

Copper catalyzed coupling reaction

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Abstract:

In Ullmann condensation reaction carried using Copper as catalyst & bond formation between carbon-carbon & carbon- heteroatom is important in the organic synthesis. Copper is environmentally friendly catalyst & another importance it is inexpensive. Selectivity & scope of the copper catalyst is similar to the palladium catalyst cross coupling reaction.

Keywords: Bond formation, Copper

Introduction:

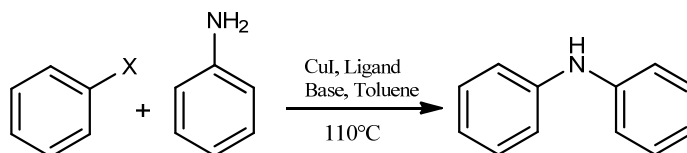
Transition metal catalysed C-N bond-forming mostly used in pharmaceutical industry. Catalysis is important in the organic reaction. Last three decades Palladium catalyst use for the C-C & C- Heteroatom coupling reaction but some limitation of N-arylation of amine. So another Metal i.e Copper use widely in cross coupling reaction. A classical Ullman reaction, C-C & C- heteroatom bond formation.[1] An organocuprate use for the formation of C-C bond. After palladium catalyst use for cross coupling reaction rarely use copper catalyst in reaction, but classical Ullmann & Goldberg reaction unshakable position.[2] Now a day copper complexes use as catalyst in the cross coupling reaction which are parallel to the palladium catalyzed reaction. A role of catalyst is oxidative addition of starting material, transmetallation & reductive elimination reactions. Copper is productive & versatile catalyst than neighboring Nickel.

In comparisons with the Copper over palladium Copper has following advantages. Copper has oxidation state ranging from 0 to +3 but Palladium having range of 0 to +4 oxidation state but 0 and +2 are the only stable oxidation state which are used in coupling reactions. A cross coupling reaction of copper is take place in +1 & +3 oxidation state.[3] Another important of copper over palladium is the accessibility of odd electron in states of copper, implying that copper can take part in redox single electron transfer process. Copper has odd

electron so it take part in redox single electron transfer process. Which are similar to the Sandmeyer reaction.[4] A free radical mechanism is carried out in presence of copper catalyst in the Sandmeyer reaction. Copper reagent is poorly soluble in the reaction medium and also cheaper as compare to Palladium copper is used as either oxidant & used as electrophilic coupling partner. In Cu (I) catalyzed reaction is carried out different ligand. A catalyst is regenerated at the reductive elimination step.

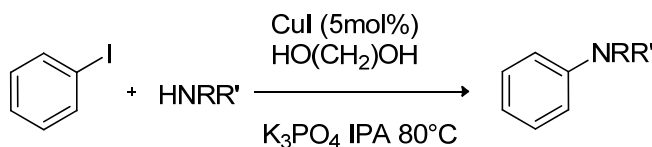
Arylation of aromatic amine:

An aromatic amine is arylated using aromatic halide & copper catalyst i.e Cu(I), Cu(II) Copper oxide reaction is take place at higher temp & long time heating a reaction mixture. But using a copper catalyst along with appropriate bidentate ligand reaction is take place at lower Temp in presences of non-polar solvent. Arylation of aniline by iodo benzene in presences of Copper iodide, ligand, base in Toluene at 110° C arylation is carried in mostly with Iodo, Bromo derivatives & unlike chloro derivatives.[5]



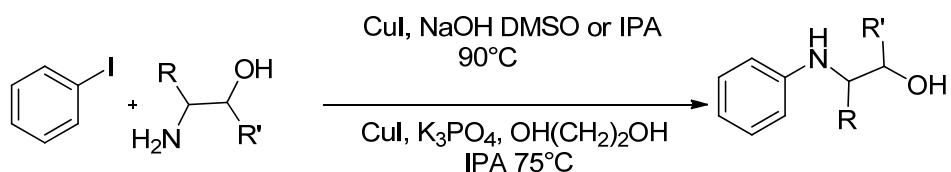
Arylation of aliphatic amines

In the conventional Ullmann reaction is the arylation of aliphatic amines, give poor yields so ligand assisted reaction forward reaction. Some Ullmann type reaction is take place without catalyst & ligand e.g CsOAc used in the Arylation of primary aliphatic amine using iodo benzene under mild conditions. A Cu catalyst secondary acyclic amine has low reactivity due to the steric hindrances. Arylation of primary aliphatic amine, & saturated heterocycles using catalyst K_2CO_3 , K_3PO_4 ligand Ethylene glycol, amino acids using polar & non polar solvent.[6]



