Innovare Academic Sciences

International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 6, Issue 6, 2014

Original Article

IONIC LIQUID PROMOTED SYNTHESIS OF 2-PHENYLIMIDAZO [1,2-*a*]PYRIDINE DERIVATIVES AND THEIR ANTIBACTERIAL SCREENING

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Received: 15 May 2014 Revised and Accepted: 13 Jun 2014

ABSTRACT

Objective: We aimed to evaluate the use of ionic liquid in the synthesis of substituted Imidazo [1,2-*a*]pyridine derivatives and their antibacterial activity against Gram-positive and Gram-negative bacteria.

Methods: The substituted-2-Phenylimidazo[1,2-*a*]pyridine derivatives have been Synthesized by a one pot two component reaction of 2-aminopyridine and α-halo acetophenone in the presence of green recoverable ionic liquid and ethanol. The newly synthesized compounds were characterized by elemental analysis, IR, ^{1}H and ^{13}C NMR. All the synthesized compounds were screened for their antibacterial activity.

Results: Excellent yield of 2-Phenylimidazo[1,2-*a*]pyridine derivatives 3a-r were obtained in ionic liquid method than ethanol. The results of biologically activities show synthesized compounds would be of better use in drug development to combat bacterial infection in future.

Conclusion: All the synthesized compounds were screened for antibacterial activity. Ampicillin, and cefixime were used as antibacterial references.

Keywords: Ionic Liquid (IL), 2-aminopyridine, α-halo-acetophenone, Antibacterial investigation.

INTRODUCTION

Bacterial infections caused by the species of genius Staphylococcus and the species of the genus Enterococcus are major health concern. Increasing incidence of bacterial infections in hospitals and their ability to develop resistance to multiple antibiotics has been reported [1]. At the beginning of the new century, it a major challenge of modern drug discovery is the design of concise and effective methodologies for preparing combinatorial libraries of small molecules for research. So far, a number of strategies have been developed for meeting such a challenge [2]. In this regard, extensive synthesis and designing of new structural motifs, in order to overcome the aforementioned problems and improve broad spectrum antimicrobial activity are highly desirable. Nitrogen-bridgehead fused heterocycles containing an imidazole ring are a common structural motif in pharmacologically important molecules, with activities spanning a diverse range of targets. Probably the most widely used heterocyclic system from this group is imidazo[1,2-*a*]pyridine. Imidazopyridine derivatives are of wide interest because of their diverse biological activities and clinical applications such as antiviral [3], antiulcer [4], antibacterial [5, 6], antifungal [7, 8], antiprotozoal [9, 10], antiherpes [11], anti-inflammatory [12, 13]. Several annulated pyridines isolated from natural sources possess broad spectrum of therapeutic activity. Members of this class were found to be protectors against gastric erosion [14]. They have also been characterized as selective cyclic-dependent kinase inhibitors [15], calcium channel blockers [16], β-amyloid formation inhibitors [17], and benzodiazepine receptor agonists [18] and they constitute a novel class of orally active nonpeptide bradykininB_2 receptor antagonists [19].

In the designing of new drugs, the development of hybrid molecules through the combination of different pharmacophores may lead to the formation of different compounds with interesting biological and pharmacological profiles. Prompted by these observations, in the present study, the synthesis of 2-phenyl derivatives of imidazo[1,2-*a*]pyridines including different pharmacophores have been carried out. Majority of the reported imidazo[1,2-*a*]pyridines synthesis methods proceed via the condensation reaction of the α-halocarbonyl compounds with 2-aminopyridine derivatives under neutral or weak basic conditions. The increase in environmental consciousness among the chemical researchers and industries and the challenge for a sustainable environment, calls for the development of clean synthetic procedures that can avoid the use of harmful organic solvents, or even better, do not need solvents at all. In continuation of our interest in green chemistry, we hereby wish to report the neat reaction of 2-aminopyridine with α-haloacetophenone under Ionic liquid medium, affording 2-phenyl substituted imidazo[1,2-*a*]pyridine derivatives in good to excellent yields.

Ionic Liquid in organic synthesis has received much attention because of it's provide faster chemistry and formation of cleaner products compared to conventional heating. This technology has recently been recognized as a useful tool for the synthesis of heterocyclic compounds [20, 21]. In conjunction with our interest in developing new protocols in combinatorial synthesis, we explore the use of ionic liquid in synthesis of imidazo[1,2-*a*]pyridine derivatives.

