Chapter I

A brief review on approaches towards the transformative reactions of Carbon-Hetero and Carbon-Carbon bonds formation

I.1. Introduction

Organic compounds are primarily made up of carbon-carbon and carbon-hetero bonds. Carbon-hetero bonds are commonly formed with nitrogen, oxygen, and sulfur, but bonds with other heteroatoms such as selenium, tellurium, and phosphorus are rare. Carbon-carbon and carbon-hetero bond formations are extensively studied in organic synthetic chemistry and are the cornerstone of conventional organic synthesis. These bond-formation reactions play a crucial role in synthesizing pharmaceutically active compounds, bioactive natural products, agrochemicals, and polymers. Synthetic chemists typically use classical metal-catalyzed cross-coupling methods to set up these reactions. A heterocyclic compound is a cyclic compound containing at least one carbon-hetero bond. Figure I.1 shows some cyclic organic compounds reported in the literature with one or more carbon-carbon and carbon-hetero bonds in their skeleton.

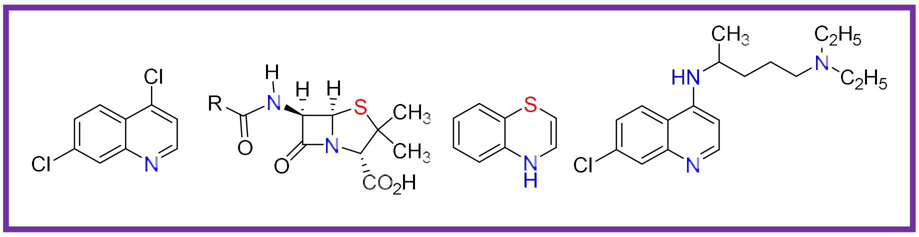


Figure I.1 Some known heterocyclic skeleton

Transformative reactions involving the formation of carbon-carbon and carbon-hetero atomic bonds have gained enormous significance in both biological and industrial fields, as well as in any urbanized human society. Many pharmaceutical products that mimic natural products with biological activity contain these types of bonds. Consequently, researchers are constantly exploring ways to invent and construct better pharmaceuticals, pesticides, insecticides, rodenticides, and weed killers by following natural models. Heteroatomic compounds play an active role in biochemical processes and are essential constituents of living cells. These transformative reactions also have significant applications as additives and modifiers in a wide range of industries, including cosmetics, reprography and information storage, plastics, solvents, antioxidants and vulcanization accelerators. Additionally, they are a powerful tool for constructing naturally occurring biologically active compounds, such as amino acids, glycosides, and naturally occurring heteroatomic compounds. They have also been extensively used as ligands in the synthesis of several transition metal catalysts, which are applied in the synthesis of a large number of organic compounds containing carbon-carbon and carbon-hetero bonds.

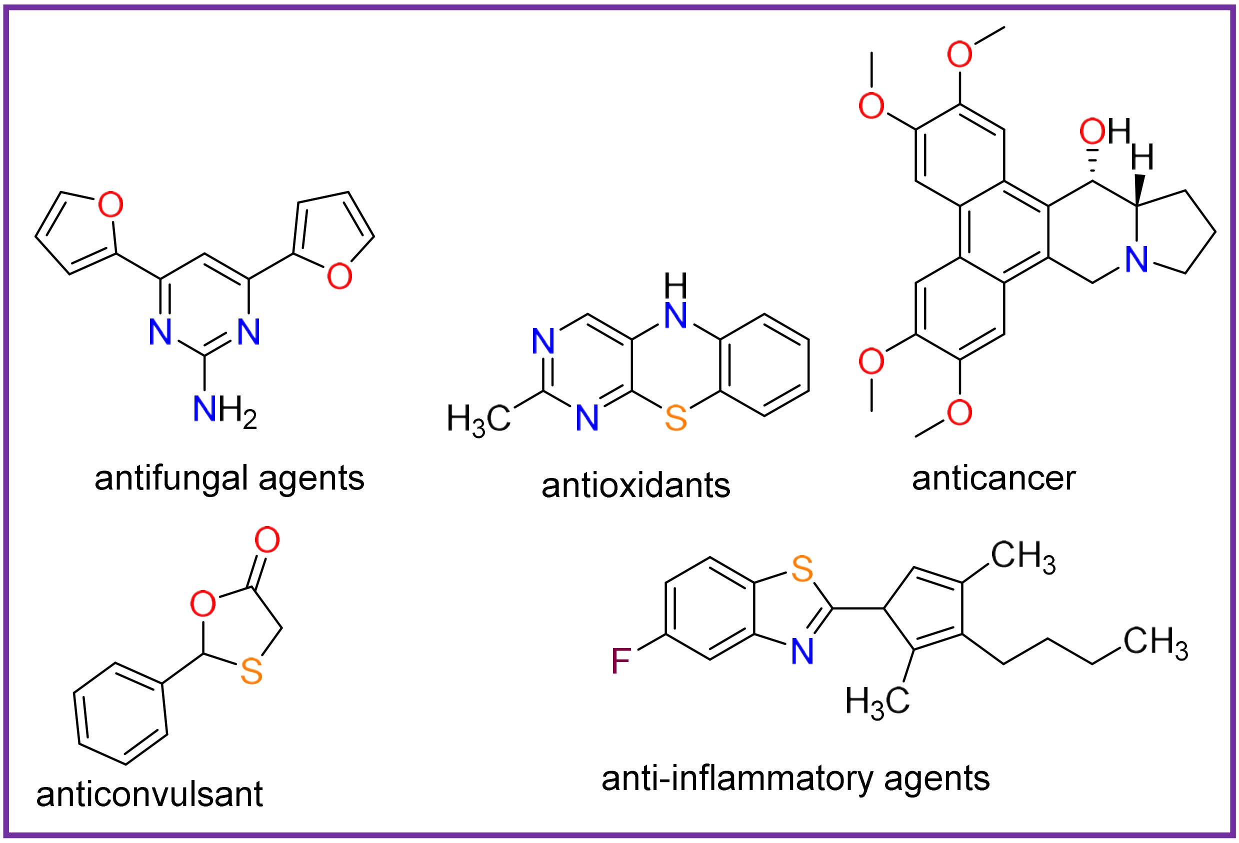


Figure I.2 Biologically active molecules having heterocyclic moiety

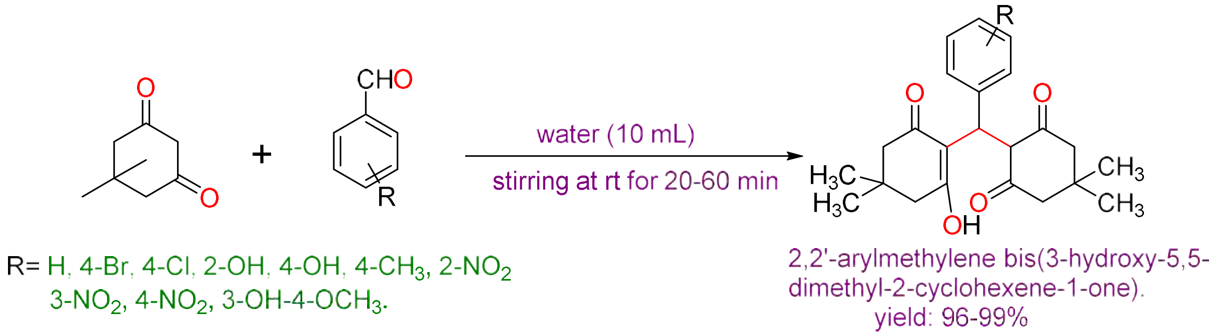
Transformative reactions that involve the formation of carbon-carbon and carbon-hetero bonds play a crucial role in constructing molecular skeletons for drug synthesis in the pharmaceutical industry (Figure I.2). Well-designed methodologies for establishing these types of bonds are essential. According to literature surveys, more than 85-95% of new drugs contain heteroatomic bonds, which provide valuable insights into biological systems. The vast array of possible combinations involving carbon, hydrogen and heteroatoms leads to compounds with diverse physical, chemical and biological properties. Among the 20 million chemical compounds identified by the end of the second millennium, over two-thirds contain carbon-carbon bonds, and approximately half of them feature heteroaromatic bonds. It is clear why organic researchers continue to explore cutting-edge procedures and strategically employ known methods for synthesizing complex heteroatomic compounds. Organic chemists are dedicated to creating these bonds through innovative and efficient synthetic modifications

I.2. Approach towards the transformation of carbon-carbon and carbon-hetero bond formation

A number of methodologies have been reported in the literature for transformative reactions involving carbon-carbon and carbon-hetero bond formation. A brief review has been discussed in this section.

