# 1. Introduction:

Chemistry steadily and firmly flourishes towards executing and fulfilling the demands of growing civilization. As a result, during the last century, it has gifted numerous products like medicines, high-performance materials, pesticides to the human society. New demands arise on a continuous basis and regularly, thereby forcing chemistry to acclimatize with the growing trends and needs of the hour. There is always a constant and growing need for the development of innovative compounds which increases the complexity of the targeted molecule in the arena of industrial and academic research.

In this context, research towards the design of reaction strategies, for carbon-carbon and carbon-heteroatom bond formation reactions, constitutes an exciting and never ending field in the arena of synthetic organic chemistry. These bond forming reactions are considered and reckoned as extremely powerful tools for the synthesis of a wide range of essential compounds existing in the fields and areas of agrochemicals, pharmaceuticals, natural products and fine chemicals etc. Literature from the last few years has reveals a number of reaction protocols for the stated bond forming reactions. These classes of reactions involve mainly transition metal catalyzed cross-coupling reactions which utilize copper, palladium, nickel, cobalt etc. as major transition metals for their catalytic performance. On the other hand, a majority of these bond formation reactions which have an oxidation step, which is considered as one of the most important step in the catalytic cycle. In the present thesis, we would like to focus on some of these types of oxidative C-C and C-heteroatom bond formation reactions.

At first, we intend to document some major C-C bond formation reactions till date. This class of reaction has attracted a great deal of attention since a very long time. Traditionally, Friedel Crafts reaction, nucleophillic addition and substitution reaction, Wurtz type reactions are considered as the key methods for C-C bond formation to connect two simpler molecules and provide a bigger or complex molecule. The efficacy of C-C bond formation reactions has been increased by introducing transition metal catalysis. The chemistry of first transition metal catalyzed C-C bond formation reaction was presented by Glaser [1] in 1869. It was a homocoupling reaction of phenyl acetylene in the presence of Cu catalyst, furnishing 1,4-diphenyl-1,3-butadiyne (**Scheme 1**).
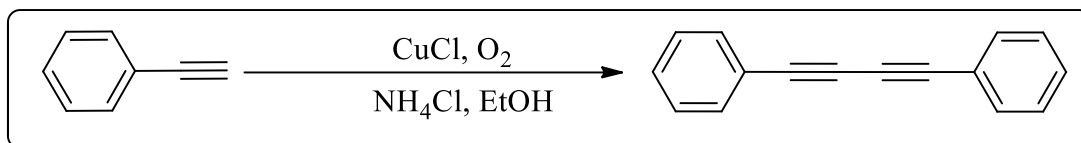
Scheme 1: Cu catalyzed Glaser coupling reaction

After few years past, in 1901, another Cu catalyzed homocoupling reaction [2] was reported by Ullmann. The reaction protocol involved stoichiometric amount of Cu metal mediated dimerization of 2-bromo and 2-chloronitrobenzene (**Scheme 2**).
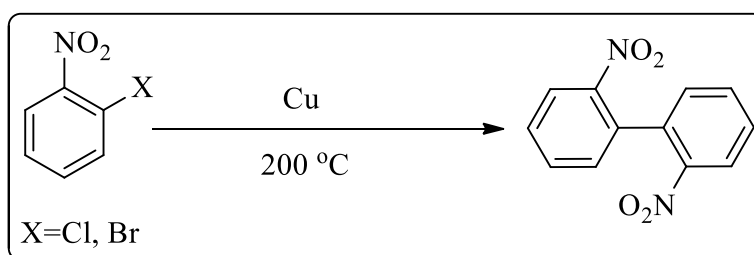