MATERIALS AND METHODS

General Procedures

All the products were synthesized and characterized by their spectral analysis. All reagents were obtained from Merck Chemical Limited. Solvent used were of laboratory grade and, when necessary, were purified and dried by standard methods. Completion of the reaction was monitored by thin layer chromatography on precoated sheets of silica gel-G (Merck, Germany). Melting point were measured in open capillary tubes and are uncorrected, IR spectra were recorded on a SHIMADZU FT-IR spectrometer using KBr pellets and band position are reported in wave number(cm^{-1}). ^{1}H and ^{13}C NMR spectra were recorded on a JEOL AL(300MHz) and (75MHz) respectively NMR spectrometer in $CDCl_3$ using TMS as an internal standard (chemical shift in δ ppm). Elemental analysis was carried out on Elemental Bario EL- III Carlo Erba 1108 CHN analyzer.

Conventional method

A mixture 0.01mol of α-halo ketone and 0.01mol of 2–aminopyridine in ethanol(10ml) was heated on a water bath for 22-23h. The mixture was cooled, filtered and product washed with dilHCl and cold ethanol. It was purified by recrystallization from ethanol to give **3a-r.** The analytical and spectral characterized data of compounds synthesized are recorded in Table 1.

Table 1: Characterization data of Imidazo[1,2-*a*]pyridine derivatives 3a-r

Entry	R	Z	Yield % in Conv	Yield % in IL	Molecular Formula	Elemental analysis % Found (Calcd)
3a	H	H	62	90	$C_{13}H_{10}N_2$	C, 80.32 (80.38); H, 5.10 (5.18); N, 14.46 (14.42)
3b	H	CH_3	61	92	$C_{14}H_{12}N_2$	C, 80.75(80.74); H, 5.13 (5.81); N, 13.42 (13.45)
3c	H	OCH_3	63	94	$C_{14}H_{12}N_2O$	C, 74.87 (74.98);; H, 5.33 (5.39); N, 12.52 (12.49);
3d	H	F	60	90	$C_{13}H_9N_2F$	C, 73.49 (73.59); H, 4.30 (4.27); N, 13.19(13.22);
3e	H	Cl	58	90	$C_{13}H_9N_2Cl$	C, 68.29 (68.27); H, 3.93 (3.96); N, 12.22 (12.25);
3f	H	Br	59	89	$C_{13}H_9N_2Br$	C, 57.17(57.16); H, 3.33(3.32); N, 10.22 (10.25)
3g	Cl	H	60	91	$C_{13}H_9N_2Cl$	C, 68.30 (68.27); H, 3.93 (3.96); N, 12.25 (12.25);
3h	Cl	CH_3	61	91	$C_{14}H_{11}N_2Cl$	C,69.11 (69.28);H, 4.12 (4.57); N, 11.24 (11.54),
3i	Cl	OCH_3	62	92	$C_{14}H_{11}N_2OCl$	C, 64.39 (64.44); H, 4.29 (4.28); N, 10.82 (10.82);
3j	Cl	F	45	88	$C_{13}H_8ClFN_2$	C, 63.01 (63.30); H, 3.12 (3.27); N, 11.22 (11.36);
3k	Cl	Cl	54	86	$C_{13}H_8Cl_2N_2$	C,59.09 (59.34);H,2.98 (3.06); N, 10.18 (10.65);
3l	Cl	Br	57	89	$C_{13}H_8BrClN_2$	C, 50.17 (50.76); H, 2.30 (2.62); N, 8.98 (9.11);
3m	OH	H	62	91	$C_{13}H_{10}N_2O$	C, 74.11 (74.27); H, 4.36 (4.79); N, 13.08 (13.33);
3n	OH	CH_3	64	92	$C_{14}H_{12}N_2O$	C,74.15 (74.98); H,5.16 (5.39); N, 12.24 (12.49),
3o	OH	OCH_3	67	95	$C_{14}H_{12}N_2O_2$	C, 69.39 (69.99); H, 4.85 (5.03); N, 11.27 (11.66);
3p	OH	F	56	93	$C_{13}H_9FN_2O$	C, 68.01 (68.42); H, 3.12 (3.97); N,12.02 (12.27);
3q	OH	Cl	59	92	$C_{13}H_9ClN_2O$	C,63.19 (63.81);H,3.27 (3.71);N, 11.18; (11.45);
3r	OH	Br	58	90	$C_{13}H_9BrN_2O$	C,53.67,(54.00); H, 3.10 (3.14); N, 9.18; (9.69);

