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Amino acid derived ionic liquid supported iron Schiff base catalyzed greener approach for the aerobic oxidation of amines to nitriles

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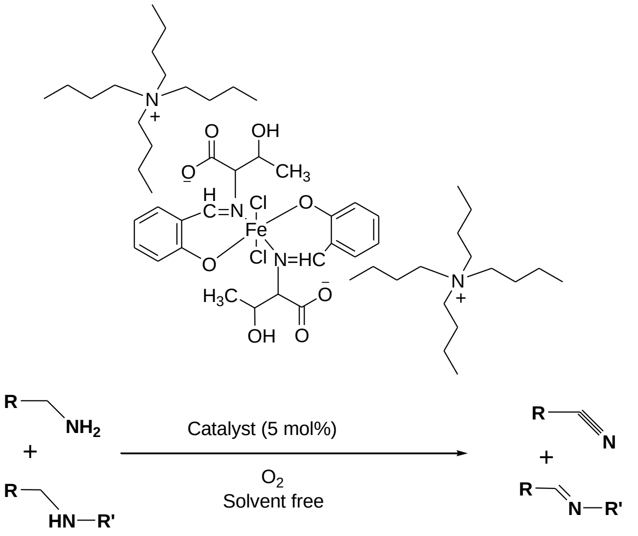
ABSTRACT

Amino acid DL-threonine derived ionic liquid was treated with salicylaldehyde to give corresponding Schiff base which subsequently complexed with iron and used as a green catalyst for aerobic oxidation of amines under solvent-less conditions. The developed catalyst was readily synthesized, reusable and exhibited superior catalytic activity owing to the synergistic effect of ionic liquid moiety. The developed catalyst was found to be quite stable and could be reused for several runs without any significant loss in catalytic activity.

Owing to the growing environmental concerns and depletion of fossil fuels, utilization of renewable natural resources as starting materials in chemical industry is receiving considerable interest in recent decades. Natural amino acids and their derivatives provide the most abundant renewable natural sources which can be effectively used as feed stocks for producing valuable chemicals for various applications[1,2]. Ionic liquids owing to their excellent thermal stability, tunable solubility, efficient recycling and lower volatility have considerable to be green alternatives to volatile organic compounds in various chemical and bio-chemical transformations[3-9]. However, despite of their widespread applications, doubts have been raised about the genuine green nature of the ionic liquids. For example, some ILs are volatile, combustible, toxic, and also exert detrimental effects on the environment[10-14]. Thus, the development of environmentally compatible or biodegradable ILs is highly desired from environmental and economic viewpoints. After the first successful synthesis by Fukumoto et al. in 2005,[15] a number of amino acid-based ionic liquids have been prepared by using amino acids as anions or cations[16-22]. These ILs owing to their biodegradable characteristics and high biocompatibility are considered to be safer and environmentally benign alternatives of the functionalized task specific ionic liquids. Recently, metal complexes of Schiff bases, derivatives of *ortho*-hydroxy aldehydes and amino acids[23], have been developed and used for the biological applications. However, the potential of such ionic liquids for catalytic applications is remained unexplored.

