Selective Synthesis of Imines *via* Oxidative Coupling of Primary Amines and Oxidation of Secondary Amines by Peroxides and other Competent Oxidants: (A Short Review)

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ABSTRACT

Imines are certainly important constituents of many biomolecules, pharmaceuticals, agrochemicals, and fine chemicals. This review article highlights the standard protocols reported so far for the selective synthesis of imines via catalyzed and non-catalyzed (i) oxidative coupling of primary amines and (ii) oxidation of secondary amines in the presence of some competent/resourceful oxidants other than molecular O_2 such as tert-butyl hydroperoxide (TBHP), H_2O_2, hypervalent iodines, persulfate, hypochlorite,electroactive species and graphene oxide. Indeed, the use of such oxidants offers a cost-effective experimental set-up, operational simplicity and also minimization of by-products. The cooperativity between catalyst, amine substrate, and oxidant is discussed in this review to understand the proposed mechanisms.Three consolidated data tables (Table 1, 2 & 3) are prepared to provide the summary of optimized reaction conditions (type of catalyst, type of oxidant, choice of solvent, amine-to-oxidant ratio, reaction time/temperature,conversion of amine, yield/selectivity of imine) of each article published to have a comparison.

Keywords: Amines, Imines, Oxidative coupling, Oxidation, Peroxides.

INTRODUCTION

Imines are called Schiff bases, in which the nitrogen atom is bonded with the alkyl group. The imine functional group (C=N), also known as Schiff-base,is an important constituent of many naturally occurring bimolecular, synthetic organic moieties and pharmaceuticals[1] (Fig.1). Imines are essential reactants in many named organic syntheses such as (i) Povarov reaction[2] to synthesize quinolines, (ii) Staudinger reaction to synthesize β-lactams[3], (iii) Imine Diels-Alder reaction to synthesize tetrahydropyridines[4], (iv) Aza-Baylis–Hillman reaction to synthesize allylic amines[5] and many multicomponent reactions to synthesize N-heterocycles[6]. Further, they were also recognized as critical intermediates in the Eschweiler-Clarke reaction[7], Amadori rearrangement[8], Pudovik reaction[9], and Kabachnik-Fields reaction[10]. Imines play a crucial role in the synthesis of diverse chemical and biologically active compounds, including amines, chiral amines, amides, pyrrolines, hydroxylamines,

and oxaziridines. The biochemical functioning of imines discloses that they are substrates/intermediates of many enzymatic reactions[11]. Besides, the Schiff bases are one of the classic imine ligands to prepare many catalytically and analytically useful coordination compounds[12].
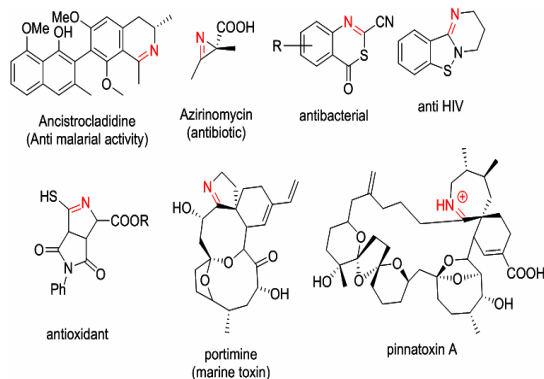

Fig. 1. Examples of naturally occurring biologically active Imines

Given the importance of imines, various conventional and catalytic methods have been developed to produce imines using appropriate substrates[13]. The synthesis of imines via (i) Schmidt reaction (the acid-catalyzed reaction of hydrogen azide with electrophiles, such as carbonyl compounds, tertiary alcohols, or alkenes)[14], (ii) alcohol-amine coupling[15], (iii) aldehyde-amine coupling[16], (iv) oxidative coupling of amines[17], (v) oxidation of amines[18], (vi) alkyne-amine coupling[19], and (vii) reaction of nitroarenes with aldehydes[20] using an appropriate catalyst or without the need of a catalyst were reported. Among the reported methods, both the oxidative coupling of amines and oxidation of amines using appropriate catalysts and eco-friendly oxidants have been emerging as operationally simple and efficient methodologies for the selective synthesis of imines. The utility of molecular O_2, TBHP, H_2O_2, and some organic/inorganic oxidants (hypervalent iodine compounds, hypochlorites, persulfates) is found in the literature. Although molecular O_2 is widely used as a green oxidant in these conversions, considerable efforts have also been made using TBHP and H_2O_2 as suitable oxidants in these conversions in view of their easy availability. Moreover, unlike molecular O_2, no special experimental setup and pressure control precaution are required when these peroxide oxidants used.

The main focus point of this review article is to provide a summary of the literature reports on catalyzed/non-catalyzed oxidative conversion of amines to corresponding imines (Schiff-base) using efficient oxidants other than molecular O_2 i.e., liquid-phase oxidants such as TBHP, H_2O_2, hypervalent iodine compounds, persulfates. Literature on catalyst-free and external oxidant-free oxidative coupling or oxidation of amines to produce imines is also captured in our review work for comparison. Based on the literature collection, the oxidative coupling of primary amines and oxidation of secondary amines are discussed in the following three sections:

1. TBHP mediated oxidative self/cross-coupling of primary amines and oxidation of secondary amines to imines.
2. H_2O_2 mediated oxidative self/cross-coupling of amines and oxidation of amines to imines
3. Miscellaneous oxidative self/cross-coupling of amines and oxidation of amines to imines

Further, a consolidated data table (Table 1, 2 & 3) concerning the optimized reaction conditions reported in each published article for the selective synthesis of imines is also presented at the end of each section of this article to have a comparison and broad idea.

1. TBHP mediated oxidative self/cross-coupling of amines and oxidation of amines to imines

Ge *et al.,* described the designing of Mn/Co-containing metal-organic framework (Mn/Co-MOF) for the oxidative coupling of various benzyl amines for the high yield synthesis of (up to 100%) corresponding imines in CH_3OH at room temperature (RT)[21] (Scheme 1). The reaction conditions were optimized by varying the solvent (CH_3CN, toluene, CH_2Cl_2, ethanol, and methanol), oxidant (molecular O_2, H_2O_2, TBHP, air, and benzoyl peroxide), and time. The authors extended the optimized catalytic conditions (1mmol substrate, 2mmol TBHP, and 10 mg catalyst in 2 mL methanol at RT for 3 h) further towards the cross oxidative-coupling of different benzyl amines and aliphatic amines. The authors also disclosed the results of catalyst recycling and reusability. This bimetallic heterogeneous MOF was found to be stable and efficient up to six catalytic runs of oxidative coupling of amines.

The bimetallic MOF catalyst was prepared by treating the acetate salts of Mn(II) and Co(II) with organic ligand namely 1,3,5-benzenetricarboxylic acid (H_3BTC) in DMA by applying ultrasound conditions. The MOF catalyst was characterized by scanning electron microscopy, energy dispersive spectroscopy, X-ray photoelectron spectroscopy, X-ray diffraction, thermogravimetry, and N_2 sorption.
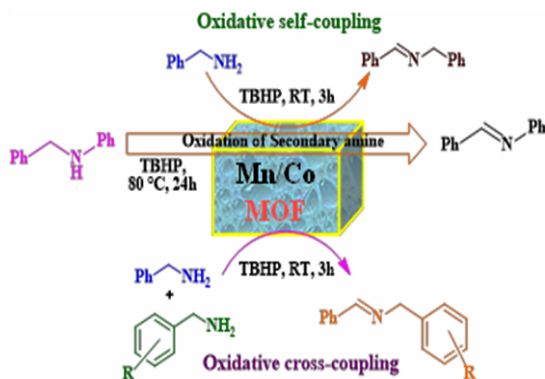
Scheme 1. Mn/Co-MOF catalyzed self-, cross-oxidative coupling of amines and oxidation of amines by TBHP for the selective synthesis of imines

A report by Wang *et al.,* described the synthesis of a recyclable hetero-bimetallic cluster type MOF [$Fe_2Mn(\mu_3$-O)(BPTC)$_2$(DMF)$_2$(H_2O)] (BPTC=biphenyl-3,4',5-tricarboxylic acid) and its application in the synthesis of various imines via homo and cross-oxidative coupling of relevant amines using TBHP as an oxidant[22] (Scheme 2). The heterobimetallic MOF catalyst was synthesized by established procedures. The catalytic conditions were optimized by studying the oxidative coupling of benzylamine in various solvents (toluene, DCM, MeCN, MeOH, n-hexane) and oxidants (TBHP, H_2O_2, and Molecular O_2). The optimized reaction conditions at RT use TBHP as an oxidant and MeOH as a solvent. Later, substrate scope was examined to produce both symmetrical and un-symmetrical imines. The influence of electronic effects by substituents of amines in their oxidative coupling phenomenon was also reported. According to the control experiments, a synergism i.e. cooperative catalysis was exhibited by both Mn and Fe sites of the catalyst during the oxidative coupling of amines. Catalyst recovery and recycling experiments indicate that this catalyst is stable up to eight catalytic runs without any change in the conversion of amine substrate and selectivity toward imine product.


Scheme 2. Fe-Mn based heterobimetallic MOF catalyzed self-, cross-oxidative coupling of amines by TBHP for the selective synthesis of imines.

Tantirungrotechai and colleagues described the usefulness of Cu-coordinated chitosan beads as an effective heterogeneous catalyst in the oxidative homo and cross-coupling of a range of amines for the high-yield synthesis of corresponding imines[23] (Scheme 3). Firstly the authors described the synthesis and characterization of the Cu/chitosan beads. Different copper precursors (Cu(OAc)$_2$, CuCl$_2$, CuO, and CuI) were used to prepare the Cu/chitosan beads. These beads were characterized by various analytical techniques like TGA, ICP-MS, XPS, Auger, ESR, XRD, and FTIR spectra to know their surface properties, chemical composition, and crystalline phases. The beads resulting from Cu(OAc)$_2$ have shown nearly all spherical shapes compared to those obtained from other copper precursors. Initially, the authors studied the oxidative coupling of benzylamine under different conditions to optimize the catalytic conditions. The beads obtained from Cu(OAc)$_2$, with 3.5% mole loading of Cu, have shown superior catalytic activity in the TBHP mediated oxidative coupling and showed 99% conversion of benzylamine and 98% yield of corresponding imine in CH_3CN at 80°C after 30 min of reaction time. The oxidative coupling conducted in the absence of a catalyst provided only a 15% yield of imine under the operated conditions. Later, the optimized reaction conditions were effectively implemented in the oxidative coupling (homo and cross) of a diverse range of amines (25 examples) to produce the corresponding imines. Finally, the authors also performed the catalyst recovery and recycling experiments and noticed that the Cu/chitosan bead catalysts are stable for upto ten catalytic cycles without showing any decrease in reactivity.

