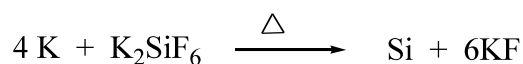


1. Historical

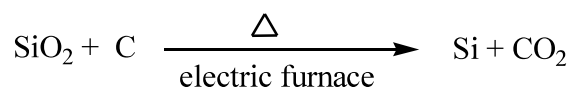
Silicon is the second most abundant element apart from oxygen found on the surface of the Earth. Silicon occurs in the form of silicon dioxide (SiO₂) and as other complex silicate minerals. Measured by mass, silicon accounts for *ca* 27.7% of the Earth's crust. Silicon belongs to group 14 of the periodic table and is placed immediately below carbon, with atomic number 14. Its ground state electronic configuration is 1s²2s²2p⁶3s²3p². Silicon is present in three isotopic forms with abundance silicon-28 (92.18%); silicon-29 (4.17%) and silicon-30 (3.11%).¹

Silicon was first identified by Antoine Lavoisier in 1787 as a component of quartz. The discovery of elemental silicon however is credited to Berzelius who in 1824 heated metallic potassium with potassium fluorosilicate to isolate a brown powder. Treatment with water gave pure elemental silicon (**Scheme 1**).²



Scheme 1

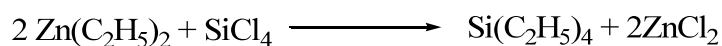
Today, silicon is prepared commercially by reducing silicon dioxide, usually in the form of white quartz, with carbon in an electric arc furnace (**Scheme 2**).³



Scheme 2

1.1 Organosilicon Chemistry

Tetraethylsilane was the first organosilicon compound to be synthesized. This organosilicon compound was synthesized in 1863 by Friedel and Crafts who reported its preparation when tetrachlorosilane was treated with diethylzinc (**Scheme 3**).⁴

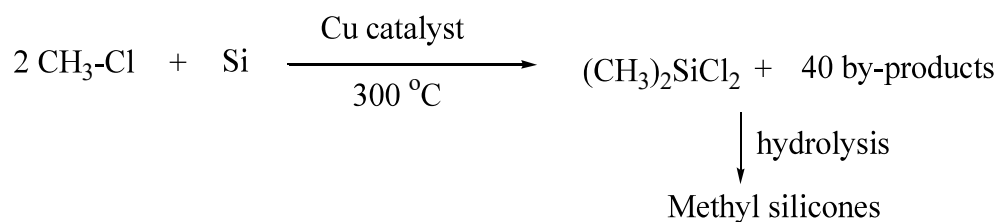
**Scheme 3**

In 1900, Victor Grignard discovered organomagnesium halides (Grignard reagents). After the discovery of Grignard reagents important advances were made in alkylsilane synthesis.

In 1904, Frederick Stanley Kipping used the newly discovered Grignard reagents to form silicon-carbon bonds from silicon tetrachloride.⁵ Kipping and his co-workers advantageously used this method over a period of the next four decades and published a series of papers on organosilicon compounds.⁶ Due to his immense pioneering work in the chemistry of organosilanes, Kipping is today regarded as the father of modern organosilicon chemistry.

Several other scientists who also independently contributed immensely to the early development of organosilicon chemistry were: Dilthey, Ladenburg ($\text{SiCl}_4 + \text{R}_2\text{Hg}$), Pape ($\text{SiCl}_4 + \text{EtCl} + 2 \text{Na}$), Polis ($\text{SiCl}_4 + \text{PhCl} + 2 \text{Na}$) *etc.*

In 1945, Rochow discovered a direct process for the synthesis of organochlorosilanes by passing a vapour of organic chlorides over heated silicon in the presence of a copper catalyst (**Scheme 4**).⁷ Thus dialkylchlorosilanes (Me_2SiCl_2) were readily provided and employed in silicone polymer production. By this process a new area was opened in organosilicon chemistry, the establishment of silicone polymer industry and also organosilicon-based reagents.

**Scheme 4**

At this stage rapid development in organosilicon chemistry occurred, with the hydrolysis of organohalosilanes.

Silanols and silicones

Rochow, Sommer and Whitmore hydrolyzed the organohalosilanes to form commercially useful silanols and silicones. Silicones which possess the Si-O-Si bonds in polymeric chains are classified as fluids, resins and elastomers. Silicones are characterized by their thermal and oxidative stability, chemical inertness, resistance to withering, good dielectric strength and low surface tension. Silicones find diverse uses as lubricants, wetting agents, defoamers, surfactants, protective coatings, hydraulic and dielectric oils, in paints, enamels and varnishes, as water repellants in textiles, cosmetic and pharmaceutical formulations.⁸

Organosilicon-based reagents

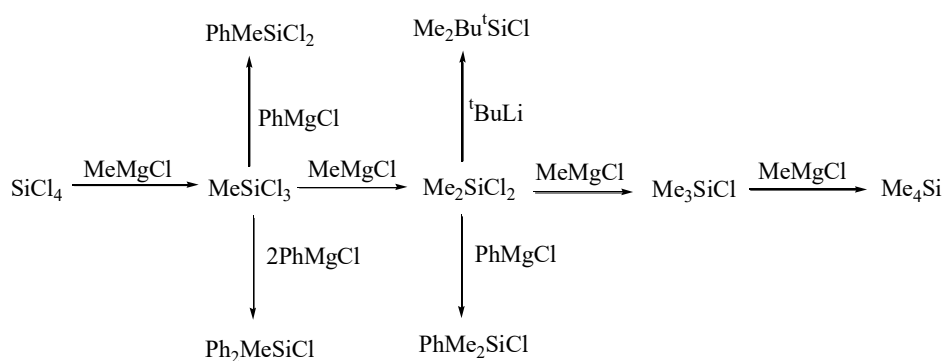
Interest in the use of organosilicon compounds in organic synthesis came in the late nineteen sixties. In 1968, the trialkylsilyl group was first introduced as a protecting group for hydroxyl functionality.⁹⁻¹⁴ The silyl ether produced was known to possess high solubility in organic solvents compared to the parent compound, possessed thermal stability and had compatibility for gas chromatography experiments.

Further academic studies showed that the silyl protecting group can be cleaved under extremely selective conditions.

The stability of the organosilyl-reagents, their ready availability, low toxicity, chemoselectivity, variety of regio- and stereo- specific transformations they can undergo mark their use as anion masking groups. Today applications in carbon-

carbon bond formations have marked their use as an integral part in the synthesis of several complex natural products and target-oriented synthesis.

For the specific preparation of various different types of silyl groups, silicon tetrachloride is manufactured by the direct action of chlorine on elemental silicon or by the action of chlorine on silica and coke. The silicon tetrachloride so prepared is next subjected to stepwise substitution using Grignard reagents, as first shown by Kipping for the conversion to the desired product (**Scheme 5**).



Scheme 5

The differing alkyl/aryl moieties in the silyl-group alter the reactivity of the silyl group rendering their flexible application in target-oriented, regio- and stereo-specific transformations.

There are several other methods for the preparation of organosilyl-based reagents. For example, polyiodosilanes can be obtained in especially good yields by reacting silylamines and hydrogen iodide in the presence of a Lewis acid. Silicon hydrides can be converted to halosilanes by electrophilic or nucleophilic substitution and one halosilane can be conveniently converted to a different halosilane by halide exchange using various reagents.¹⁵ The halosilanes so prepared can be further converted to a wide variety of silyl-based reagents such as silyl cyanides,¹⁶ silyl azides,¹⁷ silyl nitronates,¹⁸ silyl sulfides,¹⁹ bis(silylsulfates),²⁰ silyl phosphates²¹ etc.

The uniqueness of the silyl- group

The synthetic potential of organosilicon reagents is a consequence of certain unique properties of the silyl- group. Even though elemental carbon and silicon belong to Group 14 in the Periodic Table, silicon is more electropositive than carbon since silicon has an outer valence shell electronic configuration $[3s^2, 3p^2, 3d^0]$ and differing from carbon in its possession of vacant d-orbitals, the vacant d-shell introduces unique properties to organosilicon species.

Table 1: Electronegativities according to the Pauling scale²²

Element	Electronegativity
Hydrogen	2.2
Carbon	2.5
Silicon	1.9
Nitrogen	3.0
Phosphorus	2.2
Oxygen	3.4
Sulphur	2.6
Fluorine	4.0
Chlorine	3.2

A brief list of the differences between elemental carbon and silicon are listed in **Tables 1, 2 and 3**.

Like carbon, silicon forms bonds with several other elements. Selected bond dissociation energies and bond lengths are given in **Table 2**.

Table 2: Bond lengths and dissociation energies of carbon and silicon^{23, 24}

Bond	Length Å	Dissociation energy kJ mol⁻¹
Si-C	1.89	318
C-C	1.54	334
C-O	1.41	340
Si-O	1.63	531
C-Cl	1.78	335
Si-Cl	2.05	471
C-F	1.39	452
Si-F	1.60	808
C-I	2.14	213
Si-I	2.44	332
C-H	1.09	420
Si-H	1.48	339

The similarities and differences between C and Si are briefly highlighted in **Table 3**.

Table 3: The similarities and differences properties of carbon and silicon

Sl. No	Carbon	Silicon
01	Atomic no. 6	Atomic no. 14
02	Electronic configuration: $1s^2 2s^2 2p^2$	Electronic configuration: $1s^2 2s^2 2p^2 3s^2 3p^2$
03	Atomic radius: 0.77 Å	Atomic radius: 1.17 Å
04	Bond formation with orbitals of principal quantum number 2. Hence, carbon-carbon bonds are shorter bonds when compared to silicon-carbon bonds. ²³	Bond formation with orbitals of principal quantum number 3. Hence, the silicon-carbon and silicon-silicon bonds are longer bonds when compared to carbon-carbon bonds. ²³
05	The C-C bond distance (1.54 Å) is shorter, which leads to steric hindrance, when compared to carbon-silicon bonds. S_N2 reactions occur less facile when compared to with carbon-silicon bonds. ^{23, 24}	The C-Si bond distance (1.88 Å) is longer, which leads to less steric hindrance, when compared to carbon-carbon bonds. S_N2 reactions occur when carbon-silicon bond undergoes facile heterolytic bond fission with nucleophiles. ^{23, 24}
06	Carbon forms stable tetravalent compounds. ²⁵	Silicon forms tetra-, penta-, and hexa-valent compounds. ²⁶
07	The chemistry of the divalent carbon species i.e. carbenes has been studied extensively due to reactivity of divalent carbon species. ^{27, 28}	Silylene chemistry of the divalent silicon species is studied less extensively due to the very high reactivity of the divalent silicon species. ²⁹
08	Carbon forms stable double bonds ³⁰ and triple bonds. ³¹	Silicon forms double bonds and triple bonds only under controlled conditions. ^{32, 33}
09	Carbon compounds exhibit chirality and shows optical activity. ^{34, 35}	Silicon compounds also exhibit chirality and hence optical activity. ³⁶
10	Reaction mechanism are not very clear in certain reactions. ²⁵	Reaction mechanisms are easy to comprehend especially those reactions involving silicon centers. ³⁷
11	Carbon has no low lying 'd' orbitals and nucleophilic attack is different when compared to silicon compounds. In carbon, S_N1 type reaction mechanism can take place more facilely when carbon is involved. ²⁵	Silicon has low lying 'd' orbitals. These d orbitals stabilize the nucleophilic attack to promote the reactions via addition-elimination mechanism. S_N1 type reactions are comparatively less when silicon is involved. ³⁸
12	Pauling electronegativity, carbon is always more electro-negative than silicon. The electronegativity of 'C' is 2.35 ^{22, 23}	Pauling electronegativity, silicon is more electro-positive than carbon or hydrogen. The electronegativity of 'Si' is 1.64 ^{22, 23}

Reactivity of Carbon-Silicon Bond

Silicon is more electropositive than carbon (**Table 1**), resulting in polarization of silicon-carbon bond as $\text{Si}^{\delta+}-\text{C}^{\delta-}$. This polarisation encourages nucleophilic attack to occur at silicon. Owing to the bond polarization, the silicon-carbon bond is cleaved by strong nucleophiles like fluoride, chloride etc. with nucleophilic attack occurring on the silicon. The final bond formed between the nucleophile and silicon is usually stronger than the bond which is broken as shown in **Table 2**.

However, in the presence of strong electrophiles, electrophilic attack is directed towards carbon.

The unique properties of the C-Si bond have led to important effects of stabilization due to silicon. The most important of these effects are the **α -silyl effect** and **β -silyl effect**.

*The α -silyl effect*³⁹

Silicon has more electropositive character as compared to carbon and hydrogen, therefore, silicon favours the formation of α -carbanions. The stabilization of a carbanion α - to silicon group is called the **α -silyl effect**.

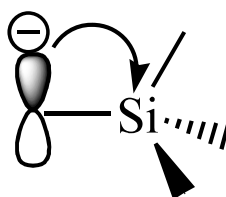


Figure 1: α -silyl effect.

This **α -silyl effect** has been described to $(\sigma^*-p)_\pi$ overlap between the antibonding σ^* molecular orbital of Si - C bond with the adjacent filled p- orbital of

the carbanion and empty 3d orbital on silicon allow $p_{\pi} - d_{\pi}$ bonding thus leading to stabilization of α -carbanion to silicon (**Fig. 1**).

*The β -silyl effect*⁴⁰

The polarization supports formation of carbocation at the β -position. The stabilization of a carbocation β - to silicon is a stereoelectronic phenomenon known as the β -silyl effect. The stabilization is attributed due to the stabilizing interaction between Si-C bond and empty p_{π} orbital of the β -carbocation (σ - π conjugation). The β -silyl effect is conformationally dependent in that the carbon silicon σ -bond and the vacant p-orbital must be in a common plane (**Fig. 2**).⁴¹

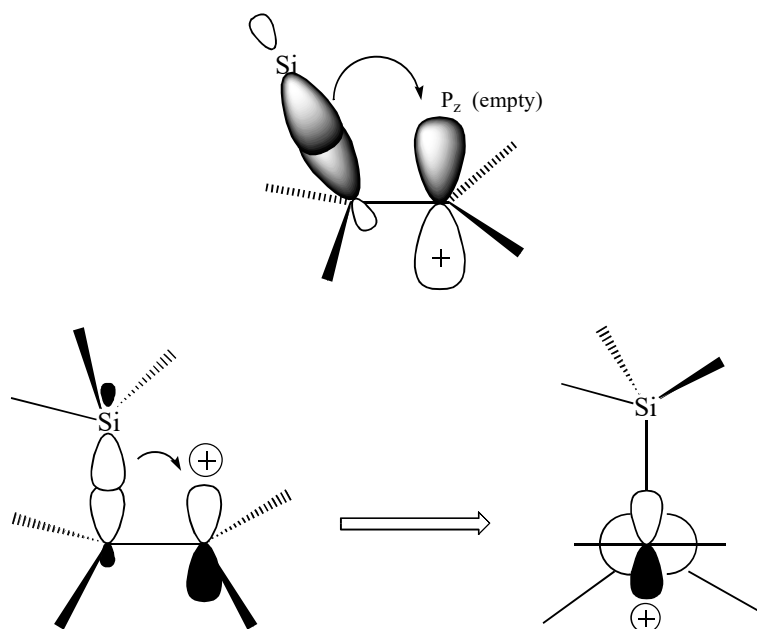


Figure 2: β -silyl effect

The β -silyl effect was first described by Ushakov and Itenberg.⁴² Subsequently it was studied by Sommer and Whitmore.⁴³ The β -effect has been attributed to $(\sigma-p)_{\pi}$ overlap between bonding α - level of the C-Si bond and with the adjacent empty p-orbital of the carbocation needed to align parallel for optimal overlap (**Fig. 2**).

Summary of Organosilicon Chemistry

Fleming has summarized all known organosilicon chemistry into eight generalizations. These generalizations are as follows:

- Nucleophilic substitution at silicon is faster than at carbon.
- Double bonds to silicon are weak.
- Single bonds from silicon to an electronegative atom like oxygen and halogens are strong.
- With alkoxide and halide nucleophiles, substitution at silicon is faster than at hydrogen.
- Silicon stabilizes an α - carbon-metal bond.
- A silicon-carbon bond stabilizes a β -carbocation.
- Silicon-hydrogen bonds can add across unsaturated linkage.
- The steric effects at silicon are not large.

Fleming has suggested that silicon bonded to carbon should be considered as a “super-proton” whereas when bonded silicon to oxygen it should be treated as an “enfeebled-proton”.⁴⁴

Most of the organosilicon chemistry explained based on the above properties/stabilizations of silicon.

Classification of Organosilicon Compounds

All organosilicon compounds are classified into several categories based upon the attachment of silyl- group to individual functionalities and their relation to the Si-C bond. The silyl group in all organosilicon compounds act as a masking agent. The silicon group is normally present during the course of the reaction. The silyl-group is therefore reported to act as a ‘*ferryman*’³⁷ and is usually absent from the final product. However the temporary presence of silicon in the compounds can selectively direct the reaction in a regio- and stereo-selective manner.

Some of the most important classes of organosilicon compounds are: Acylsilanes⁴⁵⁻⁴⁷, Alkynylsilanes⁴⁸⁻⁴⁹, Allylsilanes⁵⁰⁻⁵², Aminosilanes⁵³, Arylsilanes⁵⁴⁻⁵⁶, β -Ketosilanes⁵⁷, Silyl enol ethers⁵⁸⁻⁶⁰, Vinylsilanes⁶¹⁻⁶⁵ *etc.*

Current work

This thesis deals with the synthesis of some novel unsymmetrical 1,2-dihalocyclo alkenes and their Suzuki cross coupling reactions, a new palladium complex as a catalyst for the Sonogashira reaction of aryl bromides to synthesize some novel aryl substituted trimethylsilyl acetylenes and click reaction to synthesize trimethylsilyl containing triazole scaffolds.

A brief discussion of the important Pd-catalyzed reactions viz., (i) Suzuki reaction and (ii) Sonogashira reaction and some classes of organosilicon compounds is given as introduction in Part A of this thesis.

Part B deals with an introduction to some recent developments in alkynyl silane chemistry and some heterocyclic based silanes (triazoles and coumarins)

PART A**1. 2 Recent developments in Cross Coupling Reaction**

The substitution of an aryl, vinyl, or alkyl halide or pseudo halide by a nucleophile that takes place with catalysis by a transition-metal complex is generally referred to as a cross-coupling reaction if it follows the mechanistic course of oxidative addition, transmetalation, and reductive elimination. While many types of cross-coupling reactions have been known for several decades, advances in recent years have greatly increased their scope and practicality. This progress has had a significant impact on academic research, and cross-coupling reactions are now widely employed in a variety of synthetic venues, from the total synthesis of natural products to the preparation of new materials to bioorganic chemistry. In addition, due to this progress, these reactions are increasingly being applied in industrial settings. This includes a high level of use not only in research but also in the preparation of large samples for clinical trials as well as for manufacturing. A number of industries have been impacted, including those that produce pharmaceuticals, agrochemicals, and polymers. This progress has been greatly facilitated by an increased understanding of the mechanism by which these and related reactions proceed. Furthermore, a tremendous upsurge in the development of new ligands has contributed substantially to the recent advances. Now, these and other transition metal-catalyzed processes are no longer considered out of the ordinary and, instead, have become part of the everyday repertoire of the synthetic chemist. One common group of these processes utilizes carbon-based nucleophiles, such as aryl, vinyl, or alkyl derivatives of magnesium (Kumada-Corriu), boron (Suzuki-Miyaura), tin (Stille-Migita), zinc (Negishi), or silicon (Hiyama). In another very important cross-coupling process, a terminal alkyne serves as a pronucleophile

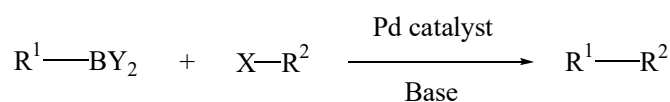
in the presence (Sonogashira) or absence (Heck alkylation) of a copper co-catalyst.⁶⁶

1.2.1 Suzuki Reaction

In 1986, Suzuki and Miyaura reported the cross-coupling between alkylboron reagents and aryl halides catalysed by palladium catalyst. Since its disclosure, it has been an attractive solution to challenging synthetic problems and has been used frequently in total synthesis for the construction of complex molecular frameworks.

Suzuki shared the 2010 Nobel Prize in Chemistry with Richard F. Heck and Ei-ichi Negishi for their effort for discovery and development of palladium-catalyzed cross couplings in organic synthesis.

Suzuki coupling is widely used to synthesize poly-olefins, styrenes, and substituted biphenyls. Several reviews have been published describing advancements and the development of the Suzuki reaction. The general scheme for the Suzuki reaction is shown below. (**Scheme 6**)



Y = hydroxy or alkoxy
X = I, Br, OTf and Cl

Scheme 6

1.2.1.1 Mechanism of Suzuki Cross Coupling Reaction

The mechanism of the Suzuki reaction is best viewed from the perspective of the palladium catalyst. The first step is the oxidative addition of palladium to the halide **2** to form the organopalladium species **3**. Reaction with base gives intermediate **4**, which via transmetalation⁶⁷ with the boronate complex **6** forms the organopalladium species **8**. Reductive elimination of the desired product **9** restores the original palladium catalyst **1** which completes the catalytic

cycle (**Fig. 3**). The Suzuki coupling takes place in the presence of a base and for a long time the role of the base was never fully understood. The base was first believed to form a trialkyl borate (R_3B-OR), in the case of a reaction of an trialkylborane (BR_3) and alkoxide (^-OR); this species could be considered as being more nucleophilic and then more reactive towards the palladium complex present in the transmetalation step.⁶⁸⁻⁷⁰ Duc and coworkers investigated the role of the base in the reaction mechanism for the Suzuki coupling and they found that the base has three roles: Formation of the palladium complex $[ArPd(OR)L_2]$, formation of the trialkyl borate and the acceleration of the reductive elimination step by reaction of the alkoxide with the palladium complex.⁶⁸

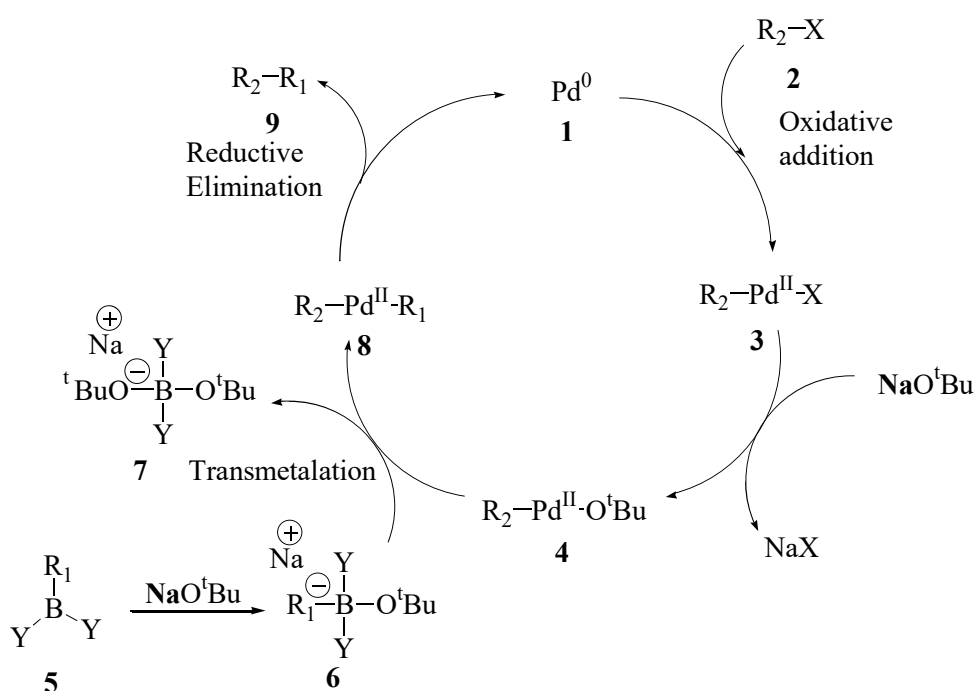


Figure 3

Oxidative addition:

In most of the cases oxidative addition is the rate determining step of the catalytic cycle.⁷¹ During this step, the palladium catalyst is oxidized from palladium (0) to palladium (II). The palladium catalyst **1** is coupled with the alkylhalide **2** to

yield an organopalladium complex **3**. As shown in the diagram the oxidative addition step breaks the carbon-halogen bond where the palladium is now bound to both the halogen and the R group (**Fig. 4**).