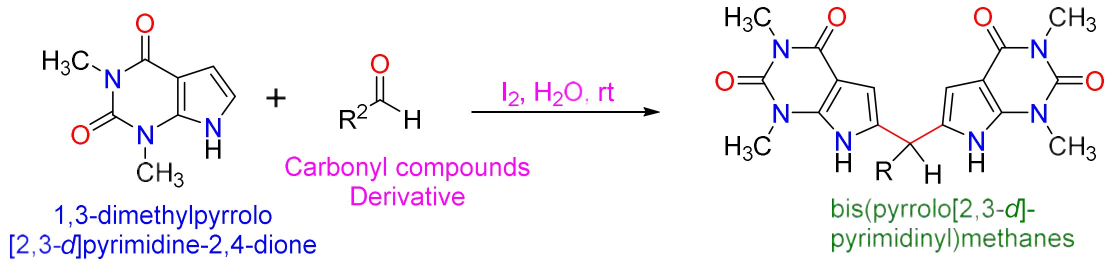
I.2.1. Reactions of C-C bond formation

Bayat *et al.*[1] developed an efficient protocol for the synthesis of 2, 2′-aryl methylene bis (3-hydroxy-5, 5-dimethyl-2-cyclohexene-1-one) derivatives. This was achieved by the reaction of dimedone with various aromatic aldehydes in water at room temperature (Scheme I.1). The work-up procedure is simple and does not require any column chromatographic purification. The structures of the prepared products were identified from their IR, ^{1}H NMR, ^{13}C NMR spectra, mass spectra and elemental analysis.



Scheme I.1 Synthesis of 2, 2′-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one in water

In 2014, M. Sharma *et al.*[2] developed a green method for carbon-carbon bond formation in H_2O medium. They synthesized a novel class of compounds called bis(pyrrolo[2,3-*d*]-pyrimidinyl)methanes from 1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione and benzaldehyde in the presence of iodine as a catalyst (Scheme I.2).



R= CH_3, $(CH_3)_2CH$, C_6H_{11}, C_6H_5, 4-Me-C_6H_4, 4-OMe-C_6H_4,
4-Cl-C_6H_4, 4-Br-C_6H_4, 4-NO_2-C_6H_4.

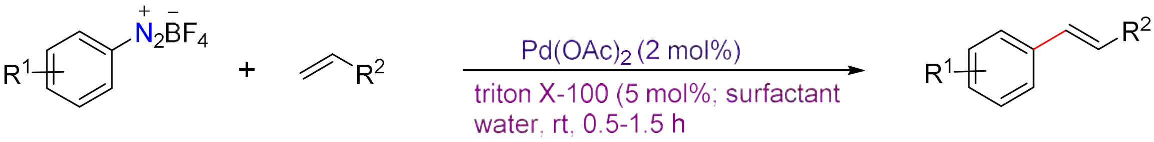
Scheme I.2 I_2 catalyst carbon–carbon bond formation reaction in H_2O medium

In 2014, Pramod B. Thakur *et al.*[3] developed a novel protocol for a new C-C bond for the catalyst-free synthesized 3-hydroxy-2-oxindole scaffolds in water medium from isatin and 3-methyl-2-pyrazolin-5-one (Scheme 1.3).

R^1=H, CH_3, C_6H_5, $CH_2C_6H_5$; R^2=H, Cl
R^3=H, F, Cl, I, NO_2, CH_3, OCH_3, OCF_3
R^4=H, Cl, CH_3; R^5= CH_3, n-Pr, CF_3

Scheme I.3 Synthesis of 3-hydroxy-2-oxindole scaffolds in H_2O medium condition.

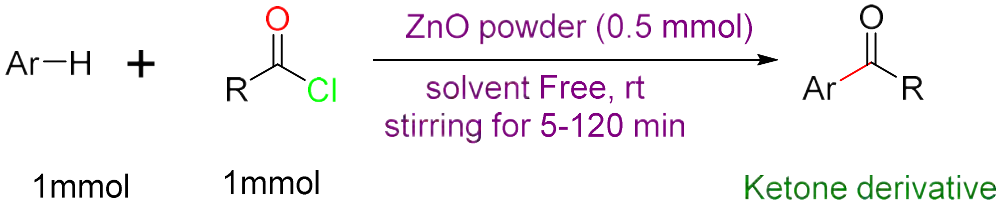
In 2012, Gaikwad and Pore introduced a modified, eco-friendly, and simple method[4] for the Matsuda Heck coupling reaction of olefins with arene diazonium tetrafluoroborate salt. This reaction is catalyzed by in situ generated palladium nanoparticles in the presence of Triton X-100 as a surfactant in water at ambient temperature. Please refer to Scheme I.4 for further details.



R^1= H, 2-Me, 2,6-di-Me, 3-NO_2, 4-Cl, 4-OMe
R^2= C_6H_5, COOMe, COOBu

Scheme 1.4 Matsuda-Heck coupling of olefins

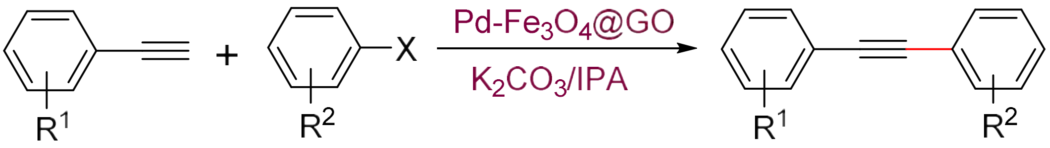
In 2004, Mona Hosseini Sarvari and Hashem Sharghi developed an efficient neat protocol[5] for Friedel-Crafts acylation of aromatic compounds using nontoxic, inexpensive and reusable ZnO powder as a solid catalyst (Scheme I.5)



Ar= Phenyl, substituted phenyl, naphthyl,
anthracenyl, furyl.
R= CH_3, C_6H_5, $C_6H_5CH_2$, 2-Cl-C_6H_4

Scheme I.5 Synthesis of substituted ketones via ZnO-catalyzed Friedel-Crafts acylation

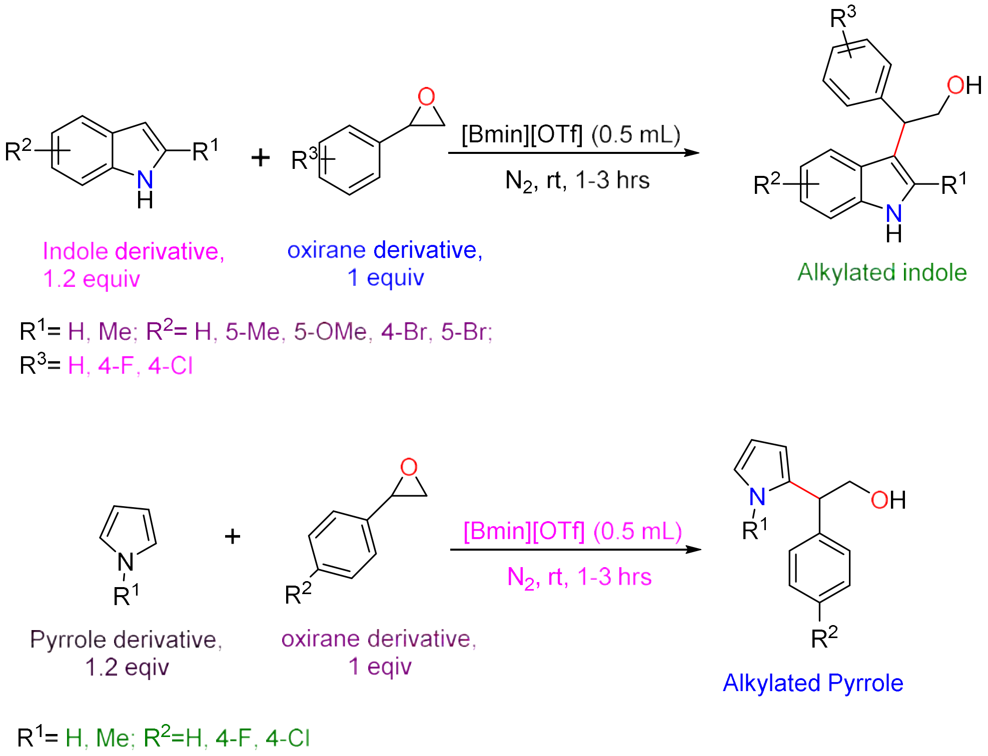
In 2023, M. A. Pawar *et al.*[6] demonstrated a modified Sonogashira coupling by catalyzing the reaction of aryl halide and substituted phenylacetylene with K_2CO_3 using magnetically separable Pd-Fe_3O_4@GO in IPA medium (Scheme I.6).