Scheme 3. Cu-coordinated chitosan beads as a catalyst in self-, cross-oxidative coupling of amines by TBHP for the selective synthesis of imines

Chen and colleagues reported the use of a porphyrin like tetradentatenon-heme based ligand TPA (tris(2-pyridylmethyl)-amine) to design a bioinspired and catalytically active ($MnCl_2$(TPA)) complex for TBHP mediated oxidative coupling of primary amines to imines in at RT[24] (Scheme 4). The influence of reaction parameters (catalyst dosage, solvent, reaction temperature, time, etc.) on the catalytic performance was also investigated in detail. When the Mn(II) was replaced with Fe(III), Co(II), Ni(II), Cu(II), and Zn(II), the conversion of amine and the yield of the imine were not appreciable. The ($MnCl_2$(TPA)) complex was able to catalyze the oxidative coupling of more challenging 1-heptylamine.
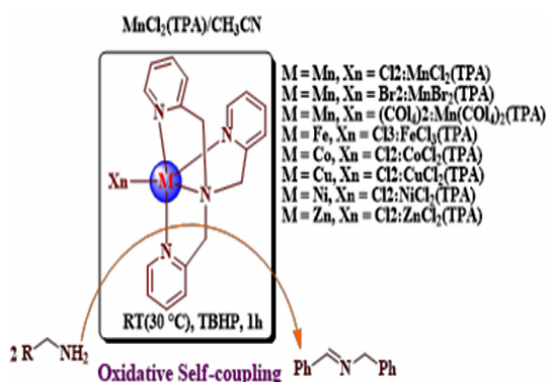
Scheme 4. ($MnCl_2$(TPA)) complex catalyst for TBHP mediated oxidative coupling of primary amines to imines

Zhao *et al.,* prepared a bimetallic heterogeneous catalyst $[Co(L)_2]_2[Mo_6O_{19}]$ (L= 2-acetylpyridine thiosemicarbazone) and proved its efficiency as a catalyst in the oxidative coupling of amines under mild conditions[25] (Scheme 5). Firstly, the authors described the synthesis of the above bimetallic catalyst by treating the appropriate

precursors of Co(II) and precursors of Mo(III) and the characterization by EA, IR,UV–Vis, PXRD spectra, XPS, and single-crystal X-ray diffraction. Later, the efficacy of bimetallic catalyst was evaluated in the oxidative coupling of a range of primary amines using TBHP as an oxidant and observed good conversion of amine substrates and good yields of imine products in methanol. A total of 9 derivatives were obtained under the optimized catalytic conditions. Further, the kinetics of the above catalytic reaction indicate it follows the pseudo-first-order kinetics model. The bimetallic catalyst was recycled three times without any appreciable loss in its activity.
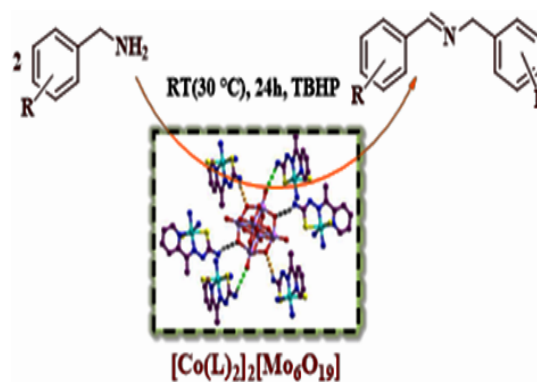
Scheme 5. Co-Mo bimetallic catalyst for TBHP mediated oxidative coupling of primary amines to imines

Zhang *et al.,* reported the heterogeneous α-MnO_2catalyzed TBHP mediated oxidative self-coupling reaction of amines for the facile synthesis imines at RT in CH_3CN[26] (Scheme 6). A total of 13 (thirteen) benzylic, heterocyclic, and aliphatic imines were synthesized at room temperature by this approach. This catalytic protocol has shown the obtainment of appreciable conversion of amine substrates and good yields of imine products. The authors provided the results of *in-situ* NMR and GC-FID/MS analysis to support the proposed mechanism. Further, the results of in-situ ATR-IR disclose the involvement of a non-radical path in the oxidative coupling of amines in the presence of α-MnO_2 catalyst. Control experiments revealed that the α-MnO_2 catalyst has exhibited long-life stability in more than 100 h in the continuous synthetic experimentation of imines. The α-MnO_2 catalyst was reused three times. It is also noticeable that other oxides of Mn such as β-MnO_2, δ-MnO_2, Mn_2O_3, and Mn_3O_4 had not performed the reaction well. Besides, other transition metal oxides such as Fe_2O_3, V_2O_5, CuO, Co_3O_4, and MoO_3 were found to be inactive under the operated conditions mentioned in the article.
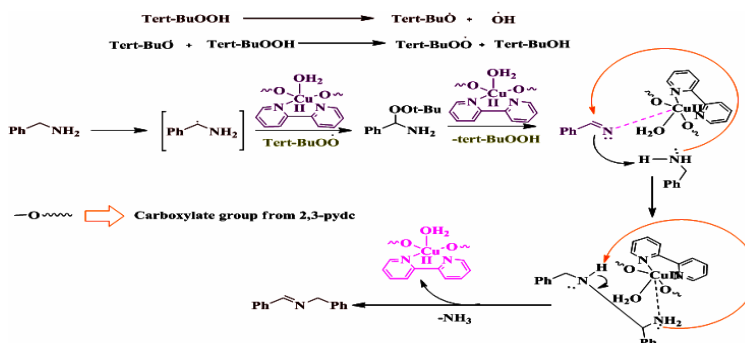
Oxidative Self-coupling

$$2 R\!\!-\!\!NH_2 \xrightarrow[\text{RT, 4h}]{\text{alpha-MnO}_2,\ \text{TBHP, CH}_3\text{CN}} Ph\!\!-\!\!N\!\!-\!\!Ph$$
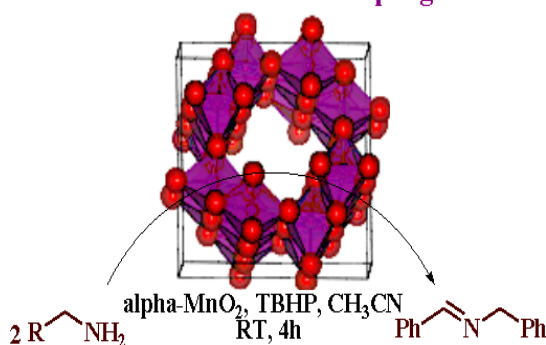
Scheme 6. α-MnO₂ catalyzed TBHP mediated oxidative self-coupling reaction of amines for the selective synthesis of imines

Mondal and colleagues employed a 1D-coordination polymer of Cu(II) composed of 2,3-pyridinedicarboxylic acid (2,3-pydc) and 2,2-bipyridine (2,2-bpy) as catalyst by in the TBHP mediated self-oxidative coupling of

benzylamine for the high yield synthesis of corresponding imine without additional solvent[27] (Scheme 7). The authors initially described the synthesis of 1D-coordination polymer, [{Cu₂(2,3-pydc)₂(2,2-bpy)(H₂O)₂}.4H₂O]ₙ(A) and its structural characterization by different physicochemical techniques such as IR-spectroscopy, UV-Vis spectroscopy, elemental analysis and TGDTA analysis including X-ray single crystal structure. Indeed, previously Yin et al reported the synthesis of this 1D-polymer catalyst[27]. However, Mondal and the team followed a different method to synthesize this 1D-polymer and re-established its structural parameters. The authors claimed that this is the first example of a Cu-based 1D-coordination polymer that is used as a catalyst in the oxidative coupling of amines. After the optimization of catalytic conditions, the authors discussed the reaction mechanism and proposed a tert-butylperoxy radical-involved reaction path.

Scheme 7. Reported mechanism of 1D-polymer [{Cu₂(2,3-pydc)₂(2,2-bpy)(H₂O)₂}.4H₂O]ₙ catalyzed TBHP mediated oxidative coupling of amines for the selective synthesis of imines

Kim and Thakur reported the efficiency of Mn(III)TPPCl/TBHP(TPPCl=5,10,15,20-tetra (4-pyridyl)-21H,23Hporphine chloride) system in CH₃CN to convert the benzyl amines into corresponding N-benzylbenzaldimines via the self-oxidative coupling at RT[28] (Scheme 8). A total of eight (8) examples of imine derivatives in high yields were synthesized. Based on the control experiments,

the proposed reaction mechanism initiated by the Mn(V)=O species that generated by the interaction of Mn(III)-TPPCl with TBHP. The Mn(V)=O species will then convert to Mn(IV)=O, Mn(IV)-OH and Mn(III)-OH species to facilitate the oxidative self-coupling of the benzylamine finally to N-benzylbenzaldimine. Further, this work discussed also the influence of steric hindrance by substituent on amines.
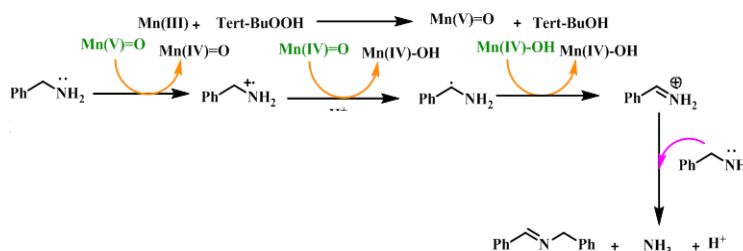
Scheme 8. Reported mechanism of Mn(III)-TPPCl complex catalyzed TBHP mediated oxidative coupling of amines for the selective synthesis of imines.

