Synthesis and Trifluoromethylation of Allylsilanes

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Author's Declaration

The work presented in this thesis was conducted at the Chemistry Research Laboratory at the University of Oxford under the supervision of Professor Véronique Gouverneur. All the work is my own, except where otherwise stated, and has not been submitted for any other degree at this or any other university.

Oscar Galicia López

September 2013

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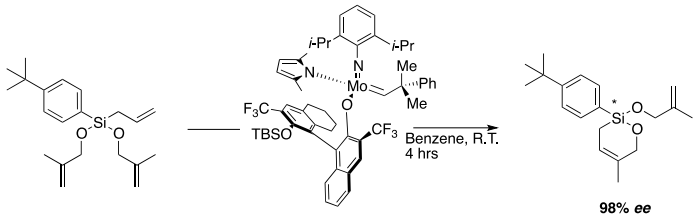
The first part of this thesis presents a novel approach for synthesising enantioenriched cyclic allylsilanes via asymmetric ring-closing metathesis (ARCM). The second part of this thesis focuses on the reactivity of allylsilanes in electrophilic trifluoromethylation under transition metal and photoredox catalysis.

Chapter 1 provides a general introduction to existing methods for preparing compounds containing Si-stereogenic centres. The motivation for using ARCM to form Si-stereogenic centres is discussed. To set the stage for this work, the development of olefin metathesis as a tool in organic synthesis is briefly summarised.

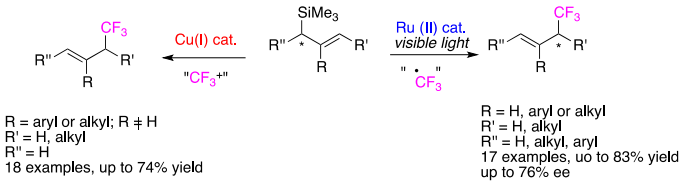
Chapter 2 describes the synthesis of various prochiral silicon-containing trienes and their reactivity in Ru-, Mo- and W-catalysed ring-closing metathesis. . Following extensive screening of chiral catalysts, few catalysts were identified that enabled selective ARCM to access Si-stereogenic products in up to 98% ee. A systematic investigation of the relationship between the structure of the starting material (*i.e.*, hydrocarbon chain length, steric and electronic properties of the silicon substituents) and the resulting efficacy in ARCM was undertaken, the results from these experiments are discussed. Importantly, this study represents the first example in which ARCM has been successfully used to desymmetrise prochiral substrates to form a new chiral Si centre (Scheme 1).



Scheme 1 Enantioselective synthesis of Si-stereogenic compounds through ARCM.

Chapter 3 provides a general introduction to the field of trifluoromethylation, with a special focus on recent applications of transition metal catalysts in Csp^2–CF_3 and Csp^3–CF_3 bond formation. A myriad of effective nucleophilic, electrophilic and radical trifluromethylating reagents have been developed during the past several years; the properties of these reagents and their compatibility with various modes of catalysis are summarised to provide a context for the second part of this thesis research.

Chapter 4 presents two novel methods for effecting trifluoromethylation of allylsilanes . First, it was discovered that the combination of an electrophilic trifluoromethlyating reagent and a copper catalyst effectively mediated trifluoromethylation of allylsilanes. The silicon substituent was crucial for improving the nucleophilicity of the substrate and dictating the regioselectivity of the Csp^3–CF_3 bond-forming step. With this method, alkyl or aryl substitution at the β-position of the allylsilane was critical for reactivity. Second, in a complementary study, it was found that copper could be replaced by a ruthenium photocatalyst and visible light. This latter method allowed for trifluoromethylation of substrates that were ineffective with copper catalysis. Mechanistic studies of both reaction systems were undertaken, and plausible reaction pathways for both reactions are proposed.



Scheme 2 Trifluoromethylation of allylsilanes under Cu catalysis or Ru photoredox catalysis.

Chapter 5 gives full experimental procedures and characterisation data for all compounds.

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Table of Contents

Abstract i
Acknowledgements ii
Contents iv
Abbreviations and Acronyms vii

Chapter 1: Introduction

1.1 Silicon and Organosilanes Overview 1
1.2 Synthesis of Si-stereogenic silanes by chiral auxiliary-induced asymmetric synthesis 3
1.3 Catalytic asymmetric synthesis of Si-stereogenic silanes 6
1.4 Enzymatic method 10
1.5 Application of Si-stereogenic silanes 12
1.6 Novel approach to the synthesis of enantiopure compounds 15
1.7 Olefin Metathesis 17
1.8 Reactivity of Grubbs catalysts 22
1.9 Catalyst decomposition 25
1.10 Ring-Closing Metathesis 27
1.11 Asymmetric Ring-Closing Metathesis 28
1.12 Importance of *syn* and *anti* alkylidene isomers 32
1.13 Mo Catalyst decomposition 34
1.14 Stereogenic Molybdenum catalysts 35
Objectives 41

Chapter 2: Asymmetric Ring Closing Metathesis under Chiral Mo and W Complexes 43

2.0 Introduction 43
2.1 Ring-Closing Metathesis
Silicon-stereogenicity 45
2.2 Synthesis of Substrates 45
First Generation of Prochiral Si-trienes 45
Second Generation of Prochiral Si-trienes 48
2.3 Ring-closing metathesis using achiral catalyst 54
2.4 Asymmetric Ring-Closing Metathesis 60
General Considerations 60

Five-membered ring 63
Six-membered ring series 64
Isomerisation at Mo-catalyst 72
2.5 Mechanistic considerations 77
2.6 Seven-membered ring series 82
2.7 Conclusions 87

Chapter 3: Trifluoromethylation 90

3.1 The Trifluoromethyl group 90
3.2 Nucleophilic Trifluoromethylation 92
3.3 Electrophilic Trifluoromethylation 96
3.4 Radical Trifluoromethylation 97
3.5 Trifluoromethylation of Arene and Heteroarene Substrates 99
3.6 Trifluoromethylation of Carbonyl-Containing Substrates 110
3.7 Allylic Trifluoromethylation 114
Objectives 122

Chapter 4: Trifluoromethylation of Organosilanes 124

4.1 The Role of Organosilanes in Fluorination Processes 124
4.2 Initial Investigations 125
Reactivity of Allylsilanes in the Presence of Electrophilic Trifluoromethylating Reagents 125
4.3 Activation of the Electrophilic "$^{+}CF_3$" reagents 127
4.4 Synthesis of model substrates 131
4.5 Further Investigations 132
Trifluoromethylation 132
4.6 Design of Linear, Branched and Cyclic Allylsilanes 143
Synthesis of enol phosphates 143
Synthesis of Allylsilanes 149
Synthesis of Cyclic Allylsilanes 154
4.7 Trifluoromethylation 156
Trifluoromethylation of Cyclic Allylsilanes 165
4.8 Mechanistic Insights 166
Possible mechanism for the trifluoromethylation of allylsilanes under copper catalysis 173
4.9 Trifluoromethylation of Allylsilanes under Photoredox Catalysis 175

4.9 Conclusions 181

Chapter 5: Experimental Section **183**

References **268**

Abbreviations and Acronyms

$[\alpha]_D$	specific rotation
Ac	acetyl
Ad	adamantyl
ADMET	acyclic diene metathesis polymerisation
Ar	aryl
ARCM	asymmetric ring-closing metathesis
AROM/CM	asymmetric ring-opening metathesis cross metathesis
A(1,2)	1,2-allylic strain
atm	atmosphere
BINAP	1,1'-Binaphthalene-2,2'-diyl)bis(3,5-dimethyl-diphenylphosphine
BINOL	1,1'-bi-2-naphthol
Bn	benzyl
br	broad
i-Bu	isobutyl
n-Bu	normal-butyl
s-Bu	secondary-butyl
t-Bu	tertiary-butyl
^oC	degrees centigrade
cat.	catalyst
CI	chemical ionisation
CM	cross metathesis
CO	carbon dioxide
COD	cyclooctadiene
conc.	concentration
COSY	correlation spectroscopy
Cy	cyclohexyl
δ	chemical shift
d	doublet
DCM	dichloromethane
DIPEA	N,N-diisopropylethylamine
DMAP	4-dimethylaminopyridine
DMF	*N*,*N*-dimethylformamide
e	electron
ee	enantiomeric excess
eq	equatorial
e.r.	enantiomeric ratio
EI	electron impact
equiv.	equivalents
ESI	electrospray ionisation
Et	ethyl
FI	field ionisation
GC	gas chromatography
g	grams
G I	Grubbs I
G II	Grubbs II
h	hours
HG II	Hoveyda-Grubbs II

HMDS	hexamethyldisilazane
HMBC	heteronuclear multiple-bond correlation
HMQC	heteronuclear multiple-quantum correlation
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	hertz
IR	infa-red
IPA	*iso*-propyl alcohol
J	coupling constant
k_{rel}	relative rate constant
Keq	equilibrium constant
LDA	lithium diisopropylamide
LG	leaving group
μL	microlitres
μmol	micromoles
m	multiplet
m	meta
M	molar or molecular ion
mbar	millibar
m-CPBA	*meta*-chloroperbenzoic acid
Me	methyl
Mes	mesityl
mg	milligrams
mL	millilitres
mmol	millimoles
MOM	methyloxylmethyl
m.p.	melting point
ms	millisecond
MS	mass spectrometry
m/z	mass/charge ratio
ν	wavelength
N	normal
NHC	N-heterocyclic carbene
NMR	nuclear magnetic resonance
NOE	nuclear Overhouser effect
α-Np	1-napthyl
Nu	nucleophile
o	ortho
p	para
Ph	phenyl
ppm	parts per million
i-Pr	isopropyl
n-Pr	normal-propyl
psi	pounds per square inch
q	quartet
qu	quintet
RCM	ring-closing metathesis
Rel	relative
R*f*	retention factor
ROM	ring-opening metathesis
RRM	ring-rearrangement metathesis
RT	room temperature
s	singlet

sec	seconds
sec	secondary
SET	single electron transfer
S_N1	nucleophilic substitution unimolecular
S_N2	nucleophilic substitution bimolecular
t	triplet or time
TBAF	tetrabutylammonium fluoride
TBS	*tert*-butyldimethylsilyl
TFA	trifluoroacetic acid
Tfa	trifluoroacetyl
TMS	trimethylsilyl
TES	triethylsilyl
temp	temperature
tert	tertiary
Tf	triflate
THF	tetrahydrofuran
TLC	thin layer chromatography
TMEDA	tetramethylethanediamine
Tol	toluene or tolyl
Ts	tosyl
UV	ultra violet

1 Silicon Chemistry

1.1 Silicon and Organosilanes Overview.

At 28% by mass, silicon is the second most abundant element on Earth after oxygen.[1] It is widely distributed as silicon dioxide or silicates, and is not found as the pure free element in nature. A valuable form of silicon to synthetic chemists are organosilanes. Friedel and Crafts prepared the first organosilane compound in 1863 by reacting silicon tetrachloride with diethylzinc to form tetraethylsilane.[2]

Organosilane reagents play important roles in many areas of organic synthesis acting as protecting groups,[3] reducing agents[4] and partners in cross-coupling reactions.[5] In order to understand the reactivity of organosilanes, it is first necessary to understand the properties of the element silicon. The atomic number of silicon is 14; it is directly beneath carbon on the periodic table and is thus typically tetravalent. Much like carbon, silicon is found singly bonded to four other atoms using sp^3 hybridisation.[6,7,8] This might suggest a similarity in reactivity to carbon; however, the presence of d-orbitals in silicon gives it the ability to bond to more than four atoms, allowing it to become hypervalent (pentavalent or hexavalent).[9] The ability of silicon to form hypervalent intermediates results in electropositive character at silicon, which is demonstrated by the ability of silicon to act as Lewis acid. For tetracoordinated carbon and silicon species the preferred molecular geometry is tetrahedral, as shown in (Figure 1.1.1).

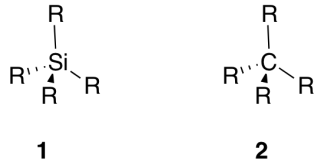


Figure 1.1.1 Structural geometries of tetracoordinated silicon and carbon.

The atomic radius of silicon (1.06 Å) is larger than the atomic radius of carbon (0.66 Å), but silicon is much less electronegative than carbon (1.90 and 2.55 respectively, on the Mulliken–Jaffe scale).[10,11] As silicon has a lower electronegativity than most other atoms, substituents bonded to silicon typically exert an electron-withdrawing effect, creating a partial positive charge on silicon atom and partial negative charges on the surrounding atoms (Table 1.1.1). This is represented in Figure 1.1.2, which contrasts the partial charge distribution of a C–H bond to a Si–H bond.[12]

Element	Electronegativity[a]
Si	1.90
C	2.55
H	2.20
F	3.98
Cl	3.16
O	3.44
N	3.04

Table 1.1.1 Electronegativity values for silicon and other common atoms.

[a] Mulliken-Jaffe Scale[10]



Figure 1.1.2 Partial charge distribution in C–H and C–Si bonds.

It is noteworthy that, a C–Si bond (1.87 Å) is substantially longer than a C–C bond (1.54 Å).[13] As alluded to above, a key difference between carbon and silicon is that silicon can participate

in hypervalent bonding to five or six ligands. Hypervalent organosilanes are prone to stereomutation *via* Berry pseudorotation[14] (Figure 1.1.3).

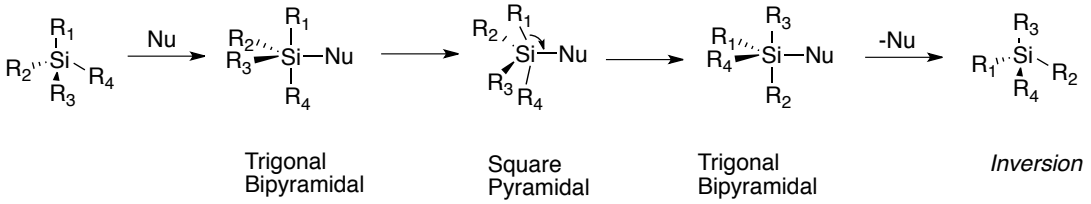
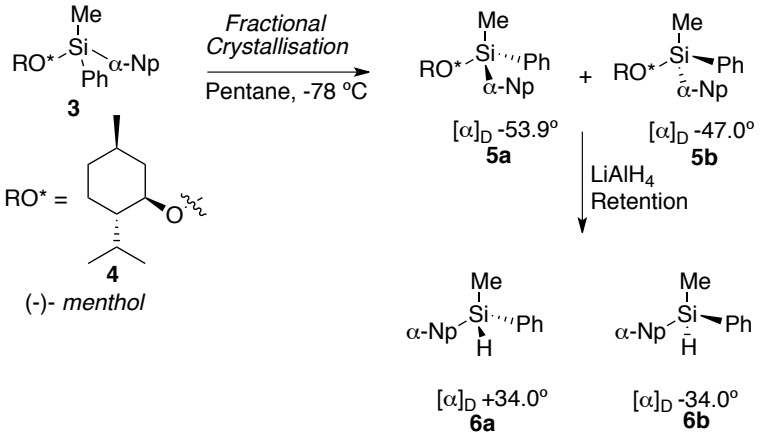


Figure 1.1.3 Mechanism of stereomutation *via* Berry pseudorotation.

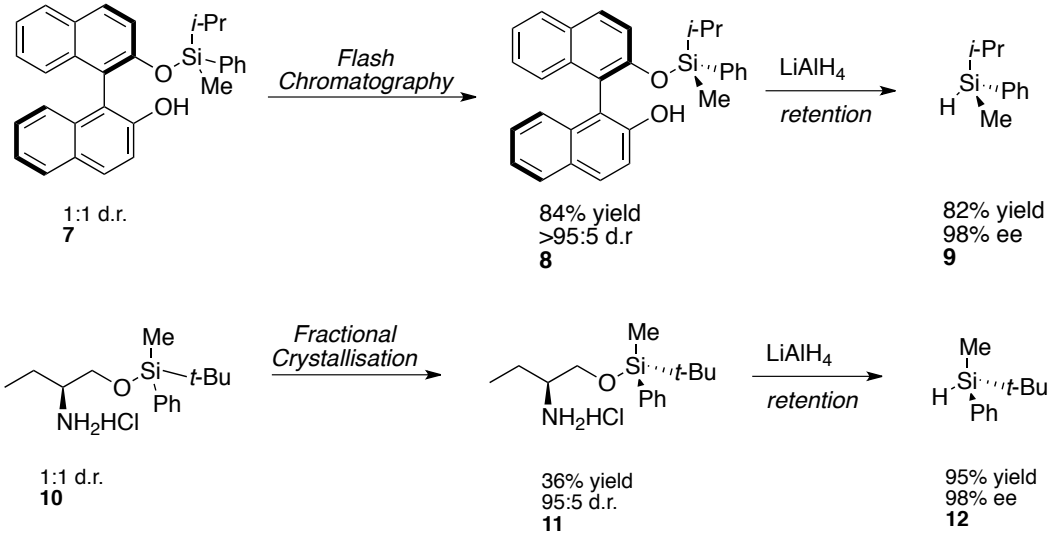
1.2 Synthesis of Si-stereogenic silanes by chiral auxiliary–induced asymmetric synthesis.

In 1907, Kipping and co-workers reported the first example of a racemic Si-stereogenic silane by treating silicon tetrachloride with Grignard reagents.[15] In the following years, much effort was devoted to the synthesis of non-racemic chiral compounds. It took 60 years before Sommer and co-workers reported the first acyclic silicon-stereogenic silane by employing the chiral auxiliary (–)-menthol.[16,17] Although the route proposed required laborious separation of the diastereomers formed, it ushered in a new era in asymmetric organosilicon chemistry (Scheme 1.2.1). Separation of the diastereomeric mixture was possible by fractional crystallisation in pentane at -78°C. Reductive cleavage of the silicon–oxygen linkage liberated the enantioenriched silane without erosion of the stereochemical information at silicon. The absolute configuration of **6a** and **6b** was determined by X-ray diffraction crystallography.



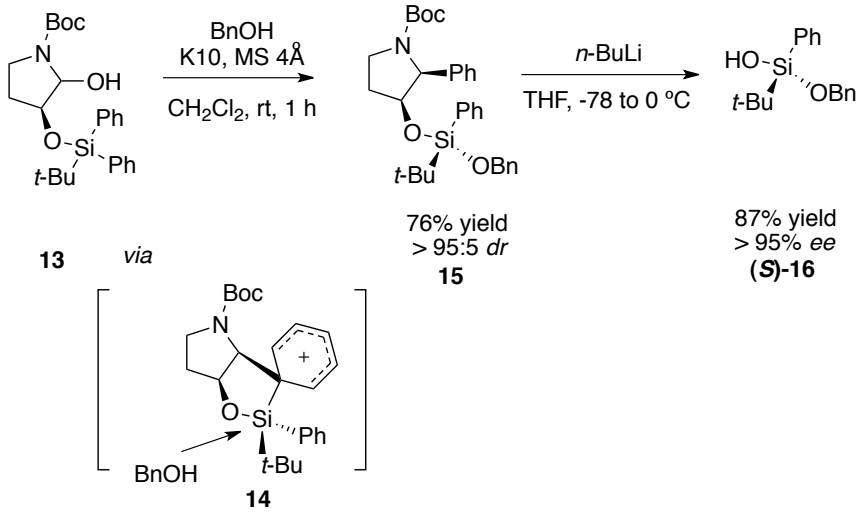
Scheme 1.2.1 Synthesis of an optically pure Si-stereogenic silane by chemical resolution.

Schaumann and co-workers later studied alternative procedures for resolving racemic chiral silanes.[18] They found that enantiomerically pure [1,1´]binaphthalenyl-2.2´diols (BINOLs) were effective resolving agents, and separation was possible by silica gel chromatography (Scheme 1.2.2). On the other hand, the use of 2-aminobutanol allowed the separation of the two diasteroisomers by fractional crystallisation, highlighting the need for a different purification strategy depending on the resolving agent employed.



Scheme 1.2.2 Preparation of optically active silanes by chemical resolution.

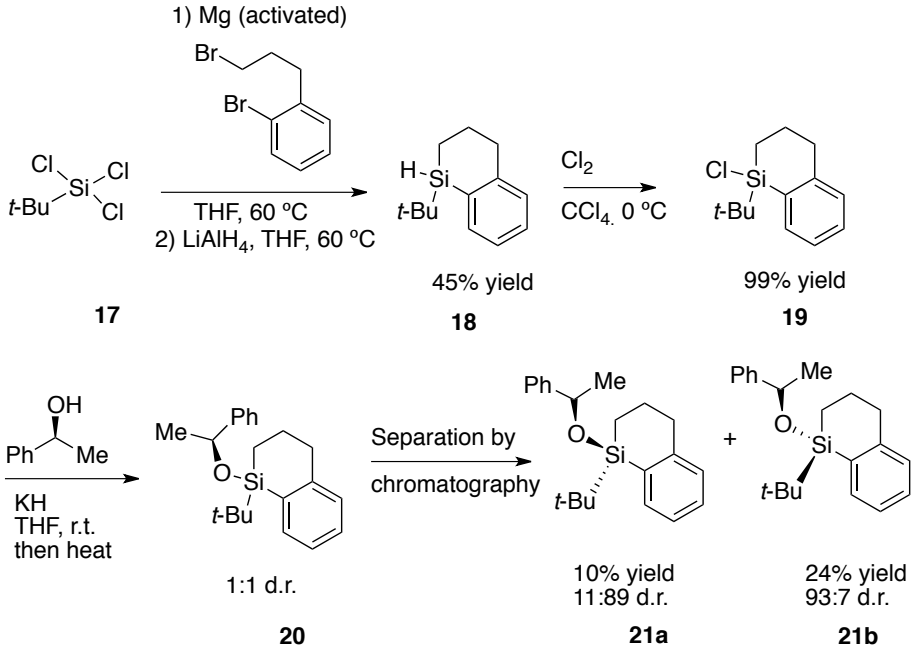
Concurrently, Tomooka *et al.* reported another method to access Si-stereogenic silanes using montmorillonite K10 clay which promotes 1,4-aryl migration (Scheme 1.2.3).[6,19] The reaction likely proceeds via formation of an *N*-acyliminium ion, followed by an intramolecular Friedel–Crafts reaction onto the aryl group through the cyclic five-membered intermediate **14** featuring a β-silyl cation. Nucleophilic attack by benzyl alcohol at silicon afforded **15**. Treatment of **15** with *n*-BuLi resulted in elimination of the desired chiral benzyloxysilanol (*S*)-**16** with high enantioselectivity (95% *ee*). This methodology does rely on the use of stoichiometric amount of the chiral auxiliary.



Scheme 1.2.3 1,4-Aryl migration leading to enantioenriched silanol (*S*)-**16.**

Oestreich *et al.* developed a novel method to synthesise rigid cyclic Si-stereogenic silanes by resolution of silyl ethers.[20] When the silane is part of a ring, the conformational freedom around silicon is restricted, increasing the level of organisation in stereoselectivity-determining transition states.[21,22] This strategy involved a four-step procedure starting from *tert*-butyltrichlorosilane **17**. The reaction of double Grignard addition to *tert*-butyltrichlorosilane **17** was quenched with an excess of $LiAlH_4$ giving the desired silane **18**. Chlorination and subsequent substitution by a homochiral alcohol afforded the Si-stereogenic

silanes as a 1:1 mixture of diastereomers. Separation of the two diastereomeric silyl ethers by chromatography proved to be difficult, with the diastereomerically enriched products isolated only in low yields.

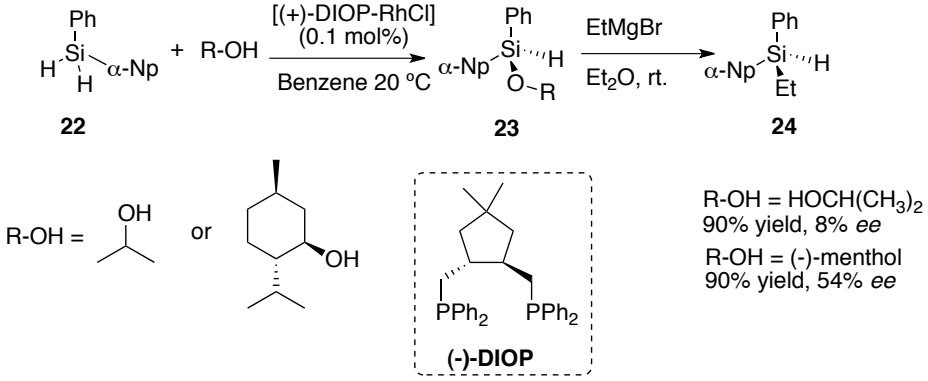


Scheme 1.2.4 Synthesis of rigid cyclic Si-stereogenic silanes by resolution.

1.3 Catalytic asymmetric synthesis of Si-stereogenic silanes

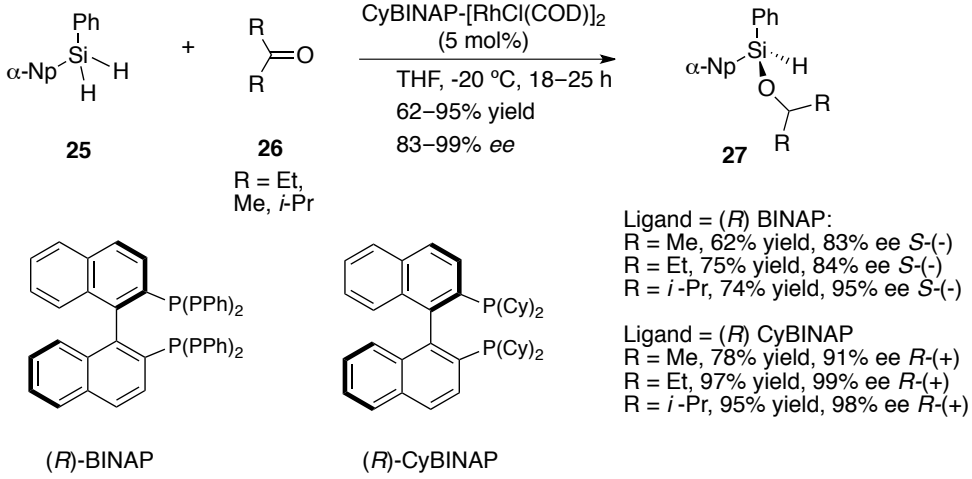
Catalytic asymmetric reactions are highly sought after processes in chemistry as they are often economical, environmentally friendly and energy-saving. Organosilicon chemistry has greatly benefited from catalysis in recent years. As described previously, most processes for the preparation of Si-stereogenic silanes in enantiopure form are based on classical resolution or chiral auxiliary approaches, which require the presence of a stoichiometric amount of a chiral group. The knowledge gained from these pioneering investigations paved the way for catalytic asymmetric syntheses of Si-stereogenic silanes. Only a few reports using transition metal catalysis have been reported to date. Corriu *et al* successfully synthesised a Si-stereogenic

silane using a chiral rhodium-DIOP catalyst (Scheme 1.3.1). The desymmetrisation of a prochiral silane occurred *via* alcoholysis and, 54% *ee* was achieved in the presence of an optically pure alcohol ((–)-menthol).[23]



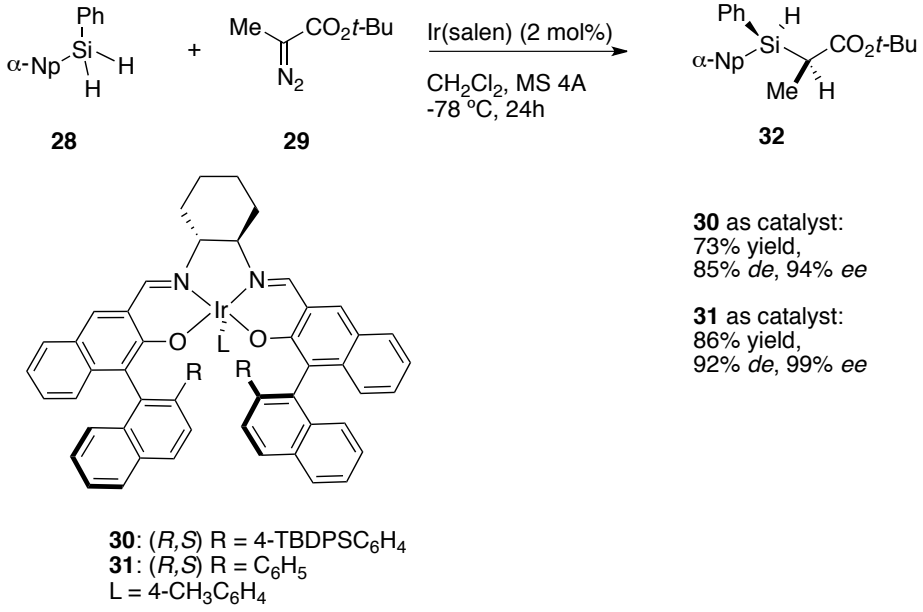
Scheme 1.3.1 Synthesis of Si-stereogenic silane by asymmetric alcoholysis.

Takaya developed the catalytic asymmetric synthesis of Si-stereogenic centres using rhodium (I) complexes possessing CyBINAP as a chiral ligand.[24] Enantioenriched alkoxysilanes were afforded in up to 99% *ee* with this catalytic system, which differentiates between the two enantiotopic hydrogens attached to the silicon atom. It is important to note that the absolute configuration of the products obtained with (*R*)-CyBINAP and (*R*)-BINAP are opposite (Scheme 1.3.2).



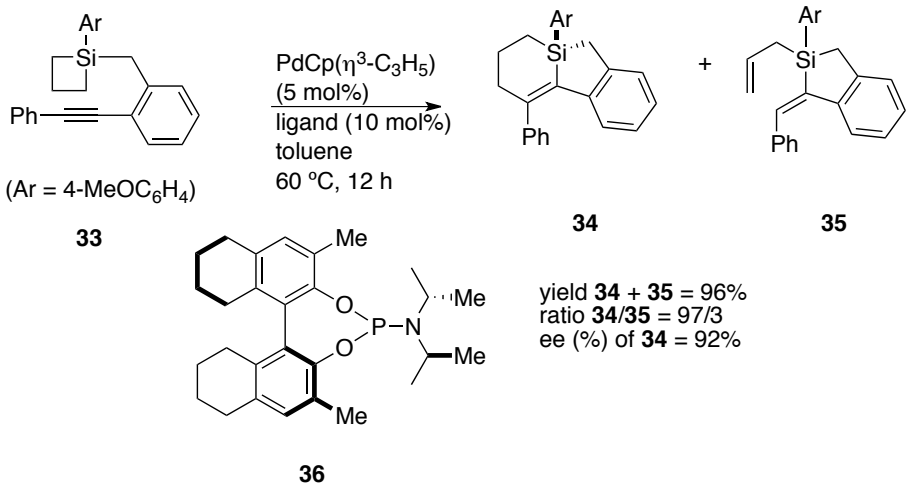
Scheme 1.3.2 Synthesis of enantioenriched Si centre by asymmetric hydrosilylation of ketones.

Katsuki *et al*, have shown that iridium (III)-salen complexes are useful as asymmetric carbene-transfer catalysts (Scheme 1.3.3). The reaction with (1-naphthyl)phenylsilane and *tert*-butyl α-diazopropionate proceeded via an enantioselective Si–H insertion to form just one of the four possible diasteromers in up to 99% *ee* and 92% *de.*[25] This example is significant because it demonstrates the formation of a new Si–C bond with excellent enantiocontrol.



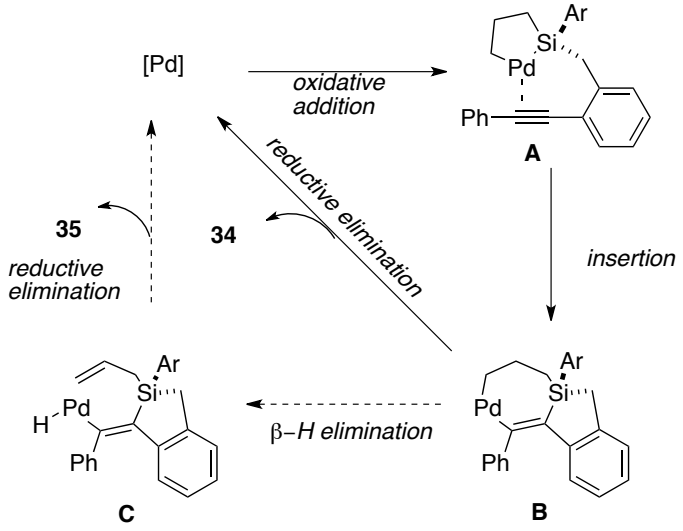
Scheme 1.3.3 Enantioselective Si–H insertion to form a stereogenic silicon centre.

In 2011, Hayashi and Shintani explored the possibility of constructing Si-stereogenicity by desymmetrisation of alkyne-tethered silacyclobutanes mediated by a chiral palladium catalyst (Scheme 1.3.4).[26] After exploring diverse chiral phosphoramidite ligands, the best result was obtained by conducting the reaction in toluene at 60 °C in the presence of ligand **36** and 5 mol% of $PdCp(C_3H_5)$, which gave **34** in high yield (96%) and high enantioselectivity (92% ee). Variation of the aryl group on silicon and of the alkyne was well tolerated, with products delivered in good yields (73–96%) and enantiomeric excess up to 95%.



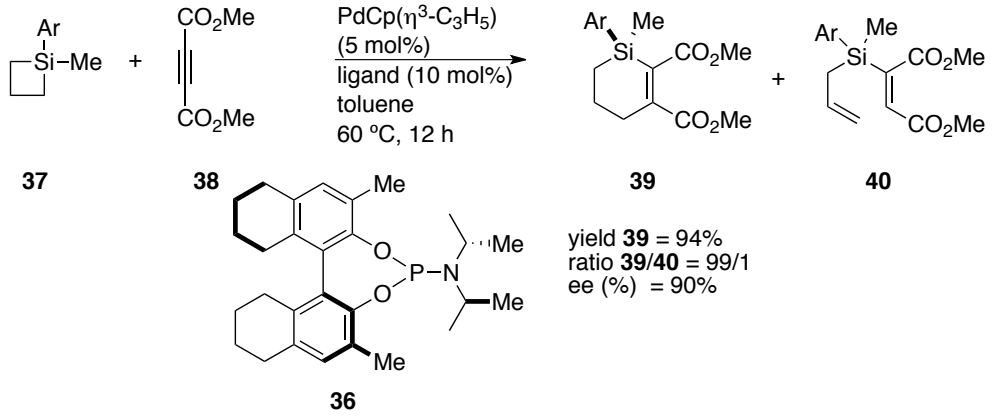
Scheme 1.3.4 Palladium catalysed desymmetrisation of silacyclobutane.

The authors proposed a catalytic cycle with the oxidative addition of Pd(0) into the C-Si bond of the silacyclobutane. Alkyne insertion to form the 1-pallada-4-sila-2-cycloheptene provides the desired product after reductive elimination. More sterically hindered phosphoramidites ligands such as **36** were most effective at preventing undesired β-hydride elimination (**35**).



Scheme 1.3.5 Proposed catalytic cycle for the formation of **34**.

Very recently, the same group extended this methodology to an intermolecular variant to form Si-stereogenic centres from the desymmetrisation of silacyclobutanes with electron-deficient alkynes in the presence of a palladium catalyst with a chiral ligand (Scheme 1.3.6).[27] The same conditions were applied to the intermolecular reaction to afford the desired silicon-stereogenic 1-sila-2-cyclohexene **39** in 94% yield and up to 90% *ee*.



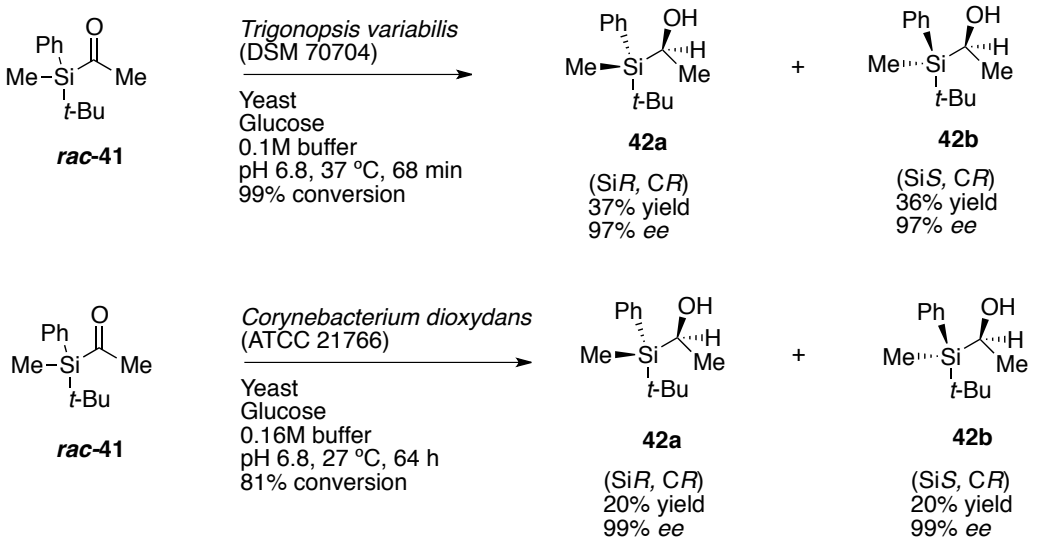
Scheme 1.3.6 Intermolecular palladium-catalysed desymmetrisation of silacyclobutanes with electron deficient alkynes.

1.4 Enzymatic method

An alternative method to access chiral organosilanes is *via* an enzymatic route. Although much less explored in comparison to metal catalysis, resolution, and chiral auxiliary approaches, it benefits from remarkably high chemo-, regio-, and stereoselectivity. The first example of enzymatic synthesis was reported in 1985, and since then many types of lipases and esterases have been explored.[28]

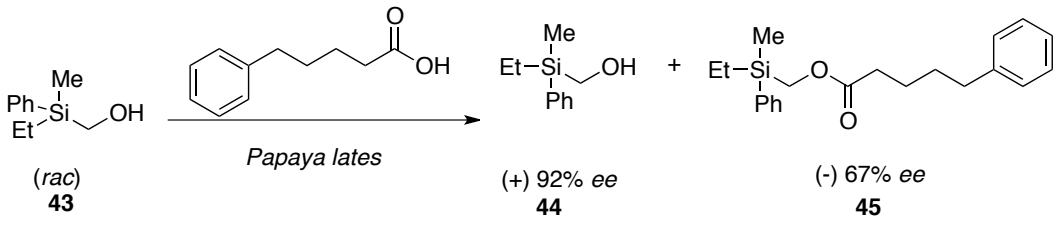
In 1991, Tacke *et al.* reported the enantioselective synthesis of (Si*R*,C*R*) and (Si*S*,C*R*)-*tert*-butyl(l-hydroxyethyl)methylphenylsilane compounds by microbial reduction of racemic acetyl(*tert*-butyl)methylphenylsilane in the presence of *Trigonopsis variabilis* (DSM 70704) in high yield (73%) and excellent *ee* (97%).[29] Using the *Corynebacterium dioxydans* (ATCC

21766) the bioconversion was lower (40% yield), but the desired product was still obtained in excellent *ee* (99%) (Scheme 1.4.1).



Scheme 1.4.1 Synthesis of enantioenriched silanes by enzymatic catalysis.

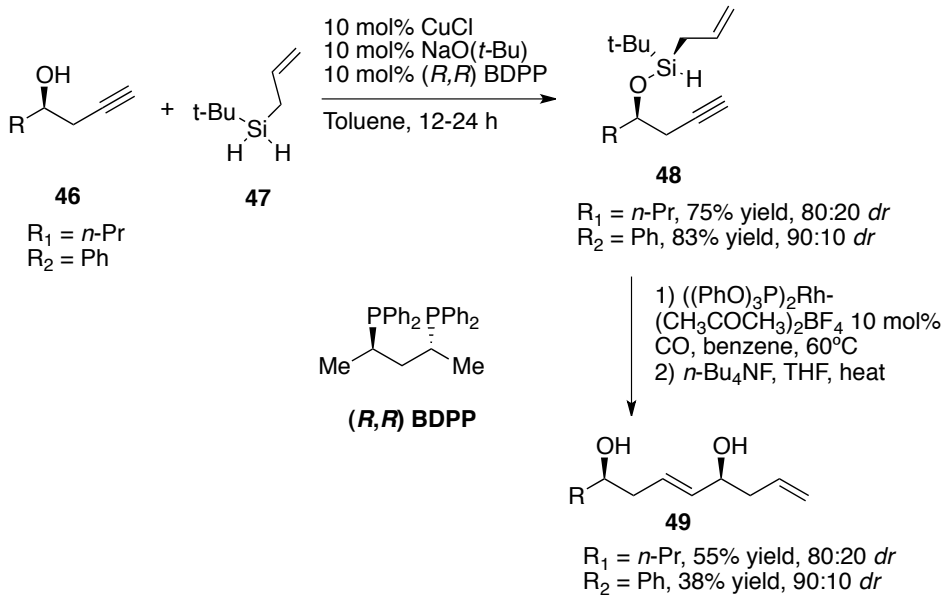
In 1994, Tanaka *et al.* reported an esterification reaction catalysed by hydrolases. In the reaction between the silicon-containing alcohol **43** and 5-phenylpentanoic the esterified compound was afforded in 60% yield. Importantly, the unreacted starting material was recovered in 92% *ee* (Scheme 1.4.2).[30]



Scheme 1.4.2 Enzymatic kinetic resolution of racemic silanols.

1.5 Application of Si-stereogenic silanes.

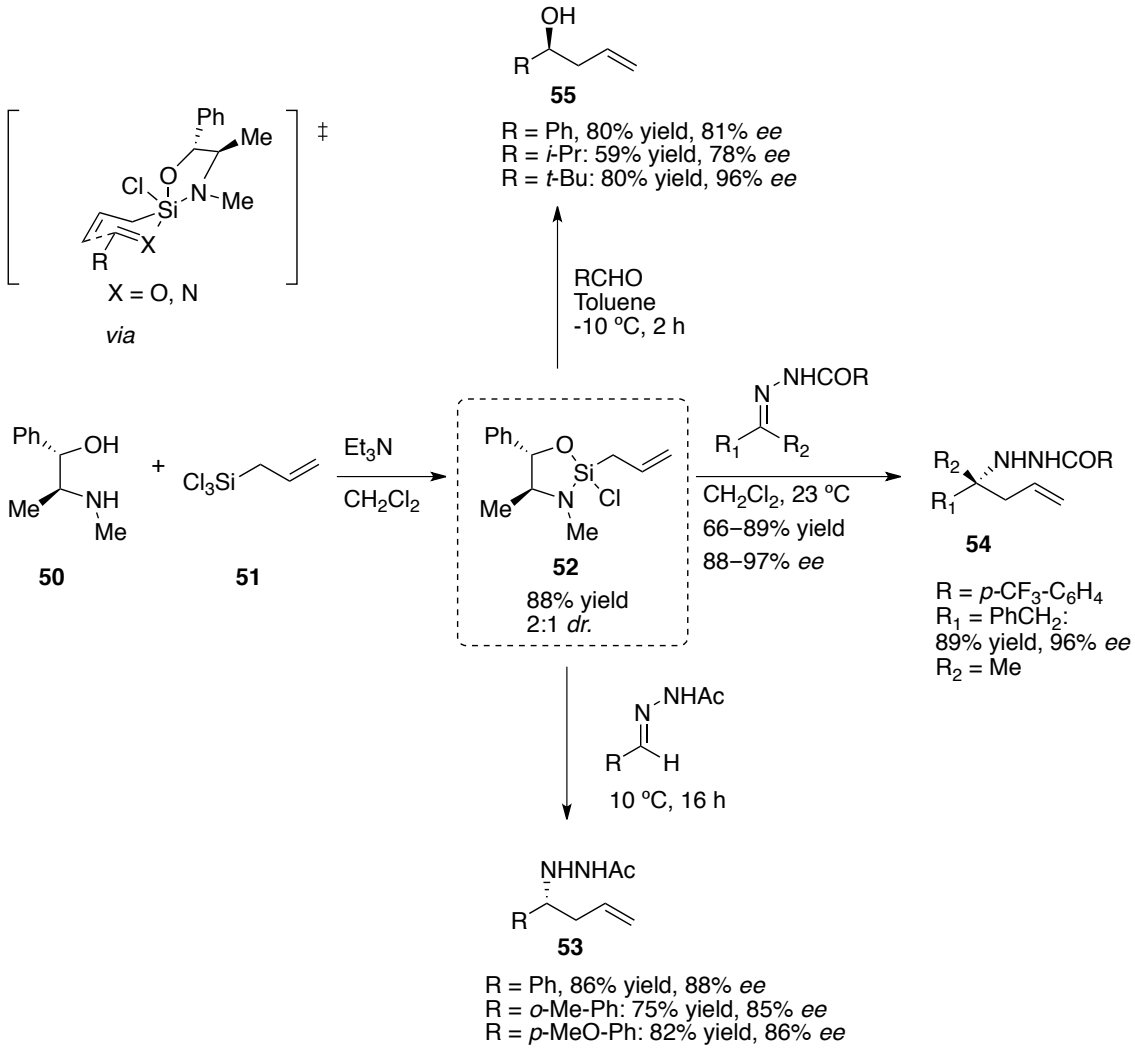
Chirality transfer from silicon to carbon has become of particular interest due to the large variety of organic transformations that can be carried out in this way.[31] However, this field has progressed slowly due to the difficulties in accessing Si-stereogenic silanes. In 2003, Leighton and co-workers reported a tandem silylformylation/allylsilylation reaction with alkynes. The reaction between propargylic alcohol and *tert*-butylallyl silane in the presence of CuCl and a chiral ligand led to the formation of diastereomerically enriched silanes. Subsequent allylformylation mediated by a Rh complex, carbonylation and deprotection yielded the 1,5-*syn*-diol without erosion of diastereoselectivity (Scheme 1.5.1). [32]



Scheme 1.5.1 Copper-catalysed silane alcoholysis leading to 1,5-diol.

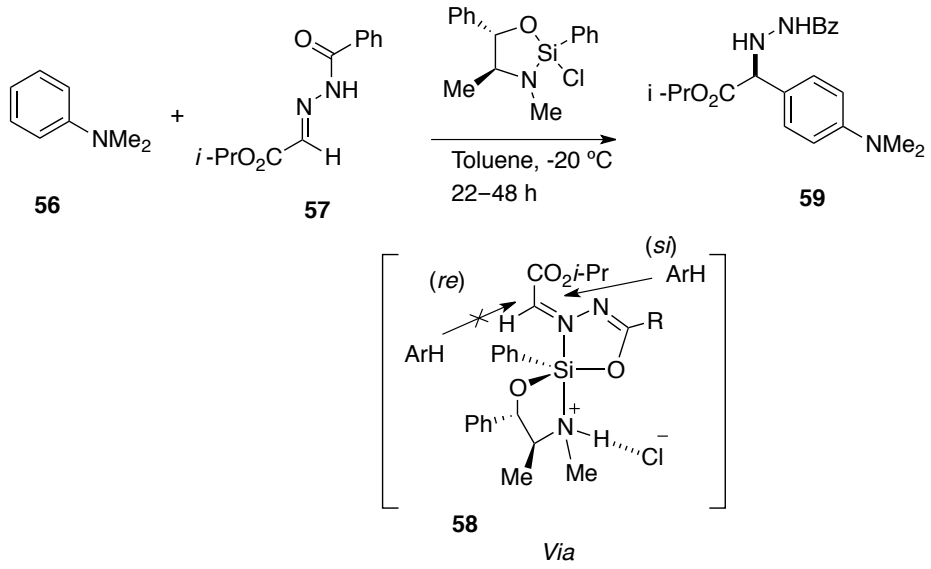
In 2003, Leighton used chiral silanes as Lewis acids by taking advantage of the ability of strained silacycles to become hypervalent[33] and reported the allylation and crotylation of aldehydes, ketones, and imines.[34] Although the pseudoephedrine-derived chiral allylsilane **52** was a 2:1 mixture of diastereomers, the enantioselectivities obtained in these transformations

were high (78–96% ee). The mechanistic basis behind the high levels of enantiocontrol remains unclear. However, it was suggested that both diastereomers could induce the same sense of enantioinduction in the product, or a pseudorotation-decomplexation sequence could lead to interconversion to give one enantiomer. The authors proposed a mechanism based on the coordination of the carbonyl or imine to the Lewis acidic silane reagent, which controls the enantioselectivity through formation of a chair-like transition state (Scheme 1.5.2).



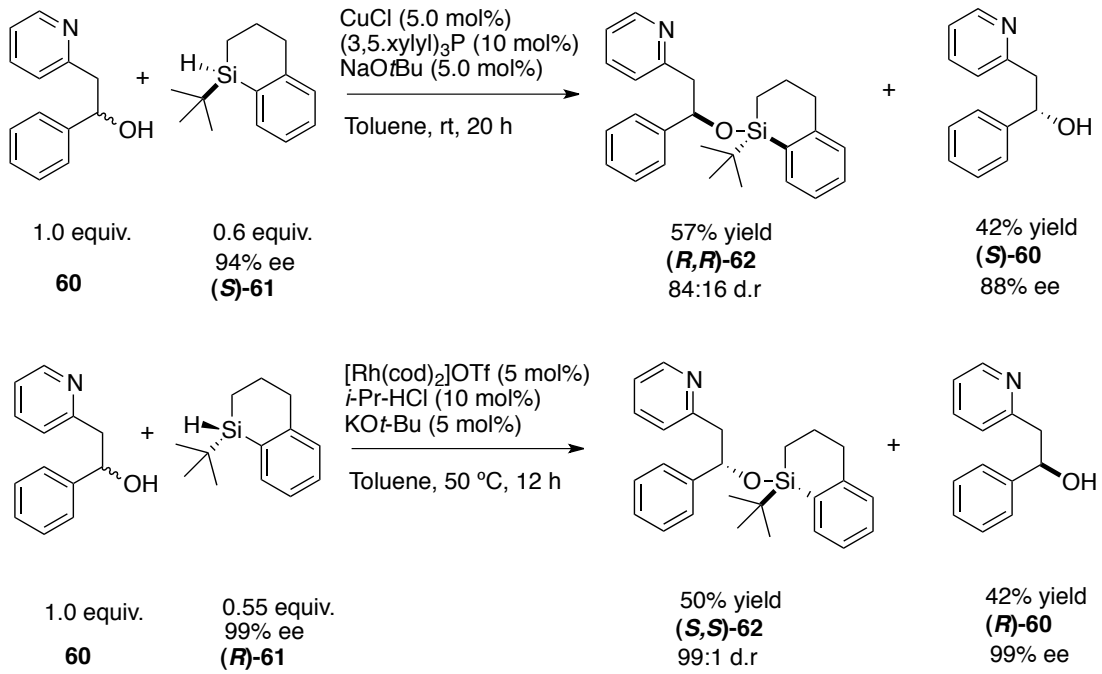
Scheme 1.5.2 Using silicon Lewis acidity to promote allylations.

Using a similar Si-stereogenic promoter, Leighton reported an enantioselective Friedel–Crafts reaction of electron–rich arenes and heteroarenes with benzoylhydrazone in up to 95% *ee*.[35] Similarly to **52**, and despite the low *dr* of the pseudoephedrine-derived silane, the reaction proceeded with excellent enantiocontrol. The authors proposed that the reaction proceeds *via* a trigonal bipyramidal silane (**58**) and the phenyl group on the silicon blocks access to the (*re*) face, instead favouring attack from the (*si*) face. This reasoning is consistent with **59** being the major enantiomer (Scheme 1.5.3). The silicon-based Lewis acid has also been used in other organic transformations such as, [3+2] cycloadditions,[36] Diels-Alder cycloadditions[37] and Mannich reactions.[38]



Scheme 1.5.3 Enantioselective Friedel–Crafts alkylation promoted by strained chiral silanes.

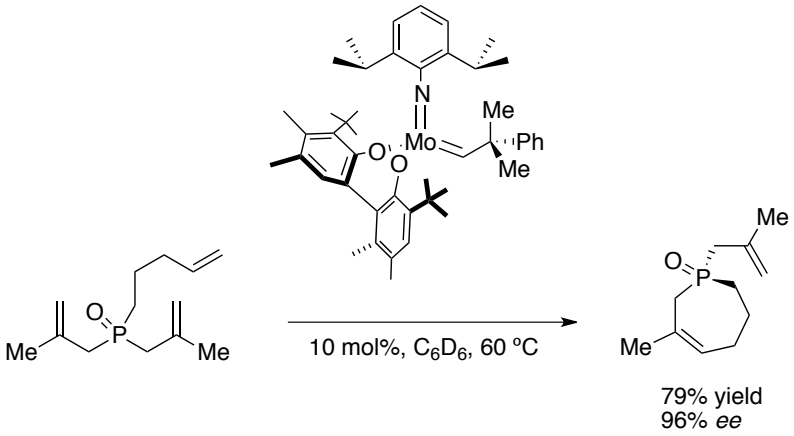
Oestreich *et al.* have extensively studied the synthesis of enantiopure silanes with the aim of investigating the chirality transfer from silicon to carbon. His group has reported the application of Si-stereogenic silanes for the control of asymmetric kinetic resolution. Under copper or rhodium catalysis, dehydrogenative silylation of secondary alcohols is possible with high enantiomeric excess and diasterocontrol (Scheme 1.5.4).[39]



Scheme 1.5.4 Kinetic resolution of alcohols under Rh or Cu catalysis.

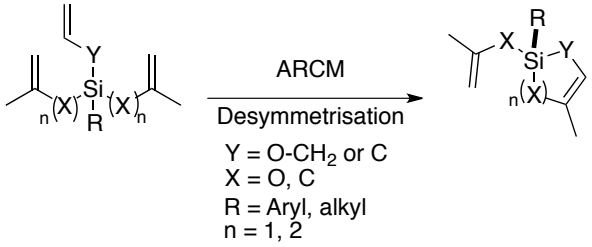
1.6 Novel approach to the synthesis of enantiopure compounds.

Despite the significant progress in this area, access to Si-stereogenic organosilanes with high enantiopurity remains a challenge due to the limited number of available methodologies. In the first part of this thesis, a novel conceptual approach to the synthesis of chiral Si-stereogenic compounds is presented. This strategy is based on the Ring-Closing Metathesis (RCM) reaction. Previous work in the Gouverneur group has shown that stereogenicity at atoms other than carbon can be generated successfully by RCM.[40] Desymmetrisation of prochiral phosphine oxide and phosphinates containing trienes was possible by Asymmetric Ring Closing-Metathesis (ARCM), leading to enantioenriched products with high enantiomeric excess.



Scheme 1.6.1 Desymmetrisation of prochiral phosphine oxide by ARCM.

Thus, we reasoned that ARCM could be extended to Si-containing templates. Overall, this approach would be strategically unique compared to other methods to construct Si-stereogenicity and would potentially be a valuable reaction for the preparation of enantioeriched Si-stereogenic compounds (Scheme 1.6.2).



Scheme 1.6. 2 Desymmetrisation of prochiral Silicon-trienes by ARCM.

1.7 Olefin Metathesis

Overview Olefin Metathesis

The first observation of the redistribution of the olefinic bonds in propene to give ethylene and 2-butene, at high temperature (725 °C), was reported in 1931.[41] Later, in 1964, Du Pont, Standard Oil and Phillips Petroleum disclosed the first transposition of double bonds mediated by $Mo(CO)_6$ supported on alumina.[42] It was not until 1967 that Calderon first named this mysterious reaction, 'metathesis'.[43] Without doubt, this discovery stands as one of the most spectacular reactions in terms of synthetic strategy and is widely used in organic synthesis[44] and polymer science.[45]

This new reaction caught the attention of industry due to its potential to effect the high-value transformation of propene into ethylene and butene under catalytic conditions (WO_3/SiO_2, WCl_6 or $MoCl_5$).[46] Calderon suggested a mechanism involving a π-cyclobutane–metal complex as an intermediate, but the cyclobutane itself was never observed, and it was not found to enter the metathesis catalytic cycle.[45] Later, in 1971, Pettit proposed the idea of a tetramethylene intermediate forming a σ-metal bond with multiple three-centre two-electron bonds.[47] Similarly, Grubbs proposed the formation of a "quasicyclo-butane" formed from a [2+2] cycloaddition of the two olefins.[48] These first ideas, however, could not fully explain the empirical patterns of the olefin transposition. Although these initial mechanistic proposals were ultimately dismissed, these contributions provided a framework through which a better understanding of the metathesis reaction could be achieved.

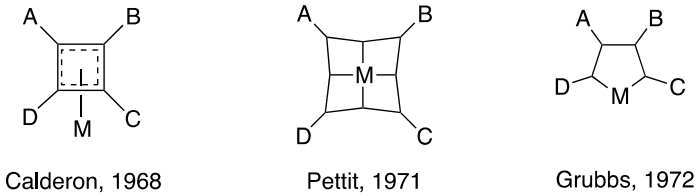


Figure 1.7.1 Representative proposals of intermediates for olefin metathesis.

Concurrent to these studies, Chauvin and Hérisson published their theory for the mechanism of olefin metathesis, which is today accepted as the actual mechanism.[49] It involves a metal–carbenoid species that coordinates to the olefin, followed by the formation of a metallacyclobutane *via* a [2+2] cycloaddition and finally cycloreversion to give the product. The first step is coordination of an olefin to a metal–alkylidene species (I–III). Formation of a metallacyclobutane *via* a [2+2] cycloaddition is followed by liberation of the product along with the formation of a new catalytically active metal–alkylidene (IV). This species coordinates with another olefin molecule and progresses through the same sequence of transformations to effect the net transposition of double bonds, as shown in Figure 1.7.2.

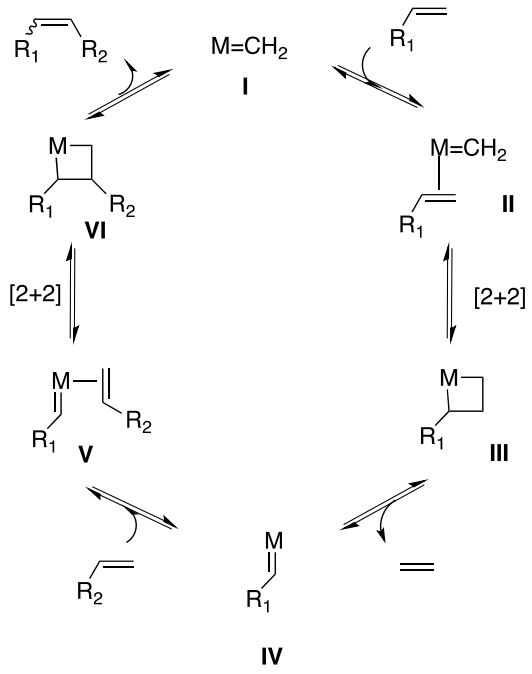
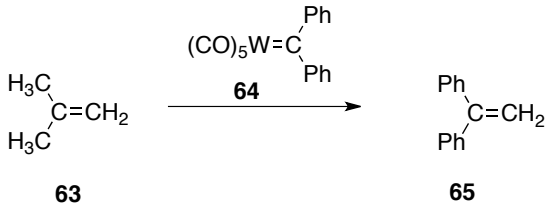


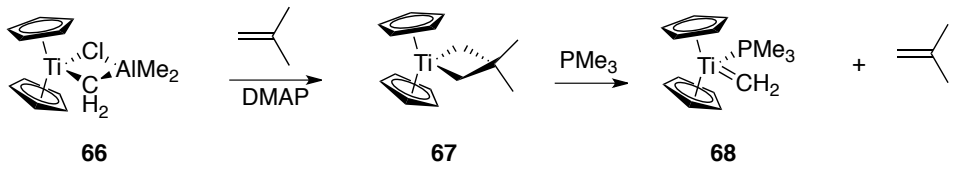
Figure 1.7.2 Mechanism of olefin metathesis proposed by Chauvin and Hérisson.

This mechanism is generally accepted and has proven to be consistent with a growing body of theoretical and experimental evidence, including characterisation of many of the postulated intermediates.[50] This important contribution by Chauvin paved the way for further progress in the development of new catalysts, particularly those containing carbenes. In 1976, these ideas allowed Casey and Burkhardt to report the first well-defined [$W(CO)_5(=CPh_2)$] carbene, which underwent olefin metathesis (Scheme 1.7.1).[51]



Scheme 1.7.1 Reactivity of the first well-defined W–carbenes.

Grubbs *et al*. made an important contribution by confirming the intermediacy of the metallacyclobutane proposed by Chauvin. Grubbs showed that the Tebbe complex [$Cp_2Ti(CH_2)(ClAlMe_2)$] reacted with olefins in the presence of dimethylaminopyridine (DMAP) to give stable titanacyclobutanes that slowly catalyse metathesis and are diagnostic intermediates in olefin metathesis.[52]



Scheme 1.7.2 Grubbs studies on Tebbe´s complex.

Previous reports from Casey and Burkhardt led Schrock, Osborn and Basset to synthesise metal complexes with high-oxidation states (**69**–**72**); these complexes were able to catalyse cross-metathesis of *cis*-2-pentene.[53]

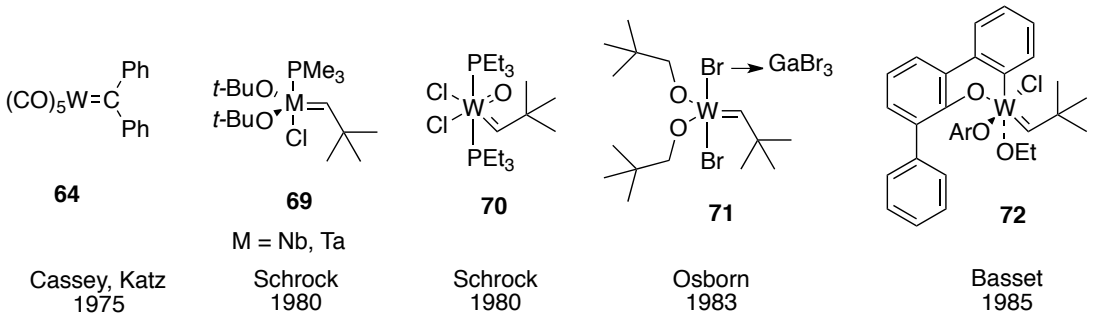


Figure 1.7.3 Early W–, Nb–, Ta– and W–carbene metathesis catalysts.

Complex **64** initiates metathesis at a low rate with a variety of alkenes. The reason for the low catalyst activity is the low oxidation state of the metal, due to the nature of the CO ligands. Based on previous results, Schrock,[54] Osborn[55] and Basset[56] (Figure 1.7.3) synthesised additional stable W–alkylidene catalysts for further evaluation in metathesis reactions. The main difference between these complexes and previous versions is the polarity at the central metal (**69**–**72**), which affects the reactivity of the catalyst. By taking these considerations into account, it was possible to synthesise highly active Mo and W species. In 1990, Schrock reported a range of imido alkylidene catalysts containing two bulky alkoxide ligands, which contributed to the stability of the complexes.[57] These catalysts are still among the most active known to date and have since been made commercially available. As such, they have found numerous applications in organic synthesis (Figure 1.7.4).

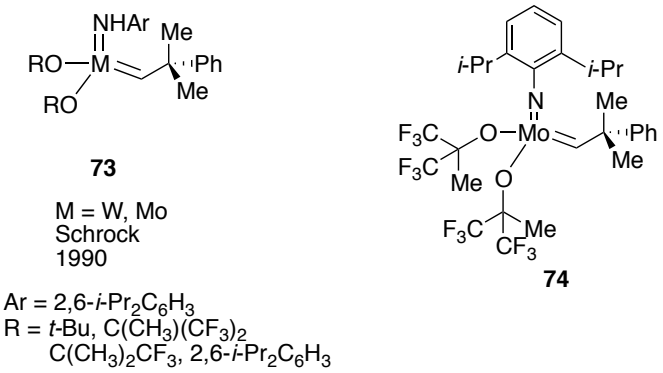


Figure 1.7.4 General structure of Schrock catalysts and the commercially available catalyst (**74**).

However, there are some disadvantages associated with Schrock´s catalysts, as they are incompatible with a number of polar functional groups and are highly sensitive to air, requiring the use of a glovebox to ensure that a sufficiently inert atmosphere is maintained. Grubbs has made a remarkable contribution with regard to catalyst stability through the design and optimisation of catalysts containing ruthenium instead of tungsten or molybdenum.[58] Although complexes **75** and **76** are not as active as their Mo counterparts, they are more versatile due to wider functional group tolerance (Figure 1.7.5). Moreover, Ru complexes are air-stable and reasonably resistant to water, alcohols and carboxylic acids.[59] In 1995 Grubbs made an important structural variation in order to increase the initiation rate of this family of catalysts. Grubbs reported that catalyst initiation occurs *via* the dissociation of phosphine ligands to generate a highly active 14-electron Ru species. Armed with this knowledge, in 1999 Grubbs,[60] Nolan[61] and Hermann[62] replaced one of the phosphines by a strong σ-donating, *trans*-labilising *N*-heterocyclic carbene ligand (NHC), resulting in a set of "second generation" catalysts. The use of NHC ligands in combination with a phosphine ligand resulted in a dramatic increase in catalyst activity. Later Hoveyda *et al.* reported a modification of Grubbs' "second generation" catalyst by introducing a chelating styrenyl ether moiety, leading to the first example of a phosphine-free catalyst **79** (Figure 1.7.5).[63] This particularly stable and reactive catalyst became very attractive for further optimisation due to the

extensive modifications in terms of steric and electronic effects that can be envisioned on the styrenyl group. This catalyst can be used in heterogeneous form with the attachment of the catalyst to solid supports.[64]

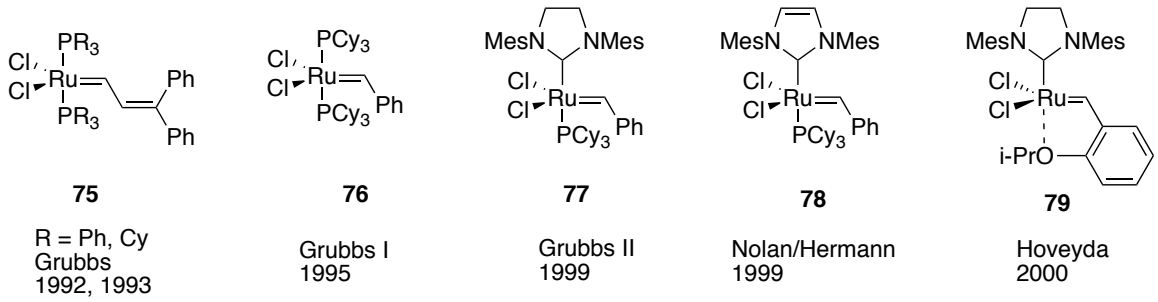


Figure 1.7.5 Ruthenium-based olefin metathesis catalysts.

1.8 Reactivity of Grubbs catalysts.

Grubbs I (**76**) is a five-coordinate 16-electron species, exhibiting a trigonal bipyramidal geometry. It showed good functional group tolerance but limited activity. Grubbs II catalyst (**77**), on the other hand, was found to exhibit enhanced activity in olefin metathesis, primarily due to the substitution of one phosphine ligand with a NHC ligand. It is believed that the NHC increases the lability of the *trans* phosphine ligand and therefore facilitates its dissociation.[65] However, studies by Grubbs and Chen indicated that phosphine dissociation is slower for Grubbs II than for Grubbs I. [66] The catalytically active species is the 14-electron complex that results from phosphine dissociation. Using gas phase mass spectrometry, it was shown that the phosphine energy dissociation energies for Grubbs I and Grubbs II are 33 and 37 kcal mol^{-1}, respectively (Figure 1.8.1).

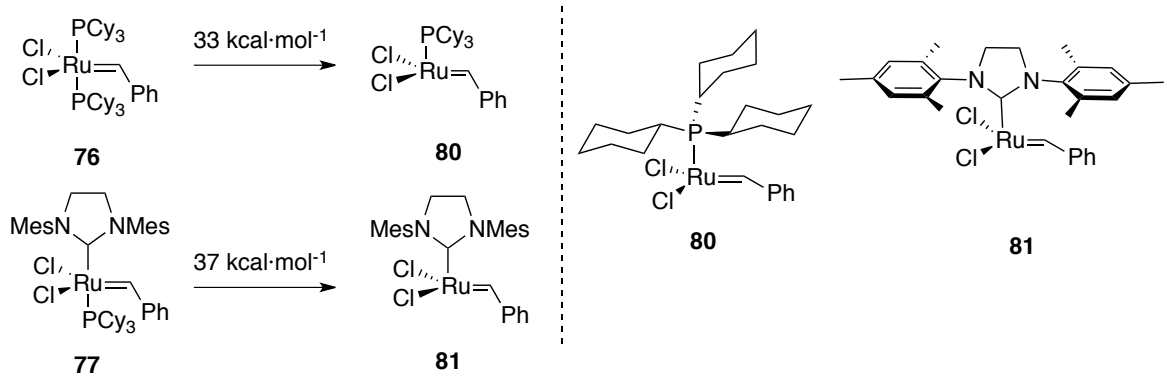


Figure 1.8.1 Energy dissociation values and steric hindrance of inversion in Grubbs I and Grubbs II catalysts.

This energetic trend for the phosphine dissociation might have its origin in the NHC ligands, which are generally thought to be strong σ-donors but poor π acceptors due to the back donation of the nitrogen lone pairs. The higher reactivity of Grubbs II has been attributed to the NHC ligand, which enhances the olefin coordination by forming a more stable metallacycle intermediate.[67] The ratio k_{-1} to k_2, ($k_2/k_{-1} > 1$) (Figure 1.8.2) which determines whether the catalyst binds to the olefin or returns to the 16 electron species (**77** or **81**) is also key to the catalyst activity.

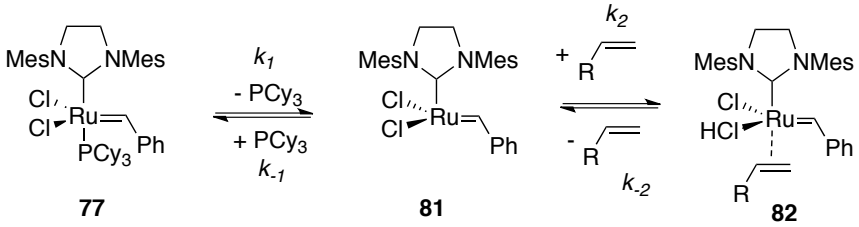


Figure 1.8.2 Dissociative mechanism for Grubbs II catalysts.

Computational studies by Chen et al.[66] confirmed that the higher catalytic activity of Grubbs II is related to steric effects. For both catalysts, the metathesis reaction involves inversion at Ru, *via* the metalocyclobutane. During the catalytic cycle of the olefin metathesis reaction, an unfavourable rotation of the C_3-symmetric phosphine ligand in Grubbs I has to occur. In this case inversion leads to a steric clash with the PCy_3 ligand (Figure 1.8.3, **III**), whereas in Grubbs

II, the C_2-symmetric NHC ligand helps to prevent this steric clash.

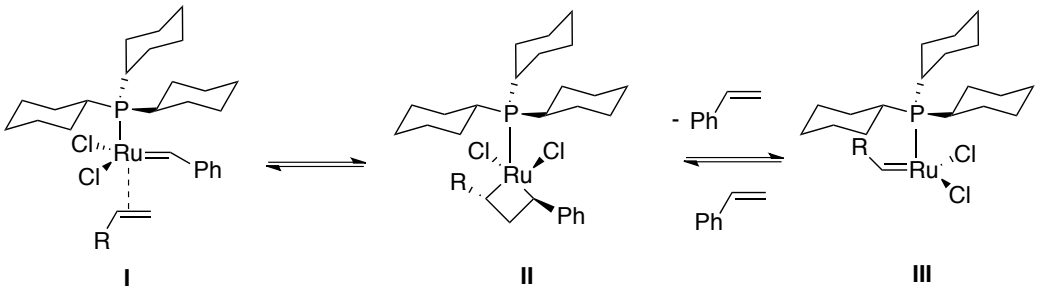


Figure 1.8.3 Steric hindrance upon metathesis in Grubbs I

Modifications on the styrenyl skeleton were studied by Grela[68] and Blechert.[69] By altering both the electronic and steric effects through incorporation of a *p*-NO_2 or *o*-Ph group, the resulting catalysts were highly active in metathesis reactions, due to the comparatively facile dissociation of the Ru–O bond to form the catalytically active 14-electron species (Figure 1.8.4). Key to the success of these catalysts is the Ru–O bond destabilisation that results from the electronic or steric effects on the aromatic ring.

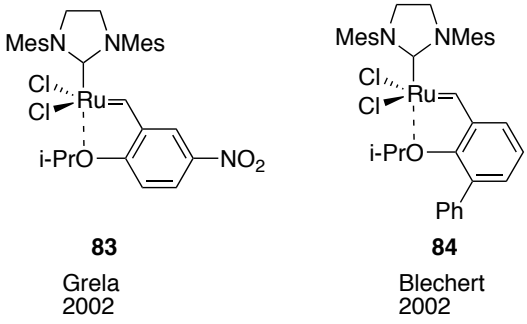


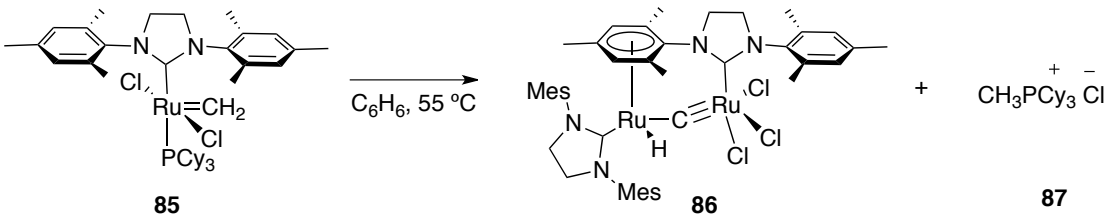
Figure 1.8.4 Modifications on the styrenyl skeleton

As mentioned previously, ruthenium and molybdenum catalysts have proven to exhibit unique reactivity and scope in olefin metathesis. While molybdenum catalysts are sensitive to moisture and air, they are effective in the presence of phosphanes, thioethers, and primary amines, which readily decompose ruthenium catalysts.[70] Ruthenium catalysts are more

tolerant to moisture and air and remain active in the presence of carboxylic acids, amides, ketones, aldehydes and alcohols.[71]

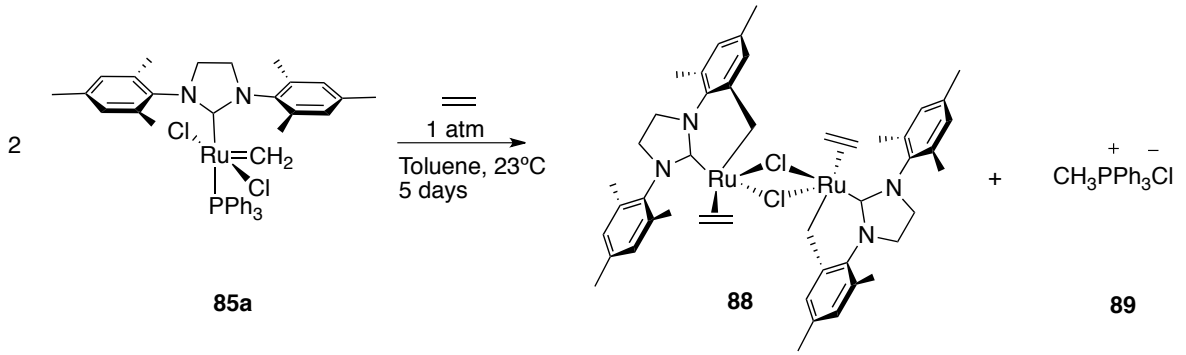
1.9 Catalyst Decomposition

In order to design more efficient catalysts for olefin metathesis, it is essential to understand the decomposition pathways of existing catalysts. Catalyst decomposition can lead to side reactions, such as olefin isomerisation.[72] Grubbs and co-workers have conducted several studies with the aim of identifying the mechanisms by which the Grubbs II catalyst decomposes. All phosphine-containing methylidene complexes have been found to decompose to generate methylphosphonium salts. When the Grubbs II catalyst was heated to 55 °C in benzene, formation of a bridging carbide complex was observed. The mechanism for this reaction remains unclear, but it has been suggested that the major decomposition pathway involves nucleophilic attack of a dissociated phosphine on the methylidene carbon.



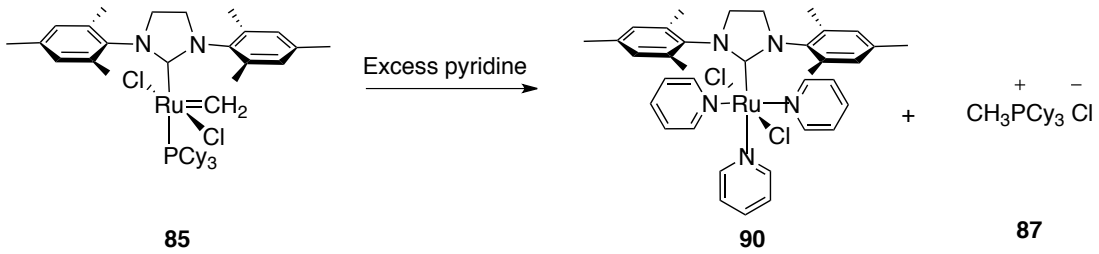
Scheme 1.9.1 Thermal decomposition of Ru catalyst.

A second deactivation pathway was identified by conducting a metathesis experiment in the presence of ethylene, which led to the formation of a dimeric species via activation of an *ortho*-methyl C–H bond on the NHC ligand (**88**).



Scheme 1.9.2 Ru catalyst decomposition via C–H activation in the presence of ethylene.

Finally, excess pyridine caused the formation of a methylphosphonium salt and the coordinatively saturated 18-e⁻ complex (**90**).



Scheme 1.9.3 Decomposition of the Ru catalyst in the presence of excess pyridine.

As a result of these studies, it was demonstrated that all of the phosphine-containing methylidene complexes decomposed following first-order kinetics to generate methylphosphonium salts. In the presence of ethylene, complex **85a** decomposed to form a Ru-dichloride dimer. This study revealed different decomposition pathways of ruthenium catalysts, which are important to inform the design of more stable and active catalysts, with ligands chosen to reduce the prevalence of side products and improve efficiency. Generally speaking, the success of olefin metathesis can be attributed to its versatility and compatibility with broad range of substrates. Metathesis catalysts became commercially available in the 1990s and 2000s and have since been applied in a myriad of interesting applications in

synthetic organic chemistry.[73] With more widespread applications, new challenges emerged. Catalysts with enhanced thermal stability, catalysts supported on solid surfaces, and chiral catalysts have all been developed. Olefin metathesis is not restricted to alkenes; alkynes are known to react under similar conditions. Both intermolecular and intramolecular reactions between an alkene and alkyne (enyne metathesis) can be catalysed by most active Ru complexes.[74] However, metathesis of two triple bonds (alkyne metathesis) is commonly carried out using Mo and W complexes. In 2005, the Royal Swedish Academy of Sciences awarded the Nobel Prize in Chemistry to Chauvin, Schrock and Grubbs in recognition of the impact of the olefin metathesis reaction on the field of Chemistry.[75]

1.10 Ring-Closing Metathesis (RCM)

Olefin metathesis reactions can be classified as cross-metathesis (CM), an intermolecular metathesis reaction between two olefins; ring-closing metathesis (RCM), an intramolecular olefin metathesis reaction; and ring-opening metathesis (ROM) and ring-opening cross-metathesis (RO/CM), the reverse of RCM. Strained cyclic olefins can be used to form polymer materials, a reaction classified as ring-opening metathesis polymerization (ROMP).[76] For the purposes of this thesis, the focus will be on intramolecular metathesis (RCM), as a key transformation for the synthesis of cyclic compounds.

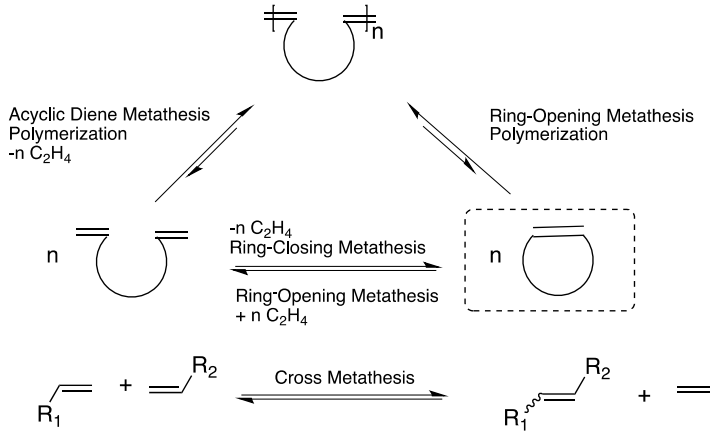
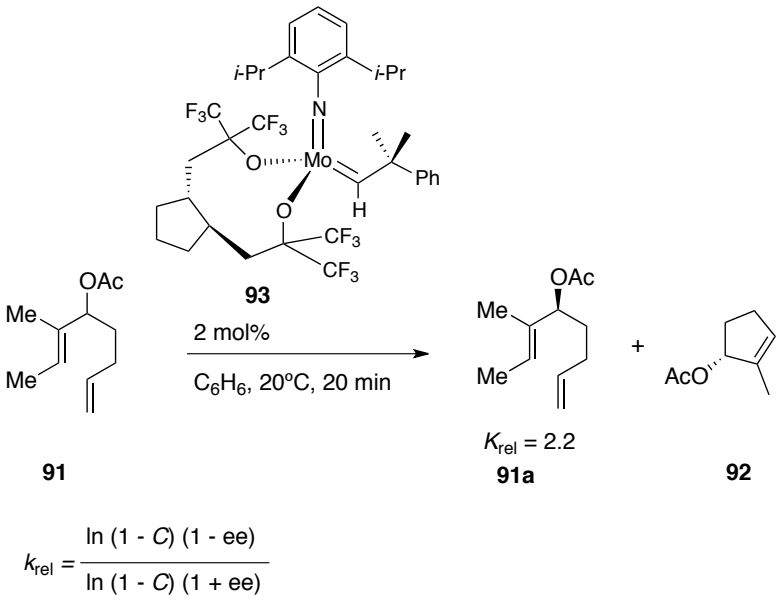


Figure 1.10.1 Different metathesis reactions.

RCM in particular has revolutionized the field of organic synthesis over the past 15 years.[76] In this relatively short period of time, olefin metathesis has developed into one of the most widely employed methods for C–C bond formation and RCM, which is thermodynamically driven by the irreversible release of ethene, is amongst the most powerful tools for ring formation. The enormous selection of heterocyclic ring systems of different sizes that can be generated by RCM has reshaped the area of total synthesis of complex molecules.

1.11 Asymmetric Ring-Closing Metathesis (ARCM)

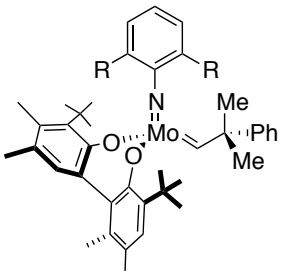
In 1996, Grubbs and Fujimura reported a novel kinetic resolution approach using Mo-catalysed ARCM. However, the initial results gave low levels of enantiodifferentiation (k_{rel}<3).[77]



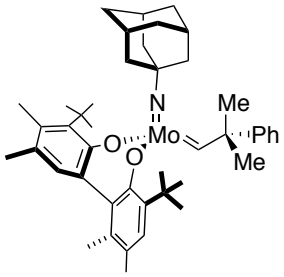
Equation k_{rel} General formula to calculate $K_{rel,}$ where C = conversion of starting material, and ee is the enantiomeric excess of the remaining starting material.

Scheme 1.11.1 Kinetic resolution using a chiral Mo catalyst.

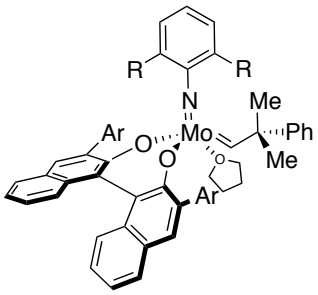
Since then, numerous efforts to develop new classes of chiral catalysts have been conducted by the Schrock and Hoveyda groups through structural modification of Mo complexes.[78]



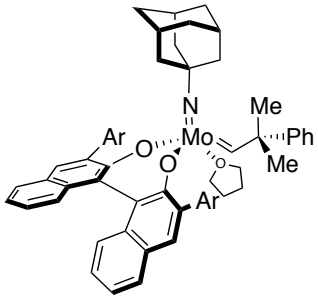
94a R = *i*-Pr
94b R = Me
94c R = Cl



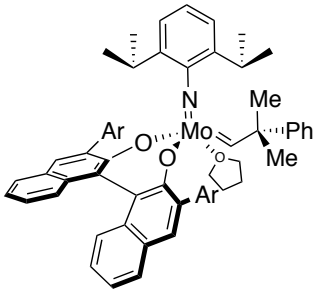
95



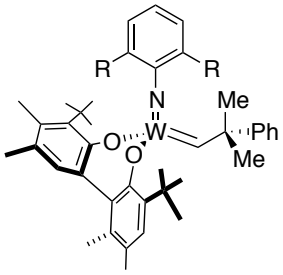
Ar = 2,4,6 *i*- Pr_3Ph
96a R = *i*-Pr
96b R = Me
96c R = Cl



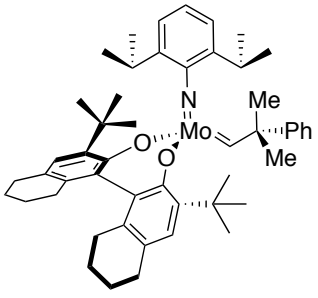
Ar = 2,4,6 *i*- Pr_3Ph
97



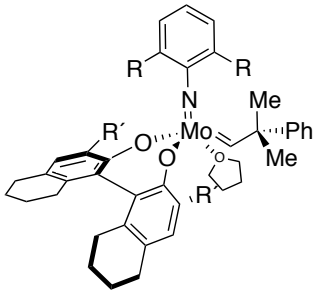
98a Ar = Mes
98b Ar = Ph



99a R = *i*-Pr
99b R = Me



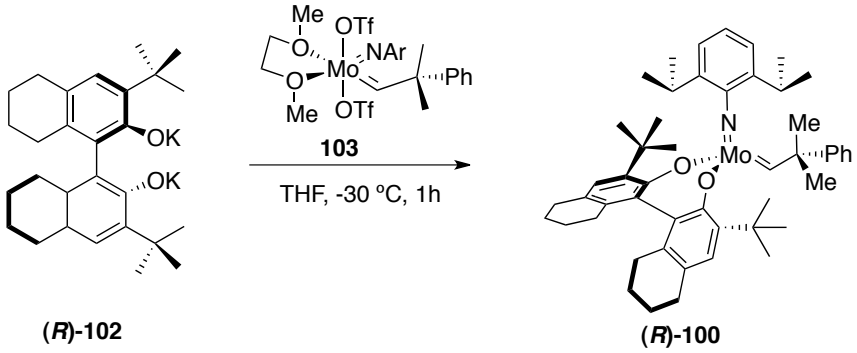
100



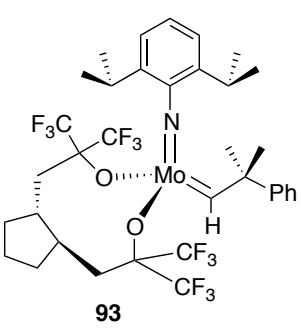
101a R = *i*-Pr, R´= Mes
101b R = *i*-Pr, R´= $CHPh_2$
101c R = Cl, R´= Mes
101d R = Cl, R´= $CHPh_2$

Figure 1.11.1 Chiral Mo catalysts.

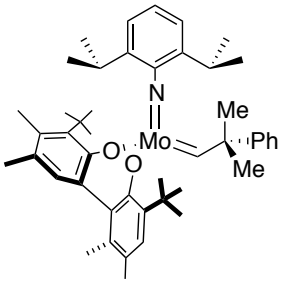
Since 1997 a variety of Mo and W complexes were synthesised with different degrees of rigidity and steric hindrance employing ligands such as biphenolate, binaptholate, and bitetralolate.[79] Catalysts can also be synthesised *in situ* from commercially available enantiopure BINOL and the molybdenum precursor **103**. The resulting complex can be stored under a nitrogen atmosphere with no detrimental effect on catalyst efficiency or selectivity.



Scheme 1.11.2 Synthesis of Mo complexes.

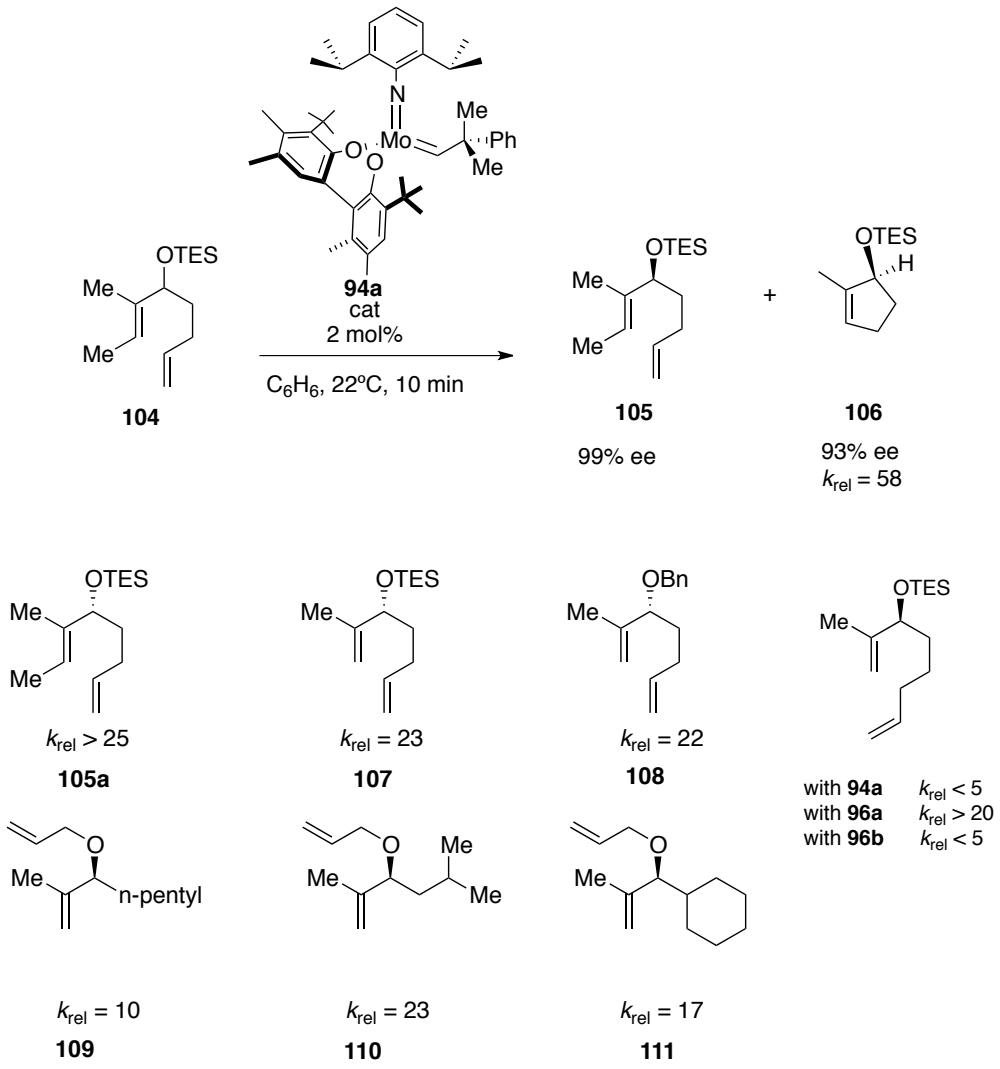


93



94a

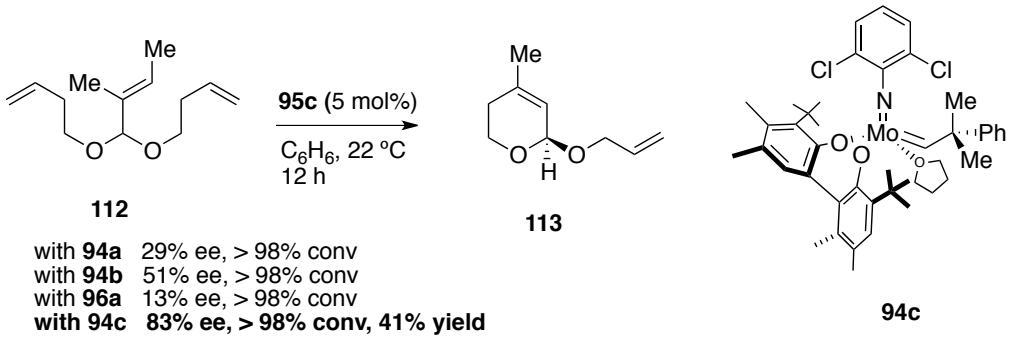
Catalysts **93** and **94a** were both examined under identical reaction conditions and tested for their reactivity and selectivity in the catalytic kinetic resolution of various dienes via ARCM. Higher levels of enantiodifferentation were obtained with **94a** compared to the chiral Mo catalyst **93**. Catalyst **94a** was the first molybdenum complex that catalysed enantioselective kinetic resolution of protected secondary alcohols *via* the formation of carbocyles.[80] The resolution was highly effective, based on conversion and product selectivity (k_{rel} = 58), and the unreacted substrate **106** was recovered in 99% *ee* (Scheme 1.11.3).