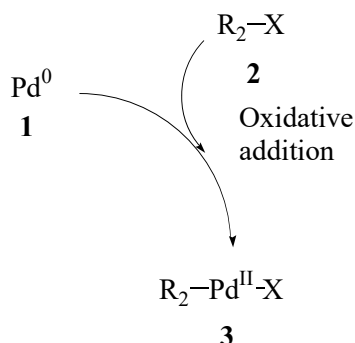


Figure 4

Oxidative addition proceeds with retention of stereochemistry with vinyl halides, while giving inversion of stereochemistry with allylic and benzylic halides.⁷² The oxidative addition initially forms the cis-palladium complex, which rapidly isomerizes to the trans-complex (**Fig. 5**).⁷³

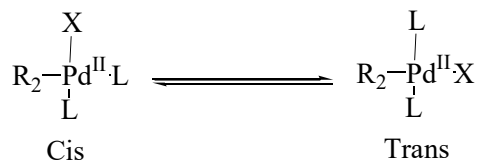
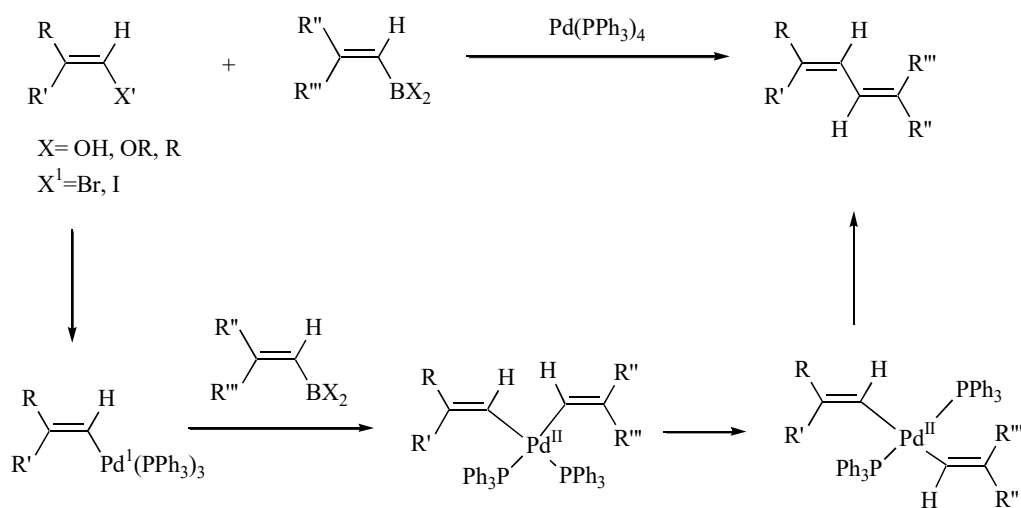


Figure 5

The Suzuki Coupling occurs with retention of configuration on the double bonds for both the organoboron reagent or the halide.⁷⁴ However, the configuration of that double bond, cis- or trans- is determined by the cis- to trans- isomerization of the palladium complex in the oxidative addition step where the trans- palladium complex is the predominant form. When the organoboron is attached to a double bond and it is coupled to an alkenyl halide the product is a diene as shown below (**Scheme 7**).



Scheme 7

Transmetalation:

Transmetalation is an organometallic reaction where ligands are transferred from one species to another. In the case of the Suzuki coupling the ligands are transferred from the organoboron species **6** to the palladium(II) complex **4** where the base that was added in the prior step is exchanged with the R_1 substituent on the organoboron species to give the new palladium(II) complex **8**. The exact mechanism of transmetalation for the Suzuki coupling remains to be discovered. The organoboron compounds do not undergo transmetalation in the absence of base and it is therefore widely believed that the role of the base is to activate the organoboron compound as well as facilitate the formation of $R_2\text{-Pd}^{\text{II}}\text{-O}^t\text{Bu}$ from $R_2\text{-Pd}^{\text{II}}\text{-X}$ (Fig. 6).⁷¹

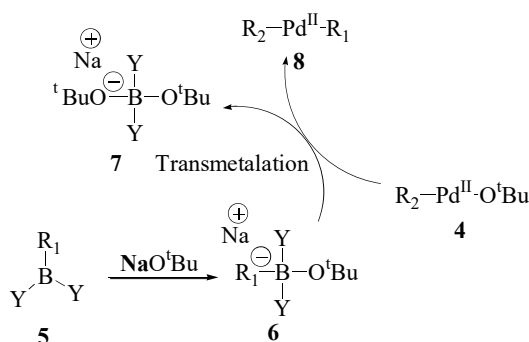
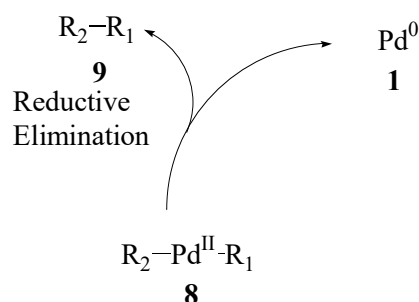


Figure 6

Reductive elimination:

The final step is the reductive elimination step where the palladium(II) complex **8** eliminates the product **9** and regenerates the palladium(0) catalyst (**1**). Using deuterium labelling, Ridgway *et al.* have shown the reductive elimination proceeds with retention of stereochemistry (**Fig. 7**).⁷⁵

**Figure 7****1.2.1.2 Organoboranes**

Aryl boronic acids are comparatively cheaper than other organoboranes and a wide variety of aryl boronic acids are commercially available. Hence, it has been widely used in Suzuki reaction as an organoborane partner. Aryltrifluoroborate salts are another class of organoboranes that are frequently used because they are less prone to protodeboronation compared to aryl boronic acids. They are easy to synthesize and can be easily purified.⁷⁶ Aryltrifluoroborate salts can be formed from boronic acids by the treatment with potassium hydrogen fluoride which can then be used in the Suzuki coupling reaction (**Scheme 8**).⁷⁷

**Scheme 8**

1.2.1.3 Metal Catalysts

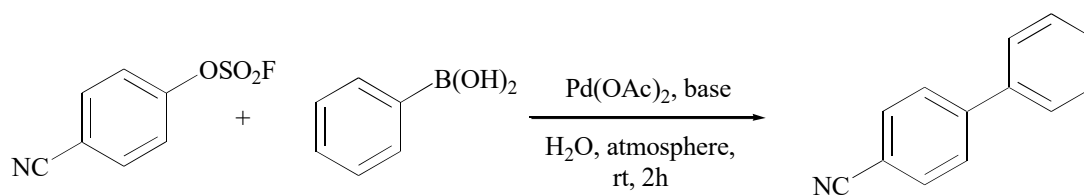
There have been variations of the Suzuki coupling reaction developed. Several reports show the use of palladium complexes $\text{Pd}(\text{OAc})_2$ ⁷⁸, PdCl_2 ⁷⁹, $(\text{PPh}_3)_2\text{PdCl}_2$ ⁸⁰, $(\text{PPh}_3)_4\text{Pd}$ ⁸¹, $\text{Pd}(\text{dppf})\text{Cl}_2$ ⁸² and $\text{Pd}(\text{dppf})\text{Cl}_2 \cdot \text{CH}_2\text{Cl}_2$ ⁸³ as catalysts for the cross coupling reactions. Various catalysts have been utilized other than the original palladium catalyst. In recent years the use of a nickel catalyst has been of interest and an advance in this area has been summarized in a recent review.⁸⁴

1.2.1.4 Advantages

The advantages of Suzuki coupling over other similar reactions are availability of common boronic acids, mild reaction conditions, and its less toxic nature. Boronic acids are less toxic and safer for the environment than organostannane and organozinc compound. It is easy to remove the inorganic by-products from reaction mixture. Hence, this reaction is beneficial for using relatively cheap and easily prepared reagents. Being able to use water as a solvent⁸⁵ makes this reaction more economical, eco-friendly, and capable of using wide variety of water soluble reagents. There are a wide variety of reagents that can be used for the Suzuki coupling, allowing for its use in many different chemical syntheses. There are reaction conditions that allow aryl- or vinyl-boronic acids and aryl- or vinyl-halides. Work has also extended the scope of the reaction to incorporate alkyl bromides.⁸⁶ In addition to different type of halides being possible for the Suzuki coupling reaction, the reaction also works with pseudohalides such as triflates (OTf), as replacements for halides. The relative reactivity for the coupling partner with the halide or pseudohalide is: $\text{R}_2\text{-I} > \text{R}_2\text{-OTf} > \text{R}_2\text{-Br} \gg \text{R}_2\text{-Cl}$. Boronic esters and organotrifluoroborate salts may be used instead of boronic acids. The catalyst can also be a palladium nanomaterial-based catalyst.⁸⁷ With a

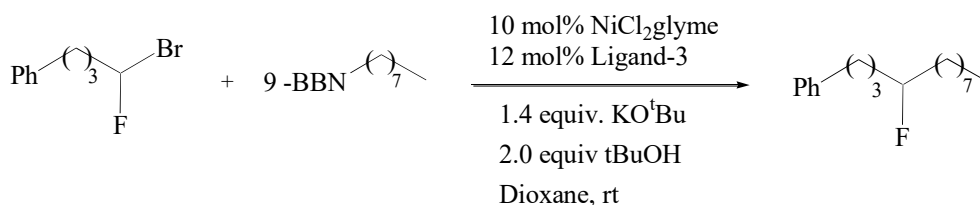
novel organophosphine ligand(SPhos), a catalyst loading of down to 0.001 mol% has been reported.⁸⁸ These advancements and the diverse number of possibilities for coupling partners, bases and solvents is a large reason why the Suzuki coupling is widely used in research and has recently been utilized in industrial processes for chemical synthesis. Applications of the Suzuki–Miyaura cross-coupling reaction in organic synthesis have been summarized by Kotha and co-workers.⁸⁹ Some of the recent literature reports on the Suzuki cross coupling reactions are given below.

Qiaobin Liang et. al., performed Suzuki–Miyaura cross-coupling reactions in water under air at room temperature without ligands or additives such as surfactants or phase-transfer reagents and proceeded smoothly to give biphenyls in excellent yields (**Scheme 9**).⁹⁰



Scheme 9

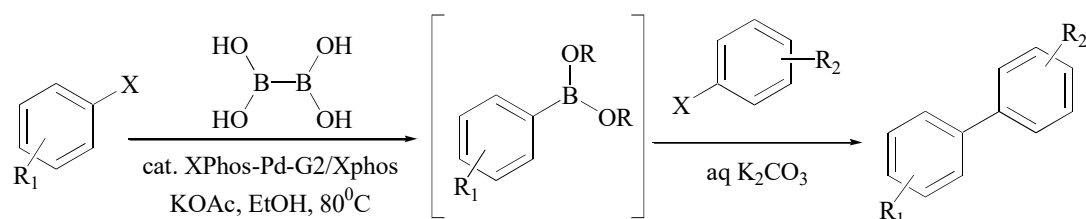
The first Suzuki cross-coupling reaction which utilizes dihalo compounds for the preparation of secondary alkyl fluorides was reported by Xiaojian Jiang et al. (**Scheme 10**).⁹¹



Scheme 10

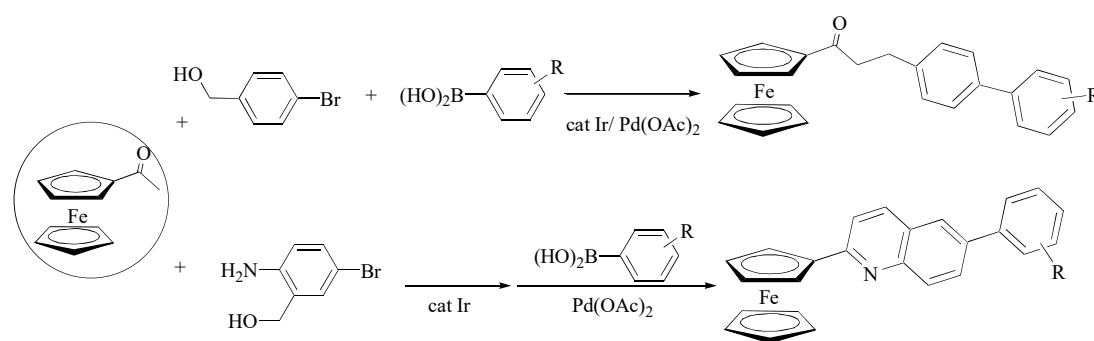
Through the use of bisboronic acid and the first- and second generation Buchwald preformed catalysts, Gary A. Molander et al., have developed a method

that allows the efficient coupling of two aryl halides in one pot without the need to synthesize the boronic acid in excess (**Scheme 11**).⁹²



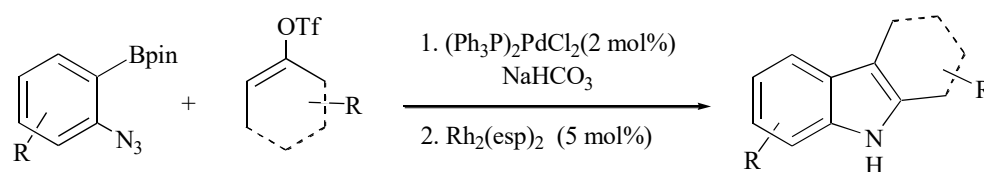
Scheme 11

An efficient PPh_3 -cyclometalated iridium(III)benzo[*H*]quinoline hydride/ $\text{Pd}(\text{OAc})_2$ -cocatalyzed three-component α -alkylation/Suzuki reaction has been reported. This method was successfully applied to a one-pot synthesis of 6-aryl-2-ferrocenylquinolines, using (2-amino-5-bromophenyl)methanol instead of 4-bromobenzylalcohol (**Scheme 12**).⁹³



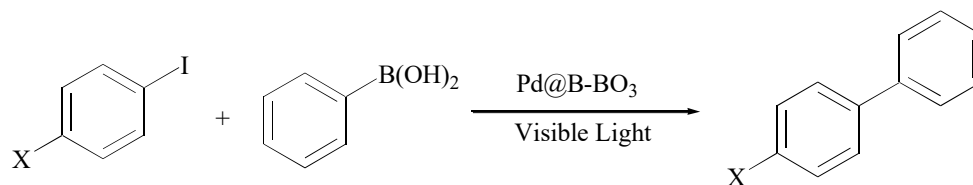
Scheme 12

The scope and limitations of a Suzuki reaction between 2-azidoarylboronic acid pinacolate esters and vinyl triflates are reported. This cross-coupling reaction enables the regioselective synthesis of indoles after a subsequent $\text{Rh}(\text{II})$ -catalyzed $\text{sp}^2\text{-C-H}$ bond amination reaction (**Scheme 13**).⁹⁴



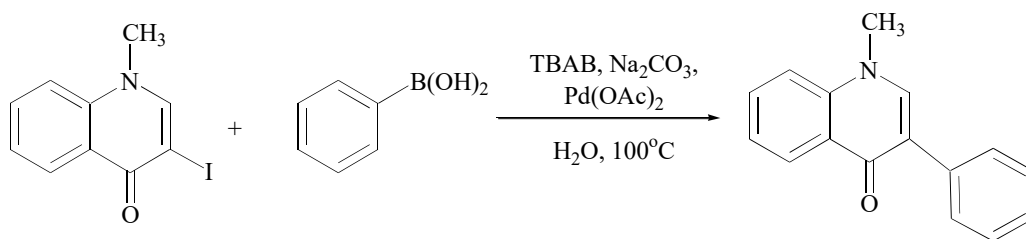
Scheme 13

Zi Jun Wang et al., reported the photocatalytic Suzuki Coupling Reaction Using Conjugated Microporous Polymer with Immobilized Palladium Nanoparticles under Visible Light (**Scheme 14**).⁹⁵



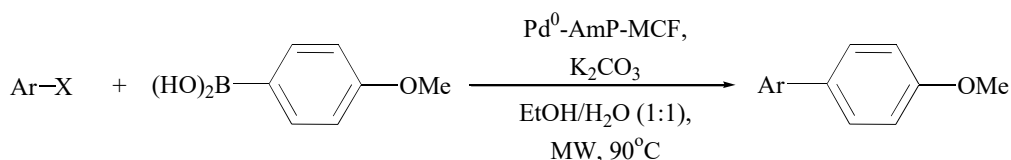
Scheme 14

Potential bioactive 3-arylquinolin-4(1H)-ones were synthesized under ohmic heating using an efficient, reusable, and ligand-free protocol developed for the Suzuki–Miyaura coupling of 1-substituted-3-iodoquinolin-4(1H)-ones with several boronic acids in water using Pd(OAc)₂ as a catalyst and tetrabutylammonium bromide (TBAB) as the phase transfer catalyst (**Scheme 15**).⁹⁶



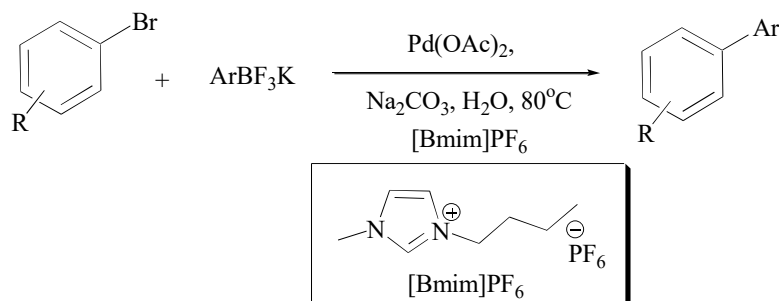
Scheme 15

Suzuki–Miyaura cross-coupling reactions of heteroaromatics catalyzed by palladium supported in the cavities of amino-functionalized siliceous mesocellular foam are reported (**Scheme 16**).⁹⁷



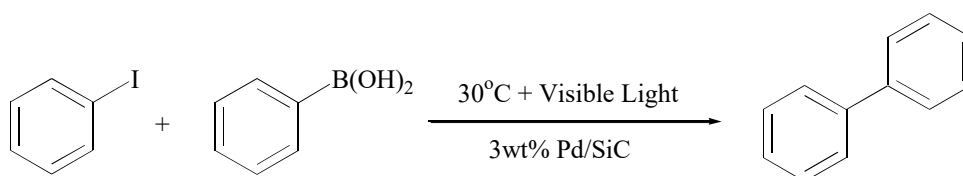
Scheme 16

The Suzuki–Miyaura coupling reactions of potassium aryltrifluoroborates with aryl bromides in water are promoted by the addition of [bmim]PF₆ using Pd(OAc)₂ as a catalyst and Na₂CO₃ as a base under air is reported (**Scheme 17**).⁹⁸



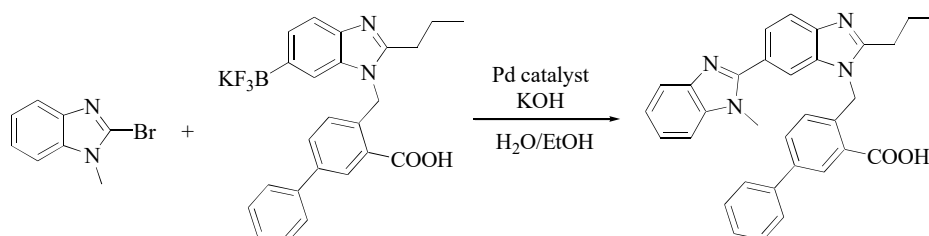
Scheme 17

The Mott-Schottky-type Pd/SiC catalyst in the coupling of iodobenzene and phenylboronic acid showed a high turnover frequency of 1053 h⁻¹ and a selectivity of nearly 100% under visible-light irradiation at 30 °C (**Scheme 18**).⁹⁹



Scheme 18

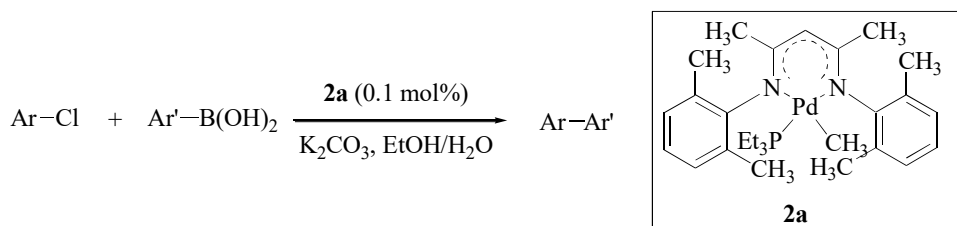
A direct and efficient total synthesis has been developed for telmisartan, a widely prescribed treatment for hypertension. The synthesis involves Suzuki reaction that can be catalyzed by either a homogeneous palladium source or graphene-supported palladium nanoparticles (**Scheme 19**).¹⁰⁰



Scheme 19

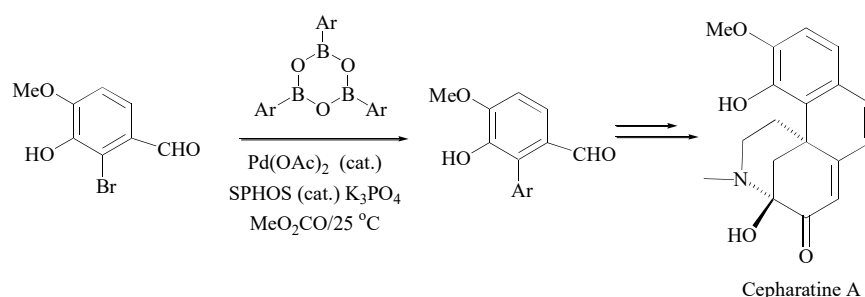
β -Diketiminatophosphane Pd complex as a powerful catalyst for the Suzuki coupling reaction of less reactive aryl chlorides under mild conditions is developed. A

wide range of sterically hindered and deactivated aryl chlorides could be efficiently coupled at a low catalyst loading of 0.1 mol % (**Scheme 20**).¹⁰¹



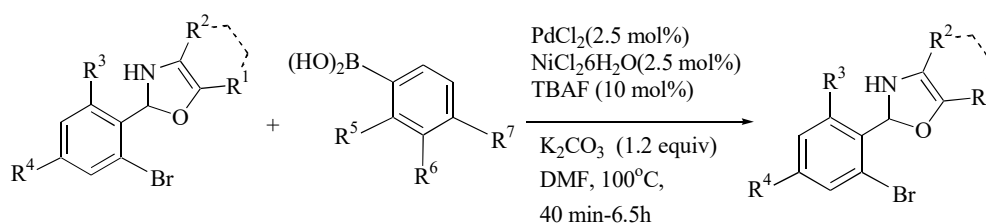
Scheme 20

Concise synthesis of the Hasubanan Alkaloid (\pm)-Cepharatine A using a Suzuki coupling reaction to effect o,p-phenolic coupling is reported (**Scheme 21**).¹⁰²



Scheme 21

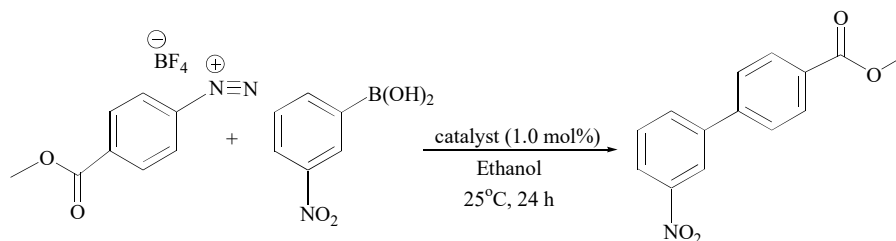
The palladium–nickel binary nanocluster is reported as a new catalyst system for Suzuki–Miyaura cross-coupling of orthoheterocycle-tethered sterically hindered aryl bromides. The inferior results obtained with the reported Pd/Ni salts/complexes or individual Pd/Ni nanoparticles as catalyst reveal the cooperative catalytic effect of the Pd and Ni nanoparticles in the Pd–Ni nanocluster (**Scheme 22**).¹⁰³



Scheme 22

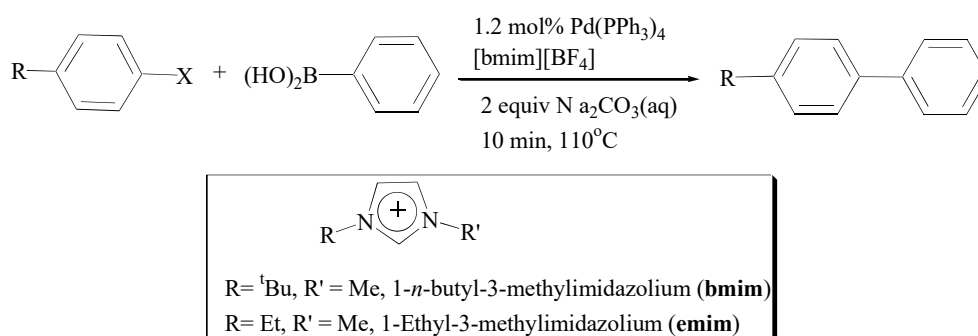
The use of aryldiazonium tetrafluoroborate salts as coupling partners in the Suzuki–Miyaura reaction was investigated from a process chemistry perspective including safety evaluation, solvent and catalyst screening and multivariate factor

optimisation. Optimised conditions were applied to a range of substrates to evaluate the scope and limitations of the reaction, and one example was carried out on mole scale to demonstrate the practicality and scalability of the process (**Scheme 23**).¹⁰⁴



Scheme 23

Palladium catalysed Suzuki cross-coupling reactions have been conducted in the ambient temperature ionic liquid, 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF₄]), exhibiting unprecedented reactivities in addition to easy product isolation and catalyst recycling (**Scheme 24**).¹⁰⁵

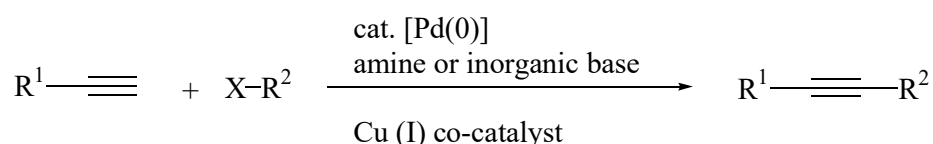


Scheme 24

1.2.2 Sonogashira Reaction

The coupling of aryl or vinyl halides with terminal acetylenes catalysed by palladium and other transition metals, commonly termed as Sonogashira cross-coupling reaction¹⁰⁶, is one of the important and widely used sp^2 - sp carbon-carbon bond formation reactions in organic synthesis, frequently employed in the synthesis of natural products, biologically active molecules, heterocycles, molecular electronics, dendrimers and conjugated polymers or nanostructures.