Anbardan *et al.,* demonstrated the ability of a Cu-MOF, namely [Cu$_2$(BDC)$_2$(DABCO)] in catalyzing oxidative homo-coupling of a range of benzylamines with different steric and electronic properties using TBHP as an oxidant to produce corresponding imines in good yields in THF at RT[29] (Scheme 9) for 24 hours. Being a heterogeneous catalyst, the Cu-MOF was found to be reusable four times without loss of catalytic activity. A comparison with other reported catalysts in the self-coupling of benzyl amines indicates that the Cu-MOF/TBHP could be a good choice/alternative catalytic system. A plausible mechanism proposed by the authors discloses the involvement of peroxy radical generated from TBHP in oxidative coupling.
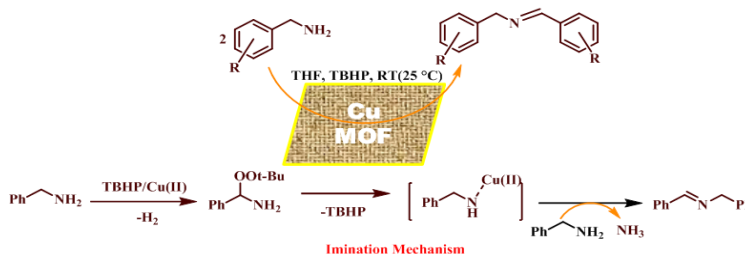
Scheme 9. Reported mechanism of [Cu$_2$(BDC)$_2$(DABCO)] catalyzed TBHP mediated oxidative coupling of amines for the selective synthesis of imines

A report by Choi and Doyle[30] demonstrated the development of [Rh$_2$(cap)$_4$]/TBHP catalytic system (cap=tetracaprolactamate) for the oxidation of diverse secondary amines to imines with high chemo- and regioselectivity in CH$_3$CN (Scheme 10). The catalytic system has shown good tolerance for pendant functional groups on secondary amines. The authors exploited the utility of the above catalytic system also in the synthesis of potential antitumor and gene-targeted drug analogs in CH$_2$Cl$_2$(Scheme 10). A total of nine (9) imine derivatives were reported in the article.
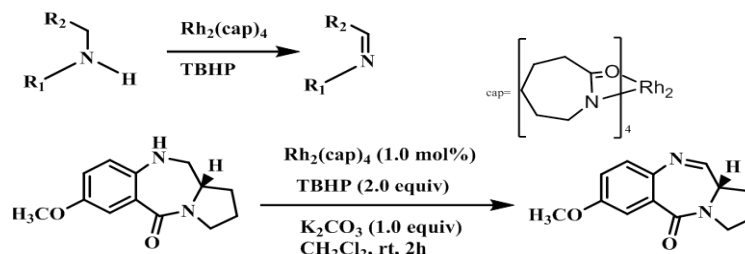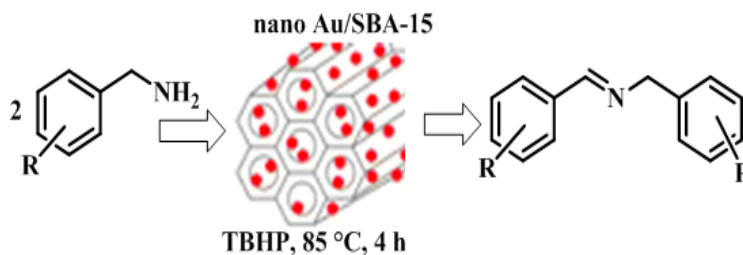

Scheme 10. [Rh$_2$(cap)$_4$]catalyzed oxidative self-coupling of amines for the selective synthesis of imines

Burri and colleagues reported the usefulness of nano-gold (NG) immobilized mesoporous SBA-15 (abbreviated as SBA-NG) as an efficient catalyst in solvent-free selective oxidation of benzylamine to N-benzylbenzaldimine[31] (Scheme 11). Firstly, the authors described the immobilization of nano-gold on SBA-15 by simultaneous deposition and reduction method and the characterization of resulting SBA-NG by N$_2$ adsorption and desorption method, BET surface area technique, XRD, IR, TEM, SEM, EDX, and XPS methods. Later, the SBA-NG catalyzed oxidation of benzylamine was studied under different conditions to optimize the catalytic conditions for the synthesis of corresponding imine. The authors studied the effect of various reaction parameters such as (i) nature of the oxidant, (ii) oxidant/amine molar ratio, (iii) reaction time, (iv) reaction temperature, (v) solvent, (vi) concentration of the SBA-NG catalyst to optimize the reaction conditions. According to the data reported, the optimized reaction conditions include the use of 70% TBHP oxidant, 0.5 TBHP/benzylamine molar ratio, 4 h of reaction time, 85 reaction temperature, solvent-free reaction system, and catalyst dosage of 50 mg. The optimized reaction conditions were extended to carry out the oxidation of some of the differently substituted benzylamines and alkylamines. By-product formation was observed mainly in the case of the oxidation of alkylamines. A free radical mechanism was proposed based on the control experiment using 4-t-butyl catechol as

a radical scavenger. Besides, catalytic recycling experiments of benzylamine oxidation disclosed that the SBA-NG catalyst is stable for up to four catalytic cycles without any decrease in activity.

Scheme 11. SBA-NG catalyzed TBHP mediated oxidative self-coupling of primary amines for the selective synthesis of imines under solvent-free conditions

Kumagai and colleagues studied the efficacy of $FeCl_2$/TEQ (TEQ = TetraQuiniline) complex with TBHP, in the chemoselective dehydrogenation of amines (primary and secondary) to the corresponding imines between 0 and 25 in CH_3CN[32] (Scheme 12). A total of seventeen (17) imine derivatives were produced. The authors mentioned that just 0.1% catalyst and 2 equivalents of TBHP are enough to accomplish the imine production. The reaction mechanism for the conversion of both primary and secondary amines into the corresponding imines was proposed based on the control experiments. The influence of the substituent position and nature of the substituent on the oxidation was also derived.
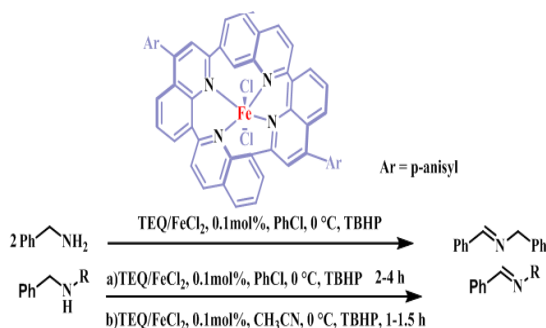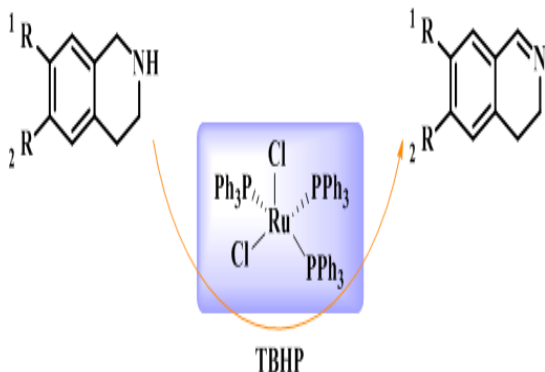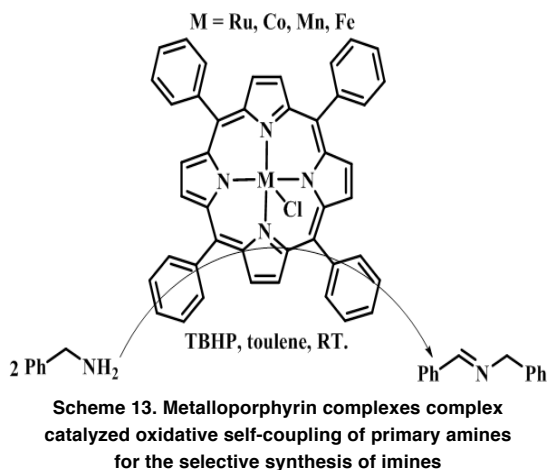

Scheme 12. Fe(III)-TetraQuiniline complexcatalyzed oxidative self-coupling of primary amines and oxidation of secondary amines for the selective synthesis of imines

Yuan *et al.,* reported that a tetraphenyl-porphyrin bound Mn(III) complex i.e., (Mn-TPPCl) is a highly efficient catalyst for the oxidative coupling of diverse amines by TBHP oxidant to produce corresponding imines[33] (Scheme 13). Firstly, the oxidative coupling of benzylamine was studied under different conditions using different metalloporphyrines, and different solvents to produce N-benzylbenzaldimine. It was observed that a solvent with a large dielectric constant (CH_2Cl_2, CH_3CN, Isopropanol), was not effective in oxidative coupling in terms of the yields of respective imine products. Hence, Toluene was selected as a solvent in the present investigation given its low dielectric constant (2.4). Among the various metalloporphyrin complexes examined (Mn, Fe, Co, Ru), the MnTPPCl complex was found to be highly efficient in terms of the conversion of benzylamine (98%) and yield of N-benzylbenzaldimine (91%). Later, the authors investigated the amine substrate scope in the MnTPPCl-catalyzed oxidative coupling. Most of the amine substrates were easily converted to corresponding imines with a high conversion rate and excellent selectivity. Especially, the amine substrates containing electron-withdrawing groups on the phenyl ring were converted easily. A total of nine (9) diverse imine derivatives were synthesized. It is noticeable that a small amount of aldehyde, a direct oxidation product of amines, was also detected for some of the substrates in the oxidative coupling reactions. The proposed mechanism indicates that the MnTPPCl/TBHP system catalyzed oxidative coupling of benzylamine involves radical species. When the reaction was monitored by *in-situ* UV-Visible spectra, the formation of an active catalytic intermediate of high valent Mn-porphyrin was detected. Meanwhile, the results of DFT calculations provide a piece of evidence for the mechanism of the nucleophilic attack of benzylamine to benzaldehyde.