R^1= H, C_2H_5
R^2= H, F, CF_3, OMe, Me,
NO_2, Cl, Br
X= I, Br, Cl

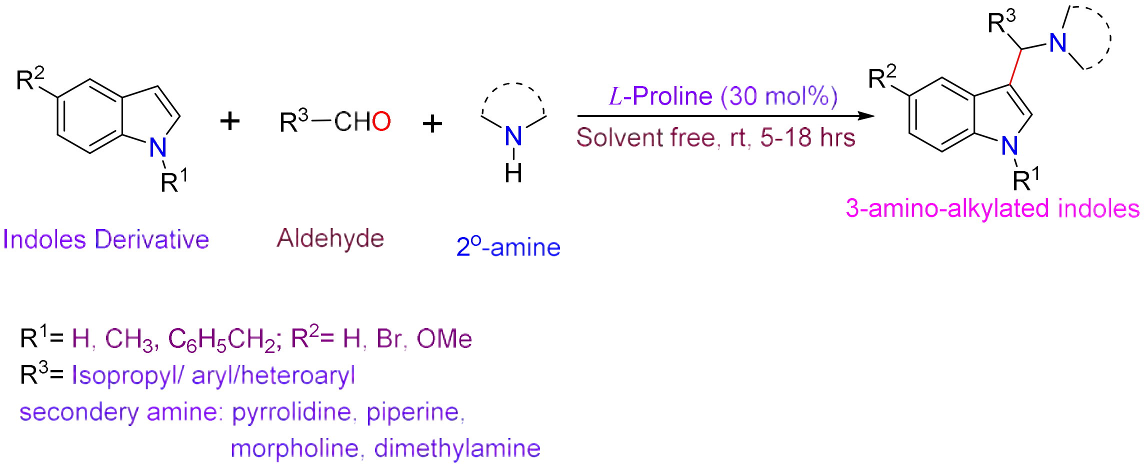
Scheme I.6 Modified Sonogashira cross-coupling reaction catalyst by Pd-Fe_3O_4@GO

In 2008, M. Lakshmi Kantam and colleagues presented a report demonstrating a recyclable and simple protocol[7] conducted at room temperature for direct alkylation of nitrogen-heterocycles, such as indoles and pyrroles, with epoxides through Friedel-Crafts reaction. The report suggests using the ionic liquid [bmim][OTf] as an effective catalyst and reaction medium (Scheme I.7).



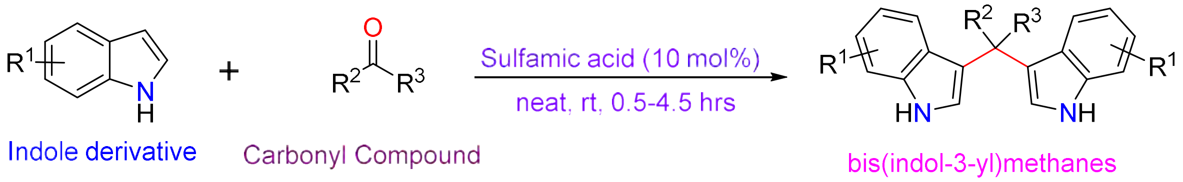
Scheme I.7 Synthesis of alkylated N-heterocycles and pyrrole through the Ionic liquids catalyzed Friedel-Crafts reaction

Kumar *et al.* developed an *L*-proline catalyzed protocol[8] for the efficient one-pot synthesis of 3-amino-alkylated indoles via a three-component Mannich-type reaction of secondary amines, aldehydes and indoles under solvent-free conditions at room temperature (Scheme I.8)



Scheme I.8 Synthesis of 3-amino-alkylated indoles catalyzed by *L*-Proline

An efficient and cost-effective protocol for the synthesis of bis(indol-3-yl)methanes from indoles and carbonyl compounds catalyzed by sulfamic acid at room temperature under neat conditions was demonstrated by An *et al.*[9] (Scheme 1.9)



R^1= H, 5-Br, 1-CH_3
R^2= H, CH_3, C_6H_{11}
R3= $C(CH_3)_3$, 4-Cl-C_6H_4, 2-NO_2-C_6H_4, 4-NO_2-C_6H_4
4-CN-C_6H_4, 4-OH-C_6H_4, 4-Br-C_6H_4

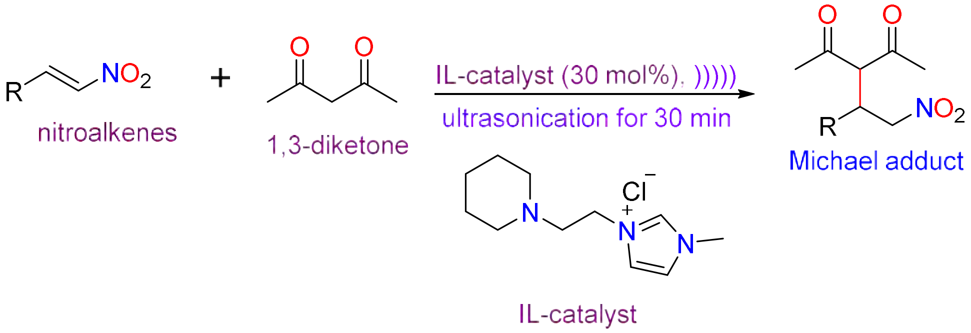
Scheme I.9 Synthesis of bis(indol-3-yl)methanes catalyzed sulfamic acid

Freitas *et al.*[10] developed a metal- and catalyst-free protocol for the efficient allylation of aldehydes to form homoallylic alcohols from aldehyde and potassium allyltrifluoroborate at room temperature under the influence of ultrasound irradiation (Scheme 1.10)

R= C_6H_5, 4-BrC_6H_4, 4-ClC_6H_4,2-FC_6H_4, 4-FC_6H_4, 2-$OCH_3C_6H_4$,
3-$OCH_3C_6H_4$, 4-$OCH_3C_6H_4$, 2-$NO_2C_6H_4$, 3-$NO_2C_6H_4$, 4-$NO_2C_6H_4$,
C_6H_5CH=CH, Naphthyl, 2-Furyl, n-Pentyl

Scheme I.10 Ultrasound-assisted catalyst-free synthesis of homoallylic alcohols

Narayanaperumal and colleagues have developed a solvent-free conjugate Michael addition method[11] using 2, 4-pentanedione and various nitroalkenes. They used catalytic amount of 1-methyl-3-(2-(piperidin-1-yl)ethyl)-1*H*-imidazol-3-ium chloride, a base-behavior task-specific ionic liquid (TSIL), and ultrasonication to obtain the desired conjugate adducts in good to excellent yields. (Scheme I.11).



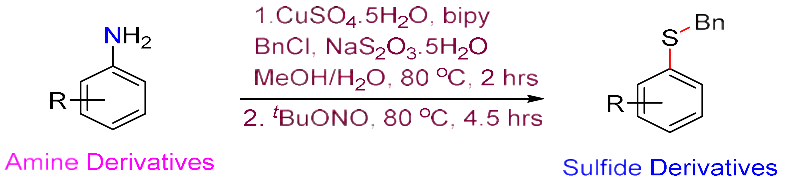
R= C_6H_5, 4-BrC_6H_4, 2-ClC_6H_4, 4-ClC_6H_4,
2-FC_6H_4, 4-FC_6H_4, 2-$OCH_3C_6H_4$,
4-$OCH_3C_6H_4$, 3-$NO_2C_6H_4$, 2-thiopheneyl

Scheme I.11 Ultrasound-assisted synthesis of Michael adducts catalyzed by Ionic liquid (IL)

I.2.2. Reactions of C-S bond formation

Some example of C-S bond formation reactions are given bellow

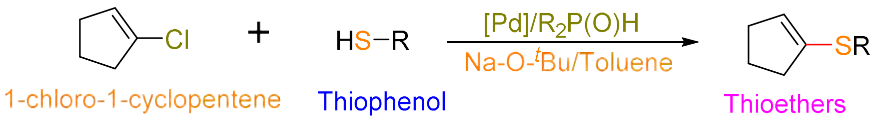
In 2014, Yiming Li and coworkers demonstrated a highly efficient Cu-catalyzed S-transfer reaction from an amine to a sulfide (Scheme I.12)[12]



R= OCH_3, F, Cl, Br, H, CH_3, ^{t}Bu, SCH_3, OH, CN,
CH_2CN, CO_2Et, CO_2Me, NO_2, Acetylene,
$CH{=}CHCO_2Et$, N=N-Ph, CH_2OH, $CONH_2$,
COPh, C=CH-CO_2Et

Scheme I.12 Cu-catalyzed s-transfer reaction from amine to sulfide

In 2002, George Y. Li demonstrated the C-S bond formation reaction from 1-chloro-1-cyclopentene generating thioethers coupling with thiophenol catalyzed by the air-stable palladium phosphinous acid complexes (Scheme I. 13)[13]



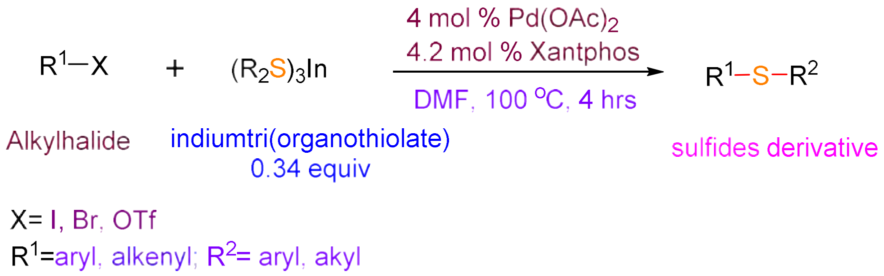
R= C_6H_5, C_6H_{13}

Scheme I. 13 Palladium-Catalyzed C-S Bond Formation of Vinyl Chlorides

In 1980, Toshihiko Migita *et al.*[14] demonstrated a successful reaction for forming a C-S bond from ArX and thiol derivatives catalyzed by the $Pd(Ph_3)_4$ complex (Scheme I.14).

