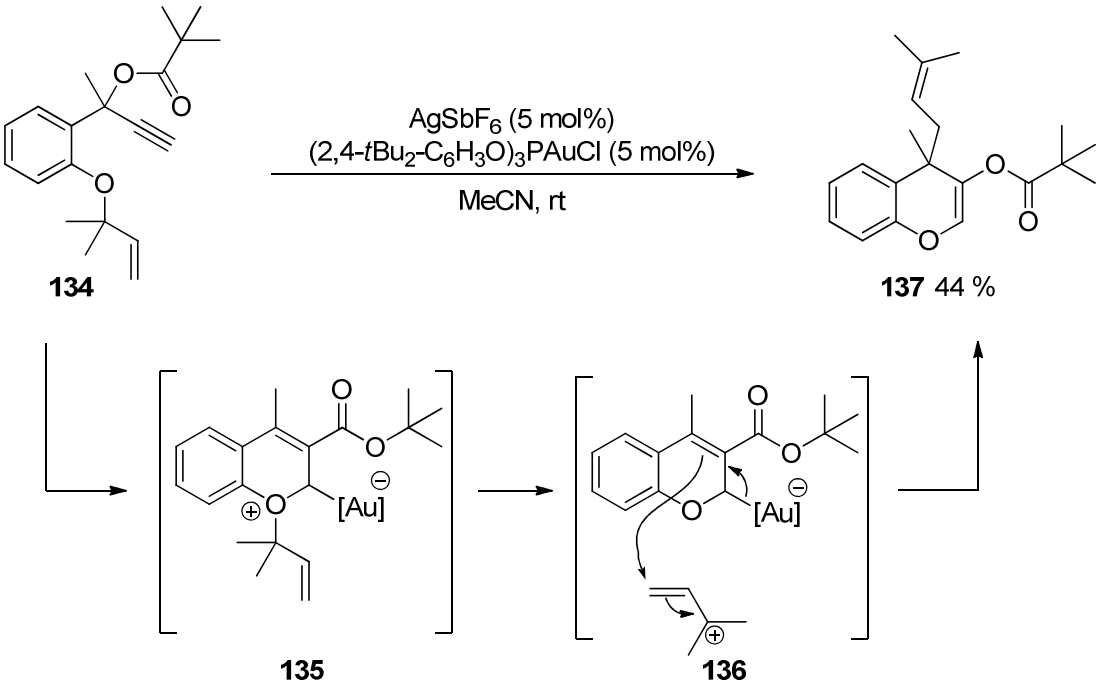
Scheme 31: X→C migration of α-alkoxy alkyl and allyl sulfide in gold catalysed processes

A similar type of migration was also presented in an intramolecular synthesis of benzopyrans **133** (Scheme 32).[52] An initial 1,2-acyloxy migration would form carbenoid **130** as introduced in the previous sections and intramolecular nucleophilic attack of the phenol ether would follow. It was proposed that subsequent expulsion of a stabilised benzylic cation would take place. Finally the reintegration of this cation in the molecule would occur by reaction with the allylgold(I) species to give **133** in good yield and enantiomeric excess.



Scheme 32: Proposed benzylic cation formation in a gold-catalysed benzopyran synthesis

This mechanism was proved in the case where a non symmetrical allyl substituent was engaged (Scheme 33). A similar migration was observed but inversion of the allylic moiety occurred to form product **137**. The possible engagement of a direct 1,4-sigmatropic rearrangement was thus ruled out giving weight to a mechanism involving the formation of an allyl cation.



Scheme 33: Allylic cation formation in a gold-catalysed benzopyran synthesis

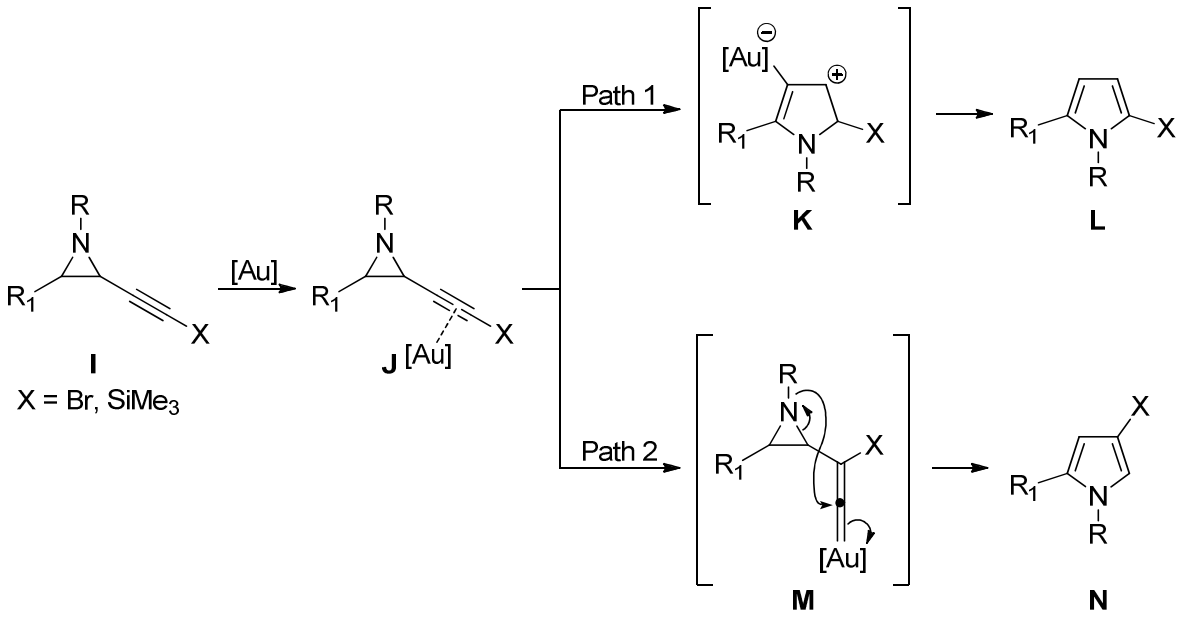
1.5 Conclusion

Homogeneous gold catalysis has proved a powerful tool for organic chemists in the last ten years. More specifically the very selective activation of C-C triple bonds of alkynes by gold complexes has attracted much interest and was employed in many processes where new C-X (X as heteroatom) and C-C bonds were formed. The high functional group tolerance and the convenience of mild reaction conditions associated with gold catalysis have also been determinant factors in the expansion of the area.

Furthermore, molecular complexity has been achieved when the fundamental process of nucleophilic attack across an alkyne was combined with migration steps. Cascade reactions involving 1,2-migration to carbenoid, 1,2-shift to non-metal-stabilised carbocation or vinylidene rearrangement were particularly efficient in that respect and more applications of these processes in synthesis should emerge in the next few years.

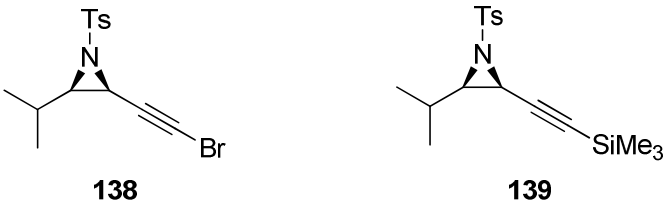
1.6 Aims and objectives

This work focused on a new gold catalysed synthesis of functionalised pyrroles from alkynyl aziridines. Our aim was to develop a regio-controlled access to 2,4- and 2,5-substituted pyrroles from the same aziridine precursor **I** under the mild conditions associated with gold catalysis (Scheme 34). Based on the known modes of reactivity of gold catalysis it was predicted that activation of the internal alkyne present in the aziridine precursor by a π-acidic gold species would render the carbons of the C-C triple bond electrophilic. A ring expansion would provide a five-membered ring cationic intermediate **K** which upon deprotonation followed by protodemetallation will lead to the formation of 2,5-substituted pyrrole **L**. Alternatively a vinylidene pathway should allow access to the 2,4-substituted pyrrole product **N**.



Scheme 34: Proposed gold-catalysed access to 2,4- and 2,5-substituted pyrroles from alkynyl aziridines.

To study this proposal aziridines **138** and **139**, bearing halogen or silyl substituents respectively, were prepared as both were shown suitable for the two pathways evoked previously (Figure 3).



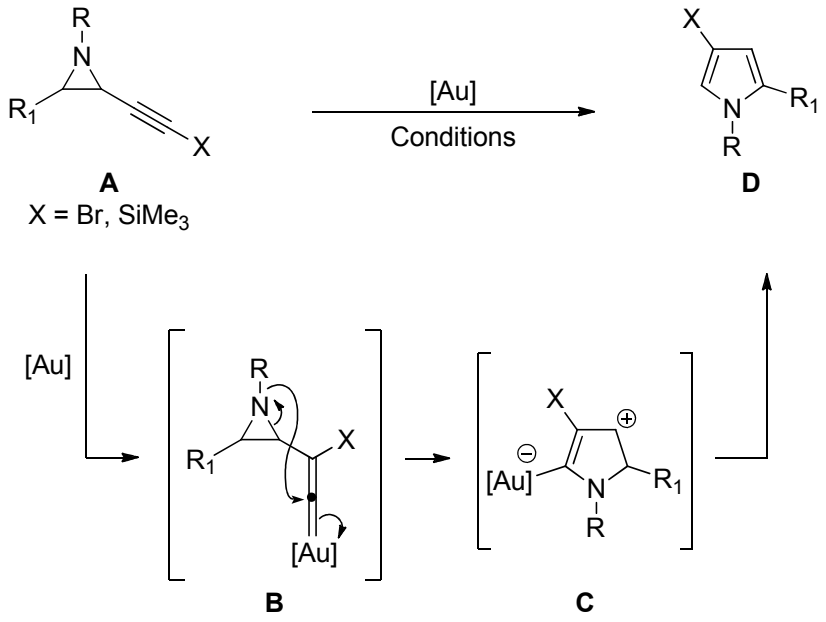
138 **139**

Figure 3: Chosen alkynyl aziridine precursors.

Chapter 2: Gold-catalysed pyrrole synthesis via vinylidene rearrangement of alkynyl aziridine

2.1 Introduction

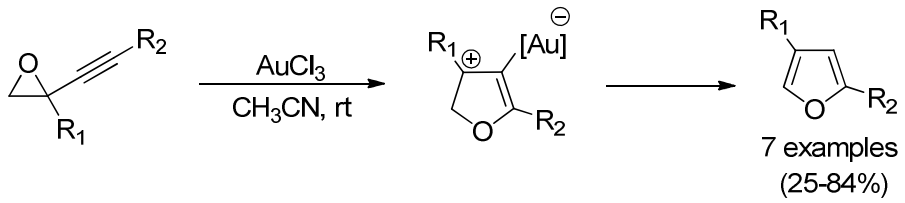
In light of the previously introduced advances in gold catalysis, a combination of a vinylidene rearrangement and a ring expansion of brominated and silylated alkynyl aziridines was proposed (Scheme 35).



Scheme 35: Proposed 2,4-substituted pyrroles synthesis through vinylidene rearrangement of alkynyl aziridines followed by a ring expansion.

According to literature precedents discussed in the previous chapter, both silyl and bromide are suitable C-C triple bond substituents for a gold-catalysed vinylidene rearrangement to take place. Under appropriate reaction conditions, formation of intermediate **B** should therefore be possible and it was anticipated that a ring expansion would occur to give organo-gold species **C**. Indeed Hashmi and Sinta have shown alkynyl oxiranes can undergo ring opening upon gold activation to give furans which is a good precedent for the transformation of **C** from **B**

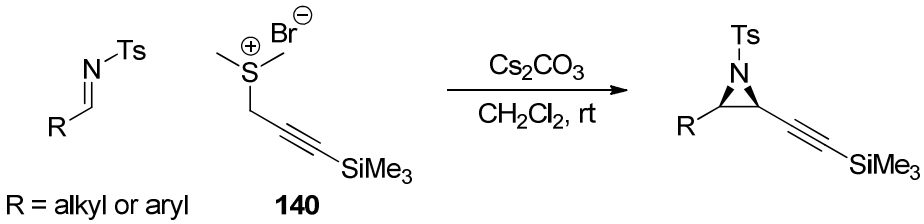
(Scheme 36). Protodeauration of intermediate **C** would then terminate the process by releasing the catalyst and the aimed 2,4-substituted pyrrole **D**.



Scheme 36: Hashmi and Sinha's gold-catalysed furan synthesis from alkynyl oxirane.

2.2 Starting material preparation

As an efficient pyrrole synthesis would be of low impact if the alkynyl aziridines could not be formed quickly from readily available and simple building blocks, it was decided to prepare those precursors according to the method of Dai, which allows a convergent coupling of tosylimines and propargylic sulfonium salts (Scheme 37).[53]

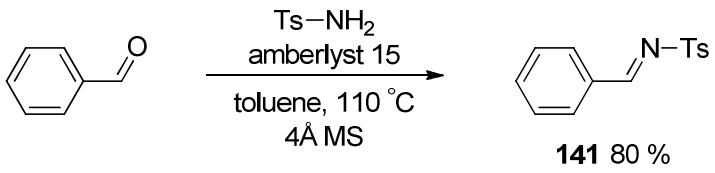


Scheme 37: Rapid access to alkynyl aziridine from imine and sulfonium salt.

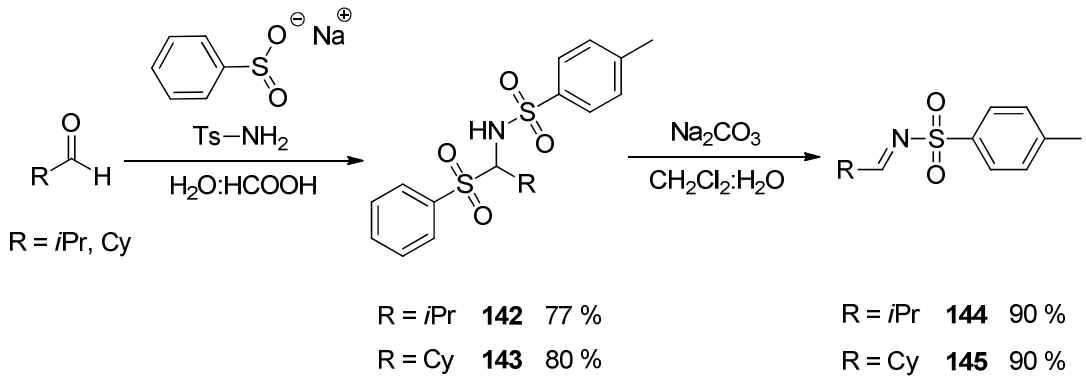
Exclusively *cis*-aziridines were obtained with this method when employing trimethylsilyl substituted sulfonium salts.

Aryltosylimine **141** was prepared by direct condensation of benzaldehyde in a Dean-Stark apparatus under acidic catalysis but attempts to access alkyltosylimines by this method were

unsuccessful (Scheme 38).[54] An alternative strategy was therefore employed to prepare these adducts from enolisable aldehydes. Alkylaldehydes were treated with 4-methylbenzenesulfonamide and sodium benzenesulfinate in a mixture of water and formic acid (Scheme 39).[55] The stable tosylamides obtained could be stored at room temperature for weeks without problem. Conversion to the corresponding tosylimines **144** and **145** was readily achieved in high yield in a mixture of CH_2Cl_2 and saturated solution of aqueous Na_2CO_3.



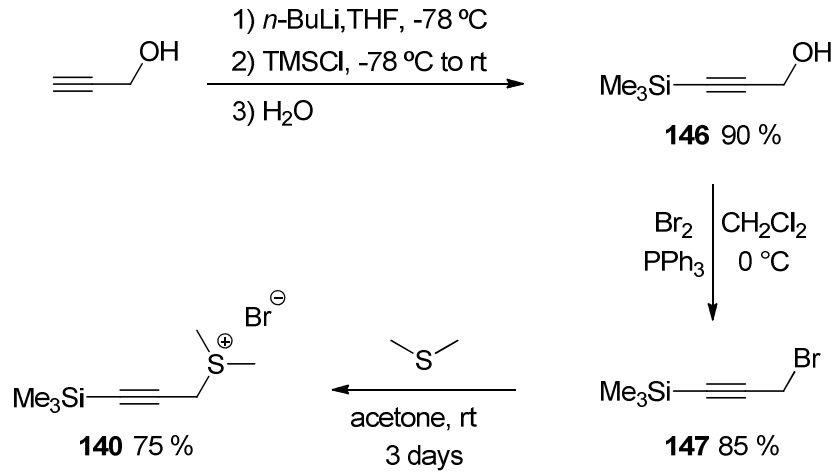
Scheme 38: Preparation of aryltosylimine 141



Scheme 39: Alternative imine preparation from enolisable alkylaldehyde.

The synthesis of the sulfonium salt **140** was also straightforwardly realised in three steps from commercially available propargyl alcohol (Scheme 40). Propargyl alcohol was doubly deprotonated with two equivalents of *n*-BuLi and the corresponding lithium species was trapped with TMSCl.[56] Propargylic alcohol **146** was obtained after aqueous workup that

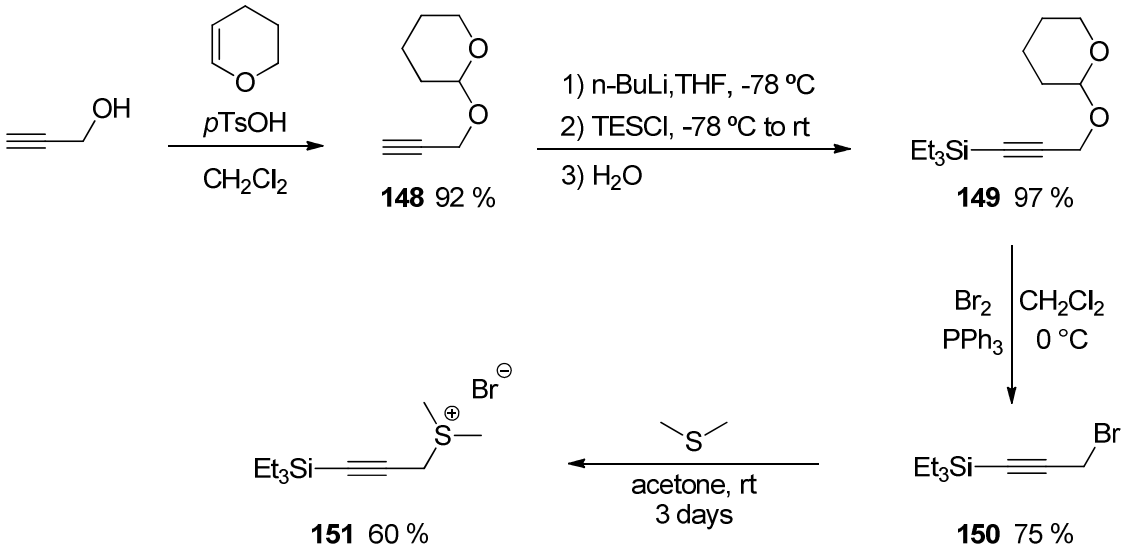
cleaved the O-Si bond. Bromide **147** was prepared using Br_2 in presence of PPh_3 and its treatment with DMS gave sulfonium salt in good yield. This last step took three days but attempts to accelerate it by heating or by stopping the reaction earlier were unsuccessful and led to dramatic yield reduction.



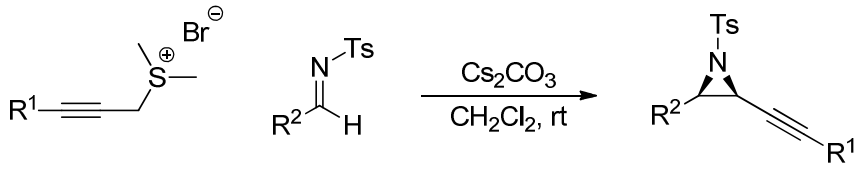
Scheme 40: Trimethylsilyl-substituted sulfonium salt preparation from propargyl alcohol.

As will be rationalised later, it was also decided to synthesise the triethylsilyl version of the sulfonium salt. Because triethylsilyl ethers are more stable than their trimethylsilyl equivalent aqueous treatment would not allow us to obtain the free propargyl alcohol in that case and another protocol was employed. Propargyl alcohol was protected with tetrahydropyran[57] as the ether could be directly converted to the bromide without an additional deprotection step (Scheme 41).[58] Triethylsilyl sulfonium salt **151** was then synthesised in average yield by treatment with DMS.

With the imines and sulfonium salts in hand, attention was turn to the preparation of the alkynyl aziridines. Four of them were formed in good yield by treatment of tosylimine and ylide with Cs_2CO_3 in CH_2Cl_2 at room temperature (Table 1).



Scheme 41: Preparation of triethylsilyl-substituted sulfonium salt.



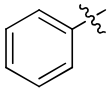
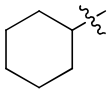
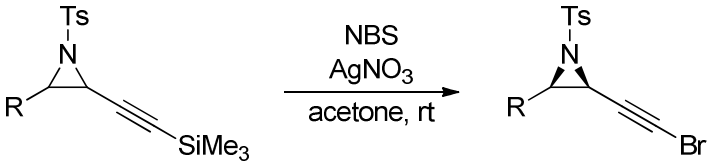
entry	R^1	R^2	Reaction Time (h)	Product	Yield (%)[a]
1	Me_3Si–		1	**152**	70
2	Me_3Si–		3	**139**	70
3	Et_3Si–		3	**153**	80
4	Me_3Si–		3	**154**	85

Table 1: Silylated alkynyl aziridine preparation. Reactions were performed using 1.2 equiv of sulfonium salt and Cs_2CO_3. [a]isolated yields

Two more brominated alkynyl aziridines were also efficiently prepared by treatment of trimethylsilyl-substituted substrates **139** and **152** with NBS and $AgNO_3$ in acetone at room temperature (Table 2).[59]



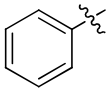
entry	R	Reaction Time (h)	Product	Yield (%)[a]
1		1	**155**	80
2		1	**138**	80

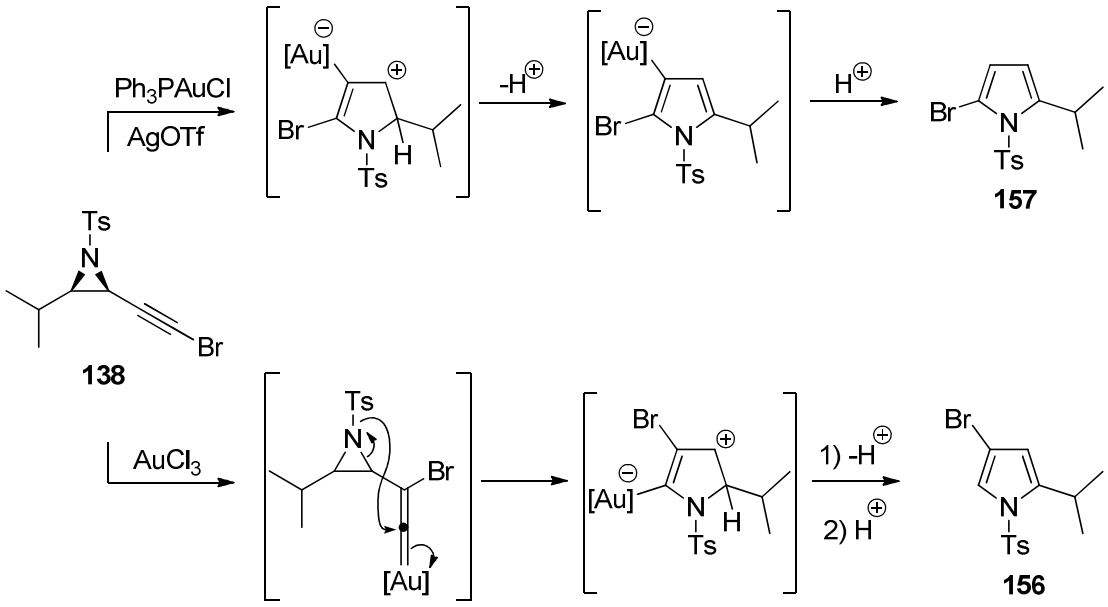
Table 2: Brominated alkynyl aziridine preparation. [a]isolated yields

2.3 Catalyst screening

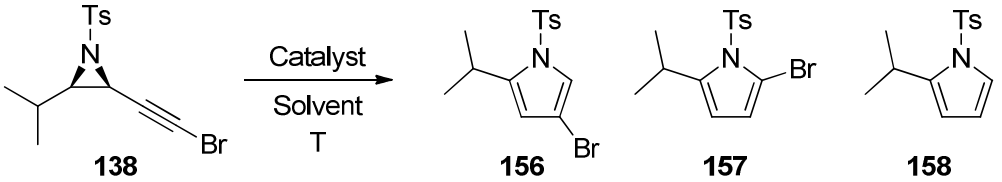
The study of the vinylidene rearrangement and ring expansion pathway was started by submitting aziridine **138** to different catalysts and sets of conditions (Table 3). Analysis of the crude mixture was performed by ^1H NMR using a known quantity of an internal standard (1,2,4,5-tetramethylbenzene). No reaction occurred when copper (entry 9), palladium (entries 10-12), platinum (entry 8), rhodium (entries 17-19), ruthenium (entry 16), silver (entries 13-15) or tungsten (entry 20) catalysts were used. On the other hand, formation of the desired 2,4-substituted pyrrole **156** was seen when $AuCl_3$ was used as catalyst (entries 2 and 3) and 2,5-substituted pyrrole **157** (not isolated) was observed with some cationic gold species (entries 6 and 7). In both cases a mono-substituted pyrrole **158** was also observed, and some starting material was often recovered unreacted. While complete conversion of alkynyl

aziridine **138** was achieved using $AuCl_3$ in toluene (0.5 M) at 50 °C after 2 h (entry 3), brominated pyrrole **156** was the minor product and monosubstituted pyrrole **158** was obtained as major.

The difference in regioselectivity when using $AuCl_3$ or a cationic catalyst can be explain by the reluctance of the latter to form a vinylidene intermediate prior to ring expansion (Scheme 42). A simple electrophilic activation of the C-C triple bond by the $PPh_3AuCl/AgOTf$ system is though to induce ring expansion and lead to the formation of 2,5-substituted pyrroles. On the other hand, $AuCl_3$ forms a vinylidene intermediate which then reacts through a ring expansion to give the observed 2,4-substituted pyrrole **156**.



Scheme 42: Proposed mechanism for 2,5 and 2,4-substituted pyrrole formation.



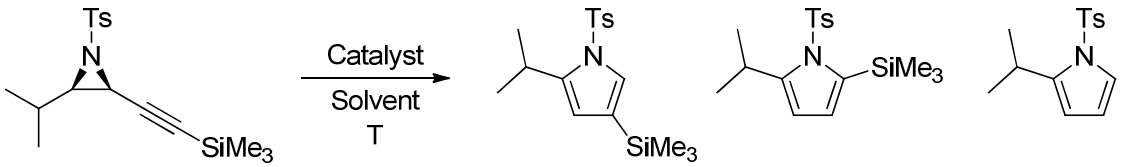
138 **156** **157** **158**

entry	Catalyst	Solvent	Temperature (°C)	Reaction Time (h)	Yield (%)[b]		
					156	**157**	**158**
1	AuCl	Toluene	23 then 50[a]	14	-	-	-[c]
2	$AuCl_3$	Toluene	23 then 50[a]	14	25	-	15[d]
3	$AuCl_3$	Toluene	50	2	20	-	60[e]
4	Me_2SAuCl	Toluene	23 then 50[a]	14	-	-	-[c]
5	PPh_3AuCl	Toluene	23 then 50[a]	14	-	-	-[c]
6	$PPh_3AuCl/AgOTf$	Toluene	23 then 50[a]	14	-	29	4[f]
7	$PPh_3Au(NTf)_2$	Toluene	23 then 50[a]	14	-	7	-[g]
8	$PtCl_2$	Toluene	23 then 50[a]	14	-	-	-[c]
9	CuI	Toluene	23 then 50[a]	14	-	-	-[c]
10	$PdCl_2$	Toluene	23 then 50[a]	14	-	-	-[c]
11	$PdCl_2(PPh_3)_2$	Toluene	23 then 50[a]	14	-	-	-[c]
12	$Pd(OAc)_2$	Toluene	23 then 50[a]	14	-	-	-[c]
13	$AgNO_3$	Toluene	23 then 50[a]	14	-	-	-[c]
14	$AgSbF_6$	Toluene	23 then 50[a]	14	-	-	-[c]
15	$AgBF_4$	Toluene	23 then 50[a]	14	-	-	-[c]
16	$RuCl_2(PPh_3)_3$	Toluene	23 then 50[a]	14	-	-	-[c]
17	$RhCl(PPh_3)_3$	Toluene	23 then 50[a]	14	-	-	-[c]
18	$(Rh(COD)Cl)_2$ + $P(pFC_6H_5)_3$	Toluene	23 then 50[a]	14	-	-	-[c]
19	$(Rh(COD)Cl)_2$ + $P(pFC_6H_5)_3$	DMF	85	14	-	-	-[c]
20	$W(CO)_5(THF)$	THF	23 then 50[a]	14	-	-	-[c]

Table 3: Catalyst screening on aziridine 138. Reactions were performed using 0.1 mmol of starting material (34 mg), 10 mol% catalyst and 0.5 mL of solvent (C = 0.2 M) under argon. [a]Reaction started at 23 °C (2 h) and heated after at 50 °C for 12 h. [b]Yields calculated by ^{1}H NMR against a known quantity of internal standard. [c]Only unreacted starting material was observed. [d]50 % starting material left. [e]C = 0.5 M, no starting material left, Isolated yields: 15 % of 156 and 60% of 158. [f]25 % starting material left. [g]46 % starting material left.

It was then decided to test the three active catalysts (Table 3, entries 3, 6, 7) on silylated alkynyl aziridine **139** (Table 4). Analysis of the crude mixtures was performed by ^{1}H NMR using a known quantity of internal standard (1,2,4,5-tetramethylbenzene). The two cationic gold catalysts (Table 4, entries 1,2) gave solely mono-substituted pyrrole **158**. In contrast to brominated substrate **138** no trace of either 2,4- or 2,5- substituted pyrrole was observed in the crude ^{1}H NMR of the mixtures.

When $AuCl_3$ was used, 2,4-substituted pyrrole **159** was formed, along with some mono-substituted product, showing vinylidene pathway could be accessed from trimethylsilane alkynyl aziridines.



139 **159** **160** **158**

entry	Catalyst	Solvent	Temp (°C)	Yield (%)[a]			
				139	**159**	**160**	**158**
1	$PPh_3Au(NTf)_2$	Toluene	50	40	-	-	11
2	$PPh_3AuCl/AgOTf$	Toluene	50	20	-	-	48
3	$AuCl_3$	Toluene	50	-	47	-	25

Table 4: Catalysis on alkynyl aziridine 139. Reactions were performed using 0.1 mmol of starting material (34 mg), 10 mol% of catalyst, 0.2 mL of solvent (C = 0.5 M) under argon and were stopped after 2h. [a]Yields calculated by ^{1}H NMR against a known quantity of internal standard.

2.4 Optimisation of 2,4-substituted pyrrole formation

Despite the observed problem of desilylation and debromination leading to formation of mono-substituted pyrrole **158**, it had been possible to identify two types of catalysts allowing access to either 2,4- or 2,5-substituted pyrroles selectively, proving that the regiodivergent strategy was valid. However, the reaction conditions had to be optimised to maximise yields while preventing the formation of the debrominated and desilylated products. It was decided to focus first on the formation of 2,4-substituted pyrroles, mechanistically more interesting than the preparation of the 2,5-substituted products.

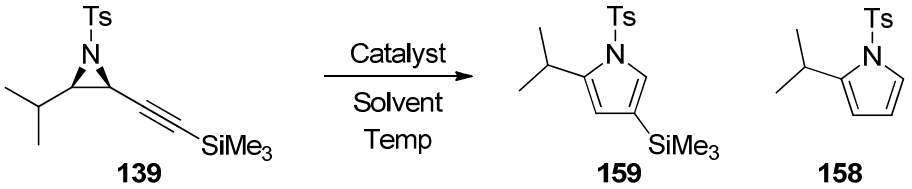
For our following studies it was decided to use trimethylsilyl-substituted alkynyl aziridine **139** instead of brominated aziridine **138** as this last one needed an extra step for its preparation.

To probe the effect of solvent, various solutions of alkynyl aziridine **139** were treated with $AuCl_3$ (Table 5).

No reaction at all was observed using CH_3CN (entry 2) and only traces of product were obtained when THF (entry 1) or $ClCH_2CH_2Cl$ (entry 3) were employed. For those two last solvents and CH_2Cl_2 (entry 5), it was also noted that significant degradation had occurred under the reaction conditions. Therefore the best result for the transformation of trimethylsilyl-substituted aziridine was still obtained when toluene was used and prevention of the formation of mono-substituted pyrrole **158** had not been possible by changing the solvent. In an attempt to assess if the presence of adventitious water in the reaction mixture was involved in the formation of mono-subtituted pyrrole, molecular sieves were probed under the reaction conditions.

Unfortunately, as reported in table 5 (entries 6, 7) the use of 4 Å activated molecular sieves reduced dramatically the conversion of starting material into pyrrole regardless of the solvent

used. The catalyst seemed to lose its reactivity under the presence of the molecular sieves and no conclusion could be made about the effects of traces of water.

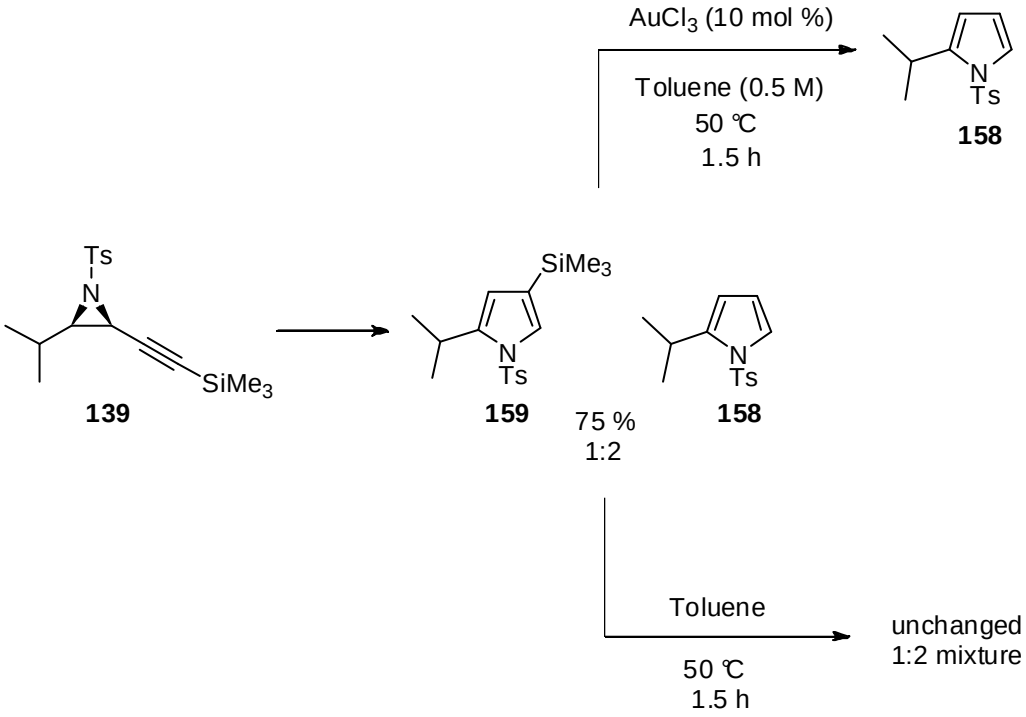


139 **159** **158**

entry	Catalyst	Solvent	Temp (°C)	Yield (%)[a]		
				139	**159**	**158**
1	$AuCl_3$	THF	50	55	5	5
2	$AuCl_3$	CH_3CN	50	100	-	-
3	$AuCl_3$	$ClCH_2CH_2Cl$	50	60	3	-
4	$AuCl_3$	Toluene	50	-	47	30
5	$AuCl_3$	CH_2Cl_2	23	22	34	2
6	$AuCl_3$	CH_2Cl_2[b]	35	70	8	-
7	$AuCl_3$	Toluene[b]	50	25	25	13

Table 5: Solvent screening. Reactions were performed using 0.1 mmol of starting material (34 mg), 10 mol% of catalyst, 0.2 mL of solvent (C = 0.5 M) under argon and were stopped after 2h. [a]Yields calculated by ^{1}H NMR against a known quantity of internal standard. [b]4 Å molecular sieve was used.

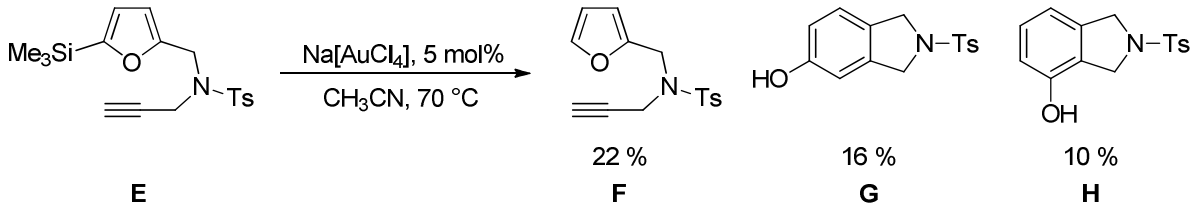
To better understand the formation of desilylated pyrrole **158** it was decided to run a simple experiment: alkynyl aziridine **139** was submitted to catalysis using our best conditions (table 5, entry 4) and the reaction was stopped this time after only 1 h (Scheme 43). The inseparable mixture of 2,4-substituted and mono-substituted pyrroles obtained was purified by flash chromatography and characterised before being separated in two portions. The first half of the mixture was simply heated in toluene while the second half was resubmitted to $AuCl_3$ catalysis.



Scheme 43: Identification of $AuCl_3$ as direct or indirect desilylating agent.

As expected, heating in toluene alone did not change the ratio of pyrroles in the mixture and total conversion to the mono-substituted pyrrole was observed in the presence of $AuCl_3$. This experiment proved that the gold species used was involved in the degradation of the silylated pyrrole after its formation.

Similar observation had already been published by Hashmi and co-workers, desilylation of furans occurred when using $NaAuCl_4$ as a gold (III) catalyst in a hydroarylation of silylated γ-alkynyl furans (Scheme 44).[60] The isolation of **F** in that case showed that desilylation of the furan precursor occured. The absence of silylated phenols as products suggested that the hydroarylation was happening after desilylation of the starting material. Moreover the ratio of phenols observed corresponded to the one obtained when a non-silylated version of the furan precursor was used (G:H; 3:2).[61]



Scheme 44: Hashmi and collaborators observed desilylation during a hydroarylation of silylated γ-alkynyl furans.

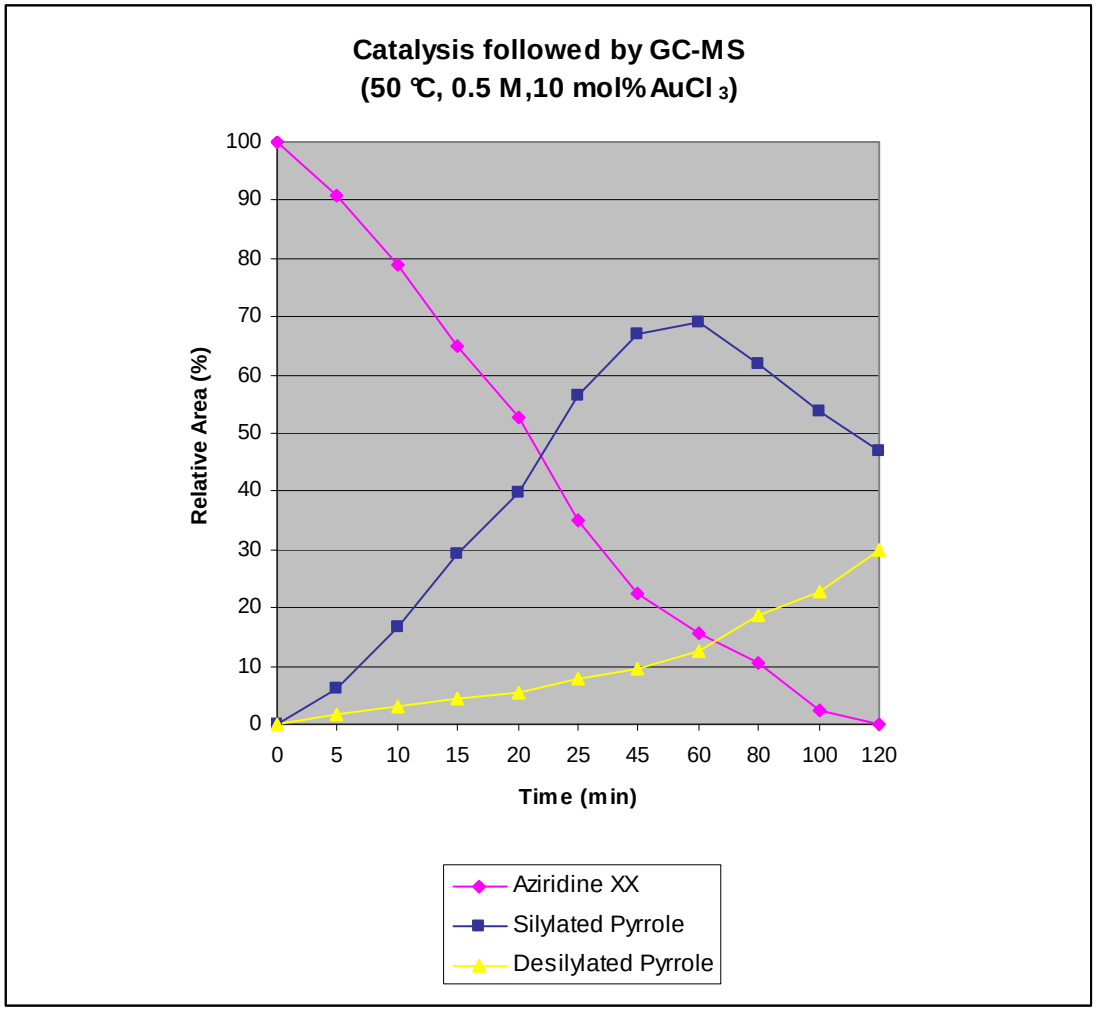
The desilylation process was thought to occur after total conversion of the starting material and so stopping the reaction at the right time would allow us to access clean trimethylsilyl-substituted pyrroles in better yields. Therefore catalysis were run again with alkynyl aziridine **139** under our best conditions and to follow the advancement of the reaction GC-MS monitoring was chosen for this experiment as pyrroles **159** and **158** were not distinguishable by simple TLC.

Toluene was used as solvent at a concentration of 0.5 M, with 10 mol% $AuCl_3$ and heating at 50 °C. The reaction mixture was sampled every 5 min in the beginning and every 20 min after 25 min. The samples were filtered through a small pad of silica to get rid of the gold residues and analysis was made by GC-MS. The reaction was stopped after 2h and the results of the study are display in Graphic 1.

Despite the represented yields in Graphic 1 being based on area ratios from uncorrected GC-MS values, a qualitative indication of the reaction could be obtained.

The study showed quick formation of the silylated pyrrole and consumption of the alkynyl aziridine. Some desilylated pyrrole was already formed after 5 min and its quantity increased relatively slowly during the reaction up to 60 min. At this point formation of desilylated pyrrole **158** accelerated slightly, and the quantity of silylated pyrrole **159** started to decrease.

From those observations it was concluded that desilylation occurred from the beginning of the reaction, as soon as some silylated pyrrole **159** was formed. Stopping the reaction at the time of maximum formation of pyrrole **159** could not be a solution as an unseparable mixture with desilylated pyrroles would be obtained.



Graphic 1: GC-MS monitoring of reaction between alkynyl aziridine 139 and $AuCl_3$.

In order to make our gold-catalysed method to form 2,4-substituted pyrroles interesting synthetically prevention of desilylation was needed from the start of the reaction.

It was thought that differencing parameters of the reaction (temperature, concentration, quantity of catalyst) could affect the profile observed in Graphic 1 and might provide us with a set of conditions to gain increased ratio of silylated pyrrole and reduced quantities of the side product. For that purpose a series of experiments followed by GC-MS were carried out (Graphics in appendix A).

The loading of $AuCl_3$ in the reaction was probed with the temperature set at 50 °C and a concentration of 0.5 M. The graphics obtained clearly showed that 2 or 5 mol% were not sufficient to form reasonable amount of products, and only a loading of 10 to 20 mol% were satisfactorily giving around 70% of silylated pyrrole at their maximum. A 20 mol% loading of catalyst was considered too much, and this parameter was fixed at 10 mol%.

The influence of concentration was then studied; reactions at 0.05 M, 0.2 M, 0.3 M, 0.4 M and 0.6 M were compared to the one obtained previously at 0.5 M. Analysis of the results showed that complete consumption of the starting material was not obtained for concentrations of 0.4 M or below. At 0.6 M the reaction rate was accelerated, as was desilylation. Deactivation of the catalyst stopped progress of the reaction after 20 min. Total conversion occurred only when the concentration was fixed at 0.5 M and after 2h (Graphic 1).

Finally the effect of temperature on the reaction was tested. Reactions were performed at 30, 40, 60 and 70 °C. At 30 °C the reaction was incomplete and no progress was observed after 90 min. At 40 °C almost all the starting material was consumed but the maximum formation of the silylated 2,4-substituted pyrrole **159** was lower than when a temperature of 50 °C was applied. Increasing the heating to 60 or 70 °C proved dramatic for the reaction as conversion stopped after 30 and 15 min respectively without improving upon the maximum quantity of product observed at 50°C.

The result for the factors studied were relatively disappointing as no improvement of the reaction had been possible. The best conditions were still obtained using toluene at 0.5 M, 50 °C with a catalyst loading of 10 mol% and desilylation had not been prevented.

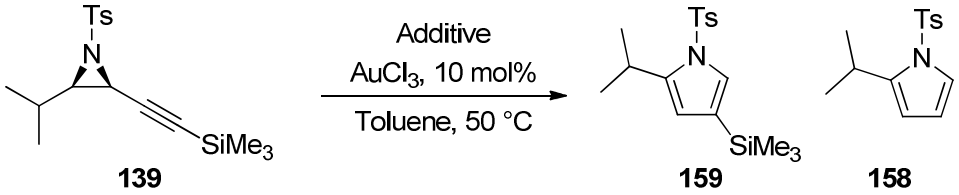
In a last effort to improve the reaction outcome, the impact of additives was investigated. Different substances were therefore tested, added to the mixture of starting material, solvent (0.5 M) and catalyst (10 mol%) at 50 °C (Table 6).

In order to check if traces of acid could account for the degradation of silylated pyrrole **159** into desilylated product **158**, *p*TsOH.H_2O and HCl were tested as additives (table 6, entry 1, 2). When 10 mol% of HCl was used degradation of the material occurred and no identifiable products were obtained. In the other hand, the reaction with one equivalent of *p*TsOH.H_2O did not go to completion (entry 1). After 2 h 9 % of starting material was still unreacted and only 1% of pyrrole **159** was present. Almost all silylated pyrrole had been transformed into monosubstituted product **158** (80% ^{1}H NMR yield). In comparison, 30% of desilylated pyrrole was previously observed when running the reaction without the acid additive for the same period (table 5, entry 4).

These results gave weight to a possible action of traces of acid formed during the course of the reaction when no additives were employed and therefore the impact of base on the transformation was probed.

Surprisingly no reaction happened at all when DIPEA was used (entry 3), and only traces of pyrroles were seen when K_2CO_3 was used (entries 4, 5).

No less than 1 equivalent of base was tried during the course of our studies as it was decided to move on to another part of the project.



139 **159** **158**

entry	Additive	Yield (%)[a]		
		139	**159**	**158**
1	*p*TsOH.H_2O (1 eq)	9	1	80
2	HCl (10 mol%)	-[b]	-	-
3	DIPEA (1 eq)	88	-	-
4	K_2CO_3 (1 eq)	89[c]	-	-
5	K_2CO_3 (dry, 1 eq)	90[c]	-	-

Table 6: Effect of additives on catalysis. Reactions were performed using 0.1 mmol of starting material (34 mg), 10 mol% of catalyst, 0.15 mL of solvent (C = 0.5 M) under argon and were stopped after 2h. [a]Yields calculated by ^{1}H NMR against a known quantity of internal standard. [b]Degradation observed. [c]Traces of products detected.

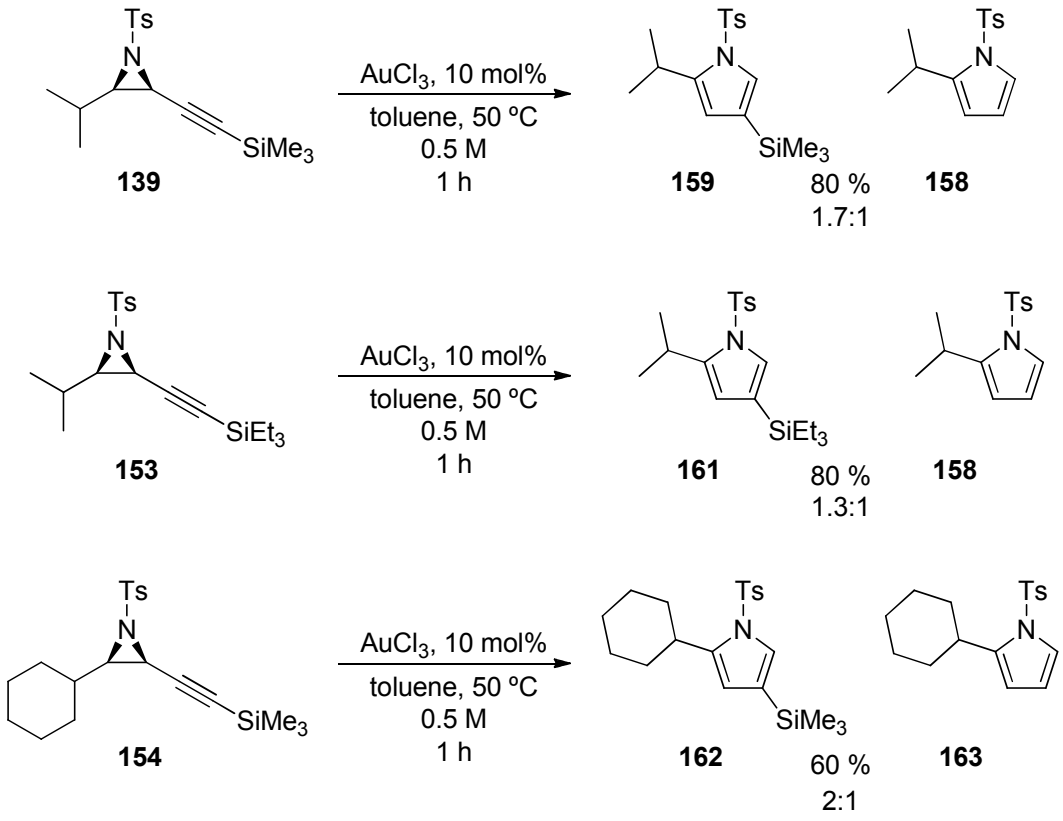
2.5 Application of the optimised conditions

Despite many attempts, the formation of the desilylated product could not be stopped but the optimised reaction conditions were applied to different alkynyl aziridines to assess if this problem could be only substrate dependent. In order to try to maximise the yield in 2,4-substituted pyrrole the best conditions obtained previously were employed with acetylenyl aziridine **139** (table 5, entry 4) using 10 mol% of $AuCl_3$ in toluene (0.5 M) at 50 °C and the reactions were stopped after 60 min as it corresponded to the maximum formation of pyrrole **159** in Graphic 1.

Alkynyl aziridine **139** was first submitted to catalysis (Scheme 45). Stopping the reaction after 1 h did provide silylated pyrrole **159** but in a poor 1.7:1 ratio with desilylated product **158** (ratio determined by ^{1}H NMR). This result was disappointing because a better ratio was expected from stopping the reaction after a 1 h period as the GC studies had indicated (Graphic 1).

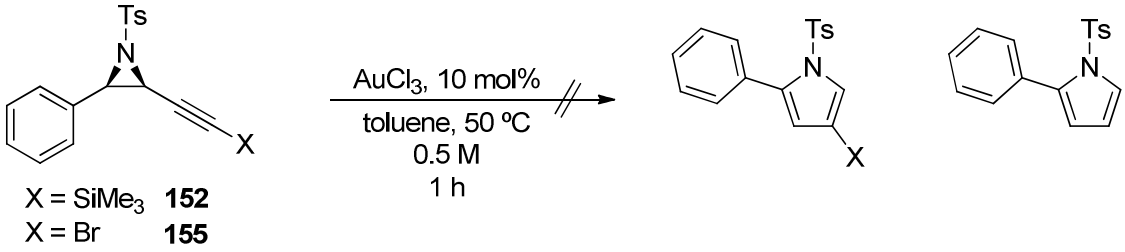
Changing the trimethylsilyl alkyne substituent with a more robust silyl group was also tried. Alkynyl aziridine **153** was prepared to that purpose but access to the TBDPS- or TBDMS-substituted alkynyl aziridines were not possible as preparation of the corresponding sulfonium salts failed. Nevertheless, substrate **153** was submitted to catalysis and pyrrole **161** was obtained (Scheme 45). Despite the formation of some desilylated pyrrole **158**, this result proved vinylidene pathway could be accessed from triethylsilane alkynyl aziridines. To the best of our knowledge this was the first time triethylsilane functional group was engaged in a gold-catalysed vinylidene rearrangement.

When alkynyl aziridine **154** bearing a cyclohexyl substituent was used, a mixture of silylated pyrrole **162** and mono-substituted pyrrole **163** was also obtained.



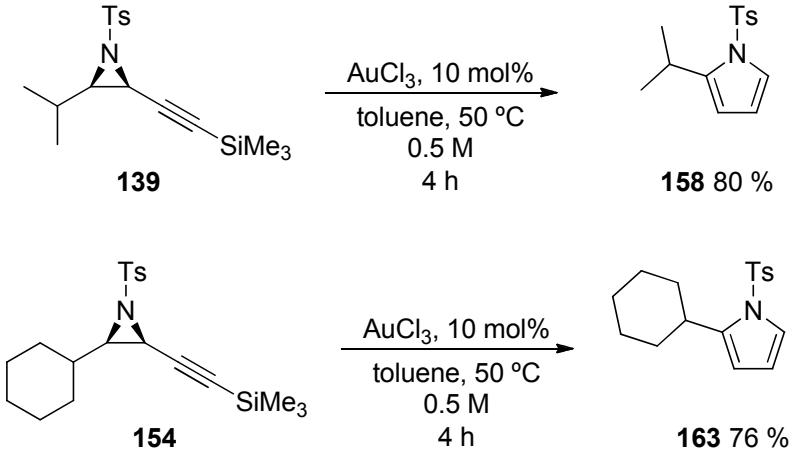
Scheme 45: Application of the optimised condition to silylated alkynyl aziridines.

After changing the alkyl substituent on the aziridine ring did not have any major impact on the outcome of the reaction it was decided to test an aryl substituent. Surprisingly, trimethylsilyl-substituted alkynyl aziridines **152** proved unreactive and the starting material was left untouched (Scheme 46). The use of the bromo-substituted aziridine **155** did not give better results, showing reluctance of phenyl-substituted aziridines to react under the reaction conditions.



Scheme 46: Reluctance of phenyl-substituted aziridines to form pyrroles under $AuCl_3$ catalysis

As the formation of the desilylated pyrrole **158** and **163** could not be avoided during the study, an experiment to maximise their formation from alkynyl aziridine **139** and **154** was tried. Leaving the reactions for 4 h under the standard reaction conditions employed previously led to total conversion of the starting material into the corresponding mono-substituted pyrrole **158** and **163** in 80% and 76% yield respectively (Scheme 47).



Scheme 47: Preparation of mono-substituted pyrroles 158 and 163

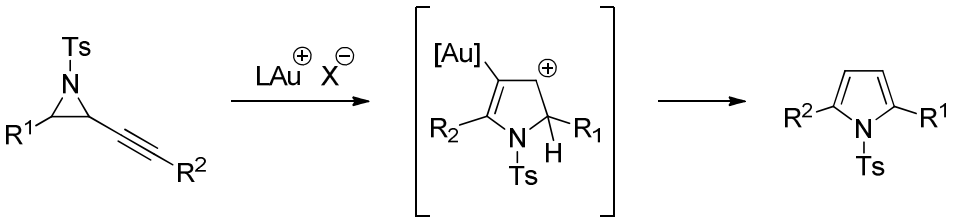
2.6 Summary

A new gold-catalysed preparation of brominated or silylated 2,4-substituted pyrroles from alkynyl aziridines was tested and discussed. Conceptually the strategy to obtain this class of pyrrole proved correct as the desired gold-catalysed vinylidene rearrangement of brominated or silylated alkynyl aziridines took place and complete regioselectivity in favour of the 2,4-pyrrole was observed using $AuCl_3$. However, despite efforts to study the effects of solvent, concentration, temperature, catalyst loading and additives, it was not possible to prevent the formation of the desilylated or debrominated side product. The optimised reaction conditions were used to give average to good yields of mixtures of 2,4-substituted silylated and desilylated products after 1h, and good yield of mono-substituted pyrrole could be obtained by extending the reaction time to 4 h.

Chapter 3: Cycloisomerisation of alkynyl aziridines by cationic gold electrophilic activation

3.1 Introduction

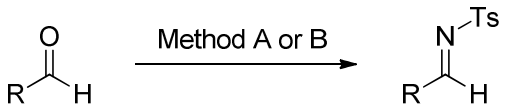
In the previous chapter brominated or silylated 2,4-substituted pyrroles have been prepared from alkynyl aziridines showing that the concept of a gold mediated vinylidene rearrangement followed by ring expansion of the generated intermediate was valid. A screen of various catalysts had indicated that $AuCl_3$ was the best gold species to facilitate this process and it had also highlighted that cationic gold catalysts were able to form 2,5-substituted pyrroles. It was therefore decided to turn attention to the formation of these products. As cationic gold complexes offered possibilities of variation through modification of their ligands and counterions it was expected that specific reaction conditions capable of forming specifically these 2,5-substituted pyrroles could be found (Scheme 48).



Scheme 48: Proposed synthesis of 2,5-substituted pyrroles from alkynyl aziridine

3.2 Starting material preparation

Following the method reported in the previous chapter, alkynyl aziridines were formed from imines and sulfonium salts (Scheme 37). A variety of substituents were investigated on these two precursors: as before, aromatic-substituted imines were obtained by direct condensation of aldehyde and sulfonamide under acidic conditions in a Dean-Stark apparatus (Table 7, method A), and a two steps process was used for enolisable aldehydes (Table 7, method B).



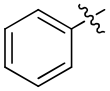
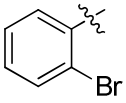
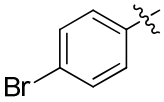
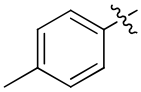
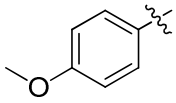
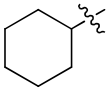
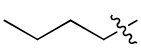
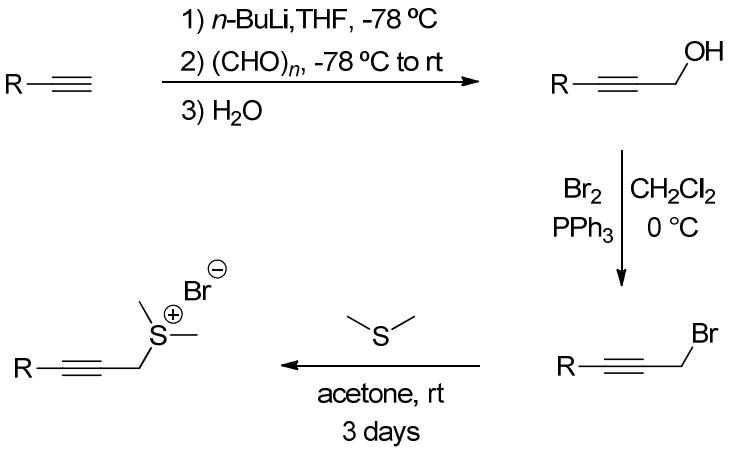
Entry	R	Method	Product	Yield (%)[a]
1		A	**141**	80
2		A	**164**	88
3		A	**165**	80
4		A	**166**	85
5		A	**167**	80
6		B	**144**	69[b]
7		B	**145**	72[b]
8		B	**168**	70[b]

Table 7: Tosylimine preparation: Method A: tosylamide, MS 4Å, amberlyst 15, toluene, 110 °C, 12 h. Method B: 1) tosylamine, sodium benzenesulfinate, H_2O:HCOOH (1:1), rt, 12h. 2) Na_2CO_3, CH_2Cl_2:H_2O (3:2), 2h. [a]Isolated yields. [b]Yield over two steps.

Sulfonium salts were prepared from commercially available terminal alkynes in a three step sequence. Low temperature deprotonation with *n*-BuLi followed by trapping with paraformaldehyde was performed to access propargylic alcohols.[62] Subsequent treatment with Br_2 in the presence of PPh_3 gave the corresponding propargylic bromides which were transformed into the sulfonium salts using dimethylsulfide (Table 8).



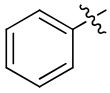
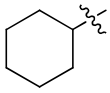
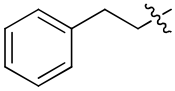
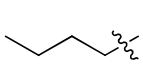
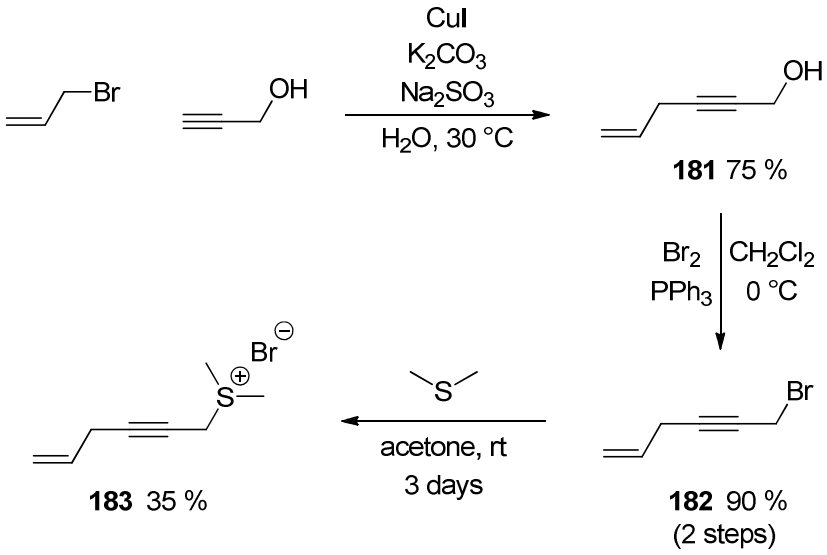
Entry	R	Alcohol		Bromide		Sulfonium salt	
		Product	Yield (%)[a]	Product	Yield (%)[a]	Product	Yield (%)[a]
1		**169**	90	**173**	92	**177**	87
2		**170**	85	**174**	91	**178**	55
3		**171**	86	**175**	75	**179**	72
4		**172**	87	**176**	95	**180**	60

Table 8: Preparation of sulfonium salts *via* hydroxymethylation followed by bromination and dimethylsulfidation. [a]Isolated yields.

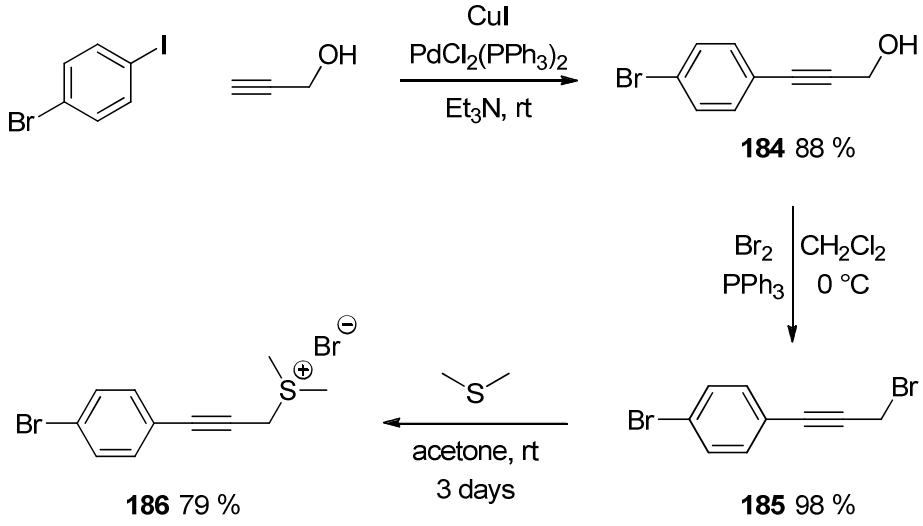
Two more sulfonium salts were prepared using alternative methods. Allylation of propargyl alcohol[63] followed by bromide formation was performed in a 90% yield over two steps.

Treatment with DMS led to the corresponding sulfonium salt **183** in low yield after 3 days (Scheme 49).



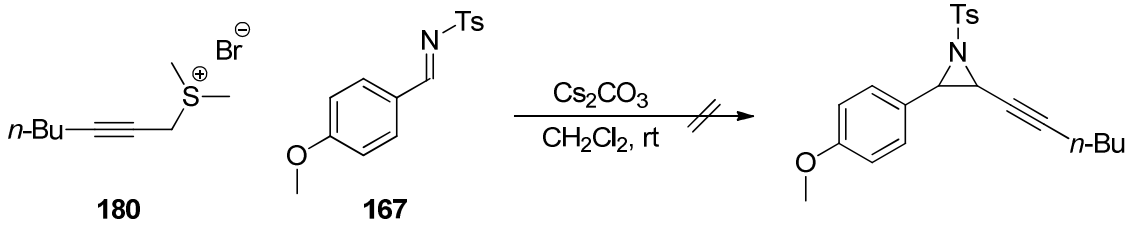
Scheme 49: Preparation of sulfonium salt 183

The 4-bromobenzene-substituted sulfonium salt **186** was also prepared from propargyl alcohol and an adapted Sonogashira reaction in triethylamine[64] introduced the aryl substituent. Functional group interconversion afforded bromide **185** which was transformed into sulfonium salt **186** in 79% yield. (Scheme 50).



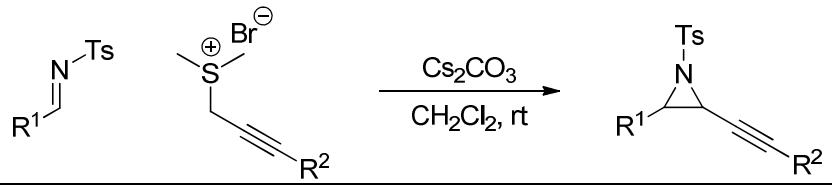
Scheme 50: Preparation of sulfonium salt 186

With those imines and sulfonium salts in hand alkynyl aziridines were synthesised using Cs_2CO_3 in CH_2Cl_2 at room temperature. In these cases, unlike when a silylated sulfonium salt was used (Chapter 2), mixtures of *cis* and *trans* products were obtained (Table 9). The formation of electron-rich aziridine derived from *p*-methoxyphenyl-substituted tosylimine was also tried but this compound proved extremely unstable and could not be isolated (Scheme 51).



180 **167**

Scheme 51: Attempted formation of *p*-methoxybenzyl-substituted alkynyl aziridine



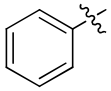
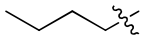
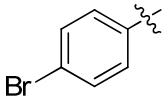
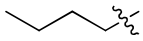
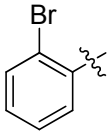
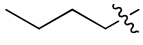
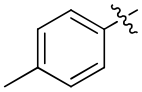
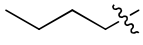
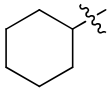
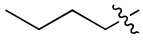
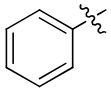
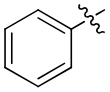
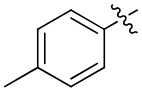
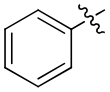
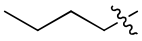
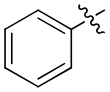
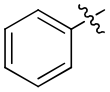
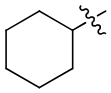
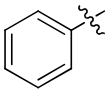
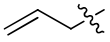
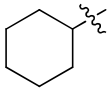
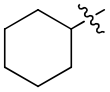
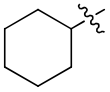
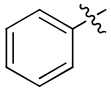
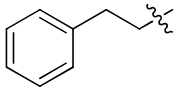
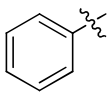
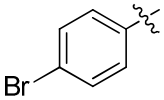
Entry	R^1	R^2	Reaction Time (h)	*cis*/*trans* Ratio	Product	Yield (%)[a]
1			2.5	9/1	**187**	65
2			3	8/1	**188**	79
3			4	20/1	**189**	73
4			8	7/1	**190**	79
5			3.5	7/1	**191**	50
6			1.5	7/1	**192**	85
7			8	>50/1	**193**	65
8			12	>50/1	**194**	40
9			2	25/1	**195**	60
10			6	>50/1	**196**	80
11			4	25/1	**197**	40
12			3.5	25/1	**198**	51
13			3	15/1	**199**	50
14			6	11/1	**200**	70
15			8	15/1	**201**	75

Table 9: Aziridine preparation from imine and sulfonium salt. Reactions were performed using 1.2 equiv of sulfonium salt and Cs_2CO_3. [a] Determined by ^{1}H NMR. [b]Isolated yields.

3.3 Survey of reaction conditions for the cycloisomerisation of alkynyl aziridines

It was decided to start our studies by using alkynyl aziridine **187** to screen different reaction conditions for the cycloisomerisation (Table 10). Analysis of the crude reaction mixture was performed by ^{1}H NMR using a known quantity of an internal standard (1,2,4,5-tetramethylbenzene). Cationic gold catalysts were used as they had proved most successful in forming 2,5-substituted pyrrole in the catalyst screening described in Chapter 2 (Table 3). The catalysts were formed *in situ* from PPh_3AuCl and a silver salt (AgX), apart from PPh_3AuNTf_2 which was used directly in its commercially available and stable cationic form.[65]

As expected 2,5-substituted pyrrole **202** was obtained when alkynyl aziridine **187** was submitted to a standard combination of PPh_3AuCl and AgOTf in toluene, but we were surprised to observe the formation of a minor second isomeric product, later identified as the 2,4-substituted pyrrole **203** (Table 10, entry 1).

It was then decided to investigate other solvents for the reaction using the same catalyst system PPh_3AuCl/AgOTf, to assess their impact on the yield and ratio of products **202** and **203**. When CH_3CN or DMF were used as the solvent no reaction occurred, probably due to poisoning of the cationic catalyst by those solvents (entry 12-13). When CH_2Cl_2, $ClCH_2CH_2Cl$, nitromethane or chloroform were employed (entries 3-6), the unexpected 2,4-isomer was obtained as the major product. Alternatively ethanol, methanol, ether, benzene and *o*-xylene (entries 7-11) favoured the formation of the 2,5-substituted pyrrole **202**.

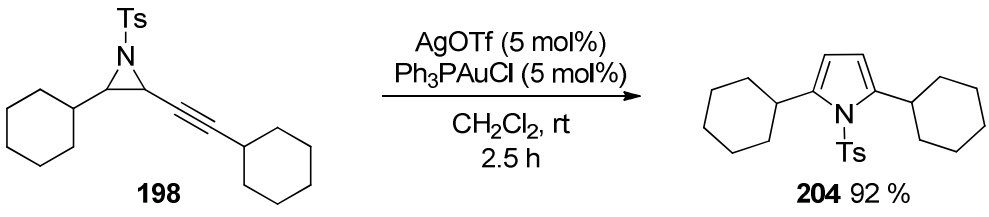
The effect of the catalyst counterion on the yield and ratio of products was then studied. A similar trend as for triflate counterion was observed with triflimidate and hexafluorophosphate counterions in toluene and CH_2Cl_2 (entries 14-17). On the other hand, switching to

hexafluoroantimonate or tetrafluoroborate led predominantly to the formation of 2,5-substituted pyrrole **202** regardless of the solvent (entries 18-20).

