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Chemistry and Applications of Organopalladium Compounds

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Abstract

Palladium and other platinum group metals are widely used because of their special characteristics. The most important reactions of Palladium are the **cross-coupling reactions**, which are palladium-catalyzed, have grown to be extremely effective processes for producing new C-C and C-N bonds. C–N and C–C bonds are used in the Synthesis of Heterocycles, Medicinal Chemistry and Natural Products.

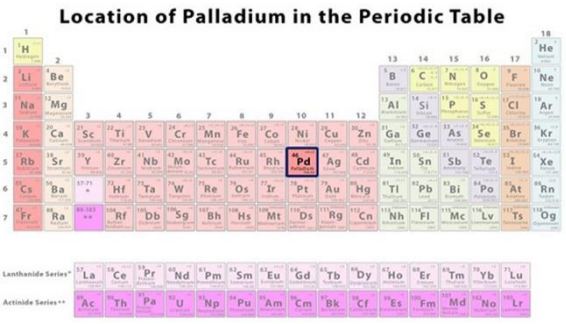
Keywords; Organopalladium, Coupling Reactions, Heck's Reactions, Suzuki's Reactions, Negishi's Reactions.

1. Introduction

Since the second half of the 20th century and up to the present, transition metals have played a significant role in organic chemistry [1-4] which has led to the invention of numerous processes for the synthesis of organic compounds that are transition metal-catalyzed.[5] Different organic compounds can be uniquely activated by transition metals, and as a result of this activation, they can promote the formation of novel bonds..[6-11] Palladium was one of the first metals to be utilized for catalyzing organic reactions. The discovery that ethylene is oxidized to acetaldehyde by air in a palladium-catalyzed reaction—which later became the Wacker process—was one occasion that sparked study into the use of palladium in organic chemistry.[12]

Later studies on palladium-catalyzed carbonylation produced novel processes for the synthesis of carbon-carbon bonds.[13-15] All life on Earth depends on the creation of new carbon-carbon bonds, which is crucial to organic chemistry. Complex compounds, can be made by linking carbon atoms together into chains. Wittig reaction, the Grignard process (1912 and the Diels-Alder reaction (1950) were all recognized with Nobel Prizes in Chemistry, highlighting the significance of the synthesis of carbon-carbon bonds. (1979)

The Nobel Prize in chemistry was awarded in 2005 for the creation of carbon-carbon double bonds using metal catalysts. Professor Richard F. Heck from the University of Delaware in Newark, Delaware, Professor Ei-ichi Negishi from Purdue University in West Lafayette, Indiana, and Professor (emeritus) Akira Suzuki from Hokkaido University in Sapporo, Japan, all share this year's Nobel Prize in Chemistry. The three chemists received awards from the Royal Swedish Academy of Sciences for "palladium-catalyzed cross couplings in organic synthesis". The three distinguished chemists' discoveries have greatly influenced academic work, the creation of new medicines and materials, and are employed in numerous industrial chemical processes for the manufacture of pharmaceuticals and other physiologically active substances.



2. Overview on Palladium

Palladium is a chemical element with the chemical symbol Pd and an atomic number of 46. Palladium is a rare and lustrous silvery-white metal.

The platinum group metals, (PGMs) which include Palladium, platinum, rhodium, ruthenium, iridium, and osmium. In (PGMs) Palladium has the lowest melting point and is the least dense of the valuable

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metals, however they all have similar chemical properties.

2.1- History

William Hyde Wollaston discovered palladium in 1803.[16, 17] In 1804 this element was named by Wollaston in honor of the asteroid Pallas, which had been found two years before. By dissolving the ore in aqua regia, neutralizing the solution with sodium hydroxide, and precipitating platinum as ammonium chloroplatinate with ammonium chloride, Wollaston discovered palladium in crude platinum ore from South America. To create the combination palladium cyanide, which was heated to release the metal palladium, he added mercuric cyanide.

2.2- Occurrence

With a 44% global production share in 2007, Russia dominated the palladium industry. South Africa came in second with a 40% share. The only other significant palladium producers are Canada (6%) and the United States (5%).[18, 19]

Palladium can be discovered in placer deposits in the Ural Mountains, Australia, Ethiopia, North and South America as a pure metal or alloyed with gold and other platinum group metals. These deposits only have a small impact on palladium output. Nickel-copper deposits in the Sudbury Basin of Ontario and the Norilsk-Talnakh deposits in Siberia are the most significant commercial sources of palladium. The Merensky Reef platinum group metals deposit in South Africa's Bushveld Igneous Complex is the other significant deposit. The two further sources of palladium in Canada and the United States are the Roby zone ore body of the Lac des Îles igneous complex in Ontario and the Stillwater igneous complex in Montana.[18]

Palladium is also produced in nuclear fission reactors and can be extracted from spent nuclear fuel though the quantity produced is insignificant.[20] Palladium is found in the rare minerals cooperite [21] and polarite.[21, 22]

2.3- Characteristics

Palladium belongs to group 10 in the periodic table but has a relatively uncommon arrangement in its outermost electron shells compared to the rest of the members of group 10, if not to all elements. It is the least dense and has the lowest melting point of the platinum group metals. In hydrochloric, nitric, and sulfuric acids, palladium dissolves slowly. This metal also does not react with oxygen at normal temperatures (and thus does not tarnish in air). Palladium heated to 800°C will form a coating of palladium(II) oxide (PdO).

At room temperature, the metal possesses the incredibly rare capacity to absorb hydrogen up to 900 times its own volume. It is thought that this produces palladium hydride (PdH2), it is still unclear whether this is a genuine chemical compound.[23] Palladium will slightly enlarge after absorbing a significant amount of hydrogen.[24]

Palladium often exists in the oxidation states 0, +1, +2, and +4. Palladium does not occur the +3 oxidation state; X-ray diffraction analysis of a variety of compounds indicates a dimer of palladium(II) and palladium(IV) instead. Despite the fact that +3 was once believed to be one of the fundamental oxidation states of palladium. Palladium(VI) was originally **detected in 2002.[25, 26]**

2.4-Applications

Palladium and other platinum group metals are widely used because of their special characteristics. In today's manufacturing process, the platinum group metals either make up one in every four products or are essential to their production.[27-29]

2.4.1- Catalytic converters

Palladium is currently most commonly used in catalytic converters.[30] Catalytic converters, which transform up to 90% of toxic gases from vehicular exhaust (hydrocarbons, carbon monoxide, and nitrogen oxide) into less damaging compounds, use more than half of the supply of palladium and its congener platinum. (nitrogen, carbon dioxide and water vapor).

Cross section of a metal-core catalytic converter

2.4.2-Electronics

Making multilayer ceramic capacitors is the second-largest use of palladium in electronics.[31] Multi-layer ceramic capacitors use palladium (and palladium-silver alloys) as its electrode material.[32] Consumer electronics employ palladium for connector platings, which is occasionally alloyed with nickel**.**

Numerous electronic products, such as computers, cell phones, component plating, low voltage electrical contacts, and SED/OLED/LCD televisions, include palladium.

2.4.3-Catalysis

Palladium is a flexible catalyst that speeds up hydrogenation and dehydrogenation reactions as well as petroleum cracking when it is finely divided, as in palladium on carbon. Palladium also works well as an electrocatalyst for the oxidation of primary alcohols to aldehydes in alkaline solutions when it is disseminated on conductive surfaces.[33] Pd is a versatile metal that can be used in homogeneous catalysis. It is employed in a wide range of ligand combinations to carry out highly selective chemical

reactions. Palladium is a powerful catalyst for forming carbon-fluoride bonds, according to a 2008 study.[34]

2.4.4-Technology

Heat-induced hydrogen diffusion through heated palladium offers a way to purifying the gas. Therefore, high pure hydrogen is produced using membrane reactors with Pd membranes. In electrochemical investigations, it is a component of the palladium-hydrogen electrode. Fuel cells use a technology called palladium to mix hydrogen and oxygen to create electricity, heat, and water. Carbon monoxide detectors use palladium(II) chloride, which has a large-scale carbon monoxide gas oxidation capacity.[35]

2.4.5-Other applications

Dentistry, medicine, and groundwater treatment all make use of palladium.[36] Palladium is also used in the manufacture of watches, blood sugar test strips, spark plugs for aircraft, surgical equipment, and electrical connectors. Professional transverse flutes are additionally made of palladium.

Palladium bullion bears the ISO currency codes XPD and 964 as a commodity. Only four metals—gold, silver, and platinum—have such codes, with palladium being one of them**.**

Since 1939, palladium has been used as a substitute for platinum or white gold as **a precious** metal in jewellery. [37]

3- The chemistry of organopalladium compounds

3.1- Palladium compounds, complexes, and ligands widely used in organic syntheses

Pd(II) salts and Pd(0) complexes, two different types of Pd substances, are utilized in chemical syntheses. Pd(II) compounds are mostly employed as catalysts or oxidizing reagents in a few processes. Catalysts are always made of Pd(0) complexes.[33] Due to the simplicity of interconversion between Pd(0) and Pd(II) intermediates, palladium compounds are highly reactive.

3.1.1- Pd(II) Compounds:

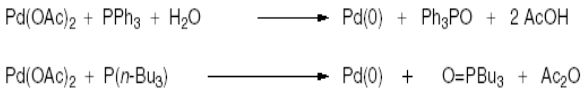
Pd(II) Compounds: can be used as both Pd(0) complex intermediates and special stoichiometric oxidising agents.

$PdCl_2$: is stable, however it has a low solubility in organic and water solvents. It dissolves in diluted HCl and, after producing a PdCl2(PhCN)2 complex, also dissolves in organic solvents. PdCl2 and PdBr2 are not monomers; in order to produce the more reactive acetonitrile complex monomers, they frequently need to be refluxed in acetonitrile.[38]

$PdX_2 + 2\ MeCN \rightarrow PdX_2(MeCN)_2$ (X = Cl, Br)

M_2PdCl_4 (M = Li, Na, K) are soluble in water, lower alcohols and some organic solvents.

$Pd(OAc)_2$: is commercially available. In organic liquids, it is stable and soluble. It is stable and soluble in organic solvents. As reducing agents for Pd(OAc)2, phosphines can be employed most conveniently. For instance, triphenylphosphine oxide and Pd(0) species are slowly generated when PPh3 is used to treat Pd(OAc)2.[39, 40] By quickly reacting Pd(OAc)2 with P(n-Bu)3 in a 1:1 ratio in THF or benzene, a highly active Pd(0) catalyst can be created.[41] P(n-Bu)3 is quickly converted to phosphine oxide, and in addition to Ac2O, a phosphine-free Pd(0) species is created. This catalyst is extremely active but unstable and needs to be employed right away; if no substrate is added, black Pd metal starts to precipitate within 30 minutes. A particularly practical method for preparing Pd is the in situ production of Pd(0) species using P(n-Bu)3 as a reducing agent.



3.1.2- Pd(0) Complexes:

$Pd(PPh_3)_4$: is a yellowish-green crystal, air-instable, light-sensitive, coordinatively saturated Pd(0) complex. Because it is overligated and contains too many ligands to allow some reactants to be coordinated, $Pd(PPh_3)_4$ is less effective as a catalyst.