Scheme 2: Cu catalyzed Ullmann homocoupling reaction

In 1943, Kharash [3] added a new dimension to transition metal catalyzed cross-coupling reaction for the formation of C-C bond. He presented $CoCl_2$ catalyzed cross-coupling reaction between vinyl and aryl bromide with aryl organomagnesium species and became the first person to develop transition metal mediated cross-coupling reaction between two coupling partners (**Scheme 3**).
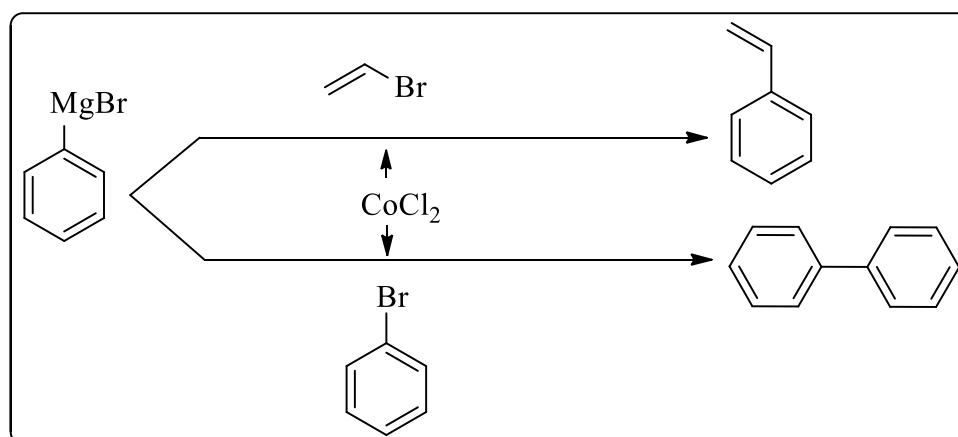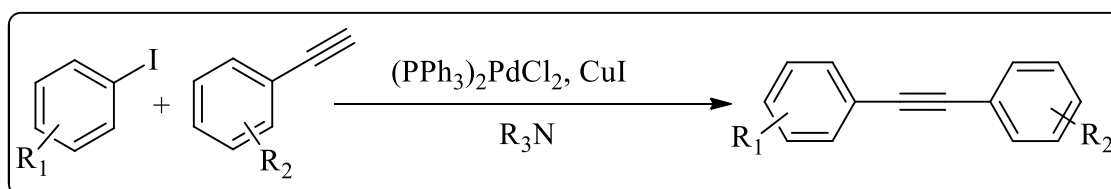

Scheme 3: First catalytic cross-coupling reaction forming C-C bond

But, it was observed that in case of cross-coupling reactions, a numbers of side products were obtained due to homocoupling, isomerization, functional group inferences and β-hydride elimination etc. This lack of selectivity issue forced the researchers to shift their attention towards the development of some innovative protocols with high selectivity. Amongst them, the chemistry of palladium catalysis in C-C bond formation reaction was a revolutionary one. Richard Heck was the first person to introduce Pd catalysis in cross-coupling reaction. In 1968, he reported [4] a cross-coupling reaction between organomercuric compound and alkene in presence of catalytic amount of Li_2PdCl_4. In subsequent years, this work was extended by Heck and Mizoroki by replacing toxic organomercuric compound by aryl halide (**Scheme 4**).
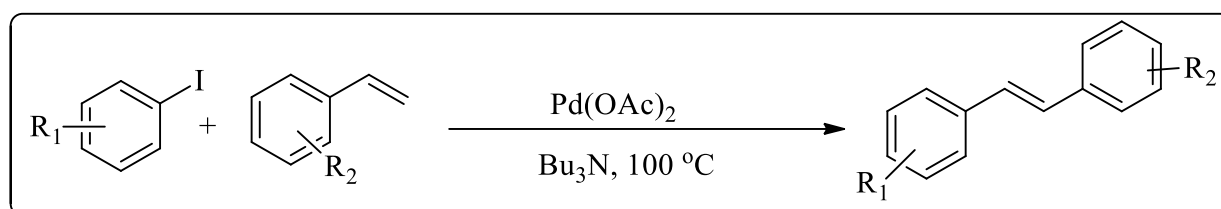

Scheme 4: First intermolecular Heck reaction

In 1975, Sonogashira, Tohda and Hagihara [5] first reported a cross-coupling reaction between terminal alkyne and aryl or vinyl halide producing a substituted alkyne product. In this reaction, co-catalyst was also used along with palladium, catalyst to promote the reaction rate in presence of an amine base (**Scheme 5**).


Scheme 5: First Sonogashira cross-coupling reaction

In the contemporary times 1977 Negishi in 1977, [6] reported a general protocol for Pd catalyzed cross-coupling reaction between organozinc compounds and organic halides, furnishing biaryl compounds (**Scheme 6**).

$$R_1X + R_2ZnX \xrightarrow[\text{Cl}_2\text{Pd(PPh}_3)_2 + 2(i\text{-Bu})_2\text{AlH}]{\text{Ni(PPh}_3)_4 \text{ or}} R_1 - R_2$$
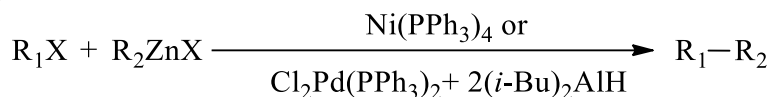
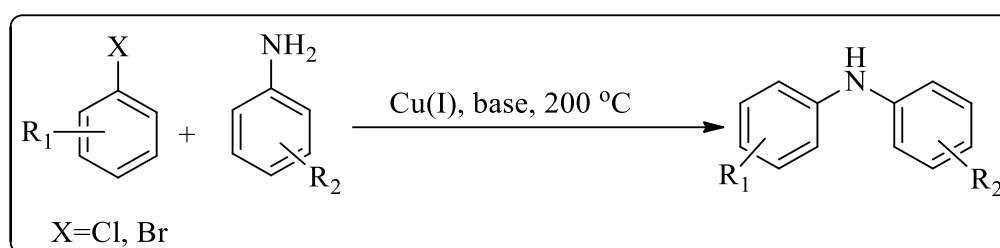Scheme 6: Negishi cross-coupling reaction