Scheme 1.11.3 Kinetic resolution of protected secondary alcohols and allylic alcohols.

It was shown that catalyst **94a** gave the best enantiocontrol for 1,6-dienes. The asymmetric induction of 1,7-dienes using catalyst **94a** was much lower (k_{rel} = < 5) (Scheme 1.11.3), suggesting that different transition states could be involved during the ring-closing metathesis event. To address the low levels of enantioinduction, it was necessary to modify the skeleton of the Mo complex in order to increase steric bulk. Indeed, complex **96a** exhibited better enantiocontrol (k_{rel} > 20). When the imido ligand contains a Me group at the ortho position, the effectiveness in the kinetic resolution significantly decreases. Thus, no single chiral Mo catalyst is efficient and selective in every asymmetric metathesis reaction. For that reason the Schrock

and Hoveyda groups have synthesised a library of catalysts.[79] More than 30 chiral Mo and W catalysts have been reported by varying the imido, alkylidene and phenoxide groups, which offers many possibilities to access more complex molecules.



Scheme 1.11.4 Asymmetric synthesis of acetals with a chiral Mo catalyst.

1.12 Importance of *syn* and *anti* alkylidene isomers.

Extensive NMR and theoretical studies have shown that both tungsten and molybdenum complexes can exist as two stereoisomeric forms, depending on whether the R group from the alkylidene group points towards or away from the imido nitrogen ligand (Figure 1.12.1).[81] Identification of these stereoisomeric forms was made possible by varying the temperature or irradiating the complex photochemically[82] to induce rotation of the M=C bond. The *syn* alkylidene (Ha) was detected by ^{1}H NMR spectroscopy between 8–14 ppm with a $^1J_{C-H}$ coupling constant of approximately 125 Hz, while the *anti* isomer appears 1–2 ppm downfield with a $^1J_{C-H}$ coupling constant of 140 Hz. At lower temperatures, the *anti* alkylidene (the more reactive and more Lewis acidic) was observed, whereas increasing the temperature led to conversion into the more stable *syn* alkylidene. The imido metal bond has significant triple character due to the electron pair on the nitrogen atom donating to an empty d orbital on the metal.[81]

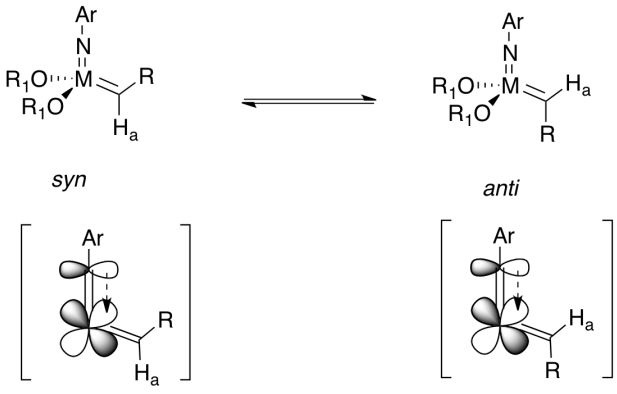


Figure 1.12.1 Interconversion of *syn* and *anti* alkylidenes.

Both steric and electronic factors are partially responsible for the higher stability of *syn* alkylidenes. Based on theoretical studies[83] an agostic interaction was proposed to exist between the metal center and the alkylidenyl C–H bond. This interaction increased the p character of the C–H bond through hyperconjugation (σ_{C-H} -> σ^*_{Mo-N}), causing the J_{C-H} coupling constant to decrease and increasing the triple bond character of the Mo=C bond. These results were supported by crystallographic studies where it was found that an *anti* alkylidene has a reduced Mo=C–C bond angle compared to the *syn* alkylidene (128.1° vs 149.5°, respectively), and the bond lengths were longer for the *anti* than the *syn* (1.927 Å vs 1.840 Å, respectively).[84] This important result confirmed the existence of an agostic interaction making the *syn* alkylidene more stable and causing this isomer to exhibit lower reactivity.

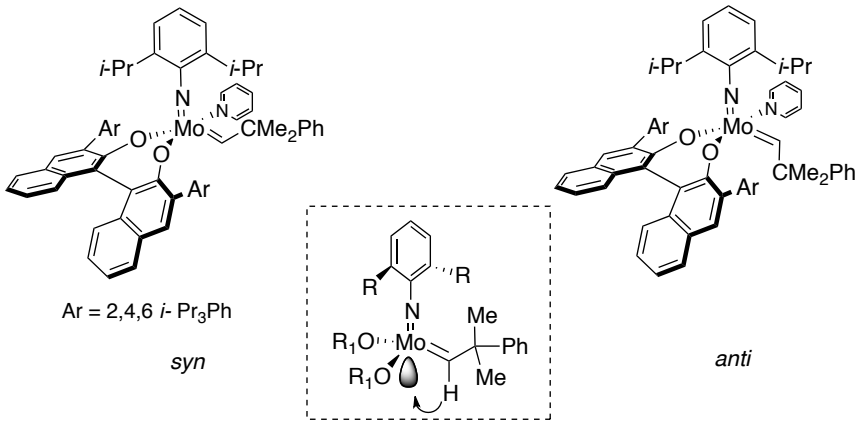


Figure 1.12.2 *Syn* alkylidene stabilisation.

On the basis of the structural differences between the *syn* and *anti* species it is clear that their reactivity profile would be different. The *syn* isomer would have more unfavorable interactions between the groups (*i*-Pr or Me) of the imido ligand and the newly formed alkylidene, making substrate binding less favorable. On the other hand, the *anti* isomer does not present clashing interactions between those groups and the newly formed alkylidene (Figures 1.12.2 and 1.12.3)

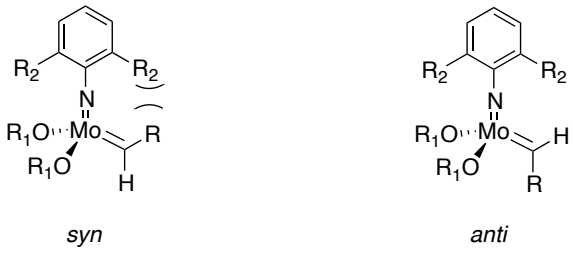
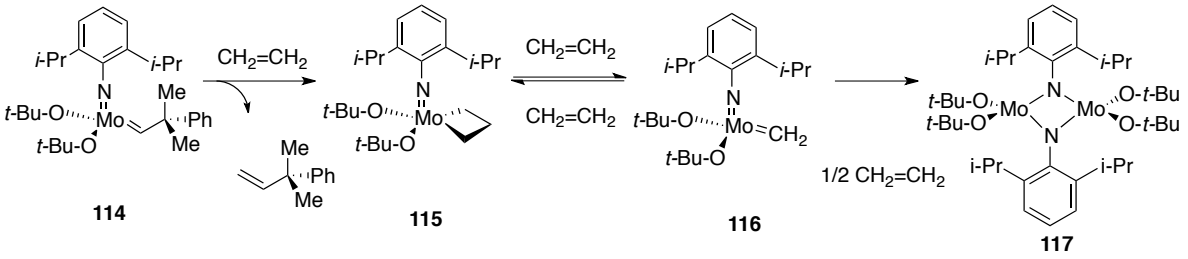


Figure 1.12.3 Steric interactions in the *syn* and *anti* species.

1.13 Mo Catalyst decomposition.

As mentioned previously, Mo catalysts are sensitive to air and moisture and must be kept under an inert atmosphere. They can also decompose under the reaction conditions. Schrock reported that a decomposition pathway takes place in which the $Mo^{(VI)}$ catalyst is reduced to $Mo^{(IV)}$ to form an imido-bridge dimeric system. This pathway was studied by ^{1}H NMR, which

showed formation of metallacyclobutane **123** and subsequent release of ethylene led to the formation of the bimolecular complex **125**.[85]



Scheme 1.13.1 Decomposition pathway of Mo catalyst.

1.14 Stereogenic Molybdenum catalysts

Despite the accomplishments of chiral Mo catalysts, the most active one is the original achiral Schrock catalyst (**93**). One of the proposed explanations to account for the lack of reactivity of sterically hindered substrates with bidentate catalysts is the structural rigidity of the catalyst. To address this issue, Schrock and Hoveyda designed a new generation of catalysts, bearing stereogenicity at molybdenum with a donor and an acceptor ligand.[85]

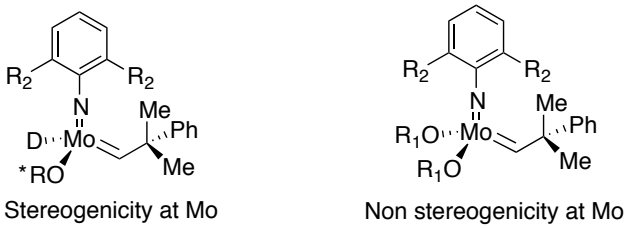


Figure 1.14.1 Chiral Mo catalysts.

According to theoretical studies, an acceptor ligand ensures sufficient metal Lewis acidity, which is necessary for efficient alkene coordination.[86] This olefin coordination requires the

distortion of the initial tetrahedral geometry in order to have a free ligation site. Therefore, it was proposed that the presence of a donor group would stabilise the vacant ligation site *via* the *trans* effect. In 2008, they reported the first example of diastereomerically enriched stereogenic-at-metal catalysts containing both an acceptor and a donor ligand.[87]

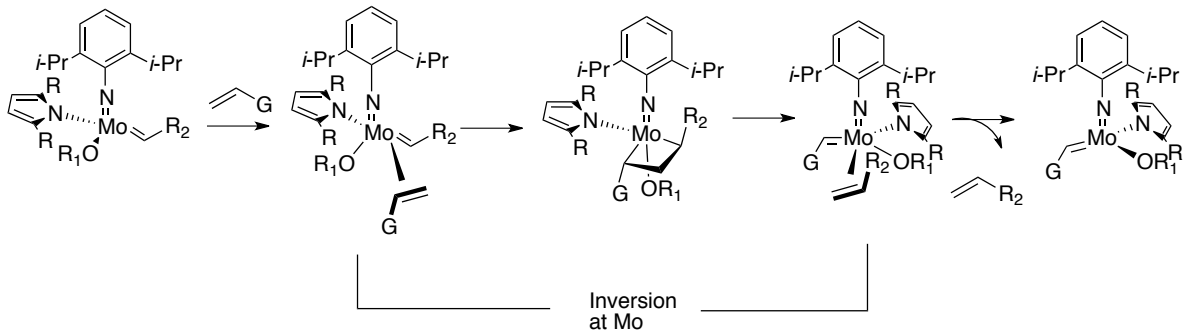


Figure 1.14.2 Electronic effects in alkene metathesis with chiral Mo catalysts.

The new chiral Mo and W complexes made by Hoveyda in collaboration with Schrock has offered unique opportunities for the preparation of enantiomerically pure carbocycles and heterocycles of great relevance, such as the asymmetric synthesis of the natural product quebrachamine.[87] These catalysts have proven to be more reactive, with shorter reaction times than the earlier biphenolate-based chiral Mo catalysts. In addition to the high conversion rates, these new catalysts generally gave higher levels of enantioselectivity. The main advantage of the new Mo complexes is the variety of alkoxides and diolates that can be used with either the imido or adamantyl based ligands (Figure 1.14.3). Moreover, this synthesis involves the *in situ* preparation of **120**$_{\mathbf{a\text{-}b}}$ and **121**$_{\mathbf{a\text{-}i}}$ without the formation of by-products that could be detrimental for the ARCM process (Figure 1.14.3). The synthesis of the chiral Mo-based catalysts starts with the bispyrrolide complexes of general formula M(NR)(CHR′)(Pyr)$_2$ and the addition of one equivalent of the alkoxide to form the monoalkoxide monopyrrolide of formula M(NR)(CHR′)(Pyr)(OR′′).[87] During the last decade, the synthesis of the new chiral Mo complexes has been widely used by the Schrock and Hoveyda groups to achieve excellent enantiocontrol in various ARCM reactions.

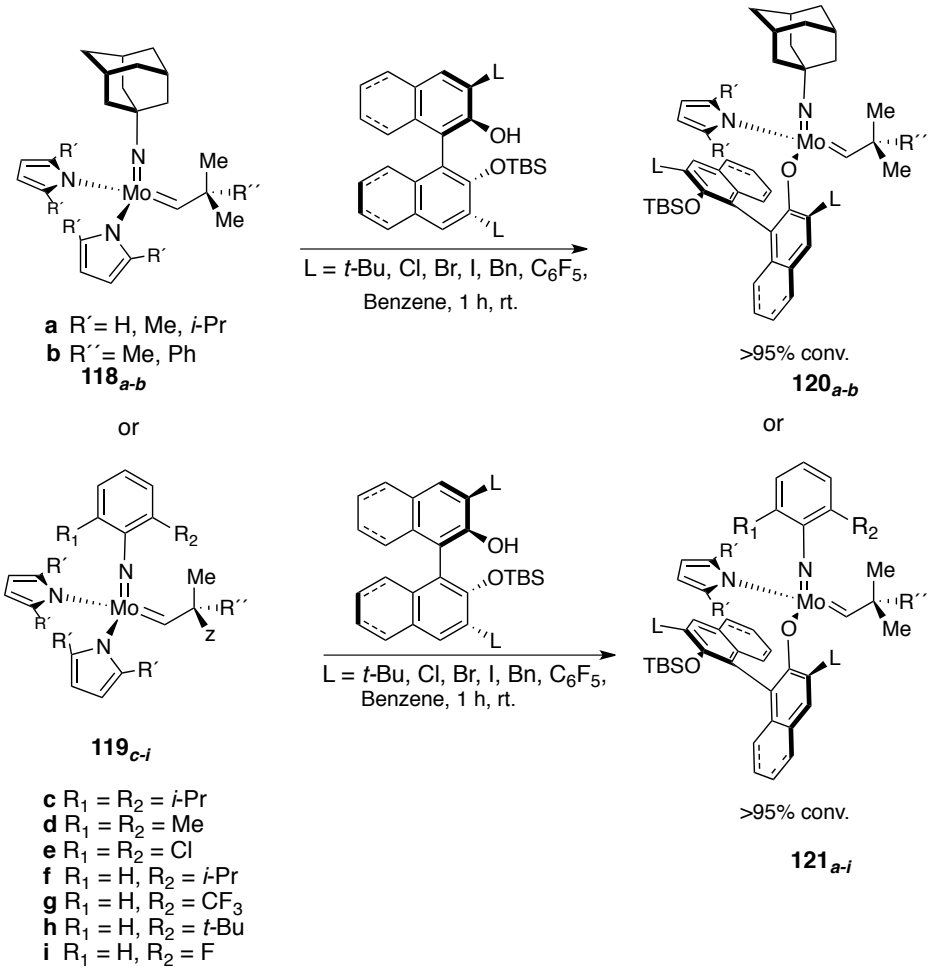
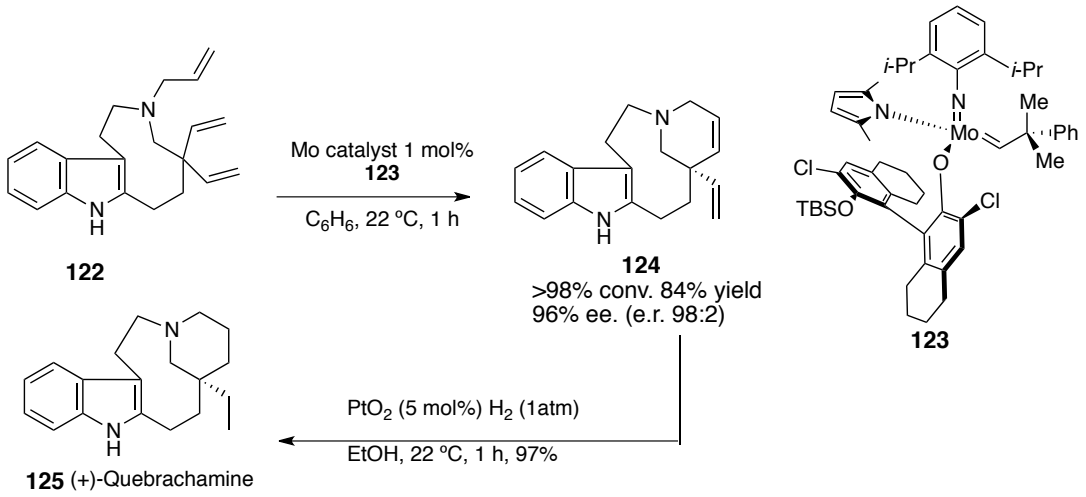


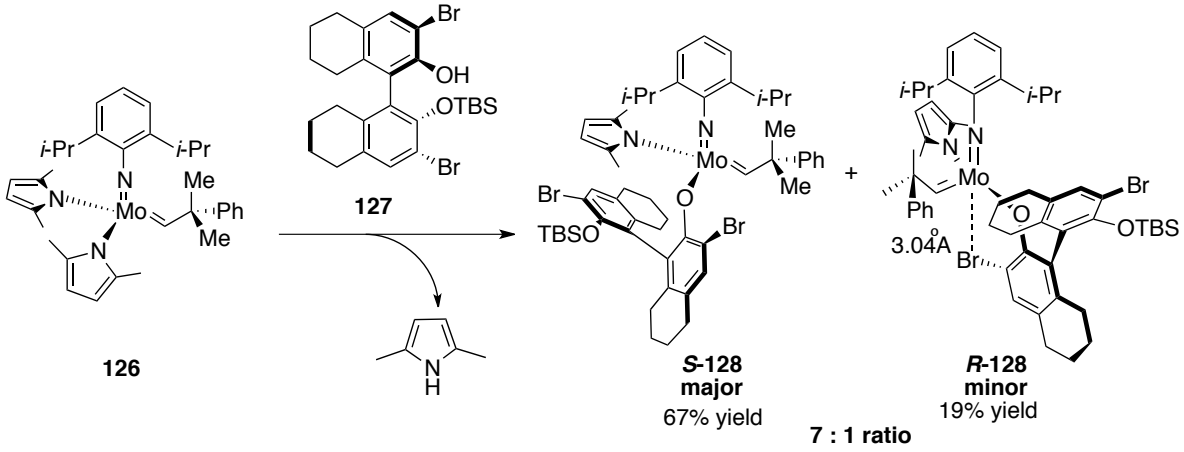
Figure 1.14.3 General synthesis of chiral Mo-catalysts.

The resulting complexes showed higher reactivity compared with the bidentate diolate complexes during ARCM.[88] Chiral Mo–aryloxides catalysts were highly effective in the synthesis of (+)-Quebrachamine (**125**), an adrenergic blocker.[89] Use of 1 mol% of catalyst **123** afforded the desired product with excellent *ee* (96%) and in 84% yield (Scheme1.14.1). Mo-based diolate complexes **94a–c**, **95** and **96a** were inactive in metathesis, even when used in high catalyst loadings and/or at high temperature.



Scheme 1.14.1 Synthesis of (+)-Quebrachamine under ARCM metathesis.

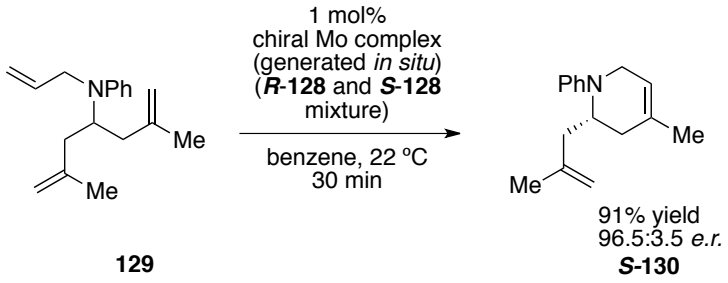
The new chiral Mo and W complexes made by Hoveyda and Schrock were formed as a diastereoisomeric mixture. In order to investigate the reactivity of the diastereoisomeric mixture during the ARCM process, Hoveyda *et al.* were able to isolate both diastereomers in a 7:1 ratio (***S*-128** and ***R*-128**), with the structures unambiguously determined by single crystal X-ray diffraction analysis.[90] These results revealed crucial factors that influence the catalyst's reactivity (Scheme 1.14.2).



Scheme 1.14.2 Synthesis of the Mo complex.

Exposing substrate **129** to ARCM conditions (1 mol% of the mixture of diastereomers of Mo complex **128**) gave product ***S*-130** in 93% *ee* and 91% isolated yield (Scheme 2.1.2).

Monitoring the reaction progress spectroscopically by ^{1}H NMR, revealed that 98% of the major isomer of complex **128** (***S*-128**) was consumed, whereas the minor diastereomer (***R*-128**) remained intact (95%) during the ARCM reaction.



Scheme 1.14.3 ARCM of **129** using the catalyst **128** generated *in situ.*

With pure samples of ***R*-128** and ***S*-128,** the ability of each diastereomer to promote the ARCM was examined.

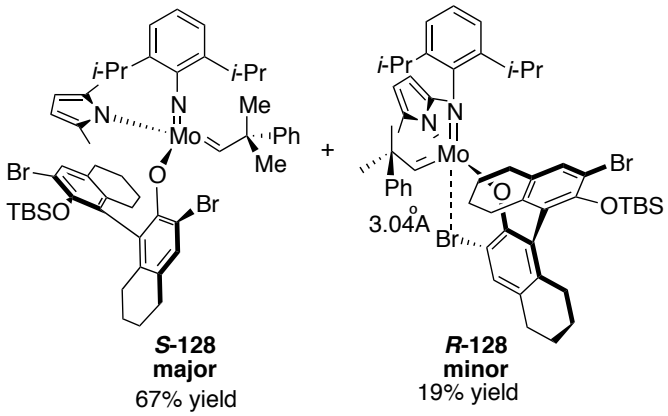
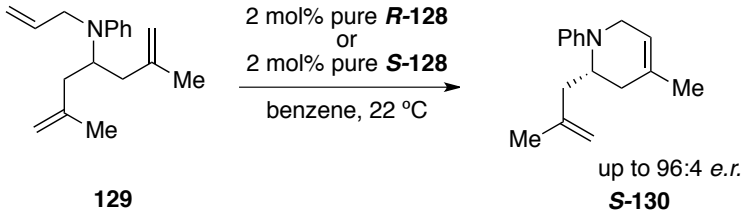


Figure 1.14.4 Diastereomers of Mo-based complex.

Careful examination of ***S*-128** and ***R*-128** identified that the bromide substituent in ***S*-128,** situated at the front position, appears to block the coordination of an olefin with the alkylidene. However, by rotation of the Mo-O bond, the approach and coordination of alkenes would appear more feasible, as can be seen in Figure 1.14.4. In structure ***R*-128**, the large

tetrahydronaphthyl ring blocks coordination, in addition a Br-Mo interaction with a distance of 3.04 Å restricts rotation about the Mo-O bond.[88]

When substrate **129** was subjected to ARCM conditions in the presence of either complex ***R*-128** or ***S*-128**, the formation of ***S*-130** was achieved with excellent enantiocontrol, up to 96:4 er, but at significantly different rates (Table 1.14.1). The formation of the same enantiomer of ***S*-130** implied that isomerisation of the two diastereomers of the chiral complex **128** occurs faster relative to ring closing metathesis and only the more reactive diastereomer initiated the subsequent ring-closing metathesis to form the ***S*-130** product.



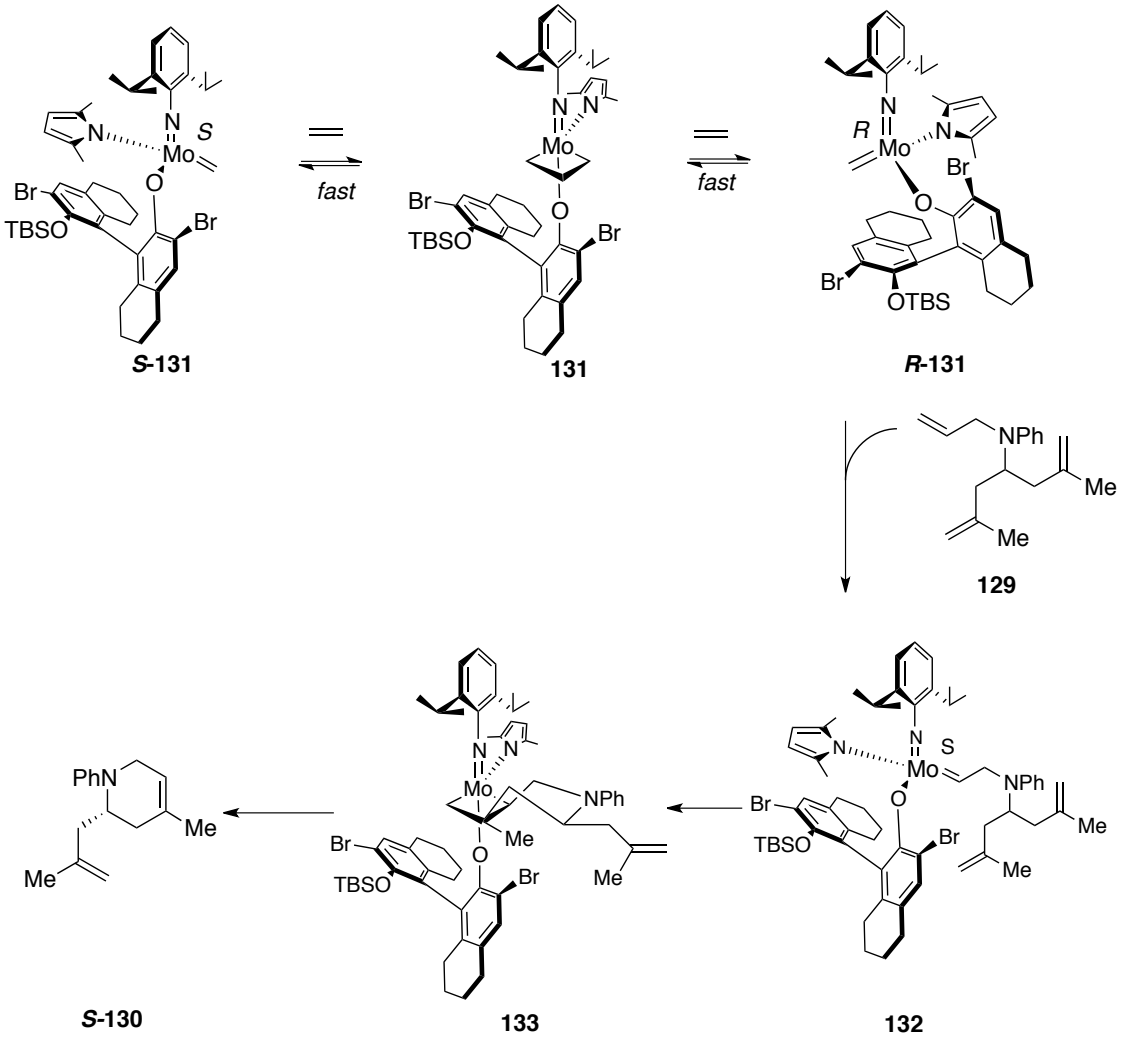
Entry	Complex	Time (min)	Conv(%)[a]	er (S:R)[b]
1	***S*-128**	2	4	76:24
2	***S*-128**	20	>98	96.5:3.5
3	***R*-128**	30	5	85.5:14.5
4	***R*-128**	180	>98	96:4

a) Based on 400 MHz ^{1}H NMR analysis of unpurified mixtures. b) Based on HPLC analysis

Table 1.14.1 ARCM in the presence of complex ***S*-128** and ***R*-128.**

Detailed mechanistic studies by Hoveyda *et al* showed that, in the presence of small amounts of ethylene (formed from initial RCM events), catalyst isomerisation occurs.[90] Scheme 1.14.4 shows that the isomerisation process leads to the formation of a mixture of diastereomers ***S*-131** and ***R*-131** with only the more reactive diastereomer ***R*-131** initiating subsequent ring-closures (as determined *via* ^{1}H NMR). Based on these observations the authors proposed a

mechanism for the ARCM reaction, where the stereochemical outcome is independent of the initial d.r of the Mo-based complex.

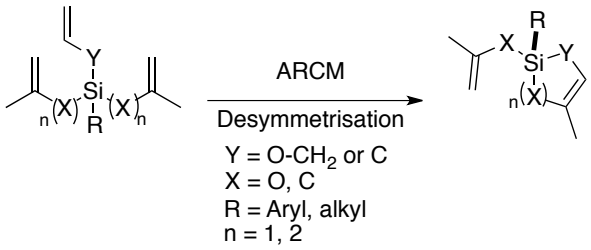


Scheme 1.14.4 Mo isomerisation and mechanism to afford ***S*-138.**

Objectives

On the basis of the great advantages that the catalysis area has gained in the construction of stereogenicity at atoms other than carbon, we embarked on a research program aimed at investigating the desymmetrisation of prochiral silicon trienes using chiral catalysts. This was

possible due to the collaboration of the Gouverneur and Hoveyda groups; which had previously reported the desymmetrisation of prochiral phosphine oxide and phosphinates containing trienes by ARCM with excellent ee.[40] These outstanding results encouraged us to pursue the study of chiral Si-stereogenic compounds in order to expand and overcome limitations of the existing methodologies. To date, ARCM has never been reported to create Si-stereogenicity. In Chapter 2, combinatorial screening of an array of catalysts for the ARCM of silicon prochiral derivatives, monitoring enantioselectivities of each reaction, will be described. The reaction scope, conditions, and design of substrates will be addressed; also the screening of various catalyst-substrate combinations towards a catalytic system that yields products in high enantiomeric excess is discussed. A library of 21 chiral catalysts complexes were explored in asymmetric catalysis (ARCM).



Scheme 1.14.5 Prochiral Si-trienes under ARCM.

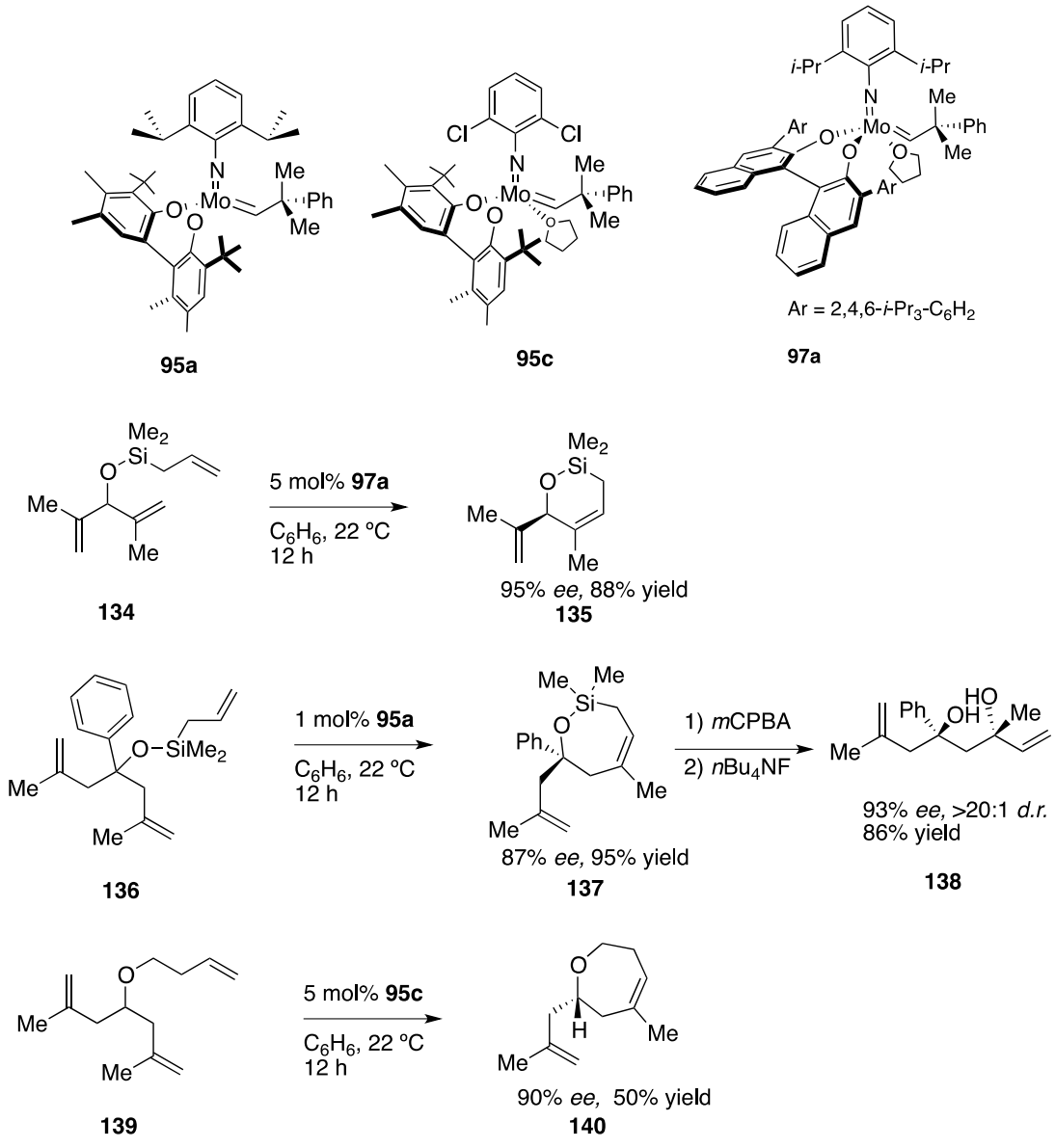
Chapter 2

2.0 Asymmetric Ring Closing Metathesis (ARCM) under Chiral Mo and W Complexes.

Asymmetric catalysis is economically an attractive strategy to synthesise enantiopure products. The development of this area is strongly related with the design of new chiral catalysts. However, despite significant progress in catalyst optimisation by rational ligand design, factors that influence selectivity and catalyst turnover are not fully understood and much trial-and-error experimentation is still employed. The development of ARCM to provide products in (high) enantiomeric excess still represents a challenge in pharmaceutical, agricultural and synthetic organic chemistry as well as in natural product synthesis.[44a]

In the case of asymmetric synthesis, a prochiral molecule serves as the starting point. Then, a chiral catalyst is used to transform a prochiral substrate into an enantiopure product. The main advantage of a catalytic method is that only small amounts of chiral catalyst are needed to produce the enantiopure product without the introduction of additional steps. Chiral catalysts are commonly based on (transition) metals modified with enantiopure organic ligands.[57] Chiral tungsten and molybdenum high oxidation state alkylidene complexes have been useful for a variety of catalytic metathesis reactions, however it is necessary to have a library of chiral Mo-complexes. Desymmetrisation of readily available prochiral trienes is significantly more efficient than kinetic resolution, as all of the material is converted to product. Examples of ARCM have been reported as depicted in Scheme 2.1.1.[91] ARCM of prochiral trienes proceeded to give the enantiopure dihydrofurans and dihydropyrans. Desymmetrisation of prochiral trienes, led to the formation of the desired 6 and 7 membered rings, and subsequent transformation allowed access to chiral acyclic dienes. However, those transformations showed a high degree of substrate to catalyst specificity.

Encouraged by these observations, an investigation on the asymmetric ring-closing metathesis of silicon prochiral trienes derivatives under chiral molybdenum and tungsten catalyts was initiated within the group.



Scheme 2.1.1 Desymmetrisation of prochiral trienes.

2.1 Ring-Closing Metathesis

Silicon-stereogenicity

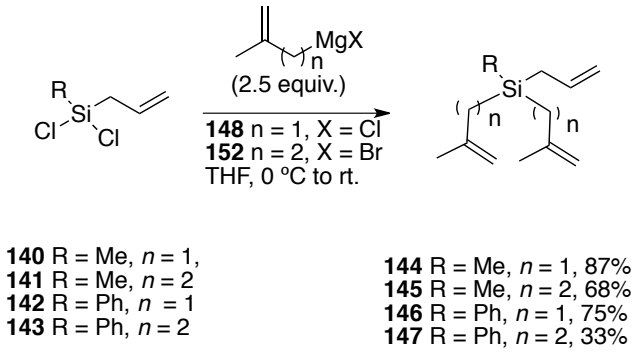
With the purpose of investigating the reactivity and selectivity of the RCM process, a range of trienic silanes containing unsubstituted allyl or homomethyl allyl groups attached to the central silicon atom were then tested. These substrates were designed such that a single regioisomer would be obtained upon RCM. The RCM was initially validated with achiral Grubbs catalyst, the resulting racemic products would serve as reference samples for *ee* determination by chiral HPLC/GC analysis. The size of the ring is an important parameter to be considered in the RCM reaction; for this reason, prochiral substrates leading to the formation of 5, 6 and 7 membered-rings were designed for investigation. The electronic effect was also evaluated by the variation of carbon *vs* oxygen attached to silicon atom. In all cases it was anticipated that catalyst initiation should occur on the unsubstituted alkene, allowing for subsequent discrimination of the two enantiotopic olefins upon ring-closure.

2.2 Synthesis of Substrates

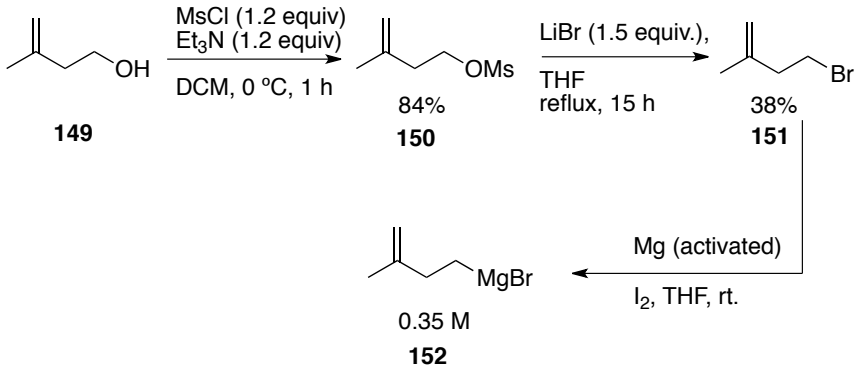
First Generation of Prochiral Si-trienes

The first series of substrates (**144**–**147**), depicted in Scheme 2.2.1 was synthesised from commercially available dichloromethyl- or dichlorophenylallylsilane and the corresponding Grignard reagent. The desired prochiral Si-containing trienes (all C-substituents) were suitable for desymmetrisation. The Grignard reagent (2-methylallylmagnesium chloride) **148** is commercially available. The homologue (3-methylallylmagnesium halide) **152** was prepared according to literature procedures from 3-methyl-buten-1-ol.[92,93] Thus, treatment of 3-methyl-buten-1-ol with methanesulfonyl chloride (MsCl) and triethylamine afforded the corresponding mesylate in 84% yield. Subsequent nucleophilic displacement with LiBr led to

the desired bromide in 38% yield after distillation. After titration the final concentration of the Grignard reagent was 0.35 M (Scheme 2.2.2).[94]



Scheme 2.2.1 General synthesis to the first generation of prochiral Si-trienes.

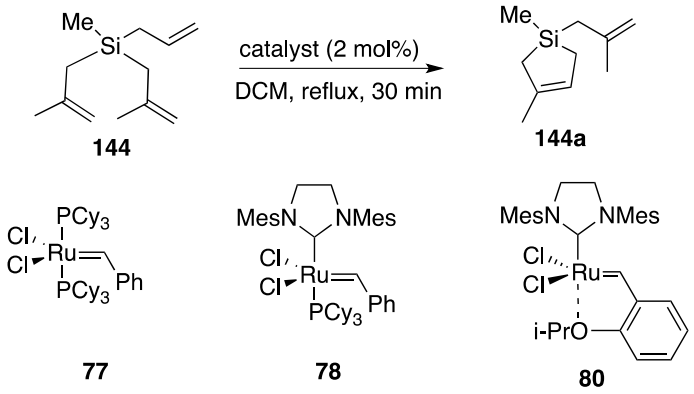


Scheme 2.2.2 Synthesis of Grignard **152.**

To assess the suitability of the Si-containing trienes (**144**–**147**) for desymmetrisation, a series of achiral ruthenium catalysts were selected based on their ease of handling and availability. Substrate **144** was chosen to carry out this study with the commercially available achiral ruthenium metathesis catalysts (**77**, **78** and **80**).

All RCM reactions were carried out in the presence of 2 mol% catalyst in DCM at reflux. Complex **78** exhibited the best reactivity (Table 2.2.1, entry 2), with optimal catalyst concentration found to be 0.01 M. By ^{1}H NMR spectra on the crude reaction mixture, the

starting material was fully consumed and no side-products were observed. The desired products were purified by a plug of silica gel. Higher concentrations (0.1 and 1 M) led to the formation of cross metathesis dimerised side products as a mixture of E and Z geometrical isomers with low selectivity (E/Z) ratio of 2:1.



Entry	Catalyst[a]	Yield / %[b]
1	**77**	0[c]
2	**78**	87
3	**80**	57

[a] Reaction carried out using 2 mol% catalyst, 0.01 M DCM under nitrogen atmosphere, [b] Isolated yield after silica gel chromatography, [c] Starting material recovered.

Table 2.2.1 Screening of achiral ruthenium metathesis catalysts.

Grubbs II (**78**) or Hoveyda-Grubbs (**80**) catalysts afforded the desired product 1,3-dimethyl-1-(2-methylprop-2-en-1-yl)-2,5-dihydro-1*H*-silole **144a** in good and moderate yields (87% and 57%) respectively. Grubbs I (**77**) catalyst was unable to react with (allyl(methyl)bis(2-methylprop-2-en-1-yl)silane) **144**. On the basis of the distinct reactivity afforded by the different Grubbs catalysts, the Grubbs II generation catalyst was selected to carry out subsequent RCM transformations.

In order to verify the effect of varying all C-substituents at the prochiral Si-trienes, a new generation of substrates was designed. We envisioned that modification of the substituents at

the silicon centre would have both electronic and steric effects. Oxysilanes, classified in general as type **I** and **II,** are depicted in Figure 2.2.1.

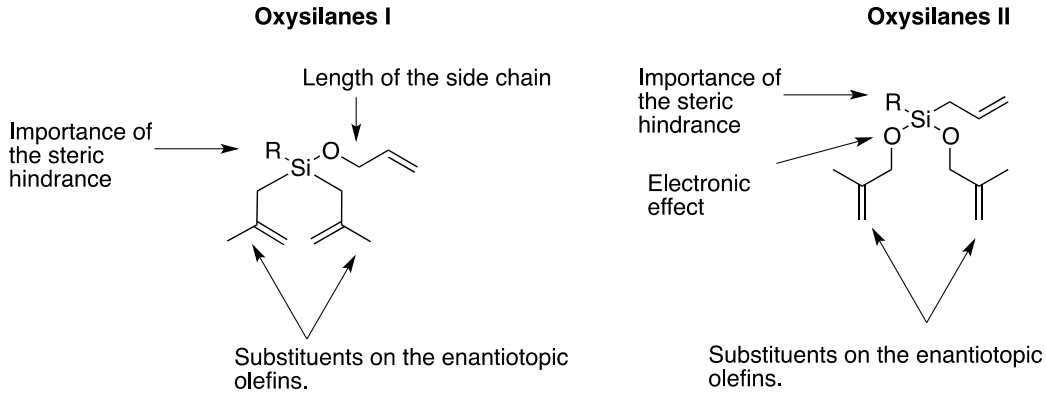
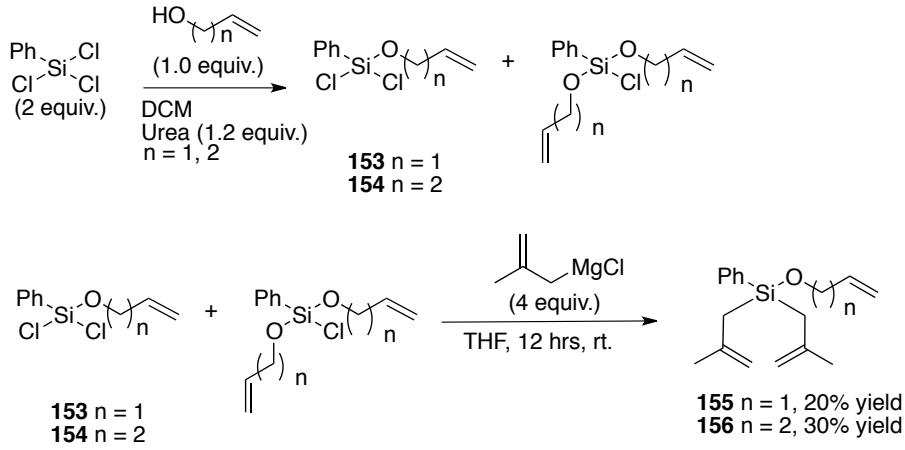


Figure 2.2.1 Prochiral Si-containing trienes.

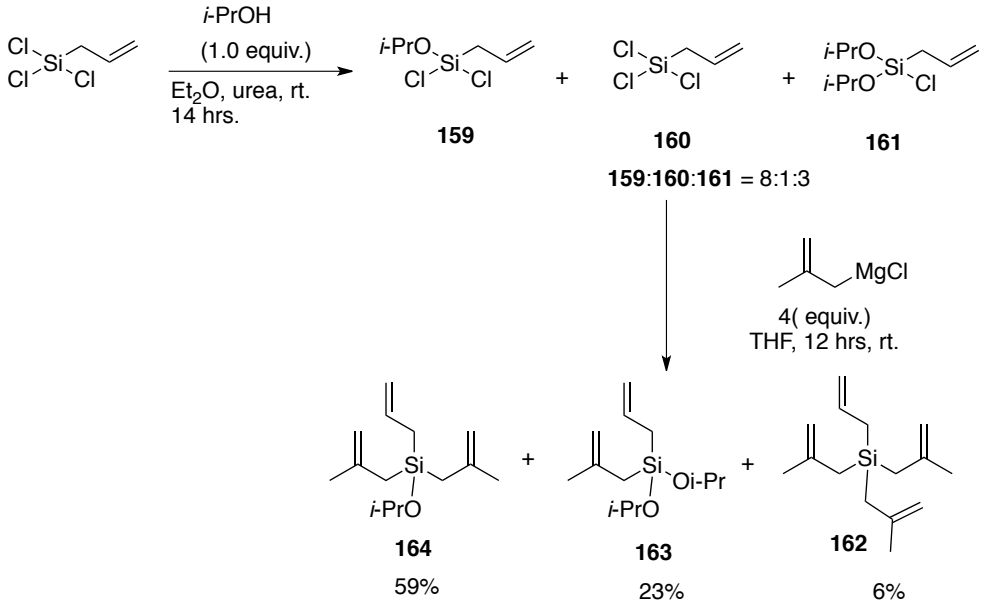
Second Generation of Prochiral Si-trienes.

Various type **I** oxysilanes were synthesised by the mono addition of an alcohol bearing the desired alkene functionality to phenyltrichlorosilane. Subsequent addition of the required Grignard reagent would give the target compounds. In an attempt to favour the monoaddition product, an excess of phenyltrichlorosilane was used. Slow addition of the alcohol was found to be crucial to minimise double addition. Isolation of the monoaddition product by distillation proved to be problematic (**153**, **154**), hence the reaction mixture was used without purification. Addition of 2-methylallylmagnesium chloride to the mixture of chlorosilanes **153** and **154** afforded the expected oxysilanes (allyloxy)[bis(2-methylprop-2-en-1-yl)]phenylsilane (**155**) and (but-3-en-1-yloxy)[bis(2-methylprop-2-en-1-yl)]phenylsilane (**156**) in 20% and 30% yield, respectively. Yields for **155** and **156** are low due to the difficulties encountered upon purification by silica gel chromatography (Scheme 2.2.3).



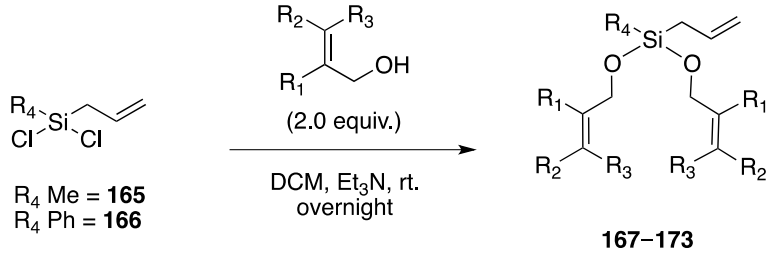
Scheme 2.2.3 General synthesis of type **I** oxysilanes.

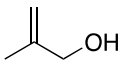
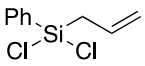
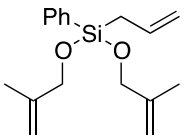
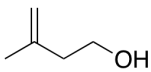
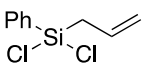
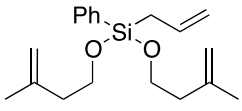
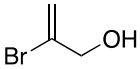
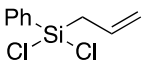
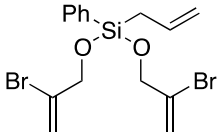
(Allyl(isopropoxy)bis(2-methylprop-2-en-1-yl)silane **164** was synthesised in a concise two-step procedure from allyltrichlorosilane. Initial monoaddition of *i*-PrOH to allyltrichlorosilane resulted in incomplete conversion affording a mixture of the mono **159** and bis-alkoxide **161** products. Isolation of allyl(dichloro)isopropoxysilane **159** from the resulting mixture by distillation proved to be difficult. Thus, the reaction mixture was used without further purification. Subsequent addition of 4 equivalents of the Grignard reagent afforded a mixture, which was purified by column chromatography to yield the desired product **164** in 59% yield.

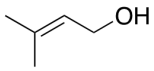
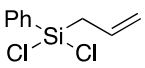
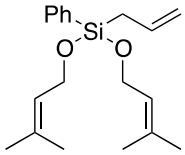
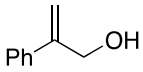
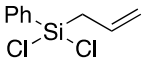
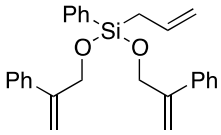
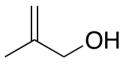
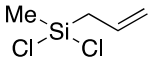
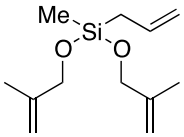
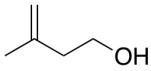
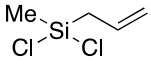
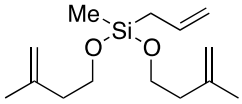


Scheme 2.2.4 Synthesis of allyldichloro(isopropoxy)silane.

The synthesis of oxysilanes type **II** required two different synthetic approaches, so that products (**167–173**) were synthesised with a single-step procedure depicted in Table 2.2.2. Substrates **176–183** were formed by a two-step methodology (Table 2.2.3). The commercially available allyldichloro(methyl)silane (**165**) and allyldichloro(phenyl)silane (**166**) were used as the starting materials for the synthesis of compounds **167–173**. Following a single-step procedure, these reagents were treated with 2 equivalents of the requisite commercially available alcohol and triethylamine in DCM, and allowed to warm from 0°C to room temperature overnight (Table 2.2.2). This afforded the desired prochiral trienic oxysilanes in good yields after purification by silica gel chromatography (51–85%).



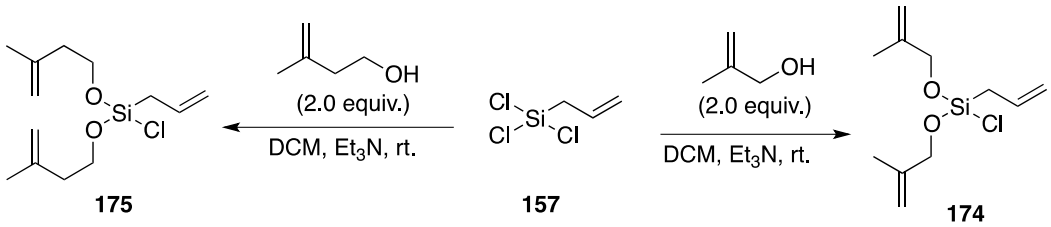
Entry	Allyl Alcohol	Dichlorosilane	Product	Yield (%)[a]
1			 **167**	51
2			 **168**	75
3			 **169**	61

4			 **170**	75
5			 **171**	65
6			 **172**	72
7			 **173**	85

a) isolated yield.

Table 2.2.2 Synthesis of oxysilanes (Type **II**).

Substrates **176**–**183** were synthesised following a two-step procedure. First, the intermediate allylchlorobis((2-methylallyl)oxy)silane **174** or the homologue **175** were formed by double addition of homoallylic alcohol to trichloroallylsilane in the presence of triethylamine (Scheme 2.2.5).



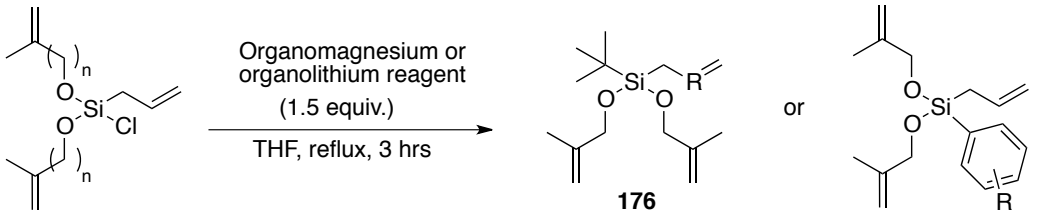
175 **157** **174**

Scheme 2.2.5 Synthesis of the intermediates **174** and **175.**

Intermediates **174** and **175** were too unstable to be purified by silica gel chromatography. Distillation under reduced pressure yielded a colourless oil, however a ^{1}H NMR spectrum of

the product showed a complex mixture of products still present after distillation. The nature of the impurities were not identified, but it is probably that monosubstitution product and starting material were present in the mixture. Then, slow addition of arylmagnesium halide or *tert*-butyllithium yielded the desired products. After careful purification by silica gel chromatography, the oxysilanes **176–183** were isolated in moderate yields (Table 2.2.3, 45–66%).

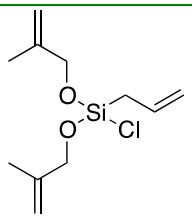
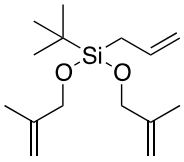
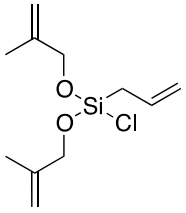
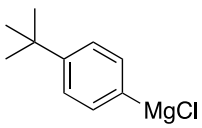
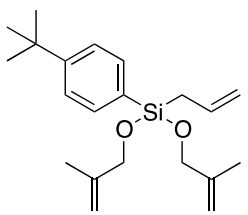
Substrates featuring an extra methylene unit to form a seven Si-cyclic membered compound were also synthesised following the same procedure (Entries 7 and 8, Table 2.2.3).

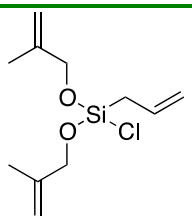
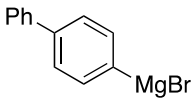
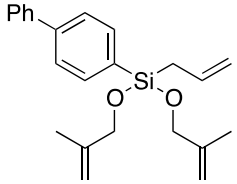
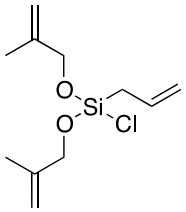
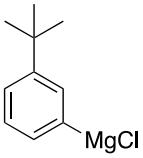
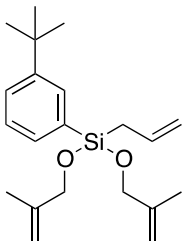
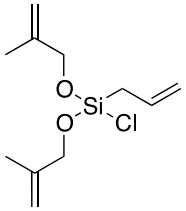
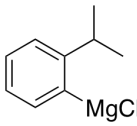
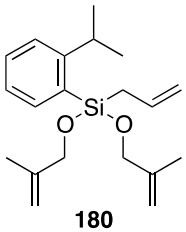
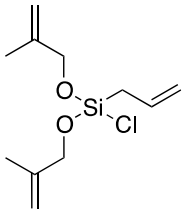
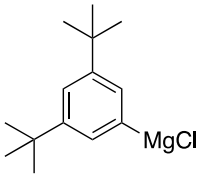
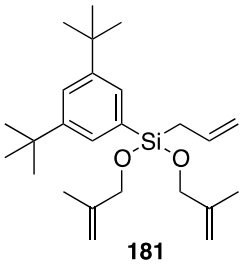
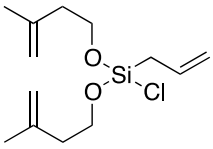
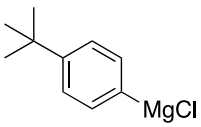
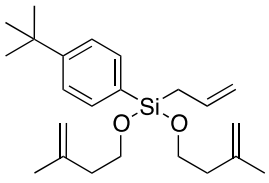


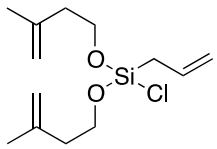
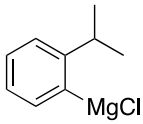
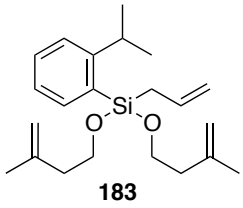
174 n = 1
175 n = 2

176

177–183

Entry	Chlorosilane	Organomagnesium or Organolithium reagents	Product	Yield(%)[a]
1[b]			 **176**	45
2			 **177**	50

3			 **178**	50
4			 **179**	55
5			 **180**	65
6			 **181**	50
7			 **182**	47

8			 **183**	66

[a] isolated yield. [b] *t*-BuLi in pentane (-20 °C) during 1 h.

Table 2.2.3 Synthesis of type **II** oxysilanes.

2.3 Ring-closing metathesis using achiral catalyst

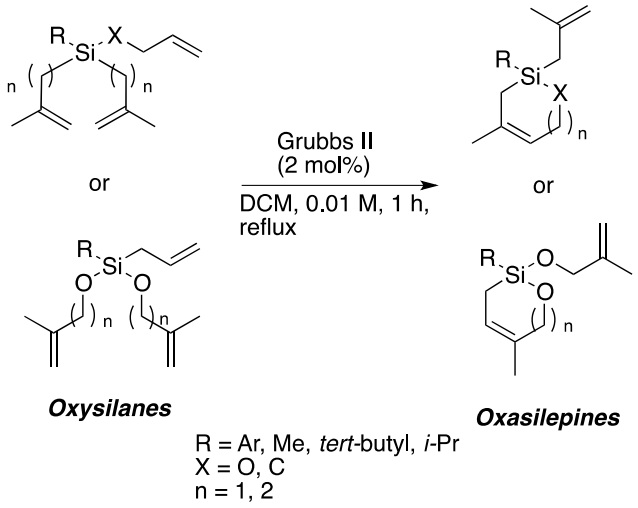
With the new prochiral Si-trienes in hand, the desymmetrisation *via* RCM was subsequently investigated. Grubbs II catalyst was used to promote RCM for all synthesised prochiral trienes under the optimised conditions (Grubbs II catalyst 2 mol%, 0.01 M in DCM, 1 hour at reflux, Table 2.3.1).

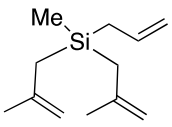
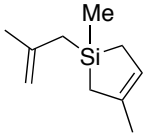
In all cases, the conversion was >98%, with the exception of substrate **169** bearing a Br atom (Table 2.3.1, entry 14). Phosphine-containing catalysts such as Grubbs II have been reported to fail in the cross-metathesis of vinyl halides.[95] Computational studies have shown that the main limitation for the metathesis of vinyl halides using a Ru-alkylidene catalyst is the steric hindrance caused by the size of the halide substituents to the olefin bond.[96]

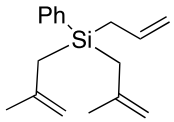
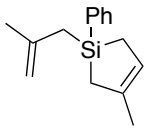
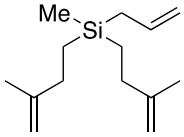
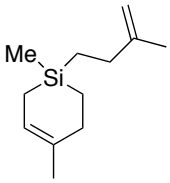
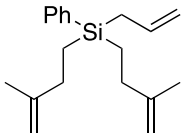
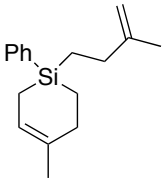
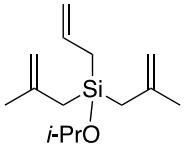
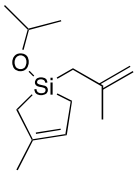
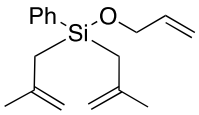
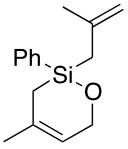
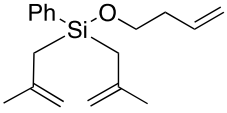
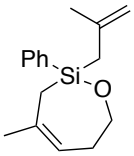
The desired products were isolated from moderate to excellent yields (65–98%, Table 2.3.1). Analysing these results, the electronic factor of mono and bis-oxysilane substrates did not affect catalyst activity (Table 2.3.1, entries 5–7). Substituent variation at the silicon atom, such as tert-butyl or (substituted) aryl groups, did not affect the reactivity of the RCM reaction (Table 2.3.1, entries 13, 15–19). The formation of the corresponding six and seven membered ring products was achieved in high yields (Table 2.3.1, entries 20–22). Examination of the crude ^{1}H NMR revealed no by-product formation (homodimerisation or isomerisation of the

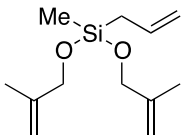
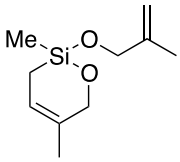
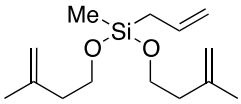
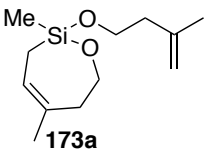
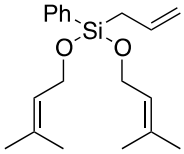
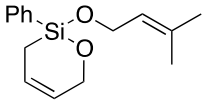
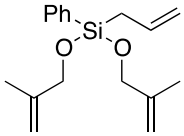
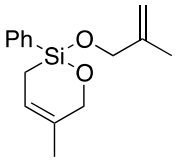
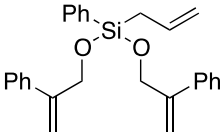
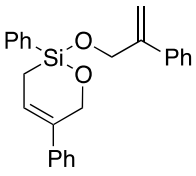
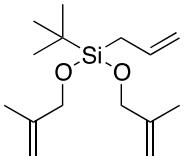
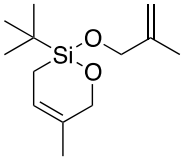
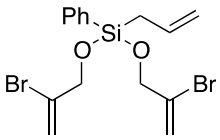
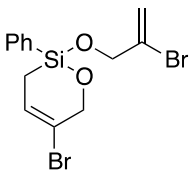
endocyclic olefin), demonstrating the high selectivity of the RCM reaction towards the formation of the desired cyclic product.

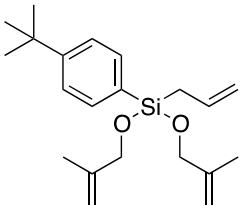
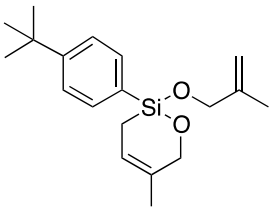
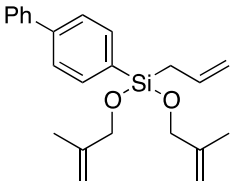
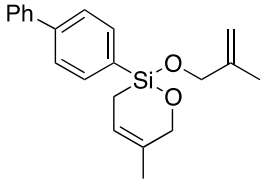
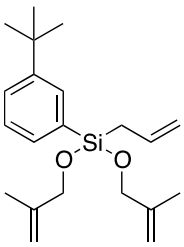
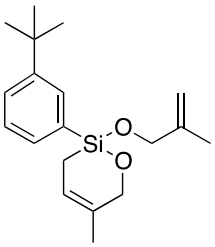
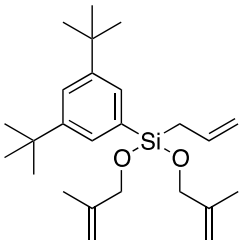
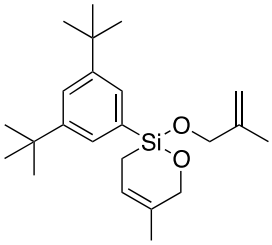
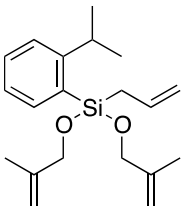
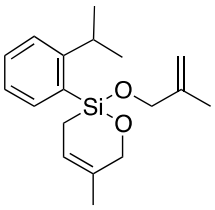
A major issue encountered with the prochiral Si-trienes all carbon substituents (**144**–**147**) was the inability to separate the corresponding enantiomers by chiral HPLC or HPLC/GC (Table 2.3.1 entries 1–4) due to the low polarity of the cyclic products. The separation of the enantiomers by stationary phase chromatography was possible when the prochiral Si-trienes contained at least one oxygen atom.

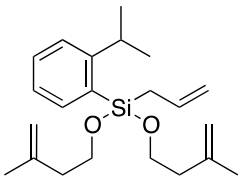
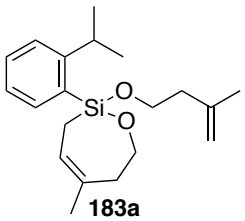
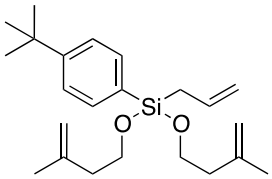
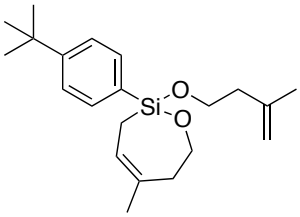
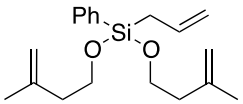
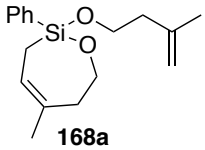


Entry	Substrate	Product[a]	% Conv.[b]	% Yield[c]
1		 **144a**	>98	87

2		 **146a**	>98	75
3		 **145a**	>98	98
4		 **147a**	>98	85
5		 **164a**	>98	65
6		 **155a**	> 98	75
7		 **156a**	> 98	75

8		 **172a**	>98	78
9		 **173a**	>98	85
10		 **170a**	> 98	75
11		 **172a**	> 98	85
12		 **171a**	> 98	55
13		 **176a**	> 98	83
14		 **169a**	0	0

15		 **177a**	>98	88
16		 **178a**	>98	88
17		 **179a**	> 98	87
18		 **181a**	> 98	90
19		 **180a**	> 98	80

20		 **183a**	> 98	86
21		 **182a**	> 98	88
22		 **168a**	>98	86

[a] All reactions carried out with 2 mol% Grubbs II, 0.01 M DCM at reflux under N_2 atmosphere. [b] Determined by ^1H NMR spectroscopy based on the starting material [c] Yields of isolated products after silica gel chromatography.

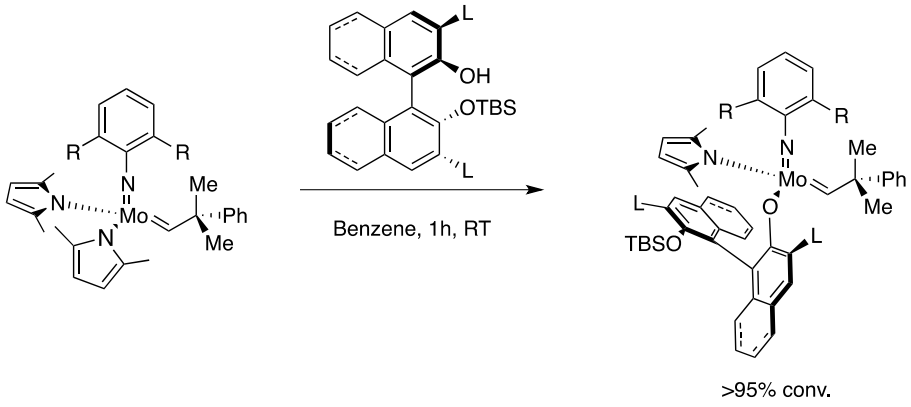
Table 2.3.1 Subjecting prochiral Si-substrates under RCM conditions.

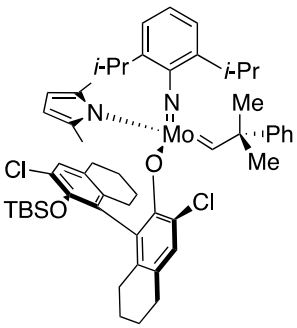
2.4 Asymmetric Ring-Closing Metathesis

General Considerations

This study was conducted in collaboration with Professor Amir. H. Hoveyda in (Boston College, Boston USA). Having validated the ability of the prochiral Si-trienes to undergo desymmetrisation to form a Si-stereogenic centre in the racemic series, we sought to extend this approach to the synthesis of enantioenriched Si-stereogenic heterocycles by the use of a chiral metathesis catalyst. This methodology would be very attractive as a new catalytic synthetic approach to create enantiopure Si-stereogenic oxasilepines.

All reactions were carried out in sealed 1 dram vials in a glovebox. The substrates were dried by azeotropic evaporation with benzene (x3) on a Schlenk line before use. Solvents were purged with Ar and purified under a positive pressure of dry argon by a modified Innovative Technologies purification system. Benzene (Aldrich) was passed successively through activated copper and alumina columns. Due to the air and water sensitivity of the catalysts, the reactions were not monitored by TLC, but rather quenched after 5 h by exposure to air. After evaporation of the solvent, the product conversion was determined by analysis of the ^{1}H NMR spectrum of the crude reaction mixture. The products were purified by flash chromatography on silica gel and the enantiomeric excess determined by chiral HPLC/GC analysis. Mo-monoalkoxide-monopyrrolide and Mo-bisalkoxide complexes bearing chiral aryloxide ligands were generated *in-situ* and used under an inert atmosphere in a dry box according to previously reported procedures.[87] W-monoalkoxide-monopyrrolide complexes were already synthesised and stored in the freezer at -60°C in the Hoveyda Laboratory. Figure 2.4.1 illustrates the library of the chiral catalysts that were employed in this work.





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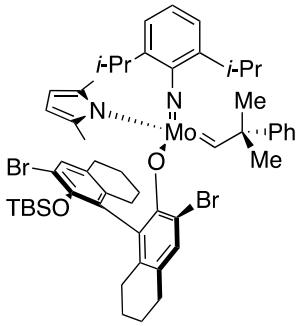

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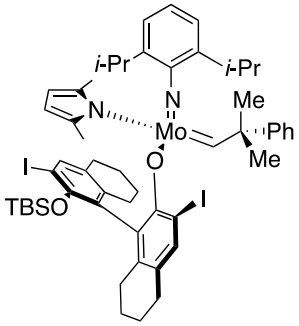

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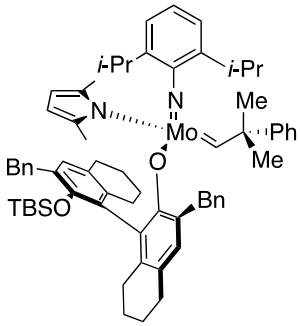

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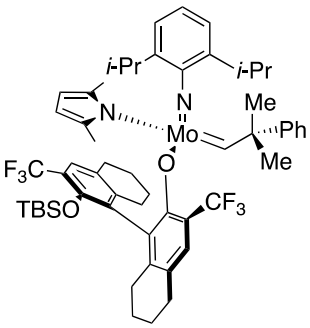

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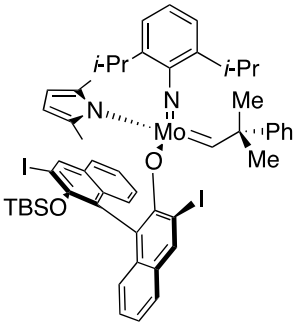

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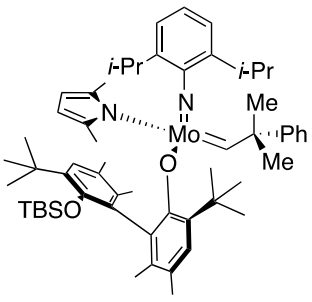

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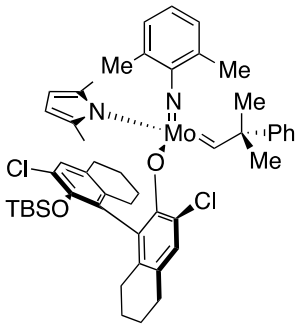

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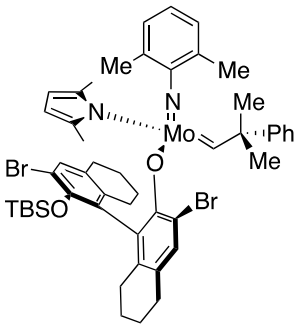

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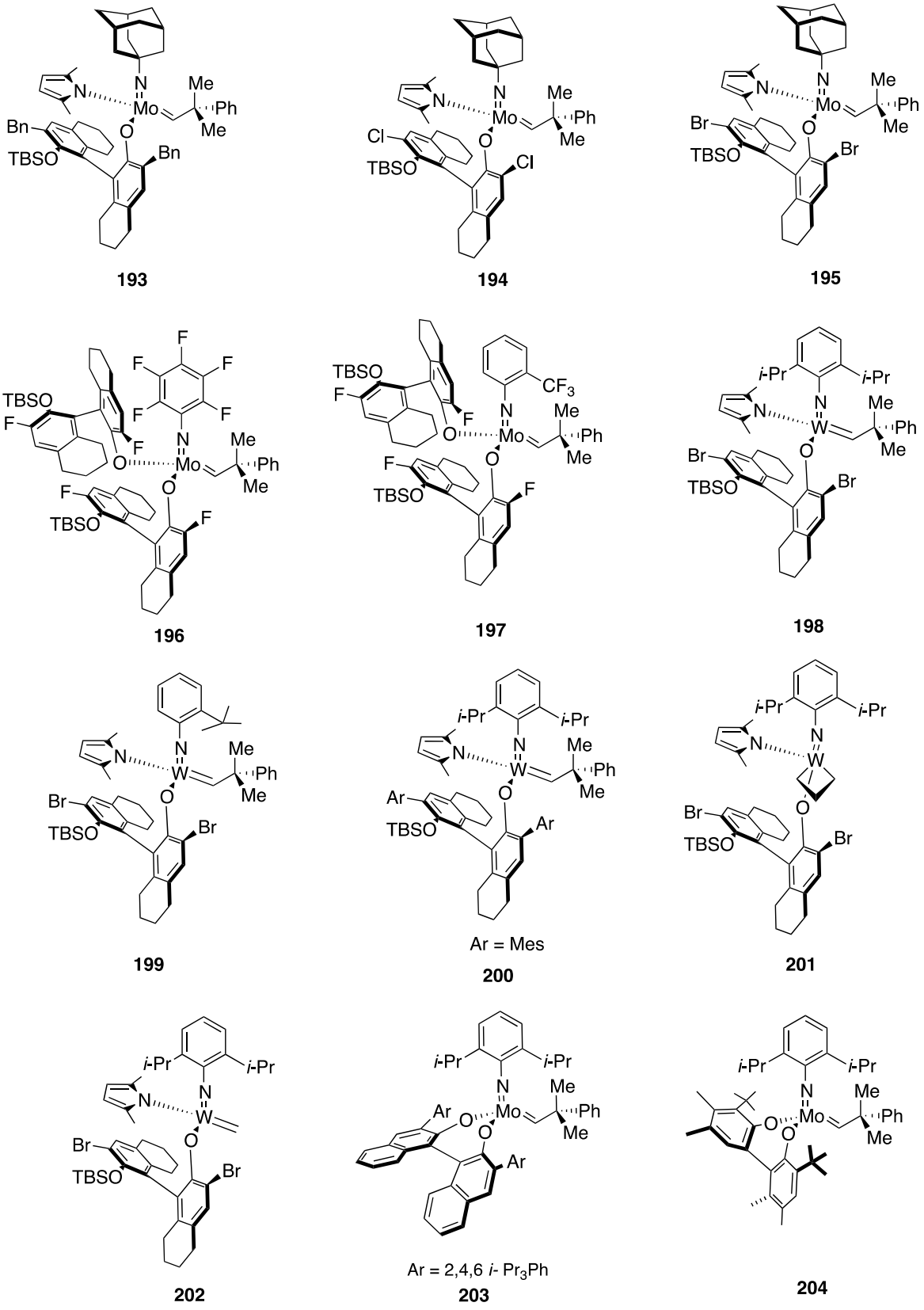
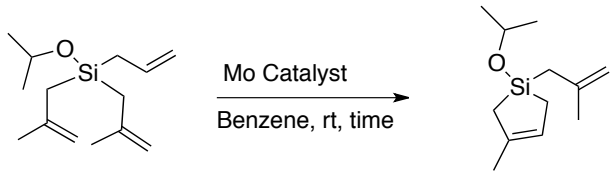


Figure 2.4.1 Library of chiral catalysts used for ARCM.

Five-membered ring

To begin our investigations, seven different chiral Mo-based catalysts were individually allowed to react with the prochiral Si-triene (allyl(isopropoxy)bis(2-methylprop-2-en-1-yl)silane) **164**, which bears an isopropoxyl group at silicon atom. Results are presented in table 2.4.



164 **164a**

Entry	Catalyst[a]	mol %	Time / h	% Conv.[b]	% ee[c]
1	**185**	2	1	9	10
2	**195**	2	1	12	>2
3	**195**	5	1	86	<2
4	**184**	5	1	67	4
5	**191**	5	1	49	14
6	**194**	5	1	>98	4
7	**187**	5	4	83	< 2
8	**193**	5	4	22	18

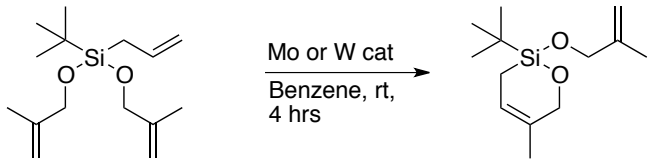
[a] Reactions carried out under N_2 atmosphere, [b] Conversion to desired product measured by 400 MHz ^{1}H NMR of the crude reaction mixture, [c] Determined by chiral GC analysis of purified product.

Table 2.4.1 Screening of catalysts for ARCM with substrate **164.**

Exposing substrate **164** under ARCM conditions afforded low conversions and enantioselectivities in all cases (0-18% *ee*) (Table 2.4.1 entries 1–8). Conversion was only increased by either increasing the catalyst loading to 5 mol% or by using the more reactive dichloride catalysts **184** and **191** (Table 2.4.1 entries 4, 5). However, enantioselectivity remained low in all cases (4–14%). Catalysts **187** and **193** bearing benzyl groups on the aryloxide ligand gave 83% and 22% conversion respectively, however poor enantioselectivity was observed (up to 18% ee) (entries 7, 8).

Six-membered ring series

We next examined allyl(tert-butyl)bis[(2-methylprop-2-en-1-yl)oxy]silane (**176**) featuring a bulkier *tert*-butyl group substituent at the silicon centre. As this substrate does not bear a chromophoric group, the analysis of the enantiomeric excess of the product was carried out by chiral gas chromatography.



176 **176a**

Entry	Catalyst[a]	mol %	Conc. (M)	% Conv.[b]	% *ee*[c]
1	**185**	5	0.01	98	35
2	**186**	5	0.01	98	39
3	**188**	5	0.01	86	34
4	**190**	**5**	**0.01**	**23**	**83**
5	**202**	5	0.01	93	33
6	**201**	5	0.01	92	37
7	**197**	5	0.01	98	5
8	**196**	5	0.01	98	5
9[d]	**190**	5	0.01	50	64
10[d]	**190**	2	0.01	60	65

[a] Reactions carried out under N_2 atmosphere, [b] Conversion to desired product measured by 400 MHz ^{1}H NMR of the crude reaction mixture, [c] Determined by chiral GC analysis of purified product, [d] Reaction time of 14 hours.

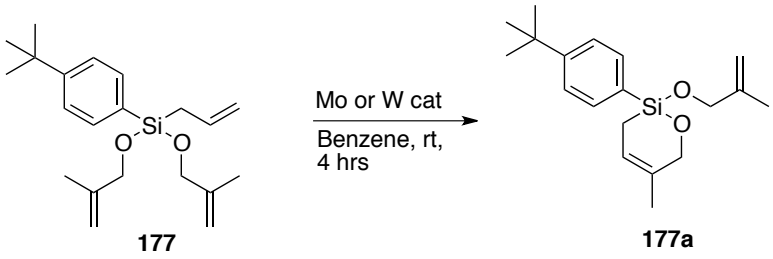
Table 2.4.2 Screening of catalysts for ARCM with substrate **176.**

When **176** was treated with 5 mol% of catalyst **190** the desired cyclic Si-stereogenic oxasilane **176a** was obtained in 29% conversion and 83% *ee* (Table 2.4.2 entry 4). A potential reason for the low reactivity may be the increased steric interactions between the *tert*-butyl groups of the aryloxide ligand and the substrate hindering the formation of the metallacycle. When the reaction was stirred for 14 hours, the conversion increased to 60% to the detriment of the

enantioselectivity (Table 2.4.2 entry 9). The catalyst loading could be reduced to 2 mol% without altering the conversion or enantioselectivity (Table 2.4.2 entries 9-10).

Dibromine, diiodine, and ditrifluoromethyl catalysts (**185**, **186**, and **188** respectively) afforded the cyclic Si-stereogenic oxasilane in excellent conversion (86-98%) but poor enantioselectivity (34–39% *ee*) (Table 2.4.2 entries 1–3). Tungsten catalysts (**202** and **201**) also afforded good conversions (up to 93%) and up to 37% *ee* (Table 2.4.2 entries 5, 6). Finally, catalysts **197** and **196** gave excellent conversions (98%) despite low enantioselectivity of 5% ee. These catalysts have a fluorine substituent at the 3 and 3' position of the aryl oxide ligand, which is a relatively small group, but also very electronegative atom. Incorporation of electron-withdrawing groups within either the imido or diolate moieties of a chiral Mo complex can result in enhanced Lewis acidity of the metal centre and higher catalyst activity.[84] Thus, the excellent conversions may reside on the higher Lewis acidity of the metal due to these important variations.

In order to examine the effect of bearing a more bulky group on the silicon atom, substrate allyl(4-tert-butylphenyl)bis[(2-methylprop-2-en-1-yl)oxy]silane**,** (**177**) was exposed to the ARCM conditions.



177 **177a**

Entry	Catalyst[a]	mol %	Conc. (M)	% Conv.[b]	% *ee*[c]
1	**185**	5	0.01	98	<2
2	**186**	5	0.01	84	-
3	**188**	5	0.01	79	97
4	**190**	5	0.01	25	98

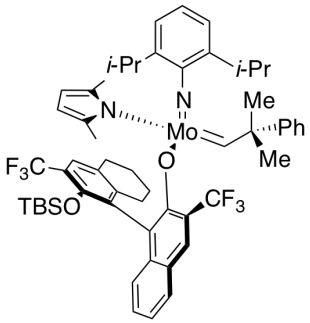
5	**202**	5	0.01	78	98
6	**201**	5	0.01	77	98
7	**197**	5	0.01	98	68
8	**196**	5	0.01	43	76
9	**199**	5	0.01	>95	10
10	**200**	5	0.01	0	-

[a] Reactions carried out under N_2 atmosphere, [b] Conversion to desired product measured by 400 MHz ^{1}H NMR of the crude reaction mixture, [c] Determined by chiral HPLC analysis of purified product.

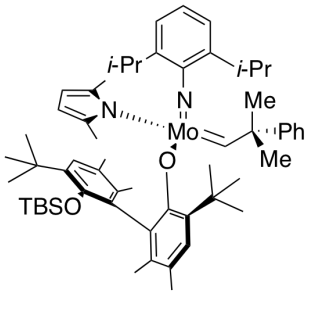
Table 2.4.3 Screening of catalysts for ARCM with substrate **177.**

For substrate **177**, a library of 10 catalysts was used for screening purposes. Several catalysts showed conversions above 76% with three catalysts giving the product in more than 95% ee. We were delighted to find that, when substrate **177** was subjected to ARCM, the desired enantioenriched Si-stereogenic oxasiline **177a** (2-(4-*tert*-butylphenyl)-5-methyl-2-[2-methylprop-2-en-1yl)oxy]-3,6-dihydro-2*H*-1,2-oxasiline) was afforded in good conversion 98% and enantioselectivities superior to 95% (Table 2.4.3, entry 5).

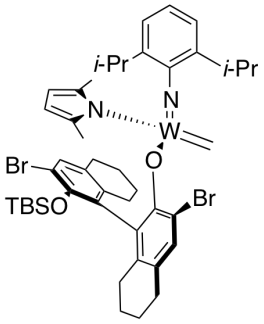
To verify the exceptional behaviour of substrate **177** with catalyst **202**, the reaction was performed using the catalyst library based on W or Mo complexes. Interestingly, catalysts **188**, **190**, and **201** led to the formation of mainly one enantiomer (superior to 95% *ee*) and high conversions (Table 2.4.3 entries 3–6).



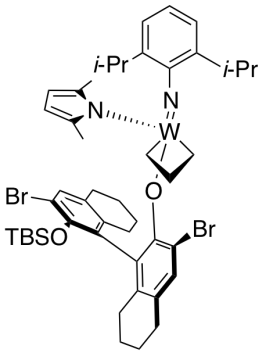
188



190



202



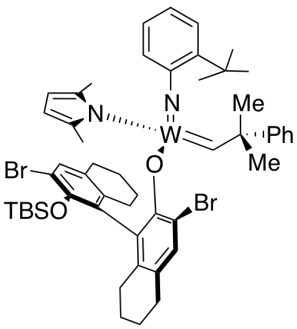
201

Catalyst **188** bears trifluoromethyl substituents (highly electron withdrawing groups making the catalyst more active) at the 3 and 3´positions of the aryloxide whereas catalyst **190** has

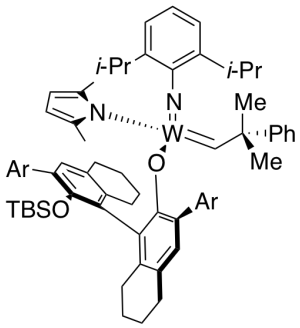
tert-butyl groups. A more bulky moiety in the chiral ligand (aryloxide) seemed to be important in order to obtain higher enantioselectivities.

Catalyst **188** gave 79% conversion and excellent *ee* (97%), while with catalyst **190** conversion was reduced probably due to steric hindrance (25%) but the enantioselectivity remained high (99% *ee*). Tungsten catalysts **202** and **201** were also effective for ARCM to yield the desired Si-stereogenic oxasilane in 78% conversion and > 95% *ee*. Although catalyst **197** (pentafluoro-imido ligand) underwent successful ring-closure to yield the desired product in 98% conversion, the enantioselectivity decreased to 68% ee. With catalyst **196** the conversion was reduced to 43% but higher enantioselectivity was observed (76% *ee*). The transformations depicted in Table 2.4.3 show a high degree of substrate to catalyst specificity, which highlights the necessity of having a library of chiral metathesis catalysts.

A modification of the imido aryl ligand **199** (bearing a *tert*-butyl group at the *ortho* position) resulted in loss of the enantioselectivity to 10%, however the activity of the catalyst was maintained (Table 2.4.3, entry 9). This structural modification at the imido ligand did have a significant effect over the enantiocontrol, suggesting that the substitution at the imido ligand is crucial to achieve high enantiomeric excess. On the other hand, catalyst **200** did not exhibit any catalytic activity under ARCM conditions probably due to steric factors of the catalyst and substrate **177** was recovered.



199

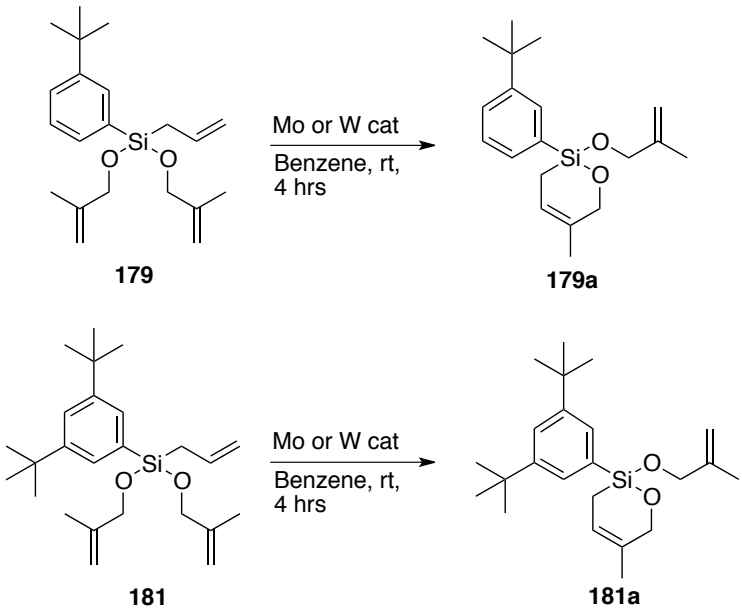


Ar = Mes

200

The high enantioselectivities observed with substrates **176** and **177** encouraged further investigations on varying the substitution pattern of the aryl group. Varying the position of the alkyl (*tert*-butyl and isopropyl) groups would provide a better understanding of the effect of

this structural modification on the enantiocontrol during the ARCM reaction. To validate our hypothesis, substrates allyl(3-*tert*-butylphenyl)bis[(2-methylprop-2-en-1-yl)oxy]silane **179** and allyl(3,5-di-*tert*-butylphenyl)bis[(2-methylprop-2-en-1-yl)oxy]silane **181** were exposed to ARCM conditions.

