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GREEN SYNTHESIS OF IMODAZO [1, 2A] PYRIDINE

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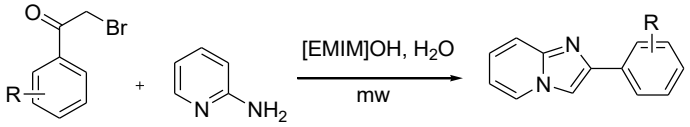
Absrtact:
An efficient ionic liquid [EMIM][OH] catalyzed water mediated condensation of phenacyl bromide and 2 amino pyridine in presence of microwave irradiation has been carried out for the synthesis of imodazo[1, 2a]pyridine derivatives. This method is simple, clean and rapid path for environmental benign synthesis of imodazo[1, 2a]pyridine.
Key-words: Imodazo[1, 2a]pyridine, ionic liquid, microwave assisted synthesis, water, phenacyl bromide

Introduction:

In is today's need to follow green chemistry principles for the organic synthesis. Many different techniques like microwave, ultra-sonication, grinding and use of water as reaction medium are getting more importance in organic synthesis.

Imidazo[1,2a] pyridines are important heterocyclic compounds because of their biological activities and interesting therapeutic properties such as anticancer[1], anti-inflammatory behavior[2], antibacterials[3],antiulcer[4], Hypnotic[5], calcium channel blockers[6]. Researchers synthesize imidazo[1, 2-a] pyridine from various starting materialse.g. condensation of 2-amino pyridine, aldehydes and isocynates[7], 2-amino pyridine, aldehydes and TMSCN[8], 2-amino pyridine, alkenes / alkynes and aldehydes[9] and 2-amino pyridine and α-halo-carbonyl compounds[10].Various catalysts are used for the synthesis of imidazo[1, 2-a] pyridine such as ammonium chloride[11], $InCl_3$[12], [bmim] Br[8]etc.
Considering these biological importance of imidazo[1, 2-a] pyridine and today's need of green methodology for synthesis we report here the microwave assisted ionic liquid catalyzed water mediated synthesis of imidazo[1, 2-a] pyridine.



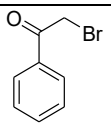
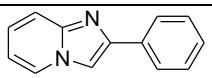
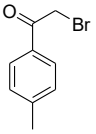
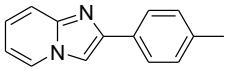
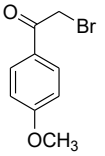
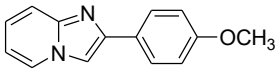
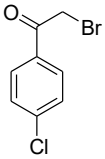
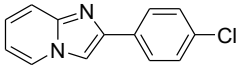
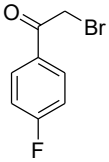
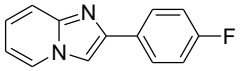
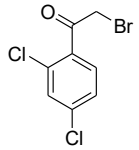
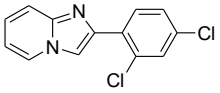
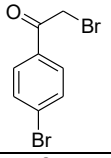
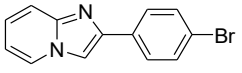
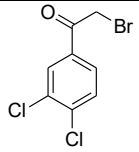
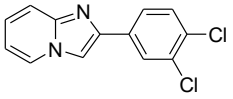
Scheme I

Materials and methods

Chemical reagents were purchased from SD fine chemical companies, sigma Aldrich India in high purity, used without further purification. All the materials purchased were of commercial grade reagent. Melting points were determined in open capillaries using an Electrothermal Mk3 apparatus. All experiments under microwave irradiation were carried out inmicrowave synthesis system 700W model manufactured by RAGA's Scientific Microwave Synthesis System Pvt.Ltd,Pune, India has a maximum power output of 700W and 2450 MHz frequency. FTIR spectra were recorded on a Perkin-Elmer FTIR spectrometer 65 in KBr pellets. ^{1}H NMR spectra were recorded on a Bruker 400 MHz FT-NMR spectrometer instrument usingDMSO-d6 (deutrated dimethyl sulfoxide) as a solventchemical shift values are recorded in units δ (ppm) relative to tetramethylsilane (Me_4Si) as an internal standard.The progresses of the reactions were monitored by TLC (Thin Layer Chromatography).