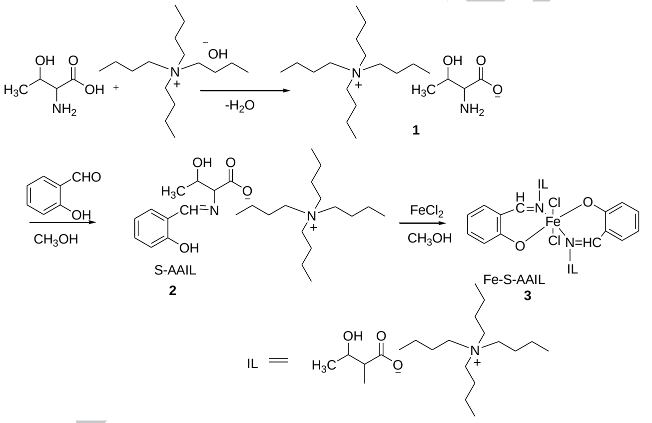
Oxidation of benzylamines to corresponding nitriles is an important synthetic transformation as they have found widespread applications as important building blocks in dyes, natural products, herbicides, agrochemicals, pharmaceuticals, and various fine chemicals.[24-25] In addition, owing to the ease of functionalization, nitriles can also be converted into other functional groups, such as carboxylic acids, amides, aldehydes and heterocycles, etc.[26-28] Traditional methods for the preparation of benzonitriles on laboratory as well as on industrial scale are the Rosenmund–von Braun reaction of aryl halides[29-30] and the diazotization of anilines followed by subsequent Sandmeyer reaction.[31] However, these methods are associated with certain drawbacks such as the use of toxic cyanides and the generation of stoichiometric amounts of metallic wastes. Thus, the direct synthesis of nitriles *via* oxidative dehydrogenation of primary amines is an attractive approach for the clean synthesis of these important precursors. Apart from the use of stoichiometric oxidants which generate huge amount of undesirable waste[32-34] a number of catalytic methodologies has been reported in recent decades. Particularly, catalytic methods using molecular oxygen as an oxidant[35-36] are more desirable from the consideration of green and sustainable chemistry. So far the cobalt, copper, palladium, ruthenium and vanadium based catalysts have been reported for the aerobic oxidation of benzylamines to nitriles.[37-40] However, many of these catalytic systems have certain drawbacks such as high cost, poor product yields and use of toxic and volatile organic solvents. Catalytic aerobic oxidation of amines to nitriles in the presence of ILs has also been reported.[41] However, the use of pure ILs as reaction media can lead to product separation difficulties and metal immobilized IL's may lead to the leaching of metal thus affecting the recyclability of catalyst.

Herein we wish to report for the first time the use of tetrabutyl ammonium salt of amino acid Schiff base, derivative of salicylaldehyde and DL-threonine functionalized with iron (II) as a recyclable catalyst for the aerobic oxidation of amines to corresponding nitriles (Scheme 1).



Scheme 1: Aerobic oxidation of amines

The step-wise synthesis of the required Schiff base functionalized amino acid derived ionic liquid (S-AAIL) is illustrated in the Scheme 2. The successful synthesis of Schiff base ionic liquid was confirmed by FTIR, ^1H and ^{13}C NMR analyses (Supporting Fig S1). The synthesized ionic liquid was treated with iron (II) chloride to obtain corresponding iron Schiff base supported amino acid ionic liquid, denoted as Fe-S-AAIL **3** (Scheme 2). The succesful synthesis of the final catalyst **3** was confirmed by ESI-MS analysis (Supporting Fig. S2).



Scheme 2: Synthesis of Fe-S-AAIL

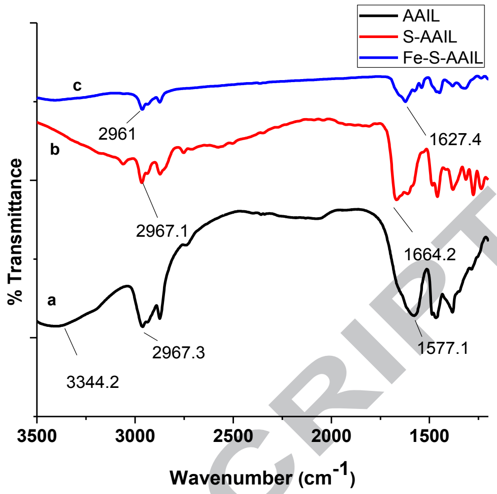


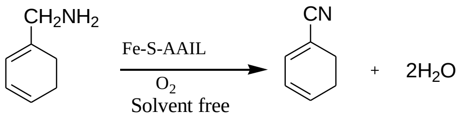
Fig. 1: FT-IR spectra of Ionic liquid, S-AAIL and Fe-S-AAIL

The chemical changes occurred during the functionalization of ionic liquid was monitored by FTIR spectroscopy. The presence of strong and broad absorption band at vibrational frequency of 3344 cm^{-1} in amino acid ionic liquid was attributed to the N-H stretching of amine group (Fig. 1a). After the reaction of amino acid IL with salicyaldehyde, the significant reduction in amine absorption band and appearance of a new sharp band around 1664 cm^{-1} which is the characteristic peak of C=N stretch, confirmed the successful formation of Schiff base from the condensation of NH_2 group of ionic liquid and CHO group of salicyladehyde (Fig. 1b). The complexation of Schiff base with iron(II) chloride was ascertained by downward shifting of characteristic peak of nitrile group from 1664 to 1627 cm^{-1} as shown in Fig. 1c. Furthermore, the ^1H and ^{13}C chemical shifts in $CDCl_3$ for S-AAIL **2** as given in Fig. S1 were in well agreement with the literature values.[42] The iron content in the synthesized ionic liquid was found to be 4.3%.

