Novel transition metal-catalysed reactions of allenes and bisallenes

César Hurtado Rodrigo

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

Doctor of Philosophy

Supervised by Dr. María Paz Muñoz Herranz

School of Chemical Sciences

University of East Anglia, Norwich

May 2016

©This copy of the thesis has been supplied on condition that anyone who consults it is understood to recognise that its copyright rests with the author and that use of any information derived there from must be in accordance with current UK Copyright Law. In addition, any quotation or extract must include full attribution.

Declaration

The research described in this thesis is, to the best of my knowledge, original except where due reference is made.

Parts of this work have been already published:

Chapter 2 is based on:

C. Hurtado-Rodrigo, S. Hoehne, M. P. Muñoz, *Chem. Commun*., **2014**, *50*, 1494-1496. **DOI:** 10.1039/C3CC48017H

M. P. Muñoz, C. Hurtado-Rodrigo, *The chemistry of gold-allene complexes*, PATAI'S Chemistry of Functional Groups, John Wiley & Sons, Ltd, **2014**, pp 567-630.

César Hurtado Rodrigo

Norwich, May 2016

Dedicated to

María Rosa Rodrigo, Susana de Val and Luis Fernando Hurtado

Acknowledgements

I would like to express my sincere gratitude to my supervisor Dr. María Paz Muñoz Herranz for her enormous constant support and guidance during my PhD, and also for giving me the honour to be the first PhD student of her career. It has been a real pleasure to work with you during these almost four years.

I am also very grateful to our postdoctoral researcher Dr. Teresa Quiros who has helped me both personally and professionally during my PhD, and for all those unforgettable moments in and out the lab, which I will never forget. Thanks friend!

Special thanks must go to my friend and also lab mate Lisa Cooper for helping me during these amazing years together. Also for her help with my English lessons and for all the laughs in and out of the lab. I want to give you a big thanks for cheering me up during the time that I have been writing up this thesis, you have shown me that the distance will never break our friendship.

I would like to thank my friends from the chemistry building, especially people from the third floor, Luis, Alex, Ryan, Ketan, Flavia, Yohan, Fran, Sheldon, Rhoda, Xiao, Paulina and James and especially my great Spanish friends Sonia and Dani, Mariajo for all her support during this time. To my big bro Victor for those countless good moments along my life in Norwich in and out of the lab and finally, in recognition of my friend and lab mate Sarah who sadly is not with us, thanks for all Sarah.

I wish to thank my friends from Spain who have been always supporting me and encouranging me to finish my PhD, thanks for being always there Mario, Juli, Victor, Jorge Noe, Raquel and Julieta.

I am also thankful to share such good moments together with my friends Carlos, Alvaro, Mundo, Raul and David. Cristina and Dani, Cristina Fernandez, Peri, Sam and Clara, Monica, Desi, Davide and Anthony.

My warmest thanks goes to the person who I am extremely proud of, my mum Maria Rosa, for her unconditional love every moment of her life, supporting all my decisions and encouraging me during this difficult way, even being far from her, I owe you all. I would also like to thank to the person who has shown me that in Norwich or whenever he will be always close to me, thanks brother.

To conclude, my deepest thanks is to my girlfriend Susana for her love even being far from her. Thanks for encouraging me during this difficult way and also for sharing a new story in our amazing life together.

Thanks to UEA and INTERREG program for the funding the present thesis.

Abstract

The research in this thesis is focused on new intermolecular additions of diverse nucleophiles to allenic and bisallenic motifs catalysed by transition metals. In the first project we developed a new Au-catalysed azidation of allenes for the synthesis of functionalised allylic azides, which are important precursors to many functional groups. A cationic Au(I)-catalyst was found as a suitable activator for the allenic π-system favouring the attack of challenging azides as nucleophiles and giving access to the desired allylic azides. Deuterium-labelling experiments revealed that the reaction goes *via* a vinyl gold intermediate, which allowed an orthogonal functionalisation of the allenes, using as electrophile iodine to break the Au-C giving valuable iodo-alkenyl azides. Besides, preliminary mechanistic studies by NMR disclosed a possible inner-sphere mechanism with the formation of Au-N_3 complexes with a continuous exchange of counterions involved in the reaction.

The second part of the present thesis was aimed to develop a novel platinum-catalysed carbo- and heterocyclization of 1,5-bisallenes to obtain 6- or 7-membered rings with and extra oxygen functional group incorporated in the skeleton of the molecule. These cyclic compounds are interesting building blocks encountered into the core of several natural products, especially in terpene and sesquiterpene family. Cationic Pt(II)-catalysts with electron-withdrawing ligands were found appropriate to lead the ring closing of these 1,5-bisallenes. The reaction seems to be triggered by the attack of oxygen nucleophiles to the activated terminal π-system of the bisallene showing different coordination modes, which give access to isomeric 6- or 7-membered rings. Deuterium labelling and preliminary mechanistic experiments revealed, that the formation of the products goes *via* a vinyl platinum intermediate in the different cyclization modes. Besides, the reaction has been monitored by ^{1}H NMR in order to study the decomposition level of the bisallenes under catalytic conditions and the possible interconversion between the isomeric cyclic products.

Table of Contents

Abbreviations

Å	angstrom
Ar	aromatic
AcO	acetoxy group
app	apparent
Bn	benzyl
$(BOC)_2O$	*tert*-butyoxycarbonyl anhydride
bs	broad singlet
bt	broad triplet
n-Bu	*n*-butyl lithium (in hexanes, 2.5M)
t-Bu	tertiary butyl
calc.	calculated
^oC	degrees Celsius
cm^{-1}	inverse centimetre (unit for wavenumber)
d	doublet
dd	doublet doublet
ddd	doublet doublet doublet
dt	doublet triplet
DCM	dichloromethane
DFT	Density Functional Theory
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
DMAP	4-dimethylaminopyridine
dppp	diphenylphosphinopropane
ee	enantiomeric excess
EDG	electron donating groups

Eq.	equivalent
Et	ethyl
EWG	electron withdrawings groups
FT-IR	Fourier Transform-Infrared Spectroscopy
g	gram (s)
h	hour (s)
H_{Ar}	aromatic proton
Hex	hexane
HR	high resolution
HRMS	High resolution mass spectrometry
Hz	hertz
IR	infrared
M	metal
m	multiplet
Me	methyl
mg	milligrams
MHz	megahertz
min	minute (s)
mmol	millimol
mL	millilitre
mp	melting point
MS	mass spectrometry
MsO	mesylate group
Mw	microwave
m/z	mass-to-charge
nm	nanometer

NIS	*N*-iodosuccinimide
NMR	Nuclear Magnetic Resonance
NOESY	Nuclear Overhauser Effect Spectroscopy
NSI	Nano Spray Ionisation
Nu	nucleophile
p	pentet
PET	petroleum ether
Ph	phenyl
ppm	parts per million
i-Pr	isopropyl-
py	pyridine
q	quartet
quat.	quaternary
rt	room temperature
s	singlet
sext.	sextet
T	temperature
t	triplet
tt	triplet triplet
TBAF	*tetra*-*n*-butylammonium fluoride
TBDMS	*tert*-butyldimethylsilane
td	triplet doublet
OTf	triflate group
TFA	trifluoroacetic acid
THF	tetrahydrofuran
THP	tetrahydropyranyl ethers

TLC	Thin Layer Chromatography
TMS	tetramethylsilane
TsO	tosylate group
tq	triplet quartets
UV	ultraviolet
VT	variable temperature
δ	chemical shift
$\tilde{\nu}$	wave frequency
λ	wavelength
J	coupling constant
µl	microlitre

Chapter 1.

General introduction on allenes:

history, structure and synthesis

1.1. History

The chemistry of allenes has flourished exponentially during the last few years, due to the extraordinary versatility inherent to their structure. The origin of allene chemistry arose when in 1875, the first chemist awarded with the Nobel prize, Jacobus Henricus Van't Hoff published in *"La Chimie dans l'space"*[1] his theory about these optically active compounds, and using homemade cardboard structures he predicted the existence of two stereogenic axes in the allene moiety (Figure **1**). There have been many attempts to synthesise these cumulenic structures,[2] and it was in 1887 that Burton and Pechmann,[3] obtained "glutinic acid" **1** (Figure **2**) when trying to justify the non-existence of these "unstable structures". However, due to the lack of analytical instrumentation in that age, the confirmation of the glutinic acid structure was not reported until 1954 by Jones and coworkers.[4]

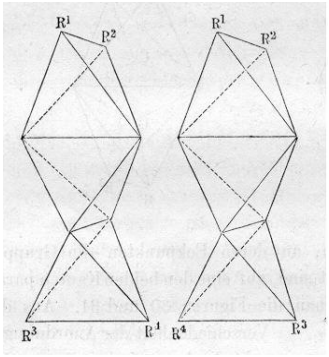
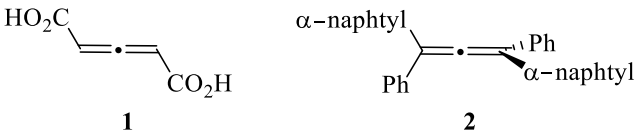


Figure 1. Predicted structure of an allene using tetrahedral models by Van't Hoff.[1] Figure reproduced from: https://webspace.yale.edu/chem125/125/history99/6Stereochemistry/vanthoff/tetrahedra.html

In 1935, Kohler, Walker and Tisher published the resolution of this racemic allenic carboxylic acid,[5] and a year later Maitland and Mills verifying experimentally Van't Hoff's prediction, synthesised the first enantiomerically pure axial chiral allene **2** (Figure **2**).[6]



1 **2**

Figure 2. Glutinic acid **1**, (*S*)-(+)1,3-di(α-napthyl)1,3-diphenylallene **2**

In 1924 Staudinger and Ruzicka published a work based on the discovery of the structure of the first naturally occurring allene, Pyrotholone, obtained from *Chrysanthemum cinerariaefolium*.[7] However, advances in spectroscopy later confirmed that instead of an allenic skeleton this molecule showed a conjugated diene moiety.[8] A few years later, the genuine first naturally occurring allene was discovered: Mycomycin **3** (Figure **3**),[9] a fungal metabolite with a high antibiotic activity.[10]

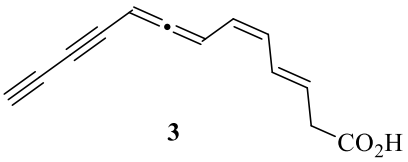


Figure 3. Mycomycin **3**, first discovered naturally occurred allene

1.2. Structure and characterisation of allenes

The structure of allenes consists of a linear 3-carbon skeleton formed by two π-bonds, which are orthogonal to each other connected by a *sp*-carbon. If the two terminal sp^2-hybridised carbons bear different substituents, these species are provided with axial chirality.

1.2.1. Symmetry of allenes

The two perpendicular angles of the allene give rise to a tetrahedral conformation (D_{2d}): there is a C_2 axis lying through the 3 aligned carbons and two perpendicular C_2 axes passing through the *sp*-hybridised carbon of the allene. Moreover, the main C_2 axis contains 2 symmetry planes, which divide the allene in two sections each containing two substituents. The arrangement of these two planes of symmetry is known as S_d symmetry and it is characteristic of allenes (Figure **4**).[11]

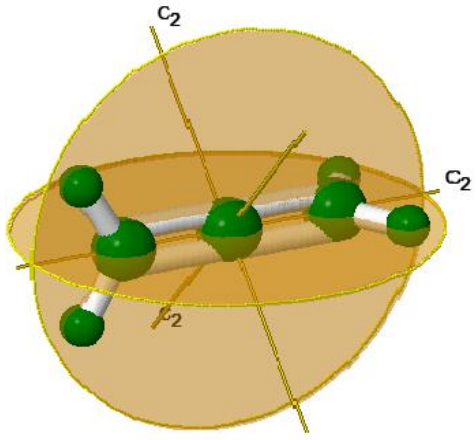


Figure 4. Axes and planes of symmetry of allenes. Figure made with tools provided in: http://symmetry.otterbein.edu/gallery/index.html

The tetrahedral D_{2d} conformation of allenes is adopted only by members in the cumulene family with an odd number of carbons. Analogues with an even number of carbons show planar conformation (D_{2h} symmetry) when the molecule is not substituted.[12] Recently Tykwinski and coworkers published a wide range of properties, syntheses and varieties of cumulenes with an even number of cumulenic carbons.[13]

1.2.2. Bond lengths and angles

The study of the structural features of allenes is essential to understand the nature, reactivity, selectivity and chirality of this functional group. Theoretical analysis on bond lengths and bond angles were published and confirmed quantitative and qualitatively by different methods.[14] It was observed that the length of C=C of the allene molecule (C_3H_4) is 0.03 Å shorter than C=C of an ethene[15] and 0.06 Å longer than acetylene.[16]

Depending on the technique used for the measurement (IR, Raman, Mw) the length of C=C belonging to the simplest allene is ≈ 1.308 ± 0.008 Å, with slight modifications depending on the nature of the functional groups in substituted allenes.[17] This C=C=C group provides rigidity to the molecules, explaining their interesting peculiarities.[11a]

1.2.3. Infrared (IR) and Ultraviolet-Visible (UV) spectroscopy

As the two π-systems of the allene are perpendicular to each other, the conjugation between them is roughly non-existent. Thus, allenes do not exhibit any absorption of light above 200 nm, so that UV-visible spectroscopy is rarely used for the detection and identification of allenes.[18]

One of the most common empirical methodologies to characterise allenes is infrared spectroscopy (IR). The linear C=C=C shows two easily recognisable bands in the IR spectra. One corresponds to the asymmetric stretching vibration of the C=C=C bonds between 1930 – 1950 cm^{-1} and the second one is the symmetric stretching vibration of C=C=C at ≈ 1075 cm^{-1}. In symmetrically substituted allenes the symmetric stretch mode of C=C=C is not active in IR because there is no change in the dipole moment, whereas it will be present in a Raman spectrum.[18-19]

1.2.4. Nuclear magnetic resonance Spectroscopy (NMR)

NMR techniques are essential in the determination and identification of organic molecules, and also a very useful methodology for the determination of allene structures. The chemical shift of the allenic protons appears slightly more deshielded than the ethylene protons. This can be explained by the central *sp*-carbon and the anisotropic contribution of the non-conjugated π-orbitals of the allene, which has an influence on the proton shielding.[18] Also, four-bond coupling constant (J^4) in allenes is normally observed, for example the J^4 between two protons in the simplest allene, was reported with a value of ≈ 6.50 - 7.00 Hz. This long-range coupling constant suggests some σ→π interactions, which are supported by experimental and theoretical calculations.[18-20]

^{13}C NMR is a valuable tool for the identification of allene moieties. The *sp*-hybridised carbon bears an intense paramagnetic effect, showing low field chemical shifts, up to 200 ppm. Also, as with ^{1}H NMR, the nature of the allene structure has an important role in these high frequency values. Table **1** shows chemical shift values in ^{13}C NMR for allenes and cumulenes. It can be observed that the *sp*-carbon of the cumulated alkenes with an odd number of carbons (non-planar molecules, C_2 and C_3 in entries **1**, **3** and **5**) display higher chemical shifts. In contrast, the *sp*-carbon of cumulenes with an even number of carbons (planar symmetry, C_2 entries **2** and **4**) display lower chemical shifts.[18]

Entry	Compound	^{13}C NMR Chemical shifts *(ppm, relative to TMS)*		
		C_1	C_2	C_3
1	$H_2C_1=C_2=C_1H_2$	73.6	212.5	-
2	$H_2C_1=C_2=C_2=C_1H_2$	118.0	171.1	-
3	$Ph_2C_1=C_2=C_1Ph_2$	112.5	208.3	-
4	$Ph_2C_1=C_2=C_2=C_1Ph_2$	122.7	152.0	
5	$Ph_2C_1=C_2=C_3=C_2=C_1Ph_2$	117.8	181.6	119.3

Table 1. ^{13}C NMR values for allenes and cumulenes [18]

1.2.5. Axial chirality in allenes

The unique structural nature of allenes reveals an uncommon axial chiral property, and two different substituents in each sp^2-carbon make allenes optically active. This allene feature is due to its tetrahedral symmetry (D_{2d}), the two non-conjugated π-systems and also the impossibility of free rotation due to the rigidity of the molecule in standard conditions.

The absolute configuration of the enantiomeric species can be determined according to the configurational nomenclature of Cahn, Ingold and Prelog.[21]

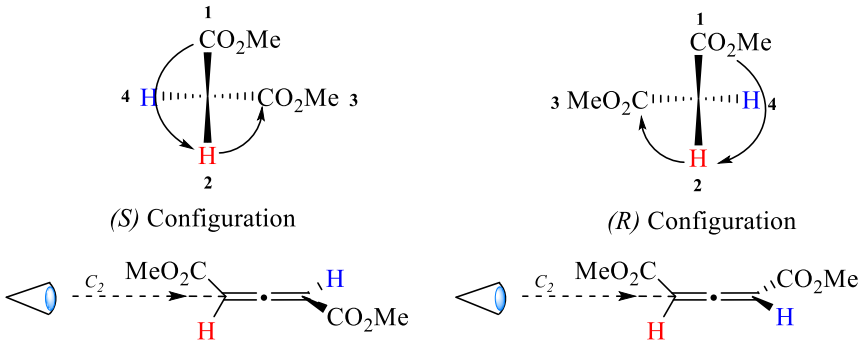


Figure 5. Representation of axial chirality of allenes

These rules propose that to enumerate the *(S)* or *(R)* stereoisomers, allenes are viewed through their C_2 axis (see Figure **4**), placing first the atom with higher atomic number directly attached to the sp^2-carbon topmost of the vertical axis (see number **1** Figure **5**). Then, in the horizontal axis (see **3** in Figure **5**) the atom with higher atomic number will take precedence over the other substituent (see number **4** in Figure **5**). The stereochemistry of these cumulenic alkenes will be determined *via* clockwise *(R)* or counter-clockwise *(S)* screw pattern of atomic number (Figure **5**).[22]

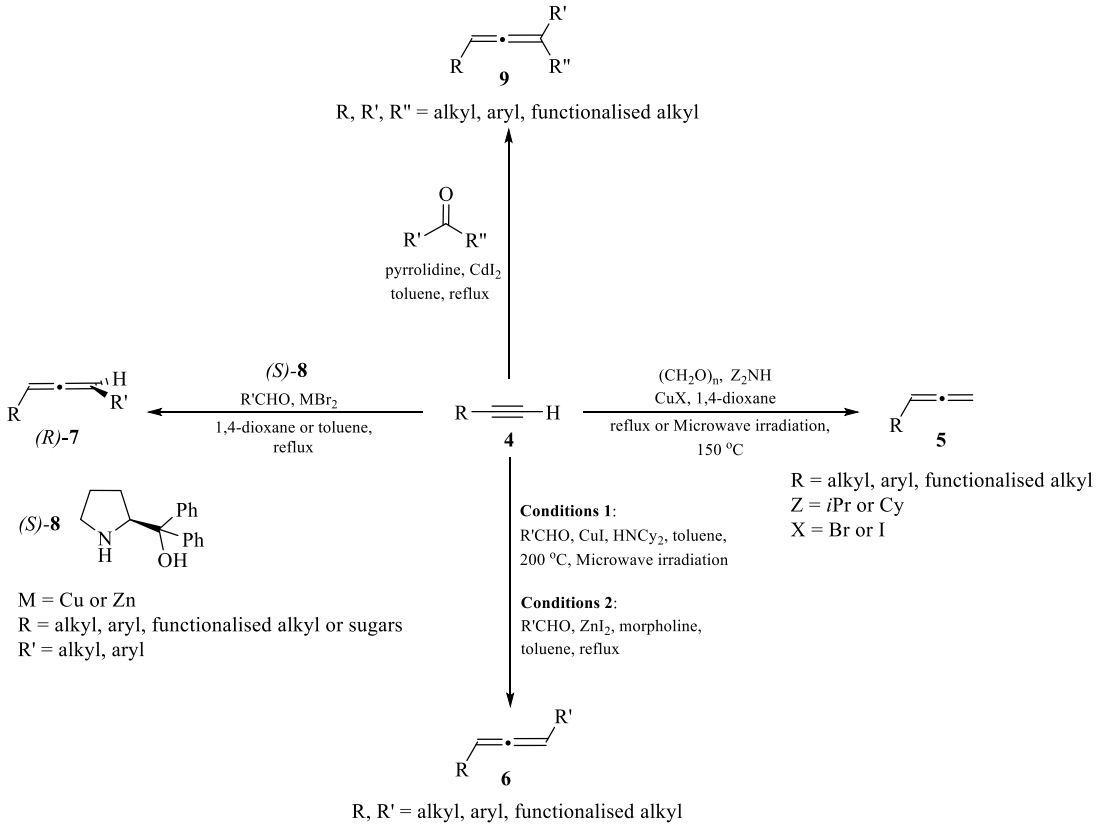
1.3. Synthesis of allenes

There are a significant number of publications, reviews or books dedicated to the synthesis of allenes.[19, 21a, 22b, 23] Originally, these species were considered unstable and laborious to make. Moreover, the detection and determination of these species due to the lack of progress in analytical techniques delayed advances on their synthesis as starting materials and their versatility in synthetic chemistry. However, in the last 20 years, the chemistry of these cumulenic alkenes has blossomed exponentially due to the development of robust methods for the synthesis of mono, di, tri and tetrasubstituted allenes,[23d, 23f, 23g, 24] in racemic or enantiomeric form.[22b, 23f, 23g, 25] In this introduction we will emphasise the most important reactions to synthesise allenes related to the ones used on the experimental work of this thesis.

1.4. Synthesis of allenes from alkynes

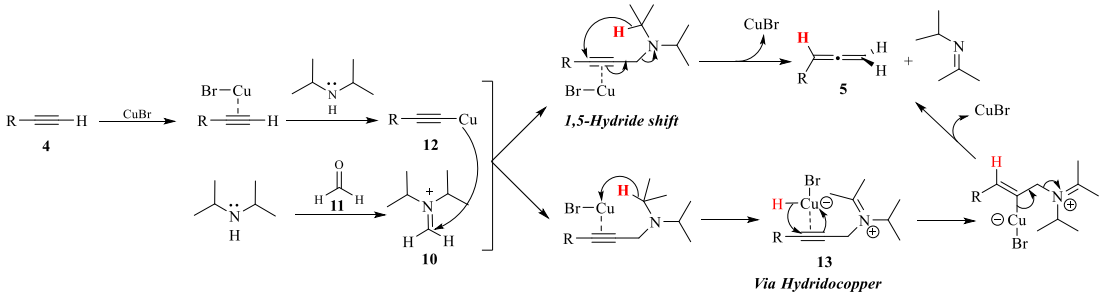
1.4.1. Homologation reaction of acetylene derivatives

Since Pierre Crabbé and coworkers discovered the first one-step homologation of acetylenes into allenes using paraformaldehyde, an amine and a copper catalyst in 1979,[26] numerous modifications have been developed to enhance the scope of the reaction. The versatility and robustness of this reaction has been shown using different metals such as Cu, Zn or Cd, various amines or chiral amines, different temperatures, aldehydes, ketones, and there are two examples of this reaction assisted by microwave irradiation. For example, monosubstituted allenes **5** (Scheme **1**) can be synthesised by modified Crabbé-homologations changing the amine, copper salts or starting materials.[26-27] 1,3-Disubstituted allenes **6** and 1,1,3-trisubstituted allenes **9** have been synthesised from aldehydes or ketones instead of paraformaldehyde, using zinc[28] or cadmium[29] as catalysts. Also, with the right choice of amine, the group of Mukay obtained allene **6** under microwave irradiation.[30] Optically active 1,3-disubstituted allenes such as *(R)*-**7**,[25a, 31] have been synthesised using copper(II) and zinc(II) catalysts and aldehydes, using chiral amine *(S)*-**8** as an organocatalyst in moderate to good yields and high *ee* (%).



Scheme 1. Allene formation by acetylene homologation

The mechanism of the Crabbé homologation is proposed to proceed by addition of copper-acetylide ion **12**, formed by complexation of the copper to terminal alkyne **4** and deprotonation by the amine, to an iminium ion **10** generated *in situ* from a Mannich-type reaction between the aldehyde **11** and the amine. Subsequently, an intramolecular 1,5-hydride shift occurs from the α-proton of the amine group on the propargylamine intermediate to the copper-activated triple bond achieving the allene **5** (Scheme **2**, top right).

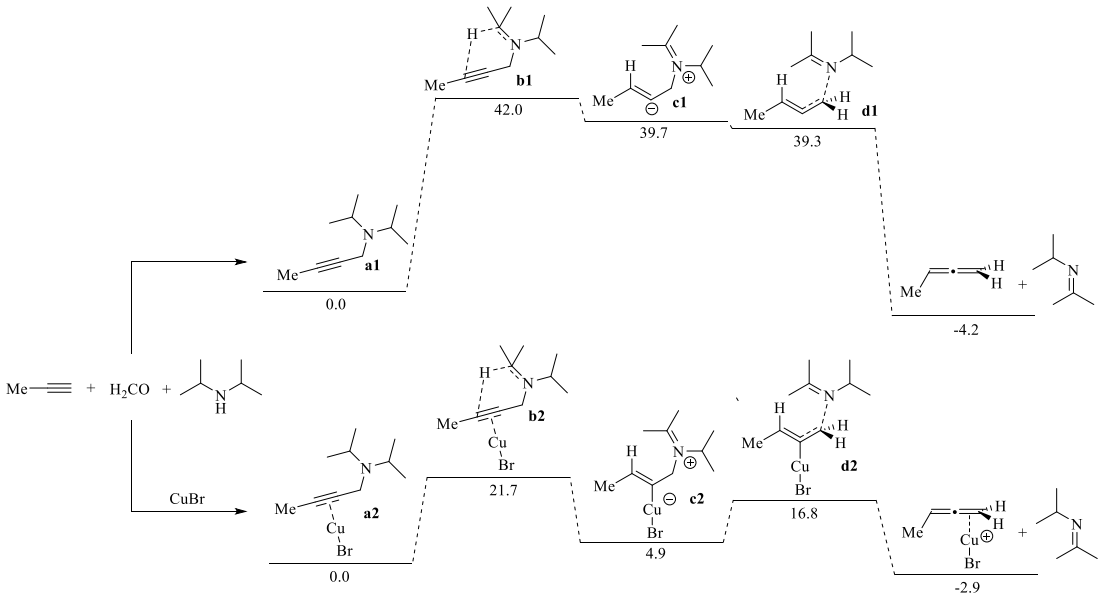


Scheme 2. Proposed mechanisms of the Crabbé homologation using CuBr, diisopropyl amine and paraformaldehyde

The first attempt to study the mechanism of this acetylenic homologation was reported by Pierre Crabbé and coworkers in 1980. They reported the formation of a hydridocopper(I) complex **13** (Scheme **2**, bottom right). In this case a hydride is transferred from the propargylamine intermediate giving the allene with the concomitant release of the iminium

product.[32] At the same time, Fillion and coworkers published the mechanistic study of this homologation, as part of their attempt to study the mechanism of the Mannich reaction.[33] They suggested that one of the hydrogen atoms from the diisopropylamine migrates *via* a 1,5-hydride shift to the internal acetylene carbon activated by CuBr to obtain the desired allene (See Scheme **2**).

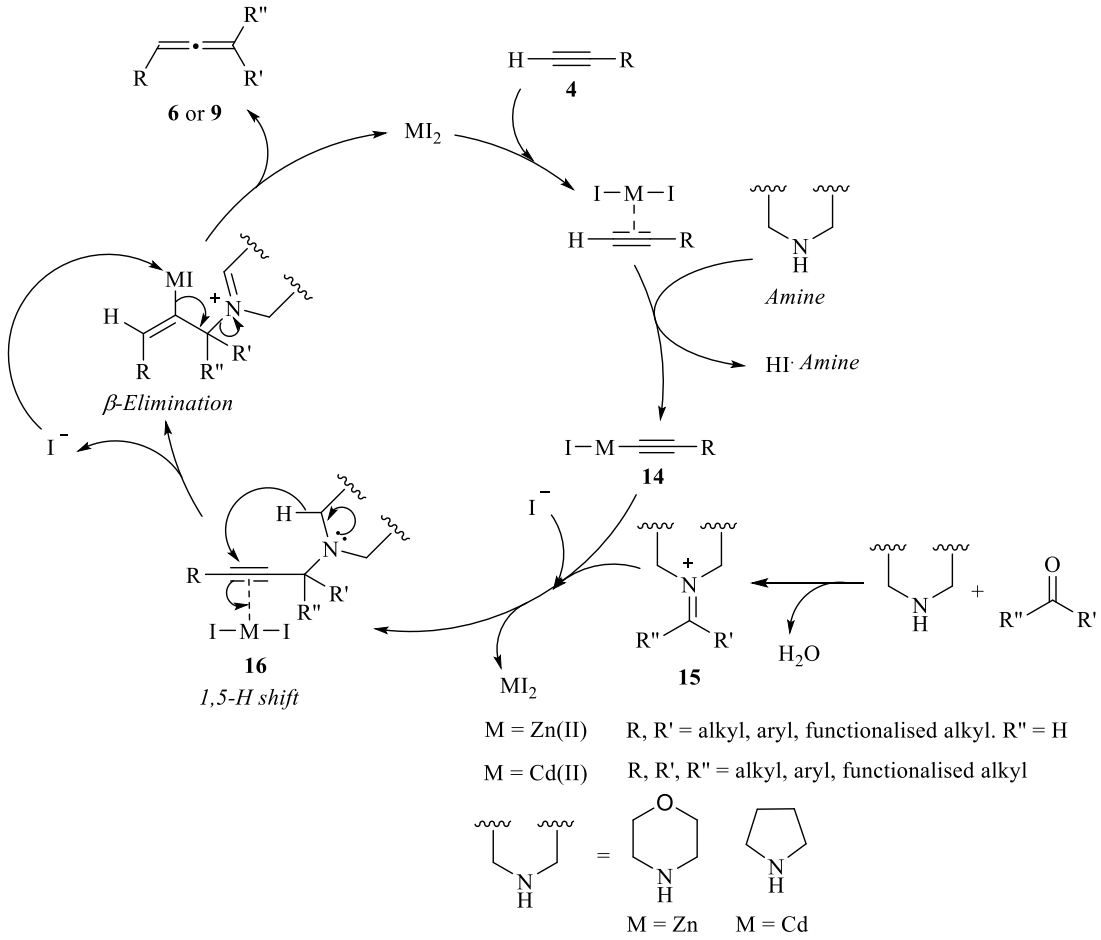
Recently, an interesting computational mechanistic study of this reaction has been published.[34] López and coworkers evaluated the role of the copper examining the reaction with and without the catalyst. They proposed that the copper is essential in the reaction to activate the alkyne (**a2** Scheme **3**). Subsequent hydride shift through the transition state (**b2**, Scheme **3**) shows quite low activation energies in comparison with absence of catalyst. Besides, copper stabilizes the zwitterionic vinyl carbanion intermediate (**c2** Scheme **3**), triggering the formation of the allene. In previous proposals the role of copper was as a Brønsted acid/base catalyst abstracting the proton from the diisopropylamine and managing the 1,5-hydride shift.[32] However, in their work López and coworkers invoked that the H-shift from the amine derivative to the triple bond occurs without any copper-H interaction, and their computational study suggests that the activation of the alkyne with copper occurs from the opposite face to the hydride transfer (Scheme **3**).[34]



Scheme 3. Computational mechanistic study of methyl allene formation *via* Crabbé homologation. Relative Gibbs free energies in Kcal/mol[34]

A similar mechanism has been postulated by the group of Ma, employing as catalysts ZnI_2 and CdI_2 to achieve 1,3-di-**6** and 1,1,3-trisubstituted **9** allenes (Scheme **4**). In both proposals the metal coordinates with the triple bond forming, after deprotonation, the

intermediate **14**, similar to the copper analogue **12** (Scheme **2**). These species react with the iminium ion **15** preformed *in situ* with morpholine and aldehydes if ZnI_2 is the catalyst, or pyrrolidine and ketones if the reaction is catalysed by CdI_2, generating the propargylic amine **16** (Scheme **4**). The catalyst coordinates to the triple bond in **16**, and after a 1,5-hydride shift and subsequent *β*-elimination generates the desired products **6** and **9**.



Scheme 4. Proposed mechanism for the synthesis of 1,3-disubstituted **6** and 1,1,3-trisubstituted **9** allenes, *via* acetylene homologation

This homologation reaction has been employed in the synthesis of naturally occurring allenes with good yields and high enantioselectivities. Recently, Ma and coworkers reported the highly enantioselective synthesis of linear allenes extracted from seed oils such as laballenic acid **17**, lamenallenic acid **18** or the hydroxy acid **19**, used as antifungals, using $CuBr_2$ as catalyst and (*S*)-**8** (see Scheme **1**) as an organocatalyst (Figure **6**).[35] With the same reaction conditions Ma developed the synthesis of the insect pheromone **20**,[25a] first isolated in 1970 by Horler from male "dried bean beetles" *Acanthoscelides obtectus*.[36]

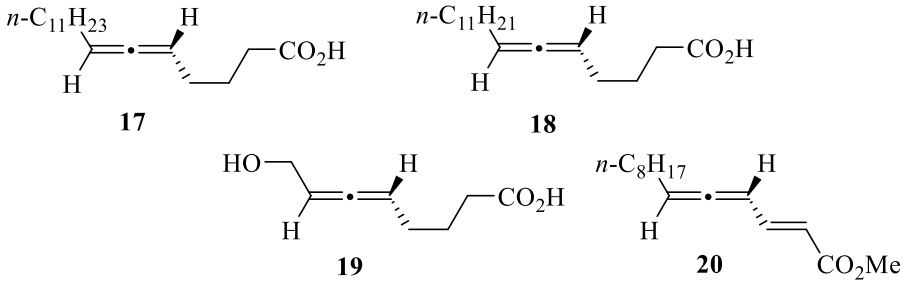
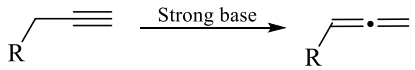


Figure 6. Laballenic acid **17**, lamenallenic acid **18**, hydroxy acid **19** and insect pheromone **20**

1.4.2. Synthesis of allenes by isomerization of alkynes

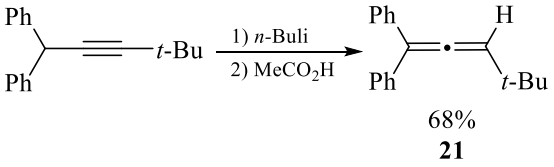
An isomerization reaction is a process where the constitution of the molecule is modified, maintaining the same molecular weight and the same empirical formula.[24b] The formation of the allenes by isomerization of the analoguous alkyne is one of the earliest ways of synthesis reported.[24b, 37] This reaction is carried out with terminal alkynes normally in the presence of strong bases (*n*-Buli, *t*-BuOK, KOH, $NaNH_2$) and high temperatures (Scheme **5**).[38]



R = aryl, carbonyl, alkynyl, alkenyl, RS-, RO-, R_2N-

Scheme 5. Synthesis of allenes by isomerization reaction

Trisubstituted allenes can also be synthesised *via* an isomerization reaction from internal alkynes. In this particular case, metalation and subsequent protonolysis gave access to allene **21** (Scheme **6**).[24b]



Scheme 6. Synthesis of trisubstituted allene **21** by isomerization reaction

1.4.3. Synthesis of allenes by metal-mediated S_N2' substitution

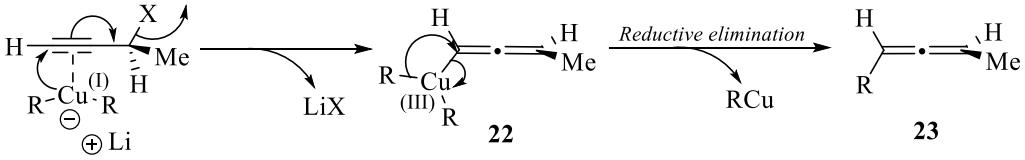
One of the most effective and commonly used methodologies for the synthesis of allenes is the metal-mediated substitution reaction of propargyl derivatives (S_N2'). These reactions can occur through a stereoselective addition of the organometallic compound from the same face (*syn*) or the opposite face (*anti*) of the leaving group depending on the nature of the substrate, the reductive agent, the leaving group or the temperature.[24c]

1.4.3.a. Organocopper-mediated synthesis of allenes

Since the first report of an organocopper-mediated S_N2' substitution reaction by P. Rona and P. Crabbé in 1968,[39] this method has been widely used for the synthesis of allenes by C-C bond formation using carbon-based organocuprates, and for the synthesis of halo-, stannyl-, or silylallenes, even in the enantiomeric version, from the propargylic electrophiles and heterocuprates.[22b, 23f-h] Alongside this, P. Crabbé and coworkers also studied organocuprates combined with Grignard and organozinc reagents to expand the scope of this reaction upon different substrates.[23f, 24d]

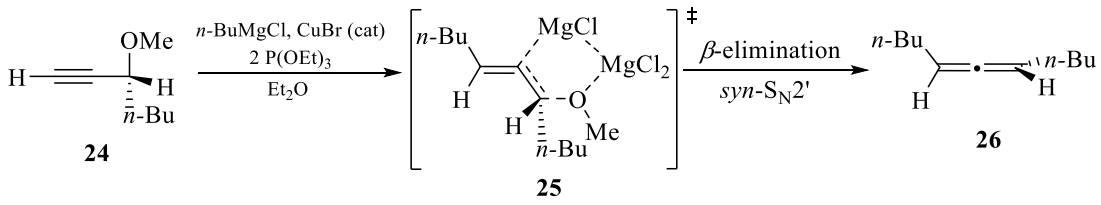
The mechanism for this reaction is proposed to be triggered by the interaction between a *d*-orbital of the copper and the π* orbitals of the electrophilic alkyne (Figure **7**), with the formation of a Cu(III) intermediate **22**, which, after reductive elimination gives rise to the allene **23** *via* a formal *anti*-S_N2'.[24d]

Figure 7. Interaction between an electrophilic alkyne and *d*-orbital of copper catalyst



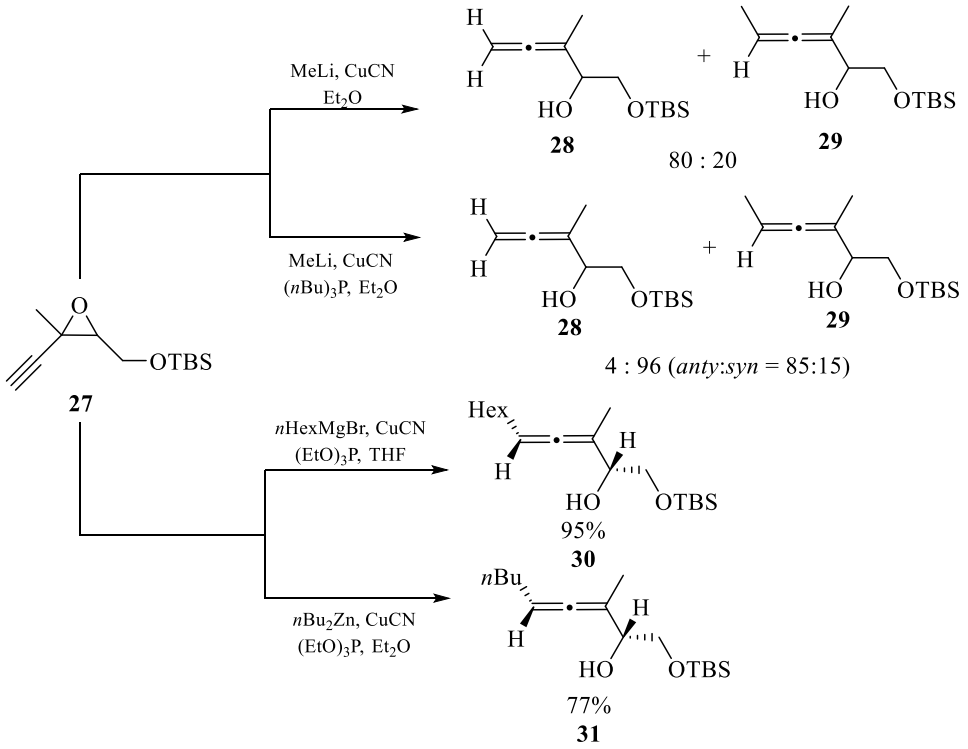
Scheme 7. Mechanism for the synthesis of allenes by S_N2' *anti*-stereoselective *via* organocuprates

Chirality transfer from the propargyl starting material to the allene using this methodology is possible. An example is shown in Scheme **8**, where formal *syn*-S_N2' was proposed to explain the transfer of chirality from the propargyl ether **24** (Scheme **8**). The reaction was carried out using copper(I), a Grignard reagent and $P(OEt)_3$ as additives, used to avoid the *anti*-S_N2'. The use of chloride to preform the Grignard reagent was a determinant in the selective *β*-elimination step. Due to its electronegativity and the small size, the chloride favours the transition state **25** by chelation with the strong Lewis acid $MgCl_2$, favouring the *syn*-S_N2' to achieve allene **26**.[24d, 40]



Scheme 8. Proposed mechanism for the synthesis of allenes *via syn*-S_N2' with organocuprates

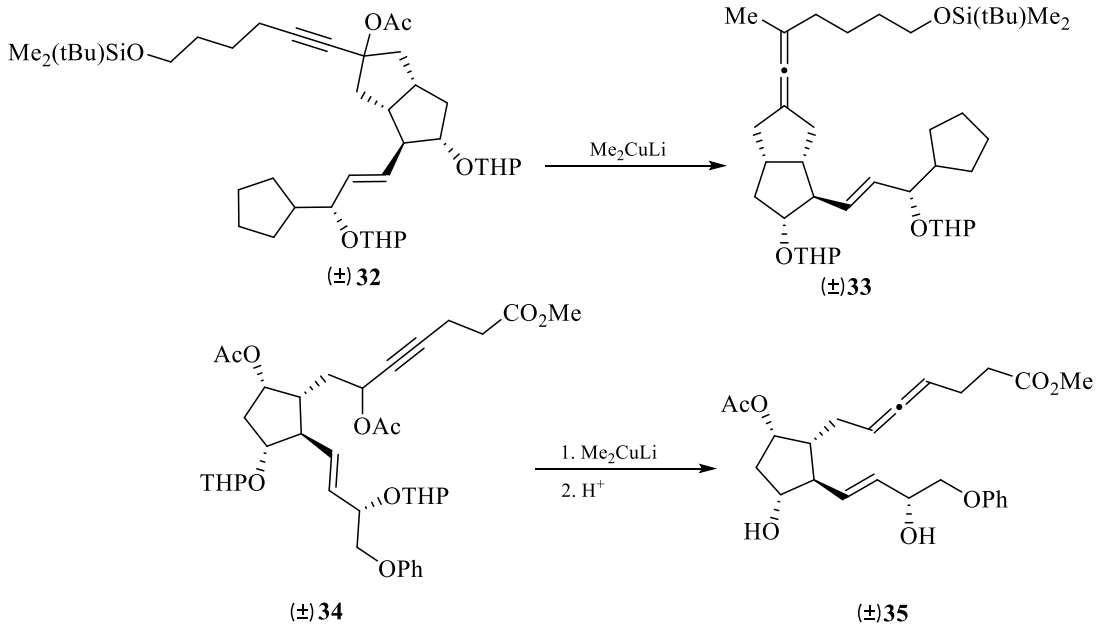
Frequently, cuprates are used in combination with Grignard and organozinc precursors to modify the reactivity of those species. The use of phosphines as additives has shown to improve the *regio*- and *anti*-stereoselectivity leading the reaction toward the desired product (Scheme **9**). For example, propargyl epoxide **27**, in the presence of lithium organocuprate is thought to react according to the mechanism proposed previously, generating a σ-copper(III) intermediate similar to **22** (Scheme **7**), achieving allene **29** in low ratio, accompanied by α-allenol **28**, which could come from the protodemetalation of the same intermediate (Scheme **9**). Interestingly, the addition of phosphines enhances the formation of the desired allene **29**.[41] The use of CuCN, Gridnard reagents and phosphines with the same substrate showed high yields, excellent selectivities and high *anti*-diastereoselectivity of allenes **30** and **31**.



Scheme 9. Different outcomes in the S_N2' substitution of propargyl epoxyde **27** with lithium cuprates, magnesium cuprates and zinc cuprates

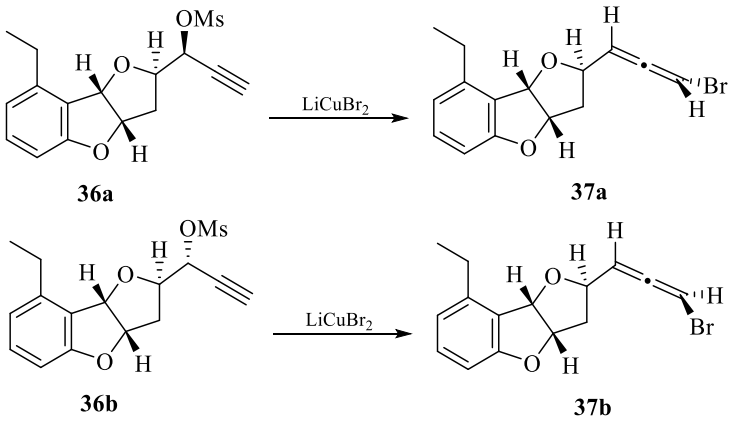
Organocuprates have been highly relevant in the total synthesis of many natural products and pharmacologically active target molecules.[35] As an example, the methylated

carbacyclin derivative (±) **33** (Scheme **10**), which is a promising anti-thrombotic agent, or the allenic prostaglandin analogue of enprostil (±) **35**,[42] the most relevant and marketed allenic prostaglandin, which is usually administered an as inhibitor of gastric acid secretion, or to reduce postprandial serum gastrin levels. Both were synthesised by an S_N2'-reduction of the propargyl acetates (±) **32** and (±) **34** respectively with the concomitant release of the leaving group.[35]



Scheme 10. Synthesis of racemic carbacyclin derivative **33** and racemic allenic prostaglandins analog **35**

This organocopper-mediated substitution has been applied to the synthesis of enantiomerically enriched haloallenes **37a** and **37b**, important allene skeletons found in many natural products.[10, 23f] For example panacene **37a** and **37b** (Scheme **11**) were the first isolated bromoallene found in nature in 1977, obtained from *Aplysia brasiliana*, a sea hare indigenous and it is used as a feeding deterrent to predatory fishes. The synthesis was developed *via anti*-S_N2'-substitution of propargyl derivative **36a** and **36b** using $LiCuBr_2$.[43]



Scheme 11. Synthesis of panacenes **37a** and **37b**

(±)-Laurallene **38** (Figure **8**), (±)-kumausallene **39** or (±)-obtusallene **40** are a few more examples of these complex bromoallene natural products.[10, 23f, 44]

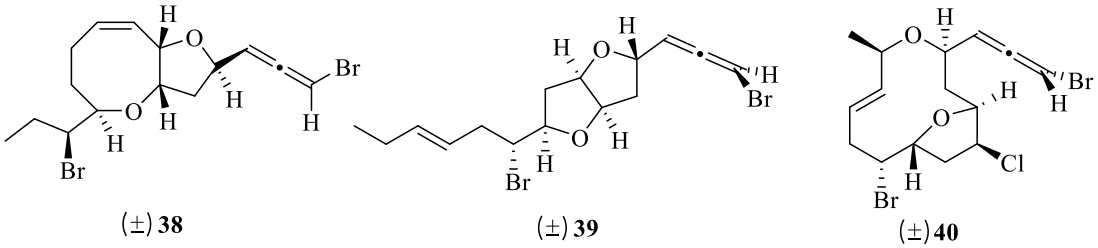
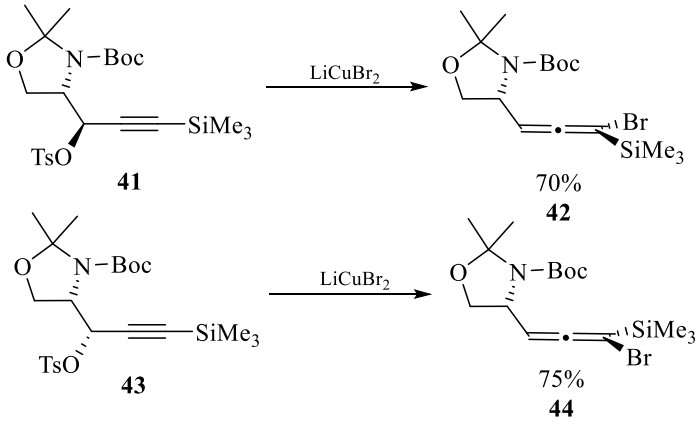


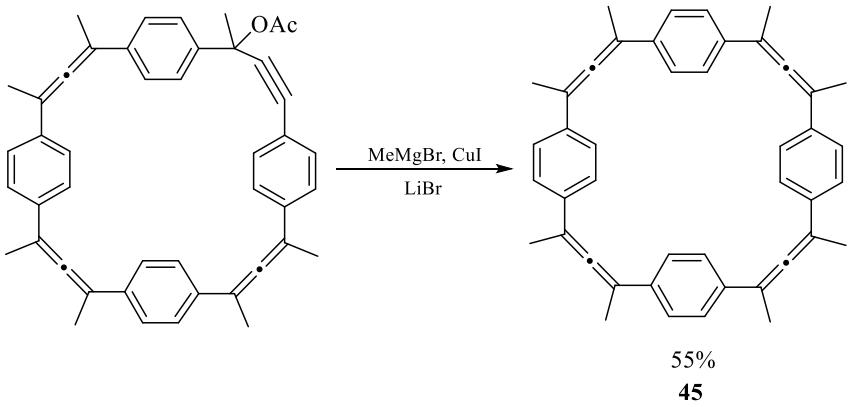
Figure 8. (±)-Laurallene **38**, (±)-kumausallene **39**, (±)-obtusallene **40**

The synthesis of these species can be performed selectively *via syn* or *anti* S_N2' depending on the halocuprate reagent of the type $LiCuX_2$ (X = Cl, Br, I).[24d] For example, silylated bromoallenes **42** and **44** (Scheme **12**) were synthesised stereoespecifically under mild conditions, *via* copper-mediated *anti*-S_N2' substitution from alkyne *anti*-**41** or *syn*-**43**.[24d]



Scheme 12. Synthesis of enantiomerically pure bromoallenes of serine-derivatives

This methodology has also been used on the synthesis of advanced molecular materials.[45] Krause and coworkers in 1999 reported the first allenophane **45** (Scheme **13**) synthesised *via* copper-mediated S_N2' substitution in moderate yields.[46]

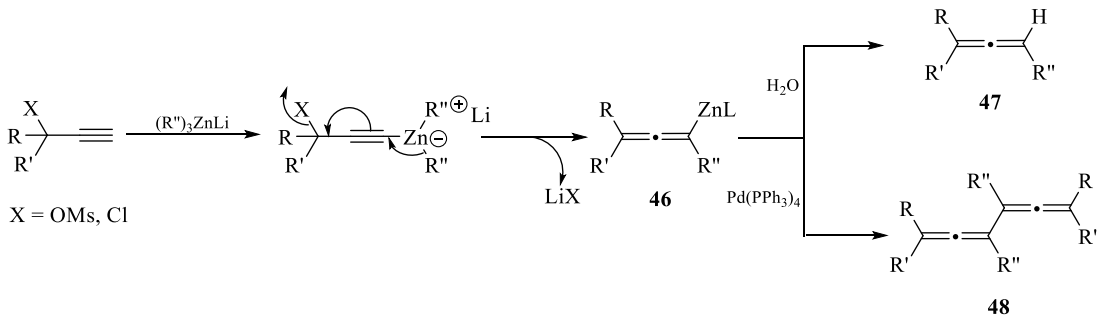


Scheme 13. Synthesis of the first allenophane **45**

Other complex chiral molecular materials have been synthesised employing axial chiral allenes as building blocks conferring structural stability and interesting chiroptical properties.[45, 47] Additionally, these macromolecules are being employed as chiral ligands for metal complexes, chiral sensors, hosts for small guest molecules or ligands for asymmetric catalysis.[23f, 45-46]

1.4.3.b. Organozinc-mediated synthesis of allenes

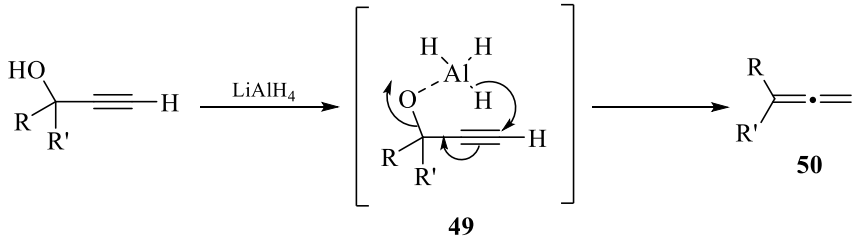
The synthesis of allenes *via* organozinc compounds is an attractive pathway to synthesise allenes and bisallenes. Generally, this organometallic reagent is used with cuprates as mentioned before,[24c, 24d] or Pd catalysts.[23d, 24c, 48] For example, the reaction of lithium triorganozincates with propargyl mesylates was proposed to occur through an S_N2'-type mechanism, achieving the allenylzinc intermediate **46**, which after quenching with water affords allene **47**, or by a Pd(0)-catalysed dimerization forms 1,2-bisallene **48** (Scheme **14**).



Scheme 14. Synthesis of allenes and bisallenes *via* lithium triorganozincates

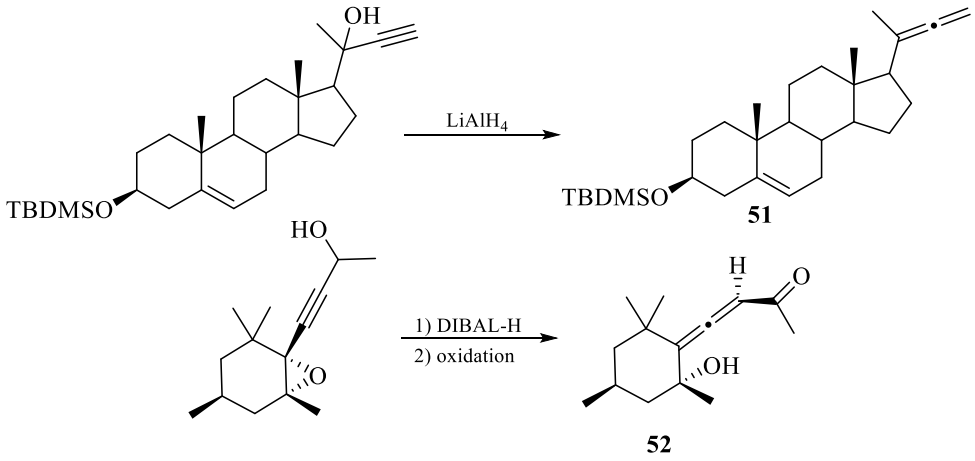
1.4.3.c. Aluminium-mediated synthesis of allenes

Aluminium hydride reagents such as diisobutylaluminium hydride (DIBAL-H) or lithium aluminium hydride ($LiAlH_4$) are also employed in substitution reactions *via* the S_N2' pathway to synthesise allenes from propargylic alcohols, epoxides or ethers. The mechanism of this substitution reaction is proposed to be triggered by intermediate **49** (Scheme **15**), where the aluminium coordinates to the oxygen, followed by hydride attack to the triple bond leading to the subsequent S_N2'-type process with the release of the oxygen as leaving group, generating 1,1-disubstituted allenes **50**. This methodology is commonly used as a powerful tool to synthesise α-allenol derivatives.[24c] The stereoselectivity of this process can be modulated to be either *syn* or *anti*, depending on the hydride source, the temperature of the reaction, leaving groups used or the propargylic substrates.[24c, 49]



Scheme 15. Synthesis of allenes *via* S_N2'-reaction using $LiAlH_4$

The high efficiency of this methodology has been applied in the synthesis of natural products such as allenic steroid **51** (Scheme **16**),[10, 50] or the "grasshopper ketone" **52**, isolated in 1968 from secretion of flightless grasshopper *Romalea microptera* showing repellent effects on its predators.[51] This famous allenic carotenoid belongs to the most numerous allenic naturally occurring group. Structurally, these species exhibit the allene moiety as well as a cyclohexylidene ring in their skeleton.[10] Dinoxanthin, neoxanthin, peridinin or fucoxanthin are carotenoids in marine animals which skeleton is formed by at least one of these building blocks showing properties varied as immune enhancements, antioxidation and photoprotection.[10]

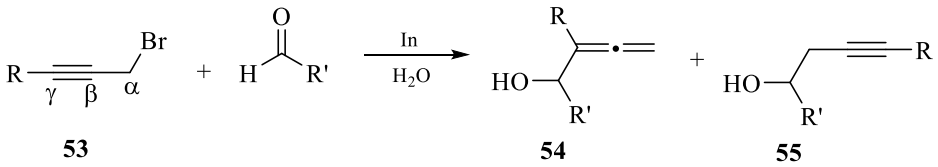


Scheme 16. Synthesis of allenic steroids **51** and "grasshopper ketone" **52** by reduction of propargylic alcohols using aluminium hydrides [35]

1.4.3.d. Indium-mediated synthesis of allenes

Indium is a versatile metal-reagent, which in the presence of propargyl halides generates allenylindium intermediates. These species are effective cross-coupling partners in reactions with organo-palladium complexes[52] and afford α-allenyl alcohols in the reaction with carbonyl groups.[53] Besides, allenylindiums can be generated in aqueous media, accentuating the importance of these reagents in organic synthesis and making it possible for reactions of these precursors to occur with non-soluble compounds in organic solvents such as carbohydrates.[53a, 54]

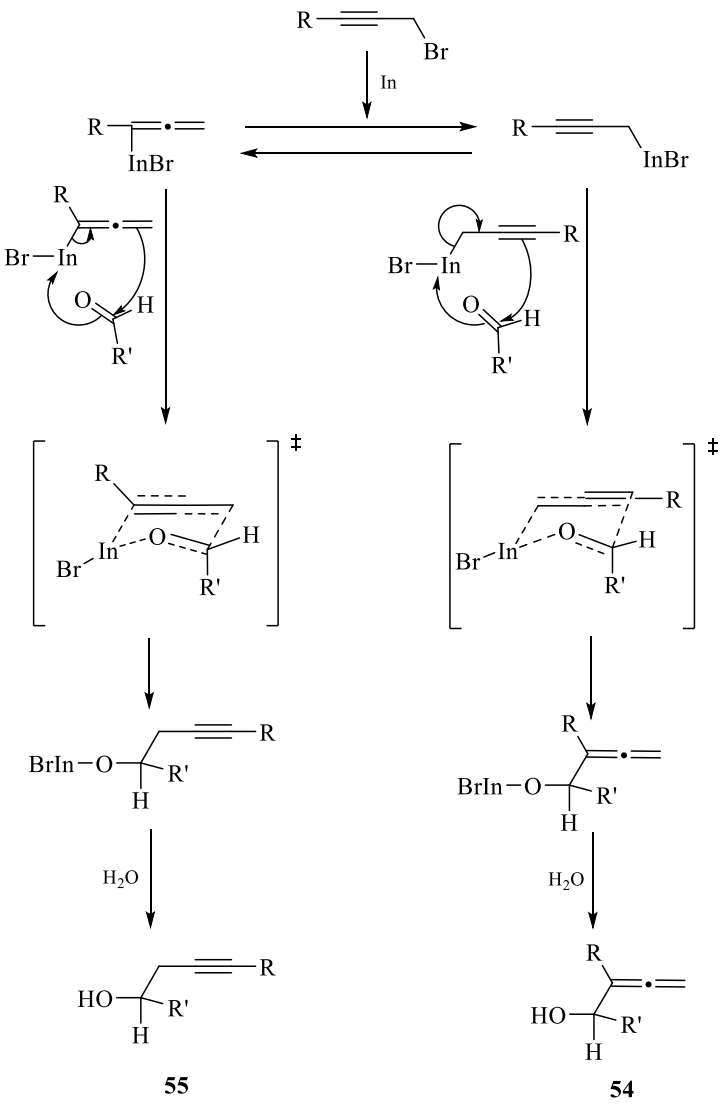
Chan and coworkers reported the first indium-mediated coupling of aliphatic or aryl aldehydes with 2-propynyl bromide derivatives **53** to produce α-allenols **54** as well as β-propargylic alcohols **55** (Scheme **17**).[53b] In order to synthesise selectively α-allenol derivatives **54**, the use of γ-substituted propargyl bromide **53** was essential.[53b] In a different approach, this selectivity issue was solved by the group of Alcaide and coworkers by using THF as a solvent and a saturated solution of ammonium chloride as an additive, in the reaction of *β*-lactam-containing propargyl derivatives as substrates.[55]



R = H, R' = *n*-C_8H_{17} Total yield = 97%, Ratio (**54**:**55**) = (12:88)
R = Ph, R' = *n*-C_8H_{17} Total yield = 89%, Ratio (**54**:**55**) = (95:5)

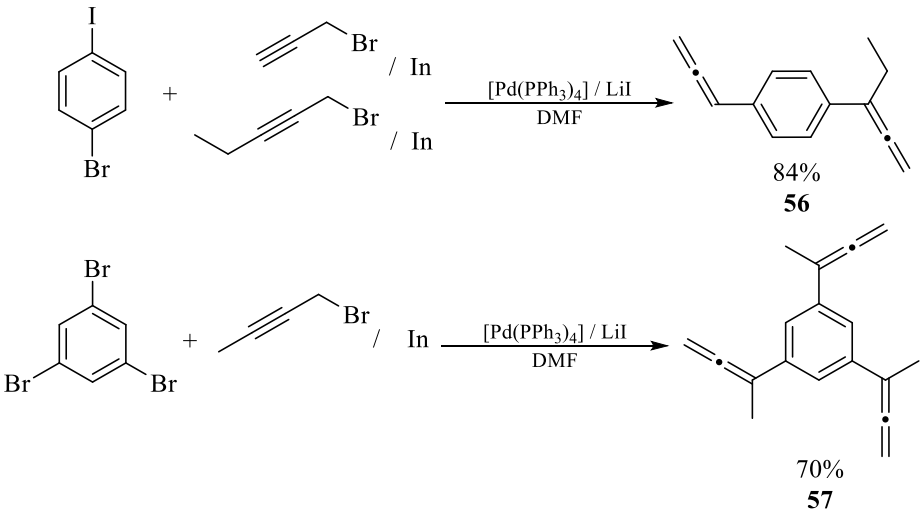
Scheme 17. Indium-mediated coupling of aldehydes with 2-propynyl systems

The proposed mechanism to explain the formation of the propargylic alcohol **55** and the α-allenol **54** goes *via* a Barbier-type reaction between an γ-alkyl halide **53** and a carbonyl group, catalysed by indium metal. In the example of Alcaide *et al*, the use of the ammonium salt was crucial to minimise the nucleophilic addition of the allenylindium intermediate to the carbonyl group, using water as the solvent (Scheme **18**).[53a]



Scheme 18. Proposed mechanism for the indium-mediated synthesis of α-allenols [54a]

Allenylindium intermediates can also be involved in metal-catalysed cross-coupling reactions. The group of Lee reported a versatile one-pot palladium-catalysed reaction of aromatic halides and allenylindium intermediates to obtain bisallene **56** and trisallene **57** (Scheme **19**) with high chemo- and regioselectivity.[52]

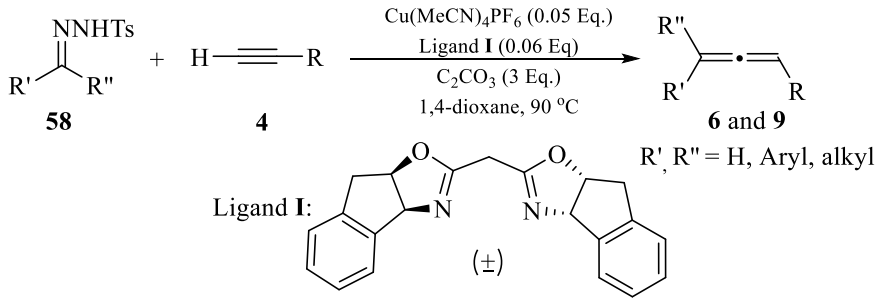


Scheme 19. Palladium-catalysed cross-coupling reactions of *in situ* generated allenylindium reagents with organic halides

1.4.4. Synthesis of allenes *via* Cu(I)-catalysed coupling of *N*-tosylhydrazones and alkynes

Metal-catalysed coupling reactions are efficient ways to synthesise allenes, with palladium and copper catalysts being the most investigated.[23f, 56] *N*-Tosylhydrazone and diazo derivatives are important precursors in these metal-catalysed coupling reactions with terminal alkynes to generate C-C bonds in high yields.[56e, 57]

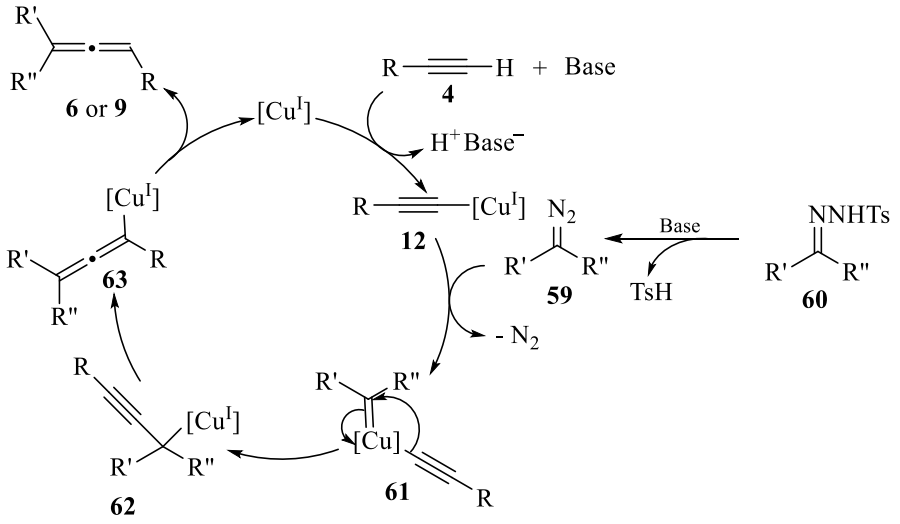
In 2011 Wang, inspired by the published work of Suarez and Flu,[57b] developed the first synthesis of functionalised di- and trisubstituted allenes **6** and **9** (Scheme **20**) from terminal alkynes **4** and *N*-tosylhydrazones **58** *via* copper(I) catalysis under mild conditions (Scheme **20**).[58]



Scheme 20. Synthesis of di- and trisubstituted allenes **6** and **9** by coupling of *N*-hydrazones **58** and terminal alkynes **4** catalysed by copper(I)

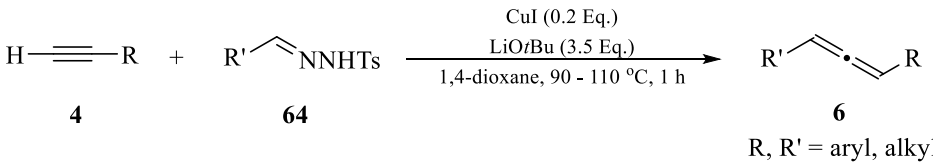
Wang proposed a mechanism initiated by the formation of copper(I) acetylide species **12** (Scheme **21**) from the terminal alkyne **4** and the copper(I) salt in the presence of base. Then, the diazo intermediate **59** generated *in situ* by deprotonation of *N*-tosylhydrazone **60**, reacts

with acetylide **12** generating copper-carbene complex **61**. 1,2-Migratory insertion of the alkynyl group would form intermediate **62**, which suffers a 1,3-copper migration to obtain intermediate **63**. Allenes **6** and **9** were formed after protonolysis of intermediate **63** with the concomitant regeneration of the copper(I) catalyst.[56c, 58]



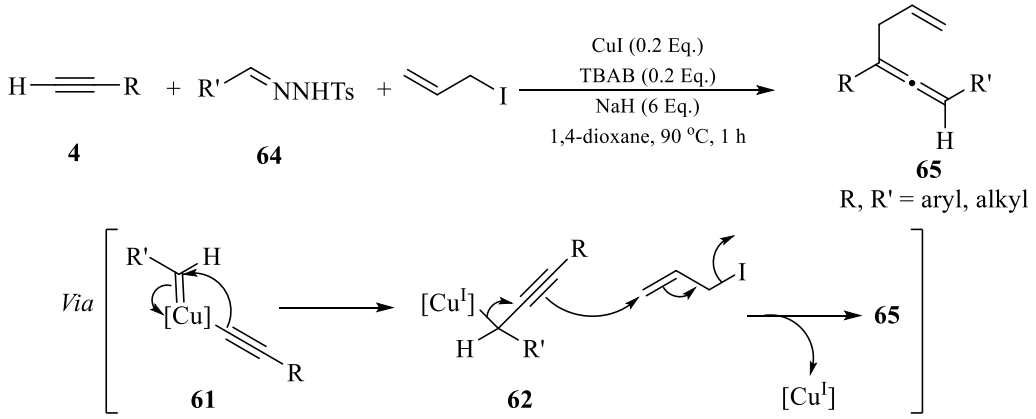
Scheme 21. Proposed mechanism of the Cu(I)-mediated synthesis of trisubstituted allenes through coupling of *N*-tosylhydrazones with terminal alkynes**.**

In 2013 the group of Wang published two articles reporting a few modifications on this reaction. In their first article, they reported the use of a cheaper copper(I) salt (CuI) to trigger the formation of the copper-carbene complex **61** (see Scheme **21**) in the synthesis of the 1,3-disubstituted allene **6** from terminal alkyne **4** and *N*-tosylhydrazones **64**, easily preformed from the corresponding aldehyde (Scheme **22**).[59]



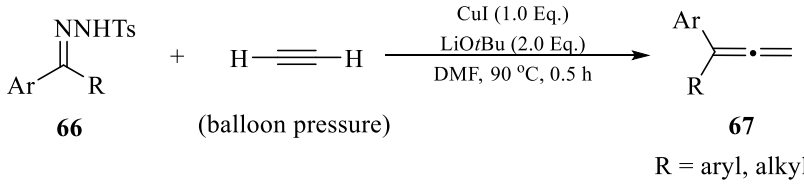
Scheme 22. Synthesis of 1,3-disubstituted allenes by coupling of *N*-tosylhydrazones and terminal alkynes

Wang and coworkers were also able to develop an efficient synthesis for trisubstituted allyl allenes **65** (Scheme **23**) by modifying the final protonation step. Thus, instead of a protonolysis of the nucleophilic organocopper intermediate **63** (Scheme **21**), a carbon-based electrophile was used to trap the organocopper species **62** (Scheme **23**) leading towards the formation of allyl substituted allenes **65**.[56d]



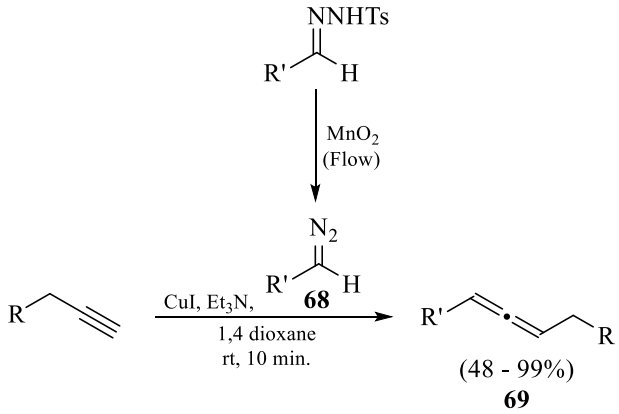
Scheme 23. Synthesis of allyl allenes by coupling of *N*-tosylhydrazones, terminal alkynes and allyl halides

Recently, Wang and coworkers have also published a novel synthesis of 1,1-disubstituted allenes **67**, promoted by a copper-carbene migratory insertion (Scheme **24**). In this work, ethyne gas and *N*-tosylhydrazones **66** derived from aromatic ketones were used, obtaining allenes **67** in high yields.[56b]



Scheme 24. Synthesis of 1,1-disubstituted allenes by coupling of *N*-tosylhydrazones and ethyne catalysed by CuI

Simultaneously, Ley and coworkers reported an excellent work based on Wang's proposed mechanism (see Scheme **21**), incorporating the concept of flow chemistry for the *in situ* formation of the unstable diazo compounds **68** (Scheme **25**) at room temperature, carrying out the reaction under milder conditions to obtain 1,3-disubstituted allenes **69**.[56c]



Scheme 25. Synthesis of di-substituted allenes by coupling of diazo compounds with terminal alkynes catalysed by Cu

Chapter 2.

Gold-catalysed hydroazidation of allenes

2.1. Introduction

"Golden times" or "a golden age" are colloquial expressions that are reminiscent of prospering situations or epochs with satisfactory economical wealth. This concept was acquired because in the past gold was employed as a valuable currency.

Among its properties, gold is corrosion and moisture resistant, a good thermal and electrical conductor (collectors for solar cells, components of circuits), and it is the most ductile and malleable metal. Gold is neither toxic, nor an allergen and it is not harmful to the environment. Therefore gold is commonly used in dental issues such as orthodontic appliances, crowns, bridges or fillings, and in drugs for medical disorders such as rheumatoid arthritis or tumours / cancer of stomach and intestines.[60]

In contrast, the growth of gold in chemistry was not as expected. Schmidbaur, in an interesting review about how gold chemistry has blossomed, said "*an old rule of catalyst research appears to regard gold as black sheep among the noble metals, for it has so far found practically no catalytic application"*,[61] in other words, gold was eclipsed by other catalytically active metals such as platinum, palladium, rhodium, osmium, or ruthenium and mercury, "platinum group metals (pgm)", which were physically and chemically similar.

Besides, another reason for its exclusion of research could be supported on the lack of chemisorption on gold in heterogeneous catalysis, with the "pgm" group of metals being more catalytically effective.[62]

About 655 publications in gold chemistry were reported until 1977, highlighting remarkable work on gold catalysed heterogeneous hydrogenation of olefins reported by Bond and coworkers.[63] During this period several alternatives for selective oxidation of hydrocarbons,[64] in particular the oxidation of carbon monoxide were widely investigated. Haruta, in one of his communications mentioned, *"The chemical industry would be transformed if selective oxidation of hydrocarbons could be achieved efficiently using cheap and clean oxygen from the air. Doing that with gold as a catalyst is a method gaining in allure".*[65] In 1987 Haruta and his colleagues published the awaited oxidation of carbon monoxide at low-temperatures by heterogeneous gold catalysis.[64, 66] Simultaneously, Hutchings and coworkers reported a hydrochlorination of ethyne under heterogeneous gold catalysis.[67] After these two works, the importance of gold as catalyst was established, and more or less at the same time Ito and coworkers developed the first homogeneous asymmetric gold catalysis,[68] followed by interesting works in this field by Fukuda and Utimoto[69] in addition to Teles and coworkers.[70] Several homogeneous gold-catalysed examples were

revealed previously, however, from 2000 until our days the number of publications in this field has grown exponentially.[71]

2.2. Relativistic effects

The unique chemical features of gold are remarkably affected by relativistic effects in comparison with the "pgm" (Figure **9**). These effects consider velocity as meaningful relative to the speed of light "*c*" due to the high speed of the electrons moving close to a heavy nucleus. As a consequence, radial contraction is given, where the s and p orbitals are contracted. In contrast, d and f orbitals are expanded, being more shielded from the nucleus and suffering a weaker attraction from the core with subsequent energetic destabilisation.[72]

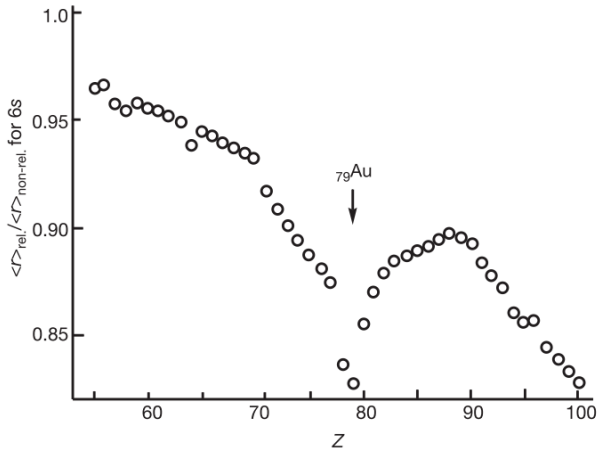


Figure 9. Relativistic contraction of the 6s orbital in different elements. This figure was reproduced directly from: D.J. Gorin, F.D. Toste, *Nature*, **2007**, *446*, 394-403.[72-73]

This contracted 6s orbital forms strong covalent bonds (Au-Ligand), confirming the greater first ionization potential (9.22 eV.) compared with silver (7.57 eV.). In contrast, the second ionization potential is 0.09 eV lower than silver, since the electrons that remain in the 5d-level are higher in energy (Figure **10**). Thus, gold has a remarkable electron affinity (2.31 eV) if it is compared with silver (1.23 eV), therefore, it shows high electronegativity (2.4) manifesting the formation of auride (Au^{-I}) compounds (CsAu or RbAu) with semiconductor properties.[74] Besides, Au^{I}–Au^{I} species display bond strength similar to strong hydrogen bonds and they can be used for their optical properties and medical applications.[75]

The yellow colour of gold is another confirmation of relativistic effects. The small bandgap between the Fermi level and the 5d electrons (Figure **10**) favours the absorption into visible light, reflecting red and yellow light.[72-73]

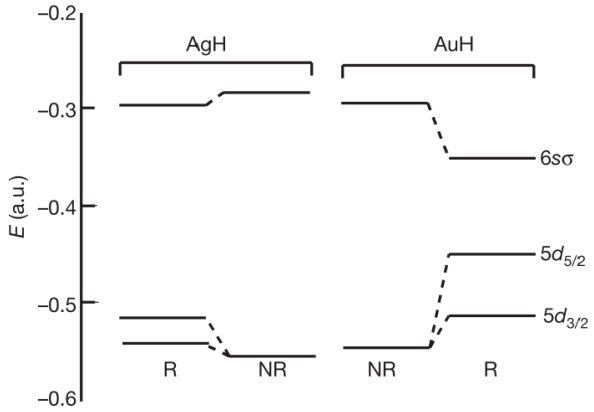


Figure 10. AuH and AgH bond energies. Relativistic (R) and non-relativistic (NR) orbitals. This figure was reproduced from: D.J. Gorin, F.D. Toste, *Nature*, **2007**, *446*, 394-403.[72-73]

The relativistic contraction of the s orbital also affects the catalytic properties of gold. The high electronegativity of Au(I) is linked with a strong Lewis acidity, whereas, cationic Au(I) species possess a "soft" Lewis acidity activating efficiently π-systems (alkynes, allenes and alkenes).[73] Oxidation of Au(I) to Au(III) is rarely given in catalysis. However the use of an external oxidant makes it possible for oxidation to Au(III) and the subsequent reduction in oxidative coupling reactions.[76] According to this, Au(I) is able to catalyse reactions without exclusion of air or in aqueous media.[73]

2.3. Chemistry of gold-allene complexes

After the consolidation of gold as a powerful catalyst in organic chemistry, a large number of works in hetero- and homogeneous catalysis have been reported. Focusing our interest on homogeneous gold catalysis, electrophilic activation of unsaturated moieties has drawn much attention. However, in this introduction to the experimental work carried out, only the remarkable versatility of allenes as substrates for gold-catalysed functionalization will be described.[77]

The allene skeleton is associated with selectivity problems as well as higher reactivity than alkynes and alkenes (Figure **11**). In addition to the regio- (to provide constitutional isomers), stereo- (*cis*- or *trans*-addition to obtain stereoisomers) and chemoselectivity (single or double addition) found in reactions with alkynes and alkenes, due to their two orthogonal π-systems allenes also have positional selectivity issues, the challenge being addition towards a specific double bond.[77-78]

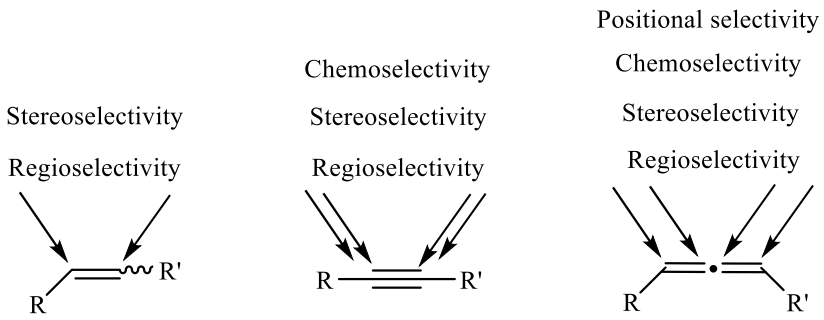


Figure 11. Diverse selectivity modes in unsaturated compounds [77-78]

Coordination of gold to allenes also displays more complexity than the complexation with alkynes or simple alkenes. Gold can coordinate to allenes in a common η^2-coordination mode with either one of the double bonds of the allene **70** (Figure **12**). Similarly to the coordination of gold with simple alkenes, depending on the electronic properties of ligands employed and the substituents of the allene skeleton, the gold will be shifted towards the central carbon as in **71** or one of the terminal carbons of the allene as in **72** (Figure **12**).[77, 79] However, there is yet another possibility for coordination. Structure **73** (Figure **12**) shows a coordinative mode where gold is σ-bounded to the *sp*-hybridized carbon of the allene (η^1-coordination). This structure can be seen as the σ-allyl cation **73**, a zwitterionic carbene **74** or η^1-bent allene **75** (Figure **12**). This η^1-coordination mode has been proposed in transition states,[80] reactive intermediates for C-X bond formation, or in axis-to-center chirality transfer reactions with allenes.[77, 79]

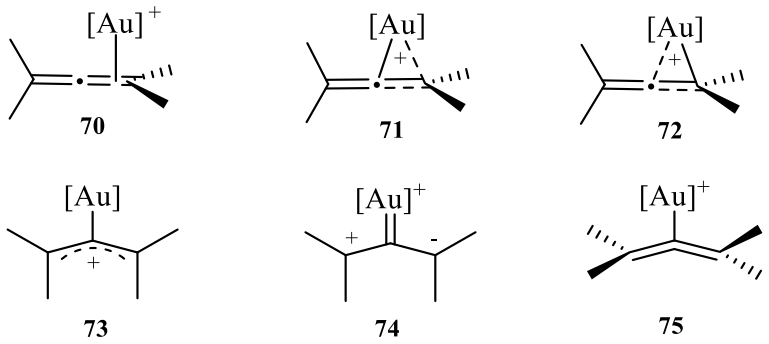
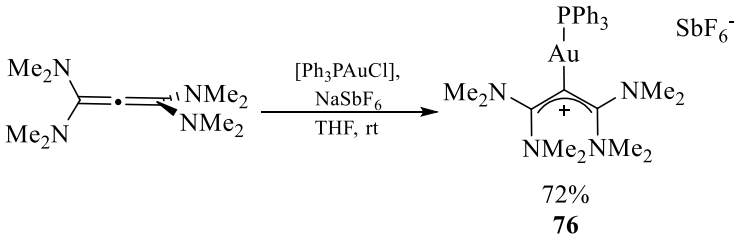


Figure 12. Modes of coordination of gold with allenes[77]

These modes of gold-allene coordination have been supported by computational (DFT calculations) and (VT) NMR studies,[81] revealing how these species can interconvert and that the η^2-coordination favours preferentially to the less hindered π-system of the allene in the ground state. Mile and coworkers reported experimental data, where they detected a η^1-gold-allene radical using ESR spectroscopy at 77 K.[77, 82] In addition, an example of a gold-allene

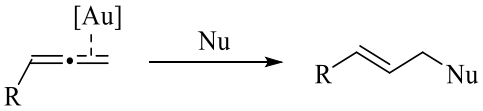
with η^1-coordination has been isolated (**76**, Scheme **26**) using a strongly-electron donating tetraaminoallene as substrate.[77, 81, 83]



Scheme 26.Example of η^1-coordination mode of gold-complexes using high electron-donating groups

2.4. Gold-catalysed reactions of allenes with nucleophiles

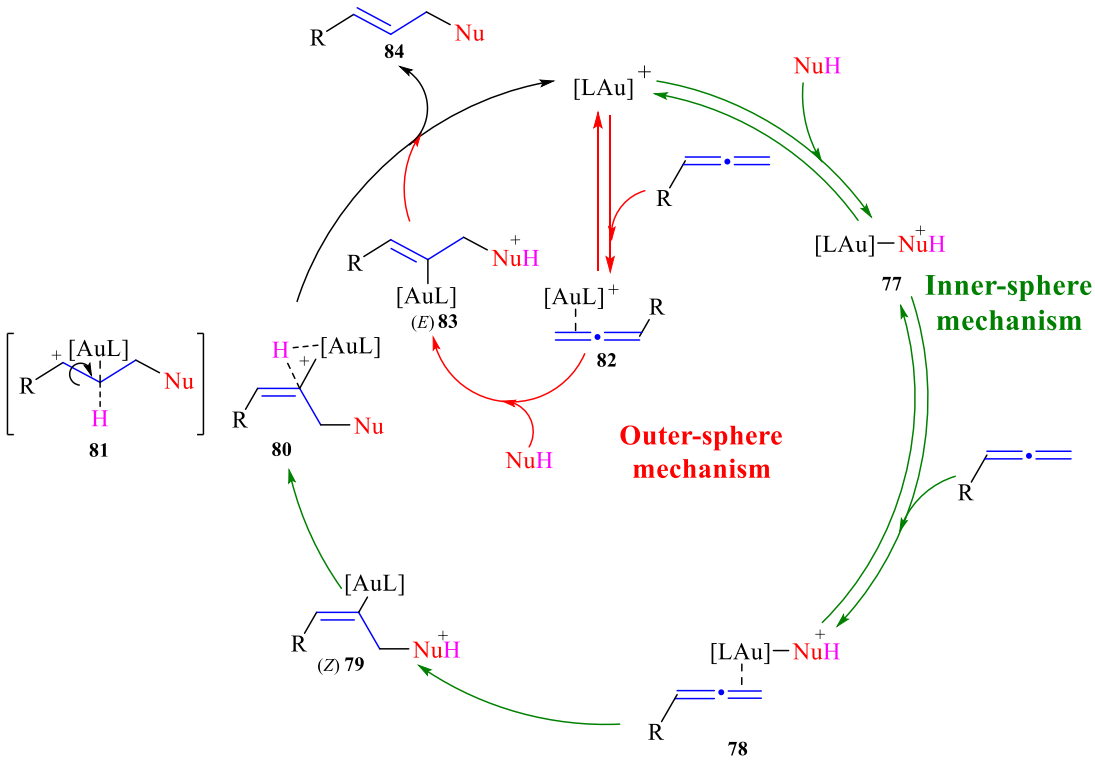
Gold-allene interactions are frequently electrophilic activations, with nucleophilic attack of carbon-based nucleophiles (arenes, carbon pronucleophiles) and heteroatoms (nitrogen, oxygen and sulfur) in inter- and intramolecular versions the most reported. Gold-catalysed hydrofunctionalisation of allenes for the synthesis of heterocycles (intramolecular reaction) has been studied extensively during the past years.[77, 84] Gold-catalysed addition of external nucleophiles to allenes (intermolecular reactions) has received less attention (Scheme **27**). The present chapter of this thesis deals with the external addition of nucleophiles to allenes to give allyl derivatives, and this introduction will focus on this topic only.



Scheme 27. General example of a gold-catalysed intermolecular reactions of allenes with nucleophiles to give allyl derivatives

2.5. Gold-catalysed intermolecular reactions of allenes with nucleophiles

The formation of *E*-allylated compounds by complexation of nucleophiles to allenes is generally assisted by an electrophilic activation of gold to one of the π-systems of the allene leading to the formation of a vinyl-gold complex as an intermediate. However, the attack of the external nucleophile can be managed depending on the interactions with the metal and its nature. Thus, two mechanisms are proposed for this reaction: inner- and outer-sphere mechanisms (Scheme **28**).



Scheme 28. Inner- and outer-sphere mechanism for the gold-catalysed intermolecular reaction of allenes with nucleophiles

In the inner-sphere mechanism (green in Scheme **28**), it has been proposed that the external nucleophile coordinates with gold first (**77**, Scheme **28**). Then, η^2-coordination of the Au-Nu with one of the π-systems of the allene generates the tricoordinate complex **78**, which after the intramolecular attack of the nucleophile, gives rise to *Z*-vinyl-gold complex **79**. During the gold-elimination process, isomerization by rotation of a C-C bond has been proposed (**80**, **81**), which gives the *E*-allyl product **84**.[77]

In the outer-sphere mechanism (red in Scheme **28**), the gold is proposed to behave as a π-acid, activating the allene (**82**, Scheme **28**) for the subsequent nucleophilic attack on the activated sp^2-carbon from the opposite face, to give the *E*-vinyl-gold intermediate **83**, which after protodemetalation gives the allyl derivative **84**.

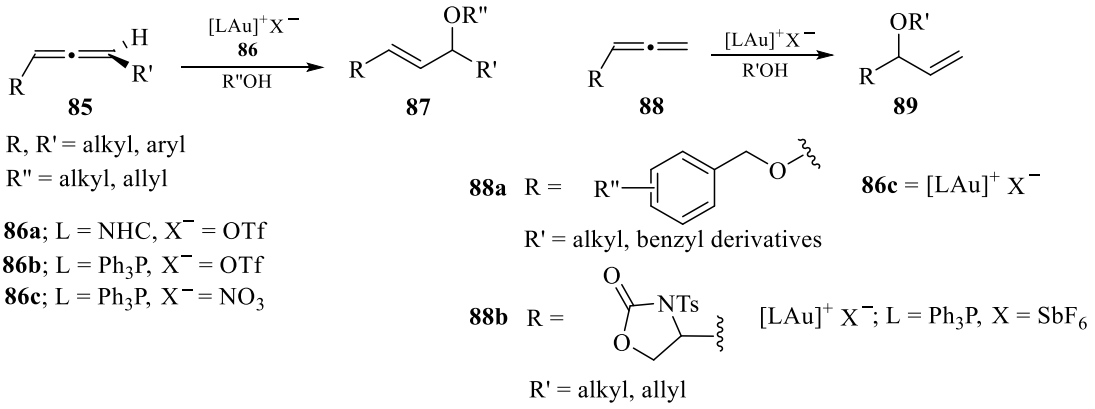
2.5.1. Gold-catalysed intermolecular reactions of allenes with oxygen nucleophiles

The addition of oxygen nucleophiles to allenes is widely employed to obtain versatile allyl ethers with high atom economy and in high yields. However it should be noted that the addition of oxygen nucleophiles in the enantioselective version has not been reported so far.

In 1998 Shulz and Teles published the first gold-catalysed reaction of allenes and alcohols.[70] However, the groups of Zhang,[85] Yamamoto[86] and Widenhoefer[87] developed the bulk of the hydroalkoxylations of allenes catalysed by gold to obtain *E*-allyl ethers

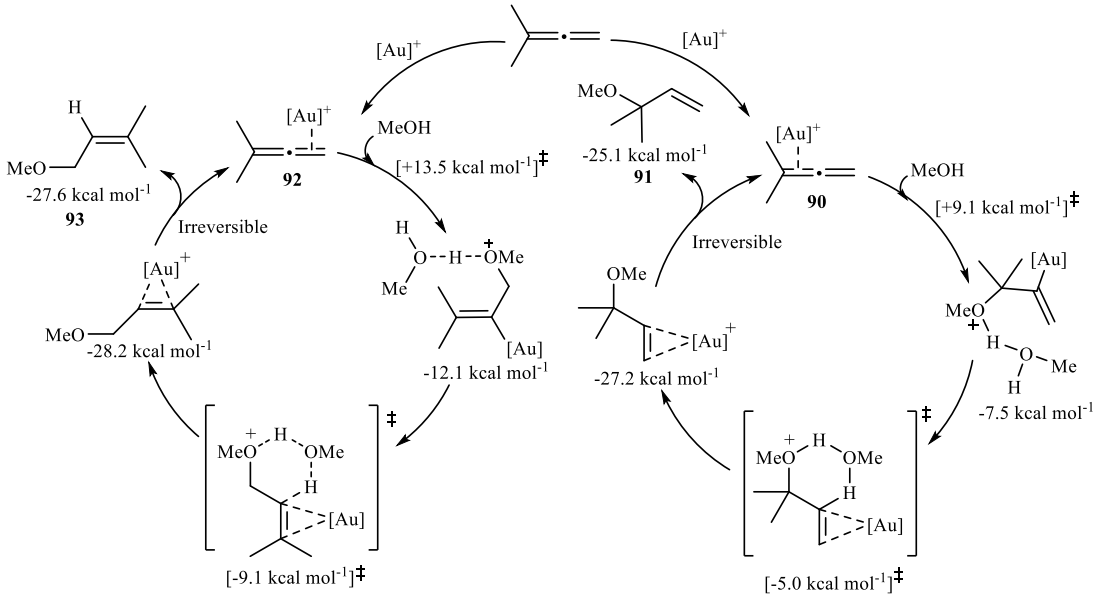
(Scheme **29**). Recently, an interesting review from Muñoz covers all these reported gold-catalysed hydroalkoxylations.[88]

Cationic *N*-heterocyclic carbenes (NHC-Au complexes) **86a**[87b] or phosphine-Au complexes **86b** and **86c**[85a, 86a] have been used as the best catalytic systems for these reactions. Hydroalkoxylation reactions using NHC-Au complexes **86a** (Scheme **29**) led to the attack through an outer-sphere mechanism.[87] Whereas, the use of phosphine-Au complexes **86b** and **86c** proposed the formation of tricoordinated gold-complex **78** (Scheme **28**) following an inner-sphere mechanism to obtain allyl derivatives **87** (Scheme **29**).[77, 86] Generally, the addition of the oxygen nucleophiles is favoured to the less hindered double bond of the allene **87** (Scheme **29**).[86-87] However, the regioselectivity towards the most hindered carbon of the allene can be enhanced when an excess of alcohol is used.[77, 89] If the allene is substituted with heteroatoms such as alkoxyallenes[85b] **88a** or 4-vinylidene-2-oxazolidinones[89a] **88b** (Scheme **29**), the nucleophilic attack occurs at the most substituted carbon **89** (Scheme **29**).



Scheme 29. Gold-catalysed intermolecular hydroalkoxylation of allenes

DFT calculations on the Au(I)-catalysed hydroalkoxylation of simple allenes showed that the addition of the nucleophile is the rate limiting step and occurs *via* an outer-sphere mechanism, with the attack to either terminal sp^2-carbons of the allene moiety in **90** and **92** (Scheme **30**).[90] The study showed that although the product of the attack to the less substituted carbon is thermodynamically more stable **93**, the nucleophilic addition to the more substituted carbon **91** is kinetically favoured. Energy values confirmed that the hydroalkoxylation reaction is irreversible so it was proposed that the kinetically favoured product **91** isomerised to the thermodynamically more stable and most experimentally observed product **93** in a process catalysed by gold *via* a cyclic transition state.[77, 90]

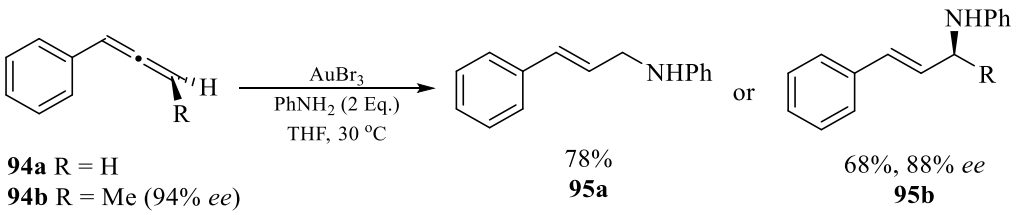


Scheme 30. DFT studies for Au(I)-catalysed hydroalkoxylation of allenes

2.5.2. Gold-catalysed intermolecular hydroamination of allenes

The addition of nitrogen nucleophiles to allenes catalysed by gold is an attractive pathway to synthesise enamines, imines, hydrazones or allyl amines with high atom economy and good yields. It is important to mention that amines can coordinate easily with the metal centre, therefore the electrophilic activation of the allene can be conditioned by the nature of the catalyst or the Au-N interactions.[77, 91]

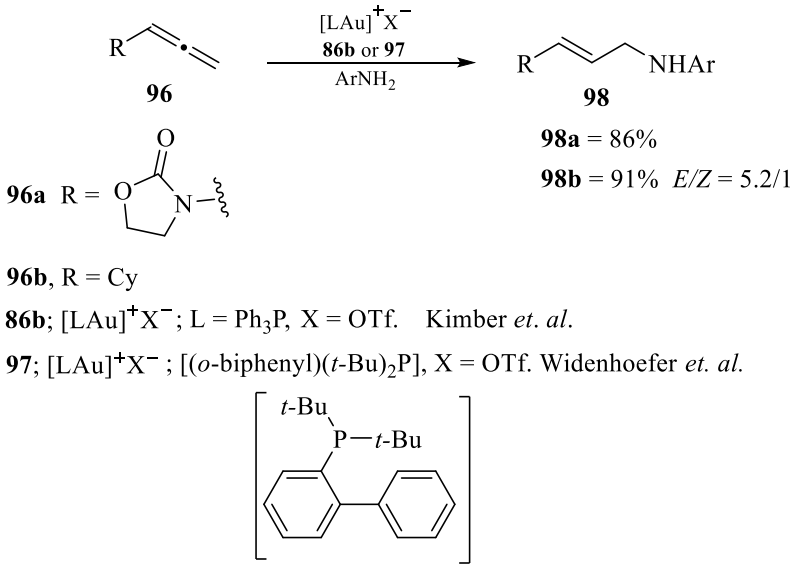
The first Au(III)-catalysed intermolecular hydroamination of chiral **94b** and non-chiral **94a** allenes using aniline as a nucleophile was reported by Nishina and Yamamoto (Scheme **31**).[92] In this work, high chirality transfer and selectivity problems (regio-, stereo-, chemo- and positional selectivity)[78] were solved, obtaining enantiomerically enriched *E*-allylated products **95b**. The suggested mechanism proposed the formation of a tricoordinate gold-complex **78** (Scheme **28**).[77, 92]



Scheme 31. Au(III)-catalysed intermolecular hydroamination of chiral and non-chiral allenes using aniline as nucleophile [77]

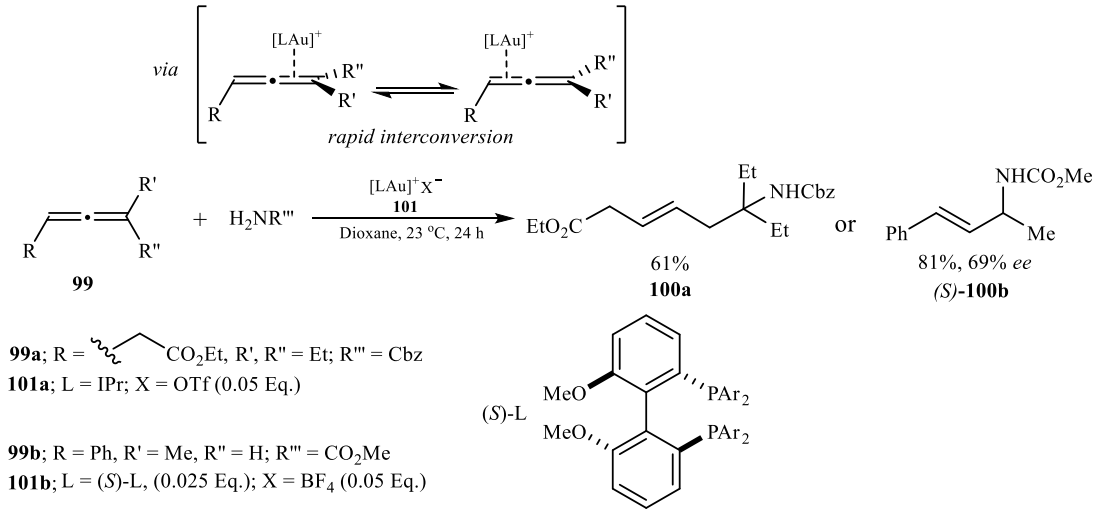
Aryl amines have also been used by Widenhoefer[93] with mono-, 1,1- and 1,3-disubstitued allenes, and also by the group of Kimber[77, 94] with valuable allenamides as

substrates, obtaining high yields and good regioselectivities. In his work, Kimber achieved the Markovnikov *E*-allylamino carbamates **98a** (Scheme **32**) proposing an outer-sphere mechanism, where the Au(I)-π-allyl complex could be stabilised by conjugation with the nitrogen of the allenamide with the subsequent addition of the nucleophile to less hindered carbon of the allene.[94] On the other hand, Widenhoefer proposed the formation of *E*-allylamines **98b** (Scheme **32**) *via* two alternative inner- or outer-sphere mechanisms, without enough experimental evidence to decide between them.[93]



Scheme 32. Synthesis of *E*-allylamino carbamates and *E*-allylamines.

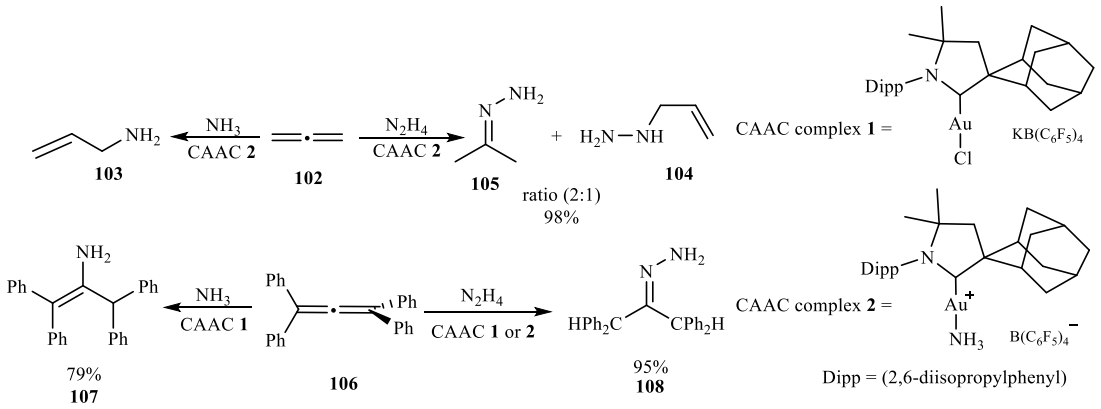
It is interesting to emphasise the work of Widenhoefer and coworkers to obtain *E*-allylamines **100a** and **100b** (Scheme **33**) using *N*-unsubstituted carbamates as nucleophiles with mono-, 1,1-, 1,1,3- and tetrasubstituted allenes,[95] as well as its enantioselective version[96] with 1,3-disubstituted allenes catalysed by gold complexes. Generally, the addition of nucleophiles occurs at the terminal sp^2-carbon of the allene moiety, whereas, in this hydroamination reaction catalysed by NHC-Au complexes the attack occurs at the most hindered carbon of the allene (**100a**, Scheme **33**). The proposed interpretation of this unusual addition resides in an outer-sphere mechanism with the rapid and reversible interconversion of the Au(I)-π-allene, and the attack occurring to the most hindered carbon (Scheme **33**).[95] In the enantioselective version, the authors used chiral bis(gold) phosphine complexes **101b**. One of the two gold centers is proposed to catalyse the C-N bond formation process, and the other metal-centre increases the conversion to the desired product. Also, the *N*-allyl carbamate product can coordinate with the second gold-centre, modifying the catalytically active species and promoting racemization of enantiomerically pure allenes **99b** (Scheme **33**).[77, 96]



Scheme 33. Synthesis of *N*-unsubstituted allyl carbamates catalysed by Au(I)

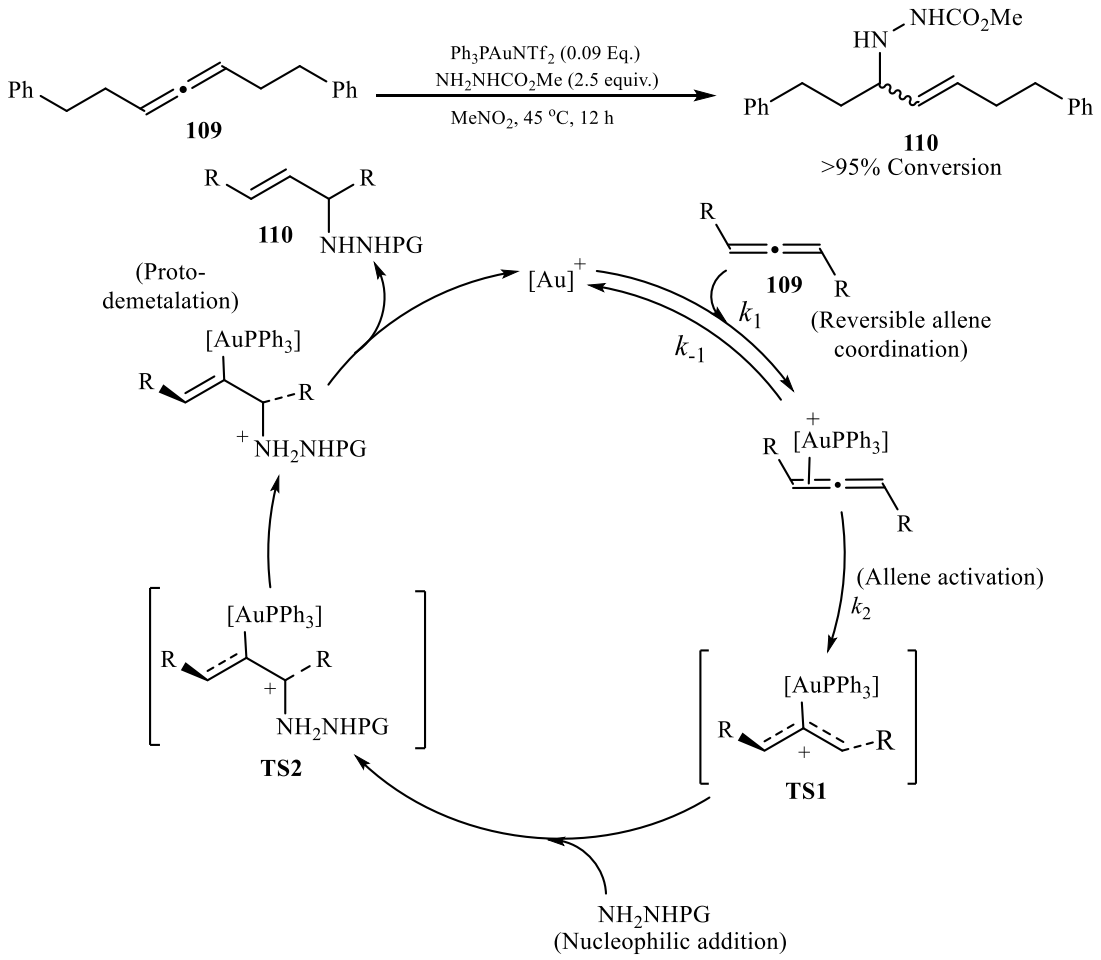
Less reactive aliphatic secondary amines (such as morpholine) have also been used as nucleophiles by the groups of Bertrand[97] and Yamamoto.[86b, 98] Their intermolecular additions to allenes, catalysed by Au(I)-complexes gave rise to Markovnikov *E*-allyl products in good yields. Both reactions are proposed to take place through an inner-sphere mechanism. However it should be noted that the authors found evidences of gold-amine complexes in the reactions.

Although the nucleophile generally attacks the sp^2-carbons of the allene, it has been observed that selectivity problems arise when small nucleophiles are employed (ammonia and hydrazine). In this case, the addition occurs at the central, terminal or both carbons of the allene, depending on steric factors. The group of Bertrand used simple ammonia or the parent hydrazine as nucleophiles for the addition to allenes employing CAAC-Au-complexes to obtain imines or hydrazones derivatives in good yields from the unusual attack of the nitrogen nucleophile to the central carbon of the allene (Scheme **34**).[99] DFT calculations on this reaction were recently published using hydrazine as *N*-nucleophile.[91b] In this study, an outer-sphere mechanism is proposed. Thus, when 1,2-propadiene **102** (Scheme **34**) is used as substrate, the addition of ammonia led to the attack at the sp^2-carbon to form **103**, whereas, the addition of hydrazine took place on both terminal and central carbon of the allene generating allyl hydrazine **104** and imine **105** respectively. Additionally, the attack of hydrazine and ammonia to the central carbon of the allene was also observed employing tetraphenyl-1,2-butadiene **106** as substrate (Scheme **34**). In this case, the energy profile suggests a rapid but reversible nucleophilic addition to the terminal sp^2-carbon of the allene, and slower but irreversible attack to the central carbon of the allene skeleton, obtaining products **107** and **108**.[77, 91b, 99]



Scheme 34. Au(I)-catalysed hydroamination of allenes using ammonia and hydrazine as nucleophiles

The group of Toste[80] reported a full mechanistic study of the Au(I)-catalysed intermolecular addition of nitrogen nucleophiles to allenes. In this work, the authors used hydrazide as the nucleophile, the symmetrical 1,7-diphenylhepta-3,4-diene **109** as the substrate and $Ph_3PAuNTf_2$ as an effective catalyst source to obtain allyl derivatives **110** in high yields (Scheme **35**). Kinetic analysis, NMR experiments, DFT calculations, chirality transfer and reversibility experiments as well as experiments to analyse the electronic properties in the ligand of the gold-complex led to the proposal of an outer-sphere mechanism where allene activation by Au(I) is the rate-limiting step, with a transition state invoking an η^1-gold-bent allene coordination complex before the nucleophilic attack.[77, 79-80]

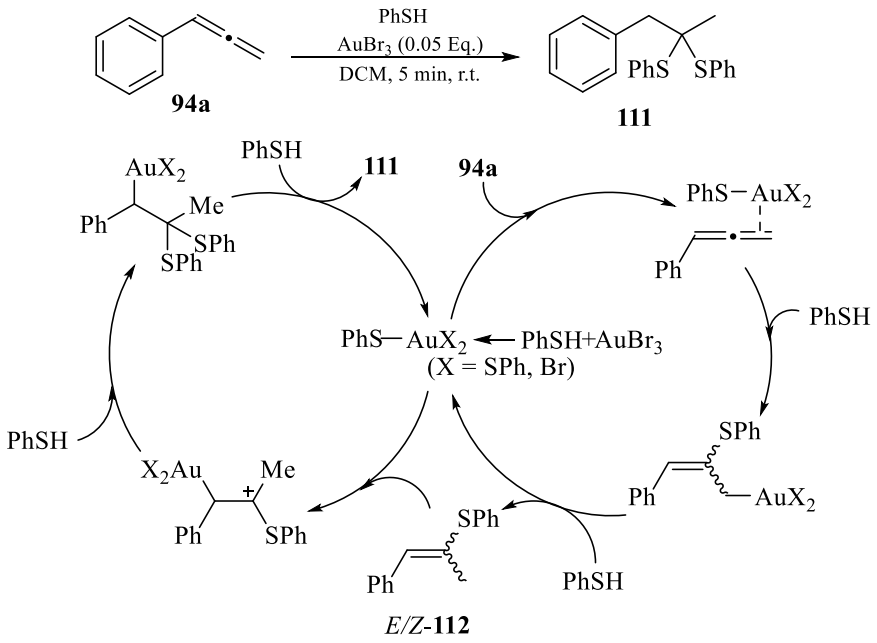


Scheme 35. Proposed mechanistic study for the Au(I)-catalysed addition of hydrazides to allenes

Another example of C-N bond formation employing allenes as substrates is the one reported by the group of Zhang, where sulfonamides are used as nucleophiles to obtain valuable Markovnikov *N*-allyl sulfonamides in high yields.[77, 100]

2.5.3. Gold-catalysed intermolecular hydrothiolation of allenes

The affinity of gold for sulfur is known. Several gold complexes are employed using sulfur ligands to catalyse reactions or as precursors to insert new ligands due to the lability of sulfur. There is only one example of gold-catalysed intermolecular hydrothiolation of allenes reported so far.[101] This work published by the group of Yamamoto shows a double addition of sulfur nucleophiles to the central *sp*-carbon of the allene, obtaining dithioacetal products **111** (Scheme **36**). The reaction is catalysed by $AuBr_3$ using exclusively mono-aryl allenes such as **94a** as substrates and aryl sulfides as nucleophiles. In the mechanism, a double catalytic cycle was suggested. The formation of a gold-sulfide complex by *in situ* ligand exchange, and the vinyl sulfide **112** as an intermediate are essential steps in the proposed catalytic cycle (Scheme **36**).[77, 101]

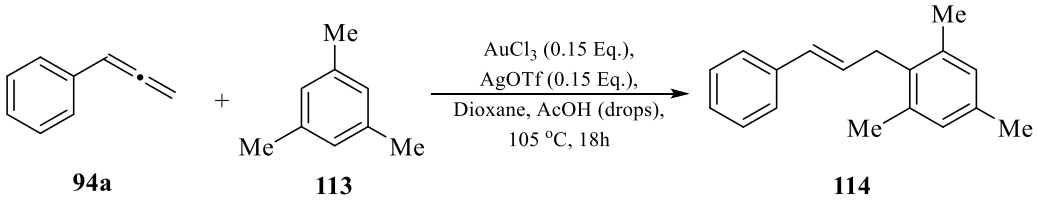


Scheme 36. Reaction and proposed mechanism of gold-catalysed hydrothiolation of allenes

2.5.4. Gold-catalysed intermolecular hydroarylation of allenes

Electron-rich aromatic compounds can also be used as nucleophiles in reactions with allenes catalysed by gold-complexes. High selectivity has been observed in the examples reported so far to obtain *E*-allyl derivatives from the attack to the less hindered sp^2-carbon of the allene. Outer-sphere mechanism is the most accepted mechanistic proposal for these reactions, where the gold activates the allene by an η^2-coordination, and the aromatic compound is added to the allene in a Friedel-Crafts-type reaction.[77]

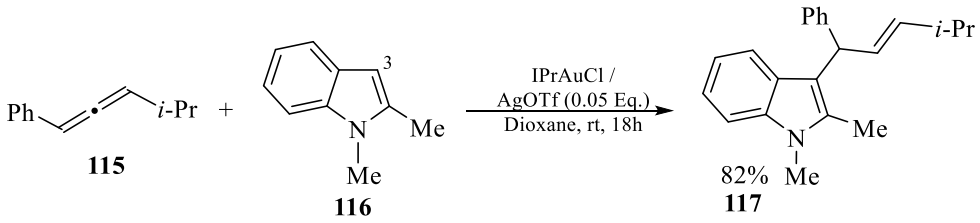
The first gold-catalysed hydroarylation was reported by Skouta and Li,[102] employing electron-rich aromatic compounds such as anisole, mesitylene **113** or tetramethylbenzene (Scheme **37**) as nucleophiles to obtain the Markovnikov *E*-allylated product **114**. However, no reaction was observed with indole or benzene. Although an inner-sphere mechanism invoking aryl-Au(III) species was initially proposed, the authors did not report supporting evidence for this proposal.[102]



Scheme 37. Au(III)-catalysed intermolecular reaction of aryl compounds to allenes

Similar results were obtained by Gagné and coworkers employing (4-$ClC_6H_4O)_3PAuCl/AgBF_4$ as the catalytic system.[103] The *E*-allylated product was obtained in moderate to good yields when electron-rich methoxy-substituted arenes were used as nucleophiles and unhindered monosubstituted allenes and 1,1-dimethylallene were employed as substrates. However, heterocyclic systems (pyrrole, indole and furan) did not give rise to the desired products.[77, 103]

After the attempts of the groups of Li[102] and Gagné[104] to catalyse addition of heterocycles to allenes, Widenhoefer and coworkers[105] used NH- and N-Me-indoles **116** (Scheme **38**) as nucleophiles for the addition to NHC-Au-activated allenes, such as **115,** to obtain *E*-allyl product **117**. Outer-sphere attack to the Au(I)-π-allene complex from the C(3) position of the indole *via* an iminium ion was proposed.



