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Catalytic role of ionic liquid (bmim)HSO_4 for a highly efficient one pot conversion of aldehydes to nitriles and ketones to amides

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Abstract
A simple and efficient method has been developed for one pot conversion of aldehydes to nitriles and ketones to amides using acidic ionic liquid, 1-butyl-3-methylimidazoliumhydrogensulphate (bmim)HSO_4. Comparative studies using microwave irradiation and conventional heating have been carried out. Reproducibility of recycled ionic liquid has also been studied.

Keywords*: Ionic liquid, microwave irradiation, aldehydes, nitriles, ketones, amides.*

I. Introduction

Room temperature ionic liquids, as an alternate to classical environmentally damaging solvents have gained a great deal of attention in recent years[1]. Among various ionic liquids, imidazolium based cations[2] associated with weakly coordinated anions are most popular due to their peculiar physical and chemical properties. Ionic liquids have advantages[3] like negligible vapour pressure, thermal stability, recyclibility, enhancing the rate of reaction selectivity, tendency to dissolve many organic/inorganic substrates and catalytic efficiency. Moreover due to their highly polar nature, they absorb microwaves very effectively and thus are rapidly heated without any pressure increase[4].

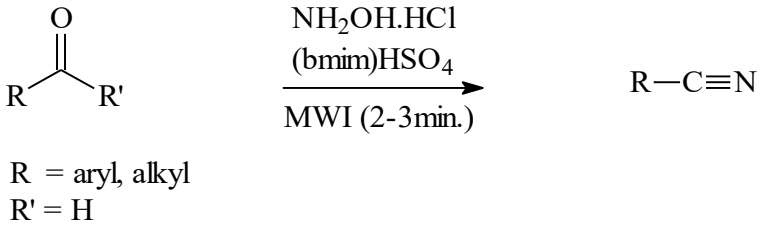
More recently the focus has been shifted to task specific ionic liquids (TSIL) [5] i.e. ionic liquids having a functional group that catalyze or take part in the reaction. As a result of their green credentials and potential to enhance rates and selectivity, they are finding increasing impetus in organic synthesis. Ionic liquids based on acidic counter ions have shown great promise to catalyze various organic reactions such as Friedel-Craft [6], Heck [7], Bignelli [8], Diels Alder [9], Pechmann condensation[10] etc.

The conversion of aldehydes into corresponding nitriles is a functional group transformation which finds significant practical importance, such as in the synthesis of various bioactive molecules[11], preparation of thiazole analogues as inhibitors of super oxide[12a], tetrazole derivatives as anti picornavirus drugs[12b], benzamidines possessing activity of fibrinogen antagonists[12c] and 1,2-diarylimidazoles as anti-inflammatory agents[12d]. Nitriles are also useful precursors for synthesis of amines, amides, ketones, carboxylic acids and esters [13]. Among a plethora of methods available for synthesis of nitriles, the most common is dehydration of aldoximes using classical reagents [14] in a two step process. Several methods have also been explored for the direct conversion of aldehydes into nitriles without isolation of nitrogen-containing intermediates. Some one pot conversions involve the use of selenium dioxide[15a], hydroxylamine hydrochloride and sodium iodide in acetonitrile[15b], HY-zeolite[15c], hydroxylamine, phthalic anhydride[15d], pyridine in refluxing toluene[15e], pyridine hydrochloride[15f] etc. However, most of these methods suffer from serious drawbacks such as low yields, harsh reaction conditions, tedious work up, opaque reaction mechanisms or long reaction times. Therefore, it is worthwhile to develop a simple, convenient and practical approach for the one pot conversion of aldehydes to nitriles.