Catalytic Activity

At first the oxidation of benzylamine (1 mmol) using catalyst **3** (5 wt%) at 35 °C for 0.5 h under oxygen atmosphere furnished the 45% conversion (Table 1, entry 1). Next, with increasing the temperature from 35 to 60 °C while keeping all other parameters constant, the conversion was found to be increased to 54%. Furthermore when the temperature was raised to 80 °C, a noteworthy enhancement in the conversion (69 %) was obtained and at a temperature of 100 °C a maximum conversion of 99% was obtained under otherwise identical experimental conditions (entries 3-4). Consequently on the basis of performed experiments, 100 °C was considered to be the optimum temperature for the present study. Next, we investigated the effect of catalyst amount by varying its amount from 1.5 to 7.5 wt% under described reaction conditions. The conversion was found to be increased with increasing the catalyst amount from 1.5 to 5%, however further increase in catalyst amount (7.5%) did not give any perceptible enrichment in the conversion (entry 8). A controlled experiment at 100 °C in the absence of catalyst did not give the desired product even after the prolonged reaction time (entry 10). Nevertheless, reaction time also had significant effect and reduction in reaction time from 0.5 to 0.25 h under optimized reaction conditions (entry 9), exhibited adverse effect on conversion. Thus, based on the above studies, the optimized reaction conditions for the aerobic oxidation are: temperature 100 °C, time 0.5 h and catalyst amount 5 wt%. In order to see the effect of ionic liquid, we synthesized iron(II) Schiff base from the reaction of salicylaldehyde and phenylene diamine and tested it for the oxidation of benzylamine under optimized reaction conditions (Table 1, entry 11). The poor reaction was found to be slow and afforded only 67% conversion to the desired nitrile. This finding suggested that the synergistic effect of both components i.e amino acid ionic liquid and iron(II) Schiff base may provide an improved activity of the developed catalyst.

Table 1: Results of optimization experiments[a]

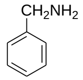
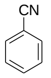
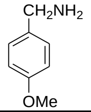
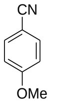
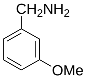
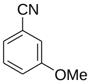
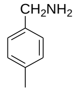
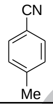
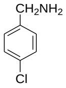
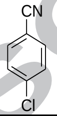
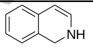
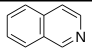
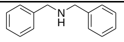
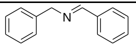


Entry	Cat. amount (wt%)	Time (h)	Temp (°C)	Conv. (%)[b]	Yield (%)[b]
1	5.0	0.5	35	45	42
2	5.0	0.5	60	54	51
3	5.0	0.5	80	69	66
4	5.0	0.5	100	99	97
5	1.5	0.5	100	61	60
6	2.5	0.5	100	74	72
7	3.5	0.5	100	82	80
8	7.5	0.5	100	97	94
9	5.0	0.25	100	-	-
10	-	0.5	100	-	-
11	5.0	0.5	100	67	64

[a]Reaction conditions: benzylamine (1 mmol), O_2 (1 atm); [b]Conversion was determined by GC and GC-MS; [c]Isolated yield, [d]reaction was conducted in the absence of catalyst

Following to optimized reaction conditions, activity of catalyst was further explored and extended for a variety of substituted benzylamines having electron donating or electron withdrawing groups. The aerobic oxidation of benzylamines having electron donating groups (Table 2, entries 2,4) afforded slightly better conversions as compared to the benzylamines having electron withdrawing groups like Cl (entries 3,5). Apart from the aromatic amines, the oxidation of aliphatic amines proceeded smoothly and afforded excellent yield of the desired nitriles (Table 2, entry 6-9). Furthermore, the oxidation of secondary amines like 1,2,3,4 tetrahydro isoquinoline and dibenzylamine under the optimized reaction conditions yielded higher yield of the corresponding imines without any evidence for the formation of any by-product (entries 10-11).