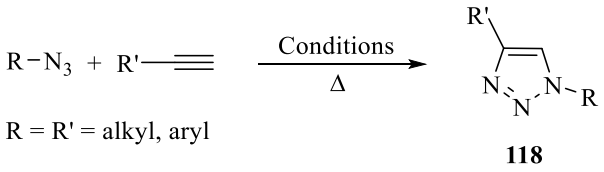
115 **116** **117**

Scheme 38. Synthesis of allyl *N*-Me-indoles **117** catalysed by Au(I) using substituted allenes

The enantioselective version of the previous reaction[105] was developed by the group of Che.[106] In this work, the authors employed a binuclear Au(I)-phosphine complex using (*S*)-(–)-MeO-BIPHEP (BIPHEP = biphenylphosphine) ligand. DFT calculations suggested Au^I-Au^I interactions, where one of the metal centres binds to the indole and the other one to the allene simultaneously, both being essential to improve the enantioselectivity of the reaction.

2.6. Allyl azides

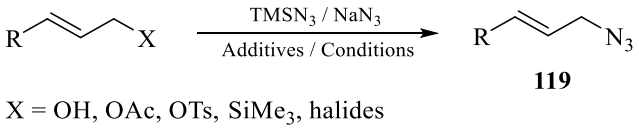
Organic azides were discovered in 1894 by Peter Griess,[107] however, the versatility of these functional groups was widely expanded in the 1950s and 1960s with the uses of aryl, alkyl and acyl azides in industry,[108] or in pharmaceuticals, with special attention in the treatment of HIV.[109] A remarkable example for the use of azides in organic synthesis is the 1,3-dipolar azide-alkyne (Scheme **39**) cycloaddition developed by Huisgen[110] as a powerful tool in the synthesis of triazoles **118** with high stereoselectivity and in mild conditions or a copper-catalysed version of this reaction reported by Sharpless,[111] and also microwave assisted to reduce the time.[110b, 112]



Scheme 39. General synthesis of triazoles *via* 1,3-dipolar addition

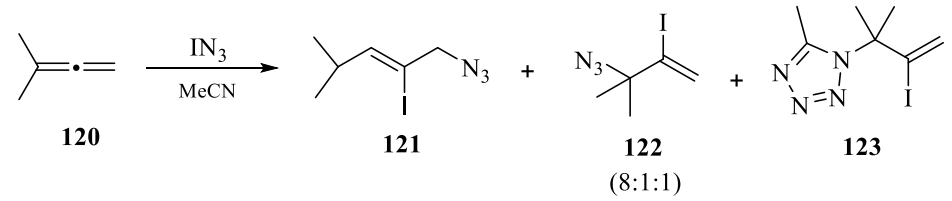
In this thesis azides have been employed as nucleophiles to generate allylic azides in the reaction with the activated allenes. NaN_3 or $TMSN_3$ are the most common and easily manageable nucleophilic azide sources, in addition to organoaluminium[113] or trialkyl tin azides[114] generally preformed *in situ*. Formation of extremely toxic and explosive HN_3 from NaN_3 and $TMSN_3$ is commonly observed due to small traces of protic components, a process difficult to avoid in the reaction media. Although the true nucleophile in our reaction, this hazardous acid is considered explosive due to its violent decomposition forming nitrogen and hydrogen, in addition it produces stable complexes with haemoglobin, blocking the oxygen transport (same effects with CN groups) or lowered blood pressure,[115] so special precautions that were undertaken for the generation and use of this reagent will be described in the results and discussion section.

Allylic azides, the desired products in our reactions, are common building blocks for the synthesis of natural products or nitrogen containing heterocycles or also to introduce complex functional groups into simple molecules. These allylic skeletons can undergo dimerizations *via* 1,3-dipolar additions[116] or give [3,3]-sigmatropic rearrangements.[117] Besides, they are useful precursors to many functional groups[109b, 109c] such as amines[118] and nitriles.[119] Allylic azides **119** (Scheme **40**) can be obtained by substitution reactions of allylic alcohols,[120] allylic esters,[118a, 121] allylic halides[116, 122] and allyl silanes[123] using as catalysts Ag, Mo(IV), Pd(0, II and IV) and triphosgene.



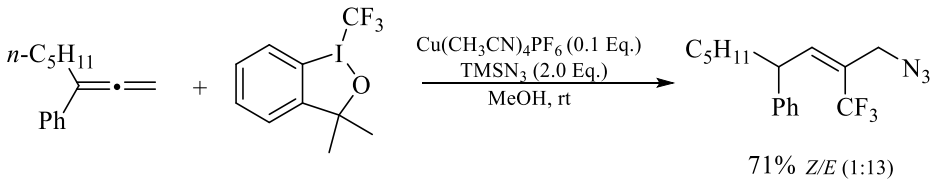
Scheme 40. Classic approach for the synthesis of allyl azides

The first reported example of synthesis of these allylic structures using allenes as substrates was the monoaddition of iodine azide to allene **120**.[117] **121** was obtained as major product, as well as **122** and the tetrazole **123**, which results from the attack of MeCN to the iodonium ion intermediate with the subsequent azide attack to the nitrilium species (Scheme **41**).



Scheme 41. Iodine azide addition to allenes

Recently, a copper(I)-catalysed trifluoromethyl-azidation of allenes (Scheme **42**) has been developed by Liu and coworkers.[124] This method shows good regio- (terminal sp^2-carbon) and stereoselectivity (*E*-isomer), with moderate to good yields, using $TMSN_3$ as azide source.



Scheme 42. Copper(I)-catalysed trifluoromethyl-azidation of allenes

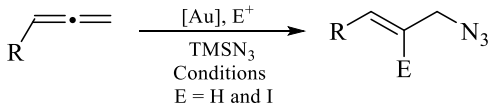
Cheng and coworkers[125] have reported an intermolecular carboazidation of allenes catalysed by palladium complexes with aryl iodides using $TMSN_3$ as azide source. The reaction works efficiently, however regio- and stereoselectivity was low, because of the rapid 1,3-shift of the azido group which was observed.

2.7. Aims and objectives

The aim of this work was to develop a new method for the synthesis of allyl azides. This was explored by employing allenes as substrates, catalysing the reaction by using gold complexes and using the more challenging azides as nucleophiles. Once the new methodology was developed, we aimed to add to the synthesis the possibility of an orthogonal functionalisation of the allenes, *via* vinyl gold intermediate, whose Au-C bond is cleaved by using iodine as an electrophile. In a further step, this allyliodide will be functionalised using cross-coupling reactions, as well as 1,3-dipolar additions.

2.8. Results and discussion

In the following chapter I will describe a novel gold-catalysed intermolecular addition of azides to substituted allenes, developed in our group that adds to the pool of available reactions for the synthesis of these interesting allylic azides, with some extra benefits (Scheme **43**).[126]

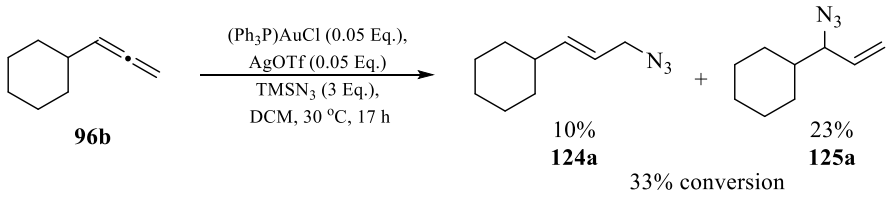


Scheme 43. General Scheme to the Au(I)-catalysed intermolecular addition of azides to allenes

This project started as a collaboration with Prof. Hashmi (University of Heidelberg) and one of his Master student (Stephanie Hoene), who carried out the preliminary screening of different parameters to get the best reaction conditions. In the next few pages, a summary of her work will be presented, showing the high sensitivity of this methodology to reaction conditions such as solvents, counterions, catalysts and additives.

2.8.1. Screening of conditions

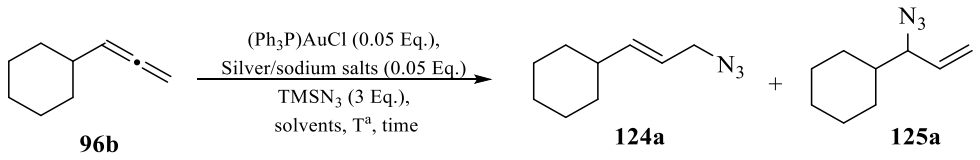
Preliminary results showed that $TMSN_3$ was the best azide source,[127] due to the low solubility of NaN_3 in organic solvents. The combination of Ph_3PAuCl/AgOTf to generate the cationic Au(I)-complex was chosen. Commercially available cyclohexylallene **96b** was employed as the standard substrate for the screening at different temperatures (Scheme **44**). Solvents tested with the previous conditions, included THF, MeCN, toluene and DCM. The reaction worked in THF, toluene and DCM, however the affinity of gold catalysts for chlorinated solvents was confirmed with the best results achieved with DCM. In addition, the reaction was also tested at different temperatures, with no further improvement.



Scheme 44. Best conditions and yields achieved after the screening of silver salts, solvents, azide sources and also different temperatures. Conversion was obtained by integration of a characteristic signal of each compound in the ^1H NMR spectra of the crude of reaction in relation to the starting material observed at the end of the reaction

The "soft" Lewis acidity of cationic Au(I)-complexes is widely employed in electrophilic activations of unsaturated moieties such as alkynes, alkenes and allenes. Thus, the need of halide abstractors and the concomitant formation of counterions in many cases is important for the catalytic activity of the Au(I)-complexes with unsaturated moieties. There are many reports focused on this topic, which highlight the importance of gold-counterion interactions in the catalytic process.[128] Depending on the size and electronic properties, counterions can be placed on the metal coordination sphere providing stronger or weaker interactions to the metal centre modulating the catalytic activity. Different silver and sodium salts were tested in the reaction as halide abstractors to preform the gold cationic complex

$[Ph_3PAu]^+X^-$, in order to enhance the catalytic activity of the Au(I)-complex (see Scheme **45** and Table **2**). NaBArF and $AgNTf_2$ (Entries **1** and **2**) in presence of the standard Au(I)-catalyst showed no conversion to the desired products. In contrast, moderate activity was observed when SbF_6^- or OTf^- were used as counterions were used (Entries **3** and **4**), giving slight conversion to the desired *E*-allyl azide **124a** as well as the *anti*-Markovnikov allyl azide **125a** (Table **2**). The best results were obtained using AgOTf as the halide abstractor (Entry **4**), which is reported to have strong interactions with the metal centre due to its small size.



Scheme 45. Screening of different silver and sodium salts to preform cationic Au(I)-complexes

Entry	Salts	Solvent	T (°C)	T (h)	Conversion % (Ratio, **124a**:**125a**)[a]
1	NaBArF	toluene	80	18	0
2	$AgNTf_2$	toluene	80	18	0
3	$AgSbF_6$	DCM	30	20	20 (1.2:1)
4	AgOTf	DCM	45	17	33 (1:2.3)

[a] Conversion was obtained by integration of a characteristic signal of each compound in the ^{1}H NMR spectra of the crude of reaction in relation to the starting material observed at the end of the reaction.

Table 2. Screening of different halide abstractors as source of the counterions

Phosphine-Au(I) complexes and NHC-Au(I) complexes generally show similar reactivities. In some cases complexes with these two ligands show different catalytic activity. NHC-ligands are strong σ-donors, but also π-donation to the metal centre L−M ($\pi \rightarrow d$) is given, as well as M−L ($d \rightarrow \pi^*$) backdonation. Phosphine ligands are also σ-donors with the contribution of 2 electrons to the metal centre, however, this ability can be modulated depending on the nature of their substituents. They can also accept electron-density from the metal, but, due to the lack of π^* orbitals in the ligand, the M−L backdonation is from d M$\rightarrow \sigma^*$ L.[83f, 129] In addition to the standard $(Ph_3P)AuCl$, several ligands were also tested in our azidation reaction to tune the activity of the catalyst. *N*-heterocyclic carbenes (NHC), nitrogen acyclic carbenes (NAC) and triphenylphosphite ligands (Figure **13**) were employed. The results revealed that the strong σ-donation of the NHC-Au(I)-complexes is not favourable, giving scarce conversions to the desired allyl azides. In contrast, phosphine and phosphite ligands displayed generally good reactivities and selectivities towards the desired allyl azides under the reaction conditions. Phosphite ligands display a weak σ-coordination with the metal

centre and higher π-acceptor character, and in our reaction they gave higher selectivities and better yields towards the allyl azides.[130]

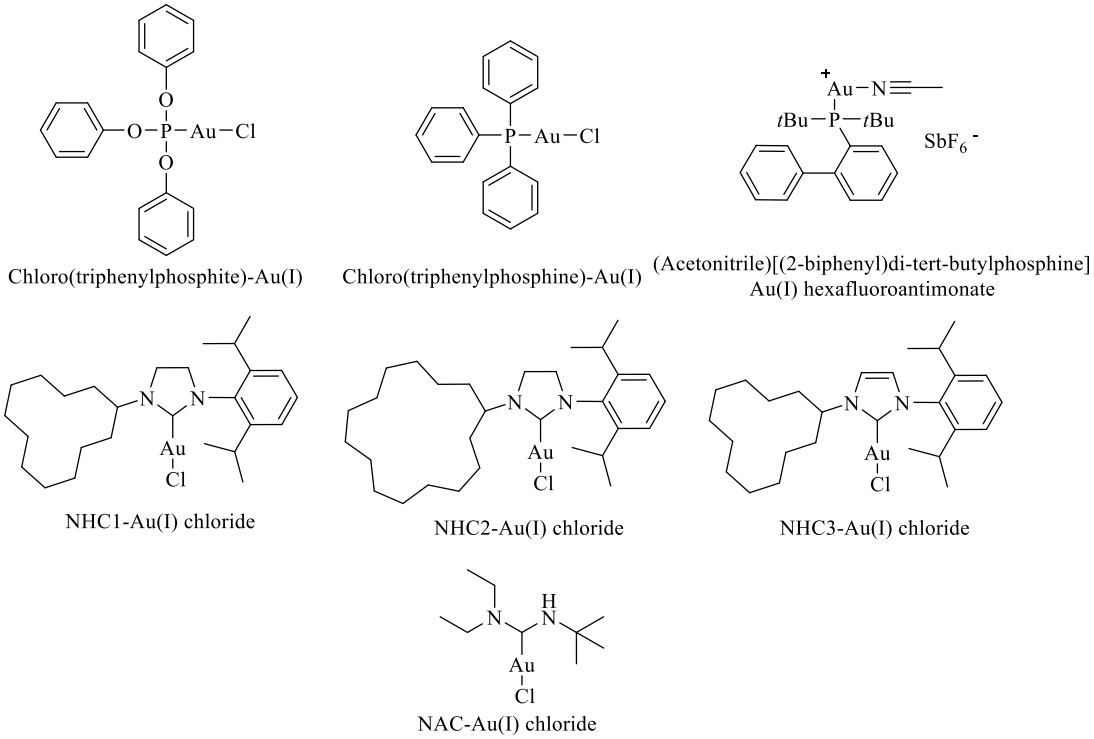
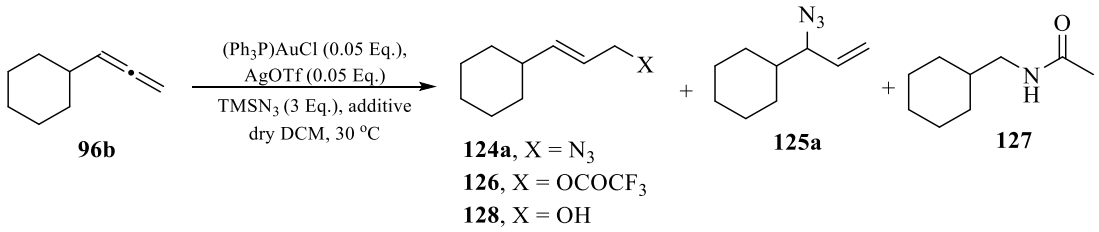


Figure 13. Au(I)-complexes screened in the intermolecular addition of azides to allenes. NHC1-, NHC2-, NHC3- and NAC-Au(I) chloride were synthesised by Hashmi's group and sent by them

In general, strong electrophiles, such as proton sources or electrophilic halogens, are required to break the Au-C bond of the vinyl gold intermediate proposed in the final step of the mechanism of these reactions.[131] However, in this work and in contrast to the previous intermolecular additions of alcohols or amines as nucleophiles to allenes (see introduction of the present chapter), $TMSN_3$ does not have any proton source. Therefore an additional proton is essential for the protonolysis step, to close the catalytic cycle with the concomitant regeneration of the Au(I)-complex.[132] The formation *in situ*[114a, 133] of the HN_3 with $TMSN_3$ and TFA gave the best conversions in the reaction with the phosphine-Au(I) complex (other acids did not work well, see Table **3**), obtaining the allyl azides **124a** and **125a** and also the product from the addition of CF_3COO^- to the activated terminal allene moiety (**126**, Scheme **46**) and the unexpected acetamide **127**, which will be further mentioned later in this chapter (Scheme **46**).[131c, 134]



Scheme 46. Acid screening to generate *in situ* the hydrazoic acid and its subsequent addition to the allene moiety

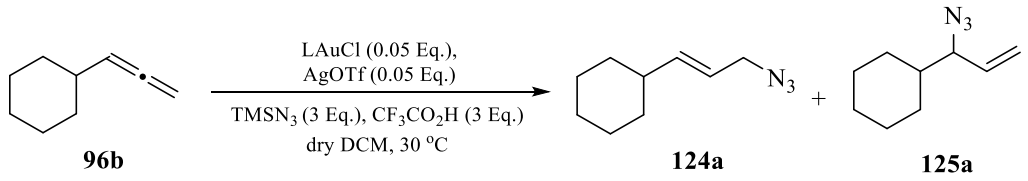
Entry	Acid (Eq.)	T (ºC)	t (h)	Conversion %, (Ratio, **124a**:**125a**:**126**:**127**:**128**)[a]
1	-	45	17	33, (1:2.3:0:0:0)
2	AcOH (1.5)	30	19	7, **124a**
3	H_2O (3.0)	30	25	23, (1.9:0:0:0:1)
4	H_2SO_4 (3.0)	30	18	-
5[b]	H_2SO_4 (3.0) / H_2O (5.0)	30	18	38, (1.7:1:0:1.2)
6	CF_3COOH (3.0)	30	18	100, (5:1:4:4:0)
7	CF_3SO_3H (3.0)	30	18	decomposition

[a] Conversion was obtained by integration of a characteristic signal of each compound in the ^1H NMR spectra of the crude of reaction in relation to the starting material observed at the end of the reaction. **[b]** Reaction carried out with $(PhO)_3PAuCl$ as catalysts.

Table 3. Screening of acids to generate *in situ* the HN_3 and its subsequent addition as nucleophile to activated allenes

HN_3 is classified as a very dangerous compound due to its high toxicity and its explosive character at higher concentrations.[115, 135] In order to minimise the risk to handle this compound, a few modifications on the reaction were performed, such as temperatures lower than 35 ºC and diluted solutions of this strong acid (< 20 % weight).[136]

With the new conditions in hand, a new catalyst screening was performed, using again the complexes shown in Figure **13**. However, no significant changes were observed with NHC-Au complexes that gave low conversion and selectivity towards the trifluoroacetate adduct **126**. Full conversion was obtained with $(Ph_3P)AuCl$ and $(PhO)_3PAuCl$, achieving higher isolated yields using $(Ph_3P)AuCl$/AgOTf (Table **4**) as a catalytic source



96b **124a** **125a**

Scheme 47. Catalyst screening with the new conditions

Entry	LAuCl	t (h)	Conversion (%)	Isolated yield %, (Ratio, **124a**:**125a**)
1[a]	L = (Ph_3P)	2.5	100	33, (1:1)
2[a]	L = $(PhO)_3P$	22	100	50, (1:1)

[a] Isolated yields were obtained by column chromatography in silica gel

Table 4. Screening of catalysts under the best reaction conditions

These final conditions were employed by my colleague with several mono- and disubstituted allenes achieving low to moderate yields as well as good selectivities of *E*-allyl azide **124a** and **125a**.

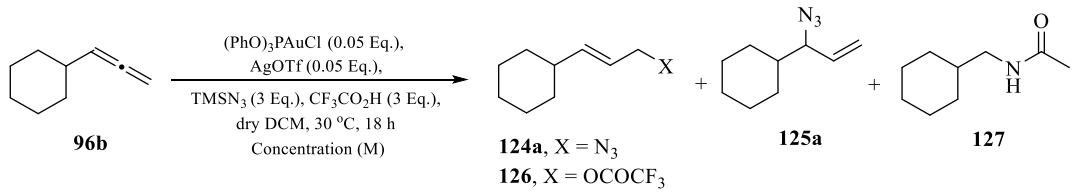
My contribution to the project started by expanding the scope of the reaction with different substituted substrates using the best reaction conditions achieved by my colleague. However, we encountered some reproducibility issues, with different conversions, isolated yields and selectivities. In order to address these issues and get a more robust and reproducible procedure for this reaction, I started a new screening of reaction conditions, taking into account the order in which the different components were added to the reactions, as well as different purification techniques.

In the previous screening, $(PhO)_3PAuCl$, AgOTf and the allenic substrate were sequentially added and dissolved in dry DCM in a Schlenk tube under inert atmosphere to preform the Au(I)-π-allene intermediate. To generate the hydrazoic acid *in situ*, $TMSN_3$ and TFA were dissolved in dry DCM at 0ºC in a second Schlenk tube under inert atmosphere. Then, the catalyst solution was taken out with a syringe under argon and added at 0ºC to the hydrazoic acid solution. Then, the reaction was heated at 30ºC until complete conversion.

Hydrazoic acid is a highly volatile acid and should be handled at lower temperatures. In order to minimise the loss of product during the addition process of the Au(I)-π-allene solution to the second Schlenk, a new experimental procedure was devised. In this case, in a dried and flushed with N_2 Schlenk tube, cationic Au(I)-complex was preformed in dry DCM at 0ºC and this temperature was kept during the addition of the rest of the components to avoid loss of the volatile acid. The allene, $TMSN_3$ and TFA were added sequentially under N_2 at 0ºC

and stirred for 2 minutes. The mixture was then warmed up to room temperature or heated at 30ºC until complete conversion.

This new procedure prevents the loss of product during the addition to the second Schlenk flask and ensures the accuracy of the final concentration, which also proved to be an important factor in the reaction. To test this, three reactions at different concentrations of substrate were performed (see Table **5**). The best results were achieved using 0.41 M as the new concentration of allene in dry DCM with improved selectivity to the allyl azide **124a** and **125a**, minimising the formation of product **126** but with the formation of the amide **127** (Table **5**, Entry **3**).



Scheme 48. Best reaction conditions employing different concentrations

Entry	Concentration (M)	Ratio (**124a**:**125a**)[a]	Ratio **126**[a]	Ratio **127**[a]
1[b]	0.11	3.3:1	0.9	-
2[b]	0.27	2.1:1	0.6	1.04
3[c]	0.41	3.9:1	0.6	2.4

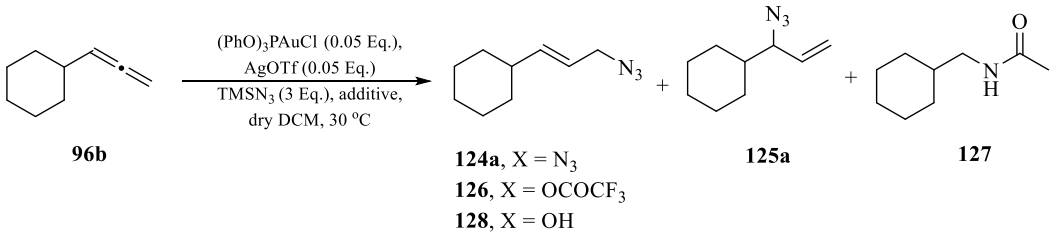
[a] Ratios were obtained by integration of a characteristic signal of each compound in the ^{1}H NMR spectra of the crude of reaction in relation to the starting material observed at the end of the reaction. **[b]** After 22 h, conversion ≈ 25%. **[c]** Full conversion after 18 h.

Table 5. Screening of the best reaction conditions using different concentrations

AgOTf is one of the best gold partners to generate cationic Au(I)-complexes by acting as a halide abstractor and counterion or just by itself as an effective catalyst.[128a, 137] It is known that silver salts are highly hygroscopic and it is recommended to handle them under anhydrous conditions.[138] Up to this point, all the reactions had been carried out with the same AgOTf batch, weighed in the open air and were slightly moist from being stored in a desiccator for a long time. Thus, a brand new batch was purchased. Surprisingly, the first reaction carried out with this new and anhydrous AgOTf batch with the conditions shown in Entry **1** (Table **6**) did not reach complete conversion (≈ 50%) after 48 h, so this result suggested that the traces of H_2O present in the old AgOTf batch could have an essential role in the reaction. Results in Table **3**, show that a proton source is needed to carry out the protonolysis of the vinyl gold intermediate. However, it is important to note that the reaction shown in Entry **1** (Table **3**),

without a proton source, only with $TMSN_3$ at 45 ºC, gave 33% conversion. This result implies that traces of water were present in the reaction media, probably from the moist AgOTf batch.

It is known, that the hydrazoic acid can be generated with different proton sources such as MeOH[139] and acids.[115, 140] Also reported is the synthesis of hydrazoic acid *in situ* with water as proton source or in a mixture with AcOH.[114a, 133, 136] However, observing our previous results, water does not seem to be a strong enough acid to give the full protonolysis of the key intermediate in our reaction.[115, 141] A few experiments were performed in order to understand the role of water in the reaction (Table **6**). Entries **1** and **2** show the differences between the moist AgOTf batch and the new one, observing that approximately 50% of the allene did not react even after longer times. Water was confirmed as a suitable proton source in combination with TFA, achieving full conversion with the phosphite-Au(I) catalysts after 22 h (Entry **6** to **8** and **11**). By increasing the amount of water used in the reaction, the selectivity towards the desired allyl azides improved, but also resulted in significant amounts of allyl alcohol **128** being observed (Entries **8** and **11**). We also tested other proton sources as additives (see entries **10**, **12**, **13** and **14**). Entries **11** to **14** (Table **6**) show that the majority of the proton sources worked efficiently. AcOH, $NH_4OH_{(ac)}$ 5.0 N and MeOH (Entries **12**, **13** and **14**) gave lower selectivity to the allyl azide **124a** and **125a** than with H_2O (Entry **11**). Therefore, we chose as our best conditions, the combination of $TMSN_3$ (3 Eq.), TFA (3 Eq.) and H_2O (5 Eq.) at room temperature (Entry **11**).



96b

124a, X = N_3
126, X = $OCOCF_3$
128, X = OH

125a

127

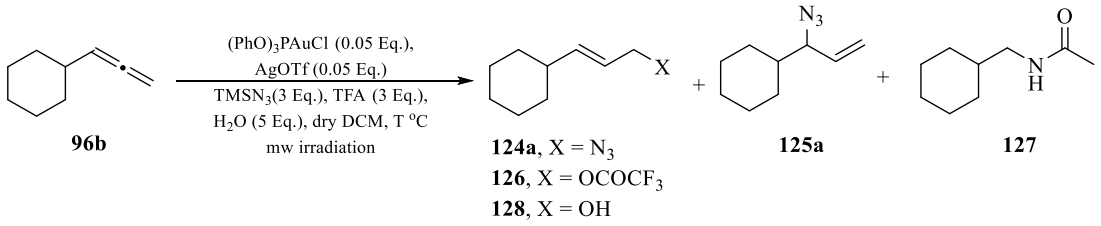
Scheme 49. Reaction performed with different amounts and mixtures of acids and proton sources

Entry	Additive (Eq.)	t (h)	Conversion % (Ratio, **124a**:**125a**:**126**:**127**:**128**)[a]
1	TFA (3)	48	50, (2.1:1:0:0:0)
2[b]	TFA (3)	22	100, (9.4:2.4:1:5.7:0)
3	H_2O (3)	22	73, (9.7:2.8:0:1:2.8)
4[c]	H_2O (3)	23	23, (3:1:0:0:1.6)
5[c]	H_2O (3)/TFA (3)	22	40, (5.2:1:2.4:3.2:0)
6	H_2O (3)/TFA (3)	23	100, (10.7:3.2:1:7:0)
7	H_2O (5)/ TFA (3)	22	100, (13.7:4.4:1:8.4:0)
8	H_2O (7)/ TFA (3)	22	100, (24.4:6.4:2.2:12.2:1)
9	H_2SO_4 (3)	23	Decomposition
10	H_2SO_4 (3)/H_2O (5)	24	10, **124a**
11[d]	H_2O (5)/TFA (3)	22	100, (22.8:5.6:1:12:1.2)
12[d]	AcOH (5)/TFA (3)	24	100, (18.2:4.8:1:9:0)
13[d]	$NH_4OH_{(aq)}$ 5 N /TFA (3)	22	100, (21.4:5:1.8:11.5:1)
14[d]	MeOH (5)/TFA (3)	22	96, (16.5:4.2:1:5.7:0)

[a] Conversion was obtained by integration of a characteristic signal of each compound in the ^1H NMR spectra of the crude of reaction in relation to the starting material observed at the end of the reaction. **[b]** This reaction was performed using the old batch of AgOTf. **[c]** This reaction was performed using as catalyst Ph_3PAuCl (0.05 Eq.). **[d]** Reaction performed at room temperature.

Table 6. Screening of the best reaction conditions with or without additives (proton sources).

With these optimum conditions in hand, a few reactions (Table **7**) were set up under microwave irradiation,[142] in order to accelerate efficiently the synthesis of allyl azides **124a** and **125a** and trying to reduce the reaction times. Unfortunately, despite the dramatic reduction of reaction time and the complete conversion of the starting material, microwave heating seems to favour the addition of $CF_3CO_2^-$ and HO^- to the allene, decreasing the desired allyl azides **124a** and **125a**, and therefore we decided to abandon this approach.



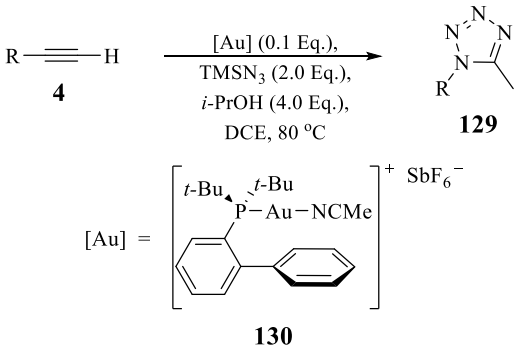
Scheme 50. Au(I)-catalysed addition of azides to allenes under microwave irradiation

Entry	t (h)	T (º C)	Conversion (%), (Ratio, **124a**:**125a**:**126**:**127**:**128**)[a]
1	5	70	100, (4.4:1.1:1.7:4.7:1)
2	4	40	100, (11:3:1:6.5:1.1)
3	3	40	100, (16.3:4:1.5:8:1)

[a] Conversions and ratios were measured by ^{1}H NMR

Table 7. Results obtained with the best reaction conditions under microwave irradiation

The effect of the additives, solvents, and nucleophiles in the reaction could be understood if we take into account their competition in solution to stabilise the cationic Au(I)-complex as ligands or counterions.[130a] Echavarren and coworkers reported the synthesis of tetrazoles **129** (Scheme **51**) from alkynes *via* C-C bond cleavage employing similar reaction conditions to the ones reported in this study.[143] In their work, cationic JohnPhos/Au(I)-catalyst **130** were employed, and a further addition of a proton source (*i*-PrOH or AcOH) was used to improve the yield of tetrazole **129**. They proposed that under Au(I)-catalysed conditions, the Brønsted acid [JohnPhosAu(*i*-PrOH)]SbF_6 is formed, which triggered the transformation to the tetrazole.

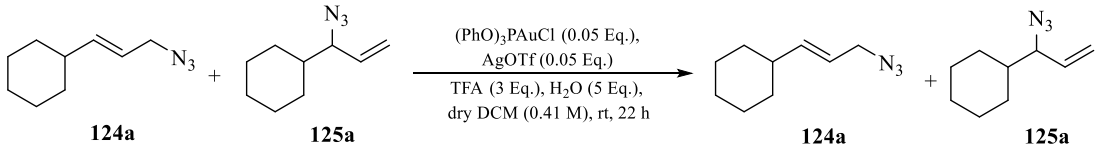


Scheme 51. Synthesis of tetrazoles *via* Au(I)-catalysed reaction of alkynes

The results obtained by the group of Echavarren, support the idea of the competition of ligands and counterions to stabilise the cationic Au(I)-complex, with the alcohol coordinated to the metal-centre generating the Brønsted acid-catalyst. In our case, the role of water could be similar and the Brønsted acid-catalyst [$(PhO)_3PAu(H_2O)$]OTf could actually

be the catalytically active species in our reaction conditions. There are examples reported by the groups of Nolan[144] or Bochmann[145] isolating and employing gold-hydroxide complexes (Au-OH) which support the possible formation of the $[(PhO)_3PAu(H_2O)]OTf$ as our active catalyst species.

At this point it is worth noting the problems encountered with isolated yields in the reaction. The products obtained in our model reaction have very similar polarities, and their purification by column chromatography was a challenge. In addition the ratios obtained from NMR crudes before purification did not correspond with the isolated yields of the products achieved. Thus, an experiment was performed to investigate the decomposition of the allyl azides **124a** and **125a** under the reaction conditions and during purification.



Scheme 52. Reaction performed to investigate the decomposition of allyl azides **124a** and **125a** under the reaction conditions

An inseparable mixture of the isolated allyl azides **124a** and **125a** (4.8:1, Entry **1**, Table **8**) was exposed to the best reaction conditions without any azide source. After 22 h, the solution was filtered through celite, washed with DCM and concentrated. Then, the crude of the reaction was weighed, a ^{1}H NMR of the reaction crude was obtained (Entry **2**, Table **8**) and the ratios compared with the ratio of the starting mixture. It is observed, that there is a slight variation in the ratios before and after the reaction. The crude was then purified by flash column chromatography over silica gel using Hex/EtOAc (7:1). After concentration of the sample, only half of product was isolated confirming the loss of product during the purification process (Entry **3**, Table **8**). Once again, the ^{1}H NMR of allyl azides revealed a small variation in the ratios of the isolated allyl azides **124a** and **125a** (Entry **3**).

Entry	Weight (mg)	Ratios allyl azides **124a**:**125a**[a]
1 (Before reaction)	20.0	(4.8:1)
2 (After 22 h reaction, before purification)	21.1	(4.2:1)
3 (Isolated azides **124a** and **125a**)	11.0	(3.6:1)

[a] Ratios were obtained by integration of the signals of each allyl azide in the ^{1}H NMR spectra of the crude of reaction.

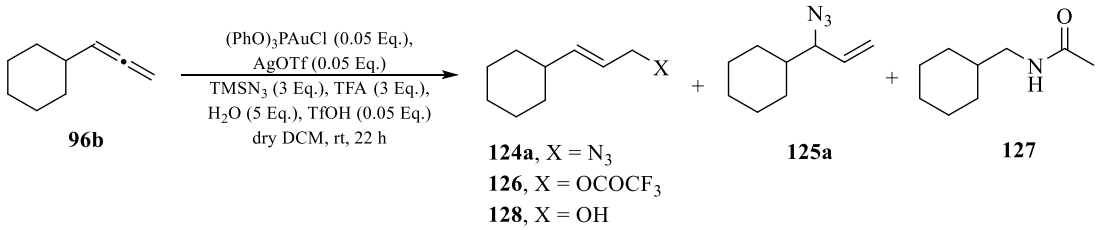
Table 8. Results obtained in the experiment performed to confirm the decomposition of the allyl azides **124a** and **125a** under the reaction conditions and during purification.

These results could suggest that allyl azides **124a** and **125a** interact with the slightly acidic silica gel during the purification step, favouring their decomposition. The hydroazidation reaction was performed using the model allene **96b** under the same reaction conditions as before and the products were purified using basic alumina as the stationary phase (Entry **2**, Table **9**). As shown in Table **9**, five different products could be identified in the ^{1}H NMR crude, however after purification only our target allyl azides **124a** and **125a** as well as the interesting acetamide **127** were efficiently isolated, in 19% higher yield than with silica gel. It might be possible that the ester is hydrolysed to the alcohol and this polar allyl alcohol is held in the stationary phase favouring the isolation of the desired products.

Entry	Stationary phase	Ratio, **124a**:**125a**:**126**:**127**:**128** before purification	Isolated yield %, ratios
1	Silica gel	(18:4.7:1.3:13:1)	40, **124a:125a:126** (29:8:1); 15, **127**
2	Basic alumina	(20:5.2:1:12:1)	59, **124a:125a** (3.7:1); 15, **127**

Table 9. Results obtained before and after purification by column chromatography using different stationary phases

To conclude the screening of the optimum reaction conditions, the control experiments were performed (Table **10**).



Scheme 53. Control experiments

Entry	$(PhO)_3PAuCl$	AgOTf	$TMSN_3$	TFA	H_2O	TfOH	Conversion %, (Ratio)[a]
1	-					-	0
2	-	-				-	0
3	-	-	-			-	0
4				-		-	73 **124a**:**125a**:**127**:**128** (10:2.8:1:2.8)
5[b]					-	-	50 **124a**:**125a** (2.1:1)
6		-					0
7	-	-					0

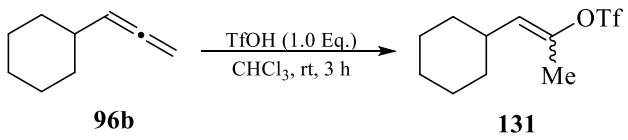
[a] Conversion was obtained by integration of a characteristic signal of each compound in the ^1H NMR spectra of the crude of reaction in relation to the starting material observed at the end of the reaction. **[b]** The reaction time was 48 h.

Table 10. Results obtained during the control experiments

Table **10** revealed that silver triflate is not the active catalyst in the hydroazidation reaction (Entry **1**). However, the role of the AgOTf as halide abstractor is essential to generate the catalytically active species in this reaction $(PhO)_3PAuOTf$ (Entries **4** and **5**). In the absence of silver, $(PhO)_3PAuCl$ does not behave as a suitable catalyst to activate the allene to the subsequent nucleophilic attack (Entry **6**). As previously stated, reactions using either TFA or H_2O only in the presence of the phosphite-Au complex gave 73% and 50% conversion respectively (Entries **4** and **5**), supporting the need of the combination of TFA/H_2O for full conversion.

On the other hand, combination of AgOTf with H_2O can generate the Brønsted acid TfOH. Also, acid-catalysed reactions by Brønsted acids to allenes are known.[146] In order to confirm that our nucleophilic addition to allenes is catalysed by Au(I)-complexes and not by Brønsted acids, two reactions were set up. A catalytic amount of triflic acid and $(PhO)_3PAuCl$ were added in the absence of AgOTf, giving no conversion (Entry **6**). Then, in the absence of gold and silver, a catalytic amount of TfOH (0.05 Eq.) was added as Brønsted acid-catalyst, and again, starting material was only recovered (Entry **7**). In addition, our group have

performed studies on the reactivity of allenes in the presence of stoichiometric amounts of TfOH that give rise to vinyl triflates **131** (Scheme **54**). These compounds were not identified in the crude of the hydroazidation reaction.[147]



Scheme 54. Formation of vinyl triflates employing Brønsted acids

2.8.2. Synthesis of allenes

Due to their high demand as precursors in organic chemistry, several allenes are commercially available and could be purchased from chemical companies such as Sigma Aldrich or Alfa Aesar to be employed neat in the hydroazidation reaction (See Figure **14**).

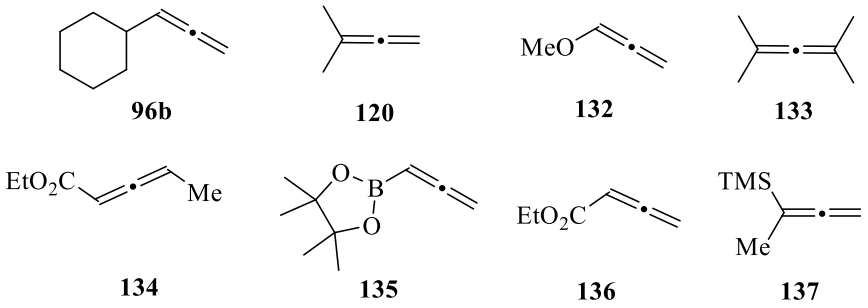
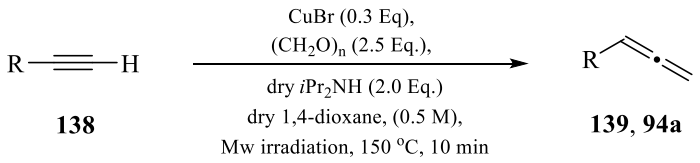


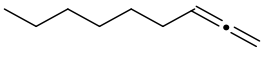
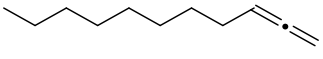
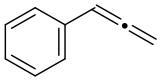
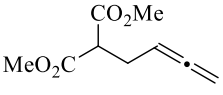
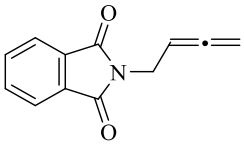
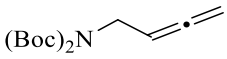
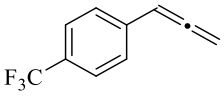
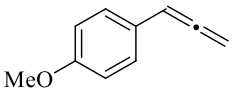
Figure 14. Commercially available allenic precursors employed in the gold-catalysed hydroazidation reaction

On the other hand, the majority of monosubstituted allenic precursors synthesised in the laboratory were generated *via* microwave assisted Crabbé homologation of the commercially available alkynes **138** (See Table **11** and Scheme **1** and **2** for the mechanism).[27b, 39a]



138 **139**, **94a**

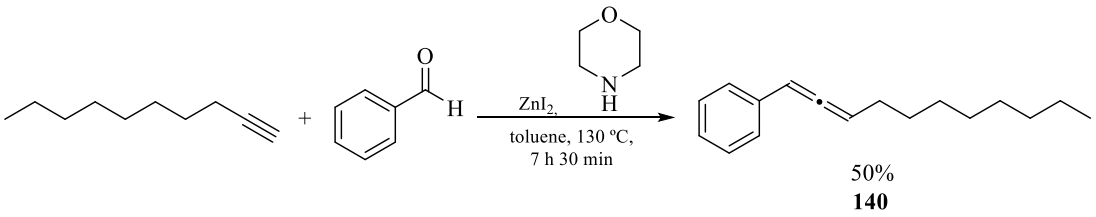
Scheme 55. Synthesis of allenes *via* microwave assisted Crabbé homologation

Entry	Allene **139x**, **94a**	Isolated Yields %
1	 **139a**	49
2	 **139b**[a]	45
3	 **94a**	46
4	 **139c**	53
5	 **139d**	89
6	 **139e**[b]	48
7	 **139f**	35
8	 **139g**	44

[a] This compound was synthesised by Stephanie Hohne using different concentration (0.3 M). **[b]** This compound was synthesised by Stephanie Hohne.

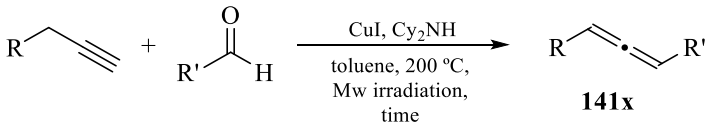
Table 11. Allenes synthesised *via* microwave assisted Crabbé homologation.

The majority of 1,3-disubstituted substrates were obtained by modified Crabbé homologations optimised for each substrate. 1,3-Disubstituted allene **140** (Scheme **56**) was obtained by a modified Crabbé homologation of the corresponding alkyne with zinc iodide. The iminium ion was preformed *in situ* in a Mannich type reaction from benzaldehyde and morpholine giving access to allene **140** in moderate yield.[28]



Scheme 56. Synthesis of 1,3-disubstituted allene **140** *via* modified Crabbé homologation of the corresponding alkyne

Alternatively, microwave heating was employed to synthesise 1,3-disubstituted allenes **141x** (Scheme **57**) *via* modified Crabbé homologation catalysed by CuI with alkyl aldehydes and Cy_2NH in toluene (See Table **12**).[30]



Scheme 57. Synthesis of 1,3-disubstituted allenes **141x** *via* microwave assisted Crabbé homologation

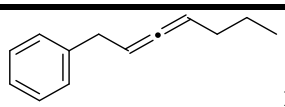
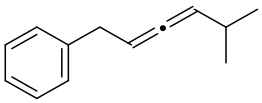
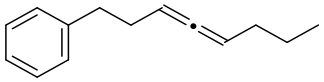
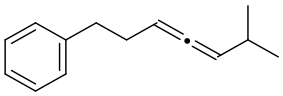
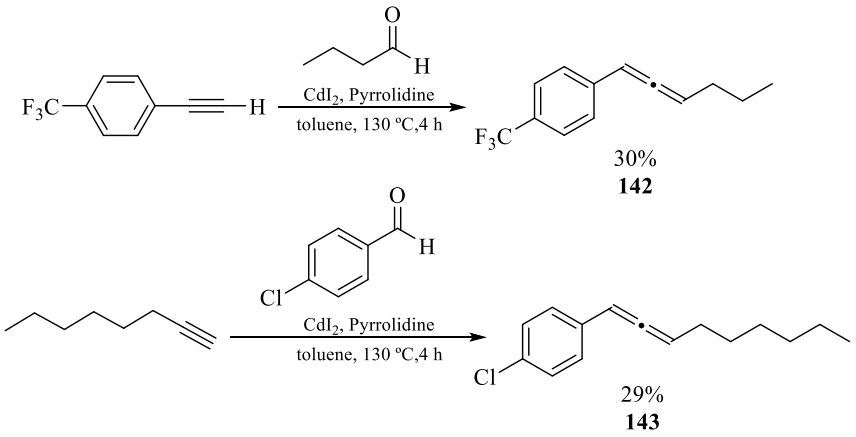
Entry	R	R'	Time	Allene **141x**	Isolated Yields (%)
1	Bn	*n*-Pr	3 h 30 min	 **141a**	39
2	Bn	*i*-Pr	4 h 30 min	 **141b**	28
3	$Ph(CH_2)_2$	*n*-Pr	3 h 30 min	 **141c**	63
4	$Ph(CH_2)_2$	*i*-Pr	3 h 30 min	 **141d**	77

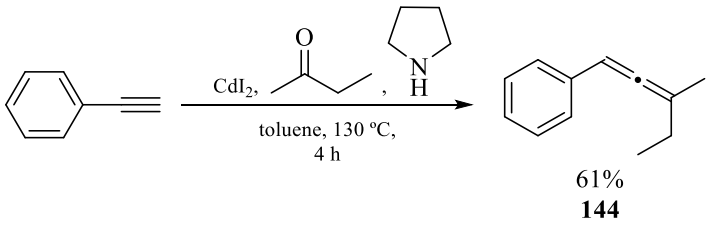
Table 12. Results obtained on the synthesis of 1,3-disubstituted allenes **141x** *via* microwave assisted Crabbé homologation

Following a similar methodology, 1,3-disubstituted allenes **142** and **143** were obtained in moderate yield by a modified cadmium(II)iodide allenylation of terminal alkynes with aldehydes using pyrrolidine as a base (Scheme **58**. See Scheme **4** for the mechanism).[29]



Scheme 58. Synthesis of 1,3-disubstituted allenes by a modified CdI_2 allenylation of terminal alkynes

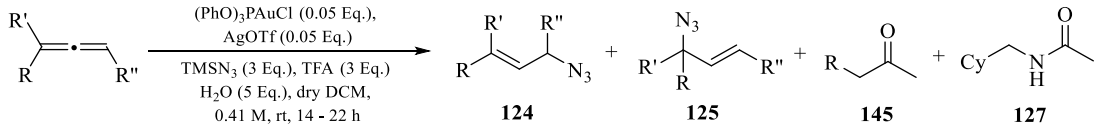
The same reaction conditions were also employed to synthesise 1,1,3-trisubstituted allene **144** with a ketone, instead of aldehydes, and a terminal alkyne (Scheme **59**. See Scheme **4** mechanism).[29]



Scheme 59. Synthesis of 1,1,3-trisubstituted allenes by a CdI_2 allenylation of terminal alkynes and ketones

2.8.3. Gold-catalysed intermolecular addition of azides to allenes

With the best reaction conditions in hand $(PhO)_3PAuCl/AgOTf$ as catalytic system, $TMSN_3$ as azide source, TFA and H_2O as additives in dry DCM, the scope of the gold-catalysed hydroazidation reaction with different allenes was explored. We observed that the reaction is quite general toward the formation of allyl azides **124** and **125** as major products, and in some cases we also isolated ketones **145** and amide **127** as side products in low yields.



Scheme 60. Reaction scope of the gold-catalysed hydroazidation of substituted allenes

Entry	Allene	R, R' and R''[e]	Isolated Yield %, **124**:**125** ratio	Isolated Yield %, Side products
1	**96b**	R = Cy	59, **124a**:**125a** (3.7:1)	15, **127**
2	**139a**	R = *n*-hexyl	48, **124b**:**125b** (1.9:1)	16, **145a**
3[a]	**139b**	R = *n*-octyl	47, **124c**:**125c** (1.8:1)	-
4	**94a**	R = Ph	62, **124d**	-
5	**139c**	R = $(MeO_2C)_2CHCH_2$	43, **124e**:**125e** (3.8:1)	17, **145b**
6	**139d**	R = phthalimide-*N*-CH_2	48, **124f**; 7, **125f**	32, **145c**
7[b]	**139e**	R = $(BOC)_2NCH_2$	38, **124g**	-
8[c]	**120**	R = R' = Me	**124h**:**125h** (3.7:1)	-
9	**140**	R = Ph, R'' = *n*-octyl	76, **124i**	-
10	**141a**	R = Bn, R'' = *n*-Pr	67, **124j**:**125j** (3.7:1)	-
11	**141b**	R = Bn, R'' = *i*-Pr	55, **124k**:**125k** (1.67:1)	-
12	**141c**	R = $Ph(CH_2)_2$, R'' = *n*-Pr	70, **124l**:**125l** (1:1.13)	-
13	**141d**	R = $Ph(CH_2)_2$, R'' = *i*-Pr	80, **124m**:**125m** (1:1)	-
14[d]	**139f**	R = *p*-CF_3Ph	74, **124n**	-
15[d]	**142**	R = *p*-CF_3Ph, R'' = *n*-Pr	67, **124o**	-
16	**143**	R = *p*-ClPh, R'' = *n*-octyl	72, **124p**	-

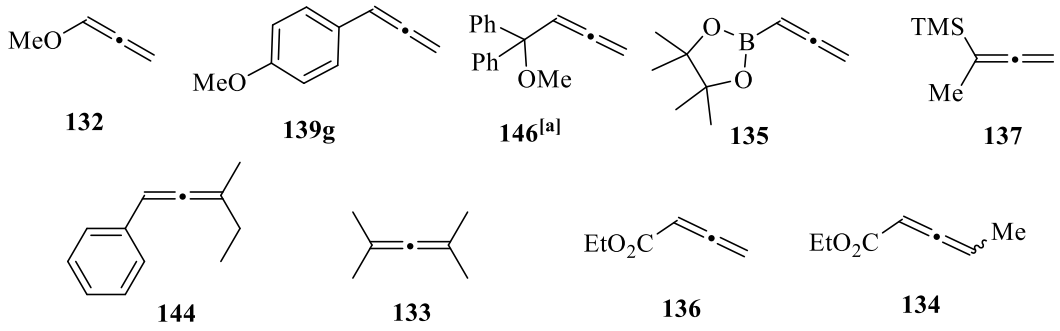
[a] Run without water (0.08 M). **[b]** Deprotection of one Boc-group was observed under the best reaction condition. **[c]** 100% conversion; products were not isolated due to volatility issues. **[d]** The reaction was carried out at 30 ºC during 60 h. **[e]** R', R'' = H, when not stated otherwise.

Table 13. Scope of reaction for the gold-catalysed hydroazidation reaction of substituted allenes

As shown in Table **13**, the reaction works efficiently for mono- and 1,3-disubstituted allenes with different functional groups in moderate to good yields. *E*-Allyl azides **124** from the attack to the less hindered carbon of the allene are generally obtained as the main or the only product. In previous works on gold-catalysed hydroamination reaction of substituted allenes, the control of the regioselectivity on the reaction was achieved when aromatic ring substituents were directly linked to the allene moiety.[93, 96, 100] Our reaction follows the same trend, with the azide attack only occurring to the sp^2-carbon opposite to the aromatic group on mono- and 1,3-disubstituted aryl allenes, giving only *E*-allyl azides **124d**, **124i**, **124n**, **124o** and **124p** (Entries **4**, **9**, **14**, **15** and **16**). However, if the aromatic group is not directly linked

to the allene, the attack of the azide can happen in both sp^2-carbons of the allene even with bulkier alkylated substituents such as *i*-propyl (Entries **10-13**). This suggests that the electronic effects prevail over the steric effects controlling the regioselectivity of the reaction.

Generally, as shown in Table **13**, the reaction works with a wide range of substituted allenes with different functionalities such as alkyl, aryl, nitrogen-protected or even malonate groups. However, substituted allenes with methoxy groups (**132**, **139g**, **146**, Figure **15**) or linked with substituents sensitive to acidic conditions (**135** and **137**), decomposed under the reaction conditions. In addition, tri-**144** and tetrasubstituted allene **133** were also tested giving complex mixtures with traces of the desired products as well as other side products that were very difficult to identify. Ethyl 2,3-butanodionate **136** and ethyl 2,3-pentanodienoate **134** showed very slow conversion to the desired allyl azides after 5 days of reaction.



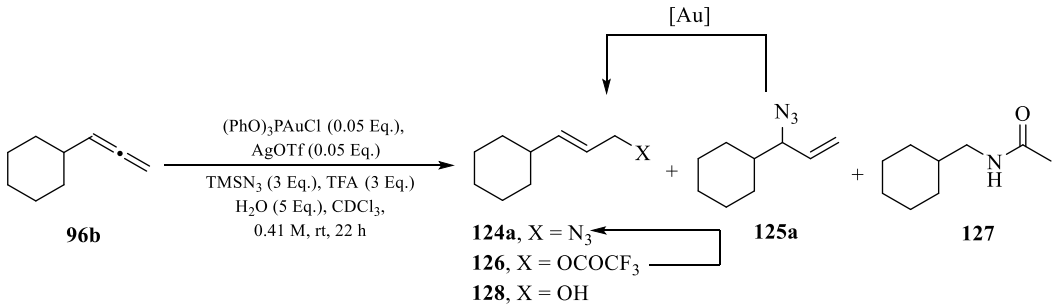
[a] This allene was available in the group.

Figure 15. Substituted allenes that did not work under the best reaction conditions

2.8.4. Isomerisation of allyl azides 124 and 125

Generally, allylic azides can equilibrate in solution, even at room temperature *via* [3,3]-sigmatropic rearrangement.[148] A previous experiment performed to investigate the possible decomposition of allyl azides under the best reaction conditions suggested that the allylic azides **124a** and **125a** could isomerise when catalysed by gold. However, these results were not conclusive (see Scheme **52**, Table **8**). Thus, a further experiment was performed in order to see the possible interconversion of the allylic products. To do so, the reaction of allene **96b** under the best conditions was monitored by ^{1}H NMR at room temperature in $CDCl_3$. Plotting the conversion *versus* time over 12 h, it was observed that the concentration of allyl azide **125a** increases rapidly and then decreases during the first 3 hours, as the concentration of the thermodynamically more stable allyl azide **124a** increases (see Table **14** and Figure **16**, allyl azides **124a** and **125a** during the first 3 h). It was also observed that the concentration of the allylic product **126**, increases during the first hour and then decreases with time. Possibly the free azide could displace the trifluoroacetate in compound **126** to generate *E*-allyl azide

124a *via* S_N2-type reaction. The ratio of products was maintained after 12 hours with no major changes observed after 22 h.



Scheme 61. NMR experiment under the best reaction conditions

Time (h)	Conversion %					
	96b	**124a**	**125a**	**126**	**127**	**128**
0	100	0	0	0	0	0
1	24.2	20.2	30.9	9.26	15.4	0.00
3	0.00	53.4	17.1	4.10	24.9	0.51
5	0.00	57.4	14.2	3.27	24.9	0.14
7	0.00	56.7	13.5	4.04	25.7	0.13
9	0.00	54.8	13.1	4.13	27.1	1.38
11	0.00	54.3	12.5	4.24	27.2	1.41
22	0.00	57.0	12.8	4.73	23.1	1.62

Table 14. Results obtained monitoring the reaction by ^1H NMR. (See appendix for further information about the integral values)

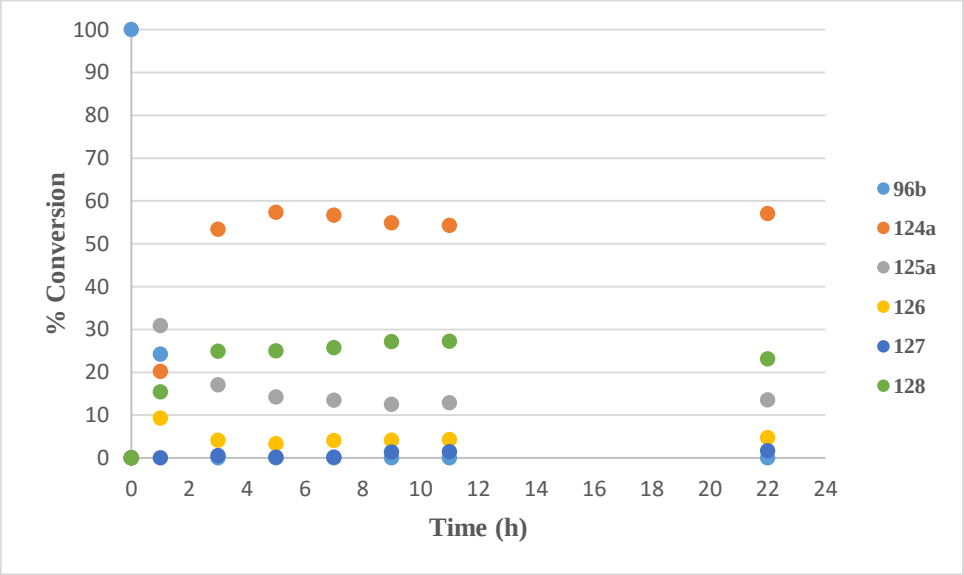
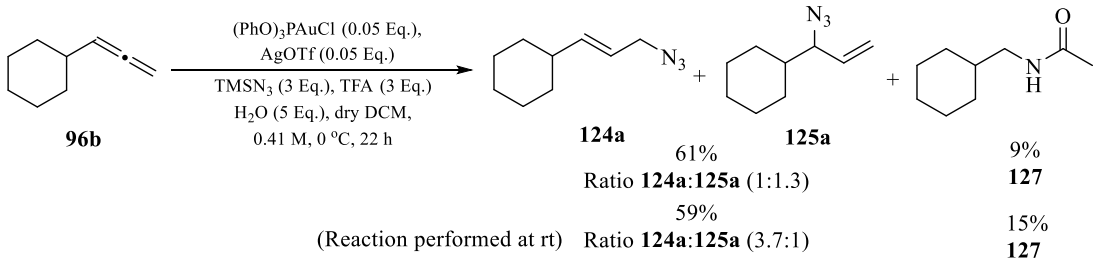


Figure 16. Catalytic NMR experiment

To analyse the effect of the temperature on the interconversion, a reaction was carried out at 0ºC for 22 h (Scheme **62**). The isolated yield of the inseparable mixture of the allyl azides was higher than previously reported at room temperature (see Table **13**, Entry **1**) and also the ratio of allyl azide **125a** was higher than the *E*-allyl azide **124a**. As it was discussed, there are examples on the hydroalkoxylation reaction of allenes where the kinetically favoured addition of nucleophiles happens to the most hindered carbon of the allene *via* an outer-sphere mechanism under an excess of alcohol. DFT analysis revealed, that the kinetically favoured product is able to isomerise to the thermodynamically more stable allyl ether catalysed by gold-complexes (see Scheme **30**).[89b, 90] Similarly in our case, we could suggest that in the presence of cationic phosphite-Au(I)-complexes, the kinetically favoured allyl azide product **125a** interconverts to give the thermodynamically more stable *E*-allyl azide **124a**.



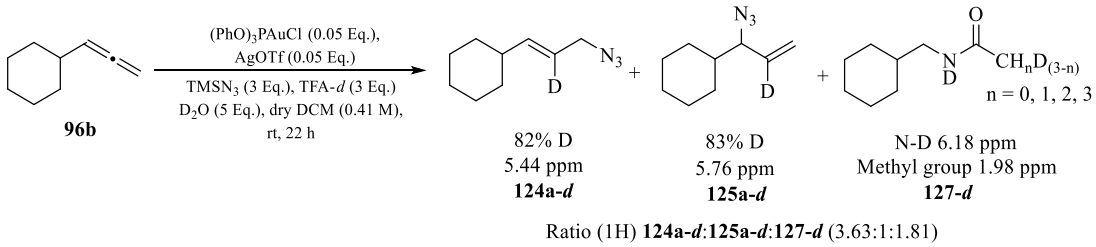
Scheme 62. Reaction carried out at 0 ºC during 22 h

There are more examples where the attack to the most substituted carbon of the allene is favoured. In those cases, it is proposed that the intermediate Au(I)-π-allene complex formed during the reaction, interconverts rapidly and reversibly at room temperature between the two π-systems of the allene, and the product of the attack to the most substituted carbon was kinetically favoured affording the observed product (Scheme **31**).[95]

2.8.5. Deuterium-labelling experiments

Deuterium-labelling experiments were performed in order to confirm the vinyl-gold intermediates and to understand the formation of amide **127**. According to this, TFA-*d* and D_2O were employed to preform *in situ* the deuterated hydrazoic acid. Allyl azides **124a-*d*** and **125a-*d*** were obtained with high deuterium incorporation in the expected positions, supporting the involvement of the vinyl-gold intermediates (Scheme **63**). Compounds **126-*d*** and **128-*d***, were also detected, but the deuterium incorporation could not be accurately quantified by NMR, due to the low concentration of those compounds in the sample. Besides, amide **127-*d*** was characterised as a mixture of compounds with different deuterium incorporation in the methyl group adjacent to the carbonyl group and also the amidic nitrogen (see Figures **17** and

18).



Scheme 63. Deuterium-labelling experiments

^{1}H NMR in $CDCl_3$:

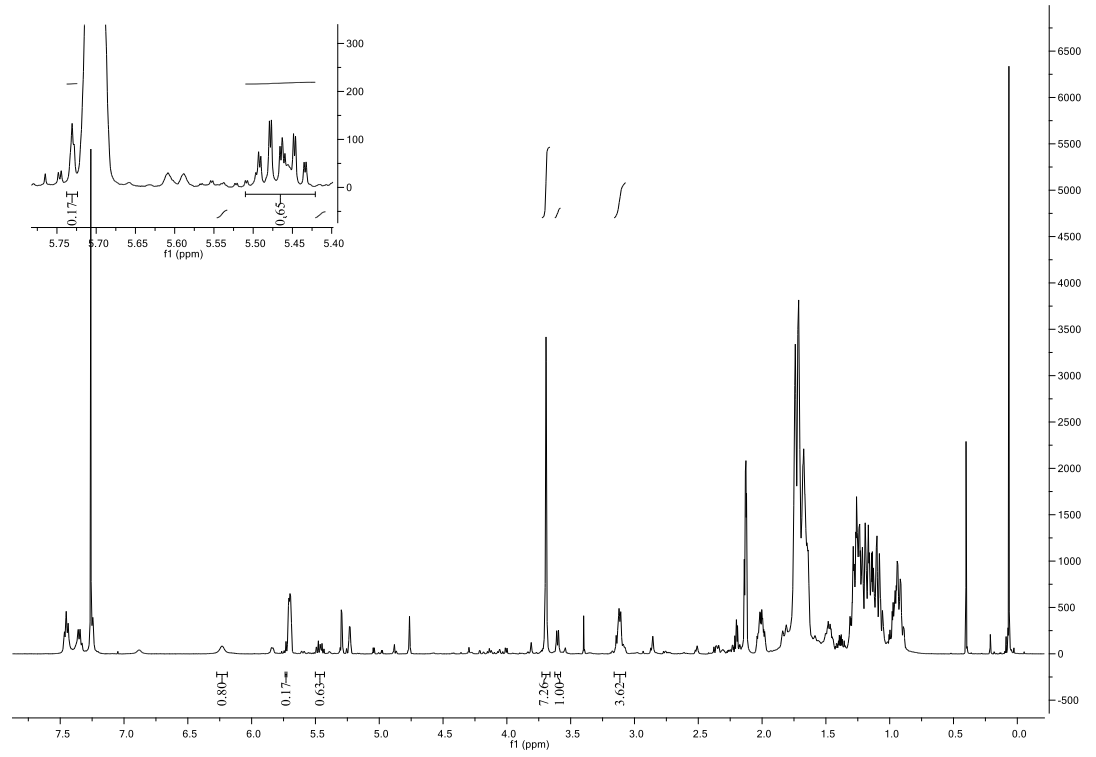


Figure 17. ^{1}H NMR of the crude of the deuterium-labelling experiments

^{2}H NMR in $CHCl_3$:

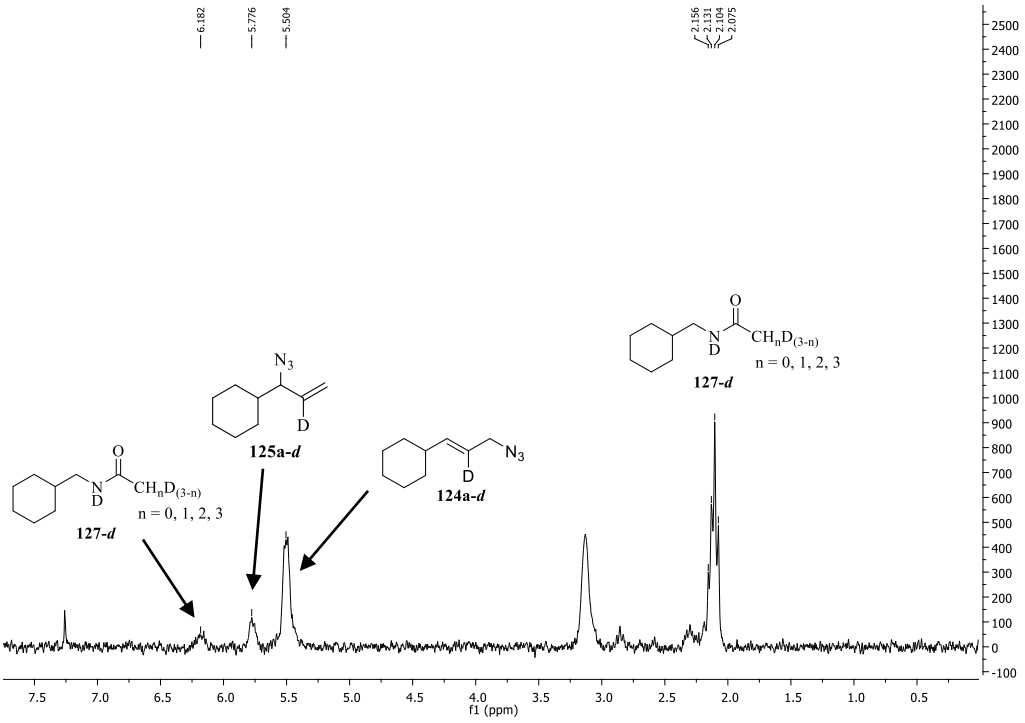
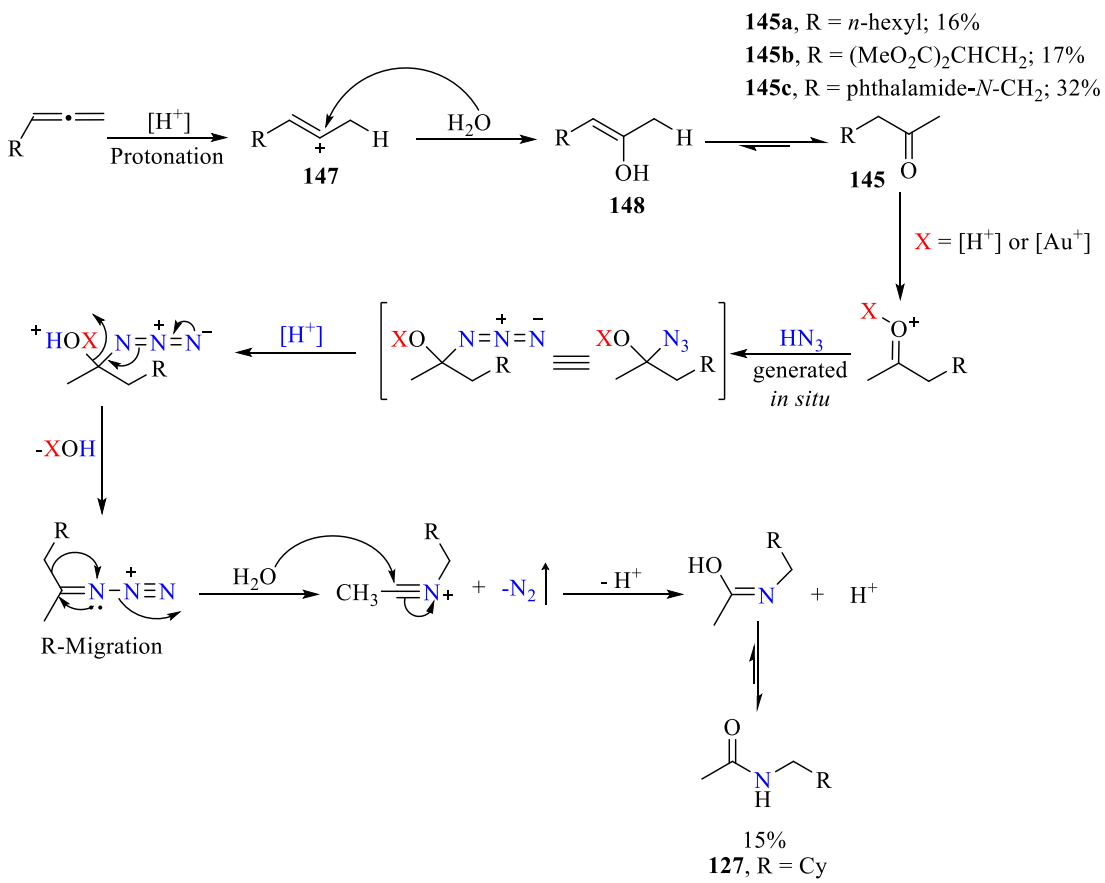


Figure 18. ^{2}H NMR of deuterium-labelling experiments

2.8.6. Formation of side products: Proposed mechanisms

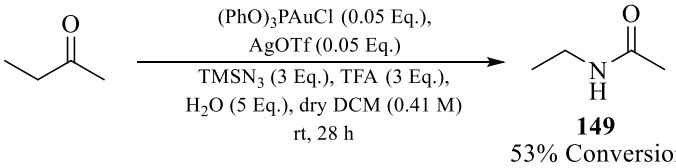
Table **13** showed that monosubstituted allenes **139a**, **c** and **d** gave as side products ketones **145a**, **b** and **c** in low yields. Based on previous investigations in the group, we propose that these secondary products are formed by protonation of the allenic precursor with the strong acid present in the reaction (**147**, Scheme **64**) and the subsequent attack of water into the central carbon of the starting allene moiety to form enol **148** that tautomerises to the ketone **145** (Scheme **64**). Interestingly, the electronic nature of the allenic substituents **139a**, **c** and **d** does not follow a trend that could explain why the formation of ketones is favoured with those allenic precursors.

Amide **127** was obtained as a secondary product under different reaction conditions with allene **96b**. After further investigation and taking into account that ketones were also obtained as secondary products under reaction conditions, it was postulated that amide **127** could come from an acid- or gold-mediated Schmidt reaction from the corresponding ketone **145** with the generated *in situ* hydrazoic acid (Scheme **64**).[149] Due to the Lewis acidic character of gold, it could coordinate with the oxygen of the ketone, favouring the attack of the azide to the carbonyl group. Migration of one of the substituents of the ketone, extrusion of N_2 and the subsequent attack of the water to the nitrilium ion would give rise to amide **127**. This proposal is supported by the results of the deuteration experiments shown before.



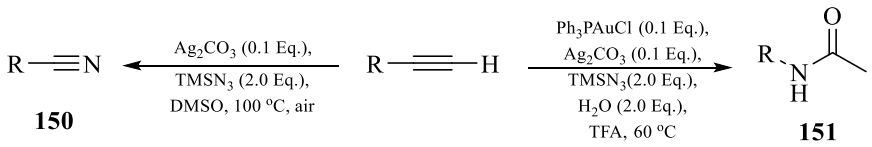
Scheme 64. Proposed mechanism for acid- or gold-mediated Schmidt reaction from allenes *via* the corresponding ketone

In order to further support this proposal, an extra experiment was carried out using a commercially available ethyl methyl ketone, which was submitted to reaction conditions. The results revealed that after 28 h, 53% conversion of amide **149** was obtained (Scheme **65**).[126] However, further investigations are required to confirm if the reaction is actually catalysed by gold or by the acid.



Scheme 65. Schmidt reaction of ethyl methyl ketone under the hydroazidation reaction conditions

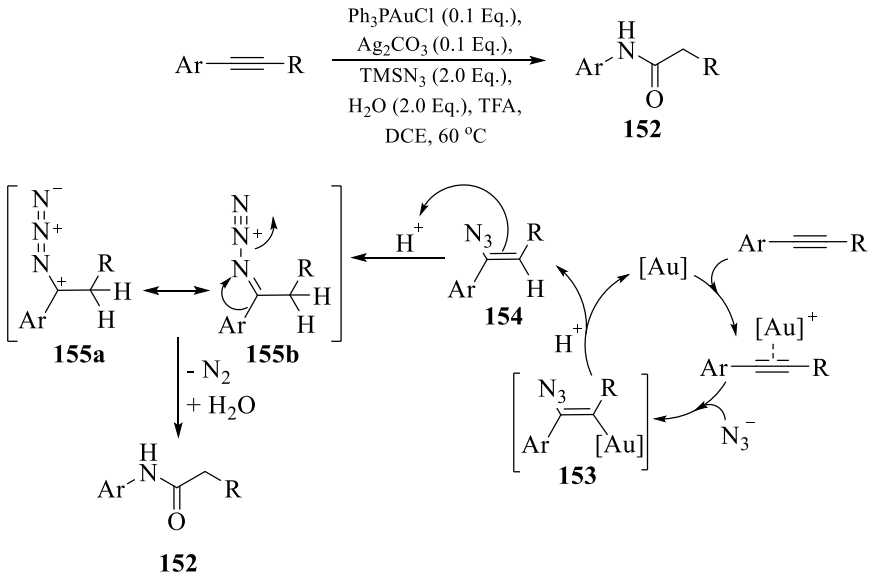
It should be mentioned here two consecutives articles published a few months before we reported our work, by the group of Jiao, to generate nitriles **150**[150] and amides **151**[151] from alkynes catalysed by silver and gold respectively (Scheme **66**).



Scheme 66. Silver- and gold-catalysed reactions of alkynes to give nitriles **150** and amides **151** and **152** respectively

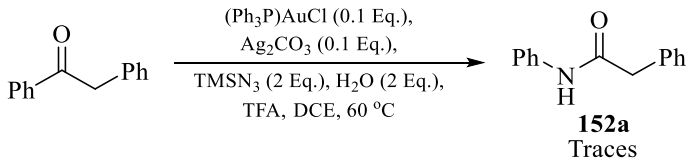
It was found that in the formation of nitriles **150**, traces of H_2O in DMSO as solvent, were responsible for the Ag-C cleavage of the vinyl azide intermediate, which also supports our theory of the wet silver effect mentioned in the previous section.[150]

The formation of amides **151** and **152** from alkynes *via* C_{sp}^2-C_{sp} cleavage (Scheme **66** and **67**) were performed using fairly similar reaction conditions to the ones reported in our gold-catalysed hydroazidation of allenes. In this case, $(Ph_3P)AuCl/AgOTf$ as catalytic source, TFA and also H_2O were used. As it is shown in the proposed mechanism (Scheme **67**), protonolysis of the vinyl gold intermediate **153** gives access to alkenyl azide **154**, which after protonation gives rise to resonance forms **155a** and **155b**, that then suffer the Schmidt rearrangement[149b, 152] process to give amide **152** with loss of N_2.[151, 153]



Scheme 67. Gold-catalysed nitrogenation of alkynes to amides and the proposed mechanism suggested

Jiao *et al.* also found ketones as side products in this reaction, and they proposed a gold-catalysed hydration of alkynes to ketones. To test if ketones were the precursors of the amides in their conditions, the authors carried out the reaction of a ketone under their best reaction conditions, similar to ours, but they only obtained traces of **152a** (Scheme **68**).[151]



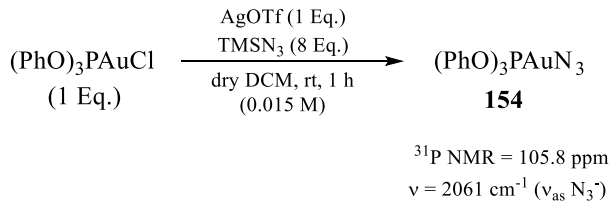
Scheme 68. Reaction carried out by the group of Jiao to investigate ketones as side products

2.8.7. Preliminary mechanistic studies of the catalytic cycle

Once the formation of the vinyl-gold intermediate was confirmed by deuterium-labelling experiments, a preliminary mechanistic study was carried out, in order to investigate if the reaction goes *via* outer- or inner-sphere mechanism.

2.8.7.a. Synthesis of gold-azide complex

An inner-sphere mechanism is characterised by the coordination of a nucleophile, (N_3^- in our case) with the cationic Au(I) species, $[LAu]^+$, to generate $[LAuN_3]$ as an active catalytic complex (see Scheme **28**, intermediate **77**). $[(Ph_3P)AuN_3]$ is a known gold complex, easy to synthesise[154] and is commonly used as a precursor for other ligands,[155] in organic synthesis[156] and frequently in photolysis chemistry.[157] However, the formation of the gold-azido complex **154** with the phosphite ligands that would be involved in our inner-sphere cycle had not been reported so far. In order to generate this complex, a reaction was carried out using similar conditions as the one employed to generate $[(Ph_3P)AuN_3]$ (Scheme **69**).



Scheme 69. Synthesis of gold-azide complex **154**

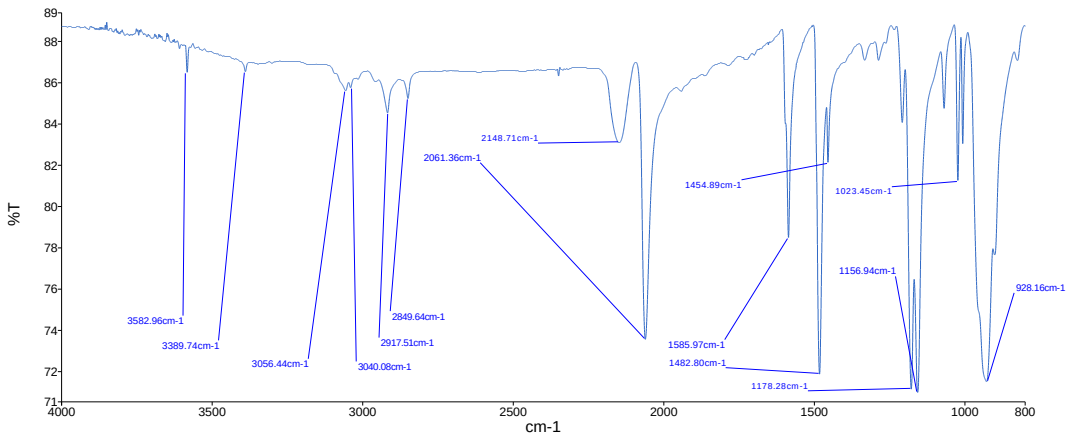
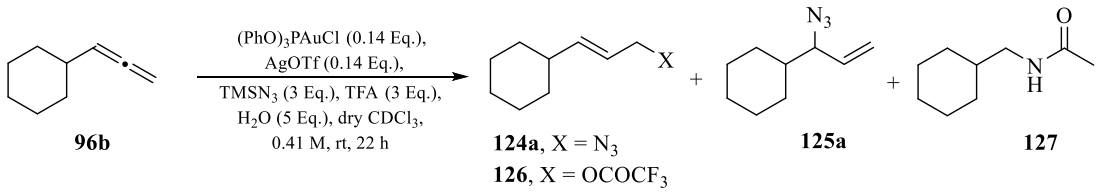


Figure 19. IR spectra of $[(PhO)_3PAuN_3]$

This novel gold-azido complex **154** is very unstable and it has to be kept in the freezer and in the dark. All attempts to crystallise it were unsuccessful because it decomposes quickly. Thus, this complex could not be isolated and employed as a catalysts or to study its implication in the catalytic cycle.

In a further attempt to identify the gold-azido complex **154**, a new reaction was carried out (Scheme **70**) and monitored by IR, hoping that the asymmetric stretch band of the azide in the complex [$(PhO)_3PAu\text{-}N_3$] would be easily recognised at $\nu_{as} \approx 2061$ cm^{-1} ([$(Ph_3P)AuN_3$] = 2050 cm^{-1})[155, 156b] (See Table **15**).



Scheme 70. Reaction monitored by IR

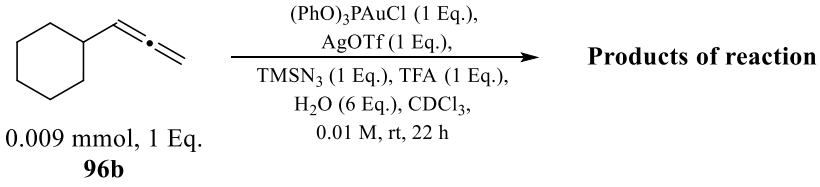
Entry	Time	(N_3) ν_{as} (cm^{-1})
1	30 min	2097.24
2	1 h 45 min	2098. 82
3	6 h	2098.82
4	9 h 30 min	2101.14

Table 15. Results obtained monitoring the reaction by IR. See appendix for the IR spectra.

The strong band of the azide group is present at around 2100 - 2097 cm^{-1} (See Table 15). However, this band also corresponds to the band of the $TMSN_3$ starting material and to the allyl azides **124a** and **125a** (ν_{as} = 2097 cm^{-1}), which are the products of the reaction (confirmed by NMR after 22 h). If it exists, the corresponding band of the [$Au\text{-}N_3$], would be overlapping with these products and therefore the identification of the gold-azido complex **154** during the reaction will be complicated using this technique.

2.8.7.b. Stoichiometric NMR Experiments

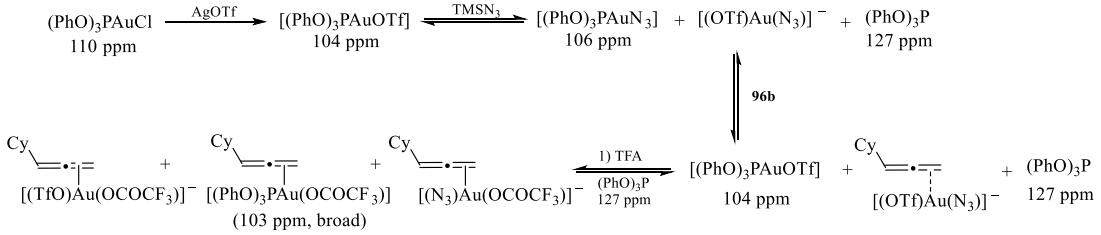
After the attempts to identify the formation of the $(PhO)_3PAuN_3$ complex, a stoichiometric NMR study was performed to study the nature of the active species generated during the reaction. Three stoichiometric experiments were carried out at room temperature and under nitrogen varying the order in which the different components of the reactions are added and recording ^1H, ^{31}P NMR spectra and after each addition.



Experiment A:

$(PhO)_3PAuCl + AgOTf + TMSN_3 +$ **96b** $+ TFA$

Interestingly, after addition of the $TMSN_3$ to the cationic complex a broad peak at 106 ppm was observed in accordance with the results obtained from the gold-azide complex **154** $[(PhO)_3PAuN_3]$ (see Scheme **69**). The broad peak could indicate a rapid equilibrium between the complex with the TfO^- and the N_3^- as counterions (Scheme **71** and Figure **20**). Additionaly, a small signal at 127 ppm was observed characteristic of free phosphite. This could indicate displacement of phosphite ligand after addition of $TMSN_3$, which would generate the anionic Au-species $[(OTf)Au(N_3)]^-$ and the gold-azide complex $[(PhO)_3PAuN_3]$. After addition of the allene, a broad peak at 104 ppm was observed, suggesting regeneration of the $[(PhO)_3PAuOTf]$ complex, with possible coordination of the allene to the complex bearing the triflate and the N_3. When TFA was added, the sharp peak of the corresponding free phosphite increased and a broad signal around 100 – 103 ppm appeard. This broad signal could suggest a rapid coordination of $[(PhO)_3PAu(OCOCF_3)]$ with the allene and a complex equilibrium of ligands and counterions (See experiment C for further information about $[(PhO)_3PAu(OCOCF_3)]$ complex).



Scheme 71. ^{31}P NMR-profile for stoichiometric Experiment **A**

^{31}P NMR profile of Experiment A:

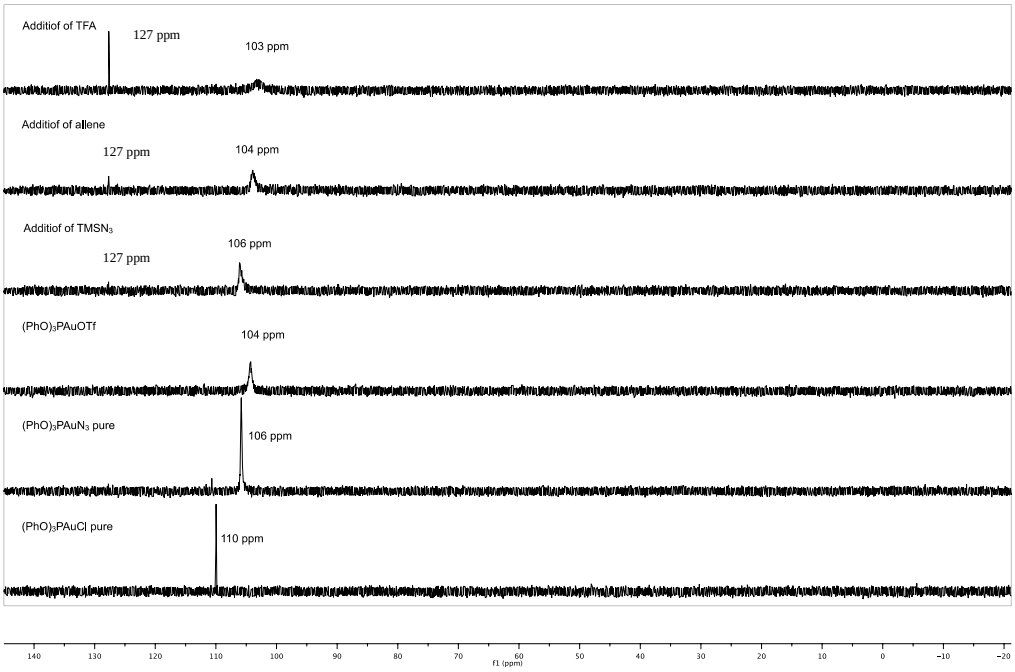
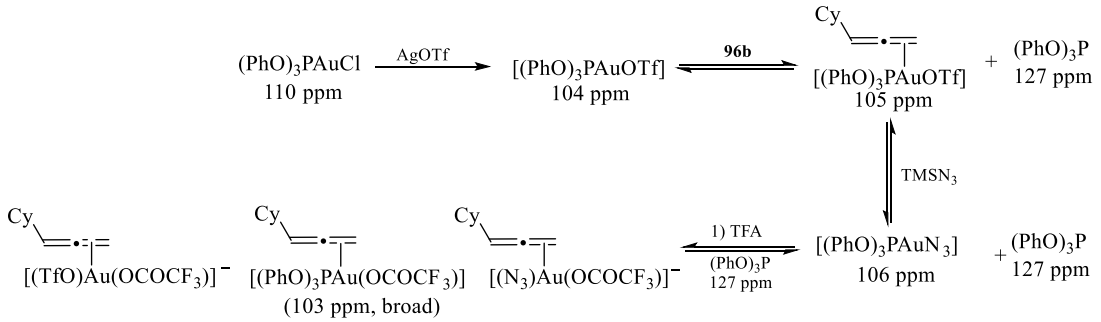


Figure 20. ^{31}P NMR profile of Experiment **A**

Experiment B:

$$(PhO)_3PAuCl + AgOTf + \mathbf{96b} + TMSN_3 + TFA$$

After addition of the allene to the cationic Au(I)-complex, a broad signal at 105 ppm was observed. This signal revealed the possible rapid coordination of the cationic Au(I)-complex with the allene. The peak of the gold-azido compound **154** was observed after addition of the $TMSN_3$ as well as a small peak corresponding to the free phosphite (127 ppm) which can indicate the formation of the anionic Au-species $[(OTf)Au(N_3)]^-$. After addition of TFA, a broad signal around 103 ppm and the sharp peak of the free phosphite suggests a similar complex equilibrium of the three different allene-Au(I) complexes with different counterions and ligands.



Scheme 72. ^{31}P NMR-profile for stoichiometric Experiment **B**

^{31}P NMR profile of Experiment B:

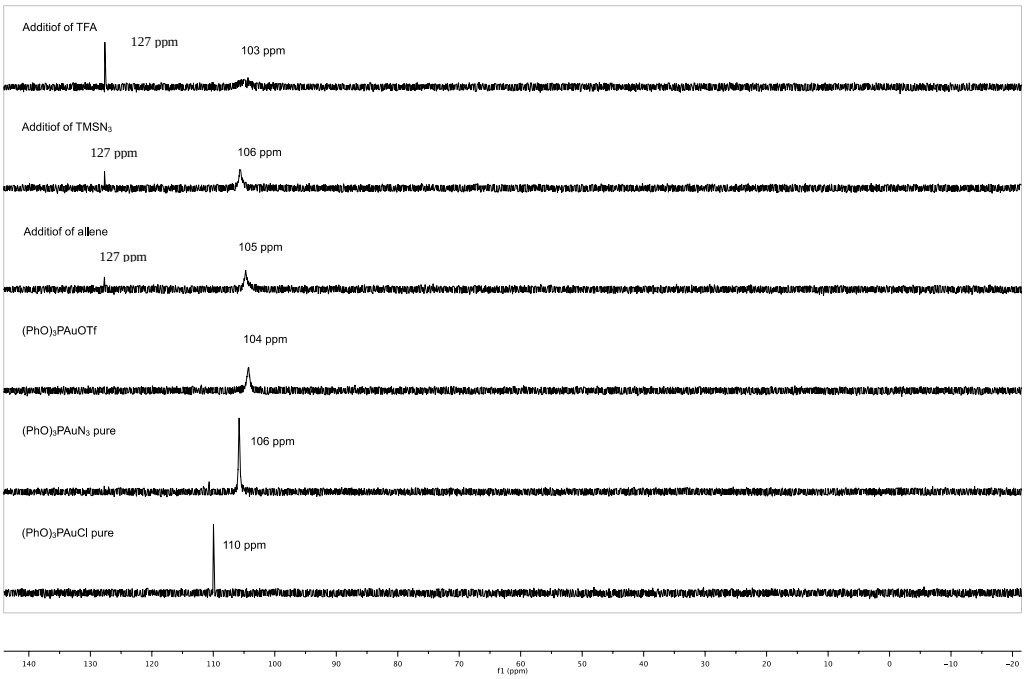
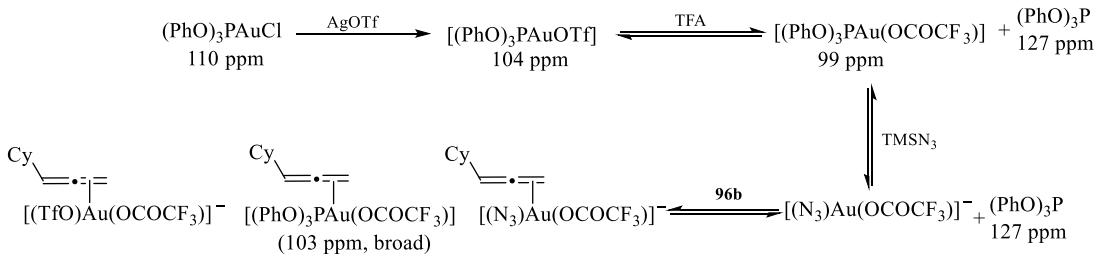


Figure 21. ^{31}P NMR profile of Experiment **B**

Experiment C

$$(PhO)_3PAuCl + AgOTf + TFA + TMSN_3 + \mathbf{96b}$$

Experiment **C** shows that after the addition of TFA to the cationic complex, the triflate counterion is replaced by the TFA anion giving a shift from 104 to 99 ppm upon generating complex $[(PhO)_3PAu]^+ {}^-OCOCF_3$ and also the free $(PhO)_3P$ at 127 ppm. Then, when the $TMSN_3$ is added, the peak at 127 ppm of the free phosphite ligand increases, which could suggest an equilibrium between $[(PhO)_3PAu]^+ {}^-OCOCF_3$ and the anionic complex $[(N_3)Au(OCOCF_3)]^-$. Subsequently when the allene **96b** was added broad peaks were observed suggesting a complex equilibrium as in experiments **A** and **B**.



Scheme 73. ^{31}P NMR-profile for stoichiometric Experiment **C**

^{31}P NMR profile of Experiment C:

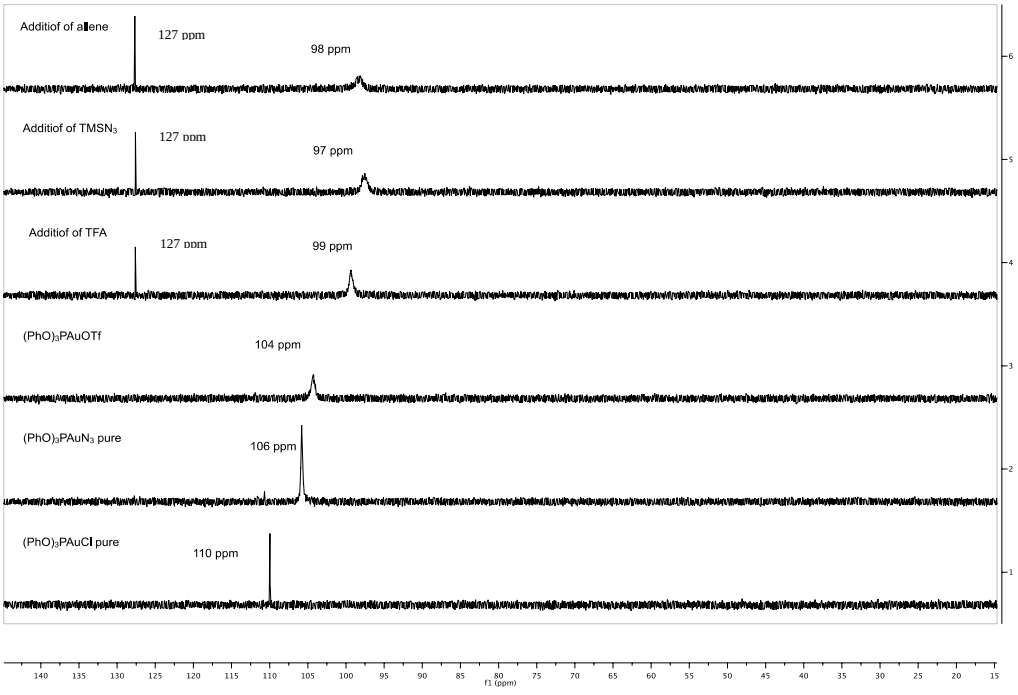


Figure 22. ^{31}P NMR profile of Experiment **C**

It has been reported that broad signals in ^{31}P NMR suggest the competition of the ligands for the metal centre, which helps to support our findings.[80] However, the broadening could also be indicative of di-aurated intermediates[158] and further investigations are needed to clarify their involvement in our case.

It has been proposed that the phosphite ligand coordinates weakly to the metal centre and it is easier to replace by other ligands.[130b] Although more evidence is needed to fully support an inner-sphere mechanism,[86b, 99a] it seems that in our reaction the displacement of the ligand and coordination of azide to the gold centre is the key for the catalytic activity. This could explain why other stronger σ-bonded ligands to the metal do not favour the azidation

reaction, and the inferior reactivity of complexes with the phosphine or NHC-ligands previously used in our screening of catalysts.

To compare the kinetic behaviour of the three systems, ^{1}H NMR analysis was also performed and the reactions were followed over a period of 6 to 23 h.

The signals used to measure integrals were:

Starting material and products	***δ* (ppm)**	**Signals**	***J* values (Hz)**	**Number of protons**
96b	5.07	q	6.50	1
124a	3.69	d	6.70	2
125a	3.60	t	7.73	1
127	3.10	t	6.44	2
128	3.38	m	-	2
126	4.77	d	6.76	2

Table 16. Signals employed to measure the kinetic behaviour of the different species

Similar rates for the formation of products were observed in all the experiments after addition of all components, which suggest that similar catalytic species are involved in the reaction and supports the involvement of a complex equilibrium with exchange of ligands and counterions. Vinyl-gold intermediates could not be identified by ^{1}H NMR in any of the experiments probably because fast protonolysis is occurring. This suggests that the rate limiting step in the reaction could lie on the equilibrium between the gold-catalyst, the azide, the allene and the rest of counterions involved in this reaction.

^{1}H NMR profile of Experiment A:

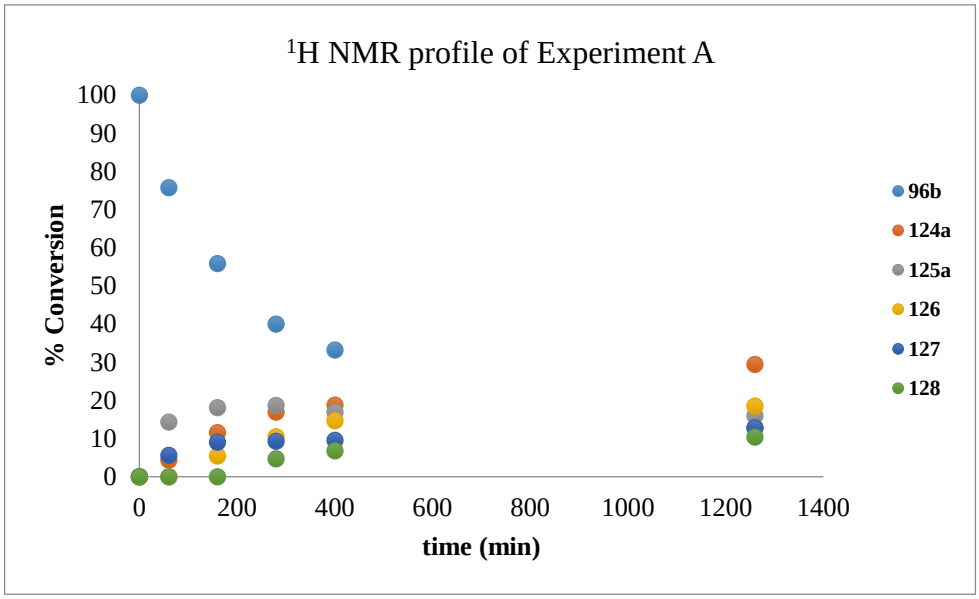


Figure 23. ^{1}H NMR profile of conversion in Experiment **A**

^{1}H NMR profile of Experiment B:

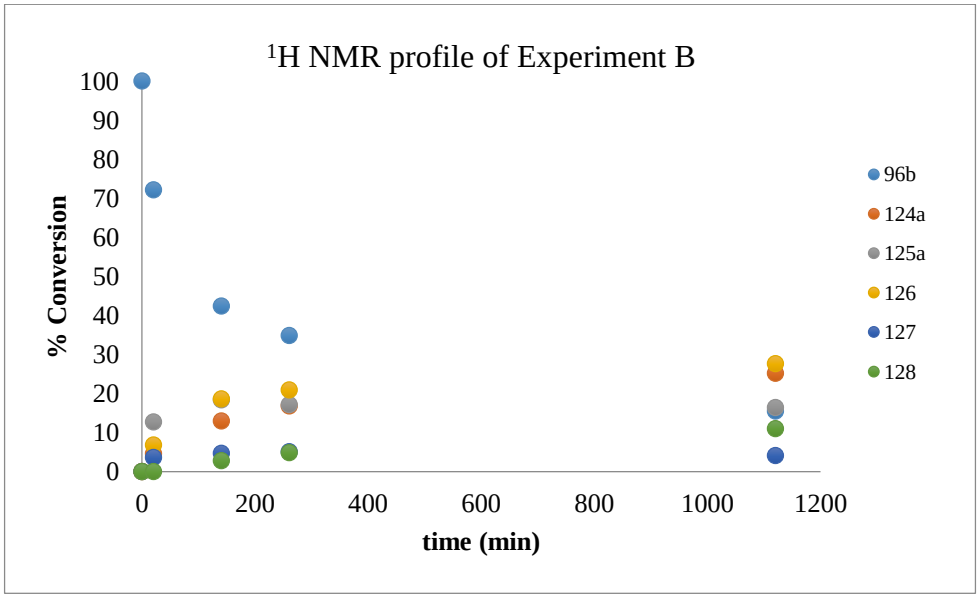


Figure 24. ^{1}H NMR profile of conversion in Experiment **B**

^{1}H NMR profile of Experiment C:

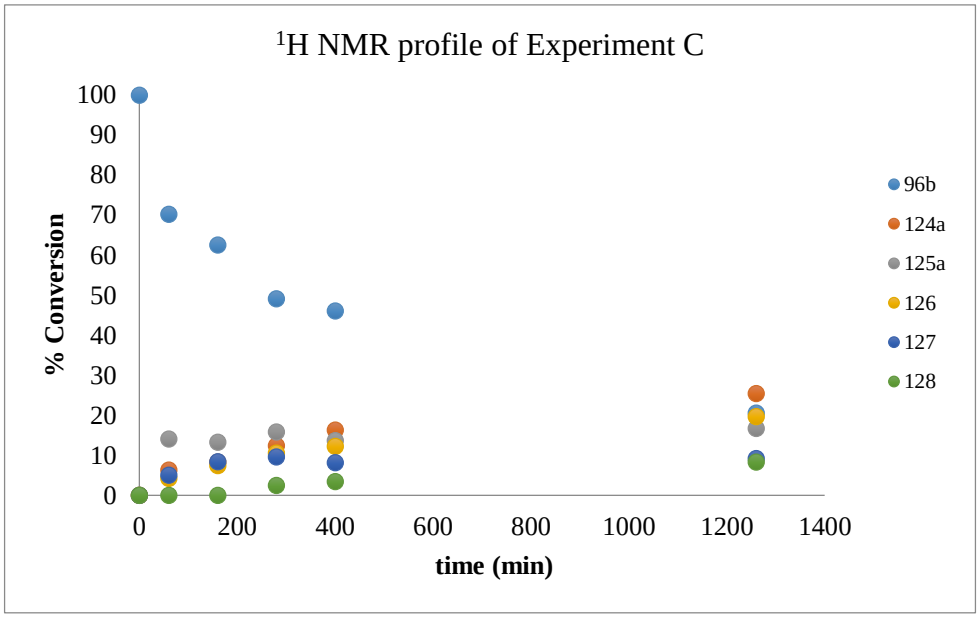
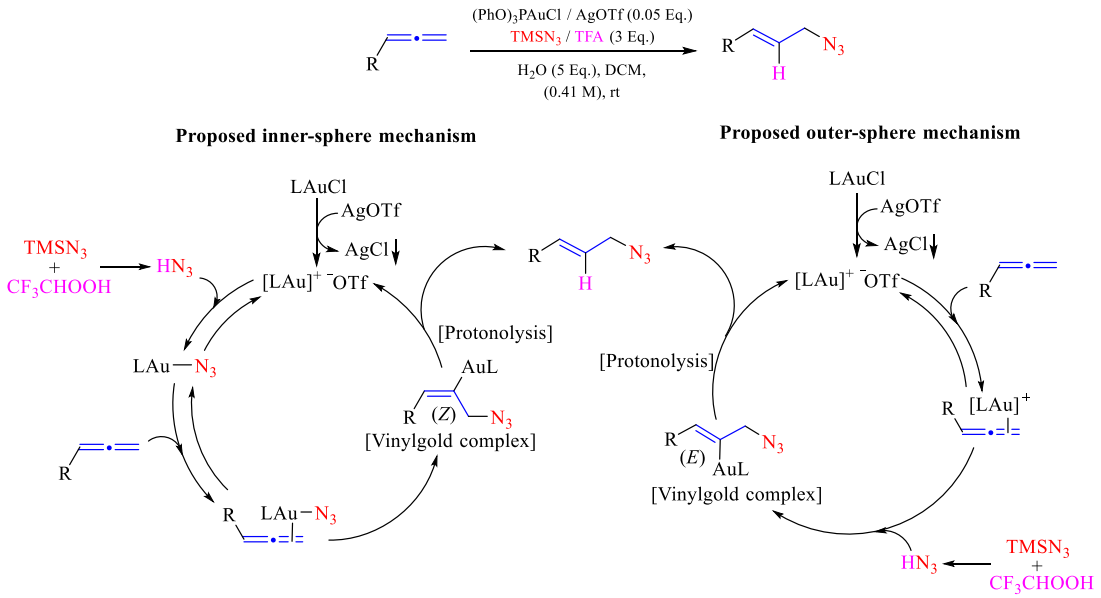


Figure 25. ^{1}H NMR profile of conversion in experiment **C**

In summary, although it is difficult to propose a full accurate mechanism for this reaction with only the results obtained, there are evidences that point to an inner–sphere process, with the possible formation of gold-azide complexes as well as a complex equilibrium of the different gold-complexes involving the azide, the allene and the rest of the counterions and ligands. However an outer-sphere mechanism cannot be completely ruled out at this point, and both possibilities have been included in Scheme **74** to explain our results.



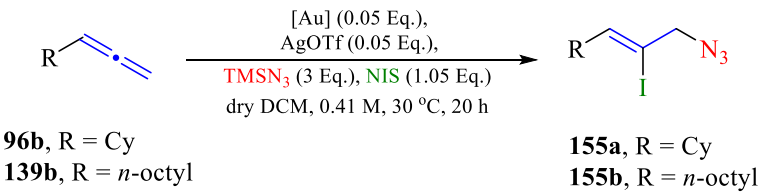
Scheme 74. Proposed mechanisms for Au(I)-catalysed intermolecular addition of azides to allenes *via* inner- or outer-sphere mechanism

2.8.8. Applicability and versatility of this transformation

Isotopic labelling experiments confirmed that the proton provided, by TFA performed the protonolysis of the vinyl-gold intermediate in this reaction (Scheme **63**). However, several electrophiles have also been employed to break the Au-C bond.[131g, 132b, 134b, 159] In order to expand the potential of this methodology iodine was employed as an electrophile instead TFA, to generate interesting iodo-alkenyl azides.

In the absence of any proton source (e.g. TFA), the formation of IN_3 *in situ* under reaction conditions could happen as it has been shown in the work of Hassner and coworkers with allenes (see Scheme **41**)[117] and also with alkenes[160] without any transition metal complex present in the reaction. However, when we carried out a reaction under our standard reaction conditions in the absence of gold and silver, using NIS and $TMSN_3$ to generate the IN_3 *in situ* with the model allene **96b**, no conversion to the desired iodo-alkenyl azides was observed, leading to recover the starting material.

Allenes **96b** and **139b** were exposed to our best reaction conditions (Scheme **75**), replacing the TFA by the NIS, in the absence of water. However, only 71% conversion was achieved using $(PhO)_3PAuCl$/AgOTf as the catalytic source (Table **17**, Entry **1**). Consequently, a new catalyst screening was performed, using NHC-Au complexes as well as different phosphine ligands.



96b, R = Cy
139b, R = *n*-octyl

155a, R = Cy
155b, R = *n*-octyl

Scheme 75. Gold-catalysts screening for the intermolecular iodoazidation of allenes

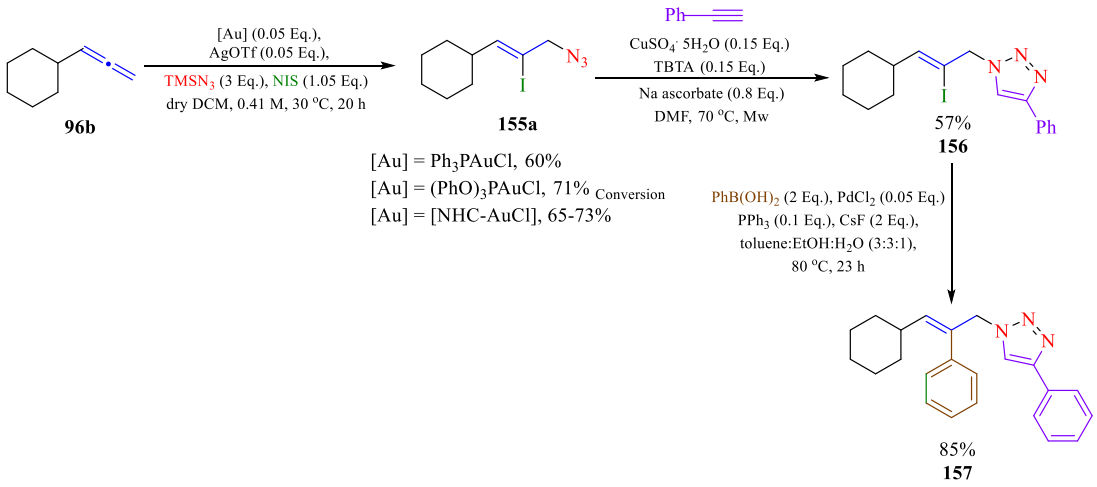
Entry	[Au]	allene	Conversion (%)	Isolated Yield (%)
1	$(PhO)_3PAuCl$	**96b**	71	-
2	Ph_3PAuCl	**96b**	100 (*E*/*Z* = 1:1)	60, *Z*-**155a**
3[a]	NHC-1	**96b**	84	73, *Z*-**155a**
4[a]	NHC-2	**96b**	78	-
5[a]	NHC-3	**96b**	83	65, *Z*-**155a**
6[a]	Cat-Au^+ SbF_6^-	**96b**	46	-
7[a]	NHC-1	**139b**	100	40, *Z*-**155b**

[a] See **Figure 13** for the structure of the Au-complexes.

Table 17. Results obtained in the gold-catalysts screening for the intermolecular iodoazidation of allenes

N-heterocyclic carbenes (Table **17**, Entries **3**, **4**, **5** and **7**) gave high conversions and excellent regioselectivities to the desired iodo-alkenyl azides **15**, product, from the attack of the azide to the terminal carbon of the allene. Besides, complete conversion was obtained using Ph_3PAuCl as a catalyst to a mixture of *E*-**155a**/*Z*-**155a** (1:1). It should be mentioned, that *E*-**155a** isomerises into *Z*-**155a** in solution after a few hours.

In order to show the potential of this methodology, a further orthogonal functionalization of allyl azide **155b** was performed after the Au(I)-catalysed azidation. Thus, Au(I)-catalysed iodoazidation of allene **96b** gave access to iodo-alkenyl azide *Z*-**155a** (Scheme **76**). The resulting product was submitted to click chemistry,[112, 161] giving the allylic triazole **156** in moderate yield. Compound **156** was further functionalised coupling a phenyl group in the allylic skeleton *via* Suzuki-Miyaura cross-coupling[162] to achieve the complex compound **157** in good yield.

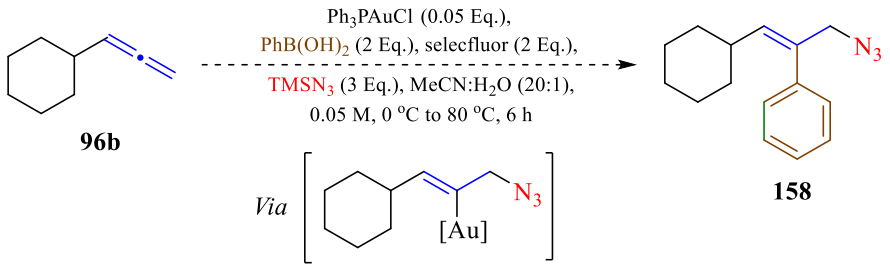


Scheme 76. Orthogonal functionalization of allenes using the Au(I)-catalysed azidation methodology

2.8.9. Attempts to develop a gold-catalysed oxidative cross-coupling reaction of allenes

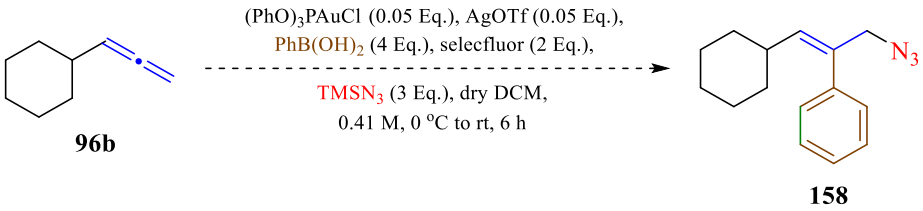
Zhang and coworkers developed an interesting gold-catalysed oxidative cross-coupling reaction of propargylic acetates and arylboronic acids to give α-arylenones in one-step.[163] In their mechanistic proposal, an uncommon oxidation of the vinyl-Au(I) intermediate to Au(III) by an external fluorinating reagent was invoked as the key step.

In order to improve the synthetic utility of this methodology, an attempt to a direct oxidative cross-coupling of the vinyl-gold intermediate generated in our reaction was performed under Zhang's conditions. Unfortunately, no evidence of product **158** from the oxidative cross-coupling reaction was observed by NMR. It was however seen that the signals of the starting material **96b** disappeared after 6 h, possibly due to the allene decomposition at 80 °C (Scheme **77**).



Scheme 77. Reaction carried out in order to trap the vinyl-gold intermediate *via* oxidative cross-coupling

A new reaction was also performed in another attempt to trap the vinyl-gold intermediate under our standard conditions and in absence of water and TFA, but with the boronic acid and selectfluor. After 6 hours, the unreacted allene **96b** was recovered without any sign of the desired compound **158** (Scheme **78**).



Scheme 78. Reaction carried out in order to trap the vinyl-gold intermediate *via* oxidative cross-coupling under our best reaction conditions

It should be taken into account that the starting materials, the reaction conditions and catalytic sources employed in the work reported by Zhang are quite different to our system. Further investigation into trapping the vinyl-gold intermediates will be performed in the group in the future, also taking into account recent examples of cross-coupling reactions by combining gold and other metals.[76, 164]

2.9. Conclusions

A novel Au(I)-catalysed intermolecular addition of azides to substituted allenes has been developed by using as the catalytic source $(PhO)_3PAuOTf$, and $TMSN_3$ with TFA to generate *in situ* hydrazoic acid, whose proton was involved in the Au-C cleavage of the vinyl-gold intermediate. The reaction is quite general and works efficiently for monosubstituted, 1,1- and 1,3-disubstituted allenes obtaining moderate to good yields. Regioselectivity issues were solved generating *E*-allyl azides as the only product including aryl functional groups directly linked to the allene moiety. To further show the synthetic potential of this reaction, iodine was employed as an electrophile achieving interesting alkenyl-iodo azides.

Further expansion of the scope and also further analysis of the side products and the complete mechanistic study of this transformation will be carried out in our laboratory in the

future, in order to fully develop this methodology as a new synthetic tool for the formation of very useful allylic azides.