$Pd(t\text{-}Bu_3P)_2$: a significant ligand, the large and electron-rich $P(t\text{-}Bu)_3$ has drawn attention. It's interesting to note that the commercially available and stable Pd(0) complex $Pd(t\text{-}Bu_3P)_2$ has a significant degree of coordination unsaturation. The bulkiness of the ligand is undoubtedly responsible for the stability of this unsaturated phosphine complex. This complex is an extremely active catalyst in several processes, particularly for aryl chlorides.[42]

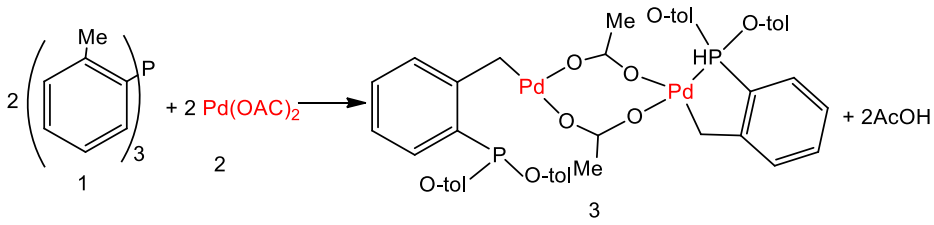
$Pd_2(dba)_3$-$CHCl_3$: (dba = dibenzylideneacetone) is another Pd(0) complex that is readily accessible on the market. It appears as purple needles and contains one molecule of $CHCl_3$ after $Pd(dba)_2$, which was first generated during preparation, recrystallizes from $CHCl_3$, where Pd(dba)2 is equivalent to $Pd_2(dba)_3$-dba.[43]

Colloidal Pd nanoparticles protected with tetraalkylammonium salts, lately come to light as potent catalysts. Without phosphine ligands, they are employed for Heck and Suzuki-Miyaura reactions, [44, 45] Aryl iodides and diazonium salts are examples of active substrates. $Pd(OAc)_2$ is most

commonly utilized without a ligand, creating some sort of colloidal or soluble Pd(0) species in situ. These Pd(0) catalysts are thought to function as homogeneous catalysts as they lack ligands.[46]

3.1.3- Ligands:

phosphine ligands :a number of phosphine ligands are used. The majority of them are marketed for sale.[47] PPh_3 is by far the substance that is utilized the most. Recrystallization from ethanol easily gets rid of any contaminated phosphine oxide. Heck utilized bulky tri(o-tolyl)phosphine for the first time, which is a particularly powerful ligand.[48] This phosphine's Pd complex is not only active, but also has a longer catalytic life**.** The palladacycle 1, also known as the Herrmann complex, which is stable to air and moisture and is marketed, provides an explanation for this.[49] It makes a great underligated single phosphine Pd(0) catalyst precursor. However, this catalyst only works at 110 °C and not at low temperatures.



Scheme 1

Tricyclohexylphosphine and $P(n\text{-}Bu)_3$, as well as arylphosphines like tri(2,4,6-trimethoxyphenyl)phosphine (TTMPP) and tri(2,6-dimethoxyphenyl)phosphine (TDMPP), are more electron-donating alkylphosphines that are effectively used in a variety of catalytic processes.. The "oxidative addition" phase is sped up by these phosphines, which are electron-rich. Furthermore, it was discovered that P(t-Bu)3 was an essential ligand, particularly for aryl chloride reactions.

Since Koie and coworkers initially described the use of $P(t\text{-}Bu)_3$ in the Pd-catalyzed amination of aryl chlorides in 1998 [50], numerous bulky and electron-rich phosphines connected to $P(t\text{-}Bu)_3$ have been synthesized and used.These di- and trialkylphosphines [51] have a limited air sensitivity. However, their air-stable phosphonium salts can be employed for catalytic processes since phosphines can be extracted from them by treating them with bases.[52]

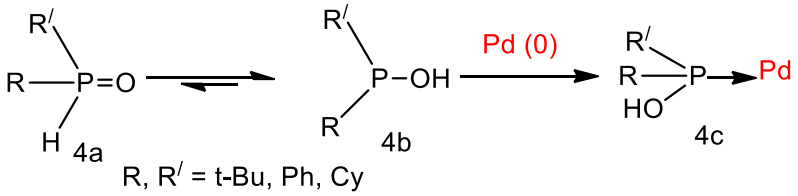
Sulfonated phosphine ligands: Sulfonated triphenylphosphine [TPPTS (triphenyl-phosphine, m-trisulfonated); tri(m-sulfophenyl)phosphine] and mono-sulfonated triphenylphosphine [TPPMS (triphenylphosphine, monosulfonated); 3-diphenyl-phosphino)benzenesulfonic acid] are commercially available ligands and their sodium salts are water-soluble.[53, 54] The moderately soluble TPPMS is selected since the Na salt of the ligand TPPTS is very soluble and may be excessively soluble in water. 2-(diphenylphosphinoethyl)trimethyl ammonium halide is a different phosphine that is soluble in water. Water can be used to conduct Pd-catalyzed reactions, which is reported to have an accelerating impact in some catalytic reactions.[55] Pd complexes coordinated by these phosphines are soluble in water.[56]

Bidentate phosphines: for examples DPPP (diphenyl- phosphinopropane), DPPB (diphenylphosphinobutane) and DPPE (diphenylphosphinoethane) play important roles in some reactions. Other bidentate phosphines include DPPF (1,1'-bis(diphenyl-phosphino)ferrocene), which differs from other bidentate phosphines by exhibiting its own individual activity.

Tedicyp (cis,cis,cis-1,2,3,4-tetrakis(diphenylphosphino-methyl) cyclopentane), a tetra-podal phosphine ligand, has been discovered to be a good ligand and its Pd complex exhibits high turnover rates.[57, 58]

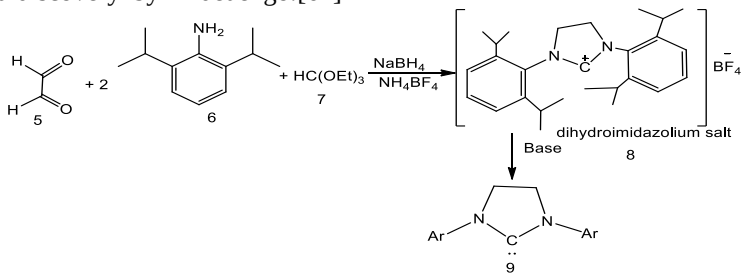
Phosphite ligands:, Triisopropyl phosphite and triphenyl phosphite, for example, are weaker electron donors than the equivalent phosphines but are useful in particular processes due to their higher ability to operate as a π--acceptor. Trimethylolpropanephosphite (TMPP), also known as 4-ethyl-2,6,7-trioxa-1-phospha-bicyclo-[2.2.2]-octane, is a cyclic phosphite that exhibits significant catalytic activity in specific processes. Although not readily available commercially, it is simple to prepare.[59, 60]

Phosphinous acids ligands: Recently Li[61] reported that When transition metals are present, air-stable phosphine oxides 4a [R'RP(O)H] tautomerize to the less stable phosphinous acids 4b [R'RPOH], which then coordinate to Pd centers through phosphorus atoms to form Pd phosphinous acid complexes 4c that act as active catalysts for inactive aryl chlorides.[61, 62]



Scheme 2

Heterocyclic carbene ligands: are currently drawing interest as novel ligands. Carbenes are unstable. and reactive species that are challenging to separate. They can be stabilized and isolated, as is well known, by coordinating to W, Mo, and Cr metal complexes.[63] Imidazol-2-ylidenes with high substituents on nitrogens are stable carbenes and can be isolated, according to a recent discovery by Ardeuengo.[64] They are known as "phosphine mimics" and are effective ligands for transition metal complexes because they are bulky, electron-rich, and so active for aryl chloride reactions. Dihydroimidazolium salts 8, which are made easily from primary amine 6, glyoxal 5 and ortho-formate 7, can be used to produce the carbenes.[65] Scheme 3



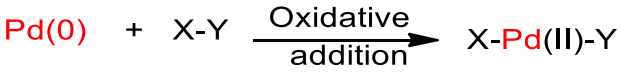
Scheme 3

Alkyl-substituted imidazolium salts are ionic liquids that are frequently employed as special solvents for a variety of processes, including Pd-catalyzed reactions.[66, 67]

3.2 Fundamental Reactions of Pd Compounds

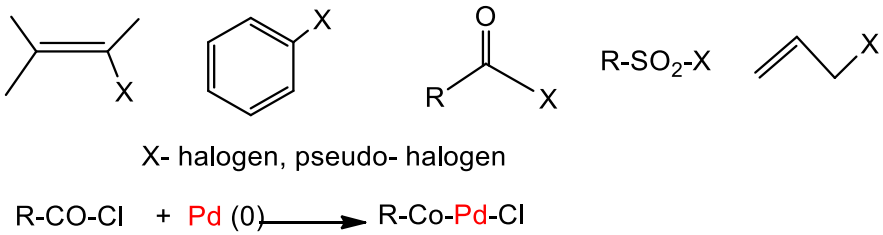
3.2.1 Oxidative Addition

In organic chemistry uses the word "oxidation" differently than organometallic chemistry, where it refers to processes like the conversion of secondary alcohols to ketones. "Oxidative addition" refers to the addition of a molecule X—Y to Pd(0) after its covalent link is broken, creating two new bonds. [68] Due to the connection between the two Pd electrons that were previously not in a bond, Pd increases its formal oxidation state by two units, going from Pd(0) to Pd.(II). This technique is comparable to how alkyl halides and magnesium are used to create Grignard reagents Mg(0) is oxidized to Mg(II) by the "oxidative" addition of alkyl halides to create two covalent bonds, which is how Grignard reagents are created. Scheme 4



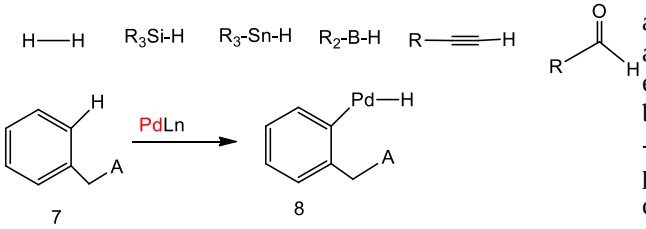
Scheme 4

Higher electron density of Pd makes oxidative addition easier, and generally, -donor ligands like R3P coupled to Pd make oxidative addition easier. Alkenes and CO, on the other hand, have a tendency Substrates with halogen bonds to restrict oxidative addition.[33, 69] Oxidative addition occurs with alkenyl, aryl, acyl, and sulfonyl halides. Scheme 5



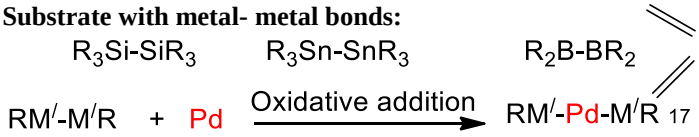
Scheme 5

The following H-C and H-M-bonded molecules are combined through oxidative addition to produce Pd hydrides. It is known that the C-H bonds of terminal alkynes and aldehydes serve as the catalyst for the oxidative addition of other molecules. The process, known as "orthopalladation," creates a Pd—H bond and palladacycles on the aromatic C—H bond in position 3 by adding donor atoms including N, S, O, and P. Scheme 6.

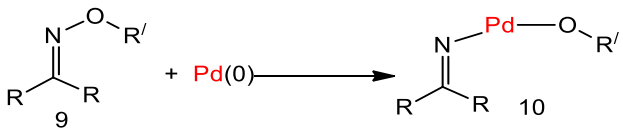


Scheme 6

Substrate with metal- metal bonds:



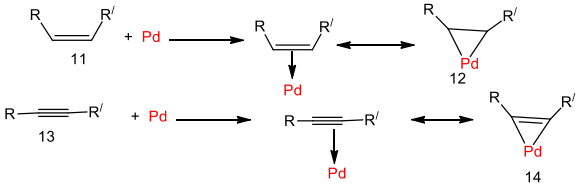
In oxime derivatives 9, the N-O bond breaks through oxidative addition to create a Pd-imino bond 10. Scheme 7



Scheme 7

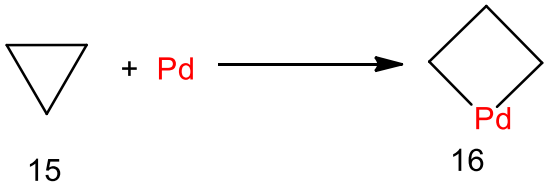
Substrate with metal- metal bonds:

As previously mentioned, oxidative addition entails the breakage of covalent bonds. In addition, bond cleavage is not necessary for oxidative addition in a broader sense. Alkene and alkyne -complexes, for instance, are thought to generate η2* complexes through oxidative addition. The ensuing alkene complexes are better defined as the palladacyclopropane 12 and the alkyne complex may be viewed as the palladacyclopropene 14. Two separate Pd—C bonds are created. As a result, formal oxidation of Pd occurs as a result of the coordination of the alkene and alkyne. Scheme 8.



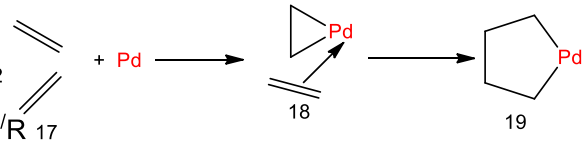
Scheme 8

By oxidative addition cyclopropane **15** with bond cleavage, palladacyclobutane **16** is created. Scheme 9



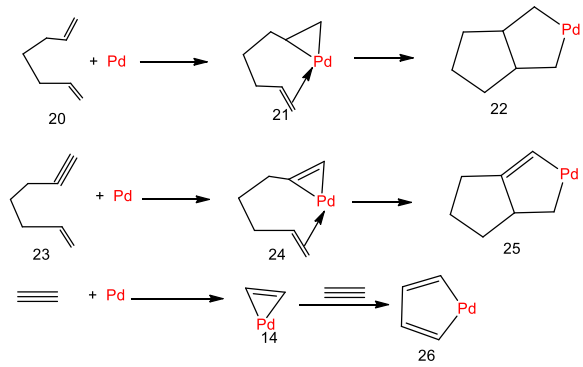
Scheme 9

Oxidative cyclization is a different type of oxidative addition that doesn't involve bond breakage. The addition processes involving two molecules of ethylene **17** are catalysed by Pd. The two double bonds undergo an intermolecular process known as π--complexation, which is followed by cyclization to produce palladacyclo-pentane **19**. Oxidative cyclization is the term for this.[33] Scheme 10.