Ionic liquid mediated synthesis of (3a-r)

A mixture 1mmol of α-haloacetophenone,1mmol of 2–aminopyridine and ionic liquid was taken in a round bottom flask, and solution was magnetically stirred for 1-2h. The progress of reaction was monitored by TLC(Merck silica gel $60F_{254}$) using petether:ethylacetate 8:2. After completion of the reaction, the product was extracted with ethylacetate. The combined organic layer was dried over anhydrous Na_2SO_4 and the solvent was distilled out under reduced pressure. The products obtained wererecrystallized by ethanol to give **3a-r** in 85-95% yield. The analytical and spectral characterized data of synthesized compounds are the same as prepared by conventional method.

2-Phenylimidazo[1,2-*a*]pyridine (3a)

Brown solid, m.p. 130-132°C. IR (KBr) (ν_{max}/cm^{-1}), 1615 (C=N), 1525, 1555, 1600 (aromatic carbon), 3050 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 6.72 (dt, 1H), 7.14-7.18 (m, 1H), 7.31 (t, 1H), 7.40-7.43 (m, 2H), 7.64 (dd, 1H), 7.87 (s, 1H), 7.95-7.97 (m, 2H), 8.12 (d, 1H);^{13}C NMR (75 MHz,$CDCl_3$): δ 118.9, 120.0, 121.7, 126.2, 127.3, 128.5, 128.9, 131.5, 135.6,136.4, 145.5.

2-(4-methylphenyl)imidazo[1,2-*a*]pyridine (3b)

Light brown solid, m.p. 145-146°C. IR (KBr) (ν_{max}/cm^{-1}), 1615 (C=N), 1609, 1525, 1555 (aromatic carbon), 2920, 2842 (aliphatic hydrogen), 3048 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 2.35 (s, 3H), 6.72 (dt, 1H), 7.21-7.27 (m, 2H), 7.63 (d, 1H), 7.86 (s, 1H), 7.80-7.84 (m, 2H), 8.10 (d, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.2, 118.4, 119.8, 120.1, 121.5, 127.8, 128.6, 128.8, 131.2,135.7, 136.6, 145.

2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (3c)

Brown solid, m.p. 134-136 °C. IR (KBr) (ν_{max}/cm^{-1}), 1610 (C=N), 1600, 1522, 1550 (aromatic carbon), 2912, 2832 (aliphatic hydrogen), 3040 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 3.82 (s, 3H), 6.70 (dt, 1H), 6.85 (d, 2H), 7.12-7.16 (m, 1H), 7.50 (d,,1H), 7.78 (s, 1H), 7.82 (d, 2H), 8.02 (d, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.0, 118.5, 120.1, 120.2, 121.3, 126.4, 128.5, 128.7, 131.3, 131.9, 134.5, 136.4, 140.5.

2-(4-flouorophenyl)imidazo[1,2-*a*]pyridine (3d)

Yellow solid, m.p. 158- 160 °C.IR (KBr) (ν_{max}/cm^{-1}), 1620 (C=N), 1612, 1535, 1560 (aromatic carbon), 3050 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 6.83 (dt, 1H), 7.09-7.14 (m, 2H), 7.16-7.20 (m, 2H), 7.65 (d,1H), 7.29(m, 1H), 7.81 (s, 1H), 8.11 (td, 1H); ^{13}C NMR (100MHz,$CDCl_3$): δ 118.6, 120.6, 126.3, 128.3, 128.6, 132.1, 135.1, 135.8, 134.5, 145.9, 149.5.

2-(4-chlorophenyl)imidazo[1,2-*a*]pyridine (3e)

Brown solid, m.p. 202-204 °C. IR (KBr) (ν_{max}/cm^{-1}), 1620 (C=N), 1610, 1520, 1555 (aromatic carbon), 3050 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 6.83 (dt, 1H), 7.22 (d, 1H), 7.14-16 (d, 2H), 7.18-7.21 (m, 2H), 7.30 (m, 1H), 7.81 (s, 1H), 8.09 (td, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 118.3, 120.5, 121.4, 123.9, 125.7, 128.2, 128.8, 131.8, 135.1, 142.1, 144.7.