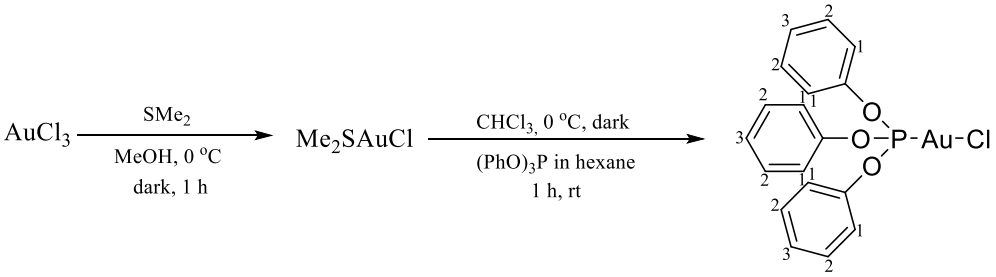
2.10. Experimental section

General experimental details

All reagents were purchased from commercial sources and used without further purification, unless noted otherwise. Solvents were dried using nitrogen atmosphere and used fresh every day for reaction. Deuterated solvents were acquired from Apollo Scientific or Fluorochem and stored over molecular sieves. All the preparative procedures were carried out in the absence of moisture and air under a nitrogen atmosphere, unless stated otherwise. Glassware, standard Schlenk tubes, and Schlenk tubes from Carousel 12 Plus Reaction Station from Radleys were flame-dried and flushed with nitrogen. Thin layer chromatography was performed on Aluminium oxide TLC-Cards with Fluorescent indicator 254 nm over aluminium oxide matrix from Sigma-Aldrich, and on Silica TLC-plates (60 F_{254} Merck). Components were visualized by illumination with UV light (λ = 254 nm), or by staining using potassium permanganate solution or phosphomolibdic acid solution in EtOH. Purification was performed by flash column chromatography using silica gel from Macherey-Nagel GmbH & Co. KG (particle size of 40 to 63 µm) as stationary phase, flash column chromatography using silica gel from Sigma-Aldrich, high purity grade (Merck grade 9385), pore size 60 Å, 230 - 400 mesh particle size, flash column chromatography using Aluminium Oxide activated, basic, Brockmann I of pore size 58 Å, pH 9.5 ± 0.5 in H_2O and over pre-coated TLC plates from Macherey-Nagel. GmbH & Co, Sil. G-25, 0.25 mm layer. Accurate weight were obtained with a Denver Instrument SI-234. Reactions under microwave irradiation were carried out in a Biotage Initiator$^+$ Microwave system. The addition and treatment of cadmium iodide was carried out into a MBraun-workstation Globe Box, Unilab Plus/Pro-Sp/dp. ^{1}H, ^{2}H, ^{13}C, ^{31}P, ^{195}Pt, ^{19}F, NMR spectra were recorded at room temperature on a Bruker Avance III 500 MHz NMR spectrometer, fitted with a 5 mm broadband observed, BBFO^{plus} Z-gradient SmartProbe^{TM} probe or using a Bruker Avance III nanobay 400 MHz NMR spectrometer, fitted with a 5 mm broadband observe BBFO^{plus} Z-gradient probe and a Varian INOVA 300 MHz. Calibration was made using the deuterated solvent $CDCl_3$ (δH = 7.26 ppm and δC = 77.16 ppm), CD_3OD (δH = 3.31 ppm and δC = 49.00 ppm), CD_3CN (δH = 1.94 ppm and δC = 1.32 ppm) Tol- d_8 (δH = 2.08 ppm and δC = 20.4 ppm).[165] Chemical shifts (δ) are given in parts per million (ppm) and coupling constants values (J) are given in Hertz (Hz). ^{13}C NMR was recorded using broad-band proton decoupling. Low resolution mass spectra were recorded using electrospray (ESI) technique in the positive and negative ion mode with a Shimadzu LCMS spectrometer. Phenomenex pre-column filter (Security Guard, ODS C18, 4 x 3 mm

i.d.) was used to prevent rapid deterioration of the pre-column. Elution was carried out using a mobile phase comprising methanol, at a flow rate of 0.2 mL min^{-1}. All solvents were HPLC grade. High-resolution mass spectra were obtained from the EPSRC Mass Spectrometry Service at the University of Swansea by EI, NSI, ESI, APCI or ASAP techniques, using a Waters XEVO G2-S or Thermo Scientific LTQ Orbitrap XL. Melting points were measured with a BÜCHI Melting Point B-545. Infrared spectra were acquired using a Perkin Elmer System 400 FT-IR spectrophotometer. Solid samples were run as thin films of their solution in DCM. Liquid samples were run neat. Diffractometer: Rigaku AFC_{12} goniometer equipped with an enhanced sensitivity (HG) Saturn724+ detector mounted at the window of an FR-E+ SuperBright molybdenum rotating anode generator with HF Varimax optics (100µm focus). Cell determination and Data collection: CrystalClear-SM Expert 2.0 r7 (Rigaku, 2011). Data reduction and cell refinement & Absorption correction: Crysalis PRO 171.37.35 (Rigaku Oxford Diffraction 2015). Structure solution: SHELXST (G. M. Sheldrick, Acta Cryst. (2008) A64 112–122). Structure refinement: SHELXL97 (G. M. Sheldrick (1997), University of Göttingen, Germany). Graphics: Mercury 3.5.1 (CCDC 2014). Publication material: WinGX: Farrugia, L. J. (2012). J. Appl. Cryst. 45, 849-854.

Synthesis of chloro(triphenylphosphite)-Au(I)



The synthesis was undertaken according to the modified procedure described by Toste and coworkers.[166] Under N_2 atmosphere, Au(III) chloride (125 mg, 0.41 mmol, 1.0 Eq.) was dissolved in 2.5 mL of absolute methanol. The solution was stirred for a few minutes at 0 ºC and under exclusion of light. Dimethyl sulfide (Me_2S) (76 µl, 1.03 mmol, 2.5 Eq.) was added dropwise. Decolouration of the solution and formation of a white precipitate was observed immediately. The reaction was stirred for 1 h and then the stirring was stopped and the solid left to settle. The yellow solution was extracted with a syringe and the solid was washed with MeOH (2.0 mL), Et_2O (2.0 mL), and petroleum ether (2.0 mL). The solvent was removed by a syringe in all cases and after the last washed, the vial was dried under vacuum for a few min. Dry chloroform (2.5 mL) was added to the solid and stirred in the dark at 0 ºC for a few min. Then, a solution of triphenylphosphite $(PhO)_3P$ (119 µl, 0.45 mmol, 1.1 Eq.) in hexane (3.7 mL) was added dropwise whereby the white solid dissolved. The solution was stirred for 1 h

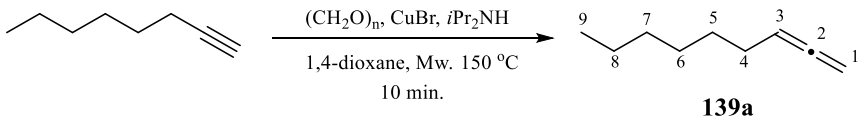
at room temperature. After the reaction was completed, the solvent was removed under vacuum, the resulting solid was triturated with hexane and filtered under vacuum. 154 mg, 0.28 mmol of a beige powder was obtained (69%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.41 (t, J = 7.9 Hz, 6H; H_{Ar}-2), 7.32 – 7.27 (m, 3H; H_{Ar}-3), 7.24 – 7.19 (m, 6H; H_{Ar}-1). ^{31}P NMR (202 MHz, $CDCl_3$, 25 ºC) δ = 109.96.

General procedure for the synthesis of allenes via Crabbe homologation assisted by microwave irradiation[27b]

Allenes **96b**, **120**, **132**, **133**, **134**, **135**, **136** and **137**, are commercially available (Sigma-Aldrich) and were used without further purification.

CuBr (0.3 Eq.) and paraformaldehyde (2.5 Eq.) were added into a previously oven-dried microwave vial under N_2. Then the corresponding alkyne (1.0 Eq. 0.5 M) was added dissolved in dry 1,4-dioxane, followed by the dropwise addition of dry iPr$_2$NH (2.0 Eq.) under inert atmosphere. The reaction mixture was heated at 150 ºC under microwave irradiation during 10 – 20 min until complete conversion, followed by TLC. The crude of the reaction was directly purified by column chromatography over silica gel using Hex or PET / Et_2O or EtOAc as eluent.

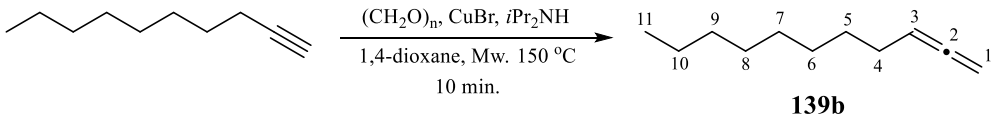
Synthesis of Nona-1,2-diene (139a)[167]



139a

From 1-octyne (850 µl, 5.67 mmol), CuBr (244 mg, 1.70 mmol), paraformaldehyde (426 mg, 14.18 mmol), dry iPr$_2$NH (1.6 mL, 11.34 mmol) and 12.0 mlL of dry 1,4-dioxane. Obtained after column chromatography, Hex/EtOAc, (90:1) then (60:1): **139a**, 342 mg, 2.75 mmol (49%): yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 5.09 (p, J = 6.7 Hz, 1H; H-3), 4.65 (dt, J = 6.7, 3.3 Hz, 2H; H-1), 2.04 – 1.95 (m, 2H; H-4), 1.45 – 1.36 (m, 2H; H-5), 1.36 – 1.23 (m, 6H; H-6 to H-8), 0.89 (t, J = 6.7 Hz, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 208.7 (C_q; C-2), 90.3 (CH; C-3), 74.6 (CH_2; C-1), 31.8 (CH_2), 29.3 (CH_2), 28.9 (CH_2), 28.4 (CH_2), 22.8 (CH_2; C-4 to C-8), 14.2 (CH_3; C-9).

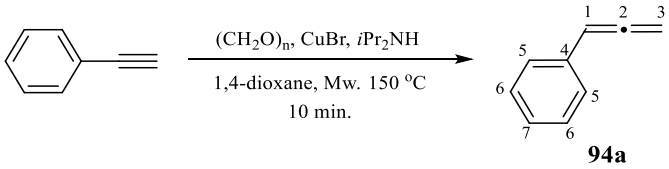
Synthesis of Undeca-1,2-diene (139b)[27c, 168]



139b

From 1-decyne (653 µl, 3.60 mmol, 0.30 M), CuBr (155 mg, 1.10 mmol), paraformaldehyde (270 mg, 9.00 mmol), dry *i*Pr_2NH (1.0 mL, 7.20 mmol) and 12.0 mL of dry 1,4-dioxane. Obtained after column chromatography, hexane: **139b**, 245 mg, 1.61 mmol (45%): pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 5.09 (p, *J* = 6.7 Hz, 1H, H-3), 4.65 (dt, *J* = 6.7, 3.2 Hz, 2H, H-1), 1.96 – 2.02 (m, 2H, H-4), 1.27 – 1.42 (m, 12H), 0.88 (t, *J* = 6.9 Hz, 3H, H-11). *This allene was preapared by Stefanie Hohne using modified conditions from the described in the general procedure.*

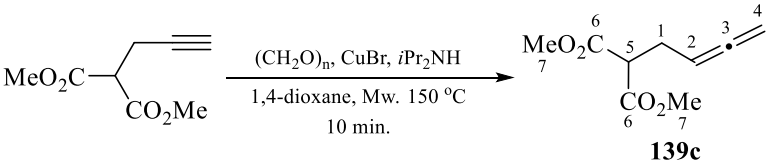
Synthesis of (1,2-propadien-1-yl)-benzene (94a)[169]



94a

From phenylacetylene (538 µl, 4.90 mmol), CuBr (210 mg, 1.47 mmol), paraformaldehyde (368 mg, 12.24 mmol), dry *i*Pr_2NH (1.4 mL, 9.79 mmol) and 10.0 mL of dry 1,4-dioxane. Obtained after column chromatography, Hex / EtOAc, (90:1) then (60:1): **94a**, 262 mg, 2.25 mmol (46%): yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.34 – 7.28 (m, 4H; H_{Ar}-5 and H_{Ar}-6), 7.23 – 7.17 (m, 1H; H_{Ar}-7), 6.17 (t, *J* = 6.8 Hz, 1H; H-1), 5.15 (d, *J* = 6.8 Hz, 2H; H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.9 (C_q; C-2), 134.1 (C_q; C-4), 128.8 (2 x CH_{Ar}; C-6), 127.0 (CH_{Ar}; C-7), 126.8 (2 x CH_{Ar}; C-5), 94.1 (CH; C-1), 78.9 (CH_2; C-3).

Synthesis of dimethyl 2-(2,3-butadienyl)malonate (139c)[170]

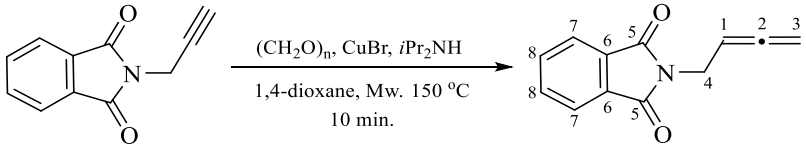


139c

From dimethyl propargyl malonate (1.3 mL, 8.81 mmol, 0.80 M), CuBr (759 mg, 5.29 mmol), paraformaldehyde (1.32 g, 44.08 mmol), dry *i*Pr_2NH (4.9 mL, 35.26 mmol) and 11.0 mL of dry 1,4-dioxane. Obtained after column chromatography, Hex / EtOAc, (6:1) then (4:1): **139c**, 860 mg, 4.67 mmol (53%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.13 (p,

J = 6.7 Hz, 1H; H-2), 4.72 (dt, *J* = 6.7, 3.2 Hz, 2H; H-4), 3.74 (s, 6H; H-7), 3.51 (t, *J* = 7.5 Hz, 1H; H-5), 2.59 (ddt, *J* = 7.5, 6.7, 3.2 Hz, 2H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 208.8 (C_q; C-3), 169.4 (2 x C_q; C-6), 86.7 (CH; C-2), 76.4 (CH_2; C-4), 52.7 (2 x CH_3; C-7), 51.4 (CH; C-5), 27.5 (CH_2; C-1).

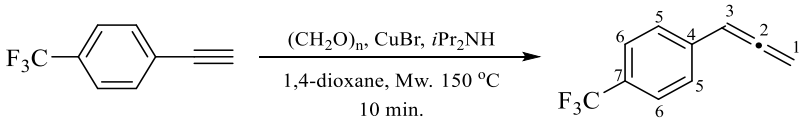
Synthesis of *N*-[2-(2,3-butadien-1-yl)-]phtalamide (139d)[27b, 171]



139d

From *N*-propargylphthalimide (870 mg, 4.69 mmol), CuBr (202 mg, 1.41 mmol), paraformaldehyde (352 mg, 11.74 mmol), dry *i*Pr_2NH (1.3 mL, 9.39 mmol) and 10.0 mL of dry 1,4-dioxane. Obtained after column chromatography, Hex / EtOAc, (5:1): **139d**, 836 mg, 4.20 mmol (89%): white solid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.86 (m, 2H; H_{Ar}-7 or H_{Ar}-8), 7.72 (m, 2H; H_{Ar}-7 or H_{Ar}-8), 5.27 (m, 1H; H-1), 4.80 (dt, *J* = 6.5, 3.1 Hz, 2H; H-3), 4.30 (dt, *J* = 6.0, 3.1 Hz, 2H; H-4). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 208.8 (C_q; C-2), 168.0 (2 x C_q; C-5), 134.1 (2 x CH_{Ar}; C-7 or C-8), 132.3 (2 x C_q; C-6), 123.5 (2 x CH_{Ar}; C-7 or C-8), 86.4 (CH_2; C-1), 78.0 (CH_2; C-3), 36.3 (CH_2; C-4).

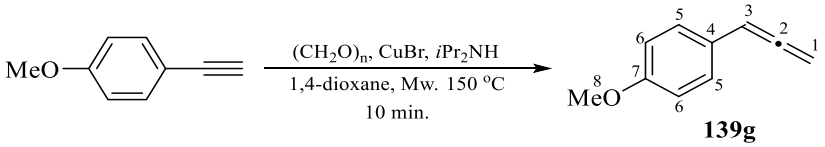
Synthesis of 4-(1,2-propadien-1-yl)-α,α,α-trifluorotoluene (139f)[172]



139f

From 4-ethynyl-α,α,α-trifluorotoluene (575 µl, 3.53 mmol), CuBr (152 mg, 1.06 mmol), paraformaldehyde (265 mg, 8.82 mmol), dry *i*Pr_2NH (990 µl, 7.05 mmol) and 7.4 mL of dry 1,4-dioxane. Obtained after column chromatography, Hex / EtOAc (90:1): **139f**, 225 mg, 1.22 mmol (35%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.55 (d, *J* = 8.2 Hz, 2H; H_{Ar}-6), 7.39 (d, *J* = 8.2 Hz, 2H; H_{Ar}-5), 6.19 (t, *J* = 6.8 Hz, 1H; H-3), 5.22 (d, *J* = 6.8 Hz, 2H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 210.6 (C_q, C-2), 138.1 (C_q, C-4), 128.9 (q, $J_{C\text{-}F}$ = 32.3 Hz; C_q-7), 126.9 (2 x CH_{Ar}; C-5), 125.7 (q, $J_{C\text{-}F}$ = 3.8 Hz; 2 x CH_{Ar}-6), 124.4 (q, $J_{C\text{-}F}$ = 271.8 Hz; CF_3), 93.4 (CH; C-3), 79.5 (CH_2; C-1).

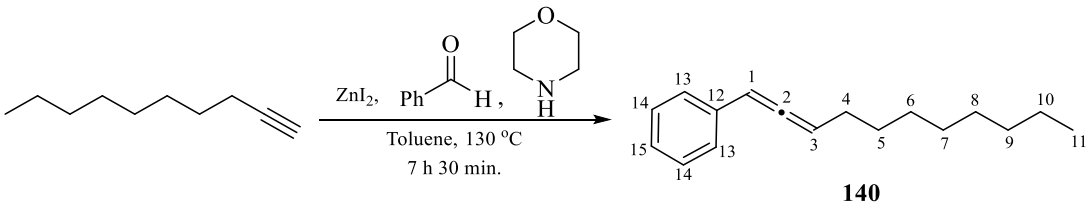
Synthesis of 1-(1,2-propadien-1-yl)-4-methoxybenzene (139g)[173]



From 1-ethynyl-4-methoxybenzene (834 µl, 6.43 mmol), CuBr (277 mg, 1.93 mmol), paraformaldehyde (483 mg, 16.08 mmol), dry *i*Pr_2NH (1.8 mL, 12.86 mmol) and 12.0 mL of dry 1,4-dioxane. Obtained after column chromatography, Hex / EtOAc, (90:1) then (40:1): **139g**, 416 mg, 2.85 mmol (44%): yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.25 – 7.20 (m, 2H; H_{Ar}-5), 6.88 – 6.83 (m, 2H; H_{Ar}-6), 6.13 (t, *J* = 6.8 Hz, 1H; H-3), 5.12 (d, *J* = 6.8 Hz, 2H; H-1), 3.80 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.5 (C_q, C-2), 158.9 (C_q, C-7), 127.9 (2 x CH_{Ar}; C-5), 126.3 (C_q, C-4), 114.3 (2 x CH_{Ar}; C-6), 93.5 (CH; C-3), 78.9 (CH_2; C-1), 55.5 (CH_3; C-8).

<u>Synthesis of 1,3-disubstituted allenes from 1-alkynes and aldehydes</u>[10a]

Synthesis of 1,2-undecadien-1-yl-benzene (140)[174]



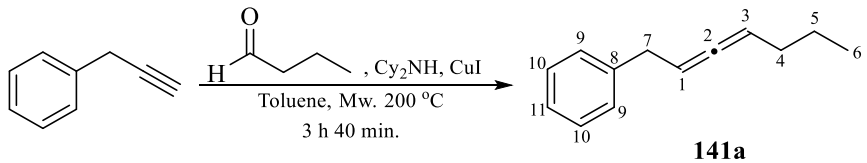
The synthesis was undertaken according to the procedure described by Ma and co-workers.[10a] Zinc Iodide (ZnI_2) (1.8 g, 5.79 mmol, 0.8 Eq.) was added under N_2 into a flamed-dried two-necks round bottom flask equipped with a condenser. Benzaldehyde (1.3 mL, 13.02 mmol, 1.8 Eq.) and 1-decyne (1.3 mL, 7.23 mmol, 1.0 Eq., 0.24 M) were added sequentialy dissolved in dry toluene under N_2 flow. The suspension was stirred at room temperature for 5 min. Then dry morpholine (0.9 mL, 10.12 mmol, 1.4 Eq.) was added dropwise under N_2. The reaction mixture was refluxed at 130 °C during 7 h 30 min. After cooled down, the solution was filtered through a pad of silica gel over celite (1:1), washed with Et_2O (30 mL) and concentrated under vacuum. The crude was purified by column chromatography over silica gel using hexane as eluent. **140**, 823 mg, 3.61 mmol was obtained as a yellow-pail oil (50%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.33 – 7.27 (m, 4H; H_{Ar}-13 and H_{Ar}-14), 7.22 – 7.14 (m, 1H; H_{Ar}-15), 6.15 – 6.10 (m, 1H; H-1), 5.57 (q, *J* = 6.7 Hz, 1H; H-3), 2.16 – 2.09 (m, 2H; H-4), 1.54 – 1.44 (m, 2H; H-5), 1.40 – 1.33 (m, 2H; H-6), 1.33 – 1.21 (m, 8H), 0.92 – 0.84 (m, 3H; H-11). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 205.3 (C_q; C-2), 135.3 (C_q; C-12), 128.7 (2 x CH_{Ar}; C-14), 126.7 (CH_{Ar}; C-15), 126.7 (2 x CH_{Ar}; C-13), 95.3 (CH; C-3), 94.7 (CH; C-

1), 32.0 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.3 (CH_2; C-6), 29.3 (CH_2; C-5), 28.9 (CH_2; C-4), 22.8 (CH_2), 14.3 (CH_3; C-11).

Experimental procedure for the microwave-assisted modified Crabbé homologation applied to the synthesis of 1,3-disubstituted allenes

The synthesis was undertaken according to the procedure described by Mukai and co-workers.[30] Alkyne (1.0 Eq., 0.5 M), aldehyde (1.5 Eq.), cyclohexylamine (Cy_2NH) (1.51 Eq.), copper(I) iodide (CuI) (0.1 Eq.), and toluene were added to a microwave vial. The vessel was sealed, and the reaction mixture was heated at 200 °C under microwave irradiation until complete conversion, followed by TLC. After cooling, the mixture was filtered through celite, washed with DCM and concentrated under vacuum. The crude of reaction was purified by column chromatography over silica gel using Hex or PET / Et_2O or EtOAc as eluent.

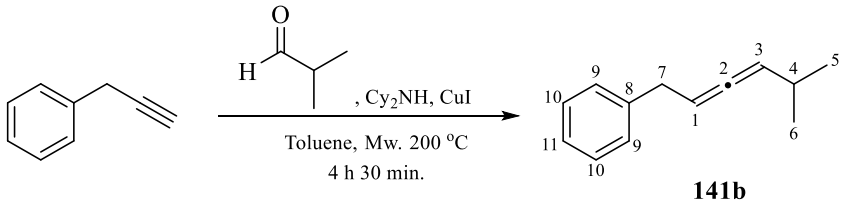
Synthesis of hepta-2,3-dienyl-benzene (141a)



141a

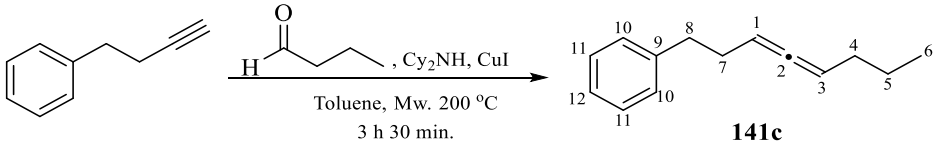
From 3-phenyl-1-propyne (294 µl, 2.37 mmol), butyraldehyde (320 µl, 3.55 mmol), Cy_2NH (711 µl, 3.57 mmol), CuI (45 mg, 0.24 mmol) and 4.7 mL of toluene. Obtained after column chromatography using Hex / EtOAc (90:1) as eluent: **141a**, 160 mg, 0.93 mmol (39%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.32 – 7.27 (m, 2H; H_{Ar}-10), 7.25 – 7.22 (m, 2H; H_{Ar}-9), 7.22 – 7.16 (m, 1H; H_{Ar}-11), 5.28 – 5.20 (m, 1H; H-1 or H-3), 5.17 – 5.08 (m, 1H; H-1 or H-3), 3.34 (dd, J = 7.0, 2.7 Hz, 2H; H-7), 2.02 – 1.93 (m, 2H; H-4), 1.42 (sex, J = 7.3 Hz, 2H; H-5), 0.92 (t, J = 7.3 Hz, 3H; H-6). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 204.7 (C_q, C-2), 140.8 (C_q, C-8), 128.6 (2 x CH_{Ar}; C-9 or C-10), 128.5 (2 x CH_{Ar}; C-9 or C-10), 126.2 (CH_{Ar}; C-11), 91.4 (CH; C-1 or C-3), 90.4 (CH; C-1 or C-3), 36.1 (CH_2; C-7), 31.1 (CH_2; C-4), 22.5 (CH_2; C-5), 13.8 (CH_3; C-6). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3063 (C-H_{Ar}), 3028 (C-H_{Ar}), 2959 (C-H_{Alkane}), 2929 (C-H_{Alkane}), 2872 (C-H_{Alkane}), 1962 (C=C=C), 1494, 1454, 1260, 882, 741 (C-$H_{Ar(bend)}$), 697. HRMS (FTMS + p APCI (NEAT)): Calc. for $C_{13}H_{17}$ $[M+H]^+$: 173.1325. Found: 173.1324.

Synthesis of (5-methyl-hexa-2,3-dienyl)-benzene (141b)



From 3-phenyl-1-propyne (294 µl, 2.37 mmol), isobutyraldehyde (324 µl, 3.55 mmol), Cy_2NH (711 µl, 3.57 mmol), CuI (45 mg, 0.24 mmol) and 4.7 mL of toluene. Obtained after column chromatography using Hex / EtOAc (90:1) as eluent: **141b**, 113 mg, 0.66 mmol (28%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.32 – 7.28 (m, 2H; H_{Ar}-10), 7.26 – 7.23 (m, 2H; H_{Ar}-9), 7.23 – 7.18 (m, 1H; H_{Ar}-11), 5.34 – 5.27 (m, 1H; H-3 or H-1), 5.18 – 5.11 (m, 1H; H-3 or H-1), 3.35 (dd, *J* = 6.9, 2.8 Hz, 2H; H-7), 2.32 – 2.22 (m, 1H; H-4), 0.99 (d, *J* = 6.9 Hz, 3H; H-5 or H-6), 0.99 (d, *J* = 6.8 Hz, 3H; H-5 or H-6). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 203.0 (C_q, C-2), 140.8 (C_q, C-8), 128.7 (2 x CH_{Ar}; C-9 or C-10), 128.4 (2 x CH_{Ar}; C-9 or C-10), 126.2 (CH_{Ar}; C-11), 99.1 (CH; C-1 or C-3), 91.8 (CH; C-1 or C-3), 36.2 (CH; C-4), 28.1 (CH_2; C-7), 22.7 (CH_3; C-5 or C-6), 22.6 (CH_3; C-5 or C-6). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3029 (C-H_{Ar}), 2963 (C-H_{Alkane}), 2928 (C-H_{Alkane}), 1955 (C=C=C), 1725, 1608 (C=C_{Ar}), 1452, 1261, 1080, 1027, 800, 699 (C-$H_{Ar(bend)}$). HRMS (FTMS + p APCI (NEAT)): Calc. for $C_{13}H_{17}$ $[M+H]^+$: 173.1325. Found: 173.1324.

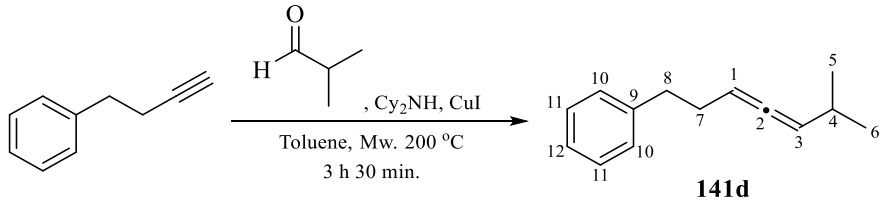
Synthesis of octa-3,4-dienyl-benzene (141c)



From 4-phenyl-1-butyne (297 µl, 2.11 mmol), butyraldehyde (286 µl, 3.17 mmol), Cy_2NH (634 µl, 3.19 mmol), CuI (40 mg, 0.21 mmol) and 4.2 mL of toluene. Obtained after column chromatography using hexane as eluent: **141c**, 248 mg, 1.33 mmol (63%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.31 – 7.26 (m, 2H; H_{Ar}-11), 7.22 – 7.16 (m, 3H; H_{Ar}-10 and H_{Ar}-12), 5.16 – 5.11 (m, 1H; H-1), 5.11 – 5.04 (m, 1H; H-3), 2.72 (t, *J* = 7.7 Hz, 2H; H-8), 2.35 – 2.25 (m, 2H; H-7), 1.99 – 1.86 (m, 2H; H-4), 1.44 – 1.32 (m, 2H; H-5), 0.95 – 0.88 (m, 3H; H-6). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 204.2 (C_q; C-2), 142.1 (C_q; C-9), 128.7 (2 x CH_{Ar}; C-10), 128.4 (2 x CH_{Ar}; C-11), 125.9 (CH_{Ar}; C-12), 91.5 (CH; C-3), 90.3 (CH; C-1), 35.6 (CH_2; C-8), 31.1 (CH_2; C-4), 30.9 (CH_2; C-7), 22.5 (CH_2; C-5), 13.8 (CH_3; C-6). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3086 (C-H_{Ar}), 3063 (C-H_{Ar}), 3027, 2959 (C-H_{Alkane}), 2929 (C-H_{Alkane}),

2871 (C-H_{Alkane}), 1962 (C=C=C), 1604 (C=C_{Ar}), 1454, 876. HRMS (FTMS + p APCI (NEAT)): Calc. for $C_{14}H_{19}$ $[M+H]^+$: 187.1481. Found: 187.1480.

Synthesis of (6-methyl-hepta-3,4-dienyl)-benzene (141d)

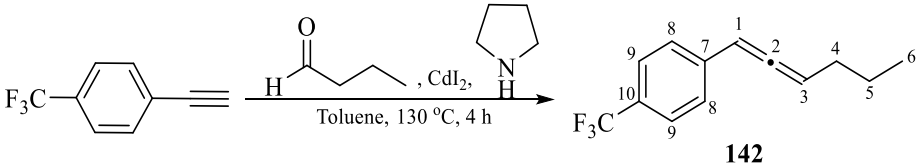


141d

From 4-phenyl-1-butyne (270 µl, 1.92 mmol), isobutyraldehyde (263 µl, 2.88 mmol), Cy_2NH (576 µl, 2.90 mmol), CuI (37 mg, 0.19 mmol) and 3.8 mL of toluene. Obtained after column chromatography using hexane as eluent: **141d**, 277 mg, 1.49 mmol (77%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.31 – 7.26 (m, 2H; H_{Ar}-11), 7.23 – 7.17 (m, 3H; H_{Ar}-10 and H_{Ar}-12), 5.23 – 5.17 (m, 1H; H-1), 5.16 – 5.11 (m, 1H; H-3), 2.73 (t, *J* = 7.8 Hz, 2H; H-8), 2.36 – 2.28 (m, 2H; H-7), 2.29 – 2.20 (m, 1H; H-4), 0.99 (d, *J* = 6.7 Hz, 6H; H-5 and H-6). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 202.5 (C_q; C-2), 142.1 (C_q; C-9), 128.6 (2 x CH_{Ar}; C-10), 128.4 (2 x CH_{Ar}; C-11), 125.9 (CH_{Ar}; C-12), 99.2 (CH; C-3), 91.7 (CH; C-1), 35.7 (CH_2; C-8), 31.0 (CH_2; C-7), 28.1 (CH; C-4), 22.6 (2 x CH_3; C-5 and C-6). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3086 (C-H_{Ar}), 3027 (C-H_{Ar}), 2960 (C-H_{Alkane}), 2925 (C-H_{Alkane}), 2866 (C-H_{Alkane}), 1960 (C=C=C), 1604 (C=C_{Ar}), 1454, 1363 (^{i}Pr), 872. HRMS (FTMS + p APCI (NEAT)): Calc. for $C_{14}H_{19}$ $[M+H]^+$: 187.1481. Found: 187.1480.

<u>Experimental procedure for a modified Crabbé homologation with CdI_2 applied to the synthesis of 1,3-disubstituted allenes</u>

Synthesis of 4-(1,2-hexadien-1-yl)-α,α,α-trifluorotoluene (142)

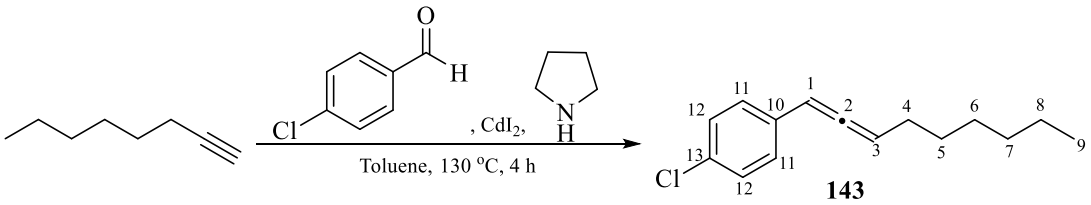


142

The synthesis was undertaken according to a modified procedure described by Ma and coworkers.[29] To a flame-dried Schlenk tube, cadmium iodide (CdI_2) (861 mg, 2.35 mmol, 0.8 Eq.) was added inside a globe box. The Schlenk tube was then taken out, dried under vacuum with a flame until the white CdI_2 turned to yellow-green. Allowed to cool. Dry toluene (12.0 mL), 4-ethynyl-α,α,α-trifluorotoluene (479 µl, 2.94 mmol, 1.0 Eq.), butyraldehyde (477 µl, 5.29 mmol, 1.8 Eq.) and pyrrolidine (343 µl, 4.11 mmol, 1.4 Eq.) were added sequentially under N_2 flow. The Schlenk tube was then equipped with a condenser and placed in a pre-

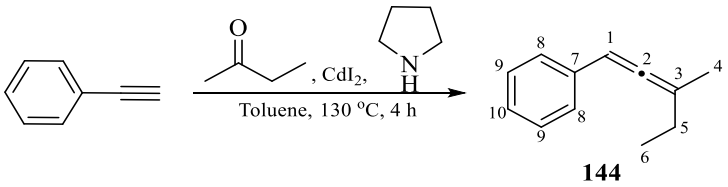
heated oil bath at 130 °C. The reaction mixture was heated at this temperature during 4 h. After cooled down, the crude was filtered through a pad of celite / silica gel (1:1), washed with Et_2O (30 mL) and concentrated under vacuum. The crude of the reaction was purified by column chromatography over silica gel using hexane as eluent. **142**, 202 mg, 0.89 mmol was obtained as a yellow oil (30%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.53 (d, J = 8.2 Hz, 2H; H_{Ar}-9), 7.38 (d, J = 8.2 Hz, 2H; H_{Ar}-8), 6.15 (dt, J = 6.7, 3.0 Hz, 1H; H-1), 5.63 (q, J = 6.7 Hz, 1H; H-3), 2.17 – 2.09 (m, 2H; H-4), 1.56 – 1.47 (m, 2H; H-5), 0.98 (t, J = 7.4 Hz, 3H; H-6). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 206.3 (C_q, C-2), 139.3 (C_q, C-7), 128.6 (q, J_{C-F} = 32.1 Hz; C_q-10), 126.8 (2 x CH_{Ar}; C-8), 125.6 (q, J_{C-F} = 3.8 Hz; 2x CH_{Ar}-9), 124.4 (q, J_{C-F} = 274.9 Hz; CF_3), 95.6 (CH; C-1), 93.9 (CH; C-3), 30.7 (CH_2; C-4), 22.4 (CH_2; C-5), 13.9 (CH_3; C-6). ^{19}F NMR (471 MHz, $CDCl_3$, 25 °C) δ = - 62.36. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3025 (C-H_{Ar}), 2966 (C-H_{Alkane}), 2927 (C-H_{Alkane}), 2853 (C-H_{Alkane}), 1954 (C=C=C), 1618 (C=C_{Ar}), 1457 (C-H_{Alkane}), 1325 (C-F), 1166, 1126, 1067. HRMS (FTMS + ASAP (OIL)): Calc. for $C_{13}H_{12}F_3$ $[M-H]^+$: 225.0886. Found: 225.0887.

Synthesis of 1-chloro-4-(1,2-nonadien-1-yl)-benzene (143)[175]



From 1-octyne (937 µl, 6.35 mmol, 1.0 Eq.), cadmium iodide (CdI_2) (1.9 g, 5.08 mmol, 0.8 Eq.), 4-chlorobenzaldehyde (1.6 g, 11.43 mmol, 1.8 Eq.), pyrrolidine (742 µl, 8.89 mmol, 1.4 Eq.) and dry toluene (26.0 mL). Obtained after column chromatography using hexane as eluent: **143**, 431 mg, 1.84 mmol (29%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.27 – 7.24 (m, 2H; H_{Ar}-12), 7.23 – 7.19 (m, 2H; H_{Ar}-11), 6.08 (dt, J = 6.6, 3.0 Hz, 1H; H-1), 5.58 (q, J = 6.6 Hz, 1H; H-3), 2.16 – 2.09 (m, 2H; H-4), 1.51 – 1.43 (m, 2H; H-5), 1.40 – 1.33 (m, 2H; H-6), 1.33 – 1.22 (m, 4H; H-7 and H-8), 0.88 (t, J = 6.9 Hz, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 205.4 (C_q, C-2), 133.9 (C_q, C-10 or C-13), 132.2 (C_q, C-10 or C-13), 128.8 (2 x CH_{Ar}; C-12), 127.9 (2 x CH_{Ar}; C-11), 95.7 (CH; C-1), 93.8 (CH; C-3), 31.8 (CH_2; C-7 or C-8), 29.2 (CH_2; C-5), 29.0 (CH_2; C-6), 28.8 (CH_2; C-4), 22.8 (CH_2; C-7 or C-8), 14.2 (CH_3; C-9).

Synthesis of (3-methyl-1,2-pentadien-1-yl)-benzene (144)[176]



The synthesis was undertaken according to the procedure described by Ma and co-workers.[29] To a flame-dried Schlenk tube, cadmium iodide (CdI_2) (574 mg, 1.57 mmol, 0.8 Eq.) was added inside a globe box. The Schlenk tube was then taken out, dried under vacuum with a flame until the white CdI_2 turned to yellow-green. Allow to dry. Dry toluene (10.0 mL), phenylacetylene (215 µl, 1.96 mmol, 1.0 Eq.), 2-butanone (193 µl, 2.15 mmol, 1.1 Eq.) and pyrrolidine (180 µl, 215 mmol, 1.1 Eq.) were added sequentially under N_2 flow. The Schlenk tube was then equipped with a condenser and placed in a pre-heated oil bath at 130 ºC. The reaction mixture was heated at this temperature during 4 h. After cooled down, the solution was filtered through a pad of celite / silica gel (1:1), washed with Et_2O (20 mL) and concentrated under vacuum. The crude of the reaction was purified by column chromatography over silica gel using hexane as eluent. **144**, 188 mg, 1.19 mmol was obtained as a yellow oil (61%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.28 – 7.24 (m, 4H; H_{Ar}-8 and H_{Ar}-9), 7.18 – 7.11 (m, 1H; H_{Ar}-10), 6.10 – 6.04 (m, 1H; H-1), 2.14 – 2.02 (m, 2H; H-5), 1.80 (d, *J* = 2.8 Hz, 3H; H-4), 1.05 (t, *J* = 7.4 Hz, 3H; H-6). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 202.5 (C_q, C-2), 136.3 (C_q, C-7), 128.6 (2 x CH_{Ar}; C-8 or C-9), 126.6 (2 x CH_{Ar}; C-8 or C-9), 126.5 (CH_{Ar}; C-10), 105.6 (C_q, C-3), 94.6 (CH; C-1), 27.3 (CH_2; C-5), 18.9 (CH_3; C-4), 12.4 (CH_3; C-6).

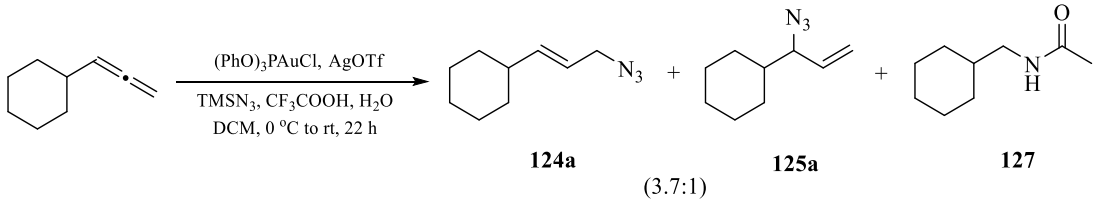
General procedure for gold-catalysed hydroazidation of allenes under best reaction conditions

$(PhO)_3PAuCl$, (0.05 Eq.) and AgOTf (0.05 Eq.) were added into a previously vacuum-dried Schlenk flask under N_2. The solids were dissolved in a small amount of dry dichloromethane and stirred for a few minutes at 0 ºC to preform the cationic complex. Then, the corresponding allene (1.0 Eq., 0.41M - absolute concentration) was added dropwise neat or dissolved in dry DCM at 0 ºC. $TMSN_3$ (3.0 Eq.), distilled water (5.0 Eq.), and CF_3COOH (3.0 Eq.) were sequencially added dropwise at 0 ºC. The mixture was warmed up and stirred at room temperature until complete conversion, followed by TLC. The crude was filtered through celite and washed with dichloromethane. The solvent was removed under vacuum, and the product was purified by column chromatography over basic alumina using Hex / Et_2O or EtOAc as eluent.

Yields were lowered in some cases due to purification issues.

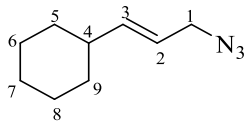
All the products obtained were air stable and in solution, but we kept them in the fridge or freezer and in the dark to avoid decompostion.

Synthesis of allyl azides 124a, 125a and *N*-cyclohexylmethyl-acetamide 127



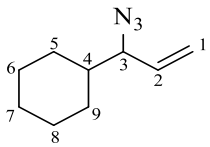
From allene **96b** (119 µl, 0.82 mmol), $(PhO)_3PAuCl$ (22 mg, 0.04 mmol), silver triflate (10 mg, 0.04 mmol), $TMSN_3$ (323 µl, 2.45 mmol), distilled water (74 µl, 4.09 mmol), trifluoroacetic acid (196 µl, 2.45 mmol) and 2.0 mL of dry DCM. Obtained after column chromatography, Hex / EtOAc, (90:1) then (2:1): **124a**:**125a** (3.7:1) as an inseparable mixture, 80 mg, 0.48 mmol (59%): pale-yellow oil, and **127**, 19 mg, 0.12 mmol (15%): yellow oil.

(3-Azido-1-propenyl)-cyclohexane (124a)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.73 – 5.68 (m, 1H; H-3), 5.44 (dtd, J = 15.4, 6.7, 1.3 Hz, 1H; H-2), 3.69 (d, J = 6.7 Hz, 2H; H-1), 2.05 – 1.97 (m, 1H; H-4), 1.77 – 1.63 (m, 5H), 1.32 – 0.94 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 143.2 (CH; C-3), 120.3 (CH; C-2), 53.1 (CH_2; C-1), 40.6 (CH; C-4), 32.9 (2 x CH_2; C-5 and C-9), 26.2 (CH_2; C-7), 26.1 (2 x CH_2; C-6 and C-8).

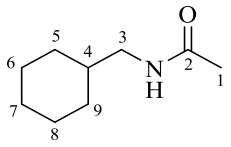
(1-Azido-allyl)-cyclohexane (125a)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.79 – 5.74 (m, 1H; H-2), 5.31 – 5.21 (m, 2H; H-1), 3.60 (t, J = 7.7 Hz, 1H; H-3), 1.69 – 1.78 (m, 5H), 1.41 – 1.35 (m, 1H; H-4), 0.83 – 1.30 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 134.6 (CH; C-2), 119.0 (CH_2; C-1), 71.1 (CH; C-3), 41.8 (CH; C-4), 29.5 (CH_2), 29.4 (CH_2), 26.4 (CH_2), 26.1 (CH_2), 26.0 (CH_2).

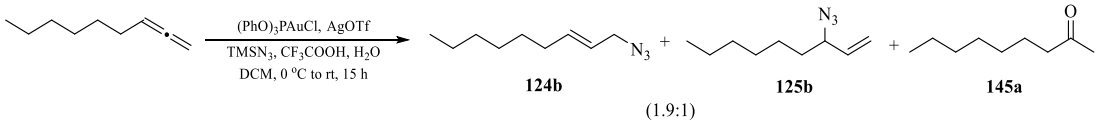
124a and **125a** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 2924 ($C\text{-}H_{Alkane}$), 2097 (N=N=N), 1646 ($C{=}CH_2$), 1450, 1260, 971 ($C{=}C_{(Bend)}$), 802. MS (ESI^+ in MeOH): *m/z* (%): 138.0 $[M\text{-}N_2{+}H]^+$. HRMS (FTMS + APCI): Calc. for $C_9H_{16}N_3$ $[M+H]^+$: 166.1339. Found: 166.1336. Calc. for $C_9H_{16}N_1$ $[M\text{-}N_2{+}H]^+$: 138.1277. Found: 138.1276.

***N*-Cyclohexylmethyl-acetamide (127)**[177]



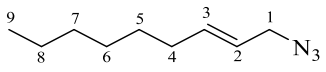
^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.50 (bs, 1H; NH), 3.09 – 3.05 (t, *J* = 6.4 Hz, 2H; H-3), 1.98 (s, 3H, H-1), 1.78 – 1.62 (m, 5H), 1.50 – 1.38 (m, 1H; H-4), 1.29 – 1.09 (m, 3H), 0.99 – 0.83 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 170.2 (C_q; C-2), 46.0 (CH_2; C-3), 38.0 (CH; C-4), 30.9 (CH_2), 26.5 (CH_2), 25.9 (CH_2), 23.5 (CH_3; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3592 (N-H), 3090, 2922 ($C\text{-}H_{Alkane}$), 2851 ($C\text{-}H_{Alkane}$), 1680 (C=O), 1560 ($N\text{-}H_{(Bend)}$), 1448, 1301, 991. HRMS (FTMS + APCI (OIL + NH_4OAc)): Calc. for $C_9H_{18}O_1N_1$ $[M+H]^+$: 156.1383. Found: 156.1380.

Synthesis of allyl azides 124b and 125b and 2-nonanone 145a



From allene **139a** (100 mg, 0.80 mmol), $(PhO)_3PAuCl$ (22 mg, 0.04 mmol), silver triflate (10 mg, 0.04 mmol), $TMSN_3$ (318 µl, 2.42 mmol), distilled water (73 µl, 4.02 mmol), trifluoroacetic acid (193 µl, 2.42 mmol) and 2.0 mL of dry DCM. Obtained after column chromatography, Hex / Et_2O, (60:1) then (2:1): **124b:125b** (1.9:1) as an inseparable mixture, 65 mg, 0.38 mmol (48%): pale-yellow oil, and **145a**, 9 mg, 0.06 mmol (16%): pale-yellow liquid.

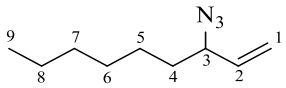
1-Azido-2-nonene (124b)



^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.79 – 5.72 (m, 1H; H-3), 5.51 (dtt, *J* = 15.0, 6.7, 1.4 Hz, 1H; H-2), 3.70 (d, *J* = 6.7 Hz, 2H; H-1), 2.12 – 2.05 (m, 2H; H-4), 1.43 – 1.35 (m, 2H; H-5), 1.35 – 1.23 (m, 6H), 0.88 (t, *J* = 6.6 Hz, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ =

137.5 (CH; C-3), 122.8 (CH; C-2), 53.1 (CH_2; C-1), 32.4 (CH_2; C-4), 31.8 (CH_2; C-5), 29.2 (CH_2), 28.9 (CH_2), 22.7 (CH_2), 14.2 (CH_3; C-9).

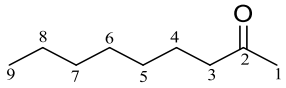
3-Azido-1-nonene (125b)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 5.74 – 5.69 (m, 1H; H-2), 5.28 – 5.24 (m, 2H; H-1), 3.83 – 3.77 (m, 1H; H-3), 1.59 – 1.46 (m, 2H; H-4), 1.44 – 1.38 (m, 2H; H-5), 1.35 – 1.23 (m, 6H), 0.91 – 0.85 (m, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 136.1 (CH; C-2), 118.0 (CH_2; C-1), 65.3 (CH; C-3), 34.4 (CH_2; C-4), 29.1 (CH_2; C-5), 29.0 (CH_2), 25.6 (CH_2), 22.7 (CH_2), 14.2 (CH_3; C-9).

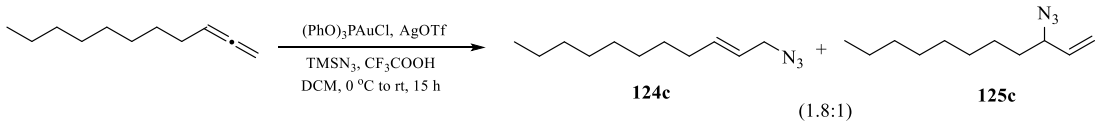
124b and **125b** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3068 (C-H_{Alkene}), 2958, 2929 (C-H_{Alkane}), 2857 (C-H_{Alkane}), 2097 (N=N=N), 1643 (C=C), 1237, 969. HRMS (FTMS + APCI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_9H_{18}N_1$ $[M-N_2+H]^+$: 140.1434. Found: 140.1430

2-nonanone (145a)[178]



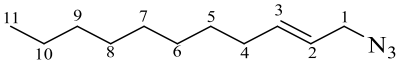
^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 2.41 (t, J = 7.5 Hz, 2H; H-3), 2.13 (s, 3H; H-1), 1.61 – 1.52 (m, 2H; H-4), 1.33 – 1.20 (m, 8H), 0.88 (t, J = 7.0 Hz, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 209.6 (C_q; C-2), 44.0 (CH_2; C-3), 31.8 (CH_2), 30.19 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 24.0 (CH_2), 22.8 (CH_2), 14.2 (CH_3; C-9).

Synthesis of allyl azides 124c and 125c



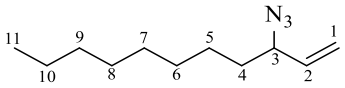
From allene **139b** (50 mg, 0.33 mmol, 0.08 M), $(PhO)_3PAuCl$ (9 mg, 0.02 mmol), silver triflate (4 mg, 0.02 mmol), $TMSN_3$ (131 µl, 0.98 mmol), trifluoroacetic acid (75 µl, 0.98 mmol) and 4.0 mL of dry DCM. Obtained as inseparable mixture after column chromatography, hexane, then Hex / Et_2O, (5:1): **124c**:**125c** (1.8:1), 30 mg, 0.15 mmol (47%): colourless oil.

1-Azido-2-undecene (124c)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.79 – 5.72 (m, 1H; H-3), 5.55 – 5.49 (m, 1H; H-2), 3.69 (d, *J* = 6.7 Hz, 2H; H-1), 2.11 – 2.06 (m, 2H; H-4), 1.61 – 1.46 (m, 2H; H-5), 1.40 – 1.27 (m, 10H), 0.88 (t, *J* = 6.8 Hz, 3H; H-11). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 137.7 (CH; C-3), 123.0 (CH; C-2), 53.3 (CH_2; C-1), 32.6 (CH_2; C-4), 32.2 (CH_2), 29.8 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 23.0 (CH_2), 14.4 (CH_3; C-11).

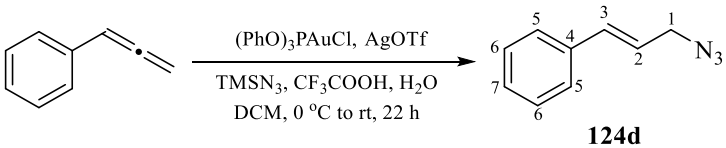
3-Azido-1-undecene (125c)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.77 – 5.72 (m, 1H; H-2), 5.28 – 5.24 (m, 2H; H-1), 3.83 – 3.79 (m, 1H; H-3), 1.59 – 1.23 (m, 12H), 0.88 (t, *J* = 6.8 Hz, 3H; H-11). *Protons of **124c** overlapped with protons of **125c***. ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 136.3 (CH; C-2), 118.2 (CH_2; C-1), 65.5 (CH; C-3), 34.6 (CH_2), 32.2 (CH_2), 30.1 (CH_2), 29.8 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 26.1 (CH_2), 14.4 (CH_3; C-11).

124c and **125c** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 2957 (C-H_{Alkane}), 2926 (C-H_{Alkane}), 2855 (C-H_{Alkane}), 2098 (N=N=N), 1645 (C=C), 1242, 970. HRMS (FTMS + APCI) Calc. for $C_{11}H_{22}N$ $[M\text{-}N_2+H]^+$: 168.1747. Found: 168.1743. Calc. for $C_{11}H_{22}N_3$ $[M+H]^+$: 196.1808. Found: 196.1805. *This synthesis was made by Stefanie Hohne.*

Synthesis of (3-azido-1-propenyl)-benzene (124d)[120c, 179]

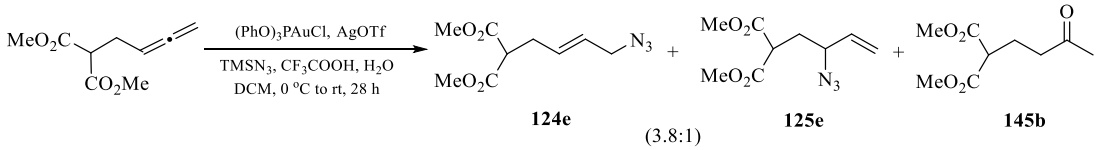


124d

From allene **94a** (100 mg, 0.86 mmol), $(PhO)_3PAuCl$ (23 mg, 0.04 mmol), silver triflate (11 mg, 0.04 mmol), $TMSN_3$ (340 µl, 2.58 mmol), distilled water (78 µl, 4.30 mmol), trifluoroacetic acid (207 µl, 2.58 mmol) and 2.1 mL of dry DCM. Obtained after column chromatography, Hex / Et_2O, (20:1): **124d**, 85 mg, 0.53 mmol (62%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.44 – 7.39 (m, 2H; H_{Ar}-5), 7.37 – 7.32 (m, 2H; H_{Ar}-6), 7.31 – 7.27 (m, 1H; H_{Ar}-7), 6.66 (d, *J* = 15.8 Hz, 1H; H-3), 6.25 (dt, *J* = 15.8, 6.7 Hz, 1H; H-2), 3.95 (dd, *J* = 6.7, 0.7 Hz, 2H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 136.1 (C_q; C-4), 134.7 (CH; C-3), 128.8 (2 x CH_{Ar}; C-5), 128.3 (CH_{Ar}; C-7), 126.8 (2 x CH_{Ar}; C-6), 122.5 (CH; C-2),

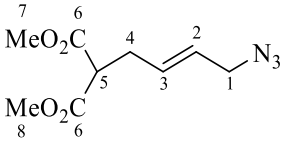
53.2 (CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3029 (C-H_{Alkene}), 2993, 2927 (C-H_{Alkane}), 2099 (N=N=N), 1702, 1654 (C=C), 1598, 1492, 1235, 967. MS-EI: $C_9H_9N_3$ *m/z* (%) 159 [M^+] (3), 118 (31), 117 (100), 115 (32), 105 (20), 91 (28), 77 (20).

Synthesis of allyl azides 124e, 125e and 2-(3-oxo-butyl)-malonic acid dimethyl ester 145b



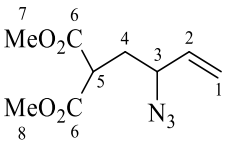
From allene **139c** (100 mg, 0.54 mmol), $(PhO)_3PAuCl$ (15 mg, 0.03 mmol), silver triflate (7 mg, 0.03 mmol), $TMSN_3$ (214 µl, 1.63 mmol), distilled water, (49 µl, 2.72 mmol), trifluoroacetic acid (130 µl, 1.63 mmol) and 1.3 mL of dry DCM. Obtained after column chromatography, Hex / EtOAc, (30:1) then (2:1): **124e:125e** (3.8:1) as inseparable mixture, 53 mg, 0.23 mmol (43%): yellow oil, and **145b**, 19 mg, 0.09 mmol (17%): yellow oil.

2-(4-Azido-2-butenyl)-malonic acid dimethyl ester (124e)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.78 – 5.68 (m, 1H; H-3 or H-2), 5.68 – 5.59 (m, 1H; H-3 or H-2), 3.74 (s, 6H; H-7 and H-8), 3.69 (d, *J* = 6.3 Hz, 2H; H-1), 3.47 (t, *J* = 7.5 Hz, 1H; H-5), 2.68 (m, 2H; H-4). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 169.2 (2 x C_q; C-6), 131.6 (CH; C-3), 126.5 (CH; C-2), 52.8 (CH_2; C-1), 52.5 (CH; C-5), 51.5 (CH_2; C-4), 31.6 (CH_3; C-7 or C-8), 29.9 (CH_3; C-7 or C-8).

2-(2-Azido-3-butenyl)-malonic acid dimethyl ester (125e)

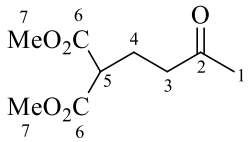


^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.63 – 5.60 (m, 1H; H-2), 5.35 – 5.31 (m, 2H; H-1), 3.75 (s, 6H; H-7 and H-8), 3.57 – 3.05 (m, 1H; H-3), 3.46 – 3.42 (m, 1H; H-5), 2.19 – 2.03 (m, 2H; H-4). *^{13}C NMR signals could not be extracted from the spectra of the mixture 2e+2e' due to the low concentration of 2e'.*

124e and **125e** as inseparable mixture: IR (Film, cm^{-1}): $\tilde{\nu}$ = 2924 (C-H_{Alkane}), 2853 (C-H_{Alkane}), 2099 (N=N=N), 1736 (C=O), 1630 (C=C), 1437, 1260 (C-O), 973, 801, 749. MS (ESI+ in

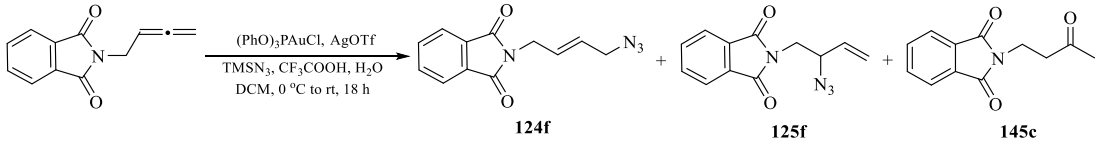
MeOH): m/z = 225.05 $C_9H_{15}KO_4$ $[M\text{-}N_3\text{+}K\text{+}H]^+$. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_9H_{17}N_4O_4$ $[M\text{+}NH_4]^+$: 245.1244 Found: 245.1247.

2-(3-Oxo-butyl)-malonic acid dimethyl ester (145b)[180]



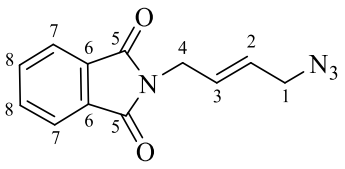
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC, TMS) δ = 3.72 (s, 6H; H-7), 3.43 (t, J = 7.2 Hz, 1H; H-5), 2.53 (t, J = 7.2 Hz, 2H; H-3), 2.17 (m, 2H; H-4), 2.13 (s, 3H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 207.2 (C_q; C-2), 169.7 (2 C_q; C-6), 52.7 (2 x CH_3; C-7), 50.4 (CH; C-5), 40.5 (CH_2; C-3), 30.1 (CH_3; C-1), 22.6 (CH_2; C-4). IR (Film, cm^{-1}): $\tilde{\nu}$ = 2941 (C-H_{Alkane}), 2854 (C-H_{Alkane}), 1732 (C=O), 1436, 1275 (C-O), 1156 (C-O), 750. HRMS (FTMS + p APCI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_9H_{18}NO_5$ $[M\text{+}NH_4]^+$: 220.1179 Found: 220.1176.

Synthesis of allyl azides 124f, 125f and *N*-(3-oxo-butyl)-phtalimide 145c



From allene **139d** (100 mg, 0.50 mmol), $(PhO)_3PAuCl$ (14 mg, 0.02 mmol), silver triflate (6 mg, 0.02 mmol), $TMSN_3$ (198 µl, 1.51 mmol), distilled water (45 µl, 2.51 mmol), trifluoroacetic acid (172 µl, 1.51 mmol) and 1.2 mL of dry DCM. Obtained after column chromatography, Hex / EtOAc, (10:1) then (2:1): **124f**, 55 mg, 0.23 mmol (48%): yellow oil; **125f**, 9 mg, 0.04 mmol (7%): yellow oil; **145c**, 35 mg, 0.16 mmol (32%): white solid.

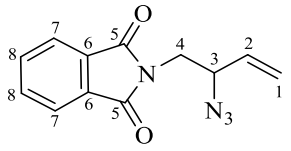
***N*-(4-Azido-2-butenyl)-phtalimide (124f)**



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.89 – 7.84 (m, 2H; H_{Ar}-7 or H_{Ar}-8), 7.75 – 7.71 (m, 2H; H_{Ar}-7 or H_{Ar}-8), 5.89 – 5.73 (m, 1H; H-3), 5.83 (dtt, J = 15.4, 5.6, 1.1 Hz, 1H; H-2), 4.33 (dd, J = 5.6, 1.1 Hz, 2H; H-4), 3.77 (d, J = 5.6 Hz, 2H; H-1); ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 167.9 (2 x C_q; C-5), 134.2 (2 x CH_{Ar}; C-7 or C-8), 132.2 (2 x C_q; C-6), 128.4 (CH; C-3), 127.4 (CH; C-2), 123.5 (2 x CH_{Ar}; C-7 or C-8), 52.1 (CH_2; C-1), 38.9 (CH_2; C-4). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3070 (C-H_{Alkene}), 2922 (C-H_{Alkane}), 2851 (C-H_{Alkane}), 2097 (N=N=N), 1771 (C=O),

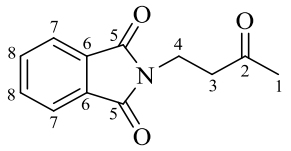
1710, 1626 (C=C), 1466, 1426, 1391, 1187, 949. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{12}H_{14}N_5O_2$ $[M+NH_4]^+$: 260.1142 Found: 260.1145.

***N*-(2-Azido-3-butenyl)-phtalimide (125f)**



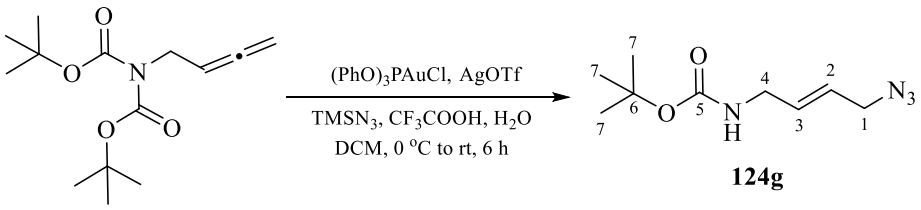
^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.89 – 7.85 (m, 2H; H_{Ar}- 7 or H_{Ar}-8), 7.77 – 7.69 (m, 2H; H_{Ar}-7 or H_{Ar}-8), 5.86 – 5.77 (m, 1H; H-2), 5.42 – 5.38 (m, 1H; H-1), 5.38 – 5.36 (m, 1H; H-1), 4.37 – 4.30 (m, 1H; H-3), 3.83 (dd, *J* = 13.9, 8.3 Hz, 1H; H-4), 3.72 (dd, *J* = 13.9, 6.3 Hz, 1H; H-4). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 168.2 (2 x C_q; C-5), 134.3 (2 x CH_{Ar}; C-7 or C-8), 132.7 (CH; C-2), 132.0 (2 x C_q, C-6), 123.7 (2 x CH_{Ar}; C-7 or C-8), 121.2 (CH_2; C-1), 62.5 (CH; C-3), 40.9 (CH_2; C-4). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3034 (C-H_{Alkene}), 2923 (C-H_{Alkane}), 2852 (C-H_{Alkane}), 2098 (N=N=N), 1771 (C=O), 1717, 1614 (C=CH_2), 1466, 1426, 1391, 717. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{12}H_{14}N_5O_2$ $[M+NH_4]^+$: 260.1142 Found: 260.1143.

***N*-(3-Oxo-butyl)-phtalimide (145c)**[181]



^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.86 – 7.81 (m, 2H; H_{Ar}-7 or H_{Ar}-8), 7.74 – 7.68 (m, 2H; H_{Ar}-7 or H_{Ar}-8), 3.98 – 3.93 (m, 2H; H-4), 2.87 (t, *J* = 7.4 Hz; 1H, H-3), 2.18 (s, 3H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 205.9 (C_q; C-2), 168.2 (2 x C_q; C-5), 134.2 (2 x CH_{Ar}; C-7 or C-8), 132.2 (2 x C_q; C-6), 123.4 (2 x CH_{Ar}; C-7 or C-8), 41.7 (CH_2; C-4), 33.1 (CH_2; C-3), 30.1 (CH_3; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3095 (C-H_{Ar}), 2957 (C-H_{Alkane}), 2926 (C-H_{Alkane}), 2856 (C-H_{Alkane}), 1709 (C=O), 1634 (C=C_{Ar}), 1467, 1435, 1260, 1029. HRMS (FTMS + p APCI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{12}H_{12}NO_3$ $[M+H]^+$: 218.0812 Found: 218.0810. M.P. = 111 – 113 °C.

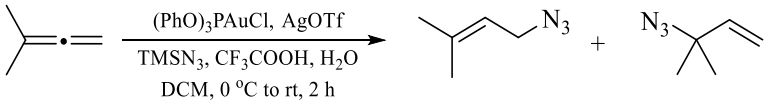
Synthesis of (4-azido-2-butenyl)-carbamic acid tert-butyl ester (124g)



124g

From allene **139e** (100 mg, 0.39 mmol), $(PhO)_3PAuCl$ (11 mg, 0.02 mmol), silver triflate (5 mg, 0.02 mmol), $TMSN_3$ (154 µl, 1.17 mmol), distilled water (35 µl, 1.96 mmol), trifluoroacetic acid (94 µl, 1.17 mmol) and 957 µl of dry DCM. Obtained after column chromatography, Hex / EtOAc, (10:1): **124g**, 32 mg, 0.15 mmol (38%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.80 – 5.76 (m, 1H; H-3 or H-2), 5.76 – 5.71 (m, 1H; H-3 or H-2), 4.15 – 4.11 (m, 2H; H-4 or H-1), 4.11 – 4.06 (m, 2H; H-4 or H-1), 1.47 (s, 9H; H-7). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 154.5 (C_q; C-5), 126.0 (CH; C-2 or C-3), 125.9 (CH; C-2 or C-3), 79.4 (C_q; C-6), 53.2 (CH_2; C-1 or C-4), 53.0 (CH_2; C-1 or C-4), 28.7 (3 x CH_3; C-7). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3332 (N-H), 2976 (C-H_{Alkane}), 2925 (C-H_{Alkane}), 2853 (C-H_{Alkane}), 2100 (N=N=N), 1706 (C=O), 1685 (C=C), 1609 (N-$H_{(Bend)}$), 1410, 1368 (*t*-Bu), 1257, 1170, 887. *HRMS could not be obtained due to rapid decomposition of this product.*

Synthesis of allyl azides 124h and 125h

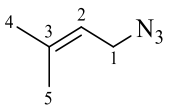


124h **125h**

(3.7:1)

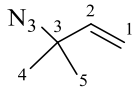
From allene **120** (20 mg, 0.29 mmol), $(PhO)_3PAuCl$ (8 mg, 0.01 mmol), silver triflate (4 mg, 0.01 mmol), $TMSN_3$ (116 µl, 0.88 mmol), distilled water (26 µl, 1.47 mmol), trifluoroacetic acid (70 µl, 0.88 mmol) and 718 µl of dry DCM. Obtained: 100% conversion **124h:125h** (3.7:1). *This product could not be isolated due to volatility issues.*

1-Azido-3-methyl-2-butene (124h)[120d, 120e]



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.35 – 5.29 (m, 1H; H-2), 3.76 (d, *J* = 7.5 Hz, 2H; H-1), 1.79 (s, 3H; H-4 or H-5), 1.71 (s, 3H; H-4 or H-5). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 130.7 (C_q; C-3), 117.3 (CH; C-2), 48.3 (CH_2; C-1), 25.7 (CH_3; C-4 or C-5), 18.0 (CH_3; C-4 or C-5).

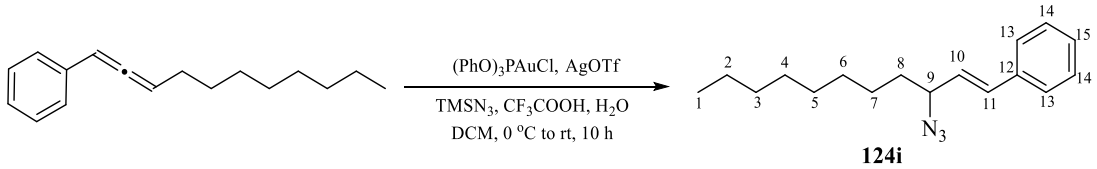
3-Azido-3-methyl-1-butene (125h)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 5.85 (dd, J = 17.3, 10.6 Hz, 1H; H-2), 5.22 (dd, J = 17.3, 0.5 Hz, 1H; H-1), 5.16 (dd, J = 10.6, 0.5 Hz, 1H; H-1), 1.33 (s, 6H; H-4 and H-5). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 141.1 (CH; C-2), 114.0 (CH_2; C-1), 62.4 (C_q; C-3), 26.0 (2 x CH_3; C-4 and C-5).

124h and **125h** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 2962 (C-H_{Alkane}), 2905 (C-H_{Alkane}), 2109 (N=N=N), 1679 (C=C), 1587, 1484, 1261, 1092, 1025, 940.

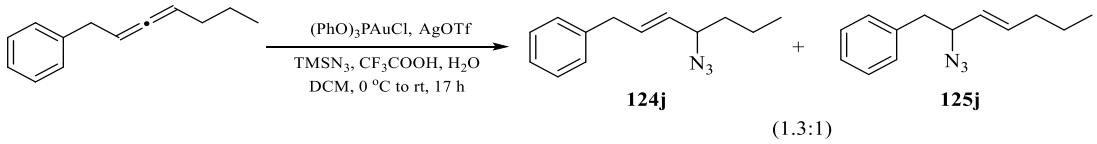
Synthesis of (3-azido-1-undecenyl)-benzene (124i)



124i

From allene **140** (100 mg, 0.44 mmol), $(PhO)_3PAuCl$ (12 mg, 0.02 mmol), silver triflate (6 mg, 0.02 mmol), $TMSN_3$ (173 µl, 1.31 mmol), distilled water (39 µl, 2.19 mmol), trifluoroacetic acid (105 µl, 1.31 mmol) and 1.1 mL of dry DCM. Obtained after column chromatography, using as eluent hexane: **124i**, 91 mg, 0.33 mmol (76%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.43 – 7.40 (m, 2H; H_{Ar}-13), 7.37 – 7.32 (m, 2H; H_{Ar}-14), 7.30 – 7.26 (m, 1H; H_{Ar}-15), 6.61 (d, J = 15.8 Hz, 1H; H-11), 6.12 (dd, J = 15.8, 8.1 Hz, 1H; H-10), 4.00 (q, J = 7.2 Hz, 1H; H-9), 1.70 – 1.56 (m, 2H; H-8), 1.45 – 1.36 (m, 2H; H-7), 1.36 – 1.23 (m, 10H), 0.91 – 0.87 (m, 3H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 136.2 (C_q; C-12), 133.2 (CH; C-11), 128.8 (2 x CH_{Ar}; C-14), 128.2 (CH_{Ar}; C-15), 127.5 (CH; C-10), 126.8 (2 x CH_{Ar}; C-13), 65.1 (CH; C-9), 34.9 (CH_2; C-8), 32.0 (CH_2; C-7), 29.6 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 26.1 (CH_2), 22.8 (CH_2), 14.2 (CH_3; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3061 (C-H_{Alkene}), 3028 (C-H_{Ar}), 2957 (C-H_{Alkane}), 2927 (C-H_{Alkane}), 2856 (C-H_{Alkane}), 2097 (N=N=N), 1599 (C=C), 1494 (C-H_{Alkane}), 1466, 1450, 1260, 1095, 966, 803, 749 (C=$C_{(Bend)}$), 692. HRMS (FTMS + p APCI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{17}H_{26}N_1$ $[M–N_2+H]^+$: 244.2060 Found: 244.2056. Calc. for $C_{17}H_{25}$ $[M–N_3]^+$: 229.1951 Found: 229.1948.

Synthesis of allyl azides 124j and 125j

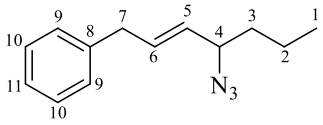


124j **125j**

(1.3:1)

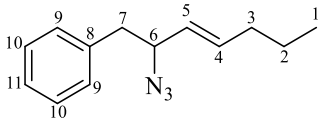
From allene **141a** (100 mg, 0.58 mmol), $(PhO)_3PAuCl$ (16 mg, 0.03 mmol), silver triflate (7 mg, 0.03 mmol), $TMSN_3$ (229 µl, 1.74 mmol), distilled water (52 µl, 2.90 mmol), trifluoroacetic acid (139 µl, 1.74 mmol) and 1.4 mL of dry DCM. Obtained as inseparable mixture after column chromatography, using as eluent hexane: **124j**:**125j** (1.3:1), 84 mg, 0.39 mmol (67%): yellow oil.

(4-Azido-2-heptenyl)-benzene (124j)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.35 – 7.25 (m, 2H; H_{Ar}), 7.25 – 7.22 (m, 1H; H_{Ar}-11), 7.21 – 7.17 (m, 2H; H_{Ar}), 5.90 – 5.84 (m, 1H; H-6), 5.49 – 5.44 (m, 1H; H-5), 3.84 (q, *J* = 7.3 Hz, 1H; H-4), 3.49 – 3.38 (m, 2H; H-7), 1.59 – 1.44 (m, 2H; H-3), 1.44 – 1.33 (m, 2H; H-2), 0.88 (t, *J* = 7.3 Hz, 3H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 139.7 (C_q; C-8), 133.7 (CH; C-6), 129.5 (CH; C-5), 128.7 (2 x CH_{Ar}), 128.7 (2 x CH_{Ar}), 126.8 (CH_{Ar}; C-11), 64.5 (CH; C-4), 38.7 (CH_2; C-7), 36.8 (CH_2; C-3), 22.4 (CH_2; C-2), 13.9 (CH_3; C-1).

(2-Azido-3-heptenyl)-benzene (125j)

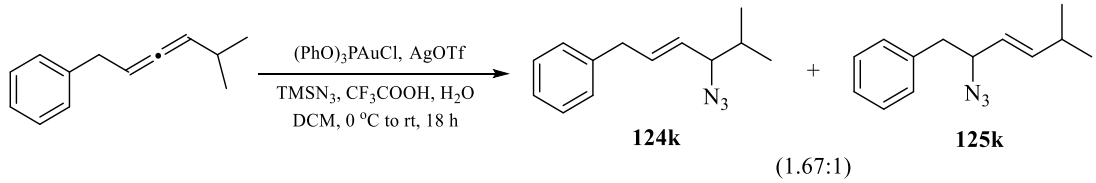


^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.35 – 7.28 (m, 2H; H_{Ar}), 7.25 – 7.22 (m, 1H; H_{Ar}-11), 7.21 – 7.17 (m 2H; H_{Ar}), 5.70 – 5.63 (m, 1H; H-4), 5.43 – 5.39 (m, 1H; H-5), 4.05 (q, *J* = 7.3 Hz, 1H; H-6), 2.80 (d, *J* = 7.3 Hz, 2H; H-7), 2.08 – 2.00 (m, 2H; H-3), 1.44 – 1.33 (m, 2H; H-2), 0.92 (t, *J* = 7.3 Hz, 3H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 137.7 (C_q; C-8), 135.9 (CH; C-4), 129.6 (2 x CH_{Ar}), 128.5 (2 x CH_{Ar}), 127.3 (CH; C-5), 126.4 (CH_{Ar}; C-11), 65.9 (CH; C-6), 41.5 (CH_2; C-7), 34.4 (CH_2; C-3) 19.3 (CH_2; C-2), 13.6 (CH_3; C-1).

124j and **125j** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3098 (C-H_{Alkene}), 3045 (C-H_{Ar}), 2960 (C-H_{Alkane}), 2931 (C-H_{Alkane}), 2873 (C-H_{Alkane}), 2097 (N=N=N), 1603 (C=C), 1454 (C-

H_{Alkane}), 1237, 970, 747 ($C{=}C_{(Bend)}$), 698. HRMS (FTMS + p APCI (OIL + NH_4OAc)): Calc. for $C_{13}H_{21}N_4$ $[M+NH_4]^+$: 233.1761 Found: 233.1760.

Synthesis of allyl azides 124k and 125k

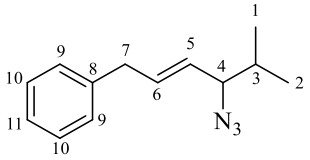


124k **125k**

(1.67:1)

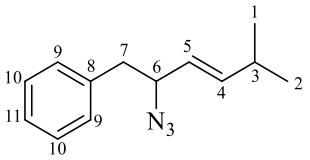
From allene **141b** (86 mg, 0.50 mmol), $(PhO)_3PAuCl$ (14 mg, 0.02 mmol), silver triflate (6 mg, 0.02 mmol), $TMSN_3$ (197 µl, 1.50 mmol), distilled water (45 µl, 2.50 mmol), trifluoroacetic acid (120 µl, 1.50 mmol) and 1.2 mL of dry DCM. Obtained as an inseparable mixture after column chromatography, using as eluent hexane: **124k**:**125k** (1.67:1), 59 mg, 0.27 mmol (55%): yellow oil.

(4-Azido-5-methyl-2-hexenyl)-benzene (124k)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.34 – 7.29 (m, 2H; H_{Ar}), 7.25 – 7.17 (m, 3H; H_{Ar}), 5.88 (dtd, *J* = 15.2, 6.9, 0.6 Hz, 1H; H-6), 5.48 (ddt, *J* = 15.2, 8.5, 1.5 Hz, 1H; H-5), 3.63 (dd, *J* = 8.5, 6.9 Hz, 1H; H-4), 3.48 – 3.44 (m, 2H; H-7), 1.79 – 1.67 (m, 1H; H-3), 0.95 (d, *J* = 6.9 Hz, 3H; H-1 or H-2), 0.91 (d, *J* = 6.9 Hz, 3H; H-1 or H-2). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 139.8 (C_q; C-8), 134.8 (CH; C-6), 128.7 (2 x CH_{Ar}), 128.7 (2 x CH_{Ar}), 127.8 (CH; C-5), 126.4 (CH_{Ar}; C-11), 71.1 (CH; C-4), 38.8 (CH_2; C-7), 32.7 (CH; C-3), 19.0 (CH_3; C-1 or C-2), 19.0 (CH_3; C-1 or C-2).

(2-Azido-5-methyl-3-hexenyl)-benzene (125k)

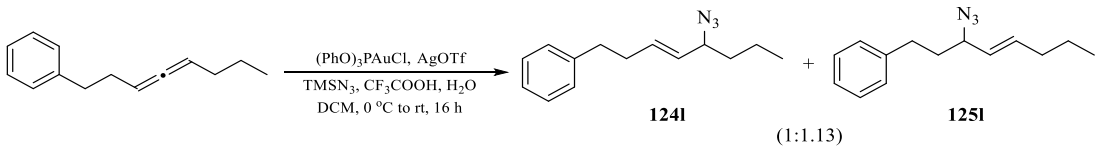


^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.36 – 7.28 (m, 2H; H_{Ar}), 7.25 – 7.18 (m, 3H; H_{Ar}), 5.64 (ddd, *J* = 15.4, 6.8, 0.6 Hz, 1H; H-4), 5.37 (ddd, *J* = 15.4, 8.1, 1.3 Hz, 1H; H-5), 4.06 – 4.00 (m, 1H; H-6), 2.83 – 2.79 (m, 2H; H-7), 2.37 – 2.28 (m, 1H; H-3), 1.00 (d, *J* = 6.8 Hz, 3H; H-1 or H-2), 0.99 (d, *J* = 6.8 Hz, 3H; H-1 or H-2). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ

= 143.0 (CH; C-4), 137.7 (C_q; C-8), 129.6 (2 x CH_{Ar}), 128.5 (2 x CH_{Ar}), 126.8 (CH_{Ar}; C-11), 124.1 (CH; C-5), 65.8 (CH; C-6), 41.5 (CH_2; C-7), 31.0 (CH; C-3), 22.5 (CH_3; C-1 or C-2), 22.4 (CH_3; C-1 or C-2).

124k and **125k** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3064(C-H_{Alkene}), 3030 (C-H_{Ar}), 2962 (C-H_{Alkane}), 2929 (C-H_{Alkane}), 2095 (N=N=N), 1610 (C=C), 1454 (C-H_{Alkane}), 1260, 1094, 1029, 803, 699 (C=$C_{(Bend)}$). HRMS (FTMS + p APCI (OIL + NH_4OAc)): Calc. for $C_{13}H_{21}N_4$ $[M+NH_4]^+$: 233.1761 Found: 233.1760.

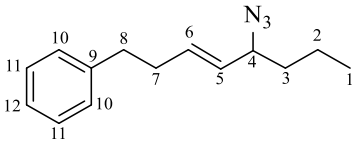
Synthesis of allyl azides 124l and 125l



124l **125l** (1:1.13)

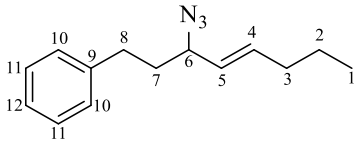
From allene **141c** (100 mg, 0.54 mmol), $(PhO)_3PAuCl$ (15 mg, 0.03 mmol), silver triflate (7 mg, 0.03 mmol), $TMSN_3$ (212 µl, 1.61 mmol), distilled water (48 µl, 2.69 mmol), trifluoroacetic acid (129 µl, 1.61 mmol) and 1.3 mL of dry DCM. Obtained as inseparable mixture after column chromatography, using as eluent hexane: **124l**:**125l** (1:1.13), 85 mg, 0.37 mmol (70%): yellow oil.

(5-Azido-3-octenyl)-benzene (124l)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.33 – 7.27 (m, 2H; H_{Ar}), 7.23 – 7.16 (m, 3H; H_{Ar}), 5.77 – 5.68 (m, 1H; H-6), 5.41 – 5.33 (m, 1H; H-5), 3.78 – 3.74 (m, 1H; H-4), 2.77 – 2.70 (m, 2H; H-8), 2.47 – 2.37 (m, 2H; H-7), 1.55 – 1.47 (m, 2H; H-3), 1.36 – 1.25 (m, 2H; H-2), 0.90 (t, J = 7.4 Hz, 3H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 141.5 (C_q; C-9), 134.3 (CH; C-6), 128.7 (CH; C-5), 128.7 (2 x CH_{Ar}), 128.5 (2 x CH_{Ar}), 126.1 (CH_{Ar}; C-12), 64.6 (CH; C-4), 36.8 (CH_2; C-3), 35.8 (CH_2; C-8), 34.1 (CH_2; C-7), 19.2 (CH_2; C-2), 13.8 (CH_3; C-1).

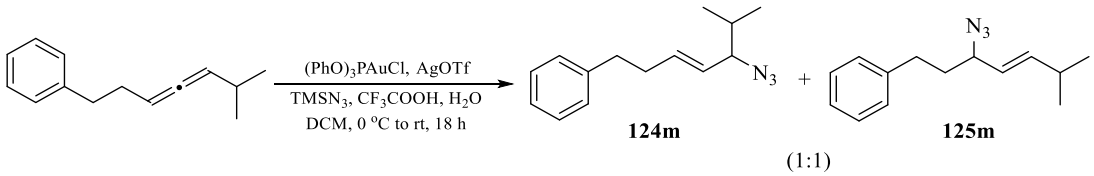
(3-Azido-4-octenyl)-benzene (125l)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.33 – 7.27 (m, 2H; H_{Ar}), 7.23 – 7.16 (m, 3H; H_{Ar}), 5.74 – 5.67 (m, 1H; H-4), 5.44 – 5.38 (m, 1H; H-5), 3.82 – 3.78 (m, 1H; H-6), 2.70 – 2.65 (m, 2H; H-8), 2.11 – 2.05 (m, 2H; H-3), 1.91 – 1.75 (m, 2H; H-7), 1.47 – 1.41 (m, 2H; H-2), 0.93 (t, J = 7.4 Hz; 3H, H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 141.3 (C_q; C-9), 136.0 (CH; C-4), 128.6 (4 x CH_{Ar}; C-10 and C-11), 127.6 (CH; C-5), 126.2 (CH_{Ar}; C-12), 64.1 (CH; C-6), 36.4 (CH_2; C-7), 34.4 (CH_2; C-3), 32.2 (CH_2; C-8), 22.4 (CH_2; C-2), 13.7 (CH_3; C-1).

124l and **125l** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3064 (C-H_{Alkene}), 3028 (C-H_{Ar}), 2960 (C-H_{Alkane}), 2932 (C-H_{Alkane}), 2873 (C-H_{Alkane}), 2095 (N=N=N), 1604 (C=C), 1455 (C-H_{Alkane}), 1238, 1030, 970, 747 (C=$C_{(Bend)}$). HRMS (FTMS+ p APCI (OIL + NH_4OAc)): Calc. for $C_{14}H_{23}N_4$ $[M+NH_4]^+$: 247.1917. Found 247.1917, Calc. for $C_{14}H_{20}N_1$ $[M–N_2+H]^+$: 202.1590. Found 202.1591.

Synthesis of allyl azides 124m and 125m

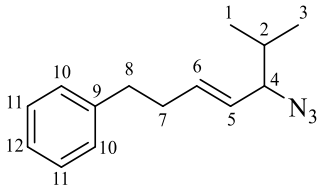


124m **125m**

(1:1)

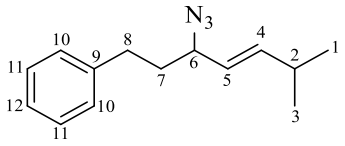
From allene **141d** (100 mg, 0.54 mmol), $(PhO)_3PAuCl$ (15 mg, 0.03 mmol), silver triflate (7 mg, 0.03 mmol), $TMSN_3$ (212 µl, 1.61 mmol), distilled water (48 µl, 2.69 mmol), trifluoroacetic acid (129 µl, 1.61 mmol) and 1.3 mL of dry DCM. Obtained as inseparable mixture after column chromatography, using as eluent hexane: **124m**:**125m** (1:1), 98 mg, 0.43 mmol (80%): yellow oil.

(5-Azido-6-methyl-3-heptenyl)-benzene (124m)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.33 – 7.27 (m, 2H; H_{Ar}), 7.23 – 7.16 (m, 3H; H_{Ar}), 5.76 – 5.71 (m, 1H; H-6), 5.43 – 5.37 (m, 1H; H-5), 3.55 (dd, *J* = 8.5, 6.8 Hz, 1H; H-4), 2.80 – 2.71 (m, 2H; H-8), 2.49 – 2.40 (m, 2H; H-7), 1.71 – 1.63 (m, 1H; H-2), 0.90 (d, *J* = 6.8 Hz, 3H; H-1 or H-3), 0.84 (d, *J* = 6.8 Hz, 3H; H-1 or H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 141.3 (C_q; C-9), 135.3 (CH; C-6), 128.6 (2 x CH_{Ar}), 128.5 (2 x CH_{Ar}), 126.9 (CH; C-5), 126.2 (CH_{Ar}; C-12), 71.3 (CH; C-4), 35.9 (CH_2; C-8), 34.1 (CH_2; C-7), 32.6 (CH; C-2), 19.0 (CH_3; C-1 or C-3), 18.9 (CH_3; C-1 or C-3).

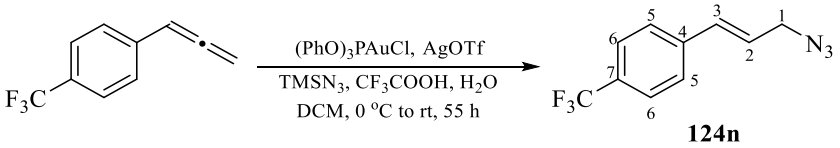
(3-Azido-6-methyl-4-heptenyl)-benzene (125m)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.33 – 7.27 (m, 2H; H_{Ar}), 7.23 – 7.16 (m, 3H; H_{Ar}), 5.71 – 5.67 (m, 1H; H-4), 5.38 – 5.32 (m, 1H; H-5), 3.80 – 3.73 (m, 1H; H-6), 2.71 – 2.64 (m, 2H; H-8), 2.39 – 2.32 (m, 1H; H-2), 1.91 – 1.75 (m, 2H; H-7), 1.04 (dd, *J* = 6.8, 2.0 Hz, 6H; H-1 and H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 143.2 (CH; C-4), 141.5 (C_q; C-9), 128.6 (4 x CH_{Ar}; C-10 and C-11), 126.1 (CH_{Ar}; C-12) 124.4 (CH; C-5), 64.0 (CH; C-6), 36.4 (CH_2; C-7), 32.2 (CH_2; C-8), 31.1 (CH; C-2), 22.6 (CH_3; C-1 or C-3), 22.5 (CH_3; C-1 or C-3).

124m and **125m** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3064 (C-H_{Alkene}), 3028 (C-H_{Ar}), 2961 (C-H_{Alkane}), 2927 (C-H_{Alkane}), 2870 (C-H_{Alkane}), 2095 (N=N=N), 1603 (C=C), 1454 (C-H_{Alkane}), 1367 (^{i}Pr), 1241, 971, 747 (C=$C_{(Bend)}$). HRMS (FTMS+ p APCI (OIL + NH_4OAc)): Calc. for $C_{14}H_{23}N_4$ $[M+NH_4]^+$: 247.1917. Found: 247.1917.

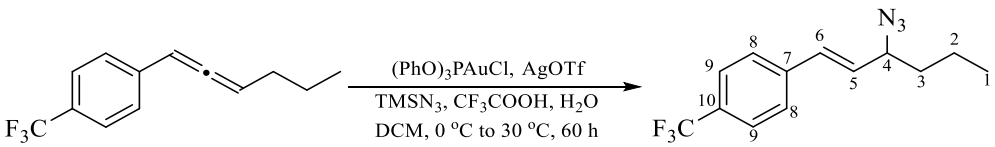
Synthesis of 1-(3-azido-1-propenyl)-4-trifluoromethyl-benzene (124n)[121b]



124n

From allene **139f** (100 mg, 0.54 mmol), $(PhO)_3PAuCl$ (15 mg, 0.03 mmol), silver triflate (7 mg, 0.03 mmol), $TMSN_3$ (214 µl, 1.63 mmol), distilled water (49 µl, 2.72 mmol), trifluoroacetic acid (186 µl, 1.63 mmol) and 1.3 mL of dry DCM. The reaction was then warmed up at 30 °C during 55 h. Obtained after column chromatography using Hex / Et_2O (80:1) as eluent. **124n**, 91 mg, 0.40 mmol (74%): pale-yellow oil. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.59 (d, J = 8.2 Hz, 2H; H_{Ar}-6), 7.50 (d, J = 8.2 Hz, 2H; H_{Ar}-5), 6.69 (d, J = 15.8 Hz, 1H; H-3), 6.33 (dt, J = 15.8, 6.4 Hz, 1H; H-2), 3.99 (dd, J = 6.4, 0.8 Hz, 2H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 139.6 (C_q; C-4), 132.9 (CH; C-3), 130.1 (q, $J_{C\text{-}F}$ = 32.4 Hz, C_q; C-7), 126.9 (2 x CH_{Ar}; C-5), 125.8 (q, $J_{C\text{-}F}$ = 3.8 Hz, 2 x CH_{Ar}-6), 125.4 (CH; C-2), 124.2 (q, $J_{C\text{-}F}$ = 271.9 Hz, CF_3) , 52.9 (CH_2; C-1). ^{19}F NMR (471 MHz, $CDCl_3$) δ = - 62.59. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3098 (C-H_{Alkene}), 3042 (C-H_{Ar}), 2927 (C-H_{Alkane}), 2855 (C-H_{Alkane}), 2102 (N=N=N), 1616 (C=C), 1415 (C-H_{Alkane}), 1326 (C-F), 1124, 1016, 748 (C=$C_{(Bend)}$).

Synthesis of 1-(3-azido-1-hexenyl)-4-trifluoromethyl-benzene (124o)

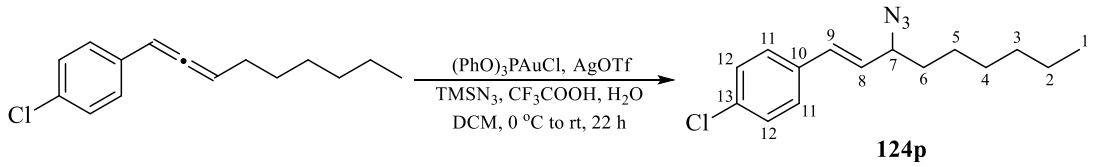


124o

From allene **142** (100 mg, 0.44 mmol), $(PhO)_3PAuCl$ (12 mg, 0.02 mmol), silver triflate (6 mg, 0.02 mmol), $TMSN_3$ (174 µl, 1.32 mmol), distilled water (40 µl, 2.21 mmol), trifluoroacetic acid (106 µl, 1.32 mmol) and 1.1 mL of dry DCM. The reaction was then warmed up at 30 °C during 60 h. Obtained after column chromatography using pentane / Et_2O (80:1) as eluent. **124o**, 79 mg, 0.30 mmol (67%): yellow oil. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.59 (d, J = 8.2 Hz, 2H; H_{Ar}-9), 7.50 (d, J = 8.2 Hz, 2H; H_{Ar}-8), 6.64 (d, J = 15.8 Hz, 1H; H-6), 6.20 (dd, J = 15.8, 7.8 Hz, 1H; H-5), 4.07 – 4.01 (m, 1H; H-4), 1.71 – 1.55 (m, 2H; H-3), 1.51 – 1.37 (m, 2H; H-2), 0.96 (t, J = 7.3 Hz, 3H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 139.7 (C_q, C-7), 131.7 (CH; C-6), 130.2 (CH; C-5), 130.0 (q, $J_{C\text{-}F}$ = 32.5 Hz; C_q; C-10), 127.9 (2 x CH_{Ar}; C-8), 125.8 (q, $J_{C\text{-}F}$ = 3.8 Hz; 2 x CH_{Ar}; C-9), 124.2 (q, $J_{C\text{-}F}$ = 271.9 Hz; CF_3), 64.4 (CH; C-4), 36.9 (CH_2; C-3), 19.3 (CH_2; C-2), 13.9 (CH_3; C-1). ^{19}F NMR (471 MHz, $CDCl_3$) δ = - 62.58. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3088 (C-H_{Alkene}), 3021 (C-H_{Ar}), 2963 (C-H_{Alkane}), 2936 (C-H_{Alkane}), 2876 (C-H_{Alkane}), 2100 (N=N=N), 1617 (C=C), 1325 (C-F), 1166, 1067, 967, 748

(C=$C_{(Bend)}$). HRMS (FTMS + p APCI (OIL + NH_4OAc)): Calc. for $C_{13}H_{15}F_3N$ $[M–N_2+H]^+$: 242.1151. Found: 242.1148. Calc. for $C_{13}H_{14}F_3$ $[M–N_3]^+$: 227.1042. Found: 227.1040. Calc. for $C_{13}H_{14}F_3N_3$ $[M]^+$: 269.1140. Found: 269.1143.

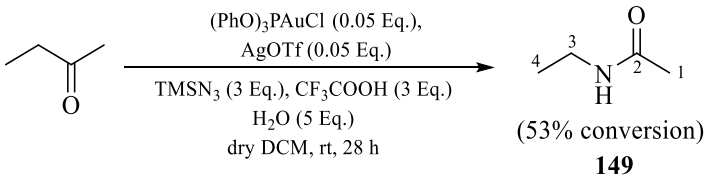
Synthesis of 1-(3-azido-1-nonenyl)-4-chloro-benzene (124p)



124p

From allene **143** (107 mg, 0.46 mmol), $(PhO)_3PAuCl$ (12 mg, 0.02 mmol), silver triflate (6 mg, 0.02 mmol), $TMSN_3$ (180 µl, 1.37 mmol), distilled water (41 µl, 2.28 mmol), trifluoroacetic acid (109 µl, 1.37 mmol) and 1.1 mLof dry DCM. Obtained after column chromatography using Hex / Et_2O (80:1) as eluent. **124p**, 91 mg, 0.33 mmol (72%): yellow oil. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.34 – 7.32 (m, 2H; H_{Ar}-12), 7.31 – 7.29 (m, 2H; H_{Ar}-11), 6.55 (d, *J* = 15.8 Hz, 1H; H-9), 6.08 (dd, *J* = 15.8, 8.0 Hz, 1H; H-8), 4.01 – 3.95 (m, 1H; H-7), 1.70 – 1.53 (m, 2H; H-6), 1.44 – 1.21 (m, 8H), 0.89 (t, *J* = 7.0 Hz, 3H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 134.7 (C_q; C-10 or C-13), 133.9 (C_q; C-10 or C-13), 131.9 (CH; C-9), 129.0 (2 x CH_{Ar}), 128.2 (CH; C-8), 128.0 (2 x CH_{Ar}), 64.9 (CH; C-7), 34.9 (CH_2; C-6), 31.8 (CH_2; C-5), 29.1 (CH_2; C-4), 26.0 (CH_2; C-3), 22.7 (CH_2; C-2), 14.2 (CH_3; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3082 (C-H_{Alkene}), 3011 (C-H_{Ar}), 2956 (C-H_{Alkane}), 2929 (C-H_{Alkane}), 2857 (C-H_{Alkane}), 2097 (N=N=N), 1603 (C=C), 1491 (C-H_{Alkane}), 1238, 1091, 967, 750 (C=$C_{(Bend)}$). HRMS (T: +p EI) : Calc. for $C_{15}H_{21}{}^{35}ClN$ $[M–N_2+H]^+$: 250.1357. Found: 250.1354. Calc. for $C_{15}H_{21}{}^{37}ClN$ $[M–N_2+H]^+$: 252.1328. Found: 252.1323. Calc. for $C_{15}H_{20}{}^{35}Cl$ $[M–N_3]^+$: 235.1248. Found: 235.1247. Calc. for $C_{15}H_{20}{}^{37}Cl$ $[M–N_3]^+$: 237.1219. Found: 237.1215. $C_{15}H_{20}{}^{35}ClN_3$ $[M]^+$: 277.1346 Found: 277.1346.

Gold-catalysed Schmidt reaction of ethyl methyl ketone[182]



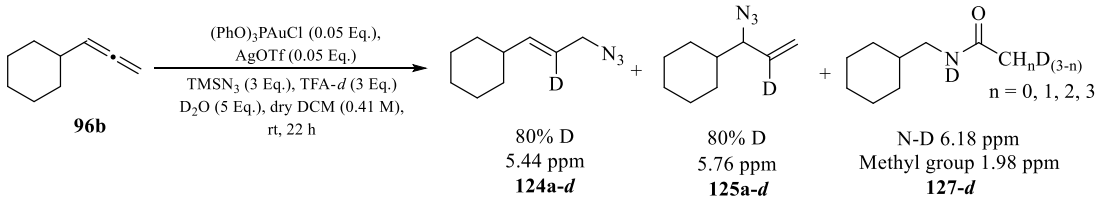
(53% conversion)

149

$(PhO)_3PAuCl$ (16 mg, 0.03 mmol, 0.05 Eq.) and silver triflate (8 mg, 0,03 mmol, 0.05 Eq.) were added under N_2 into a vacuum-dried Schlenk flask. The solids were dissolved in 1.4 mL of dry DCM and stirred for a few minutes at 0 °C. Then ethyl methyl ketone (62 µl, 0.58 mmol, 1.0 Eq., 0.41 M – absolute concentration) was added dropwise at 0 °C. $TMSN_3$ (229 µl, 1.74 mmol, 3.0 Eq.), distilled water (52 µl, 2.90 mmol, 5.0 Eq.) and CF_3COOH, (139 µl, 1.74

mmol, 3.0 Eq.) were sequentially added dropwise at 0 ºC. The mixture was then warmed up at room temperature and stirred for 28 h. The crude was filtered through celite, and washed with dichloromethane. The solvent was removed under vacuum, and the crude was analysed without purification by ^{1}H NMR. A 53% conversion to *N*-ethylacetamide **149** was observed.[183] ^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 6.87 (bs, 1H; NH), 3.41 – 3.32 (m, 2H; H-3), 2.17 (s, 3H; H-1), 1.19 (t, J = 7.2 Hz, 3H; H-4).

Experimental procedure for the deuteration experiment



$(PhO)_3PAuCl$ (22 mg, 0.04 mmol, 0.05 Eq.) and silver triflate (10.5 mg, 0.04 mmol, 0.05 Eq.) were added into a washed with D_2O and flame-vacuum-dried Schlenk flask under N_2. The solids were dissolved in dry DCM (2.0 mL) and stirred for a few minutes at 0 ºC. Then, allene **96b** (119 µl, 0.82 mmol, 1.0 Eq., 0.41 M – absolute concentration) was added dropwise to the Schlenk flask. $TMSN_3$ (323 µl, 2.45 mmol, 3.0 Eq.), D_2O (74 µl, 4.09 mmol 5.0 Eq.) and TFA-*d* (189 µl, 2.45 mmol, 3.0 Eq.) were sequencially added dropwise at 0 ºC. The mixture was then warmed up at room temperature and stirred during 22 h. The crude was filtered through celite and the solvent was removed under vacuum. The mixture was analysed by ^{1}H and ^{2}H NMR in $CDCl_3$ without purification.

We observed deuterium incorporation in the following positions:

124a-*d*: the signal at 5.44 ppm showed 80% of deuterium incorporation.

125a-*d*: the signal at 5.76 ppm showed 80% of deuterium incorporation.

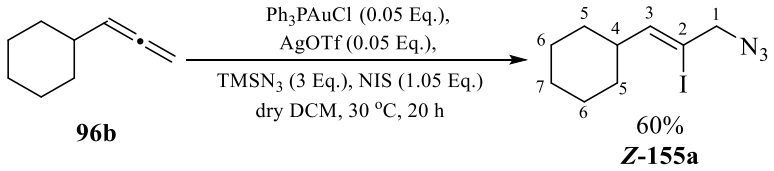
127-*d*: we observed deuterium incorporation at the amidic proton 6.18 ppm, before purification and a mixture of d_0, d_1, d_2, d_3 in the signal at 1.98 ppm (methyl group).

General procedure for gold-catalysed iodoazidation of allenes

The Au(I)-complex (0.05 Eq.), silver triflate (0.05 Eq.) and NIS (1.05 Eq.) were added into a vacuum-dried Schlenk flask under N_2. The corresponding allene (1.0 Eq., 0.1 M) in dry DCM and $TMSN_3$ (3.0 Eq.) were added sequentially and stirred for a few minutes at 0 ºC. The mixture was then warmed up at 30 ºC and stirred until complete conversion, followed by TLC. The crude was filtered through celite and washed with DCM. The solvent was removed under

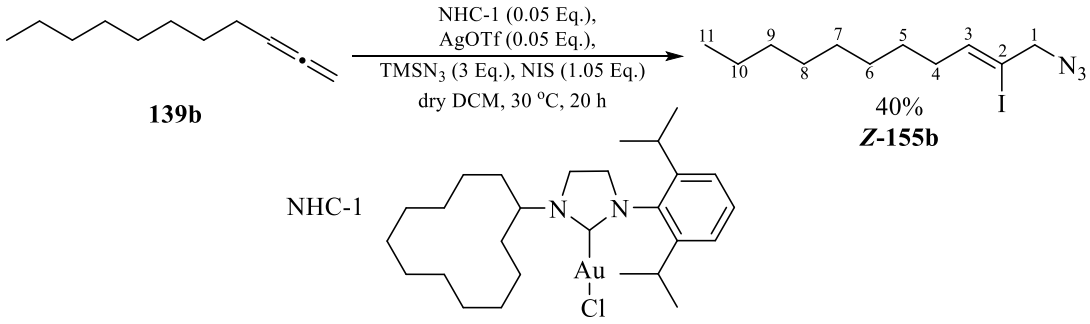
vacuum, and the product was purified by column chromatography over silica gel using Hex / Et_2O as eluent.

Synthesis of (3-azido-2-iodo-1-propenyl)-cyclohexane (*Z*-155a)



From allene **96b** (60 µl, 0.41 mmol, 0.41 M), Ph_3PAuCl (10 mg, 0.02 mmol), silver triflate (5 mg, 0.02 mmol), $TMSN_3$ (163 µl, 1.23 mmol), NIS (96 mg, 0.43 mmol.) and 4.0 mL of dry DCM. The reaction was then warmed up at 30 °C during 20 h. Obtained after column chromatography, Hex / EtOAc (50:1) then (20:1) then (1:1). ***Z*-155a**, 72 mg, 0.25 mmol (60%): pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25° C) δ = 5.68 (d, J = 8.6 Hz, 1H; H-3), 4.05 (s, 2H; H-1), 2.22 – 2.32 (m, 1H; H-4), 1.63 – 1.77 (m, 5H), 1.11 – 1.40 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C) δ = 145.2 (CH; C-3), 96.6 (C_q; C-2), 62.7 (CH_2; C-1), 45.2 (CH; C-4), 31.6 (2 x CH_2; C-5), 25.9 (CH_2; C-7), 25.6 (2 x CH_2; C-6). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3011 (C-H_{Alkene}), 2926 (C-H_{Alkane}), 2815 (C-H_{Alkane}), 2096 (N=N=N), 1635 (C=C), 1448 (C-H_{Alkane}), 1318, 1029, 893, 838. MS (ESI$^+$ in MeOH): *m/z* (%) = 264.0 [M-N_2+H]$^+$. HRMS (FTMS + p APCI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_9H_{18}IN_4$ [M+NH_4]$^+$, 309.0569. Found, 309.0571.

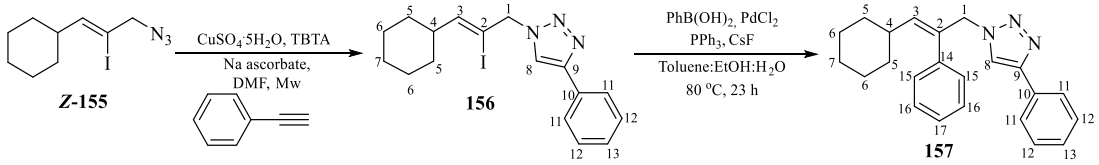
Synthesis of 1-azido-2-iodo-2-undecene (*Z*-155b)



From allene **139b** (50 mg, 0.33 mmol, 0.08 M), NHC-1 (10 mg, 0.02 mmol), silver triflate (4 mg, 0.02 mmol), $TMSN_3$ (131 µl, 0.99 mmol), NIS (76 mg, 0.34 mmol) and 4.0 mL of dry DCM. The reaction was then warmed up at 30 °C and stirred during 4 days. Obtained after column chromatography, Hex / EtOAc, (100:1). ***Z*-155b**, 42 mg, 0.13 mmol (40%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.87 (tt, J = 6.6, 0.9 Hz, 1H; H-3), 4.08 (s, 2H; H-1), 2.18 (m, 2H; H-4), 1.30 – 1.27 (m, 12H), 0.88 (t, J = 6.9 Hz, 3H; H-11). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 139.2 (CH; C-3), 98.2 (C_q; C-2), 61.5 (CH_2; C-1), 34.9 (CH_2;

C-4), 30.8 (CH_2), 28.3 (CH_2), 28.2 (CH_2), 28.1 (CH_2), 27.0 (CH_2), 21.6 (CH_2), 13.1 (CH_3; C-11). IR (Film, cm^{-1}): $\tilde{\nu}$ = 2955 (C-H_{Alkane}), 2925 (C-H_{Alkane}), 2855 (C-H_{Alkane}), 2099 (N=N=N), 1639 (C=C), 1465 (C-H_{Alkane}), 1269, 889, 829, 722 (C=$C_{(Bend)}$). MS (ESI^+ in MeOH): m/z = 321.0 $[M]^+$, 322.0 $[M+H]^+$. HRMS (FTMS p APCI (DCM + NH_4OAc)): Calc. for $C_{11}H_{20}IN_3$ $[M^+]$, 321.0696. Found, 321.0693. Calc. for $C_{11}H_{21}IN$ $[M-N_2+H]^+$, 294.0713. Found, 294.0714. *This synthesis was performed by Stefanie Hohne.*

Orthogonal functionalization of allenes using the gold-catalysed azidation methodology

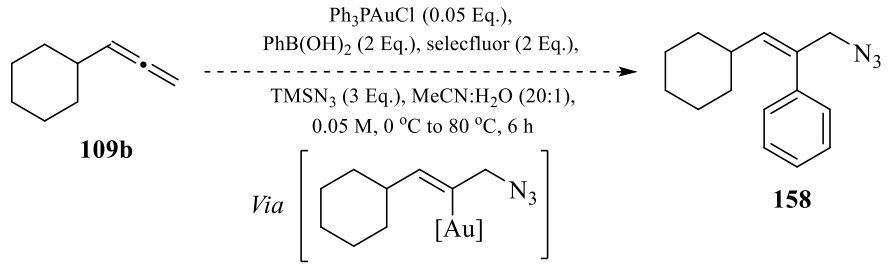


1-(3-Cyclohexyl-2-iodo-allyl)-4-phenyl-1*H*-[1,2,3]triazoles (156). Copper(II) sulfate pentahydrate (9 mg, 0.04 mmol, 0.15 Eq.), sodium ascorbate (38 mg, 0.19 mmol, 0.8 Eq.) and tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA) (19 mg, 0.04 mmol, 0.15 Eq.) were added into a (2.0-5.0 mL) microwave vial. Then (*Z*)-(3-azido-2-iodoprop-1-en-1-yl)cyclohexane ***Z*-155a** (70 mg, 0.24 mmol 1.0 Eq.) dissolved in 3.0 mL of DMF and phenylacetylene (30 µl, 0.24 mmol, 1.0 Eq.) were added. The microwave vial was sealed and the suspension was heated in the microwave at 70 °C for 1 h. The reaction mixture was quenched with water and extracted with DCM (x 3). The combined organic phases were dried over anhydrous sodium sulfate and filtered. After removing the solvent in vacuum the product was purified by column chromatography over silica gel with Hex / EtOAc (5:1) then (3:1) as eluent. **156**, 54 mg, 0.14 mmol was obtained as a pale-yellow solid (57%). ^{1}H NMR (500 MHz, $CDCl_3$, 25° C) δ = 7.77 (d, *J* = 7.5 Hz, 2H; H_{Ar}-11), 7.72 (s, 1H; H-8), 7.35 (t, *J* = 7.5 Hz, 2H; H_{Ar}-12), 7.26 (t, *J* = 7.5 Hz, 1H; H_{Ar}-13), 5.70 (d, *J* = 8.5 Hz ,1H; H-3), 5.17 (s, 2H; H-1), 2.20 (m, 1H; H-4), 1.68 – 1.62 (m, 4H; H-5), 1.17 – 1.11 (m, 6H; H-6 and H-7). ^{13}C NMR (126 MHz, $CDCl_3$, 25° C) δ = 147.9 (C_q; C-9), 146.5 (CH; C-3), 130.5 (C_q; C-10), 128.8 (2 x CH_{Ar}; C-12), 128.2 (CH_{Ar}; C-13), 125.7 (2 x CH_{Ar}; C-11), 119.5 (CH; C-8), 95.3 (C_q; C-2), 61.7 (CH_2; C-1), 45.1 (CH; C-4), 31.1 (2 x CH_2; C-5), 25.7 (CH_2; C-7), 25.3 (2 x CH_2; C-6). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3023 (C-H_{Alkene}), 2923 (C-H_{Alkane}), 2850 (C-H_{Alkane}), 1638 (C=C), 1447 (C-H_{Alkane}), 1345, 1225, 1075, 1044, 973, 762 (C=$C_{(Bend)}$). HRMS (FTMS p NSI ((DCM / MeOH + NH_4OAc)): Calc. for $C_{17}H_{20}IN_3$ $[M+H]^+$, 394.0775. Found, 394.0775.

1-(3-Cyclohexyl-2-phenyl-allyl)-4-phenyl-1*H*-[1,2,3]triazoles (157). Phenylboronic acid (22 mg, 0.18 mmol, 2.0 Eq.), $PdCl_2$ (0.8 mg, 0.005 mmol, 0.05 Eq.), PPh_3 (2.4 mg, 0.009 mmol, 0.1 Eq.) and CsF (27 mg, 0.18 mmol, 2.0 Eq.) were added into a N_2 flushed Schlenk flask. Then (*Z*)-1-(3-cyclohexyl-2-iodoallyl)-4-phenyl-1*H*-1,2,3-triazole **156** (36 mg, 0.09

mmol, 1.0 Eq.) dissolved in a mixture of toluene : EtOH : H_2O (1.3 mL : 1.3 mL : 0.4 mL) was added. The mixture was degassed by bubbling N_2 into the solution for 5 minutes and then stirred at 80 °C for 18 h. The reaction mixture was quenched with H_2O and extracted with DCM (x 3). The combined organic phases were dried over anhydrous sodium sulfate and filtered. After removing the solvent in vacuum the product was purified by column chromatography over silica gel and Hex / EtOAc (5:1) as eluent. **157**, 26 mg, 0.07 mmol, was obtained as a white-yellow solid (85%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.68 (dd, *J* = 7.4, 1.2 Hz, 2H; H_{Ar}-11), 7.47 (s, 1H; H-8), 7.31(t, *J* = 7.4 Hz, 2H; H_{Ar}-12), 7.27 – 7.20 (m, 2H; H_{Ar}-16), 7.20 – 7.13 (m, 2H; H_{Ar}-13 and H_{Ar}-17), 7.00 (dd, *J* = 6.8, 1.5 Hz, 2H; H_{Ar}-15), 5.54 (d, *J* = 10.1 Hz; 1H, H-3), 5.11 (s, 2H; H-1), 2.04 – 1.98 (m, 1H; H-4), 1.62 – 1.57 (m, 5H), 1.09 – 1.02 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 147.7 (C_q, C-9), 139.8 (CH; C-3), 137.5 (C_q, C-14), 133.2 (C_q, C-2), 130.9 (C_q; C-10), 128.8 (2 x CH_{Ar}), 128.7 (2 x CH_{Ar}), 128.4 (2 x CH_{Ar}), 128.1 (CH_{Ar}; C-13), 127.7 (CH_{Ar}; C-17), 125.8 (2 x CH_{Ar}; C-11), 119.5 (CH; C-8), 57.9 (CH_2; C-1), 37.7 (CH; C-4), 33.1 (2 x CH_2; C-6), 25.9 (CH_2; C-7), 25.5 (2 x CH_2; C-5). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3098 (C-H_{Ar}), 2924 (C-H_{Alkane}), 2850 (C-H_{Alkane}), 1646 (C=C), 1608 (C=C_{Ar}), 1444 (C-H_{Alkane}), 1338, 1225, 973, 764 (C=$C_{(Bend)}$). HRMS (FTMS p APCI ((DCM) / MeOH + NH_4OAc)): Calc. for $C_{23}H_{25}N_3$ $[M+H]^+$, 344.2127. Found, 344.2121. M. P. = 128 – 130 ºC. *This synthesis was performed by María Paz Muñoz.*

Attempts to trap the vinyl-gold intermediate via oxidative cross-coupling



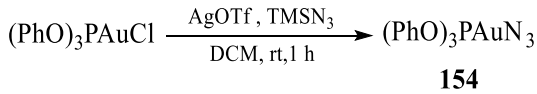
The oxidative cross-coupling was attempted using Zhang's conditions:[184]

Ph_3PAuCl (10 mg, 0.02 mmol, 0.05 Eq.), selectfluor (290 mg, 0.82 mmol, 2.0 Eq.) and $PhB(OH)_2$ (200 mg, 1.64 mmol, 4.0 Eq.) were added into a vacuum-dried Schlenk flask under N_2. The solids were dissolved in 8.2 mL of a mixture MeCN / H_2O (20:1) and stirred for a few minutes at 0 ºC. Then, **96b** (60 µl, 0.41 mmol, 1.0 Eq., 0.05 M – absolute concentration) and $TMSN_3$ (161 µl, 1.23 mmol, 3.0 Eq.) were added dropwise at 0 ºC (ice bath). The mixture was then warmed up at 80 ºC following the reaction by TLC. After 6 h the crude was filtered through a pad of celite / $MgSO_4$, washed with DCM and concentrated under vacuum. The crude was analysed by NMR. However no signals corresponding of the expected product **158** were observed. The allene signals disappeared possibly by decomposition at 80 ºC.

