Chapter-1

Introduction

Transition metal catalysis has spawned a new sector in organic synthesis in the last decade, allowing for numerous so far impossible synthetic reactions[1]. In addition, transition-metal-catalyzed coupling processes have advanced significantly and are now one of the most efficient and direct techniques for forming carbon-nitrogen and carbon-carbon bonds[2]. Transition-metal catalyzed coupling reactions were regarded as the most reliable, accurate, and powerful tools in chemists'[3] arsenal due to their wide range of variations and alterations. Several transition metal-catalyzed coupling reactions involving organometallic reagents, including organoboron[4], organotin[5], organomagnesium[6], organolithium[7], organozinc[8], and organosilane[9], have been assigned in textbooks. The Ulmann coupling and condensation reactions Suzuki-Miyaura, Buchwald-Hartwig, Chan-Lam, and Mizoroki Heck reactions are excellent instances of direct C-X and C-C bond formation[10].In 2010, the Nobel Prize in Chemistry was awarded for the achievement of transition-metal-catalyzed coupling processes[11].

Due to the distinctive drawbacks of the catalytic systems, transition-metal-catalyzed coupling processes are still limited in applications and encounter obstacles to some extent. Most transition-metal catalystsareusually costly, and the supporting ligands are even more expensive and sometimes difficult to prepare; most transition metals are toxic to varying degrees[12], and removing trace amounts of transition-metal residues from desired products is quite costly and challenging; while crucial, especially in the pharmaceutical industry[13]. Many transition-metal catalysts are

sensitive to oxygen (O_2) and moisture and requirecareful handling. In several cases, special additives and co-catalysts are also critical to promoting transformations' efficiency and selectivity[14]. Furthermore, the high consumption of transition metals does not match the criteria for long-term development[15].

As a result, transition-metal-free synthetic procedures for synthesizing carbon-carbon and carbon-nitrogen bonds must be developed without sacrificing product selectivity, energy efficiency, or environmental safety.

Several transition-metal-free processes for forming C-C and C-N bonds have recently been established. Oxidative coupling reactions involving TBHP, a transition metal-free catalyst, have gotten a lot of interest[16]. Although these reactions do not require metal salts, the stability and toxicity of these molecules have caused them to be given special attention. More recently, the combination of tetrabutylammonium iodide (TBAI)/NaI/I_2/Triethylamine as a catalyst and *tert*-butyl hydroperoxide (TBHP) as a strong oxidation system has gotten a lot of attention[17].

1.1 Brief Introduction of *tert*-Butyl hydroperoxide (TBHP)

tert-Butyl hydroperoxide (^tBuOOH) is an essential organic compound with the molecular formula $(CH_3)_3COOH$(fig 1.1). Hydroperoxide is one of the most widely used reagents in various oxidation processes, like in oxidations of multiple substrates to give epoxides[18-20],ketones, aldehydes[21],allylic alcohols[22],and nitro or imine compounds[23]. Compared to hydrogen peroxide and organic peracids, *tert*-butyl hydroperoxide is less reactive and more soluble in organic solvents. Overall, it is famous for the convenient handling properties of its solutions. Its solutions in organic solvents are highly stable.The clear, colorless liquid is widely available as 70–90%

aqueous solutions and anhydrous in hydrocarbon solvents. Aqueous solutions may be dried by a phase-separation procedure, followed by azeotropic distillation to remove the last vestiges of water if necessary. In view of the lability of the hydroxyl group in tertiary alcohols, it was early suspected that pure hydrogen peroxide in a nonaqueous solution would react with *tert*-butyl alcohol reversibly to form *tert*-butyl hydroperoxide (TBHP)[24].

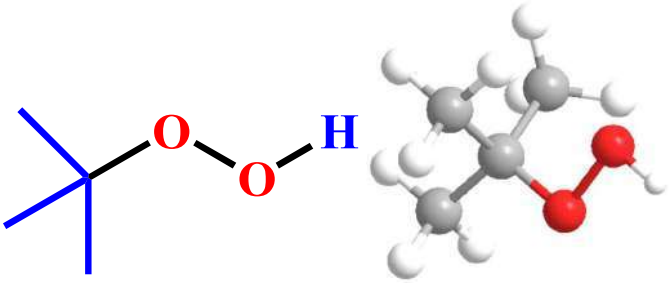


Fig 1.1: Structure of TBHP

In recent times, several advancements have been made in combining *tert*-butyl hydroperoxide (TBHP) as a co-oxidant using catalytic amounts of iodine. The increased utility is mainly due to its inexpensive, environmentally benign nature, good efficiency, and compatibility to work in place of rare or toxic heavy metal oxidants[25].TBHP oxidant system works efficiently for numerous C–C and C– X (X = heteroatom) bond-forming organic transformations under mild reaction conditions to offer the desired products in excellent yields[26](fig 1.2).

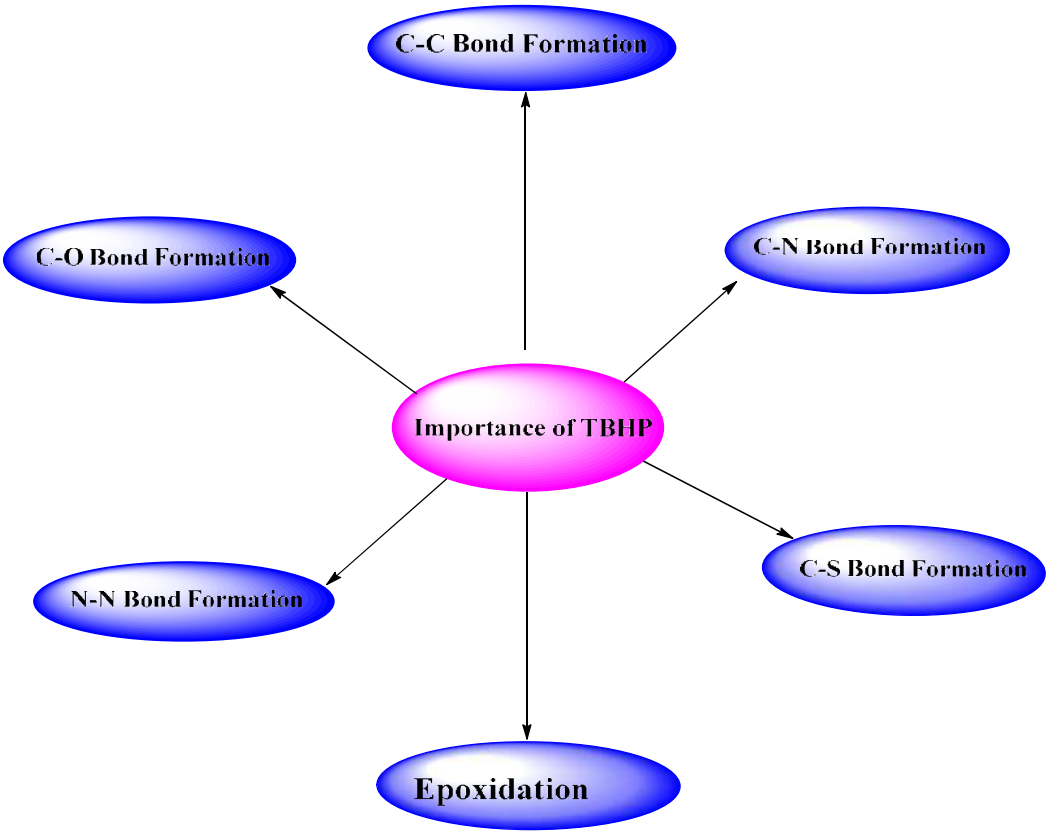


Fig 1.2: Importance of TBHP as an oxidant

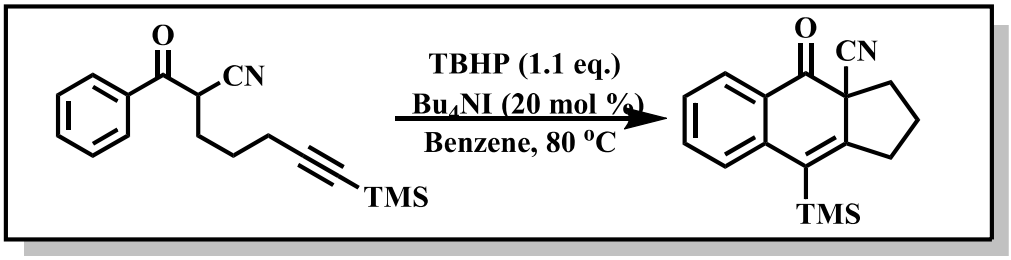
1.2 Application of TBHP

1.2.1 TBHP Mediated C-C Bond Formation:

C-C Bond formation provides the requisite connectivity for synthesizing a large and complex molecular structure from simple precursors. A recently developed protocol in this field is metal-freecatalyzed C-H bond functionalization via cross dehydrogenative cupling (CDC). Representative examples of various formsof C-C bond formations are discussed below.

1.2.1.1 Synthesis of [6,6,5] tricyclic frameworks

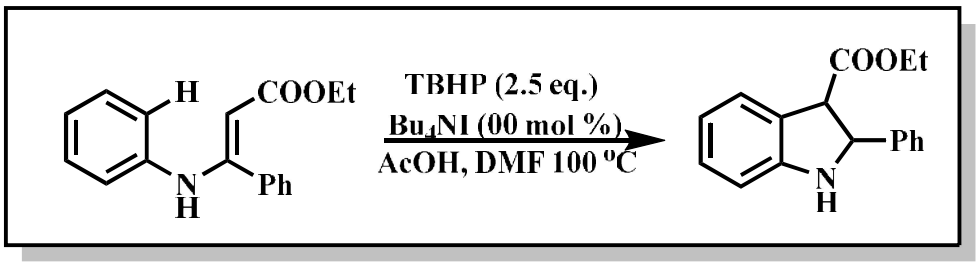
Intramolecular cyclization of the α-cyano-TMS (TMS- = Me3Si-)/aryl-capped alkynyl aryl alkyl ketones was described by Shia et al. [27] in the presence of catalyst TBAI and oxidant TBHP. In this approach, under metal-free conditions [6,6,5] tricyclic frameworks were synthesized (Scheme 1.1).