Scheme 10

The palladacyclopentane 22 is produced by the oxidative cyclization of 1,6-diene and goes further transformations. Similar to this, palladacyclopentene 25 is produced via the oxidative cyclization of α,ω--enyne. These five-membered rings are formed incrementally, and their formation can be explained in terms of the formation of palladacyclopropene or palladacyclopropane. Then, palladacyclopentane 22 and pallada-cyclopentene 25 are created by the inter- and intramolecular insertion of alkene into the three-membered rings. Acetylene reacts with Pd(0) to produce palladacyclopropene 14, which is then converted into palladacyclo-pentadiene 26 via intermolecular acetylene insertion. Scheme 11.



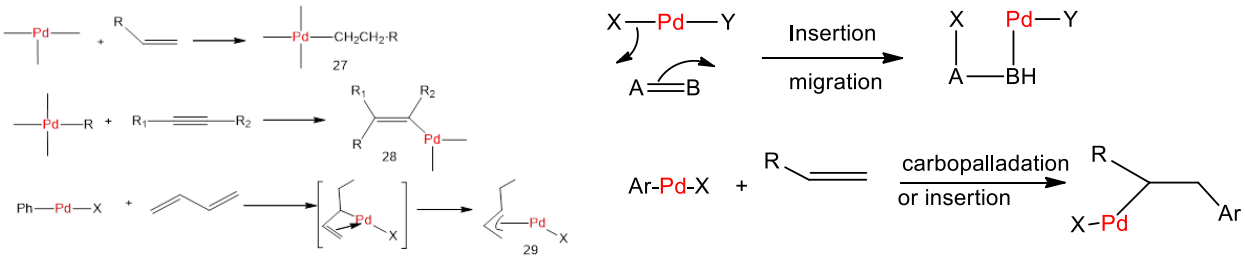
Scheme 11

3.2.2 Insertion

Different unsaturated ligands, such as alkynes, alkenes, and CO, officially insert into an adjacent Pd-ligand bond to create 12 in Pd complexes. The term "insertion" is a little deceptive. The ideal way to

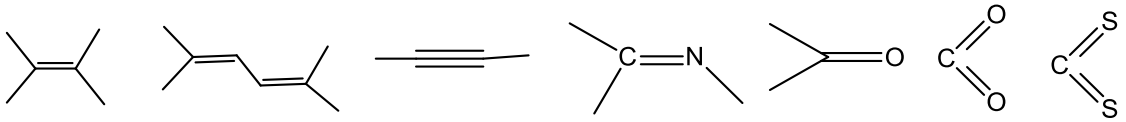
conceptualise the insertion is as a transfer of a nearby ligand from the Pd to the Pd-bound unsaturated ligand.[33]

The insertion is reversible. There are two forms of insertion. They are α,α- (or 1,1-) and α,β- (or 1,2-) insertions. α,β-insertion is the most insertion observed of unsaturated bonds like alkenes and alkynes.[68]



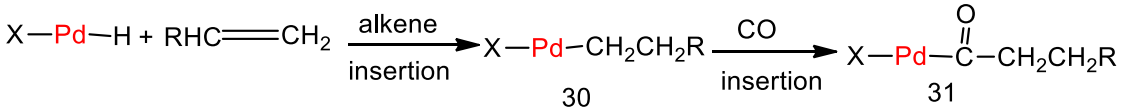
The following unsaturated bonds undergo *α,β*-insertion:

The insertion of alkene to Pd-H, which is called 'hydropalladation' of an alkene, yields the alkylpalladium complex **27**, and insertion of alkyne to Pd-R links creates the vinylpalladium complex **28**. Alkylpalladium complex 27 is produced by the so-called "hydropalladation" of an alkene, while vinylpalladium complex **28** is produced by the insertion of an alkyne into a Pd-R bond. Alkynes can be thought of as being "ciscarbopalladated" in this reaction. Conjugated dienes react with Pd complexes to create the π-allyl complex **29**. The -allylpalladium complex **29** is created when one of butadiene's double bonds is inserted into the Ph-Pd bond.[33]Scheme 12



Scheme 12

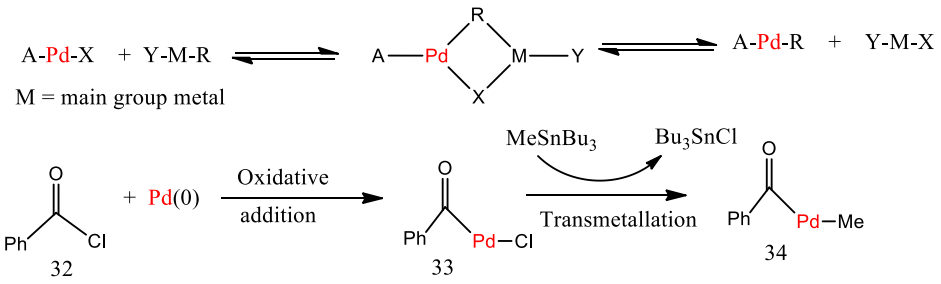
Mg and Pd complexes both undergo insertion and oxidative addition. The main reaction pathway for Grignard reagents is the insertion of a carbonyl group, whereas the Pd complexes can undergo both oxidative addition and insertion with a range of -bonds.It should be emphasised as well that several sequential insertions are possible. For instance, the alkyl complex 30 is produced by adding an alkene to a Pd-C or Pd-H bond. Next, CO is added to produce the acyl complex 31.[70] Scheme 13



Scheme 13

3.2.3 Transmetallation

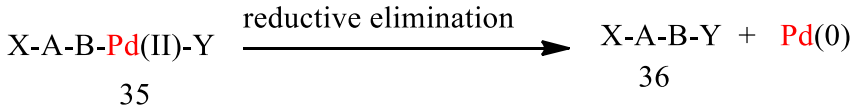
Pd complexes (A-Pd-X) produced by oxidative addition react with organometallic compounds M-R and hydrides M-H of main group metals (M= Mg, Zn, B, Al, Sn, Si, Hg), and the organic group or hydride is transferred to Pd by replacing X with R or H. In other words, transmetallation, also known as Pd alkylation or hydride production, occurs. The main group metal M must be more electropositive than Pd for transmetallation to occur, and this electropositivity difference between the two metals is thought to be the driving factor behind transmetallation. The sequence of oxidative addition-transmetallation is well recognised. Benzoylpalladium chloride 33 is produced by the reaction of benzoyl chloride with Pd(0), and benzoyl-methylpalladium 34 is produced by transmetallation with methyltributyltin. [33] Scheme14



Scheme 14

3.2.4 Reductive Elimination

Similar to the term "oxidative," "reductive" in organometallic chemistry refers to a process that is different from reduction in organic chemistry. The opposite of oxidative addition is the unimolecular breakdown route known as reductive elimination.Two cis-configured ligands are lost from the Pd centre in 35 during reductive elimination (or reductive coupling), and their combination results in a single elimination product 36.[33] Scheme 15

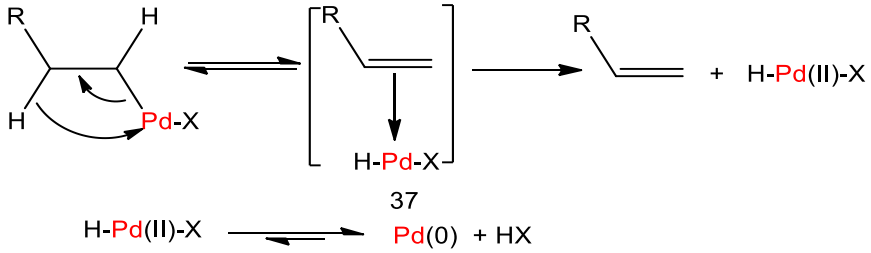


Scheme 15

3.2.5 β-H Elimination (β-Elimination, Dehydropalladation)

Synthesis of Pd hydride (H-Pd-X) and an alkene are produced as a result of the syn elimination of hydrogen from carbon at the β-position to Pd in alkylpalladium complexes. Either "β-hydride elimination" or "-hydrogen elimination" is the name given to this procedure. Because the β-H is eliminated as the Pd-hydride, the phrase "- β-hydride elimination" is most commonly used. (H-Pd-X). Dehydropalladation, used in a cis way, is the correct and unambiguous term for this process.

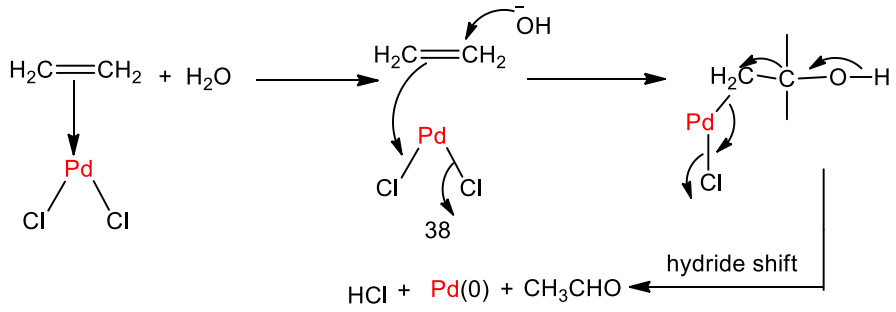
The reaction is known as " β-hydride elimination" because the -H is eliminated as a hydride by dehydropalladation to form H-Pd(II)-X (Pd-hydride) and an alkene, the latter of which is in coordination to the Pd centre to form 37. Lastly, H-Pd(II)-X affords Pd(0) and HX by reductive elimination in the presence of a base. Scheme 16



Scheme 16

3.3 Electrophilic Attack by Organopalladium Species

Pd complexes can be used to create a wide variety of beneficial reactions that are completely different from common chemical reactions. The coordination's impact is striking. Due to their abundance of electrons, unsaturated organic molecules like CO, alkenes, and alkynes are relatively inert towards nucleophiles. When these unsaturated molecules coordinate to electron deficient Pd, their reactivity is reversed. This is a significant outcome of the coordination. One of the most distinctive and advantageous reactions of Pd complexes is the reaction of nucleophiles with the coordinated unsaturated bonds. Coordinated alkenes are attacked by numerous nucleophiles. According to 38, the Wacker process typically involves the OH anion attacking ethylene coordinated to Pd(II) in order to produce acetaldehyde.[71] Scheme 17

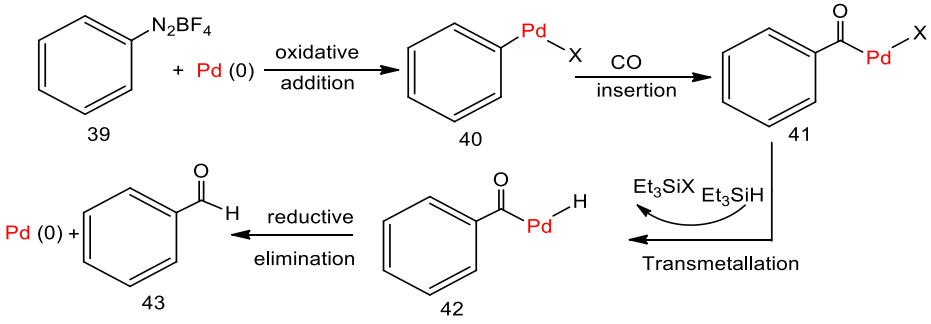


Scheme 17

3.4 Termination of Pd-Catalyzed Reactions and a Catalytic Cycle

In many instances, when Pd(0) complexes are attacked by nucleophiles, the reactions involving these complexes proceed with a catalytic quantity of Pd(0) molecules. The most beneficial aspect of synthetic reactions involving Pd complexes are the catalytic reactions that may be carried out with only a little quantity of pricey Pd complexes. The phenyldiazonium salt **39** undergoes oxidative addition, followed by CO insertion to produce the acylpalladium intermediate **41** as a typical example of the catalytic cycle. Then, benzaldehyde **43** is produced by reductive elimination from **42** following transmetallation with triethylsilane.[72]