A second experiment was carried out under the conditions of our azidation reaction:

$(PhO)_3PAuCl$, (11 mg, 0.02 mmol, 0.05 Eq.), silver triflate (5 mg, 0.02 mmol, 0.05 Eq.), selectfluor (290 mg, 0.82 mmol, 2.0 Eq.) and $PhB(OH)_2$ (200 mg, 1.64 mmol, 4.0 Eq.) were added into a vacuum-dried Schlenk flask under N_2. The solids were dissolved in 1.0 mL of dry DCM and stirred for a few minutes at 0 ºC. Then, allene **96b** (60 µl, 0.41 mmol, 1.0 Eq., 0.41 M – absolute concentration) and $TMSN_3$ (161 µl, 1.23 mmol, 3.0 Eq.) were added dropwise at 0 ºC. The mixture was warmed up at room temperature, following the reaction by TLC. After 6 h the crude was filtered through celite, washed with DCM and concentrated under vacuum. The crude was analysed by NMR. Signals of the unreacted allene and phenyl boronic acid were observed.

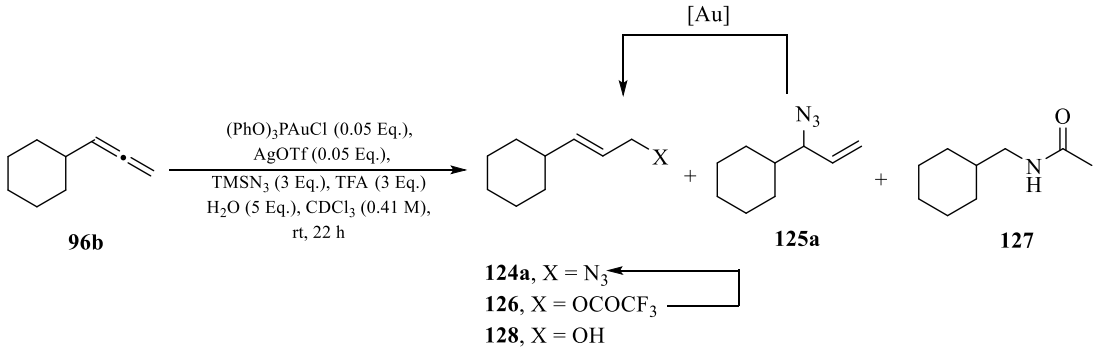
Synthesis of gold-azide complex (154)



154

$(PhO)_3PAuCl$ (15 mg, 0.03 mmol, 1.0 Eq., 0.015 M), and AgOTf (7 mg, 0.03 mmol, 1.0 Eq.) were dissolved in 2.0 mL of dry DCM under N_2. An excess of $TMSN_3$ (29 µl, 0.22 mmol, 8.0 Eq.) was added and the mixture was stirred at room temperature for 1 h. The reaction crude was filtered through celite and concentrated under vacuum. The solid was washed with hexane to remove the excess of azide to give $(PhO)_3PAuN_3$ (**154**) as a gummy oil. This complex has to be kept in the fridge and in the dark but decomposed very quickly. No HRMS could be obtained due to fast decomposition. All the attempts to crystallise the complex have failed so far. ^1H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.43 (app t, J = 7.4 Hz, 6H), 7.31 (tq, J = 7.4, 1.2 Hz, 3H), 7.23 (app dd, J = 7.4, 1.2 Hz, 6H). ^{31}P NMR (202 MHz, $CDCl_3$, 25º C): δ = 105.8 ppm. IR (Film, cm^{-1}): $\tilde{\nu}$ = 2060 (N=N=N).[156b, 185]

Catalytic NMR experiment



$(PhO)_3PAuCl$, (0.05 Eq., 22 mg, 0.04 mmol), AgOTf, (0.05 Eq., 10.5 mg, 0.04 mmol) and (1 Eq., 119 µl, 0.82 mmol) of allene **96b** in $CDCl_3$ (2.0 mL, 0.41 mM) were added into a dried-vacuum Schlenk flask under innert atmosphere and stirred for a few minutes at 0ºC. Then, $TMSN_3$, (3.0 Eq., 323 µl, 2.45 mmol), distilled water, (5.0 Eq., 74 µl, 4.09 mmol), and trifluoroacetic acid, (3.0 Eq., 196 µl, 114.02 mmol) were added dropwise at 0 ºC. The mixture was then warmed up and stirred at room temperature during 22 h. Samples (0.1 mL) were extracted directly from the Schlenk according to the time with a syringe and diluted with $CDCl_3$ for the NMR experiment.

Chapter 3.

Platinum-catalysed carbo- and heterocyclisation of 1,5-bisallenes.

3.1. Introduction

In this chapter, platinum catalysts and the new reactivity we have encountered with 1,5-bisallenes will be studied in depth. Platinum is known to be the most precious metal. Its high value resides from its extensive use in industrial applications and the scarce amount extracted in mines.

Platinum is a malleable and ductile metal, very heavy and with excellent high temperature features. Moreover, this metal is unaffected by air or water (corrosion resistant) and HCl or HNO_3. However, it can be dissolved in aqua regia, concentrated acids and alkalis. Because of its inactivity to air and water, platinum is a suitable metal to be employed in jewellery or in medical devices, sensors, thermocouples, petrochemical reforming, silicone industry and in high temperature engineering.[186] Half of the bulk extracted of this novel metal is employed as a catalysts in vehicles, because it is highly effective in oxidation reactions it can transform harmful emissions of carbon monoxide into CO_2 and H_2O due to its high melting point.

Platinum also has a remarkable use in coordination chemistry. The *cis*-diaminedichloro-platinum(II) and its derivatives are currently the most widely used anticancer drugs. In contrast, platinum salts can produce negative health effects such as DNA alterations, damage to organs, or even cancer.[187] In catalysis, platinum has been essential in heterogeneous catalytic reactions.[188] However, platinum complexes have also been employed in homogeneous catalysis. They are generally considered as a π-acid, activating unsaturated moieties such as alkenes, alkynes, dienes and allenes, they are also involved in cycloisomerisations, intra- and intermolecular additions to the activated π-systems as well as being applied to the synthesis of bioactive natural products.[189]

The wide versatility of platinum is remarkable in many branches of the chemistry. However, following the trend of the present thesis only the platinum-catalysed intermolecular addition of external nucleophiles to allenes will be covered.

Platinum and gold display similar reactivities with allenes, and in both cases their general behaviour is as a Lewis acid, activating the π-systems of the allene, favouring the nucleophilic addition to the activated allenic carbon.

Generally, platinum-allene interactions occur *via* η^2-coordination, with a symmetric or unsymmetric coordination such as **159**, **160**, **161** (Figure **26**) depending on the electronic properties of the ligand or the allene's substituents.[190] However, η^1-coordination modes with the platinum only coordinated to the central carbon of the allene have also been proposed, such

as η^1-bent-allene **164**, the allyl cation **162** or the zwitterionic carbene **163**, recently postulated by our group (Figure **26**).[191]

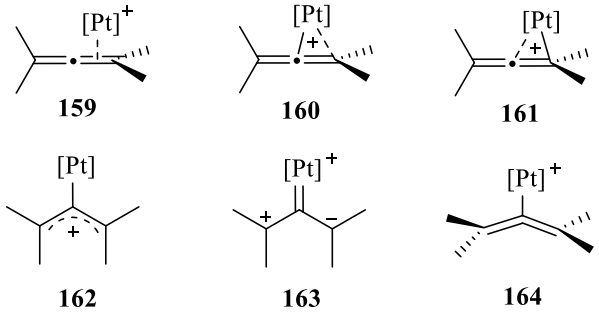
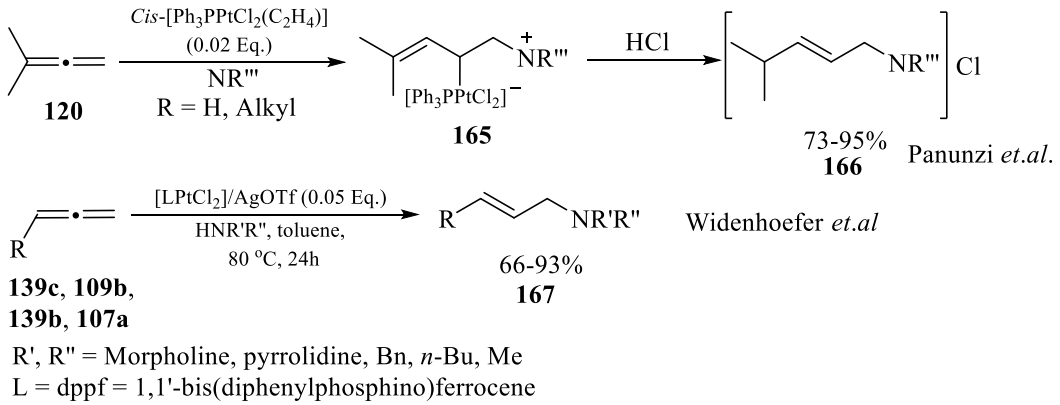


Figure 26. Platinum-allene coordination modes

3.2. Platinum-catalysed intermolecular reactions of allenes

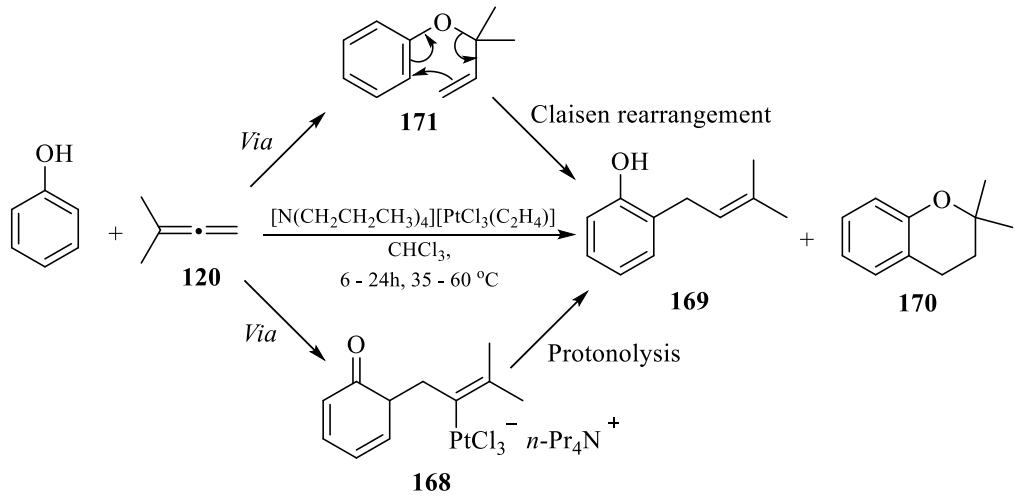
Intramolecular formation of C-C or C-X bonds (X = heteroatoms) catalysed by platinum is a well-known method for cycloisomerisations towards the formation of carbo- and heterocycles with high atom economy and excellent yields.[189b, 189d, 189e, 192] In contrast, the intermolecular addition of external nucleophiles to allenes catalysed by platinum complexes is less explored; therefore, this chapter will outline this interesting topic.

The first intermolecular addition of nucleophiles to allenes catalysed by platinum complexes was reported by the group of Panunzi in 1978,[193] using amines as nucleophiles and dimethylallene as the substrate. In this case, platinum complexes activate the less hindered C=C of the allene, favouring the subsequent attack of the amine to afford the isolated platinum σ-alkenyl complexes $(Ph_3P)PtCl_2(\eta^1\text{-}Me_2C{=}CCH_2NR_3)$ **165** (Scheme **79**). This intermediate was then exposed to acidic conditions (HCl) to give the desired *E*-allyl amines **166**. Similar results have been obtained by the group of Widenhoefer, using $Pt(dppf)Cl_2$/AgOTf as the catalytic source, exclusively with monoallenes as substrates (Scheme **79**). The authors proposed an outer-sphere mechanism in this reaction, where η^2-coordination of the catalytic platinum complex with the less hindered double bond of the allene drives the addition of alkylated secondary amines generating a *Z*-vinyl-platinum intermediate, which after Pt-C cleavage forms *E*-allyl amines **167**.



Scheme 79. Platinum-catalysed intermolecular addition of nitrogen nucleophiles.

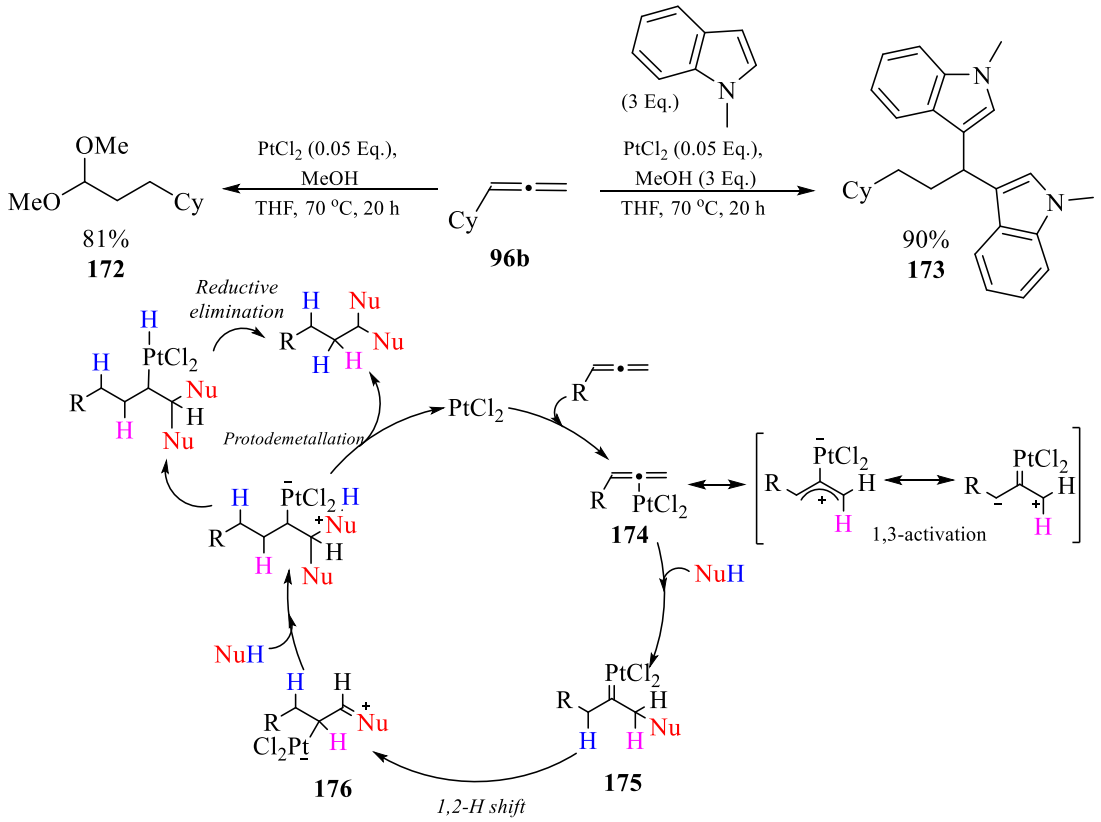
Oxygen nucleophiles were also employed by the group of Panunzi,[194] using 1,1-dimethylallene **120** and phe. However, instead of the expected oxygen attack to the allene, the phenol behaves as an electron-rich aromatic nucleophile leading to the attack at the less hindered sp^2-carbon of the allene to form the vinyl-platinum intermediate **168** (Scheme **80**), and giving the corresponding allylated product **169** as well as chroman derivatives **170** in low yields. The authors proposed, that the allylated derivative **169** is obtained first, and this cyclises to chromane **170**. Also, if the phenol acts as an oxygen nucleophile, the intermediate generated from oxygen attack to the hindered carbon of the allene **171** and a subsequent Claisen rearrangement also can generate the allylated product **169**.



Scheme 80. Platinum-catalysed alkenylation of phenols with 1,1-dimethylallenes

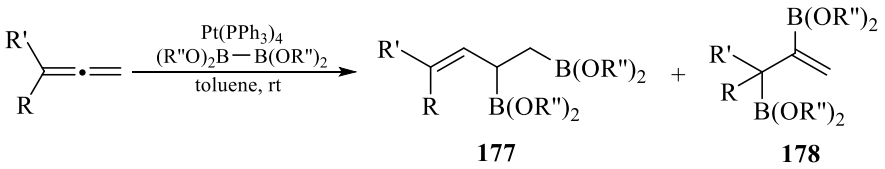
Our group has developed a new platinum-catalysed addition of nucleophiles to allenes, showing a different reactivity than previously observed. In this reaction, a selective double addition of alcohols or indoles to the terminal double bond of the allene moiety gives rise to aliphatic acetals **172**[191a] or bisindolyl derivatives **173**[191b] respectively (Scheme **81**). The initially proposed mechanism suggested the coordination of platinum *via* the *sp*-carbon of the

allene **174** as a zwitterionic platinum carbene, followed by the addition of the nucleophile to the terminal C=C of the allene **175**, generating the platinum carbene. Then, 1,2-H shift supported by the nucleophile, activates the terminal sp^2-carbon of the intermediate **176** to the second nucleophilic attack, giving after protodemetalation the desired acetal **172** or bisindol derivative **173**. Mechanistic studies are ongoing in the group at the moment and a more complex mechanistic picture has been uncovered.



Scheme 81. Platinum-catalysed double addition to allenes of alcohols and indoles as nucleophiles

Another example of double addition to allenes catalysed by platinum(0) has been reported by the group of Miyaura using diborons as nucleophiles.[195] The regioselectivity of the addition is influenced by size of the ligands on the metal (phosphine ligands) and the electronic nature of the substituents on the allene. High steric hindrance, forces the addition to the terminal and central carbons of the allene **177** (Scheme **82**). In contrast, smaller phosphine ligands and monosubstituted allenes favour the attack to the most hindered C=C and the central carbon of the allene **178**. DFT calculations were also performed confirming the high electronic influence on the B-B addition to monosubstituted allenes.[196] This group postulate that monosubstituted allenes with EDG (Me or NH_2) favour the insertion of B-B to the internal π-system of the allene. In contrast, for EWG (CN) the terminal one is preferred over the internal C=C. These electronic influences could be explained on concept of charge transfer from the π-system of the allene and "d" orbitals involved from the metal.



R = R' = H, alkanes, **94a**, Ph, OMe, SMe
(OR") = ($O_2C_2Me_4$)

Scheme 82. Platinum-catalysed intermolecular diboration of allenes

3.3. Introduction to the chemistry of bisallenes

As it has been shown, allenes are involved in many reaction processes displaying different reactivities. However, if two conjugated or non-conjugated cumulated alkenes are linked, the versatility of these systems hugely increases, offering the possibility of developing new methodologies with high atom economy in carbo- and heterocyclisations,[24a, 48, 197] or being incorporated in the scaffold of natural products.[198]

The first reported bisallene **179** (Figure **27**) was synthesised by Marvel and coworkers in 1936.[199] 1,1,6,6-tetraphenyl-1,2,4,5-hexatetraene **180** was obtained by Khun and Fischer [200] in 1961, then in 1967 Jacobs and Prempree [201] obtained the conjugated bisallene **181**.[48]

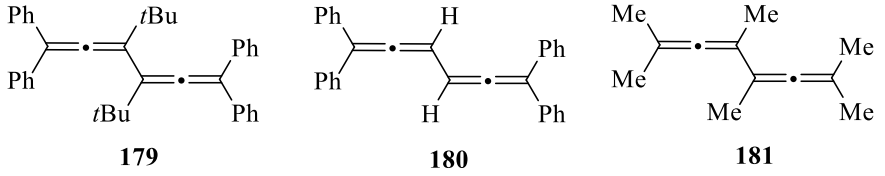
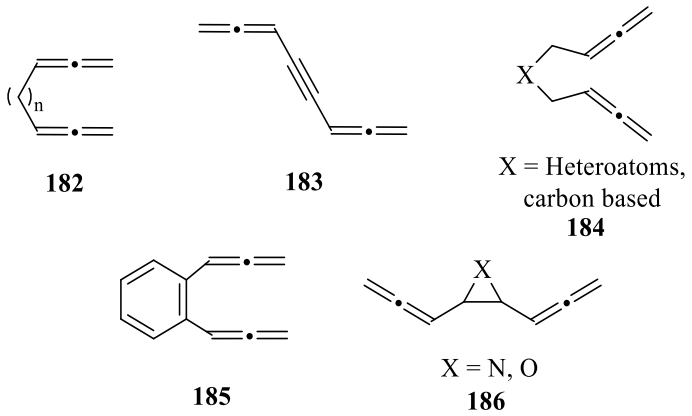


Figure 27. First reported bisallenes **179**, bisallene synthesised by Kuhn and Fischer **180**, bisallene developed by Jacobs and Prempree **181**

As it is shown in Figure **27**, conjugated bisallenes were initially investigated. However, non-conjugated bisallenes (**182**, **184** and **186** Figure **28**) are the most employed nowadays due to their high versatility in cyclisation chemistry. Non-conjugated bisallenes can be linked by a wide variety of tethers such as alkyl chains **182**, chains containing heteroatoms (S, N, O) **184** and epoxides or aziridines **186**, incorporating extra functionalities into the skeleton of these structures (Figure **28**).



182 **183** **184** **185** **186**

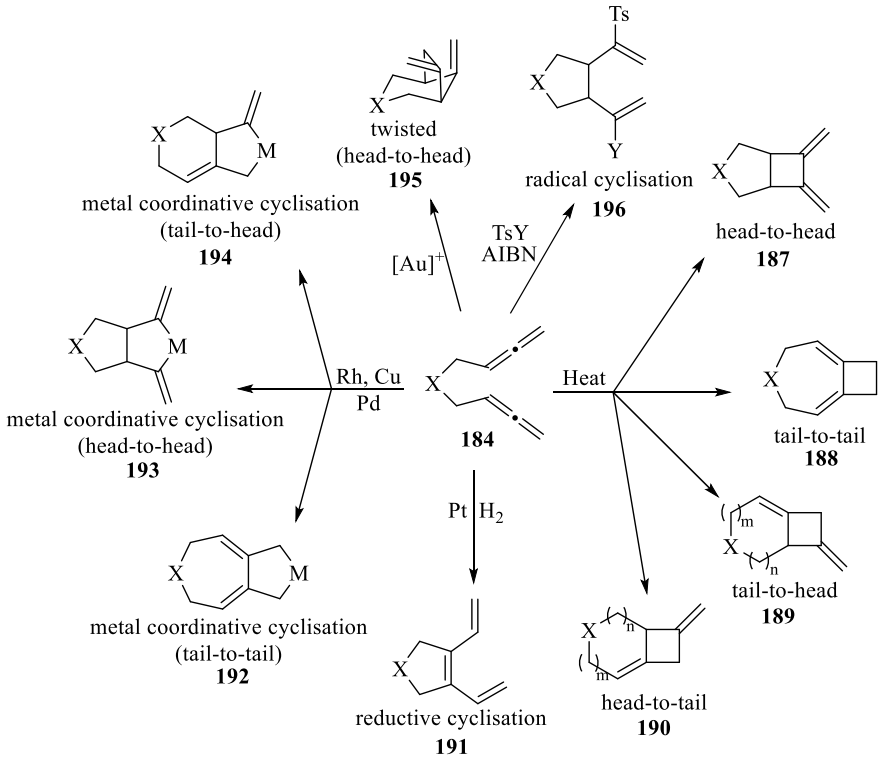
Figure 28. Examples of conjugated and non-conjugated bisallenes linked by different tethers [48]

3.4. Reactivity of 1,5-bisallenes

The rapid development of the chemistry of bisallenes has given rise to an extensive number of reports about the synthesis and reactivity of these substrates.[48, 197c, 202] Bisallenic intermediates generated *in situ via* [2,3]-sigmatropic rearrangements from bispropargyl derivatives have also been employed effectively in the synthesis of complex carbo- and heterocycles.[203] Moreover, base-catalysed rearrangement of bis(π-conjugated propargyl) derivatives is also used to generate carbocycles *in situ* through bisallenic intermediates.[204]

In the present thesis, only the synthesis and chemistry of non-conjugated 1,5-bisallenes **184** will be covered (Figure **28**). These motifs are involved in cycloadditions, cyclo- and carbometalations, radical or even multicomponent cascade reactions[205] to generate 5-7 membered rings displaying interesting reactivities.[197b] Scheme **83** shows an overview of the many possible cyclisation modes among the 4 π-systems reported in the literature.

Intramolecular [2+2] cycloaddition is one of the most explored reactions of allenes to generate cyclobutenes or cyclobutanes, which concern 4 possible cyclisation modes: head-to-head **187**, tail-to-tail **188**, tail-to-head **189** and head-to-tail **190** (Scheme **83**).[197f, 206] On the other hand, carbocyclisations mediated by transition-metals such as Rh,[207] Pd[206c, 207b, 208] or Cu[209] are also a powerful tool to create new C-C bonds using 1,5-bisallenes as substrates. In this case, the metal can coordinate with the bisallene forming metalacycles *via* reactions tail-to-tail **192** (Scheme **83**) forming 7-membered rings, head-to-head **193**, or tail-to-head **194** where the metal coordinates between the terminal C=C of one allene and the external π-system of the other allene moiety. Reductive elimination on those metalacycles would give similar products to the thermal cycloadditions.



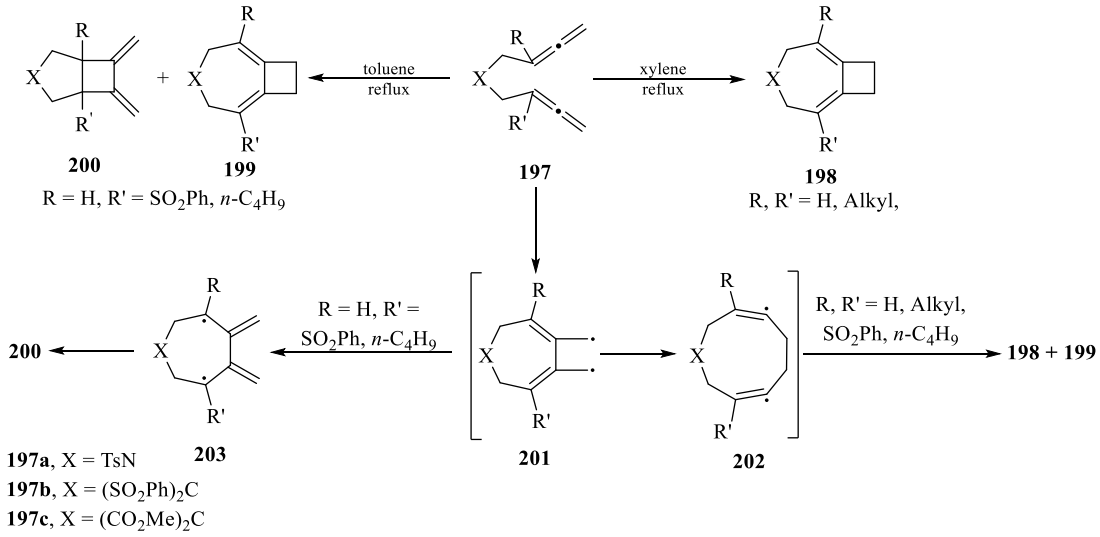
Scheme 83. Coordination modes and reactivities in the chemistry of 1,5-bisallenes

Besides, 5-membered ring derivatives have also been synthesised using non-conjugated 1,5-bisallenes *via* radical cyclisation **196**,[210] as well as platinum-catalysed reductive cyclisation under hydrogenation conditions **191**.[211] Finally, an uncommon gold-catalysed twisted head-to-head carbocyclisation has been reported to give intriguing bicycles **195** in high yields when nitrogen containing groups were used as tethers in the bisallenes.[212]

3.4.1. Thermal carbocyclisation of 1,5-bisallenes

Thermally induced cyclisation of bisallenes is a well-known method for the formation of 4-membered rings *via* formal [2+2] cycloaddition. However, so far there are only two examples that employ 1,5-bisallenes.[206c, 213] In both cases, the tail-to-tail cyclisation mode (**188**, Scheme **83**) gives access to bicyclic products **198** and **199** (Scheme **84**). This synthesis is sensitive to reaction conditions such as concentration of **197**, as well as the tethers employed to link the two allene moieties, where higher yields are obtained in the presence of bulky groups such as $(SO_2Ph)_2C$ and $(CO_2Me)_2C$ it is probably due to the Thorpe-Ingold effect.[197a, 214] The proposed mechanism suggests the formation of bicycles **198**, **199** and **200** (Scheme **84**) *via* diradical intermediates **201**, **202** and **203**. Products **198** and **199** can be generated by exo- or endocyclic diradical intermediates **201** and **202** respectively. Interestingly, SO_2Ph and *n*-C_4H_9 groups incorporated in the internal 3-position of the allene (R'), induce a remarkable

effect in the [2+2] cycloaddition reaction, generating bicycle **199** and also product **200** *via* head-to-head cyclisation of diradical intermediate **203** (Scheme **84**).[197a]

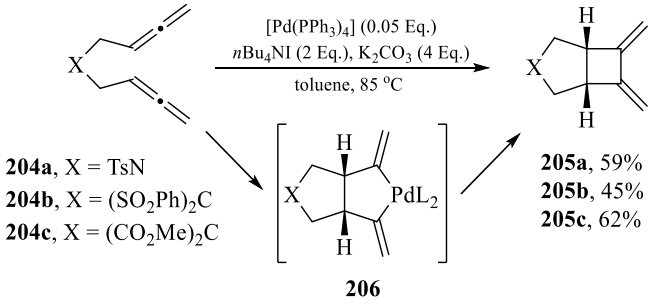


Scheme 84. Thermally induced carbocyclisation of 1,5-bisallenes and proposed mechanism

3.4.2. Transition metal-catalysed reactions of 1,5-bisallenes

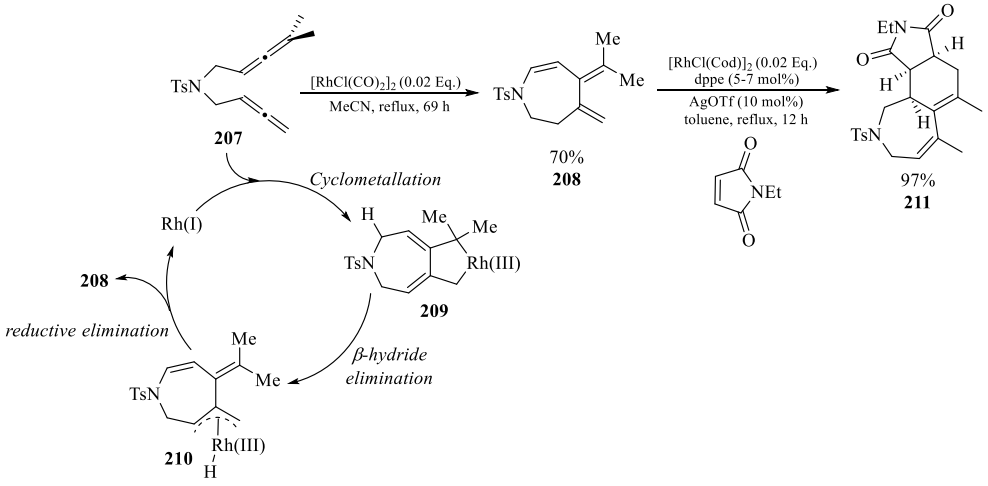
Carbocyclisation of diynes, enynes, dienes or allenenes catalysed by metals such as (Rh, Pd and Au) is a well-known method to form carbo- and heterocyclic products in good yields, and high stereoselectives.[189e, 215] Nowadays, electrophilic activation of allenes by transition metals to obtain complex molecules is extensively used.[24c, 202, 216] As a consequence, the next few pages will outline the high reactivity and atom economy of non-conjugated bisallenes with metals.

The proposed mechanism to obtain bicycle[3.2.0] **205** *via* thermal diradical endocyclisation of bisallene **197** with bulky groups in the tether is shown in Scheme **84** in the previous section.[206c] Alternatively, the formation of compound **205** has also been reported by the same authors in the reaction of bisallenes **204** catalysed by Pd(0) through a head-to-head coordination of the metal with the bisallene, forming palladacycle **206** (Scheme **85**). The intermediate **206** then undergoes reductive elimination to achieve the desired product **205**. K_2CO_3 and nBu$_4$NI are essential to generate bicycle[3.2.0] **205** in good yields. It is likely that nBu$_4$NI is involved in a ligand exchange process which facilitates the reductive elimination step.[206c]



Scheme 85. Palladium(0)-catalysed intramolecular [2+2] cycloaddition reaction of 1,5-bisallenes

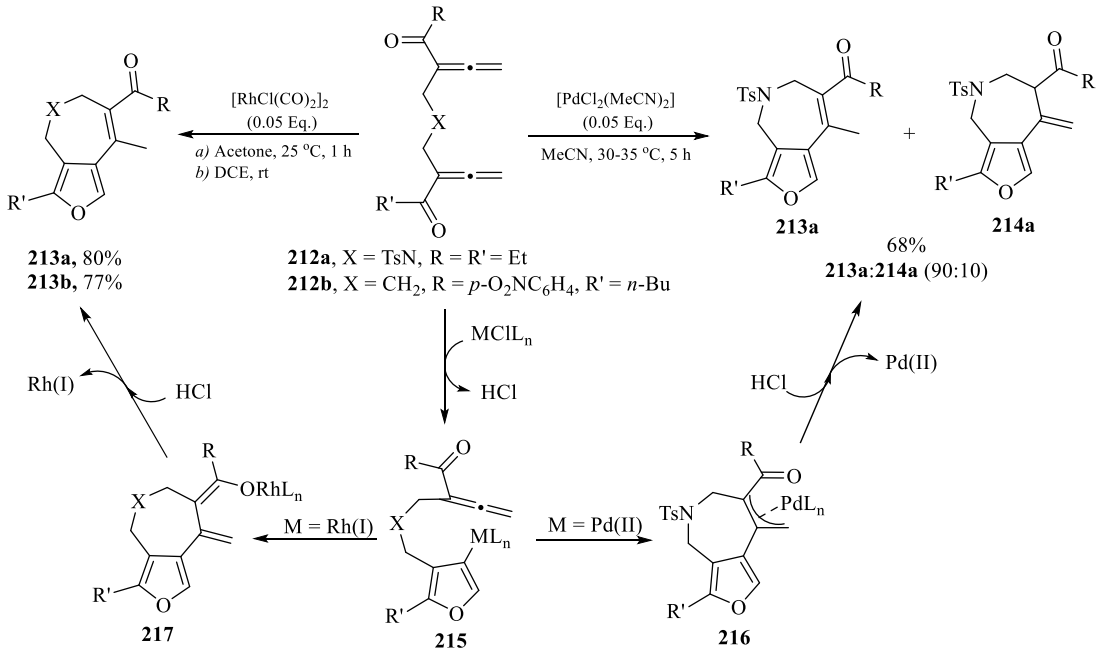
Bisallene **207** (Scheme **86**) was employed in the group of Ma to obtain 7-membered rings **208** in the presence of Rh(I) catalysts. In this case, a plausible mechanism suggests a tail-to-tail cyclometalation to form **209.** Regioselective β-hydride elimination **210**, followed by reductive elimination achieved the 7-membered ring **208** in good yields.[207a] In order to show the synthetic utility of conjugated triene **208**, the same authors described a few examples of their reaction with dienophiles to obtain complex tricyclic compounds **211** in excellent yields *via* Rh-catalysed [4+2] cycloaddition.[217]



Scheme 86. Rh(I)-catalysed cyclisation of 1,5-bisallenes to obtain 7-membered rings. Synthesis of complex tricyclic compounds **211** *via* [4+2] cycloaddition of **208** with dienophiles

Palladium and rhodium catalysts have been used in the biscyclisation of symmetrical **212a** and unsymmetrical 1,5-bis(1,2-allenylketones) **212b** to obtain furo[3,4]azepine derivatives **213a**, **213b** and **214a** (Scheme **87**). Symmetrical bisallenylketones **212a** in the presence of Pd(II) afforded bicycle **213a** as well as its regioisomer **214a** in a ratio (90:10) with a moderate yield. However, Rh(I) catalysts give access to a highly selective biscyclisation of bisallene **212a** to afford furo[3,4]azepine derivatives **213a** as the only isomer in a high yield. In addition, the reaction of unsymmetrical bisallenylketones **212b** was also catalysed by Rh(I) to selectively achieve product **213b** in good yields.[197a, 207b] The author suggested that both

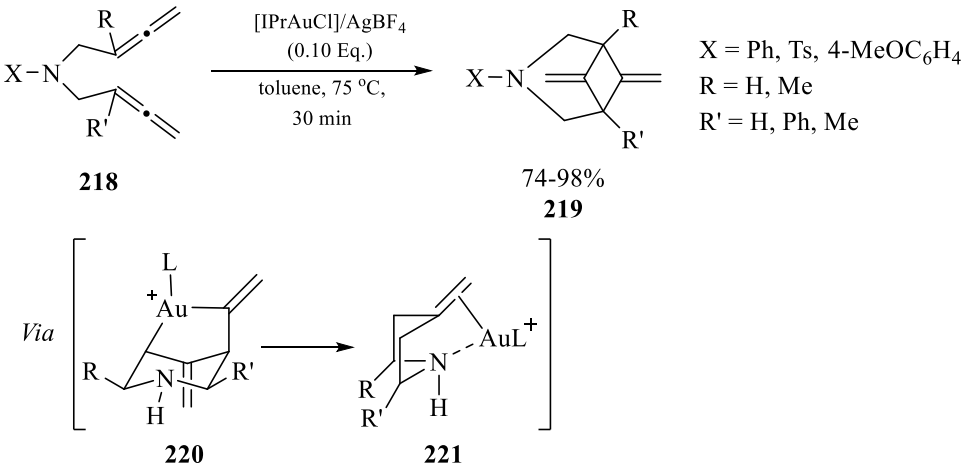
metals trigger the cycloisomerisation of one 1,2-allenyl ketone moiety *via* intermediate **215** (Scheme **87**). Then, palladium(II)-catalysed carbometalation of the other allene moiety forms the π-allyl intermediate **216**, which after protonolysis affords products **213a** and **214a**. In contrast, the oxophilicity of rhodium favours intermediate **217** that after protonolysis gives access to bicycles **213** only.[197a, 207b]



Scheme 87. Pd(II)- and Rh(I)-catalysed biscyclisation of symmetrical and unsymmetrical 1,5-bis(1,2-allenylketones) to obtain furo[3,4]azepine derivatives

1,ω-Bisallenols have also been employed to obtain 2,5-dihydrofuran-fused bicycles in the presence of palladium(II)-complexes. The mechanism was related to the one proposed in Scheme **87**, *via* π-allylpalladium (see intermediates **216** and **217**, Scheme **87**).[208]

The use of gold in electrophilic activation of bisallenes is surprisingly scarce in comparison with monoallenes as it was shown in the previous chapter. However, the group of Chung described an uncommon twisted head-to-head [2+2] cycloaddition obtaining azabicyclo[3.1.1] heptanes **219** in high yields from bisallenes with nitrogen-containing groups in the tether (Scheme **88**). It is noteworthy the high sensitivity of the process to reaction conditions, catalyst and also the substrate, as it works only with the cationic IPrAu-complex and *N*-tethered analogs **218**.[212] DFT calculations proposed that the cationic gold species coordinates, with an internal π-system of one of the allenes, which make it more subsceptible for attack than the other allenyl moiety generating an unsual gold-metallacycle intermediate **220** (Scheme **88**). After reductive elimination from **220**, the gold complex remains coordinated with the C=C as well as with the nitrogen **221**, to then give product **219**.[212]

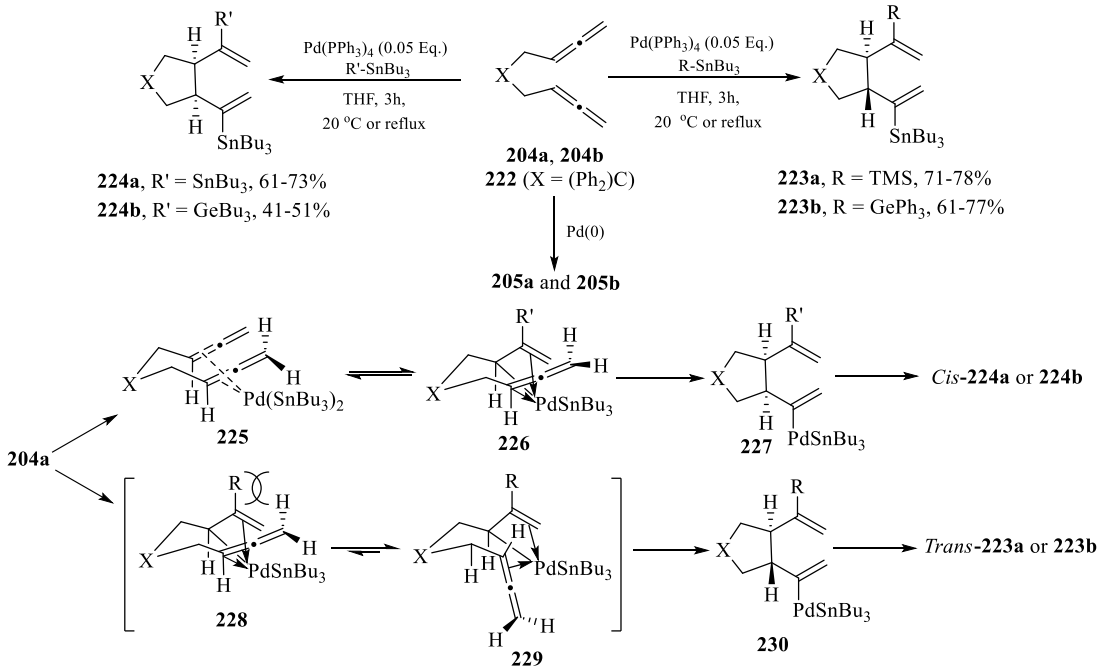


Scheme 88. Gold-catalysed twisted head-to-head [2+2] cycloadditions of 1,5-bisallenes to obtain bicycle **219**. Proposed mechanisms to the synthesis of compound **219**

3.4.3. Transition metal-catalysed reactions of 1,5-bisallenes adding an additional partner

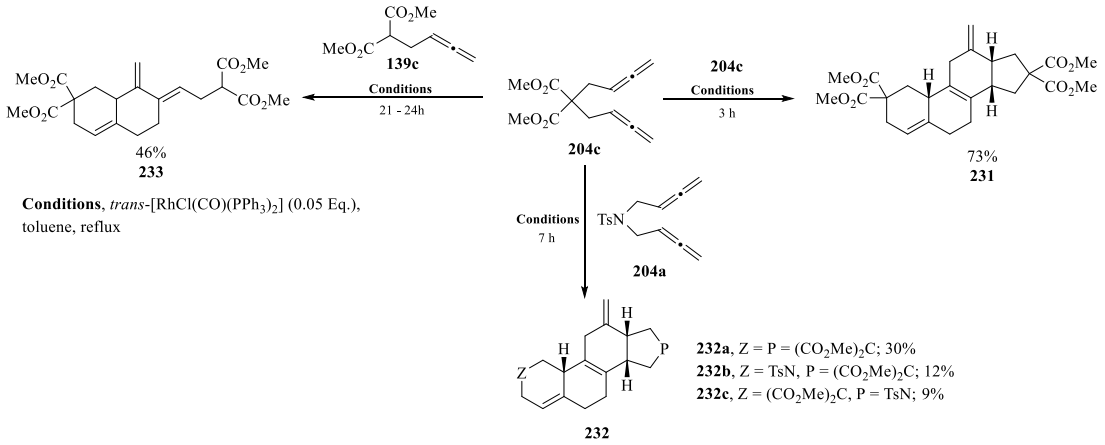
In addition to the previous carbocyclisations with 1,5-bisallenes catalysed by transition metals, the ring-construction process can also take place in presence of additional compounds (CO, organic compounds, H_2, or external nucleophiles) that are incorporated in the resulting molecule.

The first example reported was a palladium(0)-catalysed addition-cyclisation reaction using as additives (trimethylsilyl)tributylstannane to generate 5-membered rings **223** and **224** (Scheme **89**).[218] Stereoselectivity issues were found during the cyclisation process, mainly due to sensitivity to reaction conditions, reagents and steric factors. Germylstannanes were also employed showing similar reactivities.[210b] In both cases, *cis*-products **224** are favoured when $SnBu_3$ or $GeBu_3$ are used. In contrast the *trans*-isomers **223** were obtained in the presence of bulkier "R" groups such as TMS or $GePh_3$. It is important to note the greater steric effect of TMS in comparison with Bu_3Sn, mainly due to the short distance of Si-C bond, which increases the size of the group. The mechanism goes through an oxidative addition to generate Bu_3SnPdR species, which reacts with the bisallene to generate the σ,π-allylpalladium complexes **229** or **226**. Intermediate **229** is favoured when the bulky "R" = TMS is employed, generating the vinyl-$PdSnBu_3$ intermediate **230**, which after reductive elimination give access to the *trans*- products **223**. In contrast, the *cis*-**224** are favoured when a rapid carbocyclisation of intermediate **225** and / or through σ,π-allylpalladium intermediate **226**, generates the vinyl-$PdSnBu_3$ **227**, giving rise to the desired *cis*-products *via* reductive elimination. In addition, if intermediates **227** and **230** undergo long reaction processes, [2+2] cycloaddition would generate bicycle[3.2.0] **205** (Scheme **88**).



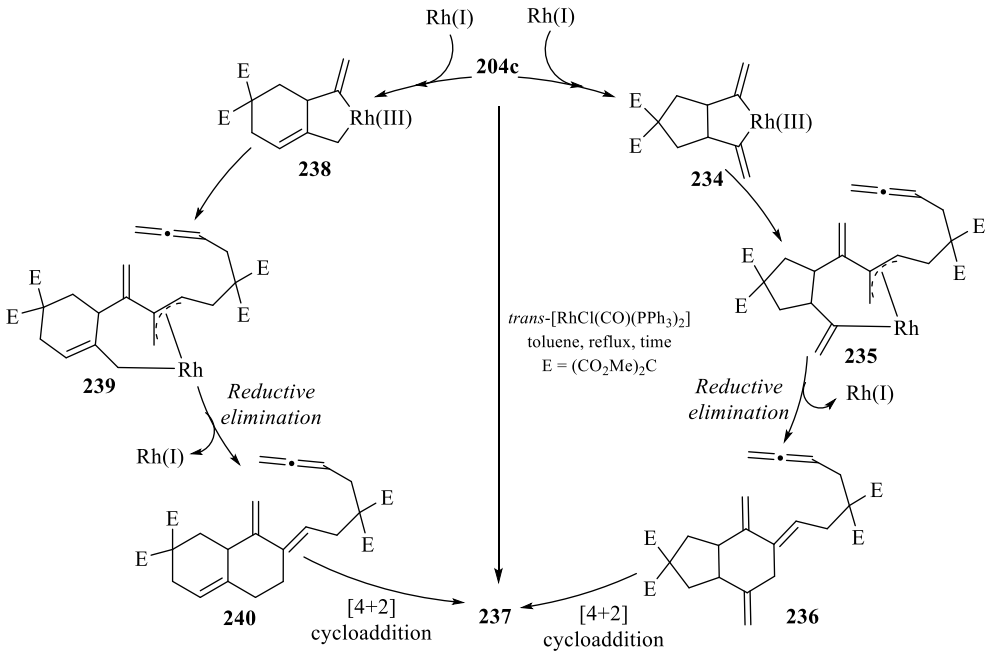
Scheme 89. Palladium(0)-catalysed cyclisation of 1,5-bisallenes with tributylstannane derivatives

Interestingly, the group of Ma has reported a highly efficient methodology to synthesise steroid derivatives in the reaction of 1,5-bisallenes catalysed by *trans*-[RhCl(CO)(PPh_3)$_2$] where the additional partner was the same or a different bisallene. For example, compound **231** (Scheme **90**) was obtained by reaction of two 1,5-bisallenes **204c**, achieving higher yields if a lower concentration of the substrate was utilised.[219] With the optimised conditions in hand, the synthesis of heterosteroids **232** was also achieved using two different 1,5-bisallenes. As a result, three different products **232a**,**b**,**c** were isolated in moderate yields.[220] Bisallene **204c** in the presence of monoallene **139c** under the same reaction conditions, gave rise to an attractive bicycle with an exocyclic conjugated diene **233** in its scaffold. This product **233**, was alkylated and subsequently cyclised *via* a Diels-Alder reaction to achieve tetracyclic skeletons diastereoselectively.[197a, 221]



Scheme 90. Synthesis of heterosteroid derivatives catalysed by Rh(I) with 1,5-bisallenes

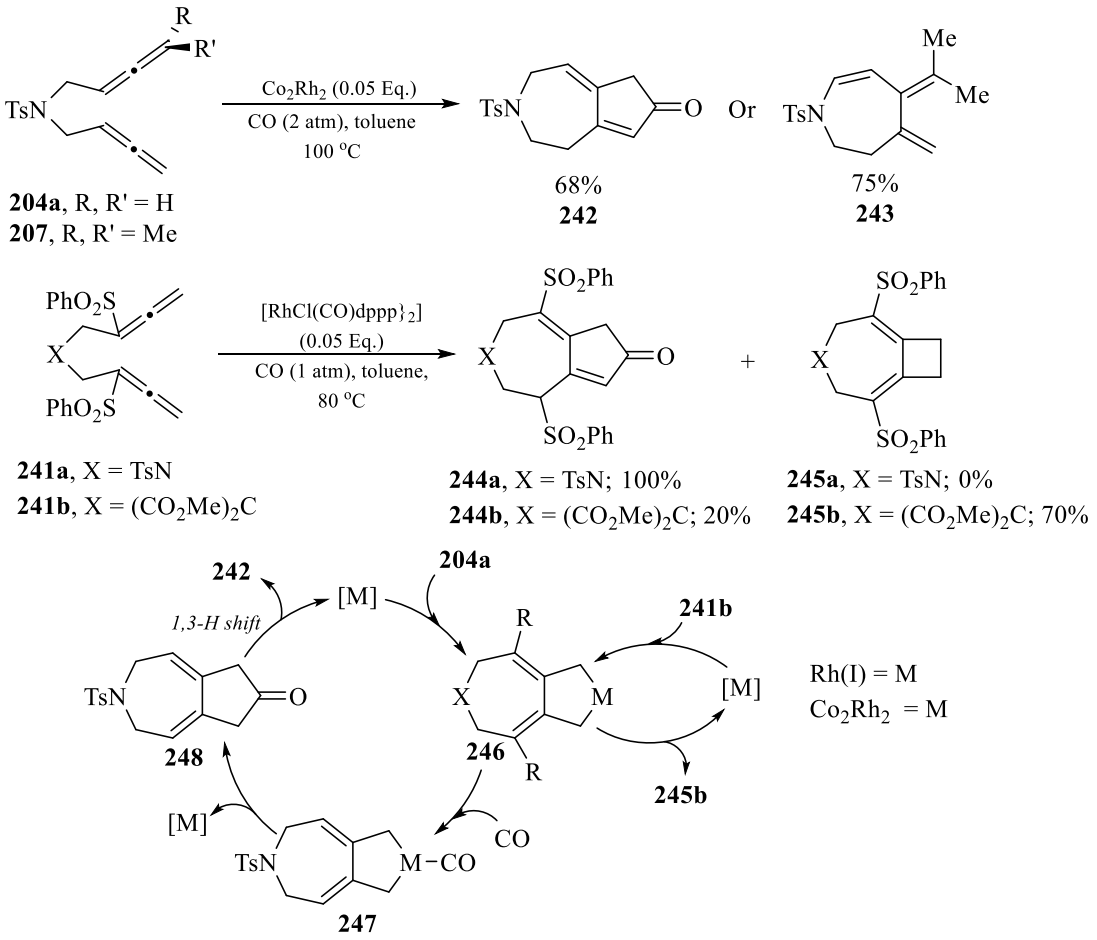
Two plausible mechanisms were proposed by the authors. Both would start with the formation of rhodacycles **234** and **238** (Scheme **91**) from bisallene **204c** (Scheme **90**). Then, carbometallation with the second bisallene would generate intermediates **235** and **239**, which after reductive elimination would give rise to species **236** and **240**. Subsequently, the conjugated diene incorporated in the scaffold of the bicycle and the last allene moiety can undergo a Diels-Alder reaction to achieve steroid **237**.[219]



Scheme 91. Proposed mechanisms for the rhodium-catalysed synthesis of steroid derivatives with 1,5-bisallenes

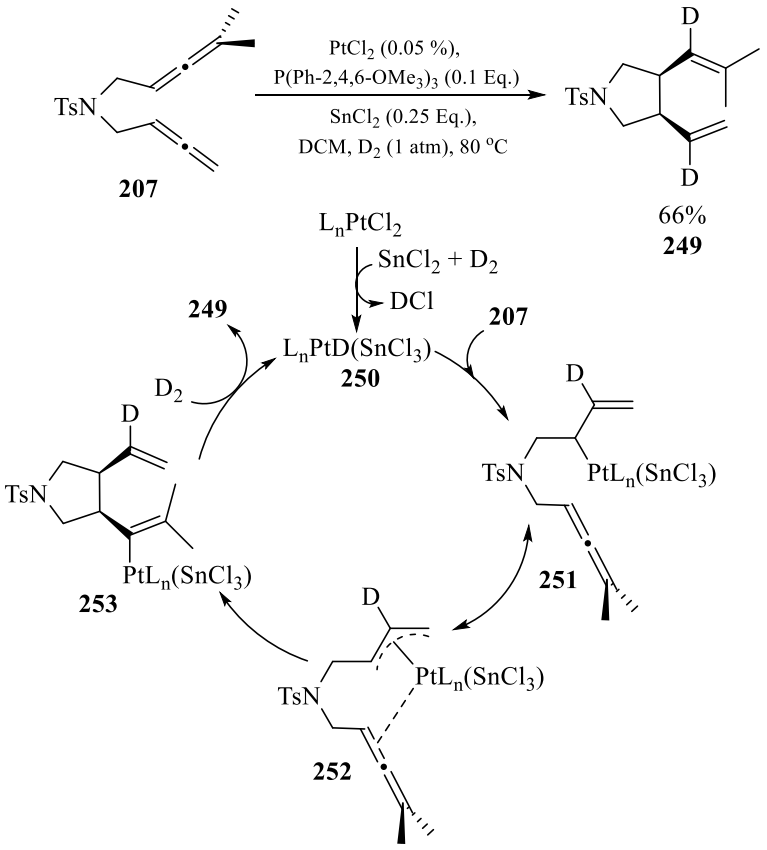
1,5-bisallenes have also been employed in a Pauson-Khand type reaction catalysed by rhodium or cobalt/rhodium nanoparticles. Thus, transition metal-catalysed [2+2+1] cycloaddition reactions in presence of CO give access to cyclopentenone-fused bicyclic products **242** and **244**, in moderate to good yields, as well as the product from a [2+2]

cycloaddition **245** (Scheme **92**).[206c] One of the first works of this Pauson-Khand transformation was reported by the group of Chung,[222] who was able to achieve cyclopentenone **242** in the presence of Co/Rh heterobimetallic nanoparticles and the essential CO atmosphere in moderate yields (Scheme **92**). It should be mentioned that 7-membered ring **243** was obtained using substituted bisallene **207** under these reaction conditions. On the other hand, Mukai and coworkers[223] also reported this [2+2+1] cycloaddition under carbon monoxide atmosphere, affording the Pauson-Khand type products **244** (Scheme **92**), catalysed by Rh(I). Bis(phenylsulfonylallene) derivatives were employed in this work, and the voluminous SO_2Ph group in the bisallene scaffold was essential to avoid the formation of rhodacycles **234** and **238** (Scheme **91**), as well as carry out the [2+2+1] carbonylative cycloaddition under smooth conditions. A proposed mechanism was also reported, where the Pauson-Khand type [2+2+1] and [2+2] cycloaddition products would come from tail-to-tail metal-coordinative cyclisation to generate rhodacycle **246**. From this intermediate, reductive elimination would give rise to bicycle **245**. On the other hand, the insertion of CO would give **247** and the subsequent reductive elimination would form cyclopentenone **248**, which isomerizes *via* 1,3-H shift, possibly to decrease the ring strain of the 1,3-diene intermediate **248**, to give the desired products **242** and **244**.



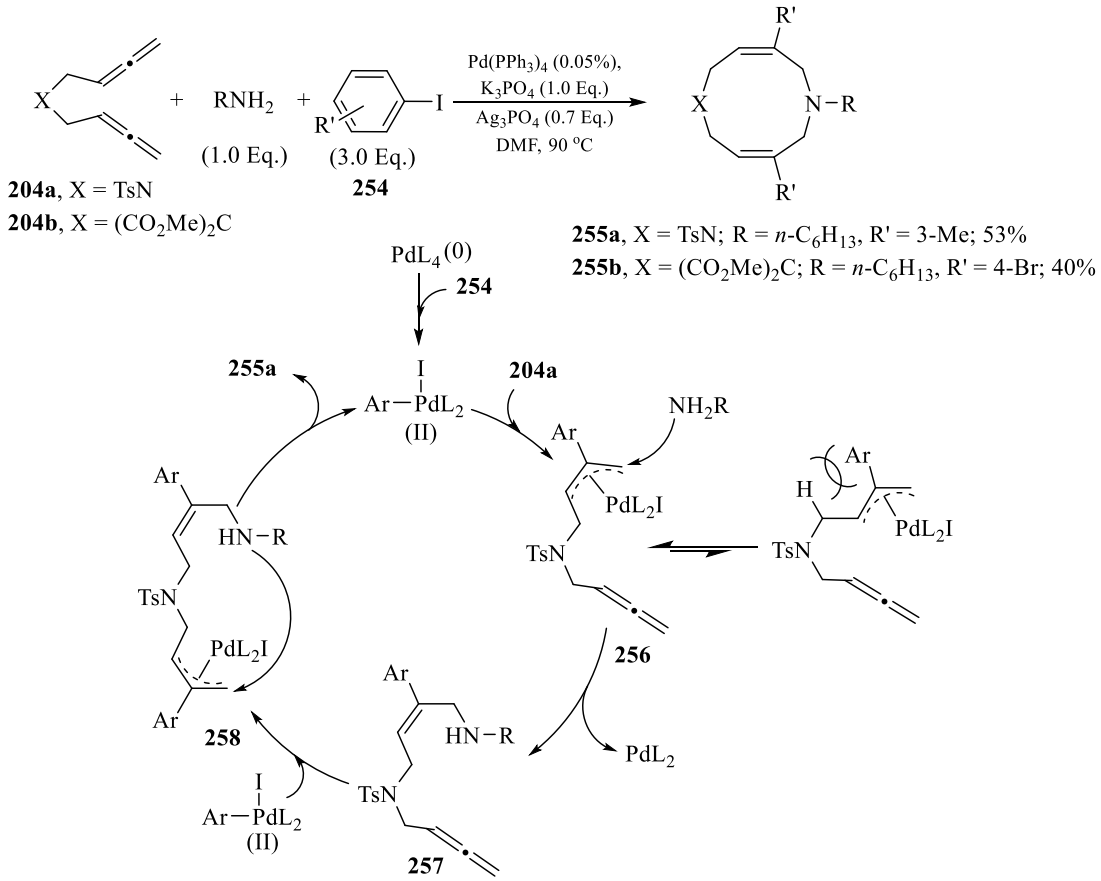
Scheme 92. Transition metal catalysed Pauson-Khand type reactions of 1,5-bisallenes and its mechanistic insight

5-Membered rings **249** (Scheme **93**) have also been obtained *via* regio- and *cis*-diastereoselective reductive cyclisation of 1,5-bisallenes catalysed by platinum-hydride complexes generated *in situ* under hydrogenation conditions. In an attempt to confirm the mechanism, reaction with D_2 was performed. Deuterio-platinum complex **250** initiates the deuteriometalation of one allene moiety, this gives access to the allyl-platinum intermediate **251**, which coordinates with the internal π-system of the other allene moiety **252** to create a new C-C bond **253**. Subsequently, protodemetalation of the vinyl-platinum complex **253** with D_2 generates the desired *cis*-cyclopentane derivative **249** in moderate yields and regenerate the catalytic Pt-D.[211]



Scheme 93. Regio- and stereoselective reductive cyclization of 1,5-bisallenes under hydrogenation conditions catalysed by platinum complexes

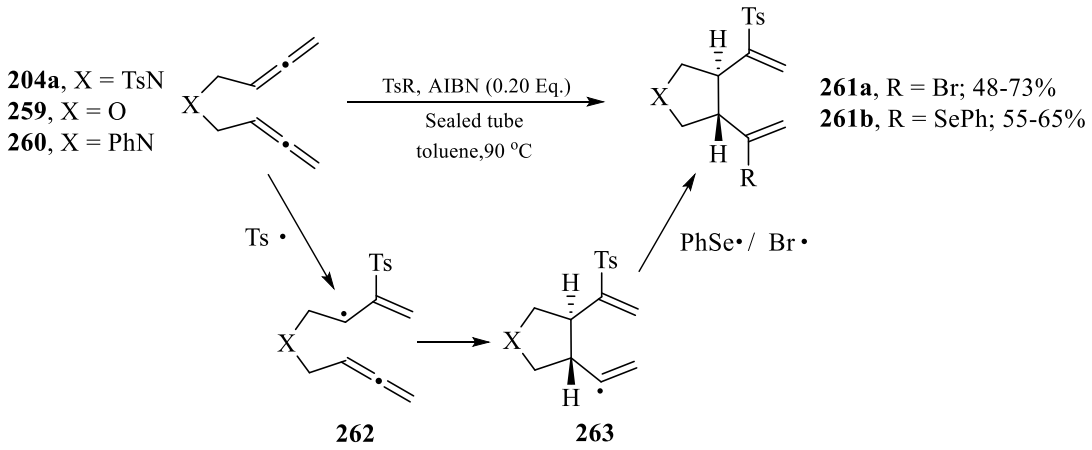
Transition metal-catalysed addition of nucleophiles to allenes is the main approach of the present thesis, thus, it is essential to mention the only intermolecular addition of nucleophiles to 1,5-bisallenes catalysed by metals reported so far. In this work, the group of Ma developed the synthesis of regio- and stereoselective 10-membered ring heterocycles **255** catalysed by palladium(0), with aryliodides **254**, Ag_3PO_4 as an additive, amines as nucleophiles and K_3PO_4 as a base (Scheme **94**). A proposed mechanism was also reported by the authors, which suggests a sequential inter-/intramolecular reaction of 1,5-bisallenes triggered by the nucleophilic attack of the amine to two π-allylpalladium intermediates **256** and **258** (Scheme **94**). Carbopalladation of one allene moiety with the preformed Ar-Pd-I complex generates stereoselectively the *anti*-π-allylpalladium intermediate **256**, due to steric interactions of the "Ar" group incorporated. Intermolecular nucleophilic attack of the amine to π-allyl-Pd **256** would form intermediate **257**. Then, the carbopalladation of the other allene moiety gives access to a new *anti*-π-allylpalladium intermediate **258**, favouring the regioselective intramolecular attack of the nucleophile, achieving product **255a**.[224]



Scheme 94. Palladium-catalysed sequential inter-, intramolecular reaction of 1,5-bisallenes to obtain 10-membered rings.

3.4.4. Radical cyclisation of 1,5-bisallenes

As well as addition of external partners in the metal-catalysed examples, it is important to note the reactivity reported in the addition of free radicals to 1,5-bisallenes without any metal involved in the reaction. Thus, *trans*-fused cyclopentane derivatives **261** (Scheme **95**) can be obtained selectively in presence of a catalytic amount of AIBN, with incorporation of tosyl and bromides or tosyl and selenophenyl groups in the scaffold of the 5-membered ring. As shown in the proposed mechanism (Scheme **95**) a tosyl radical, generated *in situ* is added to the *sp*-carbon of one allene **262** in the propagation step. This triggers the stereoselective radical C-C bond formation with the other allene moiety **263**, creating a new radical in the central carbon of the allene, which is trapped by selenophenyl or bromide radicals, giving access to the *trans*-product **261**.[197a, 210a]



Scheme 95. Synthesis of *trans*-fused cyclopentane derivatives *via* radical C-C bond formation with 1,5-bisallenes as substrates

3.5. Aims and objectives

The aim of this work was to investigate the novel reactivity of 1,5-bisallenes with transition metal-catalysts, to synthesise 7-membered rings with the incorporation of an oxygen group into the skeleton of the final product. These structures are commonly integrated in the core of many natural products and in important biologically active molecules, especially in terpene and sesquiterpene families (Figure **29**).[225] The construction of these medium size rings is still a challenge for organic chemists, in comparison with the formation of 5 to 6-membered rings, due to ring strain and entropic reasons.[225c, 226] 7-Membered rings have also been obtained previously in reactions of 1,5-bisallenes catalysed by Rh(I) (See Scheme **87** and **93**)[207a] or by a thermal [2+2] cycloaddition (See Scheme **84**) between the two terminal π–systems of the bisallene (*tail-to-tail*).[206c]

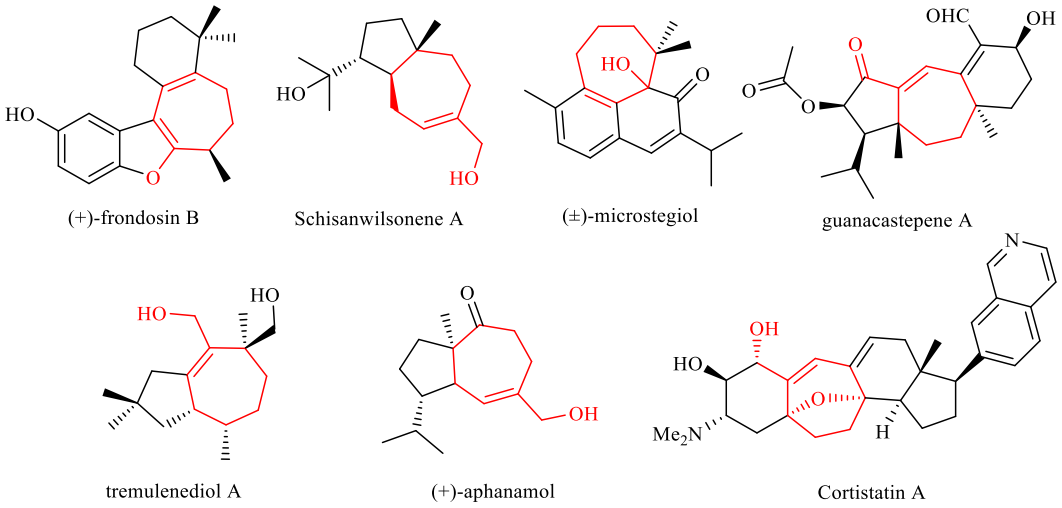


Figure 29. Natural products and biologically active molecules with a 7-membered ring in their core bearing an additional oxygen functional group. (+)-frondosin B,[227] schisanwilsonene A,[228] (±)-microstegiol,[229] guanacastepene A,[230] tremulenediol A,[231] (+)-aphanamol,[225d] cortistatin A[232]

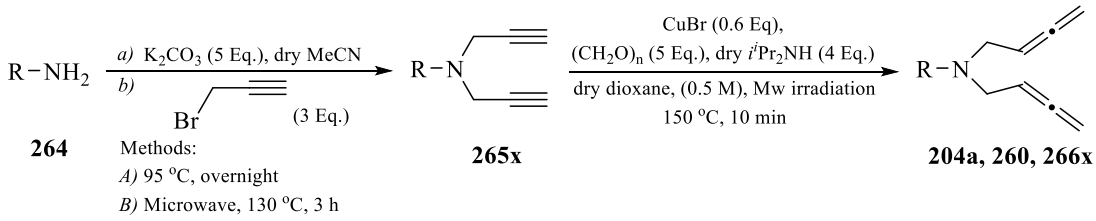
3.6. Results and discussion

3.6.1. Synthesis of starting materials

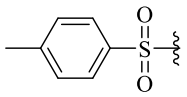
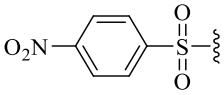
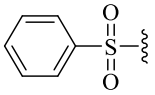
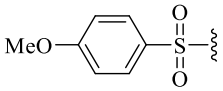
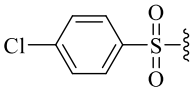
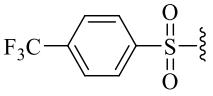
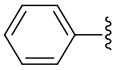
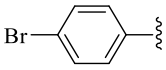
3.6.1.a. Synthesis of the simplest symmetrical monosubstituted bisallenic precursors

The skeleton of the simplest non-conjugated 1,5-bisallene used in this work is formed by two allenes linked through a methylene group to heteroatoms (oxygen and nitrogen) or carbon-based tethers such as $(CO_2Me)_2C$ or $(PhO_2S)_2C$. The synthesis of these bisallenic precursors was generally carried out in two steps: bispropargylation of the commercially available tether with propargyl bromide, followed by the formation of the 1,5-bisallene *via* microwave assisted Crabbé homologation.[27b]

Formation of *N*-tethered bispropargyl derivatives **265x** (Scheme **96**) was performed using two sets of conditions (See Table **18**), deprotonation of the amine derivatives **264** with K_2CO_3 under reflux overnight (method A) or assisted by microwave irradiation at 130 °C during 3 h (method B). As shown in Table **18**, microwave heating reduced drastically the reaction time and also higher yields were obtained in comparison with method A (See Entries **1**, **3** and **6**). Subsequently, the synthesis of *N*-tethered 1,5-bisallenes **204a**, **260** and **266x** was performed *via* microwave assisted Crabbé homologation.



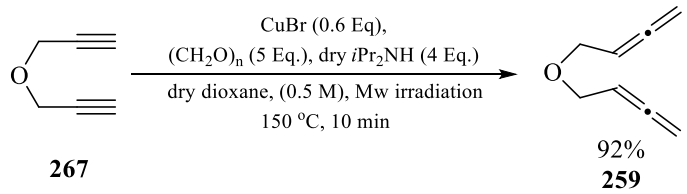
Scheme 96. Synthesis of the simplest *N*-tethered 1,5-bisallenes *via* microwave assisted Crabbé homologation

Entry	R	**265x** Isolated Yield (%)		Bisallene **204a**, **260** or **266x** Isolated Yield (%)
		Method A	Method B	
1		**265a**, 92	**265a**, 99	**204a**, 70 **204a-*d*4**, 61[a],[b]
2		**265c**, 95	**265c**, 64	**266c**, 73[a]
3		**265d**, 72	**265d**, 98	**266d**, 93
4		**265e**, 93	-	**266e**, 52
5		**265f**, 92	-	**266f**, 52
6		**265g**, 95	**265g**, 99	**266g**, 63
7		**265i**, 45	-	**266i**, 63
8		**265j**, 95	-	**260**, 68
9		-	**265k**, 95	**266k**, 60

[a] Reaction time 12 min. **[b]** Synthesised using deuterated paraformaldehyde $(CD_2O)_n$. Bisallene **204-*d*4** was fully deuterated in the two terminal positions of the two allenes.

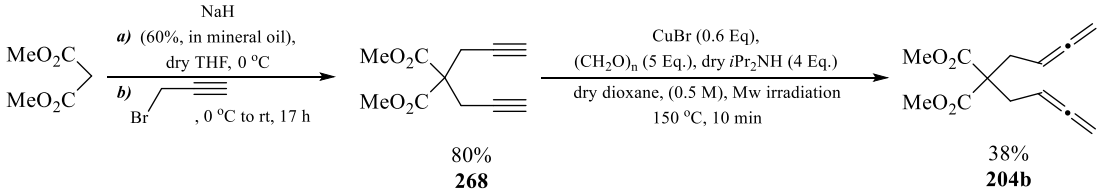
Table 18. Formation of bispropargyl derivatives **265x**. Synthesis of *N*-tethered 1,5-bisallenes **204a**, **260** and **266x** *via* microwave assisted Crabbé homologation

Oxygen-tethered bisallene **259** was synthesised directly from the commercially available dipropargyl ether **267** *via* microwave assisted Crabbé homologation (Scheme **97**).



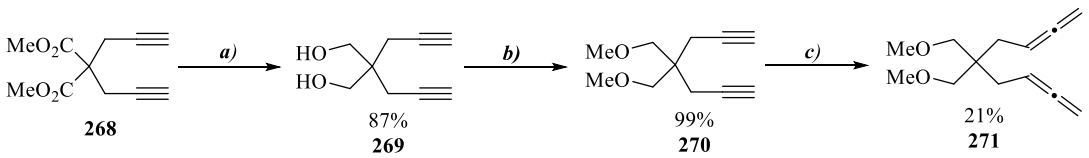
Scheme 97. Synthesis of bis(2,3-butadienyl) ether **259** *via* microwave assisted Crabbé homologation

Bispropargylation of dimethylmalonate with NaH in dry THF at 0 °C and the subsequent Crabbé homologation assisted by microwaves gave access to 1,5-bisallene **204b** in moderate yield (Scheme **98**).



Scheme 98. Synthesis of bispropargyl derivative **268** and the formation of bisallene **204b** *via* microwave assisted Crabbé homologation

Bisallene **271** (Scheme **99**) was obtained in three steps starting with reduction of bispropargylic malonate **268** with $LiAlH_4$, dimethylation of diol **269**, and finally microwave assisted Crabbé homologation to generate the allenic precursor **271** from bispropargylic derivative **270**.

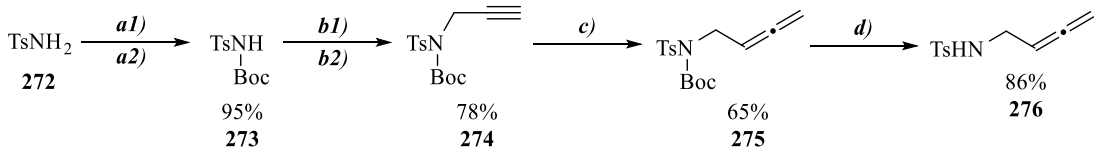


a) $LiAlH_4$ (3 Eq.), dry Et_2O, 0 °C to rt, 4 h. *b)* MeI (5 Eq.), NaH (60%, mineral oil) (2.2 Eq.), dry THF, 0 °C to rt, 8 h. *c)* $(CH_2O)_n$ (5 Eq.), CuBr (0.6 Eq.), dry iPr_2NH (4 Eq.), 0.5 M, dry 1,4-dioxane, Mw irradiation, 150 °C, 20 min

Scheme 99. Synthesis of bisallene **271**

3.6.1.b. Synthesis of unsymmetrical 1,5-bisallenes

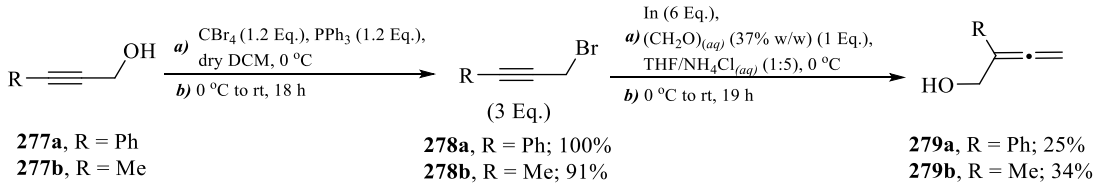
Unsymmetrical mono/disubstituted 1,5-bisallenes were synthesised employing *p*-toluensulfonamide as tether in all the examples. This primary sulfonamide **272** was protected with di-*tert*-butyl dicarbonate to obtain product **273** (Scheme **100**). Propargylation of the protected amide **273** gave rise to propargyl sulfonamide derivative **274**, which underwent microwave assisted Crabbé homologation to give allene **275** in moderate yield. Deprotection of the substituted amide with TMSCl/MeOH gave access to monosubstituted allene **276**, which was used as the starting material for the coupling with 1,1-disubstituted allenols *via* Mitsunobu reaction (See Scheme **101** and **104**).[212, 233]



a1) $TsNH_2$ (1 Eq.), NEt_3 (1.2 Eq.), DMAP (0.02 Eq.), 0.41 M, dry THF. *a2)* $(Boc)_2O$ (1 Eq.), dry THF, rt, 17 h. *b1)* K_2CO_3 (2.5 Eq.), dry MeCN. *b2)* Propargyl bromide (80% toluene) (1.3 Eq.), 0.19 M, dry MeCN, 95 °C, reflux, 20 h. *c)* $(CH_2O)_n$ (2.5 Eq.), CuBr (0.3 Eq.),dry iPr_2NH (2 Eq.), dry 1,4-dioxane, 0.5 M, Mw. 150 °C, 10 min. *d)* TMSCl (15 Eq.), MeOH (15 Eq.), 32 h, rt.

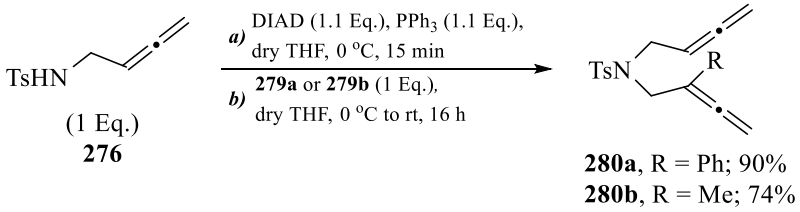
Scheme 100. Synthesis of allenic precursor **276**

Synthesis of 1,1-disubstituted allenols **279** (Scheme **101**) was carried out in two steps starting with bromination *via* Appel reaction[234] of substituted 2-propyn-1-ol **277** to give γ-substituted prop-2-ynyl bromide derivatives **278**, and indium-mediated Barbier-type reaction of propargyl derivatives **278**, to give **279a** and **279b** in moderate yields.[54a]



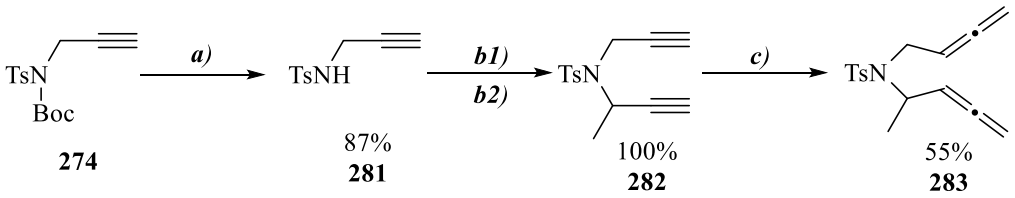
Scheme 101. Synthesis of substituted allenolic precursors **279** from 2-propyn-1-ol derivatives **277**

Allene **276** (Scheme **102**) and the substituted allenols **279a** and **279b** were assembled to generate non-symmetrical 1,5-bisallenes **280a** and **280b** *via* Mitsunobu reaction.



Scheme 102. Synthesis of non-symmetrical monosubstituted 1,5-bisallenes **280a** and **280b**

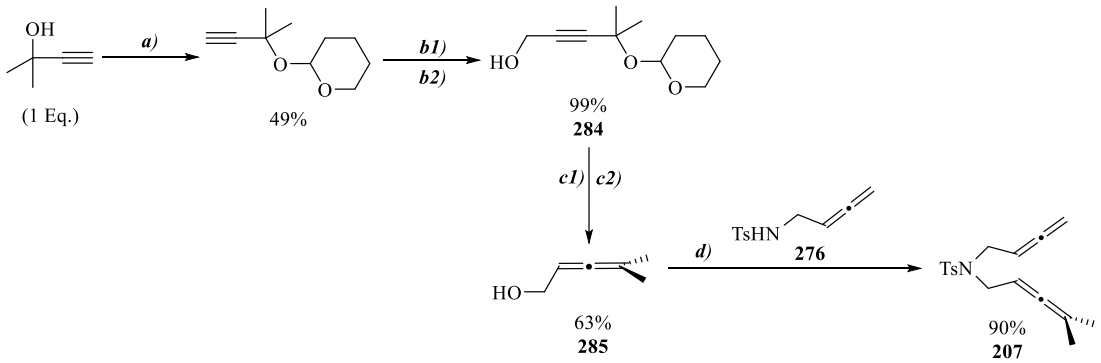
Non-symmetrical bisallene **283** with a methyl group in the carbon next to the nitrogen, was synthesised using as starting material propargylic *p*-toluenesulfonamide **274** (Scheme **103**). Deprotection of the amine under acidic conditions (**281**)**,** propargylation with 3-bromo-1-butyne (**282**) followed by Crabbé homologation, gave access to bisallene **283** in moderate yield.



a) TFA (4.3 Eq.), DCM, 0.65 M, 0 °C to rt, 2 h. ***b1)*** K_2CO_3 (2.5 Eq.), dry MeCN. ***b2)*** 3-bromo-1-butyne (1.5 Eq), Mw, 125 °C, 3 h. ***c)*** $(CH_2O)_n$ (5 Eq.), CuBr (0.6 Eq.), dry *i*Pr_2NH (4 Eq.), 0.5 M, dry 1,4-dioxane, Mw, 150 °C, 10 min

Scheme 103. Synthesis of non-symmetrical monosubstituted 1,5-bisallene **283**

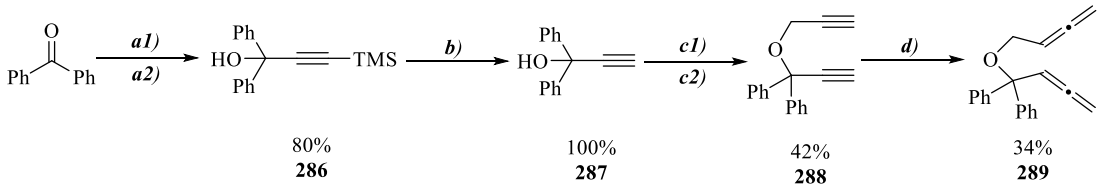
The synthesis of non-symmetrical bisallene **207** (Scheme **104**), was carried out *via* Mitsunobu reaction using as a precursor, allene **276** and the substituted allenol **285** previously synthesised by an S_N2' type reaction from the propargylic derivative **284**.[207a]



a) 3,4-Dihydro-2*H*-pyran (1.1 Eq.), *p*-TsOH (0.01 Eq.), 0 °C, 5 h. ***b1)*** *n*-Buli (2.5 M, in hexane) (1.1 Eq.), 1.1 M, dry Et_2O, -78 °C, 45 min. ***b2)*** $(CH_2O)_n$ (3 Eq.), - 78 °C, 30 min, then rt, 16 h. ***c1)*** $LiAlH_4$ (3 Eq.), 0.21 M, dry Et_2O, 0 °C. ***c2)*** 0 °C to rt, 6 h. *d)* DIAD (1.1 Eq.), PPh_3 (1.1 Eq.), dry THF, 16 h, rt.

Scheme 104. Synthesis of allenol precursor **285**. Synthesis of disubstituted 1,5-bisallene **207**

Oxygen-tethered bisallene **289** (Scheme **105**), disubstituted with two phenyl groups on the carbon adjacent to the oxygen, was synthesised using as the starting material commercially available benzophenone. Alkynylation with ethynyltrimethylsilane gave compound **286**. Deprotection of the alkyne with TBAF (**287**) and propargylation of the alcohol gave access to the bispropargylic ether **288**. Then, microwave assisted Crabbé homologation of compound **288** generated bisallene **289** in moderate yield.

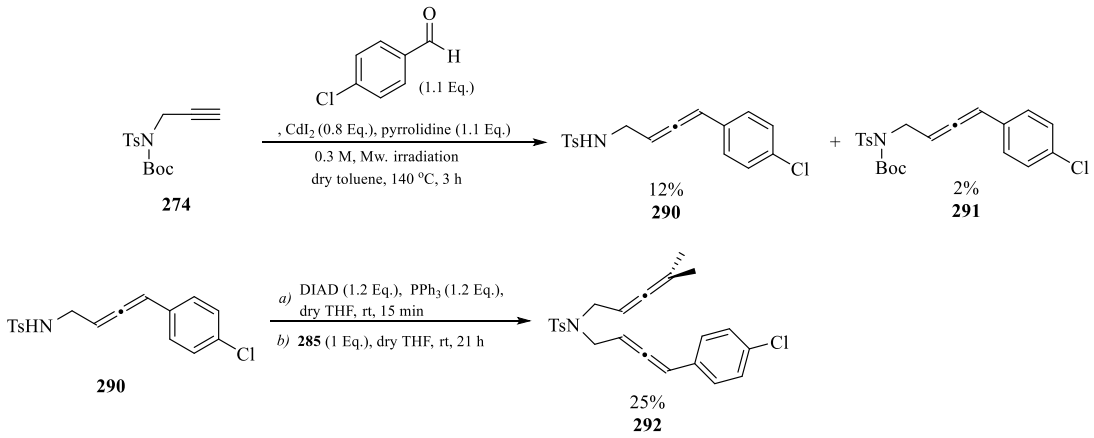


a1) ethynyltrimethylsilane (1.5 Eq.), *n*-Buli (2.5 M in hexane) (1.5 Eq.), 0.23 M, dry THF, -78 °C, 30 min. ***a2)*** - 78 °C, 30 min, then rt, 20 h. ***b)*** TBAF · 3 H_2O, 0.33 M, 0 °C, 1 h 30 min. ***c1)*** NaH (60% in mineral oil) (1.4 Eq.), 0.21 M, dry THF, 0 °C. ***c2)*** Propargyl bromide (80% in toluene) (1.5 Eq.), 0 °C to rt, 17 h. ***d)*** $(CH_2O)_n$ (5 Eq.), CuBr (0.6 Eq.),dry *i*Pr_2NH (4 Eq.), 0.5 M, dry 1,4-dioxane, Mw, 150 °C, 10 min.

Scheme 105. Synthesis of oxygen-tethered bisallene **289**

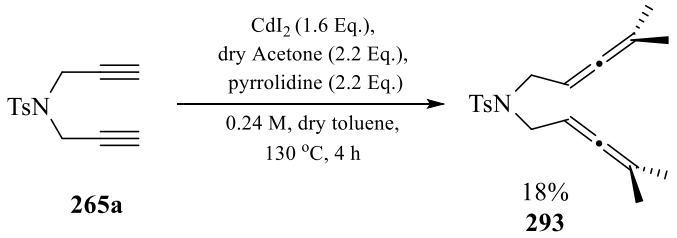
Unsymmetrical bisallene **292** was synthesised in two steps from propargylic *p*-toluensulfonamide **274** (Scheme **106**). In the first step, a modified cadmium-mediated

allenylation of terminal alkynes with aldehydes gave traces of allene **291**.[29] Due to the harsh conditions employed, deprotected allene **290** was also isolated although in low yield. This allene **290** and disubstituted allenol **285** gave access to the unsymmetrical bisallene **292** *via* Mitsunobu reaction.



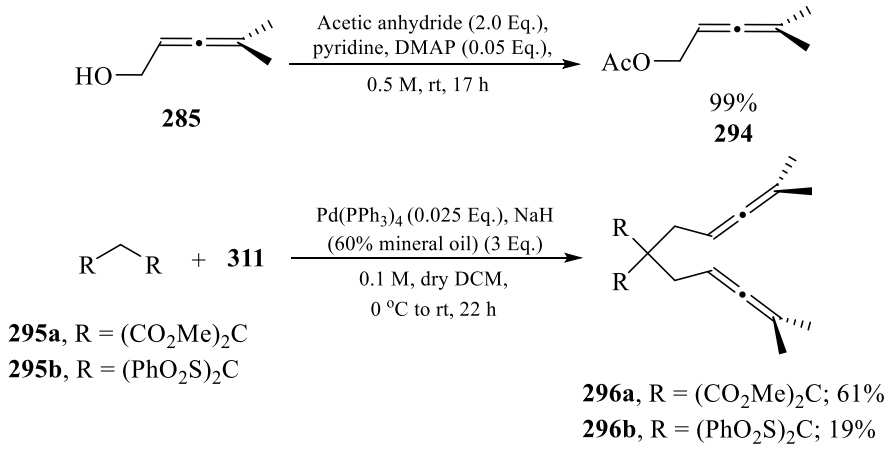
Scheme 106. Synthesis of trisubstituted bisallene **292**

Symmetrically substituted bisallene **293** was synthesised *via* cadmium-mediated bisallenilation of bispropargylic sulfonamide **265a** with acetone in low yield (Scheme **107**).[29]



Scheme 107. Cadmium-mediated synthesis of tetrasubstituted bisallene **293**

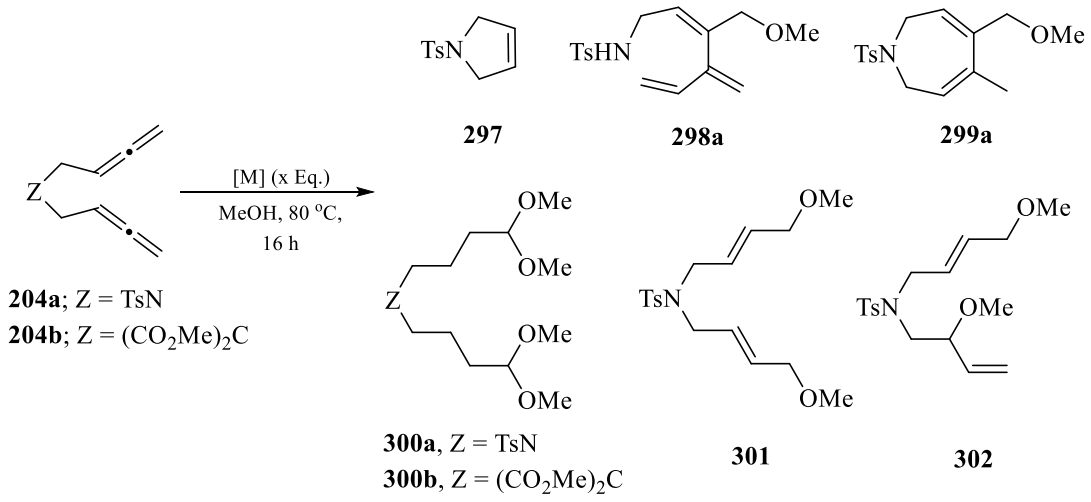
In a different approach, carbon-based thether 1,5-bisallenes **296** were synthesised by palladium-catalysed oxidative addition of allenyl acetates **294** to dimethyl malonate **295a** or bis(phenylsulfonyl)methane **295b** following a described procedure (Scheme **108**).[207a]



Scheme 108. Synthesis of allenyl acetate **294** and carbon-based bisallenes **296a** and **296b**.

3.6.2. Catalysts screening

Bisallenes **204a** and **204b** were employed as model substrates in a preliminary catalyst screening in the search for new reactivity of these compounds in presence of methanol as solvent and as nucleophile, towards the synthesis of ideally 7-membered rings of the type of **299**, with an additional methoxy group incorporated in the final skeleton (Scheme **109** and Table **19**).



Scheme 109. Reaction of 1,5-bisallenes with different transition metal-catalysts

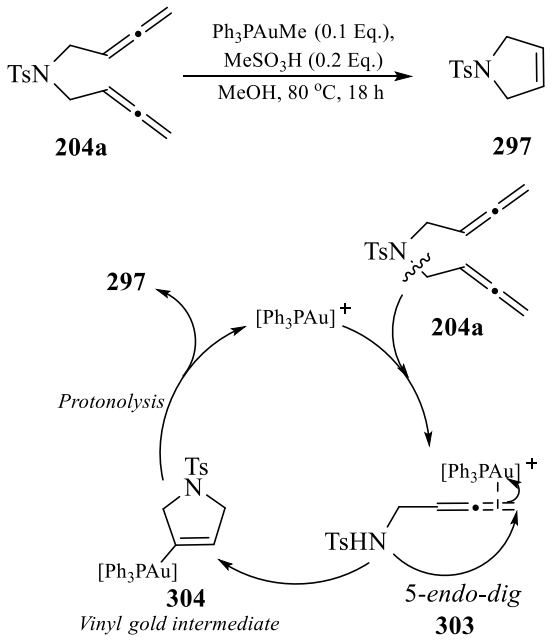
Entry	Bisallene	[M] (x Eq.)	Products, Isolated Yield, %
1	**204b**	$PtCl_2$ (0.1)	**204b**, 40
2	**204b**	$Fe(CO)_5$ (0.1)	No reaction
3	**204b**	$NiCl_2$ (0.1)	No reaction
4	**204b**	$PdCl_2$ (0.1)	No reaction
5	**204b**	$[RhCl(cod)]_2$ (0.1)	Polymer
6	**204a**	$PtCl_2$ (0.1)	**298a**, 19; **299a**, 4; **300a**, 33
7	**204a**	$Fe(CO)_5$ (0.1)	No reaction
8	**204a**	$NiCl_2$ (0.1)	No reaction
9	**204a**	$PdCl_2$ (0.1)	No reaction
10	**204a**	$[RhCl(cod)]_2$ (0.1)	No reaction
11[a]	**204a**	Ph_3PAuMe (0.1), $MeSO_3H$ (0.2)	**297**, 7; **301**, 59; **302**, 18
12[a]	**204a**	$AgNO_3$ (0.1)	No reaction
13[a]	**204a**	CuCl (0.1)	No reaction
14[a]	**204a**	$FeCl_3 \cdot H_2O$ (0.1)	No reaction
15[a]	**204a**	$Hg(NO_3)_2$ (Excess)	No reaction
16[a]	**204a**	$Fe(NO_3)_3 \cdot 9H_20$ (0.1)	No reaction
17[a]	**204a**	$[(CH_3CN)_3RuCp]PF_6$ (0.1); $CeCl_3$ (0.1)	Complex mixture

[a] The reaction was carried out during 18 h.

Table 19. Results obtained from the reaction of 1,5-bisallenes **204a** and **204b** in the presence of different transition metalcomplexes. *This screening was performed by Dr María Paz Muñoz*

No reaction was observed with the following transition metal-catalysts: Fe(0) and Fe(III) (Entries **2**, **7**, **14** and **16**), Ni(II) (Entries **3** and **8**), Pd(II) (Entries **4** and **9**), Rh(I) (Entries **5** and **10**), Ag(I) (Entry **12**), Cu(I) (Entry **13**), Hg(II) (Entry **15**), Ru(II) (Entry **16**).

Transition metals with remarkable Lewis acidic character, Pt(II) (Entries **1** and **6**) and Au(I) (Entry **11**), reacted with the bisallenes **204a** and **204b** (See Table **19**). Au(I)-catalyst gave access to compounds **297**, **301** and **302** in moderate yields. Allylic products **301** and **302** (Scheme **109**) were generated by a gold-catalysed intermolecular addition of MeOH to the terminal position of both allenes (**301**), or addition to one terminal[85a, 86a, 87a] and one internal[85b, 89a] position of the allenes (**302**). (See previous chapter, gold-catalysed intermolecular addition of alcohols to allenes).[87b, 235] 3-Pyrroline **297** was also isolated as a product of reaction using cationic Au(I) as the catalyst. This 5-membered ring could be obtained by cleavage of a N-C bond with the concomitant loss of the allene chain, in an unknown process. Then, subsequent attack of the nitrogen to the activated terminal position of the other allene *via* 5-*endo*-*dig* cyclisation **303** would generate the vinyl gold intermediate **304**, which after protonolysis gives product **297** (See Scheme **110**). The cleavage of the N-C bond with loss of one allenyl chain could be involved in the decomposition of these bisallenes in the reaction with platinum catalysts that will be discussed further in the next few pages. No other cyclisation products were observed with Au(I)-catalysts under these conditions and therefore we abandoned this line of investigation.

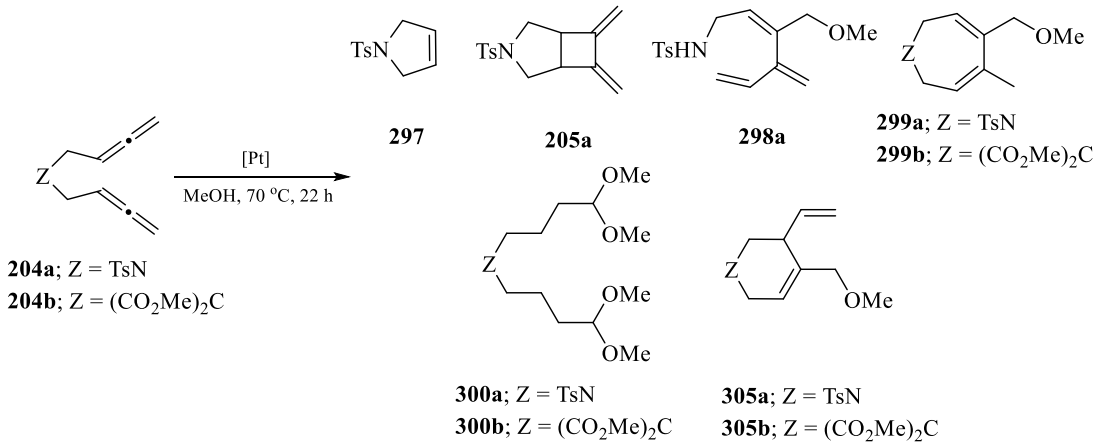


Scheme 110. Proposed mechanism for the formation of 3-pyrroline **297**

The desired 7-membered ring **299a** with an alkoxy group incorporated into its skeleton was only achieved when platinum(II) dichloride was employed as catalyst in presence of

bisallene **204a**. Additionally, the linear triene **298a**, was also obtained and products **300a** (Entry **6**) and **300b** (Entry **1**) were also observed as main products by an unusual platinum-catalysed double dihydroalkoxylation of each allene of the bisallenes **204a** and **204b** respectively. This new reactivity opened new research avenues in the group and the reaction with alcohols and indoles as nucleophiles that has been mentioned in the introduction (see scheme **82**), is currently being investigated and exploited.[191a]

In order to optimise the formation of the cyclic product in the platinum-catalysed reaction, I perfomed a new screening of platinum-complexes with different silver salts, as halogen abstractors to preform *in situ* the cationic complexes with different counterions, in the presence of MeOH and bisallenes **204a** and **204b** (See Scheme **111** and Table **20**).



Scheme 111. Reaction of bisallenes with different platinum complexes

Entry	Bisallene	[Pt] (0.05 Eq.)	AgX (0.1 Eq.)	Products, Isolated Yield, %
1	**204a**	$PtCl_2$	-	**298a**, 37; **299a**, 4; **300a**, 33
2[a],[c]	**204a**	$PtCl_2$	-	**300a**, 66
3[c]	**204a**	$PtCl_2(MeCN)_2$	-	**298a**, 36; **299a**, 5; **300a**, 14
4[c]	**204a**	$PtCl_4$	-	**300a**, 74
5[c]	**204a**	$PtCl_2(MeCN)_2$	AgOTf	**298a**, 24; **305a**, 17
6	**204a**	$PtCl_4$	AgOTf	**297**, 11; **299a**, 20; **305a**, 5
7	**204a**	$PtCl_2(MeCN)_2$	$AgSbF_6$	**297**, 10; **298a**, 9; **299a**, 18; **305a**, 8
8	**204a**	$PtCl_2(MeCN)_2$	NaBArF	**297**, 16; **298a**, 34; **299a**, 13; **305a**, 11
9[c]	**204a**	$PtCl_2(MeCN)_2$	$AgNTf_2$	**297**, 19; **298a**, 16; **299a**, 9; **305a**, 5
10[c]	**204a**	$PtCl_2(MeCN)_2$	$NaBPh_4$	**297**, 3; **205a**, 4
11[b],[c]	**204a**	$PtCl_4$	AgOTf	**297**, 24; **298a**, 8; **299a**, 7; **305a**, 16
12	**204a**	$K[Pt(C_2H_4)Cl_3 \cdot H_2O$	$AgSbF_6$	**305a**, 4; Complex mixture
13	**204b**	$PtCl_2(MeCN)_2$	$AgSbF_6$	**299b**, 11; **305b**, 7
14[d]	**204a**	$PtCl_2(MeCN)_2$	$AgSbF_6$	**298a**, 30; **299a**, 13; **305a**, 11

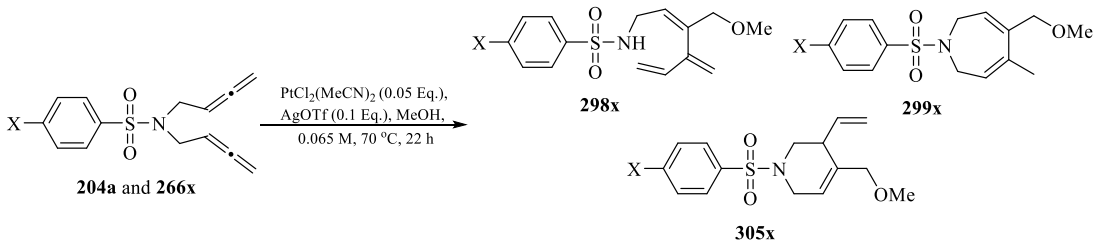
[a] The reaction was carried out in toluene, using 4 Eq. of MeOH. **[b]** The reaction was carried out at room temperature. **[c]** Reaction time 20 h. **[d]** Products were purified with new high purity silica gel.

Table 20. Results obtained from the reaction of 1,5-bisallenes **204a** and **204b** in the presence of different platinum complexes

The results shown in Table **20** suggest that the selectivity towards the cyclic products is very sensitive to reaction conditions and platinum complexes. The formation of cationic platinum(II) and platinum(IV) complexes avoided the formation of the bisacetal products **300** but a new 6-membered ring **305** was also observed in different amounts depending on the

cationic platinum complexes employed (Table **20**). The use of AgOTf and $AgSbF_6$ to form the cationic complexes gave the best selectivity towards the 7-membered rings **299b** (Entry **13**) and **299a** (Entries **5**, **6** and **14**), with also formation of triene **298a**. Besides, it was observed that products were not very stable to column chromatography and probably this could explain the low isolated yields obtained. In order to solve this issue, a new high purity silica gel was used as stationary phase obtaining better yields in comparison with those previously obtained (see comparison of Entry **7** and Entry **14**, Table **20**).

The highest selectivity towards 7-membered cycle **299a** was obtained using $PtCl_2(MeCN)_2$ as catalyst (0.05 Eq.) and 0.1 Eq. of AgOTf as halide abstractor, in MeOH at 70 ºC (See Table **20**, Entry **5**), and these were chosen as the optimum reaction conditions to study the scope of the reaction with different 1,5-bisallenes. We first used different sulfonamide derivatives as tethers in order to study the effect of the electronic nature of the bisallene in the reaction (see Scheme **112** and Table **21**).



Scheme 112. Platinum-catalysed alkoxycyclisation of sulfonamide derivatives

Entry	Bisallene	X	Isolated Yields, %		
			298x	**299x**	**305x**
1	**204a**	Me	**298a**, 30	**299a**, 13	**305a**, 11
2	**266c**	NO_2	**298c**, 29	**299c**, 25	-
3	**266d**	H	**298d**, 18	**299d**, 8	**305d**, 11
4[a]	**266e**	MeO	**298e**, 4	-	**305e**, 4
5	**266f**	Cl	**298f**, 8	**299f**, 27	**305f**, 13

[a] Products **298e** and **305e** were isolated by prep-TLC

Table 21. Results obtained with sulfonamide derivatives under the best reaction conditions so far

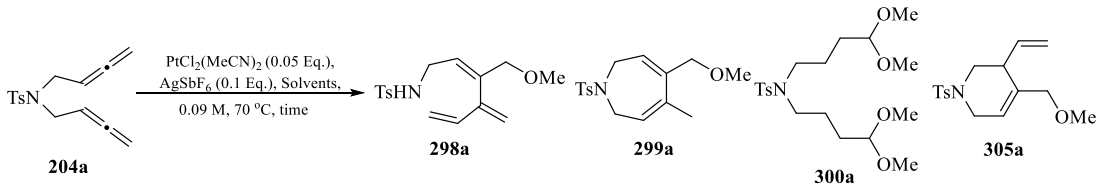
As it is observed in Table **21**, the strong electron withdrawing influence of nitro group in para position avoids formation of the 6-membered ring (Entry **2**). The 7-Membered ring is not formed when the strong donating group MeO- is used (Entry **4**). The triene **298x** was formed as main product in most of the cases except when a chloride group in para position of aromatic ring was used, which favoured the formation of the two cyclic products (Entry **5**).

However, it is important to highlight the low yields obtained in all the cases, even when high purity silica gel is employed to isolate the products. These results suggest that possibly the starting material is decomposing under reaction conditions as mentioned in the work reported by Jang and coworkers.[211]

In order to enhance the selectivity as well as the isolated yield we decided to perform a new screening of conditions.

3.6.3. Solvent Screening

Previous results confirmed that cationic platinum complexes, pre-formed from $PtCl_2(MeCN)_2$, were essential to avoid the formation of the bisacetals **300** leading to the synthesis towards 6-membered cycle **305** or 7-membered cycle **299** (See Table **20**). However, all the reactions were performed using methanol as solvent and as the nucleophile so far. In order to check the possible influence of the concentration of methanol in the reaction, a screening of different ratios of MeOH in THF were studied using standard bisallene **204a** (see Table **22**). In this screening $AgSbF_6$ was used as halide abstractor.



Scheme 113. Platinum(II)-catalysed carbocyclisation of 1,5-bisallenes with different ratios of MeOH in THF or MeCN

Entry	Solvents (ratio)	t (h)	NMR Ratio (**298x**:**299x**:**300x**:**305x**) before purification / Isolated Yield, %[e]
1[a]	MeOH	30	(9.1:1:0:3.2)
2	THF:MeOH (1:1)	5	(4.1:1:0:10)
3	THF:MeOH (5:1)	5	(5.6:1:0:24)
4	THF:MeOH (9:1)	2 h 40 min	(1:0:0:2.7) / **298a**, 11; **305a**, 39
5	THF:MeOH (18:1)	4	(1.7:0:0:1) / **298a**, 37; **305a**, 36
6	THF:MeOH (30:1)	7	(1:0:0:1.6)
7[b]	THF:MeOH (9:1)	1 h 30 min	(1:0:0:1.5) / **298a**, 7; **305a**, 33
8[c]	THF:MeOH (9:1)	1 h 45 min	**300a**, 71
9[d]	MeCN:MeOH (18:1)	26	**298a**; 20% conversion

[a] The reaction was carried out at room temperature. **[b]** The concentration of the bisallene was 0.2 M. **[c]** The reaction was performed using $PtCl_4$ (0.05 Eq.) and $AgSbF_6$ (0.1 Eq.) as catalyst. **[d]** The reaction was heated at 90 °C. **[e]** 100% conversion observed in all the reactions.

Table 22. Results obtained after screening of different proportions of MeOH in THF and MeCN

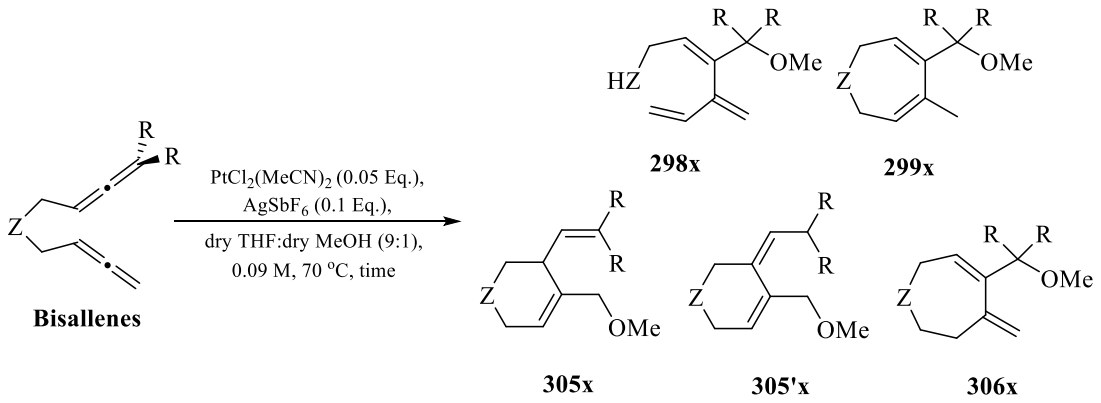
The reaction was very sensitive to modifications on the ratios of THF/MeOH. When the amount of MeOH descreases in comparison to THF, the formation of the 6-membered ring **305a** was preferred over the formation of the 7-membered ring **299a**. The mixture THF/MeOH (9:1) gave cyclic compound **305a** as main product, even employing different concentrations of the bisallene **204a** (Entries **4** and **7**). Formation of **298a** was observed in all the reactions. Comparing the ratio of products before and after purification, it was clear that purification issues were still present (compare ratio of products before and after purification in Entry **5**, for example).

The results shown in Table **22** also revealed that the reaction gives less selectivity at room temperature (Entry **1**). Moreover, cationic platinum(IV)-complex (Entry **8**), with the mixture THF/MeOH (9:1) gave access to a rapid conversion to bisacetal **300a** in good yield, but not to the heterocycles **299a** and **305a**.

Vinylcyclohexanes derivatives **305** are important building blocks in the synthesis of natural products.[128c, 236] Besides, cyclisation to give 6-membered rings is less common in 1,5-bisallene chemistry (see introduction of this chapter). Therefore, we decided to explore the scope of the reaction using the optimised conditions for the formation of substituted vinylcyclohexanes with MeOH as nucleophile in a 9:1 mixture of THF:MeOH.

3.6.4. Scope of platinum-catalysed alkoxycyclisation reaction of 1,5-bisallenes

With an efficient mixture of solvents as well as the suitable catalyst in hand, the scope of this transformation was explored with several bisallenes.



Scheme 114. Platinum-catalysed alkoxycyclisation of 1,5-bisallenes under the best reaction conditions

Entry	Bisallenes	t (h)	Ratio (**298x**:**299x**:**305x**:**305'x**:**306x**) before purification / Isolated Yield, %[a]
1	**204a**; Z = TsN; R = H	2 h 40 min	(1:0:2.7:0:0) / **298a**, 11; **305a**, 39
2	**266c**; Z = *p*-NO_2-$PhSO_2N$; R = H	2 h 10 min	(3.6:2.4:1:0:1.6) / (**298c**+**306c** (4:1)), 30;[b] **299c**, 25
3	**266d**; Z = $PhSO_2N$; R = H	2 h 15 min	(3.4:0:1.5:1:0) / (**298d**+**305'd** (1.1:1)), 43;[b] **305d**, 19
4	**266e**; Z = *p*-MeO-$PhSO_2N$; R = H	1 h 30 min	(2:0:1:0:0) / **298e**, 44; **305e**, 26
5	**266f**; Z = *p*-Cl-$PhSO_2N$; R = H	2 h 25 min	(1:4.5:6.3:3.2:0) / **298f**, 2; **299f**+**305f'** (1.5:1), 31[b]; **305f**, 17
6	**266g**; Z = *p*-CF_3-$PhSO_2N$; R = H	2 h	(1.1:1.2:2.1:1:0) / **298g**, 1; **299g**+**305g' (traces)** 5;[b] **305g**, 6
7	**266i**; Z = CH_3SO_2N; R = H	1 h 30 min	(10.4:1:3.8:0:0) / **298i**+**305i** (1:2.9), 31;[b] **299i**, traces
8	**207**; Z = TsN; R = Me	> 48 h[c]	**305l**, 16

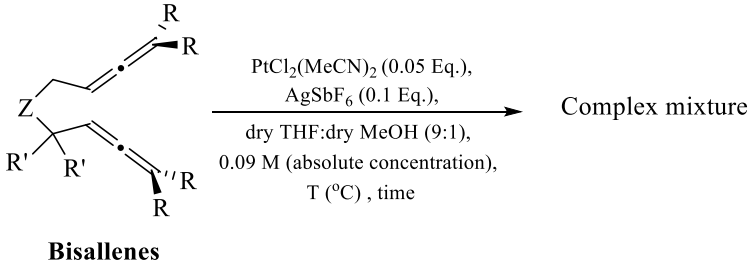
[a] Complete conversion unless otherwise stated. **[b]** Obtained as inseparable mixture. **[c]** Conversion < 100 %.

Table 23. Scope of platinum-catalysed alkoxycyclisation of 1,5-bisallenes

Vinylcyclohexene derivatives **305x** were observed with all the bisallenes employed. Electron donating groups (Entries **1**, **3**, **4**, **7** and **8**, Table **23**) favoured the formation of 6-membered rings **305x** and trienes **298x** in moderate to low isolated yields. In contrast, electron withdrawing groups (Entries **2**, **5** and **6**) gave mixtures of the cyclic products and trienes **298x** in low isolated yields. A new 7-membered cycle **306c**, isomer of **299c** was identified in the reaction of the nitro derivative (Entry **2**). Besides, an isomer **305f'**of vinylcyclohexene derivative **305f** was obtained using chloride derivative **266f**. Bisallene **207**, sterically hindered

in one allene led the nucleophilic attack to the non-substituted allene, giving as the only product the 6-membered cycle **305l** in low yield (Entry **8**).

When we tried the platinum-catalysed alkoxycyclisation of 1,5-bisallenes with other tethers different from sulfonamides, we observed complex reaction mixtures as shown in Table **24**. With the more substituted bisallenes long reaction times (Entry **5**, Table **24**) or microwave heating were employed without success (Entries **6** and **7**).



Scheme 115. Unsuccesful alkoxycyclisation of 1,5-bisallenes under the best reaction conditions so far

Entry	Bisallenes	t (h)	T °C	Products
1	**204b**; Z = $(CO_2Me)_2C$; R = R_1 = H	> 48 h	70	Traces of **299b** and **305b**
2	**260j**; Z = PhN; R, R_1 = H	> 24 h	70	Complex mixture
3	**266k**; Z = *p*-Br-PhN; R, R_1 = H	> 24 h	70	Complex mixture
4	**289**; Z = O; R = H; R_1 = Ph	> 24 h	70	Complex mixture
5	**293**; Z = TsN; R = Me, R_1 = H	40 h	90	Complex mixture
6[a]	**296a**; Z = $(CO_2Me)_2C$; R = Me; R_1 = H	10 h	90	Complex mixture
7[a]	**296b**; Z = $(PhO_2S)_2C$; R = Me; R_1 = H	4 h	90	Complex mixture

[a] Reaction was carried out under microwave irradiation.

Table 24. Unsuccesful alkoxycyclisation of 1,5-bisallenes under the best reaction conditions so far

These results emphasised the important role of sulfonamide groups as tethers in bisallene chemistry.[207a, 213, 223b] In our hands, only sulfonamide-tethered bisallenes reacted under the optimal reaction conditions. However, it is worth remembering that using MeOH as solvent and as nucleophile, bisallene **204b** with dimethylmalonate as tether gave the cyclisation products, in low isolated yields (Entry **13**, Table **20**).