Murahashi *et al.,*[34] reported that the oxidation of secondary amines provided two different products when there was a change in the catalytic system (Catalyst/oxidant). The oxidation of secondary amines catalyzed by $(PPh_3)_3$-Ru-Cl_2/ TBHP gave an imine product. On the other hand, the same oxidation by Na_2WO_4/H_2O_2 gave nitrones and reasoned that there are two different catalyst

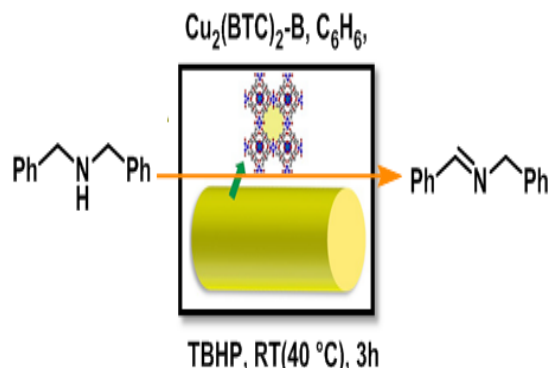species i.e., M-OOH and M=O species to change the product distribution.

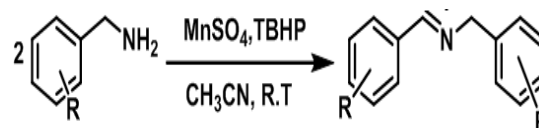**Scheme 13. Metalloporphyrin complexes complex catalyzed oxidative self-coupling of primary amines for the selective synthesis of imines**

Scheme 14. Oxidation of secondary amines by (PPh$_3$)$_2$-Ru-Cl$_2$/TBHP catalytic system

According to the proposed mechanism, a Ru-amine complex (Ru-NR$_2$CH$_2$RI) formed at the beginning of the catalytic cycle is subjected to β-elimination to produce an imine-Ru-hydride complex. Finally, TBHP oxidizes the imine-Ru-hydride complex and produces the desired imine.

Baiker and his colleagues prepared three new microporous Cu-MOFs, namely bulk Cu$_3$(BTC)$_2$, Cu$_3$(BTC)$_2$-A, Cu$_3$(BTC)$_2$-B (BTC=benzene-1,3,5-tricarboxylate)and examined their efficiency in the oxidation of dibenzylamine to obtain corresponding imine[35] (Scheme 15). These nanosized MOFs were prepared according to standard hydrothermal/solvothermal methodologies. A polymer poly(acrylic acid sodium salt) (PAA-Na) and CTAB were used as capping agents to prepare the MOF-3, only PAA-Na was used to obtain MOF-2, and no capping agent was used to obtain the MOF-1. All the materials were well characterized by XRD, SEM, TEM, and

N$_2$ adsorption-desorption. Among the three nano-MOFs, the nano-MOF-3 was catalytically more active in the oxidation of dibenzylamine using TBHP oxidant. However, when compared to the previous literature reports the catalytic activity displayed by nano-MOF-3 is not appreciable. It was reasoned that blocking of active sites on these MOFs by the functional groups of the capping agent decreased the catalytic activity.


Scheme 15. Cu-MOFcatalyzed oxidation of secondary amines for the selective synthesis of imines in the presence of TBHP

Kim and colleagues demonstrated the efficacy of a straightforward and economical catalytic system comprising MnSO$_4$/TBHP for the oxidative coupling of benzylamines to N-benzylbenzaldimines in CH$_3$CN at room temperature[36] (Scheme 15). Notably, the reaction proved ineffective in the absence of the Mn(II) catalyst. Furthermore, there was no evidence of benzaldehyde formation during the oxidative coupling process. Following a reaction period of 3.5 h, nine differently substituted imines were obtained in high yields using this methodology. The investigation revealed the impact of both steric and electronic factors on the rate of oxidative coupling. According to the proposed reaction mechanism, an active oxo-Mn species (Mn(IV)=O), formed through the interaction between MnSO$_4$ and TBHP, initiates the subsequent steps of oxidative coupling, leading to the production of the corresponding imines.

Scheme 16. Mn(II)catalyzed oxidative self-coupling of primary amines for the selective synthesis of imines in the presence of TBHP

A patent by Feng *et al.,* reported the catalytic efficiency of various transition metal oxides (oxides of V, Mn, Fe, Co, Cu, Mo) and oxidants (TBHP and H_2O_2) in the oxidation of various primary and secondary amines to produce the imines[37] (Scheme 17). A total of thirteen (13) representations were mentioned by varying the solvent, oxidant, and catalyst. According to the results, the combination of

βMnO_2+TBHP provided the best results for the high-yield synthesis of imines (Yield of 92% and selectivity of 95%).
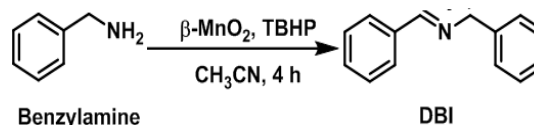
Scheme 17. MnO_2/TBHP catalyzed selective oxidative coupling of primary amines to imines

Table 1: Optimized catalytic conditions reported for the TBHP mediated oxidative coupling/oxidation of amines to imines

S. No	Catalyst	Solvent	Temperature (°C)	Time	Substrate	Oxidant	Conv. / yield/sel. (%)	Reference
1	Mn/Co-MOF(H_3BTC) (10 mg)	MeOH	RT	4 h	Benzyl amine (1 mmol)	TBHP (2 mmol)	100/100/ -	21
2	[$Fe_3(\mu_3$-O)(CH_3COO$)_6$] (8 mg)	MeOH	R.T.	12 h	Benzyl amine (1 mmol)	TBHP (0.3 mL)	90/90/99	22
3	Cu/chitosan beads (Cu(OAc$)_2$) (10mg)	CH_3CN	80	30 min	Benzyl amine (0.5 mmol)	TBHP (1 mmol)	>99/98/-	23
4	MnCl$_2$(TPA)0.2mol%	CH_3CN	RT	1 h	Benzyl amine (1 mmol)	TBHP (2 mmol)	98.2/93.4/-	24
5	[Co(L)$_2$]$_2$[Mo$_6$O$_{19}$] (0.006 mmol)	CH_3OH	RT	24 h	Benzyl amine (0.5 mmol)	TBHP (3 mmol)	-/92/-	25
6	α-MnO$_2$ (0.05 mmol)	CH_3CN	RT	4 h	Benzyl amine (0.5 mmol)	TBHP (1 mmol)	96/-/95	26
7	[{Cu$_2$(2,3-pydc)$_2$ (2,2 -bpy) (H$_2$O)$_2$}. 4H$_2$O]$_n$ (15 mg)	Solvent -free	45	30 min	Benzyl amine (10 mmol)	TBHP (15mmol)	-/91/-	27
8	Mn(III)TPPCl/TBHP (0.01 mmol)	CH_3CN	RT	1 h	Benzyl amine (1 mmol)	TBHP (1 mmol)	-/94/-	28
9	[Cu$_2$(BDC)$_2$(DABCO)] (10 mol%)	THF	RT	24 h	Benzyl amine (1 mmol)	TBHP (2 mmol)	-/75/-	29
10	[Rh$_2$(cap)$_4$](1.0 mol%)	CH_3CN	RT	16 h	Benzyl amine (1 mmol)	TBHP (2 mmol)	95/94/-	30
11	SBA-NG(50 mg)	Solvent -free	85	4 h	Benzyl amine (1 mmol)	TBHP	98/-/99	31
12	FeCl$_2$/TEQ (TEQ=Tetra Quiniline) (0.1 mol%)	CH_3CN	RT	1.5 h	Benzyl amine (0.4 mmol)	TBHP (2 mmol)	98/93/-	32
13	(MnTPPCl) (3x10^{-4} mmol)	Toluene	RT	15 min	Benzyl amine (1 mmol)	TBHP (2mmol)	99/91/-	33
14	(PPh$_3$)$_3$RuCl$_2$ (0.04 mmol)	Benzene	RT	2 h	Cyclic amine (2 mmol)	TBHP (3.2 mmol)	--/82/--	34
15	Cu$_3$(BTC)2-B	n-hexane	40	3 h	Dibenzylamine	TBHP	Dibenzylimine 53/41/-	35
16	MnSO$_4$ (0.05 mmol)	CH_3CN	RT	3.5 h	Benzyl amine (1 mmol)	TBHP (1 mmol)	-/93/-	36
17	β-MnO$_2$(0.05 mmol)	CH_3CN	RT	4 h	Benzylamine (0.5 mmol)	TBHP (1 mmol)	64/--/98	37

2. H_2O_2 mediated oxidative self/cross-coupling of amines and oxidation of amines

Chu and Li reported the effectiveness of H_2O_2 as an oxidant in the heterogeneous V_2O_5 catalyzed oxidation of a range of benzylamines to corresponding imines at RT in water[38] (Scheme 18). Firstly, the authors studied the oxidation of

p-chlorobenzylamine as a model reaction under different reaction conditions such as variation in oxidant and catalyst concentrations, and reaction time. There was no progress in the reaction in the absence of either an oxidant or catalyst. The reaction conditions for the above reaction were optimized with 3 equiv. of H_2O_2 oxidant, 0.08 equiv.

of V_2O_5 catalyst and 3.5 h of reaction time at RT. Later, these optimized conditions were used to study the substrate scope. When the benzylamines contain electron-withdrawing substituents, the reaction was accomplished at RT in water. On the contrary, with the benzylamines containing electron-donating substituent, the oxidation reaction was accomplished at 50°C. According to the proposed reaction mechanism, $HOV(O_2)_2$ is the active catalyst species formed by the interaction of H_2O_2 with V_2O_5. This active catalytic species then interacts with benzylamine to continue the next successive steps to yield the corresponding imine.
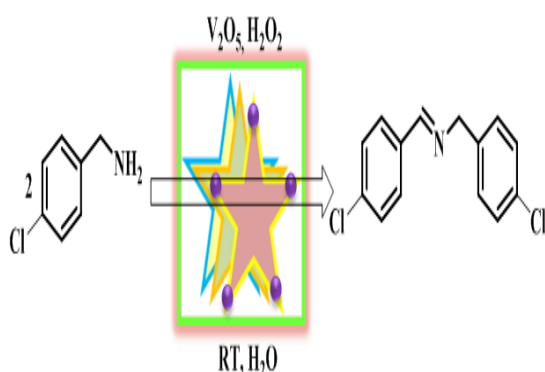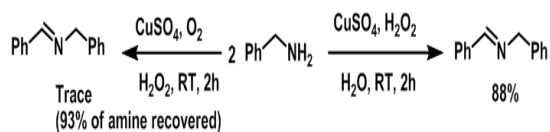

Scheme 18. V_2O_5 catalyzed oxidative self-coupling of primary amines for the selective synthesis of imines in the presence of H_2O_2

Ogawa and colleagues observed that Cu(II)SO_4 performed well in the selective oxidation of some benzyl and aliphatic amines to the corresponding imines by H_2O_2 in water at RT for 1.5 h[39] (Scheme 19). According to the proposed reaction mechanism, a Cu-amine complex, formed by the reaction of amine with $CuSO_4$, reacts with H_2O_2 and generates the imine intermediate. After this, the amine substrate couples with the imine intermediate to produce the desired imine product.

