Oxidative Bromination and Ring Expansion in Organic Chemistry

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Finally, special thanks go to my country for allowing me to have this opportunity to study a PhD degree.

List of abbreviations

DMSO: Dimethyl sulfoxide.

NBS: *N*-Bromosuccinimide.

DCE: Dichloroethane.

TEA: Triethylamine.

THF: Tetrahydrofuran.

Bmim[Br]: 1-Butyl-3-methylimidazolium bromide.

DCM: Dichloromethane

TFA: Trifluoroacetic anhydride.

EWG: Electron withdrawing group.

EDG: Electron donating group.

TIPS: Triisopropylsilyl.

NCS: *N*-Chlorosuccinimide.

NIS: *N*-Iodosuccinimide.

BTPPMS: Benzyltriphenylphosphonium peroxymonosulfate.

m-CPBA: *m*-Chloroperoxybenzoic acid.

NMR: Nuclear magnetic resonance spectroscopy.

TFE: 2,2,2-Trifluoroethanol.

IR: Infrared.

MS: Mass spectrometry.

HRMS: High resolution mass spectrometry.

TMOP: 2,4,6-Trimethoxyphenyl.

THP: Tetrahydropyranyl.

TBS: *tert*-Butyldimethylsilyl.

TBAF: Tetrabutylammonium fluoride.

OBR: Ohira-Bestmann reagent.

rt: Room temperature.

PTSA: *p*-Toluenesulfonic acid.

LDA: Lithium diisopropylamide.

dppf: 1,1-Bis(diphenylphosphino)ferrocene.

h: hour

TOPP: Tribiphenyl-2-yl phosphite.

DMAD: Dimethyl but-2-ynedioate.

DBU: 1,8-Diazabicyclo[5.4.0]undec-7-ene.

PEPPSI-IPr**:** [1,3-Bis(2,6-Diisopropylphenyl)imidazol-2-ylidene](3-chloropyridyl)palladium(II) dichloride.

HPLC: High-performance liquid chromatography.

ee: Enantiomeric excess.

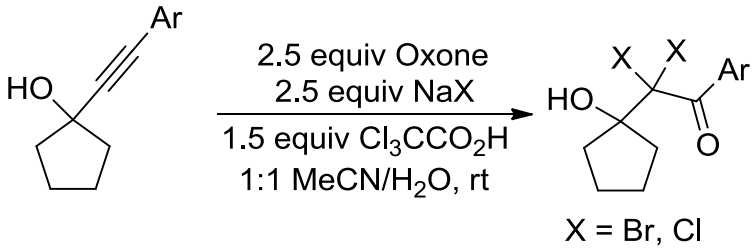
ESI: Electrospray ionisation.

IE: Electron ionisation.

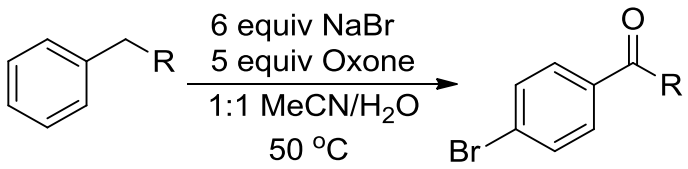
APCI: Atmospheric-pressure chemical ionisation.

Abstract

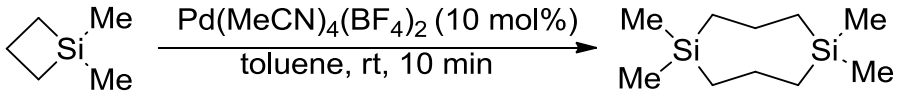
This thesis is composed of two independent research projects. The first major project discussed is electrophilic halogenation using inorganic halides in the presence of oxidant. This includes the conversion of tertiary propargyl alcohols in to α,α-dihaloketones.

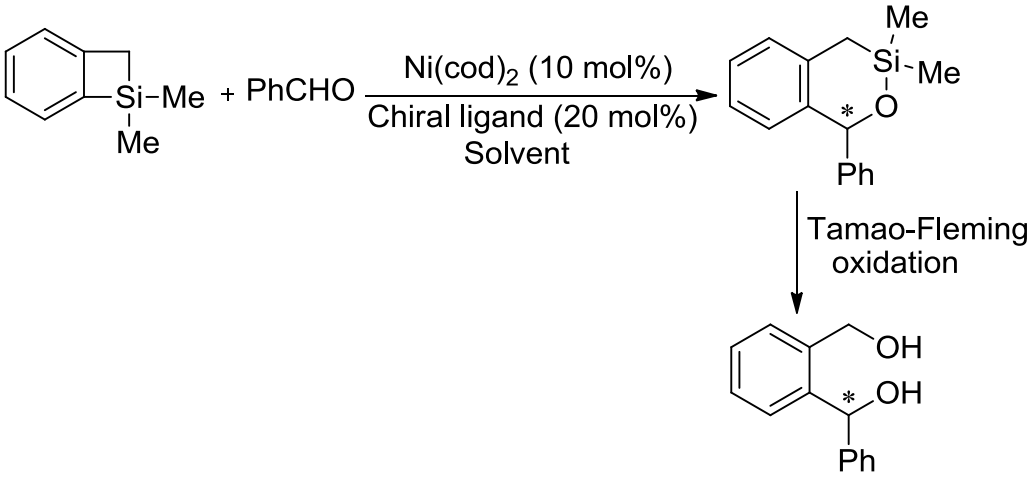


In addition, the oxidative bromination of a range of alkylbenzene derivatives using the inexpensive oxidant Oxone and sodium bromide is described with up to 4 C-H bonds being functionalised in this process.



The second part of this thesis focuses on using silacyclobutanes in our aim to access new silicon-containing chemical space. Silacyclobutanes are useful in organic synthesis because of their exciting reactivity based on their high Lewis acidity and ring strain. We describe our efforts at developing catalytic conditions for the Pd-mediated dimerisation of silacyclobutanes, as well as our preliminary results on the nickel-catalysed enantioselective ring expansion of benzosilacyclobutane with aldehydes. After Tamao-Fleming oxidation, this reaction produces extremely useful chiral benzylic alcohols.

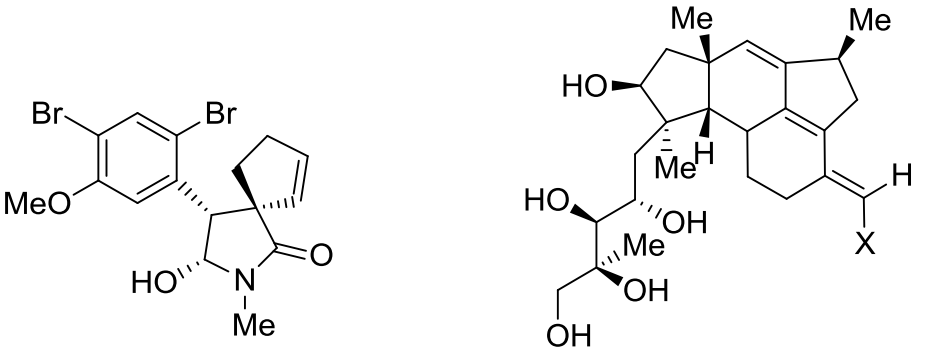



Si–Me
Me
+ PhCHO
Ni(cod)2 (10 mol%)
Chiral ligand (20 mol%)
Solvent
Me
Si
Me
O
*
Ph
Tamao-Fleming
oxidation
OH
OH
*
Ph

Chapter 1: Oxidative Bromination

1 Introduction

The introduction of bromine atoms into organic molecules is a fundamental reaction in organic synthesis. These bromides may be important compounds in their own right (Figure 1)[1,2] or they may be useful building blocks in organic synthesis. For example, transition-metal-catalyzed cross-coupling reactions[3] and nucleophilic substitutions[4] of organic bromides are common processes. Moreover, organic bromides are widely used as intermediates in the industrial manufacture of pharmaceuticals, agrochemicals, and polymers.[5,6]



1 Amathaspiramide E
antiviral

2a X = Cl neomangicol A
2b X = Br neomangicol B

Figure 1

Traditional bromination methods involving the direct or indirect use of molecular bromine show a maximum of 50% efficiency in atom consumption of bromine. These methods can also generate toxic, and corrosive hydrogen bromide, which leads to environmental pollution. Moreover, the difficulty of handling liquid bromine, is such that special care is needed for its transport and storage. During the past few years, bromination methods which avoid the use of hazardous and highly toxic molecular bromine have been extensively studied, including NBS-NaOH[7], NBS-PTSA[8], HBr-DMSO[9], and H_2O_2-HBr[10]. Recently, the oxidative bromination process has been developed as a more efficient, environmentally friendly, atom-economic (100% consumption of bromine) method.

Oxidative bromination is a method which generates electrophilic bromine from the reaction between Br^- and oxidants such as H_2O_2[11], Oxone[12], $(NH_4)_2S_2O_8$[13], *t*-BuOOH[14], peracid[15], and others with or without the use of a catalyst. This process involves using different salts as a source of bromide, such as KBr, NaBr, Bu_4NBr, and NH_4Br, and requires a two-phase system (water and organic solvent).

1.1 Br_2 bromination

Different methods of bromination of organic molecules using molecular bromine have been studied. Previously, the most popular method was by using molecular bromine as a reagent in chlorinated solvents.

Bromination of alkenes is an effective method for the functionalisation of hydrocarbons.[16] This process proceeds through an electrophilic addition mechanism and formation of a bromonium ion intermediate (Figure 2).

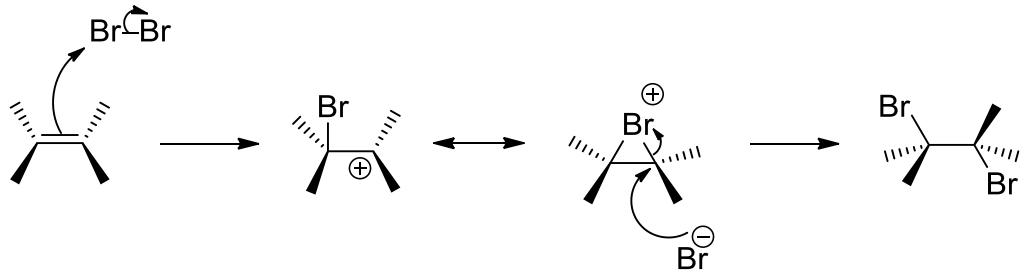
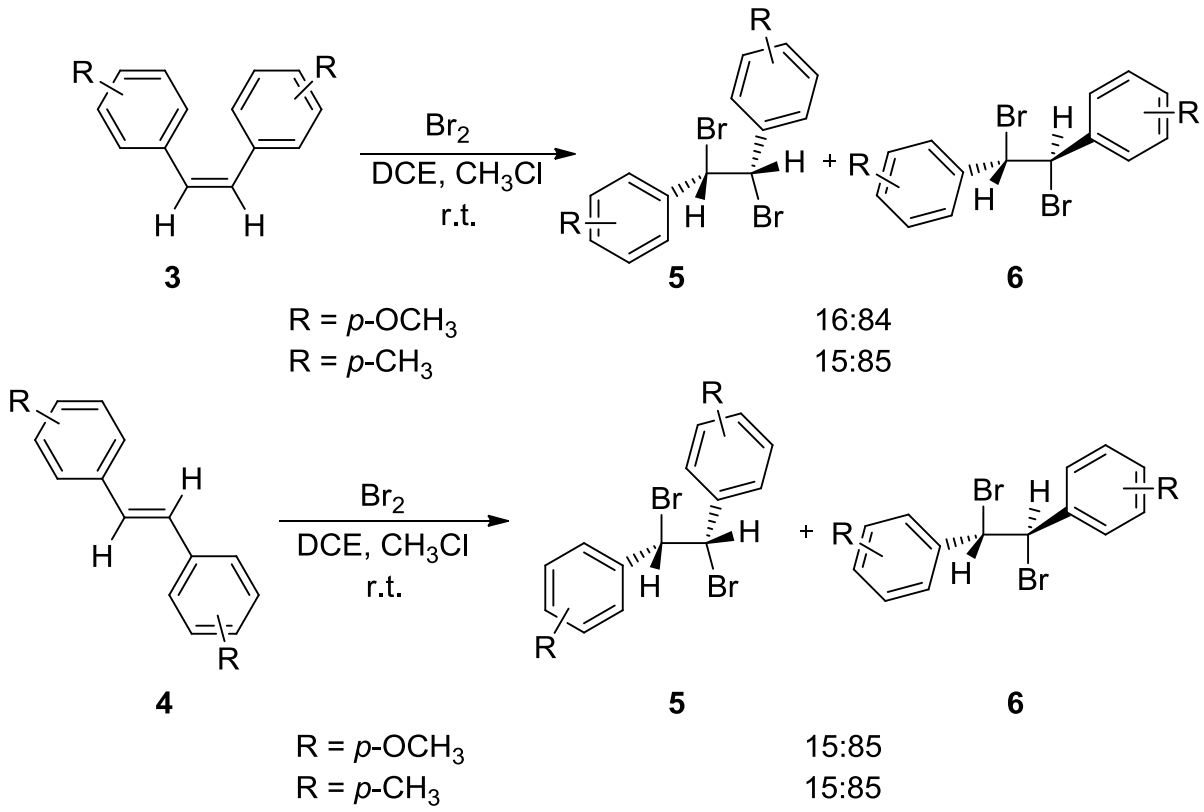


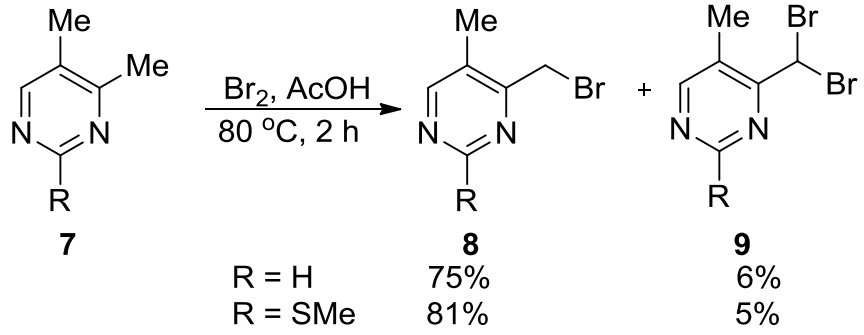
Figure 2

Bellucci and co-workers reported the electrophilic bromination of *cis*- and *trans*-stilbenes (**3**, **4**) in aprotic solvents DCE and CH_3Cl using molecular bromine at room temperature. The reaction stereoselectively generated the *anti* dibromide product in all cases (Scheme 1).[16] This result confirms the formation of a cationic intermediate that can rotate to place the bulky phenyl groups as far apart as possible.



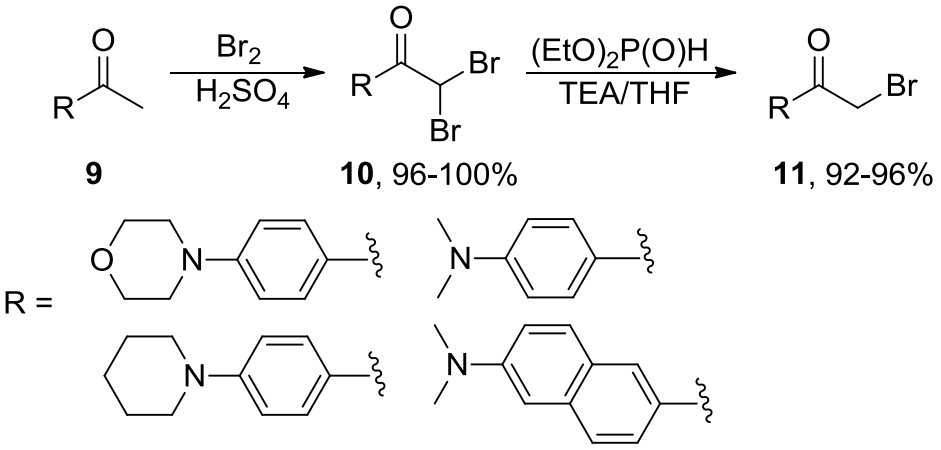
Scheme 1

In 1991, a study on polymethylpyrimidines **7** by Strekowski *et al.*[17] demonstrated highly regioselective bromination. The method for bromination of polymethylpyrimidines was already reported but the product was formed in low yield.[18] In this method they used bromine in acetic acid at 80 ^{o}C to effect this transformation which provided product **8** in good yield, and dibromination product **9** in low yield (Scheme 2).



Scheme 2

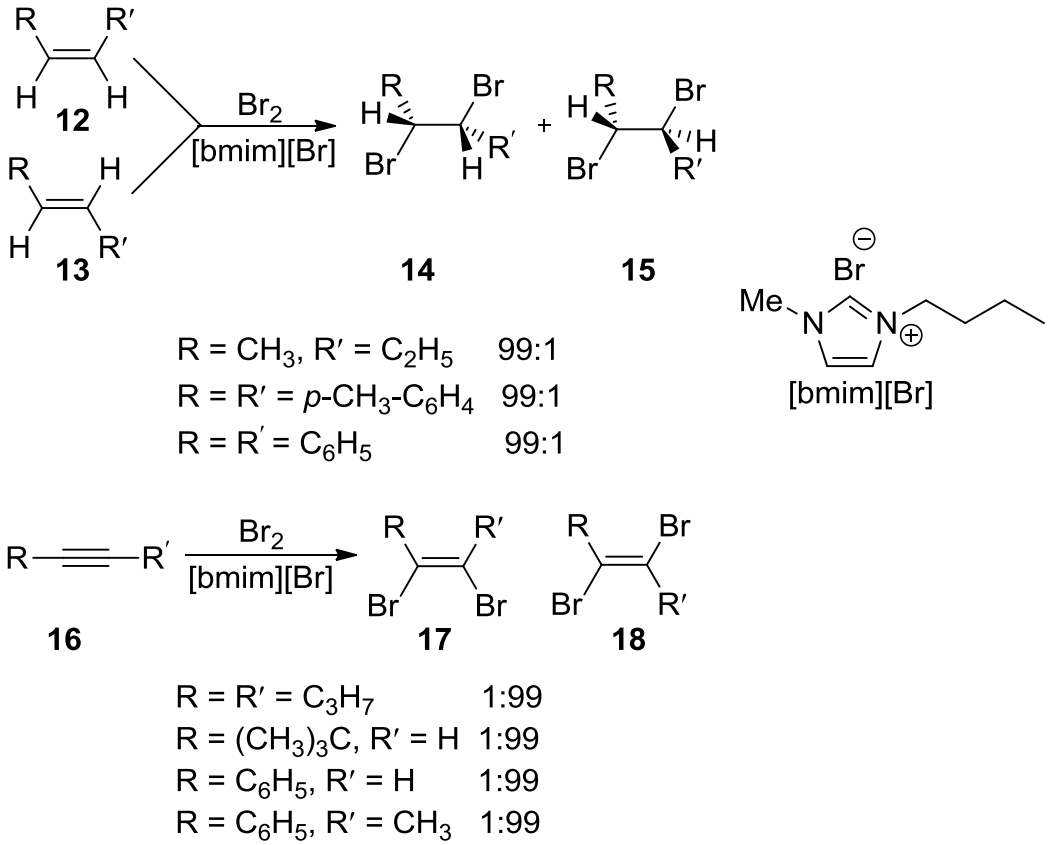
Diwu and co-workers reported that amino substituted arylmethylketones can be selectively brominated (Scheme 3). They tried different brominating reagents and solvents to effect the transformation of these compounds and to improve the yield, but they found that bromine in sulfuric acid was the best conditions for dibromination of the amino-substituted arylmethylketones without concomitant bromination of the ring. This was due to the presence of sulfuric acid, which completely stopped the ring bromination. These dibrominated compounds could be easily monodebrominated with diethyl phosphite in the presence of triethylamine.[19]



Scheme 3

Most reactions using molecular bromine as a source of bromine in direct brominations require harsh reaction conditions and chlorinated solvents as well as generating toxic and corrosive hydrogen bromide. These issues have made it necessary to develop more convenient processes as alternatives to the traditional methods such as: Br_2-ionic liquid[20] and Br_2-Lewis acid.[21] For example, the stereoselective bromination of alkenes and alkynes can be achieved with the use of the room-temperature ionic liquids, 1-butyl-3-methyllimidazolium hexafluorophosphate, 1-butyl-3-methylimidazolium tetrafluoroborate, 1-butyl-3-methylimidazolium bromide, and 1-butyl-3-methylimidazolium chloride. This method is considered a "green" recyclable procedure and is an

alternative to the use of chlorinated solvents. Using Br_2 in [bmim][Br] with alkenes **12**, and **13** and alkynes **16** gave the product with high anti stereoselectivity (Scheme 4).[21]

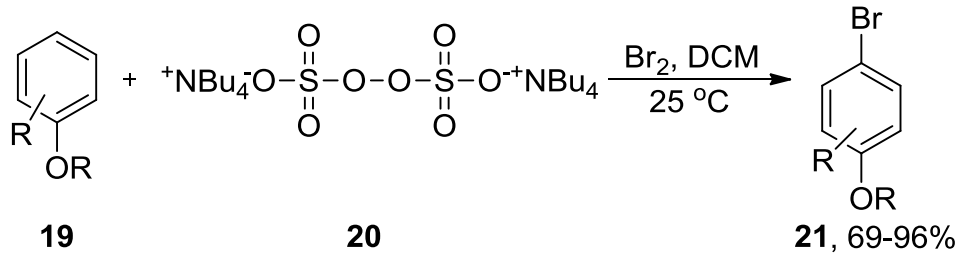


Scheme 4

Bromination of aromatic compounds is also a very important reaction in organic synthesis as aryl bromides are extremely useful compounds which can undergo reactions such as cross-coupling. [22.23]

The most well-known methods for the synthesis of brominated aromatic compounds are based on using bromine. For example, molecular bromine in organic solvent used to be the most popular method for direct bromination of aromatic compounds, but the disadvantage of this method is that it is difficult to control especially for electron-rich aromatics. Thus, several alternative methods have been developed for this process.[24]

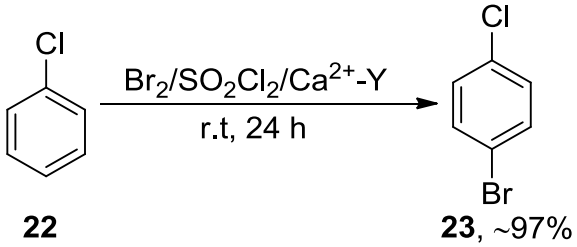
In 2004, Kim *et al.* [24] described one of these new methods. Activated aromatic compounds **19** were converted to brominated compounds **21** with complete regioselectivity in good to excellent yields by using peroxide **20** as an oxidant with molecular bromine in DCM at room temperature (Scheme 5).



19 **20** **21**, 69-96%

Scheme 5

Another example of bromination of aromatic compounds was discovered by the Gnaim group. The *para*-bromination of chlorobenzene **22** was effected in good to excellent yields using a new system of Br_2/SO_2Cl_2/zeolite (Scheme 6). Different zeolites were prepared with metal cations but they found the Ca^{2+}-Y zeolite the most stable and effective catalyst under their reaction conditions. [25]



22 **23**, ~97%

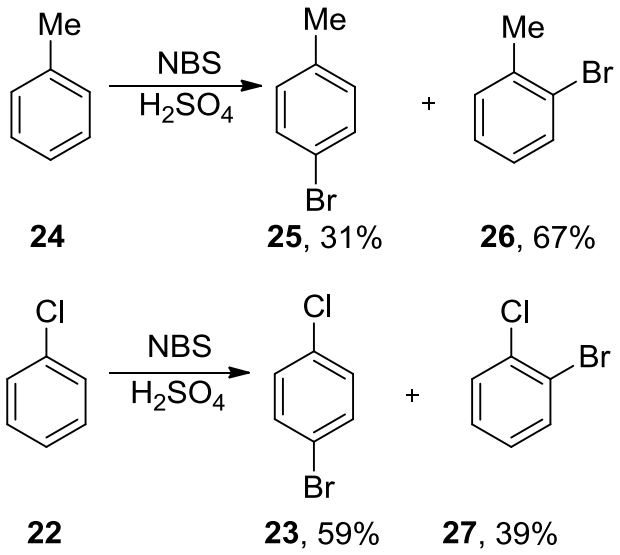
Scheme 6

Again, the use of molecular bromine as brominating agent has several disadvantages as mentioned above. To overcome these problems, *N*-bromosuccinimide (NBS) has been used instead as a brominating reagent, as it is easy to handle, transformations can occur under various reaction conditions, and NBS does not produce HBr in the reaction.

1.2 NBS bromination

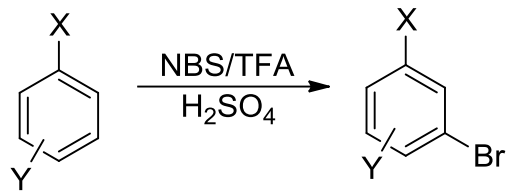
A. Bromination of aromatic compounds

Among the first examples of using *N*-bromosuccinimide (NBS) for the bromination of aromatic compounds were those reported in 1964 by Lambert. They successfully brominated both toluene **24** and chlorobenzene **22** using NBS in aqueous H_2SO_4 and *ortho* and *para* isomers of both compounds were isolated in moderate yields (Scheme 7). However, this study was limited to these substrates.[26]



Scheme 7

Since then, efforts have been aimed towards developing the bromination of aromatics using NBS as a source of electrophilic bromine under milder conditions. In 1999, the Duan group reported a convenient new method for the bromination of deactivated aromatic compounds by using NBS in trifluoroacetic acid (TFA) as solvent in the presence of catalytic sulfuric acid at room temperature. This reagent system was able to brominate a number of highly deactivated aromatic substrates in good to excellent yields (Scheme 8). [27]

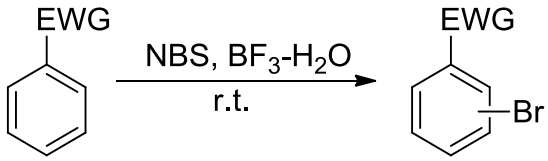


28 **29**, 45-91%

X = CF_3, NO_2, CO_2H, CHO, H
Y = H, *p*-Cl, *p*-CF_3, *m*-CF_3, *m*-NO_2

Scheme 8

The Olah group found that bromination of deactivated arenes could be easily achieved using the NBS/BF_3-H_2O system at room temperature to give the corresponding monobrominated products **31** in 77-96% yields (Scheme 9). The formation of monobrominated products with *N*-bromosuccinimide (NBS) showed very high selectivity and good yields without any organic solvent present. In this reaction NBS was used as a source of Br^+ in combination with BF_3-H_2O which is economic, easy to prepare, and provides sufficiently high acidity.[28]

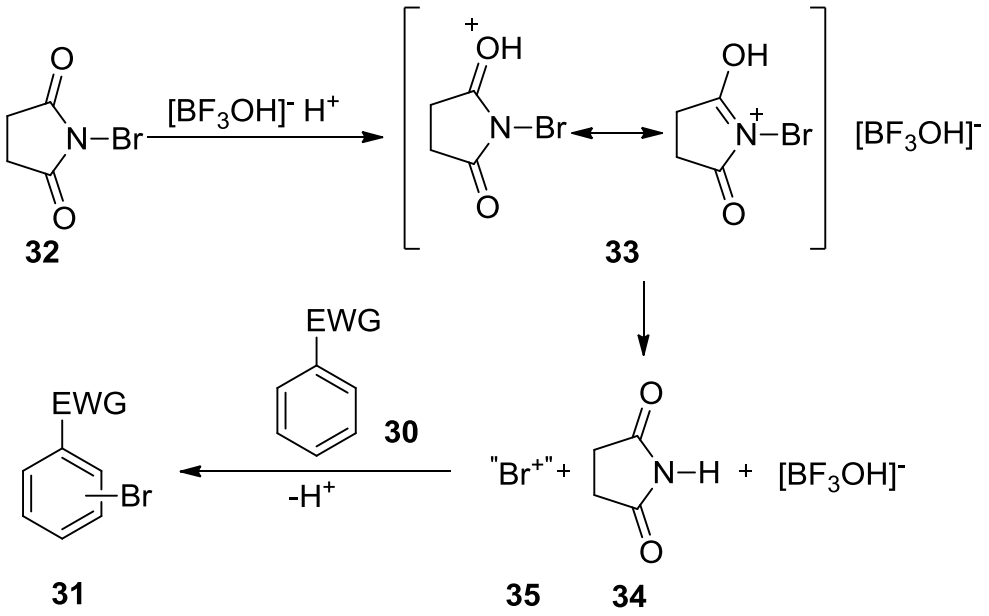


30 **31,** 77-96%

EWG = Electron withdrawing group

Scheme 9

The authors proposed that in the presence of BF_3-H_2O, and under mild conditions, a superelectrophilic protosolvated halogenating species **33** is generated. This intermediate can lead to the generation of protosolvated $[X]^+$ **35**. Finally, this species can react with the arenes **30** to end up with halogenated products **31** (Scheme 10).

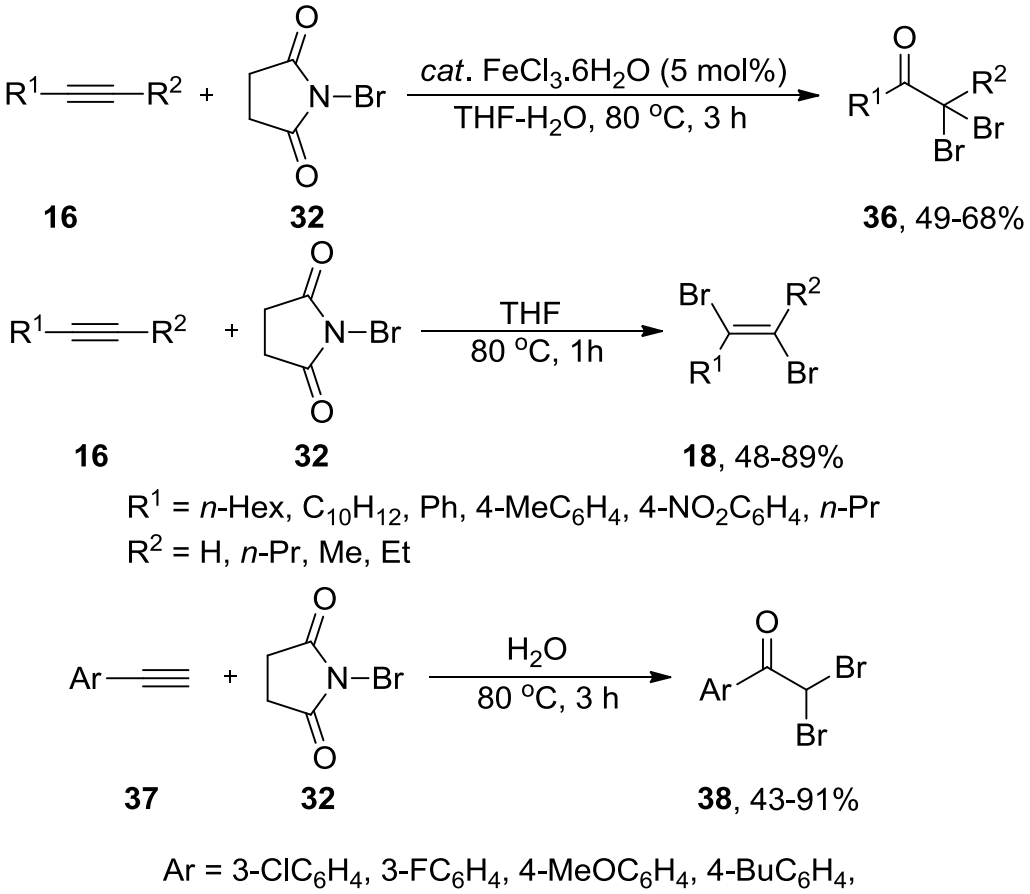


Scheme 10

B. Bromination of alkynes

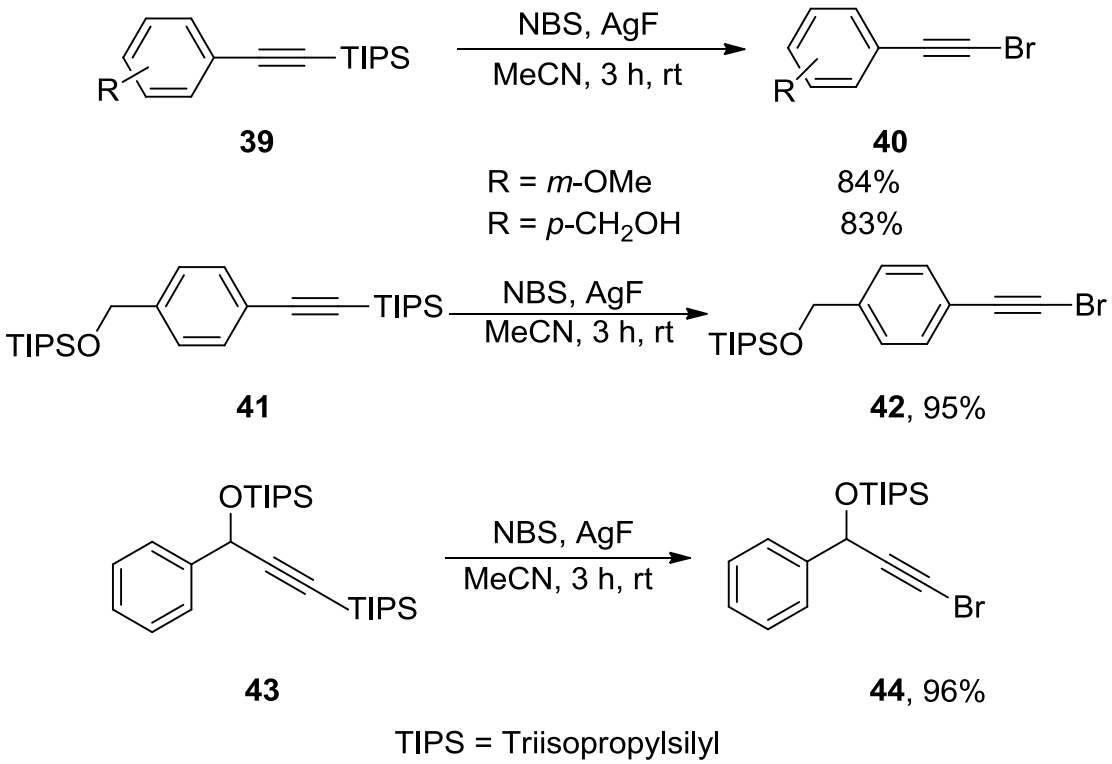
Bromination of alkynes with a bromine source such as NBS is a classic method for the synthesis of *α,α*-dibromoketones and *α,β*-dibromoketones as well as bromoacetylenes.[29, 30]

Liu *et al.* [29]reported their study for oxyhalogenation of alkynes **16** using NBS in THF and H_2O in the presence of $FeCl_3.6H_2O$ as catalyst to produce the corresponding *α,α*-dibromoketones **36** in good yields (Scheme 11). The *α,β*-dibromo alkenes **18** were also prepared in this process but in THF as solvent and without a catalyst. Moreover, without using a catalyst terminal aromatic alkynes **37** were converted into *α,α*-dibromoketones **38** in good yields in water.



Scheme 11

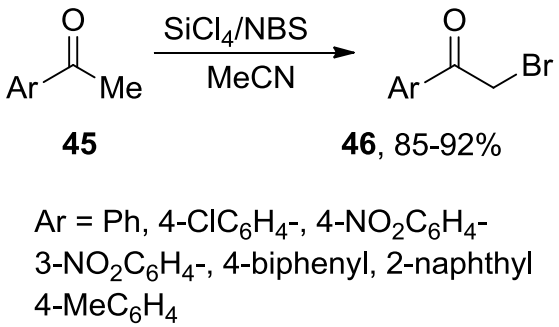
In 2006, Lee and co-workers developed a new method for the synthesis of haloalkynes.[30] This involved the preparation of bromoacetylenes from bulky trialkylsilyl acetylenes through the addition of AgF and NBS in MeCN. These conditions successfully led to high yields of bromoacetylenes (Scheme 12).



Scheme 12

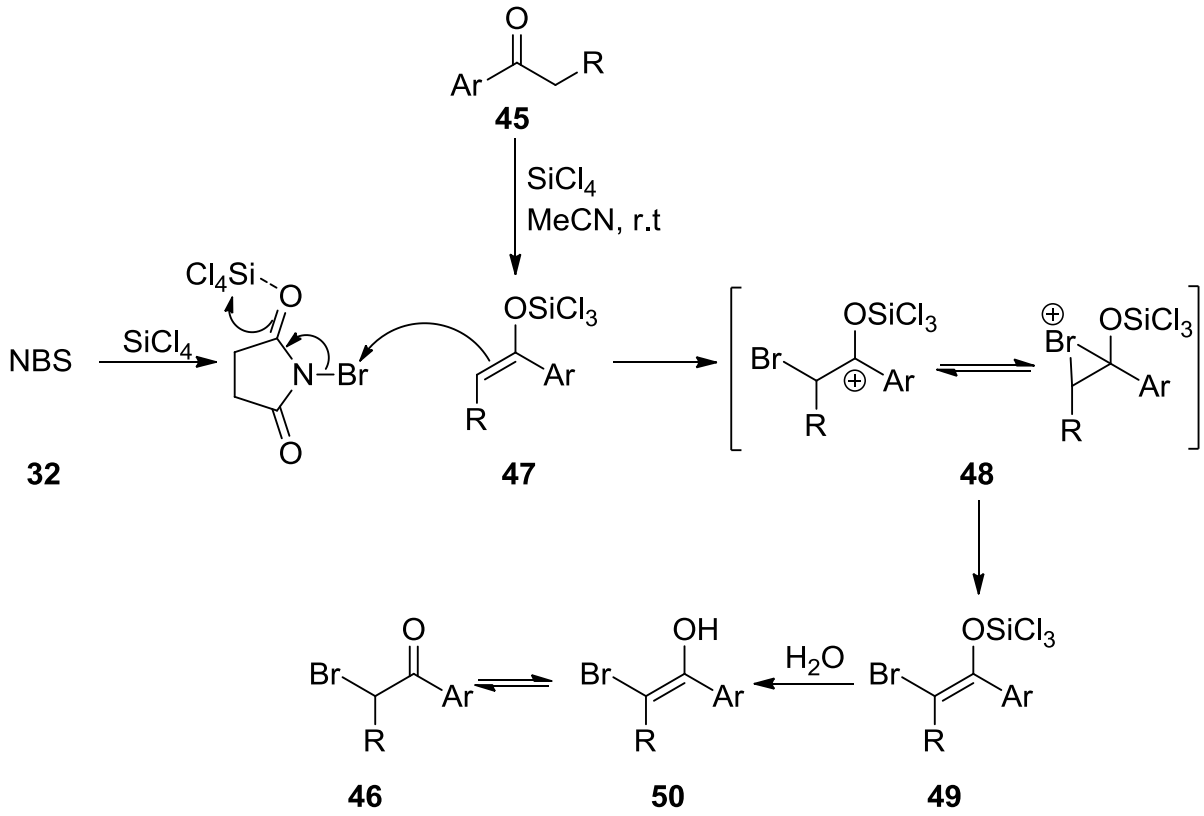
C. Bromination of carbonyl compounds

The transformation of carbonyl compounds into α-halocarbonyl derivatives has been widely studied under various halogenation conditions. [31-33] Novak and Salama demonstrated that the combination of NBS and $SiCl_4$ in MeCN was an efficient system for the α-monobromination of carbonyl compounds **45** as well as benzylic halogenations. This method gave the α-monobromination products in good to high yields with high regioselectivity (Scheme 13).[34]



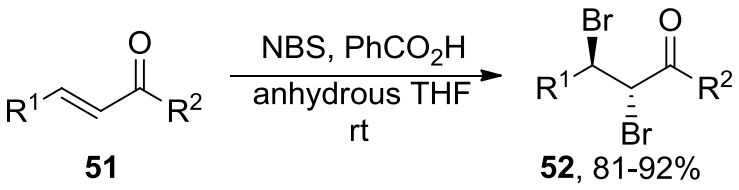
Scheme 13

The proposed mechanism for this method is shown in Scheme 14. The silyl enol ether **47** is generated first through the reaction of the ketone **45** with $SiCl_4$ and the further addition of $SiCl_4$ may coordinate with the NBS to enhance the activity of the halogen atom. Then, intermediate **47** attacks the halogen of NBS to form the halogenated silyl enolate **49**. After the aqueous work-up product **46** is formed.



Scheme 14

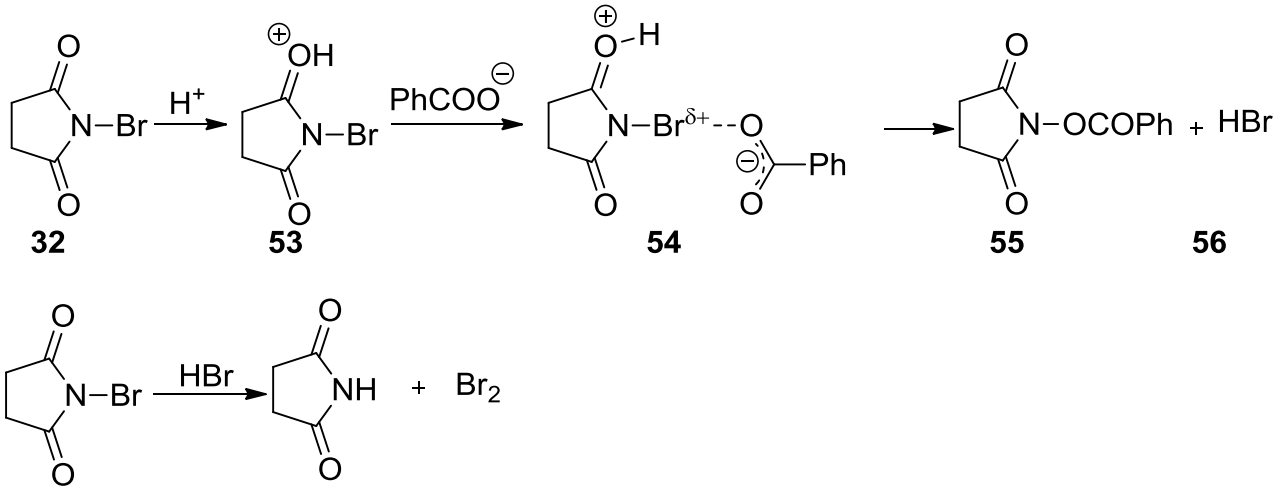
In 2013, examples of the conversion of unsaturated carbonyl compounds into α,β-dibromination products was presented by the Xue group. They applied the combination of NBS and benzoic acid as a dibromination agent for the first time in the reaction of unsaturated carbonyl compounds. The dibromination products were prepared at room temperature, and were formed in good to excellent yields (Scheme 15).[35]

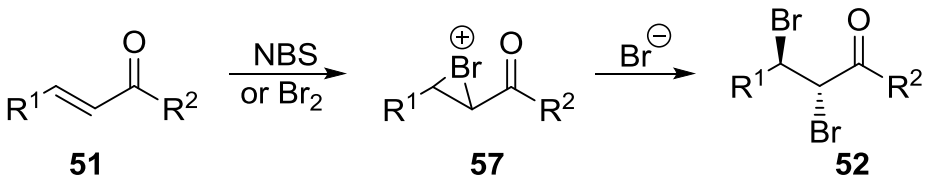


R^1 = 4-ClC_6H_4, R^2 = Ph
R^1 = Ph, R^2 = Ph
R^1 = 4-$CH_3C_6H_4$, R^2 = Ph
R^1 = 4-BrC_6H_4, R^2 = Ph
R^1 = 2-naphthyl R^2 = Ph
R^1 = 2-thienyl, R^2 = Ph
R^1 = Ph, R^2 = Me

Scheme 15

The proposed mechanism for this reaction is shown in Scheme 16. First, the interaction between NBS and benzoic acid leads to the generation of complex **54** through the protonation of NBS **32**. Subsequently both 2,5-dioxopyrrolidin-1-yl benzoate **55** and HBr **56** are generated. Next, the excess NBS **32** could react with the HBr **56** to generate the elemental bromine. Then, the carbonyl compound could react with NBS or Br_2 to form the bromonium ion intermediate **57**, which is then trapped by the bromide anion and the dibrominated product **52** is formed.[35]



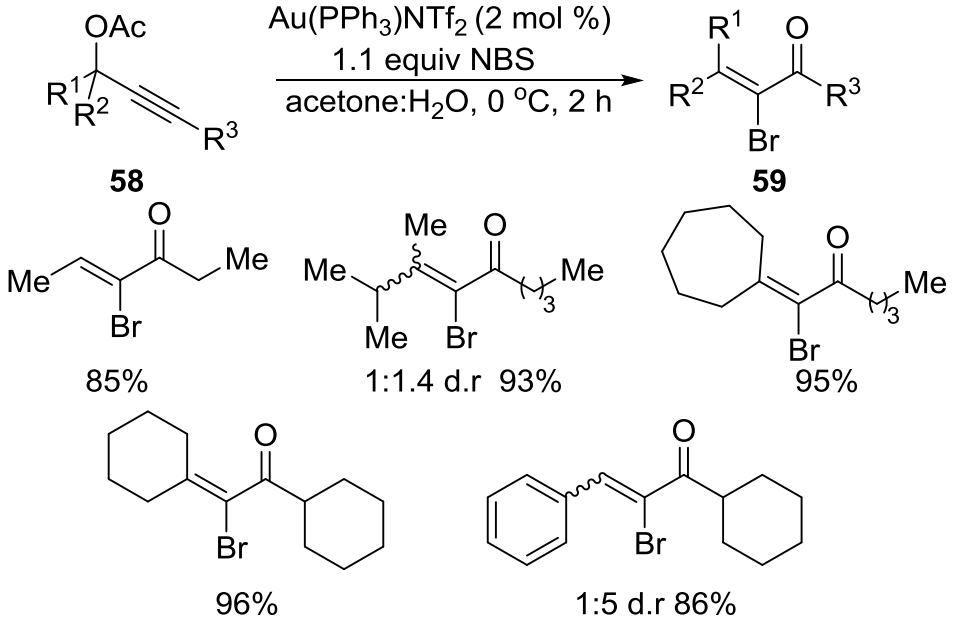


Scheme 16

D. Bromination of propargyl acetates and propargyl alcohols

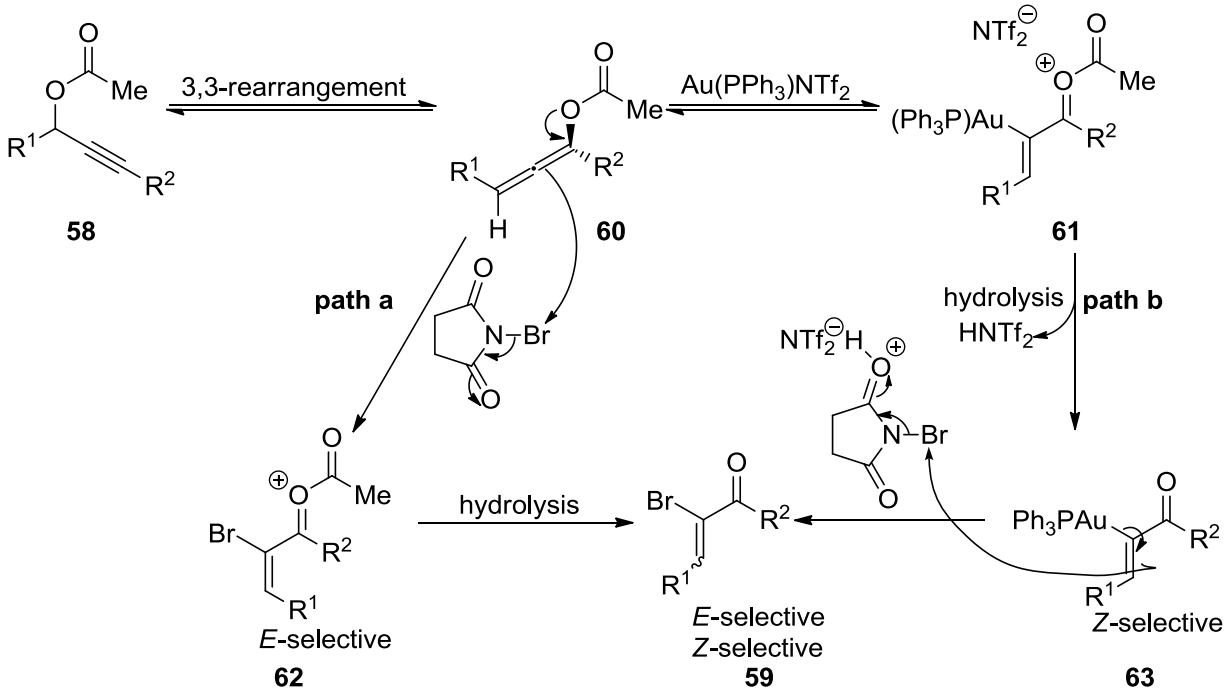
Propargyl alcohols and propargyl acetates are widely used in organic synthesis due to their availability as starting materials and the fact that they can be readily prepared from aldehydes/ketones and terminal alkynes.[36]

The Zhang group reported a new method for the preparation of α-haloenones by using propargyl acetates **58** with an $Au(PPh_3)NTf_2$ catalyst in the presence of NXS as a source of halogen in acetone/H_2O solvent. This reaction worked very well with NCS, NIS and NBS to produce the α-haloenones. α-Bromoenone **59** products were prepared by using 1.1 equivalents of NBS under the reaction conditions, which resulted in excellent yields (Scheme 17).[37]



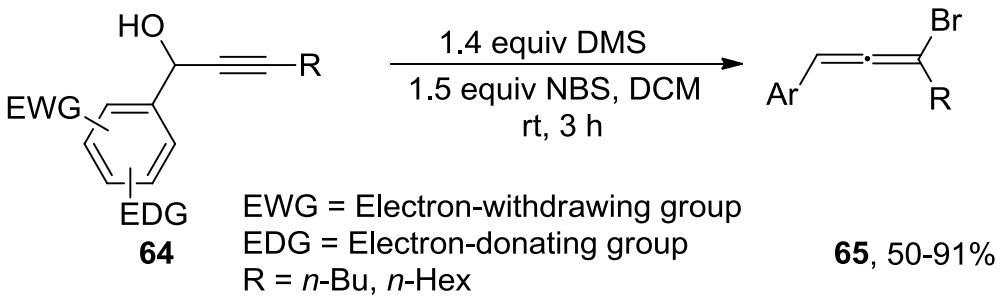
Scheme 17

A plausible mechanism for this reaction is shown in Scheme 18. The propargyl acetate **58** could be activated through a 3,3-rearrangement to generate carboxyallene intermediate **60**. Then, this intermediate can react with NBS to form oxocarbenium **62** (path a) which can result in (*E*-isomer) product **59.** Alternatively, intermediate **60** could be activated by a further amount of Au^{I} catalyst to form Au-containing cation **61** (path b) which can lead to the formation of intermediate **63** upon hydrolysis, then react with NBS to give *Z*-isomer **59**.