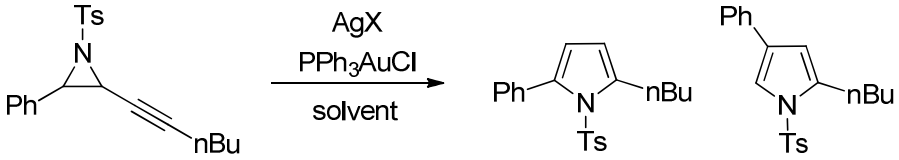
Surprisingly, the 2,5-substituted pyrrole was obtained as the sole product when a tosylate counterion was employed (entries 22-23). This catalytic system seemed less active than the other cationic gold species as heating to 70 °C was needed to obtain total conversion of the starting material (entry 24).

Finally the use of the P(*p*CF_3-C_6H_4)$_3$ ligand, which is more electron-deficient than PPh_3 was investigated. It was thought that using this ligand could be beneficial for the reaction as more alkynophilic character should be induced in the gold complex. It has, subsequently to our study, been shown that the ligand, like the counterion, could affect the reactivity of the gold complex by affecting the electron density on the metal or by influencing the position of the counterion.[66] When using this P(*p*CF_3-C_6H_4)$_3$ ligand, a reduction of the rate of the reaction was observed and the ratio of products obtained were no better than when PPh_3 was employed (entries 25-27).

When the non-aromatic substituted alkynyl aziridine **198** was used in CH_2Cl_2 with the cationic gold system Ph_3PAuCl/AgOTf, formation of only 2,5-substituted pyrrole **204** was observed (Scheme 52). This result showed that only aromatic-substituted alkynyl aziridines were able to form the 2,4-substituted isomer, probably through an aryl-migration pathway.



Scheme 52: Reaction of a non-aromatic-substituted alkynyl aziridine under cationic gold catalysis.



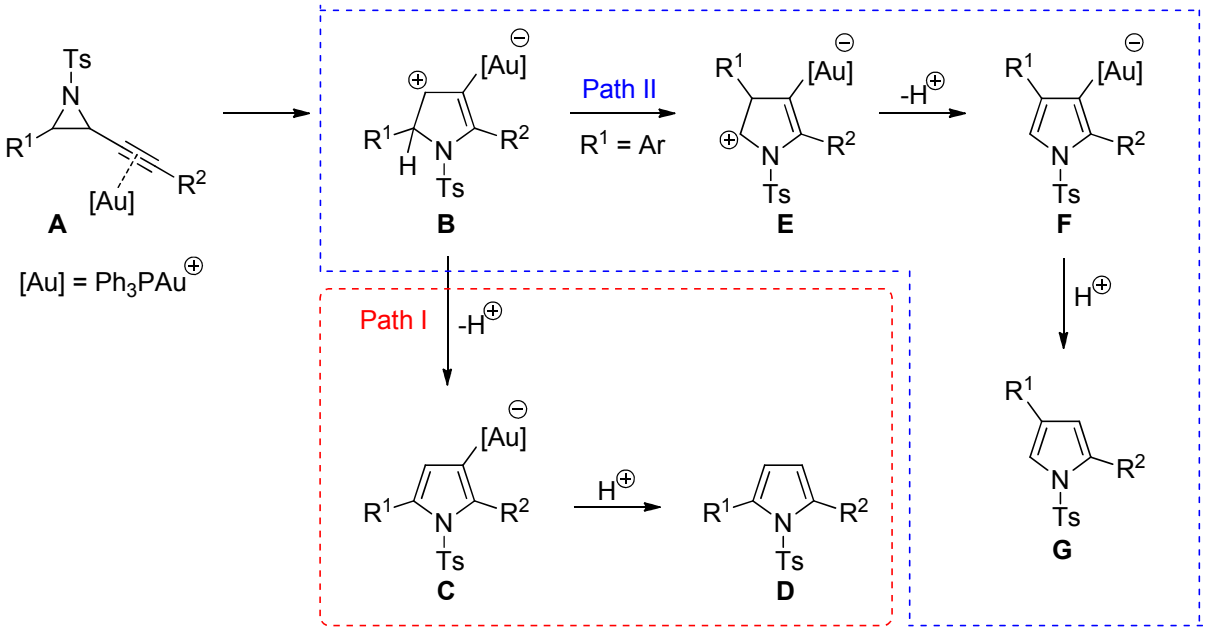
187 **202** **203**

Entry	X	Solvent	Reaction Time (h)	Yield (%)[a,b]	Ratio[c] (**202**:**203**)
1	OTf	toluene	4	75	24:1
2	OTf	toluene[d]	0.75	81	2.3:1
3	OTf	CH_2Cl_2	0.75	60	1:7.6
4	OTf	$ClCH_2CH_2Cl$	1	50	1:24
5	OTf	CH_3NO_2	20	29	0:1
6	OTf	CH_3Cl	20	72	1.1:1
7	OTf	EtOH	2	56	>50:1
8	OTf	MeOH	0.75	45	>50:1
9	OTf	Et_2O	20	79	>50:1
10	OTf	benzene	20	66	6.3:1
11	OTf	*o*-xylene	20	79	15:1
12	OTf	DMF[e]	20	-	-
13	OTf	CH_3CN[e]	20	-	-
14	NTf_2	CH_2Cl_2	20	42	1:5
15	NTf_2	toluene	20	45	2.8:1
16	PF_6	CH_2Cl_2	36	60	2:1
17	PF_6	toluene	48	63	20:1
18	SbF_6	CH_2Cl_2	2.5	40	1:4.7
19	SbF_6	toluene	20	34	1:2.4
20	BF_4	CH_2Cl_2	20	<10	1:1.8
21	NO_3	CH_2Cl_2	20	-	-
22	OTs	$ClCH_2CH_2Cl$	24	<10	1:0
23	OTs	Toluene	24	<10	1:0
24	OTs	$ClCH_2CH_2Cl$[f]	3	98	1:0
25	OTf	CH_2Cl_2[g]	1.5	60	1:3.6
26	OTf	Toluene[g]	20	74	5.2:1
27	OTf	$ClCH_2CH_2Cl$[g]	20	64	1:2.4

Table 10: Survey of reaction conditions for cycloisomerisation of alkynyl aziridines. [a]AgX (5 mol%), PPh_3AuCl (5 mol%), 187 (0.1 mmol), solvent (0.5 mL) with all reactions run at rt unless otherwise specified. [b]Yields calculated by ^1H NMR against a known quantity of internal standard. [c]Determined by ^1H NMR. [d]Reaction performed at 50 °C. [e]No reaction occurred. [f]Reaction performed at 70 °C. [g]$P(pCF_3\text{-}C_6H_4)_3AuCl$ was used instead of PPh_3AuCl.

3.4 Reaction mechanism proposition

Based on this survey of reaction conditions a mechanism explaining the regiodivergence observed was proposed (Scheme 53).

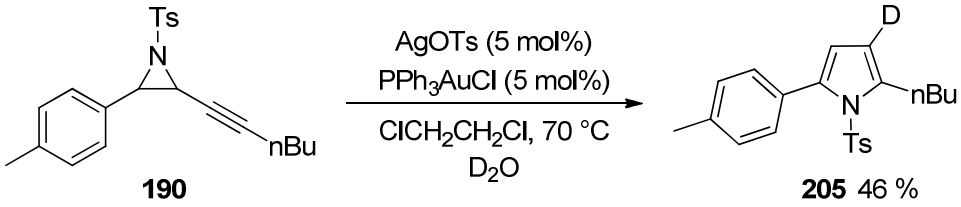


Scheme 53: Possible regiodivergent pathways

The results summarised in Table 10 could be explained by considering the basicity of the counterions used in System A, B and C. When a relatively basic counterion such as tosylate was present (System C), deprotonation of intermediate **B** (Scheme 53) followed by protodemetallation would be efficient and would lead to the formation of the 2,5-substituted isomer **D** (Scheme 53, Path I). In the absence of such a counterion, an aromatic or weakly Lewis basic solvent would also facilitate this pathway (System B) as observed in the optimisation of the reaction conditions (Table 10, entries 7-11). When both counterion and solvent were insufficiently basic (System A), an alternative pathway involving a 1,2-aryl shift

would take precedence, giving intermediate **E** and ultimately the 2,4-substituted pyrrole **G** (Scheme 53, Path II).

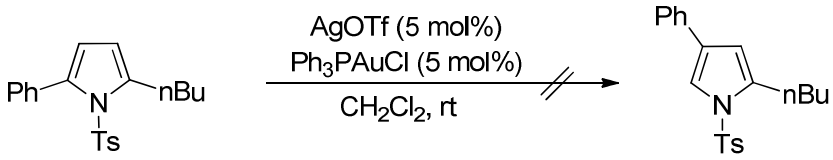
The intermediacy of the vinyl gold intermediate **B** was supported by the selective incorporation of deuterium at the metal position when an experiment was conducted using $Ph_3PAuCl/AgOTs$ in D_2O-washed $ClCH_2CH_2Cl$ (Scheme 54).



190 **205** 46 %

Scheme 54: Cyclisation of alkynyl aziridine 190 in the presence of D_2O-washed $ClCH_2CH_2Cl$

It is important to note that submitting 2,5-substituted pyrrole **202** to the reaction conditions of System A did not lead to formation of any 2,4-substituted isomer (Scheme 55).



202 **203**

Scheme 55: Attempt to interconvert 2,5-substituted pyrrole into 2,4-substituted product

The scope of the formation of both 2,4- and 2,5-substituted pyrroles was then studied as the possibility of controlling the substituent pattern of the product through reaction conditions change could have important applications in the synthesis of pyrroles. Moreover the high yielding formation of 2,5-substituted pyrrole **202** when using AgOTs presented the potential for the development of a clean and efficient method to access this class of products.

3.5 A comparaison of the reaction conditions against structural alteration

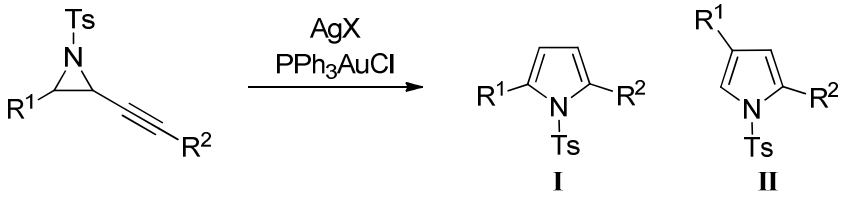
In light of the results of the study into optimisation of the reaction conditions, it was decided to proceed with three sets of catalytic systems: System A employing AgOTf in CH_2Cl_2 at room temperature; System B employing AgOTf in toluene at room temperature; System C employing AgOTs in $ClCH_2CH_2Cl$ at 70 °C (Table 11).

System A was selected because it favoured the formation of 2,4-substituted pyrroles in good yield. On the other hand, both System B and C allowed access to 2,5-pyrroles preferentially. Despite System C being superior in terms of yield and selectivity, System B was used as a chlorinated-solvent free option, this being more attractive for industrial applications.

Various aryl-substituted alkynyl aziridines were submitted to the three sets of conditions. As predicted by the previously proposed mechanism (Scheme 57), System C gave almost quantitative yield of the single 2,5-substituted pyrrole isomer for all the substrates.

As observed during the reaction conditions survey, System B generally gave a mixture of isomers in favour of the 2,5-substituted pyrrole while System A favoured formation of the 2,4-substituted product.

Aziridines with electron-deficient aryl substituents gave less of the 2,4-substituted pyrrole product with Systems A and B than when a phenyl group was used (entries 4-5 and 7-8). On the other hand, the more electron-rich the aromatic moiety the greater the selectivity for the 2,4-substituted pyrrole (entries 1-2, 10-11, 13-14, 16-17). These results were in line with the proposed mechanism as electron-rich aryl substituents would be more prone to perform a 1,2-shift than electron-deficient ones.



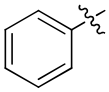
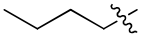
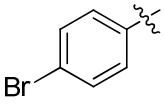
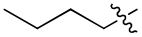
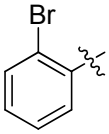
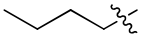
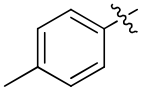
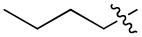
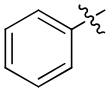
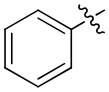
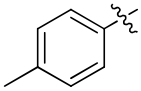
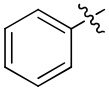
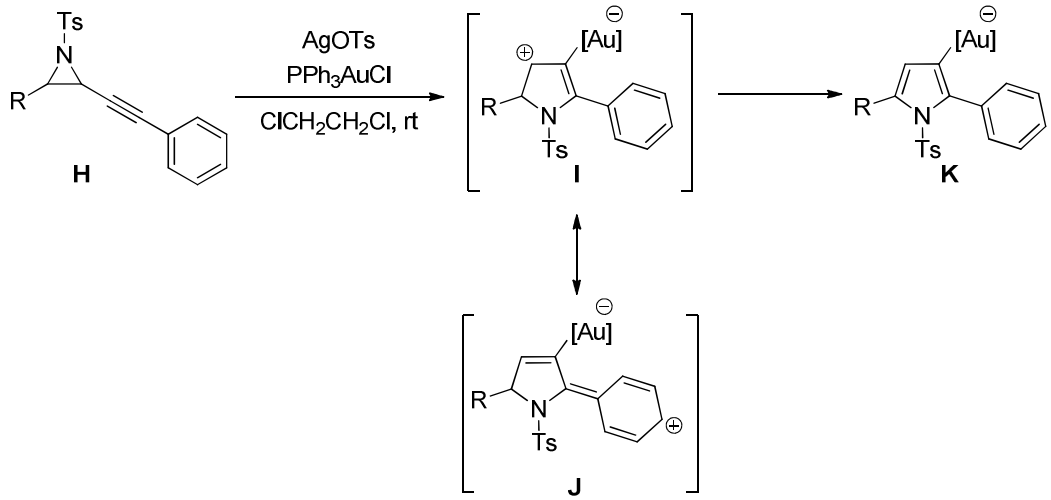
Entry	R_1	R_2	Reaction Time (h)	System[a]	Products		Yield (%)[b,c]	Ratio (**I**:**II**)
					I	**II**		
1			2	**A**			60	1:7.6
2			5	**B**	**202**	**203**	75	24:1
3			3.5	**C**			98	1:0
4			2.5	**A**			74	1:1.1
5			12	**B**	**206**	**207**	85	1:0
6			4	**C**			98	1:0
7			3	**A**			90	3:1
8			12	**B**	**208**	**209**	75	50:1
9			4	**C**			98	1:0
10			1.5	**A**			32	1:50
11			1	**B**	**210**	**211**	30	1.5:1
12			5	**C**			98	1:0
13			0.5	**A**			98	1:6
14			5	**B**	**212**	**213**	79	1.4:1
15			3	**C**			98	1:0
16			0.5	**A**			65	0:1
17			1	**B**	**214**	**215**	60	0:1
18			3.5	**C**			98	1:0

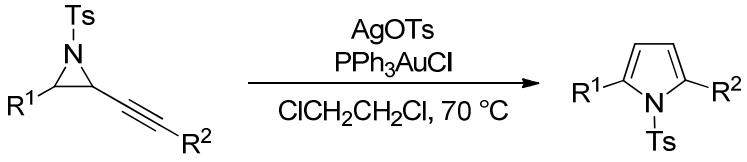
Table 11: Gold-catalysed synthesis of 2,4 and 2,5-substituted pyrroles. [a]System A employed AgOTf in CH_2Cl_2 at RT; System B employed AgOTf in toluene at RT; System C employed AgOTs in $ClCH_2CH_2Cl$ at 70 °C. [b]All reactions were carried out using 0.2 mmol of substrate with 5 mol% of gold and silver species at 0.2 M. [c]Isolated percentage yields of pyrrole products with ratio of isomers determined by ^1H NMR.

3.6 Synthesis of 2,5-substituted pyrroles

The optimised conditions for the formation of 2,5-substituted pyrroles (System C) were then applied to the other alkynyl aziridines prepared (Table 9) including those with alkyl substitutents on the three-membered ring (Table 12, entries 1-7). Almost quantitative yields were obtained and the purification of those 2,5-substituted products consisted only of an expedient and economical filtration through a plug of silica followed by solvent removal under reduced pressure. In only three cases purification by flash chromatography was necessary after the filtration step (entries 1, 3 and 8). Notably the reaction was efficient at room temperature when the alkyne moiety was substituted by a phenyl group. This could be rationalised by an extra stabilisation of intermediate **I** in the presence of the phenyl group (Scheme 56). Its formation would therefore be more favoured in that case than when a non-stabilising alkyl substituent was employed and cyclisation would proceed without the need for heating.



Scheme 56: Extra stabilisation by phenyl substituent allowing room temperature cyclisation



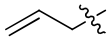
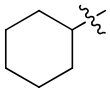
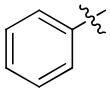
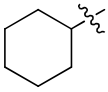
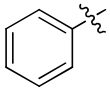
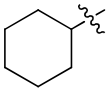
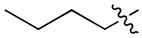
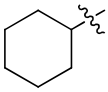
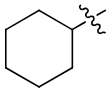
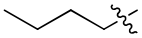
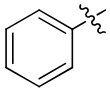
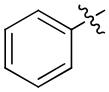
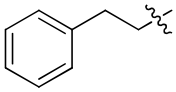
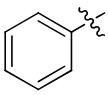
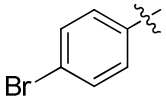
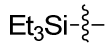
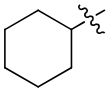
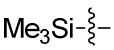
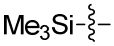
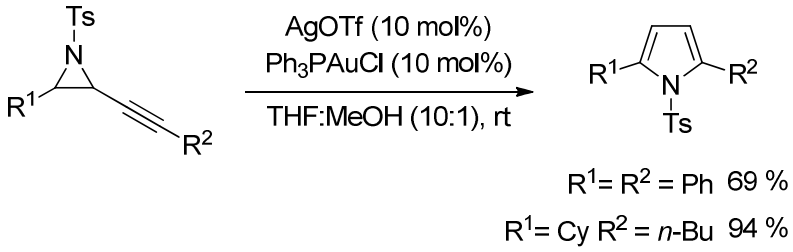
Entry	R^1	R^2	Reaction Time (h)	Product	Yield (%)[a,b]
1			12	**216**	95
2			3	**217**	98
3			12	**218**	95[c]
4			12	**219**	98[c]
5			4	**220**	98
6			3	**204**	98
7			12	**202**	98[c]
8			4	**221**	95
9			3	**222**	98
10			12	**158**	98[c,d]
11			12	**163**	98[c,d]
12			12	**158**	98[c,d]

Table 12: Preparation of 2,5-substituted pyrroles. [a]All reactions were carried out using 0.2 mmol of substrate with 5 mol% of gold and silver species at 0.2 M. [b]Isolated yields. [c]Reaction at rt. [d]Desilylated pyrrole isolated.

As well as alkyl and phenyl substituents, other functional groups such as allyl and *p*-bromobenzene (entries 1 and 9) were successfully employed. The products of these reactions were particularly interesting as they would provide opportunities for later elaboration to more complex molecules.[67]

The use of silylated alkynyl aziridines (entries 10-12) gave monosubstituted pyrroles under the cationic gold reaction conditions as when $AuCl_3$ was used as catalyst in Chapter 2 (Scheme 47). However, the transformation was more efficient this time as 98% yields were achieved compare to the 80% previously reported.

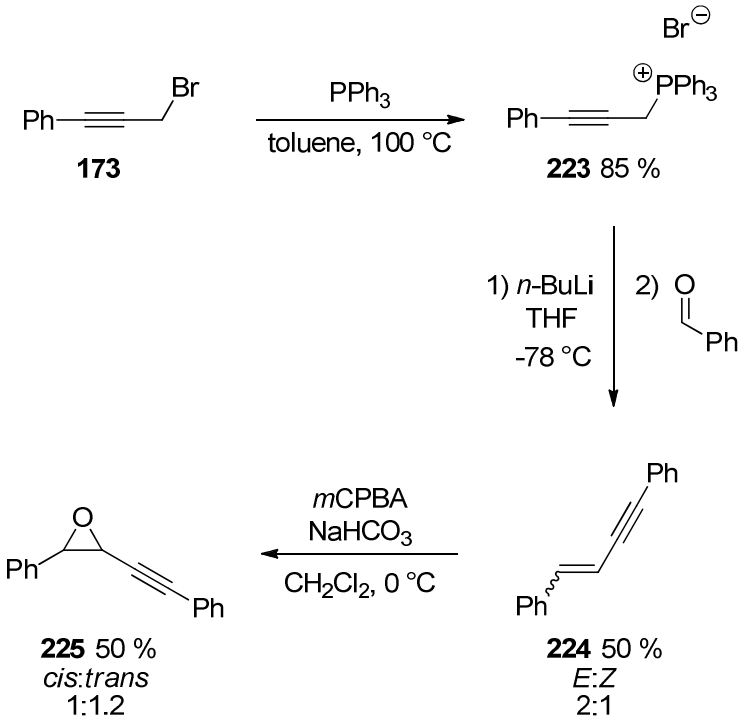
Subsequent to our publication,[68] Dai and co-workers reported a similar gold-catalysed preparation of functionalised pyrroles from *N*-tosyl-substituted alkynyl aziridines (Scheme 57).[69] The cationic gold system Ph_3PAuCl/AgOTf was employed in a mixture of THF and MeOH to give 2,5-substituted pyrroles in good yields. No 2,4-pyrroles were reported when aromatic substituents were submitted to these reaction conditions. This was in agreement with our results as 2,5-substituted pyrrole was formed predominantly when MeOH was used as solvent with the catalytic system Ph_3PAuCl/AgOTf (Table 10, entry 8). Moreover our reaction conditions employing Ph_3PAuCl/AgOTs gave better yields every time similar alkynyl aziridines were used.



Scheme 57: Dai and co-workers gold-catalysed synthesis of 2,5-substituted pyrroles

3.7 Attempts to extend the method to the formation of furans

A study was undertaken to investigate whether aryl-substituted alkynyl epoxides would show similar reactivity and allow the preparation of 2,4-disubstituted furans by aryl shift. Phosphonium salt **223** was synthesised and engaged in a Wittig reaction with benzaldehyde. The enyne obtained was reacted with mCPBA under basic conditions to access a mixture of *cis* and *trans* oxirane **225** (Scheme 58).



Scheme 58: Alkynyl oxirane preparation

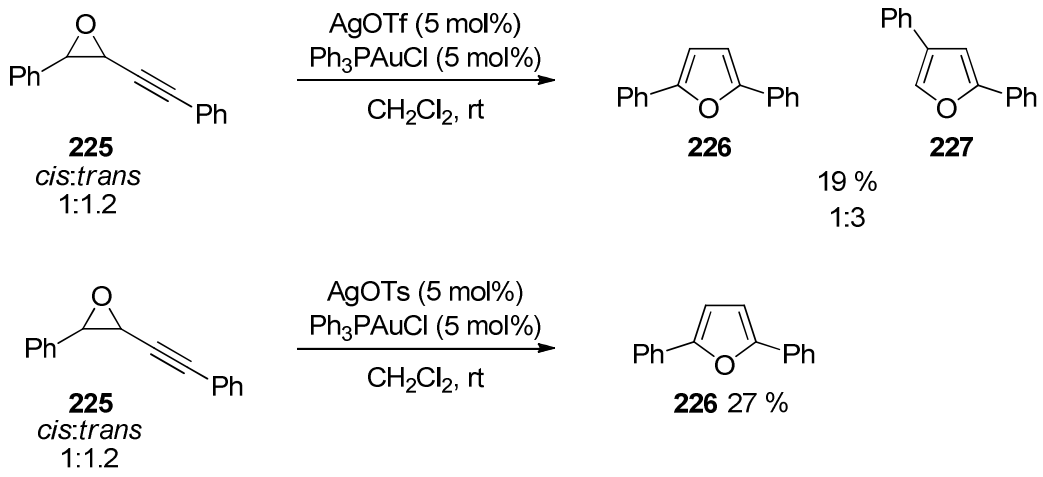
Alkynyl epoxide **225** was submitted to the optimal conditions for the selective formation of either 2,4 or 2,5-substituted pyrroles (Scheme 59).

Under the conditions shown to favour formation of 2,4-substituted pyrrole, a mixture of furans was also obtained. 2,4-Substituted furan **227** was identified as the major product and

the 2,5-substituted furan as the minor. When AgOTs was used only the 2,5-substituted furan was observed.

Both results showed that alkynyl epoxides reacted in a similar way as alkynyl aziridines under cationic gold catalysis. The shift of an aryl moiety was favoured when a triflate counterion was employed and 2,5-disubstituted epoxide **226** was obtained as sole isomer when a tosylate one was used.

Unfortunately contrary to their pyrrole equivalents which were accessed efficiently, 2,4- and 2,5-disubstituted furans were obtained in very low yields by this method.

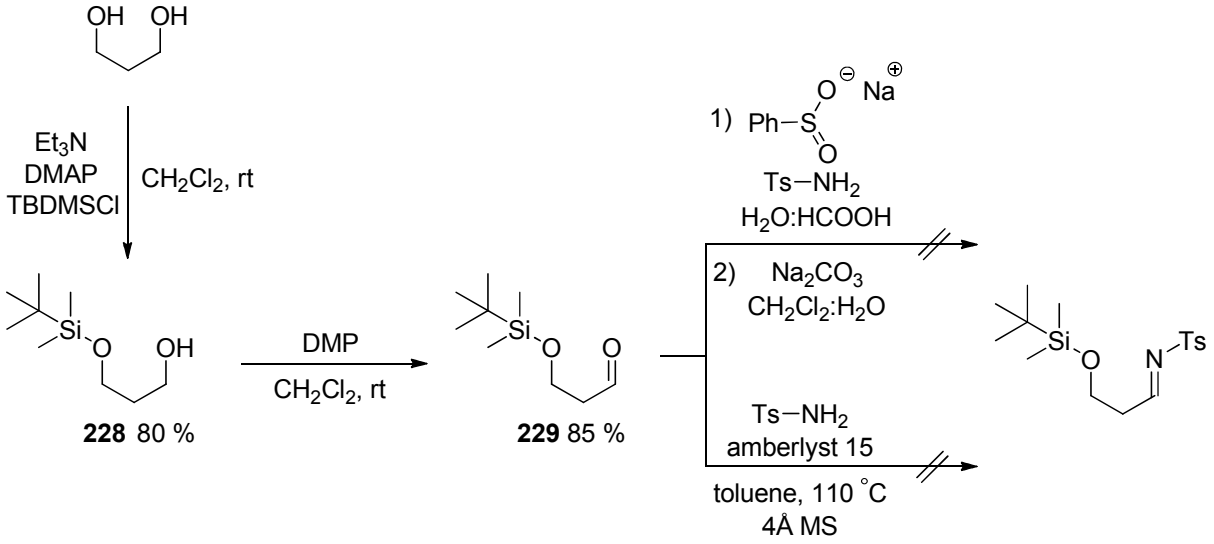


Scheme 59: Furan formation under the optimal reaction conditions for alkynyl aziridine cyclisation

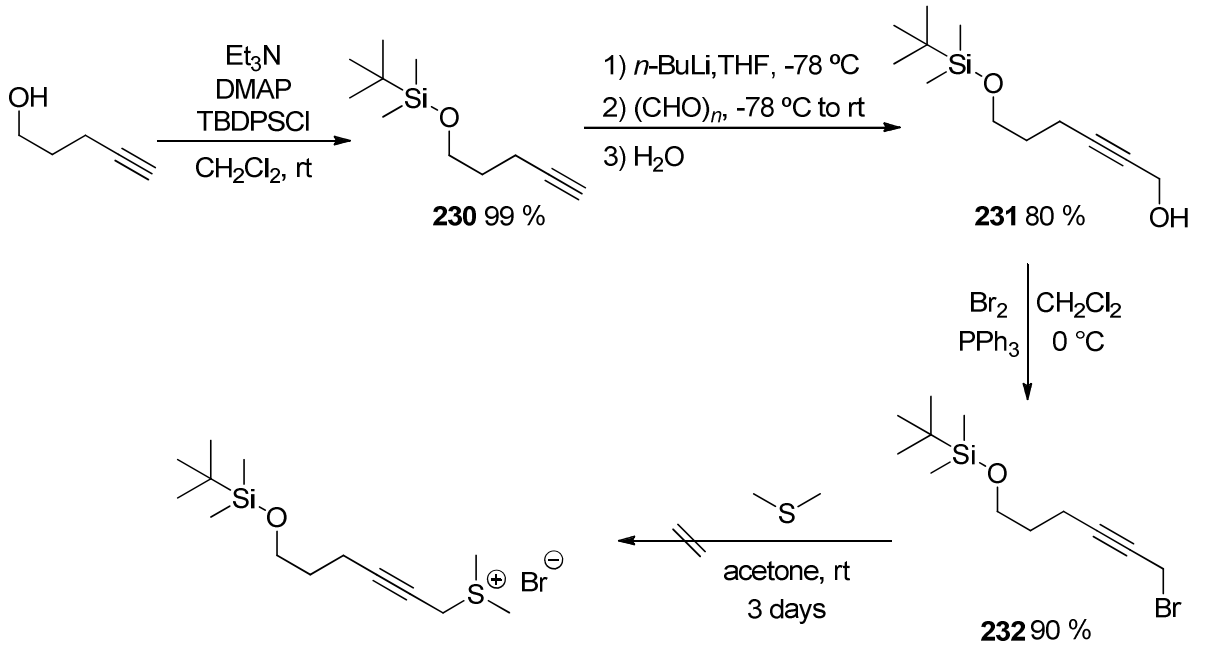
3.8 Attempts to extend the method to the formation of more complex pyrroles

The method developed for the formation of tosylated 2,5-substituted pyrroles was a success as almost quantitative yields were obtained for all the alkynyl substrates tested during the course of our studies. However more complex substituents such as TBDMS-protected alcohols could

not be incorporated in the imine or sulfonium salt alkynyl aziridine precursors (Scheme 60 and 61).



Scheme 60: Failed attempts to form imine from aldehyde 229

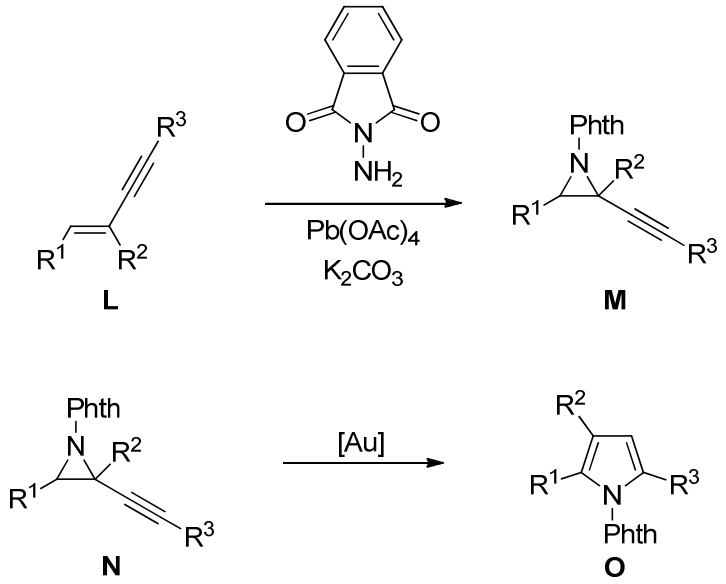


Scheme 61 : Failed attempts to form sulfonium salt from bromide 232

The method used for the formation of alkynyl aziridines was showing its limitations and it was decided to investigate other modes of preparation.

Many aziridination techniques had been developed in the past but most employed fastidious linear synthesis and their use would considerably reduce the interest of our gold-catalysed transformation.

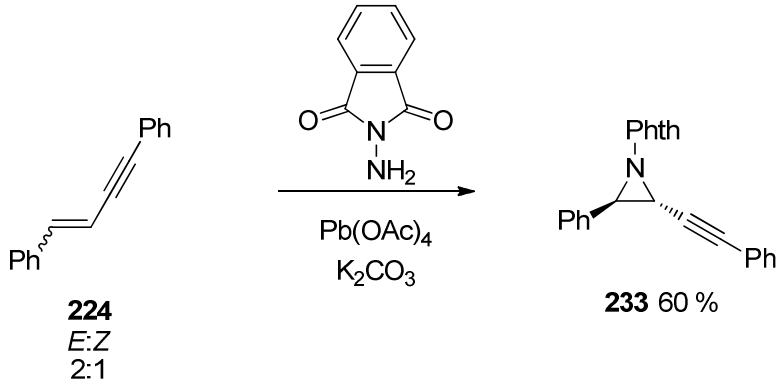
Therefore attention was turned to another expedient method that had been used to form *N*-phthalimide alkynyl aziridines **M** from 1,3-enynes **L** under oxidative conditions (Scheme 62).[70] It was expected that formation of the corresponding pyrrole would be possible under gold catalysis in a similar way as for the tosylated alkynyl aziridines studied previously. Moreover this technique was anticipated to allow access to trisubstituted alkynyl aziridines which could potentially allow formation of trisubstituted pyrroles.



Scheme 62: Direct aziridination of 1,3-enynes and a possible route to trisubstituted pyrroles

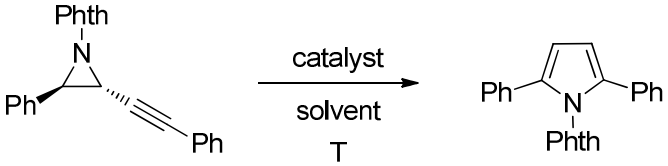
Therefore 1,3-enyne **224** was prepared from bromide **173** following a sequence previously described for epoxide **225** formation (Scheme 58). The *N*-phthalimide alkynyl aziridine **233**

was obtained by treatment of enyne **224** with *N*-aminophthalimide in the presence of $Pb(OAc)_4$ and base (Scheme 63). The use of very toxic $Pb(OAc)_4$ was not ideal but enabled access to the aziridine required to investigate the ring expansion.



Scheme 63: Preparation of *N*-phthalimide alkynyl aziridine 233

Compound **233** was submitted to different reaction conditions summarised in Table 13. The reaction conditions discussed previously leading to the selective preparation of 2,5-substituted *N*-tosyl pyrroles proved almost ineffective as only very little *N*-phthalimide pyrrole was formed according to ^{1}H NMR of the crude mixture (Table 13, entries 1). Most of the starting material was recovered but partial degradation was also observed. A similar result was obtained when dichloro(pyridine-2-carboxylato)gold was employed (entry 7). The use of $AuCl_3$ at 70 °C or $Ph_3PAuCl/AgOTf$ at room temperature led to complex mixtures with the formation of small amounts of product and total consumption of the starting material (entries 2, 9). Moreover no reaction occurred in the presence of AuCl or $PtCl_2$ in $ClCH_2CH_2Cl$ regardless of the temperature (entries 3-6).



233 **234**

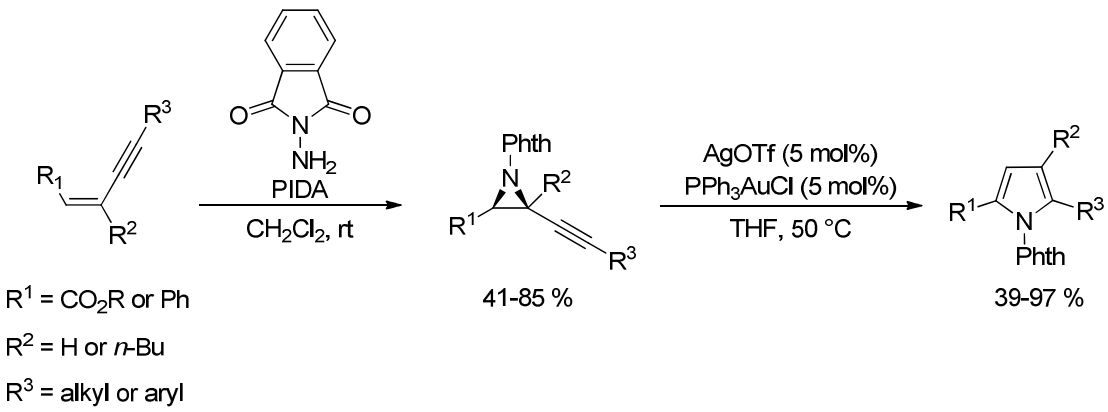
Entry	Catalyst	Solvent	T (°C)	Yield (%)[a,b]
1	$PPh_3AuCl/AgOTs$	$ClCH_2CH_2Cl$	70	5[c]
2	$PPh_3AuCl/AgOTf$	CH_2Cl_2	23	7[d]
3	AuCl	$ClCH_2CH_2Cl$	23	-[e]
4	AuCl	$ClCH_2CH_2Cl$	70	-[e]
5	$PtCl_2$	$ClCH_2CH_2Cl$	23	-[e]
6	$PtCl_2$	$ClCH_2CH_2Cl$	70	-[e]
7	Au(III)[f]	$ClCH_2CH_2Cl$	70	9[c]
8	$AuCl_3$	$ClCH_2CH_2Cl$	23	-[e]
9	$AuCl_3$	$ClCH_2CH_2Cl$	70	5[d]

Table 13: Catalysts screening to form 2,5-substituted pyrroles from alkynyl aziridine 233. [a]All reactions were run for 12 h using 0.2 mmol of substrate with 5 mol% of gold and silver species at 0.2 M. [b]Yields calculated by ^{1}H NMR against a known quantity of internal standard. [c]Most starting material was left untouched. [d]Complex mixture, no starting material recovered. [e]No pyrrole product observed by crude ^{1}H NMR, partial degradation of the starting material occurred. [f]Dichloro(pyridine-2-carboxylato) gold was used.

At that stage it was envisioned to screen other gold catalysts and to study the impact of solvent on the reaction. However, Liu and co-workers published their work on the preparation of functionalised pyrroles from similar *N*-phthalimide-substituted alkynyl aziridines and it was decided to halt the project (Scheme 64).[71]

The method described by Liu and co-workers employed the cationic gold system $Ph_3PAuCl/AgOTf$ in THF at 50 °C and good yields of pyrrole were reported from strictly *cis*-alkenyl aziridines. The same combination of gold complex and silver salt had been tested in

our study on aziridine **233**, but had been employed at room temperature in CH_2Cl_2 and very low conversion to pyrrole **234** had been observed at the time (Table 13, entry 2). To access the aziridine precursor a similar method to ours was employed from enynes but the toxic $Pb(OAc)_4$ was replaced by PIDA. This reaction tolerated a range of alkyl and aryl functional groups for substituents R^2 and R^3 (Scheme 64) but it was limited to esters and phenyl in position 2 of the aziridine ring (R^1 in Scheme 64). Despite this restriction, disubstituted and trisubstituted enynes were accessed and gold catalysis under the reported conditions led to the formation of a series of disubstituted or trisubstituted pyrroles.



Scheme 64: Liu and co-workers gold-catalysed synthesis of *N*-phthalimide substituted pyrrole.

3.9 Summary

A new and efficient gold-catalysed 2,4- and 2,5-substituted pyrrole synthesis from *N*-tosyl alkynyl aziridine has been developed. The effect of the counterion on the outcome of the reaction was demonstrated and allowed preferentially formation of one isomer or the other. $Ph_3PAuOTs$ proved to be the catalyst of choice to form 2,5-substituted pyrrole in an atom-economic manner as almost quantitative yields were obtained. Changing the catalyst to

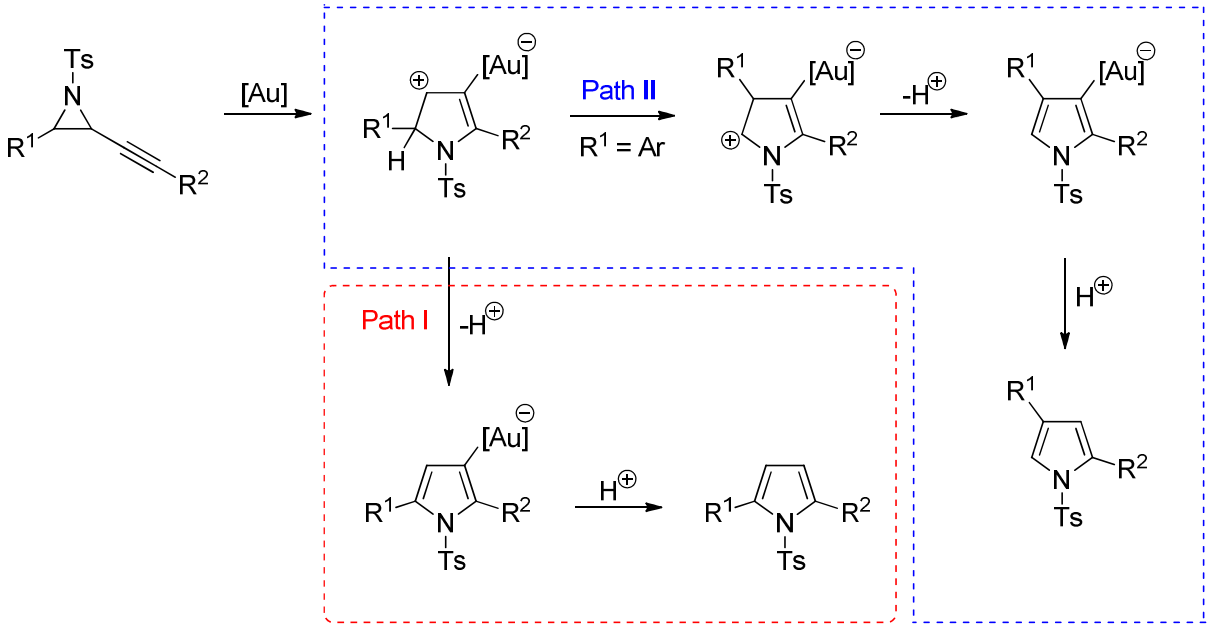
$Ph_3PAuOTf$ afforded the 2,4-substituted isomer highlighting the importance of counterion selection for gold catalysed processes as it can play an important role in determining the reaction pathway. Furthermore the applicability of the reaction developed for this pyrrole synthesis was also investigated on *N*-phthalimide alkynyl aziridine and alkynyl oxirans proving unfortunately that the optimised reaction conditions could not be directly transposed. Improvement of the scope of the reaction would probably be possible but would need advances in the access of the *N*-tosyl alkynyl aziridine precursors as this proved to be a limiting factor in this project.

Chapter 4: Mechanistic studies

4.1 Introduction

The preceding chapter described the development of new gold-catalysed pyrrole syntheses. The use of OTf or OTs as the counterion to gold was proven to be critical in determining whether the reaction pathway led to the formation of either a 2,5- or 2,4-substituted pyrrole as the major product. During studies into the role of the counterion, solvent effect, and the impact of the alkynyl aziridine aryl substituent a reaction mechanism was proposed which rationalised the reaction outcomes through a 1,2-aryl shift (Scheme 65).

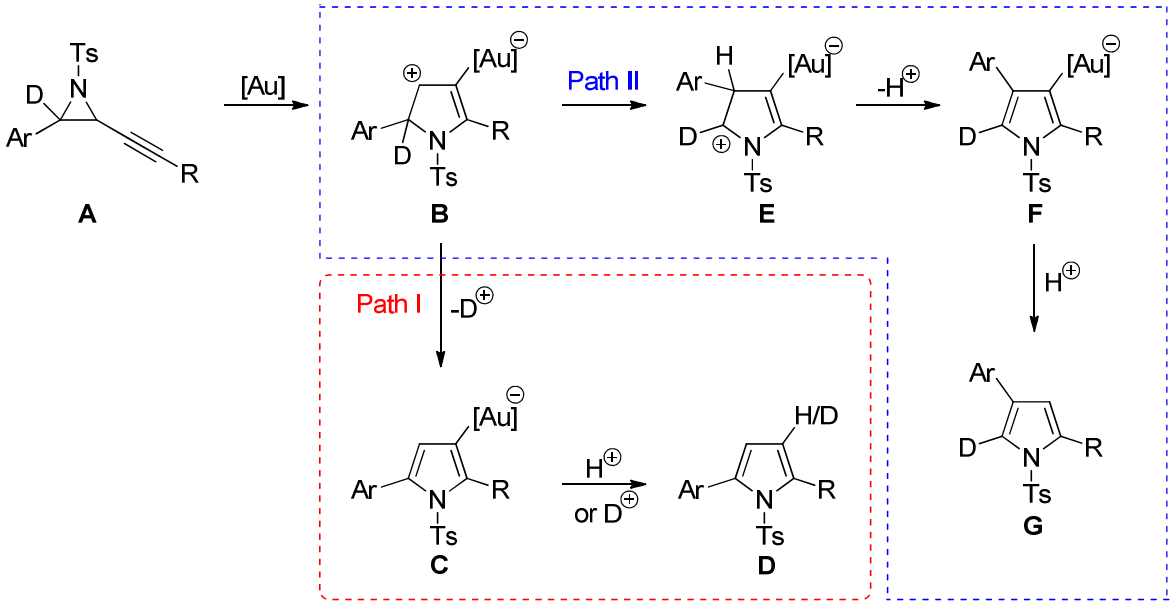
In order to prove this hypothesis correct or not, deuterium labelling was explored to tell us about the movement of the protons during the course of the reaction, and ^{13}C labelling was investigated to learn about the behaviour of the carbon skeleton.



Scheme 65: Mechanism proposed in Chapter 3

4.2 Deuterium labelled studies

In order to probe the proposed reaction mechanism, it was decided to synthesise an alkynyl aziridine bearing a deuterium label at the benzylic position (Scheme 66, structure **A**). Indeed, with such an aziridine isolation of compound **G** would prove the 1,2-aryl shift, and isolation of compound **D** would validate Path I under the standard reaction conditions.

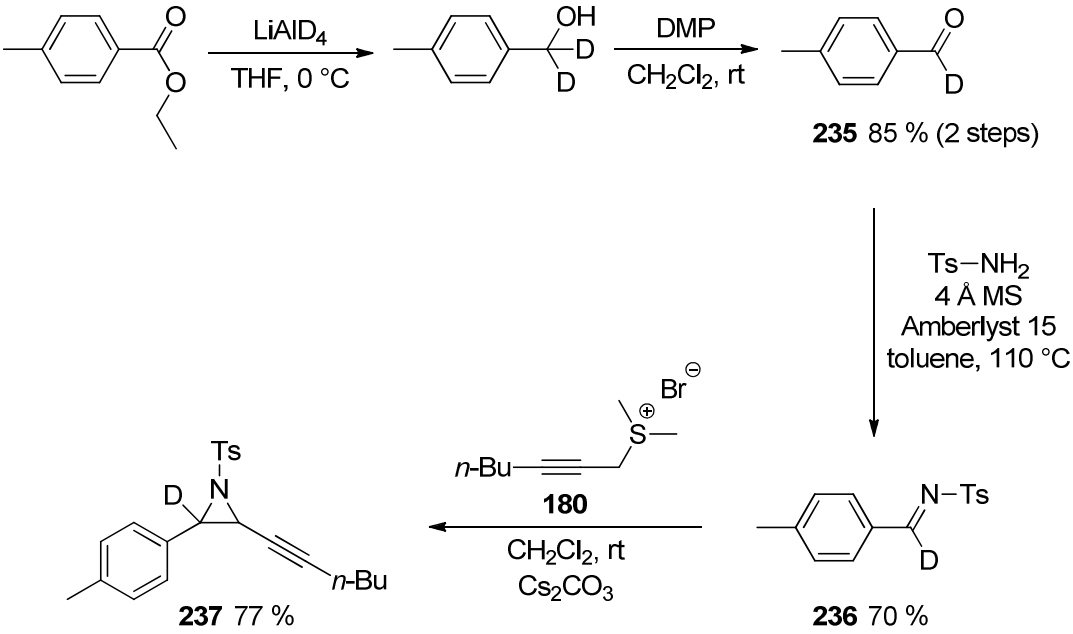


Scheme 66: Anticipated outcome of the reaction of deuterium labelled alkynyl aziridine

It was decided to prepare deuterium labelled alkynyl aziridine **237** bearing a tolyl group because this substituent had given among the greatest amount of rearrangement product (Chapter 3, Scheme 11). The *n*-butyl functionality was preferred to a phenyl one in order to simplify the aromatic region of ^{1}H NMR spectra and so facilitate interpretation of results.

Ethyl 4-methylbenzoate was reduced using $LiAlD_4$ to give the deuterated 4-methylbenzyl alcohol[72] and oxidation using the Dess-Martin procedure gave the desired aldehyde **235** in high yield (Scheme 67). The corresponding deuterated imine **236** was formed by condensation

with tosylamine under the previously described conditions and used to prepare deuterated alkynyl aziridine **237**.

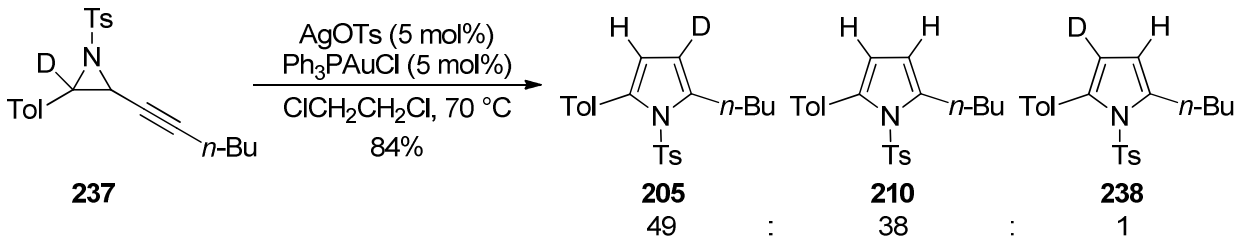


Scheme 67: Preparation of deuterated alkynyl aziridine 237

Aziridine **237** was then subjected to the two sets of reaction conditions previously developed: $Ph_3PAuCl/AgOTs$ in $ClCH_2CH_2Cl$ at 70 °C and $Ph_3PAuCl/AgOTf$ in CH_2Cl_2 at room temperature.

4.2.1 Deuterium labelled studies employing $Ph_3PAuCl/AgOTs$

As in the non-labelled series, the use of AgOTs with PPh_3AuCl led exclusively to 2,5-substituted pyrroles (Scheme 68).



Scheme 68: Deuterium labelling study employing $Ph_3PAuCl/AgOTs$

The ^1H NMR of the mixture of products obtained (Figure 4) clearly showed the presence of non-deuterated pyrrole product **210** which had been previously synthesised and characterised (Figure 5). According to the ^1H NMR spectra of this non-deuterated pyrrole **210** (Figure 5), the doublet at 6.04 ppm corresponded to H^4 as this proton is only coupled with its neighbour H^3. The pattern observed for H^3 at 6.02 ppm was a more complex doublet of triplets due to coupling not only with H_4 but also with the first CH_2 of the *n*-Bu moiety (^4J coupling).

In addition to the signals from compound **210** two unequal singlets were observed at 6.04 and 6.02 ppm (Figure 4). Considering the previous pattern attribution for H^3 and H^4, the new singlet at 6.04 ppm was assigned to a proton at position 4 in pyrrole **205** with an adjacent deuterium in position 3. The presence of the second small singlet at 6.02 ppm was attributed to a small amount of deuterated pyrrole **238** bearing a proton in position 3 and deuterium in position 4 this time.

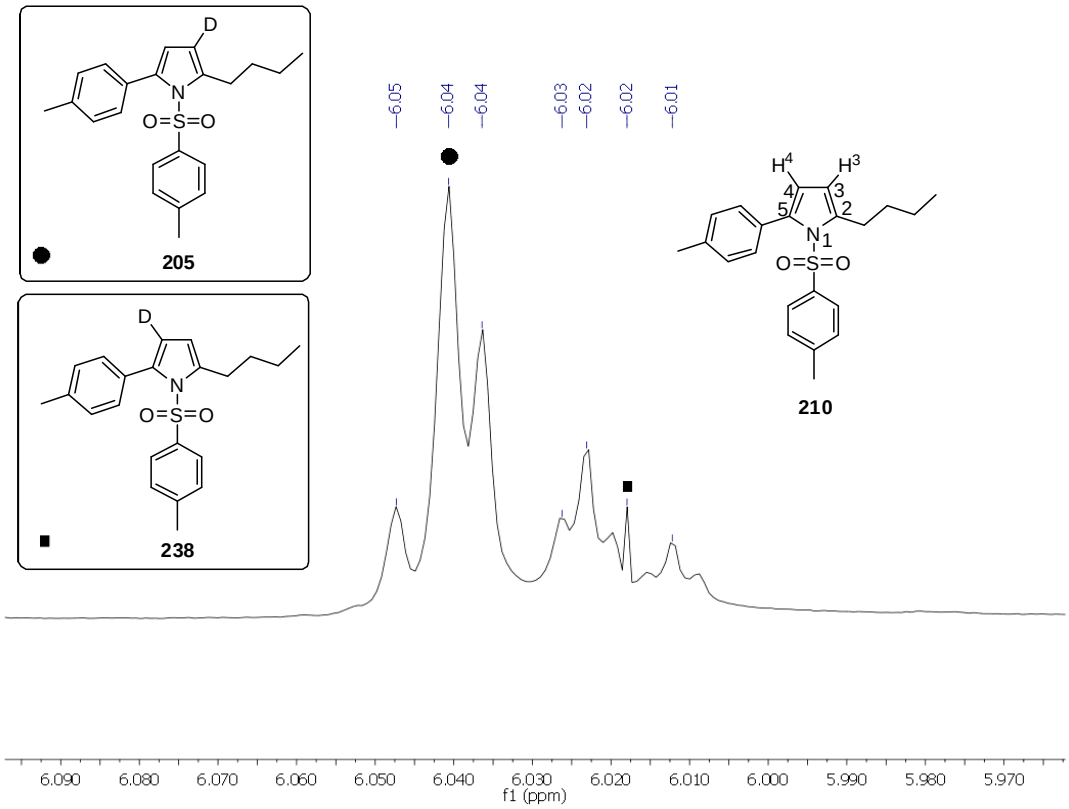


Figure 4: Selected area of ^{1}H NMR from the mixture of pyrroles obtained after reaction on deuterated alkynyl aziridine 237 using $PPh_3AuCl/AgOTs$

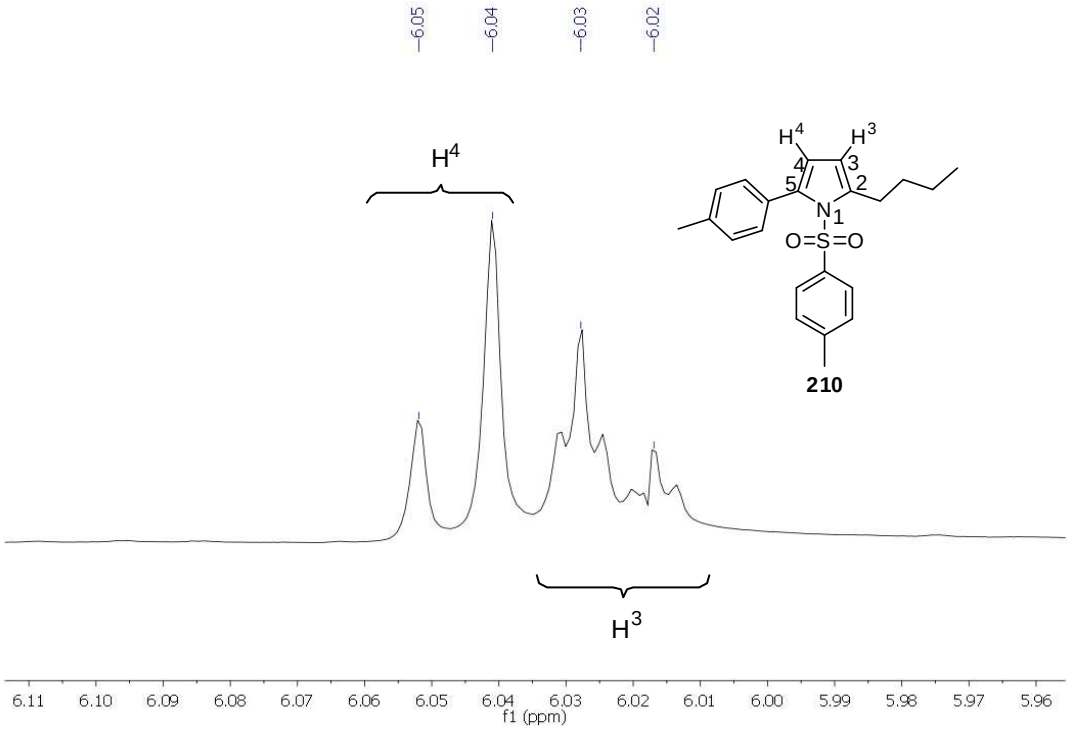
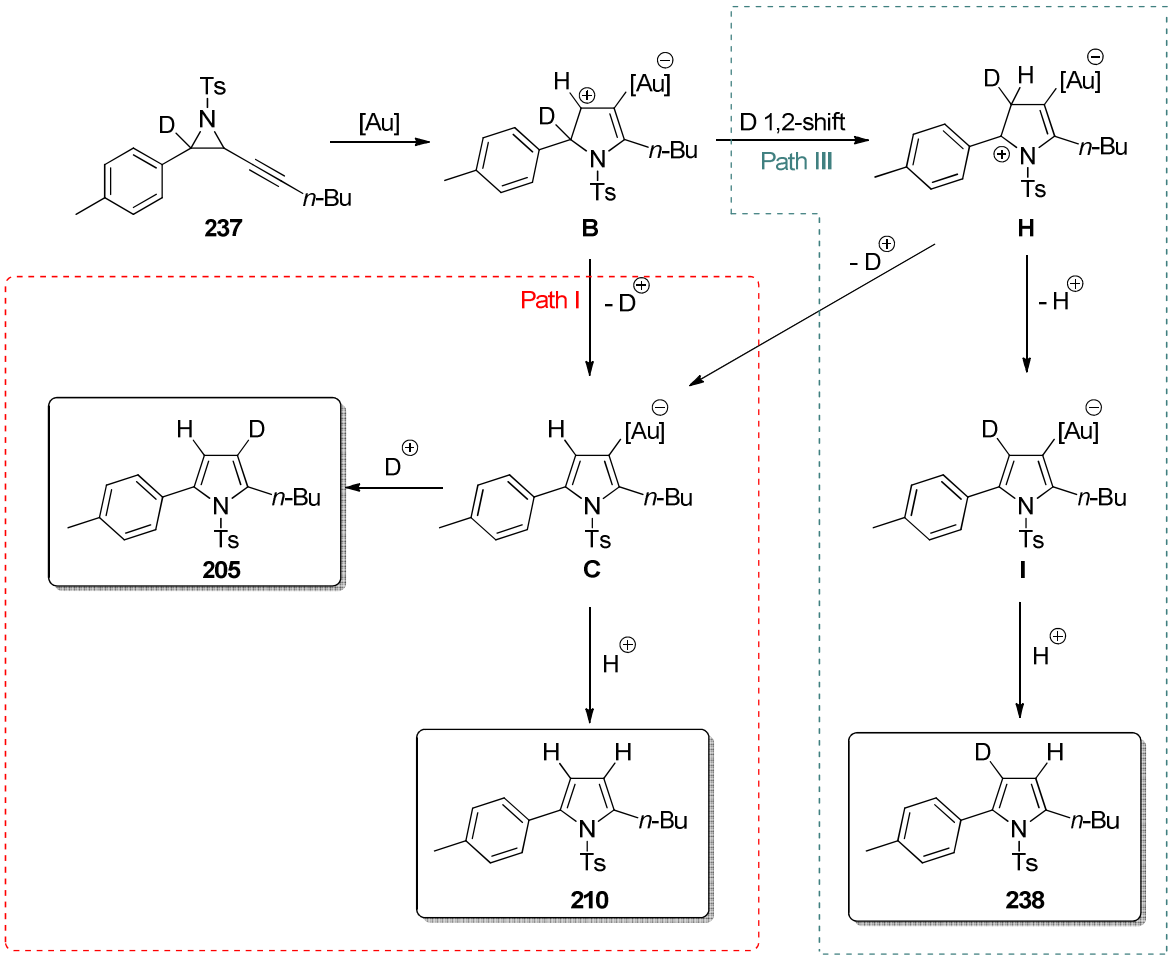


Figure 5: ^{1}H NMR of non-deuterated pyrrole 210

At the light of these experimental results a refined reaction mechanism was proposed (Scheme 69).



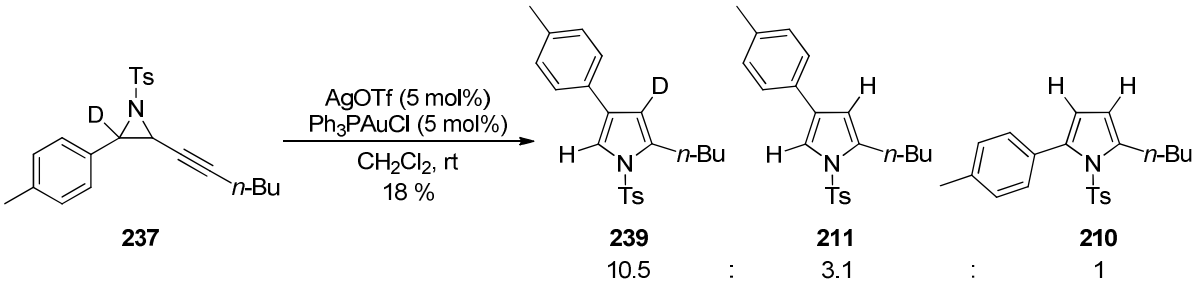
Scheme 69: Mechanistic rationale for the deuterium labelling study using $Ph_3PAuCl/AgOTs$

After cationic gold activation of deuterated alkynyl aziridine **237**, cycloisomerisation would lead to intermediate **B**. Through path I, abstraction of the deuterium at that stage would give intermediate **C** which could evolve into product **205** by reincorporating the lost deuterion. The second product **210** would be obtained by proton exchange with the reaction mixture, from traces of water or acid for example. Another possibility from intermediate **B** would be the 1,2-shift of the deuterium to give **H** through path III. This migration could be rationalised

by the formation of a tertiary carbocation stabilised by the adjacent heteroatom and aryl group. From **H,** product **I** would be obtained by loss of proton, subsequent protodemetalation would give deuterated pyrrole **238**.

4.2.2 Deuterium labelled studies employing $Ph_3PAuCl/AgOTf$

When deuterium labelled alkynyl aziridine **237** was reacted with AgOTf and Ph_3PAuCl, a mixture of 2,5-substituted (minor) and 2,4-substituted (major) pyrroles was produced as expected (Scheme 70). Surprisingly a yield of 18% of pyrrole mixture was obtained while 32% were reported in the non-deuterated series (Chapter 3, Table 11, entry 10). Repeating the reaction afforded the same 18% yield of products. When another deuterium-labelled alkynyl aziridine bearing a phenyl-substituted alkyne (instead of an *n*-butyl moiety as for **237**) was reacted with AgOTf and Ph_3PAuCl, complete degradation occurred.



237 **239** : **211** : **210**

10.5 : 3.1 : 1

Scheme 70: Deuterium labelling study employing $Ph_3PAuCl/AgOTf$

The ^1H NMR of the mixture of pyrroles (Figure 6) showed evidence of the presence of small amount of previously synthesised non-deuterated product **211**. The ^1H NMR of this non-labelled 2,4-substituted pyrrole (Figure 7) showed two resonances coupled together, a doublet at 7.54 ppm (H^5) and a doublet of triplets at 6.30 ppm (H^3), the pattern due to long range

coupling with the -CH_2 of the *n*-butyl moiety (^4J coupling). The products of deuterated alkynyl aziridine **237** gave a mixture of pyrroles in which the doublet of triplets at 6.30 ppm was easily identified. The doublet at 7.54 ppm could not be seen, probably being covered by the presence of a net singlet from deuterium-labelled pyrrole **239** at 7.54 ppm.

Moreover trace amount of non-deuterated product **210** was also identified by a doublet at 6.04 ppm and a doublet of triplets at 6.02 ppm (not represented in Figure 6, 7).

With these data the mechanism was then re-examined.

As in the former deuterium labelled study employing AgOTs, the presence of traces of pyrrole **210** was explained by path I, through loss of deuterium from intermediate **B** followed by protodeauration. Pyrroles **205** and **238**, from path I and path III respectively, were probably below ^{1}H NMR detection limit and were not observed.

The formation of pyrroles **211** and **239** could be explained through path II. Intermediate **B** would lead to **J** after a 1,2-aryl shift (Scheme 71). A subsequent 1,2-H migration would deliver intermediate **K**, perhaps leading to a more stabilised tertiary carbocation. Loss of deuterium at that stage would give **M** and protodemetalation or deuterium exchange would form pyrroles **211** and **239**. However, loss of proton from **K** would give intermediate **L** and compound **240** should have been detected in the ^{1}H NMR of the mixture.

Lack of product **240** raised questions about the validity of the proposed mechanism for the formation of the 2,4-substituted products and the mechanistic investigations were pursued.

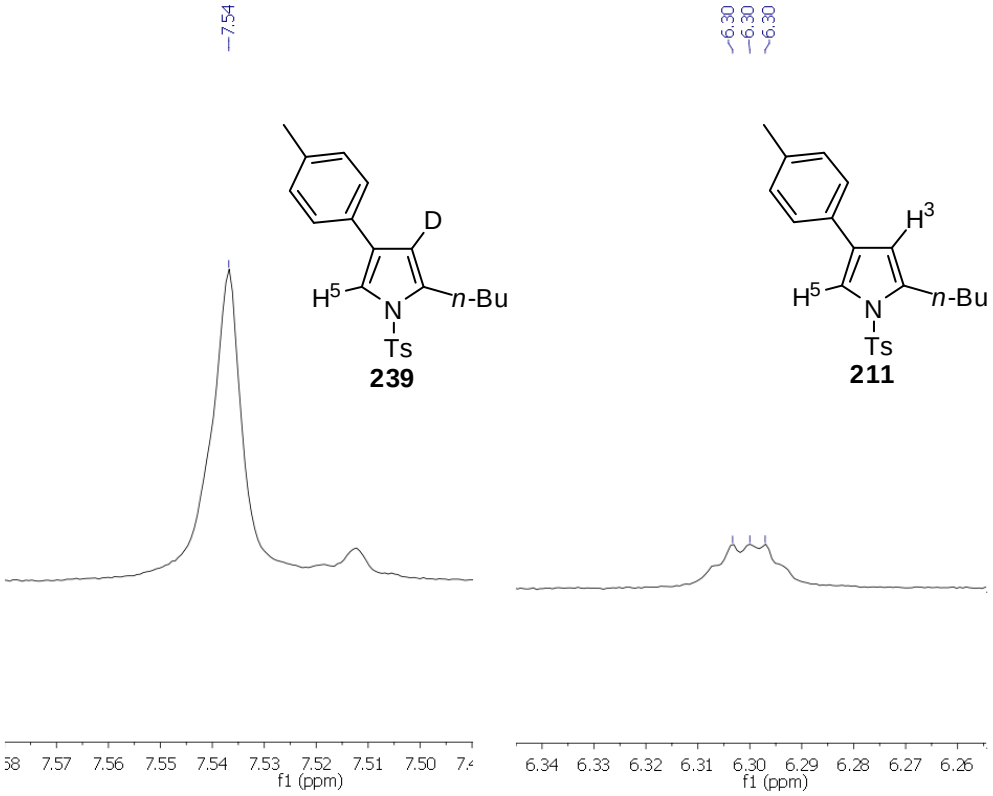


Figure 6: Selected parts of ^{1}H NMR of pyrrole mixture obtained employing $Ph_3PAuCl/AgOTf$

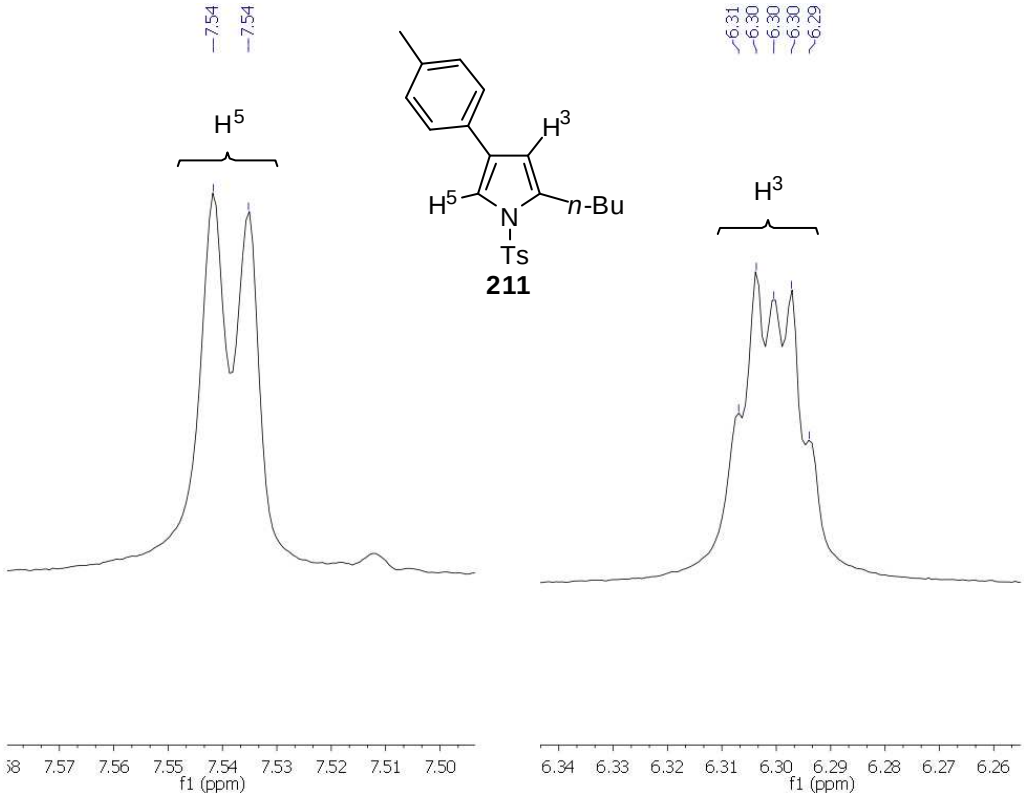
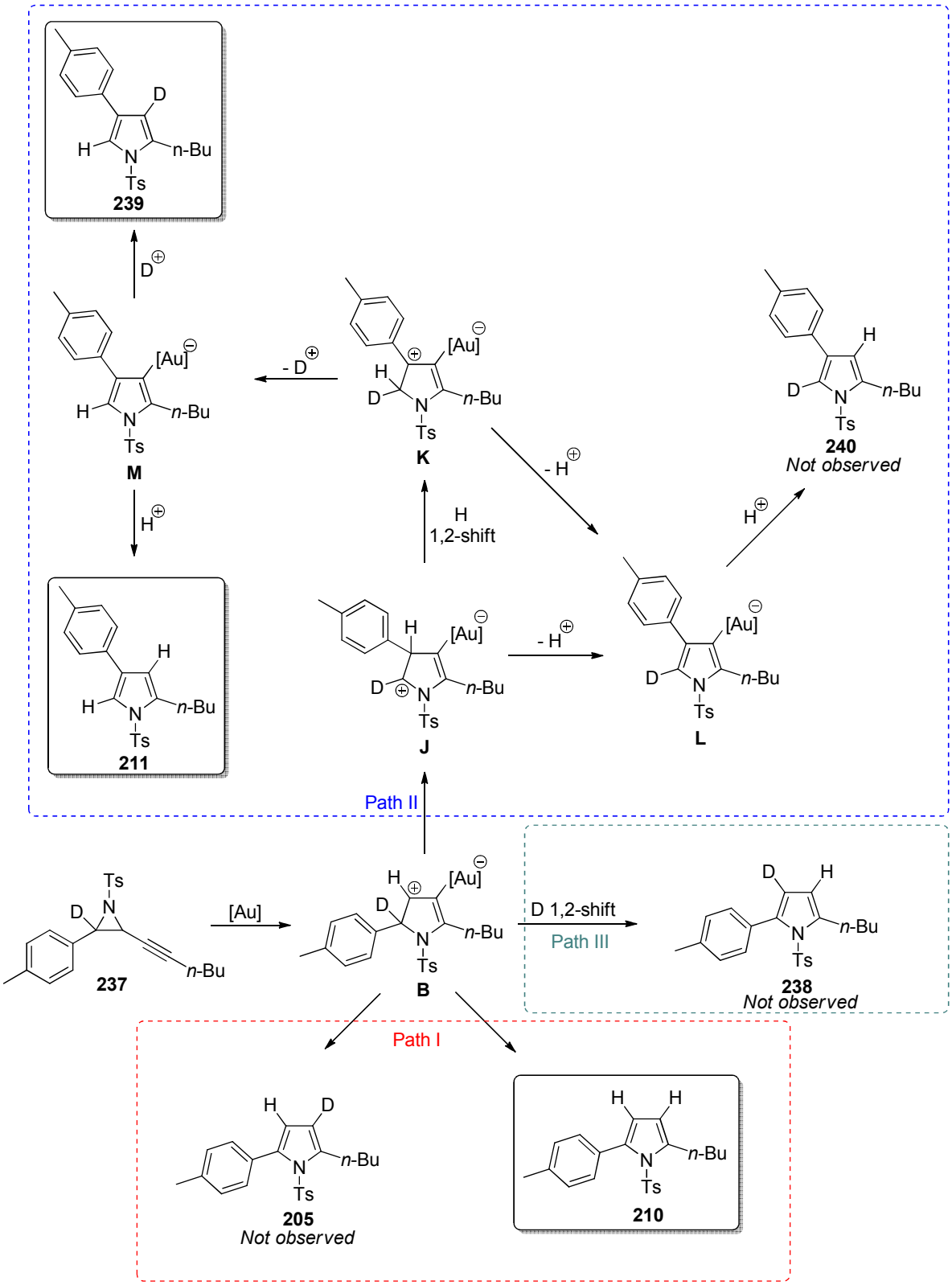


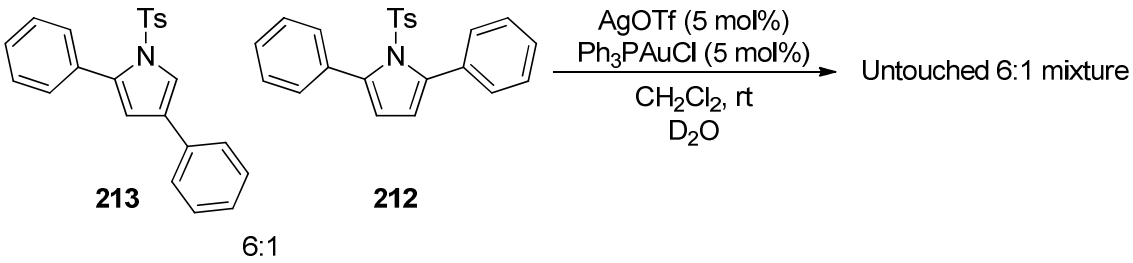
Figure 7: ^{1}H NMR of non-deuterated pyrrole 211



Scheme 71: Mechanistic rationale for the deuterium labelled study using $Ph_3PAuCl/AgOTf$

4.3 ^{13}C labelled studies

Although control studies had shown no H/D exchange under the reaction conditions (Scheme 72), more information was required to ascertain a likely mechanism.