A feature article by Ogawa and colleagues[40] revealed that a $CuSO_4/H_2O_2$ catalytic system was superior to $CuSO_4/O_2$ in accomplishing the oxidative self-coupling of benzylamines to imines (Scheme 20). Later, the benzylamines possessing electron withdrawing/donating substituents were employed to evaluate the substrate scope. Nevertheless, all of these reactions were accomplished smoothly to give corresponding imines in good yields. The authors also reported the oxidation of some aliphatic amines using the same catalytic protocols. After the success of catalytic self-coupling of amines, the results of oxidative cross-coupling followed by heterocyclization using the same catalytic system were presented.
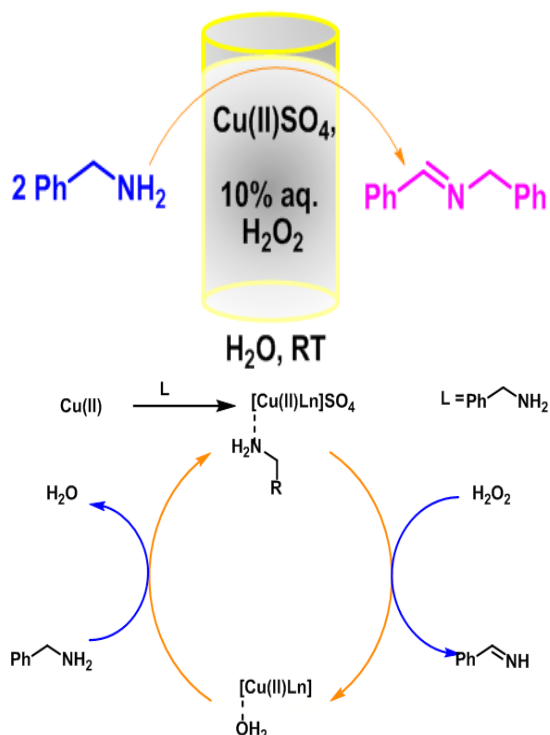

Scheme 19. Proposed mechanism of Cu(II)catalyzed oxidative self-coupling of primary amines for the selective synthesis of imines in the presence of H_2O_2


Scheme 20. Cu(II)catalyzed H_2O_2 mediated oxidative self-coupling of primary amines for the selective synthesis of imines

Reddy and Sayari investigated the transition metal silicates catalyzed oxidation of primary amines using H_2O_2 as an oxidant. This article described that vanadium silicates are more selective towards the formation of imines than other transition metal silicates investigated (Scheme 21)[41].
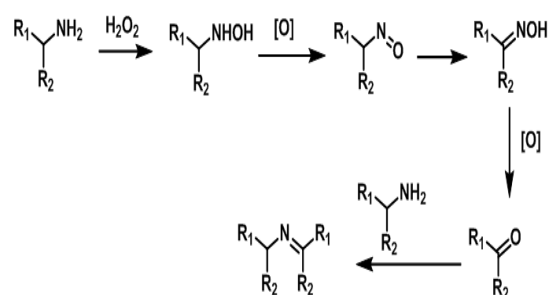

Scheme 21. Reaction pathway of Vanadium silicates catalyzed H_2O_2 mediated oxidative coupling of amines

Gopiraman and Chung observed the generation of H_2O_2 by the activation of atmospheric oxygen and benzylamine by CuO/CNP catalyst. The H_2O_2 now reacts with another benzylamine molecule to form an imine-intermediate[42] (Scheme 22). After this, the imine intermediate was found to decompose by another nucleophilic benzylamine molecule to form the desired imine product.
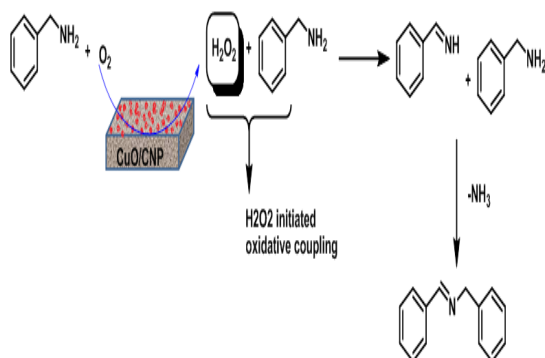
Scheme 22. Reaction pathway of CuO/CNP catalyzed oxidative coupling of primary amine to imines involving H_2O_2

Guo *et al.*, reported the application of a recyclable MOF of vanadium(IV), derived from organic linkers of triphenyls, denoted as BIT-66, $[(V_3O_3(H_2O)(BTB)_2]$(BTB=1,3,5-tris(4-carboxy-phenyl)benzene) as a photocatalyst for the H_2O_2 mediated oxidative coupling of benzylamine to corresponding imine[43] (Scheme 23). Indeed, the main objective of this study was BIT-66 catalyzed oxidative coupling of amine in the presence of molecular O_2. Firstly, the authors studied the reaction under different conditions to optimize the catalytic conditions. According to the results, the BIT-66 material displayed superior photocatalytic activity in producing imines under visible light in the presence of molecular O_2 than H_2O_2.
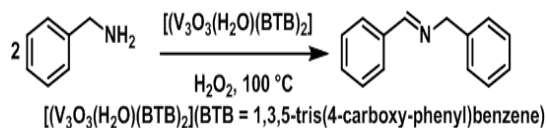
Scheme 23. BIT-66 as a photocatalyst for the H_2O_2 mediated oxidative coupling of benzylamine to imine

Huang and the team developed a gold-based nanocomposite photocatalyst that is intercalated between a MOF and COF (covalent organic framework) for the selective oxidation of amine (Scheme 24)[44]. The MOF namely UiO-66-NH$_2$ and the COF composed of PAPB-PDA were used to fabricate the above nano-composite catalyst. The

proposed mechanism of photocatalytic oxidation of amines demonstrated the participation of *in situ* generated H_2O_2 as an additional oxidant during the catalytic cycle of amine oxidation to produce selectively the imines.
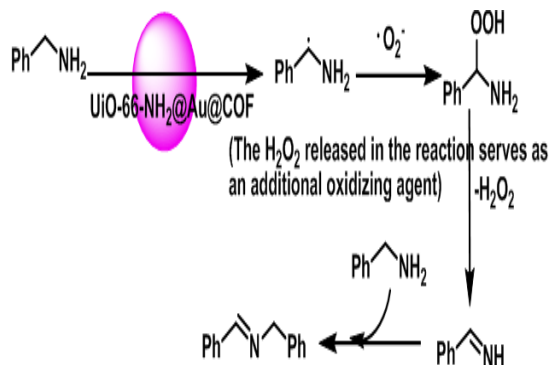
**Scheme 24. MOF-Au-COF catalyzed oxidative self-coupling of imines**

Ravula *et al.*, investigated the utility of a heterogeneous mixed oxide (Mo/Ce-Si) catalyst in the solvent-free oxidative coupling of amines for the selective synthesis of imines[45]. Among the three oxidants (molecular O_2, TBHP, H_2O_2) employed in the oxidative coupling of benzylamine at 140°C, the best results were obtained by employing molecular O_2 as the oxidant i.e., in terms of substrate conversion (100%) and imine product selectivity (98%). Nevertheless, the oxidative coupling conducted in the presence of H_2O_2 at 80°C has also displayed good conversion (99%) of the substrate and a reasonable selectivity for imine (83%) (Scheme 25). Higher temperatures are not suitable for H_2O_2 based oxidative conversions.
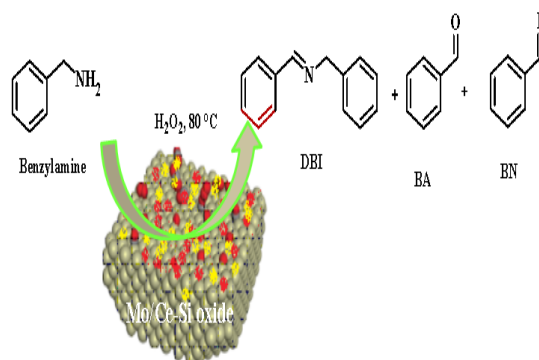
Scheme 25. H_2O_2 mediated Mo/Ce-Si oxide catalyzed oxidative coupling of amines

Wu *et al.*, reported a solvent-free and metal-free oxidation of benzylamines to produce the imines at 100 using H_2O_2 as an oxidant[46]

(Scheme 26). The optimized conditions reported were viz. substrate 1mmol; H_2O_2 1 mmol; 100; 16 hours. A total of eight (8) imine derivatives were synthesized using this protocol. However, this protocol was not effective for aliphatic amine oxidation.
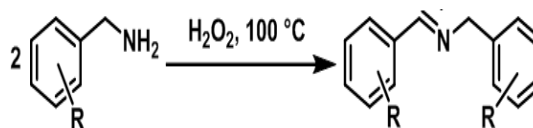
Scheme 26. A metal-freeoxidative self-coupling of primary amines using only H_2O_2 oxidant