Scheme 1.1 Bu_4NI-catalyzed intramolecular cyclization of the α-cyano-TMS/aryl-capped alkynyl aryl alkyl ketones**.**

1.2.1.2 Synthesis of 1H-indole derivatives

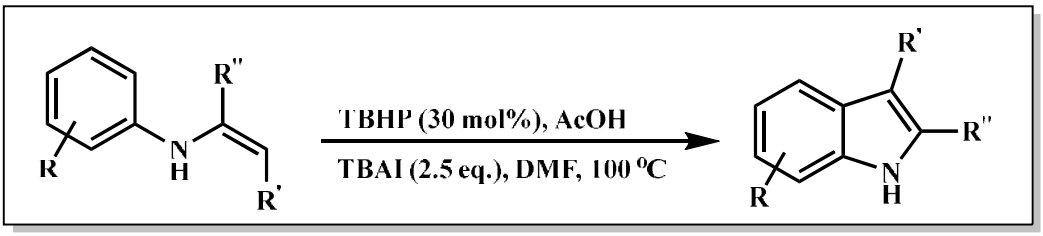
The synthesis of 1H-indole derivatives was reported by Li et al. [28] group through the intramolecular cross dehydrogenative coupling (CDC) approach using TBAI as a catalyst. In this approach, N-arylenamines afforded their corresponding 1H-indoles through intramolecular oxidative coupling using TBAI as a catalyst & TBHP as an oxidant (Scheme1.2).



Scheme1. 2 Bu_4NI-catalyzed intramolecular oxidative coupling of N-arylenamines

1.2.1.3 Synthesis of indole derivatives via cross-dehydrogenative coupling(CDC)

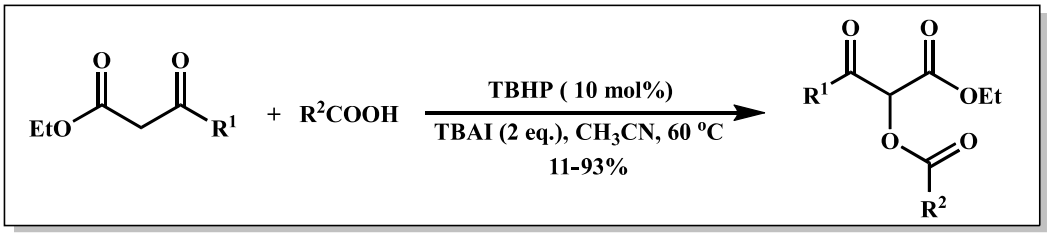
Using TBAI and TBHP, L. Xingshu et al. [29] have directly synthesized 1H-indole derivatives via a cascade of intramolecular cross-coupling of N-arylenamines. The addition of TEMPO did not suppress the reaction, indicating that a radical pathway is not the dominant mechanism in this system. Iodide salts, including LiI, NaI, and NH_4I, were used to test this unusual example of the TBAI-catalyzed C–C bond-forming CDC reaction, but the results were poor (Scheme 1.3).



Scheme 1.3 TBAI/TBHP-Mediated indole synthesis

1.2.1.4 Oxidative Coupling of β-ketoesters with carboxylic acids

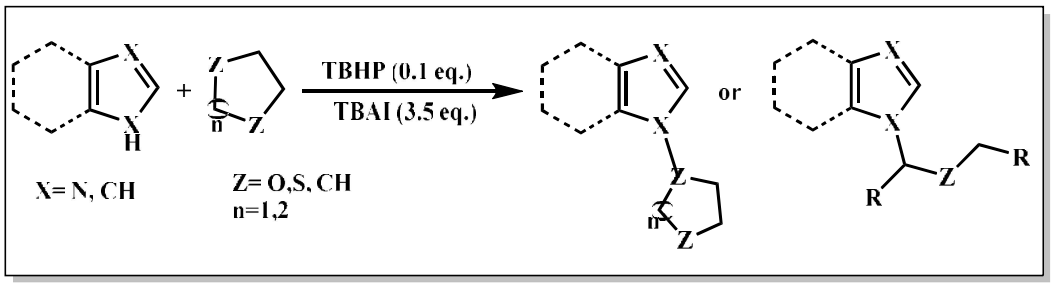
Using TBAI as a catalyst and TBHP as the terminal oxidant, X. Xiangsheng et al. [30] presented a method for synthesizingα-carboxylic-β-keto esters by oxidative coupling of carbonyl compounds with carboxylic acids. Under these conditions, many ketones and 1,3-dicarbonyl compounds react with carboxylic acids to give the corresponding α-acyloxy ketones in good to outstanding yields(Scheme 1.4).



Scheme 1.4 TBAI-Catalyzed synthesis of α-carboxylic-β-ketoesters

1.2.1.5 Coupling of azoles with α-C(sp3)-H of ethers and thioethers

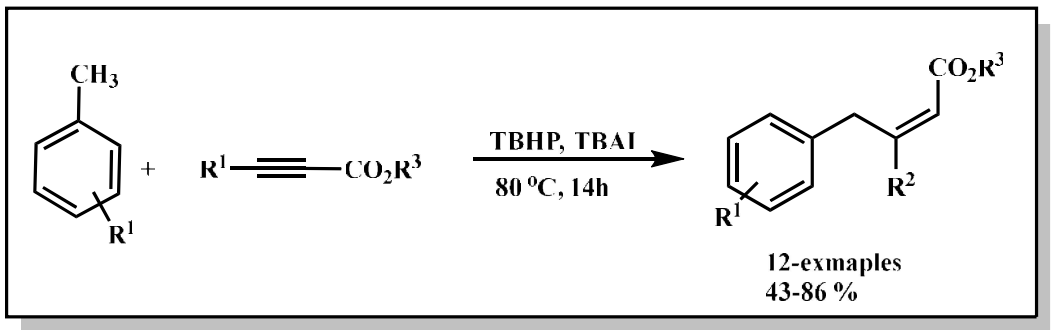
Using TBAI as a catalyst and TBHP as an oxidant, S. P. Parvinder et al. [31] devised a technique for synthesizing N-substituted azoles by combining azoles with ethers and thioethers via α -C(sp3)-H activation(Scheme 1.5).



Scheme 1.5 TBAI/TBHP-catalyzed synthesis of *N*-substituted azoles

1.2.1.6 sp^3 C–H bond functionalization of toluene derivatives

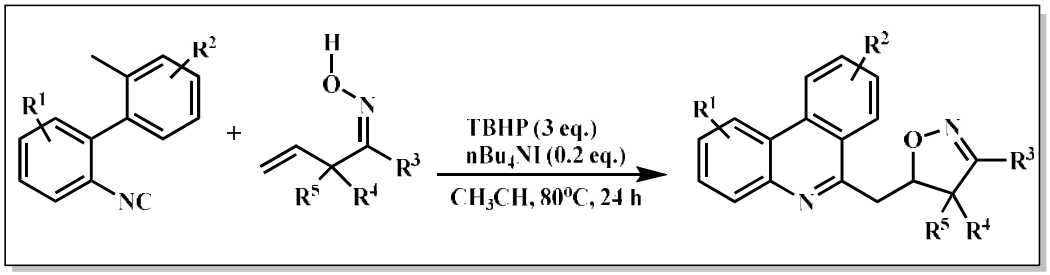
F. Shahsavari et al. [32] reported sp3 C–H bond functionalization of toluene substrates to establish a facile process for synthesizing allylbenzene derivatives using TBHP as the oxidant and TBAI as the catalyst in good to moderate yields (Scheme 1.6).



Scheme 1.6 TBAI- catalyzed synthesis of allylbenzene derivatives

1.2.1.7 Synthesis of isoxazoline-functionalized phenanthridines

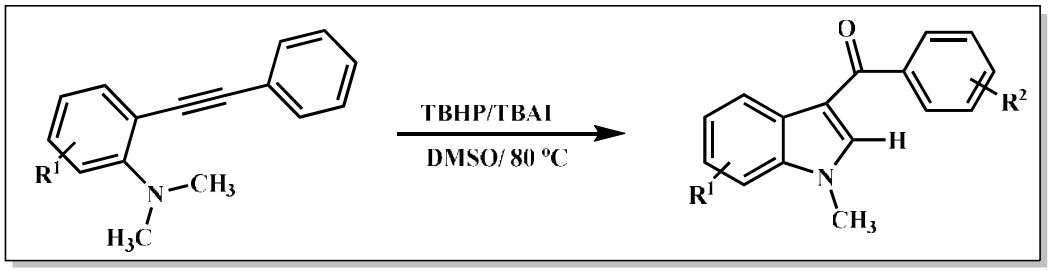
X. L. Yang et al.[33]described a new and practical synthesis of isoxazoline-functionalized phenanthridine derivatives usinga combination of TBAI and TBHPfrom 2-isocyanobiaryls and β,γ-unsaturated ketoximes by iminoxyl radical-participated cascade cyclization /addition / cyclization under oxidative conditions at 80 °C for 24 h(Scheme 1.7).



Scheme 1.7 TBHP-mediated synthesis of isoxazoline-functionalized phenanthridines.

1.2.1.8 Domino synthesis of 3-aroylindoles via two sp3 C–H activation.

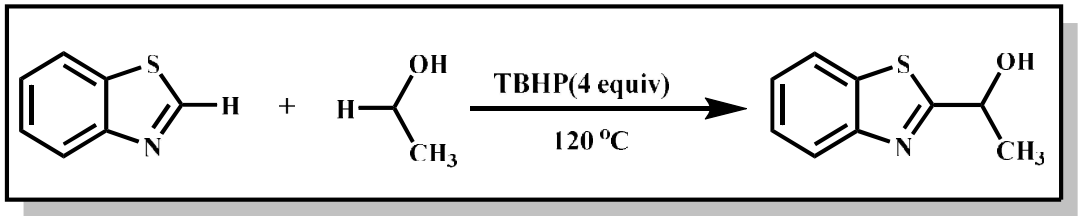
B. K. Patel et al. [34] discovered a metal-free technique for producing 3-aroylindole from *o*-alkynyl-N,N-dialkylamines by activating two sp3 C–H bonds in the presence of TBAI as a catalyst and TBHP as an oxidant (Scheme 1.8).