Although we showed improved selectivity towards a specific cyclisation mode, the low yields and limited scope were still a challenge in this methodology. We therefore decided to use internal references to report NMR yields and compare with yields of isolated products. We also investigated the decomposition of the starting material under the reaction conditions, and we performed a new screening of platinum-complexes under optimal reaction conditions for the formation of the 6-membered rings.

3.6.5. Internal references to quantify NMR yields

Quantification by ^{1}H NMR spectroscopy is a simple and robust technique commonly used nowadays.[237] In this approach, an internal standard, consisting of a known amount of a compound chemically inert and soluble in the solvent employed is added. All the products of the reaction can be quantified at the same time, providing that clean isolated signals for each can be analysed in the ^{1}H NMR spectra, by comparing their integrals with the integral of the internal standard.

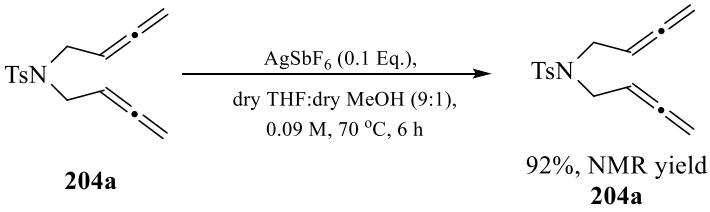
We tried several known internal standards under the optimal reaction conditions using bisallene **266c** as starting material: TBDMSCl, hexamethyldisilane, ferrocene, 3,4,5-trichloropyridine and dimethyl sulfone. However, the first three were not suitable for our quantification due to different reasons: accurate integration of the silane derivatives was difficult due to the strong signals of these derivatives; there was overlap of the signals of the ferrocene with signals from the reaction products; so we discharged them as internal standards. Coordination of the 3,4,5-trichloropyridine to the platinum displacing the acetonitrile ligands changed the reaction course. However, a stock solution with a known amount of 3,4,5-trichloropyridine in $CDCl_3$ was prepared and a sample added as internal standard to the crude of reaction allowed us to measure accurately the integrals of the products of reaction. In addition, dimethyl sulfone was also employed as internal standard added from the beginning to the reaction media, not interfering during the reaction process.

3.6.6. Experiments to study the level of decomposition of the starting material under reaction conditions

As it was mentioned before, the group of Jang in the platinum-catalysed reductive cyclisation of 1,5-bisallenes, confirmed the decomposition of the starting material under their reaction conditions.[211] It was also reported that substituents at the allene terminus slow down the rate of decomposition of the allenes.[238]

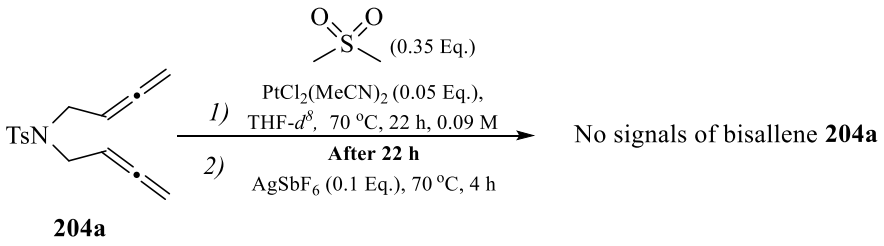
In order to quantify the grade of decomposition of starting material under our reaction conditions, model bisallene **204a** was used in three different experiments with modifications on the parameters of the reaction:

Experiment **A**: the reaction was performed in absence of the platinum-catalyst. After 6 hours, the NMR yield was measured using as internal reference and accurate volume of a stock solution of 3,4,5-trichloropyridine in $CDCl_3$ added to the crude of the reaction. Low decomposition levels of the bisallene were observed (Scheme **116**).



Scheme 116. Experiment **A**. Reaction carried out to observed the decomposition of starting material without the platinum-catalyst

Experiment **B**: the reaction was performed using bisallene **204a**, platinum-catalyst, and THF-d^8, without halide abstractor during the first 22 hours in an NMR tube, heated and stirred in an oil bath and monitored by ^{1}H NMR using as internal reference dimethyl sulfone (2.869 ppm) (Scheme **117**).



Scheme 117. Experiment **B**, was performed to quantify the level of decomposition of the starting material in absence of nucleophile and halide abstractor.

Figure **30** shows the ^{1}H NMR spectra of experiment **B**, obtained during the first 22 hours without silver salt. The concentration of the bisallene was plot over time to show the rate of decomposition of bisallene **204a** under reaction conditions (Figure **31**). It was observed that 40% of bisallene had disappeared after 3 h, 55% after 8.5 h and 22 h later only 26% of the starting material remains in solution. After 22 h, 0.1 Eq. of $AgSbF_6$ was added to the NMR tube under inert atmosphere. Inmediately after the addition and 4 hours later, two ^{1}H NMR spectra were run, observing a much faster decomposition of **204a** after formation the cationic platinum-complex (Figure **30** and **31**-orange dots).

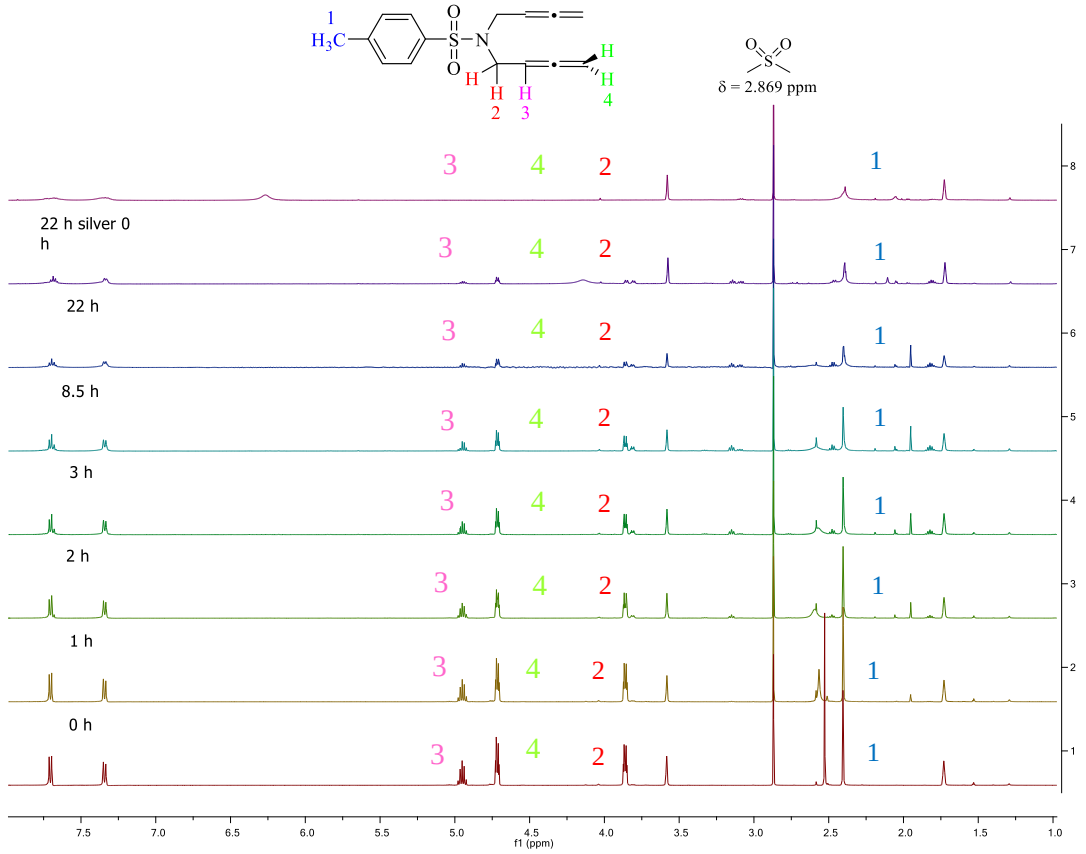


Figure 30. Results obtained monitoring the reaction by ^{1}H NMR of experiment **B** shown in Scheme **118**

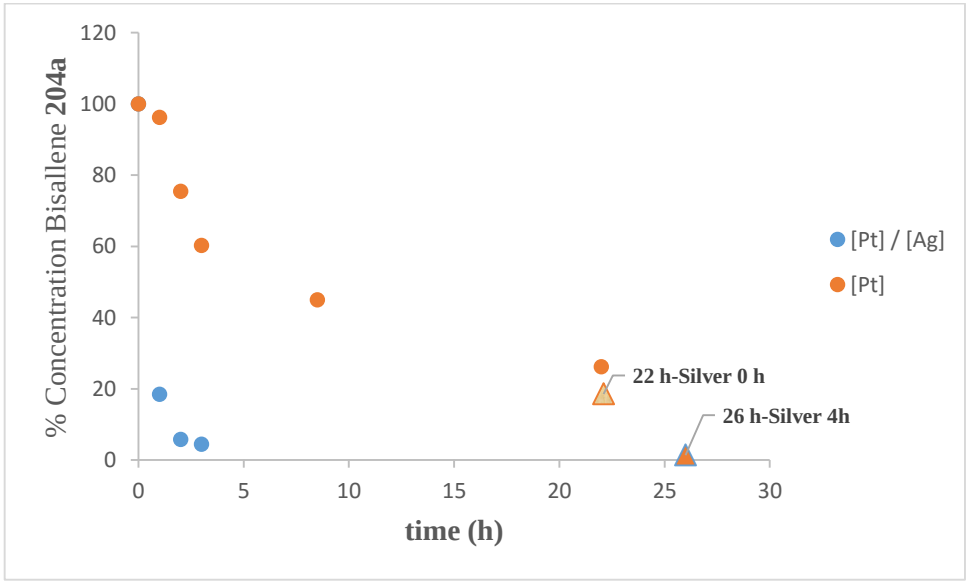
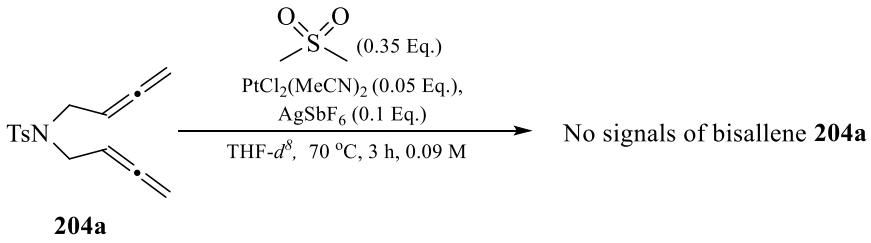


Figure 31. Results obtained in experiment **B** (orange) and **C** (blue)

Experiment **C**: the reaction was performed using the model bisallene **204a**, preforming *in situ* the cationic platinum-complex in THF-d^8 in absence of MeOH in an NMR tube, heated and stirred in an oil bath and monitored by ^{1}H NMR using dimethyl sulfone as internal reference (Scheme **118**).



Scheme 118. Experiments **C** to quantify the grade of decomposition of 1,5-bisallenes without nucleophile

^{1}H NMR spectra of experiment **C** (Figure **32**), and the plot of the concentration of the bisallene over time (Figure **31**-blue dots), showed a much rapid decomposition of the starting material in only 3 hours of reaction in the presence of the cationic complex.

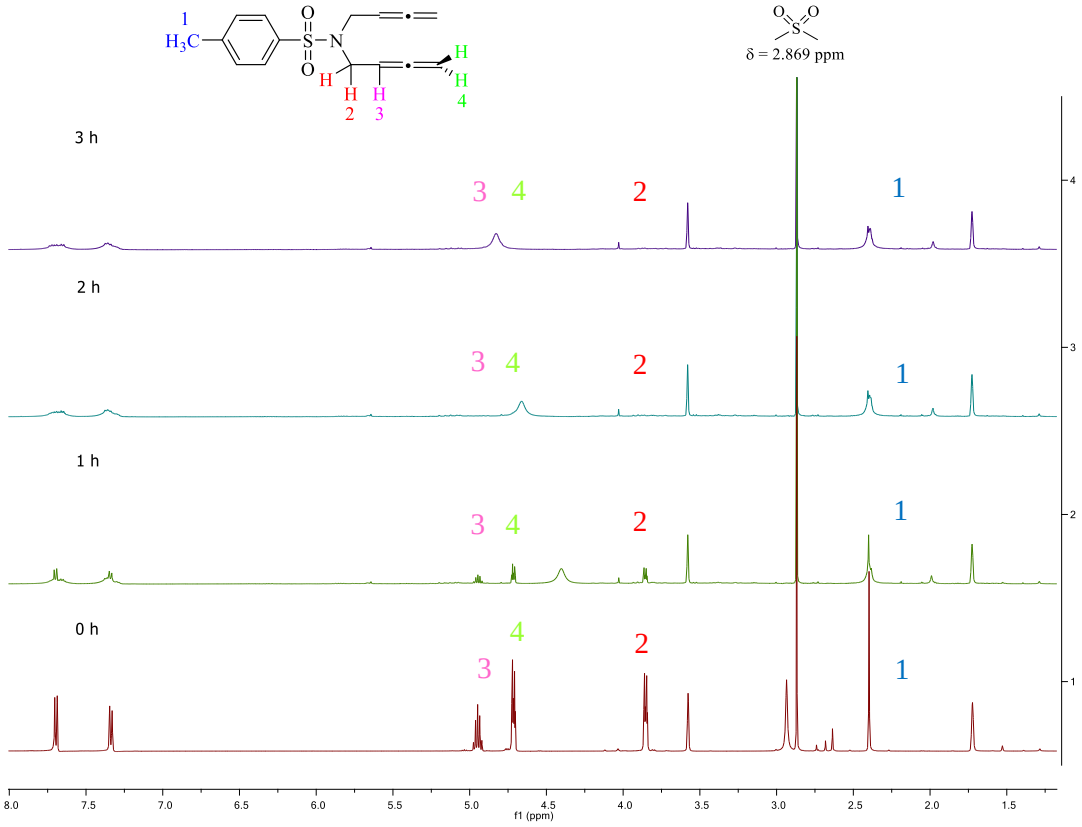


Figure 32. Results obtained monitoring by ^{1}H NMR of experiment **C** shown in Scheme **118**

It should be noted that the tosyl group of the sulfonamide does not disappear during the reaction. In contrast, the signals corresponding to the allenic skeleton desapeared under reaction conditions supporting the loss of the allenyl chain mentioned in the formation of compound **297** in Scheme **110** (See Figure **30** and **32**). The rapid decomposition of starting material in the presence of the cationic complex suggests that the reaction has to be completed in a short time. Therefore, a new search for a better platinum catalysts able to perform the cyclisation faster and under milder conditions was carried out.

3.6.7. New screening of platinum catalysts

Platinum catalysts **308**, **310** and **312** were purchased from commercial sources and were used without further purification. Catalyts **307**[239] and **311**[240] were synthesised by Dr Quiros in our laboratory. $PtCl_2$(dppp) **309** was synthesised from $PtCl_2$ using known methodologies.[241]

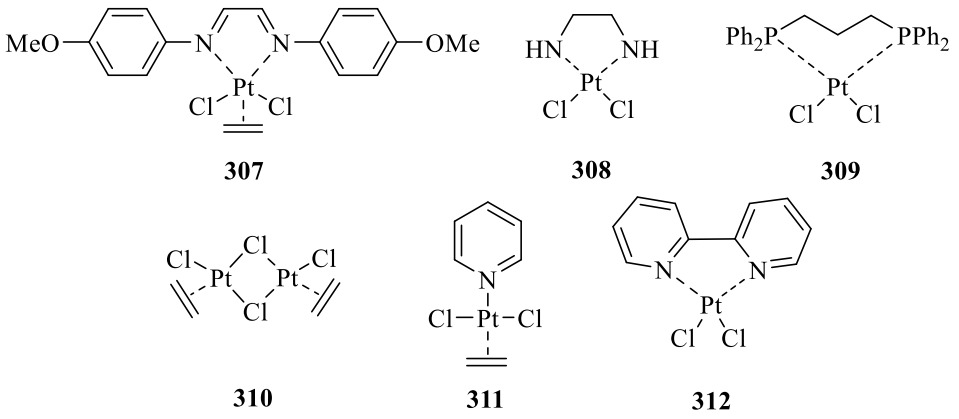
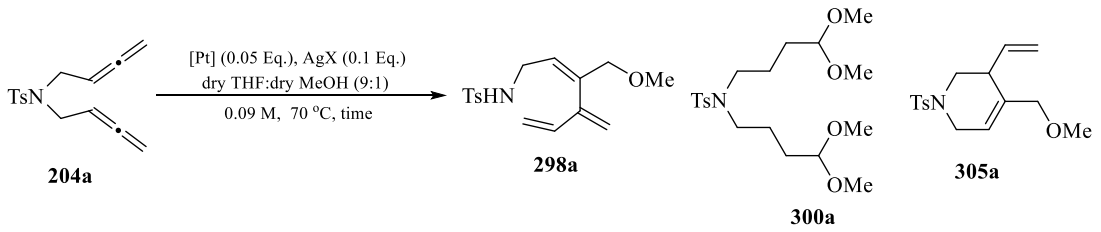


Figure 33. Platinum(II)-catalysts tested under reaction conditions.

In contrast with the electron withdrawing character of nitrile ligand employed so far, strong electron donating pyridine ligands such as **311** and **312** were used. Additionaly, uncommon platinum(II)-pentacoordinate complex **307** with strong electron donation from the ligand to the metal centre was also tested. Reactions with complexes containing a labile ethylene ligand that can be displaced by allenes were tested and compare in the reaction with and without halide abstractors, hoping that the π-systems of the allene η^2-bounded to the neutral platinum complex will be efficiently activated for the nucleophilic attack triggering the expected carbocyclisation of the bisallenes. Furthermore, bulky ligands such as (dppp) **309**,[241] bridging chloride ligands **310** and chelating ethylenediamine ligand (en) **308** were also employed in this screening.



204a **298a** **300a** **305a**

Scheme 119. Reaction conditions to the new screening of platinum-catalysts

Entry	[Pt]	AgX	t (h)	Isolated yields (%)[a]		
				298a	**300a**	**305a**
1	**308**	$AgSbF_6$	2 h 40 min	15	-	18
2	**312**	$AgSbF_6$	6 h	Complex mixture		
3	**307**	$AgSbF_6$	2 h	53[b]	-	-
4	**307**	-	> 27 h	Complex mixture[c]		
5	**311**	$AgSbF_6$	2 h	24	-	16
6	**311**	-	16 h	Complex mixture		
7	**310**	-	20 h	-	83[b]	-
8	**309**	$AgSbF_6$	24 h	No reaction		

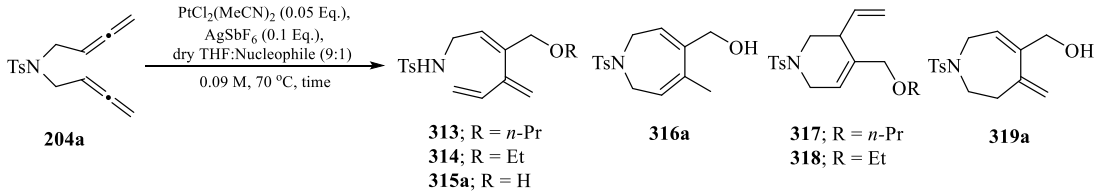
[a] 100% conversion. **[b]** NMR yield. **[c]** Not 100 % conversion.

Table 25. Results obtained after new screening of platinum-complexes under reaction conditions

A complex mixture was obtained when platinum complex **312** was employed in the reaction (Entry **2,** Table **25**). Unsuccesful results were also achieved with platinum catalysts **307** and **311** (Entries **4** and **6**). High selectivity and moderate yield of triene **298a** was obtained with catalyst **307** in the presence of 0.1 Eq. of $AgSbF_6$ (Entry **3**). Di-μ-chloro-dichlorobis(ethylene)diplatinum(II) **310** (Entry **7**) gave in good yield bisacetal **300a**. 6-Membered cycle **305a** and triene **298a** where obtained in low yields using platinum complexes **308** and **311** (Entries **1** and **5** respectively). The new screening of platinum catalysts revealed that electron donor ligands or bulky phosphines do not favour any cyclisation mode. Thus, the electron withdrawing nature of nitrile ligands and $AgSbF_6$ as halide abstractor seems to be the best combination to lead the reaction towards the desired products.

3.6.8. Scope with different oxygen-nucleophiles

This methodology is extremely sensitive to reaction conditions (catalysts, counterions, solvents). Despite all the extensive screening described so far, the nature of the nucleophile has not been mentioned yet. In this regard, *n*-PrOH, EtOH and H_2O were used under optimal conditions employing $PtCl_2(MeCN)_2/AgSbF_6$ as catalyst and bisallene **204a** as the model substrate.



Scheme 119. Platinum-catalysed alkoxy- and hydroxycyclisations of 1,5-bisallenes

Entry	Nucleophile	t (h)	Isolated Yields, %[a]
1	*n*-PrOH	1 h 40 min	**313**, 24; **317**, 20
2	EtOH	1 h 45 min	**314**, 20; **318**, 23
3[b]	H_2O	5 h 30 min	**315a**, 2; **316a**, 16; **319a**, 21

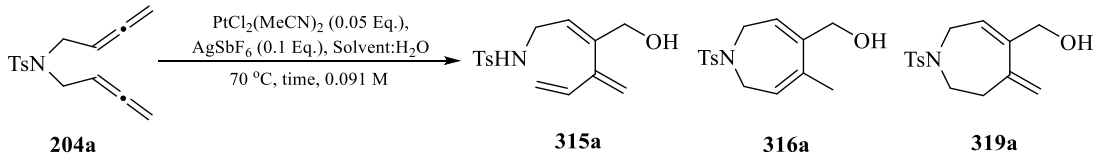
[a] 100% conversion. **[b]** NMR yield using 3, 4, 5-trichloropyridine as internal standard added to the crude of reaction

Table 26. Results obtained after platinum-catalysed reaction of 1,5-bisallenes with *n*-PrOH, EtOH and H_2O as nucleophiles

6-Membered rings **317** and **318**, as well as the corresponding trienes **313** and **314** were obtained when *n*-PrOH and EtOH were used as nucleophiles (Entries **1** and **2**, Table **26**). However, with water as the nucleophile, high selectivity to the 7-membered cycles (**316a** and **319a**, Entry **3**) was observed in moderate yield. Additionally, triene **315a** was obtained in only 2% in this reaction. These results showing the divergent reactivity towards the 7-membered cycles prompted us to investigate further H_2O as nucleophile in the reaction.

3.6.9. Optimisation conditions using H_2O as nucleophile

Following the trend of the previous mixtures of THF/MeOH, a small screening of ratios of water in different solvents was performed. To do so, we employed $PtCl_2(MeCN)_2$ and $AgSbF_6$ as catalytic source and the model bisallene **204a** at 70 °C.



Scheme 120. Optimisation of the ratio solvent:H_2O for the platinum-catalysed hydroxycyclisation of 1,5-bisallene **204a**

Entry	Solvent:H_2O (ratio)	t (h)	NMR Yields, %[a],[b]		
			315a	**316a**	**319a**
1[c]	THF:H_2O (9:1)	5 h 30 min	2	16	21
2	THF:H_2O (18:1)	5 h 45 min	2	7	33
3	THF:H_2O (20:1)	5 h	22	11	17
4	THF:H_2O (3 Eq.)	26 h	31	-	-
5	Toluene:H_2O (18:1)	> 48 h	Complex mixture		
6	1,4-dioxane:H_2O (18:1)	4 h	6	1	1

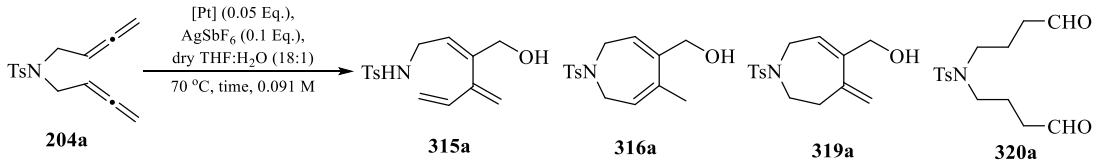
[a] 100% conversion of starting material. **[b]** NMR yield using 3,4,5-trichloropyridine as internal standard added to the crude of reaction. **[c]** As in Table **26**, entry **3**.

Table 27. Results obtained under reaction conditions using different ratio of solvents and water as nucleophile

The best results for the formation of product **319a** were obtained when a mixture of THF:H_2O (18:1) was employed (Entry **2**, Table **27**). Isomer **316a** and triene **315a** were obtained in all the cases, being the triene the only product detected when only 3 Eq. of H_2O were added (Entry **4**). Toluene and 1,4-dioxane did not give better results (Entries **5** and **6**).

3.6.10. Screening of platinum-catalysts with the new conditions using H_2O as nucleophile

With the optimal mixture of solvents achieved in the previous step (Entry **2**, Table **27**), a new screening of platinum-catalysts was also performed with water, using bisallene **204a** as the starting material (Table **28**). Unfortunately, none of the platinum complexes tested enhanced neither the selectivity nor the yields of the desired products. Also, the bisaldehyde **320a** generated by platinum-catalysed dihydroxylation of each of the allenes was observed in reactions without the silver salt present (Entries **3**, **4**, **5** and **6**).[191a]



Scheme 121. Screening of platinum-catalysts with the new optimal conditions using water as nucleophile

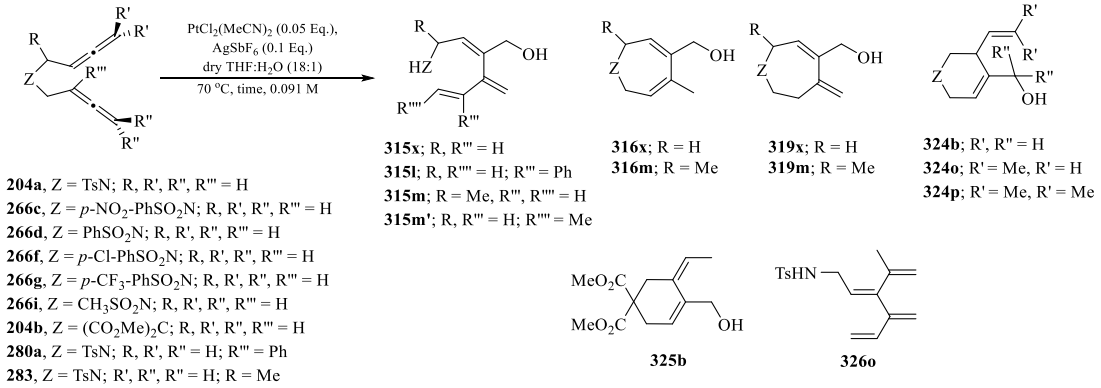
Entry	[Pt]	t (h)	NMR Yields (%)				
			315a	**316a**	**319a**	**320a**	**204a**
1	**308** $PtCl_2$(en)	23 h	5	6	17	-	-
2	**312** $PtCl_2$(bipy)	> 48 h	No reaction				
3	$PtCl_2(MeCN)_2$[a]	4 h	-	-	-	91	-
4	**307** $PtCl_2(C_2H_4)(RNCHCHNR)$[a],[b]	26 h	0	6	10	4	5
5	**310** $[Pt_2Cl_2(\mu\text{-}Cl)_2(C_2H_4)_2]$[a]	> 48 h	0	6	4	21	9
6	**321** [PtCl(terpy)]Cl[a]	50 h	0	0	0	5	64
7	**322** [PtCl(terpy)]SbF_6	53 h	6	4	9	-	30
8	**323** *cis/trans*-$PtCl_2(PPh_3)_2$	24 h	No reaction				

[a] The reaction was carried out without halide abstractor. **[b]** R = (*p*-OMe(C_6H_4)).

Table 28. Screening of platinum-complexes using water as nucleophile

3.6.11. Scope of platinum-catalysed hydroxycyclisation reaction of 1,5-bisallenes

The scope of the reaction was studied with water as nucleophile and several substituted 1,5-bisallenes using the best conditions so far for the formation of the 7-membered rings (Scheme **122**, Table **29**).



204a, Z = TsN; R, R', R", R'" = H
266c, Z = *p*-NO_2-$PhSO_2N$; R, R', R", R'" = H
266d, Z = $PhSO_2N$; R, R', R", R'" = H
266f, Z = *p*-Cl-$PhSO_2N$; R, R', R", R'" = H
266g, Z = *p*-CF_3-$PhSO_2N$; R, R', R", R'" = H
266i, Z = CH_3SO_2N; R, R', R", R'" = H
204b, Z = $(CO_2Me)_2C$; R, R', R", R'" = H
280a, Z = TsN; R, R', R" = H; R'" = Ph
283, Z = TsN; R', R", R" = H; R = Me
207, Z = TsN; R, R", R'" = H; R" = Me
293, Z = TsN; R, R'" = H; R', R" = Me

315x; R, R'" = H
315l; R, R'"" = H; R'" = Ph
315m; R = Me, R'", R'"" = H
315m'; R, R'" = H; R'"" = Me

316x; R = H
316m; R = Me

319x; R = H
319m; R = Me

324b; R', R" = H
324o; R' = Me, R' = H
324p; R' = Me, R' = Me

325b

326o

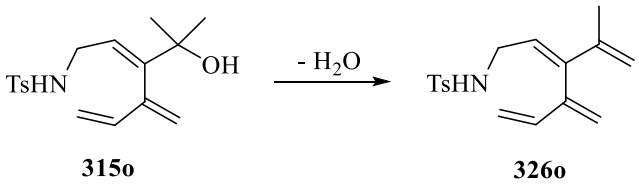
Scheme 122. Scope platinum-catalysed hydroxycyclisation of 1,5-bisallenes under the best reaction conditions

Entry	Bisallene	t (h)	Products (ratios after purification)/ Isolated Yields, %[a]
1	**204a**	5 h 45 min	**315a**:**316a**:**319a** (1:1.4:5)/ 41[b]
2	**266c**	5 h	**316c**:**319c** (1:1.1)/ 54[b]
3	**266d**	5 h 30 min	**315d**:**316d**:**319d** (2:1:3.8)/ 53[b]
4	**266f**	22 h	**315f**:**316f**:**319f** (1:4.7:6.9)/ 35[b]
5	**266g**	4 h 30 min	**316g**:**319g** (1:2.6)/ 34[b]
6	**266i**	5 h 30 min	**315i**:**316i**:**319i** (3:1:3)/ 52[b]
7	**204b**	30 h	**324b**:**325b** (1:1.3)[c]/ 11[b]; **316b**, 9
8	**280a**	24 h + 6 h[c]	**315l**, 8
9	**283**	24 h	**316m**:**319m** (1:1.4)/ 21[b]; **315m**:**315m'** (1.2:1) 22[b]
10	**207**	6 h[c]	**324o**, 28; **326o**, 24
11	**293**	48 h[d]	**324p**, 16

[a] 100% conversion. **[b]** Obtained as inseparable mixture. **[c]** Microwave heating 90 °C. **[d]** Not 100 % conversion.

Table 29. Results obtained with bisallenic precursors after optimised reaction conditions

7-membered cyclisation products **319x** were obtained as the main products with non-substituted *N*-tethered bisallenes, in inseparable mixtures with isomers **316x** and trienes **315x** (Table **29**). It should be mentioned, that electron-withdrawing groups on the tether avoided the formation of triene **315** (Entries **2** and **5**). The triene was also not observed when malonate was used as tether (Entry **7**). Formation of 6-membered rings **324x** was obtained when bulky substituents were incorporated on the terminal carbon of the bisallenes (Entries **10** and **11**). Tetraene **326o** was also isolated from bisallene **207** (Scheme **123**), possibly formed by loss of water from the triene **315o**, originally formed in the reaction, due to the harsher conditions employed (Entry **10**, Table **29**).



315o **326o**

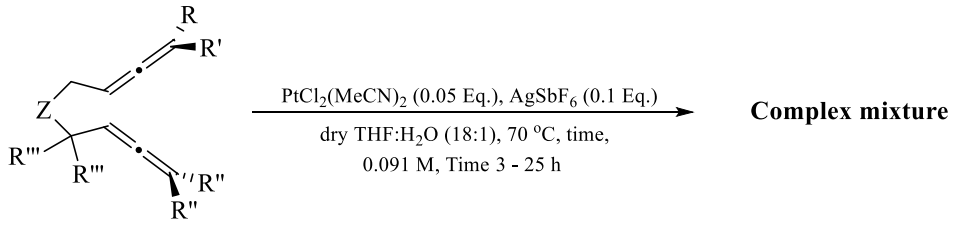
Scheme 123. Proposed formation of tetraene **326o** from triene **315o**

When malonate was used as tether, as well as the 7-membered cycle **316b**, the 6-membered ring **324b** was obtained in low yield in an inseparable mixture with its conjugated isomer **325b** (Entry **7**, Table **29**). Formation of **324b** and **325b** could be explained by isomerisation of π-allyl-Pt complexes formed during the reaction similarly to the isomerisation between 7-membered cycles that will be mentioned later on in this chapter.[242]

Triene **315l** was obtained as the only product in low yield when bisallene **280a** with an aromatic ring on the internal position of one allene was exposed to optimal reaction conditions (Entry **8**).

Substituted bisallene **283** with a methyl group adjacent to the *N*-tether gave in low yield an inseparable mixture of the isomeric 7-membered rings **316m** and **319m**, as well as two isomeric trienes **315m** and **315m'** (Entry **9**, Table **29**). Products **316m**, **319m** and **315m** come from the attack of the water to the terminal position of the non-substituted allene, while addition of water to the most hindered allene will explain the unexpected formation of triene **315m'**.

Other substituted 1,5-bisallenes were also tested under optimal conditions with unsuccessful results. In all the cases complex mixtures were observed by ^{1}H NMR (Scheme **124**).



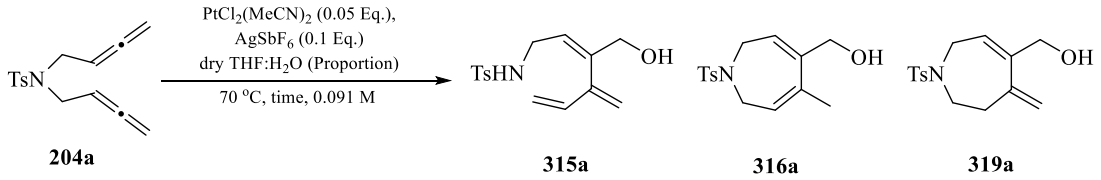
266e; Z = *p*-OMe-PhSO$_2$N; R, R', R'', R''' = H
266k; Z = *p*-Br-PhN; R, R', R'', R''' = H
289; Z = O; R, R', R'' = H; R''' = Ph
292; Z = TsN; R = *p*-Cl-Ph; R', R''' = H; R'' = Me
296a; Z = $(CO_2Me)_2C$; R, R', R'' = Me; R''' = H
296b; Z = $(PhO_2S)_2C$; R, R', R'' = Me; R''' = H

Scheme 124. Unsuccesful alkoxycyclisation of 1,5-bisallenes under the best reaction conditions so far

3.6.12. New optimization studies

The remarkable increase in selectivity towards 7-membered rings **316** and **319** with H_2O as the nucleophile should be highlighted. Although still not very high, possibly due to decomposition of the starting materials under the reaction conditions, the isolated yields of the cycles containing the OH functionality were improved despite the difficulties in the purification by column chromatography. However, no control over the formation of isomer **316** or **319**, and considerable amounts of the triene **315**, were still present in many cases. Trying to improve further this reaction with H_2O as nucleophile, we decided to investigate the effect of the concentration of H_2O in THF that showed a great improvement in the case of the MeOH.

An additional screening of the reaction using different ratios of THF:H_2O was carried out using $PtCl_2(MeCN)_2/AgSbF_6$ as catalytic source and model bisallene **204a**.



Scheme 125. Platinum-catalysed hydroxycyclisation of bisallenes with the different ratios of THF:H_2O

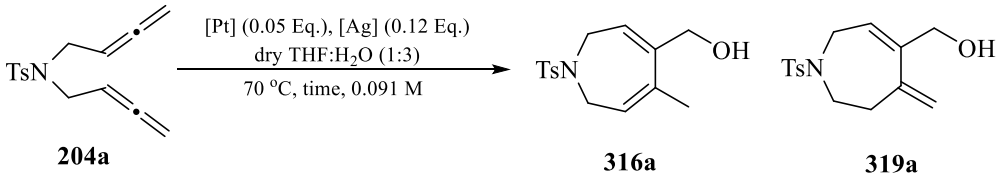
Entry	THF:H_2O (ratio)	t (h)	NMR Yields (%)[a][b]		
			315a	**316a**	**319a**
1[d]	(18:1)	5 h 45 min	**315a**:**316a**:**319a** (1:1.4:5)/ 41[c]		
2[d]	(9:1)	5 h 30 min	2	16	21
3[e]	(3:1)	12 h	2	7	33
4	(1:1)	20 h	2	7	47
5	(1:3)	12 h	**316a**:**319a** (1:9.8)/ 43[c]		

[a] All the NMR yields were measured using as internal standard 3,4,5-trichloropyridine added to the crude of reaction. **[b]** 100% conversion of starting material. **[c]** The products were isolated as inseparable mixture and the ratio was measured after purification. **[d]** These results were obtained in the previous solvents screening **[e]** Reaction was carried out using 0.06 M as absolute concentration.

Table 30. Results obtained after the screening of different proportions of solvents and nucleophile

Selectivity towards the 7-membered cycle **319a** with the exocyclic double bond was achieved with the increment of water in the reaction, with the best results and complete conversion to the cycles with no formation of the triene achieved when a mixture THF:H_2O (1:3) was used during 12 hours (Entry **5**). However, it is worth noting that the reaction time was slower, which has some implications in the decomposition of the starting material and

yields. Thus, in a new attempt to decrease the reaction time under these new conditions, a new screening of platinum complexes previously synthesised in the lab such as *cis*-$PtCl_2(PhCN)_2$, *trans*-$PtCl_2(PhCN)_2$ and *trans*-$PtCl_2(MeCN)_2$), or from commercial sources (*cis*-$PtCl_2(MeCN)_2$) was performed, in which we changed the substituents on the nitrile ligands and their configuration around of the platinum.



204a **316a** **319a**

Scheme 126. Reaction screening of platinum complexes with nitrile ligands

Entry	[Pt]	[Ag]	t (h)	NMR yields (%)[a],[b]	
				316a	**319a**
1	*cis*-$PtCl_2(MeCN)_2$	$AgSbF_6$	12 h	**316a**:**319a** (1:9.8)/ 43[d]	
2	*trans*-$PtCl_2(PhCN)_2$	$AgSbF_6$	8 h	5	9
3	*cis*-$PtCl_2(PhCN)_2$	$AgSbF_6$	6 h	5	18
4	*cis*-$PtCl_2(MeCN)_2$	$AgPF_6$	6 h 15 min	7	25
5[c]	*cis*-$PtCl_2(MeCN)_2$	$AgSbF_6$	1 h 30 min	5	34
6	*trans*-$PtCl_2(MeCN)_2$	$AgSbF_6$	20 h	**316a**:**319a** (1:8.4)/ 38[d]	

[a] NMR yields using 3,4,5-trichloropyridine as internal reference added to the crude of reaction. **[b]** 100% conversion of starting material. **[c]** Microwave heating at 60 ºC. **[d]** The products were isolated as inseparable mixture and the ratio was measured after purification.

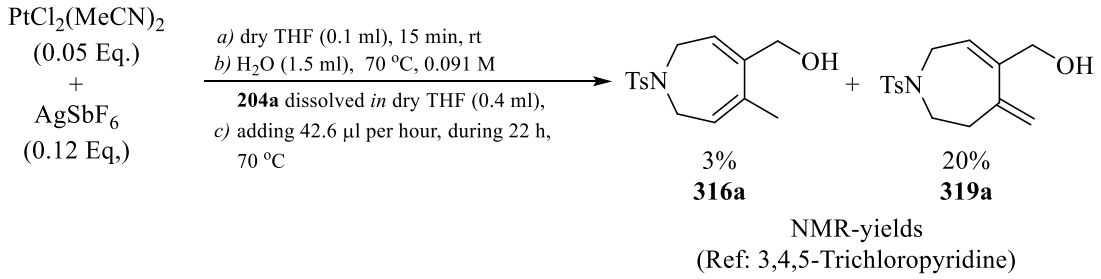
Table 31. Results obtained after the screening of different platinum-complexes under the new optimal conditions

Although full consumption of the starting material was observed with shorter times, yields of the cycles were still very low. A small trend between the *trans*- and *cis*-$PtCl_2(RCN)_2$ was observed, with the *cis*-platinum complex giving faster reactions. These results support the importance of the *cis*- and *trans*-isomerisation in square planar configurations on d^8 transition metal complexes, and suggest that a *cis*-complex is the best pre-catalyst in our case, and isomerisation of the *trans* to *cis*- in solution before the catalytic cycle to form the products.

In a final attempt to decrease the decomposition of the starting material, two experimental procedures were designed to incorporate the use of an automatic syringe pump. The bisallene or the cationic complex were added slowly to the reaction mixture, in order to minimise their interaction.

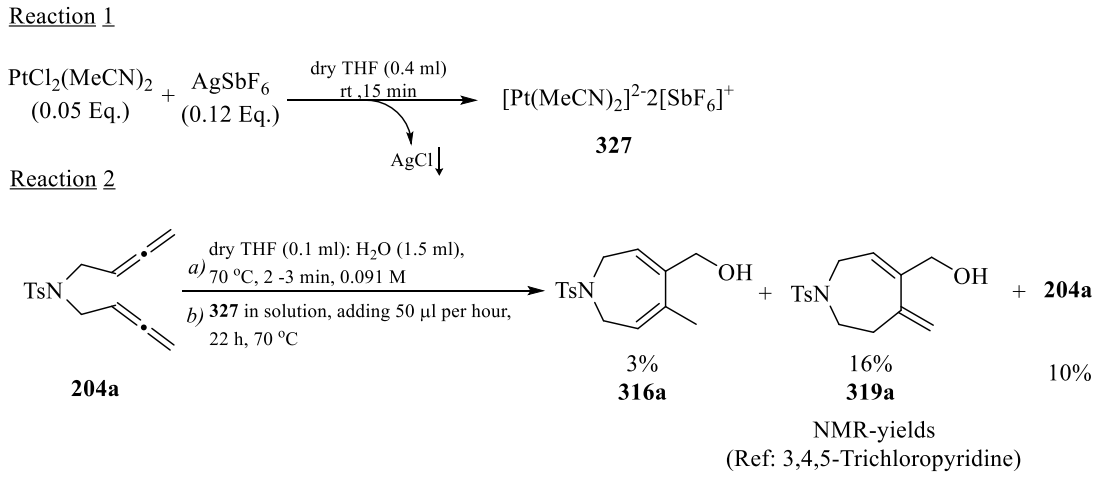
Experiment **1**: Bisallene **204a** was dissolved in dry THF and added slowly using the automatic syringe pump to a microwave vial containing the preformed catalytic complex and

the water under inert atmosphere. Unfortunately, after complete conversion of the starting material, the yield did not improve. However it should be noted that the selectivity of the reaction to the desired cyclic products remains, with the 7-membered ring **319a** being the major product of reaction.



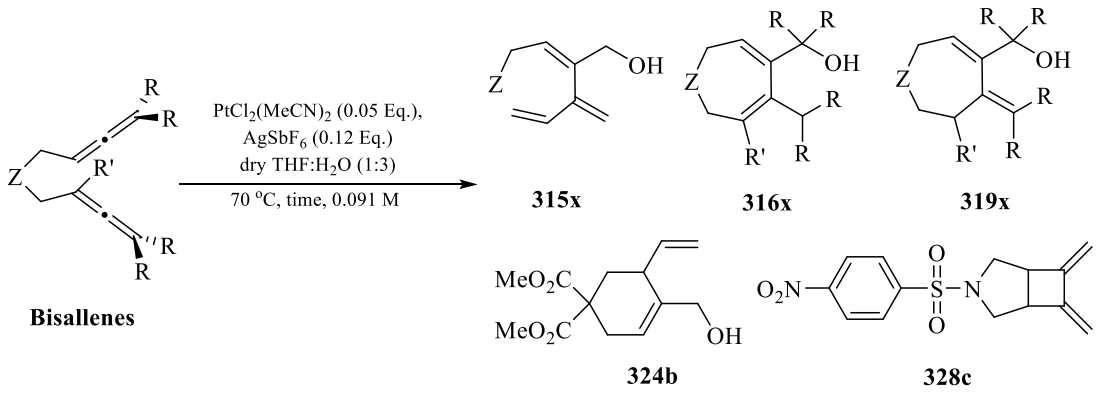
Scheme 127. Experiment performed to minimise the loss of starting material under reaction conditions supported by an automatic syringe pump

Experiment **2**: The cationic complex $[Pt(MeCN)_2]^{2-}$ $2[SbF_6]^{+}$ was preformed in a Schlenk tube with dry THF during 15 min at room temperature. The complex in solution was decantated and added to a different Schlenk under inert atmosphere containing a mixture of water (1.5 mL), dry THF (0.1 mL) and bisallene **204a**, *via* the syringe pump at 50 µl per hour. Not 100% conversion, decomposition and low NMR yields of 7-membered rings were observed after 22 h, and therefore we did not use this experimental procedure in our further studies.



Scheme 128. Experiment carried out adding sequentially the load of platinum-complex in solution previously preformed in order to avoid the rapid decomposition of the starting material

As no further improvement was achieved, we decided to re-investigate the scope of the reaction of several 1,5-bisallenes with the latest conditions with *cis*-$PtCl_2(MeCN)_2/AgSbF_6$ and a 1:3 ratio of THF:H_2O (Scheme **129**, Table **32**).



Scheme 129.Scope of the platinum-catalysed hydroxycyclisation of 1,5-bisallenes

Entry	Bisallenes	t (h)	**315x**:**316x**:**319x** (ratio)/ Isolated Yield, %[a]
1	**204a**; Z = TsN; R, R' = H	12 h	(0:1:9.8)/ 43
2	**266d**; Z = $PhSO_2N$; R, R' = H	12 h	(0:1:7.8)/ 52
3	**266c**; Z = *p*-NO_2-$PhSO_2N$; R, R' = H	6 h	(0:1:5.9)/ 35; **328c**, 3
4	**266f**, Z = *p*-Cl-$PhSO_2N$; R, R' = H	22 h	(0:1:7.6)/ 46
5	**266e**, Z = *p*-OMe-$PhSO_2N$; R, R' = H	12 h	(0:1:10)/ 42
6	**266g**, Z = *p*-CF_3-$PhSO_2N$; R, R' = H	12 h	(0:1:8.5)/ 52
7	**266i**, Z = CH_3SO_2N; R, R' = H	12 h	(2.1:1:8.5)/ 31
8[b]	**259**, Z = O; R, R' = H	1 h 30 min	**315q**, 13; **319q** (traces)
9[c]	**280b**; Z = TsN; R = H; R' = Me	15 h 30 min	**319r** (traces)
10	**204b**; Z = $(CO_2Me)_2C$; R, R' = H	24 h	**316b**:**319b**:**324b** (3.1:1:9.3)/ 6

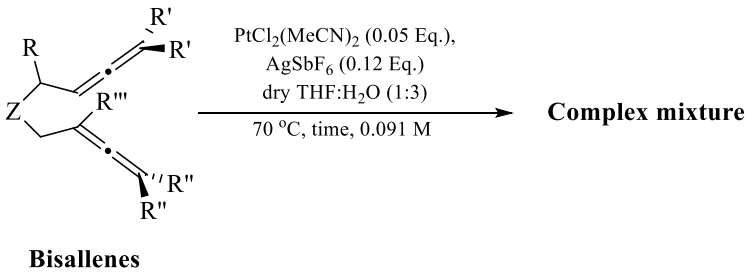
[a] The products were obtained as inseparable mixture. **[b]** The reaction was carried out at 55 °C. **[c]** Microwave heating 70 °C. **[d]** 100% conversion

Table 32. Screening of substrates under the best reaction conditions using THF:H_2O (1:3) as mixture of solvents

N-Sulfonamide derivatives (Entries **1** – **7**, Table **32**) displayed excellent selectivity towards 7-membered rings **316x** and **319x**. In all the examples, cyclisation **319x** prevails over the other products in moderate yields, and triene **315** is mainly avoided. It is interesting to highlight the good result with bisallene **266e**, with the *para*-MeO-sulfonamide, which gave a complex mixture in the previous conditions with THF:H_2O (18:1) (See Table **29**), supporting the huge sensitivity of this methodology to modifications in the reaction conditions. Under these conditions, the bisallene bearing the electron withdrawing NO_2 group (Entry **3**) gave, in addition to the 7-membered cycles, bicycle-[3.2.0] **328c**.[206c, 213] *O*-tethered bisallene **259** (Entry **8**) also reacted under these conditions, obtaining the triene **315q** and traces of the cyclic compound **319q**, however only triene **315q** could be isolated after column chromatography. Traces of the product **319r** were also observed on the NMR-crude, however it decomposed

after purification (Entry **9**, Table **32**). A carbon-based tether was also employed (Entry **10**), giving mixtures of the 6- and 7-membered rings as inseparable mixture in low yield.

Complex mixtures were obtained with the 1,5-bisallenes shown in Table **33**.



Scheme 130. Bisallenic precursors that did not work under catalytic conditions

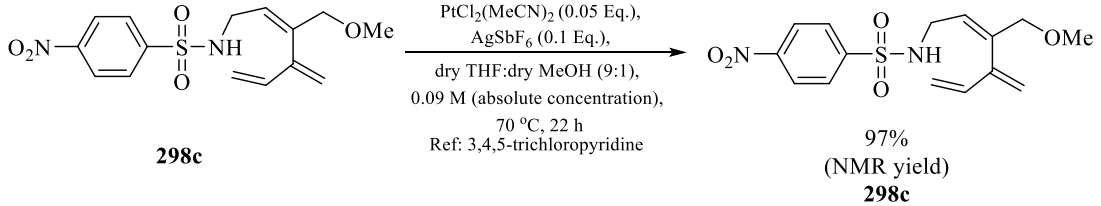
Entry	1,5-bisallenes	t (h)
1	**272**; Z = $(MeOCH_2)_2C$; R, R', R'', R''' = H	19 h
2	**280a**; Z = TsN; R, R', R'' = H; R''' = Ph	> 48 h
3	**283**; Z = TsN; R = Me; R', R'', R''' = H	9 h 40 min
4[a]	**207**; Z = TsN; R, R'', R''' = H; R' = Me	24 h

[a] Microwave heating 70 °C.

Table 33. Unsuccesful alkoxycyclisation of 1,5-Bisallenes under the best reaction conditions so far

3.6.13. Mechanistic insights and deuterium-labelling experiments

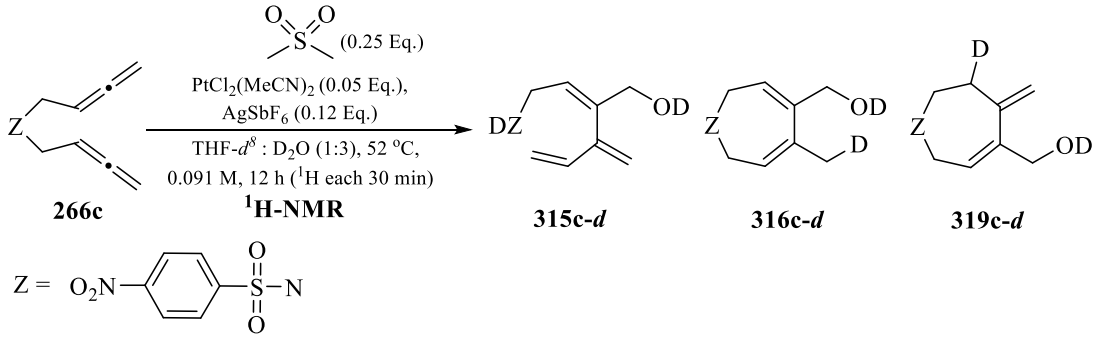
In order to gain some insight into the mechanism of the reactions, we first studied the stability of the products and the possible interconversion between the isomeric cycles and the triene during the reaction under platinum catalysis. Thus, isolated triene **298c** was re-submitted to the reaction conditions with MeOH as nucleophile in a mixture THF:MeOH, 9:1 (Scheme **131**). We observed that triene **298c** did not decompose or cyclise during the reaction after 22 h at 70 °C. This experiment also suggests that the low yields obtained in the isolation of triene **298** can come from decomposition or other issues during the purification by column chromatography with silica gel.



Scheme 131. Reaction performed to observed the decomposition level of product **298c** under reaction conditions

We also tried the study of the interconversion between the two 7-membered rings **316a** and **319a** in solution and their possible decomposition under reaction conditions with and without the cationic platinum complex. However, due to the problems with the isolation of these compounds as previously mentioned, the results obtained were not conclusive.

Nevertheless, an additional experiment was performed to support the possible interconversion of the 7-membered cycles. In this case, the reaction was monitored directly by ^{1}H NMR using an internal standard (dimethyl sulfone). To do so, an NMR tube was loaded with bisallene **266c**, the cationic platinum complex, $PtCl_2(MeCN)_2/AgSbF_6$, a mixture THF-d^8:D_2O (1:3) and the reference dimethyl sulfone under nitrogen. The mixture was heated at 52 ^{o}C in the spectrometer (note the lower temperature due to experimental set up in the NMR). The reaction was monitored by ^{1}H NMR every 30 min during 12 h. As expected, 7-membered ring **319c-*d*** was formed as main product, however, triene **315c-*d*** was also observed in considerable amount in contrast with the results obtained with water as nucleophile in the bigger scale reaction at 70 ^{o}C (Entry **3**, Table **32**).



Scheme 132. Monitoring reaction by ^{1}H NMR using as internal reference dimethyl sulfide

Figure **40** shows the ^{1}H NMR spectra acquired during the reaction at 52 ^{o}C. It should be highlighted the low resolution of the NMR spectra during the first 3 hours of reaction, possibly due to the high concentration of water and fluxional behaviour of the allene(s)-platinum complexes. This experiment was repeated twice showing a similar profile at the beginning of the reaction. Although integrals of the bisallene **266c** could not be accurately measured, we were able to extract some data to show the consumption of bisallene (Figure **35**). The integrals of the three products of the reaction could be accurately measured and the concentrations calculated using the internal reference dimethyl sulfone. The profile of the reaction is shown in figure **35**. Fast consumption of the bisallene **266c** was observed at the beginning of the reaction, but analysis of the mass balance showed that not all the starting material was forming the observed products, confirming again the decomposition of the bisallenes in the presence of cationic platinum complexes. Interstingly, no full conversion was observed, and traces of the bisallene are observed even at longer times. Formation of products

315c-*d* and **316c-*d*** is mainly achieved during the first 15000 s (4 - 5 hours), then concentration of both seems to be stabilised, which would ruled out that **315c-*d*** as intermediate in the formation of the isomeric **319c-*d*** or interconversion between the two cycles once they are formed. On the other hand, 7-membered ring **319c-*d*** is obtained as main product, in a fast process at the beginning of the reaction and then at a slower rate, which could indicate catalyst decomposition.

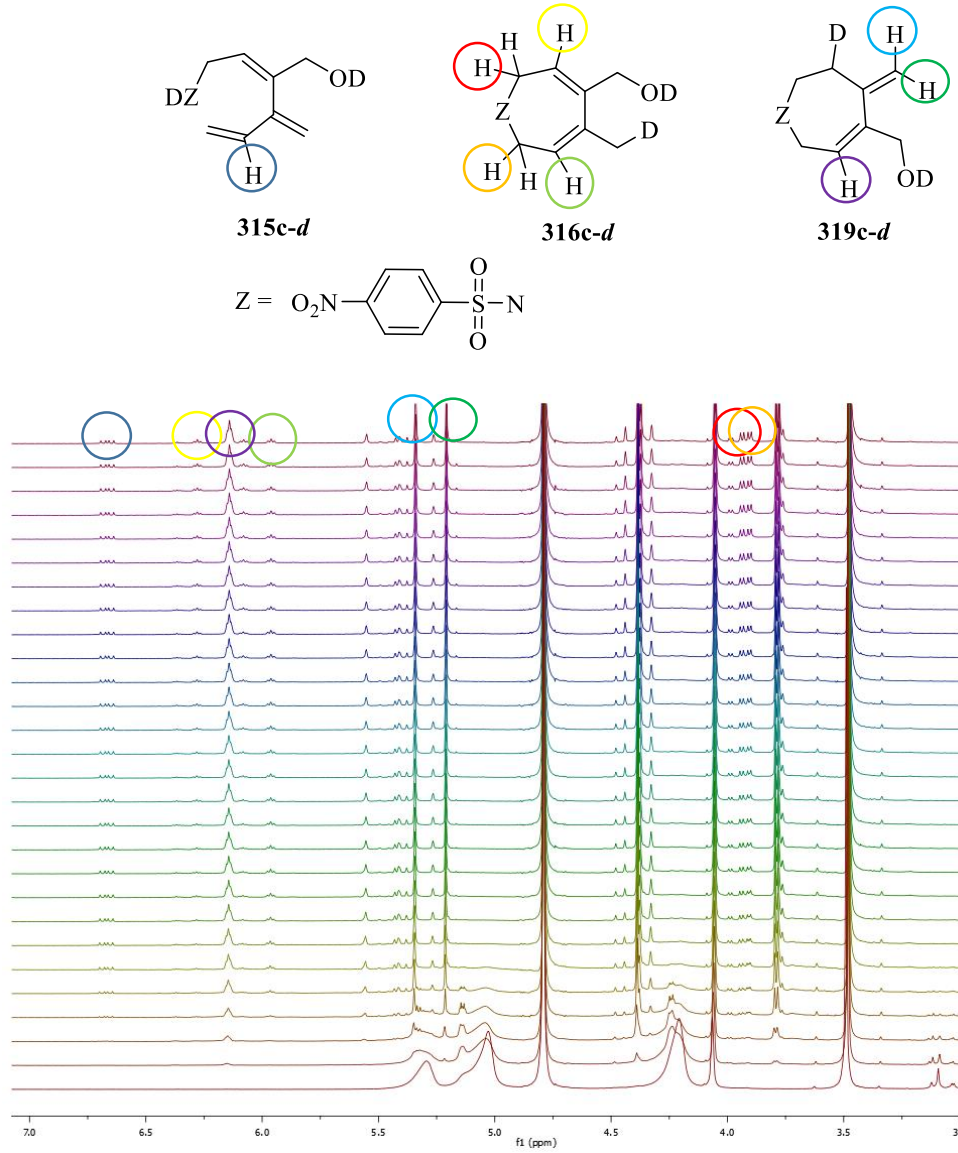


Figure 34. ^{1}H NMR acquired during the reaction into the NMR at 52 ºC under the best reaction conditions

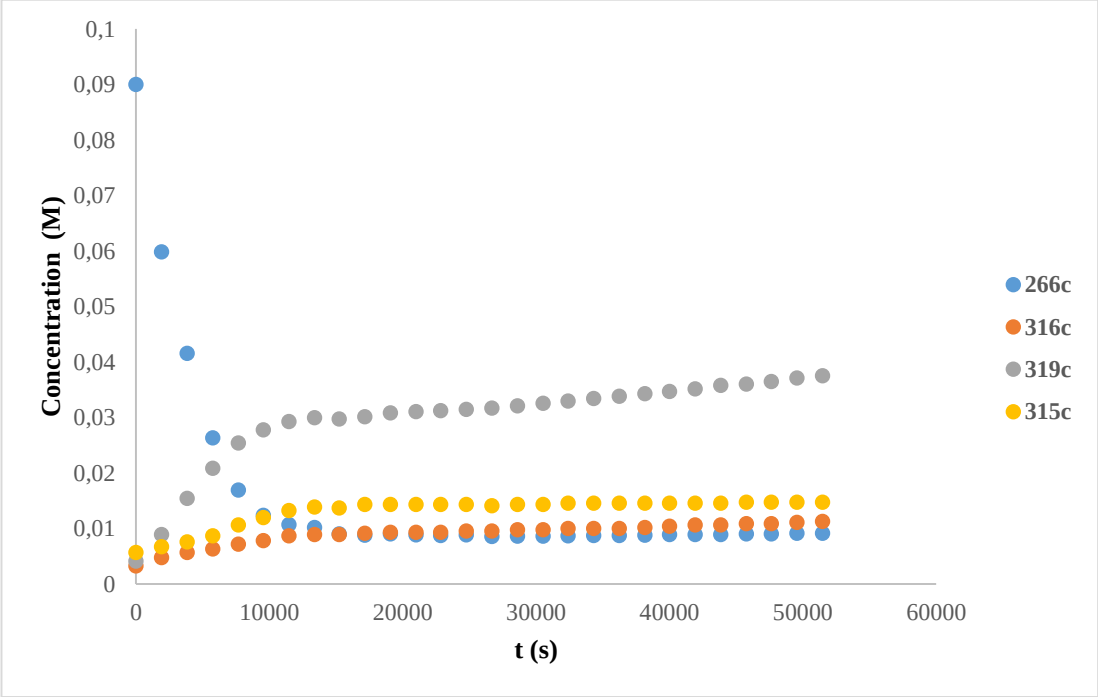
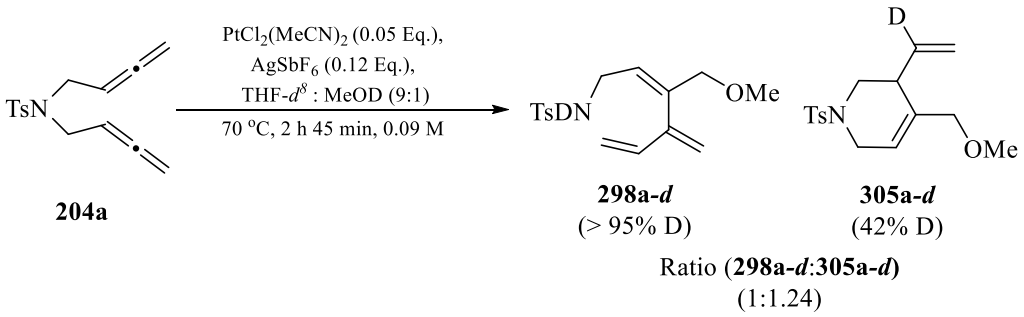


Figure 35. Data plot with the results obtained monitoring the reaction of bisallenes by ^{1}H NMR

In order to get an insight into the intermediates involved in these new catalytic cycles, deuterium-labelling experiments were performed using MeOD and D_2O as nucleophiles in THF-d^8, *N*-sulfonamide bisallenes **204a** and **266d**, and $PtCl_2(MeCN)_2/AgSbF_6$ as catalyst.

1,5-Bisallene **204a** was reacted under optimal reaction conditions with MeOD as the nucleophile to give the monodeuterated compound **305a-*d*** (42% D) and triene **298a-*d*** with high deuterium incorporation in the sulfonimidic nitrogen (> 95% D).



Scheme 133. Deuterium-labelling experiment using MeOD as nucleophile

^{1}H NMR in $CDCl_3$:

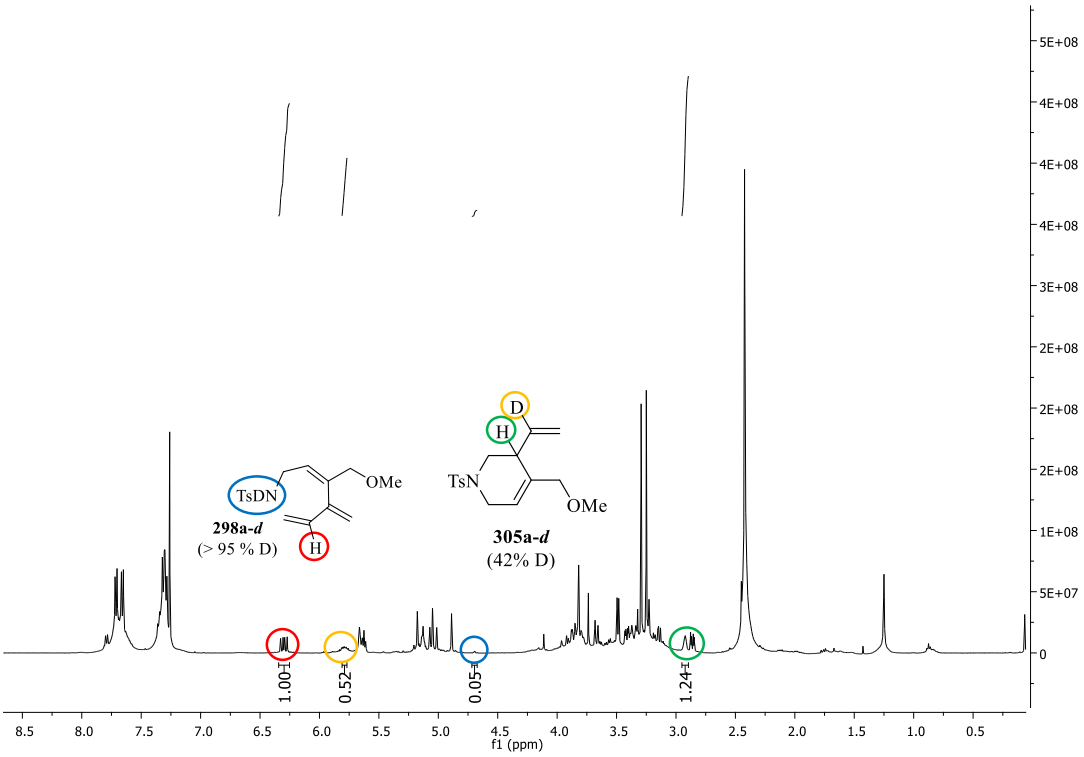


Figure 36. ^{1}H NMR of deuterium-labelling experiments

^{2}H NMR in $CHCl_3$: (traces of THF and THF-d^8 present)

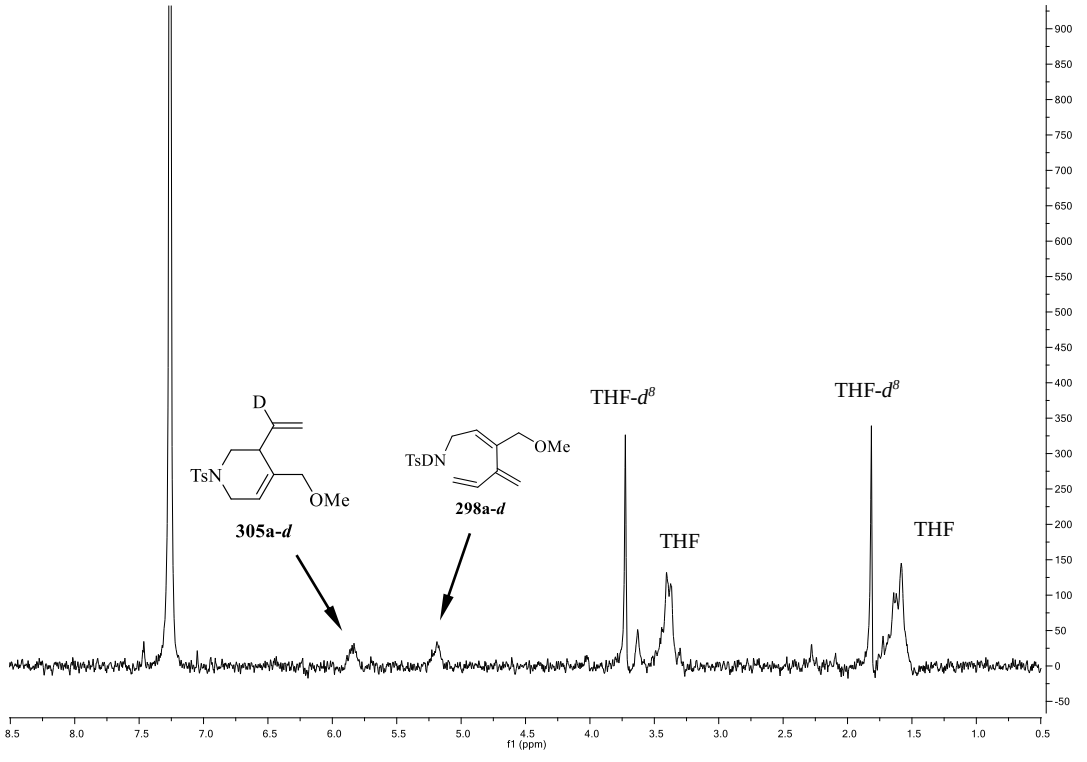
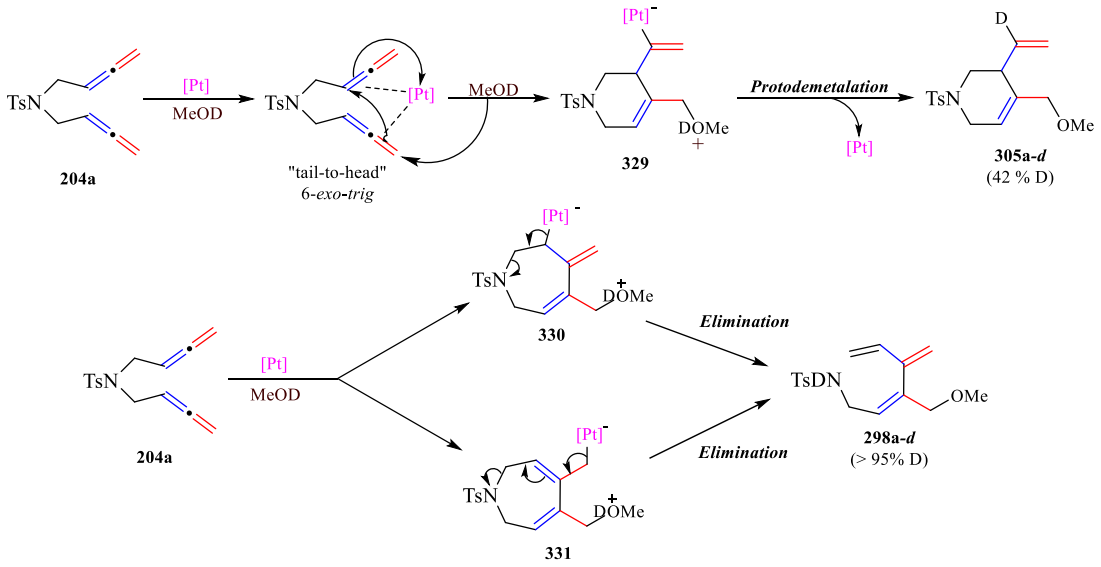


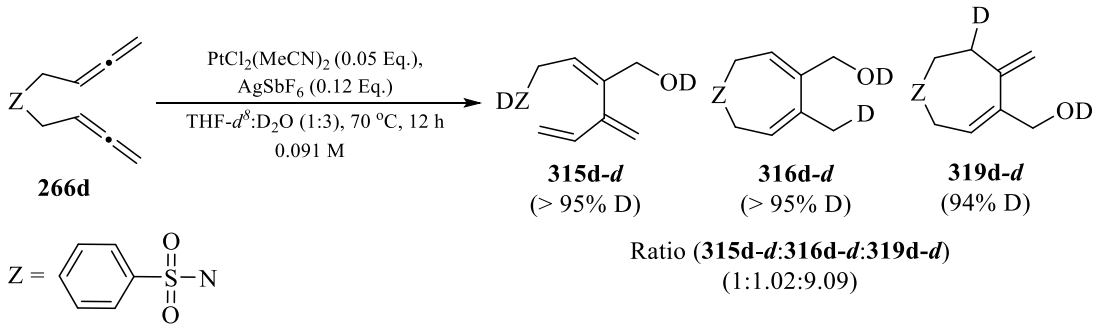
Figure 37. ^{2}H NMR of deuterium-labelling experiments

^{1}H NMR (Figure **36**) and ^{2}H NMR (Figure **37**) revealed the incorporation of deuterium on the internal position of the exocyclic vinyl group in compound **305a-*d***. This suggests that protodemetalation of a vinyl-platinum intermediate **329** (Scheme **134**) could be taking place in the final step of the catalytic cycle. This intermediate could be formed by attack of the MeOD to the terminal carbon of one allene, triggering the concomitant *tail-to-head* (external – internal π-systems of the bisallene) 6-*exo-trig* cyclisation of the bisallene **204a** (Scheme **134**), which after Pt-C cleavage with deuterium gives 6-membered ring **305a-*d***. Besides, triene **298a-*d*** was also formed in the reaction, displaying high deuterium incorporation in the N-D bond. We propose, that this compound comes from the elimination reaction of intermediate platinum complex **330** and / or **331**, formed by 7-*endo* or *exo-dig* cyclisation triggered by the attack of the MeOD to the terminal carbon of the allene (Scheme **134**). These cyclisations could also happen stepwise, by attack of the nucleophile to the terminal carbon of the allene to form an acyclic vinyl-platinum intermediate that undergoes carbocyclisation with the other allene to give the two intermediates.



Scheme 134. Proposal mechanism to synthesise 6-membered ring **305a-*d*** *via tail-to-head* 6-*exo-trig* cyclisation and the formation of triene **298a-*d*** by the elimination reaction from its intermediates platinum-complexes **329**, **330** and or **331**.

On the other hand, bisallene **266d** was employed as substrate in the deuterium-labelling experiment using D_2O as nucleophile under the optimal conditions with the mixture THF-d^8:D_2O (1:3).



Scheme 135. Deuterium-labelling experiments using D_2O as nucleophile

Deuterium incorporation into the 7-membered cycle **319d-*d*** was observed in the internal allylic position of the exocyclic double bond. Besides, mono, di or tri-deuteration was obtained in the exocyclic methyl group of **316d-*d***. Triene **315d-*d*** was also formed in low yield, with high deuterium incorporation in the nitrogen (Figure **38** and **39**).

^{1}H NMR in $CDCl_3$:

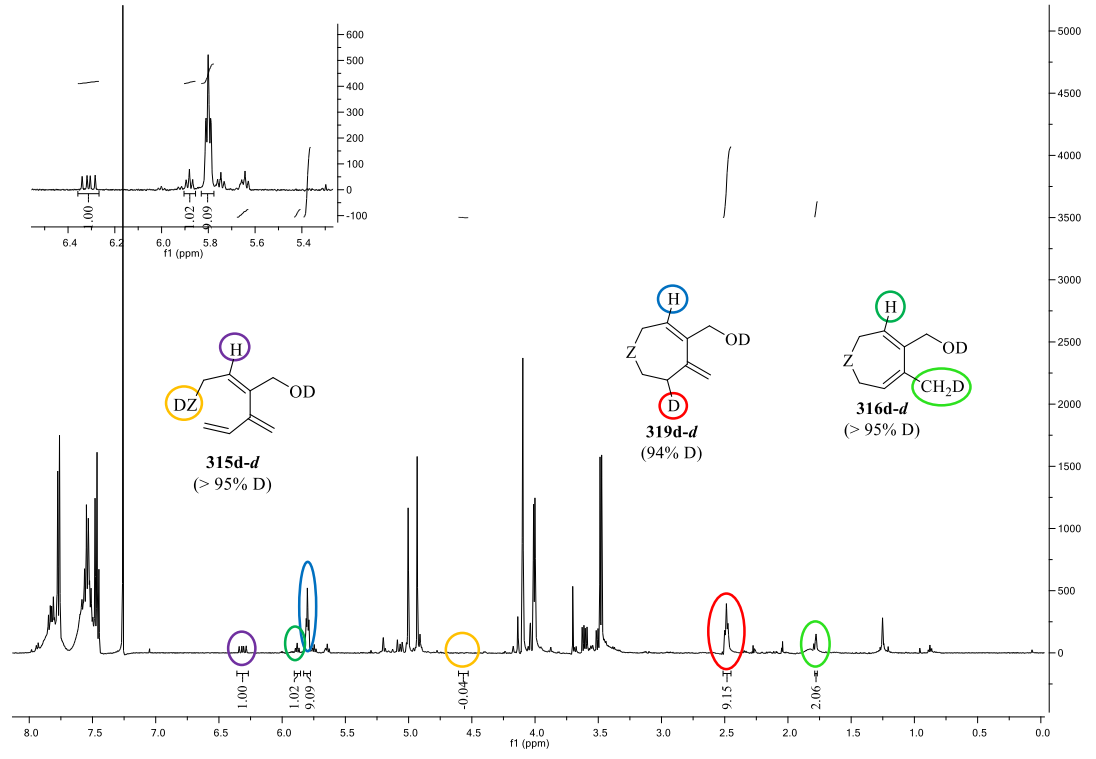


Figure 38. ^{1}H NMR of deuterium-labelling experiments

^{2}H NMR in $CHCl_3$: (traces of THF-d^8 were present)

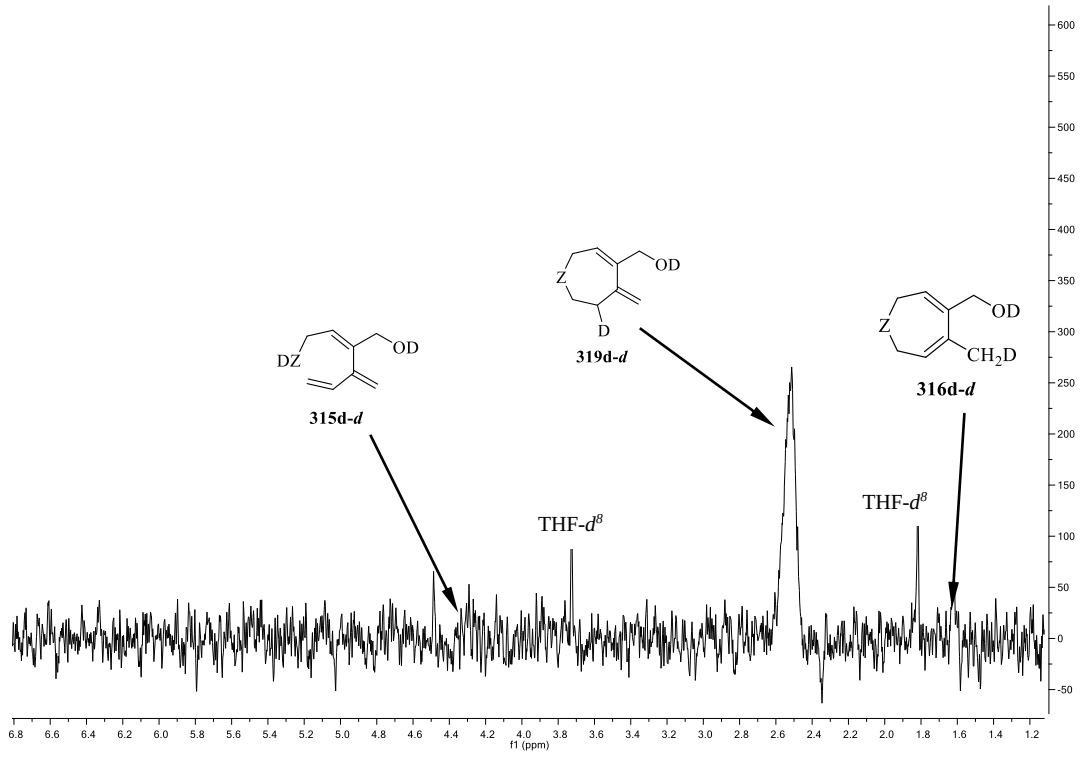
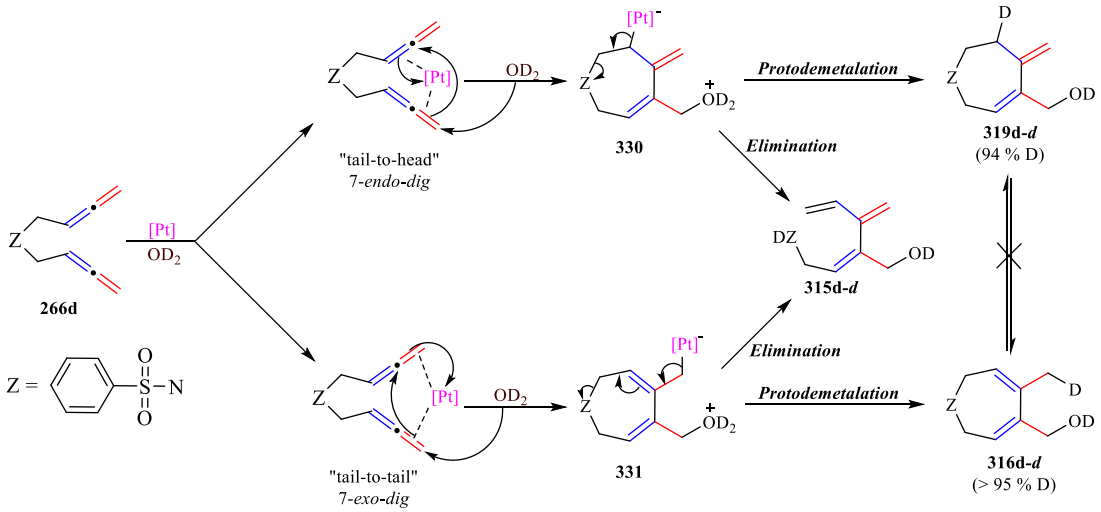


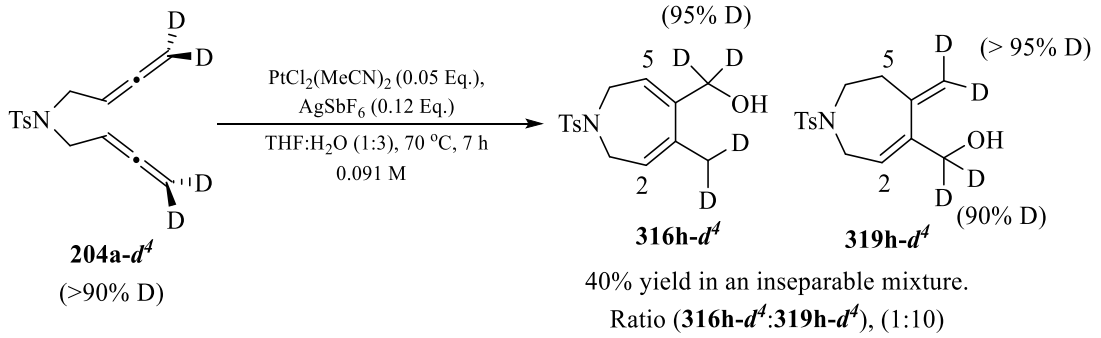
Figure 39. ^{2}H NMR of deuterium-labelling experiments

These results suggest the attack of the water to the terminal carbon of one allene triggering a 7-*endo*- or exo-*dig* cyclisation in a *tail-to-head* or *tail-to-tail* mode to give the isomeric allyl-Pt intermediates **330** and **331** (Scheme **136**). Irreversible protodemetalation of the Pt-C bond in both intermediates will lead to **319d-*d*** and **316d-*d*** respectively. As it has been discussed in the previous experiment monitoring the reaction by ^{1}H NMR (See Figure **34** and **35**) the isomerisation of cycles **316** and **319** in solution was not observed. Deuterium experiments also showed no deuterium scrambling after complete conversion of the three products, which supports the non-intercoversion of the final cycles. However, interconversion of the allyl-Pt intermediates cannot be completely ruled out. The allyl-Pt intermediates **330** and **331** will also explain the formation of the triene **315d-*d*** by irreversible elimination aided by the electron withdrawing properties of the sulfonamide as in the case of the methanol (Scheme **136**).



Scheme 136. Proposed mechanisms to generated 7-membered cycles **316d-*d*** and **319d-*d*** and triene **315d-*d***

Deuterated 1,5-bisallene **204a-d_4** in the terminal positions of the allene was reacted under optimal conditions with H_2O as nucleophile, to obtained **316a-d_4** and **319a-d_4**, with no significant loss of deuterium in the expected positions. No deuterium incorporation was detected on C-5 and C-2 in the skeleton of both cycles, which again suggests that the two 7-membered cycles **316** and **319** do not interconvert under reaction conditions.



Scheme 137. Reaction carried out under optimal conditions using deuterated bisallene **204a-d^4**

Further mechanistic studies to understand the different reactivity of water and alcohols, the sensitivity of the reaction to the different parameters studied, as well as the elimination and protodemetalation steps are currently being carried out in the group. Intra- versus intermolecular protodemetalation steps, as well as the possibility of alternative mechanisms involving Pt-hydrides are being considered.

3.7. Conclusions

We have discovered a new platinum-catalysed carbocyclisation of 1,5-bisallenes to give 6- or 7-membered cycles with an extra oxygen nucleophile incorporated in the skeleton of rings, depending on the nucleophile used.

The reaction works better with cationic platinum complexes bearing electron-withdrawing ligands and with bisallenes containing a sulfonamide as the tether. However, the reaction is very sensitive to slight modifications of these parameters, and complete selectivity is still a challenge. Rapid decomposition of the model bisallenic starting material under catalytic conditions has been proven by NMR experiments, with isolation no higher than 60%.

Deuterium-labelling experiments confirmed the involvement of allyl- or vinyl-platinum intermediates in the different cyclisation modes observed to synthesise 7-membered rings *via* 7-*exo*- and 7-*endo*-*dig* cyclisations, and 6-membered rings *via* 6-*exo*-*trig* cyclisation. A possible mechanism for the formation of the trienes has been proposed *via* elimination from the key allyl-platinum intermediates.

Selectivity of the reaction using MeOH, the scope with different bisallenes and also the mechanistic study of this reaction are in progress in our group.

.

3.8. Experimental section

Synthesis of *cis*-bis(acetonitrile)dichloroplatinum(II) and *trans*-bis(acetonitrile)dichloroplatinum(II)[243]

$$PtCl_2 \xrightarrow[90\ ^oC,\ 4\ h]{\text{dry MeCN}} \textit{cis}\text{-}[PtCl_2(MeCN)_2] + \textit{trans}\text{-}[PtCl_2(MeCN)_2]$$

Platinum(II) chloride ($PtCl_2$) (200 mg, 0.75 mmol, 1.0 Eq.) was added under N_2 into a flamed-dried Schlenk flask. Dry MeCN (2.0 mL, 38.30 mmol, 50.0 Eq.) was added. The Schlenk was equipped with a condenser and the solution was refluxed at 90 ºC for 4 h. The crude of reaction was filtered, under vacuum, obtaining *trans*-bis(acetonitrile)dichloroplatinum(II) as a grey solid (108 mg, 0.31 mmol, 41%). The mother liquor was concentrated, under vacuum, obtaining of *cis*-bis(acetonitrile)dichloroplatinum(II) as a yellow solid (53 mg, 0.15 mmol, 20%). *Cis*-$[PtCl_2(MeCN)_2]$ ^{1}H NMR (400 MHz, $CDCl_3$, 25 ºC) δ = 2.17 (s, 6H). ^{195}Pt NMR (108 MHz, $CDCl_3$, 25 ºC) δ = - 2684.72. IR (Film, cm^{-1}): $\tilde{\nu}$ = 2923 (C-H_{Alkane}), 2351 (C≡N), 2339 (C≡N), 1406, 1354, 1019, 772. *Trans*-$[PtCl_2(MeCN)_2]$ ^{195}Pt NMR (108 MHz, Tol, 25 ºC) δ = - 2789.32. IR (Film, cm^{-1}): $\tilde{\nu}$ = 2925, 2338 (C≡N), 1409, 1359, 1019.

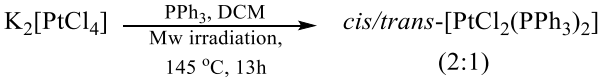
Synthesis of *cis* and *trans*-bis(benzonitrile)dichloroplatinum(II)[244]

$$PtCl_2 \xrightarrow[100\ ^oC,\ 1\ h]{\text{PhCN}} \textit{Cis}\text{-}[PtCl_2(PhCN)_2] \text{ and } \textit{trans}\text{-}[PtCl_2(PhCN)_2]$$

Platinum(II) dichloride ($PtCl_2$) (40 mg, 0.15 mmol, 1.0 Eq.) and neat benzonitrile (1.7 mL, 0.02 mmol, 0.1 Eq.) were added to a flame-dried Schlenk flask under N_2. The solution was refluxed at 100 ºC during 1 h. The suspension was cooled down, filtered through celite and concentrated under vacuum. Then, the yellow solid was treated with hot benzene and filtered under vacuum. The insoluble *cis*-$[PtCl_2(PhCN)_2]$ was washed with petroleum ether and dried under vacuum. Obtained 8 mg, 0.02 mmol (11%) as a yellow solid. The mother liquor was concentrated obtaining *trans*-$[PtCl_2(PhCN)_2]$ as a white solid, 23 mg, 0.05 mmol (32%). *Cis*-$[PtCl_2(PhCN)_2]$. ^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.80 (dd, J = 8.2, 1.2 Hz, 2H; *o*-Ph), 7.77 – 7.72 (m, 1H; *p*-Ph), 7.60 – 7.54 (m, 2H; *m*-Ph). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 135.3 (CH_{Ar}; *p*-Ph), 133.8 (CH_{Ar}; *m*-Ph), 129.5 (CH_{Ar}; *o*-Ph), 119.4 (C_q; Ph), 109.1 (C_q; CN). ^{195}Pt NMR (108 MHz, $CDCl_3$, 25 ºC) δ = - 2514.0. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3097 (C-H_{Ar}), 3061 (C-H_{Ar}), 3038 (C-H_{Ar}), 2286 (C≡N), 1592, 1446, 1199, 998, 761, 683. *Trans*-$[PtCl_2(PhCN)_2]$ ^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.83 – 7.78 (m, 2H; *o*-Ph), 7.77 – 7.72 (m, 1H; *p*-Ph), 7.57 (t, J = 8.1 Hz, 2H; *m*-Ph).^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 135.4 (CH_{Ar}; *p*-Ph), 133.9 (CH_{Ar}; *m*-Ph), 129.6 (CH_{Ar}; *o*-Ph). *(C_q; Ph) and (C_q; CN) could not be*

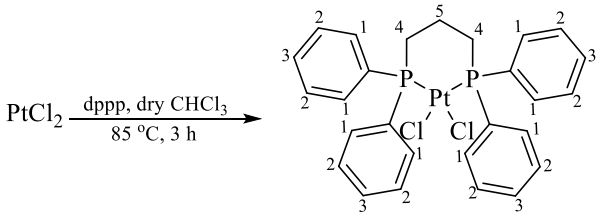
identified due to the low concentration of the sample. ^{195}Pt NMR (108 MHz, $CDCl_3$, 25 ºC) δ = - 2488.00. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3096 (C-H_{Ar}), 3033 (C-H_{Ar}), 2288 (C≡N), 1592, 1446, 1120, 762.

Synthesis of *cis/trans*-dichlorobis(triphenylphosphine)platinum (II)[245]



The synthesis was undertaken according to the procedure described by Oemke and co-workers.[245] Potassium tetrachloroplatinate ($K_2[PtCl_4]$) (47 mg, 0.11 mmol, 1.0 Eq.) and triphenylphosphine (PPh_3) (60 mg, 0.23 mmol, 2.0 Eq.) were added to a microwave vial under normal atmosphere and dissolved in 2.6 mL of DCM. The vial was sealed and the reaction was heated at 145 ºC under microwave irradiation during 13 h. To the yellow solution was added slowly Et_2O and then the suspension was cooled down at 0 ºC (ice bath) during 10 min. The white powder was filtered and washed with small portions of Et_2O. The product was recrystallized from $CHCl_3$ and heptane. Obtained as a white powder, 46 mg, 0.06 mmol (51%). *Cis/Trans(2:1)*[$PtCl_2(PPh_3)_2$], ^{31}P NMR (202 MHz, $CDCl_3$, 25 ºC) δ = 21.81_{Trans} (PPh_3), 14.31_{Cis} (PPh_3), 13.27_{Cis} (d, $J_{P\text{-}Pt}$ = 2785.3 Hz). ^{195}Pt NMR (108 MHz, $CDCl_3$, 25 ºC) δ = - $4172.9_{(Trans)}$, - $4581.8_{(Cis)}$.

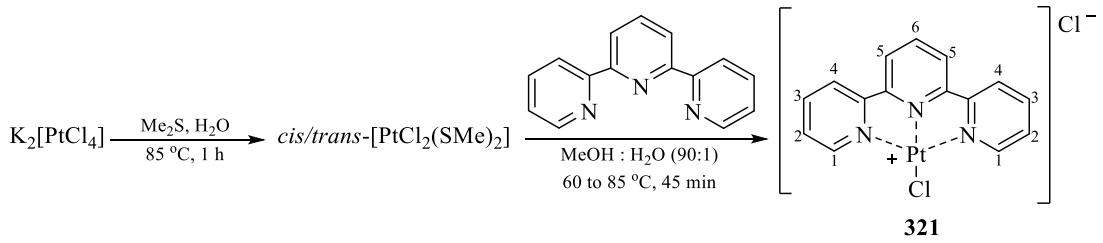
Synthesis of [1,3-bis(diphenylphosphino)propane]dichloroplatinum (II) (309)[245]



309

The synthesis was undertaken according to the procedure described by Bennett and co-workers.[246] Platinum(II) dichloride ($PtCl_2$) (70 mg, 0.26 mmol, 1.0 Eq.) and 1,3-bis(diphenylphosphino)propane (dppp) (108 mg, 0.26 mmol, 1.0 Eq.) were added to a flame-dried Schlenk flask under N_2. The solids were dissolved in 10.0 mL dry $CHCl_3$. Then, the Schlenk was equipped with a condenser and the suspension was refluxed during 3 h. Then over the warm solution was added *n*-hexane to obtain a white precipitate. The solid was filtered and washed with *n*-hexane. Obtained as a white solid **309**, 178 mg, 0.26 mmol (99%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.81 – 7.73 (m, 8H; H_{Ar}-2), 7.48 – 7.44 (m, 4H; H_{Ar}-1), 7.43 – 7.37 (m, 8H; H_{Ar}-8), 2.61 – 2.40 (m, 4H; H-4), 2.13 – 1.94 (m, 2H; H-5). ^{31}P NMR (202 MHz, $CDCl_3$, 25 ºC) δ = - 5.59 (d, $J_{P\text{-}Pt}$ = 3407.6 Hz).

Synthesis of chloro (2,2',6',2''-terpyridine) platinum chloride (321)[247]

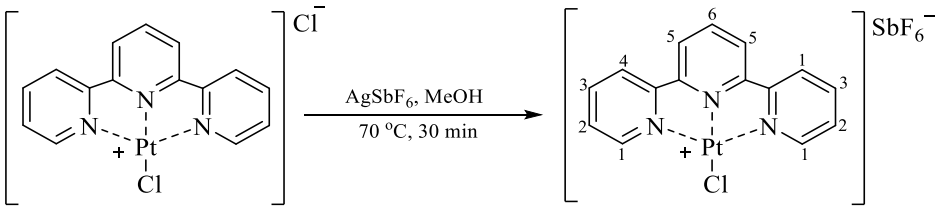


321

Potassium tetrachloroplatinate ($K_2[PtCl_4]$) (300 mg, 0.72 mmol, 1.0 Eq., 0.12 M) was added dissolved in 6.0 mL of distilled H_2O in a two-necks round bottom flask with a condenser. The mixture was stirred at room temperature during 5 min. Then, dimethylsulfide (Me_2S) was added dropwise and the solution was refluxed at 85 ºC during 1 h. The yellow solution was cooled down at room temperature, extracted with DCM (x 3), washed with brine, dried over $MgSO_4$ anhydrous and concentrated under vacuum. *Cis/trans*-$[PtCl_2(SMe)_2]$ was obtained, 207 mg, 0.53 mmol (73%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = $2.58_{(Trans)}$ (s, 6H; 2 x Me), $2.58_{(Trans)}$ (d, $J_{H\text{-}Pt}$ = 50.6 Hz,), $2.47_{(Cis)}$ (s, 6H; 2 x Me), $2.47_{(Cis)}$ (d, $J_{H\text{-}Pt}$ = 41.0 Hz). ^{195}Pt NMR (108 MHz, $CDCl_3$, 25 ºC) δ = - $3396.3_{(Trans)}$. ^{195}Pt NMR (108 MHz, $CDCl_3$, 25 ºC) δ = - $3396.3_{(Cis)}$

Cis/trans-$[PtCl_2(SMe)_2]$ (45 mg, 0.12 mmol, 1.0 Eq.) was dissolved in 2.0 mL of a mixture MeOH : H_2O (90:1) in a two-necks round bottom flask with a condenser. The suspension was warmed up at 60 ºC during 10 min. Terpyridine (terpy) (29 mg, 0.12 mmol, 1.1 Eq.) was dissolved in 300 µl of MeOH and added to the round bottom flask. The mixture was refluxed at 80 ºC during 45 min. The orange solution was cooled down at room temperature and concentrated under vacuum. The red-orange residue was dissolved in boiling methanol to remove the excess of terpy and cooled down at room temperature. The product was precipitated adding 50 mL of Et_2O and then filtered under vacuum. Obtained 34 mg, 0.06 mmol (55%) **321** as a red solid. ^{1}H NMR (500 MHz, CD_3OD, 25 ºC) δ = 9.16 – 9.11 (m, 2H; H-1), 8.58 – 8.43 (m, 7H; H-3, H-4, H-5 and H-6), 7.92 (m, 2H; H-2). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3087 (Terpy), 2929 (Terpy), 1605, 1474 (Terpy), 1401, 779.

Synthesis of chloro (2,2':6',2''-terpyridine)-hexafluoroantimonate platinum (322)[247-248]



321 **322**

[PtCl(terpy)]Cl **321** (10 mg, 0.02 mmol, 1.0 Eq.) was dissolved in 2.0 mL of MeOH in a microwave vial under normal atmosphere, changing the colour immediately from red to bright yellow. The vial was sealed and the mixture was heated at 70 °C during 5 min. Then $AgSbF_6$ (6 mg, 0.02 mmol, 1.0 Eq.) was added dissolved in 1.0 mL of MeOH. The suspension was heated at 70 °C during 30 min. The solution was cooled down and concentrated under vacuum. Obtained 8 mg, 0.01 mmol, as a yellow-orange solid **322** (61%). ^{1}H NMR (500 MHz, CD_3CN, 25 °C) δ = 9.05 (d, J = 5.8 Hz, 2H; H-6), 8.65 – 8.60 (m, 2H; H-5), 8.60 – 8.55 (m, 4H; H-3 and H-4), 8.50 (t, J = 7.9 Hz, 1H; H-1), 8.01 – 7.95 (m, 2H; H-2). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3066 (Terpy), 3011 (Terpy), 1607, 1475 (Terpy), 1399, 772, 653.

Synthesis of *N*-bispropargyl derivatives

Procedure (a):

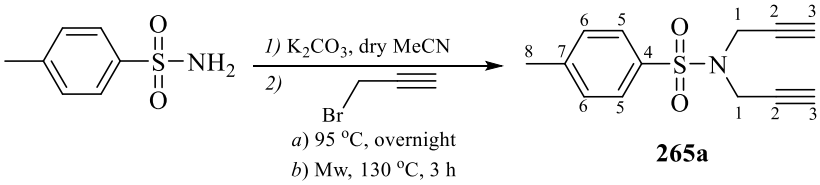
Potassium carbonate (K_2CO_3) (5.0 Eq.) was added into a flame-dried two-necks round bottom flask equipped with a condenser under N_2 atmosphere. The corresponding substituted primary amine (1.0 Eq., 0.26 M – absolute concentration) was added dissolved in dry acetonitrile under N_2. The suspension was stirred at room temperature for 3 min and then propargyl bromide (80% in toluene, 3.0 Eq.) was added dropwise. The reaction mixture was heated at 90 – 95 °C until complete conversion, followed by TLC. The crude was quenched with H_2O at 0 °C (ice bath) and extracted with Et_2O (x 3). The ether extracts were combined and washed with brine, dried over $MgSO_4$ anhydrous and concentrated under vacuum. The product was purified by column chromatography over silica gel using Hex or PET / Et_2O or EtOAc as eluent.

Procedure (b):

Potassium carbonate (K_2CO_3) (5.0 Eq.) was added into a previously vacuum-dried microwave vial under N_2 conditions. Then the corresponding substituted primary amine (1.0 Eq., 0.26 M – absolute concentration) was added dissolved in dry acetonitrile under N_2. The suspension was stirred at room temperature during 3 min and then propargyl bromide (80% in toluene, 3.0 Eq.) was added dropwise under N_2. The vial was sealed under inert atmosphere

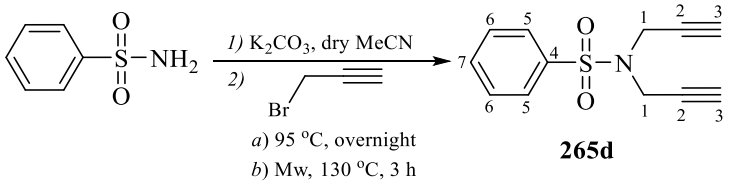
and the reaction mixture was heated under microwave irradiation at 130 °C during 3 h. The crude was quenched with H_2O at 0 °C (ice bath) and extracted with Et_2O (x 3). The ether extracts were combined and washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The product was obtained without further purification.

Synthesis of 4-methyl-*N*,*N*-di-prop-2-ynyl-benzenesulfonamide (265a)[249]



Procedure (a). From *p*-toluenesulfonamide (4.0 g, 23.51 mmol), K_2CO_3 (16.2 g, 117.57 mmol), propargyl bromide (7.9 mL, 70.54 mmol) and 92.0 mL of dry acetonitrile. Obtained without further purification a brown solid **265a**, 5.3 g, 21.64 mmol (92%). ***Procedure (b).*** From *p*-toluenesulfonamide (450 mg, 2.63 mmol), K_2CO_3 (1.8 g, 13.14 mmol), propargyl bromide (877 µl, 7.88 mmol) and 10.0 mL of dry acetonitrile. Obtained without further purification a brown solid **265a**, 642 mg, 2.59 mmol (99%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.72 (d, J = 8.2 Hz, 2H; H_{Ar}-5), 7.30 (d, J = 8.2 Hz, 2H; H_{Ar}-6), 4.17 (d, J = 2.4 Hz, 4H; H-1), 2.43 (s, 3H; H-8), 2.15 (t, J = 2.4 Hz, 2H; H-3). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C) δ = 144.1 (C_q; C-4 or C-7), 135.3 (C_q; C-4 or C-7), 129.7 (2 x CH_{Ar}; C-6), 128.0 (2 x CH_{Ar}; C-5), 76.3 (2 x C_q; C-2), 74.2 (2 x CH; C-3), 36.3 (2 x CH_2; C-1), 21.7 (CH_3; C-8).

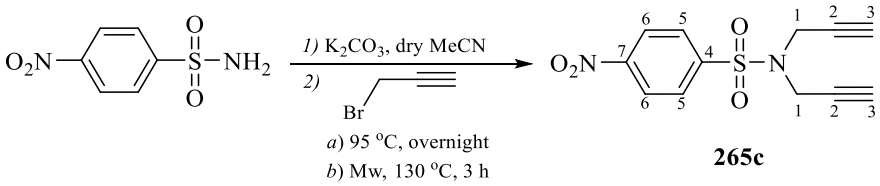
Synthesis of *N*,*N*-di-prop-2-ynyl-benzenesulfonamide (265d)



Procedure (a). From benzenesulfonamide (1.0 g, 6.36 mmol), K_2CO_3 (4.4 g, 31.81 mmol), propargyl bromide (2.1 mL, 19.08 mmol) and 24.0 mL of dry acetonitrile. Obtained after column chromatography, Hex / EtOAc, (6:1) then (4:1), 1.1 g, 4.50 mmol (72%): **265d** white solid. ***Procedure (b).*** From benzenesulfonamide (600 mg, 3.82 mmol), K_2CO_3 (2.6 g, 19.08 mmol), propargyl bromide (1.3 mL, 11.45 mmol) and 14.0 mL of dry acetonitrile. Obtained without further purification a brown solid **265d**, 1.4 g, 6.23 mmol (98%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.87 – 7.81 (m, 2H; H_{Ar}-5), 7.63 – 7.57 (m, 1H; H_{Ar}-7), 7.55 – 7.48 (m, 2H; H_{Ar}-6), 4.18 (d, J = 2.4 Hz, 4H; H-1), 2.14 (t, J = 2.4 Hz, 2H; H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 138.3 (C_q; C-4), 133.3 (CH_{Ar}; C-7), 129.1 (2 x CH_{Ar}; C-5), 128.0 (2 x CH_{Ar}; C-6), 76.2 (2 x C_q; C-2), 74.2 (2 x CH; C-3), 36.4 (2 x CH_2; C-1). IR (Film, cm^{-1}):

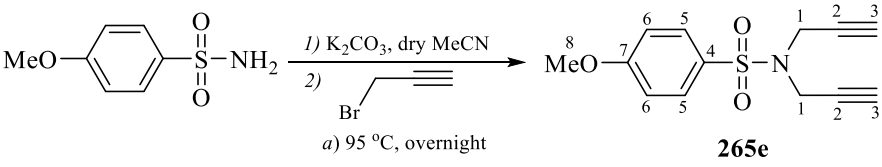
$\tilde{\nu}$ = 3264 (C≡CH), 3073 (C-H_{Ar}), 2994, 2942 (C-H_{Alkane}), 2891 (C-H_{Alkane}), 2121 (C≡C), 1449 (C-H_{Alkane}), 1339 (S=O), 1164 (S=O), 1071 (C-N), 889. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{12}H_{12}NO_2S$ $[M+H]^+$: 234.0583. Found: 234.0583. M.P. = 68 – 70 °C.

Synthesis of 4-nitro-*N*,*N*-di-prop-2-ynyl-benzenesulfonamide (265c)



Procedure (a). From 4-nitrobenzenesulfonamide (1.0 g, 4.95 mmol), K_2CO_3 (3.4 g, 24.76 mmol), propargyl bromide (1.7 mL, 14.86 mmol) and 26.0 mL of dry acetonitrile. Obtained without further purification an orange solid **265c**, 1.3 g, 4.70 mmol (95%). ***Procedure (b).*** From 4-nitrobenzenesulfonamide (600 mg, 2.97 mmol), K_2CO_3 (2.0 g, 14.83 mmol), propargyl bromide (991 µl, 8.90 mmol) and 13.0 mL of dry acetonitrile. Obtained without further purification an orange solid **265c**, 524 mg, 1.88 mmol (64%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 8.47 – 8.29 (m, 2H; H_{Ar}-5), 8.07 – 8.01 (m, 2H; H_{Ar}-6), 4.23 (d, J = 2.4 Hz, 4H; H-1), 2.19 (t, J = 2.4 Hz, 2H; H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 150.5 (C_q; C-7), 144.3 (C_q; C-4), 129.2 (2 x CH_{Ar}; C-6), 124.3 (2 x CH_{Ar}; C-5), 75.6 (2 x C_q; C-2), 74.9 (2 x CH; C-3), 36.6 (2 x CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3269 (C≡CH), 3104 (C-H_{Ar}), 3069 (C-H_{Ar}), 2998 (C-H_{Alkane}), 2118 (C≡C), 1607 (C=C_{Ar}), 1530 (N-O), 1350 (S=O), 1167 (S=O), 1061 (C-N), 931. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{12}H_{10}N_2O_4SNa$ $[M+Na]^+$: 301.0253. Found: 301.0258. M. P. = 113 – 115 °C.

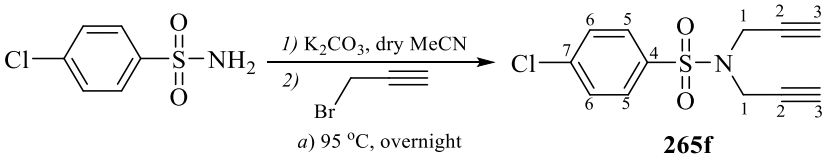
Synthesis of 4-methoxy-*N*,*N*-di-prop-2-ynyl-benzenesulfonamide (265e)



Procedure (a). From 4-methoxybenzenesulfonamide (1.4 g, 7.53 mmol), K_2CO_3 (5.2 g, 37.66 mmol), propargyl bromide (2.5 mL, 22.60 mmol) and 29.0 mL of dry acetonitrile. Obtained after column chromatography, Hex / EtOAc (5:1) then (3:1): **265e**, 1.8 g, 7.00 mmol (93%): white solid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.79 – 7.74 (m, 2H; H_{Ar}-5), 6.99 – 6.94 (m, 2H; H_{Ar}-6), 4.16 (d, J = 2.4 Hz, 4H; H-1), 3.87 (s, 3H; H-8), 2.16 (t, J = 2.4 Hz, 2H; H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 163.5 (C_q; C-7), 130.2 (2 x CH_{Ar}; C-5), 129.8 (C_q; C-4), 114.2 (2 x CH_{Ar}; C-6), 76.4 (2 x C_q; C-2), 74.2 (2 x CH; C-3), 55.8 (CH_3; C-8), 36.3

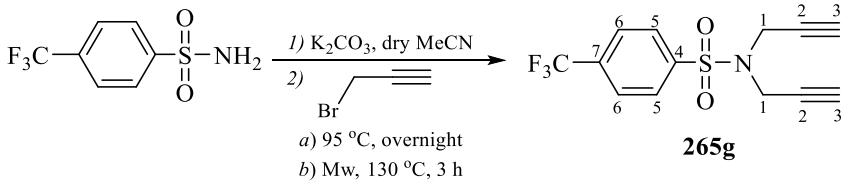
(2 x CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3290 (C≡CH), 3104 (C-H_{Ar}), 3014 (C-H_{Ar}), 2897 (C-H_{Alkane}), 2846 (C-H_{Alkane}), 2125 (C≡C), 1596 (C=C_{Ar}), 1498, 1350 (S=O), 1262 (C-O), 1159 (S=O), 1096 (C-N), 1027 (C-O), 805. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{13}H_{14}NO_3S$ $[M+H]^+$: 264.0689. Found: 264.0686. M.P. = 49 – 51 °C.

Synthesis of 4-chloro-*N*,*N*-di-prop-2-ynyl-benzenesulfonamide (265f)



Procedure (a). From 4-chlorobenzenesulfonamide (1.0 g, 5.31 mmol), K_2CO_3 (3.7 g, 26.54 mmol), propargyl bromide (1.8 mL, 15.92 mmol) and 25.0 mL of dry acetonitrile. Obtained after column chromatography, Hex / EtOAc (4:1): **265f**, 1.3 g, 4.86 mmol (92%): yellow-white solid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.81 – 7.75 (m, 2H; H_{Ar}-5), 7.52 – 7.45 (m, 2H; H_{Ar}-6), 4.18 (d, J = 2.4 Hz, 4H; H-1), 2.18 (t, J = 2.4 Hz, 2H; H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 139.9 (C_q; C-7), 136.9 (C_q; C-4), 129.4 (2 x CH_{Ar}; C-5), 129.4 (2 x CH_{Ar}; C-6), 76.0 (2 x C_q; C-2), 74.5 (2 x CH; C-3), 36.4 (2 x CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3295 (C≡CH), 3097 (C-H_{Ar}), 2987, 2935 (C-H_{Alkane}), 2857 (C-H_{Alkane}), 2122 (C≡C), 1587 (C=C_{Ar}), 1355 (S=O), 1166 (S=O), 1096 (C-N), 893. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{12}H_1{}^{35}ClNO_2S$ $[M+H]^+$: 268.0194. Found: 268.0197. Calc. for $C_{12}H_1{}^{37}ClNO_2S$ $[M+H]^+$: 270.0163. Found: 270.0163. M.P. = 65 – 67 °C.

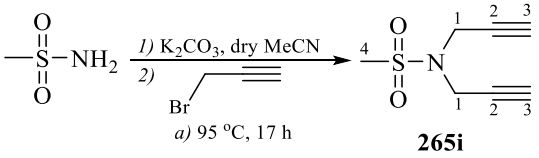
Synthesis of *N*,*N*-di-prop-2-ynyl-4-trifluoromethyl-benzenesulfonamide (265g)



Procedure (a). From 4-(trifluoromethyl)benzenesulfonamide (377 mg, 1.67 mmol), K_2CO_3 (1.1 g, 8.37 mmol), propargyl bromide (560 µl, 5.02 mmol) and 22.0 mL of dry acetonitrile. Obtained without further purification a brown solid **265g**, 479 mg, 1.59 mmol (95%). ***Procedure (b).*** From 4-(trifluoromethyl)benzenesulfonamide (347 mg, 1.54 mmol), K_2CO_3 (1.1 g, 7.70 mmol), propargyl bromide (514 µl, 4.62 mmol) and 7.0 mL of dry acetonitrile. Obtained without further purification a brown solid **265g**, 461 mg, 1.53 mmol (99%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.98 (d, J = 8.2 Hz, 2H; H_{Ar}-5), 7.79 (d, J = 8.2 Hz, 2H; H_{Ar}-6), 4.20 (d, J = 2.4 Hz, 4H; H-1), 2.17 (t, J = 2.4 Hz, 2H; H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 142.0 (C_q; C-4), 128.5 (2 x CH_{Ar}; C-5), 126.3 (q, $J_{C\text{-}F}$ = 3.5 Hz; 2 x

CH_{Ar}; C-6), 75.8 (2 x C_q; C-2), 74.6 (2 x CH; C-3), 36.5 (2 x CH_2; C-1). *Signals (C_q; C-7) and (C_q; CF_3) could not be identified.* ^{19}F NMR (471 MHz, $CDCl_3$, 25 °C) δ = - 63.11. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3291 (C≡CH), 3104 (C-H_{Ar}), 3060 (C-H_{Ar}), 2936 (C-H_{Alkane}), 2856 (C-H_{Alkane}), 2124 (C≡C), 1323 (S=O), 1168 (S=O), 1133 (C-F), 1095 (C-N), 843. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{13}H_{11}F_3NO_2S$ $[M+H]^+$: 302.0457. Found: 302.0453. M.P. = 44 – 46 °C.

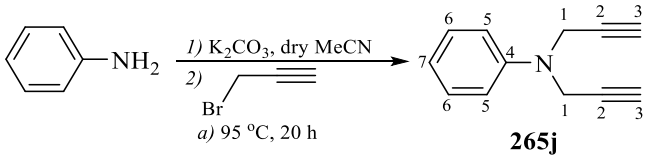
Synthesis of *N,N*-di-prop-2-ynyl-methanesulfonamide (265i)



265i

Procedure (a). From methanesulfonamide (2.3 g, 24.42 mmol), K_2CO_3 (16.9 g, 122.09 mmol), propargyl bromide (8.2 mL, 73.26 mmol) and 30.0 mL of dry acetonitrile. Obtained after column chromatography using PET / EtOAc as eluent (10:1) then (5:1) a yellow solid **265i**, 1.8 g, 10.78 mmol (45%). ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 4.19 (d, *J* = 2.4 Hz, 4H; H-1), 2.97 (s, 3H; H-4), 2.39 (t, *J* = 2.4 Hz, 2H; H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 76.8 (2 x C_q; C-2), 74.7 (2 x CH; C-3), 38.7 (CH_3; C-4), 36.6 (2 x CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3288 (C≡CH), 2979 (C-H_{Alkane}), 2933 (C-H_{Alkane}), 2853 (C-H_{Alkane}), 2120 (C≡C), 1347 (S=O), 1155 (S=O), 1080 (C-N), 951, 892. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_7H_{10}NO_2S$ $[M+H]^+$: 172.0427. Found: 172.0426. M.P. = 35 – 36 °C.