The palladium catalysed C-C bond formation process which is able to couple a terminal sp hybridized carbon from an alkyne with a sp^2 carbon of an aryl or vinyl halide (or triflate) is commonly termed as a Sonogashira coupling (**Scheme 25**).¹⁰⁷



R^1 = Aryl, heteroaryl, alkyl, SiR_3

R^2 = Aryl, heteroaryl, vinyl

X = I, Br, Cl, OTf

Scheme 25

The Sonogashira cross-coupling reaction was first reported by Kenkichi Sonogashira, Yasuo Tohda, and Nobue Hagihara in their 1975 publication.¹⁰⁸ It is an extension to the Cassar and Dieck and Heck reactions, which afford the same reaction products, but use harsh reaction conditions, such as high temperature, to do so. Both of these reactions make use of a palladium catalyst to carry out the coupling, while Sonogashira uses both palladium and copper catalysts simultaneously. This results in the increased reactivity of the reagents and the ability of the reaction to be carried out at room temperature, making the Sonogashira cross-coupling reaction a highly useful reaction, particularly in the alkylation of aryl

and alkenyl halides.¹⁰⁹ The reaction's remarkable utility can be evidenced by the amount of research still being done on understanding and optimizing its synthetic capabilities. The Sonogashira reaction achieved in recent years concerning catalysts, reaction conditions and substrates.^{110, 111}

1.2.2.1 Mechanism of Sonogashira Cross coupling reaction¹¹²

The mechanism involves two cycles: the palladium cycle and the copper cycle.

The Palladium cycle (Fig. 8)

- An inactive palladium Pd^{II} catalyst is activated by a reduction to the Pd^0 compound.
- The active palladium catalyst is the 14 electron compound Pd^0L_2 , complex A, which reacts with the aryl or vinyl halide in an oxidative addition to produce a Pd^{II} intermediate, complex B. This step is believed to be the rate-limiting step of the reaction.
- Complex B reacts in a transmetallation with the copper acetylide, complex F, which is produced in the copper cycle, to give complex C, expelling the copper halide, complex G.
- Both organic ligands are trans oriented and convert to cis in a trans-cis isomerization to produce complex D.
- In the final step, complex D undergoes reductive elimination to produce the alkyne, with regeneration of the palladium catalyst.

The copper cycle (Fig. 8)

- It is suggested that the presence of base results in the formation of a pi-alkyne complex, complex E, which makes the terminal proton on the alkyne more acidic, leading to the formation of the copper acetylide, compound F.

- Compound F continues to react with the palladium intermediate B, with regeneration of the copper halide, G

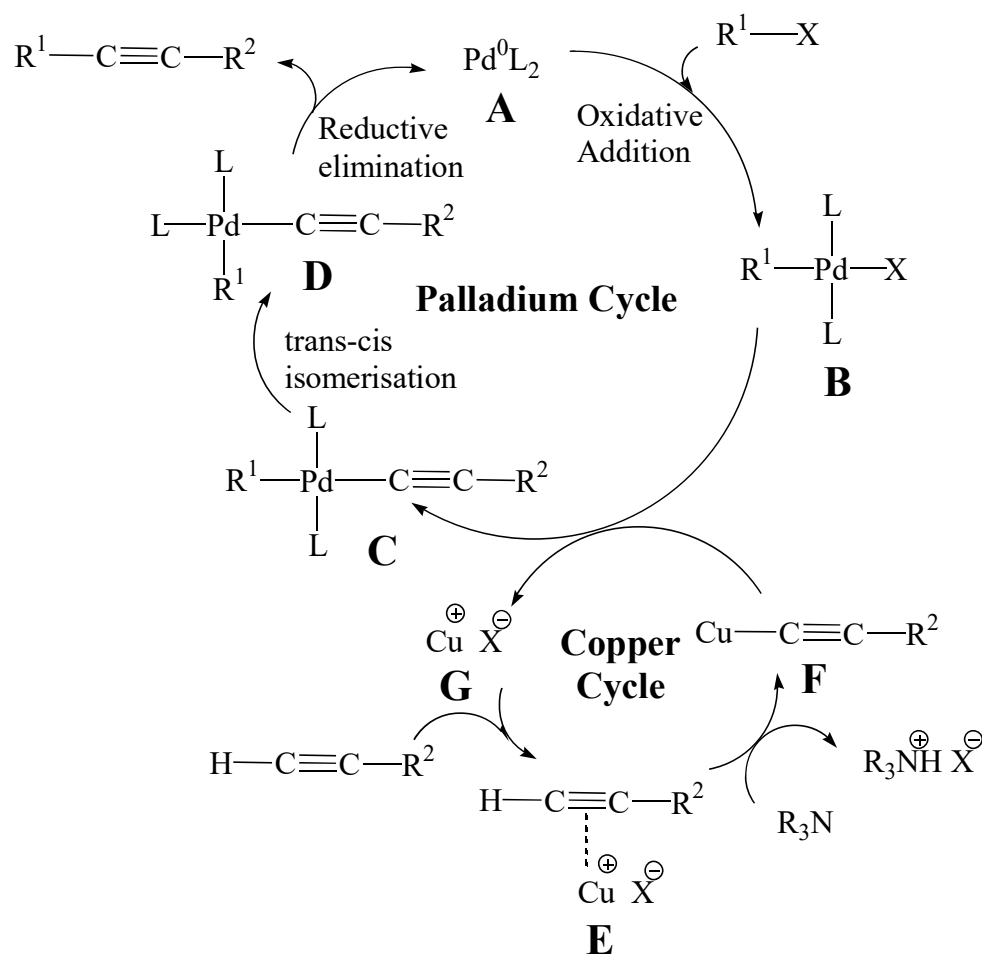


Figure 8: Mechanism of Sonogashira Reaction

Mechanistic studies suggest that these catalytic cycles represent the preferred reaction pathway, however there is debate about the exact identity of some intermediates, which may depend upon reaction conditions. For example, it has been shown that monoligated $\text{Pd}^0(\text{PR}_3)$ complexes (B) can be formed when dealing with bulky phosphanes and have been suggested as possible catalytic species in coupling reactions.¹¹³ In contrast, some results point to the formation of anionic palladium species, which would be the real catalysts instead of the coordinatively unsaturated Pd^0L_2 . Generally seen in the presence of anions and halides, it is known that

$\text{Pd}^0(\text{PPh}_3)_2$ does not exist in solution when generated in the presence of halide anions because they coordinate the Pd^0 center to form anionic species of the type $[\text{L}_2\text{Pd}^0\text{Cl}]^-$ which can participate in cross-coupling reactions.¹¹⁴

1.2.2.2 Catalyst

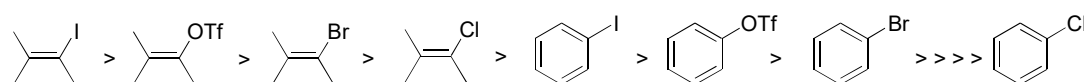
Typically, two catalysts are needed for this reaction: a zerovalent palladium complex and a halide salt of copper (I). Examples of such palladium catalysts include compounds in which palladium is ligated to phosphines $[\text{Pd}(\text{PPh}_3)_4]$. A common derivative is $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, but bidentate ligand catalysts, such as $\text{Pd}(\text{dppe})\text{Cl}_2$, $\text{Pd}(\text{dppp})\text{Cl}_2$, and $\text{Pd}(\text{dppf})\text{Cl}_2$ have also been used.¹¹² The drawback to such catalysts is the need for high loadings of palladium (up to 5 mol %), along with a larger amount of a copper co-catalyst.¹¹² Pd^{II} is often employed as a pre-catalyst since it exhibits greater stability than Pd^0 over an extended period of time and can be stored under normal laboratory conditions for months.¹¹⁵ The Pd^{II} catalyst is reduced to Pd^0 in the reaction mixture by either an amine, a phosphine ligand, or a reactant, allowing the reaction to proceed.¹¹⁶ The oxidation of triphenylphosphine to triphenylphosphine oxide can also lead to the formation of Pd^0 in situ when catalysts such as bis(triphenylphosphine)palladium(II) chloride are used.

Copper(I) salts, such as copper iodide, react with the terminal alkyne and produce a copper(I) acetylide, which acts as an activated species for the coupling reactions. Cu(I) is a co-catalyst in the reaction, and is used to increase the rate of the reaction.¹⁰⁹

1.2.2.3 Reaction conditions

The Sonogashira reaction is typically run under mild conditions.¹¹⁷ The cross-coupling is carried out at room temperature with a base, typically an amine, such as diethylamine,¹⁰⁸ that also acts as the solvent. The reaction medium must be basic to neutralize the hydrogen halide produced as the byproduct of this coupling reaction, so alkylamine compounds such as triethylamine and diethylamine are sometimes used as solvents, but also DMF or ether can be used as solvent. Other bases such as potassium carbonate or cesium carbonate are occasionally used. In addition, deaerated conditions are formally needed for Sonogashira coupling reactions because the palladium (0) complexes are unstable in the air, and oxygen promotes the formation of homocoupled acetylenes. Recently, developments of air-stable organopalladium catalysts enable this reaction to be conducted in the ambient atmosphere.

Depending on the sp^2 -carbon halide-or triflate used, these reaction conditions have varying results.



The rate of reaction of sp^2 carbons. Vinyl iodide > vinyl triflate > vinyl bromide > vinyl chloride > aryl iodide > aryl triflate > aryl bromide >>>> aryl chloride.¹¹²

1.2.2.4 Complications

Due to the crucial role of base, specific amines must be added in excess or as solvent for the reaction to proceed. It has been discovered that secondary amines such as piperidine, morpholine, or diisopropylamine in particular can react efficiently and reversibly with *trans*- $RPdX(PPh_3)_2$ complexes by substituting one

PPh₃ ligand. The equilibrium constant of this reaction is dependent on R, X, a factor for basicity, and the amine's steric hindrance.¹¹⁸ The result is competition between the amine and the alkyne group for this ligand exchange, which is why the amine is generally added in excess to promote preferential substitution.

1.2.2.5 Copper-free reaction

While a copper co-catalyst is added to the reaction to increase reactivity, the presence of copper can result in the formation of alkyne dimers. This leads to what is known as the Glaser coupling reaction, which is an undesired formation of homocoupling products of acetylene derivatives upon oxidation. As a result, when running a Sonogashira reaction with a copper co-catalyst, it is necessary to run the reaction in an inert atmosphere to avoid the unwanted dimerization. Copper-free variations to the Sonogashira reaction have been developed to avoid the formation of the homocoupling products.^{115, 119} The exact mechanism by which the copper-free reaction occurs is still under debate.¹⁰⁹ One mechanism (**Fig. 9**) seems to indicate the following:

- As in the original mechanism, oxidative addition of the aryl halide or triflate to the Pd(0) catalysts.
- Since the amines associated with this reaction are not basic enough to deprotonate the reacting alkyne, it is believed that complexation to the Pd(0) catalyst requires displacement of one ligand to create an intermediate complex.
- As a result, this new intermediate can then facilitate deprotonation of the terminal alkyne proton and subsequent ligand exchange with the leaving group X.
- Reductive elimination gives rise to the desired coupling product.

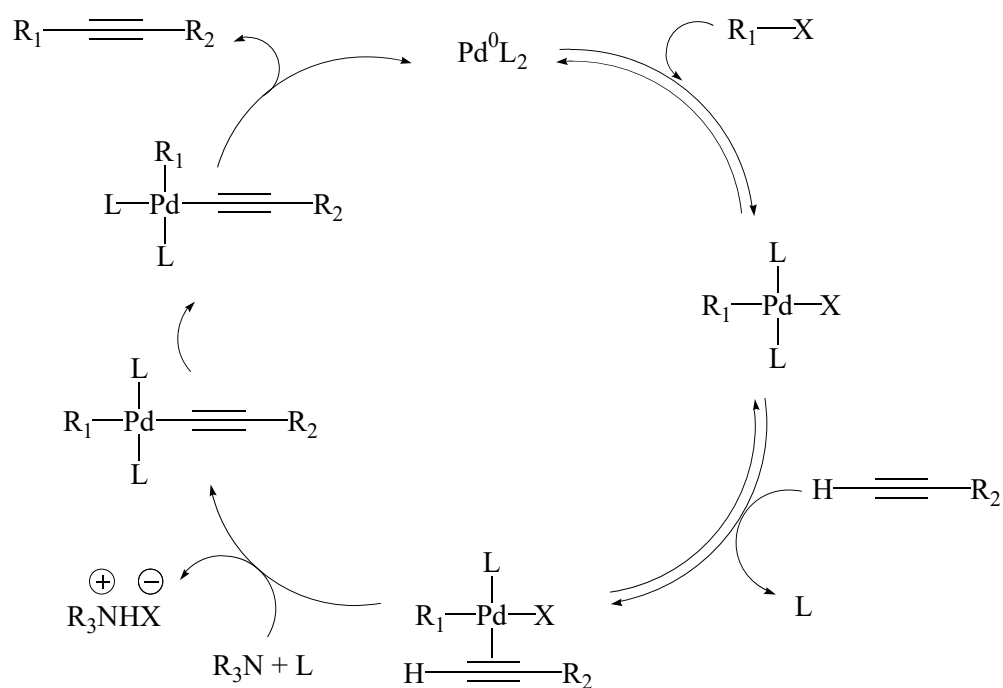


Figure 9: Proposed copper free mechanism for Sonogashira Reaction¹¹⁹

Due to mounting evidence that amines may also be involved in various steps exclusive of (via a new mode of reactivity) and/or preceding deprotonation events, an alternate mechanism¹²⁰ (**Fig. 10**) suggests the following:

- Amines can interfere with the oxidative addition through an accelerating effect brought upon to the formation of more reactive $[\text{Pd}(0)\text{L}(\text{amine})]$ complexes.
- As a result, they can also substitute one ligand in the complex formed after the addition.
- Depending on the rate of the competition between amine and alkyne in the substitution of one ligand in this complex, an inter-play between the original mechanism and the newer one seems likely.

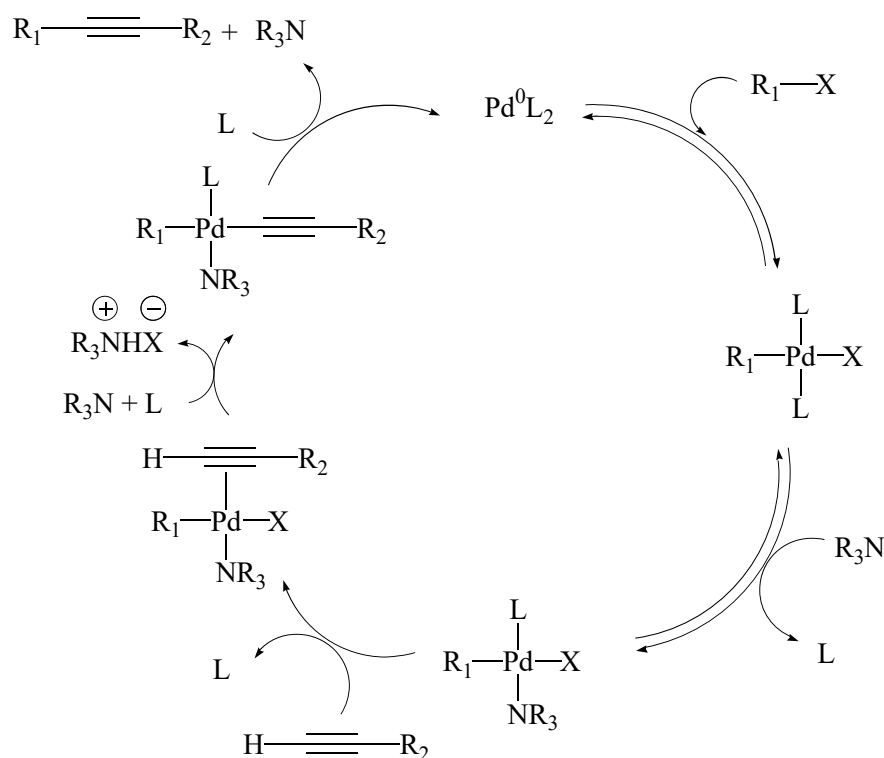


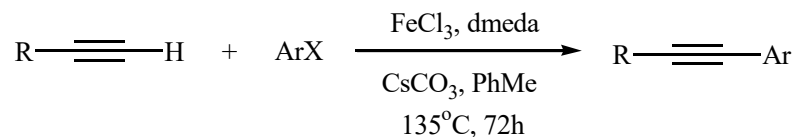
Figure 10: Alternative copper-free mechanism¹²⁰

The crucial difference between the two mechanisms is that the former would be preferred if the amine is a weaker ligand than the reacting alkyne, while the latter mechanism would be preferred if the amine were a better ligand than the alkyne.¹²⁰

1.2.2.6 Catalyst variations

Recently, a nickel-catalyzed Sonogashira coupling has been developed which allows for the coupling of non-activated alkyl halides to acetylene without the use of palladium, although a copper co-catalyst is still needed.¹²¹ It has also been reported that gold can be used as a heterogeneous catalyst, which was demonstrated in the coupling of phenylacetylene and iodobenzene with an Au/CeO₂ catalyst.^{122, 123} In this case, catalysis occurs heterogeneously on the Au nanoparticles,^{123, 124} with Au(0) as the active site.¹²⁵ Selectivity to the desirable cross coupling product was also found to be enhanced by supports such as CeO₂ and La₂O₃.¹²⁵ Additionally, iron-catalyzed Sonogashira couplings have been investigated as relatively cheap and non-toxic

alternatives to palladium. Here, FeCl₃ is proposed to act as the transition-metal catalyst and Cs₂CO₃ as the base, thus theoretically proceeding through a palladium-free and copper-free mechanism (**Scheme 26**).¹²⁶



Scheme 26

While the copper-free mechanism has been shown to be viable, attempts to incorporate the various transition metals mentioned above as less expensive alternatives to palladium catalysts have shown a poor track record of success due to contamination of the reagents with trace amounts of palladium, suggesting that these theorized pathways are extremely unlikely, if not impossible, to achieve.¹²⁷

Studies shown that organic and inorganic starting materials can also contain enough (ppb level) palladium for the coupling.¹²⁸

Gold and Palladium Combined

A highly efficient gold and palladium combined methodology for the Sonogashira coupling of a wide array of electronically and structurally diverse aryl and heteroaryl halides have been reported.¹²⁹ The orthogonal reactivity of the two metals shows high selectivity and extreme functional group tolerance in Sonogashira coupling. A brief mechanistic study reveals that the gold-acetylide intermediate enters into palladium catalytic cycle at the transmetalation step.

Palladium-phosphorus complexes

The issues dealing with recovery of the often expensive catalyst after product formation poses a serious drawback for large-scale applications of homogeneous

catalysis. Structures known as metalodendrimers combine the advantages of homogeneous and heterogeneous catalysts, as they are soluble and well defined on the molecular level, and yet they can be recovered by precipitation, ultrafiltration, or ultracentrifugation.¹³⁰ Some recent examples can be found about the use of dendritic palladium complex catalysts for the copper-free Sonogashira reaction. Thus, several generations of bidentate phosphanated palladium (II) polyamino dendritic catalysts have been used solubilized in triethylamine for the coupling of aryl iodides and bromides at 25-120 °C, and of aryl chlorides, but in very low yields.¹³¹ The dendrimeric catalysts could usually be recovered by simple precipitation and filtration and reused up to five times, with diminished activity produced by dendrimer decomposition and not by palladium leaching being observed. These dendrimeric catalysts showed a negative dendritic effect; that is, the catalyst efficiency decreases as the dendrimer generation increases. The recyclable polymeric phosphane ligand shown below is obtained from ring-opening metathesis polymerization of a norbornene derivative, and has been used in the copper cocatalyzed Sonogashira reaction of methyl piodobenzoate and phenylacetylene using $\text{Pd}(\text{dba})_2 \cdot \text{CHCl}_3$ as a palladium source.¹³² Despite recovery by filtration, polymer catalytic activity decreased by approximately 4-8% in each recycles.

Palladium-nitrogen complexes

Pyridines and pyrimidines have shown good complexation properties for palladium and have been employed in the formation of catalysts suitable for Sonogashira couplings. The dipyrimidyl-palladium complex shown below (**Fig. 11**) has been employed in the copper-free coupling of iodo-, bromo- and chlorobenzene with phenylacetylene using N-butylamine as base in THF solvent at 65 °C.

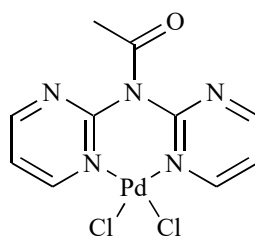


Figure 11: Dipyrimidyl-palladium complex.

Furthermore, all structural features of this complex have been characterized by extensive X-ray analysis, verifying the observed reactivity.¹³³

More recently, the dipyridylpalladium complex has been obtained and has been used in the copper-free Sonogashira coupling reaction of aryl iodides and bromides in N-methylpyrrolidinone (NMP) using tetra-n-butylammonium acetate (TBAA) as base at room temperature. It is interesting to note that this complex has also been used for the coupling of aryl iodides and bromides in refluxing water as solvent and in the presence of air, using pyrrolidine as base and TBAB as additive,¹³⁴ although its efficiency was higher in N-methylpyrrolidinone (NMP) as solvent.

N-heterocyclic carbene (NHC) palladium complexes¹³⁵

Nucleophilic N-heterocyclic carbenes (NHCs) behave like typical σ -donor ligands that can substitute 2-electron ligands (i.e., amines, phosphanes) in metal coordination chemistry, and at times even more efficiently; therefore, they have found application to numerous areas of organometallic homogeneous catalysis.¹³⁶ The most easily available are stable carbenes derived from imidazole, not the least because numerous imidazolium precursor compounds can be made along various reliable routes, with the combination of the imidazolium salt with a palladium source under basic conditions generating the NHC-palladium complex. At 1 mol%, the NHC-derived palladium(II) complex shown in **Fig. 12** has been known

to promote the coupling of aryl bromides at 80 °C in DMF using triethylamine as base, although requiring the presence of catalytic amounts of copper(I) iodide and triphenylphosphine as well.¹³⁵

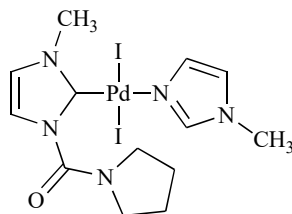


Figure 12: NHC-derived Pd(II) complex

1.2.2.7 Use of arenediazonium

Arenediazonium salts have been reported as an alternative to aryl halides for the Sonogashira coupling reaction. Gold(I) chloride has been used as co-catalyst combined with palladium(II) chloride in the coupling of arenediazonium salts with terminal alkynes, a process carried out in the presence of bis-2,6-diisopropylphenyl dihydroimidazolium chloride (IPr NHC) (5 mol%) to in situ generate a NHC–palladium complex, and 2,6-di-tert-butyl-4-methylpyridine (DBMP) as base in acetonitrile as solvent at room temperature.¹²⁹ This coupling can be carried out starting from anilines by formation of the diazonium salt followed by in situ Sonogashira coupling, where anilines are transformed into diazonium salt and furtherly converted into alkyne by coupling with phenylacetylene.