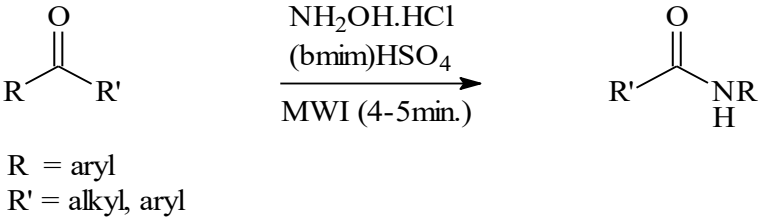
Preparation of amides from ketones is also an important functional group transformation in organic synthesis[16]. Amides are useful precursors for the industrial production of polyamides such as Nylon 6[17]. The Beckman rearrangement is a fundamental and useful reaction, long recognized as an extremely valuable and versatile method for the preparation of amides or lactams. The conventional Beckmann rearrangement usually requires the use of strong Lewis or Bronsted acids such as concentrated sulfuric acid, hydrogen chloride in acetic anhydride, phosphorous pentachloride, hydroxylamine-O-sulfonic acid and HCOOH[18]. But these processes cause corrosion and generally give low yields. Moreover, the recovery of catalyst is also a problem with these procedures. High selectivity can be achieved in liquid phase rearrangements[19], in which the solvent plays an important role. However, literature reports only a few methods for solvent free and one-pot conversions of ketones into amides[20].

Due to our continuous endeavour to develop greener methodologies[21] and on going work on (bmim)HSO_4[22] we have presented an alternate benign protocol for one-pot conversion of aldehydes to

corresponding nitriles (Scheme 1) and ketones into amides (Scheme 2). The potential use of room temperature ionic liquid (bmim)HSO_4 as bronsted acid[23] helps in catalyzing this conversion.



Scheme 1



Scheme 2

II. Experimental

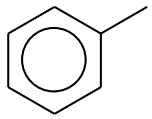
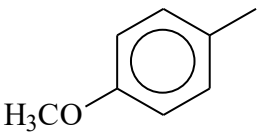
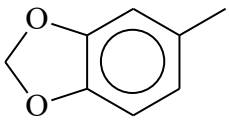
2.1 Preparation of Nitriles/Amides using (bmim)HSO_4 under Microwave Irradiation

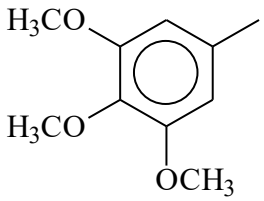
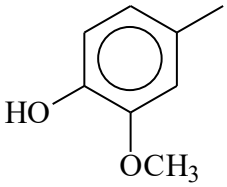
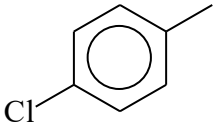
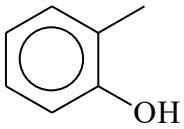
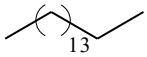
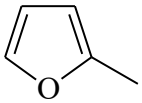
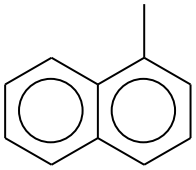
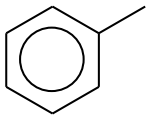
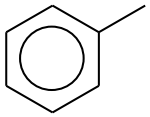
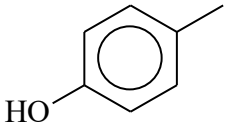
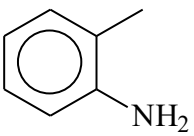
A mixture of aldehyde/ketone (1.0mmol) and hydroxylamine hydrochloride (1.0mmol) was mixed with (bmim)HSO_4 (0.19mmol) in a 50ml conical flask, covered with a watch glass. The mixture was then subjected to microwave irradiation at 320W in a domestic microwave oven [LGMS-194A(800W)] for the specified time (Table 1). The reaction mixture was allowed to cool, extracted with diethyl ether (3x10mL), washed with brine and the combined organic extracts were dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave the corresponding nitrile/amide which was further purified by chromatography on silica gel [hexane:EtOAc (5:1)].

2.2 Preparation of Nitriles/Amides using Thermal Heating

A mixture of aldehyde/ketone(1.0mmol) and hydroxylamine hydrochloride (1.0mmol) was mixed with (bmim)HSO_4 (0.19mmol) in 50mL round bottomed flask fitted with a guard tube. The mixture was heated for the time specified in Table 1, worked up and purified as above (method 2.1) to get the desired product.