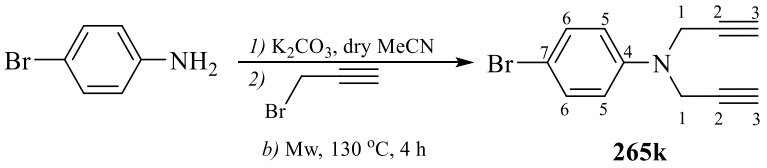
Synthesis of phenyl-di-prop-2-ynyl-amine (265j)[250]



265j

Procedure (a). From aniline (1.0 mL, 10.97 mmol), K_2CO_3 (7.6 g, 54.87 mmol), propargyl bromide (2.9 mL, 32.92 mmol) and 42.0 mL of dry acetonitrile. Obtained without further purification a yellow solid **265j**, 1.8 g, 10.40 mmol (95%). ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.32 – 7.27 (m, 2H; H_{Ar}-6), 7.00 – 6.95 (m, 2H; H_{Ar}-5), 6.92 – 6.87 (m, 1H; H_{Ar}-7), 4.13 (d, *J* = 2.3 Hz, 4H; H-1), 2.25 (t, *J* = 2.3 Hz, 2H; H-3). *This data matched the reported for this compound.*

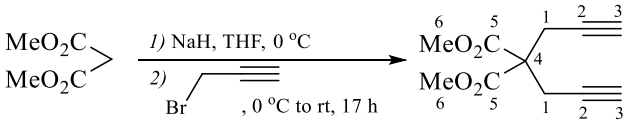
Synthesis of (4-bromo-phenyl)-di-prop-2-ynyl-amine (265k)



265k

Procedure (b). From 4-bromoaniline (353 mg, 2.07 mmol), K_2CO_3 (1.4 g, 10.33 mmol), propargyl bromide (690 µl, 6.20 mmol) and 17.0 mL of dry acetonitrile. Obtained without further purification a yellow solid **265k**, 1.8 g, 10.40 mmol (95%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.40 – 7.35 (m, 2H; H_{Ar}-6), 6.87 – 6.78 (m, 2H; H_{Ar}-5), 4.09 (d, J = 2.4 Hz, 4H; H-1), 2.26 (t, J = 2.4 Hz, 2H; H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 146.8 (C_q; C-4), 132.1 (2 x CH_{Ar}; C-6), 117.4 (2 x CH_{Ar}; C-5), 112.2 (C_q; C-7), 78.9 (2 x C_q; C-2), 73.1 (2 x CH; C-3), 40.7 (2 x CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3292 (C≡CH), 3080 (C-H_{Ar}), 3045 (C-H_{Ar}), 2926 (C-H_{Alkane}), 2833 (C-H_{Alkane}), 2115 (C≡C), 1592 (C=C_{Ar}), 1495, 1227, 1161 (C-N), 948, 902, 811. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{12}H_{10}{}^{79}BrN$ [M]$^+$: 246.9991. Found: 246.9994. Calc. for $C_{12}H_{10}{}^{81}BrN$ [M]$^+$: 248.9971. Found: 248.9971. Calc. for $C_{12}H_{11}{}^{79}BrN$ [M+H]$^+$: 248.0025. Found: 248.0070. Calc. for $C_{12}H_{11}{}^{81}BrN$ [M+H]$^+$: 250.0004. Found: 251.0082.

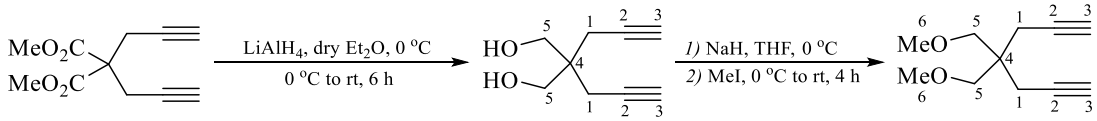
Synthesis of dimethyl 2,2-di(prop-2-ynyl)malonate (268)[249]



268

To a suspension of sodium hydride (NaH) (60% mineral oil, 2.3 g, 57.75 mmol, 2.2 Eq.) in dry THF (40.0 mL) at 0 °C (ice bath), was added dropwise dimethylmalonate (5.0 mL, 43.75 mmol, 1.0 Eq., 1.1 M). After 5 min stirring, propargyl bromide (80% in toluene, 7.3 mL, 65.63 mmol, 2.5 Eq.) was added and the resulting solution was warmed up at room temperature and stirred during 17 h. The solution was quenched with $NaHCO_{3(ac)}$ (15 mL) at 0 °C (ice bath), extracted with EtOAc (x 3), washed with brine, dried over $MgSO_4$ anhydrous and concentrated under vacuum. The product **268** was obtained without further purification as a brown solid (5.5 g, 26.25 mmol, 99%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 3.77 (s, 6H; H-6), 3.01 (d, J = 2.6 Hz, 4H; H-1), 2.04 (t, J = 2.6 Hz, 2H; H-3). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C) δ = 169.2 (2 x C_q; C-5), 78.4 (2 x C_q; C-2), 71.9 (2 x CH; C-3), 56.6 (C_q; C-4), 53.3 (2 x CH_3; C-6), 22.8 (2 x CH_2; C-1).

Synthesis of 4,4-bis-methoxymethyl-hepta-1,6-diyne (270)[251]



268 **269** **270**

The synthesis was undertaken according to the procedure described by Malacria and coworkers.[251] To a suspension of lithium aluminium hydride ($LiAlH_4$) (325 mg, 8.56 mmol, 3.0 Eq.) in dry Et_2O (8.0 mL) at 0 °C (ice bath), was added dimethyl 2,2-di(prop-2-ynyl)malonate **268** (594 mg, 2.85 mmol, 1.0 Eq., 0.16 M – absolute concentration) dissolved in 10.0 mL of dry Et_2O under N_2. The solution was warmed up at room temperature and stirred during 5 h. The excess of $LiAlH_4$ was quenched at 0 °C (ice bath) adding H_2O (2.0 mL), an aqueous NaOH solution (2.0 mL, 15% w/w), and then H_2O (2.0 mL). The white suspension was filtered over celite, washed with DCM (20 mL), dried over $MgSO_4$ anhydrous and concentrated under vacuum. 2,2-Di-prop-2-ynyl-propane-1,3-diol **269**[252] was obtained without further purification as a white solid (378 mg, 2.48 mmol, 87%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 3.75 (s, 4H; H-5), 2.38 (d, J = 2.7 Hz, 4H; H-1), 2.05 (t, J = 2.7 Hz, 2H; H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 80.4 (2 x C_q; C-2), 71.3 (2 x CH; C-3 or CH_2; C-5), 66.8 (2 x CH; C-3 or CH_2; C-5), 42.2 (C_q; C-4), 21.9 (2 x CH_2; C-1).

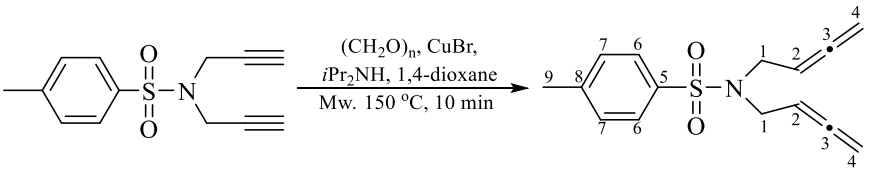
To a suspension of NaH (60% mineral oil, 219 mg, 5.46 mmol, 2.2 Eq.) in dry THF (4.0 mL) at 0 °C (ice bath), was added 2,2-di-prop-2-ynyl-propane-1,3-diol **269** (378 mg, 2.48 mmol, 1.0 Eq., 0.31 M – absolute concentration) dissolved in dry THF (4.0 mL). After 5 min, iodomethane (773 µl, 12.42 mmol, 5.0 Eq.) was added and the resulting solution was stirred at room temperature during 6 h. The mixture was quenched with $NH_4Cl_{(ac)}$ (5 mL) at 0 °C (ice bath), extracted with Et_2O (x 3), washed with brine, dried over $MgSO_4$ anhydrous and concentrated under vacuum. The product **270** was obtained without further purification as a yellow oil (447 mg, 2.48 mmol, 100%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 3.36 (s, 4H; H-5), 3.35 (s, 6H; H-6), 2.35 (d, J = 2.7 Hz, 4H; H-1), 1.98 (t, J = 2.7 Hz, 2H; H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 80.9 (2 x C_q; C-2), 73.6 (2 x CH_2; C-5), 70.5 (2 x CH; C-3), 59.6 (2 x CH_3; C-6), 41.8 (C_q; C-4), 22.0 (2 x CH_2; C-1).

General procedure for the synthesis of 1,5-bisallenes by microwave-assisted Crabbé homologation from bispropargyl derivatives[27b]

CuBr (0.6 Eq.) and paraformaldehyde (5.0 Eq.) were added into a oven-dried microwave vial under N_2. Then the corresponding bispropargylic derivative (1.0 Eq., 0.5 M – absolute concentration) was added dissolved in dry 1,4-dioxane, followed by the addition of iPr$_2$NH (4.0 Eq.) dropwise under inert atmosphere. The reaction mixture was heated at 150 °C

under microwave irradiation during 10 – 20 min until complete conversion, followed by TLC. The crude of the reaction was purified by column chromatography over silica gel using Hex or PET / Et_2O or EtOAc as eluent.

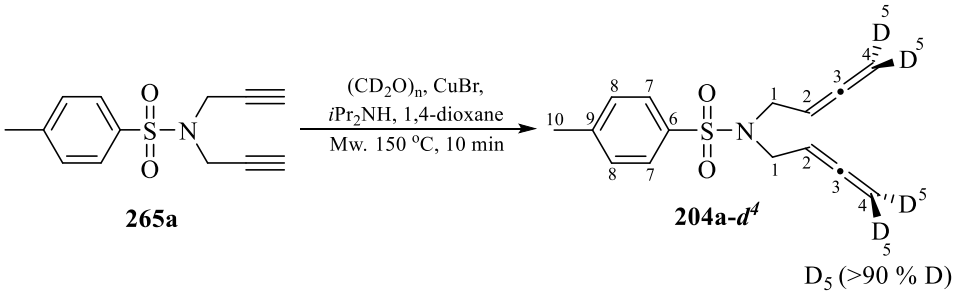
Synthesis of *N,N*-di-buta-2,3-dienyl-4-methyl-benzenesulfonamide (204a)[210a, 253]



265a **204a**

From compound **265a** (1.6 g, 6.38 mmol), CuBr (549 mg, 3.83 mmol), paraformaldehyde (958 mg, 31.88 mmol), *i*Pr_2NH (3.6 mL, 25.51 mmol) and 13.0 mL of dry 1,4-dioxane. Obtained after column chromatography, PET / EtOAc, (7:1), **204a**, 1.2 g, 4.46 mmol (70%): yellow solid. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.72 – 7.68 (m, 2H; H_{Ar}-6), 7.29 (d, *J* = 8.2 Hz, 2H; H_{Ar}-7), 4.97 – 4.90 (m, 2H; H-2), 4.71 (dt, *J* = 6.6, 2.4 Hz, 4H; H-4), 3.90 (dt, *J* = 7.0, 2.4 Hz, 4H; H-1), 2.42 (s, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.8 (2 x C_q; C-3), 143.4 (C_q; C-8), 137.7 (C_q; C-5), 129.8 (2 x CH_{Ar}; C-7), 127.3 (2 x CH_{Ar}; C-6), 85.8 (2 x CH; C-2), 76.3 (2 x CH_2; C-4), 45.8 (2 x CH_2; C-1), 21.7 (CH_3; C-9).

Synthesis of d_4-*N,N*-di-buta-2,3-dienyl-4-methyl-benzenesulfonamide (204a-*d*^{4})



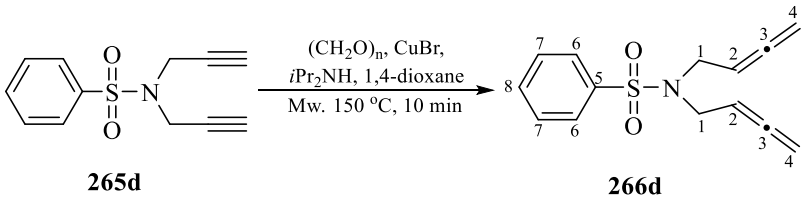
265a **204a-*d*^{4}**

D_5 (>90 % D)

From compound **265a** (410 mg, 1.66 mmol), CuBr (143 mg, 0.99 mmol), paraformaldehyde-d_2 (265 mg, 8.28 mmol, 98% D), *i*Pr_2NH (928 µl, 6.62 mmol) and 3.3 mL of dry 1,4-dioxane. Obtained after column chromatography, PET / EtOAc, (20:1) then (7:1) then (4:1): **204a-*d*^{4}**, 284 mg, 1.02 mmol (61%): white solid. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.73 – 7.68 (m, 2H; H_{Ar}-8), 7.29 (d, *J* = 8.2 Hz, 2H; H_{Ar}-7), 4.94 (t, *J* = 7.1 Hz, 2H; H-2), 4.73 – 4.68 (m, D-5, >90 %D), 3.90 (d, *J* = 7.1 Hz, 4H; H-1), 2.42 (s, 3H; H-10). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.9 (2 x C_q; C-3), 143.4 (C_q; C-9), 137.7 (C_q; C-6), 129.8 (2 x CH_{Ar}; C-8), 127.3 (2 x CH_{Ar}; C-7), 86.0 (2 x CH; C-2), 45.8 (2 x CH_2; C-1), 21.7 (CH_3; C-10). *C_q; C-4 could not be found due to deuteration.* ^2H NMR (77 MHz, $CDCl_3$, 25 °C), δ = 4.74 (s, 4D; D-5). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3079 (C-H_{Ar}), 2924 (C-H_{Alkane}), 2865 (C-H_{Alkane}), 1938

(C=C=C), 1597 (C=C_{Ar}), 1345 (S=O), 1161 (S=O), 1095 (C-N), 941, 814. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{15}H_{14}D_4NO_2S$ $[M+H]^+$: 280.1304. Found: 280.1300. M.P. = 49 – 50 °C.

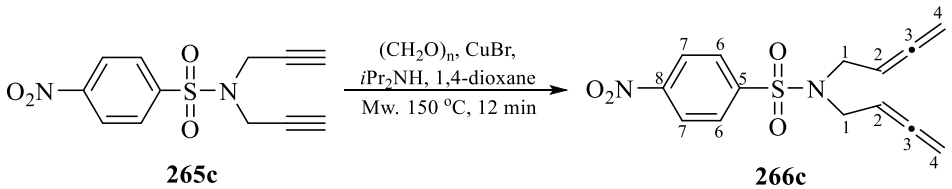
Synthesis of *N,N*-di-buta-2,3-dienyl-benzenesulfonamide (266d)



265d **266d**

From compound **265d** (1.0 g, 4.32 mmol), CuBr (372 mg, 2.59 mmol), paraformaldehyde (649 mg, 21.61 mmol), *i*Pr_2NH (2.4 mL, 17.29 mmol) and 9.0 mL of dry 1,4-dioxane. Obtained after column chromatography, Hex / EtOAc (12:1): **266d**, 707 mg, 2.71 mmol (63%): yellow solid. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.84 – 7.80 (m, 2H; H_{Ar}-6), 7.60 – 7.54 (m, 1H; H_{Ar}-8), 7.53 – 7.48 (m, 2H; H_{Ar}-7), 4.99 – 4.89 (m, 2H; H-2), 4.71 (dt, *J* = 6.6, 2.4 Hz, 4H; H-4), 3.92 (dt, *J* = 6.9, 2.4 Hz, 4H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.8 (2 x C_q; C-3), 140.7 (C_q; C-5), 132.7 (CH_{Ar}; C-8), 129.2 (2 x CH_{Ar}; C-7), 127.3 (2 x CH_{Ar}; C-6), 85.7 (2 x CH; C-2), 76.4 (2 x CH_2; C-4), 45.8 (2 x CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3065 (C-H_{Ar}), 2991, 2924 (C-H_{Alkane}), 2862 (C-H_{Alkane}), 1954 (C=C=C), 1342 (S=O), 1160 (S=O), 1095 (C-N), 851, 749. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{14}H_{16}NO_2S$ $[M+H]^+$: 262.0896. Found: 262.0897. M.P. = 38 – 40 °C.

Synthesis of *N,N*-di-buta-2,3-dienyl-4-nitro-benzenesulfonamide (266c)

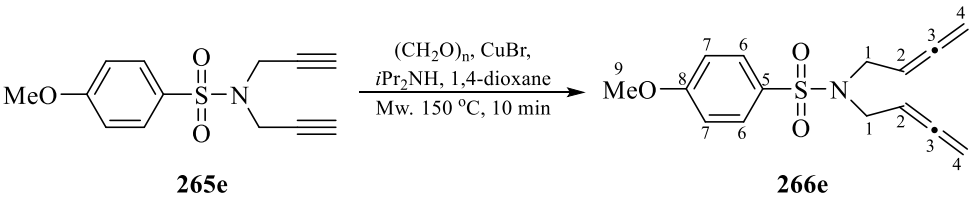


265c **266c**

From compound **265c** (524 mg, 1.88 mmol), CuBr (162 mg, 1.13 mmol), paraformaldehyde (283 mg, 9.43 mmol), *i*Pr_2NH (1.1 mL, 7.54 mmol) and 3.8 mL of dry 1,4-dioxane. Obtained after column chromatography, PET / EtOAc, (30:1) then (7:1) then (4:1): **266c**, 423 mg, 1.38 mmol (73%): yellow solid. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 8.35 (d, *J* = 8.9 Hz, 2H; H_{Ar}-6), 8.01 (d, *J* = 8.9 Hz, 2H; H_{Ar}-7), 4.96 (p, *J* = 6.8 Hz, 2H; H-2), 4.74 (dt, *J* = 6.8, 2.4 Hz, 4H; H-4), 3.96 (dt, *J* = 6.8, 2.4 Hz, 4H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.9 (2 x C_q; C-3), 150.1 (C_q; C-8), 146.8 (C_q; C-5), 128.5 (2 x CH_{Ar}; C-7), 124.5 (2 x CH_{Ar}; C-6), 85.4 (2 x CH; C-2), 76.9 (2 x CH_2; C-4), 45.9 (2 x CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3108 (C-H_{Ar}), 2933 (C-H_{Alkane}), 1954 (C=C=C), 1528 (N-O), 1348 (S=O), 1157 (S=O),

1062 (C-N), 855. HRMS (FTMS + p APCI (DCM)): Calc. for $C_{14}H_{15}N_2O_4S$ $[M+H]^+$: 307.0747. Found: 301.0748. M.P. = 68 – 69 °C.

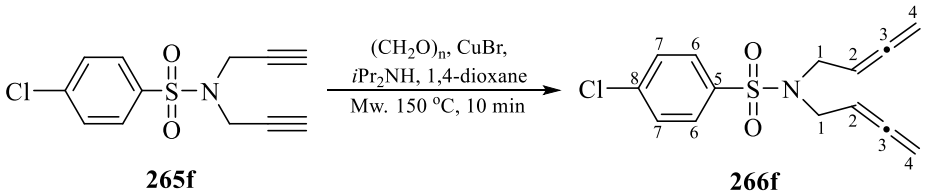
Synthesis of *N,N*-di-buta-2,3-dienyl-4-methoxy-benzenesulfonamide (266e)



265e **266e**

From compound **265e** (596 mg, 2.26 mmol), CuBr (195 mg, 1.36 mmol), paraformaldehyde (340 mg, 11.31 mmol), *i*Pr_2NH (1.3 mL, 9.04 mmol) and 4.5 mL of dry 1,4-dioxane. Obtained after column chromatography, Hex / EtOAc, (5:1): **266e**, 342 mg, 1.17 mmol (52%): brown oil. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.78 – 7.72 (m, 2H; H_{Ar}-6), 6.99 – 6.93 (m, 2H; H_{Ar}-7), 4.98 – 4.91 (m, 2H; H-2), 4.72 (dt, *J* = 6.8, 2.4 Hz, 4H; H-4), 3.89 (dt, *J* = 6.8, 2.4 Hz, 4H; H-1), 3.87 (s, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.8 (2 x C_q; C-3), 162.9 (C_q; C-8), 132.3 (C_q; C-5), 129.4 (2 x CH_{Ar}; C-7), 114.3 (2 x CH_{Ar}; C-6), 85.8 (2 x CH; C-2), 76.3 (2 x CH_2; C-4), 55.7 (CH_3; C-9), 45.8 (2 x CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3066 ($C\text{-}H_{Ar}$), 2941 ($C\text{-}H_{Alkane}$), 2840 ($C\text{-}H_{Alkane}$), 1954 (C=C=C), 1596 ($C{=}C_{Ar}$), 1498, 1341 (S=O), 1260 (C-O), 1156 (S=O), 1095 (C-N), 836, 756. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{15}H_{18}NO_3S$ $[M+H]^+$: 292.1002. Found: 292.0997.

Synthesis of *N,N*-di-buta-2,3-dienyl-4-chloro-benzenesulfonamide (266f)

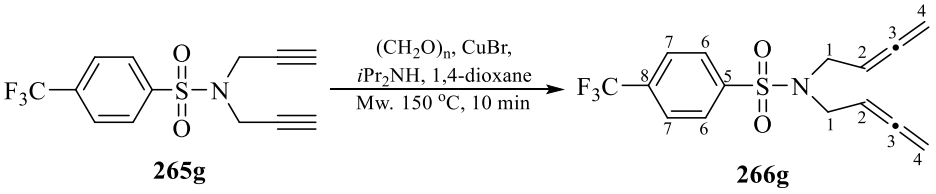


265f **266f**

From compound **265f** (575 mg, 2.07 mmol), CuBr (178 mg, 1.24 mmol), paraformaldehyde (310 mg, 10.34 mmol), *i*Pr_2NH (1.2 mL, 8.27 mmol) and 4.0 mL of dry 1,4-dioxane. Obtained after column chromatography, Hex / EtOAc, (6:1): **266f**, 318 mg, 1.07 mmol (52%): white solid. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.79 – 7.73 (m, 2H; H_{Ar}-6), 7.50 – 7.45 (m, 2H; H_{Ar}-7), 4.95 (p, *J* = 6.8 Hz, 2H; H-2), 4.73 (dt, *J* = 6.8, 2.5 Hz, 4H; H-4), 3.91 (dt, *J* = 6.8, 2.5 Hz, 4H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.9 (2 x C_q; C-3), 139.3 (C_q; C-8), 139.1 (C_q; C-5), 129.5 (2 x CH_{Ar}; C-7), 128.8 (2 x CH_{Ar}; C-6), 85.6 (2 x CH; C-2), 76.6 (2 x CH_2; C-4), 45.8 (2 x CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3090 ($C\text{-}H_{Ar}$), 2991 ($C\text{-}H_{Alkane}$), 2925 ($C\text{-}H_{Alkane}$), 2862 ($C\text{-}H_{Alkane}$), 1954 (C=C=C), 1585 ($C{=}C_{Ar}$), 1476, 1344 (S=O), 1161 (S=O), 1086 (C-N), 849, 617. HRMS (FTMS + p APCI (DCM)): Calc. for

$C_{14}H_{15}NO_2S^{35}Cl$ $[M+H]^+$: 296.0507 Found: 296.0504. Calc. for $C_{14}H_{15}NO_2S^{37}Cl$ $[M+H]^+$: 298.0476 Found: 298.0471. M. P. = 37 – 39 °C.

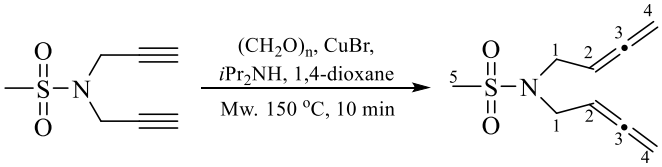
Synthesis of *N,N*-di-buta-2,3-dienyl-4-trifluoromethyl-benzenesulfonamide (266g)



265g **266g**

From compound **265g** (461 mg, 1.53 mmol), CuBr (132 mg, 0.92 mmol), paraformaldehyde (230 mg, 7.66 mmol), *i*Pr_2NH (860 µl, 6.13 mmol) and 3.1 mL of dry 1,4-dioxane. Obtained after column chromatography, PET / EtOAc, (20:1): **266g**, 319 mg, 0.97 mmol (63%): yellow oil. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.95 (d, J = 8.2 Hz, 2H; H_{Ar}-6), 7.77 (d, J = 8.2 Hz, 2H; H_{Ar}-7), 4.96 (p, J = 6.7 Hz, 2H; H-2), 4.72 (dt, J = 6.7, 2.4 Hz, 4H; H-4), 3.94 (dt, J = 6.7, 2.4 Hz, 4H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.8 (2 x C_q; C-3), 144.4 (C_q; C-5), 134.3 (q, J_{C-F} = 33.2 Hz, C_q; C-8), 127.8 (2 x CH_{Ar}; C-6), 126.4 (q, J_{C-F} = 3.6 Hz, 2 x CH_{Ar}-7), 85.5 (2 x CH; C-2), 76.7 (2 x CH_2; C-4), 45.8 (2 x CH_2; C-1). *The signal of C_q; CF_3 could not be extracted from the spectra.* ^{19}F NMR (471 MHz, $CDCl_3$, 25 °C) δ = - 63.04 (CF_3). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3107 (C-H_{Ar}), 3073 (C-H_{Ar}), 2927 (C-H_{Alkane}), 2860 (C-H_{Alkane}), 1956 (C=C=C), 1348 (S=O), 1166 (S=O), 1134 (C-F), 1063 (C-N), 1017, 846. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{15}H_{15}F_3NO_2S$ $[M+H]^+$: 330.0770. Found: 330.0771.

Synthesis of *N,N*-di-buta-2,3-dienyl-methanesulfonamide (266i)

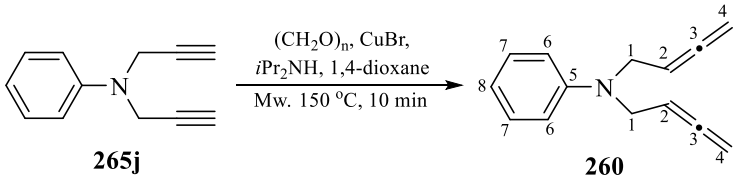


265i **266i**

From compound **265i** (1.2 g, 6.91 mmol), CuBr (105 mg, 0.73 mmol), paraformaldehyde (230 mg, 6.09 mmol), *i*Pr_2NH (3.9 mL, 27.64 mmol) and 13.8 mL of dry 1,4-dioxane. Obtained after column chromatography, PET / EtOAc, (7:1) then (4:1): **266i**, 868 mg, 4.36 mmol (63%): orange oil. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.14 (p, J = 6.7 Hz, 2H; H-2), 4.84 (dt, J = 6.7, 2.4 Hz, 4H; H-4), 3.92 (dt, J = 6.7, 2.4 Hz, 4H; H-1), 2.89 (s, 3H; H-5). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.9 (2 x C_q; C-3), 86.0 (2 x CH; C-2), 76.8 (2 x CH_2; C-4), 45.5 (2 x CH_2; C-1), 40.5 (CH_3; C-5). IR (Film, cm^{-1}): $\tilde{\nu}$ = 2987 (C-H_{Alkane}), 2919 (C-H_{Alkane}), 2853 (C-H_{Alkane}), 1953 (C=C=C), 1436 (C-H_{Alkane}), 1323 (S=O), 1145 (S=O), 1062

(C-N), 961, 844. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_9H_{14}NO_2S$ $[M+H]^+$: 200.0740. Found: 200.0741.

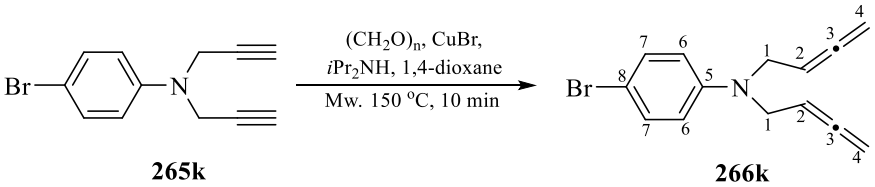
Synthesis of *N,N*-di-2,3-butadien-1-yl-benzenamine (260)[212]



265j **260**

From compound **265j** (1.8 g, 10.40 mmol), CuBr (895 mg, 6.24 mmol), paraformaldehyde (1.6 g, 51.99 mmol), *i*Pr_2NH (5.9 mL, 41.59 mmol) and 13.0 mL of dry 1,4-dioxane. Obtained after column chromatography, Hex / EtOAc, (13:1): **260**, 1.4 g, 7.08 mmol (68%): brown oil. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.24 – 7.19 (m, 2H; H_{Ar}-7), 6.76 (m, 2H; H_{Ar}-6), 6.71 (t, *J* = 7.3 Hz, 1H; H_{Ar}-8), 5.18 (p, *J* = 6.6 Hz, 2H; H-2), 4.76 (dt, *J* = 6.6, 2.8 Hz, 4H; H-4), 3.98 (dt, *J* = 6.6, 2.8 Hz, 4H; H-1). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ = 209.2 (2 x C_q; C-3), 148.0 (C_q; C-5), 129.2 (2 x CH_{Ar}; C-7), 117.0 (CH_{Ar}; C-8), 113.2 (2 x CH_{Ar}; C-6), 87.1 (2 x CH; C-2), 76.2 (2 x CH_2; C-4), 49.6 (2 x CH_2; C-1).

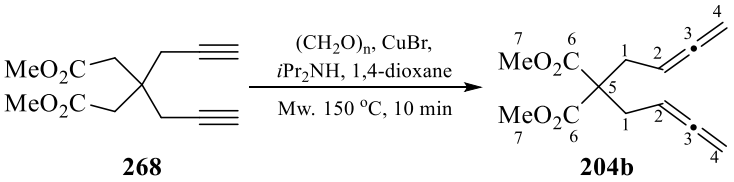
Synthesis of (4-bromo-phenyl)-di-buta-2,3-dienyl-amine (266k)



265k **266k**

From compound **265k** (247 mg, 1.00 mmol), CuBr (86 mg, 0.60 mmol), paraformaldehyde (150 mg, 5.00 mmol), *i*Pr_2NH (560 µl, 4.00 mmol) and 2.0 mL of dry 1,4-dioxane. Obtained after column chromatography, Hex / EtOAc, (40:1) then (10:1): **266k**, 163 mg, 0.59 mmol (60%): yellow oil. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.30 – 7.26 (m, 2H; H_{Ar}-7), 6.64 – 6.58 (m, 2H; H_{Ar}-6), 5.14 (p, *J* = 6.2 Hz, 2H; H-2), 4.80 – 4.72 (m, 4H; H-4), 3.94 (dt, *J* = 6.2, 2.9 Hz, 4H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.1 (2 x C_q; C-3), 147.1 (C_q; C-5), 131.9 (2 x CH_{Ar}; C-7), 114.8 (2 x CH_{Ar}; C-6), 108.8 (C_q; C-8), 86.8 (2 x CH; C-2), 76.6 (2 x CH_2; C-4), 49.7 (2 x CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3060 (C-H_{Ar}), 2987 (C-H_{Alkane}), 2924 (C-H_{Alkane}), 2870 (C-H_{Alkane}), 1953 (C=C=C), 1591 (C=C_{Ar}), 1497 (C-H_{Alkane}), 1353, 1222, 847. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{14}H_{15}N^{79}Br$ $[M+H]^+$: 276.0382. Found: 276.0380. Calc. for $C_{14}H_{15}N^{81}Br$ $[M+H]^+$: 278.0358. Found: 276.0358.

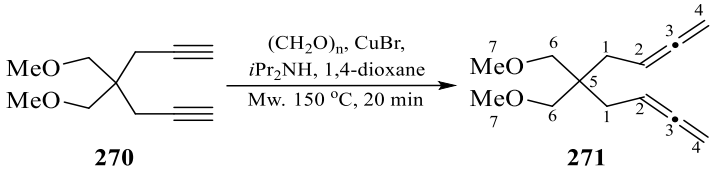
Synthesis of 2,2-di-2,3-butadien-1-yl-1,3-dimethyl malonate (204b)[41]



268 **204b**

From compound **268** (600 mg, 2.88 mmol), CuBr (248 mg, 1.73 mmol), paraformaldehyde (433 mg, 14.42 mmol), *i*Pr_2NH (1.6 mL, 11.53 mmol) and 5.8 mL of dry 1,4-dioxane. Obtained after column chromatography, PET / EtOAc, (20:1) then (6:1): **204b**, 226 mg, 1.08 mmol (38%): yellow oil. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 4.93 (tt, *J* = 8.0, 6.7 Hz, 2H; H-2), 4.66 (dt, *J* = 6.7, 2.4 Hz, 4H; H-4), 3.72 (s, 6H; H-7), 2.64 (dt, *J* = 8.0, 2.4 Hz, 4H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 210.2 (2 x C_q; C-3), 171.1 (2 x C_q; C-6), 84.2 (2 x CH; C-2), 74.8 (2 x CH_2; C-4), 58.0 (C_q; C-5), 52.6 (2 x CH_3; C-7), 32.1 (2 x CH_2; C-1).

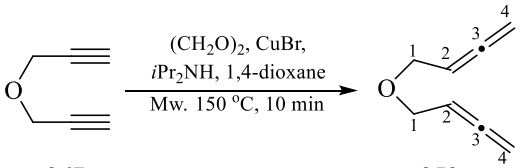
Synthesis of 5,5-bis-methoxymethyl-nona-1,2,7,8-tetraene (271)



270 **271**

From 4,4-bis-methoxymethyl-hepta-1,6-diyne **270** (447 mg, 2.48 mmol), CuBr (214 mg, 1.49 mmol), paraformaldehyde (373 g, 12.40 mmol), *i*Pr_2NH (1.4 mL, 9.92 mmol) and 5.0 mL of dry 1,4-dioxane. Obtained after column chromatography, PET / EtOAc, (30:1): **271**, 108 mg, 0.52 mmol (21%): yellow oil. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.05 (tt, *J* = 8.2, 6.7 Hz, 2H; H-2), 4.62 (dt, *J* = 6.7, 2.4 Hz, 4H; H-4), 3.31 (s, 6H; H-7), 3.21 (s, 4H; H-6), 2.04 (dt, *J* = 8.2, 2.4 Hz, 4H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 210.1 (2 x C_q; C-3), 85.3 (2 x CH; C-2), 74.9 (2 x CH_2; C-4 or C-6), 73.7 (2 x CH_2; C-4 or C-6), 59.4 (2 x CH_3; C-7), 42.7 (C_q; C-5), 31.6 (2 x CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 2983 (C-H_{Alkane}), 2923 (C-H_{Alkane}), 2890 (C-H_{Alkane}), 2855 (C-H_{Alkane}), 1955 (C=C=C), 1735, 1459 (C-H_{Alkane}), 1107 (C-O), 967, 840. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{13}H_{21}O_2$ $[M+H]^+$: 209.1536. Found: 209.1536.

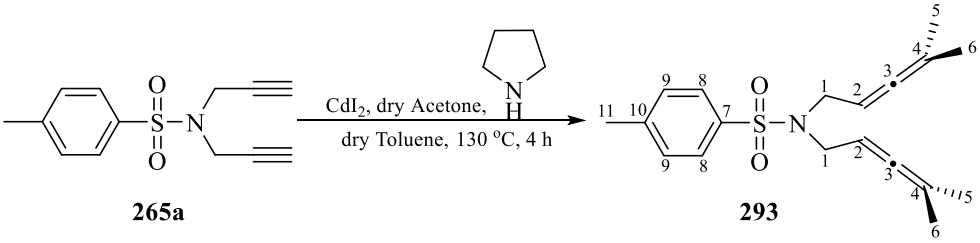
Synthesis of bis(2,3-butadienyl) ether (259)[210, 254]



267 **259**

From compound **267** (600 µl, 6.97 mmol), CuBr (600 mg, 4.19 mmol), paraformaldehyde (1.0 g, 34.88 mmol), *i*Pr$_2$NH (3.9 mL, 27.90 mmol) and 14.0 mL of dry 1,4-dioxane. Obtained after column chromatography, PET / Et$_2$O, (20:1): **259**, 783 mg, 6.41 mmol (92%): yellow liquid. ^{1}H NMR (500 MHz, CDCl$_3$, 25 °C) δ = 5.24 (p, J = 6.8 Hz, 2H; H-2), 4.79 (dt, J = 6.8, 2.4 Hz, 4H; H-4), 4.04 (dt, J = 6.8, 2.4 Hz, 4H; H-1). ^{13}C NMR (126 MHz, CDCl$_3$, 25 °C) δ = 209.5 (2 x C$_q$; C-3), 87.7 (2 x CH; C-2), 75.8 (2 x CH$_2$; C-4), 67.7 (2 x CH$_2$; C-1).

Synthesis of 4-methyl-*N*,*N*-bis-(4-methyl-penta-2,3-dienyl)-benzenesulfonamide (293)

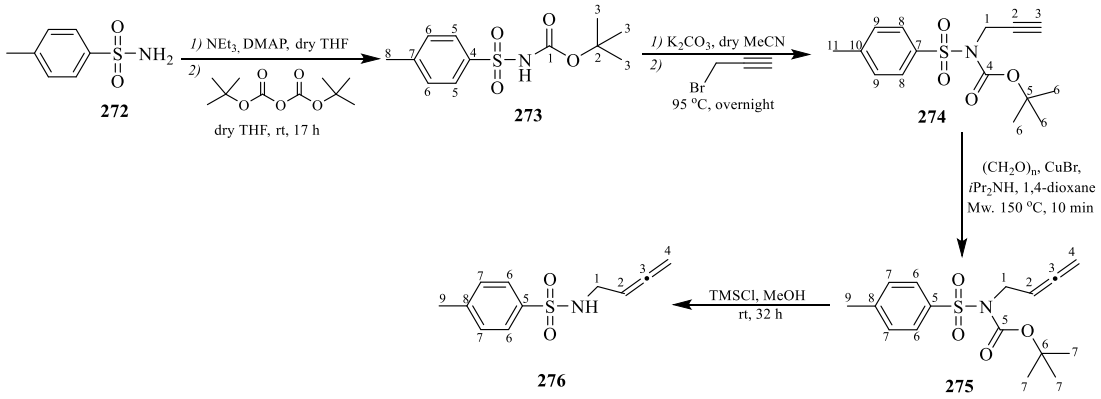


265a **293**

The synthesis was undertaken according to the procedure described by Ma and co-workers.[29] To a flame-dried Schlenk tube CdI$_2$ (1.2 g, 3.24 mmol, 1.6 Eq.) was added inside a globe box. Then the Schlenk was taken out the globe box and dried under vacuum with a flame until the white CdI$_2$ turned to yellow-green and allow to cool down. 4-Methyl-*N*,*N*-di-prop-2-ynyl-benzenesulfonamide **265a** (500 mg, 2.02 mmol, 1.0 Eq., 0.24 M) dissolved dry toluene (8.3 mL), dry acetone (327 µl, 4.45 mmol, 2.2 Eq.) and pyrrolidine (372 µl, 4.45 mmol, 2.2 Eq.) were added sequentially under N$_2$ flow. The Schlenk tube was then equipped with a condenser and placed in a pre-heated oil bath at 130 °C during 4 h. After cooled down, the reaction mixture was filtered through a pad of celite / silica gel (1:1), washed with Et$_2$O (30 mL) and concentrated under vacuum. The crude of the reaction was purified by column chromatography over silica gel using Hex / Et$_2$O as eluent. 110 mg, 0.36 mmol was obtained of **293** as a white solid (18%). ^{1}H NMR (500 MHz, CDCl$_3$, 25 °C) δ = 7.71 (d, J = 8.2 Hz, 2H; H$_{Ar}$-8), 7.27 (d, J = 8.2 Hz, 2H; H$_{Ar}$-9), 4.81 – 4.74 (m, 2H; H-2), 3.81 (d, J = 6.9 Hz, 4H; H-1), 2.41 (s, 3H; H-11), 1.64 (d, J = 2.8 Hz, 12H; H-5 and H-6). ^{13}C NMR (126 MHz, CDCl$_3$, 25 °C) δ = 203.6 (2 x C$_q$; C-3), 143.1 (C$_q$; C-10), 138.2 (C$_q$; C-7), 129.8 (2 x CH$_{Ar}$; C-9), 127.3 (2 x CH$_{Ar}$; C-8), 96.6 (2 x C$_q$; C-4), 84.4 (2 x CH; C-2), 46.1 (2 x CH$_2$; C-1), 21.6 (CH$_3$; C-

11), 20.5 (4 x CH_3; C-5 and C-6). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3098 (C-H_{Ar}), 3065 (C-H_{Ar}), 2986 (C-H_{Alkane}), 2924 (C-H_{Alkane}), 2856 (C-H_{Alkane}), 1975 (C=C=C), 1736, 1603 (C=C_{Ar}), 1446 (C-H_{Alkane}), 1346 (S=O), 1162 (S=O), 1100 (C-N), 984, 902, 817. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{19}H_{25}NO_2SNa$ $[M+Na]^+$: 354.1498. Found: 354.1500. M.P. = 45 – 46 °C.

Synthesis of *N*-(buta-2,3-dienyl)-4-methylphenylsulfonamide (276)[255]



To a suspension of *p*-toluensulfonamide **272** (4.0 g, 23.36 mmol, 1.0 Eq., 0.41 M – absolute concentration) in dry THF (37.0 mL) was added dropwise NEt_3 (3.9 mL, 28.04 mmol, 1.2 Eq.) and *N*,*N*-dimethylaminopyridine (DMAP) (57 mg, 0.47 mmol, 0.02 Eq.) under N_2. Then, di-tert-butyl dicarbonate (5.1 g, 23.36 mmol, 1.0 Eq.) dissolved in dry THF (20.0 mL) was added dropwise. The white suspension was stirred at room temperature during 17 h. The mixture was then quenched with a solution of HCl (20 mL, 0.2 M) at 0 °C (ice bath), and the product was extracted with EtOAc (x 3), washed with H_2O, brine (x 2), dried over $MgSO_4$ anhydrous and concentrated under vacuum. *N*-[(4-methylphenyl)sulfonyl]-,1,1-dimethylethyl ester carbamic acid **273**[256] was obtained without further purification (6.0 g, 22.09 mmol, 95%): white solid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.90 (d, J = 8.2 Hz, 2H; H_{Ar}-5), 7.34 (d, J = 8.2 Hz, 2H; H_{Ar}-6), 7.10 (bs, 1H; NH), 2.45 (s, 3H; H-8), 1.39 (s, 9H; H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 149.1 (C_q; C-1), 144.9 (C_q; C-7), 136.0 (C_q; C-4), 129.7 (2 x CH_{Ar}; C-6), 128.4 (2 x CH_{Ar}; C-5), 84.2 (C_q; C-2), 28.0 (3 x CH_3; C-3), 21.8 (CH_3; C-8).

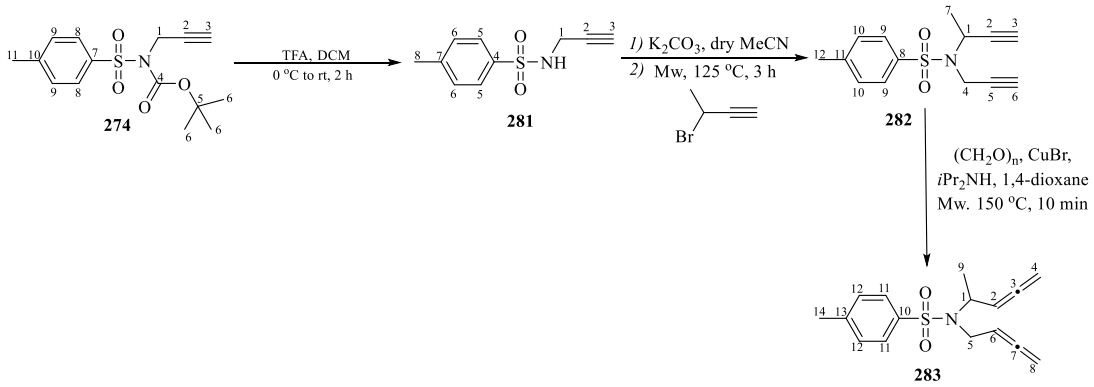
To a suspension of K_2CO_3 (4.3 g, 31.33 mmol, 2.5 Eq.) in dry MeCN (40.0 mL) was added **273**, (3.4 g, 12.53 mmol, 1.0 Eq., 0.19 M – absolute concentration) dissolved in dry MeCN (27.0 mL) under N_2. The solution was stirred at room temperature for 3 min and then propargyl bromide (80% in toluene, 1.8 mL, 16.29 mmol, 1.3 Eq.) was added dropwise. The reaction mixture was refluxed at 95 °C during 20 h. The solution was quenched with H_2O at 0 °C (ice bath), extracted with Et_2O (x 3), washed with brine, dried over $MgSO_4$ anhydrous and concentrated under vacuum. *N*-[(4-methylphenyl)sulfonyl]-*N*-2-propyn-1-yl-,1,1-dimethylethyl ester carbamic acid **274**[257] was obtained without further purification (3.0 g,

9.74 mmol, 78%): brown solid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.93 – 7.88 (m, 2H; H_{Ar}-8), 7.31 (d, *J* = 8.2 Hz, 2H; H_{Ar}-9), 4.63 (d, *J* = 2.4 Hz, 2H; H-1), 2.44 (s, 3H; H-11), 2.32 (t, *J* = 2.4 Hz, 1H; H-3), 1.35 (s, 9H; H-6). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 150.3 (C_q; C-4), 144.6 (C_q; C-10), 136.7 (C_q; C-7), 129.4 (2 x CH_{Ar}; C-9), 128.4 (2 x CH_{Ar}; C-8), 85.1 (C_q; C-2), 79.0 (C_q; C-5), 72.2 (CH; C-3), 35.8 (CH_2; C-1), 28.0 (3 x CH_3; C-6), 21.8 (CH_3; C-11). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3285 (C≡CH), 3094 (C-H_{Ar}), 2983 (C-H_{Alkane}), 2936 (C-H_{Alkane}), 2132 (C≡C), 1732 (C=O), 1598 (C=C_{Ar}), 1360 (S=O), 1312 (*t*-Bu), 1280 (C-O), 1156 (S=O), 1071 (C-N), 913, 847. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{15}H_{19}NO_4SNa$ $[M+Na]^+$: 332.0927. Found: 332.0924. M.P. = 70 – 72 °C.

CuBr (335 mg, 2.34 mmol, 0.3 Eq.) and paraformaldehyde (585 mg, 19.47 mmol, 2.5 Eq.) were added into a oven-dried microwave vial under N_2. Then the compound **274** (2.4 g, 7.79 mmol, 1.0 Eq., 0.5 M) dissolved in 15.6 mL of dry 1,4-dioxane and dry *i*Pr_2NH (2.2 mL, 15.58 mmol, 2.0 Eq.) were added sequentially dropwise under inert atmosphere. The reaction mixture was heated at 150 °C under microwave irradiation during 15 min. The product **275**[255] was purified by column chromatography over silica gel using PET / EtOAc (7:1) as eluent. 1.6 g, 5.09 mmol was obtained as a yellow oil (65%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.84 – 7.80 (m, 2H; H_{Ar}-9), 7.33 – 7.28 (m, 2H; H_{Ar}-10), 5.29 (p, *J* = 6.4 Hz, 1H; H-2), 4.79 (dt, *J* = 6.4, 2.7 Hz, 2H; H-4), 4.46 (dt, *J* = 6.4, 2.7 Hz, 2H; H-1), 2.44 (s, 3H; H-12), 1.36 (s, 9H; H-7).^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.2 (C_q; C-3), 150.8 (C_q; C-5), 144.3 (C_q; C-8 or C-11), 137.4 (C_q; C-8 or C-11), 129.3 (2 x CH_{Ar}; C-10), 128.3 (2 x CH_{Ar}; C-9), 87.5 (CH; C-2), 84.4 (CH_2; C-4), 67.2 (CH_2; C-1), 45.3 (C_q; C-6), 28.0 (CH_3; C-12), 21.8 (3 x CH_3; C-7).

The deprotection step was undertaken according to the procedure described by Gore and coworkers.[258] To a solution of **275** (1.6 g, 5.10 mmol, 1.0 Eq.) in MeOH (3.1 mL, 15.0 Eq.) was added dropwise trimethylsilyl chloride (TMSCl) (9.7 mL, 76.44 mmol, 15.0 Eq.) and stirred for 37 h at room temperature. Then, the reaction was quenched with $NaHCO_{3(aq)}$ (50 mL), extracted with DCM (x 3), washed with $NaHCO_{3(aq)}$, brine, dried over $MgSO_4$ anhydrous and concentrated under vacuum. The resulting crude was purified by column chromatography over silica gel using PET / EtOAc (4:1) as eluent. 970 mg, 4.35 mmol was obtained as a white solid **276** (86%).[37] ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.75 (d, *J* = 8.2 Hz, 2H; H_{Ar}-6), 7.31 (d, *J* = 8.2 Hz, 2H; H_{Ar}-7), 5.07 (p, *J* = 6.6 Hz, 1H; H-2), 4.77 (dt, *J* = 6.6, 3.3 Hz, 2H; H-4), 4.46 (bs, 1H; NH), 3.63 – 3.56 (m, 2H; H-1), 2.43 (s, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 208.1 (C_q; C-3), 143.7 (C_q; C-8), 137.2 (C_q; C-5), 129.9 (2 x CH_{Ar}; C-7), 127.3 (2 x CH_{Ar}; C-6), 87.3 (CH; C-2), 78.3 (CH_2; C-4), 41.5 (CH_2; C-1), 21.7 (CH_3; C-9).

Synthesis of *N*-buta-2,3-dienyl-4-methyl-*N*-(1-methyl-buta-2,3-dienyl)-benzenesulfonamide (283)[222, 259]



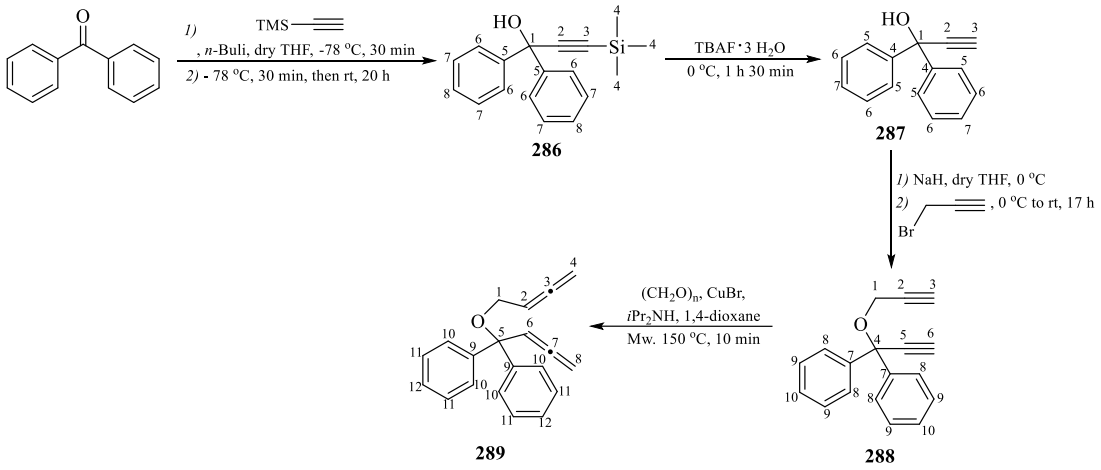
CF_3COOH (2.1 mL, 27.80 mmol, 4.3 Eq.) was added dropwise to a solution of **274** (2.0 g, 6.46 mmol, 1.0 Eq., 0.65 M) in 10.0 mL of DCM at 0 °C (ice bath). The resulting solution was warmed up to room temperature and stirred during 2 h. The reaction was quenched with $NaHCO_{3(aq)}$, extracted with EtOAc (x 3), washed with $NaHCO_{3(aq)}$ (20 mL), brine (20 mL), dried over $MgSO_4$ anhydrous, and concentrated under vacuum. The crude was purified by column chromatography over silica gel using Hex / EtOAc (6:1) as eluent. 4-methyl-*N*-2-propyn-1-yl-benzenesulfonamide **281**[257] was obtained as a white solid (1.2 g, 5.62 mmol, 87%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.80 – 7.75 (m, 2H; H_{Ar}-5), 7.34 – 7.29 (m, 2H; H_{Ar}-6), 4.51 (bt, *J* = 5.3 Hz, 1H; NH), 3.84 (dd, *J* = 6.1, 2.5 Hz, 2H; H-1), 2.44 (s, 3H; H-8), 2.11 (t, *J* = 2.5 Hz, 1H; H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 144.0 (C_q; C-7), 136.7 (C_q; C-4), 129.9 (2 x CH_{Ar}; C-6), 127.6 (2 x CH_{Ar}; C-5), 78.1 (C_q; C-2), 73.2 (CH; C-3), 33.1 (CH_2; C-1), 21.7 (CH_3; C-8).

K_2CO_3 (668 mg, 4.83 mmol, 2.5 Eq.) and **281** (404 mg, 1.93 mmol, 1.0 Eq., 0.23 M) were added into a vacuum-dried microwave vial under N_2. Then, 8.4 mL of dry MeCN were added and the suspension was stirred at room temperature for 3 min. 3-Bromo-1-butyne (279 µl, 2.90 mmol, 1.5 Eq.) was added dropwise under N_2. The vial was sealed under N_2 and the reaction mixture was heated under microwave irradiation at 125 °C during 3 h. The crude was quenched with H_2O at 0 °C (ice bath), extracted with Et_2O (x 3), washed with brine, dried over $MgSO_4$ anhydrous and concentrate under vacuum. The product **282**[260] was obtained without further purification as a brown solid (504 mg, 1.93 mmol, 100%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.79 – 7.74 (m, 2H; H_{Ar}-9), 7.29 (d, *J* = 8.2 Hz, 2H; H_{Ar}-10), 4.89 (qd, *J* = 7.1, 2.3 Hz, 1H; H-1), 4.21 (dd, *J* = 18.4, 2.3 Hz, 1H; H-4), 4.01 (dd, *J* = 18.4, 2.5 Hz, 1H; H-4), 2.42 (s, 3H; H-12), 2.22 (d, *J* = 2.3 Hz, 1H; H-3), 2.21 (t, *J* = 2.3 Hz, 1H; H-6), 1.54 (d, *J* = 7.1 Hz, 3H; H-7). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 143.8 (C_q; C-11), 136.5 (C_q; C-8), 129.7 (2 x CH_{Ar}; C-10), 127.8 (2 x CH_{Ar}; C-9), 81.0 (C_q; C-2 or C-5), 80.0 (C_q; C-2 or C-5), 73.9 (CH;

C-3), 72.6 (CH; C-6), 46.3 (CH; C-1), 33.6 (CH_2; C-4), 22.1 (CH_3; C-7), 21.7 (CH_3; C-12). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3286 (C≡CH), 3069 (C-H_{Ar}), 3039 (C-H_{Ar}), 2987 (C-H_{Alkane}), 2932 (C-H_{Alkane}), 2864 (C-H_{Alkane}), 2125 (C≡C), 1600 (C=C_{Ar}), 1339 (S=O), 1157 (S=O), 1106 (C-N), 1037, 896. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{14}H_{16}NO_2S$ $[M]^+$: 262.0896. Found: 262.0892.

CuBr (166 mg, 1.16 mmol, 0.6 Eq.) and paraformaldehyde (290 mg, 9.65 mmol, 5.0 Eq.) were added into a oven-dried microwave vial under N_2. Then **282** (504 mg, 1.93 mmol, 1.0 Eq., 0.5 M) dissolved in 3.9 mL of dry 1,4-dioxane and dry *i*Pr_2NH (1.1 mL, 7.72 mmol, 4.0 Eq.) were added dropwise under inert atmosphere. The reaction mixture was heated at 150 °C under microwave irradiation during 10 min. The crude of the reaction was purified by column chromatography over silica gel using PET / EtOAc (20:1) then (7:1) as eluent. 309 mg, 1.07 mmol was obtained as an orange oil **283** (55%).[222, 259] ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.74 – 7.70 (m, 2H; H_{Ar}-11), 7.28 (d, *J* = 8.2 Hz, 2H; H_{Ar}-12), 5.23 – 5.15 (m, 1H; H-6), 4.98 – 4.93 (m, 1H; H-2), 4.79 – 4.74 (m, 2H; H-4), 4.74 – 4.70 (m, 2H; H-8), 4.66 – 4.58 (m, 1H; H-1), 3.88 (ddt, *J* = 15.8, 6.0, 2.8 Hz, 1H; H-5), 3.74 (ddt, *J* = 15.8, 7.3, 2.4 Hz, 1H; H-5), 2.42 (s, 3H; H-14), 1.22 (d, *J* = 6.9 Hz, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 208.8 (C_q; C-3 or C-7), 208.7 (C_q; C-3 or C-7), 143.3 (C_q; C-13), 138.3 (C_q; C-10), 129.7 (2 x CH_{Ar}; C-12), 127.3 (2 x CH_{Ar}; C-11), 91.9 (CH; C-2), 89.5 (CH; C-6), 77.8 (CH_2; C-4), 76.3 (CH_2; C-8), 51.8 (CH; C-1), 42.8 (CH_2; C-5), 21.6 (CH_3; C-14), 18.8 (CH_3; C-9).

Synthesis of (1-buta-2,3-dienyloxy-buta-2,3-dienyl)-dibenzene (289)



To a solution of ethynyltrimethylsilane (980 µl, 6.79 mmol, 1.5 Eq.) in dry THF (10.0 mL) at -78 °C (dry ice / acetone) was added *n*-Buli (2.5 M in hexane, 2.7 mL, 6.78 mmol, 1.5 Eq.), and the mixture was stirred during 30 min at this temperature. Then, benzophenone (824 mg, 4.52 mmol, 1.0 Eq., 0.23 M – absolute concentration) dissolved in dry THF (10.0 mL) was added dropwise to the flask under N_2 and stirred at - 78 °C for 30 min. The solution was

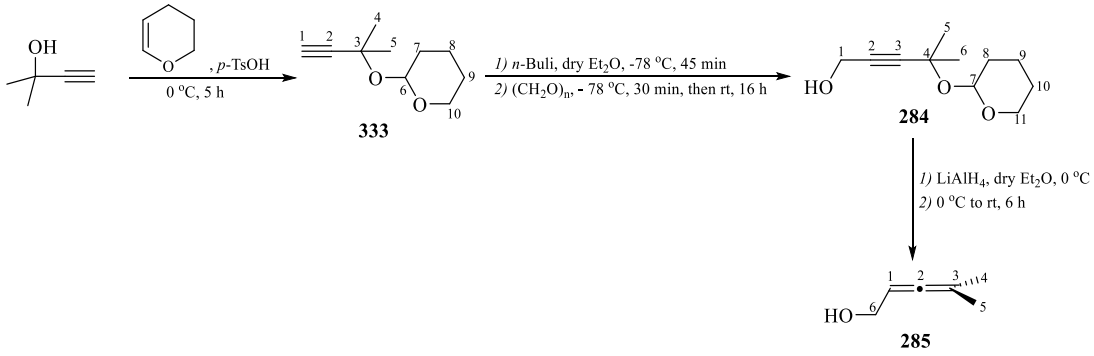
warmed up at room temperature and stirred for 20 h. The reaction was quenched with H_2O, extracted with Et_2O (x 3), washed with brine, dried with $MgSO_4$ anhydrous and concentrated under vacuum. The product **286**[261] was obtained without further purification as a yellow oil (1.0 g, 3.61 mmol, 80%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.63 – 7.59 (m, 4H; H_{Ar}-6), 7.35 – 7.30 (m, 4H; H_{Ar}-7), 7.29 – 7.23 (m, 2H; H_{Ar}-8), 2.84 (bs, 1H; OH), 0.23 (s, 9H; H-4). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 144.9 (2 x C_q; C-5), 128.4 (4 x CH_{Ar}; C-6 or C-7), 127.8 (2 x CH_{Ar}; C-8), 126.1 (4 x CH_{Ar}; C-6 or C-7), 107.8 (C_q; C-2), 92.1 (C_q; C-1), 74.8 (C_q; C-3), 0.00 (3 x CH_3; C-4).

To a solution of **286** (1.0 g, 4.63 mmol, 1.0 Eq., 0.33 M – absolute concentration) in THF (7.0 mL) at 0 °C (ice bath) was added dropwise a solution TBAF · $3H_2O$ in THF (7.0 mL). The mixture was stirred at 0 °C (ice bath) during 1 h 30 min. The crude was concentrated under vacuum and the product was purified by column chromatography over silica gel using Hex / EtOAc, (6:1) then (2:1): **287**[262] 962 mg, 4.62 mmol (100%): orange solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 7.64 – 7.59 (m, 4H; H_{Ar}-5), 7.38 – 7.32 (m, 4H; H_{Ar}-6), 7.31 – 7.26 (m, 2H; H_{Ar}-7), 2.89 (s, 1H; H-3), 2.78 (s, 1H; OH). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C) δ = 144.5 (2 x C_q; C-4), 128.5 (4 x CH_{Ar}; C-6), 128.0 (2 x CH_{Ar}; C-7), 126.1 (4 x CH_{Ar}; C-5), 86.5 (C_q; C-2), 75.7 (CH; C-3), 74.5 (C_q; C-1).

To a suspension of NaH (60% mineral oil, 164 mg, 4.11 mmol, 1.4 Eq.) in dry THF (8.0 mL) at 0 °C (ice bath) was added **287** (611 mg, 2.93 mmol, 1.0 Eq., 0.21 M – absolute concentration) dissolved in dry THF (6.0 mL). After 10 min, propargyl bromide (80% in toluene, 490 µl, 4.40 mmol 1.5 Eq.) was added and the resulting solution was stirred at room temperature during 17 h. The mixture was quenched with $NH_4Cl_{(aq)}$ (10 mL) at 0 °C (ice bath), extracted with Et_2O (x 3), washed with brine, dried over $MgSO_4$ anhydrous and concentrated under vacuum. The product **288** was purified by column chromatography over silica gel using Hex / EtOAc, (90:1) then (15:1), (300 mg, 1.22 mmol, 42%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.58 – 7.55 (m, 4H; H_{Ar}-8), 7.35 – 7.30 (m, 4H; H_{Ar}-9), 7.29 – 7.25 (m, 2H; H_{Ar}-10), 4.19 (d, J = 2.5 Hz, 2H; H-1), 2.94 (s, 1H; H-6), 2.42 (t, J = 2.5 Hz, 1H; H-3). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 142.3 (2 x C_q; C-7), 128.4 (4 x CH_{Ar}; C-9), 128.2 (2 x CH_{Ar}; C-10), 126.8 (4 x CH_{Ar}; C-8), 82.5 (C_q; C-2 or C-5), 80.2 (C_q; C-2 or C-5), 78.6 (C_q, C-3 or C-6), 74.0 (C_q, C-3 or C-6), 53.5 (CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3290 (C≡CH), 3068 (C-H_{Ar}), 3033 (C-H_{Ar}), 2963 (C-H_{Alkane}), 2914 (C-H_{Alkane}), 2866 (C-H_{Alkane}), 2118 (C≡C), 1489, 1261 (C-O), 1027 (C-O), 867. HRMS (FTMS + p APCI (OIL + NH_4OAc)): Calc. for $C_{18}H_{14}O$ $[M]^+$: 246.1039. Found: 246.1035. Calc. for $C_{18}H_{13}O$ $[M-H]^+$: 245.0961. Found: 245.0957. Calc. for $C_{18}H_{15}O$ $[M+H]^+$: 247.1117. Found: 247.1114.

CuBr (105 mg, 0.73 mmol, 0.6 Eq.) and paraformaldehyde (230 mg, 6.09 mmol, 5.0 Eq.) were added into a oven-dried microwave vial under N_2. Then compound **288** (300 mg, 1.22 mmol, 1.0 Eq., 0.5 M) dissolved in 2.5 mL of dry 1,4-dioxane and dry *i*Pr_2NH (683 µl, 4.87 mmol, 4.0 Eq.) were added sequentially dropwise under inert atmosphere. The reaction mixture was heated at 150 ºC under microwave irradiation during 10 min. The crude of the reaction was purified by column chromatography over silica gel using Hex / EtOAc (20:1) as eluent. (1-Prop-2-ynyloxy-prop-2-ynyl)-bis(benzene) **289**,[255] was obtained as a yellow oil (114 mg, 0.41 mmol, 34%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.45 – 7.41 (m, 4H; H_{Ar}-10), 7.32 – 7.28 (m, 4H; H_{Ar}-11), 7.25 – 7.20 (m, 2H; H_{Ar}-12), 5.83 (t, *J* = 6.7 Hz, 1H; H-6), 5.32 (p, *J* = 6.6 Hz, 1H; H-2), 4.79 (d, *J* = 6.7 Hz, 2H; H-8), 4.79 (dt, *J* = 6.6, 2.8 Hz, 2H; H-4), 3.94 (dt, *J* = 6.6, 2.8 Hz, 2H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 209.0 (C_q; C-3 or C-7), 208.8 (C_q; C-3 or C-7), 144.5 (2 x C_q; C-9), 128.0 (4 x CH_{Ar}; C-11), 127.5 (4 x CH_{Ar}; C-10), 127.3 (2 x CH_{Ar}; C-12), 95.3 (CH; C-6), 88.9 (CH; C-2), 83.6 (C_q; C-5), 78.2 (CH_2; C-8), 76.0 (CH_2; C-4), 62.3 (CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3060 (C-H_{Ar}), 3032 (C-H_{Ar}), 2926 (C-H_{Alkane}), 2861 (C-H_{Alkane}), 1959 (C=C=C), 1661 (C=C_{Ar}), 1450 (C-H_{Alkane}), 1053, 1032 (C-O), 851. HRMS (FTMS + p APCI (OIL + NH_4OAc)): Calc. for $C_{20}H_{19}O$ $[M+H]^+$: 275.1430. Found: 275.1426.

Synthesis of 4-methyl-penta-2,3-dien-1-ol (285)[263]



This synthesis was undertaken according to the procedure described by Poli and co-workers.[263c] *p*-Toluenesulfonic acid monohydrate (*p*-TsOH) (571 mg, 3.0 mmol, 0.01 Eq.) and 300 mL of dry DCM were added to a 500 mL round bottom flask under inert atmosphere. The temperature was cooled down at 0 ºC (ice bath) and 2-methyl-3-butyn-2-ol (29.0 mL, 300 mmol, 1.0 Eq., 1.0 M) was added. The mixture was stirred at 0 ºC during 5 min. Then 3,4-dihydro-2*H*-pyran (30.0 mL, 330 mmol, 1.1 Eq.) was added neat dropwise at 0 ºC. The reaction mixture was stirred at the same temperature during 5 h. The solution was quenched with a saturated solution of $NaHCO_{3(aq)}$ at 0 ºC, extracted with DCM (x 3), washed with brine, dried over $MgSO_4$ anhydrous and concentrated under vacuum. The crude was purified by column chromatography over silica gel using Hex / Et_2O (90:1) then (20:1) as eluent. Compound

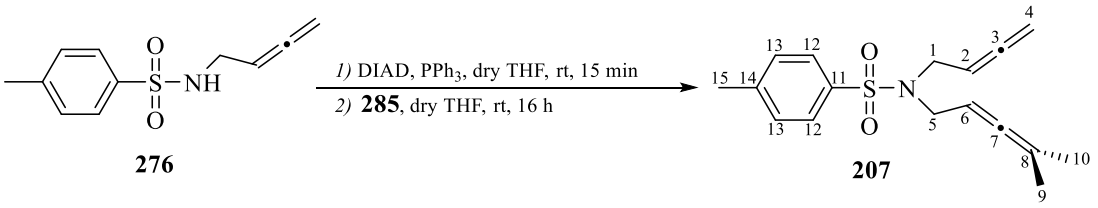
333[263c] was obtained as a colourless oil (28.9 g, 145.7 mmol, 49%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 5.06 (dd, *J* = 5.0, 3.4 Hz, 1H; H-6), 4.00 – 3.90 (m, 1H; H-10), 3.56 – 3.45 (m, 1H; H-10), 2.43 (s, 1H; H-1), 1.90 – 1.78 (m, 1H; H-9), 1.77 – 1.66 (m, 1H; H-7), 1.60 – 1.51 (m, 4H; 1 x H-7, 2 x H-8 and 1 x H-9), 1.54 (s, 3H; H-4 or H-5), 1.50 (s, 3H; H-4 or H-5). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 96.3 (CH; C-6), 86.5 (C_q; C-2), 72.0 (CH; C-1), 71.0 (C_q; C-3), 63.5 (CH_2; C-10), 32.0 (CH_2; C-7), 30.7 (CH_3; C-4 or C-5), 29.9 (CH_3; C-4 or C-5), 25.5 (CH_2; C-8), 20.6 (CH_2; C-9).

Compound **333** (6.0 g, 35.66 mmol, 1.0 Eq., 1.1 M) was added dissolved in 33.0 mL of dry Et_2O into a flame-dried Schlenk flask under N_2. The solution was stirred during 5 min at - 78 ºC (dry ice / acetone). Then *n*-Buli (16.0 mL, 39.23 mmol, 1.1 Eq.) was added cautiously, maintaining the temperature under - 60 ºC during the addition. The reaction mixture was stirred at - 78 ºC during 45 min. Then, paraformaldehyde (3.21 g, 106.99 mmol, 3.0 Eq.) was added in small portions under N_2. After 15 min the solution was warmed up at room temperature and stirred until complete conversion, following the reaction by TLC. The reaction was quenched with H_2O at 0 ºC, extracted with Et_2O (x 3), washed with brine, dried over $MgSO_4$ anhydrous and concentrated under vacuum. The product was purified by column chromatography over silica gel using Hex / Et_2O (4:1) then (2:1) as eluent. Compound **284**[263c, 264] was obtained as a colourless oil (7.0 g, 35.31 mmol, 99%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 5.05 (dd, *J* = 4.9, 3.3 Hz, 1H; H-7), 4.28 (s, 2H; H-1), 3.98 – 3.89 (m, 1H; H-11), 3.55 – 3.44 (m, 1H; H-11), 2.34 (bs, 1H; OH), 1.89 – 1.75 (m, 1H; H-10), 1.75 – 1.64 (m, 1H; H-8), 1.57 – 1.49 (m, 4H; 1 x H-8, 2 x H-9 and 1 x H-10), 1.52 (s, 3H; H-5 or H-6), 1.47 (s, 3H; H-5 or H-6). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 95.9 (CH; C-7), 88.0 (C_q; C-3), 82.5 (C_q; C-2), 71.0 (C_q; C-4), 63.2 (CH_2; C-11), 51.1 (CH_2; C-1), 32.0 (CH_2; C-8), 30.6 (CH_3; C-5 or C-6), 30.0 (CH_3; C-5 or C-6), 25.5 (CH_2; C-9), 20.3 (CH_2; C-10).

Compound **284** (7.8 g, 39.40 mmol, 1.0 Eq., 0.21 M) dissolved in dry Et_2O (67.0 mL) was added dropwise under N_2 to a flame-dried round bottom flask with a suspension of $LiAlH_4$ (4.5 g, 118.20 mmol, 3.0 Eq.) in dry Et_2O (120.0 mL) at 0 °C (ice bath). Then the solution was warmed up at room temperature and stirred during 6 h, followed by TLC. The excess of $LiAlH_4$ was quenched at 0 °C adding H_2O (4.0 mL), an aqueous NaOH solution (4.0 mL, 15 % w/w), and then H_2O (8.0 mL). The white suspension was filtered on celite, and washed with Et_2O (100 mL). The organic layer was dried over $MgSO_4$ anhydrous and concentrated under vacuum. The product was purified by column chromatography over silica gel using Hex / Et_2O (10:1) then (4:1) as eluent. The compound **285** was obtained as a yellow-pale oil (2.4 g, 24.92 mmol, 63%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 5.23 – 5.15 (m, 1H; H-1), 4.07 (d, *J* = 5.6 Hz, 2H; H-6), 1.72 (d, *J* = 2.6 Hz, 6H; H-4 and H-5), 1.42 (bs, 1H; OH). ^{13}C NMR (126 MHz,

$CDCl_3$, 25 °C) δ = 200.6 (C_q; C-2), 90.0 (CH; C-1), 61.1 (CH_2; C-6), 20.7 (2 x CH_3; C-4 and C-5).

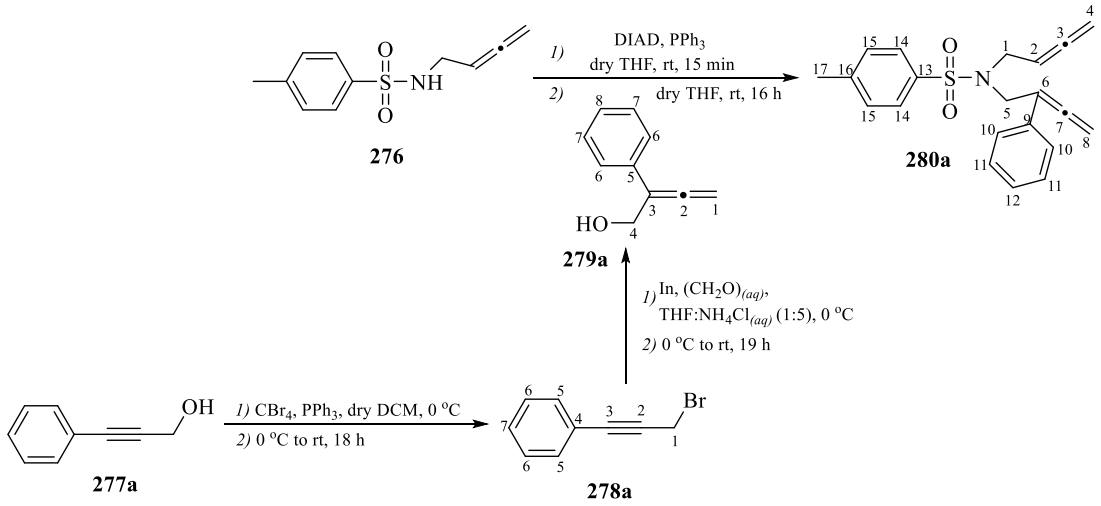
Synthesis of *N*-(buta-2,3-dienyl)-*N*-(4-methylpenta-2,3-dienyl) 4-tolylsulfonamide (207)[265]



276 **207**

The synthesis was undertaken according to the procedure described by Chung and co-workers.[222] To a flame-dried Schlenk flask were added sequentially 5.0 mL of dry THF, diisopropyl azadicarboxilate (DIAD) (208 µl, 1.05 mmol, 1.1 Eq.) and triphenylphosphine (PPh_3) (277 mg, 1.05 mmol, 1.1 Eq.) under N_2 flow. The yellow suspension was stirred 15 min at room temperature. Then compound **276** (214 mg, 0.96 mmol, 1.0 Eq., 0.1 M – absolute concentration) and allenol **285** (94 mg, 0.96 mmol, 1.0 Eq.) were added dissolved in dry THF (5.0 mL) under N_2 flow. The reaction was stirred at room temperature until complete conversion, followed by TLC. The solution was concentrated under vacuum and purified by column chromatography over silica gel using Hex / Et_2O (90:1) as eluent. The compound **207** was obtained as a white solid (262 mg, 0.86 mmol, 90%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.72 – 7.68 (m, 2H; H_{Ar}-12), 7.28 (d, *J* = 8.2 Hz, 2H; H_{Ar}-13), 4.94 (p, *J* = 6.8 Hz, 1H; H-2), 4.80 – 4.73 (m, 1H; H-6), 4.70 (dt, *J* = 6.8, 2.4 Hz, 2H; H-4), 3.90 (dt, *J* = 6.8, 2.4 Hz, 2H; H-1), 3.82 (d, *J* = 6.9 Hz, 2H; H-5), 2.42 (s, 3H; H-15), 1.64 (d, *J* = 2.8 Hz, 6H; H-9 and H-10). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.6 (C_q; C-3 or C-7), 203.6 (C_q; C-3 or C-7), 143.3 (C_q; C-14), 137.9 (C_q; C-11), 129.8 (2 x CH_{Ar}; C-13), 127.3 (2 x CH_{Ar}; C-12), 96.9 (C_q; C-8), 86.0 (CH; C-2), 84.3 (CH; C-6), 76.2 (CH_2; C-4), 46.6 (CH_2; C-5), 45.3 (CH_2; C-1), 21.6 (CH_3; C-15), 20.5 (2 x CH_3; C-9 and C-10).

Synthesis of *N*-(buta-2,3-dienyl)-4-methyl-*N*-(2-phenylbuta-2,3 dienyl)benzenesulfonamide (280a)[222]



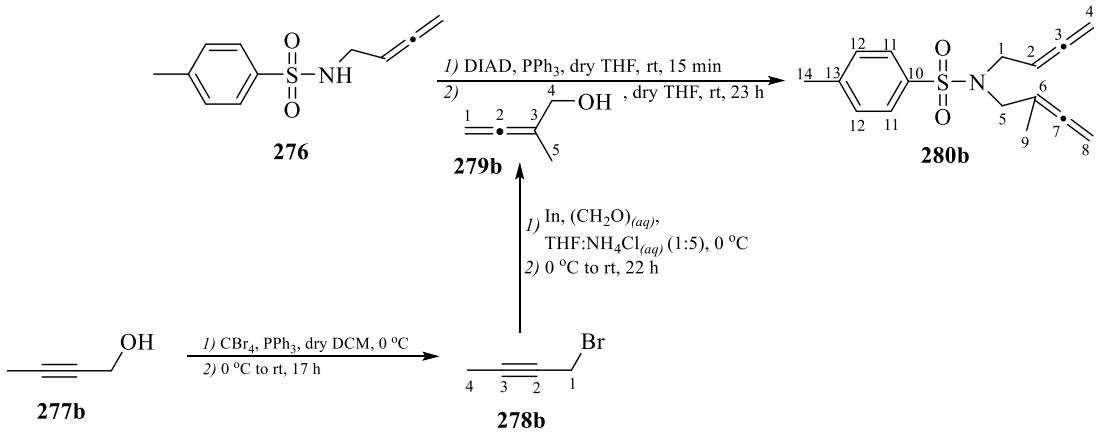
To a solution of **277a** (1.5 mL, 11.98 mmol, 1.0 Eq., 0.1 M) in 120.0 mL of dry DCM at 0 °C (ice bath), were added tetrabromomethane (CBr_4) (4.8 g, 14.37 mmol, 1.2 Eq.) and triphenylphospine (PPh_3) (3.8 g, 14.37 mmol, 1.2 Eq.) in small portions under N_2 flow. The solution was warmed up at room temperature and stirred during 18 h. The solvent was evaporated under vacuum and the crude was purified by column chromatography over silica gel using PET / Et_2O (6:1) as eluent. Compound **278a**[266] was obtained as a yellow oil (2.3 g, 11.98 mmol, 100%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.40 – 7.35 (m, 2H; H_{Ar}-5), 7.29 – 7.22 (m, 3H; H_{Ar}-6 and H_{Ar}-7), 4.10 (s, 2H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 132.0 (2 x CH_{Ar}; C-5), 129.0 (CH_{Ar}; C-7), 128.5 (2 x CH_{Ar}; C-6), 122.3 (C_q; C-4), 86.9 (C_q; C-2), 84.4 (C_q; C-3), 15.4 (CH_2; C-1).

This synthesis was undertaken according to the procedure described by Alcaide and co-workers.[55] To an aqueus solution of paraformaldehyde (37% w/w H_2O, 492 µl, 6.40 mmol, 1.0 Eq.) in a mixture THF:$NH_4Cl_{(aq)}$ (1:5), (20 mL) at 0 ° C (ice bath) was added indium powder (4.4 g, 38.40 mmol, 6.0 Eq.) in small portions. This mixture was stirred vigorously during 3 min. Then **278a** (3.7 g, 19.20 mmol, 3.0 Eq.) dissolved in 23.0 mL of the mixture (THF: $NH_4Cl_{(aq)}$) was added dropwise at 0 °C. The reaction was warmed up at room temperature and stirred during 19 h. Then, 15 mL of H_2O was added and the white solution was extracted with Et_2O (x 4), washed with brine, dried over $MgSO_4$ anhydrous and concentrated under vacuum. The crude was purified by column chromatography over silica gel using PET / Et_2O (4:1) as eluent. The compound **279a**[267] was obtained as a yellow oil (238 mg, 1.63 mmol, 25%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.43 (d, J = 7.8 Hz, 2H; H_{Ar}-6), 7.35 (t, J = 7.8 Hz, 2H; H_{Ar}-7), 7.27 – 7.21 (m, 1H; H_{Ar}-8), 5.26 (t, J = 2.7 Hz, 2H; H-1), 4.58 (t, J = 2.7 Hz, 2H; H-4). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 207.7 (C_q; C-2), 133.9 (C_q; C-5), 128.8 (2 x CH_{Ar};

C-7), 127.4 (CH_{Ar}; C-8), 126.3 (2 x CH_{Ar}; C-6), 106.1 (C_q; C-3), 80.5 (CH_2; C-1), 61.7 (CH_2; C-4).

To a flame-dried Schlenk flask were added sequentially 3.0 mL of dry THF, diisopropyl azadicarboxilate (DIAD) (354 µl, 1.80 mmol, 1.1 Eq.) and triphenylphosphine (PPh_3) (471 mg, 1.80 mmol, 1.1 Eq.) under N_2 flow. The yellow suspension was stirred 15 min. Then, **276** (364 mg, 1.63 mmol, 1.0 Eq., 0.2 M) and **279a** (239 mg, 1.63 mmol, 1.0 Eq.) were added dissolved in dry THF (5.5 mL) under N_2 flow. The reaction was stirred at room temperature until complete conversion, followed by TLC. The crude of reaction was concentrated under vacuum and purified by column chromatography over silica gel using PET / EtOAc (7:1) as eluent. Compound **280a**[44a] was obtained as a yellow oil (136 mg, 0.39 mmol, 24%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.70 (d, J = 8.2 Hz, 2H; H_{Ar}-14), 7.48 – 7.44 (m, 2H; H_{Ar}), 7.34 – 7.30 (m, 2H; H_{Ar}), 7.29 (d, J = 7.9 Hz, 2H; H_{Ar}), 7.25 – 7.21 (m, 1H; H_{Ar}-12), 5.05 (t, J = 2.5 Hz, 2H; H-8), 4.85 (p, J = 6.7 Hz, 1H; H-2), 4.63 (dt, J = 6.7, 2.5 Hz, 2H; H-4), 4.33 (t, J = 2.5 Hz, 2H; H-5), 3.86 (dt, J = 6.7, 2.5 Hz, 2H; H-1), 2.43 (s, 3H; H-17). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 210.0 (C_q; C-3 or C-7), 209.6 (C_q; C-3 or C-7), 143.5 (C_{qAr}), 137.3 (C_{qAr}), 133.8 (C_{qAr}), 129.8 (2 x CH_{Ar}), 128.7 (2 x CH_{Ar}), 127.6 (2 x CH_{Ar}), 127.4 (CH_{Ar}; H-12), 126.6 (2 x CH_{Ar}), 100.8 (C_q; C-6), 85.3 (CH; C-2), 79.1 (CH_2; C-4 or C-8), 76.1 (CH_2; C-4 or C-8), 47.2 (CH_2; C-1 or C-5), 45.8 (CH_2; C-1 or C-5), 21.7 (CH_3; C-17).

Synthesis of *N*-2,3-butadien-1-yl-4-methyl-*N*-(2-methyl-2,3-butadien-1-yl)-benzenesulfonamide (280b)[212]



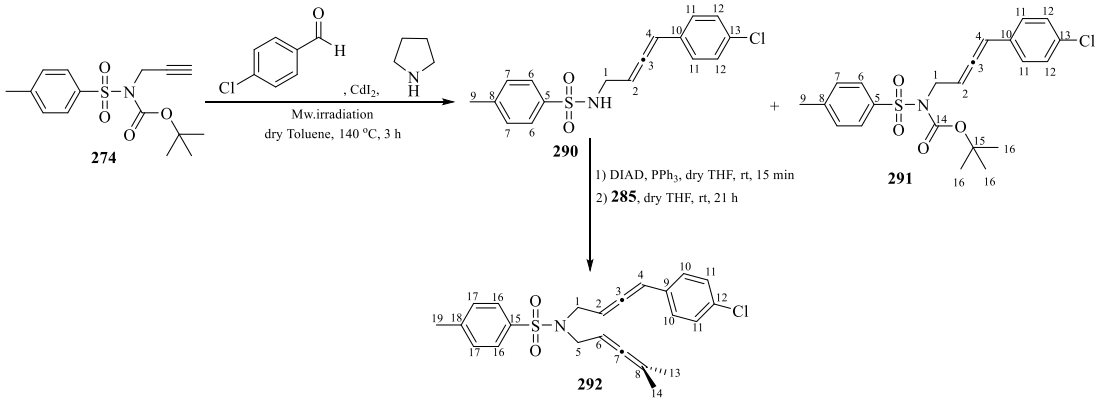
To a solution of **277b** (800 µl, 10.69 mmol, 1.0 Eq., 0.1 M) in 106.0 mL of dry DCM at 0 °C (ice bath), were added tetrabromomethane (CBr_4) (4.3 g, 12.83 mmol, 1.2 Eq.) and triphenylphospine (PPh_3) (3.4 g, 12.83 mmol, 1.2 Eq.) in small portions under N_2 flow. The solution was warmed up at room temperature and stirred 17 h. The solvent was evaporated under vacuum and the mixture was purified by column chromatography over silica gel using PET / Et_2O (20:1) as eluent. Compound **278b**[268] was obtained as a yellow liquid (1.3 g, 9.76

mmol, 91%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 3.84 (q, *J* = 2.5 Hz, 2H), 1.82 (t, *J* = 2.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C) δ = 83.9 (C_q; C-3), 74.5 (C_q; C-2), 15.8 (CH_2; C-1), 4.1 (CH_3; C-4).

This synthesis was performed according to the procedure described by Alcaide and co-workers.[55] To a solution of paraformaldehyde (37% w/w H_2O, 868 µl, 11.65 mmol, 1.0 Eq.) in a mixture THF:$NH_4Cl_{(aq)}$ (1:5), (20 mL) at 0 ° C (ice bath) was added indium powder (8.0 g, 69.93 mmol, 6.0 Eq.) in small portions. This mixture was stirred vigorously during 3 min and then **278b** (4.6 g, 34.96 mmol, 3.0 Eq.) dissolved 29.0 mL of the mixture THF:$NH_4Cl_{(aq)}$ (1:5) was added dropwise at 0 °C. The reaction was warmed up at room temperature and stirred during 22 h. 18 mL of H_2O was added and the white solution was extracted with Et_2O (x 4), washed with brine, dried with $MgSO_4$ anhydrous and concentrated under vacuum. The crude was purified by column chromatography over silica gel using Et_2O as eluent. Product **279b**[269] was obtained as a yellow liquid (321 mg, 3.82 mmol, 34%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 4.81 (sep *J* = 3.1 Hz, 2H; H-1), 4.03 (bt, *J* = 3.1 Hz, 2H; H-4), 1.72 (t, *J* = 3.1 Hz, 3H; H-5). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 204.8 (C_q; C-2), 99.7 (C_q; C-3), 77.3 (CH_2; C-1), 63.9 (CH_2; C-4), 15.3 (CH_3; C-5).

To a flame-dried Schlenk flask were added sequentially 2.0 mL of dry THF, diisopropyl azadicarboxilate (DIAD) (186 µl, 0.95 mmol, 1.1 Eq.) and triphenylphosphine (PPh_3) (248 mg, 0.95 mmol, 1.1 Eq.) under N_2 flow. The yellow suspension was stirred 15 min. Then, **276** (192 mg, 0.86 mmol, 1.0 Eq., 0.1 M – absolute concentration) and allenol **279b** (72 mg, 0.86 mmol, 1.0 Eq.) were added dissolved in 6.0 mL of dry THF under N_2 flow. The reaction was stirred at room temperature until complete conversion, followed by TLC. The crude of reaction was concentrated under vacuum and purified by column chromatography over silica gel using PET / Et_2O (10:1) as eluent. Product **280b** was obtained as a white solid (184 mg, 0.64 mmol, 74%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.72 – 7.67 (m, 2H; H_{Ar}-11), 7.29 (d, *J* = 8.2 Hz, 2H; H_{Ar}-12), 4.87 – 4.80 (m, 1H; H-2), 4.66 (dt, *J* = 6.6, 2.4 Hz, 2H; H-4), 4.63 – 4.58 (m, 2H; H-8), 3.87 (dt, *J* = 7.2, 2.4 Hz, 2H; H-1), 3.81 (t, *J* = 2.4 Hz, 2H; H-5), 2.42 (s, 3H; H-14), 1.67 (t, *J* = 3.1 Hz, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 209.8 (C_q; C-3 or C-7), 207.8 (C_q; C-3 or C-7), 143.3 (C_q; C-13), 137.8 (C_q; C-10), 129.8 (2 x CH_{Ar}; H-12), 127.3 (2 x CH_{Ar}; H-11), 94.1 (C_q; C-6), 85.2 (CH; C-2), 76.0 (CH_2; C-4), 75.2 (CH_2; C-8), 50.3 (CH_2; C-5), 45.8 (CH_2; C-1), 21.7 (CH_3; C-14), 16.0 (CH_3; C-9).

Synthesis of *N*-[4-(4-chloro-phenyl)-buta-2,3-dienyl]-4-methyl-*N*-(4-methyl-penta-2,3-dienyl)-benzenesulfonamide (292)

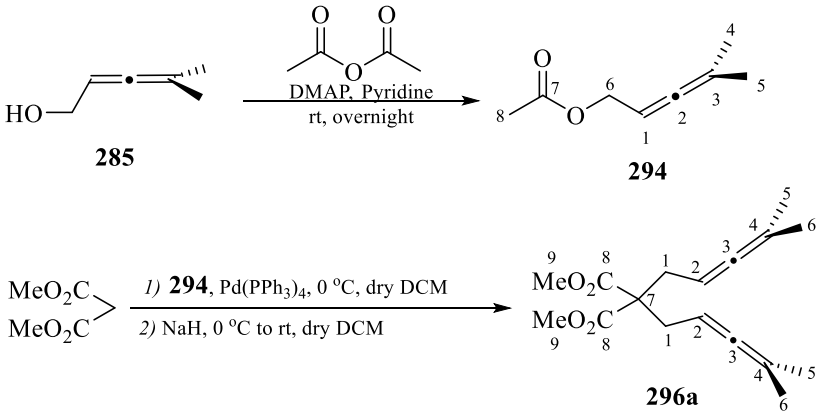


The first step was undertaken according to a modified procedure described by Ma and co-workers.[29] To a flame-dried microwave vial, CdI_2 (1.0 g, 2.74 mmol, 0.8 Eq.) was added inside a globe box. Then the vial was sealed and dried under vacuum with a flame until the white CdI_2 turned to yellow-green. Then allow to cool. Compound **274** (1.1 g, 3.42 mmol, 1.0 Eq., 0.3 M – absolute concentration) and 4-chlorobenzaldehyde (529 mg, 3.76 mmol, 1.1 Eq.) dissolved in 10.0 mL of dry toluene and pyrrolidine (314 µl, 3.76 mmol, 1.1 Eq.) were added sequentially under N_2 flow. The reaction mixture was heated by microwave irradiation at 140 °C during 3 h. After cooled down, the reaction mixture was filtered through a pad of celite / silica gel (1:1), washed with Et_2O (15 mL) and concentrated under vacuum. The crude of the reaction was purified by column chromatography over silica gel using Hex / EtOAc (20:1) then (15:1) then (4:1) as eluent. Product **290** (142 mg, 0.42 mmol, 12%, brown oil) and **291**, (21 mg, 0.05 mmol, 2%, brown oil) were obtained. **(290)** ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.74 (d, J = 8.2 Hz, 2H; H_{Ar}-6), 7.28 (d, J = 8.6 Hz, 2H; H_{Ar}-12), 7.25 (d, J = 8.2 Hz, 2H; H_{Ar}-7), 7.12 (d, J = 8.6 Hz, 2H; H_{Ar}-11), 6.18 (dt, J = 6.1, 3.1 Hz, 1H; H-4), 5.55 (q, J = 6.1 Hz, 1H; H-2), 4.53 (bt, J = 5.9 Hz, 1H; NH), 3.71 (m, 2H; H-1), 2.42 (s, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 204.8 (C_q; C-3), 143.8 (C_q; C-8), 137.0 (C_q; C-5), 133.3 (C_q; C-13), 131.9 (C_q; C-10), 129.9 (2 x CH_{Ar}; C-11), 129.0 (2 x CH_{Ar}; C-7), 128.2 (2 x CH_{Ar}; C-12), 127.3 (2 x CH_{Ar}; C-6), 97.2 (CH; C-4), 92.6 (CH; C-2), 41.6 (CH_2; C-1), 21.7 (CH_3; C-9). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3441 (N-H), 3098 (C-H_{Ar}), 2981 (C-H_{Alkane}), 2927 (C-H_{Alkane}), 2857 (C-H_{Alkane}), 1953 (C=C=C), 1492 (C-H_{Alkane}), 1360 (S=O), 1155 (S=O), 1090 (C-N), 1013, 835. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{17}H_{17}{}^{35}ClNO_2S$ $[M+H]^+$: 334.0663. Found: 334.0664, Calc. for $C_{17}H_{17}{}^{37}ClNO_2S$ $[M+H]^+$: 336.0632. Found: 336.0632. **(291)** ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.80 (d, J = 8.2 Hz, 2H; H_{Ar}-6), 7.29 – 7.25 (m, 2H; H_{Ar}), 7.25 – 7.19 (m, 4H; H_{Ar}), 6.21 (dt, J = 6.2, 2.6 Hz, 1H; H-4), 5.76 (q, J = 6.2 Hz, 1H; H-2), 4.56 (d, J = 2.6 Hz, 1H; H-1), 4.55 (dd, J = 2.6, 1.0 Hz, 1H; H-1), 2.44 (s, 3H; H-

9), 1.29 (s, 9H; H-16). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 206.1 (C_q; C-3), 150.7 (C_q; C-14), 144.4 (C_q; C-8), 137.4 (C_q; C-5), 132.9 (C_q; C-13), 132.4 (C_q; C-10), 129.3 (2 x CH_{Ar}; C-11), 128.8 (2 x CH_{Ar}; C-7), 128.5 (2 x CH_{Ar}; C-12), 128.2 (2 x CH_{Ar}; C-6), 96.5 (CH; C-4), 92.7 (CH; C-2), 84.7 (C_q; C-15), 45.2 (CH_2; C-1), 27.9 (3 x CH_3; C-16), 21.8 (CH_3; C-9). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3096 (C-H_{Ar}), 3054 (C-H_{Ar}), 2987 (C-H_{Alkane}), 2925 (C-H_{Alkane}), 2853 (C-H_{Alkane}), 1953 (C=C=C), 1729 (C=O), 1491 (C-H_{Alkane}), 1360 (S=O), 1257 (C-O), 1155 (S=O), 1014 (C-O), 813. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{22}H_{28}{}^{35}ClN_2O_4S$ $[M+NH_4]^+$: 451.1453. Found: 451.1450. Calc. for $C_{22}H_{28}{}^{37}ClN_2O_4S$ $[M+NH_4]^+$: 453.1423. Found: 453.1418.

To a flame-dried Schlenk flask were added sequentially 2.0 mL of dry THF, diisopropyl azadicarboxilate (DIAD) (92 µl, 0.47 mmol, 1.1 Eq.) and triphenylphosphine (PPh_3) (123 mg, 0.47 mmol, 1.1 Eq.) under N_2 flow. The yellow suspension was stirred 15 min. Then, **290** (142 mg, 0.42 mmol, 1.0 Eq., 0.04 M – absolute concentration) and allenol **285** (42 mg, 0.42 mmol, 1.0 Eq.) were added dissolved in 8.0 mL of dry THF under N_2 flow. The reaction was stirred at room temperature until complete conversion, followed by TLC. The crude of reaction was concentrated under vacuum and purified by column chromatography over silica gel using Hex / EtOAc (30:1) then (15:1) then (10:1) as eluent. Product **292** was obtained as a yellow oil (44 mg, 0.11 mmol, 25%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.71 (d, *J* = 8.2 Hz, 2H; H_{Ar}-16), 7.28 (d, *J* = 8.2 Hz, 2H; H_{Ar}-17), 7.26 – 7.23 (m, 2H; H_{Ar}-10), 7.16 – 7.12 (m, 2H; H_{Ar}-11), 6.09 (dt, *J* = 6.5, 2.3 Hz, 1H; H-4), 5.42 (q, *J* = 6.5 Hz, 1H; H-2), 4.77 – 4.68 (m, 1H; H-6), 4.03 (ddd, *J* = 15.0, 6.5, 2.3 Hz, 1H; H-1), 3.97 (ddd, *J* = 15.0, 7.3, 2.3 Hz, 1H; H-1), 3.90 (dd, *J* = 14.8, 7.3 Hz, 1H; H-5), 3.80 (dd, *J* = 14.8, 7.3 Hz, 1H; H-5), 2.41 (s, 3H; H-19), 1.51 (d, *J* = 2.7 Hz, 3H; H-13), 1.51 (d, *J* = 2.7 Hz, 3H; H-14). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 206.4 (C_q; C-3 or C-7), 203.8 (C_q; C-3 or C-7), 143.4 (C_q), 137.8 (C_q), 132.9 (C_q; C-9 or C-12), 132.3 (C_q; C-9 or C-12), 129.9 (2 x CH_{Ar}; C-17), 128.9 (2 x CH_{Ar}; C-10), 128.2 (2 x CH_{Ar}; C-11), 127.3 (2 x CH_{Ar}; C-16), 97.0 (C_q; C-8), 95.2 (CH; C-4), 91.3 (CH; C-2), 84.0 (CH; C-6), 46.7 (CH_2; C-5), 45.1 (CH_2; C-1), 21.7 (CH_3; C-19), 20.4 (2 x CH_3; C-13 and C-14). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3069 (C-H_{Ar}), 3035 (C-H_{Ar}), 2980 (C-H_{Alkane}), 2922 (C-H_{Alkane}), 2854 (C-H_{Alkane}), 1951 (C=C=C), 1641, 1597 (C=C_{Ar}), 1491 (C-H_{Alkane}), 1346 (S=O), 1159 (S=O), 1093 (C-N), 1014, 900, 835. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)) Calc. for $C_{23}H_{25}{}^{35}ClNO_2S$ $[M+H]^+$: 414.1289. Found: 414.1288. Calc. for $C_{23}H_{25}{}^{37}ClNO_2S$ $[M+H]^+$: 416.1259. Found: 416.1257.

Synthesis of dimethyl 2,2-bis-(4-methyl-penta-2,3-dienyl)-malonate (296a)[265]

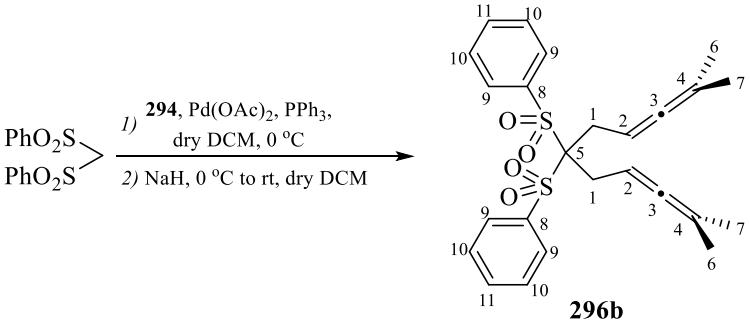


The synthesis was followed according to the procedure described by Tsuji and coworkers.[270] To a solution of allenol **285** (440 mg, 4.45 mmol, 1.0 Eq., 0.5 M) in pyridine (9.0 mL) was added in small portions 4-dimethylaminopyridine (DMAP) (27 mg, 0.22 mmol, 0.05 Eq.). Then acetic anhydride (846 µl, 8.96 mmol, 2.0 Eq.) was added dropwise and the reaction was stirred during 17 h at room temperature. The reaction was quenched with $NaHCO_{3(aq)}$ (25 mL) at 0 °C (ice bath), extracted with Et_2O (x 4), washed with HCl (0,2 M) (x 3), washed once with brine, dried over $MgSO_4$ anhydrous and concentrated under vacuum. The product **294** was obtained without further purification.[265, 270] (621 mg, 4.43 mmol, 99%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.13 – 5.06 (m, 1H; H-1), 4.50 (d, J = 6.8 Hz, 2H; H-6), 2.06 (s, 3H; H-8), 1.70 (d, J = 2.8 Hz, 6H; H-4 and H-5). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 203.5 (C_q; C-2), 171.0 (C_q; C-7), 97.4 (C_q; C-3), 84.9 (CH; C-1), 63.5 (CH_2; C-6), 21.2 (CH_3; C-8), 20.4 (2 x CH_3; C-4 and C-5).

The synthesis was undertaken according to a procedure described by Ma and coworkers.[271] To a flame-dried Schlenk flask were added sequentially $Pd(PPh_3)_4$ (43 mg, 0.04 mmol, 0.025 Eq.) in dry DCM (7.0 mL), **294** (631 mg, 4.50 mmol, 3.0 Eq.) dissolved in 8.0 mL of dry DCM and dimethylmalonate (172 µl, 1.50 mmol, 1.0 Eq., 0.1 M – absolute concentration) dropwise and under N_2. Then the mixture was cooled down at 0 °C (ice bath) and stirred at this temperature during 5 min. NaH (60% mineral oil, 180 mg, 4.50 mmol, 3.0 Eq.) was added in small portions under N_2 flow. The reaction was warmed up at room temperature and stirred during 22 h. The reaction was quenched at 0 °C with $NH_4Cl_{(aq)}$ (10 mL), extracted with DCM (x 3), washed with brine, dried over $MgSO_4$ anhydrous and concentrated under vacuum. The product was purified by column chromatography using PET / EtOAc (60:1) then (40:1) as eluent. **296a** (267 mg, 0.91 mmol, 61%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 4.81 – 4.72 (m, 2H; H-2), 3.71 (s, 6H; H-9), 2.60 (d, J = 7.7 Hz, 4H; H-1), 1.65 (d, J = 2.9 Hz, 12H; H-5 and H-6). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ =

204.0 (2 x C_q; C-3), 171.4 (2 x C_q; C-8), 95.2 (2 x C_q; C-4), 82.8 (2 x CH; C-2), 58.2 (C_q; C-7), 52.5 (2 x CH_3; C-9), 32.5 (2 x CH_2; C-1), 20.6 (4 x CH_3; C-5 and C-6).

Synthesis of [[2,2-bis-(4-methyl-penta-2,3-dienyl]-bis(sulfonyl)]-bis-benzene (296b)



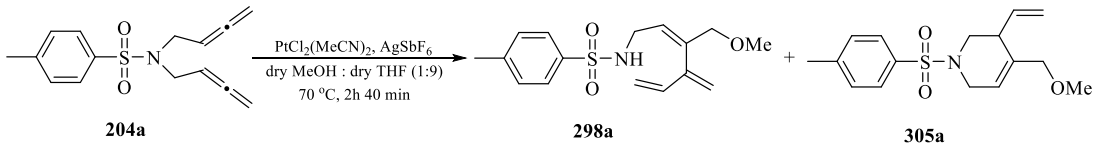
296b

The synthesis was undertaken according to a procedure described by Ma and coworkers.[271] To a flame-dried Schlenk flask was added $Pd(OAc)_2$ (13 mg, 0.06 mmol, 0.05 Eq.) and triphenylphosphine (PPh_3) (30 mg, 0.11 mmol, 0.10 Eq.) dissolved in dry DCM (5.0 mL). The solution was stirred for few minutes. Then, allene **294** (474 mg, 3.38 mmol, 3.0 Eq.) dissolved in 6.5 mL of dry DCM and neat bis(phenylsulfonyl)methane (334 mg, 1.13 mmol, 1.0 Eq., 0.1 M – absolute concentration) were added under N_2 flow. Then the mixture was cooled down at 0 °C (ice bath) and stirred at this temperature during 5 min. NaH (60% mineral oil, 135 mg, 3.38 mmol, 3.0 Eq.) was added in small portions under N_2 flow. The reaction was warmed up at room temperature and stirred during 20 h. The reaction was quenched at 0 °C with $NH_4Cl_{(aq)}$ (10 mL), extracted with DCM (x 3), washed with brine, dried over $MgSO_4$ anhydrous and concentrated under vacuum. The product was purified by column chromatography using PET / EtOAc (4:1) as eluent. **296b** (100 mg, 0.22 mmol, 19%): brown gummy oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 8.12 – 8.07 (m, 4H; H_{Ar}-9), 7.73 – 7.67 (m, 2H; H_{Ar}-11), 7.61 – 7.55 (m, 4H; H_{Ar}-10), 5.23 – 5.11 (m, 2H; H-2), 3.02 (d, J = 7.1 Hz, 4H; H-1), 1.71 (d, J = 2.8 Hz, 12H; H-6 and H-7). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 204.1 (2 x C_q; C-3), 137.2 (2 x C_q; C-8), 134.6 (2 x CH_{Ar}; C-11), 131.6 (4 x CH_{Ar}; C-10), 128.6 (4 x CH_{Ar}; C-9), 96.6 (2 x C_q; C-4 or 2 x CH; C-2), 91.1 (2 x C_q; C-4 or 2 x CH; C-2), 81.9 (C_q; C-5), 29.1 (2 x CH_2; C-1), 20.3 (4 x CH_3; C-6 and C-7). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3097 (C-H_{Ar}), 3069 (C-H_{Ar}), 2980 (C-H_{Alkane}), 2925 (C-H_{Alkane}), 2854 (C-H_{Alkane}), 1971 (C=C=C), 1602 (C=C_{Ar}), 1447 (C-H_{Alkane}), 1330 (S=O), 1311, 1146 (S=O), 1079, 1000, 858. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{25}H_{32}NO_4S_2$ $[M+NH_4]^+$: 474.1767. Found: 474.1760.

General procedure for platinum-catalysed alkoxycyclisation of 1,5-bisallenes under the best conditions found

To a microwave vial were added $PtCl_2(MeCN)_2$ (0.05 Eq.) and $AgSbF_6$ (0.1 Eq.). Then the vial was closed with a stopper and flushed with N_2 during 3 min. A small amount of dry THF was added and the solution was stirred at room temperature for a few minutes to preform the cationic complex. The corresponding 1,5-bisallene (1.0 Eq., 0.09 M – absolute concentration) dissolved in dry THF and dry MeOH (THF:MeOH 9:1) were added sequentially under N_2. Then the vial was sealed under N_2 and placed in a pre-heated oil bath at 70 ºC until completed conversion, following the reaction by TLC. The crude was filtered through celite, washed with dichloromethane and concentrated under vacuum. The mixture was purified by column chromatography using (Sigma-Aldrich Silica gel) and PET, Hex / Et_2O, EtOAc as eluents.

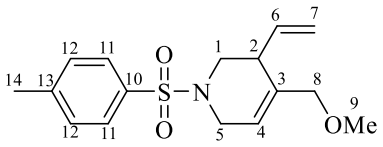
Synthesis of products 298a and 305a



204a **298a** **305a**

From 1,5-bisallene **204a** (50 mg, 0.18 mmol), $PtCl_2(MeCN)_2$ (3 mg, 0.01 mmol), silver hexafluoroantimonate (6 mg, 0.02 mmol), dry MeOH (200 µl, 4.94 mmol) and 1.8 mL of dry THF. Obtained after column chromatography using Hex / EtOAc (8:1) then (6:1) then (4:1) as eluent: **305a**, 22 mg, 0.07 mmol (39%): yellow oil, and **298a**, 6 mg, 0.02 mmol (11%): yellow oil.

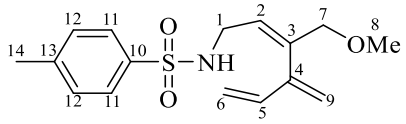
4-Methoxymethyl-1-(toluene-4-sulfonyl)-3-vinyl-1,2,3,6-tetrahydro-pyridine (305a)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.59 (d, J = 8.2 Hz, 2H; H_{Ar}-11), 7.25 (d, J = 8.2 Hz, 2H; H_{Ar}-12), 5.73 (ddd, J = 17.1, 10.2, 8.5 Hz, 1H; H-6), 5.62 – 5.58 (m, 1H; H-4), 5.11 – 5.05 (m, 2H; H-7), 3.82 – 3.78 (m, 1H; H-8), 3.78 – 3.72 (m, 1H; H-5), 3.60 (dd, J = 12.3, 0.8 Hz, 1H; H-8), 3.35 (dd, J = 11.4, 3.6 Hz, 1H; H-1), 3.32 – 3.26 (m, 1H; H-5), 3.19 (s, 3H; H-9), 2.89 – 2.83 (m, 1H; H-2), 2.80 (dd, J = 11.4, 4.1 Hz, 1H; H-1) 2.36 (s, 3H; H-14). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 143.7 (C_q; C-13), 137.0 (CH; C-6), 135.3 (C_q; C-10), 133.3 (C_q; C-3), 129.8 (2 x CH_{Ar}; C-12), 127.9 (2 x CH_{Ar}; C-11), 120.1 (CH; C-4), 117.3 (CH_2; C-7), 73.5 (CH_2; C-8), 58.1 (CH_3; C-9), 47.8 (CH_2; C-1), 44.9 (CH_2; C-5), 40.5 (CH; C-2), 21.7

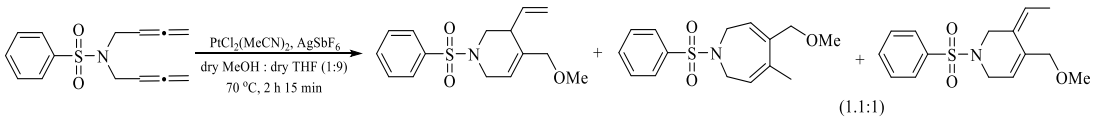
(CH_3; C-14). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3097 (C-H_{Alkene}), 3072 (C-H_{Ar}), 2924 (C-H_{Alkane}), 2858 (C-H_{Alkane}), 1737 (C=C), 1640 (C=CH_2), 1597 (C=C_{Ar}), 1456 (C-H_{Alkane}), 1344 (S=O), 1210 (C-O), 1165 (S=O), 1093 (C-N), 958, 820. HRMS (FTMS + APCI (DCM + NH_4OAc)): Calc. For $C_9H_{18}ON$ $[M+H]^+$: 325.1589. Found: 325.1580.

***N*-(3-Methoxymethyl-4-methylene-hexa-2,5-dienyl)-4-methyl benzenesulfonamide (298a)**



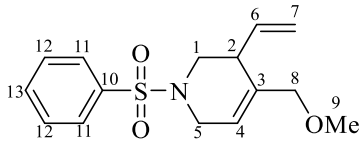
^1H NMR (300 MHz, $CDCl_3$, 25 ^oC) δ = 7.72 (d, J = 8.2 Hz, 2H; H_{Ar}-11), 7.29 (d, J = 8.2 Hz, 2H; H_{Ar}-12), 6.29 (dd, J = 17.4, 10.4 Hz, 1H; H-5), 5.62 (t, J = 7.0 Hz, 1H; H-2), 5.17 (s, 1H; H-9), 5.05 (d, J = 10.4 Hz, 1H; H-6), 5.03 (d, J = 17.4 Hz, 1H; H-6), 4.89 (s, 1H; H-9), 4.56 (bt, J = 5.9 Hz, 1H; NH), 3.85 – 3.77 (s, 2H; H-7), 3.54 – 3.43 (m, 2H; H-1), 3.28 (s, 3H; H-8), 2.42 (s, 3H; H-14). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ^oC) δ = 143.6 (C_q; C-13), 143.5 (C_q; C-10), 139.8 (C_q; C-3 or C-4), 137.1 (CH; C-5), 129.8 (2 x CH_{Ar}; C-12), 127.3 (2 x CH_{Ar}; C-11), 123.6 (CH; C-2), 118.8 (CH_2; C-9), 116.4 (CH_2; C-6), 75.1 (CH_2; C-7), 58.3 (CH_3; C-8), 41.6 (CH_2; C-1), 21.6 (CH_3; C-14). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3282 (N-H), 3098 (C-H_{Alkene}), 3082, 3061 (C-H_{Ar}), 2925 (C-H_{Alkane}), 2855 (C-H_{Alkane}), 1727 (C=C), 1598 (C=C_{Ar}), 1450 (C-H_{Alkane}), 1310 (S=O), 1240 (C-O), 1161 (S=O), 1094 (C-N), 911. HRMS (ESI-HRMS): Calc. for $C_{16}H_{25}O_3N_2S$ $[M+NH_4]^+$: 325.1589 Found: 325.1580.

Synthesis of products 299d, 305d and 305'd



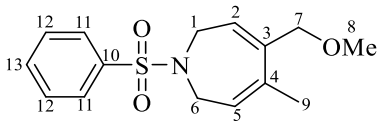
From 1,5-bisallene **266d** (206 mg, 0.79 mmol), $PtCl_2(MeCN)_2$ (14 mg, 0.04 mmol), silver hexafluoroantimonate (27 mg, 0.08 mmol), dry MeOH (866 µl, 21.40 mmol) and 7.8 mL of dry THF. Obtained after column chromatography using PET / EtOAc (10:1) then (7:1) then (4:1) as eluent: **305d**, 48 mg, 0.16 mmol (21%): colourless oil; and **299d**:**305'd** (1.1:1) as inseparable mixture, 33 mg, 0.39 mmol (15%): yellow oil.

1-Benzenesulfonyl-4-methoxymethyl-3-vinyl-1,2,3,6-tetrahydro-pyridine (305d)



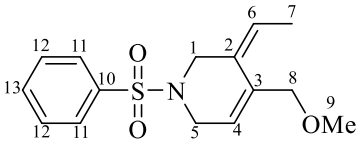
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.81 – 7.77 (m, 2H; H_{Ar}-11), 7.62 – 7.57 (m, 1H; H_{Ar}-13), 7.56 – 7.51 (m, 2H; H_{Ar}-12), 5.80 (ddd, *J* = 17.1, 10.2, 8.4 Hz, 1H; H-6), 5.69 – 5.66 (m, 1H; H-4), 5.18 – 5.12 (m, 2H; H-7), 3.89 – 3.85 (m, 1H; H-8), 3.85 – 3.81 (m, 1H; H-5), 3.70 – 3.65 (m, 1H; H-8), 3.45 (dd, *J* = 11.4, 3.4 Hz, 1H; H-1), 3.42 – 3.35 (m, 1H; H-5), 3.26 (s, 3H; H-9), 2.97 – 2.91 (m, 1H; H-2), 2.89 (dd, *J* = 11.4, 4.1 Hz, 1H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 136.9 (CH; C-6), 136.4 (C_q; C-3), 135.3 (C_q; C-10), 132.9 (CH_{Ar}; C-13), 129.2 (2 x CH_{Ar}; C-12), 127.8 (2 x CH_{Ar}; C-11), 120.0 (CH; C-4), 117.4 (CH_2; C-7), 73.5 (CH_2; C-8), 58.2 (CH_3; C-9), 47.8 (CH_2; C-1), 44.8 (CH_2; C-5), 40.5 (CH; C-2). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3097 (C-H_{Alkene}), 3065 (C-H_{Ar}), 2963 (C-H_{Alkane}), 2923 (C-H_{Alkane}), 2852 (C-H_{Alkane}), 1710 (C=C), 1607 (C=C_{Ar}), 1457 (C-H_{Alkane}), 1321 (S=O), 1150 (C-O), 1133 (S=O), 1081 (C-N), 961. HRMS (FTMS + p NSI (DCM) / MeOH + NH_4OAc)): Calc. for $C_{15}H_{20}O_3NS$ $[M+H]^+$: 294.1158. Found: 294.1161.