Scheme 1.8 TBHP mediated synthesis of 3-aroylindole

1.2.1.9 C-2-Alkylation of azoles

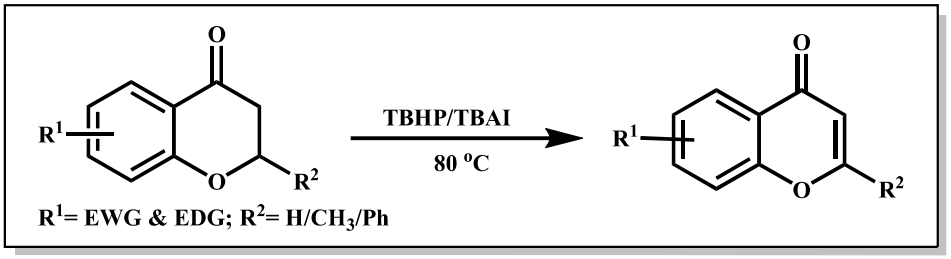
Under metal/base-free conditions, Wang and coworkers developed the direct C-2-alkylation of azoles with alcohols/ethers by oxidative C-H activation [35]. In the presence of TBHP, the cross dehydrogenative coupling between α-sp3 C-H in alcohols/ethers and 2-position sp2 C-H in azoles was carried out effortlessly. This gentle technique produced a variety of valuable azole derivatives in high yields(Scheme1.9).



Scheme 1.9 Direct C-2-alkylation of azoles via dehydrogenative cross-coupling

1.2.1.10 Preparation of double bond

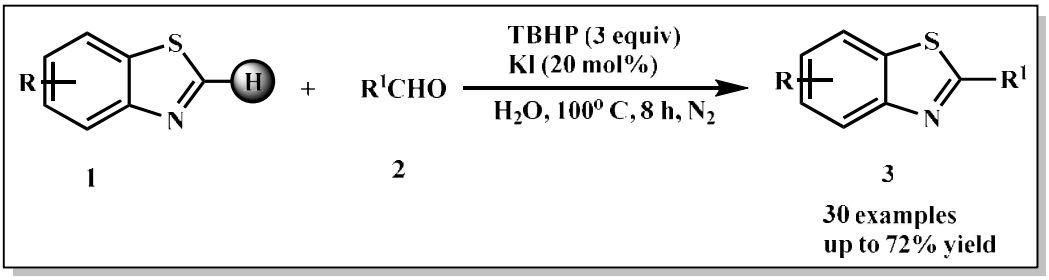
H. A. Agisho and coworkers [36] described the production of a new C=C double bond in the presence of a catalytic quantity of tetrabutylammonium iodide and the oxidant TBHP, resulting in good to outstanding yields of the related products (Scheme1.10).



Scheme 1.10 TBAI/TBHP catalyzed the formation of a new C=C bond

1.2.1.11 Oxidative coupling of benzothiazoles with aldehydes

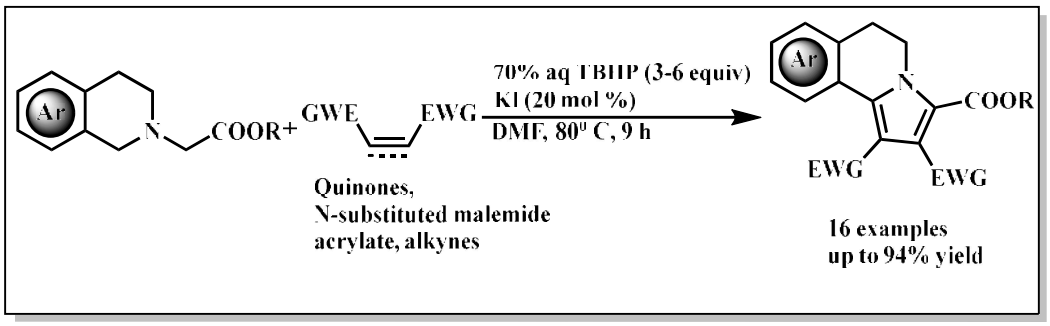
In 2014, Cui and coworkers[37] developed the oxidative coupling of benzothiazoles with aldehydes using KI/TBHP under transition-metal-free conditions (Scheme 1.11).



Scheme 1.11 Oxidative Coupling of benzothiazoles with aldehydes

1.2.1.12 1,3-Dipolar cycloaddition/oxidation/aromatization cascade reaction

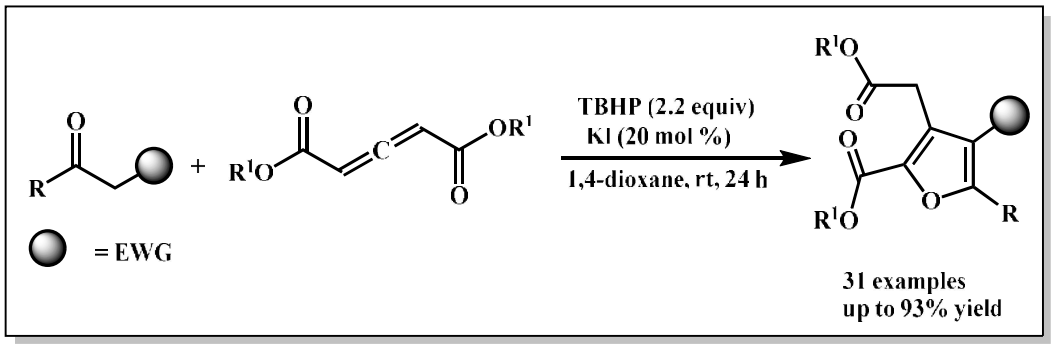
In 2016, Li and Gao et al. [38] reported a 1,3-dipolar cycloaddition /oxidation /aromatization cascade reaction between tetrahydroisoquinolines and commercially available dipolarophiles (1,4-naphthoquinone, N-substituted maleimide, acrylate), to provide diverse pyrrolo [2,1-a] isoquinolines in acceptable yields (Scheme 1.12).



Scheme1.12 1,3-Dipolar cycloaddition/oxidation/aromatization

1.2.1.13 Tandem Michael addition/oxidative annulations

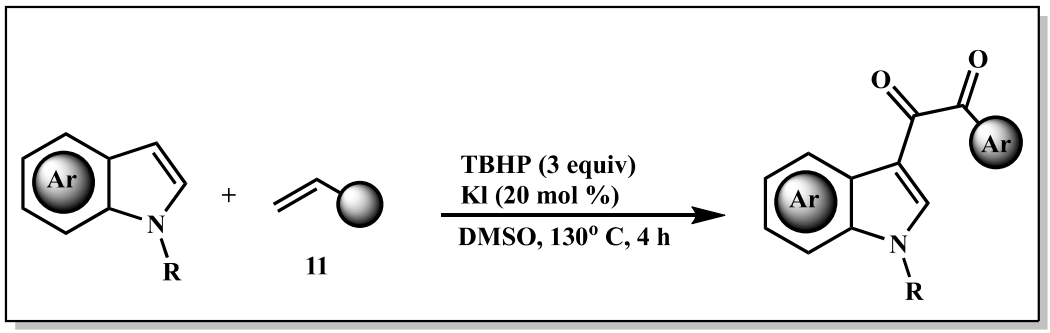
In 2016, Luo and coworkers [39] reported the synthesis of polysubstituted furan derivatives via intermolecular tandem Michael addition/oxidative annulations of allene-1,3-dicarboxylic esters and 1,3-dicarbonyl compounds (Scheme 1.13).



Scheme1.13 Synthesis of polysubstituted furan

1.2.1.14 Regioselective synthesis of C-3 dicarbonyl indole derivatives

In 2019, Guo and coworkers [40] developed a straightforward and highly atom economic approach for the regioselective synthesis of C-3 dicarbonyl indole derivatives using combination of KI and TBHP (Scheme 1.14).



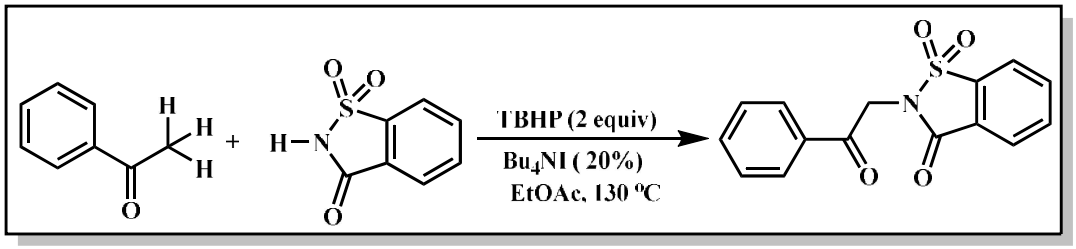
Scheme 1.14 Synthesis of C-3 dicarbonyl indole derivatives

1.2.2 TBHP Mediated C-N Bond Formation

Methods for generating C-N bonds are critical because nitrogen-containing core units are common in natural products and materials research. In recent years, the academic and industrial worlds have been paying close attention to C-N bond-forming processes under metal-free circumstances. Representative examples of various C-N bond formations are shown below.

1.2.2.1 Oxidative imidation of ketones

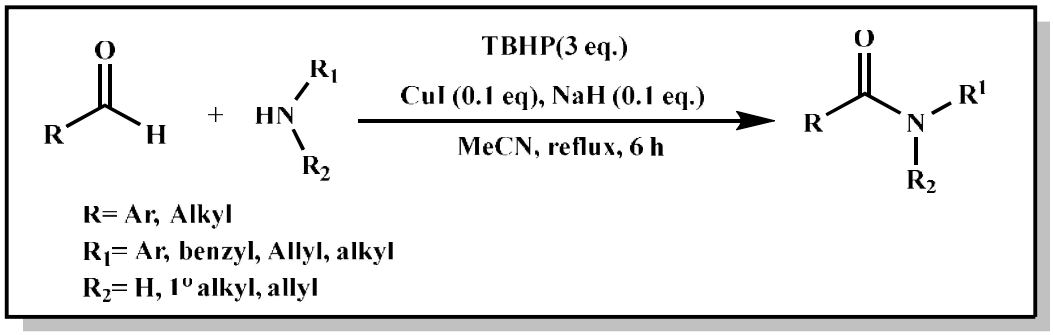
Zhang and coworkers[41] described a method for generating α-amino ketones by oxidative imidation of ketones using imides catalyzed by TBAI (Scheme 1.15). Different ketones were smoothly linked with various imides, such as saccharin, phthalimide, and succinimide, to produce their corresponding α-amino ketones in high yields. Under TBAI/TBHP catalytic conditions, this is the first C–N bond production incidence by cross-coupling of sp3 C-H bonds in simple ketones and N-H bonds in imides.