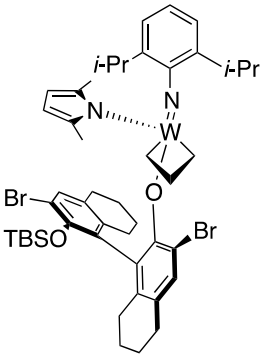


Entry	Substrate	Catalyst[a]	mol %	Conc. (M)	% Conv.[b]	% *ee*[c]
1	**179**	**185**	5	0.01	95	10
2	**179**	**189**	5	0.01	95	11
3	**179**	**188**	5	0.01	46	5
4	**179**	**202**	5	0.01	71	10
5	**179**	**201**	5	0.01	72	10
6	**181**	**202**	5	0.01	85	45
7	**181**	**201**	**5**	**0.01**	**71**	**51**
8	**181**	**186**	5	0.01	36	40
9	**181**	**188**	5	0.01	71	40
10	**181**	**190**	5	0.01	24	45
11	**181**	**203**	5	0.01	10	-
12	**181**	**204**	5	0.01	9	-
13	**181**	**199**	5	0.01	95	10
14	**181**	**200**	5	0.01	0	-

[a] Reactions carried out under N_2 atmosphere, [b] Conversion to desired product measured by 400 MHz ^{1}H NMR of the crude reaction mixture, [c] Determined by chiral HPLC analysis of purified product.

Table 2.4.4 Screening of catalysts for ARCM with substrates **179** and **181**

After selection of the best chiral catalysts from the previous experiments, complexes **185–186** and **188–204** were selected for this transformation. Among the chiral catalysts examined during this screening, most of them gave high conversion to the desired product (46–95%). However, all of them induced very low enantioselectivities (< 11% ee) (Table 2.4.4, entries 1–5).



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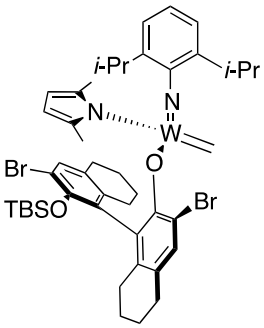
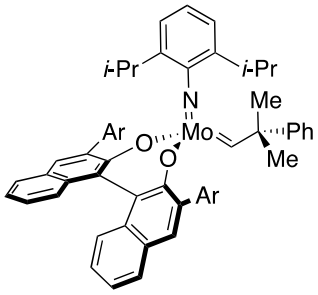


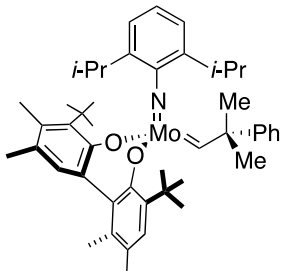
202

Subjecting substrate **181** under the ARCM conditions, only catalyst **199** led to full conversion after 4 hours but no enantiomeric excess was observed (Table 2.4.4, entry 13). Except for catalyst **202**, all complexes converted less than 71% of the substrate **181**. In addition, all the enantioselectivities obtained were low to moderate, the highest being 51% (Table 2.4.4, entry 7). The stereochemical erosion observed for the formation of **179a** and **181a** showed that indeed very small changes in the substrate have dramatic influence on the enantiocontrol, emphasising the necessity of having chiral catalyst libraries.



Ar = 2,4,6 *i*- Pr_3Ph

203

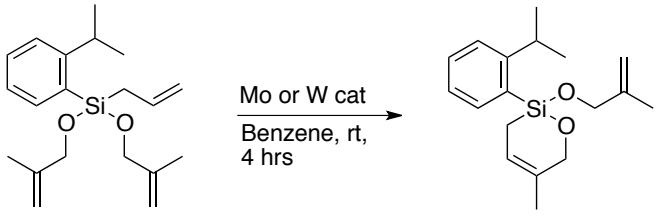


204

Finally, biphenolate catalysts **203** and **204** were explored under ARCM conditions, these catalysts presented very low activity, less than 10% conversion. The rigidity or the steric factors of these catalysts may decrease the catalytic activity. ARCM is generally extremely sensitive to changes in the substrate or in the catalyst. Small modifications in the substrate can have a tremendous effect on the enantiocontrol of the reaction, as was already shown above. The same holds for the substrates;

a catalyst that converts a certain substrate with high enantioselectivity can provide low selectivity for a related substrate.

Based on previous observations, we extended this approach to substrate **180**, which bears an isopropyl substituent at the *ortho*-position of the aryl group. However, this experiment resulted in the same low ee values, ranging from 2% to 33% for catalyst **199** and moderate conversion, as observed in Table 2.4.5.



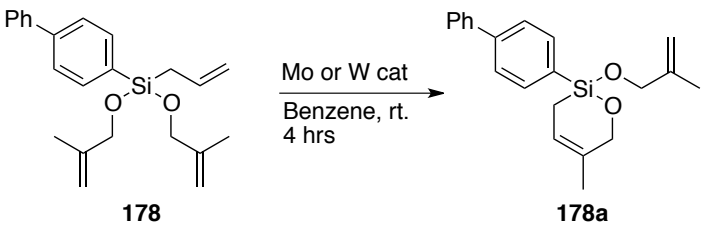
180 **180a**

Entry	Catalyst[a]	mol %	Conc. (M)	% Conv.[b]	% *ee*[c]
1	**185**	5	0.01	95	<2
2	**188**	5	0.01	62	<2
3	**190**	5	0.01	36	<2
4	**201**	5	0.01	71	<2
5	**199**	5	0.01	95	8
6	**200**	5	0.01	0	-

[a] Reactions carried out under N_2 atmosphere, [b] Conversion to desired product measured by 400 MHz ^{1}H NMR of the crude reaction mixture, [c] Determined by chiral HPLC analysis of purified product.

Table 2.4.5 Screening of catalysts for ARCM with substrate **180.**

Based on previous observations, substrate allyl(biphenyl-4-yl)bis[(2-methylprop-2-en-1-yl)oxy]silane (**178**) was designed with substitution at the *para*-position of the phenyl ring, which seems to be a critical position for the enantiocontrol during the ARCM process.

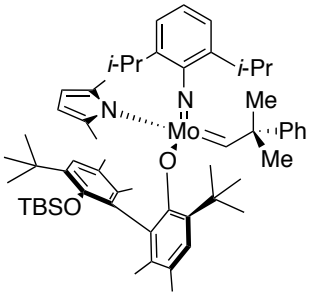


178 **178a**

Entry	Catalyst[a]	mol %	Conc. (M)	% Conv.[b]	% *ee*[c]
1	**185**	5	0.01	98	8
2	**185**	2	0.01	67	8
3	**186**	5	0.01	86	2
4	**188**	5	0.01	38	5
5	**189**	5	0.01	60	12
6	**190**	5	0.01	10	24
7	**197**	5	0.01	86	6
8	**196**	5	0.01	91	7
9	**198**	5	0.01	<2	-
10	**202**	5	0.01	82	<2
11	**201**	5	0.01	74	<2
14[d]	**185**	5	0.01	65	<2
15[d]	**201**	5	0.01	16	-
16[e]	**190**	5	0.01	20	8

[a] Reactions carried out under N_2 atmosphere, [b] Conversion to desired product measured by 400 MHz ^{1}H NMR of the crude reaction mixture, [c] Determined by chiral HPLC analysis of purified product, [d] Addition of 1 equivalent of diallylether, [e] Reaction time 16 hours.

Table 2.4.6 Screening of catalysts for ARCM with substrate **178**.



190

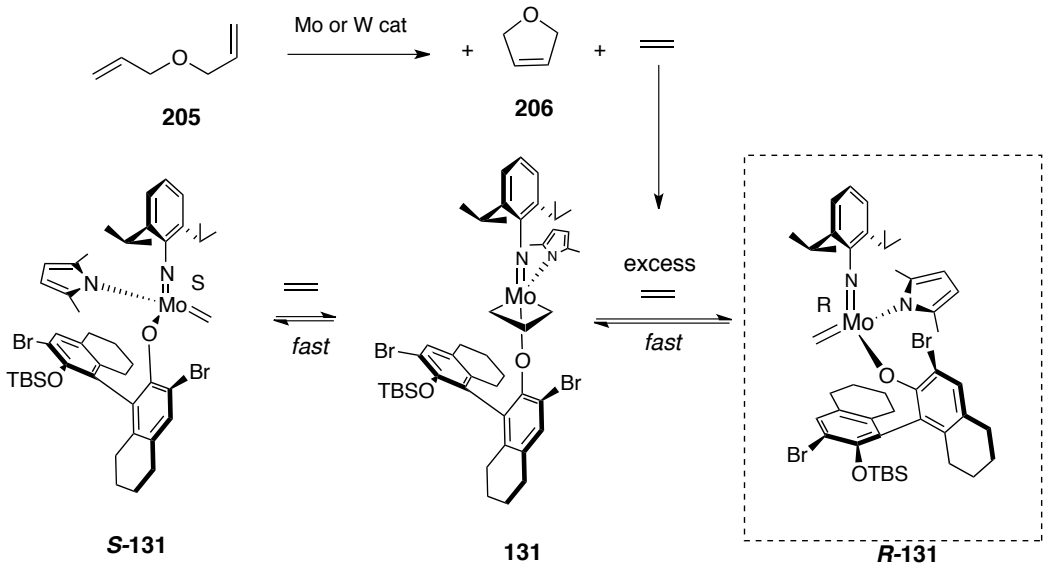
Screening of catalyst loadings found 5 mol% as the optimum, giving conversions up to 98%, however enantioselectivity was low (8% ee) (Table 2.4.6 entry 1). When the catalyst loading was reduced to 2 mol% the conversion dropped to 67% and the enantioselectivity remained low (8% ee) (Table 2.4.6 entry 2). Varying the substituent group at the 3 and 3´positions of the aryl oxide ligand (I and CF_3 groups) **186** and **188** gave good conversion with the iodine substituted catalyst (86%), but low enantioselectivity was observed (2% ee) (Table 2.4.6 entries 3,4). Having the electron withdrawing CF_3 group did not improve either the conversion or the enantioselectivity.

Interestingly catalyst **190**, bearing a *tert*-butyl group at the 3 and 3´ positions of the aryloxide of the catalyst led to the highest level of enantiocontrol (24% ee) albeit with poor conversion (10%) (Table 2.4.6 entry 6). This modest result of enantiocontrol highlighted the importance of the steric factors in the catalyst **190** and in the prochiral siloxane. When we increased the

reaction time to 16 hours, the conversion increased to 20% but the enantiomeric excess was eroded (Table 2.4.6 entry 16). We also explored tungsten catalysts **198**, **201**, **202**. No reaction was observed with catalyst **198** (Table 2.4.6 entry 9). However, complexes **201** and **202** afforded good conversions of 74% and 82% respectively, but no enantiomeric excess was observed (Table 2.4.6 entries 9-11).

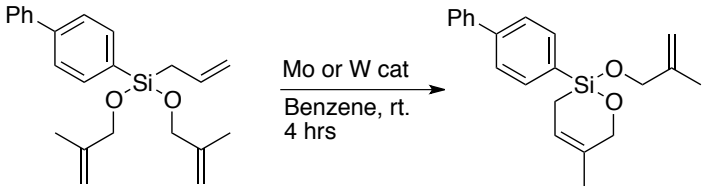
Isomerisation at Mo catalyst.

Diallyl ether has been used in cross metatheses to form *in situ* ethylene. Hoveyda and co-workers have reported that when ethylene is in the reaction mixture, isomerisation at the Mo catalyst occurs very quickly.[90] This leads to the formation of a mixture of diasteroisomers, of which only the more reactive diasteroisomer is able to perform the ARCM leading to high enantioselectivity. We carried out experiments in the presence of one equivalent of diallylether **205**, as a source of ethylene. Catalysts **185** and **201** were exposed under these conditions, but low conversion and low *ee* were obtained (Table 2.4.6 entries 14, 15).



Scheme 2.4.1 Addition of diallylether to generate ethylene *in situ.*

In order to determine the effect of the solvent upon the conversion and enantioselectivity, DCM and THF were examined with substrate **178**, however moderate conversion (33–84%), and no enantiomeric excess was observed (Table 2.4.7 entries 1-4).



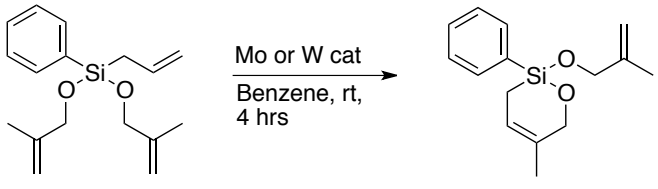
178 **178a**

Entry	Catalyst[a]	Solvent	mol %	Conc. (M)	% Conv.[b]	% *ee*[c]
1	**185**	DCM	5	0.01	33	5
2	**185**	THF	5	0.01	56	<2
3	**201**	DCM	5	0.01	50	<2
4	**201**	THF	5	0.01	84	<2

[a] Reactions carried out under N_2 atmosphere, [b] Conversion to desired product measured by 400 MHz ^{1}H NMR of the crude reaction mixture, [c] Determined by chiral HPLC analysis of purified product.

Table 2.4.7 Screening of catalysts for ARCM with substrate **178**.

Having investigated substrates with steric demanding units such as **176**, **177**, **178, 179**, **180**, and **181**, substrate **167** (allyl(methyl)bis[(2-methylprop-2-en-1-yl)oxy]silane) was studied with a range of catalysts **185**–**202** under ARCM conditions (5 mol% catalyst during 4 hours).



167 **167a**

Entr	Catalyst[a]	mol %	Conc. (M)	% Conv.[b]	% *ee*[c]
1	**185**	5	0.1	98	8
2	**185**	5	0.01	98	38
3	**185**	2	0.01	82	20

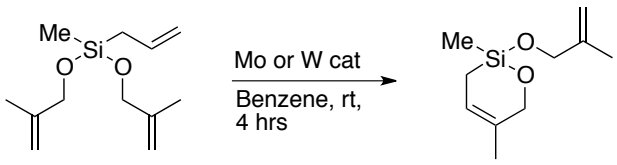
4	**186**	5	0.01	42	<2
5	**188**	5	0.01	30	<2
6	**189**	5	0.01	90	<2
7	**190**	5	0.01	<2	-
8	**198**	5	0.01	<2	-
9	**202**	5	0.01	80	52
10	**201**	5	0.01	62	66
11[d]	**190**	5	0.01	25	9

[a] Reactions carried out under N_2 atmosphere, [b] Conversion to desired product measured by 400 MHz ^{1}H NMR of the crude reaction mixture, [c] Determined by chiral HPLC analysis of purified product, [d] Reaction time 16 hours.

Table 2.4.8 Screening of catalysts for ARCM with substrate **167**.

Concentration of the reaction also had an effect, on increasing from 0.01M to 0.1M the conversion remained high (98%), while enantioselectivity was almost lost (8% ee). 5 mol% of the catalyst **185** was found to be the optimum giving up to 98% conversion and moderate enantioselectivity (38% ee) (Table 2.4.8, entry 2). When the catalyst loading was reduced to 2 mol% the conversion and enantioselectivity dropped to 82% and 20%, respectively (Table 2.4.8, entry 3). Thus, all the reactions were carried out at 0.01M in benzene. Varying the substituent group at the 3 and 3´positions of the aryl oxide ligands (I and CF_3 groups) **186** and **188** resulted in a decrease in the conversion (42%) and loss of enantiocontrol (2% ee) (Table 2.4.8, entries 4–5). Catalyst **190**, bearing a *ter*t-butyl group at the 3 and 3´ positions did not allow the RCM to occur (Table 2.4.8, entry 7). We also explored tungsten catalysts **185**, **202** and **201**. Catalyst **198** is analogous to Mo-based catalyst **185**, but in this case no conversion was observed. However, in both cases, complexes **202** and **201** afforded good levels of conversion, 80% and 62%, respectively with an enantiomeric excess of 52% for **202** and 66% for **201** (Table 2.4.8, entries 9–10). When the reaction time was increased to 16 hours, the conversion went up to 25% in a racemic fashion 9% ee (Table 2.4.8, entry 11).

Substrate **172** (allyl{bis[(2-methylprop-2-en-1-yl)oxy]}silane) bearing a relatively small methyl group at the silicon centre was examined under ARCM, however no enantiomeric excess was observed.



172 **172a**

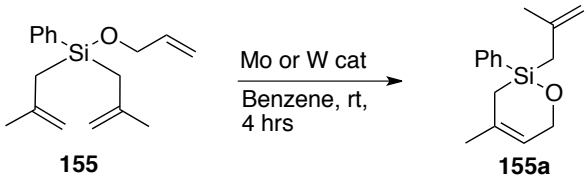
Entry	Catalyst[a]	mol %	Time / h	% Conv.[b]	% ee[c]
1	**185**	2	4	82	7
2	**192**	2	4	64	10
3	**195**	2	4	77	4
4	**191**	10	14	>98	3
5	**185**	10	14	>98	<2

[a] Reactions carried out under N_2 atmosphere, [b] Conversion to desired product measured by 400 MHz ^{1}H NMR of the crude reaction mixture, [c] Determined by chiral GC analysis of purified product.

Table 2.4.9 Screening of catalysts for ARCM with substrate **172**.

Screening with dibromide catalysts (isopropyl, methyl aryl imido ligand and adamantyl imido ligand, **185**, **192**, **195**) using 2 mol% of catalyst gave moderate conversion up to 82% but very low enantioselectivity (Table 2.4.9, entries 1–3, <2 up to 10% *ee.*). Increasing the catalyst loading up to 10 mol% gave full conversion to the desired product, however poor enantioselectivities were observed (Table 2.4.9, entries 4–5). The adamantyl group on catalyst **195** resulted in lower conversion and did not show enantiocontrol over the ARCM reaction (Table 2.4.9, entry 3).

Substrate **155** ((allyloxy)[bis(2-methylprop-2-en-1-yl)]phenylsilane) was examined under ARCM. This substrate led to the formation of the 6-membered ring **155a** (4-methyl-2-(2-methylprop-2-en-1-yl)-2-phenyl-3,6-dihydro-2*H*-1,2-oxasiline).



155 **155a**

Entry	Catalyst[a]	% Conv.[b]	% ee[c]
1	**185**	95	35
2	**186**	92	12
3	**188**	86	10
4	**189**	98	20
5	**190**	75	3
6	**202**	94	2
7	**201**	94	3
8	**197**	96	9
9	**196**	70	8

[a] Reactions carried out under N_2 atmosphere, [b] Conversion to desired product measured by 400 MHz ^{1}H NMR of the crude reaction mixture, [c] Determined by chiral HPLC analysis of purified product.

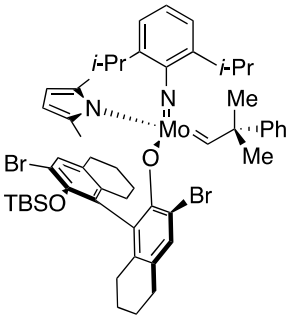
Table 2.4.10 Screening of catalysts for ARCM with substrate **155.**

Our screening started with catalyst **185**, which provided excellent conversion (95%) and 35% *ee* (Table 2.4.10 entry 1). In an attempt to enhance enantioselectivity, catalysts with a bulkier substituent at the 3 and 3' position of the aryl oxide ligand were used. Iodine was selected as it Van der Waals radius of 198 pm is larger than bromine (185 pm). Screening of catalysts **186** and **189** with substrate **155** afforded the desired six-membered product in excellent conversion (92 and 98%), however the enantioselectivity remained low (12–20% *ee*) (Table 2.4.9 entries 2, 4). The other catalysts screened with substrate **155** showed excellent conversions (70–96%), but disappointingly, none of the catalysts could provide high enantiomeric excess (Table 2.4.9 entries 3-9).

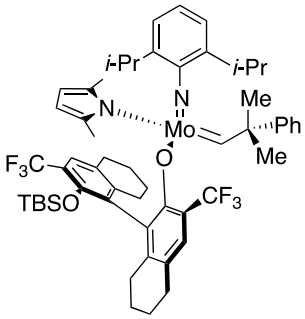
2.5 Mechanistic considerations

The contrasting behavior of the two substrates **176** and **177** with the rest of the substrates under ARCM is still unclear. However, there are some pieces of evidence that suggest the importance of having a bulky substituent at the *p*-position of the aryl group or directly attached to the silicon atom (*t*-butyl group). Hoveyda and co-workers showed a possible mechanism leading to the formation of N-aryl-tetrahydropyridines in high yields (> 78%) and > 97% ee. Based on Hoveyda's mechanistic studies, we propose a plausible transition state leading to the formation of the enantiopure Si-stereogenic oxasilepine **177a** under the ARCM process. The loss of selectivity exhibited with most of the substrates under molybdenum or tungsten catalysts may be due to the lack of unfavourable interactions between the catalyst and the substrate during the transition state. Prochiral oxysilanes showed moderate to excellent conversion to the desired six-membered Si-stereogenic oxasilepines. Oxysilanes bearing one or two oxygen atoms do not present different reactivity during the ARCM process, delivering the desired products. The structural differences between the *o*-, *m*-, and *p*-(*tert*-butyl or isopropyl) substitution at the aromatic ring attached to the silicon, seem small, but during the ARCM reaction lead to substantially different conversions and ee values of the desired products. Bonds lengths must be considered; C–Si (1.87 Å) *vs* C–C bond (1.53 Å) may have a huge impact during the formation of a compact and organised transition state.

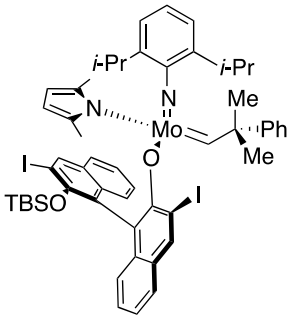
Unfortunately, we were unable to unambiguously determine the absolute configuration of the ring-closed products by X-ray crystal structure. 2-(4-*Tert*-butylphenyl)-5-methyl-2-[2-methylprop-2-en-1yl)oxy]-3,6-dihydro-2*H*-1,2-oxasiline is not crystalline at room temperature or at low temperature. Numerous attempts at growing crystals were carried out by variation of the solvent, temperature or method of crystallisation.



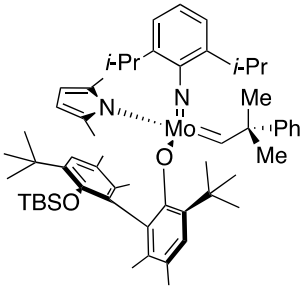
185



188



189



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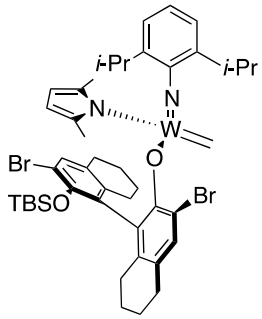
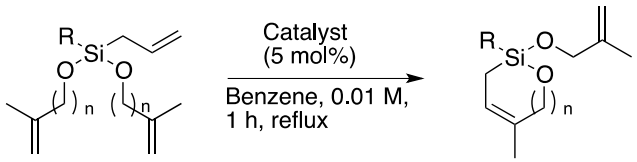
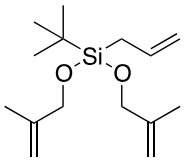
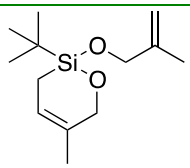
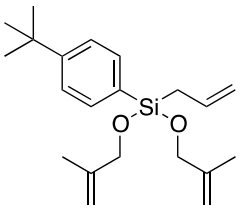
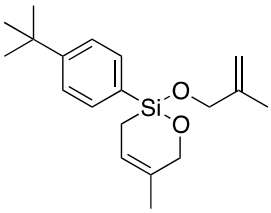
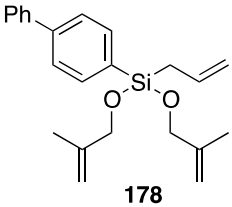
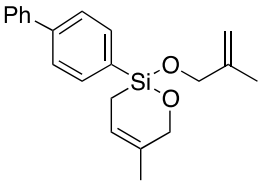


202



Entry	Substrate	Catalyst	Product	% ee
1	 **176**	190	 **176a**	83
2	 **177**	188	 **177a**	97
3	 **178**	189	 **178a**	12

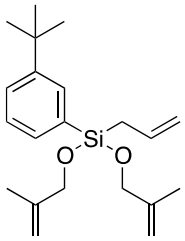
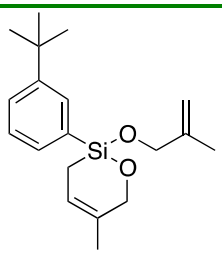
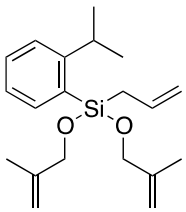
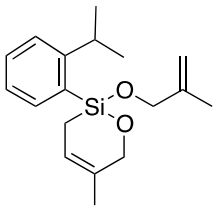
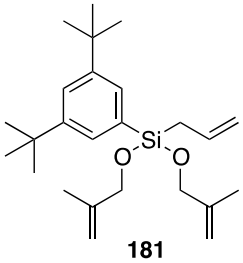
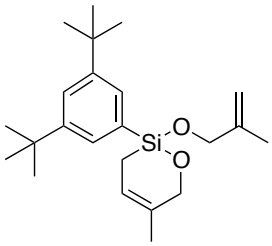
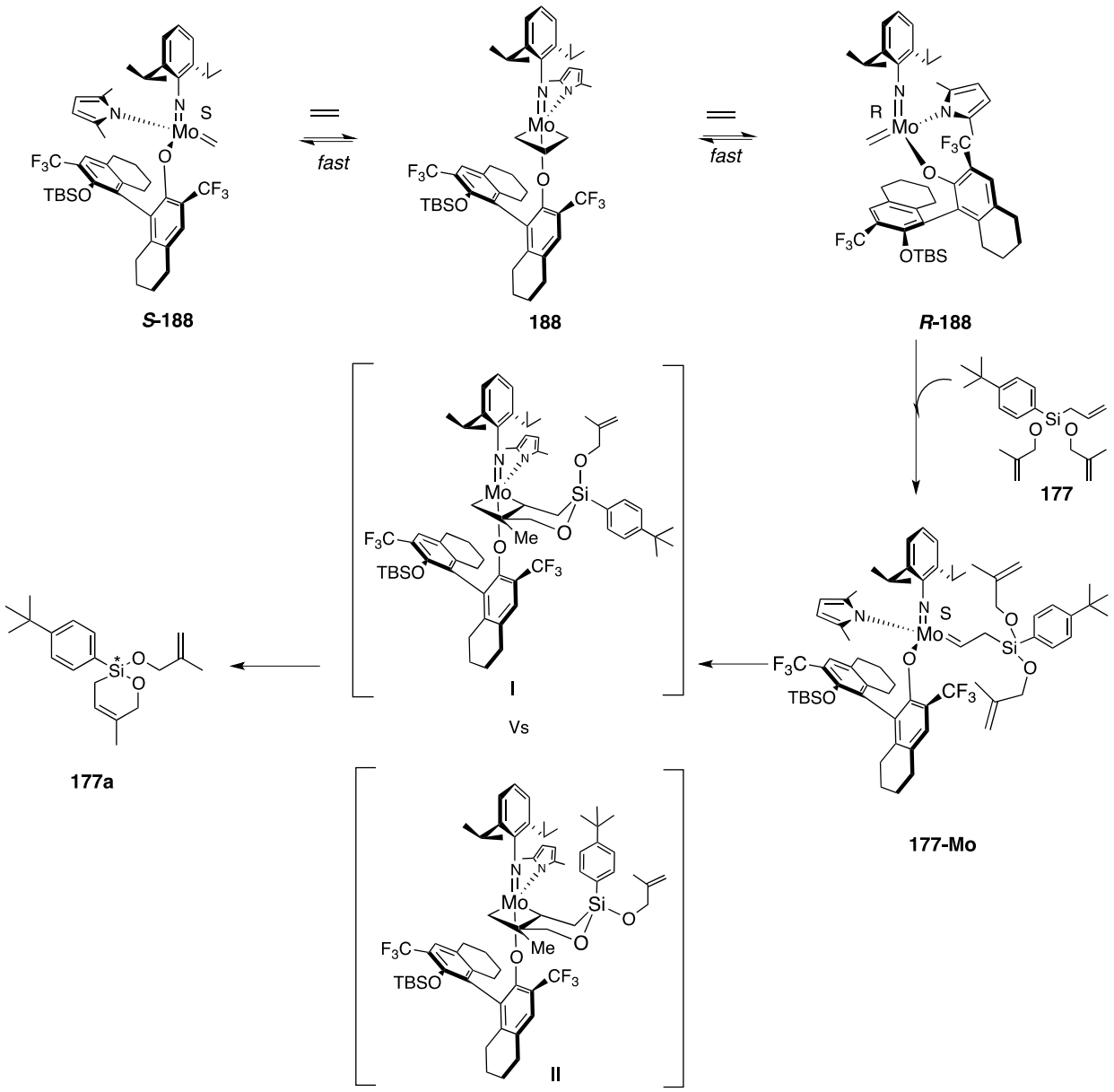
4	 **179**	189	 **179a**	11
5	 **180**	190	 **180a**	<2
6	 **181**	202	 **181a**	45

Table 2.5.1 Formation of six-membered ring oxasilepines.

Substrates **176** and **177** gave the highest enantioselectivity so far in the presence of various chiral Mo/W catalysts. The formation of a six-membered product may imply the formation of a chair-like transition state. A possible mechanism for this transformation may involve a six-membered transition state, where the bulkier substituent prefers to occupy the pseudo equatorial position (**TS-I**) during the ARCM process. Having the *tert*-butyl group at the *para*-position on the aromatic ring attached to silicon seems to be crucial to form an enriched oxasiline.



Scheme 2.5.1 Possible mechanism leading the formation of **177a**.

Scheme 2.5.1 shows a possible mechanism leading to the formation of (2-(4-*tert*-butylphenyl)-5-methyl-2-[2-methylprop-2-en-1yl)oxy]-3,6-dihydro-2*H*-1,2-oxasiline) **177a**.

Fast isomerisation of **188** would form the more active species ***R*-188**, which after coordination with the unsubstituted alkene, gives the intermediate **177-Mo**. The next step involves the formation of the metallacycle, which determines the formation of the two possible chair-like

transition states (**I** and **II**). We supposed that the bulkier group would occupy the equatorial position, avoiding the interactions between the *tert*-butyl group of the aryl group attached to silicon with the isopropyl groups from the imido ligand. Then, the enantioenriched oxasiline is formed, regenerating the catalyst. Substrate allyl(4-tert-butylphenyl)bis[(2-methylprop-2-en-1-yl)oxy]silane **177** was found to give high enantiocontrol during the screening experiments, providing the product >95% ee. This proposed pathway would lead to the formation of the **177a** enantiomer, however the determination of the absolute configuration is critical to establish a conclusive pathway. The role of the *tert*-butyl group attached to silicon may be crucial in this particular asymmetric catalysis.

Whereas catalyst **188** converted substrate **177** with >95% enantioselectivity, only moderate levels of enantiomeric excess were possible with substrate **176**. Catalyst **190** gave the best enantiocontrol (83%) with substrate **176**. This was the highest enantioselectivity obtained for this product so far. The use of catalyst **190** bearing a bulky (*tert*-butyl at the alkoxyde ligand) group resulted in the highest enantioselectivity. The difference of this catalyst with all the others is remarkable, in particular due to the steric hindrance induced by the *tert*-butyl groups (catalyst and substrate) is much higher compared to the methyl-moiety. Other catalysts displayed high levels of activity, but gave much lower levels of enantiocontrol. A plausible explanation is that not all catalysts provide sufficient steric bulk to induce enantioselectivity.

A transition state was proposed for the transformation with substrate **176**, the *tert*-butyl group would occupy the equatorial position TS(**I**), leading to the formation of a preferential enantiomer (**176a**).

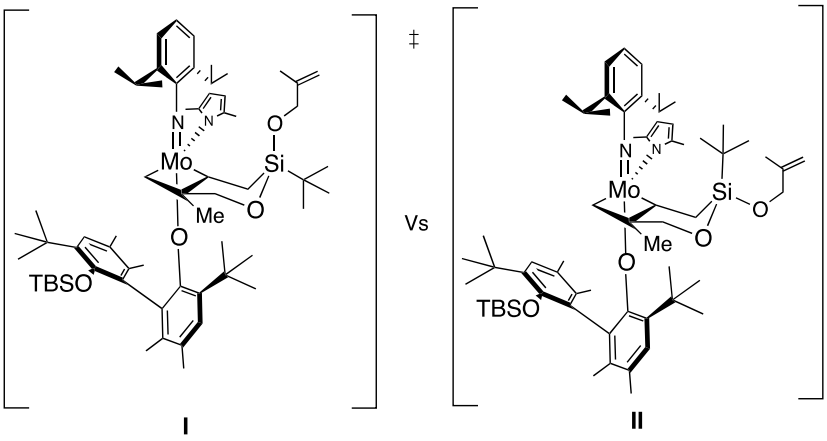
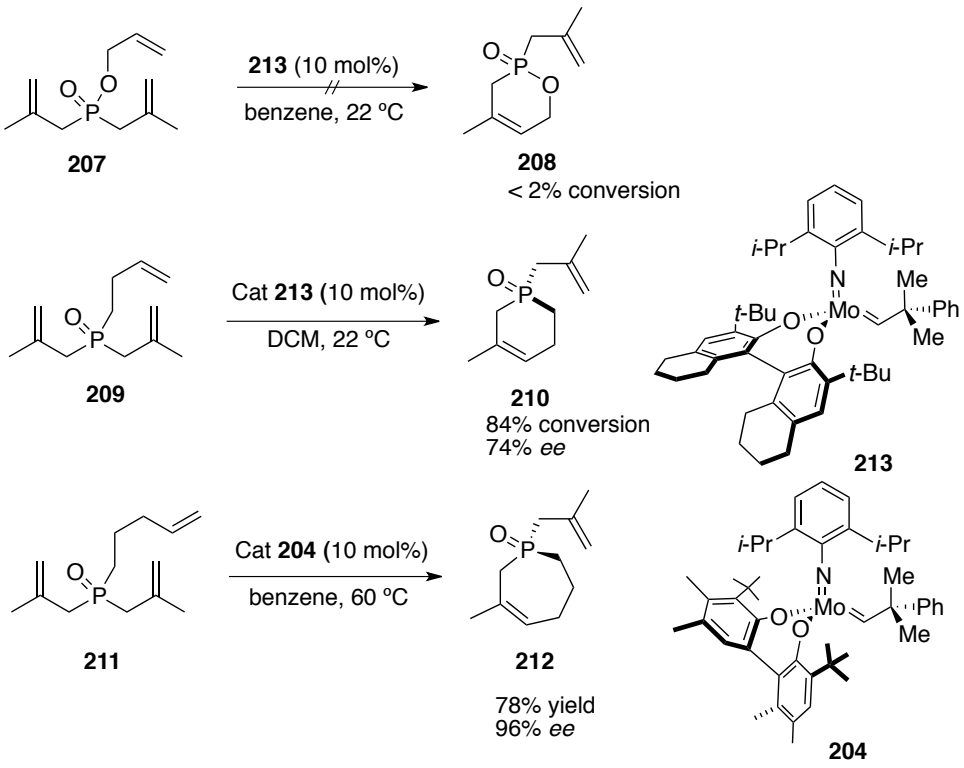


Figure 2.5.1 Proposed TS leading to the formation of **176a**.

All other prochiral Si-trienes gave low to moderate enantiomeric excess, suggesting that transition states (**I**) and (**II**) are equal in energy with no preferential formation of one transition state. These results highlight that the enantioselectivity is determined by both, the substitution pattern at silicon and interactions between the catalyst-subtrate that occur during the ARCM process.

2.6 Seven-Membered ring series

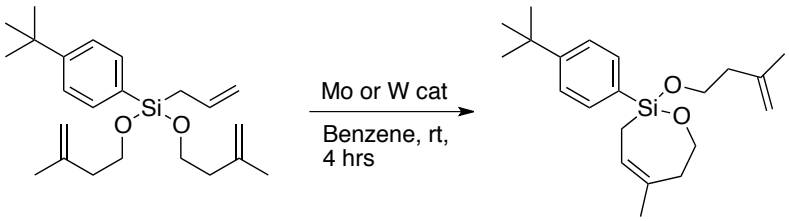
The concept of desymmetrisation of prochiral phosphines oxides and phosphinates by ARCM has also reported by our group.[40] In this work, formation of enantioenriched six and seven-membered rings were presented, highlighting that the enantioselectivity and the catalyst reactivity depends on substrate and solvent (Scheme 2.6.1). Based on the precedents that seven-membered rings phosphine oxides can also be formed in high enantiomeric excess, the investigation of prochiral Si-trienes leading to the formation of seven-membered ring products, was performed.



Scheme 2.6.1 ARCM of phosphino oxides by Mo-catalysts.

For a direct comparision of the reactivity and enantioselectivity during the ARCM process versus the six-membered ring products, desymmetrisation on the prochiral Si-trienes **176**–**181** was explored. These experiments were conducted on the homologues Si-trienes containing an extra methylene unit, leading to the formation of the desired seven-membered oxasilepines.

Substrate **182** (allyl(4-*tert*-butylphenyl)bis[(3-methylbut-3-en-1-yl)oxy]silane) was subjected to ARCM conditions, the results are depicted in Table 2.6.1. Formation of a seven-membered oxasilepine was obtained in moderate to excellent conversion (49%–90%) and no homodimerisation side products were observed.



182 **182a**

Entry	Catalyst[a]	mol %	Conc. (M)	% Conv.[b]	% *ee*[c]
1	**185**	5	0.01	90	8
2	**188**	5	0.01	40	9
3	**189**	5	0.01	83	10
4	**190**	5	0.01	60	9
5	**202**	5	0.01	74	8
6	**201**	5	0.01	80	7
7	**196**	5	0.01	86	7

[a] Reactions carried out under N_2 atmosphere, [b] Conversion to desired product measured by 400 MHz ^{1}H NMR of the crude reaction mixture, [c] Determined by chiral HPLC analysis of purified product.

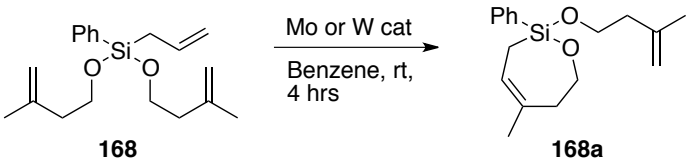
Table 2.6.1 Screening of catalysts for ARCM with substrate **182.**

All reactions showed conversion above 60%, except for catalyst **188**, which delivered 40% conversion. For the investigated catalytic systems the enantiomeric excess showed a range of 7–10%. Among the chiral catalysts (including the catalysts that displayed high activity and gave the best enantioselectivities for substrates **176** and **177**) examined during this study, all gave very low levels of enantiocontrol.

While excellent conversions were still possible with the seven-membered ring product **182a**, only low levels of enantiocontrol were observed. The addition of an extra methylene unit may disrupt the preference transition state leading to full erosion of the enantioselectivity.

It is clear from Table 2.6.1 that addition of one methylene unit to the enantiotopic groups of the substrate led to erosion of the enantioselectivity. Substrate allyl{bis[(3-methylbut-3-en-1-yl)oxy]}phenylsilane (**168**) was investigated under ARCM conditions with some of the chiral catalysts. Dibromide alkoxy ligand stereogenic at metal catalysts **185**, **192** and **195** afforded the desired 7-membered Si-stereogenic silane in good conversion (60–77%) but low

enantioselectivity (4–18%) (Table 2.6.2, entries 1–3). As observed for catalyst **187**, conversion remained high, but resulted in loss of enantioselectivity (Table 2.6.2, entry 4).



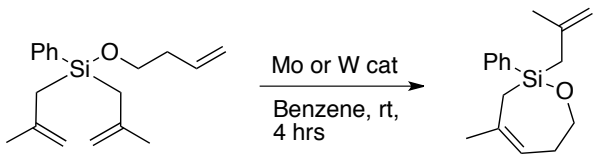
168 **168a**

Entry	Catalyst[a]	mol %	Time / h	% Conv.[b]	% ee[c]
1	**185**	2	5	77	14
2	**192**	2	5	60	18
3	**195**	2	5	72	4
4	**187**	5	4	85	< 2

[a] Reactions carried out under an N_2 atmosphere, [b] Conversion to desired product measured by 400 MHz ^{1}H NMR of the crude reaction mixture, [c] Determined by chiral HPLC analysis of purified product.

Table 2.6.2 Screening of catalysts for ARCM with substrate **168**.

Finally, substrate **156** ((but-3-en-1-yloxy)[bis(2-methylprop-2-en-1-yl)]phenylsilane) was designed to investigate the influence of forming a seven-membered-ring product. This substrate differs from the previous one (**168**) by bearing an oxygen atom attached to silicon, but this structural difference did not improve the enantioselectivity.



156 **156a**

Entry	Catalyst[a]	% Conv.[b]	% ee[c]
1	**185**	95	4
2	**186**	90	16
3	**188**	51	5
4	**189**	50	<2
5	**190**	44	<2

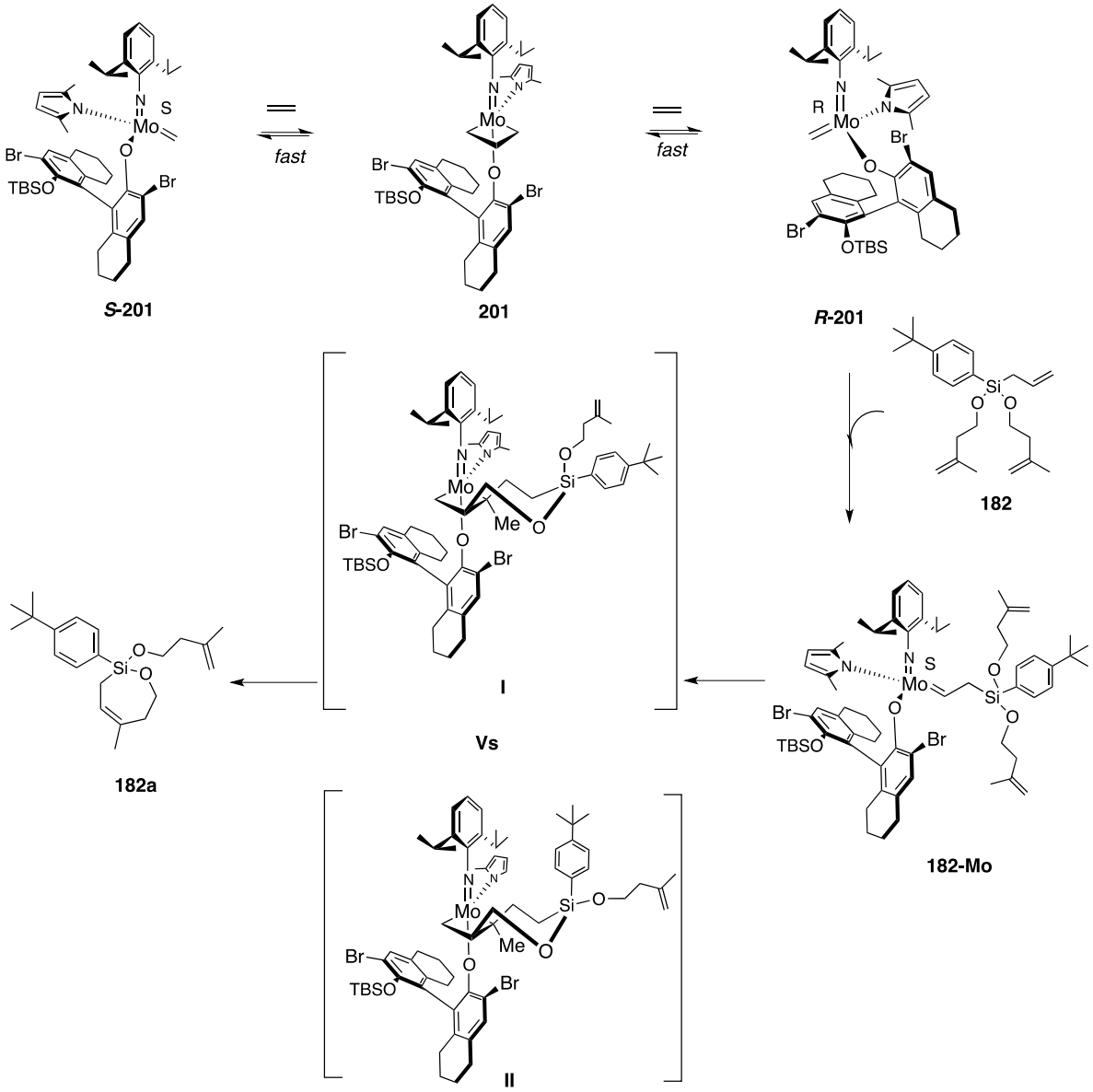
6	**202**	20	<2
7	**201**	61	<2
8	**197**	54	<2

[a] Reactions carried out under an N_2 atmosphere, [b] Conversion to desired product measured by 400 MHz ^1H NMR of the crude reaction mixture, [c] Determined by chiral HPLC analysis of purified product.

Table 2.6.3 Screening of catalysts for ARCM with substrate **156**.

The results depicted in Table 2.6.1, Tables 2.6.2 and 2.6.3, indicate that the formation of enantioenriched seven-membered products was not possible with the chiral catalysts screened. Subjecting substrate **156** under ARCM conditions with catalyst **185** gave the desired seven-membered product in excellent conversion (95%) but enantioselectivity remained low, 4% *ee* (Table 2.4.12 entry 1). Screening of various catalysts formed the desired seven-membered product in moderate conversions (44%–61%) with no enantioselectivity observed (Table 2.6.3 entries 3–8).

These results may suggest that there is not a preferential TS, thus the formation of both enantiomers occurs. Forming a seven-membered ring transition state may be too disrupted for this class of oxasilepines. A possible mechanism leading to the formation of 2-(4-*tert*-butylphenyl)-5-methyl-2-[(3-methylbut-3-en-1-yl)oxy]-2,3,6,7-tetrahydro-1,2 oxasilepine (**182a**) is depicted in Scheme 2.6.2.



Scheme 2.6.2 Possible mechanism leading to the formation of **182a**.

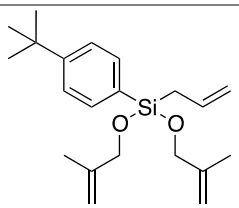
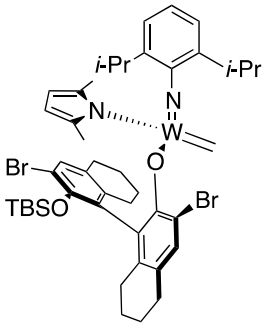
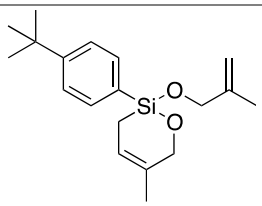
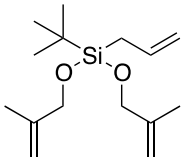
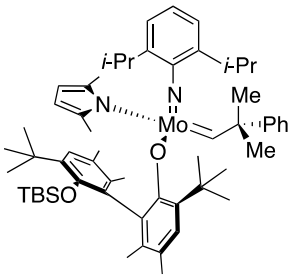
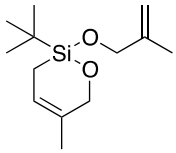
2.7 Conclusions

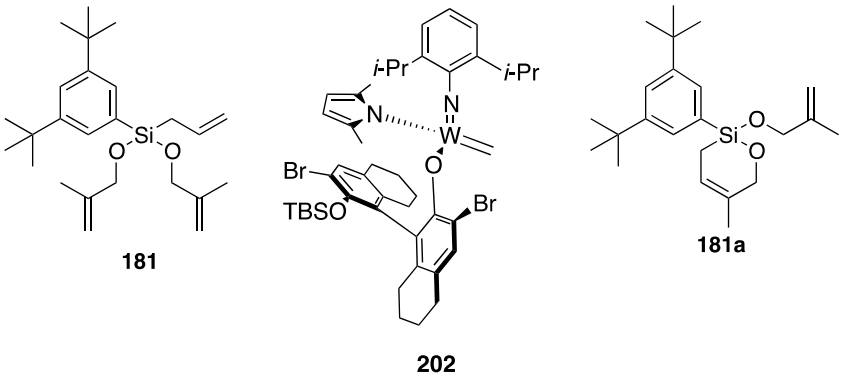
A variety of small ring unsaturated oxasilanes have been synthesised through Mo and W-catalysed asymmetric metathesis efficiently. The catalytic ARCM is one of the most widely applied homogeneous catalysis to create stereogenicity at carbon, phosphorus and this work shows that is possible at silicon. Based on these results, the rational design of chiral catalysts

appears challenging, which makes screening of large ligand libraries a more practical strategy to find a catalyst for a certain substrate.

Among the 21 chiral Mo or W catalysts examined in this work, most of them induced very low enantioselectivities (lower than 10% ee) and only few catalysts gave moderate and high enantioenriched oxysilepines (**188**, **190**, **201** and **202**). These results emphasise the importance of the combinatorial screening of the catalyst library. In order to identify a more detailed picture of a preferential transition state, it may be necessary to carry out theoretical studies.

The best enantioselectivities achieved with the Si-prochiral trienes and catalysts are depicted in Table 2.7.1.

Entry	Substrate	Catalyst	Product	% Conv.[b]	% *ee*[c]
1	 **177**	 **202**	 **177a**	78	98
2	 **176**	 **190**	 **176a**	23	83

3			71	51

181 **202** **181a**

Table 2.7.1 Summary with the best results (substrate-catalyst).

Another factor to be considered is the bonds length, C–Si bond is substantially longer than a C–C bond (1.87 Vs 1.53 Å), this situation may also affect the formation of a compact 6-membered transition state.

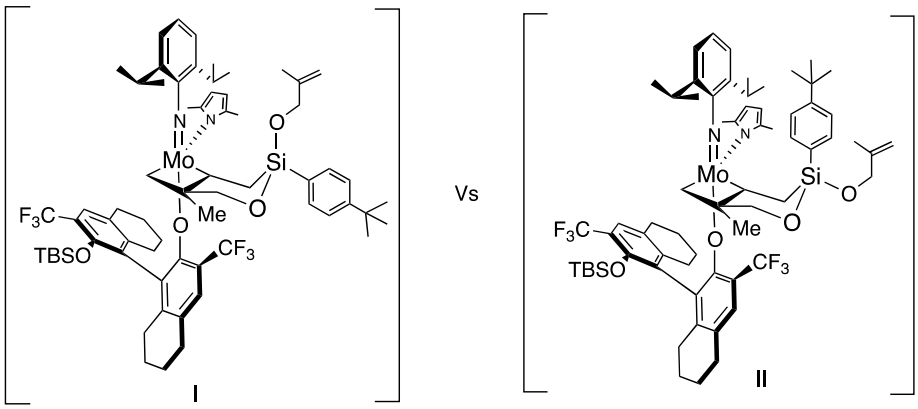


Figure 2.7.1 Probable TS leading to the formation of 6-membered ring.

Chapter 3

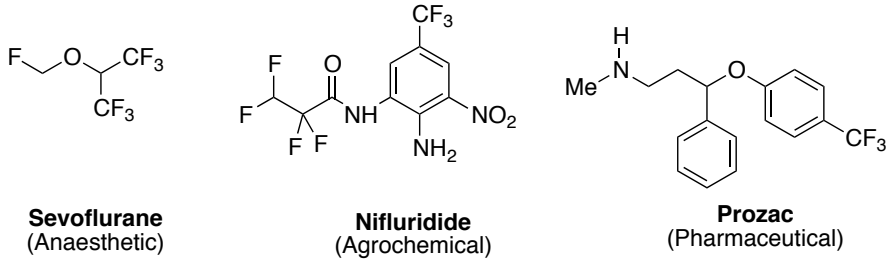
3.1 The trifluoromethyl group

During the past decade, the incorporation of CF_3 groups into organic compounds has become a topic of increasingly widespread interest in the fields of organic, inorganic and medicinal chemistry. [97] Organic molecules containing a CF_3 group possess a broad array of chemical and biological activities. CF_3 groups are electron-withdrawing substituents (χ = 3.5) and its incorporation generally leads to an increase of lipophilicity and metabolic stability when compared to the non-fluorinated compounds (Table 3.1.1).[98]

Substituent X =	π	Substituent X =	π
H	0.0	CH_3	0.56
F	0.14	CF_3	0.88
Cl	0.71	OCF_3	1.04
Br	0.86	SF_5	1.23
I	1.12	SCF_3	1.44

Table 3.1.1 Lipophilicity increments **π** as assessed for monosubstituted benzene C_6H_5-X

Several organofluorine compounds have been approved as drugs for the treatment of a variety of human diseases. Half of the top-selling drugs in 2005, 20% of all pharmaceuticals, and 30–40% of agrochemicals contain at least one fluorine atom.[99] Numerous compounds containing CF_3 groups possess anti-inflammatory, antiparasitic and central nervous system activities.[100] Since Fluoxetine (Prozac®) was approved by the FDA in 1987 as an antidepressant drug, it has become the most widely prescribed drug for this purpose.[101]



Sevoflurane (Anaesthetic) **Nifluridide** (Agrochemical) **Prozac** (Pharmaceutical)

Figure 3.1.1 A selection of bioactive molecules containing CF_3 groups.

Although numerous pharmaceuticals contain CF_3 groups, traditional trifluoromethylation methods introduce the trifluoromethyl groups in the early stages of synthesis, which is disadvantageous in the lead optimisation phase of drug discovery. Ideally, for these applications, CF_3 groups could be introduced at later stages of the synthetic route with exquisite control over chemo-, regio-, and stereoselectivity.

This chapter summarises some of the most relevant methods for appending a trifluoromethyl group onto a molecule of interest (arenes, heteroarenes, carbonyl-containing compounds, and allyl-containing compounds) using three modes of reactivity. Nucleophilic, electrophilic and radical trifluoromethylation are reactions typically proceeding with cooperative action of a metal catalysis (*e.g.*, Cu or Ru).[102] Representative reagents for direct trifluoromethylation, which have been developed in recent years, are shown in Figure 3.1.2.

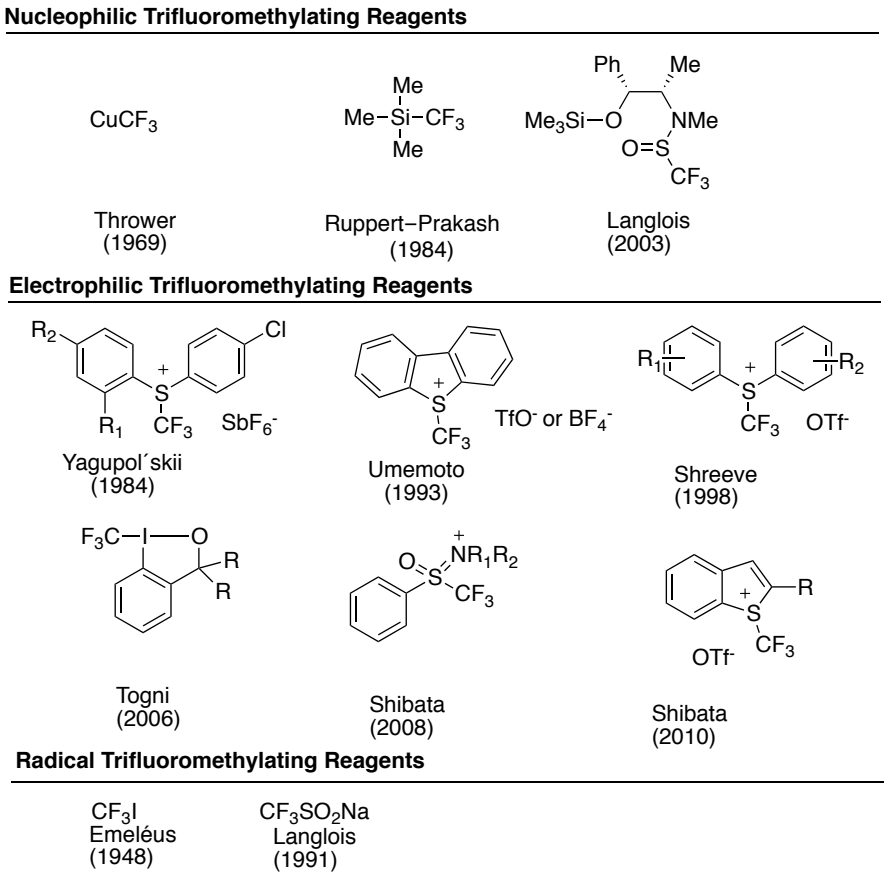
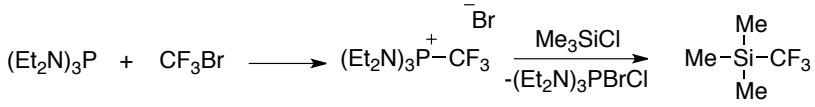


Figure 3.1.2 The three main class of trifluoromethylating reagents, with representative examples.

3.2 Nucleophilic Trifluoromethylation

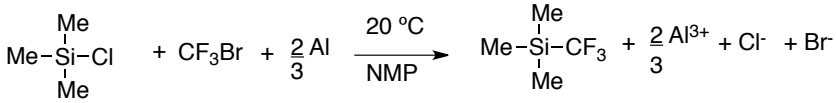
The Ruppert–Prakash reagent (trifluoromethyl trimethylsilane, $TMSCF_3$) has been widely used as a trifluoromethylating reagent during the last few decades. In 1984, Ruppert and co-workers described the synthesis of $TMSCF_3$,[103] which proceeded via the formation of the intermediate phosphonium salt. The addition of trimethylchlorosilane (TMSCl) led to the $TMSCF_3$ reagent, obtained as a colourless liquid.

In 1989, Prakash extended this methodology to the preparation of other perfluoroalkylated silanes.[104] The Ruppert–Prakash reagent is now commercially available; however, the synthesis requires the use of CF_3Br, a reagent that is now regulated by Montreal protocol restrictions, and as result, its production is limited.



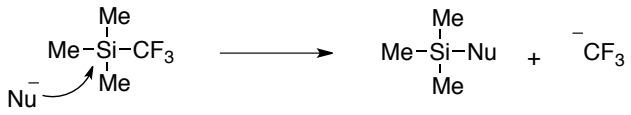
Scheme 3.2.1 Synthesis of trimethyl(trifluoromethyl)silane ($TMSCF_3$).

Alternative efficient methods for the synthesis of the reagent Ruppert-Prakash, avoiding the use of carcinogenic reagents such as $(Et_2N)_3P$ or HMPA have been developed by Grobe and Hegge.[105] They used aluminium powder in NMP for the reduction of trifluorobromomethane (CF_3Br) in the presence of TMSCl. Additionally; the reaction was carried out using an autoclave, which allowed recycling the unused CF_3Br (Scheme 3.2.2).



Scheme 3.2.2 Alternative synthesis for the $TMSCF_3$ reagent.

The Ruppert–Prakash reagent has been extensively used for the functionalisation of a variety of compounds containing a carbonyl moiety, or other electrophilic functional group.[106,107] In order to generate the reactive trifluoromethyl anion, the Ruppert–Prakash reagent requires activation with a nucleophilic initiator, which is generally a fluoride anion.[108]



Scheme 3.2.3 Generation of the reactive CF_3^- anion.

A major drawback of generating a CF_3 anion in this manner is its instability, which is strongly affected by the short C–F bond length and the high electronegativity of the fluorine atoms. Since the trifluoromethyl anion rapidly decomposes to form singlet difluorocarbene and a fluoride ion, a metal is frequently incorporated to stabilise this reactive species (Figure 3.2.1).

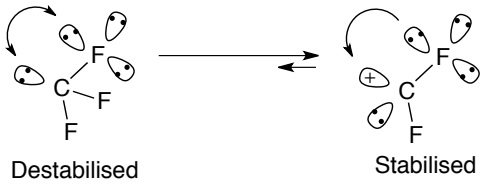


Figure 3.2.1 Decomposition of the CF_3 anion.

It is proposed that the coordination of a transition metal stabilises the CF_3^- anion through dispersion of its electron density into the vacant molecular orbitals of the metal;[109] copper is commonly used in this capacity.

Copper has an electron configuration of $[Ar]3d^{10}4s^1$ and forms a variety of coordination complexes with oxidation states of +1, +2 and +3.[110] After palladium, it has become one of the most popular metal catalysts in cross-coupling reactions. Compared to other transition metal catalysts, copper is typically inexpensive, readily available, stable to air and easy to handle.[111]

In 1969, Thrower and Kobayashi reported the synthesis of the organometallic complex, $CuCF_3$.[112] However, this complex was poorly defined, and its exact structure and composition

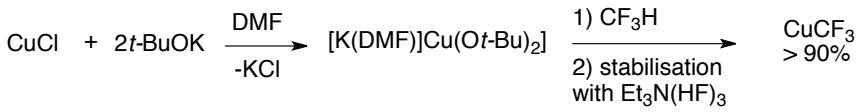
remained unknown. During the following years, many complexes of this type, based on Cu were reported; however, definitive evidence to corroborate their structures remained elusive.[113] These complexes reacted sluggishly in trifluoromethylation reactions with aromatic iodides or bromides at high temperatures, giving the desired aryl-CF_3 along with several by-products.

In terms of reaction mechanism, copper has a propensity for participating in single-electron transfer processes,[114] unlike metals such as palladium, which typically proceed via two-electron redox events. Thus, in addition to standard oxidative addition/reductive elimination cross-coupling sequences, alternative free-radical mechanisms should also be taken into consideration in Cu-catalyzed trifluoromethylation reactions, as discussed in the ensuing sections.

Despite the accomplishments highlighted above using copper and the Ruppert–Prakash reagent to generate a versatile $CuCF_3$ species, a lingering limitation is the high cost of performing this chemistry on larger scale. In this respect, alternative CF_3^- sources are potentially attractive.

Fluoroform (trifluoromethane; CF_3H) is a by-product that is formed in the synthesis of diverse products such as Teflon (DuPont), polyvinylidene fluoride (PVDF), refrigerants and other commercial organofluorine compounds. Due to its increasingly widespread availability as a by-product of industrial processes, it would be valuable to be able to convert CF_3H into a stable and reactive trifluoromethylating reagent. Fluoroform is the weakest acid of all the haloforms, some of the p*K*a values are: CF_3H = 28, CCl_3H = 15.5, CBr_3H = 14.7.[115] When deprotonated by strong bases such as $KCH_2S(O)Me$, fluoroform is an attractive nucleophilic CF_3^- source. However, a problem with this approach is the notorious, facile decomposition of CF_3^- to difluorocarbene at room temperature. Moreover, fluoroform has a low boiling point (–83 °C), which makes it difficult to handle in synthetic laboratories.

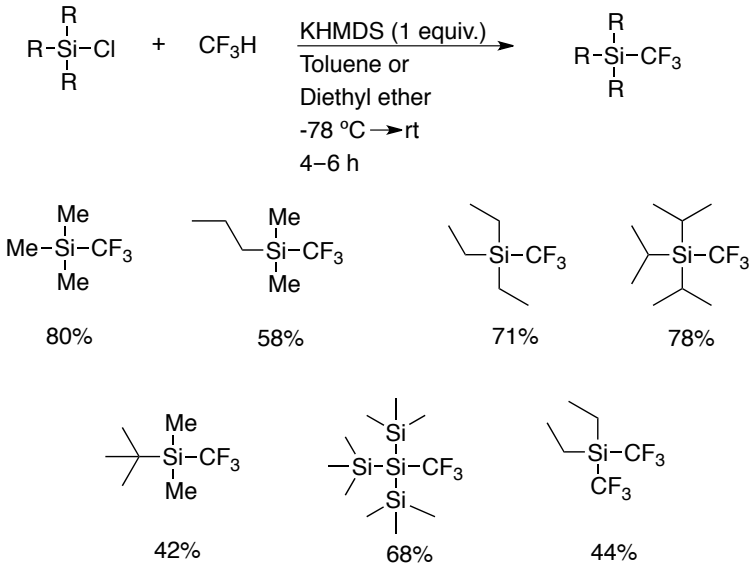
In 2011, Grushin and co-workers made another relevant contribution to the field of nucleophilic trifuoromethylation by achieving the first example of direct cupration of fluoroform (Scheme 3.2.3). [116] They reported that $Et_3N{\cdot}3HF$ in DMF was able to stabilise the resulting $Cu–CF_3$ complex, and that mixture could be used directly in the trifluoromethylation of arylboronic acids, haloarenes and haloheteroarenes. Although this method requires an excess of CF_3H (2–3 equivalents) and stoichiometric amounts of CuI for the preparation of the $Cu–CF_3$ species, it is a valuable contribution in terms of generating a reactive $Cu–CF_3$ species from an alternative, widely available source of CF_3^- anion (Scheme 3.2.4).



Scheme 3.2.4 Synthesis of $CuCF_3$ from fluoroform.

Based on this research, Prakash and co-workers reported the direct transformation of CF_3H to various (trifluoromethyl)silanes, including the synthesis of $TMSCF_3$, a reagent which has made an enormous impact in the field of nucleophilic trifluoromethylation (*vide supra*).[117] These reactions were performed by dissolving CF_3H in toluene (for TMSCl) or diethyl ether (for other chlorosilanes) at –78°C. Deprotonation with KHMDS, followed by addition of the chlorosilane and subsequent warming to room temperature over 4–6 hours gave the desired products (Scheme 3.2.5).

This new synthetic route is important due to the economical and operational limitations for current routes to produce the Ruppert–Prakash reagent.



Scheme 3.2.5 Synthesis of various trifluoromethylsilanes from fluoroform.

3.3 Electrophilic Trifluoromethylation.

Another common reactivity mode to accomplish trifluromethylation is to use electrophilic trifluoromethylating reagents, "CF_3^+", and to date, a range of different CF_3^+ reagents have been reported. They essentially fit into two families: (1) O–, S–, Se–, and Te–CF_3 chalcogenium salts **I** and (2) hypervalent iodine(III) reagents **II**, as shown in Figure 3.3.1 These two classes of reagents have been successfully developed by the groups of Yagupolskii,[118] Umemoto,[119] Shreeve,[120] Magnier,[121] Togni[122], and Shibata.[123] The reactivity of the first class of reagents relies on the attachment of a charged chalcogenium atom to the CF_3 moiety. It has been shown that the relative trifluoromethylating power of these chalcogenium salts follows a reactivity trend in the order Te < Se < S and that reagents bearing electron-withdrawing substituents are more reactive than those with electron-donating groups.[119]

These reactivity trends suggest that nucleophilic attack at the CF_3 group is driven by the relief of charge on the neighboring chalcogen. Hypervalent iodonium species (Togni's reagents) are the most recently reported class of electrophilic reagents. [124] Due to their high stability and

reactivity, both reagent types **I** and **II** have been applied extensively, and some CF_3^+ reagents are now commercially available.

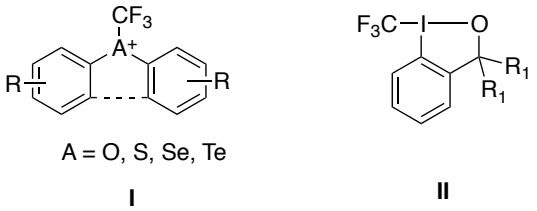
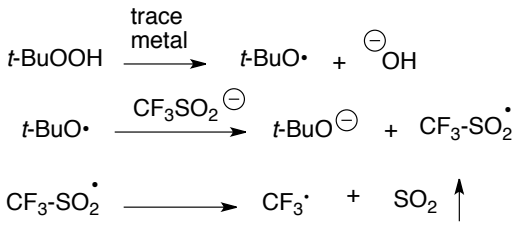


Figure 3.3.1 General structure of electrophilic trifluoromethylating reagents.

3.4 Radical Trifluoromethylation

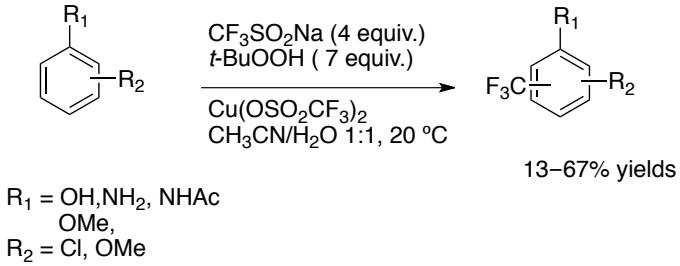
Historically, radical trifluoromethylation is the oldest method for installing a trifluoromethyl group onto an organic compound, and mechanistically, it is distinct from nucleophilic and electrophilic trifluoromethylation.[125] The trifluoromethyl radical can be generated under oxidative, reductive, thermal, and photoredox conditions. The most common source of CF_3• is iodotrifluoromethane CF_3I, although other sources of CF_3• have been reported, such as triflyl chloride (CF_3SO_2Cl), bromotrifluoromethane (CF_3Br) and bis(trifluoromethyl)-mercury.[126] In fact, CF_3Cl and CF_3Br are so readily homolysed by sunlight that their presence in the atmosphere has led to ozone layer depletion. Thus, the Montreal Protocol has discontinued their use. Some existing alternatives contain toxic metals, such as mercury or tellurium, which makes them unattractive and impractical.

In 1991, Langlois and co-workers[127] reported the use of sodium trifluoromethanesulfinate (CF_3SO_2Na) as an alternative source for the generation of the CF_3• species (Scheme 3.4.1). The CF_3 radical was generated through the oxidation of CF_3SO_2Na with *t*-butyl hydroperoxide (*t*-BuOOH) in the presence of catalytic amounts of $Cu(OSO_2CF_3)_2$.



Scheme 3.4.1 Generation of CF_3 radical species.

In this report, a series of aromatic compounds bearing electron-releasing groups were subjected to oxidative conditions. The desired Ar-CF_3 products were obtained in moderate yields (13-67%), with the presence of bistrifluoromethylated products (Scheme 3.4.2).



Scheme 3.4.2 Trifluoromethylation of aromatic compunds with Langlois reagent.

Out of the approaches for the generation of CF_3• species, those involving activation by light are particularly attractive. In 1936, Burstall reported the synthesis of the tris(bipyridine)ruthenium(II) dichloride $[Ru(bpy)_3]Cl_2$ (byp = 2,2´-bipyridine), which has become one of the most widely used catalysts in photocatalysis.[128] As a consequence, many organic transformations mediated by light gained popularity during the last century.[129] In the past decade, radical trifluoromethylation mediated by photocatalysis has emerged as a valuable method. The main advantage of this approach is that it operates under mild reaction conditions.

$[Ru(bpy)_3]^{2+}$ complexes have unique photochemical and electrochemical properties. They absorb in the visible range (λ_{max} = 450 nm). Irradiation with light leads to efficient excitation of

an electron, which can then participate in single electron transer (SET). The Ru^{2+*} excited state species is also known as a MLCT (metal-to-ligand charge transfer) state. This high-energy species can operate either as a single-electron oxidant or reductant. The operative pathway (oxidative or reductive quenching cycle) will depend on the chemical species in the reaction mixture (Figure 3.4.1).[130]

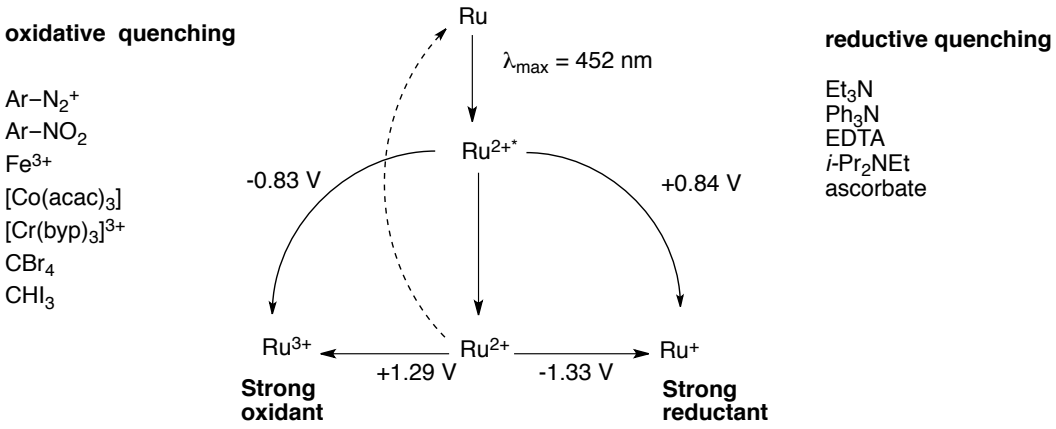
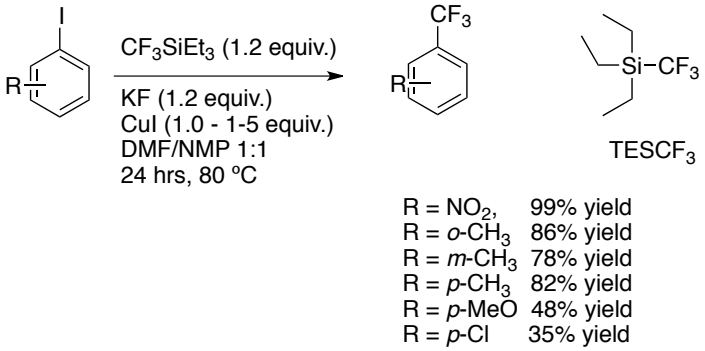


Figure 3.4.1 Photoredox catalytic cycle of $[Ru(bpy)_3]^{2+}$ and representative oxidative and reductive quenchers

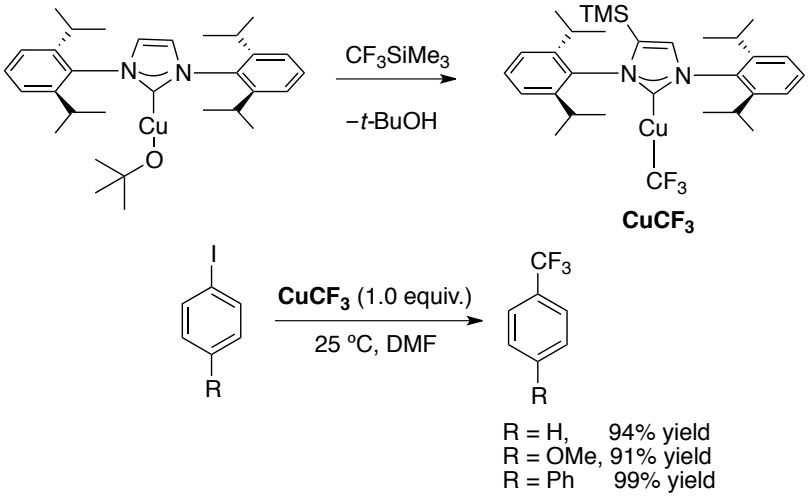
3.5 Trifluoromethylation of Arene and Heteroarene Substrates.

Urata was a pioneer in developing nucleophilic trifluoromethylation of aryl iodides using triethyl(trifluoromethyl)silane (TES–CF_3) and CuI.[131] The reaction led to the desired aromatic trifluoromethylated products in moderate to excellent yields. However, the main drawback was the high copper loading (CuI, 1–1.5 equiv.), which was necessary to give full conversion. Additionally, the narrow substrate scope was a further limitation of this method (Scheme 3.5.1).



Scheme 3.5.1 Nucleophilic trifluoromethylation of aryl iodines.

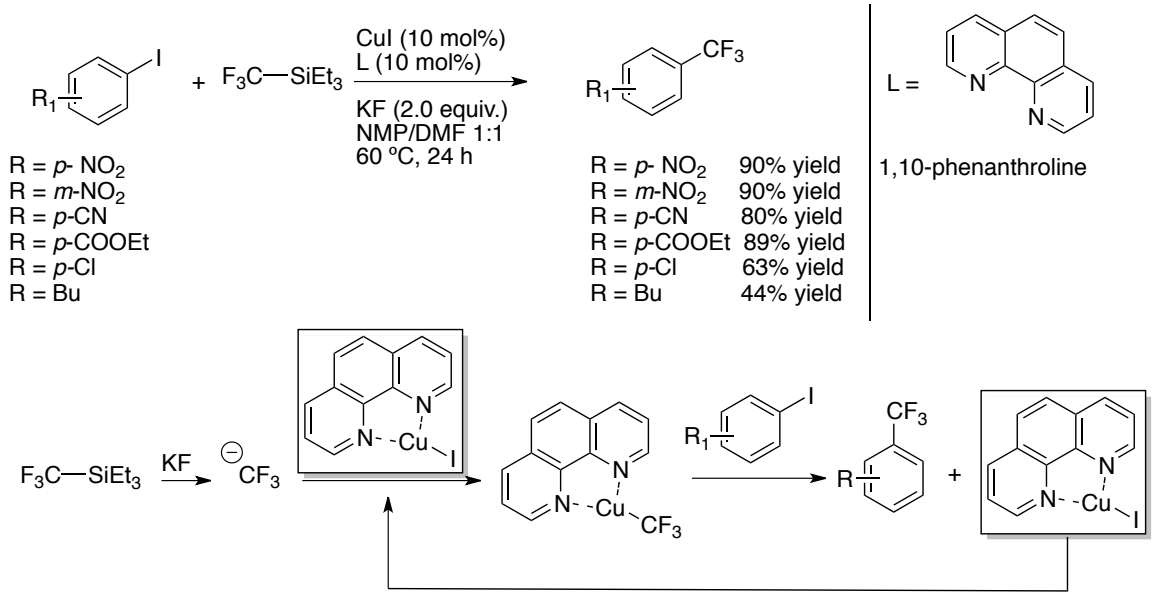
In 2008, Vicic *et al.* described the synthesis of the first well-defined Cu–CF_3 complex that could efficiently mediate trifluoromethylation of aryl iodides under mild conditions (Scheme 3.5.2).[132] Importantly, this work offered definitive evidence for the existence of a thermally stable $CuCF_3$ complex, which was unambiguously characterised by single-crystal X-ray diffraction. This investigation further revealed the importance of the ancillary ligand in stabilising the $CuCF_3$ species to prevent decomposition.



Scheme 3.5.2 First example of a well-defined $CuCF_3$ reagent.

Amii and co-workers disclosed the first example of copper-catalysed trifluoromethylation of aryl iodides using CuI and a diamine ligand (Scheme 3.5.3).[133] The first step in the catalytic

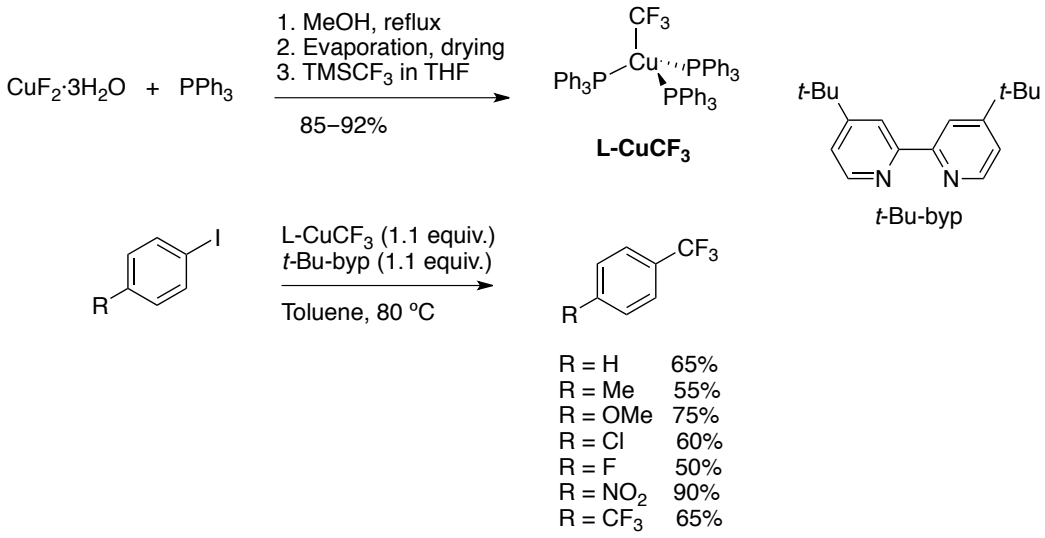
cycle is generation of the trifluoromethyl anion species, which readily reacts with the [Cu(L)(I)] complex (L = 1,10-phenanthroline) to give the putative [Cu(L)(CF_3)] species. The authors, however, did not isolate this intermediate or detect it spectroscopically. The reaction between [Cu(L)(CF_3)] and aryl iodides is assumed to proceed through σ-bond metathesis, affording the desired products, with regeneration of the catalytically active CuI species, which closes the catalytic cycle. This method could achieve the formation of the desired trifluoromethyl arene products in moderate to good yields (44–90%). The main drawback was that only aryl iodides with electron withdrawing groups gave optimal results.



Scheme 3.5.3 Catalytic trifluoromethylation of aryl iodides in the presence of a diamine ligand.

In 2011, Grushin reported another example of a well-defined, air-stable $CuCF_3$ reagent stabilised by triphenyl phosphine ligands.[134] Complex **L-CuCF$_3$** itself was unreactive as a trifluoromethylating reagent, but the addition of 4,4'-di-*tert*-butyl-2,2'-bipyridine (*t*-Bu-bpy) enabled the reaction to take place. Addition of *t*-Bu-bpy facilitated dissociation of PPh_3, resulting in the immediate formation of the active complex [(*t*-Bu-bpy)Cu(PPh_3)(CF_3)]. This reactive $CuCF_3$ species converted aryl iodides to the desired trifluoromethylated products in

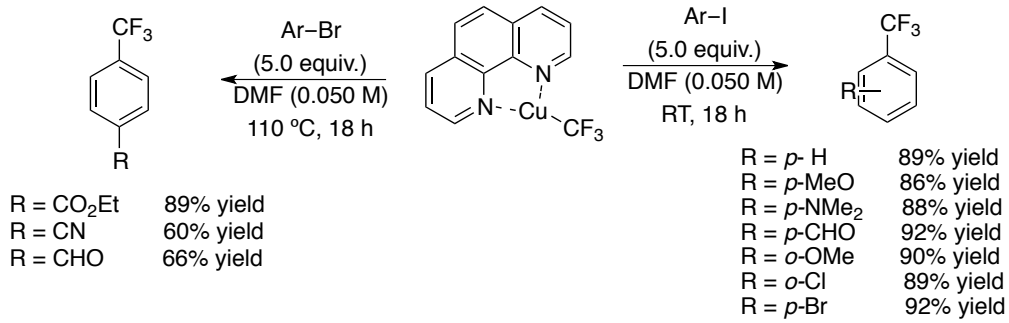
moderate to good yields. However, the main limitations were the need for stoichiometric amounts of copper and the fact that only aryl iodides with electron-withdrawing groups gave good results (Scheme 3.5.4).



Scheme 3.5.4 Cu–CF_3 reagent stabilised by PPh_3.

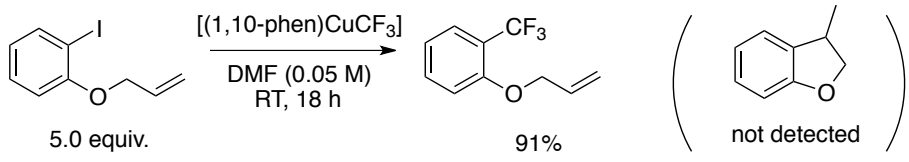
Hartwig documented the reactivity of the complex [(1,10-phen)$CuCF_3$],[135] which was an intermediate in the reaction reported by Amii and co-workers. In Hartwig's work, the complex was isolated and fully characterised by NMR spectroscopy and elemental analysis. The ^{19}F NMR analysis showed two species in solution; one component [(1,10-phen)$_2$Cu][Cu(CF_3)$_2$], which resonates at δ = -30.8 ppm, and the other one [(1,10-phen)$CuCF_3$] resonates at δ = -22.6 ppm. The isolated complex [(1,10-phen)$CuCF_3$] reacted with aryl iodides under mild conditions. For aryl bromide substrates, it was necessary to increase the temperature to afford the desired products in moderate to good yields (Scheme 3.5.5). The reaction proceeded effectively with aryl halides containing electron-donating groups and electron-withdrawing groups. A practical disadvantage was that the reaction conditions employed an excess (5 equivalents) of the aryl halide.

Recently, the complex [(1,10-phen)$CuCF_3$] became commercially available as Trifluoromethylator™, an easily handled, thermally stable, single-component reagent for the trifluoromethylation of aryl iodides.



Scheme 3.5.5 Cu–CF_3 trifluoromethylating reagent for aryl iodides and bromides.

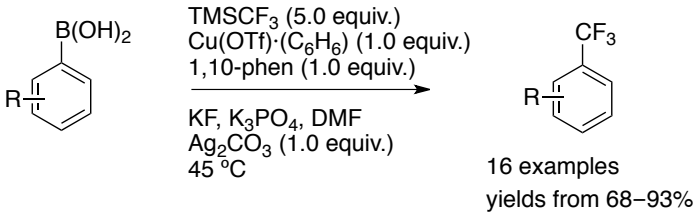
In order to elucidate the mechanism of this transformation, 2-(allyloxy)iodobenzene was subjected to the standard trifluoromethylation conditions with [(1,10-phen)$CuCF_3$]. If the reaction involved aryl radical intermediates, it was surmised that the arene would cyclise. In the event, no cyclised product was detected and the trifluoroarene was isolated in 91% yield (Scheme 3.5.6). This experiment led to the conclusion that the reaction did not proceed *via* a radical aryl intermediate.



Scheme 3.5.6 Mechanistic experiment ruling out a radical pathway.

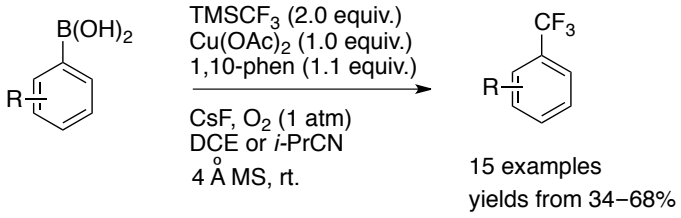
Qing and co-workers reported the trifluoromethylation of aryl boronic[136] acids under oxidative conditions in the presence of Cu(I). Based on previous findings, bidentate diamine ligands were used to stabilise the reactive Cu–CF_3 species. It was surmised that the 1,10-phen ligand

donated sufficient electron density to copper such that further oxidation of the complex to Cu(II) or Cu(III) was viable. Reductive elimination from one of these high oxidation state intermediates would deliver the desired trifluoromethylated product (Scheme 3.5.7). The trifluoromethylation reaction gave the desired products in good yields, though stoichiometric amounts of the copper and excess $TMSCF_3$ reagent were needed.



Scheme 3.5.7 Nucleophilic trifluoromethylation of aryl boronic acids mediated by copper.

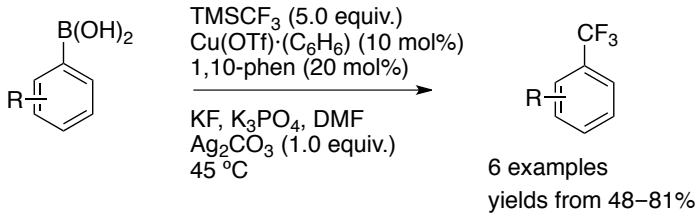
Similar to Qing's work, a protocol involving oxidative trifluoromethylation of aryl and heteroaryl boronic acids was reported by Buchwald. The main difference was the replacement of $Cu(OTf)\cdot(C_6H_6)$ with $Cu(OAc)_2$ as the metal mediator and Ag_2CO_3 with oxygen as the oxidant (Scheme 3.5.8).[137]



Scheme 3.5.8 Nucleophilic trifluoromethylation of aryl boronic acids.

Further developments by the Qing group led to the discovery of a catalytic trifluoromethylation of arylboronic acids.[138] It was hypothesized that the rate of decomposition of the CF_3^- anion was much higher than the rate of reductive elimination (which regenerates the copper catalyst). Thus, they carried out the experiments under the same reaction conditions as described previously with slow addition of the $TMSCF_3$ reagent.

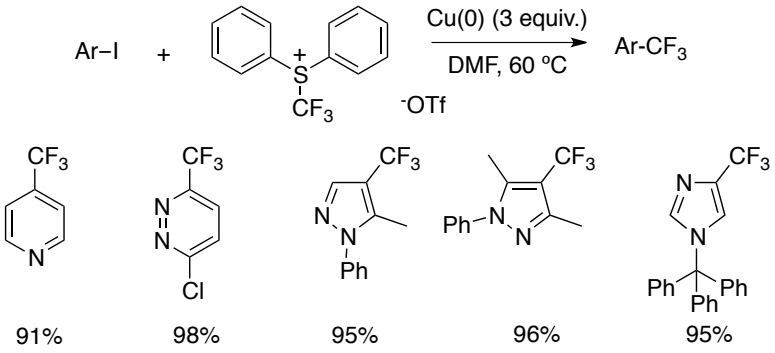
This modification allowed the active Cu complex to regenerate itself and coordinate with another CF_3^- anion prior to decomposition (Scheme 3.5.9).



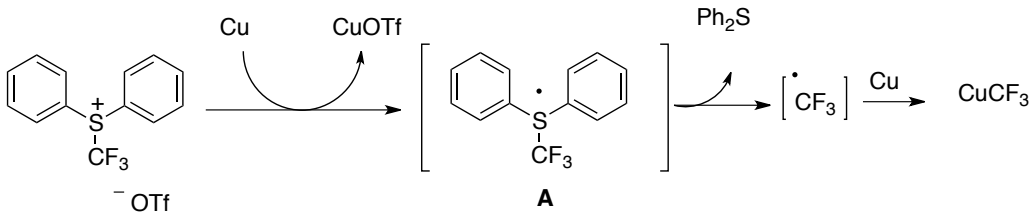
Scheme 3.5.9 Copper-catalysed nucleophilic trifluoromethylation of aryl boronic acids.

Alternatively, in a complementary approach, *S*-(trifluoromethyl)-dibenzothiophenium salts or hypervalent iodine(III) salts in combination with copper have led to successful electrophilic trifluoromethylation of aryl- and heteroarylboronic acids.

Xiao and co-workers reported an example of electrophilic trifluoromethylation of heteroaryl iodides using (trifluoromethyl)diphenylsulfonium triflate in the presence of copper (Scheme 3.5.10).[139] This was the first report of trifluoromethylation of iodo-substituted heteroarenes in high yields using an electrophilic CF_3^+ source. The mechanism proposed for this transformation involves the formation of $CuCF_3$ species, generated by reduction of the (trifluoromethyl)diphenylsulfonium triflate with copper *via* single eletron transfer (SET). Subsequently, intermediate **A** decomposes to form a CF_3• radical, which reacts with Cu(0) to generate $CuCF_3$ (Scheme 3.5.11). However, a drawback of this chemistry is that it requires super-stoichiometric amounts of copper (3 equivalents).