Scheme 18

Jiang *et al.*[38] have reported a convenient and highly regioselective method of preparation of bromoallenes **65** from propargyl alcohols **64** which involves a combination of *N*-bromosuccinimide and DMS in DCM at room temperature (Scheme 19). The propargyl alcohol substrates are converted into bromoallene products without being affected by the electron-donating group or electron-withdrawing group located at the *para* or *meta* position of the aromatic ring. However, any of these groups located at the *ortho* position lowers the yield of the product obtained.

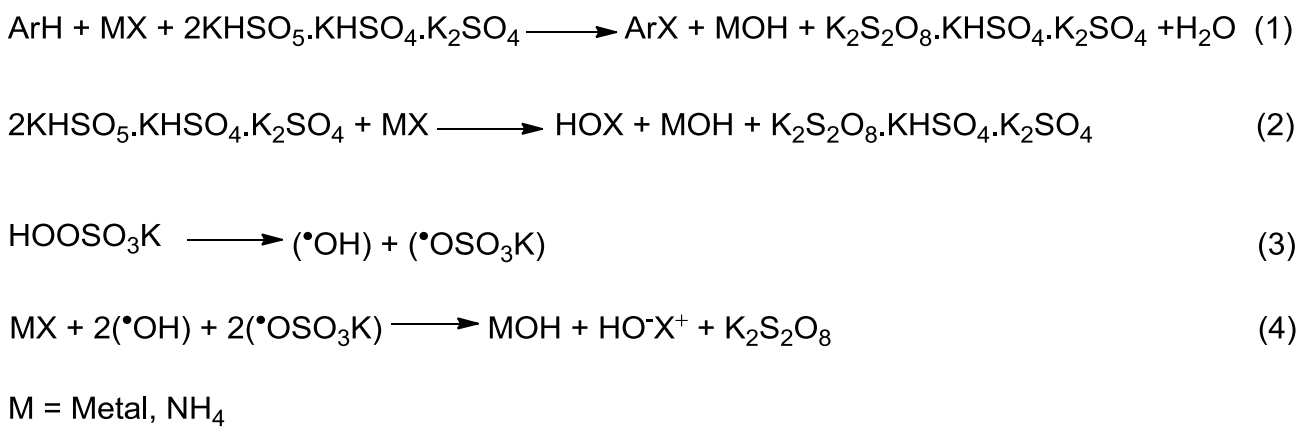


Scheme 19

All the above methods which involve the use of organic reagents such as NBS have some drawbacks such as difficulty-of-use, relatively high cost, low atom efficiency, or supply issues. Therefore, the need to find alternative methods for bromination continues to attract attention. For example, researchers have been seeking to develop more convenient approaches to the preparation of bromoorganic compounds by using readily available, inexpensive, and easy-to-handle inorganic halides which have been reported in various reactions as electrophilic halogenation reactions.

1.3 Electrophilic bromination with bromides

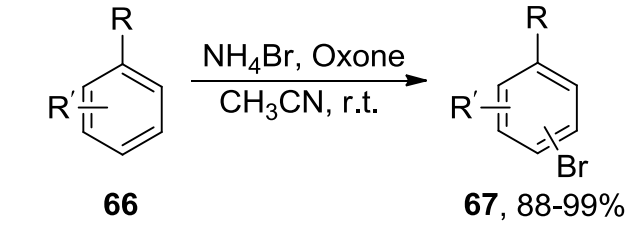
Electrophilic bromination of organic compounds with halides involves the reaction of an oxidant with the halides to form the corresponding hypohalous acid (HOBr).[39] The general mechanism of an oxidant such as Oxone® reacting with halides is shown in Scheme 20. This intermediate (HOX) has a high degree of instability due to its ionic nature and it is very reactive toward aromatic nuclei. The HOX forms from the dissociation of Oxone® into radicals then one of these radicals $^{\bullet}OH$ oxidizes the MX to give HOX and MOH (Equation 4).[40]



Scheme 20

A. Bromination of aromatic compounds

Several methods have been described for bromination of organic compounds under oxidative conditions. For example, a number of different aromatic substrates have been reacted using ammonium bromide and potassium peroxymonosulfate which is an inexpensive, stable oxidizing reagent, in CH_3CN. This method selectively monobrominates various activated aromatic compounds in high yields (Scheme 21).[41]



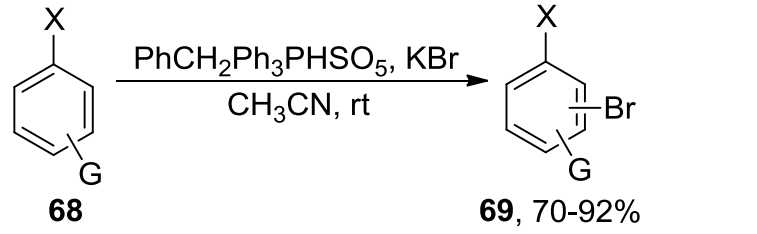
Scheme 21

The mechanism of this reaction is similar to that shown in Scheme 20. In the presence of Oxone® the oxybromination of an aromatic compound occurs as in Equation (1).

$$ArH + NH_4Br + 2KHSO_5.KHSO_4.K_2SO_4 \longrightarrow$$

$$ArBr + NH_4OH + K_2S_2O_8.KHSO_4.K_2SO_4 + H_2O \quad (1)$$

Adibi and co-workers have reported that benzyltriphenylphosphonium peroxymonosulfate (BTPPMS) can be used as oxidant for the bromination of electron-rich aromatic rings in the presence of potassium bromide as bromine source under non-aqueous conditions. Using BTPPMS as a mild, efficient, stable, and cheap reagent for the first time provides monobrominated products in moderate to high yields (Scheme 22).[42]



68 **69**, 70-92%

G = H, Electron-releasing or -withdrawing substituent

X = OH, NH_2, $NHCOCH_3$

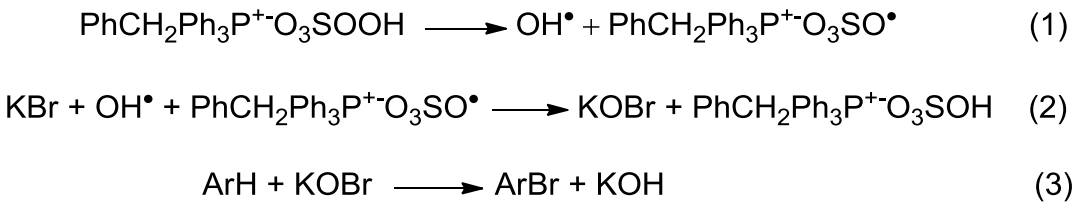
Scheme 22

The authors proposed that there are two mechanisms for the bromination of aromatic compounds in the presence of BTPPMS. In the first mechanism the bromination proceeds through the formation of potassium hypobromite as shown in Equation (1) and (2).

$$ArH + KBr + PhCH_2Ph_3PHSO_5 \longrightarrow ArBr + KOH + PhCH_2Ph_3PHSO_4 \quad (1)$$

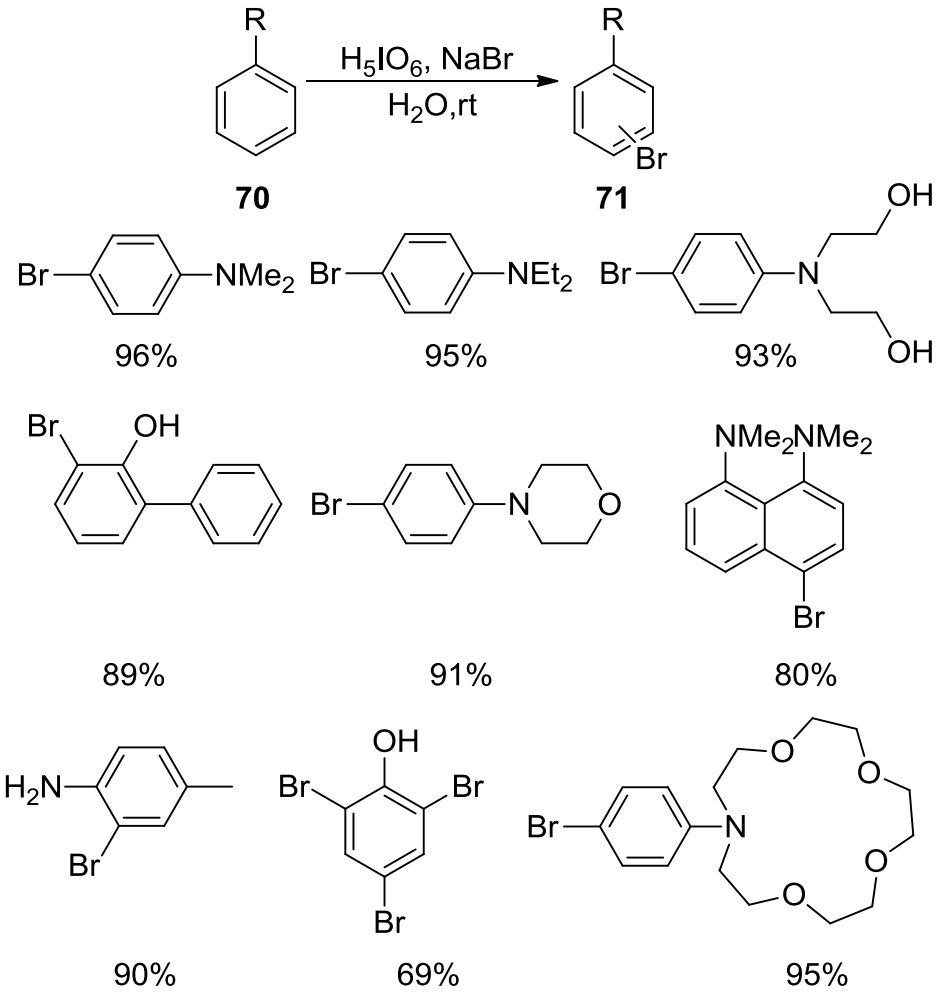
$$PhCH_2Ph_3PHSO_5 + KBr \longrightarrow KOBr + PhCH_2Ph_3PHSO_4 \quad (2)$$

The second proposed mechanism occurs through a radical route by homolytic cleavage of the O–O bond in the peroxymonosulfate anion ($^{-}O_3S$–O–OH) followed by KOBr formation and arene bromination (Scheme 23).[42]



Scheme 23

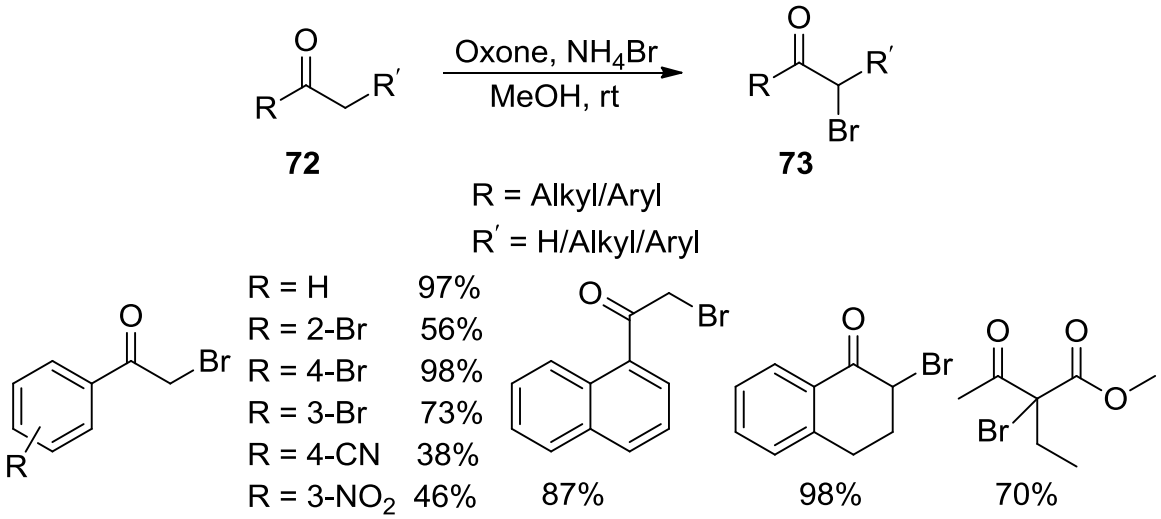
Without using an organic cosolvent the bromination of aromatic compounds has also been achieved at room temperature in short reaction times using orthoperiodic acid (H_5IO_6) as oxidant and sodium bromide as a safe source of bromide in water (Scheme 24).[43]



Scheme 24

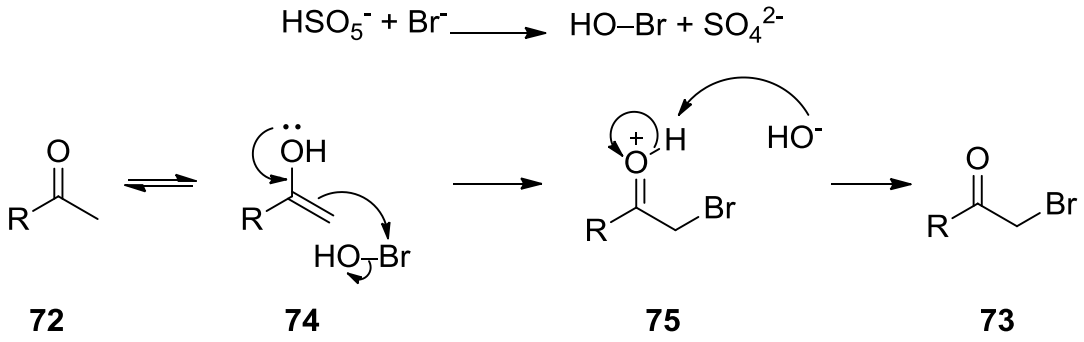
B. Bromination of carbonyl compounds

α-Bromoketones are widely used as intermediates in organic synthesis. The α-bromination of various ketones such as cyclic, aralkyl, acyclic, 1,3-diketones and *β*-ketoesters, and the α- and *α,α*-dibromination of 1,3-diketones and *β*-ketoesters have been achieved by an efficient and economic method using ammonium bromide and Oxone at room temperature without catalyst. Selective α-monobromination can be achieved in moderate to excellent yields (Scheme 25).[44]



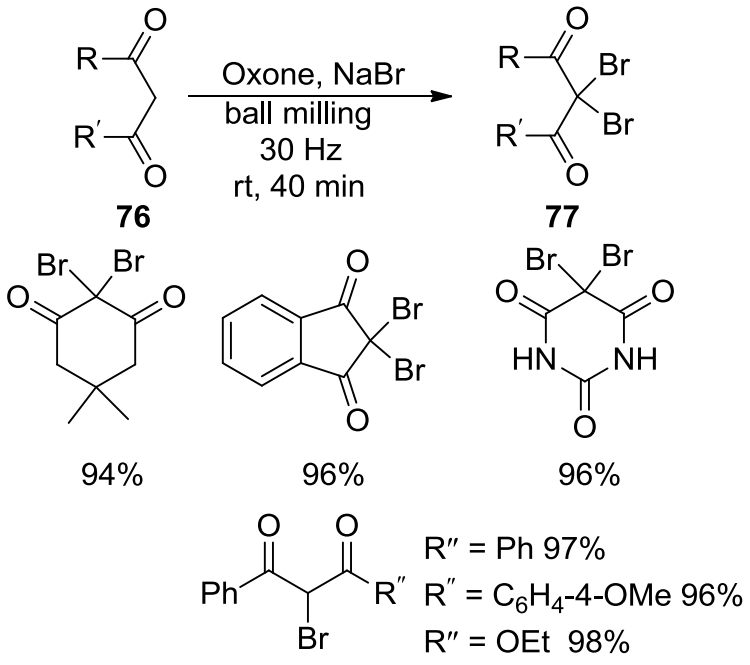
Scheme 25

A plausible mechanism for this reaction is shown in Scheme 26. The α-bromination of ketones proceeds through the formation of hypobromous acid, which then reacts with ketones **72** to give the desired product **73**.



Scheme 26

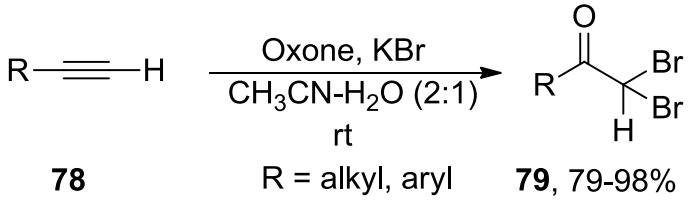
Solvent-free bromination of 1,3-dicarbonyl compounds **76** using a combination of sodium bromide and Oxone was investigated under mechanical milling conditions (Scheme 27). α,α-Dibromo derivatives **77** were obtained in 94-96% yields when cyclic 1,3-dicarbonyl compounds were subjected to the reaction conditions, whilst acyclic 1,3-dicarbonyl compounds afforded α-monobromo derivatives in 96-98% yields.[45]



Scheme 27

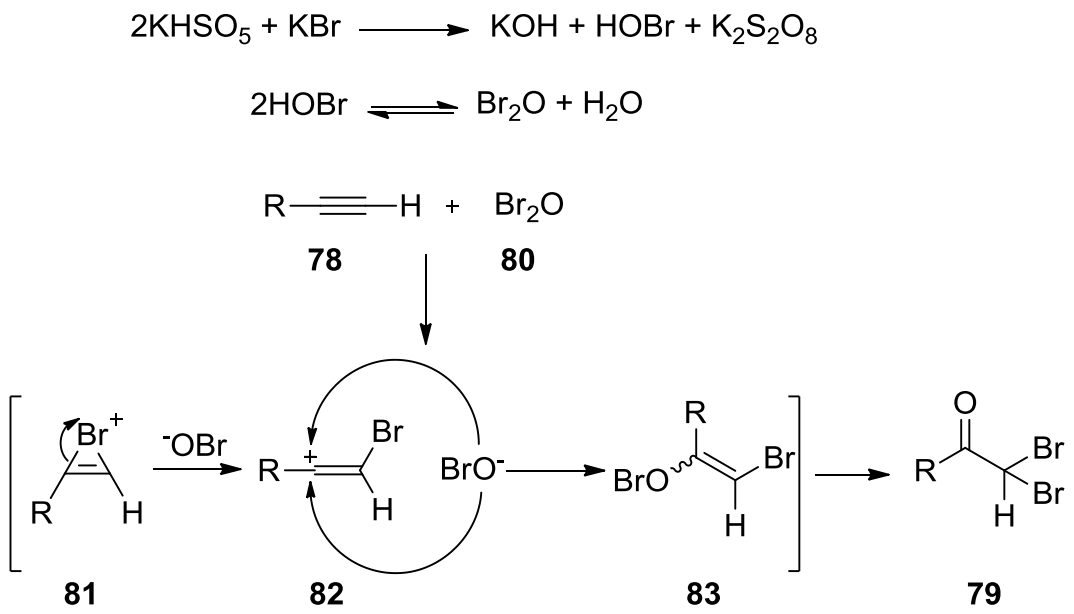
C. Bromination of alkynes

Madabhushi *et al*.[46] studied oxybromination of terminal alkynes using Oxone® and KBr as a simple and efficient method for synthesis of α,α-dibromoketones in high yields (Scheme 28). In this reaction various alkynes were converted into α,α-dibromoketones in the presence of a combination of acetonitrile and water at room temperature. However, no reaction was observed in the absence of water.



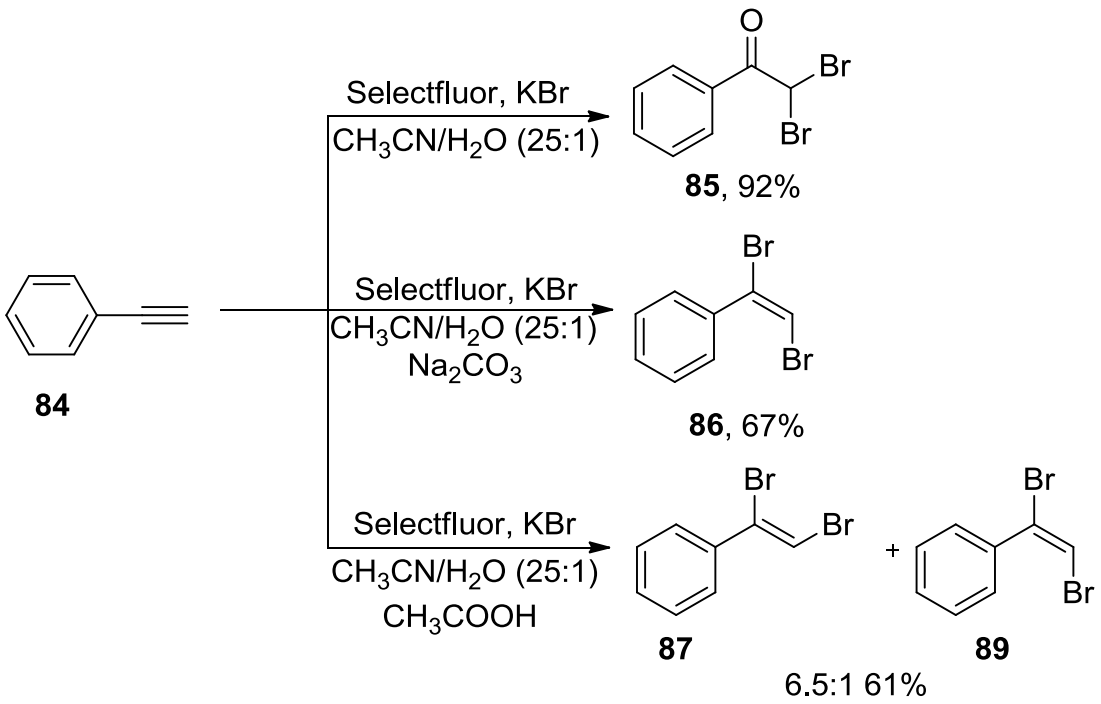
Scheme 28

They proposed a plausible mechanism for the formation of α,α-dibromoketones **79** (Scheme 29). In the first step hypobromous acid is generated under the reaction conditions. Then, the hypobromous acid is converted into dibromo monoxide (Br_2O) **80**. Next, the Br_2O species reacts with alkyne **78** to form a cyclic alkyne-bromonium ion complex **81**, which then generates a more stable vinyl carbocation intermediate. Finally, this intermediate undergoes a nucleophilic addition reaction with BrO^- affording α,α-dibromoketones **79**.



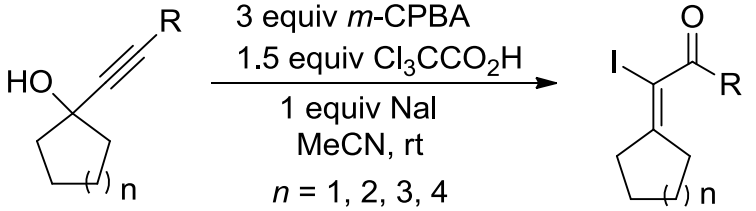
Scheme 29

Shreeve and co-workers have reported the use of Selectfluor as oxidant to generate electrophilic bromine Br^+ from potassium bromide. They found that treatment of phenylacetylene **84** with Selectfluor/KBr/H_2O afforded α,α-dibromoacetophenone **85** in 92% yield. However, in the presence of a small amount of acid or base the product was different. When Na_2CO_3 was added to the reaction mixture the product was *trans*-1,2-dibromostyrene **86** in 67% yield. In the case of using acetic acid a mixture of *cis* and *trans* products were formed but the major product was *cis*-1,2-dibromostyrene (Scheme 30).[47]



Scheme 30

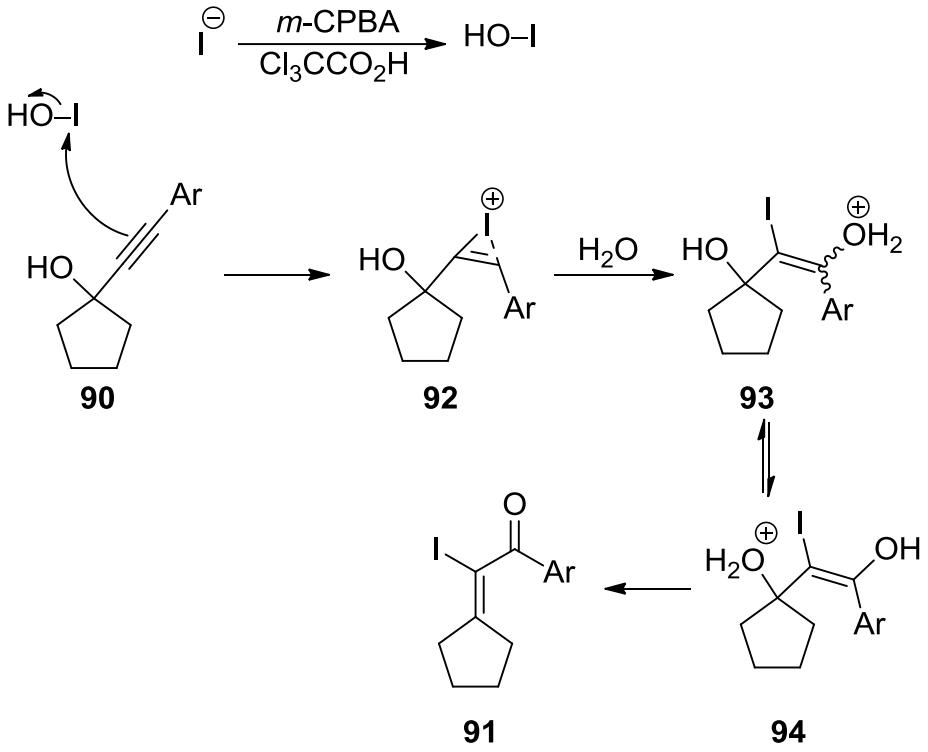
In a similar way our group recently published their work using sodium iodide with *m*-CBPA as oxidant to generate I^+. They stated that tertiary propargyl alcohols **90** undergo rearrangement to produce α-iodoenones **91** in good yields (Scheme 31).[48]



Scheme 31

The mechanism for the rearrangement of tertiary propargylic alcohols is shown in Scheme 32. First, hypoiodous acid (HOI) is formed from the reaction of sodium iodide with *m*-CPBA and

trichloroacetic acid. Then, hypoiodous acid reacts with the alkyne to form an iodonium cation intermediate **92**. Finally, the addition of water produces intermediate **93** which undergoes proton transfer and loss of water to give the α-iodoenone product **91**.



Scheme 32

1.4 Summary

In summary different methods for the bromination of various organic compounds have been discussed in this chapter. These methods involve using different sources of bromine such as molecular bromine (Br_2), *N*-bromosuccinimide (NBS), and bromide. The last source is cheap, readily available, and easy-to-handle. The use of inorganic bromide in electrophilic bromination reactions is one of the most important advances in recent years for the synthesis of bromo compounds.

2 Objective and aim

The objective of this study was to investigate the reactivity of sodium halides under oxidative conditions with a range of substrates. For this purpose, reactions with tertiary propargyl alcohols, homopropargyl alcohols, alkenes, and alkylbenzenes were carried out.

3 Results and Discussion

As discussed in the previous chapter, tertiary propargyl alcohols undergo rearrangement when treated with sodium iodide in the presence of an oxidant (Scheme 31). In our study we aimed to use sodium bromide or sodium chloride in place of sodium iodide to investigate whether a similar rearrangement process would occur under similar conditions (Figure 3).

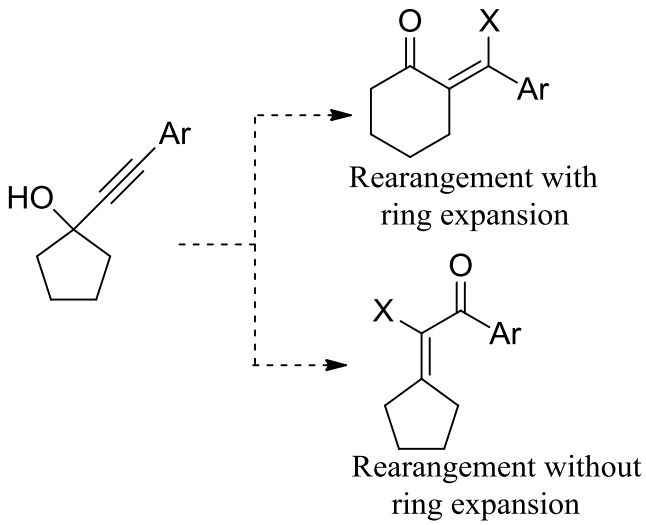
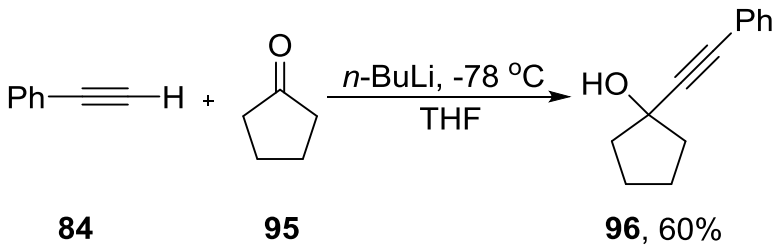


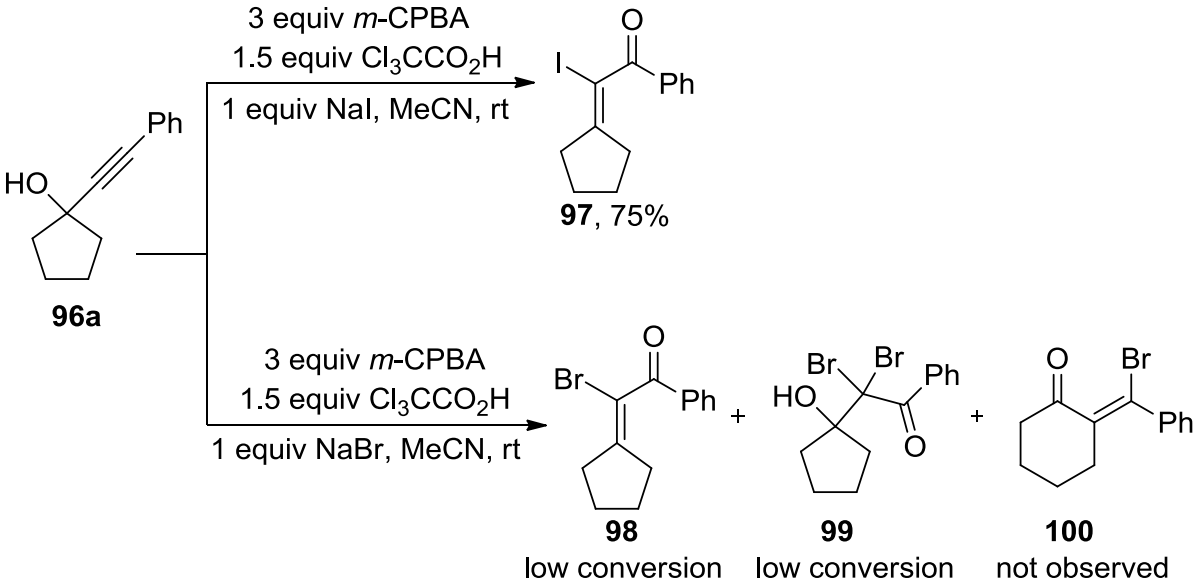
Figure 3

As shown in Figure 3, we envisioned two possible outcomes at the beginning of our investigation: (a) rearrangement with ring expansion; and /or (b) rearrangement without ring expansion. Tertiary propargyl alcohols **96a** were prepared from aldehydes/ketones and terminal alkynes using a known procedure (Scheme 33).[36]



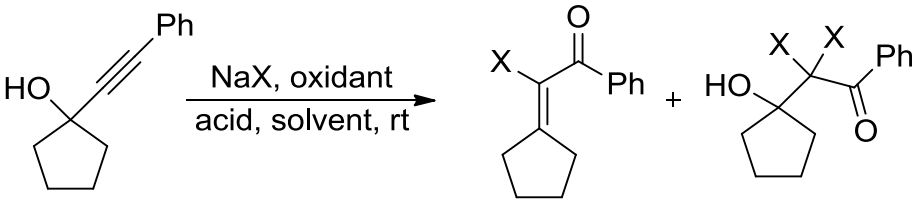
Scheme 33

Using our previously developed rearrangement conditions, alcohol **96** was mixed with NaI and *m*-chloroperbenzoic acid in the presence of trichloroacetic acid dissolved in acetonitrile, and the expected α-iodoenone **97** was formed in 75% yield (Scheme 34). However, exchanging NaI for NaBr only led to low yield of the analogous α-bromoenone **98.** Another product was formed during the reaction which after further investigation by ^{1}H NMR analysis was identified as the α,α-dibromoketone **99** but this were formed in low yield also. Moreover, it was observed that the rearrangement process occurred without ring expansion product **100** being formed.



Scheme 34

At this stage, we decided to investigate this process and develop optimised conditions. Initially different oxidants were tested and it was observed that Oxone® was the most effective oxidant (Table 1, entries 1-6). Then, the effect of using different acids, or no acid was investigated but only low or no conversion products were observed (entries 7-11). The use of different solvents in place of acetonitrile led to no reaction (entries 12-14).



96a **97** (X=I) **98** (X=Br) **99** (X=Br) **101** (X=Cl)

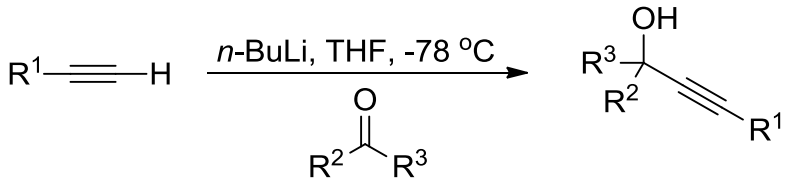
Entry	X	Oxidant	Acid	Solvent	Yield[a] (%)
1	Br	*m*CPBA	TCA	MeCN	22 (**98**), 9 (**99**)
2	Br	Oxone®	TCA	MeCN	35 (**98**), 9 (**99**)
3	Br	KIO_4	TCA	MeCN	0 (**98**), 0 (**99**)
4	Br	$PhI(OAc)_2$	TCA	MeCN	18 (**98**), 3 (**99**)
5	Br	H_2O_2	TCA	MeCN	–
6	Br	$NaBO_4$	TCA	MeCN	–
7	Br	Oxone®	TFA	MeCN	29 (**98**), 8 (**99**)
8	Br	Oxone®	AcOH	MeCN	–
9	Br	Oxone®	–	MeCN	30 (**98**), 10 (**99**)
10	Br	Oxone®	$TsOH·H_2O$	MeCN	–
11	Br	Oxone®	TfOH	MeCN	–
12	Br	Oxone®	TCA	MeOH	–
13	Br	Oxone®	TCA	CH_2Cl_2	–
14	Br	Oxone®	TCA	TFE	–
15	Br	Oxone®	TCA	$MeCN/H_2O$	63[b] (**99**)
16	Br	Oxone®	–	$MeCN/H_2O$	65[b] (**99**)
17	Cl	Oxone®	TCA	$MeCN/H_2O$	95[b] (**101**)
18	I	Oxone®	TCA	$MeCN/H_2O$	31 (**97**)
19	I	*m*CPBA	TCA	$MeCN/H_2O$	14 (**97**)

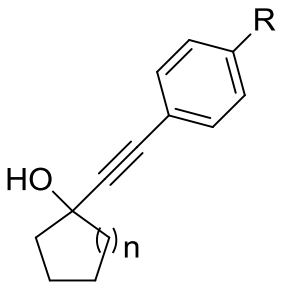
[a] Yield determined by ^1H NMR analysis. [b] Yield of pure isolated product.

Table 1

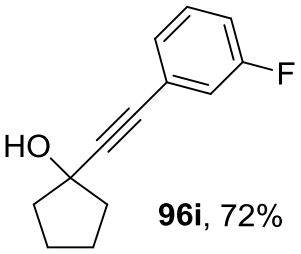
All attempts to isolate a pure sample of **98** by chromatography were unsuccessful due to the presence of **99** as impurity. We postulated that the availability of water during the reaction led to formation of the product **99**. At this point, we decided to add water to the reaction mixture and use a 1:1 mixture of acetonitrile and water. This had the desired effect as product **99** was isolated in 63% yield (entry 15). We repeated the reaction without the acid and this led to formation of product **99** in similar yield (entry 16), but it was more difficult to purify. Therefore, we decided to continue with trichloroacetic acid as an additive in the reaction. Replacing NaBr with NaCl led to complete conversion to the analogous chloride **101** in 95% yield (entry 17). However, repeating the reaction with NaI instead of NaBr under the conditions investigated led to formation of product **97** only with no sign of the α,α-diiodoketone product (entries 18-19).

In order to expand the substrate scope, tertiary propargyl alcohols (**96b**-**96k**) were prepared in an analogous fashion to **96a** in good yields (Scheme 35).

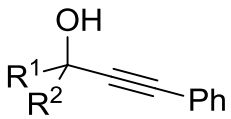




	n	R	Yield
96b	1	Me	77%
96c	1	Et	63%
96d	1	OMe	77%
96e	1	*t*-Bu	51%
96f	2	*t*-Bu	60%
96g	3	*t*-Bu	44%
96h	4	*t*-Bu	45%



96i, 72%

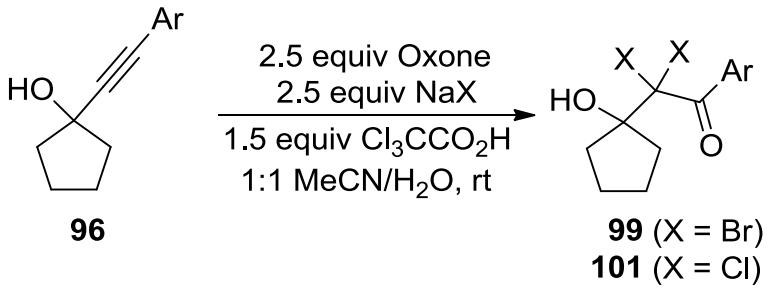


96j, R^1 = Me, R^2 = Et 85%

96k, R^1 = Me, R^2 = *t*-Bu 66%

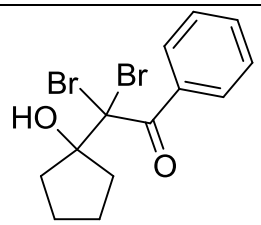
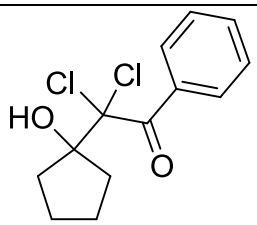
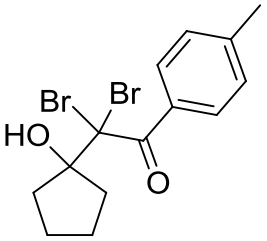
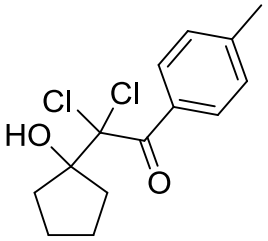
Scheme 35

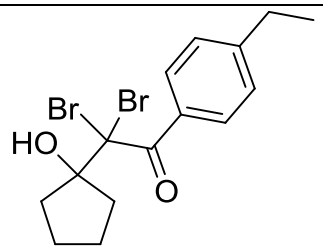
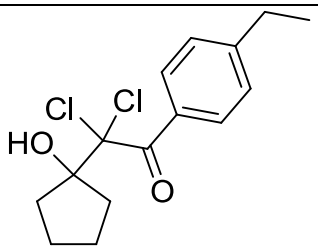
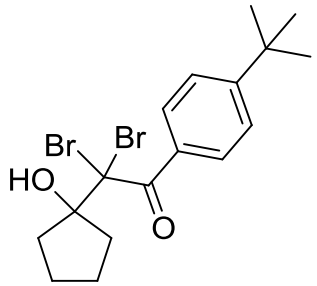
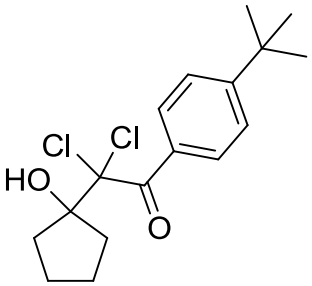
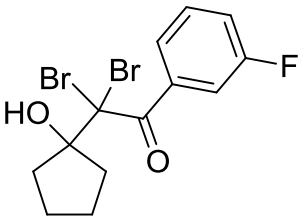
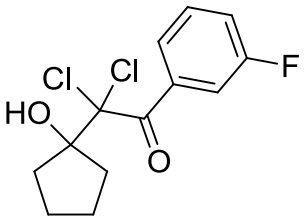
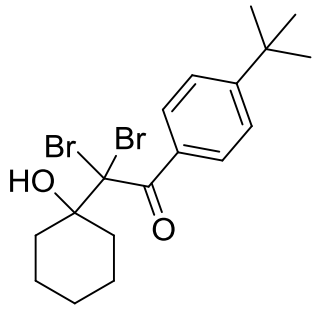
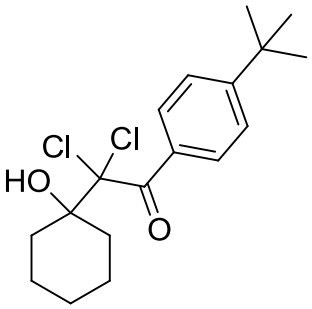
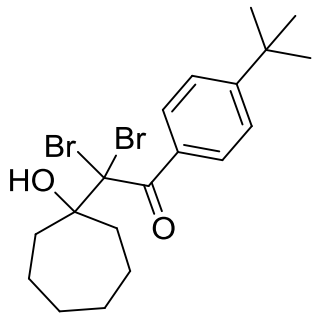
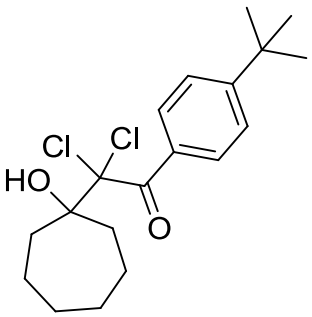
These alcohols (**96b-96k**) were subjected to the developed reaction conditions and the reaction worked in most cases studied. Different aromatic substituents, five-, six-, seven-, and-eight membered rings and open-chain substrates were all tolerated and led to formation of α,α-dihaloketones **99** and **101** in moderate to good yields (Table 2). In some cases, purification of the crude reaction mixture by silica gel chromatography led to partial decomposition of the product. For example, with **96d** and **96k,** the crude reaction mixtures were very messy, and pure samples were difficult to isolate. Also, attempts to purify the products **99h** and **101h** on silica gel led to diminished yields (entry 8).