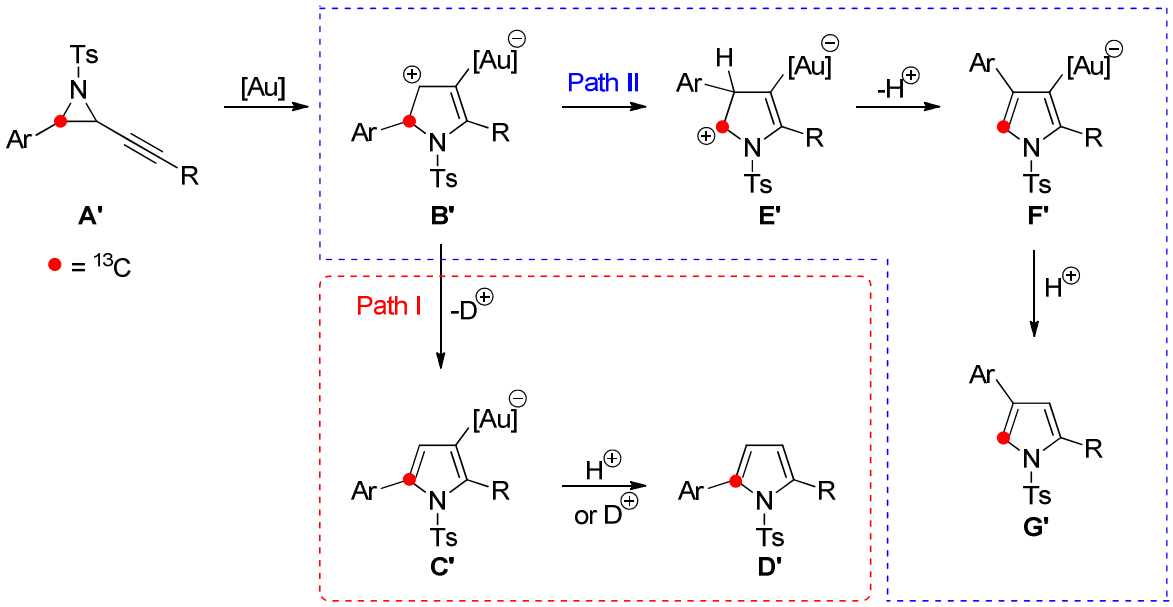
Scheme 72: Control study ruling out H/D exchange under the reaction conditions

It was therefore decided to continue with ^{13}C labelling studies in order to obtain information about the behaviour of the carbon skeleton during the reaction.

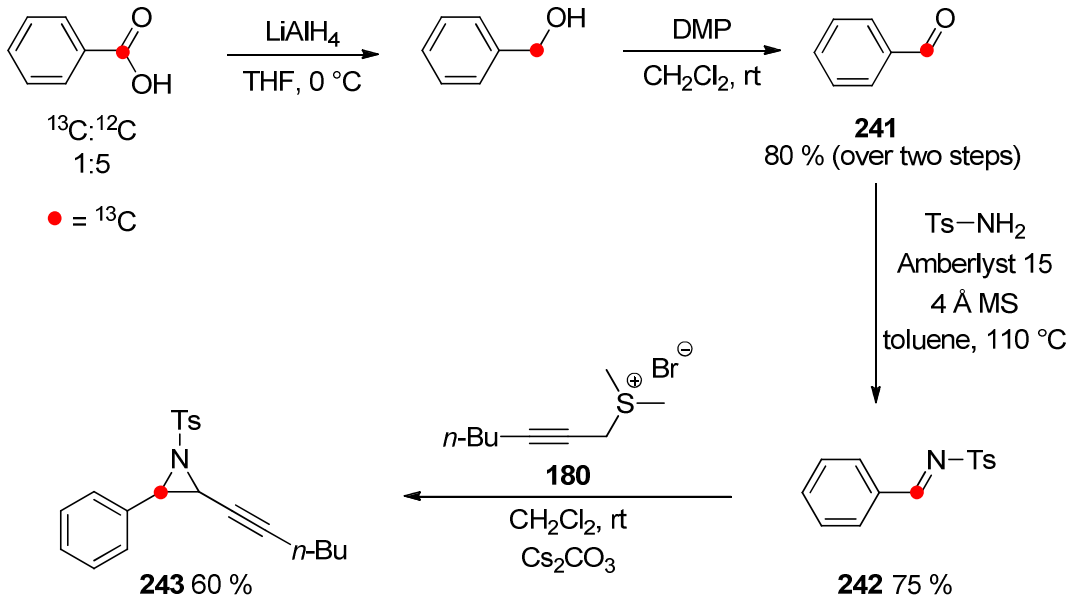
An alkynyl aziridine bearing a ^{13}C-enriched center bonded to an aryl moiety on the three-membered ring was employed (Structure **A'**, Scheme 73). With the ^{13}C-enriched carbon in that position, it was expected to give weight to the proposed Path I by forming product **D'**. Isolation of pyrrole **G'** would allow us to validate the 1,2-aryl shift pathway that could not be proved by the deuterium experiments.

The ^{13}C-enriched alkynyl aziridine **243** was prepared from commercially available ^{13}C-enriched benzoic acid, as 1:5 ^{13}C:^{12}C mixture, in a four-step sequence (Scheme 74). Reduction of the carboxylic acid with $LiAlH_4$ was followed by Dess-Martin oxidation to give aldehyde **241**.[73,74] Condensation with tosylamine under acidic conditions afforded the

corresponding imine **242**. Reaction with sulfonium salt **180** and Cs_2CO_3 gave the ^{13}C-enriched alkynyl aziridine **243**.



Scheme 73: Anticipated outcome of the reaction of ^{13}C-enriched alkynyl aziridine

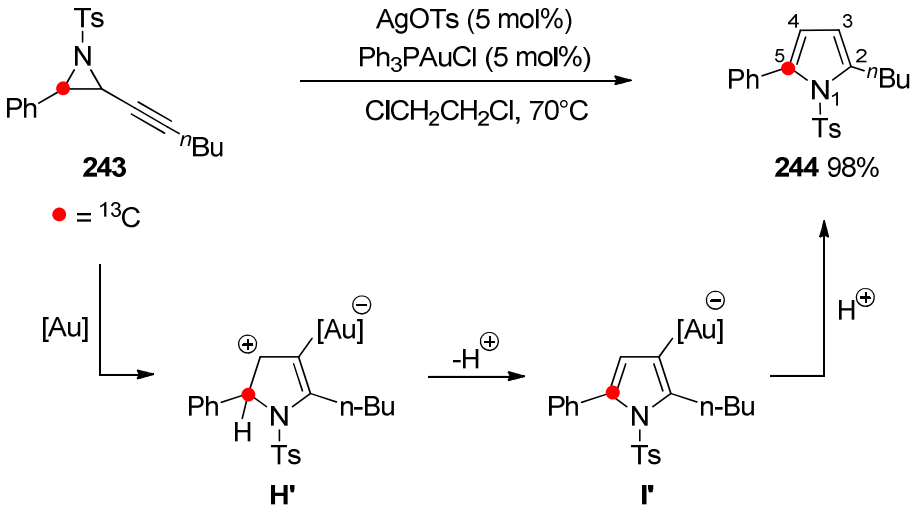


Scheme 74: Preparation of ^{13}C-enriched alkynyl aziridine 243

Aziridine **243** was then subjected to the two sets of reaction conditions previously developed: $Ph_3PAuCl/AgOTs$ in $ClCH_2CH_2Cl$ at 70 °C and $Ph_3PAuCl/AgOTf$ in CH_2Cl_2 at room temperature.

4.3.1 ^{13}C labelling study employing $Ph_3PAuCl/AgOTs$

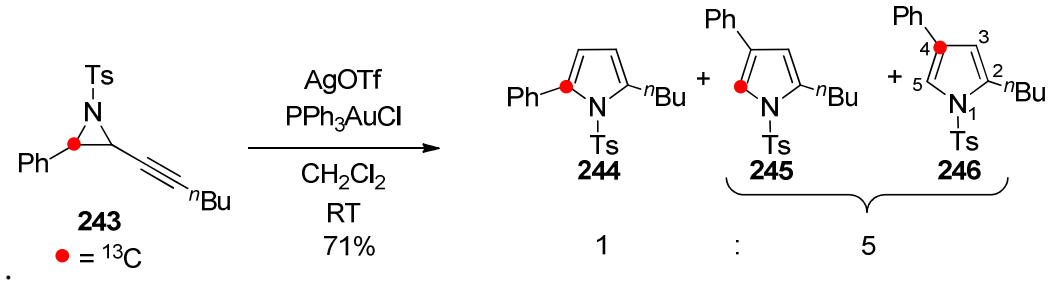
Under catalysis with **243** $Ph_3PAuCl/AgOTs$, alkynyl aziridine **243** afforded the expected 2,5-substituted pyrrole **244** exclusively. ^{13}C enrichment was observed at only one resonance in the ^{13}C NMR spectrum (Appendix B), corresponding to C-5, as expected from the proposed mechanism (Scheme 75).



Scheme 75: ^{13}C labelling study using $AgOTs/PPh_3AuCl$ with alkynyl aziridine 243.

4.3.2 ^{13}C labelling study employing $Ph_3PAuCl/AgOTf$

When ^{13}C-enriched alkynyl aziridine **243** was submitted to catalysis using $Ph_3PAuCl/AgOTf$ a mixture of three ^{13}C-enriched isomers was obtained (Appendix B) rather than the two expected. All resonances could be attributed to either the 2,5- or 2,4-pyrrole isomers (Scheme 76).



Scheme 76: ^{13}C labelling study using $AgOTf/PPh_3AuCl$ with alkynyl aziridine 243.

Two products were readily identifiable as the ^{13}C-enriched 2,5-substituted pyrrole **244** described above, and the expected 2,4-substituted pyrrole **245** with ^{13}C-enrichment at 117.7 ppm in the ^{13}C NMR spectrum (Figure 8).

The other ^{13}C-enriched quaternary signal at 126.8 ppm was explained by the 2,4-substituted pyrrole **246** with ^{13}C-enrichement at C-4, the carbon directly linked to the aryl motif.

HMBC experiments were run to confirm this analysis. Clear ^{3}J coupling between the C-4 ^{13}C-enriched quaternary centre and the protons of the aryl group was observed, proving pyrrole **246** structure and enrichment site.

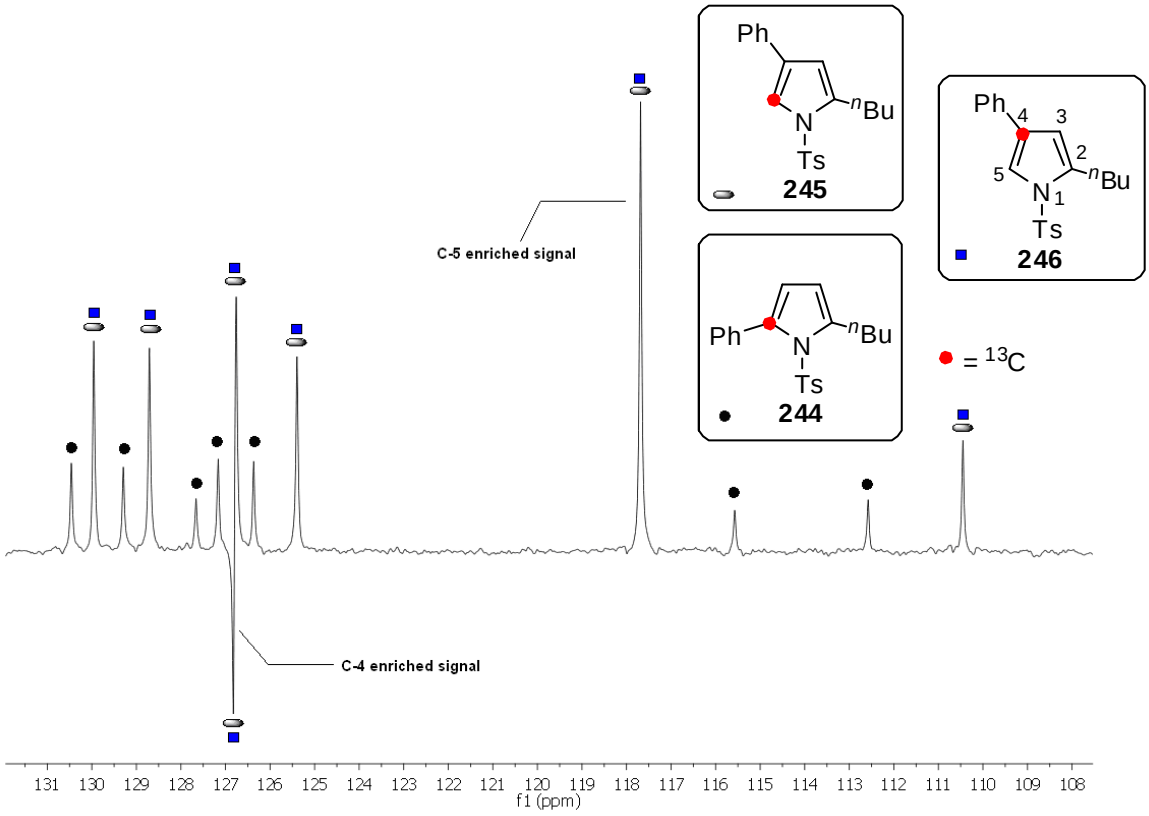
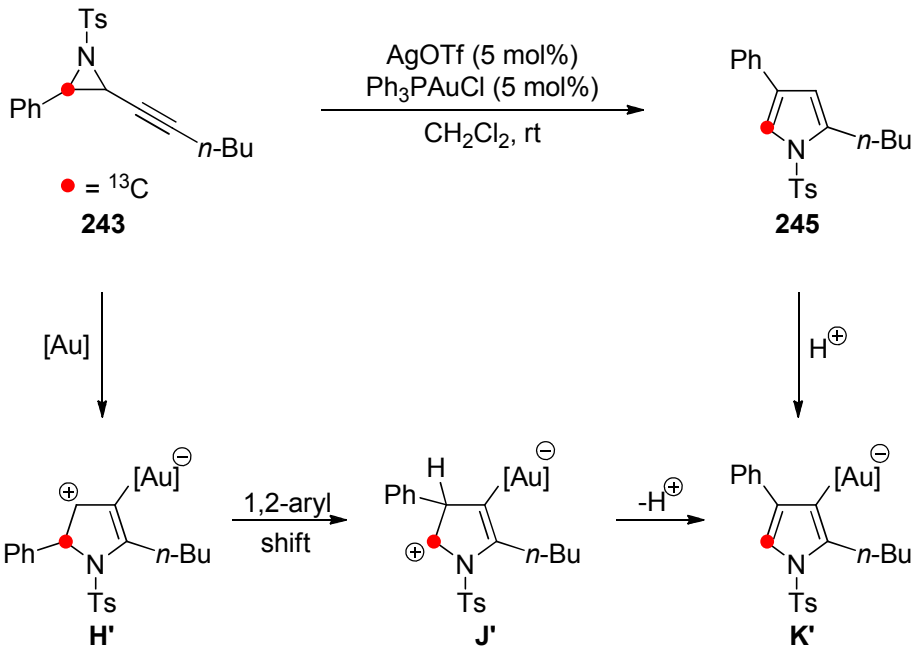


Figure 8: ^{13}C NMR of mixture of pyrroles after treatment of alkynyl aziridine 243 with AgOTf/Ph_3PAuCl.

The formation of ^{13}C-enriched pyrrole **245**, showing the aryl moiety had migrated during the course of the reaction, was in agreement with Path II of the mechanistic proposal suggesting a 1,2-aryl shift (Scheme 73 and 77).

The presence of ^{13}C-enriched pyrrole **246** could not be explained by this pathway. Taken with the D-labelling data, it was apparent that an alternate pathway was operating.



Scheme 77: Proposed mechanism for the formation of 2,4-substituted pyrrole 245

4.4 New mechanistic proposal

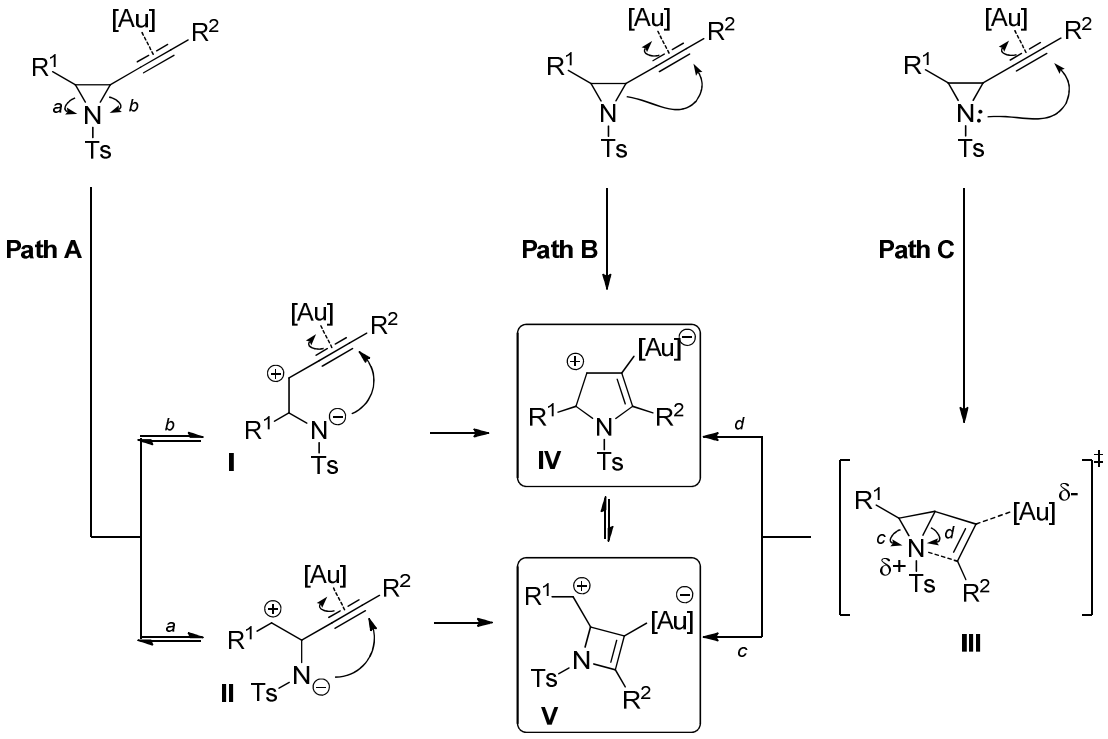
When activated by a gold catalyst, alkynyl aziridines could cycloisomerise to form five-membered ring intermediates as was proposed previously (Structure **B**, Scheme 73). But in fact three distinct pathways could be suggested for that first step (Scheme 78).

A stepwise ring-expansion could take place with reversible alkynyl aziridine ring opening followed by attack of the nitrogen on the alkyne-gold complex (Path A). As two possible ring openings of the three-membered ring could be possible, intermediates **I** and **II** would be formed and would lead to **IV** or **V** respectively after cyclisation onto the alkyne.

In Path B, direct migration of one of the C-N σ-bond from the aziridine to the activated alkyne would happen to form **IV**.

Alternatively, the lone pair of the aziridine nitrogen could perform a nucleophilic attack across the alkyne rendered electrophilic by the catalyst (Path C). Intermediate **V** and **IV** could then be formed from strain release by path *c* or *d* respectively.

Despite being very different from one another mechanistically, none of these three pathways could be ruled out. Nevertheless, the most important for our study was that two pathways were allowing the formation of a four- and five-membered ring intermediate. Path B could also lead to intermediate **V** if interconvertion between **IV** and **V** was possible.

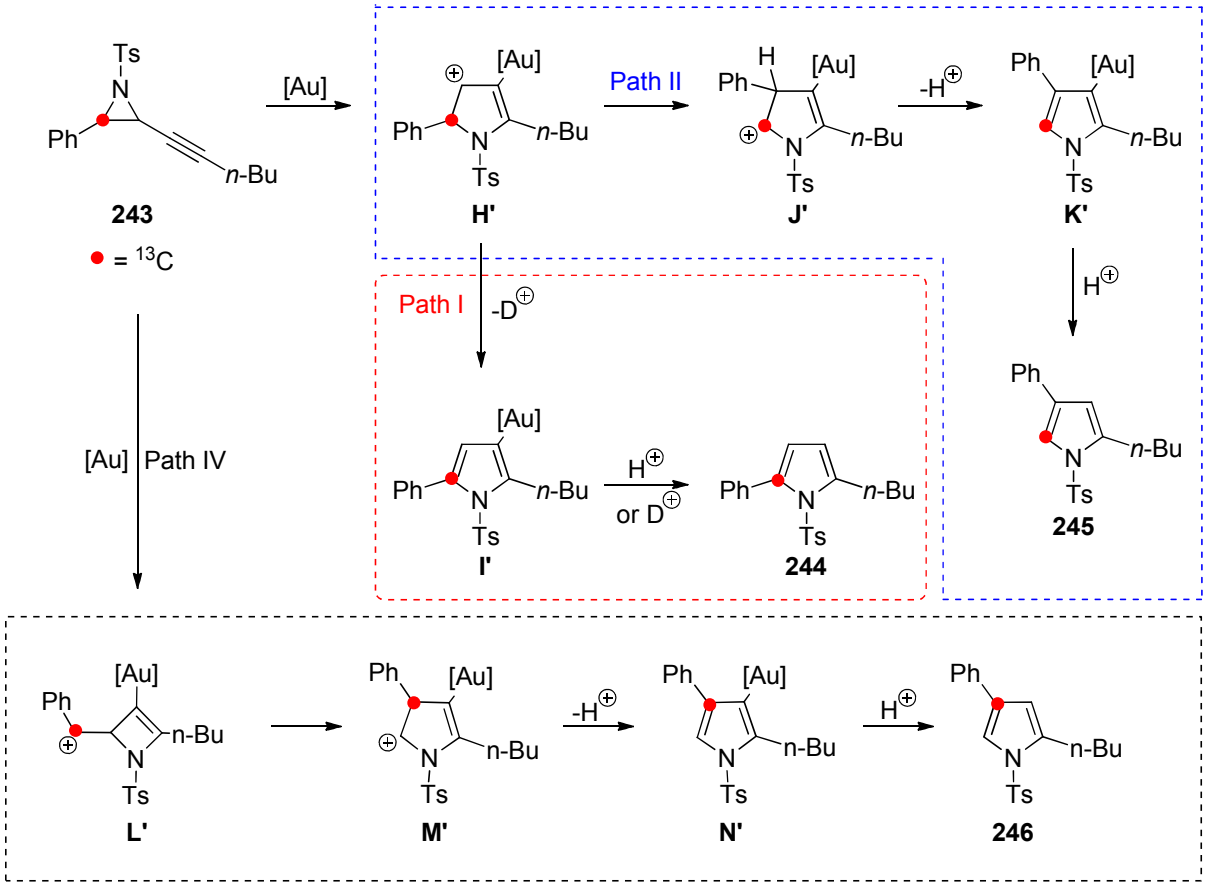


Scheme 78: Distinct pathways for the alkynyl aziridine opening

The ^{13}C labelling study showed previously that the five-membered ring intermediate could explain the formation of ^{13}C-enriched 2,5-substituted pyrrole **244** (Scheme 75) and ^{13}C-enriched 2,4-substituted pyrrole **245** (Scheme 77).

On the other hand, it was thought that the four-membered ring intermediate could explain the formation of ^{13}C-enriched 2,4-substituted pyrrole **246** (Scheme 79).

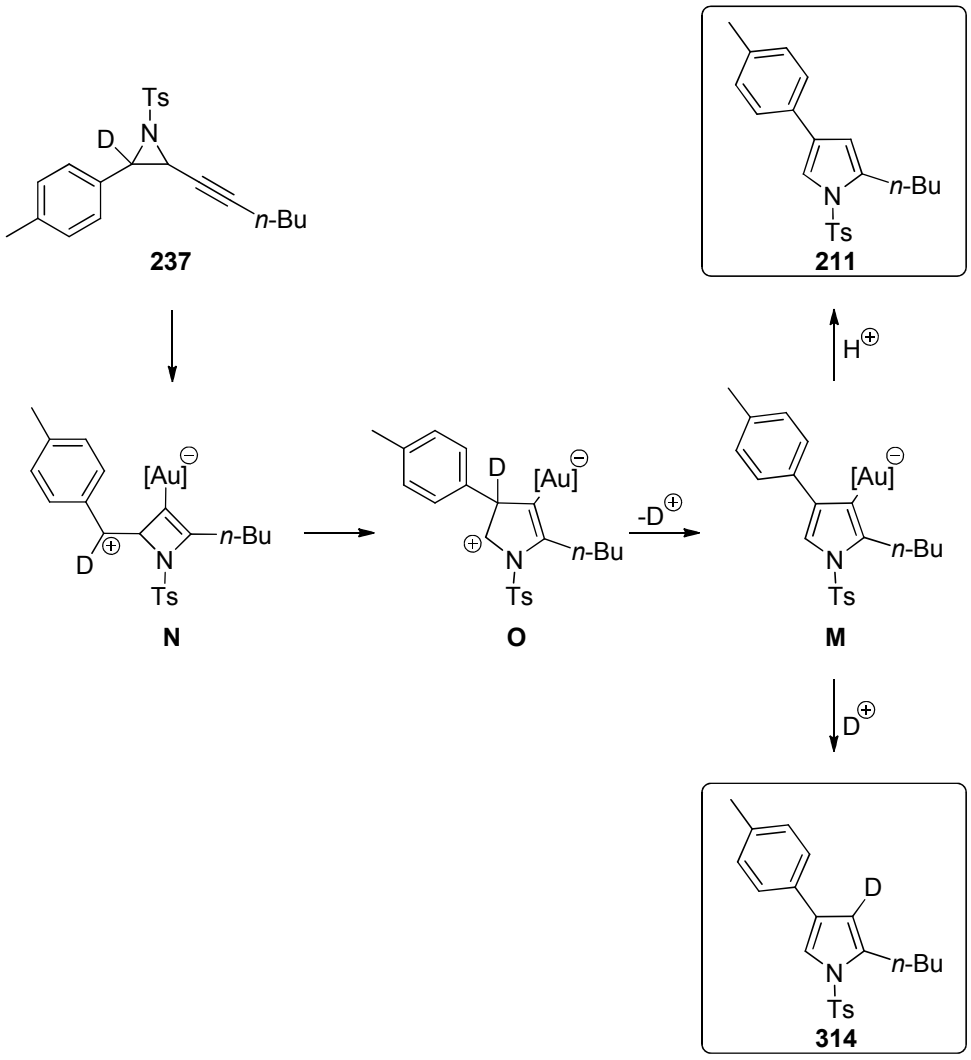
In this case, the secondary carbocation of intermediate **L'** would be stabilised by the adjacent aryl group. This species would then evolve into intermediate **M'** by a 1,2-vinyl migration. Proto-deauration would finally give ^{13}C-enriched 2,4-substituted pyrrole **246**.



Scheme 79: New mechanism proposal for the cycloisomerisation of alkynyl aziridine 243 using $Ph_3PAuCl/AgOTf$.

As well as explaining the formation of a pyrrole with ^{13}C-enrichment at C-4 this mechanism also accounts for the results of the deuterium labelling experiments where almost only deuterium insertion was observed in position 3 (Scheme 70).

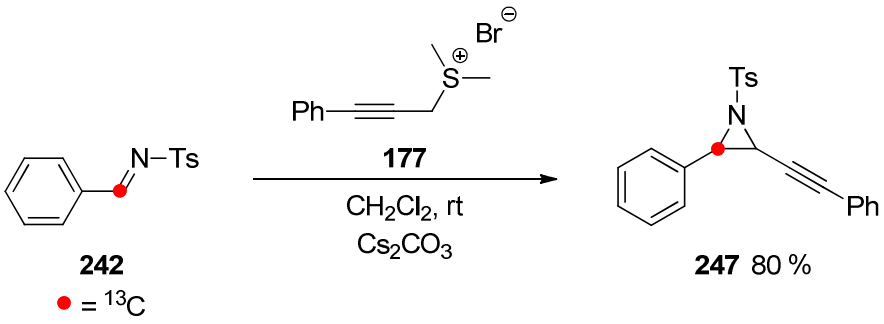
Under this new mechanism, starting with deuterium-labelled aziridine **237**, the transformation of four-membered ring intermediate **N** into structure **O** (Scheme 80) positions deuterium at C-4. Aromatisation proceeds by loss of deuterium to form the organo-gold species **M**. Gold-deuterion exchange would then lead to deuterated 2,4-substituted pyrrole **314**. On the other hand proto-demetalation of intermediate **M** would give 2,4-substituted product **211**.



Scheme 80: Mechanistic rationale for the deuterium labelling study using $Ph_3PAuCl/AgOTf$.

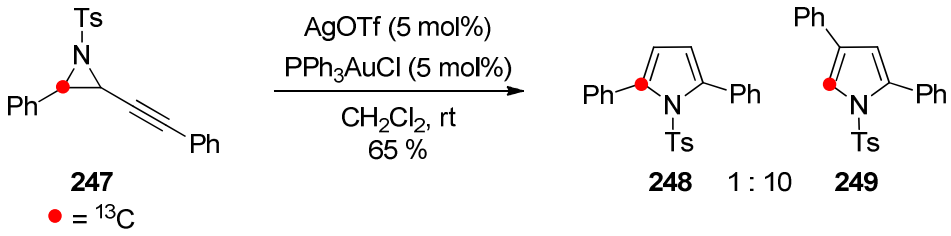
4.5 Tests on the new mechanism

In order to confirm the new mechanistic proposal preparation of ^{13}C-enriched alkynyl aziridine **247** from ^{13}C-enriched imine **242** was performed (Scheme 81).



Scheme 81: preparation of ^{13}C-enriched alkynyl aziridine 247

The new substrate was then submitted to catalysis using $Ph_3PAuCl/AgOTf$. In contrast to the use of ^{13}C-enriched alkynyl aziridine **243**, ^{13}C NMR of the purified pyrrole mixture did not reveal any trace of ^{13}C-enrichment at C-4 of a 2,4-substituted product (Scheme 82, Appendix B).

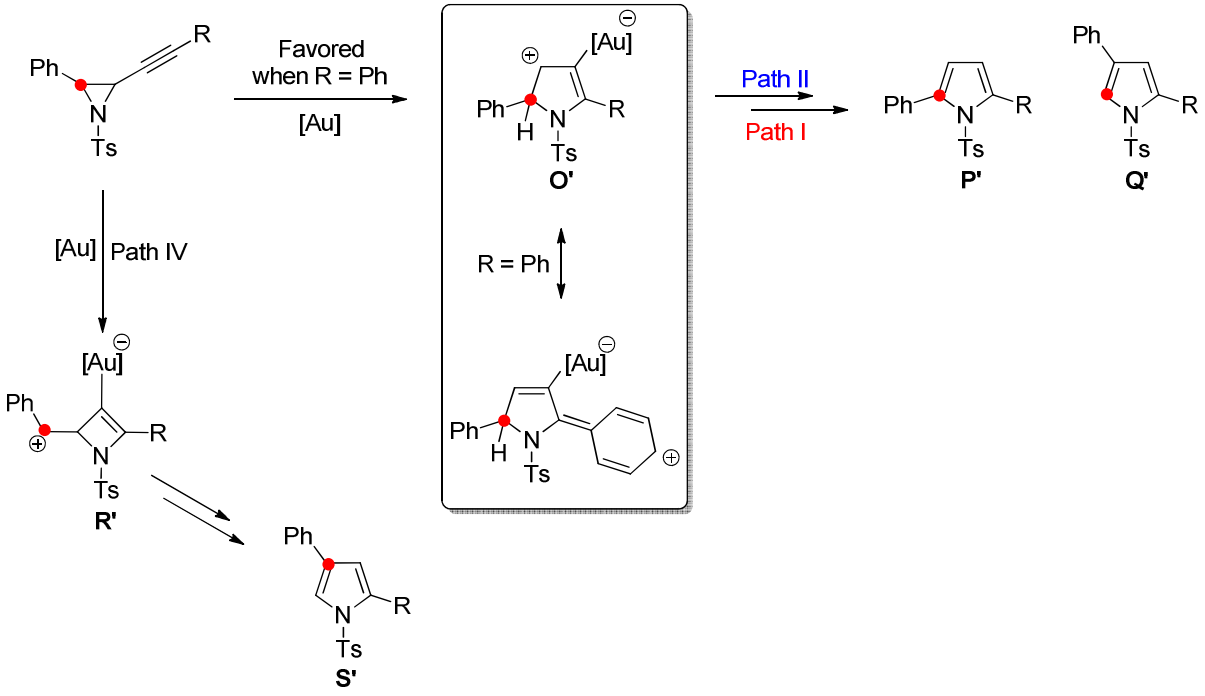


Scheme 82: ^{13}C labelling study using AgOTf/Ph_3PAuCl with alkynyl aziridine 247

In light of this result the new mechanism was reevaluated, paying particular attention to the two intermediates **H'** and **L'** where the process diverged (Scheme 79). The only variation in

the two ^{13}C-enriched alkynyl aziridines considered was the substituent to the alkyne which was either an alkyl or a phenyl moiety. Switching this group would not appear to significantly affect the stability of 4-membered ring **L'** (Scheme 79), but it could have a significant effect on the 5-membered ring intermediate **H'**.

The presence of a phenyl substituent allows greater stabilisation of **O'** by extended delocalisation of aromatic electrons (Scheme 83), thus potentially favouring **O'** at the expense of **R'**. This could explain the formation of only one ^{13}C-enriched 2,4-disubstituted pyrrole in the case of a phenyl-substituted alkynyl aziridine. In the absence of this extra stabilisation, using n-butyl-substituted alkynyl aziridine **243**, the two pathways could be competitive and give the mixture of two 2,4-substituted pyrroles isomers.



Scheme 83: Extra stabilisation of intermediate O'.

It was then decided to prepare three other ^{13}C-enriched substrates to assess the validity of this explanation (Figure 9).

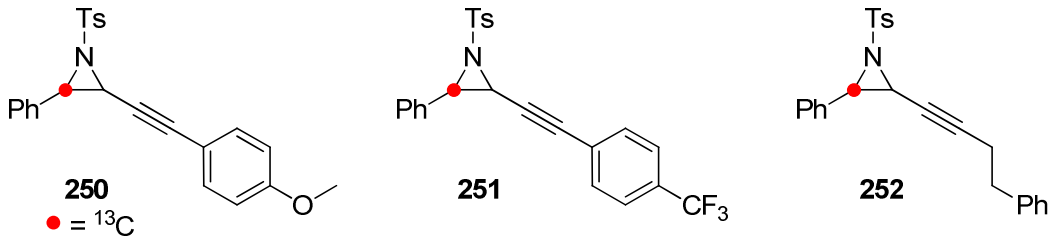


Figure 9: Proposed ^{13}C-enriched substrates to test the validity of mechanistic proposal

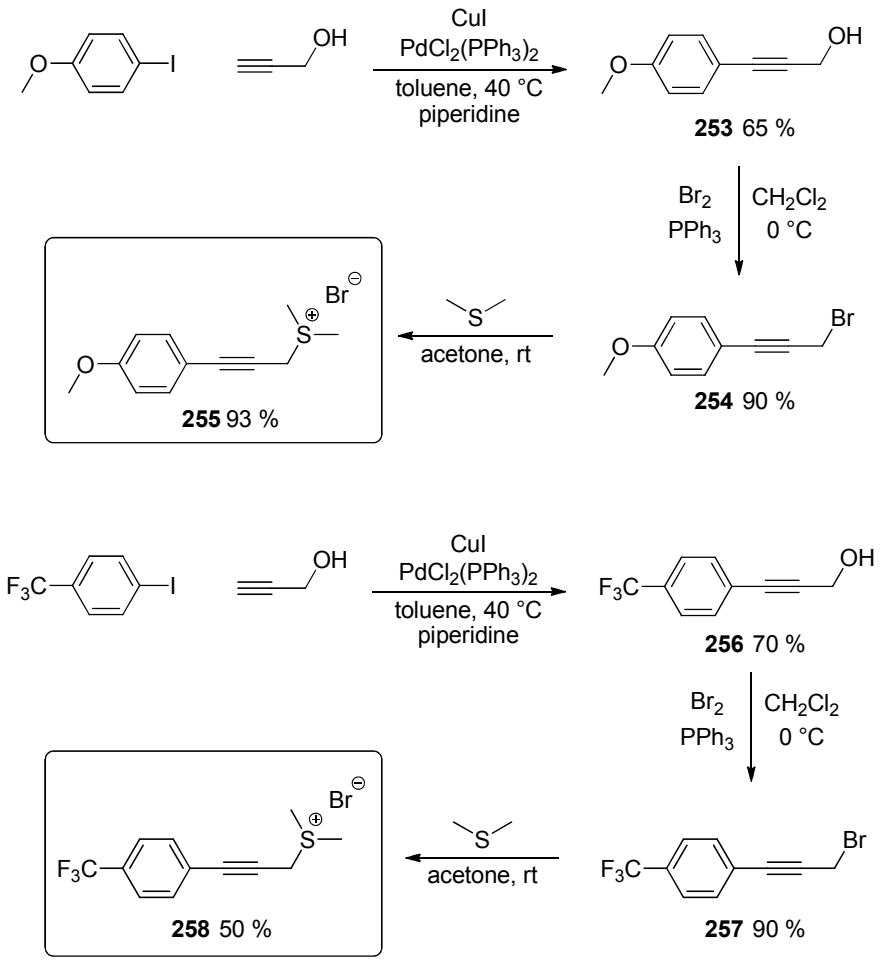
^{13}C-Enriched alkynyl aziridine **252**, bearing an alkyl moiety, was synthesised in order to confirm that no further stabilisation of five-membered ring intermediate **O'** (Scheme 83) would lead to a mixture of 2,4-substituted pyrroles **P'**, **S'** with **Q'** as when *n*-butyl-substituted alkynyl aziridine **243** was employed.

^{13}C-enriched alkynyl aziridine **250**, bearing an electron-rich aryl group, was expected to stabilise intermediate **O'** (Scheme 83) to a greater extent than when ^{13}C-phenyl-substituted alkynyl aziridine **247** was used. Therefore formation of pyrroles **P'** and **Q'** only was anticipated.

In the other hand, ^{13}C-enriched alkynyl aziridine **251**, bearing an electron-deficient aryl group, was expected to destabilise intermediate **O'** (Scheme 83) relative to phenyl substituted **247** and so would potentially give a mixture of ^{13}C-enriched pyrroles **P'**, **S'** and **Q'** by enabling Path IV to be competitive.

To access to these ^{13}C-enriched alkynyl aziridines, sulfonium salts **255** and **258** were prepared (Scheme 84).

Sonogashira type reaction between propargyl alcohol and 4-methoxyiodobenzene gave alcohol **253**. Treatment with PPh_3 and bromine led to bromide **254** which was reacted with dimethylsulfide to form sulfonium salt **255**. The same sequence of reactions was used to form sulfonium salt **258** from 4-(trifluoromethyl)iodobenzene.



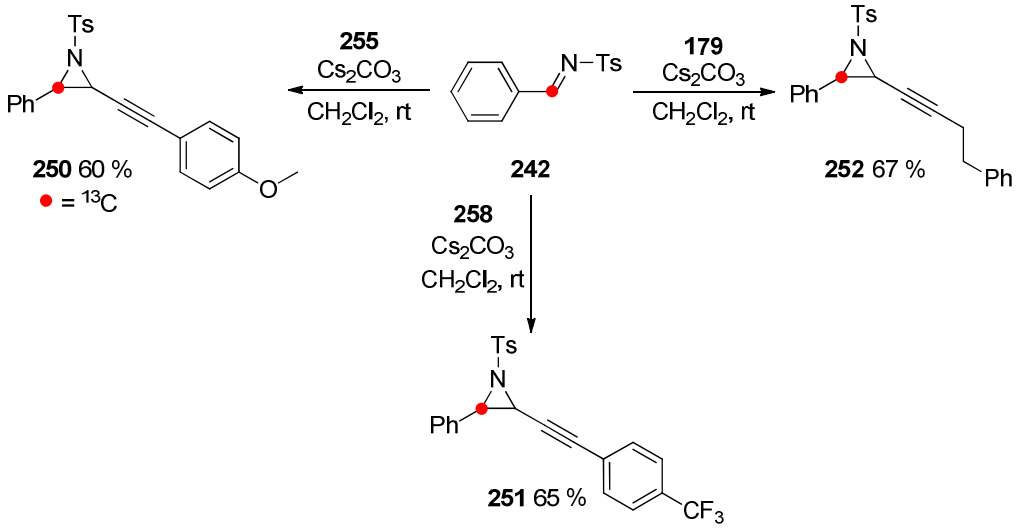
Scheme 84: Preparation of sulfonium salt 255 and 258

^{13}C-enriched alkynyl aziridines **250**, **251** and **252** were then synthesised via reaction of sulfonium salts **255**, **258** and **179** with ^{13}C-enriched imine **242** (Scheme 85).

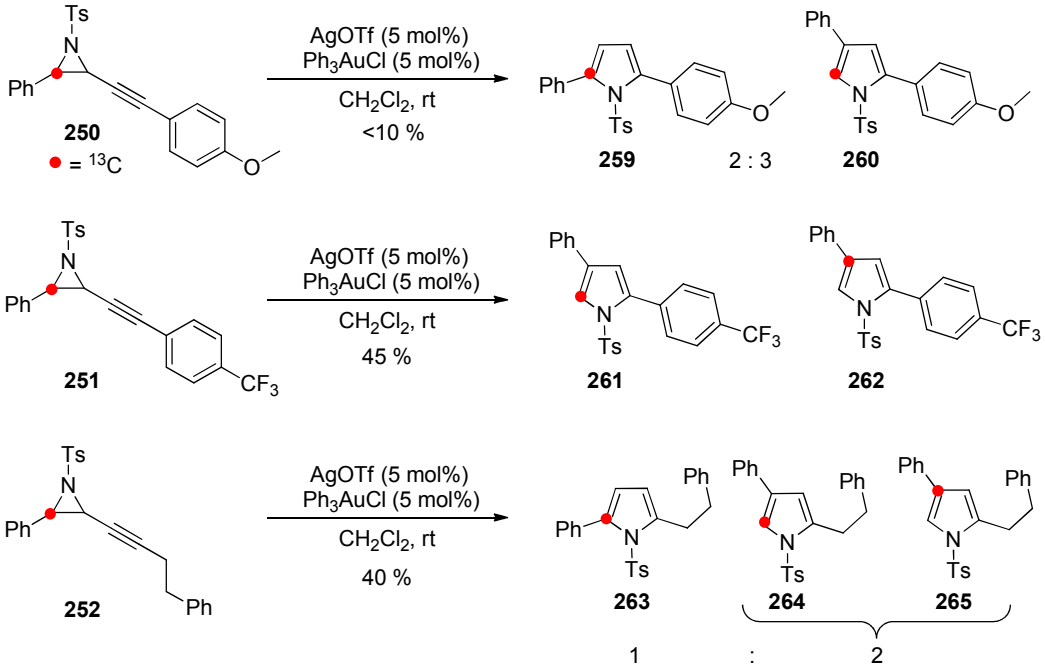
The impact of the alkyne substituent was probed by running catalysis on those new alkynyl aziridines with the system AgOTf/PPh_3AuCl (Scheme 86).

As predicted the presence of an electron donating aryl substituent on ^{13}C-enriched alkynyl aziridine **250** led to formation of only ^{13}C-enriched 2,4-substituted pyrrole isomer **260** (Appendix B). Moreover, electron deficient aryl-substituted alkynyl aziridine **251** and alkyl substituted **252** gave mixtures of ^{13}C-enriched 2,4-substituted pyrroles as was anticipated (Appendix B).

These results were in perfect agreement with the mechanism proposal where a competition between five-membered ring **O'** and a four-membered ring **R'** was suggested for the cycloisomerisation of aryl-substituted alkynyl aziridines (Scheme 83).



Scheme 85: Preparation of ^{13}C-enriched alkynyl aziridines 250, 251 and 252



Scheme 86: Mixture of isomers obtained when submitting ^{13}C-enriched alkynyl aziridine 250, 251 and 252 to $Ph_3PAuCl/AgOTf$

4.6 Summary

The reaction mechanisms proposed in Chapter 3 were put to the test using deuterium labelling and ^{13}C labelling studies. The deuterium experiments were consistent with the proposed pathway for the formation of 2,5-substituted pyrroles. Further confirmation came from using ^{13}C-enriched alkynyl aziridines under the same cationic gold catalytic system employing $Ph_3PAuCl/AgOTs$. On the other hand the studies showed that formation of 2,4-substituted pyrroles with $Ph_3PAuCl/AgOTf$ was a more complex process than expected, and a new mechanism has been proposed to account for experimental outcomes. The ^{13}C labelling could prove that two different pathways were active leading to 2,4-substituted pyrroles. A ring expansion via a five membered ring was shown to give 2,5-substituted pyrrole and a 2,4-substituted isomer from a 1,2-aryl shift. Another pathway, through a four membered ring this time, was shown to lead to a 2,4-substituted pyrrole by alternative skeletal rearrangement. When alkynyl aziridine bearing an electron deficient or an alkyl substituted alkyne was used, competition between the five and four membered ring intermediate led to the formation of the two 2,4-substituted pyrroles with labelling at two sites. The use of alkynyl aziridine bearing an electron-rich substituted alkyne gave only 2,4-substituted pyrrole with enrichment at only one site thanks to an extra-stabilisation of the five membered ring intermediate favouring this pathway.

Those results showed how seemingly relatively simple gold-catalysed reactions could reveal themselves to be complex when mechanistic studies were run to explain their outcome. It also showed the importance of such studies to allow strongly supported mechanistic proposal to be made.

4.7 Overall summary

Two new gold-catalysed strategies have been developed to access a range of substituted pyrroles from alkynyl aziridines.

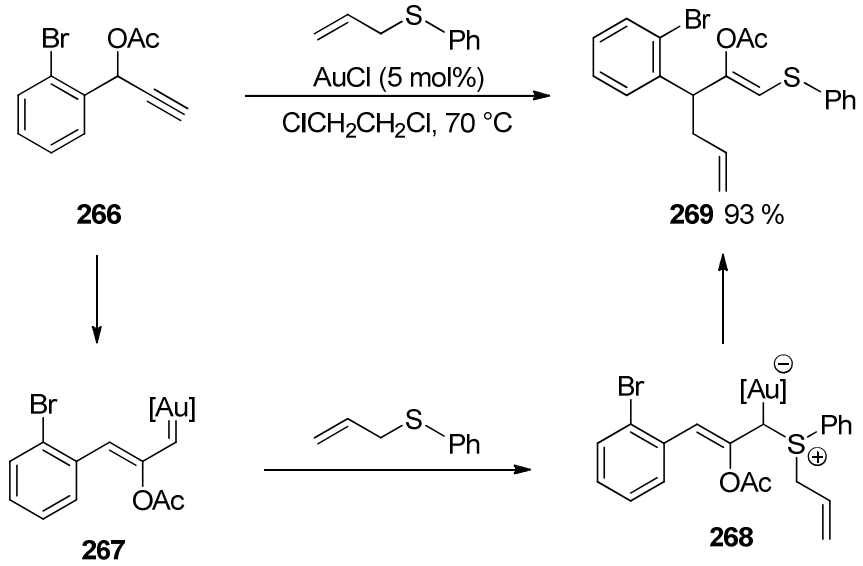
Brominated or silylated 2,4-substituted pyrroles were prepared regioselectively *via* a $AuCl_3$-catalysed vinylidene rearrangement when brominated or silylated alkynyl aziridines were employed. Despite the formation of debrominated or desilylated side product, the concept of the reaction involving a rarely described gold-vinylidene intermediate was validated.

Another strategy using cationic gold catalysis has also been successfully developed to synthesise 2,4- and 2,5-substituted pyrroles from alkynyl aziridines. The catalytic system Ph_3PAuCl/AgOTs allowed us to access 2,5-substituted pyrroles in almost quantitative yield. The 2,4-substituted isomers were formed preferentially when Ph_3PAuCl/AgOTf was employed. A study of the reaction mechanism employing ^{13}C and deuterium-labelling supports a straightforward 3,5-ring expansion to the formation of 2,5-substituted pyrroles, with no skeletal rearrangement. On the other hand, a competition between two pathways was revealed for the formation of the 2,4-substituted pyrroles. Depending on the initial ring opening step, both a 1,2-aryl migration in a five membered ring intermediate, or a 1,2-vinyl migration in a four membered ring intermediate are proposed to account for the observed reaction outcomes.

Chapter 5: Synthesis of α,β-unsaturated imides from ynamides

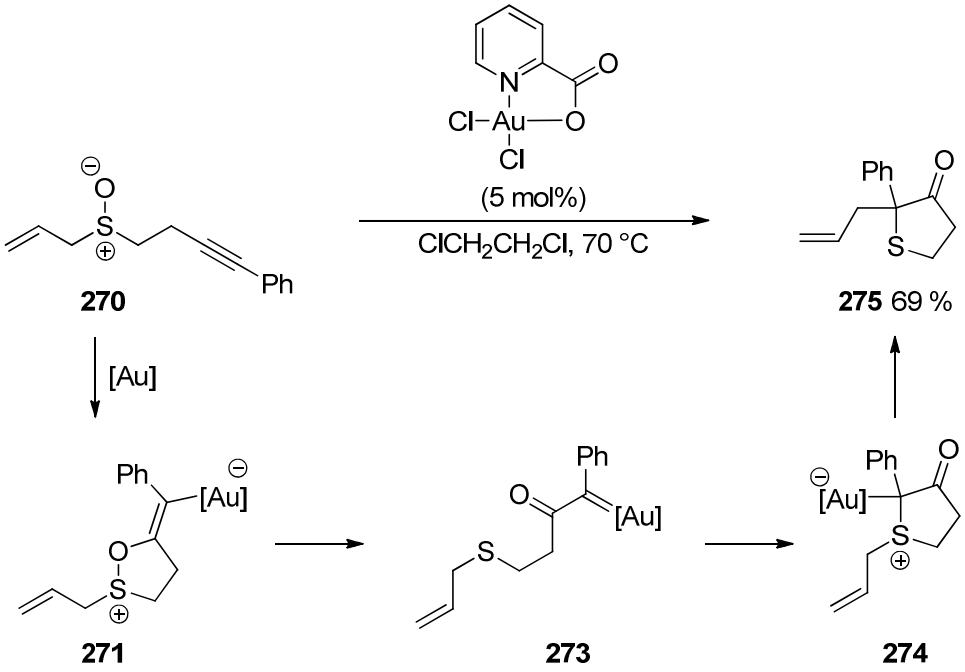
5.1 Introduction

As discussed in Chapter 1 (section 1.6.1), previous studies have shown the ability of propargylic carboxylates to rearrange under gold catalyst activation to form gold carbenoid species. Various nucleophiles have been employed to react on these intermediates and sulfides were for example recently used to perform an intermolecular coupling under gold catalysis (Scheme 87).[75] Generation of gold carbenoid species **267** by rearrangement followed by nucleophilic attack of the sulfide led to formation of an ylide **268**. This intermediate could then rearrange again when an allyl substituted sulfide was employed, allowing complex molecules to be obtained from simple building blocks.



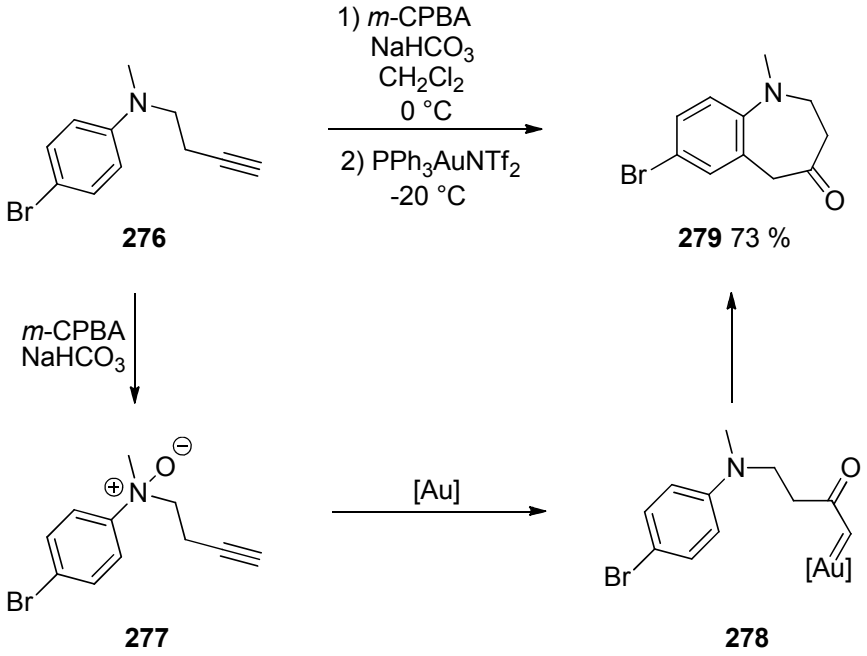
Scheme 87: Coupling reaction between alkyne and sulfide developed in the group

Following those results, further processes employing even simpler alkynes were developed. The use of an internal sulfoxide **270**, while reducing unfavourable gold-sulfur interactions, allowed an internal redox process to simultaneously generate the carbenoid and sulfide components necessary for ylide **274** formation (Scheme 88).



Scheme 88: Alkyne as direct precursor for the formation of sulfur ylide

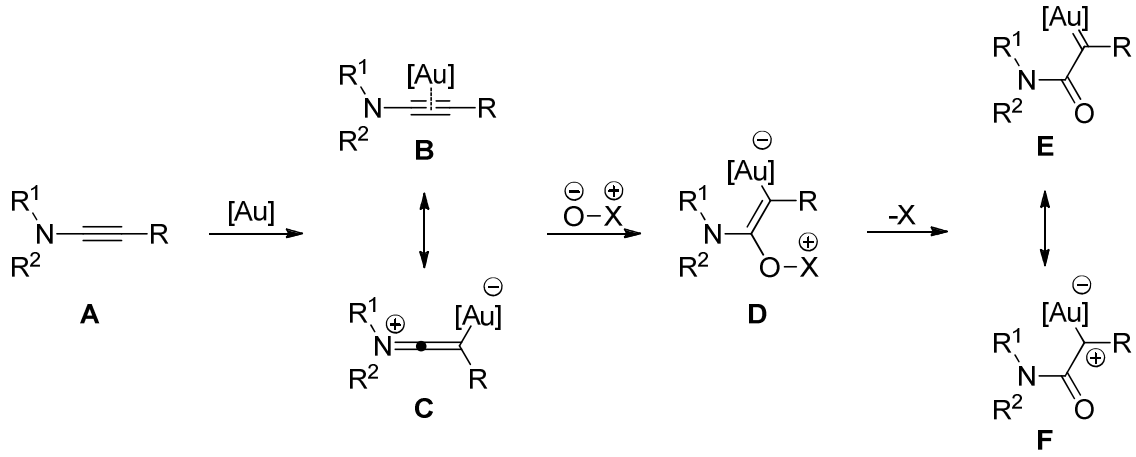
Zhang and co-workers had also recently published results showing the use of an in situ formed *N*-oxide **277** in an intramolecular preparation of α-oxogold carbenoid species **278**. This very reactive intermediate was employed in a cyclisation process leading to tetrahydrobenz[b]azepin-4-one **279** (Scheme 89).[76]



Scheme 89: Preparation of tetrahydrobenz[b]azepin-4-ones

Considering the previous work above, it was thought that the formation of a gold carbenoid from an alkyne and an external oxidizing agent, where the oxygen delivery system would not be incorporated in the product, would be of significant interest.

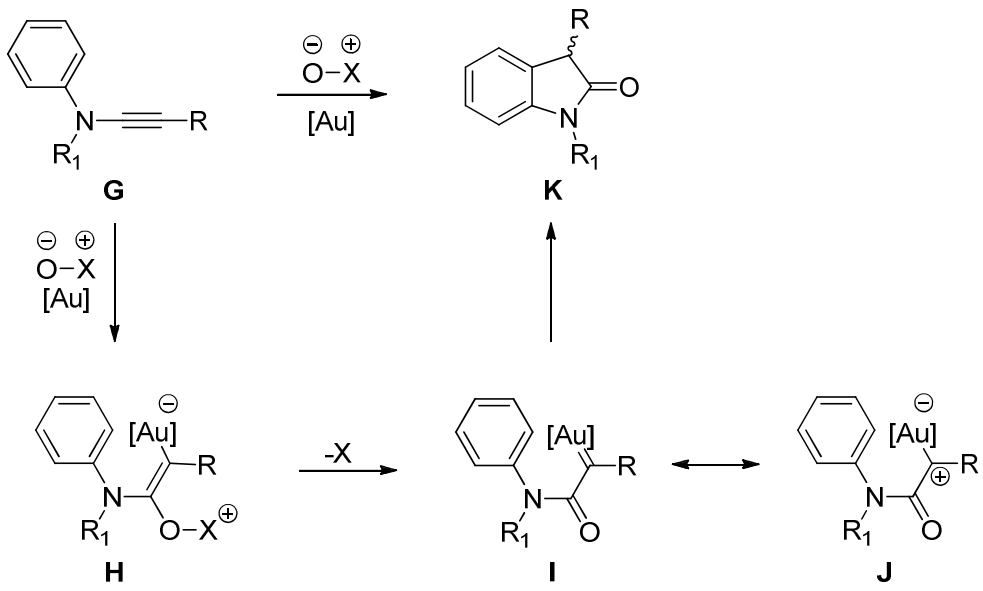
To ensure site-specificity of carbenoid introduction, controlled by the cyclisation in intramolecular processes, ynamides were selected as substrates (Scheme 90).[77]



Scheme 90: Ynamides as equivalents of α,α-disubstituted imidocarbenoids

Indeed, heteroatom lone pair participation should favour a gold-ketene-iminium resonance form **C** and develop an electrophilic site adjacent to the nitrogen (Scheme 90). It was therefore anticipated that nucleophilic addition of an external oxidant, a sulfoxide or *N*-oxide for example, would occur selectively to form intermediate **D**. Cleavage of the O-X bond would lead to the formation of an α-oxo gold carbenoid species **E** which could be used in different subsequent reactions.

A phenyl substituted ynamide **G** could for example lead to the formation of carbenoid intermediate **I** (Scheme 91). Cyclisation could then be envisaged to give indolinone product **K**.

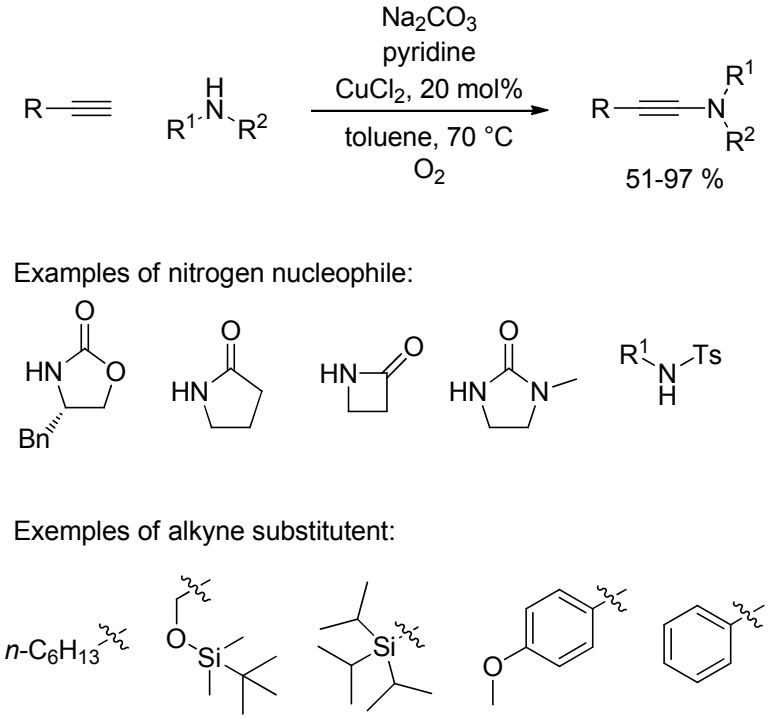


Scheme 91: Proposed cyclisation of phenyl-substituted imidocarbenoid intermediate

In order to assess this concept, ynamides bearing a *N*-phenyl substituent were prepared.

5.2 Starting material preparation

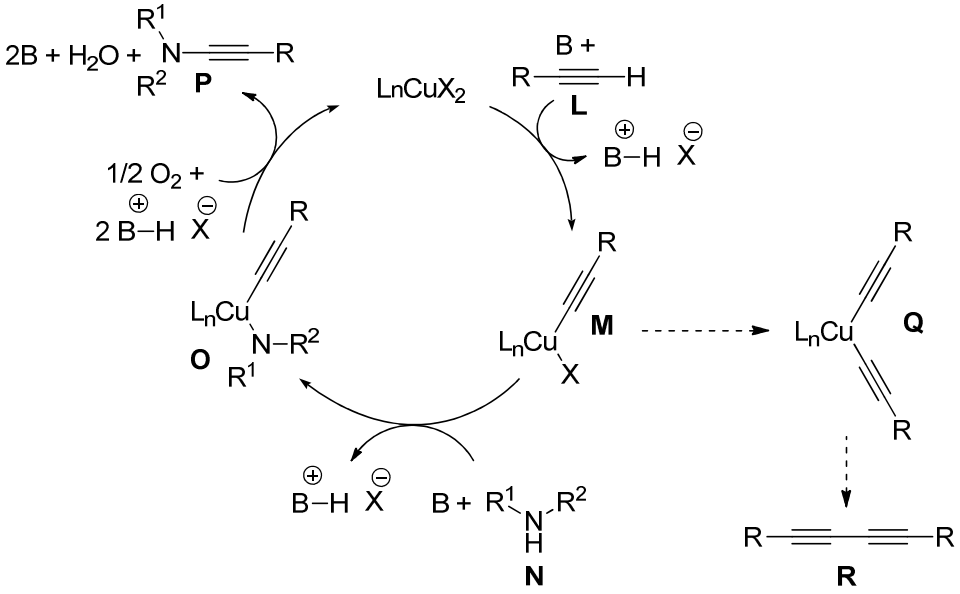
Synthesis of the ynamide precursors was achieved employing a copper-catalysed coupling between a terminal alkyne and an amide under aerobic conditions (Scheme 92).[78] This atom-economical method allowed the use of a range of electron-withdrawing secondary amides and a variety of substituents were tolerated. Furthermore good to excellent yields of ynamides were reported.



Scheme 92: Stahl aerobic method to synthesise ynamides from terminal alkynes

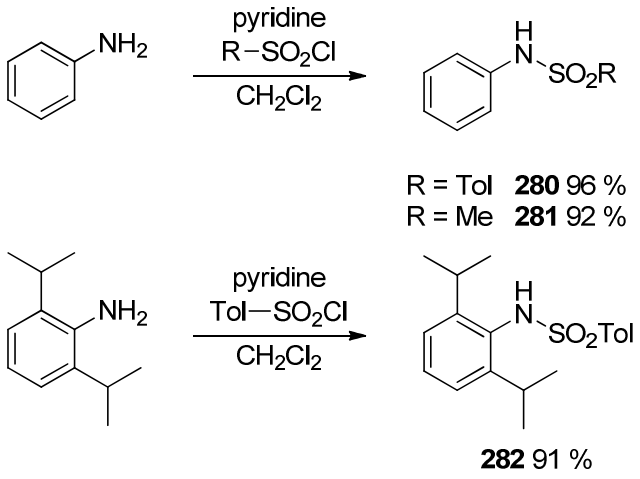
The reaction mechanism was proposed to feature a catalytic sequential activation of alkyne **L** and amide **N** to give organocopper intermediate **O** (Scheme 93). A C-N reductive elimination step would provide the ynamide product **P** and the catalyst would be reoxidised under the

aerobic conditions. An excess of nitrogen nucleophile was required to prevent the formation of a bisalkynyl copper complex **Q** responsible for the formation of diyne side product **R**.



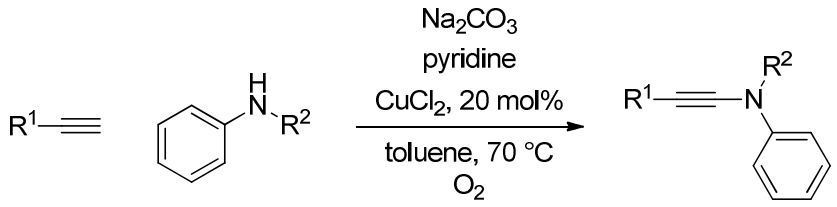
Scheme 93: Proposed mechanism for the copper-catalysed ynamide preparation from alkyne

Tosyl and mesyl-substituted anilines **280** and **281** were prepared in good yield by simple slow addition of the appropriate sulfonylchloride to a mixture of aniline and pyridine in CH_2Cl_2 (Scheme 94).[79] Diisopropylaniline was also employed under the same conditions to give **282** in 91% yield.



Scheme 94:Preparation of sulfonylanilines

Coupling reactions were performed using commercially available alkynes, $CuCl_2$, pyridine and Na_2CO_3 in toluene at 70 °C under O_2 atmosphere (table 14). Excellent yields of product were obtained with the mesylated or tosylated anilines and as expected a range of substituent could be employed including alkyl chloride, propargylic methoxyether and phenyl (table 14, entries 2, 3, 4). It is important to note that the excess of secondary amine employed to prepare each ynamide was always easily recovered after purification by flash chromatography.



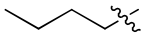
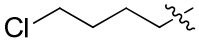
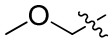
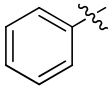
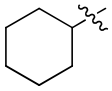
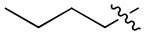
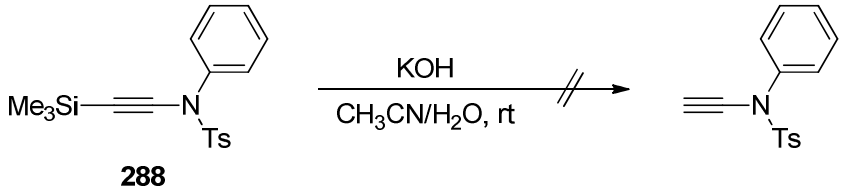
entry	R_1	R_2	Product	Yield (%)[a,b]
1			**283**	98
2			**284**	98
3			**285**	86
4			**286**	92
5			**287**	98
6			**288**	98
7			**289**	98

Table 14: Ynamide preparation from terminal alkyne. [a]All reactions performed using alkyne (2 mmol), amine (10 mmol), Na_2CO_3 (4 mmol), $CuCl_2$ (0.4 mmol) and toluene (10 mL).[b]Isolated yields.

The use of amide **282** led to the formation of the diyne side product and no trace of ynamide was observed. The steric hindrance due to the two isopropyl substituent was thought to be responsible for the lack of reactivity of this substrate.

To complete our selection of substrates desilylation of ynamide **288** using KOH in a 1:1 mixture of H_2O and CH_3CN was tried but degradation occurred and the expected ynamide could not be isolated (Scheme 95).



288

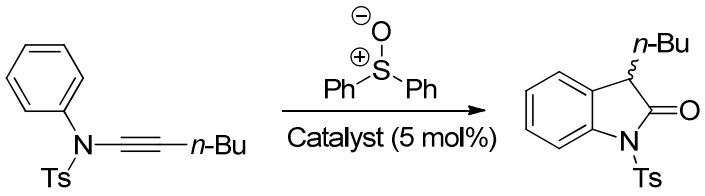
Scheme 95: Attempt of ynamide 288 desilylation using KOH.

Unfortunately, apart form ynamide **288**, all the other substrates proved unstable and were starting to form an unidentified side product 30 min after purification.

Therefore those substrates were engaged in catalysis immediately after synthesis and purification.

5.3 Optimisation of the reaction conditions

Ynamide **283** was submitted to various catalysts and reaction conditions using commercially available diphenylsulfoxide as a starting point (table 15). Only traces of an unknown compound were observed by TLC regardless of the solvent used and increase of the temperature led to degradation of the starting material. Varying the catalyst from $PtCl_2$ to cationic gold or $AuCl_3$ was not successful as no trace of the expected product was observed by ^1H NMR of the crude reaction mixtures.