Scheme1.15 TBAI-catalyzed oxidative imidation of ketones with imides

1.2.2.2 Oxidative amidation of aldehyde

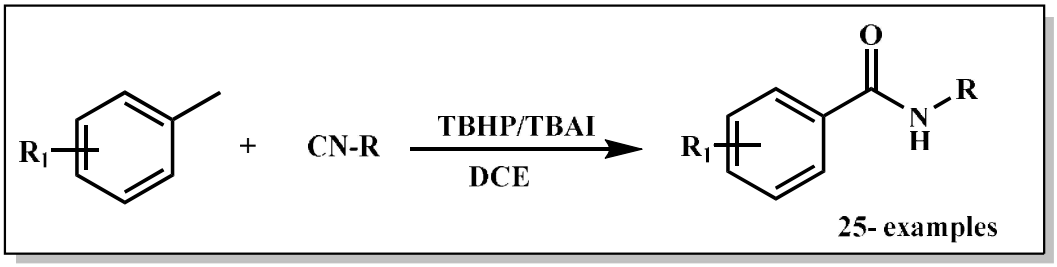
In the presence of TBHP, a combination of copper (I) iodide and an N-heterocyclic carbene [42] catalyzes the oxidative amidation of aldehydes with amines. The simple and practical approach covers a wide range of substrates and uses inexpensive and abundant reagents.



Scheme1.16 TBHP initiated oxidative amidation of aldehyde

1.2.2.3 Coupling reaction between isocyanide and aryl methanes

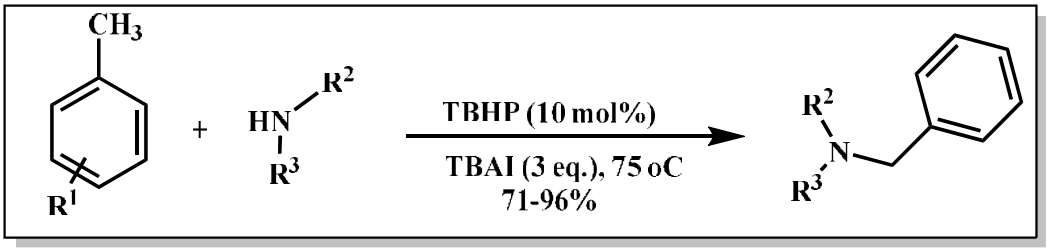
The reaction of aryl methanes with isocyanides in the presence of TBAI as a catalyst and TBHP as an oxidant was developed by L. Zhiqiang et al. [43] as a novel approach for the synthesis of amides (Scheme1.17).



Scheme 1.17 TBAI-catalyzed reaction of methylarene with isocyanide

1.2.2.4 Amination of benzylic C–H bonds

Using TBHP as an oxidant, Z. Chengjia et al. [44] achieved organocatalytic amination of benzylic C–H bonds and imidation of imides. This procedure makes the synthesis of imidazole and purine nucleoside compounds simple (Scheme 1.18).

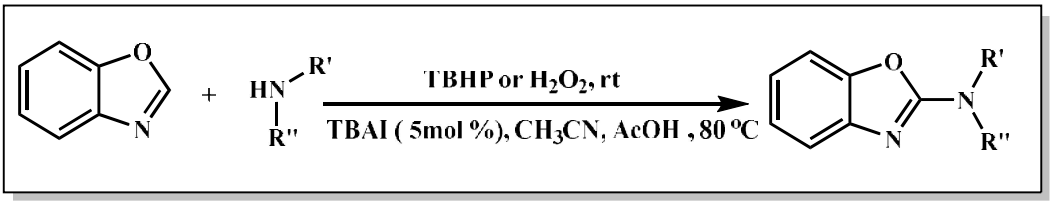


Scheme 1.18 TBAI/TBHP-mediated amination of toluenes

1.2.2.5 Amination of benzoxazoles with amines

An efficient and metal-free approach for synthesizing 2-amino-benzoxazole derivatives was reported by N. J. Boris et al. [45] from direct amination of benzoxazoles with amines through C-N bond formation using aqueous solutions of

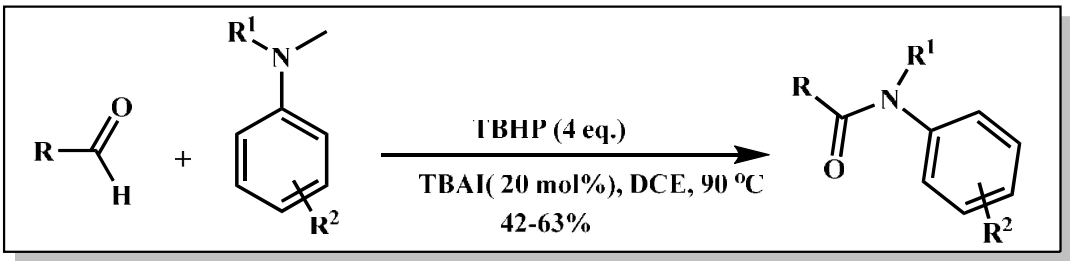
H_2O_2 or TBHP as a co-oxidant and TBAI as a catalyst (Scheme 1.19). This reaction is the first example of an iodide catalyzed oxidative amination of heteroarenes.



Scheme 1.19 TBAI-catalyzed synthesis of 2-amino-benzoxazoles

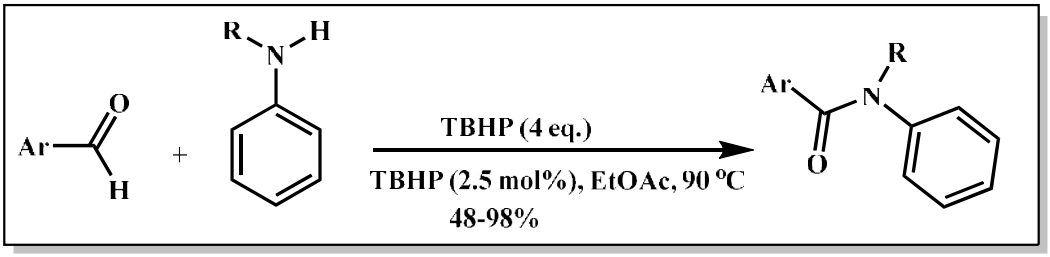
1.2.2.6 Amide bond formation from aldehydes and aromatic tertiary amines

1.2.2.6.1 M. Wen-Peng et al. [46] used TBAI as a catalyst and TBHP as an oxidant to describe an unexpected amide bond synthesis from aldehydes and aromatic tertiary amines or N-alkylanilines(Scheme 1.20).



Scheme 1.20. TBAI/TBHP-mediated synthesis of amides from tertiary amines

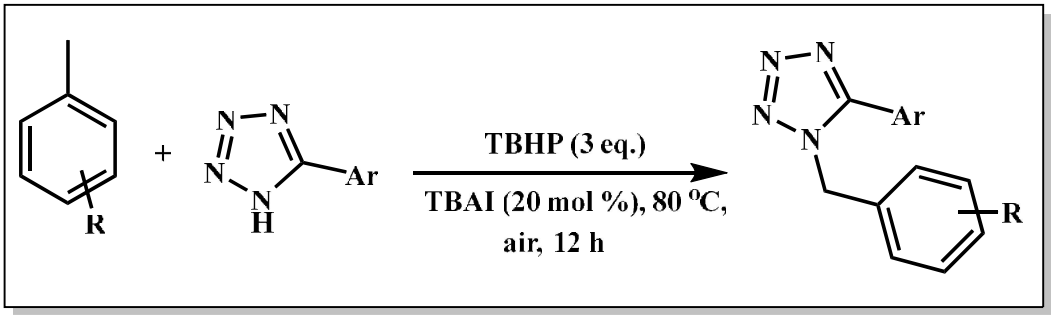
1.2.2.6.2 In refluxing ethyl acetate, W. Shan et al. produced a similar method with reduced TBAI loading. In this report, aliphatic amines, such as triethylamine and tributylamine, can also be used as coupling partners (Scheme 1.21). In both investigations, the initial step was proposed to be the oxidation of tertiary amines to produce secondary amines, followed by the interaction of secondary amines with aldehydes to give amides.



Scheme 1.21 TBAI/TBHP-mediated synthesis of amides from tertiary amines

1.2.2.7 Alkylation of aryl tetrazoles

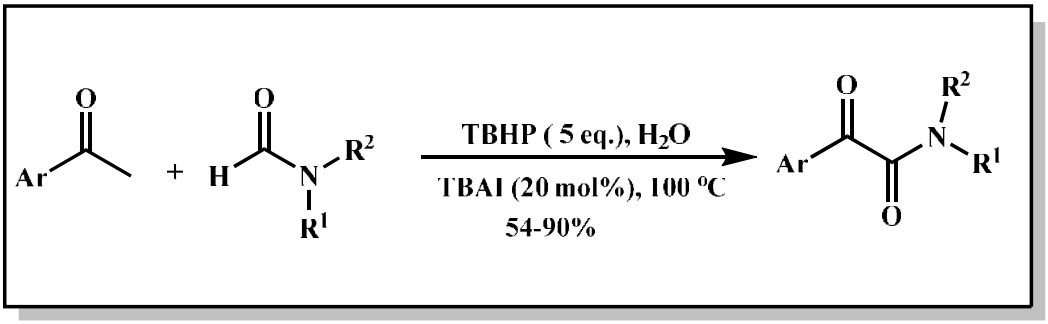
An efficient approach for synthesizing benzylated and alkylated aryl tetrazoles from aryl tetrazoles and methylarene was developed by W. Linag et al. [47] through direct C–N bond formation involving sp3 C-H activation using TBHP as the oxidant and TBAI as the catalyst (Scheme 1.22).