96

99 (X = Br)
101 (X = Cl)

Entry	Product with NaBr	Yield (%)	Product with NaCl	Yield (%)
1	 **99a**	63	 **101a**	95
2	 **99b**	87	 **101b**	52

3	 **99c**	47	 **101c**	79
4	 **99e**	50	 **101e**	64
5	 **99i**	88	 **101i**	76
6	 **99f**	60	 **101f**	78
7	 **99g**	95	 **101g**	61

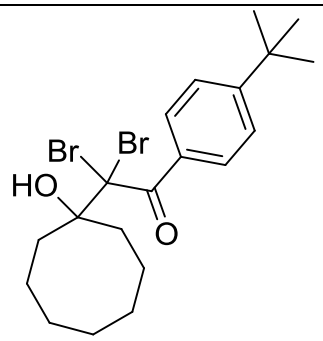
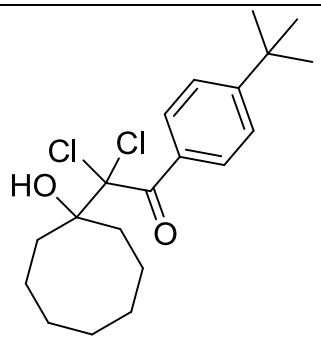
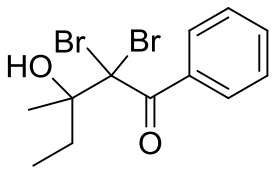
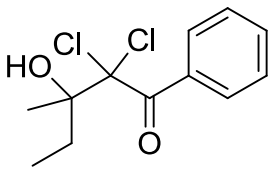
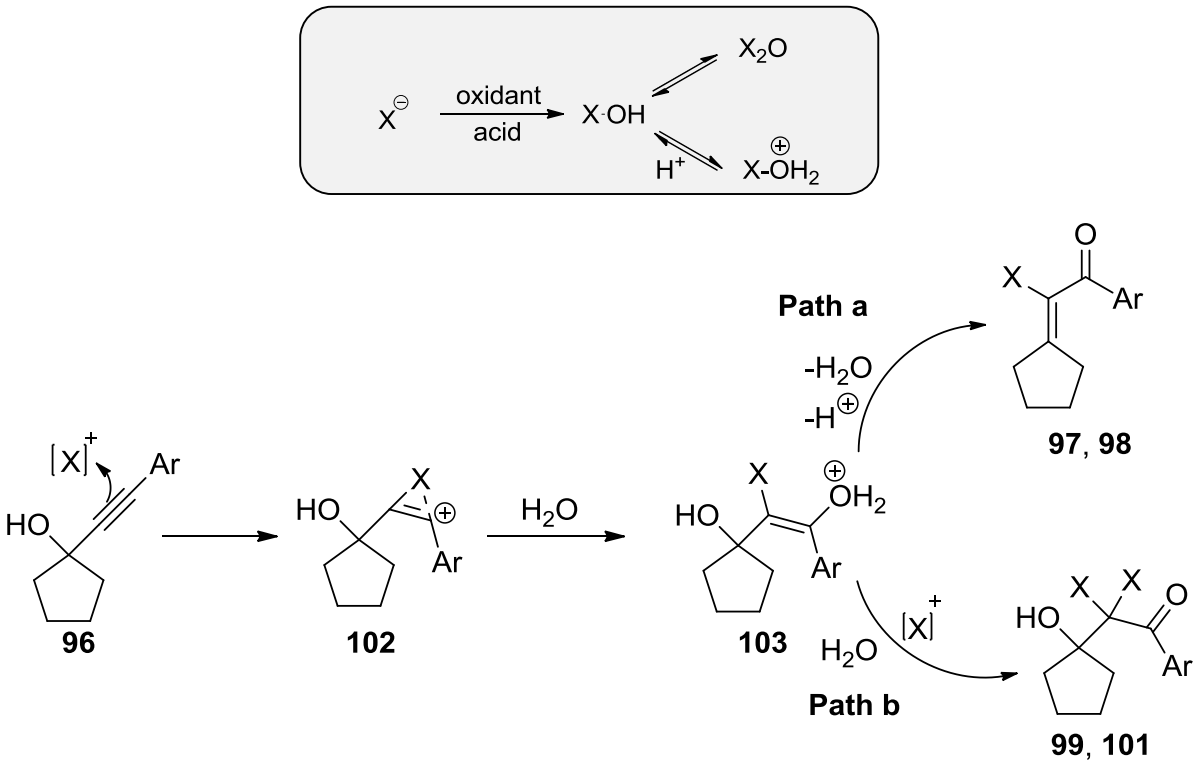
8	 **99h**	29	 **101h**	15
9	 **99j**	72	 **101j**	79

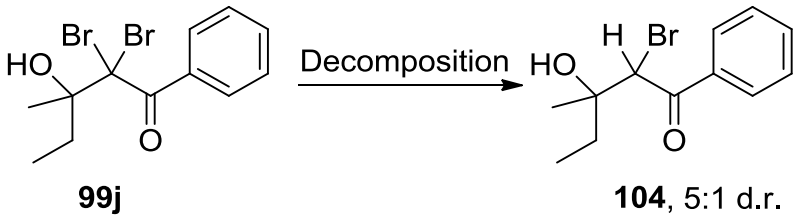
Table 2

The proposed mechanism of this process is shown in Scheme 36. The first step is oxidation of the halide to form the corresponding hypohalous acid. Then, we hypothesised that the hypohalous acid could be either protonated to generate a more reactive halogenating species or be converted into the halogen monoxide (X_2O) species.[49] Next, one of these species reacts with the alkyne **96** to generate the intermediate **102** and addition of water forms the hypothetical intermediate **103**. This intermediate leads to generation of the α-haloenone **97** or **98** by elimination of water (path a) or it reacts with a further equivalent of one of the halogen species to give an α,α-dihaloketone **99** or **101** (path b). Path a is more favoured in the absence of water, but in the presence of water the path b is favoured with bromide and chloride. Only the α-iodoenone is formed with iodide which is possibly due to the large size of iodine causing unfavourable steric interactions or iodide leads to formation of different species under the reaction conditions. Indeed, the reaction with NaI requires acidic conditions, whereas the reactions with NaCl and NaBr do not.



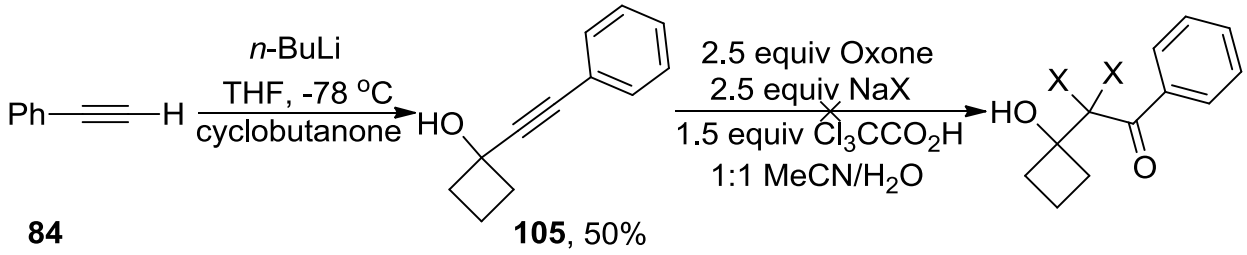
Scheme 36

Similar to the chemistry reported before for mono-dehalogenation of α,α-dihaloketones.[50,51] it was observed that after several weeks at room temperature under an air atmosphere, the product **99j** had decomposed into compound **104** as a 5:1 mixture of diastereomers (Scheme 37). The structure of the sample was identified by ^{1}H NMR analysis.



Scheme 37

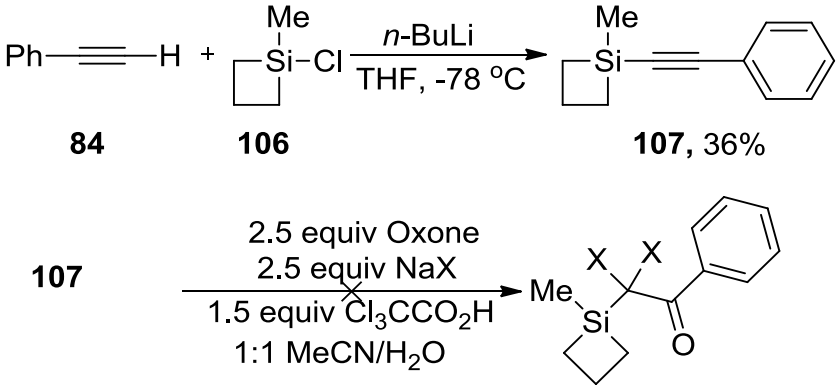
In a further effort to expand the scope of the reaction to include the smaller ring sizes, 1-(phenylethynyl)cyclobutane-1-ol **105** was prepared in an analogous fashion to propargyl alcohols. When our optimised conditions were tried with this substrate there was no product obtained and we recovered the starting material (Scheme 38).



84 **105**, 50%

Scheme 38

1-(Phenylethynyl)silacyclobutane **107** was readily prepared from the 1-chloro-1-methylsilacyclobutane **106** and phenylacetylene **84** and was subjected to our conditions, but unfortunately there was no sign of the desired product (Scheme 39).

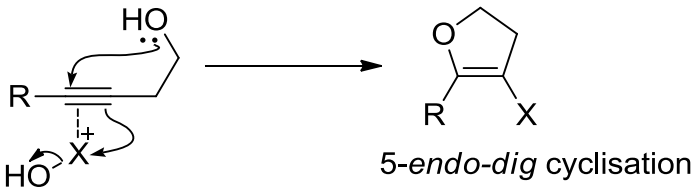


84 **106** **107,** 36%

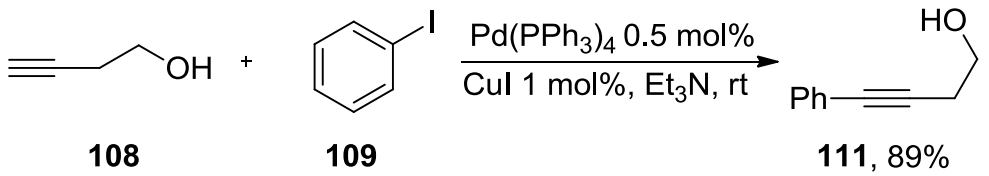
107

Scheme 39

After our success with propargyl alcohols, we wished to investigate homopropargyl alcohols under these reaction conditions. The presence of the alcohol could allow a 5-*endo-dig* cyclisation to occur instead of rearrangement (Scheme 40). Accordingly, we prepared homopropargyl alcohol **110** from 3-butyn-1-ol **108** in 89% yield by a Sonogashira coupling reaction (Scheme 41).[52]

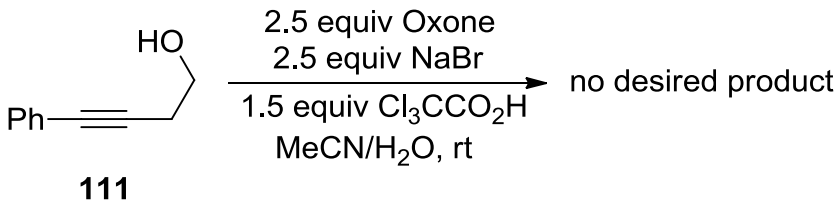


Scheme 40



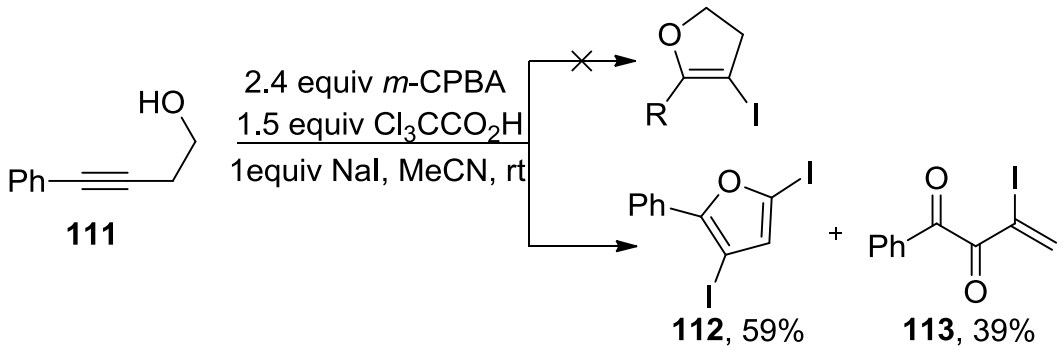
Scheme 41

Homopropargyl alcohol **111** was subjected to our reaction conditions, Oxone® and sodium bromide at room temperature, but unfortunately, no conversion of the starting material was observed (Scheme 42).



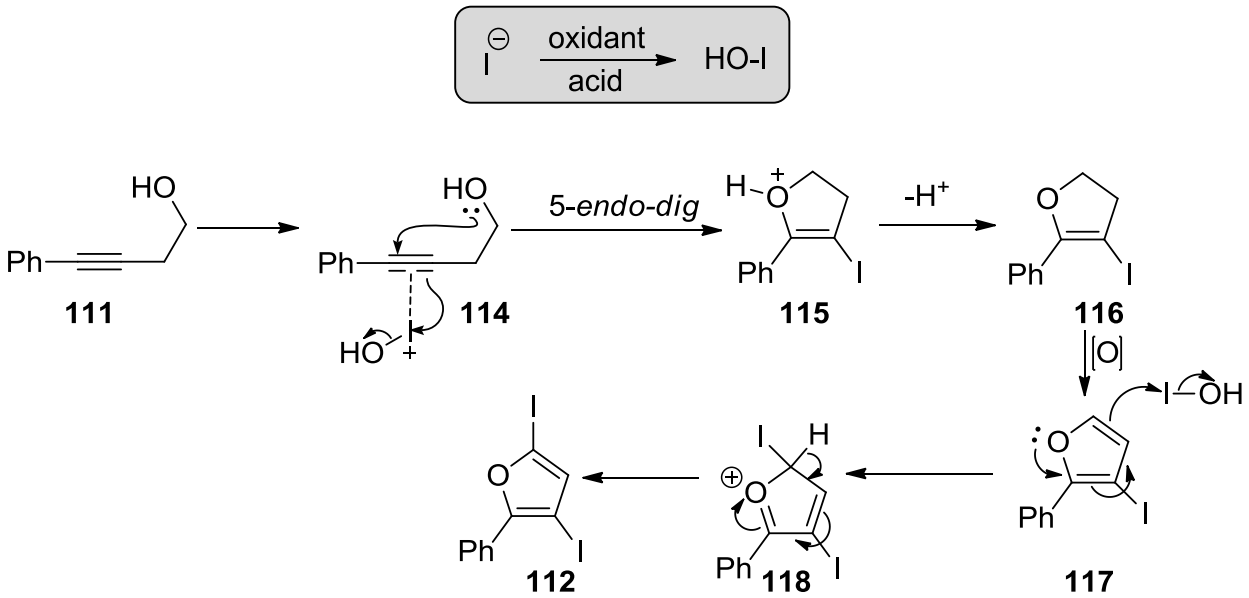
Scheme 42

At this point, we decided to use alternative conditions which had been previously published by our group.[48] Treatment of alcohol **111** with NaI and *m*-chloroperbenzoic acid in the presence of trichloroacetic acid in acetonitrile led to formation of cyclic product **112** and acyclic compound **113** the strctures of 3-iodo-1-phenylbut-3-ene-1,2-dione which were determined by ^{1}H NMR analysis (Scheme 43). Neither of these was the expected products, but the oxidative halogenations did work under these conditions. In order to improve this reaction to form one product, several different experiments were run, but unfortunately, all our attempts were unsuccessful and mixtures of these two compounds were obtained in all cases.



Scheme 43

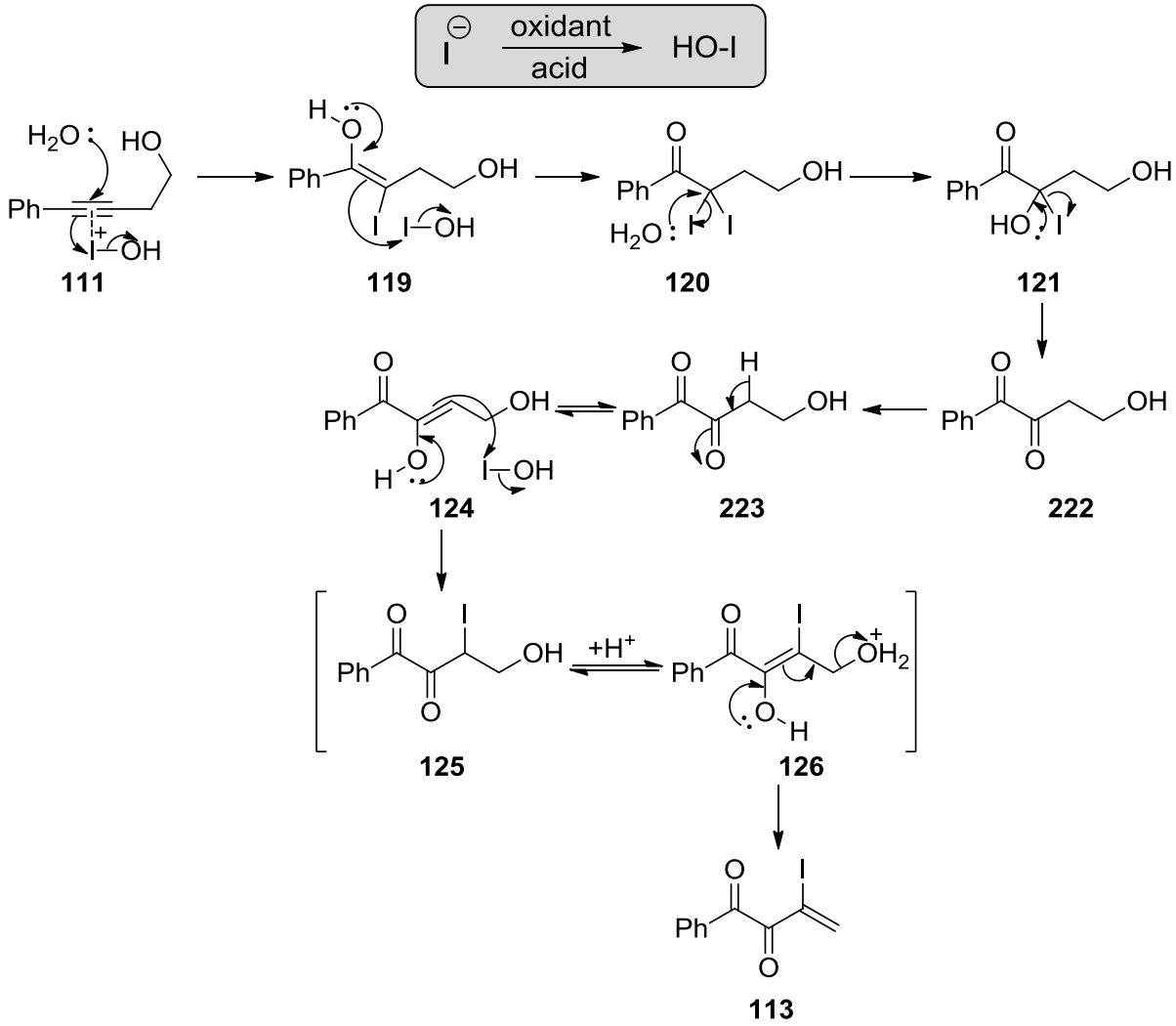
Mechanisms for formation of **112** and **113** can be proposed. Both mechanisms involve oxidation of the halide to generate a reactive halogenating species. Then, to form cyclised product **112** the first step is the cyclisation of **114** promoted by activation of the triple bond by hypoiodous acid (Scheme 44). Then, deprotonation of **115** forms **116** which is oxidised to **117**. Subsequent halogenation of **117** by a second equivalent of hypoiodous acid generates **112**.



Scheme 44

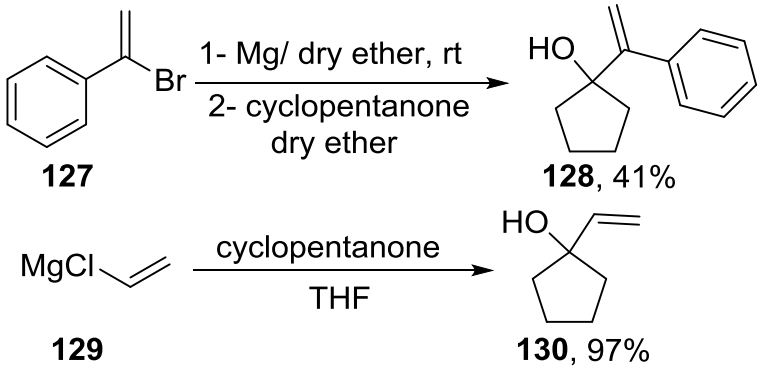
Alternatively, hypoiodous acid coordinates with the C-C triple bond and activates it to attack by H_2O to form **119.** This can react with a second equivalent of hypoiodous acid to generate diiodo intermediate **120**. Subsequent displacement by water can form diketone **121**. Next, under acidic

conditions the enol **124** could be iodinated to form **125** and then eliminate water to form the final product **113** (Scheme 45).



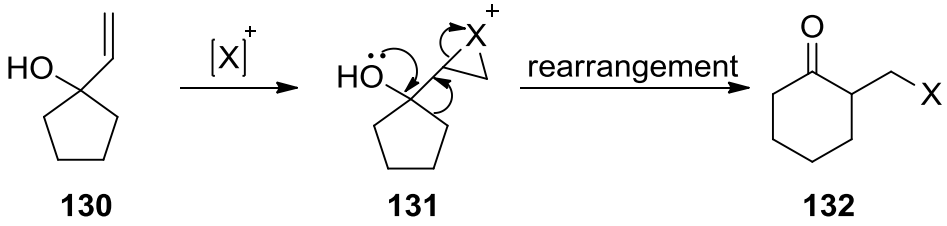
Scheme 45

We next sought to explore the effect of the reaction conditions on alkene substrates. Accordingly, tertiary propargyl alcohols **128** and **130** bearing alkene substitution were prepared in good yields by Grignard addition to cyclopentanone (Scheme 46).[53,54]



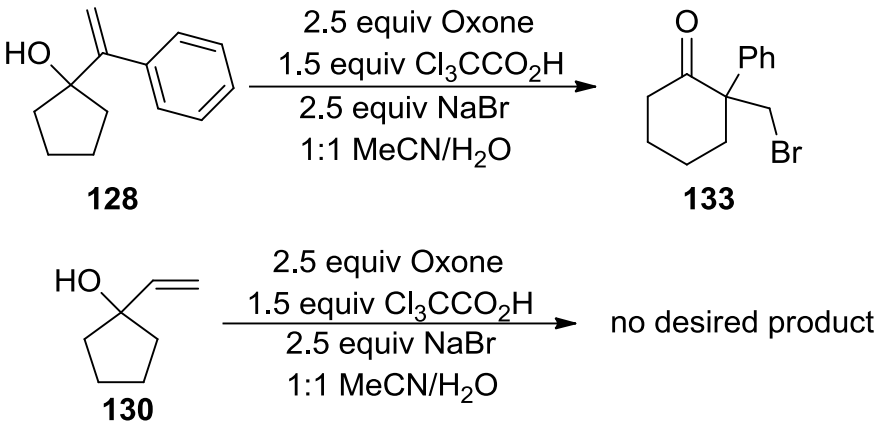
Scheme 46

Based on our previous work, i.e. Scheme 35, we hypothesised that halogenating species $[X]^+$ could react with alkene **130** to generate halonium intermediate **131**. Next, rearrangement could occur to form the ring expansion product **132**, i.e. undergo a (semipinacol rearrangement) (Scheme 47).



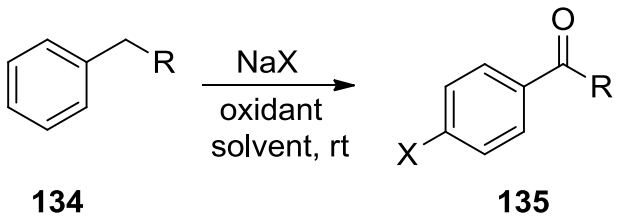
Scheme 47

With substrates **128** and **130** in hand, both were treated with our standard reaction conditions, but unfortunately with alkene **130** there was no product obtained, whereas with **128** a small amount of the desired ring expansion product **133** was observed. This was determined by ^{1}H NMR analysis of the crude reaction mixture, but a pure sample of the compound could not be obtained (Scheme 48). At this point we decided to abandon this reaction.



Scheme 48

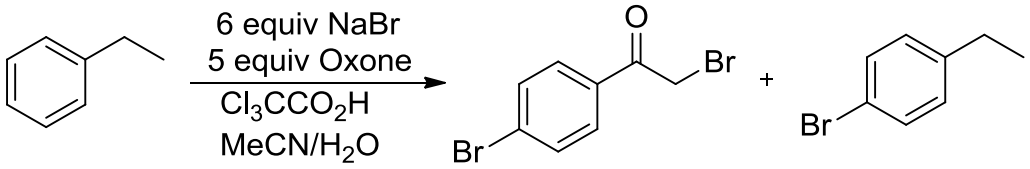
Despite the limited success with alkenes, we hoped to extend our work to simple alkylbenzenes to find out if functionalization of these substrates is possible under our conditions. We hypothesised that the halogenation of aromatic rings and oxidation of benzylic methylenes to ketones could occur in one step. Both transformations are known using similar condition to ours,[55,56] but not occurring simultaneously (Scheme 49).



Scheme 49

We began our investigation by treating ethyl benzene **134** with our previously developed conditions of sodium halides in the presence of Oxone and trichloroacetic acid in a mixture of acetonitrile and water at room temperature in the light (Table 3, entry 1). In the event, α-bromoketone **135** was formed but in low conversion. The reaction was attempted again in the dark (entry 2) but this also led to the product being formed in low yield. When the reaction mixture was heated at 50 ^{o}C in the dark, an increase in the yield of the product **135** was observed along with the formation of another product **136** (entry 3). Repeating the reaction and heating at 50 ^{o}C but in the light led to an improvement in the yield of the product **135** and it was isolated in 65% yield (entry 4). Then, we

ran the reaction without the trichloroacetic acid and this time the product **135** was isolated in 65% yield (entry 5). Hence, the acid is not necessary for this reaction to proceed. We were surprised that bromination adjacent to the ketone also occurred, and were intrigued to know whether this took place before or after ketone formation.



134 **135** **136**

Entry	Temperature (°C)	Conditions	Yield (%)[a]
1	20	in the light	<5(**135**)
2	20	in the dark	6 (**135**)
3	50	in the dark	16 (**135**), 13 (1**36**)
4	50	in the light	65 (**135**)
5	50	in the light	65 (**135**)[b]

[a] Yield of isolated compound. [b] No Cl_3CCO_2H added.

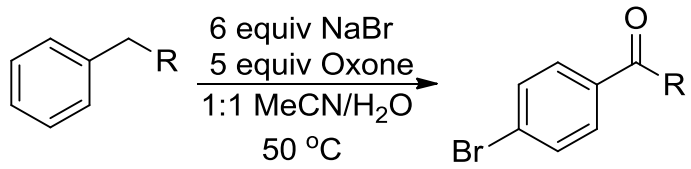
Table 3

In the crude reaction mixture, small amounts of the *ortho*- and *meta*- bromination products could be observed by ^{1}H NMR analysis but these could be easily removed by recrystallization. When we repeated the reaction with sodium chloride in place of sodium bromide low conversion of starting material was observed, so we decided to concentrate on sodium bromide.

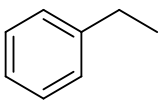
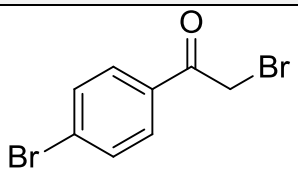
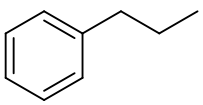
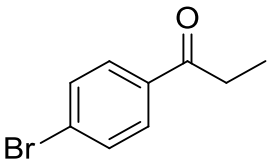
With these conditions in hand, the scope of this reaction was investigated (Table 4). When *n*-propylbenzene **134b** and *n*-butylbenzene **134c** were subjected to the reaction conditions both bromination of the aromatic ring and oxidation of the benzylic position occurred, although bromination adjacent to the ketone was not observed. Products **135b** and **135c** were isolated in good yields (entries 2 and 3), with the latter product being formed at room temperature. In a similar

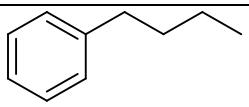
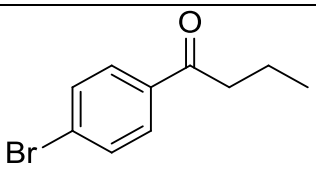
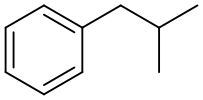
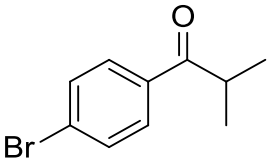
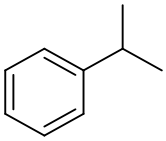
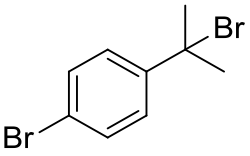
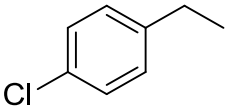
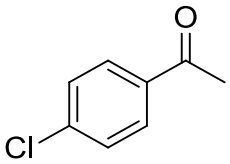
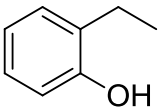
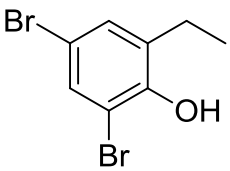
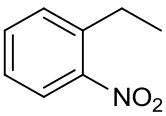
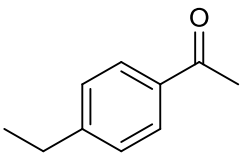
fashion isobutylbenzene **134d** was converted to ketone **135d** but in moderate yield (entry 4). Cumene **134e** was converted to the benzylic bromide **135e** in 57% yield (entry 5). This suggests that benzylic bromination rather than oxygenation occurs in these reactions.

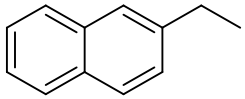
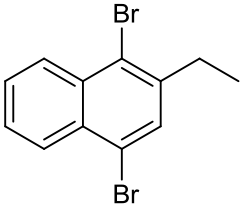
With a desire to increase the scope of this process further, a variety of substrates with aryl substituents were studied to explore their effect on reactivity. With a 4-chloro substituent, substrate **134f** was oxidized at the benzylic position to provide 73% yield of ketone **135f** (entry 6). Again, no bromination adjacent to the ketone occurred. With a phenol substituent no benzylic oxidation occurred due to the effect of the phenol group and instead double bromination of the ring was observed (entry 7). Surprisingly, substrates **134h** and **134i** containing electron-withdrawing substituents did not react under these conditions (entries 8, 9). 2-Ethylnaphthalene **134j** was not oxidized at the benzylic position either, but dibromination product **135j** was obtained in 32% yield (entry 10).



134 **135**

Entry	Substrate	Product	Yield[a] (%)
1	 **134a**	 **135a**	65
2	 **134b**	 **135b**	86

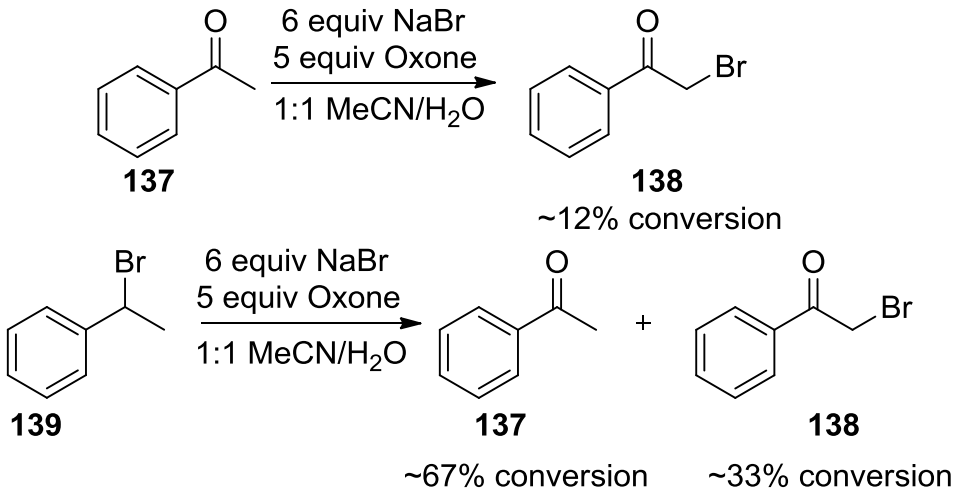
3	 **134c**	 **135b**	63[b]
4	 **134d**	 **135d**	30
5	 **134e**	 **135e**	57[b]
6	 **134f**	 **135f**	73[b]
7	 **134g**	 **135g**	74
8	 **134h**	no reaction	–
			

9	**134i**  **134j**	no reaction	–
10		 **135j**	32[b]

[a] Yield of isolated compound. [b] Reaction performed at room temperature.

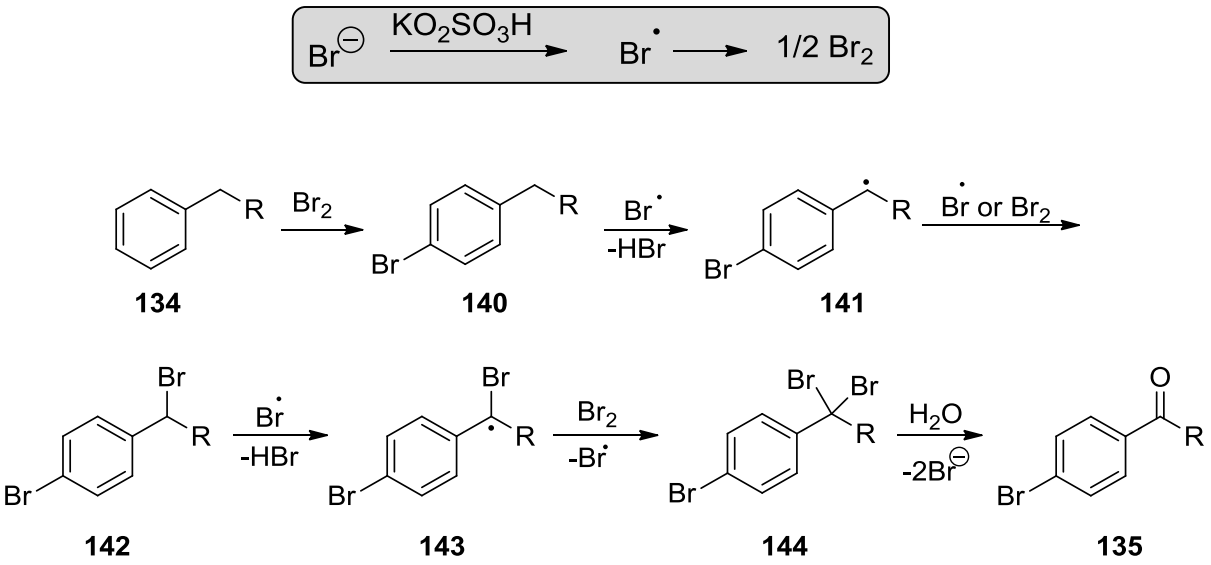
Table 4

In order to elucidate the mechanism of this process, two experiments were performed under the reaction conditions. Firstly, acetophenone **137** was treated with the reaction conditions and 12% of starting material was converted to α-bromination product **138** without ring bromination occurring (Scheme 50). In a second experiment, we treated 1-bromoethylbenzene **139** with the reaction conditions and two compounds were observed in an approximately 2:1 ratio; acetophenone **137** and α-bromination product **138**. These results suggest that bromination of the aromatic ring must occur before benzylic oxidation and the bromine adjacent to the ketone is installed via the tribromide not the ketone.



Scheme 50

A plausible mechanism for the functionalization of alkylbenzenes with sodium bromide is depicted in Scheme 51. First, oxidation of sodium bromide generates bromine radical and elemental bromine. Then, bromination of the alkylbenzene ring can occur to give intermediate **140**. Subsequent benzylic hydrogen atom abstraction can form **141,** which can combine with one of the bromine species to form the benzyl bromide **142**. Intermediate **142** can undergo a second hydrogen abstraction and **143** combine with another Br_2 or $Br^{\cdot}$ to afford dibromide **144**. Finally, in the presence of water dibromide intermediate **144** can be converted to ketone **135**.



Scheme 51

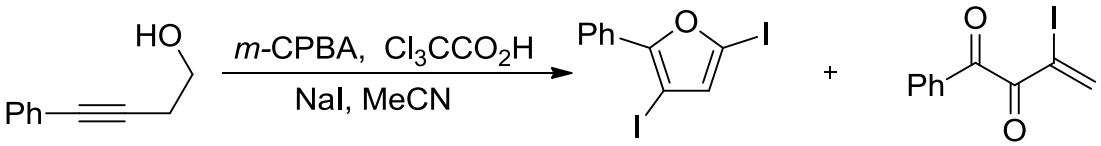
4 Conclusion

In summary, the reaction of tertiary propargyl alcohols has been developed under oxidative conditions with sodium bromide and chloride to generate *α,α*-dihalo-*β*-hydroxy ketones in good to excellent yields. This is a simple and efficient method for halogenations. Moreover, it was found that the presence of water in the reaction is responsible for generating the α,α-dihaloketones, whereas the α-haloenone is favored under anhydrous conditions. This work has been published.[57]

Also, we have developed an efficient method for the oxidative bromination of a range of simple alkylbenzenes up to 4 C-H bonds can be functionalised in this process by using a mixture of the inexpensive oxidant Oxone and NaBr. These results have also been published.[58]

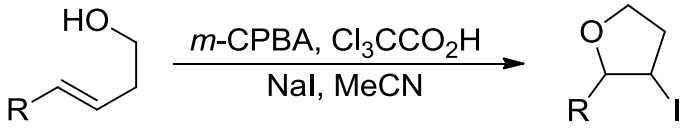
5 Future work

Future work in this area will need to focus on the improvement of the reaction of homopropargyl alcohols under oxidative conditions, as two compounds were formed in our preliminary work. More work is required to selectively form one of these two compounds as the major product (Scheme 52).



Scheme 52

Also, the cyclisation of the analogous alkenes could be investigated to produce tetrahydrofurans (Scheme 53).



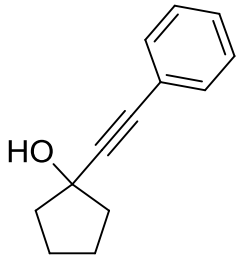
Scheme 53

6 Experimental

General. ^{1}H NMR spectra were recorded at 400 MHz. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard ($CDCl_3$: 77.4 ppm). Mass spectrometry (m/z) was performed in ESI mode, with only molecular ions being reported. Infrared (IR) spectra ν_{max} are reported in cm^{-1}. Bands are characterised as broad (br), strong (s), medium (m) and weak (w). Reagents were purchased from Sigma Aldrich and Fisher Scientific, they were used as received without further purification. Tetrahydrofuran was distilled from sodium wire and benzophenone under an atmosphere of nitrogen.

General procedure for the preparation of tertiary propargyl alcohols:

Synthesis of 1-(phenylethynyl)cyclopentanol, 96a:



Prepared by a procedure reported by Moran et al.[48] Phenylacetylene (0.54 mL, 4.9 mmol) was dissolved in THF (20 mL) at -78 ^{o}C under a N_2 atmosphere and *n*-BuLi (2.4 M, 2 mL, 4.9 mmol) was added dropwise. After 0.5 hour, the resulting mixture was added *via* cannula to a solution of cyclopentanone (0.43 mL, 4.9 mmol) in THF (20 mL) and stirred at -78 ^{o}C overnight. The reaction

was quenched by addition of water (5 mL) and extracted with ethyl acetate (2 x 10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under vacuum. The residue was purified by flash chromatography on silica gel (20:1 petroleum ether 40-60/EtOAc) to provide **96a** as a yellow oil (0.054 g, 60%).

IR (neat): 990 (m), 1488 (m), 2963 (w), 3335 (br) cm^{-1}.

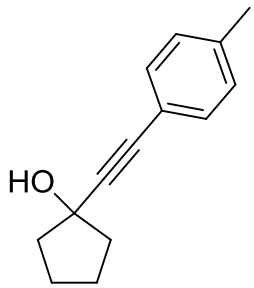
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.75-1.81 (2H, m), 1.84-1.91 (2H, m), 2.02-2.09 (4H, m), 2.17 (1H, s), 7.27-7.31 (3H, m), 7.40-7.44 (2H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ 23.8 (2C), 42.8 (2C), 75.2, 83.4, 93.2, 123.2, 128.5, 128.6 (2C), 131.9 (2C).

MS: m/z (M + 23) 209.0

HRMS: m/z calc'd for $[M + Na]^+$ $C_{13}H_{14}NaO$ 209.0937, found 209.0945.

Synthesis of 1-(*p*-tolylethynyl)cyclopentanol, 96b:



Synthesised according to the representative procedure for the formation of **96a,** using 4-ethynyltoluene (0.62 mL, 4.9 mmol) and cyclopentanone (0.43 mL, 4.9 mmol) to give **96b** (0.753 g, 77%) as a white solid.

Melting point: 50-51 °C. (Lit.:[48] 55-57 °C)

IR (neat): 995 (s), 2953 (m), 3215 (br) cm^{-1}.

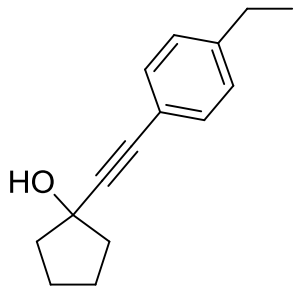
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.72-1.92 (5H, m), 1.96-2.11 (4H, m), 2.34 (3H, s), 7.10 (2H, d, *J* = 7.4 Hz), 7.31 (2H, d, *J* = 7.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 23.9 (2C), 43.0 (2C), 75.3, 83.5, 92.5, 120.1, 129.3 (2C), 131.8 (2C), 138.6.

MS: m/z (M – 17) 183.1

HRMS: m/z calc'd for $[M - OH]^+$ $C_{14}H_{15}$ 183.1168, found 183.1164.

Synthesis of 1-((4-ethylphenyl)ethynyl)cyclopentanol, 96c:



Synthesised according to the representative procedure for the formation of **96a,** using 1-ethyl-4-ethynylbenzene (0.68 mL, 4.9 mmol) and cyclopentanone (0.43 mL, 4.9 mmol) to provide **96c** (0.660 g, 63%) as a yellow oil.

IR (neat): 991 (s), 2963 (m), 3336 (br) cm^{-1}.

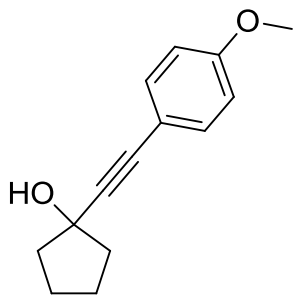
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (3H, t, *J* = 7.4 Hz), 1.73-1.94 (5H, m), 1.97-2.11 (4H, m), 2.63 (2H, q, *J* = 7.4 Hz), 7.13 (2H, d, *J* = 8.1 Hz), 7.34 (2H, d, *J* = 8.1 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 15.7, 23.9 (2C), 29.1, 43.0 (2C), 75.3, 83.5, 92.5, 120.4, 128.1 (2C), 132.0 (2C), 145.0.

MS: m/z (M – 17) 197.1

HRMS: m/z calc'd for $[M - OH]^+$ $C_{15}H_{17}$ 197.1336, found 197.1322.

Synthesis of 1-((4-methoxyphenyl)ethynyl)cyclopentan-1-ol, 96d:



Synthesised according to the representative procedure for the formation of **96a,** using 1-ethynyl-4-methoxybenzene (0.64 mL, 4.9 mmol) and cyclopentanone (0.43 mL, 4.9 mmol) to provide **96d (**0.813 g, 77%) as colourless oil.

$IR_{(neat)}$: 990 (s), 1170 (s), 1508 (s), 1605 (m), 2962 (w), 3394 (br) cm^{-1}.

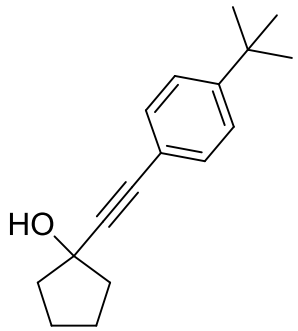
^1H NMR (400 MHz, $CDCl_3$): δ 1.72-1.92 (4H, m), 1.96-2.10 (5H, m), 3.80 (3H, s), 6.82 (2H, d, *J* = 8.8 Hz), 7.35 (2H, d, *J* = 8.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 23.8 (2C), 42.9 (2C), 55.6, 75.3, 83.3, 91.8, 114.2 (2C), 115.3, 133.4 (2C), 159.8.

MS: m/z (M – 17) 199.1

HRMS: m/z calc'd for $[M - OH]^+$ $C_{14}H_{15}O$ 199.1128, found 199.1115.

Synthesis of 1-((4-*tert*-butylphenyl) ethynyl)cyclopentanol, 96e:



Synthesised according to the representative procedure for the formation of **96a,** using 4-*tert*-butylphenylacetylene (0.88 mL, 4.9 mmol) and cyclopentanone (0.43 mL, 4.9 mmol) to provide **96e** (0.611 g, 51%) as a white solid.

Melting point: 63-65 ^{o}C. (Lit.:[48] 65-67 ^{o}C)

IR (neat): 996 (s), 2958 (m), 3255 (br) cm^{-1}.

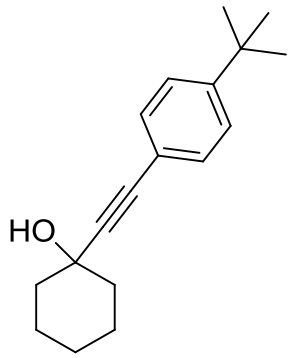
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (9H, s), 1.73-1.94 (5H, m), 1.97-2.12 (4H, m), 7.31 (2H, d, J = 8.5 Hz), 7.35 (2H, d, J = 8.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 23.9 (2C), 31.5 (3C), 35.1, 42.9 (2C), 75.3, 83.5, 92.5, 120.2, 125.6 (2C), 131.7 (2C), 150.8.

MS: m/z (M – 17) 225.1

HRMS: m/z calc'd for $[M - OH]^+$ $C_{17}H_{21}$ 225.1649, found 225.1634.

Synthesis of 1-((4-(tert-butyl)phenyl)ethynyl)cyclohexan-1-ol, 96f:



Synthesised according to the representative procedure for the formation of **96a,** using 4-*tert*-butylphenylacetylene (0.88 mL, 4.9 mmol) and cyclohexanone (0.51 mL, 4.9 mmol) to provide **96f** (0.750 g, 60%) as a white solid.

Melting point: 55-58 ^{o}C. (Lit.:[48] 55-57 ^{o}C)

IR (neat): 962 (s), 2930 (m), 3255 (br) cm^{-1}.