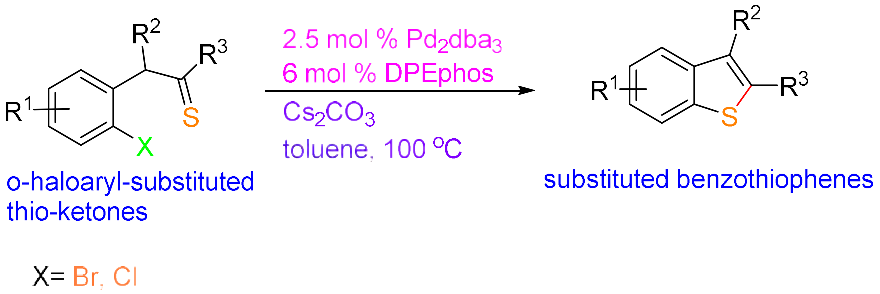
Scheme I.14 $Pd(Ph_3)_4$ catalysed C-S bond formation reaction

In 2008, J. Lee and colleagues[15] conducted a chemical reaction that involved the formation of a C-S bond using indiumtri(organothiolate) as the nucleophilic coupling partner. This procedure allowed for the creation of a wide range of sulfides including aryl-aryl, aryl-alkyl, aryl-vinyl, and alkyl-vinyl sulfides in good to excellent yields. When alkenyl halides were used in the reactions, the double-bond geometry was retained, as shown in Scheme I.15.



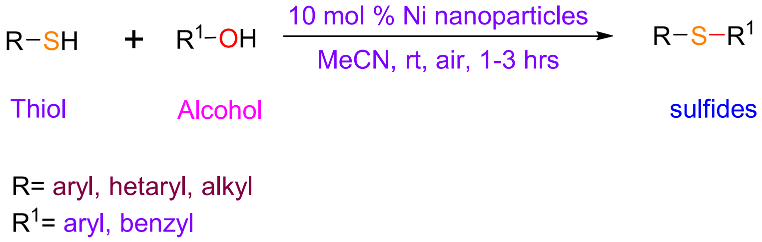
Scheme I. 15 Pd-catalyzed C-S bond formation reaction using indiumtri(organothiolate)

In 2006, Michael C. Willis and colleagues made a significant breakthrough in organic synthesis by developing a method for synthesizing benzothiophenes derivatives.[16] The procedure involves an intramolecular thio-enolate S-arylation reaction using the DPE-phos ligand. Enolates are produced from *o*-haloaryl-substituted thio-ketones, and the reaction is catalyzed by Pd_2dba_3, resulting in the formation of products in moderate to good yields (Scheme 1.16).



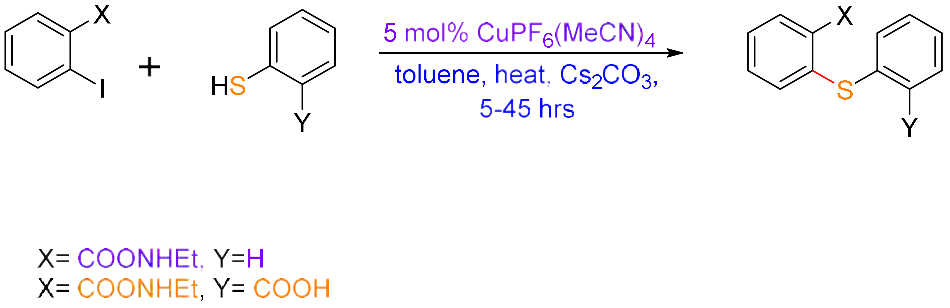
Scheme I.16 Synthesis of benzothiophenes catalyzed by Pd$_2$dba$_3$ in the DPE-phos ligand

In 2007, A. Saxena et al. reported an interesting cross-coupling reaction using Ni nanoparticles (15-18 nm).[17] Additionally, the formation of thioethers from thiols and alcohols under mild conditions at room temperature has also been observed. The reaction involved a variety of aryl and alkyl thiols, along with a wide range of alcohols, resulting in high yields (Scheme I.17).



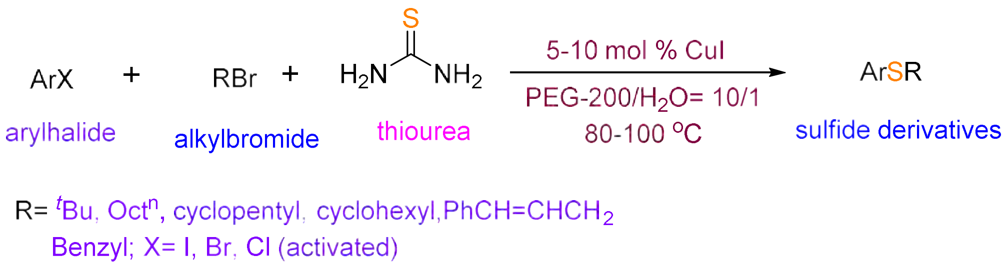
Scheme I.17 Synthesis of thiol ethers catalyst by 15-18 mm Ni nanoparticles

In 1999, A. V. Kalinin and his colleagues reported the use of a catalytic system incorporating the CuPF$_6$(MeCN)$_4$ complex.[18] This system was used as a catalyst to synthesize diaryl thioethers from *o*-substituted aryl iodides and aryl thiols in the presence of Cs$_2$CO$_3$ under heating conditions (Scheme I.18).



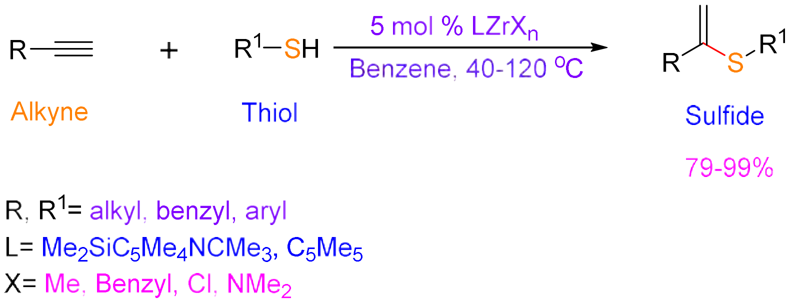
Scheme I.18 C-S coupling reaction catalyst by CuPF$_6$(MeCN)$_4$ catalyst

In 2010, H. Firouzabadi *et al.* used thiourea as a thiol surrogate to report CuI-catalyzed synthesis of thioethers from aryl halides and alkyl bromides. The reaction was carried out in wet PEG-200 at 80-100 °C under an inert atmosphere. This thioetherification synthesis protocol could benefit from a variety of readily available alkyl bromides. Thiourea in wet PEG-200 was also used as a sulfur donor in addition to reactions involving various organyl halides and electron-deficient alkenes. Both intra- and intermolecular reactions with substituted thiourea derivatives have been reported in the C-S cross-coupling synthesis of 2-(arylthio) arylcyanamides as well as CuO-mediated reaction involving selenourea (Scheme I.19)[19]



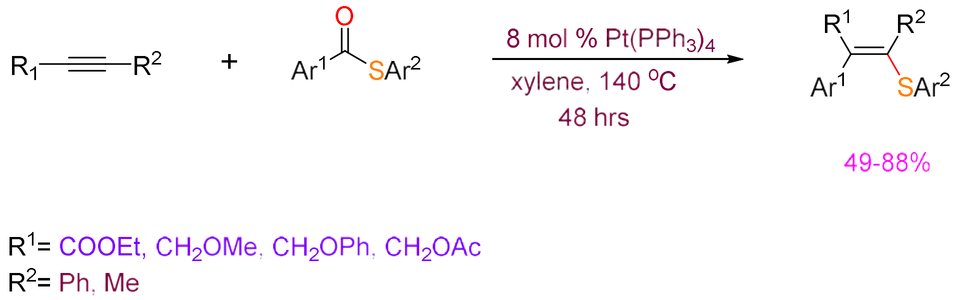
Scheme I.19 Synthesis of thioethers catalyzed by CuI in PEG-200

In 2010, C. J. Weiss *et al.* reported the application of organozirconium (IV)-mediated intermolecular hydrothiolation of terminal alkynes with aliphatic, aromatic, and benzylic thiols using various precatalysts. The reaction exhibits exceptional selectivity, with selectivities reaching up to 99% and yields typically exceeding 90%. The reaction has also been successfully demonstrated on a large scale, resulting in a 72% isolated yield and 99% Markovnikov selectivity. They also reported indicating that the activation parameters for CGCZrMe$_2$-mediated 1-pentanethiol hydrothiolation of 1-hexyne, measured between 50-80 °C, are in line with a turnover-limiting alkyne insertion into the Zr-SR bond, followed by a thiol-induced Zr-C protonolysis (Scheme I.20)[20]



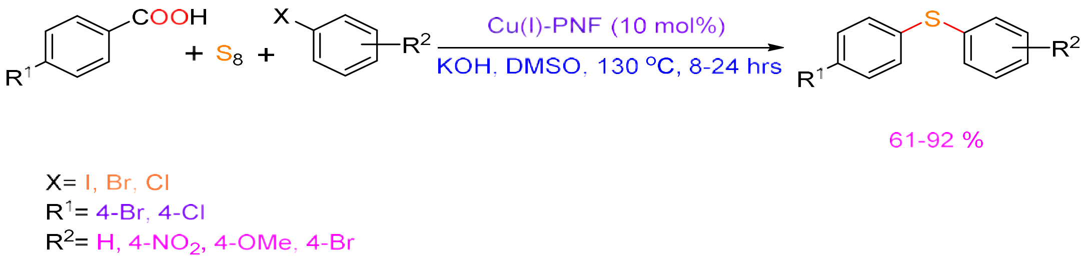
Scheme I.20 lanthanide-mediated selective hydrothiolation of terminal alkynes with thiols