283 **290**

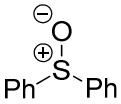
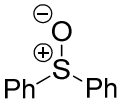
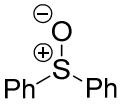
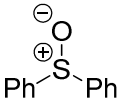
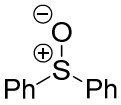
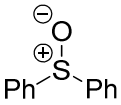
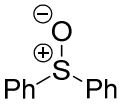
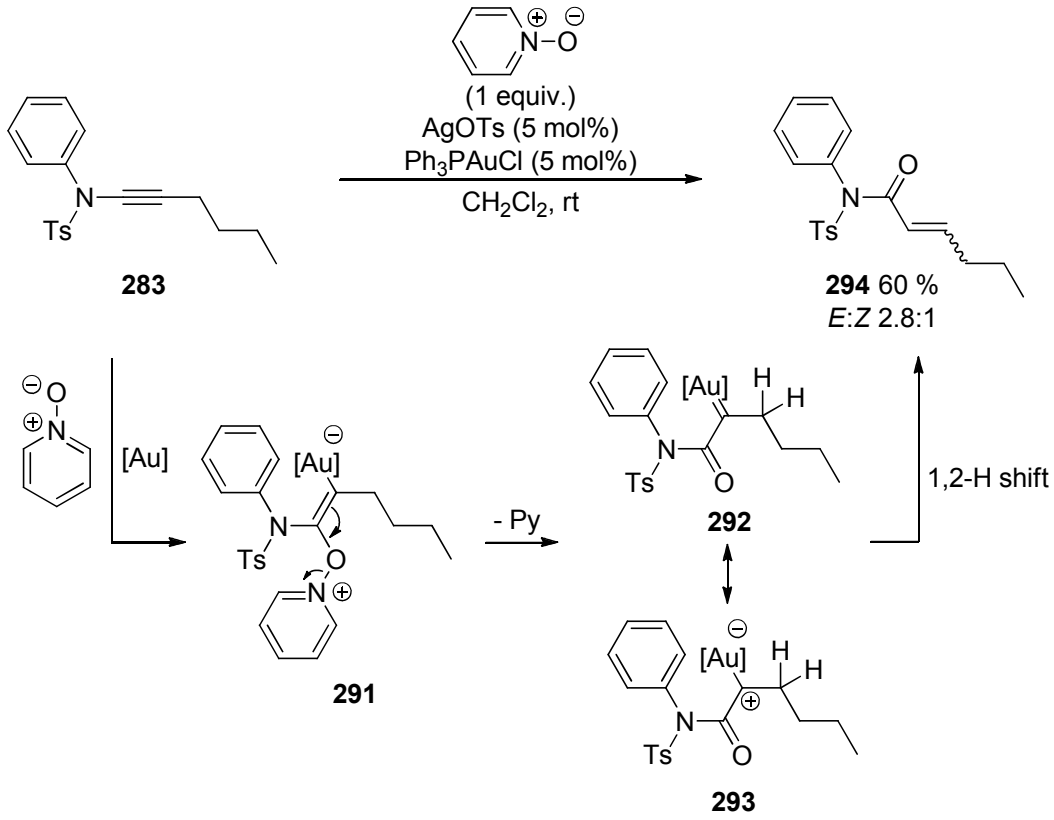
entry	Oxidant	Catalyst	Solvent	Temperature (°C)	Yield (%)[a]
1		$PtCl_2$	toluene	23	-
2		$PtCl_2$	toluene	80	-[b]
3		$PPh_3AuCl/AgOTf$	CH_3CN	23	-
4		$PPh_3AuCl/AgOTf$	CH_2Cl_2	23	-
5		$PPh_3AuCl/AgOTs$	CH_2Cl_2	23	-
6		$PPh_3AuCl/AgOTf$	$ClCH_2CH_2Cl$	70	-[b]
7		$AuCl_3$	CH_2Cl_2	23	-

Table 15: Use of diphenylsulfoxide as oxidant in attempts to form indolinones. [a]Reactions performed on 0.1 mmol starting material with 1eq sulfoxide and 5 mol% catalyst at a concentration of 0.2 M. [b]Complete degradation of the starting material was observed.

Diphenylsulfoxide was then replaced by the stable, crystalline and commercially available pyridine *N*-oxide. This reagent was expected to be more nucleophilic than the sulfoxide as extra stabilisation by electron delocalisation in the aromatic pyridine ring was possible. Moreover the oxygen of the *N*-oxide should also be more accessible because it is less sterically hindered than in diphenylsulfoxide.

Ynamide **283** was therefore submitted to catalysis using Ph_3PAuCl/AgOTs and pyridine *N*-oxide (Scheme 96). Pleasingly total conversion of the starting material into a new product was observed after 12 h at room temperature. However, after filtration of the reaction mixture through a pad of silica and evaporation of the solvent, crude ^1H NMR did not reveal any traces of the expected cyclised compound. Isolation of the reaction products was performed and they were identified as (*E*)- and (*Z*)-α,β-unsaturated imides **294**.

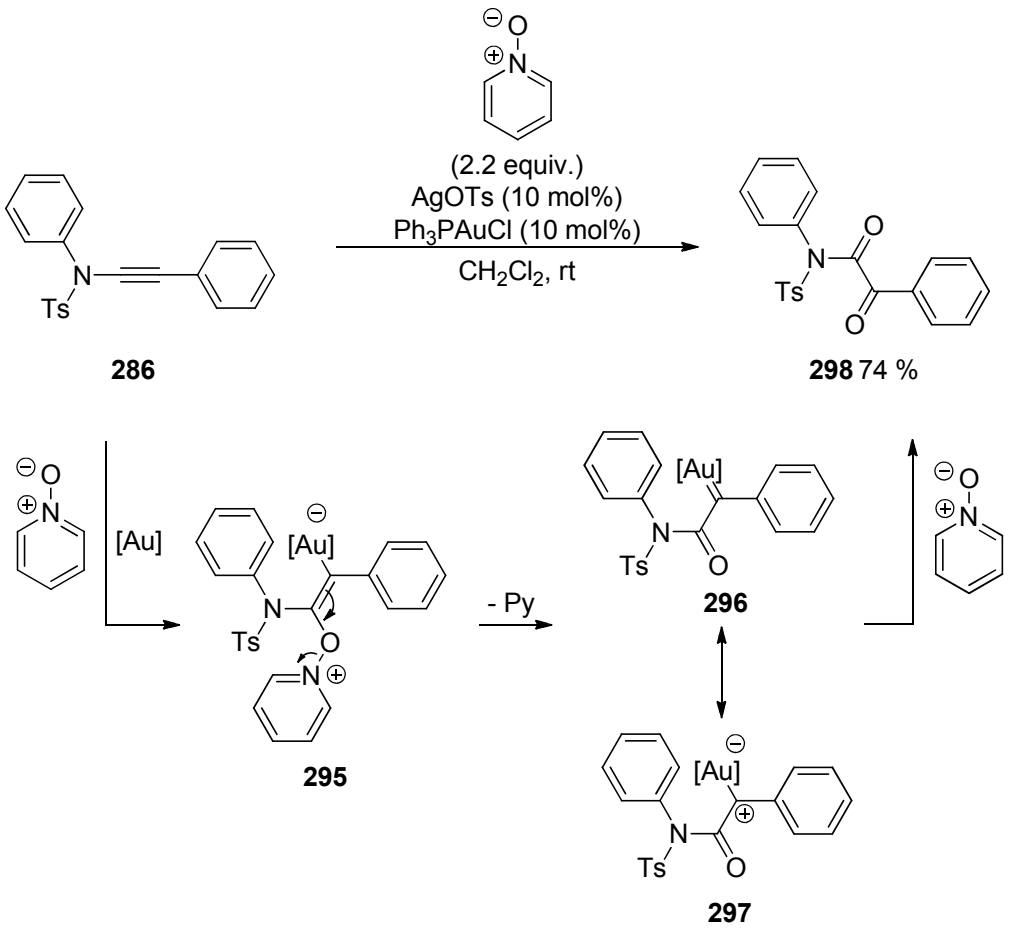
The products of the reaction were though to come from formation of intermediate **291** by nucleophilic attack of pyridine *N*-oxide onto the gold-activated ynamide (Scheme 96). Cleavage of the O-N bond would release pyridine and generate intermediate **292**/**293** displaying carbenoid character. A 1,2-H insertion on the carbene would then form the observed (*E*)- and (*Z*)-α,β-unsaturated imides **294**.



Scheme 96: Gold-catalysed reaction of ynamide 283 with pyridine *N*-oxide

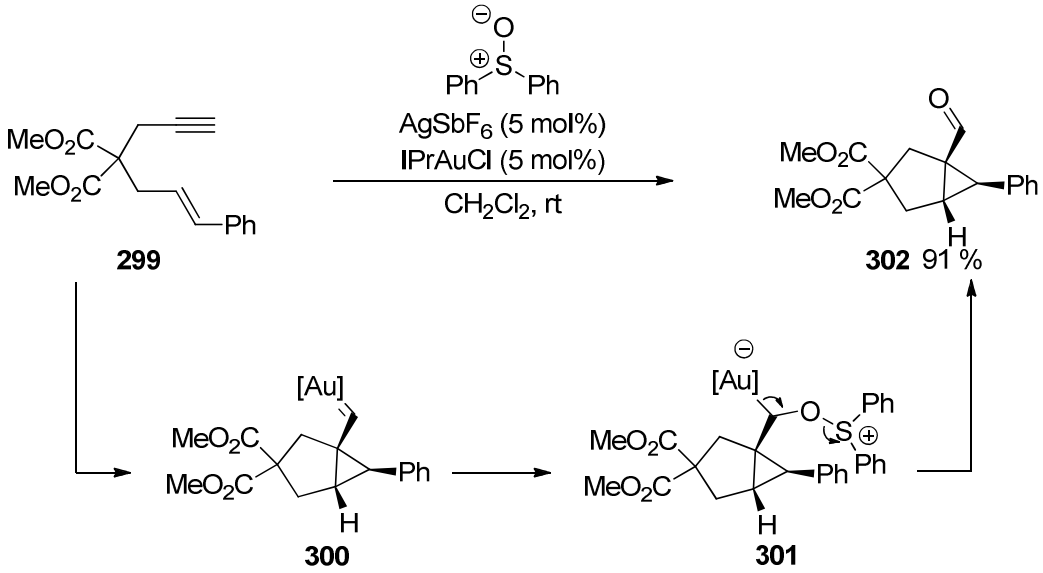
In order to avoid 1,2-H insertion in the carbenoid species formed *in situ*, phenyl-substituted ynamide **286** was used with Ph_3PAuCl/AgOTs and pyridine *N*-oxide. In that case formation of the cyclised indolinone product was expected.

This time with only one equivalent *N*-oxide the reaction did not go to completion and a different product was formed according to TLC and ^1H NMR of the crude mixture. A second test was attempted with 2.2 equivalents of *N*-oxide and total consumption of the ynamide precursor was observed after 12 h. The product of the reaction was isolated and identified as dioxidated oxoacetamide **298** (Scheme 97).



Scheme 97: Gold-catalysed formation of oxoacetamide 298 from ynamide 286

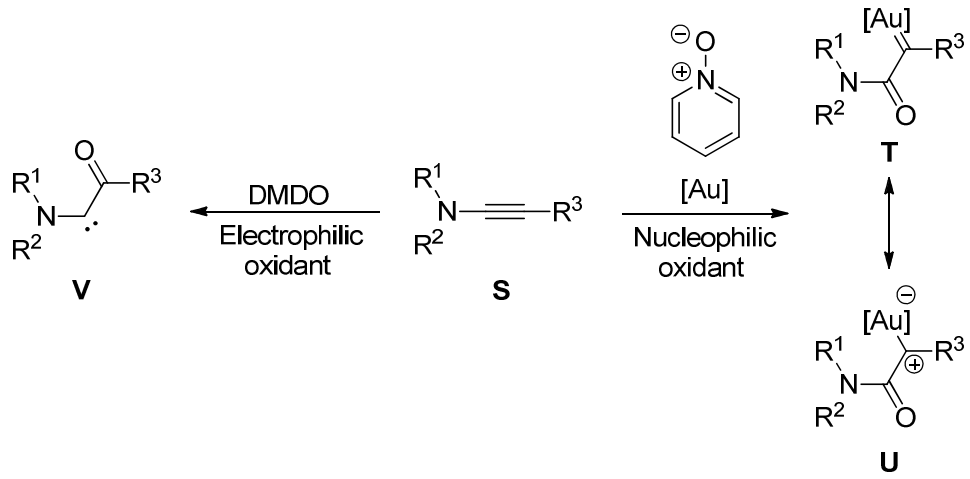
Access to the dioxidated product **298** was explained by oxidation of the carbenoid intermediate **296** formed during the course of the reaction, justifying the need for two equivalents of *N*-oxide to completely convert the starting material into product (Scheme 97). This result was consistent with previous work from Toste and co-workers where diphenyl sulfoxide could be used to trap different preformed gold carbene intermediates to give carbonyl compounds in good yield (Scheme 98).[80]



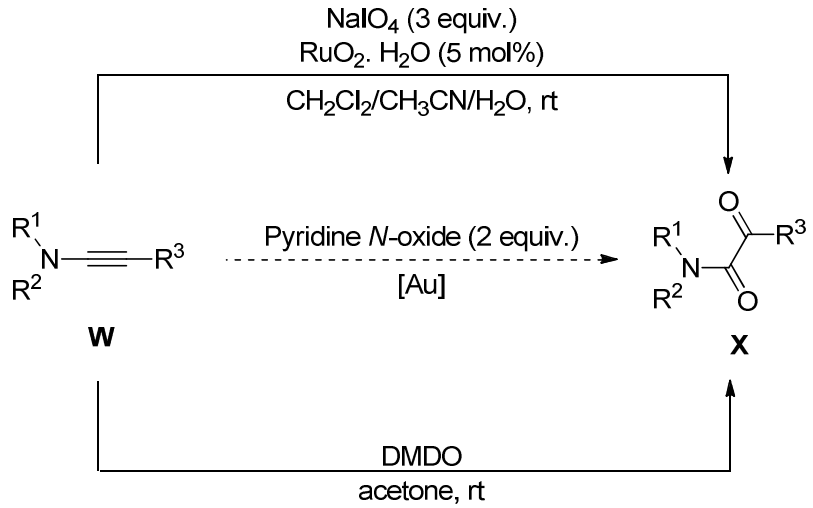
Scheme 98: Toste and co-workers trapping of gold carbene with Ph_2SO

Carbene formation from oxidation of ynamides had already been reported in the literature employing DMDO as electrophilic oxidant (Scheme 99). The novelty brought by the use of a gold catalyst and pyridine *N*-oxide was that opposite regiochemistry to that previously established was obtained (**T** vs **V**).[81]

Furthermore the gold-catalysed formation of the dioxidated oxoacetamide from ynamide and *N*-oxide complements the existing reaction employing electrophilic oxidants to form this class of compounds (Scheme 100).[82]



Scheme 99: Opposite regioselectivity of electrophilic versus nucleophilic oxidation of ynamides



Scheme 100: Preparation of dioxidated oxoacetamide by electrophilic or nucleophilic oxidation

When the trimethylsilyl substituted ynamide **288** (Table 14, entry 6) was reacted with $PPh_3AuCl/AgOTs$ and pyridine *N*-oxide, very complex mixtures of products and degradation were observed.

Despite evidence for the formation of the expected gold carbenoid species during the course of the reaction with ynamides **283** and **286**, no cyclised products had been observed. But the possibility to access α,β-unsaturated imides in two steps from a sulfonamide and a terminal

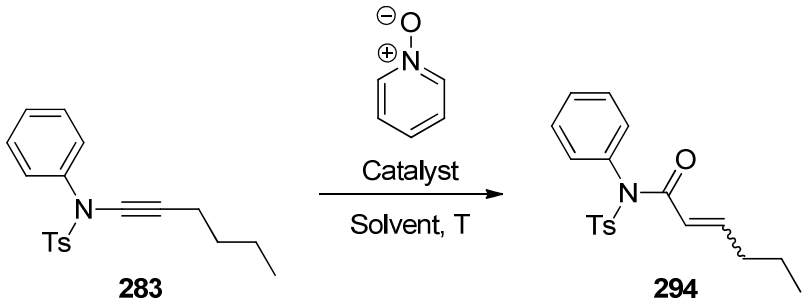
alkyne represented an attractive transformation and therefore the reaction was explored in greater details.

Screening of reaction conditions was performed using ynamide **283** as test substrate and pyridine *N*-oxide as nucleophile (Table 16).

Every gold (I) and gold (III) species tried gave the expected α,β-unsaturated imide in average to good yields (Table 16, entries 1-8) and platinum salts were inactive for this transformation (Table 16, entries 9, 10). Test reactions using NBS or *p*-TsOH in place of the metal salts were unsuccessful and starting material was recovered. Moreover employment of TfOH led to degradation of the starting material without observable formation of the expected α,β-unsaturated imide product.

Considering all the systems tested, two sets of conditions were particularly interesting: System A used air-stable dichloro(pyridine-2-carboxylato)gold (III) precatalyst (Au-**I**)[83] in $ClCH_2CH_2Cl$ at 70 °C (Table 16, entry 20) and was the quickest to completely convert the starting material into product in high yield. System B avoided the use of chlorinated solvent, employing $AuBr_3$ at room temperature in THF and was giving the best (*E*)-selectivity in high yield (Table 16, entry 17).

Therefore it was decided that both system would be applied to a selection of different ynamide in order to probe the scope of the reaction.



283 **294**

entry	Catalyst	Solvent	Time (h)	Temperature (°C)	Yield in % (*E*:*Z* ratio)[a,b]
1	Me_2SAuCl	CH_2Cl_2	12	RT	61 (3.9:1)
2	$PPh_3AuCl/AgOTs$	$ClCH_2CH_2Cl$	12	70	80 (3.7:1)
3	PPh_3AuNTf_2	CH_2Cl_2	12	RT	44 (1:1)
4	AuCl	CH_2Cl_2	12	RT	61 (3.8:1)
5	AuCl	$ClCH_2CH_2Cl$	0.25	80	76 (2.3:1)
6	$NaAuCl_4.H_2O$	CH_2Cl_2	12	RT	54 (2.4:1)
7	Au-**I**	CH_2Cl_2	12	RT	48 (3.0:1)
8	Au-**I**	Toluene	12	RT	52 (2.5:1)
9	$PtBr_2$	Toluene	12	70	-[c]
10	$PtCl_2$	Toluene	12	70	-[c]
14	$AuCl_3$	CH_2Cl_2	12	RT	42 (3.3:1)
15	$AuBr_3$	$ClCH_2CH_2Cl$	0.33	70	82 (2.5:1)
16	$AuBr_3$	Toluene	3	RT	84 (2.0:1)
17	$AuBr_3$	THF	12	RT	86 (3.2:1)
18	$AuBr_3$	CH_3NO_2	24	RT	60 (3.8:1)
19	Au-**I**	$ClCH_2CH_2Cl$	2	50	66 (2.3:1)
20	Au-**I**	$ClCH_2CH_2Cl$	0.17	70	82 (2.3:1)[d]
21	Au-**I**	$ClCH_2CH_2Cl$	0.25	80	45 (2.5:1)

Table 16: Survey of reaction conditions. [a]Reactions were performed using 0.1 mmol of ynamide, 5 mol% of catalyst, 0.11 mmol of pyridine *N*-oxide and 0.5 mL of solvent (0.2 M). [b]NMR yields against a known quantity of internal standard and ratios determined by ^{1}H NMR. [c]The starting material was partially recovered. [d]71 % isolated yield after flash chromatography.

5.4 Application of the optimised conditions

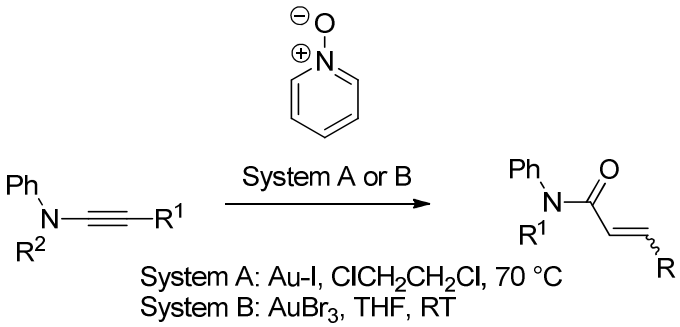
The ynamides prepared previously were then submitted to the two sets of condition selected after the optimisation work: System A employing dichloro(pyridine-2-carboxylato)gold (III) precatalyst (Au-**I**) in $ClCH_2CH_2Cl$ at 70 °C; System B employing $AuBr_3$ at room temperature in THF.

Both *N*-tosyl and *N*-mesyl substituted ynamides gave the expected mixture of (*E*) and (*Z*) α,β-unsaturated imides in good yield with the (*E*) isomer as the major (Table 17).

Other functionalities than simple alkyl were tolerated, notably an alkyl chloride (entry 2) and an alkoxy group (entry 3). In this last case complete selectivity toward the synthetically valuable (*E*)-α,β-unsaturated imide was even achieved. Apart from this example and when the symmetrical cyclohexane substituent was used (entry 5), only moderate (*E*):(*Z*)selectivity was observed and System B proved superior than System A in every cases for the preparation of the (*E*)-isomer. System A always gave slightly better yield of the mixture of isomers than System B.

During the course of our studies Zhang and co-workers reported a similar use of pyridine *N*-oxides in a new synthesis of dihydrofuran-3-ones (Scheme 101).[84] Like in the reaction described above it was thought that nucleophilic attack of the pyridine *N*-oxide derivative across the terminal alkyne would take place to give intermediate **308**.

Formation of an α-oxo gold carbenoid species **C** would result from expulsion of the pyridine derivative (Scheme 101). Internal nucleophilic attack of the carbenoid by the alcohol would then terminate the process and give product **311**.



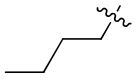
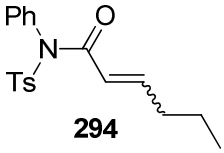
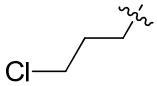
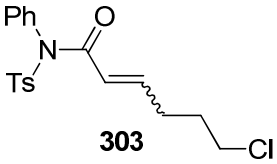
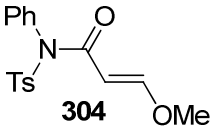
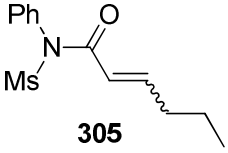
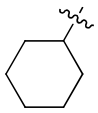
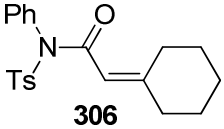
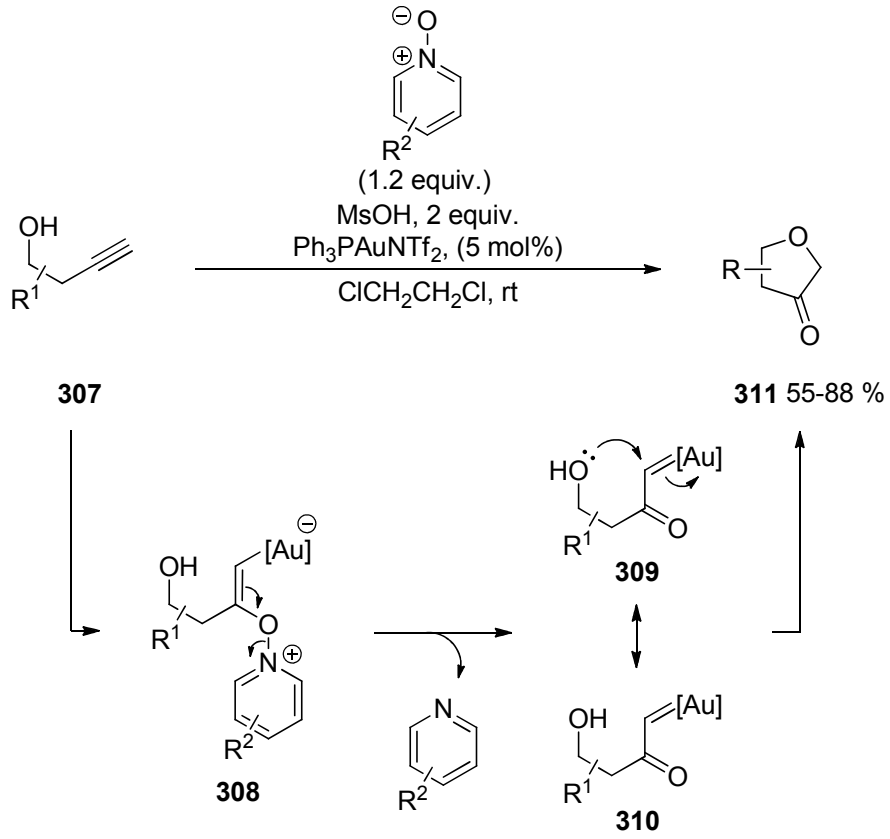
Entry	R^1	R^2	Product	System	Yield in % (E:Z ratio)[a,b]
1		Ts	 **294**	A	71 (2.3:1)
				B	70 (3.7:1)
2		Ts	 **303**	A	73 (1.9:1)
				B	70 (3.5:1)
3		Ts	 **304**	A	70[c]
				B	65[c]
4		Ms	 **305**	A	75 (3.0:1)
				B	71 (4.0:1)
5		Ts	 **306**	A	80
				B	78

Table 17: Synthesis of α,β-unsaturated imides. [a]Reaction were performed using 0.3 mmol of ynamide, 5 mol% of catalyst, 0.33 mmol of pyridine *N*-oxide and 1.5 mL of solvent. [b]Isolated yields, ratio of isomers determined by ^{1}H NMR after purification. [c]Only *E*-isomer was observed.



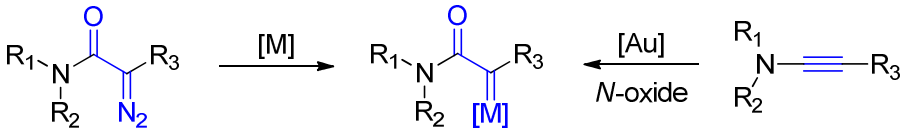
Scheme 101: Zhang and co-workers gold-catalysed preparation of dihydrofuran-3-ones

A broad range of functional groups were tolerated such as halogenated alkyls, azides or various substituted aromatic rings. But the drawback of the method was the need for an acid in the reaction mixture. It was proposed that the pyridine formed during the course of the reaction deactivated the catalyst as than 10% yield of product was reported when no acid was employed. It was worth to note that such effect were not observed in the case of the (*E*) and (*Z*) α,β-unsaturated imides synthesis reported above.

5.5 Summary

A new gold catalysed reaction has been developed employing an external oxidizing agent to form a gold carbenoid intermediate from ynamides. Despite the fact that none of the expected indolinones was formed, the predicted site-specific introduction of the gold carbenoid moiety was demonstrated. This intermediate was indeed employed for the preparation of a variety of α,β-unsaturated imides in good yields with a good functionality tolerance. It was also shown that access to one oxoacetamide compound was possible in good yield and under mild reaction conditions when an aryl substituted substrate was used with two equivalents of *N*-oxide.

Those results also demonstrate that ynamides can be employed as direct equivalents to α,α-disubstituted-diazo amides for regiospecific access to gold carbenes (Scheme 102). Therefore the gold-catalysed methods described above might lead to further developments in synthesis while avoiding the use of the potentially hazardous diazo functionality.



Scheme 102: Ynamides as equivalents to α,α-disubstituted-diazo amides

Chapter 6: Experimental

6.1 Instruments

Asynt DrySin heating blocks on stirrer hotplates were employed for reactions with temperature controlled *via* external probe. Infra-red spectra were recorded neat on a Perkin–Elmer Spectrum 100 FT-IR spectrometer. Only selected absorbencies (ν_{max}) are reported in cm-1. High resolution mass spectra (HRMS) were recorded on a VG ProSpec or a VG-ZabSpec at 70 eV when utilising electron impact ionisation (EI). A Micromass LCT using a methanol mobile phase was used for HRMS utilising electrospray ionisation. In both case (EI or ES), HRMS was obtained using a lock-mass to adjust the calibrated mass scale. MS data are reported as *m/z*. NMR: Spectra were recorded on Bruker AC300 (^{1}H = 300 MHz, ^{13}C = 75.5 MHz), Bruker AV300 (^{1}H = 300 MHz, ^{13}C = 75.5 MHz) or Bruker AV400 (^{1}H = 400 MHz, ^{13}C = 101 MHz), in the solvents indicated; Chemical shifts (δ) are given in ppm relative to TMS. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: $\delta_C \equiv 77.0$ ppm; residual $CHCl_3$ in $CDCl_3$: $\delta_H \equiv 7.26$ ppm; DMSO-d_6: $\delta_C \equiv$ 39.52 ppm; residual DMSO-d_5 in DMSO-d_6: $\delta_H \equiv 2.50$ ppm). Coupling constants (J) are reported in Hz. Multiplicity is denoted in ^{1}H NMR by: s (singlet), d (doublet), t (triplet), q (quadruplet), quint (quintuplet), sept (septuplet) and m (multiplet). ^{13}C NMR spectra were recorded using the PENDANT pulse sequence from the Bruker standard pulse program library. Melting points were recorded using open glass capillaries on a Stuart Scientific apparatus and are uncorrected.

6.2 Reactions

Reactions were followed by thin layer chromatography (TLC) using Macherey Nagel silica gel 60F254 analytical plates (plastic support) which were developed using standard visualizing agents: UV fluorescence (254 and 366 nm), and potassium permanganate/Δ. Purification by Flash chromatography was performed using Fluorochem silica gel 60 (0.043-0.063 mm).

All reactions in non-aqueous solvents were conducted in flame-dried glassware under a argon atmosphere and with magnetic stirring. Volumes of less than 0.2 mL were measured and dispensed with gastight syringes. Evaporation and concentration under reduced pressure was performed at 10-700 mbar at 40 °C. All pure products of reactions were dried under high vacuum (1 mbar).

6.3 Chemicals and Reagents

All reagents were obtained from commercial sources and used without further purification. All reactions were carried out under argon in flame-dried glassware and with magnetic stirring. The solvents used were purified by distillation over the drying agents indicated and were transferred under argon: tetrahydrofuran (sodium benzophenone ketyl), diethyl ether (sodium benzophenone ketyl), toluene (sodium), dichloromethane (CaH_2) and dichloroethane (CaH_2). Pyridine and triethylamine were distilled from CaH_2 and were stored over 4 Å molecular sieves. *N*-bromosuccinimide was recrystallised from hot water and was dried thoroughly under high vacuum. Dess-Martin periodinane was prepared from 2-iodoxybenzoic

acid (IBX)[85] following a known procedure.[86] The following cooling bath were used; 0 °C (ice/water) and -78 °C (dry ice/acetone).

6.4 Procedure and Characterisation

6.4.1 Procedure and characterisation for Chapters 2, 3 and 4

Aryltosylimine preparation: General procedure 1 (GP1):

To a solution of aldehyde (10 mmol) in toluene (30 mL) were added 4-methyl-benzenesulfonamide (9 mmol, 1.54 g), amberlyst 15 ion-exchange resin (1 g) and activated 4Å powdered molecular sieve (1 g). The reaction mixture was heated at reflux (110 ºC) for 12 h in a Dean-Stark apparatus. The temperature was cooled down to room temperature and the reaction mixture was filtered. The solvent was removed under reduced pressure and the residue was triturated with hexane. The crystals obtained were filtered off, washed with *n*-pentane (2 × 40 mL) and dried to give pure imine.

Preparation of propargylic alcohols from terminal alkynes and formaldehyde: General procedure 2 (GP2)

n-BuLi (20 mmol, 8.0 mL of a 2.5M solution in hexane) was added dropwise to a solution of alkyne (20 mmol) in THF (80 mL) at -78 ºC. The reaction mixture was stirred 30 min at -78 ºC before paraformaldehyde (20 mmol, 0.60 g) was added. The temperature was raised to room temperature and the reaction mixture stirred for 12 h. NH_4Cl solution (50 mL) was added to quench the reaction and the THF was removed under reduced pressure. Et_2O (40 mL) was added and the phases were separated. The aqueous phase was washed with Et_2O (3 ×

40 mL) and the combined organic extracts were washed with brine (30 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification by flash chromatography of the residue gave the corresponding propargylic alcohol.

Formation of aziridines from imine and sulfonium salt: General Procedure 3 (GP 3):

The corresponding sulfonium salt (1.2 mmol) and then the Cs_2CO_3 (1.2 mmol) were added sequentially to a solution of imine (1.0 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was stirred at room temperature until completion and filtered through a pad of silica to remove the inorganic salts. The filtrate was then concentrated under reduced pressure and the residue was purified by flash chromatography to afford the alkynyl aziridine.

$AuCl_3$ catalysed pyrrole formation: General Procedure 4 (GP 4):

To $AuCl_3$ (0.01 mmol, 3.0 mg) under argon was added a solution of the corresponding aziridine (0.1 mmol) in toluene (0.2 mL) and the mixture was immediately heated at 50 °C. Stirring was maintened for the indicated time and a quick filtration through a pad of silica was performed using ethyl acetate. The solvents were removed under reduced pressure and the residue purified by flash chromatography [hexanes:ethyl acetate:triethylamine (25:1:1%)].

Sonogashira coupling of aryliodides with propargyl alcohol: General procedure 5 (GP5)

To a solution of aryliodide (25 mmol) in toluene (30 mL) at room temperature were added $Pd(PPh_3)_2Cl_2$ (0.75 mmol, 530 mg), CuI (1.5 mmol, 285 mg) and piperidine (47.8 mmol, 4.72 mL). After stirring 5 min at room temperature, propargyl alcohol (25.5 mmol, 1.48 mL) was added dropwise. The reaction mixture was then heated at 40 °C for 12h. After cooling down to room temperature, the reaction was filtered through a plug of silica, eluting with EtOAc. The filtrate was concentrated under reduced pressure and purification of the residue by flash chromatography gave pure propargylic alcohol.

Gold-catalysed cycloisomerisations of alkynyl aziridines using Ph_3PauCl/AgOTs: general procedure 6 (GP6):

The catalyst system was prepared by addition of anhydrous $ClCH_2CH_2Cl$ (0.5 mL) to Ph_3PAuCl (0.01 mmol, 5.0 mg) and AgOTs (0.01 mmol, 2.8 mg) in a flame-dried Schlenk flask under argon. After stirring for 10 min at room temperature, a white precipitate of AgCl was observed and a solution of the corresponding acetylenyl aziridine (0.2 mmol) in anhydrous $ClCH_2CH_2Cl$ (0.5 mL) was added. The reaction mixture was stirred at the indicated temperature until complete consumption of aziridine before being filtered through a pad of silica. The filtrate was then concentrated under reduced pressure. When required the residue was purified by flash chromatography as indicated.

Gold-catalysed cycloisomerisations of alkynyl aziridines using Ph_3PauCl/AgOTf: general procedure 7 (GP7):

The catalyst system was prepared by addition of anhydrous CH_2Cl_2 (0.5 mL) to Ph_3PAuCl (0.01 mmol, 5.0 mg) and AgOTf (0.01 mmol, 2.5 mg) in a flame-dried Schlenk flask under

argon. After stirring for 10 min at room temperature, a white precipitate of AgCl is observed and a solution of the corresponding acetylenyl aziridine (0.2 mmol) in anhydrous CH_2Cl_2 (0.5 mL) was added. The reaction mixture was stirred at room temperature until complete consumption of aziridine before being filtered through a pad of silica. The filtrate was then concentrated under reduced pressure. The residue was purified by flash chromatography as indicated.

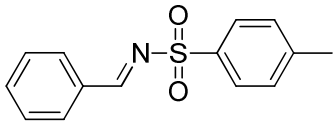
Preparation of propargylic bromides from propargylic alcohols: General procedure 8 (GP8)

To a solution of PPh_3 (1.1 equiv.) in CH_2Cl_2 at 0 °C was added Br_2 (1.9 equiv.) dropwise. The reaction mixture was stirred for 20 min at 0 °C before a solution of alcohol (1 equiv.) in CH_2Cl_2 was added dropwise. The reaction mixture was warmed to room temperature and stirred for 1 h. Water (25 mL) was added to quench the reaction and the two phases were separated. The aqueous phase was washed with CH_2Cl_2 (3 × 20 mL) and the combined organic extracts were washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification by flash chromatography of the residue gave the corresponding propargylic bromide.

Sulfonium salt preparation: General procedure 9 (GP9)

Dimethylsulfide (15.0 mmol, 932 mg, 1.1 ml) was added to a solution of bromide (5 mmol) in acetone (5 mL) and the reaction mixture was stirred at room temperature for 3 days. A white solid was formed which was filtered off, washed with diethyl ether (4 × 10 mL) and dried to afford the corresponding pure sulfonium salt.

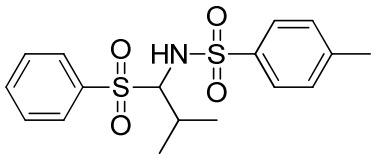
N-Benzylidene-4-methylbenzenesulfonamide (141)



Following GP1 using benzaldehyde (1.06 g, 1.02 mL) gave imine **141** as a white solid (1.86 g, 80%); mp 104-105 ºC; ν_{max} (neat)/cm^{-1} 2932, 2864, 1650, 1570,1415, 1381, 1320, 1280, 1158, 1092, 1064, 960, 861, 820, 753; δ_H (300 MHz; $CDCl_3$) 2.43 (3H, s, CH_3), 7.34 (2H, d, *J* 8.2, 2 × CH), 7.45-7.50 (2H, m, 2 × CH), 7.60-7.87 (5H, m, 5 × CH), 9.03 (1H, s, CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 128.0 (2C, 2 × CH), 129.1 (2C, 2 × CH), 129.8 (2C, 2 × CH), 131.2 (2C, 2 × CH), 132.3 (CH), 134.9 (C_{quat}), 136.6 (C_{quat}), 144.5 (C_{quat}), 170.1 (CH).

Data were in agreement with those reported in the literature.[87]

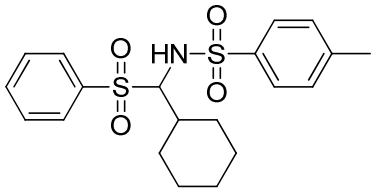
***N*-(1-Benzenesulfonyl-2-methyl-propyl)-4-methylbenzenesulfonamide (142)**



To a 1:1 mixture of water (50 mL) and formic acid (50 mL) were added 4-methyl-benzenesulfonamide (34 mmol, 5.82 g,), 2-methylpropionaldehyde (40 mmol, 2.94 g, 2.3 mL) and sodium benzenesulfinate (40 mmol, 6.57 g). The reaction mixture was stirred for 12 h at room temperature and the resulting white precipitate was filtered off, washed with water (2 × 35 mL) and then pentane (2 × 35 mL) to give pure 4-methylbenzene sulfonamide **142** as a white solid (11.32 g, 77%); 114-115 °C; ν_{max} (neat)/cm^{-1} 3298, 3056, 2967, 1342, 1306, 1166, 1134, 1082, 1055, 886, 806; δ_H (300 MHz; $CDCl_3$) 0.84 (3H, d, *J* 6.9, CH_3), 1.04 (3H, d, *J* 6.9, CH_3), 2.40 (3H, s, CH_3), 2.73 (1H, m, CH), 4.52 (1H, dd, *J* 10.7 and 3.2, CH), 5.17 (1H, d, *J* 10.7, NH), 7.17 (2H, d, *J* 8.2, 2 × CH), 7.45-7.51 (4H, m, 4 × CH), 7.62-7.66 (1H, m,

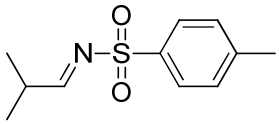
CH), 7.82 (2H, d, *J* 7.2, 2 × CH); δ_C (75 MHz; $CDCl_3$) 16.5 (2C, 2 × CH_3), 20.9 (CH), 21.5 (CH_3), 77.5 (CH), 126.6 (2C, 2 × CH), 129.1 (2C, 2 × CH), 129.3 (2C, 2 × CH), 129.6 (2C, 2 × CH), 134.0 (CH), 137.0 (C_{quat}), 137.9 (C_{quat}), 143.7 (C_{quat}).

_N_-(Benzenesulfonyl-cyclohexyl-methyl)-4-methylbenzenesulfonamide (143)



To a 1:1 mixture of water (50 mL) and formic acid (50 mL) were added 4-methyl-benzenesulfonamide (34 mmol, 5.82 g,), cyclohexanecarboxaldehyde (40 mmol, 4.49 g, 4.9 mL) and sodium benzenesulfinate (40 mmol, 6.57 g). The reaction mixture was stirred for 12 h at room temperature and the resulting white precipitate was filtered off, washed with water (2 × 35 mL) and then pentane (2 × 35 mL) to give pure 4-methylbenzene sulfonamide **143** as a white solid (12.69 g, 80%); 119-121 °C; ν_{max} (neat)/cm^{-1} 3300, 3056, 2934, 1446, 1337, 1304, 1161, 1145, 1078, 1055, 810, 750; δ_H (300 MHz; $CDCl_3$) 0.86-1.11 (2H, m, CH_2), 1.15-1.46 (2H, m, CH_2), 1.49-2.01 (6H, m, 3 × CH_2), 2.40 (3H, s, CH_3), 4.48 (1H, dd, *J* 10.7 and 3.4, CH), 5.52 (1H, d, *J* 10.7, NH), 7.16 (2H, d, *J* 8.0, 2 × CH), 7.44-7.53 (4H, m, 4 × CH), 7.60-7.65 (1H, m, CH), 7.79-7.81 (2H, m, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.5 (CH_3), 25.5 (2C, 2 × CH_2), 25.7 (2C, 2 × CH_2), 29.6 (CH_2), 36.8 (CH), 77.2 (CH), 126.2 (2C, 2 × CH), 128.7 (2C, 2 × CH), 128.9 (2C, 2 × CH), 129.2 (2C, 2 × CH), 133.5 (CH), 137.0 (C_{quat}), 137.8 (C_{quat}), 143.2 (C_{quat}).

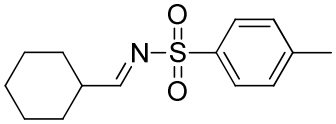
_N_-Isobutylidene-4-methyl-benzenesulfonamide (144)



A Na_2CO_3 solution (70 mL) was added to a solution of 4-methylbenzenesulfonamide **142** (10 mmol, 3.67 g) in CH_2Cl_2 (100 mL). The reaction mixture was stirred at room temperature for 2 h and the two phases were separated. The aqueous phase was washed with CH_2Cl_2 (3 × 50 mL) and the combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give pure imine **144** as a white solid (2.02 g, 90%); mp 78-80 ºC; ν_{max} (neat)/cm^{-1} 3305, 3066, 2971, 1632, 1601, 1458, 1313, 1161, 1140, 1088, 817, 749; δ_H (300 MHz; $CDCl_3$) 1.20 (6H, d, *J* 7.2, 2 × CH_3), 2.41 (3H, s, CH_3), 2.72 (1H, m, CH), 7.31 (2H, d, *J* 8.2, 2 × CH), 7.80 (2H, d, *J* 8.2, 2 × CH), 8.51 (1H, d, *J* 4.3, CH); δ_C (75 MHz; $CDCl_3$) 17.9 (2C, 2 × CH_3), 21.5 (CH_3), 34.6 (CH), 128.0 (2C, 2 × CH), 129.7 (2C, 2 × CH), 134.6 (C_{quat}), 144.6 (C_{quat}), 181.8 (CH).

Data were in agreement with those reported in the literature.[55]

_N_-Cyclohexylmethylene-4-methyl-benzenesulfonamide (145)

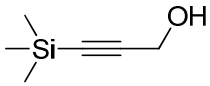


A Na_2CO_3 solution (70 mL) was added to a solution of 4-methylbenzenesulfonamide **143** (10 mmol, 4.07 g) in CH_2Cl_2 (100 mL). The reaction mixture was stirred at room temperature for 2 h and the two phases were separated. The aqueous phase was washed with CH_2Cl_2 (3 × 50 mL) and the combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give pure imine **145** as a white solid (2.39 g, 90%); mp 103-105 ºC; ν_{max}

(neat)/cm^{-1} 3307, 3062, 2960, 1630, 1602, 1452, 1385, 1310, 1180, 1159, 1130, 1092, 810, 750, 690; δ_H (300 MHz; $CDCl_3$) 1.16-1.37 (4H, m, 2 × CH_2), 1.63-1.88 (6H, m, 3 × CH_2), 2.42-2.44 (4H, m, CH and CH_3), 7.32 (2H, d, *J* 8.3, 2 × CH), 7.79 (2H, d, *J* 8.3, 2 × CH), 8.46 (1H, d, *J* 4.4, CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 25.1 (2C, 2 × CH_2), 25.6 (CH_2), 28.4 (2C, 2 × CH_2), 43.7 (CH), 128.0 (2C, 2 × CH), 129.7 (2C, 2 × CH), 134.8 (C_{quat}), 144.5 (C_{quat}), 181.0 (CH).

Data were in agreement with those reported in the literature.[55]

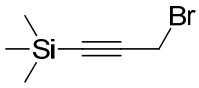
3-(Trimethylsilyl)-2-propyn-1-ol (146)



n-BuLi (108 mmol, 43.2 mL of a 2.5M solution in hexane) was added dropwise to a solution of propargyl alcohol (54 mmol, 3.03 g, 3.1 mL) in THF (150 mL) at -78 ºC. The reaction mixture was stirred for 30 min at -78 ºC before TMSCl (157 mmol, 17.06 g, 20 mL) was added. The temperature was raised to room temperature and the reaction mixture stirred for 4 h. NH_4Cl solution (40 mL) was added to quench the reaction and the THF was removed under reduced pressure. Et_2O (40 mL) was added and the phases were separated. The aqueous phase was washed with Et_2O (3 × 40 mL) and the combined organic extracts were washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification by distillation under reduced pressure (95 ºC, 60 mmHg) gave alcohol **146** as a colourless liquid (6.36 g, 90%); ν_{max} (neat)/cm^{-1} 3342, 2960, 2180, 1255, 1043, 847, 701; δ_H (300 MHz; $CDCl_3$) 0.17 (9H, s, 3 × CH_3), 1.86 (1H, s, OH), 4.26 (2H, s, CH_2); δ_C (75 MHz; $CDCl_3$) -0.7 (3C, 3 × CH_3), 51.1 (CH_2), 90.1 (C_{quat}), 103.1 (C_{quat}).

Data were in agreement with those reported in the literature.[88]

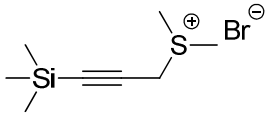
1-Bromo-3-(trimethylsilyl)-2-propyne (147)



Following GP8 using PPh_3 (11 mmol, 2.88 g), Br_2 (10.9 mmol, 0.55 mL) and alcohol **146** (1.28 g) in CH_2Cl_2 (30 mL). Purification by flash chromatography (*n*-pentane) gave bromide **147** as a colourless oil (1.62 g, 85%); ν_{max} (neat)/cm^{-1} 2970, 2172, 1247, 1219, 1039, 841, 745; δ_H (300 MHz; $CDCl_3$) 0.18 (9H, s, 3 × CH_3), 3.91 (2H, s, CH_2); δ_C (75 MHz; $CDCl_3$) -0.4 (3C, 3 × CH_3), 14.5 (CH_2), 92.3 (C_{quat}), 100.0 (C_{quat}).

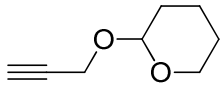
Data were in agreement with those reported in the literature[89]

Dimethyl(3-(trimethylsilyl)prop-2-yn-1-yl)sulfonium bromide (140)



Following GP9 using bromide **147** (955 mg) gave dimethyl(3-(trimethylsilyl)prop-2-yn-1-yl)sulfonium bromide **140** (949 mg, 75%); mp 156-157 °C;ν_{max} (neat)/cm^{-1} 3013, 2918, 2181, 1318, 1253, 1190, 1038, 991, 845, 761, 639 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 0.22 (9H, s, 3 × CH_3), 3.18 (6H, s, 2 × CH_3), 4.93 (2H, s, CH_2); δ_C (75 MHz; $CDCl_3$) -0.7 (3C, 3 × CH_3), 24.1 (2C, 2 × CH_3), 33.2 (CH_2), 89.7 (C_{quat}), 97.5 (C_{quat}); HRMS *m/z* (TOF ES+) 173.0819. $C_8H_{17}SSi$ requires 173.0815.

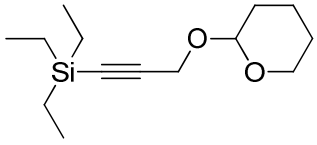
2-Prop-2-ynyloxy-tetrahydropyran (148)



Dihydropyran (50 mmol, 4.21 g, 4.6 mL) and *p*-toluenesulfinic acid monohydrate (1 mmol, 0.20 g) were added to a solution of propargylic alcohol (50 mmol, 2.80 g, 2.9 mL) in CH_2Cl_2 (30 mL) at 0 ºC. After 30 min the reaction mixture was allowed to stirr at to room temperature. After 3 h the reaction was quenched by the addition of Na_2CO_3 solution (15 mL). The phases were separated and the aqueous phase was washed with CH_2Cl_2 (3×15 mL). The combined organic extracts were washed with brine (15 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the residue by flash chromatography [hexane:ethylacetate (20:1)] gave ether **148** as colourless oil (6.460 g, 92%); ν_{max} (neat)/cm^{-1} 3288, 2941, 2873, 2121, 1445, 1387, 1263, 1181, 1122, 1020, 959, 899, 667; δ_H (300 MHz; $CDCl_3$) 1.52-1.88 (6H, m, 3 × CH_2), 2.41 (1H, m, CH), 3.50-3.57 (1H, m, CH), 3.80-3.88 (1H, m, CH), 4.26 (2H, dd, *J* 15.0 and 2.5, 2 × CH), 4.82 (1H, m, CH); δ_C (75 MHz; $CDCl_3$) 19.0 (CH_2), 25.3 (CH_2), 30.2 (CH_2), 54.0 (CH_2), 61.8 (CH_2), 73.8 (CH), 79.5 (C_{quat}), 96.6 (CH).

Data were in agreement with those reported in the literature.[90]

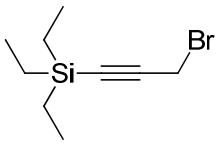
Triethyl(3-(tetrahydro-2*H*-pyran-2-yloxy)prop-1-ynyl)silane (149)



n-BuLi (7.05 mmol, 2.8 mL of a 2.5M solution in hexane) was added dropwise to a solution of protected alcohol **148** (7.13 mmol, 1.0 g) in THF (20 mL) at -78 ºC. The reaction mixture was stirred for 30 min at -78 ºC before TESCl (6.41 mmol, 1.08 mL) was added. The

temperature was raised to room temperature and the reaction mixture stirred for 4 h. NH_4Cl solution (20 mL) was added to quench the reaction and the THF was removed under reduced pressure. Et_2O (30 mL) was added and the phases were separated. The aqueous phase was washed with Et_2O (3 × 30 mL) and the combined organic extracts were washed with brine (15 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the residue by flash chromatography [hexane:ethylacetate (20:1)] gave ether **149** as a pale yellow liquid (1.76 g, 97%); δ_H (300 MHz; $CDCl_3$) 0.60 (6H, q, *J* 8.0 and 7.7, 3 × CH_2), 0.98 (9H, t, *J* 8.0 and 7.7, 3 × CH_3), 1.50-1.88 (6H, m, 2 × CH_3), 3.44-3.56 (1H, m, CH), 3.81-3.89 (1H, m, CH), 4.29 (2H, s, CH_2), 4.86 (1H, m, CH); δ_C (75 MHz; $CDCl_3$) 4.4 (3C, 3 × CH_2), 7.8 (3C, 3 × CH_3), 18.8 (CH_2), 25.2 (CH_2), 30.1 (CH_2), 54.0 (CH_2), 61.8 (CH_2), 90.1 (C_{quat}), 96.8 (CH), 103.2 (C_{quat}); HRMS *m/z* (TOF ES+) 277.1602. $C_{14}H_{26}O_2NaSi$ requires 277.1600.

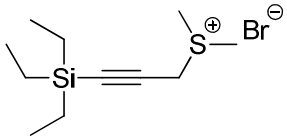
3-(Bromo-prop-1-ynyl)-triethylsilane (150)



Following GP8 using PPh_3 (7.6 mmol, 1.99 g), Br_2 (7.5 mmol, 0.38 mL) and ether **149** (1.76 g) in CH_2Cl_2 (20 mL). Purification by flash chromatography (*n*-pentane) gave bromine **150** as a colourless oil (1.75 g, 75%); ν_{max} (neat)/cm^{-1} 2959, 2914, 2176, 1456, 1413, 1235, 1038, 1019, 955, 895; δ_H (300 MHz; $CDCl_3$) 0.61 (6H, q, *J* 7.7, 3 × CH_2), 0.99 (9H, t, *J* 7.7, 3 × CH_3), 3.93 (2H, s, CH_2); δ_C (75 MHz; $CDCl_3$) 4.5 (3C, 3 × CH_2), 7.6 (3C, 3 × CH_3), 14.8 (CH_2), 89.6 (C_{quat}), 100.3 (C_{quat}).

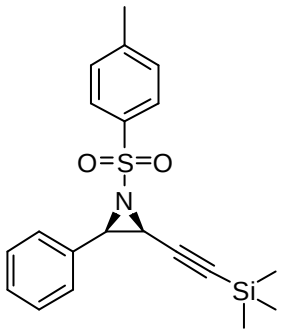
Data were in agreement with those reported in the literature.[91]

Dimethyl(3-(triethylsilyl)prop-2-yn-1-yl)sulfonium bromide (151)



Following GP9 using bromide **150** (1.166 g) gave sulfonium salt **151** as a white solid (886 mg, 60%); mp 149-150 °C; ν_{max} (neat)/cm^{-1} 3013, 2918, 2181, 1318, 1253, 1190, 1038, 991, 845, 761, 639; δ_H (300 MHz; $CDCl_3$) 0.61 (6H, q, *J* 7.7, 3 × CH_2), 0.96 (9H, t, *J* 7.7, 3 × CH_3), 3.21 (6H, s, 2 × CH_3), 5.06 (2H, s, CH_2); δ_C (75 MHz; $CDCl_3$) 4.0 (3C, 3 × CH_2), 7.4 (3C, 3 × CH_3), 24.4 (2C, 2 × CH_3), 33.7 (CH_2), 90.9 (C_{quat}), 95.4 (C_{quat}); HRMS *m/z* (TOF ES+) 215.1291. $C_{11}H_{23}SSi$ requires 215.1284.

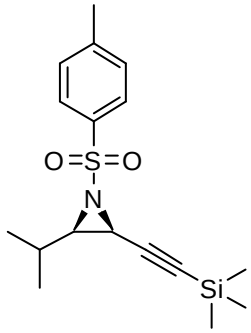
***cis*-2-Phenyl-1-(toluene-4-sulfonyl)-3-((trimethylsilyl)ethynyl)aziridine (152)**



Following GP3 using imine **141** and sulfonium salt **140** for 1 h. Purification by flash chromatography [hexane:ethylacetate:triethylamine (20:1:1%)] gave *cis*-aziridine **152** as a yellow solid (258 mg, 70%); mp 80-81 °C; ν_{max} (neat)/cm^{-1} 3028, 2850, 2176, 1586, 1444, 1326, 1251, 1160, 860, 795, 650; δ_H (300 MHz; $CDCl_3$) -0.01 (9H, s, 3 × CH_3), 2.43 (3H, s, CH_3), 3.63 (1H, d, *J* 6.9, CH), 3.94 (1H, d, *J* 6.9, CH), 7.27-7.35 (7H, m, 7 × CH), 7.87 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) -0.7 (3C, 3 × CH_3), 21.7 (CH_3), 35.9 (CH), 46.4 (CH), 91.5 (C_{quat}), 97.4 (C_{quat}), 127.9 (4C, 4 × CH), 128.0 (2C, 2 × CH), 128.4 (CH), 129.9 (2C, 2 ×

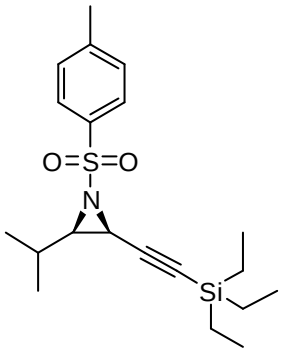
CH), 131.9 (C_{quat}), 134.5 (C_{quat}), 144.9 (C_{quat}); HRMS *m/z* (TOF ES+) 392.1112. $C_{20}H_{23}NO_2NaSSi$ requires 392.1116.

cis-2-Isopropyl-1-(toluene-4-sulfonyl)-3-((trimethylsilyl)ethynyl)aziridine (139)



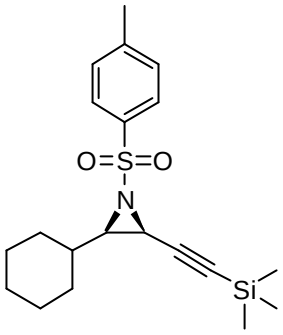
Following GP3 using imine **144** and sulfonium salt **140** for 3 h. Purification by flash chromatography [hexane:ethylacetate:triethylamine (25:1:1%)] gave *cis*-aziridine **139** as a white solid (235 mg, 70%); mp 59-61 °C; ν_{max} (neat)/cm^{-1} 2966, 2913, 2178, 1601, 1472, 1405, 1351, 1322, 1308, 1291, 1250, 1154, 1092, 1076, 945, 873, 840, 814, 759; δ_H (300 MHz; $CDCl_3$) 0.12 (9H, s, 3 × CH_3), 0.79 (3H, d, *J* 6.8, CH_3), 0.98 (3H, d, *J* 6.8, CH_3), 1.50-1.60 (1H, m, CH), 2.45 (3H, s, CH_3), 2.49 (1H, dd, *J* 6.9 and 2.6, CH), 3.38 (1H, d, *J* 6.9, CH), 7.34 (2H, d, *J* 8.3, 2 × CH), 7.84 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) -0.4 (3C, 3 × CH_3), 18.4 (CH_3), 20.1 (CH_3), 21.7 (CH_3), 28.4 (CH), 33.9 (CH), 51.0 (CH), 90.0 (C_{quat}), 97.9 (C_{quat}), 128.2 (2C, 2 × CH), 129.6 (2C, 2 ×CH), 134.6 (C_{quat}), 144.7 (C_{quat}); HRMS *m/z* (TOF ES+) 358.1281. $C_{17}H_{21}NO_2NaS$ requires 358.1273.

***cis*-2-Isopropyl-1-(toluene-4-sulfonyl)-3-((triethylsilyl)ethynyl)aziridine (153)**



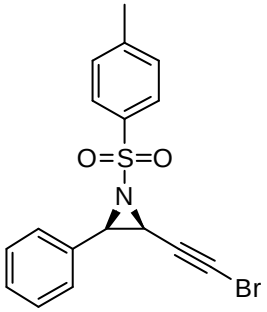
Following GP3 using imine **144** and sulfonium salt **151** for 3 h. Purification by flash chromatography [hexane:ethylacetate:triethylamine (25:1:1%)] gave *cis*-aziridine **153** as a white solid (302 mg, 80%); mp 49-50 °C; ν_{max} (neat)/cm^{-1} 3047, 2958, 2875, 2230, 1323, 1160, 1093, 876, 725; δ_H (300 MHz; $CDCl_3$) 0.55 (6H, q, *J* 8.0, 3 × CH_2), 0.81 (3H, d, *J* 6.7, CH_3), 0.93 (9H, t, *J* 8.0, 3 × CH_3), 0.98 (3H, d, *J* 6.7, CH_3), 1.58-1.65 (1H, m CH), 2.44 (3H, s, CH_3), 2.51 (1H, dd, J 9.7 and 6.9, CH), 3.37 (1H, d, *J* 6.9, CH), 7.33 (2H, d, *J* 8.3, 2 × CH), 7.83 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 4.1 (3C, 3 × CH_2), 7.3 (3C, 3 × CH_3), 18.5 (CH_3), 20.2 (CH_3), 21.7 (CH_3), 28.5 (CH), 34.0 (CH), 51.0 (CH), 87.5 (C_{quat}), 99.0 (C_{quat}), 128.1 (2C, 2 ×CH), 129.6 (2C, 2 × CH), 134.7 (C_{quat}), 144.6 (C_{quat}); HRMS *m/z* (TOF ES+) 400.1733. $C_{20}H_{31}NO_2NaS$ requires 400.1742.

***cis*-2-Cyclohexyl-1-(toluene-4-sulfonyl)-3-((trimethylsilyl)ethynyl)aziridine (154)**



Following GP3 using imine **145** and sulfonium salt **140** for 3 h. Purification by flash chromatography [hexane:ethylacetate:triethylamine (20:1:1%)] gave *cis*-aziridine **154** as a beige solid (319 mg, 85%); mp 76-77 °C; ν_{max} (neat)/cm^{-1} 2937, 2902, 2852, 2178, 1598, 1448, 1410, 1368, 1326, 1245, 1222, 1158, 1135, 1089, 1061, 958, 838, 824, 815, 749, 701; δ_H (300 MHz; $CDCl_3$) 0.13 (9H, s, 3 × CH_3), 0.90-1.34 (6H, m, 3 × CH_2), 1.43-1.79 (5H, m , 2 × CH_2 and CH), 2.43 (3H, s, CH_3), 2.55 (1H, dd, *J* 6.9 and 2.6, CH), 3.35 (1H, d, *J* 6.9, CH), 7.33 (2H, d, *J* 8.2, CH_2), 7.83 (2H, d, *J* 8.2, CH_2); δ_C (75 MHz; $CDCl_3$) -0.5 (3C, 3 × CH_3), 21.6 (CH_3), 25.2 (CH_2), 25.4 (CH_2), 25.9 (CH_2), 28.8 (CH_2), 30.3 (CH_2), 33.4 (CH), 37.3 (CH), 49.3 (CH), 89.7 (C_{quat}), 98.0 (C_{quat}), 128.0 (2C, 2 × CH), 129.6 (2C, 2 × CH), 134.4 (C_{quat}), 144.6 (C_{quat}); HRMS *m/z* (TOF ES+) 398.1590. $C_{20}H_{29}NO_2NaSSi$ requires 398.1586.

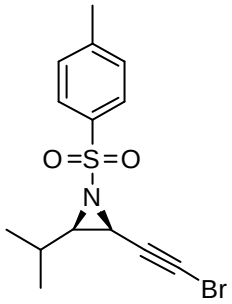
cis-2-Bromoethynyl-3-phenyl-1-(toluene-4-sulfonyl)aziridine (155)



Silver nitrate (0.07 mmol, 12 mg) and NBS (0.77 mmol, 136 mg) were added to a solution of aziridine **152** (0.70 mmol, 258 mg) in acetone (10 mL) and the mixture was stirred at room temperature for 1 h. Water (10 mL) was added and the organic phase was separated. The aqueous phase was extracted with ethyl acetate (3 × 10 mL). The combined organics were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The residue was then purified by flash chromatography [hexane:ethyl acetate:triethylamine (8:1:1%)] to give *cis*-aziridine **155** as a white solid (210 mg, 80%); mp 90-92 °C; ν_{max} (neat)/cm^{-1} 3047,

2858, 2190, 1550, 1401, 1323, 1164, 876, 790, 672; δ_H (300 MHz; $CDCl_3$) 2.44 (3H, s, CH_3), 3.64 (1H, d, *J* 6.8, CH), 3.97 (1H, d, *J* 6.8, CH), 7.31-7.36 (7H, m, 7 × CH), 7.87 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.7 (CH_3), 36.2 (CH), 46.0 (CH), 48.4 (C_{quat}), 72.5 (C_{quat}), 127.6 (2C, 2 × CH), 127.9 (2C, 2 × CH), 128.2 (2C, 2 × CH), 128.6 (CH), 129.9 (2C, 2 ×CH), 131.6 (C_{quat}), 134.4 (C_{quat}), 145.1 (C_{quat}); HRMS *m/z* (TOF ES+) 397.9837. $C_{17}H_{14}NO_2NaS^{79}Br$ requires 397.9826.

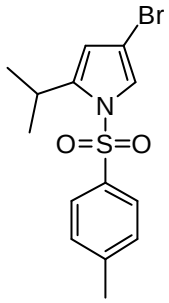
cis-2-Bromoethynyl-3-isopropyl-1-(toluene-4-sulfonyl)-aziridine (138)



Silver nitrate (0.07 mmol, 12 mg) and NBS (0.77 mmol, 136 mg) were added to a solution of aziridine **139** (0.70 mmol, 234 mg) in acetone (10 mL) and the mixture was stirred at room temperature for 1 h. Water (10 mL) was added and the organic phase was separated. The aqueous phase was extracted with ethyl acetate (3 × 10 mL). The combined organics were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The residue was then purified by flash chromatography [hexane:ethyl acetate:triethylamine (15:1:1%)] to give *cis*-aziridine **138** as a white solid (191 mg, 80%); mp 71-72 °C; ν_{max} (neat)/cm^{-1} 3050, 2963, 2145, 1326, 1164, 1089, 941, 873, 829, 815, 758; δ_H (300 MHz; $CDCl_3$) 0.81 (3H, d, *J* 6.8, CH_3), 0.99 (3H, d, *J* 6.8, CH_3), 2.45 (3H, s, CH_3), 2.52 (1H, dd, *J* 6.8 and 2.9, CH), 3.38 (1H, d, *J* 6.8, CH), 7.35 (2H, d, *J* 8.3, 2 × CH), 7.83 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 18.7 (CH_3), 20.1 (CH_3), 21.7 (CH_3), 28.4 (CH), 34.1 (CH), 44.5 (CH), 50.8 (C_{quat}),

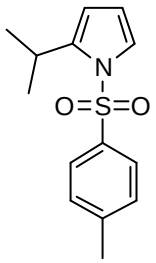
73.1 (C_{quat}), 128.2 (2C, 2 × CH), 129.7 (2C, 2 × CH), 134.3 (C_{quat}), 144.9 (C_{quat}); HRMS *m/z* (TOF ES+) 363.9992. $C_{14}H_{16}NO_2NaS^{79}Br$ requires 363.9983.

4-bromo-2-isopropyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (156).



Following GP4 using aziridine **138** (34 mg) for 2 h gave a pyrroles **156** as a brown oil (5 mg, 15%); ν_{max} (neat)/cm^{-1} 3002, 2971, 1588, 1359, 1181, 715, 678. δ_H (300 MHz; $CDCl_3$) 1.09 (6H, d, *J* 6.8, 2 × CH_3), 2.41 (3H, s, CH_3), 3.26 (1H, sept, *J* 6.8, CH), 6.02 (1H, d, *J* 1.9, CH), 7.25 (1H, d, *J* 1.9, CH), 7.30 (2H, d, *J* 8.3, 2 × CH), 7.63 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.4 (CH_3), 23.4 (2C, 2 × CH_3), 26.1 (CH), 100.4 (C_{quat}), 112.5 (CH), 120.5 (CH), 126.5 (2C, 2 × CH), 129.8 (2C, 2 × CH), 135.9 (C_{quat}), 143.6 (C_{quat}), 144.9 (C_{quat}); HRMS *m/z* (TOF ES+) 363.9980. $C_{14}H_{16}NO_2NaS^{79}Br$ requires 363.9983.

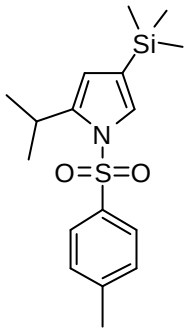
2-Isopropyl-1-(toluene-4-sulfonyl)-1H-pyrrole (158).



Following GP4 using aziridine **138** (34 mg) for 2 h gave **158** as a white solid (16 mg, 60%).

Following GP4 using aziridine **154** (34 mg) for 4 h gave **158** as a white solid (21 mg, 80%). Following GP6 using aziridine**139** at 70 °C for 12 h or aziridine **153** at 70 °C for 12 h gave pyrrole **158** as a white solid (51 mg, 98%); mp 85-86 °C; ν_{max} (neat)/cm^{-1} 3010, 2967, 2871, 1597, 1366, 1179, 1189, 812, 704, 682; δ_H (300 MHz; $CDCl_3$) 1.13 (6H, d, *J* 6.7, 2 × CH_3), 2.41 (3H, s, CH_3), 3.29 (1H, sept, *J* 6.7, CH), 6.05 (1H, m, CH), 6.22 (1H, dd, *J* 3.4 and 3.3, CH), 7.26 (1H, dd, *J* 3.3 and 1.6, CH), 7.28 (2H, d, *J* 8.3, 2 × CH), 7.61 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 23.8 (2C, 2 × CH_3), 26.3 (CH), 109.8 (CH), 111.4 (CH), 122.2 (CH), 126.5 (2C, 2 × CH), 129.9 (2C, 2 × CH), 136.9 (C_{quat}), 143.1 (C_{quat}), 144.6 (C_{quat}); HRMS *m/z* (TOF ES+) 286.0874. $C_{14}H_{17}NO_2NaS$ requires 286.0878.

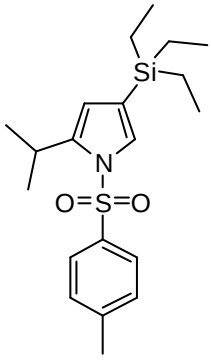
2-Isopropyl-1-(toluene-4-sulfonyl)-4-(trimethylsilyl)-1*H*-pyrrole (159)



Following GP4 using aziridine **139** (34 mg) for 1 h gave a mixture of pyrroles **159** and **158** (25 mg, 1.7:1 **159**:**158**); ν_{max} (neat)/cm^{-1} 3013, 2976, 1591, 1369, 1254, 1185, 818, 711, 681. **2-Isopropyl-1-(toluene-4-sulfonyl)-4-(trimethylsilyl)-1*H*-pyrrole**: δ_H (300 MHz; $CDCl_3$) 0.19 (9H, s, 3 × CH_3), 1.13 (6H, d, *J* 6.8, 2 × CH_3), 2.42 (3H, s, CH_3), 3.25 (1H, sept, *J* 6.8, CH), 6.07 (1H, d, *J* 1.7, CH), 7.27 (1H, d, *J* 1.7, CH), 7.30 (2H, d, *J* 8.3, 2 × CH), 7.62 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) -0.7 (3C, 3 × CH_3), 21.6 (CH_3), 23.8 (2C, 2 × CH_3), 26.2 (CH), 113.7 (CH), 121.3 (C_{quat}), 126.5 (2C, 2 × CH), 127.0 (CH), 129.7 (2C, 2 × CH), 137.1

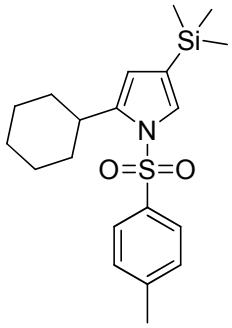
(C_{quat}), 143.6 (C_{quat}), 144.5 (C_{quat}); HRMS *m/z* (TOF ES+) 358.1271. $C_{17}H_{25}NO_2NaSSi$ requires 358.1273.

2-Isopropyl-1-(toluene-4-sulfonyl)-4-(triethylsilyl)-1*H*-pyrrole (161)



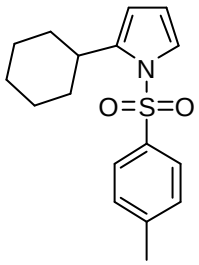
Following GP4 using aziridine **bd** (38 mg) for 1 h gave a mixture of pyrroles **161** and **158** (26 mg, 80%, 1.3:1 **161**:**158**); ν_{max} (neat)/cm^{-1} 3020, 2988, 1596, 1390, 1375, 1260, 1180, 825, 715. **2-Isopropyl-1-(toluene-4-sulfonyl)-4-(triethylsilyl)-1*H*-pyrrole**: δ_H (300 MHz; $CDCl_3$) 0.67 (6H, q, *J* 7.5, 3 × CH_2), 0.93 (9H, t, *J* 7.5, 3 × CH_3), 1.09 (6H, d, *J* 6.8, 2 × CH_3), 2.38 (3H, s, CH_3), 3.21 (1H, sept, *J* 6.8, CH), 6.00 (1H, d, *J* 1.6, CH), 7.23 (1H, d, *J* 1.6, CH), 7.25 (2H, d, *J* 8.4, 2 × CH), 7.55 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 3.7 (3C, 3 × CH_2), 7.4 (3C, 3 × CH_3), 21.5 (CH_3), 23.8 (2C, 2 × CH_3), 26.2 (CH), 114.3 (CH), 117.9 (C_{quat}), 126.3 (2C, 2 × CH), 128.1 (CH), 129.8 (2C, 2 × CH), 136.9 (C_{quat}), 143.5 (C_{quat}), 144.4 (C_{quat}); HRMS *m/z* (TOF ES+) 400.1739. $C_{20}H_{31}NO_2NaSSi$ requires 400.1742.