Scheme 18



Scheme 18

3.5 Reactions Involving Pd(II) Compounds and Pd(0) Complexes

Oxidative reactions with Pd(II) salts and catalytic reactions with Pd(0) complexes are the two categories of organic reactions involving Pd. Pd(II) salts [$PdCl_2$, $Pd(OAc)_2$] are special oxidising or dehydrogenating agents, and the reactions promoted by Pd(II) can be expressed by the following general equations

Oxidative (dehydrogenative) reactions with Pd(II) compounds

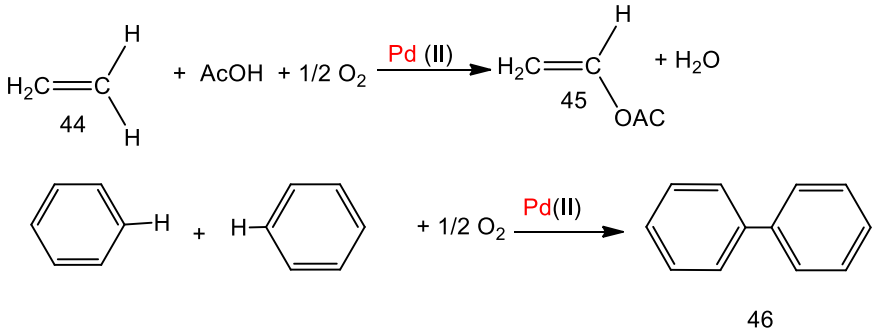
$$A\text{-}H + B\text{-}H + PdX_2 \longrightarrow A\text{-}B + Pd(0) + 2HX \quad \text{eq. 1}$$

$$Pd(0) + 2HX + 1/2\ O_2 \xrightarrow{[OX]} PdX_2 + H_2O \quad \text{eq. 2}$$

$$A\text{-}H + B\text{-}H + 1/2\ O_2 \xrightarrow[[OX]]{PdX_2} A\text{-}B + H_2O \quad \text{eq. 3}$$

Two hydrogen atoms are combined to form Pd(0) and the product A-B after being extracted from the two substrates A-H and B-H. (eq. 1). This reaction is stoichiometric with Pd(II), but when Pd(0) is oxidised in situ to Pd(II) with the proper oxidants (OX), the reaction becomes catalytic (eq. 2), and the entire reaction can be summarised by a third equation.(eq. 3).

Examples of formal dehydrogenation reactions include the oxidative coupling of benzene and the production of vinyl acetate **45** from ethylene **44**. Scheme 19



Scheme 19

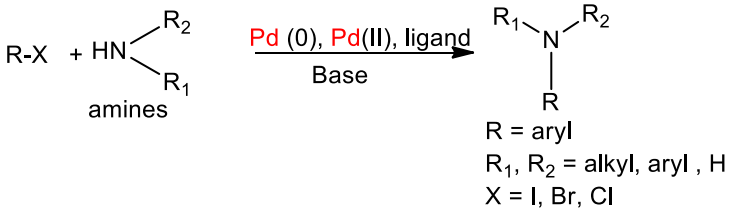
3.6. Palladium-Catalyzed Cross-Coupling Reactions: Generation of Carbon–Nitrogen Bond

Due to the widespread availability of C-N functional groups in natural products, pharmaceuticals, catalysts, and organic materials, as well as their presence in aromatic amines, C-N bond formation is of special interest in organic chemistry. The first amino group was created by Ullmann and Goldberg by combining activated aryl (pseudo)halides with amine nucleophiles. Due to its sharpness and the waste it produces, the use of stoichiometric quantities of copper salts limited this methodology's ability to produce useful materials. Later, the Pd-catalyzed amination reactions, created in the 1990s by Buchwald and Hartwig, have become the most common method for forming C-N bonds.[73-76]

3.6.1 The Buchwald–Hartwig amination reaction.

One useful technique in synthesis chemistry is the amination of aryl, vinyl, and heteroaryl halides and pseudohalides via Pd-catalyzed C-N coupling. Stephen L. Buchwald and John F. Hartwig first described the aryl halide and amine C-N cross-coupling process in 1983.

The Goldberg reaction, nucleophilic aromatic substitution, and other extremely harsh methods were replaced by the synthetic effectiveness of this reaction, which also pointedly increased the substrate scope with the aid of a flexible strategy for the synthesis of (hetero) arylamines on both a small-scale academic level and a large-scale industrial level.[77-79] Scheme 20



Scheme 20

4. Applications of Palladium-Catalyzed C−N Cross-Coupling Reactions

The synthesis of aromatic amines in a variety of basic and practical research fields has been made possible by the Pd-catalyzed cross-coupling of amines with aryl halides and pseudohalides to generate C-N bonds.[80-82] The use of this technique has been extraordinarily varied due to the pervasiveness of arylated amines in pharmaceuticals, organic materials, natural products, and catalysts. Protocols have become more widely applicable and trustworthy as a result of the ongoing development of better ligands and precatalysts.[73, 83-85]

Monodentate symmetrical ligands of the PR3- or PAr_3-type, as well as ligands with various alkyl substituents [for example, n-BuP(Ad)2], have frequently been used.[86, 87] Nevertheless, BINAP **14**, **17** and Xantphos 18, 19 have emerged as the ligands utilised in Narylation processes the most frequently. The supporting ligands DPEPhos, dppf, CyPF-t-Bu, and dppp are further common examples of bidentate ligands. A third class of often used ligands is the dialkylbiarylphosphines **22** Diakylbiarylphosphines can be modified to enhance the desired reactivity or selectivity because of their structural diversity. Moreover, Pd-catalyzed C-N cross-coupling occasionally makes use of ligands like BippyPhos **23** and MorDalPhos **24**. When exposed to base, these air-stable compounds easily transform into the active catalyst. Precatalysts have been described in four generations since their discovery, with progressively easier activation.[88-91] Out of all the precatalysts that are currently accessible, base-

activated precatalysts have been used the most in C-N coupling reactions.

4.1 Applications of C−N Coupling in the Synthesis of Heterocycles

In the fields of natural product synthesis, medicinal chemistry [92], and organic materials, nitrogen-based heterocycles are essential building components. Pd-catalyzed C-N coupling chemistry-based methods for their preparation often offer sizable advantages over conventional ones. Often, structurally complicated heterocycles can be easily produced by tandem procedures comprising at least one C-N bond formation event. The requirement for isolating or purifying intermediate products can often be avoided by performing multistep reactions in a single pot. Therefore, it is typically possible to use one catalyst to complete processes requiring many Pd-catalyzed reactions. This method has been used to manufacture a variety of heterocycles, from tiny molecules to big polycyclic ones that contain many heteroatoms.

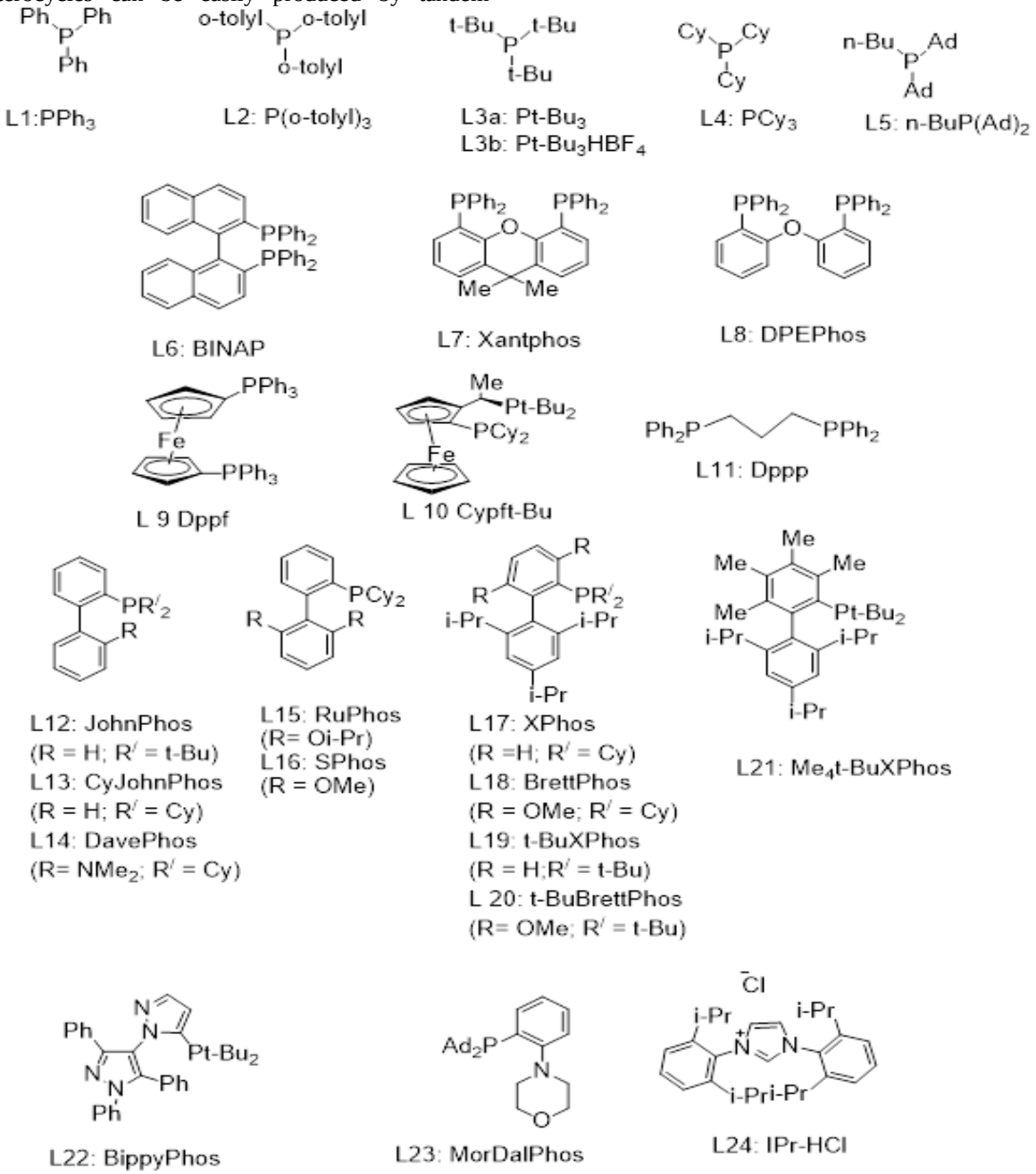


Figure 1: displays a list of the ligands that were most commonly utilized in the examples of C-N coupling in this analysis.