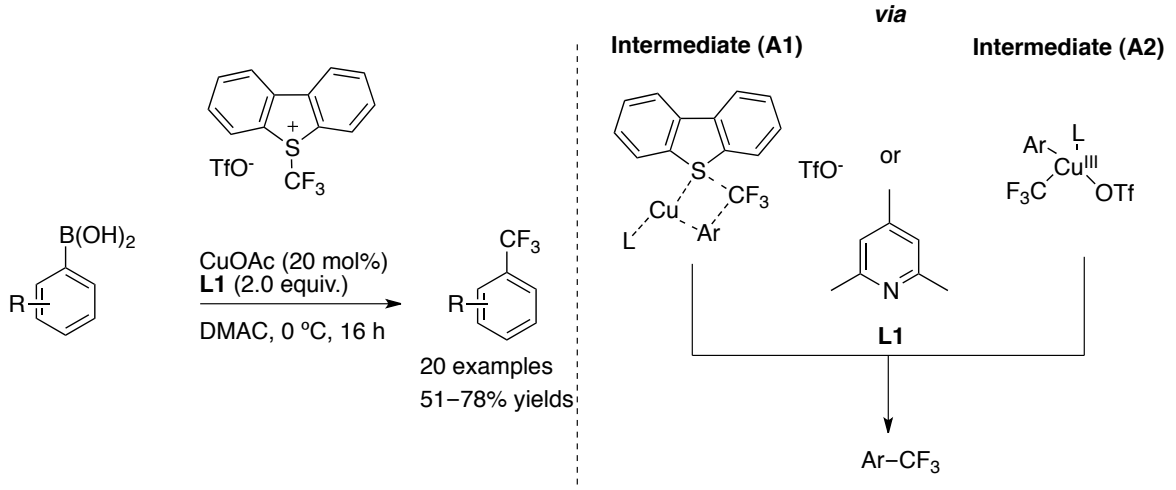


Scheme 3.5.10 The first example of trifluoromethylation of heteroaryl iodides.



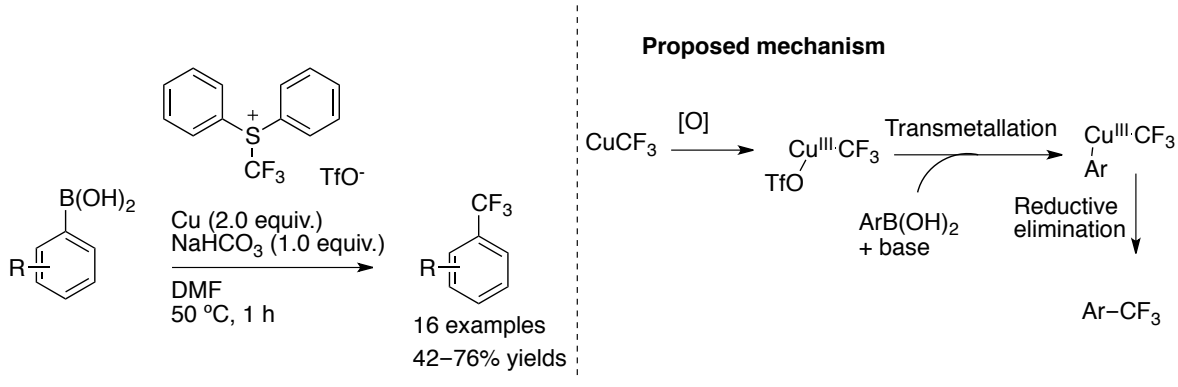
Scheme 3.5.11 Possible reaction mechanism for the formation of $CuCF_3$ *via* SET.

Liu *et al*. developed a Cu-catalysed method for the trifluoromethylation of aryl-, heteroaryl-, and vinyl boronic acids using Umemoto's electrophilic CF_3^+ source. [140] For this reaction, the authors suggested two possible pathways. The first possibility is that the CF_3^+ reagent reacts with the [Cu–aryl] species (**A1**) through σ-bond metathesis to form the aryl–CF_3 bond without the intervening formation of a $CuCF_3$ species. The other possibility is *via* transmetallation of the aryl boronic acid to form a [Cu(I)–aryl] intermediate, followed by oxidative addition of the trifluoromethylating reagent to form a Cu(III) species (**A2**). Reductive elimination would then give the desired aryl–CF_3 product. *N*,*N*-Dimethylacetamide (DMAC) was used as solvent and 2,4,6-trimethylpyridine (**L1**) as the ligand, presumably to stabilise either the Cu(I) or Cu(III) intermediates, and moderate yields from 51% to 78% were obtained (Scheme 3.7.12).



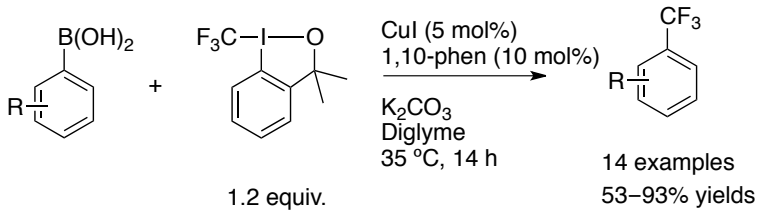
Scheme 3.5.12 Copper-mediated trifluoromethylation of arylboronic acids by electrophilic CF_3^+ reagents.

In a very similar approach, Xiao and co-workers also examined the trifluoromethylation of arylboronic acids using the *S*-(trifluoromethyl)diphenylsulfonium salt and 2 equivalents of Cu(0).[141] Under these reaction conditions, the authors reasoned that the formation of $CuCF_3$ species was possible. Regarding the mechanism, it was suggested that the formation of $CuCF_3$ species proceeds *via* SET, followed by oxidation to Cu(III) and transmetallation with the aryl boronic acid. In the final step, reductive elimination gives the desired aryl–CF_3 product. Yields were moderate, ranging from 42 to 76% (Scheme 3.7.13).



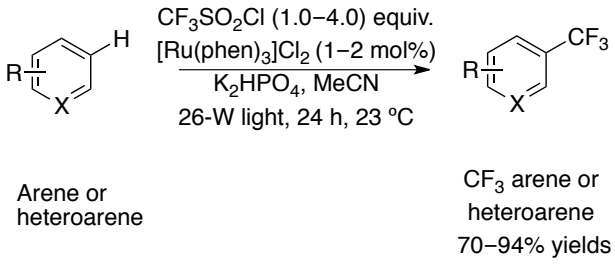
Scheme 3.5.13 Copper-mediated trifluoromethylation of arylboronic acids by electrophilic CF_3^+ reagents.

Shen and co-workers reported an example of copper-catalysed trifluoromethylation of arylboronic acids using the Togni reagent (Scheme 3.5.14).[142] This transformation was the first example of a reaction of this type using a hypervalent iodine reagent as the electrophilic CF_3^+ source. Similar to the conditions used in the nucleophilic trifluoromethylation reaction described above, in this case it was also necessary to use a stabilizing ligand. Detailed investigations revealed that 1,10-phenanthroline was the optimal ligand for this transformation. The reaction proceeded in moderate to excellent yields, and the substrate scope encompassed heteroarylboronic acids as well as some alkenylboronic acids.



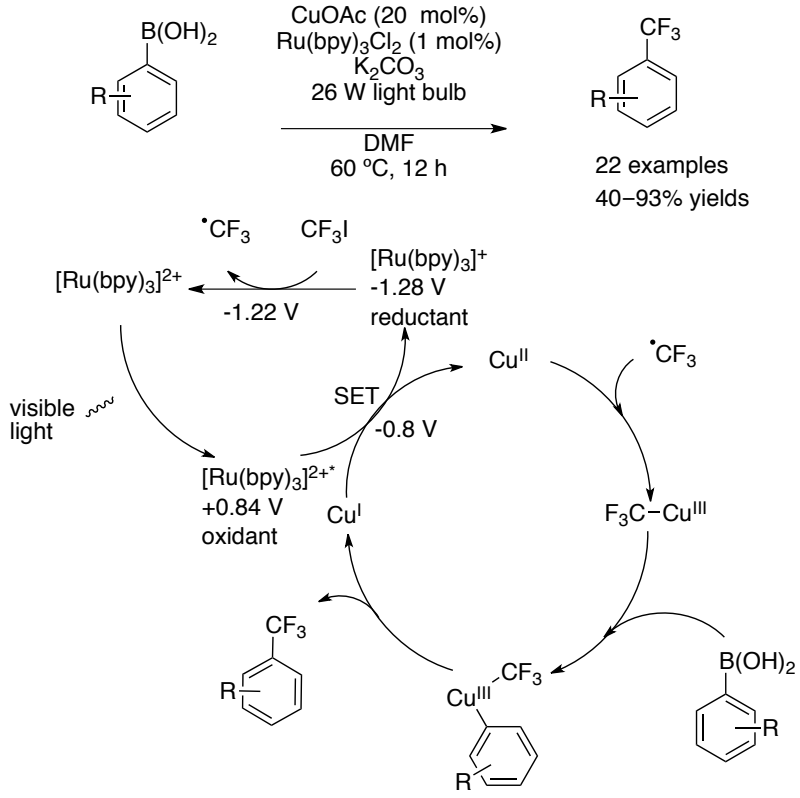
Scheme 3.5.14 Copper-catalysed trifluoromethylation with Togni's **I** reagent.

Direct trifluoromethylation of C–H bonds is an attractive approach because it would obviate the need of prefunctionalisation the (hetero)arene substrate. Recently, MacMillan and co-workers achieved a major breakthrough in the field of photoredox radical trifluoromethylation (Scheme 3.5.15).[143] A photoredox-active ruthenium(II) catalyst and CF_3SO_2Cl were used to generate the CF_3• radical species, which readily performed the trifluoromethylation of (hetero)arenes. This methodology is attractive for the derivatisation of biologically active lead compounds in discovery campaigns.



Scheme 3.5.15 Ru-photoredox-catalysed trifluoromethylation of arenes and heteroarenes.

In 2012, Sanford reported an elegant cross-coupling reaction of arylboronic acids with CF_3I mediated by a photoredox catalyst, $[Ru(bpy)_3]^{2+}$, and a Cu catalyst.[144] The merger of these two modes of catalysis led to the formation of the aryl–CF_3 products in moderate to excellent yields (Scheme 3.5.16). The mechanism suggested for this transformation involves photoexcitation of Ru^{2+} to Ru^{2+*}, followed by electron transfer to a Cu(I) species to form Cu(II). Once the reducing Ru^{+} species is formed, reduction of CF_3I leads to the formation of the CF_3• radical species. The CF_3• radical reacts with Cu(II) to form the key [Cu(III)–CF_3] intermediate. Subsequent transmetalation with the arylboronic acid leads to formation of the $[Cu^{III}(aryl)(CF_3)]$ intermediate, which undergoes reductive elimination to release the trifluoromethylated product, with concomitant regeneration of the Cu^{I} catalyst (Scheme 3.5.16).

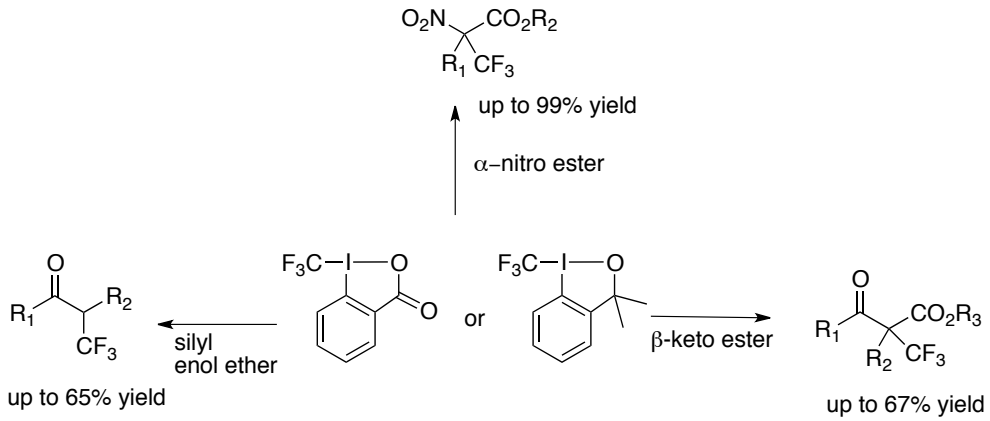


Scheme 3.5.16 Trifluomethylation of arylboronic acids mediated by copper and photoredox catalysis.

3.6 Trifluoromethylation of Carbonyl-Containing Substrates.

Togni trifluoromethylating reagents have been used for the α-trifluoromethylation of various activated carbonyl-containing compounds and their derivatives. For example, silyl enol ethers and silyl ketene acetals have been converted in this manner to the corresponding α-trifluoromethyl ketones or esters, respectively.[125]

In a different approach, Togni and co-workers reported that the addition of catalytic CuCl enabled α-nitro esters to be converted to the desired α-nitro-α-trifluoromethyl esters in moderate to excellent yields, thereby providing a route to the corresponding α-trifluormethyl-α-amino acids.[124]

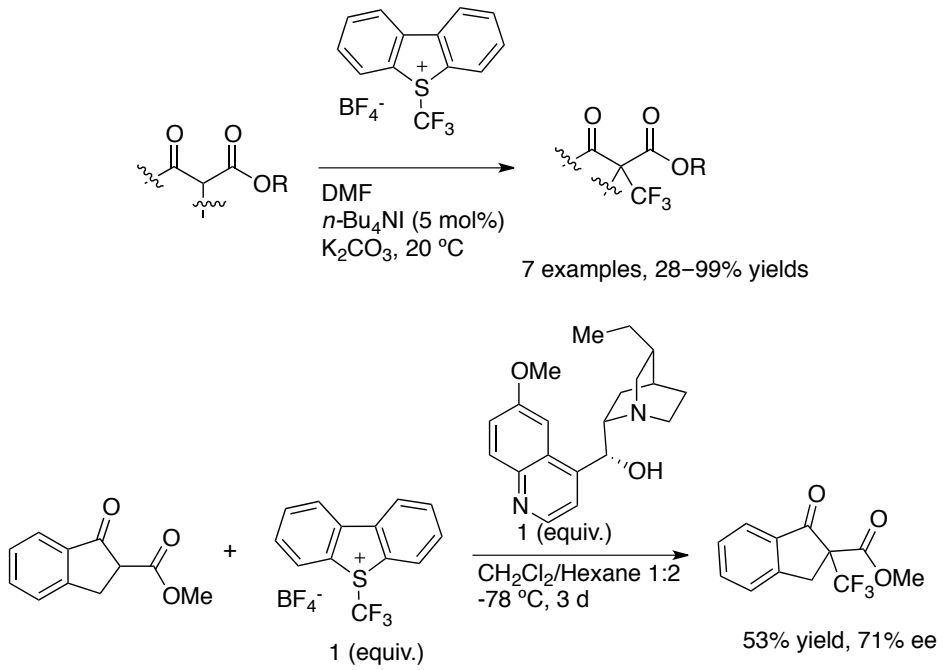


Scheme 3.6.1 Selected trifluoromethylation reactions using hypervalent iodine reagents.

The Umemoto and Shibata trifluoromethylating reagents have also been successfully applied in the trifluoromethylation of carbon-based nucleophiles. Cyclic and acyclic β-ketoesters, enamines, phosphines, and thiolates have been trifluoromethylated in moderate to excellent yields.[145]

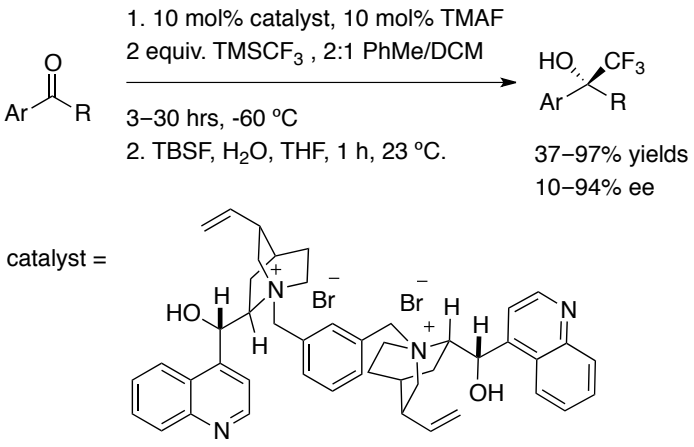
In 2003, Cahard and Ma reported a direct α-trifluoromethylation of carbonyl-containing compounds using the Umemoto reagent.[146] They demonstrated that using mild phase-transfer

catalysis conditions, α-substituted-β-ketoesters underwent α-trifluoromethylation with the CF_3^+ source, a reaction that presumably proceeds *via* the tetrabutylammonium enolate (Scheme 3.6.2). Later, the same group described an enantioselective variant using stoichiometric quantities of chiral cinchona alkaloid dihydroquinine to deprotonate the β-ketoester and form the chiral ammonium enolate.[125] This chiral Brønsted base approach provided the α-trifluoromethyl-β-ketoester in up to 71% ee (Scheme 3.6.2).



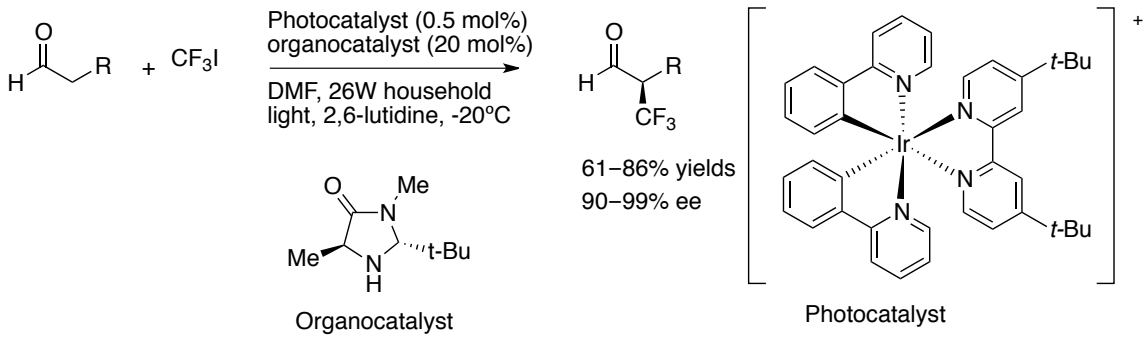
Scheme 3.6.2 Trifluoromethylation of carbonyl-containing compounds using the Umemoto reagent.

Kobayashi and co-workers described the use of chiral ammonium catalysts in combination with the Ruppert–Prakash reagent, a nucleophilic trifluoromethylating source (Scheme 3.6.3). In this report, aryl ketones furnished the corresponding trifluoromethylated alcohols in low to high yields and with varying enantioselectivities.[147]

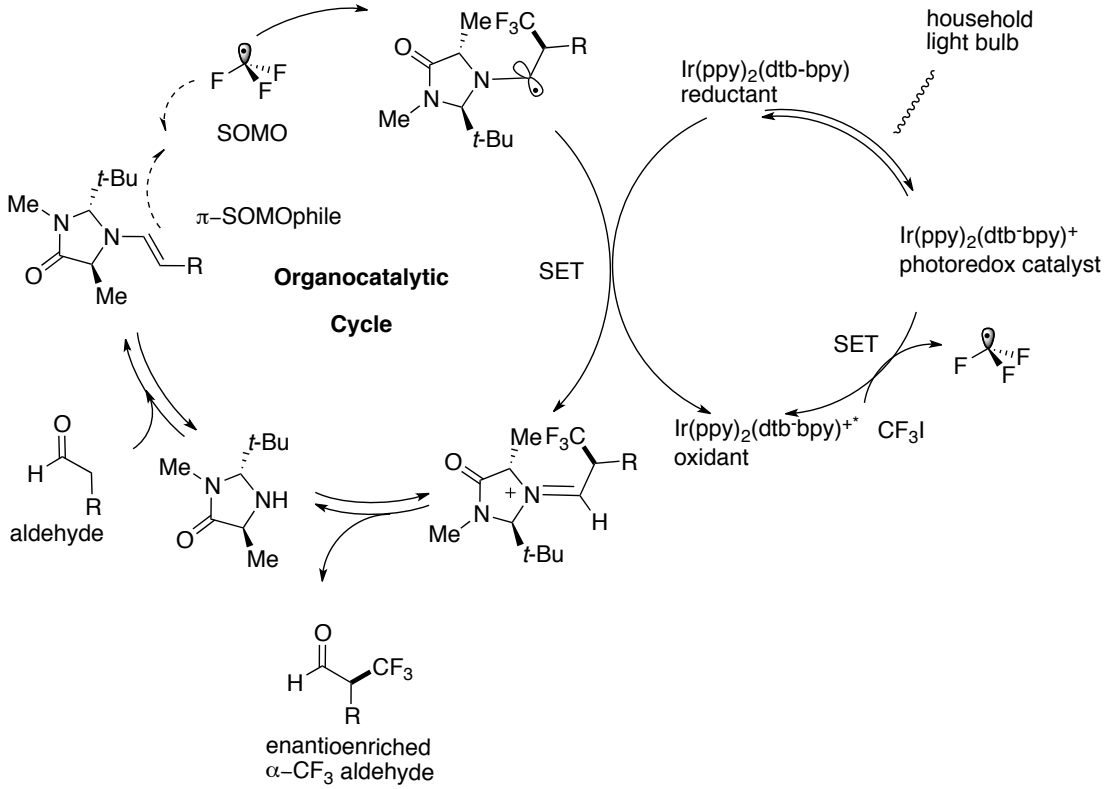


Scheme 3.6.3 Catalytic enantioselective trifluoromethylation of aromatic ketones by chiral ammonium catalysts.

In 2009, MacMillan and co-workers demonstrated that in the presence of visible light, $Ir(ppy)_2(dtbbpy)PF_6$ or $[Ru(bpy)_3]Cl_2$ were effective one-electron reductants for the generation of the trifluoromethyl radical from CF_3I.[148] The trifluoromethyl radical efficiently attacked the transiently generated enamine, formed through condensation of the aldehyde with the secondary amine catalyst. This elegant method to form α-CF_3 aldehydes led to the construction of a variety of enantioenriched trifluoromethylated building blocks.

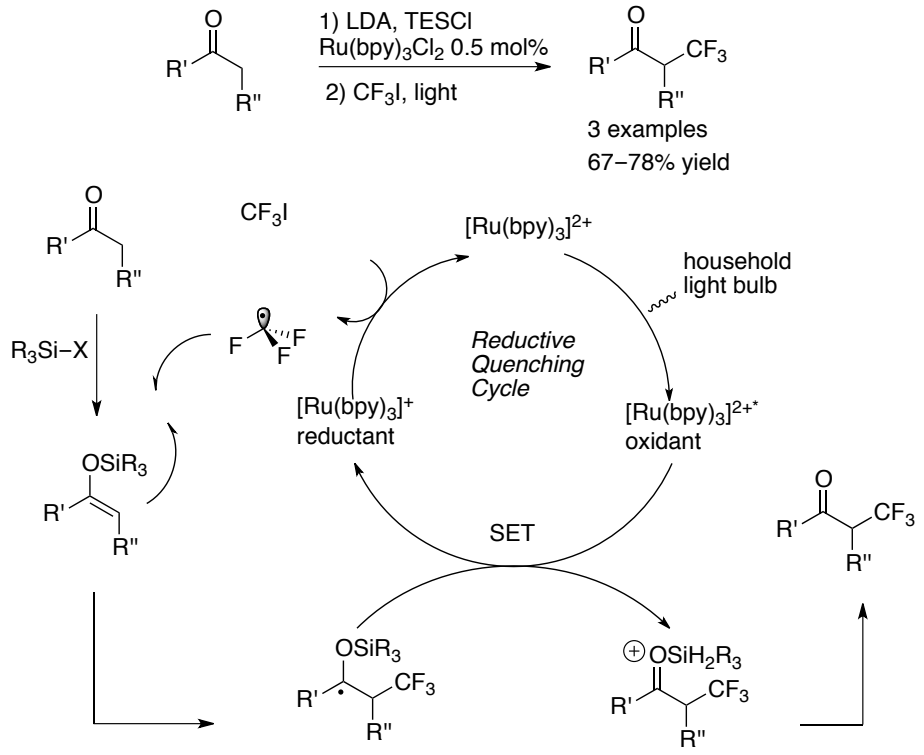


Scheme 3.6.4 Direct α-trifluoromethylation of aldehydes under photoredox catalysis.



Scheme 3.6.5 Plausible mechanism for the enantioselective α-trifluoromethylation of aldehydes under photoredox catalysis.

The MacMillan group extended their previous protocol for the generation of CF_3• radicals *via* photoredox catalysis to the synthesis of other α-trifluoromethyl carbonyl-containing compounds (ketones, esters, and amides).[149] The carbonyl compounds were converted to enolsilane derivatives, which are suitable nucleophiles for reactions with alkyl radicals in the presence of $Ru(bpy)_3Cl_2$ as a photocatalyst and a household light bulb. The CF_3• radical combines with the enolsilane to give a trifluoromethyl enolsilane radical, followed by a SET to generate a silyloxocarbenium species leading to the formation of the racemic α-CF_3 carbonyl-containing compound (Scheme 3.6.6).



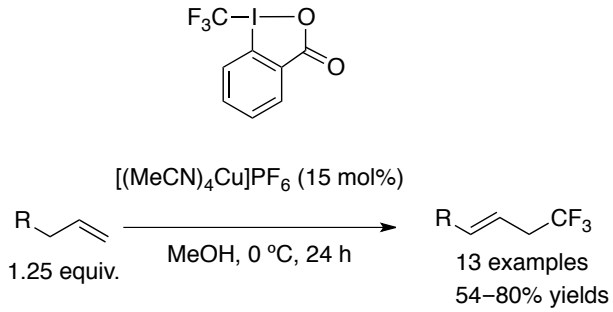
Scheme 3.6.6 Plausible mechanism for the α-trifluoromethylation of carbonyl-containing compounds under photoredox catalysis.

3.7 Allylic Trifluoromethylation

Significant efforts have been devoted to the construction of C_{sp^3}–CF_3 stereogenicity, with most cases involving carbonyl-containing compounds (*vide supra*). In the absence of an activating carbonyl moiety, examples are far less common. In this context, the direct selective installation of a CF_3 group on an allylic position remains a challenging synthetic problem. Isolated examples of Pd-catalyzed allylic trifluoromethylation of allylstannanes with CF_3I were reported by Matsubara and co-workers.[150] However, organotin compounds are toxic, which reduces the method´s practical utility.

Research on copper-catalysed trifluoromethylation for the synthesis of allylic–CF_3 products is less developed, and research in this area began in earnest only at the beginning of this decade.

In 2011 Buchwald and co-workers examined the reactivity of 4-phenyl-1-butene in the presence of Cu catalysts and Togni reagent **298** in different solvents.[151] They found $[(MeCN)_4Cu]PF_6$ was the best catalyst and MeOH was the optimal solvent to achieve the desired allylic trifluoromethylation with high *E*/*Z* selectivity (98:2). This reaction tolerated a range of functional groups, including unprotected alcohols, protected amines, esters, amides and alkyl bromides.



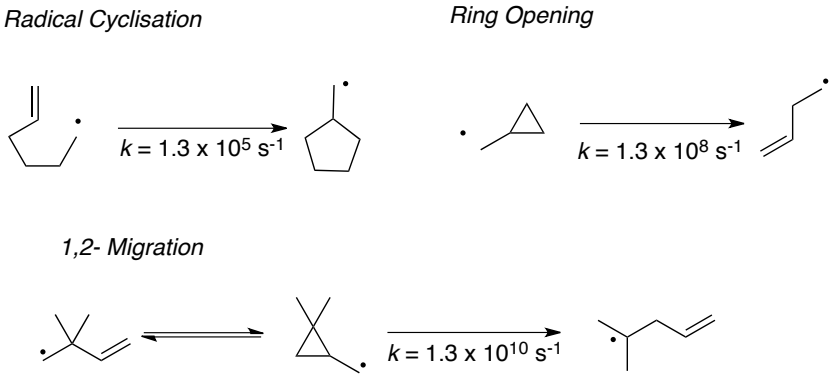
Scheme 3.7.1 Synthesis of allylic–CF_3 products *via* C–H functionalisation.

For this transformation two pathways were hypothesised, the first proceeding *via* generation of an allylic radical intermediate, the second *via* electrophilic trifluoromethylation to generate a cationic species. The desired allylic–CF_3 products are then formed through either SET or by proton elimination, respectively. In order to determine whether or not the mechanism proceeded *via* an allylic radical, the trifluoromethylation of cyclopropane substrate (a "radical clock") was examined.

"Radical clocks" are employed as mechanistic probes to determine the presence of a radical intermediate. Classic examples of these reactions include cyclisations, ring openings, and 1,2-migrations.[152] The 5-exo-cyclisation of the 5-hexenyl radical to the cyclopentylcarbinyl radical is commonly used as a radical clock. Newcomb observed that substitution variants of the 5-hexenyl "radical clock" led to cyclise at faster rates. For example, 6,6-diphenyl-5-hexenyl and

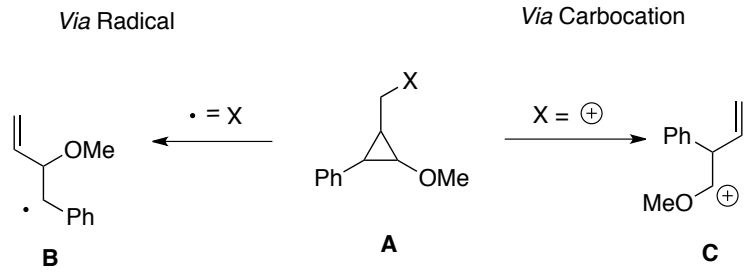
6-cyano-5- hexenyl radical cyclisations proceeded at 25°C with rate constants of 5.4×10^7 s^{-1} and 1.6×10^8 s^{-1}, respectively.[153]

One of the most studied "radical clock" reactions is the ring opening of cyclopropylcarbinyl. This reaction, driven by the relief of ring strain, proceeds with a rate constant of 1.3×10^8 s^{-1}.



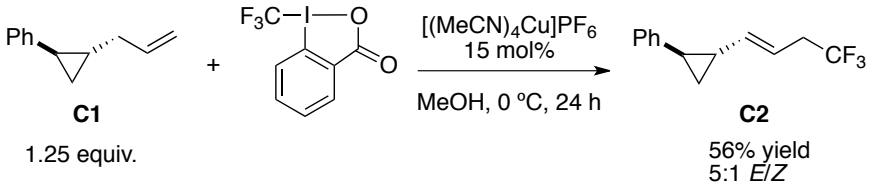
Scheme 3.7.2 Examples of radical clock reactions.

However, the structural reorganisation of the radicals in most of the ring opening reactions are the same as those that would occur from the corresponding carbocations. Therefore, the qualitative evidence provided from these reactions is not conclusive and additional studies are required in order to determine the reaction mechanism. In this sense, Newcomb designed a hypersensitive mechanistic probe (Scheme 3.7.3, **A**) for distinguishing between radical and carbocation intermediates.[154] This probe was designed based on the notion that when the ring opening ocurrs in cyclopropylcarbinyl systems, a phenyl group would stabilise the radical centre (Scheme 3.7.3 **B**) more strongly than an alkoxy group would. However, the converse will take place if the reaction proceeds through a carbocation intermediate (Scheme 3.7.3 **C**).



Scheme 3.7.3 Mechanistic probe to distinguish radical or carbocation pathways.

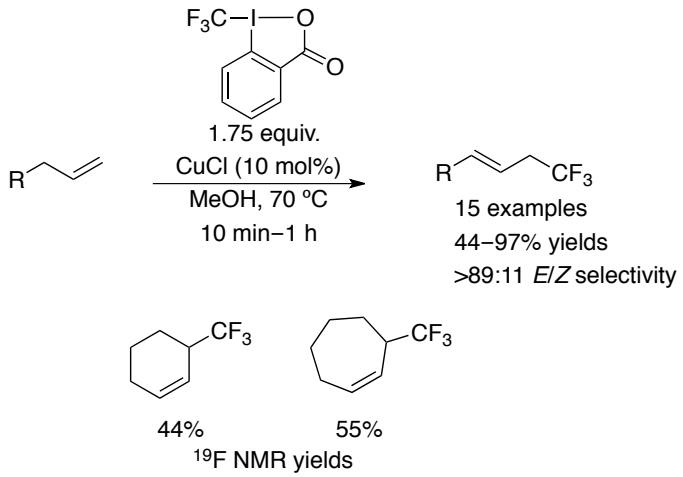
When Buchwald subjected a radical clock **C1** (Scheme 3.7.4) to trifluoromethylation reaction conditions (MeOH, Togni I reagent, $[(MeCN)_4Cu]PF_6$ 15 mol%), the trifluoromethylated cyclopropane **C2** (Scheme 3.7.4) was formed in moderate yield (56%), but only traces of the ring-opened product were observed. Further experiments did not help to elucidate the reaction mechanism. Overall, from their findings, they were unable to distinguish between the radical and electrophilic trifluoromethylation pathways.



Scheme 3.7.4 Radical clock study to probe the reaction mechanism.

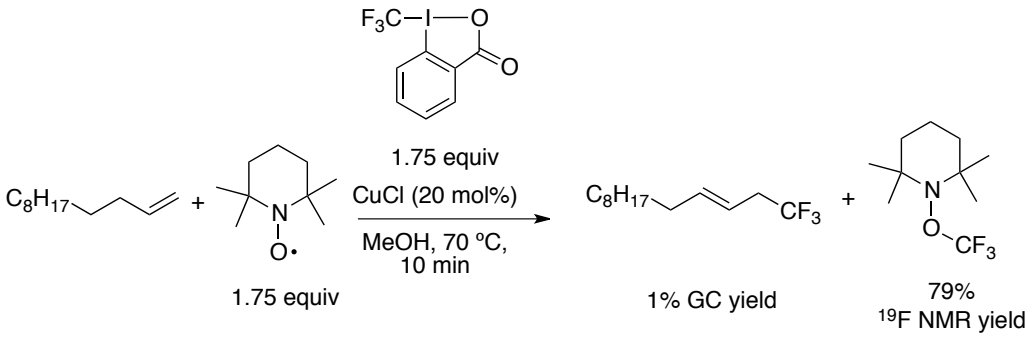
Wang reported a similar copper-catalyzed trifluoromethylation reaction of terminal alkenes.[155] In the report, CuCl was used as the catalyst in combination with Togni reagent **I** as the CF_3^+ source in methanol at 70 °C, which led to efficient formation of the desired allylic–CF_3 products. Terminal olefins featuring ester, amide and phthalimide functional groups were tolerated under the reaction conditions to give the desired products in moderate to high yields (44–97%) with high control over *E:Z* selectivity. Only two examples of branched allylic–CF_3

products were reported in moderate yield (as determined by ^{19}F NMR spectroscopy in the presence of an internal standard) (Scheme 3.7.5).



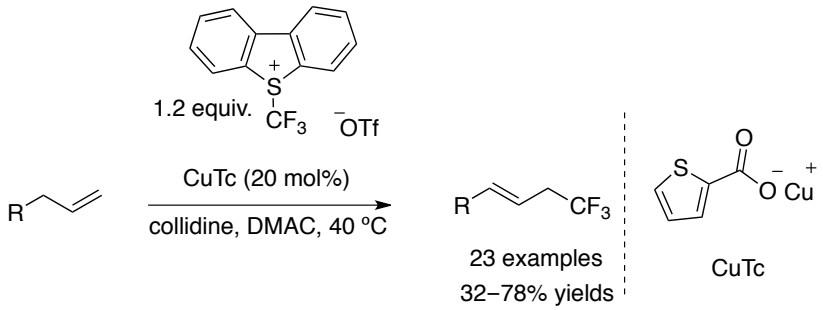
Scheme 3.7.5 Allylic trifluoromethylation of terminal alkenes via C–H functionalisation.

In order to gain further understanding of the reaction mechanism, the reaction was run under the standard conditions in the presence of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), which is known to operate as a radical scavenger. The reaction led to the formation of the TEMPO–CF_3 species, and only 1% of the desired allylic–CF_3 product (detected by gas chromatography). This experimental result provided supportive evidence that a CF_3• radical is involved in the reaction mechanism (Scheme 3.7.6).



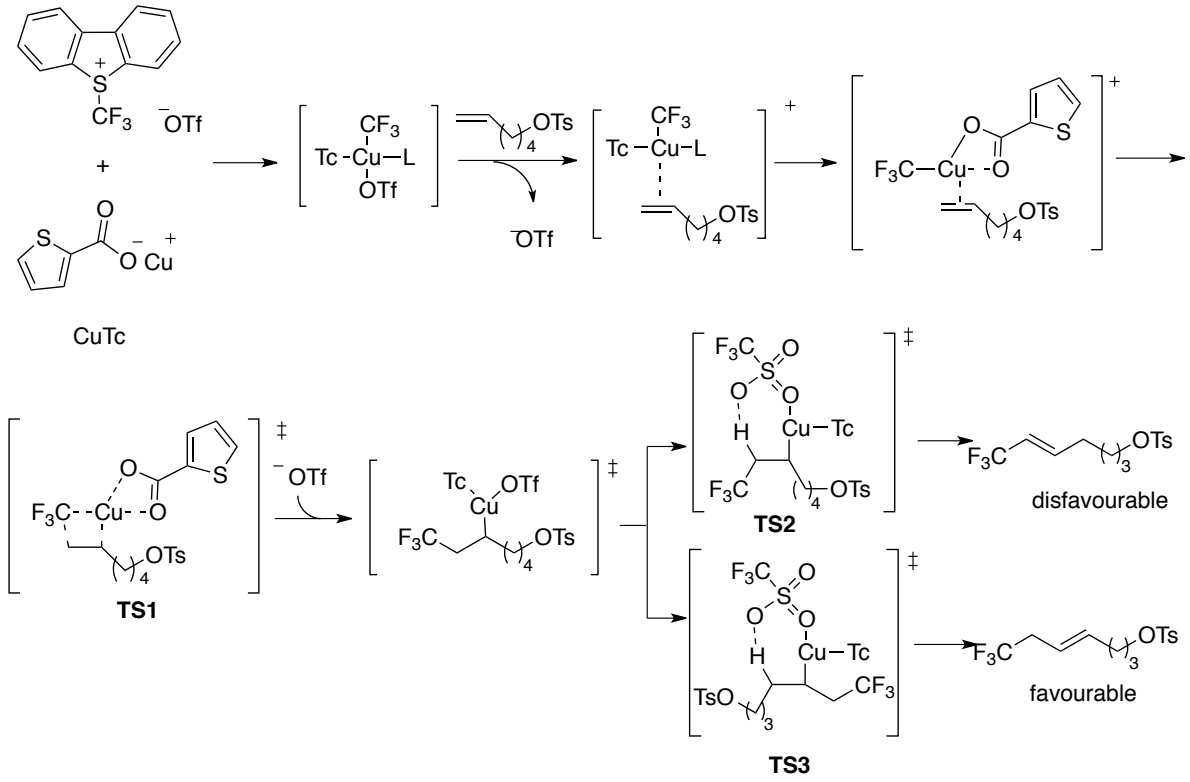
Scheme 3.7.6 Reaction in the presence of TEMPO.

In 2011, Liu also disclosed a method for allylic trifluoromethylation of terminal alkenes through allylic C–H bond activation using Umemoto's reagent as the electrophilic CF_3^+ source.[156] This reaction was mediated by a copper catalyst, with CuTc (Copper(I) Thiophene-2-carboxylate) proving to be optimal. The addition of a base as an additive was necessary for the reaction to proceed in good yields (up to 78%).



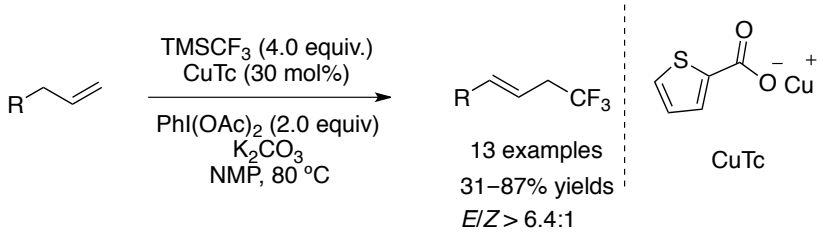
Scheme 3.7.7 Allylic trifluoromethylation of terminal alkenes *via* C–H functionalisation.

This reaction also tolerated functional groups such as esters, amides, and phtalimides, giving moderate to high yields (44–97%). However, 2-substituted terminal alkenes or internal alkenes were unreactive under these conditions, even at higher temperatures. Based on theoretical calculations and experimental results, Liu and co-workers suggested that the intermediacy of an allylic radical species is unlikely. Instead, they suggested the formation of a $[Cu^{III}CF_3]$ intermediate that may proceed through a Heck-type four membered-ring transition state (TS1), which is the rate-limiting step of the reaction. The counteranion (TfO^-) is suggested to assist the activation of the C-H bond, accelerating the elimination step to release the desired allylic CF_3 product. Theoretical calculations indicate the formation of the vinylic–CF_3 by-product is not energetically favourable, probably due to steric hindrance factors (Scheme 3.7.8, **TS2**). In fact, 2-substituted terminal alkenes or internal alkenes did not react under the reaction conditions, even when the reaction temperature was increased to 80 °C.



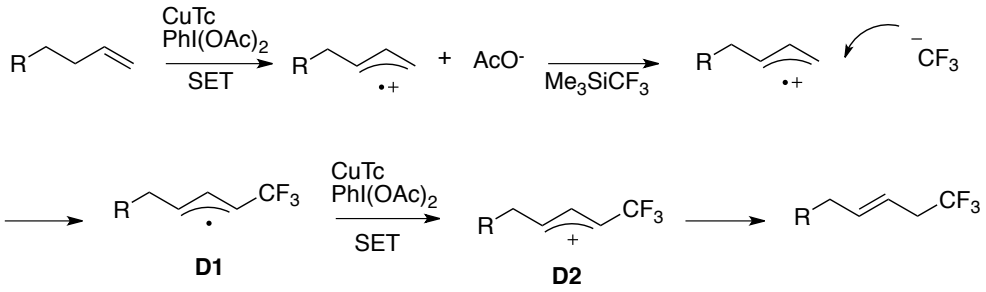
Scheme 3.7.8 Possible intermediate leading to the formation of the allylic–CF_3 product.

Recently, Qing and co-workers investigated nucleophilic trifluoromethylation of terminal alkenes under oxidative conditions using the Ruppert–Prakash reagent.[157] They found that with CuTc and $TMSCF_3$, trifluoromethylation of alkenes could indeed be accomplished in the presence of the strong oxidant $PhI(OAc)_2$, leading to the formation of allylic–CF_3 products in moderate to good yields (Scheme 3.7.9).



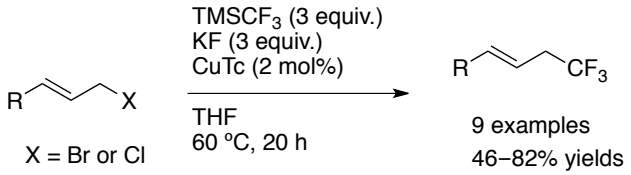
Scheme 3.7.9. Nucleophilic trifluoromethylation of terminal alkenes under oxidative conditions.

Regarding the mechanism, the authors suggested that CuTc in combination with $PhI(OAc)_2$ may oxidise the terminal alkene to a radical cation intermediate *via* single electron transfer. Subsequent attack of the CF_3^- anion onto the radical cation would lead to the formation of the radical intermediate **D1**. Then, single-electron oxidation gives the cationic intermediate **D2**, which forms the desired product by deprotonation.



Scheme 3.7.10 Possible mechanism for the nucleophilic trifluormethylation of terminal alkenes.

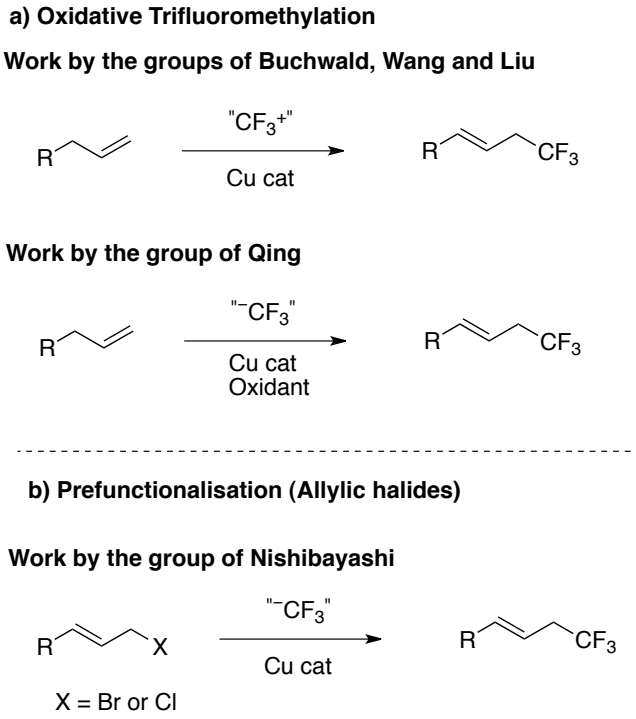
Nishibayashi and co-workers developed a copper-catalysed trifluoromethylation reaction of allylic halides to afford the desired allylic–CF_3 products in good to moderate yields (46–82%) and with high regioselectivity (Scheme 3.6.10)[158]. Although the mechanistic details of this transformation remain unclear, the authors suggested that the reaction involves initial formation of a $CuCF_3$ species. Oxidative addition of the allylic halide results in the formation of a Cu(III) species. Finally, reductive elimination gives the corresponding allylic–CF_3 product. Disadvantages of this transformation include the fact that it requires expensive allylic halides and 3 equivalents of the $TMSCF_3$ reagent, making it less attractive as a trifluoromethylation method.



Scheme 3.7.10 Cu-catalysed trifluoromethylation of allylic halides.

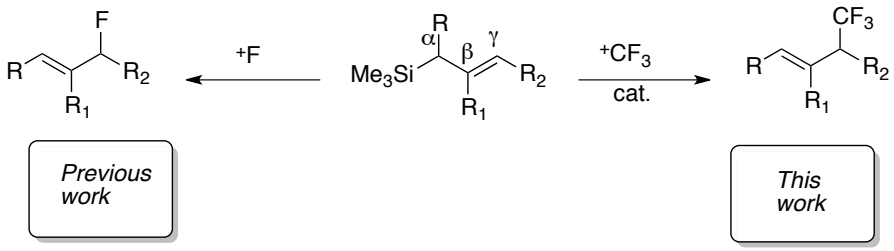
3.8 Objectives.

The methods of Buchwald,[151] Wang,[155] Liu,[156] Qing[157] and Nishibayashi[158] are important contributions, enabling the efficient preparation of linear allylic–CF_3 products. However all of these reactions are limited in terms of accessing branched acyclic allylic–CF_3 products. Only two examples of branched cyclic products were prepared through application of the C–H functionalisation methodology in Wang's report**.** This limitation underscores the fact that in contrast to C(sp)^2–CF_3 bond formation, which has evolved quickly during the past several years, C(sp)^3–CF_3 bond formation remains a significant challenge, particularly in the absence of an activating carbonyl moiety. Thus, a major part of the research conducted for this thesis focused on exploring new methods for synthesising allylic–CF_3 products with improved substrate scope and enhanced regio- and stereocontrol. Figure 3.8.1 summarises the main strategies introduced above for accessing allylic–CF_3 products under copper-catalysed conditions. The development of asymmetric variants of these transformations under Cu-catalyzed conditions remains a tremendous challenge. Several catalytic asymmetric approaches for constructing C(sp^3)–CF_3 stereogenicity are being investigated in the Gouverneur group at the present time.



Scheme 3.8.1 Cu-catalysed allylic trifluoromethylation.

To address this synthetic problem, an alternative strategy was considered in which an allylsilane substrate would be used, with the silyl group increasing the nucleophilicity of the proximal alkene and controlling the regioselectivity of the C–CF_3 bond-forming step. Since a wide variety of electrophilic CF_3^+ reagents are available and allylsilanes are readily straightforward to prepare, it was envisioned that this approach would offer a practically useful means of forming linear and branched allylic–CF_3 products.

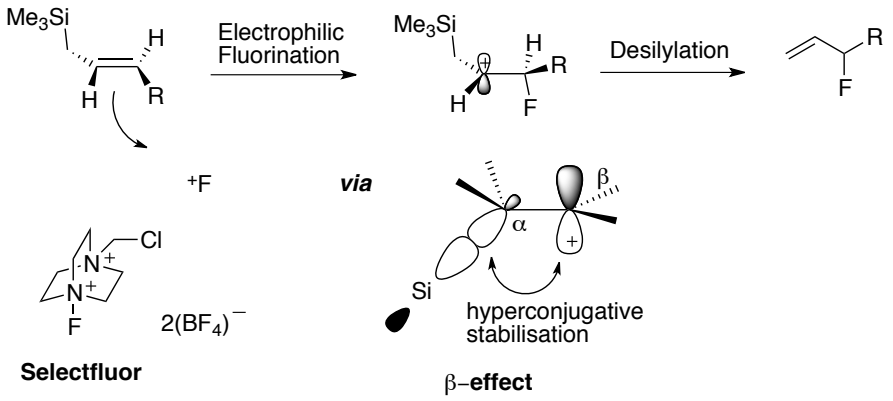


Scheme 3.8.2 Trifluoromethylation of allylsilanes under metal catalysis.

Chapter 4

4.1 The Role of Organosilanes in Fluorination Processes.

Silyl groups are known to offer beneficial effects in enhancing reactivity and allowing for stereocontrol in olefin substitution reactions. The Gouverneur group has previously taken advantage of these characteristics to develop a class of electrophilic fluorodesilylation reactions, which collectively serve as versatile methodology for accessing fluorinated building blocks, including enantioenriched derivatives.[159] In this process, the electrophilic source of fluorine is (1-chloromethyl-4-fluorodiazoniabicyclo[2.2.2]octane bis(tetrafluoroborate)), which is commercially known as Selectfluor™. The reactivity and selectivity of electrophilic substitution reactions of organosilanes is principally determined by the β-effect of silicon, in which $\sigma_{Si-C} \rightarrow C$ 2p hyperconjugation leads to stabilisation of a vicinal carbocation by 29–30 kcal/mol. In comparison, silicon stabilises a vicinial radical by 2.6–4.5 kcal/mol.[160] This remarkable level of cation stabilisation is possible when the occupied C–Si σ bond is periplanar to the empty p orbital, as maximum orbital overlap is attained in this conformation. The β-effect results in regioselective addition of the electrophilic source of fluorine to the alkene. Desilylation then gives clean transposition of the double bond, leading to the formation of the allylic fluoride. This process proceeds *via* an S_E2' mechanism, and a general depiction of the reaction is shown in Scheme 4.1.1.



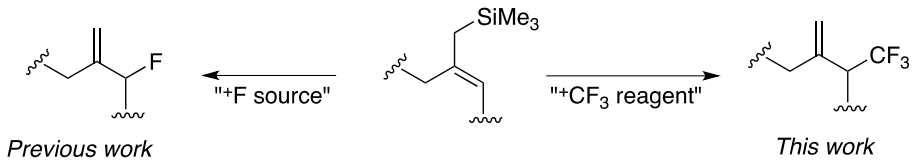
Scheme 4.1.1 Electrophilic fluorodesilylation process.

4.2 Initial investigations

4.2.1 Reactivity of Allylsilanes in the Presence of Electrophilic Trifluoromethylating Reagents.

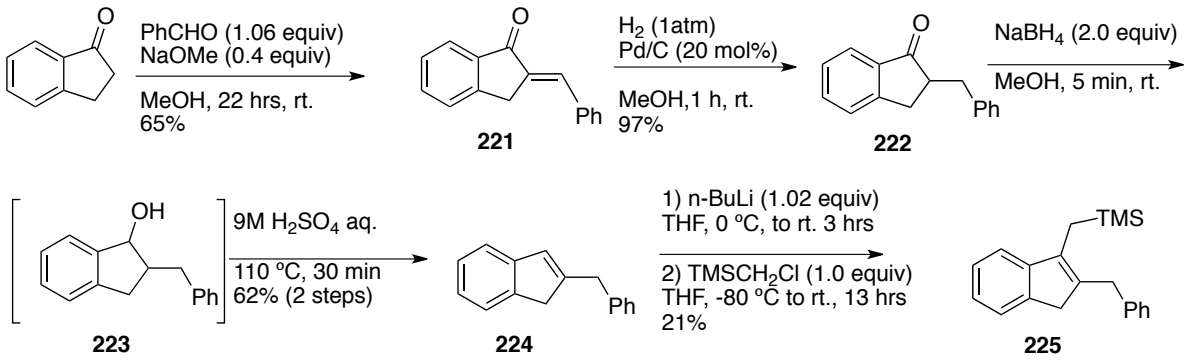
Since the Gouverneur group's first report on electrophilic fluorination of allylsilanes in 2003,[161] it has been found that these reactions exhibit broad substrate scope and tolerate a variety of functional groups.[162] The method offers access to complex targets such as fluorinated analogues of vitamin D, sphingosine and fluorinated carbohydrate analogues.[163]

The introduction of a CF_3 group onto a target molecule is challenging and is commonly performed by applying a stepwise *de novo* approach. Increasingly, late-stage methods for introducing CF_3 groups are sought after, particularly in medicinal chemistry settings. Thus, based on this previous knowledge, it was envisioned that this approach could be extended to the synthesis of allylic–CF_3 compounds using a suitable CF_3^+ reagent (Scheme 4.2.1).



Scheme 4.2.1 Proposed strategy for electrophilic trifluoromethylation of allylsilanes.

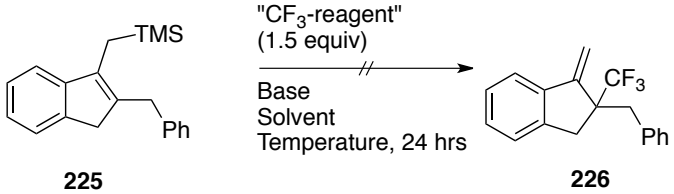
Initial studies were carried out in our group with the model substrate ((2-benzyl-1*H*-inden-3-yl)methyl)trimethylsilane. This substrate was prepared from the commercially available indanone in a multi-step sequence. First, an aldol reaction gave product **221** in moderate yield (65%). Next, selective hydrogenation of the alkene with palladium on carbon (20 mol%) in methanol afforded **222**. Reduction of the ketone with 2 equivalents of $NaBH_4$, followed by elimination gave product **224** in 62% yield. Deprotonation with one equivalent of *n*-BuLi , followed by treatment with chloromethyltrimethylsilane, provided ((2-benzyl-1*H*-inden-3-yl)methyl)trimethylsilane in low yield (21%) (Scheme 4.2.2).

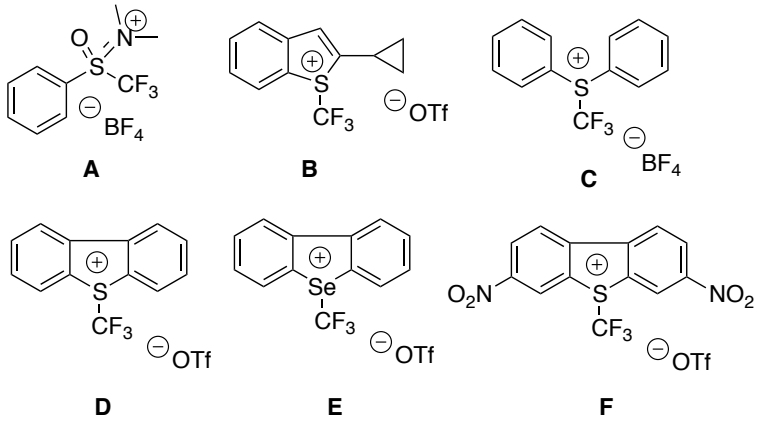


Scheme 4.2.2 Synthesis of model substrate ((2-benzyl-1*H*-inden-3-yl)methyl)trimethylsilane **225**.

Initial studies were carried out on model substrate **225** using Umemoto and Shibata reagents **A**–**F** in acetonitrile at room temperature for 24 hours. Under these conditions, none of the desired allylic–CF_3 product was observed (Table 4.2.1). When the reaction was run at room temperature, the starting material was fully recovered. When the reaction was heated to 70 °C, decomposition of the starting material was observed (Table 4.2.1, Entry 10). Use of various bases as additives did not promote the desired trifluoromethylation reaction.

Varying the solvent, temperature, addition of additives and the CF_3^+ source did not lead to the formation of the desired allylic-CF_3 product. The lack of reactivity indicated that Umemoto and Shibata reagents **A–F** are insufficiently electrophilic to react with the model substrate, ((2-benzyl-1*H*-inden-3-yl)methyl)trimethylsilane **225**. This prompted us to consider alternative CF_3^+ sources, as described in the next section.





Entry	$^{+}CF_3$ Reagent	Solvent	Temp °C	Base	Yield (%)
1	A	CH_3CN	RT	-	NR
2	B	CH_3CN	RT	-	NR
3	C	CH_3CN	RT	-	NR
4	D	CH_3CN	RT	-	NR
5	E	CH_3CN	RT	-	NR
6	F	CH_3CN	RT	-	NR
7	B	CH_3CN	RT	DBU(1.2 equiv.)	NR
8	B	CH_3CN	RT	Cs_2CO_3 (2 equiv.)	NR
9	B	CH_3CN	RT	$TMAF{\cdot}4H_2O$	NR
10	B	CH_3CN	70°	-	Decomposition
11	B	DMF	70°	-	NR

Table 4.2.1 Initial attempts at trifluoromethylation of allylsilanes.

4.3 Activation of the Electrophilic "$^{+}CF_3$" reagent

Proof of concept

We recognised that several key modifications were required to demonstrate the viability of this concept. Based on the previous results, it was reasoned that steric hindrance might be an impediment for the approach of the trifluoromethyl group to the alkene. Therefore, a new class of less sterically encumbered allylsilane substrates in which the γ-position was not disubstituted were synthesised (Figure 4.3.1).

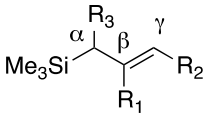
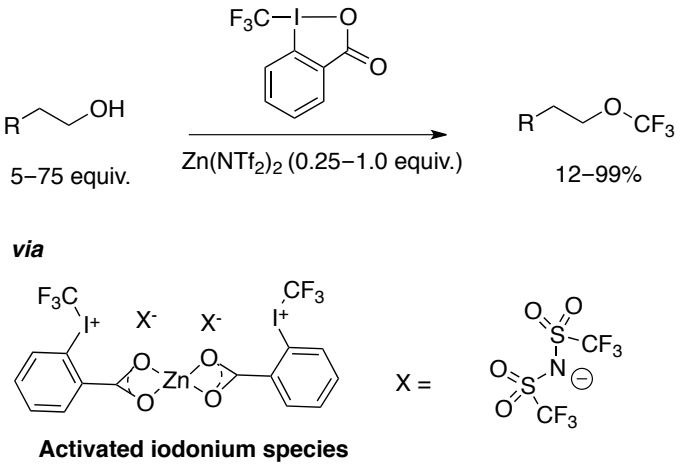


Figure 4.3.1 New class of allylsilane substrates

As mentioned before, Umemoto and Shibata trifluoromethylating reagents **A**–**F** appeared to be insufficiently electrophilic to react with alkenes temporarily activated with a regiodirecting trialkylsilyl group.

Togni[164] and MacMillan[148] have reported independently that Togni reagents **I** and **II** can be activated by Lewis acids to generate a highly electrophilic iodonium species (Scheme 4.3.2). In 2009, Togni reported the trifluoromethylation of aliphatic alcohols using a hypervalent iodine(III) reagent activated by the Lewis acid, ($Zn(NTf_2)_2$).[164] The assumption that the reaction proceeded *via* the activated iodonium species was proven by X-ray diffraction and mass spectrometry.

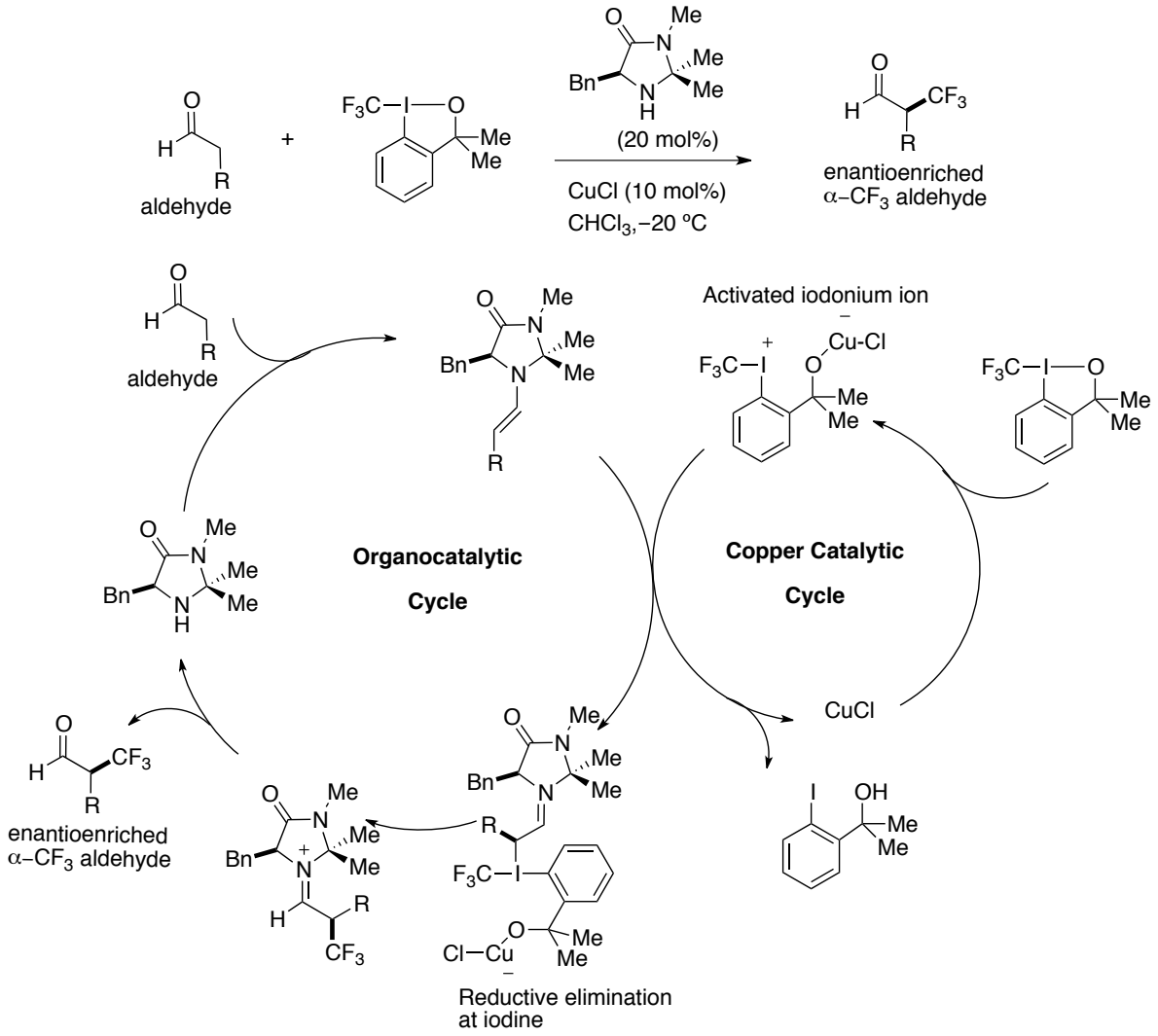


Scheme 4.3.1 Formation of the electrophilic iodonium species.

Inspired by Togni's report that the hypervalent iodine (III) reagents could be activated towards nucleophilic attack in the presence of a Lewis acid, Macmillan proposed an enantioselective route towards the sysnthesis of enantioenriched α- CF_3 aldehydes. The

authors speculated that the reaction could proceed *via* condensation of a chiral amine catalyst and the aldehyde forming a chiral enamine (π-electron rich), which could then react with the activated iodonium species. In practice, the reaction proceeded in high (66–86%) and with enantioselectivities up to 94% ee when $Sm(OTf)_2$, $FeCl_2$ or CuCl were used as catalysts. Chloroform was the best solvent probably due to the lack of coordination with the metal catalyst.

Regarding the reaction mechanism, the authors proposed that the Togni reagent **II** was activated through the coordination of the Lewis acids and that these metal additives did not serve as single-electron reductants. Coordination of the metal to the oxygen of the benziodoxole facilitates cleavage of the I–O bond. The resulting activated iodonium species reacts with the enamine forming a λ_3-iodane intermediate. This intermediate undergoes reductive elimination to generate the enantioenriched α-trifluoromethyl aldehyde (Scheme 4.5.7). The recent reports by Buchwald and Wang on copper-catalysed allylic trifluoromethylation with Togni reagent **I**, however, proposed the possibility of radical intermediates under similar conditions.



Scheme 4.3.2 Probable mechanism for the formation of enantioenriched α-CF_3 aldehydes.

Based on previous literature precedents, it was thus hypothesised that an appropriate Lewis acid could activate Umemoto, Shibata and Togni trifluoromethylating reagents to react with the alkenes temporarily activated with the regiodirecting trialkylsilyl group (Figure 4.3.2). With the purpose of investigating the reactivity of less sterically allylsilanes encumbered, two new model substrates were synthesised.

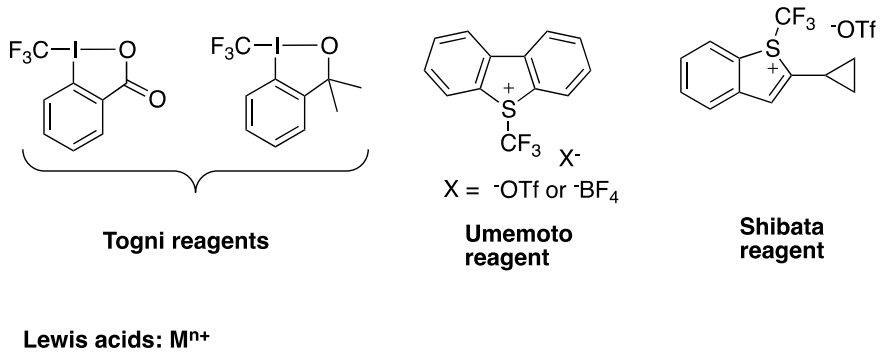
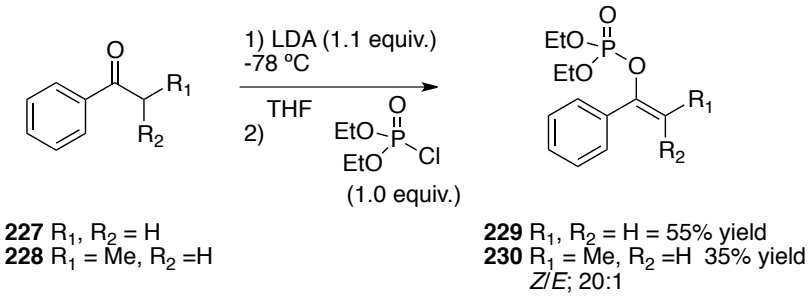


Figure 4.3.2 Electrophilic CF_3^+ reagents used in this study.

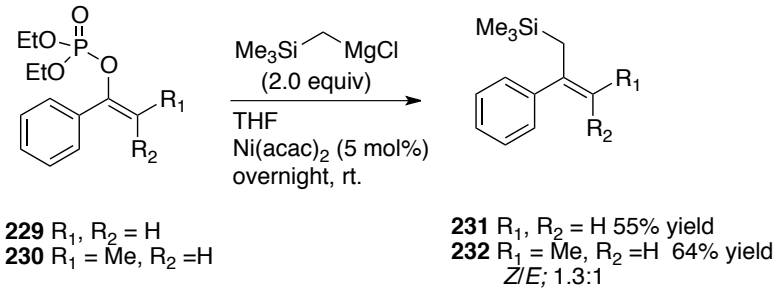
4.4 Synthesis of model substrates

Having recognised the possible importance of the structure of the substrate on reactivity, we next synthesised a couple of allylsilanes using a two-step procedure described by Kumada *et al.*[165] First, the required enol phosphates were prepared from the reaction of diethyl chlorophosphate with a lithium enolate, the latter of which was generated from the corresponding ketone and lithium diisopropylamide (LDA). The enol phosphates, diethyl (1-phenylvinyl) phosphate (**229**) and (*Z*)-diethyl(1-phenyl-1-propenyl) phosphate (**230**), were isolated in moderate yield (35% and 55% yield, respectively), and **230** was obtained as a 1:20 mixture of *E:Z* isomers .



Scheme 4.4.1 Synthesis of the enol phosphates.

The target allylsilanes, **231** (2-phenylallyl)trimethylsilane and **232** ((*Z*)-trimethyl(2-phenylbut-2-en-1-yl)silane), were then synthesised using Kumada–Tamao cross-coupling between trimethylsilylmethylmagnesium chloride and enol phosphates **229** and **230** (Scheme 4.4.2). With the synthesis of these model substrates completed, new catalytic modes of activating the CF_3^+ reagents were next examined.

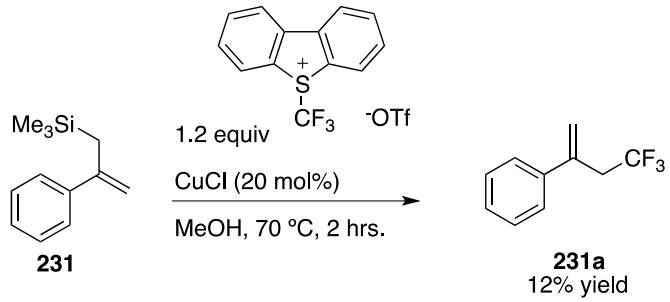


Scheme 4.4.2 Synthesis of allylsilanes **231** and **232**.

4.5 Further Investigations

Trifluoromethylation

In order to test the proposed Lewis acid activation strategy, initial investigations were performed with allylsilane **231** in the presence of Umemoto's reagent and CuCl (20 mol%) in methanol at 70 °C (Scheme 4.5.1).

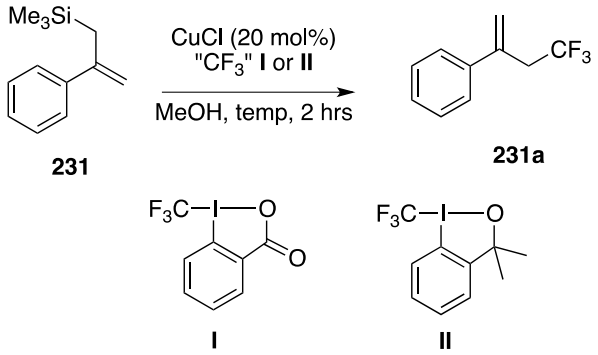


Scheme 4.5.1 Trifluoromethylation of **231** using Umemoto's reagent.

Preliminary results showed the Umemoto reagent could be suitable for activation in the presence of copper salts, (20 mol% CuCl) (2-phenylallyl)trimethylsilane **231** and methanol at 70 °C. The reaction resulted in the formation of (4,4,4-trifluorobut-1-en-2-yl)benzene **231a** in 12% yield, observed through ^{19}F NMR spectroscopy using fluorobenzene as an internal standard.

By ^{19}F NMR spectroscopy, the diagnostic peak for compound **231a** in $CDCl_3$ is a triplet at -64.9 ppm with a coupling constant of $^{3}J_{F-H}$ = 10.5 Hz. By ^{1}H NMR spectroscopy the diagnostic peaks are the two inequivalent vinylic protons at 5.4 and 5.6 ppm. Upfield at 3.3 ppm, a quartet is observed with a coupling constant of $^{3}J_{H-F}$ = 10.7 Hz.

This result encouraged us to further investigate the reactivity of substrate **331** under copper catalysis with hypervalent iodine(III) reagents **I** and **II** (Table 4.5.1).

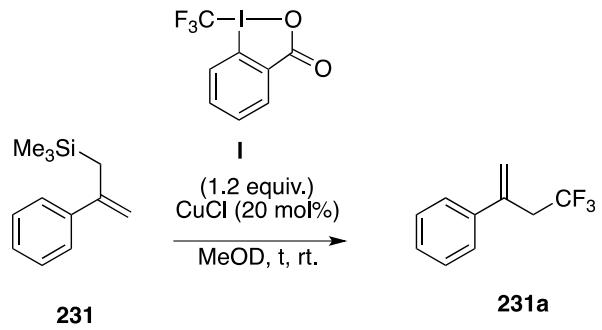


Entry[a]	Cu Source	"CF_3" (equiv)	Temp (°C)	Conv. (%)[b]	Yield (%)[c]
1	CuCl	**I** (1.2)	rt	85	67
2	**CuCl**	**I (1.2)**	**70**	**89**	**73**
3	CuCl	**II** (1.2)	70	72	51
4	CuCl	**I** (1.5)	70	87	58
5	**none**	**I (1.2)**	**70**	**<2**	**<2**

[a] **231** (0.2 mmol, 1.0 equiv), **I** or **II** (0.24 mmol, 1.2 equiv), Cu^{I} (0.04 mmol, 20 mol%), in MeOH (0.4 mmol) at 70 °C for 2 h. [b] Determined by ^{1}H NMR spectroscopy based on the starting material. [c] Determined by ^{19}F NMR spectroscopy using fluorobenzene as an internal standard.

Table 4.5.1 Optimisation of trifluoromethylating reagent.

The reaction of (2-phenylallyl)trimethylsilane (**231**) and Togni reagent **I**, (1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one), or Togni reagent **II,** (3,3-dimethyl-1-(trifluoromethyl)-1,2-benzodioxol), under the similar conditions as our initial experiments gave the desired product **231a** in high conversion. Yields were determined by ^{19}F NMR spectroscopy using fluorobenzene as an internal standard. Use of Togni reagent **I** under the standard conditions at room temperature afforded the desired product **231a** in 85% conversion and 67% yield (Table 4.5.1, entry 1). Increasing the temperature to 70 °C was beneficial for the reaction, improving both the conversion and yield to 89% and 73% respectively (Table 4.5.1, Entry 2). Togni reagent **II** was less efficient than **I**; however, it nonetheless gave the product in 51% yield (Table 4.5.1, Entries 2 and 3). Increasing the amount of the trifluoromethylating reagent **I** did not improve the yield, and formation of unidentified byproducts was observed (Table 4.5.1, entry 4). When the reaction was carried out under the standard conditions in the absence of CuCl, no product was detected (Table 4.5.1, entry 5). The formation of **231a** as a function of time was monitored by ^{1}H and ^{19}F NMR spectroscopy in deuterated methanol (CD_3OD) with Togni reagent **I** and CuCl at room temperature. This revealed that the transformation occurred rapidly during the first 5 minutes, reaching a maximum after 20 minutes. After 3 hours, the reaction carried on slowly without significant progress.



Scheme 4.5.2 Rate profile with substrate **231** under the trifluoromethylation conditions.

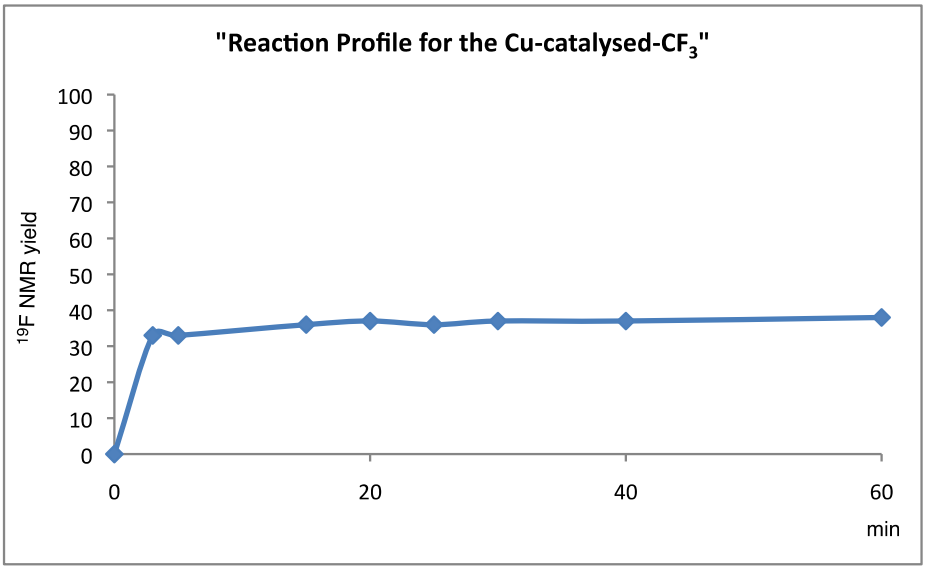
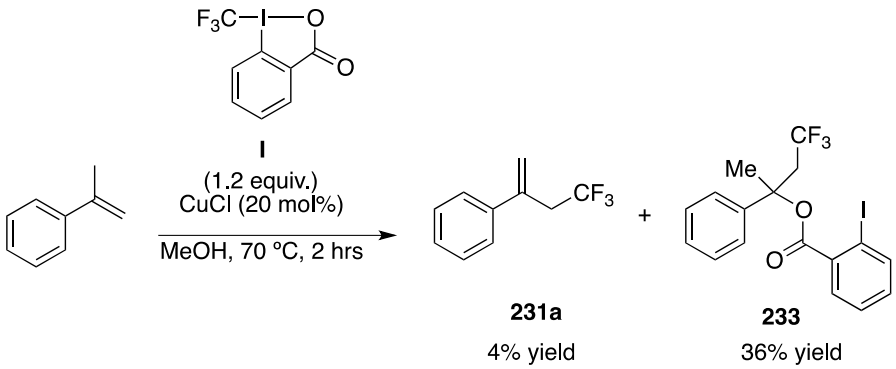


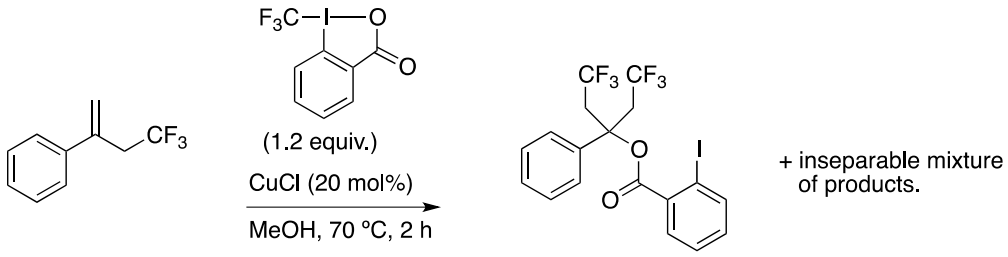
Figure 4.5.1 Reaction progress over time under the standard trifluoromethylation conditions.

The results with substrate **231** demonstrated that silyl-activated alkenes could be used to access allylic–CF_3 products. However, at this stage, it was necessary to examine the role of the silyl group in more detail, in terms of its influence in controlling the regiochemical course of the trifluoromethylation reaction. A control experiment was carried out under the standard conditions in which α–methylstyrene, Togni reagent **I** and 20 mol% CuCl were combined in MeOH at 70 °C. The main product **233** was isolated in 36%, along with only 4% of the desired product **231a** (Scheme 4.5.3).



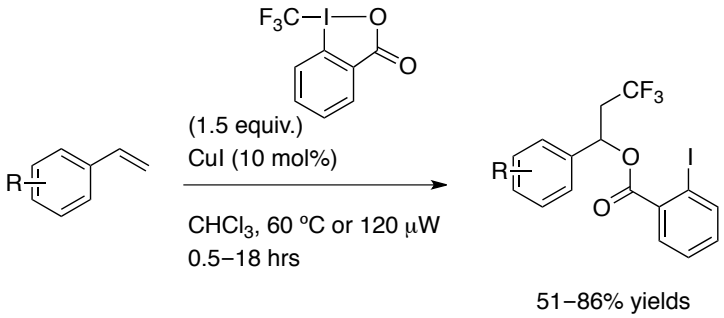
Scheme 4.5.3 Control experiment to demonstrate the importance of the silyl group.

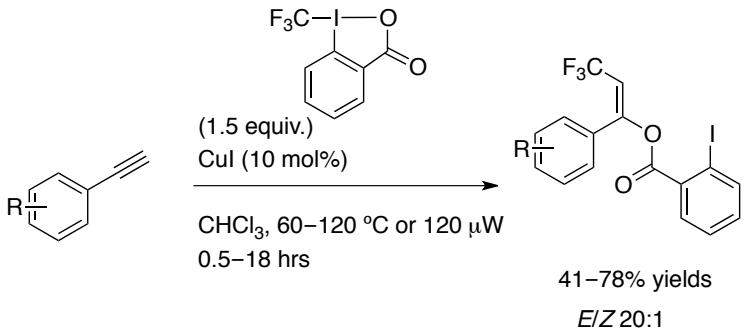
When the isolated product, 4,4,4-trifluorobut-1-en-2-yl)benzene (**231a**), was further exposed to the trifluoromethylating conditions, Togni reagent **I** (1.2 equivalents), CuCl (20 mol%), in MeOH, a complex mixture of products was formed. By ^{1}H NMR analysis, the vinylic protons were not observed and by ^{19}F NMR, a new triplet was observed at -60.4 ppm with a coupling constant $^{3}J_{F\text{-}H}$ = 9.5 Hz. By mass spectrometry, this new product was tentatively assigned as the bis-trifluoromethylated product.



Scheme 4.5.4 Formation of bis-trifluoromethylated product.

These results are in agreement with Szabó's observations[166] on the trifluoromethylation of alkenes and alkynes under copper catalysis (Scheme 4.5.5). In his work, reactions were carried out at temperatures from 60 °C to 120 °C in the presence of Togni reagent **I** and CuI (10 mol%) in chloroform. When the reaction was run at high temperatures (100–120 °C), the yields dropped substantially, probably due to the limited thermostability of the Togni reagent **I**.[141a]

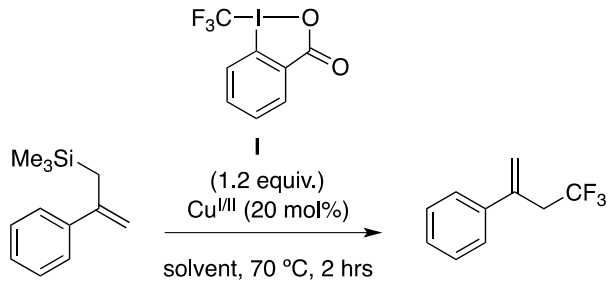




Scheme 4.5.5 Trifluoromethylation by copper-catalysed addition of Togni reagent **I** to alkenes and alkynes.

Regarding the mechanism, the authors suggested that the reaction proceeded *via* a radical mechanism. The addition of 2,2,6,6-tetramethyl-1-piperidinyl (TEMPO), a radical scavenger, to the standard conditions completely inhibited the reaction. Interestingly, the reaction was accelerated with substrates containing electron-donating groups (*e.g.*, methoxy) at the *p*-position.

Collectively, our results and those of Szabó showcase the importance of the silyl group for accessing the desired allylic–CF_3 products. Having demonstrated the importance of the silyl group, we next carried out further optimisation of the reaction with substrate **231** with respect to the Cu salt, and solvent (Table 4.5.2).



Entry[a]	Cu Source	Solvent	Conv. (%)[b]	Yield (%)[b]
1	CuI	MeOH	100	32
2	$[Cu(OTf)]_2PhH$	MeOH	100	37

3	$[(MeCN)_4Cu]PF_6$	MeOH	100	55
4	CuTc	MeOH	75	71
5	$CuCl_2$	MeOH	90	28
6	CuCl	*t*-BuOH	61	39
7	CuCl	DCM	81	51
8	CuCl	DMF	87	51
9	CuCl	toluene	86	22
10	CuCl	MeOH/ *i*-Pr_2NEt (1.2)	94	47

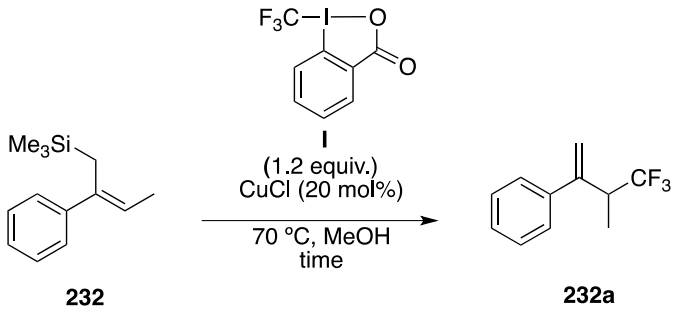
[a] **231** (0.2 mmol, 1.0 equiv), **I** (0.24 mmol, 1.2 equiv), $Cu^{I/II}$ salt (0.04 mmol, 20 mol%), solvent at 70 °C for 2 h. [b] Isolated yield.

Table 4.5.2 Optimisation of the $Cu^{I/II}$ source and solvent,.

Having already established the optimal temperature (70 °C), CF_3 source and quantity of Togni reagent **I** (1.2 equiv.), alternative copper catalysts were next examined. CuI, $[Cu(OTf)]_2C_6H_6$, CuTc and $[(MeCN)_4Cu]PF_6$ led to 100% conversion but gave only moderate yields ranging from 32% to 55% (Table 4.5.2, Entries 1–3). CuTc was as effective as CuCl as the catalyst, affording the desired product in 71% yield and 75% conversion; however, CuTc is expensive compared to CuCl or CuI (Table 4.5.2, Entries 1–4). $CuCl_2$ gave 90% conversion, but the desired product was obtained in a poor yield of 28% yield (Table 4.5.2, Entry 5). Alternative solvents, such as dichloromethane (DCM), *N*,*N*-dimethylformamide (DMF), *t*-BuOH and toluene, did not improve the reaction yield (39–51%) (Table 4.5.2, Entries 6–9). The addition of *N*,*N*-diisopropylethylamine (DIPEA) did not improve the yield, giving only 47% yield of the desired product (Table 4.5.2, Entry 10).

The above optimisation studies led to the identification of the optimal reaction conditions, 20 mol% CuCl and 1.2 equiv Togni reagent **I** in MeOH at 70 °C, for this novel method of achieving trifluoromethylation of (2-phenylallyl)trimethylsilane. These conditions led to the formation of (4,4,4-trifluorobut-1-en-2-yl)benzene in high conversion and good isolated yield (73%) (Table 4.5.1, Entry 2). This result encouraged us to explore the potential application of this methodology to create stereogenicity in the $C(sp^3)$–CF_3 bond-forming step. Thus, it was

envisioned that the use of allylsilanes could enable access to branched allylic–CF_3 moieties. To test this hypothesis, (*Z*)-trimethyl(2-phenylbut-2-en-1-yl)silane was selected for validation studies.

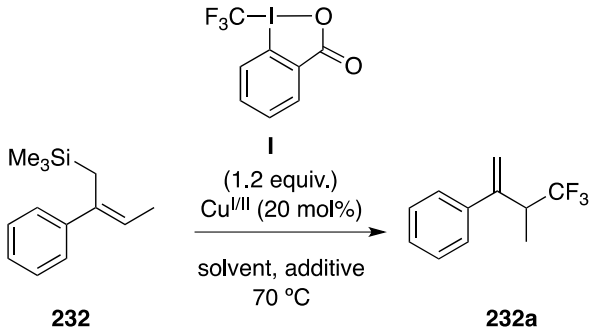


Entry[a]	Metal salt	Time (h)	Temp (°C)	Yield (%)[b]
1	none	12	rt	NR[c]
2	CuCl	20	70	53
3	CuCl	2	70	53

[a] **232** (0.25 mmol), **I** (0.30 mmol, 1.2 equiv), CuCl (0.05 mmol, 20 mol%), MeOH (0.5 mL). [b] Isolated yield.

Table 4.5.3 Reaction of allylsilane **232** with Togni reagent **I** under different conditions.

Despite the fact that the alkene in substrate **232** is more electron-rich than that of allylsilane **231**, the yield was found to be lower under identical reaction conditions (Table 4.5.1, Entry 2 versus Table 4.5.3, Entry 3). This reactivity difference could be attributed to the γ-substituent on allylsilane **232**, which adds steric hindrance as the CF_3 source approaches the alkene. Therefore, different Cu sources, solvents and additives were examined in this reaction (Table 4.5.4).



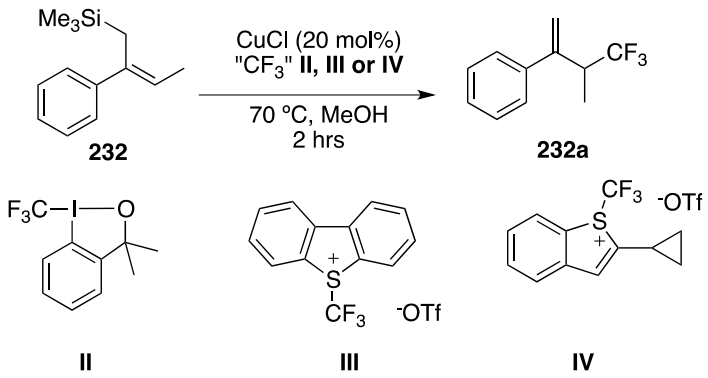
Entry[a]	Metal salt	"CF_3" (equiv)	Solvent	Time (h)	Yield (%)[b]
1	CuI	**I** (1.2)	MeOH	20	50
2	$[(MeCN)_4Cu]PF_6$	**I** (1.2)	MeOH	17	23
3	CuTC	**I** (1.2)	MeOH	20	17
4	$[Cu(OTf)]_2C_6H_6$	**I** (2.0)	MeOH	2	14
5	$CuCl_2$	**I** (1.2)	MeOH	20	12
6	CuOAc	**I** (1.2)	MeOH	20	7
7	CuCl	**I** (1.2)	DMF	20	34
8	CuCl	**I** (1.2)	DMAc	20	13
9	CuCl	**I** (1.2)	*i*-PrOH	20	17

[a] **232** (0.25 mmol), **I** (0.30 mmol, 1.2 equiv), $Cu^{I/II}$ (0.05 mmol, 20 mol%), in solvent (0.5 mL) at 70 ˚C for 2 h. [b] Isolated yield.

Table 4.5.4 Screening of $Cu^{I/II}$ sources, solvents and additives.

By exploring other Cu sources (Table 4.5.4, Entries 1–6), it was found that the desired product could be isolated in up to 50% yield when CuI was used. Cu species such as $[Cu(OTf)]_2C_6H_6$, CuTc (copper(I)-thiophene-2-carboxylate), $[(CH_3CN)_4Cu]PF_6$, $CuCl_2$ and CuOAc, on the other hand, afforded **232a** in low yields (7–23%) (Entries 2–6). Use of $CuCl_2$, a stronger Lewis acid, led to a 12% yield, substantially lower than with CuCl (53% yield). 2-Phenylbutene was observed as a side product, particularly when using $[(CH_3CN)_4Cu]PF_6$ as the catalyst. This could be formed due to the presence of fluoride anions and the use of a protic solvent, which together could induce protodesilylation.

Our optimisation studies also revealed that methanol was the best solvent; aprotic solvents such as DMF or DMAc gave poor yields (13–34%), and *i*-PrOH gave 17% yield (Table 4.5.4, Entries 1, 7–9). Other electrophilic CF_3 sources such as Togni reagent **II**, Umemoto reagent **III** and Shibata reagent **IV**, were also explored but were found to be ineffective (Table 4.5.5)



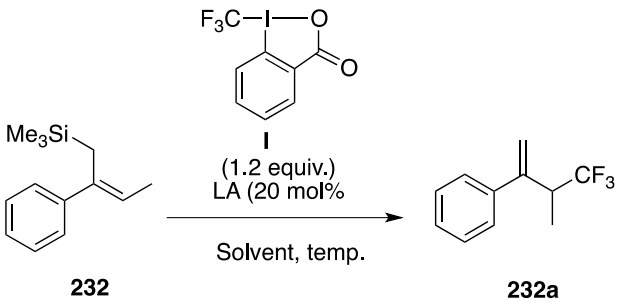
Entry	"CF_3" (equiv)	Yield (%)[b]
1	**II** (1.2)	29
2	**III** (1.2)	ND[c]
3	**IV** (1.2)	ND[c]

[a] **232** (0.25 mmol), "CF_3" (0.30 mmol, 1.2 equiv), in solvent (0.5 mL) at 70 °C for 2 h. [b] Isolated yield. [c] Decomposition.