Table 2: Optimized catalytic conditions reported for the H_2O_2 mediated oxidative coupling/oxidation of amines to imines

| S. No	Catalyst	Solvent	Temperature (°C)	Time	Amine Substrate	Oxidant	Conv. /yield/sel. (%)	Reference
1	V_2O_5(0.08 equiv)	Water	RT	>10 h	Benzyl amine (1 equiv)	H_2O_2 (3 equiv)	-/64/-	38
2	Cu(II)SO$_4$(0.2 mol%)	Water	RT	1.5 h	Benzyl amine (1 mmol)	H_2O_2 (2 mmol)	-/91/-	39
3	Cu(II)SO$_4$(0.2 mol%)	Water	RT	2 h	Benzyl amine (2 mmol)	H_2O_2 (2mmol)	-/88/-	40
4	Vanadium silicates (0.2 g)	Methanol	RT	2h	Propylamine (2 g)	H_2O_2 (1.92g)	Mixture of amines and oximes	41
5	CuO/CNP(25 mg)	Solvent-free	110	12 h	Benzylamine (10 mmol)	O_2/H_2O_2	-/98/-	42
6	BIT-66 (V-MOF) (5 mg)	CH$_3$CN	RT	12 h	Benzyl amine (0.5 mmol)	H_2O_2 (1.5 mmol)	7.9/-/	43
7	UiO-66-NH$_2$@Au$_{0.5}$@COF (20 mg)	Acetone	RT	20	Benzylamine (1 mmol)	O_2/H_2O_2	66.9/-/-	44
8	Mo/Ce-Si Oxides (150 mg)	Solvent-free	80	5 h	Benzylamine (4.6 mmol)	H_2O_2 (5 mmol)	-/-/83	45
9	Catalyst-free	Solvent-free	100	16 h	Benzyl amine (1 mmol)	H_2O_2 (1 mmol)	-/69/-	46

3. Miscellaneous oxidative self/cross-coupling of amines and oxidation of amines

In this section, a review of the reported examples of oxidative self/cross-coupling of primary amines and oxidation of secondary amines that were mediated by some competent oxidizing agents other than TBHP,H_2O_2 and molecular O_2 is presented. These processes includes the utilization of molecular iodine, hypervalent iodine compounds, hypochlorites, persulfates, electrochemical cells (anodic oxidation), and enzymes.

Wang *et al.,* reported a metal-free aqueous synthesis of imines *via* molecular iodine mediated i.e., I_2-mediated oxidation of some cyclic and acyclic amines in the presence of a base (Scheme 27)[47]. Firstly, the authors described the optimization of reaction conditions using 1,2,3,4-Tetrahydroisoquinoline as the model substrate to produce the corresponding imine. The effect of reaction parameters such as the effect of the base, and the temperature was assessed.

There was no effect of radical scavengers/

initiators TEMPO or BHT on the reaction and mentioned that there is no evidence of a radical mechanism during the I_2-mediated oxidation to amines. The optimized reaction conditions were successfully applied in the oxidation of a diverse range of cyclic and acyclic amines. A total of eleven (11) imine derivatives were synthesized in this work. The Optimized reaction conditions include aminesubstrate (0.5 mmol), I_2(0.5 mmol), K_2CO_3 (1 mmol), H2O, and reflux. The proposed reaction mechanism indicates initially a base-promoted iodination of amine substrate produces an N-iodo intermediate. Later, the cleavage of the N-I bond of the N-iodo intermediate, followed by deprotonation by base provides the corresponding imine.
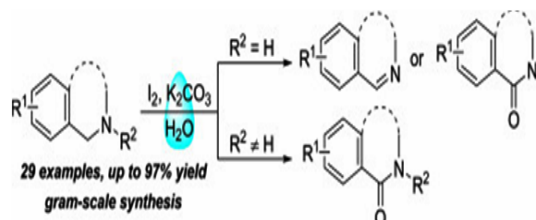

Scheme 27. Aqueous synthesis of imines via I_2/base-mediated oxidation of amines

Nicolaou and colleagues evaluated the performance of o-iodoxybenzoic acid (IBX) in the oxidative conversion of various secondary amines selectively to corresponding imines in DMSO at 45°C[48]. The problem of regioselectivity in imine product distribution with respect to the substituent on the secondary amine during its oxidation process was addressed. However, attempts made to convert the primary and tertiary amines into imines via the IBX-mediated oxidation processes were not successful.
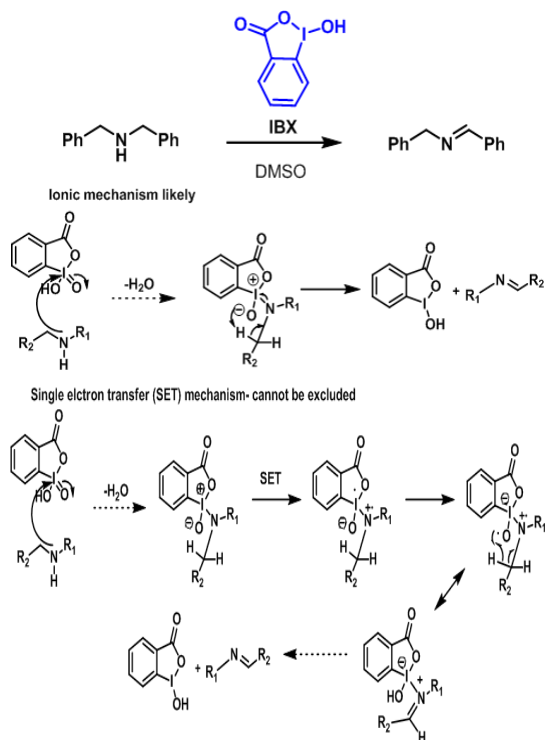

Scheme 28. IBX mediated secondary amine oxidation to imines and the reported mechanism

Galletti *et al.,* reported that imine is formed as an intermediate during the TEMPO-catalyzed oxidation of various secondary amines to aldehydes using $NaIO_4$ as an oxidant[49]. A plausible mechanism is proposed to support the formation of an imine intermediate (Scheme 29).
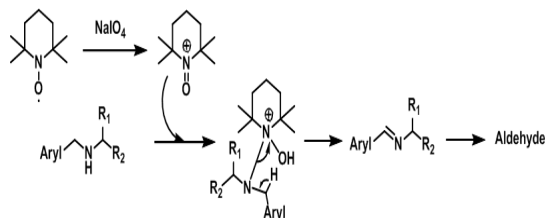
Scheme 29. Oxidation of secondary amines to imines by TEMPO/periodate catalytic system

Orru and colleagues optimized the conditions for the oxidation of some unactivated amines selectively to the imines using IBX as an oxidant in CH_2Cl_2[50]. Indeed this was an intermediate step in the oxidative Ugi-type and aza-Friedel–Crafts reactions. Nevertheless, a total of five imine intermediates were isolated and characterized in this work.
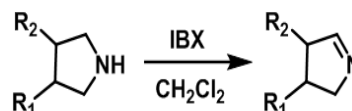
Scheme 30. Synthesis of imines from unactivated amines oxidized by IBX

Porta *et al.,* compared the difference in the function of molecular O_2 and Iodosobenzene (ISB) as oxidants in the $RuCl_2(PPh_3)_3$ complex catalyzed oxidation of a secondary amine (dibenzylamine) in toluene at 80°C[51]. When the reaction was studied in the presence of molecular O_2, it took 5 h to achieve 35% amine conversion and 60% imine product (benzylbenzaldimine)selectivity. The selectivity of the product was improved to 70% by replacing the $RuCl_2(PPh_3)_3$ with $[Ru(DMSO)_4Cl_2]$. A simple tri-hydrated $RuCl_3$ precursor was not effective in this reaction. However, this catalytic system was not unique to all the amine substrates.

Later, the authors investigated the efficacy of Iodosylbenzene as an oxidant in the abovementioned amine oxidation in CH_2Cl_2 (Scheme 31) and noticed that it took only a few minutes to accomplish the reaction at RT by providing imines with 75% selectivity. However, there were by-products like benzonitrile observed to some extent. The proposed mechanism indicated the *in situ* formation of benzaldehyde from benzylamine and its condensation with additional benzylamine molecules to produce the imine.
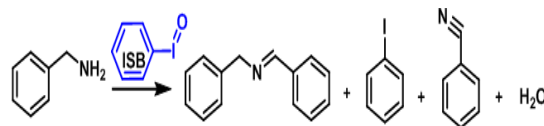
**Scheme 31. ISB promoted oxidation of primary amine to imine**

Larsen and Jorgenson investigated secondary amine oxidation under two different conditions. The first condition was the catalyst-free amine oxidation in the presence of only iodosobenzene (ISB) oxidant[52]. The second condition was the amine oxidation using the combination of ISB with porphyrin complexes of Mn(III) and Fe(III) or a

Salen complex of Mn(III). High yields of imine products were obtained from the amines in catalyzed reactions than the uncatalyzed reactions. Mn(III)-Salen complex exhibited superior catalytic activity than the two other complexes reported. It is interesting to note that based on some experimental data, two different reaction mechanisms have been proposed for the catalyzed and uncatalyzed oxidation of amines.
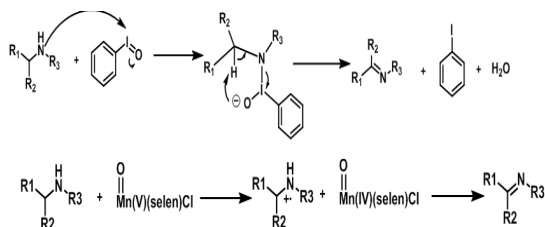
Scheme 32. Oxidation mechanism of secondary amines to imines by Mn(III)-Salen/ISB catalytic system

Ochiai and colleagues reported that Iodosobenzene (ISB) mediated oxidation of cyclic amines generates the corresponding imines in CH_2Cl_2 at RT as shown below[53]. However, the efficiency of ISB was not found to be consistent for the oxidation of all the cyclic amines reported in this article.
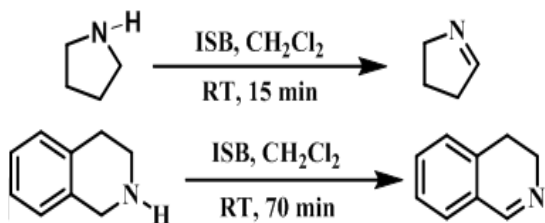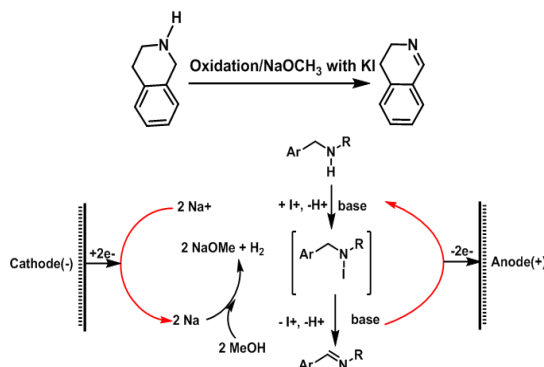

**Scheme 33. Oxidation of cyclic amines by ISB**

Okimoto *et al.,* reported the impact of KI in the electrochemical oxidation of benzylic amines to imines[54]. The combination of supporting electrolyte NaOMe with KI provided better results for the electrochemical conversion of amines that NaOMe alone and reasoned that the iodide ions can acts as electron carriers. When the amount of current was ~3 F/mol, the yield of respective imine was increased up to 90%. The effect of the amount of current and other electrolytes was also discussed.