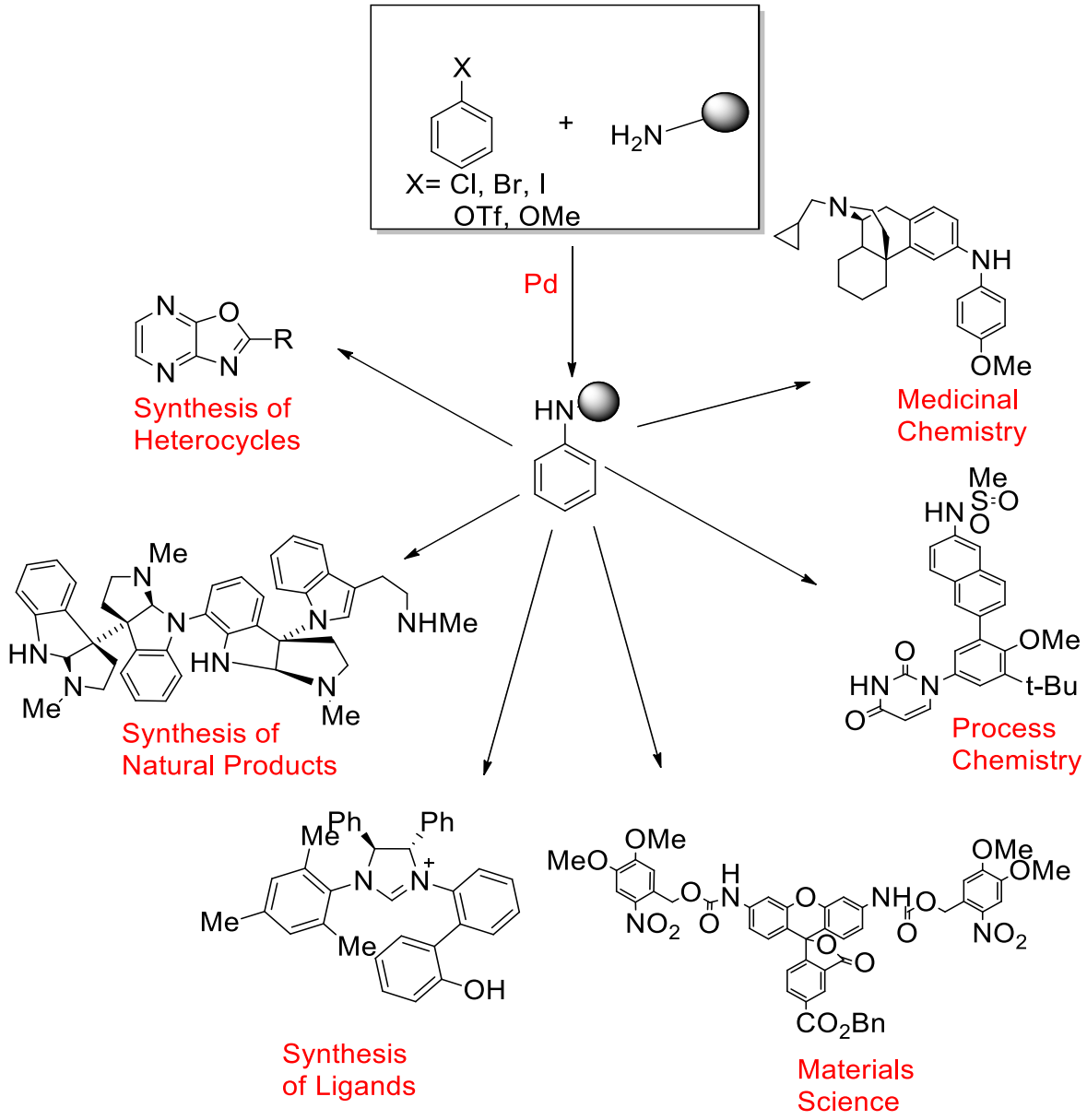


Figure 2. Main fields of application of Pd-catalyzed C−N cross-coupling reactions.

4.2 Applications of C−N Coupling in Medicinal Chemistry

Pd-catalyzed C-N coupling reactions have had the most influence is medicinal chemistry.[93-95] The development of compound libraries for application in medicinal chemistry has been sped up by the ease of the synthetic processes and the adaptability of the results. The production of complex drug-like molecules has recently been studied using high-throughput techniques for Pd-catalyzed C-N coupling at the nanomolar scale. Moreover, the functional group tolerance of these procedures has made it possible for C-N bonds to form along the entirety of synthetic routes.

4.3 Applications of C−N Coupling in Process Chemistry

In recent years, the applications of Pd-catalyzed N-arylation processes in process chemistry have expanded quickly.[95-97] In many instances, the intended cross-coupling reaction can be adjusted to proceed successfully on a wide scale with little catalyst loading, possibly enabling the process to be profitable. New techniques for large-scale metal scavenging, such as the use of functionalized silicas48 and fixed-bed adsorption processes49, which enable isolation of the desired coupling product with low levels of residual palladium, as required by regulatory bodies for active pharmaceutical ingredients, have also aided in the

development of process-scale C-N cross-coupling reactions for the synthesis of pharmaceuticals.
Process chemists frequently use C-N cross-coupling reactions to bypass time-consuming synthesis steps or low yielding processes when the medicinal chemistry pathway is not scaleable. Pd-catalyzed methods are also seen as a good substitute for potentially hazardous procedures or the usage of harmful chemicals. Sometimes, after the coupling reaction has been optimised for manufacturing conditions, the identical N-arylation reactions are used in the discovery and process routes.

4.4 Applications in the Synthesis of Natural Products

Whole synthesis frequently involves extremely difficult transformations in Pd-catalyzed C-N coupling reactions. They are frequently N-arylations that create heterocycles that are incorporated into the final natural product structure. Furthermore, the adaptability of C-N couplings permits the addition of nitrogen centres carrying protective groups, which may be necessary for later steps in the synthesis. In very convergent synthetic methods, Pd-catalyzed C-N couplings have been reported to either form C-N bonds between two sophisticated pieces or to functionalize complicated structures at a late stage.

4.5 Applications in Materials Chemistry and Chemical Biology

N-arylation reactions are frequently used in materials research because they are common in highly conjugated systems in organic materials and because nitrogen-containing functional groups can act as donors. Furthermore, C-N cross-coupling reactions are also used to generate a variety of useful compounds for chemical biology applications (such as biological probes). Several C-N couplings are frequently performed in a single step, either by utilizing aryl halides with numerous reactive sites or by using coupling partners with multiple nucleophilic nitrogens.

4.6 Applications in the Synthesis of Ligands and Catalysts

Nitrogen atoms are frequently included in the ligands for new catalytic processes because of their capacity to coordinate to transition metals. In the synthesis of ligands, Pd-catalyzed N-arylation reactions are used to construct heterocycles or insert chelating functional groups into a current framework. The core of the structure can have many nitrogen atoms connected to it in order to access multidentate ligands. There have also been examples of C-N coupling reactions carried out on both free ligands and ligands that are already bonded to a metal. Another developing application of N-arylation is the preparation of amine-containing organocatalysts for enantioselective catalysis.

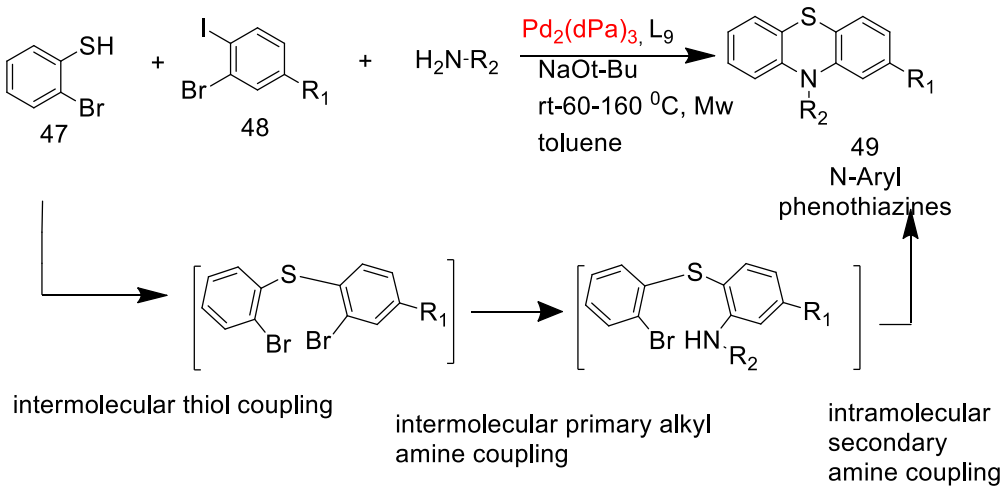
4.6.1 ALKYLAMINES

Primary Alkylamines

One of the most developed Pd-catalyzed C-N cross-coupling reactions is the N-arylation of primary alkylamines. Avoiding the development of undesirable tertiary anilines as a result of the competing diarylation reaction is the basic problem of this transformation. Hence, selecting a supporting ligand wisely is essential for obtaining the appropriate reaction selectivity. The C-N coupling of primary alkylamines has been demonstrated to be possible using a variety of Pd catalysts, with the earliest examples recorded by Wolfe and Buchwald [98] and Hartwig and coworkers [99, 100] based on L6 and L10, respectively, displaying the greatest generality. Since then, a strong ligand known as dialkylbiarylphosphine, L18, [101], has come to light. It exhibits high activity and selectivity for a variety of aryl halides, including aryl chlorides and (pseudo)aryl halides, at extremely low catalyst loadings.[102]

4.7 Applications of the Coupling of Primary Alkylamines in the Synthesis of Heterocycles.

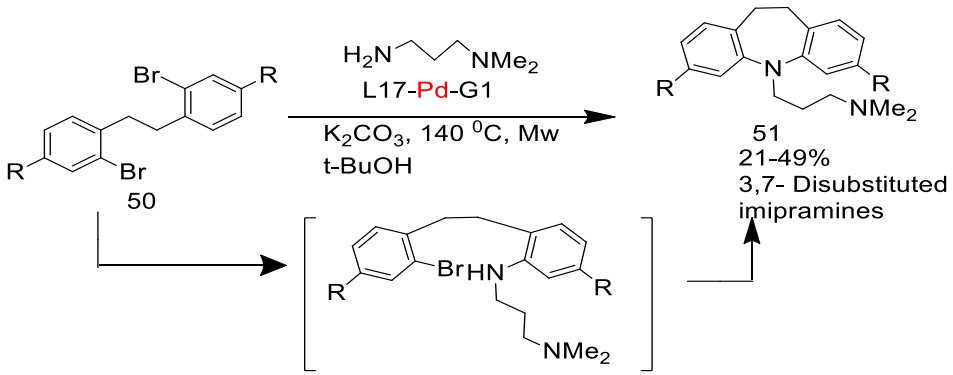
Jørgensen and colleagues presented two strategies for the Pd-catalyzed cross-coupling of primary alkylamines to yield nitrogen-based heterocycles. The first methodology was a one-pot procedure that converted biologically intriguing N-alkyl- and N-arylphenothiazines **49** from 2-bromothiophenol **47**, a primary amine, and a functionalized 1-bromo-2-iodobenzene **48**.[103] Scheme 20
The consecutive inter- and intramolecular N-arylation processes were preceded by a C–S bond formation phase using the more activated aryl iodide due to the strong nucleophilic nature of thiols. Trace amounts of the desired product were produced when triaryl- or trialkylphosphine-based catalysts (L1, L2, L3a) were used, while dialkylbiarylphosphine-based catalysts (L14, L17) encouraged the undesirable intermolecular interaction between the amine and the aryl iodide.



Scheme 20

4.8 Applications of the Coupling of Primary Alkylamines in Medicinal Chemistry.

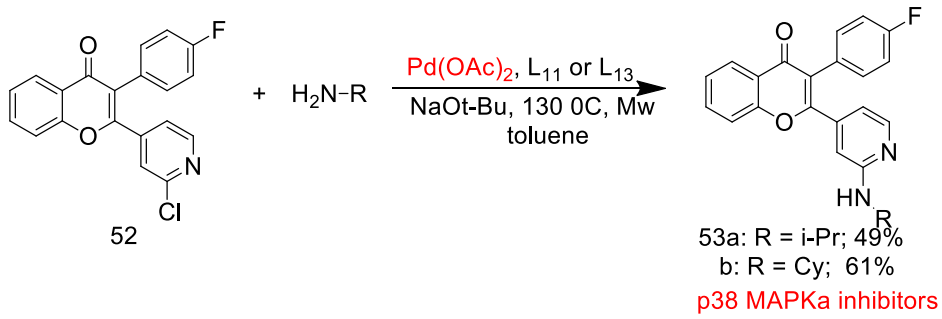
Jensen and colleagues created a number of 3,7-disubstituted analogues of the tricyclic antidepressant imipramine (R = H) 51. [103] In a single pot, the bisaryl bromides 50 were used to produce the dibenzazepines. A first-generation L17 palladium precatalyst with a weak base in t-BuOH permitted the two N-arylation processes.[104] Scheme 21.



Scheme 21

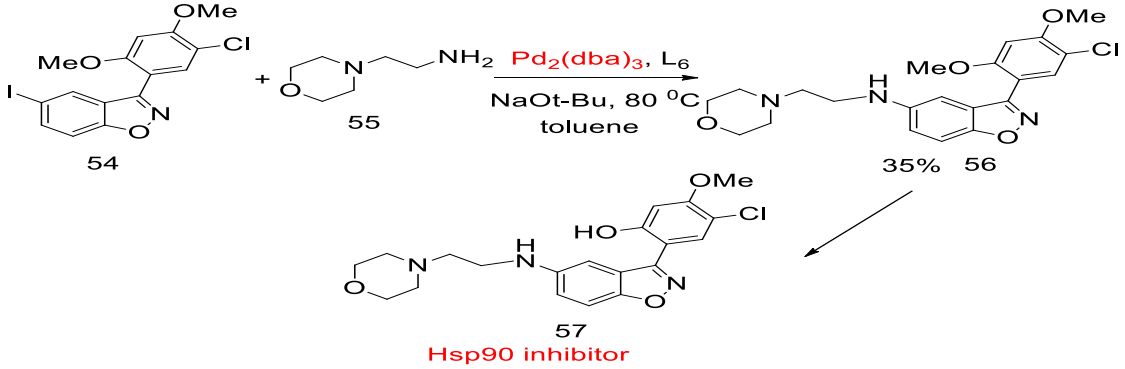
Figure 3 Tricyclic antidepressant imipramine

In order to facilitate the reaction of primary amines and aryl chloride **52** to produce the compounds **53a** and **53b**, which were examined as potential treatments for human breast cancer, L11 or L13 were suitable supporting ligands.[105] Scheme 22.