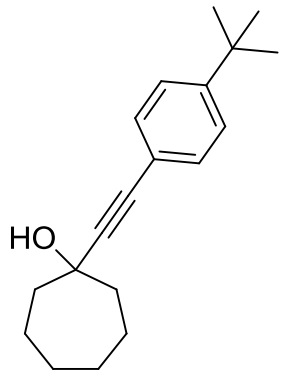
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (9H, s), 1.51-1.76 (8H, m), 1.95-2.07 (3H, m), 7.32 (2H, d, *J* = 8.3 Hz), 7.37 (2H, d, *J* = 8.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 23.8 (2C), 25.5, 31.5 (3C), 35.1, 40.4 (2C), 69.5, 84.8, 92.6, 120.1, 125.5 (2C), 131.7 (2C), 151.8.

MS: m/z (M + 17) 239.1

HRMS: m/z calc'd for $[M - OH]^+$ $C_{18}H_{23}$ 239.1800, found 239.1792.

Synthesis of 1-((4-*tert*-butylphenyl)ethynyl)cycloheptanol, 96g:



Synthesised according to the representative procedure for the formation of **96a,** using 4-*tert*-butylphenylacetylene (0.88 mL, 4.9 mmol) and cycloheptanone (0.57 mL, 4.9 mmol) to provide **96g** (0.580 g, 44%) as a white solid.

Melting point: 89-90 ^{o}C. (Lit.:[48] 90-92 ^{o}C)

IR (neat): 994 (s), 2971 (m), 3339 (br) cm^{-1}.

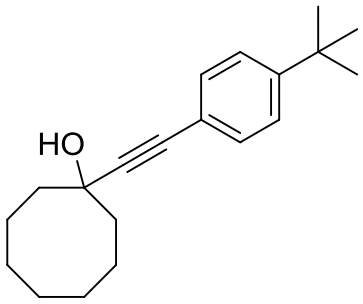
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (9H, s), 1.43-1.57 (3H, m), 1.59-1.76 (7H, m), 1.84 (1H, m), 1.98-2.06 (3H, m), 7.31 (2H, d, *J* = 7.3 Hz), 7.37 (2H, d, *J* = 7.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 22.5 (2C), 28.3 (2C), 31.5 (3C), 35.1, 38.8 (2C), 72.2, 83.7, 93.4, 120.2, 125.5 (2C), 131.7 (2C), 151.7.

MS: m/z (M + 23) 293.2

HRMS: m/z calc'd for $[M + Na]^+$ $C_{19}H_{26}NaO$ 293.1876, found 293.1876.

Synthesis of 1-((4-(*tert*-butyl)phenyl)ethynyl)cyclooctan-1-ol, 96h:



Synthesised according to the representative procedure for the formation of **96a,** using 4-*tert*-butylphenylacetylene (0.8 mL, 4.43 mmol) and cyclooctanone (0.58 mL, 4.43 mmol) to provide **96h** (0.573 g, 45%) as a white solid.

Melting point: 114- 116 ºC. (Lit.:[48] 115-116 ºC)

$IR_{(neat)}$: 980 (s), 2917 (m), 3263 (br) cm^{-1}.

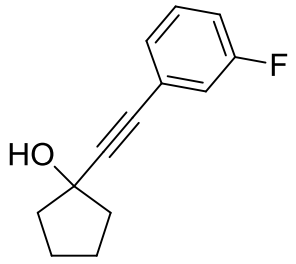
^1H NMR (400 MHz, $CDCl_3$): δ 1.29 (9H, s), 1.45-1.55 (2H, m), 1.59-1.74 (8H, m), 1.94-2.08 (4H, m), 2.36 (1H, br), 7.30 (2H, d, *J* = 8.6 Hz), 7.35 (2H, d, *J* = 8.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 22.6 (2C), 24.9, 28.3 (2C), 31.5 (3C), 35.1, 38.8 (2C), 72.2, 83.8, 93.4, 120.3, 125.6 (2C), 131.8 (2C), 151.8.

MS: m/z (M -17) 267.2

HRMS: m/z calc'd for $[M - OH]^+$ $C_{20}H_{27}$ 267.2118, found 267.2098.

Synthesis of 1-((3-fluorophenyl)ethynyl)cyclopentanol, 96i:



Synthesised according to the representative procedure for the formation of **96a,** using 1-ethynyl-3-fluorobenzene (0.57 mL, 4.9 mmol) and cyclopentanone (0.43 mL, 4.9 mmol) to provide **96i** (0.720 g, 72%) as a colourless oil.

IR (neat): 993 (s), 1579 (s) 1608 (m), 2962 (w), 3336 (br) cm^{-1}.

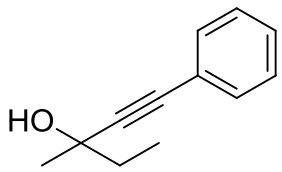
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.73-1.94 (4H, m), 1.98-2.11 (5H, m), 7.01 (1H, tdd, *J* = 8.6, 2.6, 1.4 Hz), 7.14 (1H, ddd, *J* = 9.6, 2.4, 1.4 Hz), 7.22 (1H, dt, *J* = 7.8, 1.3 Hz), 7.22-7.29 (1H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ 23.9 (2C), 42.9 (2C), 75.2, 82.3 (d, *J* = 3.4 Hz), 94.2, 115.9 (d, *J* = 20.3 Hz), 118.8 (d, *J* = 23 Hz), 125.1 (d, *J* = 9.5 Hz), 127.9 (d, *J* = 3.2 Hz), 130.2 (d, *J* = 9.5 Hz), 162.6 (d, *J* = 248 Hz).

MS: m/z (M – 17) 187.1

HRMS: m/z calc'd for $[M - OH]^+$ $C_{13}H_{12}F$ 187.0929, found 187.0913.

Synthesis of 3-methyl-1-phenylpent-1-yn-3-ol, 96j:



Synthesised according to the representative procedure for the formation of **96a,** using phenylacetylene (0.54 mL, 4.9 mmol), and butanone (0.44 mL, 4.9 mmol) to provide **96j** (0.725 g, 85%) as a yellow oil.

IR (neat):1112 (m), 1139 (m), 2952 (m), 3269 (br) cm^{-1}.

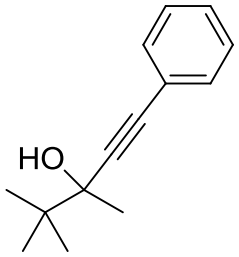
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.11 (3H, t, *J* =7.4 Hz), 1.57 (3H, s), 1.79 (2H, qd, *J* = 2.9 Hz), 2.14 (1H, br), 7.27-7.32 (3H, m), 7.38-7.45 (2H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ 9.4, 29.7, 37.0, 69.5, 83.7, 93.0, 123.1, 128.6 (3C), 132.0 (2C).

MS: m/z (M) 174.1

HRMS: m/z calc'd for $[M]^+$ $C_{12}H_{14}O$ 174.1039, found 174.1051.

Synthesis of 3,4,4-trimethyl-1-phenylpent-1-yn-3-ol, 96k:



Synthesised according to the representative procedure for the formation of **96a,** using phenylacetylene (0.76 mL, 6.9 mmol) and pinacolone (0.86 mL, 6.9 mmol) to provide **96k (**0.921 g, 66%) as a colourless oil.

$IR_{(neat)}$: 901 (m), 1070 (m), 2966 (m), 3457 (br) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.11 (9H, s), 1.53 (3H, s), 2.00 (1H, s), 7.27-7.33 (3H, m), 7.38-7.45 (2H, m).

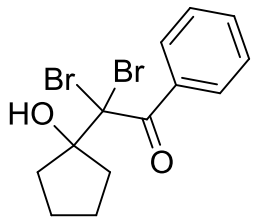
^{13}C NMR (100 MHz, $CDCl_3$): δ 25.1, 25.5 (3C), 38.8, 74.6, 84.2, 93.2, 123.3, 128.4, 128.5 (2C), 132.0 (2C).

MS: m/z (M – 17) 185.1

HRMS: m/z calc'd for $[M - OH]^+$ $C_{14}H_{17}$ 185.1330, found 185.1324.

Representative procedure for oxidative bromination/ chlorination of tertiary propargylic alcohols:

Synthesis of 2,2-dibromo-2-(1-hydroxycyclopentyl)-1-phenylethanone, 99a:



1-(Phenylethynyl)cyclopentanol (50 mg, 0.2 mmol, 1 equiv) **96a**, Oxone® (412 mg , 0.6 mmol, 2.5 equiv), NaBr (69 mg, 0.6 mmol, 2.5 equiv), and trichloroacetic acid (66 mg, 0.4 mmol, 1.5 equiv) were dissolved in acetonitrile (1 mL) at room temperature under a nitrogen atmosphere. Water (1 mL) was added dropwise to the mixture and it was stirred overnight. The reaction mixture was quenched with saturated aqueous sodium thiosulfate solution (5 mL) and extracted with DCM (5 mL x 2). The combined organic layers were washed with saturated aqueous sodium bicarbonate solution (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by flash chromatography on silica gel (20:1 petroleum ether 40-60/EtOAc) to give the product **99a** as a yellow oil (62 mg, 63%).

$IR_{(neat)}$: 686 (s), 810 (s), 1229 (m), 1665 (m), 2954 (w), 3539 (br) cm^{-1}.

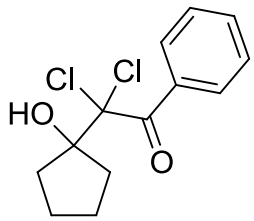
^1H NMR (400 MHz, $CDCl_3$): δ 1.71-1.81 (2H, m), 1.88-1.97 (2H, m), 2.03 -2.12 (2H, m), 2.37-2.46 (2H, m), 3.56 (1H, s), 7.46 (2H, t, *J* = 8.0 Hz), 7.58 (1H, t, *J* = 7.4 Hz), 8.40 (2H, d, *J* = 7.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 26.1 (2C), 39.6 (2C), 42.4, 89.8, 128.2 (2C), 131.8 (2C), 133.3, 133.9, 191.0.

MS: m/z (M + 23) 383.0

HRMS: m/z calc'd for $[M + Na]^+$ $C_{13}H_{14}Br^{79}$ Br^{81} NaO_2 382.9252, found 382.9248.

Synthesis of 2,2-dichloro-2-(1-hydroxycyclopentyl)-1-phenylethanone, 101a:



Synthesised according to the representative procedure for the formation of **99a,** using 1-(phenylethynyl)cyclopentanol (50 mg, 0.26 mmol, 1 equiv)**96a**. The obtained product was purified by flash chromatography (20:1 petroleum ether 40-60/EtOAc) to end up with **101a** as a colourless oil (67 mg, 95%).

$IR_{(neat)}$: 687 (s), 829 (m), 1234 (m), 1677 (m), 2956 (w), 3550 (br) cm^{-1}.

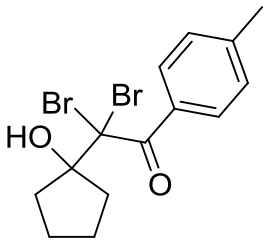
^1H NMR (400 MHz, $CDCl_3$): δ 1.67-1.78 (2H, m), 1.85-2.04 (4H, m), 2.25-2.37 (2H, m), 3.42 (1H, br), 7.48 (2H, t, J = 7.6 Hz), 7.60 (1H, t, J = 7.6 Hz), 8.32 (2H, d, J = 7.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 25.9 (2C), 38.5 (2C), 89.8, 90.7, 128.4 (2C), 131.6 (2C), 132.5, 134.2, 190.9.

MS: m/z (M + 23) 295.0

HRMS: m/z calc'd for $[M + Na]^+$ $C_{13}H_{14}Cl^{35}$ Cl $^{37}NaO_2$ 295.0273, found 295.02731.

Synthesis of 2,2-dibromo-2-(1-hydroxycyclopentyl)-1-(*p*-tolylethanone), 99b:



Synthesised according to the representative procedure for the formation of **99a,** using 1-(*p*-tolylethynyl)cyclopentanol (50 mg, 0.24 mmol, 1 equiv) **96b**. The obtained product was purified by flash chromatography (40:1 petroleum ether 40-60/EtOAc) to end up with **99b** as a brown solid (62 mg, 87%).

Melting point: 67-69 ^{o}C.

$IR_{(neat)}$: 601 (s), 831 (m), 1659 (m), 2955 (w), 3512 (br) cm^{-1}.

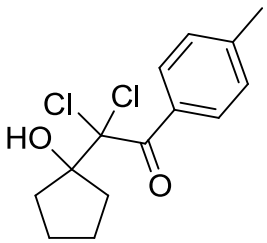
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.71-1.80 (2H, m), 1.88-1.98 (2H, m), 2.04-2.11 (2H, m), 2.37-2.46 (2H, m), 2.43 (3H, s), 3.6 (1H, br), 7.2 (2H, d, *J* = 8.6 Hz), 8.3 (2H, d, *J* = 8.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 22.1 (2C), 26.1 (2C), 39.6, 74.6, 89.8, 128.9 (2C), 130.5, 132.0 (2C), 145.2, 190.6.

MS: m/z (M + 23) 399.0.

HRMS: m/z calc'd for $[M + Na]^+$ $C_{14}H_{16}NaBr^{79}Br^{81}O_2$ 398.9389, found 398.9389.

Synthesis of 2,2-dichloro-2-(1-hydroxycyclopentyl)-1-(*p*-tolylethanone), 101b:



Synthesised according to the representative procedure for the formation of **99a,** using 1-(*p*-tolylethynyl)cyclopentanol (50 mg, 0.42 mmol, 1 equiv) **96b**. The obtained product was purified by flash chromatography (40:1 petroleum ether 40-60 /EtOAc) to end up with **101b** as a white solid (37 mg, 52%).

Melting point: 95-97 ^{o}C.

$IR_{(neat)}$: 665 (s), 853 (m), 1254 (m), 1671 (s), 2926 (w), 3516 (m) cm^{-1} .

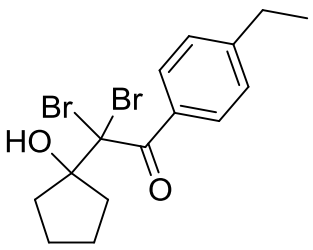
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.76-1.82 (2H, m), 1.92-2.10 (4H, m), 2.32-2.42 (2H, m), 2.50 (3H, s), 3.54 (1H, br), 7.34 (2H, d, *J* = 8.9 Hz), 8.30 (2H, d, *J* = 8.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 22.1 (2C), 25.8 (2C), 38.4, 89.7, 90.6, 129.1 (2C), 129.7, 131.7 (2C), 145.4, 190.4.

MS: m/z (M + 23) 309.0

HRMS: m/z calc'd for $[M + Na]^+$ $C_{14}H_{16}Cl^{35}Cl^{37}NaO_2$ 309.0419, found 309.0404.

Synthesis of 2,2-dibromo-1-(4-ethylphenyl)-2-(1-hydroxycyclopentyl)ethanone, 99c:



Synthesised according to the representative procedure for the formation of **99a,** using 1-((4-ethylphenyl)ethynyl)cyclopentanol (50 mg, 0.23 mmol, 1 equiv) **96c**. The product obtained was purified by flash chromatography (20:1 petroleum ether 40-60/EtOAc) to end up with **99c** as a colourless oil (42 mg, 47%).

$IR_{(neat)}$: 628 (s), 1229 (m), 1655 (m), 2960 (m), 3465 (br) cm^{-1}.

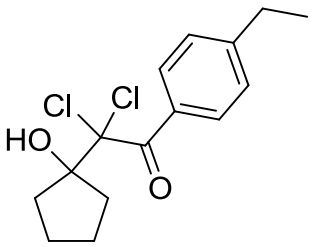
^1H NMR (400 MHz, $CDCl_3$): δ 1.28 (2H, t, *J* = 7.4 Hz), 1.70–1.81 (2H, m), 1.87-1.98 (2H, m), 2.03-2.11 (2H, m), 2.36-2.46 (2H, m), 2.75 (3H, q, *J* = 7.4 Hz), 3.61 (1H, br), 7.28 (2H, d, *J* = 8.2 Hz), 8.35 (2H, d, *J* = 7.9 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 15.4 (2C), 26.1, 29.3 (2C), 39.6, 74.6, 89.8, 127.7 (2C), 130.6, 132.1 (2C), 151.2, 190.6.

MS: m/z (M + 23) 411.0

HRMS: m/z calc'd for $[M + Na]^+$ $C_{15}H_{18}Br^{79}Br^{81}NaO_2$ 410.9565, found 410.9561.

Synthesis of 2,2-dichloro-1-(4-ethylphenyl)-2-(1-hydroxycyclopentyl)ethanone, 101c:



Synthesised according to the representative procedure for the formation of **99a,** using 1-((4-ethylphenyl)ethynyl)cyclopentanol (50 mg, 0.23 mmol, 1 equiv) **96c**. The obtained product was purified by flash chromatography (20:1 petroleum ether 40-60/EtOAc) to end up with **101c** as a yellow oil (55 mg, 79%).

$IR_{(neat)}$: 855 (m), 1251(m), 1671 (m), 2956 (w), 3551(br) cm^{-1}.

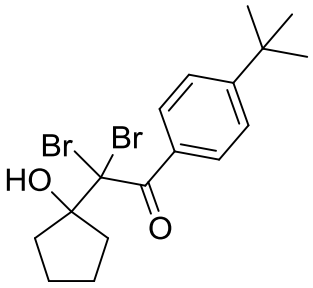
^1H NMR (400 MHz, $CDCl_3$): δ 1.28 (2H, t, *J* = 7.6 Hz), 1.66-1.77 (2H, m), 1.85-2.03 (4H, m), 2.25-2.35 (2H, m), 2.75 (3H, q, *J* = 7.6 Hz), 3.48 (1H, s), 7.30 (2H, d, *J* = 8.3 Hz), 8.26 (2H, d, *J* = 8.34 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 15.4, 25.9 (2C), 29.4, 38.6 (2C), 89.9, 90.7, 128.0 (2C), 129.9, 132 (2C), 151.6, 190.5.

MS: m/z (M + 23) 323.1

HRMS: m/z calc'd for $[M + Na]^+$ $C_{15}H_{18}Cl^{35}Cl^{34}NaO_2$ 323.0576, found 323.0574.

Synthesis of 2,2-dibromo-1-(4-(*tert*-butyl)phenyl)-2-(1-hydroxycyclopentyl)ethanon, 99e:



Synthesised according to the representative procedure for the formation of **99a,** using 1-((4-*tert*-butylphenyl) ethynyl)cyclopentanol (50 mg, 0.26 mmol, 1 equiv) **96e.** The obtained product was purified by flash chromatography (20:1 petroleum ether 40-60/EtOAc) to end up with **99e** as a white solid (86 mg, 50 %).

Melting point: 74-76 ºC.

$IR_{(neat)}$: 628 (s), 854 (s), 1248 (m), 1660 (m), 2959 (w), 3533 (br) cm^{-1}.

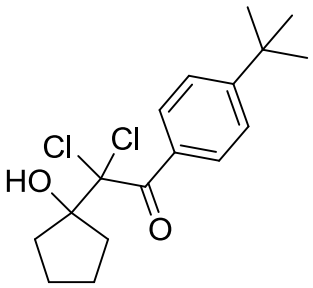
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (9H, s), 1.70-1.81 (2H, m), 1.87-1.98 (2H, m), 2.09-2.12 (2H, m), 2.36-2.46 (2H, m), 3.61 (1H, br), 7.46 (2H, d, J = 9.2 Hz), 8.36 (2H, d, J = 9.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 26.2, 31.4 (3C), 35.6 (2C), 39.7 (2C), 74.6, 89.9, 125.2 (2C), 130.3, 132 (2C), 158.1, 190.5.

MS: m/z (M + 23) 439.0

HRMS: m/z calc'd for $[M + Na]^+$ $C_{17}H_{22}NaBr^{79}Br^{81}O_2$ 438.9878, found 438.9872.

Synthesis of 1-(4-(*tert*-butyl)phenyl)-2,2-dichloro-2-(1-hydroxycyclopentyl)ethanone, 101e:



Synthesised according to representative procedure for the formation of **99a,** using 1-((4-*tert*-butylphenyl) ethynyl)cyclopentanol (50 mg, 0.20 mmol, 1 equiv) **96e**. The obtained product was purified by flash chromatography (20:1 petroleum ether 40-60/EtOAc) to end up with **101e** as a colourless oil (55 mg, 64%).

$IR_{(neat)}$: 669 (s), 857 (s), 1253 (m), 1672 (m), 2960 (w), 3534 (br) cm^{-1}.

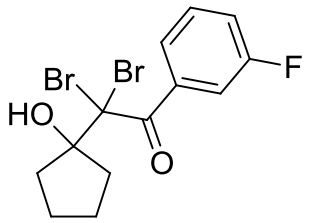
^1H NMR (400 MHz, $CDCl_3$): δ 1.34 (9H, s), 1.66-1.79 (2H, m), 1.85-2.03 (4H, m), 2.25-2.37 (2H, m), 3.47 (1H, br), 7.49 (2H, d, J = 8.2 Hz), 8.27 (2H, d, J = 8.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 25.9, 31.3 (3C), 35.6 (2C), 38.5 (2C), 90.7, 90.8, 125.5 (2C), 129.6, 131.8 (2C), 158.3, 190.4.

MS: m/z (M + 23) 351.1

HRMS: m/z calc'd for $[M + Na]^+$ $C_{17}H_{22}Cl^{35}Cl^{37}NaO_2$ 351.0889, found 351.0889.

Synthesis of 2,2-dibromo-1-(3-flurophenyl)-2-(1-hydroxycyclopentyl)ethanone, 99i:



Synthesised according to the representative procedure for the formation of **99a,** using 1-((3-fluorophenyl)ethynyl)cyclopentanol (50 mg , 0.24 mmol, 1 equiv) **96i**. The obtained product was purified by flash chromatography (5:1 petroleum ether 40-60/EtOAc) to end up with **99i** as a colourless oil (81 mg, 88%).

$IR_{(neat)}$: 681 (m), 1254 (s), 1669 (m), 2954 (w), 3542 (br) cm^{-1}.

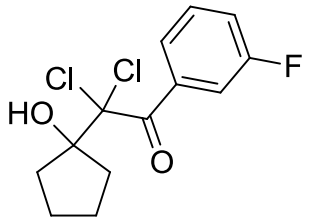
^1H NMR (400 MHz, $CDCl_3$): 1.70-1.82 (2H, m), 1.87-1.98 (2H, m), 2.01-2.11 (2H, m), 2.34-2.45 (2H, m), 3.41 (1H, br), 7.28 (1H, dt, *J* = 8.2, 2.5 Hz), 7.44 (1H, dt, *J* = 5.7, 8.0 Hz), 8.08 (1H, dt, *J* = 10, 2.3 Hz), 8.21 (1H, d, *J* = 7.9 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 26.1 (2C), 39.6 (2C), 74.3, 89.8, 118.7 (d, *J* = 24 Hz) 121.1 (d, *J* = 21 Hz), 127.7 (d, *J* = 3.0 Hz), 129.8 (d, *J* = 7.7 Hz), 135.3 (d, *J* = 6.8 Hz), 162.7 (d, *J* = 231 Hz), 189.7.

MS: m/z (M + 23) 400.9

HRMS: m/z calc'd for $[M + Na]^+$ $C_{13}H_{13}Br^{79}Br^{81}FNaO_2$ 400.9159, found 400.9150.

Synthesis of 2,2-dichloro-1-(3-fluorophenyl)-2-(1-hydroxycyclopentyl)ethanone, 101i:



Synthesised according to the representative procedure for the formation of **99a,** using 1-((3-fluorophenyl)ethynyl)cyclopentanol (50 mg, 0.24 mmol, 1 equiv) **99i**. The obtained product was purified by flash chromatography (5:1 petroleum ether 40-60/EtOAc) to end up with **101i** as a colourless oil (54 mg, 76%).

$IR_{(neat)}$: 699(s), 1257 (s), 1682 (m), 2957 (w), 3558 (br) cm^{-1}.

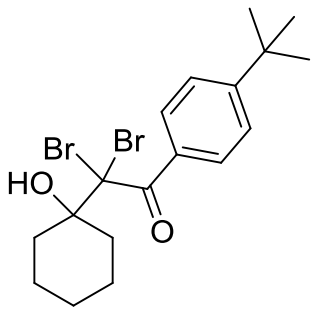
^1H NMR (400 MHz, $CDCl_3$): δ 1.68-1.80 (2H, m), 1.86-2.02 (4H, m), 2.26-2.35 (2H, m), 3.26 (1H , s), 7.30 (1H, dt, *J* = 2.4, 8.1 Hz), 7.45 (1H, dt, *J* = 5.8, 8.1 Hz), 8.0 (1H, dt, *J* = 2.1, 10 Hz), 8.12 (1H, d, *J* = 8.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 25.9 (2C), 38.5 (2C), 89.7, 90.6, 118.5 (d, *J* =24 Hz), 121.3 (d, *J* = 21 Hz), 127.4 (d, *J* = 3.0 Hz), 130.1 (d, *J* = 8.0 Hz), 134.5 (d, *J* = 7.0 Hz), 162.8 (d, *J* = 208 Hz), 189.5.

MS: m/z (M + 23) 313.0

HRMS: m/z calc'd for $[M + Na]^+$ $C_{13}H_{13}Cl^{35}Cl^{37}FNaO_2$ 313.0169, found 313.0164.

Synthesis of 2,2-dibromo-1-(4-(*tert*-butyl)phenyl)-2-(1-hydroxycyclohexyl)ethanone, 99f:



Synthesised according to the representative procedure for formation of **99a,** using 1-(*p*-tolylethynyl)cyclopentanol (50 mg , 0.19 mmol, 1 equiv) **96f**. The obtained product was purified by

flash chromatography (20:1 petroleum ether 40-60/EtOAc) to end up with **99f** as a yellow solid (50 mg, 60%).

Melting point: 94-95 ^{o}C.

$IR_{(neat)}$: 623 (s), 851 (m), 1243 (m), 1660 (m), 2926 (br), 3511 (w) cm^{-1}.

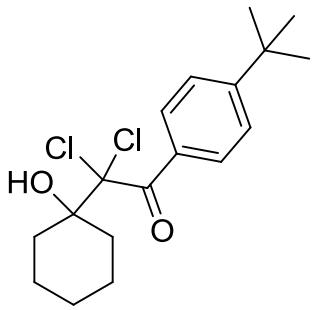
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (9H, s), 1.60-1.78 (6H, m), 1.98-2.07 (2H, m), 2.11-2.19 (2H, m), 3.92 (1H, br), 7.46 (2H, d, J = 9.0 Hz), 8.26 (2H, d, J = 8.7 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8 (2C), 25.8 (2C), 31.3 (3C), 31.7, 35.5, 72.2, 80.2, 125.3 (2C), 130.5, 131.4 (2C), 157.9, 191.6.

MS: m/z (M + 39) 469.0

HRMS: m/z calc'd for $[M + K]^{+}$ $C_{18}H_{24}Br^{79}Br^{81}KO_2$ 468.9775, found 468.9768.

Synthesis of 1-(4-(*tert*-butyl)phenyl)-2,2-dichloro-(1-hydroxycyclohexyl)ethanone, 101f:



Synthesised according to the representative procedure for the formation of **99a,** 1-(*p*-tolylethynyl)cyclopentanol (50 mg, 0.19 mmol, 1 equiv) **96f**. The obtained product was purified by flash chromatography (20:1 petroleum ether 40-60/EtOAc) to end up with **101f** as a yellow solid (51 mg, 78%).

Melting point: 77-80 ^{o}C.

$IR_{(neat)}$: 634 (s), 708 (m), 1252(m), 1666 (m), 2932 (br), 3528 (w) cm^{-1}.

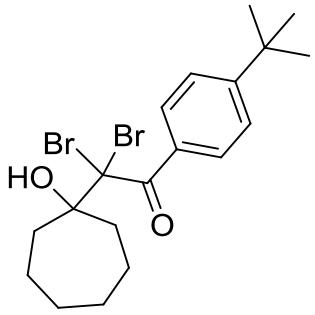
^1H NMR (400 MHz, $CDCl_3$): δ 1.34 (9H, m), 1.54-1.80 (6H, m), 1.83-1.93 (2H, m), 2.06 -2.14 (2H, m), 3.73 (1H, br), 7.48 (2H, d, J = 8.7 Hz), 8.20 (2H, d, J = 8.4 Hz).

^{13}C NMR (100MHz, $CDCl_3$): δ 21.8 (2C), 25.8 (2C), 31.3 (3C), 31.6, 35.5, 80.2, 91.9, 125.3 (2C), 130.5, 131.4 (2C), 157.9, 191.6.

MS: m/z (M + 23) 356.1

HRMS: m/z calc'd for $[M + Na]^+$ $C_{18}H_{24}Cl^{35}Cl^{37}NaO_2$ 365.1053, found 365.1053.

Synthesis of 2,2-dibromo-1-(4-(*tert*-butyl)phenyl)-2-(1-hydroxycycloheptyl)ethanone, 99g:



Synthesised according to the representative procedure for the formation of **99a,** using 1-((4-*tert*-butylphenyl)ethynyl)cycloheptanol (50 mg, 0.18 mmol, 1 equiv) **96g**. The obtained product was purified by flash chromatography (20:1 petroleum ether 40-60/EtOAc) to end up with **99g** as a brown oil (73 mg, 95%).

$IR_{(neat)}$: 623 (s), 854 (s), 1233(m), 1660 (m), 2926 (w), 3501 (br) cm^{-1}.

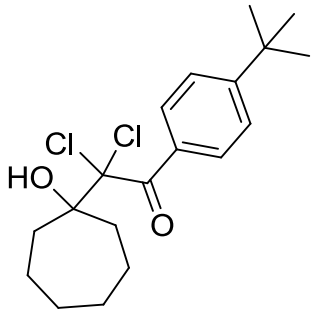
^1H NMR (400 MHz, $CDCl_3$): δ 1.35 (9H, s), 1.50-1.60 (4H, m), 1.62-1.71 (4H, m), 1.77-1.87 (2H, m), 2.12-2.20 (2H, m), 4.30 (1H, br), 7.45 (2H, d, J = 8.5Hz), 8.24 (2H, d, J = 8.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 23.1, 24.2, 28.8, 29.2, 31.3 (3C), 35.5, 37.5, 42.7, 82.7, 70.4, 125 (2C), 127.9, 131.5 (2C), 157.6, 193.1.

MS: m/z (M + 23) 467.0

HRMS: m/z calc'd for $[M + Na]^+$ $C_{19}H_{26}Br^{79}Br^{81}NaO_2$ 467.0191, found 467.0174.

Synthesis of 1-(4-(*tert*-butyl)phenyl)-2,2-dichloro-2-(1-hydroxycycloheptyl)ethanone, 101g:



Synthesised according to the representative procedure for the formation of **99a,** using 1-((4-*tert*-butylphenyl)ethynyl)cycloheptanol (50 mg, 0.18 mmol, 1 equiv) **96g**. The obtained product was purified by flash chromatography (20:1 petroleum ether 40-60/EtOAc) to end up with **101g** as a yellow oil (26 mg, 61%).

$IR_{(neat)}$: 670 (s), 864 (s), 1250 (s), 1670 (m), 2926 (w) cm^{-1}.

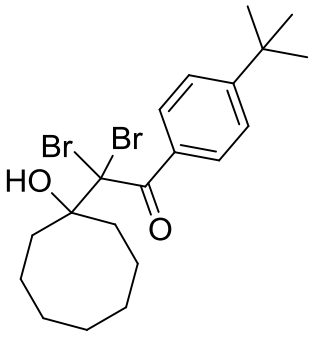
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (9H, s), 1.53-1.59 (4H, m), 1.61-1.69 (4H, m), 1.75-1.83 (2H, m), 2.09-2.14 (2H, m), 4.07 (1H, br), 7.46 (2H, d, J = 8.7 Hz), 8.17 (2H, d, J = 8.7 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 23.8, 26.4, 28.1, 29.5, 31.3 (3C), 35.5, 36.6, 42.0, 83.0, 92.6, 125.3 (2C), 130.7, 131.4 (2C), 157.9, 192.5.

MS: m/z (M + 23) 379.1

HRMS: m/z calc'd for $[M + Na]^+$ $C_{19}H_{26}Cl^{35}Cl^{37}NaO_2$ 379.1202, found 379.1223.

Synthesis of 2,2-dibromo-1-(4-(*tert*-butyl)phenyl)-2-(1-hydroxycyclooctyl)ethan-1-one, 99h:



According to representative procedure for the formation of **99a,** using 1-((4-*tert*-butylphenyl)ethynyl) cyclooctanol (50 mg, 0.17 mmol, 1 equiv) **96h**, The obtained product was purified by flash chromatography (20:1 petroleum ether 40-60/EtOAc) to end up with **99h** which was obtained not clean and afforded as colourless oil (0.022 g, 29%).

$IR_{(neat)}$: 853 (s), 1244 (m), 1659 (m), 2922 (w), 3500 (br) cm^{-1}.

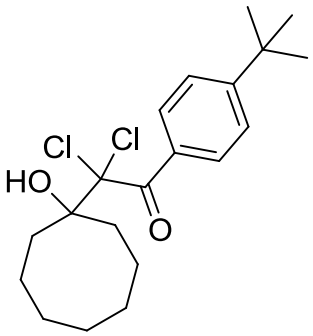
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.35 (9H, s), 1.47-1.74 (12H, m), 2.09-2.21 (2H, m), 4.31 (1H, br), 7.45 (2H, d, *J* = 8.3 Hz), 8.22 (2H, d, *J* = 8.3 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): 21.7 (2C), 22.9, 25.1 (2C), 28.0 (2C), 31.4 (3C), 35.5, 72, 81.6, 125.1 (2C), 127.9, 131.4 (2C), 157.6, 193.5.

MS: m/z (M + 23) 481.0

HRMS: m/z calc'd for $[M + Na]^+$ $C_{20}H_{28}Br^{79}Br^{81}NaO_2$ 481.0348 found 481.0321.

Synthesis of 1-(4-(*tert*-butyl)phenyl)-2,2-dichloro-2-(1-hydroxycyclooctyl)ethan-1-one, 101h:



According to representative procedure for the formation of **99a**, using 1-((4-*tert*-butylphenyl)ethynyl) cyclooctanol (50 mg, 0.17 mmol, 1 equiv) **96h**, The obtained product was purified by flash chromatography (20:1 petroleum ether 40-60/EtOAc) to end up with **101h** which was obtained not clean and afforded as colourless oil (0.009 g, 15%).

$IR_{(neat)}$: 855 (m), 1249 (m), 1670 (m), 2923 (w), 3513 (br) cm^{-1}.

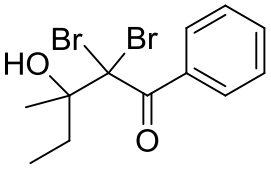
^1H NMR (400 MHz, $CDCl_3$): δ 1.34 (9H, s), 1.47-1.75 (9H, m), 1.81-1.93 (2H, m), 2.10-2.17 (3H, m), 4.08 (1H, br), 7.47 (2H, d, *J* = 8.5 Hz), 8.15 (2H, d, *J* = 8.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 22.4 (2C), 25.0 (2C), 28.0 (3C), 31.3 (3C), 33.2, 35.5, 82.0, 125.3 (2C), 130.9, 131.3 (2C), 157.9, 193.0.

MS: m/z (M + 23) 393.1

HRMS: m/z calc'd for $[M + Na]^+$ $C_{20}H_{28}Cl^{35}Cl^{37}NaO_2$ 393.1359 found 393.1358.

Synthesis of 2,2-dibromo-3-hydroxy-4-methyl-1-phenylpentan-1-on, 99j:



Synthesised according to the representative procedure for the formation of **99a,** using 3-methyl-1-phenylpent-1-yn-3-ol (50 mg, 0.28 mmol, 1 equiv) **96j**. The obtained product was purified by flash

chromatography (100:1 petroleum ether 40-60/EtOAc) to end up with **99j** as an orange oil (0.070 g, 72%).

$IR_{(neat)}$: 687 (s), 808 (m), 1227 (m), 2970 (w), 3520 (br) cm^{-1}.

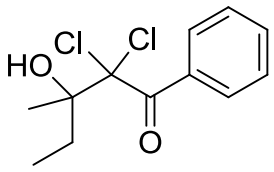
^1H NMR (400 MHz, $CDCl_3$): δ 1.08 (3H, t, *J* = 7.5 Hz), 1.61 (3H, br), 2.06 (2H, q, *J* = 7.7 Hz), 4.04 (1H, br), 7.46 (2H, t, *J* = 8.2 Hz), 7.54 (1H, t, *J* = 7.4 Hz), 8.28 (2H, d, *J* = 7.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 8.8, 22.8, 30.1, 74.9, 81.0, 128.7 (2C), 131.3 (2C), 133.7, 134.5, 193.0.

MS: m/z (M + 23) 370.9

HRMS: m/z calc'd for $[M + Na]^+$ $C_{12}H_{14}Br^{35}Br^{37}NaO_2$ 370.9253, found 370.9243.

Synthesis of 2,2-dichloro-3-hydroxy--methyl-1-phenylpentan-1-one, 101j:



Synthesised according to the representative procedure for the formation of **99a,** using 3-methyl-1-phenylpent-1-yn-3-ol (50 mg, 0.28 mmol, 1 equiv) **96j**. The obtained product was purified by flash chromatography (100:1 petroleum ether 40-60/EtOAc) to end up with **101j** as a yellow oil (0.058 g, 79%).

$IR_{(neat)}$: 688 (s), 824 (m), 1231 (m), 1676 (m), 2974 (w), 3533 (br) cm^{-1}.

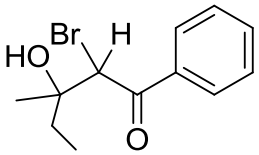
^1H NMR (400 MHz, $CDCl_3$): δ 1.07 (3H, t, *J* = 7.5 Hz), 1.54 (3H, br), 1.88-2.07 (2H, m), 3.82 (1H, br), 7.45 (2H, t, *J* = 8.2 Hz), 7.58 (1H, t, *J* = 7.5 Hz), 8.22 (2H, d, *J* = 7.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 8.3, 21.5, 29.2, 81.1, 91.5, 128.3 (2C), 131.2 (2C), 133.4, 133.9, 192.5.

MS: m/z (M + 23) 283.0

HRMS: m/z calc'd for $[M + Na]^+$ $C_{12}H_{14}Cl^{35}Cl^{37}NaO_2$ 283.0263, found 283.0258.

Synthesis of 2-bromo-3-hydroxy-3-methyl-1-phenylpentan-1-one, 104:



Upon standing at room temperature under an air atmosphere after several weeks, compound **99j** had decomposed and was purified by preparatory TLC (silica gel, 20:1 petroleum ether/EtOAc) to give the product **104** as a 5:1 mixture of diastereomers as a yellow oil.

Data given for the major diastereomer **104**. Whereas, the data for minor diastereomer was not obtained due to the small amount.

$IR_{(neat)}$: 685 (s), 1223 (m), 1667 (m), 2973 (w), 3481 (br) cm^{-1}.

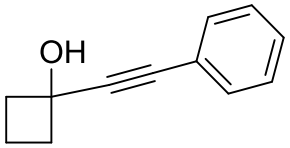
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.94-1.00 (3H, t, J = 7.4 Hz), 1.39 (3H, s), 1.74-1.87 (2H, m), 4.07 (1H, br), 5.15 (1H, s), 7.51 (2H, t, J = 7.4 Hz), 7.62 (1H, t, J = 8.0 Hz), 7.99 (2H, d, J = 6.9 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 8.2, 23.7, 33.3, 62.6, 73.6, 129.2 (2C), 129.3 (2C), 134.7, 135.2, 196.3.

MS: m/z (M + 23) 293.0

HRMS: m/z calc'd for $[M + Na]^+$ $C_{12}H_{15}BrNaO_2$ 293.0148, found 293.0158.

Synthesis of 1-(phenylethynyl)cyclobutan-1-ol, 105:[59]



Synthesised according to the representative procedure for the formation of **96a,** using phenylacetylene (0.54 mL, 4.9 mmol), cyclobutanone (0.37 mL, 4.9 mmol) to give **105** (0.419 g, 50%) as a white solid.

Melting point: 43-46 ^{o}C.

$IR_{(neat)}$: 692 (s), 783 (s), 1150 (s), 1421 (m), 1488 (m), 2937 (w), 2988 (w), 3289 (br) cm^{-1}.

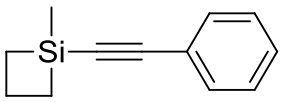
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.83-1.92 (2H, m), 2.35 (2H, qd, *J* = 9.3, 2.2 Hz), 2.49-2.57 (2H, m), 3.50 (1H, s), 7.29-7.32 (3H, m), 7.44 (2H, dd, *J* = 6.2, 3.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 13.3, 38.9 (2C), 68.6, 83.8, 92.8, 123.1, 128.2 (2C), 128.3, 132.0 (2C).

MS: m/z (M + 23) 195.1

HRMS: m/z calc'd for $[M + Na]^+$ $C_{12}H_{12}NaO$ 195.0780, found 195.0882.

Synthesis of 1-methyl-1-(phenylethynyl)silacyclobutane, 107:[60]



Synthesised according to the representative procedure for the formation of **96a,** using 1-chloro-1-methylsilacyclobutane (0.6 mL, 4.9 mmol) **106** and phenylacetylene (0.5 mL, 4.9 mmol) **84** to give **107** (0.327 g, 36%) as a colourless oil.

$IR_{(neat)}$: 720 (s), 868 (m), 1487 (m), 2926 (w) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.57 (3H, s), 1.12-1.23 (2H, m), 1.31-1.43 (2H, m), 2.11-2.25 (2H, m), 7.31-7.37 (3H, m), 7.51-7.58 (2H, m).

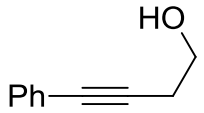
^{13}C NMR (100 MHz, $CDCl_3$): δ 0.2, 15.7 (2C), 18.6, 92.6, 107.4, 123.0, 128.5 (2C), 129.0, 132.2 (2C).

MS: m/z (M) 186.1

HRMS: m/z calc'd for $[M]^+$ $C_{12}H_{14}Si$ 186.0859, found 186.0854.

Representative procedure for Sonogashira coupling for the synthesis of homo propargyl alcohol:

Synthesis of 4-phenylbut-3-yn-1-ol, **111:**[52]



To a solution of tetrakis(triphenylphosphine)palladium (22 mg, 0.02 mmol), copper iodide (8 mg, 0.04 mmol) in Et_3N (24 mL) was added iodobenzene (0.45 mL, 3.9 mmol) **109** and 3-butyn-1-ol (0.3 mL, 3.9 mmol) **108** at room temperature and it was stirred overnight under nitrogen. The crude mixture was filtered through Celite and the solid was washed with Et_3N. Then, the liquid partition was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (9:1 petroleum ether 40-60/EtOAc) to give the product **111** as a yellow oil (0.505 g, 89%).

$IR_{(neat)}$: 914 (m), 2883 (m), 3342 (br) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.68 (2H, t, J = 6.4 Hz), 3.80 (2H, q, J = 6.1 Hz), 7.27-7.30 (3H, m), 7.39-7.43 (2H, m).

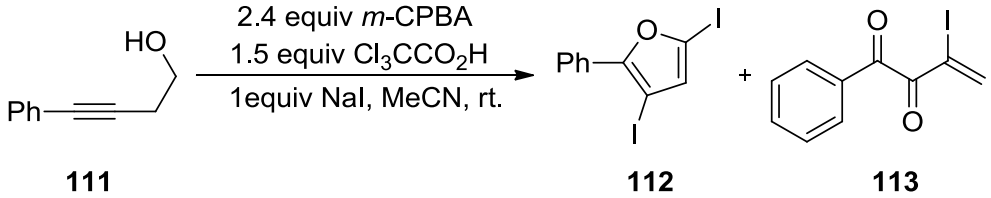
^{13}C NMR (100 MHz, $CDCl_3$): δ 24.1, 61.4, 82.7, 86.7, 123.6, 128.2, 128.5 (2C), 132.0 (2C).

MS: m/z (M + 1) 147.0

HRMS: m/z calc'd for $[M + H]^+$ $C_{10}H_{11}O$ 147.0804, found 147.0802.

Representative procedure for oxidative iodination of homopropargyl alcohol.

Synthesis of 3,5-diiodo-2-phenylfuran and 3-iodo-1-phenylbut-3-ene-1,2-dione, 112, 113:



111 **112** **113**

4-Phenylbut-3-yn-1-ol **111** (50 mg, 0.34 mmol, 1 equiv), 3-chloroperbenzoic acid (185 mg , 0.82 mmol, 2.4 equiv), NaI (51 mg, 0.34 mmol, 1 equiv) and trichloroacetic acid (83 mg, 0.5 mmol, 1.5 equiv) were dissolved in acetonitrile (2 mL) at room temperature under a nitrogen atmosphere and it was stirred overnight. The reaction mixture was quenched with saturated aqueous sodium thiosulfate solution (5 mL) and extracted with DCM (5 mL x 2). The combined organic layers were washed with saturated aqueous sodium bicarbonate solution (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by flash chromatography on silica gel (50:1 petroleum ether 40-60/EtOAc) to give a 1:1 mixture of the two products 3, 5-diiodo-2-phenylfuran **112** which was collected first then followed by the product 3-iodo-1-phenylbut-3-ene-1,2-dione **113** in column tubes.

3, 5-diiodo-2-phenylfuran, 112: brown oil (40 mg, 59%).

$IR_{(neat)}$: 657 (s), 1670 (m), 2921 (m) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 6.70 (1H, s), 7.34 (1H, t, *J* = 7.2 Hz), 7.42 (2H, t, *J* = 7.5 Hz), 7.91 (2H, d, *J* = 7.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 62.3, 89.2 (2C), 126.4 (2C), 129.1 (2C), 129.6, 130.1, 158.2.

MS: m/z (M) 395.8

HRMS: m/z calc'd for $[M]^+$ $C_{10}H_6I_2O$ 395.8503, found 395.8508.

3-iodo-1-phenylbut-3-ene-1,2-dione, 113: yellow oil (38 mg, 39%).

$IR_{(neat)}$: 1600 (m), 1736 (m), 2921 (m) cm^{-1}.

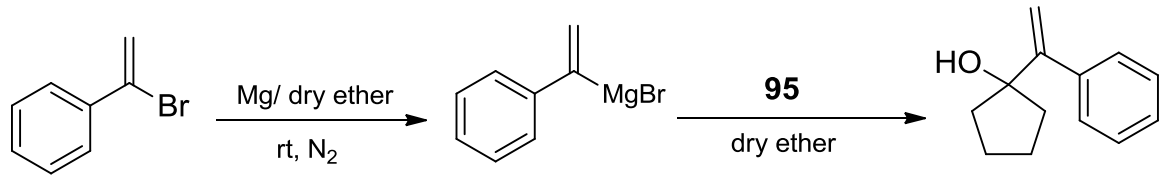
^1H NMR (400 MHz, $CDCl_3$): δ 6.83 (1H, d, *J* = 2.3 Hz), 6.85 (1H, d, *J* = 2.3 Hz), 7.46 (2H, t, *J* = 7.7 Hz), 7.59 (1H, t, *J* = 7.4 Hz), 7.81 (2H, d, *J* = 7.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 108.3, 129.8 (2C), 130.2 (2C), 133.4, 134.1, 138.6 (CH_2), 192.0 (2C).