Part B

The recent developments in the chemistry viz., synthesis of the following classes of organosilicon compounds are presented:

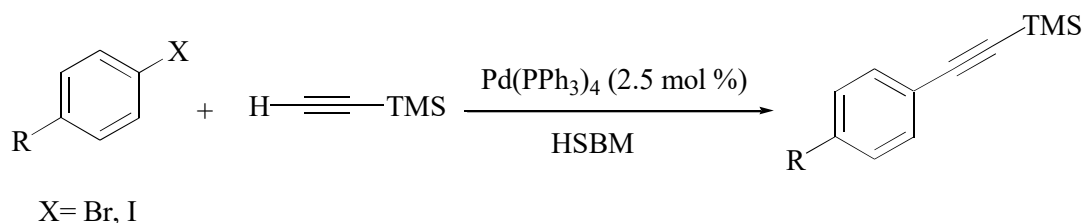
- i. *Alkynylsilanes and*
- ii. *Some heterocyclic based silanes (triazoles and coumarins)*

1.3 A brief reviews of Alkynylsilanes

Alkynylsilanes form an important class of compounds in organosilicon chemistry. In these compounds the silyl group is attached to the carbon-carbon triple bond. In the past ten years alkynylsilanes have proved to be versatile building blocks in organic synthesis. They have been extensively used in protecting groups for terminal alkynes,¹³⁷ in Hiyama coupling,¹³⁸ in metathesis reactions,¹³⁹ in Lewis acid-catalyzed electrophilic substitutions¹⁴⁰ and also in Sonogashira coupling.¹⁴¹

1.3.1 Synthesis of trimethylsilyl ethyne derivatives using Sonogashira Cross coupling reaction

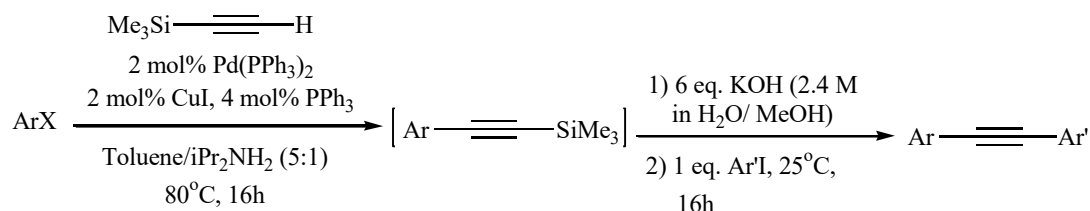
The solvent-free Sonogashira reaction utilizing high speed ball milling of a variety of *para*-substituted aryl halides were performed with trimethylsilylacetylene. Iodo- and bromo-substituted aromatics successfully undergo Sonogashira coupling to form arylalkynylsilanes (**Scheme 27**).¹⁴²



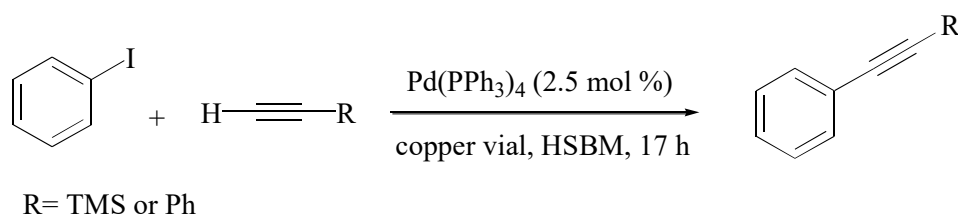
Scheme 27

Unsymmetrical diarylalkynes are accessible by a one-pot procedure from two different aryl halides and (trimethylsilyl)acetylene. A Pd/Cu-catalyzed Sonogashira

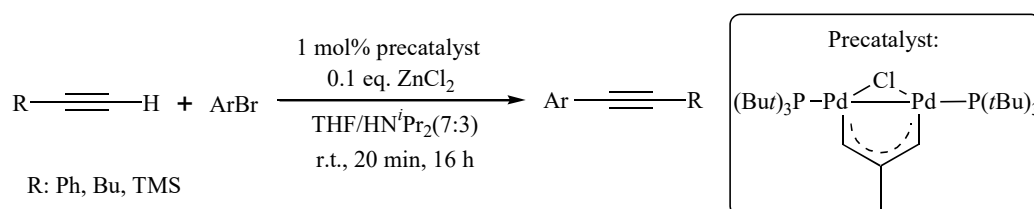
coupling of an aryl halide with (trimethylsilyl)acetylene is followed by desilylation of the formed aryl(trimethylsilyl)acetylene with aqueous potassium hydroxide and a second Sonogashira coupling with an aryl iodide (**Scheme 28**).¹⁴³

**Scheme 28**

A. F. Dennis, et.al., have first time reported the use of the vial and ball material as a catalyst in a ball milled solvent free Sonogashira cross coupling reaction to synthesize various trimethylsilylethyne derivatives (**Scheme 29**).¹⁴⁴

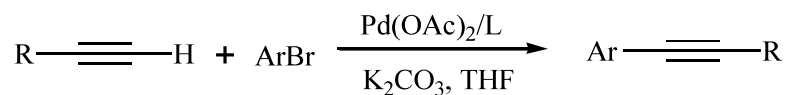
**Scheme 29**

A. D. Finke, et. al., have reported substoichiometric amounts of ZnCl_2 promoted a room temperature, $\text{Pd}/\text{P}(t\text{-Bu})_3$ -catalyzed cross-coupling of aryl bromides with alkynes. A $\text{Pd}(\text{I})$ dimer is a particularly active precatalyst for this reaction (**Scheme 30**).¹⁴⁵

**Scheme 30**

A copper and amine free Sonogashira coupling reaction employing amino phosphines as ligands was reported by Cheng, et. al., Under optimized reaction

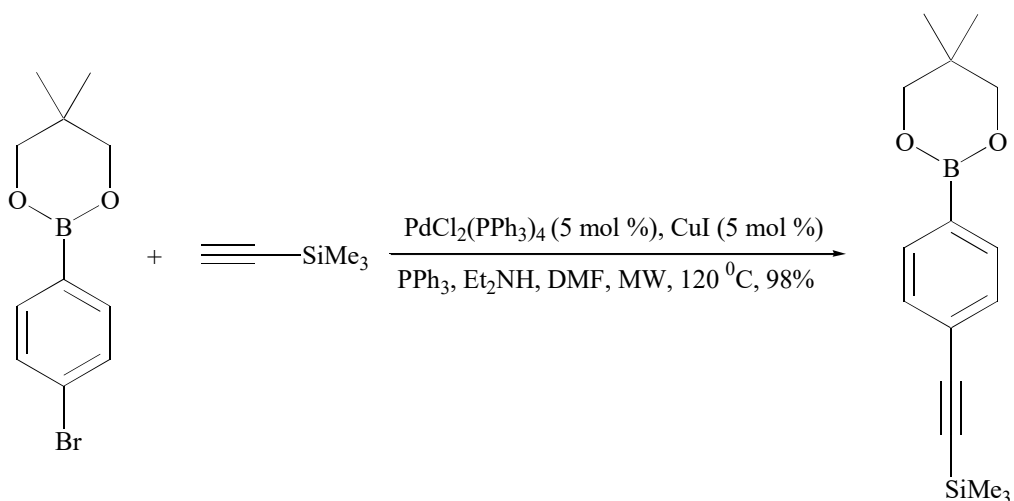
conditions, the Sonogashira coupling reaction occurred selectively when an enyne substrate was employed and no Heck reaction product was detected; acetone-masked acetylene and trimethylsilylacetylene can also be efficiently coupled, providing a method to make terminal alkynes (**Scheme 31**).¹⁴⁶



R: alkyl, aryl and TMS

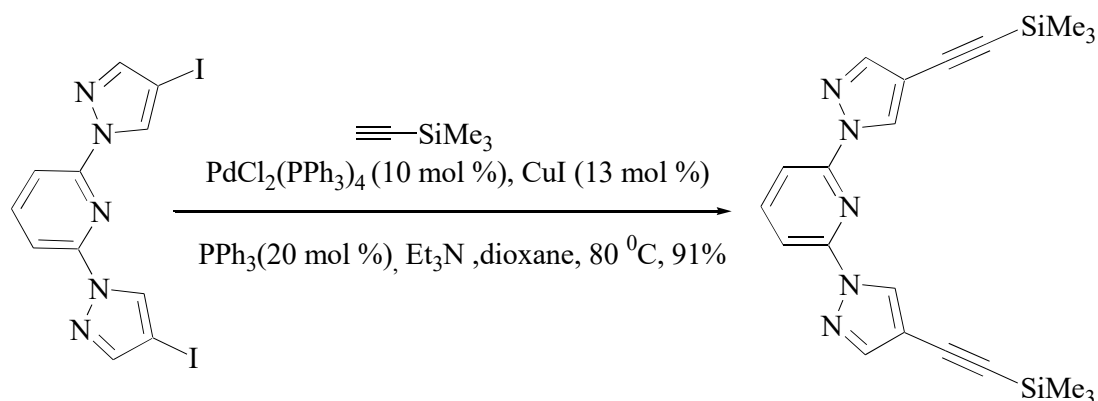
Scheme 31

Bromoaryl boronates when coupled to trimethylsilylacetylene under microwave-facilitated Sonogashira reaction conditions to gave acetylenes (**Scheme 32**).¹⁴⁷



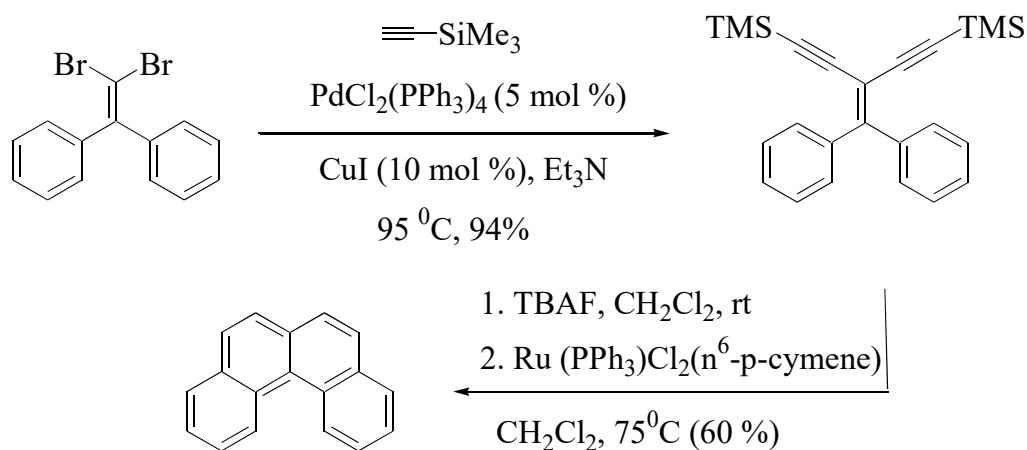
Scheme 32

An example of the application of the Sonogashira methodology to the alkynylation of an iodinated pyrazole ring is the double alkynylation of the 2,6-bis(pyrazol-1-yl)pyridine system with TMSA, affording the bis-alkynylated system, which is useful in coordination chemistry (**Scheme 33**).¹⁴⁸



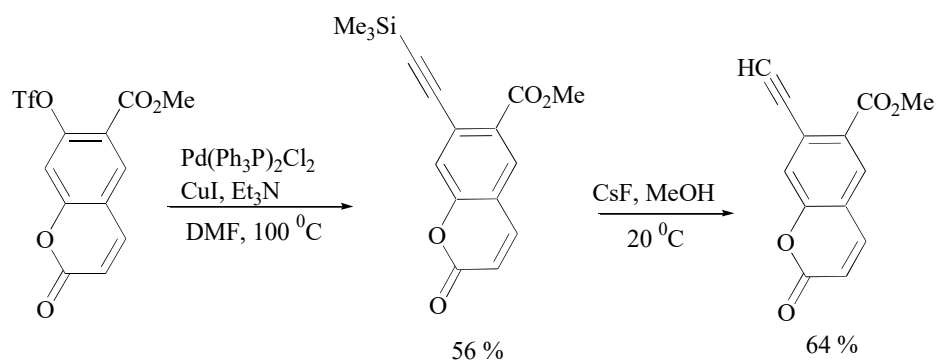
Scheme 33

An illustrative example is the synthesis of [4] helicene, was achieved starting from dibrominated diphenylethene. Double Sonogashira cross-coupling reaction of this compound with TMSA gives *gem*-enediyne, which was desilylated and cyclized under transition metal catalysis using a ruthenium complex to give polycyclic aromatic hydrocarbons (Scheme 34).¹⁴⁹



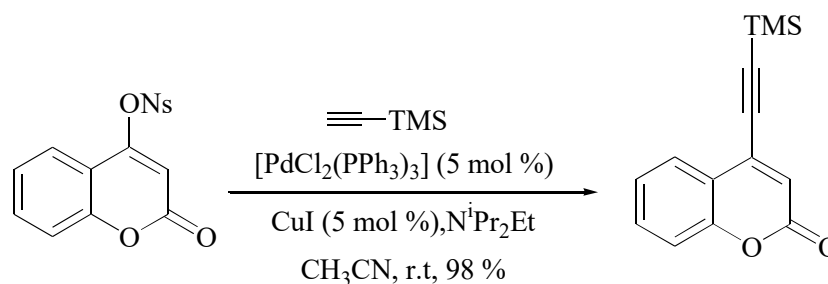
Scheme 34

The reaction of the triflate with trimethylsilyl acetylene in the presence of $\text{Pd}(\text{Ph}_3\text{P})_2\text{Cl}_2/\text{CuI}/\text{Et}_3\text{N}$ gave 7-trimethylsilylalkynylcoumarin. It undergoes desilylation with cesium fluoride to form 7-alkynylcoumarin (Scheme 35).¹⁵⁰



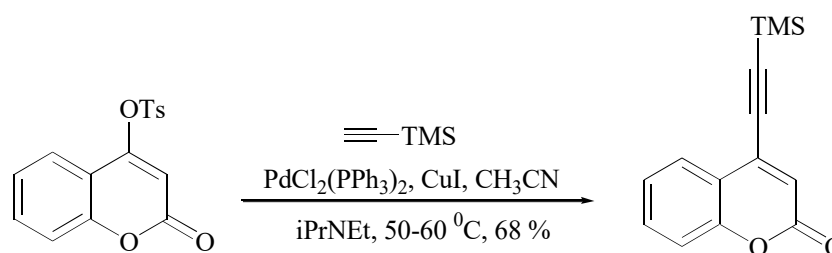
Scheme 35

The reactivity of various vinyl nosylates with palladium catalysts in cross-coupling reactions to form products is reported (Scheme 36).¹⁵¹



Scheme 36

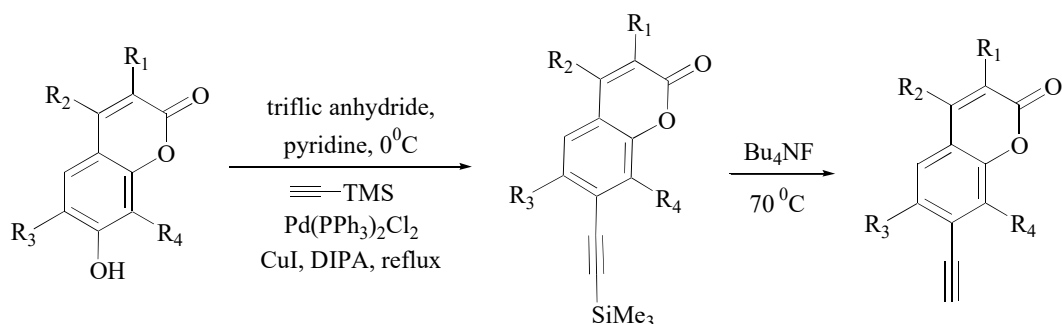
The palladium catalyzed carbon-carbon bond formation between 4-tosylcoumarins and terminal acetylenes via under Sonogashira reaction conditions to generate 4-alkynylcoumarin is given (Scheme 37).¹⁵²



Scheme 37

The 7-hydroxy coumarin is activated through the formation of triflate intermediates followed by substitution with the trimethylsilylprotected acetylene.

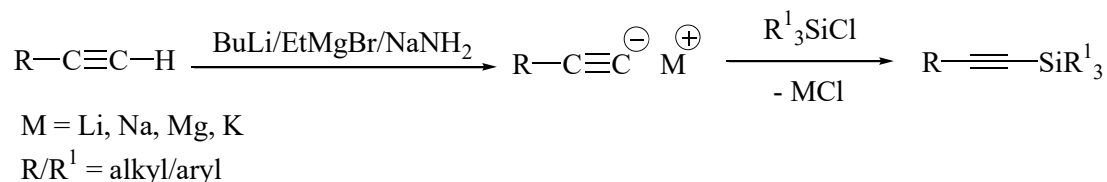
After removing the protecting group (trimethylsilyl group), the final 7-ethynylcoumarin products are obtained (**Scheme 38**).¹⁵³



Scheme 38

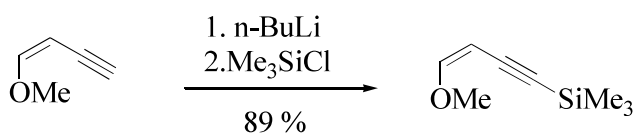
1.3.2 Some other methods of synthesis of trimethylsilylethynes:

Terminal alkynes are converted readily into alkynylsilanes, usually by the reaction of the alkyne anion with a suitable silyl chloride. The alkynyl anion may be generated using a wide variety of reagents such as BuLi, EtMgBr, NaNH₂ *etc* (**Scheme 39**).¹⁵⁴



Scheme 39

Direct silylation of a terminal alkyne with chlorotrimethylsilane provides the simplest procedure for the synthesis of conjugated enynes having a silyl substituent at the alkynyl carbon (**Scheme 40**).¹⁵⁵

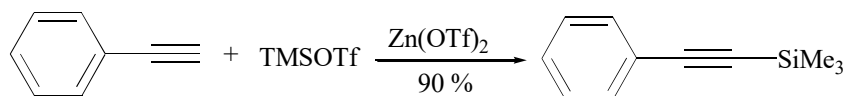


Scheme 40

Recently Zhu and Shaw reported the zinc triflate-mediated silylation of terminal alkynes with chlorosilane/silyltriflate with yields greater than 90% and this

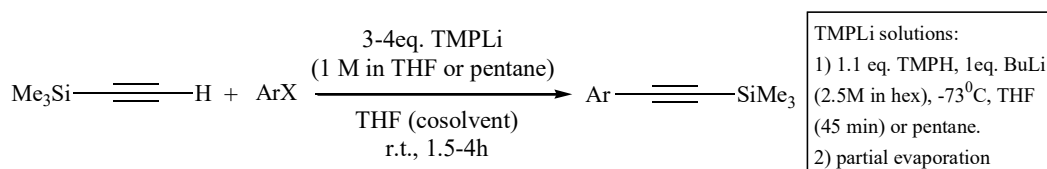
method avoids the use of stoichiometric quantities of bases and metal mediators

(Scheme 41).^{156,157}



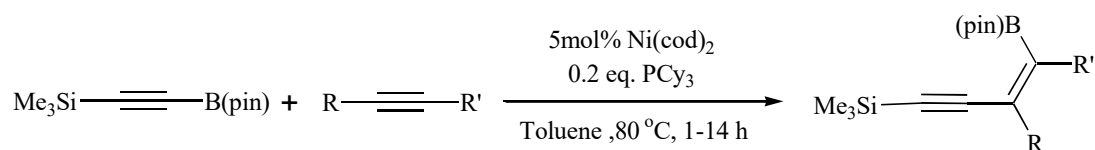
Scheme 41

The use of TMPLi base in a pentane/THF mixture at 25°C or use of a metal alkoxide base in dioxane at elevated temperature enable base-mediated, transition-metal-free alkynylations of aryl chlorides that proceed via benzyne intermediates is also reported. Fluoro, trifluoromethyl, silyl, cyano, and alcohol functionalities are compatible with the reaction conditions (Scheme 42).¹⁵⁸



Scheme 42

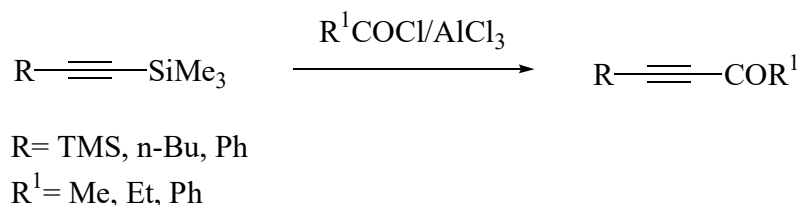
Alkynylboration of alkynes with alkynyl(pinacol)boranes in the presence of nickel catalysts gave *cis*-1-borylbut-1-en-3-yne derivatives. Some boryl-substituted enynes were reacted with sp^2 halides under Suzuki-Miyaura coupling conditions (Scheme 43).¹⁵⁹



Scheme 43

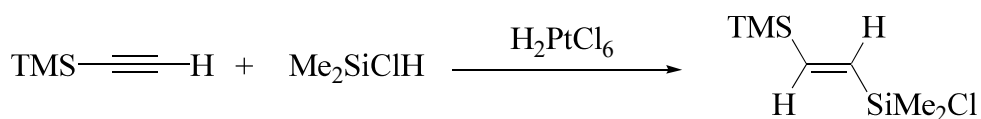
1.3.3 Reactions of trimethylsilylalkynes

Alkynylsilanes undergo electrophilic substitution reactions with a wide variety of acid chlorides in presence of a Lewis acid to obtain the corresponding α,β -acetylenic ketones (**Scheme 44**).¹⁶⁰



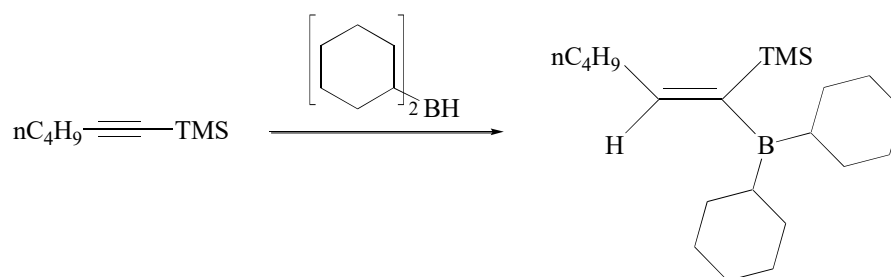
Scheme 44

1-Trimethylsilylalkynes undergo addition reactions with silanes in the presence of a suitable catalyst to form (*E*)-vinylsilanes. The platinum catalysed hydrosilylation proceed via *syn*-addition of silane to the alkyne exclusively resulting in (*E*)-product (**Scheme 45**).¹⁶¹



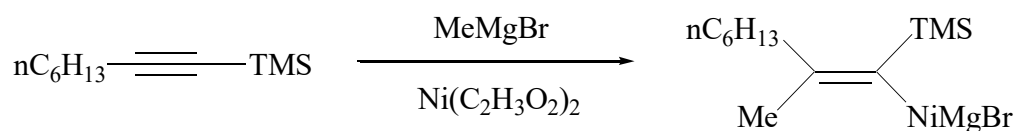
Scheme 45

Dialkylboranes undergo *syn*-addition to 1-trimethylsilylalkynes to yield vinylboranes in which the silicon and boron are bonded to same carbon atom. The *regio*-selectivity can be explained by an intermediate involving β -carbocation to silicon which is known to be stabilized by β -silyl effect (**Scheme 46**).¹⁶²



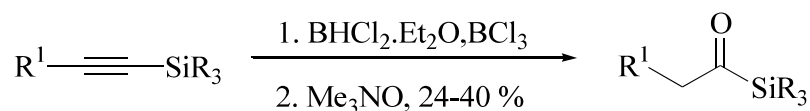
Scheme 46

Methyl Grignard reagents catalysed by nickel add regioselectively to 1-trimethylsilylalkynes (**Scheme 47**).¹⁶³