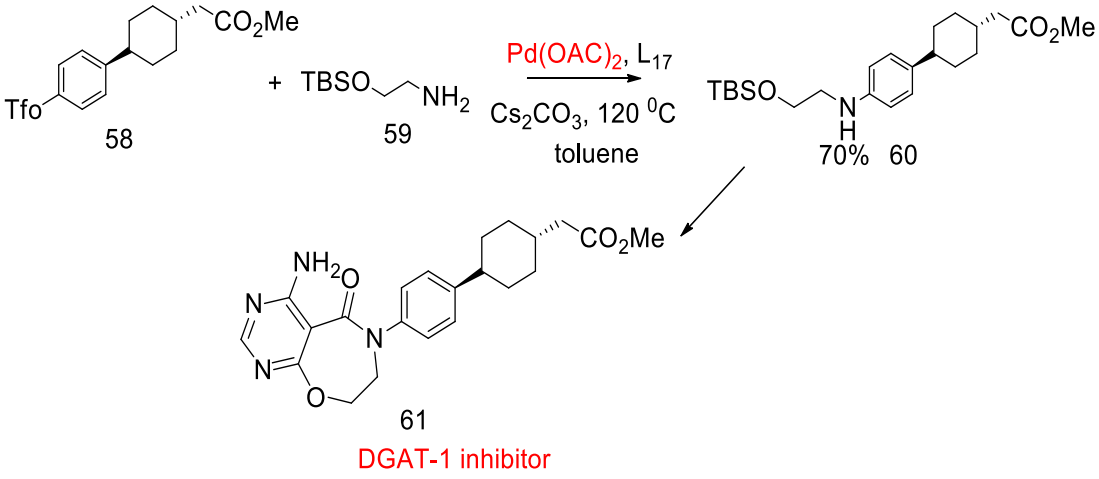
Scheme 22

Scheme 23 provides additional illustrations of the *N*-arylation of primary linear alkylamines. By carefully combining aryl iodide with 1-(2-aminoethyl)piperidine **55** **54**, Gopalsamy et. al. (Wyeth) synthesized Hsp90 inhibitor **57** as a possible anticancer drug.[106]



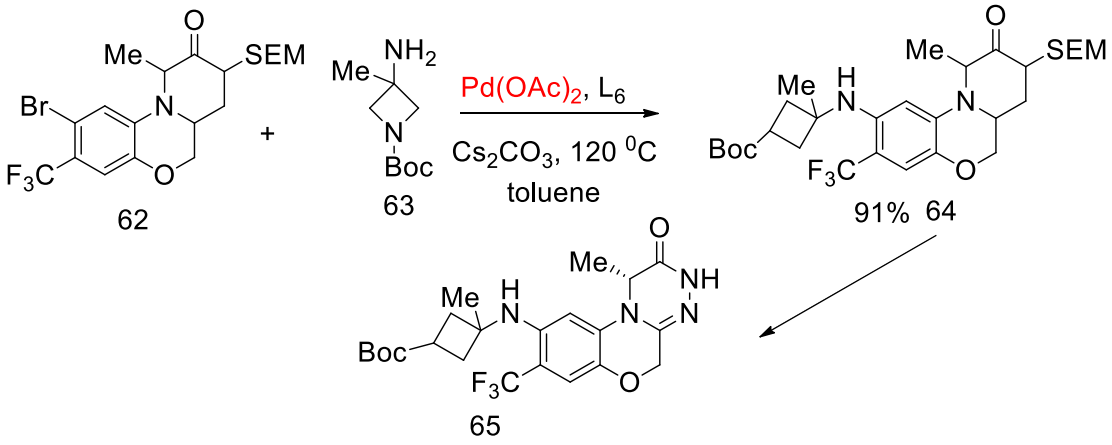
Scheme 23

Pd(OAc)$_2$/L17 was used by Dow and colleagues (Pfizer) to create the DGAT-1 inhibitor 61 for research on the treatment of type II diabetes or obesity.[107] This led to a 70% yield coupling of the enantioenriched aryl triflate **58** to the O-protected main amine. Scheme 24



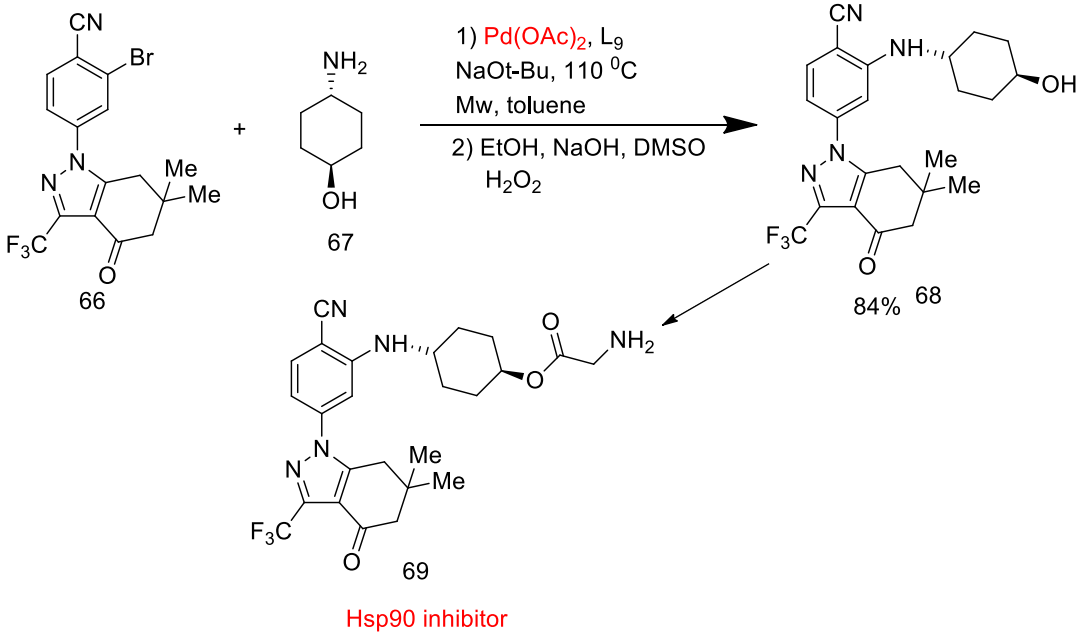
Scheme 24

Similar to this, primary aminocycloalkanes are frequent building blocks in pharmaceutical targets. By combining aryl bromide **62** with aminoazetidine **63**, George and colleagues (AbbVie) produced compound **65**, a promising protein kinase Cθ inhibitor for the treatment of autoimmune diseases. This reaction produced an outstanding yield (91%). [108] Scheme 25



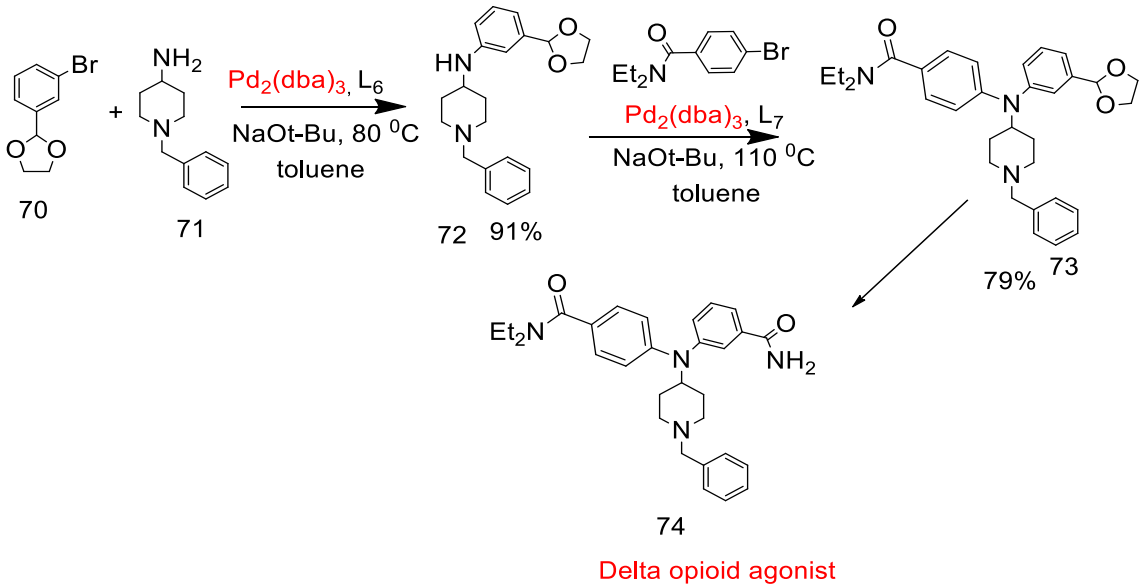
Scheme 25

A number of Hsp90 inhibitors generated from indazol-4-one were also created by Huang and colleagues (Pfizer) using Pd-catalyzed cross-coupling processes, like the N-arylation of cyclohexyl amine 67.[109] Scheme 26



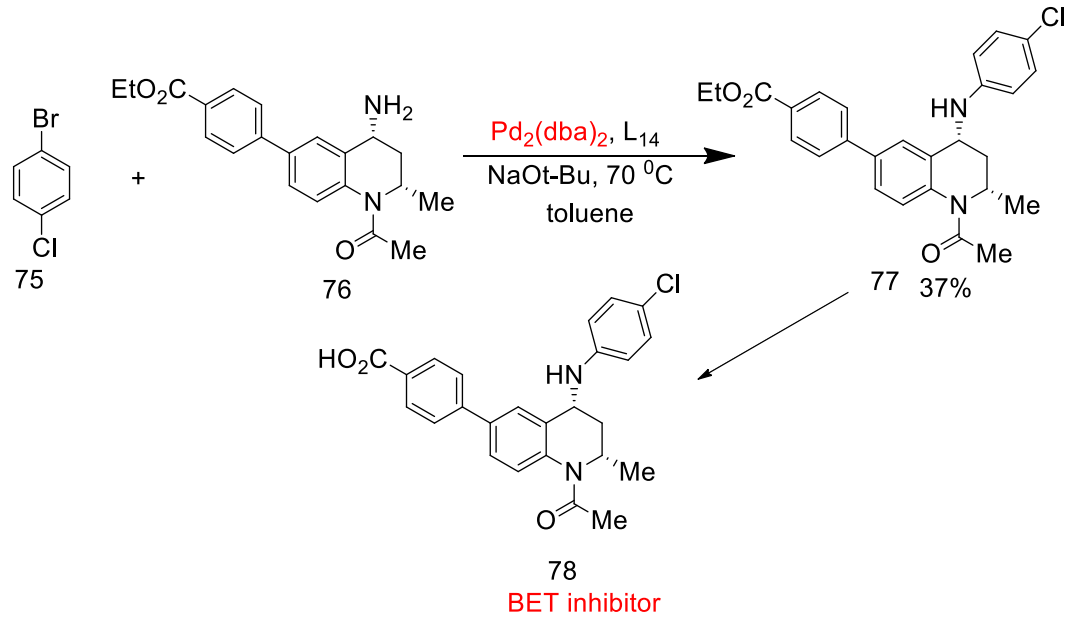
Scheme 26

Two alkylamine C-N bond-forming reactions were crucial steps in Griffin and colleagues' (AstraZeneca) synthetic pathway to δopioid agonist **74**.[110] (Scheme 27). Alkyldiarylamine analogues **74** were easily produced by sequential N-arylation reactions of 4-aminopiperidine **71**. There were two kinds of L6 and L7-based catalysts used.