2-cyclohexyl-1-(toluene-4-sulfonyl)-4-(trimethylsilyl)-1*H*-pyrrole (162)



Following GP4 using aziridine **154** (38 mg) for 1 h gave a mixture of pyrroles **162** and **163** (21 mg, 60%, 2:1 **162**:**162**); ν_{max} (neat)/cm^{-1} 3012, 2963, 1596, 1456, 1368, 1252, 1188, 990, 815, 711, 688. **2-cyclohexyl-1-(toluene-4-sulfonyl)-4-(trimethylsilyl)-1*H*-pyrrole**: δ_H (300 MHz; $CDCl_3$) 0.19 (9H, s, 3 × CH_3), 1.07-1.34 (6H, m, 3 × CH_2), 1.60-1.80 (4H, m, 2 × CH_2), 2.40 (3H, s, CH_3), 2.87 (1H, t, *J* 10.8, CH), 6.01 (1H, d, *J* 1.7, CH), 7.23 (1H, d, *J* 1.7, CH), 7.28 (2H, d, *J* 8.3, 2 × CH), 7.63 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) -0.7 (3C, CH_3), 21.5 (CH_3), 26.0 (CH_2), 26.7 (2C, 2 × CH_2), 34.4 (2C, 2 × CH_2), 36.0 (CH), 113.9 (CH), 121.0 (C_{quat}), 126.6 (3C, 3 × CH), 129.8 (2C, 2 × CH), 136.8 (C_{quat}), 142.5 (C_{quat}), 144.5 (C_{quat}); HRMS *m/z* (TOF ES+) 398.1580. $C_{20}H_{29}NO_2NaSSi$ requires 398.1586.

2-Cyclohexyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (163)



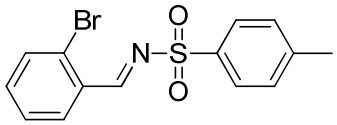
Following GP4 using aziridine **154** (38 mg) for 4 h gave pyrrole **163** as a white solid (23 mg, 76%).

Following GP6 using aziridine **154** at 70 °C for 12 h gave pyrrole **163** as a white solid (59 mg, 98%); mp, 70-72 °C; ν_{max} (neat)/cm^{-1} 3015, 2969, 2873, 1599, 1450, 1362, 1188, 1181,

810, 701, 684; δ_H (300 MHz; $CDCl_3$) 1.09-1.38 (6H, m, 3 × CH_2), 1.64-1.83 (4H, m, 2 × CH_2), 2.44 (3H, s, CH_3), 2.94 (1H, t, *J* 11.0, CH), 6.04 (1H, dd, *J* 3.4 and 1.7, CH), 6.24 (1H, dd, *J* 3.4 and 3.3, CH), 7.27 (1H, dd, *J* 3.3 and 1.7, CH), 7.31 (2H, d, *J* 8.3, 2 × CH), 7.65 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.5 (CH_3), 25.9 (CH_2), 26.6 (2C, 2 × CH_2), 34.4 (2C, 2 × CH_2), 36.0 (CH), 110.1 (CH), 111.3 (CH), 121.8 (CH), 126.5 (2C, 2 × CH), 129.8 (2C, 2 × CH), 136.8 (C_{quat}), 142.0 (C_{quat}), 144.6 (C_{quat}); HRMS *m/z* (TOF ES+) 326.1187. $C_{17}H_{21}NO_2NaS$ requires 326.1191.

Data were in agreement with those reported in the literature.[69]

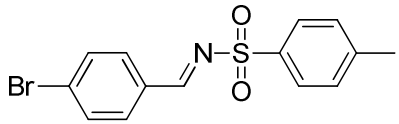
_N_-(2-bromobenzylidene)-4-methylbenzenesulfonamide (164)



Following GP1 using 2-bromobenzaldehyde (1.85 g, 1.16 mL) gave imine **164** as a white solid (2.68 g, 88%); mp 137-138 ºC; ν_{max} (neat)/cm^{-1} 3002, 2854, 1643, 1582,1428, 1376, 1315, 1260, 1150, 1088, 952, 860, 749; δ_H (300 MHz; $CDCl_3$) 2.43 (3H, s, CH_3), 7.35 (2H, d, *J* 8.4, 2 × CH), 7.40-7.50 (2H, m, 2 × CH), 7.62 (1H, dd, *J* 7.9 and 1.6, CH), 7.88 (2H, d, *J* 8.4, 2 × CH), 9.43 (1H, s, CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 126.3 (CH), 127.9 (2C, 2 × CH), 127.9 (C_{quat}), 129.5 (CH), 130.5 (2C, 2 × CH), 131.1 (C_{quat}), 133.7 (CH), 134.5 (C_{quat}), 135.7 (CH), 144.9 (C_{quat}), 169.2 (CH).

Data were in agreement with those reported in the literature.[92]

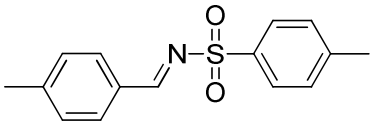
_N_-(4-bromobenzylidene)-4-methylbenzenesulfonamide (165)



Following GP1 using 4-bromobenzaldehyde (1.85 g) gave imine **165** as a white solid (2.44 g, 80%); mp 188-190 ºC; ν_{max} (neat)/cm^{-1} 3066, 2986, 2909, 1649, 1599,1585, 1481, 1315, 1302, 1282, 1158, 1087, 1064, 1008, 868, 812, 704; δ_H (300 MHz; $CDCl_3$) 2.46 (3H, s, CH_3), 7.36 (2H, d, *J* 8.0, 2 × CH), 7.64 (2H, d, *J* 7.7, 2 × CH), 7.81 (2H, d, *J* 8.0, 2 × CH), 7.90 (2H, d, *J* 7.7, 2 × CH), 9.00 (1H, s, CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 128.2 (2C, 2 × CH), 129.9 (2C, 2 × CH), 130.2 (C_{quat}), 131.2 (C_{quat}), 132.4 (2C, 2 × CH), 132.6 (2C, 2 × CH), 133.6 (C_{quat}), 144.8 (C_{quat}), 168.8 (CH).

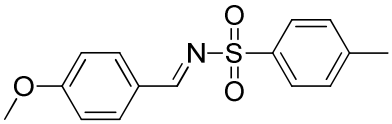
Data were in agreement with those reported in the literature.[87]

4-methyl-_N_-(4-methylbenzylidene)benzenesulfonamide (166)



Following GP1 using 4-methylbenzaldehyde (1.20 g, 1.18 mL) gave imine **166** as a white solid (2.09 g, 85%); mp 103-104 ºC; ν_{max} (neat)/cm^{-1} 3044, 1593, 1561, 1512, 1367, 1314, 1302, 1288, 1155, 1085, 1019, 874, 790, 761; δ_H (300 MHz; $CDCl_3$) 2.43 (6H, s, 2 × CH_3), 7.28 (2H, d, *J* 7.9, 2 × CH), 7.34 (2H, d, *J* 7.9, 2 × CH), 7.81 (2H, d, *J* 8.2, 2 × CH), 7.88 (2H, d, *J* 8.2, 2 × CH), 9.00 (1H, CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 22.0 (CH_3), 128.0 (2C, 2 × CH), 129.7 (2C, 2 × CH), 129.9 (2C, 2 × CH), 131.4 (2C, 2 × CH), 135.4 (C_{quat}), 144.4 (2C, 2 × C_{quat}), 146.4 (2C, 2 × C_{quat}).

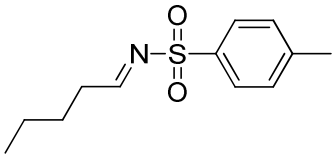
_N_-(4-methoxylbenzylidene)-4-methylbenzenesulfonamide (167)



Following GP1 using 4-methoxylbenzaldehyde (1.36 g, 1.22 mL) gave imine **167** as a white solid (2.08 g, 80%); mp 123-125 ºC; ν_{max} (neat)/cm^{-1} 3023, 2970, 1657, 1578,1420, 1327, 1279, 1164, 1088, 965, 869, 850, 757, 656; δ_H (300 MHz; $CDCl_3$) 2.43 (3H, s, CH_3), 3.89 (3H, s, CH_3), 6.98 (2H, d, *J* 8.3, 2 × CH), 7.32 (2H, d, *J* 8.3, 2 × CH), 7.85-7.91 (4H, m, 4 × CH), 8.95 (1H, s, CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 55.9 (CH_3), 114.7 (2C, 2 × CH), 125.2 (C_{quat}), 127.9 (2C, 2 × CH), 129.7 (2C, 2 × CH), 133.7 (2C, 2 × CH), 135.3 (C_{quat}), 144.3 (C_{quat}), 165.3 (C_{quat}), 169.2 (CH).

Data were in agreement with those reported in the literature.[87]

4-methyl-_N_-pentylidenebenzenesulfonamide (168)

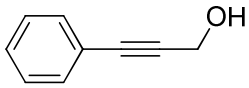


To a 1:1 mixture of water (15 mL) and formic acid (15 mL) were added 4-methyl-benzenesulfonamide (9 mmol, 1.54 g,), valeraldehyde (10 mmol,) and sodium benzenesulfinate (10 mmol, 1.64 g). The reaction mixture was stirred for 12 h at room temperature and the resulting white precipitate was filtered off, washed with water (2 × 10 mL) and then pentane (2 × 10 mL). The solid was dissolved in CH_2Cl_2 (25 mL) and a Na_2CO_3

solution was added (20 mL). The reaction mixture was stirred at room temperature for 2h and the two phases were separated. The aqueous phase was washed with CH_2Cl_2 and the combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give pure imine **168** as a beige solid (1.50 g, 70%); mp 92-95 ºC; ν_{max} (neat)/cm^{-1} 3992, 3050, 2956, 1633, 1600, 1453, 1369, 1320, 1151, 1117, 1086, 807, 754, 688; δ_H (300 MHz; $CDCl_3$) 0.91 (3H, t, *J* 7.3, CH_3), 1.35 (2H, m, CH_2), 1.62 (2H, m, CH_2), 2.45 (3H, m, CH_3), 2.53 (2H, m, CH_2), 7.35 (2H, d, *J* 8.0, 2 × CH), 7.81 (2H, d, *J* 8.0, 2 × CH), 8.58 (1H, d, *J* 4.5, CH); δ_C (75 MHz; $CDCl_3$) 13.6 (CH_3), 21.5 (CH_3), 22.3 (CH_2), 26.7 (CH_2), 35.6 (CH_2), 128.0 (2C, 2 × CH), 129.7 (2C, 2 × CH), 134.7 (C_{quat}), 144.6 (C_{quat}), 178.8(CH).

Data were in agreement with those reported in the literature.[55]

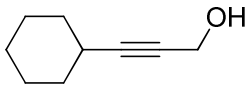
3-phenylprop-2-yn-1-ol (169)



Following GP2 using phenylacetylene (2.04 g, 2.19 mL). Purification by flash chromatography [hexane:ethylacetate (4:1)] gave alcohol **169** as a colourless oil (2.37 g, 90%); ν_{max} (neat)/cm^{-1} 3345, 2923, 2875, 2863, 2240, 1601, 1499, 1115, 1033, 960, 785, 726; δ_H (300 MHz; $CDCl_3$) 3.12 (1H, s, OH), 4.53 (2H, s, CH_2), 7.24-7.39 (3H, m, 3 × CH), 7.42-7.51 (2H, m, 2 × CH); δ_C (75 MHz; $CDCl_3$) 51.3 (CH_2), 85.4 (C_{quat}), 87.3 (C_{quat}), 122.5 (C_{quat}), 128.2 (2C, 2 × CH), 128.3 (2C, 2 × CH), 131.5 (CH).

Data were in agreement with those reported in the literature.[93]

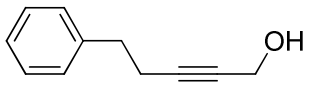
3-Cyclohexylprop-2-yn-1-ol (170)



Following GP2 using cyclohexylacetylene (2.16 g, 2.61 mL). Purification by flash chromatography [hexane:ethylacetate (3:1)] gave alcohol **170** as a colourless oil (2.35 g, 85%); ν_{max} (neat)/cm^{-1} 3345, 2933, 2866, 2655, 2289, 1450, 1368, 1360, 1302, 1244, 1136, 1079, 982, 860, 765; δ_H (300 MHz; $CDCl_3$) 1.20-1.58 (6H, m, 3 × CH_2), 1.62-1.85 (4H, m, 2 × CH_2), 2.36 (1H, m, CH), 4.24 (2H, s, CH_2); δ_C (75 MHz; $CDCl_3$) 24.9 (2C, 2 × CH_2), 25.8 (CH_2), 29.1 (CH), 32.6 (2C, 2 × CH_2), 51.5 (CH_2), 78.2 (C_{quat}), 90.7 (C_{quat}).

Data were in agreement with those reported in the literature.[93]

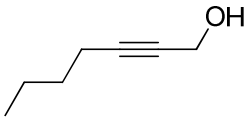
5-phenylpent-2-yn-1-ol (171)



Following GP2 using 4-phenyl-1-butyne (2.60 g, 2.81 mL). Purification by flash chromatography [hexane:ethylacetate (6:1)] gave alcohol **171** as a colourless oil (2.75 g, 86%); ν_{max} (neat)/cm^{-1} 3360, 3091, 3061, 2955, 2286, 2230, 1605, 1523, 1497, 1155, 1011, 955, 736, 712; δ_H (300 MHz; $CDCl_3$) 1.53 (1H, s, OH), 2.50-2.59 (2H, m, CH_2), 2.90 (2H, t, *J* 7.6, CH_2), 4.28 (2H, t, *J* 2.0, CH_2), 7.23-7.35 (3H, m, 3 × CH), 7.36-7.42 (2H, m, 2 × CH); δ_C (75 MHz; $CDCl_3$) 20.9 (CH_2), 35.0 (CH_2), 51.4 (CH_2), 79.1 (C_{quat}), 85.8 (C_{quat}), 126.3 (2C, 2 × CH), 128.4 (3C, 3 × CH), 140.5 (C_{quat}); HRMS *m/z* (TOF EI+) 160.0892. $C_{11}H_{12}O$ requires 160.0888.

Data were in agreement with those reported in the literature.[93]

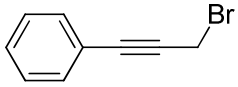
Hept-2-yn-1-ol (172)



Following GP2 using hex-1-yne (1.64 g, 2.30mL). Purification by flash chromatography [hexane:ethylacetate (5:1)] gave alcohol **172** as a colourless oil (2.37 g, 87%); ν_{max} (neat)/cm^{-1} 3355, 2930, 2885, 2226, 1459, 1139, 1011, 816, 731; δ_H (300 MHz; $CDCl_3$) 0.91 (3H, t, *J* 7.2, CH_3), 1.34-1.54 (4H, m, 2 × CH_2), 2.10 (1H, s, OH), 2.20 (2H, t, *J* 6.8, CH_2), 4.25 (2H, m, CH_2); δ_C (75 MHz; $CDCl_3$) 13.6 (CH_3), 18.4 (CH_2), 21.8 (CH_2), 30.7 (CH_2), 51.5 (CH_2), 78.2 (C_{quat}), 86.6 (C_{quat}).

Data were in agreement with those reported in the literature.[94]

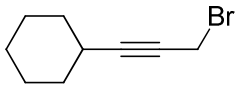
(3-Bromoprop-1-ynyl)benzene (173)



Following GP8 using PPh_3 (19.7 mmol, 5.16 g), Br_2 (19.5 mmol, 0.98 mL) and alcohol **169** (2.37 g) in CH_2Cl_2 (50 mL). Purification by flash chromatography (*n*-pentane) gave bromide **173** as a colourless oil (3.21 g, 92%); ν_{max} (neat)/cm^{-1} 3057, 2223, 1676, 1591, 1493, 1273, 1120, 1003, 988, 860; δ_H (300 MHz; $CDCl_3$) 4.17 (2H, s, CH_2), 7.30-7.40 (3H, m, 3 × CH), 7.42-7.51 (2H, m, 2 × CH); δ_C (75 MHz; $CDCl_3$) 15.3 (CH_2), 84.2 (C_{quat}), 86.7 (C_{quat}), 122.1 (C_{quat}), 128.3 (2C, 2 × CH), 128.8 (2C, 2 × CH), 131.8 (CH).

Data were in agreement with those reported in the literature.[95]

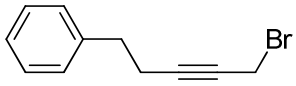
(3-Bromoprop-1-ynyl)cyclohexane (174)



Following GP8 using PPh_3 (24.8 mmol, 6.49 g), Br_2 (24.5 mmol, 1.23 mL) and alcohol **170** (2.35 g) in CH_2Cl_2 (60 mL). Purification by flash chromatography (*n*-pentane) gave bromide **174** as a colourless oil (3.11 g, 91%); δ_H (300 MHz; $CDCl_3$) 1.15-1.57 (6H, m, 3 × CH_2), 1.60-1.79 (4H, m , 2 × CH_2), 2.35-2.42 (1H, m, CH), 3.93 (2H, d, *J* 2.1, CH_2); δ_C (75 MHz; $CDCl_3$) 15.8 (CH_2), 24.7 (2C, 2 × CH_2), 25.8 (CH_2), 29.3 (CH), 32.3 (2C, 2 × CH_2), 75.3(C_{quat}), 92.1 (C_{quat}).

Data were in agreement with those reported in the literature. [96]

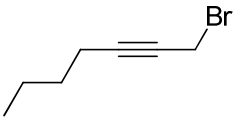
(5-Bromopent-3-ynyl)benzene (175)



Following GP8 using PPh_3 (18.9 mmol, 4.95 g), Br_2 (18.7 mmol, 0.94 mL) and alcohol **171** (2.75 g) in CH_2Cl_2 (50 mL). Purification by flash chromatography (hexane) gave bromide **175** as a colourless oil (2.87 g, 75%); ν_{max} (neat)/cm^{-1} 3029, 2935, 2870, 2235, 1609, 1520, 1499, 1344, 1202, 1160, 816; δ_H (300 MHz; $CDCl_3$) 2.59 (2H, tt, *J* 7.5 and 2.4, CH_2), 2.88 (2H, t, *J* 7.5, CH_2), 3.96 (2H, t, *J* 2.4, CH_2), 7.23-7.30 (3H, m, 3 × CH), 7.31-7.44 (2H, m, 2 × CH); δ_C (75 MHz; $CDCl_3$) 15.5 (CH_2), 21.1 (CH_2), 34.5 (CH_2), 76.0 (C_{quat}), 87.2 (C_{quat}), 126.3 (CH), 128.3 (2C, 2 × CH), 128.4 (2C, 2 × CH), 140.2 (C_{quat}); HRMS *m/z* (TOF EI+) 222.0040. $C_{11}H_{11}{}^{79}Br$ requires 222.0044.

Data were in agreement with those reported in the literature.[97]

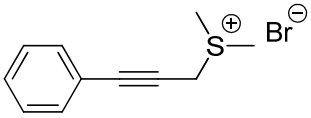
1-Bromohept-2-yne (176)



Following GP8 using PPh_3 (10.2 mmol, 2.67 g), Br_2 (10.1 mmol, 0.51 mL) and alcohol **172** (2.37 g) in CH_2Cl_2 (30 mL). Purification by flash chromatography (*n*-pentane) gave bromide **176** as a colourless oil (1.54 g, 95%); ν_{max} (neat)/cm^{-1} 2959, 2914, 2882, 2239, 1612, 1572, 1463, 1310, 1269, 1101, 996; δ_H (300 MHz; $CDCl_3$) 0.91 (3H, t, *J* 7.1, CH_3), 1.39-1.50 (4H, m, 2 × CH_2), 2.24 (2H, m, CH_2), 3.93 (2H, t, *J* 2.3, 2H); δ_C (75 MHz; $CDCl_3$) 13.5 (CH_3), 18.5 (CH_2), 21.9 (CH_2), 30.4 (CH_2), 31.5 (CH_2), 75.2 (C_{quat}), 88.3 (C_{quat}).

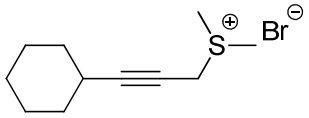
Data were in agreement with those reported in the literature.[98]

Dimethyl(3-phenylprop-2-ynyl)sulfonium bromide (177)



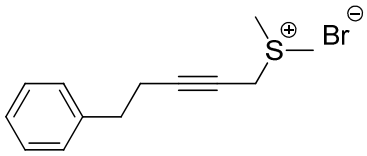
Following GP9 using bromide **173** (975 mg) sulfonium salt **177** as a white solid (1.11 g, 87%); mp 138-139 °C; ν_{max} (neat)/cm^{-1} 2977, 2908, 2867, 2235, 1487, 1422, 1408, 1187, 1044, 1009, 979, 762, 691, 635; δ_H (300 MHz; DMSO- d_6) 3.00 (6H, s, 2 × CH_3), 4.82 (2H, s, CH_2), 7.41-7.48 (3H, m, 3 × CH), 7.58-7.62 (2H, m, 2 × CH); δ_C (75 MHz; DMSO- d_6) 26.0 (2C, 2 × CH_3), 34.5 (CH_2), 78.5 (C_{quat}), 91.2 (C_{quat}), 123.3 (C_{quat}), 131.1 (2C, 2 × CH), 132.1 (CH), 134.3 (2C, 2 × CH); HRMS *m/z* (TOF ES+) 177.0734. $C_{11}H_{13}S$ requires 177.0738.

(3-cyclohexylprop-2-yn-1-yl)dimethylsulfonium bromide (178)



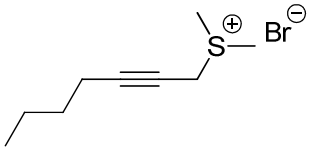
Following GP9 using bromide **174** (1.00 g) gave sulfonium salt **178** as a white solid (723 mg, 55%); mp 110-111 °C;ν_{max} (neat)/cm^{-1} 3001, 2951, 2929, 2889, 2233, 1458, 1419, 1325, 1248, 1187, 1153, 1050, 1001, 928, 721, 638; δ_H (300 MHz; $CDCl_3$) 1.12-1.85 (10H, m, 5 × CH_2), 2.44 (1H, m, CH), 3.18 (6H, s, 2 × CH_3), 4.95 (2H, s, CH_2); δ_C (75 MHz; $CDCl_3$) 18.0 (CH), 24.2 (2C, 2 × CH_3), 24.7 (2C, 2 × CH_2), 25.5 (CH_2), 32.3 (2C, 2 × CH_2), 33.4 (CH_2), 65.1 (C_{quat}), 96.7 (C_{quat}); HRMS *m/z* (TOF ES+) 183.1210. $C_{11}H_{19}S$ requires 183.1202.

Dimethyl(5-phenylpent-2-yn-1-yl)sulfonium bromide (179)



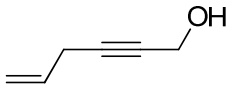
Following GP9 using bromide **175** (1.12 g) gave sulfonium salt **179** as a white solid (1.026 g, 72%); mp 103-104 °C; ν_{max} (neat)/cm^{-1} 2988, 2918, 2231, 1601, 1494, 1452, 1410, 1323, 1261, 1206, 1151, 1056, 1005, 939, 742, 701; δ_H (300 MHz; $CDCl_3$) 2.65 (2H, tt, *J* 6.9 and 2.1, CH_2), 2.84 (2H, t, *J* 6.9, CH_2), 2.87 (6H, s, 2 × CH_3), 4.85 (2H, t, *J* 2.1, CH_2), 7.17-7.24 (3H, m, 3 × CH), 7.26-7.33 (2H, m, 2 × CH); δ_C (75 MHz; $CDCl_3$) 20.3 (CH_2), 24.0 (2C, 2 × CH_3), 33.3 (CH_2), 34.0 (CH_2), 66.3 (C_{quat}), 91.4 (C_{quat}), 126.8 (CH), 128.4 (2C, 2 × CH), 128.7 (2C, 2 × CH), 139.6 (C_{quat}); HRMS *m/z* (TOF ES+) 205.1055. $C_{13}H_{17}S$ requires 205.1051.

Hept-2-ynyldimethylsulfonium bromide (180)



Following GP9 using bromide **176** (875 mg) gave sulfonium salt **180** as a white solid (711 mg, 60%); mp 74-75 °C ; νmax (neat)/cm-1 2997, 2954, 2931, 2888, 2230, 1456, 1423, 1320, 1251, 1183, 1148, 1047, 1004, 930, 725, 639; δ_H (300 MHz; $CDCl_3$) 0.88 (3H, t, *J* 2.2, CH_3), 1.30-1.53 (4H, m, 2 × CH_2), 2.26 (2H, dt, *J* 6.9 and 2.2, CH_2), 3.19 (6H, s, 2 × CH_3), 4.94 (2H, t, *J* 2.2, CH_2); δ_C (75 MHz; $CDCl_3$) 18.4 (CH_2), 21.9 (CH_2), 24.3 (2C, 2 × CH_3), 28.6 (CH_3), 30.3 (CH_2), 33.4 (CH2), 65.2 (C_{quat}), 92.7 (C_{quat}); HRMS *m*/*z* (TOF ES+) 157.1054. $C_9H_{17}S$ requires 157.1051.

Hex-5-en-2-yn-1-ol (181)

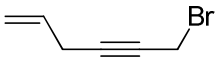


To a solution of propargyl alcohol (10 mmol, 0.60 mL) in water (10 mL) were added allyl bromide (15 mmol, 0.64 mL), K_2CO_3 (10 mmol, 1.38 g), Na_2SO_3 (5 mmol, 630 mg) and CuI (0.2 mmol, 38 mg). The reaction mixture was stirred at 30 °C for 12h. After cooling down to room temperature, NH_4Cl solution (20 mL) and CH_2Cl_2 (20 mL) were added to the reaction mixture. The phases were separated and the aqueous phase was washed with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by distillation (75 °C at 20 mmHg) to give alcohol **181** as a colourless oil (720 mg, 75%); ν_{max} (neat)/cm^{-1} 3445, 3010, 2991, 2231, 1645, 1582, 1554, 1465, 1366, 1267, 1186, 1149, 930, 902, 845, 770; δ_H (300

MHz; $CDCl_3$) 2.85 (1H, s, OH), 3.01 (2H, m, CH_2), 4.29 (2H, m, CH_2), 5.12 (1H, ddt, *J* 8.8 and 1.7 and 1.7, CH), 5.32 (1H, ddt, *J* 17.2 and 1.7 and 1.7, CH), 5.81-5.84 (1H, m, CH); δ_C (75 MHz; $CDCl_3$) 23.0 (CH_2), 50.9 (CH_2), 80.6 (C_{quat}), 82.6 (C_{quat}), 116.9 (CH_2), 132.3 (CH).

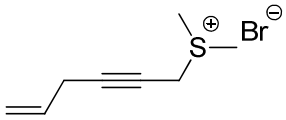
Data were in agreement with those reported in the literature.[99]

6-Bromohex-1-en-4-yne (182)



Following GP8 using PPh_3 (8.2 mmol, 2.15 g), Br_2 (8.15 mmol, 0.41 mL) and alcohol **181** (720 mg) in CH_2Cl_2 (20 mL). Purification by flash chromatography (*n*-pentane) gave bromide **182** as a colourless oil (1.07 g, 90%); ν_{max} (neat)/cm^{-1} 3015, 2999, 2236, 1645, 1560, 1523, 1466, 1209, 1153, 1026, 963, 812; δ_H (300 MHz; $CDCl_3$) 3.20 (2H, m, CH_2), 3.95 (2H, m, CH_2), 5.05-5.07 (1H, m, CH), 5.20 (1H, ddt, *J* 17.6 and 1.8 and 1.8, CH), 5.72-5.76 (1H, m, CH); δ_C (75 MHz; $CDCl_3$) 15.9 (CH_2), 24.6 (CH_2), 79.1 (C_{quat}), 81.2 (C_{quat}), 116.7 (CH_2), 132.3 (CH); HRMS *m/z* (TOF EI+) 157.9735. C_6H_7Br requires 157.9731.

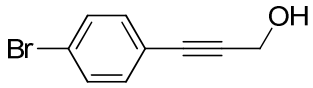
Hex-5-en-2-yn-1-yldimethylsulfonium bromide (183)



Following GP9 using bromide **182** (795 mg) gave sulfonium salt **183** as a white solid (387 mg, 35%); ν_{max} (neat)/cm^{-1} 3090, 3020, 2915, 2191, 1825, 1640, 1323, 1193, 1035, 991, 925, 840, 760, 642; δ_H (300 MHz; $CDCl_3$) 3.41 (6H, s, 2 × CH_3), 3.70 (2H, m, CH_2), 4.80 (2H, s, CH_2), 5.47 (1H, dd, *J* 11.0 and 1.8, CH), 5.56 (1H, dd, *J* 18.0 and 1.8, CH), 6.01 (1H, m, CH);

δ_C (75 MHz; $CDCl_3$) 23.3 (CH_2), 24.6 (2C, 2 × CH_3), 34.3 (CH_2), 76.6 (C_{quat}), 81.5 (C_{quat}), 117.5 (CH_2), 133.1 (CH); HRMS *m/z* (TOF ES+) 141.0740. $C_8H_{13}S$ requires 141.0732.

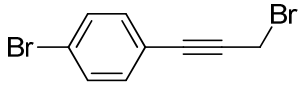
3-(4-bromophenyl)prop-2-yn-1-ol (184)



Following GP5 using 1-bromo-4-iodobenzene (7.07 g). Purification by flash chromatography [hexane:ethylacetate (5:1)] gave alcohol **184** as a brown oil (4.64 g, 88%); ν_{max} (neat)/cm^{-1} 3335, 2870, 2226, 1579, 1560, 1486, 1405, 1387, 1262, 1166, 1080, 1015, 955, 831, 753; δ_H (300 MHz; $CDCl_3$) 1.87 (1H, s, OH), 4.48 (2H, s, CH_2), 7.28 (2H, d, *J* 8.4, 2 × CH), 7.42 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 14.9 (CH_2), 86.7 (C_{quat}), 86.9 (C_{quat}), 121.5 (C_{quat}), 123.2 (CH_2), 131.7 (2C, 2 × CH), 133.3 (2C, 2 × CH); HRMS *m/z* (TOF EI+) 209.9676. $C_9H_7O^{79}Br$ requires 209.9680.

Data were in agreement with those reported in the literature.[93]

1-Bromo-4-(3-bromoprop-1-ynyl)benzene (185)

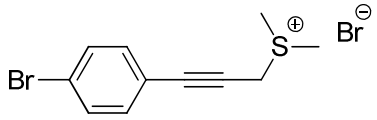


Following GP8 using PPh_3 (11 mmol, 2.88 g), Br_2 (10.9 mmol, 0.55 mL) and alcohol **184** (2.11 g) in CH_2Cl_2 (30 mL). Purification by flash chromatography (*n*-pentane) gave bromide **185** as a colourless oil (2.68 g, 98%); ν_{max} (neat)/cm^{-1} 3010, 2230, 1906, 1603, 1591, 1489, 1396, 1278, 1216, 1206, 1120, 1075, 988, 906, 845; δ_H (300 MHz; $CDCl_3$) 4.15 (2H, s, CH_2),

7.29 (2H, d, *J* 8.3, 2 × CH), 7.45 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 14.9 (CH_2), 85.2 (C_{quat}), 85.5 (C_{quat}), 121.1 (C_{quat}), 123.3 (C_{quat}), 131.6 (2C, 2 × CH), 133.2 (2C, 2 × CH).

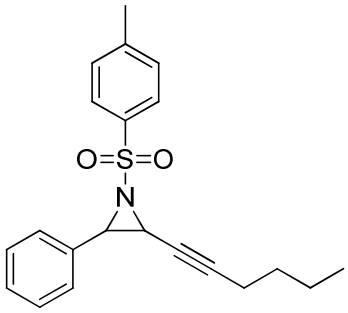
Data were in agreement with those reported in the literature.[100]

(3-(4-bromophenyl)prop-2-yn-1-yl)dimethylsulfonium bromide (186)



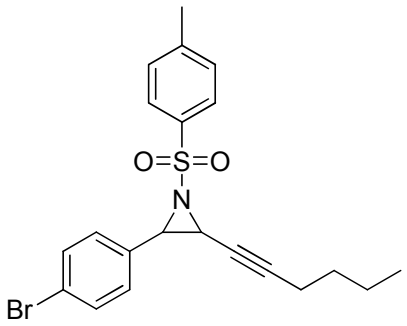
Following GP9 using bromide **185** (1.369 g) gave sulfonium salt **186** as a white solid (1.327 g, 79%); mp 132-134 °C; ν_{max} (neat)/cm^{-1} 3012, 2929, 2884, 2241, 1628,1401, 1325, 1221, 1163, 1135, 1112, 1072, 1039, 1001, 982, 840, 805, 778, 722; δ_H (300 MHz; $CDCl_3$) 3.39 (6 H, s, 2 × CH_3), 5.51 (2H, s, CH_2), 7.44 (2H, d, *J* 8.4, 2 × CH), 7.55 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 23.9 (2C, 2 × CH_3), 30.2 (CH_2), 79.9 (C_{quat}), 87.5 (C_{quat}), 122.6 (C_{quat}), 122.8 (C_{quat}), 132.1 (2C, 2 × CH), 135.6 (2C, 2 × CH); HRMS *m/z* (TOF ES+) 254.9845. $C_{11}H_{12}S^{79}Br$ requires 254.9838.

2-Hex-1-ynyl-3-phenyl-1-(toluene-4-sulfonyl)aziridine (187)



Following GP3 using imine **141** and sulfonium salt **180** for 2.5 h. Purification by flash chromatography [hexane:ethylacetate (12:1)] gave aziridine **187** as a beige solid (229 mg, 65%, 9:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 3053, 2957, 2926, 2243, 1320, 1162, 1091, 1021, 875, 787; HRMS *m/z* (TOF ES+) 376.1344. $C_{21}H_{23}NO_2NaS$ requires 376.1347; aziridine *cis*-**187**: δ_H (300 MHz; $CDCl_3$) 0.74 (3H, t, *J* 7.2, CH_3), 1.03-1.15 (2H, m, CH_2), 1.19-1.28 (2H, m, CH_2), 1.99 (2H, td, *J* 6.8 and 1.7, CH_2), 2.41 (3H, s, CH_3), 3.63 (1H, dt, *J* 6.9 and 1.7, CH), 3.93 (1H, d, *J* 6.9, CH), 7.25-7.33 (7H, m, 7 × CH), 7.87 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.4 (CH_3), 18.2 (CH_2), 21.4 (CH_2), 21.6 (CH_3), 30.0 (CH_2), 36.2 (CH), 46.1 (CH), 72.1 (C_{quat}), 86.7 (C_{quat}), 127.7 (2C, 2 × CH), 127.9 (4C, 4 × CH), 128.2 (CH), 129.8 (2C, 2 × CH), 132.2 (C_{quat}), 134.7 (C_{quat}), 144.7 (C_{quat}).

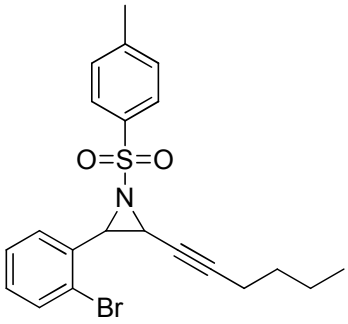
2-(4-Bromophenyl)-3-hex-1-ynyl-1-(toluene-4-sulfonyl)aziridine (188)



Following GP3 using imine **165** and sulfonium salt **180** for 3 h. Purification by flash chromatography [hexane:ethylacetate (35:1)] gave aziridine **188** as a yellow solid (341 mg, 79%, 8:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 3053, 2959, 2929, 2861, 2243, 1594, 1488, 1405, 1375, 1322, 1159, 1088, 1010, 900, 851, 839, 805, 775; HRMS *m/z* (TOF ES+) 454.0445. $C_{21}H_{22}NO_2NaS^{79}Br$ requires 454.0452; aziridine *cis*-**188:** δ_H (300 MHz; $CDCl_3$) 0.77 (3H, t, *J* 7.2, CH_3), 1.04-1.30 (4H, m, 2 × CH_2), 2.01 (2H, td, *J* 6.9 and 1.7, CH_2), 2.44 (3H, s, CH_3), 3.62 (1H, dt, *J* 6.9 and 1.7, CH), 3.88 (1H, d, *J* 6.9, CH), 7.19 (2H, d, *J* 8.5, 2 × CH), 7.34

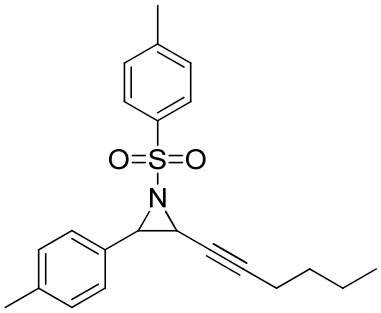
(2H, d, *J* 8.4, 2 × CH), 7.42 (2H, d, *J* 8.5, 2 × CH), 7.86 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.5 (CH_3), 18.3 (CH_2), 21.5 (CH_2), 21.7 (CH_3), 30.0 (CH_2), 36.2 (CH), 45.5 (CH), 71.9 (C_{quat}), 87.0 (C_{quat}), 122.4 (C_{quart}), 127.9 (3C, 3 × CH), 129.4 (3C, 3 × CH), 129.8 (CH), 131.1 (CH), 131.4 (C_{quat}), 134.6 (C_{quat}), 144.9 (C_{quat}).

2-(2-Bromophenyl)-3-hex-1-ynyl-1-(toluene-4-sulfonyl)aziridine (189)



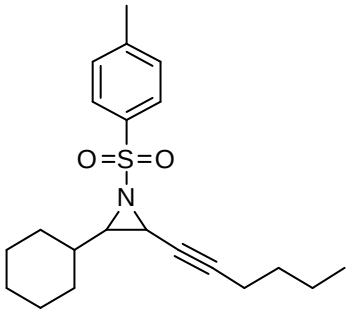
Following GP3 using imine **164** and sulfonium salt **180** for 4 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave aziridine **189** as yellow solid (315 mg, 73%, 20:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 2957, 2931, 2871, 2249, 1331, 1159, 1090, 1018, 870, 778, 752; HRMS *m/z* (TOF ES+) 454.0467. $C_{21}H_{22}NO_2NaS^{79}Br$ requires 454.0452; aziridine *cis*-**189:** δ_H (300 MHz; $CDCl_3$) 0.70 (3H, t, *J* 7.2, CH_3), 0.91-1.20 (4H, m, 2 × CH_2), 1.93 (2H, td, *J* 6.7, CH_2), 2.45 (3H, s, CH_3), 3.70 (1H, dt, *J* 6.9 and 1.7, CH), 4.12 (1H, d, *J* 6.9, CH), 7.12-7.27 (3H, m, 3 × CH), 7.36 (2H, d, *J* 8.4, 2 × CH), 7.52 (1H, dd, *J* 7.8 and 1.3, CH), 7.90 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.4 (CH_3), 18.2 (CH_2), 21.3 (CH_2), 21.7 (CH_3), 29.9 (CH_2), 36.2 (CH), 46.8 (CH), 71.9 (C_{quat}), 86.0 (C_{quat}), 123.3 (C_{quart}), 126.9 (CH), 128.0 (2C, 2 × CH), 129.5 (3C, 3 × CH), 129.9 (CH), 132.1 (CH), 132.4 (C_{quat}), 134.5 (C_{quat}), 144.9 (C_{quat}).

2-Hex-1-ynyl-1-(toluene-4-sulfonyl)-3-*p*-tolylaziridine (190)



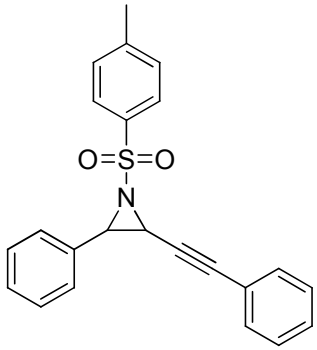
Following GP3 using imine **166** and sulfonium salt **180** for 4 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave aziridine **190** as a white solid (290 mg, 79%, 7:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 3052, 2958, 2928, 2860, 2246, 1917, 1595, 1517, 1492, 1321, 1162, 1089, 1018, 899, 853, 809, 768, 706; HRMS *m/z* (TOF ES+) 390.1492. $C_{22}H_{25}NO_2NaS$ requires 390.1504; aziridine *cis*-**190:** δ_H (300 MHz; $CDCl_3$) 0.76 (3H, t, *J* 7.2, CH_3), 1.06-1.31 (4H, m, 2 × CH_2), 2.02 (2H, td, *J* 6.9 and 1.8, CH_2), 2.32 (3H, s, CH_3), 2.42 (3H, s, CH_3), 3.60 (1H, dt, *J* 6.9 and 1.8, CH), 3.89 (1H, d, *J* 6.9, CH), 7.09 (2H, d, *J* 8.1 and 2 × CH), 7.21 (2H, d, *J* 8.1, 2 × CH), 7.33 (2H, d, *J* 8.4, 2 × CH), 7.87 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.4 (CH_3), 18.3 (CH_2), 21.2 (CH_2), 21.5 (CH_3), 30.0 (CH_2), 36.1 (CH), 46.2 (CH), 72.3 (C_{quat}), 86.6 (C_{quat}), 127.6 (2C, 2 × CH), 127.9 (2C, 2 × CH), 128.6 (2C, 2 × CH), 129.7 (2C, 2 × CH), 131.3 (C_{quat}), 134.8 (C_{quat}), 138.0 (C_{quat}), 144.7 (C_{quat}).

2-cyclohexyl-3-(hex-1-ynyl)-1-(toluene-4-sulfonyl)aziridine (191)



Following GP3 using imine **145** and sulfonium salt **180** for 3 h. Purification by flash chromatography [hexane:ethylacetate (4:1)] gave aziridine **191** as a white solid (180 mg, 50%, 7:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 2926, 2854, 2248, 1598, 1449, 1367, 1314, 1304, 1154, 1121, 1088, 1021, 962, 905, 882, 813, 789, 727, 672; HRMS *m/z* (TOF ES+) 382.1821. $C_{21}H_{29}NO_2NaS$ requires 382.1817; aziridine *cis*-**191:** δ_H (300 MHz; $CDCl_3$) 0.87 (3H, t, *J* 7.2, CH_3), 0.90-1.16 (5H, m, 2 × CH_2 and CH), 1.25-1.48 (6H, m, 3 × CH_2), 1.53-1.78 (4H, m, 2 × CH_2), 2.17 (2H, dt, *J* 6.8 and 1.8, CH_2), 2.44 (3H, s, CH_3), 2.54 (1H, dd, *J* 9.7 and 6.9, CH), 3.35 (1H, dt, *J* 6.9 and 1.8, CH), 7.32 (2H, d, *J* 8.3, 2 × CH), 7.82 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 18.4 (CH_2), 21.6 (CH_3), 21.7 (CH_2), 25.3 (2C, 2 × CH_2), 25.4 (2C, 2 × CH_2), 26.0 (CH_2), 29.0 (CH_2), 30.3 (CH_2), 33.9 (CH_3), 37.1 (CH), 49.5 (CH), 72.8 (C_{quat}), 85.2 (C_{quat}), 128.0 (2C, 2 × CH), 129.6 (2C, 2 × CH), 134.7 (C_{quat}), 144.5 (C_{quat}).

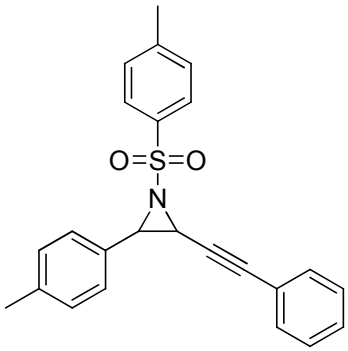
2-Phenyl-3-phenylethynyl-1-(toluene-4-sulfonyl)aziridine (192)



Following GP3 using imine **141** and sulfonium salt **177** for 1.5 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave aziridine **192** as a white solid (317 mg, 85%, 7:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 3032, 2950, 2926, 2230, 1597, 1490, 1457, 1441, 1319, 1157, 1087, 1071, 873, 854, 784, 757, 708; HRMS *m/z* (TOF ES+) 396.1041. $C_{23}H_{19}NO_2NaS$ requires 396.1034; aziridine *cis*-**192:** δ_H (300 MHz; $CDCl_3$) 2.42 (3H, s, CH_3), 3.85 (1H, d, *J* 6.9, CH), 4.07 (1H, d, *J* 6.9, CH), 7.14-7.38 (12H, m, 12 × CH), 7.90 (2H, d, *J* 8.3, 2 × CH);

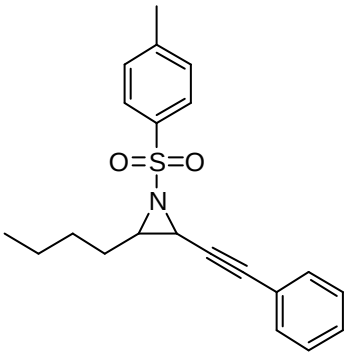
δ_C (75 MHz; $CDCl_3$) 21.7 (CH_3), 36.3 (CH), 46.5 (CH), 81.6 (C_{quat}), 85.1 (C_{quat}), 121.8 (C_{quart}), 127.8 (2C, 2 × CH), 128.0 (4C, 4 × CH), 128.1 (2C, 2 × CH), 128.5 (CH), 128.8 (CH), 129.9 (2C, 2 × CH), 131.8 (2C, 2 × CH), 132.1 (C_{quat}), 134.6 (C_{quat}), 144.9 (C_{quat}).

2-Phenylethynyl-1-(toluene-4-sulfonyl)-3-*p*-tolylaziridine(193)



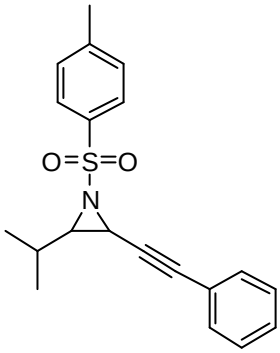
Following GP3 using imine **166** and sulfonium salt **177** for 8 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] aziridine **193** as a white solid (252 mg, 65%, 50:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 3053, 2957, 2926, 2228, 1597, 1519, 1491, 1317, 1155, 1089, 1021, 877, 824, 806, 757; HRMS *m/z* (TOF ES+) 410.1199. $C_{24}H_{21}NO_2NaS$ requires 410.1191; aziridine *cis*-**193**: δ_H (300 MHz; $CDCl_3$) 2.30 (3H, s, CH_3), 2.41 (3H, s, CH_3), 3.82 (1H, d, *J* 6.9, CH), 4.01 (1H, d, *J* 6.9, CH), 7.10 (2H, d, *J* 8.0, 2 × CH), 7.18-7.27 (7H, m, 7 × CH), 7.31 (2H, d, *J* 8.5, 2 × CH), 7.88 (2H, d, *J* 8.5, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.2 (CH_3), 21.7 (CH_3), 36.3 (CH), 46.5 (CH), 81.8 (C_{quat}), 85.2 (C_{quat}), 121.9 (C_{quart}), 127.7 (2C, 2 × CH), 128.0 (2C, 2 × CH), 128.1 (2C, 2 × CH), 128.7 (3C, 3 × CH), 129.0 (CH), 129.8 (2C, 2 × CH), 131.9 (2C, 2 × CH), 134.7 (C_{quat}), 138.3 (C_{quat}), 144.9 (C_{quat}).

2-Butyl-3-(phenylethynyl)-1-(toluene-4-sulfonyl)aziridine (194)



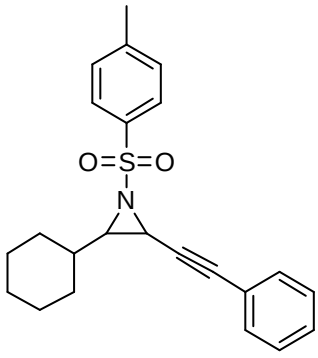
Following GP3 using imine **168** and sulfonium salt **177** for 12 h. Purification by flash chromatography [hexane:ethylacetate (60:1)] aziridine **194** as a light yellow solid (141 mg, 40%, 50:1 *cis*:*trans*)); ν_{max} (neat)/cm^{-1} 2965, 2930, 2860, 2249, 1601, 1491, 1316, 1304, 1292, 1152, 1087, 934, 842, 809, 753, 730, 715, 688, 672; HRMS *m/z* (TOF ES+) 376.1340. $C_{21}H_{23}NO_2NaS$ requires 376.1347; aziridine *cis*-**194**: δ_H (300 MHz; $CDCl_3$) 0.84 (3H, t, *J* 7.0, CH_3), 1.26-1.32 (4H, m, 2 × CH_2), 1.55-1.75 (2H, m, CH_2), 2.45 (3H, s, CH_3), 2.63 (1H, q, *J* 13.0 and 6.9, CH), 3.59 (1H, d, *J* 6.9, CH), 7.28-7.41 (7H, m, 7 × CH), 7.87 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.8 (CH_3), 21.6 (CH_3), 22.1 (CH_2), 27.9 (CH_2), 28.7 (CH_2), 34.4 (CH), 45.3 (CH), 82.0 (C_{quat}), 84.2 (C_{quat}), 121.9 (C_{quat}), 128.0 (2C, 2 × CH), 128.2 (CH), 128.8 (CH), 129.7 (2C, 2 × CH), 131.9 (2C, 2 × CH), 134.7 (C_{quat}), 144.7 (C_{quat}).

2-isopropyl-3-(phenylethynyl)-1-(toluene-4-sulfonyl)aziridine (195)



Following GP3 using imine **144** and sulfonium salt **177** for 4 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave aziridine **195** as a yellow solid (203 mg, 60%, 25:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 2965, 2923, 2881, 1601, 1493, 1441, 1406, 1362, 1316, 1304, 1186, 1151, 1087, 1059, 980, 945, 873, 820, 768, 750, 711, 687, 670; HRMS *m/z* (TOF ES+) 362.1189. $C_{20}H_{21}NO_2NaS$ requires 362.1191; aziridine *cis*-**195**: δ_H (300 MHz; $CDCl_3$) 0.80 (3H, d, *J* 6.7, CH_3), 1.00 (3H, d, *J* 6.7, CH_3), 1.60-1.72 (1H, m, CH), 2.41 (3H, s, CH_3), 2.59 (1H, dd, *J* 9.7 and 6.9, CH), 3.56 (1H, d, *J* 6.9, CH), 7.22-7.37 (7H, m, 7 × CH), 7.83 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 18.6 (CH_3), 20.1 (CH_3), 21.6 (CH_3), 28.5 (CH), 34.2 (CH), 51.3 (CH), 82.0 (C_{quat}), 83.9 (C_{quat}), 122.0 (C_{quat}), 128.1 (2C, 2 × CH), 128.2 (2C, 2 × CH), 128.8 (CH), 129.7 (2C, 2 × CH), 131.9 (2C, 2 ×CH), 134.7 (C_{quat}), 144.7 (C_{quat}).

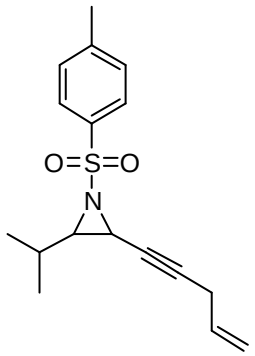
2-cyclohexyl-3-(phenylethynyl)-1-(toluene-4-sulfonyl)aziridine (196)



Following GP3 using imine **145** and sulfonium salt **177** for 6 h. Purification by flash chromatography [hexane:ethylacetate (4:1)] gave aziridine **196** as a white solid (303 mg, 80%, 50:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 2925, 2853, 2250, 1601, 1491, 1448, 1326, 1155, 1090, 981, 951, 911, 860, 826, 755, 715, 690, 667; HRMS *m/z* (TOF ES+) 402.1510. $C_{23}H_{25}NO_2NaS$ requires 402.1504; aziridine *cis*-**196**: δ_H (300 MHz; $CDCl_3$) 0.80-1.24 (6H, m, 3 × CH_2), 1.32-1.82 (5H, m, 2 × CH_2 and CH), 2.40 (3H, s, CH_3), 2.63 (1H, dd, *J* 9.6 and 6.9, CH), 3.54 (1H, d, *J* 6.9, CH), 7.21-7.36 (7H, m, 7 × CH), 7.82 (2H, d, *J* 8.3, 2 × CH); δ_C (75

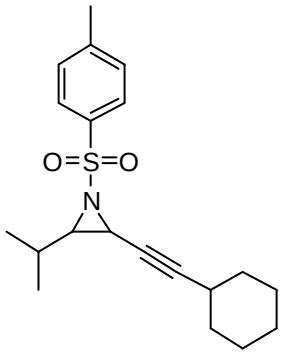
MHz; $CDCl_3$) 21.6 (CH_3), 25.3 (CH_2), 25.5 (CH_2), 26.0 (CH_2), 29.1 (CH_2), 30.5 (CH_2), 33.9 (CH), 37.4 (CH), 49.8 (CH), 82.3 (C_{quat}), 83.8 (C_{quat}), 122.0 (C_{quat}), 128.1 (3C, 3 × CH), 128.8 (2C, 2 × CH), 129.7 (2C, 2 × CH), 131.9 (2C, 2 × CH), 134.6 (C_{quat}), 144.6 (C_{quat}).

2-Isopropyl-3-(pent-4-en-1-ynyl)-1-(toluene-4-sulfonyl)aziridine (197)



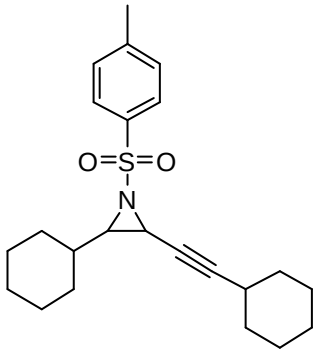
Following GP3 using imine **144** and sulfonium salt **183** for 4 h. Purification by flash chromatography [hexane:ethylacetate (12:1)] aziridine **197** as a yellow oil (121 mg, 40%, 25:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 3089, 3047, 2958, 2875, 2230, 1830, 1630, 1323, 1160, 1093, 980, 940, 876, 725; HRMS *m/z* (TOF ES+) 326.1182. $C_{17}H_{21}NO_2NaS$ requires 326.1191; aziridine *cis*-**197**: δ_H (300 MHz; $CDCl_3$) 0.81 (3H, d, *J* 6.7, CH_3), 0.99 (3H, d, *J* 6.7, CH_3), 1.58-1.69 (1H, m, CH), 2.45 (3H, s, CH_3), 2.52 (1H, dd, *J* 9.8 and 6.9, CH), 2.95 (2H, dd, *J* 5.2 and 1.8, CH_2), 3.41 (1H, dt, *J* 6.9 and 1.8, CH), 5.09 (1H, dd, *J* 10.0 and 1.7, CH), 5.23 (1H, dd, *J* 17.0 and 1.7, CH), 5.70-5.79 (1H, m, CH), 7.34 (2H, d, *J* 8.3, 2 × CH), 7.84 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 18.6 (CH_3), 20.1 (CH_3), 21.6 (CH_3), 23.0 (CH_2), 28.3 (CH), 34.0 (CH), 51.0 (CH), 76.4 (C_{quat}), 81.6 (C_{quat}), 116.3 (CH_2), 128.1 (2C, 2 × CH), 129.6 (2C, 2 × CH), 131.7 (CH), 134.7 (C_{quat}), 144.7 (C_{quat}).

2-(Cyclohexylethynyl)-3-isopropyl-1-(toluene-4-sulfonyl)aziridine (199)



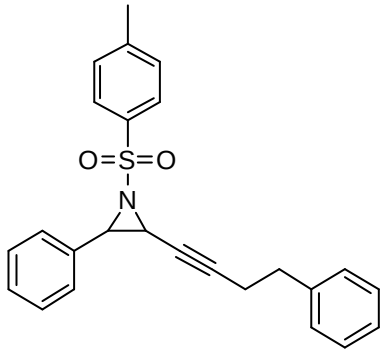
Following GP3 using imine **144** and sulfonium salt **178** for 4 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave aziridine **199** as a white solid (196 mg, 50%, 15:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 2965, 2927, 2854, 2241, 1598, 1449, 1406, 1314, 1304, 1151, 1088, 946, 899, 876, 866, 813, 801, 775; HRMS *m/z* (TOF ES+) 368.1666. $C_{20}H_{27}NO_2NaS$ requires 368.1660; aziridine *cis*-**199**: δ_H (300 MHz; $CDCl_3$) 0.77 (3H, d, *J* 6.7, CH_3), 0.96 (3H, d, *J* 6.7, CH_3), 1.24-1.48 (6H, m, 3 × CH_2), 1.54-1.80 (4H, m, 2 × CH_2), 2.37-2.44 (4H, m, CH and CH_3), 3.37 (1H, *J* 6.9 and 1.3, CH), 7.31 (2H, d, *J* 8.2, 2 × CH), 7.81 (2H, d, *J* 8.2, 2 × CH); δ_C (75 MHz; $CDCl_3$) 18.5 (CH_3), 20.1 (CH_3), 21.6 (CH_3), 24.5 (2C, 2 × CH_2), 25.7 (CH_2), 28.3 (CH), 32.1 (2C, 2 × CH_2), 34.1 (2 × CH_2), 50.9 (CH), 72.6 (C_{quat}), 89.1 (C_{quat}), 128.0 (2C, 2 × CH), 129.5 (2C, 2 × CH), 134.7 (C_{quat}), 144.5 (C_{quat}).

2-cyclohexyl-3-(cyclohexylethynyl)-1-(toluene-4-sulfonyl)aziridine (198)



Following GP3 using imine **145** and sulfonium salt **178** for 2 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave aziridine **198** as a white solid (196 mg, 51%, 25:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 2967, 2871, 2249, 1598, 1448, 1319, 1153, 1192, 815, 709, 686; HRMS *m/z* (TOF ES+) 408.1976. $C_{23}H_{31}NO_2NaS$ requires 408.1973; aziridine *cis*-**198**: δ_H (300 MHz; $CDCl_3$) 0.85-1.15 (5H, m, 2 × CH_2 and CH), 1.24-1.43 (9H, m, 4 × CH_2 and CH), 1.59-1.78 (8H, m, 4 × CH_2), 2.43 (3H, s, CH_3), 2.53 (1H, dd, *J* 9.6 and 7.0, CH), 3.35 (1H, dd, *J* 6.9 and 1.5, CH), 7.31 (2H, d, *J* 8.3, 2 × CH), 7.81 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 24.4 (2C, 2 × CH_2), 25.3 (CH_2), 25.4 (CH_2), 25.7 (CH_2), 26.0 (2C, 2 × CH_2), 28.8 (CH_2), 29.0 (CH_2), 32.0 (2C, 2 × CH_2), 33.8 (CH_3), 37.2 (CH), 49.4 (CH), 72.8 (C_{quat}), 88.9 (C_{quat}), 128.0 (2C, 2 × CH), 129.5 (2C, 2 × CH), 134.7 (C_{quat}), 144.5 (C_{quat}).

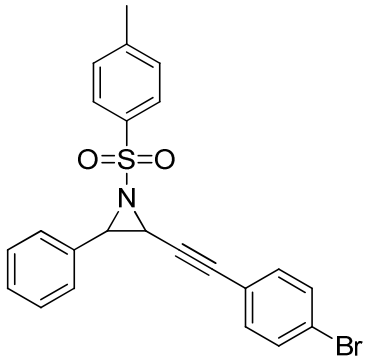
2-phenyl-3-(4-phenylbut-1-yn-1-yl)-1-(toluene-4-sulfonyl)aziridine (200)



Following GP3 using imine **141** and sulfonium salt **179** for 3 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave aziridine **200** as a yellow oil (281 mg, 70%, 11:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 2987, 2931, 2248, 1597, 1495, 1453, 1384, 1327, 1291, 1233, 1158, 1090, 1021, 875, 814, 742, 695; HRMS *m/z* (TOF ES+) 424.1340. $C_{25}H_{23}NO_2NaS$ requires 424.1347; aziridine *cis*-**200**: δ_H (300 MHz; $CDCl_3$) 2.27-2.34 (2H, m, CH_2), 2.44 (3H, s, CH_3), 2.50-2.66 (2H, m, CH_2), 3.63 (1H, dt, *J* 6.9 and 1.8, CH), 3.95 (1H, d, *J* 6.9, CH), 6.96-7.01 (2H, m, 2 × CH), 7.24-7.27 (3H, m, 3 × CH), 7.30 (5H, s, 5 × CH),

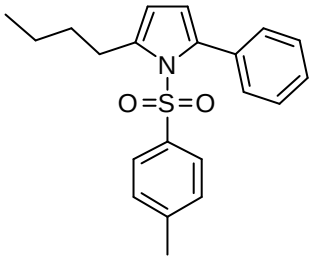
7.34 (2H, d, *J* 8.3, 2 × CH), 7.89 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 20.8 (CH_3), 21.7 (CH_3), 34.4 (CH_2), 36.2 (CH), 46.1 (CH), 73.0 (C_{quat}), 85.9 (C_{quat}), 126.2 (CH), 127.8 (2C, 2 × CH), 127.9 (2C, 2 × CH), 128.0 (2C, 2 × CH), 128.3 (5C, 5 × CH), 129.8 (2C, 2 × CH), 132.2 (C_{quat}), 134.8 (C_{quat}), 140.2 (C_{quat}), 144.8 (C_{quat}).

2-((4-bromophenyl)ethynyl)-3-phenyl-1-(toluene-4-sulfonyl)aziridine (201)



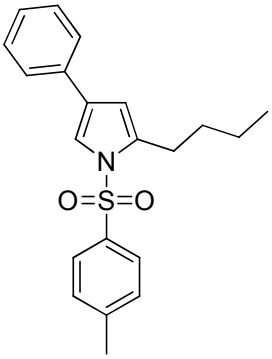
Following GP3 using imine **141** and sulfonium salt **186** for 8 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] aziridine **201** as a brown solid (339 mg, 75%, 15:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 3066, 2233, 1599, 1450, 1334, 1233, 1160, 1087, 1023, 885, 818, 745, 698; HRMS *m/z* (TOF ES+) 474.0144. $C_{23}H_{18}NO_2NaS^{79}Br$ requires 474.0139; aziridine *cis*-**201**: δ_H (300 MHz; $CDCl_3$) 2.43 (3H, s, CH_3), 3.85 (1H, d, *J* 6.9, CH), 4.09 (1H, d, *J* 6.9, CH), 7.02 (2H, d, *J* 8.6, 2 × CH), 7.31-7.36 (9H, m, 9 × CH), 7.92 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.7 (CH_3), 26.9 (CH), 42.2 (CH), 80.0 (C_{quat}), 92.3 (C_{quat}), 121.9 (C_{quart}), 123.1 (C_{quat}), 127.1 (CH), 128.0 (2C, 2 × CH), 128.3 (2C, 2 × CH), 128.6 (2C, 2 × CH), 129.4 (2C, 2 × CH), 131.5 (2C, 2 × CH), 134.7 (2C, 2 × CH), 136.9 (C_{quat}), 137.8 (C_{quat}), 138.4 (C_{quat}).

2-Butyl-5-phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (202)



Following GP6 using aziridine **187** or **194** at room temperature for 12 h gave **202** as yellow oil (69 mg, 98%); ν_{max} (neat)/cm^{-1} 3060, 2956, 2928, 2861, 1733, 1597, 1528, 1482, 1444, 1366, 1169, 1116, 1092, 911, 809, 759; δ_H (300 MHz; $CDCl_3$) 0.97 (3H, t, *J* 7.3, CH_3), 1.37-1.50 (2H, m, CH_2), 1.65-1.75 (2H, m, CH_2), 2.37 (3H, s, CH_3), 2.92 (2H, t, *J* 7.7, CH_2), 6.04 (1H, d, *J* 3.3, CH), 6.07 (1H, d, *J* 3.3, CH), 7.15 (2H, d, *J* 8.4, 2 × CH), 7.28 (2H, d, *J* 8.4, 2 × CH), 7.33 (5H, m, 5 × CH); δ_C (75 MHz; $CDCl_3$) 14.0 (CH_3), 21.6 (CH_3), 22.5 (CH_2), 29.3 (CH_2), 31.6 (CH_2), 112.6 (CH), 115.6 (CH), 126.4 (2C, 2 × CH), 127.2 (2C, 2 × CH), 127.7 (CH), 129.3 (2C, 2 × CH), 130.4 (2C, 2 × CH), 133.3 (C_{quat}), 136.4 (C_{quat}), 138.0 (C_{quat}), 139.9 (C_{quat}), 144.2 (C_{quat}); HRMS *m/z* (TOF ES+) 376.1350. $C_{21}H_{23}NO_2NaS$ requires 3761347.

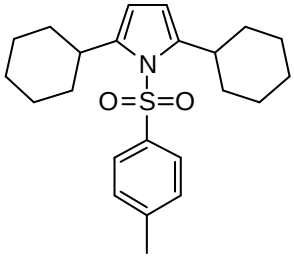
2-Butyl-4-phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (203)



Following GP7 using aziridine **187** (70 mg) for 2 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave a mixture of 2,4-substituted pyrrole **203** and 2,5-substituted

pyrrole **202** (42 mg, 60%, 1:7.6 **202**:**203**); ν_{max} (neat)/cm^{-1} 2958, 2929, 2871, 1723, 1596, 1526, 1494, 1448, 1401, 1361, 1306, 1292, 1188, 1168, 1120, 1089, 1038, 1009, 920, 812, 789, 761, 693; HRMS *m/z* (TOF ES+) 376.1356. $C_{21}H_{23}NO_2NaS$ requires 376.1347; **2-Butyl-4-phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole 203**: δ_H (300 MHz; $CDCl_3$) 0.91 (3H, t, *J* 7.3, CH_3), 1.31-1.43 (2H, m, CH_2), 1.54-1.61 (2H, m, CH_2), 2.41 (3H, s, CH_3), 2.69 (2H, t, *J* 7.6, CH_2), 6.33 (1H, dt, *J* 1.9 and 1.0, CH), 7.29 (2H, d, *J* 8.4, 2 × CH), 7.32 (2H, d, *J* 8.4, 2 × CH), 7.37 (1H, d, *J* 8.2, CH), 7.51 (2H, dd, *J* 8.4, 8.2, 2 × CH), 7.58 (1H, d, *J* 1.9, CH), 7.69 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.9 (CH_3), 21.6 (CH_3), 22.4 (CH_2), 26.9 (CH_2), 30.7 (CH_2), 110.4 (CH), 117.7 (CH), 125.4 (2C, 2 × CH), 126.7 (3C, 3 × CH),126.8 (C_{quat}), 127.8 (2C, 2 × CH), 130.0 (2C, 2 × CH), 133.7 (C_{quat}), 136.3 (C_{quat}), 136.9 (C_{quat}), 144.8 (C_{quat}).

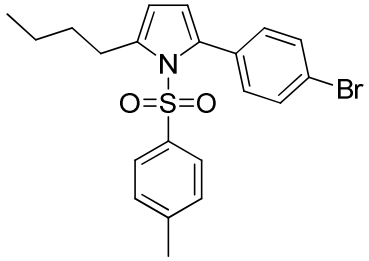
2,5-dicyclohexyl-1-(toluene-4-sulfonyl)-1H-pyrrole (204)



Following GP6 using aziridine**198** at 70 °C for 3 h gave **204** as a colorless oil (67 mg, 98%); ν_{max} (neat)/cm^{-1} 2924, 2853, 1726, 1681, 1601, 1524, 1497, 1443, 1367, 1358, 1309, 1271, 1195, 1177, 1154, 1120, 1097, 1087, 1069, 1045, 891, 810, 784, 738, 688, 652; δ_H (300 MHz; $CDCl_3$) 1.14-1.40 (8H, m, 4 × CH_2), 1.62-1.72 (8H, m, 4 × CH_2), 1.90 (4H, m, 2 × CH_2), 2.38 (3H, s, CH_3), 3.05 (2H, m, 2 × CH), 5.94 (2H, s, 2 × CH) 7.22 (2H, d, *J* 8.3, 2 × CH), 7.38 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.5 (CH_3), 26.2 (2C, 2 × CH_2), 26.8 (4C, 4 × CH_2), 34.8 (4C, 4 × CH_2), 37.3 (2C, 2 × CH), 109.4 (2C, 2 × CH), 125.5 (2C, 2 ×CH), 129.7

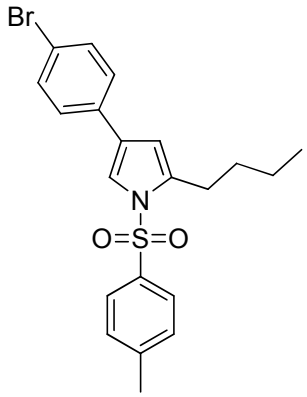
(2C, 2 ×CH), 138.2 (C_{quat}), 143.9 (C_{quat}), 144.0 (2C, 2 × C_{quat}); HRMS *m/z* (TOF ES+) 408.1969. $C_{23}H_{31}NO_2NaS$ requires 408.1973.

2-(4-Bromophenyl)-5-butyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (206)



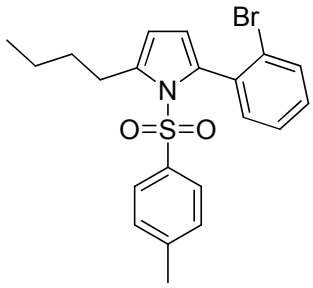
Following GP6 using **188** aziridine (86 mg) at 70 °C for 4 h gave **206** as a brown oil (84 mg, 98%); ν_{max} (neat)/cm^{-1} 3048, 2953, 2929, 2826, 1592, 1368, 1170, 1092, 1023, 810, 750, 732, 650, 660; δ_H (300 MHz; $CDCl_3$) 1.03 (3H, t, *J* 7.3, CH_3), 1.43-1.55 (2H, m, CH_2), 1.70-1.80 (2H, m, CH_2), 2.43 (3H, s, CH_3), 2.97 (2H, t, *J* 7.7, CH_2), 6.10-6.14 (2H, m, 2 × CH), 7.21-7.27 (4H, m, 4 × CH), 7.34 (2H, d, *J* 8.4, 2 × CH), 7.52 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.9 (CH_3), 21.5 (CH_3), 22.5 (CH_2), 29.2 (CH_2), 31.6 (CH_2), 112.8 (CH), 116.1 (CH), 121.9 (C_{quat}), 126.3 (2C, 2 × CH), 129.4 (2C, 2 × CH), 130.4 (2C, 2 × CH), 131.9 (2C, 2 × CH), 132.3 (C_{quat}), 136.2 (C_{quat}), 136.8 (C_{quat}), 140.4 (C_{quat}), 144.4 (C_{quat}); HRMS *m/z* (TOF ES+) 454.0437. $C_{21}H_{22}NO_2NaS^{79}Br$ requires 454.0452.