2-(4-Bromophenyl)imidazo[1,2-*a*]pyridine (3f)

Brown solid, m.p. 220-222 °C. IR (KBr) (ν_{max}/cm^{-1}), 1618 (C=N), 1610, 1520, 1555 (aromatic carbon), 3048 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 6.67 (dt, 1H), 7.01 (m, 1H), 7.35-7.40 (m, 2H), 7.44-7.51 (m, 2H), 7.51 (d, 1H), 7.81 (s, 1H), 8.10 (d, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 118.1, 120.4, 121.9, 123.7, 125.4, 128.1, 128.7, 131.2, 134.8, 141.9, 144.2.

6-chloro-2-phenylimidazo[1,2-*a*]pyridine (3g)

Yellow solid, m.p. 199-203 °C. IR (KBr) (ν_{max}/cm^{-1}), 1625 (C=N), 1555, 1525 (aromatic carbon), 3052 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 7.21-7.24 (m,1H), 7.36 (t, 1H), 7.42-7.46 (m, 2H), 7.71 (d, 1H), 7.84(s, 1H), 7.91-7.94 (m, 2H), 8.20 (d, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 120.9, 121.1, 121.5, 122.4, 127.5, 128.1, 128.9, 132.1, 133.4, 136.7, 144.7.

6-Chloro-2-(4-methylphenyl)imidazo[1,2-*a*]pyridine (3h)

Light brown solid, m.p. 223-225 °C. IR (KBr) (ν_{max}/cm^{-1}), 1620 (C=N), 1615, 1530, 1560 (aromatic carbon), 2920, 2842 (aliphatic hydrogen), 3048 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 2.35 (s, 3H), 7.15-7.20 (m, 2H), 7.35 (t, 1H), 7.42-7.47 (m, 2H), 7.65 (d, 1H), 7.83 (s, 1H), 8.19 (d, 1H); ^{13}C NMR (100MHz, $CDCl_3$): δ 14.2, 120.0, 120.8, 121.5, 122.1, 127.9, 128.5, 128.8, 132.9, 133.1, 136.1, 144.6.

6-chloro-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (3i)

Brown solid, m.p. 245-246 °C. IR (KBr) (ν_{max}/cm^{-1}), 1618 (C=N), 1610, 1520, 1555 (aromatic carbon), 2915, 2840 (aliphatic hydrogen), 3045 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 3.84 (s, 3H), 6.80-6.85 (m, 2H), 7.30-7.35 (m, 2H), 7.41 (t, 1H),7.68 (d, 1H), 7.81 (s, 1H), 7.82 (s, 1H), 8.18 (d, 1H); ^{13}C NMR (75 MHz,$CDCl_3$): δ 39.3, 120.4, 120.9, 121.7, 122.6, 126.9, 128.8, 133.2, 133.7, 134.1, 140.7, 144.5.

6-Chloro-2-(4-fluorophenyl)imidazo[1,2-*a*]pyridine (3j)

Yellow solid, m.p. 267-269 °C. IR (KBr) (ν_{max}/cm^{-1}), 1625 (C=N), 1615, 1535, 1560 (aromatic carbon), 3050 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 6.83 (dt, 1H), 7.10-7.15 (m, 2H), 7.17-7.22 (m, 2H), 7.45 (t, 1H), 7.82 (s, 1H),7.71 (d, 1H), 8.15 (d,

1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 120.9, 121.2, 121.5, 122.3, 128.5, 128.9, 133.1, 133.9, 135.9, 144.7, 149.2.

6-Chloro-2-(4-chlorophenyl)imidazo[1,2-*a*]pyridine (3k)

Brown solid, m.p. 243-245 °C. IR (KBr) (ν_{max}/cm^{-1}), 1622 (C=N) 1612, 1520, 1560 (aromatic carbon), 3050 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 7.30-7.35 (m, 2H), 7.39-7.44 (m, 2H), 7.49 (t, 1H), 7.74 (d, 1H) 7.81(s, 1H), 8.16 (d, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 120.4, 120.7, 121.4, 122.7, 128.6, 128.9, 133.1, 133.5, 135.3, 142.6, 144.9.