General procedure for the synthesis of Imidazo[1,2-a] pyridines:
A mixture of phenacyl bromide(1 mmol), 2 amino pyridine (0.8 mmol) and [EMIM][OH] (0.2 mmol) was taken in a 10 ml glass vial equipped with a cap. The tube was kept in the irradiation cavity in the monomode microwave oven and irradiated with microwaves at 140 watt at 180^0C for the specified time as mentioned in Table 1. The progress of reaction was monitored by TLC. After completion of reaction, the reaction mixture was filtered, washed with water and purified by recrystalization with ethanol to afford the pure product.

Table 1: Synthesis of imidazo[1, 2-a] pyridine from phenacyl bromide and 2 amino pyridine

Entry	Phenacyl Bromide	Product	Time in sec	Yeild in %	M.P.
1			120	85	136-137[13]
2			120	82	144-145[14]
3			120	78	135-136[13]
4			90	84	206-207[13]
5			90	80	163-164[14]
6			75	85	182[14]
7			90	80	215-216[14]
8			75	82	172[15]

Result and discussion:
Phenacyl bromide (1.2 mmol) and 2 aminopyridine (1 mmol) on irradiating with microwaves in presence of [EMIM][OH] in water the reaction was completed in just 1 -2 min affording imidazo[1,

2-a] pyridine (Scheme1). Progress of reaction was monitored by thin layer chromatography using ethyl acetate/hexane in appropriate proportions as eluent. The present report offers cleaner and simpler experimental and work-up procedures. After completion of reaction, the reaction mixture was filtered, washed with water and recrystallized. There was no need of chromatographic purification techniques. The method was quite simple and the products were formed within a few minutes in very good yields. The reason of rapid reaction time is rapid rise in temperature because of strong absorption of microwaves in presence of ionic liquid. The scope and generality of this method was checked using different substituted phenacyl bromides. The α-bromoacetophenone with electron-rich substituent as well as electron-poor substituent undergoes condensation reaction with 2-aminopyridine equally well to afford the corresponding products. All the imidazo[1, 2-a] pyridine derivatives were characterized by melting point, IR, ^{1}H NMR spectral analysis.

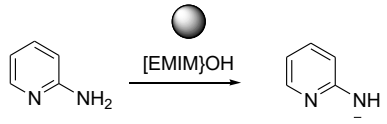
Spectral data of representative compound is mentioned below:

2-(4-Methylphenyl)imidazo[1,2-α]pyridine:IR (KBr), ν (cm^{-1}): 3461, 3130, 2838, 1634, 1507, 1485, 1370, 1247, 1148, 823, 743; 1H-NMR: δ = 2.37 (s, 3 H), 6.72 (s, 1 H), 7.12 (s, 1 H), 7.24 (s, 2 H), 7.64–7.65 (d, 1 H), 7.60 (s, 1 H), 7.78–7.83 (d, 3 H), 8.05 (s, 1 H).

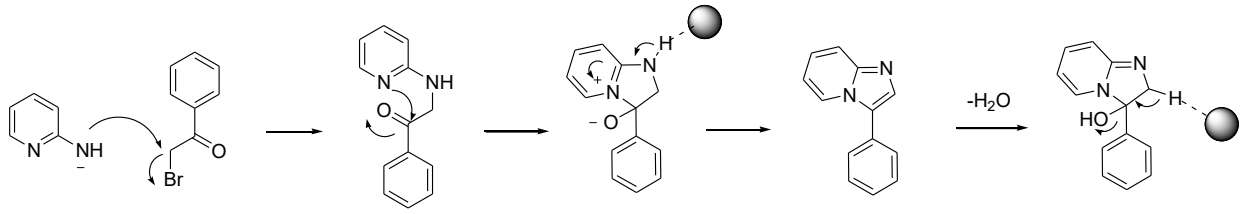
2-(4-Methoxyphenyl)imidazo[1,2-α]pyridine: IR (KBr), ν (cm^{-1}): 3468, 3136, 2838, 1634, 1507, 1483, 1374, 1249, 1032, 839, 744; 1H-NMR: δ = 3.86 (s, 3 H), 6.72–6.75 (t, 1 H), 6.94–6.98 (d, 2 H), 7.11–7.16 (t,1 H), 7.59-7.62 (d, 1 H), 7.75 (s, 1 H), 7.86-7.89 (d, 2 H), 8.1 (d, 1 H).

Mechanism:

i) Base abstract proton to form anion



ii) attack of anion of 2 aminopyridine on phenacyl bromide followed by cyclisation and dehydration



Conclusion:

In summary, we report here a simple, environment benign ionic liquid catalyzed, water mediated method for the synthesis of biologically important imidazo[1, 2-a] pyridine derivatives under microwave irradiation.

Acknowledgement:

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