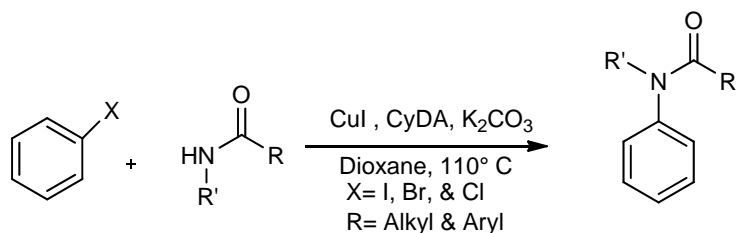
Arylation of Substituted alkyl amines

Arylation of aminoalcohol using aryl iodides using copper iodide as a catalyst NaOH, DMSO –water (2:1) or IPA as solvent at 90° C while another reaction should be perform using Copper iodide, ethylene glycol, (stoichiometric) , K₃PO₄, IPA at 75°C.[7]

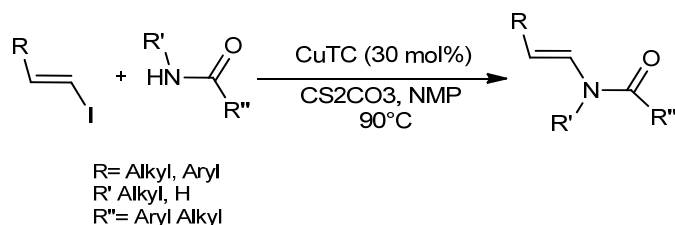


Arylation of amides

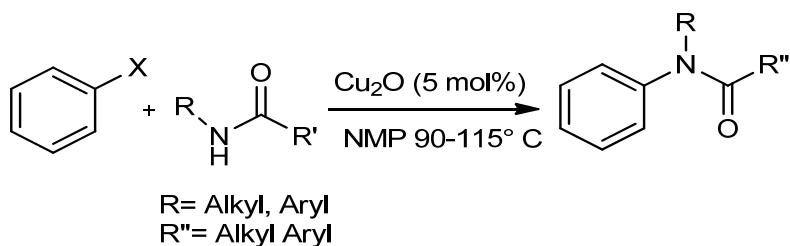
A copper catalyst coupling of amide to aryl halide or vinyl halide in presences of mostly bidendentate amine ligands, base K₂CO₃, K₃PO₄, & using various solvent like toluene, dioxane, THF, DMF this reaction is known as Goldberg reaction. A Goldberg reaction is similar to the Ullmann reaction. A reaction should be carried out in reflux Temp. or lower temp. In the reaction not use strong base because amidate formed binds to copper & copper inhibits its catalytic process. The arylation of amide is chemoselective in this reaction disubstitution on the Nitrogen amine is impossible. A aryl chlorides including electron donating group increase the reactivity of aryl chloride so its react with amide using dimethyl cyclohexyldiamine (DMCyDA) as a ligand & Chlorobenzene used as solvent. [8] In this reaction Cu(I) catalyst used as (5- 20 mol%)



A Goldberg reaction is carried out as absences of ligand. In this reaction Liebeskind's catalyst copper(I) thiophene- 2- carboxylate (CuTC) is used. Reaction is performed in the polar solvent like NMP & DMSO is used while anhydrous Cs₂CO₃ or Rb₂CO₃ base are used under N₂ atmosphere.[9]

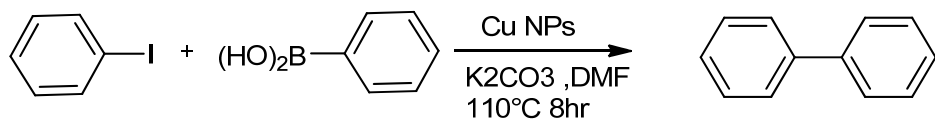


Generally coupling of amide with aryl halide using Copper iodide, ligand, base, but a coupling of amide with aryl halide in the absence of metal complex, ligands but using Cu_2O , Cs_2CO_3 , Sodium tert-butoxide, NMP at $90-110^\circ\text{C}$ it gives coupling product.[10]