Compound **113** decomposed, so mass spectrometry (m/z) could not be obtained.

Representative procedure for the preparation of the cycloalkanones:

Synthesis of 1-(1-phenylvinyl)cyclopentan-1-ol, 128: [53]



127 **128**

In a round bottom flask, magnesium turnings (0.25 g) in dry Et_2O (10 mL) were stirred. Then, 1,2-diiodoethane (0.140 g) was added. Once the magnesium was activated, α-bromostyrene (0.86 mL, 6.7 mmol) **127** was added dropwise and the mixture heated to reflux for 2 h. After cooling to room temperature, a solution of cyclopentanone (0.56 mL, 6.7 mmol) **95** in Et_2O (3 mL) was added dropwise *via* cannula over 20 min to the reaction mixture which was stirred for 16 hours at room temperature. Then, HCl (6 M, 3 mL) was added and the aqueous layer was extracted with ether (2 x 5 mL). Then, the combined organic layers were washed with water (5 mL), dried with anhydrous magnesium sulfate, filtered and concentrated under vacuum. The product was purified by flash

chromatography (20:1 petroleum ether 40-60/EtOAc) to give the product **128** (0.516 g, 41%) as a yellow oil.

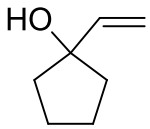
$IR_{(neat)}$: 699 (s), 774 (m), 910 (m), 1192 (m), 1492 (m), 2960 (w), 3428 (br) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 1.64-1.92 (8H, m), 2.53 (1H, br), 5.07 (1H, d, *J* = 0.98 Hz), 5.4 (1H, d, *J* = 0.98 Hz), 7.27-7.34 (3H, m), 7.38 (2H, dd, *J* = 7.7, 1.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 22.0 (2C), 38.7 (2C), 84.0, 114.1 127.4 (2C), 128.2, 129.5 (2C), 138.1, 154.5.

MS: (M – OH) 170.1

Synthesis of 1-vinylcyclopentan-1-ol, 130:[54]



Vinyl magnesium chloride (4.5 mL, 7.3 mmol, 1.6 M solution in THF) was dissolved in THF (20 mL). Then, cyclopentanone (0.44 mL, 4.9 mmol) **95** was added. The mixture was stirred for 16 hours under a nitrogen atmosphere. Aqueous NH_4Cl (1 M, 5 mL) was added and the mixture extracted with ether (2 x 10 mL). The organic layers were combined and dried with anhydrous magnesium sulfate, filtered and concentrated under vacuum to give the product **130** (0.801 g, 97%) as an orange oil.

$IR_{(neat)}$: 1409 (m), 1640 (m), 2872 (w), 2959 (s), 3353 (br) cm^{-1}.

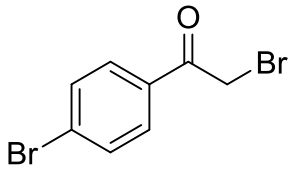
^1H NMR (400 MHz, $CDCl_3$): δ 1.56-1.72 (6H, m), 1.74-1.88 (2H, m), 1.93 (1H, s), 4.98 (1H, d, *J* = 10.5 Hz), 5.22 (1H, d, *J* = 17.2 Hz), 5.97 (1H, dd, *J* = 10.9, 16.9 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 23.8, 40.3 (2C), 82.3, 111.2 (2C), 144.6.

MS: m/z (M – OH) 95.1

Representative procedure for oxidative bromination of alkylbenzenes:

Synthesis of 2-bromo-1-(4-bromophenyl)ethan-1-one, 135a:[61]



Ethyl benzene (100 mg, 0.94 mmol, 1 equiv) **134a**, Oxone (1.4 g, 4.7 mmol, 5 equiv), and NaBr (338 mg, 3.29 mmol, 6 equiv) were dissolved in acetonitrile (3 mL) at room temperature under a nitrogen atmosphere. Water (3 mL) was added dropwise to the mixture and it was stirred overnight. The reaction mixture was quenched with saturated aqueous sodium thiosulfate solution (5 mL) and extracted with CH_2Cl_2 (2 x 10 mL), dried over anhydrous magnesium sulfate, filtered and concentrated under vacuum. The crude product **135a** did not require further purification and was isolated as a pale brown solid (170 mg, 65%).

Melting point: 75-77 ^oC. (Lit.:[61]108-109 ^oC)

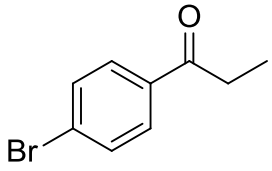
$IR_{(neat)}$: 546 (s), 1693 (m), 2952 (w) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 4.40 (2H, s), 7.64 (2H, d, *J* = 8.3 Hz), 7.85 (2H, d, *J* = 8.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 30.7, 129.7, 130.8 (2C), 132.6 (2C), 133.0, 190.8.

MS: m/z (M) 277.8.

Synthesis of 1-(4-bromophenyl)propan-1-one, 135b:[62]



Synthesised according to the representative procedure for the formation of **135a,** using propylbenzene (100 mg, 0.83 mmol, 1 equiv) **134b**, Oxone (1.2 g, 4 mmol, 5 equiv), and NaBr (298

mg, 2.9 mmol, 6 equiv). The crude product did not require further purification and **135b** was isolated as a brown oil (153 mg, 86%)**.**

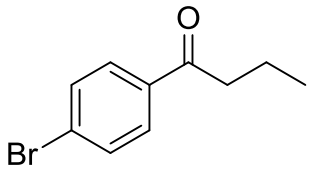
$IR_{(neat)}$: 1685 (m), 2975 (w) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 1.21 (3H, t, *J* = 7.2 Hz), 2.89-3.0 (2H, m), 7.59 (2H, d, *J* = 8.6 Hz), 7.82 (2H, d, *J* = 8.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 8.4, 32.1, 128.3, 129.8 (2C), 132.1 (2C), 135.9, 200.0

MS: m/z (M) 212.0

Synthesis of 1-(4-bromophenyl)butan-1-one, 135c:[63]



Synthesised according to the representative procedure for the formation of **135a,** using butylbenzene (100 mg, 0.7 mmol) **134c**, Oxone (1 g, 3.5 mmol, 5 equiv), and NaBr (252 mg, 2.45 mmol, 6 equiv). The product was purified by flash chromatography (9:1 petroleum ether 40-60/EtOAc) to provide the product **135c** as a brown oil (100 mg, 63%).

$IR_{(neat)}$: 565 (m), 1686 (m), 2959 (w) cm^{-1}.

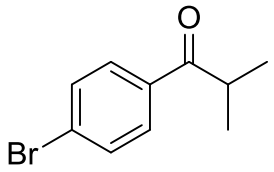
^1H NMR (400 MHz, $CDCl_3$): δ 0.99 (3H, t, *J* = 7.2 Hz), 1.71-1.80 (2H, m), 2.90 (2H, t, *J* = 7.4 Hz), 7.59 (2H, d, *J* = 8.8 Hz), 7.82 (2H, d, *J* = 8.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 18.0, 40.8, 128.3, 130.0 (2C), 132.2 (2C), 136.1, 199.6.

MS: m/z (M) 226.0

HRMS: m/z calc'd for $[M]^+$ $C_{10}H_{11}BrO$ 225.9993, found 226.0001.

Synthesis of 1-(4-bromophenyl)-2-methylpropan-1-one, 135d:[64]



Synthesised according to the representative procedure for the formation of **135a**, using (3-methylbut-1-en-2-yl) benzene (100 mg, 0.7 mmol) **134d**, Oxone (1 g, 3.5 mmol, 5 equiv), and NaBr (252 mg, 2.45 mmol, 6 equiv). The product was purified by flash chromatography (9:1 petroleum ether 40-60 /EtOAc) to provide the product **135d** as a yellow oil (47 mg, 30%).

$IR_{(neat)}$: 1682 (m), 2969 (w) cm^{-1}.

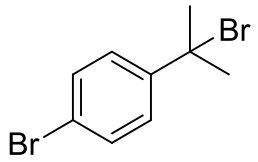
^1H NMR (400 MHz, $CDCl_3$): δ 1.21 (6H, d, *J* = 6.9 Hz), 3.45-3.54 (1H, m), 7.60 (2H, d, *J* = 8.8 Hz), 7.82 (2H, d, *J* = 8.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4 (2C), 35.4, 127.9, 129.9 (2C), 131.9 (2C), 134.9, 203.4.

MS: m/z (M + 1) 227.0

HRMS: m/z calc'd for $[M + H]^+$ $C_{10}H_{12}OBr$ 227.0066, found 227.0072.

Synthesis of 1-bromo-4-(2-bromopropan-2-yl)benzene, 135e:



Synthesised according to the representative procedure for the formation of **135a,** using cumene (100 mg, 0.83 mmol) **134e**, Oxone (1.2 g, 4 mmol, 5 equiv), and NaBr (298 mg, 2.9 mmol, 6 equiv). The crude product did not require further purification and **135e** was isolated as a brown oil (131 mg, 57%).

$IR_{(neat)}$: 545 (s), 1589 (m), 2973 (w) cm^{-1}.

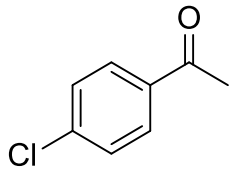
^1H NMR (400 MHz, $CDCl_3$): δ 1.55 (6H, s), 7.35 (2H, d, *J* = 8.2 Hz), 7.45 (2H, d, *J* = 8.2 Hz)

^{13}C NMR (100 MHz, $CDCl_3$): δ 32.1 (2C), 72.7, 120.9, 126.7 (2C), 131.6 (2C), 148.5.

MS: (M – Br) 196.9

HRMS: m/z calc'd for $[M - Br]^+$ $C_9H_{10}Br$ 196.9960, found 196.9959.

Synthesis of 1-(4-chlorophenyl)ethan-1-one, 135f:[65]



Synthesised according to the representative procedure for the formation of **135a**, using 1-chloro-4-ethylbenzene (100 mg, 0.7 mmol) **134f**, Oxone (1 g, 3.5 mmol, 5 equiv), and NaBr (252 mg, 2.45 mmol, 6 equiv). The crude product **135f** did not require further purification and was isolated as a brown oil (79 mg, 73%).

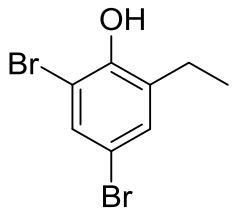
$IR_{(neat)}$: 822 (s), 1681 (s) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 2.57 (3H, s), 7.41 (2H, d, *J* = 8.6 Hz), 7.87 (2H, d, *J* = 7.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 26.9, 129.2 (2C), 130.1 (2C), 135.7, 139.9, 197.2.

MS: m/z (M) 154.0

Synthesis of 2,4-dibromo-6-ethylphenol, 135g:



Synthesised according to the representative procedure for the formation of **135a**, using 2-ethylphenol (100 mg, 0.8 mmol) **134g**, Oxone (1.2 g, 4 mmol, 5 equiv), and NaBr (291 mg, 2.8 mmol, 6 equiv). The product was purified by flash chromatography (9:1 petroleum ether 40-60/EtOAc) to provide the product **135g** as a brown oil (165 mg, 74%).

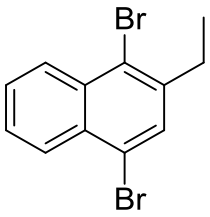
$IR_{(neat)}$: 556 (m), 1138 (s), 1222 (m), 1317 (m), 1454 (m), 1566 (w), 2967 (w), 3506 (br) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20 (3H, t, *J* = 7.4 Hz), 2.66 (2H, q, *J* = 7.4 Hz), 5.52 (1H, s), 7.21 (1H, d, *J* = 2.3 Hz), 7.43 (1H, d, *J* = 2.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 24.2, 111.0, 112.7, 131.6, 131.9, 133.9, 149.7.

MS: m/z (M) 278.0

Synthesis of 1,3-dibromo-2-ethylnaphthalene, 135j:



Synthesised according to the representative procedure for the formation of **135a,** using 2-ethylnaphthalene (100 mg, 0.6 mmol) **134j**, Oxone (922 mg, 3 mmol, 5 equiv), and NaBr (216 mg, 2.1 mmol, 6 equiv). The product was purified by flash chromatography (9:1 petroleum ether 40-60 /EtOAc) to provide the product **135j** as a yellow oil (60 mg, 32%).

$IR_{(neat)}$: 751 (s), 959 (s), 1256 (m), 1488 (m), 1583 (m), 2966 (w) cm^{-1}.

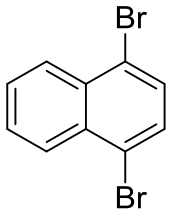
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (3H, t, *J* = 7.7 Hz), 2.93-3.05 (2H, m), 7.56-7.65 (2H, m), 7.69 (1H, s), 8.20 (1H, d, *J* = 8.0 Hz), 8.35 (1H, d, *J* = 8.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 14.6, 30.8, 122.7, 123.4, 127.5, 127.8, 128.1, 128.4, 131.5, 131.8, 133.8, 142.5.

MS: m/z (M) 312.0

HRMS: m/z calc'd for $[M]^+$ $C_{12}H_{10}Br_2$ 311.9144, found 311.9161.

Synthesis of 1,4-dibromonaphthalene, 43:[66]



Synthesised according to the representative procedure for the formation of **33,** using naphthalene (100 mg, 0.7 mmol), Oxone (1 g, 3.5 mmol, 5 equiv), and NaBr (252 mg, 2.45 mmol, 6 equiv).

The product was purified by flash chromatography (petroleum ether 40-60) to provide the product **43** as a white solid (62 mg, 77%).

Melting point: 80-82 °C. (Lit.:[66] 80-81 °C)

$IR_{(neat)}$: 748 (s), 959 (s), 1250 (m), 1364 (m), 1582 (m), 3066 (w) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (2H, dd, *J* = 6.5, 3.3 Hz), 7.61 (2H, s), 8.23 (2H, dd, *J* = 6.5, 3.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 122.9 (2C), 128.1 (2C), 128.5 (2C), 130.4 (2C), 133.3 (2C).

MS: m/z (M) 284.0

HRMS: m/z calc'd for $[M]^+$ $C_{10}H_6Br_2$ 283.8831, found 283.8841.

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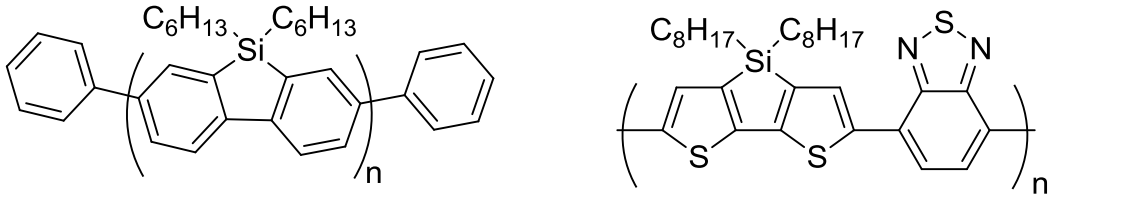
Chapter 2: Ring Expansion

1 Introduction

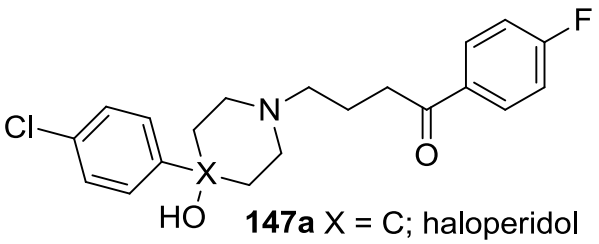
Silicon is the most abundant element on Earth after oxygen. However, its use in organic chemistry is limited. This is despite the fact that replacement of carbon atoms for silicon atoms in small chemical compounds can have a significant positive impact on the properties of the compound.[1,2] Polycyclic aromatic compounds have become important because of their optical and electronic properties, and it has been found that many silicon containing molecules possess superior properties than their carbon analogues. For example, dibenzosiloles have been shown to have unique optoelectronic characteristics and are widely used as light-emitting diodes **145**[3], solar cells **146**[4] (Figure 4), detectors for explosives[5] and thin-film transistors.[6]



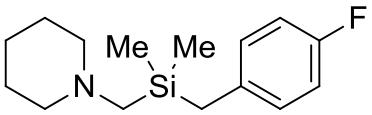
145 a blue light emitting polymer **146** a potential photovoltaic polymer

Figure 4

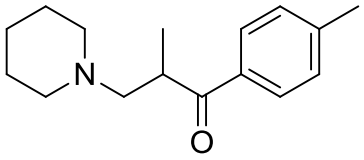
There are currently no drugs on the market that contain a silicon atom, despite research indicating that molecules with silicon atoms may have improved properties compared to their carbon analogues.[7] For example, sila-haloperidol **147b**, a dopamine receptor antagonist, displays higher subtype selectivity and a different mode of metabolism to haloperidol **147a**.[8] The installation of the silicon atom leads to changes in properties including molecule shape, due to the different bond lengths and atom size, different bond polarisations and increased lipophilicity. Silperisone **148** is a centrally acting muscle relaxant which has been shown to have fewer propensities to cause CNS depression or motor side effects than tolperisone **149** and other antispastic drugs (Figure 5).[9,10]



147a X = C; haloperidol
147b X = Si; sila-haloperidol



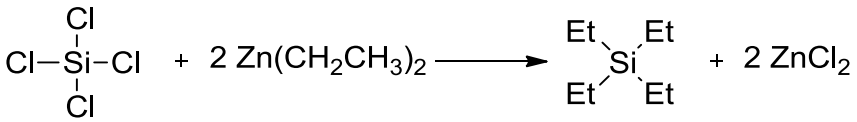
148 silperisone



149 tolperisone

Figure 5

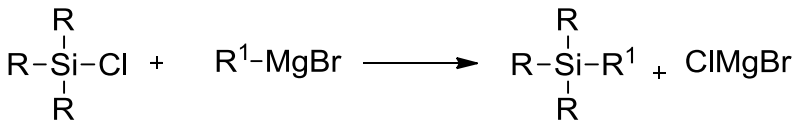
Many different routes have been created and applied to the synthesis of organosilicon compounds. Friedel and Crafts reported the first method, they investigated the reaction of silicon tetrachloride **150** with diethyl zinc **151** to form tetraethylsilane **152** which was the first compound prepared with a Si-C bond (Scheme 54).[11]



150 **151** **152** **153**

Scheme 54

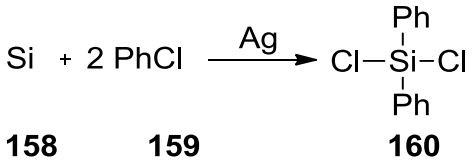
Further research in this area by Kipping demonstrated the reaction of chlorosilanes **154** with Grignard reagents **155** for the convenient preparation of silanes **156** (Scheme 55).[12]



154 **155** **156** **157**

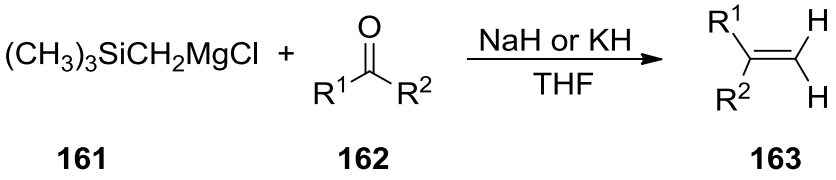
Scheme 55

Another widely cited study in this specialised field was carried out by Rochow and Muller, who discovered a direct process for preparing halogenated organosilane derivatives **160** *via* the direct reaction of elemental silicon **158** with chlorobenzene **159** mediated by Ag metal (Scheme 56).[13]



Scheme 56

Most of the development of organosilicon chemistry started towards the end of the 1960s, when Peterson demonstrated the olefination reaction through using trimethylsilylmethylmagnesium chloride **161** as an effective intermediate in the conversion of carbonyl compound **162** to the corresponding olefin **163** (Scheme 57).[14] At this point, swift development of organosilicon chemistry ensued.



Scheme 57

1.1 The chemical properties of silicon

Silicon is in group 14 (3_S^2 3_P^2) and is listed under carbon in the periodic table. Due to this, it can be assumed silicon and carbon have similar characteristics. For example, it is common to find silicon singly bonded to four other atoms using sp^3 atomic orbital hybridization. In terms of the tetracoordinated species, the molecular geometry is tetrahedral, which is presented in Figure 6.

Figure 6

There are several important differences in chemical properties between carbon and silicon which are summarized in Table 5.[7,9] The first difference concerns the availability of 3d orbitals on silicon. Single bonds from silicon to electronegative elements O and F are stronger than the bonds between carbon and these elements. Nevertheless, Si-C and Si-H bonds are not as strong as the bond between C-H and C-C bonds, and this is because of the large 3p orbital on silicon, which does not overlap well with the 2p orbital on C, O and N. Therefore, multiple bonds that involve silicon are unstable, so Si=C, Si=O and Si=N bonds are not found in general.

Properties	Carbon	Silicon
Atomic number	6	14
Electronic configuration	$1s^2 2s^2 2p^2$	$1s^2 2s^2 2p^6 3s^2 3p^2 3d^0$
Electronegativity	2.50	1.74
Atomic radius	66 pm	106 pm
Bond length	C-C 1.54 Å	Si-C 1.87 Å
Bond energy	C-C 79.8 kcal/mol	Si-C 76.0 kcal/mol

Table 5

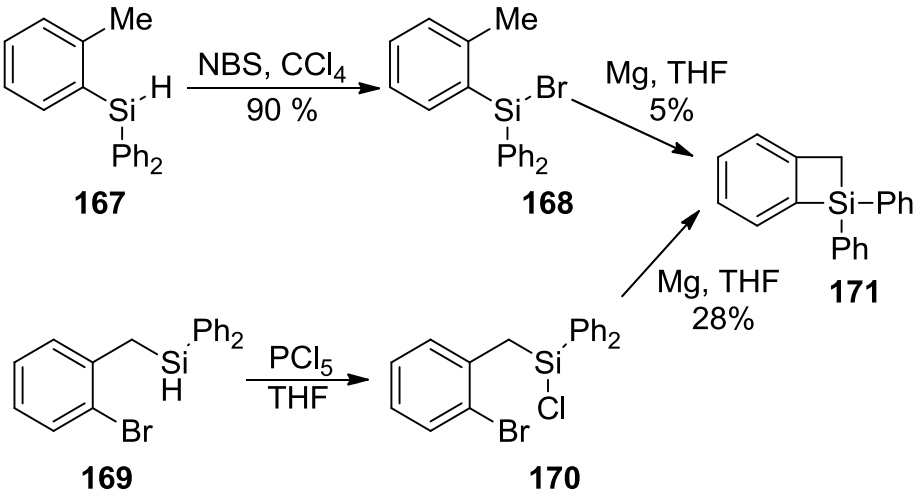
Other differences between silicon and carbon atoms are the size and electronegativity; silicon is bigger and less electronegative than carbon. This can result in differences in bond polarizations of analogous carbon-element and silicon-element bonds. Another difference is that silicon-containing bonds are around 20% longer than carbon-containing bonds; the length of a C-Si bond is 1.87 Å, however the length of a C-C bond is 1.54 Å. Therefore, there are differences in the size and shape of analogous silicon and carbon compounds. [2,7,9]

1.2 Synthesis of silacyclobutanes

Silacycles have become an important class of small molecules in recent years. In particular, silacyclobutane derivatives have attracted attention due to their ring strain and Lewis acidity.

Silacyclobutanes have another special and remarkable feature, which is the activity of the Si-C bonds, which enables intermolecular rearrangement reactions, ring-opening addition reactions and ring-insertion reactions.[15,16]

The chemistry of four-membered ring silacycles has been widely studied since 1964, when Gilman and Atwell reported the first synthesis of a benzosilacyclobutene. This was the first example of a metallabenzocyclobutene. Gilman and Atwell prepared benzosilacyclobutenes using two different approaches; the first comprised the reaction of diphenyl *o*-tosylsilane **167** with NBS in CCl_4, which produced bromodiphenyl(*o*-tolyl)silane **168** in 90% yield. This was treated with magnesium in THF to produce benzosilacyclobutene **171** in 5% yield. Secondly, benzosilacyclobutenes were made in a yield of 28% through treating bromobenzyldiphenylsilane **169** with phosphorus pentachloride to produce (2-bromobenzyl)chlorodiphenylsilane **170**, followed by reaction with magnesium in THF to produce **171** (Scheme 58).[17-19]

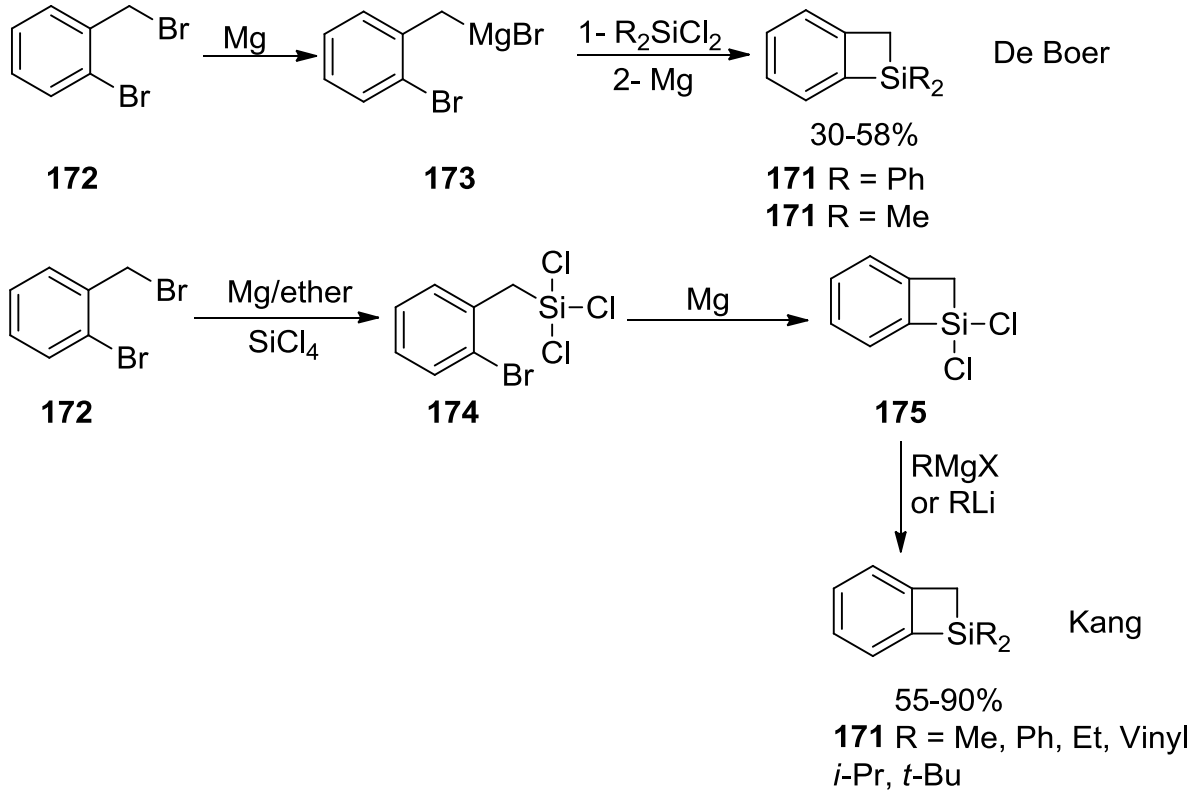


167 **168** **171** **169** **170**

Scheme 58

Alternative syntheses of benzosilacyclobutenes **171** have been reported by de Boer and Kang both starting from 2-bromobenzyl bromide **172**.[20] de Boer synthesised these species by treating the starting material with magnesium to produce (2-bromobenzyl) magnesium bromide, which reacted with both dichlorodiphenylsilane and dichlorodimethylsilane and with an excess of magnesium to

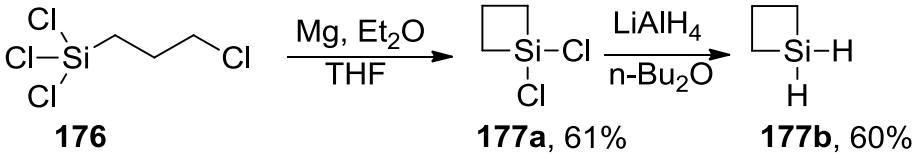
generate good yields of products **171** (R = Ph or Me) (30% and 58% respectively). On the other hand, Kang developed another synthetic route in order to prepare benzosilacyclobutenes **171** from the reaction of the Grignard reagent derived from 2-bromobenzyl bromide with tetrachlorosilane. This then reacted with an excess of magnesium which generated cyclized intermediate 1,1-dichlorobenzosilacyclobutene **175**. Subsequently, the 1,1-dichlorobenzosilacyclobutene **175** reacted with either Grignard reagents or *tert*-butyllithium in order to generates the product in moderate to high yields (55-90%). This method resulted in benzosilacyclobutene derivatives with different alkyl substituents on silicon (Scheme 59).[20]



Scheme 59

In addition, silacyclobutanes can be prepared using other synthetic approaches, such as the cyclization of compounds that have CH_2=CH– and ≡C–H groups catalyzed by hexachloroplatinic acid, or through heating the reaction mixture without a catalyst under pressure.[21]

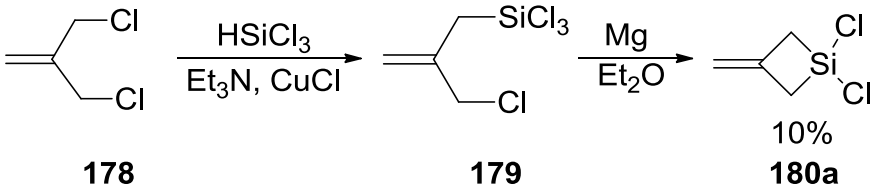
Laane reported the first preparation of silacyclobutane derivatives in 1967. 1,1-Dichloro-1-silacyclobutane **177a** was generated through reacting 3-chloropropyltrichlorosilane **176** with magnesium in THF or ether in a yield of 61%. Reduction of 1,1-dichloro-1-silacyclobutane **177a** can be achieved with lithium aluminium hydride in *n*-butyl ether at 0 °C. The silacyclobutane **177b** was generated in a yield of 60% (Scheme 60).[22]



176 **177a**, 61% **177b**, 60%

Scheme 60

A different approach to silacyclobutanes was developed by William P. Weber and co-workers in 1990, to synthesise 3-methylene-1,1-dichlorosilacyclobutane **180a** from readily available starting materials in two steps. The first step was the reaction of 3-chloro-2-chloromethyl-1-propene **178** with trichlorosilane in triethylamine as solvent and a catalytic amount of cuprous chloride to produce trichloro(2-(chloromethyl)allyl)silane **179**. This was followed by an intermolecular Grignard ring closure to furnish the final product **180** in a low yield of 10% (Scheme 61).[23]

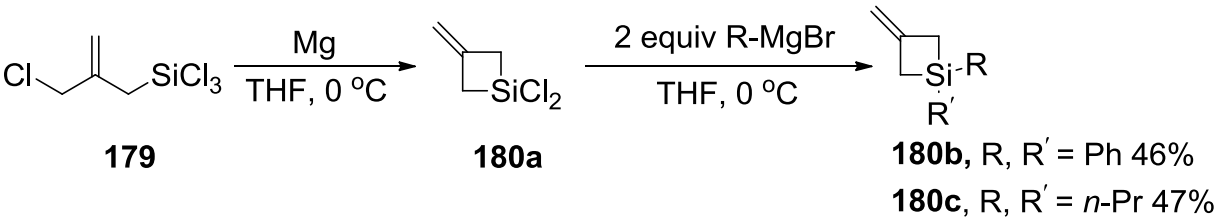


178 **179** **180a**

Scheme 61

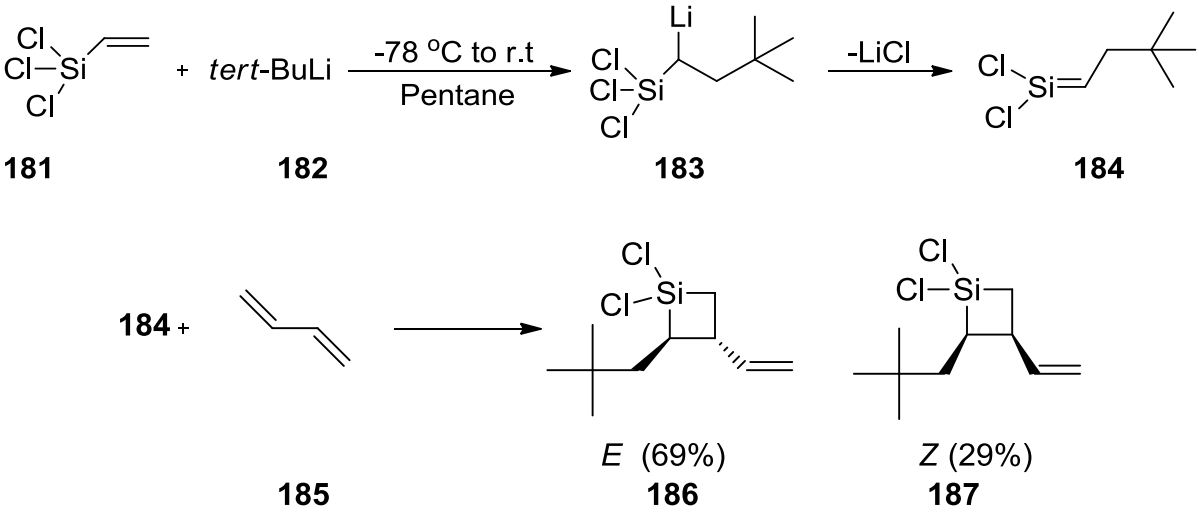
Furthermore, Oshima and Utimoto prepared 3-methylenesilacyclobutanes **180a** in good yields by a two steps process which involved the treatment of 2-(chloromethyl)-3-(trichlorosilyl)propene **179** with magnesium in THF at 0 °C, which was then followed by two equivalents of phenylmagnesium bromide in THF being added at 0 °C to produce 3-methylene-1,1-diphenylsilacyclobutane **180b** in

46% yield. When propylmagnesium bromide was used in place of phenylmagnesium bromide the 3-methylene-1,1-dipropylsilacyclobutane **180c** was formed in a 47% yield (Scheme 62).[24]



Scheme 62

In 1991, Sewald *et al.*[25] investigated another method to synthesise silacyclobutanes; this method was based on there being three chlorine substituents on the silicon atom and a vinyl group. Mechanistically, they suggested that the first step was addition of *tert*-butyllithium **182** to vinyltrichlorosilane **181** to produce α-lithiated adduct (3,3-dimethyl-1-(trichlorosilyl)butyl)lithium **183**. Then, through elimination of LiCl, the dichloroneopentylsilene intermediate **184** was formed which was followed by the use of a trapping reagent, 1,3-butadiene **185**, to produce a 69:29 *E/Z* mixture of isomeric 2-neopentyl-3-vinyl-1-silacyclobutanes **186** and **187** in 80% yield (Scheme 63).

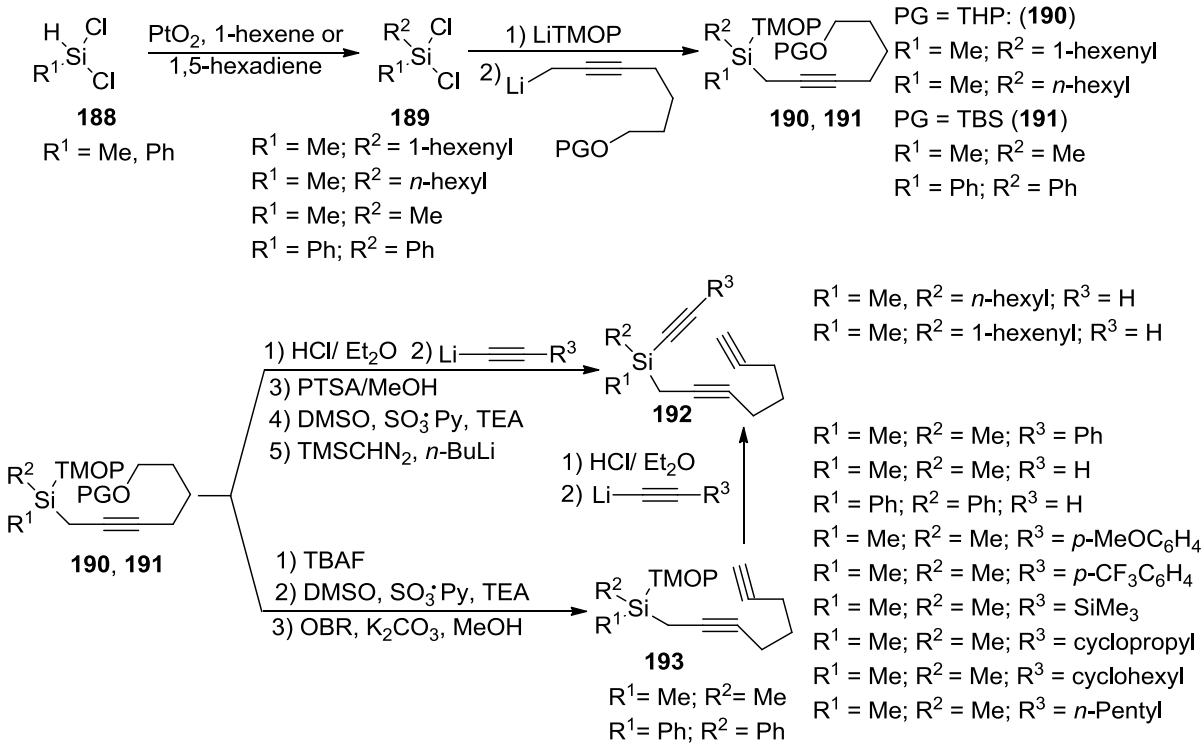


Scheme 63

Petit and co-workers created a very efficient method to functionalize benzosilacyclobutene compounds in high yields from acyclic sila-triynes by a niobium-catalyzed [2 + 2 + 2]

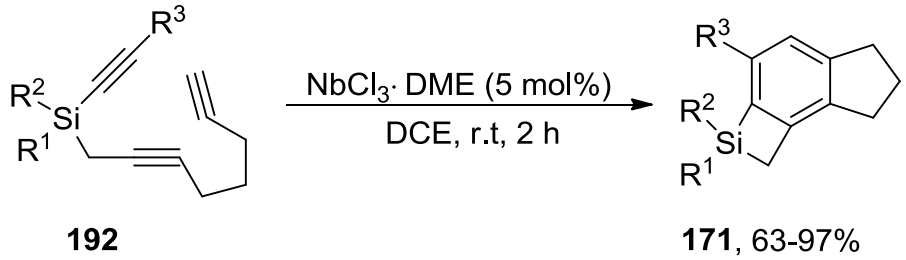
cycloaddition. They revealed that benzosilacyclobutenes are capable of being synthesised with different substituents on the silicon atom in addition to the aromatic ring.[19]

First of all they prepared the acyclic sila-triyne derivatives **190** and **191** (Scheme 64). Disubstituted dichlorosilanes **189** are either commercially available or formed by the hydrosilylation of 1-hexene or 1,5-hexadiene with methyldichlorosilane **188** followed by the addition of the bulky 2,4,6-trimethoxyphenyllithium (Li-TMOP) reagent. Finally, addition of alkyl lithium derivatives selectively generated intermediate **190** or **191**. To introduce the other triple bonds on compounds **190** or **191** two pathways were created; the first one used the tetrahydropyranyl (THP) protecting group which led to the synthesis of **192** after several steps: removal of TMOP, nucleophilic substitution, alcohol deprotection, Parikh-Doering oxidation, and Colvin homologation. The second pathway involved the use of *tert*-butyldimethylsilyl (TBS) as a protecting group, and the first step was alcohol deprotection using tetrabutylammonium fluoride (TBAF). This was followed by oxidation and homologation with the Ohira-Bestmann reagent (OBR) which led to the generation of intermediate **193.** After this, TMOP was replaced by chlorine in order to attach the final alkyne in **192**.



Scheme 64

Following on from this, the researchers used their conditions to catalyze the cycloaddition of these acyclic sila-triyne substrates at room temperature using $NbCl_3$·DME (5 mol %) as catalyst. After optimization, this was found to be the most efficient catalyst with DCE as solvent. After 2 h, the highly functionalized benzosilacyclobutenes **171** could be isolated in high yields (63-97%) (Scheme 65).[19]

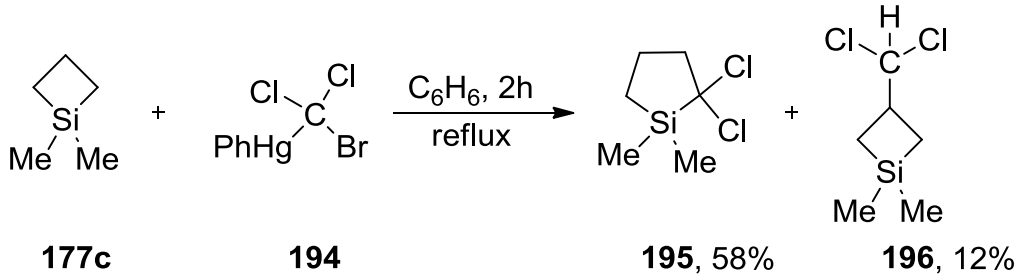


Scheme 65

1.3 Overview of silacyclobutane ring expansion reactions

In recent years, several reactions have been reported with silacyclobutanes and their derivatives that exploit both the ring strain and the activity of the Si-C bonds in these compounds. For example,

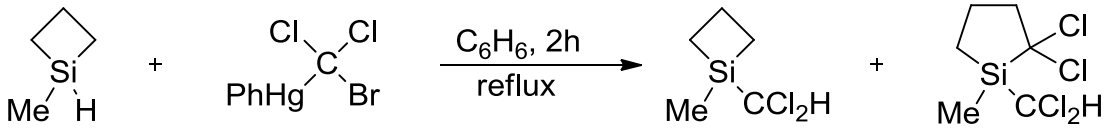
ring expansion reactions with electrophilic carbenes have been investigated by Seyferth *et al.*[26] These are the first examples of CCl_2 being inserted into a silicon-carbon bond in a strained cyclic system. The study revealed that treating silacyclobutane **177c** with phenyl(bromodichloromethyl) mercury **194** in refluxing benzene for two hours generated a mixture of products that came about from either Si-C or C-H bond insertions. However, the results revealed the ring expansion of silacyclopentanes from Si-C bond insertion was the major pathway (Scheme 66).



177c **194** **195**, 58% **196**, 12%

Scheme 66

So as to understand the variations in reactivity between Si-C bond and Si-H bond insertion by dichlorocarbenes generated from phenyl(bromodichloromethyl)mercury **194**, many different reactions were investigated. In the case of using 1-methyl-1-silacyclobutane **177e** (Scheme 67), it was shown that Si-H bond insertion was preferred over Si-C bond insertion and an 11:1 ratio of products was formed.[26]

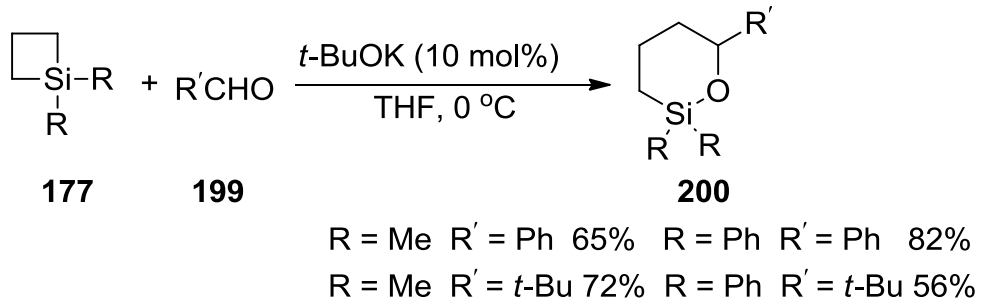


177e **194** **197**, 68% **198**, 6%

Scheme 67

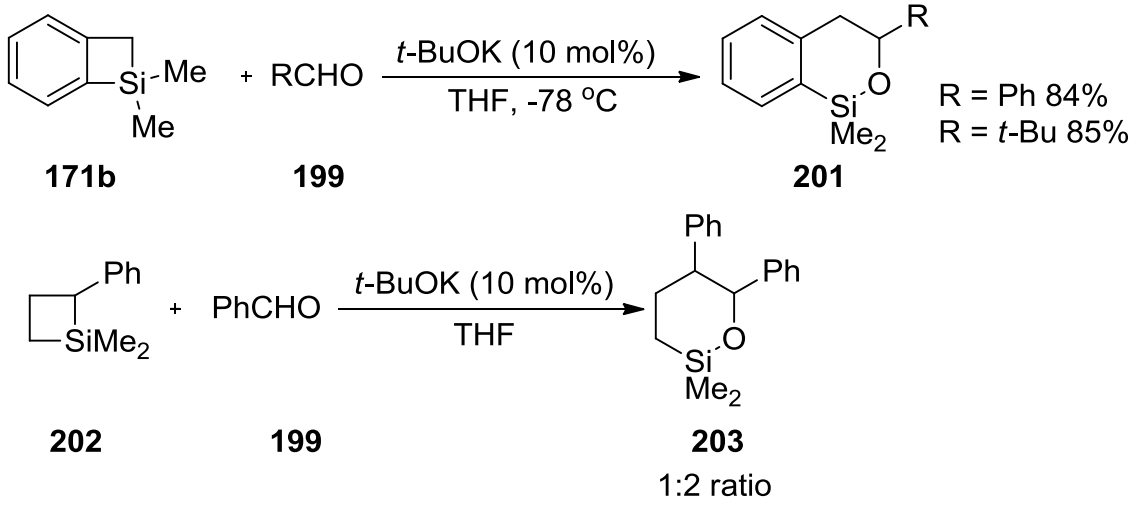
Oshima *et al.*[27] reported different modes of ring expansion through the use of various nucleophiles and nucleophilic carbenoid reagents in order to synthesize various five- and six-membered silacycles. They reported that the treatment of silacyclobutane **177** with a catalytic amount of

potassium *t*-butoxide with benzaldehyde **199** in THF at 0 °C for 2 h led to formation of six-membered cyclic silyl ethers **200** in high yields (Scheme 68).