Suzuki and Miyaura, in 1979 [7] established an inventive synthetic protocol for cross-coupling reaction, which utilized organoboron compounds and aryl halides as coupling partner for biaryl synthesis. This reaction protocol was easily accepted by research community because of facile reaction condition and remarkable features inherited with the starting material organoboron compounds such as resistance towards heat, moisture and air. They are also commercially available and tolerant towards a wide range of functionalities (**Scheme 7**). Owing to the tremendous contribution
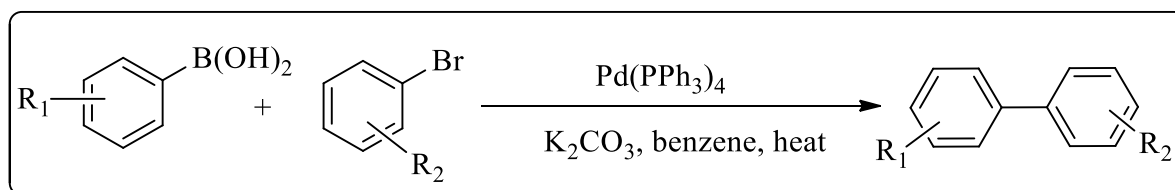
Scheme 7: Suzuki-Miyaura cross-coupling reaction

towards organic synthetic chemistry for providing novel routes for C-C bond formation reaction, Suzuki, Heck and Negishi were awarded the 2010 Nobel Prize in Chemistry. Apart from these, large numbers of successful achievements were found in the area of C-C bond formation reaction. Some of the common reactions amongst them include Stille, Beletskaya, Kumada, Corriu, Kochi, Tsuji, Trost etc. In all of the stated reactions, oxidative addition is found to be a major step and so, they can be termed as oxidative C-C bond formation reaction. Although these reaction schemes provided some general procedure for construction of molecules having C-C bond, but, in most of the cases they involved high temperature, expensive ligands, inert atmosphere etc. which are usually against the principle of green chemistry. Therefore, nowadays, researchers are paying considerable attention for fine tuning of these reaction avoiding ligands and higher temperature etc.

Parallel to this, we also emphasize on C-heteroatom bond formation reactions which include mainly C-N, C-O and C-S type bond formations. However, we have limited ourselves to a discussion of C-N and C-O bond forming reactions. The C-N bond formation reactions find great importance due to the vast application of *N*-containing compounds in the field of pharmaceuticals, natural product and industrial chemistry [8]. These compounds are mainly synthesized by carrying out cross-coupling reaction between a nitrogen nucleophile and an aryl coupling partners using Cu and Pd metal catalysts. Ullmann in 1903, first described [9] a copper catalyzed C-N bond formation reaction by implementing a cross-coupling reaction between aniline and aryl halide (**Scheme 8**).

Scheme 8: Ullmann cross-coupling for C-N bond forming reaction

This reaction scheme was also explored towards C-O and C-S bond formation by using *O*- and *S*- nucleophiles respectively producing diaryl ether and diaryl thioether. The first palladium catalyzed cross-coupling reaction for the construction of C-N bond was developed by Buchwald and Hartwig [10] and it gained considerable recognition in the research community (**Scheme 9**). It was a cross-coupling reaction between organic halide and *N*-nucleophile and had high substrate diversity and functional group tolerance.
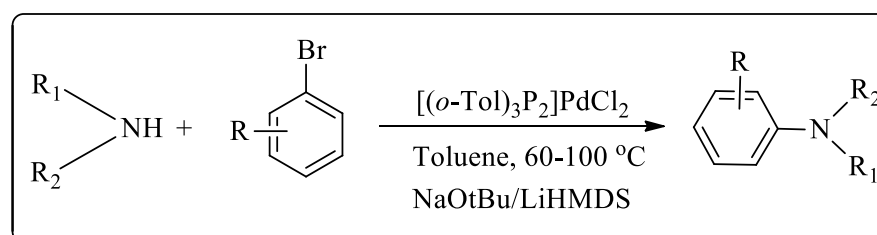
Scheme 9: Buchwald Hartwig C-N bond forming reaction