Table 2: Fe-S-AAIL catalyzed oxidation of amines[a]

Entry	Substrate	Product	Time (h)	Conv.[b] (%)	Yield[c] (%)
1			0.5	>99	95
2			0.5	>99	98
3			0.5	93	91
4			0.5	>99	98
5			0.5	89	88
6	$CH_3(CH_2)_6NH_2$	$CH_3(CH_2)_5CN$	0.5	>99	99
7	$CH_3(CH_2)_8NH_2$	$CH_3(CH_2)_7CN$			
8	$CH_3(CH_2)_{10}NH_2$	$CH_3(CH_2)_9CN$			
9	$CH_3(CH_2)_{12}NH_2$	$CH_3(CH_2)_{11}CN$			
10			1	>99	99
11			10	87	86

[a]Reaction conditions: benzylamine (1 mmol), O_2 (1 atm); [b]Conversion was determined by GC and GC-MS; [c]Isolated yield, [d]reaction was conducted in the absence of catalyst.

In addition a Hammett plot (Figure 3) was also drawn to show the effect of substituents in benzylamines ($XC_6H_4CH_2NH_2$; X=H,p-Me, p-OMe, and p-Cl) on the reaction rate. As shown, a good linear correlation between values of log (k_X/k_H) and $(R_2=0.997)$ was observed for the aerobic oxidation of amines (X=, p-H, p-Me, p-OMe, and p-Cl). The resulting Hammett parameter reaction constant ρ=-0.015, indicates that a carbocation type intermediate is involved in the oxidation process. Further highest value of σ (substituent constant) for p-OMe indicated that electron donating group favors such reaction.

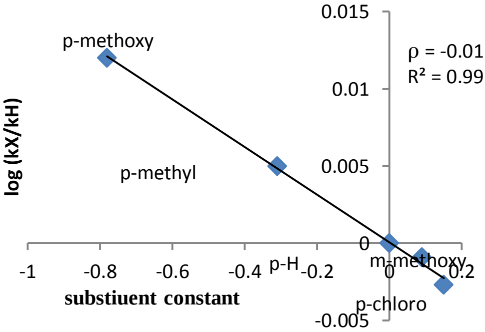


Fig. 2: Hammett plot

Furthermore, the recycling and reusability of the catalyst was examined by performing the aerobic oxidation of benzylamine as a model reaction under optimized reaction conditions. At the end of the reaction, the reaction mixture was diluted with dichloromethane and the catalyst was separated by filtration. The recovered catalyst was used as such for subsequent five runs (Fig. 3). In all cases, the yield of the product remained almost same which indicated that the synthesized iron catalyst was quite stable and can be reused for several runs without significant loss in activity. Furthermore, the iron content in fresh and recovered catalyst after five runs was found to be nearly same i.e. 4.3 and 4.2 %, confirmed that no leaching had occurred during the reaction

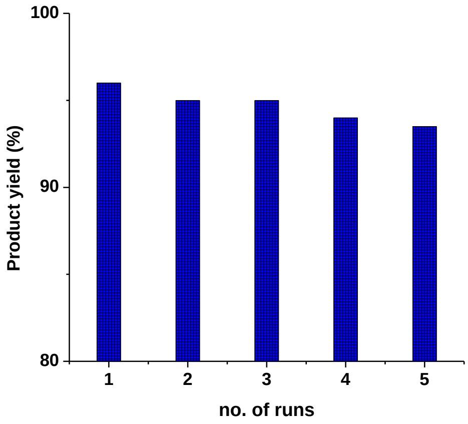


Fig. 3: Recycling of the Fe-S-AAIL

Conclusion

In summary, we have developed an efficient, green and reusable amino acid derived ionic liquid supported iron Schiff base for aerobic oxidation of various benzylamines, aliphatic amines and secondary amines to the corresponding nitriles and imines, respectively with 1 atm of dioxygen. The developed method offers a number of advantage such as i) easy synthesis of the catalyst; ii) chemically bonded iron prevents the leaching; iii) recyclability of the catalyst without significant loss; iv) solvent free conditions offering green approach and higher product yields. We believe that the potential of these novel task specific metal containing ionic liquids can further be explored for developing several other organic transformations in future.