6-Chloro-2-(4-bromophenyl)imidazo[1,2-*a*]pyridine (3l)

Brown solid, m.p. 227-229 °C. IR (KBr) (ν_{max}/cm^{-1}), 1620 (C=N) 1610, 1525, 1560 (aromatic carbon), 3050 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 7.35-7.40 (m, 2H), 7.45-7.48 (m, 2H), 7.52 (t, 1H), 7.78 (d, 1H), 7.81(s, 1H), 8.15 (d,1H); ^{13}C NMR (100MHz, $CDCl_3$): δ 120.4, 120.9, 121.6, 122.1, 128.2, 128.8, 133.2, 133.6, 134.3, 141.7, 144.7.

2-phenylimidazo[1,2-*a*]pyridine-8-ol (3m)

Brown solid, m.p. 189-191 °C. IR (KBr) (ν_{max}/cm^{-1}), 1610 (C=N) 1600, 1520, 1550 (aromatic carbon), 3050 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 6.72 (dt, 1H), 7.14-7.18 (m, 1H), 7.31 (t, 1H), 7.40-7.43 (m, 2H), 7.64 (dd, 1H), 7.87 (s, 1H), 7.95-7.97 (m, 2H), 8.12 (td, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 118.3, 120.2, 121.2, 127.5, 127.8, 128.9, 129.4, 132.3, 134.6, 136.9, 144.8.

2-(4-methylphenyl)imidazo[1,2-*a*]pyridine-8-ol (3n)

Light brown solid, m.p. 202-204°C. IR (KBr) (ν_{max}/cm^{-1}), 1608 (C=N), 1600, 1520, 1550 (aromatic carbon), 2920, 2842 (aliphatic hydrogen), 3045 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 2.35 (s, 3H), 6.71 (dt, 1H), 7.16-7.21 (m, 2H), 7.33 (t, 1H), 7.41-7.46 (m, 2H), 7.67 (dd, 1H), 7.87 (s, 1H), 8.12 (d, 1H); ^{13}C NMR (75 MHz,$CDCl_3$): δ 14.2, 118.1, 120.2, 121.1, 127.4, 127.7, 128.2, 128.8, 132.4, 134.7, 136.5, 144.7.

2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine-8-ol (3o)

Brown solid, m.p. 219-221 °C. IR (KBr) (ν_{max}/cm^{-1}), 1605 (C=N), 1600, 1515, 1550 (aromatic carbon), 2915, 2840 (aliphatic hydrogen), 3045 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 3.84 (s, 3H), 6.71 (dt, 1H), 6.78 (d, 2H), 7.34 (t, 1H), 7.76 (d, 2H), 7.80 (s, 1H), 7.64 (dd, 1H), 8.11 (td, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.2, 118.5, 120.7, 121.6, 126.7, 127.7, 128.2, 132.8, 134.0, 134.5, 140.9, 144.8.

2-(4-fluorophenyl)imidazo[1,2-*a*]pyridine-8-ol (3p)

Yellow solid, m.p. 246-248 °C. IR (KBr) (ν_{max}/cm^{-1}), 1612 (C=N), 1605, 1525, 1552 (aromatic carbon), 3050 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 6.80 (dt,1H), 7.08 (d, 2H), 7.16 (d, 2H), 7.31 (t, 1H), 7.90 (s, 1H),7.76 (dd, 1H), 8.16 (td, 1H), ^{13}C NMR (100MHz, $CDCl_3$): δ 118.8, 121.8, 122.7, 128.2, 128.9, 129.5, 132.9, 134.7, 136.2, 144.9, 150.4.

2-(4-chlorophenyl)imidazo[1,2-*a*]pyridine-8-ol (3q)

Brown solid, m.p. 215-217 °C. IR (KBr) (ν_{max}/cm^{-1}), 1610 (C=N), 1605, 1520, 1555 (aromatic carbon), 3048 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 6.79 (dt, 1H), 7.02 (d, 2H), 7.18 (d, 2H), 7.31 (t, 1H), 7.89 (s, 1H), 7.76 (dd, 1H), 8.15 (td, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 118.6, 120.9, 121.8, 127.7, 128.6, 128.7, 132.7, 134.6, 142.1, 144.8.