Table 4.5.5 Screening of trifluoromethylating reagents.

Togni reagent **II** was less efficient than **I**, yielding only 29% of the desired product (Table 4.5.5, entry 1). Sulfonium salts **III** and **IV** favoured protodesilylation, possibly due to the counteranion.

Having recognised the activation of the Togni reagent by copper salts, a series of alternative Lewis acids were tested with the model substrate **232**.



Entry[a]	Lewis acid	Solvent	Time (h)	Temp (°C)	Yield (%)[b]
1	$SnCl_4$	CH_2Cl_2	24	rt	44
2	$BF_3{\cdot}Et_2O$	CH_2Cl_2	24	rt	NR
3	$Sm(OTf)_4$	CH_2Cl_2	24	rt	NR
4	$Fe(OAc)_2$	MeOH	2	70	52

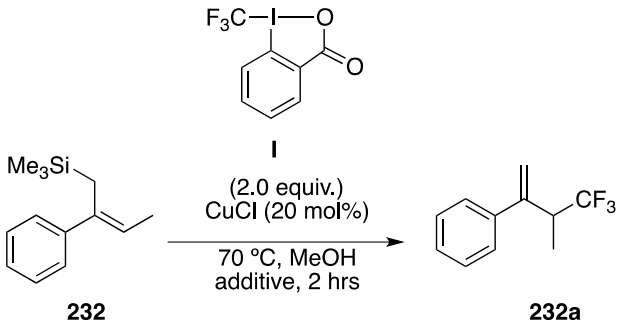
[a] **232** (0.25 mmol), **I** (0.30 mmol, 1.2 equiv), LA (0.05 mmol, 20 mol%), in solvent (0.5 mL) for 24 h. [b] Isolated yield.

Table 4.5.6 Screening of Lewis acids under the trifluoromethylating conditions.

Interestingly, when $BF_3{\cdot}Et_2O$ or $Sm(OTf)_4$ (non-redox-active Lewis acids) were evaluated as catalysts, the desired product was not observed (Table 4.5.6, Entries 2 and 3). $SnCl_4$ and $Fe(OAc)_2$, on the other hand, were capable of promoting the trifluoromethylation reaction in moderate yields (44% and 52%, respectively), providing similar efficiency as CuCl, which gave 53% yield. Considering only these observations, it seems that Togni reagent **I** is being activated by Cu(I) through an SET process rather than *via* Lewis acid activation.

Having established suitable trifluoromethylation conditions for the synthesis of the branched allylic–CF_3 product, our attention next turned to suppressing the protodesilylation process. We supposed that an *in situ* generated Brønsted acid like 2-iodobenzoic acid could decompose the starting material under the reaction conditions. Thus, it was reasoned that the use of an organic base would prevent the formation of by-products, such as 2-phenylbutene. Pleasingly, using *i*-Pr_2NEt or Et_3N, there was a significant improvement in the isolated yield up to 75%

(Table 4.5.7, Entries 1–2). Other bases such as DMAP, DBU or TMEDA did not improve the reaction.



Entry	Metal salt	Additive	Solvent	Yield (%)[b]
1	CuCl	*i*-Pr_2NEt	MeOH	75
2	CuCl	Et_3N	MeOH	61
3	CuCl	DMAP	MeOH	trace
4	CuCl	DBU	MeOH	14
5	CuCl	TMEDA	MeOH	23

[a] **232** (0.25 mmol), **I** (0.30 mmol, 1.2 equiv), CuCl (0.05 mmol, 20 mol%), in solvent (0.5 mL) at 70 ˚C for 2 h. [b] Isolated yield.

Table 4.5.7 Screening of organic bases in the trifluoromethylation reaction.

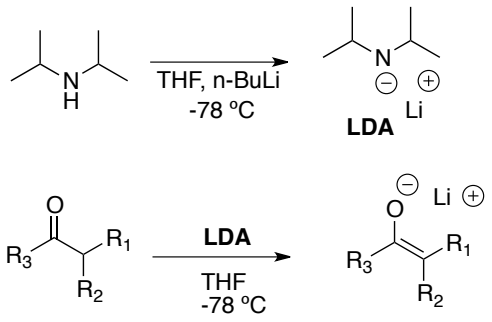
Having established the optimal conditions for the trifluoromethylation reaction with two substrates, (2-phenylallyl)trimethylsilane **231** (1.2 equiv. Togni reagent **I**, 20 mol% CuCl, MeOH, 70 °C) and (*Z*)-trimethyl(2-phenylbut-2-en-1-yl)silane **232** (2.0 equiv. Togni reagent **I**, 20 mol% CuCl, MeOH 70 °C), we next sought to test the scope of the reaction. To this end, a library of branched allylsilanes was synthesised.

4.6 Design of Linear, Branched and Cyclic Allylsilanes.

Synthesis of enol phosphates.

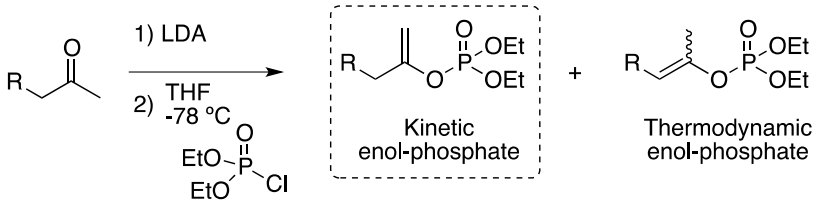
Linear and branched allylsilanes were synthesised following the same two-step procedure described previously. First, the ketone of interest was treated with lithium diisopropylamide

(LDA), which was formed by treating a cooled (-78 °C) tetrahydrofuran (THF) solution of diisopropylamine with *n*-butyllithium. LDA has a pK_a value of 36. Therefore, it was suitable for the deprotonation of carbonyl compounds at the α-position (Scheme 4.6.1).



Scheme 4.6.1 Preparation of the enolates with LDA solution.

Once the enolate was formed, diethyl chlorophosphate was added very slowly at -78 °C. The reaction was allowed to warm to room temperature, giving the desired enol phosphate. The major issue in this transformation is the selectivity (kinetic *versus* thermodynamic), however, by controlling the temperature and solvent (THF) the kinetic product was favoured over the thermodynamic product.[167]



Scheme 4.6.2 Formation of the kinetic enol-phosphate.

Enol phosphates bearing aryl substituents were isolated in moderate yields (55–72%), but a clear effect was not observed on reactivity due to the *p*-substitution (EDG or EWG), such as -OMe, -Me, -F, -CF_3 (Table 4.6.1, Entries 1–4). The reaction proceeded with excellent *E*/*Z* selectivity (1:20). The stereochemistry was determined by analysis of Nuclear Overhauser

Effects (NOEs) *via* NMR spectroscopy. For the assigment of the stereochemistry of the enol phosphates, strong NOE enhancements were observed between the protons **Ha** and **Hb**, indicating that these structures featured a *Z*-geometry.

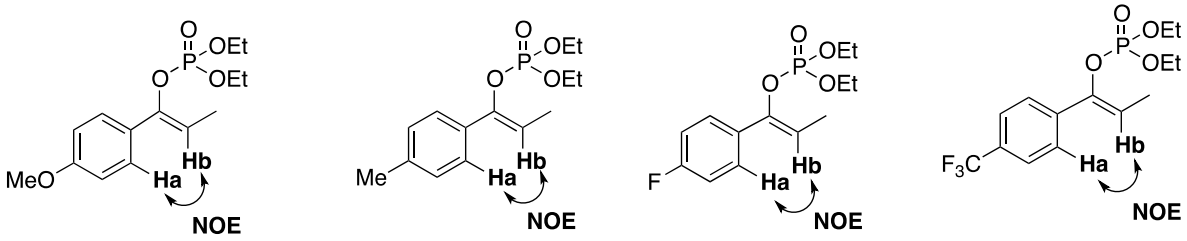
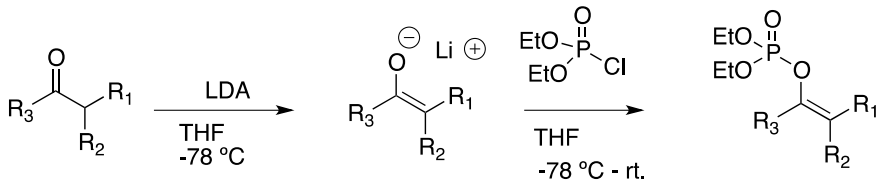
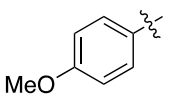
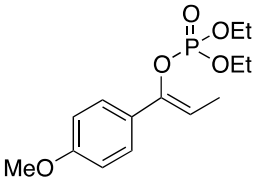
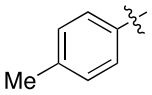
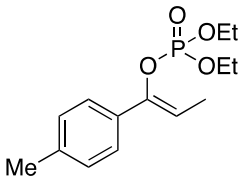
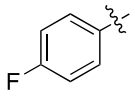
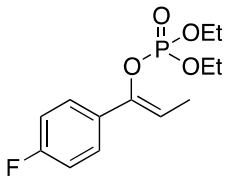
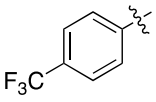
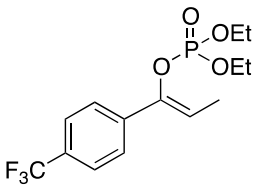
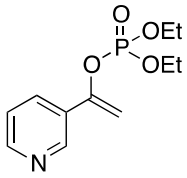
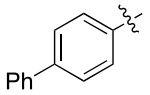
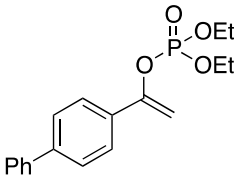
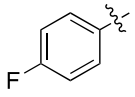
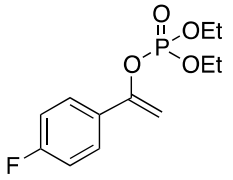
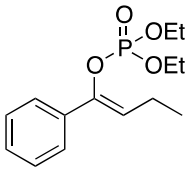
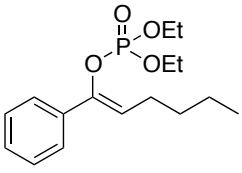


Figure 4.6.1 Key NOE data for the assigment of the stereochemistry.

Diethyl [1-(pyridine-3-yl)vinyl] phosphate (Table 4.6.1, Entry 5) was isolated in a moderate yield of 51%. Terminal enol phosphates (R_1 and R_2 = H) were synthesised in good yields (up to 84%). Variation of the R_1 substituents (Et, or *n*-Bu) was tolerated (68–79%) (Table 4.6.1, Entries 8, 9), as was replacement of the aryl group at R_3 with an alkyl substituent (50–75%) (Table 4.6.1, Entries 10–12).



Entry	R_3	R_2	R_1	Product	Yield % (*E*/*Z*)
1		H	Me		55 (1:20)

2		H	Me		66 (1:20)
3		H	Me		66 (1:20)
4		H	Me		72 (1:20)
5		H	H		51
6		H	H		84
7		H	H		67
8		H	Et		79 (1:20)
9		H	*n*-Bu		68 (1:20)

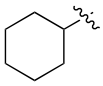
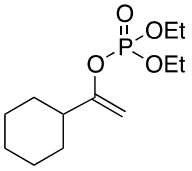
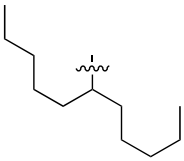
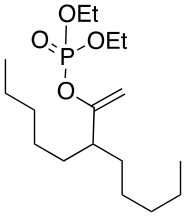
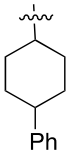
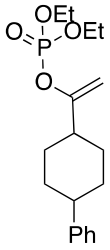
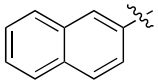
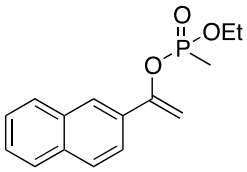
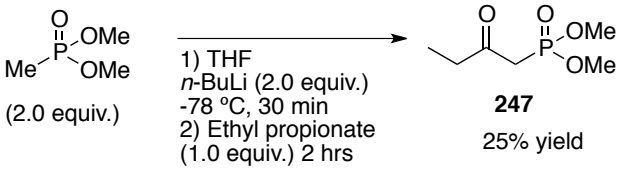
10		H	H		50
11		H	H		75
12		H	H		52
13		H	H		90

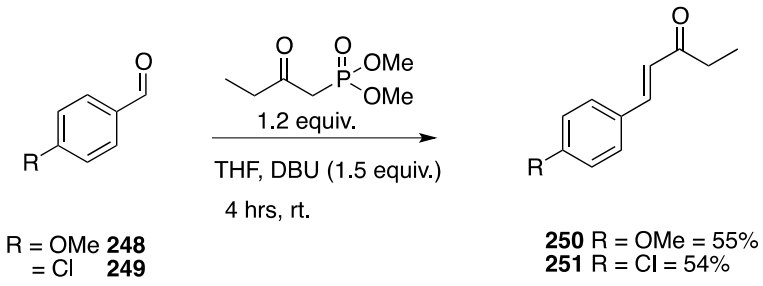
Table 4.6.1 Synthesis of enol phosphates.

Dienol phosphates were next targeted. β-Ketophosphonate **247** was obtained from the corresponding commercially available ester and dimethyl methylphosphonate in the presence of *n*-BuLi in THF at -78 °C. **247** proved to be difficult to purify, requiring distillation, and was isolated in only 25% yield.



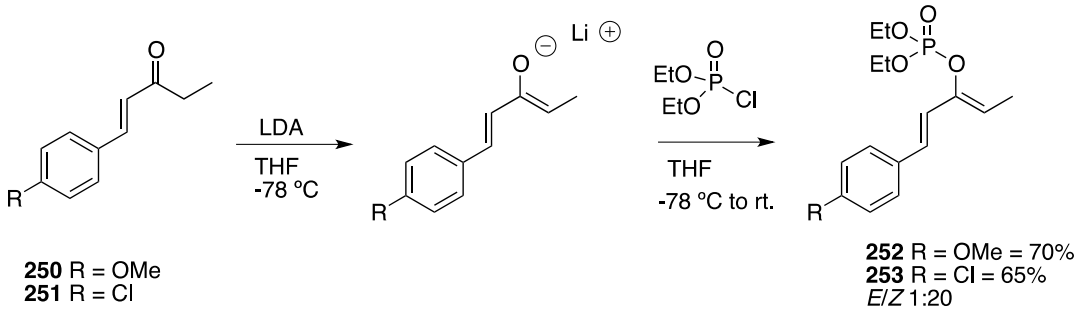
Scheme 4.6.3 Synthesis of β-ketophosphonate.

A Horner–Wadsworth–Emmons reaction between β-ketophosphonate **247** an aldehydes **248** and **249** gave α,β-unsaturated ketones **250** and **251** in moderate yields (55 and 54% yield, respectively) (Scheme 4.4.1). The reaction was carried out under anhydrous conditions in the presence of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene). In the synthesis of **250**, several unidentified side products were observed, and the starting material was fully consumed. The methoxy group at the *p*-position of the aryl group might be the responsible for the higher reactivity. However, 4-chlorobenzaldehyde presented lower reactivity under the same reaction conditions, as a result, starting material was observed from the crude reaction mixture by ^{1}H NMR. In both cases, the *E*-isomer was formed, this stereochemical outcome was confirmed by ^{1}H NMR spectroscopy. The two vinylic protons have a coupling constant $^{3}J_{H\text{-}H}$ of 16 Hz.



Scheme 4.6.4 Formation of α,β-unsaturated ketones.

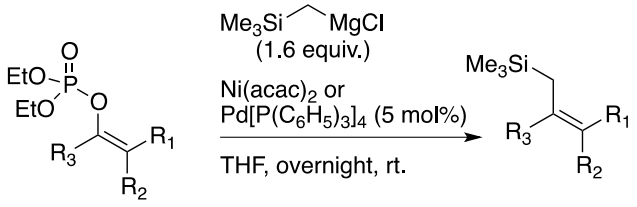
Enol phosphates **252** and **253** were synthesised according to the previously described procedure. These substrates were found to be unstable at room temperature, and decomposition was observed when the compounds were stored at room temperature overnight. Therefore, α,β-unsaturated enol phosphates **252** and **253** were stored at 0°C.



Scheme 4.6.5 Synthesis of α,β-unsaturated enol phosphates.

Synthesis of Allylsilanes

Allylsilanes were synthesised from the corresponding enol phosphates using a procedure developed by Kumada. Nickel acetylacetonate ($Ni(acac)_2$)-catalysed cross coupling of the enol phosphates with trimethylsilylmethylmagnesium chloride gave the desired allylsilanes. Tetrakis(triphenylphosphine)palladium(0) $[P(C_6H_5)_3]_4Pd$ has also been found to be a suitable catalyst for this reaction. The enol phosphates were dissolved in diethyl ether, and then the catalysts, $Ni(acac)_2$ or $[P(C_6H_5)_3]_4Pd$ (5 mol%), were added. Next, a 1 M solution of trimethylsilylmagnesium chloride in diethyl ether was gradually added, and the reaction was stirred at room temperature for 15 hours.



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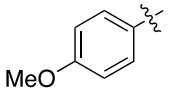
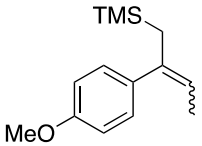
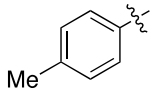
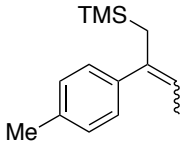
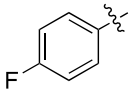
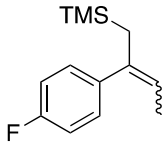
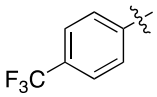
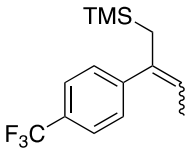
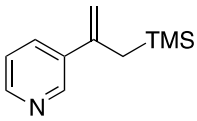
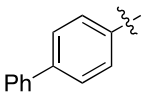
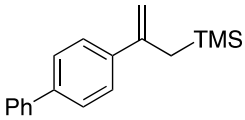
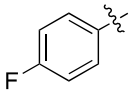
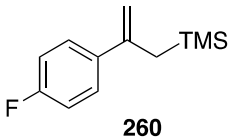
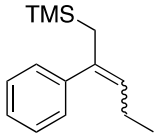
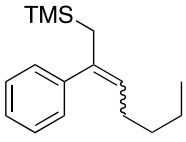
1		H	Me	 **254**	33 (1:1.5)

2		H	Me	 **255**	66 (1:1.1)
3		H	Me	 **256**	68 (1.3:1)
4		H	Me	 **257**	49 (1:1.1)
5		H	H	 **258**	33
6		H	H	 **259**	38
7		H	H	 **260**	67
8		H	Et	 **261**	66 (1:1.8)
9		H	*n*-Bu	 **262**	61 (1:1.4)

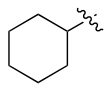
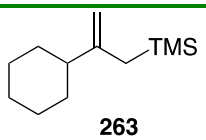
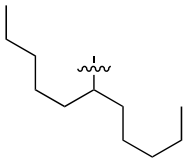
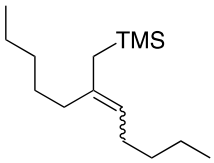
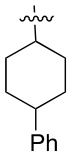
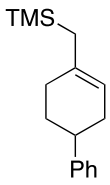
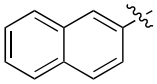
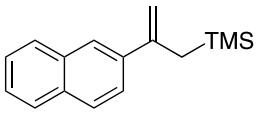
10		H	H	 **263**	51
11		H	H	 **264**	61 (1:1.5)
12		H	H	 **265**	37
13		H	H	 **266**	49

Table 4.6.2 Synthesis of branched and linear allylsilanes.

In this way, a diverse collection of substrates was synthesised in order to assess the scope of the trifluoromethylation reaction. Enol phosphates featuring electron-withdrawing and electron-donating groups at the *para* position of the aromatic ring were synthesised following the Kumada procedure. After careful purification by silica gel chromatography, the desired allylsilanes were isolated in low to moderate yields (33–68%), with E/Z isomeric ratios between 1:1.1 and 1:3.1 (Table 4.6.2, Entries 1–4). Full consumption of the starting material was observed by ^{1}H NMR analysis of the crude reaction mixture. However, small amounts (<5%) of the corresponding vinylsilane were detected by ^{1}H NMR spectroscopy in most cases (observed as singlets in the region from 5.2 ppm to 5.6 ppm), which complicated purification.

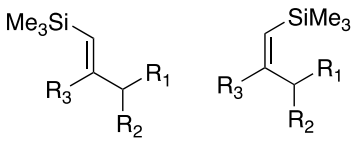


Figure 4.6.2 Vinylsilanes detected as side products.

In addition, allylsilanes bearing Me or OMe groups at the *p*-position were found to be unstable, and decomposition was observed when these compounds were allowed to stand at room termperature for 1 week. In order to avoid decomposition, the allylsilanes were stored at 0 °C.

Figure 4.6.3 depicts the ^{1}H NMR spectrum of a representative product, [2-(4-methoxyphenyl)but-2-en-1-yl]trimethylsilane, **254**. The diagnostic peaks for branched allylsilanes are observed in the regions between 5.0–5.7 ppm and 1.5–2.0 ppm. The vinylic proton (4) couples with the vicinal protons (CH_3), so that a quartet is observed at 5.5 ppm for the major isomer (*Z*), with a coupling constant of $^{3}J_{H\text{-}H}$ = 6.6 Hz. The TMS signal appears at -0.12 ppm for the major isomer.

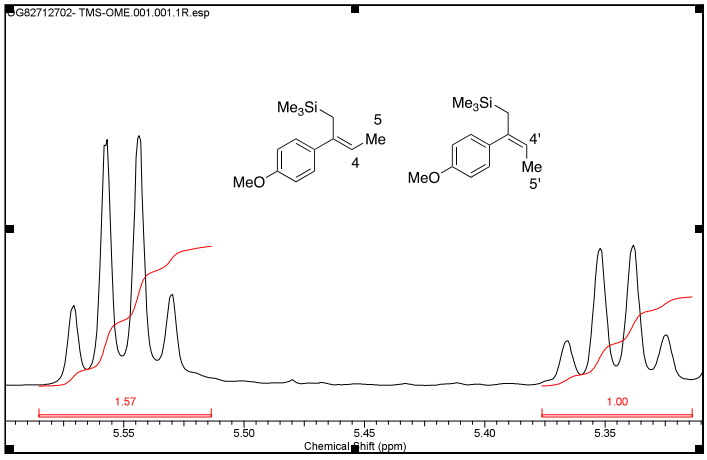


Figure 4.6.3 ^{1}H NMR spectrum of allylsilane **254**.

Diethyl [1-(pyridine-3-yl)vinyl] phosphate was converted to the desired pyridine-containing allylsilane in a low yield of 33%. However, this provided sufficient quantity to study the suitability of this substrate in the trifluoromethylation reaction (Table 4.6.2, Entry 5). Enol

phosphates with terminal alkyl substituents (R_1 = Et and *n*-Bu) gave the corresponding allylsilanes in moderate yields (66 and 61% yield, respectively) as an inseparable mixture of *E*:*Z* isomers (1:1.4 and 1:1.8) (Table 4.6.2, Entries 8, 9). Subjecting the terminal enol phosphates (R_1, R_2 = H) to the coupling conditions led to the formation of the allylsilanes **259** and **260** in moderate yields (38 and 67%, respectively). **259** and **260** are unsubstituted terminal allylsilanes, which we hoped would provide information on the importance of the substitution at the γ-position.

Figure 4.6.4 shows the ^{1}H NMR spectrum of a representative unsubstituted terminal allylsilane, **259**. In this case, the diagnostic peaks appear in the same region as those of **254**, but exhibit a different coupling pattern for the vinylic protons. The two terminal protons appear as singlets at 4.9 and 5.2 ppm; as expected, only one TMS signal is detected at 0 ppm.

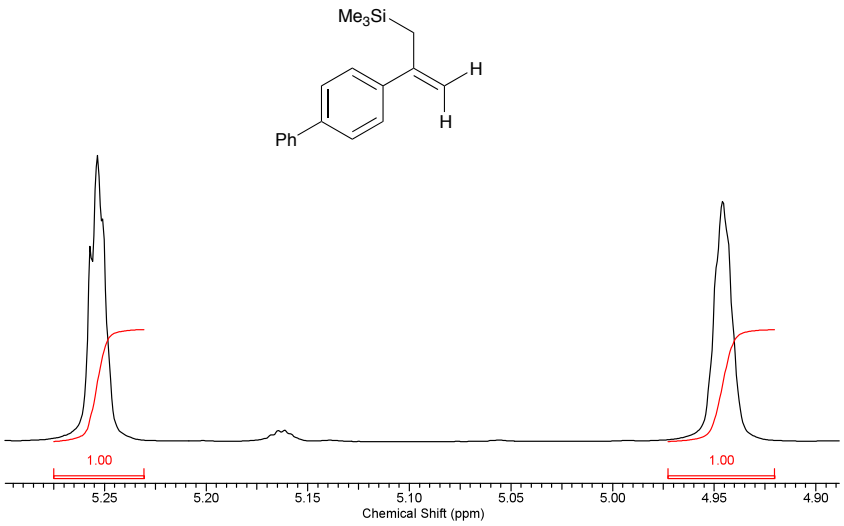
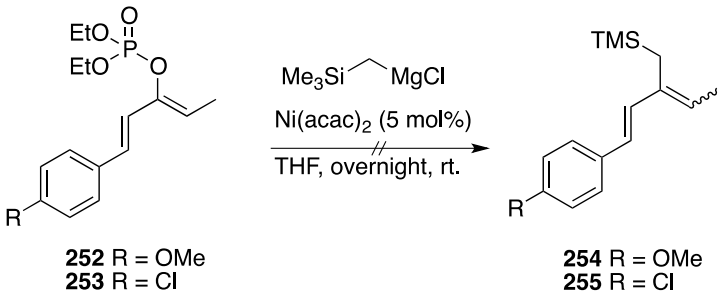


Figure 4.6.4 ^{1}H NMR spectrum of allylsilane **259**.

Substrates featuring alkyl groups at R_3 successfully underwent the Kumada coupling reaction, in moderate yields (Table 4.6.2, Entries 10–12). Substrate **265** was designed in order to study the degree of diastereocontrol in the trifluoromethylation reaction.

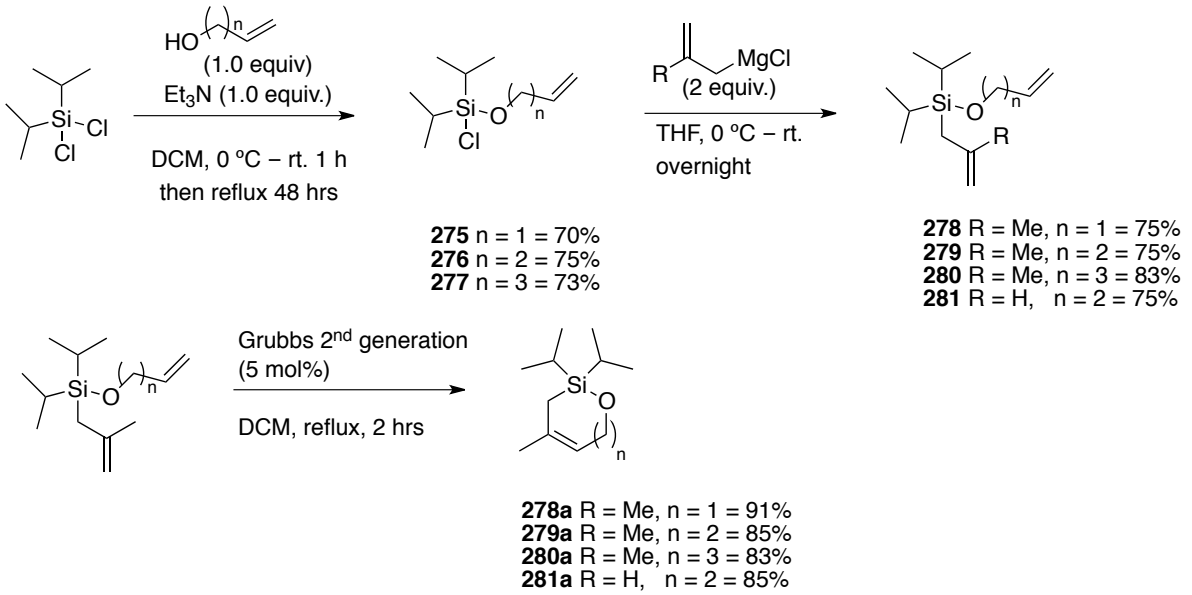
Synthesis of allylsilanes **254** and **255** was also attempted following the previous procedure. However, upon analysis of the crude ^{1}H NMR spectrum, decomposition was observed, leading to a complex mixture of unidentified side products.



Scheme 4.6.6 Kumada coupling reaction with substrates **252** and **253**.

Synthesis of Cyclic Allylsilanes

In order to understand the effect of ring size on reactivity, we also investigate the trifluoromethylation of cyclic allylsilanes. These substrates were prepared following the same procedure previously described in Chapter 2, Section 2.2. The desired model substrates were synthesised in a concise three-step procedure from the commercially available diisopropylsilyl dichloride (Scheme 4.6.7)

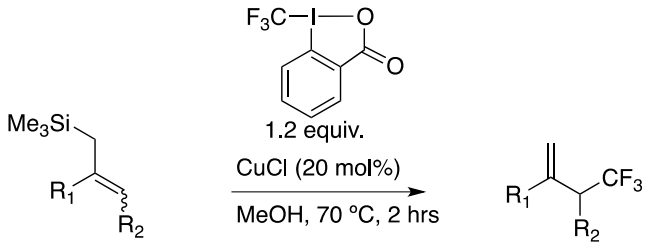


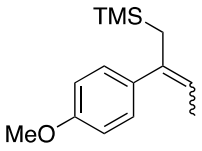
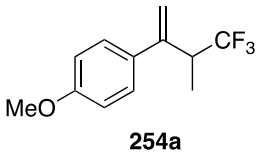
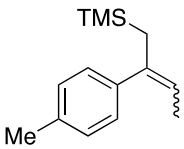
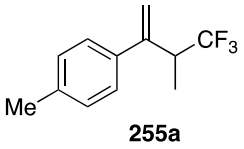
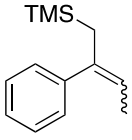
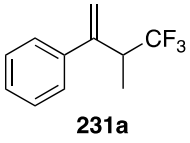
Scheme 4.6.7 Synthesis of six, seven and eight-membered silacycles.

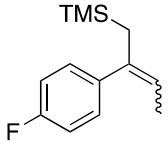
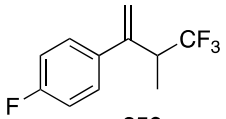
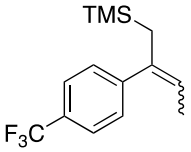
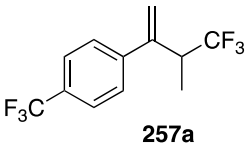
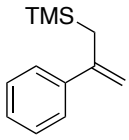
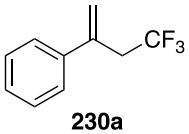
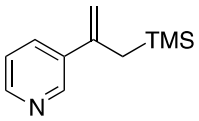
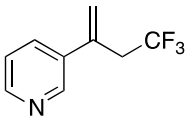
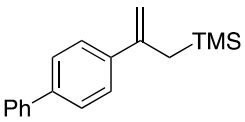
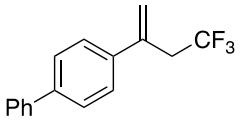
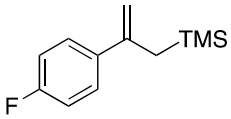
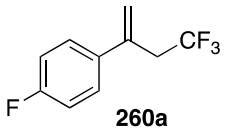
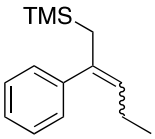
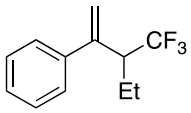
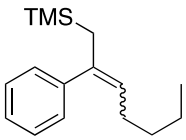
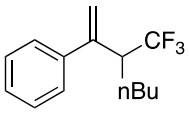
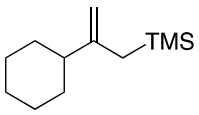
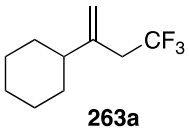
Intermediates **275**–**277** were synthesised from commercially available reagents by the addition of the selected alcohol to a dichlorodiisopropylsilane solution in DCM at 0 °C. After distillation under reduced pressure, the desired alkoxydiisopropylsilyl chlorides were isolated in moderate yields (70–75%). Subsequent addition of a Grignard reagent (2-methylallylmagnesium chloride or allylmagnesium chloride) gave bis-alkenyl compounds **278**–**281** in 75–83% yield. Ring-closing metathesis using the second generation Grubbs catalyst (5 mol%) in dichloromethane (0.01 M) at 40 °C afforded six, seven and eight membered rings **278a**–**281a** in excellent yields (83–91%). Analysis of the crude ^{1}H NMR spectrum, formation of dimerised side products were not observed. Purification of the cyclic products was performed by filtration through a short plug of silica gel.

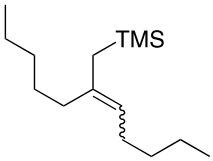
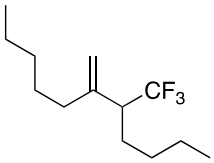
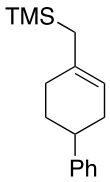
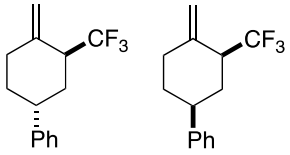
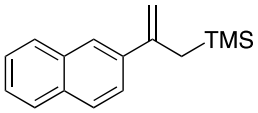
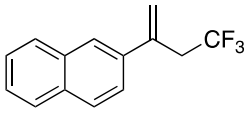
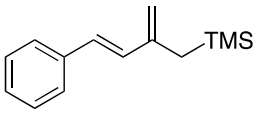
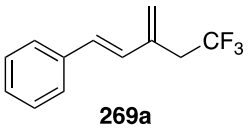
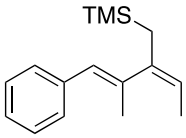
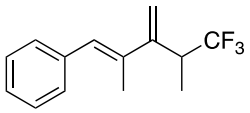
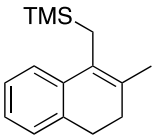
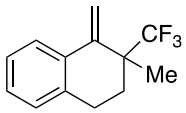
4.7 Trifluoromethylation

With the substrates in hand, the scope and limitations of the trifluoromethylation reaction were assessed. Using the optimised conditions for unsubstituted allylsilanes (1.2 equiv Togni reagent **I** and 20 mol% CuCl in MeOH; see Section 4.3.1) and substituted allylsilanes (2.0 equiv Togni reagent **I**, 20 mol% CuCl and 2.0 equiv *i*-Pr_2EtN in MeOH), allylsilanes substrates **254**–**266** were tested. The general procedure involved stirring the mixture for 2 h at 70 °C, working up the reaction, and purifying the crude mixture by SiO_2 gel column chromatography (Table 4.7.1).



Entry[a]	Substrate	CF_3 equiv. I	Product	Yield [%][b,c]
1		2.0	 **254a**	40
2		2.0	 **255a**	40
3		2.0	 **231a**	75

4		2.0	 **256a**	17
5		2.0	 **257a**	6
6		1.2	 **230a**	70
7		1.2	 **258a**	42
8		1.2	 **259a**	74
9		1.4	 **260a**	59
10		2.0	 **261a**	42 (86)
11		2.0	 **262a**	48 (96)
12		2.0	 **263a**	42

13		2.0	 **264a**	40 (58)
14[f]		1.2	 **265a**	44 *anti*/*syn* 4.6:1
15		1.2	 **266a**	83
16		1.2	 **269a**	84
17[d]		1.2	 **267a**	38 (57)
18[e]		2.0	 **268a**	trace

[a] Reaction conditions: allylsilane (1 equiv), CuCl (20 mol %), CF_3 reagent **I** (1.2 equiv) in MeOH at 70 °C for 2 h on a 0.25–0.5 mmol scale. [b] Yield of isolated product. [c] Numbers in parentheses refer to yields based on recovery of unreacted allylsilane. [d] Reaction time was 12 h. [e] Reaction time was 24 h. [f] Reaction time was 3 h. The d.r. was determined by ^{19}F NMR analysis of the crude mixture.

Table 4.7.1 Trifluoromethylation of allylsilanes under copper catalysis.

Varying the group at the *para* position affected the reactivity of the allylsilanes. With substrates featuring electron-releasing groups (Table 4.7.1, entries 1 and 2), the starting material was predominantly consumed to give unidentified side products. It is believed that electron-donating groups accelerate the desired trifluoromethylation reaction and side

reactions, leading to complicated product mixtures. By ^{1}H and ^{19}F NMR spectroscopy, trifluoromethyl-containing compounds have distinctive diagnostic peaks.

By ^{1}H NMR spectroscopy, the trifluoromethyl group has an influence on the chemical shifts of nearby protons, however the effect is less pronounced than with a fluorine substituent. As a representative example, deshielding of the geminal proton (CH_3-C*H*-CF_3, δ = 3.39 ppm) and the observed qd multiplicity are diagnostic for the presence of the CF_3 group in product **254a**. The multiplicity pattern results from the overlap of the coupling constants $^{3}J_{H–F}$ = 8.8 Hz and $^{3}J_{H–H}$ = 7.3 Hz. This was confirmed by analysis of the shift for the vicinal proton (C*H*$_3$-CH-CF_3, δ = 1.29 ppm), a doublet with a coupling constant $^{3}J_{H-H}$ = 7.3 Hz. In the ^{19}F NMR spectrum, a doublet was observed at δ = -70.62 ppm with a coupling constant $^{3}J_{F-H}$ = 8.8 Hz (Figure 4.7.1).

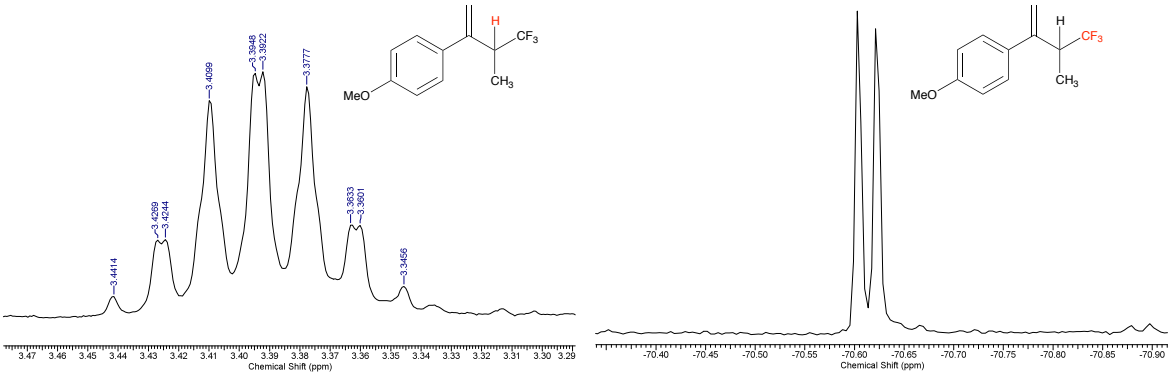


Figure 4.7.1 ^{1}H and ^{19}F NMR spectrum of **254a**.

Substrates bearing EWGs at the *para*-position (–F and –CF_3) gave different result from those with EDGs, giving lower yields and recovery of ~40% of the starting material in both cases (Table 4.7.1, entries 4–5). Excess Togni reagent **I** (2 equiv) and *i*-Pr_2EtN (2 equiv) were used to increase the yield of the branched allyl–CF_3 products. Trifluoromethylation of bulky branched substrates proved to be more difficult than substrates that were unsubstituted at the γ

position, which did not require excess amounts of the Togni reagent. Figure 4.7.2 shows the ^{1}H NMR spectrum of a representative unsubstituted allylic–CF_3 product, **259a**. The diagnostic peaks are as follows: the two terminal alkene protons in the region of 5.5 ppm and the quartet at 3.7 ppm with a coupling constant $^{3}J_{H\text{-}F}$ = 10.5 Hz. In the ^{19}F NMR spectrum, the CF_3 signal is observed as a triplet at -64.4 ppm, with a coupling constant of 10.4 Hz (Figure 4.7.2).

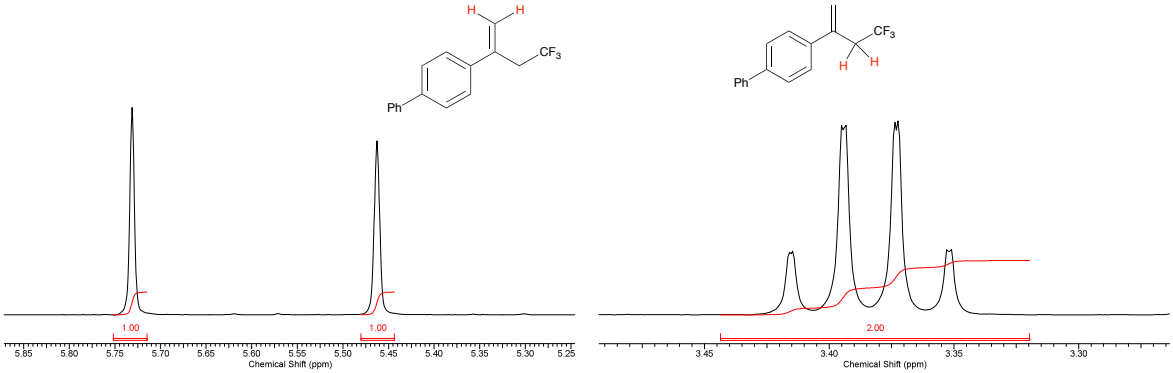


Figure 4.7.2 ^{1}H NMR spectrum of **259a.**

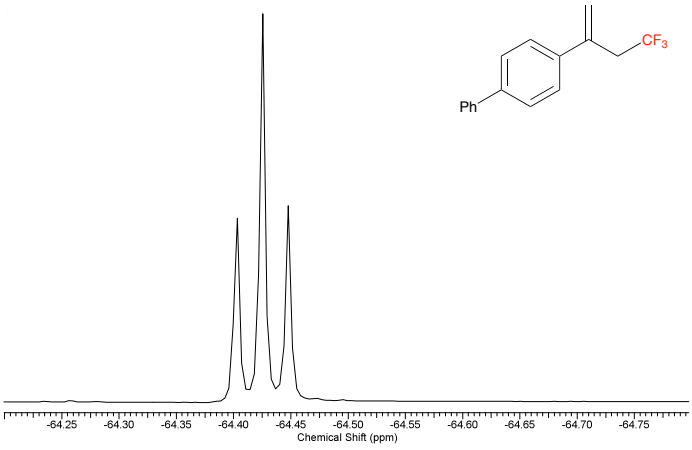
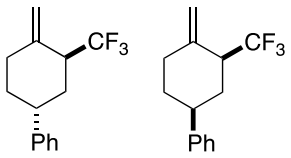


Figure 4.7.3 ^{19}F NMR spectrum of **259a**.

This novel methodology tolerates the presence of a pyridine ring (42% yield, Table 4.7.1, entry 7). Allylsilanes with Et or *n*-Bu substituents at R_1 led to the formation of the corresponding branched allylic–CF_3 products in moderate yields (42 and 48%, respectively) (Table 4.7.1,

Entries 10, 11). Secondary and primary alkyl groups were tolerated at the β-position, giving yields around 40% (Table 4.7.1, Entries 12–13). These transformations required 2 equivalents of Togni reagent **I** in order to maximise yields (as observed with Entries 1–5). These data suggest that β and γ-substitution on the allylsilanes plays a critical role in the trifluoromethylation reaction. Therefore, additional information was sought using other β-substituted substrates in the reaction. 2-Naphthyl and 2-styryl substituted products were isolated in 83% and 84% yields, respectively (Table 4.7.1, Entries 15 and 16). When the 2-styryl allylsilane subunit was further substituted, there was a significant drop in yield of the desired allyl–CF_3 product (38%) (Entry 17). Interestingly, no reaction was observed for substrate **266a** (Table 4.7.1, Entry 18). This result suggests that steric hindrance can limit formation of an quaternary allylic C(sp^3)–CF_3 centre.

In order to assess the level of diasterocontrol in the trifluoromethylation reaction, substrate **265**, which possesses a stereogenic centre proximal to the site of trifluoromethylation, was subjected to the trifluoromethylation conditions. The reaction proceeded with modest diastereocontrol in favour of the *anti* diastereomer (d.r. = 4.6:1) in a moderate yield (44%) (Figure 4.7.4).



anti/*syn* 4.6:1

Figure 4.7.4 Diastereomers **265a.**

The relative stereochemistry of the major diastereomer **265a** was assigned using 2D HMQC (Heteronuclear Multiple-Quantum Correlation), NOESY (Nuclear Overhauser Effect Spectroscopy) and ^{19}F–^{1}H HOESY (Heteronuclear Overhauser Effect Spectroscopy). The

trifluoromethyl group in the molecule allowed the use of heteronuclear NOE and HOESY experiments. First, protons Ha–Hf were assigned by combining NMR experiments, and as a result, Hc was assigned to the triplet at 3.05 ppm (J = 13.0 Hz) in the ^{1}H NMR (Figure 4.7.5). According to the literature, the cyclohexane axial–axial coupling constant is 13.1 Hz.[168]

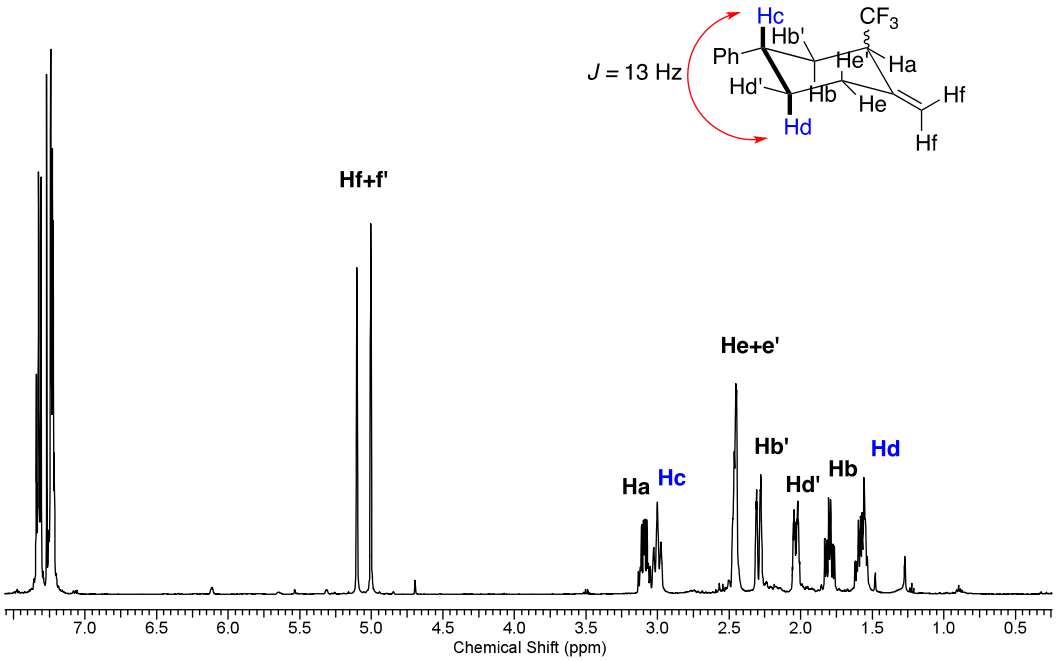


Figure 4.7.5 ^{1}H NMR spectrum of **265a**.

NOESY and HOESY experiments provided complementary data for the elucidation of the relative stereochemistry. The key enhancements at Hc, Hb, Hd' and Hb protons corroborated with the assignment of the phenyl group, Hd' and Hb' at equatorial positions (Figure 4.7.6). HOESY experiments revealed strong correlations between the CF_3 group with protons Hb' and Hc. However, no response was observed between the CF_3 group and the Hd, Hb and Hd' protons (Figure 4.7.7). This data indicated that the phenyl ring must be *anti* to the CF_3 group.

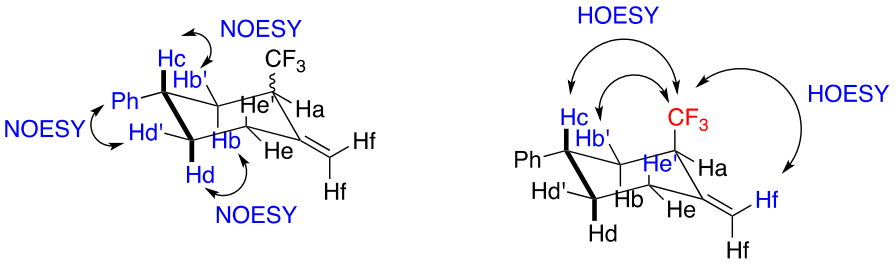


Figure 4.7.6 Correlations observed with NOESY and HOESY experiments.

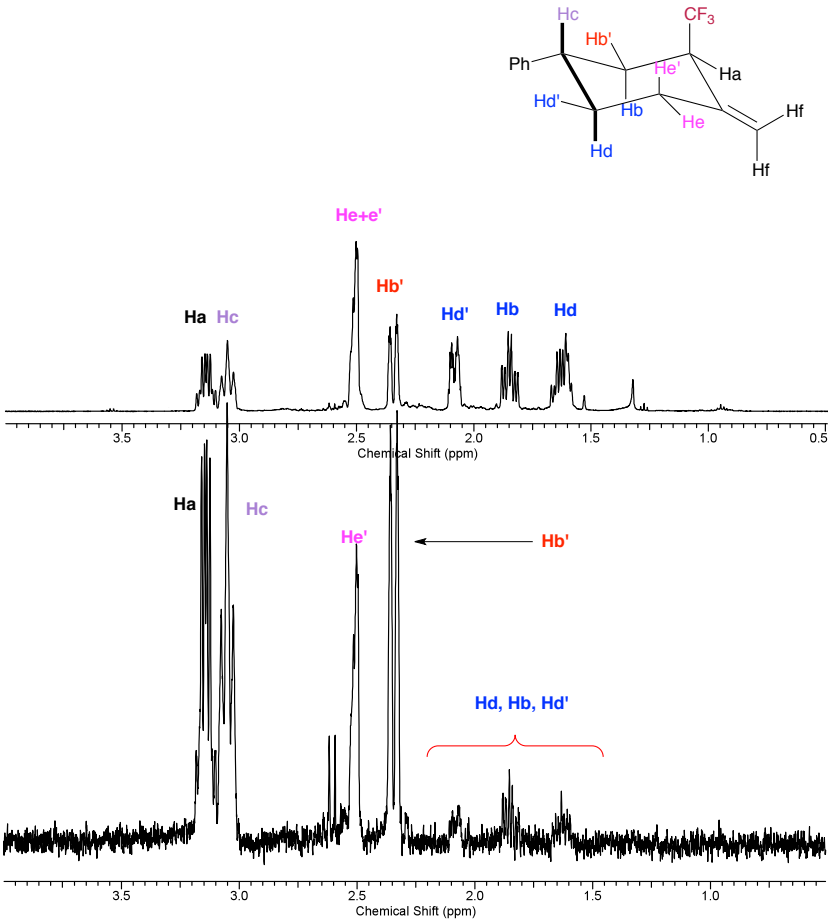
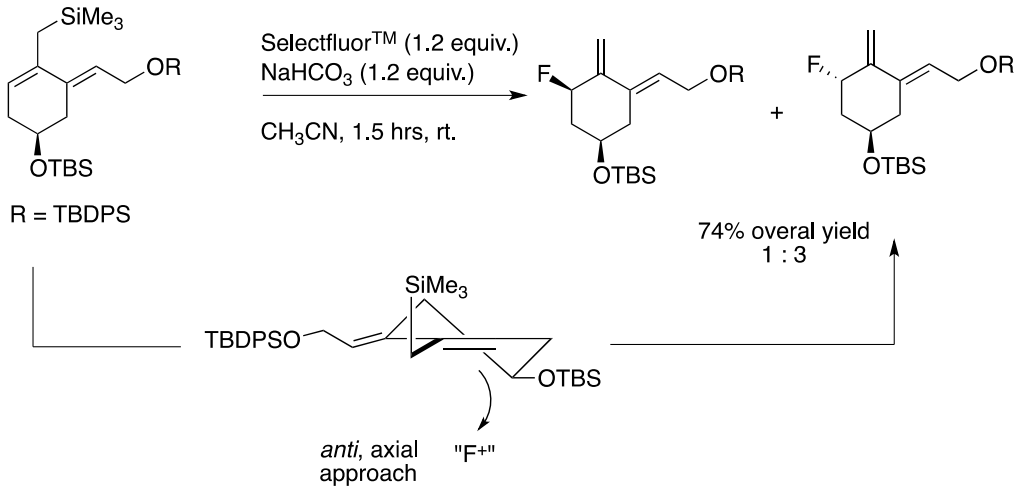


Figure 4.7.7 ^{19}F–^{1}H HOESY spectroscopy of **265a**.

In the ^{19}F NMR spectrum, the major diastereomer was observed at -66.5 ppm (d, J = 11 Hz). Two-dimensional ^{19}F–^{1}H HOESY spectroscopy revealed correlations between the CF_3 group and the Hb' and Hc protons. These NMR results were supportive evidence that the CF_3 group

and the Hb' and Hc protons adopt a *syn* conformation. It was thus reasoned that the phenyl ring must be *anti* to the CF_3 group.

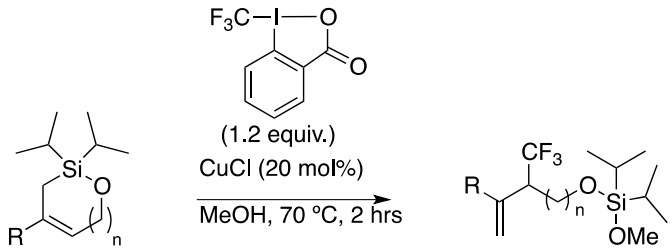
In previous work, it was shown that a structurally related allylsilane, when subjected to electrophilic fluorination, led to an advanced intermediate of an 1α-fluoro vitamin D_3 analogue with a similar sense and level of diastereocontrol (d.r. = 3:1 in favour of the *anti* isomer).[163] The observed level of diastereocontrol was explained by considering the half-chair conformation of the allylsilane. The electrophilic F^+ reagent preferentially approaches along an axial trajectory, which is *anti* to silicon, leading to the formation of the major product. The other possibility is axial approach *syn* to the silyl group, leading to the formation of the minor product. Along this second trajectory, the F^+ reagent encounters substantial steric hindrance, therefore, we postulate that the present trifluoromethylation reaction of substrate **265** under copper catalysis is governed by the same principles.

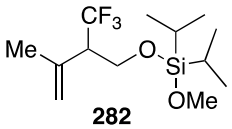
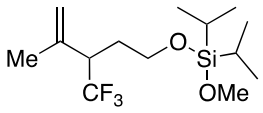
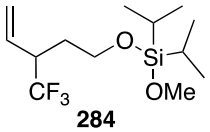
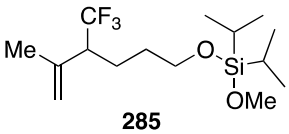


Scheme 4.7.1 Preferential *anti* axial approach.

Cyclic Allylsilanes.

Conformational analysis of different cycloalkenes has been the topic of numerous previous research papers.[169] Conformational analysis of silicon containing rings (cyclic allylsilanes), on the other hand, has not been reported. As discussed in Chapter 1, C–Si bonds are longer (1.86 Å) than C–C bonds(1.53 Å). As a result, it is reasonable to question whether the conformational behaviour of cyclic allylsilanes (6-, 7- and 8-membered rings) differs from that of cycloalkenes. Conformationally restricted cyclic substrates **278a–281a** were used to investigate the fate of the silyl group under copper catalysis.



Entry	R	n	Product	Yield (%)[b]
1	Me (**278a**)	1	 **282**	ND[c]
2	Me (**279a**)	2	 **283**	46%
3	H (**281a**)	2	 **284**	Trace[e]
4	Me (**280a**)	3	 **285**	41%

[a] Reaction conditions: allylsilane (1 equiv), CuCl (20 mol %), CF_3 reagent **I** (1.2 equiv) in MeOH at 70 °C for 2 h on a 0.25–0.5 mmol scale. [b] Yield of isolated product. [c] Decomposition of the starting material [e] Determined by ^{19}F NMR spectroscopy

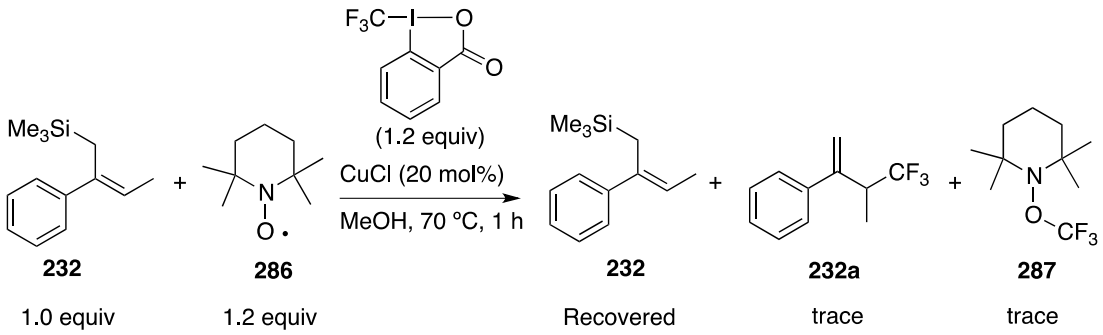
Table 4.7.2 Trifluoromethylation of cyclic allylsilanes

When substrate **278a** was subjected to the standard trifluoromethylation conditions (1.2 equiv Togni reagent **I** and 20 mol% CuCl in MeOH), none of the desired product was detected

by ^{1}H or ^{19}F NMR spectroscopy. Only decomposition of the starting material and formation of many unidentified trifluoromethylated byproducts were observed (Table 4.7.2, Entry 1). By increasing the size of the ring by introducing a extra methylene unit, as in 2,2-diisopropyl-4-methyl-2,3,6,7-tetrahydro-1,2-oxasilepine (**279a**), the outcome of the reaction dramatically changed, yielding the trifluormethylated oxysilane in 46% yield, along with 43% of the recovered starting material (Table 4.7.2, Entry 2). This result suggested that the conformational preferences of the eight-membered cyclic allylsilanes are crucial for the trifluoromethylation reaction. Additionally these results demonstrate the fact that the silyl group can be used for tracking possible intermediates during the reaction. Interestingly, substrate **281a**, which does not bear a methyl group at the β-position decomposed in the reaction, yielding only trace quantities of the desired product, as detected by ^{19}F NMR spectroscopy (Table 4.7.2, Entry 3). This experiment highlighted the importance of the substituent at the β-position in facilitating the trifluoromethylation reaction. This result suggests the involvement an unstable intermediate that is prone to decomposition. Eight-membered cyclic substrate **280a**, which bears a methyl group at the β-position, was converted to the desired allylic–CF_3 product **285** in 41% yield, with 44% recovered starting material. When another equivalent of Togni reagent **I** was added to the reaction mixture, formation of the desired product remained constant, while decomposition of the starting material increased.

4.8 Mechanistic Insights

Experiments were performed to gain further understanding of the reaction mechanism. First, the trifluoromethylation reaction of allylsilane **232** was carried out in the presence of the radical scavenger, 2,2,6,6-tetramethyl-1-piperidinyloxy (**286**, TEMPO) (Scheme 4.8.1)

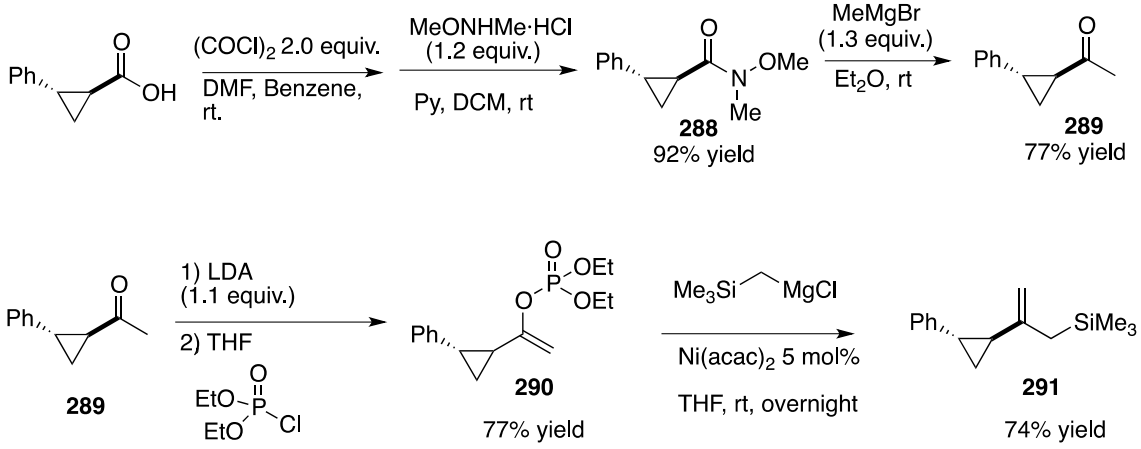


Scheme 4.8.1 Reaction of allylsilane **330** in the presence of a radical scavenger.

Under the optimised conditions, the reaction was completely inhibited by TEMPO, consistent with a radical process. Starting material **232** was recovered along with only trace quantities of the product, (4,4,4-trifluorobut-1-en-2-yl)benzene (**232a**) (δ = -70.6 ppm in the ^{19}F NMR) and TEMPO–CF_3 (**287**) (δ = -55.6 ppm in the ^{19}F NMR). This result suggests that an electrophilic $CF_3^{\bullet}$ radical may be involved as a reactive species in the reaction mechanism. In order to support the idea that the reaction proceeds *via* a radical species, additional experiments were necessary. For this purpose, a radical clock, trimethyl[2-(*trans*-2-phenylcyclopropyl)allyl]silane (**291**) was prepared as a mechanistic probe.

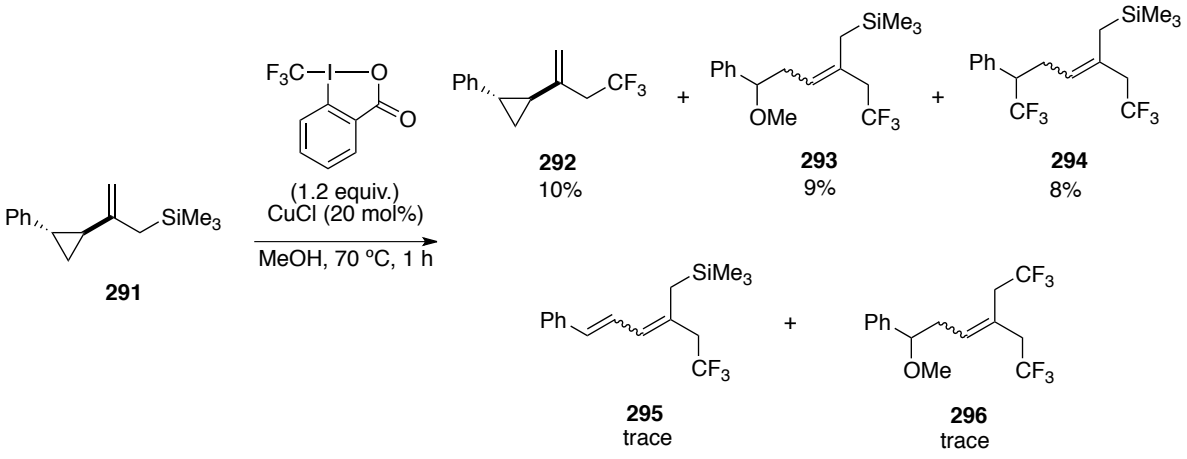
1-(*trans*-2-(Phenyl)cyclopropyl)ethanone **291** was synthesised from commercially available *trans*-2-phenyl-1-cyclopropane carboxylic acid (Scheme 4.8.2). The acyl chloride was prepared by treating the carboxylic acid with oxalyl chloride in the presence of DMF at room temperature. Subsequent nucleophilic acyl substitution with *N*,*O*-dimethylhydroxyamide led to the formation of Weinreb amide **288** in excellent yield (92%). The addition of methylmagnesium bromide provided ketone intermediate **289.**[170]

Trimethyl[2-(*trans*-2-phenylcyclopropyl)allyl]silane (**291**) was then synthesised following the general two-step procedure previously described above in the substrate synthesis section.



Scheme 4.8.2 Synthesis of the radical clock allylsilane **291**.

Trimethyl[2-(*trans*-2-phenylcyclopropyl)allyl]silane (**291**) was subjected to the standard reaction conditions (1.2 equiv Togni reagent **I** and 20 mol% CuCl in methanol at 70 °C. This experiment led to the formation of a complex mixture of products (Scheme 4.8.3), which could be separated using preparative TLC on SiO_2 gel.



Scheme 4.8.3 Trifluoromethyation of **291** under the standard conditions.

The major products were the allylic–CF_3 cyclopropane, *trans*-[2-(4,4,4-trifluoro-2-buytenyl)cyclopropyl]benzene (**292**), isolated in 10% yield, the ring-opened methoxy product,

[5-methoxy-5-phenyl-2-(2,2,2-trifluoroethyl)-2-pentenyl]-trimethylsilane (**293**), in 9% yield and (bis)trifluoromethylated product **294**. Trace amounts of products **295** and **296** could also be detected (Scheme 4.8.3). The mechanism by which Togni reagent **I** is activated by CuCl and reacts with the cyclopropane is not conclusive. The formation of products **292**, **293** and **294** suggests that there are two possible pathways for the metal catalyst to interact with the Togni reagent to increase its reactivity towards the allylsilane. In the first scenario, the metal could act as a Lewis acid, coordinating to the oxygen of the benziodoxole, facilitating cleavage of the I–O bond to form the activated iodonium species (Figure 4.8.1).

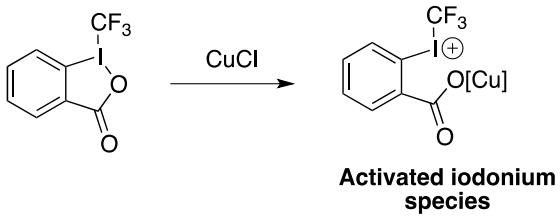
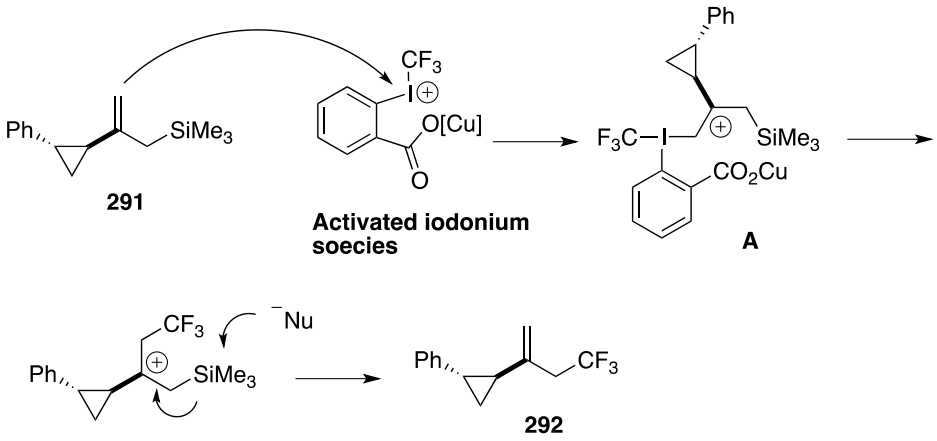


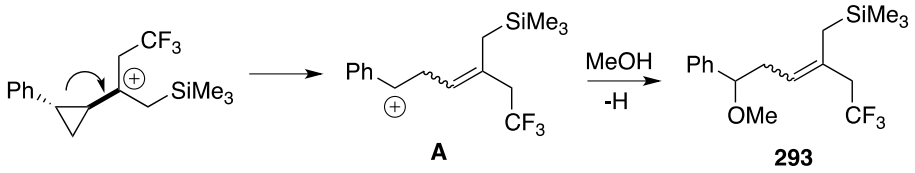
Figure 4.8.1 Formation of the activated iodonium species.

This highly electrophilic iodonium species could then react with the allylsilane to form λ_3-iodane intermediate **A** (Scheme 4.8.4). Reductive elimination at iodine forms a carbocation intermediate, which is stabilised by the β-effect of silicon. Subsequent desilylation process then affords allylic–CF_3 product **292**.



Scheme 4.8.4 Possible mechanism *via* two-electron transfer.

A rearrangement could also take place, where the cyclopropyl ring opens to afford benzylic carbocation **A** (Scheme 4.8.5). Intermolecular trapping by the solvent (MeOH) would form product **293**.



Scheme 4.8.5 Possible pathway to the formation of **293**.

The formation of the (bis)trifluoromethylated product **294** is potentially consistent with a radical pathway involving a $CF_3^{\bullet}$ species. In this scenario, CuCl acts as single-electron reductant and reduces Togni reagent **I** to the corresponding radical anion **A** (Figure 4.8.3).

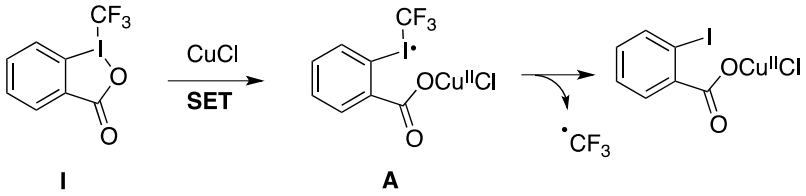
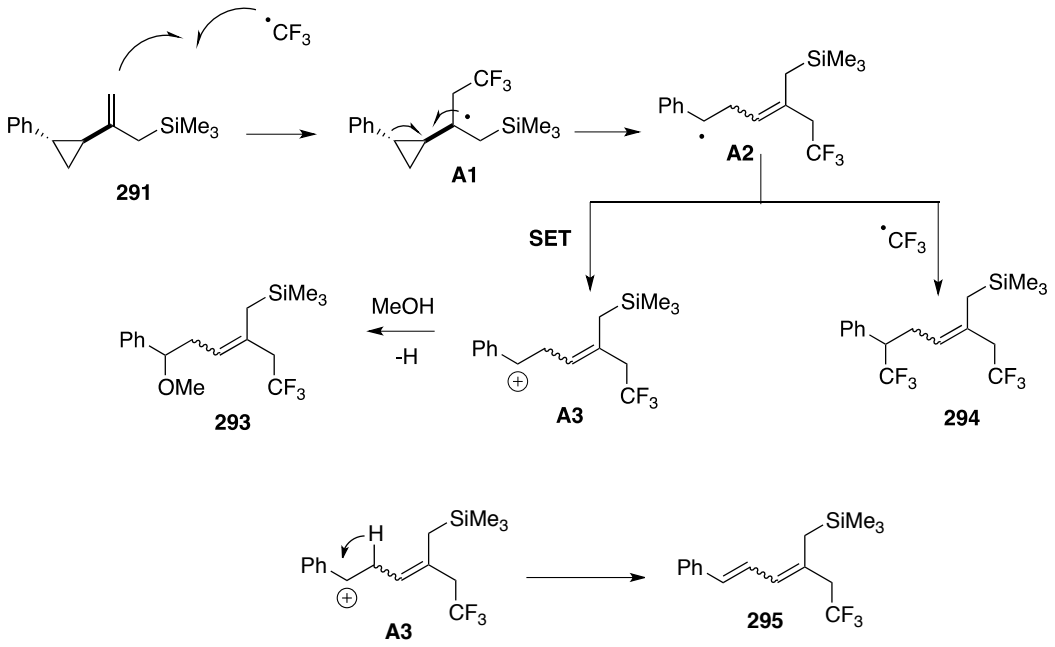


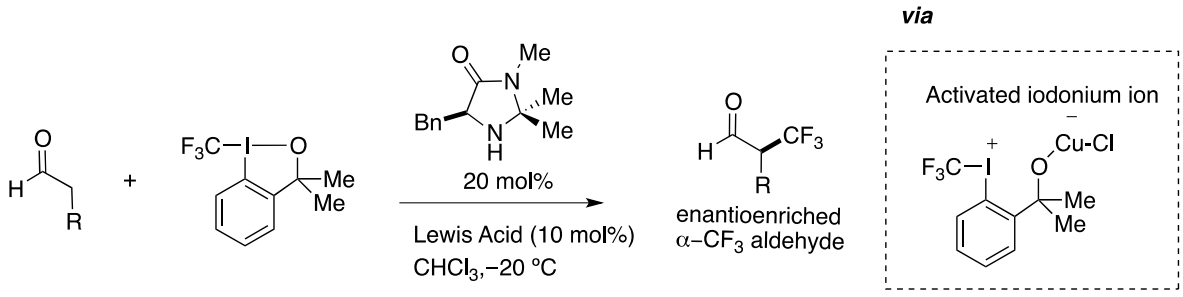
Figure 4.8.2 Possible pathway for generating the $CF_3^{\bullet}$ radical.

Then, this species (**A**, Figure 4.8.3) generates the $CF_3^{\bullet}$ radical, which reacts with the alkene to form radical intermediate **A1** (Scheme 4.8.6). Stabilisation by ring opening leads to a trifluoromethylated benzylic radical. This species reacts with a second $CF_3^{\bullet}$ radical, giving **294**. Formation of **293** is possible *via* SET from intermediate **A2** to form benzylic carbocation **A3**, which is trapped by the solvent. **295** could be generated by proton elimination from the intermediate **A3** (Scheme 4.8.6).



Scheme 4.8.6 Possible SET mechanism explaining the formation of **293**, **294** and **295**.

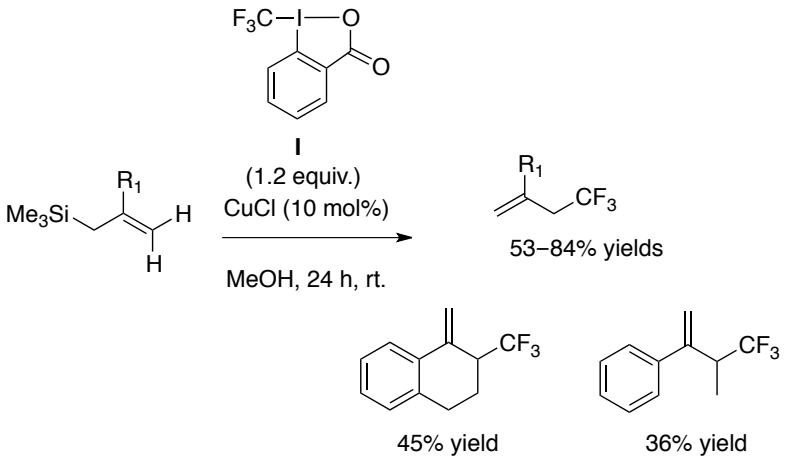
The mechanism for the formation of these products is in agreement with MacMillan's report on the enantioselective α-trifluoromethylation of aldehydes.[148] MacMillan proposed that the reaction proceeded through the activation of the Togni reagent by a Lewis acid. However, a alternative mechanistic scenario where the CuCl acts as single-electron transfer agent to generated a CF_3• radical was not dismissed.



Scheme 4.8.7 Enantioselective α-trifluoromethylation of aldehydes.

During the preparation of this work, Sodeoka and co-workers reported a manuscript describing the trifluoromethylation of allylsilanes under copper catalysis.[171] Linear allylic–CF_3

products were synthesized in moderate to good yields, but only two examples of branched allylic–CF_3 products in poor yields were included (Scheme 4.8.8).



Scheme 4.8.8 Trifluoromethylation of allylsilanes under copper catalysis.

The mechanism suggested by Sodeoka and co-workers involved an electrophilic CF_3^+ species, generated through activation of Togni reagent **I** by CuCl. They speculated that the trifluoromethylation of allylsilanes proceeds through the formation of a carbocation at the position β to silicon, followed by attack of the solvent, methanol, to release the desired allylic–CF_3 product. The authors dismissed the possibility of radical intermediates. When a substrate with an EDG group at the *p*-position was exposed to the trifluoromethylation conditions, formation of (bis)trifluoromethylated and dimerised side products was observed (Figure 4.8.3). To suppress formation of the undesired products, the reactions were instead carried out at 0 °C.

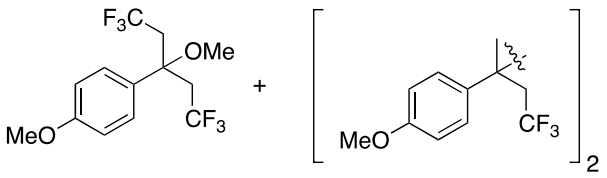
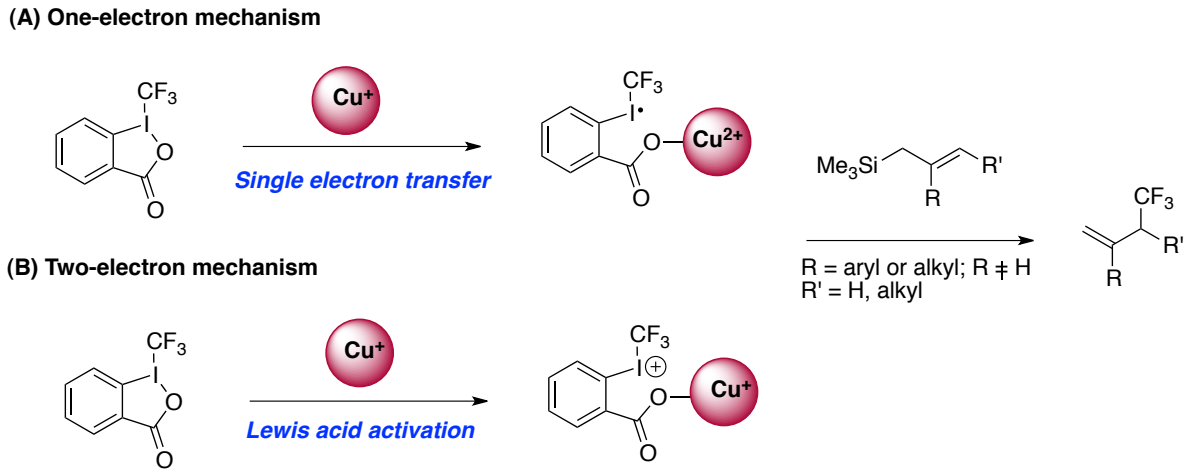


Figure 4.8.3 Side products detected during the trifluoromethylation reaction.

Possible mechanism for the trifluoromethylation of allylsilanes under copper catalysis.

Based on the results discussed above (radical scavenger and radical clock) and the literature precedents,[148,151,155171] we propose that two mechanisms are operative: one-electron transfer and two-electron transfer.



Scheme 4.8.9 Possible pathways for the activation of Togni reagent **I**.

In the first mechanistic scenario, Cu(I) catalytically activates Togni reagent **I** *via* single electron transfer (SET), a process that leads to CF_3-containing radical species **A** (Scheme 4.8.10). Decomposition of intermediate **A** releases the electrophilic CF_3• radical. This radical reacts with the allylsilane **232**, resulting in trifluoromethylated benzylic radical intermediate **B**, which is stabilised by the proximal silyl group. Oxidation of **B** with either Cu(II) or **I** gives intermediate **C**, a carbocation that is more stabilised by the β-silyl group than **B**. Subsequent desilylation with methanol gives the desired allylic–CF_3 product **232a**. A mechanism with the Cu(I) catalyst acting as a Lewis acid could also be operative. In this second scenario, activation of **I** leads to cationic species **D**. Electrophilic trifluoromethylation of the allylsilane then takes place, affording intermediate **C** either directly or *via* reductive elimination from λ^3-iodane species **E**. However, the S_N2 attack on the activated iodonium species is unlikely mechanism

since the carbon of the trifluoromethyl group is shielded by the three fluorine atoms. The inversion barrier for the CF_3 anion requires 119 kcal/mol[172] and 39 kcal/mol[173] for the CF_3 radical species. Therefore, a λ^3-iodane intermediate is more likely to occur, further desilylation process would then give product **232a.** Herein, we propose a reaction mechanism where both the cationic and the radical mechanisms could be operating in parallel and progressing at different rates.

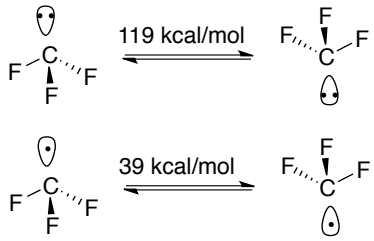
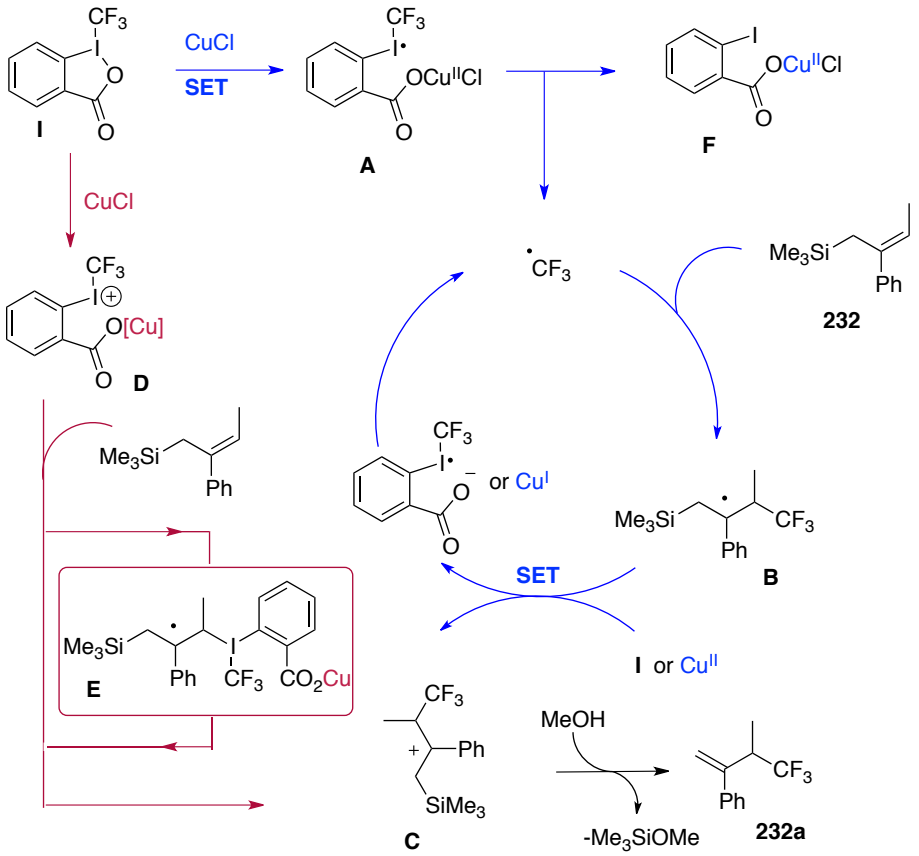


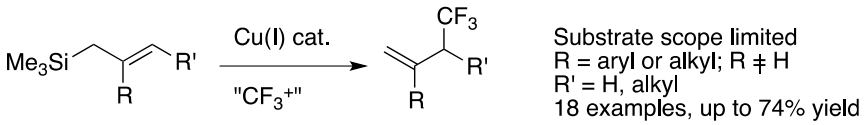
Figure 4.8.4 Inversion barrier for the CF_3 anion and radical.



Scheme 4.8.10 Plausible mechanism for trifluoromethylation of allylsilanes mediated by CuCl.

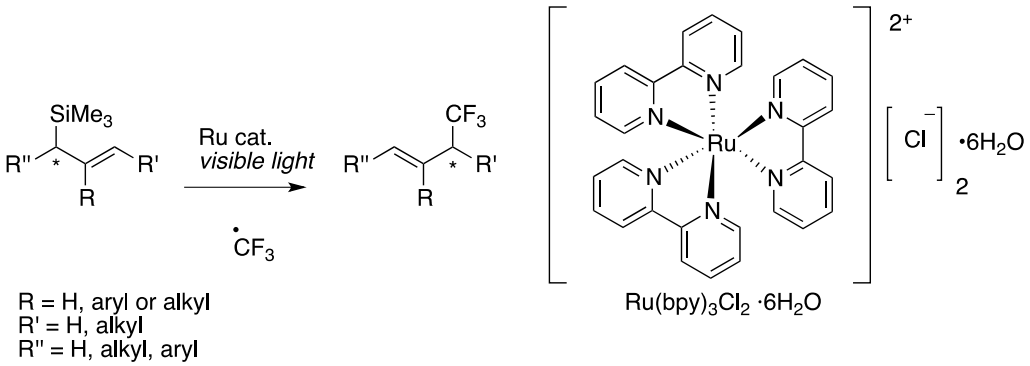
4.9 Trifluoromethylation of Allylsilanes under Photoredox Catalysis.

In the previous section, we demonstrated that alkenes temporarily activated with a regiodirecting allylic trialkylsilyl group can undergo trifluoromethylation with Togni reagent **I** under copper catalysis in MeOH. In this reaction, the trialkylsilyl group is responsible for the regioselectivity, providing the allylic trifluoromethylated products with complete selectivity for functionalization at the γ-position relative to silicon. The scope included formation of the branched cyclic allylic–CF_3 products (including compounds featuring C(sp^3)–CF_3 stereogenicity) and acyclic allylic–CF_3 products. However, the substrate scope of this reaction is limited to the formation of *gem*-disubstituted products (R≠H). Preliminary mechanistic analysis suggests that this transformation involves a *net* electrophilic transfer of the CF_3 group by way of an intervening CF_3• radical species, (generated by SET processes).



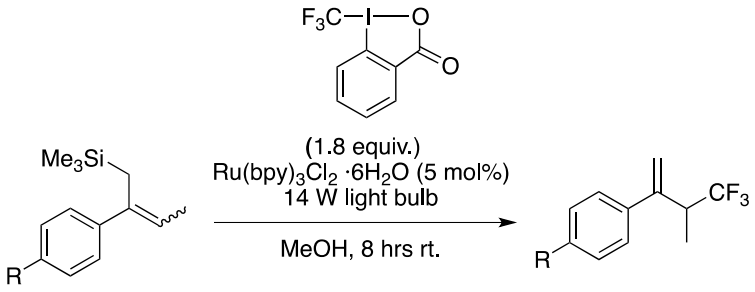
Scheme 4.9.1 Trifluoromethylation of allylsilanes under copper catalysis.

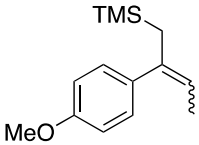
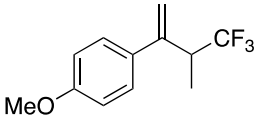
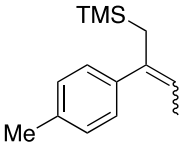
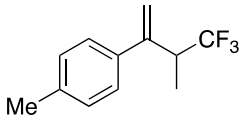
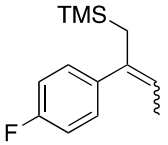
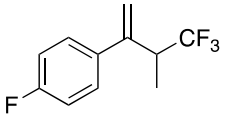
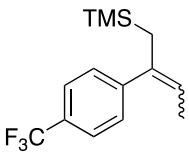
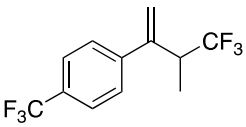
To address the limited substrate scope, our group considered an alternative catalytic manifold for generating CF_3• species: a Ru/visible-light photoredox catalysis system. Based on the successful trifluoromethylation of (hetero)arenes[143] and alkenes[174] under photoredox catalysis, it was hypothesised that this mode of activation may be suitable for the trifluoromethylation of allylsilanes. The trialkylsilyl group would be used to control the reactivity and regio- and stereoselectivity in combination with the appropiate CF_3 source (Scheme 4.9.2).



Scheme 4.9.2 Proposed trifluoromethylation reaction of allylsilanes under photoredox conditions.

Initial investigations were focused on trifluoromethylation of allylsilanes bearing EWG or EDG at the *p*-position of the aromatic ring.



Entry	Substrate	Product	Yield (%)[a]
1			29
2			27
3			10
4[b]			11

[a] Yield of isolated product. [b] Yield determined by ^{1}H NMR.

Table 4.9.1 Trifluoromethylation of allylsilanes with different *p*-substituents.

When the substrates were exposed to the trifluoromethylation conditions, yields of desired products were low due to the presence of many unidentified side products containing trifluoromethyl groups. Comparing this data with the results under copper catalysis revealed a similar pattern. In both reactions, the electronic properties of the *p*-substituent influenced the observed product formation in the same way. The highest conversions were obtained with electron-releasing groups (OMe, Me) in the *p*-position of the aromatic ring (Figure 4.9.1). However, these groups also led to the formation of unidentified byproducts.

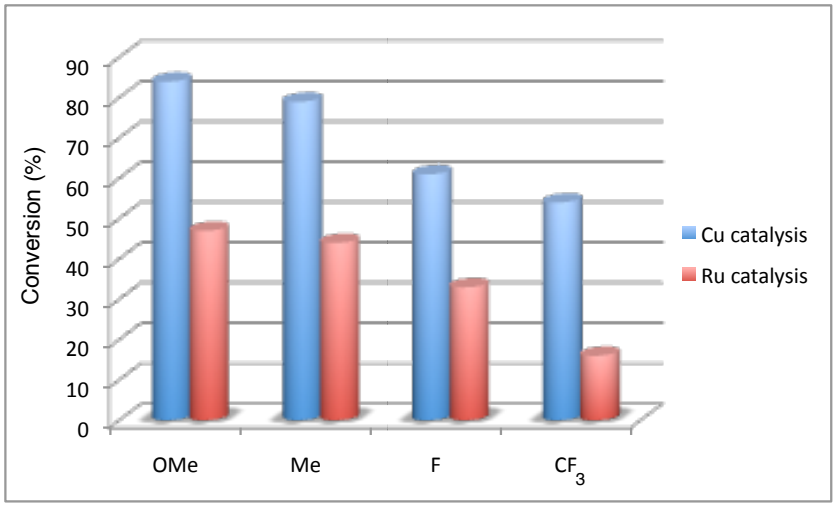
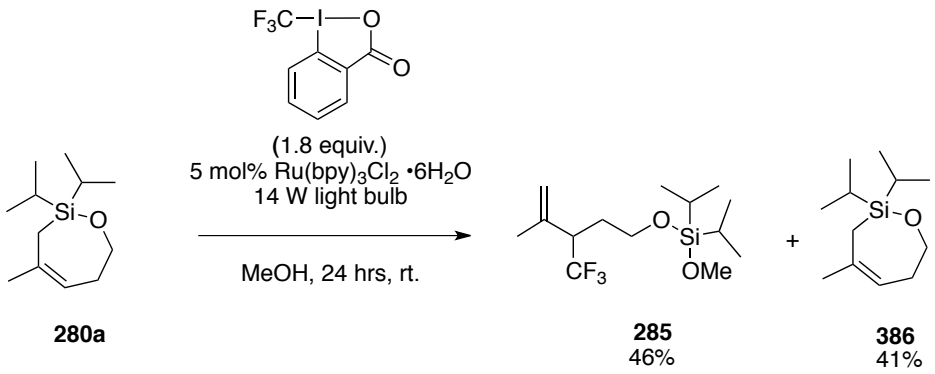


Figure 4.9.1 Comparision of both catalytic approaches (Cu and Ru catalysis).