Another massive development was put forward by Chan and Lam in 1998 for construction of C-N, C-O and C-S bonds [11] by using Cu catalysis. They disclosed a method using arylboronic acid as a successful coupling partner for *N*-arylation, *O*-arylation and *S*-arylation using corresponding nucleophiles under mild condition (**Scheme 10**). The method received popularity within a very short time due to the simple reaction condition and useful starting material.
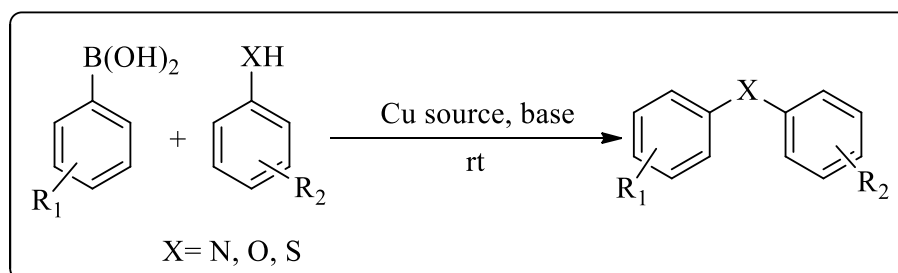
Scheme 10: Chan-Lam cross-coupling reaction

After these pioneering developments, many efforts were given towards the concerned topic using various phosphine or *N*-based ligand system because ligands play a significant role in the activity of the catalyst. Most of the ligands promote the oxidative addition pathway of the transition metal catalyzed cross-coupling reaction and hence take a major role in boosting up the reaction.

Although the development of these classes of transition metal catalyzed C-C and C-heteroatom cross-coupling reactions, provided new routes in synthetic organic chemistry, yet most of the reaction protocols were associated with some major drawbacks like high temperature, toxic solvents etc. Most importantly, the ligands were also found to be toxic and expensive. Therefore, researchers are trying to find solutions to overcome these problems. Nowadays, nanocatalysis comes out to be an excellent area which can triumph over expensive ligand assisted condition. The metal or metal oxides nanoparticles (NPs) are very reactive catalyst having a high surface to volume ratio [12]. Literature reveals a variety of reports in which Pd or Cu based NPs have been executed in ligand free C-C and C-heteroatom bond formation reaction. But, the procedures for NPs synthesis are not very smooth; as a result, lots of researches are going on for facile development of NPs synthesis. Similarly, some highly active catalysts are also designed

which can lower the activation energy of the reaction pathway and can provide room temperature feasibility for the reaction.

On the other hand, heterogeneous catalysis is a growing area of research nowadays. Even though homogeneous catalyst affords high selectivity and enhanced reaction rate, it added some shortcomings such as imperfect separation from the reaction mixture and lack of reusability. These shortcomings restrict homogeneous catalyst for widespread application in industrial purposes. In contrast, today's world prefers more economical pathways for a chemical reaction; thereby, heterogeneous catalysis occupies a superior position to homogeneous catalysis from economical point of view also. So, at present, plethora of reports are found on heterogeneous catalysis for C-C and C-heteroatom bond formation reactions where homogeneous metal catalysts or complexes are embedded on different solid surfaces like clay [13], zeolite [14], charcoal [15], silica [16], microporous silica [17], graphene oxide [18] etc. Therefore, it is of high demand and need of the hour to develop mild protocol for C-C and C-heteroatom bond formation reaction by employing heterogeneous catalysis.

Another uprising field, being noticed in the recent decade, is the functionalization of aromatic compounds via the construction of C-heteroatom bond. C-heteroatom bond containing moieties like aromatic amines, nitro arenes, phenols, aromatic azides are considered as universal building blocks for various pharmaceutical compounds and also establish their application in natural product chemistry. So, researchers are paying more attention towards aromatic functionalization using easily available useful substrate. Lots of reports are found on this subject matter which exploits aryl halides as substrate for the desired transformation. But, aryl halides are not considered as environment friendly species as they produce halogenated by products. In case of aryl chlorides, harsh conditions needed for the required transformation. Again, aryl bromides and iodides are very costly. So, to overcome these problems, in recent times, arylboronic acids are used for the transformation reactions whose by products are not harmful to the environment and they can undergo reaction under milder condition as compared to halides. These classes of reactions can also be termed as oxidative C-heteroatom bond formation reactions because these reactions experience transformations from a less electronegative boron atom to a higher electronegative atom compared to boron.

So, considering from all quarters and the above factors, in the present thesis we focus on development of some mild and efficient protocols for oxidative C-C and C-heteroatom bond formation reaction.

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