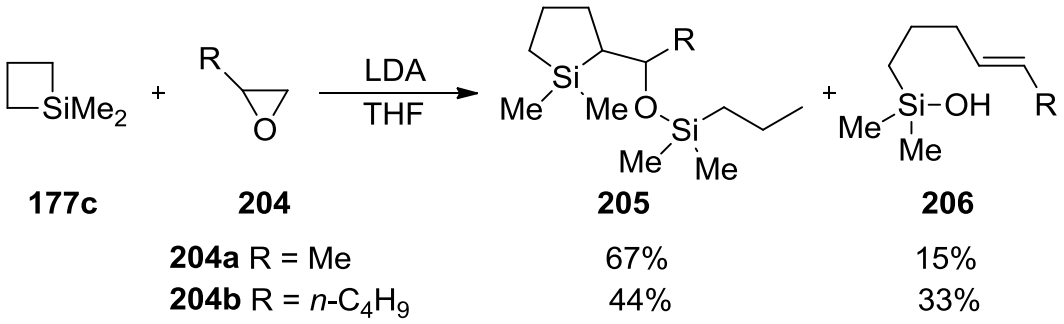
Scheme 68

The treatment of 1,1-dimethyl-2,3-benzo-1-sila-2-cyclobutene **171b** with aldehydes at -78 °C generated the analogous products in high yields. Other unsymmetrically substituted silacyclobutanes were investigated, for example, 1,1-dimethyl-2-phenyl-1-silacyclobutane **202** was mixed with benzaldehyde using the same conditions to generate the corresponding oxasilacyclohexanes **203** as a 1:2 mixture of (syn/anti) stereoisomers (Scheme 69).[27]



Scheme 69

As a result of continuing research with silacylobutane, the same researchers reported the reaction of 1,1-dimethyl-1-silacyclobutane **177c** with epoxides **204**. For example, treatment of **177c** and 1,2-epoxypropane **204a** or 1,2-epoxyhexane **204b** with lithium diisopropylamide produced two products, the silacyclopentane **205** and an olefinic silanol **206** (Scheme 70).[27]

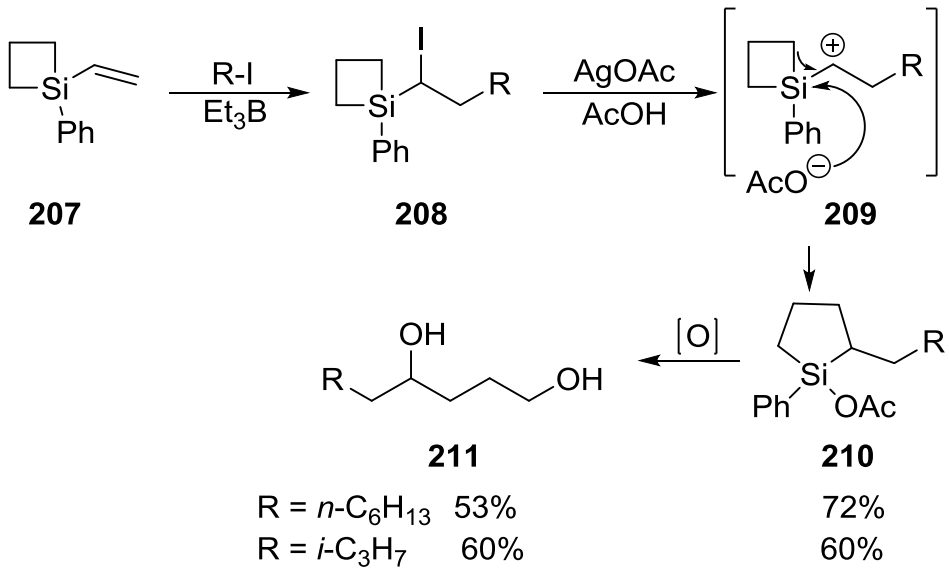


177c **204** **205** **206**

204a R = Me	67%	15%
204b R = *n*-C_4H_9	44%	33%

Scheme 70

In 1991, Oshima *et al.*[28]described the ring expansion of silacyclobutanes. Starting from 1-vinylsilacyclobutane **207**, radical addition of an alkyl iodide resulted in the formation of the iodo product **208**. Then, upon treatment with silver acetate in acetic acid at room temperature silacyclobutylalkyl cation intermediate **209** was formed which rearranged to acetoxysilacyclopentane **210** in up to 72% yield (Scheme 71). They suggested that the reaction proceeds through silver ion-mediated iodine removal to provide silacyclobutylalkyl cation **209**. Subsequently, the acetate anion attacks the silicon atom of **209** which leads to migration of one of the C-Si bonds to the α-carbon atom to afford silacyclopentane **210**. Treatment of the acetoxysilacyclopentanes **210** with H_2O_2-KF led to oxidative cleavage of the carbon-silicon bonds to produce 1,4-diols **211**.



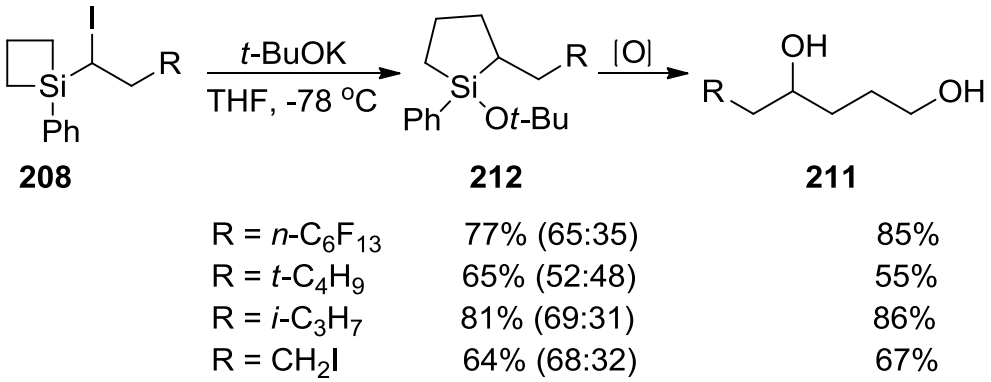
207 **208** **209**

211 **210**

R = *n*-C_6H_{13}	53%	72%
R = *i*-C_3H_7	60%	60%

Scheme 71

In addition, reaction of 1-(1-iodoalkyl)-1-phenyl-1-silacyclobutane **208** with *t*-BuOK leads to formation of silacyclopentanes in good yields. Subsequent oxidative cleavage of the two C-Si bonds affords access to 1,4-diols **211** (Scheme 72).[28]

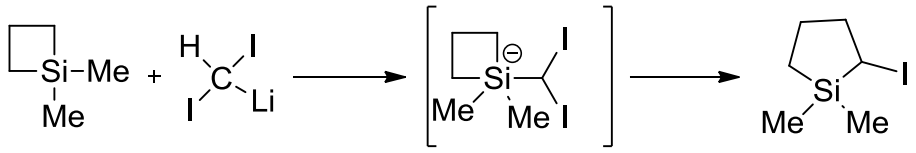


208 **212** **211**

R = *n*-C_6F_{13}	77% (65:35)	85%
R = *t*-C_4H_9	65% (52:48)	55%
R = *i*-C_3H_7	81% (69:31)	86%
R = CH_2I	64% (68:32)	67%

Scheme 72

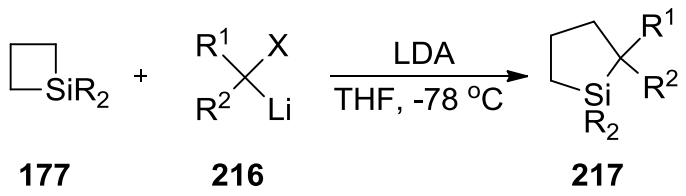
The Ohima group examined the insertion of nucleophilic lithium carbenoid reagents into Si-C bonds of silacyclobutanes to produce silacyclopentanes **215** through a pentacoordinate silicate intermediate **214** (Scheme 73).[29, 30]



177c **213** **214** **215**

Scheme 73

Many different silacyclobutane derivatives have been treated with these reaction conditions: lithium diisopropylamide with lithium carbenoids **216** in THF at -78 °C to generate silacyclopentane derivatives **217** in good yields. The substituents on silicon did not have impact upon the reaction pathway as shown in table 6 .[29,30]

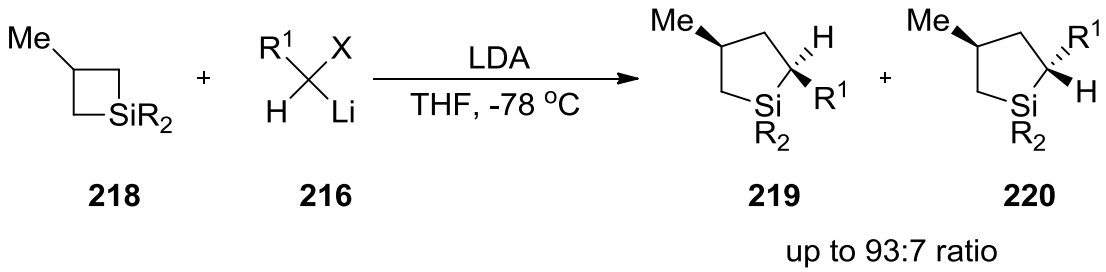


177 **216** **217**

R	R^1	R^2	X	Yield (%)
Me	H	I	I	83
Me	H	Br	Br	62
Me	H	Cl	Cl	49
Me	*n*-Bu	I	I	59
Me	H	Ph	Br	61
Me	H	Me_3Si	I	56
Ph	H	Br	Br	72
Ph	H	Cl	Cl	74
Ph	H	Ph	Br	46
Ph	H	Me_3Si	I	58
n-Bu	H	I	I	85
n-Bu	H	Br	Br	79
O^iPr	H	I	I	83

Table 6

Silacyclobutanes with a methyl substituent at the 3-position have been treated with lithium carbenoids to produce the corresponding silacyclopentanes with high stereoselectivity, up to 93:7 syn/anti ratio (Scheme 74).[29,30]

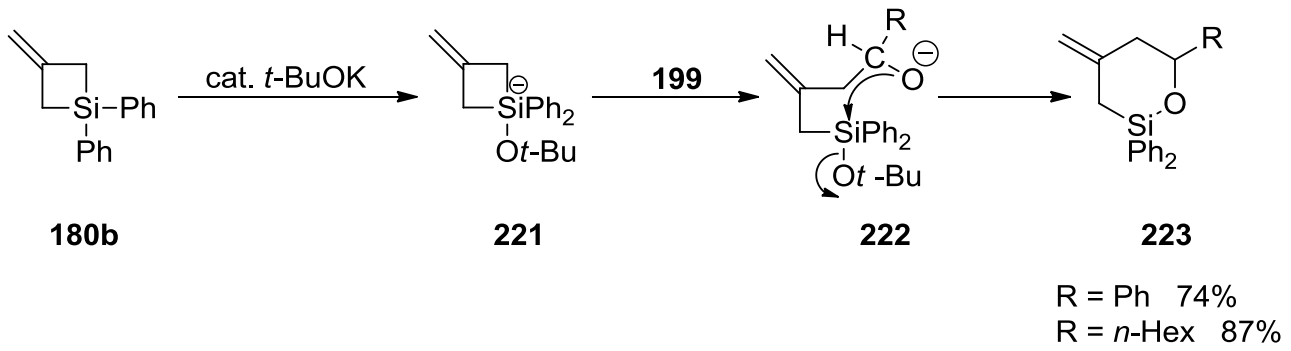


218 **216** **219** **220**

up to 93:7 ratio

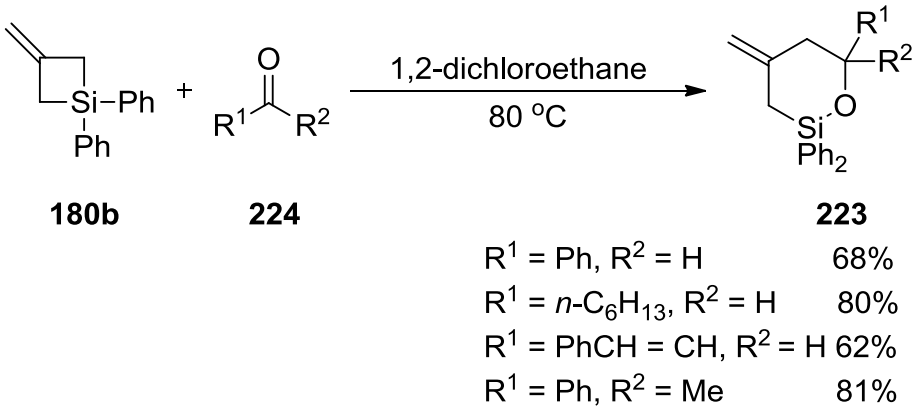
Scheme 74

In 1995, the same researchers reported that 3-methylene-1,1-diphenylsilacyclobutane mixed with aldehydes **199** in the presence of a catalytic amount of *t*-BuOK in 1,2-dichloroethane generate 5-methylene-2-oxa-1-silacyclohexane **223** in high yields (Scheme 75).[24]



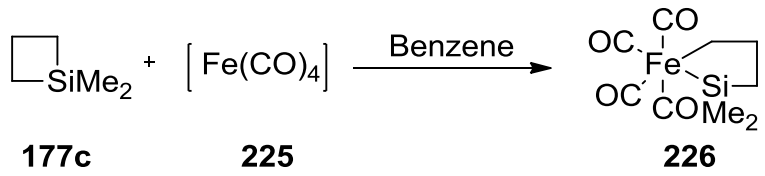
Scheme 75

However, it was discovered that when 3-methylene-1,1-diphenylsilacyclobutane **180b** was treated with either aldehyde or ketone **224** at reflux in DCE without catalyst, 5-methylene-2-oxa-1-silacyclohexane **223** was produced in good yields. This reaction occurred due to the ability of silicon to stabilise β-carbocations (Scheme 76).[24]



Scheme 76

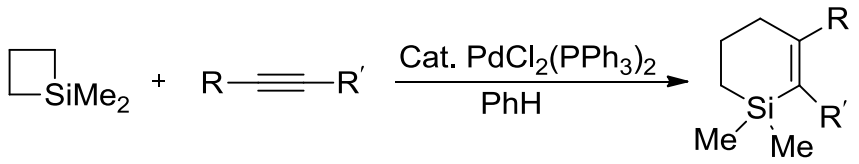
Silacyclobutanes have been utilised in catalytic ring expansion reactions *via* Si-C activation by many different metals, for example Ni, Pd, Pt, Cu, Ag, and Zn salts. Lappert *et al.* examined the first example of the insertion of a transition metal complex, pentacarbonyliron into a strained organosilicon heterocycle, 1,1-dimethyl-1-silacyclobutane **177c** to produce 2,2-dimethyl-1,1,1,1-tetracarbonyl-1-ferra-2-silacyclopentane **226** (Scheme 77).[31]



177c **225** **226**

Scheme 77

Sakurai and Imai noted the first example of a $PdCl_2(PPh_3)_2$ catalyzed alkyne **16** insertion into silacyclobutane to produce silacyclohexene derivatives **227** in moderate yields (Scheme 78).[32]



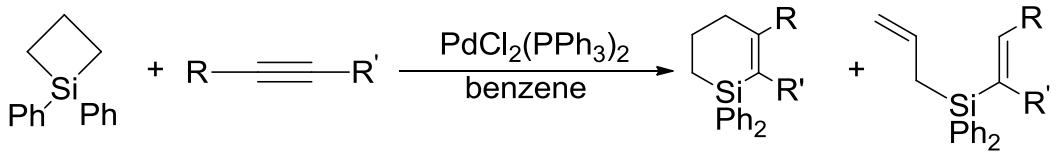
177c **16** **227**

R = R′ = COOMe
R = COOMe, R′ = H
R = Ph, R′ = H

17-45%

Scheme 78

Oshima *et al*.[33] reported that both silacyclohexene derivatives **228** and allylvinylsilane derivatives **229** were formed when 1,1-diphenyl-1-silacyclobutane **177d** was mixed with acetylene **16** in the presence of catalytic $PdCl_2(PPh_3)_2$ (Scheme 79). The ratio of acetylene-insertion products (silacyclohexenes) **228** and ring-opened allylvinylsilane products **229** was revealed to depend on the acetylenic starting material.

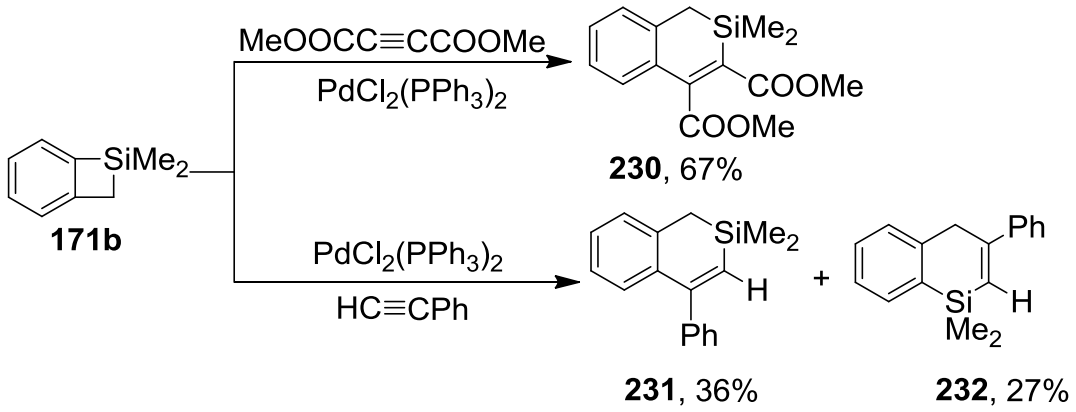


177d **16** **228** **229**

R = R' = CO_2Me	86%	7%
R = CO_2Me, R' = H	50%	26%
R = Ph, R' = H	16%	60%

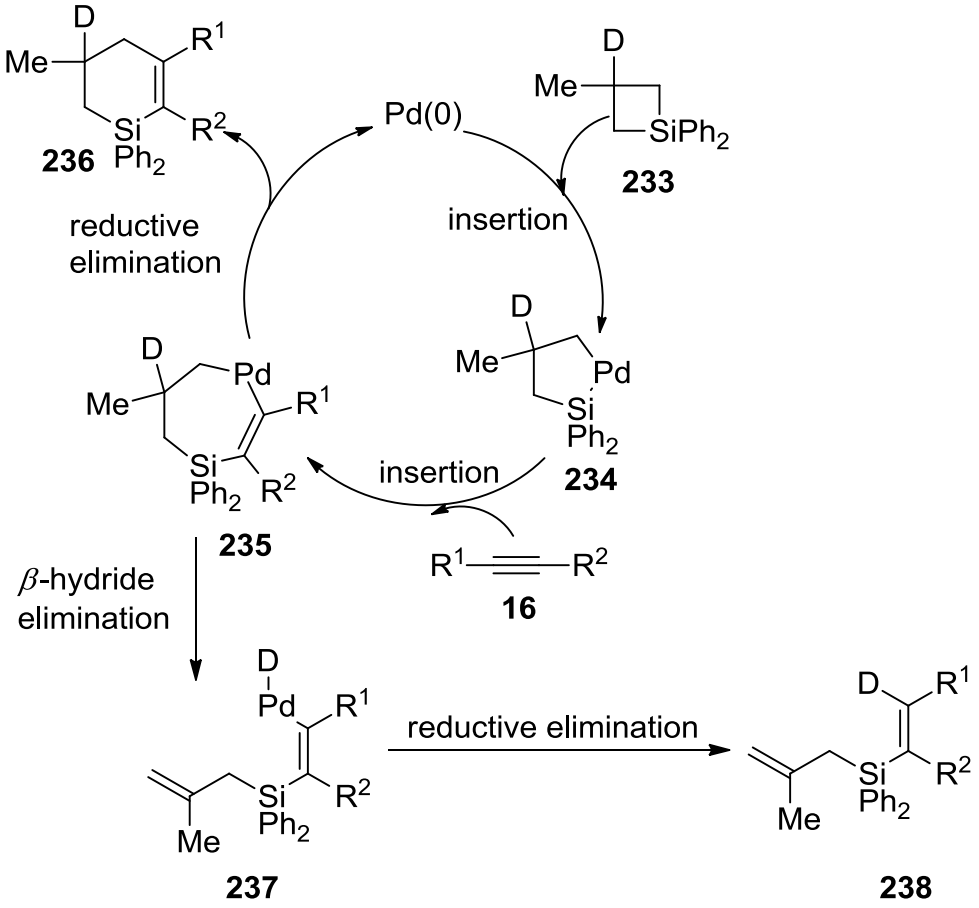
Scheme 79

Treatment of benzosilacyclobutane **171b** with dimethyl acetylenedicarboxylate or phenylacetylene under Pd catalysis provided the corresponding dihydrosilanaphthalenes (Scheme 80).



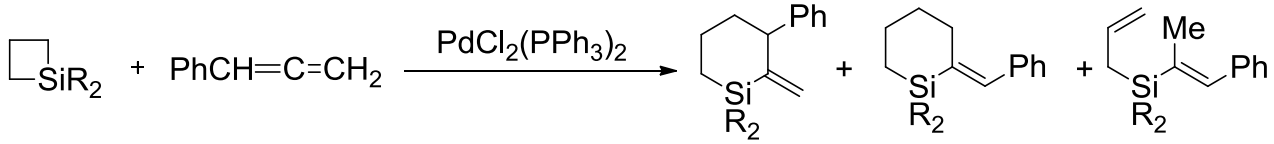
Scheme 80

The postulated mechanism of this reaction involves insertion of Pd(0) into the Si-C bond leading to the formation of five-membered palladasilacyclopentane **234**. This is followed by insertion of the acetylenic compound **16** to generate the seven-membered ring intermediate **235**, which can produce product **236** with regeneration of Pd(0) through reductive elimination. Alternatively, allylvinylsilane product **238** can be formed by *β*-hydride elimination then followed by reductive elimination (Scheme 81).



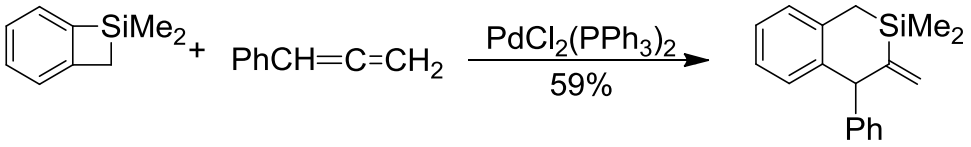
Scheme 81

When the reaction was repeated with phenylallene rather than phenylacetylene, it resulted in the formation of a mixture of three compounds. However, phenylallene inserted into benzosilacyclobutane to form 1,2,3,4-tetrahydro-2-silanaphthalene **243** as a single product (Scheme 82). [33]



177 **239** **240** **241** **242**

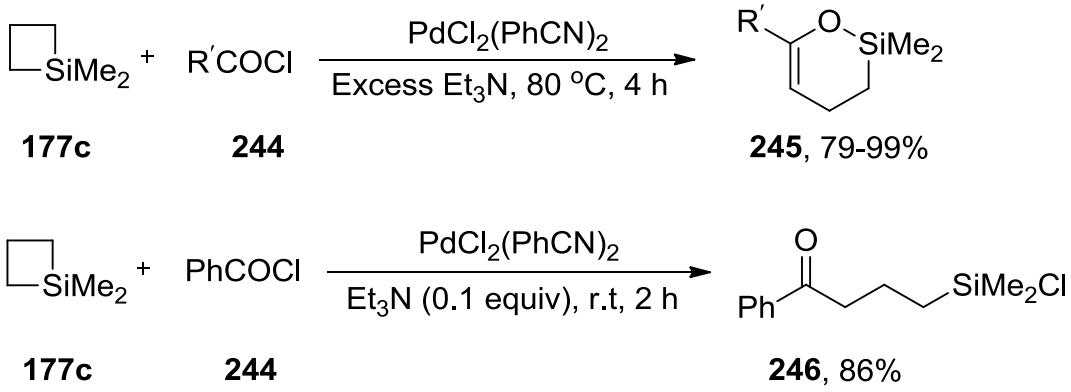
R = Me	47%	29%	11%
R = Ph	77%	8%	5%



171b **239** **243**

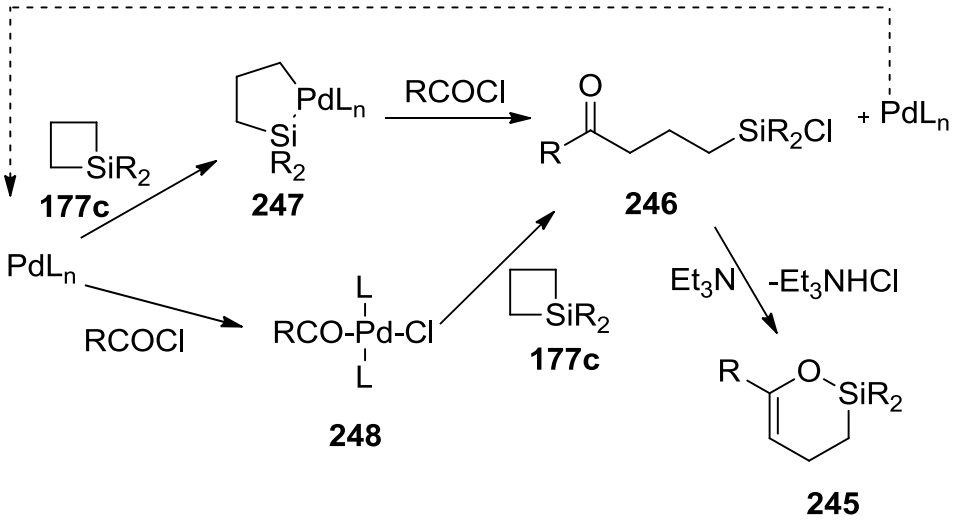
Scheme 82

The Tanaka group showed that the reaction between silacyclobutanes **177c** and acid chlorides **244** using a palladium or platinum catalyst with a large excess of tertiary amine at 80 ^{o}C can generate cyclic silyl enol ethers **245** in very high yields. On the other hand, running the reaction with a limited quantity of the amine (0.1 equivalent) and at room temperature led to the formation of 3-(chlorosilyl)propyl ketones **246** instead (Scheme 83).



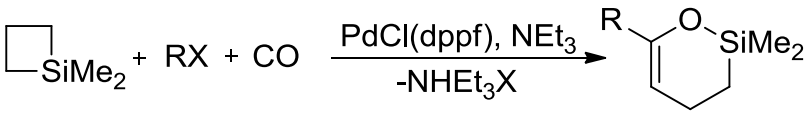
Scheme 83

The proposed mechanism of this reaction is shown in Scheme 84. The oxidative addition of silacyclobutane to palladium(0) (or platinum(0)) produces five-membered silacycle intermediate **247**, which then inserts in to the acid chloride to provide 1-phenyl-4-(chlorodimethylsilyl)-1-butanone **246**. In the presence of excess amine, intermediate **246** can cyclize to silyl enol ether **245**. Alternatively, the oxidative insertion of palladium(0) (or platinum(0)) can take place with the acid chloride to produce a chloro(acyl)-palladium(II) or platinum (II) species **248**. Subsequently, insertion of silacyclobutane **177c** can occur to produce 1-phenyl-4-(chlorodimethylsilyl)-1-butanone **246**.[34]



Scheme 84

The Tanaka group also described an alternative one-pot synthesis of cyclic enol ethers **245**; the palladium catalyzed ring expansion of 1,1-dimethyl-1-silacyclobutane **177c** with aromatic halides **249** in a carbon monoxide atmosphere (1 atm). Electron-rich and electron-deficient aromatic iodides substituents have been shown to be appropriate substrates to access cyclic silyl enol ethers **245** in excellent yields (Scheme 85).

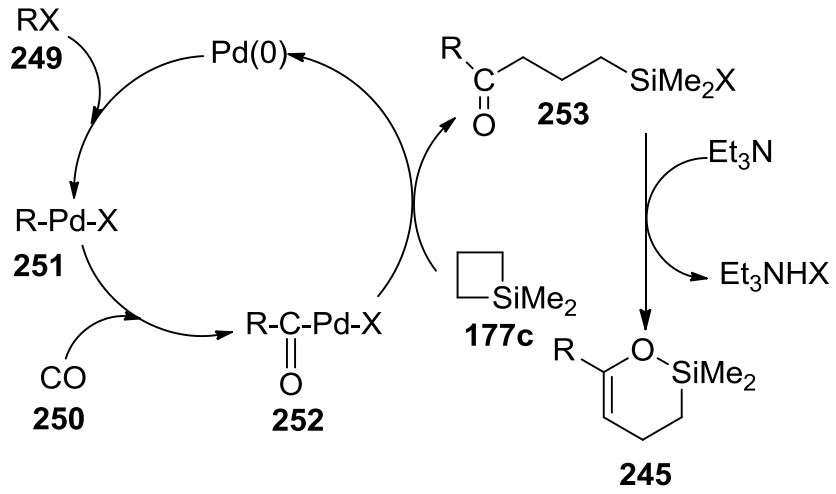


R = Ph	X = I	97%
R = *p*-$MeOC_6H_4$	X = I	94%
R = PhCH=CH	X = I	97%
R = *p*-$EtO_2CC_6H_4$	X = I	99%
R = *p*-FC_6H_4	X = I	93%
R = *p*-NCC_6H_4	X = Br	96%

Scheme 85

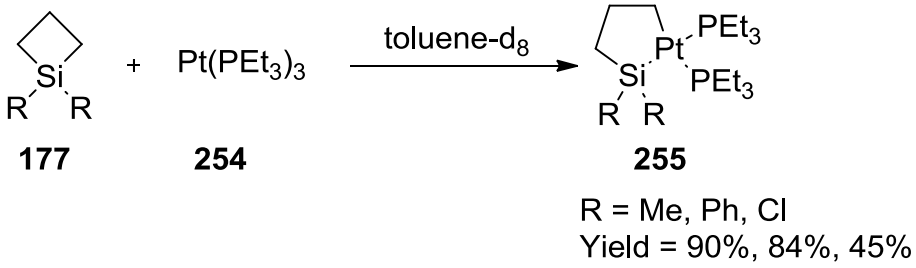
A plausible mechanism for the three-component coupling reaction is described in Scheme 86. Firstly, oxidative addition of Pd(0) to an organic halide **249** occurs to generate an aryl-palladium **251**, which undergoes CO **250** insertion to produce an acylpalladium intermediate **252**. After this

has been formed, silacyclobutane inserts into intermediate **252** to produce γ-(chlorosilyl)propyl ketone **253**, which cyclises in the presence of amine to generate cyclic enol ether **245**.[35]



Scheme 86

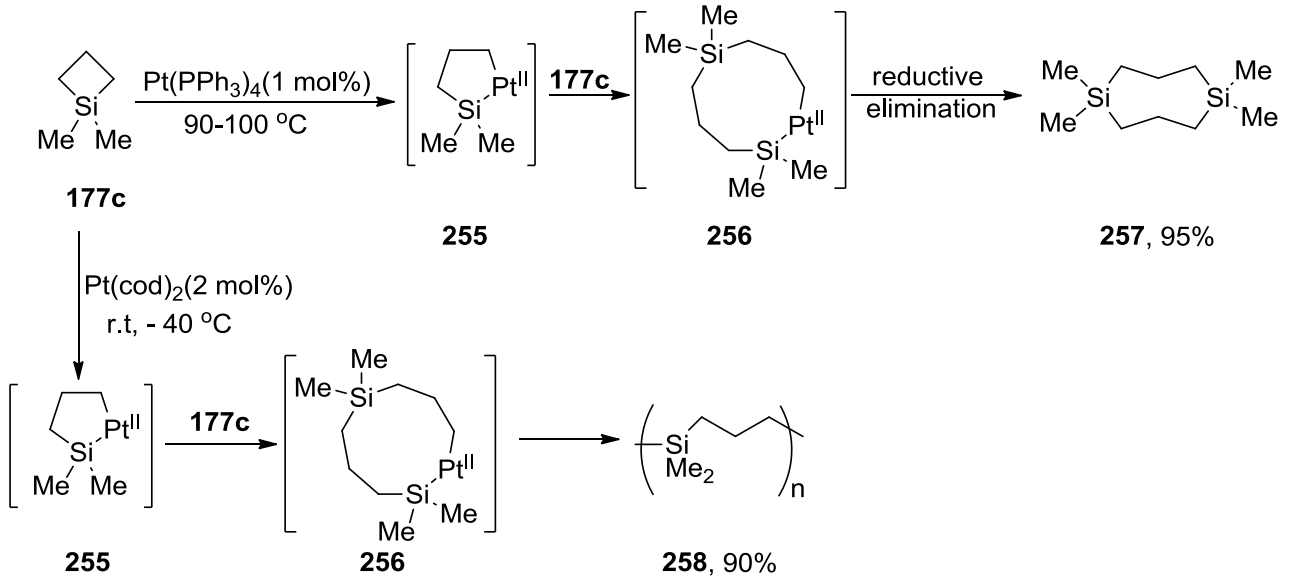
Tanaka *et al*.[36] demonstrated that Si-C bonds of silacyclobutanes easily undergo oxidative addition to $Pt(PEt_3)_3$ in toluene-d_8 upon heating in a sealed NMR tube at 60 °C. The researchers synthesised the intermediate 1-platina-2-silacyclopentane complex **255** and then studied its reactivity (Scheme 87). Many different reactions have been examined under the same conditions which have revealed that the reactivity of 1,1-disubstituted silacyclobutanes towards the oxidative addition of transition metal Pt(0) follows the order of R = Me > Ph > Cl.



Scheme 87

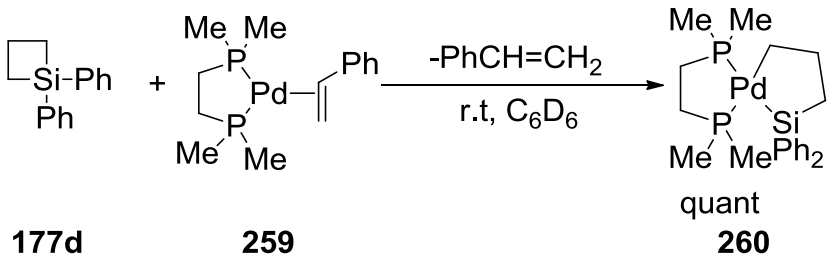
As revealed in Scheme 88, the dimer **257** is easily prepared from **177c** through platinum catalysis in the presence of phosphine ligands by reaction with another molecule of silacyclobutane **177c** through 1-platina-2-silacyclononane intermediate **256.** This intermediate is not as stable as **255**

because of the bigger ring size and the dimer **257** forms through reductive elimination. Polymerization product **258** is formed when Pt catalysis without phosphine ligands is employed.



Scheme 88

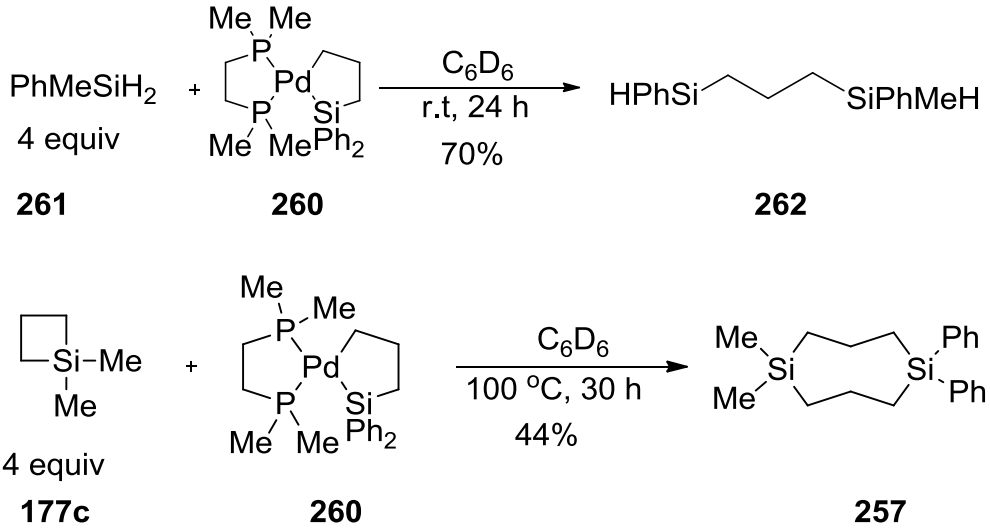
What is more, Tanaka *et al*.[37] reported the first example of an isolable alkyl(silyl)palladium species. The 1-pallada-2-silacyclopentane complex **260** was formed in quantitative yield after 10 minutes through treating Pd(η^{2}-PhCH=CH_2) (dempe) with 1,1-diphenylsilacyclobutane **177d** in C_6D_6 at room temperature (Scheme 89).



Scheme 89

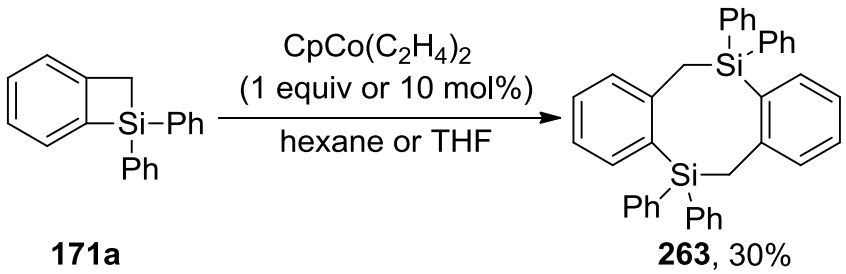
When the 1-pallada-2-silacyclopentane complex **260** was mixed with four equivalents of methylphenylsilane **261** in C_6D_6 in a sealed NMR tube at room temperature a ring-opening reaction occurred and the 1,3-bis(hydrosilyl) propane **262** product was generated in a yield of 70%. On the other hand, when the 1-pallada-2-silacyclopentane complex **260** was mixed with 1,1-

dimethylsilacyclobutane **177c** in C_6D_6 in a sealed NMR tube and heated at 100 ^oC, the 1,5-disilacyclooctane (pseudo-dimer) product **257** was generated in a yield of 44% (Scheme 90).



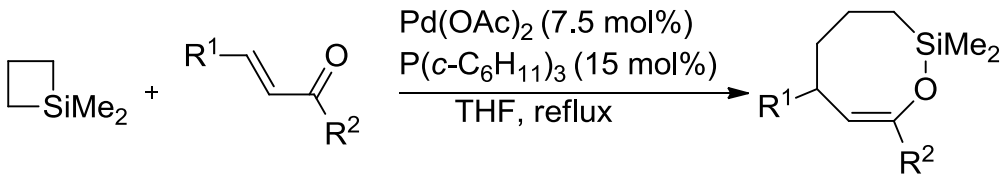
Scheme 90

In 2007, another example of the dimerisation process was shown by Agenet and co-workers.[38] They showed 1,1-diphenylbenzosilacyclobutene **171a** can undergo dimerisation in the presence of catalytic or stoichiometric amounts of $CpCo(C_2H_4)_2$ to afford the dimer **263** in moderate yield (Scheme 91).[38]



Scheme 91

Oshima *et al.*[39] reported the palladium-catalysed formal cycloaddition of silacyclobutanes with enones to provide numerous eight-membered cyclic silyl enol ethers (Scheme 92). They have also described the palladium-catalysed formal intermolecular cycloaddition of silacyclobutanes with alkynes to generate eight-membered rings.

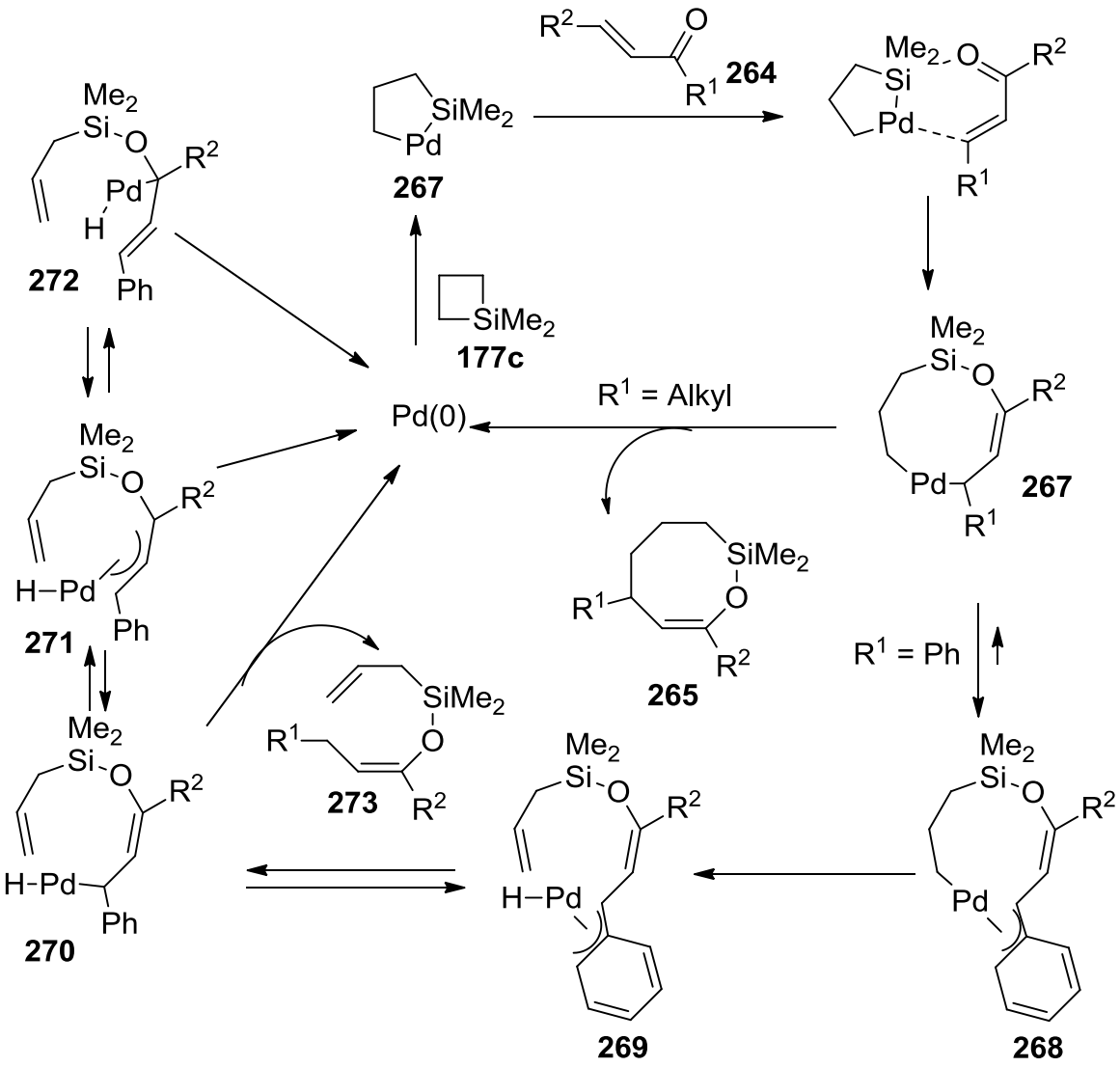


177c **264** **265**

R^1 = *n*-Pr, R^2 = Ph	80%
R^1 = *n*-Pr, R^2 = 4-PhC_6H_4	89%
R^1 = *n*-Pr, R^2 = 4-FC_6H_4	82%
R^1 = *n*-Pr, R^2 = 4-$CF_3C_6H_4$	90%
R^1 = *n*-Pr, R^2 = 2-Naphthyl	78%
R^1 = Me, R^2 = Ph	75%
R^1 = *n*-Pr, R^2 = 2-Thienyl	62%
R^1 = $PhCH_2O(CH_2)_9$, R^2 = Ph	76%

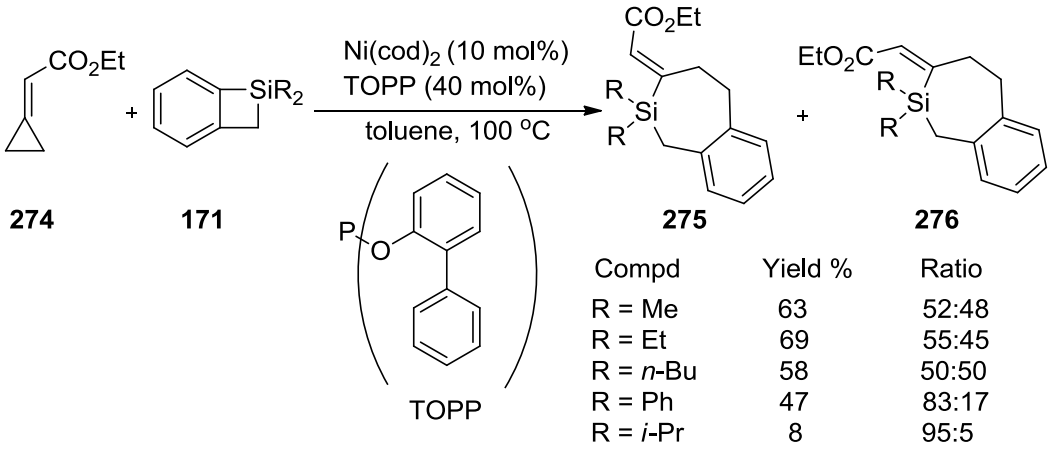
Scheme 92

The mechanism of this formal cycloaddition of silacyclobutane **177c** with enones **264** is revealed in Scheme 93. The palladasilacyclopentane intermediate **266** is formed by the oxidative addition of silacyclobutane to palladium(0). After this, the insertion of the enone **264** can occur into the Si-Pd bond to generate nine-membered palladacycle **267**. With β-alkyl-substituted enones, there is fast reductive elimination to produce the eight-membered cyclic silyl enol ethers **265** whilst regenerating Pd(0). On the other hand, with R^1 = Ph, the π-benzylpalladium intermediate **268** is formed leading to *β*-hydride elimination rather than reductive elimination to produce palladium hydride intermediate **269**. This can undergo σ to π isomerisations leading to palladium intermediates **270**, **271**, and **272**, which can undergo reductive elimination to produce the ring opened product **273**.[39]



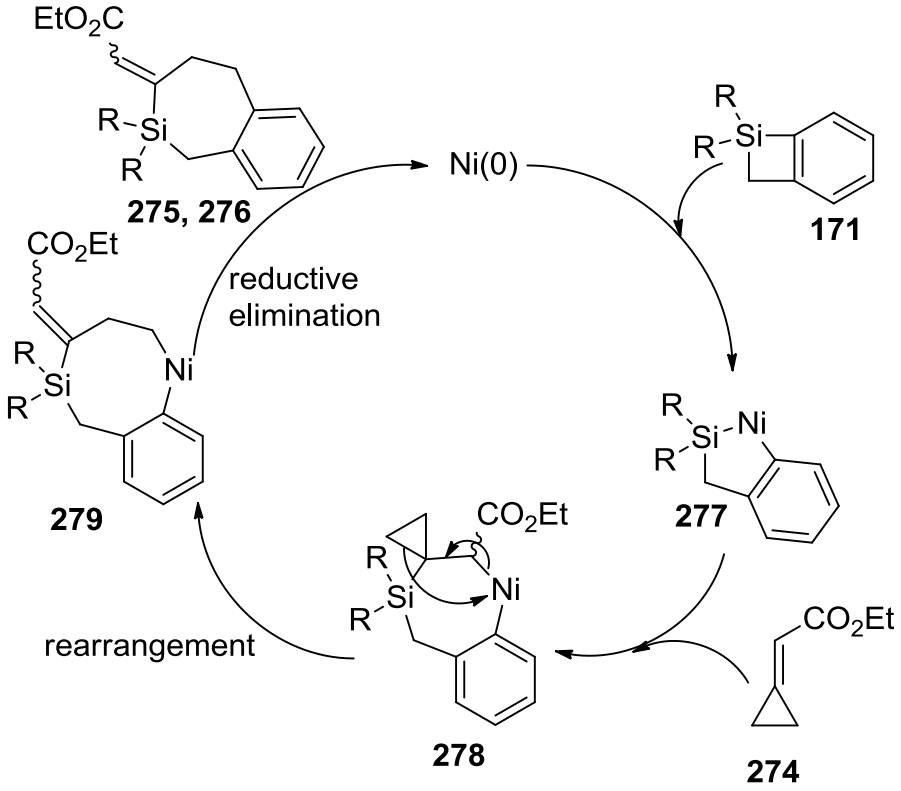
Scheme 93

Another example of a ring expansion reaction has been reported by the Saito group (Scheme 94).[40] In this reaction, benzosilacyclobutane derivatives reacted with ethyl cyclopropylideneacetate **274** through the use of catalytic $Ni(cod)_2$ and TOPP ligand (tribiphenyl-2-yl phosphite) in toluene at 100 ^oC over 5 h to provide seven membered ring products **275**, and **276**. However, little to no preference for alkene geometrical isomers was observed.