Scheme 1.22 Synthesis of benzylated and alkylated aryl tetrazoles

1.2.2.8 Synthesis of α-ketoamides from aryl methyl ketones

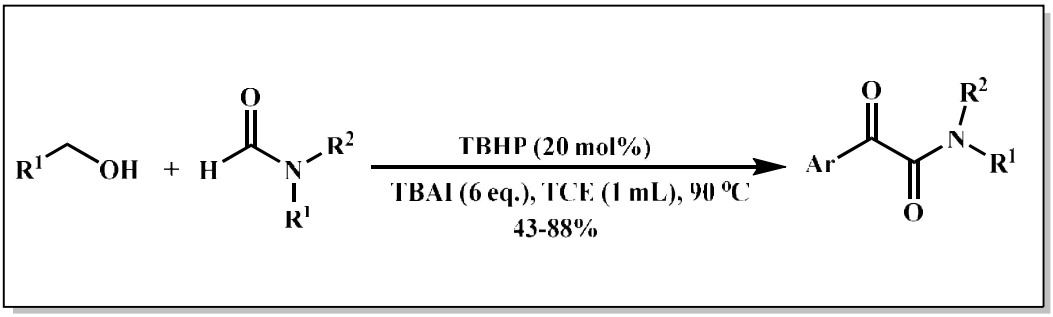
The direct synthesis of α-ketoamides from aryl methyl ketones and dialkyl formamides was developed by B. Q. Ling et al. [48] using TBHP as the oxidant and TBAI as the catalyst in aqueous media(Scheme 1.23).



Scheme 1.23. TBAI/TBHP-mediated synthesis of α-ketoamides

1.2.2.9 Synthesis of amides from alcohols and N,N-disubstituted formamides

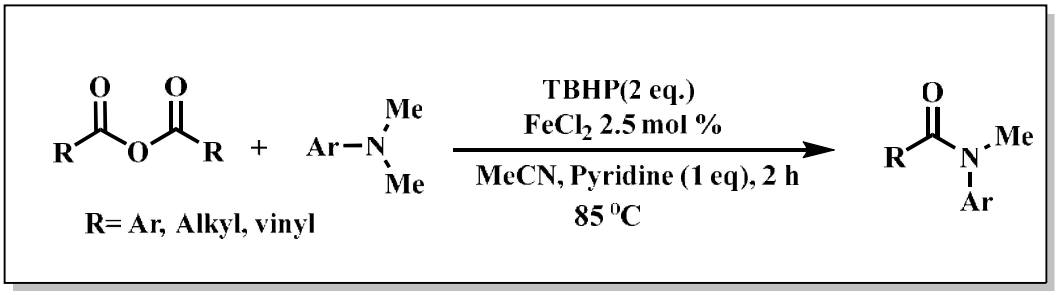
Z. Chengjian et al. [49]reported an efficient approach for synthesizing amides from alcohols and dialkyl formamides using TBHP as the oxidant and TBAI as the catalyst. Various amides were formed in good yields(Scheme 1.24).



Scheme 1.24 TBAI/TBHP-Mediated synthesis of amides from alcohols.

1.2.2.10 Synthesis of tertiary amides from tertiary amines and anhydrides

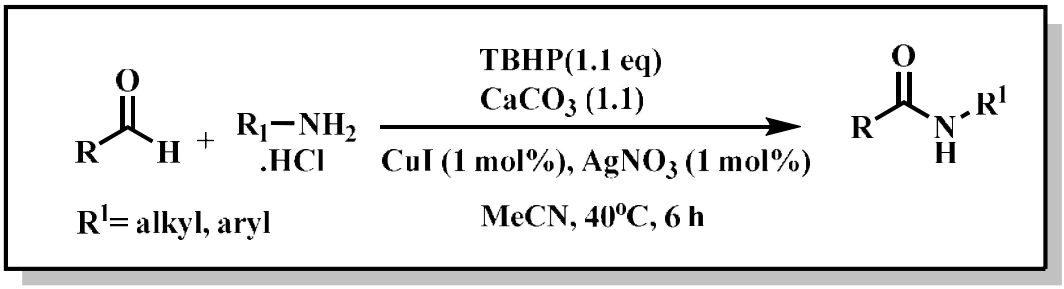
W.-J. Yoo reported[50] a general and efficient approach for synthesizing tertiary amides from readily available tertiary amines and anhydrides using $FeCl_2$ as the catalyst and TBHP as the oxidant in water (T-Hydro). Mechanistic studies indicated that the *in situ* generated α-amino peroxide of tertiary amine and iminium ion act as key intermediates (Scheme1.25).



Scheme 1.25 Synthesis of tertiary amides from tertiary amines and anhydrides

1.2.2.11 Oxidative amidation of aldehydes using amine HCl salts

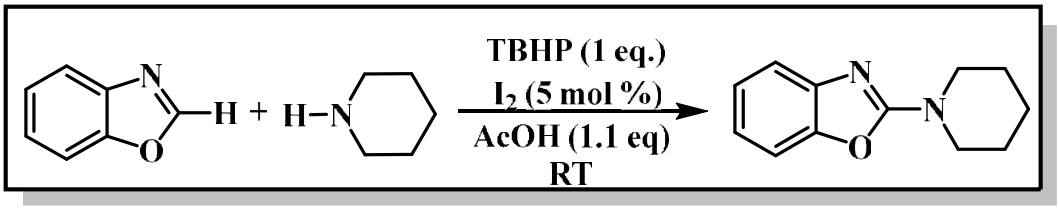
In the presence of a copper catalyst, amine HCl salts and TBHP as an oxidant are used in a mild and effective oxidative amidation of aldehydes[51](Scheme 1.26).



Scheme 1.26 Synthesis of tertiary amides

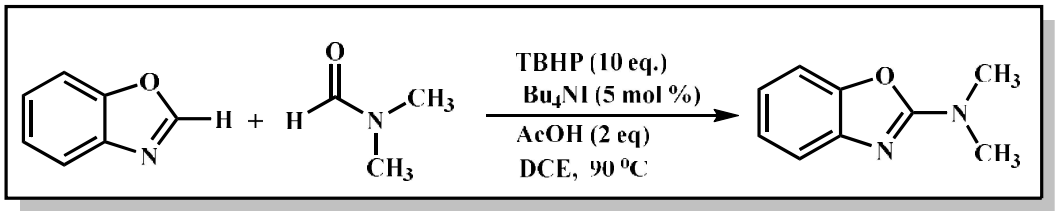
1.2.2.12 Oxidative aminations of benzoxazole

1.2.2.12.1 Prabhu[52] group has developed a simple metal-free method for oxidative amination of benzoxazole with secondary or primary amines via C-H bond functionalization (Scheme I.27). This method of making C-N bonds is user-friendly because it creates tertiary butanol and water as a by-product, both of which are ecologically beneficial. To produce therapeutically active aminated benzoxazoles in high yields, various benzoxazole derivatives with electron-donating and electron-withdrawing groups were combined with both primary and secondary amines.



Scheme 1.27 Oxidative amination of benzoxazole

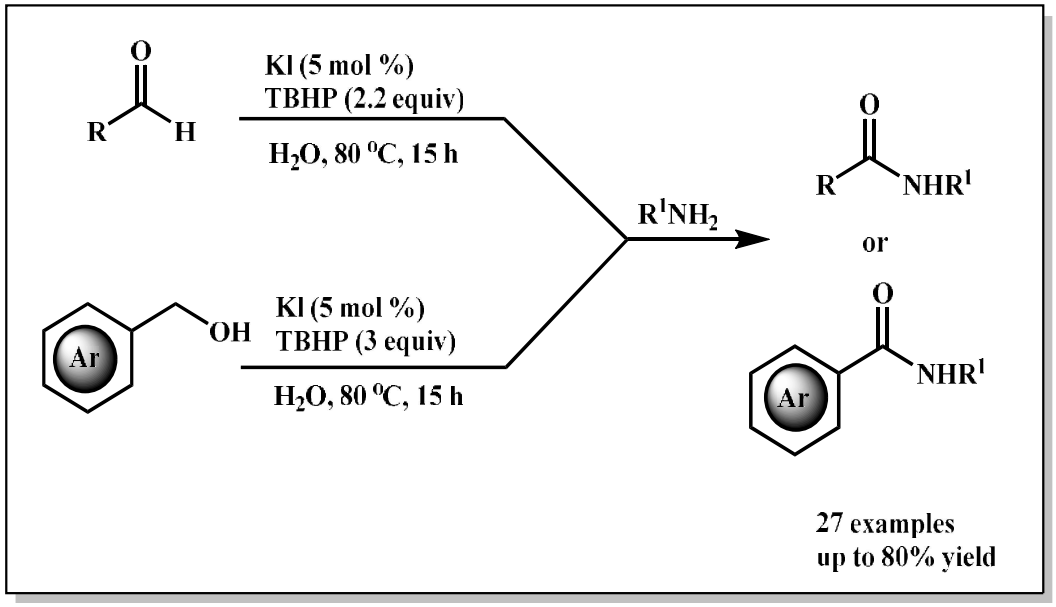
1.2.2.12.2 Wang's group [53] developed a metal-free and easy amination process for benzoxazoles employing formamides as a nitrogen source (Scheme 1.28). A series of substituted benzoxazoles combined smoothly with a series of formamides to produce excellent yields of the desired amination products.