4-(4-Bromophenyl)-2-butyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (207)



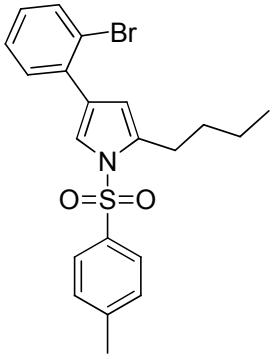
Following GP7 using aziridine **188** (86 mg) for 2 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave a mixture of 2,4-substituted pyrrole **207** and 2,5-substituted pyrrole **206** (63 mg, 74%, 1:1.1 **206**:**207**); ν_{max} (neat)/cm^{-1} 2957, 2928, 2870, 1728, 1596, 1524, 1476, 1465, 1397, 1364, 1302, 1259, 1188, 1168, 1119, 1090, 1071, 1009, 919, 810, 728, 703; HRMS *m/z* (TOF ES+) 454.0446. $C_{21}H_{22}NO_2NaS^{79}Br$ requires 454.0452. **4-(4-Bromophenyl)-2-butyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole 207:** δ_H (300 MHz; $CDCl_3$) 0.97 (3H, t, *J* 7.3, CH_3), 1.39-1.50 (2H, m, CH_2), 1.59-1.69 (2H, m, CH_2), 2.48 (3H, s, CH_3), 2.75 (2H, t, *J* 7.7, CH_2), 6.34 (1H, dt, *J* 1.9 and 1.0, CH), 7.37 (2H, d, *J* 8.4, 2 × CH), 7.43 (2H, d, *J* 8.6, 2 × CH), 7.54 (2H, d, *J* 8.6, 2 × CH), 7.63 (1H, d, *J* 1.9, CH), 7.76 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.9 (CH_3), 21.6 (CH_3), 22.4 (CH_2), 26.9 (CH_2), 30.7 (CH_2), 110.0 (CH), 117.7 (CH), 120.4 (C_{quat}), 126.9 (2C, 2 × CH),126.8 (2C, 2 × CH), 130.0 (2C, 2 × CH), 131.8 (2C, 2 × CH), 132.7 (C_{quat}), 136.2 (C_{quat}), 137.2 (C_{quat}), 140.4 (C_{quat}), 144.9 (C_{quat}).

2-(2-Bromophenyl)-5-butyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (208)



Following GP6 using aziridine **189** (86 mg) at 70 °C for 4 h gave **208** as a brown oil (84 mg, 98%); ν_{max} (neat)/cm^{-1} 3049, 2956, 2928, 2861, 1736, 1597, 1459, 1365, 1170, 1091, 1025, 1095, 810, 755; δ_H (300 MHz; $CDCl_3$) 0.94 (3H, t, *J* 7.3, CH_3), 1.38-1.45 (2H, m, CH_2), 1.62-1.70 (2H, m, CH_2), 2.39 (3H, s, CH_3), 2.80-2.89 (2H, m, CH_2), 6.07 (1H, dt, *J* 3.4 and 1.0, CH), 6.15 (1H, d, *J* 3.4, CH), 7.19-7.30 (4H, m, 4 × CH), 7.42 (2H, d, *J* 8.4, 2 × CH), 7.59 (2H, d, *J* 7.7, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.9 (CH_3), 21.6 (CH_3), 22.5 (CH_2), 28.6 (CH_2), 31.3 (CH_2), 111.4 (CH), 115.7 (CH), 126.0 (C_{quat}), 126.1 (CH), 126.6 (2C, 2 × CH), 129.5 (CH), 129.6 (2C, 2 × CH), 132.2 (CH), 133.1 (CH), 134.6 (2C, 2 × C_{quat}), 136.9 (C_{quat}), 138.7 (C_{quat}), 144.4 (C_{quat}); HRMS *m/z* (TOF ES+) 454.0460. $C_{21}H_{22}NO_2NaS^{79}Br$ requires 454.0452.

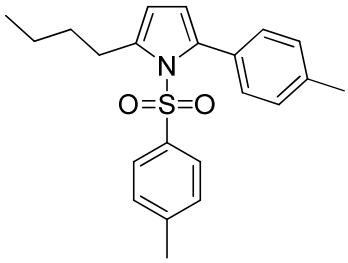
4-(2-Bromophenyl)-2-butyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (209)



Following GP7 using aziridine **189** (86 mg) for 3 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave a mixture of 2,4-substituted pyrrole **209** and 2,5-substituted

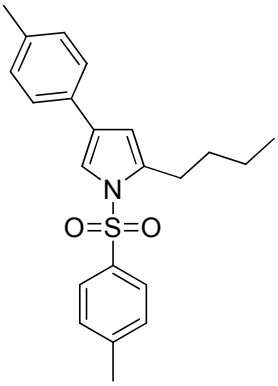
pyrrole **208** (77 mg, 90%, 3:1 **208**:**209**); ν_{max} (neat)/cm^{-1} 3051, 2957, 2928, 2861, 1597, 1527, 1460, 1364, 1170, 1125, 1096, 1025, 908, 810, 755, 729; HRMS *m/z* (TOF ES+) 454.0460. $C_{21}H_{22}NO_2NaS^{79}Br$ requires 454.0452. **4-(2-Bromophenyl)-2-butyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole 209:** δ_H (300 MHz; $CDCl_3$) 0.90 (3H, t, *J* 7.2, CH_3), 1.33-1.45 (2H, m, CH_2), 1.53-1.63 (2H, m, CH_2), 2.42 (3H, s, CH_3), 2.63-2.78 (2H, m, CH_2), 6.28 (1H, m, CH), 7.12 (1H, ddd, *J* 7.9, 1.7, 1.2, CH), 7.19-7.43 (4H, m, 4 × CH, underneath major isomer), 7.60-7.64 (2H, m, 2 × CH), 7.72 (2H, d, *J* 8.4, 2 × CH).

2-Butyl-1-(toluene-4-sulfonyl)-5-*p*-tolyl-1*H*-pyrrole (210)



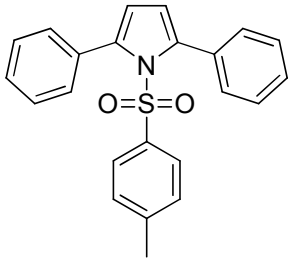
Following GP6 using aziridine **190** (73 mg) at 70 °C for 5 h gave pyrrole **210** as brown oil (71 mg, 98%); ν_{max} (neat)/cm^{-1} 3052, 2958, 2930, 2870, 1738, 1590, 1462, 1369, 1178, 1090, 1028, 1093, 815, 757; δ_H (300 MHz; $CDCl_3$) 0.97 (3H, t, *J* 7.3, CH_3), 1.37-1.49 (2H, m, CH_2), 1.64-1.75 (2H, m, CH_2), 2.44 (3H, s, CH_3), 2.47 (3H, s, CH_3), 2.91 (2H, t, *J* 7.6, CH_2), 6.03 (1H, dt, *J* 3.3 and 1.0, CH), 6.04 (1H, d, *J* 3.3, CH), 7.14-7.16 (4H, m, 4 × CH), 7.23 (2H, d, *J* 8.0, 2 × CH), 7.29 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.9 (CH_3), 21.3 (CH_3), 21.5 (CH_3), 22.5 (CH_2), 29.3 (CH_2), 31.6 (CH_2), 112.6 (CH), 115.3 (CH), 126.3 (2C, 2 × CH), 127.9 (2C, 2 × CH), 129.3 (2C, 2 × CH), 130.3 (2C, 2 × CH), 130.5 (C_{quat}), 136.4 (C_{quat}), 137.5 (C_{quat}), 138.2 (C_{quat}), 139.6 (C_{quat}), 144.1 (C_{quat}); HRMS *m/z* (TOF ES+) 390.1502. $C_{22}H_{25}NO_2NaS$ requires 390.1504.

2-Butyl-1-(toluene-4-sulfonyl)-4-*p*-tolyl-1*H*-pyrrole (211)



Following GP7 using aziridine **190** (74 mg) for 1.5 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave a mixture of 2,4-substituted pyrrole **211** and 2,5-substituted pyrrole **210** (23 mg, 32%, 1:50 **210**:**211**); ν_{max} (neat)/cm^{-1} 3058, 2954, 2921, 1724, 1596, 1490, 1445, 1365, 1161, 1093, 912, 814, 755; HRMS *m/z* (TOF ES+) 368.1691. $C_{22}H_{26}NO_2NaS$ requires 368.1684. **2-Butyl-1-(toluene-4-sulfonyl)-4-*p*-tolyl-1*H*-pyrrole 211:** δ_H (300 MHz; $CDCl_3$) 0.90 (3H, t, *J* 7.3, CH_3), 1.30-1.43 (2H, m, CH_2), 1.53-1.63 (2H, m, CH_2), 2.35 (3H, s, CH_3), 2.40 (3H, s, CH_3), 2.68 (2H, t, *J* 7.4, CH_2), 6.30 (1H, dt, *J* 1.9, 0.9, CH), 7.16 (2H, d, *J* 8.2, 2 × CH), 7.28 (2H, d, *J* 8.4, 2 × CH), 7.40 (2H, d, *J* 8.2, 2 × CH), 7.54 (1H, d, *J* 1.9, CH), 7.68 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.9 (CH_3), 21.1 (CH_3), 21.6 (CH_3), 22.4 (CH_2), 26.9 (CH_2), 30.7 (CH_2), 110.5 (CH), 117.3 (CH), 125.3 (2C, 2 × CH), 126.7 (2C, 2 × CH),129.4 (2C, 2 × CH), 129.9 (2C, 2 × CH), 130.8 (C_{quat}), 136.4 (C_{quat}), 136.5 (2C, 2 × C_{quat}), 136.9 (C_{quat}), 144.7 (C_{quat}).

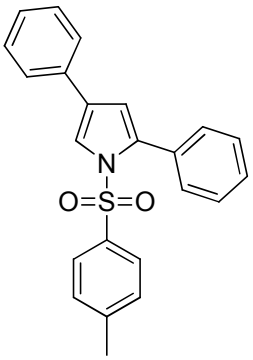
2,5-Diphenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (212)



Following GP6 using aziridine **192** (75 mg) at 70 °C for 3 h gave **212** as a yellow oil (74 mg, 98%); ν_{max} (neat)/cm^{-1} 3048, 2949, 2925, 1717, 1592, 1491, 1437, 1367, 1167, 1088, 914, 812, 754; δ_H (300 MHz; $CDCl_3$) 2.34 (3H, s, CH_3), 6.24 (2H, s, 2 × CH), 7.05 (4H, m, 4 × CH), 7.37-7.44 (6H, m, 6 × CH), 7.50-7.53 (4H, m, 4 × CH); δ_C (75 MHz; $CDCl_3$) 21.5 (CH_3), 117.3 (2C, 2 × CH), 127.0 (4C, 4 × CH), 127.5 (2C, 2 × CH), 127.9 (2C, 2 × CH), 128.7 (4C, 4 × CH), 129.6 (2C, 2 × CH), 133.3 (2C, 2 × C_{quat}), 134.6 (C_{quat}), 141.2 (2C, 2 × C_{quat}), 144.3 (C_{quat}); HRMS *m/z* (TOF ES+) 396.1039. $C_{23}H_{19}NO_2NaS$ requires 396.1034.

Data were in agreement with those reported in the literature.[69]

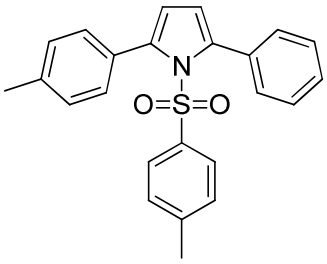
2,4-Diphenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (213)



Following GP7 using aziridine **192** (75 mg) for 1.5 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave a mixture of 2,4-substituted pyrrole **213** and 2,5-substituted pyrrole **212** (74 mg, 98%, 1:6 **212**:**213**); ν_{max} (neat)/cm^{-1} 3061, 3048, 2923, 1725, 1596, 1492,

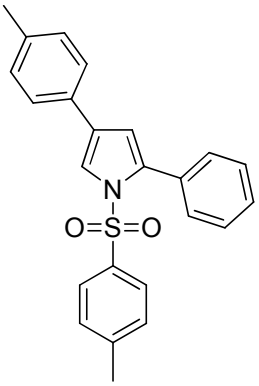
1449, 1363, 1307, 1188, 1168, 1091, 1069, 1046, 1028, 1004, 911, 812, 759; HRMS *m/z* (TOF ES+) 396.1047. $C_{23}H_{19}NO_2NaS$ requires 396.1034. **2,4-Diphenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole 213:** δ_H (300 MHz; $CDCl_3$) 2.34 (3H, s, CH_3), 6.49 (1H, d, *J* 1.6, CH), 7.08 (2H, d, *J* 8.1, 2 × CH), 7.24-7.37 (10H, m, 10 × CH), 7.53 (2H, d, *J* 7.3, 2 × CH), 7.73 (1H, d, *J* 1.6, CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 114.3 (CH), 119.5 (CH), 125.5 (2C, 2 × CH), 127.0 (CH), 127.1 (2C, 2 × CH),127.4 (2C, 2 × CH), 127.5 (C_{quat}), 128.4 (CH), 128.8 (2C, 2 × CH), 129.4 (2C, 2 × CH), 130.8 (2C, 2 × CH), 130.9 (C_{quat}), 132.8 (C_{quat}), 134.9 (C_{quat}), 136.5 (C_{quat}), 144.7 (C_{quat}).

2-Phenyl-1-(toluene-4-sulfonyl)-5-*p*-tolyl-1*H*-pyrrole (214)



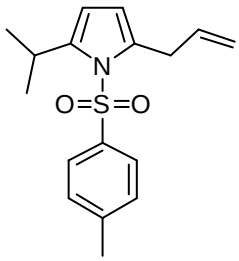
Following GP6 using aziridine **193** (77 mg) at 70 °C for 3.5 h gave **214** as a colourless oil (75 mg, 98%); ν_{max} (neat)/cm^{-1} 3056, 2960, 2937, 1730, 1580, 1491, 1438, 1360, 1167, 1091, 910, 813, 759; δ_H (300 MHz; $CDCl_3$) 2.38 (3H, s, CH_3), 2.41 (3H, s, CH_3), 6.22 (1H, d, *J* 3.9, CH), 6.23 (1H, *J* 3.9, CH), 7.09 (5H, m, 5 × CH), 7.21 (2H, d, *J* 7.8, 2 × CH), 7.23-7.35 (6H, m, 6 × CH); δ_C (75 MHz; $CDCl_3$) 21.4 (CH_3), 21.6 (CH_3), 117.0 (CH), 117.4 (CH), 127.0 (2C, 2 × CH), 127.5 (2C, 2 × CH), 127.8 (CH), 128.3 (2C, 2 × CH), 128.7 (2C, 2 × CH), 129.5 (2C, 2 × CH), 129.6 (2C, 2 × CH), 130.5 (C_{quat}), 133.4 (C_{quat}), 134.6 (C_{quat}), 137.8 (C_{quat}), 140.9 (C_{quat}), 141.4 (C_{quat}), 144.3 (C_{quat}); HRMS *m/z* (TOF ES+) 410.1188. $C_{24}H_{21}NO_2NaS$ requires 410.1191.

2-Phenyl-1-(toluene-4-sulfonyl)-4-*p*-tolyl-1*H*-pyrrole (215)



Following GP7 using aziridine **193** (77 mg) for 30 min. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave 2,4-substituted pyrrole **215** as a light brown oil (50 mg, 65%); ν_{max} (neat)/cm^{-1} 3051, 2950, 2930, 1720, 1590, 1492, 1440, 1360, 1165, 1091, 911, 811, 756; δ_H (300 MHz; $CDCl_3$) 2.33 (3H, s, CH_3), 2.34 (3H, s, CH_3), 6.45 (1H, d, *J* 1.9, CH), 7.07 (2H, d, *J* 8.0, 2 × CH), 7.17 (2H, d, *J* 8.0, 2 × CH), 7.23-7.43 (9H, m, 9 × CH), 7.67 (1H, d, *J* 1.9, CH); δ_C (75 MHz; $CDCl_3$) 21.1 (CH_3), 21.6 (CH_3), 114.4 (CH), 119.2 (CH), 125.4 (2C, 2 × CH), 127.1 (2C, 2 × CH), 127.4 (2C, 2 × CH),127.6 (C_{quat}), 128.3 (CH), 129.4 (2C, 2 × CH), 129.5 (2C, 2 × CH), 130.4 (C_{quat}), 130.8 (2C, 2 × CH), 131.3 (C_{quat}), 135.5 (C_{quat}), 136.8 (C_{quat}), 136.9 (C_{quat}), 144.7 (C_{quat}); HRMS *m/z* (TOF ES+) 410.1177. $C_{24}H_{21}NO_2NaS$ requires 410.1191.

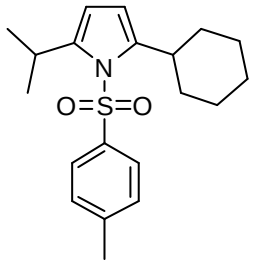
2-Allyl-5-isopropyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (216)



Following GP6 using aziridine **197** at 70 °C for 12 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave **216** as a colourless oil (57 mg, 95%); ν_{max} (neat)/cm^{-1} 3089,

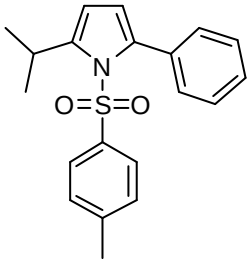
3010, 2967, 2871, 1831, 1635, 1597, 1366, 1179, 1189, 980, 925, 818, 706, 686; δ_H (300 MHz; $CDCl_3$) 1.24 (6H, d, *J* 6.7, 2 × CH_3), 2.44 (3H, s, CH_3), 3.50 (1H, sept, *J* 6.7, CH), 3.60 (2H, dd, 3.6 and 1.1, CH_2), 5.11 (1H, m, CH), 5.16 (1H, m, CH), 5.85-5.99 (2H, m, 2 × CH), 6.05 (1H, d, *J* 3.4, CH), 7.31 (2H, d, *J* 8.2, 2 × CH), 7.50 (2H, d, *J* 8.2, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.5 (CH_3), 24.0 (2C, 2 × CH_3), 27.3 (CH), 33.7 (CH_2), 108.9 (CH), 111.9 (CH), 116.7 (CH_2), 125.7 (2C, 2 × CH), 129.8 (2C, 2 × CH), 135.2 (CH), 135.4 (C_{quat}), 137.7 (C_{quat}), 144.2 (C_{quat}), 145.5 (C_{quat}); HRMS *m/z* (TOF ES+) 326.1198. $C_{17}H_{21}NO_2NaS$ requires 326.1191.

2-cyclohexyl-5-isopropyl-1-(toluene-4-sulfonyl)-1H-pyrrole (217)



Following GP6 using aziridine **199** at 70 °C for 3 h gave **217** as a colorless oil (67 mg, 98%); ν_{max} (neat)/cm^{-1} 2968, 2926, 2853, 1681, 1598, 1528, 1493, 1447, 1370, 1357, 1304, 1193, 1180, 1167, 1142, 1111, 1095, 1060, 1016, 810, 783, 747, 703, 682, 665; δ_H (300 MHz; $CDCl_3$) 1.17 (6H, d, *J* 6.7, 2 × CH_3), 1.21-1.49 (4H, m, 2 × CH_2), 1.52-1.82 (4H, m, 2 × CH_2), 1.91 (2H, d, *J* 12.1, CH_2), 2.38 (3H, s, CH_3), 3.05 (1H, m, CH), 3.42 (1H, sept, *J* 6.7, CH), 5.95 (1H, d, *J* 3.5, CH), 5.98 (1H, d, *J* 3.5, CH), 7.22 (2H, d, *J* 8.4, 2 × CH), 7.28 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.5 (CH_3), 24.0 (2C, 2 × CH_3), 26.2 (CH_2), 26.7 (2C, 2 × CH_2), 27.5 (CH), 34.8 (2C, 2 × CH_2), 37.4 (CH), 109.2 (CH), 109.4 (CH), 125.4 (2C, 2 × CH), 129.7 (2C, 2 × CH), 138.0 (C_{quat}), 144.0 (C_{quat}), 144.5 (C_{quat}), 145.0 (C_{quat}); HRMS *m/z* (TOF ES+) 368.1676. $C_{20}H_{27}NO_2NaS$ requires 368.1660.

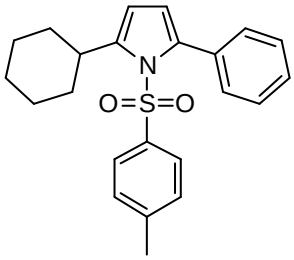
2-isopropyl-5-phenyl-1-(toluene-4-sulfonyl)-1H-pyrrole (218)



Following GP6 using aziridine **195** at room temperature for 12 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave **218** as a yellow oil (64 mg, 95%); ν_{max} (neat)/cm^{-1} 3062, 2953, 2931, 2859, 1731, 1595, 1531, 1481, 1445, 1370, 1168, 1116, 1090, 912, 807, 757; δ_H (300 MHz; $CDCl_3$) 1.29 (6H, d, *J* 6.7, 2 × CH_3), 2.36 (3H, s, CH_3), 3.62 (1H, sept, *J* 6.7, CH), 6.07 (2H, m, 2 × CH), 7.13 (2H, d, *J* 8.4, 2 × CH), 7.25 (2H, d, *J* 8.8, 2 × CH), 7.32 (5H, s, 5 × CH); δ_C (75 MHz; $CDCl_3$) 21.5 (CH_3), 23.8 (2C, 2 × CH_3), 28.1 (CH), 111.0 (CH), 115.9 (CH), 126.2 (2C, 2 × CH), 127.2 (2C, 2 × CH), 127.6 (CH), 129.2 (2C, 2 × CH), 130.2 (2C, 2 × CH), 133.5 (C_{quat}), 136.3 (C_{quat}), 138.8 (C_{quat}), 144.1 (C_{quat}), 147.2 (C_{quat}); HRMS *m/z* (TOF ES+) 362.1186. $C_{20}H_{21}NO_2NaS$ requires 362.1191.

Data were in agreement with those reported in the literature.[69]

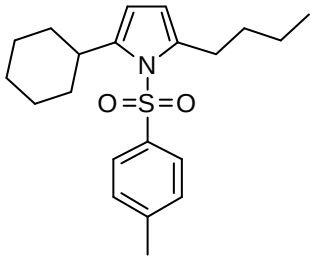
2-Cyclohexyl-5-phenyl-1-(toluene-4-sulfonyl)-1H-pyrrole (219)



Following GP6 using aziridine **196** at room temperature for 12 h gave **219** as a brown solid (74 mg, 98%); mp 143-145 °C; ν_{max} (neat)/cm^{-1} 2929, 2854, 1716, 1598, 1531, 1445, 1363, 1309, 1215, 1196, 1179, 1167, 1091, 1079, 1062, 1049, 1018, 895, 811, 798, 756, 747; δ_H (300 MHz; $CDCl_3$) 1.38-1.68 (4H, m, 2 × CH_2), 1.90-2.01 (4H, m, 2 × CH_2), 2.24-2.30 (2H, m, CH_2), 2.52 (3H, s, CH_3), 3.42 (1H, t, *J* 11.2, CH), 6.20 (1H, dd, *J* 3.3 and 0.8, CH), 6.24 (1H, d, *J* 3.3, CH), 7.29 (2H, d, *J* 8.1, 2 × CH), 7.41 (2H, d, *J* 8.1, 2 × CH), 7.48 (5H, s, 5 × CH); δ_C (75 MHz; $CDCl_3$) 21.5 (CH_3), 26.5 (CH_2), 26.7 (2C, 2 × CH), 34.6 (2C, 2 × CH_2), 37.9 (CH), 111.0 (CH), 115.9 (CH), 126.2 (2C, 2 × CH), 127.2 (2C, 2 × CH), 127.6 (CH), 129.2 (2C, 2 ×CH), 130.2 (2C, 2 × CH), 133.5 (C_{quat}), 136.4 (C_{quat}), 138.4 (C_{quat}), 144.1 (C_{quat}), 146.2 (C_{quat}); HRMS *m/z* (TOF ES+) 376.1350. $C_{23}H_{25}NO_2NaS$ requires 376.1347.

Data were in agreement with those reported in the literature.[69]

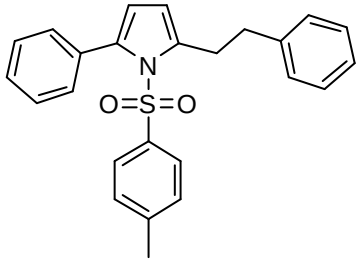
2-Butyl-5-cyclohexyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (220)



Following GP6 using aziridine **191** at 70 °C for 4 h gave **220** as a brown oil (70 mg, 98%); ν_{max} (neat)/cm^{-1} 2925, 2855, 1740, 1681, 1601, 1528, 1493, 1448, 1369, 1359, 1340, 1192, 1174, 1152, 1117, 1093, 892, 810, 770, 751, 722, 665; δ_H (300 MHz; $CDCl_3$) 0.99 (3H, t, *J* 7.3, CH_3), 1.15-1.38 (4H, m, 4 × CH_2), 1.61-1.70 (6H, m, 3 × CH_2), 1.85 (2H, m, CH_2), 2.02 (2H, d, *J* 12.3, CH_2), 2.48 (3H, s, CH_3), 2.83 (2H, t, *J* 12.3, CH_2), 3.18 (1H, m, CH), 6.02 (1H, d, *J* 3.5, CH), 6.04 (1H, d, *J* 3.5, CH), 7.34 (2H, d, *J* 8.4, 2 × CH), 7.52 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.9 (CH_3), 21.6 (CH_3), 22.4 (CH_2), 26.2 (CH_2), 26.7 (2C, 2 × CH_2), 28.8 (CH_2), 31.1 (CH_2), 34.8 (2C, 2 × CH_2), 37.2 (CH), 109.0 (CH), 111.0 (CH), 125.6 (2C, 2 × CH), 129.7 (2C, 2 × CH), 137.7 (C_{quat}), 138.0 (C_{quat}), 144.0 (C_{quat}), 144.2 (C_{quat}); HRMS *m/z* (TOF ES+) 382.1828. $C_{21}H_{29}NO_2NaS$ requires 382.1817.

Data were in agreement with those reported in the literature.[69]

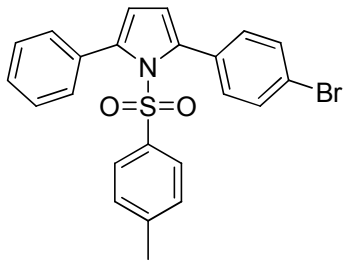
2-phenethyl-5-phenyl-1-(toluene-4-sulfonyl)-1H-pyrrole (221)



Following GP6 using aziridine **200** at 70 °C for 4 h. Purification by flash chromatography [hexane:ethylacetate (20:1)] gave **221** as a yellow oil (76 mg, 95%); ν_{max} (neat)/cm^{-1} 3027,

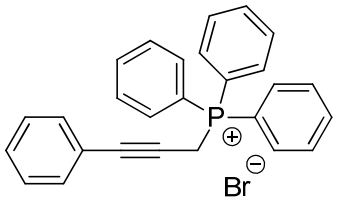
2920, 2851, 1596, 1494, 1452, 1363, 1295, 1170, 1098, 1071, 1028, 908, 809, 759, 729, 694; δ_H (300 MHz; $CDCl_3$) 2.38 (3H, s, CH_3), 3.05-3.10 (2H, m, CH_2), 3.23-3.28 (2H, m, CH_2), 6.06 (1H, d, *J* 3.3, CH), 6.09 (1H, d, *J* 3.3, CH), 7.15 (2H, d, *J* 8.3, 2 × CH), 7.21-7.33 (7H, m, 7 × CH), 7.35 (5H, m, 5 × CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 31.8 (CH_2), 36.3 (CH_2), 113.5 (CH), 115.6 (CH), 126.0 (CH), 126.4 (2C, 2 × CH), 127.2 (2C, 2 × CH), 127.8 (CH), 128.3 (2C, 2 × CH), 128.5 (2C, 2 × CH), 129.3 (2C, 2 × CH), 130.5 (2C, 2 × CH), 133.2 (C_{quat}), 136.2 (C_{quat}), 138.4 (C_{quat}), 138.8 (C_{quat}), 141.5 (C_{quat}), 144.3 (C_{quat}); HRMS *m/z* (TOF ES+) 424.1340. $C_{25}H_{23}NO_2NaS$ requires 424.1347.

2-(4-bromophenyl)-5-phenyl-1-(toluene-4-sulfonyl)-1H-pyrrole (222)



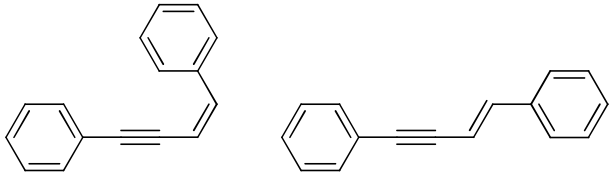
Following GP6 using aziridine **201** at 70 °C for 3 h gave pyrrole **222** as a brown oil (88 mg, 98%); ν_{max} (neat)/cm^{-1} 2233, 1705, 1596, 1439, 1371, 1176, 1092, 920, 810, 729, 703; δ_H (300 MHz; $CDCl_3$) 2.38 (3H, s, CH_3), 6.26 (2H, d, *J* 3.5, 2 × CH), 7.05-7.12 (4H, m, 4 × CH), 7.28-7.55 (9H, m, 9 × CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 117.3 (CH), 118.3 (CH), 126.8 (2C, 2 × CH), 127.6 (2C, 2 × CH), 127.8 (C_{quat}), 128.7 (2C, 2 × CH), 128.8 (2C, 2 × CH), 128.9 (2C, 2 × CH), 129.5 (2C, 2 × CH), 133.0 (C_{quat}), 133.4 (CH), 134.3 (C_{quat}), 134.8 (C_{quat}), 139.2 (C_{quat}), 141.9 (C_{quat}), 144.7 (C_{quat}); HRMS *m/z* (TOF ES+) 474.0144. $C_{23}H_{18}NO_2NaS^{79}Br$ requires 474.0139.

(3-phenyl-1,2-propandienyl)triphenylphosphonium bromide (223)



Triphenylphosphine (10.5 mmol, 2.75 g) was added to a solution of bromide **173** (10.5 mmol, 2.04 g) in toluene (45 mL) and the reaction mixture was heated at 75 °C. After 12 h stirring was pursued at room temperature for 1 h. The solid was filtered off, washed with *n*-pentane (4 × 15 mL) and dried to give phosphonium bromide **223** as a white solid (3.93 g, 82 %); mp 180-181 ºC; ν_{max} (neat)/cm^{-1} 2987, 2901, 2803, 1585,1487, 1455, 1440, 1394, 1380, 1108, 1066, 993, 906; δ_H (300 MHz; $CDCl_3$) 5.19 (2H, d, *J* 15.1, CH_2), 6.95-7.20 (4H, m, 4 × CH), 7.45-7.70 (16H, m, 16 × CH); δ_C (75 MHz; $CDCl_3$) 20.2 (CH_2), 80.0 (C_{quat}), 81.2 (C_{quat}), 118.0 (3 × C_{quat}), 128.4 (2C, 2 × CH), 129.0 (C_{quat}), 130.3 (6C, 6 × CH), 131.5 (CH), 134.0 (2C, 2 × CH), 134.1 (6C, 6 × CH), 135.3 (3C, 3 × CH).

Mixture of (*E*)- and (*Z*)-But-1-en-3-yne-1,4-dibenzene (224)

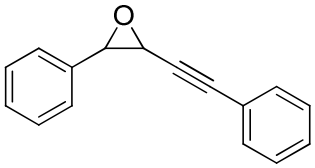


n-BuLi (3.28 mmol, 1.32 mL of a 2.5M solution in hexane) was added dropwise to a solution of phosphonium bromide **223** (3.28 mmol, 1.51 g) in THF (40 mL) at 0 ºC. The reaction mixture was cooled down to -78 ºC and was stirred 30 min. Benzaldehyde (3.28 mmol, 0.35 mL) was added dropwise and the reaction mixture was stirred at room temperature for 12 h. NH_4Cl solution (20 mL) was added to quench the reaction and the THF was removed under reduced pressure. CH_2Cl_2 (20 mL) was added and the phases were separated. The aqueous

phase was washed with CH_2Cl_2 (3 × 20 mL) and the combined organic extracts were washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification by flash chromatography of the residue gave enyne **224** as a yellow solid (422 mg, 63%, 2:1 *E*:*Z*); ν_{max} (neat)/cm^{-1} 3058, 3026, 2190, 1948,1879, 1593, 1487, 1440, 1119, 1069, 1027, 950, 913, 782, 747, 721, 686; δ_H (300 MHz; $CDCl_3$) 5.92 (1H, d, *J* 12.0, CH, from *Z* isomer), 6.39 (1H, d, *J* 16.1, CH, from *E* isomer), 6.70 (1H, d, *J* 12.0, CH, from *Z* isomer), 7.05 (1H, d, *J* 16.1, CH, from *E* isomer), 7.25-7.55 (18H, m, 18 × CH), 7.93 (2H, d, *J* 7.6, 2 × CH, from *Z* isomer); δ_C (75 MHz; $CDCl_3$) 141.3 (CH, from *E* isomer), 138.7 (CH, from *Z* isomer), 136.6 (C_{quat}, CH, from *Z* isomer), 136.4 (C_{quat}, from *E* isomer), 131.5 (2C, 2 × CH, from *E* isomer), 131.4 (2C, 2 × CH, from *Z* isomer), [128.7-128.1] (18C, unidentified), 126.3 (2C, 2 × CH, CH from *Z* isomer and CH, from *E* isomer), 108.2 (CH, from *E* isomer), 107.4 (CH, CH, from *Z* isomer), 91.8 (C_{quat}, from *Z* isomer), 88.9 (C_{quat}, from *E* isomer), 88.3 (C_{quat}, from *E* isomer), 87.7 (C_{quat}, from *Z* isomer).

Data were in agreement with those reported in the literature.[101]

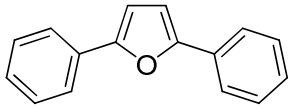
2-Phenyl-3-(phenylethynyl)oxirane (225)



mCPBA (4.1 mmol, 1.09 g of a 77% mixture with water) was added in one portion to a solution of enyne **224** (2 mmol, 408 mg) and $NaHCO_3$ (6.2 mmol, 521 mg) in CH_2Cl_2 (10 mL). The reaction mixture was stirred 12 h at room temperature. Water was then added and the phases were separated. The aqueous phase was washed with CH_2Cl_2 (3 × 10 mL) and the combined organic extracts were washed with brine (10 mL), dried (Na_2SO_4) and concentrated

under reduced pressure. Purification of the residue by flash chromatography [hexane:ethylacetate (90:1)] gave oxirane **225** as a white solid (220 mg, 50%, *cis*: *trans* 1:1.2); ***cis*-2-Phenyl-3-(phenylethynyl)oxirane**: δ_H (300 MHz; $CDCl_3$) 3.60 (1H, d, *J* 2.1, CH), 4.17 (1H, d, *J* 2.1, CH), 7.30-7.52 (10H, m, 10 × CH); δ_C (75 MHz; $CDCl_3$) 49.9 (CH), 60.4 (CH), 83.9 (C_{quat}), 85.3 (C_{quat}), 121.9 (C_{quat}), 125.6 (2C, 2 × CH), 128.4 (2C, 2 × CH), 128.6 (2C, 2 × CH), 128.8 (CH), 128.9 (CH), 132.0 (2C, 2 × CH), 135.8 (C_{quat}). ***trans*-2-Phenyl-3-(phenylethynyl)oxirane**: δ_H (300 MHz; $CDCl_3$) 3.99 (1H, d, *J* 4.3, CH), 4.25 (1H, d, *J* 4.3, CH), 7.33-7.54 (10H, m, 10 × CH); δ_C (75 MHz; $CDCl_3$) 48.7 (CH), 59.3 (CH), 83.7 (C_{quat}), 86.1 (C_{quat}), 122.0 (C_{quat}), 127.0 (2C, 2 × CH), 127.9 (2C, 2 × CH), 128.3 (2C, 2 × CH), 128.5 (CH), 128.8 (CH), 131.9 (2C, 2 × CH), 134.3 (C_{quat}).

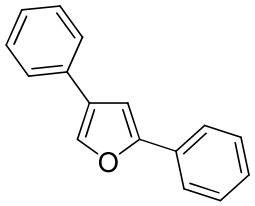
2,5-diphenylfuran (226)



Following GP6 using oxirane **225** (44 mg) at 70 °C for 4 h. Purification by flash chromatography [hexane:ethylacetate (4:1)] gave **226** as a colourless oil (12 mg, 27%); ν_{max} (neat)/cm^{-1} 3120, 3004, 2960, 1730, 1602, 1532, 1475, 1266, 1080, 980, 932, 852, 796; δ_H (300 MHz; $CDCl_3$) 6.75 (2H, s, 2 × CH), 7.26-7.30 (2H, m, 2 × CH), 7.38-7.44 (4H, m, 4 × CH), 7.72-7.79 (4H, m, 4 × CH); δ_C (75 MHz; $CDCl_3$) 107.2 (2C, 2 × CH), 123.7 (4C, 4 × CH), 127.4 (2C, 2 × CH), 128.7 (4C, 4 × CH), 130.8 (2C, 2 × C_{quat}), 153.4 (2C, 2 × C_{quat}).

Data was in agreement with the one reported in the literature.[102]

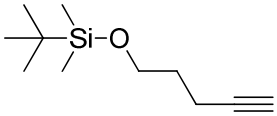
2,4-diphenyl (227)



Following GP7 using oxirane **225** (44 mg) for 15 min. Purification by flash chromatography [hexane:ethylacetate (4:1)] gave a mixture of 2,4-substituted furan **227** and 2,5-substituted furan **226** (8 mg, 19%, 1:3 **226**:**227**); ν_{max} (neat)/cm^{-1} 3130, 3012, 2933, 2902, 1740, 1609, 1482, 1230, 1152, 1075, 998, 956, 810, 789; δ_H (300 MHz; $CDCl_3$) 6.90 (1H, s, CH), 7.18-7.40 (6H, m, 6 × CH), 7.41-7.73 (5H, m, 5 × CH); δ_C (75 MHz; $CDCl_3$) 104.0 (CH), 123.9 (C_{quat}), 125.8 (2C, 2 × CH), 127.1 (2C, 2 × CH), 127.6 (2C, 2 × CH), 128.4 (2C, 2 × CH), 128.7 (CH), 128.8 (CH), 130.7 (CH), 132.4 (C_{quat}), 137.9 (C_{quat}), 154.9 (C_{quat}).

Data was in agreement with the one reported in the literature.[103]

***tert*-butyldimethyl(pent-4-ynyloxy)silane (230)**

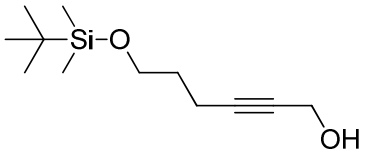


TBDMSCl (11 mmol, 1.66 g) was added to a solution of pent-4-yn-1-ol (10 mmol, mL), DMAP (0.1 mmol, 12 mg) and triethylamine (22 mmol, 3.0 mL) in CH_2Cl_2 (50 mL). The reaction mixture was stirred at room temperature for 48 h. A NH_4Cl solution (20 mL) was added to quench the reaction and the two phases were separated. The aqueous phase was washed with CH_2Cl_2 (3 × 15 mL) and the combined organic extracts were washed with brine (15 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography [hexane:ethylacetate (4:1)] to give silyl ether **230** as a colourless oil

(1.95 g, 99%); ν_{max} (neat)/cm^{-1} 3315, 2958, 2935, 2870, 1530, 1479, 1430, 1356, 1280, 1262, 1104, 979, 844, 802, 795; δ_H (300 MHz; $CDCl_3$) 0.04 (6H, s, 2 × CH_3), 0.89 (9H, s, 3 × CH_3), 1.71 (2H, tt, *J* 7.1 and 6.1, CH_2),1.91 (1H, t, *J* 2.8, CH), 2.26 (2H, td, *J* 7.1 and 2.8, CH_2), 3.68 (2H, t, *J* 6.1, CH_2); δ_C (75 MHz; $CDCl_3$) -5.4 (2C, 2 × CH_3), 14.8 (CH_2), 18.3 (C_{quat}), 25.9 (3C, 3 × CH_3), 31.5 (CH_2), 61.5 (CH_2), 68.2 (C_{quat}), 84.2 (CH).

Data were in agreement with those reported in the literature.[104]

6-(*tert*-butyldimethylsilyloxy)hex-2-yn-1-ol (231)

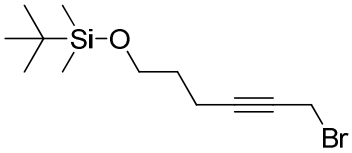


n-BuLi (10 mmol, 4.0 mL of a 2.5M solution in hexane) was added dropwise to a solution of silylether **230** (10 mmol) in THF (40 mL) at -78 ºC. The reaction mixture was stirred 30 min at -78 ºC before paraformaldehyde (10 mmol, 300 mg) was added. The temperature was raised to room temperature and the reaction mixture stirred for 12 h. NH_4Cl solution (20 mL) was added to quench the reaction and the THF was removed under reduced pressure. Et_2O (20 mL) was added and the phases were separated. The aqueous phase was washed with Et_2O (3 × 20 mL) and the combined organic extracts were washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the residue by flash chromatography [hexane:ethylacetate (2:1)] gave alcohol **231** as a colourless oil (1.82 g, 80%); ν_{max} (neat)/cm^{-1} 3345, 2956, 2935, 2853, 1478, 1389, 1364, 1307, 1260, 1108, 983, 850, 812; δ_H (300 MHz; $CDCl_3$) 0.04 (6H, s, 2 × CH_3), 0.88 (9H, s, 3 × CH_3), 1.70 (2H, tt, *J* 7.0 and 6.1, CH_2), 2.16 (1H, s, OH), 2.28 (2H, tt, *J* 7.1 and 2.1, CH_2), 3.67 (2H, t, *J* 6.1, CH_2), 4.21 (2H, t, *J* 2.1,

CH_2); δ_C (75 MHz; $CDCl_3$) -5.4 (2C, 2 × CH_3), 15.1 (CH_2), 18.3 (C_{quat}), 25.9 (3C, 3 × CH_3), 31.5 (CH_2), 51.1 (CH_2), 61.5 (CH_2), 78.4 (C_{quat}), 85.9 (C_{quat}).

Data were in agreement with those reported in the literature.[104]

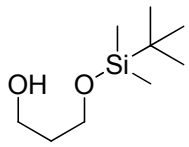
(6-bromohex-4-ynyloxy)*tert*-butyldimethylsilane (232)



To a solution of PPh_3 (8.7 mmol, 2.28 g) in CH_2Cl_2 (25 mL) at 0 °C was added Br_2 (8.6 mmol, 0.43 mL) dropwise. The reaction mixture was stirred for 30 min at 0 °C before a solution of alcohol **231** (7.9 mmol, 1.82 g) in CH_2Cl_2 (10 mL) was added dropwise. The reaction mixture was warmed to room temperature and stirred for 1h. Water (25 mL) was added to quench the reaction and the two phases were separated. The aqueous phase was washed with CH_2Cl_2 (3 × 20 mL) and the combined organic extracts were washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the residue by flash chromatography [hexane:ethylacetate (15:1)] gave bromide **232** as a yellow oil (2.07g, 90%); ν_{max} (neat)/cm^{-1} 3009, 2966, 2856, 2241, 1532, 1480, 1359, 1258, 1208, 1116, 1106, 932, 875, 810; δ_H (300 MHz; $CDCl_3$) 0.05 (6H, s, 2 × CH_3), 0.89 (9H, s, 3 × CH_3), 1.70 (2H, tt, *J* 7.0 and 6.1, CH_2), 2.32 (2H, tt, *J* 7.0 and 2.2, CH_2), 3.68 (2H, t, *J* 6.1, CH_2), 3.91 (2H, t, *J* 2.2, CH_2); δ_C (75 MHz; $CDCl_3$) -5.4 (2C, 2 × CH_3), 15.3 (CH_2), 15.6 (CH_2), 18.3 (C_{quat}), 25.9 (3C, 3 × CH_3), 31.3 (CH_2), 61.4 (CH_2), 75.4 (C_{quat}), 87.8 (C_{quat}).

Data were in agreement with those reported in the literature.[104]

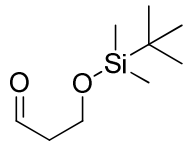
3-(*tert*-butyldimethylsilyloxy)propan-1-ol (228)



TBDPSCl (7.6 mmol, 1.15 g) was added to a solution of 1,3-propandiol (30 mmol, 2.75 mL), DMAP (0.38 mmol, 46 mg) and triethylamine (15.2 mmol, 2.1 mL) in CH_2Cl_2 (100 mL). The reaction mixture was stirred at room temperature for 48 h. A NH_4Cl solution (40 mL) was added to quench the reaction and the two phases were separated. The aqueous phase was washed with CH_2Cl_2 (3 × 20 mL) and the combined organic extracts were washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography [hexane:ethylacetate (4:1)] to give alcohol **228** as a colourless oil (1.15 g, 80%); ν_{max} (neat)/cm^{-1} 2990, 2982, 1474, 1366, 1216, 1105, 1092, 762, 705; δ_H (300 MHz; $CDCl_3$) 0.08 (6H, s, 2 × CH_3), 0.90 (9H, s, 3 × CH_3), 1.77 (2H, quint, *J* 5.8, CH_2), 3.81-3.84 (4H, m, 2 × CH_2); δ_C (75 MHz; $CDCl_3$) -5.4 (2C, 2 × CH_3), 18.3 (C_{quat}), 25.9 (3C, 3 × CH_3), 34.1 (CH_2), 62.5 (CH_2), 63.0 (CH_2).

Data were in agreement with those reported in the literature.[105]

3-(*tert*-butyldimethylsilyloxy)propanal (229)

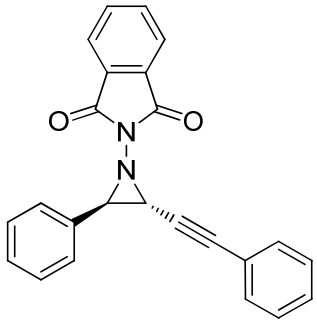


A solution of DMP (7.3 mmol, 3.10 g) in CH_2Cl_2 (10 mL) was added to a solution of alcohol **228** (6.08 mmol, 1.15 g) in CH_2Cl_2 (50 mL) at room temperature. After stirring 2 h, $Na_2S_2O_3$ solution (15 mL) was added to quench the reaction. The two phases were separated and the aqueous phase was washed with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were

washed with brine (15 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography [hexane:ethylacetate (20:1)] to give alcohol **229** as a colourless oil (973 mg, 85%); ν_{max} (neat)/cm^{-1} 2960, 2941, 2875, 2735, 1727, 1530, 1478, 1390, 1260, 1163, 1105, 978, 826, 803, 770; δ_H (300 MHz; $CDCl_3$) 0.02 (6H, s, 2 × CH_3), 0.85 (9H, s, 3 × CH_3), 2.55 (2H, td, *J* 6.0 and 2.1, CH_2), 3.95 (2H, t, *J* 6.0, 2 × CH), 9.76 (1H, t, *J* 2.1, CH); δ_C (75 MHz; $CDCl_3$) -5.5 (2C, 2 × CH_3), 18.1 (C_{quat}), 25.7 (3C, 3 × CH_3), 46.5 (CH_2), 57.3 (CH_2), 201.8 (C_{quat}).

Data were in agreement with those reported in the literature[106]

trans-2-Phenyl-3-(phenylethynyl)aziridin-1-yl)isoindoline-1,3-dione (233)

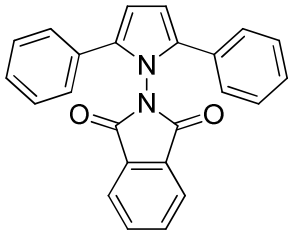


A solution of $(PbOAc)_4$ (4 mmol, 1.77 g) in CH_2Cl_2 (10 mL) was added over 20 min to a mixture of enyne **224** (2 mmol, 408 mg), *N*-aminophthalimide (4 mmol, 648 mg) and K_2CO_3 (20 mmol, 2.76 g) in CH_2Cl_2 (50 mL) at 0 °C. The reaction mixture was then stirred 12 h at room temperature. Water (15 mL) was added to quench the reaction and the phases were separated. The aqueous phase was washed with CH_2Cl_2 (3 × 20 mL) and the combined organic extracts were washed with brine (30 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the residue by flash chromatography [hexane:ethylacetate (5:1)] gave *trans*-aziridine **233** as a yellow solid (480 mg, 60%); mp 112-114 °C; ν_{max}

(neat)/cm^{-1} 3063, 2250, 1735, 1605, 1532, 1376, 1136, 1055, 963, 870, 865, 732; δ_H (300 MHz; $CDCl_3$) 3.56 (1H, d, *J* 5.1, CH), 4.48 (1H, d, *J* 5.1, CH), 7.20-7.30 (5H, m, 5 × CH), 7.36-7.43 (3H, m, 3 × CH), 7.47-7.50 (2H, m, 2 × CH), 7.69-7.72 (2H, m, 2 × CH), 7.82-7.84 (2H, m, 2 × CH); δ_C (75 MHz; $CDCl_3$) 40.6 (CH), 50.9 (CH), 82.8 (C_{quat}), 85.7 (C_{quat}), 121.8 (2C, 2 × C_{quat}), 123.1 (2C, 2 × CH), 127.0 (2C, 2 × CH), 128.2 (2C, 2 × CH), 128.4 (CH), 128.6 (2C, 2 × CH), 130.2 (2C, 2 × CH), 131.6 (2C, 2 × CH_2), 134.1 (2C, 2 × C_{quat}), 135.0 (CH), 165.3 (2C, 2 × C_{quat}).

Data were in agreement with those reported in the literature.[107]

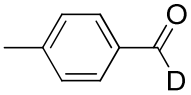
2-(2,5-diphenyl-1H-pyrrol-1-yl)isoindoline-1,3-dione (234)



Following GP7 using alkynyl aziridine **233** at 70 °C for 12 h. Purification by flash chromatography [hexane:ethylacetate (4:1)] gave **234** as a yellow solid (3 mg, 5%); mp 170-172 °C; δ_H (300 MHz; $CDCl_3$) 6.51 (2H, s, 2 × CH), 7.20-7.23 (2H, m, 2 × CH), 7.25-7.30 (4H, m, 4 × CH), 7.42-7.46 (4H, m, 4 × CH), 7.65-7.70 (2H, m, 2 × CH), 7.76-7.80 (2H, m, 2 × CH); δ_C (75 MHz; $CDCl_3$) 109.3 (2C, 2 × CH), 124.1 (2C, 2 × CH), 127.8 (2C, 2 × CH), 127.9 (4C, 4 × CH), 128.6 (4C, 4 × CH), 129.1 (2C, 2 × C_{quat}), 131.0 (2C, 2 × C_{quat}), 134.7 (2C, 2 × CH), 137.6 (2C, 2 × C_{quat}), 165.1 (2C, 2 × C_{quat}).

Data was in agreement with the one reported in the literature.[107]

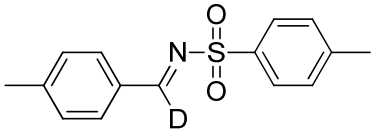
4-methylbenzaldehyde-α-*d* (235)



Ethyl 4-methylbenzoate (2.5 mmol, 0.39 mL) was added to a suspension of $LiAlD_4$ (3.5 mmol, 147 mg) in Et_2O (5 mL) at 0 °C.The reaction mixture was stirred at room temperature for 1 h. After cooling down to 0 °C water (2.5 mL) was added to quench the reaction. A solution of HCl (10%, 2.5 mL) was added to solubilise the suspension and the two phases were separated. The aqueous phase was washed with Et_2O (3 × 10 mL). The combined organic abstracts were wased with brine (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure to give 4-methylbenzyl alcohol-α,α-*d*.

A solution of the crude deuterated alcohol in CH_2Cl_2 (2 mL) was added to a solution of DMP (3 mmol, 1.26 g) in CH_2Cl_2 (5 mL). The reaction mixture was stirred at room temperature for 2 h and a solution of $Na_2S_2O_3$ (5 mL) was added to quench the reaction. The two phases were separated and the aqueous phase was washed with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by distillation under reduced pressure (78 °C at 10 mmHg) to give aldehyde **235** as a colourless liquid (455 mg, 85%); δ_H (300 MHz; $CDCl_3$) 2.43 (3H, s, CH_3), 7.30 (2H, d, *J* 7.9, 2 × CH), 7.75 (2H, d, *J* 7.9, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.9 (CH_3), 129.7 (2C, 2 × CH), 129.9 (2C, 2 × CH), 134.2 (C_{quat}), 145.5 (C_{quat}).

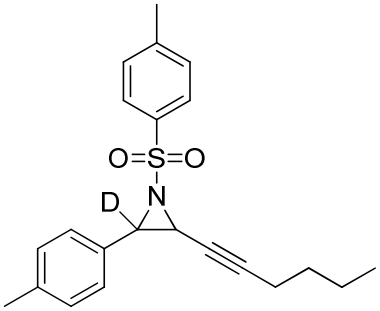
***N*-(Deuteriophenylmethylene)-4-methylbenzenesulfonamide (236)**



A mixture of 4-methylbenzaldehyde-α-*d* (2 mmol, 428 mg), *p*-toluenesulfonamide (1.9 mmol, 325 mg), amberlyst (150 mg) and 4Å molecular sieve (150 mg) in toluene was stirred at 130

°C in a Dean-stark apparatus. After 12h, the reaction mixture was cooled down to room temperature and filtered. The filtrate was concentrated under reduced pressure and the residue was recristalised (ethyl acetate/n-pentane) to give imine **236** as a white solid (383 mg, 70%); 99-100 °C; ν_{max} (neat)/cm^{-1} 3356, 3260, 1582, 1552, 1508, 1494, 1445, 1409, 1387, 1318, 1303, 1288, 1155, 1089, 1033, 1018, 905, 858, 821, 809, 785, 753, 705; δ_H (300 MHz; $CDCl_3$) 2.43 (6H, s, 2 × CH_3), 7.28 (2H, d, *J* 7.9, 2 × CH), 7.34 (2H, d, *J* 7.9, 2 × CH), 7.81 (2H, d, *J* 8.2, 2 × CH), 7.88 (2H, d, *J* 8.2, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 22.0 (CH_3), 128.0 (2C, 2 × CH), 129.8 (2C, 2 × CH), 129.9 (2C, 2 × CH), 131.4 (2C, 2 × CH), 135.5 (C_{quat}), 144.4 (2C, 2 × C_{quat}), 146.4 (2C, 2 × C_{quat}); HRMS *m/z* (TOF ES+) 297.0791. $C_{15}H_{14}DNO_2NaS$ requires 297.0784.

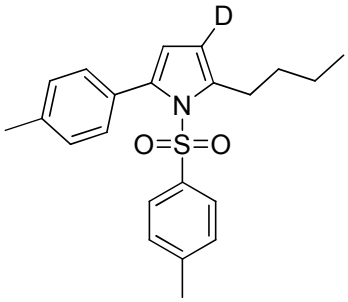
2-Deuterio-3-Hex-1-ynyl-1-(toluene-4-sulfonyl)-2-*p*-tolylaziridine (237)



Following GP 3 using imine **236** and sulfonium salt **180** for 3 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave aziridine **237** as a beige solid (143 mg, 77%, 12:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 2961, 2926, 2874, 2248, 1921, 1598, 1518, 1458, 1410, 1363, 1323, 1301, 1181, 1161, 1133, 1090, 1019, 914, 894, 838, 805, 757, 704; δ_H (300 MHz; $CDCl_3$) 0.76 (3H, t, *J* 7.2, CH_3), 1.05-1.18 (2H, m, CH_2), 1.22-1.31 (2H, m, CH_2), 2.02 (2H, td, *J* 6.9 and 1.8, CH_2), 2.32 (3H, s, CH_3), 2.43 (3H, s, CH_3), 3.60 (1H, t, *J* 1.8, CH), 7.09 (2H, d, *J* 8.1, 2 × CH), 7.21 (2H, d, *J* 8.1, 2 × CH), 7.33 (2H, d, *J* 8.4, 2 × CH), 7.87 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.4 (CH_3), 18.3 (CH_2), 21.2 (CH_3), 21.5 (CH_2), 21.6 (CH_3),

30.0 (CH_2), 36.1 (CH), 72.3 (C_{quat}), 86.6 (C_{quat}), 127.6 (2C, 2 × CH), 127.9 (2C, 2 × CH), 128.6 (2C, 2 × CH), 129.1 (C_{quat}), 129.7 (2C, 2 × CH), 134.8 (C_{quat}), 138.0 (C_{quat}), 144.7 (C_{quat}); HRMS *m/z* (TOF ES+) 391.1563. $C_{22}H_{24}DNO_2NaS$ requires 391.1566.

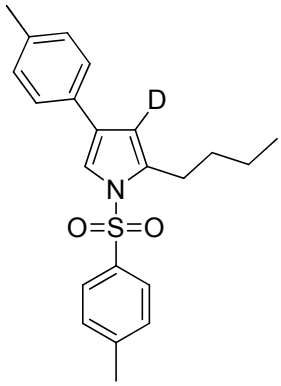
Mixture of 2-butyl-3-deuterio-1-(toluene-4-sulfonyl)-5-*p*-tolyl-1*H*-pyrrole (205) and 2-Butyl-1-(toluene-4-sulfonyl)-5-*p*-tolyl-1*H*-pyrrole (210)



Following GP 6 using aziridine **237** (0.2 mmol, 70 mg) for 2.5 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave a mixture of deuterated pyrrole **205**, pyrrole **210** and deuterated pyrrole **238** as a colourless oil (69 mg, 84%, **205**:**210**:**238** 49:38:1); ν_{max} (neat)/cm^{-1} 2956, 2927, 2862, 1597, 1529, 1494, 1455, 1405, 1367, 1291, 1187, 1172, 1092, 1017, 810, 703, 660; HRMS *m/z* (TOF ES+) 391.1572. $C_{22}H_{24}DNO_2NaS$ requires 391.1566.

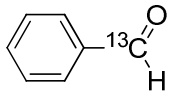
2-butyl-3-deuterio-1-(toluene-4-sulfonyl)-5-*p*-tolyl-1*H*-pyrrole 205: δ_H (300 MHz; $CDCl_3$) 0.96 (3H, t, *J* 7.3, CH_3), 1.36-1.49 (2H, m, CH_2), 1.64-1.74 (2H, m, CH_2), 2.37 (3H, s, CH_3), 2.39 (3H, s, CH_3), 2.90 (2H, t, *J* 7.7, CH_2), 6.04 (1H, s, CH), 7.12-7.16 (4H, m, 4 × CH), 7.23 (2H, d, *J* 8.0, 2 × CH), 7.29 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.9 (CH_3), 21.3 (CH_3), 21.5 (CH_3), 22.5 (CH_2), 29.3 (CH_2), 31.6 (CH_2), 115.2 (CH), 126.3 (2C, 2 × CH), 127.9 (2C, 2 × CH), 129.3 (2C, 2 × CH), 130.3 (2C, 2 × CH), 130.5 (C_{quat}), 136.4 (C_{quat}), 137.5 (C_{quat}), 138.2 (C_{quat}), 139.6 (C_{quat}), 144.1 (C_{quat}).

2-butyl-3-deuterio-1-(toluene-4-sulfonyl)-4-*p*-tolyl-1*H*-pyrrole (239)



Following GP7 using aziridine **237** (74 mg) for 1 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave a mixture of 2,4-substituted pyrrole **239**, 2,4-substituted pyrrole **211** and 2,5-substituted pyrrole **210** (13 mg, 18%, 10.5:3.1:1 **239**:**211**:**210**); δ_H (300 MHz; $CDCl_3$) 0.90 (3H, t, *J* 7.3, CH_3), 1.30-1.43 (2H, m, CH_2), 1.53-1.64 (2H, m, CH_2), 2.35 (3H, s, CH_3), 2.40 (3H, s, CH_3), 2.68 (2H, t, *J* 7.4, CH_2), 7.16 (2H, d, *J* 8.2, 2 × CH), 7.28 (2H, d, *J* 8.4, 2 × CH), 7.40 (2H, d, *J* 8.2, 2 × CH), 7.54 (1H, s, CH), 7.68 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.9 (CH_3), 21.1 (CH_3), 21.6 (CH_3), 22.4 (CH_2), 26.9 (CH_2), 30.7 (CH_2), 117.3 (CH), 125.3 (2C, 2 × CH), 126.7 (2C, 2 × CH),129.4 (2C, 2 × CH), 129.9 (2C, 2 × CH), 130.8 (C_{quat}), 136.4 (C_{quat}), 136.5 (C_{quat}), 136.6 (C_{quat}), 136.9 (C_{quat}), 144.7 (C_{quat}); HRMS *m/z* (TOF ES+) 391.1559. $C_{22}H_{24}DNO_2NaS$ requires 391.1566.

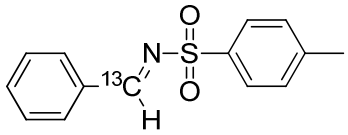
^{13}C-enriched benzaldehyde (241)



A solution of ^{13}C-enriched benzoic acid (5 mmol, 610 mg, ^{13}C:^{12}C 1:5) in Et_2O (5 mL), was added dropwise to a suspension of $LiAlH_4$ (12 mmol, 504 mg) in Et_2O (25 mL) at 0 °C. After 20 min stirring the reaction mixture was heated at 50 °C for 2 h. After cooling down to 0 °C water (15 mL) was added to quench the reaction. A solution of HCl (10%, 5 mL) was added to solubilise the suspension and the two phases were separated. The aqueous phase was washed with Et_2O (3 × 15 mL). The combined organic abstracts were wased with brine (15 mL), dried (Na_2SO_4), and concentrated under reduced pressure to give ^{13}C-enriched benzyl alcohol.

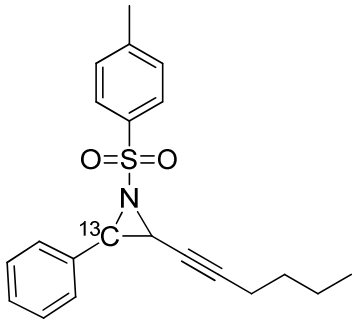
A solution of the crude ^{13}C-enriched benzyl alcohol in CH_2Cl_2 (5 mL) was added to a solution of DMP (7.5 mmol, 3.16 g) in CH_2Cl_2 (30 mL). The reaction mixture was stirred at room temperature for 4 h and a solution of $Na_2S_2O_3$ (15 mL) was added to quench the reaction. The two phases were separated and the aqueous phase was washed with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were washed with brine (15 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by distillation under reduced pressure (75 °C at 10 mmHg) to give ^{13}C-enriched benzaldehyde **241** as a colourless liquid (425 mg, 80%); δ_H (300 MHz; $CDCl_3$) 7.50-7.73 (3H, m, 3 × CH), 7.75-7.92 (2H, m, 2 × CH), 10.07 (1H, s, CH); δ_C (75 MHz; $CDCl_3$) 129.2 (2C, 2 × CH), 130.0 (2C, 2 × CH), 134.7 (CH), 136.7 (C_{quat}), 192.6 (^{13}C-enriched signal, CH).

^{13}C enriched *N*-Benzylidene-4-methylbenzenesulfonamide (242)



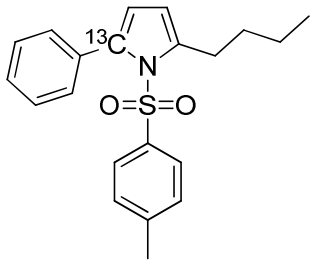
A 1:5 mixture of benzaldehyde-α-^{13}C and benzaldehyde (5.5 mmol, 589 mg), *p*-toluenesulfonamide (5.0 mmol, 856 mg), amberlyst 15 (380 mg) and 4Å molecular sieve (380 mg) in toluene (30 mL) was stirred at 130 °C in a Dean-Stark apparatus. After 12h, the reaction mixture was cooled down to room temperature and filtered. The filtrate was concentrated under reduced pressure and the residue was recristalised (ethyl acetate/n-pentane) to give ^{13}C-enriched imine **242** as a white solid (907 mg, 70%); mp 102-103 °C; ν_{max} (neat)/cm^{-1} 2922, 2853, 2179, 1598, 1449, 1413, 1364, 1326, 1291, 1245, 1158, 1135, 1090, 1061, 994, 959, 859, 838, 824, 815, 749, 701; δ_H (300 MHz; $CDCl_3$) 2.41 (3H, s, CH_3), 7.35 (2H, d, *J* 8.0, 2 × CH), 7.49 (2H, d, *J* 8.0, 2 × CH), 7.59-7.64 (1H, m, CH), 7.88-7.94 (4H, m, 4 × CH), 9.03 (1H, s, CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 128.0 (2C, 2 × CH), 129.1 (2C, 2 × CH), 129.8 (2C, 2 × CH), 131.3 (2C, 2 × CH), 132.4 (C_{quat}), 134.9 (CH), 135.1 (C_{quat}), 144.6 (C_{quat}), 170.1 (^{13}CH, enriched signal); HRMS *m/z* (TOF ES+) 283.0592. $C_{13}{}^{13}CH_{13}NO_2NaS$ requires 283.0598.

^{13}C enriched 2-(Hex-1-ynyl)-3-phenyl-1-(toluene-4-sulfonyl)aziridine (243)



Following GP3 using ^{13}C enriched imine **242** and sulfonium salt **180** for 3 h. Purification by flash chromatography [hexane:ethylacetate (12:1)] gave ^{13}C-enriched aziridine **243** as a white solid (212 mg, 60%, 8:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 2960, 2934, 2252, 1601, 1497, 1455, 1381, 1319, 1305, 1292, 1230, 1187, 1158, 1088, 1038, 1025, 871, 811, 784, 754, 738, 717,695, 672; δ_H (300 MHz; $CDCl_3$) 0.75 (3H, t, *J* 7.2, CH_3), 1.01-1.32 (4H, m, 2 × CH_2), 1.98 (2H, td, *J* 6.8 and 1.7, CH_2), 2.42 (3H, s, CH_3), 3.63 (1H, dt, *J* 6.9 and 1.7, CH), 3.94 (1H, d, *J* 6.9, CH), 7.21-7.39 (7H, m, 7 × CH), 7.88 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.4 (CH_3), 18.2 (CH_2), 21.4 (CH_2), 21.6 (CH_3), 30.0 (CH_2), 36.2 (CH), 46.1 (^{13}CH, enriched signal, CH), 72.1 (C_{quat}), 86.7 (C_{quat}), 127.7 (2C, 2 × CH) 127.9 (4C, 4 × CH), 128.2 (CH), 129.8 (2C, 2 × CH), 132.2 (C_{quat}), 134.7 (C_{quat}), 144.6 (C_{quat}); HRMS *m/z* (TOF ES+) 377.1376. $C_{20}{}^{13}CH_{23}NO_2NaS$ requires 377.1381.

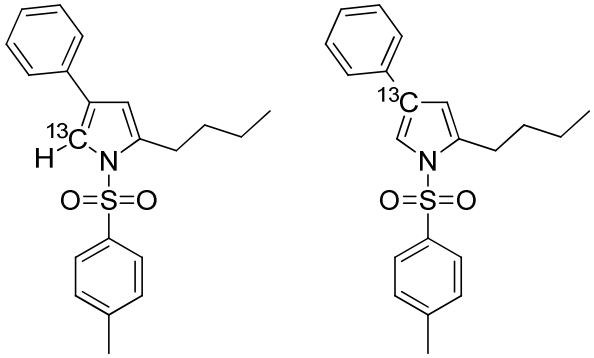
13C-enriched 2-Butyl-5-phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (244)



Following GP6 using ^{13}C enriched aziridine **243** (71 mg) at 70 °C for 4 h gave pyrrole **244** (69 mg, 98%); ν_{max} (neat)/cm^{-1} 3060, 2956, 2928, 2861, 1737, 1596, 1527, 1482, 1444, 1366, 1169, 1116, 1092, 911, 809, 759; δ_H (300 MHz; $CDCl_3$) 0.97 (3H, t, *J* 7.3, CH_3), 1.38-1.50 (2H, m, CH_2), 1.66-1.76 (2H, m, CH_2), 2.36 (3H, s, CH_3), 2.92 (2H, t, *J* 7.7, CH_2), 6.04 (1H, d, *J* 3.3, CH), 6.08 (1H, d, *J* 3.3, CH),7.14 (2H, d, *J* 8.4, 2 × CH), 7.28 (2H, d, *J* 8.4, 2 × CH), 7.32 (5H, s, 5 × CH); δ_C (75 MHz; $CDCl_3$) 14.0 (CH_3), 21.6 (CH_3), 22.5 (CH_2), 29.3 (CH_2), 31.6 (CH_2), 112.6 (CH), 115.6 (CH), 126.4 (2C, 2 × CH), 127.2 (2C, 2 × CH), 127.7 (CH),

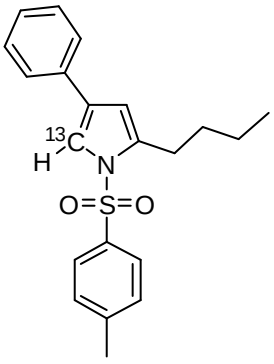
129.3 (2C, 2 × CH), 130.4 (2C, 2 × CH), 133.3 (C_{quat}), 136.4 (C_{quat}), 138.0 (^{13}C, enriched signal, C_{quat}), 139.9 (C_{quat}), 144.2 (C_{quat}); HRMS *m/z* (TOF ES+) 377.1373. $C_{20}{}^{13}CH_{23}NO_2NaS$ requires 377.1381.

Mixture of ^{13}C enriched 2-butyl-4phenyl-1-(toluene-4-sulfonyl)-1H-pyrroles with 2-butyl-5phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (244).



Following GP7 using ^{13}C enriched aziridine **243** (71 mg) at room temperature for 2 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave a mixture of 2,4-substituted pyrroles **245, 246** and 2,5-substituted pyrroles **244** (50 mg, 71%, **244:(245+246)** 1:5); HRMS *m/z* (TOF ES+) 377.1378. $C_{20}{}^{13}CH_{23}NO_2NaS$ requires 377.1381.

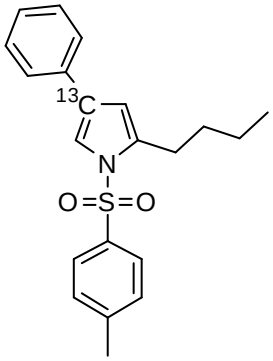
^{13}C enriched 2-butyl-4phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrroles (245):



δ_H (300 MHz; $CDCl_3$) 0.91 (3H, t, *J* 7.3, CH_3), 1.31-1.43 (2H, m, CH_2), 1.54-1.61 (2H, m, CH_2), 2.41 (3H, s, CH_3), 2.69 (2H, t, *J* 7.6, CH_2), 6.33 (1H, dt, *J* 1.9 and 1.0, CH), 7.29 (2H, d, *J* 8.4, 2 × CH), 7.32 (2H, d, *J* 8.4, 2 × CH), 7.37 (1H, d, *J* 8.2, CH), 7.51 (2H, dd, *J* 8.4 and

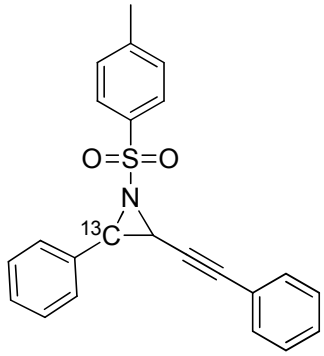
8.2, 2 × CH), 7.58 (1H, d, *J* 1.9, CH), 7.69 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.9 (CH_3), 21.6 (CH_3), 22.4 (CH_2), 26.9 (CH_2), 30.7 (CH_2), 110.4 (CH), 117.7 (^{13}CH, enriched signal, CH), 125.4 (2C, 2 × CH), 126.7 (2C, 2 × CH), 126.8 (CH), 126.9 (C_{quat}), 128.7 (2C, 2 × CH), 130.0 (2C, 2 × CH), 133.7 (C_{quat}), 136.3 (C_{quat}), 136.9 (C_{quat}), 144.8 (C_{quat}).