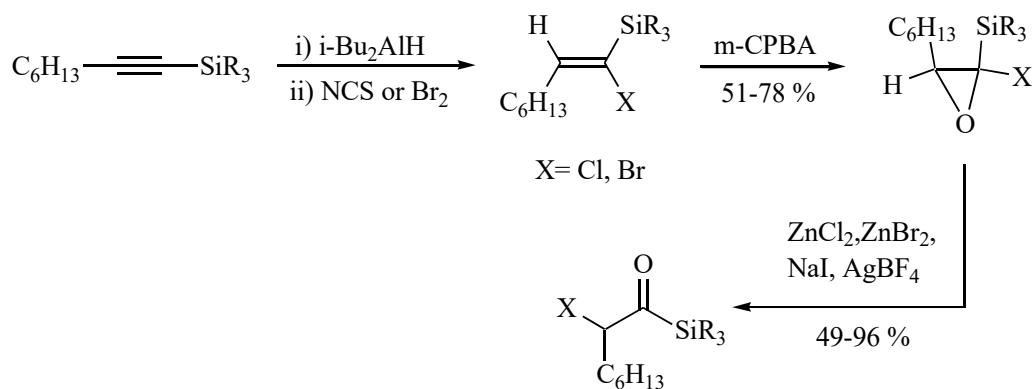
Scheme 47

Hassner and Soderquist reported the first method for the synthesis of acylsilanes by the hydroboration-oxidation of silylacetylenes further hydrolysis form acylsilanes (**Scheme 48**).¹⁶⁴



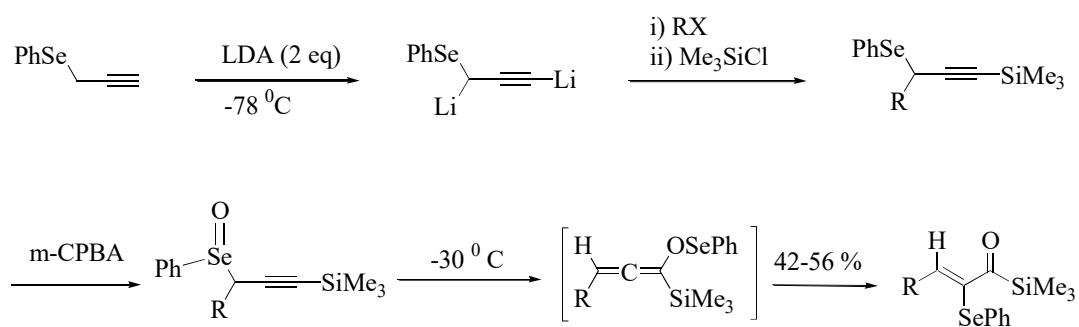
Scheme 48

Oshima and Utimoto found that α -haloacylsilanes could be formed from the reaction of 2-halo-2-trimethylsilyloxiranes with metal salts such as ZnCl_2 , ZnBr_2 , NaI , and AgBF_4 (**Scheme 49**).¹⁶⁵



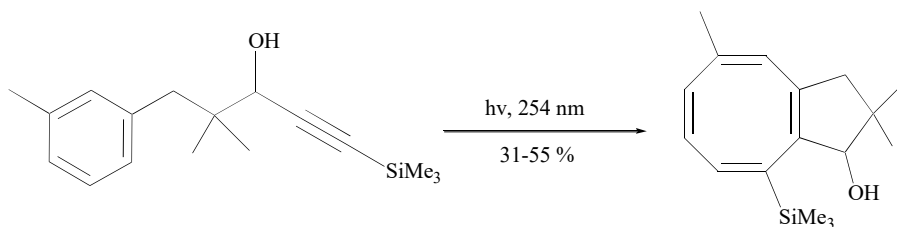
Scheme 49

Reich reported that the rearrangement of selenoxide derived from the phenyl propargyl selenide to the preparation of seleno-substituted α,β -unsaturated acylsilane (**Scheme 50**).¹⁶⁶



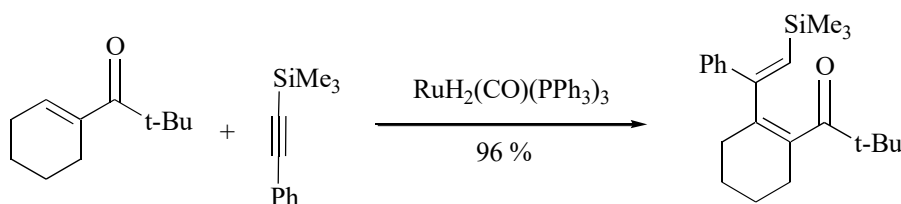
Scheme 50

Intramolecular [2+2] photocycloaddition across the *ipso*- and *ortho*- positions of the pendant phenyl chromophore produce optically active cyclooctatetraenes. The photocycloaddition is highly regioselective (Scheme 51).¹⁶⁷



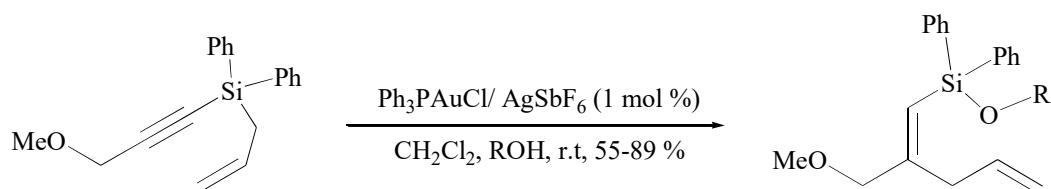
Scheme 51

Murai *et al.* reported that silyl-substituted dienones were accessed by ruthenium catalyzed C-H activation followed by hydorruthenation of a silylalkyne (Scheme 52).¹⁶⁸



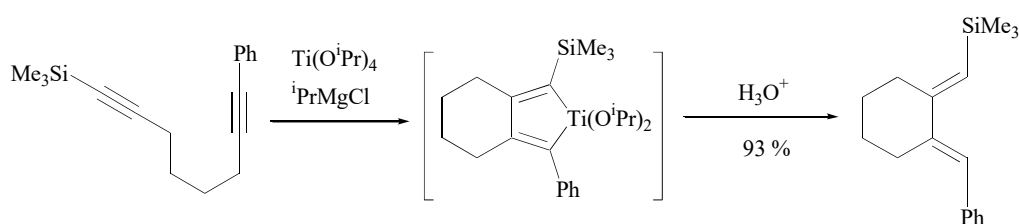
Scheme 52

Intramolecular allylation of silyl alkynes catalyzed by gold generate alkoxy vinyl silanes (Scheme 53).¹⁶⁹



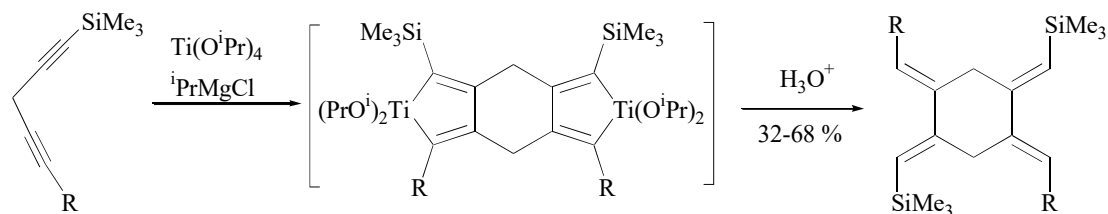
Scheme 53

1-Silyl-1,3-butadienes and 1,4-bis(silyl)-1,3-butadienes can be easily prepared by hydrolysis of the corresponding titanacyclopentadienes or zirconacyclopentadienes. Sato et al. reported a titanium mediated intramolecular alkyne coupling to generate silyl-1,3-dienes (Scheme 54).¹⁷⁰



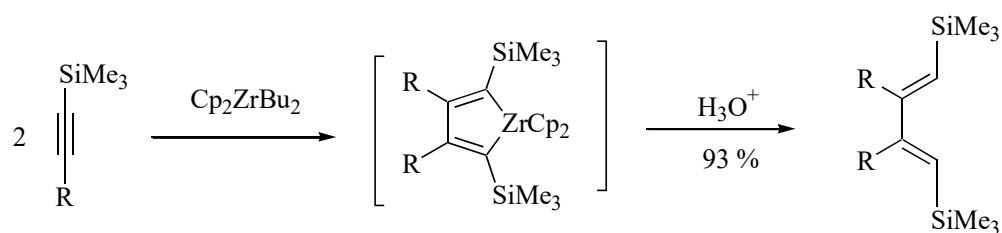
Scheme 54

Later they reported a dimerization of diynes to yield tetraalkylidene cyclohexanes (Scheme 55).¹⁷¹



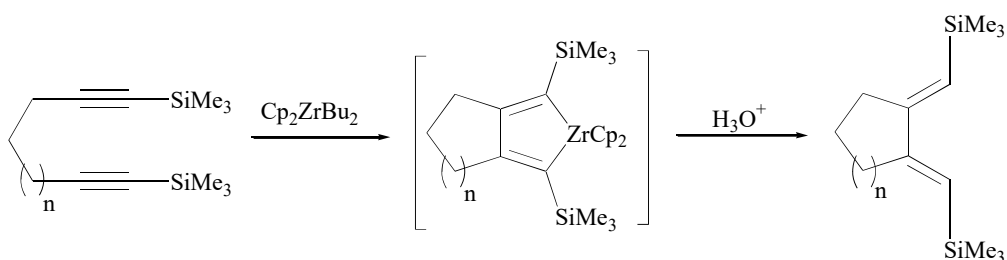
Scheme 55

Negishi, Takahashi and co-workers have developed pair selective coupling of alkynes mediated by zirconium (Scheme 56).¹⁷² Cp₂ZrBu₂ (Negishi reagent), which is generated by Cp₂ZrCl₂ and n-BuLi in situ, is treated with silyl-substituted alkynes to give bis(silyl)-zirconacyclopentadienes. Hydrolysis process gives 1,4-bis-(silyl)-1,3-dienes in high stereoselectivity.



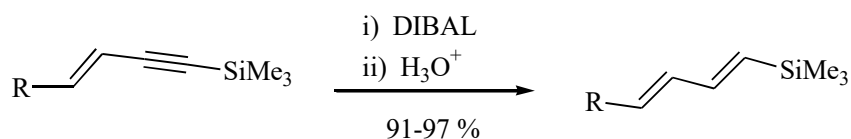
Scheme 56

Exocyclic 1,4-bis(silyl)-1,3-butadienes are synthesized by a similar method (Scheme 57).¹⁷³



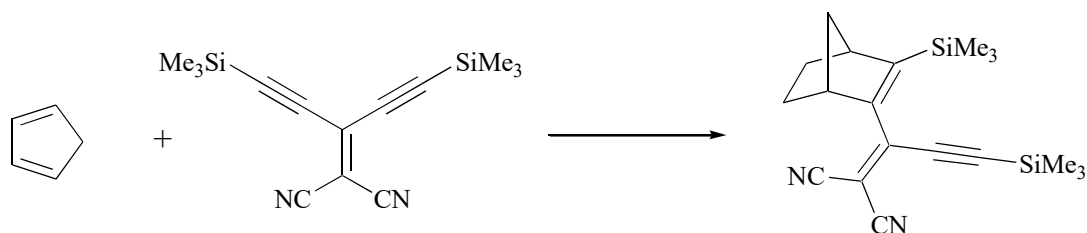
Scheme 57

Hydroalumination of (E)-1-trimethylsilyl-3-buten-1-yne with diisobutylaluminum hydride followed by base hydrolysis affords (1E, 3Z)-1-trimethylsilyl-1,3-dienes (Scheme 58).¹⁷⁴



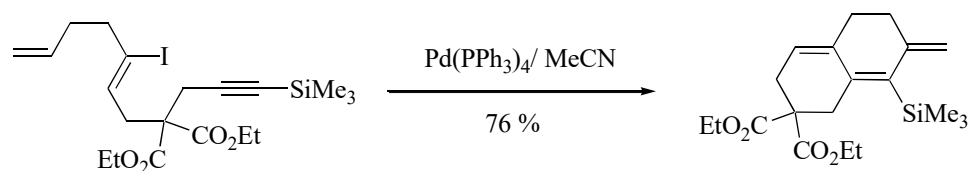
Scheme 58

Diels-Alder reaction of dialkyne with cyclopentadiene yields a diene having a silyl substituent at the terminal carbon (Scheme 59).¹⁷⁵



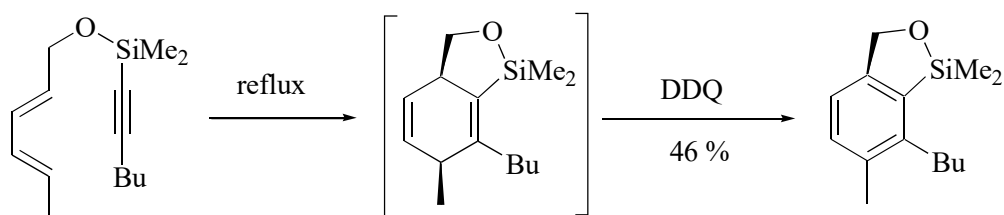
Scheme 59

Tandem cyclization reactions of a 1-trimethylsilyl-substituted vinyl iodide with enynes at appropriate positions gives an interesting route for the synthesis of silyl substituted dienes in a polycyclic system (**Scheme 60**).¹⁷⁶



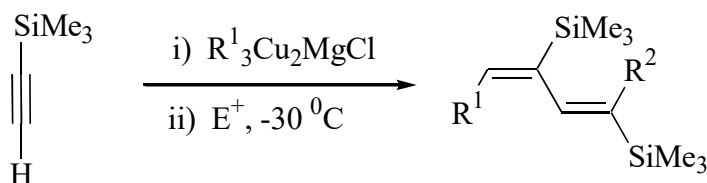
Scheme 60

Intramolecular hetero Diels-Alder reactions of an alkynyl silyl ether of sorbyl alcohol upon heating in toluene led to an adduct that was immediately oxidized with DDQ to the aromatic compound (**Scheme 61**).¹⁷⁷



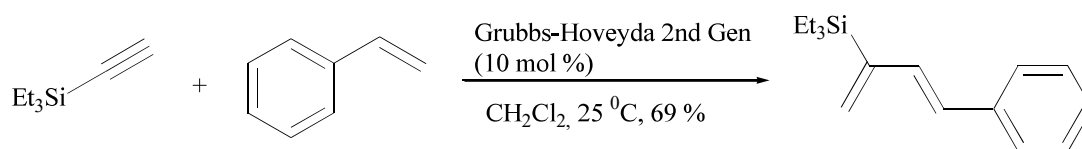
Scheme 61

Copper-magnesium reagents react with trimethylacetylene followed by an electrophile to give 1,3-bis(silyl)-1,3-butadiene (**Scheme 62**).¹⁷⁸



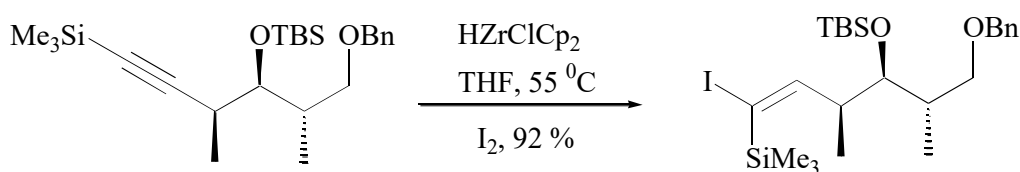
Scheme 62

The preparation of highly substituted silicon dienes by using ene-yne cross-metathesis involving reactions between trimethylsilylacetylene and styrene with rubbs-Hoveyda second generation catalyst gave the desired product (**Scheme 63**).¹⁷⁹



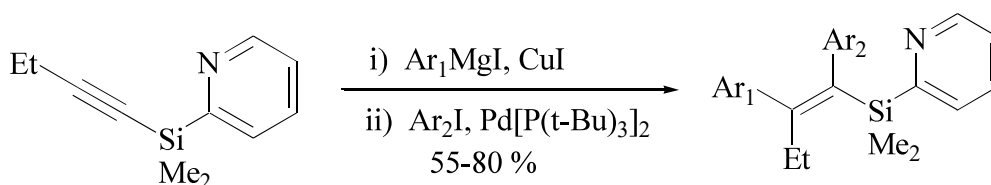
Scheme 63

Hydrozirconations with Schwartz reagent followed by addition of iodine results in the stereo defined formation of halosilylalkenes which have been applied to the total synthesis of complex polyketide natural products (Scheme 64).¹⁸⁰



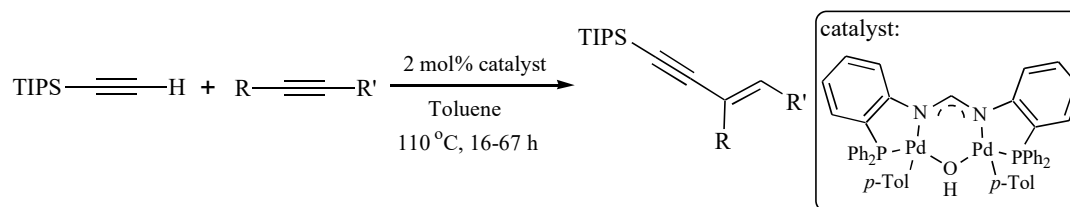
Scheme 64

Tetrasubstituted vinylsilanes can be accessed from carbocupration and Kumada coupling of 2-pyridylsilylalkynes through the regioselective carbometallation of 2-pyridylsilylalkynes with aryl Grignard reagents in the presence of catalytic copper (I) iodide (Scheme 65).¹⁸¹



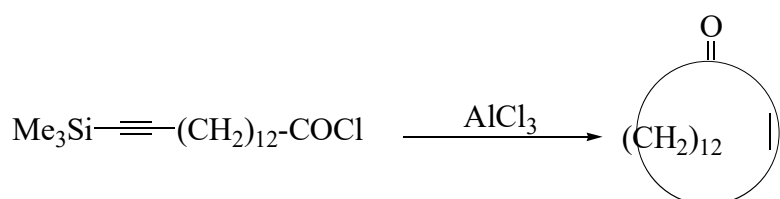
Scheme 65

Dinuclear and mononuclear palladium complexes with N,N' -bis[2-(diphenylphosphino)phenyl]amidinate (DPFAM) as a ligand catalyzed the cross-addition of triisopropylsilylacetylene (TIPSA) to unactivated internal alkynes, giving enynes selectively is reported (Scheme 66).¹⁸²



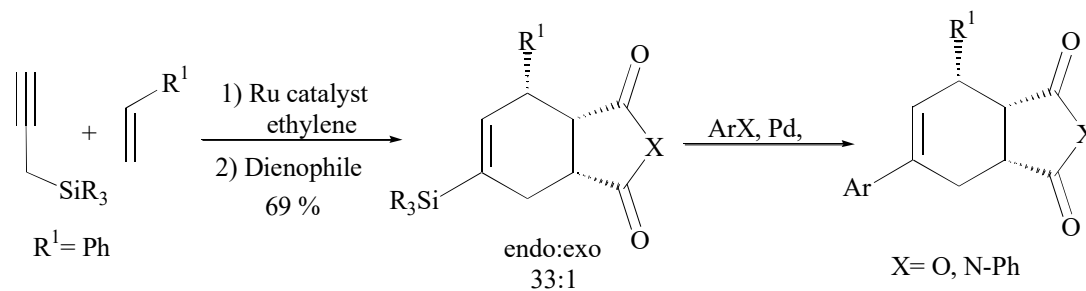
Scheme 66

Alkynylsilanes have been reported to undergo electrophilic substitution at the site of the silicon an intramolecular electrophilic substitution have been used for the synthesis of a macrocyclic ketone (Scheme 67).^{183, 184}



Scheme 67

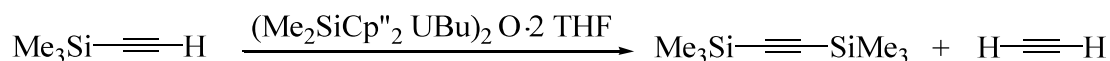
Alkynyl silanes have been successfully employed in ene-yne cross metathesis. The resulting dienes have found application in stereoselective Diels-Alder reactions and the Diels-Alder adducts further used in ene-yne cross-coupling reactions (Scheme 68).¹⁸⁵



Scheme 68

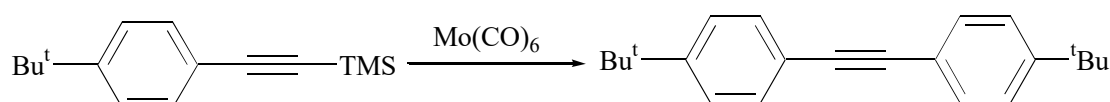
Eisen showed that trimethylsilylacetylene, upon treatment with an *ansa*-dimethylsilyl and oxo-bridged uranium metallocene (Me₂SiCp''₂UBu)₂O•2THF, underwent self metathesis to form bis(trimethylsilylacetylene) and acetylene. This is

an unique example of structure-reactivity domain in an organoactinide complex (Scheme 69).¹⁸⁶



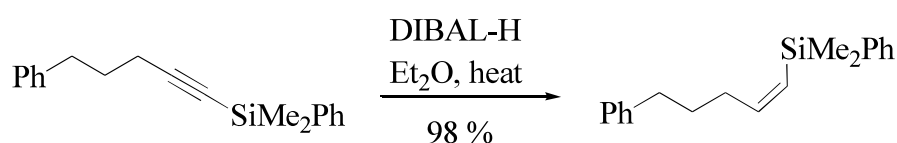
Scheme 69

Silyl alkynes have also been used in metathesis reactions to obtain substituted diaryl alkynes using molybdenum hexacarbonyl complex (Scheme 70).¹⁸⁷



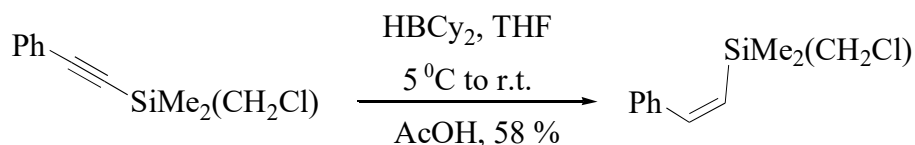
Scheme 70

The formal *syn*-addition of hydrogen across silylalkynes with aluminium and boron hydrides is reported. For example, diisobutylaluminium hydride adds efficiently across aliphatic silylalkynes (Scheme 71).¹⁸⁸



Scheme 71

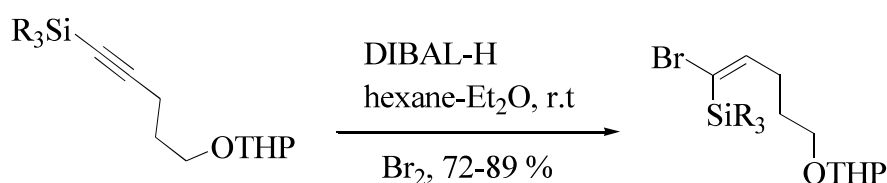
Dicyclohexylborane reduction of alkynylsilanes by Soderquist is employed less frequently but tolerates more exotic substituents on silicon (Scheme 72).¹⁸⁹



Scheme 72

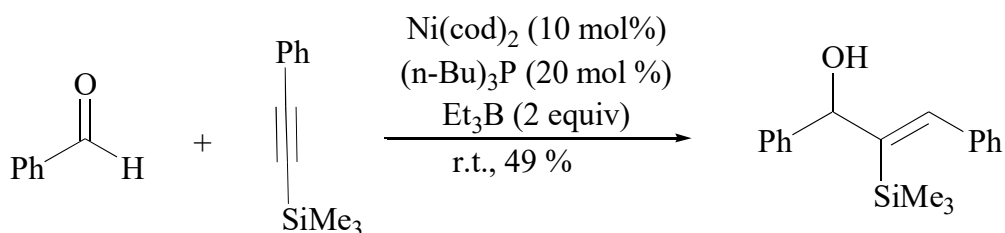
The *cis*-addition of metal hydride species over triple bonds is responsible for the formation of *cis*-vinylsilane from silylalkyne. For example, hydroalumination of

silylalkynes with diisobutylaluminium hydride followed by addition of iodine or bromine results in the stereo defined formation of halosilylalkenes (**Scheme 73**).¹⁹⁰