Kuniyasu and co-workers considered the mechanistic aspects of the carbochalcogenetation of alkynes and addressed its possible implementation in synthetic procedures. They found that, in particular, unsymmetrical alkynes underwent decarbonylative aryl thiolation by thioethers under Pt-catalyzed conditions. The proposed mechanism involved alkyne insertion into the M-S bond followed by reductive elimination as the key steps of the catalytic cycle. Similarly, the Pt-catalyzed furyl thiolation, thienyl thiolation and pyridyl thiolation of alkynes were described. One interesting development resulting from this methodology is the Pd-catalyzed regioselective iminothiolation of alkynes (Scheme I.21)[21]



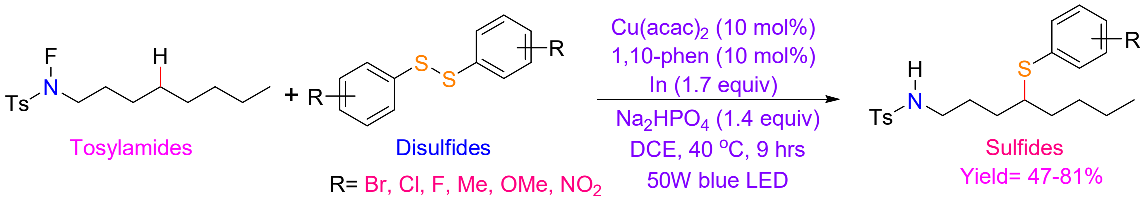
Scheme I.21 Pt-catalyzed decarbonylative aryl thiolation of unsymmetrical alkynes

In 2019, Z. Taherinia *et al.* introduced a modified method supported by a CuI-catalyzed three-component reaction of aromatic acid with elemental sulfur and aryl halides producing unsymmetrical diaryl sulfides was described (Scheme I.22)[22]



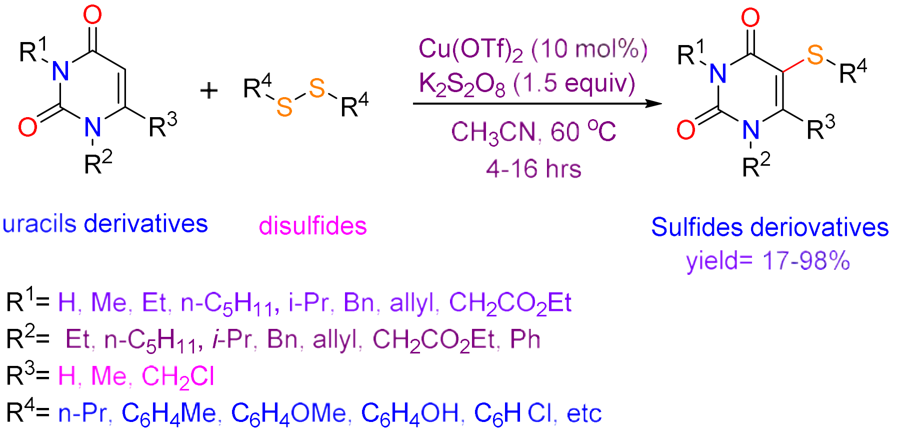
Scheme I.22 Thio arylation of aromatic acid with elemental sulfur catalyst by CuI

In 2020, Yuman Qin *et al.* demonstrated a chemical reaction that forms a bond between carbon and sulfur atoms through C(Sp^2)-H sulfenylation of alkyl tosylamides at the δ-position. This reaction is referred to as C-S coupling. The reaction occurred when N-fluoro-tosylamide and diaryl disulfide were mixed at 40 °C in the presence of Cu(acac)$_2$, 1, 10-phen, Na$_2$HPO$_4$, and indium powder under blue LED light. This protocol was found to be compatible with various diaryl disulfides, as well as dibenzyl disulfides and diphenyl diselenides. (Scheme I.23)[23]



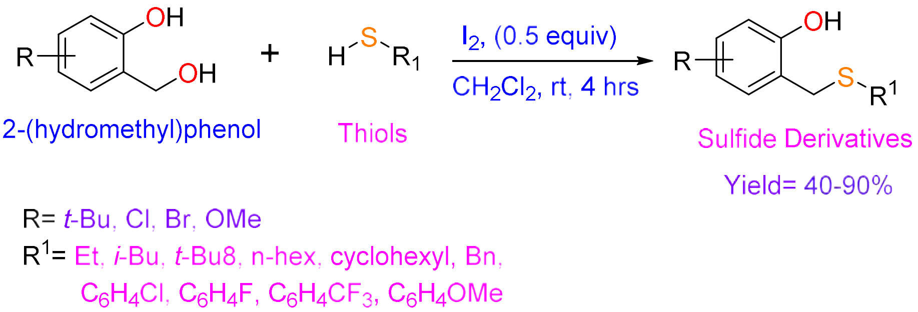
Scheme I.23 Sulfenylation of tosylamides with disulfides

In 2019, the Yotphan group unveiled a groundbreaking method for selectively introducing sulfur-containing groups onto uracils. This groundbreaking achievement was made possible by utilizing copper as a catalyst and either disulfide or a specific compound referred to as NH_4SCN. The reaction was successfully carried out in acetonitrile, with $Cu(OTf)_2$ and $K_2S_2O_8$ serving as co-catalysts, resulting in consistently excellent outcomes. Remarkably, the process exhibited remarkable tolerance towards a diverse range of functional groups. Furthermore, it was observed that the reaction proved to be notably more efficient with electron-rich diaryl disulfides than with their electron-deficient counterparts. Rigorous control experiments unequivocally established that the transformation followed a radical mechanism, solidifying the method's validity and potential impact. (Scheme I. 24)[24]



Scheme I.24 C(Sp^2)-H thiolation of uracils with disulfides

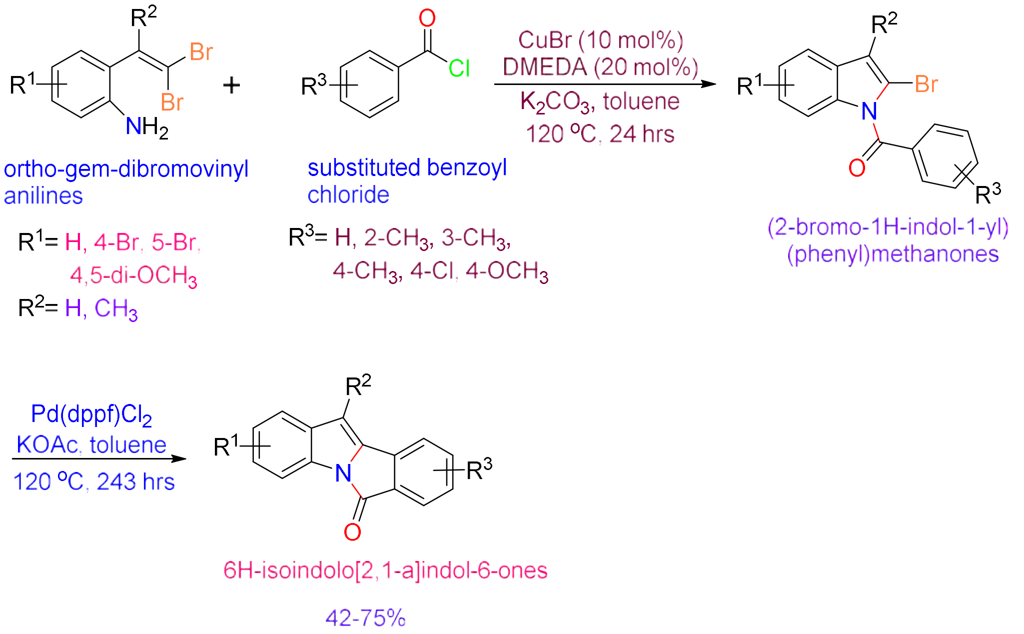
In 2018, the Lee group reported a new method to create sulfides through a dehydrative C-S bond formation. This method involves using 2-(hydromethyl)phenol and thiols in the presence of I_2. The reaction is gentle yet efficient, taking only 4 hrs to complete at room temperature. It's worth noting that the protocol is compatible with both aryl thiol and aliphatic thiol. In fact, slightly higher selectivity was observed with aliphatic thiols in competition experiments. Additionally, products with good yields can be obtained on a gram scale by using long-chain aliphatic thiol. (Scheme I. 25)[25]