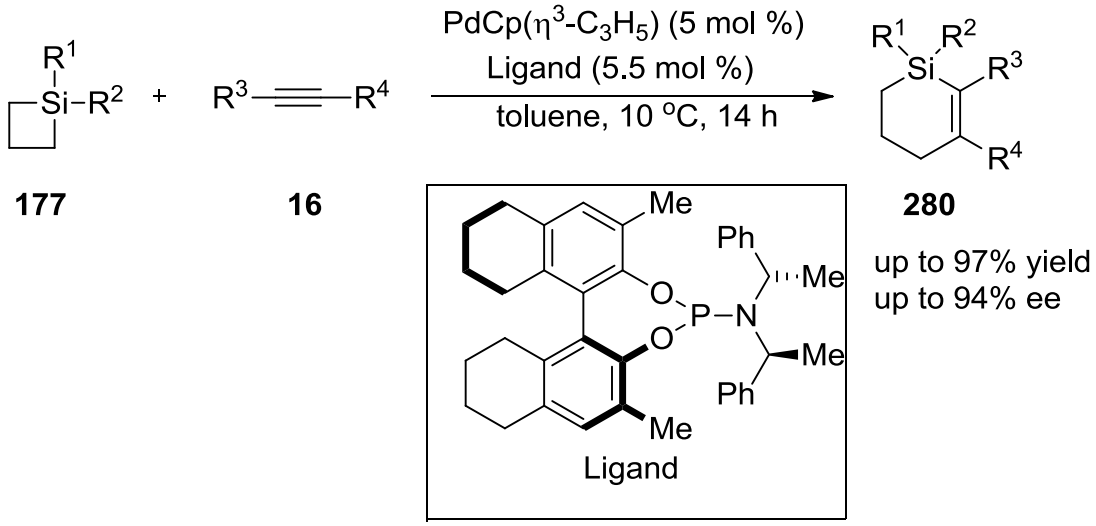
Scheme 94

The mechanism of the ring expansion reaction of benzosilacyclobutane **171** is shown in Scheme 95. The Ni(0) undergoes oxidative insertion into the Si-C bond of benzosilacyclobutane **171** to provide the five-membered ring intermediate **277**. This combines with **274** to produce the seven-membered ring nickelacycle **278** through insertion of the Si-C bond. Opening of the cyclopropane ring and rearrangement leads to **279** and finally **275** and **276** are formed through reductive elimination.[40]



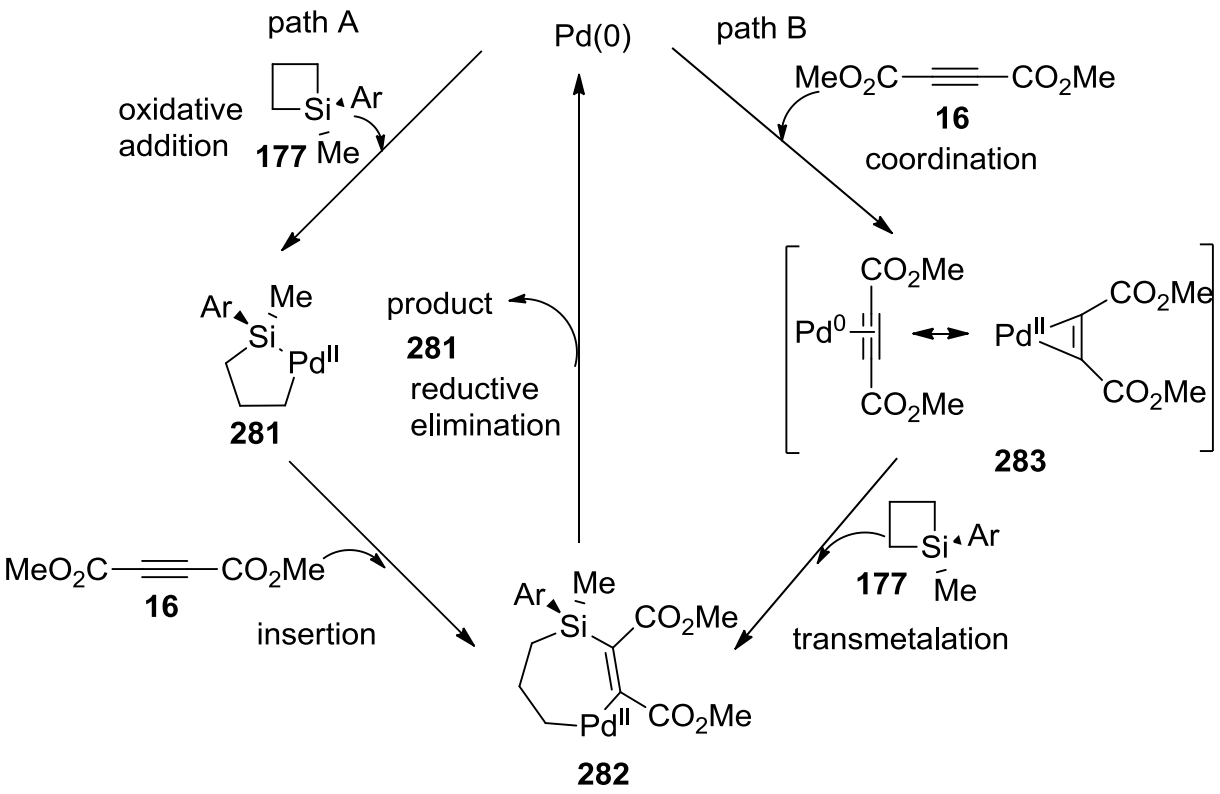
Scheme 95

In 2012, Hayashi *et al.*[41] reported a palladium-catalyzed enantioselective desymmetrization of silacyclobutanes with electron-deficient alkynes to produce silicon-stereogenic 1-sila-2-cyclohexenes **280** with high enantioselectivity and very high yields. The researchers used PdCp(η^3-C_3H_5) as catalyst (a chiral monophos ligand) in toluene at 10 °C to bring about the transformation (Scheme 96).



Scheme 96

Two conceivable mechanisms are suggested for the catalytic cycle (Scheme 97). First, 1-pallada-2-silacyclopentane intermediate **281** can be formed through oxidative addition of a C-Si bond of silacyclobutane **177** to palladium(0) (path A). Subsequent insertion of alkyne **16** would give 1-pallada-4-sila-2-cycloheptene intermediate **282**, which can undergo reductive elimination to produce the product **280** and Pd(0). Alternatively, in path B, which is more likely than path A, the coordination of alkyne **16** to palladium(0) results in the formation of a 1-pallada-2-cyclopropene intermediate **283**. Then, transmetalation of silacyclobutane can provide 1-pallada-4-sila-2-cycloheptene intermediate **282**, followed by reductive elimination to give the product **280** and Pd(0).[41]



Scheme 97

1.4 Summary

Silicon is a cheap nontoxic element of increasing importance to chemists as incorporating silicon atom into molecules can have beneficial effects over the carbon analogues. However, known synthetic chemistry with silicon is far behind carbon. Despite being in the same group as carbon, the reactivity of silicon is markedly different.

Silacycles have played very important role in recent organic chemistry due to the ring strain of a four-membered ring and Lewis acidity, these molecules have been used in a wide range of chemical transformation, one of these we discussed above ring expansion reactions with electrophilic reagent as well as ring expansion reactions *via* Si-C activation by many different transition metals.

2 Aim and objective

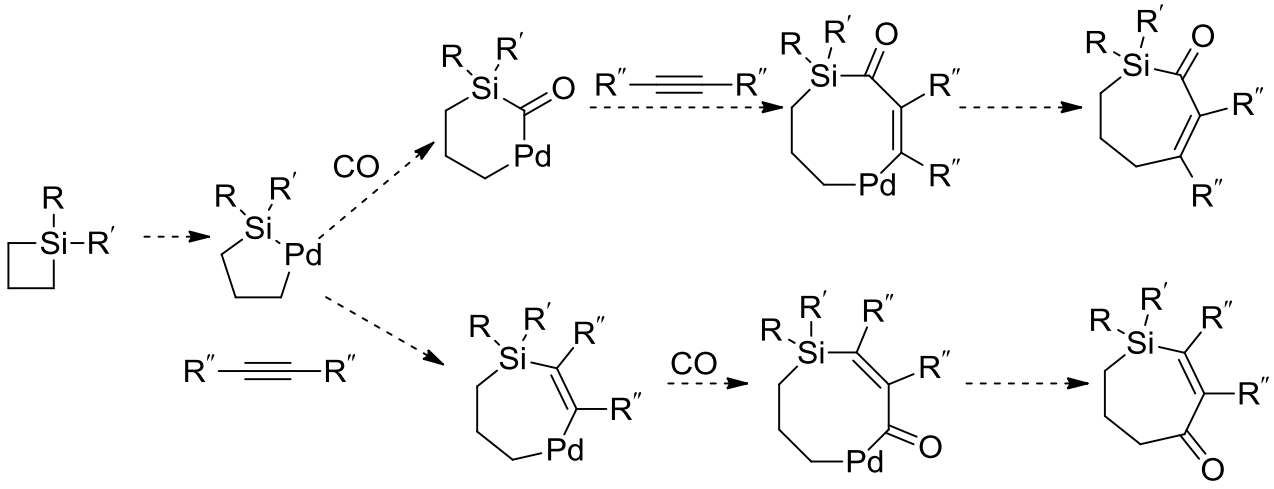
The aim of this project was to investigate the reactivity of silacycles in order to access new chemical space. The synthetic chemistry of silicon is underdeveloped and we aimed to address this shortfall through two strategies;

• First strategy Pd-catalyzed dimerization of silacycobuanes and benzosilacyclobutenes.

• Second strategy Ni and Pd –catalyzed reactions of benzosilacyclobutenes: enantioselective ring expansion.

3 Results and Discussion

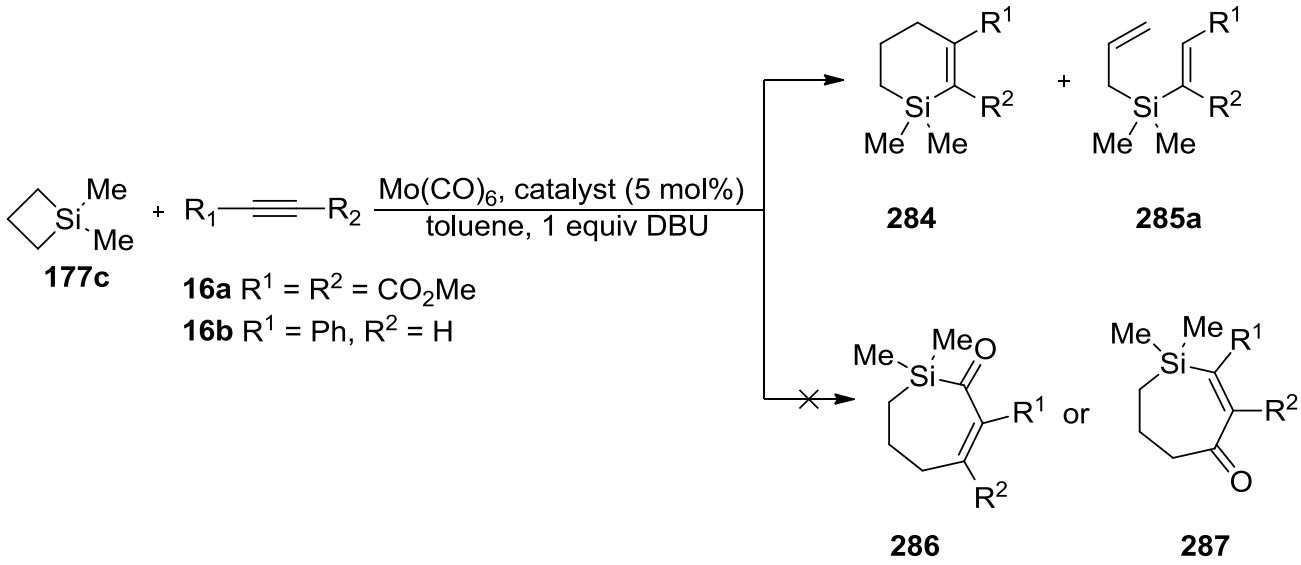
In 1975, Sakurai and Imai reported the Pd-catalyzed ring expansion of 1,1-dimethylsilacyclobutane with alkynes as shown in Scheme 78.[32] Based on this report, the aim was to investigate the insertion of CO into the palladium-silacycle and the subsequent reaction with alkynes (Scheme 98). Importantly, this investigation would enable access to unknown silacycles. CO could potentially be inserted into either the Pd-Si or the Pd-C bond leading to different products, although the former was probably more likely in analogy with alkyne insertion. Alternatively, alkyne insertion could occur first followed by carbonylation.

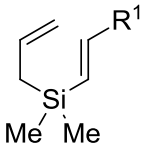


Scheme 98

Larhed *et al.*[42] have developed a method for the aminocarbonylation of nitro group substituted aryl iodides and aryl bromides utilizing $Mo(CO)_6$ as a source of CO using a bridged two-vessel system. Following their procedure, the study began with commercially available 1,1-dimethylsilacyclobutane **177c** and dimethyl but-2-ynedioate (DMAD) **16a** in the presence of a catalytic amount of $Pd(OAc)_2$, 0.5 equiv of $Mo(CO)_6$ and 1 equiv of DBU in toluene at room temperature but there was no product observed (Table 7, entry 1). The reaction was attempted again at 65 °C, but only starting materials were returned (entry 2). Attempting the reaction in the microwave at 65 °C, also led to no desired product **5** being formed (entry 3). However, further

increases in the temperature to 100 ^{o}C (entry 4) led to formation of dimethyl 1,1-dimethyl-1-sila-2-cyclohexene-2,3- dicarboxylate **284** and methyl (*E*)-4,4-dimethyl-4-sila-2,6-heptadienoate **285**. This suggests that CO insertion is not facile. In a further attempt phenylacetylene was used in place of DMAD with $Pd(OAc)_2$ as catalyst, but again no product was obtained. However, the use of $Pd(PPh_3)_2Cl_2$ as catalyst provided the allylvinylsilane as the major product (entries 5 and 6).



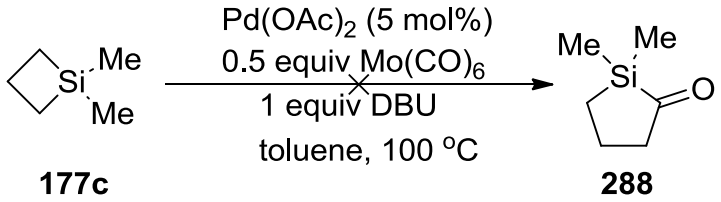
Entry	Conditions	Alkyne	Major product	Yield[a] %
1	$Pd(OAc)_2$, 0.5 equiv $Mo(CO)_6$, r.t for 10 min.	**16a**	N.R	0
2	$Pd(OAc)_2$, 0.5 equiv $Mo(CO)_6$, r.t for 10 min, then 65 ^oC for 1 h.	**16a**	N.R	0
3	$Pd(OAc)_2$, 0.5 equiv $Mo(CO)_6$, 65 ^oC, microwave.	**16a**	N.R	0
4	$Pd(OAc)_2$, 1 equiv $Mo(CO)_6$, 100 ^oC.	**16a**	**284 + 285a**	44(**284**) 16(**285a**)
5	$Pd(OAc)_2$, 0.5 equiv $Mo(CO)_6$, 100 ^oC.	**16b**	N.R	N.R
6	$Pd(PPh_3)_2Cl_2$, 0.5 equiv $Mo(CO)_6$, 100 ^oC.	**16b**		42 (**285b**)

[a] Determined by ^1H NMR analysis.

Table 7

At this point it was decided to attempt the reaction without any alkyne present by subjecting 1,1-dimethylsilacyclobutane to $Pd(OAc)_2$ with 0.5 equiv of $Mo(CO)_6$ and 1 equiv of DBU in toluene in the microwave at 65 ^oC in order to investigate the possible formation of the five-membered ring product **288** by CO insertion (Table 8, entry 1). Unfortunately, there was no sign of the desired product from ^1H NMR analysis of the crude reaction mixture. When repeating the treatment of 1,1-dimethysilacyclobutane **177c** with $Pd(OAc)_2$, $Mo(CO)_6$ and DBU at room temperature (entry 2), it was found that a small amount of a new compound was observed in the ^1H NMR spectrum of the crude reaction mixture. Analysis suggested that dimerisation had occurred, but in low yield. As shown earlier, a stoichiometric amount of Pd salt and high temperature has been shown to be

necessary for the dimerisation of silacyclobutanes (Scheme 90). Potentially, this was a catalytic version of this process occurring at room temperature that had been uncovered.



177c **288**

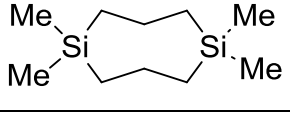
Entry	Conditions	Alkyne	Major product	Yield
1	65 °C for 30 min, microwave.	no alkyne	N.R	0
2	r.t.	no alkyne		Trace

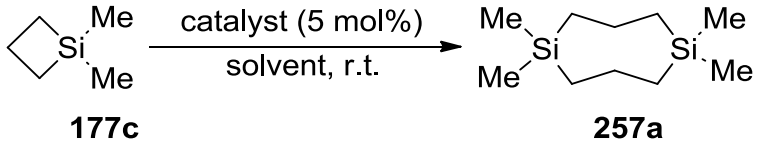
Table 8

3.1 Pd-catalysed dimerisation of silacyclobutanes

It was envisaged that the dimerisation process did not require $Mo(CO)_6$ or DBU, so the optimisation was begun by stirring 1,1-dimethylsilacyclobutane **177c** in toluene at room temperature under a nitrogen atmosphere for 24 h in the presence of $Pd(OAc)_2$ (5 mol%). We were delighted to discover the same product as before but in just 6% yield. Unfortunately, a pure sample of **257a** could not be obtained (Table 9, entry 1).

The next step to optimise the reaction conditions was to investigate a variety of palladium salts. A range of Pd(0) and Pd(II) salts were tested (entries 2-7) but unfortunately none of these led to formation of the product. Eventually it was found that $Pd(MeCN)_4(BF_4)_2$ was the most effective catalyst with an improvement in yield of the desired product to 14% (entry 8). The reaction was attempted again in order to investigate the effect of temperature on the reaction, and the yield was

increased to 35% upon heating to 40 °C (entry 9). However, when the reaction was repeated with a further increase of temperature up to 60 °C, there was no additional increase in yield (entry 10).



177c **257a**

Entry	Catalyst	Solvent	Temp (°C)	Yield %
1	$Pd(OAc)_2$	toluene	r.t.	6
2	$Pd(PPh_3)_4$	toluene	r.t.	-
3	$Pd_2(dba)_3.CHCl_3$	toluene	r.t.	-
4	Pd/C	toluene	r.t.	-
5	$PdCl_2$	toluene	r.t.	-
6	$Pd(OCOCF_3)_2$	toluene	r.t.	-
7	PEPPSI-IPr	toluene	r.t.	-
8	$Pd(MeCN)_4(BF_4)_2$	toluene	r.t.	14
9	$Pd(MeCN)_4(BF_4)_2$	toluene	40	35
10	$Pd(MeCN)_4(BF_4)_2$	toluene	60	34
11	$Pd(MeCN)_4(BF_4)_2$	toluene	r.t.	39[a]
12	$Pd(MeCN)_4(BF_4)_2$	1,4-dioxane	r.t.	-
13	$Pd(MeCN)_4(BF_4)_2$	MeCN	r.t.	-
14	$Pd(MeCN)_4(BF_4)_2$	benzene	r.t.	-
15	$Pd(MeCN)_4(BF_4)_2$/CuCl	toluene	r.t	-[b]
16	$Pd(MeCN)_4(BF_4)_2/H_2O$	toluene	r.t.	-[c]

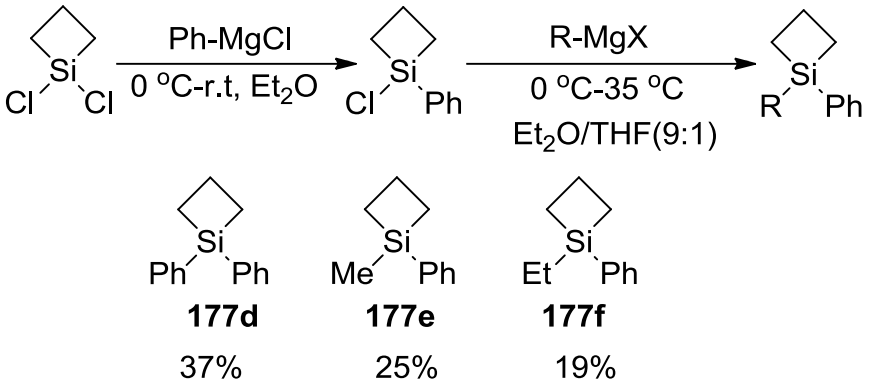
[a] 10 mol% catalyst was used. [b] 5 mol% of CuCl added to reaction mixture. [c] 1 equiv of H_2O added to reaction mixture.

Table 9

In a further attempt to improve the yield of this reaction, the amount of catalyst was increased to 10 mol%. In the event, the yield was increased to 39% of isolated compound which occurred at room temperature in just 10 min (entry 11). However, further increases in the amount of catalyst failed to lead to any additional yield. NMR analysis of the reaction indicated complete consumption of starting material. In order to investigate the effect of solvent on the reaction outcome, 1,4-dioxane, acetonitrile and benzene were tried but no product was obtained (entries 12-14). Moreover, the addition of 5 mol% CuCl or water inhibited the reaction completely (entries 15, 16). Under the optimal conditions it was pleasing to see that the reaction took place with complete consumption of the starting material providing a pure sample of dimer with no other products beings isolable by chromatography.

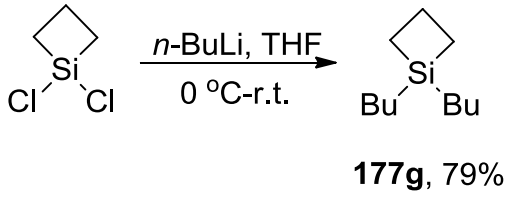
This process was surprising as previous work has shown that to effect this dimerisation requires stoichiometric palladium and a high temperature of 100 ^{o}C.[37] This process is catalytic in palladium and occurs at room temperature. Initial interpretation would suggest that **177c** undergoes oxidative addition by Pd(0) to form a palladacycle which quickly reacts with another equivalent of **177c** (in preference to CO or alkyne). These results call in to question the proposed mechanisms in several publications, as it seems unlikely that Pd(0) undergoes oxidation addition to silacyclobutanes under their reaction conditions (Scheme 81).

At this stage it was decided to investigate the scope of this Pd-catalysed dimerisation reaction, and various silacyclobutane derivatives **177d**, **177e** and **177f** were prepared (Scheme 99). These were synthesised from commercially available 1,1-dichlorosilacyclobutane by addition of two successive Grignard reagents to give the silacyclobutane derivatives in good yields.[41]



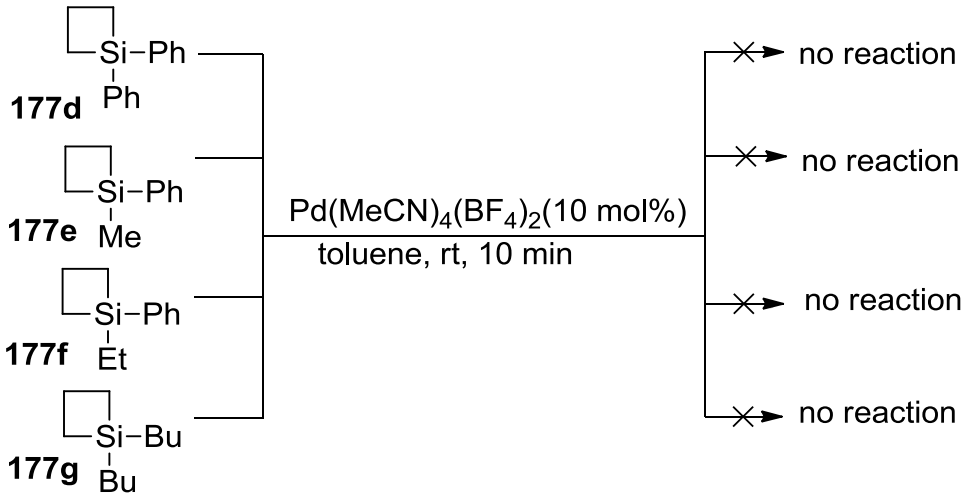
Scheme 99

1,1-Dibutylsilacyclobutane was obtained in very good yield through addition of *n*-butyl lithium to 1,1-dichlorosilacyclobutane in THF (Scheme 100).



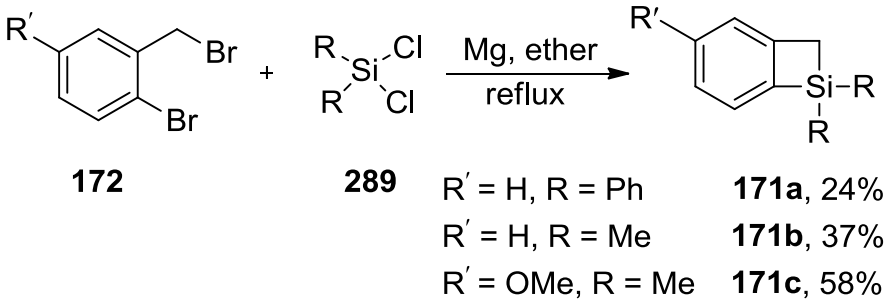
Scheme 100

With these four substrates in hand, the dimerisation was attempted using the developed conditions, but no reaction occurred and the starting materials were returned in all cases. It is proposed that the dimerisation did not occur due to steric bulk preventing the initial oxidative addition step required in this process (Scheme 101).



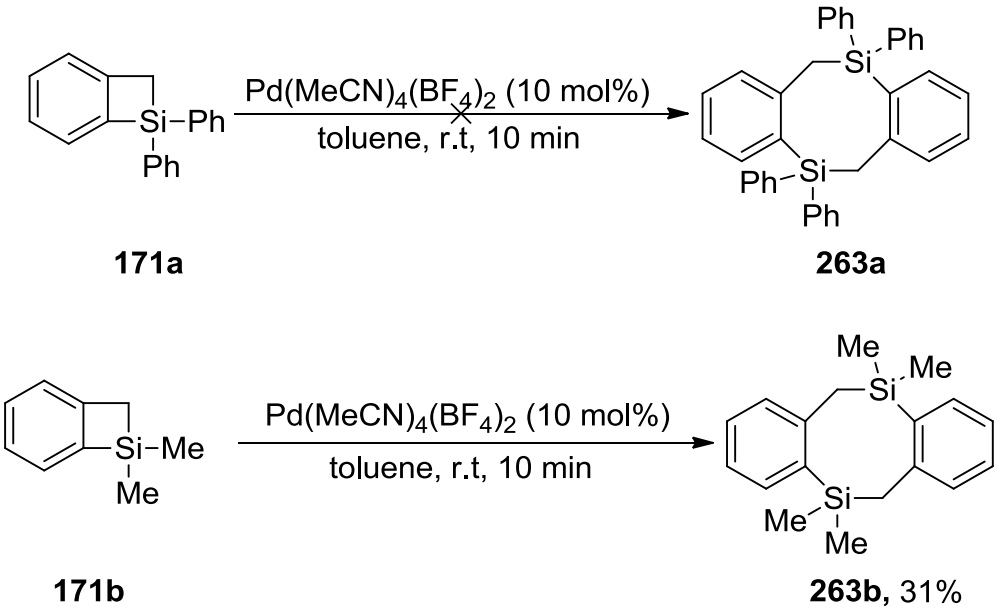
Scheme 101

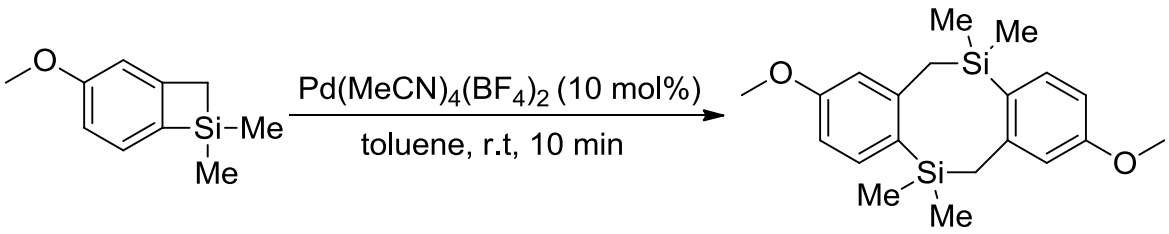
In a further attempt to investigate the substrate scope of the dimerisation reaction, benzosilacyclobutane derivatives **171a**, **171b**, and **171c** were prepared from the reaction of 1-bromo-2-(bromomethyl)benzene **172** with magnesium in ether with dichlorosilanes **289** (Scheme 102).[43]



Scheme 102

When the 1,1-dimethylbenzosilacyclobutane **171b** was treated with the optimized dimerisation conditions (Scheme 103), the dimer **263b** was formed with a yield of 31%. Moreover, the 4-methoxy-7,7-dimethyl-7-silabicyclo[4.2.0]octa-1(6),2,4-triene **171c** was also subjected to the reaction conditions and the dimer **263c** was isolated in 12% yield. In contrast, the 1,1-diphenylbenzosilacyclobutane **171a** did not undergo the dimerisation process.

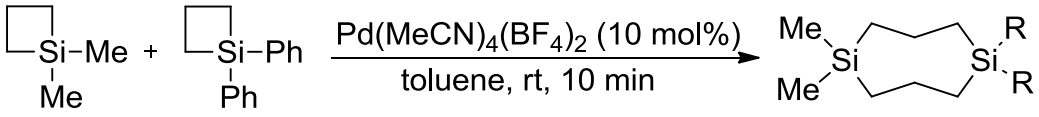




171c **263c**, 12%

Scheme 103

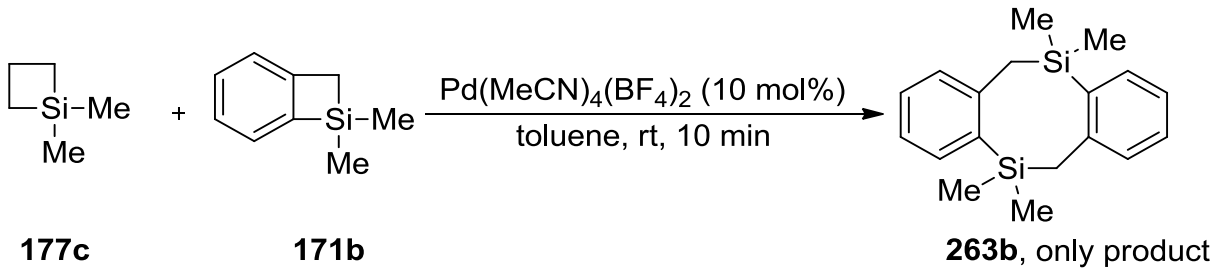
The next goal was to determine whether there were any differences in the reactivity of the different palladium species toward silacyclobutanes during the reaction. It was noted that when a 1:1 mixture of silacyclobutanes **177c** and **177d** was subjected to the reaction conditions, a 1:1 mixture of the two products **257cc** and **257cd** were formed (according to ^{1}H NMR analysis) (Scheme 104). It was also pleasing to find that a 1:2 mixture of silacyclobutanes **177c** and **177d** led to formation of a 1:2 ratio of **257cc** and **257cd**. These results show that even though the initial oxidative addition only occurs with **177c** the subsequent insertion of a second silacyclobutane occurs with **177c** and **177d** at a similar rate.



177c		**177d**	**257cc:257cd**
1	:	1	1:1
1	:	2	1:2

Scheme 104

Moreover, in order to determine the effect of the aromatic ring on activation of the C-Si bond in 1,1-diphenylbenzosilacyclobutane compared to 1,1-dimethylsilacyclobutane, a 1:1 mixture of **177c** and **171b** was subjected to the reaction conditions (Scheme 105). When the ^{1}H NMR spectrum of the resulting crude reaction mixture was obtained only one product was observed dimethyl dimer **263b**. This suggests that **171b** reacts more quickly than **177c** in both stages of the dimerisation process.

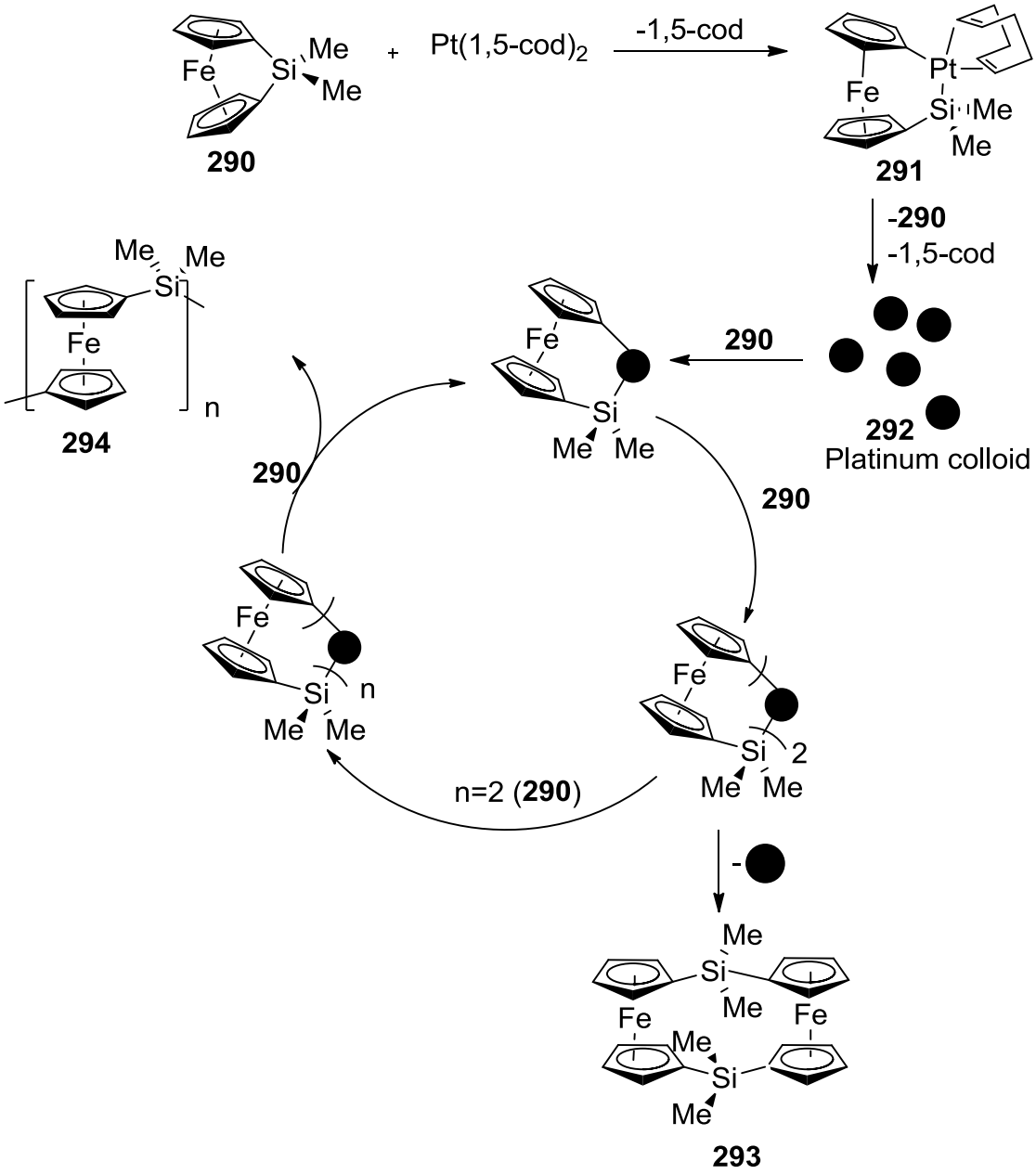


Scheme 105

In an attempt to understand the reaction mechanism of the dimerisation process a number of further experiments were undertaken. Silacyclobutane **177c** was treated with the standard reaction conditions and one equivalent of galvinoxyl. It was observed that there was no effect on the rate or outcome of the reaction which indicates that this is not a radical process. Another experiment was performed whereby one equivalent of mercury was added to the reaction mixture. In the event, when the ^{1}H NMR spectrum of the crude reaction mixture was obtained complete inhibition of the dimerisation was observed.

Manners and co-workers detected dimerisation compounds during their exploration of the ring-opening polymerization (ROP) of silicon-bridged ferrocenophanes (Scheme 106).[44,45] They investigated the effect of mercury on the ROP and suggested that a heterogeneous mechanism is operating. Treatment of **290** with Pt(1,5-cod)$_2$ led to formation of the [2] platinasilaferrocenophane **291** *via* oxidative-addition to Pt(0). Subsequent elimination of the remaining 1,5-cod ligand led to formation of the platinum colloids **292**. Finally, oxidative-addition and reductive elimination generates the products **293** and **294**.

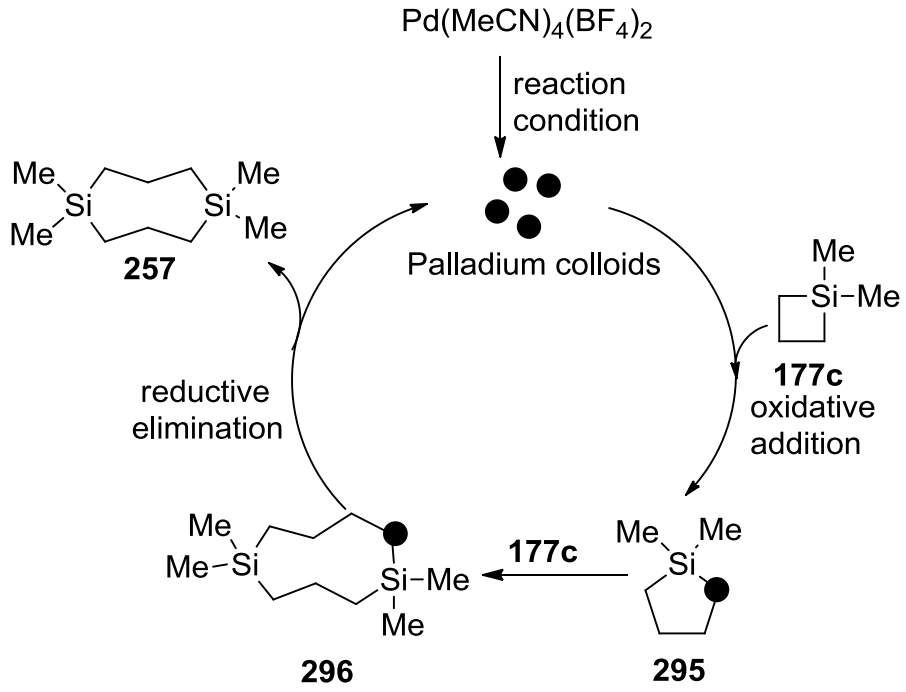
Importantly, in comparison with their result the fact that the addition of mercury to the reaction conditions resulted in inhibition of dimerisation is believed to be the result of a heterogeneous catalytic mechanism.



Scheme 106

Similarly, in our dimerisation it is presumed that a key step in the mechanism is the palladium salt $Pd(MeCN)_4(BF_4)_2$ generates palladium colloids first under the reaction conditions (Scheme 107). This step is more likely to occur according to our study rather than the oxidative addition of Pd(0) into silacyclobutane as previously discussed. Then, these colloids undergo oxidative addition to the silacyclobutane **177c** to form the palladacycle intermediate **295**. This species can react with another

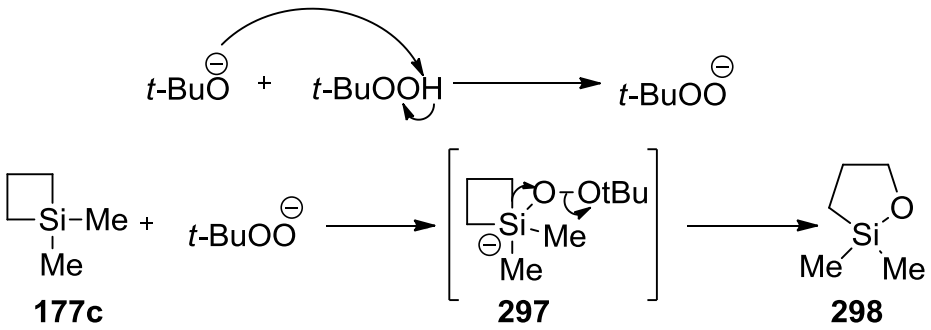
molecule of silacyclobutane **177c** to give a nine-membered palladacycle **296**. Finally, reductive elimination forms the product **257**.



Scheme 107

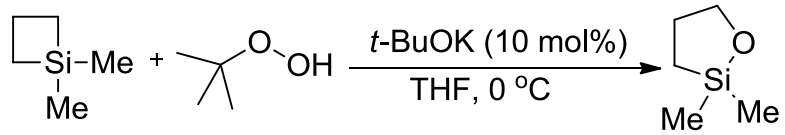
3.2 Base catalysed ring expansion of silacyclobutanes

Previous work by Oshima has shown that potassium *t*-butoxide catalyses the reaction between silacyclobutanes and aldehydes to yield six-membered cyclic silyl ethers as shown in Scheme 68.[27] We hypothesised that addition of a nucleophilic peroxide to 1,1-dimethylsilacyclobutane **177c** would lead to formation of pentacoordinate siliconate intermediate **297** which would then rearrange to afford five-membered ring product **298** (Scheme 108).



Scheme 108

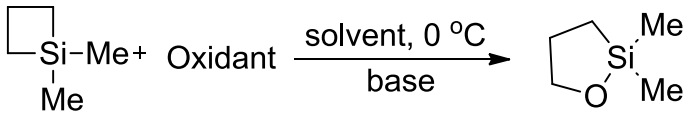
Accordingly, treatment of **177c** with catalytic potassium *tert*-butoxide and *tert*-butyl hydroperoxide led to oxidative ring expansion product 2,2-dimethyl-1,2-oxasilolane **298** but in very low yield (Scheme 109).



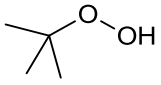
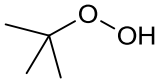
177c **298**

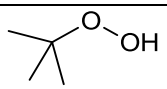
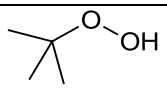
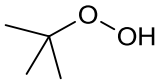
Scheme 109

In order to improve the yield of this reaction, an optimisation study was conducted (Table 10). The reaction was repeated with an increase in the amount of base to one and three equivalents to see if the yield improved (entries 1, 2), but, unfortunately, no conversion of the starting material was evident. Then, the effect of oxidant was investigated; hydrogen peroxide was used instead of *tert*-butyl hydroperoxide in both solvents THF and ether but no product was observed in either case (entries 3, 4). In addition, the effect of changing the base was investigated; by using NaOEt but this led to no conversion of the starting material (entry 5). However, product **298** could be obtained in 23% yield using the original conditions in ether instead of THF (entry 6). When the reaction was repeated with10 mol% *t*-BuOK in ether conversion increased and the product **298** was isolated in 43% yield (entry 7).



177c **298**

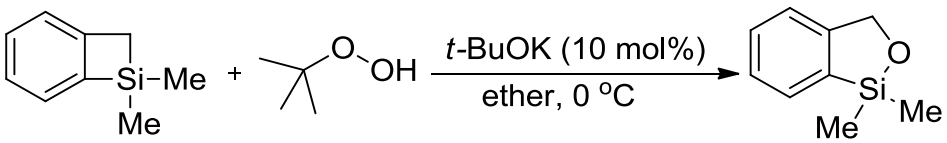
Entry	Oxidant	Base	Solvent	Yield %
1		*t*-BuOK 3 equiv	THF	-
2		*t*-BuOK 1 equiv	THF	-

3	H_2O_2	*t*-BuOK 10 mol%	THF	-
4	H_2O_2	*t*-BuOK 10 mol%	ether	-
5		NaOEt	ether	-
6		*t*-BuOK 5 mol%	ether	23
7		*t*-BuOK 10 mol %	ether	43

[a] Yield of pure compound.

Table 10

With these reaction conditions in hand, attention was turned to 1,1-dimethylbenzosilacyclobutane **171b.** Based on our previous study of the dimerisation process this substrate was expected to be more reactive than **177c**, however in the event, the reaction mixture contained more than one product and the starting material. Unfortunately, a pure sample of **299** could not be separated from the byproducts by flash chromatography (Scheme 110).