Scheme 27

Prinjha, Bamborough, and their colleagues (GlaxoSmithKline) documented the N-arylation of chiral aminopiperidine 76 to access an anti-inflammatory compound 78.[111] Scheme 28

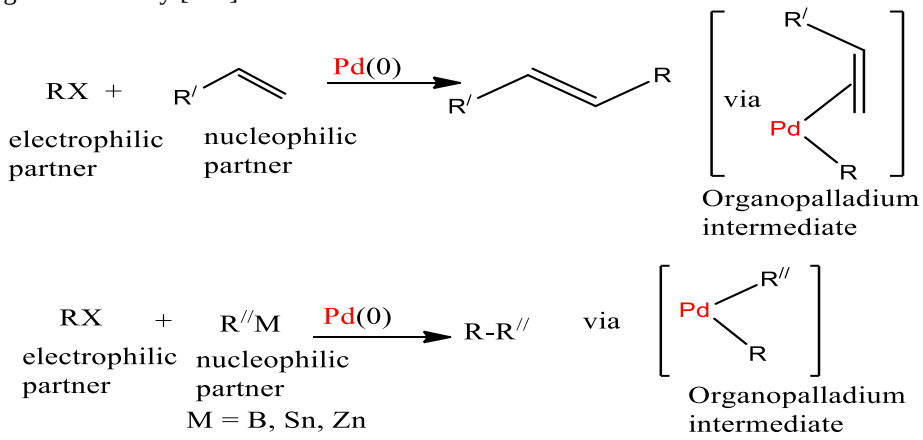


Scheme 28

5. Palladium-Catalyzed Cross-Coupling Reactions: Generation of Carbon–Carbon Bond

There have been numerous attempts to create novel processes involving the formation of C-C bonds because they are one of the most potent tools in synthetic organic chemistry. These attempts are documented in the literature. Numerous catalyst systems have been developed and a wide variety of novel organic molecules have been synthesised as a result of testing a wide range of ligands. Additionally, numerous supported zerovalent palladium nanoparticles and heterogenized palladium complexes were commonly pursued for more sustainable recycling purposes.[112, 113] Cross-coupling reactions facilitated by palladium have become extensively used in the synthesis of functionalized structures, fine chemicals, complex and pharmaceutical intermediates. Heck, Negishi, and Suzuki received the 2010 Nobel Prize in Chemistry

for their groundbreaking work using palladium catalysts in organic chemistry.[114]



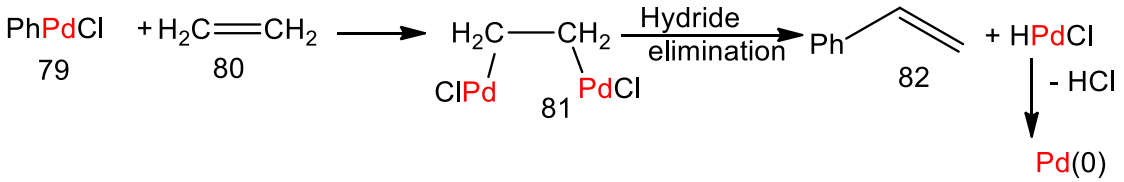
Scheme 29

Palladium-catalyzed cross couplings work on the basis that two molecules are bonded together on the metal by the synthesis of metal-carbon bonds. The carbon atoms bonded to the palladium are brought very near to one another in this manner. They couple with one another in the following phase, which causes a new carbon-carbon single bond to form. According to this concept, there are two cross-coupling reactions that have become crucial in organic synthesis.[115] Scheme 29

Both reactions use an organohalide RX (or related molecule) as the electrophilic coupling partner and are catalysed by zerovalent palladium. The nucleophilic coupling partner in the two processes, however, varies. It is an olefin in the first type, while it is an organometallic complex R"M in the second type. Scheme 29 palladium-catalyzed cross-coupling reactions complement one another in this manner with respect to the nucleophilic coupling partner.

5.1-Heck's pioneering work on cross couplings involving olefins

In 1968 Heck stated that in situ-produced methyl- and phenylpalladium halides (RPdX; R = Me, Ph; X = halide) are added to olefins at room temperature.[13, 116-119] Styrene **82** was produced by adding phenylpalladium chloride (PhPdCl) **79** to ethylene **80** and then elimination the palladium. Scheme 30



Scheme 30

Heck significantly altered his reaction in 1972, increasing the reaction's usefulness for synthesis purposes. The reaction of an aryl halide and an olefin in the presence of a palladium catalyst led to the arylation of an olefin as a result of this novel modification.[120] Figure 4

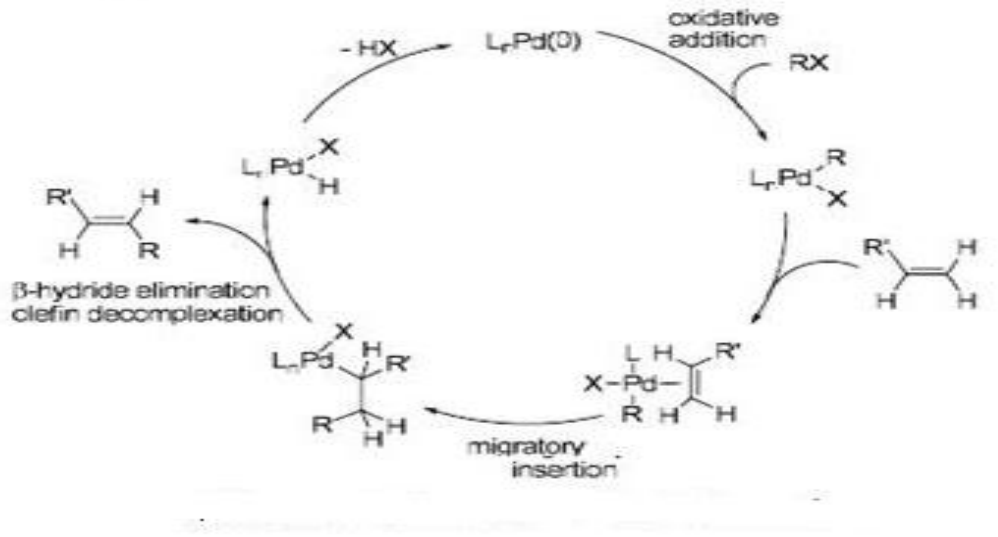


Figure 4 Mechanism of Heck reaction

5.2-Negishi's development of a mild cross coupling

Negishi began a sequence of investigations in 1976 to investigate additional chemoselective organometallic species in the palladium-catalyzed couplings with organo-halides. He used substances with organozirconium or organoaluminum as coupling partners.[121]

In an advance in cross coupling that was catalysed by palladium, Negishi introduced organozinc compounds as the nucleophilic coupling partners in 1977.[122, 123]

The Negishi reaction, which is the name of the novel coupling reaction, has become an essential method for creating carbon-carbon single bonds. Schem 31

$$RZnY + R'X \xrightarrow{\text{Pd-catalyst}} R\text{-}R + MX$$

R, R/ = aryl, vinyl, alkyl
X = halide, triflate, etc

Scheme 31

5.3-Suzuki's discovery of a practical process

Suzuki and coworkers discovered that organoboron compounds can be used as coupling partners in the palladium-catalyzed cross coupling of vinyl and aryl halides.[124] Scheme 32

$$RBY_2 + R'X \xrightarrow[\text{base}]{\text{Pd- catalyst}} R\text{-}R' + MX$$

R,R/ = aryl, vinyl, alkyl
X = halide, triflate, etc

Scheme 32

Later, the process was expanded to incorporate couplings with alkyl groups. The Suzuki reaction is the name of the process. A further important finding was the discovery that arylboronic acids can take part as coupling partners in the cross-coupling reaction that is catalysed by palladium.[125-127]

The mechanism of the Negishi and Suzuki cross-coupling reactions

The cross-coupling reactions by Negishi and Suzuki used organohalide (or an analogous compound such as an organotriflate or a diazo compound) pairs with an organozinc or an organoboron compound, respectively, in the presence of a catalytic amount of a palladium(0) complex. During the reaction, a fresh carbon-carbon single bond is created. Figure 5

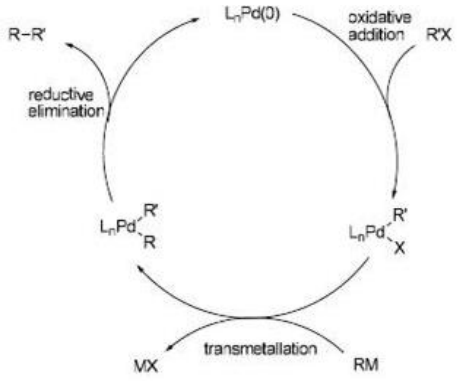


Figure 5

6. Application of palladium-catalyzed cross couplings

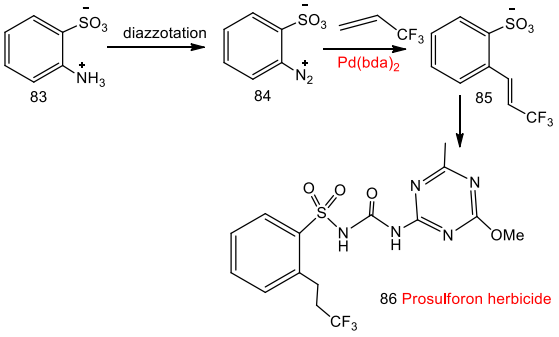
Heck, Negishi, and Suzuki's invention of palladium-catalyzed carbon-carbon bond forming processes has greatly influenced synthetic organic chemistry and has found numerous uses in target-oriented synthesis. Numerous natural products [128-130] and biologically active compounds with complicated

molecular structures have been synthesized using these three cross-coupling reactions.[131-133] They have also been used in the pharmaceutical and fine chemical sectors.[76, 134-138]

6.1 In the fine chemical and pharmaceutical industries

The Heck reaction has been used for a number of large-scale industrial applications, and the cross-

Scheme 33.



Scheme 33

The asthma medication Singulair **87** (Merck, 1993) and the anti-inflammatory drug Naproxen **88** (Albermarle, Hoechst AG, 1994) are two additional instances of pharmaceuticals produced industrially using the Heck reaction.[141] Figure 6

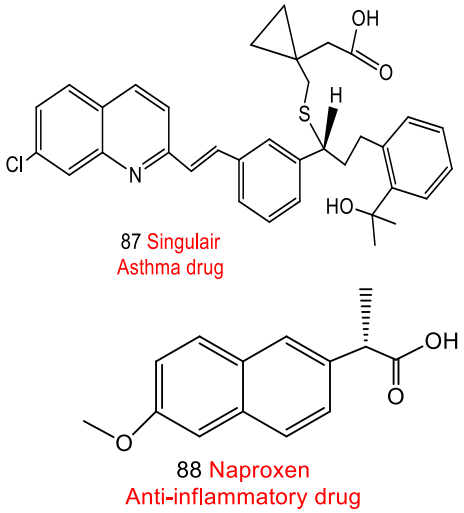
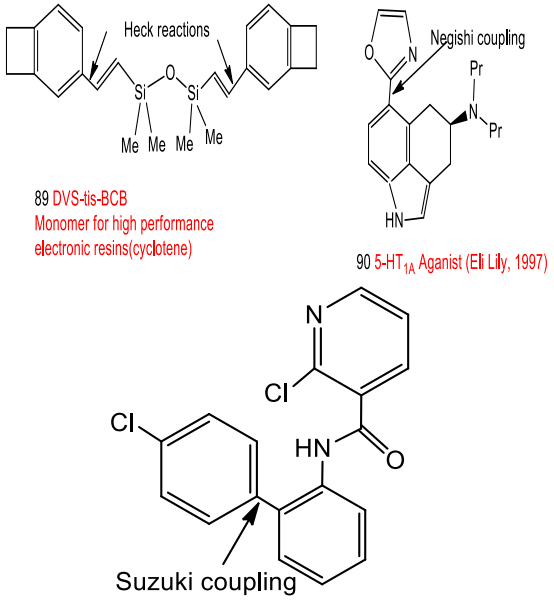


Figure 6

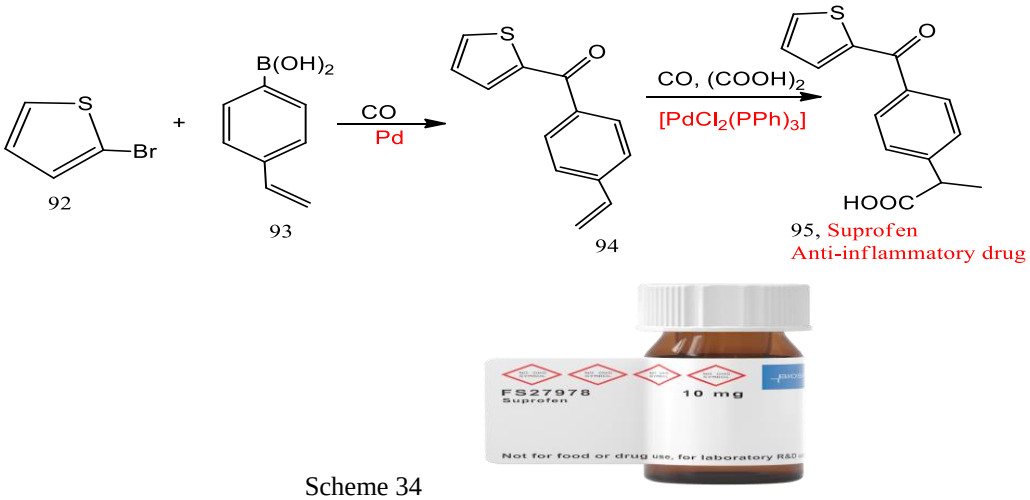
coupling reactions facilitated by palladium are appropriate for large-scale execution. On a multiton basis each year, a number of these processes are carried out. Ciba-Geigy created a method for mass producing the sulfonyl urea herbicide Prosulforon **86**.[139] A diazonium salt produces an aryl palldium intermediate in the crucial Heck reaction, which combines with the olefin.[140]

DVS-bis-BCB (Cyclotene)[142], which is an advanced electronics resin used in a number of crucial microelectronic applications, is one example of how the Heck, Negishi, and Suzuki reactions are used in the production of fine compounds in industry. Some applications of the Heck, Negishi, and Suzuki reactions in 5-HT1AAgonist[79] which is used to address depression and social phobia conditions, as well as generalised anxiety disorder.[143] and the fungicide Boscalid.[144, 145] Figure 7.