Scheme I. 25 Dehydrative C-S coupling of 2-(hydromethyl)phenols and thiols

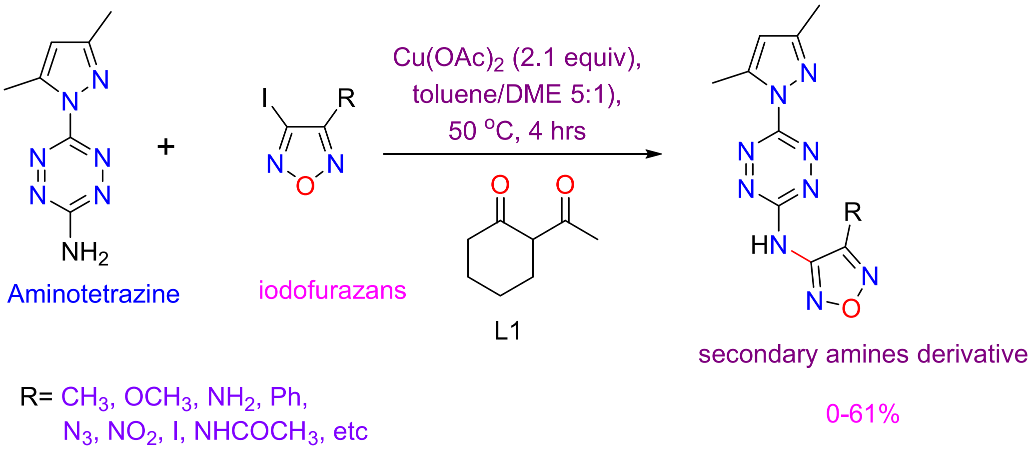
I.2.3. Reactions of C-N bond formation

In 2012, Bao and his colleagues synthesized a series of 6*H*-isoindolo[2, 1-*a*]indol-6-ones through a one-pot sequential coupling reaction. The first step in this sequence is a Cu-catalyzed C-N coupling cyclization, followed by Pd-catalyzed C-H activation. They initiated the sequence by reacting ortho-gem-dibromo vinyl anilines and substituted benzoyl chloride in the presence of CuBr (10%), *N, N*-dimethyl ethylenediamine (DMEDA) (20%) as a ligand, and K_2CO_3 (1.0 equiv.) in toluene at 120 °C. This reaction resulted in the formation of (2-bromo-1*H*-indol-1-yl) (phenyl)methanone in moderate to good yields (Scheme I. 26)[26]



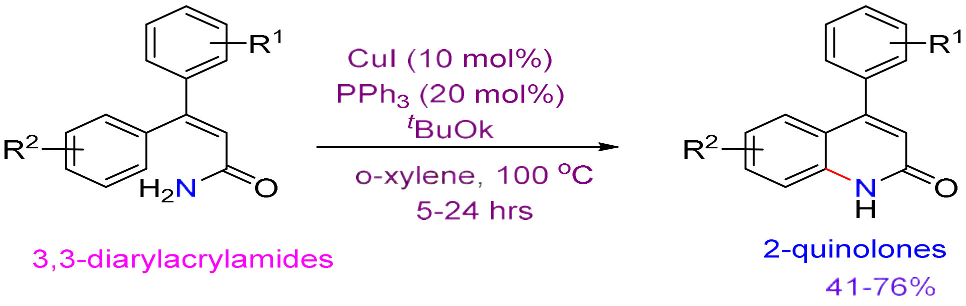
Scheme I. 26 Synthesis of 6*H*-isoindolo[2,1-*a*]indol-6-ones

In 2012, A.B. Sheremetev *et al.* developed a robust method for coupling various furazanyl iodides with 1, 2, 4, 5-tetrazines. This is the only report where electron-deficient nitrogen-rich heterocyclic iodides were coupled with electron-deficient nitrogen-rich heterocyclic amines. To achieve this, aminotetrazine was allowed to react with substituted iodofurazans in the presence of $Cu(OAc)_2$ and 2-acetyl cyclohexanone as the supporting ligand. The reaction was carried out at 50 °C for 4 hrs, resulting in the formation of coupled secondary amines in good yields. (Scheme I. 27)[27]



Scheme I. 27 Coupling reaction of furazanyl iodides with s-tetrazinylamines

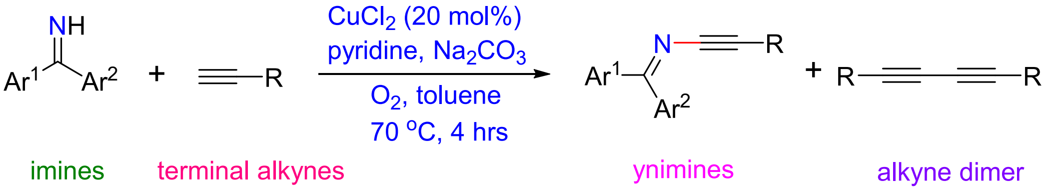
In 2012, R. Berrino and colleagues developed a method to synthesize 2-quinolones through an intra-molecular process that involved C-H functionalization and C-N bond formation. The process involved treating 3, 3-diaryl acryl amides with CuI (10 mol %), PPh_3 (20 mol %), and KO-^{t}Bu in ortho-xylene at 100 °C for 5 to 24 hrs under aerobic conditions. The 2-quinolones were obtained in good yields using this method. (Scheme I. 28)[28]



R^1= H, 4-CH_3, 3-CH_3, 4-^tBu, 4-OCH_3,
3,5-di-CH_3, 4-Cl, 4-F, 4-Br
R^2= H, 4-CH_3, 3-CH_3, 4-^tBu, 4-OCH_3, 3,5-di-CH_3
4-Cl, 4-F, 4-Br, 2-CH_3, 2-Cl, 2-Br

Scheme I. 28 Synthesis of 2-quinolones based on an intra-molecular C–H functionalization/C–N bond forming process

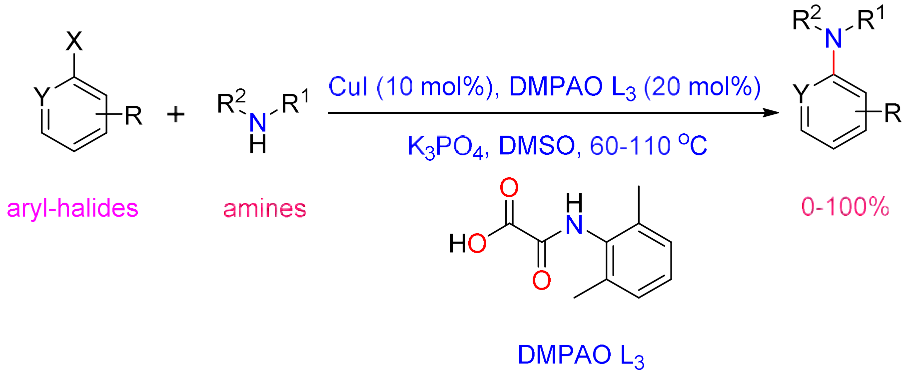
In 2012, Evano and colleagues reported a successful synthesis of ynimines through a Cu-mediated oxidative cross-coupling of imines with terminal alkynes (Scheme I. 29)[29]



R= Ph, 4-F-C_6H_4, C_6H_{13}, C_3H_7, CH_2-cyclohexane,
cyuclohexane,cyclopropane, -$Si(CH_3)_3$,
cyclohexane-1-yl, -CH_2-O-Bz, etc.
Ar^1= Ph, 3-CH_3-C_6H_4, ^tBu
Ar^2= 2,3-di-CH_3-C_6H_3, 2,6-di-F-C_6H_3, 2-OCH_3-C_6H_4,
2-Br-C_6H_4, ^tBu

Scheme I. 29 Synthesis of ynimines via Cu-mediated oxidative cross-coupling of imines with terminal alkynes

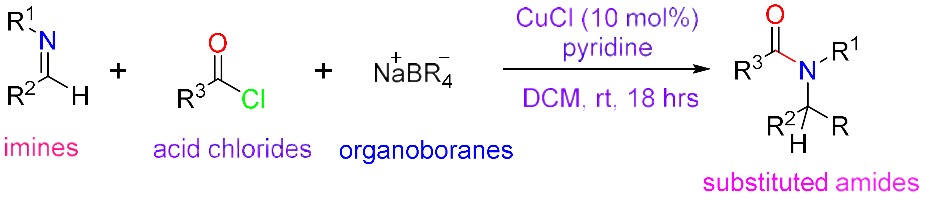
Yao, Ma, and their co-workers reported in 2012 that 2-(2,6-dimethylphenylamino)-2-oxoacetic acid (DMPAO)L_3 can be used as an inexpensive and powerful ligand for Cu-catalyzed aryl amination of aryl halides and amines, producing high yields of *N*-arylated products (Scheme I. 30)[30]



R= $4\text{-}CH_3$, $3\text{-}CH_3$, $2\text{-}CH_3$, $4\text{-}SCH_3$, $3\text{-}COCH_3$,
$4\text{-}NO_2$, $3\text{-}OCH_3$, $4\text{-}OCH_3$, $2\text{-}OCH_3$, 4-Ph,
$3\text{-}NO_2$, $4\text{-}CO_2CH_3$, 4-CN, 3-F
R^1= H, CH_3, CH_2CHCH_2, C_3H_7,
R^2=CH_2Ph, cyclohexane, CH_2CHCH_2, C_3H_7,
CH_2CH_2OH, C_3H_6OH, $C_2H_4OCH_3$
R^1=R^2= $-C_5H_{10}-$, $-C_4H_8-$, $-CH_2CH(OH)CH_2-$ $-CH(CH_3)C_3H_6-$,
$-CH_2CH_2OCH_2CH_2-$, etc.
Y=C, N

Scheme I. 30 Synthesis of *N*-arylated product catalyzed by CuI, (DMPAO) L_3

In 2012, Arndtsen and colleagues developed a copper-catalyzed Petasis-type reaction utilizing imines, acid chlorides and organoboranes to access alpha-substituted amides (Scheme I.31)[31]