Scheme 1.28. Metal-free direct amination of benzoxazoles

1.2.2.13 Amide bond formation from benzyl alcohols/aldehydes

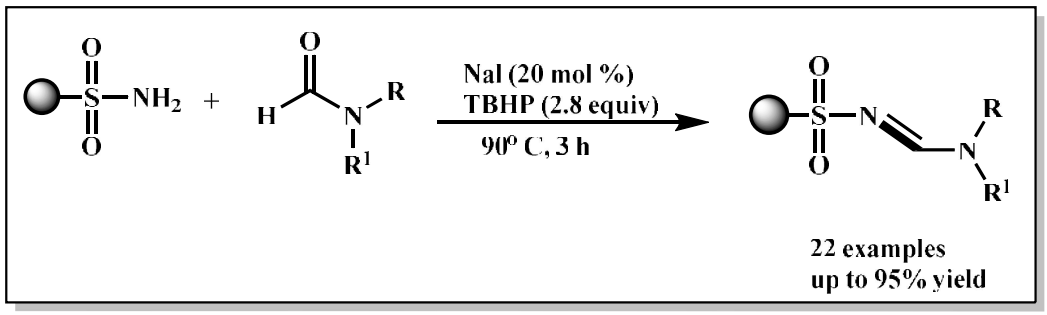
Reddy's group[54] was the first to publish the excellent yields of amide from benzyl alcohols/aldehydes with primary amines using KI as a catalyst and TBHP as an oxidant. (Scheme 1.29).



Scheme 1.29 Amide bond formation

1.2.2.14 Synthesis of N-sulfonyl formamidine

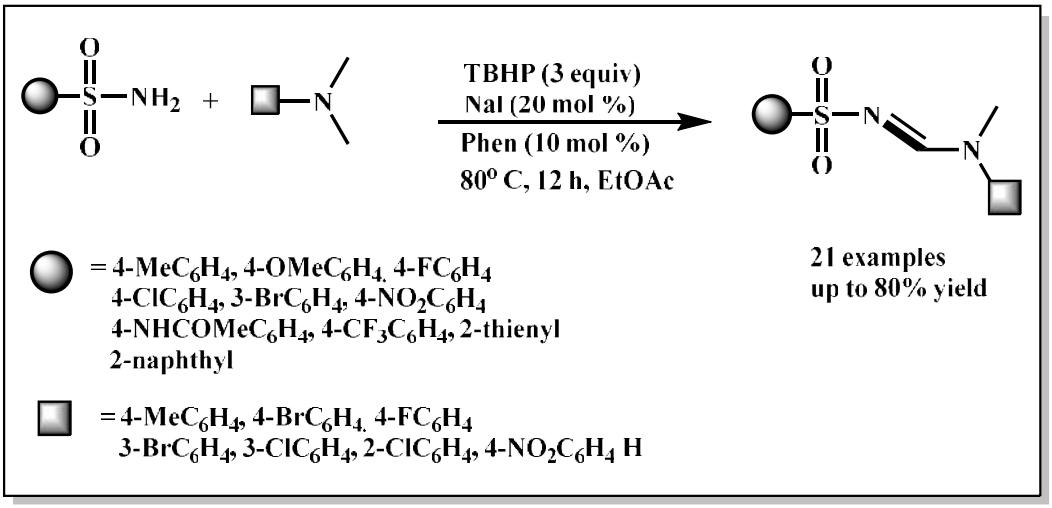
1.2.2.14.1 Wan's and coworkers [55] have developed a well-designed and simple method for rapidly assembling N-sulfonyl formamidine by a NaI-triggered condensation of sulfonyl hydrazides and formamides (Scheme 1.30).



Scheme 1.30 Synthesis of N-sulfonyl formamidine

1.2.2.14.2 Mao and collaborators developed an important route involving the de-tetra-hydrogenative cross-coupling (DTCC) reaction between commercially available and abundant substrates (N,N-dimethylaniline, and sulfonamide) under transition-metal-

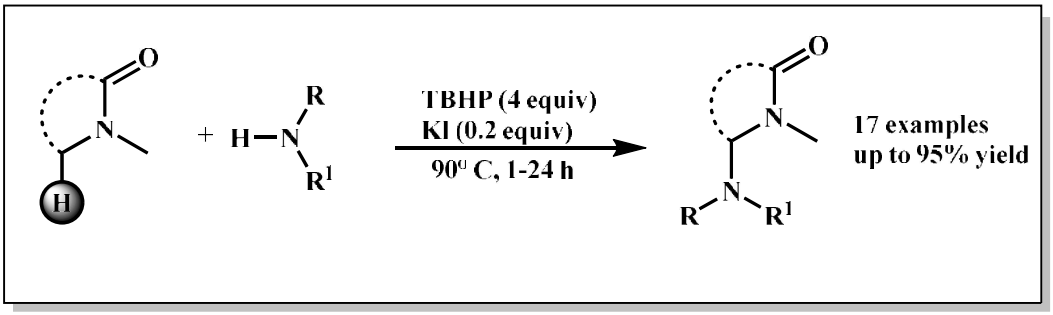
free conditions, inspired by earlier success (Wan's report) in the synthesis of sulfonyl amidines. (Scheme1.31).[56]



Scheme1.31 Synthesis of N-sulfonyl formamidine

1.2.2.15 Imidation of the C(sp3)–H bond

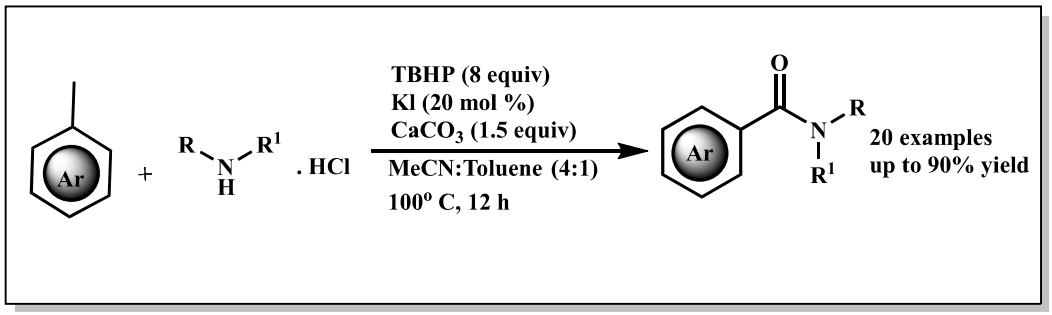
Liu and Meng reported the KI-catalyzed imidation of the C(sp3)–H bond next to the amide nitrogen atom using TBHP as an oxidant in this vein[57] (Scheme 1.32).



Scheme 1.32 Imidation of the C(sp3)–H bond

1.2.2.16 Synthesis of amide from methyl arenes and the HCl salt of amines

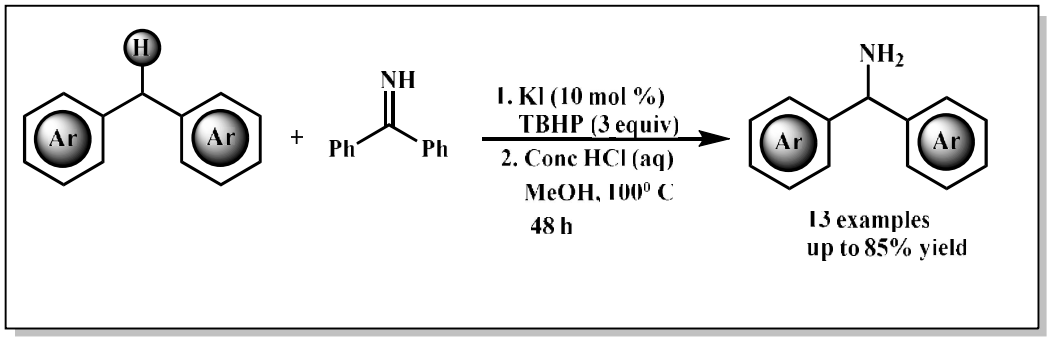
Heydari and coworkers[58] originally devised a unique and straightforward technique for directly synthesizing amide derivatives from methylarenes and the HCl salt of amines in 2014(Scheme 1.33).



Scheme 1.33 Synthesis of amide

1.2.2.17 Cross-dehydrogenative amination

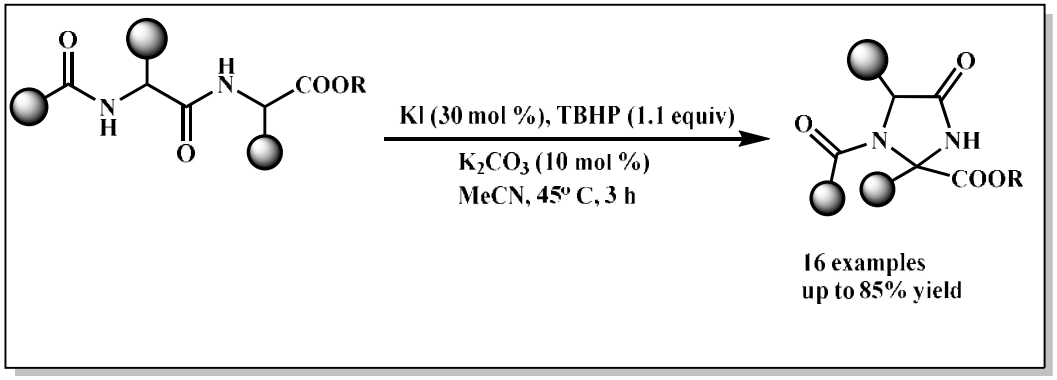
The Li group discovered an interesting cross-dehydrogenative amination reaction of diaryl methanes without using a metal catalyst, using benzophenone imine as an aminating agent (Scheme 1.34).[59]



Scheme 1.34 Cross-dehydrogenative amination

1.2.2.18 Intramolecular dehydrogenative cyclization of N-acyl dipeptide esters

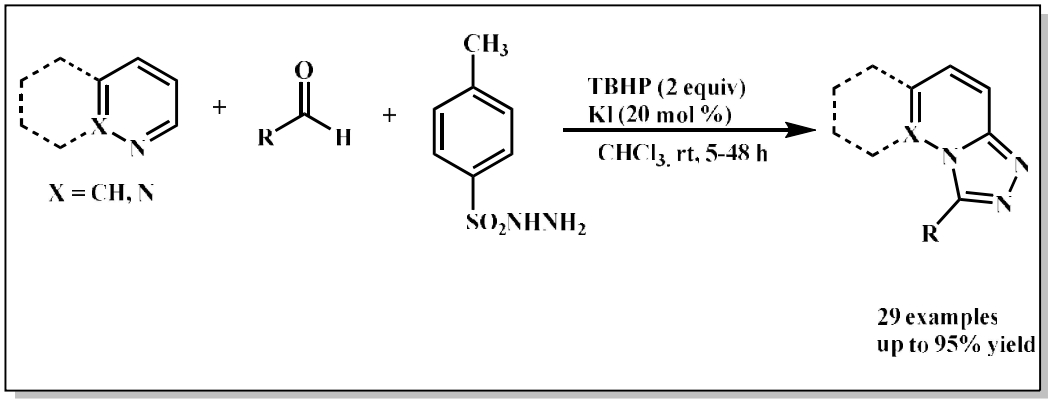
Yu and coworkers [60] developed the intramolecular dehydrogenative cyclization of N-acyl dipeptide esters to imidazolidin-4-ones using 30 mol percent KI as the catalyst, 1.1 equivalent of TBHP as the oxidant, and 10 mol percent of K_2CO_3 as the base in MeCN at 45 °C (Scheme 1.35).