Lower conversions and yields were observed with electron-withdrawing groups (F and CF_3) (Table 4.9.1, Entries 3–4). In the *p*-CF_3 case, 30% of the starting material, **257** ({2-[4-(trifluoromethyl)phenyl]but-2-en-1yl}trimethylsilane), was recovered. This result suggests that the low reactivity of substrates with an EWG reduces the formation of unidentified side products.

Cyclic allylsilane **280a** was also examined under photoredox conditions. The reaction led to the formation of **285** in moderate yield (46%) and 41% of the starting material was recovered

(Scheme 4.9.3). Interestingly, in this case the reaction proceeded smoothly with no decomposition observed in the crude ^{1}H NMR spectrum.

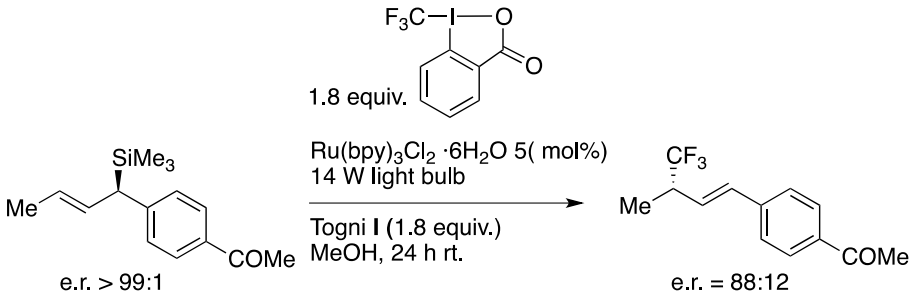


Scheme 4.9. 3 Trifluoromethylation of cyclic allylsilane under photoredox conditions.

These results provided supportive evidence that the proposed catalytic manifold for the generation of a CF_3• species using the high-performing Ru/visible light catalytic system was indeed effective. Further investigations in the Gouverneur group in collaboration with Dr. S. Mizuta, Dr. K. M. Engle, S. Verhoog and M. O'Duill provided significant new insights into this trifluoromethylation methodology mediated by photoredox catalysis.[175] This catalytic activation mode allowed our group to achieve a major breakthrough in the trifluoromethylation of allylsilanes not containing *gem*-disubstitution at the β-position. This reaction was only possible under photoredox conditions, as our previously developed copper catalysed method was unsuccesful.

Previously in this chapter, we demonstrated that copper-catalysed trifluoromethylation with substrate **265** proceededs with the CF_3 source approaching *anti* to silicon. Further studies showed that under photoredox catalysis, trifluoromethylation of enantioenriched allylsilanes took place with chirality transfer from the C–Si bond to the C–CF_3 bond with high enantiocontrol (76% ee), with the reaction again proceeding with preferential *anti* approach of

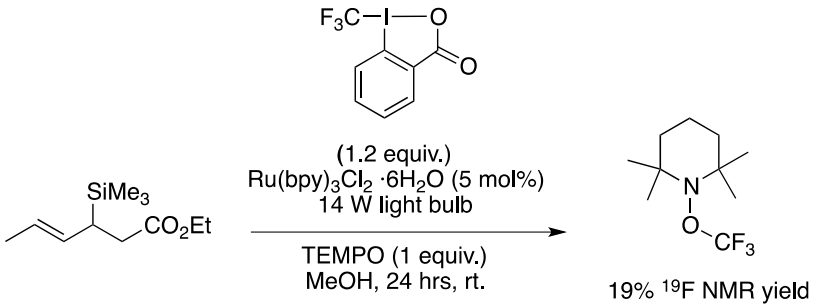
the CF_3 source. This is consistent with the well-established *anti*-$S_{E'}$ mode of addition observed for other electrophiles. [176]



Scheme 4.9.4 Chirality transfer from an enantiopure allylsilane.

The mechanism by which the electrophilic trifluoromethylating reagent is activated by the Ru photocatalyst was not immediately apparent during the development of this tranformation. In order to gain further understanding of the reaction mechanism, a series of experiments were performed.

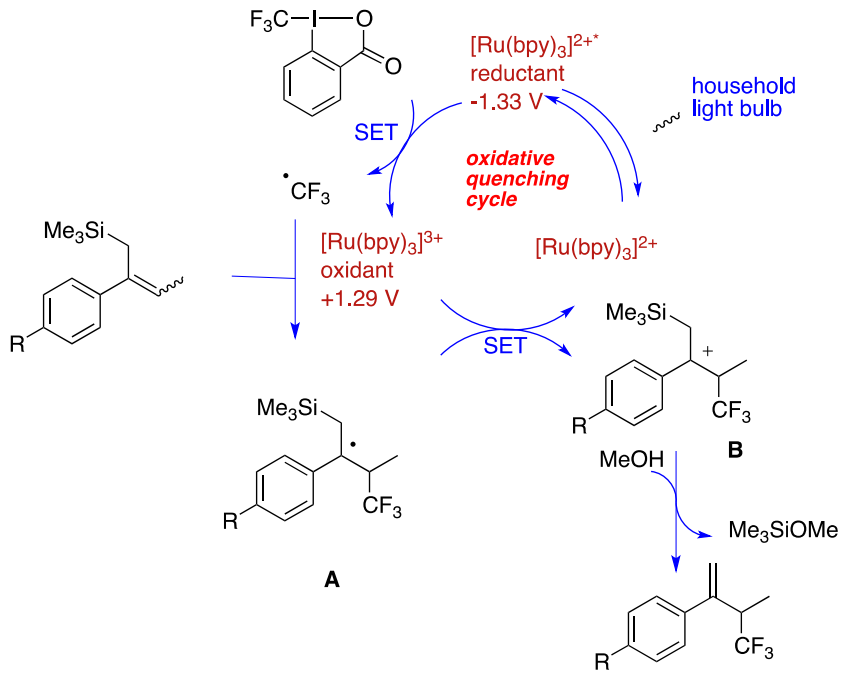
Trifluoromethylation of the allylsilane was carried out in the presence of TEMPO under Ru/visible-light photocatalysis (Scheme 4.9.5).



Scheme 4.9.5 Attempted trifluoromethylation of allylsilane in the presence of TEMPO, a radical scavenger.

Under these conditions, the desired trifluoromethylated product was not detected. Instead, the TEMPO–CF_3 product was formed (19% yield by ^{19}F NMR spectroscopy). This result suggested that $CF_3^{\bullet}$ is involved as a reactive species in the reaction.

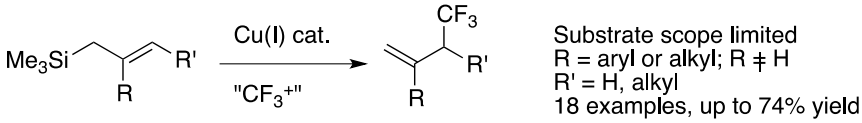
Recently, our group reported a detailed study of the reduction potentials for trifluoromethylating reagents (sulfonium salts and hypervalent iodine(III) compounds).[177] In this study, it was found that *S*-(trifluoromethyl)thiophenium salts (Shibata reagents) were also suitable sources of $CF_3^{\bullet}$ under photoredox catalysis. Cyclic voltammetry experiments provided key data for the elucidation of the probable reaction mechanism. The reduction potential for Togni reagent **I** by cyclic voltammetry (-0.68 V *vs* SCE in CH_3CN) was found to be compatible with the reduction step using excited state $Ru(bpy)_3^{2+*}$; this implies that single-electron transfer (SET) reduction of Togni reagent would be concurrent with the oxidation of $Ru(bpy)_3^{2+*}$ to $Ru(bpy)_3^{3+}$ (-0.81 V *vs* SCE in CH_3CN).[178, 179] Based on previous studies, a plausible reaction mechanism for the trifluoromethylation reaction is depicted in Scheme 4.9.2. The trifluoromethyl radical generated by reduction of Togni reagent **I**, reacts regio- and stereoselectively with the allylsilane. The resulting radical species, **A** (Scheme 4.9.2), could then undergo a second SET with the strong oxidant $Ru(bpy)_3^{3+}$ (+1.29 V *vs* SCE in CH_3CN), regenerating the ground-state photocatalyst $Ru(bpy)_3^{2+}$. Intermediate **B** (Scheme 4.9.6), a carbocationic species is stabilised by the β-silyl group, and subsequent desilylation is mediated by methanol to form the desired allylic–CF_3 product.



Scheme 4.9.6 Possible mechanism leading to the formation of the allylic–CF_3 products under photoredox conditions.

4.9 Conclusions

In summary, in this chapter the development of new catalytic methodologies to access allylic–CF_3 products has been presented. The first approach, trifluoromethylation of allylsilanes under copper catalysis, could be used to form various branched cyclic and acyclic allylic–CF_3 products, including compounds featuring C(sp^3)–CF_3 stereogenicity. Preliminary analysis suggests that the mechanism is complex and involves multiple reaction pathways featuring radical and/or cationic intermediates. The substrate scope of this reaction is limited to the formation of *gem*-disubstituted products (R≠H).



In the second approach, an alternative mechanism for generating $CF_3^{\bullet}$ species was also demonstrated using a high-performing Ru/visible-light catalytic system. Trifluoromethylation of substrates not containing *gem*-substitution at the β-position was successfully achieved. Cyclic voltammetry measurements suggest that an oxidative quenching cycle is operative in the photoredox catalytic cycle. However, further investigations into the mechanism are currently underway. Use of an enantioenriched chiral allylsilane substrate allowed for chirality transfer during the reaction, giving access to enantioenriched branched allylic–CF_3 products.

Chapter 5

Experimental Section

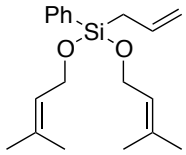
General remarks

All solvents and chemicals were used as purchased unless stated otherwise. All NMR spectra were recorded in deutereated solvents on Bruker AV400 and AV500 spectrometers calibrated using residual solvent as an internal reference. NMR data were processed using MestReNova-LITE software. Proton and carbon-13 NMR spectra are reported as chemical shifts (δ) in parts per million (ppm) relative to residual undeuterated solvent peak using the Bruker internal referencing procedure (edlock) and coupling constant (*J*) are measured in hertz (Hz). The following abbreviations are used to describe multiplets: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). High resolution mass spectra (HRMS, m/z) were recorded on a Bruker MicroTOF spectrometer using positive electrospray ionization (ESI+) or chemical ionization (CI+). Infrared spectra were recorded either as solids (KBr disc) or as a liquid film where indicated on NaCl discs using a Bruker Tensor 27 FT-IR spectrometer. Absorptions are reported in wavenumbers (cm^{-1}) and only peaks of interest are reported. Melting points of solids were measured on a Griffin apparatus and are uncorrected. IUPAC names were obtained using the ACD/ILab service. All reactions were performed in dried apparatus with magnetic stirring under an inert atmosphere of argon or nitrogen. All solvents were dried on a column of alumina prior to use. Thin layer chromatography (TLC) was performed using Merck aluminium-foil baked plates precoated with Kieselgel 60 F245. The products were visualized using UV fluorescence (254 nm) or potassium permanganate stain. Silica gel column chromatography was performed over Merck silica gel C60 (40-60 μm) using eluent systems as described for each experiment.

CuCl was purchased from Sigma-Aldlich. Other reagents were obtained from commercial sources. Togni's trifluoromethylating reagent **I** was prepared in multi-grams scale according to

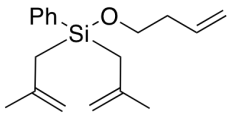
literature procedures.[124c] Known compounds have been checked against literature references and only two pieces of analytical data are given.

Allyl{bis[(3-methylbut-2-en-1-yl)oxy]}phenylsilane: 170.



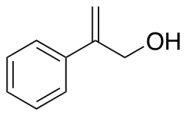
To a 0.1 M solution of allylphenyldichlorosilane (0.75 mL, 4.0 mmol, 1.0 eq) in DCM (30 mL) and urea (1.1 mL, 8.4 mmol, 2.1 eq) was added dropwise a 1 M solution of 3-methyl-2-buten-1-ol (0.90 mL, 8.4 mmol, 2.1 eq) in DCM at room temperature. The reaction mixture was maintained stirring 16 hours. The reaction mixture was quenched with water and extracted with DCM. The combined organic layers were washed with water and brine, dried over magnesium sulphate and filtered. The solvent was subsequently removed *in vacuo* and the crude oil purified *via* flash chromatography *Rf* = 0.5 (Hexane:Et_2O 95:5) to yield a colourless oil, (yield 695 mg, 75%). **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 1.61 (6H, s, CH=CCH_3), 1.73 (6H, s, CH=CCH_3), 1.90 (2H, d, $^3J_{(H,H)}$ 8.0 Hz, SiCH_2), 4.31 (4H, m, SiOCH_2), 4.89 (1H, dq, $^3J_{(H,H)}$ 10.0 Hz, $^4J_{(H,H)}$ 2.0 Hz, CH=CH_{2cis}), 4.93 (1H, dq, $^3J_{(H,H)}$ 17, $^4J_{(H,H)}$ 2 x 2.0 Hz, CH=CH_{2trans}), 5.39 (2H, tqq, $^3J_{(H,H)}$ 7.0 Hz, $^4J_{(H,H)}$ 2.0 Hz, $^4J_{(H,H)}$ 1.5 Hz, Me_2C=C*H*), 5.81 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 8.0 Hz, C*H*=CH_2), 7.40 (3H, m, Ph$H_{ortho/para}$), 7.66 (2H, m, PhH_{meta}); **^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm):** 17.9 (s, *C*H_3), 21.0 (s, Si*C*H_2), 25.7 (s, *C*H_3), 59.9 (s, SiO*C*H), 114.8 (s, CH=*C*H_2), 123.6 (s, *C*H=CMe_2), 127.7 (s, ArC_{ortho}), 130.0 (s, ArC_{para}), 132.8 (s, $SiCH_2$*C*H=CH_2), 133.1 (s, ArC_{ipso}), 134.5 (s, ArC_{meta}), 134.7 (s, Me_2*C*=CH_2); **IR (film): υ_{max} (cm^{-1})** 3076, 1638 , 1031, **: HMRS** (ESI, *m/z*) calc for $C_{19}H_{28}O_2SiNa$ $[M+Na]^+$: 339.1756 found: 339.1753.

(But-3-en-1-yloxy)[bis(2-methylprop-2-en-1-yl)]phenylsilane: 156.



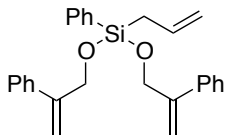
To a 0.1 M solution of phenyltrichlorosilane (0.86 mL, 5.6 mmol, 2.0 eq) in DCM and urea (168 mg, 2.8 mmol, 1.1 eq) was added dropwise a solution 0.1 M of 3-buten-1-ol (0.24 mL, 2.8 mmol, 1.1 eq) in DCM at room temperature. The reaction mixture was maintained stirring for 12 hours. Without further purification the solution was transferred *via* cannula to a one-neck round-bottomed flask and the solvent was removed in *vacuo*. The crude dichloride silane was redisolved in THF (1 M) and added dropwise to a solution of 2-methylallylmagnesium chloride in THF (5 eq, 0.5 M solution). The reaction mixture was left to stir at room temperature for 16 hours; then was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine and dried over magnesium sulphate, filtered and the solvent removed *in vacuo.* The crude was a colourless oil, purified by flash chromatography, *Rf* = 0.7 (Hexane:Et_2O 95:5), to yield (286 mg, 30%). **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 1.69 (6H, br s, CH_3), 1.96 (4H, s, SiCH_2MeC=CH_2), 2.35 (2H, q, 7 Hz, Si-OCH_2CH_2), 3.77 (2H, t, 7 Hz, Si-OCH_2CH_2), 4.61 (2H, br s, MeC=CH_2), 4.67 (2H, br s, MeC=CH_2), 5.12 (1H, dt, $^3J_{(H,Hcis)}$ 10.0, $^2J_{(H,H)}$ 1.5 Hz, CH=C$H_{2(cis)}$), 5.36 (1H, dt, $^3J_{(H,Htrans)}$ 17.0, $^2J_{(H,H)}$ CH=C$H_{2(trans)}$), 5.94 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 8.0 Hz, CH=CH_2), 7.39 (3H, m, C$H_{ortho/para}$), 7.61 (2H, m, CH_{meta}); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 25.35 (s CH$_3$), 25.42 (s, SiCH$_2$), 37.1 (s, Si-OCH$_2$$CH_2$), 63.0 (s, Si-O$CH_2CH_2$), 110.3 (s, MeC=$CH_2$), 116.5 (s, CH=$CH_2$), 127.7 (s, CH$_{ortho}$), 129.7 (s, CH$_{para}$), 134.1 (s, CH=CH$_2$), 135.2 (s, CH$_{meta}$), 135.7 (s, SiC_{ipso}), 142.1 (s, MeC=CH$_2$); **IR (film): υ_{max} (cm^{-1})** 3074, 1636**; HMRS** (ESI, *m/z*) calc for $C_{18}H_{26}OSiNa$ $[M+Na]^+$: 309.1651 found: 309.1657.

2-phenylprop-2-en-1-ol[180].



Procedure: To a solution of phenylmagnesium chloride (12.5 mL, 1 M in THF, 12.5 mmol) in THF (50 mL) was added CuI (152 mg, 0.8 mmol). The reaction was then allowed to stir at room temperature for 30 minutes. A solution of propargyl alcohol (291 µL, 280 mg, 5.0 mmol) in THF (10 mL) was then added. After the reaction was allowed to stir at reflux for 20 hours, the reaction was quenched by the addition of NH_4Cl (100 mL) and extracted with Et_2O (200 mL). The organic phase was dried over sodium sulfate, filtered and the solvent was removed *in vacuo*. After purification by silica gel chromatography with 10% EtOAc in hexane as eluent, the expected compound was obtained as a colourless oil (428 mg, 64% yield). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 4.61 (d, $^3J_{(H,H)}$ = 6.0 Hz, 2H), 5.40 (s, 1H), 4.61 (d, $^3J_{(H,H)}$ = 6.0 Hz, 2H), 5.55 (s, 1H), 7.60-7.62 (m, 5H),; **^{13}C NMR (100.6MHz, $CDCl_3$) (δ ppm)**: 65.5, 113.1, 126.9, 127.6, 129.2, 141.0, 147.2 NMR data are consistent with the reported in the literature.

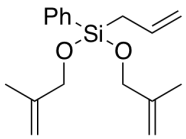
Allyl(phenyl)bis[2-phenylprop-2-en-1-yl)oxy]silane: 171.



To a 0.1 M solution of allylphenyldichlorosilane (0.37 mL, 2.0 mmol, 1.0 eq) in DCM (15 mL) and Et_3N (0.54 mL, 4.2 mmol, 2.1 eq) was added dropwise a 1 M solution of 2-phenyl-2-propen-1-ol (560 mg, 4.2 mmol, 2.1 eq) in DCM at room temperature. The reaction mixture was maintained stirring for 16 hours. The reaction mixture was quenched with water and extracted with DCM. The combined organic layers were washed with water and brine, dried over magnesium sulphate and filtered. The solvent was subsequently removed in *vacuo* and

the crude oil purified via flash chromatography *Rf* = 0.6 (Hexane:Et_2O 95:5), to yield a colourless oil yield (535 mg, 65%).**^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 1.98 (2H, d, $^3J_{(H,H)}$ 8.0 Hz, SiCH_2), 4.68 (4H, s, SiOCH_2), 4.93 (1H, dd, $^3J_{(H,H)}$ 10.0 Hz, $^4J_{(H,H)}$ 2.0 Hz, CH=CH_{2cis}), 4.98 (1H, dt, $^3J_{(H,H)}$ 17.0, $^4J_{(H,H)}$ 2.0 Hz, CH=CH_{2trans}), 5.48 (4H, m, (C_6H_5)C=CH_2), 5.86 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 8.0 Hz, CH=CH_2), 7.67-7.27 (15H, m, Ph$H_{m,o,p}$),; **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 20.9 (s, SiCH_2), 64.6 (s, SiOCH), 112.0 (s, PhC=CH_2), 115.1 (s, CH=CH_2), 126.0, 12.7, 127.8, 128.3, 130.3, 132.3, 132.4, 138.7, 146.2; **IR (film): υ_{max} (cm^{-1})** 3080, 1850, 1600, 1256**;** **HMRS** (ESI, *m/z*) calc for $C_{27}H_{28}O_2SiNa$ $[M+Na]^+$: 435.1756 found: 435.1753.

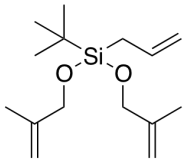
Allyl(methyl)bis[(2-methylprop-2-en-1-yl)oxy]silane: 167.



To a 0.1 M solution of allylphenyldichlorosilane (0.37 mL, 2.0 mmol, 1.0 eq) in DCM (15 mL) and Et_3N (0.54 mL, 4.2 mmol, 2.2 eq), was added dropwise a 1 M solution of 2-methyl-2-propen-1-ol (414 mL, 4.2 mmol, 2.2 eq) in DCM at room temperature. The reaction mixture was maintained stirring for 16 hours. The reaction mixture was quenched with water and extracted with DCM. The combined organic layers were washed with water, brine, and dried over magnesium sulphate and filtered. The solvent was subsequently removed *in vacuo* and the crude oil purified via flash chromatography *Rf* = 0.6 (Hexane:Et_2O 95:5), to yield a colourless oil (288 mg, 51%). **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 1.73 (6H, s, C=CH_2CH_3), 4.20 (4H, m, SiOCH_2), 1.93 (2H, d, $^3J_{(H,H)}$ 8 Hz, SiCH_2), 4.86 (2H, s, MeC=CH_2), 4.91 (1H, dt, $^3J_{(H,H)}$ 10.0 Hz, $^4J_{(H,H)}$ 2.0 Hz, CH=CH_{2cis}), 4.97 (1H, dt, $^3J_{(H,H)}$ 17.0, $^4J_{(H,H)}$ 2.0 Hz, CH=CH_{2trans}), 5.06 (2H, s, MeC=CH_2), 5.86 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 8.0 Hz, CH=CH_2), 7.39 (3H, m, Ph$H_{ortho/para}$), 7.66 (2H, m, PhH_{meta}); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 19.0 (s, CH_3), 20.9 (s, SiCH_2), 65.5 (s, SiOCH), 109.7 (s, MeC=CH_2), 115.0 (s, CH=CH_2), 127.8 (s, ArC_{ortho}), 130.2 (s,

ArC_{para}), 132.6 (s, SiCH$_2$*C*H=CH$_2$), 132.7 (s, ArC_{ipso}), 134.4 (s, ArC_{meta}), 143.7 (s, Me*C*=CH$_2$),; **IR (film): υ_{max} (cm^{-1})** 3076, 1638, 1031; **HMRS** (ESI, *m/z*) calc for $C_{17}H_{25}O_2SiNa$ $[M+Na]^+$: 289.1624 found: 289.1620.

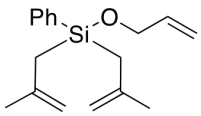
Allyl(tert-butyl)bis[(2-methylprop-2-en-1-yl)oxy]silane: 176.



To a 0.1 M solution of trichloroallylsilane (0.71 mL, 5.0 mmol, 1.0 eq) in DCM and Et_3N (1.4 mL, 10.5 mmol, 2.1 eq) was added dropwise a 0.1 M solution of 2-methyl-2-propen-1-ol in DCM (0.84 mL, 10.0 mmol, 2.0 eq) at room temperature. The reaction mixture was maintained stirring for 12 hours. Without further purification the solution was transferred *via* cannula to a one-neck round-bottomed flask and the solvent was removed *in vacuo* (4.6 mmol, 1.13 g). The crude was redisolved in pentane (1 M) and added dropwise at -78ºC to a 1.9 M solution of *t*-Butyllithium in pentane (2.9 mL, 5.5 mmol, 1.2 eq). The reaction mixture was left to stir to room temperature for 16 hours. It was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent removed *in vacuo* and the crude oil was purified by flash chromatography, *Rf* = 0.5 (Hexane:Et_2O 95:5), to yield a colourless oil (402 mg, 30%). **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 1.01 (9H, s, C(C*H*$_3$)$_3$), 1.72 (6H, s, C=CH$_2$C*H*$_3$), 1.78 (2H, d, $^3J_{(H,H)}$ 8.0 Hz, SiC*H*$_2$), 4.21 (4H, m, SiOC*H*$_2$), 4.84 (2H, s, MeC=C*H*$_2$), 4.91 (1H, dt, $^3J_{(H,H)}$ 10.0 Hz, $^4J_{(H,H)}$ 2.0 Hz, CH=C*H*$_{2cis}$), 4.97 (1H, m, CH=C*H*$_{2trans}$), 5.04 (2H, s, MeC=C*H*$_2$), 5.91 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 8.0 Hz, C*H*=CH$_2$); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 19.0 (s, *C*H$_3$), 19.3 (s, Si*C*H$_2$), 19.3 (s, Si*C*H$_2$), 26.7 (s, C(*C*H$_3$)$_3$), 67.0 (s, SiO*C*H$_2$), 109.5 (s, MeC=*C*H$_2$), 114.6 (s, CH=*C*H$_2$), 134.2 (s, SiCH$_2$*C*H=CH$_2$), 144.5 (s, Me*C*=CH$_2$); **IR (film): υ_{max}**

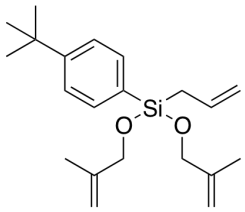
(cm^{-1}) 3076, 1638, 1031; **HMRS** (ESI, *m/z*) calc for $C_{15}H_{28}NaO_2Si$ $[M]^+$: 291.1751 found: 291.1749.

Allyloxy)[bis(2-methylprop-2-en-1-yl)]phenylsilane: 155.



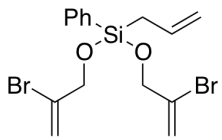
To a 0.1 M solution of phenyltrichlorosilane (0.43 mL, 2.8 mmol, 2.0 eq) in DCM and urea (84 mg, 1.4 mmol, 1.0 eq) was added dropwise a 0.1 M solution of allylalcohol in DCM (0.11 mL, 1.4 mmol, 1.0 eq) at room temperature. The reaction mixture was maintained stirring for 12 hours. Without further purification the solution was transferred *via* cannula to one-neck round-bottomed flask and the solvent removed *in vacuo*. The crude dichloride silane was redisolved in THF (1 M) and was added dropwise to a solution of 2-methylallylmagnesium chloride in THF (5.0 eq, 0.5 M solution). The reaction mixture was left to stir at room temperature for 16 hours. It was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent removed *in vacuo* and the crude was purified by flash chromatography, *Rf* = 0.5 (Hexane:Et_2O 95:5), to yield a colourless oil (78 mg, 20%). **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 7.61 (2H, m, CH_{meta}), 7.39 (3H, m, C$H_{ortho/para}$), 5.94 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 8.0 Hz, CH=CH_2), 5.36 (1H, ddt, $^3J_{(H,H)}$ 17.0, $^2J_{(H,H)}$ 1.5, $^4J_{(H,H)}$ 1.5 Hz, CH=C$H_{2(trans)}$), 5.12 (1H, ddt, $^3J_{(H,H)}$ 10.0, $^2J_{(H,H)}$ 1.5, $^4J_{(H,H)}$ 1.5 Hz, CH=C$H_{2(cis)}$), 4.67 (2H, br s, MeC=C$H_a$$H_b$), 4.61 (2H, br s, MeC=C$H_a$$H_b$), 4.28 (2H, m, Si-OC$H_2$CH), 1.98 (4H, s, SiC$H_2$MeC=$CH_2$), 1.69 (6H, br s, C$H_3$); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 142.0 (s, MeC=CH_2), 136.7 (s, ArC_{ipso}), 135.4 (s, ArC_{meta}), 134.1 (s, CH=CH_2), 129.7 (s, ArC_{para}), 127.6 (s, ArC_{ortho}), 114.4 (s, CH=$C$$H_2$), 110.3 (s, MeC=$C$$H_2$), 64.2 (s, Si-O$C$$H_2$), 25.4 (s, Si$C$$H_2$), 25.3 (s $C$$H_3$). **IR (film): υ (cm^{-1})** 2980, 1656, **HMRS** (ESI, *m/z*)**:** m/z calc for $C_{17}H_{24}OSi$ $[M]^+$: 272.1596; found: 272.1591.

Allyl(4-tert-butylphenyl)bis[(2-methylprop-2-en-1-yl)oxy]silane: 177.



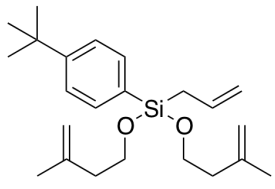
To a 0.1 M solution of trichloroallylsilane (0.71 mL, 5.0 mmol, 1.0 eq) in DCM and Et_3N (1.4 mL, 10.5 mmol, 2.1 eq) was added dropwise a solution 0.1 M of 2-methyl-2-propen-1-ol in DCM (0.84 mL, 10.0 mmol, 2.0 eq) at room temperature. The reaction mixture was maintained stirring for 12 hours. Without further purification the solution was transferred *via* cannula to one-neck round-bottomed flask and the solvent was removed in *vacuo* (1.1 g, 4.6 mmol). The crude was redisolved in THF (1 M) and was added drop wise at -78ºC to a solution of 4-tert-butylphenylmagnesium bromide solution in THF (11 mL, 5.5 mmol, 1.1 eq. 0.5 M in Et_2O). The reaction mixture was warmed up to room temperature and stirred for 16 hours. Then, was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent was removed *in vacuo* and the crude purified by flash chromatography, *Rf* = 0.6 (Hexane:Et_2O 95:5) to yield a colourless oil (860, mg 50%). **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 1.34 (9H, s, C(CH_3)$_3$), 1.73 (6H, s, CH_3), 1.93 (2H, d, $^3J_{(H,H)}$ 8.0 Hz, SiCH_2), 4.20 (4H, m, SiOCH_2), 4.86 (2H, s, MeC=CH$_a$$H_b$), 4.91 (1H, dt, $^3J_{(H,H)}$ 10.0 Hz, $^4J_{(H,H)}$ 2.0 Hz, CH=CH_{2cis}), 4.97 (1H, ddt, $^3J_{(H,H)}$ 17.0, $^4J_{(H,H)}$ 2.0 Hz, CH=CH_{2trans}), 5.07 (2H, s, MeC=CH_aH$_b$), 5.87 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 8.0 Hz, CH=CH$_2$), 7.41 (2H, m, PhH_{ortho}), 7.60 (2H, m, PhH_{meta}); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 19.0 (s, CH$_3$), 21.7 (s, SiCH$_2$), 31.2 (s, C(CH$_3$)$_3$), 34.7 (s, C(CH$_3$)$_3$), 66.5 (s, SiOCH$_2$), 109.6 (s, MeC=CH$_2$), 114.8 (s, CH=CH$_2$), 124.8 (s, ArC_{ortho}), 129.2 (s, ArC_{ipso}), 132.8 (s, SiCH$_2$$C$H=CH$_2$), 134.4 (s, Ar$C_{meta}$), 143.7 (s, Me$C$=CH$_2$), 153.2 (s, Ar$C_{para}$); **IR (film): υ_{max} (cm^{-1})** 3076, 1638, 1031; **HMRS** (ESI, *m/z*) calc for $C_{21}H_{32}O_2SiNa$ [M+Na]$^+$: 367.2069 found: 367.2070.

Allyl{bis[(2-bromoprop-2-en-1-yl)oxy]}silane: 169.



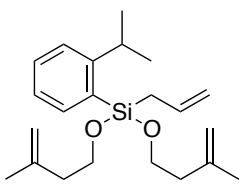
To a 0.1 M solution of allylphenyldichlorosilane (0.92 mL, 5.0 mmol, 1.0 eq) in DCM (25 mL) and Et_3N (1.4 mL, 10.0 mmol, 2.0 eq) was added dropwise a 1 M solution of 2-bromo-2-propen-1-ol (0.83 mL, 10 mmol, 2.0 eq) in DCM at room temperature. The reaction mixture was maintained stirring for 16 hours. The reaction mixture was quenched with water and extracted with DCM. The combined organic layers were washed with water and brine, dried over magnesium sulphate and filtered. The solvent was subsequently removed *in vacuo* and the crude oil purified *via* flash chromatography, *Rf* = 0.5 (Hexane:Ether 95:5) to yield a colourless oil (1.2 g, 61%). **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 1.93 (2H, d, $^3J_{(H,H)}$ 8.0 Hz, SiCH_2), 4.38 (4H, m, SiOCH_2), 4.96 (1H, dt, $^3J_{(H,H)}$ 10.0 Hz, $^4J_{(H,H)}$ 2.0 Hz, CH=CH_{2cis}), 5.04 (1H, dt, $^3J_{(H,H)}$ 17.0, $^4J_{(H,H)}$ 2.0 Hz, CH=CH_{2trans}), 5.59 (2H, s, BrC=CH_aH_b), 5.84 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 8.0 Hz, CH=CH_2), 6.02 (2H, s, BrC=CH_aH_b), 7.44 (3H, m, Ph$H_{ortho/para}$) 7.66 (2H, m, PhH_{meta}); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 20.9 (s, SiCH$_2$), 65.5 (s, SiOCH), 109.7 (s, BrC=CH$_2$), 115.0 (s, CH=CH$_2$), 127.8 (s, ArC_{ortho}), 130.2 (s, ArC_{para}), 132.6 (s, SiCH$_2C$H=CH$_2$), 132.7 (s, ArC_{ipso}), 134.4 (s, ArC_{meta}), 143.7 (s, MeC=CH$_2$); **IR (film): υ_{max} (cm^{-1})** 3076, 1638, 1031, **HRMS (CI+):** m/z calc for $C_{15}H_{18}O_2Br_2O_2SiNa$ $[M+Na]^+$: 438.9333; found: 438.9335.

Allyl(4-*tert*-butylphenyl)bis[(3-methylbut-3-en-1-yl)oxy]silane: 182.



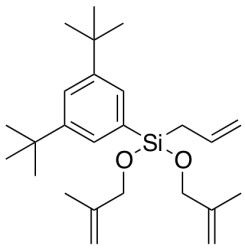
To a 0.1 M solution of trichloroallylsilane (0.71 mL, 5.0 mmol, 1eq) in DCM and Et_3N (1.4 mL, 10.5 mmol, 2.1 eq) was added dropwise a solution 0.1 M of 3-methyl-3-buten-1-ol in DCM (1.0 mL, 10.0 mmol, 2.0 eq) at room temperature. The reaction mixture was maintained stirring for 48 hours under reflux. Without further purification the solution was transferred *via* cannula to one-neck round-bottomed flask and the solvent was removed *in vacuo* (1.0 g, 4.0 mmol). The crude was redisolved in THF (1 M) and was added dropwise at 0 ºC to a solution of 4-tert-butylphenylmagnesium bromide in THF (10 mL, 5.0 mmol, 1.0 eq. 0.5 M). The reaction mixture was warmed up to room temperature and stirred for 16 hours. It was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent removed *in vacuo* to yield and the crude oil was purified by flash chromatography, *Rf* = 0.6 (Hexane:Et_2O 95:5) to yield a colourless oil (860 mg, 47%). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.36 (9H, s, C(CH_3)$_3$), 1.76 (6H, s, CH_3), 1.92 (2H, d, , $^3J_{(H,H)}$ 11.6 Hz, CH_2), 2.30 (4H, t, $^3J_{(H,H)}$ 7.2 Hz, SiCH_2), 3.90 (4H, td, $^3J_{(H,H)}$ 7.6 Hz, $^4J_{(H,H)}$ 2.4 Hz SiOCH_2), 4.86 (2H, s, MeC=CH$_a$H$_b$), 4.81 (1H, dt, $^3J_{(H,H)}$ 7.6 Hz, $^4J_{(H,H)}$ 2.4 Hz, CH=CH_{2cis}), 4.95 (1H, ddt, $^3J_{(H,H)}$ 17.0, $^4J_{(H,H)}$ 2.0 Hz, CH=CH_{2trans}), 5.07 (2H, s, MeC=CH_aH$_b$), 5.87 (1H, ddt, $^3J_{(H,Htrans)}$ 17.2, $^3J_{(H,Hcis)}$11.2, $^3J_{(H,H)}$ 8.0 Hz, CH=CH$_2$), 7.44 (2H, m, PhH_{ortho}), 7.61 (2H, m, PhH_{meta}); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 20.9 (s, CH$_3$), 22.8 (s, SiCH$_2$), 31.2 (s, C(CH$_3$)$_3$), 34.7 (s, C(CH$_3$)$_3$), 40.7 (s, SiOCH$_2C$H$_2$), 61.8 (s, SiOCH$_2$), 111.7 (s, MeC=CH$_2$), 114.7 (s, CH=CH$_2$), 124.7 (s, ArC_{ortho}), 129.6 (s, ArC_{ipso}), 133.0 (s, SiCH$_2C$H=CH$_2$), 134.4 (s, ArC_{meta}), 142.7 (s, MeC=CH$_2$), 153.1 (s, ArC_{para}); **IR (film): υ_{max} (cm^{-1})** 2965, 1632, 1089; **HMRS** (ESI, *m/z*) calc for $C_{23}H_{36}O_2SiNa$ [M+Na]$^+$: 395.2377 found: 395.2376.

Allyl(3-isopropylphenyl)bis[(3-methylbut-3-en-1-yl)oxy]silane: 183.



To a 0.1 M solution of trichloroallylsilane (0.71 mL, 5.0 mmol, 1eq) in Et_2O and Et_3N (1.4 mL, 10.5 mmol, 2.1 eq) was added dropwise a 0.1 M solution of 3-methyl-3-buten-1-ol 3-buten-1-ol in DCM (1.0 mL, 10.0 mmol, 2.0 eq) at room temperature. The reaction mixture was maintained stirring for 12 hours. Without further purification the solution was transferred *via* cannula to one-neck round-bottomed flask and the solvent was removed *in vacuo* (1.1 g, 4.0 mmol). The crude was redisolved in THF (1 M) and was added dropwise at 0 ºC to a solution of 2-isopropyl-butylphenylmagnesium bromide in THF (10 mL, 5.0 mmol, 1.0 eq. 0.5 M). The reaction mixture was warmed up to room temperature for 16 hours. It was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent removed *in vacuo* and the oil which was purified by flash chromatography, *Rf* = 0.6 (Hexane:Et_2O 95:5) to yield a colourless oil (984 mg, 66%). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.27 (6H, d, , $^3J_{(H,H)}$ 6.8 Hz, CH(CH_3)$_3$), 1.77 (6H, s, CH_3), 1.92 (2H, d, $^3J_{(H,H)}$ 11.6 Hz, CH_2), 2.36 (4H, t, $^3J_{(H,H)}$ 7.2 Hz, SiOCH$_2$CH_2), 3.31 (1H, sep, $^3J_{(H,H)}$ 6.8 Hz, CH),), 3.90 (4H, m, SiOCH_2), 4.74 (2H, s, MeC=CH$_a$$H_b$), 4.80 (2H, s, MeC=C$H_aH_b$), 4.91 (1H $^3J_{(H,Hcis)}$11.2, $^3J_{(H,H)}$ 8.0 Hz, CH=CH$_2$), 4.96 (1H, ddt, $^3J_{(H,H)}$ 17.5, $^4J_{(H,H)}$ 2.0 Hz, CH=CH_{2trans}), 5.81 (1H, ddt, $^3J_{(H,Htrans)}$ 17.5, $^3J_{(H,Hcis)}$11.2, $^3J_{(H,H)}$ 8.0 Hz, CH=CH$_2$), 7.20 (1H, t, $^3J_{(H,H)}$ 6.4 Hz PhH_{meta}), 7.36 (1H, d, $^3J_{(H,Htrans)}$ 7.5 Hz PhH_{ortho}), 7.41 (1H, t, $^3J_{(H,H)}$ 6.4 Hz PhH_{para}), 7.70 (1H, d, $^3J_{(H,H)}$ 6.4 Hz, PhH_{meta}); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 22.1 (s, CH$_3$), 22.8 (s, SiCH$_2$), 24.8 (s, CH(CH$_3$)$_2$), 33.4 (s, CH(CH$_3$)$_2$), 40.7 (s, SiOCH$_2$$CH_2$), 61.7 (s, SiO$CH_2$), 111.7 (s, MeC=$CH_2$), 114.4 (s, CH=$CH_2$), 125.1 (s, Ar$C_{ortho}$), 124.7 (s, Ar$C_{meta}$), 130.6 (s, Ar$C_{ortho}$), 130.7 (s, Ar$C_{ipso}$), 132.9 (s, SiCH$_2$$C$H=CH$_2$), 135.9 (s, Ar$C_{meta}$), 142.6 (s, Me$C$=CH$_2$), 155.6 (s, Ar$C_{para}$); **IR (film): υ_{max} (cm^{-1})** 2964, 1632, 1090; **HMRS** (ESI, *m/z*) calc for $C_{22}H_{34}O_2SiNa$ $[M+Na]^+$: 381.2220 found: 381.2215.

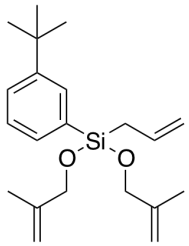
Allyl(3,5-di-*tert*-butylphenyl)bis[(2-methylprop-2-en-1-yl)oxy]silane: 181.



To a 0.1 M solution of trichloroallylsilane (0.71 mL, 5.0 mmol, 1eq) in DCM and Et_3N (1.4 mL, 10.5 mmol, 2.1 eq) was added dropwise a 0.1 M solution of 2-methyl-2-propen-1-ol in DCM (0.84 mL, 10.0 mmol, 2.0 eq) at room temperature. The reaction mixture was maintained stirring for 12 hours. Without further purification the solution was transferred *via* cannula to one-neck round-bottomed flask and the solvent was removed in *vacuo* (1.1 g, 4.0 mmol). The crude was redisolved in THF (1 M) and was added drop wise at 0ºC to a solution of 3,5-di*tert*butyl-phenylmagnesium bromide in THF (10 mL, 5.0 mmol, 1.0 eq. 0.5 M). The reaction mixture was warmed up to room temperature and stirred for 16 hours. It was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent was removed in *vacuo* and the crude oil purified by flash chromatography, *Rf* = 0.6 (Hexane:Et_2O 95:5) to yield a colourless oil (900 mg, 45%). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.34 (18H, s, C(CH_3)$_3$), 1.73 (6H, s, CH_3), 1.93 (2H, d, $^3J_{(H,H)}$ 8.4 Hz, SiCH_2), 4.21 (4H, s, SiOCH_2), 4.87 (2H, s, MeC=CH_aH_b), 4.95 (1H, dt, $^3J_{(H,H)}$ 10.0 Hz, $^4J_{(H,H)}$ 2.0 Hz, CH=CH_{2cis}), 4.97 (1H, ddt, $^3J_{(H,H)}$ 17.0, $^4J_{(H,H)}$ 2.0 Hz, CH=CH_{2trans}), 5.09 (2H, s, MeC=CH_aH_b), 5.91 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 8.0 Hz, CH=CH_2), 7.53 (3H, m, Ph$H_{ortho,\ para}$); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 19.0 (s, CH_3), 21.3 (s, SiCH_2), 31.2 (s, C(CH_3)$_3$), 34.8 (s, C(CH_3)$_3$), 66.5 (s, SiOCH_2), 109.5 (s, MeC=CH_2), 114.6 (s, CH=CH_2), 124.2 (s, ArC_{ortho}), 128.4 (s, ArC_{ipso}), 131.4 (s, $SiCH_2CH=CH_2$), 133.0 (s, ArC_{meta}), 143.7 (s, MeC=CH_2), 149.7 (s, ArC_{para}); **IR (film): υ_{max} (cm^{-1})**

2964, 2867, 1632, 1104; **HMRS** (ESI, *m/z*) calc for $C_{25}H_{40}NaO_2Si$ $[M]^+$: 423.2690 found: 423.2686.

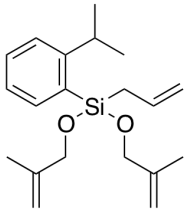
Allyl(3-*tert*-butylphenyl)bis[(2-methylprop-2-en-1-yl)oxy]silane: 179.



To a 0.1 M solution of trichloroallylsilane (0.71 mL, 5.0 mmol, 1eq) in DCM and Et_3N (1.4 mL, 10.5 mmol, 2.1 eq) was added dropwise a 0.1 M solution of 2-methyl-2-propen-1-ol in DCM (0.84 mL, 10.0 mmol, 2.0 eq) at room temperature. The reaction mixture was maintained stirring for 12 hours. Without further purification the solution was transferred *via* cannula to one-neck round-bottomed flask and the solvent was removed *in vacuo* (1.1 g, 4.0 mmol). The crude was redisolved in THF (1 M) and was added dropwise at 0 ºC to a solution of 3-tert-butylphenylmagnesium bromide in THF (10 mL, 5.0 mmol, 1.1 eq. 0.5 M). The reaction mixture was warmed up to room temperature and stirred for 16 hours. It was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent was removed in *vacuo* and the crude oil purified by flash chromatography, *Rf* = 0.6 (Hexane:Et_2O 95:5) to yield a colourless oil (860 mg, 55%). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.33 (9H, s, $C(CH_3)_3$), 1.73 (6H, s, CH_3), 1.94 (2H, d, $^3J_{(H,H)}$ 7.6 Hz, $SiCH_2$), 4.20 (4H, s, $SiOCH_2$), 4.87 (2H, s, $MeC=CH_aH_b$), 4.93 (1H, dt, $^3J_{(H,H)}$ 10.0 Hz, $^4J_{(H,H)}$ 2.0 Hz, $CH=CH_{2cis}$), 4.95 (1H, ddt, $^3J_{(H,H)}$ 16.0, $^4J_{(H,H)}$ 2.0 Hz, $CH=CH_{2trans}$), 5.00 (2H, s, $MeC=CH_aH_b$), 5.92 (1H, ddt, $^3J_{(H,Htrans)}$ 16.0, $^3J_{(H,Hcis)}$10.5, $^3J_{(H,H)}$ 8.0 Hz, $CH=CH_2$), 7.34 (1H, t, $^3J_{(H,H)}$ 6.4 Hz PhH_{meta}), 7.46 (2H, m, $PhH_{ortho,\ para}$), 7.71 (1H, s, PhH_{ortho}); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 19.0 (s, CH_3), 21.1 (s, $SiCH_2$), 31.3 (s, $C(CH_3)_3$), 34.6 (s, $C(CH_3)_3$), 66.5 (s, $SiOCH_2$), 109.6 (s, $MeC=CH_2$), 114.8 (s, $CH=CH_2$), 127.2 (s, ArC_{ortho}),

127.5 (s, ArC_{ortho}), 131.3 (s, ArC_{meta}), 131.5 (s, ArC_{ipso}), 132.1 (s, SiCH$_2$*C*H=CH$_2$), 132.8 (s, ArC_{meta}), 143.8 (s, Me*C*=CH$_2$), 150.1 (s, ArC_{para}); **IR (film): υ_{max} (cm^{-1})** 2964, 2867, 1632, 1104; **HMRS** (ESI, *m/z*) calc for $C_{21}H_{32}O_2Si$ $[M]^+$: 344.2172 found: 344.2173.

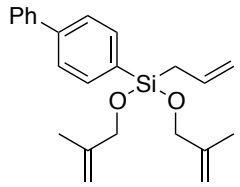
Allyl(3-isopropylphenyl)bis[(2-methylprop-2-en-1-yl)oxy]silane: 180.



To a 0.1 M solution of trichloroallylsilane (0.71 mL, 5.0 mmol, 1eq) in DCM and Et_3N (630 mg, 10.5 mmol, 2.1 eq) was added dropwise a solution 0.1 M of 2-methyl-2-propen-1-ol (0.82 mL, 10.0 mmol, 2.0 eq) in DCM at room temperature. The reaction mixture was maintained stirring for 12 hours. Without further purification the solution was transferred *via* cannula to one-neck round-bottomed flask and the solvent was removed in *vacuo* (1.0 g, 4.0 mmol). The crude was redisolved in THF (1 M) and was added drop wise at 0ºC to a solution of 2-iso-propylphenylmagnesium bromide in THF (10 mL, 5.0 mmol, 1.0 eq. 0.5 M). The reaction mixture was warmed up to room temperature and stirred for 16 hours. It was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent removed *in vacuo* and the crude oil which was purified by flash chromatography, *Rf* = 0.6 (Hexane:Et_2O 95:5) to yield a colourless oil (940 mg, 65%). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.27 (6H, d, $^3J_{(H,H)}$ 6.4 Hz, CH(C*H*$_3$)$_3$), 1.77 (6H, s, C*H*$_3$), 1.92 (2H, dt, $^3J_{(H,H)}$ 7.6 Hz, $^4J_{(H,H)}$ 2.0 Hz, C*H*$_2$), 3.29 (1H, sep, $^3J_{(H,H)}$ 6.8 Hz, C*H*), 4.19, (2H, s, SiOC*H*$_2$), 4.21, (2H, s, SiOC*H*$_2$), 4.86 (2H, s, MeC=CH$_a$*H*$_b$), 4.90 (1H, m, CH=C*H*$_2$), 4.98 (1H, ddt, $^3J_{(H,H)}$ 17.0, $^4J_{(H,H)}$ 2.0 Hz, CH=C*H*$_{2trans}$), 5.07 (2H, s, MeC=C*H*$_a$H$_b$), 5.81 (1H, ddt, $^3J_{(H,Htrans)}$ 17.5, $^3J_{(H,Hcis)}$11.2, $^3J_{(H,H)}$ 8.0 Hz, C*H*=CH$_2$), 7.21 (1H, t, $^3J_{(H,H)}$ 6.4 Hz Ph*H*$_{meta}$), 7.36 (1H, d, $^3J_{(H,Htrans)}$ 7.5 Hz Ph*H*$_{ortho}$), 7.44 (1H, t, $^3J_{(H,H)}$ 6.4 Hz

PhH_{para}), 7.77 (1H, d, $^{3}J_{(H,H)}$ 6.4 Hz, PhH_{meta}); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 19.0 (s, CH_3), 22.2 (s, SiCH_2), 24.9 (s, CH(CH_3)$_2$), 33.6 (s, $CH(CH_3)_2$), 66.4 (s, SiOCH_2), 109.6 (s, MeC=CH_2), 114.9 (s, CH=CH_2), 125.1 (s, ArC_{ortho}), 130.4 (s, ArC_{ortho}), 130.7 (s, ArC_{ipso}), 132.8 (s, $SiCH_2CH=CH_2$), 135.9 (s, ArC_{meta}), 143.7 (s, MeC=CH_2), 155.7 (s, ArC_{para}); **IR (film): υ_{max} (cm^{-1})** 2964, 1632, 1100; **HMRS** (ESI, *m/z*) calc for $C_{20}H_{30}O_2Si[M]^+$: 330.2015 found: 330.2018

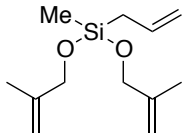
Allyl(biphenyl-4-yl)bis[(2-methylprop-2-en-1-yl)oxy]silane: 178.



To a 0.1 M solution of trichloroallylsilane (0.71 mL, 5.0 mmol, 1eq) in DCM and urea (630 mg, 10.5 mmol, 2.1 eq) was added dropwise a 0.1 M solution of 2-methyl-2-propen-1-ol in DCM (0.84 mL, 10.0 mmol, 2.0 eq) at room temperature. The reaction mixture was maintained stirring for 12 hours. Without further purification the solution was transferred *via* cannula to one-neck round-bottomed flask and the solvent was removed *in vacuo* (1.1 g, 4.5 mmol). The crude was redisolved in THF (1 M) and was added dropwise at 0ºC to a solution of 4-biphenylmagnesiumbromide in THF (11 mL, 5.5 mmol, 1.1 eq. 0.5 M). The reaction mixture was warmed up to room temperature and stirred for 16 hours. It was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent removed *in vacuo* and the crude oil was purified by flash chromatography, *Rf* = 0.6 (Hexane:Et_2O 95:5) to yield a colourless oil (860 mg, 50%). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.65 (6H, s, C=CH_2CH_3), 1.88 (2H, d, $^{3}J_{(H,H)}$ 8 Hz, SiCH_2), 4.13 (4H, m, SiOCH_2), 4.78 (2H, s, MeC=CH_2), 4.97 (1H, dt, $^{3}J_{(H,H)}$ 17.0, $^{4}J_{(H,H)}$ 2.0 Hz, CH=CH_{2trans}), 4.88 (1H, ddt, $^{3}J_{(H,Htrans)}$ 17.0, $^{3}J_{(H,Hcis)}$10.0, $^{3}J_{(H,H)}$ 8.0 Hz, CH=CH_2), 5.00 (2H, s, MeC=CH_2), 7.66-7.26 (9H, m, PhH), **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 19.0 (s, CH_3), 21.0 (s, SiCH_2), 66.6 (s, SiOCH), 109.7 (s, MeC=CH_2), 115.1 (s, CH=CH_2),

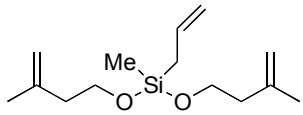
126.5, 127.2, 127.5, 128.8, 131.4, 132.6, 134.9, 140.9, 142.9, 143.7 (s, Me*C*=CH_2); **IR (film): υ_{max} (cm^{-1})** 3050, 1631m 1031; **HMRS** (ESI, *m/z*) calc for $C_{23}H_{28}NaO_2Si$ $[M+Na]^+$: 387.1751 found: 387.1755.

Allyl{bis[(2-methylprop-2-en-1-yl)oxy]}silane: 172.



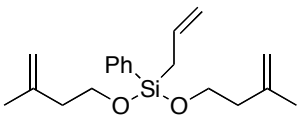
To a 0.1 M solution of allylmethyldichlorosilane (0.29 mL, 2.0 mmol, 1.0 eq) in DCM (15 mL) and Et_3N (0.54 mL, 4.2 mmol, 2.2 eq), was added dropwise a 1 M solution of 2-methyl-2-propen-1-ol (414 mL, 4.2 mmol, 2.2 eq) in DCM at room temperature. The reaction mixture was maintained stirring for 16 hours. The reaction mixture was quenched with water and extracted with DCM. The combined organic layers were washed with water, brine, and dried over magnesium sulphate and filtered. The solvent was subsequently removed *in vacuo* and the crude oil purified via flash chromatography *Rf* = 0.6 (Hexane:Et_2O 95:5), to yield a colourless oil (449 mg, 72%). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 0.16 (3H, s, SiCH_3), 1.70 (2H, d, $^3J_{(H,H)}$ 8 Hz, SiCH_2), 1.72 (6H, s, CH_3C=CH_2), 4.15 (4H, s, SiOCH_2), 4.85 (2H, m, MeC=CH_{2b}), 4.92 (1H, ddt, $^3J_{(H,H)}$ 10, $^2J_{(H,H)}$ 3, $^4J_{(H,H)}$ 2 x 1.0 Hz, CH=C$H_{2(cis)}$), 4.97 (1H, ddt, $^3J_{(H,H)}$ 17, $^2J_{(H,H)}$ 3, $^4J_{(H,H)}$ 2 x 1 Hz, CH=C$H_{2(trans)}$), 5.84 (1H, dddd, $^3J_{(H,Htrans)}$ 17, $^3J_{(H,Hcis)}$10, $^3J_{(H,H)}$ 2 x 8.00 Hz, C*H*=CH_2), 5.00 (2H, s, MeC=CH_{2a}); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** -1.3 (s, Si*C*H_3), 18.9 (s, *C*H_3C=CH_2), 21.8 (s, Si*C*H_2), 66.3 (s, SiO*C*H_2), 109.8 (s, MeC=*C*H_2), 114.4 (s, CH=*C*H_2), 133.0 (s, *C*H=CH_2), 143.9 (s, Me*C*=CH_2); **IR (film): υ (cm^{-1})** 3060, 1648, 1033; **HRMS (CI+):** m/z calc for $C_{12}H_{23}O_2Si$ $[M+H]^+$: 227.1467; found: 227.1471.

Allyl(methyl)bis[(2-methylbut-3-en-1-yl)oxy]silane: 173.



To a 0.1 M solution of allylmethyldichlorosilane (0.29 mL, 2.0 mmol, 1.0 eq) in DCM (15 mL) and Et_3N (0.54 mL, 4.2 mmol, 2.2 eq), was added dropwise a 1 M solution of 3-methyl-1-buten-1-ol (424 mL, 4.2 mmol, 2.2 eq) in DCM at room temperature. The reaction mixture was maintained stirring for 16 hours. The reaction mixture was quenched with water and extracted with DCM. The combined organic layers were washed with water, brine, and dried over magnesium sulphate and filtered. The solvent was subsequently removed *in vacuo* and the crude oil purified via flash chromatography *Rf* = 0.6 (Hexane:Et_2O 95:5), to yield a colourless oil (431 mg, 85%). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 0.13 (3H, s, SiCH_3), 1.65 (2H, d, $^3J_{(H,H)}$ 8.0 Hz, SiCH_2CH), 1.74 (6H, s, C=CH$_2$CH_3), 2.88 (4H, dd, $^3J_{(H,H)}$ 8, 8 Hz, SiOCH$_2$CH_2), 3.80 (4H, dd, $^3J_{(H,H)}$ 8, 8 Hz, SiOCH_2CH$_2$), 4.71 (2H, dd, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 1.0 Hz, MeC=C$H_{2(cis)}$), 4.77 (2H, m, MeC=C$H_{2(trans)}$), 4.89 (1H, dt, $^3J_{(H,H)}$ 11, $^2J_{(H,H)}$ 1 Hz, CH=C$H_{2(cis)}$), 4.95 (1H, ddd, $^3J_{(H,H)}$ 17, $^2J_{(H,H)}$ 2, $^4J_{(H,H)}$ 1 Hz, CH=C$H_{2(trans)}$), 5.80 (1H, m, CH=CH$_2$); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** -1.3 (s, SiCH$_3$), 21.8 (s, SiCH$_2$), 23.5 (s, SiOCHCH$_3$), 40.7 (s, SiOCH$_2$$CH_2$), 61.4 (s, SiO$CH_2$), 111.6 (s, MeC=$CH_2$), 114.3 (s, CH=$CH_2$), 133.3 (s, CH=CH$_2$), 142.6 (s, MeC=CH$_2$); **IR (film): υ (cm^{-1})** 3076, 1638, 1031; **HRMS (CI+):** m/z calc for $C_{13}H_{25}O_2Si$ [M+H]$^+$: 241.1624; found: 241.1627.

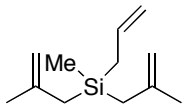
Allyl{bis[(3-methylbut-3-en-1-yl)oxy]}phenylsilane: 168.



To a 1 M solution of allylphenyldichlorosilane (0.5 mL, 2.69 mmol, 1.2 eq) in DCM (15 mL) and triethylamine (0.75 mL, 5.38 mmol, 2.4 eq) in DCM, at 0 °C was added dropwise and solution of 3-methyl-3-buten-1-ol (0.45 mL, 4.48 mmol, 2.2 eq). The reaction mixture was maintained

stirring at reflux for 19 hours after which the reaction mixture was quenched with water and extracted with DCM. The combined organic extracts were washed with water and brine, and dried over sodium sulphate and filtered. The solvent was subsequently removed in *vacuo* and the crude oil purified via filtration through a short plug of alumina to yield as a clear oil 640 mg (75%) R_f = 0.4 (Hexane:Ether 95:5) **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.78 (6H, br s, CH_3), 1.94 (2H, ddd, $^3J_{(H,H)}$ 8.0, $^4J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 1.0 Hz, SiCH_2CH), 2.36 (4H, t, $^3J_{(H,H)}$ 2 x 7.0 Hz $SiOCH_2CH_2$), 3.92 (4H, td, $^3J_{(H,H)}$ 2 x 7.0, $^2J_{(H,H)}$ 2.5 Hz SiOCH_2CH_2), 4.77 (2H, s, MeC=CH_2), 4.83 (2H, s, MeC=CH_2), 4.94 (1H, ddt, $^3J_{(H,H)}$ 10.0, $^2J_{(H,H)}$ 1.5, $^4J_{(H,H)}$ 2 x 1.0 Hz, CH=C$H_{2(cis)}$), 5.00 (1H, ddt, $^3J_{(H,H)}$ 17.0, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 2 x 1.0 Hz, CH=C$H_{2(trans)}$), 5.87 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 2 x 8.0 Hz, CH=CH_2), 7.43 (3H, m, C$H_{ortho/para}$), 7.69 (2H, m, CH_{meta}); **^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm):** 20.8 (s, Si$C$$H_2$CH), 22.8 (s, $C$$H_3$C=$CH_2$), 40.7 (s, $SiOCH_2CH_2$MeC=CH_2), 61.8 (s, $SiOCH_2CH_2$MeC=CH_2), 111.9 (s, MeC=$C$$H_2$), 114.9 (s, CH=$C$$H_2$), 127.8 (s, $C$$H_{ortho}$), 130.2 (s, $C$$H_{para}$), 132.8 (s, CH=CH_2), 133.1 (s, SiC_{ipso}), 134.5 (s, $C$$H_{meta}$), 142.6, (s, Me$C$=$CH_2$); **IR (film): υ (cm^{-1})** 3074 (=C-H), 1650 (C=C), 1096 (C-O); **HRMS (CI+):** m/z calc for $C_{19}H_{29}O_2Si$ $[M+H]^+$: 317.1937; found: 317.1943.

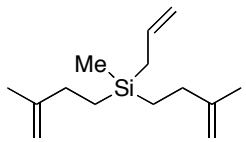
Allyl(methyl)bis(2-methylprop-2-en-1-yl)silane: 144.



To a 0.1 M solution of allylmethyldichlorosilane (0.29 mL, 2.0 mmol, 1.0 eq) in THF (15 mL) was added dropwise a solution of 2-methylallylmagnesium chloride in THF (3.0 eq, 0.5 M solution). The reaction mixture was left to stir at room temperature for 16 hours. It was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent removed *in vacuo* and the crude was purified by flash chromatography, *Rf* = 0.5 (Hexane), to yield a colourless oil (337 mg, 87%). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 0.08

(3H, s, CH_3), 1.62 (4H, s, SiCH_2MeC=CH_2), 1.63 (2H, ddd, $^3J_{(H,H)}$ 8.0, $^4J_{(H,H)}$ 1.5, $^4J_{(H,H)}$ 1.0 Hz SiCH_2CH), 1.74 (6H, dd, $^4J_{(H,Htrans)}$ 2.0, $^4J_{(H,Hcis)}$ 1.0 Hz, C=CH_2CH_3), 4.54 (2H, br s, MeC=CH_2), 4.65 (2H, dq, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 1.0 Hz, MeC=CH_2), 4.89 (1H, ddt, $^3J_{(H,H)}$ 10.0, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 2 x 1.5 Hz, CH=C$H_{2(cis)}$), 4.90 (1H, ddt, $^3J_{(H,H)}$ 16.0, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 2 x 1.5 Hz, CH=C$H_{2(trans)}$), 5.81 (1H, ddt, $^3J_{(H,Htrans)}$ 16.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 2 x 8.0 Hz, CH=CH_2); **^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm):** -1.8, (s, SiCH$_3$), 21.9, (s, SiCH$_2$CH), 25.2 (s, SiCH$_2$MeC=CH_2), 25.4, (s, CH$_3$C=CH_2), 109.1 (s, MeC=CH$_2$), 113.6 (s, CH=CH$_2$), 134.6 (s, CH=CH_2), 143.0 (s, MeC=CH_2); **IR (film): υ (cm^{-1})** 3076, 1636, **HRMS (CI+):** m/z calc for $C_{12}H_{23}Si$ $[M+H]^+$: 195.1569; found: 195.1566.

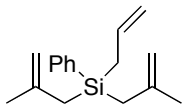
Allyl(methyl)bis(3-methylbut-3-en-1-yl)silane: 145.



To a 0.1 M solution of allylmethyldichlorosilane (0.29 mL, 2.0 mmol, 1.0 eq) in THF (15 mL) was added dropwise a solution of Grignard **152** THF (3.0 eq, 0.35 M solution). The reaction mixture was left to stir at room temperature for 16 hours. It was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent removed *in vacuo* and the crude was purified by flash chromatography, *Rf* = 0.5 (Hexane), to yield a colourless oil (301 mg, 68%). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 0.13 (3H, br s, SiCH_3), 0.79 (4H, ddd, $^3J_{(H,H)}$ 8.0, $^2J_{(H,H)}$ 5.0, $^3J_{(H,H)}$ 4.5 Hz, SiCH_2 CH_2MeC=CH_2), 1.66 (2H, d, $^3J_{(H,H)}$ 8.0 Hz, SiCH_2CH), 1.74 (6H, t, $^4J_{(H,Htrans)}$ 1.0, $^4J_{(H,Hcis)}$ 1.0 Hz, C=CH_2CH_3), 2.05 (4H, dt, $^3J_{(H,H)}$ 8.5, $^2J_{(H,H)}$ 2.0 Hz, SiC$H_2$$CH_2$MeC=$CH_2$), 4.68 (2H, q, $^4J_{(H,H)}$ 3 x 1.0 Hz, MeC=C$H_{2(cis)}$), 4.72 (2H, q, $^4J_{(H,H)}$ 3 x 1.0 Hz, MeC=C$H_{2(trans)}$), 4.88 (1H, dd, $^3J_{(H,H)}$ 10.00, $^2J_{(H,H)}$ 2.0 Hz, CH=C$H_{2(cis)}$), 4.93 (1H, dd, $^3J_{(H,H)}$ 17.0, $^2J_{(H,H)}$ 2.0 Hz, CH=C$H_{2(trans)}$), 5.82 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$ 10.0, $^3J_{(H,H)}$ 2 x 8.0 Hz, CH=CH_2); **^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm):** -4.4 (s, SiCH$_3$), 12.8 (s, SiCH$_2$$CH_2$MeC=$CH_2$), 22.1 (s, CH$_3$),

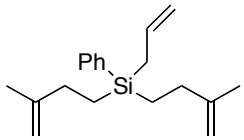
23.1 (s, Si*C*H_2CH), 30.9 (s, SiCH$_2$*C*H$_2$MeC=CH$_2$), 108.5 (s, MeC=*C*H$_2$), 113.7 (s, CH=*C*H$_2$), 133.9 (s, *C*H=CH$_2$), 142.9 (s, MeC=CH$_2$); **IR (film): υ (cm^{-1})** 3076, 1649; **HRMS (CI+):** m/z calc for $C_{14}H_{27}Si$ $[M+H]^+$: 223.1882; found: 223.1887.

Allyl[bis(2-methylprop-2-en-1-yl)]phenylsilane: 146.



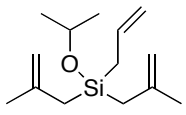
To a 0.1 M solution of allylphenyldichlorosilane (0.92 mL, 5.0 mmol, 1.0 eq) in THF (25 mL) was added dropwise a solution of 2-methylallylmagnesium chloride in THF (3.0 eq, 0.5 M solution). The reaction mixture was left to stir at room temperature for 16 hours. It was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent removed *in vacuo* and the crude was purified by flash chromatography, *Rf* = 0.5 (Hexane) to yield a colourless oil (960 mg, 75%). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.67 (6H, br s, C*H*$_3$), 1.97 (4H, s, SiC*H*$_2$MeC=CH$_2$), 2.04 (2H, dt, $^3J_{(H,H)}$ 8.0, $^4J_{(H,H)}$ 2 x 1.5 Hz, SiC*H*$_2$CH), 4.65 (2H, br s, MeC=C*H*$_{2(cis)}$), 4.73 (2H, dq, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 3 x 1.5 Hz, MeC=C*H*$_{2(trans)}$), 5.00 (1H, dq, $^3J_{(H,H)}$ 10.0, $^2J_{(H,H)}$ 1.5, $^4J_{(H,H)}$ 2 x 1.5 Hz, CH=C*H*$_{2(cis)}$), 5.05 (1H, dq, $^3J_{(H,H)}$ 17.0, $^2J_{(H,H)}$ 1.5, $^4J_{(H,H)}$ 2 x 1.5 Hz, CH=C*H*$_{2(trans)}$), 7.42 (3H, m, C*H*$_{ortho/para}$), 5.94 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 2 x 8.0 Hz, C*H*=CH$_2$), 7.64 (2H, m, C*H*$_{meta}$); **^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm):** 20.0, (s, Si*C*H$_2$CH), 24.0 (s, Si*C*H$_2$MeC=CH$_2$), 25.6, (s, *C*H$_3$), 110.2 (s, MeC=*C*H$_2$), 114.7 (s, CH=*C*H$_2$), 127.7 (s, *C*H$_{ortho}$), 129.3 (s, *C*H$_{para}$), 134.1 (s, *C*H=CH$_2$), 134.4 (s, *C*H$_{meta}$), 136.2 (s, Si*C*$_{ipso}$), 142.7 (s, MeC=CH$_2$); **IR (film): υ (cm^{-1})** 3074, 1636; **HRMS (CI+):** m/z calc for $C_{17}H_{25}Si$ $[M+H]^+$: 257.1726; found: 257.1724.

Allyl[bis(3-methylbut-3-en-1-yl)]phenylsilane: 147.



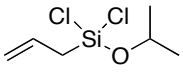
To a 0.1 M solution of allylmethyldichlorosilane (0.47 mL, 2.56 mmol, 1.0 eq) in THF (15 mL) was added dropwise a solution of Grignard **152** THF (3.0 eq, 0.35 M solution). The reaction mixture was left to stir at room temperature for 16 hours. It was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent removed *in vacuo* and the crude was purified by flash chromatography, *Rf* = 0.5 (Hexane) to yield as a clear oil 555 mg (33%). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.08 (4H, dt, $^2J_{(H,H)}$ 8.0, $^3J_{(H,H)}$ 2 x 5.0 Hz, SiCH_2CH$_2$MeC=CH$_2$), 1.80 (6H, t, $^4J_{(H,Htrans)}$ 1.5, $^4J_{(H,Hcis)}$ 1.5 Hz, C=CH$_2$CH_3), 1.96 (2H, dt, $^3J_{(H,H)}$ 8.0, $^4J_{(H,H)}$ 2 x 1.5 Hz, SiCH_2CH), 2.11 (4H, dt, $^2J_{(H,H)}$ 8.5, $^3J_{(H,H)}$ 2 x 4.5 Hz, SiCH$_2$CH_2MeC=CH$_2$), 4.76 (2H, dq, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 3 x 1.0 Hz, MeC=C$H_{2(cis)}$), 4.80 (2H, dq, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 3 x 1.0 Hz, MeC=C$H_{2(trans)}$), 4.95 (1H, ddt, $^3J_{(H,H)}$ 10.0, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 2 x 1.0 Hz, CH=C$H_{2(cis)}$), 5.00 (1H, ddt, $^3J_{(H,H)}$ 17.0, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 2 x 1.0 Hz, CH=C$H_{2(trans)}$), 5.88 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 2 x 8.0 Hz, CH=CH$_2$),), 7.38 (3H, m, C$H_{ortho/para}$), 7.51 (2H, m, CH_{meta}); **^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm):** 10.3 (s, SiCH$_2$CH$_2$MeC=CH$_2$), 20.2, (s, SiCH$_2$CH), 22.2 (s, CH$_3$), 31.6 (s, SiCH$_2$$CH_2$MeC=CH$_2$), 108.7 (s, MeC=$CH_2$), 113.9 (s, CH=$CH_2$), 127.8 (s, CH$_{ortho}$), 127.9 (s, CH$_{para}$), 129.2 (s, CH=CH$_2$), 134.2 (s, CH$_{meta}$), 136.2 (s, SiC_{ipso}), 148.3 (s, MeC=CH$_2$); **IR (film): υ (cm^{-1})** 3071, 1650; **HRMS (CI+):** m/z calc for $C_{19}H_{29}Si$ $[M+H]^+$: 285.2039; found: 285.2028.

Allyl(isopropoxy)bis(2-methylprop-2-en-1-yl)silane: 164.



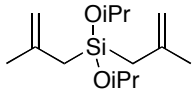
To a 0.1 M solution of trichloroallylsilane (0.71 mL, 5.0 mmol, 1eq) in DCM and Et_3N (630 mg, 10.5 mmol, 2.1 eq) was added dropwise a solution 0.1 M of isopropanol (0.38 mL, 5.0 mmol, 1.0 eq) in DCM at room temperature. The reaction mixture was maintained stirring for 12 hours. Without further purification the solution was transferred *via* cannula to one-neck round-bottomed flask and the solvent was removed in *vacuo*. The crude was redisolved in THF (1 M) and was added dropwise at 0 °C to a solution of 2-methylallylmagnesium chloride 0.5 M solution in THF (15.0 mmol, 3.0 eq.). The reaction mixture was warmed up to room temperature and stirred for 16 hours. It was quenched with saturated ammonium chloride solution and extracted with Et_2O. The combined organic extracts were washed with water, brine, dried over magnesium sulphate and filtered. The solvent removed *in vacuo* and the crude oil which was purified by flash chromatography, *Rf* = 0.6 (Hexane:Et_2O 95:5) to yield a colourless oil (702 mg, 59%). **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.17 (6H, d, $^3J_{(H,H)}$ 6.0 Hz, SiOCH(CH_3)$_2$), 1.69 (4H, br,s, SiCH_2MeC=CH_2), 1.74 (2H, dt, $^3J_{(H,H)}$ 8.0, $^4J_{(H,H)}$ 2 x 1.5 Hz, SiCH_2CH), 1.79 (6H, dd, $^4J_{(H,Htrans)}$ 1.5, $^4J_{(H,Hcis)}$ 1.0 Hz, C=CH_2CH_3), 4.10 (1H, spt, $^3J_{(H,H)}$ 6.0 Hz, SiOC*H*Me$_2$), 4.59 (2H, dq, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 3 x 1.0 Hz, MeC=C$H_{2(cis)}$), 4.67 (2H, dq, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 3 x 1.5 Hz, MeC=C$H_{2(trans)}$), 4.91 (1H, ddt, $^3J_{(H,H)}$ 10.0, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 2 x 1.0 Hz, CH=C$H_{2(cis)}$), 4.95 (1H, ddt, $^3J_{(H,H)}$ 17.0, $^2J_{(H,H)}$ 2.0, $^4J_{(H,H)}$ 1.0 Hz, CH=C$H_{2(trans)}$), 5.86 (1H, ddt, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$10.0, $^3J_{(H,H)}$ 8.0 Hz, C*H*=CH_2); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 22.1, (s, Si*C*H_2CH), 25.4 (s, Si*C*H_2MeC=CH_2), 25.8 (s, *C*H_3C=CH_2), 25.8 (s, SiOCH(*C*H_3)$_2$), 65.5 (s, SiO*C*HMe$_2$), 109.7 (s, MeC=*C*H_2), 114.3 (s, CH=*C*H_2), 133.9 (s, *C*H=CH_2), 142.6 (s, Me*C*=CH_2); **IR (film): υ (cm^{-1})** 3076, 1638, 1031; **HRMS (CI+):** m/z calc for $C_{14}H_{27}OSi$ $[M+H]^+$: 239.1831; found: 239.1833.

Allyl(dichloro)isopropoxysilane (intermediate of 164):



^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.28 (6H, d, $^3J_{(H,H)}$ 6.0 Hz, SiOCH(CH_3)$_2$), 2.09 (2H, dt, $^3J_{(H,H)}$ 7.5, $^4J_{(H,H)}$ 2 x 1.5 Hz, SiCH_2CH), 4.45 (1H, spt, $^3J_{(H,H)}$ 6 x 6.0 Hz, SiOCHMe$_2$), 5.10 (1H, dq, $^3J_{(H,H)}$ 10.5, $^2J_{(H,H)}$ 1.5, $^4J_{(H,H)}$ 2 x 1.5 Hz, CH=C$H_{2(cis)}$),), 5.12 (1H, dq, $^3J_{(H,H)}$ 16.5, $^2J_{(H,H)}$ 1.5, $^4J_{(H,H)}$ 2 x 1.5 Hz, CH=C$H_{2(trans)}$), 5.78 (1H, ddt, $^3J_{(H,Htrans)}$ 16.5, $^3J_{(H,Hcis)}$10.5, $^3J_{(H,H)}$ 2 x 7.5 Hz, CH=CH$_2$. This intermediate was too unstable to obtain ^{13}C NMR or mass spectroscopy.

By-product formed in the synthesis of 164:

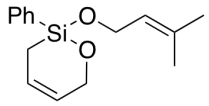


^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.19 (12H, d, $^3J_{(H,H)}$ 6.0 Hz, SiOCH(CH_3)$_2$), 1.69 (4H, s, SiCH_2), 1.81 (6H, s, C=CH$_2$CH_3), 4.20 (2H, spt, $^3J_{(H,H)}$ 6.0 Hz, SiOCHMe$_2$), 4.62 (2H, MeC=CH_2), 4.91 (2H, s, MeC=CH_2); **^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm):** 21.3, (s, SiCH_2), 25.0 (s, CH_3C=CH$_2$), 25.5 (s, SiOCH(CH_3)$_2$), 65.0 (s, SiOCHMe$_2$), 109.8 (s, MeC=CH_2), 142.40 (s, MeC=CH$_2$); **IR (film): υ (cm^{-1})** 3076**,** 1650, 1032.

General Procedure (A) for RCM with achiral catalysts:

To a 0.01 M solution of silane in DCM, was added 2 mol% Grubbs second generation catalyst and the reaction heated to reflux for 30 minutes. The reaction mixture was concentrated in vacuo to yield a brown oil which was purified via flash column chromatography to yield a colourless oil.

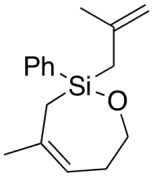
2-[(3-methylbut-2-en-1-yl)oxy]-2-phenyl-3,6-dihydro-2*H*-1,2-oxasiline: 170a.



Synthesised according to general procedure **(A)** from **170** (200 mg, 0.63 mmol), to yield **170a** as a clear oil (134 mg, 78%) R_f = 0.3 (95:5 Hex:Et$_2$O); **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):**

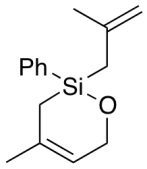
1.58 (2H, m, SiCH_2), 1.77 (6H, s, Me_2C=CH), 4.35 (2H, m, SiOCH_2), 4.70 (2H, m, SiOCH_2), 5.41 (1H, m, $SiCH_2CH$), 5.72 (1H, m, $SiCH_2CHCH$), 5.94 (1H, m, $SiOCH_2CHCH$), 7.68-7.41 (5H, m, Ar*H*); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 9.3 (s, Si*C*H_2), 19.0 (s, *Me*C=CH_2), 20.3 (s, *Me*C=CH), 66.7 (s, SiO*C*H_2C=CH), 68.0 (s, SiO*C*H_2C=CH), 109.9 (s, Me_2C=*C*H), 118.2 (s, MeC=*C*H), 127.3 (s, ArC_{para}), 130.4 (s, ArC_{ortho}), 133.6 (s, Me_2C=CH), 134.0 (s, ArC_{meta}), 135.4 (s, Me_2C=CH), 142.8 (s, ArC_{ipso}); **IR (film): υ_{max} (cm^{-1})** 3076, 1650, 1009; **HMRS** (ESI, *m/z*) calc for $C_{15}H_{20}O_2Si$ $[M]^+$: 260.1233 found: 260.1235.

4-methyl-2-(2-methylprop-2-en-1-yl)-2-phenyl-2,3,6,7-tetrahydro-1,2-oxasilepine: 156a.



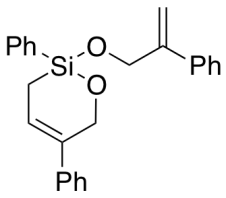
Synthesised according to general procedure **(A)** from **156** (200 mg, 0.77 mmol), to yield **156a** as a clear oil (142 mg, 75%) R_f = 0.3 (95:5 Hex:Et_2O); **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 2.05-1.7 (10H, m, Si(CH_2CCH_3)$_2$), 2.32 (1H, m, $SiOCH_2CH_bHCH_2$), 2.42 (1H, m, $SiOCH_2CH_aHCH_2$), 4.01 (2H, m, SiOCH_2CH_2), 4.56 (1H, s, MeC=CH_aH_b), 4.65 (1H, s, MeC=CH_aH_b), 5.47 (1H, m, $SiO(CH_2)_2CH$), 7.42 (3H, m, C$H_{ortho/para}$), 7.63 (2H, m, CH_{meta}); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 21.5 (s, Si*C*H_2C=CH_2), 25.2 (s, Si*C*H_2CMe), 27.2 (s, *C*H_3C=CH_2), 27.5 (s, *C*H_3C=CH), 32.0 (s, $SiOCH_2CH_2CH$), 64.8 (s, SiO*C*H_2CH_2), 109.7 (s, MeC=*C*H_2), 121.6 (s, *C*H=CMe), 128.0 (s, ArC_{ortho}), 129.8 (s, ArC_{para}), 134.04 (s, ArC_{meta}), 136.9 (s, Me*C*=CH), 137.0 (s, Me*C*=CH_2), 142.8 (s, ArC_{ipso}); **IR (film): υ (cm^{-1})** 3071, 1650, 1121; **HMRS** (ESI, *m/z*) calc for $C_{16}H_{22}OSi$ $[M]^+$: 258.1440 found: 258.1445.

4-methyl-2-(2-methylprop-2-en-1-yl)-2-phenyl-3,6-dihydro-2*H*-1,2-oxasiline: 155a.



Synthesised according to general procedure **(A)** from **155** (200 mg, 0.76 mmol), to yield **155a** as a clear oil (134 mg, 75%) R_f = 0.6 (Hex:Et_2O 99:1); **^{1}H NMR (500 MHz, CD_2Cl_2) δ (ppm):** 1.70 (3H, s, CH_3), 1.74 (3H, s, CH_3), 1.86-1.88 (2H, m, Si(CH_2CH_2), 2.37 (2H, m, $SiCH_2C$=CH), 3.99 (2H, m, $SiOCH_2$), 4.55 (1H, s, MeC=CH_aH_b), 4.64 (1H, s, MeC=CH_aH_b), 5.46 (1H, m, $SiOCH_2CH$), 7.40 (3H, m, C$H_{ortho/para}$), 7.62 (2H, m, CH_{meta}); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 21.5 (s, $SiCH_2C=CH_2$), 25.2 (s, $SiCH_2CMe$), 26.9 (s, $CH_3C=CH_2$), 27.0 (s, $CH_3C=CH$), 64.8 (s, $SiOCH_2$), 109.7 (s, $MeC=CH_2$), 121.6 (s, CH=CMe), 128.0 (s, ArC_{ortho}), 129.8 (s, ArC_{para}), 134.0 (s, ArC_{meta}), 136.9 (s, MeC=CH), 137.0 (s, $MeC=CH_2$), 142.8 (s, ArC_{ipso}); **IR (film): υ (cm^{-1})** 3091, 1660, 1121; **HMRS** (ESI, *m/z*) calc for $C_{15}H_{20}OSi$ $[M]^+$: 244.1283 found: 244.1285 Enantiomers separated by chiral HPLC using a chiral AD-H column, 220nm, (Hexane 100%), 0.5 mL/min, 22.9 min and 24.9.0 min.

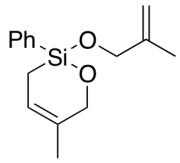
2,5-diphenyl-2-[(2-phenylprop-2-en-1-yl)oxy]-3,6-dihydro-2-*H*-1,2oxasiline: 171a



Synthesised according to general procedure **(A)** from **171** (200 mg, 0.48 mmol), to yield **171a** as a clear oil (103 mg, 55%) R_f = 0.6 (95:5 Hex:Et_2O); **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 1.81 (2H, m, $SiCH_2$), 4.80 (2H, s, $SiOCH_2C=CH_2$), 5.02 (2H, m, $SiOCH_2$), 5.49 (1H, s, $SiOCH_2=CH_b$), 5.53 (1H, s, $SiOCH_2=CH_a$), 6.23 (1H, m, $SiCH_2CH$), 7.73-7.41 (15H, m, Ar*H*); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 10.6 (s, $SiCH_2$), 65.2 (s, $SiOCH_2C=CH_2$), 67.1 (s, $SiOCH_2C=CH_2$), 112.5 (s, $PhC=CH_2$), 123.0, 126.3, 126.4, 127.6, 128.1, 128.7, 128.8, 130.9, 133.7, 134.0, 139.0, 140.1,

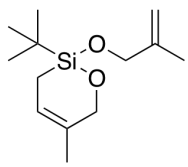
140.8, 146.8; **IR (film): υ (cm^{-1})** 3079, 1650, 1230, **HMRS** (ESI, *m/z*) calc for $C_{25}H_{24}O_2Si$ $[M]^+$: 384.1546 found: 384.1546.

5-Dimethyl-2-[(2-methylprop-2-en-1-yl)oxy]-2-pheny-3,6-dihydro-2*H*-1,2-oxysilane: 172a.



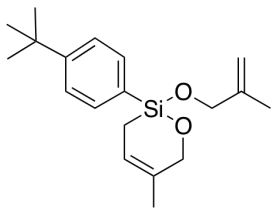
Synthesised according to general procedure **(A)** from **172** (200 mg, 0.63 mmol), to yield **172a** as a clear oil (155 mg, 85%) R_f = 0.6 (95:5 Hex:Et_2O); **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 1.55 (2H, m, SiC*H*$_2$), 1.65 (3H, s, *Me*C=CH_2), 1.76 (3H, s, *Me*C=CH), 4.23 (2H, s, SiOC*H*$_2$C=CH_2), 4.50 (1H, m, $SiOCH_aH_bC$=CH), 4.56 (1H, m, SiOC*H*$_a$H$_2$C=CH), 4.88 (1H, m, MeC=CH_aH_b), 5.05 (1H, m, MeC=C*H*$_a$H$_b$), 5.68 (1H, m, $SiCH_2CH$), 7.68-7.44 (5H, m, Ar*H*); **^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm):** 9.5 (s, Si*C*H$_2$), 19.0 (s, *Me*C=CH_2), 20.3 (s, *Me*C=CH), 66.9 (s, SiO*C*H$_2$C=CH_2), 68.4 (s, SiO*C*H$_2$C=CH), 109.8 (s, MeC=*C*H), 118.4 (s, MeC=*C*H$_2$), 128.2 (s, Ar*C*$_{ortho}$), 130.6 (s, Ar*C*$_{para}$), 134.3 (s, Me*C*=CH_2), 134.7 (s, Ar*C*$_{meta}$), 135.5 (s, Me*C*=CH), 144.5 (s, Ar*C*$_{ipso}$); **IR (film): υ (cm^{-1})** 3076, 1650, 1240; **HRMS (CI+):** m/z calc for $C_{15}H_{21}O_2Si$ $[M+H]^+$: 261.1311; found: 261.1315. Enantiomers separated by chiral HPLC using a chiral OD-R column, 220nm, (Hexane 100%), 0.5 mL/min, 47.2 min and 58.0 min.

2-*tert*-butyl-5-methyl-2-[(2-methylprop-2-en-1-yl)oxy]-3,6-dihydro-2*H*-1,2-oxasiline: 176a.



Synthesised according to general procedure **(A)** from **176** (200 mg, 0.74 mmol), to yield **176a** as a clear oil 147 mg (92%) R_f = 0.3 (95:5 Hex:Et_2O); **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 0.99 (9H, s, C(CH_3)$_3$), 1.25 (2H, m, SiCH_2), 1.65 (3H, s, *Me*C=CH_2), 1.76 (3H, s, *Me*C=CH), 4.16 (2H, s, SiOCH_2C=CH_2), 4.46 (2H, m, SiOCH_2C=CH), 4.80 (1H, m, MeC=CH_2), 5.68 (1H, m, SiCH_2C*H*), 5.05 (1H, m, MeC=CH_2); **^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm):** 9.5 (s, Si*C*H_2), 17.9 (s, (CH_3)$_3$*C*), 18.9 (s, *Me*C=CH_2), 20.1 (s, *Me*C=CH), 25.5 (s, (CH_3)$_3$C), 66.4 (s, SiO*C*H_2C=CH_2), 68.1 (s, SiO*C*H_2C=CH), 109.2 (s, MeC=*C*H), 118.5 (s, MeC=*C*H_2), 134.7 (s, Me*C*=CH_2), 134.7 (s, Me*C*=CH), 144.5 (s, Ar*C*$_{ipso}$); **IR (film): υ (cm^{-1})** 3076, 1650, 1090; **HRMS (CI+):** m/z calc for $C_{13}H_{24}O_2Si$ $[M]^+$: 240.1546; found: 240.1541 Enantiomers separated by chiral GC using a β-dex column, 50 °C, 20 psi, 200.7 min and 204.1 min.

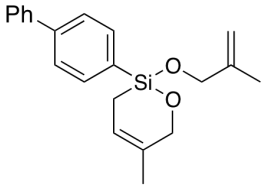
2-(4-*tert*-butylphenyl)-5-methyl-2-[2-methylprop-2-en-1yl)oxy]-3,6-dihydro-2*H*-1,2-oxasiline: 177a.



Synthesised according to general procedure **(A)** from **177** (200 mg, 0.58 mmol), to yield **177a** as a clear oil (161 mg, 88%) R_f = 0.3 (95:5 Hex:Et_2O); **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 1.36 (9H, s, Si-C(CH_3)$_3$), 1.53 (2H, m, SiCH_2), 1.65 (3H, s, *Me*C=CH_2), 1.76 (3H, s, *Me*C=CH), 4.23 (2H, s, SiOCH_2C=CH_2), 4.50 (1H, m, SiOCH_a*H*$_b$C=CH), 4.55 (1H, m, SiOC*H*$_a$H$_b$C=CH), 4.88 (1H, m, MeC=C*H*$_a$H$_b$), 5.05 (1H, m, MeC=C*H*$_{2a}$), 5.67 (1H, m, SiCH_2C*H*), 7.47 (2H, d, $^3J_{(H,H)}$ 8.0, Ar*H*$_{meta}$), 7.61 (2H, d, $^3J_{(H,H)}$ 8.0, Ar*H*$_{orto}$); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 9.6 (s, Si*C*H_2), 19.1 (s, *Me*C=CH_2), 20.3 (s, *Me*C=CH), 31.3 (s, C(*C*H$_3$)$_3$), 35.0 (s, *C*(CH$_3$)$_3$), 66.9 (s, SiO*C*H_2C=CH_2), 68.3 (s, SiO*C*H_2C=CH), 109.7 (s, MeC=*C*H), 118.5 (s, MeC=*C*H_2), 125.2 (s, Ar*C*$_{para}$), 130.7 (s, Ar*C*$_{ortho}$), 134.2 (s, Me*C*=CH_2), 134.2 (s, Ar*C*$_{meta}$), 135.5 (s, Me*C*=CH), 144.6 (s, Ar*C*$_{ipso}$), 153.9 (s, Ar*C* $_{ipso}$);

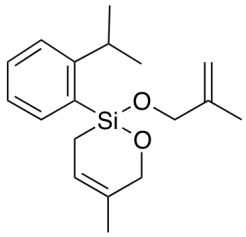
IR (film): υ (cm^{-1}) 3076, 1650, 1230, 1200; **HRMS (CI+):** m/z calc for $C_{19}H_{28}NaO_2Si$ $[M]^+$: 339.1751; found: 339.1753. Enantiomers separated by chiral HPLC using a chiral OZ-H column, 220nm, (Hexane 100%), 0.5 mL/min, 45.8 min and 48.7 min.

2-(biphenyl-4-yl)-5-methyl-2-[2-methylprop-2-en-1yl)oxy]-3,6-dihydro-2*H*-1,2-oxasiline: 178a.