^{13}C enriched 2,5- diphenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (246):



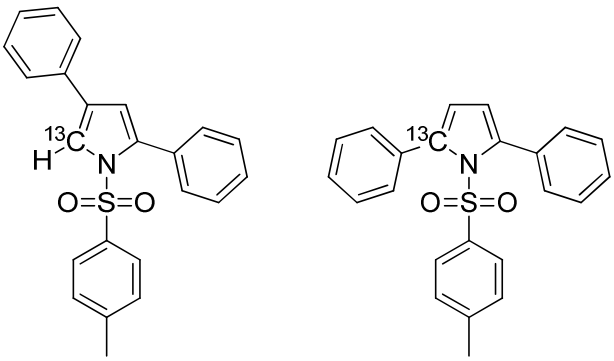
δ_H (300 MHz; $CDCl_3$) 0.91 (3H, t, *J* 7.3, CH_3), 1.31-1.43 (2H, m, CH_2), 1.54-1.61 (2H, m, CH_2), 2.41 (3H, s, CH_3), 2.69 (2H, t, *J* 7.6, CH_2), 6.33 (1H, dt, *J* 1.9 and 1.0, CH), 7.29 (2H, d, *J* 8.4, 2 × CH), 7.32 (2H, d, *J* 8.4, 2 × CH), 7.37 (1H, d, *J* 8.2, CH), 7.51 (2H, dd, *J* 8.4 and 8.2, 2 × CH), 7.58 (1H, d, *J* 1.9, CH) 7.69 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 13.9 (CH_3), 21.6 (CH_3), 22.4 (CH_2), 26.9 (CH_2), 30.7 (CH_2), 110.4 (CH), 117.7 (CH), 125.4 (2C, 2 × CH), 126.7 (2C, 2 × CH), 126.8 (CH), 126.9 (^{13}CH, enriched signal, C_{quat}), 128.7 (2C, 2 × CH), 130.0 (2C, 2 × CH), 133.7 (C_{quat}), 136.3 (C_{quat}), 136.9 (C_{quat}), 144.8 (C_{quat}).

^{13}C-enriched 2-phenyl-3-(phenylethynyl)-1-(toluene-4-sulfonyl)aziridine (247)



Following GP1 using ^{13}C enriched imine **242** and sulfonium salt **177** for 1.5 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave ^{13}C-enriched aziridine **247** (298 mg, 80%, 12:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 3032, 2950, 2926, 2240, 1597, 1490, 1457, 1441, 1319, 1157, 1087, 1071, 873, 854, 784, 757, 708; δ_H (300 MHz; $CDCl_3$) 2.44 (3H, s, CH_3), 3.87 (1H, d, *J* 6.9, CH), 4.09 (1H, d, *J* 6.9, CH), 7.12-7.28 (4H, m, 4 × CH), 7.29-7.45 (8H, m, 8 × CH), 7.92 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.7 (CH_3), 36.3 (CH), 46.5 (^{13}CH, enriched signal, CH), 81.6 (C_{quat}), 85.1 (C_{quat}), 121.8 (C_{quat}), 127.8 (2C, 2 × CH), 128.0 (4C, 4 × CH), 128.1 (2C, 2 × CH), 128.5 (CH), 128.8 (CH), 129.9 (2C, 2 × CH), 131.8 (2C, 2 × CH), 132.1 (C_{quat}), 134.6 (C_{quat}), 144.9 (C_{quat}); HRMS *m/z* (TOF ES+) 397.1074. $C_{22}{}^{13}CH_{18}NO_2NaS$ requires 397.1068.

Mixture of 13C-enriched 2,4-diphenyl-1-(toluene-4-sulfonyl)-1H-pyrrole (249) and 2,5-diphenyl-1-(toluene-4-sulfonyl)-1H-pyrrole (248)



Following GP7 using ^{13}C enriched 2-phenyl-3-(phenylethynyl)-1-(toluene-4-sulfonyl)aziridine (75 mg) at room temperature for 2 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave a mixture of 2,4-substituted **249** and 2,5-substituted pyrroles **248** (49 mg, 65%, **248**:**249** 1:10); HRMS *m/z* (TOF ES+) 397.1075. $C_{22}{}^{13}CH_{19}NO_2NaS$ requires 397.1068.

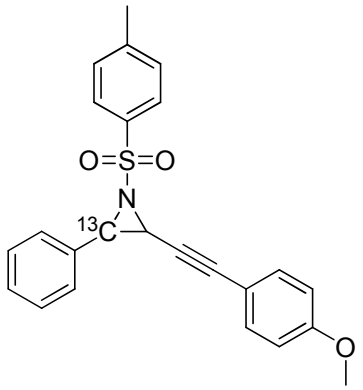
^{13}C enriched 2,4-diphenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole:

δ_H (300 MHz; $CDCl_3$) 2.34 (3H, s, CH_3), 6.49 (1H, d, *J* 2.0, CH), 7.24-7.37 (10H, m, 10 × CH), 7.53 (2H, d, *J* 7.1, 2 × CH), 7.73 (1H, d, *J* 2.0, CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 114.3 (CH), 119.5 (^{13}C-enriched signal, CH), 125.5 (2C, 2 × CH), 127.0 (CH), 127.1 (2C, 2 × CH), 127.4 (2C, 2 × CH), 128.4 (CH), 128.8 (2C, 2 × CH), 129.4 (2C, 2 × CH), 130.8 (2C, 2 × CH), 131.2 (C_{quat}), 133.3 (C_{quat}), 135.4 (C_{quat}), 136.9 (C_{quat}), 141.2 (C_{quat}), 144.7 (C_{quat}).

^{13}C enriched 2,5- diphenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole:

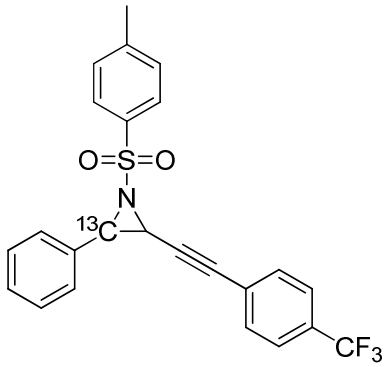
δ_H (300 MHz; $CDCl_3$) 2.34 (3H, s, CH_3), 6.24 (2H, m, 2 × CH), 7.06 (4H, m, 4 × CH), 7.35-7.46 (6H, m, 6 × CH), 7.49-7.53 (4H, m, 4 × CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 117.3 (2C, 2 × CH), 127.0 (4C, 4 × CH), 127.5 (2C, 2 × CH), 127.9 (2C, 2 × CH), 128.8 (4C, 4 × CH), 129.6 (2C, 2 × CH), 133.3 (2C, 2 × C_{quat}), 134.6 (C_{quat}), 141.3 (2C, ^{13}C-enriched signal, 2 × C_{quat}), 144.3 (C_{quat}).

13C-enriched 2-((4-methoxyphenyl)ethynyl)-3-phenyl-1-(toluene-4-sulfonyl)aziridine (250)



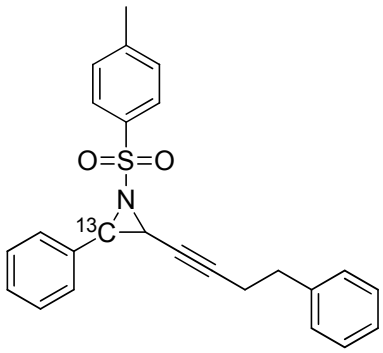
Following GP1 using ^{13}C enriched imine **242** and sulfonium salt **255** for 45 min. Purification by flash chromatography [hexane:ethylacetate (20:1)] gave ^{13}C-enriched aziridine **250** (242 mg, 60 %, 16:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 3036, 2933, 2838, 2228, 1603, 1509, 1455, 1327, 1291, 1247, 1156, 1089, 1027, 976, 872, 831, 812, 786, 733, 697; δ_H (300 MHz; $CDCl_3$) 2.43 (3H, s, CH_3), 3.76 (3H, s, CH_3), 3.86 (1H, d, *J* 6.9, CH), 4.07 (1H, d, *J* 6.9, CH), 6.73 (2H, d, *J* 8.9, 2 × CH), 7.11 (2H, d, *J* 8.9, 2 × CH), 7.30-7.41 (7H, m, 7 × CH), 7.91 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.7 (CH_3), 36.5 (CH), 46.5 (^{13}CH, enriched signal, CH), 55.2 (CH_3), 80.2 (C_{quat}), 85.3 (C_{quat}), 113.8 (2C, 2 × CH), 127.8 (2C, 2 × CH), 128.0 (5C, 5 × CH, C_{quat}), 128.4 (CH), 129.8 (2C, 2 × CH), 132.2 (C_{quat}), 133.4 (2C, 2 × CH), 134.7 (C_{quat}), 144.9 (C_{quat}), 159.9 (C_{quat}); HRMS *m/z* (TOF ES+) 426.1089. $C_{23}{}^{13}CH_{21}NO_3NaS$ requires 426.1095.

^{13}C-enriched 2-phenyl-1-(toluene-4-sulfonyl)-3-((4-trifluoromethyl)phenyl)ethynyl)aziridine (251)



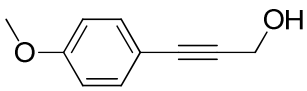
Following GP1 using ^{13}C enriched imine **242** and sulfonium salt **258** for 30 min. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave ^{13}C-enriched aziridine **251** (287 mg, 65%%, 15:1 *cis*:*trans*); ν_{max} (neat)/cm^{-1} 3065, 3012, 1617, 1596, 1496, 1456, 1405, 1378, 1320, 1157, 1127, 1106, 1088, 1059, 1016, 973, 870, 838, 812, 785, 737, 696; δ_H (300 MHz; $CDCl_3$) 2.44 (3H, s, CH_3), 3.90 (1H, d, *J* 6.8, CH), 4.13 (1H, d, *J* 6.8, CH), 7.27 (2H, d, *J* 8.1, 2 × CH), 7.31-7.42 (7H, m, 7 × CH), 7.48 (2H, d, *J* 8.1, 2 × CH), 7.94 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 35.8 (CH), 46.5 (^{13}CH, enriched signal, CH), 83.5 (C_{quat}), 84.3 (C_{quat}), 125.0 (CH), 125.1 (CH), 125.5 (C_{quat}), 127.7 (2C, 2 × CH), 128.0 (2C, 2 × CH), 128.1 (2C, 2 × CH), 128.6 (CH), 129.9 (2C, 2 × CH), 130.2 (C_{quat}), 130.6 (C_{quat}), 131.9 (C_{quat}), 132.1 (2C, 2 × CH), 134.4 (C_{quat}), 145.1 (C_{quat}); HRMS *m/z* (TOF ES+) 465.0934. $C_{23}{}^{13}CH_{18}NO_2F_3NaS$ requires 465.0942.

^{13}C-enriched 2-phenyl-3-(4-phenylbut-1-yn-1-yl)-1-(toluene-4-sulfonyl)aziridine (252)



Following GP1 using ^{13}C enriched imine **242** and sulfonium salt **179** for 4h. Purification by flash chromatography [hexane:ethylacetate (20:1)] gave ^{13}C-enriched aziridine **252** (269 mg, 67%, 14:1 *cis*:*trans*). ν_{max} (neat)/cm^{-1} 3029, 2925, 2248, 1597, 1495, 1454, 1384, 1327, 1291, 1235, 1158, 1090, 1021, 875, 814, 783, 742, 695; δ_H (300 MHz; $CDCl_3$) 2.27-2.33 (2H, m, CH_2), 2.44 (3H, s, CH_3), 2.50-2.65 (2H, m, CH_2), 3.62 (1H, dt, *J* 6.9 and 1.8, CH), 3.94 (1H, d, *J* 6.9, CH), 6.95-7.01 (2H, m, 2 × CH), 7.14-7.24 (3H, m, 3 × CH), 7.29 (5H, s,5 × CH), 7.34 (2H, d, *J* 8.3, 2 × CH), 7.88 (2H, d, *J* 8.3, 2 × CH); δ_C (75 MHz; $CDCl_3$) 20.8 (CH_2), 21.7 (CH_3), 34.1 (CH_2), 36.1 (CH), 46.1 (^{13}CH, enriched signal, CH), 73.0 (C_{quat}), 85.8 (C_{quat}), 126.2 (2C, 2 × CH), 127.8 (2C, 2 × CH), 127.9 (2C, 2 × CH), 128.0 (2C, 2 × CH), 128.3 (5C, 5 × CH), 129.8 (2C, 2 × CH), 132.2 (C_{quat}), 134.7 (C_{quat}), 140.2 (C_{quat}), 144.8 (C_{quat}); HRMS *m/z* (TOF ES+) 425.1373. $C_{24}{}^{13}CH_{23}NO_2NaS$ requires 425.1381.

3-(4-Methoxyphenyl)prop-2-yn-1-ol (253)

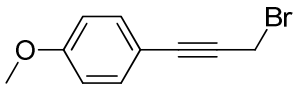


Following GP5 using 4-iodoanisole (5.85 g). Purification by flash chromatography [hexane:ethylacetate (2:1)] gave alcohol **253** as a brown solid (2.64 g, 65%);δ_H (300 MHz; $CDCl_3$) 1.83 (1H, s, OH), 3.81 (3H, s, CH_3), 4.49 (2H, s, CH_2), 6.85 (2H, d, *J* 6.5, 2 × CH), 7.40 (2H, d, *J* 6.5, 2 × CH); δ_C (75 MHz; $CDCl_3$) 51.7 (CH_2), 55.3 (CH_3), 85.7 (C_{quat}), 85.9

(C_{quat}), 114.0 (2C, 2 × CH), 114.6 (C_{quat}), 133.2 (2C, 2 × CH), 159.8 (C_{quat}); HRMS *m/z* (TOF EI+) 162.0683. $C_{10}H_{10}O_2$ requires 162.0681.

Data were in agreement with those reported in the literature.[108]

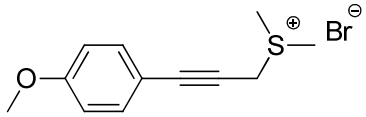
1-(3-Bromoprop-1-ynyl)-4-methoxybenzene (254)



Following GP8 using PPh_3 (11 mmol, 2.88 g), Br_2 (10.9 mmol, 0.55 mL) and alcohol **253** (1.62 g) in CH_2Cl_2 (30 mL). Purification by flash chromatography (hexane) gave bromine **254** as a colourless oil (2.02 g, 90%); ν_{max} (neat)/cm^{-1} 2228, 1609, 1602, 1518, 1471, 1102, 1001, 960, 820; δ_H (300 MHz; $CDCl_3$) 3.79 (3H, s, CH_3), 4.17 (2H, s, CH_2), 6.84 (2H, d, *J* 9.0, 2 × CH), 7.39 (2H, d, *J* 9.0, 2 × CH); δ_C (75 MHz; $CDCl_3$) 16.0 (CH_2), 55.3 (CH_3), 83.0 (C_{quat}), 86.9 (C_{quat}), 114.0 (2C, 2 × CH), 114.1 (C_{quat}), 133.5 (2C, 2 × CH), 160.0 (C_{quat}).

Data were in agreement with those reported in the literature.[95]

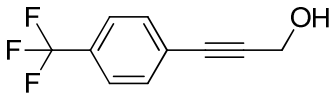
(3-(4-methoxyphenyl)prop-2-yn-1-yl)dimethylsulfonium bromide (255)



Following GP9 using bromide **254** (1.125 g) gave sulfonium salt **255** (1.335 g, 93%); mp 124-125 °C;ν_{max} (neat)/cm^{-1} 2969, 2907, 2864, 2216, 1605, 1565, 1509, 1459, 1421, 1325, 1296, 1276, 1246, 1180, 1169, 1105, 1046, 1021, 1009, 828, 800, 703; δ_H (300 MHz; $CDCl_3$) 3.31 (6H, s, 2 × CH_3), 3.81 (3H, s, CH_3), 5.31 (2H, s, CH_2), 6.85 (2H, d, *J* 8.8, 2 × CH), 7.40 (2H,

d, *J* 8.8, 2 × CH); δ_C (75 MHz; $CDCl_3$) 24.6 (2C, 2 × CH_3), 34.2 (CH_2), 55.3 (CH_3), 73.0 (C_{quat}), 91.2 (C_{quat}), 112.5 (C_{quat}), 114.2 (2C, 2 × CH), 133.7 (2C, 2 × CH), 160.6 (C_{quat}); HRMS *m/z* (TOF ES+) 207.0844. $C_{12}H_{15}OS$ requires 207.0840.

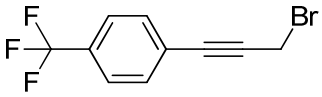
3-(4-Trifluoromethylphenyl)prop-2-yn-1-ol (256)



Following GP5 using 1-iodo-4-(trifluoromethyl)benzene (6.80 g, 3.67 mL). Purification by flash chromatography [hexane:ethylacetate (4:1)] gave alcohol **256** as a brown solid (2.75 g, 90%); ν_{max} (neat)/cm^{-1} 3350, 3080, 2890, 2275, 1622, 1532, 1405, 1328, 1186, 1129, 953, 786, 732, 689; δ_H (300 MHz; $CDCl_3$) 1.91 (1H, t, *J* 5.5, OH), 4.54 (2H, d, *J* 5.5, CH_2), 7.50 (2H, d, *J* 8.5, 2 × CH), 7.54 (2H, d, *J* 8.5, 2 × CH); δ_C (75 MHz; $CDCl_3$) 51.5 (CH_2), 84.3 (C_{quat}), 89.6 (C_{quat}), 122.5 (C_{quat}), 125.2 (2C, 2 × CH), 126.4 (C_{quat}), 130.2 (C_{quat}), 131.9 (2C, 2 × CH).

Data were in agreement with those reported in the literature.[93]

1-(3-Bromoprop-1-ynyl)-4-(trifluoromethyl)benzene (257)

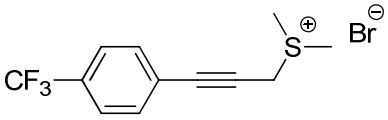


Following GP8 using PPh_3 (11 mmol, 2.88 g), Br_2 (10.9 mmol, 0.55 mL) and alcohol **256** (2.00 g) in CH_2Cl_2 (30 mL). Purification by flash chromatography (*n*-pentane) gave bromine **257** as a yellow oil (2.36 g, 90%); ν_{max} (neat)/cm^{-1} 3012, 2232, 2199, 1930, 1725, 1669, 1516, 1407, 1423, 1329, 1129, 1073, 1052, 1022, 850, 769; δ_H (300 MHz; $CDCl_3$) 4.16 (2H, s, CH_2), 7.54 (2H, d, *J* 8.4, 2 × CH), 7.57 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 14.4

(CH_2), 85.1 (C_{quat}), 86.6 (C_{quat}), 125.3 (2C, 2 × CH), 125.9 (C_{quat}), 130.6 (C_{quat}), 132.1 (2C, 2 × CH); HRMS *m/z* (TOF EI+) 261.9590. $C_{10}H_6{}^{79}BrF_3$ requires 261.9605.

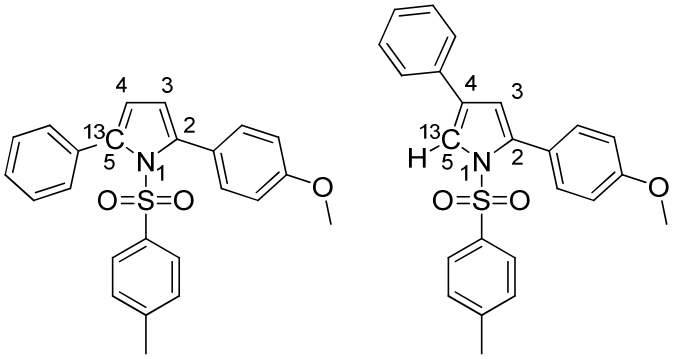
Data were in agreement with those reported in the literature.[109]

Dimethyl(3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-yl)sulfonium bromide (258)



Following GP9 using bromide **257** (1.315 g) gave sulfonium salt **258** (1.625 g, 50%); mp 139-140 °C, ν_{max} (neat)/cm^{-1} 3006, 2924, 2891, 2245, 1618,1407, 1319, 1231, 1162, 1126, 1107, 1067, 1045, 1017, 1001, 982, 840, 712; δ_H (300 MHz; $CDCl_3$) 3.36 (6H, s, 2 × CH_3), 5.43 (2H, s, CH_2), 7.60-7.70 (4H, m, 4 × CH); δ_C (75 MHz; $CDCl_3$) 24.9 (2C, 2 × CH_3), 33.7 (CH_2), 76.9 (C_{quat}), 89.5 (C_{quat}), 124.3 (C_{quat}), 125.7 (2C, 2 × CH), 131.4 (C_{quat}), 131.8 (C_{quat}), 132.5 (2C, 2 × CH); HRMS *m/z* (TOF ES+) 245.0607. $C_{12}H_{12}F_3S$ requires 245.0612.

Mixture of ^{13}C-enriched 2-(4-methoxyphenyl)-5-phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (259) and 2-(4-methoxyphenyl)-4-phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (260)



Following GP7 using ^{13}C enriched aziridine **250** (80 mg) for 45 min. Purification by flash chromatography [hexane:ethylacetate (20:1)] gave a mixture of 2,4-substituted **260** and 2,5-substituted pyrroles **259** (8 mg, <10%, **259**:**260** 2:3).

Only a complexe and dirty mixture of pyrroles was obtained. Caracteristic pics of 2,4 and 2,5-substituted expected pyrroles are visible in ^{1}H NMR:

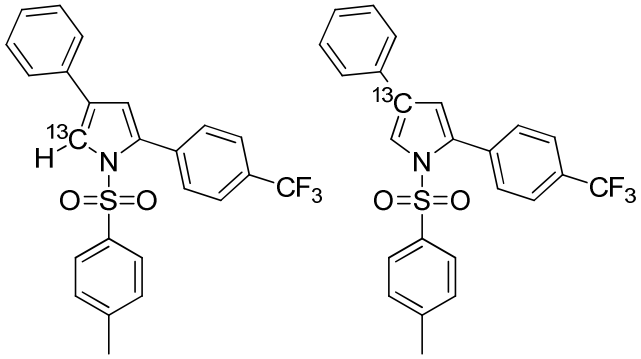
2-(4-methoxyphenyl)-5-phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (259): δ_H (300 MHz; $CDCl_3$) 2.35 (3H, s, CH_3), 3.87 (3H, s, CH_3), 6.16 (1H, d, *J* 3.3, CH), 6.23 (1H, d, *J* 3.3, CH), 6.85-7.50 (13H, m, 13 × CH).

^{13}C NMR shows a ^{13}C-enriched signal at 140.7 ppm characteristic of ^{13}C enrichement at C-5 for a 2,5-pyrrole. The rest of the ^{13}C NMR spectrum could not be interpretate.

2-(4-methoxyphenyl)-4-phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (260): δ_H (300 MHz; $CDCl_3$) 2.35 (3H, s, CH_3), 3.88 (3H, s, CH_3), 6.43 (1H, d, *J* 2.0, CH), 6.85-7.50 (13H, m, 13 × CH), 7.70 (1H, d, *J* 2.0, CH).

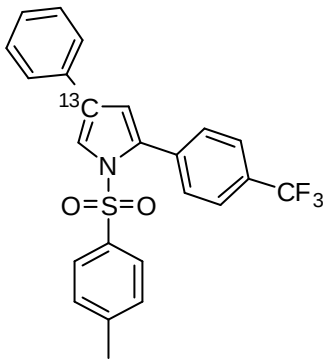
^{13}C NMR shows a ^{13}C-enriched signal at 119.2 ppm characteristic of ^{13}C enrichement at C-5 for a 2,4-pyrrole. The rest of the ^{13}C NMR spectrum could not be interpretate.

^{13}C-enriched 4-Phenyl-1-(toluene-4-sulfonyl)-2-(4-(trifluoromethyl)phenyl)-1*H*-pyrroles (261) and (262)



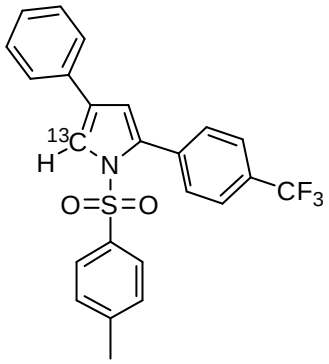
Following GP7 using ^{13}C-enriched 2-phenyl-1-(toluene-4-sulfonyl)-3-((4-trifluoromethyl)phenyl)ethynyl)aziridine (88 mg) at for 2 h. Purification by flash chromatography [hexane:ethylacetate (25:1)] gave a mixture of 2,4-substituted pyrroles **261** and **262** (39 mg, 45%); HRMS *m/z* (TOF ES+) 465.0939. $C_{23}{}^{13}CH_{18}NO_2F_3NaS$ requires 465.0942.

^{13}C-enriched 4-Phenyl-1-(toluene-4-sulfonyl)-2-(4-(trifluoromethyl)phenyl)-1*H*-pyrrole (262):



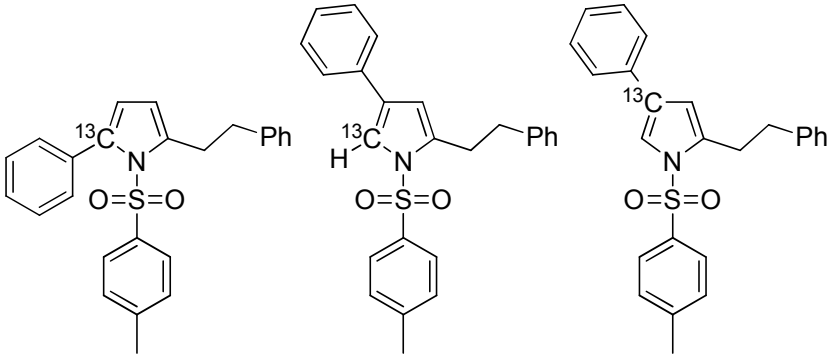
δ_H (300 MHz; $CDCl_3$) 2.36 (3H, s, CH_3), 6.55 (1H, d, *J* 1.9, CH), 7.13 (2H, d, *J* 8.1, 2 × CH), 7.26-7.31 (3H, m, 3 × CH), 7.37-7.46 (4H, m, 4 × CH), 7.51-7.55 (2H, m, 2 × CH), 7.61 (2H, d, *J* 8.1, 2 × CH), 7.76 (1H, d, *J* 1.9, CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3),115.4 (CH), 120.4 (CH), 122.7 (C_{quat}), 124.4 (CH), 125.5 (2C, 2 × CH), 127.0 (2C, 2 × CH), 127.3 (CH), 128.0 (^{13}C-enriched signal, C_{quat}), 128.9 (2C, 2 × CH), 129.6 (2C, 2 × CH), 130.2 (d, J_{C-F} 32.8, C_{quat}), 130.9 (2C, 2 × CH), 132.9 (2C, 2 × CH), 134.9 (C_{quat}), 135.2 (C_{quat}), 135.4 (C_{quat}) 145.1 (C_{quat}).

^{13}C-enriched 4-Phenyl-1-(toluene-4-sulfonyl)-2-(4-(trifluoromethyl)phenyl)-1*H*-pyrrole (261):



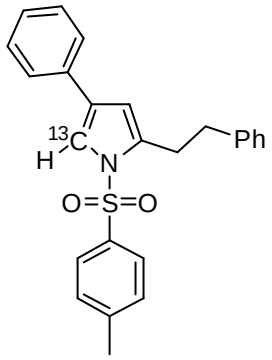
δ_H (300 MHz; $CDCl_3$) 2.36 (3H, s, CH_3), 6.55 (1H, d, *J* 1.9, CH), 7.13 (2H, d, *J* 8.1, 2 × CH), 7.26-7.31 (3H, m, 3 × CH), 7.37-7.46 (4H, m, 4 × CH), 7.51-7.55 (2H, m, 2 × CH), 7.61 (2H, d, *J* 8.1, 2 × CH), 7.76 (1H, d, *J* 1.9, CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3),115.4 (CH), 120.4 (CH), 122.7 (C_{quat}), 124.4 (^{13}C-enriched signal, CH), 125.5 (2C, 2 × CH), 127.0 (2C, 2 × CH), 127.3 (CH), 128.0 (C_{quat}), 128.9 (2C, 2 × CH), 129.6 (2C, 2 × CH), 130.2 (d, $J_{C\text{-}F}$ 32.8, C_{quat}), 130.9 (2C, 2 × CH), 132.9 (2C, 2 × CH), 134.9 (C_{quat}), 135.2 (C_{quat}), 135.4 (C_{quat}) 145.1 (C_{quat}).

^{13}C-enriched 2-phenethyl-4-phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrroles and 2-phenethyl-5-phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (263)



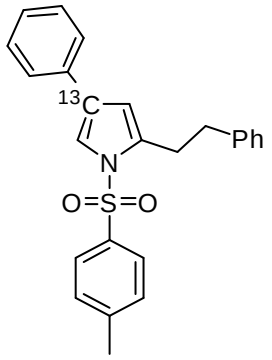
Following GP7 using ^{13}C-enriched aziridine **252** (81 mg) at for 2 h. Purification by flash chromatography [hexane:ethylacetate (20:1)] gave a mixture of 2,4-substituted **264, 265** pyrroles and 2,5-substituted pyrrole **263** (32 mg, 40%, **263:(264+265)** 1:2); HRMS *m/z* (TOF ES+) 425.1376. $C_{24}{}^{13}CH_{23}NO_2NaS$ requires 425.1381.

^{13}C-enriched 2-phenethyl-4-phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (264):



δ_H (300 MHz; $CDCl_3$) 2.34 (3H, s, CH_3), 2.85-2.90 (2H, m, CH_2), 2.94-2.99 (2H, m, CH_2), 6.35 (1H, dt, *J* 2.0 and 0.9, CH), 7.12-7.28 (8H, m, 8 × CH), 7.30-7.33 (2H, m, 2 × CH), 7.42-7.45 (2H, m, 2 × CH), 7.54 (1H, d, *J* 2.0, CH), 7.63 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 29.3 (CH_2), 35.4 (CH_2), 111.2 (CH), 118.0 (^{13}C-enriched signal, CH), 125.5 (2C, 2 × CH), 126.1 (CH), 126.8 (2C, 2 × CH), 126.9 (CH), 127.0 (C_{quat}), 127.3 (4C, 4 × CH), 128.4 (2C, 2 × CH), 130.1 (2C, 2 × CH), 133.6 (C_{quat}), 136.0 (C_{quat}), 138.5 (C_{quat}), 141.2 (C_{quat}), 144.9 (C_{quat}).

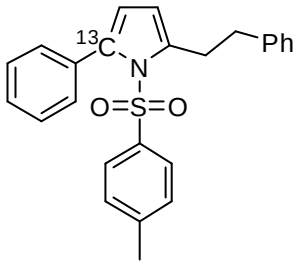
^{13}C-enriched 2-phenethyl-4-phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrroles (265):



δ_H (300 MHz; $CDCl_3$) 2.34 (3H, s, CH_3), 2.85-2.90 (2H, m, CH_2), 2.94-2.99 (2H, m, CH_2), 6.35 (1H, dt, *J* 2.0 and 0.9, CH), 7.12-7.28 (8H, m, 8 × CH), 7.30-7.33 (2H, m, 2 × CH), 7.42-7.45 (2H, m, 2 × CH), 7.54 (1H, d, *J* 2.0, CH), 7.63 (2H, d, *J* 8.4, 2 × CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 29.3 (CH_2), 35.4 (CH_2), 111.2 (CH), 118.0 (CH), 125.5 (2C, 2 × CH), 126.1 (CH), 126.8 (2C, 2 × CH), 126.9 (CH), 127.0 (^{13}C-enriched signal, C_{quat}), 127.3 (4C, 4

× CH), 128.4 (2C, 2 × CH), 130.1 (2C, 2 × CH), 133.6 (C_{quat}), 136.0 (C_{quat}), 138.5 (C_{quat}), 141.2 (C_{quat}), 144.9 (C_{quat}).

^{13}C-enriched 2-phenethyl-5-phenyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole (263):



δ_H (300 MHz; $CDCl_3$) 2.36 (3H, s, CH_3), 3.05 (2H, m, CH_2), 3.24 (2H, m, CH_2), 6.02-6.09 (2H, m, 2 × CH), 7.13 (2H, d, *J* 8.0, 2 × CH), 7.19-7.31 (7H, m, 7 × CH), 7.34 (5H, 5 × CH); δ_C (75 MHz; $CDCl_3$) 21.6 (CH_3), 31.8 (CH_2), 36.3 (CH_2), 113.5 (CH), 115.7 (CH), 126.0 (CH), 126.4 (2C, 2 × CH), 127.3 (2C, 2 × CH), 127.8 (CH), 128.4 (2C, 2 × CH), 128.5 (2C, 2 × CH), 129.4 (2C, 2 × CH), 130.5 (2C, 2 × CH), 133.2 (C_{quat}), 136.3 (C_{quat}), 138.5 (^{13}C-enriched signal, C_{quat}), 138.8 (C_{quat}), 141.6 (C_{quat}), 144.4 (C_{quat}).

6.4.2 Procedure and characterisation for Chapter 5

Formation of 4-methylbenzenesulfonamides and methanesulfonamides: General procedure 10 (GP10):[110]

A solution of the corresponding sulfonyl chloride (36 mmol) in CH_2Cl_2 (20 mL) was added dropwise to a mixture of primary amine (30 mmol) and pyridine (15 mL) in CH_2Cl_2 (80 mL) at rt. After stirring one night, a 1M aqueous HCl solution (20 mL) was added to quench the reaction. The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extracts were washed with H_2O (1 × 20 mL) and brine (1 ×

20 mL) and dried over Na_2SO_4. After filtration, concentration under reduced pressure was performed and the residue was purified by flash chromatography.

Formation of ynamides: General procedure 11 (GP11)[78]

$CuCl_2$ (56 mg, 0.4 mmol), Amide (10 mmol) and Na_2CO_3 (424 mg, 4 mmol) were added to a flame-dried 500 mL three-necked round-bottomed flask under argon. The flask was purged with oxygen for 15 min and a solution of pyridine (0.32 mL, 4 mmol) in dry toluene (10mL) was added. A balloon filled with oxygen was connected to the flask and the stirred mixture was heated a 70 °C. After 15 min, addition of a solution of alkyne (2 mmol) in dry toluene by syringe pump (4h) was started. The mixture was allowed to stir at 70 °C for another 4h and was then cooled to rt. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography.

α,β-Unsaturated imides preparation: General procedures 12 (GP12):

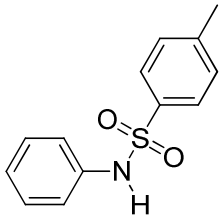
System A (GP12A):

A solution of the corresponding ynamide (0.3 mmol, 1 eq) in $ClCH_2CH_2Cl$ (1.5 mL) was added to a mixture of dichloro(2-pyridinecarboxylato)gold (6 mg, 0.015 mmol, 5 mol %) and pyridine-*N*-oxide (32 mg, 0.33 mmol, 1.1 eq) in a flame-dried Schlenk flask under argon. The reaction mixture was stirred at 70 °C until complete consumption of the starting material before being filtered through a pad of silica. The filtrate was then concentrated under reduced pressure and purification of the residue was performed by flash chromatography.

System B (GP12B):

A solution of the corresponding ynamide (0.3 mmol, 1 eq) in THF (1.5 mL) was added to a mixture of goldtribromide (7 mg, 0.015 mmol, 5 mol %) and pyridine-*N*-oxide (32 mg, 0.33 mmol, 1.1 eq) in a flame-dried Schlenk flask under argon. The reaction mixture was stirred at rt until complete consumption of the starting material before being filtered through a pad of silica. The filtrate was then concentrated under reduced pressure and purification of the residue was performed by flash chromatography.

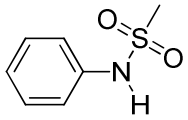
4-Methyl-*N*-phenylbenzenesulfonamide (280)



Following GP10 using 4-methylbenzenesulfonyl chloride (6.86 g) and aniline (2.70 mL). Purification by flash chromatography [hexanes:EtOAc (10:1)] gave amide **280** as a white solid (7.20 g, 97 %); mp: 102-104 °C; ν_{max} (neat)/cm^{-1} 3237, 3061, 2980, 2899, 1597, 1481, 1414, 1336, 1319, 1291, 1223, 1186, 1153, 1089, 1031, 909, 810, 753, 693; δ_H (300 MHz; $CDCl_3$) 2.37 (3H, s, CH_3), 6.94 (1H, br s, NH), 7.06-7.12 (3H, m, 3 × CH), 7.20-7.26 (4H, m, 4 × CH), 7.67 (2H, d, *J* 8.3, 2 × CH); δ_C (400 MHz; $CDCl_3$) 21.5 (CH_3), 121.6 (2C, 2 × CH), 125.3 (CH), 127.3 (2C, 2 × CH), 129.3 (2C, 2 × CH), 129.7 (2C, 2 × CH), 136.1 (C_{quat}), 136.5 (C_{quat}), 143.9 (C_{quat}); HRMS *m/z* (TOF ES+) 270.0561. $C_{13}H_{13}NO_2NaS$ requires 270.0565.

Data were in agreement with those reported in the literature.[111]

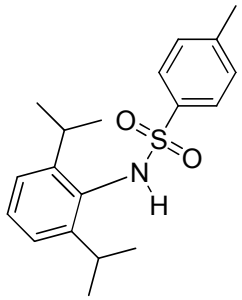
_N_-Phenylmethanesulfonamide (281)



Following GP10 using methylsulfonyl chloride (2.80 mL) and aniline (2.70 mL). Purification by flash chromatography [hexanes:EtOAc (5:1)] gave amide **281** as a white solid (4.74 g, 92 %); mp (°C) 99-103; ν_{max} (neat)/cm^{-1} 3253, 3019, 2933, 1595, 1494, 1471, 1392, 1319, 1300, 1275, 1145, 1075, 1028, 975, 959, 918, 894, 751, 692; δ_H (300 MHz; $CDCl_3$) 3.02 (3H, s, CH_3), 7.15-7.21 (2H, m, NH, CH), 7.24-7.27 (2H, m, 2 × CH), 7.32-7.39 (2H, m, 2 × CH); δ_C (400 MHz; $CDCl_3$) 39.2 (CH_3), 120.8 (2C, 2 × CH), 125.4 (CH), 129.6 (2C, 2 × CH), 136.6 (C_{quat}); HRMS *m/z* (TOF EI+) 171.0356. $C_7H_9NO_2S$ requires 171.0354.

Data were in agreement with those reported in the literature.[112]

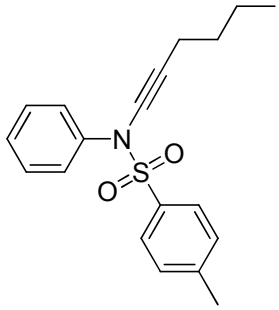
_N_-(2,6-Diisopropylphenyl)-4-methylbenzenesulfonamide (282)



Following GP10 using 4-methylbenzenesulfonyl chloride (6.86 g) and 2,6-diisopropylaniline (5.70 mL). Purification by flash chromatography [hexanes:EtOAc (15:1)] gave amide **282** as a white solid (9.10 g, 91 %); mp (°C) 156-159; ν_{max} (neat)/cm^{-1} 3254, 2970, 2927, 2868, 1596, 1444, 1398, 1329, 1304, 1156, 1089, 912, 811, 789, 710; δ_H (300 MHz; $CDCl_3$) 0.97 (12H, d, *J* 6.8, CH_3), 2.38 (3H, s, CH_3), 3.09 (2H, sept, *J* 6.8, CH), 5.99 (1H, s, NH), 7.08 (2H, d, *J* 7.6, CH), 7.17-7.25 (3H, m, CH), 7.56 (2H, d, *J* 8.3, CH); δ_C (400 MHz; $CDCl_3$) 21.5 (CH_3),

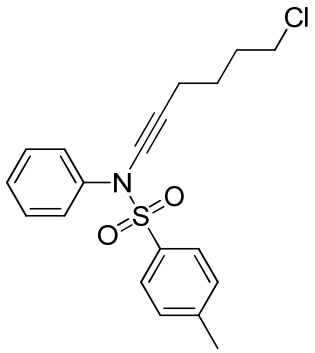
23.8 (4C, CH_3), 28.4 (2C, 2 × CH), 123.9 (2C, 2 × CH), 127.4 (2C, 2 × CH), 128.8 (CH), 129.2 (C_{quat}), 129.5 (2C, 2 × CH), 137.3 (C_{quat}), 143.5 (C_{quat}), 148.3 (C_{quat}); HRMS *m/z* (TOF ES+) 354.1509. $C_{19}H_{25}NO_2NaS$ requires 354.1504.

_N_-(Hex-1-yn-1yl)-4-methyl-_N_-phenylbenzenesulfonamide (283)



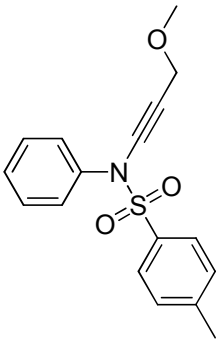
Following GP11 using amide **280** (2.47 g) and hex-1-yne (0.24 mL). Purification by flash chromatography [hexanes:EtOAc (20:1)] gave ynamide **283** as a colorless oil (320 mg, 98%); ν_{max} (neat)/cm^{-1} 2957, 2930, 2871, 2254, 1594, 1488, 1455, 1369, 1269, 1173, 1156, 1089, 923, 892, 812, 755, 704, 690, 678; δ_H (300 MHz; $CDCl_3$) 0.85 (3H, t, *J* 7.2, CH_3), 1.26-1.50 (4H, m, 2 × CH_2), 2.24 (2H, t, *J* 6.9, CH_2), 2.38 (3H, s, CH_3), 7.17-7.29 (7H, m, 7 × CH), 7.49 (2H, d, *J* 8.3, 2 × CH); δ_C (400 MHz; $CDCl_3$) 13.6 (CH_3), 18.2 (CH_2), 21.7 (CH_3), 21.9 (CH_2), 30.9 (CH_2), 70.4 (C_{quat}), 73.8 (C_{quat}), 126.1 (2C, 2 × CH), 127.8 (CH), 128.3 (2C, 2 × CH), 128.9 (2C, 2 × CH), 129.3 (2C, 2 × CH), 133.0 (C_{quat}), 139.4 (C_{quat}), 144.6 (C_{quat}); HRMS *m/z* (TOF ES+) 350.1185. $C_{19}H_{21}NO_2NaS$ requires 350.1191.

_N_-(6-Chlorohex-1-yn-1yl)-4-methyl-_N_-phenylbenzenesulfonamide (284)



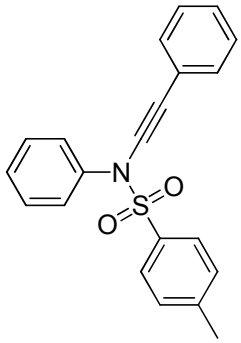
Following GP11 using amide **280** (2.47 g) and 6-chlorohex-1-yne (0.25 mL). Purification by flash chromatography [hexanes:EtOAc (15:1)] gave ynamide **284** as a colorless oil (354 mg, 98%); ν_{max} (neat)/cm^{-1} 2952, 2869, 2254, 2032, 1594, 1488, 1368, 1266, 1173, 1089, 1027, 923; δ_H (300 MHz; $CDCl_3$) 1.66 (2H, m, CH_2), 1.87 (2H, m, CH_2), 2.36 (2H, t, *J* 6.8, CH_2), 2.44 (3H, s, CH_3), 3.55 (2H, t, *J* 6.5, CH_2), 7.22-7.25 (3H, m, 3 × CH), 7.29-7.33 (4H, m, 4 × CH), 7.54 (2H, d, *J* 8.4, 2 × CH); δ_C (400 MHz; $CDCl_3$) 17.8 (CH_2), 21.7 (CH_3), 26.0 (CH_2), 31.5 (CH_2), 44.5 (CH_2), 69.4 (C_{quat}),74.5 (C_{quat}), 126.1 (2C, 2 × CH), 128.0 (CH), 128.2 (2C, 2 × CH), 129.0 (2C, 2 × CH), 129.4 (2C, 2 × CH), 133.0 (C_{quat}), 139.2 (C_{quat}), 144.7 (C_{quat}); HRMS *m/z* (TOF ES+) 384.0812. $C_{19}H_{20}NO_2NaS^{35}Cl$ requires 384.0801.

_N_-(3-methoxyprop-1-yn-1-yl)-4-methyl-_N_-phenylbenzenesulfonamide (285)



Following GP11 using amide **280** (2.47 g) and 3-methoxyprop-1-yne (0.17 mL). Purification by flash chromatography [hexanes:EtOAc (15:1)] gave ynamide **285** as a colourless oil (540 mg, 86%); ν_{max} (neat)/cm^{-1} 2925, 2860, 2824, 2244, 1595, 1489, 1454, 1370, 1292, 1172, 1160, 910, 894, 861, 812, 755, 685, 654; δ_H (300 MHz; $CDCl_3$) 2.40 (3H, s, CH_3), 3.30 (3H, s, CH_3), 4.22 (2H, s, CH_2), 7.19-7.30 (7H, m, 7 × CH), 7.54 (2H, d, *J* 8.4, 2 × CH); δ_C (400 MHz; $CDCl_3$) 21.7 (CH_3), 57.2 (CH_3), 60.0 (CH_2), 66.9 (C_{quat}), 80.3 (C_{quat}), 126.3 (2C, 2 × CH), 128.2 (2C, 2 × CH), 128.3 (CH), 129.5 (2C, 2 × CH), 129.8 (2C, 2 × CH), 133.1 (C_{quat}), 138.7 (C_{quat}), 145.0 (C_{quat}); HRMS *m/z* (TOF ES+) 338.0815. $C_{17}H_{17}NO_3NaS$ requires 338.0827.

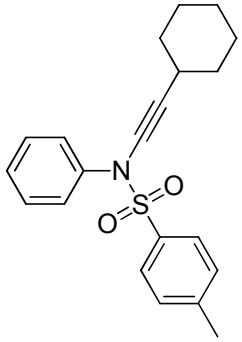
_N_-(3-methoxyprop-1-yn-1-yl)-4-methyl-_N_-phenylbenzenesulfonamide (286)



Following GP11 using amide **280** (2.47 g) and phenyacetylene (0.11 mL). Purification by flash chromatography [hexanes:EtOAc (20:1)] gave ynamide **286** as a pale yellow solid (639 mg, 92%); mp 104-105 °C; ν_{max} (neat)/cm^{-1} 3058, 2922, 2240, 1593, 1488, 1442, 1455, 1369, 1293, 1203, 1164, 1081, 1066, 1023, 924, 893, 813, 783, 758, 690, 680; δ_H (300 MHz; $CDCl_3$) 2.45 (3H, s, CH_3), 7.28-7.35 (9H, m, 9 × CH), 7.37-7.41 (3H, m, 3 × CH), 7.63 (2H, d, *J* 8.3, 2 × CH); δ_C (400 MHz; $CDCl_3$) 21.7 (CH_3), 70.5 (C_{quat}), 83.0 (C_{quat}), 122.7 (C_{quat}), 126.3 (2C, 2 × CH), 128.0 (CH), 128.3 (5C, 5 × CH), 129.1 (2C, 2 × CH), 129.5 (2C, 2 ×

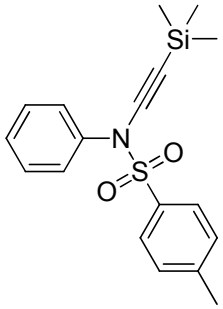
CH), 131.5 (2C, 2 × CH), 133.0 (C_{quat}), 139.0 (C_{quat}), 145.0 (C_{quat}); HRMS *m/z* (TOF ES+) 370.0872. $C_{21}H_{17}NO_2NaS$ requires 370.0878.

_N_-(Cyclohexylethynyl)-4-methyl-_N_-phenylbenzenesulfonamide (287)



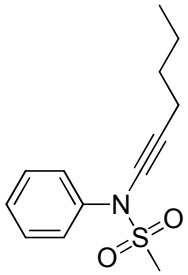
Following GP11 using amide **280** (2.47 g) and cyclohex-1-yne (0.26 mL). Purification by flash chromatography [hexanes:EtOAc (20:1)] gave ynamide **287** as a colorless oil (343 mg, 98%); ν_{max} (neat)/cm^{-1} 2932, 2853, 2251, 1738, 1596, 1488, 1447, 1366, 1268, 1174, 1154, 1088, 1029, 921; δ_H (300 MHz; $CDCl_3$) 1.30-1.36 (2H, m, CH_2), 1.36-1.54 (4H, m, 2 × CH_2), 1.62-1.71 (2H, m, CH_2), 1.74-1.81 (2H, m, CH_2), 2.43 (3H, s, CH_3), 2.47-2.55 (1H, m, CH), 7.24-7.28 (4H, m, 4 × CH), 7.28-7.33 (3H, m, 3 × CH), 7.55 (2H, d, *J* 8.3, 2 × CH); δ_C (400 MHz; $CDCl_3$) 21.7 (CH_3), 24.7 (2C, 2 × CH_2), 25.9 (CH_2), 28.8 (CH), 32.7 (2C, 2 × CH_2), 74.2 (C_{quat}), 74.3 (C_{quat}), 126.0 (2C, 2 × CH), 127.8 (CH), 128.3 (2C, 2 × CH), 128.9 (2C, 2 × CH), 129.2 (2C, 2 × CH), 132.9 (C_{quat}), 139.5 (C_{quat}), 144.6 (C_{quat}); HRMS *m/z* (TOF ES+) 376.1339. $C_{21}H_{23}NO_2NaS$ requires 376.1347.

4-Methyl-N-phenyl-N-((trimethylsilyl)ethynyl)benzenesulfonamide (288)



Following GP11 using amide **280** (2.75 g) and ethynyltrimethylsilane (0.28 mL). Purification by flash chromatography [hexanes:EtOAc (20:1)] gave ynamide **288** as a colourless solid (670 mg, 98%); mp 120-122 °C; ν_{max} (neat)/cm^{-1} 2961, 2165, 1591, 1490, 1365, 1248, 1185, 1160, 1139, 1085, 934, 908, 843, 831, 780, 712, 692; δ_H (300 MHz; $CDCl_3$) 0.17 (9H, s, 3 × CH_3), 2.45 (3H, s, CH_3), 7.22-7.27 (3H, m, 3 × CH), 7.29-7.34 (4H, m, 4 × CH), 7.57 (2H, d, *J* 8.4, 2 × CH); δ_C (400 MHz; $CDCl_3$) 0.0 (3C, 3 × CH_3), 21.7 (CH_3), 73.3 (C_{quat}), 95.3 (C_{quat}), 126.2 (2C, 2 × CH), 128.2 (CH), 128.4 (2C, 2 × CH), 129.0 (2C, 2 × CH), 129.3 (2C, 2 × CH), 132.9 (C_{quat}), 138.6 (C_{quat}), 144.9 (C_{quat}); HRMS *m/z* (TOF ES+) 366.0963. $C_{18}H_{21}NO_2NaSSi$ requires 366.0960.

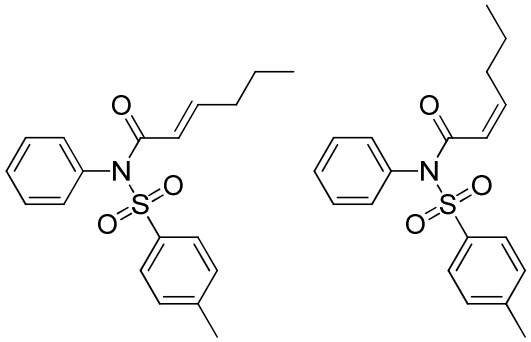
***N*-(Hex-1-yn-1-yl)-*N*-phenylmethanesulfonamide (289)**



Following GP11 using amide **281** (1.71 g) and hex-1-yne (0.24 mL). Purification by flash chromatography [hexanes:EtOAc (20:1)] gave ynamide **289** as a colorless oil (576 mg, 98%); ν_{max} (neat)/cm^{-1} 2957, 2929, 2858, 2256, 1593, 1490, 1456, 1362, 1322, 1270, 1168, 1155, 1075, 1027, 958, 924, 901, 825, 757, 737, 691; δ_H (300 MHz; $CDCl_3$) 0.92 (3H, t, *J* 7.2, CH_3),

1.37-1.48 (2H, m, CH_2), 1.49-1.60 (2H, m, CH_2), 2.35 (2H, t, *J* 7.0, CH_2), 3.07 (3H, s, CH_3), 7.30-7.43 (3H, m, 3 × CH), 7.51 (2H, d, *J* 7.9, 2 × CH); δ_C (400 MHz; $CDCl_3$) 13.6 (CH_2), 18.2 (CH_2), 22.0 (CH_2), 30.9 (CH_2), 36.1 (CH_3), 71.1 (C_{quat}), 73.1 (C_{quat}), 125.4 (2C, 2 × CH), 128.0 (CH), 129.3 (2C, 2 × CH), 139.1 (C_{quat}); HRMS *m/z* (TOF EI+) 251.0981. $C_{13}H_{17}NO_2S$ requires 251.0980.

(*E*) and (*Z*),*N*-Phenyl-*N*-tosylhex-2-enamides (294)

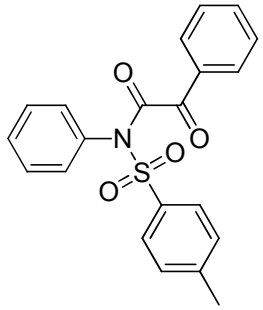


Following GP12A using ynamide **283** (98 mg) for 10 min. Purification by flash chromatography [hexanes:EtOAc (15:1)] gave imide (*E*)-**294** as a colourless oil (50 mg, 49 %) and imide (*Z*)-**294** as a colourless oil (22 mg, 21 %). Total yield in imide **294**: 70 % [*E*:*Z* (2.3:1)].

Following GP12B using ynamide **283** (98 mg) for 18 h. Purification by flash chromatography [hexanes:EtOAc (15:1)] gave imide (*E*)-**294** as a colourless oil (57 mg, 56 %) and imide (*Z*)-**294** as a colourless oil (15 mg, 14 %). Total yield in imide **294**: 70 % [*E*:*Z* (3.7:1)]; imide (*Z*)-**294**: ν_{max} (neat)/cm^{-1} 2964, 2931, 2877, 1688, 1623, 1597, 1488, 1455, 1420, 1357, 1241, 1174, 1149, 1120, 1087, 1074, 1002, 877, 819, 793, 733, 696, 685; δ_H (300 MHz; $CDCl_3$) 0.87 (3H, t, *J* 7.4, CH_3), 1.31-1.44 (2H, m, CH_2), 2.46 (3H, s, CH_3), 2.52 (2H, dtd, *J* 7.5 and 7.3, 1.8, CH_2), 5.41 (1H, dt, *J* 11.6 and 1.8, CH), 5.98 (1H, dt, *J* 11.6 and 7.3, CH), 7.22-7.25 (2H, m, 2 × CH), 7.34 (2H, d, *J* 8.4, 2 × CH), 7.42-7.50 (2H, m, 2 × CH), 7.93 (2H, d, *J* 8.4, 2

× CH); δ_C (400 MHz; $CDCl_3$) 13.7 (CH_3), 21.7 (CH_3), 22.2 (CH_2), 31.1 (CH_2), 120.3 (CH), 129.2 (2C, 2 × CH), 129.3 (2C, 2 × CH), 129.6 (2C, 2 × CH), 129.7 (CH), 130.3 (2C, 2 × CH), 136.4 (C_{quat}), 136.5 (C_{quat}), 144.6 (C_{quat}), 151.4 (CH), 165.3 (C_{quat}); HRMS *m/z* (TOF ES+) 366.1135. $C_{19}H_{21}NO_3NaS$ requires 366.1140; imide (*E*)-**294:** ν_{max} (neat)/cm^{-1} 2963, 2929, 2876, 1689, 1635, 1595, 1488, 1455, 1361, 1291, 1255, 1165, 1121, 1088, 975, 904, 814, 726, 695, 682; δ_H (300 MHz; $CDCl_3$) 0.78 (3H, t, *J* 7.4, CH_3), 1.23-1.35 (2H, m, CH_2), 1.97 (2H, dtd, *J* 7.3 and 7.2 and 1.5, CH_2), 2.45 (3H, s, CH_3), 5.44 (1H, dt, *J* 15.1 and 1.5, CH), 6.95 (1H, dt, *J* 15.1 and 7.1, CH), 7.23-7.29 (2H, m, 2 × CH), 7.34 (2H, d, *J* 8.4, 2 × CH), 7.45-7.53 (3H, m, 3 × CH), 7.93 (2H, d, *J* 8.4, 2 × CH) ; δ_C (400 MHz; $CDCl_3$) 13.5 (CH_3), 21.2 (CH_2), 21.7 (CH_3), 34.4 (CH_2), 121.3 (CH), 129.2 (2C, 2 × CH), 129.3 (2C, 2 × CH), 129.7 (2C, 2 × CH), 129.8 (CH), 130.4 (2C, 2 × CH), 136.1 (C_{quat}), 136.3 (C_{quat}), 144.7 (C_{quat}), 151.0 (CH), 165.3 (C_{quat}); HRMS *m/z* (TOF ES+) 366.1141. $C_{18}H_{21}NO_2NaS$ requires 366.1140.

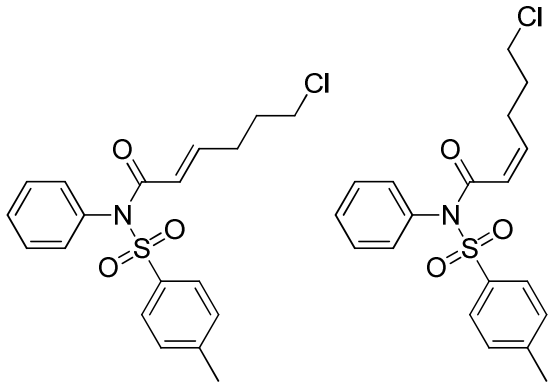
2-Oxo-*N*,2-diphenyl-*N*-tosylacetamide (298)



The catalyst system was prepared by addition of CH_2Cl_2 (1 mL) to $AuClPPh_3$ (5 mg, 0.01 mmol, 10 mol%) and AgOTs (2.8 mg, 0.01 mmol, 10 mol%) in a flame-dried Schlenk flask under argon. After stirring for 10 min at rt, a white precipitate of AgCl was observed and ynamide **286** (0.1 mmol, 35 mg) and pyridine-*N*-oxide (22 mg, 0.22 mmol, 2.2 eq) were added. The reaction mixture was stirred at rt for 3 h before being filtered through a pad of

silica. The filtrate was then concentrated under reduced pressure and purification of the residue by flash chromatography [hexanes:EtOAc (20:1)] gave oxoacetamide **298** as a colourless oil (30 mg, 79 %); ν_{max} (neat)/cm^{-1} 2921, 2988, 1685, 1672, 1595, 1487, 1449, 1374, 1325, 1306, 1229, 1191, 1173, 1148, 1086, 1073, 1034, 955, 912, 812, 758, 737, 710, 694, 662; δ_H (300 MHz; $CDCl_3$) 2.48 (3H, s, CH_3), 7.13 (2H, d, *J* 6.9, 2 × CH), 7.33-7.44 (5H, m, 5 × CH), 7.50-7.55 (2H, m, 2 × CH), 7.60-7.70 (1H, m, CH), 7.75 (2H, d, *J* 8.4, 2 × CH), 7.88-7.90 (2H, m, 2 × CH); δ_C (400 MHz; $CDCl_3$) 21.8 (CH_3), 128.9 (2C, 2 × CH), 129.1 (2C, 2 × CH), 129.5 (2C, 2 × CH), 129.6 (2C, 2 × CH), 129.8 (2C, 2 × CH), 130.2 (CH), 130.6 (2C, 2 × CH), 132.7 (C_{quat}), 133.5 (C_{quat}), 134.1 (C_{quat}), 134.6 (CH), 145.9 (C_{quat}), 166.7 (C_{quat}), 187.6 (C_{quat}); HRMS *m/z* (TOF ES+) 402.0765. $C_{21}H_{17}NO_4NaS$ requires 402.0776.

(*E*) and (*Z*)-6-Chloro-*N*-Phenyl-*N*-tosylhex-2-enamides (303)

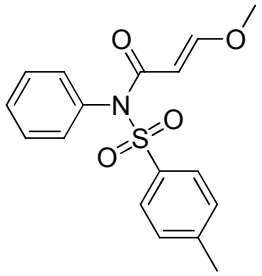


Following GP12A using ynamide **284** (109 mg) for 10 min. Purification by flash chromatography [hexanes:EtOAc (15:1)] gave imide (*E*)-**303** as a colourless oil (54 mg, 48 %) and imide (*Z*)-**303** as a colourless oil (29 mg, 25 %). Total yield in enamide **303**: 73 % [*E*:*Z* (1.9:1)].

Following GP12B using ynamide **284** (109 mg) for 18 h. Purification by flash chromatography [hexanes:EtOAc (15:1)] gave imide (*E*)-**303** as a colourless oil (61 mg, 54

%) and imide (*Z*)-**303** as a colourless oil (18 mg, 16 %). Total yield in imide **303**: 70 % [*E*:*Z* (3.5:1)]; imide (*E*)-**303**: ν_{max} (neat)/cm^{-1} 2960, 2924, 2853, 1689, 1637, 1594, 1488, 1361, 1169, 1087, 907, 813, 725, 694, 681; δ_H (300 MHz; $CDCl_3$) 1.69 (2H, m, CH_2), 2.17 (2H, dtd, *J* 7.3 and 7.1 and 1.4, CH_2), 2.45 (3H, s, CH_3), 3.39 (2H, t, *J* 6.4, CH_2), 5.51 (1H, dt, *J* 15.0 and 1.5, CH), 6.90 (1H, dt, *J* 15.0 and 7.2, CH), 7.23-7.29 (2H, m, 2 × CH), 7.34 (2H, d, *J* 8.4, 2 × CH), 7.46-7.55 (3H, m, 3 × CH), 7.92 (2H, d, *J* 8.4, 2 × CH); δ_C (400 MHz; $CDCl_3$) 21.7 (CH_3), 29.2 (CH_2), 30.4 (CH_2), 43.6 (CH_2), 122.4 (CH), 129.2 (2C, 2 × CH), 129.3 (2C, 2 × CH), 129.7 (2C, 2 × CH), 129.9 (CH), 130.2 (2C, 2 × CH), 135.9 (C_{quat}), 136.2 (C_{quat}), 144.8 (C_{quat}), 148.5 (CH), 164.9 (C_{quat}); HRMS *m/z* (TOF ES+) 400.0754. $C_{19}H_{20}NO_3NaS^{35}Cl$ requires 400.0750; imide (*Z*)-**303**: ν_{max} (neat)/cm^{-1} 2924, 2855, 1688, 1627, 1595, 1489, 1454, 1415, 1359, 1242, 1159, 1088, 907, 881, 812, 726, 694, 684; δ_H (300 MHz; $CDCl_3$) 1.84 (2H, dt, *J* 14.0 and 6.8, CH_2), 2.46 (3H, s, CH_3), 2.68 (2H, ddt, *J* 7.5 and 7.5 and 1.7, CH_2), 3.47 (2H, t, *J* 6.8, CH_2), 5.47 (1H, dt, *J* 11.5 and 1.7, CH), 5.95 (1H, dt, *J* 11.5 and 7.5, CH), 7.23-7.26 (2H, m, 2 × CH), 7.35 (2H, d, *J* 8.3, 2 × CH), 7.45-7.49 (3H, m, 3 × CH), 7.92 (2H, d, *J* 8.3, 2 × CH); δ_C (400 MHz; $CDCl_3$) 21.7 (CH_3), 26.6 (CH_2), 31.7 (CH_2), 44.2 (CH_2), 121.5 (CH), 129.2 (2C, 2 × CH), 129.4 (2C, 2 × CH), 129.7 (2C, 2 × CH), 129.8 (CH), 130.3 (2C, 2 × CH), 136.2 (C_{quat}), 136.3 (C_{quat}), 144.8 (C_{quat}), 148.7 (CH), 165.0 (C_{quat}); HRMS *m/z* (TOF ES+) 400.0751. $C_{19}H_{20}NO_3NaS^{35}Cl$ requires 400.0750;

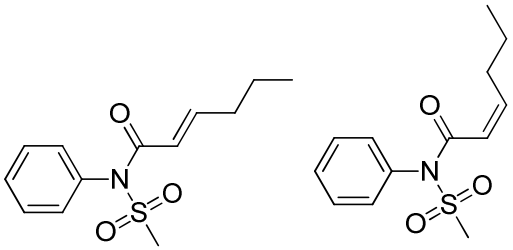
(*E*)-3-Methoxy-*N*-phenyl-*N*-tosylacrylamide (304)



Following GP12A using ynamide **285** (95 mg) for 12 h. Purification by flash chromatography [hexanes:EtOAc (20:1)] gave imide **(*E*)-304** as a colourless oil (70 mg, 70 %).

Following GP12B using ynamide **285** (95 mg) for 18 h. Purification by flash chromatography [hexanes:EtOAc (20:1)] gave imide **(*E*)-304** as a colourless oil (65 mg, 65 %); ν_{max} (neat)/cm^{-1} 2976, 2936, 1682, 1605, 1488, 1453, 1438, 1354, 1331, 1256, 1169, 1113, 1084, 931, 906, 810, 723, 692, 683; δ_H (300 MHz; $CDCl_3$) 2.45 (3H, s, CH_3), 3.46 (3H, s, CH_3), 4.82 (1H, d, *J* 12.1, CH), 7.27-7.30 (2H, m, 2 × CH), 7.34 (2H, d, *J* 8.4, 2 × CH), 7.46-7.56 (4H, m, 4 × CH), 7.93 (2H, d, *J* 8.4, 2 × CH); δ_C (400 MHz; $CDCl_3$) 21.7 (CH_3), 58.1 (CH_3), 97.0 (CH), 129.1 (2C, 2 × CH), 129.3 (2C, 2 × CH), 129.6 (2C, 2 × CH), 129.8 (CH), 130.4 (2C, 2 × CH), 136.4 (C_{quat}), 136.7 (C_{quat}), 144.6 (C_{quat}), 164.6 (CH), 166.5 (C_{quat}); HRMS *m/z* (TOF ES+) 354.0766. $C_{17}H_{17}NO_4NaS$ requires 354.0776.

(*E*) and (*Z*)-*N*-(Methylsulfonyl)-*N*-phenylhex-2-enamides (305).

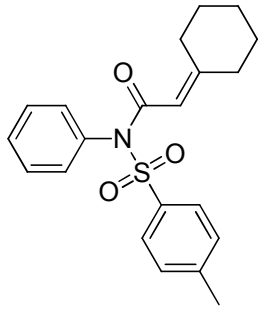


Following GP12A using ynamide **289** (109 mg) for 10 min. Purification by flash chromatography [hexanes:EtOAc (15:1)] gave imide (*E*)-**305** as a colourless oil (45 mg, 56

%) and imide (*Z*)-**305** as a colourless oil (15 mg, 19 %). Total yield in imide **305**: 75 % [*E*:*Z* (3:1)].

Following GP12B using ynamide **289** (109 mg) for 18 h. Purification by flash chromatography [hexanes:EtOAc (15:1)] gave imide (*E*)-**305** as a colourless oil (46 mg, 58 %) and imide (*Z*)-**305** as a colourless oil (11 mg, 13 %). Total yield in imide **305**: 71 % [*E*:*Z* (4:1)]; imide (*Z*)-**305:** ν_{max} (neat)/cm^{-1} 2963, 2932, 2876, 1682, 1622, 1594, 1487, 1450, 1345, 1322, 1253, 1189, 1165, 1120, 840, 760, 736, 696; δ_H (300 MHz; $CDCl_3$) 0.95 (3H, t, *J* 7.4, CH_3), 1.41-1.51 (2H, m, CH_2), 2.66 (2H, dtd, *J* 7.5 and 7.4 and 1.8, CH_2), 3.48 (3H, s, CH_3), 5.46 (1H, dt, *J* 11.5 and 1.8, CH), 6.12 (1H, dt, *J* 11.5 and 7.4, CH), 7.26-7.30 (2H, m, 2 × CH), 7.45-7.50 (3H, m, 3 × CH); δ_C (400 MHz; $CDCl_3$) 13.8 (CH_3), 22.2 (CH_2), 31.3 (CH_2), 41.9 (CH_3), 119.8 (CH), 129.8 (2C, 2 × CH), 129.9 (CH), 130.0 (2C, 2 × CH), 135.6 (C_{quat}), 152.7 (CH), 166.5 (C_{quat}); HRMS *m/z* (TOF ES+) 290.0823. $C_{13}H_{17}NO_3NaS$ requires 290.0827; imide (*E*)-**305**: ν_{max} (neat)/cm^{-1} 2964, 2937, 2880, 1685, 1634, 1592, 1488, 1455, 1349, 1320, 1291, 1255, 1182, 1152, 1123, 963, 907, 765, 726, 695; δ_H (300 MHz; $CDCl_3$) 0.83 (3H, t, *J* 7.4, CH_3), 1.28-1.44 (2H, m, CH_2), 2.05 (2H, dtd, *J* 7.3 and 7.2 and 1.5, CH_2), 3.48 (3H, s, CH_3), 5.51 (1H, dt, *J* 15.2 and 1.5, CH), 7.10 (1H, dt, *J* 15.2 and 7.1, CH) 7.26-7.32 (2H, m, 2 × CH), 7.47-7.52 (3H, m, 3 × CH); δ_C (400 MHz; $CDCl_3$) 13.5 (CH_3), 21.2 (CH_2), 34.4 (CH_2), 41.9 (CH_3), 121.0 (CH), 129.8 (2C, 2 × CH), 130.0 (CH), 130.1 (2C, 2 × CH), 135.3 (C_{quat}), 151.8 (CH), 166.4 (C_{quat}); HRMS *m/z* (TOF ES+) 290.0830. $C_{13}H_{17}NO_3NaS$ requires 290.0827.

2-Cyclohexylidene-*N*-phenyl-*N*-tosylacetamide (306).



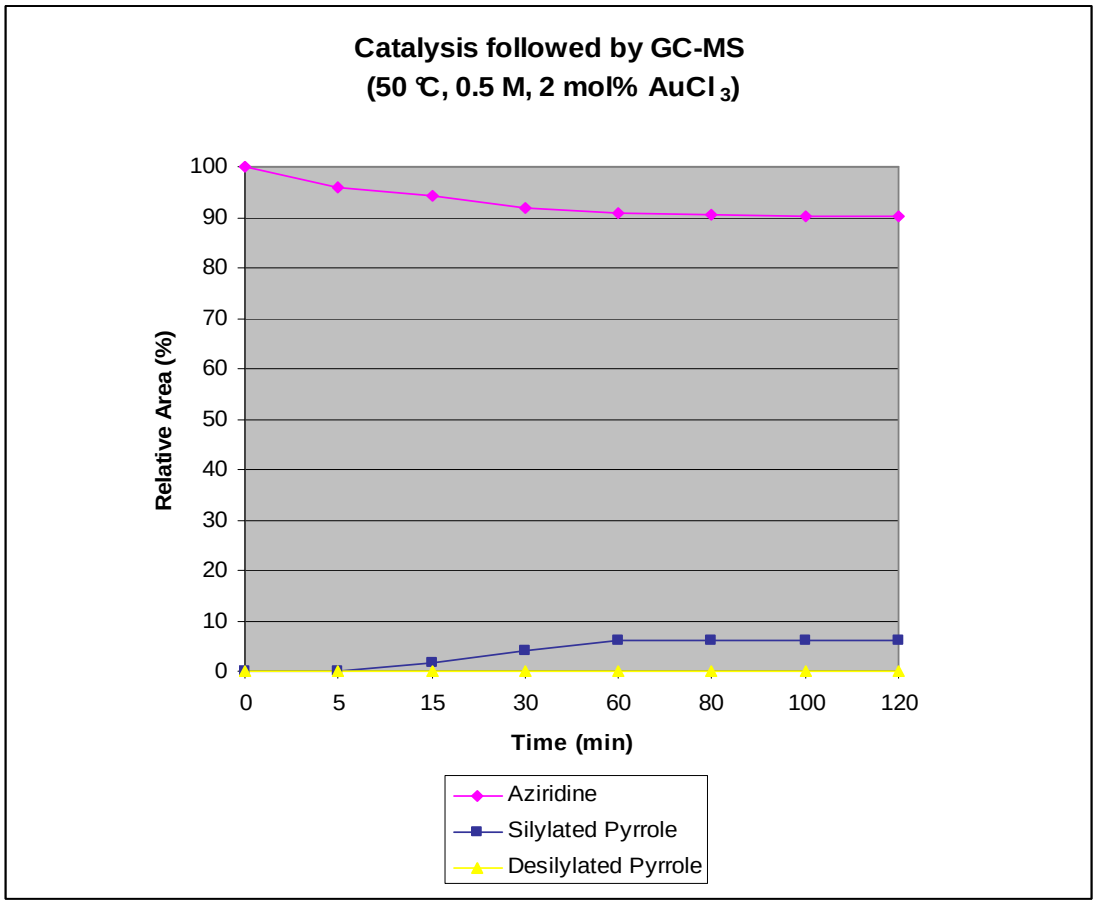
Following GP12A using ynamide **287** (109 mg) for 20 min. Purification by flash chromatography [hexanes:EtOAc (20:1)] gave imide **306** as a colourless oil (88 mg, 80 %).