Scheme1.35 Cyclization of N-acyl dipeptide esters

1.2.2.19 The Synthesis of 4,3-fused 1,2,4-triazoles

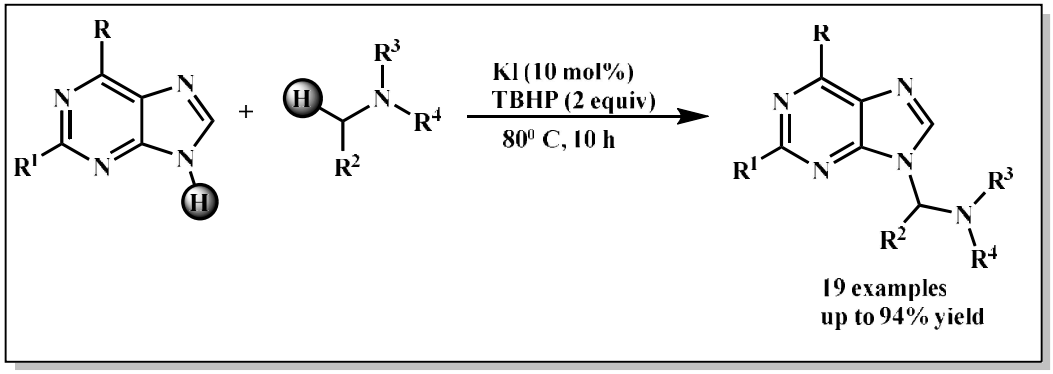
Kalita and collaborators[61] described an efficient one-pot multicomponent domino reaction between aldehydes, *p*-toluene sulfonylhydrazide, and aromatic N-heterocycles to provide 4,3-fused 1,2,4-triazoles under environmentally friendly conditions (Scheme 1.35).



Scheme 1.36 Synthesis of 4,3-fused 1,2,4-triazoles

1.2.2.20 N-Amidoalkylation of purine

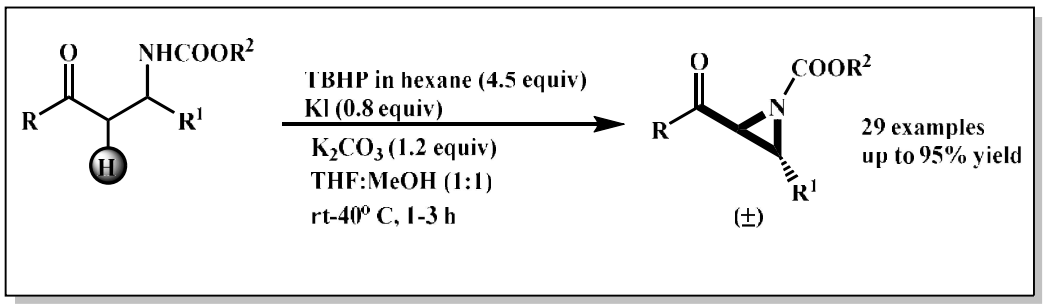
Lin and coworkers[62]used N,N-dialkylamines as suitable alkylating agents to achieve regioselective N-amidoalkylation of purine derivatives via C(sp3)–H bond activation (Scheme 1.36).



Scheme 1.37 Synthesis of N-amidoalkylation of purine

1.2.2.21 The stereoselective Synthesis of *trans*-disubstituted aziridines

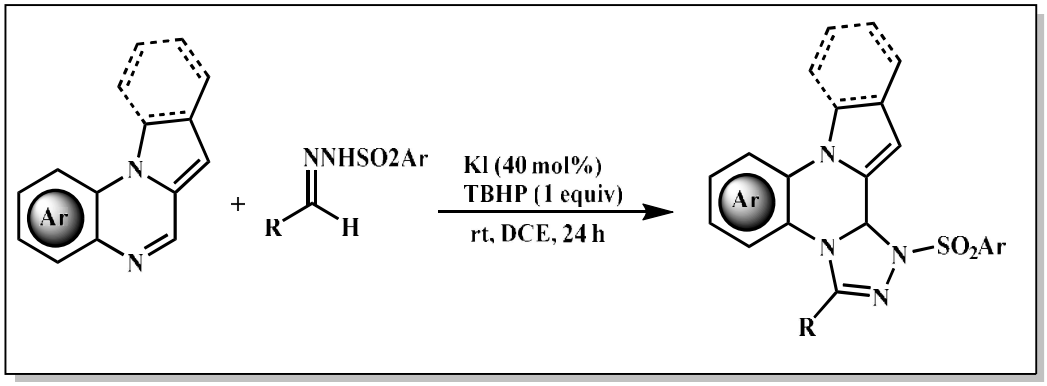
Xu and coworkers [63] reported an unusual approach for the stereoselective synthesis of *trans*-disubstituted aziridines via intramolecular oxidative C(sp3)–H amination of β-amino ketones at the start of 2020 (Scheme 1.37).



Scheme 1.38 Synthesis of *trans*-disubstituted aziridines

1.2.2.22 The Synthesis of [1,2,4]triazolo[3,4-c]quinoxaline scaffolds

Liu and coworkers[64] also revealed a synthetically feasible [3 + 2] cycloaddition reaction involving pyrrolo[1,2-a]quinoxaline and N-arylsulfonylhydrazones to produce fused [1,2,4]triazolo[3,4-c]quinoxaline scaffolds (Scheme 1.38).



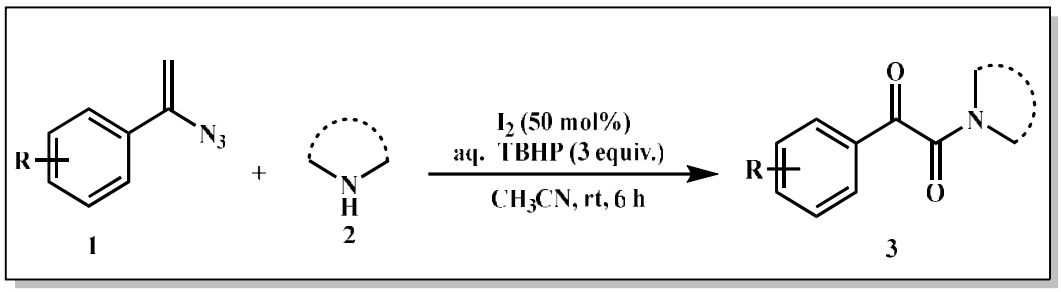
Scheme 1.39 Synthesis of [1,2,4]triazolo[3,4-c]quinoxaline scaffolds

1.2.3 Recent Application of TBHP in C-C & C-N Bond Formation (2020-2022)

Recent progress in TBHP initiated C-C & C-N bond formation has been so rapid that it is impossible to review the subject adequately here. Indeed, some of the synthetic developments pertinent to the present dissertation have been selected for special mention. Inevitably this approach left out several exemplary contributions, and an apology is tendered in advance to authors whose work is not included.

1.2.3.1 Synthesis of α-ketoamides

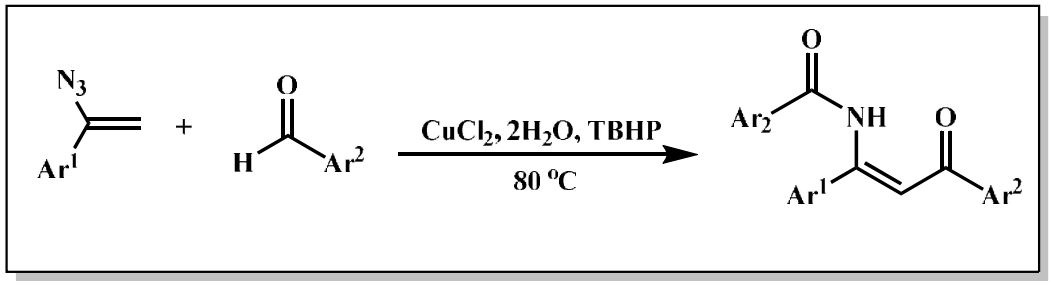
Under favorable circumstances, a facile and practical synthesis method for α-ketoamides has been devised. At room temperature, aryl vinyl azides and secondary amines were used to make α-ketoamides in a simple way(Scheme 1.39).[65]



Scheme1.40 Synthesis of α-ketoamides

1.2.3.2 Synthesis of β-acylatedenaminones

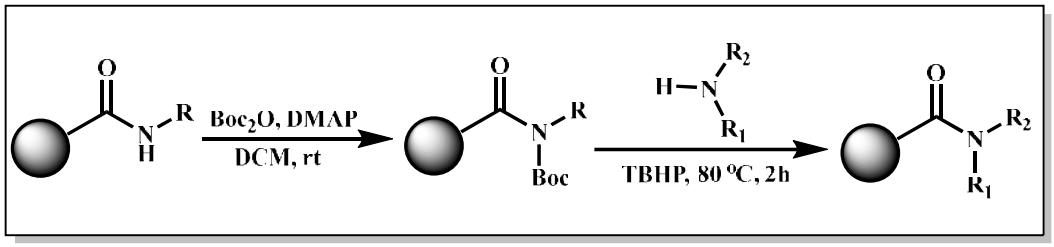
A simple and effective oxidative functionalization of vinyl azides with aldehydes yielded a wide range of β-acylated enaminones. The cross-coupling was carried out in the presence of $CuCl_2.H_2O$/TBHP, and the necessary β-acylated enaminones were generated in a (Z)-stereo-selective and atom economic manner, making this technique highly appealing. The new C–C and C–N bonds were created using a one-pot approach that included radical addition and recombination [66] (Scheme 1.40).