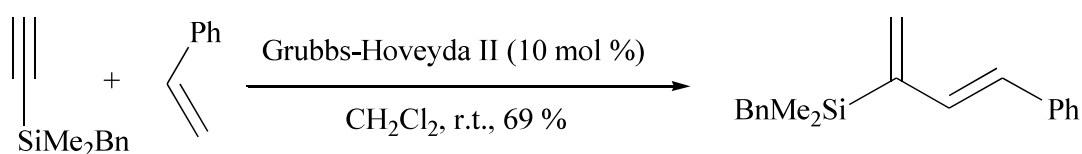
Scheme 73

The uses of nickel hydride species which are formed *in situ* from the reaction of bis(1,5-cyclooctadiene)nickel (0) [Ni(cod)₂] with triethylborane or triisopropylsilane and these react with trimethylsilylacetylenes and aldehydes to give products (**Scheme 74**).¹⁹¹

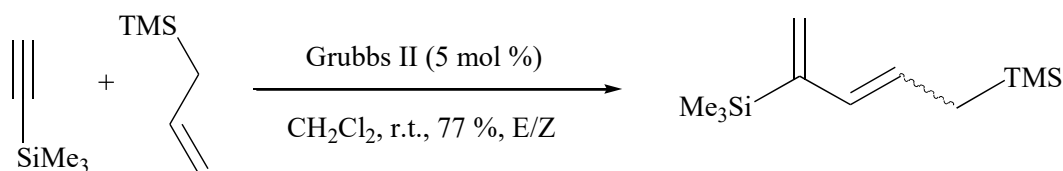


Scheme 74

Silylalkynes react with ruthenium-catalyst to form ruthenium-catalysed enyne cross-metathesis with terminal olefins to provide conjugated diene products. The catalyst first reacts with the terminal alkyne, followed by the alkene, leading to 2-silylbuta-1,3-diene products. (**Scheme 75, 76**).^{192,193}

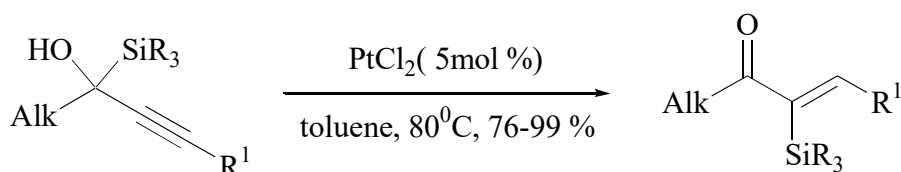


Scheme 75



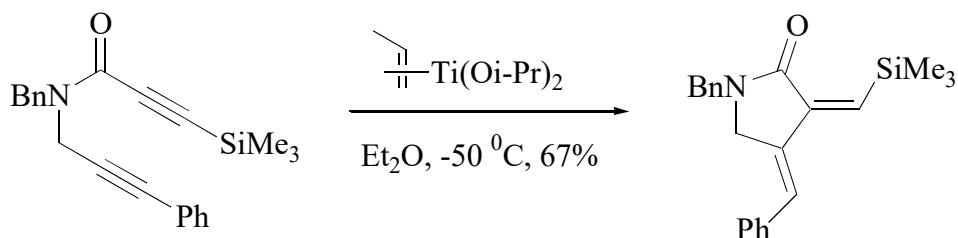
Scheme 76

Propargylic α -hydroxysilanes with platinum (II) undergo a mechanistically related rearrangement promoted by π -Lewis acids to giving (*Z*)-enone products (Scheme 77).¹⁹⁴



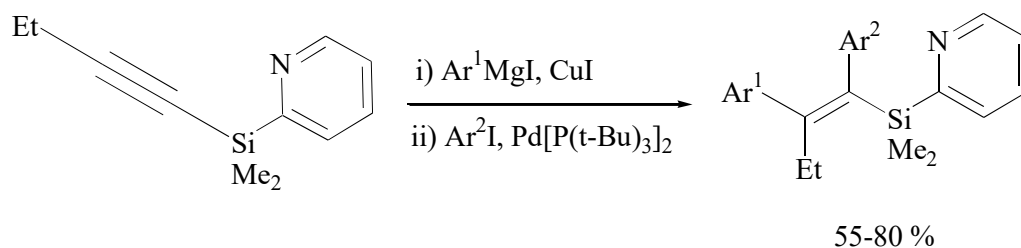
Scheme 77

Tethering of the coupling partners provides 1,2,2-vinylsilane products similar to those derived from the silyl carbocyclisation of 1,6-diynes using an acidic quench (Scheme 78).¹⁹⁵



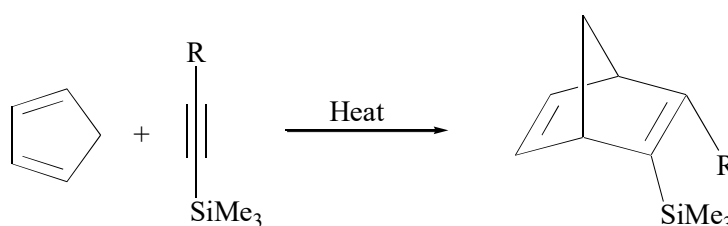
Scheme 78

Tetra substituted vinylsilanes can also be accessed through the regioselective carbometallation of 2-pyridylsilylalkynes with aryl Grignard reagents in the presence of catalytic copper (I) iodide followed by carbocupration and Kumada coupling of 2-pyridylsilylalkynes (Scheme 79).¹⁹⁶



Scheme 79

Using the Diels-Alder reaction: the synthesis of trimethylsilyl-substituted norbornadienes from trimethylsilylalkynes with cyclopentadiene is reported (Scheme 80).¹⁹⁷

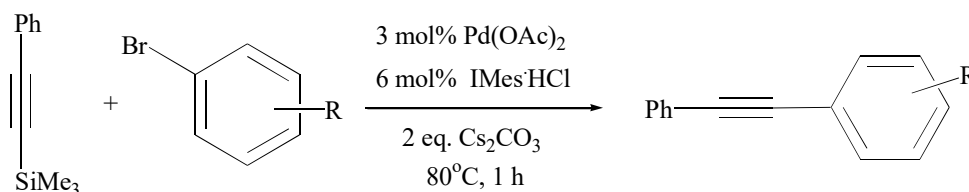


Scheme 80

1.3.3.1 Sila Sonogashira reaction

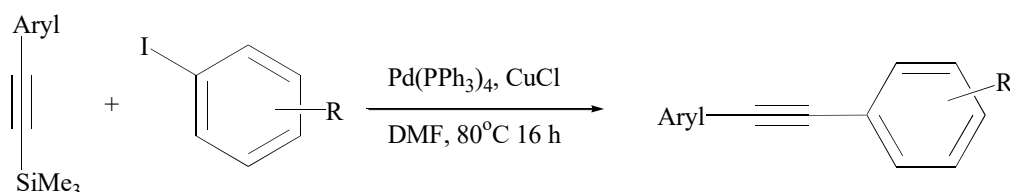
A direct cross-coupling of alkynylsilanes with aryl halides/triflates catalysed by palladium complex is called Sila-Sonogashira reaction.

Chuluo Yang and Steven P. Nolan have used a palladium/imidazolium chloride system to mediate the cross-coupling reaction of aryl halides with alkynylsilanes. The combination of 3 mol % Pd(OAc)₂ and 6 mol % IMes·HCl in the presence of Cs₂CO₃ as base proves to be a highly efficient system in assisting coupling of aryl bromides with alkynylsilanes (Scheme 81)¹⁹⁸.

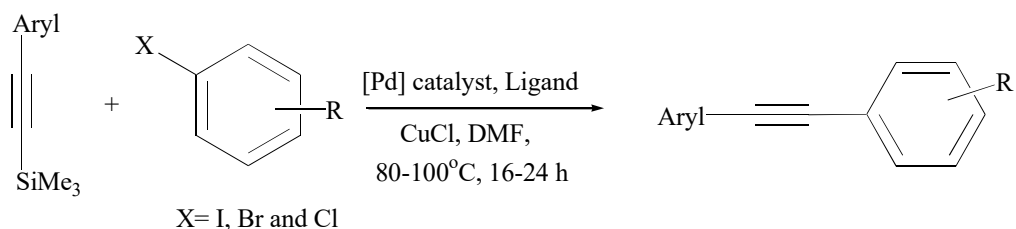


Scheme 81

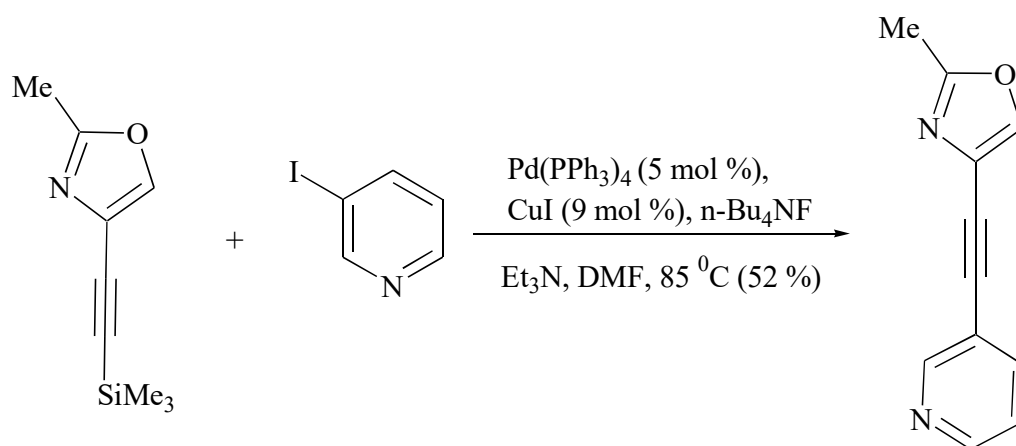
Nishihara, Y. *et al.*, have reported the palladium-catalyzed cross-coupling reactions of aryl iodides with alkynylsilanes in the presence of a substoichiometric amount (50 mol %) of copper(I) chloride as an activator in DMF under strictly non-basic reaction conditions afford the corresponding unsymmetrical diarylethyne in moderate to excellent yields (**Scheme 82**)¹⁹⁹.

**Scheme 82**

Nishihara, Y. *et al.*, have also reported the cross-coupling reactions of alkynylsilanes with aryl iodides/bromides/chlorides in the presence of various palladium complexes and ligands. They also mentioned that these reactions proceed through a direct activation of a carbon-silicon bond in alkynylsilanes by CuCl to generate the corresponding alkynylcopper species via transmetalation from silicon to copper. Mechanistic investigations on the reaction of alkynylsilanes with aryl bromides confirmed that the trimethylsilyl bromide generated in situ retarded both transmetalation steps between CuCl and alkynylsilane, and between palladium(II) species formed by oxidative addition and alkynylcopper species (**Scheme 83**)²⁰⁰.

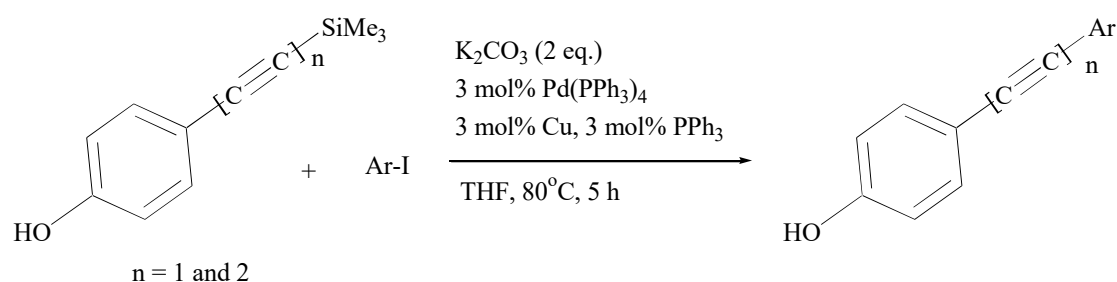
**Scheme 83**

Sila-Sonogashira reaction of oxazole derived trimethylsilylethyne with 3-iodopyridine is reported. It involves, *in situ* TBAF-promoted desilylation of oxazole derivative and a subsequent palladium-copper-catalyzed cross coupling reaction with 3-iodopyridine gave alkyne. The product formed is used as an antagonist in the treatment of drug abuse. (Scheme 84).²⁰¹



Scheme 84

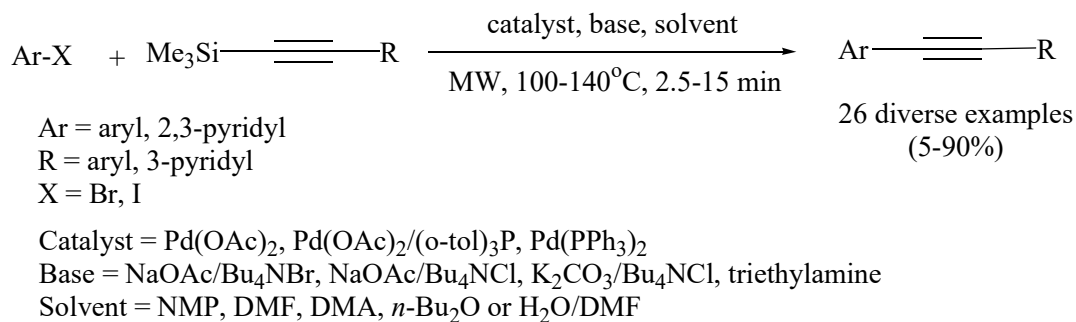
Masayuki S. *et al.*, have successfully synthesized phenolic-hydroxy-substituted diarylethyne and 1,4-diarylbutadiynes from trimethylsilylalkynes and aryl iodides via silyl-group-migration-induced deprotection of alkynes and the usual Sonogashira coupling (Scheme 85)²⁰².



Scheme 85

The palladium catalyzed synthesis of diaryl acetylenes has been demonstrated by Ulrich S. Sorenson and Esteban Pombo-Villar from Novartis Pharma AG. A direct coupling of activated aryl- and heteroaryl bromides and iodides with 1-aryl-2-

trimethylsilylacetylenes has been developed for the synthesis of diarylacetylenes, avoiding the use of copper (I) iodide as a co-catalyst. Microwave dielectric heating has shown improvement in reaction yields over the conventional oil bath heating (Scheme 86)²⁰³.

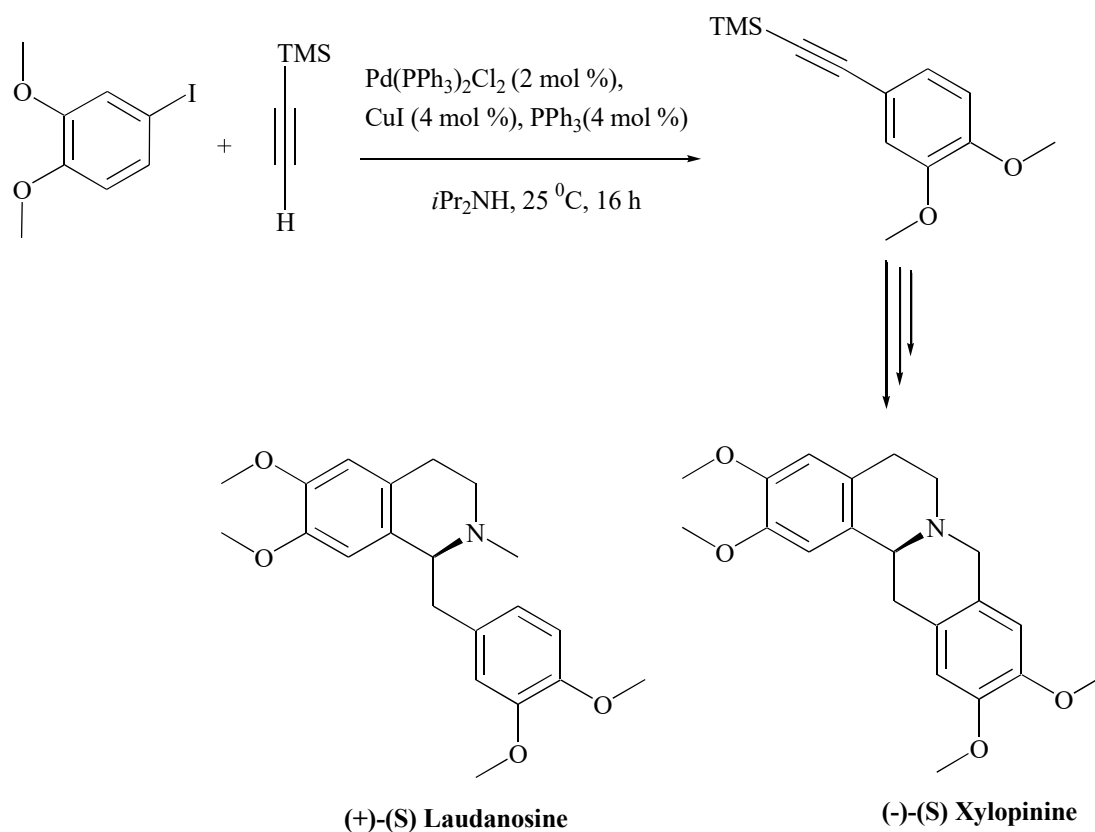


Scheme 86

1.3.4 Some important applications of alkynylsilanes:

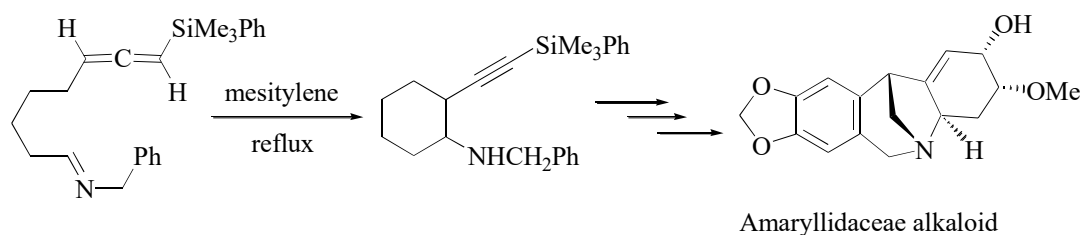
Many metabolites found in nature contain alkyne or enyne moieties, and therefore, the Sonogashira reaction has found frequent utility in their syntheses.²⁰⁴ Several of the most recent and promising applications of this coupling methodology toward the total synthesis of natural products exclusively employed the typical copper-cocatalyzed reaction.

The recent examples of the use of aryl iodides for the preparation of intermediates under typical Sonogashira conditions, which, after cyclization, yield natural products such as the benzyloquinoline alkaloids (+)-(S)-laudanosine and (-)-(S)-xylopinine (Scheme 87)²⁰⁵.



Scheme 87

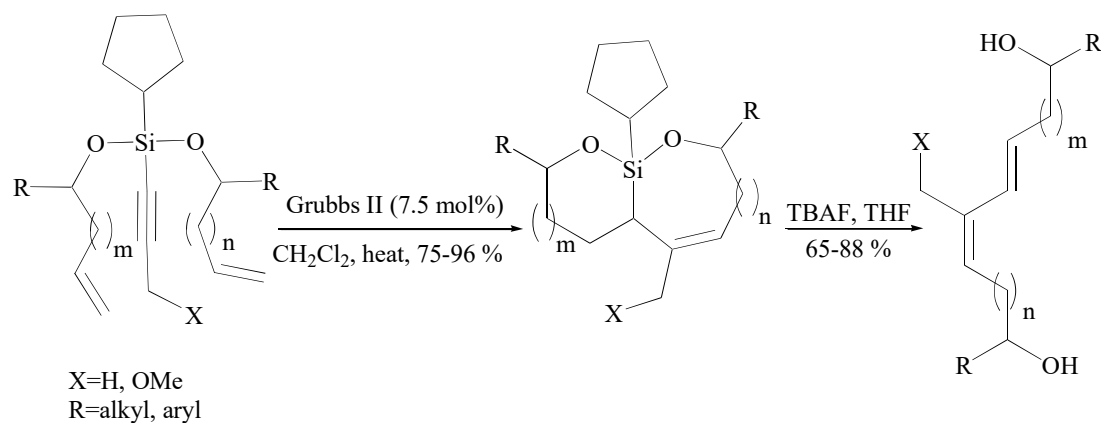
Weinreb *et al.* developed the methodology of the intramolecular allenylsilane imino-ene reaction to prepare silylacetylenes. The bulky silyl group was used in this reaction to give a single stereoisomer. Weinreb applied this methodology in the total synthesis of *amaryllidaceae* alkaloids (Scheme 88).²⁰⁶



Scheme 88

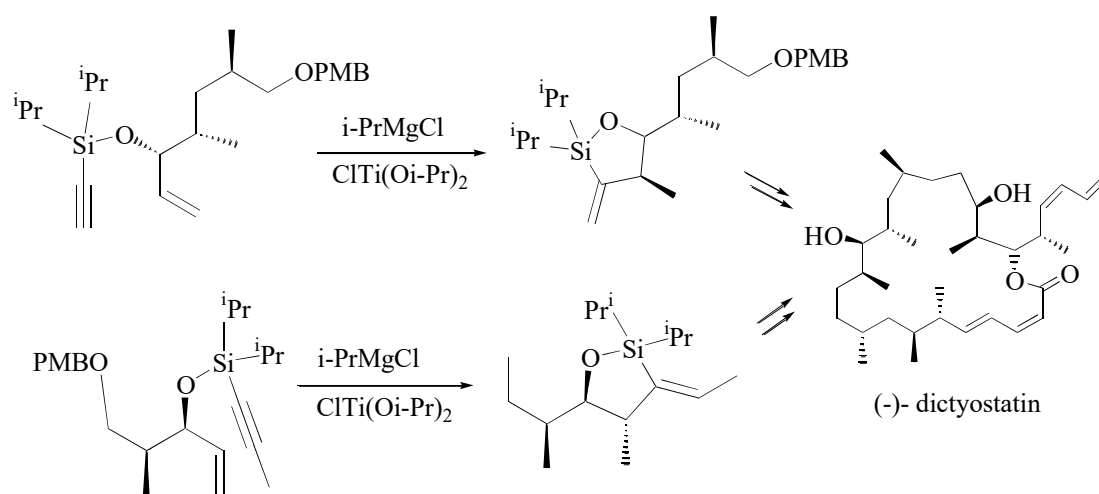
Lee and co-workers have reported the enyne metathesis to silylalkynes appended with two alkenes. These dienynes participate smoothly in the tandem ene-

yne-ene metathesis to afford 6,7- and 7,8-bicyclic siloxanes (**Scheme 89**).²⁰⁷ The *Z,E*-diene carbon frame work that is obtained on desilylation of these siloxacyclic products features in many natural products such as Tartrolon B.²⁰⁸ and (-)-Cochleamycin A.¹⁵⁰



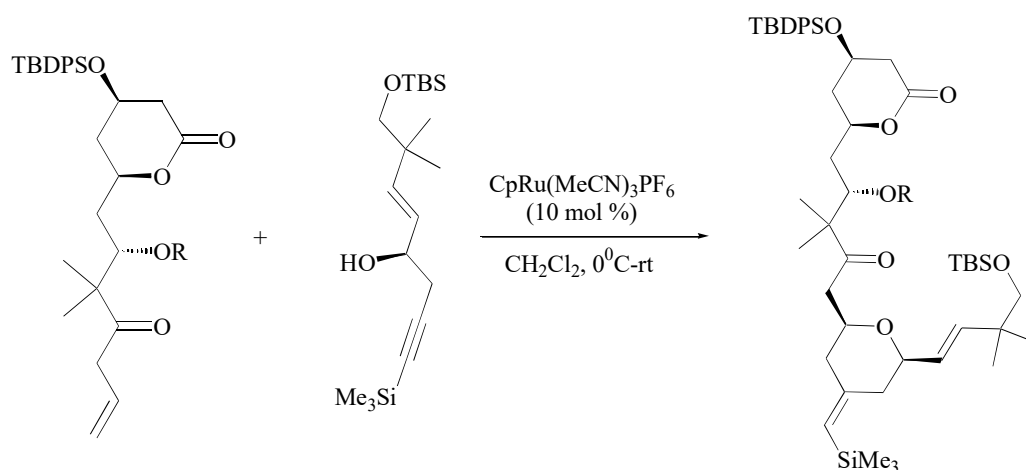
Scheme 89

An important application of silyl acetylenes is the development of η^2 -propeneTi(O^{*i*}Pr)₂ effected cyclization of silyloxyenyynes. The reaction proceeded with excellent diastereoselectivity to provide cyclic siloxanes with an anti-relationship between the oxygen and methyl bearing carbon. This technology has been used for the preparation of an effective anti-cancer agent as dictyostatin (**Scheme 90**).²⁰⁹