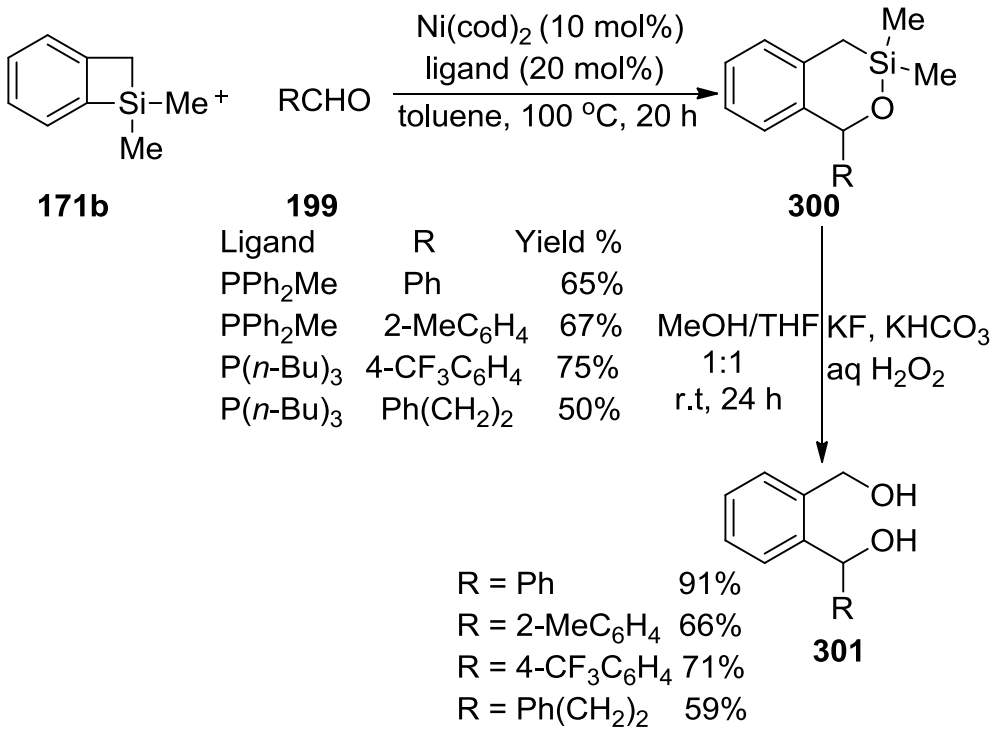
171b **299**

Scheme 110

More work is required for this process to investigate the reactivity of various silacyclobutane derivatives, and this study is under investigation by another member of our group.

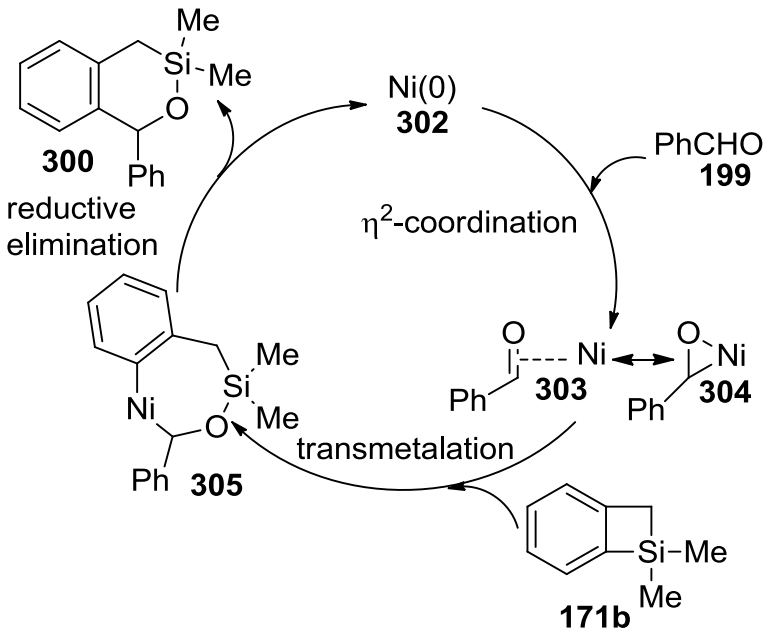
33 Enantioselective Ni-catalysed ring expansion of benzosilacyclobutane

Oshima and co-workers reported a method for the ring expansion of benzosilacyclobutane with aldehydes by nickel catalysis to give oxasilacyclohexene products.[46] Treatment of 1,1-dimethylbenzosilacyclobutanes in the presence of $Ni(cod)_2$ (10 mol%) and PPh_2Me (20 mol%) in toluene at 100 °C with aromatic and aliphatic aldehydes led to formation of the corresponding ring expanded products **300** in very good yields. Subsequent Tamao-Fleming oxidation provided diol products **301** in good yields (Scheme 111).



Scheme 111

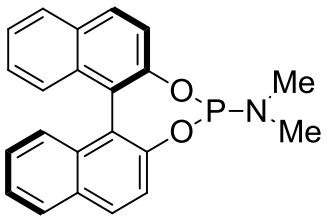
The proposed mechanism for this reaction is shown in Scheme 112. First, a nickel(0) species **302** coordinates with aldehyde **199** to give η^2-coordinated complex **303** or intermediate **304**, which is followed by transmetalation with benzosilacyclobutane **171b** to form the intermediate **305**. Subsequent reductive elimination generates the final product **300** and regenerates **302**.



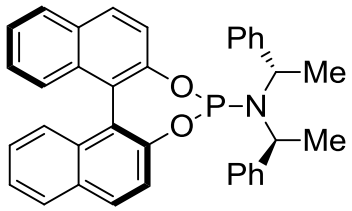
Scheme 112

This process appears to be a useful access to chiral secondary alcohols, and we decided to investigate the development of an enantioselective version of this process. Initial experimentation was carried out with 1,1-dimethylbenzosilacyclobutane (**171b,** 1 equiv) which was mixed with readily available benzaldehyde (**199**, 1.2 equiv) in the presence of $Ni(cod)_2$ (10 mol%) and PPh_2Me (20 mol%) in toluene to afford the racemic product **300**. Then, HPLC analysis was attempted to find suitable separation conditions for the product **300**, but unfortunately, the peaks for the racemic product **300** could not be observed. We converted **300** to the secondary alcohol **301** under Tamao-Fleming oxidation and HPLC separation conditions on a chiralcel IA column were developed.

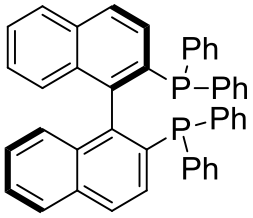
Next, we turned our attention to the use of chiral phosphine ligands in order to render this process enantioselective. When phosphoramidite ligands were used such as (*R*)L1 at room temperature, the corresponding alcohol **301** was obtained in low yield and poor enantioselectivity (Table 11, entry 1, 4% ee). However, with an increase in the reaction temperature to 100 ^oC with the same ligand an improvement in enantiomeric excess to 23% was observed (entry 2). Then a series of chiral phosphine ligands shown in Figure 7, were tested to determine the effect of the ligand structure on the enantioselectivity.



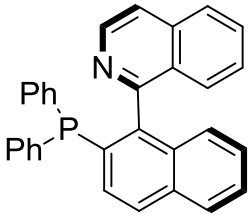
306, **L1**



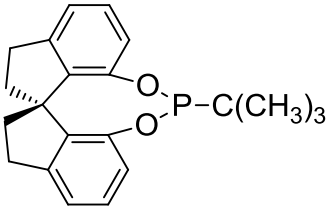
307, **L2**



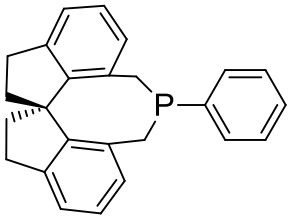
308, **L3**



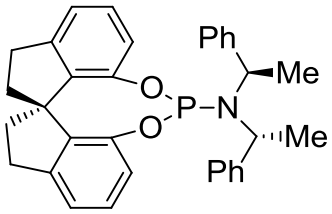
309, **L4**



310, **L5**



311, **L6**

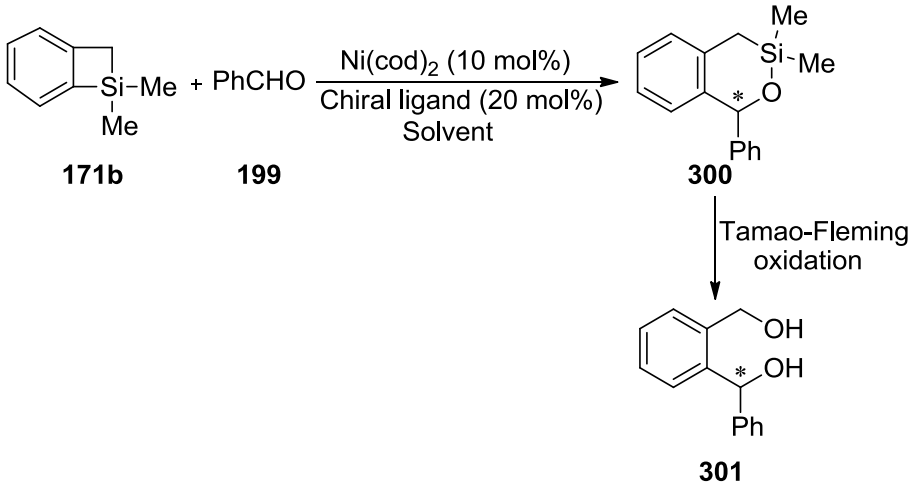


312, **L7**

Figure 7

A modest improvement in enantiomeric excess was obtained using (*S*,*R*,*R*)L2 as ligand (entry 3, 31% ee). However, when using biphosphine ligand (*R*)L3 and monophosphine ligand (*S*)L4 no reaction was observed in either case (entries 4, 5). In further attempts to improve the enantiomeric excess values, chiral spiro-monophosphorus ligands with a 1,1-spirobiindane backbone were tested (entries 6-10). Ligands L5, L6, and L7 were found to be the most efficient and gave the desired

product **301** with moderate yields and the enantioselectivity of the reactions improved dramatically to 39, 55, and 63% ee respectively at room temperature.



171b **199** **300** **301**

Entry	L(10 mol%)	Reaction Conditions	Yield [%][a]	Ee of **301** [%][b]
1	(*R*)L_1	RT, 24 h	19	4
2	(*R*)L_1	100 ^oC, 24 h	12	-23
3	(*S*, *R*, *R*)L_2	RT, 24 h	24	-31
4	(*R*)L_3	100 ^oC, 24 h	-	-
5	(*S*)L_4	100 ^oC, 24 h	-	-
6	(*S*)L_5	100 ^oC, 24 h	41	40.5
7	(*S*)L_5	RT, 24 h	17	39
8	(*R*)L_6	100 ^oC, 24 h	30	-37
9	(*R*)L_6	RT, 3d	33	-55
10	(*R*)L_7	RT, 24 h	23	-63

General conditions: 1 equiv of **171b**, 1.2 equiv of 15, 10 mol% $Ni(cod)_2$, 20 mol% Chiral ligand, 2 mL of MeCN, [a] Yield over two steps. [b] Determined by chiral HPLC on a chiralcel IA column.

Table 11

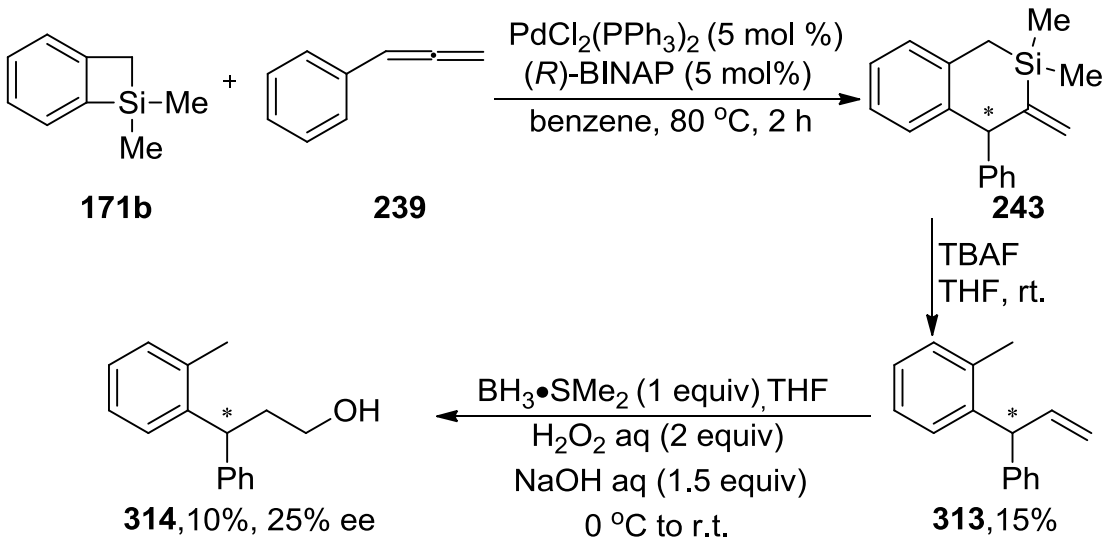
Further work is required to improve the yield and enantioselectivity of this process.

3.4 Enantioselective Pd-catalysed ring expansion of benzosilacyclobutane

To continue the study of silacyclobutanes, we were interested in developing the Pd-catalysed ring expansion of 1,1-dimethylbenzosilacyclobutane **171b** with phenylallene **239** as shown in Scheme 82. To date there has been only one example of a report on the reaction of benzosilacyclobutane with phenylallene, which is that by Oshima.[33] We wished to develop a general enantioselective version of this process.

In order to determine enantiomeric excess values, starting material **171b** was mixed with phenylallene **239** in the presence of 5 mol% $PdCl_2(PPh_3)_2$ in benzene under reflux for 2 h to give the racemic product **243**. Then, HPLC analysis was attempted with different chiral columns to determine suitable separation conditions. However, complete separation of the racemate peaks was not possible. It was decided to protodesilyate compound **243** with excess TBAF to the product **313** (Scheme 113). Again attempts to separate the racemate **313** by chiral HPLC was problematic.

In a further attempt, product **313** was converted to the corresponding alcohol **314** through hydroboration–oxidation, following the process described by Shintani *et al*.[47] Finally, separation conditions for product **314** were obtained on a chiralcel IB column. At this point, the effect of the chiral ligand (*R*)-BINAP was investigated. Performing the reaction led to 25% ee, but the compound **314** was not completely pure, and the HPLC trace was not perfect. Time constraints meant that no further work was conducted on this process (Scheme 113).


PdCl2(PPh3)2 (5 mol %)
(R)-BINAP (5 mol%)
benzene, 80 °C, 2 h
Si–Me
Me
171b
239
Me
Si–Me
Ph
243
TBAF
THF, rt.
BH3•SMe2 (1 equiv), THF
H2O2 aq (2 equiv)
NaOH aq (1.5 equiv)
0 °C to r.t.
OH
Ph
314,10%, 25% ee
Ph
313,15%

Scheme 113

4 Conclusion and future work

We have developed the dimerisation of silacyclobutanes under palladium catalysis at room temperature. We have shown that the dimerisation did not occur with different substrates of silacyclobutane due to steric bulk preventing the initial oxidative addition step. We determined that a heterogeneous catalytic mechanism is operating here in comparison to the proposed mechanisms in several related publications. The addition of mercury to the reaction conditions was the key point to prove this mechanism and we have shown that the palladium colloids are formed under reaction conditions as the first step. This work has been published.[51]

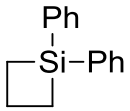
For future work the preparation of chiral secondary alcohols by chiral Ni catalysis has been initated, which provides the product in moderate enantioselectivity. However, more work is required to improve this process. In addition, the preliminary results discussed above provide the foundation for future work on palladium-catalysed enantioselective ring expansion reactions of silacyclobutanes with allenes.

5 Experimental

General.^{1}H NMR spectra were recorded at either 400 MHz or 500 MHz. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard ($CDCl_3$: 77.4 ppm). Mass spectrometry (m/z) was performed in ESI, IE and APCI mode, with only molecular ions being reported. Infrared (IR) spectra ν_{max} are reported in cm^{-1}. Bands are characterised as broad (br), strong (s), medium (m) and weak (w). Reagents were purchased from Sigma Aldrich and Fisher Scientific, they were used as received without further purification. Dimethyl silacyclobutane **177c** is commercially available, tetrahydrofuran was distilled from sodium wire and benzophenone under an atmosphere of nitrogen.

General procedure for the preparation of silacyclobutane serivatives:

Synthesis of 1,1-diphenylsilacyclobutane, 177d:



Prepared by a procedure reported by Hayashi *et al*.[41] Phenylmagnesium chloride (4 mL, 8.08 mmol, 2 M solution in THF) was added dropwise over 30 min to a solution of 1,1-dichlorosilacyclobutane (1.18 mL, 9.70 mmol) in Et_2O (20 mL) at 0 ^{o}C. The mixture was stirred overnight at room temperature and filtered through Celite. The filter was washed with Et_2O. The resulting solution was concentrated under vacuum, and the residue was dissolved in ether (27 mL) and THF (3 mL). Phenylmagnesium chloride (4.8 mL, 9.7 mmol, 2 M solution in THF) was added dropwise over 30 min at 0 ^{o}C, and the mixture was stirred for three days at 35 ^{o}C. The reaction was quenched with a

saturated aqueous solution of NH_4Cl (10 mL) and extracted with ether (5 mL x 2). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel (petroleum ether 40-60/ether) to afford compound **177d** as a colourless oil (0.674 g, 37%).

$IR_{(neat)}$: 693 (s), 1426 (m), 2966 (w) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 1.57 (4H, t, *J* = 8.3 Hz), 2.33 (2H, q, *J* = 8.4 Hz), 7.43-7.52 (6H, m), 7.66-7.72 (4H, m).

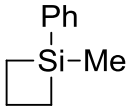
^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2 (2C), 18.7, 128.3 (4C), 130.0 (2C), 134.8 (4C), 136.7 (2C).

^{29}Si NMR (99 MHz, $CDCl_3$): δ – 6.88

MS: m/z (M) 224.1

HRMS: m/z calc'd for $[M]^+$ $C_{15}H_{16}Si$ 224.1021, found 224.1020.

Synthesis of 1-methyl-1-phenylsilacyclobutanes, 177e:



Synthesised according to the representative procedure for **177d,** using phenylmagnesium chloride (4 mL, 8.08 mmol, 2 M solution in THF) and methylmagnesium bromide (3 mL, 9.69 mmol, 3 M solution in THF), the product was obtained and purified by flash chromatography (petroleum ether 40-60/ether on silica) affording the title compound **177e** as a colourless oil (0.3247 g, 25%).

$IR_{(neat)}$: 694 (s), 1427 (m), 2962 (w) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 0.66 (3H, s), 1.20-1.33 (2H, m), 1.34-1.47 (2H, m), 2.23-2.35 (2H, m), 7.45-7.51 (3H, m), 7.69-7.76 (2H, m).

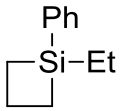
^{13}C NMR (100 MHz, $CDCl_3$): δ -1.4, 14.7 (2C), 18.6, 128.2 (2C), 129.7, 133.8 (2C), 138.9.

^{29}Si NMR (99 MHz, $CDCl_3$): δ -12.22

MS: m/z (M + 1) 163.1

HRMS: m/z calc'd for $[M + H]^+$ $C_{10}H_{15}Si$ 163.0938 found, 163.0934.

Synthesis of 1-ethyl-1-phenylsilacyclobutane, 177f:



Synthesised according to the representative procedure for **177d,** using phenylmagnesium chloride (4 mL, 8.08 mmol, 2 M solution in THF) and ethylmagnesium chloride (3 mL, 9.69 mmol, 2 M solution in THF), the product was obtained and purified by flash chromatography (petroleum ether 40-60 /ether on silica) affording the title compound **177f** as a colourless oil (0.267 g, 19%).

$IR_{(neat)}$: 694 (s), 1427 (m), 2957 (w) cm^{-1}.

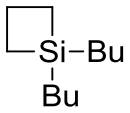
^{1}H NMR (400 MHz, $CDCl_3$): δ1.01-1.11 (2H, m), 1.13-1.20 (2H, m), 1.26-1.34 (3H, m), 2.18-2.29 (2H, m), 7.42-7.49 (3H, m), 7.65-7.71 (2H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ 7.3, 7.6, 12.7 (2C), 18.7, 128.2 (2C), 129.7, 134.0 (2C), 138.3.

MS: m/z (M) 176.1

HRMS: m/z calc'd for $[M]^+$ $C_{11}H_{16}Si$ 176.1021 found, 176.1023.

Synthesis of 1,1-dibutylsilacyclobutane, 177g:[48]



Under N_2, 1,1-dichlorosilacyclobutane (0.58 mL, 4.9 mmol) was dissolved in THF (20 mL) at 0 °C. *n*-BuLi (6 mL, 2.5 M in hexanes) was add dropwise over 30 min. Then the reaction was stirred overnight at room temperature. The reaction was quenched by addition of saturated aqueous NH_4Cl

solution (10 mL) and extracted with ether (5 mL x 2). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product **177g** did not require further purification and was isolated as yellow oil (0.0714 g, 79 %).

$IR_{(neat)}$: 714 (s), 1463 (m), 2858 (m), 2914 (w) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 0.51 (8H, t, *J* = 7.2 Hz), 0.86 (6H, t, *J* = 7.2 Hz), 1.18-1.35 (10H, m).

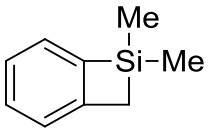
^{13}C NMR (100 MHz, $CDCl_3$): δ 12.6 (2C), 14.2 (2C), 18.1 (2C), 18.9, 26.6 (2C), 27.2 (2C).

MS: m/z (M + 18) 202.1

HRMS: m/z calc'd for $[M + NH_4]^+$ $C_{11}H_{28}NSi$ 202.1986, found 202.1991.

General procedure for the preparation of benzosilacyclobutane derivatives:

Synthesis of 7,7-dimethyl-7-silabicyclo[4.2.0]octa-1(6),2,4-triene, 171b:[43]



Under nitrogen atmosphere, magnesium turnings (3.5 g) and acid washed sand (3.5 g) in 20 mL of diethyl ether was stirred. Then, 1,2-diiodoethane (0.25 g) was added. Once the magnesium was activated, a solution of 2-bromobenzyl bromide (15 g, 0.12 mmol), dimethyldichlorosilane (11 g, 0.04 mmol) in diethyl ether (130 mL) was added dropwise via addition funnel over 5 hours. The mixture was refluxed overnight. The resulting mixture was cooled in an ice bath and hydrolysed with aqueous solution 10% ammonium chloride (100 mL), filtered and the organic layer was separated. The organic layer was washed with water (100 mL), dried, and concentrated under vacuum to afford **171b** as a colourless oil (6.36 g, 37%).

$IR_{(neat)}$: 819 (s), 1041 (m), 1434 (m), 2960 (w) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ –0.71 (6H, s), 0.97 (2H, s), 5.93-6.06 (2H, m), 6.09-6.19 (2H, m).

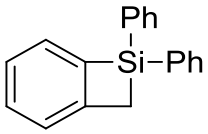
NMR (100 MHz, $CDCl_3$): δ –0.1 (2C), 20.5, 126.5, 127.3, 130.8, 130.8, 146.4, 151.0.

^{29}Si NMR (99 MHz, $CDCl_3$): δ –9.26.

MS: m/z (M) 148.1

HRMS: m/z calc'd for $[M]^+$ $C_9H_{12}Si$ 148.0708, found 148.0712.

Synthesis of 7,7-diphenyl-7-silabicyclo[4.2.0]octa-1(6),2,4-triene, 171a:[17]



Synthesised according to the representative procedure for the formation of **171b**, using diphenyldichlorosilane (4.5 g, 0.016 mmol) to end up with **171a** which was purified by flash chromatography (petroleum ether 40-60 on silica) as a yellow solid (0.020 g, 24 %).

Melting point: 75-78 °C. (Lit.:[17] 75-76 °C)

$IR_{(neat)}$: 693 (s), 1426 (m), 1492 (m), 3023 (w) cm^{-1}.

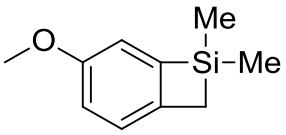
^1H NMR (400 MHz, $CDCl_3$): δ 2.69 (2H, s), 6.86-6.92 (2H, m), 7.08-7.20 (4H, m), 7.33-7.49 (8H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ 22.6, 124.7, 128.0, 128.3 (4C), 129.4 (3C), 129.8, 134.7, 135.8 (4C), 136.1 (2C), 138.6.

MS: m/z (M) 272.1

HRMS: m/z calc'd for $[M]^+C_{19}H_{16}Si$ 272.1016, found 273.1014.

Synthesis of 4-methoxy-7,7-dimethyl-7-silabicyclo[4.2.0]octa-1(6),2,4-triene, 171c:



Synthesised according to the representative procedure for the formation of **171a**, using dimethyldichlorosilane (4 g, 0.01 mmol), the product **7** was obtained and purified by flash chromatography (petroleum ether 40-60 on silica) affording the title compound **171c** as a colourless oil (5.200 g, 58%).

$IR_{(neat)}$: 892 (s), 1046 (s), 1234 (m), 1581 (m), 2952 (w) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.5 (6H, s), 2.17 (2H, s), 3.8 (3H, s), 6.77 (1H, s), 6.86 (1H, d, *J* = 7.4 Hz), 7.3 (1H, dd, *J* = 8.1, 1.7 Hz).

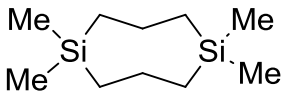
^{13}C NMR (100 MHz, $CDCl_3$): 0.1 (2C), 20.2, 55.3, 111.6, 114.5, 132.0, 136.9, 152.5, 162.5.

MS: m/z (M + 1) 179.1

HRMS: m/z calc'd for $[M + H]^+$ $C_{10}H_{15}OSi$ 179.0887, found 179.0886.

General procedure for dimerisation of silacyclobutanes:

Synthesis of 1,1,5,5-tetramethyl-1,5-disilocane, 257a:[36]



A mixture of 1,1-dimethylsilacyclobutane (50 mg, 0.5 mmol) and tetrakis(acetonitrile)palladium(II) tetrafluoroborate (22 mg, 0.05 mmol) in toluene (2 mL) was stirred for ten minutes at room temperature. The mixture was filtered through Celite and the filter pad washed with ethyl acetate (10 mL). Concentration under vacuum afforded **257a** as a colourless oil (0.019 g, 39%).

$IR_{(neat)}$: 1220 (m), 1359 (m), 1708 (s) cm^{-1}.

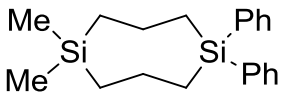
^{1}H NMR (400 MHz, $CDCl_3$): δ – 0.05 (12H, s), 0.74 (8H, t, *J* = 7.0 Hz), 1.77 (4H, q, *J* = 7.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ – 2.1 (4C), 18.3 (4C), 18.7 (2C).

^{29}Si NMR (99MHz, $CDCl_3$): δ 2.38.

MS: $[M - CH_3]^+$ 185.1.

Synthesis of 1,1-dimethyl-5,5-diphenyl-1,5-disilocane 257cd:[37]



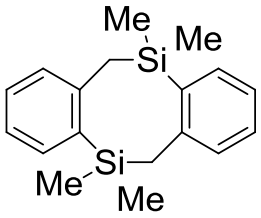
A mixture of dimethylsilacyclobutane **177c** (28 mg, 0.2 mmol, 1 equiv), 1,1-diphenylsilacyclobutane **177d** (50 mg, 0.2 mmol, 1 equiv), and tetrakis(acetonitrile)palladium(II) tetrafluoroborate (8 mg, 0.02 mmol) in toluene (3 mL) was stirred overnight at room temperature. The mixture was filtered through Celite and the filter pad washed with ethyl acetate (10 mL). Concentration under vacuum provided a 1:1 mixture of **257cc** and **257cd** as a colorless oil. Separation of these compounds by flash chromatography was not successful.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.01 (6H, s), 0.85 (4H, t, *J* = 6.8 Hz), 1.44 (4H, t, *J* = 6.8 Hz), 1.94 (4H, q, *J* = 6.8 Hz), 7.27–7.63 (10H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ –2.5 (2C), 14.7 (2C), 18.1 (2C), 18.3 (2C), 127.8 (4C), 128.9 (4C), 134.3 (2C), 137.5 (2C).

^{29}Si NMR (99MHz, $CDCl_3$): δ –7.66, 2.72.

Synthesis of 5,5,11,11-tetramethyl-5,6,11,12-tetrahydrodibenzo[b,f][1,5]disilocine, 263b:[36]



Synthesised according to the representative procedure for the formation of **257a**, using 7,7-diphenyl-7-silabicyclo[4.2.0]octa-1(6),2,4-triene **171b** (250 mg, 1.68 mmol), the product was obtained and purified by flash chromatography on silica (petroleum ether 40-60) affording the title compound **263b** as a colourless oil (0.077 g, 31%).

$IR_{(neat)}$: 724 (s), 799 (s), 1430 (m), 2946 (w) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.33 (6H, s), 0.38 (6H, s), 2.33 (2H, d, *J* = 13.5 Hz), 2.77 (2H, d, *J* = 13.5 Hz), 6.90 (2H, td, *J* = 7.4, 1.0 Hz), 6.95 (2H, d, *J* = 7.6 Hz), 7.10-7.16 (4H, m).

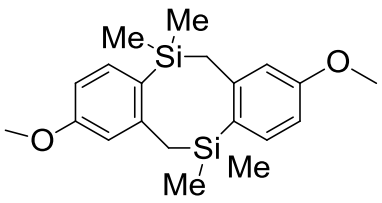
^{13}C NMR (100 MHz, $CDCl_3$): δ –3.2 (2C), –1.1 (2C), 29.4 (2C), 123.9 (2C), 127.9 (2C), 129.5 (2C), 134.5 (2C), 135.1 (2C), 146.0 (2C).

^{29}Si NMR (99 MHz, $CDCl_3$): δ –2.00.

MS: m/z (M + 1) 297.1

HRMS: m/z calc'd for $[M + H]^+$ $C_{18}H_{25}Si_2$ 297.1489, found 297.1487.

Synthesis of 2,9-dimethoxy-5,5,11,11-tetramethyl-5,6,11,12-tetrahydrodibenzo[b,f][1,5] disilocine, 263c:



Synthesised according to the representative procedure for the formation of **257a**, using 4-methoxy-7,7-dimethyl-7-silabicyclo[4.2.0]octa-1(6),2,4-triene **171c** (55 mg, 0.31 mmol), the product was obtained and purified by flash chromatography (petroleum ether 40-60 on silica) affording the title compound **263c** as a yellow oil (0.06 g, 12 %).

$IR_{(neat)}$: 828 (s), 1229 (m), 1589 (m), 2954 (w) cm^{-1}.

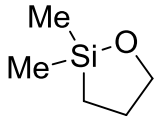
^1H NMR (400 MHz, $CDCl_3$): δ 0.27 (6H, s), 0.33 (6H, s), 2.26 (2H, d, *J* = 12.9 Hz), 2.72 (2H, d, *J* = 12.9 Hz), 3.72 (6H, s), 6.45 (1H, d, *J* = 2.5 Hz), 6.47 (1H, d, *J* = 2.5 Hz), 6.5 (2H, d, *J* = 2.5 Hz), 7.03 (1H, s), 7.05 (1H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ –2.9 (2C), –0.9 (2C), 29.7 (2C), 55.2 (2C), 109.1 (2C), 114.1 (2C), 125.5 (2C), 136.5 (2C), 148.1 (2C), 160.8 (2C).

MS: m/z (M + 1) 357.1

HRMS: m/z calc'd for $[M + H]^+$ $C_{20}H_{29}O_2Si_2$ 357.1701, found 357.1694.

Synthesis of 2,2-dimethyl-1,2-oxasilolane, 298:[49]



1,1-Dimethylsilacyclobutane (50 mg, 0.49 mmol, 1 equiv) and *t*-butylhydroperoxide (44 mg, 0.49 mmol, 1 equiv) were dissolved in THF (3 mL) and stirred under a nitrogen atmosphere at 0 °C. Then, *t*-BuOK (16 mg, 0.1 mmol) was added to the mixture. After 2 h, the mixture was poured into ice water and extracted with ethyl acetate (2 x 10 mL). The combined organic layers were washed with brine and dried with anhydrous magnesium sulfate, filtered and concentrated under vacuum to provide **298** as a yellow liquid (0.024 g, 43%).

$IR_{(neat)}$: 772 (s), 1250 (s), 2954 (w), 3315 (br) cm^{-1}.

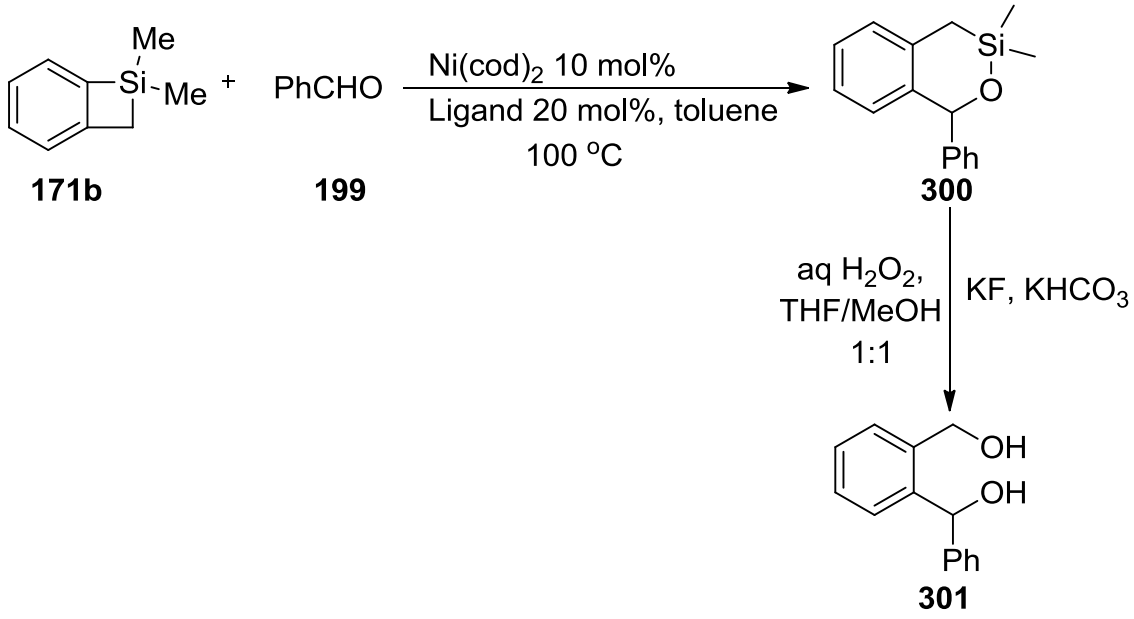
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.07 (6H, s), 0.53 (2H, t, *J* = 8.3 Hz), 1.54–1.73 (2H, m), 3.60 (2H, t, *J* = 6.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 0.3 (2C), 14.0, 26.6, 65.5.

MS: m/z (M) 116.1

HRMS: m/z calc'd for $[M]^+$ $C_5H_{12}OSi$ 116.0652, found 116.0657.

Synthesis of 2-(hydroxy(phenyl)methyl)phenol, 301:[46]



In a glovebox, a round bottom flask, under nitrogen, was charged with $Ni(cod)_2$ (18 mg, 0.067 mmol) and PPh_2Me (27 mL, 0.13 mmol). Then, the flask was removed from the glovebox, and toluene (3 mL) was added. The mixture was stirred for 10 min at 0 °C, then a solution of benzaldehyde (82 mL, 0.80 mmol) in toluene (3 mL) and 7,7-dimethyl-7-silabicyclo[4.2.0]octa-1(6),2,4-triene **171b** (100 mg, 0.067 mmol) were added successively. The resulting mixture was stirred overnight at 100 °C. After cooling to room temperature, the reaction was concentrated under vacuum and the crude mixture was transferred to next step without purification.

Procedure for Tamao-Fleming Oxidation of 3,3-dimethyl-1-phenyl-3,4-dihydro-1*H*-benzo[*d*][1,2]oxasiline:

The crude 3,3-dimethyl-1-phenyl-3,4-dihydro-1*H*-benzo[*d*][1,2]oxasiline **300** (200 mg, 0.786 mmol) product was dissolved in THF (1 mL) and a solution of KF (91 mg, 1.57 mmol) and $KHCO_3$ (157 mg, 1.57 mmol) in MeOH (1 mL) was added. Then, aq. H_2O_2 (35%, 0.5 mL, 0.16 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 24 hours, and then an aqueous solution of sodium thiosulfate was added. The organic and the aqueous layers were separated and the latter was extracted with ether (2 x 5 mL). The combined organic layers were dried ($MgSO_4$), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by flash chromatography (2:1 petroleum ether 40-60/EtOAc) to end up with **301** (0.043 g, 26%) as a colourless oil.

$IR_{(neat)}$: 1001 (s), 1449 (m), 1492 (m), 3301 (w) cm^{-1}.

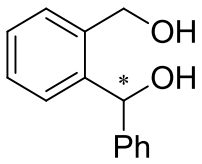
^1H NMR (400 MHz, $CDCl_3$): δ 3.08 (1H, s), 3.93 (1H, s), 4.45 (1H, d, *J* = 11.1 Hz), 4.60 (1H, d, *J* = 11.1 Hz), 6.01 (1H, s), 7.19-7.37 (9H, m).

^{13}CNMR (100 MHz, $CDCl_3$): δ 63.8, 74.3, 126.6, 127.4, 128.3 (2C), 128.4, 128.4, 128.9 (2C), 130.3, 138.5, 142.2, 142.5.

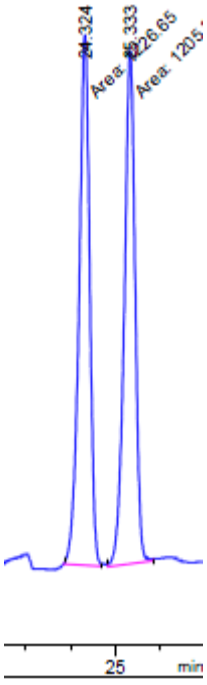
MS: m/z (M + 23) 237.1

HRMS: m/z calc'd for $[M + Na]^+$ $C_{14}H_{14}NaO_2$ 237.0886, found 237.0888.

2-(hydroxy(phenyl)methyl)phenol, 301

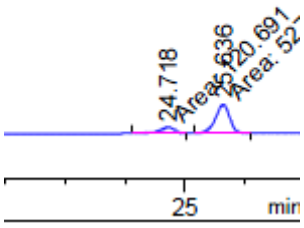


HPLC: The ee was determined on a Chiralpak IA 254 nm hexane/EtOH gradient (100:0 to 80:20 over 27 min), 1 ml/min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.324	MM	0.2742	1226.64929	74.55486	50.4395
2	25.333	MM	0.2784	1205.27222	72.14515	49.5605

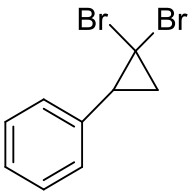
Figure 8



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.718	MM	0.2929	120.69054	6.86810	18.6171
2	25.636	MM	0.2759	527.58563	31.86602	81.3829

Figure 9

Synthesis of (2,2-dibromocyclopropyl)benzene, 315:[50]



In a round bottom flask styrene (3.4 mL, 30 mmol), crushed KOH (2.5 g, 45 mmol), and tetraethylammonium bromide (315 mg, 1.5 mmol) were dissolved in DCM (15 mL). Then, bromoform (3.4 mL, 36 mmol) was added dropwise over 1 h at 40 ºC and the mixture was stirred for 24 hours at room temperature. The solution was filtered through a short pad of silica gel and the filtrate was concentrated under vacuo. The mixture was purified by flash chromatography (petroleum ether 40-60 on silica) to give the product **315** as a yellow oil (8.21 g, 99%).

$IR_{(neat)}$: 650 (s), 767 (m), 1496 (m), 3026 (w) cm^{-1}.

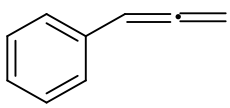
^1H NMR (400 MHz, $CDCl_3$): δ 2.52 (1H, dd, *J* = 10.4, 6.2 Hz), 2.63 (1H, dd, *J* = 10.4, 7.9 Hz), 3.47 (1H, dd, *J* = 7.9, 6.2 Hz), 7.73-7.92 (5H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ 27.4, 28.9, 36.1, 127.8, 128.5 (2C), 129.1 (2C), 136.1.

MS: m/z (M – 79.9) 195.0

HRMS: m/z calc'd for $[M - Br]^+$ C_9H_8Br 194.9804, found 194.9816.

Synthesis of phenylallene, 239:[50]



(2,2-Dibromocyclopropyl)benzene **315** (2 g, 7.2 mmol) was dissolved in THF (20 mL). Then, methyl magnesium bromide (3.6 mL, 10.8 mmol, 3 M solution in Et_2O) was slowly added. The reaction mixture was stirred for 2 h at room temperature, at which point diethyl ether (15 mL) and water (3 mL) was added. The organic layer was separated, and then aqueous HCl (3 N, 5 mL) was added to the organic layer and extracted with Et_2O (2 x 5 mL). The combined organic layers were washed with brine, dried over ($MgSO_4$), filtered and concentrated under vacuum to give the product **239** as a colourless liquid (0.568 g, 68%).

$IR_{(neat)}$: 693 (s), 761 (m), 1673 (m), 1673 (m), 3031 (w) cm^{-1}.

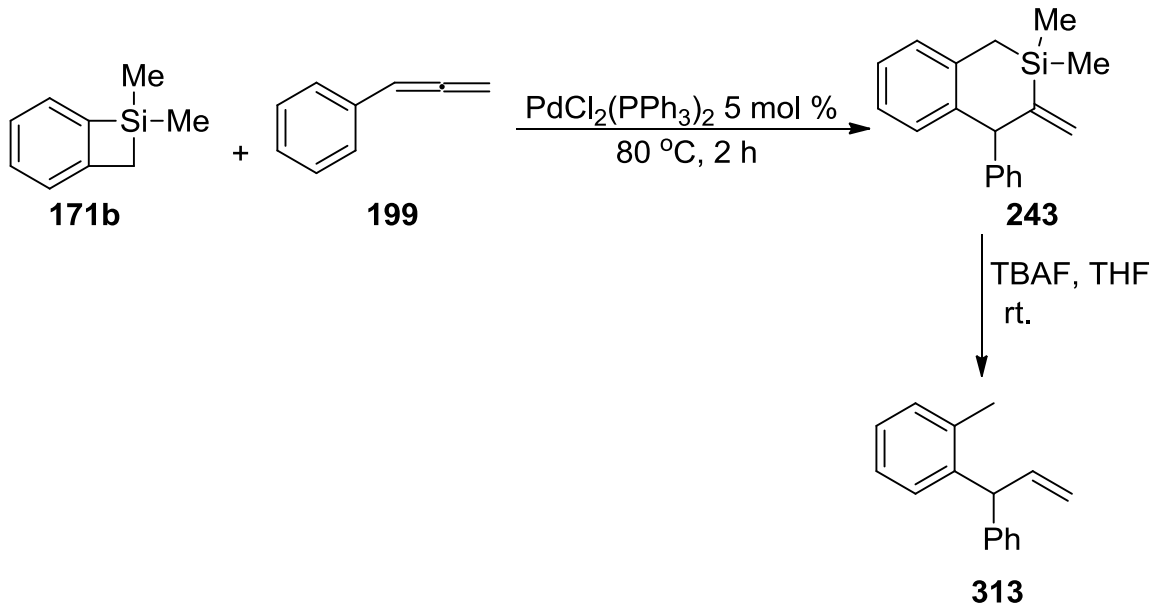
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.25 (2H, d, *J* = 6.7 Hz), 6.28 (1H, t, *J* = 6.7 Hz), 7.26 –7.34 (1H, m), 7.37–7.44 (4H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ 79.1, 94.2, 127.0 (2C), 127.2, 128.9 (2C), 134.2, 210.1.

MS: m/z (M + 1) 117.1

HRMS: m/z calc'd for $[M + H]^+$ C_9H_9 117.0699, found 117.0700.

Synthesis of 1-methyl-2-(1-phenylallyl)benzene, 313:[33]



Phenylallene **239** (100 mg, 0.86 mmol), 7,7-dimethyl-7-silabicyclo[4.2.0]octa-1(6),2,4-triene **177b** (127 mg, 0.86 mmol), and $PdCl_2(PPh_3)_2$ (30 mg, 0.043 mmol) were dissolved in benzene (4 mL) under a nitrogen atmosphere. The mixture was stirred for 2 h at 80 °C, and then the mixture was cooled to room temperature and concentrated under vacuum. Then, 2,2-dimethyl-3-methylene-4-phenyl-1,2,3,4-tetrahydrobenzo[*c*]siline product **243** (43 mg, 0.16 mmol) was used without purification and was dissolved in THF (2 mL) and tetra-*n*-butylammonium fluoride (0.35 mL, 1 M solution in THF) was added. Then, the mixture was stirred overnight at room temperature and quenched with water (5 mL) and extracted with EtOAc (2 x 10 mL). The organic layers were combined and dried with anhydrous magnesium sulfate, filtered and concentrated under vacuum. The product was purified by flash chromatography (5:1 petroleum ether 40-60/EtOAc) to end up with **313** (0.005 g, 15%) as a colourless oil.

$IR_{(neat)}$: 725 (s), 1489 (m), 1637 (m), 2924(w), 3059 (w) cm^{-1}.

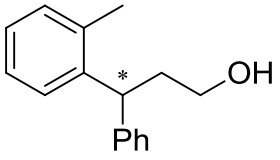
^1H NMR (400 MHz, $CDCl_3$): δ 2.24 (3H, s), 4.84 (1H, d, *J* = 17.1 Hz), 4.90 (1H, d, *J* = 6.3 Hz), 5.22 (1H, d, *J* = 10.2 Hz), 6.28 (1H, ddd, *J* = 17.1, 10.2, 6.5 Hz), 7.10 –7.30 (9H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ 20.1, 51.4, 116.7, 126.3, 126.5, 126.7, 128.6, 128.7, 129.2 (2C), 130.8, 136.7, 140.8, 141.6, 142.8 (2C).

MS: m/z (M) 208.1

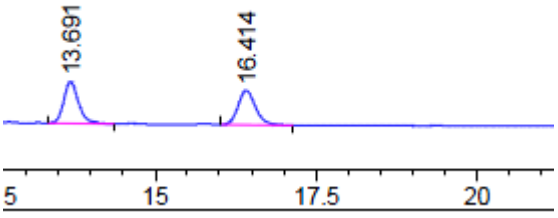
HRMS: m/z calc'd for $[M]^+C_{16}H_{16}$ 208.1247, found 208.1258.

To determine enantioselectivites, compound **313** was converted to the corresponding alcohol **314** through a hydroboration–oxidation sequence[47] but due to the small amount of the compound **314** the characterisation data could not be obtained.



314

HPLC: The ee was determined on a Chiralpak IB 254 nm hexane/i-PrOH gradient (100:0 to 90:10 over 20 min), 0.8 mL/min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.691	BB	0.2459	394.78207	24.50697	50.7367
2	16.414	BB	0.2896	383.31699	20.18122	49.2633

Figure 10

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