Scheme 1.41 Synthesis of β-acylated enaminones

1.2.3.3 TBHP-Initiated transamidation of secondary amides

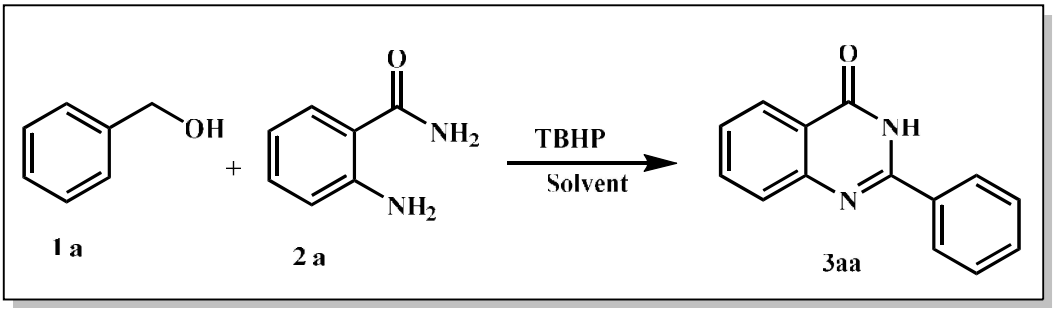
Ankush Mishra et al. have developed a facile, efficient, and eco-friendly method for transamidation of a secondary amide using TBHP as a radical initiator (Scheme 1.41).[67]



Scheme 1.42 Transamidation of secondary amides

1.2.3.4 Aqueous Domino synthesis of quinazolinones and quinoxalines

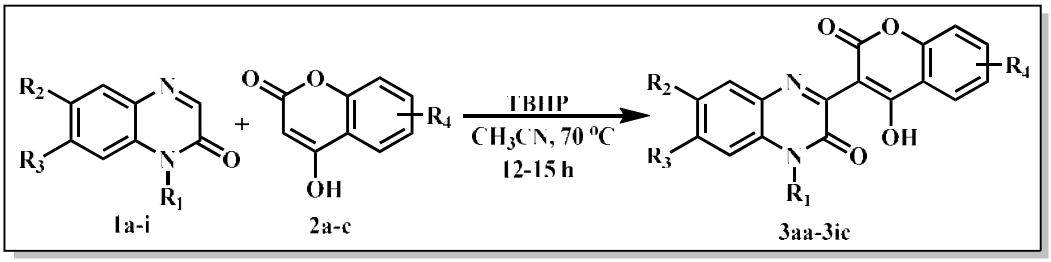
Photoinducedcatalyst-free reactions in aqueous media constitute a big step forward in developing a green and sustainable approach to domino Synthesis of quinazolinones and quinoxalines using TBHP as the oxidant [68] (Scheme 1.42).



Scheme 1.43 Synthesis of quinazolinones and quinoxalines

1.2.3.5 C-3 Functionalization of quinoxalin-2(1H)-ones

Suraj Sharma and coworkers [69] reported an efficient and atom-economical approach under metal-free conditions to C-3 functionalization of quinoxalin-2(1H)-ones with 4-hydroxycoumarins, 4-hydroxy-6-methyl-2-pyrone, and 2-hydroxy-1,4-naphthoquinone through the free radical cross-coupling pathway using TBHP as the oxidant (Scheme 1.43).



Scheme 1.44 C-3 Functionalization of quinoxalin-2(1H)-ones

1.2.3.6 Four component synthesis of enaminones

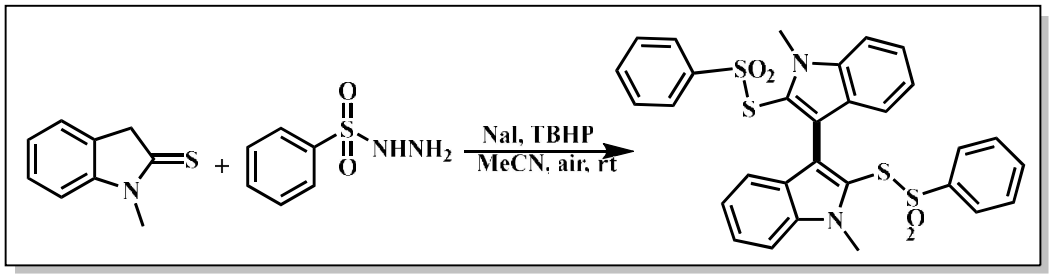
Jiantao Zhang et al. [70] reported an efficient, metal-free four-component multicomponent approach to get enaminones with various functional groups under

mild conditions. Additionally, the products could be converted to thiadiazoles (Scheme1.44).

Scheme1.45 Four component synthesis of enaminones

1.2.3.7 Synthesis of achiral axial 3, 3′-biindole-2, 2′-dibenzenesulfonothioate

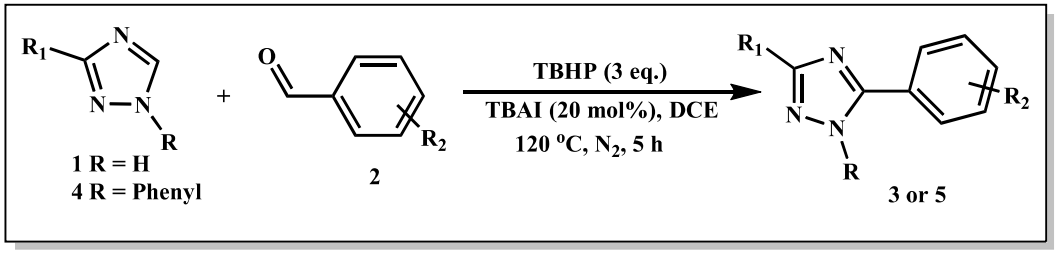
Lin Xu and coworkers[71] reported a new transition metal-free approach for synthesizing achiral axial 3,3'-biindole-2,2'-dibenzenesulfonothioate derivatives from indole-2-thiones with arylsulfonyl hydrazides under mild conditions using NaI as the catalyst and TBHP as the oxidant (Scheme 1.45).



Scheme 1.46 Synthesis of achiral axial 3, 3′-biindole-2, 2′-dibenzenesulfonothioate

1.2.3.8 Synthesis of 3,5–disubstituted–1,2,4–triazoles

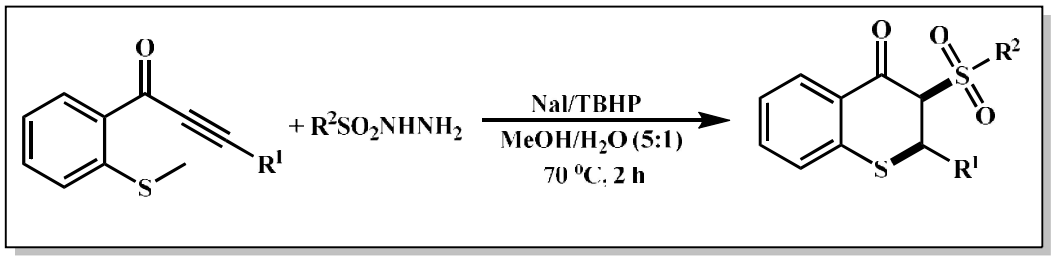
A simple, efficient, and environmentally friendly approach has been developed for the synthesis of 3,5–disubstituted–1,2,4–triazoles and 1,3,5–trisubstituted–1,2,4–triazoles from 3–monosubstituted–1,2,4–triazoles and 1,3–disubstituted–1,2,4–triazoles, respectively, with the help of TBAI / TBHP under mild reaction condition [72] (Scheme1.46).



Scheme1.47 Synthesis of 3,5–disubstituted–1,2,4–triazoles

1.2.3.9 Transition-metal-free synthesis of 3-sulfonylated thioflavones

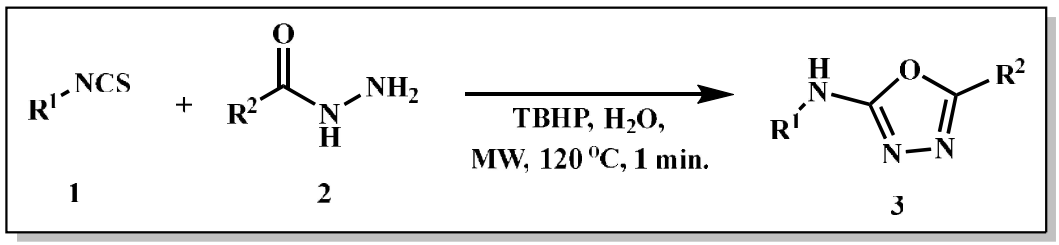
Zhi-Wen Feng [73] described an efficient transition-metal-free sulfonylation cyclization reaction of methylthiolated alkynones with sulfonyl hydrazides to 3-sulfonylated thioflavones using NaI/TBHP under mild reaction conditions(Scheme 1.47).



Scheme 1.48 Transition-metal-free synthesis of 3-sulfonylated thioflavones

1.2.4.10 One-pot synthesis of 2-amino-1,3,4-oxadiazoles

Dilep Kumar Sigalapalli and coworkers[74] reported Microwave-Assisted one-pot synthesis of 2-amino-1,3,4-oxadiazoles from the corresponding isothiocyanates and hydrazides using TBHP and water (Scheme1.48).



Scheme1.49 One-pot synthesis of 2-amino-1,3,4-oxadiazoles

Considering the importance of TBHP in C-C & C-N bond formation, it is our interest to investigate the TBHP-initiated C-C & C-N bond formation via oxidative coupling of methylarenes with active methylene compounds, benzyl bromide with amine, benzylmercaptan with amine and indole with active methylene compounds. The studies have been described in subsequent chapters 2-5.

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