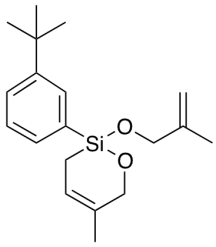
Synthesised according to general procedure **(A)** from **178** (200 mg, 0.54 mmol), to yield **178a** as a clear oil (162 mg, 88%) R_f = 0.3 (95:5 Hex:Et_2O); **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.57 (2H, m, SiCH_2), 1.64 (3H, s, *Me*C=CH_2), 1.76 (3H, s, *Me*C=CH), 4.25 (2H, s, SiOCH_2C=CH_2), 4.52 (1H, m, SiOC$H_a$$H_b$C=CH), 4.58 (1H, m, SiOC$H_a$$H_b$C=CH), 4.88 (1H, s, MeC=C$H_a$$H_b$), 5.07 (1H, s, MeC=C$H_a$$H_b$), 5.66 (1H, m, SiC$H_2$C*H*), 7.77-7.37 (9H, m, Ar*H*),; **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** 9.5 (s, Si*C*H_2), 19.0 (s, *Me*C=CH_2), 20.2 (s, *Me*C=CH), 66.7 (s, SiO*C*H_2C=CH_2), 68.0 (s, SiO*C*H_2C=CH), 109.9 (s, MeC=*C*H), 118.2 (s, MeC=*C*H_2), 127.2, 126.6, 127.5, 128.7, 132.2 (s, Me*C*=CH_2), 134.5, 134.9 (s, Me*C*=CH), 140.9 (s, ArC_{ipso}), 143.0, 143.8; **IR (film): υ (cm^{-1})** 3076 2900, 1800, 1650; **HMRS** (ESI, *m/z*) calc for $C_{21}H_{24}O_2Si$ $[M]^+$: 336.1546 found: 336.1550. Enantiomers separated by chiral HPLC using a chiral OD-H column, 220nm, (Hexane 100%), 0.5 mL/min, 69.6 min and 94.1 min.

2-(2-isopropylphenyl)-5-methyl-2-[2-methylprop-2-en-1yl)oxy]-3,6-dihydro-2*H*-1,2-oxasiline: 180a.



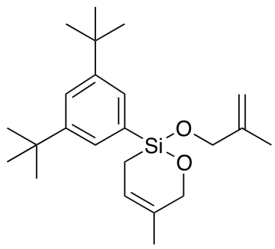
Synthesised according to general procedure **(A)** from **180** (200 mg, 0.60 mmol), to yield **180a** as a clear oil (164 mg, 90%) R_f = 0.6 (95:5 Hex:Et_2O); **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 1.26 (8H, m, SiCH_2, Si-CH(CH_3)$_2$), 1.61 (3H, s, *Me*C=CH_2), 1.71 (3H, s, *Me*C=CH), 3.19 (1H, sept, $^3J_{(H,H)}$ 6.8 Hz, C*H*), 4.14 (2H, dd, $^4J_{H\text{-}H}$ 12.5, $^4J_{H\text{-}H}$ 10.8, SiOCH_2C=CH_2), 4.47 (1H, m, SiOCH$_a$$H_b$C=CH), 4.55 (1H, m, SiOC$H_aH_b$C=CH), 4.82 (1H, s, MeC=CH_aH$_b$), 5.00 (1H, s, MeC=CH$_a$$H_b$), 5.60 (1H, m, SiCH$_2$C*H*), 7.21 (1H, t, $^3J_{(H,H)}$ 6.4 Hz PhH_{meta}), 7.36 (1H, d, $^3J_{(H,H\textit{trans})}$ 7.5 Hz PhH_{ortho}), 7.41 (1H, t, $^3J_{(H,H)}$ 6.4 Hz PhH_{para}), 7.70 (1H, d, $^3J_{(H,H)}$ 6.4 Hz, PhH_{meta}); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 10.5 (s, Si*C*H$_2$), 19.1 (s, *Me*C=CH_2), 24.8 (s, *Me*C=CH), 31.5 (s, CH(*C*H$_3$)$_2$), 34.1 (s, *CH*(CH$_3$)$_2$), 66.5 (s, SiO*C*H$_2$C=CH_2), 67.7 (s, SiO*C*H$_2$C=CH), 109.7 (s, MeC=*C*H), 118.1 (s, MeC=*C*H$_2$), 125.0, 125.2, 130.7, 131.3 (s, Me*C*=CH_2), 134.7, 135.2 (s, Me*C*=CH), 143.8, 155.4; **IR (film): υ (cm^{-1})** 3076, 1650, 1340, 990; **HRMS (CI+):** m/z calc for $C_{18}H_{26}O_2Si$ $[M]^+$: 302.1702; found: 302.1702. Enantiomers separated by chiral HPLC using a chiral OD-R column, 220nm, (Hexane 100%), 0.5 mL/min, 27.2 min and 33.0 min.

2-(3-*tert*-butylphenyl)-5-methyl-2-[2-methylprop-2-en-1yl)oxy]-3,6-dihydro-2*H*-1,2-oxasiline: 179a.



Synthesised according to general procedure **(A)** from **179** (200 mg, 0.58 mmol), to yield **179a** as a clear oil (159 mg, 87%) R_f = 0.3 (95:5 Hex:Et_2O); **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 1.33 (9H, s, Si-C(CH_3)$_3$), 1.53 (2H, m, SiCH_2), 1.62 (3H, s, *Me*C=CH_2), 1.73 (3H, s, *Me*C=CH), 4.21 (2H s, SiOCH_2C=CH_2), 4.47 (1H, m, SiOCH$_a$$H_b$C=CH), 4.55 (1H, m, SiOC$H_aH_b$C=CH), 4.85 (1H, s, MeC=CH_aH$_b$), 5.04 (1H, s, MeC=CH$_a$$H_b$), 5.64 (1H, m, SiCH$_2$CH), 7.33 (1H, t, $^3J_{(H,H)}$ 6.4 Hz PhH_{meta}), 7.46 (2H, m, Ph$H_{ortho,\ para}$), 7.70 (1H, s, PhH_{ortho}); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 9.3 (s, SiCH$_2$), 19.0 (s, *Me*C=CH_2), 20.2 (s, *Me*C=CH), 31.3 (s, C(CH$_3$)$_2$), 34.6 (s, C(CH$_3$)$_3$, 66.6 (s, SiOCH$_2$C=CH_2), 68.0 (s, SiOCH$_2$C=CH), 109.8 (s, MeC=CH), 118.3 (s, MeC=CH$_2$), 127.4, 127.6, 130.7, 131.1, 133.0 (s, MeC=CH$_2$), 134.8 (s, MeC=CH), 143.9, 150.2; **IR (film): υ (cm^{-1})** 3076, 1650, 1230, 1100; **IR (film): υ (cm^{-1})** 3076 (=C-H), 1650 (C=C); **HRMS (CI+):** m/z calc for $C_{19}H_{28}NaO_2Si$ [M]$^+$: 339.1751; found: 339.1753. Enantiomers separated by chiral HPLC using a chiral OD-R column, 220nm, (Hexane 100%), 0.5 mL/min, 47.2 min and 58.0 min.

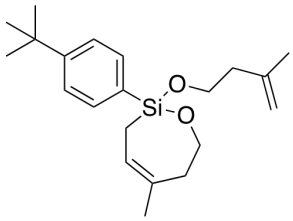
2-(3,5-di-*tert*-butylphenyl)-5-methyl-2-[2-methylprop-2-en-1yl)oxy]-3,6-dihydro-2*H*-1,2-oxasiline: 181a.



Synthesised according to general procedure **(A)** from **181** (200 mg, 0.50 mmol), to yield **181a** as a clear oil (165 mg, 89%) R_f = 0.6 (95:5 Hex:Et_2O); **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):**

1.33 (18H, s, Si-C(C*H*$_3$)$_3$), 1.53 (2H, m, SiC*H*$_2$), 1.62 (3H, s, *Me*C=CH$_2$), 1.73 (3H, s, *Me*C=CH), 4.21 (2H, s, SiOC*H*$_2$C=CH$_2$), 4.50 (1H, m, SiOCH$_a$*H*$_b$C=CH), 4.53 (1H, m, SiOC*H*$_a$H$_b$C=CH), 4.86 (1H, s, MeC=C*H*$_a$H$_b$), 5.06 (1H, s, MeC=CH$_a$*H*$_b$), 5.65 (1H, m, SiCH$_2$C*H*), 7.51 (3H, s, Ph*H*); **^{13}C NMR (125 MHz, CDCl$_3$) δ (ppm):** 9.4 (s, Si*C*H$_2$), 20.2 (s, *Me*C=CH$_2$), 22.6 (s, *Me*C=CH), 31.4 (s, C(*C*H$_3$)$_2$), 34.8 (s, *C*(CH$_3$)$_3$), 66.6 (s, SiO*C*H$_2$C=CH$_2$), 68.0 (s, SiO*C*H$_2$C=CH), 109.8 (s, MeC=*C*H), 118.4 (s, MeC=*C*H$_2$), 124.6, 127.9, 132.3 (s, Me*C*=CH$_2$), 134.8, 144.0, 149.8; **IR (film): υ (cm^{-1})** 3076 (=C-H), 1650 (C=C); **IR (film): υ (cm^{-1})** 3080, 1750, 1600, 900; **HMRS** (ESI, *m/z*) calc for C$_{23}$H$_{36}$O$_2$Si [M]$^+$: 372.2485 found: 372.2490. Enantiomers separated by chiral HPLC using a chiral OD-R column, 220nm, (Hexane 100%), 0.5 mL/min, 33.2 min and 36.0 min.

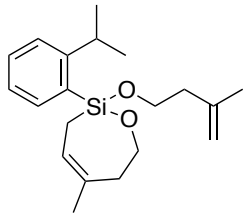
2-(4-*tert*-butylphenyl)-5-methyl-2-[(3-methylbut-3-en-1-yl)oxy]-2,3,6,7-tetrahydro-1,2-oxasilepine: 182a.



Synthesised according to general procedure **(A)** from **182** (200 mg, 0.53 mmol), to yield **182a** as a clear oil (147 mg, 86%) R_f = 0.5 (95:5 Hex:Et$_2$O); **^{1}H NMR (500 MHz, CDCl$_3$) δ (ppm):** 1.29-1.33 (11H, m, SiC*H*$_2$, SiC(C*H*$_3$)$_3$), 1.72 (3H, s, *Me*C=CH$_2$), 1.75 (3H, s, *Me*C=CH), 2.30 (2H, t, $^3J_{(H,H)}$ 7.0 Hz, SiOCH$_2$C*H*$_2$), 2.43 (2H, t, $^3J_{(H,H)}$ 5.0 Hz, SiOCH$_2$C*H*$_2$), 3.85 (2H, s, SiOC*H*$_2$C=CH$_2$), 4.05 (2H, m, SiOC*H*$_2$C=CH), 4.88 (1H, s, MeC=C*H*$_a$H$_b$), 4.77 (1H, s, MeC=C*H*$_{2a}$), 5.5 (1H, m, SiCH$_2$C*H*), 7.41 (2H, d, $^3J_{(H,H)}$ 8.0 Hz, Ar*H*), 7.56 (2H, d, $^3J_{(H,H)}$ 8.0 Hz, Ar*H*); **^{13}C NMR (125 MHz, CDCl$_3$) δ (ppm):** 14.4 (s, Si*C*H$_2$), 22.7 (s, *Me*C=CH$_2$), 25.1 (s, *Me*C=CH), 31.3 (s, C(*C*H$_3$)$_3$), 34.7 (s, *C*(CH$_3$)$_3$), 36.6 (s, SiOCH$_2$*C*H$_2$CCH$_2$), 40.7 (s, SiOCH$_2$*C*H$_2$), 61.8 (s, SiO*C*H$_2$C=CH$_2$), 63.5 (s, SiO*C*H$_2$C=CH), 111.6 (s, MeC=*C*H), 119.3 (s, MeC=*C*H$_2$), 124.7, 133.8 (s, Me*C*=CH$_2$), 134.0, 134.9, 142.8 (s,

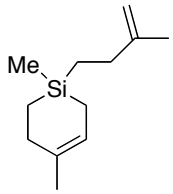
Me*C*=CH), 152.9; **IR (film): υ (cm^{-1})** 3076, 1650, 1400, 1324, 1109, 910; **HRMS (CI+):** m/z calc for $C_{21}H_{32}NaO_2Si$ $[M]^+$: 367.2064; found: 367.2054.

2-(2-isopropylphenyl)-5-methyl-2-[(3-methylbut-3-en-1-yl)oxy]-2,3,6,7-tetrahydro-1,2-oxasilepine: 183a.



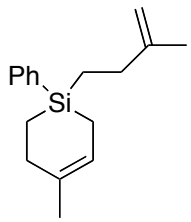
Synthesised according to general procedure **(A)** from **183** (200 mg, 0.55 mmol), to yield **183a** as a clear oil (158 mg, 86%) R_f = 0.3 (95:5 Hex:Et_2O); **^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):** 1.25 (6H, m, $CH(CH_3)_2$), 1.72 (3H, s, *Me*C=CH_2), 1.73 (3H, s, *Me*C=CH), 1.82 (2H, d, 7.6 Hz, $^3J_{(H,H)}$7.5 Hz , $SiCH_2$), 2.29 (2H, t, $^3J_{(H,H)}$ 7.0 Hz, $SiOCH_2CH_2$), 2.42 (2H, t, $^3J_{(H,H)}$ 5.0 Hz, $SiOCH_2CH_2$), 3.28 (1H, sep, $^3J_{(H,H)}$ 6.8 Hz, $CH(CH_3)_2$), 3.81 (2H, m, $SiOCH_2C=CH_2$), 4.10 (2H, m, $SiOCH_2C=CH$), 4.69 (1H, s, $MeC=CH_{2b}$), 4.75 (1H, s, $MeC=CH_{2a}$), 5.5 (1H, m, $SiCH_2CH$), 7.18 (1H, t, $^3J_{(H,H)}$ 6.5 Hz PhH_{meta}), 7.33 (1H, d, $^3J_{(H,Htrans)}$ 7.5 Hz PhH_{ortho}), 7.34 (1H, t, $^3J_{(H,H)}$ 6.5 Hz PhH_{para}), 7.62 (1H, d, $^3J_{(H,H)}$ 6.5 Hz, PhH_{meta}); **^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm):** 14.4 (s, $SiCH_2$), 22.7 (s, *Me*C=CH_2), 25.1 (s, *Me*C=CH), 31.3 (s, $CH(CH_3)_2$), 34.7 (s, $CH(CH_3)_2$), 36.6 (s, $SiOCH_2CH_2CCH_2$), 40.7 (s, $SiOCH_2CH_2$), 61.8 (s, $SiOCH_2C=CH_2$), 63.5 (s, $SiOCH_2C=CH$), 111.6 (s, MeC=*C*H), 119.3 (s, $MeC=CH_2$), 124.7 (s, ArC_{ortho}), 133.8 (s, Me*C*=CH_2), 134.0 (s, ArC_{meta}), 134.9 (s, ArC_{para}), 142.8 (s, Me*C*=CH), 152.9 (s, ArC_{ipso}); **IR (film): υ (cm^{-1})** 3076, 2980, 1650, 1220; **HRMS (CI+):** m/z calc for $C_{21}H_{32}NaO_2Si$ $[M]^+$: 367.2064; found: 367.2059. Enantiomers separated by chiral HPLC using a chiral OD-R column, 220nm, (Hexane 100%), 0.5 mL/min, 32.2 min and 36.0 min.

1,4-Dimethyl-1-(3-methylbut-3-en-1-yl)-1,2,3,6-tetrahydrosiline: 145a.



Synthesised according to general procedure **(A)** from **145** (60 mg, 0.27 mmol), to yield **145a** s a clear oil 50 mg (98%) R_f = 0.35 (99:1 Hex:Et_2O) **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 0.16 (3H, s, CH_3), 0.89 (2H, t, $^3J_{(H,H)}$ 7.0 Hz, $SiCH_2CH_2MeC{=}CH_2$), 1.27 (2H, dd, $^2J_{(H,H)}$ 7.0, $^3J_{(H,H)}$ 5.5 Hz, $SiCH_2CH$), 1.31 (2H, t, $^3J_{(H,H)}$ 7.0 Hz, $SiCH_2CH_2MeC{=}CH$), 1.67 (3H, br s, $SiCH_2CH_2CH_3C{=}CH$), 1.74 (3H, br s, $SiCH_2CH_2CH_3C{=}CH_2$), 2.15 (2H, t, $^3J_{(H,H)}$ 7.0 Hz, $SiCH_2CH_2MeCH{=}CH_2$), 2.26 (2H, t, $^3J_{(H,H)}$ 7.0 Hz, $SiCH_2CH_2MeC{=}CH$), 4.72 (1H, s, $MeC{=}CH_2$), 4.77 (1H, s, $MeC{=}CH_2$), 5.47 (1H, ddq, $^3J_{(H,Ha)}$ 6.5, $^3J_{(H,Hb)}$ 5.0, $^4J_{(H,H)}$ 3 x 1.0 Hz, $SiCH_2CH$); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** -3.1 (s, $SiCH_3$), 9.9 (s, $SiCH_2CH_2MeC{=}CH_2$), 12.9 (s, $SiCH_2CH$), 14.1 (s, $SiCH_2CH_2MeC{=}CH$), 22.3 (s, $CH_3C{=}CH_2$), 25.6 (s, $CH_3C{=}CH$), 28.0 (s, $SiCH_2CH_2MeC{=}CH_2$), 34.1 (s, $SiCH_2CH_2MeC{=}CH$), 111.6 (s, $MeC{=}CH_2$), 119.1 (s, $CH{=}CMe$), 137.2 (s, $MeC{=}CH$), 142.8 (s, $MeC{=}CH_2$); **IR (film): υ (cm^{-1})** 3076, 1650, 1560, 1340, 1010; **HRMS (CI+):** m/z calc for $C_{12}H_{23}Si$ $[M+H]^+$: 195.1569; found: 195.1570.

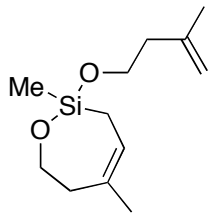
4-Methyl-1-(3-methylbut-3-en-1-yl)-1-phenyl-1,2,3,6-tetrahydrosiline: 147a.



Synthesised according to general procedure **(A)** from **147** (0.10 g, 0.35 mmol), to yield **147a** as a clear oil 76 mg (85%) R_f = 0.3 (Hex) **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.02 (2H, m, $SiCH_2CH_2MeC{=}CH_2$), 1.04 (2H, m, $SiCH_2CH_2MeC{=}CH$), 1.54 (2H, ddd, $^2J_{(H,H)}$ 7.0, $^3J_{(Ha,H)}$ 6.5, $^3J_{(Hb,H)}$

5.0 Hz, SiCH_2CH), 1.73 (3H, br s, SiCH$_2$CH$_2$CH_3C=CH), 1.76 (3H, br s, SiCH$_2$CH$_2$CH_3C=CH$_2$), 2.07 (2H, $^2J_{(H,H)}$ 8.0, $^3J_{(H,H)}$ 4.5 Hz, SiCH$_2$CH_2MeCH=CH$_2$), 2.26 (2H, td, $^3J_{(H,H)}$ 7.0, $^2J_{(H,H)}$ 6.5 Hz, SiCH$_2$CH_2MeC=CH), 4.72 (1H, s, MeC=CH_2), 4.76 (1H, s, MeC=CH_2), 5.64 (1H, ddq, $^3J_{(H,Ha)}$ 6.5, $^3J_{(H,Hb)}$ 5.0, $^4J_{(H,H)}$ 1.0 Hz, SiCH$_2$CH), 7.40 (3H, m, C$H_{ortho/para}$), 7.58 (2H, m, CH_{meta}); **^{13}C NMR (101 MHz, CDCl$_3$) δ (ppm)** 148.3 (s, MeC=CH$_2$), 137.6 (s, MeC=CH), 137.4 (s, SiC_{ipso}), 134.0 (s, CH$_{meta}$), 129.0 (s, CH$_{para}$), 127.8 (s, CH$_{ortho}$), 119.4 (s, CH=CMe), 108.7 (s, MeC=CH$_2$), 31.7 (s, SiCH$_2$$CH_2$MeC=CH), 27.9 (s, SiCH$_2$$CH_2$MeC=CH$_2$), 25.8 (s, CH$_3$C=CH), 22.3 (s, CH$_3$C=CH$_2$), 11.3 (s, SiCH$_2CH_2$MeC=CH), 10.1 (s, SiCH$_2$CH), 10.3 (s, SiCH$_2CH_2$MeC=CH$_2$); **IR (film): υ (cm^{-1})** 3069, 1650, 1440, 1100.

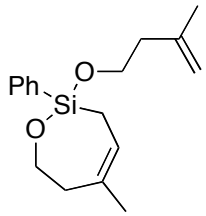
2,5-Methyl-2-[(3-methylbut-3-en-1-yl)oxy]-2,3,6,7-tetrahydro-1,2-oxasilepine: 173a.



Synthesised according to general procedure **(A) 173a** as a clear oil 75 mg (85%) R_f = 0.3 (95:5 Hex:Et$_2$O) **^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm):** 0.10 (3H, s, SiCH_3), 1.45 (1H, dd, $^3J_{(H,H)}$ 13.0, 7.0 Hz, SiCH_{2b}CH=CMe), 1.64 (1H, dd, $^3J_{(H,H)}$ 13.0, 7.0 Hz, SiCH_{2a}CH=CMe), 1.73 (3H, s, *Me*C=CH), 1.75 (3H, s, *Me*C=CH$_2$), 2.28 (2H, t, $^3J_{(H,H)}$ 7.0 Hz, SiOCH$_2$CH_2MeC=CH$_2$), 2.36 (2H, m, SiOCH$_2$CH_2(Me)C=CH), 3.81 (2H, t, $^3J_{(H,H)}$ 7.0 Hz, SiOCH_2CH$_2$MeC=CH$_2$), 3.91 (1H, ddd, $^3J_{(H,H)}$ 11.0, 7.0 Hz, $^2J_{(H,H)}$ 4.0 Hz, SiOCH_{2b}CH$_2$(Me)C=CH), 4.03 (1H, ddd, $^3J_{(H,H)}$ 10.0, 7.0 Hz, $^2J_{(H,H)}$ 4.0 Hz, SiOCH_{2a}CH$_2$C(Me)=CH), 4.72 (1H, s, MeC=CH_2), 4.77 (1H, s, MeC=CH_2), 5.48 (1H, dd, $^3J_{(H,Ha)}$ 7.5, $^3J_{(H,Hb)}$ 7.0 Hz, SiCH$_2$CH); **^{13}C NMR (101 MHz, CDCl$_3$) δ (ppm):** -3.7 (s, SiCH$_3$), 14.1 (s, SiCH$_2$CH), 22.6 (s, CH$_3$C=CH$_2$), 25.2 (s, CH$_3$C=CH), 36.6 (s, SiOCH$_2$$CH_2$MeC=CH), 40.7 (s, SiOCH$_2$$CH_2$MeC=CH$_2$), 61.5 (s, SiO$CH_2CH_2$MeC=CH$_2$), 63.3 (s, SiO$CH_2CH_2$MeC=CH), 111.6 (s, MeC=$CH_2$), 119.4 (s, MeC=$C$H), 134.9. (s, Me$C$=CH), 142.8 (s, Me$C$=CH); **IR (film): υ (cm^{-1})**

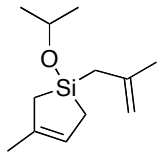
3073, 1648, 1129, **HRMS (CI+):** m/z calc for $C_{12}H_{23}O_2Si$ $[M+H]^+$: 227.1467; found: 227.1471. Enantiomers separated by chiral GC using a β-dex column, 100 °C, 20 psi, 20.7 min and 21.2 min.

5-Methyl-2-[(3-methylbut-3-en-1-yl)oxy]-2-phenyl-2,3,6,7-tetrahydro-1,2-oxasilepine: 168a.



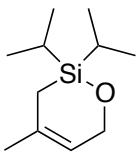
Synthesised according to general procedure **(A)** from **168** (200 mg, 0.63 mmol), to yield **168b** as a clear oil 150 mg (86%) R_f = 0.3 (95:5 Hex:Et_2O) **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.75 (3H, s, CH_3C=CH_2), 1.78 (3H, s, SiCH_2HC=CCH_3), 1.82 (1H, d, $^3J_{(H,H)}$ 6.0 Hz, SiCH_bHCH), 1.86 (1H, d, $^3J_{(H,H)}$ 7.0 Hz, SiCH_aHCH), 2.33 (2H, m, SiOCH_2CH_2MeC=CH_2), 2.47 (2H, m, SiOCH_2CH_2MeC=CH), 3.87 (2H, m, SiOC$H_2$$CH_2$MeC=$CH_2$), 4.18 (2H, t, $^3J_{(H,H)}$ 6.0 Hz, SiOC$H_2$$CH_2$MeC=CH), 4.75 (1H, s, MeC=CH_2), 4.80 (1H, s, MeC=CH_2), 5.55 (1H, ddq, $^3J_{(H,Ha)}$ 7.0, $^3J_{(H,Hb)}$ 6.0, $^4J_{(H,H)}$ 1.5 Hz, SiCH_2CH), 7.41 (3H, m, C$H_{ortho/para}$), 7.66 (2H, m, CH_{meta}); **^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm):** 14.4 (s, SiCH_2CH), 22.8 (s, $C$$H_3$C=$CH_2$), 25.2 (s, $C$$H_3$C=CH), 36.7 (s, Si$OCH_2C$$H_2$MeC=CH), 40.7 (s, Si$OCH_2C$$H_2$MeC=$CH_2$), 61.9 (s, SiO$C$$H_2$$CH_2$MeC=$CH_2$), 63.7 (s, SiO$C$$H_2$$CH_2$MeC=CH), 111.7 (s, MeC=$C$$H_2$), 119.3 (s, CH=CMe), 127.8 (s, $C$$H_{ortho}$), 130.1 (s, $C$$H_{para}$), 134.04 (s, $C$$H_{meta}$), 134.5 (s, Me$C$=CH), 135.1 (s, Si$C_{ipso}$), 142.7 (s, Me$C$=$CH_2$); **IR (film): υ ($cm^{-1}$)** 3071, 1650, 1121; **HRMS (CI+):** m/z calc for $C_{17}H_{25}O_2Si$ $[M+H]^+$: 289.1624; found: 289.1625 Enantiomers separated by chiral HPLC using a chiral OD-R column, 220nm, (Hexane 100%), 0.5 mL/min, 47 min and 56 min.

1-Isopropoxy-3-methyl-1-(2-methylprop-2-en-1-yl)-2,5-dihydro-1*H*-silole: 164a.



Synthesised according to general procedure **(A)** from **164** (100 mg, 0.42 mmol), to yield **164a** as a clear oil 80 mg (92%) R_f = 0.14 (99:1 Hex:Et_2O) **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.17 (6H, d, $^3J_{(H,H)}$ 6.0 Hz, SiOCH(CH_3)$_2$), 1.27 (2H, br s, SiCH_2MeCH=CH_2), 1.29 (2H, br s, SiCH_2MeC=CH), 1.37 (2H, m, SiCH_2CH), 1.77 (3H, s, SiCH$_2$CH_3CH=CH_2), 1.79 (3H, s, SiCH$_2$CH_3C=CH), 4.03 (1H, spt, $^3J_{(H,H)}$ 6 x 6.0 Hz, SiOCHMe$_2$), 4.58 (1H, s, MeC=CH_2), 4.64 (1H, s, MeC=CH_2), 5.53 (1H, t, $^3J_{(H,H)}$ 4.0 Hz, SiCH$_2$CH); **^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm):** 16.4 (s, SiCH$_2$CH=CMe), 21.8 (s, SiCH$_2$MeC=CH), 22.9 (s, CH$_3$C=CH), 25.0 (s, CH$_3$C=CH$_2$), 25.6 (s, SiOCH(CH$_3$)$_2$), 26.9 (s, SiCH$_2$MeC=CH$_2$), 65.9 (s, SiOCHMe$_2$), 109.2 (s, MeC=CH$_2$), 124.1 (s, CH=CMe), 139.5 (s, MeC=CH), 142.6 (s, MeC=CH$_2$); **IR (film): υ (cm^{-1})** 3076, 1638, 1240, 1026; **HRMS (CI+):** m/z calc for $C_{12}H_{23}OSi$ $[M+H]^+$: 211.1518; found: 211.1510. Enantiomers separated by chiral GC using a β-dex column, 60 °C, 20 psi, 120 min and 123 min.

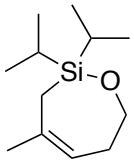
2,2-diisopropyl-3-methyl-2.3.6-tetrahydro-1,2-oxasilepine: 278a.



Synthesised according to general procedure **(A)** from **278** (300 mg, 1.32 mmol), to yield **278a** as a clear oil (241 mg, 91%) R_f = 0.6 (Hex:Et_2O 99:1); **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.05 (m, 14H, CH_3), 1.06 (s, 2H, SiCH_2), 1.81 (s, 3H, CH_3), 4.45 (s, 2H, SiOCH_2), 5.35 (1H, m, SiOCH$_2$CH); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** δ 10.7 (Si(CH(CH$_3$)$_2$)$_2$), 12.9 (Si(CH(CH$_3$)$_2$)$_2$),

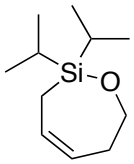
17.0 (CH$_2$Si), 28.0 (CH$_3$), 63.9 (OCH$_2$), 122.6 (CH=CMe), 132.2 (MeC=CH); **IR (film): υ (cm^{-1})** 2940, 2864, 2360, 1462, 1095; **HMRS** (ESI, *m/z*) calc for $C_{11}H_{22}OSi$ [M]$^+$: 198.1440 found: 198.1445.

2,2-diisopropyl-4-methyl-2.3.6.7-tetrahydro-1,2-oxasilepine[185]: 279a.



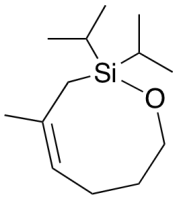
Synthesised according to general procedure **(A)** from **279** (300 mg, 1.32 mmol), to yield **279a** as a clear oil (231 mg, 85%) R_f = 0.6 (Hex:Et$_2$O 99:1); **^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm):** 1.05 (m, 14H, CH_3), 1.61 (s, 2H, SiCH_2), 1.81 (s, 3H, CH$_3$), 2.28 (m, 2H, SiOCH$_2$CH_2) 3.85 (s, 2H, SiOCH_2), 5.35 (1H, m, SiOCH$_2$CH); **^{13}C NMR (100 MHz, CDCl$_3$) δ (ppm):** δ 12.9 (Si(CH(CH$_3$)$_2$)$_2$), 17.3 (CH$_2$Si), 17.5 (Si(CH(CH$_3$)$_2$)$_2$), 27.5 (CH$_3$), 32.0 (SiOCH$_2$$CH_2$), 64.0 (O$CH_2$), 120.6 ($C$H=CMe), 136.2 (Me$C$=CH). Characterisation data correspond to the literature.

2,2-diisopropyl-2,3,6,7-tetrahydro-1,2-oxasilepine[185]: 281a.



Synthesised according to general procedure **(A)** from **280** (300 mg, 1.32 mmol), to yield **281a** as a clear oil (217 mg, 90%) R_f = 0.6 (Hex:Et$_2$O 99:1); **^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm):** 1.01 (m, 14H, CH_3), 1.62 (d, 2H, $^3J_{H\text{-}H}$ = 7 Hz, SiCH_2), 2.35 (m, 2H, SiOCH$_2$CH_2) 3.92 (t, 2H, $^3J_{H\text{-}H}$ = 5 Hz, 2H, SiOCH_2), 5.48 (m, 1H, SiOCH$_2$CH), 5.8 (m, 1H, CHCH); **^{13}C NMR (100 MHz, CDCl$_3$) δ (ppm):** δ 11.4 (Si(CH(CH$_3$)$_2$)$_2$), 17.3 (CH$_2$Si), 17.5 (Si(CH(CH$_3$)$_2$)$_2$), 32.4 (SiOCH$_2$$CH_2$), 63.3 (O$CH_2$), 126.6 ($C$H=CH), 127.3 (CH=C$H$). Characterisation data correspond to the literature.

2,2-diisopropyl-5-methyl-3,6,7,8-tetrahydro-2*H*-1,2-oxasilocine: 280a.

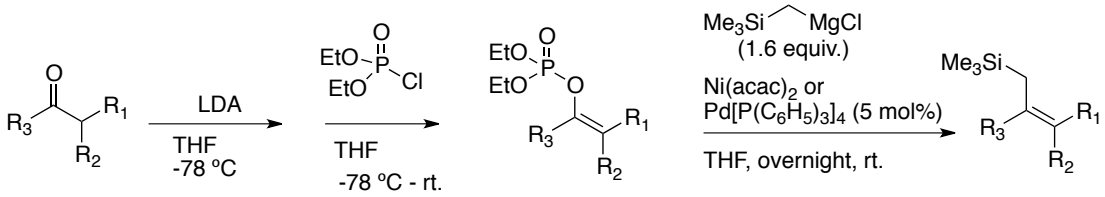


Synthesised according to general procedure **(A)** from **280** (300 mg, 1.32 mmol), to yield **280a** as a clear oil (241 mg, 83%) R_f = 0.6 (Hex:Et_2O 99:1); **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.03-1.07 (m, 14H, CH_3), 1.60 (s, 2H, SiCH_2), 1.61-1.66 (m, 2H, $SiOCH_2CH_2$), 1.81 (s, 3H, CH_3), 2.10-2.15 (m, 2H, $SiOCH_2CH_2CH_2$) 3.71 (m, 2H, $SiOCH_2$), 5.05 (1H, m, $SiOCH_2CH$); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** δ 12.0 ($Si(CH(CH_3)_2)_2$), 17.5 (CH_2Si), 17.7 ($Si(CH(CH_3)_2)_2$), 23.4 ($SiOCH_2CH_2CH_2$) 27.1 (CH_3), 30.8 ($SiOCH_2CH_2$), 60.0 (OCH_2), 120.1 (CH=CMe), 134.7 (MeC=CH); **IR (film): υ (cm^{-1})** 2940, 2864, 2060, 1562, 1010; FI Mass (EI) m/z Anal. Calcd for $C_{13}H_{26}OSi$ 226.1753, found $[M]^+$ 226.1757.

2. Experimental Procedures and Characterisation Data

2-1. Synthesis of allylsilane Starting materials

General Procedure for the synthesis of allylsilanes:[181]

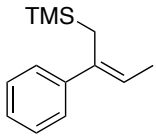


To a solution of diisopropylamine (3.6 mL, 25.8 mmol) in anhydrous tetrahydrofuran (20 mL) was added a 2.5 M solution of *n*- n-butyllithium in hexane (10.3 mL, 25.8 mmol) at 0 ˚C under an N_2 atmosphere. The lithium diisopropylamide solution was cooled to −78 ˚C and the ketone (22.4 mmol) was added dropwise over a period of 10 min. The mixture was stirred at −78 ˚C for 30 min, diethyl chlorophosphate (3.9 mL, 26.8 mmol) was added, and the mixture was

allowed to warm to room temperature over 1 h. Following completion of the reaction, the mixture was diluted with diethyl ether (50 mL), and washed with water (50 mL), 1 N aq. HCl (50 mL), and sat. aq. $NaHCO_3$(50 mL). The organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude diethyl enol phosphate product was purified by column chromatography using the indicated solvent system.

For the subsequent step, a three necked round bottom flask was equipped with a stirring bar. To the flask were successively added the Ni or Pd catalyst (2.5 to ~ 5 mol%), a 1.0 M solution of trimethylsilylmethylmagnesium chloride (13.4 mL, 13.4 mmol) in diethyl ether and the diethyl enol phosphate (6.7 mmol). The mixture was stirred at room temperature for 15 h, then cooled to 0 ^oC with an ice bath, prior to the addition of 1 N aq. HCl (10 mL). The organic layer was separated, and the aqueous layer was extracted with diethyl ether (2×100 mL). The combined organic layer was washed with sat. $NaHCO_3$ (50 mL), diluted water (50 mL) and brine(50 mL), and then dried over $MgSO_4$ and concentrated *in vacuo*. The pure allylsilane was isolated by column chromatography on silica gel using the indicated solvent system.

(*Z*)-trimethyl(2-phenylbut-2-en-1-yl)silane: **232.**

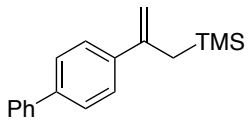


The title compound was prepared according to the general procedure. From propiophenone (3.0 g, 22.4 mmol) and diethyl chlorophosphate (3.9 mL, 26.8 mmol). Lithium diisopropylamide solution was prepared from diisopropylamine (3.6 mL, 25.8 mmol), anhydrous tetrahydrofuran (20 mL) and 2.5 M solution of *n*-butyllithium in hexane (10.3 mL, 25.8 mmol). The crude residue was purified by SiO_2 gel column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) to afford (Z)-diethyl(1-phenyl-1-propenyl) phosphate (2.13 g, 35%) as a colourless oil. **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20 (dt, J = 2.2, 7.1 Hz, 6H), 1.87 (dd, J = 3.1, 7.0

Hz, 3H), 3.96–4.17 (m, 4H), 5.65 (dq, *J* =2.2, 7.0 Hz, 1H), 7.24–7.51 (m , 5H). ^{1}H NMR spectra corresponded to the literature data.[165]

The second step was performed according to the general procedure using the following: $[P(C_6H_5)_3]_4Pd$ (200 mg, 0.17 mmol), a 1 M solution of trimethylsilylmethylmagnesium chloride (13.4 mL, 13.4 mmol) in diethyl ether and the obtained diethyl enol phosphate (1.8 g, 6.7 mmol) with for stirring 15 h. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired allylsilane (878 mg, 64%) as a colourless oil. **^{1}H NMR (400 MHz, $CDCl_3$):** δ –0.10 (s, 9H), 1.77 (d, *J* = 6.8 Hz, 3H), 2.03 (s, 3H), 5.65 (q, *J* = 6.8 Hz, 1H), 7.20–7.36 (m, 5 H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ –1.0, 14.8, 20.6, 119.5, 126.3, 126.5, 128.0, 138.9, 144.9. Characterisation data correspond to the literature data.[165]

{2-[(1,1'-biphenyl)-4-yl]allyl}trimethylsilane: 259.

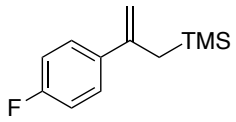


The title compound was prepared according to the general procedure. From 1-[1,1'-biphenyl]-4-ylethanone (1.9 g, 10.0 mmol) and diethyl chlorophosphate (1.7 mL, 11.0 mmol). Lithium diisopropylamide solution was prepared from diisopropylamine (1.5 mL, 11.0 mmol), anhydrous tetrahydrofuran (15 mL) and 1.6 M solution of *n*-butyllithium in hexane (7.5 mL, 12.0 mmol). The crude residue was purified by SiO_2 gel column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) to afford 1-[(1, 1'-biphenyl)-4-yl]vinyl diethyl phosphate (2.8 g, 84%) as a colourless oil. **IR (neat)** 2984, 1682, 1632, 1604, 1487, 1403, 1266, 1001, 848, 767, 735, 697 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 1.37 (dt, *J* = 1.2, 7.3 Hz, 6H), 4.16–4.23 (m, 4H), 5.26 (dd, *J* = 2.2, 2.8 Hz, 1H), 5.34 (t, *J* = 2.7 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 2H), 7.59–7.63 (m, 4H), 7.65–7.69 (m, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 16.1 (d, *J* = 6.7 Hz), 64.5 (d, *J* = 6.2 Hz), 97.2 (d, *J* = 3.7 Hz), 125.6, 127.0, 127.1, 127.6, 128.8, 133.2 (d, *J* = 7.3 Hz), 140.3, 141.8,

152.1 (d, *J* = 7.7 Hz), **HRMS** (ESI) m/z Anal. Calcd for $C_{18}H_{21}NaO_4P$ 355.1070, found $[M+Na]^+$ 355.1062.

The second step was performed according to the general procedure using the following: $Ni(acac)_2$ (102 mg, 0.40 mmol), a 1 M solution of trimethylsilylmethylmagnesium chloride (16 mL, 16.0 mmol) in diethyl ether and the obtained diethyl enol phosphate (2.8 g, 8.4 mmol) were stirring for 15 h. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired allylsilane (878 mg, 38%) as a white solid. **IR (neat)** 2956, 1488, 1320, 1249, 1126, 1070, 924, 844, 771, 737 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ –0.14 (s, 9H, SiMe_3), 2.10 (s, 2H, SiCH_2), 4.94 (s, 1H, C=CH_a), 5.25 (s, 1H, C=CH_b), 7.37 (t, *J* = 8.5 Hz, 1H, Ph_{para}), 7.47 (t, *J* = 8.9 Hz, 2H, Ph_{meta}), 7.52 (d, *J* = 9.5 Hz, 2H, Ph_{ortho}), 7.59 (d, *J* = 9.8 Hz, 2H, Ph_{meta}), 7.65 (d, *J* = 9.5 Hz, 2H, Ph_{ortho}); **^{13}C NMR (125 MHz, $CDCl_3$):** δ –1.3 (SiMe_3), 26.0 (SiCH_2), 110.1 (C=CH_2), 126.7, 126.8, 126.9, 127.2, 128.7, 139.9, 140.7, 141.6, 146.0; **HRMS** (EI) m/z Anal. Calcd for $C_{18}H_{22}Si$ 266.1491, found $[M]^+$ 266.1499.

[2-(4-fluorophenyl)allyl]trimethylsilane: 260.

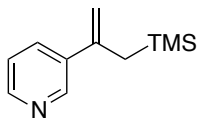


The title compound was prepared according to the general procedure from 4'-fluoroacetophenone (1.2 mL, 10.0 mmol) and diethyl chlorophosphate (1.7 mL, 12.0 mmol). Lithium diisopropylamide solution was prepared from diisopropylamine (1.5 mL, 11.0 mmol), anhydrous tetrahydrofuran (15 mL) and 1.6 M solution of *n*-butyllithium in hexane (6.8 mL, 11.0 mmol). The crude residue was purified by SiO_2 gel column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) to afford diethyl [1-(4-fluorophenyl)vinyl]phosphate (2.0 g, 72%) as a yellow oil. IR (neat) 2987, 1739, 1636, 1605, 1509, 1370, 1266, 1232, 1097, 996, 841, 812cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 1.37 (dt, *J* = 1.0, 7.0 Hz, 6H), 4.20–4.27 (m, 4H), 5.19 (t, *J* = 2.7 Hz,

1H), 5.21 (t, *J* = 2.5 Hz, 1H), 7.03 (t, *J* = 8.8 Hz, 2H), 7.56 (dd, *J* = 5.4, 6.2 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 16.0 (d, *J* = 6.6 Hz), 64.5 (d, *J* = 6.6 Hz), 97.1 (dd, *J* = 1.9, 3.8 Hz), 115.3 (d, *J* = 21.8 Hz), 127.2 (d, *J* = 7.6 Hz), 130.5 (dd, *J* =3.8, 6.1 Hz), 151.4 (d, *J* = 7.6 Hz), 163.1 (d, *J* = 247.3 Hz); **HRMS** (ESI) m/z Anal. Calcd for $C_{12}H_{16}FNaO_4P$ 297.0662, found $[M+Na]^+$ 297.0661.

The second step was performed according to the general procedure using the following: $Ni(acac)_2$ (65 mg, 0.25 mmol), a 1.0 M solution of trimethylsilylmethylmagnesium chloride (7.5 mL, 7.5 mmol) in diethyl ether and the obtained diethyl enol phosphate (1.4 g, 5.0 mmol) were stirring for 15 h. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired allylsilane (700 mg, 67%) as a colourless oil. **IR (neat)** 2956, 2360, 2341, 1667, 1508, 1373, 1096, 1077, 1054, 944, 837, 765, 730, 720 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ –0.17 (s, 9H, SiMe_3), 1.92 (s, 2H, SiCH_2), 4.77 (s, 1H, C=CH_a), 5.00 (s, 1H, C=CH_b), 6.90 (t, *J* = 1.2, 8.8 Hz, 2H, Ph_{meta}), 7.28 (ddd, *J* = 1.0, 5.3, 8.8 Hz, 2H, Ph_{ortho}); **^{13}C NMR (100 MHz, $CDCl_3$):** δ –1.5 (s, SiMe_3), 26.3 (s, SiCH$_2$), 110.0 (C=CH$_2$), 114.8 (d, *J* = 20.6 Hz, Ph_{ortho}), 127.8 (d, *J* = 5.9 Hz, Ph_{meta}), 138.8 (d, *J* = 3.2 Hz, Ph_{ipso}), 145.6 (C=CH$_2$), 162.2 (d, *J* = 244.5 Hz, Ph_{para}); **HRMS** (EI) m/z Anal. Calcd for $C_{12}H_{17}FSi$ 208.1084, found $[M]^+$ 208.1078.

3-[3-(trimethylsilyl)prop-1-en-2-yl]pyridine: 258.

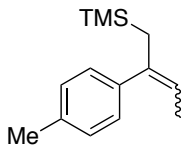


The title compound was prepared according to the general procedure. From 3-acetylpyridine (1.4 mL, 13.0 mmol) and diethyl chlorophosphate (2.2 mL, 15.6 mmol). Lithium diisopropylamide solution was prepared from diisopropylamine (2.0 mL, 14.3 mmol), anhydrous tetrahydrofuran (20 mL) and 1.6 M solution of *n*-butyllithium in hexane (9.0 mL, 14.3 mmol). The crude residue was purified by SiO_2 gel column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) to afford diethyl [1-(pyridine-3-yl)vinyl] phosphate (1.7 g, 51%) as a

colourless oil. **IR (neat)** 2985, 1637, 1418, 1270, 1165, 997, 837, 715; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.35 (td, J = 1.0, 7.0 Hz, 6H), 4.14–4.22 (m, 4H), 5.29 (dt, J = 2.0, 3.1 Hz, 1H), 5.32 (t, J = 3.0 Hz, 1H), 7.26 (ddd, J = 0.6, 4.9, 8.0 Hz, 1H), 7.83 (ddd, J = 1.6, 2.2, 8.0 Hz, 1H), 8.5 (d, J = 3.8, 1H), 8.80 (d, J = 1.3 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$,):** δ 16.0, (d, J = 7.2 Hz), 64.6, (d, J = 6.3 Hz), 98.9 (d, J = 3.2 Hz), 123.0, 130.1 (d, J = 7.2 Hz), 132.5, 146.5, 149.78, 149.83; **HRMS** (ESI) m/z Anal. Calcd for $C_{11}H_{16}NNaO_4P$ 280.0709, found $[M+Na]^+$ 280.0705.

The second step was performed according to the general procedure using the following: $Ni(acac)_2$ (85 mg, 0.33 mmol), a 1 M solution of trimethylsilylmethylmagnesium chloride (10 mL, 10.0 mmol) in diethyl ether and the obtained diethyl enol phosphate (1.7 g, 6.6 mmol) were stirring for 15 h. The crude residue was purified by SiO_2 gel column chromatography to afford the desired allylsilane (420 mg, 33%) as a yellow oil. **IR (neat)** 3230, 2954, 2360, 1616, 1475, 1411, 1247, 1160, 1022, 942, 850, 719 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ –0.09 (s, 9H, SiMe_3), 2.01 (br. d, J = 1.0 Hz, 2H, SiCH_2), 4.96 (d, J = 1.0 Hz, 1H, C=CH_a), 5.17 (d, J = 1.0 Hz, 1H, C=CH_b), 7.23 (dd, J = 5.1, 7.6 Hz, 1H,), 7.68 (dt, J = 1.9, 7.9, 1H), 8.48 (d, J = 4.0 Hz, 1H), 8.67 (s, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ –1.45 (SiMe_3), 25.8 (SiCH_2), 111.8 (C=CH_2), 122.9, 133.5, 138.1, 143.5 (C=CH_2), 147.6, 148.3; **HRMS** (ESI) m/z Anal. Calcd for $C_{11}H_{18}NSi$ 192.1203, found $[M+H]^+$ 192.1196.

[2-(*p*-tolyl)but-2-en-1-yl]trimethylsilane: 232.



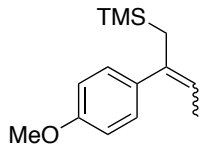
The title compound was prepared according to the general procedure. From 4'-methylpropiophenone (4.4 mL, 30 mmol) and diethyl chlorophosphate (5.2 mL, 36.0 mmol). Lithium diisopropylamide solution was prepared from diisopropylamine (4.6 mL, 33.0 mmol), anhydrous tetrahydrofuran (30 mL) and 1.6 M solution of *n*-butyllithium in hexane (20 mL,

33.0 mmol). The crude residue was purified by SiO_2 gel column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) to afford (Z)-diethyl[1-(*p*-tolyl)-1-en-1yl phosphate (5.0 g, 53%) as a colourless oil. **IR (neat)** 2984, 1269, 1027, 977, 890, 811 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 1.26 (dt, *J* = 1.3, 7.3 Hz, 6H), 1.88 (dd, *J* = 3.2, 7.0 Hz, 3H), 2.34 (s, 3H), 4.02–4.15 (m, 4H), 5.61 (dq, *J* =1.9, 7.0 Hz, 1H), 7.13 (d, *J* = 7.9 Hz, 2H), 7.40 (d, *J* = 7.9 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$,):** δ 11.7 (d. *J* = 1.9 Hz), 16.0 (d, *J* = 6.6 Hz), 21.1, 64.1 (d, *J* = 6.6 Hz), 111.2 (d, *J* = 6.6 Hz), 125.2, 128.8, 132.9, 137.9, 146.8 (d, *J* = 9.1 Hz); **HRMS** (ESI) m/z Anal. Calcd for $C_{14}H_{21}NaO_4P$ 307.1070, found $[M+Na]^+$ 307.1067.

The second step was performed according to the general procedure using the following: $Ni(acac)_2$ (82 mg, 0.31 mmol), a 1 M solution of trimethylsilylmethylmagnesium chloride (13 mL, 13.0 mmol) in diethyl ether and the obtained diethyl enol phosphate (1.8 g, 6.3 mmol) were stirring for 15 h. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired allylsilane (912 mg, 66%, isomeric ratio =1:1.1) as a colourless oil.

Characterisation data for the mixture of *E*/Z isomers (isomeric ratio=1:1.1): **IR (neat)** 2954, 1608, 1510, 1463, 1287, 1247, 1177, 1037, 837 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ –0.14 (s, 4.5 H, SiMe_3), –0.11 (s, 4.5 H) 1.61 (d, *J* = 6.9 Hz, 1.5 H, CHCH_3), 1.73 (d, *J* = 6.9 Hz, 1.5H), 1.89 (s, 1H, SiCH_2), 2.00 (s, 1H, SiCH_2), 2.34 (s, 3H, CH_3), 2.36 (s, 3H,), 5.37 (q, *J* = 6.6 Hz, 0.5H, C*H*CH_3), 5.61 (q, *J* = 6.7 Hz, 0.5H,), 7.08–7.10 (m, 1.5H), 7.15 (d, *J* = 8.2 Hz, 0.5 H), 7.22 (d, *J* = 8.2 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ –1.4 (SiMe_3), –0.9, 14.78 (Si*C*H_2), 14.88, 20.5 (CH*C*H_3), 21.0, 21.1 (CH_3) 29.6, 118.5 (C=*C*H), 118.8, 126.3, 128.48, 128.55, 128.7, 135.7, 135.9, 138.6, 138.7, 139.1, 142.0 (*C*=CH); **HRMS** (EI) m/z Anal. Calcd for $C_{14}H_{22}Si$ 218.1491, found $[M]^+$ 218.1491.

2-(4-methoxyphenyl)but-2-en-1-yl]trimethylsilane: 254.



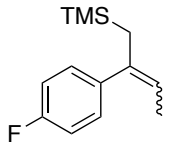
The title compound was prepared according to the general procedure. From 4'-methoxylpropiophenone (2.6 mL, 15.0 mmol) and diethyl chlorophosphate (2.6 mL, 18.0 mmol). Lithium diisopropylamide solution was prepared from diisopropylamine (2.3 mL, 16.5 mmol), anhydrous tetrahydrofuran (20 mL) and 2.5 M solution of *n*-butyllithium in hexane (6.6 mL, 16.5 mmol). The crude residue was purified by SiO_2 gel column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) to afford a mixture of *E*/Z isomers of diethyl [1-(4-methoxyphenyl)prop-1-en-1-yl]phosphate (2.5 g, 55%, *E* : *Z* = 1 : 4.1) as a colourless oil. IR (neat) 2980, 1410, 1325, 1269, 1165, 1120, 1023, 889 cm^{-1}.

Characterisation data for the Z isomer: **^{1}H NMR (500 MHz, $CDCl_3$):** δ 1.25 (dt, *J* = 1.3, 7.3 Hz, 6H), 1.86 (dd, *J* = 2.8, 7.3 Hz, 3H), 3.81 (s, 3H), 4.02–4.17 (m, 4H), 5.25 (dq, *J* = 2.2, 7.3 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 1H), 7.44 (d, *J* = 8.8 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 11.7 (d, *J* = 1.9 Hz), 16.1 (d, *J* = 6.6 Hz), 55.3, 64.2 (d, *J* = 5.7 Hz), 110.3 (d, *J* = 6.6 Hz), 113.5, 126.7, 128.5, 129.9, 146.6 (d, *J* = 8.5 Hz), 159.5; HRMS (ESI) m/z Anal. Calcd for $C_{14}H_{21}NaO_5P$ 323.1019, found $[M+Na]^+$ 323.1015.

The second step was performed according to the general procedure using the following: $Ni(acac)_2$ (108 mg, 0.41 mmol), a 1 M solution of trimethylsilylmethylmagnesium chloride (17 mL, 17.0 mmol) in diethyl ether and the obtained diethyl enol phosphate (2.5 g, 8.3 mmol) were stirring for 15 h. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane/EtO_2 99:1) as an eluent afforded the desired allylsilane (610 mg, 33%, isomeric ratio = 1 : 1.5) as a colourless oil.

Characterisation data for the mixture of *E*/Z isomers (isomeric ratio=1:1.5): **IR (neat)** 2954, 1511, 1415, 1247, 1159, 934, 838, 806, 760 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ –0.16 (s, 3.6H), 0.12 (s, 5.4H, Si*Me*$_3$), 1.61 (d, *J* = 6.9 Hz, 1.2H), 1.72 (d, *J* = 6.8 Hz, 1.8H, CHC*H*$_3$), 1.84 (s, 0.8H), 1.97 (s, 1.2H, SiC*H*$_2$), 3.80 (s, 1.8H, O*Me*), 3.82 (s, 1.2H), 5.34 (q, *J* = 5.9 Hz, 0.4 H), 5.55 (q, *J* = 6.8 Hz, 0.6 H, C*H*CH$_3$), 6.82 (d, *J* = 8.5 Hz, 1.2 H, Ph$_{meta}$), 6.85 (d, *J* = 8.5 Hz, 0.8 H), 7.12 (d, *J* = 8.5 Hz, 0.8 H$_{ortho}$), 7.25 (d, *J* = 8.5 Hz, 1.2 H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ –1.4 (Si*Me*$_3$), –0.9, 14.8 (SiC*H*$_2$), 14.9, 20.6 (CHC*H*$_3$), 29.7, 55.15 (O*Me*), 55.19, 113.2 (C=*C*H), 113.3, 118.2, 118.4, 127.4, 129.7, 134.4, 137.5 (*C*=CH), 138.20, 138.23; **HRMS** (EI) m/z Anal. Calcd for $C_{14}H_{22}OSi$ 234.1440, found $[M]^+$ 234.1445.

[2-(4-fluorophenyl)but-2-en-1-yl]trimethylsilane: 256.

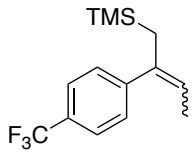


The title compound was prepared according to the general procedure. 4'-fluoropropiophenone (1.4 mL, 10.0 mmol) and diethyl chlorophosphate (1.7 mL, 12.0 mmol). Lithium diisopropylamide solution was prepared from diisopropylamine (1.5 mL, 11.0 mmol), anhydrous tetrahydrofuran (15 mL) and 2.5 M solution of *n*-butyllithium in hexane (4.4 mL, 11.0 mmol). The crude residue was purified by SiO_2 gel column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) to afford (Z)-diethyl [1-(4-fluorophenyl)prop-1-en-1-yl]phosphate (1.9 g, 66%) as a colourless oil. IR (neat) 2985, 1686, 1509, 1267, 1163, 1024, 979, 892, 812; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 1.26 (dt, *J* = 1.2, 7.3 Hz, 6H), 1.87 (dd, *J* = 2.8, 7.0 Hz, 3H), 4.04–4.15 (m, 4H), 5.59 (dq, *J* =2.2, 7.0 Hz, 1H), 7.01 (t, *J* = 8.5 Hz, 2H), 7.48 (dd, *J* = 5.5, 8.5 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$,):** δ 11.7, 16.0 (d, *J* = 6.6 Hz), 64.3, (d, *J* = 5.8 Hz), 112.1 (d, *J* = 6.6 Hz), 115.1 (d, *J* = 21.85), 127.2 (d, *J* = 7.6 Hz), 131.9 (dd, *J* = 1.9, 3.8 Hz), 145.9 (d, *J* = 8.5 Hz), 162.6 (d, *J* = 245.4 Hz); **HRMS** (ESI) m/z Anal. Calcd for $C_{13}H_{18}FNaO_4P$ 311.0819, found $[M+Na]^+$ 311.0815.

The second step was performed according to the general procedure using the following: $Ni(acac)_2$ (180 mg, 0.70 mmol), a 1 M solution of trimethylsilylmethylmagnesium chloride (27 mL, 27 mmol) in diethyl ether and the obtained diethyl enol phosphate (4.0 g, 13.8 mmol) were stirring for 15 h. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired allylsilane (2.1 g, 68%, isomeric ratio=1:3.1) as a colourless oil.

Characterisation data for the mixture of *E*/Z isomers (isomeric ratio=1:3.1): **IR (neat)** 2920, 1488, 1320, 1249, 1126, 1070, 924, 844, 771, 737 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ –0.16 (s, 2.2H), –0.13 (s, 6.8H, SiMe_3), 1.58 (d, *J* = 6.9 Hz, 0.8H), 1.72 (d, *J* = 6.8 Hz, 2.2H, CHCH_3), 1.84 (s, 0.5H), 1.96 (s, 1.5H, SiCH_2), 5.38 (q, *J* = 6.6 Hz, 0.3H), 5.55 (q, *J* = 6.8 Hz, 0.7H, CHCH_3), 6.97 (t, *J* = 8.8 Hz, 2.2 H, Ph_{meta}), 7.01 (t, *J* = 8.8 Hz, 0.8H), 7.15 (dd, *J* = 5.4, 8.8 Hz, 0.8H), 7.28 (dd, *J* = 5.4, 8.8 Hz, 2.2H, Ph_{ortho}); **^{13}C NMR (125 MHz, $CDCl_3$):** δ –1.4 (SiMe_3), –9.9, 14.77 (SiCH_2), 14.82, 20.8, 29.7 (CHCH$_3$), 114.68 (d, *J* = 20.8 Hz, C=CH), 114.73 (d, *J* = 20.9 Hz), 119.2, 119.6, 127.9 (d, *J* = 8.5 Hz, Ph_{meta}), 130.1 (d, *J* = 7.6 Hz), 137.7, 137.96, 138.0 (d, *J* = 3.8 Hz, Ph_{ortho}), 141.0 (d, *J* = 3.7 Hz), 161.4 (d, *J* = 242.6 Hz, Ph_{para}), 161.6 (d, *J* = 244.4 Hz); **HRMS** (EI) m/z Anal. Calcd for $C_{13}H_{19}FSi$ 222.1240, found $[M]^+$ 222.1247.

{2-[4-(trifluoromethyl)phenyl]but-2-en-1yl}trimethylsilane: 257.



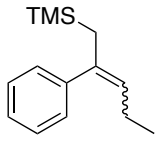
The title compound was prepared according to the general procedure. From 4'-trifluoromethylpropiophenone (2.0 g, 10.0 mmol) and diethyl chlorophosphate (1.7 mL, 12.0 mmol). Lithium diisopropylamide solution was prepared from diisopropylamine (1.5 mL, 11.0 mmol), anhydrous tetrahydrofuran (15 mL) and 2.5 M solution of *n*-butyllithium in hexane (4.4 mL, 11.0 mmol). The crude residue was purified by SiO_2 gel column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) to afford (*Z*)-diethyl{1-[4-(trifluoromethyl)phenyl]prop-1-en-1-

yl} phosphate (2.6 g, 72%) as a colourless oil. IR (neat) 2970, 2360, 1738, 1512, 1366, 1229, 1216, 1023, 811; **^{1}H NMR (500MHz, $CDCl_3$):** δ 1.26 (dt, J = 1.3, 7.0 Hz, 6H), 1.93 (dd, J = 3.2, 7.3 Hz, 3H), 4.06–4.18 (m, 4H), 5.81 (dq, J = 2.3, 7.3 Hz, 1H), 7.58 (d, J = 8.5 Hz, 2H), 7.62 (d, J = 8.5 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 11.9 (d, J = 1.9 Hz), 16.0 (d, J = 5.6 Hz), 64.5, (d, J = 5.8 Hz), 114.6 (d, J = 6.6 Hz), 125.2 (q, J = 4.0 Hz), 124.0 (q, J = 270.1 Hz), 125.4, 129.9 (q, J = 32.5 Hz), 139.1, 145.6 (d, J = 7.6 Hz); **HRMS** (ESI) m/z Anal. Calcd for $C_{14}H_{18}F_3NaO_4P$ 361.0787, found $[M+Na]^+$ 361.0781.

The second step was performed according to the general procedure using the following: $Ni(acac)_2$ (94 mg, 0.36 mmol), a 1 M solution of trimethylsilylmethylmagnesium chloride (15 mL, 15.0 mmol) in diethyl ether and the obtained diethyl enol phosphate (2.5 g, 7.4 mmol) were stirring for 15 h. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired allylsilane (1.0 g, 49% isomeric ratio =1 : 6) as a colourless oil.

Characterisation data for the major isomer: **IR (neat)** 2956, 1603, 1508, 1366, 1249, 1230, 1131, 913, 841, 746 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ –0.12 (s, 9H, SiMe_3), 1.76 (d, J = 6.8 Hz, 3H, CHCH_3), 2.01 (s, 2H, SiCH_2), 5.68 (q, J = 6.8 Hz, 1H, CHCH$_3$), 7.42 (d, J = 8.5 Hz, 2H, Ph_{meta}), 7.53 (d, J = 8.5 Hz, 2H, Ph_{ortho}); **^{13}C NMR (125 MHz, $CDCl_3$):** δ –0.96 (SiMe_3), 14.9 (SiCH$_2$), 20.5 (CHCH$_3$), 121.7 (C=CH), 124.4 (q, J = 270.0 Hz, CF$_3$), 125.0 (q, J = 4.0 Hz, Ph_{meta}), 126.6 (Ph_{ortho}), 128.4 (q, J = 33.2, Ph_{para}), 138.0 (C=CH), 148.5; **^{19}F NMR (376 MHz, $CDCl_3$):** δ –62.2 (s, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{13}H_{19}F_3Si$ 272.1208, found $[M]^+$ 272.1207.

Trimethyl(2-phenylpent-2-en-1-yl)silane: 261.

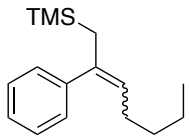


The title compound was prepared according to the general procedure. From butyrophenone (3.0 g, 20.5 mmol) and diethyl chlorophosphate (3.6 mL, 24.6 mmol). Lithium diisopropylamide solution was prepared from diisopropylamine (3.3 mL, 23.5 mmol), anhydrous tetrahydrofuran (20 mL) and 2.5 M solution of n-butyllithium in hexane (9.4 mL, 23.5 mmol). The crude residue was purified by SiO_2 gel column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) to afford (*Z*)-diethyl(1-phenyl-1-butenyl) phosphate (4.6 g, 79%) as a colourless oil. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.07 (t, *J* = 7.6 Hz, 3H), 1.17–1.23 (m, 6H), 2.33–2.39 (m, 2H), 3.96–4.12 (m, 4H), 5.50–5.56 (m, 1H), 7.23–7.32 (m, 3H), 7.46–7.50 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 13.6, 15.9 (d, *J* = 6.4 Hz), 19.6, 22.5, 64.2 (d, *J* = 6.4 Hz), 119.4 (d, *J* = 6.4 Hz), 125.4, 128.0, 128.1, 135.7, 145.3 (d, *J* = 9.5 Hz).

The second step was performed according to the general procedure using the following: $Ni(acac)_2$ (128 mg, 0.5 mmol), a 1 M solution of trimethylsilylmethylmagnesium chloride (20 mL, 20.0 mmol) in diethyl ether and the obtained diethyl enol phosphate (2.8 g, 10.0 mmol) were stirring for 15 h. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired allylsilane (1.45 g, 66%, isomeric ratio=1:1.8) as a yellow oil.

Characterisation data for the mixture of *E*/Z isomers (isomeric ratio=1:1.8): **IR (neat)** 2958, 1493, 1248, 1159, 837, 773, 754, 696 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ –0.04 (s, 9H, Si*Me*$_3$), 1.05 (t, *J* = 7.3 Hz, 1.1H), 1.16 (t, *J* = 7.3 Hz, 1.9H, CH_2CH_3), 1.98 (br. s, 0.7H), 2.10 (br. s, 1.3H, SiCH_2), 2.21–2.26 (m, 1.3H, $CHCH_2CH_3$), 5.34–5.41 (m, 0.35H), 5.55–5.62 (m, 0.65H, $CHCH_2$), 7.27–7.44 (m, 5H, Ar); **^{13}C NMR (100 MHz, $CDCl_3$):** δ –1.4 (Si*Me*$_3$), –0.9, 14.3 (SiCH_2), 15.1, 20.9 (CH_2CH_3), 22.5, 29.6 (CH_2CH_3), 126.3 (*C*=CH), 126.4, 126.6, 127.1, 127.77, 127.82, 128.0, 128.5, 137.3, 142.5 (*C*=CH), 144.9; **HRMS** (EI) m/z Anal. Calcd for $C_{14}H_{22}Si$ 218.1491, found $[M]^+$ 218.1482.

Trimethyl(2-phenylhept-2-en-1-yl)silane: 262.



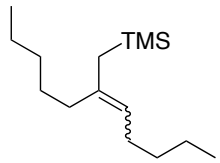
The title compound was prepared according to the general procedure. From pentyl phenyl ketone (3.0 g, 20.0 mmol) and diethyl chlorophosphate (3.6 mL, 24.6 mmol). Lithium diisopropylamide solution was prepared from diisopropylamine (3.3 mL, 23.5 mmol), anhydrous tetrahydrofuran (20 mL) and 2.5 M solution of n-butyllithium in hexane (9.4 mL, 23.5 mmol). The crude residue was purified by SiO_2 gel column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) to afford (Z)-diethyl(1-phenyl-1-hexenyl) phosphate (4.2 g, 68%) as a yellow oil. **IR (neat)** 2960, 1446, 1268, 1026, 977, 889, 800, 765, 695 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 0.88 (t, J = 7.3 Hz, 3H), 1.18 (t, J = 7.3 Hz, 6H), 1.33–1.45 (m, 4H), 2.31 (dq, J = 2.5, 7.2 Hz, 2H), 3.95–4.09 (m, 4H), 5.51 (dt, J = 1.8, 7.3 Hz, 1H), 7.18–7.27 (m, 3H), 7.45 (d, J = 7.1 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 13.8, 15.9 (d, J = 7.2 Hz), 22.3, 25.7, 64.1 (d, J = 6.4 Hz), 117.8 (d, J = 6.4 Hz), 125.3, 127.9, 128.0, 135.7, 145.3 (d, J = 8.7 Hz); **HRMS** (ESI) m/z Anal. Calcd for $C_{16}H_{25}NaO_4P$ 335.1388, found $[M+Na]^+$ 335.1383.

The second step was performed according to the general procedure using the following: $Ni(acac)_2$ (96 mg, 0.38 mmol), a 1 M solution of trimethylsilylmethylmagnesium chloride (15 mL, 15.0 mmol) in diethyl ether and the obtained diethyl enol phosphate (2.3 g, 7.5 mmol) were stirring for 15 h. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired allylsilane (2.12 g, 61%, isomeric ratio = 1 : 1.4) as a yellow oil.

Characterisation data for the mixture of *E*/Z isomers (isomeric ratio = 1 : 1.4): **IR (neat)** 2955, 1248, 836, 774, 754, 697 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ –0.04 (s, 5.4H SiMe_3), –0.03 (s, 3.6H), 0.93–1.06 (m, 3H, CH_2CH_3), 1.39–1.52 (m, 4H, CH_2CH_2), 1.96 (d, J = 5.7 Hz, 0.8 H), 2.07–2.11 (m, 2H, $SiCH_2$), 2.22 (t, J = 6.8 Hz, 1.2 H, $CHCH_2$), 5.39 (q, J = 6.8 Hz, 0.4H), 5.61 (q, J = 6.3

Hz, 0.6 H, C=C*H*), 7.22–7.44 (m, 5H, Ar); **^{13}C NMR (100 MHz, $CDCl_3$):** δ –1.40, –0.94 (Si*Me*$_3$), 14.0, 14.1 (Si*C*H$_2$), 20.9 *C*H$_3$), 22.3, 22.6 (*C*H$_2$CH$_3$), 28.8, 29.0 (*C*H$_2$CH$_2$CH$_3$), 29.8, 32.1 (*C*H$_2$CH$_2$CH$_2$CH$_3$) , 32.8, 125.5 (C=*C*H), 126.21, 126.24, 126.4, 126.6, 127.8, 128.0, 128.6, 137.7, 137.8 (*C*=CH), 142.6, 145.0; **HRMS** (EI) m/z Anal. Calcd for $C_{16}H_{26}Si$ 246.1804, found $[M]^+$ 246.1802.

Trimethyl(2-pentyl-2-heptenyl)silane: 264.



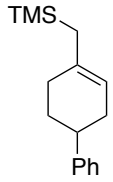
The title compound was prepared according to the general procedure. From 6-undecanone (3.8 g, 20.0 mmol) and diethyl chlorophosphate (3.6 mL, 24.6 mmol). Lithium diisopropylamide solution was prepared from diisopropylamine (3.3 mL, 23.5 mmol), anhydrous tetrahydrofuran (20 mL) and 2.5 M solution of *n*-butyllithium in hexane (9.4 mL, 23.5 mmol). The crude residue was purified by SiO_2 gel column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) to afford diethyl(5-undecen-6yl)-phosphate (4.6 g, 75%, isomeric ratio = 1 : 1.8) as a yellow oil.

Characterisation data for the mixture of *E*/Z isomers (isomeric ratio = 1 : 1.8): IR (neat) 2930, 1271, 1028, 977, 801 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 0.8 (m, 6H), 1.20–1.50 (m, 16H), 1.93–2.21 (m, 4H), 4.05–4.13 (m, 4H), 4.75 (t, *J* = 5.6 Hz, 0.35H), 5.24 (t, *J* = 5.8 Hz, 0.65 H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 13.7, 13.8, 14.0, 16.0 (d, *J* = 7.2 Hz), 22.0, 22.2, 22.3, 24.7, 26.1, 26.25, 26.29, 29.57, 29.61, 31.0, 31.1, 31.3, 31.9, 33.9, 63.77, 63.84 (d, *J* = 5.6 Hz), 114.1 (d, *J* = 3.9 Hz), 114.4 (d, *J* = 7.2 Hz), 114.6 (d, *J* = 8.7 Hz), 148.4 (d, *J* = 9.5 Hz); **HRMS** (ESI) m/z Anal. Calcd for $C_{15}H_{31}NaO_4P$ 329.1858, found $[M+Na]^+$ 329.1852.

The second step was performed according to the general procedure using the following: $Ni(acac)_2$ (96 mg, 0.38 mmol), a 1 M solution of trimethylsilylmethylmagnesium chloride (15 mL, 15.0 mmol) in diethyl ether and the obtained diethyl enol phosphate (2.3 g, 7.5 mmol) were stirring for 15 h. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired allylsilane (2.3 g, 61%, isomeric ratio = 1 : 2.5) as a colourless oil.

Characterisation data for the mixture of *E*/Z isomers (isomeric ratio = 1 : 2.5): **IR (neat)** 2956, 2928, 1466, 1247, 837, 661 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 0.01 (s, 6.3H, SiMe_3), 0.04 (s, 2.7H), 0.90–0.93 (m, 6H, 2 x (CH_3)), 1.26–1.40 (m, 10H, 5 x (CH_2), 1.90–2.02 (m, 4H, C=CHCH_2, SiCH_2), 4.95 (t, *J* = 7.1 Hz, 0.7 H, C=C*H*), 5.01 (t, *J* = 6.6 Hz, 0.3 H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ –1.2, –0.6 (SiMe_3), 14.08, 14.12, 21.1, 22.43, 22.5, 22.68, 22.71, 26.7, 27.7, 28.0, 28.2, 31.7, 32.0, 32.1, 32.4, 32.8, 39.2, 121.7 (C=*C*H), 123.1, 136.8, 136.9; HRMS (EI) m/z Anal. Calcd for $C_{15}H_{32}Si$ 240.2273, found $[M]^+$ 240.2280.

Trimethyl[(4-phenyl-1-cyclohexenyl)methyl]silane: 265.

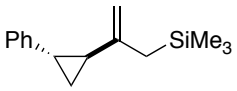


The title compound was prepared according to the general procedure. From 4-phenylcyclohexanone (3.0 g, 17.2 mmol) and diethyl chlorophosphate (3.0 mL, 20.6 mmol). Lithium diisopropylamide solution was prepared from diisopropylamine (2.8 mL, 19.8 mmol), anhydrous tetrahydrofuran (20 mL) and 2.5 M solution of *n*-butyllithium in hexane (7.9 mL, 19.8 mmol). The crude residue was purified by SiO_2 gel column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) to afford diethyl[4-phenyl-1-cyclohexenyl]phosphate (2.8 g, 52%) as a colourless oil. **IR (neat)** 2930, 1685, 1369, 1136, 1029, 968, 876, 759, 701 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.36 (t, *J* = 7.1 Hz, 6H), 1.85–2.02 (m, 2H), 2.19–2.47 (m, 4H), 2.75–2.83 (m,

1H), 4.13–4.20 (m, 4H), 5.55–5.57 (m, 1H), 7.19–7.31 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0 (d, J = 7.2 Hz), 28.0 (d, J = 4.0 Hz), 29.6, 31.5, 39.2, 64.1 (d, J = 5.6 Hz), 110.1 (d, J = 5.6 Hz), 126.2, 126.7, 128.4, 145.7, 147.4 (d, J = 9.5 Hz); HRMS (ESI) m/z Anal. Calcd for $C_{16}H_{23}NaO_4P$ 333.1232, found $[M+Na]^+$ 333.1226.

The second step was performed according to the general procedure using the following: $Ni(acac)_2$ (104 mg, 0.41 mmol), a 1 M solution of trimethylsilylmethylmagnesium chloride (16 mL, 15.0 mmol) in diethyl ether and the obtained diethyl enol phosphate (2.5 g, 8.1 mmol) were stirring for 15 h. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired allylsilane (2.3 g, 37%) as a colourless oil. **IR (neat)** 2952, 1493, 1453, 1247, 1172, 839, 754, 697 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 0.06 (s, 9H, SiMe_3), 1.50 (s, 2H, SiCH_2), 1.67–1.77 (m, 1H, CH_aCH$_2$), 1.92–2.02 (m, 2H, PhCHCH_2), 2.14–2.21(m, 2H, PhCHCH_2), 2.29– 2.33 (m, 1H, CH_bCH$_2$), 2.73–2.80 (m, 1H, PhCH), 5.33 (br. d, J = 4.3 Hz, 1H, C=CH), 7.20–7.34 (m, 5H, Ar); **^{13}C NMR (100 MHz, $CDCl_3$):** δ –1.1 (SiMe_3), 27.7 (SiCH_2), 30.3 (CH=CCH$_2$CH$_2$), 31.6 (CH=CCH$_2$$CH_2$) , 33.7 (PhCH$CH_2$), 40.1 (Ph$C$H), 118.5 (C=$C$H), 125.8, 126.9, 128.3, 153.4, 147.4; **HRMS** (EI) m/z Anal. Calcd for $C_{14}H_{24}Si$ 244.1647, found $[M]^+$ 244.1643.

Trimethyl[2-(*trans*-2-phenylcyclopropyl)allyl]silane: 291.

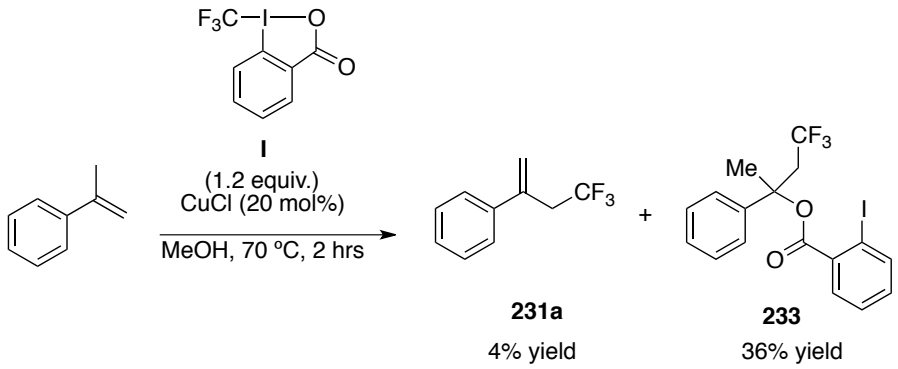


The title compound was prepared according to the general procedure. From 1-(*trans*-2-(phenyl)cyclopropyl)ethanone[9] (830 mg, 5.1 mmol) and diethyl chlorophosphate (898 µL, 6.22 mmol). Lithium diisopropylamide solution was prepared from diisopropylamine (822 µL, 5.86 mmol), anhydrous tetrahydrofuran (10 mL) and 2.5 M solution of *n*-butyllithium in hexane (3.7 mL, 5.86 mmol). The crude residue was purified by SiO_2 gel column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) to afford diethyl[1-(*trans*-2-

phenylcyclopropyl)vinyl]phosphate (1.2 g, 77%) as a yellow oil. **IR (neat)** 2984, 1645, 1266, 1165, 996, 845, 749, 692 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.15–1.31 (m, 2H), 1.35 (dt, *J* = 1.0, 7.1 Hz, 3H), 1.36 (dt, *J* = 1.0, 7.0 Hz, 3H), 1.77–1.82 (m, 1H), 2.25 (ddd, *J* = 3.3, 4.6, 9.1 Hz, 1H), 4.13–4.21 (m, 4H), 4.61 (t, *J* = 2.3 Hz, 1H), 4.88 (t, *J* = 2.3 Hz, 1H), 7.09 (d, *J* = 7.1 Hz, 2H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.20 (t, *J* = 7.3 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 14.1, 15.9 (d, *J* = 7.2 Hz), 23.1, 26.0, 64.3 (d, *J* = 4.8 Hz), 95.4 (d, *J* = 7.0 Hz), 125.86, 125.89, 128.3, 141.2, 154.2 (d, *J* = 7.9 Hz); **HRMS** (ESI) m/z Anal. Calcd for $C_{15}H_{21}NaO_4P$ 319.1075, found $[M+Na]^+$ 319.1070.

The second step was performed according to the general procedure using the following: $Ni(acac)_2$ (47.5 mg, 0.19 mmol), a 1 M solution of trimethylsilylmethylmagnesium chloride (7.4 mL, 10.0 mmol) in diethyl ether and the obtained diethyl enol phosphate (1.1 g, 3.7 mmol) with stirring for 9 h. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired allylsilane (633 mg, 74%) as a yellow oil. **IR (neat)** 2954, 1065, 1497, 1247, 836, 743, 694 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 0.17 (s, 9H SiMe_3), 1.22–1.27 (m, 1H, PhCHCH_a), 1.31–1.36 (m, 1H, PhCHCH_b), 1.61–1.67 (m, 1H, PhC*H*), 1.76 (s, 2H, SiCH_2), 2.05–2.09 (m, 1H, PhC*H*), 4.63 (s, 1H, C=CH_a), 4.69 (s, 1H, C=CH_b), 7.19 (d, *J* = 7.6 Hz, 2H, Ar), 7.27 (t, *J* = 7.6 Hz, 1H, Ar), 7.38 (t, *J* = 7.6 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ –1.2 (SiMe_3), 17.0 (Si*C*H_2), 26.0 (PhCH*C*H_2), 27.1 (PhCH*C*H), 30.1 (Ph*C*HCH_2), 104.0 (C=*C*H_2), 125.5 (Ar), 125.6 (Ar), 128.3 (Ar), 142.9 (Ar) (*C*=CH_2), 147.8; **HRMS** (EI) m/z Anal. Calcd for $C_{15}H_{22}Si$ 230.1491, found $[M]^+$ 230.1489.

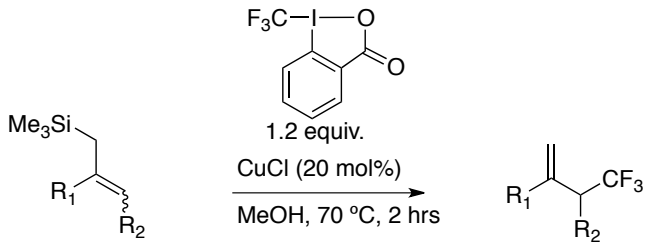
Trifluoromethylation of α-Methylstyrene with Togni's Reagent.



A 5 mL vial containing a magnetic stir bar was charged with α-methylstyrene (32.5 µL, 0.25 mmol), CuCl (5.0 mg, 20 mol%). MeOH (0.5 mL) and Togni's trifluoromethylating reagent **2a** (94.8 mg, 0.3 mmol) were added under Ar atmosphere. The reaction mixture was stirred for 2 h at 70 ˚C. Upon completion of the reaction, sat. aq. $NaHCO_3$ was added at room temperature. The resulting mixture was extracted with diethyl ether (×2), and the combined organic phase was washed sequentially with distilled water, and brine and then dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane to *n*-hexane/AcOEt = 20/1) to afford trifluoromethyl benzoate adduct (39.0 mg, 36%) as a oily solid and allylic trifluoromethyl product (2 mg, 4%).

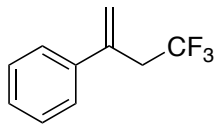
Characterisation data for 4,4,4-trifluoro-2-phenylbutan-2-yl 2-iodobenzoate: **IR (neat)** 2360, 2341, 1733, 1371, 1261, 1155, 1126, 1016 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.13 (s, 3H, Me), 3.05 (dq, J = 10.3, 15.4 Hz, 1H, CH_aCF$_3$), 3.20 (dq, J = 10.6, 15.4 Hz, 1H, CH_bCF$_3$), 7.18 (t, J = 7.6 Hz, 1H, Ar), 7.32 (t, J = 7.1 Hz, 1H, Ar), 7.38–7.47 (m, 5H, Ar), 7.86 (d, J = 7.6 Hz, 1H, Ar), 8.00 (d, J = 8.1 Hz, 1H, Ar); **^{19}F NMR (377 MHz, $CDCl_3$):** δ –60.0 (t, J = 11.5 Hz, 3F); **HRMS** (ESI) m/z Anal. Calcd for $C_{17}H_{14}F_3INaO_2$ 456.9883, found $[M+Na]^+$ 456.9873.

General Procedure for the Trifluoromethylation of Allylsilanes.



A 5 mL vial containing a stirring bar was charged with allylsilane (0.25 mmol) and CuCl (5.0 mg, 20 mol%). MeOH (0.5 mL), additive (0.5 mmol) and Togni's trifluoromethylating reagent (0.3–0.5 mmol) were added under Ar atmosphere. The reaction mixture was stirred for 2 h at 70 ˚C. Upon completion of the reaction, sat. aq. $NaHCO_3$ was added at room temperature. The resulting mixture was extracted with diethyl ether (×2), and the combined organic phase was washed sequentially with distilled water, brine and then dried over $MgSO_4$ and concentrated *in vacuo*. The crude mixture was purified by SiO_2 gel column chromatography using the indicated solvent system.

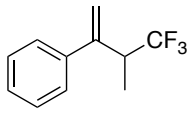
(4,4,4-trifluorobut-1-en-2-yl)benzene: 231a.



The title compound was prepared according to the general procedure under the following conditions: Trimethyl(2-phenylallyl)silane **231** (47.6 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol), Togni's trifluoromethylating reagent (94.8 mg, 0.30 mmol), stirred for 2 h at 70 ˚C. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired product (32.6 mg, 70%) as a colourless oil. **IR (neat)** 2926, 1356, 1254, 1135, 911, 841, 778, 670 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 3.30 (dq, J = 3.3, 10.7 Hz, 2H, CH_2CF_3), 5.39

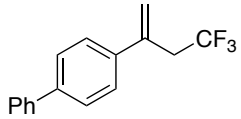
(s, 1H, C=CH_a), 5.61 (2, 1H, C=CH_b), 7.30–7.34 (m, 1H, Ph$_{para}$), 7.37 (t, J = 7.6 Hz, 2H, Ph$_{meta}$), 7.40–7.42 (m, 2H, Ph$_{ortho}$); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 39.4 (q, J = 29.4 Hz, CH$_2$CF$_3$), 119.3 (C=CH$_2$) 125.5 (q, J = 278 Hz, CF$_3$), 126.1, 128.0 (Ar), 128.4 (Ar), 137.8 (q, J = 2.9 Hz, C=CH$_2$), 139.9 (Ar); **^{19}F NMR (471 MHz, $CDCl_3$):** δ –64.9 (t, J = 10.4 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{10}H_9F_3$ 186.0664, found $[M]^+$ 186.0656.

(4,4,4-trifluoro-3-methylbut-1-en-2-yl)benzene: 232a.



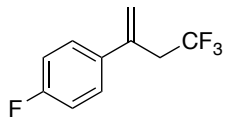
The title compound was prepared according to the general procedure the following conditions. (Z)-Trimethyl(2-phenyl-2-butenyl)silane **X** (51.1 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol), Togni's trifluoromethylating reagent (158.0 mg, 0.50 mmol) and iPr$_2$NEt (87.1 µL, 0.50 mmol), stirring for 2 h at 70 ˚C. The crude residue was purified by SiO_2 gel column chromatography (n-hexane) to afford the desired product (37.4 mg, 75%) as a colourless oil. **IR (neat)** 2973, 1463, 1337, 1258, 1169, 1130, 1063, 1001, 913, 842, 777, 698 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.40 (d, J = 7.1 Hz, 3H, Me), 3.35–3.47 (m, 1H, CHCF$_3$), 5.42 (s, 1H, C=CH_a), 5.50 (s, 1H, C=CH_b), 7.33–7.37 (m, 5H, Ar); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 14.7 (Me), 42.6 (q, J = 27.0 Hz, CHCF$_3$), 116.8 (C=CH$_2$), 126.4 (Ar), 127.1 (q, J = 279 Hz, CF$_3$), 127.7 (Ar), 128.4 (Ar), 141.7 (C=CH$_2$), 144.9 (Ar); **^{19}F NMR (377 MHz, $CDCl_3$):** δ –70.6 (d, J = 8.6 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{11}H_{12}F_3$ 200.0813, found $[M]^+$ 200.0820.

4-(4,4,4-trifluorobut-1-en-2-yl)-1,1'-biphenyl: 259a.



The title compound was prepared according to the general procedure under the following conditions. {2-[(1,1'-biphenyl)-4-yl]allyl}trimethylsilane **259** (66 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol), Togni's trifluoromethylating reagent (94.8 mg, 0.30 mmol), stirred for 2 h at 70 ˚C. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired product (49 mg, 74%) as a white solid, 82-84 °C. **IR (neat)** 2360, 1488, 1355, 1320, 1249, 1137, 1126, 1070, 924, 844, 771, 737, 692 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 3.38 (q, J = 10.5 Hz, 2H, CH_2CF$_3$), 5.42 (s, 1H, C=CH_a), 5.68 (s, 1H, C=CH_b), 7.37 (t, J = 7.6 Hz, 1H, Ar), 7.49 (t, J = 7.8 Hz, 2H, Ar), 7.50 (d, J =8.5 Hz, 2H, Ar), 7.61 (t, J = 7.8 Hz, 4H, Ar); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 39.3 (q, J = 29.2 Hz, CH$_2$CF$_3$), 119.3 (C=CH$_2$), 125.7 (q, J = 275.8 Hz, CF$_3$), 126.4, 127.0, 127.1, 127.4, 128.8, 137.4 (q, J = 2.8 Hz, C=CH$_2$), 138.7, 140.4, 140.8; **^{19}F NMR (470Hz, $CDCl_3$):** δ –64.4 (t, J = 10.4 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{16}H_{13}F_3$ 262.0969, found $[M]^+$ 262.0966.

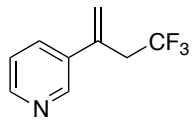
1-fluoro-4-(4,4,4-trifluorobut-1-en-2-yl)benzene: 260a.



The title compound was prepared according to the general procedure under the following conditions. [2-(4-fluorophenyl)allyl]trimethylsilane **260** (104 mg, 0.5 mmol), CuCl (10.0 mg, 0.1 mmol) Togni's trifluoromethylating reagent (221 mg, 0.70 mmol), stirred for 2 h at 70 ˚C. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired product (60.0 mg, 59%) as a colourless oil. **IR (neat)** 2920, 2361, 913, 744, 670, 617 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 3.30 (dq, J = 1.0, 10.4 Hz, 2H, CH_2CF$_3$), 5.28 (s, 1H, C=CH_a), 5.47 (s, 1H, C=CH_b), 6.96 (t, J = 8.5 Hz, 2H, Ph$_{ortho}$), 7.29 (dd, J = 5.1, 8.5 Hz, 2H, Ph$_{meta}$); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 39.6 (q, J = 29.4 Hz, CH$_2$CF$_3$), 115.3 (C=CH$_2$), 119.4 (Ar) 125.6 (q, J = 274.8 Hz, CF$_3$), 127.8 (d, J = 8.6 Hz, Ph$_{meta}$), 136.0 (d, J = 2.8 Hz, Ph$_{ortho}$), 137.0 (q, J = 2.8 Hz, C=CH$_2$),

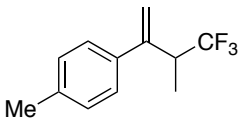
162.6 (d, *J* = 245.4 Hz, Ph_{para}); **^{19}F NMR (471 MHz, $CDCl_3$):** δ –114.2 (m, 1F), –64.5 (t, *J* = 10.4 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{10}H_8F_4$ 204.0562, found $[M]^+$ 204.0572

3-(4,4,4-trifluorobut-1-en-2-yl)pyridine: 258a.