1-Benzenesulfonyl-4-methoxymethyl-5-methyl-2,7-dihydro-1*H*-azepine (299d)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.84 – 7.77 (m, 2H; H_{Ar}-11), 7.60 – 7.54 (m, 1H; H_{Ar}-13), 7.54 – 7.46 (m, 2H; H_{Ar}-12), 5.84 (t, *J* = 7.0 Hz, 1H; H-2), 5.77 – 5.71 (m, 1H; H-5), 3.90 (s, 2H; H-7), 3.61 (d, *J* = 7.0 Hz, 2H; H-1), 3.58 (d, *J* = 7.1 Hz, 2H; H-6), 3.15 (s, 3H; H-8), 1.78 (s, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 145.5 (C_q; C-3 or C-4), 142.7 (C_q; C-3 or C-4), 139.1 (C_q; C-10), 132.7 (CH_{Ar}; C-13), 129.2 (2 x CH_{Ar}; C-12), 127.6 (2 x CH_{Ar}; C-11), 124.2 (CH; C-2), 124.1 (CH; C-5), 73.5 (CH_2; C-7), 58.0 (CH_3; C-8), 43.9 (CH_2; C-1), 43.6 (CH_2; C-6), 19.7 (CH_3; C-9*). The H_{Ar} from the aromatic ring and the H-7 from the CH_2 are overlapped with signals from compound **305'd***

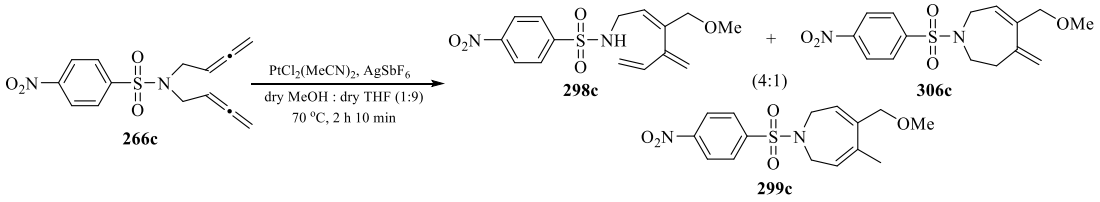
1-**Benzenesulfonyl-3-ethylidene-4-methoxymethyl-1,2,3,6-tetrahydro-pyridine (305'd)**



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.84 – 7.77 (m, 2H; H_{Ar}-11), 7.60 – 7.54 (m, 1H; H_{Ar}-13), 7.54 – 7.46 (m, 2H; H_{Ar}-12), 5.66 – 5.63 (m, 1H; H-4), 5.62 (q, *J* = 7.1 Hz, 1H; H-6), 3.93 (s, 2H; H-1), 3.90 (s, 2H; H-8), 3.85 – 3.81 (m, 2H; H-5), 3.23 (s, 3H; H-9), 1.75 (d, *J* = 7.1 Hz, 3H; H-7). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 137.2 (C_q; C-10), 133.2 (C_q; C-3), 132.9 (CH_{Ar}; C-13), 129.0 (2 x CH_{Ar}; C-12), 128.4 (C_q; C-2), 127.8 (2 x CH_{Ar}; C-11), 121.3 (2 x CH; C-4 and C-6), 72.6 (CH_2; C-8), 58.1 (CH_3; C-8), 45.2 (CH_2; C-1), 43.8 (CH_2; C-5), 13.4 (CH_3; C-7). *The H_{Ar} from the aromatic ring and the H-8 from the CH_2 are overlapped with signals from compound* ***299d***

299d and **305'd** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3098 (C-H_{Alkene}), 3070 (C-H_{Ar}), 2920 (C-H_{Alkane}), 2850 (C-H_{Alkane}), 2825 (C-H_{Alkane}), 1732 (C=C), 1447 (C-H_{Alkane}), 1335 (S=O), 1231 (C-O), 1164 (S=O), 1091 (C-N), 746. HRMS (FTMS+ p NSI ((DCM) / MeOH + NH_4OAc)): Calc. for $C_{15}H_{18}NO_3S$ $[M-2H+H]^+$: 292.1002. Found: 292.1000.

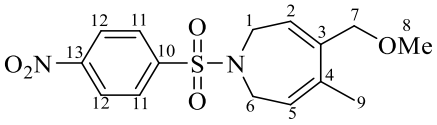
Synthesis of products 298c, 299c and 306c



266c **298c** **306c** **299c**

From 1,5-bisallene **266c** (55 mg, 0.18 mmol), $PtCl_2(MeCN)_2$ (3 mg, 0.01 mmol), silver hexafluoroantimonate (6 mg, 0.02 mmol), dry MeOH (200 µl, 4.86 mmol) and 1.8 mL of dry THF. Obtained after column chromatography using Hex / EtOAc (8:1) as eluent: **299c**, 15 mg, 0.04 mmol (25%): yellow solid; and **298c:306c** (4:1) as inseparable mixture, 18 mg, 0.05 mmol (30%): yellow oil.

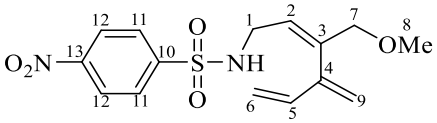
4-Methoxymethyl-5-methyl-1-(4-nitro-benzenesulfonyl)-2,7-dihydro-1*H*-azepine (299c)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 8.38 – 8.35 (m, 2H; H_{Ar}-11 or H_{Ar}-12), 8.01 – 7.98 (m, 2H; H_{Ar}-11 or H_{Ar}-12), 5.89 (t, *J* = 7.0 Hz, 1H; H-2), 5.75 (tq, *J* = 7.0, 1.3 Hz, 1H; H-5), 3.92

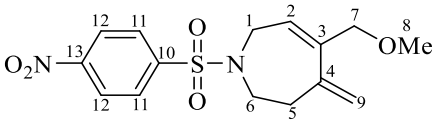
(s, 2H; H-7), 3.64 (d, *J* = 7.0 Hz, 2H; H-1), 3.63 (d, *J* = 7.0 Hz, 2H; H-6), 3.22 (s, 3H; H-8), 1.80 (s, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 150.2 (C_q; C-10 or C-13) 146.0 (C_q; C-10 or C-13), 145.3 (C_q; C-3 or C-4), 143.3 (C_q; C-3 or C-4), 128.7 (2 x CH_{Ar}; C-11), 124.5 (2 x CH_{Ar}; C-12), 123.5 (CH; C-5), 123.2 (CH; C-2), 73.4 (CH_2; C-7), 58.3 (CH_3; C-8), 43.9 (CH_2; C-6), 43.6 (CH_2; C-1), 19.8 (CH_3; C-9). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3111 (C-H_{Alkene}), 3070 (C-H_{Alkene}), 3032 (C-H_{Ar}), 2924 (C-H_{Alkane}), 2854 (C-H_{Alkane}), 1741 (C=C), 1531 (N-O), 1350 (S=O), 1164 (S=O), 1091 (C-N), 1011 (C-O), 920, 855. HRMS (FTMS + p NSI (DCM)) Calc. for $C_{15}H_{18}O_5N_2S$ $[M+H]^+$: 339.1009. Found: 339.1005.

***N*-(3-Methoxymethyl-4-methylene-hexa-2,5-dienyl)-4-nitro-benzenesulfonamide (298c)**



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 8.35 (d, *J* = 8.8 Hz, 2H; H_{Ar}-11 or H_{Ar}-12), 8.02 (d, *J* = 8.8 Hz, 2H; H_{Ar}-11 or H_{Ar}-12), 6.32 (dd, *J* = 17.4, 10.5 Hz, 1H; H-5), 5.63 (t, *J* = 7.0 Hz, 1H; H-2), 5.21 (s, 1H; H-9), 5.09 (d, *J* = 10.5 Hz, 1H; H-6), 5.04 (d, *J* = 17.4 Hz, 1H; H-6), 4.91 (s, 1H; H-9), 4.53 (bt, *J* = 5.7 Hz, 1H; NH), 3.82 (s, 2H; H-7), 3.60 – 3.55 (m, 2H; H-1), 3.31 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 150.2 (C_q; C-10 or C-13), 146.2 (C_q; C-10 or C-13), 143.6 (C_q; C-3 or C-4), 140.9 (C_q; C-3 or C-4), 137.2 (CH; C-5), 128.5 (2 x CH_{Ar}; C-11 or C-12), 124.5 (2 x CH_{Ar}; C-11 or C-12), 122.2 (CH; C-2), 119.1 (CH_2; C-9), 116.5 (CH_2; C-6), 74.9 (CH_2; C-7), 58.6 (CH_3; C-8), 41.7 (CH_2; C-1).

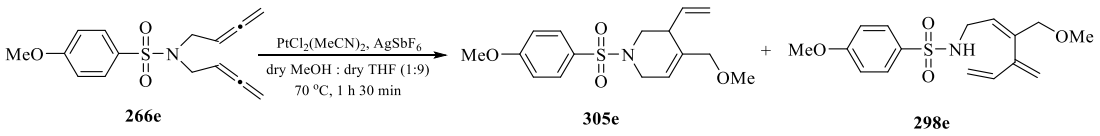
5-Methoxymethyl-4-methylene-1-(4-nitro-benzenesulfonyl)-2,3,4,7-tetrahydro-1*H*-azepine (306c)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 8.27 (d, *J* = 8.8 Hz, 2H; H_{Ar}-11 or H_{Ar}-12), 7.94 (d, *J* = 8.8 Hz, 2H; H_{Ar}-11 or H_{Ar}-12), 5.78 (t, *J* = 4.9 Hz, 1H; H-2), 4.94 (s, 1H; H-9), 4.83 (s, 1H; H-9), 4.11 (d, *J* = 4.9 Hz, 2H; H-1), 3.81 (d, *J* = 0.9 Hz, 2H; H-7), 3.53 (t, *J* = 6.4 Hz, 2H; H-6), 3.27 (s, 3H; H-8), 2.52 (t, *J* = 6.4 Hz, 2H; H-5). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 142.5 (C_q; C-10 or C-13), 140.2 (C_q; C-10 or C-13), 128.8 (2 x CH_{Ar}; C-11 or C-12), 125.5 (C_q; C-3 or C-4), 124.1 (2 x CH_{Ar}; C-11 or C-12), 115.9 (CH_2; C-9), 74.6 (CH_2; C-7), 58.4 (CH_3; C-8), 49.0 (CH_2; C-6), 44.9 (CH_2; C-5) 36.2 (CH_2; C-1). *Due to the low concentration of the compound one quarternary carbon could not be found.*

298c and **306c** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3508 (N-H), 3110 (C-H_{Alkene}), 2925 (C-H_{Alkane}), 2855 (C-H_{Alkane}), 1716 (C=C), 1611 (C=C_{Ar}), 1531 (N-O), 1454 (C-H_{Alkane}), 1350 (S=O), 1210 (C-O), 1164 (S=O), 1094 (C-N), 918, 859, 742.0. HRMS (FTMS + p NSI (DCM)): Calc. for $C_{15}H_{19}O_5N_2S$ $[M+H]^+$: 339.1009 Found: 339.1008. M.P. = 83 – 85 °C.

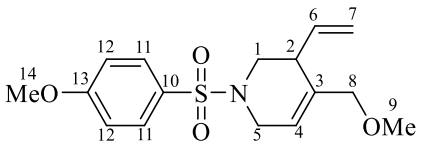
Synthesis of products 298e and 305e



266e **305e** **298e**

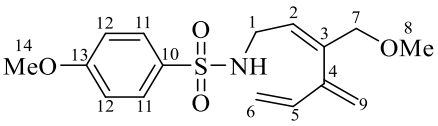
From 1,5-bisallene **266c** (74 mg, 0.25 mmol), $PtCl_2(MeCN)_2$ (4 mg, 0.01 mmol), silver hexafluoroantimonate (9 mg, 0.02 mmol), dry MeOH (280 µl, 6.91 mmol) and 2.2 mL of dry THF. Obtained after column chromatography using Hex / EtOAc (5:1) then (3:1) then (1:1) as eluent: **305e**, 22 mg, 0.07 mmol (26%): yellow oil; and **298e**, 36 mg, 0.11 mmol (44%): yellow oil.

1-(4-Methoxy-benzenesulfonyl)-4-methoxymethyl-3-vinyl-1,2,3,6-tetrahydro-pyridine (305e)



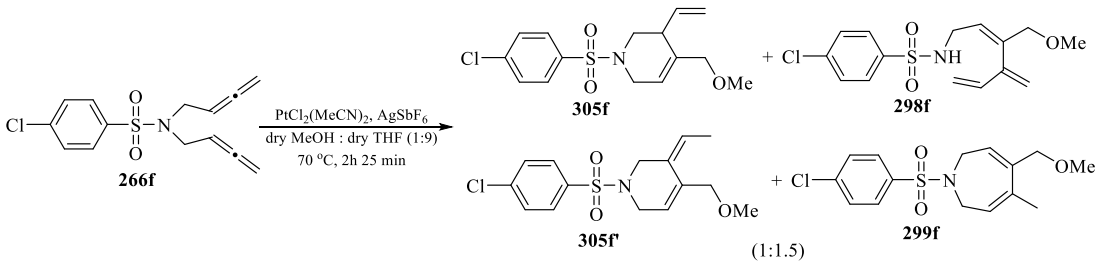
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.74 – 7.69 (m, 2H; H_{Ar}-11), 7.01 – 6.97 (m, 2H; H_{Ar}-12), 5.80 (ddd, *J* = 17.1, 10.1, 8.5 Hz, 1H; H-6), 5.70 – 5.64 (m, 1H; H-4), 5.17 – 5.14 (m, 1H; H-7), 5.14 – 5.11 (m, 1H; H-7), 3.87 (s, 3H; H-14), 3.89 – 3.84 (m, 1H; H-8), 3.84 – 3.77 (m, 1H; H-5), 3.68 (dd, *J* = 12.3, 0.7 Hz, 1H; H-8), 3.41 (dd, *J* = 11.4, 3.6 Hz, 1H; H-1), 3.41 – 3.34 (m, 1H; H-5), 3.26 (s, 3H; H-9), 2.96 – 2.90 (m, 1H; H-2), 2.87 (dd, *J* = 11.4, 4.1 Hz, 1H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 163.2 (C_q; C-13), 137.0 (CH; C-6), 135.3 (C_q; C-10), 129.9 (2 x CH_{Ar}; C-11), 128.0 (C_q; C-3), 120.1 (CH; C-4), 117.3 (CH_2; C-7), 114.3 (2 x CH_{Ar}; C-12), 73.5 (CH_2; C-8), 58.2 (CH_3; C-9), 55.8 (CH_3; C-14), 47.8 (CH_2; C-1), 44.9 (CH_2; C-5), 40.5 (CH; C-2). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3095 (C-H_{Alkene}), 3054 (C-H_{Ar}), 2921 (C-H_{Alkane}), 2856 (C-H_{Alkane}), 2820 (C-H_{Alkane}), 1732 (C=C), 1594 (C=C_{Ar}), 1460 (C-H_{Alkane}), 1344 (S=O), 1257 (C-O), 1153 (S=O), 1091 (C-N), 960. HRMS (FTMS + p NSI ((DCM) / MeOH + NH_4OAc)): Calc. for $C_{16}H_{22}O_4NS$ $[M+H]^+$: 324.1264. Found: 324.1265.

4-Methoxy-*N*-(3-methoxymethyl-4-methylene-hexa-2,5-dienyl)-benzenesulfonamide (298e)



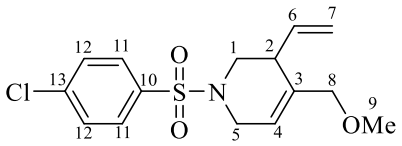
^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ =7.77 (d, J = 8.8 Hz, 2H; H_{Ar}-11), 6.96 (d, J = 8.8 Hz, 2H; H_{Ar}-12), 6.31 (dd, J = 17.3, 10.5 Hz, 1H; H-5), 5.63 (t, J = 6.6 Hz, 1H; H-2), 5.18 (s, 1H; H-9), 5.09 – 5.00 (m, 2H; H-6), 4.89 (s, 1H; H-9), 4.34 – 4.30 (m, 1H; NH), 3.87 (s, 3H; H-14), 3.82 (s, 2H; H-7), 3.48 (t, J = 6.6 Hz, 2H; H-1), 3.30 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 163.0 (C_q; C-13), 143.7 (C_q; C-3 or C-4), 139.9 (C_q; C-10), 137.2 (CH; C-5), 131.7 (C_q; C-3 or C-4), 129.4 (2 x CH_{Ar}; C-11), 123.5 (CH; C-2), 118.9 (CH_2; C-9), 116.4 (CH_2; C-6), 114.3 (2 x CH_{Ar}; C-12), 75.2 (CH_2; C-7), 58.4 (CH_3; C-8), 55.8 (CH_3; C-14), 41.6 (CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3540 (N-H), 2964 (C-H_{Alkane}), 2920 (C-H_{Alkane}), 2852 (C-H_{Alkane}), 1744 (C=C), 1712, 1632 (C=C_{Ar}), 1596, 1448 (C-H_{Alkane}), 1312 (S=O), 1260 (C-O), 1156 (S=O), 1100 (C-N). HRMS (FTMS + p NSI ((DCM) / MeOH + NH_4OAc)): Calc. for $C_{16}H_{22}O_4NS$ $[M+H]^+$: 324.1264. Found: 324.1266.

Synthesis of products 298f, 299f, 305f and 305f'



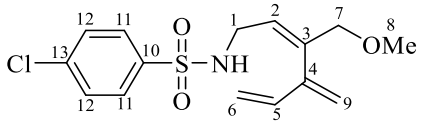
From 1,5-bisallene **266f** (72 mg, 0.24 mmol), $PtCl_2(MeCN)_2$ (4 mg, 0.01 mmol), silver hexafluoroantimonate (8 mg, 0.02 mmol), dry MeOH (270 µl, 6.59 mmol), 2.4 mL of dry THF. Obtained after column chromatography using Hex/EtOAc (8:1) then (6:1) then (2:1) as eluent: **298f**, 3 mg, 0.01 mmol (2%): yellow oil; **299f:305f'** (1.5:1) as inseparable mixture, 36 mg, 0.11 mmol (31%): yellow oil; and **305f** 22 mg, 0.07 mmol (17%): yellow oil.

1-(4-Chloro-benzenesulfonyl)-4-methoxymethyl-3-vinyl-1,2,3,6-tetrahydro-pyridine (305f)



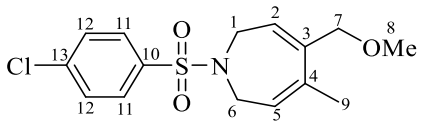
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.74 – 7.70 (m, 2H; H_{Ar}-11 or H_{Ar}-12), 7.53 – 7.48 (m, 2H; H_{Ar}-11 or H_{Ar}-12), 5.83 – 5.73 (m, 1H; H-6), 5.68 (m, 1H; H-4), 5.17 – 5.15 (m, 1H; H-7), 5.16 – 5.12 (m, 1H; H-7), 3.86 (d, *J* = 12.1 Hz, 1H; H-8), 3.85 – 3.81 (m, 1H; H-5), 3.68 (d, *J* = 12.1 Hz, 1H; H-8), 3.44 (dd, *J* = 11.3, 3.4 Hz, 1H; H-1), 3.41 – 3.35 (m, 1H; H-5), 3.26 (s, 3H; H-9), 2.96 – 2.92 (m, 1H; H-2), 2.90 (dd, *J* = 11.3, 4.1 Hz, 1H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 139.5 (C_q), 136.7 (CH; C-6), 135.4 (C_q), 135.0 (C_q), 129.5 (2 x CH_{Ar}; C-11 or C-12), 129.2 (2 x CH_{Ar}; C-11 or C-12), 119.8 (CH; C-4), 117.5 (CH_2; C-7), 73.5 (CH_2; C-8), 58.2 (CH_3; C-9), 47.8 (CH_2; C-1), 44.8 (CH_2; C-5), 40.4 (CH; C-2). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3086 (C-H_{Alkene}), 2922 (C-H_{Alkane}), 2850 (C-H_{Alkane}), 2828 (C-H_{Alkane}), 1714 (C=C), 1585 (C=C_{Ar}), 1476 (C-H_{Alkane}), 1349 (S=O), 1200 (C-O), 1165 (S=O), 1091 (C-N), 962, 828. HRMS (FTMS + p NSI ((DCM) / MeOH + NH_4OAc)): Calc. for $C_{15}H_{19}O_3NS^{35}Cl$ $[M+H]^+$: 328.0769. Found: 328.0769. Calc. For $C_{15}H_{19}O_3NS^{37}Cl$ $[M+H]^+$: 330.0738. Found: 330.0736.

4-Chloro-*N*-(3-methoxymethyl-4-methylene-hexa-2,5-dienyl)-benzenesulfonamide (298f)



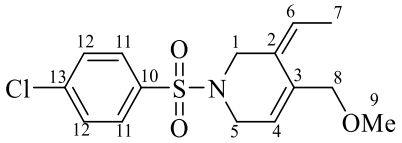
^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.79 – 7.76 (m, 2H; H_{Ar}-11 or H_{Ar}-12), 7.49 – 7.46 (m, 2H; H_{Ar}-11 or H_{Ar}-12), 6.32 (dd, *J* = 17.4, 10.4 Hz, 1H; H-5), 5.63 (tt, *J* = 7.0, 1.5 Hz, 1H; H-2), 5.20 (s, 1H; H-9), 5.08 (d, *J* = 10.4 Hz, 1H; H-6), 5.03 (d, *J* = 17.4 Hz, 1H; H-6), 4.90 (s, 1H; H-9), 4.35 (bt, *J* = 5.8 Hz, 1H; NH), 3.83 (s, 2H; H-7), 3.54 – 3.50 (m, 2H; H-1), 3.31 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 143.6 (C_q), 140.4 (C_q), 139.3 (C_q), 138.7 (C_q), 137.2 (CH; C-5), 129.5 (2 x CH_{Ar}; C-11 or C-12), 128.7 (2 x CH_{Ar}; C-11 or C-12), 122.8 (CH; C-2), 119.0 (CH_2; C-9), 116.4 (CH_2; C-6), 75.1 (CH_2; C-7), 58.5 (CH_3; C-8), 41.6 (CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3286 (N-H), 3097 (C-H_{Alkene}), 2925 (C-H_{Alkane}), 2859 (C-H_{Alkane}), 2826 (C-H_{Alkane}), 1717 (C=C), 1586, 1476 (C-H_{Alkane}), 1395 (S=O), 1337 (C-O), 1163 (S=O), 1093 (C-N), 1013 (C-O). HRMS (FTMS + p NSI ((DCM) / MeOH + NH_4OAc)): Calc. for $C_{15}H_{22}{}^{35}ClO_3N_2S$ $[M+NH_4]^+$: 345.1034. Found: 345.1040. Calc. for $C_{15}H_{22}{}^{37}ClO_3N_2S$ $[M+NH_4]^+$: 347.1003. Found: 345.1003.

1-(4-Chloro-benzenesulfonyl)-4-methoxymethyl-5-methyl-2,7-dihydro-1*H*-azepine (299f)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.76 – 7.73 (m, 2H; H_{Ar}-11 or H_{Ar}-12), 7.51 – 7.47 (m, 2H; H_{Ar}-11 or H_{Ar}-12), 5.86 (t, *J* = 7.0 Hz, 1H; H-2), 5.75 (tq, *J* = 7.1, 1.4 Hz, 1H; H-5), 3.92 (s, 2H; H-7), 3.60 (d, *J* = 7.0 Hz, 2H; H-1), 3.58 (d, *J* = 7.1 Hz, 2H; H-6), 3.20 (s, 3H; H-8), 1.80 (s, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 145.7 (C_q; C-4), 142.9 (C_q; C-3), 139.2 (C_q; C-10 or C-13), 137.8 (C_q; C-10 or C-13), 129.5 (2 x CH_{Ar}; C-11 or C-12), 129.0 (2 x CH_{Ar}; C-11 or C-12), 123.9 (CH; C-2), 123.8 (CH; C-5), 73.5 (CH_2; C-7), 58.1 (CH_3; C-8), 43.8 (CH_2; C-6), 43.6 (CH_2; C-1), 19.8 (CH_3; C-9).

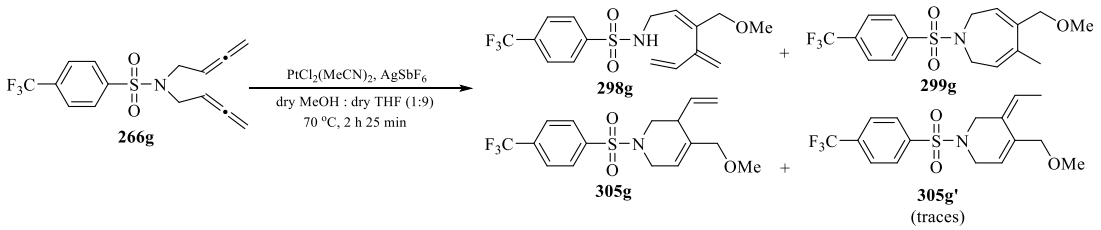
1-(4-Chloro-benzenesulfonyl)-3-ethylidene-4-methoxymethyl-1,2,3,6-tetrahydro-pyridine (305f')



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.73 – 7.70 (m, 2H; H_{Ar}-11 or H_{Ar}-12), 7.47 – 7.43 (m, 2H; H_{Ar}-11 or H_{Ar}-12), 5.67 – 5.60 (m, 2H; H-6 and H-4), 3.95 (s, 2H; H-1), 3.90 (s, 2H; H-8), 3.87 – 3.83 (m, 2H; H-5), 3.23 (s, 3H; H-9), 1.75 (d, *J* = 7.2 Hz, 3H; H-7). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 139.4 (C_q; C-10 or C-13), 136.0 (C_q; C-10 or C-13), 133.4 (C_q; C-2 or C-3), 129.3 (2 x CH_{Ar}; C-11 or C-12), 129.2 (2 x CH_{Ar}; C-11 or C-12), 128.2 (C_q; C-2 or C-3), 121.6 (CH; C-6 or C-4), 121.0 (CH; C-6 or C-4), 72.5 (CH_2; C-8), 58.1 (CH_3; C-9), 45.2 (CH_2; C-5), 43.9 (CH_2; C-1), 13.4 (CH_3; C-9).

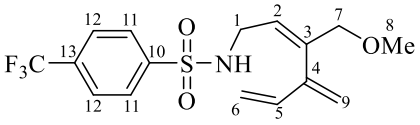
299f and **305f'** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3095 (C-H_{Alkene}), 3067 (C-H_{Ar}), 2925 (C-H_{Alkane}), 2854 (C-H_{Alkane}), 1733 (C=C), 1586, 1477 (C-H_{Alkane}), 1349 (S=O), 1299 (C-O), 1165 (S=O), 1091 (C-N), 1013 (C-O), 829, 757. HRMS (FTMS + p NSI ((DCM) / MeOH + NH_4OAc)): Calc. for $C_{15}H_{22}{}^{35}ClO_3N_2S$ $[M+H]^+$: 328.0729. Found: 328.0774. Calc. for $C_{15}H_{22}{}^{37}ClO_3N_2S$ $[M+H]^+$: 330.0738. Found: 330.0742.

Synthesis of products 298g, 299g, 305g and 305g' (traces)



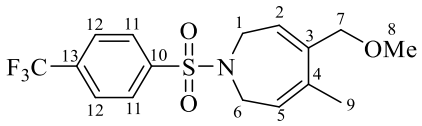
From 1,5-bisallene **266g** (195 mg, 0.59 mmol), $PtCl_2(MeCN)_2$ (10 mg, 0.03 mmol), silver hexafluoroantimonate (20 mg, 0.02 mmol), dry MeOH (652 µl, 16.11 mmol) and 5.9 mL of dry THF. Obtained after column chromatography using PET / EtOAc (14:1) then (10:1) then (8:1) then (4:1) as eluent: **298g**, 1 mg, 0.003 mmol (1%): yellow oil; **298g** and traces of **305g'** as inseparable mixture, 13 mg, 0.04 mmol (6%): yellow oil; and **305g**, 12 mg, 0.03 mmol (6%): colourless oil.

***N*-(3-Methoxymethyl-4-methylene-hexa-2,5-dienyl)-4-trifluoromethyl-benzenesulfonamide (298g)**



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.97 (d, J = 8.3 Hz, 2H; H_{Ar}-11), 7.78 (d, J = 8.3 Hz, 2H; H_{Ar}-12), 6.31 (dd, J = 17.4, 10.5 Hz, 1H; H-5), 5.62 (tt, J = 7.0, 1.4 Hz, 1H; H-2), 5.19 (d, J = 0.7 Hz, 1H; H-9), 5.07 (d, J = 10.5 Hz, 1H; H-6), 5.03 (d, J = 17.4 Hz, 1H; H-6), 4.90 (s, 1H; H-9), 4.41 (bt, J = 5.8 Hz, 1H; NH), 3.82 (d, J = 1.4 Hz, 2H; H-7), 3.58 – 3.53 (m, 2H; H-1), 3.30 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 143.6 (C_q; C-10), 140.7 (C_q; C-3 or C-4), 137.2 (CH; C-5), 134.5 (q, $J_{C\text{-}F}$ = 32.9 Hz; C_q; C-13), 127.8 (2 x CH_{Ar}; C-11), 127.2 (q, $J_{C\text{-}F}$ = 231.7 Hz; CF_3), 126.3 (q, $J_{C\text{-}F}$ = 3.8 Hz; 2 x CH_{Ar}; C-12), 122.5 (CH; C-2), 119.0 (CH_2; C-9), 116.4 (CH_2; C-6), 75.0 (CH_2; C-7), 58.5 (CH_3; C-8), 41.7 (CH_2; C-1). ^{19}F NMR (471 MHz, $CDCl_3$, 25 °C) δ = - 63.11. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3282 (N-H), 3097 (C-H_{Alkene}), 2960 (C-H_{Alkane}), 2924 (C-H_{Alkane}), 2853 (C-H_{Alkane}), 1713 (C=C), 1456 (C-H_{Alkane}), 1404, 1322 (S=O), 1167 (S=O), 1132 (C-F), 1062 (C-O), 917, 843. HRMS (FTMS + p NSI ((DCM) / MeOH + NH_4OAc)): Calc. for $C_{16}H_{19}F_3O_3NS$ $[M+H]^+$: 362.1032 Found: 362.1036.

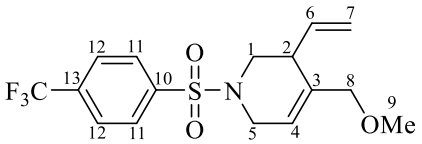
4-Methoxymethyl-5-methyl-1-(4-trifluoromethyl-benzenesulfonyl)-2,7-dihydro-1*H*-azepine (299g)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.94 (d, J = 8.2 Hz, 2H; H_{Ar}-11), 7.79 (d, J = 8.2 Hz, 2H; H_{Ar}-12), 5.86 (t, J = 7.0 Hz, 1H; H-2), 5.76 (tq, J = 7.1, 1.4 Hz, 1H; H-5), 3.91 (s, 2H; H-7), 3.64 (d, J = 7.0 Hz, 2H; H-1), 3.60 (d, J = 7.1 Hz, 2H; H-6), 3.17 (s, 3H; H-8), 1.79 (s, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 145.7 (C_q), 143.0 (C_q), 128.1 (2 x CH_{Ar}; C-11), 127.2 (q, $J_{C\text{-}F}$ = 262.3 Hz; CF_3), 126.2 (q, $J_{C\text{-}F}$ = 3.6 Hz; 2 x CH_{Ar}-C-12), 123.8 (CH; C-5), 123.6 (CH; C-2), 73.4 (CH_2; C-7), 58.1 (CH_3; C-8), 43.9 (CH_2; C-6), 43.7 (CH_2; C-1), 19.8 (CH_3; C-9). *(C_q; C-13) could not be identified.* ^{19}F NMR (471 MHz, $CDCl_3$, 25 ^{o}C) δ = - 63.07. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3118, 3052 (C-H_{Alkene}), 2924 (C-H_{Alkane}), 2852 (C-H_{Alkane}), 2826 (C-H_{Alkane}), 1738 (C=C), 1456 (C-H_{Alkane}), 1323 (S=O), 1167 (S=O), 1110 (C-O), 1062 (C-N), 1015, 845. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{16}H_{19}F_3O_3NS$ $[M+H]^+$: 362.1032 Found: 362.1036.

*Compound **305g'** was identify as inseparable mixture with compound **299g**, however, due to the low concentration was impossible to fully characterize the product.*

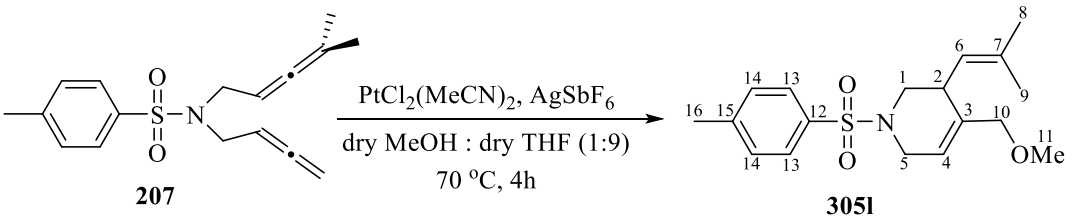
4-Methoxymethyl-1-(4-trifluoromethyl-benzenesulfonyl)-3-vinyl-1,2,3,6-tetrahydro-pyridine (305g)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.92 (d, J = 8.2 Hz, 2H; H_{Ar}-11), 7.80 (d, J = 8.2 Hz, 2H; H_{Ar}-12), 5.82 – 5.72 (m, 1H; H-6), 5.70 – 5.66 (m, 1H; H-4), 5.18 – 5.16 (m, 1H; H-7), 5.14 – 5.11 (m, 1H; H-7), 3.91 – 3.87 (m, 1H; H-5), 3.88 – 3.83 (m, 1H; H-8), 3.68 (d, J = 12.3 Hz, 1H; H-8), 3.51 – 3.45 (m, 1H; H-1), 3.45 – 3.38 (m, 1H; H-5), 3.26 (s, 3H; H-9), 2.98 – 2.94 (m, 1H; H-2), 2.94 – 2.91 (m, 1H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 136.6 (CH; C-6), 135.5 (C_q; C-10), 132.9 (C_q; C-3), 128.2 (2 x CH_{Ar}; C-11), 126.4 (q, $J_{C\text{-}F}$ = 3.7 Hz; 2 x CH_{Ar}; C-12), 119.6 (CH; C-4), 117.7 (CH_2; C-7), 73.5 (CH_2; C-8), 58.2 (CH_3; C-9), 47.8 (CH_2; C-1), 44.8 (CH_2; C-5), 40.3 (CH; C-2). *(C_q; C-13), (C_q; CF_3) could not be identified.* ^{19}F NMR (471 MHz, $CDCl_3$, 25 ^{o}C) δ = - 63.11. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3095 (C-H_{Alkene}), 2963 (C-H_{Alkane}), 2923 (C-H_{Alkane}), 2852 (C-H_{Alkane}), 1607 (C=C), 1457, 1322 (S=O), 1302 (C-O), 1170

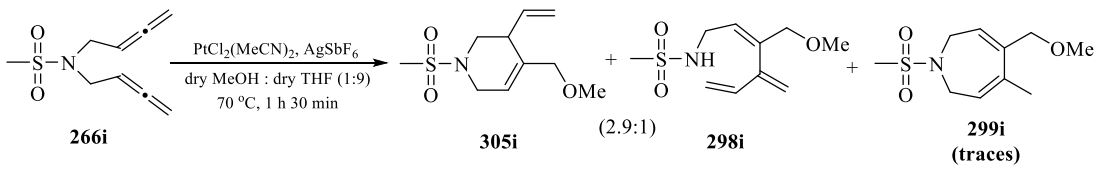
(S=O), 1133 (C-F), 961. HRMS (FTMS + p NSI ((DCM) / MeOH + NH_4OAc)): Calc. for $C_{16}H_{19}F_3NO_3S$ $[M+H]^+$: 362.1032 Found: 362.1035.

Synthesis of 4-methoxymethyl-3-(2-methyl-propenyl)-1-(toluene-4-sulfonyl)-1,2,3,6-tetrahydro-pyridine (305l)



From 1,5-bisallene **207** (66 mg, 0.22 mmol), $PtCl_2(MeCN)_2$ (4 mg, 0.01 mmol), silver hexafluoroantimonate (8 mg, 0.02 mmol), dry MeOH (240 µl, 5.95 mmol) and 2.2 mL of dry THF. Obtained after column chromatography using Hex / EtOAc (4:1) as eluent: **305l**, 11 mg, 0.03 mmol (16%): colourless oil. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.66 (d, J = 8.2 Hz, 2H; H_{Ar}-13), 7.31 (d, J = 8.2 Hz, 2H; H_{Ar}-14), 5.62 – 5.59 (m, 1H; H-4), 5.07 – 5.02 (m, 1H; H-6), 3.79 – 3.75 (m, 1H; H-10), 3.75 – 3.70 (m, 1H; H-5), 3.60 (d, J = 12.6 Hz, 1H; H-10), 3.46 – 3.39 (m, 1H; H-5), 3.24 (s, 3H; H-11), 3.20 – 3.17 (m, 1H; H-1), 3.16 – 3.13 (m, 1H; H-2), 2.98 – 2.93 (m, 1H; H-1), 2.42 (s, 3H; H-16), 1.71 (d, J = 1.1 Hz, 3H; H-8), 1.68 (d, J = 1.1 Hz, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 143.6 (C_q; C-15), 136.9 (C_q; C-12), 134.3 (C_q; C-3), 129.7 (2 x CH_{Ar}; C-14), 127.9 (2 x CH_{Ar}; C-13), 123.5 (CH; C-6), 119.2 (CH; C-4), 73.7 (CH_2; C-10), 58.1 (CH_3; C-11), 48.3 (CH_2; C-1), 44.8 (CH_2; C-5), 35.1 (CH; C-2), 26.0 (CH_3; C-9), 21.7 (CH_3; C-16), 18.3 (CH_3; C-8). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3034 (C-H_{Alkene}), 2958 (C-H_{Alkane}), 2922 (C-H_{Alkane}), 2853 (C-H_{Alkane}), 1733 (C=C), 1600 (C=C_{Ar}), 1454 (C-H_{Alkane}), 1346 (S=O), 1160 (S=O), 1100 (C-O), 1098 (C-N), 961, 819. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{18}H_{26}O_3NS$ $[M+H]^+$: 336.1628 Found: 336.1629.

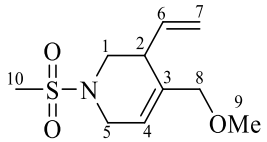
Synthesis of products 305i, 298i and 299i (traces)



From 1,5-bisallene **266i** (104 mg, 0.52 mmol), $PtCl_2(MeCN)_2$ (9 mg, 0.03 mmol), silver hexafluoroantimonate (18 mg, 0.05 mmol), dry MeOH (574 µl, 14.18 mmol) and 5.2 mL of dry THF. Obtained as inseparable mixture after column chromatography using PET / EtOAc (7:1) then (4:1) as eluent: **305i:298i** (2.9:1), 38 mg, 0.16 mmol (32%): colourless oil.

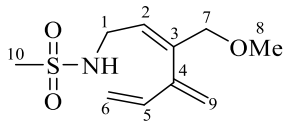
*Compound **299i** was identified by ^{1}H NMR in the reaction crude, however, due to the low concentration of product, it was difficult identify the signals accurately.*

1-Methanesulfonyl-4-methoxymethyl-3-vinyl-1,2,3,6-tetrahydro-pyridine (305i)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 5.83 – 5.74 (m, 1H; H-4), 5.78 – 5.74 (m, 1H; H-6), 5.18 – 5.12 (m, 2H; H-7), 3.95 – 3.90 (m, 1H; H-5), 3.92 – 3.87 (m, 1H; H-8), 3.73 (d, *J* = 12.0 Hz, 1H; H-8), 3.69 – 3.63 (m, 1H; H-5), 3.48 (dd, *J* = 11.9, 3.7 Hz, 1H; H-1), 3.30 (s, 3H; H-9), 3.17 (dd, *J* = 11.9, 4.1 Hz, 1H; H-1), 3.00 – 2.96 (m, 1H; H-2), 2.80 (s, 3H; H-10). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 136.7 (CH; C-6), 135.6 (C_q; C-3), 120.2 (CH; C-4), 117.5 (CH_2; C-7), 73.6 (CH_2; C-8), 58.3 (CH_3; C-9), 47.4 (CH_2; C-1), 44.7 (CH_2; C-5), 40.4 (CH; C-2), 35.5 (CH_3; C-10).

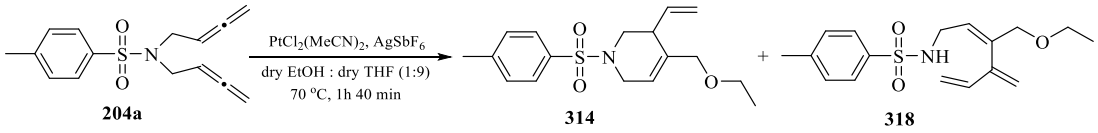
***N*-(3-Methoxymethyl-4-methylene-hexa-2,5-dienyl)-methanesulfonamide (298i)**



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 6.40 (dd, *J* = 17.3, 10.5 Hz, 1H; H-5), 5.79 – 5.74 (m, 1H; H-2), 5.30 (d, *J* = 0.8 Hz, 1H; H-9), 5.18 – 5.13 (m, 1H; H-6), 5.14 – 5.08 (m, 1H; H-6), 5.00 (s, 1H; H-9), 4.32 – 4.29 (m, 1H; NH), 3.89 (d, *J* = 1.3 Hz, 2H; H-7), 3.69 – 3.65 (m, 2H; H-1), 3.35 (s, 3H; H-8), 2.92 (s, 3H; H-10). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 143.8 (C_q; C-3 or C-4), 140.1 (C_q; C-3 or C-4), 137.2 (CH; C-5), 123.5 (CH; C-2) 119.0 (CH_2; C-9), 116.5 (CH_2; C-6), 75.1 (CH_2; C-7), 58.5 (CH_3; C-8), 41.7 (CH_2; C-1), 40.7 (CH_3; C-10).

305i and **298i** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3480 (N-H), 3081 (C-H_{Alkene}), 2980 (C-H_{Alkane}), 2929 (C-H_{Alkane}), 2854 (C-H_{Alkane}), 1638 (C=C), 1337 (S=O), 1151 (S=O), 1095 (C-O), 967, 778. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{18}H_{26}O_3NS$ $[M+H]^+$: 336.1628 Found: 336.1629.

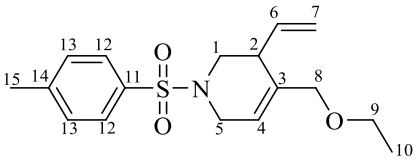
Synthesis of products 314 and 318 using EtOH as nucleophile.



204a **314** **318**

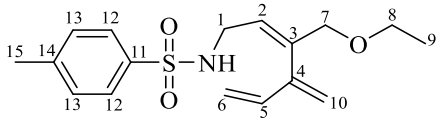
From 1,5-bisallene **204a** (50 mg, 0.18 mmol), $PtCl_2(MeCN)_2$ (3 mg, 0.01 mmol), silver hexafluoroantimonate (6 mg, 0.02 mmol), dry EtOH (288 µl, 4.94 mmol) and 1.8 mL of dry THF. Obtained after column chromatography using PET / EtOAc (4:1) as eluent: **314**, 14 mg, 0.04 mmol (23%): colourless oil; and **318**, 12 mg, 0.04 mmol (20%): colourless oil.

4-Ethoxymethyl-1-(toluene-4-sulfonyl)-3-vinyl-1,2,3,6-tetrahydro-pyridine (314)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.66 (d, *J* = 8.2 Hz, 2H; H_{Ar}-12), 7.31 (d, *J* = 8.2 Hz, 2H; H_{Ar}-13), 5.80 (ddd, *J* = 17.1, 10.1, 8.5 Hz, 1H; H-6), 5.68 – 5.65 (m, 1H; H-4), 3.87 (dd, *J* = 12.3, 2.0 Hz, 1H; H-8), 3.84 – 3.79 (m, 1H; H-5), 3.75 (dd, *J* = 12.3, 0.8 Hz, 1H; H-8), 3.45 – 3.40 (m, 2H; H-9), 3.45 – 3.35 (m, 1H; H-1), 3.37 – 3.32 (m, 1H; H-5), 2.96 – 2.92 (m, 1H; H-2), 2.87 (dd, *J* = 11.4, 4.1 Hz, 1H; H-1), 2.43 (s, 3H; H-15), 1.16 (t, *J* = 7.0 Hz, 3H; H-10). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 143.7 (C_q), 137.1 (CH; C-6), 135.6 (C_q), 133.3 (C_q), 129.8 (2 x CH_{Ar}; C-13), 127.9 (2 x CH_{Ar}; C-12), 119.7 (CH; C-4), 117.2 (CH_2; C-7), 71.5 (CH_2; C-8), 65.9 (CH_2; C-9), 47.8 (CH_2; C-1), 44.9 (CH_2; C-5), 40.6 (CH; C-2), 21.7 (CH_3; C-15), 15.3 (CH_3; C-10). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3090 (C-H_{Alkene}), 3066 (C-H_{Ar}), 3039 (C-H_{Ar}), 2966 (C-H_{Alkane}), 2919 (C-H_{Alkane}), 2850 (C-H_{Alkane}), 1648 (C=C), 1598, 1456 (C-H_{Alkane}), 1331 (S=O), 1161 (S=O), 1094 (C-N), 1042 (C-O), 908, 814. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{18}H_{26}O_3NS$ $[M+H]^+$: 322.1471. Found: 322.1472.

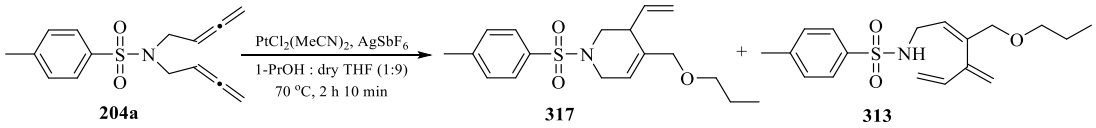
***N*-(3-Ethoxymethyl-4-methylene-hexa-2,5-dienyl)-4-methyl-benzenesulfonamide (318)**



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.72 (d, *J* = 8.2 Hz, 2H; H_{Ar}-12), 7.29 (d, *J* = 8.2 Hz, 2H; H_{Ar}-13), 6.30 (dd, *J* = 17.3, 10.5 Hz, 1H; H-5), 5.62 (tt, *J* = 7.0, 1.5 Hz, 1H; H-2), 5.17 (d, *J* = 0.8 Hz, 1H; H-10), 5.08 – 5.04 (m, 1H; H-6), 5.03 (d, *J* = 17.3 Hz, 1H; H-6), 4.88 (s, 1H; H-10), 4.28 (bt, *J* = 5.9 Hz, 1H; NH), 3.86 (d, *J* = 1.5 Hz, 2H; H-7), 3.52 – 3.47 (m, 2H; H-1),

3.44 (q, *J* = 7.0 Hz, 2H; H-8), 2.43 (s, 3H; H-15), 1.17 (t, *J* = 7.0 Hz, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 143.8 (C_q), 143.5 (C_q), 140.4 (C_q), 137.2 (CH; C-5), 137.2 (C_q), 129.8 (2 x CH_{Ar}; C-13), 127.3 (2 x CH_{Ar}; C-12), 122.7 (CH; C-2), 118.8 (CH_2; C-10), 116.3 (CH_2; C-6), 73.0 (CH_2; C-7), 66.1 (CH_2; C-8), 41.6 (CH_2; C-1), 21.7 (CH_3; C-15), 15.2 (CH_3 C-9). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3286 (N-H), 3094 (C-H_{Alkene}), 3028 (C-H_{Ar}), 2977 (C-H_{Alkane}), 2925 (C-H_{Alkane}), 2857 (C-H_{Alkane}), 1720 (C=C), 1598, 1442 (C-H_{Alkane}), 1352 (S=O), 1336, 1161 (S=O), 1094 (C-O), 1051, 912, 815. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{18}H_{26}O_3NS$ [M + H]+: 322.1471. Found: 322.1474.

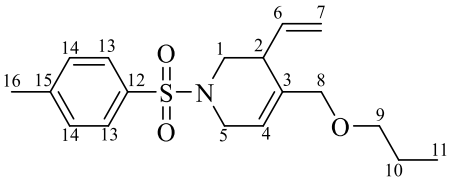
Synthesis of products 317 and 313 using 1-propanol as nucleophile



204a **317** **313**

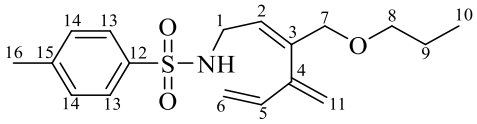
From 1,5-bisallene **204a** (53 mg, 0.19 mmol), $PtCl_2(MeCN)_2$ (3 mg, 0.01 mmol), silver hexafluoroantimonate (7 mg, 0.02 mmol), 1-Propanol (393 µl, 5.27 mmol) and 1.9 mL of dry THF. Obtained after column chromatography using PET / EtOAc (7:1) as eluent: **317**, 13 mg, 0.04 mmol (20%): colourless oil; and **313**, 15 mg, 0.05 mmol (24%): colourless oil.

4-Propoxymethyl-1-(toluene-4-sulfonyl)-3-vinyl-1,2,3,6-tetrahydro-pyridine (317)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.66 (d, *J* = 8.2 Hz, 2H; H_{Ar}-13), 7.31 (d, *J* = 8.2 Hz, 2H; H_{Ar}-14), 5.80 (ddd, *J* = 17.1, 10.1, 8.5 Hz, 1H; H-6), 5.69 – 5.64 (m, 1H; H-4), 5.18 – 5.10 (m, 2H; H-7), 3.87 (d, *J* = 12.3 Hz, 1H; H-8), 3.84 – 3.78 (m, 1H; H-5), 3.74 (d, *J* = 12.3 Hz, 1H; H-8), 3.42 (dd, *J* = 11.4, 3.6 Hz, 1H; H-1), 3.38 – 3.34 (m, 1H; H-5), 3.33 – 3.23 (m, 2H; H-9), 2.97 – 2.93 (m, 1H; H-2), 2.87 (dd, *J* = 11.4, 4.1 Hz, 1H; H-1), 2.43 (s, 3H; H-16), 1.55 (sex, *J* = 7.3 Hz, 1H; H-10), 0.89 (t, *J* = 7.3 Hz, 3H; H-11). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 143.7 (C_q), 137.1 (CH; C-6), 135.7 (C_q), 133.3 (C_q), 129.8 (2 x CH_{Ar}; C-14), 127.9 (2 x CH_{Ar}; C-13), 119.6 (CH; C-4), 117.2 (CH_2; C-7), 72.3 (CH_2; C-9), 71.7 (CH_2; C-8), 47.8 (CH_2; C-1), 44.9 (CH_2; C-5), 40.6 (CH; C-2), 23.0 (CH_2; C-10), 21.7 (CH_3; C-16), 10.8 (CH_3; C-11). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3083 (C-H_{Alkene}), 3069 (C-H_{Alkene}), 3035 (C-H_{Ar}), 2961 (C-H_{Alkane}), 2924 (C-H_{Alkane}), 2852 (C-H_{Alkane}), 1637 (C=C), 1597, 1457 (C-H_{Alkane}), 1347 (S=O), 1163 (S=O), 1120 (C-O), 1093 (C-N), 955, 815. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{14}H_{17}O_5N_2S$ $[M-H+O]^+$: 350.1421. Found: 350.1425.

4-Methyl-*N*-(4-methylene-3-propoxymethyl-hexa-2,5-dienyl)-benzenesulfonamide (313)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.72 (d, J = 8.2 Hz, 2H; H_{Ar}-13), 7.29 (d, J = 8.2 Hz, 2H; H_{Ar}-14), 6.30 (dd, J = 17.3, 10.5 Hz, 1H; H-5), 5.62 (tt, J = 7.0, 1.5 Hz, 1H; H-2), 5.17 (d, J = 0.8 Hz, 1H; H-11), 5.07 (d, J = 10.5 Hz, 1H; H-6), 5.04 (d, J = 17.3 Hz, 1H; H-6), 4.88 (s, 1H; H-11), 4.26 (bt, J = 5.9 Hz, 1H; NH), 3.86 (d, J = 1.5 Hz, 2H; H-7), 3.53 – 3.47 (m, 2H; H-1), 3.34 (t, J = 6.9 Hz, 2H; H-8), 2.43 (s, 3H; H-16), 1.61 – 1.52 (m, 2H; H-9), 0.90 (t, J = 7.2 Hz, 3H; H-10). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 143.8 (C_q), 143.5 (C_q), 140.5 (C_q), 137.3 (CH; C-5), 137.2 (C_q), 129.8 (2 x CH_{Ar}; C-14), 127.3 (2 x CH_{Ar}; C-13), 122.6 (CH; C-2), 118.8 (CH_2; C-11), 116.3 (CH_2; C-6), 73.2 (CH_2; C-7 or C-8), 72.5 (CH_2; C-7 or C-8), 41.6 (CH_2; C-1), 23.0 (CH_3; C-16), 21.7 (CH_2; C-9), 10.8 (CH_3; C-10). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3291 (N-H), 3090 (C-H_{Alkene}), 3066 (C-H_{Alkene}), 3039 (C-H_{Ar}), 2966 (C-H_{Alkane}), 2929 (C-H_{Alkane}), 2850 (C-H_{Alkane}), 1648 (C=C), 1598, 1456 (C-H_{Alkane}), 1331 (S=O), 1161 (S=O), 1094 (C-N), 1042 (C-O), 908, 814. HRMS (FTMS + p APCI (OIL)): Calc. for $C_{18}H_{26}O_3NS$ $[M+H]^+$: 336.1628. Found: 336.1624.

General procedures for platinum-catalysed hydroxycyclisation of 1,5-bisallenes

Procedure 1

To a microwave vial were added $PtCl_2(MeCN)_2$ (0.05 Eq.) and $AgSbF_6$ (0.1 Eq.). Then the vial was closed with a stopper and flushed with N_2 during 3 min. A small amount of dry THF was added and the solution was stirred at room temperature for a few min to preform the cationic complex. The corresponding 1,5-bisallene (1.0 Eq., 0.091 M – absolute concentration) dissolved in dry THF was added, then distilled H_2O (THF:H_2O, 18:1). The vial was sealed and placed in a pre-heated oil bath at 70 ^{o}C or under microwave irradiation until completed conversion, following the reaction by TLC. The crude was filtered through a pad of celite / $MgSO_4$ anhydrous (1:2), washed with dichloromethane and concentrated under vacuum. The mixture was purified by column chromatography using (Sigma-Aldrich Silica gel) and PET, Hex / Et_2O, EtOAc as eluents.

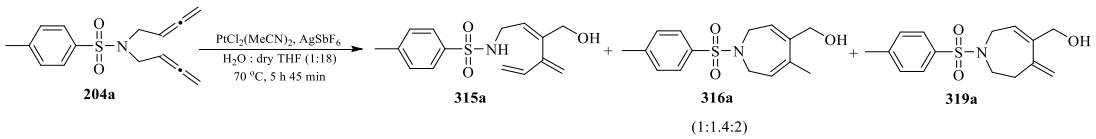
Procedure 2

To a microwave vial were added $PtCl_2(MeCN)_2$ (0.05 Eq.) and $AgSbF_6$ (0.12 Eq.). Then the vial was closed with a stopper and flushed with N_2 during 3 min. A small amount of dry THF was added and the solution was stirred at room temperature for a few min to preform

the cationic complex. The corresponding 1,5-bisallene (1.0 Eq., 0.09 M – absolute concentration) dissolved in dry THF was added, then distilled H_2O (THF:H_2O, 1:3) was added. The vial was sealed under N_2 and placed in a pre-heated oil bath at 70 °C or under microwave irradiation until completed conversion, following the reaction by TLC. The crude was filtered through a pad of celite / $MgSO_4$ anhydrous (1:2), washed with acetonitrile and concentrated under vacuum. The mixture was purified by column chromatography using (Sigma-Aldrich Silica gel) and PET, Hex / Et_2O, EtOAc as eluents.

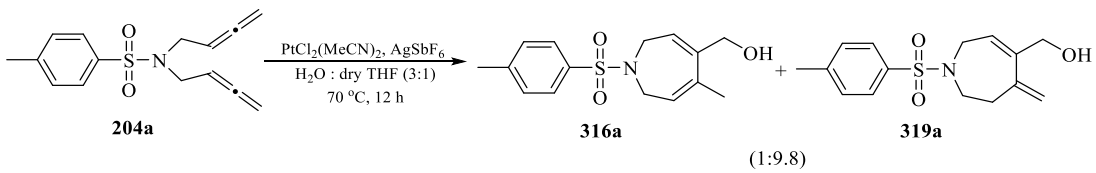
Synthesis of products 315a, 316a and 319a

Procedure 1



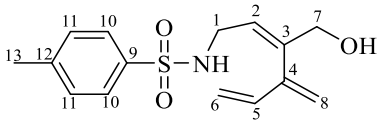
From 1,5-bisallene **204a** (116 mg, 0.42 mmol), $PtCl_2(MeCN)_2$ (7 mg, 0.02 mmol), silver hexafluoroantimonate (14 mg, 0.04 mmol), distilled water (234 µl, 10.95 mmol) and 4.0 mL of dry THF. Obtained as inseparable mixture after column chromatography using Hex / EtOAc (10:1) then (3:1) as eluent: **315a**:**316a**:**319a** (1:1.4:2), 50 mg, 0.17 mmol (41%): yellow oil.

Procedure 2



From 1,5-bisallene **204a** (100 mg, 0.36 mmol), $PtCl_2(MeCN)_2$ (6 mg, 0.02 mmol), silver hexafluoroantimonate (15 mg, 0.04 mmol), distilled water (3.0 mL, 0.17 mmol) and 1.0 mL of dry THF. Obtained as inseparable mixture after column chromatography using PET / EtOAc (5:1) then (1:1) as eluent: **316a**:**319a** (1:9.8), 46 mg, 0.16 mmol (43%): yellow oil.

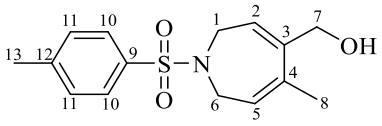
***N*-(3-Hydroxymethyl-4-methylene-hexa-2,5-dienyl)-4-methyl-benzenesulfonamide (315a)**



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.71 (d, J = 8.2 Hz, 2H; H_{Ar}-10), 7.33 – 7.29 (m, 2H; H_{Ar}-11), 6.31 (dd, J = 17.4, 10.5 Hz, 1H; H-5), 5.64 (tt, J = 6.8, 1.3 Hz, 1H; H-2), 5.19 (s, 1H;

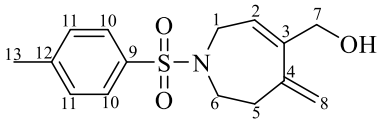
H-8), 5.08 (d, *J* = 10.5 Hz, 1H; H-6), 5.03 (d, *J* = 17.4 Hz, 2H; H-6), 4.91 (s, 1H; H-8), 4.45 (bt, *J* = 6.1 Hz, 1H; NH), 4.04 (s, 2H; H-7), 3.49 (d, *J* = 6.8 Hz, 1H; H-1), 3.48 (d, *J* = 6.1 Hz, 1H; H-1), 2.42 (s, 3H; H-13). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 143.6 (C_q), 143.5 (C_q), 142.7 (C_q), 137.1 (CH; C-5), 137.1 (C_q), 129.8 (2 x CH_{Ar}; C-11), 127.3 (2 x CH_{Ar}; C-10), 122.4 (CH; C-2), 65.8 (CH_2; C-7), 41.6 (CH_2; C-1), 21.7 (CH_3; C-13).

[5-Methyl-1-(toluene-4-sulfonyl)-2,7-dihydro-1*H*-azepin-4-yl]-methanol (316a)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.68 (d, *J* = 8.2 Hz, 2H; H_{Ar}-11), 7.30 (d, *J* = 8.2 Hz, 2H; H_{Ar}-10), 5.88 (t, *J* = 7.0 Hz, 1H; H-2), 5.73 (tq, *J* = 7.0, 1.2 Hz, 1H; H-5), 4.13 (s, 2H; H-7), 3.58 (d, *J* = 7.0 Hz, 2H; H-1), 3.57 (d, *J* = 7.0 Hz, 2H; H-6), 2.42 (s, 3H; H-13), 1.79 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 147.6 (C_q), 143.4 (C_q), 142.0 (C_q), 136.2 (C_q), 129.8 (2 x CH_{Ar}; C-11), 127.6 (2 x CH_{Ar}; C-10), 124.5 (CH; C-5), 122.5 (CH; C-2), 63.8 (CH_2; C-7), 43.8 (CH_2; C-6), 43.5 (CH_2; C-1), 21.7 (CH_3; C-13), 19.8 (CH_3; C-8).

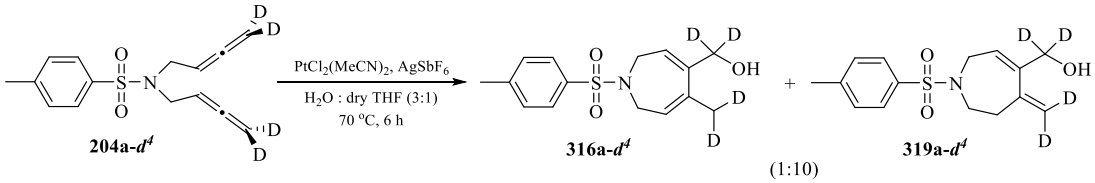
[5-methylene-1-(toluene-4-sulfonyl)-2,5,6,7-tetrahydro-1*H*-azepin-4-yl]-methanol (319a)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.63 (d, *J* = 8.2 Hz, 2H; H_{Ar}-10), 7.25 (d, *J* = 8.2 Hz, 2H; H_{Ar}-11), 5.80 (t, *J* = 5.3 Hz, 1H; H-2), 5.00 (s, 1H; H-8), 4.95 (s, 1H; H-8), 4.11 (s, 2H; H-7), 3.95 (d, *J* = 5.3 Hz, 2H; H-1), 3.44 (t, *J* = 6.4 Hz, 2H; H-6), 2.49 (t, *J* = 6.4 Hz, 2H; H-5), 2.40 (s, 3H; H-13). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 143.3 (C_q), 142.8 (C_q), 142.6 (C_q), 136.3 (C_q), 129.5 (2 x CH_{Ar}; C-11), 127.5 (2 x CH_{Ar}; C-10), 124.8 (CH; C-2), 115.1 (CH_2; C-8), 65.3 (CH_2; C-7), 48.8 (CH_2; C-6), 45.0 (CH_2; C-1), 36.3 (CH_2; C-5), 21.6 (CH_3; C-13). M.P. = 79 – 81 °C.

315a, **316a** and **319a** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3521 (O-H), 3296 (N-H), 3087 (C-H_{Alkene}), 3063 (C-H_{Alkene}), 3035 (C-H_{Ar}), 2925 (C-H_{Alkane}), 2857 (C-H_{Alkane}), 1725 (C=C), 1598, 1455 (C-H_{Alkane}), 1333 (S=O), 1159 (S=O), 1094 (C-N), 1070 (C-O), 904, 816. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{15}H_{20}O_3NS$ $[M+H]^+$: 294.1158. Found: 294.1154.

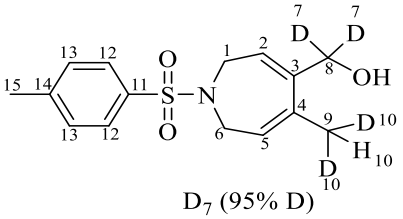
Synthesis of products 316a-*d*^{4} and 319a-*d*^{4}



Procedure 2

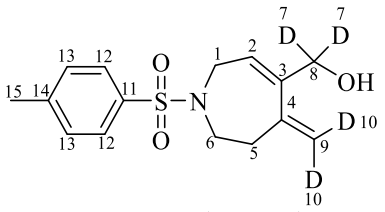
From 1,5-bisallene **204a-*d*^{4}** (150 mg, 0.54 mmol), $PtCl_2(MeCN)_2$ (9 mg, 0.03 mmol), silver hexafluoroantimonate (22 mg, 0.06 mmol), distilled water (4.5 mL, 0.25 mmol) and 1.5 mL of dry THF. Obtained as inseparable mixture after column chromatography using PET / EtOAc (2:1) as eluent: **316a-*d*^{4}**:**319a-*d*^{4}** (1:10), 63 mg, 0.21 mmol (40%): white solid.

[5-Methyl-1-(toluene-4-sulfonyl)-2,7-dihydro-1*H*-azepin-4-yl]-methanol-*d*^{4} (316a-*d*^{4})



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.61 (d, *J* = 8.2 Hz, 2H; H_{Ar}-12), 7.23 (d, *J* = 8.2 Hz, 2H; H_{Ar}-13), 5.81 (t, *J* = 7.0 Hz, 1H; H-2), 5.66 (t, *J* = 7.0 Hz, 1H; H-5), 4.07 (s, 2H; H-7, 5 % H), 3.51 (d, *J* = 7.0 Hz, 2H; H-1), 3.51 (d, *J* = 7.0 Hz, 2H; H-6), 2.36 (s, 3H; H-15), 1.70 (m, 1H; H-10). *The deuterium incorporation in C-9, could not be accurately determine due to overlapping with other signals.* ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 147.5 (C_q), 143.4 (C_q), 142.7 (C_q), 136.1 (C_q), 129.8 (2 x CH_{Ar}; C-13), 127.5 (2 x CH_{Ar}; C-12), 124.4 (CH; C-5), 122.5 (CH; C-2), 43.8 (CH_2; C-6), 43.5 (CH_2; C-1), 21.6 (CH_3; C-15). *C-8 and C-9 could not be assigned due to the high deuterium incorporation*. ^{2}H NMR (77 MHz, $CDCl_3$, 25 °C) δ = 4.11 (bs, 2^{2}H; ^{2}H-7), 1.81 (bs, 1^{2}H; ^{2}H-10), 1.79 (bs, 1^{2}H; ^{2}H-10).

[5-methylene-1-(toluene-4-sulfonyl)-2,5,6,7-tetrahydro-1*H*-azepin-4-yl]-methanol-*d*^{4} (319a-*d*^{4})



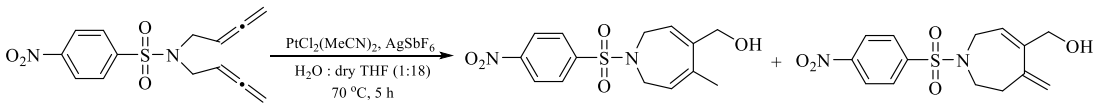
D_7 (>95% D)
D_{10} (95% D)

^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.57 (d, J = 8.2 Hz, 2H; H_{Ar}-12), 7.19 (d, J = 8.2 Hz, 2H; H_{Ar}-13), 5.73 (t, J = 5.3 Hz, 1H; H-2), 4.92 (s, 1H; H-10, 5 % H), 4.87 (s, 1H; H-10, 5 % H), 4.05 (s, 2H; H-7, < 5 % H), 3.88 (d, J = 5.3 Hz, 2H; H-1), 3.37 (t, J = 6.4 Hz, 2H; H-6), 2.42 (t, J = 6.4 Hz, 2H; H-5), 2.34 (s, 3H; H-15). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 143.3 (C_q), 142.6 (C_q), 142.5 (C_q), 136.2 (C_q), 129.5 (2 x CH_{Ar}; C-13), 127.5 (2 x CH_{Ar}; C-12), 48.8 (CH_2; C-6), 45.0 (CH_2; C-1), 36.2 (CH_2; C-5), 21.6 (CH_3; C-15). *C-8 and C-9 could not be assigned due to the high deuterium incorporation*. ^{2}H NMR (77 MHz, $CDCl_3$, 25 ^{o}C) δ = 5.06 (bs, 1^{2}H; ^{2}H-10), 5.01 (bs, 1^{2}H; ^{2}H-10), 4.11 (bs, 2^{2}H; ^{2}H-7).

316a-*d*^{4} and **319a-*d*^{4}** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3514 (O-H), 2954 (C-H_{Alkane}), 2853 (C-H_{Alkane}), 1644 (C=C), 1454 (C-H_{Alkane}), 1332 (S=O), 1157 (S=O), 1096 (C-N), 1062 (C-O), 907. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{15}H_{16}D_4O_3NS$ $[M+H]^+$: 298.1409. Found: 298.1409. M.P. = 106 – 108 ^{o}C.

Synthesis of products 316c and 319c

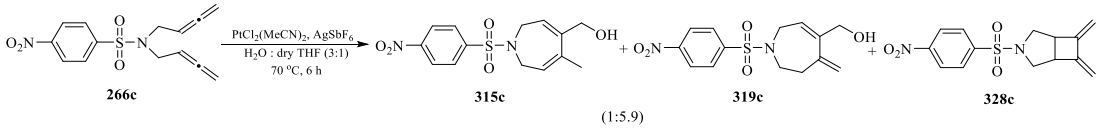
Procedure 1



266c **316c** (1:1) **319c**

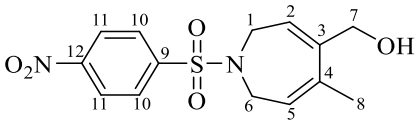
From 1,5-bisallene **266c** (103 mg, 0.34 mmol), $PtCl_2(MeCN)_2$ (6 mg, 0.02 mmol), silver hexafluoroantimonate (12 mg, 0.03 mmol), distilled water (187 µl, 10.38 mmol) and 3.4 mL of dry THF. Obtained as inseparable mixture after column chromatography using PET / EtOAc (80:1) then (50:1) then (10:1) then (2:1) as eluent: **316c**:**319c** (1:1), 55 mg, 0.18 mmol (54%): yellow solid.

Procedure 2



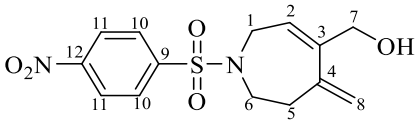
From 1,5-bisallene **266c** (204 mg, 0.67 mmol), $PtCl_2(MeCN)_2$ (12 mg, 0.03 mmol), silver hexafluoroantimonate (28 mg, 0.08 mmol), distilled water (5.5 mL, 0.30 mmol) and 1.8 mL of dry THF. Obtained after column chromatography using PET / EtOAc (2:1) as eluent: **328c,** 6 mg, 0.02 mmol (3%): yellow solid; and **315c**:**319c** (1:5.9) as inseparable mixture, 75 mg, 0.23 mmol (35%): yellow solid.

[5-Methyl-1-(4-nitro-benzenesulfonyl)-2,7-dihydro-1*H*-azepin-4-yl]-methanol (316c)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 8.37 (d, J = 8.8 Hz, 2H; H_{Ar}-11), 7.99 (d, J = 8.8 Hz, 2H; H_{Ar}-10), 5.93 (t, J = 7.1 Hz, 1H; H-2), 5.77 (tq, J = 7.2, 1.3 Hz, 1H; H-5), 4.18 (s, 2H; H-7), 3.65 (d, J = 7.1 Hz, 2H; H-1), 3.63 (d, J = 7.2 Hz, 2H; H-6), 1.82 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 150.2 (C_q; C-12), 148.2 (C_q; C-3), 145.3 (C_q; C-9), 142.8 (C_q; C-4), 128.6 (2 x CH_{Ar}; C-10), 124.5 (2 x CH_{Ar}; C-11), 123.8 (CH; C-5), 121.6 (CH; C-2), 63.6 (CH_2; C-7), 43.8 (CH_2; C-6), 43.6 (CH_2; C-1), 19.9 (CH_3; C-8).

[5-methylene-1-(4-nitro-benzenesulfonyl)-2,5,6,7-tetrahydro-1*H*-azepin-4-yl]-methanol (319c)

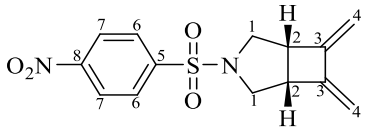


^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 8.29 (d, J = 9.0 Hz, 2H; H_{Ar}-11), 7.95 (d, J = 9.0 Hz, 2H; H_{Ar}-10), 5.84 (t, J = 4.3 Hz, 1H; H-2), 4.99 (s, 1H; H-8), 4.86 (s, 1H; H-8), 4.14 – 4.10 (m, 2H; H-1), 4.09 (s, 2H; H-7), 3.53 (t, J = 6.4 Hz, 2H; H-6), 2.53 (t, J = 6.4 Hz, 2H; H-5), 1.56 (bs, 1H; OH). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 150.0 (C_q; C-12), 145.5 (C_q; C-9), 142.8 (C_q; C-4), 142.4 (C_q; C-3), 128.7 (2 x CH_{Ar}; C-10), 124.2 (2 x CH_{Ar}; C-11), 124.1 (CH; C-2), 115.6 (CH_2; C-8), 64.8 (CH_2; C-7), 49.0 (CH_2; C-6), 45.0 (CH_2; C-1), 36.3 (CH_2; C-5).

315c and **319c** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3543 (O-H), 3104 (C-H_{Alkene}), 3031 (C-H_{Alkene}), 2926 (C-H_{Alkane}), 2863 (C-H_{Alkane}), 1606 (C=C), 1531 (N-O), 1351 (S=O), 1309,

1161 (S=O), 1094 (C-N), 1061 (C-O), 910. HRMS (FTMS + p APCI (Solid)): Calc. for $C_{14}H_{17}O_5N_2S$ $[M+H]^+$: 325.0853. Found: 325.0854. M.P. = 141 – 143 °C.

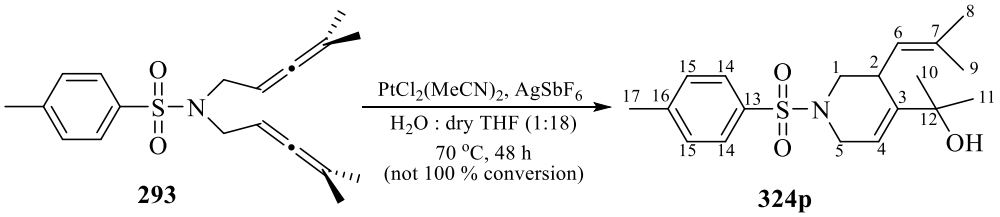
6,7-Dimethylene-3-(4-nitro-benzenesulfonyl)-3-aza-bicyclo[3.2.0]heptan (328c)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 8.35 (d, J = 8.8 Hz, 2H; H_{Ar}-7), 7.99 (d, J = 8.8 Hz, 2H; H_{Ar}-6), 5.18 (s, 2H; H-4), 4.80 (s, 2H; H-4), 3.70 (d, J = 10.2 Hz, 2H; H-1), 3.40 – 3.35 (m, 2H; H-2), 2.95 (dd, J = 10.2, 6.1 Hz, 2H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 150.3 (C_q; C-8), 148.8 (2 x C_q; C-3), 142.4 (C_q; C-5), 129.1 (2 x CH_{Ar}; C-6), 124.2 (2 x CH_{Ar}; C-7), 106.2 (2 x CH_2; C-4), 53.6 (2 x CH_2; C-1), 44.9 (2 x CH; C-2). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3110 ($C\text{-}H_{Alkene}$), 2969 ($C\text{-}H_{Alkane}$), 2923 ($C\text{-}H_{Alkane}$), 2853 ($C\text{-}H_{Alkane}$), 1527 (N-O), 1347 (S=O), 1168 (S=O), 1089 (C-N), 1015 (C-O), 897. HRMS (FTMS + p APCI (Solid)): Calc. for $C_{14}H_{15}O_4N_2S$ $[M+H]^+$: 307.0747. Found: 307.0749. M.P. = 156 – 158 °C.

Synthesis of 2-[3-(2-Methyl-propenyl)-1-(toluene-4-sulfonyl)-1,2,3,6-tetrahydro-pyridin-4-yl]-propan-2-ol (324p)

Procedure 1

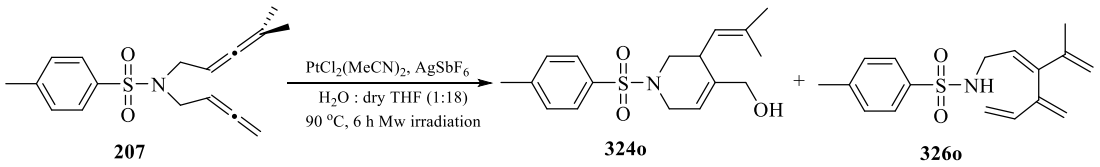


From 1,5-bisallene **293** (22 mg, 0.07 mmol), $PtCl_2(MeCN)_2$ (1 mg, 0.003 mmol), silver hexafluoroantimonate (2 mg, 0.01 mmol), distilled water (37 µl, 2.02 mmol) and 694 µl of dry THF. Obtained after column chromatography using Hex / EtOAc (10:1) then (6:1) then (2:1) as eluent: **324p**, 4 mg, 0.01 mmol (16%): colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.65 (d, J = 8.1 Hz, 2H; H_{Ar}-14), 7.31 (d, J = 8.1 Hz, 2H; H_{Ar}-15), 5.66 (dd, J = 3.5, 3.0 Hz, 1H; H-4), 5.23 – 5.18 (m, 1H; H-6), 3.92 (dd, J = 16.2, 3.5 Hz, 1H; H-5), 3.42 (dd, J = 10.8, 3.0 Hz, 1H; H-1), 3.32 – 3.30 (m, 1H; H-5), 3.30 – 3.26 (m, 1H; H-2), 2.68 (dd, J = 10.8, 3.6 Hz, 1H; H-1), 2.42 (s, 3H; H-17), 1.71 (d, J = 1.3 Hz, 3H; H-8 or H-9), 1.70 (d, J = 1.3 Hz, 3H; H-8 or H-9), 1.27 (s, 3H; H-10 or H-11), 1.24 (s, 3H; H-10 or H-11). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 146.1 (C_q), 143.6 (C_q), 133.3 (C_q), 133.3 (C_q), 129.7 (2 x CH_{Ar}; C-15), 127.9 (2 x CH_{Ar}; C-14), 126.8 (CH; C-6), 115.9 (CH; C-4), 73.1 (C_q; C-12), 49.8 (CH_2; C-1), 44.9 (CH_2; C-5), 34.8 (CH; C-2), 30.1 (CH_3; C-10 or C-11), 29.9 (CH_3; C-10 or C-11),

26.0 (CH_3; C-8 or C-9), 21.7 (CH_3; C-17), 18.2 (CH_3; C-8 or C-9). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3522 (O-H), 3054 (C-H_{Alkene}), 2970 (C-H_{Alkane}), 2923 (C-H_{Alkane}), 2853 (C-H_{Alkane}), 1721 (C=C), 1600, 1456 (C-H_{Alkane}), 1340 (S=O), 1163 (S=O), 1092 (C-N), 1060 (C-O), 960. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{19}H_{27}O_3NSNa$ $[M+Na]^+$: 372.1604. Found: 372.1602.

Synthesis of products 324o and 326o

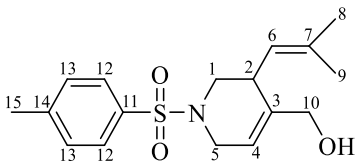
Procedure 1



207 **324o** **326o**

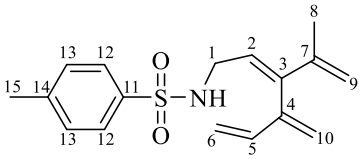
From 1,5-bisallene **207** (103 mg, 0.34 mmol), $PtCl_2(MeCN)_2$ (6 mg, 0.02 mmol), silver hexafluoroantimonate (12 mg, 0.03 mmol), distilled water (188 µl, 10.44 mmol) and 3.4 mL of dry THF. Obtained after column chromatography using Hex / EtOAc (15:1) then (10:1) then (6:1) then (2:1) as eluent: **324o**, 31 mg, 0.10 mmol (28%): yellow oil; and **326o**, 26 mg, 0.08 mmol (24%): yellow oil.

[3-(2-Methyl-propenyl)-1-(toluene-4-sulfonyl)-1,2,3,6-tetrahydro-pyridin-4-yl]-methanol (324o)



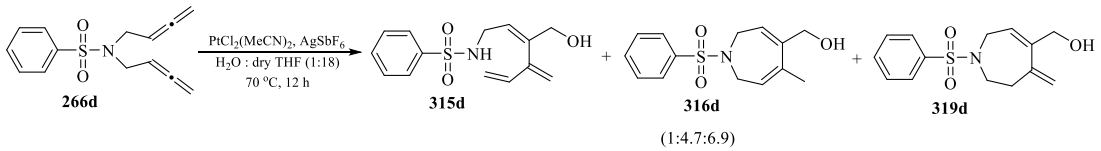
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.66 (d, J = 8.2 Hz, 2H; H_{Ar}-12), 7.32 (d, J = 8.2 Hz, 2H; H_{Ar}-13), 5.65 – 5.61 (m, 1H; H-4), 5.05 – 5.00 (m, 1H; H-6), 3.95 (s, 2H; H-10), 3.70 – 3.63 (m, 1H; H-5), 3.54 – 3.48 (m, 1H; H-5), 3.22 – 3.19 (m, 1H; H-2), 3.08 – 3.03 (m, 1H; H-1), 3.06 – 3.01 (m, 1H; H-1), 2.43 (s, 3H; H-15), 1.71 (d, J = 1.3 Hz, 3H; H-8 or H-9), 1.70 (d, J = 1.3 Hz, 3H; H-8 or H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 143.7 (C_q), 139.4 (C_q), 134.8 (C_q), 133.3 (C_q), 129.8 (2 x CH_{Ar}; C-13), 127.9 (2 x CH_{Ar}; C-12), 123.5 (CH; C-6), 117.7 (CH; C-4), 64.5 (CH_2; C-10), 48.3 (CH_2; C-1), 44.8 (CH_2; C-5), 35.4 (CH; C-2), 26.0 (CH_3; C-8 or C-9), 21.7 (CH_3; C-15), 18.4 (CH_3; C-8 or C-9). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3480 (O-H), 3063 (C-H_{Alkene}), 2977 (C-H_{Alkane}), 2926 (C-H_{Alkane}), 2881 (C-H_{Alkane}), 1714 (C=C), 1598, 1456 (C-H_{Alkane}), 1338 (S=O), 1163 (S=O), 1092 (C-N), 1071 (C-O), 816. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{17}H_{24}O_3NS$ $[M+H]^+$: 322.1471. Found: 322.1469.

***N*-(3-Isopropenyl-4-methylene-hexa-2,5-dienyl)-4-methyl-benzenesulfonamide (326o)**



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.73 (d, *J* = 8.2 Hz, 2H; H_{Ar}-12), 7.31 (d, *J* = 8.2 Hz, 2H; H_{Ar}-13), 6.34 (dd, *J* = 17.3, 10.3 Hz, 1H; H-5), 5.58 (t, *J* = 7.1 Hz, 1H; H-2), 5.27 (d, *J* = 1.1 Hz, 1H; H-10), 5.03 (d, *J* = 10.3 Hz, 1H; H-6), 4.96 (s, 2H; H-9), 4.92 (d, *J* = 17.3 Hz, 1H; H-6), 4.85 (s, 1H; H-10), 4.25 (bt, *J* = 6.0 Hz, 1H; NH), 3.57 – 3.53 (m, 2H; H-1), 2.43 (s, 3H; H-15), 1.81 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 144.5 (C_q), 143.9 (C_q), 143.6 (C_q), 141.3 (C_q), 138.0 (CH; C-5), 137.3 (C_q), 129.8 (2 x CH_{Ar}; C-13), 127.3 (2 x CH_{Ar}; C-12), 122.6 (CH; C-2), 119.3 (CH_2; C-10), 116.8 (CH_2; C-9), 116.6 (CH_2, C-6), 42.5 (CH_2; C-1), 21.7 (CH_3; C-15), 20.1 (CH_3; C-8). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3093 (C-H_{Alkene}), 3069 (C-H_{Alkene}), 3042 (C-H_{Alkene}), 2926 (C-H_{Alkane}), 2860 (C-H_{Alkane}), 1718 (C=C), 1598, 1451 (C-H_{Alkane}), 1333 (S=O), 1160 (S=O), 1093 (C-N), 816. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{17}H_{22}O_2NS$ $[M+H]^+$: 304.1366. Found: 304.1368.

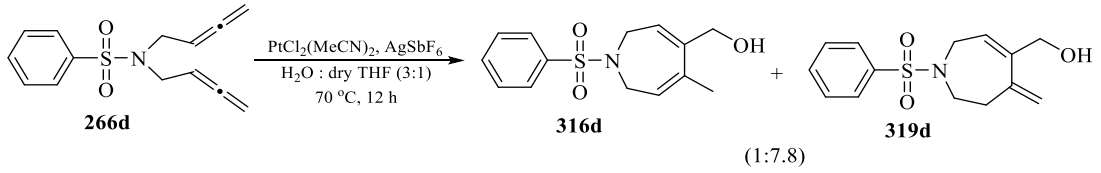
Synthesis of products 315d, 316d and 319d



Procedure 1

From 1,5-bisallene **266d** (106 mg, 0.41 mmol), $PtCl_2(MeCN)_2$ (7 mg, 0.02 mmol), silver hexafluoroantimonate (14 mg, 0.04 mmol), distilled water (225 µl, 10.53 mmol) and 4.3 mL of dry THF. Obtained as inseparable mixture after column chromatography using Hex / EtOAc (20:1) then (5:1) then (1:1) as eluent: **315f**:**316f**:**319f** (2:1:3.8), 60 mg, 0.21 mmol (53%): colourless oil.

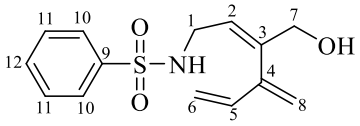
Procedure 2



From 1,5-bisallene **266d** (154 mg, 0.59 mmol), $PtCl_2(MeCN)_2$ (10 mg, 0.03 mmol), silver hexafluoroantimonate (24 mg, 0.07 mmol), distilled water (4.9 mL, 0.27 mmol) and 1.6

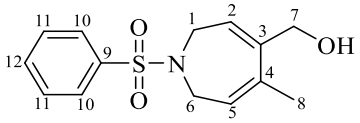
mL of dry THF. Obtained as inseparable mixture after column chromatography using PET / EtOAc (5:1) then (1:1) as eluent: **316d**:**319d** (1:7.8), 86 mg, 0.31 mmol (52%): colourless oil.

***N*-(3-Hydroxymethyl-4-methylene-hexa-2,5-dienyl)-benzenesulfonamide (315d)**



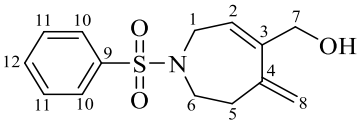
^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.87 – 7.73 (m, 2H; H_{Ar}-10), 7.58 – 7.54 (m, 1H; H_{Ar}-12), 7.51 – 7.44 (m, 2H; H_{Ar}-11), 6.28 (dd, J = 17.3, 10.5 Hz, 1H; H-5), 5.63 (t, J = 7.0 Hz, 1H; H-2), 5.17 (s, 1H; H-8), 5.07 – 5.02 (m, 1H; H-6), 5.01 – 4.98 (m, 1H; H-6), 4.89 (s, 1H; H-8), 4.72 (bt, J = 5.7 Hz, 1H; NH), 4.02 (s, 2H; H-7), 3.53 – 3.40 (m, 2H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 142.7 (C_q; C-9), 140.0 (C_q; C-3 or C-4), 139.0 (C_q; C-3 or C-4), 137.1 (CH; C-5), 132.8 (CH_{Ar}; C-12), 129.2 (2 x CH_{Ar}; C-11), 127.2 (2 x CH_{Ar}; C-10), 122.1 (CH; C-2), 119.0 (CH_2; C-8), 116.6 (CH_2; C-6), 65.7 (CH_2; C-7), 41.6 (CH_2; C-1).

(1-Benzenesulfonyl-5-methylene-2,5,6,7-tetrahydro-1*H*-azepin-4-yl)-methanol (316d)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.82 – 7.79 (m, 2H; H_{Ar}-10), 7.60 – 7.49 (m, 1H; H_{Ar}-12), 7.48 – 7.46 (m, 2H; H_{Ar}-11), 5.87 (t, J = 7.0 Hz, 1H; H-2), 5.71 (tq, J = 7.0, 1.4 Hz, 1H; H-5), 4.13 (s, 2H; H-7), 3.59 (d, J = 7.0 Hz, 2H; H-1), 3.58 (d, J = 7.0 Hz, 2H; H-6), 1.78 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 147.7 (C_q; C-3 or C-4), 142.1 (C_q; C-3 or C-4), 139.1 (C_q; C-9), 132.7 (CH_{Ar}; C-12), 129.2 (2 x CH_{Ar}; C-11), 127.5 (2 x CH_{Ar}; C-10), 124.3 (CH; C-5), 122.3 (CH; C-2), 63.7 (CH_2; C-7), 43.9 (CH_2; C-6), 43.6 (CH_2; C-1), 19.8 (CH_3; C-8).

(1-Benzenesulfonyl-5-methyl-2,7-dihydro-1*H*-azepin-4-yl)-methanol (319d)



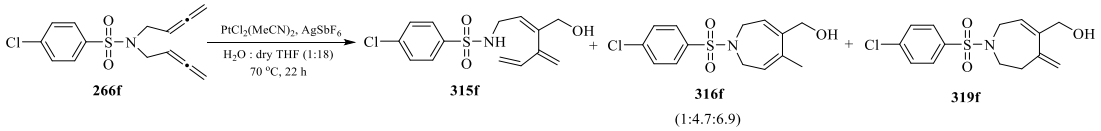
^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.78 – 7.73 (m, 2H; H_{Ar}-10), 7.59 – 7.56 (m, 1H; H_{Ar}-12), 7.49 – 7.43 (m, 2H; H_{Ar}-11), 5.80 (tt, J = 5.0, 0.9 Hz, 1H; H-2), 4.99 (s, 1H; H-8), 4.91 (s, 1H; H-8), 4.08 (d, J = 0.9 Hz, 2H; H-7), 3.99 (d, J = 5.0 Hz, 2H; H-1), 3.47 (t, J = 6.4 Hz, 2H; H-6), 2.49 (t, J = 6.4 Hz, 2H; H-5). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 142.7 (C_q; C-3 or C-4), 142.6 (C_q; C-3 or C-4), 139.3 (C_q; C-9), 132.5 (CH_{Ar}; C-12), 128.9 (2 x CH_{Ar}; C-11),

127.5 (2 x CH_{Ar}; C-10), 124.6 (CH; C-2), 115.2 (CH_2; C-8), 65.1 (CH_2; C-7), 48.8 (CH_2; C-6), 45.0 (CH_2; C-1), 36.3 (CH_2; C-5).

315d, **316d** and **319d** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3518 (O-H), 3064 (C-H_{Alkene}), 2924 (C-H_{Alkane}), 2864 (C-H_{Alkane}), 1606 (C=C), 1447 (C-H_{Alkane}), 1329 (S=O), 1159 (S=O), 1095 (C-N), 1061 (C-O), 903. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{14}H_{18}O_3NS$ $[M+H]^+$: 280.1002. Found: 280.1003.

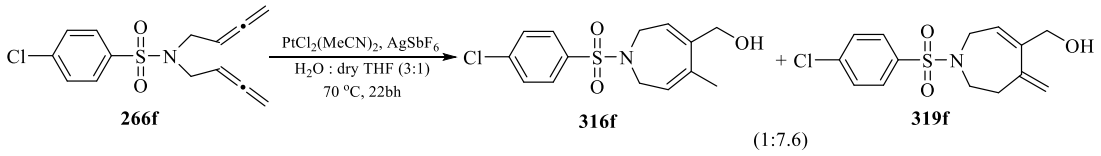
Synthesis of products 315f, 316f and 319f

Procedure 1



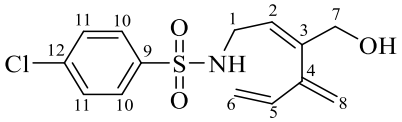
From 1,5-bisallene **266f** (109 mg, 0.37 mmol), $PtCl_2(MeCN)_2$ (6 mg, 0.02 mmol), silver hexafluoroantimonate (13 mg, 0.04 mmol), distilled water (204 µl, 11.33 mmol) and 3.7 mL of dry THF. Obtained as inseparable mixture after column chromatography using Hex / EtOAc (10:1) then (4:1) then (1:1) as eluent: **315f**:**316f**:**319f** (1:4.7:6.9), 40 mg, 0.13 mmol (35%): yellow oil.

Procedure 2



From 1,5-bisallene **266f** (161 mg, 0.59 mmol), $PtCl_2(MeCN)_2$ (10 mg, 0.03 mmol), silver hexafluoroantimonate (23 mg, 0.07 mmol), distilled H_2O (4.5 mL, 0.25 mmol) and 1.5 mL of dry THF. Obtained as inseparable mixture after column chromatography using PET / EtOAc (2:1) then (1:1) as eluent: **316f**:**319f** (1:7.6), 77 mg, 0.25 mmol (46%): yellow oil.

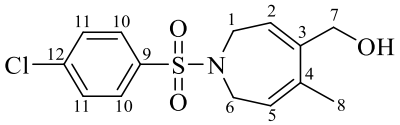
4-Chloro-*N*-(3-hydroxymethyl-4-methylene-hexa-2,5-dienyl)-benzenesulfonamide (315f)



^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.77 (d, J = 8.7 Hz, 2H; H_{Ar}-10), 7.48 (d, J = 8.7 Hz, 2H; H_{Ar}-11), 6.33 (dd, J = 17.3, 10.5 Hz, 1H; H-5), 5.66 (tt, J = 6.9, 1.4 Hz, 1H; H-2), 5.22 (s, 1H; H-8), 5.09 (d, J = 10.5 Hz, 1H; H-6), 5.04 (d, J = 17.3 Hz, 1H; H-6), 5.01$_{(overlap)}$ (s, 1H; H-8), 4.06 (s, 2H; H-7), 3.53 – 3.49 (m, 2H; H-1). *Signal H-8, overlaps with a signal from* **319f**.

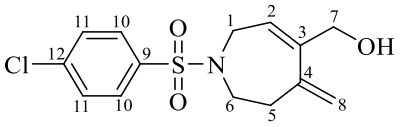
^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 143.4 (C_q), 143.0 (C_q), 139.3 (C_q), 138.5 (C_q), 129.5 (2 x CH_{Ar}; C-11), 128.7 (2 x CH_{Ar}; C-10), 121.9 (CH; C-2), 119.1 (CH_2; C-8), 116.6 (CH_2; C-6), 65.7 (CH_2; C-7), 41.6 (CH_2; C-1).

[1-(4-Chloro-benzenesulfonyl)-5-methyl-2,7-dihydro-1*H*-azepin-4-yl]-methanol (316f)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.74 (d, J = 8.7 Hz, 2H; H_{Ar}-10), 7.49 (d, J = 8.7 Hz, 2H; H_{Ar}-11), 5.91 (t, J = 7.2 Hz, 1H; H-2), 5.75 (tq, J = 7.3, 1.4 Hz, 1H; H-5), 4.16 (s, 2H; H-7), 3.60 (d, J = 7.2 Hz, 2H; H-1), 3.58 (d, J = 7.3 Hz, 2H; H-6), 1.81 (bs, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 147.9 (C_q), 142.4 (C_q), 139.2 (C_q), 129.5 (2 x CH_{Ar}; C-11), 128.9 (2 x CH_{Ar}; C-10), 124.2 (CH; C-5), 122.1 (CH; C-2), 63.8 (CH_2; C-7), 43.8 (CH_2; C-6), 43.6 (CH_2; C-1), 19.8 (CH_3; C-8). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3494 (O-H), 3097 (C-H_{Alkene}), 2923 (C-H_{Alkane}), 2860 (C-H_{Alkane}), 1727 (C=C), 1586, 1336 (S=O), 1162 (S=O), 1093 (C-N), 1064 (C-O), 913, 828. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{14}H_{17}{}^{35}ClO_3NS$ $[M+H]^+$: 314.0612. Found: 314.0616. Calc. for $C_{14}H_{17}{}^{37}ClO_3NS$ $[M+H]^+$: 316.0581. Found: 316.0585.

[1-(4-chloro-benzenesulfonyl)-5-methylene-2,5,6,7-tetrahydro-1*H*-azepin-4-yl]-methanol (319f)

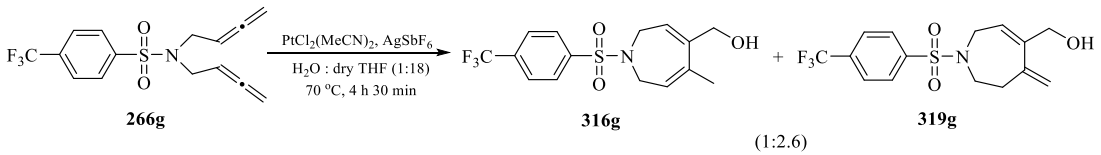


^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.69 (d, J = 8.7 Hz, 2H; H_{Ar}-10), 7.43 (d, J = 8.7 Hz, 2H; H_{Ar}-11), 5.81 (tt, J = 5.2, 1.0 Hz, 1H; H-2), 5.00 (s, 1H; H-8), 4.91 (s, 1H; H-8), 4.11 (d, J = 1.0 Hz, 2H; H-7), 4.01 (d, J = 5.2 Hz, 2H; H-1), 3.46 (t, J = 6.4 Hz, 2H; H-6), 2.50 (t, J = 6.4 Hz, 2H; H-5). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 142.7 (C_q), 142.6 (C_q), 139.0 (C_q), 138.0 (C_q), 129.2 (2 x CH_{Ar}; C-11), 129.0 (2 x CH_{Ar}; C-10), 124.4 (CH; C-2), 115.3 (CH_2; C-8), 65.0 (CH_2; C-7), 48.8 (CH_2; C-6), 45.0 (CH_2; C-1), 36.3 (CH_2; C-5).

315f:**316f**:**319f** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3498 (O-H), 3350 (N-H), 3090 (C-H_{Alkene}), 2924 (C-H_{Alkane}), 2854 (C-H_{Alkane}), 1648 (C=C), 1585, 1335 (S=O), 1161 (S=O), 1093 (C-N), 1052 (C-O), 903, 828. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{14}H_{17}{}^{35}ClO_3NS$ $[M+H]^+$: 314.0612. Found: 314.0616. Calc. for $C_{14}H_{17}{}^{37}ClO_3NS$ $[M+H]^+$: 316.0581. Found: 316.0585.

Synthesis of products 316g and 319g

Procedure 1

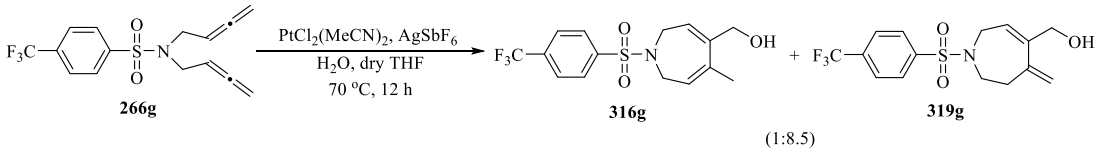


266g **316g** **319g**

(1:2.6)

From 1,5-bisallene **266g** (99 mg, 0.30 mmol), $PtCl_2(MeCN)_2$ (5 mg, 0.015 mmol), silver hexafluoroantimonate (10 mg, 0.03 mmol), distilled water (167 µl, 9.25 mmol) and 3.0 mL of dry THF. Obtained as inseparable mixture after column chromatography using Hex / EtOAc (10:1) then (5:1) then (2:1) as eluent: **316g**:**319g** (1:2.6), 35 mg, 0.10 mmol (34%): yellow solid.

Procedure 2

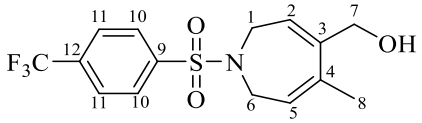


266g **316g** **319g**

(1:8.5)

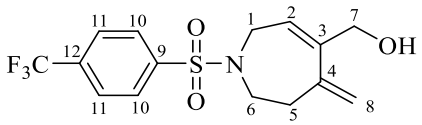
From 1,5-bisallene **266g** (149 mg, 0.45 mmol), $PtCl_2(MeCN)_2$ (8 mg, 0.02 mmol), silver hexafluoroantimonate (19 mg, 0.05 mmol), distilled water (3.8 mL, 0.21 mmol) and 1.3 mL of dry THF. Obtained after column chromatography using PET / EtOAc (1:1) as eluent: **316g**:**319g** (1:8.5), 81 mg, 0.23 mmol (52%): yellow solid.

[5-Methyl-1-(4-trifluoromethyl-benzenesulfonyl)-2,7-dihydro-1*H*-azepin-4-yl]-methanol (316g)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 7.94 (d, J = 8.2 Hz, 2H; H_{Ar}-10), 7.79 (d, J = 8.2 Hz, 2H; H_{Ar}-11), 5.92 (t, J = 7.0 Hz, 1H; H-2), 5.76 (tq, J = 7.1, 1.5 Hz, 1H; H-5), 4.18 (s, 2H; H-7), 3.64 (d, J = 7.0 Hz, 2H; H-1), 3.62 (d, J = 7.1 Hz, 2H; H-6), 1.82 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 147.9 (C_q), 143.0 (C_q), 142.5 (C_q), 128.0 (2 x CH_{Ar}; C-10), 127.3 (q, $J_{C\text{-}F}$ = 238.0 Hz, C_q; CF_3), 126.4 (q, $J_{C\text{-}F}$ = 3.7 Hz, 2 x CH_{Ar}; C-11), 124.1 (CH; C-5), 122.0 (CH; C-2), 63.8 (CH_2; C-7), 43.8 (CH_2; C-1), 43.6 (CH_2; C-6), 19.9 (CH_3; C-8). *C_q-12 could not be identified.* 19F NMR (471 MHz, CDCl3, 25 °C) δ = - 63.00. IR (Film, cm-1): ν̃ = 3522 (O-H), 3104 (C-H_{Alkene}), 3059 (C-H_{Alkene}), 2924 (C-H_{Alkane}), 2860 (C-H_{Alkane}), 1727 (C=C), 1323 (S=O), 1165 (S=O), 1132 (C-F), 1058 (C-O), 920, 844. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{15}H_{17}O_3NSF_3$ $[M+H]^+$: 348.0876. Found: 348.0876.

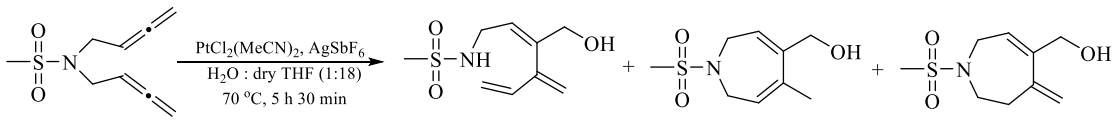
[5-Methylene-1-(4-trifluoromethyl-benzenesulfonyl)-2,5,6,7-tetrahydro-1*H*-azepin-4-yl]-methanol (319g)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.87 (d, J = 8.2 Hz, 2H; H_{Ar}-10), 7.70 (d, J = 8.2 Hz, 2H; H_{Ar}-11), 5.80 (t, J = 4.6 Hz, 1H; H-2), 4.94 (s, 1H; H-8), 4.82 (s, 1H; H-8), 4.05$_{(Overlap)}$ (s, 2H; H-7), 4.04$_{(overlap)}$ (d, 2H; H-1), 3.48 (t, J = 6.4 Hz, 2H; H-6), 2.49 (t, J = 6.4 Hz, 2H; H-5). *J coupling from the doublet at 4.04 ppm could not be obtained as it is overlapping with H-7.* ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 143.0 (C_q), 142.7 (C_q), 142.4 (C_q), 134.1 (q, J_{C-F} = 33.0 Hz, C_q; C-12), 128.0 (2 x CH_{Ar}; C-10), 126.0 (q, J_{C-F} = 3.7 Hz, 2 x CH_{Ar}; C-11), 124.1 (CH; C-2), 123.4 (q, J_{C-F} = 272.9 Hz, C_q; CF_3), 115.3 (CH_2; C-8), 64.7 (CH_2; C-7), 48.8 (CH_2; C-6), 45.0 (CH_2; C-1), 36.3 (CH_2; C-5). ^{19}F NMR (471 MHz, $CDCl_3$, 25 ^{o}C) δ = - 63.07. IR (Film, cm-1): $\tilde{\nu}$ = 3522 (O-H), 3107 (C-H_{Alkene}), 3063 (C-H_{Alkene}), 2926 (C-H_{Alkane}), 2860 (C-H_{Alkane}), 1720 (C=C), 1404, 1324 (S=O), 1165 (S=O), 1133 (C-F), 1063 (C-O), 905, 844. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{15}H_{20}O_3N_2SF_3$ $[M+NH_4]^+$: 365.1141. Found: 365.1146. M.P. of **316g** and **319g** as inseparable mixture = 104 – 106 ^{o}C.

Synthesis of products 315i, 316i amd 319i

Procedure 1

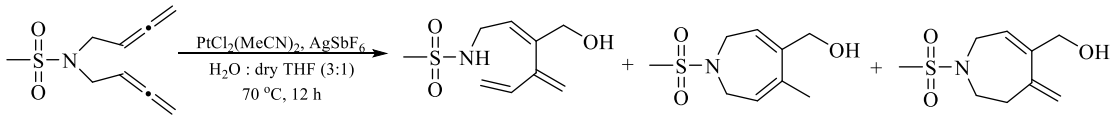


266i **315i** **316i** **319i**

(3:1:3)

From 1,5-bisallene **266i** (180 mg, 0.91 mmol), $PtCl_2(MeCN)_2$ (16 mg, 0.04 mmol), silver hexafluoroantimonate (31 mg, 0.09 mmol), distilled water (504 µl, 27.90 mmol) and 9.1 mL of dry THF. Obtained as inseparable mixture after column chromatography using EtOAc / DCM (1:1) as eluent: **315i**:**316i**:**319i** (3:1:3), 101 mg, 0.47 mmol (52%): yellow-orange oil.

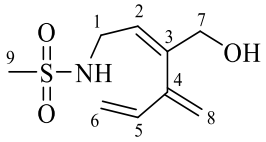
Procedure 2



266i **315i** **316i** (2.1:1:8.5) **319i**

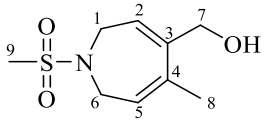
From 1,5-bisallene **266i** (151 mg, 0.76 mmol), $PtCl_2(MeCN)_2$ (13 mg, 0.04 mmol), silver hexafluoroantimonate (31 mg, 0.07 mmol), distilled water (6.3 mL, 0.35 mmol) and 2.1 mL of dry THF. Obtained after column chromatography using PET / EtOAc (1:1) as eluent: **315i**:**316i**:**319i** (2.1:1:8.5), 51 mg, 0.24 mmol (31%): yellow-orange oil.

***N*-(3-hydroxymethyl-4-methylene-hexa-2,5-dienyl)-methanesulfonamide (315i)**



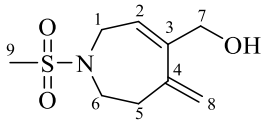
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 6.41 (dd, J = 17.4, 10.6 Hz, 1H; H-5), 5.78 (t, J = 6.8 Hz, 1H; H-2), 5.31 (s, 1H; H-8), 5.17 (d, J = 10.6 Hz, 1H; H-6), 5.13 (d, J = 17.4 Hz, 1H; H-6), 5.04 (s, 1H; H-8), 4.15 – 4.12 (m, 2H; H-7), 3.68 (d, J = 6.8 Hz, 2H; H-1), 2.94 (s, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 142.8 (C_q; C-4), 142.8 (C_q; C-3), 137.2 (CH; C-5), 122.3 (CH; C-2), 119.1 (CH_2; C-8), 116.7 (CH_2; C-6), 65.7 (CH_2; C-7), 41.7 (CH_2; C-1), 40.6 (CH_3; C-9).

(1-Methanesulfonyl-5-methyl-2,7-dihydro-1*H*-azepin-4-yl)-methanol (316i)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 6.13 (t, J = 7.0 Hz, 1H; H-2), 5.98 (tq, J = 7.0, 1.5 Hz, 1H; H-5), 4.27 (s, 2H; H-7), 3.63 (d, J = 7.0 Hz, 2H; H-1), 3.60 (d, J = 7.0 Hz, 2H; H-6), 2.81 (s, 3H; H-9), 1.93 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 148.1 (C_q; C-3), 142.6 (C_q; C-4), 124.5 (CH; C-5), 122.5 (CH; C-2), 63.8 (CH_2; C-7), 43.6 (CH_2; C-6), 43.4 (CH_2; C-1), 37.2 (CH_3; C-9), 20.0 (CH_3; C-8).

(1-methanesulfonyl-5-methylene-2,5,6,7-tetrahydro-1*H*-azepin-4-yl)-methanol (319i)

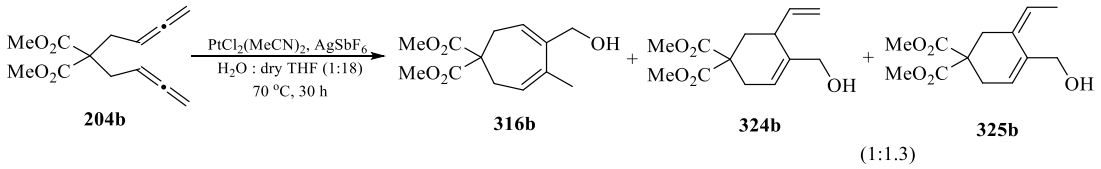


^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 5.92 (t, J = 5.2 Hz, 1H; H-2), 5.17 (s, 2H; H-8), 4.26 – 4.24 (m, 2H; H-7), 4.05 (d, J = 5.2 Hz, 2H; H-1), 3.54 (t, J = 6.5 Hz, 2H; H-6), 2.79 (s, 3H; H-9), 2.61 (t, J = 6.5 Hz, 2H; H-5). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 143.7 (C_q; C-3), 143.3 (C_q; C-4), 125.3 (CH; C-2), 115.5 (CH_2; C-8), 65.1 (CH_2; C-7), 48.7 (CH_2; C-6), 44.5 (CH_2; C-1), 38.5 (CH_3; C-9), 36.7 (CH_2; C-5).

315i:**316i**:**319i** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3512 (O-H), 3293 (N-H), 3088 (C-H_{Alkene}), 3011 (C-H_{Alkene}), 2929 (C-H_{Alkane}), 2870 (C-H_{Alkane}), 1709 (C=C), 1585, 1411 (C-H_{Alkane}), 1319 (S=O), 1147 (S=O), 1061 (C-O), 964. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_9H_{16}O_3NS$ $[M+H]^+$: 218.0845. Found: 218.0844. Calc. for $C_9H_{19}O_3N_2S$ $[M+NH_4]^+$: 235.1111 Found: 235.1111.

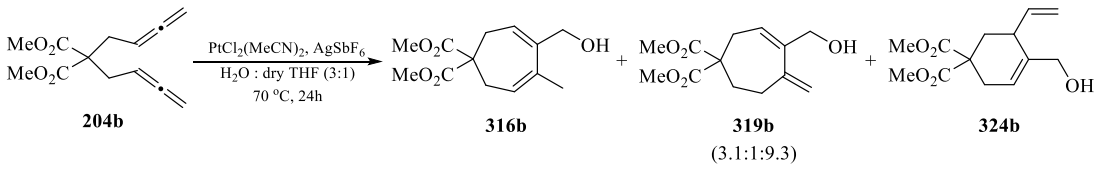
Synthesis of products 316b, 319b, 324b and 325b

Procedure 1



From 1,5-bisallene **204b** (153 mg, 0.65 mmol), $PtCl_2(MeCN)_2$ (11 mg, 0.03 mmol), silver hexafluoroantimonate (22 mg, 0.06 mmol), distilled water (359 µl, 19.91 mmol) and 6.5 mL of dry THF. Obtained after column chromatography using PET / EtOAc (10:1) then (7:1) then (2:1) as eluent: **316b**, 15 mg, 0.06 mmol (9%): colourless oil; and **324b**:**325b** (1:1.3) as inseparable mixture, 18 mg, 0.07 mmol (11%): colourless oil.

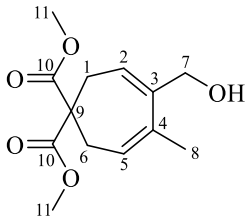
Procedure 2



From 1,5-bisallene **204b** (162 mg, 0.78 mmol), $PtCl_2(MeCN)_2$ (13 mg, 0.04 mmol), silver hexafluoroantimonate (32 mg, 0.09 mmol), distilled water (6.4 mL, 0.35 mmol) and 2.1 mL of dry THF. Obtained as inseparable mixture after column chromatography using PET /

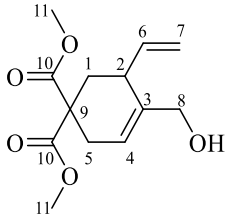
EtOAc (10:1) then (1:1) as eluent: **316b**:**319b**:**324b** (3.1:1:9.3), 11 mg, 0.04 mmol (6%): colourless oil.

4-Hydroxymethyl-5-methyl-cyclohepta-3,5-diene-1,1-dicarboxylic acid dimethyl ester (316b)



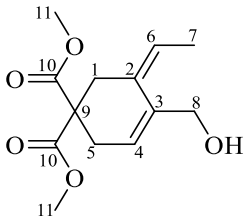
^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 6.16 (t, *J* = 6.8 Hz, 1H; H-2), 6.03 (tq, *J* = 6.8, 1.4 Hz, 1H; H-5), 4.19 (s, 2H; H-7), 3.72 (s, 6H; H-11), 2.42 (d, *J* = 6.8 Hz, 2H; H-1), 2.40 (d, *J* = 6.8 Hz, 2H; H-6), 1.85 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 172.1 (2 x C_q; C-10), 144.7 (C_q; C-3), 138.6 (C_q; C-4), 127.8 (CH; C-2 or C-5), 126.8 (CH; C-2 or C-5), 71.7 (CH_2; C-7), 64.7 (C_q; C-9), 52.8 (2 x CH_3; C-11), 32.1 (CH_2; C-1 or C-6), 31.9 (CH; C-1 or C-6), 20.2 (CH_3; C-8). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3480 (O-H), 2958 (C-H_{Alkane}), 2931 (C-H_{Alkane}), 1732 (C=O), 1442, 1270 (C-O), 1250, 1085 (C-O_{OH}). HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{13}H_{19}O_5$ $[M+H]^+$: 255.1227. Found: 255.1229. Calc. for $C_{13}H_{22}O_5N$ $[M+NH_4]^+$: 272.1492 Found: 272.1495.

4-Hydroxymethyl-5-vinyl-cyclohex-3-ene-1,1-dicarboxylic acid dimethyl ester (324b)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 5.72 – 5.68 (m, 1H; H-4), 5.58 – 5.48 (m, 1H; H-6), 5.10 (ddd, *J* = 17.1, 1.5, 0.8 Hz, 1H; H-7), 5.04 (dd, *J* = 10.0, 1.5 Hz, 1H; H-7), 3.97 – 3.88 (m, 2H; H-8), 3.65 (s, 6H; H-11), 2.96 – 2.87 (m, 1H; H-2), 2.71 – 2.66 (m, 1H; H-5), 2.47 – 2.40 (m, 1H; H-5), 2.37 (ddd, *J* = 13.5, 6.1, 2.0 Hz, 1H; H-1), 1.84 (dd, *J* = 13.5, 9.3 Hz, 1H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 172.3 (2 x C_q; C-10), 139.8 (CH; C-6), 138.1 (C_q; C-3), 122.6 (CH; C-4), 117.1 (CH_2; C-7), 65.2 (CH_2; C-8), 54.0 (C_q; C-9), 52.8 (2 x CH_3; C-11), 39.4 (CH; C-2), 34.5 (CH_2; C-1), 30.5 (CH_2; C-5).