Persulfates are well-known oxidants in synthetic organic chemistry. Wang *et al.,* reported the ultrasound-assisted sodium persulfate oxidative coupling of amines into imines[55] (Scheme 35). The results indicate that a solvent and catalyst-free low-temperature oxidative coupling of amines gave good yields of imines in shorter reaction times. The synthesis of seven differently substituted imine derivatives was

described and a plausible mechanism for persulfate-mediated amine oxidation was projected.

Scheme 34. Electrochemical oxidation of cyclic and acyclic secondary amines to imines
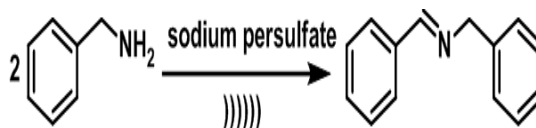
Scheme 35. A metal-free ultrasound assisted sodium persulfate oxidized coupling of amines into imines

Hudwekar *et al.,* reported the effectiveness of $K_2S_2O_8$ mediated facile oxidative self and cross-coupling of amines (Scheme 36)[56] in environmentally benign polyethylene glycol (PEG 200) solvent at RT without using any external base for the selective synthesis of imines (amine conversion 99% and imine selectivity 99%). On the other hand, the oxidative coupling conducted in normal organic solvents using oxidants such as TBHP, H_2O_2, NaO^{t}Bu, Air and even $K_2S_2O_8$ experienced both conversion and selectivity problems. The authors explained that the potassium ions form a half crown-ether type metal complex and persulfate ions improve the basicity of the reaction to stabilize the substrates and to provide high yields of imine product. Results of elemental analysis using atomic absorption spectroscopy in PEG solvent revealed that there was no contamination of metal ions. The proposed oxidative coupling mechanism indicates the possibility of two reaction pathways starting with the peroxide intermediate of benzylamine.

Synthesis of symmetrical and unsymmetrical imines
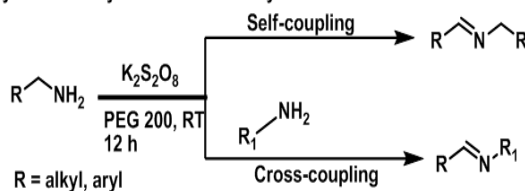
Scheme 36. $K_2S_2O_8$ mediated oxidative coupling of amines

Yamazaki reported the efficiency of the $NiSO_4/K_2S_2O_8$ catalytic system in the catalytic oxidation of some secondary amines to provide corresponding imines in CH_2Cl_2 at RT[57]. Comparable yields of imines were also obtained when the reaction was carried out in common organic solvents. In addition, the same reaction was also carried out under solvent-free conditions, but the yields were not consistent with respect to the substrate scope.
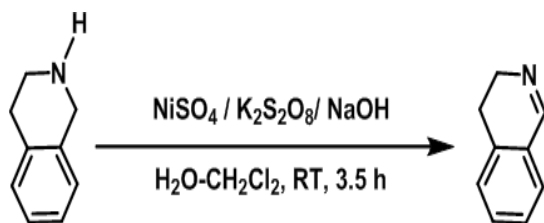
Scheme 37. Oxidation of cyclic secondary amines by Ni(II)/persulphate catalytic system

de Souza *et al.,* discovered an 'On Water' approach for the synthesis of acyclic and cyclic imines via the metal-free oxidative coupling of amines by using two cheap and commonly available oxidants namely NaOCl and commercial bleach (Scheme 38)[58]. The concentration of NaOCl was the key factor in the imine product yield. Degassed water was used as a solvent to rule out the role of dissolved O_2 and the efficacy of NaOCl as an oxidant in the amine oxidative coupling. The yields of imine products were not appreciable in organic solvents such as CH_3CN, hexane, and toluene. The conditions optimized for benzylamine oxidative coupling were then implemented successfully in the oxidative coupling of a range of other amine substrates. When the concentration of NaOCl was increased to 1.0 equiv, amide formation was noticed in the amine oxidative coupling after 24 hours. The proposed mechanism revealed the occurrence of oxidative coupling at the interface of the aqueous and organic phases of amine.

R = aryl, alkyl
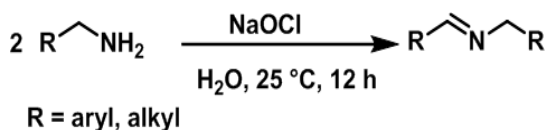
**Scheme 38. NaOCl-mediated catalyst-free oxidative coupling of amines in water**

Liu *et al.,* reported ametal-free and external oxidant-free electrochemical method for the oxidative coupling of amines to synthesize corresponding imines at RT (Scheme 39)[59]. The article emphasized that electrochemical energy is a clean and renewable energy resource, and that is not explored widely in organic synthesis. Initially, the oxidative coupling of benzylamine was investigatedas a model reaction at a constant voltage (5V) in an electrochemical cell containing a carbon anode and a carbon cathode, TEABr as an electrolyte, and CH_3CN as solvent. This approach provided a 96% yield of the desired imine product after 10 hours. An appropriate mechanism for the formation of imines via the dehydrogenation of amine was deduced. A change in the electrode, voltage, reaction time, solvent, and electrolyte showed a negative trend in the results of oxidative coupling of benzylamine. Further, the authors proposed that the surface of the carbon cathode is more suitable for electrocatalytic oxidative coupling of benzylamine than other electrodes. Under the optimized conditions, the electrochemical catalytic oxidative coupling of some other primary and secondary amines with different steric and electronic properties was also examined by the authors. Altogether, the synthesis of 17 diverse imines was described and the efficacy of electrochemical oxidative-coupling of amines for the gram-scale synthesis of imines was also described.
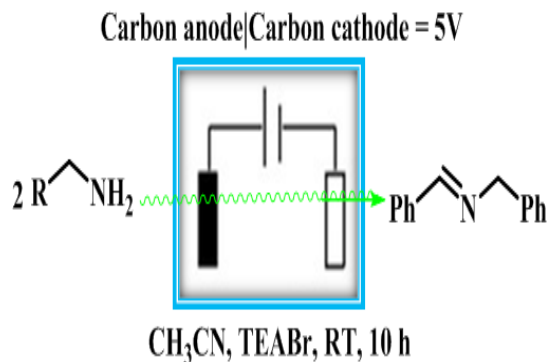
Scheme 39. Catalyst-free electrochemical oxidative coupling of benzylamine to imine

He *et al.,* performed a photoelectrochemical oxidation of benzyl amines selectively to achieve the corresponding imines using $Mo/BiVO_4$ photoanodes in a closed two-chamber, three-electrode PEC cell[60]. No external oxidant was used in this oxidation reaction. This reaction also envisioned the simultaneous formation of molecular H_2. The authors observed the effect of substituent on amine substrate during the PEC oxidation in the selective production of corresponding imine. An anaerobic reaction mechanism with the involvement of only photo-generated holes on the valence band of $Mo/BiVO_4$ photo-anode was discussed.
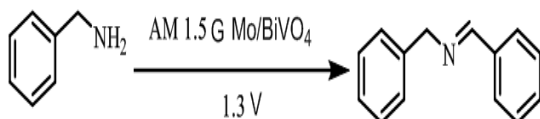
Scheme 40. Imine synthesis via Mo/BiVO$_4$ photo-anode mediated electrochemical oxidation of primary amines

Overton *et al.,* reported that the oxidation of secondary amines by the Swern oxidation method (DMSO-oxalyl chloride) yielded the corresponding imines along with considerable amounts of methylthiomethylamines as by-products.[61]
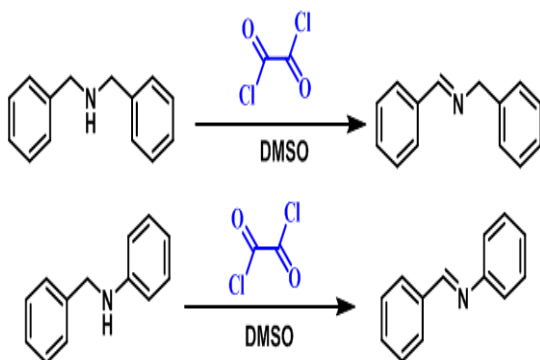
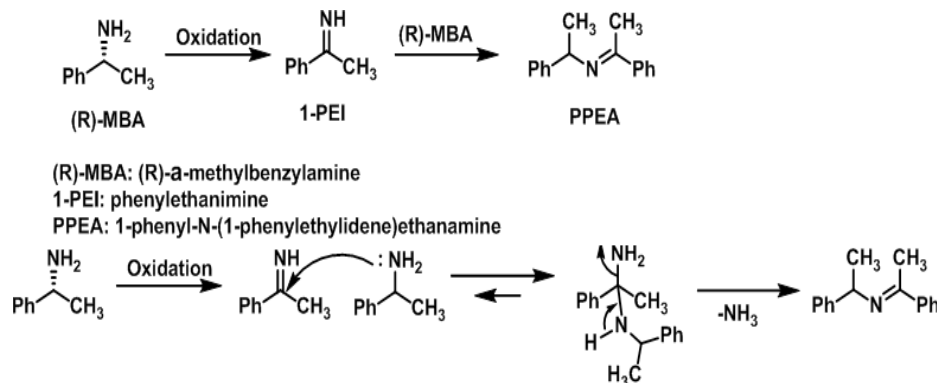**Scheme 41. DMSO-oxalyl chloride promoted Swern oxidation of primary/secondary amines to imines**