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Experimental

Techniques

The presence of functional groups in the synthesized materials was confirmed by Fourier Transform Infrared Spectra using Perkin–Elmer spectrum RX-1 IR spectrophotometer having potassium bromide window and the spectra were collected on a Nicolet 8700 FT-IR spectrometer in the region of 4000-400 cm⁻¹. ICP-AES analysis was carried out to determine the loading of iron in the synthesized catalyst **3** by inductively coupled plasma atomic emission spectrometer (ICP-AES, DRE, PS-3000UV, Leeman Labs Inc., USA). Samples for ICP-AES were prepared by leaching out 100 mg of sample with conc HNO_3, followed by heating it for 30 min and finally made up the volume to 10 ml by adding distilled water. GC-MS analysis of products was carried out by using HP 5972 MSD coupled with HP 5890 GC, HP (USA) 1998. NMR spectra were recorded at 11.14 Tesla on a Bruker Avance III 500 spectrometer using a 5 mm broad band probe. The sample concentration is 10 % (v/v) for ^{1}H NMR and 30 % (v/v) for ^{13}C NMR analysis. The ^{1}H NMR was recorded at 500 MHz, with a 900 pulse angle, and 16 no. of scans, 5 s relaxation delay with a sweep width of 6,000 Hz. The ^{13}C NMR spectrum were recorded at 125 MHz, with a 900 pulse angle, and 2k no. of scans, 5s relaxation delay with a sweep width of 30,000 Hz. Deutrated chloroform ($CDCl_3$) was used as a solvent for sample analysis with tetramethylsilane (TMS) as an internal standard.

Synthesis of amino acid ionic liquid (AAIL)

Synthesis of ionic liquid was done on the basis of literature available procedure. An aqueous solution of tetrabutyl ammonium hydroxide (40 wt% solution in water) was added drop wise to DL-threonine aqueous solution that was slightly in excess of equimolar. The reaction mixture was allowed to stir at room temperature for 15 h. At the end of the reaction, water was removed under reduced pressure by rotary evaporation at 55 °C. Further, to this concentrate was added 90 ml of CH_3CN and 10 ml of CH_3OH and the resulting mixture was stirred vigorously. Excess of amino acid was removed by filtration and the obtained filtrate was concentrated under reduced pressure. The product was dried in vacuum for 2 days at 80 °C.

Synthesis of Fe-S-AAIL

To a solution of ionic liquid (2 mmol) in 5 ml of methanol was added gradually a solution of salicylaldehyde in methanol (5 ml) at room temperature with stirring. After 2 min of addition of salicyladehyde solution, an appearance of yellow color, gives the indication of formation of Schiff base. To this, a solution of $FeCl_2$ (1 mmol) in methanol was added drop-wise and stirred at room temperature for 30 minutes. A red colour thick viscous ionic liquid of Fe Schiff base complex was obtained which was dried under vacuum oven at 60 ^{o}C for 1 h to remove the methanol and was washed thrice with methanol to remove the unreacted species and was dried again under the conditions as mentioned above. FTIR (KBr): 2961, 1627, 1588, 1367 cm^{-1}. ESI-MS (m/z): 1141 (Fig. S2).

Typical experimental procedure for aerobic oxidation of amine

A double necked round bottomed flask (10 ml), equipped with magnetic stirrer was charged with amine (1 mmol) and catalyst **3** (5 wt%) and the resulting mixture was heated at 100 ^{o}C for 0.5 h under constant purging of molecular oxygen. After completion of the reaction, the mixture was diluted with ethyl acetate and the recovered catalyst was separated by decantation. The combined organic layer was dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure to give the crude product, which was further purified by column chromatography over silica gel using a solvent system of hexane and ethyl acetate (4:1) as eluent. The conversion and selectivity of the products was determined by GC-MS (HP 5972 MSD coupled with HP 5890 GC, HP (USA) and GC analysis (Varian CP 3800 with a FID detector and CPSil capillary column of 0.25 mm diameter and 30 meter length), respectively. Identity of the isolated products was confirmed by comparing their physical and spectral data with those of authentic compounds.

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Graphical Abstract

Amino acid derived ionic liquid supported iron Schiff base catalyzed greener approach for the aerobic oxidation of amines to nitriles

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