The title compound was prepared according to the general procedure under the following conditions. 3-[3-(triimethylsilyl)prop-1-en-2-yl]pyridine **258** (57 mg, 0.3 mmol), CuCl (6.0 mg, 0.06 mmol), Togni's trifluoromethylating reagent (132 mg, 0.42 mmol), stiited for 2 h at 70 ˚C. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded the mixture of desired product (24 mg, <42%) as a yellow oil and unidentified byproducts. **IR (neat)** 2360, 2341, 1760, 1255, 1134, 748, 669 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 3.29 (q, *J* = 10.4 Hz, 2H, C$H_2$$CF_3$), 5.49 (s, 1H, C=C$H_a$), 5.66 (s, 1H, C=C$H_b$), 7.31 (dd, *J* = 5.0, 8.2 Hz, 1H), (m, 1H), 7.70 (dt, *J* = 1.9, 8.0 Hz, 1H), 8.56 (d, *J* = 4.1 Hz, 1H), 8.69 (s, 1H); **^{19}F NMR (376 MHz, $CDCl_3$):** δ –64.5 (t, *J* = 10.4 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_9H_9F_3N$ 188.0682, found $[M+Na]^+$188.0677.

1-methyl-4-(4,4,4-Trifluoro-3-methylbut-1-en-2-yl)benzene: 255a.



Procedure B: Copper catalysis.

The title compound was prepared according to the general procedure under the following conditions. [2-(*p*-tolyl)but-2-en-1-yl]trimethylsilane **255** (54.5 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol), Togni's trifluoromethylating reagent (158.0 mg, 0.50 mmol) and *i*Pr_2NEt (87.1 μL,

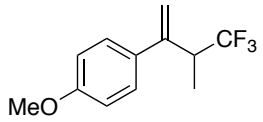
0.50 mmol), stirred for 2 h at 70 ˚C. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford (21.4 mg, 40%) as a colourless oil

Procedure C: Ruthenium Catalysis.

The title compound was prepared according to the general procedure under the following conditions. [2-(*p*-tolyl)but-2-en-1-yl]trimethylsilane **255** (54.5 mg, 0.25 mmol), $Ru(bpy)_3Cl_2$ (9.0 mg, 0.0125 mmol), Togni trifluoromethylating reagent (94.8 mg, 0.3 mmol) and MeOH (0.5 mL) with stirring for 8 h under visible light. The crude residue was purified by SiO_2 gel column chromatography (Et_2O/n-hexane = 1/99) to afford the desired product (16 mg, 27%).

IR (neat) 2985, 1729, 1268, 1027, 977, 891, 811, 753 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 1.44 (d, *J* = 7.2 Hz, 3H), 2.41 (s, 3H), 3.41–3.47 (m, 1H), 5.43 (s, 1H), 5.55 (s, 1H), 7.16 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.2 Hz); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 14.7 (q, *J* = 2.8 Hz), 21.0, 42.5 (q, *J* = 27.0 Hz), 116.0, 126.2, 127.2 (q, *J* = 277.7 Hz), 129.1, 137.6, 138.7, 144.5; **^{19}F NMR (377 MHz, $CDCl_3$):** δ –70.6 (d, *J* = 8.6 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{12}H_{13}F_3$ 214.0969, found $[M]^+$ 214.0972.

1-methoxy-4-(4,4,4-Trifluoro-3-methylbut-1-en-2-yl)benzene: 254a.



Procedure B: Copper catalysis.

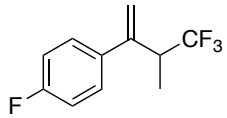
The title compound was prepared according to the general procedure under the following conditions. [2-(4-methoxyphenyl)but-2-en-1-yl]trimethylsilane **254** (58.5 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol), Togni's trifluoromethylating reagent (158.0 mg, 0.50 mmol) and *i*Pr_2NEt (87.1 µL, 0.50 mmol), stirred for 2 h at 70 ˚C. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane/Et_2O 99:1) to afford the desired product (23.4 mg, 40%) as a colourless oil.

Procedure C: Ruthenium Catalysis.

The title compound was prepared according to the general procedure under the following conditions. [2-(4-methoxyphenyl)but-2-en-1-yl]trimethylsilane **254** (58.5 mg, 0.25 mmol), $Ru(bpy)_3Cl_2$ (9.0 mg, 0.0125 mmol), Togni trifluoromethylating reagent (94.8 mg, 0.3 mmol) and MeOH (0.5 mL) with stirring for 8 h under visible light. The crude residue was purified by SiO_2 gel column chromatography (Et_2O/n-hexane = 1/99) to afford the desired product (17 mg, 29%).

IR (neat) 2992, 1609, 1511, 1247, 1178, 1019, 971, 911, 796, 748 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 1.38 (d, J = 7.1 Hz, 3H, *Me*), 3.34–3.43 (m, 1H, C*H*CF_3), 3.82 (s, 3H, O*Me*), 5.33 (s, 1H, C=CH_a), 5.44 (s, 1H, C=CH_b), 6.88 (d, J =8.8 Hz, 2H, Ar), 7.29 (d, J = 8.8 Hz, 2H, Ar); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 14.7 (*Me*), 42.5 (q, J = 27.0 Hz, *C*HCF_3), 55.3 (O*Me*), 113.7 (C=*C*H_2), 115.4 (Ar), 127.2 (q, J = 278.6 Hz, *C*F_3) 127.6 (Ar), 134.2 (Ar), 144.3 (*C*=CH_2), 159.2 (Ar); **^{19}F NMR (377 MHz, $CDCl_3$):** δ –70.6 (d, J = 8.7 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{12}H_{13}F_3O$ 230.0918, found $[M]^+$ 230.0915.

1-methyl-4-(4,4,4-trifluoro-3-methylbut-1-en-2-yl)benzene: 256a.



Procedure B: Copper catalysis.

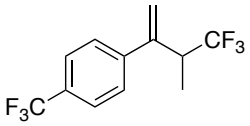
The title compound was prepared according to the general procedure under the following conditions. The title compound was prepared according to the general procedure under the following conditions. [2-(4-fluorophenyl)but-2-en-1-yl]trimethylsilane **256** (54.5 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol), Togni's trifluoromethylating reagent (158.0 mg, 0.50 mmol) and *i*Pr_2NEt (87.1 µL, 0.50 mmol), stirred for 2 h at 70 ˚C. The crude residue was purified by

SiO_2 gel column chromatography (*n*-hexane) to afford the desired product (10 mg, 17%) as a colourless oil

Procedure C: Ruthenium Catalysis.

The title compound was prepared according to the general procedure under the following conditions. . [2-(4-fluorophenyl)but-2-en-1-yl]trimethylsilane **256** (54.5 mg, 0.25 mmol), $Ru(bpy)_3Cl_2$ (9.0 mg, 0.0125 mmol), Togni trifluoromethylating reagent (94.8 mg, 0.3 mmol) and MeOH (0.5 mL) with stirring for 8 h under visible light. The crude residue was purified by SiO_2 gel column chromatography (Et_2O/n-hexane = 1/99) to afford the desired product (6 mg, 10%). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 1.39 (d, J = 7.0 Hz, 3H, *Me*), 3.30–3.40 (m, 1H, C*H*CF_3), 5.41 (s, 1H, C=CH_a), 5.46 (s, 1H, C=CH_b), 7.04 (t, J = 8.5 Hz, 2H, Ar), 7.31 (dd, J = 5.0, 8.5 Hz, 2H, Ar); **^{19}F NMR (471 MHz, $CDCl_3$):** δ –114.72–114.77 (m, 1F), –70.6 (d, J = 8.7 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{11}H_{10}F_4$ 218.0719, found $[M]^+$ 218.0726.

1-[(4,4,4-trifluoro-3-methylbut-1-en-2-yl)-4(trifluoromethyl)]benzene: 257a.



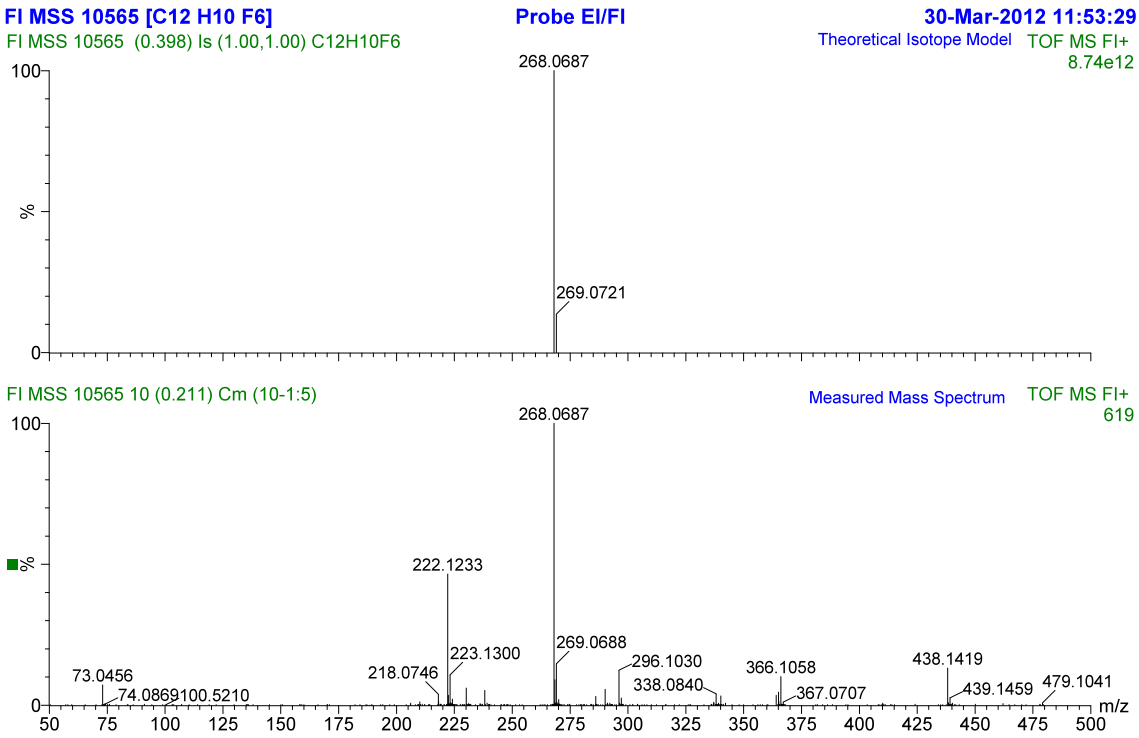
Procedure B: Copper catalysis.

The title compound was prepared according to the general procedure under the following conditions. {2-[4-(trifluoromethyl)phenyl]but-2-en-1yl}trimethylsilane **257** (67.0 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol), Togni's trifluoromethylating reagent (158.0 mg, 0.50 mmol) and *i*Pr_2NEt (87.1 µL, 0.50 mmol), stirred for 2 h at 70 ˚C. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to give trace quantities of the desired product (<3 mg, <6%).

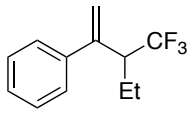
Procedure C: Ruthenium Catalysis.

The title compound was prepared according to the general procedure under the following conditions. {2-[4-(trifluoromethyl)phenyl]but-2-en-1yl}trimethylsilane **257** (67.0 mg, 0.25 mmol), $Ru(bpy)_3Cl_2$ (9.0 mg, 0.0125 mmol), Togni trifluoromethylating reagent (94.8 mg, 0.3 mmol) and MeOH (0.5 mL) with stirring for 8 h under visible light. The crude residue was purified by SiO_2 gel column chromatography (Et_2O/n-hexane = 1/99) to afford the desired product (6 mg, 11%).

HRMS (EI) m/z Anal. Calcd for $C_{12}H_{10}F_6$ 268.0687, found $[M]^+$ 268.0687

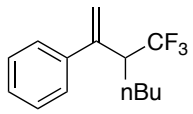


[3-(trifluoromethyl)pent-1-en-2-yl]benzene: 261a.



The title compound was prepared according to the general procedure under the following conditions. Trimethyl(2-phenyl-2-pentenyl)silane **261** (54.6 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol), Togni's trifluoromethylating reagent (158.0 mg, 0.50 mmol) and *i*Pr_2NEt (87.1 µL, 0.50 mmol), stirred for 2 h at 70 ˚C. Column chromatography (*n*-hexane) of the crude residue afforded the desired product (22.3 mg, 42%) as a colourless oil and recovered starting material (27.9 mg, 51%). **IR (neat)** 2973, 1316, 1259, 1168, 1132, 1102, 1037, 961, 912, 848, 777, 718, 700 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.00 (t, J = 7.3 Hz, 3H, *Me*), 1.73–1.84 (m, 1H, CHC$H_{2a}$$CH_3$), 1.94–2.04 (m, 1H, CHC$H_{2a}$$CH_3$), 3.16 (d quintet, J = 4.6, 9.6 Hz, 1H, C$H$$CF_3$), 5.41 (s, 1H, C=C$H_a$), 5.58 (s, 1H, C=C$H_a$), 7.32–7.36 (m, 5H, Ar); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 11.5 (*Me*), 22.7 ($C$$H_2$$CH_3$), 49.8 (q, J = 25.4 Hz, $C$$HCF_3$), 126.5 (C=$C$$H_2$), 127.0 (q, J = 277 Hz, $C$$F_3$), 127.7 (Ar), 128.4 (Ar) 142.6 (C=CH_2), 143.5 (Ar); **^{19}F NMR (377 MHz, $CDCl_3$):** δ –69.2 (d, J = 10.4 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{12}H_{13}F_3$ 214.0969, found $[M]^+$ 214.0970.

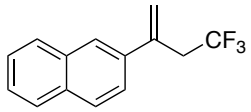
[3-(trifluoromethyl)hept-1-en-2-yl]benzene: 262a.



The title compound was prepared according to the general procedure under the following conditions. Trimethyl(2-phenylhept-2-en-1-yl)silane **262** (61.6 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol), Togni's trifluoromethylating reagent (158.0 mg, 0.50 mmol) and *i*Pr_2NEt (87.1 µL, 0.50 mmol), stirred for 2 h at 70 ˚C. Column chromatography (*n*-hexane) of the crude residue afforded the desired product (28.7 mg, 48%) as a colourless oil and recovered starting material (3.09 mg, 50%). **IR (neat)** 2959, 1467, 1263, 1165, 1132, 1097, 912, 846, 778 cm^{-1};

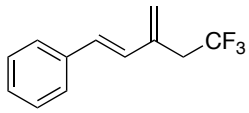
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, J = 7.3 Hz, 3H, *Me*), 1.29–1.47 (m, 4H, $CH_2CH_2CH_3$), 1.70–1.80 (m, 1H, $CH_{2a}CH_2CH_2CH_3$), 1.89–1.96 (m, 1H, $CH_{2b}CH_2CH_2CH_3$), 3.22 (d quintet, J = 4.0, 9.6 Hz, 1H, $CHCF_3$), 5.41 (s, 1H, C=CH_{2a}), 5.57 (s, 1H, C=CH_{2b}), 7.32–7.37 (m, 5H, Ar); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 13.8 (Me), 22.5 (CH_2CH_3) , 28.9 ($CH_2CH_2CH_3$), 29.1 ($CH_2CH_2CH_2CH_3$) 49.2 (q, J = 26.5 Hz, $CHCF_3$), 117.2 (C=CH_2), 126.4 (Ar), 127.0 (q, J = 278.6 Hz, CF_3), 127.6 (Ar), 128.4 (Ar), 142.6 (Ar), 143.7 (q, J = 1.9 Hz, C=CH_2); **^{19}F NMR (377 MHz, $CDCl_3$):** δ –69.3 (d, J = 8.6 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{14}H_{17}F_3$ 242.1282, found $[M]^+$ 242.1285.

2-(4,4,4-trifluobut-1-en-2-yl)naphthalene: 266a.



The title compound was prepared according to the general procedure under the following conditions. [2-(naphthalene-2-yl)allyl]trimethylsilane **266**[182] (60.0 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol), Togni's trifluoromethylating reagent (94.8 mg, 0.30 mmol), stirred for 2 h at 70 ˚C. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired product (49.0 mg, 83%) as a colourless oil. **IR (neat)** 1348, 1252, 1129, 1107, 962, 919, 893, 858, 839, 817, 750 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 3.42 (dt, J = 0.6, 10.7 Hz, 2H, CH_2CF_3), 5.49 (s, 1H, C=CH_a), 5.76 (s, 1H, C=CH_b), 7.42–7.52 (m, 2H, Ar), 7.57 (dd, J = 1.9, 8.8 Hz, 1H, Ar), 7.83–7.87 (m, 4H, Ar); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 39.4 (q, J = 29.4 Hz, CH_2CF_3), 119.8 (C=CH_2), 124.1, 125.0, 125.8 (q, J = 275.8 Hz, CF_3), 126.2, 126.4, 127.6, 128.1, 128.2, 132.9, 133.2, 137.1, 137.7 (q, J = 1.9 Hz, C=CH_2); **^{19}F NMR (471 MHz, $CDCl_3$):** δ –64.6 (t, J = 10.7 Hz 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{14}H_{11}F_3$ 236.0813, found $[M]^+$ 236.0817.

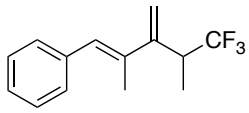
(*E*)-(5,5,5-trifluoro-3-methylene-1-pentenyl)benzene: 269a.



The title compound was prepared according to the general procedure under the following conditions. (*E*)-Trimethyl(2-methylene-4-phenyl-3-butenyl)silane **269**[183] [5] (54.1 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol) and Togni's trifluoromethylating reagent (94.8 mg, 0.30 mmol), stirred for 1 h at 70 ˚C. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired product (45.0 mg, 84%) as a colourless oil. **IR (neat)** 2962, 1260, 1091, 1019 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 3.14 (t, J = 10.6 Hz, 2H, CH_2CF$_3$), 5.33 (s, 1H, C=CH_a), 5.49 (s, 1H, C=CH_b), 6.60 (d, J = 16.4 Hz, 1H, PhCH=CH), 6.85 (d, J = 16.4 Hz, 1H, PhCH=CH), 7.25–7.29 (m, 1H, Ar), 7.35 (t, J = 7.8 Hz, 2H, Ar), 7.44 (d, J = 7.6 Hz, 2H, Ar); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 36.3 (q, J = 30.2 Hz, CH$_2$CF$_3$), 121.9 (C=CH$_2$), 125.8 (q, J = 275 Hz, CF$_3$), 126.6 (Ar) , 127.9 (Ar), 128.7 (Ar), 129.5 (PhCH=CH) 129.6, 135.5 PhCH=CH) 136.7 (C=CH$_2$); **^{19}F NMR (377 MHz, $CDCl_3$):** δ –64.3 (t , J = 12.1 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{12}H_{11}F_3$ 212.0813, found $[M]^+$ 212.0820.

Note: The title compound was found to decompose spontaneously within one week when stored at room temperature.

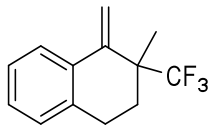
(E)-(5,5,5-trifluoro-2,4-dimethyl-3-methylene-1-pentenyl)benzene: 267a.



The title compound was prepared according to the general procedure under the following conditions. Trimethyl[2-((*Z*)-1-phenyl-1-propene-2-yl)-2-butenyl]silane **267**[184] (61.1 mg, 0.25

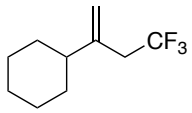
mmol), CuCl (5.0 mg, 0.05 mmol) and Togni's trifluoromethylating reagent (94.8 mg, 0.30 mmol), stirred for 12 h at 70 ˚C. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired product (22.2 mg, 38%) as a colourless oil and recovered starting material (26.3 mg, 43%). **IR (neat)** 2953, 1766, 1451, 1257, 1172, 1134, 1096, 1001, 846, 741, 699 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 1.39 (d, J = 7.3 Hz, 3H, *Me*), 2.02 (d, J = 1.3 Hz, 3H, CCH_3), 3.36–3.46 (m, 1H, CHCF$_3$), 5.33 (s, 1H, C=CH_a), 5.48 (s, 1H, C=CH_a), 6.62 (s, 1H, PhCH=C), 7.24–7.29 (m, 3H, Ar), 7.36 (t, J = 7.3 Hz, 2H, Ar); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 15.0 (q, J =2.8 Hz, *Me*), 16.5 (CCH_3, 39.6 (q, J = 26.5 Hz, CHCF$_3$), 115.0 (C=CH$_2$), 126.6 (Ar), 127.0 (Ar), 127.2 (q, J = 277.7 Hz, CF$_3$), 128.1 (PhCH=C), 129.2, 137.4 (PhCH=C), 137.8 (CH=CMe), 146.8 (q, J = 1.9 Hz, C=CH$_2$); **^{19}F NMR (377 MHz, $CDCl_3$):** δ –70.6 (t , J = 8.6 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{14}H_{15}F_3$ 240.1126, found $[M]^+$ 240.1127.

2-methyl-1-methylene-2-(trifluoromethyl)-1,2,3,4-tetrahydronaphthalene: 268a.



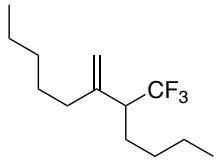
Preparation of the title compound was attempted for using the general procedure. From trimethyl[(2-methyl-3,4-dihydronaphthalen-1-yl)methyl]silane **268** (51.1 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol) and Togni's trifluoromethylating reagent (94.8 mg, 0.30 mmol) with stirring for 24 h at 70 ˚C. Column chromatography (*n*-hexane) of the crude residue afforded a mixture of the desired product and inseparable impurities (8.8 mg). **^{1}H NMR (400 MHz, $CDCl_3$):** identifiable peaks: 1.45 (s, 3H, *Me*), 5.45 (s, 1H, C=CH_a), 5.80 (s, 1H, C=CH_b); **^{19}F NMR (377 MHz, $CDCl_3$):** δ –74.6 (s, 3F).

(4,4,4-trifluorobut-1-en-2-yl)cyclohexane: 263a.



The title compound was prepared according to the general procedure under the following conditions. (2-cyclohexylallyl)trimethylsilane **263** (49.1 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol) and Togni's trifluoromethylating reagent (142 mg, 0.42 mmol), stirred for 1 h at 70 °C. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired product (20.0 mg, 42%) as a colourless oil. **IR (neat)** 2928, 1450, 1251, 1124, 840 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 1.07–1.33 (m, 6H), 1.69–1.83 (m, 4H), 1.92 (t, J = 11.7 Hz, 1H), 2.81 (q, J = 11.0 Hz, 2H, CH_2CF_3), 5.03 (s, 1H, C=CH_a), 5.05 (s, 1H C=CH_b); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.2, 26.6, 32.1, 38.9 (q, J = 28.2 Hz, *C*H_2CF_3), 43.8, 126.1 (q, J = 275.0 Hz, *C*F_3), 144.0; **^{19}F NMR (236 MHz, $CDCl_3$):** δ –64.9 (t , J = 11.1 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{10}H_{15}F_3$ 192.1126, found $[M]^+$ 192.1130.

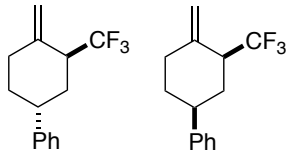
6-methylene-5-(trifluoromethyl)undecane: 264a.



The title compound was prepared according to the general procedure under the following conditions. Trimethyl(2-pentyl-2-heptenyl)silane **XX** (60.1 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol), Togni's trifluoromethylating reagent (158 mg, 0.5 mmol) and *i*Pr_2NEt (87.1 µL, 0.50 mmol), stirred for 2 h at 70 °C. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired product (23.4 mg, 40%) as a colourless oil and recovered starting material (19.3 mg, 32%). **IR (neat)** 2958, 2863, 1467, 1258, 1161,

1123, 1094, 906, 840 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 0.907 (t, J = 7.0 Hz, 3H), 0.912 (t, J = 7.3 Hz, 3H), 1.21–1.76 (m, 13H), 2.03 (t, J = 7.9 Hz, 1H), 2.62–2.70 (m, 1H, C$H$$CF_3$), 5.03 (s, 1H, C=C$H_a$), 5.07 (s, 1H, C=C$H_b$); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 13.8, 14.0, 22.5, 22.6, 27.0, 27.1, 28.9, 31.5, 34.8, 50.0 (q, J = 24.6 Hz, $C$$HCF_3$), 114.5, 127.1(q, J = 278.6 Hz, CF_3), 143.4; **^{19}F NMR (377 MHz, $CDCl_3$):** δ –69.2 (d, J = 9.2 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{13}H_{23}F_3$ 236.1752, found $[M]^+$ 236.1756.

anti-4-methylene-3-[(trifluoromethyl)cyclohexyl]benzene: 265a.

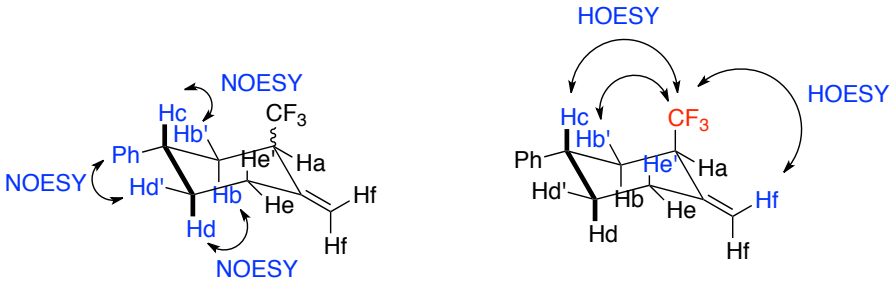


The title compound was prepared according to the general procedure under the following conditions. Trimethyl{[1,2,3,6-tetrahydro-(1,1'-biphenyl)-4-yl]methyl}silane **265** (61.1 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol) and Togni's trifluoromethylating reagent (94.8 mg, 0.30 mmol), stirred for 3 h at 70 ˚C. The diastereomeric ratio was determined by ^{19}F-NMR spectroscopy of the crude mixture (*anti : syn* = 4.6 : 1). Column chromatography (*n*-hexane) of the crude residue afforded the desired product (26.3 mg, 44%, *anti : syn* = 3 : 1) as a colourless oil. Further purification by preparative TLC enable to isolation of the pure *anti* isomer.

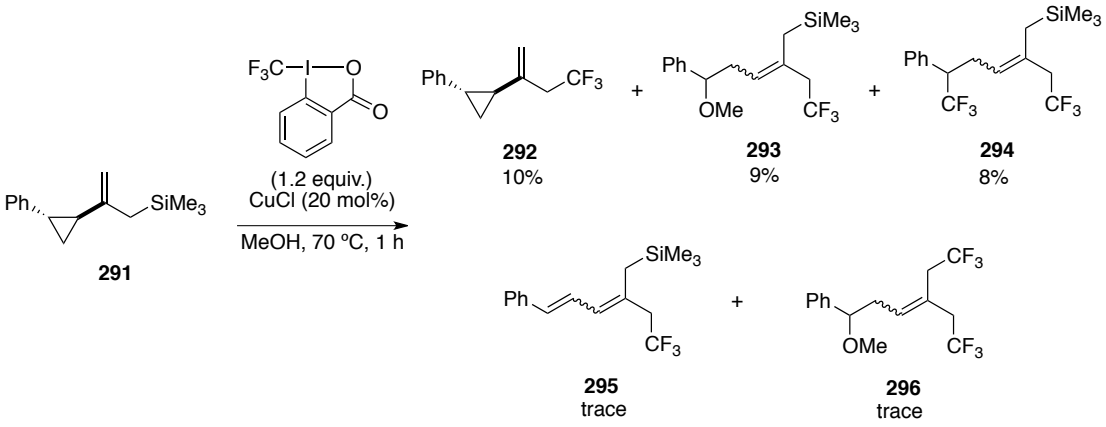
Characterisation data for the *anti* diastereomer**: IR (neat)** 2936, 1236, 1167, 1141, 1113, 1075, 1056, 1029, 980, 844 cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 1.56–1.62 (m, H_d), 1.80 (dt, J = 6.6, 13.4 Hz, H_b), 2.01–2.06 (m, $H_{d'}$), 2.29 (br. d, J = 14.2 Hz, $H_{b'}$), 2.44–2.49 (m, H_e and $H_{e'}$), 3.00 (t, J = 13.0 Hz, H_c), 3.10 (dq, J = 6.6, 11.1 Hz, H_a), 5.01 (s, H_f), 5.10 (s, $H_{f'}$), 7.22–7.26 (m, 3H, Ar), 7.32 (t, J = 7.6 Hz, 2H, Ar); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 32.4, 33.2, 34.1, 46.5 (q, J = 26.5 Hz, $C$$HCF_3$), 116.0, 126.4, 126.8, 127.2 (q, J = 279.5 Hz, CF_3), 128.5, 140.8 (q, J = 1.9 Hz, C=CH_2),

145.5; **^{19}F NMR (471 MHz, $CDCl_3$):** δ –66.5 (d, J = 11.1 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{14}H_{15}F_3$ 240.1126, found $[M]^+$ 240.1123.

NOESY/ ^{19}F-^{1}H HOESY spectroscopy was consistent with the assignment of the major product as the *anti* diastereomer.



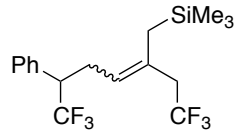
2-5. Trifluoromethylation of the radical crock with Togni's reagent



A 5 mL vial containing a magnetic stir bar was charged with trimethyl[2-(*trans*-2-phenylcyclopropyl)allyl]silane **291** (115 mg, 0.5 mmol) and CuCl (10.0 mg, 20 mol%), MeOH (1.0 mL) and Togni's trifluoromethylating reagent **I** (189.6 mg, 2.4 mmol) were added under

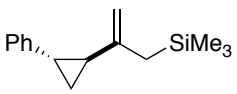
Ar atmosphere. The reaction mixture was stirred at 70 ˚C. After stirring for 1 h, sat. aq. $NaHCO_3$ was added to the mixture at room temperature. The resulting mixture was extracted with diethyl ether, and the combined organic phase was washed sequentially with distilled water, and brine and then dried over $MgSO_4$ and concentrated *in vacuo*. The crude mixture was purified by preparative T.L.C. on SiO2 gel using *n*-hexane as the eluent to obtain trimethyl[6,6,6-trifluoro-5-phenyl-2-(2,2,2-trifluoroethyl)-2-hexyl]silane (17.5 mg, 8.4%, R_f = 0.7) and *trans*-[2-(4,4,4-trifluoro-2-buytenyl)cyclopropyl]benzene (11.2 mg, 10%, R_f = 0.64). Furthermore purification by preparative T. L. C. on SiO_2 gel using diethyl ether/ *n*-hexane=1/20 as an eluent afforded [5-methoxy-5-phenyl-2-(2,2,2-trifluoroethyl)-2-pentenyl]trimethylsilane (14.4 mg, 9%, R_f = 0.47) as a colourless oil.

trimethyl[6,6,6-trifluoro-5-phenyl-2-(2,2,2-trifluoroethyl)-2-hexyl]silane: 294.



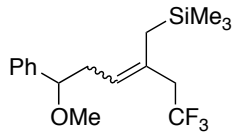
^{1}H NMR (400 MHz, $CDCl_3$): δ –0.16 (s, 9H, Si*Me*$_3$), 1.56 (s, 2H, Si*CH*$_2$), 2.54–2.67 (m, 2H, C*H*$_2$CH=C), 2.73–2.84 (m, 2H, C*H*$_2$CF$_3$), 3.26 (d quintet, *J* = 4.3, 9.6 Hz, 1H, C*H*CF$_3$), 5.05 (t, *J* = 7.1 Hz, 1H, C=C*H*), 7.27–7.36 (m, 5H, Ar); **^{19}F NMR (377 MHz, $CDCl_3$):** δ –69.7 (d, *J* = 6.9 Hz, 3F), –63.8 (t, *J* = 10.3 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{17}H_{22}F_6Si$ 368.1396, found $[M]^+$ 368.1395.

***trans*-[2-(4,4,4-trifluorobut-1-en-2-yl)cyclopropyl]benzene: 291.**



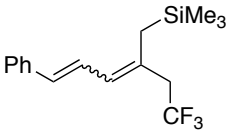
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17–1.28 (m, 2H, PhCHCH_2), 1.65–1.69 (m, 1H, CHC=CH_2), 1.94–1.98 (m, 1H, PhCH), 2.92 (q, J = 11.0 Hz, 2H, CH_2CF_3), 5.03 (s, 1H, C=CH_a), 5.04 (s, 1H, C=CH_b), 7.11 (d, J = 7.6 Hz, 2H, Ar), 7.19 (t, J = 7.1 Hz, 1H, Ar), 7.27–7.29 (m, 2H, Ar); **^{19}F NMR (377 MHz, $CDCl_3$):** δ –64.8 (t, J = 12.1 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{13}H_{13}F_3$ 226.0969, found $[M]^+$ 226.0965.

[5-methoxy-5-phenyl-2-(2,2,2-trifluoroethyl)-2-pentenyl]trimethylsilane: 293.

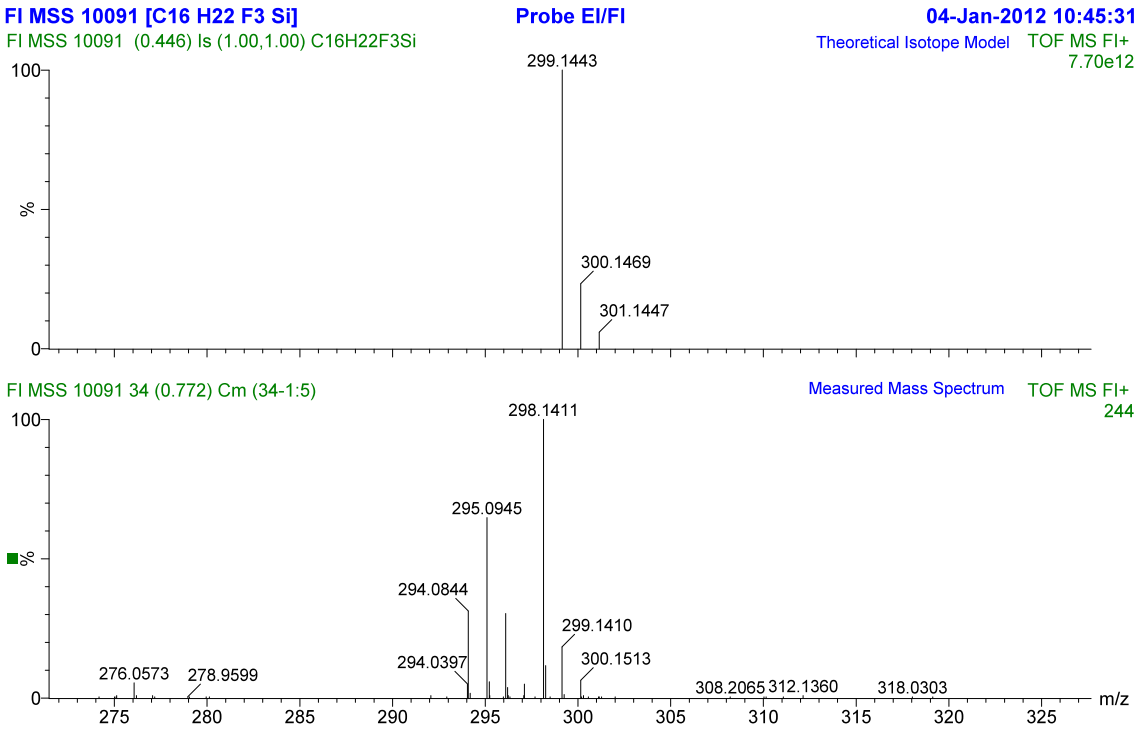


^{1}H NMR (400 MHz, $CDCl_3$): δ –0.03 (s, 9H, SiMe_3), 1.59 (s, 2H, SiCH_2), 2.38 (dt, J = 6.8, 14.6 Hz, 1H, PhCHCH_a), 2.54 (dt, J = 7.3, 14.6 Hz, 1H, PhCHCH_b), 2.61–2.78 (m, 2H, CH_2CF_3), 3.21 (s, 3H, OMe), 4.07 (t, J = 7.1 Hz, 1H, PhCH), 5.30 (t, J = 7.3 Hz, 1H, C=CH), 7.27–7.38 (m, 5H, Ar); **^{19}F NMR (377 MHz, $CDCl_3$):** δ –63.8 (t, J = 10.4 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{17}H_{25}OF_3Si$ 330.1627, found $[M]^+$ 330.1627.

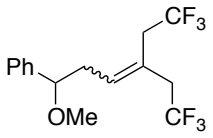
trimethyl(5-phenyl-2-(2,2,2-trifluoroethyl)penta-2,4-dien-1-yl)silane: 295.



FI Mass (EI) m/z Anal. Calcd for $C_{17}H_{22}F_3Si$ 298.1365, found $[M]^+$ 298.1411

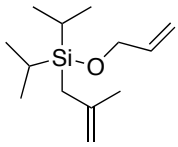


[6,6,6-trifluoro-1-metoxyl-4-(2,2,2-trifluoroethyl)hex-3-en-1-yl]benzene: 405.



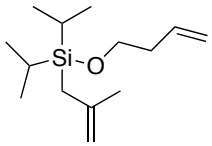
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (dt, J = 6.0, 14.5 Hz, 1H, PhCHCH_a), 2.57 (dt, J = 7.3, 14.6 Hz, 1H, PhCHCH_b), 2.75–2.90 (m, 4H, 2 x (CH_2CF$_3$)), 3.21 (s, 3H, OMe), 4.14 (t, J = 6.0 Hz, 1H, PhCH), 5.83 (t, J = 7.3 Hz, 1H, CH=C), 7.26–7.37 (m, 5H, Ar); **^{19}F NMR (377 MHz, $CDCl_3$):** δ –65.2 (t, J = 10.3 Hz, 3F), –64.4 (t, J = 10.4 Hz, 3F).

(Allyloxy)diisopropyl(2-methylallyl)silane: 278.



To a solution of (allyloxy)diisopropylsilyl chloride (1g, 4.5 mmol, 1 eq). in dry THF in 40 mL at 0 °C, was added 2-methylallylmagnesium chloride (0.5 M in THF, 18 mL, 9 mmol, 2 eq) dropwise. The reaction mixture was the stirred at toom temperature under argon. After 16 hours, the reaction was quenched with sat. $NH_4Cl_{(aq)}$ and extracted 3 times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced presure. Column chromatography (hexane) gave the product as a colourless oil in 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (sb, 14H, Si(*i*-Pr)$_2$), 1.68 (s, 2H, CH_2Si), 1.81 (s, 3H, CH_3), 4.25 (m, 2H, OCH_2), 4.66 (m, 2H, CCH_2), 5.10 (s, 1H, $^3J_{(H,H)}$ 10.0 Hz, CH=C$H_{2(cis)}$), 5.33 (d, $^3J_{(H,H)}$ 17.0 Hz, CH=C$H_{2(trans)}$), 5.99 (dt, 1H, $^3J_{(H,Htrans)}$ 17.0, $^3J_{(H,Hcis)}$ 10.0 Hz, 1H, CHCH_2); ^{13}C NMR (100 Hz, $CDCl_3$): δ 12.9 (Si(*C*H(CH_3)$_2$)$_2$), 17.5 (Si(CH(*C*H_3)$_2$)$_2$), 22.4 (*C*H_2Si), 25.3 (*C*H_3), 64.1 (O*C*H_2), 109.5 (*C*H_2), 113.3 (*C*H_2), 137.2 (*C*HCH$_2$), 143.3 (*C*CH$_2$); IR (neat) 2967, 2800, 1667, 1098, 990, 804 cm^{-1} FI Mass (EI) m/z Anal. Calcd for $C_{13}H_{26}OSi$ 226.1753, found $[M+Na]^+$ 226.1742.

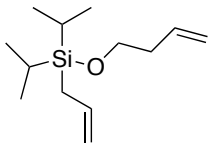
(But-3-enyloxy)(diisopropyl)(2-methylprop-2-en-1-yl)silane: 279.



To a solution of (3-butenoxy)diisopropylsilyl chloride (1g, 4.5 mmol, 1 eq). in dry THF in 40 mL at 0 °C, was added 2-methylallylmagnesium chloride (0.5 M in THF, 18 mL, 9 mmol, 2 eq) dropwise. The reaction mixture was the stirred at toom temperature under argon. After 16

hours, the reaction was quenched with sat. $NH_4Cl_{(aq)}$ and extracted 3 times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced presure. Column chromatography (hexane) gave the product as a colourless oil in 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (sb, 14H, Si(*i*-Pr)$_2$), 1.68 (s, 2H, CH_2Si), 1.80 (s, 3H, CH_3), 2.27-2.34 (m, 2H, OCH$_2$CH_2), 3.73 (t, $^3J_{(H-H)}$ = 6.8 Hz, 2H, OCH_2), 4.59-4.64 (m, 2H, CCH_2), 4.99-5.11 (m, 2H, CHCH_2), 5.78-5.90 (m, 1H, CHCH$_2$); ^{13}C NMR (100 Hz, $CDCl_3$): δ 12.9 (Si(*C*H(CH$_3$)$_2$)$_2$), 17.5 (Si(CH(*C*H$_3$)$_2$)$_2$), 17.6 (Si(CH(*C*H$_3$)$_2$)$_2$), 22.4 (*C*H$_2$Si), 25.3 (*C*H$_3$), 37.5 (OCH$_2$*C*H$_2$), 63.0 (O*C*H$_2$), 109.4 (*C*H$_2$), 116.3 (*C*H$_2$), 135.4 (*C*HCH$_2$), 143.5 (*C*CH$_2$). Characterization data correspond to the literature.[185]

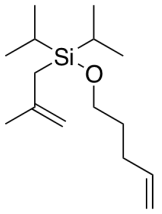
Allyl(but-3-en-yloxy)diisopropylsilane: 281.



A solution of dichloro(diisopropyl)silane (1 mL, 5.5 mmol, 1 eq), in dry THF (40 mL) was cooled to 0 °C and allylmagnesiym chloride (2M in THF, 2.8 mL, 5.6 mmol, 1 eq) was added. The reaction mixture was stirred for 2 hours at room temperature. A solution of 3 buten-1-ol (0.53 mL, 6.05 mmol, 1.1 eq), distilled triethylamine (0.85 mL, 6.05 mmol, 1.1 eq) was then added and the reaction mixture was stirred at room temperature overnight. After 16 hours, the reaction was quenched with sat. $NH_4Cl_{(aq)}$ and extracted 3 times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced presure. Column chromatography (hexane) gave the product as a colourless oil in 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (sb, 14H, Si(*i*-Pr)$_2$), 1.71 (dt, $^3J_{H-H}$ = 8.0, 1.2 Hz, 2H, CH_2Si), 2.27-2.34 (m, 2H, OCH$_2$CH_2), 3.72 (t, $^3J_{(H-H)}$ = 7.0 Hz, 2H, OCH_2), 4.81-5.10 (m, 4H, CCH_2 x 2), 5.78-5.92 (m, 2H, CHCH_2 x 2); ^{13}C NMR (100 Hz, $CDCl_3$): δ 12.5 (Si(*C*H(CH$_3$)$_2$)$_2$), 17.5

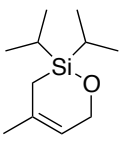
(Si(CH(*C*H$_3$)$_2$)$_2$), 18.8 (*C*H$_2$Si), 37.5 (OCH$_2$*C*H$_2$), 63.1 (O*C*H$_2$), 113.6 (*C*H$_2$), 116.3 (*C*H$_2$), 134.6 (*C*HCH$_2$), 135.3 (*C*HCH$_2$). Characterisation data correspond to the literature.

Allyl(pent-4-en-yloxy)diisopropylsilane: 280.



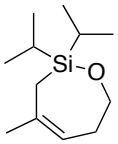
To a solution of (4hexoxy)diisopropylsilyl chloride (1g, 4.5 mmol, 1 eq). in dry THF in 40 mL at 0 °C, was added 2-methylallylmagnesium chloride (0.5 M in THF, 18 mL, 9 mmol, 2 eq) dropwise. The reaction mixture was the stirred at toom temperature under argon. After 16 hours, the reaction was quenched with sat. $NH_4Cl_{(aq)}$ and extracted 3 times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced presure. Column chromatography (hexane) gave the product as a colourless oil in 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (sb, 14H, Si(*i*-Pr)$_2$), 1.62-1.67 (m, 4H), 1.80 (s, 3H, C*H*$_3$), 2.21 (m, 2H, OCH$_2$C*H*$_2$), 3.70 (t, $^3J_{(H\text{-}H)}$ = 6.8 Hz, 2H, OC*H*$_2$), 4.59-4.64 (m, 2H, CC*H*$_2$), 4.99-5.11 (m, 2H, CHC*H*$_2$), 5.78-5.90 (m, 1H, C*H*CH$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.9 (Si(*C*H(CH$_3$)$_2$)$_2$), 17.6 (Si(CH(*C*H$_3$)$_2$)$_2$), 22.4 (*C*H$_2$Si), 25.3 (*C*H$_3$), 30.0(OCH$_2$CH$_2$*C*H$_2$) 32.0 (OCH$_2$*C*H$_2$), 62.6 (O*C*H$_2$), 109.4 (*C*H$_2$), 114.3 (*C*H$_2$), 138.5 (*C*HCH$_2$), 143.5 (*C*CH$_2$); IR (neat) 2940, 2866, 1639, 1463, 1383, 1098, 992, 911, 804, 743 cm^{-1} FI Mass (EI) m/z Anal. Calcd for $C_{15}H_{30}NaOSi$ 277.1958, found $[M+Na]^+$ 277.1954.

2,2-diisopropyl-3-methyl-2.3.6-tetrahydro-1,2-oxasilepine: 278a.



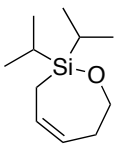
Synthesised according to general procedure **(A)** from **278** (300 mg, 1.32 mmol), to yield **278a** as a clear oil (241 mg, 91%) R_f = 0.6 (Hex:Et_2O 99:1); **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.05 (m, 14H, CH_3), 1.06 (s, 2H, SiCH_2), 1.81 (s, 3H, CH_3), 4.45 (s, 2H, SiOCH_2), 5.35 (1H, m, $SiOCH_2CH$); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** δ 10.7 (Si(CH$(CH_3)_2)_2$), 12.9 (Si(CH($CH_3)_2)_2$), 17.0 (CH_2Si), 28.0 (CH_3), 63.9 (OCH_2), 122.6 (CH=CMe), 132.2 (MeC=CH). **IR (film): υ (cm^{-1})** 2940, 2864, 2360, 1462, 1095. **HMRS** (ESI, *m/z*) calc for $C_{11}H_{22}OSi$ $[M]^+$: 198.1440 found: 198.1445.

2,2-diisopropyl-4-methyl-2,3,6,7-tetrahydro-1,2-oxasilepine[185]: 279a.



Synthesised according to general procedure **(A)** from **279** (300 mg, 1.32 mmol), to yield **279a** as a clear oil (241 mg, 91%) R_f = 0.6 (Hex:Et_2O 99:1); **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.05 (m, 14H, CH_3), 1.61 (s, 2H, SiCH_2), 1.81 (s, 3H, CH_3), 2.28 (m, 2H, $SiOCH_2CH_2$) 3.85 (s, 2H, SiOCH_2), 5.35 (1H, m, $SiOCH_2CH$); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** δ 12.9 (Si(CH$(CH_3)_2)_2$), 17.3 (CH_2Si), 17.5 (Si(CH($CH_3)_2)_2$), 27.5 (CH_3), 32.0 ($SiOCH_2CH_2$), 64.0 (OCH_2), 120.6 (CH=CMe), 136.2 (MeC=CH). Characterisation data correspond to the literature.

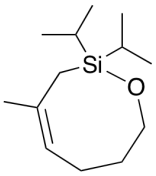
2,2-diisopropyl-2,3,6,7-tetrahydro-1,2-oxasilepine[185]: 281a.



Synthesised according to general procedure **(A)** from **281** (300 mg, 1.32 mmol), to yield **281a** as a clear oil (236 mg, 90%) R_f = 0.6 (Hex:Et_2O 99:1); **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.01 (m, 14H, CH_3), 1.62 (d, 2H, $^3J_{H\text{-}H}$ = 7 Hz, SiCH_2), 2.35 (m, 2H, $SiOCH_2CH_2$) 3.92 (t, 2H, $^3J_{H\text{-}H}$ = 5

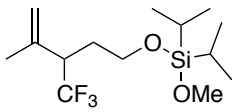
Hz, 2H, SiOCH_2), 5.48 (m, 1H, SiOCH$_2$CH), 5.8 (m, 1H, CHCH); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** δ 11.4 (Si(CH(CH$_3$)$_2$)$_2$), 17.3 (CH$_2$Si), 17.5 (Si(CH(CH$_3$)$_2$)$_2$), 32.4 (SiOCH$_2$$CH_2$), 63.3 (O$CH_2$), 126.6 ($C$H=CH), 127.3 (CH=C$H$). Characterisation data correspond to the literature.

2,2-diisopropyl-5-methyl-3,6,7,8-tetrahydro-2*H*-1,2-oxasilocine: 280a.



Synthesised according to general procedure **(A)** from **280** (300 mg, 1.32 mmol), to yield **281a** as a clear oil (241 mg, 91%) R_f = 0.6 (Hex:Et$_2$O 99:1); **^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):** 1.03-1.07 (m, 14H, CH_3), 1.60 (s, 2H, SiCH_2), 1.61-1.66 (m, 2H, SiOCH$_2$CH_2), 1.81 (s, 3H, CH$_3$), 2.10-2.15 (m, 2H, SiOCH$_2$CH$_2$CH_2) 3.71 (m, 2H, SiOCH_2), 5.05 (1H, m, SiOCH$_2$CH); **^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):** δ 12.0 (Si(CH(CH$_3$)$_2$)$_2$), 17.5 (CH$_2$Si), 17.7 (Si(CH(CH$_3$)$_2$)$_2$), 23.4 (SiOCH$_2$CH$_2$$CH_2$) 27.1 ($CH_3$), 30.8 (SiOCH$_2$$CH_2$), 60.0 (O$CH_2$), 120.1 ($C$H=CMe), 134.7 (Me$C$=CH). **IR (film): υ (cm^{-1})** 2940, 2864, 2060, 1562, 1010. FI Mass (EI) m/z Anal. Calcd for $C_{13}H_{26}OSi$ 226.1753, found [M]$^+$ 226.1757.

Diisopropyl(methoxy){[4-methyl-3-(trifluoromethyl)pent-4-en-1-yl]oxy}-silane: 283



Procedure B: Copper catalysis.

The title compound was prepared according to the general procedure under the following conditions. 2,2-diisopropyl-4-methyl-2.3.6.7-tetrahydro-1,2-oxasilepine **279a** (49.0 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol) and Togni's trifluoromethylating reagent (95 mg, 0.3 mmol)

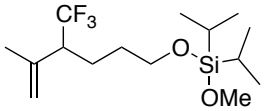
and MeOH (0.5 mL) stirred for 1 h at 70 ˚C. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired product (24.0 mg, 42%) as a colourless oil.

Procedure C: Ruthenium Catalysis.

The title compound was prepared according to the general procedure under the following conditions. 2,2-diisopropyl-4-methyl-2,3,6,7-tetrahydro-1,2-oxasilepine **279a** (54 mg, 0.25 mmol), $Ru(bpy)_3Cl_2$ (9.0 mg, 0.0125 mmol), Togni trifluoromethylating reagent (94.8 mg, 0.3 mmol) and MeOH (0.5 mL) with stirring for 24 h under visible light. The crude residue was purified by SiO_2 gel column chromatography (Et_2O/n-hexane = 1/99) to afford the desired product (30 mg, 41%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.04–1.05 (m, 14H), 1.84-1.86 (m, 1H, $SiOCH_2CH_a$), 1.84 (s, 3H, CH_3), 2.00-2.01 (m, 1H, $SiOCH_2CH_b$), 3.12 (qt, $^3J_{H\text{-}F}$ = 9.8, 4.0 Hz, 1H, $CHCF_3$), 3.61 (s, 3H, OCH_3), 3.71 (m, 1H, OCH_2CH_a), 3.87 (m, 1H, OCH_2CH_b), 5.03 (s, 1H, $C=CH_a$), 5.13 (s, 1H, CH_b); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 11.9 ($Si(CH(CH_3)_2)_2$), 17.3 (CH_2Si), 22.8 (q, J = 2.8 Hz CH_2CHCF_3), 29.7 (CH_3), 50.9 (OMe), 62.1 (OCH_2), 117.7 ($C=CH_2$), 127.0 (q, J = 279.0 Hz, CF_3), 138.6 (q, J = 1.8 Hz, $C=CH_2$); **^{19}F NMR (377 MHz, $CDCl_3$):** δ –69.1 (d , $^3J_{F\text{-}H}$ = 10.4 Hz, 3F) **HRMS** (ESI) m/z Anal. Calcd for $C_{14}H_{27}F_3NaSi$ 335.1630, found [M+Na]+ 335.1628.

Diisopropyl(methoxy){[5-methyl-4-(trifluoromethyl)hex-5-en-1-yl]oxy}-silane: 285



Procedure B: Copper catalysis.

The title compound was prepared according to the general procedure under the following conditions. 2,2-diisopropyl-5-methyl-3,6,7,8-tetrahydro-2*H*-1,2-oxasilocine **280a** (56.5 mg, 0.25 mmol), CuCl (5.0 mg, 0.05 mmol) and Togni's trifluoromethylating reagent (95 mg, 0.3

mmol) and MeOH (0.5 mL) stirred for 1 h at 70 ˚C. The crude residue was purified by SiO_2 gel column chromatography (*n*-hexane) to afford the desired product (24.0 mg, 42%) as a colourless oil.

Procedure C: Ruthenium Catalysis.

The title compound was prepared according to the general procedure under the following conditions. 2,2-diisopropyl-5-methyl-3,6,7,8-tetrahydro-2*H*-1,2-oxasilocine **280a** (56.5 mg, 0.25 mmol), $Ru(bpy)_3Cl_2$ (9.0 mg, 0.0125 mmol), Togni trifluoromethylating reagent (79.0 mg, 0.25 mmol) and MeOH (0.5 mL) with stirring for 24 h under visible light. The crude residue was purified by SiO_2 gel column chromatography (Et_2O/n-hexane = 1/99) to afford the desired product (33.0 mg, 40%). Characteristic data for diisopropyl(methoxy){[5-methyl-4-(trifluoromethyl)hex-5-en-1-yl]oxy}-silane: **IR (neat)** 2360, 2341, 1653, 1260, 1119, 668 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.04–1.05 (m, 14H), 1.44-1.53 (m, 1H, $SiOCH_2CH_aH_a$), 1.58-1.65 (m, 1H, $SiOCH_2CH_aH_b$), 1.68-1.75 (m, 1H, $SiOCH_2CH_2CH_aH_a$), 1.77 (s, 3H, CH_3), 1.81-1.85 (m, 1H, $SiOCH_2CH_2CH_aH_b$), 2.73-2.85 (qt, $^3J_{H\text{-}F}$ = 9.8, 4.0 Hz, 1H, $CHCF_3$), 3.56 (s, 3H, OCH_3), 3.73-3.81 (m, 2H, OCH_2CH_2), 4.96 (s, 1H, $C{=}CH_aH_a$), 5.06 (s, 1H, CH_aH_b); **^{13}C NMR (125 MHz, CDCl3):** δ 12.3 ($Si(CH(CH_3)_2)_2$), 17.7 (CH_2Si), 20.1 (q, J = 2.8 Hz CH_2CHCF_3), 23.0 ($OCH_2CH_2CH_2$) 30.1 (CH_3), 51.3 (OMe), 62.5 (OCH_2), 118.1 ($C{=}CH_2$), 127.4 (q, J = 279.0 Hz, CF_3), 139.0 (q, J = 1.8 Hz, $C{=}CH_2$); **^{19}F NMR (471 MHz, $CDCl_3$):** δ –69.2 (d , J = 10.4 Hz, 3F); **HRMS** (EI) m/z Anal. Calcd for $C_{15}H_{29}F_3NaO_2Si$, 349.1781, found $[M+Na]^+$ 349.1795

References

[1] Driess, M. *Nature Chem*, **2012**, *4,* 525–526.
[2] (a) Urry, G. *Acc. Chem. Res.* **1970**, *3*, 306–312. (b) Barton, T. J. Carbacyclic Silanes, In *Comprehensive Organometallic Chemistry*; Wilkinson, G.; Stone, F. G. A; Abel, E. W., Eds.; Pergamon: Oxford, 1982, p 205.
[3] Solsona, J. G.; Romea, P.; Urpi, F. *Org. Lett.* **2003,** *5*, 468–4684.
[4] Wen, K.; Chow, S.; Sanghvi, Y. S.; Theodorakis, E. A. *J. Org. Chem.* **2002**, *67*, 7887–7889.
[5] Hatanaka, Y.; Hiyama, T. *J. Org. Chem*. **1988**, *53*, 918–920.
[6] Tomooka, K.; Nakazaki, A.; Nakai, T. *J. Am. Chem. Soc.* **2000**, *122*, 408–409.
[7] Nakazaki, A.; Usuki, J.; Tomooka, K. *Synlett* **2008**, 2064–2068.
[8] Rendler, S.; Oestreich, M. *Synthesis* **2005**, *11*, 1727–1747.
[9] Brook, M. A. *Silicon in Organic, Organometallic, and Polymer Chemistry*; John Wiley & Sons: New York, **2000.**
[10] Mulliken, R. S. *J. Chem. Phys.* **1934**, *2*, 782.
[11] Huheey, E. A.; Keiter, R. L. *Inorganic Chemistry; Principles of Structure and Reactivity*, 4th ed.; Harper Collins: New York, **1993**.
[12] Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: London, **1998.**
[13] Chult, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev*. **1993**, *93*, 1371–1448.
[14] Couzijn, E. P. A.; Schakel, M.; de Kanter, F. J. J.; Ehlers, A. W.; Lutz, M.; Spek, A. L.; Lammertsma, K. *Angew. Chem., Int. Ed.* **2004,** *43*, 3440–3442, Couzijn, E. P. A.; van den Engel, D. W. F.; Slootweg, J. C.; de Kanter, F. J. J.; Ehlers, A. W.; Schakel, M.; Lammertsma, K. *J. Am. Chem. Soc.* **2009,** *131*, 3741–3751.
[15] Kipping, F. S. *Proc. Chem. Soc., London* **1907,** *23*, 9.
[16] Sommer, L. H.; Frye, C. L. *J. Am. Chem. Soc.* **1959,** *81*, 1013–1013.
[17] Sommer, L. H.; Frye, C. L.; Parker, G. A.; Michael, K. W. *J. Am. Chem. Soc.* **1964**, *86*, 3271–3276.
[18] (a) Jankowski, P.; Schaumann, E.; Wicha, J.; Zarecki, A.; Adiwidjaja, G. *Tetrahedron: Asymmetry* **1999**, *10*, 519–526. (b) Jankowski, P.; Wicha, J.; Zarecki, A.; Schaumann, E.; Adiwidjaja, G.; Asztemborska, M. *Chem. Commun.* **2000**, 1029–1030.
[19] (a) Igawa, K.; Kokan, N; Tomooka, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 728–731. (b) Nakazaki, A.; Usuki, J.; Tomooka, K. *Synlett* **2008**, 2064–2068.
[20] Rendler, S.; Auer, G.; Keller, M.; Oestreich, M. *Adv. Synth. Catal.* **2006**, *348*, 1171–1182.
[21] Oestreich, M. *Chem. Eur. J*. **2006,** *12*, 30–37.
[22] Oestreich, M.; Schmid, U. K.; Auer, G.; Keller, M. *Synthesis* **2003**, 2725–2739.
[23] (a) Corriu, R. J. P.; Moreeau, J. J. E. *J. Organomet. Chem*. **1974**, *64*, C51–C54. (b) Corriu, R. J. P.; Moreeau, J. J. E. *J. Organomet. Chem*. **1976**, *120*, 337–346.
[24] Ohta, T.; Ito, M.; Tsuneto, A.; Takaya, H. *J. Chem. Soc., Chem. Commun.* **1994**, 2525–2526.
[25] Yasutomi, Y.; Suematsu, H.; Katsuki, T. *J. Am. Chem. Soc*. **2010**, *132,* 4510–4511.
[26] Shintani, R.; Moriya, K.; Hayashi, T. *J. Am. Chem. Soc.* **2011**, *133*, 16440–16443.
[27] Shintani, R.; Moriya, K.; Hayashi, T. *Org. Lett*. **2012**, *14*, 2902–2905.
[28] (a) Ghanem, A.; Aboul-Enein, H-Y. *Tetrahedron: Asymmetry,* **2004**, *15*, 333–335. (b) Garcia-Urdiales, E.; Alfonso, I.; Gotor, V. *Chem. Rev*. **2005**, *105*, 313–354.
[29] (a) Syldatk, C.; Andree, H.; Stoffregen, A.; Wagner, F.; Stumpf, B.; Ernst, L.; Zilch, H.; Tacke, R. *Appl. Microbiol. Biotechnol*. **1987**, *27*, 152–158. (b) Syldalk, C.; Stoffregen, A.; Wuttke F.; Tacke, R. *Biotechnol. Lett*. **1988**, *10*, 731–734. (c) Fritsche, K.; Syldatk, C.; Wagner, F.; Hengelsberg, H.; Tacke, R. *Appl. Microbiol. Biotechnol*. **1989**, *31*, 107–111.
[30] Fukui, T.; Kawamoto, T.; Tanaka, A. *Tetrahedron: Asymmetry*, **1994**, *5*, 73–82.

[31] Selected examples: (a) Paquette, L. A. *Science*, **1982**, *217*, 793–800; (b) Studer, A. *Angew. Chem., Int. Ed*., **1998**, *37*, 462–465. (c) Coelho, P. J.; Blanco, L. *Tetrahedron Lett*. **2003**, *59*, 2451–2456. (d) Godineau, E.; Schenk K.; Landais, Y. *J. Org. Chem*. **2008**, *73*, 6983–6993. (f) Langer, P. *Tetrahedron*, **2009**, *65*, 5445–5614. (g) Xu, L. W.; Li, L.; Shi, Z. H. *Adv. Synth. Catal*. **2010**, *352*, 243–279.

[32] Schmidt, D. R.; O'Malle, S. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 1190–1191.

[33] (a) Kinnaird, J. W. A.; Ng, P. Y.; Kubota, K.; Wang, X.; Leighton, J. L. *J. Am. Chem. Soc.* **2002,** *124*, 7920–7921.

[34] (a) Berger, R.; Duff, K.; Leighton, J. L. *J. Am. Chem. Soc.* **2004,** *126*, 5686–5687. (b) Kubota, K.; Leighton, J. L. *Angew. Chem., Int. Ed*. **2003**, *42*, 946–948. (c) Berger, R.; Duff, K.; Leighton, J. L. *J. Am. Chem. Soc.* **2004**, *126*, 5686–5687. (d) Burns, N. Z.; Hackman, B. M.; Ng, P. G.; Powelson, I. A.; Leighton, J. L. *Angew. Chem., Int. Ed*. **2006**, *45*, 3811–3813.

[35] Shirakawa, S.; Berger, R.; Leighton, J. L. *J. Am. Chem. Soc.* **2005**, *127*, 2858–2859.

[36] Shirakawa, S.; Lombardi, P. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2005**, *127*, 9974–9975.

[37] Kubota, K.; Hamblett, C. L.; Wang, X.; Leighton, J. L. *Tetrahedron* **2006**, *62*, 11397–11401.

[38] Notte, G. T.; Leighton, J. L. *J. Am. Chem. Soc.* **2008**, *130*, 6676–6677.

[39] (a) Rendler, S.; Auer, G.; Oestreich, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 7620–7624. (b) Karatas, B.; Rendler, S.; Fröhlich, R.; Oestreich, M. *Org. Biomol. Chem*. **2008**, *6*, 1435–1440. (c) Rendler, R.; Plefka, O.; Karatas, B.; Auer, G.; Fröhlich, R.; Mück-Lichtenfeld, C.; Grimme S.; Oestreich, M. *Chem. Eur. J*. **2008**, *14*, 11512–11528.

[40]Harvey, S. J.; Malcolmson, S. J.; Dunne, K. S.; Meek, S. J.; Thompson, A. L.; Schrock, R. R.; Hoveyda, A. H.; Gouverneur V. *Angew. Chem. Int. Ed*. **2009**, *48*, 762 –766.

[41] Schneider, V.; Frolich, P. K. *Ind. Eng. Chem,* **1931**, *23*, 1405–1410.

[42] (a) Eleuterio, H. S. German Patent 1072811, 1960; US Patent 3074918, 1963. (b) Truett, W. L.; Johnson, D. R.; Robinson, I. M.; Montague, B. P. *J. Am. Chem. Soc.* **1960**, *82*, 2337–2340.

[43] (a) Calderon, N.; Chen, H. Y.; Scott, K. W. *Tetrahedron Lett.* **1967,** *34*, 3327–3329. (b) Calderon, N. *Acc. Chem. Res.* **1972**, *5*, 127–132.

[44] (a) Grubbs, R. H., Ed. *Handbook of Metathesis*; Wiley-VCH: Weinheim, 2003. (b) Furstner, A. *Angew. Chem., Int. Ed*. **2000**, *39*, 3013–3043. (c) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413–4450.

[45] Bielawski, C. W.; Grubbs, R. H. *Prog. Polym. Sci*. **2007**, *32*,1–29.

[46] Eleuterio, H. S. *J. Mol. Catal.* **1991**, *65*, 55–61.

[47] Lewandos, G. S.; Pettit, R. *J. Am. Chem. Soc.* **1971,** *93*, 7087–7088.

[48] (a) Grubbs, R. H.; Brunck, T. K. *J. Am. Chem. Soc.* **1974**, *94*, 2538–2540. (b) Biefel, C. G.; Eick, H. A.; Grubbs, R. H. *Inorg. Chem.* 1**973**, *12*, 2166–2170.

[49] Herisson, J. L.; Chauvin, Y. *Makromol. Chem.* **1971,** *141*, 161–176.

[50] Correa, A.; Cavallo, L. *J. Am. Chem. Soc.* **2006**, *128*, 13352–13353. (b) Occhipinti, G.; Bjorsvik, H. R.; Jensen, V. R. *J. Am. Chem. Soc.* **2006**, *128*, 6952–6964. (c) Adlhart, C.; Chen, P. *J. Am. Chem. Soc*. **2004**, *126*, 3496–3510.

[51] Casey, C. P.; Burkhardt, T. J. *J. Am. Chem. Soc.* **1974,** *96*, 7808–7809.

[52] Howard, T. R.; Lee, J. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **1987**, *109*, 4880–4890.

[53] (a) Rocklage, S. M.; Fellmann, J. D.; Rupprecht, G. A.; Messerle, L. W.; Schrock, R. R. *J. Am. Chem. Soc.* **1981**, *103*, 1440–1447. (b) Schrock, R. R.; Rocklage, S. M.; Wengrovius, J. H.; Rupprecht G.; Feldmann, J. *J. Mol. Catal.* **1980**, *8*, 73–83.

[54] (a) Churchill, M. R.; Rheingold, A. L.; Youngs, W. J.; Schrock, R. R. *J. Organomet. Chem.* **1981**, *204*, C17–C20. (b) Wengrovius, J. H.; Schrock, R. R.; Churchill, M. R.; Missert J. R.; Youngs, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 4515–4516.

[55] Kress, J.; Wesolek, M.; Osborn, J. A. *J. Am. Chem. Soc.* **1983**, *105*, 6346–6347.

[56] Quignard, F.; Leconte M.; Basset, J.-M. *J. Chem. Soc., Chem. Commun.* **1985**, 1816–1817.

[57] For a review on the development of Ta/Nb/W/Mo-based metathesis catalysts, see: Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592–4633.
[58] (a) Nguyen, S. T.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1993**, *115*, 9858–9859. (b) Nguyen, S. T.; Johnson, L. K.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1992**, *114*, 3974–3975.
[59] Fu, G. C.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 9856–9857.
[60] Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953–956.
[61] Huang, J.; Stevens, E. D.; Nolan, S. P.; Petersen, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 2674–2678.
[62] Weskamp, T.; Kohl, F. J.; Hieringer, W.; Gleich, D.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **1999**, *38*, 2416–2419.
[63] (a) Garber, S. B.; Kingbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179. (b) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791–799.
[64] Hoveyda, A. H.; Gillingham, D. G.; van Veldhuizen, J. J.; Kataoka, O.; Garber, S. B.; Kingsbury, J. S.; Harrity, J. P. A. *Org. Biomol. Chem.* **2004**, *2*, 8–23.
[65] Herrmann, W. A.; Köcher, C. *Angew. Chem., Int. Ed*. **1997**, *36*, 2162–2187.
[66] Torker, S.; Merki, D.; Chen, P. *J. Am. Chem. Soc.* **2008,** *130, 14*, 4808–4814.
[67] (a) Sanford, M. S.; Ulman, M.; Grubbs, R. H. *J. Am. Chem. Soc*. **2001**, *123*, 749–750. (b) Sanford, M. S.; Love, J. A.; Grubbs, R. H. *J. Am. Chem. Soc*. **2001**, *123*, 6543–6554.
[68] Demchuk, O. M.; Pietrusiewicz, K. M.; Michrowska, A.; Grela, K., *Org. Lett.* **2003**, *5*, 3217–3220.
[69] Gessler, S.; Randl, S.; Blechert, S. *Tetrahedron Lett*. **2000**, *41*, 9973–9976.
[70] (a) Wu, Z., Z.; Wheeler, D. R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 146–151. (b) Armstrong, S. K.; Christie, B. A. *Tetrahedron Lett*. **1996**, *37*, 9373–9376.
[71] Kirkland, T. A.; Lynn, D. M.; Grubbs, R. H. *J. Org. Chem*. **1998**, *63*, 9904-9909.
[72] Hong, S. H.; Wenzel, A. G.; Salguero, T. T.: Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2007**, *129*, 7961–7968.
[73] Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res*. **2001**, *34*, 18–29
[74] Diver, S. T.; Giessert, A. *J. Chem. Rev.* **2004**, *104*, 1317–1382.
[75] (a) Chauvin, Y. *Angew. Chem, Int. Ed*. **2006**, *45*, 3740–3747; (b) Schrock, R. R. *Angew. Chem., Int. Ed*. **2006**, *45*, 3748–3759. (c) Grubbs, R. H. *Angew. Chem. Int. Ed*. **2006**, *45*, 3760–3765.
[76] For recent reviews on the impact of CM and RCM on organic synthesis, see: (a) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4490–4527. (b) Gaich, T.; Mulzer, J. *Curr. Top. Med. Chem.* **2005**, *5*, 1473–1494. (c) Van de Weghe, P.; Eustache, J. *Curr. Top. Med. Chem.* **2005**, *5*, 1495–1519.
[77] Fujimura, O.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996,** *118*, 2499–2500.
[78] Alexander, J. B.; La, D. S.; Cefalo, D. R.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1998**, *120*, 4041–4042.
[79] (a) Hock, A. S.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2006**, *128,* 16373**–**16365. (b) Singh, R; Czekelius, C.; Schrock, R. R.; Müller, P. *Organometallics* **2007**, *26*, 2528–2539. (c) Marinescu, S. C.; Singh, R.; Hock, A. S.; Wampler, K. M.; Schrock, R. R.; Mtiller, P. *Organometallics* **2008**, *27,* 6570–6578.
[80] Zhu, S. S.; Cefalo, D. R.; La, D. S.; Jamieson, J. Y.; Davis, W. M.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc*. **1999**, *121*, 8251–8259.
[81] Schrock, R. R.; Crowe, W. E.; Bazan, G. C.; DiMare, M.; O'Regan, M. B.; Schofield, M. H. *Organometallics*, **1991**, *10*, 1832–1843.
[82] Oskam, J. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1992**, *114*, 7588–7590.
[83] Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592–4633.
[84] Totland, K. M.; Boyd, T. J.; Laovie, G. G.; Davis, W. M.; Schrock, R. R. *Macromolecules* **1996**, *29*, 6114–6125.

[85] Robbins, J.; Bazan, G. C.; Murdzek, J. S.; O' Regan, M. B.; Schrock, R. R. *Organometallics* **1991**, *10*, 2902–2907.
[86] Poater, A.; Solans-Monfort, X.; Clot, E.; Copéret, C.; Eisenstein, O. *J. Am. Chem. Soc*. **2007**, *129*, 8207–8216.
[87] Malcolmson, S. J.; Meek, S. J.; Sattely, E. S.; Schrock, R. R.; Hoveyda, A. H. *Nature* **2008**, *456*, 933–937.
[88] Sattely, E. S.; Meek, S. J.; Malcolmson, S. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc*. **2009**, *131*, 943–953.
[89] Deutsch, H. F.; Evenson, M. A.; Drescher, P.; Sparwasser, C.; Madsen, P. *J. Pharm. Biomed. Anal.* **1994**, *12*, 1283–1287.
[90] Meek, S. J.; Malcolmson, S. J.; Li, B.; Schrock, R. R.; Hoveyda, A .H.; *J. Am. Chem. Soc.* **2009**, *131*, 16407–16409.
[91] Weatherhead, G. S.; Houser, J. H.; Ford, J. G.; Jamieson, J. Y.; Schrock, R. R.; Hoveyda, A. H. *Tetrahedron Lett.* **2000**, *41*, 9553–9559.
[92] Paquette, L. A.; Sauer, D. R.; Cleary, D. G.; Kinsella, M. A.; Blackwell, C. M.; Anderson, L. G. *J. Am. Chem. Soc.* **1992,** *114*, 7375–7387.
[93] Leach, A. G.; Wang, R.; Wohlhieter, G. E.; Khan, S. I.; Jung, M. E.; Houk, K. N. *J. Am. Chem. Soc.* **2003,** *12*, 4271-4278.
[94] Lin, H.-S.; Paquette, L. A. *Synthetic Communications* **1994**, *24*, 2503–2506.
[95] Sashuk, V.; Samojlowicz, C.; Szadkowska, A.; Grela, K. *Chem. Commun.* **2008**, 2468–2470.
[96] Fomine, S.; Vargas-Ortega, J.; Tlenkopatchev, M.A. *J. Mol. Catal. A: Chem*. **2007**, *263*, 121–127.
[97] *Organofluorine Chemistry: Principles and Commercial Applications*; Banks, R. E.; Smart, B. E.; Tatlow, J. C.; Eds. Plenum Press: New York, **1994**.
[98] Smart, B. E. *J. Fluorine Chem.* **2001**, *109*, 3–11.
[99] Kirk, K. L. *J. Fluorine Chem.* **2006**, *127*, 1013–1029.
[100] (a) Keller, M. B. *J. Clin. Psychiatry* **2000**, *61*, 896–908. (b) Benfield, B.; Ward, A. *Drugs* **1986**, *32*, 313–334. (c) Burke, W. *J. Expert. Opin. Invest. Drugs* **2002**, *11*, 1477–1486.
[101] Wong, D. T.; Bymaster, F. P.; Engleman, E. A. *Life Sci.* **1995**, *57*, 411–441.
[102] For a review, see: Tomashenko, O. A.; Grushin, V. V. *Chem. Rev.* **2011,** *111*, 4475–4521.
[103] Ruppert, I.; Schlich, K.; Volbach, W. *Tetrahedron Lett.* **1984**, *25*, 2195–2198.
[104] (a) Prakash, G. K. S.; Yudin, A. K. *Chem. Rev.* **1997**, *97*, 757–786. (b) Singh, R. P.; Shreeve, J. M. *Tetrahedron* **2000**, *56*, 7613–7632. (c) Prakash, G. K. S.; Mandal, M. *J. Fluorine Chem.* **2001**, *112*, 123–131.
[105] Grobe, J.; Hegge, J. *Synlett*, **1995**, 641–642.
[106] Mizuta, S.; Shibata, N.; Sato, T.; Fujimoto, H.; Nakamura, S.; Toru, T. *Synlett* **2006**, 267–270.
[107] (a) Panne, P.; Naumann, D.; Hoge, B. *J. Fluorine Chem.* **2001**, *112*, 283-286. (b) Murphy-Jolly, M. B.; Lewis, L. C.; Caffyn, A. J. M. *Chem. Commun.* **2005**, *35*, 4479–4480.
[108] Singh, R. P.; Shreeve, J. M. *Tetrahedron* **2000**, *56*, 7613–7632.
[109] (a) Kobayashi, Y.; Kumadaki, I. *Tetrahedron Lett.* **1969**, *10*, 4095–4096. (b) Kobayashi, Y.; Yamamoto, K.; Kumadaki, I. *Tetrahedron Lett.* **1979**, *20*, 4071–4072.
[110] Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337–2364.
[111] Su, Y.; Jia, W.; Jiao, N. *Synthesis* **2011**, *11*, 1678–1690.
[112] (a) McLoughlin, V. C. R.; Thrower, J. U. S. Patent 3408411, **1968**. (b) McLoughlin, V. C. R.; Thrower, J. *Tetrahedron* **1969**, *25*, 5921–5940. (c) Kobayashi, Y.; Kumadaki, I. *Tetrahedron Lett.* **1969**, *10*, 4095–4096.
[113] Wiemers, D. M.; Burton, D. J. *J. Am. Chem. Soc*. **1986**, *108*, 832–834.
[114] (a) Zhang, C.; Tang, C.; Jiao, N. *Chem. Soc. Rev.* **2012**, *41*, 3464–3484. (b) Wang, X.; Ye, Y.; Zhang, S.; Feng, J.; Xu, Y.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc*. **2011**, *133*, 16410–16413.

[115] Reutov, O. A.; Butin, K. P.; Beletskaya, I. P.; *Usp. Khim.* **1974**, 43, 35.

[116] (a) Zanardi, A.; Novikov, M. A.; Martin, E.; Benet-Buchholz, J.; Grushin, V. V. *J. Am. Chem. Soc*. **2011**, *133*, 20901–20913. (b) Novak, P.; Lishchynskyi, A.; Grushin, V. V. *Angew. Chem. Int. Ed*. **2012**, *51*, 7767–7770.
[117] Prakash, G. K. S.; Jog, P. V.; Batamack, P. T. D.; Olah, G. A. *Science* **2012**, *338*, 1324–1327.
[118] Yagupol'skii, L. M.; Kondratenko, N. V.; Timofeeva, G. N. *J. Org. Chem.* **1984**, *20*, 103–106.
[119] (a) Umemoto, T.; Ishihara, S. *Tetrahedron Lett*. **1990**, *31*, 3579–3582. (b) Umemoto, T.; Ishihara, S. *J. Am. Chem. Soc*. **1993**, *115*, 2156–2164. (c) Umemoto, T.; Ishihara, S. *J. Fluorine Chem.* **1999**, *98*, 75–81. (d) Umemoto, T.; Ishihara, S.; Adachi, K. *J. Fluorine Chem*. **1995**, *74*, 77–82.
[120] Singh, R. P.; Shreeve, J. M. *Tetrahedron* **2000**, *56*, 7613–7632.
[121] Magnier, E.; Blazejewski, J.-C.; Tordeux, M.; Wakselman, C. *Angew. Chem., Int. Ed*. **2006**, *45*, 1279–1282.
[122] Eisenberger, P.; Gischig, S.; Togni, A. *Chem. Eur. J.* **2006**, *12*, 2579–2586.
[123] Matsnev, A.; Noritake, S.; Nomura, Y.; Tokunaga, E.; Nakamura, S.; Shibata, N. *Angew. Chem., Int. Ed*. **2010**, *49*, 572–576.
[124] (a) Kieltsch, I.; Eisenberger, P.; Togni, A. *Angew. Chem. Int. Ed.* **2007**, *46*, 754–757. (b) Kieltsch, I.; Eisenberger, P.; Stanek, K.; Togni, A. *Chimia* **2008**, *62*, 260–263. (c) K. Stanek, R. Koller, A. Togni, *J. Org. Chem.* **200**8, *73*, 7678–7685.

[125] Ma, J.-A.; Cahard, D. *J. Fluorine Chem.* **2007**, *128*, 975–996.
[126] (a) Heaton, C. A.; Powell, R. L. *J. Fluor. Chem.* **1989**, *45*, 86. (b) McClinton M. A.; McClinton D. A. *Tetrahedron*, **1992**, *48*, 6555–6666.
[127] Langlois, B. R.; Laurent, E.; Roidot, N. *Tetrahedron Lett.* **1991**, *32*, 7525–7528.
[128] Burstall F. H. *J. Chem. Soc*. **1936**, 173–175.
[129] (a) Sabbatini, N.; Balzani, V. *J. Am. Chem. Soc*. **1972**, *94*, 7587–7589. (b) Gafney, H. D.; Adamson, A. W. *J. Am. Chem. Soc.* **1972**, *94*, 8238–8239. (c) Wrighton, M.; Markham, J. *J. Phys. Chem*. **1973**, *77*, 3042–3044. (d) Bock C. R.; Meyer, T. J.; Whitten, D. G. *J. Am. Chem. Soc.* **1974**, *96*, 4710–4712. (e) Navon, G.; Sutin N. *Inorg. Chem*. **1974**, *13*, 2159–2164.
[130] For reviews on photoredox catalysis with visible light, see: (a) Narayanam, J. M. R.; Stephenson, C. R. J. *Chem. Soc. Rev*. **2011**, *40*, 102–113. (b) Yoon, T. P.; Ischay M. A.; Du, J. *Nat. Chem*. **2010**, *2*, 527–532 (c) Zeitler, K. *Angew. Chem. Int. Ed*. **2009**, *48*, 9785–9789.
[131] Urata, H.; Fuchikami, T. *Tetrahedron Lett.* **1991**, *32*, 91–94.
[132] Dubinina, G. G.; Furutachi, H.; Vicic, D. A. *J. Am. Chem. Soc.* **2008**, *130*, 8600–8601.
[133] Oishi, M.; Kondo H.; Amii, H. *Chem. Commun.* **2009**, 1909–1911.
[134] Tomashenko, O. A.; Escudero-Adán, E. C.; Martínez-Belmonte, M.; Grushin, V. V. *Angew. Chem. Int. Ed*. **2011**, *50*, 7655–7659.
[135] Morimoto, H.; Tsubogo, T.; Litvinas, N. D.; Hartwig J. F. *Angew. Chem. Int. Ed.* **2011**, *50*, 3793–3798.
[136] Chu, L.; Qing, F.-L. *Org. Lett*. **2010**, *12*, 5060–5063.
[137] Senecal, T. D.; Parsons, A. T.; Buchwald S. L. *J. Org. Chem*. **2011**, *76*, 1174–1176.
[138] Jiang, X.; Chu, L.; Qing, F. L. *J. Org. Chem*. **2012**, *77*, 1251–1257.
[139] Zhang, C.-P.; Wang, Z.-L.; Chen, Q.-Y.; Zhang, C.-T.; Gu, Y.-C.; Xiao, J.-C. *Angew. Chem. Int. Ed*. **2011**, *50*, 1896 –1900.
[140] Xu, J.; Luo, D.-F.; Xiao, B.; Liu, Z.-J.; Gong, T.-J.; Fu, Y.; Liu, L. *Chem. Commun.* **2011**, *47*, 4300–4302.
[141] Zhang, C.-P.; Cai, J.; Zhou, C.-B.; Wang, X.-P.; Zheng, X.; Gu, Y.-C.; Xiao, J.-C. *Chem. Commun.* **2011**, *47*, 9516–9518.
[142] Liu, T.; Shen, Q. *Org. Lett*. **2011**, *13*, 2342-2345.
[143] Nagib, D. A.; MacMillan, D. W. C. *Nature* **2011**, *480*, 224–228.
[144] Ye, Y.; Melanie, S. S. *J. Am. Chem. Soc*. **2012**, *134*, 9034–9037

[145] (a) Umemoto, T.; Adachi, K. *J. Org. Chem.* **1994**, *59*, 5692–5699.
[146] Ma, J.-A.; Cahard, D. J. *Org. Chem.* **2003**, *68*, 8726–8729.
[147] (a) Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron Lett.* **1994**, *35*, 3137–3138; b) Caron, S.; Do, N.M.; Arpin, P.; Larivee, A. *Synthesis* **2003**, 1693 – 1698.
[148] Allen, A. E.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2010**, *132*, 4986–4987.
[149] Pham, P. V.; Nagib, D. V.; MacMillan, D. W. C. *Angew. Chem. Int. Ed*. **2011**, *50*, 6119–6122.
[150] Matsubara, S.; Mitani, M.; Utimoto, K. *Tetrahedron Lett*. **1991**, *32*, 7689–7690.
[151] Parsons, A. T.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2011**, *50*, 9120–9123.
[152] Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13,* 317–323
[153] (a) Ha, C.; Horner, J. H.; Newcomb, M.; Varick, T. R.; Arnold, B. R., Lusztyk, J. *J. Org. Chem.* **1993**, *58*, 1194–1198. (b) Newcomb, M.; Varick, T. R.; Ha, C.; Manek, M. B.; Yue, X. *J. Am. Chem. Soc.* **1992**, *114*, 8158-8163.
[154] Newcomb, M.; Chestney, D. L. *J. Am. Chem. Soc. 1994, 116,* 9753–9754.
[155] Wang, X.; Ye, Y.; Zhang, S.; Feng, J.; Xu, J.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc.* **2011**, *133*, 16410–16413.
[156] Xu, J.; Fu, Y.; Luo, D.-F.; Jiang, Y.-Y.; Xiao, J-B.; Liu, Z.-J.; Gong, T.-J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 15300–15303.
[157] Chu, L.; Qing, F.L. *Org. Lett.* **2012**, *14,* 2106–2109.
[158] Miyake, Y.; Ota, S.; Nishibayashi, Y. *Chem. Eur. J.* **2012**, *18*, 13225–13258.
[159] Tredwell, M.; Gouverneur, V. *Org. Biomol. Chem*. **2006**, 26-32.
[160]) (a) Kawamura, T.; Kochi, J. K. *J. Am. Chem. Soc.* **1972**, *94*, 648–650. (b) Griller, D.; Ingold, K. U. *J. Am. Chem. Soc.* **1974**, *96*, 6715–6720. (c) Jackson, R. A.; Ingold, K. U.; Griller, D.; Nazran, A. S. *J. Am. Chem. Soc.* **1985**, *107*, 208–211. (d) Auner, N.; Walsh, R.; Westrup, J. *J. Chem. Soc., Chem. Commun.* **1986**, 207–208.
[161] Greedy, B.; Paris, J.-M.; Vidal, T.; Gouverneur, V. *Angew. Chem. Int. Ed.* **2003**, *42*, 3291–3294.
[162] (a) Pacheco, M. C.; Gouverneur, V. *Org. Lett.* **2005**, *7*, 1267–1270. (b) Tredwell, M.; Tenza, K.; Pacheco, M. C. ; Gouverneur, V. *Org. Lett.* **2005**, *7*, 4495–4497. (c) Tredwell, M.; Gouverneur, V. *Org. Biomol. Chem.* **2006**, *4*, 26–32. (d) Thibaudeau, S.; Fuller, R.; Gouverneur, V. *Org. Biomol. Chem.* **2004**, *2*, 1110–1112 (e) Lam, Y.-h.; Bobbio, C.; Cooper, I. R.; Gouverneur, V. *Angew. Chem. Int. Ed.* **2007**, *46*, 5106–5110.
[163] Giuffredi, G.; Bobbio, C.; Gouverneur, V. *J. Org. Chem.* **2006**, *71*, 5361–5364.
[164] Koller, R.; Stanek, K.; Stolz, D.; Aardoom, R.; Niedermann, K.; Togni, A. *Angew. Chem. Int. Ed.* **2009**, *48*, 4332 –4336.
[165] Hayashi, T.; Fujiwa, T.; Okamoto, Y.; Katsuro, Y.; Kumada, M. *Synthesis* **1981**, *12*, 1001–1003.
[166] Janson, P- G.; Ghoneim, I.; Ilchenko, N. O.; Szabó, K. *J. Org. Lett*. **2012**, *14*, 2882–2885.
[167] Krafft, M. E.; Holton, R. A. *Tetrahedron Lett*. **1983**, *24*, 1345–1348.
[168] Jensen, F. R.; Bushweller, C. H.; Beck, B. H. *J. Am. Chem. Soc.* **1969**, *91*, 344–351.
[169] Leong, M. K.; Mastryukov, V. S.; Boggs, J. E. *J. Mol. Struct*, **1998**, *445,* 149–160.
[170] Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815–3818.
[171] Shimizu, R.; Egami, H.; Hamashima, Y.; Sodeoka, M. *Angew. Chem. Int. Ed.* **2012**, *51*, 4577–4580.
[172] Marynick, D. S. *J. Mol. Struct.* **1982**, *87*, 161-168.
[173] Curtiss, L. A.; Pople, J. A. *Chem. Phys. Lett.* **1987**, *141*, 175–178.
[174] (a) Yasu, Y.; Koike, T.; Akita, M. *Angew. Chem. Int. Ed*. **2012**, *51*, 9567–9571. (b) Yasu, Y.; Koike, T.; Akita, M. *Org. Lett*. **2013**, *15*, 2136–2139.
[175] Mizuta, S.; Engle, K. M.; Verhoog, S.; Galicia-López, O; O'Duill, M.; Médebielle, M; Wheelhouse, K.; Rassias, G.; Thompson, A. L.; Gouverneur, V. *Org. Lett*., **2013**, *15*, 1250–1253.
[176] a) Kawamura, T.; Kochi, J. K. *J. Am. Chem. Soc.* **1972**, *94*, 648–650; b) Griller, D.; Ingold, K. U.; *J. Am. Chem. Soc.* **1974**, *96*, 6715–6720; c) Jackson, R. A.; Ingold, K. U. ; Griller, D.; Nazran, A. S.; *J.*

Am. Chem. Soc. **1985**, *107*, 208–211; d) Auner, N.; Walsh, R.; Westrup, J.; *J. Chem. Soc., Chem. Commun.* **1986**, 207–208.

[177] Mizuta, S.; Verhoog, S.; Wang, X.; Shibata, N.; Gouverneur, V.; Médebielle, M. *J. Fluorine Chem*. **2013**, dx.doi.org/10.1016/j.jfluchem.2013.07.006

[178] (a) Narayanam, J.M.R.; Stephenson, C.R.J.; *Chem. Soc. Rev.* **2011**, *40*, 102–113. (b) Teplý, F.; *Collect. Czech. Chem. Commun.* **2011**, *76*, 859–917. (c) Tucker, J.W.; Stephenson, C.R.J.; *J. Org. Chem.* **2012**, *77*, 1617–1622. (d) Xuan, J.; Xiao, W.-J.; *Angew. Chem. Int. Ed.* **2012**, *51*, 6828–6838.

[179] Haga, M.; Dodsworth, E.S.; Eryavec, G.; Seymour, P.; Lever, A.B.P.; *Inorg. Chem*. **1985**, *24*, 1901–1906.

[180]Duan, Z-C.; Hu, X-P.; Zhang, C.; Wang, D-Y.; Yu, S-B.; Zheng, Z. *J. Org. Chem*. **2009**, *74*, 9191–9194.

[181] Hayashi, T.; Fujiwa, T.; Okamoto, Y.; Katsuro, Y.; Kumada, M.; *Synthesis* **1981**, 1001–1003.

[182] Ferraris, D.; Young, B.; Cox, C.; Dudding, T.; Drury, W. J.; Ryzhkov, L.; Taggi, A. E.; Lectka, T. *J. Am. Chem. Soc.* **2002**, *124*, 67–77.

[183] Bunnelle, W. H.; Narayanan, B. A. *Org*. *Synth*. *Coll*. *Vol*. *VIII* **1993**, 602.

[184] Lam, Y.-h.; Bobbio, C.; Cooper, I. R. Gouverneur, V. *Angew. Chem. Int. Ed.* **2007**, *46*, 5106–5110.

[185] Wilkinson, S. C.; Lozano, O.; Schuler, M.; Pacheco, M. C.; Salmon, R.; Gouverneur, V. *Angew. Chem., Int. Ed*. **2009**, *48*, 7083–7086.