2-(4-bromophenyl)imidazo[1,2-*a*]pyridine-8-ol (3r)

Brown solid, m.p. 199-202°C.IR (KBr) (ν_{max}/cm^{-1}), 1610 (C=N), 1605, 1525, 1550 (aromatic carbon), 3048 (aromatic hydrogen); ^{1}HNMR (300MHz, $CDCl_3$): δ 6.78 (dt, 1H), 7.33 (t, 1H), 7.44 (d, 2H), 7.84 (d, 2H), 7.76 (dd, 1H), 8.16 (td, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 118.4, 120.4, 121.2, 127.2, 128.1, 128.5, 132.4, 134.1, 134.7, 142.5, 144.6.

RESULTS AND DISCUSSIONS

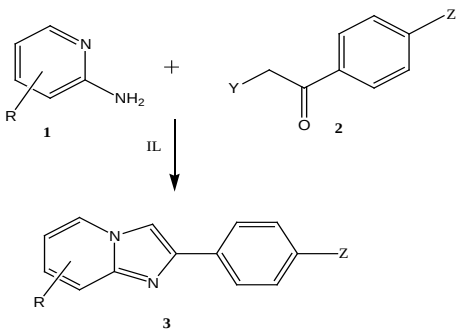
The synthesis of Imidazo[1,2-*a*]pyridine had been attempted by reacting 2-Amino pyridine with α-haloacetophenone in ionic liquid, viz(BMIM)BF_4 (as shown in scheme 1). The reaction was also carried out by conventional method using ethanol as a solvent which required refluxing for 22-23h, however, in (BMIM)BF_4, the reaction took place at room temperature in 1-2h and gave a higher yield.

The structures of the products were confirmed by ^{1}H NMR, ^{13}C NMR, IR and elemental analysis. In the IR spectra of compounds **3a-r** showed no peak for -NH_2, in the 3290-3196 region and no peak for Carbonyl carbon in the region 1790-1820 cm^{-1}. The IR spectra of compounds **3a-r** exhibited medium bands in the range 1620-1500 cm^{-1}(C=N, and aromatic carbons, stretching).

In the ^{1}H-NMR spectra of compounds **3a, 3h, 3n**showed a singlet for the methyl protons around 2.35 ppm. Compounds **3c, 3i, 3o** showed a singlet for the methoxy protons around3.84 ppm. ^{13}C-NMR data of compounds **3a-r** showed no peak for the carbonyl carbon of the acetyl group around 193 ppm, but showed signals only for aromatic and olefinic carbons in the range 114-152, in addition to the CH_3 signal around 14 ppm. This gives astrong evidence that the carbonyl carbon of haloacetophenone is converted to alkene carbon as shown in scheme 1**.**

Antibacterial activity

All the synthesized compounds were evaluated for their antibacterial activity against gram positive bacteria *S. aureus, E. faecalis* and gram negative bacteria *E. coli, E. aerogenus*. Minimum inhibitory concentration (MIC) was measured as described in the Table 2. Ampicillin, and cefixime were used as antibacterial references.



R	
1a	H
1b	Cl
1c	OH

Z	
2a	H
2b	CH3
2c	OCH3
2d	F
2e	Cl
2f	Br

Scheme 1: Synthesis of Imidazo[1,2-*a*]pyridine (3a-r)

Table 2: Minimum inhibition concentration (MICμg/ml) of the synthesized compounds (3a-r) as well as standard drugs tested for antibacterial activity