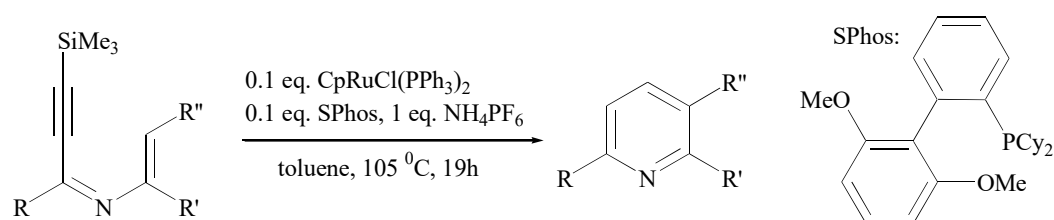
Scheme 90

The ruthenium catalyst illustrated by the coupling of homopropargylic alcohols with β,γ -unsaturated enones, resulting in hydroxyenones that cyclise *in-situ* by an intramolecular conjugate addition. Ring closure occurs with moderate to good diastereoselectivity in favour of the 2,6-*cis*-tetrahydropyran product (**Scheme 91**).²¹⁰



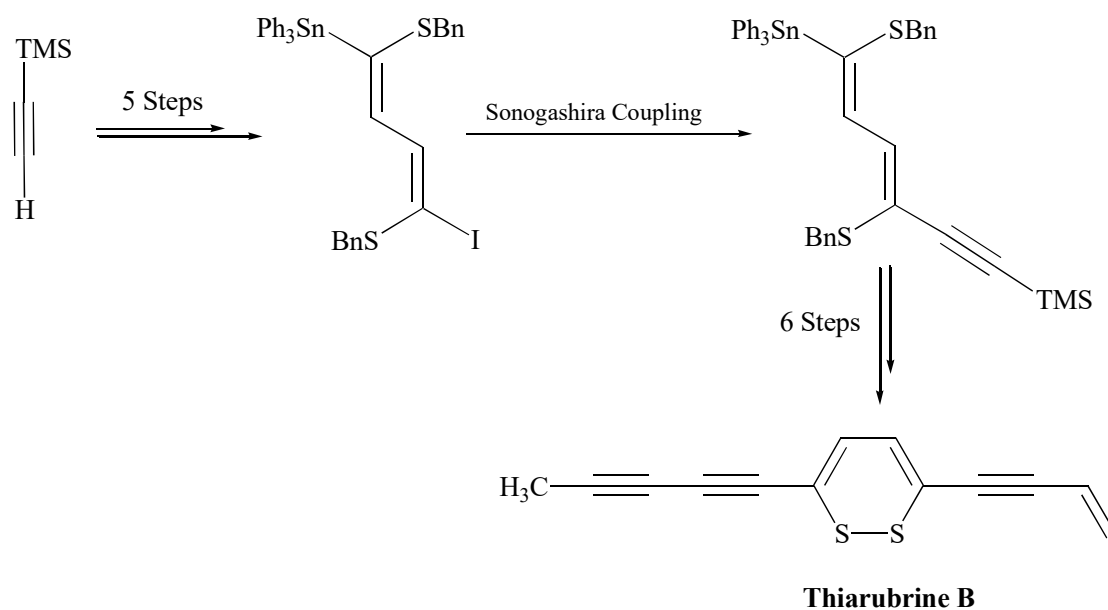
Scheme 91

The direct conversion of amides, including sensitive *N*-vinyl amides, to the corresponding trimethylsilyl alkynyl imines followed by a ruthenium-catalyzed protodesilylation and cycloisomerization gives various substituted pyridines and quinolines (**Scheme 92**).²¹¹



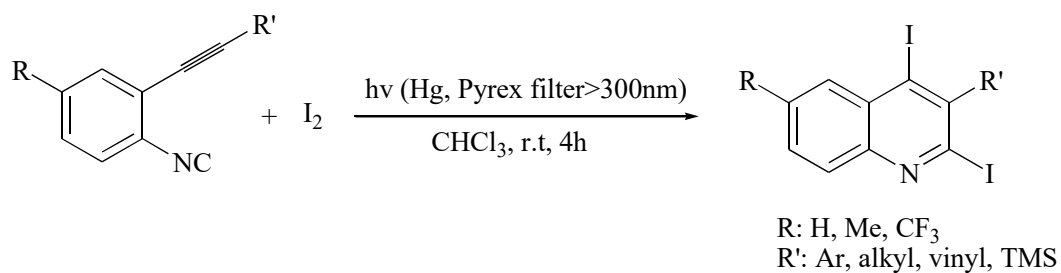
Scheme 92

In the year 1994 Eric Block reported the total synthesis of **Thiarubrine B** starting from trimethylsilyl acetylene. The synthesis involves the use of Sonogashira reaction in three different steps out of 12 linear steps (**Scheme 93**).²¹²



Scheme 93

Upon photoirradiation of *o*-alkynylaryl isocyanides in the presence of iodine, an intramolecular cyclization affords the corresponding 2,4-diiodoquinolines in good yields. 2,4-Diiodoquinolines can be employed in regioselective transition metal-catalyzed cross-coupling reactions (Scheme 94).²¹³



Scheme 94

1.4 A brief review of some silylated Triazoles and Coumarins :

1.4.1 Click Chemistry:

The concept of click chemistry is experiencing growing popularity. A large amount of literature including excellent review articles is available on this subject. In 2003, Kolb and Sharpless et al.²¹⁴ presented a review that outlined the special nature of triazole chemistry with an emphasis on the potential use of the reaction in biochemical studies that range from lead discovery and optimization to tagging of biological systems, such as proteins, nucleotides, and whole organisms. Bock et al. presented a review with an in-depth analysis of the reaction in 2006, including all essential mechanistic and methodological aspects at the time.²¹⁵ Binder et al.²¹⁶ and Lutz²¹⁷ described the polymer and materials science applications. Gil et al.,²¹⁸ Li et al.,²¹⁹ Moses and Moorhouse²²⁰ and Wu and Fokin²²¹ have reviewed the general synthetic utility of click chemistry across the fields.

Some reviews mention CuAAC as essential in particular important fields, for example, in dendrimer and polymer grafting,²²²⁻²²⁴ as well as in synthesis^{225, 226} and in chemical ligation.^{227, 228} Reviews also describe applications in synthesis of peptidomimetics,^{229, 230} in bioconjugations²³¹⁻²³³ and surface chemistry.²³⁴ It has been compared to the Staudinger ligation²²⁸ and used in profiling of proteases²³⁵ and in combinatorial drug discovery.^{236, 237} A review on a metal-chelating system has also been published.²³⁸ An excellent recent review by Meldal and Tornøe describes CuAAC in great detail.²³⁹ The design of the recent development of fluorogenic CuAAC reactions as well as their applications has been highlighted by Wang et al.²⁴⁰

1.4.2 Triazoles

Triazole refers to either one of a pair of isomeric chemical compounds with the molecular formula $C_2H_3N_3$, and has a five membered ring containing two carbon and three nitrogen atoms.

Triazoles have two isomeric forms, i.e., 1,2,3-triazole (**Fig. 13**) and 1,2,4-triazole (**Fig. 14**).

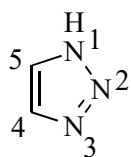


Figure 13

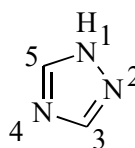


Figure 14

1,2,3-Triazoles are basic aromatic nitrogen heterocyclic compounds, which are surprisingly stable compared to other organic compounds with three adjacent nitrogen atoms. However, flash vacuum pyrolysis at 500 °C leads to loss of molecular nitrogen (N_2) to produce aziridine. Certain triazoles are relatively easy to cleave by ring-chain tautomerism.

An extensively studied reaction for the synthesis of 1,2,3-triazoles is the Huisgen 1,3-dipolar cycloaddition reaction of azides with alkynes.²⁴¹ The limitations of the original reactions, due to the high reaction temperature and to the low regioselectivity, have been overcome by the copper(I)-catalyzed 1,3-dipolar cycloaddition (CuAAC) reaction, which is the most prominent example of ‘click chemistry’, developed by the groups of Sharpless²⁴² and Meldal.²⁴³ The cycloaddition reactions of terminal alkynes with azides catalyzed by Cu (I) can be conducted at room temperature and are highly regioselective, leading exclusively to

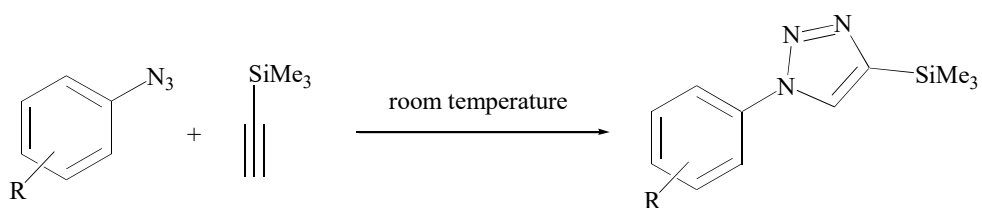
4-substituted-1,2,3-triazoles. The synthesis of 4-substituted-1,2,3-triazoles success under different reaction conditions.^{244, 245}

Nitrogen heterocycles, such as 1,2,3-triazoles, have found a wide range of important applications in the agrochemical, pharmaceutical, polymer, materials field.²⁴⁶ In addition, the 1,2,3-triazoles have shown biological properties such as antibacterial,²⁴⁷ antiallergic,²⁴⁸ and anti-HIV activities.²⁴⁹

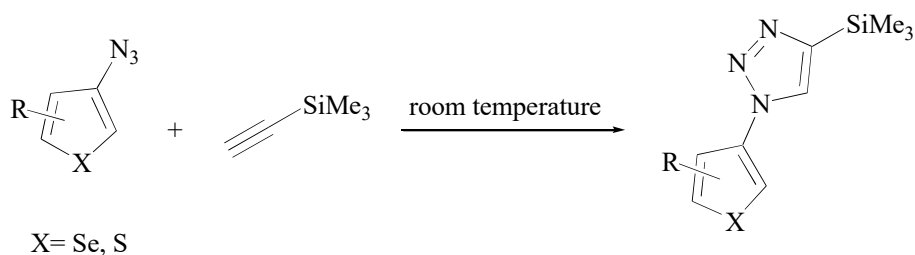
Our interest in this topic is focussed on the synthesis of trimethylsilyl containing triazole scaffolds. The following methods are reported in literature containing silylated 1,2,3-triazoles.

The reaction of some aryl azides and the 2- and 3-azidobenzo[*b*]thiophenes with (trimethylsilyl)acetylene to give 1-aryl (or 1-heteroaryl)-4-trimethylsilyl-1,2,3-triazoles via 1,3-dipolar cycloaddition is reported.²⁵⁰

The regiochemistry of 1,2,3-triazoles arising from 1,3- dipolar cycloaddition of a number of aryl and heteroaryl azides with dipolarophile (trimethylsilyl)acetylene proceed smoothly at room temperature to afford the corresponding C-4 silylated triazoles (Scheme 95, 96).²⁵¹

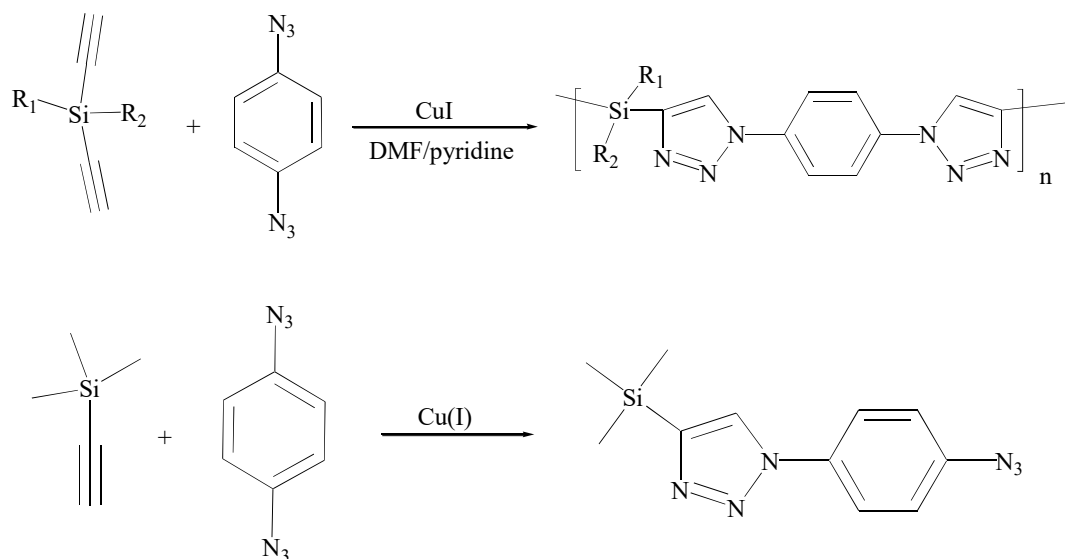


Scheme 95



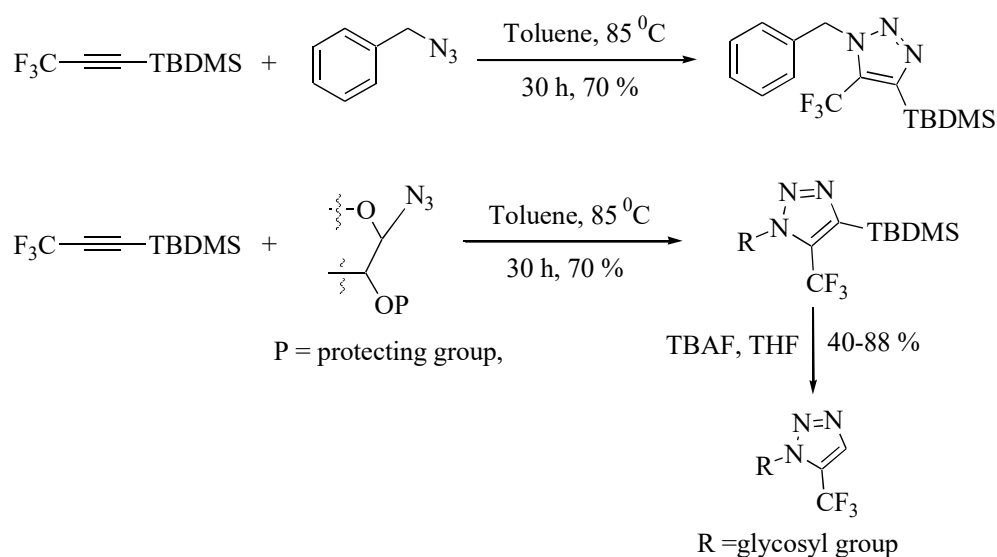
Scheme 96

Poly[silylene-(1,2,3-triazol-4-yl)-1,4-phenylene]s and 1-(4-azidophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole prepared from diethynylsilanes, trimethylsilylacetylene and diazidobenzene via Copper-Catalyzed Azide-Alkyne Cycloaddition (CuAAC) step-growth polymerization (**Scheme 97**).²⁵²



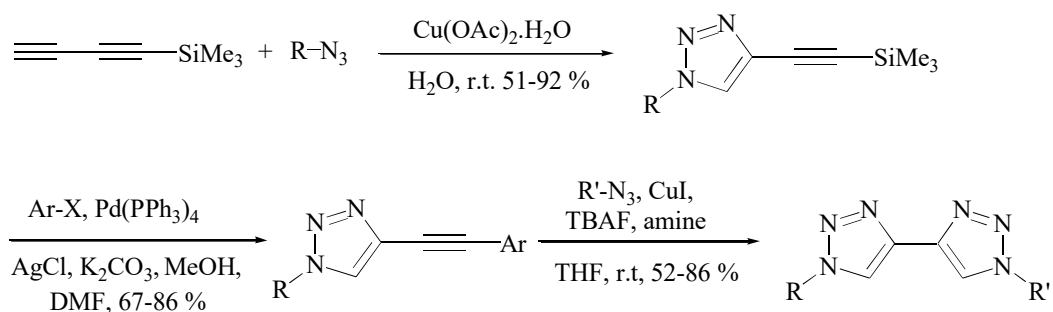
Scheme 97

The preparation of silylated 1,2,3-triazole nucleoside analogues from glycosyl azides with 3,3,3-trifluoro-1-tert-butyl dimethylsilylpropyne is reported. (**Scheme 98**).²⁵³



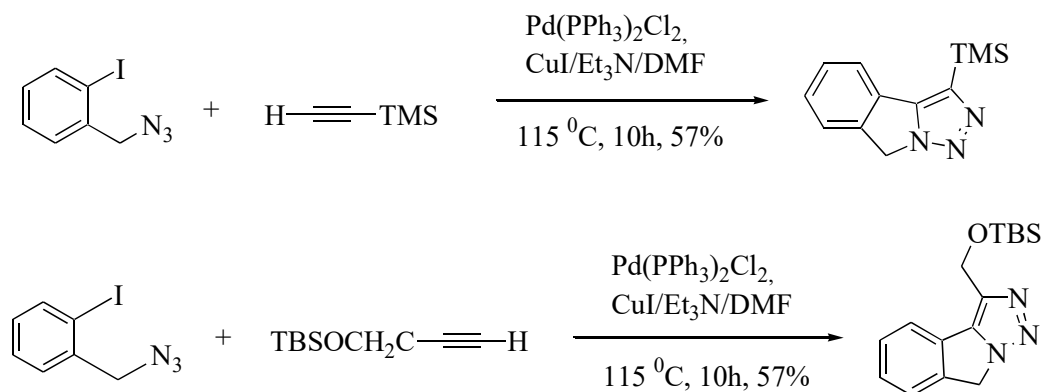
Scheme 98

The synthesis of 4-trimethylsilylalkynyl-1,2,3-triazoles and 4-arylalkynyl-1,2,3-triazoles from 1-trimethylsilyl-1,3-butadiyne with several organic azides via 1,3-cycloaddition reaction is reported. Which were transformed into 4,4'-bis-1,2,3-triazole derivatives (**Scheme 99**).²⁵⁴



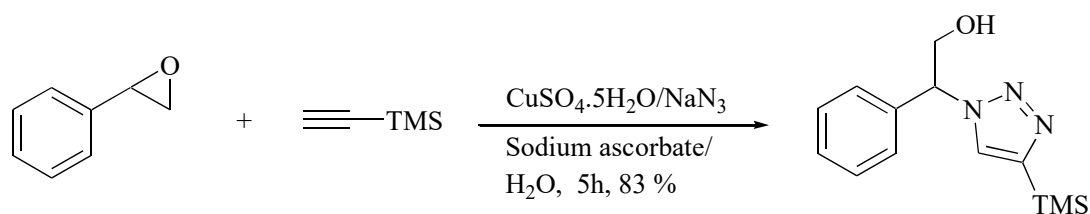
Scheme 99

The synthesis of isoindoline fused with triazoles from ortho-iodobenzyl azide and substituted silylacetylenes in presence of $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ and $\text{CuI}/\text{Et}_3\text{N}$ undergoing hetero annulations is described (**Scheme 100**).²⁵⁵



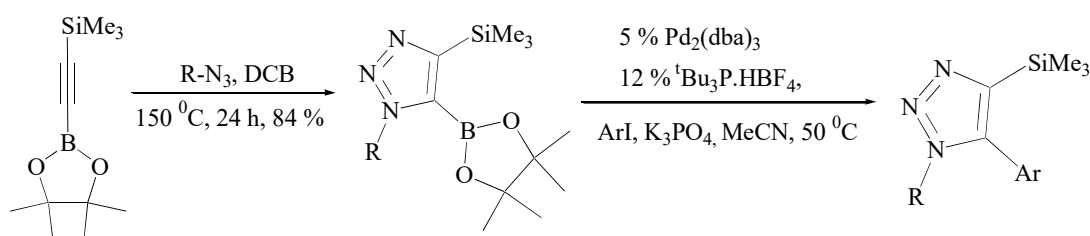
Scheme 100

A one-pot synthesis of β -hydroxy triazoles from epoxides and sodium azide under neutral conditions is reported (**Scheme 101**).²⁵⁶



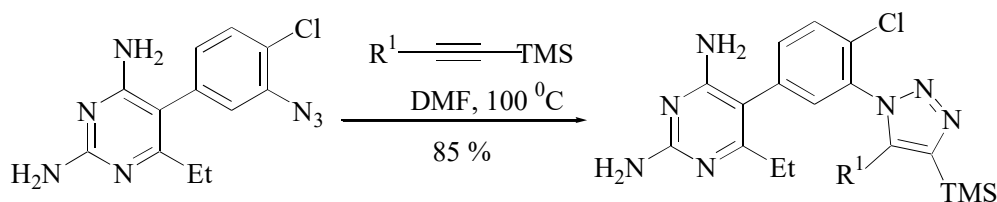
Scheme 101

The synthesis of trimethylsilyl-substituted triazole boronic esters from trimethylsilylalkynylboronates with azides is known. These subsequently undergo cross coupling with aryl iodides to provide the trimethylsilyl-substituted triazoles (Scheme 102).²⁵⁷



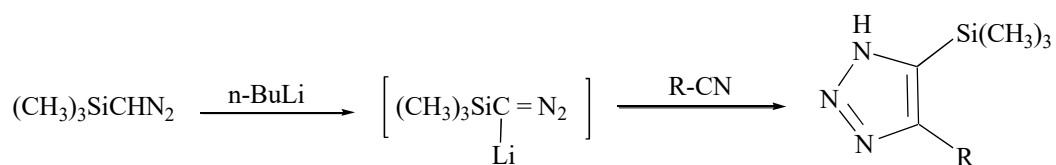
Scheme 102

Reactions between substituted aryl azide and the (trimethylsilyl)acetylene is regiospecific with the 4-(trimethylsilyl)triazole being formed (Scheme 103).²⁵⁸



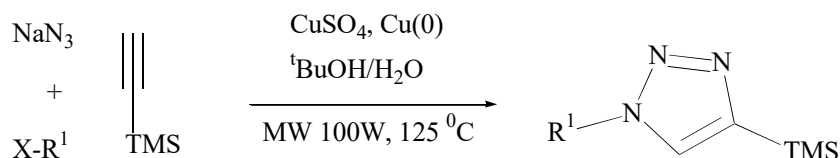
Scheme 103

The synthesis of 4-substituted 5-trimethylsilyl-1,2,3-triazoles from *n*-butyllithium with various nitriles by the 1,3-dipolar cycloaddition is reported (Scheme 104).²⁵⁹



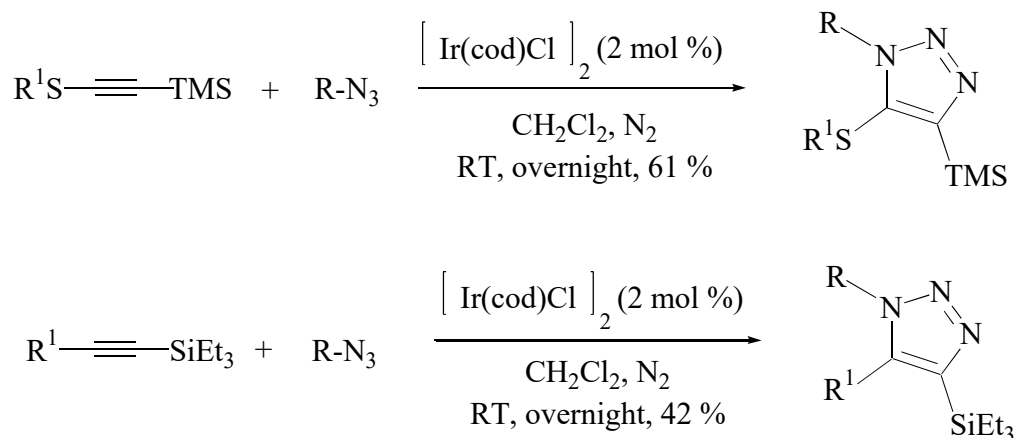
Scheme 104

A microwave-assisted one-pot synthesis of silylated-1,2,3-triazoles from ethylpropiolate and (trimethylsilyl)acetylene is reported (**Scheme 105**).²⁶⁰



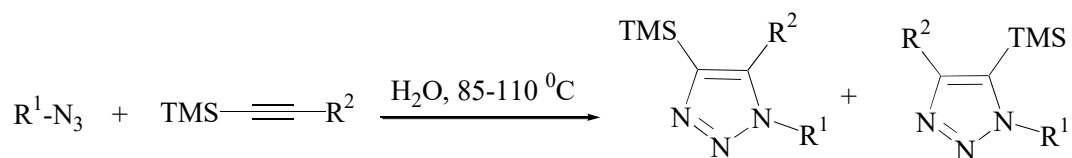
Scheme 105

An iridium-catalyzed azide-alkyne cycloaddition reaction (IrAAC) of internal alkynes or thioalkynes is described (**Scheme 106**).²⁶¹