Suzuki reaction Using nano Cu

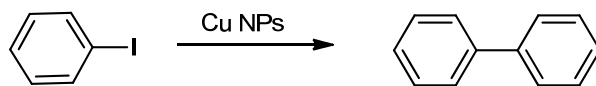
It is a cross-coupling reaction between an aryl halide with a boronic acid. It is important in organic synthesis. Suzuki cross-coupling reaction is generally carried out using Palladium, Nickel & Iron. Scientist Rothenberger et al. carried out Suzuki coupling reaction using nano copper particles. When Suzuki coupling reaction is carried out using Cu nanoparticles, it shows significant activity & reaction is completed within 8 hr at 110°C . [11]



Ullmann reaction using nano Cu

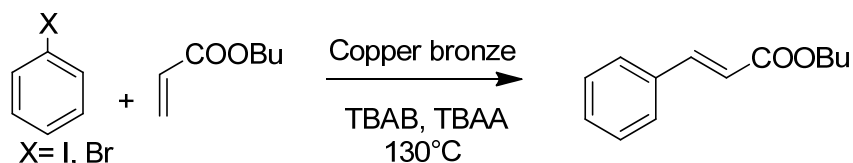
When Ullmann reaction is carried out using uncapped and undefined macrosized copper powder, it showed only 43% conversion of iodobenzene to biphenyl in 5 hrs, while nano copper prepared by Citrate method in this method got (66nm) particle size. Using this nano catalyst, 88%

conversion of Aryl iodide into the product. When finer nano copper size is 8nm it gives 95% conversion [12]



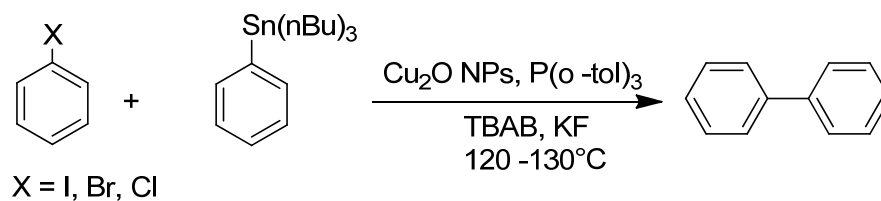
Heck reaction using nano copper

When copper bronze alloy treatment with iodo benzene a Cu(4nm) nano partical are formed. Which play active role in the reaction. In heck reaction activated alkene is treated with aryl halides using nano Copper & base at 130°C. Reaction is completed in 16 hrs. Activity of catalyst is increases after recycle it was maximum use in six cycles.[13]



Stille reaction using nano Cu

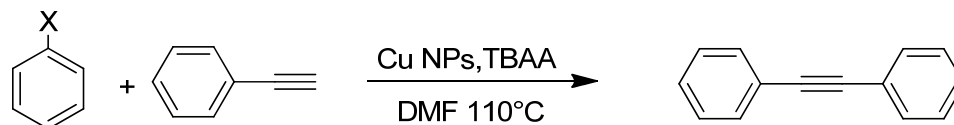
In stille reaction is cross coupling between aryl halide with organotin compounds. In nano Cu₂O using ionic liquid TBAB in the presences of Phosphorus ligand. A reaction is take place at 125-130°C [14]



Sonogashira cross-coupling

It is cross coupling reaction between terminal alkynes with aryl halides in presences of palladium catalyst & base . Now a days a copper cluster used in the reaction this cluster is can be

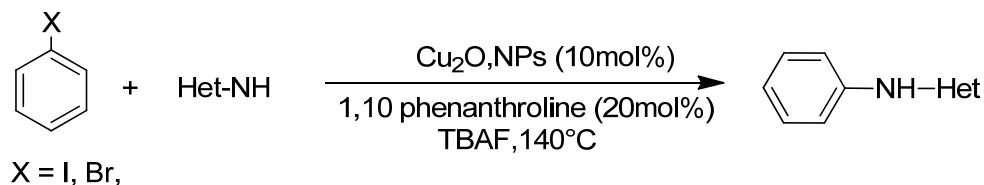
recycled upto 3 times without losing its activity while leaching data of catalyst is not available. In this reaction mechanism proposed by oxidative addition & reductive elimination.[15]



X = I, Br,

Arylation of aromatic heterocycles

Nitrogen containing heterocycles (Triazole, indole & imidazoles) is arylated using aryl & hetero halides. The reaction should be carried out using nano Cu_2O , n-butylammonium fluoride (TBAF) & 1, 10 phenanthroline at 140°C .[16]



X = I, Br,

Summary and outlook

This review gives information of recent development in the bond formation reaction using Cu as catalyst. Now a days using nano Cu^0 catalyst Suzuki, still, Heck, Sonogashira coupling reaction is carried out. As compared other metal Cu is less expensive & environmentally acceptable.

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