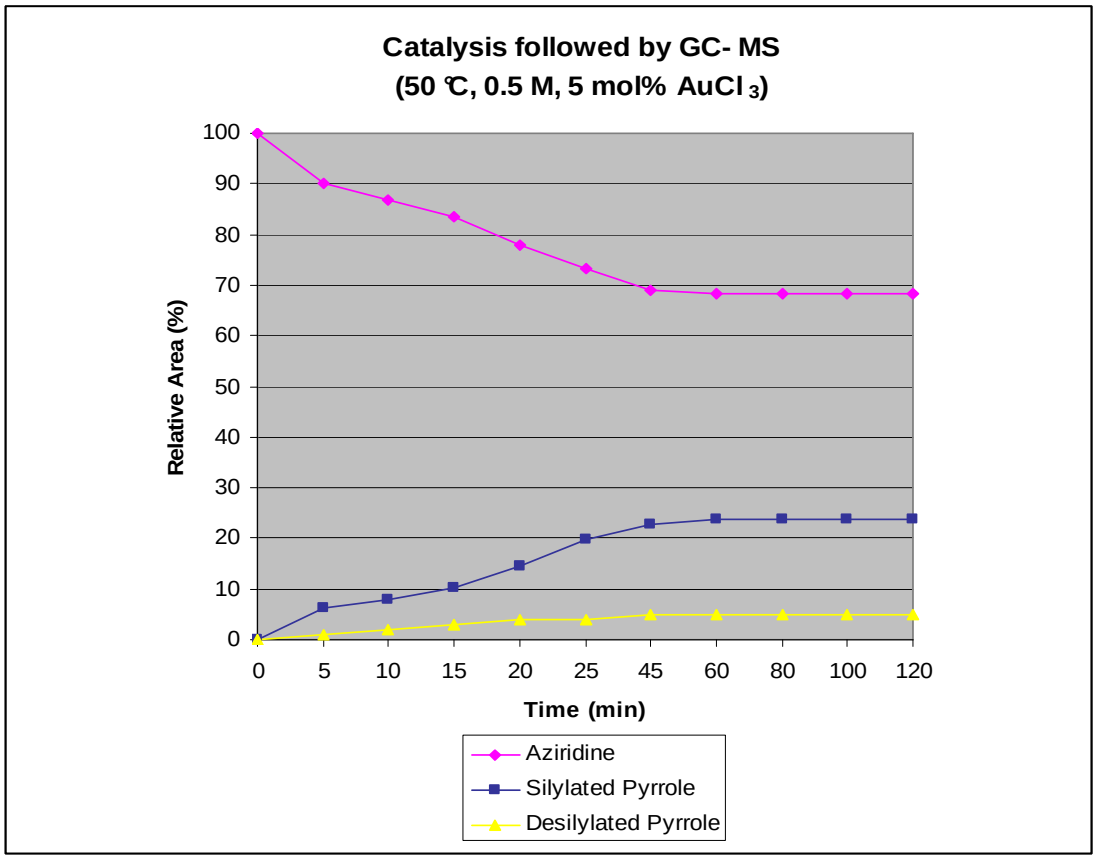
Following GP12B using ynamide **287** (109 mg) for 18 h. Purification by flash chromatography [hexanes:EtOAc (20:1)] gave imide **306** as a colourless oil (86 mg, 78 %); ν_{max} (neat)/cm^{-1} 2934, 2855, 1681, 1617, 1592, 1485, 1448, 1391, 1361, 1251, 1199, 1185, 1167, 1143, 1123, 997, 977, 933, 904, 889, 839, 814, 719, 692, 681, 653; δ_H (300 MHz; $CDCl_3$) 1.41-1.64 (6H, m, 3 × CH_2), 1.83-1.97 (2H, m, CH_2), 2.44 (3H, s, CH_3), 2.60-2.75 (2H, m, CH2), 5.21 (1H, s, CH), 7.22-7.28 (2H, m, 2 × CH), 7.33 (2H, d, *J* 8.4, 2 × CH), 7.43-7.49 (3H, m, 3 × CH), 7.92 (2H, d, *J* 8.4, 2 × CH); δ_C (400 MHz; $CDCl_3$) 21.7 (CH_3), 26.0 (CH_2), 27.7 (CH_2), 28.5 (CH_2), 30.1 (CH_2), 38.2 (CH_2), 114.0 (CH), 129.0 (2C, 2 × CH), 129.2 (2C, 2 × CH), 129.5 (3C, 3 × CH), 130.2 (2C, 2 × CH), 136.5 (C_{quat}), 136.6 (C_{quat}), 144.4 (CH), 164.8 (C_{quat}), 165.7 (C_{quat}); HRMS *m/z* (TOF ES+) 392.1281. $C_{21}H_{23}NO_3NaS$ requires 392.1296.

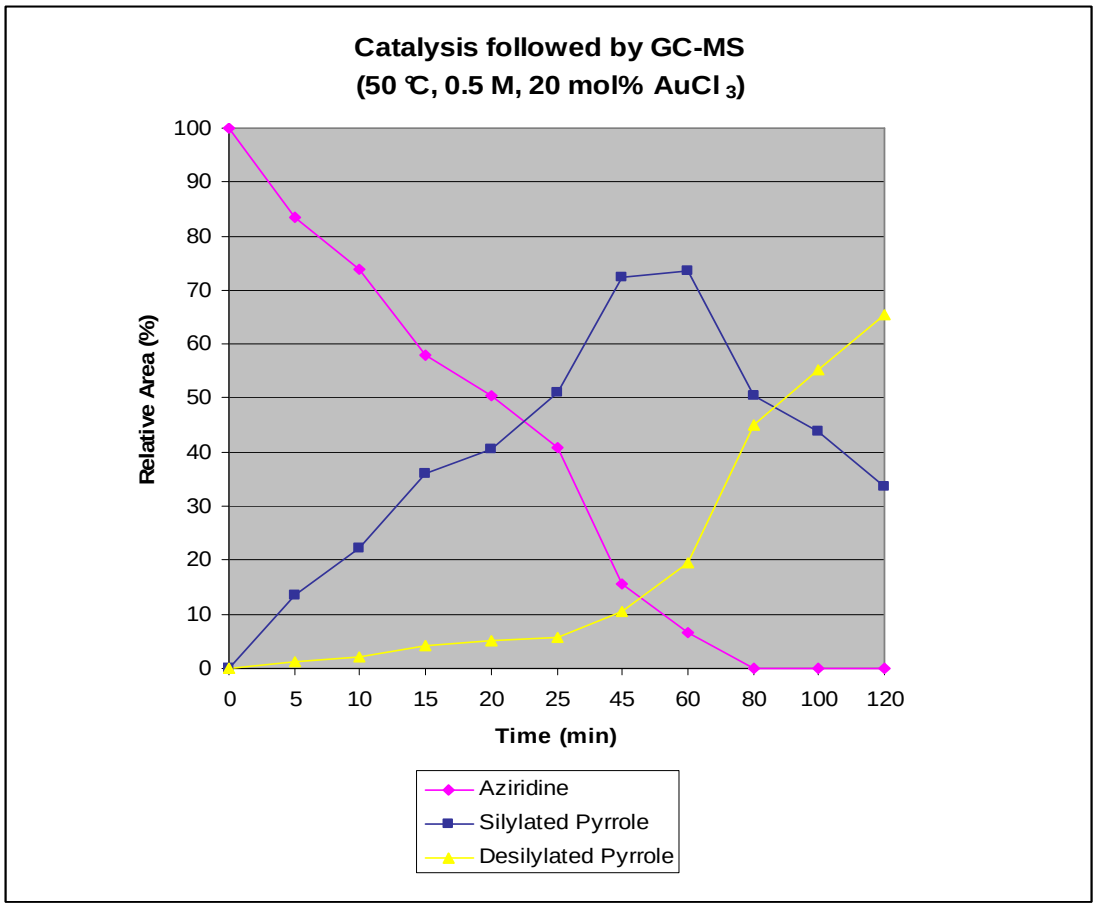
Appendices

Appendix A)

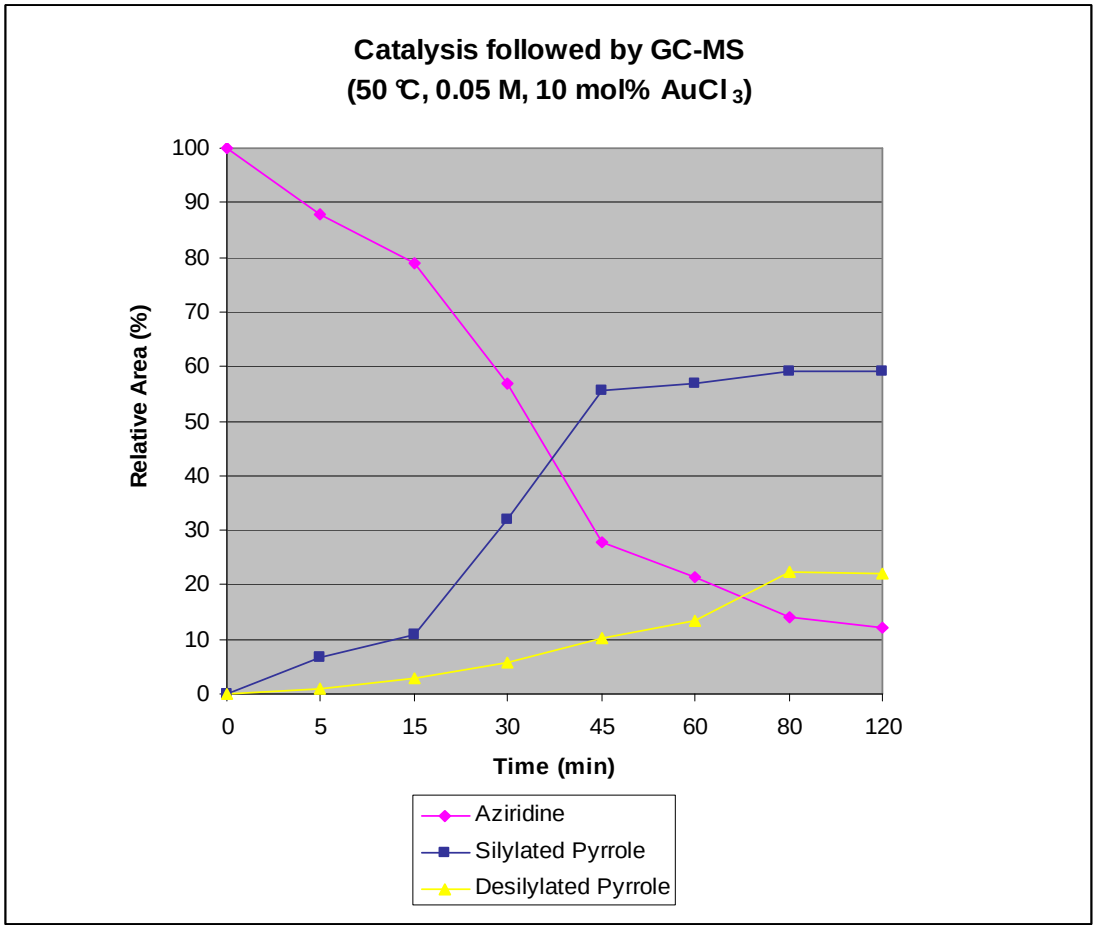
Study of the catalyst loading

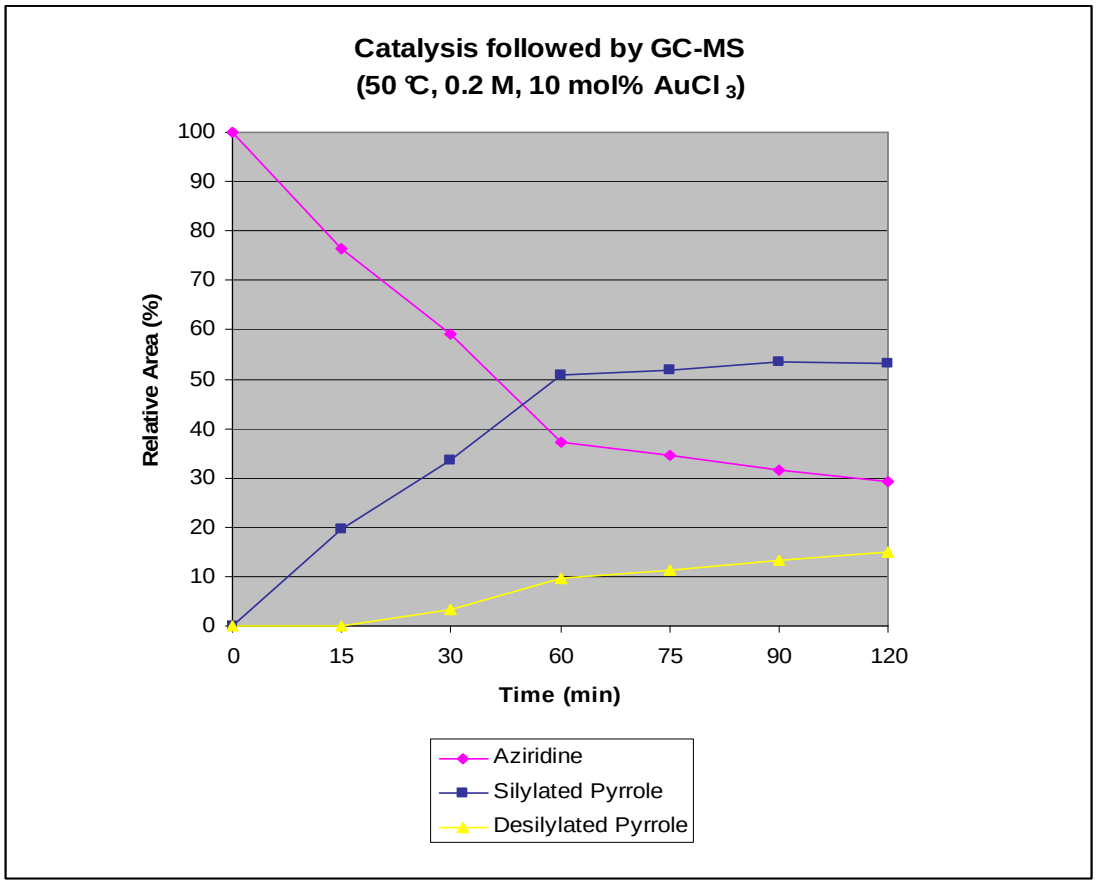


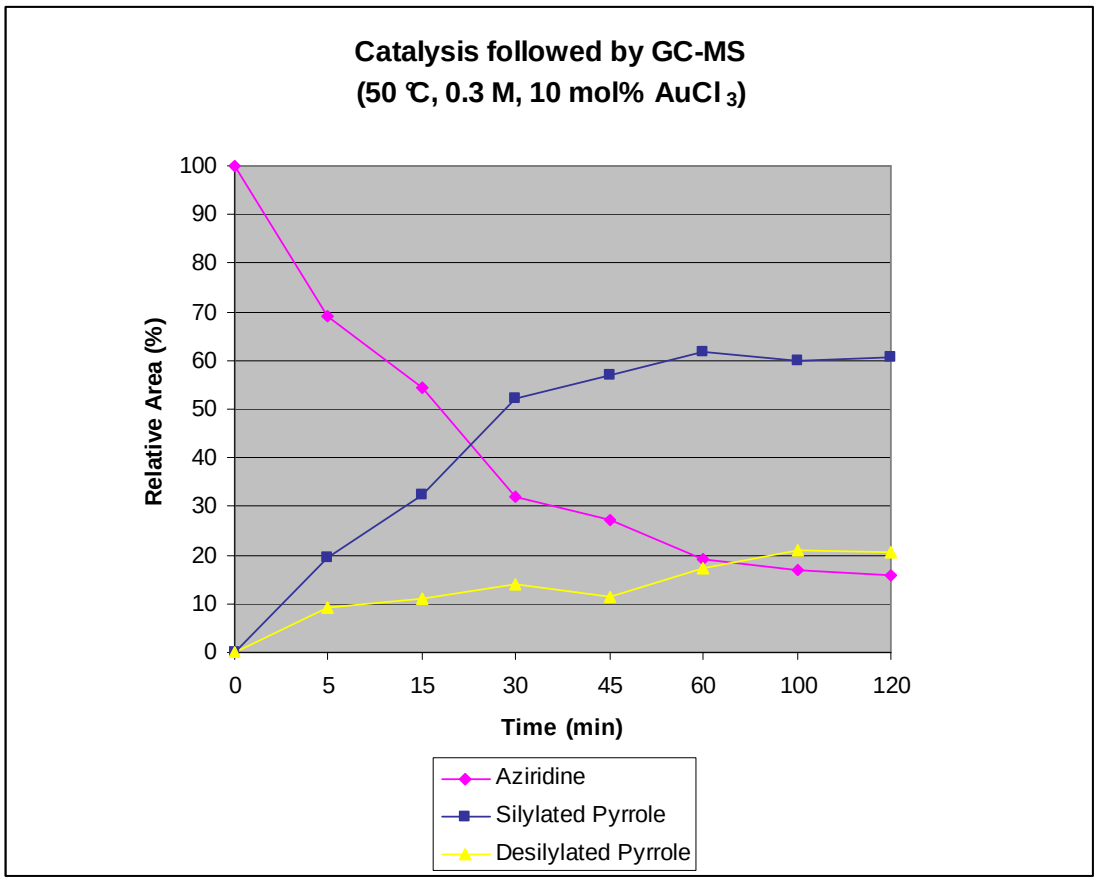

Catalysis followed by GC- MS
(50 ℃, 0.5 M, 5 mol% AuCl 3)
Relative Area (%)
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
45
60
80
100
120
Time (min)
Aziridine
Silylated Pyrrole
Desilylated Pyrrole

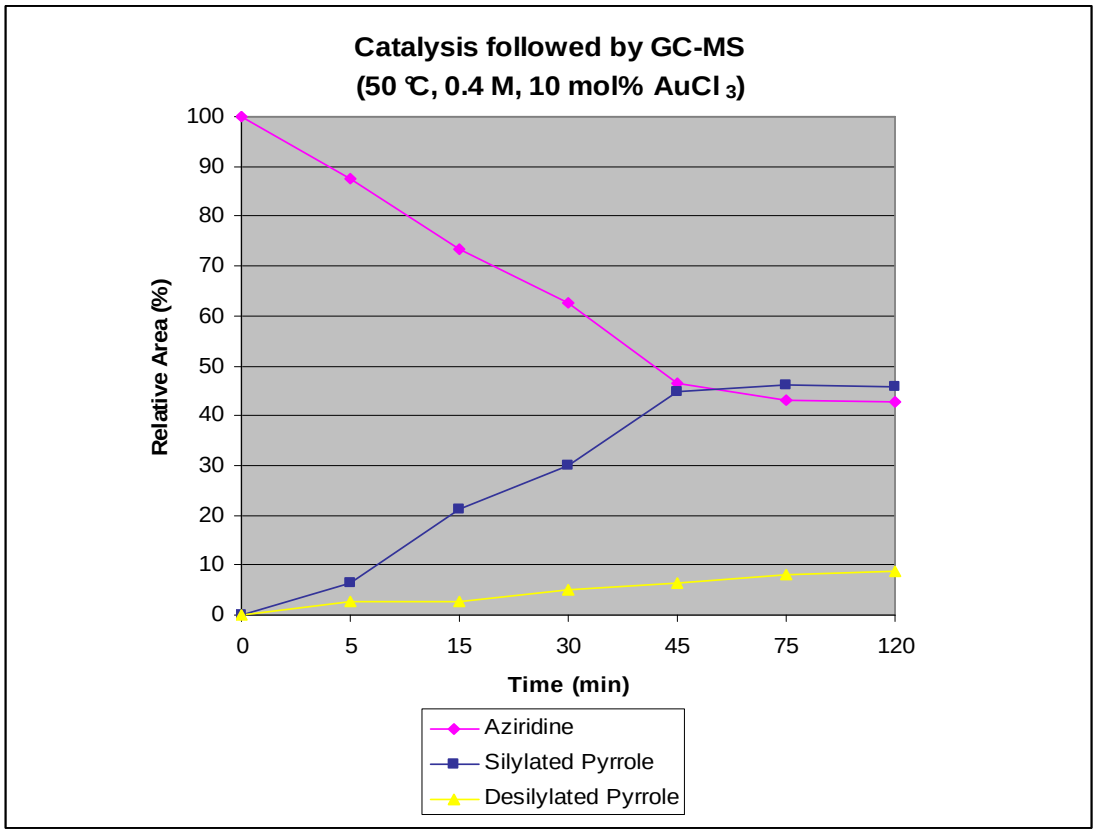

Catalysis followed by GC-MS
(50 ℃, 0.5 M, 20 mol% AuCl 3)
Relative Area (%)
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
45
60
80
100
120
Time (min)
Aziridine
Silylated Pyrrole
Desilylated Pyrrole

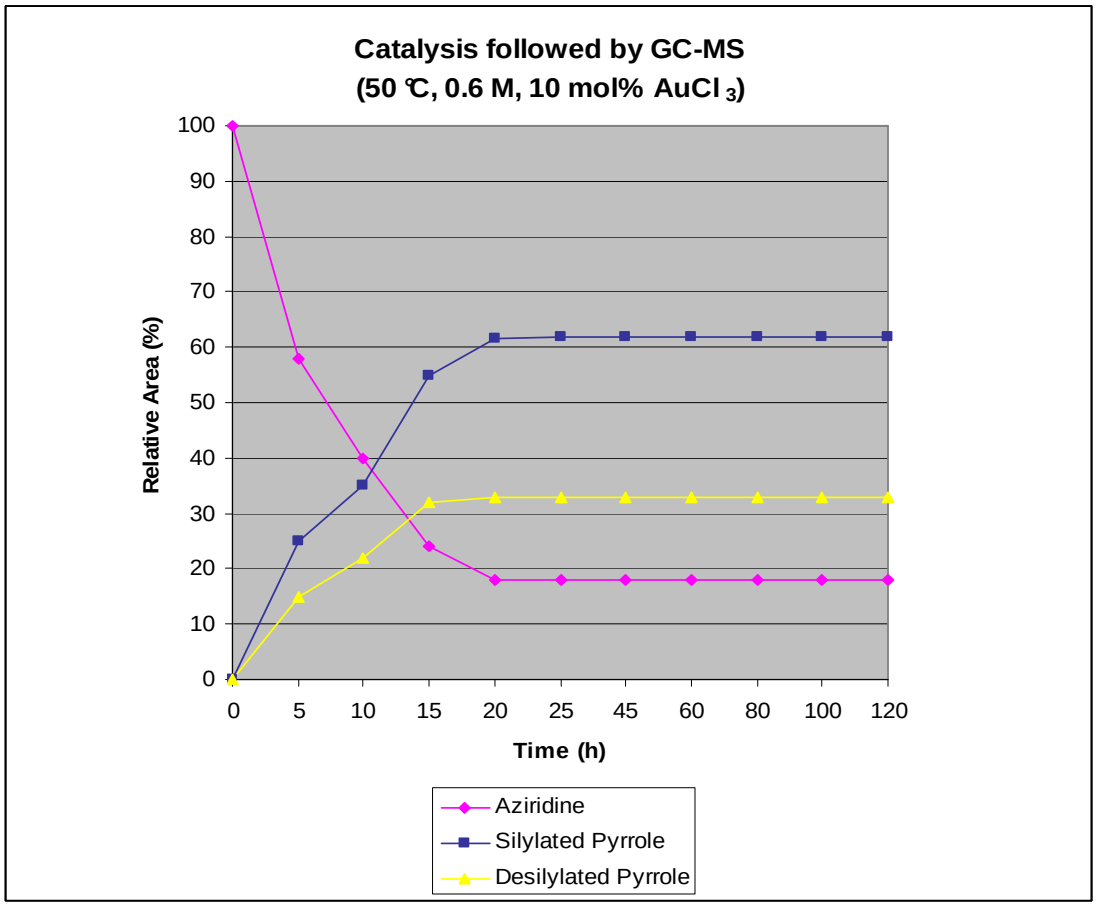
Study of the concentration



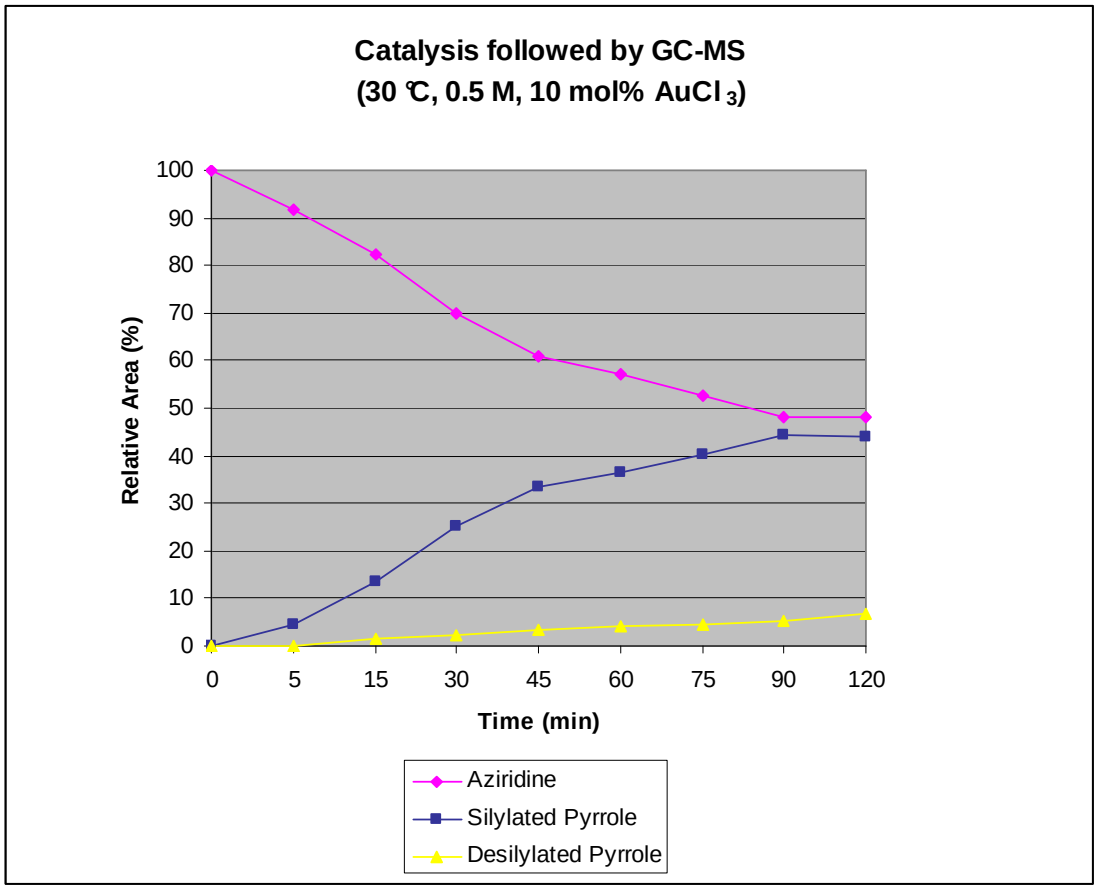

Catalysis followed by GC-MS
(50 ℃, 0.2 M, 10 mol% AuCl 3)
Relative Area (%)
100
90
80
70
60
50
40
30
20
10
0
0
15
30
60
75
90
120
Time (min)
Aziridine
Silylated Pyrrole
Desilylated Pyrrole

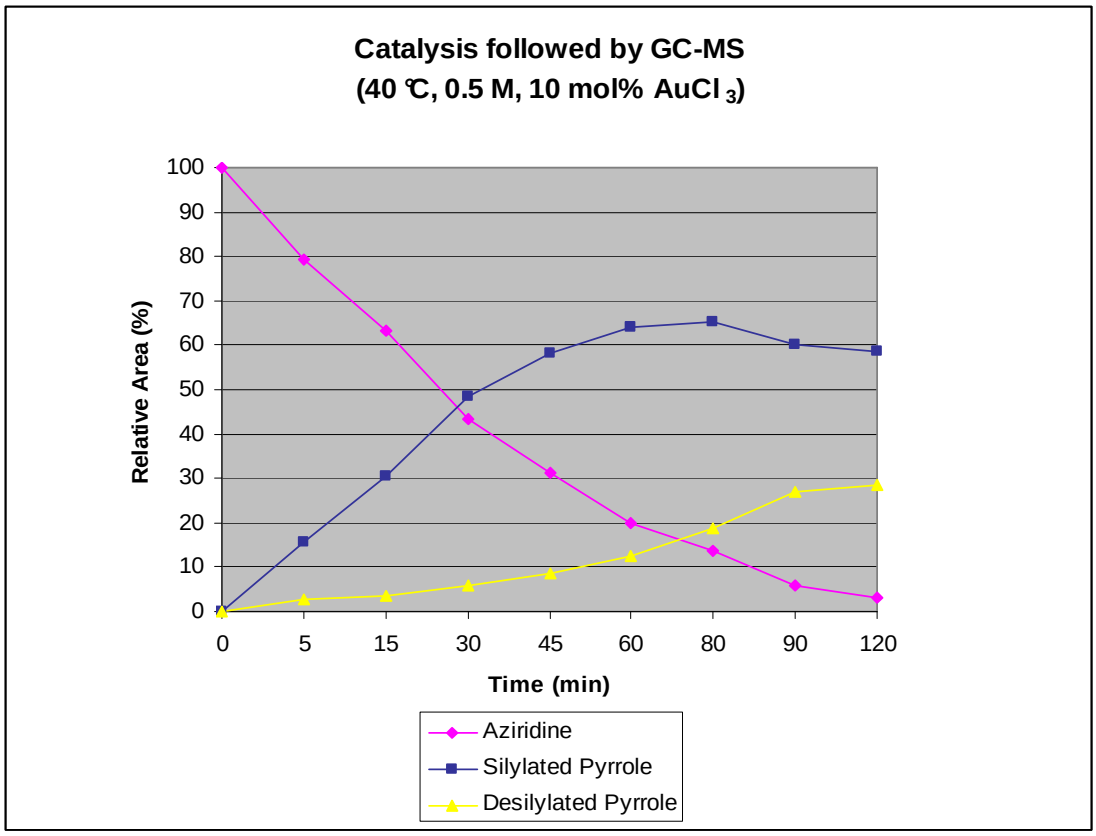

Catalysis followed by GC-MS
(50 ℃, 0.3 M, 10 mol% AuCl 3)
Relative Area (%)
100
90
80
70
60
50
40
30
20
10
0
0
5
15
30
45
60
100
120
Time (min)
Aziridine
Silylated Pyrrole
Desilylated Pyrrole

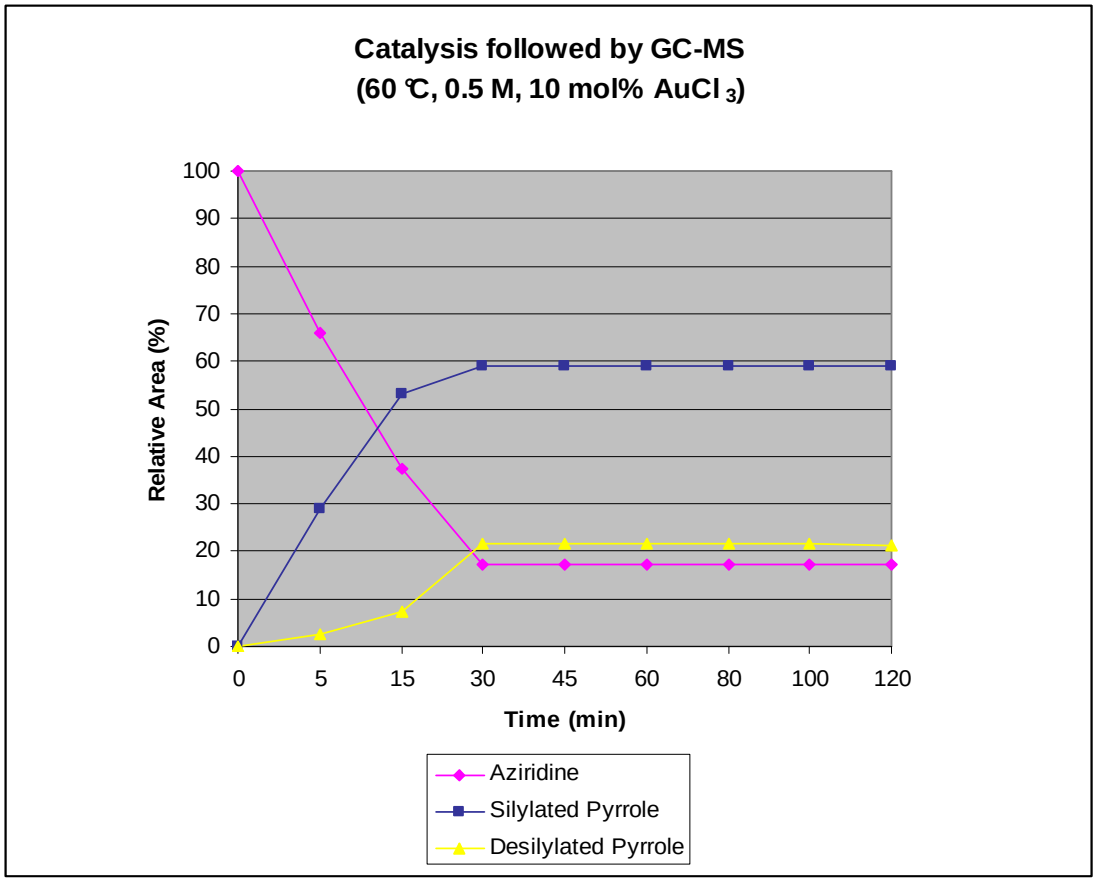

Catalysis followed by GC-MS
(50 ℃, 0.4 M, 10 mol% AuCl 3)
Relative Area (%)
100
90
80
70
60
50
40
30
20
10
0
0
5
15
30
45
75
120
Time (min)
Aziridine
Silylated Pyrrole
Desilylated Pyrrole

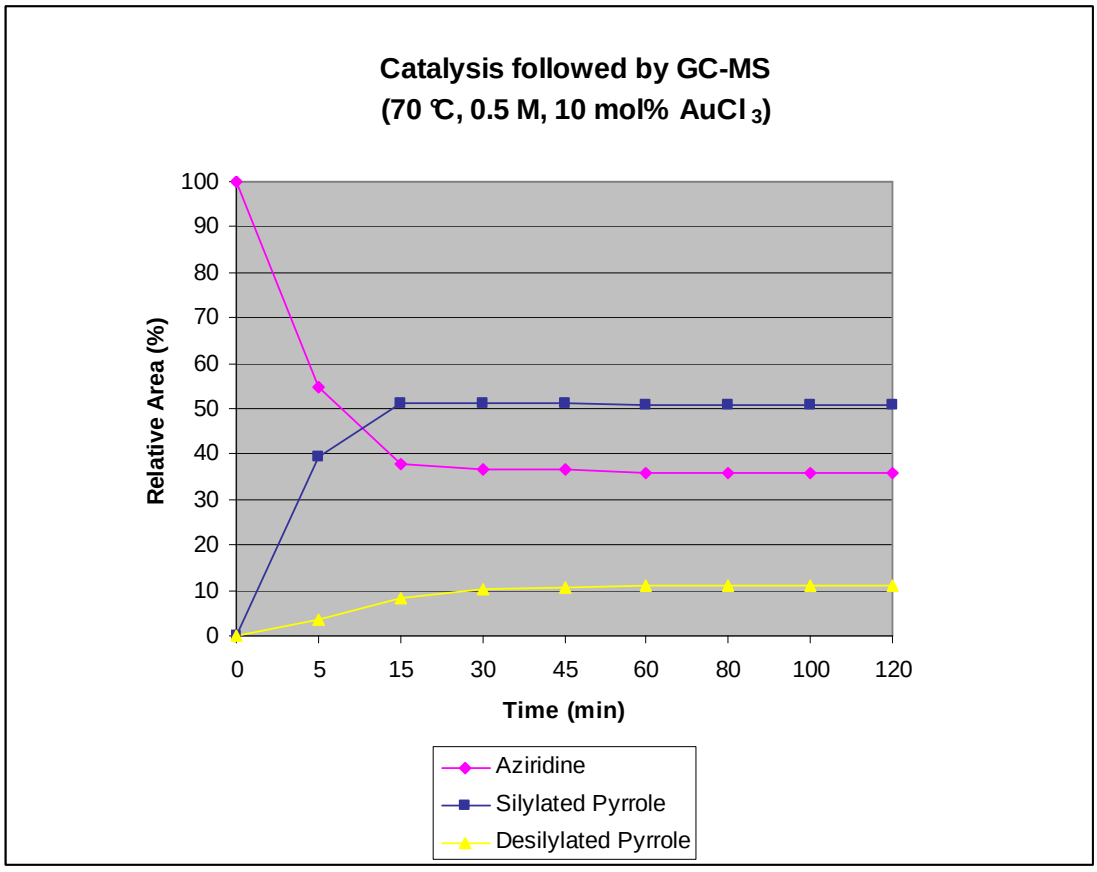

Catalysis followed by GC-MS
(50 ℃, 0.6 M, 10 mol% AuCl 3)
Relative Area (%)
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
45
60
80
100
120
Time (h)
Aziridine
Silylated Pyrrole
Desilylated Pyrrole

Study of the effect of temperature:

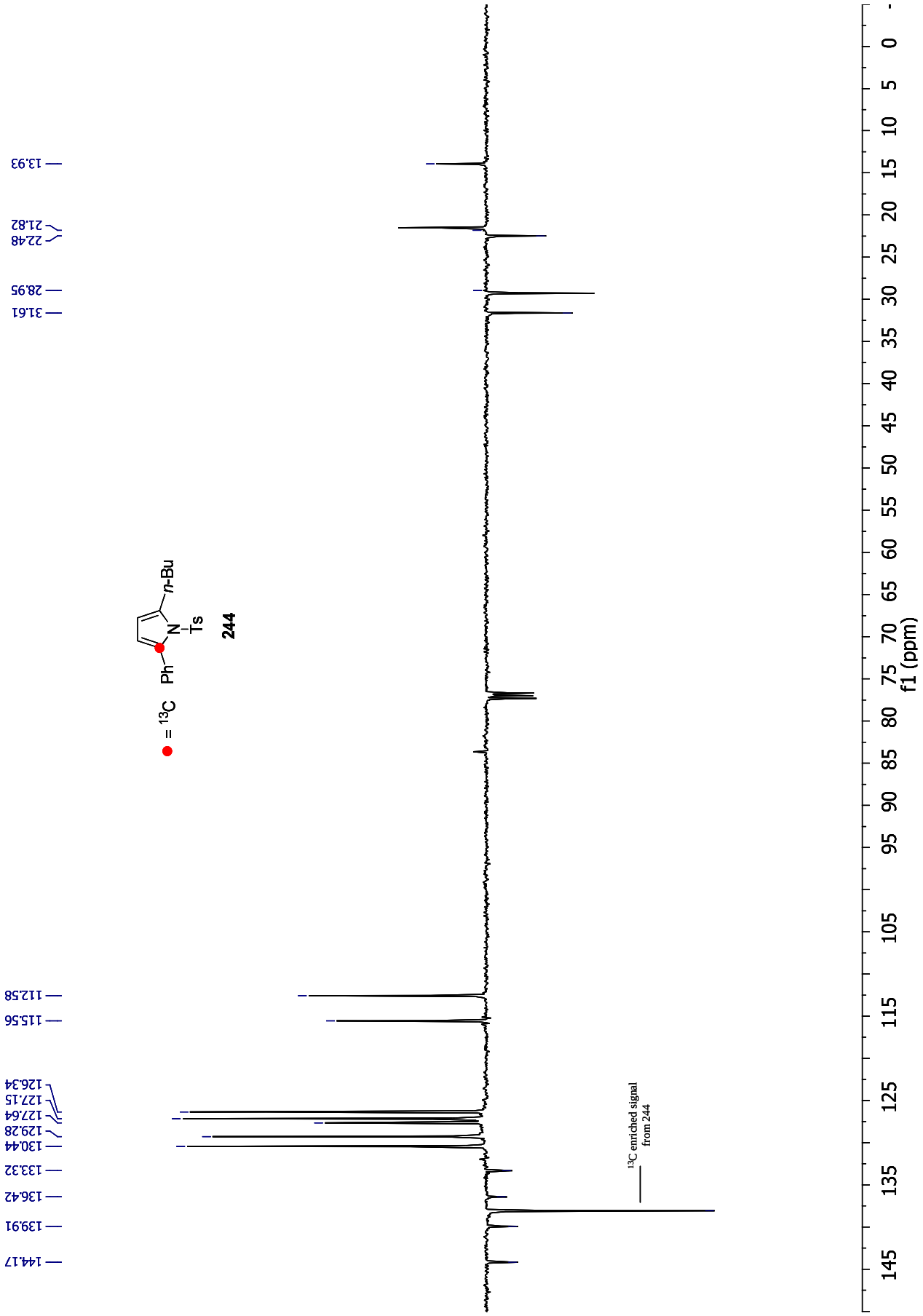


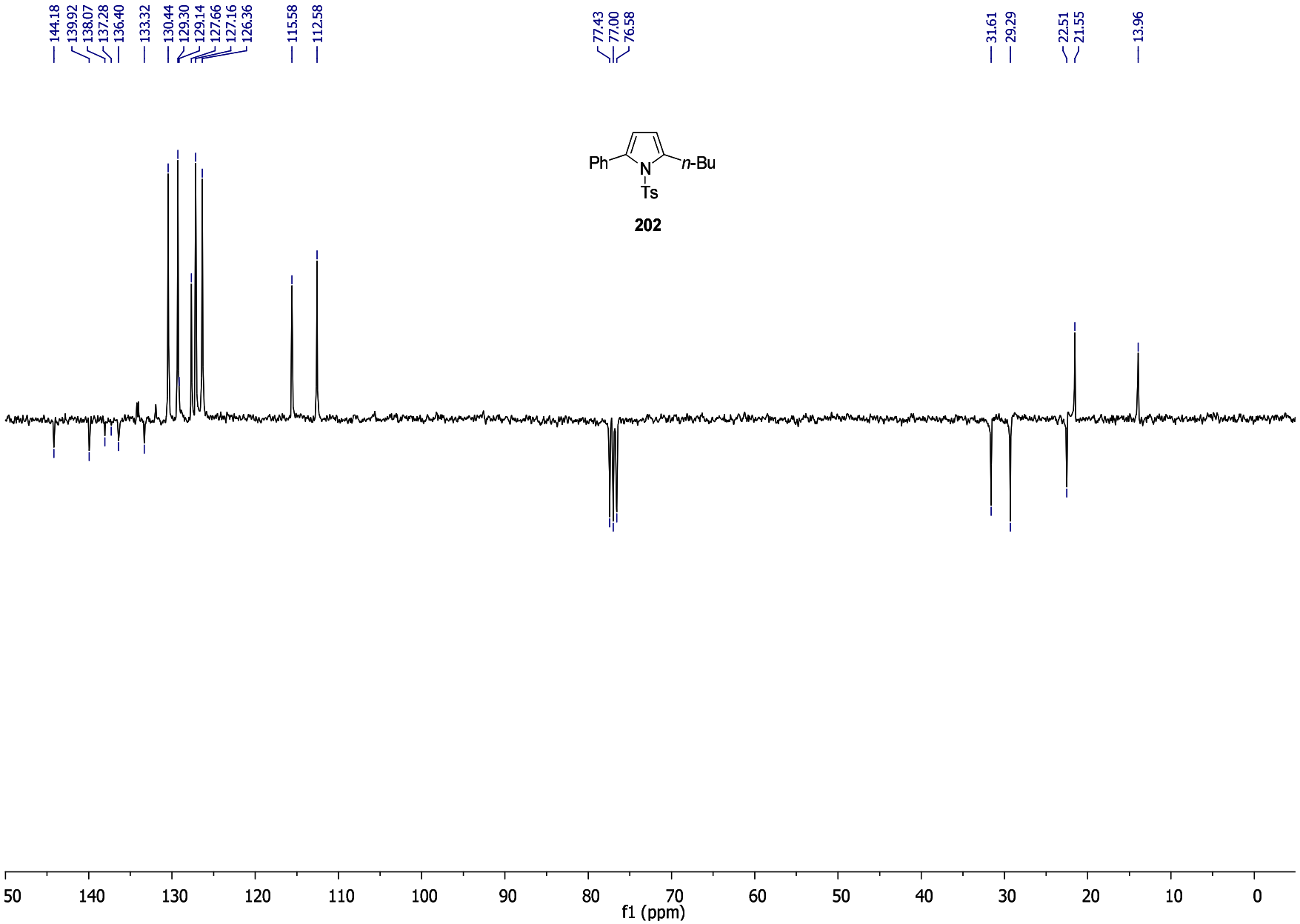

Catalysis followed by GC-MS
(40 ℃, 0.5 M, 10 mol% AuCl 3)
Relative Area (%)
100
90
80
70
60
50
40
30
20
10
0
0
5
15
30
45
60
80
90
120
Time (min)
Aziridine
Silylated Pyrrole
Desilylated Pyrrole

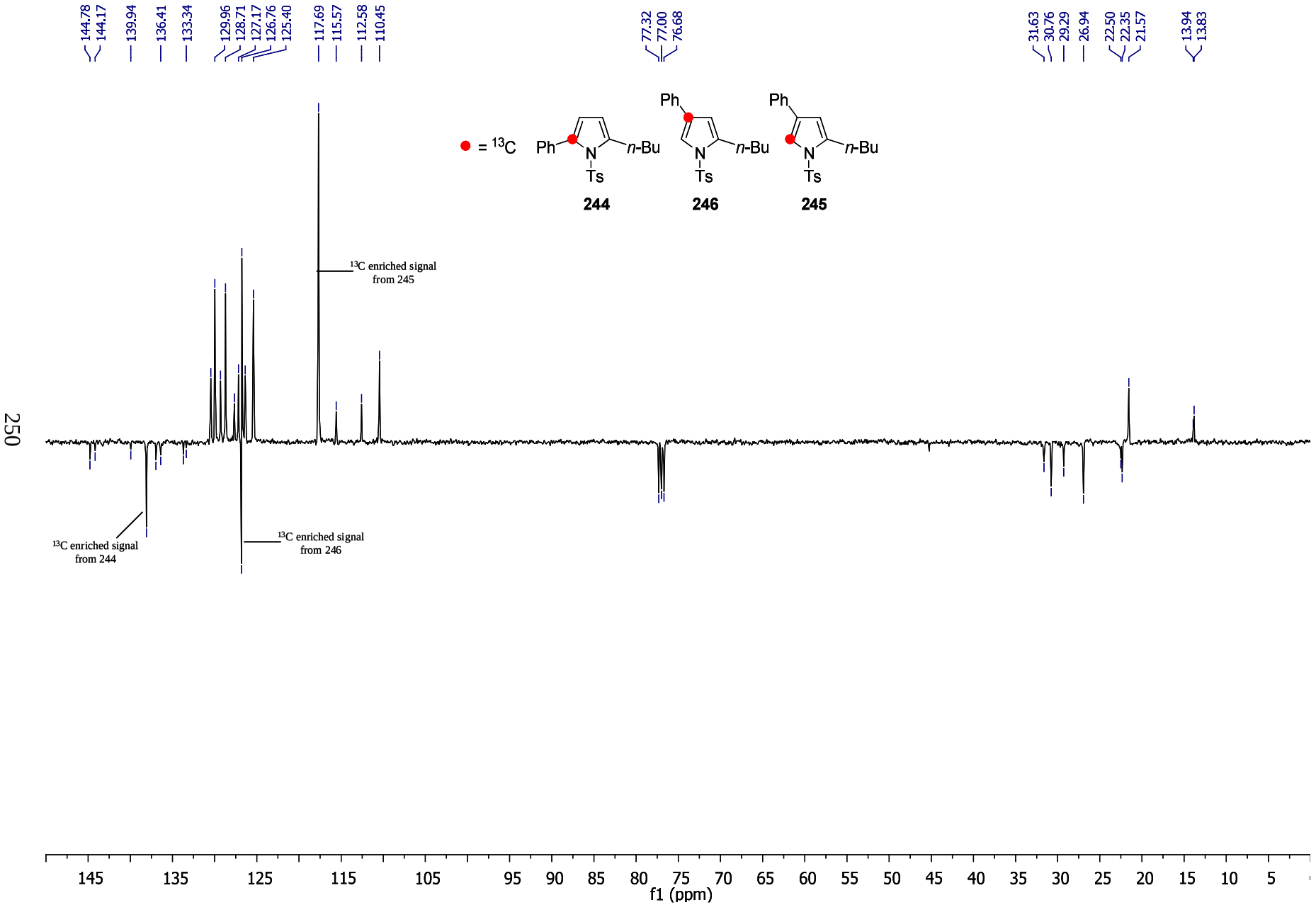

Catalysis followed by GC-MS
(60 ℃, 0.5 M, 10 mol% AuCl 3)
Relative Area (%)
100
90
80
70
60
50
40
30
20
10
0
0
5
15
30
45
60
80
100
120
Time (min)
Aziridine
Silylated Pyrrole
Desilylated Pyrrole

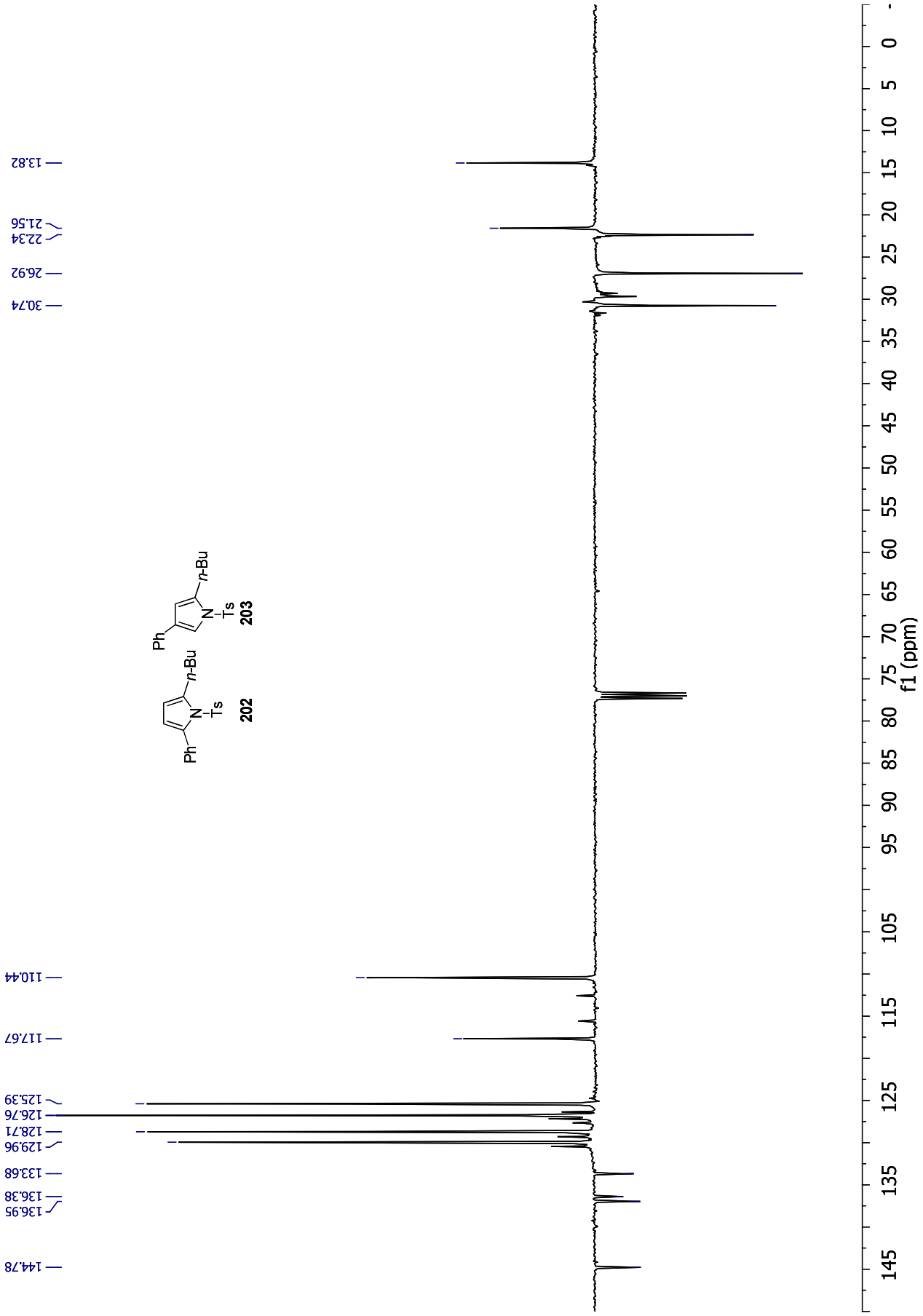

Catalysis followed by GC-MS
(70 ℃, 0.5 M, 10 mol% AuCl 3)
Relative Area (%)
100
90
80
70
60
50
40
30
20
10
0
0
5
15
30
45
60
80
100
120
Time (min)
Aziridine
Silylated Pyrrole
Desilylated Pyrrole

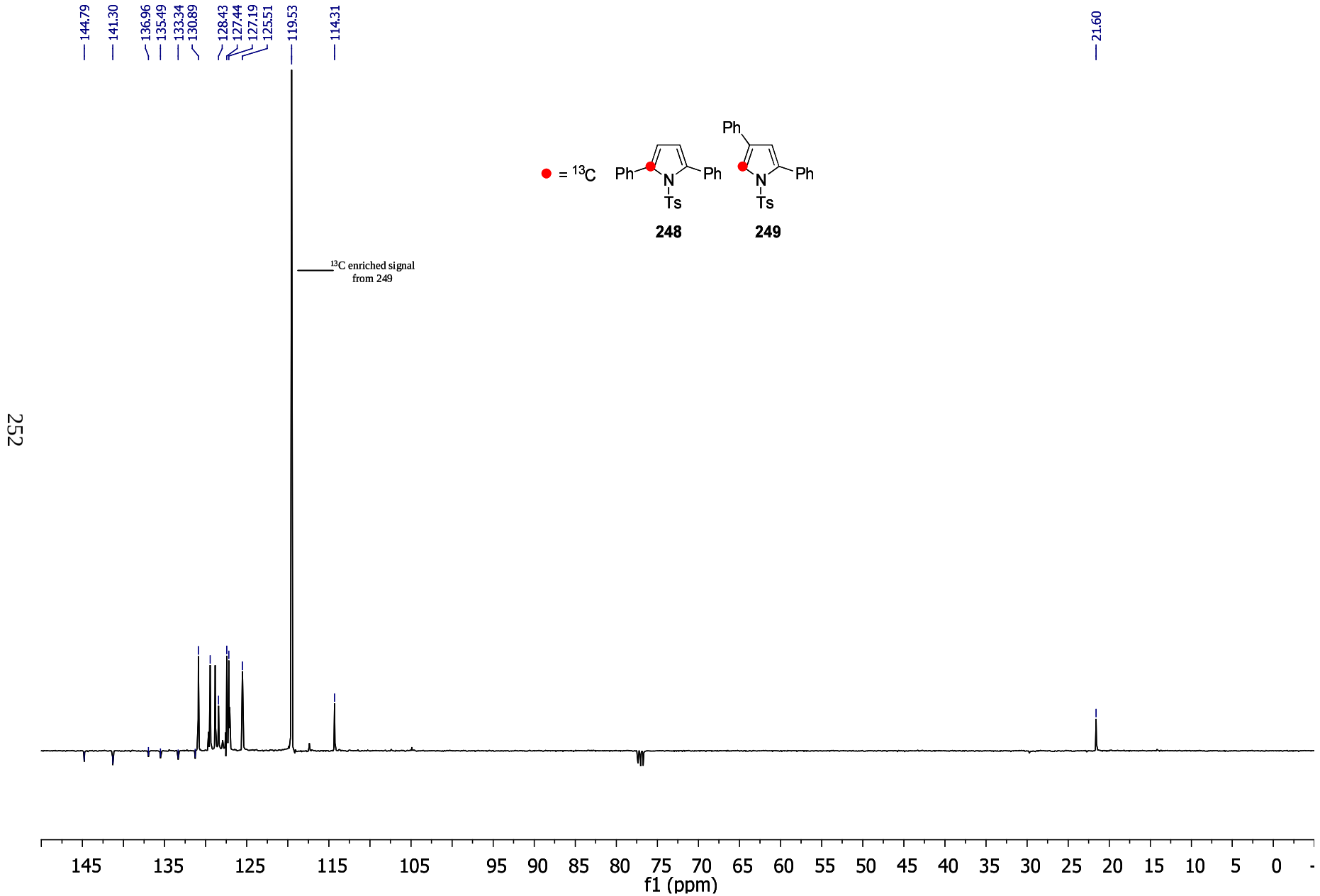
Appendix B)

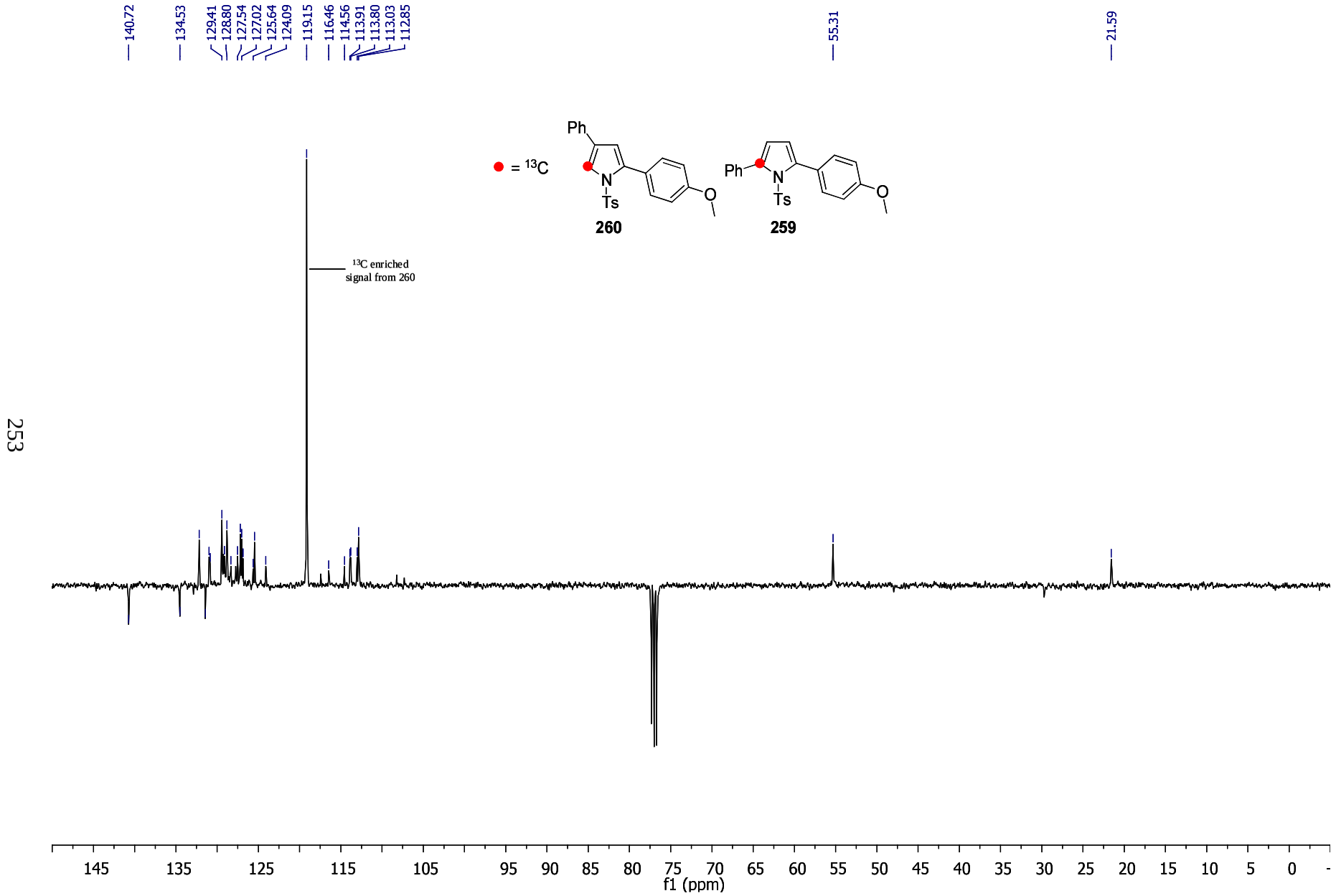

13.93
21.82
22.48
28.95
31.61
112.58
115.56
126.34
127.15
127.64
129.28
130.44
133.32
136.42
139.91
144.17
= 13C
Ph
N
Ts
n-Bu
244
13C enriched signal from 244
f1 (ppm)

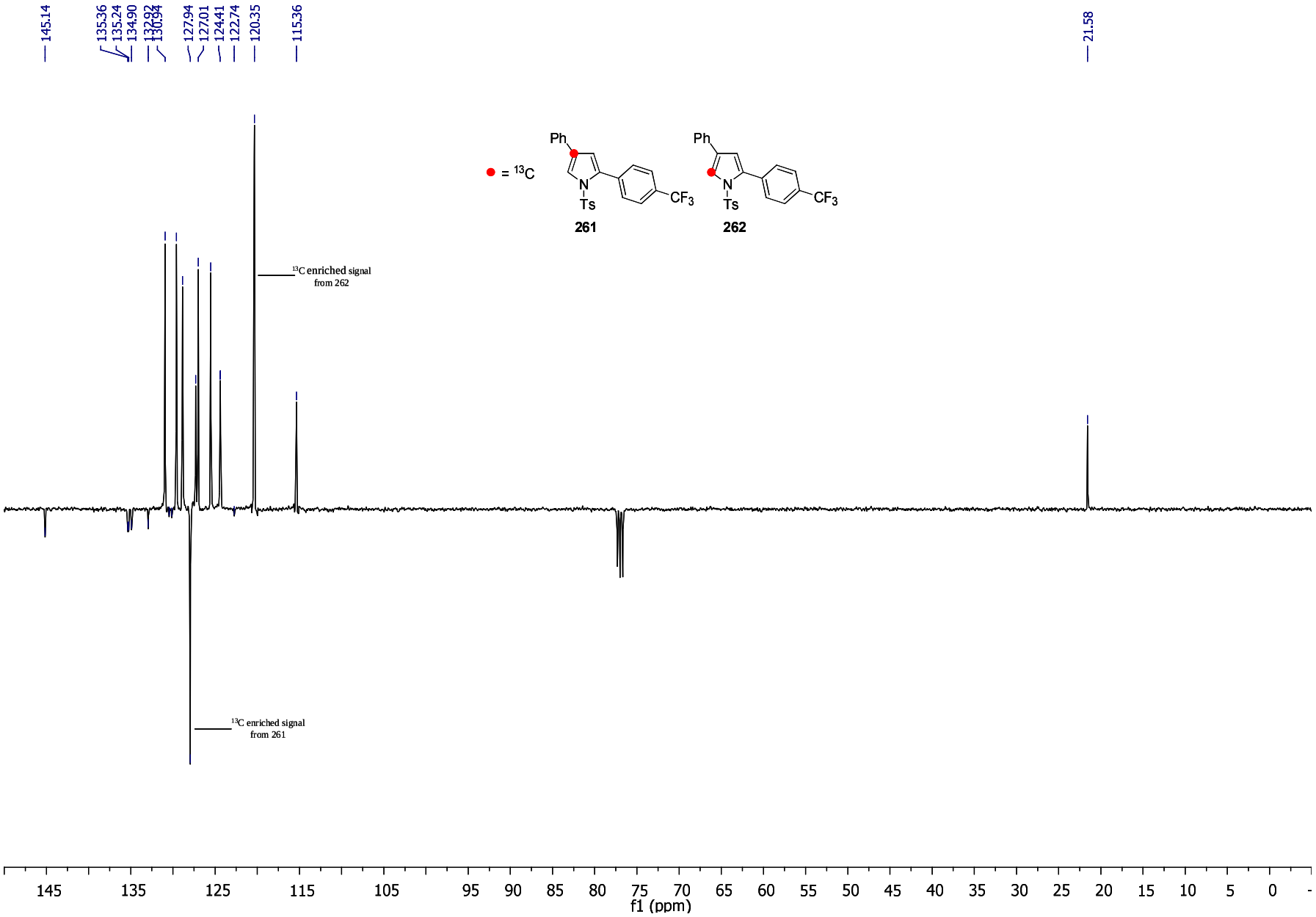

144.18
139.92
138.07
137.28
136.40
133.32
130.44
129.30
129.14
127.66
127.16
126.36
115.58
112.58
77.43
77.00
76.58
31.61
29.29
22.51
21.55
13.96
Ph
N
Ts
n-Bu
202
50
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

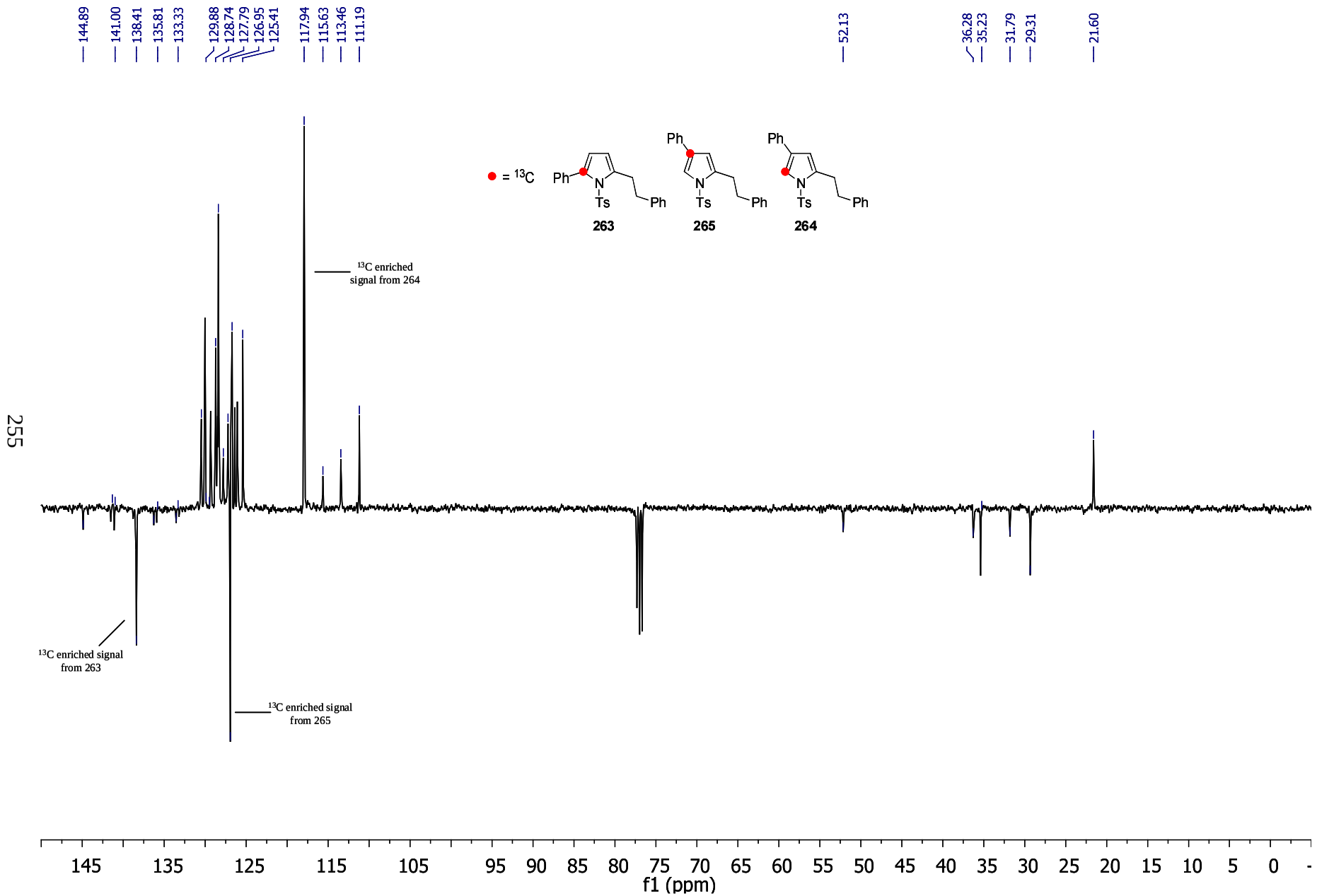

144.78
144.17
139.94
136.41
133.34
129.96
128.71
127.17
126.76
125.40
117.69
115.57
112.58
110.45
77.32
77.00
76.68
31.63
30.76
29.29
26.94
22.50
22.35
21.57
13.94
13.83
= 13C
Ph
N
Ts
n-Bu
244
246
245
13C enriched signal from 245
13C enriched signal from 244
13C enriched signal from 246
250
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
f1 (ppm)


13.82
21.56
22.34
26.92
30.74
110.44
117.67
125.39
126.76
128.71
129.96
133.68
136.38
136.95
144.78
Ph
n-Bu
N
Ts
203
Ph
n-Bu
N
Ts
202
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
105
115
125
135
145
f1 (ppm)


144.79
141.30
136.96
135.49
133.34
130.89
128.43
127.44
127.19
125.51
119.53
114.31
21.60
= 13C
Ph
Ph
N
Ts
248
Ph
Ph
N
Ts
249
13C enriched signal
from 249
252
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
f1 (ppm)


140.72
134.53
129.41
128.80
127.54
127.02
125.64
124.09
119.15
116.46
114.56
113.91
113.80
113.03
112.85
55.31
21.59
● = 13C
Ph
N
Ts
O
260
259
13C enriched signal from 260
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
f1 (ppm)


145.14
135.36
135.24
134.90
132.92
130.94
127.94
127.01
124.41
122.74
120.35
115.36
21.58
● = ^{13}C
Ph
N
Ts
CF$_3$
261
262
^{13}C enriched signal from 262
^{13}C enriched signal from 261
f1 (ppm)


144.89
141.00
138.41
135.81
133.33
129.88
128.74
127.79
126.95
125.41
117.94
115.63
113.46
111.19
52.13
36.28
35.23
31.79
29.31
21.60
= 13C
Ph
N
Ts
Ph
263
265
264
13C enriched signal from 264
13C enriched signal from 263
13C enriched signal from 265
255
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
f1 (ppm)

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