Entry	R	Z	S.aureus	E.faecalis	E. coli	E. aerogenes
3a	H	H	32.25±1.21	33.41±1.01	31.12±1.05	37.17±0.89
3b	H	CH_3	24.25±1.51	26.21±1.11	25.12±1.49	28.45±0.45
3c	H	OCH_3	12.99±1.17	14.03±0.89	13.25±1.16	18.98±1.67
3d	H	F	5.89±0.02	6.59±0.75	6.01±0.03	7.48±0.03
3e	H	Cl	2.01±0.05	3.43±1.02	3.23±0.10	4.75±0.75
3f	H	Br	3.41±0.03	7.01±0.79	3.11±0.06	6.49±0.36
3g	Cl	H	7.99±0.05	9.89±0.89	8.15±0.09	7.99±0.05
3h	Cl	CH_3	8.18±1.32	8.09±1.91	9.49±1.5	7.45±0.99
3i	Cl	OCH_3	10.09±1.27	11.05±1.31	11.27±1.43	15.28±0.64
3j	Cl	F	0.23±0.02	0.44±0.12	0.45±0.02	0.89±0.51
3k	Cl	Cl	0.31±0.01	0.21±0.02	0.39±0.05	1.42±0.04
3l	Cl	Br	0.22±0.03	0.47±0.03	0.27±0.01	1.31±0.32
3m	OH	H	7.45±1.17	19.31±1.12	18.19±1.43	22.21±1.54
3n	OH	CH_3	11.21±1.19	20.32±1.25	11.53±1.20	14.12±2.01
3o	OH	OCH_3	15.23 ±1.32	24.12±1.01	17.21±0.44	16.59±0.98
3p	OH	F	12.11±0.05	16.53±1.43	15.45±0.04	14.32±1.87
3q	OH	Cl	11.98±0.45	17.01±1.09	14.57±0.31	16.25±2.04
3r	OH	Br	11.08±0.05	16.85±1.52	13.03±1.21	14.99±1.86
Amoxicillin			14.23±1.21	1.15±0.02	15.27±1.23	4.71±0.12
Cefixime			31.01±2.11	29.18±1.52	2.57±0.15	29.03±1.57

As shown in Table 2, the synthesized scaffolds exhibited a broad spectrum activity with MIC values, defined as the lowest concentration at which no visible growth observed against both Gram-positive and Gram-negative bacteria. Among the Gram positive bacteria tested, *S. aureus* showed a relatively high sensitivity toward the title compounds. Compounds **3j, 3k,** and **3l**, gave the best inhibitory activity against *S. aureus* with MIC values <0.5 mg/ml. Furthermore, compounds **3j, 3k** and **3l** also showed potent activity against *E. faecalis* with MIC values <0.5 mg/ ml.

CONCLUSION

Synthesis of substituted Imidazo[1,2-a]pyridine derivatives using Ionic liquid as solvent found efficient and time saving. The result showed that the efficiency and the yield of the reaction in $(BMIM)BF_4$ was higher than conventional method. Synthesis was done successfully and compounds **3a-r** showed antibacterial activity against Gram-positive and Gram-negative bacteria.

ACKNOWLEDGEMENT

Financial assistance from CSIR (No. 09/149(0568)/2009-EMR-1), New Delhi is acknowledged. We are grateful to the Head, Department of Chemistry, University Of Rajasthan, Jaipur for providing laboratory facilities.