Table 1: Conversion of aldehydes into Nitriles and ketones into amides

S.No.	R	R'	MWI(320W)		Thermal Heating	
			Time (min.)	Yield(%)	Time (h)	Yield (%)
1.		–H	3	92	5	90
2.		–H	2	85	3.5	90
3.		–H	2	88	3.5	92

4.		–H	2	90	3	90
5.		–H	3	80	4	85
6.		–H	3	75	4	77
7.		–H	3	72	4	80
8.		–H	2	90	3	92
9.		–H	2	80	3	85
10.		–H	3	85	6	80
11.		$–CH_3$	4	80	5	78
12.		–Ph	4	88	5	80
13.		$–CH_3$	5	82	7	75
14.		$–CH_3$	–	–	–	–

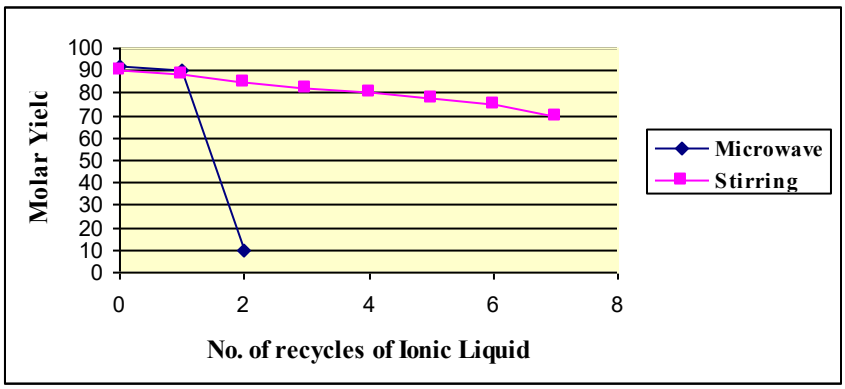
All the compounds in table 1 were characterized on the basis of ^{1}HNMR and IR spectral data which was found to be consistent with data reported in literature.

III. Results and Discussion

In view of the emerging importance of the dialkyl imidazolium based ILs as novel reaction media and as a part of our ongoing investigations on greener methodologies, we wish to report the use of (bmim)HSO_4 in the synthesis of nitriles and amides from aldehydes and ketones respectively. The synthesis of former by utilizing a simple and clean route via microwave assisted dehydration of aldoximes formed in situ by condensation of aldehydes with hydroxylamine hydrochloride in the presence of (bmim)HSO_4, has been exploited for the first time. The rate of the reaction is enhanced due to the dielectric effect of microwaves and the room temperature ionic liquid (bmim)HSO_4, helps in assigning economic value to eliminate waste. The separation of ionic liquid was brought about in an efficient and convenient manner by simply extracting the reaction mixture with diethyl ether. The solvent was distilled off (and used for subsequent workups) leading to isolation of products in good yields. A variety of aldehydes have been studied under these reaction conditions (Table 1). Heterocyclic (entry 9) and naphthyl aldehydes (entry 10) also afford products in equally good yields. The expeditious and solvent free approach has also been exploited without the use of microwave oven.

We also observed that (bmim)HSO_4 can efficiently catalyze the reaction of ketones (entry 11,12 and 13) with hydroxylamine hydrochloride to form initially the corresponding ketoximes followed by transformation to amides via Beckmann rearrangement. The structures of products were characterized from their spectral data (IR, ^{1}HNMR, ^{13}C) and compared with authentic samples.

The effectiveness of recycled ionic liquid was studied in the case of nitrile synthesis from 4-methoxybenzaldehyde (Figure). It was observed that recycled ionic liquid could be used up to 2 times on microwave irradiation before charring of ionic liquid occurred. However, the reaction time with recycled ionic liquid increased from 3 to 6 min. for complete conversion to nitrile during first recyclibility check. On the second recycled attempt, reaction resulted in formation of aldoxime with very little conversion into nitrile, even on increase of reaction time up to 6 min. More significantly, recycling of IL was accomplished at least seven times with thermal heating without any charring. Thus although microwave irradiation causes thrust in reaction by decreasing the reaction time it simultaneously lowers the activity of the catalyst.



Figure

IV. Conclusion

In conclusion, the work presented herein demonstrates the first use of ionic liquid (bmim)HSO_4 as a bronsted acid catalyst for a reliable, practical and one pot conversion of aldehydes to nitriles and ketones to amides. The notable features of the method are ease of preparation of catalyst, reduced reaction time and waste products, easy work up, solvent free reaction conditions and recyclibility of the catalyst. The method is applicable to a range of aldehydes and ketones both under microwave and thermal heating.

Acknowledgements

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