Mukaiyama and the team studied the efficiency of the N-tert-butylphenylsulfinimidoyl chloride and DBU mixture as an oxidant in the oxidation of various cyclic and acyclic secondary amines to the corresponding imines in CH$_2$Cl$_2$ at 78°C.[62] The imine product regioselectivity with respect to the substituent present on the amine substrate was discussed.
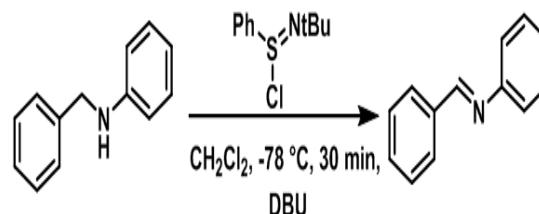
Scheme 42. N-tert-butylphenylsulfinimidoyl chloride/DBU promoted oxidation of secondary amines to imines

Asano and colleagues reported the first exampleof D-amino acid oxidase enzyme-mediated oxidative self-coupling and cross-coupling of primary amines to corresponding imines[63]. The details of the reaction mechanism are provided in Scheme 43. The authors disclosed the procedure for stabilization of intermediates such as 1-PEI (Scheme 45) in aqueous solutions in the presence of oxidase enzyme.
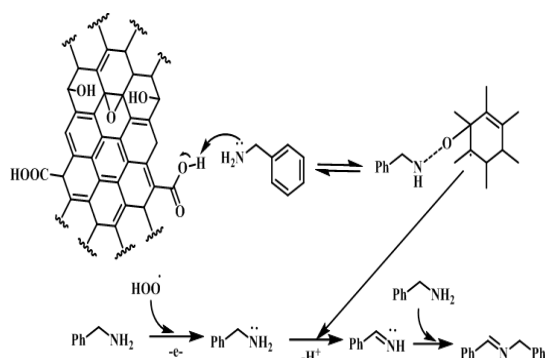

(R)-MBA: (R)-a-methylbenzylamine
1-PEI: phenylethanimine
PPEA: 1-phenyl-N-(1-phenylethylidene)ethanamine

Scheme 43. D-amino acid oxidase enzyme-mediated oxidative self-coupling of primary amines to imines

Luque and colleagues reported an external oxidant-free oxidative coupling of benzylamine catalyzed by heterogeneous and recyclable graphene oxide (GO) to produce selectively the imine (N-benzylidine-1-phenylmethanamine) under microwave reaction conditions (Scheme 44)[64]. There was no oxidative coupling of amine in the absence of oxidant and catalyst. On the other hand, when this reaction was investigated only in the presence of an oxidant H$_2$O$_2$ i.e., without a catalyst resulted in the quantitative conversion of benzylamine (99%) but produced a mixture of products (aldehyde,

amine, nitrile, oxime). The results of intended oxidative coupling reactions using normal GO/H$_2$O$_2$ or reduced GO/H$_2$O$_2$ catalytic systems also showed the problems of selectivity distribution of a mixture of products. Finally, the oxidant-free oxidative coupling of benzylamine by GO under microwave conditions was accomplished, by overcoming selectivity issues, and produced N-benzylbenzaldimine as the major product. A comparison of these results with previously reported K-10 montmorillonite catalyzed oxidative coupling of amines[65] (Scheme 45) to imines was provided to deduce the reaction mechanism.

Indeed, the report by Torok and colleagues discloses that the formation mechanism of imine takes place by any one of the two reaction pathways proposed. The unstable imine formed via dehydrogenation of benzylamine undergoes transamination with another benzylamine and produces an imine product or the unstable imine

intermediate may convert into benzaldehyde via hydrolysis which then couples with another benzylamine to form the same desired imine[50]. However, since GO contains various reactive surface oxygen sites (carboxyl, ether), an external oxidant-free mechanism was proposed for the selective formation of imine.

Scheme 44. Graphene oxide catalyzed external oxidant-free oxidative coupling
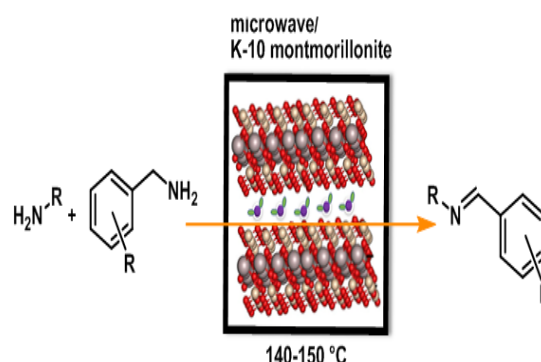
Scheme 45. Microwave-assistedMontmorillonite catalyzed oxidative cross-coupling of amines

Table 3: Optimized catalytic conditions reported for the oxidative coupling/ oxidation of amines to imines using miscellaneousoxidants (other than TBHP, H$_2$O$_2$ and molecular O$_2$)

S. No	Catalyst	Solvent	Temperature (°C)	Time	Substrate	Oxidant	Conv./yield /sel.(%)	Reference
1	Catalyst-free	Water	100	0.5	1,2,3,4-Tetrahydroiso-quinoline(cyclic amine)	I$_2$/K$_2$CO$_3$ base	-/85/-	47
2	Catalyst-free	DMSO	45	0.5 h	Dibenzylamine (0.5 mmol)	IBX(1.1 euiv)	-/83/-	48
3	TEMPO (0.04 mmol)	H$_2$O/CH$_3$CN	RT	20 min	Aromatic bicylic amine (0.04 mmol)	NaIO$_4$(0.4 equiv)	-/78/-	49
4	Catalyst-free	CH$_2$Cl$_2$	60	1 h	Meso-pyrrolidine (0.25 mmol)	IBX(1.1 equiv)	-/95/-	50
5	Catalyst-free	CH$_2$Cl$_2$	RT	5 min	Benzylamine ISB (oxidant/amine = 1)		100/75/-	51
6	Mn(III)(saen) Cl(0.0 25 mmol)	CH$_2$Cl$_2$	0	2 h	PhCH$_3$NHC(CH$_3$)$_3$ (0.5 mmol)	ISB(1 mmol)	-/80/-	52
7	Catalyst-free	CH$_2$Cl$_2$	RT	15 min	Pyrrolidine	ISB(1 equiv)	-/93/-	53
8	Catalyst-free	CH$_3$OH	15	--	Tetrahydroiso-quinoline (10 mmol)	KI (3 mmol)/ NaOCH$_3$ (5 mmol)	-/86/-	54
9	Catalyst-free	Solvent-free	-	-	-	Na$_2$S$_2$O$_8$	-	55
10	Catalyst-free	PEG-200	RT	12 h	Benzylamine (1 mmol)	K$_2$S$_2$O$_8$ (1 equiv)	99/-/99	56
11	NiSO$_4$ (2 mol%)	Aqueous-CH$_2$Cl$_2$	RT	3.5	Tetrahydroiso-quinoline (2.25 mmol)	K$_2$S$_2$O$_8$ (3.1 mmol)	-/87/-	57
12	Catalyst-free	Water	RT	12 h	Benzylamine (0.56 mmol)	NaOCl(0.5 equiv)	-/95/-	58
13	Metal-free Electro-oxidative coupling	CH$_3$CN	RT	10	Benzylamine (0.25 mmol)	Oxidant-free	-/96/-	59
14	3% Mo/BiVO$_4$ electrode	0.1 M TBAPF$_6$ CH$_3$CN	RT	3 h	Benzylamine (0.05M)	3% Mo/BiVO$_4$ electrode	-/-/99	60
15	Catalyst-free	CH$_2$Cl$_2$	RT	20 min	Dibenzylamine	DMSO	-/63.4/-	61
16	Catalyst-free	CH$_2$Cl$_2$	-78	30	N-cinnamylaniline (0.53 mmol)	Ph-S(Cl)=N(tBu) (0.96 mmol)/DBU (0.96 mmol)	-/98/-	62
17	Catalyst-free	Water	20	1 h	(R)-α-methylbenzylamine ((R)-MBA) (150 mM)	D-amino acid oxidase (2U)	-/68mM/-	63
18	Graphene Oxide (100 mg)	Water/ Ethanol	Micro-wave	0.5	Benzylamine (0.2 mL)	Oxidant-free	95/	64
19	K-10 montmorillonite (500 mg)	CH$_2$Cl$_2$	Micro-wave	Few minutes	Benzylamine	Oxidant-free	100/-/-	65

CONCLUSION

Advancements in imine synthetic methodologies by following green chemistry protocols are crucial for the chemical industry. In this context, the literature review provided here on the topic of selective and high-yield synthesis of imines by (i) oxidative-coupling of primary amines and (ii) oxidation of secondary amines revealed the scope for the development of a variety of homogeneous/ heterogeneous catalysts that includes MOFs, porous materials, supported metal oxides, mixed metal oxides, clays, nanocomposites, transition metal complexes, in the presence of green oxidants such as peroxides. In many examples, non-noble i.e. non-precious catalytic systems were only suggested as effective catalysts for the selective conversion of amines to imines. Although few specific examples of catalyst and oxidant-free synthesis of imines from amines were reported, not much scope/progress is observed. Further, the utility of H_2O_2 and TBHP-based liquid phase oxidants has shown good control over oxidative coupling and imine product distribution in the presence of a catalyst. The performance of the peroxide, persulfate, hypochlorite oxidants was not inferior to molecular O_2 in the above-mentioned oxidative conversion of amines. The proposed reaction mechanisms in the majority of the reports revealed the radical mechanism initiated by peroxide species during oxidative coupling. Considering all aspects, and especially bearing in mind the availability, low price, and non-toxicity associated with TBHP and H_2O_2, we presume that in the future additional applications of these peroxides will appear in the oxidative conversions of amines.

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Conflict of Interest

There is no conflict of interest.

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