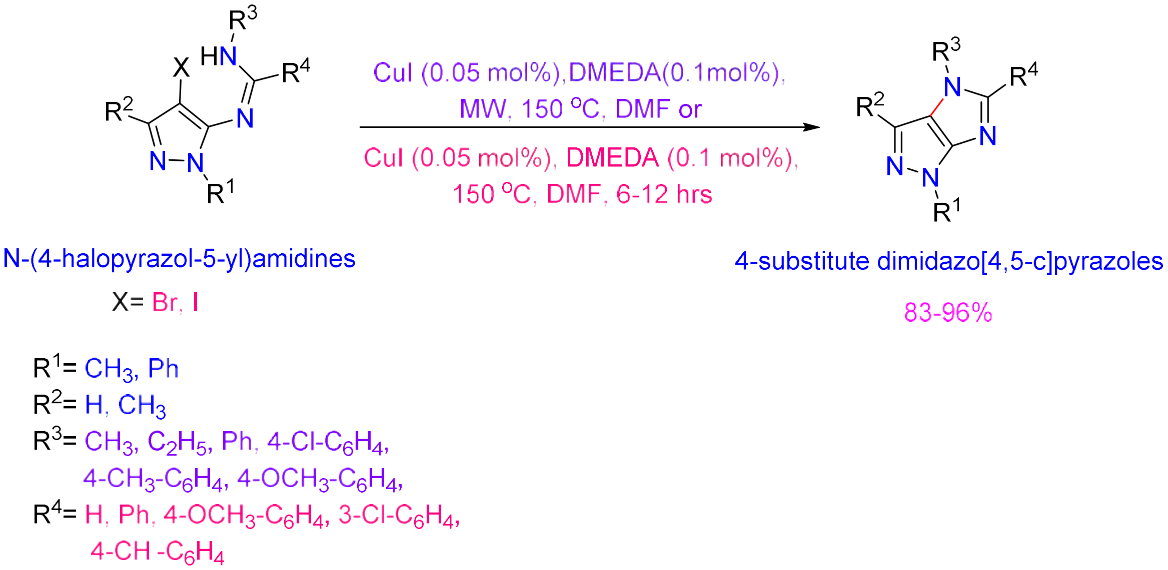


R= Ph, $4\text{-}CH_3\text{-}C_6H_4$, CH_2Ph, $4\text{-}F\text{-}C_6H_4$,
C_2H_5, thiophene-2-yl
R^1= CH_3, C_2H_5, Bn, $4\text{-}OCH_3\text{-}C_6H_4$, allyl
R^2= CH_2CH_2Ph, $4\text{-}F\text{-}C_6H_4$, $4\text{-}CH_3\text{-}C_6H_4$,
thiophen-2-yl, naphthalen-2-yl
R^3= Ph, $4\text{-}CH_3\text{-}C_6H_4$, $4\text{-}NO_2\text{-}C_6H_4$, $CH(CH_3)_2$,
thiophen-2-yl, furan-2-yl

Scheme I. 31 Synthesis of α-substituted amides catalyzed by Cu

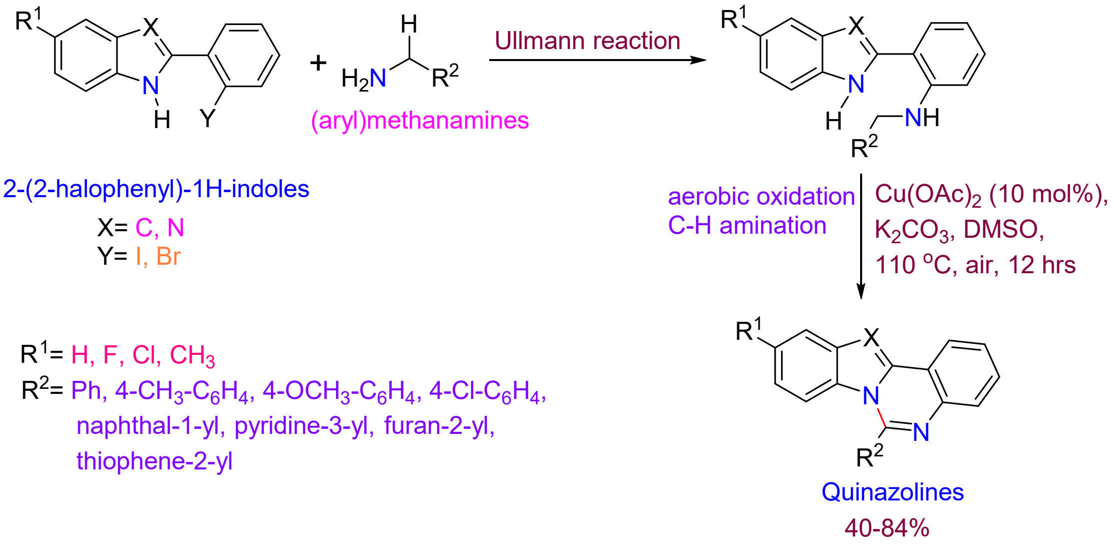
In 2012, Liubchak, Tolmachev and their colleagues developed a new method for synthesizing 4-substituted imidazo-[4, 5-*c*]pyrazoles. They suggested the cyclization of *N*-(4-halopyrazol-5-yl)amidines under Cu-catalyzed cross-coupling conditions. The reaction was carried out using

0.05 mol% of CuI, 0.1 mol% of DMEDA and an excess of K_2CO_3. The reaction was performed using both microwave and conventional heating methods, with DMF as a solvent (Scheme I. 32)[32]



Scheme I. 32 Synthesis of 4-substituted imidazo[4,5-*c*]pyrazoles under MW and conventional heating condition

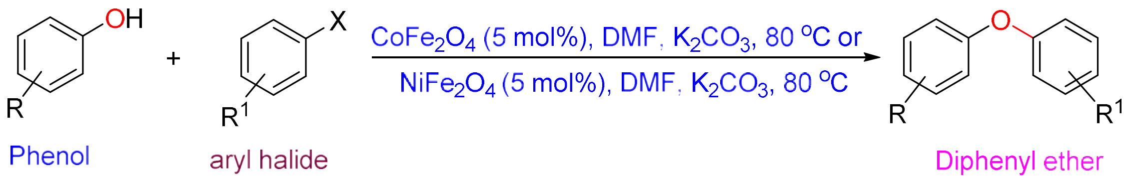
Zou, Zhang and co-workers have developed a simple and efficient method for the synthesis of indolo[1,2-*c*]- quinazolines using Cu-catalyzed and air as oxidant from readily available 2-(2-halophenyl)-1*H*-indoles and (aryl)methanamines (Scheme I. 33)[33]



Scheme I. 33 Synthesis of indolo[1,2-*c*]-quinazolines using Cu-catalyzed and air as oxidant

I.2.4. Reactions of C-O bond formation

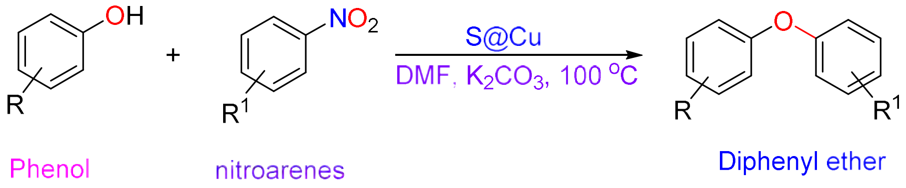
In 2015, Firouz Matloubi Moghaddam *et al.* demonstrated the formation of a C-O bond using a catalyst of $NiFe_2O_4$ and $CoFe_2O_4$ nanoparticles with phenol and aryl halide (Scheme I.34)[34]



R= H, CH_3, CH_3CO, C_6H_5CO
R^1= H, 4-OMe, 2-CHO,
X= Cl, Br, I,

Scheme I. 34 C-O bond formation reaction catalyst by $NiFe_2O_4$ and $CoFe_2O_4$ nanoparticles

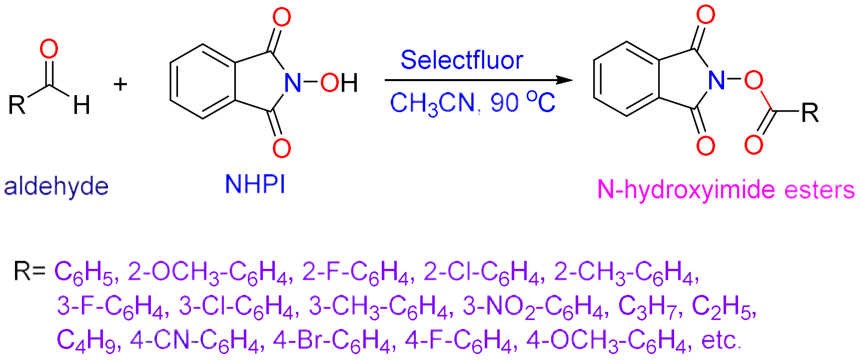
In 2016, Tanmoy Maity *et al.* demonstrated Heterogeneous *o*-arylation of nitroarenes with substituted phenols over a copper-immobilized mesoporous silica catalyst (S@Cu) in DMF medium. (Scheme I. 35)[35]