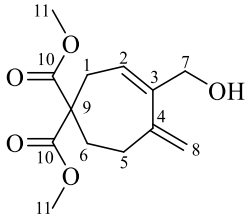
5-Ethylidene-4-hydroxymethyl-cyclohex-3-ene-1,1-dicarboxylic acid dimethyl ester (325b)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.71 – 5.68 (m, 1H; H-4), 5.66 (q, *J* = 7.0 Hz, 1H; H-6), 4.18 (d, *J* = 1.0 Hz, 2H; H-8), 3.64 (s, 6H; H-11), 2.80 (s, 2H; H-1), 2.66 (d, *J* = 3.8 Hz, 2H; H-5), 1.70 (d, *J* = 7.0 Hz, 3H; H-7). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 171.5 (2 x C_q; C-10), 138.1 (C_q; C-3), 121.3 (CH; C-6), 120.9 (CH; C-4), 63.8 (CH_2; C-8), 52.9 (2 x CH_3; C-11), 31.3 (CH_2; C-5), 30.9 (CH_2; C-1), 13.3 (CH_3; C-7). *C_q-3 and C_q-9 could not be identified.*

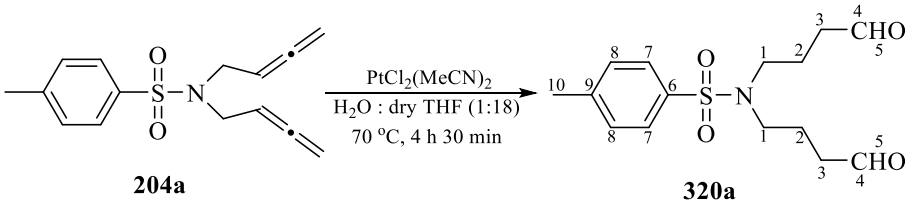
324b and **325b** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3488 (O-H), 2960 (C-H_{Alkane}), 2925 (C-H_{Alkane}), 2853 (C-H_{Alkane}), 1730 (C=O), 1439, 1274 (C-O), 1271, 1200, 1086 (C-O_{OH}). HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{13}H_{22}O_5N$ $[M+NH_4]^+$: 272.1494 Found: 272.1495.

4-Hydroxymethyl-5-methylene-cyclohept-3-ene-1,1-dicarboxylic acid dimethyl ester (319b)



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 5.80 (t, *J* = 6.7 Hz, 1H; H-2), 5.07 (s, 1H; H-8), 5.02 (s, 1H; H-8), 4.19 (s, 2H; H-7), 3.71 (s, 6H; H-11), 2.75 (d, *J* = 6.7 Hz, 2H; H-1), 2.51 – 2.48 (m, 2H; H-6), 2.28 – 2.24 (m, 2H; H-5). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 172.2 (2 x C_q; C-10), 145.9 (C_q; C-3), 142.6 (C_q; C-4), 123.9 (CH; C-2), 113.5 (CH_2; C-8), 66.2 (CH_2; C-7), 56.9 (C_q; C-9), 52.8 (2 x CH_3; C-11), 32.8 (CH_2; C-1), 32.5(CH_2; C-6), 31.1 (CH_2; C-5). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3463 (O-H), 2960 (C-H_{Alkane}), 2928 (C-H_{Alkane}), 1730 (C=O), 1270 (C-O), 1262, 1085 (C-O_{OH}). HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{13}H_{19}O_5$ $[M+H]^+$: 255.1228. Found: 255.1229. Calc. for $C_{13}H_{22}O_5N$ $[M+NH_4]^+$: 272.1494 Found: 272.1495.

Synthesis of product 320a

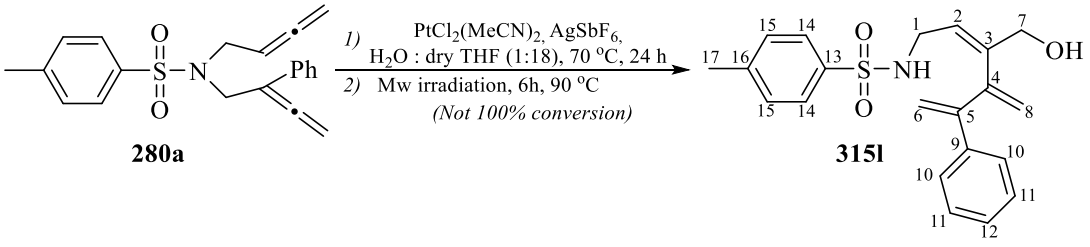


204a **320a**

Procedure 1

To a microwave vial was added $PtCl_2(MeCN)_2$ (2 mg, 0.004 mmol, 0.05 Eq.). Then the vial was closed with a stopper and flushed with N_2 during 3 min. A small amount of dry THF was added and the solution was stirred at room temperature for a few min. The 1,5-bisallene **204a** (23 mg, 0.08 mmol, 1.0 Eq., 0.091 M – absolute concentration) dissolved in dry THF was added, then distilled water (THF:H_2O, 18:1). Then the vial was sealed and placed in a pre-heated oil bath at 70 °C until completed conversion, following the reaction by TLC. The crude was filtered through a pad of celite / $MgSO_4$ anhydrous (1:2), washed with dichloromethane and concentrated under vacuum. Obtained after column chromatography using PET / EtOAc (7:1) as eluent: **320a**, 24 mg, 0.08 mmol (91%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 9.77 (t, J = 0.8 Hz, 2H; H-5), 7.68 – 7.63 (m, 2H; H_{Ar}-7), 7.32 – 7.27 (m, 2H; H_{Ar}-8), 3.14 – 3.09 (m, 4H; H-1), 2.54 (td, J = 7.0, 0.8 Hz, 4H; H-3), 2.42 (s, 3H; H-10), 1.84 (p, J = 7.0 Hz, 4H; H-2). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 201.3 (2 x C_q; C-4), 143.6 (C_q; C-9), 136.4 (C_q; C-6), 129.9 (2 x CH_{Ar}; C-8), 127.2 (2 x CH_{Ar}; C-7), 48.1 (2 x CH_2; C-1), 40.8 (2 x CH_2; C-3), 21.6 (CH_3; C-10), 21.4 (2 x CH_2; C-2). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3433, 2922 (C-H_{Alkane}), 2851(C-H_{Alkane}), 2729 (C-$H_{Aldehyde}$), 1717 (C=O), 1650 (C=C), 1454 (C-H_{Alkane}), 1334 (S=O), 1157 (S=O), 1089 (C-N). HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{15}H_{22}O_4NS$ $[M+H]^+$: 312.1264. Found: 312.1268.

Synthesis of product 315l



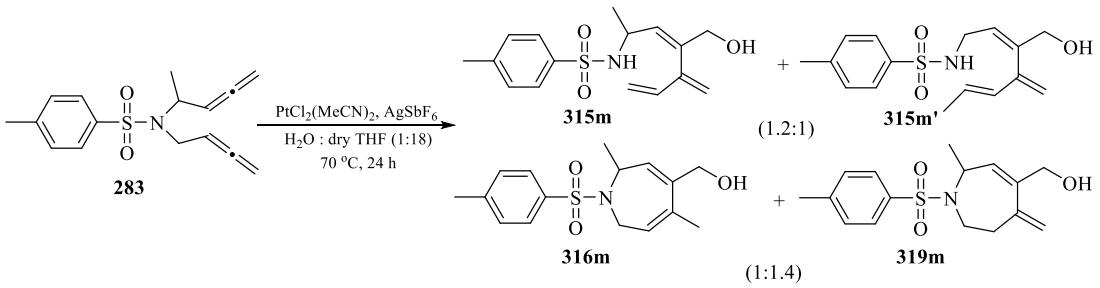
280a **315l**

Procedure 1 (under Mw irradiation)

From 1,5-bisallene **280a** (140 mg, 0.40 mmol), $PtCl_2(MeCN)_2$ (7 mg, 0.02 mmol), silver hexafluoroantimonate (14 mg, 0.04 mmol), distilled water (222 µl, 12.30 mmol) and 4.0 mL of dry THF. Obtained after column chromatography using PET / EtOAc (4:1) as eluent:

315l, 11 mg, 0.03 mmol (8%): yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.73 (d, J = 8.2 Hz, 2H; H_{Ar}-14), 7.33 – 7.26 (m, 5H; H_{Ar}), 7.17 – 7.13 (m, 2H; H_{Ar}), 5.65 (t, J = 6.8 Hz, 1H; H-2), 5.17 (s, 1H; H-6 or H-8), 5.14 (s, 1H; H-6 or H-8), 5.09 (s, 1H; H-6 or H-8), 5.02 (s, 1H; H-6 or H-8), 4.54 (bt, J = 5.9 Hz, 1H; NH), 4.12 (s, 2H; H-7), 3.64 (t, J = 6.8 Hz, 2H; H-1), 2.41 (s, 3H; H-17). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 148.6 (C_q), 144.7 (C_q), 144.5 (C_q), 140.3 (C_q), 136.9 (C_q), 129.8 (CH_{Ar}), 128.6 (2 x CH_{Ar}), 128.2 (CH_{Ar}), 127.3 (2 x CH_{Ar}; C-14), 122.5 (CH; C-2), 119.7 (CH_2; C-8 or C-6), 116.8 (CH_2; C-8 or C-6), 65.9 (CH_2; C-7), 41.8 (CH_2; C-1), 21.7 (CH_3; C-17). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3523 (O-H), 3280 (N-H), 3087 (C-H_{Alkene}), 3057 (C-H_{Alkene}), 2929 (C-H_{Alkane}), 2854 (C-H_{Alkane}), 1690 (C=C), 1493, 1327 (S=O), 1160 (S=O), 1093 (C-N), 1051 (C-O), 910. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{21}H_{24}O_3NS$ $[M+H]^+$: 370.1471 Found: 370.1473.

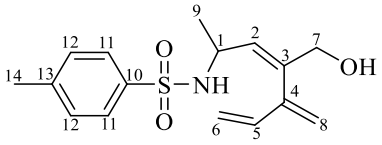
Synthesis of products 315m, 315m', 316m and 319m



Procedure 1

From 1,5-bisallene **283** (132 mg, 0.46 mmol), $PtCl_2(MeCN)_2$ (8 mg, 0.02 mmol), silver hexafluoroantimonate (16 mg, 0.05 mmol), distilled water (253 µl, 14.03 mmol) and 4.6 mL of dry THF. Obtained after column chromatography using PET / EtOAc (7:1) then (5:1) then (2:1) as eluent: **315m**:**315m'**, (1.2:1) as inseparable mixture, 31 mg, 0.10 mmol (22%): yellow oil; and **316m**:**319m** (1:1.4) as inseparable mixture, 30 mg, 0.10 mmol (21%): yellow oil.

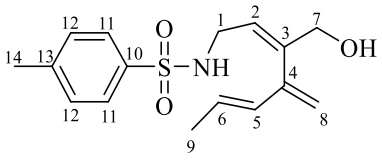
***N*-(3-Hydroxymethyl-1-methyl-4-methylene-hexa-2,5-dienyl)-4-methyl-benzenesulfonamide (315m)**



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.74 – 7.71 (m, 2H; H_{Ar}-11), 7.31 – 7.28 (m, 2H; H_{Ar}-12), 6.26 (dd, J = 17.4, 10.5 Hz, 1H; H-5), 5.51 – 5.47 (m, 1H; H-2), 5.13 (d, J = 1.0 Hz, 1H; H-8), 5.03 (d, J = 10.5 Hz, 1H; H-6), 5.00 (d, J = 17.4 Hz, 1H; H-6), 4.81 (s, 1H; H-8), 4.44

(bt, *J* = 5.9 Hz, 1H; NH), 4.02 (d, *J* = 1.2 Hz, 2H; H-7), 3.95 – 3.87 (m, 1H; H-1), 2.43 (s, 3H; H-14), 1.15 (d, *J* = 6.6 Hz, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 143.8 (C_q), 143.4 (C_q), 139.8 (C_q), 138.0 (C_q), 136.9 (CH; C-5), 129.6 (2 x CH_{Ar}; C-12), 128.7 (CH; C-2), 127.3 (2 x CH_{Ar}; C-11), 119.0 (CH_2; C-8), 116.8 (CH_2; C-6), 65.9 (CH_2; C-7), 48.7 (CH; C-1), 22.9 (CH_3; C-9), 21.7 (CH_3; C-14).

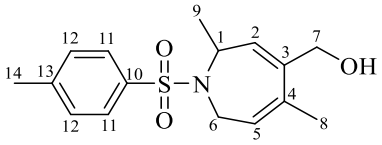
***N*-(3-hydroxymethyl-4-methylene-hepta-2,5-dienyl)-4-methyl-benzenesulfonamide (315m')**



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.71 – 7.68 (m, 2H; H_{Ar}-11), 7.28 – 7.25 (m, 2H; H_{Ar}-12), 6.01 (dq, *J* = 15.6, 1.6 Hz, 1H; H-5), 5.59 (tt, *J* = 6.9, 1.5 Hz, 1H; H-2), 5.53 (q, *J* = 6.9 Hz, 1H; H-6), 5.04 (s, 1H; H-8), 4.73 (s, 1H; H-8), 4.54 (t, *J* = 5.8 Hz, 1H; NH), 3.99 – 3.96 (m, 2H; H-7), 3.52 – 3.48 (m, 2H; H-1), 2.42 (s, 3H; H-14), 1.71 (dd, *J* = 6.9, 1.6 Hz, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 143.6 (C_q), 143.4 (C_q), 143.3 (C_q), 137.2 (C_q), 131.7 (CH; C-5), 129.8 (2 x CH_{Ar}; C-12), 128.7 (CH; C-6), 127.4 (2 x CH_{Ar}; C-11), 121.9 (CH; C-2), 116.0 (CH; C-8), 65.8 (CH_2; C-7), 41.6 (CH_2; C-1), 21.6 (CH_3; C-14), 18.2 (CH_3; C-9).

315m and **315m'** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3567 (O-H), 3334 (N-H), 2921 (C-H_{Alkane}), 2851 (C-H_{Alkane}), 1740 (C=C), 1648 (N-$H_{(Bend)}$), 1538, 1459, 1370 (S=O), 1164 (S=O), 1051 (C-O) . HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{16}H_{22}O_3NS$ $[M+H]^+$: 308.1316. Found: 308.1318.

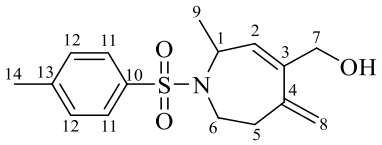
[2,5-Dimethyl-1-(toluene-4-sulfonyl)-2,7-dihydro-1*H*-azepin-4-yl]-methanol (316m)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.67 – 7.62 (m, 2H; H_{Ar}-11), 7.26 – 7.21 (m, 2H; H_{Ar}-12), 5.82 (d, *J* = 6.1 Hz, 1H; H-2), 5.83 – 5.79 (m, 1H; H-5), 4.50 – 4.42 (m, 1H; H-1), 4.04 (s, 2H; H-7), 3.74 (dd, *J* = 14.5, 6.5 Hz, 1H; H-6), 3.68 (dd, *J* = 14.5, 6.7 Hz, 1H; H-6), 2.40 (s, 3H; H-14), 1.70 (s, 3H; H-8), 1.32 (d, *J* = 6.9 Hz, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 140.3 (C_q; C-3), 138.2 (C_q; C-4), 137.7 (C_{qAr}), 131.4 (CH; C-2), 129.6 (2 x CH_{Ar};

C-12), 127.5 (2 x CH_{Ar}; C-11), 127.3 (CH; C-5), 66.0 (CH_2; C-7), 53.0 (CH; C-1), 42.7 (CH_2; C-6), 23.1 (CH_3; C-9), 21.6 (CH_3; C-14), 20.5 (CH_3; C-8).

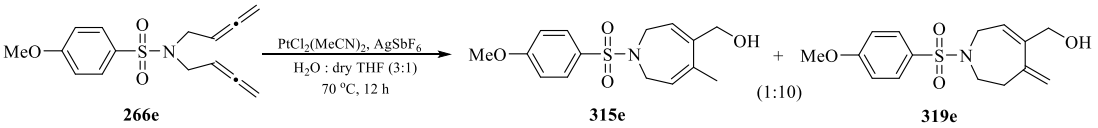
[2-methyl-5-methylene-1-(toluene-4-sulfonyl)-2,5,6,7-tetrahydro-1*H*-azepin-4-yl]-methanol (319m)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.67 – 7.63 (m, 2H; H_{Ar}-11), 7.26 – 7.21 (m, 2H; H_{Ar}-12), 5.63 (d, *J* = 5.8 Hz, 1H; H-2), 4.96 (s, 1H; H-8), 4.88 (s, 1H; H-8), 4.84 – 4.77 (m, 1H; H-1), 4.12 (d, *J* = 13.5 Hz, 1H; H-7), 4.08 (d, *J* = 13.5 Hz, 1H; H-7), 3.90 – 3.82 (m, 1H; H-6), 3.31 (dt, *J* = 13.6, 5.7 Hz, 1H; H-6), 2.51 – 2.44 (m, 2H; H-5), 2.40 (s, 3H; H-14), 1.21 (d, *J* = 7.1 Hz, 3H; H-9). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 143.1 (C_q; C-13), 142.6 (C_q; C-3), 140.0 (C_q; C-4), 138.0 (C_q; C-10), 129.5 (2 x CH_{Ar}; C-12), 129.1 (CH; C-2), 127.4 (2 x CH_{Ar}; C-11), 115.2 (CH_2; C-8), 66.2 (CH_2; C-7), 52.4 (CH; C-1), 43.1 (CH_2; C-6), 37.8 (CH_2; C-5), 21.6 (CH_3; C-14), 18.3 (CH_3; C-9).

316m and **319m** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3517 (O-H), 2973 (C-H_{Alkane}), 2921 (C-H_{Alkane}), 2852 (C-H_{Alkane}), 1597 (C=C), 1451 (C-H_{Alkane}), 1329 (S=O), 1155 (S=O), 1095 (C-N), 1051 (C-O), 976, 815. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{16}H_{25}O_3N_2S$ $[M+NH_4]^+$: 325.1580. Found: 325.1582. Calc. for $C_{16}H_{22}O_3NS$ $[M+H]^+$: 308.1315. Found: 308.1317.

Synthesis of products 315e and 319e

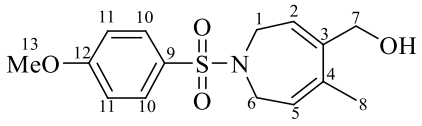


266e **315e** **319e**

Procedure 2

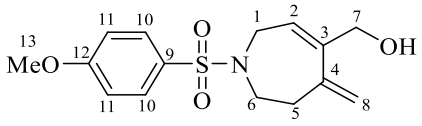
From 1,5-bisallene **266e** (160 mg, 0.55 mmol), $PtCl_2(MeCN)_2$ (9 mg, 0.03 mmol), silver hexafluoroantimonate (23 mg, 0.07 mmol), distilled water (4.5 mL, 0.25 mmol) and 1.5 mL of dry THF. Obtained as inseparable mixture after column chromatography using PET / EtOAc (1:1) as eluent: **315e**:**319e** (1:10), 71 mg, 0.23 mmol (42%): yellow oil.

[1-(4-Methoxy-benzenesulfonyl)-5-methyl-2,7-dihydro-1*H*-azepin-4-yl]-methanol (315e)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.74 – 7.70 (m, 2H; H_{Ar}-10), 6.99 – 6.95 (m, 2H; H_{Ar}-11), 5.88 (t, *J* = 7.0 Hz, 1H; H-2), 5.73 (tq, *J* = 7.0, 1.4 Hz, 1H; H-5), 4.13 (s, 2H; H-7), 3.86 (s, 3H; H-13), 3.56 (d, *J* = 7.0 Hz, 2H; H-1), 3.55 (d, *J* = 7.0 Hz, 2H; H-6), 1.79 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 162.9 (C_q; C-12), 147.7 (C_q; C-3), 142.1 (C_q; C-4), 130.7 (C_q; C-9), 129.6 (2 x CH_{Ar}; C-l0), 124.5 (CH; C-5), 122.5 (CH; C-2), 114.4 (2 x CH_{Ar}; C-ll), 63.7 (CH_2; C-7), 55.8 (CH_3; C-l3), 43.8 (CH_2; C-6), 43.5 (CH_2; C-l), 19.8 (CH_3; C-8).

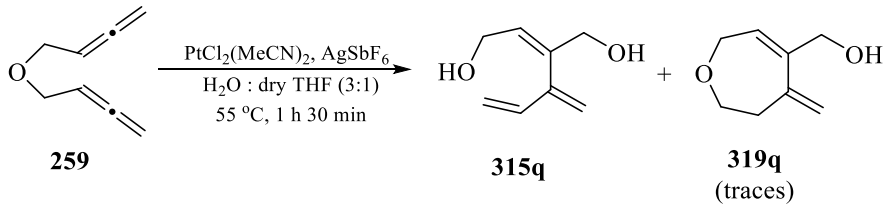
[1-(4-methoxy-benzenesulfonyl)-5-methylene-2,5,6,7-tetrahydro-1*H*-azepin-4-yl]-methanol (319e)



^{1}H NMR (500 MHz, $CDCl_3$, 25 ºC) δ = 7.70 – 7.66 (m, 2H; H_{Ar}-10), 6.94 – 6.90 (m, 2H; H_{Ar}-11), 5.80 (t, *J* = 5.0 Hz, 1H; H-2), 4.99 (s, 1H; H-8), 4.94 (s, 1H; H-8), 4.11 (s, 2H; H-7), 3.94 (d, *J* = 5.0 Hz, 2H; H-1), 3.84 (s, 3H; H-13), 3.42 (t, *J* = 6.4 Hz, 2H; H-6), 2.48 (t, *J* = 6.4 Hz, 2H; H-5). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ºC) δ = 162.9 (C_q; C-12), 142.8 (C_q; C-3 or C-4), 142.6 (C_q; C-3 or C-4), 130.9 (C_q; C-9), 129.6 (2 x CH_{Ar}; C-10), 124.6 (CH; C-2), 115.0 (CH_2; C-8), 114.1 (2 x CH_{Ar}; C-11), 65.2 (CH_2; C-7), 55.7 (CH_3; C-13), 48.7 (CH_2; C-6), 45.0 (CH_2; C-1), 36.3 (CH_2; C-5).

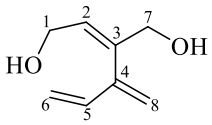
316e and **319e** as inseparable mixture. IR (Film, cm^{-1}): $\tilde{\nu}$ = 3520 (O-H), 3096 (C-H_{Alkene}), 3076 (C-H_{Alkene}), 2927 (C-H_{Alkane}), 2845 (C-H_{Alkane}), 1596 (C=C), 1498, 1332 (S=O), 1260 (C-O), 1154 (S=O), 1096 (C-N), 1063 (C-O), 899. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{15}H_{20}O_4NS$ $[M+H]^+$: 310.1108. Found: 310.1112.

Synthesis of 315q and 319q (traces)



Procedure 2

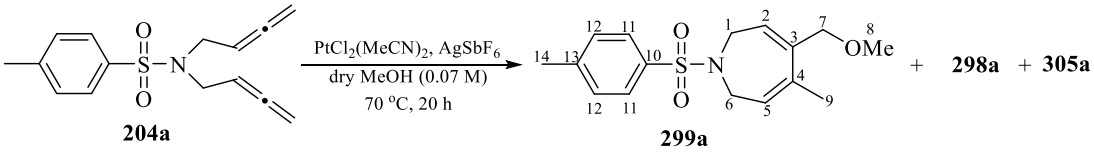
From 1,5-bisallene **259** (188 mg, 1.54 mmol), $PtCl_2(MeCN)_2$ (27 mg, 0.08 mmol), silver hexafluoroantimonate (63 mg, 0.18 mmol), distilled water (12.7 mL, 0.70 mmol) and 4.2 mL of dry THF. Obtained after column chromatography using DCM / Et_2O (1:1) as eluent: **315q**, 29 mg, 0.21 mmol (13%): yellow oil; and traces of **319q**.



^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 6.43 (dd, *J* = 17.4, 10.5 Hz, 1H; H-5), 5.91 (t, *J* = 6.7 Hz, 1H; H-2), 5.30 (s, 1H; H-8), 5.16 (d, *J* = 17.4 Hz, 1H; H-6), 5.15 (d, *J* = 10.5 Hz, 1H; H-6), 5.03 (s, 1H; H-8), 4.14 (s, 2H; H-7), 4.08 (d, *J* = 6.7 Hz, 2H; H-1). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C) δ = 144.0 (C_q; C-4), 141.0 (C_q; C-3), 137.5 (CH; C-5), 126.7 (CH; C-2), 118.9 (CH_2; C-8), 116.6 (CH_2; C-6), 66.2 (CH_2; C-7), 60.1 (CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3349 (O-H), 3087 (C-H_{Alkene}), 2925 (C-H_{Alkane}), 2856 (C-H_{Alkane}), 1738 (C=C), 1585 (N-$H_{(Bend)}$), 1432, 1364, 1231, 1086 (C-O_{OH}), 993, 907. HRMS (FTMS + p APCI (DCM)): Calc. for $C_8H_{13}O_2$ $[M+H]^+$: 141.0910. Found: 141.0906.

*Product **319q** could not be fully characterised by ^{1}H and ^{13}C NMR due to the low concentration of the product in the crude of reaction.*

Synthesis of 4-methoxymethyl-5-methyl-1-(toluene-4-sulfonyl)-2,7-dihydro-1*H*-azepine (299a)

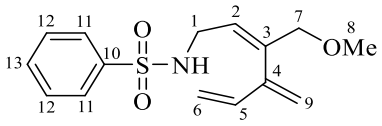


To a flame-dried Schlenk tube, were added $PtCl_2(MeCN)_2$ (6 mg, 0.02 mmol, 0.05 Eq.) and silver hexafluoroantimonate (12 mg, 0.04 mmol, 0.1 Eq.) under N_2 flow. Then, dry MeOH (2.0 mL) was added and the solution was stirred at room temperature for a few min to preform the cationic complex. 1,5-Bisallene **204a** (98 mg, 0.36 mmol, 1.0 Eq., 0.07 M –

absolute concentration) dissolved in dry MeOH (3.0 mL) was added under N_2 and the Schlenk tube was placed in a pre-heated oil bath at 70 ^oC until completed conversion, following the reaction by TLC. The crude was filtered through celite, washed with dichloromethane and concentrated under vacuum. The mixture was purified by column chromatography using (Sigma-Aldrich Silica gel) and Hex / EtOAc (10:1) and (4:1) as eluent: **299a**, 14 mg, 0.05 mmol (13%): yellow oil; **305a**, 12 mg, 0.04 mmol, (11%): yellow oil; and **298a**, 28 mg, 0.09 mmol, (25%): yellow oil.

299a ^1H NMR (300 MHz, $CDCl_3$, 25 ^oC) δ = 7.69 (d, *J* = 8.2 Hz, 2H; H_{Ar}-11), 7.30 (d, *J* = 8.2 Hz, 2H; H_{Ar}-12), 5.84 (t, *J* = 7.1 Hz, 1H; H-2), 5.74 (tq, *J* = 7.2, 1.2 Hz, 1H; H-5), 3.91 (s, 2H; H-7), 3.59 (d, *J* = 7.1 Hz, 2H; H-1), 3.56 (d, *J* = 7.2 Hz, 2H; H-6), 3.15 (s, 3H; H-8), 2.43 (s, 3H; H-14), 1.78 (s, 3H; H-9). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ^oC) δ = 144.2 (C_q), 142.2 (C_q), 141.4 (C_q), 135.0 (C_q), 128.7 (2 x CH_{Ar}; C-12), 126.5 (2 x CH_{Ar}; C-11), 123.2 (CH; C-5), 123.1 (CH; C-2), 72.3 (CH_2; C-7), 56.8 (CH_3; C-8), 42.7 (CH_2; C-6), 42.4 (CH_2; C-1), 20.5 (CH_3; C-14), 18.6 (CH_3; C-9). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3098 (C-H_{Alkene}), 3082 (C-H_{Alkene}), 2925 (C-H_{Alkane}), 2855 (C-H_{Alkane}), 1727 (C=C), 1598, 1450, 1310 (S=O), 1240 (C-O), 1161 (S=O), 1094 (C-N), 1002 (C-O), 911. HRMS (ESI-HRMS) Calc. for $C_{16}H_{22}O_3NS$ [M+H]+: 308.1320 Found: 308.1323.

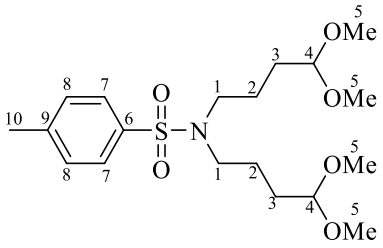
Synthesis of *N*-(3-methoxymethyl-4-methylene-hexa-2,5-dienyl)-benzenesulfonamide (298d)



To a microwave vial were added $PtCl_2(MeCN)_2$ (5 mg, 0.01 mmol, 0.05 Eq.) and $AgSbF_6$ (9 mg, 0.03 mmol, 0.1 Eq.). Then the vial was closed with a stopper and flushed with N_2 during 3 min. A small amount of dry THF was added and the solution was stirred at room temperature for a few min to preform the cationic complex. 1,5-Bisallene **266d** (72 mg, 0.27 mmol, 1.0 Eq., 0.09 M – absolute concentration) dissolved in dry THF was added, then dry MeOH (THF:MeOH 9:1). The vial was sealed under N_2 and placed in a pre-heated oil bath at 70 ^oC until completed conversion, following the reaction by TLC. The crude was filtered through celite, washed with dichloromethane and concentrated under vacuum. The mixture was purified by column chromatography using (Sigma-Aldrich Silica gel) and Hex / EtOAc (8:1) as eluent: **298d**, 34 mg, 0.12 mmol, (43%): yellow oil; and **305d**, 15 mg, 0.05 mmol, (19%): yellow oil.

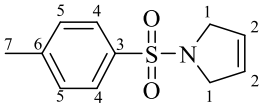
^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.87 – 7.82 (m, 2H; H_{Ar}-11), 7.60 – 7.55 (m, 1H; H_{Ar}-13), 7.54 – 7.48 (m, 2H; H_{Ar}-12), 6.30 (dd, *J* = 17.5, 10.5 Hz, 1H; H-5), 5.63 (tt, *J* = 7.0, 1.4 Hz, 1H; H-2), 5.17 (s, 1H; H-9), 5.06 (d, *J* = 10.5 Hz, 1H; H-6), 5.03 (d, *J* = 17.5 Hz, 1H; H-6), 4.89 (s, 1H; H-9), 4.34 (bt, *J* = 5.7 Hz, 1H; NH), 3.82 (s, 2H; H-7), 3.55 – 3.48 (m, 2H; H-1), 3.30 (s, 3H; H-8). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 143.7 (C_q), 140.2 (C_q), 140.1 (C_q), 137.2 (CH; C-5), 132.8 (CH_{Ar}; C-13), 129.2 (2 x CH_{Ar}; C-12), 127.3 (2 x CH_{Ar}; C-11), 123.2 (CH; C-2), 118.9 (CH_2; C-9), 116.4 (CH_2; C-6), 75.2 (CH_2; C-7), 58.4 (CH_3; C-8), 41.6 (CH_2; C-1). IR (Film, cm^{-1}): $\tilde{\nu}$ = 3269 (N-H), 3100 (C-H_{Alkene}), 2922 (C-H_{Alkane}), 2852 (C-H_{Alkane}), 1739 (C=C), 1583 (N-$H_{(Bend)}$), 1446, 1308 (S=O), 1240 (C-O), 1152 (S=O), 1090 (C-N), 1038 (C-O), 986. HRMS (FTMS + p NSI ((DCM)/MeOH + NH_4OAc)): Calc. for $C_{15}H_{23}O_3N_2S$ $[M+NH_4]^+$: 311.1424. Found: 311.1425.

***N*,*N*-Bis-(4,4-dimethoxy-butyl)-4-methyl-benzenesulfonamide (300)**



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.66 (d, *J* = 8.2 Hz, 2H; H_{Ar}-8), 7.27 (d, *J* = 8.2 Hz, 2H; H_{Ar}-7), 4.32 (t, *J* = 5.0 Hz, 2H; H-4), 3.28 (s, 12H; H-5), 3.10 (t, *J* = 7.0 Hz, 4H; H-1), 2.40 (s, 3H; H-10), 1.61 – 1.52 (m, 8H; H-3 and H-2). IR (Film, cm^{-1}): $\tilde{\nu}$ = 2926 (C-H_{Alkane}), 2870 (C-H_{Alkane}), 1719, 1682, 1335 (S=O), 1158 (S=O), 1091 (C-N), 1015 (C-O), 815. HRMS (+ESI): Calc. for $C_{19}H_{33}O_6NSNa$ $[M+Na]^+$: 426.1921. Found: 426.1924. M.P. = 115 – 117 ^{o}C.

1-(Toluene-4-sulfonyl)-2,5-dihydro-1*H*-pyrrole (314)[272]



^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ = 7.74 – 7.70 (m, 2H; H_{Ar}-4), 7.32 (d, *J* = 8.2 Hz, 2H; H_{Ar}-5), 5.65 (s, 2H; H-2), 4.12 (s, 4H; H-1), 2.43 (s, 3H; H-7). ^{13}C NMR (126 MHz, $CDCl_3$, 25 ^{o}C) δ = 143.6 (C_q; C-6), 134.5 (C_q; C-3), 129.9 (2 x CH_{Ar}; C-3), 127.6 (2 x CH; C-2), 125.6 (2 x CH_{Ar}; C-4), 55.0 (2 x CH_2; C-1), 21.7 (CH_3; C-7).

References

[1] J. H. v. t. Hoff, *La Chimie dans l'espace*, P.M. Bazendijk, Rotterdam, **1875**.
[2] **(a)** C. D. Hurd, C. N. Webb, *J. Am. Chem. Soc.* **1927**, *49*, 546-559; (b) F. Faltis, J. Pirsch, L. Bermann, *Chem. Ber.* **1930**, *63*, 691-702; (c) O. Dimroth, H. Feuchter, *Chem. Ber.* **1903**, *36*, 2238-2251.
[3] B. S. Burton, H. von Pechmann, *Chem. Ber.* **1887**, *20*, 145-149.
[4] E. R. H. Jones, G. H. Mansfield, M. C. Whiting, *J. Chem. Soc.* **1954**, 3208-3212.
[5] E. P. Kohler, J. T. Walker, M. Tishler, *J. Am. Chem. Soc.* **1935**, *57*, 1743-1745.
[6] (a) P. Maitland, W. H. Mills, *J. Chem. Soc.* **1936**, 987-998; (b) P. Maitland. W. H. Mills, *Nature* **1935**, *135*, 994.
[7] H. Staudinger, L. Ruzicka, *Helv. Chim. Acta* **1924**, *7*, 177-201.
[8] L. Crombie, S. H. Harper, D. Thompson, *J. Chem. Soc.* **1951**, 2906-2915.
[9] (a) E. A. Johnson, K. L. Burdon, *J. Bacteriol* **1947**, *54*, 281; (b) W. D. Celmer, I. A. Solomons, *J. Am. Chem. Soc.* **1952**, *74*, 1870-1871; (c) W. D. Celmer, I. A. Solomons, *J. Am. Chem. Soc.* **1952**, *74*, 2245-2248; (d) W. D. Celmer, I. A. Solomons, *J. Am. Chem. Soc.* **1952**, *74*, 3838-3842.
[10] A. Hoffmann-Roder, N. Krause, *Angew. Chem. Int.Ed.* **2004**, *43*, 1196-1216.
[11] (a) W. Runge, in *Ketenes, Allenes and Related Compounds (1980)*, John Wiley & Sons, Ltd., **2010**, pp. 45-98; (b) C. E. Dykstra, H. F. Schaefer, in *Ketenes, Allenes and Related Compounds (1980)*, John Wiley & Sons, Ltd., **2010**, pp. 1-44; (c) W. Runge, in *Ketenes, Allenes and Related Compounds (1980)*, John Wiley & Sons, Ltd., **2010**, pp. 99-154.
[12] (a) C. H. Hendon, D. Tiana, A. T. Murray, D. R. Carbery, A. Walsh, *Chem. Sci.* **2013**, *4*, 4278-4284; (b) E. Soriano, I. Fernandez, *Chem. Soc. Rev.* **2014**, *43*, 3041-3105.
[13] (a) J. A. Januszewski, D. Wendinger, C. D. Methfessel, F. Hampel, R. R. Tykwinski, *Angew. Chem. Int. Ed.* **2013**, *52*, 1817-1821; (b) J. A. Januszewski, R. R. Tykwinski, *Chem. Soc. Rev.* **2014**, *43*, 3184-3203.
[14] (a) L. J. Weimann, R. E. Christoffersen, *J. Am. Chem. Soc.* **1973**, *95*, 2074-2084; (b) R. J. Buenker, *J. Chem. Phys.* **1968**, *48*, 1368-1379.
[15] L. S. Bartell, E. A. Roth, C. D. Hollowell, K. Kuchitsu, J. E. Young, *J. Chem. Phys.* **1965**, *42*, 2683-2686.
[16] M. G. Pullen, B. Wolter, A.-T. Le, M. Baudisch, M. Hemmer, A. Senftleben, C. D. Schroter, J. Ullrich, R. Moshammer, C. D. Lin, J. Biegert, *Nat. Commun.* **2015**, *6*.
[17] (a) A. G. Maki, R. A. Toth, *J. Mol. Spectry.* **1965**, *17*, 136-155; (b) D. R. Lide, D. E. Mann, *J. Chem. Phys.* **1957**, *27*, 874-877; (c) P. D. Ellis, Y. S. Li, C. C. Tong, A. P. Zens, J. R. Durig, *J. Chem. Phys.* **1975**, *62*, 1311-1313; (d) A. Bouchy, J. Demaison, G. Roussy, J. Barriol, *J. Mol. Struct.* **1973**, *18*, 211-217.
[18] J. W. Munson, in *Ketenes, Allenes and Related Compounds (1980)*, John Wiley & Sons, Ltd., **2010**, pp. 165-188.
[19] D. R. Taylor, *Chem. Rev.* **1966**, *317*, 317.
[20] M. Karplus, *J. Am. Chem. Soc.* **1960**, *82*, 4431-4432.
[21] (a) R. Rossi, P. Diversi, *Synthesis* **1973**, *1973*, 25-36; (b) V. Prelog, G. Helmchen, *Angew. Chem. Int. Ed.* **1982**, *21*, 567-583.
[22] (a) G. Lowe, *Chem. Commun.* **1965**, 411-413; (b) R. K. Neff, D. E. Frantz, *Tetrahedron* **2015**, *71*, 7-18.
[23] (a) K. Griesbaum, *Angew. Chem. Int. Ed.* **1966**, *5*; (b) S. R. Landor, *The Chemistry of the Allenes: Synthesis*, Academic Press, **1982**; cin *Modern Allene Chemistry*, Wiley-VCH Verlag GmbH, **2008**, pp. i-xv; (d) H. Yamamoto, D. L. Usanov, in *Comprehensive Organic Synthesis II (Second Edition)* (Ed.: P. Knochel), Elsevier, Amsterdam, **2014**, pp. 209-242; (e) R. A. Biggs, W. W. Ogilvie, in *Comprehensive Organic Synthesis II (Second Edition)* (Ed.: P. Knochel), Elsevier, Amsterdam, **2014**, pp. 802-841; (f) S. Yu, S. Ma, *Chem. Commun.* **2011**, *47*, 5384-5418; (g) R. K. Neff, D. E. Frantz, *ACS Catal.* **2014**, *4*, 519-528; (h) J. Ye, S. Ma, *Org. Chem. Front.* **2014**, *1*, 1210-1224.

[24] (a) F. Lehrich, H. Hopf, J. Grunenberg, *Eur. J. Org. Chem.* **2011**, *2011*, 2705-2718; (b) A. S. K. Hashmi, in *Modern Allene Chemistry*, Wiley-VCH Verlag GmbH, **2008**, pp. 2-50; (c) A. Hoffmann-Röder, N. Krause, in *Modern Allene Chemistry*, Wiley-VCH Verlag GmbH, **2008**, pp. 51-92; (d) H. Ohno, Y. Nagaoka, K. Tomioka, in *Modern Allene Chemistry*, Wiley-VCH Verlag GmbH, **2008**, pp. 141-181.

[25] (a) X. Tang, X. Huang, T. Cao, Y. Han, X. Jiang, W. Lin, Y. Tang, J. Zhang, Q. Yu, C. Fu, S. Ma, *Org. Chem. Front.* **2015**, *2*, 688-691; (b) M. Ogasawara, *Tetrahedron: Asymmetry* **2009**, *20*, 259-271; (c) A. Hoffmann-Röder, N. Krause, *Angew. Chem. Int. Ed.* **2002**, *41*, 2933-2935; (d) Y. F. Ao, D. X. Wang, L. Zhao, M. X. Wang, *J. Org. Chem.* **2014**, *79*, 3103-3110; (e) T. Hashimoto, K. Sakata, F. Tamakuni, M. J. Dutton, K. Maruoka, *Nat. Chem.* **2013**, *5*, 240-244.

[26] (a) P. Crabbe, H. Fillion, D. Andre, J.-L. Luche, *J.Chem. Soc. Chem. Commun.* **1979**, 859-860; (b) P. Crabbé, D. André, H. Fillion, *Tetrahedron Lett.* **1979**, *20*, 893-896.

[27] (a) P. Crabbé, B. Nassim, M.-T. Robert-Lopes, *Org. Synth.* **1990**, *7*, 276; (b) H. Nakamura, T. Sugiishi, Y. Tanaka, *Tetrahedron Lett.* **2008**, *49*, 7230-7233; (c) J. Kuang, S. Ma, *J. Org. Chem.* **2009**, *74*, 1763-1765; (d) H. Luo, S. Ma, *Eur. J. Org. Chem.* **2013**, *2013*, 3041-3048.

[28] S. M. J. Kuang, *J. Am. Chem. Soc.* **2010**, *132*, 1786-1787.

[29] X. Tang, C. Zhu, T. Cao, J. Kuang, W. Lin, S. Ni, J. Zhang, S. Ma, *Nat. Commun.* **2013**, *4*, 2450.

[30] C. Mukai, S. Kitagaki, M. Komizu, *Synlett* **2011**, *2011*, 1129-1132.

[31] (a) X. Huang, T. Cao, Y. Han, X. Jiang, W. Lin, J. Zhang, S. Ma, *Chem. Commun.* **2015**, *51*, 6956-6959; (b) J. Ye, R. Lü, W. Fan, S. Ma, *Tetrahedron* **2013**, *69*, 8959-8963.

[32] Y. L. S. Searles, B. Nassim, M. -T. Robert Lopes, P. T. Tran, P. Crabbe, *J. Am. Chem. Soc. Perkin Trans.* **1984**, *1*, 747-751.

[33] D. A. H. Fillion, J.-L. Luche, **1980**, *21*, 929-930.

[34] M. González, R. Á. Rodríguez, M. M. Cid, C. S. López, *J. Comput. Chem.* **2012**, *33*, 1236-1239.

[35] N. Krause, A. Hoffmann-Röder, in *Modern Allene Chemistry*, Wiley-VCH Verlag GmbH, **2008**, pp. 997-1040.

[36] D. F. Horler, *J. Chem. Soc. C: Org.* **1970**, 859-862.

[37] T. L. Jacobs, R. Akawie, R. G. Cooper, *J. Am. Chem. Soc.* **1951**, *73*, 1273-1276.

[38] J. H. Wotiz, (Ed.: M. D. H. G. Viehe), New York, **1969**, p. 365.

[39] (a) P. Rona, P. Crabbe, *J. Am. Chem. Soc.* **1968**, *90*, 4733-4734; (b) P. Rona, P. Crabbe, *J. Am. Chem. Soc.* **1969**, *91*, 3289-3292.

[40] A. Alexakis, I. Marek, P. Mangeney, J. F. Normant, *J. Am. Chem. Soc.* **1990**, *112*, 8042-8047.

[41] N. Krause, A. Hoffmann-Röder, *Tetrahedron* **2004**, *60*, 11671-11694.

[42] P. Crabbe, H. Carpio, *J.Chem. Soc. Chem. Commun.* **1972**, 904-905.

[43] (a) K. S. Feldman, C. C. Mechem, L. Nader, *J. Am. Chem. Soc.* **1982**, *104*, 4011-4012; (b) J. Boukouvalas, M. Pouliot, J. Robichaud, S. MacNeil, V. Snieckus, *Org. Lett.* **2006**, *8*, 3597-3599.

[44] V. M. Dembitsky, T. Maoka, *Prog. Lipids. Res.* **2007**, *46*, 328-375.

[45] P. Rivera-Fuentes, F. Diederich, *Angew. Chem. Int. Ed.* **2012**, *51*, 2818-2828.

[46] S. Thorand, F. Vögtle, N. Krause, *Angew. Chem. Int. Ed.* **1999**, *38*, 3721-3723.

[47] S. Castro-Fernández, M. M. Cid, C. S. López, J. L. Alonso-Gómez, *J. Phys. Chem. A* **2015**, *119*, 1747-1753.

[48] H. Hopf, G. Markopoulos, *Beilstein J. Org. Chem.* **2012**, *8*, 1936-1998.

[49] A. Claesson, L.-I. Olsson, *J. Am. Chem. Soc.* **1979**, *101*, 7302-7311.

[50] A. Burger, J.-P. Roussel, C. Hetru, J. A. Hoffmann, B. Luu, *Tetrahedron* **1989**, *45*, 155-164.

[51] J. Meinwald, K. Erickson, M. Hartshorn, Y. C. Meinwald, T. Eisner, *Tetrahedron Lett.* **1968**, *9*, 2959-2962.

[52] K. Lee, D. Seomoon, P. H. Lee, *Angew. Chem. Int. Ed.* **2002**, *41*, 3901-3903.
[53] (a) C.-J. Li, *Tetrahedron* **1996**, *52*, 5643-5668; (b). M. B. Isaac, T.-H. Chan, *J. C. S. Chem. Commun.* **1995**, 1003-1004.
[54] (a) B. Alcaide, P. Almendros, C. Aragoncillo, *Chem. Eur. J.* **2002**, *8*, 1719-1729; (b) Z.-L. Shen, S.-Y. Wang, Y.-K. Chok, Y.-H. Xu, T.-P. Loh, *Chem. Rev.* **2013**, *113*, 271-401.
[55] B. Alcaide, P. Almendros, C. Aragoncillo, *Chem. Eur. J.* **2002**, *8*, 1719-1729.
[56] (a) H. Zhou, C. Moberg, *J. Am. Chem. Soc.* **2012**, *134*, 15992-15999; (b) F. Ye, C. Wang, X. Ma, M. L. Hossain, Y. Xia, Y. Zhang, J. Wang, *J. Org. Chem.* **2015**, *80*, 647-652; (c) J. S. Poh, D. N. Tran, C. Battilocchio, J. M. Hawkins, S. V. Ley, *Angew. Chem. Int. Ed.* **2015**, *54*, 7920-7923; (d) F. Ye, M. L. Hossain, Y. Xu, X. Ma, Q. Xiao, Y. Zhang, J. Wang, *Chem. Asian J.* **2013**, *8*, 1404-1407; (e) Q. Xiao, Y. Zhang, J. Wang, *Acc. Chem. Res.* **2013**, *46*, 236-247.
[57] (a) Q. Xiao, B. Wang, L. Tian, Y. Yang, J. Ma, Y. Zhang, S. Chen, J. Wang, *Angew. Chem. Int. Ed.* **2013**, *52*, 9305-9308; (b) A. Suárez, G. C. Fu, *Angew. Chem.* **2004**, *116*, 3664-3666.
[58] Q. Xiao, Y. Xia, H. Li, Y. Zhang, J. Wang, *Angew. Chem. Int. Ed.* **2011**, *50*, 1114-1117.
[59] M. L. Hossain, F. Ye, Y. Zhang, J. Wang, *J. Org. Chem.* **2013**, *78*, 1236-1241.
[60] S. Pricker, *Gold Bull.* **1996**, *29*, 53-60.
[61] H. Schmidbaur, *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 728-740.
[62] (a) G. C. Bond, *Catal. Today* **2002**, *72*, 5-9; (b) K.-I. Tanaka, K. Tamaru, *J. Catal.* **1963**, *2*, 366-370.
[63] G. C. Bond, P. A. Sermon, G. Webb, D. A. Buchanan, P. B. Wells, *J.Chem. Soc. Chem. Commun.* **1973**, 444b-445.
[64] G. Bond, *Gold Bull.* **2008**, *41*, 235-241.
[65] M. Haruta, *Nature* **2005**, *437*, 1098-1099.
[66] M. Haruta, T. Kobayashi, H. Sano, N. Yamada, *Chem. Lett.* **1987**, *16*, 405-408.
[67] G. J. Hutchings, *J. Catal.* **1985**, *96*, 292-295.
[68] Y. Ito, M. Sawamura, T. Hayashi, *J. Am. Chem. Soc.* **1986**, *108*, 6405-6406.
[69] Y. Fukuda, K. Utimoto, *J. Org. Chem.* **1991**, *56*, 3729-3731.
[70] J. H. Teles, S. Brode, M. Chabanas, *Angew. Chem. Int. Ed.* **1998**, *37*, 1415-1418.
[71] A. S. K. Hashmi, *Gold. Bull.* **2004**, *37*, 51.
[72] P. Pyykko, J. P. Desclaux, *Acc. Chem. Res.* **1979**, *12*, 276-281.
[73] D. J. Gorin, F. D. Toste, *Nature* **2007**, *446*, 395-403.
[74] (a) D. R. McKelvey, *J. Chem. Educ.* **1983**, *60*, 112; (b) P. Pyykkö, *Angew. Chem. Int. Ed.* **2002**, *41*, 3573-3578; (c) P. Pyykkö, *Angew. Chem. Int. Ed.* **2004**, *43*, 4412-4456.
[75] P. Pyykkö, *Chem. Rev.* **1997**, *97*, 597-636.
[76] M. N. Hopkinson, A. D. Gee, V. Gouverneur, *Chem. Eur. J.* **2011**, *17*, 8248-8262.
[77] M. P. Muñoz, C. Hurtado.-Rodrigo, in *PATAI'S Chemistry of Functional Groups*, John Wiley & Sons, Ltd, **2014**.
[78] A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2000**, *39*.
[79] V. Gandon, G. Lemière, A. Hours, L. Fensterbank, M. Malacria, *Angew. Chem. Int. Ed.* **2008**, *47*, 7534-7538.
[80] Z. J. Wang, D. Benitez, E. Tkatchouk, W. A. Goddard Iii, F. D. Toste, *J. Am. Chem. Soc.* **2010**, *132*, 13064-13071.
[81] V. Gandon, G. Lemiere, A. Hours, L. Fensterbank, M. Malacria, *Angew. Chem. Int. Ed.* **2008**, *47*, 7534-7538.
[82] J. H. B. Chenier, J. A. Howard, B. Mile, *J. Am. Chem. Soc.* **1985**, *107*, 4190-4191.
[83] (a) T. J. Brown, B. D. Robertson, R. A. Widenhoefer, *J. Organomet. Chem.* **2014**, *758*, 25-28; (b) R. J. Harris, K. Nakafuku, R. A. Widenhoefer, *Chem. Eur. J.* **2014**, *20*, 12245-12254; (c) A. Furstner, M. Alcarazo, R. Goddard, C. W. Lehmann, *Angew. Chem. Int. Ed.* **2008**, *47*, 3210-3214; (d) C. Esterhuysen, G. Frenking, *Chem. Eur. J.* **2011**, *17*, 9944-9956; (e) T. J. Brown, A. Sugie, M. G. Dickens, R. A. Widenhoefer,

Organometallics **2010**, *29*, 4207-4209; (f) T. J. Brown, A. Sugie, M. G. Leed, R. A. Widenhoefer, *Chem. Eur. J.* **2012**, *18*, 6959-6971.
[84] (a) N. Krause, C. Winter, *Chem. Rev.* **2011**, *111*, 1994-2009; (b) N. Krause, (Ed.: E. P. G. Andersson, Wiley-VCH Verlag GmbH & Co), **2012**, pp. 195-209; (c) C. Winter, N. Krause, in *Modern Gold Catalyzed Synthesis*, Wiley-VCH Verlag GmbH & Co. KGaA, **2012**, pp. 363-389; (d) B. Alcaide, P. Almendros, *Beilstein J. Org. Chem.* **2011**, *7*, 622-630; (e) A. Hoffmann-Roder, N. Krause, *Org. Biomol. Chem.* **2005**, *3*, 387-391; (f) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180-3211; (g) E. M. Barreiro, L. A. Adrio, K. K. Hii, J. B. Brazier, *Eur. J. Org. Chem.* **2013**, *2013*, 1027-1039; (h) R. A. Widenhoefer, *Chem. Eur. J.* **2008**, *14*, 5382-5391.
[85] (a) D.-M. Cui, K.-R. Yu, C. Zhang, *Synlett* **2009**, *2009*, 1103-1106; (b) D.-M. Cui, Z.-L. Zheng, C. Zhang, *J. Org. Chem.* **2009**, *74*, 1426-1427.
[86] (a) N. Nishina, Y. Yamamoto, *Tetrahedron Lett.* **2008**, *49*, 4908-4911; (b) N. Nishina, Y. Yamamoto, *Tetrahedron* **2009**, *65*, 1799-1808.
[87] (a) Z. Zhang, R. A. Widenhoefer, *Org. Lett.* **2008**, *10*, 2079-2081; (b) Z. Zhang, S. Du Lee, A. S. Fisher, R. A. Widenhoefer, *Tetrahedron* **2009**, *65*, 1794-1798.
[88] M. P. Muñoz, *Org. Biomol. Chem.* **2012**, *10*, 3584-3594.
[89] (a) Y. Horino, Y. Takata, K. Hashimoto, S. Kuroda, M. Kimura, Y. Tamaru, *Org. Biomol. Chem.* **2008**, *6*, 4105-4107; (b) M. S. Hadfield, A.-L. Lee, *Org. Lett.* **2010**, *12*, 484-487.
[90] R. S. Paton, F. Maseras, *Org. Lett.* **2009**, *11*, 2237-2240.
[91] (a) R. A. Widenhoefer, X. Han, *Eur. J. Org. Chem.* **2006**, *2006*, 4555-4563; (b) A. Couce-Rios, G. Kovács, G. Ujaque, A. Lledós, *ACS Catal.* **2015**, *5*, 815-829.
[92] N. Nishina, Y. Yamamoto, *Angew. Chem. Int. Ed.* **2006**, *45*, 3314-3317.
[93] A. N. Duncan, R. A. Widenhoefer, *Synlett* **2010**, *2010*, 419-422.
[94] A. W. Hill, M. R. J. Elsegood, M. C. Kimber, *J. Org. Chem.* **2010**, *75*, 5406-5409.
[95] R. E. Kinder, Z. Zhang, R. A. Widenhoefer, *Org. Lett.* **2008**, *10*, 3157-3159.
[96] K. L. Butler, M. Tragni, R. A. Widenhoefer, *Angew Chem Int Ed Engl* **2012**, *51*, 5175-5178.
[97] X. Zeng, M. Soleilhavoup, G. Bertrand, *Org. Lett.* **2009**, *11*, 3166-3169.
[98] N. Nishina, Y. Yamamoto, *Synlett* **2007**, *2007*, 1767-1770.
[99] (a) R. Kinjo, B. Donnadieu, G. Bertrand, *Angew. Chem. Int. Ed.* **2011**, *50*, 5560-5563; (b) V. Lavallo, G. D. Frey, B. Donnadieu, M. Soleilhavoup, G. Bertrand, *Angew. Chem. Int. Ed.* **2008**, *47*, 5224-5228.
[100] C. Zhang, S. Q. Zhang, H. J. Cai, D. M. Cui, *Beilstein J Org Chem* **2013**, *9*, 1045-1050.
[101] Menggenbateer, M. Narsireddy, G. Ferrara, N. Nishina, T. Jin, Y. Yamamoto, *Tetrahedron Lett.* **2010**, *51*, 4627-4629.
[102] R. Skouta, C.-J. Li, *Can. J. Phys.* **2008**, *86*, 616-620.
[103] M. A. Tarselli, A. Liu, M. R. Gagné, *Tetrahedron* **2009**, *65*, 1785-1789.
[104] M. A. Tarselli, A. Liu, M. R. Gagne, *Tetrahedron* **2009**, *65*, 1785-1789.
[105] K. L. Toups, G. T. Liu, R. A. Widenhoefer, *J. Organomet. Chem.* **2009**, *694*, 571-575.
[106] M. Z. Wang, C. Y. Zhou, Z. Guo, E. L. Wong, M. K. Wong, C. M. Che, *Chem Asian J* **2011**, *6*, 812-824.
[107] (a) P. Grieß, *Philos. Trans. R. Soc. London* **1864**, *13*, 377; bP. Grieß, *Justus Liebigs Ann. Chem.* **1865**, *135*, 131.
[108] (a) J. H. Boyer, F. C. Canter, *Chem. Rev.* **1954**, *54*,, 1 - 57; (b) P. A. S. Smith, *Org. React.* **1946**, *3*, 337 - 349; (c) S. Batra, A. Mishra, S. Hutait, S. Bhowmik, N. Rastogi, R. Roy, *Synthesis* **2010**, *2010*, 2731-2748.
[109] (a) G. L'Abbe, *Chem. Rev.* **1969**, *69*, 345-363; (b) S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem. Int. Ed.* **2005**, *44*, 5188-5240; (c) E. F. V. Scriven, K. Turnbull, *Chem. Rev.* **1988**, *88*, 297-368; (d) T.-S. Lin, W. H. Prusoff, *J. Med. Chem.* **1978**, *21*, 109-112.

[110] (a) R. Huisgen, *Prog. Chem. Soc.* **1961**, 357-396; (b) R. Huisgen, *Angew. Chem. Int. Ed.* **1963**, *2*, 633-696.
[111] V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2002**, *41*, 2596-2599.
[112] H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2001**, *40*, 2004-2021.
[113] (a) V. Aureggi, G. Sedelmeier, *Angew. Chem. Int. Ed.* **2007**, *46*, 8440-8444; (b) C. Arnold, D. N. Thatcher, *J. Org. Chem.* **1969**, *34*, 1141-1142.
[114] (a) H. Schäfer, W. Saak, M. Weidenbruch, *J. Organomet. Chem.* **2000**, *604*, 211-213; (b) J. S. McMurray, O. Khabashesku, J. S. Birtwistle, W. Wang, *Tetrahedron Lett.* **2000**, *41*, 6555-6558; (c) D. P. Curran, S. Hadida, S.-Y. Kim, *Tetrahedron* **1999**, *55*, 8997-9006; (d) J. V. Duncia, M. E. Pierce, J. B. Santella, *J. Org. Chem.* **1991**, *56*, 2395-2400.
[115] J. Wiss, C. Fleury, C. Heuberger, U. Onken, M. Glor, *Org. Process Research & Development* **2007**, *11*, 1096-1103.
[116] E. Manhart, K. von Werner, *Synthesis* **1978**, *1978*, 705-706.
[117] J. K. A. Hassner, *J.Org.Chem.* **1986**, *51*, 2767-2770.
[118] (a) S.-I. Murahashi, Y. Tanigawa, Y. Imada, Y. Taniguchi, *Tetrahedron Lett.* **1986**, *27*, 227-230; (b) J. E. Green, D. M. Bender, S. Jackson, M. J. O'Donnell, J. R. McCarthy, *Org. Lett.* **2009**, *11*, 807-810.
[119] W. Zhou, J. Xu, L. Zhang, N. Jiao, *Synlett* **2011**, *2011*, 887-890.
[120] (a) C. V. M. Rueping, U. Uria, *Org. Lett.* **2012**, *14*, 768-771; (b) P. Surendra Reddy, V. Ravi, B. Sreedhar, *Tetrahedron Lett.* **2010**, *51*, 4037-4041; (c) A. R. Deshmukh, A. Jayanthi, V. K. Gumaste, *Synlett* **2004**, 979-982; (d) Y. K. T. Kanai, Y. Ishii, *J. Org. Chem.* **1990**, *55*, 3274-3277; (e) J. H. Boyer, F. C. Canter, *J. Org. Chem.* **1999**, *64*, 5308-5311.
[121] (a) E. Blart, J. P. Geneˆt, M. Safi, M. Savignac, D. Sinou, *Tetrahedron* **1994**, *50*, 505-514; (b) Y. Uozumi, T. Suzuka, R. Kawade, H. Takenaka, *Synlett* **2006**, *2006*, 2109-2113; (c) P. Aufranc, J. Ollivier, A. Stolle, C. Bremer, M. Es-Sayed, A. de Meijere, J. Salaün, *Tetrahedron Lett.* **1993**, *34*, 4193-4196; (d) M. Safi, R. Fahrang, D. Sinou, *Tetrahedron Lett.* **1990**, *31*, 527-530; **(**e) S. Murahashi, Y. Taniguchi, Y. Imada, Y. Tanigawa, *J. Org. Chem.* **1989**, *54*, 3292-3303.
[122] (a) S. G. Alvarez, M. T. Alvarez, *Synthesis* **1997**, 413-414; (b) P. Deslongchamps, U. O. Cheriyan, R. J. Taillefer, *Can. J. Phys.* **1979**, *57*, 3262-3271.
[123] (a) M. Arimoto, H. Yamaguchi, E. Fujita, M. Ochiai, Y. Nagao, *Tetrahedron Lett.* **1987**, *28*, 6289-6292; (b) M. Arimoto, H. Yamaguchi, E. Fujita, Y. Nagao, M. Ochiai, *Chem. Pharm. Bull.* **1989**, *37*, 3221-3224.
[124] N. Zhu, F. Wang, P. Chen, J. Ye, G. Liu, *Org. Lett.* **2015**, *17*, 3580-3583.
[125] H.-M. Chang, C.-H. Cheng, *J. Chem. Soc. Perkin. Trans.* **2000**, 3799-3807.
[126] C. Hurtado-Rodrigo, S. Hoehne, M. P. Muñoz, *Chem. Commun.* **2014**, *50*, 1494-1496.
[127] M. Jafarzadeh, *Synlett* **2007**, *2007*, 2144-2145.
[128] (a) D. Wang, R. Cai, S. Sharma, J. Jirak, S. K. Thummanapelli, N. G. Akhmedov, H. Zhang, X. Liu, J. L. Petersen, X. Shi, *J. Am. Chem. Soc.* **2012**, *134*, 9012-9019; (b) A. Duschek, S. F. Kirsch, *Angew. Chem. Int. Ed.* **2008**, *47*, 5703-5705; (c) M. A. Tarselli, A. R. Chianese, S. J. Lee, M. R. Gagne, *Angew. Chem. Int. Ed.* **2007**, *46*, 6670-6673; (d) I. E. A. Homs, A. M. Echavarren, *Org. Lett.* **2013**, *15*, 5782-5785.
[129] (a) P. Nava, D. Hagebaum-Reignier, S. Humbel, *Chem. Phys.* **2012**, *13*, 2090-2096; (b) M. Pažický, A. Loos, M. J. Ferreira, D. Serra, N. Vinokurov, F. Rominger, C. Jäkel, A. S. K. Hashmi, M. Limbach, *Organometallics* **2010**, *29*, 4448-4458; (c) L. Cavallo, A. Correa, C. Costabile, H. Jacobsen, *J. Organomet. Chem.* **2005**, *690*, 5407-5413; (d) A. G. Orpen, N. G. Connelly, *Organometallics* **1990**, *9*, 1206-1210.
[130] (a) W. Wang, G. B. Hammond, B. Xu, *J. Am. Chem. Soc.* **2012**, *134*, 5697-5705; (b) G. C. Fortman, S. P. Nolan, *Organometallics* **2010**, *29*, 4579-4583; (c) R. E. Brooner, T. J. Brown, R. A. Widenhoefer, *Chem. Eur. J.* **2013**, *19*, 8276-8284.

[131] (a) L.-P. Liu, B. Xu, M. S. Mashuta, G. B. Hammond, *J. Am. Chem. Soc.* **2008**, *130*, 17642-17643; (b) L. Ye, L. Zhang, *Org. Lett.* **2009**, *11*, 3646-3649; (c) A. S. K. Hashmi, T. D. Ramamurthi, M. H. Todd, A. S.-K. Tsang, K. Graf, *Aust. J. Chem.* **2010**, *63*, 1619-1626; (d) S. F. Kirsch, J. T. Binder, B. Crone, A. Duschek, T. T. Haug, C. Liébert, H. Menz, *Angew. Chem. Int. Ed.* **2007**, *46*, 2310-2313; (e) M. Yu, G. Zhang, L. Zhang, *Org. Lett.* **2007**, *9*, 2147-2150; (f) B. Crone, S. F. Kirsch, *J. Org. Chem.* **2007**, *72*, 5435-5438; (g) J. Barluenga, M. A. Rodríguez, J. M. González, P. J. Campos, *Tetrahedron Lett.* **1990**, *31*, 4207-4210.

[132] (a) J. Waser, B. Gaspar, H. Nambu, E. M. Carreira, *J. Am. Chem. Soc.* **2006**, *128*, 11693-11712; (b) I. Adamo, F. Benedetti, F. Berti, P. Campaner, *Org. Lett.* **2006**, *8*, 51-54.

[133] B. Gutmann, J.-P. Roduit, D. Roberge, C. O. Kappe, *Angew. Chem. Int. Ed.* **2010**, *49*, 7101-7105.

[134] (a) W. Wang, G. B. Hammond, B. Xu, *J. Am. Chem. Soc.* **2012**, *134*, 5697-5705; (b) A. S. K. Hashmi, T. D. Ramamurthi, M. H. Todd, A. S.-K. Tsang, K. Graf, *Aust. J. Chem.* **2010**, *63*, 1619.

[135] J.-P. Hagenbuch, *Chimia* **2003**, *57*, 773-776.

[136] M. E. Kopach, M. M. Murray, T. M. Braden, M. E. Kobierski, O. L. Williams, *Org. Process Res. Dev.* **2009**, *13*, 152-160.

[137] (a) M. P. Muñoz, *Chem. Soc. Rev.* **2014**, *43*, 3164-3183; (b) C. Gronnier, P. F. Bel, G. Henrion, S. Kramer, F. Gagosz, *Org. Lett.* **2014**, *16*, 2092-2095.

[138] L. Ricard, F. Gagosz, *Organometallics* **2007**, *26*, 4704-4707.

[139] T. Jin, S. Kamijo, Y. Yamamoto, *Eur. J. Org. Chem.* **2004**, *2004*, 3789-3791.

[140] (a) C. Besset, S. Chambert, B. Fenet, Y. Queneau, *Tetrahedron Lett.* **2009**, *50*, 7043-7047; (b) M. Frick, D. McAtee, J. McAtee, C. Wysoczynski, S. Ray Partha, in *Heterocyclic Communications*, *Vol. 17*, **2011**, p. 17.

[141] M. D. Kemp, *J. Chem. Educ.* **1960**, *37*, 142.

[142] (a) D. Adam, *Nature* **2003**, *421*, 571-572; (b) C. O. Kappe, *Angew. Chem. Int. Ed.* **2004**, *43*, 6250-6284; (c) M. Nüchter, U. Müller, B. Ondruschka, A. Tied, W. Lautenschläger, *Chemical Engineering & Technology* **2003**, *26*, 1207-1216.

[143] M. Gaydou, A. M. Echavarren, *Angew. Chem. Int. Ed.* **2013**, *52*, 13468-13471.

[144] (a) S. Gaillard, A. M. Slawin, S. P. Nolan, *Chem. Commun.* **2010**, *46*, 2742-2744; (b) S. Gaillard, J. Bosson, R. S. Ramon, P. Nun, A. M. Slawin, S. P. Nolan, *Chem. Eur. J.* **2010**, *16*, 13729-13740.

[145] (a) D.-A. Rosca, J. A. Wright, M. Bochmann, *Dalton Trans.* **2015**, *44*, 20785-20807; (b) D.-A. Rosca, D. A. Smith, M. Bochmann, *Chem. Commun.* **2012**, *48*, 7247-7249; (c) D.-A. Roşca, J. A. Wright, D. L. Hughes, M. Bochmann, *Nat. Commun.* **2013**, *4*.

[146] (a) B. Bolte, F. Gagosz, *J. Am. Chem. Soc.* **2011**, *133*, 7696-7699; (b) S. Kim, D. Kang, C.-H. Lee, P. H. Lee, *J. Org. Chem.* **2012**, *77*, 6530-6537; (c) L. Zhang, S. A. Kozmin, *J. Am. Chem. Soc.* **2004**, *126*, 10204-10205; (d) T. Caneque, F. M. Truscott, R. Rodriguez, G. Maestri, M. Malacria, *Chem. Soc. Rev.* **2014**, *43*, 2916-2926; (e) A. S. Bogachenkov, A. V. Dogadina, V. P. Boyarskiy, A. V. Vasilyev, *Org. Biomol. Chem.* **2015**, *13*, 1333-1338; (f) W. Smadja, *Chem. Rev.* **1983**, *83*, 263-320; (g) M. Marin-Luna, A. Vidal, D. Bautista, R.-A. Orenes, M. Alajarin, *Org. Biomol. Chem.* **2015**.

[147] M. P. Muñoz. L. Cooper, unpublished results, *Unpublished results*.

[148] (a) A. K. Feldman, B. Colasson, K. B. Sharpless, V. V. Fokin, *J. Am. Chem. Soc.* **2005**, *127*, 13444-13445; (b) A. Gagneux, S. Winstein, W. G. Young, *J. Am. Chem. Soc.* **1960**, *82*, 5956-5957.

[149] (a) K. F. Z. Schmidt, *Angew. Chem. Int. Ed.* **1923**, *36*, 511; (b) P. A. S. Smith, *J. Am. Chem. Soc.* **1948**, *70*, 320-323.

[150] T. Shen, T. Wang, C. Qin, N. Jiao, *Angew. Chem.* **2013**, *125*, 6809-6812.

[151] C. Qin, P. Feng, Y. Ou, T. Shen, T. Wang, N. Jiao, *Angew. Chem. Int. Ed.* **2013**, *52*, 7850-7854.

[152] (a) L. E. Fikes, H. Shechter, *J. Org. Chem.* **1979**, *44*, 741-744; (b) G. L. Milligan, C. J. Mossman, J. Aube, *J. Am. Chem. Soc.* **1995**, *117*, 10449-10459.
[153] A. Hassner, E. S. Ferdinandi, R. J. Isbister, *J. Am. Chem. Soc.* **1970**, *92*, 1672-1675.
[154] (a) W. Beck, W. P. Fehlhammer, P. Pöllmann, H. Schächl, *Chem. Ber.* **1969**, *102*, 1976-1987; (b) D. I. Nichols, A. S. Charleston, *J. Chem. Soc. A: Inorg., Phys., Theoretical* **1969**, 2581-2583; (c) R. F. Ziolo, J. A. Thich, Z. Dori, *Inorg. Chem.* **1972**, *11*, 626-631.
[155] T. M. K. W. Beck, P. Klufers, G. Kramer, C. M. Rienaker, *Z. Anorg. Allg. Chem.* **2001**, *627*, 1669-1674.
[156] (a) D. V. Partyka, J. B. Updegraff, M. Zeller, A. D. Hunter, T. G. Gray, *Organometallics* **2007**, *26*, 183-186; (b) D. V. Partyka, T. J. Robilotto, M. Zeller, A. D. Hunter, T. G. Gray, *Proc. Natl. Acad. Sci. U S A* **2008**, *105*, 14293-14297.
[157] J. Strähle, *J. Organomet. Chem.* **1995**, *488*, 15-24.
[158] (a) T. J. Brown, D. Weber, M. R. Gagné, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2012**, *134*, 9134-9137; (b) A. Gomez-Suarez, S. P. Nolan, *Angew. Chem. Int. Ed.* **2012**, *51*, 8156-8159.
[159] Z. Shi, C. He, *J. Am. Chem. Soc.* **2004**, *126*, 13596-13597.
[160] A. Hassner, F. W. Fowler, *J. Org. Chem.* **1968**, *33*, 2686-2691
[161] (a) H. S. G. Beckmann, V. Wittmann, *Org. Lett.* **2006**, *9*, 1-4; (b) T. L. F. Himo, R. Hilgraf, V. V. Rostovtsev, L. Noodleman, K. B. Sharpless, V. V. Fokin, *J. Am. Chem. Soc.* **2004**, *127*, 210-216.
[162] (a) A. Suzuki, *Angew. Chem. Int. Ed.* **2011**, *50*, 6722-6737; (b) K. Z. A. Thakur, J. Louie, *Chem. Commun.* **2012**, *48*, 203-205; (c) P. R. E. Salanouve, Y. L. Janin, *Tetrahedron* **2012**, *68*, 2135-2140.
[163] G. Zhang, Y. Peng, L. Cui, L. Zhang, *Angew. Chem. Int. Ed.* **2009**, *48*, 3112-3115.
[164] (a) M. Al-Amin, K. E. Roth, S. A. Blum, *ACS Catal.* **2014**, *4*, 622-629; (b) K. E. Roth, S. A. Blum, *Organometallics* **2011**, *30*, 4811-4813; (c) Y. Shi, S. A. Blum, *Organometallics* **2011**, *30*, 1776-1779; (d) J. J. Hirner, Y. Shi, S. A. Blum, *Acc. Chem. Res.* **2011**, *44*, 603-613; (e) A. S. K. Hashmi, C. Lothschütz, R. Döpp, M. Ackermann, J. De Buck Becker, M. Rudolph, C. Scholz, F. Rominger, *Adv. Synth. Catal.* **2012**, *354*, 133-147; (f) A. S. K. Hashmi, C. Lothschütz, R. Döpp, M. Rudolph, T. D. Ramamurthi, F. Rominger, *Angew. Chem. Int. Ed.* **2009**, *48*, 8243-8246.
[165] H. E. Gottlieb, V. Kotlyar, A. Nudelman, *J. Org. Chem.* **1997**, *62*, 7512-7515.
[166] R. M. Z. P. Mauleon, A. Z. Gonzalez, F. D. Toste, *J. Am. Chem. Soc.* **2009**, *131*, 6348-6349.
[167] (a) K. M. Buchner, T. B. Clark, J. M. N. Loy, T. X. Nguyen, K. A. Woerpel, *Org. Lett.* **2009**, *11*, 2173-2175; (b) P. E. Peterson. T. A. Flood, *J. Org. Chem.* **1980**, *45*, 5006-5007.
[168] T. S. Jiro Tsuji, Ichiro Minami, *Synthesis* **1987**, 603-606.
[169] (a) H. Clavier, K. L. Jeune, I. de Riggi, A. Tenaglia, G. Buono, *Org. Lett.* **2011**, *13*, 308-311; (b) M. S. Baird, A. V. Nizovtsev, I. G. Bolesov, *Tetrahedron* **2002**, *58*, 1581-1593.
[170] (a) Z. Zhang, R. A. Widenhoefer, *Org. Lett.* **2008**, *10*, 2079 - 2081; (b) BD. Djahanbini, B. Cazes, J. Gore, *Tetrahedron* **1987**, *43*, 3441-3452.
[171] V. N. G. Lindsay, D. Fiset, P. J. Gritsch, S. Azzi, A. B. Charette, *J. Am. Chem. Soc.* **2013**, *135*, 1463-1470.
[172] (a) Q.-H. Li, J.-W. Liao, Y.-L. Huang, R.-T. Chiang, H.-M. Gau, *Org. Biomol. Chem.* **2014**, *12*, 7634-7642; (b) Q. Li, H. Gau, *Synlett* **2012**, *23*, 747-750.
[173] (a) M. Yonehara, S. Nakamura, A. Muranaka, M. Uchiyama, *Chem. Asian J.* **2010**, *5*, 452-455; (b) H. Nakamura, T. Kamakura, S. Onagi, *Org. Lett.* **2006**, *8*, 2095-2098.
[174] (a) S. M. J. Kuang, *J. Am. Chem. Soc.* **2010**, *132*, 1786-1787; (b) S. Buchwald, C. Larsen, K. Anderson, R. Tundel, *Synlett* **2006**, *2006*, 2941-2946.
[175] A. Pelter, K. Smith, K. D. Jones, *J. Chem. Soc. Perkin Trans. 1* **1992**, 747-748.
[176] B. Bolte, Y. Odabachian, F. Gagosz, *J. Am. Chem. Soc.* **2010**, *132*, 7294-7296.

[177] R. Pelagalli, I. Chiarotto, M. Feroci, S. Vecchio, *Green Chemistry* **2012**, *14*, 2251.
[178] (a) M. Benohoud, S. Tuokko, P. M. Pihko, *Chem. Eur. J.* **2011**, *17*, 8404-8413; (b) M. H. A. Arase, Y. Masuda, *Bull. Chem. Soc. Jpn.* **1984**, *57*, 209-213.
[179] Y. T. S.-I. Murahashi, Y. Imada, Y. Tanigawa, *J. Org. Chem.* **1989**, *54*, 3292-3303.
[180] M. R. Saidi, N. Azizi, E. Akbari, F. Ebrahimi, *J. Mol. Catal. A* **2008**, *292*, 44-48.
[181] (a) F. Liu, A. Martin-Mingot, M. P. Jouannetaud, C. Bachmann, G. Frapper, F. Zunino, S. Thibaudeau, *J. Org. Chem.* **2011**, *76*, 1460-1463; (b) W. K. M. Viscontini, H. A. Leidne, *Helv. Chim. Acta* **1965**, *48*, 1221-1225.
[182] C. Qin, P. Feng, Y. Ou, T. Shen, T. Wang, N. Jiao, *Angew. Chem. Int. Ed.* **2013**, *52*, 7850-7854.
[183] (a) M. Avalos, R. Babiano, J. L. Barneto, J. L. Bravo, P. Cintas, J. L. Jiménez, J. C. Palacios, *J. Org. Chem.* **2001**, *66*, 7275-7282; (b) A. R. Katritzky, A. E. Hayden, K. Kirichenko, P. Pelphrey, Y. Ji, *J. Org. Chem.* **2004**, *69*, 5108-5111.
[184] G. Zhang, Y. Peng, L. Cui, L. Zhang, *Angew. Chem. Int. Ed.* **2009**, *48*, 3112-3115.
[185] W. Beck, T. M. Klapötke, P. Klüfers, G. Kramer, C. M. Rienäcker, *Z. Anorg. Allg. Chem.* **2001**, *627*, 1669-1674.
[186] A. F. C. Barnard, *Platinum Metals Rev.* **2012**, *56*, 165-176.
[187] (a) R. P. M. D. Hall, G. B. Kauffman, *Platinum Metals Rev.* **2010**, *54*, 250-256; (b) M. Jamshidi, R. Yousefi, S. M. Nabavizadeh, M. Rashidi, M. G. Haghighi, A. Niazi, A. A. Moosavi-Movahedi, *Int. J. Biol. Macromol.* **2014**, *66*, 86-96; (c) N. Margiotta, E. Petruzzella, J. A. Platts, S. T. Mutter, R. J. Deeth, R. Ranaldo, P. Papadia, P. A. Marzilli, L. G. Marzilli, J. D. Hoeschele, G. Natile, *Dalton Trans,* **2015**, *44*, 3544-3556.
[188] F. R. Hartley, *Chemistry of the platinum group metals: recent developments*, Elsevier, **1991**.
[189] (a) A. Furstner, P. W. Davies, *Angew. Chem. Int. Ed.* **2007**, *46*, 3410-3449; (b) T. G. V. Mamane, H. Krause, A. Furstner, *J. Am. Chem. Soc.* **2004**, *126*, 8654-8655; (c) H. C. Clark, V. K. Jain, *Coordination Chemistry Reviews*, **1984**, *55*, 151-204; (d) E. Soriano, J. Marco-Contelles, *Acc. Chem. Res.* **2009**, *42*, 1026-1036; (e) IS. Oi, I. Tsukamoto , S. Miyano, Y. Inoue, *Organometallics* **2001**, *20*, 3704-3709; (f) C. Liu, C. F. Bender, X. Han, R. A. Widenhoefer, *Chem. Commun.* **2007**, 3607-3618.
[190] (a) M. Kadonaga, N. Yasuoka, N. Kasai, *Chem. Commun.* **1971**, 1597-1597; (b) S. Otsuka, A. Nakamura, K. Tani, *J. Organomet. Chem.* **1968**, *14*, P30-P32.
[191] (a) M. Paz Muñoz, M. C. de la Torre, M. A. Sierra, *Adv. Synth. Catal.* **2010**, *352*, 2189-2194; (b) M. P. Muñoz, M. C. de la Torre, M. A. Sierra, *Chem. Eur. J.* **2012**, *18*, 4499–4504.
[192] (a) L. Y. Mei, Y. Wei, X. Y. Tang, M. Shi, *J. Am. Chem. Soc.* **2015**; (b) B. Alcaide, P. Almendros, I. Fernández, T. M. d. Campo, T. Naranjo, *Adv. Synth. Catal.* **2013**, *355*, 2681-2685; (c) N. Marion, G. Lemiere, A. Correa, C. Costabile, R. S. Ramon, X. Moreau, P. de Fremont, R. Dahmane, A. Hours, D. Lesage, J. C. Tabet, J. P. Goddard, V. Gandon, L. Cavallo, L. Fensterbank, M. Malacria, S. P. Nolan, *Chem. Eur. J.* **2009**, *15*, 3243-3260; (d) R. Zriba, V. Gandon, C. Aubert, L. Fensterbank, M. Malacria, *Chem. Eur. J.* **2008**, *14*, 1482-1491; (e) K. C. N. Cadran, G. Herve, C. Aubert, L. Fensterbank, M. Malacria, J. Marco-Contelles, *J. Am. Chem. Soc.* **2004**, *126*, 3408-3409; (f) L. Charruault, V. Michelet, R. Taras, S. Gladiali, J. P. Genet, *Chem. Commun.* **2004**, 850-851; (g) C.-H. Liu, Z.-X. Yu, *Org. Chem. Front.* **2014**, *1*, 1205-1209.
[193] A. De Renzi, B. Di Blasio, A. Panunzi, C. Pedone, A. Vitagliano, *J. Chem. Soc. Dalton Trans.* **1978**, 1392-1397.
[194] A. De Renzi, A. Panunzi, A. Saporito, A. Vitagliano, *J. Chem. Soc. Perkin. Trans. 2* **1983**, 993-996.
[195] T. Ishiyama, T. Kitano, N. Miyaura, *Tetrahedron Lett.* **1998**, *39*, 2357-2360.
[196] L. C. M. Wang, Z. Wu, *Organometallics* **2008**, *27*, 6464-6471.

[197] (a) B. Alcaide, P. Almendros, C. Aragoncillo, *Chem. Soc. Rev.* **2014**, *43*, 3106-3135; (b) G. Chen, X. Jiang, C. Fu, S. Ma, *Chem. Lett.* **2010**, *39*, 78-81; (c) R. Stamm, H. Hopf, *Beilstein J. Org. Chem.* **2013**, *9*, 36-48; (d) H. Hopf, in *Modern Allene Chemistry*, Wiley-VCH Verlag GmbH, **2008**, pp. 185-241; (e) S. Braverman, Y. Duar, *J. Am. Chem. Soc.* **1990**, *112*, 5830-5837; (f) P. G. F. Toda, *Chem. Rev.* **1992**, *92*, 1685-1707; (g) C. Aragoncillo, *An. Quim.* **2010**, *106*, 268-276.

[198] K. Liu, H. Kim. P. Ghosh, N. G. Akhmedov, L. J. Williams, *J. Am. Chem. Soc.* **2011**, *133*, 14968-14971.

[199] (a) C. S. M. E. D. Farley, *J. Am. Chem. Soc.* **1936**, *58*, 29-34; (b) C. S. Marvel, W. J. Peppel, *J. Am. Chem. Soc.* **1939**, *61*, 895-897.

[200] R. Kuhn, H. Fischer, *Chem. Ber.* **1961**, *94*, 3060-3071.

[201] T. L. Jacobs, P. Prempree, *J. Am. Chem. Soc.* **1967**, *89*, 6177-6182.

[202] K. M. Brummond, J. E. DeForrest, *Synthesis* **2007**, *2007*, 795-818.

[203] (a) K. O. S. Kitagaki, K. Katoh, C. Mukai, *Org. Lett.* **2006**, *8*, 95-98; (b) S. Kitagaki, Y. Okumura, C. Mukai, *Tetrahedron Lett.* **2006**, *47*, 1849-1852; (c) S. Kitagaki, K. Katoh, K. Ohdachi, Y. Takahashi, D. Shibata, C. Mukai, *J. Org. Chem.* **2006**, *71*, 6908-6914; (d) F. Toda, K. Tanaka, I. Sano, T. Isozaki, *Angew. Chem. Int. Ed.*. **1994**, *33*, 1757-1758.

[204] (a) Y. Zafrani, H. E. Gottlieb, M. Sprecher, S. Braverman, *J. Org. Chem.* **2005**, *70*, 10166-10168; (b) Y. Zafrani, M. Cherkinsky, H. E. Gottlieb, S. Braverman, *Tetrahedron* **2003**, *59*, 2641-2649; (c) T. Mitra, S. Jana, S. Pandey, P. Bhattacharya, U. K. Khamrai, A. Anoop, A. Basak, *J. Org. Chem.* **2014**, *79*, 5608-5616; (d) I. Iwai, J. Ide, *Chem. Pharm. Bull.* **1964**, *12*, 1094-1100; (e) P. J. Garratt, S. B. Neoh, *J. Am. Chem. Soc.* **1975**, *97*, 3255-3257; (f) Y. S. P. Cheng, P. J. Garratt, S. B. Neoh, V. M. Rumjanek, *Israel Journal of Chemistry* **1985**, *26*, 101-107; (g) Y. S. P. Cheng, E. Dominguez, P. J. Garratt, S. B. Neoh, *Tetrahedron Lett.* **1978**, *19*, 691-694; (h) B. H. Bui, P. R. Schreiner, *Eur. J. Org. Chem.* **2006**, *2006*, 4187-4192; (i) S. Braverman, Y. Zafrani, H. E. Gottlieb, *Tetrahedron Lett.* **2000**, *41*, 2675-2678; (j) S. Braverman, Y. Zafrani, H. E. Gottlieb, *Tetrahedron* **2001**, *57*, 9177-9185; (k) R. Mukherjee, A. Basak, *Synlett* **2012**, *23*, 877-880.

[205] (a) W. Shu, G. Jia, S. Ma, *Angew. Chem. Int. Ed.* **2009**, *48*, 2788-2791; (b) X. Lian, S. Ma, *Chem. Eur. J.* **2010**, *16*, 7960-7964.

[206] (a) B. Alcaide, P. Almendros, C. Aragoncillo, I. Fernandez, G. Gomez-Campillos, *J. Org. Chem.* **2014**, *79*, 7075-7083; (b) B. Alcaide, P. Almendros, C. Aragoncillo, *Chem. Soc. Rev.* **2010**, *39*, 783-816; (c) X. Jiang, X. Cheng, S. Ma, *Angew. Chem. Int. Ed.* **2006**, *45*, 8009-8013.

[207] (a) S. Ma. P. Lu, *Org. Lett.* **2007**, *9*, 2095-2097; (b) Y. Deng, C. Fu, S. Ma, *Chem. Eur. J.* **2011**, *17*, 4976-4980.

[208] Y. Deng, Y. Shi, S. Ma, *Org. Lett.* **2009**, *11*, 1205-1208.

[209] M. K. S. Kitagaki, S. Narita, C. Mukai, *Org. Lett.* **2012**, *14*, 1366-1369.

[210] (a) S.-K. Kang, Y.-H. Ha, D.-H. Kim, Y. Lim, J. Jung, *Chem. Commun.* **2001**, 1306-1307; (b) Y.-T. Hong, S.-K. Yoon, S.-K. Kang, C.-M. Yu, *Eur. J. Org. Chem.* **2004**, *2004*, 4628-4635.

[211] Y.-N. Lim, H.-T. Kim, H.-S. Yoon, H.-Y. Jang, *Bull. Korean. Chem. Soc.* **2011**, *32*, 3117-3119.

[212] S. M. Kim, J. H. Park, Y. K. Kang, Y. K. Chung, *Angew. Chem. Int. Ed.* **2009**, *48*, 4532-4535.

[213] S. Ma. P. Lu, *Chin. J. Chem.* **2010**, *28*, 1600 - 1606.

[214] R. M. Beesley, C. K. Ingold, J. F. Thorpe, *J. Chem. Soc. Trans.* **1915**, *107*, 1080-1106.

[215] (a) E.-i. Negishi, C. Copéret, S. Ma, S.-Y. Liou, F. Liu, *Chem. Rev.* **1996**, *96*, 365-394; (b) K. M. Brummond, J. M. McCabe, *Tetrahedron* **2006**, *62*, 10541-10554; (c) M. M. L. Fensterbank, *Acc. Chem. Res.* **2014**, *47*, 953.

[216] M. Ogasawara, T. Hayashi, in *Modern Allene Chemistry*, Wiley-VCH Verlag GmbH, **2008**, pp. 93-140.

[217] P. Lu, J. Kuang, S. Ma, *Synlett* **2010**, *2010*, 227-230.
[218] T.-G. B. S. -K. Kang, A. N. Kulak, Y. -H. Ha, Y. Lim, J. Park, *J. Am. Chem. Soc.* **2000**, *122*, 11529 - 11530.
[219] S. Ma, P. Lu, L. Lu, H. Hou, J. Wei, Q. He, Z. Gu, X. Jiang, X. Jin, *Angew. Chem. Int. Ed.* **2005**, *44*, 5275-5278.
[220] S. Ma, L. Lu, *Chem. Asian J.* **2007**, *2*, 199-204.
[221] S. Ma. P. Lu, *Org. Lett.* **2007**, *9*, 5319-5321.
[222] J. H. Park, E. Kim, H. M. Kim, S. Y. Choi, Y. K. Chung, *Chem. Commun.* **2008**, 2388-2390.
[223] (a) F. Inagaki, S. Narita, T. Hasegawa, S. Kitagaki, C. Mukai, *Angew. Chem. Int. Ed.* **2009**, *48*, 2007-2011; (b) T. Kawamura, F. Inagaki, S. Narita, Y. Takahashi, S. Hirata, S. Kitagaki, C. Mukai, *Chem. Eur. J.* **2010**, *16*, 5173-5183.
[224] J. Cheng, X. Jiang, S. Ma, *Org. Lett.* **2011**, *13*, 5200 - 5203.
[225] (a) B. M. Fraga, *Natural Product Reports* **2013**, *30*, 1226-1264; (b) B. M. Fraga, *Natural Product Reports* **2012**, *29*, 1334-1366; (c) K. T. de Oliveira, B. M. Servilha, L. de C. Alves, A. L. Desiderá, T. J. Brocksom, in *Studies in Natural Products Chemistry, Vol. Volume 42* (Ed.: R. Atta ur), Elsevier, **2014**, pp. 421-463; (d) P. A. Wender, L. Zhang, *Org. Lett.* **2000**, *2*, 2323-2326.
[226] (a) M. A. Casadei, C. Galli, L. Mandolini, *J. Am. Chem. Soc.* **1984**, *106*, 1051-1056; (b) M. A. Battiste, P. M. Pelphrey, D. L. Wright, *Chem. Eur. J.* **2006**, *12*, 3438-3447; (c) J. H. Ryan, C. Hyland, J. Just, A. G. Meyer, J. A. Smith, C. C. Williams, in *Progress in Heterocyclic Chemistry, Vol. Volume 25* (Eds.: W. G. Gordon, A. J. John), Elsevier, **2013**, pp. 455-495; (d) X. L. C. M. Schienebeck, X.-z. Shu, and W. Tang, *Pure Appl. Chem.* **2014**, *86*, 409-417; (e) T. V. Nguyen, J. M. Hartmann, D. Enders, *Synthesis* **2013**, *45*, 845-873.
[227] M. Inoue, M. W. Carson, A. J. Frontier, S. J. Danishefsky, *J. Am. Chem. Soc.* **2001**, *123*, 1878-1889.
[228] M. Gaydou, R. E. Miller, N. Delpont, J. Ceccon, A. M. Echavarren, *Angew. Chem. Int. Ed.* **2013**, *52*, 6396-6399.
[229] R. A. Taj, J. R. Green, *J. Org. Chem.* **2010**, *75*, 8258-8270.
[230] M. Mandal, H. Yun, G. B. Dudley, S. Lin, D. S. Tan, S. J. Danishefsky, *J. Org. Chem.* **2005**, *70*, 10619-10637.
[231] H. M. L. Davies, B. D. Doan, *J. Org. Chem.* **1998**, *63*, 657-660.
[232] K. C. Nicolaou, Y.-P. Sun, X.-S. Peng, D. Polet, D. Y. K. Chen, *Angew. Chem. Int. Ed.* **2008**, *47*, 7310-7313.
[233] O. Mitsunobu, M. Yamada, *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2380-2382.
[234] R. Appel, *Angew. Chem. Int. Ed.* **1975**, *14*, 801-811.
[235] M. P. Muñoz, *Org. Biomol. Chem.* **2012**, *10*, 3584-3594.
[236] P. Webber, M. J. Krische, *J. Org. Chem.* **2008**, *73*, 9379-9387.
[237] (a) T. Rundlof, M. Mathiasson, S. Bekiroglu, B. Hakkarainen, T. Bowden, T. Arvidsson, *J. Pharm. Biomed. Anal.* **2010**, *52*, 645-651; (b) P. N. Kolesnikov, D. L. Usanov, E. A. Barablina, V. I. Maleev, D. Chusov, *Org. Lett.* **2014**, *16*, 5068-5071.
[238] (a) J. Franzén, J. Löfstedt, I. Dorange, J.-E. Bäckvall, *J. Am. Chem. Soc.* **2002**, *124*, 11246-11247; (b) G. Zhu, Z. Zhang, *Org. Lett.* **2004**, *6*, 4041-4044.
[239] B. Crociani, F. Di Bianca, R. Bertani, L. Zanotto, *Inorg. Chim. Acta* **1988**, *141*, 253-261.
[240] M. P. Rowe, W. H. Steinecker, E. T. Zellers, *Analytical Chemistry* **2007**, *79*, 1164-1172.
[241] N. C. Dopke, H. E. Oemke, *Inorg. Chim. Acta* **2011**, *376*, 638-640.
[242] (a) T. Bai, S. Ma, G. Jia, *Coordin. Chem. Rev.* **2009**, *253*, 423-448; (b) W. Kong, J. Cui, Y. Yu, G. Chen, C. Fu, S. Ma, *Org. Lett.* **2009**, *11*, 1213-1216.
[243] F. P. I. Francesco P. Fanizzi, Luciana Maresca, Giovanni Natile *J. Chem. Soc. Dalton Trans.* **1990**, 199-202; (b) R. B. Daniela Fraccarollo, Mirto Monzzon, Umberto Belluco, Rino A. Michelin, I*norg. Chim. Acta* **1992**, *201*, 15-22

[244] Y. T. Toshihiko Uchiyama, Yukio Nakamura, Toshio Miwa, Shinichi Kawaguchi, *Bull. Chem. Soc. Jpn.* **1981**, *54*, 181-185.
[245] N. C. Dopke, H. E. Oemke , *Inorg. Chim. Acta* **2011**, *376*, 638-640.
[246] T. G. Appleton, M. A. Bennett, B. Tomkins, *J. Chem. Soc. Dalton Trans*. **1976**
[247] (a) S. D. Cummings, *Coordin. Chem. Rev.* **2009**, *253*, 449-478; (b) J. R. Shapley, I. Inorganic Syntheses, *Inorganic Syntheses*, Wiley, **2004**.
[248] J. S. F. Riaan Buchner, Raymond J. Haines, Corey T. Cunningham, David R. MaMillin, *Inorg. Chem.* **1997**, *36*, 3952-3956.
[249] A. S. K. Hashmi, T. Häffner, M. Rudolph, F. Rominger, *Chem. Eur. J.* **2011**, *17*, 8195-8201.
[250] (a) D. Yim, H. Yoon, C.-H. Lee, W.-D. Jang, *Chem. Commun.* **2014**, *50*, 12352-12355; (b) W. J. Shi, J. Y. Liu, D. K. Ng, *Chem. Asian J.* **2012**, *7*, 196-200.
[251] N. Cadran, K. Cariou, G. Hervé, C. Aubert, L. Fensterbank, M. Malacria, J. Marco-Contelles, *J. Am. Chem. Soc.* **2004**, *126*, 3408-3409.
[252] (a) J. Huang, W. Xu, *J. Appl. Polym. Sci.* **2011**, *122*, 1251-1257; (b) S. Seo, T. J. Marks, *Chem. Eur. J.* **2010**, *16*, 5148-5162.
[253] T.-G. B. Suk-Ku Kang, Alexander N. Kulak, Young-Hwan Ha, Yoongho Lim, Joongmin Park, *J. Am. Chem. Soc.* **2000**, *122*, 11529-11530.
[254] X. Lian, S. Ma, *Chem. Eur. J.* **2010**, *16*, 7960-7964.
[255] H. Ohno, T. Mizutani, Y. Kadoh, A. Aso, K. Miyamura, N. Fujii, T. Tanaka, *J. Org. Chem.* **2007**, *72*, 4378-4389.
[256] (a) A. Heydari, S. E. Hosseini, *Adv. Synth. Catal.* **2005**, *347*, 1929-1932; (b) S. Z. Johannes F. Teichert, Anthoni W. van Zijl, Jan Willem Slaa, Adriaan J. Minnaard, Ben L. Feringa, *Org. Lett.* **2010**, *12*, 4658-4660.
[257] Y. Kavanagh, C. M. Chaney, J. Muldoon, P. Evans, *J. Org. Chem.* **2008**, *73*, 8601-8604.
[258] R. K. Dieter, N. Chen, V. K. Gore, *J. Org. Chem.* **2006**, *71*, 8755-8760.
[259] Y. Amako, H. Hori, S. Arai, A. Nishida, *J. Org. Chem.* **2013**, *78*, 10763-10775.
[260] N. W. Mszar, F. Haeffner, A. H. Hoveyda, *J. Am. Chem. Soc.* **2014**, *136*, 3362-3365.
[261] V. Maraval, C. Duhayon, Y. Coppel, R. Chauvin, *Eur. J. Org. Chem.* **2008**, *2008*, 5144-5156.
[262] (a) X. Zhang, W. T. Teo, Sally, P. W. H. Chan, *J. Org. Chem.* **2010**, *75*, 6290-6293; (b) X. Zhang, W. T. Teo, P. W. H. Chan, *Org. Lett.* **2009**, *11*, 4990-4993.
[263] (a) A. Doutheau, A. Saba, J. Goré, *Synthetic Communications* **1982**, *12*, 557-563; (b) H. G. Richey, L. M. Moses, *J. Org. Chem.* **1983**, *48*, 4013-4017; (c) C. Kammerer-Pentier, A. Diez Martinez, J. Oble, G. Prestat, P. Merino, G. Poli, *J. Organomet. Chem.* **2012**, *714*, 53-59.
[264] A. Boutier, C. Kammerer-Pentier, N. Krause, G. Prestat, G. Poli, *Chem. Eur. J.* **2012**, *18*, 3840-3844.
[265] P. Lu. S. Ma, *Org. Lett.* **2007**, *9*, 2095-2097.
[266] (a) F. Kleinbeck. F. D. Toste, *J. Am. Chem. Soc.* **2009**, *131*, 9178 - 9179; (b) C. K. H. Devendra J. Vyas, Martin Oestreich, *Org. Lett.* **2011**, *13*, 4462 - 4465.
[267] (a) W. K. J. Li, C. Fu, S. Ma, *J. Org. Chem.* **2009**, *74*; (b) S. P. Cook, S. J. Danishefsky, *Org. lett.* **2006**, *8*, 5693-5695.
[268] L. Zhao, X. Lu, W. Xu, *J. Org. Chem.* **2005**, *70*, 4059-4063.
[269] S. P. Cook, S. J. Danishefsky, *Org. Lett.* **2006**, *8*, 5693-5695.
[270] K. Semba, T. Fujihara, J. Terao, Y. Tsuji, *Angew. Chem. Int. Ed.* **2013**, *52*, 12400-12403.
[271] P. Lu, S. Ma, *Org. Lett.* **2007**, *9*, 2095-2097.
[272] J. A. Varela, C. González-Rodríguez, S. G. Rubín, L. Castedo, C. Saá, *J. Am. Chem. Soc.* **2006**, *128*, 9576-9577.

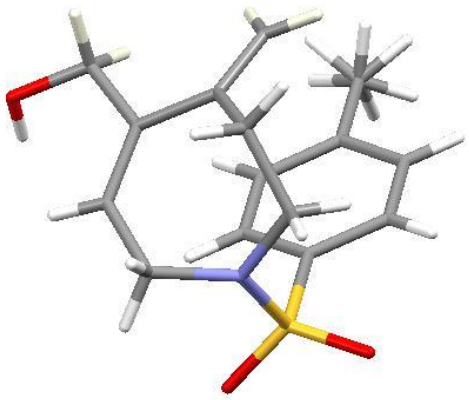
Appendix A

X-ray Data

The crystallographic data for the structures presented in the text are given in this experimental section. All the crystallographic analyses were performed by Dr. J. Christensen at NCS, UK National Crystallography Service.

Compound 319a-*d*^{4}

Crystal data and structure refinement for compound **319a-*d*^{4}**.

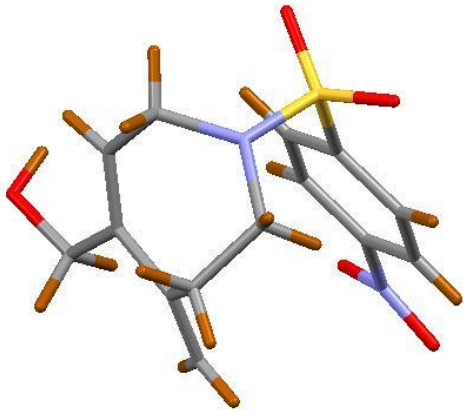


Empirical formula	$C_{15}H_{15}D_4NO_3S$	
Formula weight	297.40	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	*P*–1	
Unit cell dimensions	a = 7.7739(5) Å	α = 81.084(4)°
	b = 8.1108(5) Å	β = 77.029(4)°
	c = 11.6326(5) Å	γ = 84.725(5)°
Volume	704.87(7) Å^3	
Z	2	
Density (calculated)	1.401 Mg / m^3	
Absorption coefficient	0.236 mm^{-1}	
F(000)	312	
Crystal	Chip; colourless	

Crystal size	0.09 × 0.07 × 0.03 mm^3
θ range for data collection	2.546 – 29.975°
Index ranges	$-10 \le h \le 10$, $-11 \le k \le 11$, $-15 \le l \le 15$
Reflections collected	12909
Independent reflections	3710 [R_{int} = 0.0582]
Completeness to θ = 25.242°	100.0 %
Absorption correction	Semi–empirical from equivalents
Max. and min. transmission	1.00000 and 0.71189
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3710 / 0 / 232
Goodness-of-fit on F^2	1.044
Final R indices [$F^2 > 2\sigma(F^2)$]	$R1$ = 0.0448, $wR2$ = 0.0994
R indices (all data)	$R1$ = 0.0661, $wR2$ = 0.1086
Extinction coefficient	n/a
Largest diff. peak and hole	0.329 and –0.388 e $Å^{-3}$

Compound 319c

Crystal data and structure refinement for compound **319c**.

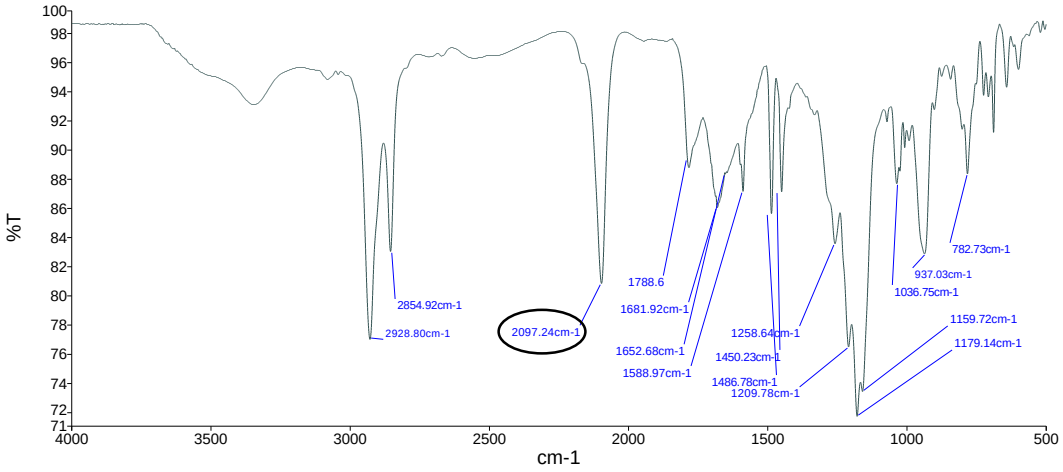


Empirical formula	$C_{14}H_{16}N_2O_5S$
Formula weight	324.35
Temperature	100(2) K

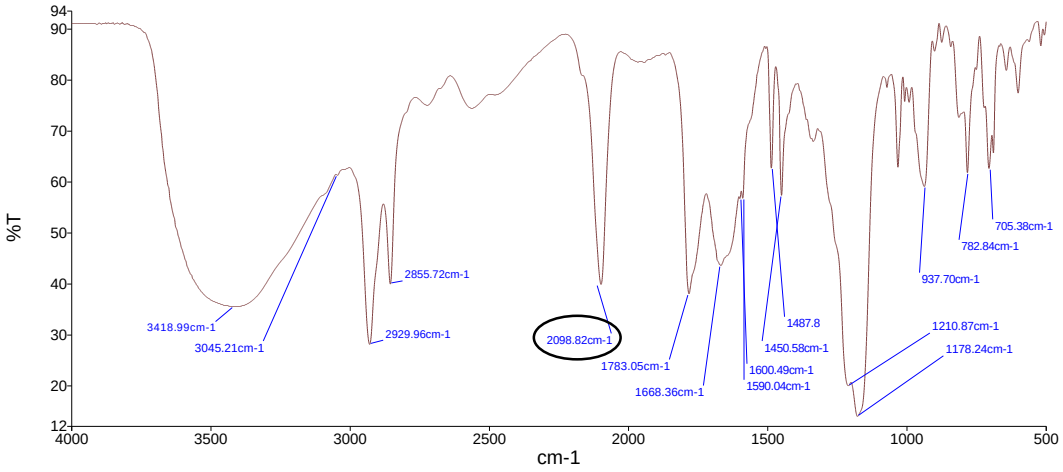
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	*P*–1	
Unit cell dimensions	a = 7.4327(3) Å	α = 84.381(3)°
	b = 7.9704(3) Å	β = 77.298(3)°
	c = 12.1638(5) Å	γ = 87.637(3)°
Volume	699.45(5) Å^3	
Z	2	
Density (calculated)	1.540 Mg / m^3	
Absorption coefficient	0.259 mm^{-1}	
F(000)	340	
Crystal	Block; colourless	
Crystal size	0.17 × 0.08 × 0.06 mm^3	
θ range for data collection	2.568 – 29.509°	
Index ranges	$-9 \le h \le 10$, $-10 \le k \le 10$, $-14 \le l \le 16$	
Reflections collected	9013	
Independent reflections	3478 [R_{int} = 0.0422]	
Completeness to θ = 25.242°	99.8 %	
Absorption correction	Semi–empirical from equivalents	
Max. and min. transmission	1.00000 and 0.71296	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3478 / 0 / 203	
Goodness-of-fit on F^2	1.042	
Final R indices [$F^2 > 2\sigma(F^2)$]	*R1* = 0.0379, *wR2* = 0.0986	
R indices (all data)	*R1* = 0.0468, *wR2* = 0.1034	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.386 and –0.412 e Å^{-3}	

Apendix B

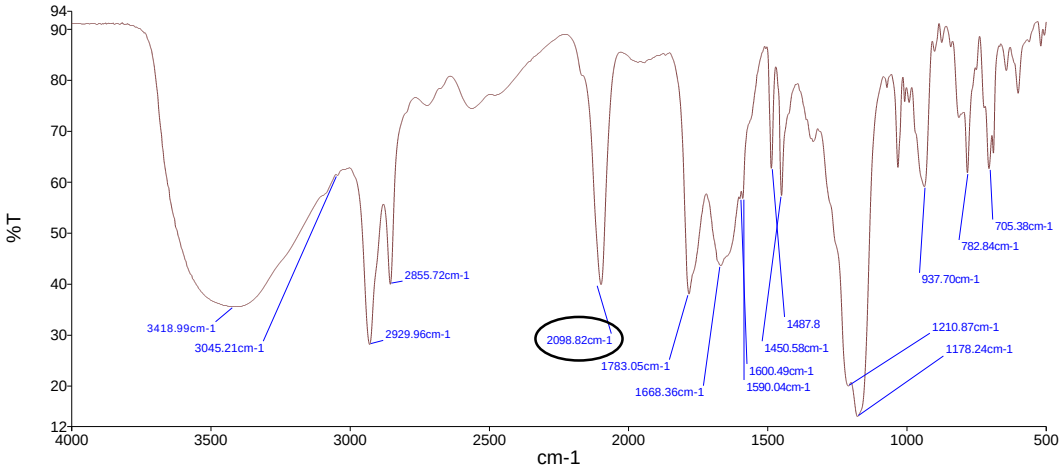
Gold-catalysed hydroazidation reaction of allenes monitored by IR



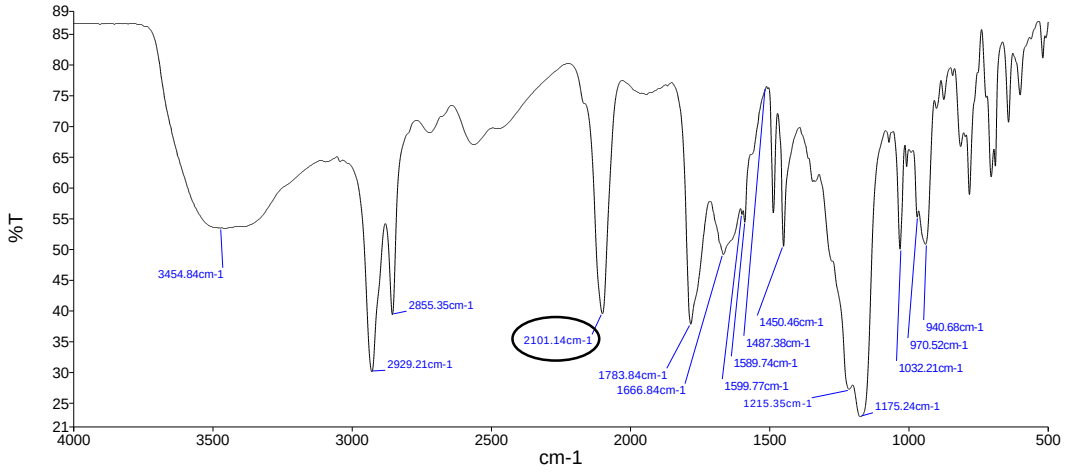
IR carried out after 30 min.



IR carried out after 1 h 45 min.



IR carried out after 6 h.



IR carried out after 9 h 30 min.

Stoichiometric NMR Experiments

Experiment **A**

Results obtained in stoichiometric experiment **A**

Addition	Time (min)	^{31}P NMR (ppm)	^{1}H NMR integral (1H)					
			96b	**124a**	**125a**	**127**	**128**	**126**
$(PhO)_3PAuCl$	0	110	-	-	-	-	-	-
AgOTf	0	-	-	-	-	-	-	-
-	30	104	-	-	-	-	-	-
$TMSN_3$	75	-	-	-	-	-	-	-
-	105	106	-	-	-	-	-	-
109b	145	-	-	-	-	-	-	-
-	205	104	5.27	0.3	1	0.00	0.39	0.00
TFA	285	-	-	-	-	-	-	-
-	305	103	3.09	0.64	1	0.3	0.5	0.00
-	425	103	2.14	0.90	1	0.56	0.5	0.00
H_2O	485	-	-	-	-	-	-	-
-	545	103	1.96	1.10	1	0.86	0.56	0.4
-	1405	-	0.8	1.84	1	1.16	0.80	0.65

Addition	Time (min)	% Conversion					
		96b	**124a**	**125a**	**127**	**128**	**126**
$(PhO)_3PAuCl$	-	-	-	-	-	-	-
AgOTf	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-

$TMSN_3$	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
109b	0	100	0.00	0.00	0.00	0.00	0.00
-	60	75.72	4.31	14.37	0.00	5.60	0.00
TFA	-	-	-	-	-	-	-
-	160	55.88	11.57	18.08	5.42	9.04	0.00
-	280	39.96	16.90	18.67	10.46	9.34	4.67
H_2O							
-	400	33.25	18.74	16.96	14.67	9.58	6.79
-	1260	12.78	29.47	15.97	18.53	12.86	10.38

Experiment **B**

Results obtained in stoichiometric experiment **B**

Addition	Time (min)	^{31}P NMR (ppm)	^{1}H NMR integral (1H)					
			96b	**124a**	**125a**	**127**	**128**	**126**
$(PhO)_3PAuCl$	0	110	-	-	-	-	-	-
AgOTf	0	-	-	-	-	-	-	-
-	30	104	-	-	-	-	-	-
109b	75	-	-	-	-	-	-	-
-	105	105	-	-	-	-	-	-
$TMSN_3$	145	-	-	-	-	-	-	-
-	205	106	4.97	0.45	1	0.3	0.36	0.00
TFA	285	-	-	-	-	-	-	-
-	305	103	4.71	0.62	1	0.56	0.63	0.00
-	425	103	3.09	0.78	1	0.66	0.60	0.15
-	545	103	3.37	1.19	1	0.89	0.6	0.25
-	1405	-	1.23	1.52	1	1.18	0.55	0.5

Addition	Time (min)	% Conversion					
		96b	**124a**	**125a**	**127**	**128**	**126**
$(PhO)_3PAuCl$	-	-	-	-	-	-	-
AgOTf	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
109b	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
$TMSN_3$	0	100	0.00	0.00	0.00	0.00	0.00
-	60	70.20	6.36	14.12	4.24	5.08	0.00

TFA	-	-	-	-	-	-	-
-	160	62.55	8.30	13.28	7.44	8.43	0.00
-	280	49.09	12.39	15.89	10.56	9.61	2.46
-	400	46.10	16.35	13.68	12.24	8.21	3.42
-	1260	20.55	25.48	16.71	19.72	9.19	8.35

Experiment **C**

Results obtained in stoichiometric experiment **C**

Addition	Time (min)	^{31}P NMR (ppm)	^{1}H NMR integral (1H)					
			96b	**124a**	**125a**	**127**	**128**	**126**
$(PhO)_3PAuCl$	0	110	-	-	-	-	-	-
AgOTf	0	-	-	-	-	-	-	-
-	30	104	-	-	-	-	-	-
TFA	75	-	-	-	-	-	-	-
-	105	99	-	-	-	-	-	-
$TMSN_3$	145	-	-	-	-	-	-	-
-	205	97.69	-	-	-	-	-	-
109b	285	-	-	-	-	-	-	-
-	305	98.16	5.68	0.36	1	0.54	0.28	0.00
-	425	98.56	2.3	0.70	1	1.01	0.25	0.15
-	545	97.96	2.03	0.98	1	1.22	0.3	0.28
-	1405	-	0.94	1.53	1	1.68	0.25	0.67

Addition	Time (min)	% Conversion					
		96b	**124a**	**125a**	**127**	**128**	**126**
$(PhO)_3PAuCl$	-	-	-	-	-	-	-
AgOTf	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
TFA	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
$TMSN_3$	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
109b	0	100	0.00	0.00	0.00	0.00	0.00
-	20	72.17	4.64	12.71	6.86	3.62	0.00
-	140	42.40	13.00	18.43	18.62	4.70	2.86
-	260	34.91	16.85	17.20	20.98	5.16	4.90
-	1120	15.56	25.19	16.46	27.65	4.12	11.03

Time (h)	^{1}H NMR integral (1H) / Conversion (%)											
	96b		**124a**		**125a**		**127**		**128**		**126**	
0	1	100	0	0	1	0	0	0	0	0	0	0
1	0.78	24.2	0.65	20.2	1	30.9	0.3	9.26	0.5	15.4	0	0.00
3	0	0.00	3.12	53.4	1	17.1	0.24	4.10	1.46	24.9	0.03	0.51
5	0	0.00	4.03	57.4	1	14.2	0.23	3.27	1.75	24.9	0.01	0.14
7	0	0.00	4.21	56.7	1	13.5	0.3	4.04	1.91	25.7	0.01	0.13
9	0	0.00	4.38	54.8	1	13.1	0.33	4.13	2.17	27.1	0.11	1.38
11	0	0.00	4.23	54.3	1	12.5	0.33	4.24	2.12	27.2	0.11	1.41
22	0	0.00	4.22	57.0	1	12.8	0.35	4.73	1.71	23.1	0.12	1.62

Table 15. Further information about the integrals related to the different products.