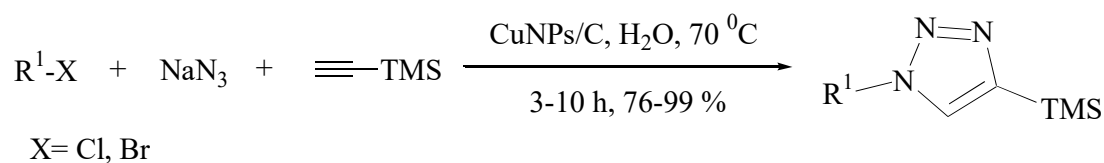
Scheme 106

The [3+2]-cycloaddition reactions of aromatic azides and silylated alkynes in aqueous media yield 1,5-disubstituted-4-(trimethyl-silyl)-1*H*-1,2,3-triazoles (**Scheme 107**).²⁶²



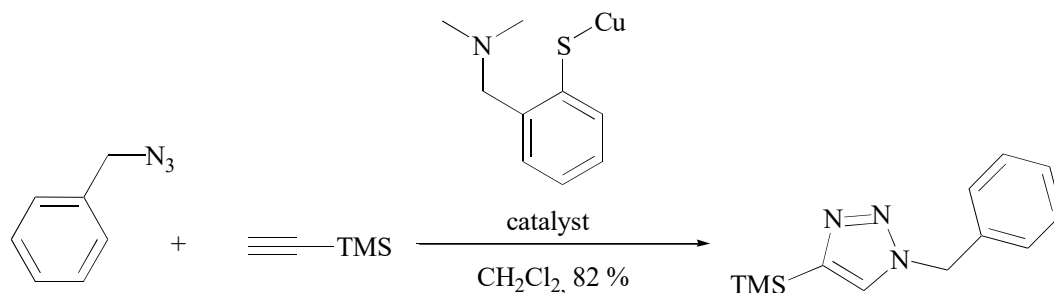
Scheme 107

The copper nanoparticles are found to be effective catalyst for the multi-component synthesis of silylated 1,2,3-triazoles from different organic halides in water (Scheme 108).²⁶³



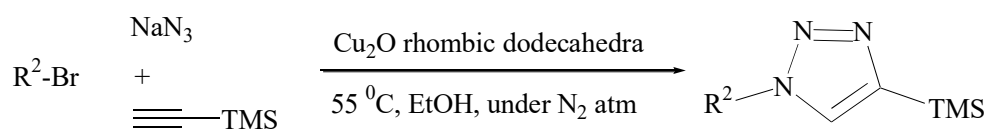
Scheme 108

A {[2-(dimethylamino)methyl]thiophenolato}copper (I) complex is used as an efficient catalyst (1 mol %) for the Huisgen reaction (CuAAC) of azides and terminal alkynes to give corresponding silyl-1,2,3-triazoles (Scheme 109).²⁶⁴



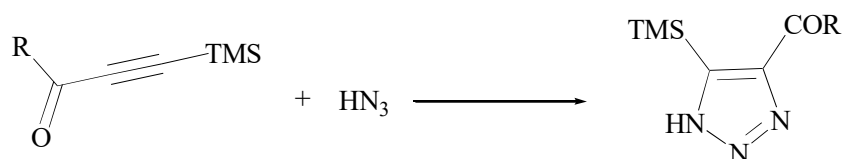
Scheme 109

The multi component synthesis of silylated-1,2,3-triazoles from the reaction of trimethylsilylacetylene, organic halides and NaN₃ in presence of Cu₂O rhombic dodecahedral nano crystals is described (Scheme 110).²⁶⁵



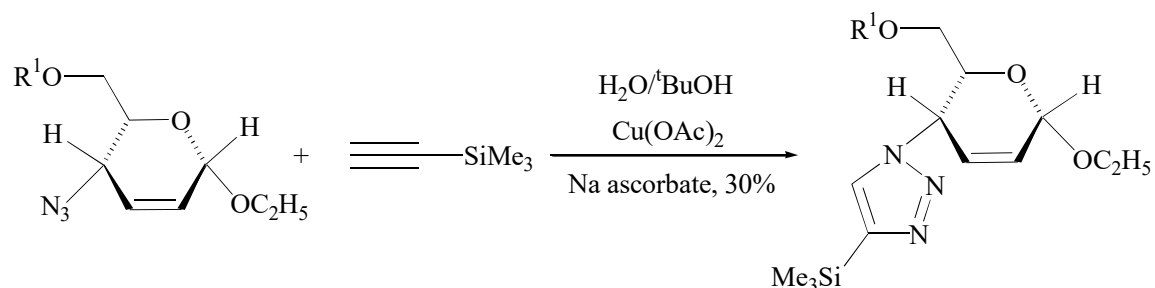
Scheme 110

Acyl(trimethylsilyl)acetylenes react with hydrazoic acid to form the 4-acyl-5-(trimethylsilyl)-1,2,3-triazoles (Scheme 111).²⁶⁶



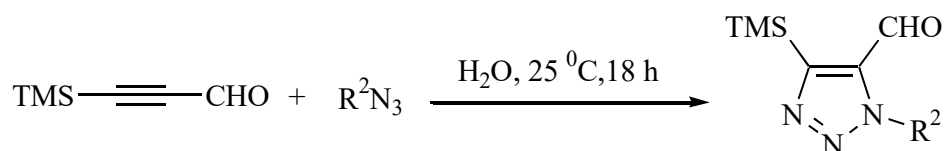
Scheme 111

The synthesis of 1-(ethyl-2,3,4-trideoxy- α -D-erythro-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazole derivatives from 4-azido-2,3,4-trideoxy- α -D-erythro-hex-2-enopyranosides with trimethylsilylacetylene is reported (Scheme 112).²⁶⁷



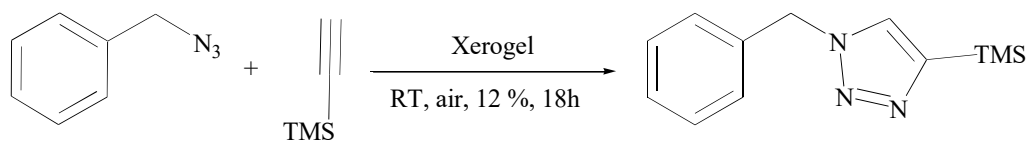
Scheme 112

The reactions of trialkylsilylpropynals with trimethylsilyl- and benzyl azides in water to give 4-trialkylsilyl-1*H*-1,2,3-triazole-5-carbaldehydes (Scheme 113).²⁶⁸



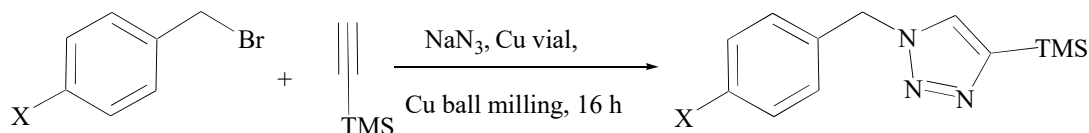
Scheme 113

A novel class of chiral coordination polymer organogels are used as catalysts in 1,3-dipolar Huisgen cycloaddition reaction are reported (**Scheme 114**).²⁶⁹



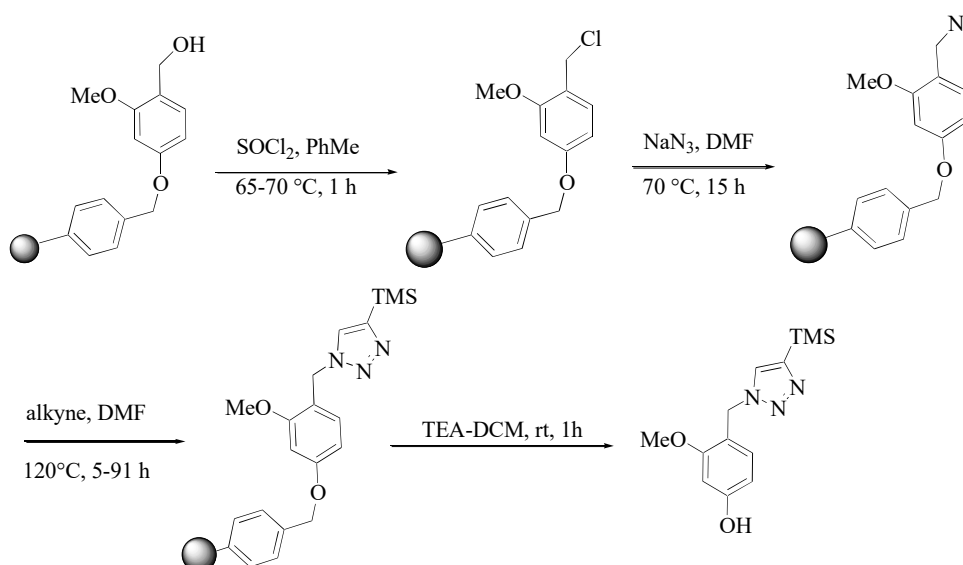
Scheme 114

The copper vial catalysed cycloaddition (CuAAC) reaction under solvent-free mechano-chemical using copper milling ball conditions to synthesize silyl-1,2,3-triazoles is reported (**Scheme 115**).²⁷⁰



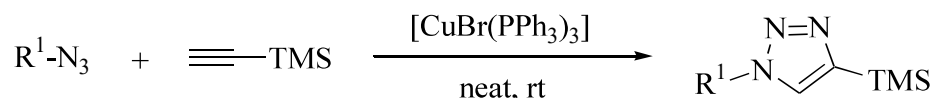
Scheme 115

The solid-phase synthesis of 4-hydroxybenzylsubstituted-silyl-1,2,3-triazoles via 1,3-dipolar cycloaddition of polymer-bound azides to various alkynes is reported (**Scheme 116**).²⁷¹



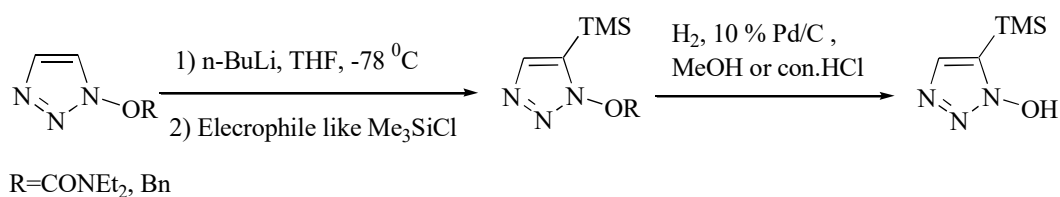
Scheme 116

[CuBr(PPh₃)₃]-catalyzed cycloaddition reactions with organoazides and alkynes to form corresponding triazoles (**Scheme 117**).²⁷²



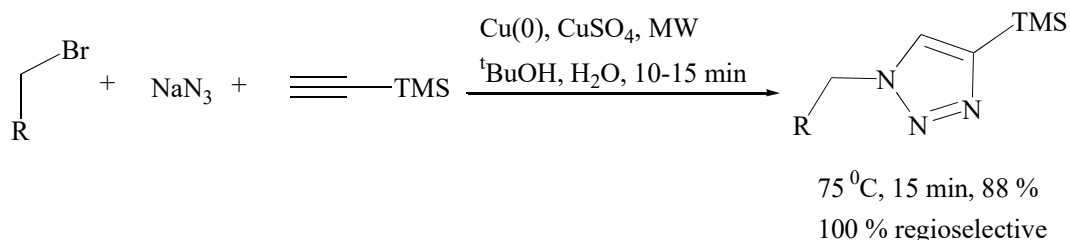
Scheme 117

The synthesis of 5-substituted 1-hydroxy-1,2,3-triazoles from 1-(benzyloxy)-1,2,3-triazole with *n*-butyllithium to form anion which when reacted with a electrophiles as carbon, halogen, sulfur, silicon, and tin substituents undergo subsequent removal of the benzyl group by palladium-catalyzed hydrogenolysis or by treatment with hydrochloric acid is reported (**Scheme 118**).²⁷³



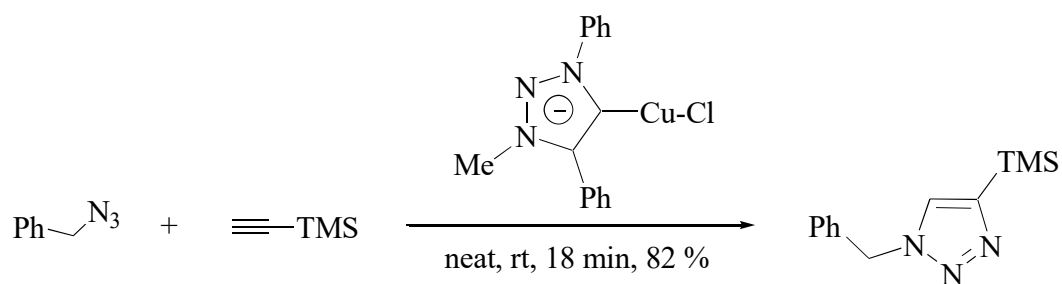
Scheme 118

A microwave-assisted reaction has been used to prepare a series of 1,4-disubstituted-1,2,3-triazoles from corresponding alkylhalides sodium azide and alkynes (**Scheme 119**).²⁷⁴



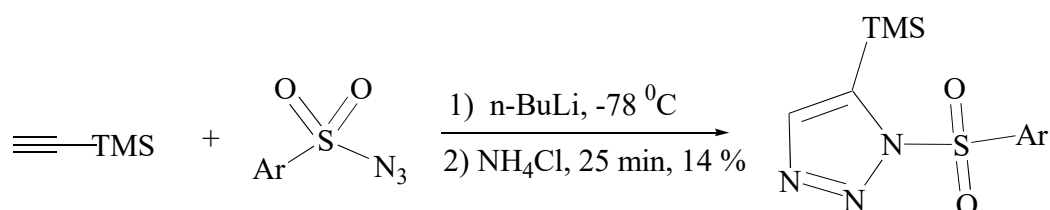
Scheme 119

The CuCl(TPh) complexes efficiently catalyze click reactions of azides with alkynes to give 1,4-substituted 1,2,3-triazoles (**Scheme 120**).²⁷⁵



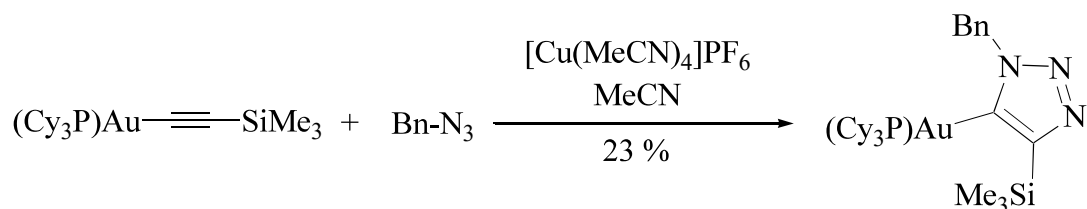
Scheme 120

The reaction of trimethylsilylacetylene with sulfonyl azides form 1,5-substituted sulfonyl triazoles (Scheme 121).²⁷⁶



Scheme 121

The gold (I) alkynyls undergo copper-catalyzed reaction with benzyl azide reaction to proceed with 1,4-regioselectivity to give triazolite products like $[(\text{PCy}_3)_3\text{Au}(1\text{-benzyl-4-trimethylsilyl}(\text{triazolato}))]$ (Scheme 122).²⁷⁷

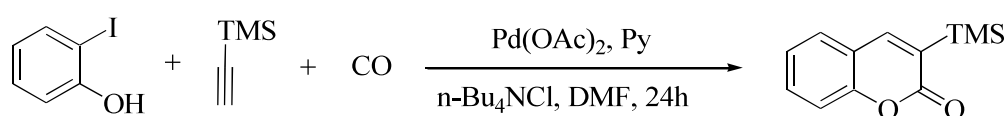


Scheme 122

1.4.2 Coumarins

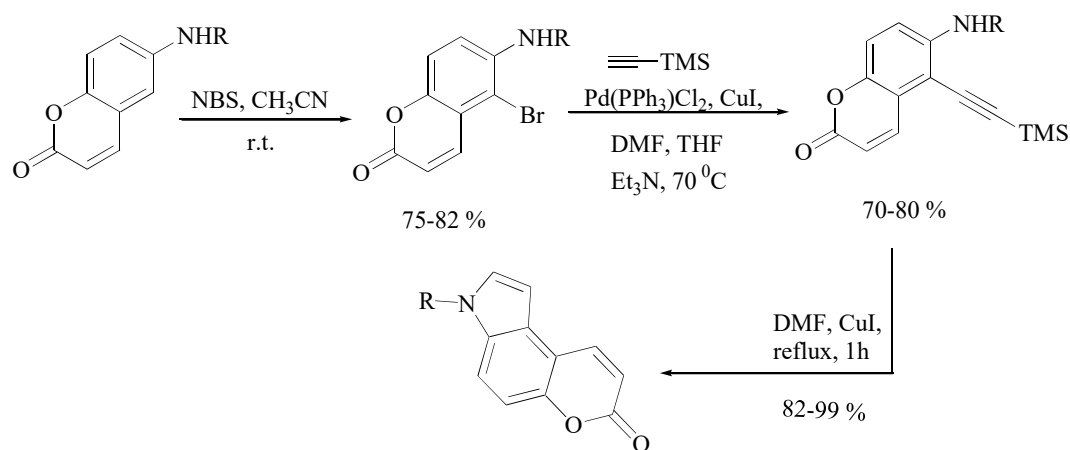
Coumarin and quinolone sub-units are found in a large number of natural products possessing biological activity and which exhibit antifungal, antibacterial, antiviral, antimicrobial, antimalarial, insecticidal, antineoplastic, antidiuretic, antiarrhythmic and sedative properties.²⁷⁸⁻²⁸²

Palladium-catalyzed carbonylative annulation of *o*-iodophenol with trimethylsilylacetylenes to form silylated coumarin scaffolds is reported (**Scheme 123**).²⁸³



Scheme 123

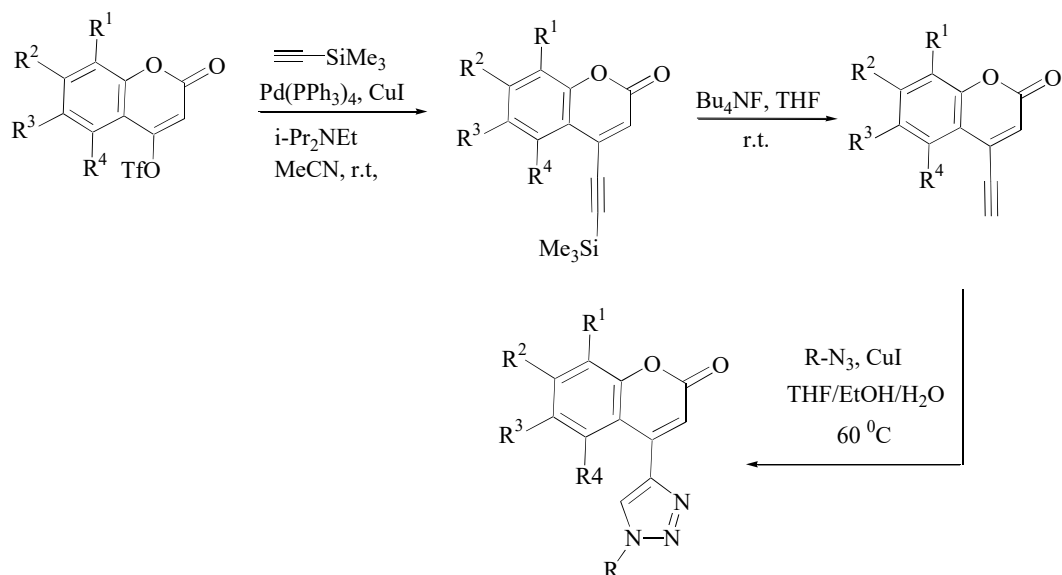
The sequential coupling and cyclization reactions between aryl halides and (trimethylsilyl)acetylene with concurrent elimination of the TMS substituent to synthesis substituted pyrano[3,2-*e*]indolone and pyrrolo[3,2-*f*]quinolone derivatives is reported (**Scheme 124**).²⁸⁴



Scheme 124

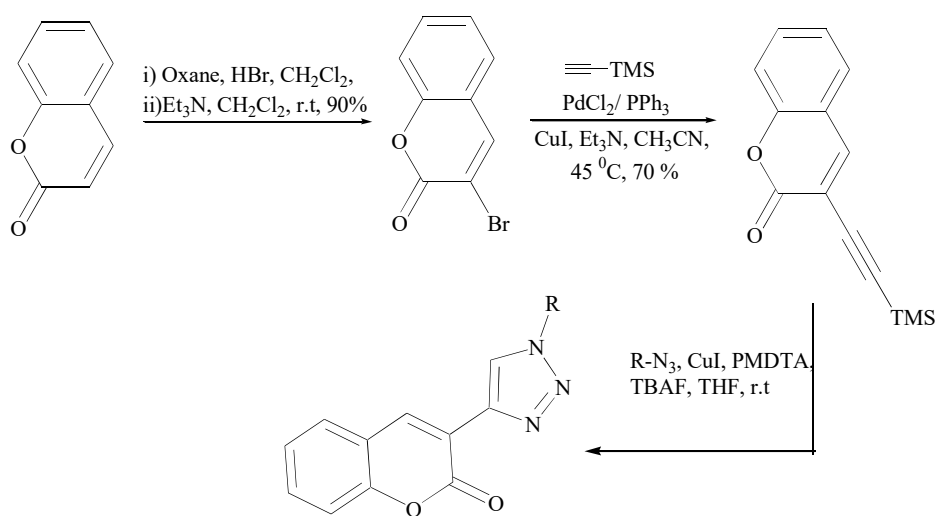
4-Trimethylsilylethynyl-substituted coumarins were synthesized using Sonogashira cross-coupling of the corresponding 4-trifluoromethylsulfonyloxy

coumarins. A series of coumarin triazolylglycosides were synthesized using copper-mediated 1,3-dipolar cycloaddition reactions of carbohydrate azides and 4-alkynyl-substituted coumarins (**Scheme 125**).²⁸⁵



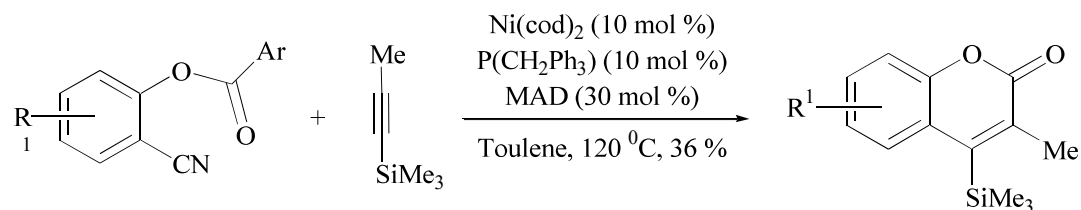
Scheme 125

3-Bromocoumarin when subjected to a Sonogashira cross-coupling reaction gave the 3-(trimethylsilyl)ethynyl coumarin. The compound was reacted with various organic azides via click chemistry to form the corresponding 3-(1,2,3-triazolyl)coumarin derivatives (**Scheme 126**).²⁸⁶



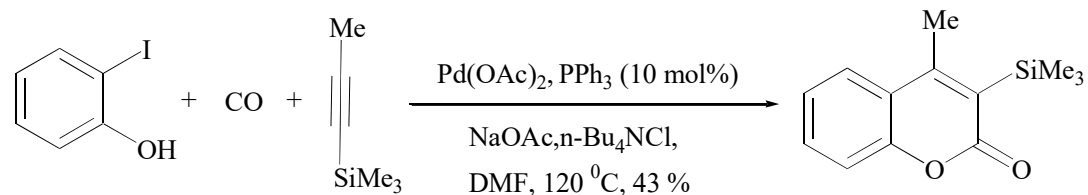
Scheme 126

An intermolecular cycloaddition reaction is reported where *o*-arylcyanobenzonitriles react with alkynes to afford coumarins in the presence of Ni(0)/P(CH₂Ph)₃/MAD as a catalyst (**Scheme 127**).²⁸⁷



Scheme 127

A variety of substituted coumarins have been prepared by the palladium-catalyzed coupling of *o*-iodophenols with internal alkynes and 1 atm of carbon monoxide. Unlike most of the previous work on the palladium-catalyzed carbonylation of alkynes, the insertion of the internal alkyne occurs in preference to the insertion of CO (**Scheme 128**).²⁸⁸



Scheme 128