R= H, CH_3, OCH_3, COMe, Et
R^1= NO_2, CN, CHO,

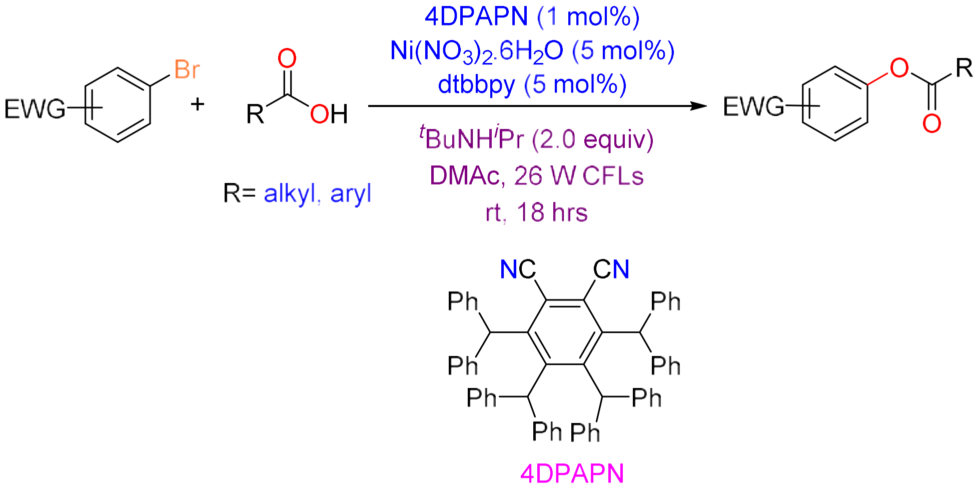
Scheme I. 35 S@Cu catalysed *o*-arylation reaction of nitroarene with aryl alcohols

In 2016, Yunhe Lv *et al.* developed a select fluor-mediated intermolecular C–O cross coupling reaction for the synthesis of *N*-hydroxyimide esters from aldehydes with *N*-hydroxyphthalimide (NHPI) (Scheme I. 36)[36]



Scheme I. 36 Scope of the reaction of aldehydes with NHPI mediated by selectfluor

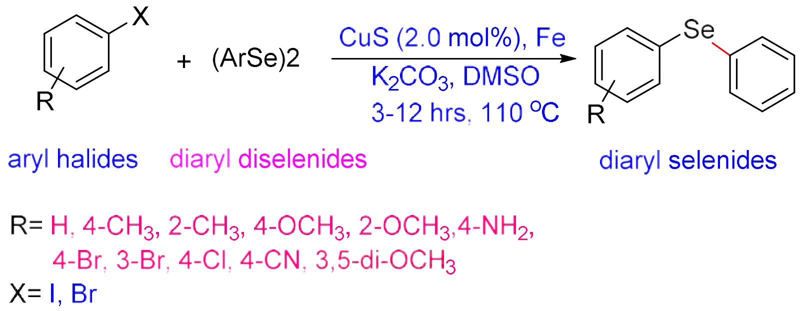
In 2018, the Zhang and Huang group created a new D-A fluorophore, 4-DPAPN, which had the right triplet energy. They utilized 4-DPAPN as a photocatalyst to develop a similar photoinduced Ni-catalyzed C-O coupling reaction with aryl bromides and carboxylic acids under mild conditions (Scheme I.37). The catalyst used was $Ni(NO_3)_2.6H_2O$/dtbbpy.[37]



Scheme I. 37 C–O coupling reactions of aryl halide with carboxylic acids using $Ni(NO_3)_2{\cdot}6H_2O$/dtbbpy as the catalyst

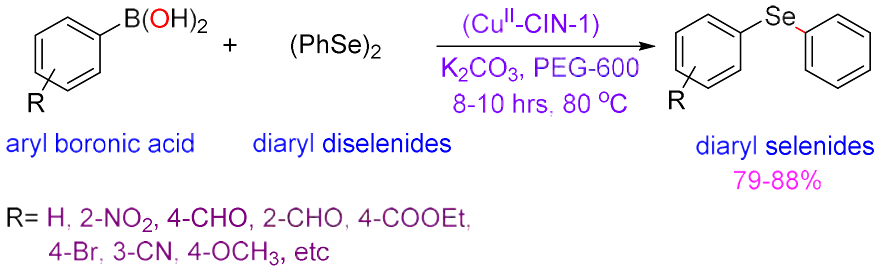
I.2.5. Reactions of C-Se bond formation

In 2010, Li *et al.* introduced a highly efficient and ligand-free CuS-catalyzed coupling reaction between aryl halides and diaryldiselenides. This reaction was accelerated by the addition of Fe powder and could be completed in only 3-12 hours at 110 °C under an argon atmosphere. The purpose of this reaction was to synthesize unsymmetrical diaryl selenides with good to excellent yields (Scheme I. 38)[38]



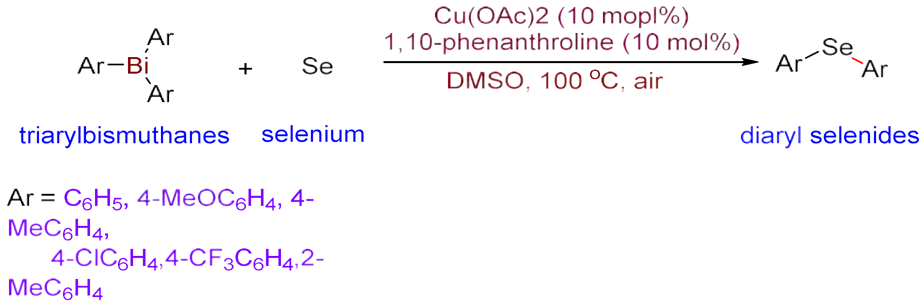
Scheme I. 38 Synthesis of unsymmetrical diaryl selenides using Fe catalysis

In 2014, S. Roy *et al*. developed an eco-friendly method for phenylselenylation of aryl boronic acid. This method was catalyzed by a highly recyclable heterogeneous Cu(II) catalyst supported on a nitrogen-rich porous covalent imine network (Cu^{II}-CIN-1) in PEG-600 solvent. The catalyst was successfully used to catalyze the cross-coupling reaction between a diverse set of aryl boronic acids and diphenyl diselenide. This resulted in the synthesis of good to excellent yields of the corresponding unsymmetrical organoselenides in PEG-600 solvent in the presence of K_2CO_3 at 80 °C for 8 hrs (Scheme I. 39).[39]



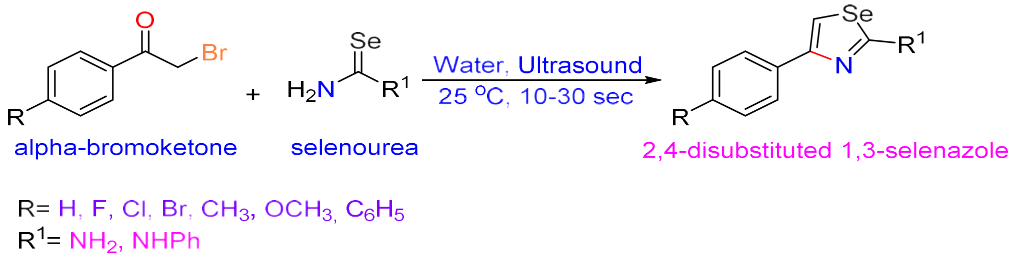
Scheme I. 39 Cu^{II}-CIN-1 catalysed phenyl selenylation of aryl boronic acid

In 2016, Matsumura and colleagues reported a copper-catalyzed synthesis of symmetrical diaryl selenides from triarylbismuthanes and selenium under aerobic conditions. The reaction involved treating Ph_3Bi with 1.5 equivalents of Se powder using 10 mol% $Cu(OAc)_2$ and 1,10-phenanthroline as the catalytic system in DMSO at 100 °C. Remarkably, this transformation proceeded without the need for any base or inorganic reagent under aerobic conditions (Scheme I. 40)[40]



Scheme I. 40 Cu-catalysed procedure for the synthesis of symmetrical diaryl selenides

In a study conducted in 2015, Gondru and colleagues devised a novel and expeditious methodology for synthesizing 2, 4-disubstituted 1, 3-selenazoles. This was accomplished by reacting α-bromoketone with selenourea at a temperature of 25 °C within an aqueous medium, facilitated by ultrasonic irradiation. The process yielded analytically pure products in a remarkably brief duration of 10 to 60 seconds, with the outcomes being of exceptional yield (Scheme I.41)[41]



Scheme I.41 Synthesis of 2, 4- disubstituted 1, 3-selenazole in H_2O medium under ultrasonic irradiation

I.3. Conclusion

Indeed, the field of organic synthesis is continually evolving, with transformative reactions involving Carbon-Carbon (C-C) and Carbon-Heteroatom (C-X) bond formations being at the forefront of chemical research. The discussion underscores the significant potential for innovation in this domain, particularly in the development of new reaction methodologies. The ongoing exploration of these reactions not only expands our understanding of chemical processes but also paves the way for the creation of novel compounds with diverse applications in medicinal chemistry, materials science and beyond.

I.4. References

References are given in BIBLIOGRAPHY under Chapter I (page 235-236).