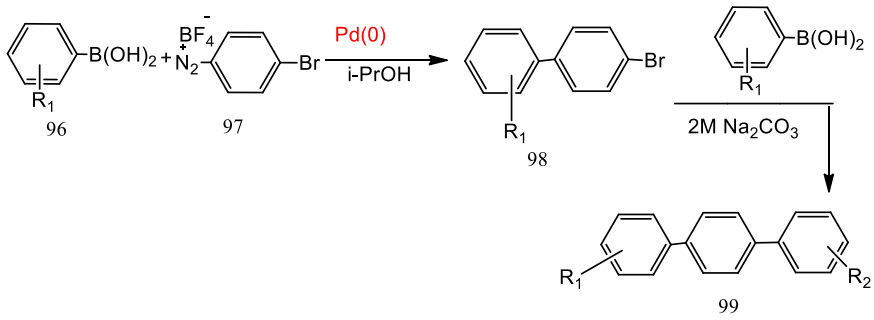
6.2 In the synthesis of other biologically active compounds

Diaryl ketone is a flexible structural motif that can be found in natural products like Cotoin and Papaveraldine, as well as in non-steroidal anti-inflammatory medications like Ketoprofen, Suprofen and UV screens (e.g. Oxybenzone, Sulisobenzone). Recently, a general method of synthesising Suprofen **95** using a three-component cross coupling reaction of carbon monoxide, aryl and heteroaryl bromide **92**, and boronic acid **93** was described. [146] Scheme 34



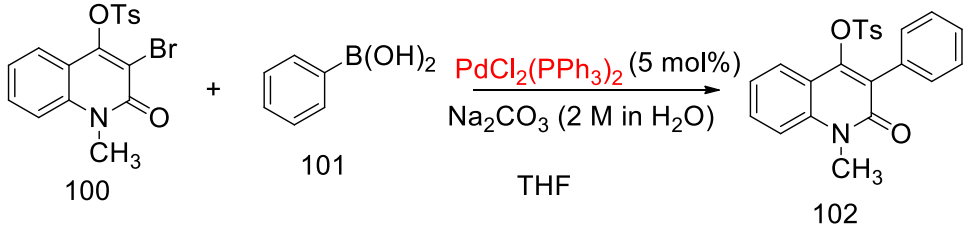
Scheme 34

Terphenyls have gained attention due to a variety of biological activities that are important, such as their strong immunosuppressive, neuroprotective, antithrombotic, anticoagulant, specific 5-lipoxygenase inhibitory, and cytotoxic effects. Terphenyl **99** and polyphenyl systems are also significant structural components in fluorescent substances [147] and liquid crystals. [148] Using the Suzuki coupling process, Taylor and Felpin have created a highly effective one-pot method of producing unsymmetrical terphenyls.[149] Scheme 35



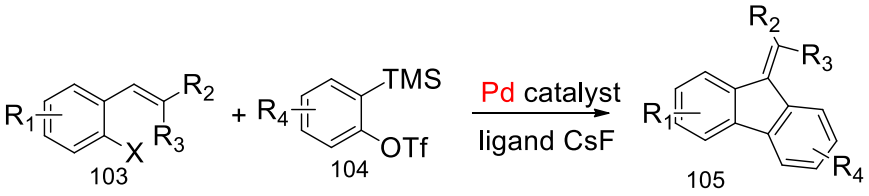
Scheme 35

There are numerous alkaloids with extraordinary biological activities that contain the quinolin-2(1*H*)-one core. Members of this class are used as anticancer, antiviral, and antihypertensive agents, among many other medicinal chemistry uses,[150] a simple and practical method for making 3, 4-Disubstituted Quinolin-2(1*H*)-ones **102** was described. [151] Scheme 36



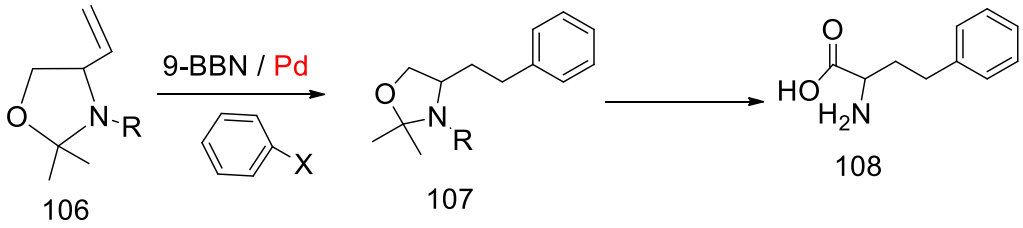
Scheme 36

Key structural components in many compounds with biological action include 9-fluorenylidenes. Substituted 9-fluorenylidenes **105** are produced in excellent yields by the annulation of arynes by substituted ortho-halostyrenes 103, which is palladium-catalyzed. Pharmaceutical [152] and cosmetically significant exist for 9H-fluoren-9-ylidenes' derivatives. Scheme 37



Scheme 37

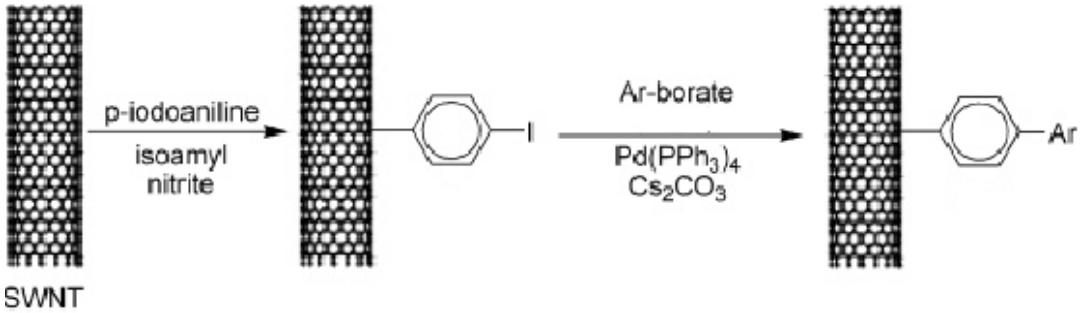
The significance of synthetic amino acids as building blocks for creating peptide-based biologically active molecules is growing in the field of biochemistry. [153] They are also utilized as molecular scaffolds, conformational restrictions, and pharmaceutically useful products. [154] Particular focus has been paid to homophenylalanine analogues as components of potential pharmaceuticals, such as 4-methoxyhomo-phenylalanine. [155] Scheme 38 shows how the compound described by Johnson et al. was synthesised. [156]



Scheme 38

6.3 In Carbon nanotubes

Unique nanostructures called carbon nanotubes have exceptional electrical and mechanical characteristics. Carbon nanotubes of the SWNT (single wall nanotube) variety are finding increasing use in pharmacology and technology. In this regard, functionalizing carbon nanotube walls is becoming more important.[157] Cheng and Adronov published a technique for Suzuki coupling reaction-based covalent functionalization of SWNTs with chromophores.[158] Porphyrin, fluorene, and bithiophene are potential candidates for the Ar group in Figure 8



7. Palladium organometallic anticancer agents

Organopalladium compounds, among others, have attracted a lot of attention in recent years due to their typically high stability under physiological conditions. A large number of these substances have demonstrated promising antiproliferative efficacy in vitro and in vivo against a variety of cisplatin-resistant and cisplatin-sensitive cancers, and they occasionally displayed a different mode of action from platinum-based medications.

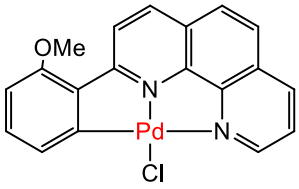
The most significant palladium organometallic compounds as potential anticancer agents:

7.1 Palladacyclic complexes

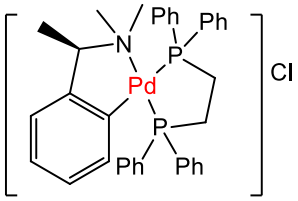
Cyclopalladated imines and tetranuclear cyclopalladates.

Palladacyclic species play a significant role among the organopalladium complexes that have received the greatest attention as prospective anticancer treatments. These compounds are often stable in both ordinary organic solvents and the

physiological environment because they contain multidentate ligands and at least one palladium - carbon link. Numerous examples of palladium complexes falling under this category were reported. Some of these show an unusual anticancer impact on both cisplatin-sensitive and cisplatin-resistant cell lines, according to the review by Fairlamb and Kapdi[148] from the beginning of 2014.. Figure 9



109



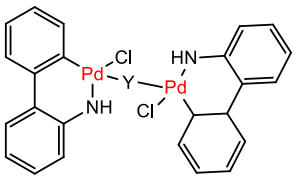
110

Figure 9 Cyclopalladated complexes with anticancer and antiparasitic activity

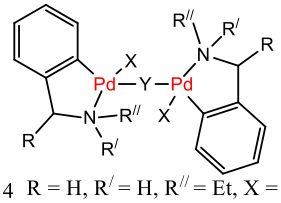
Mono- and dinuclear endo cyclopalladated benzophenone imines were synthesised and their biological activity was thoroughly examined by Albert and colleagues [159,160]. Particularly, MDA-MB-231 and MCF-7 cancer cells responded favourably to the antiproliferative activity of cyclopalladates **111** and **112** with ahydrogen on the nitrogen atom. Figure 10

7.2 Dinuclear palladacyclic complexes with bridging diphosphine ligands

In the area of polynuclear complexes, Karami et.al. revealed dinuclear cyclopalladates with exceptional anticancer activities between 2014 and 2017. Complexes **113** and **114** in particular, which include the bridging diphosphines DPPF (1,1'-bis(diphenylphosphine)-ferrocene) and BPP (1,3-bis(4-pyridyl)propane) showed high cytotoxicity against the JURKAT and SKOV3 cell lines.[161] Both substances showed considerable binding affinity for DNA and BSA and lesser cytotoxic activity towards healthy peripheral blood mononuclear cells (PBMCs). Figure 11



113 Y = dppf
Y = bpp



114 R = H, R/ = H, R// = Et, X = Cl, Y = dppe
R = H, R/ = H, R// = Et, X = Br, Y = dppe
R = Me, R/ = Me, R// = Me, X = Cl, Y = dppf

8. Conclusion

Palladium is a rare metal that works as a "matchmaker" or catalyst to combine various ingredients to create helpful products for flat-screen displays, cancer treatments, asthma medications, and more.

Additionally, palladium is now a common component of almost every car automotive catalyst, which uses it to reduce hazardous emissions from internal combustion engines. The crucial function of palladium, on the other hand, is unknown to the broader public but has since been recognized with the 2010 Nobel Prize for Chemistry.

Due to their typically great stability under physiological conditions, organopalladium compounds, among others, have attracted considerable interest in medical uses.The cross-coupling reactions, which are palladium-catalyzed, have grown to be extremely effective processes for producing new C-C and C-N bonds. Typically, with the aid of organopalladium molecules, bonds are formed between various carbon nucleophiles and less reactive organic electrophiles.

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