REFERENCES

1. Grare M, Mourer M, Fontanay S, Regnouf-de-Vains JB, Finance C, Duval RE. In vitro activity of para-guanidinoethylcalix[4]arene against susceptible and antibiotic-resistant gram-negative and gram-positive bacteria. J Antimicrob Chemother 2007;60(3):575-581.
2. Schreiber SL.Target-oriented and diversity-oriented organic synthesis in drug discovery, Science 2000;287:1964–1969.
3. Puerstinger G, Paeshuyse J, Declercq E, Neyts J. Antiviral 2, 5-disubstituted imidazo[4,5-*c*]pyridines from anti-pestivirus to anti-hepatitis C virus activity. Bioorg Med Chem Lett 2007;17:390-393.
4. Katsura Y, Nishino S, Inowe Y, Tomoi M, Takasugi H. Studies on antiulcer drugs II synthesis and antiulcer activities of imidazo[1,2-*a*]pyridinyl-2-alkylaminobenzoxazoles and 5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridinyl derivatives. Chem Pharm Bull 1992;40(2):371-380.
5. Rewankar GR, Matthews JR, Robins RK. Synthesis and antimicrobial activity of certain imidazo[1,2-*a*]pyrimidines. J Med Chem 1975;18:1253-1255.
6. Rival Y, Grassy G, Michel G. Synthesis and antibacterial activity of some imidazo[1,2-*a*]pyrimidine derivatives. Chem Pharm Bull 1992;40(5):1170-1176.
7. Fisher MH, Lusi A. Imidazo[1,2-*a*]pyridine anthelmintic and antifungal agents. J Med Chem 1972;15(9):982-985.
8. Rival Y, Grassy G, Taudou A, Ecalle R. Antifungal activity in vitro of some imidazo[l,2-*a*lpyrimidine derivatives. Eur J Med Chem 1991;26:13-18.
9. Biftu T, Feng D, Fisher M, Liang G, Qian X, Scribner A, Dennis R, Lee S, Liberator P, Brown C, Gurnett A, Leavitt P, Thompson D, Mathew J, Misura A, Samaras S, Tamas T, Sina J, McNulty K, McKnight C. Synthesis and sar studies of very potent imidazopyridine antiprotozoal agents. Bioorg Med Chem Lett 2006;16:2479-2483.
10. Ismail MA, Arafa RK, Wenzler T, Brun R, Tanious FA, Wilson WD, Boykin DW. Synthesis and antiprotozoal activity of novel bis-benzamidinoimidazo[1,2-*a*]pyridines and 5,6,7,8-tetrahydro-imidazo[1,2-*a*]pyridines. Bioorg Med Chem 2008;16:683-691.
11. Gudmundsson KS, Johns BA. Imidazo[1,2-*a*]pyridines with potent activity against herpesviruses. Bioorg Med Chem Lett 2007;17:2735-2739.
12. Maruyama Y, Anami K, Terasawa M, Goto K, Imayoshi T, Kadabe Y, Mizushima Y. Anti-inflammatory activity of an imidazopyridine derivative (miroprofen), Arzneimittelforsch 1981;31(7):1111-1115.
13. Abignente E, Carariis P, Fattorusso E, Mayol L. Research on heterocyclic compounds XXIII phenyl derivatives of fused imidazole systems. J Heterocylic Chem 1989;26:1875-1880.
14. Kaminski JJ, Wallmark B, Bruing C, Anderson BM. Antiulcer agents 5 Inhibition of gastric H+/K+-ATPase by substituted imidazo[1,2-*a*]pyridines and related analogs and its implication in modeling the high affinity potassium ion binding site of the gastric proton pump enzyme. J Med Chem 1991;34:533-541.
15. Hamdouchi C, Zhong B, Mendoza J, Collins E, Jaramillo C, De Diego JE, Robertson D, Spencer CD, Anderson BD, Watkins SA, Zhanga F, Brooks HB. Structure-based design of a new class of highly selective aminoimidazo[1,2-*a*]pyridine-based inhibitors of cyclin dependent kinases. Bioorg Med Chem Lett 2005;15:1943-1947.
16. Sanfilippo PJ, Urbanski M, Press JB, Pubinsky B, Moore JB. Synthesis of (aryloxy)alkylamines 2 novel imidazo-fused heterocycles with calcium channel blocking and local anesthetic activity. J Med Chem 1988;31(11):2221-2227.
17. Goodacre SC, Street LJ, Hallett DJ, Crawforth JM, Kelly S, Owens AP, Blackaby WP, Lewis RT, Stanley J, Smith AJ, Ferris P, Sohal B, Cook SM, Pike A, Brown N, Wafford KA, Marshall G, Astro JL, Atack JR. Imidazo[1,2-*a*]pyrimidines as functionally selective and orally bioavailable $GABA_A\alpha2/\alpha3$ binding site agonists for the treatment of anxiety disorders. J Med Chem 2006;49(1):35-38.

18. Denora N, Laquintana V, GiuseppinaPisu M, Dore R, Murru L, Latrofa A, Trapani G, Sanna E. 2-Phenyl-imidazo[1,2-*a*]pyridine compounds containing hydrophilic groups as potent and selective ligands for peripheral benzodiazepine receptors synthesis, binding affinity and electrophysiological studies. J Med Chem 2008;51:6876-6878.
19. Abe Y, Kayakiri H, Satoh S, Inoue T, Sawada Y, Imai K, Inamura N, Asano M, Hatori C, Katayama A, Oku T, Tanaka H. A novel class of orally active non-peptide bradykinin B_2 receptor antagonists 3 discovering bioisosteres of the imidazo[1,2-*a*]pyridine moiety. J Med Chem 1998;41:4062-4079.
20. Fukuyama T, Shinmen M, Nishitani S, Sato M, Rfu I. A copper-free sonogashira coupling reaction in ionic liquids and its application to a microflow system for efficient catalyst recycling.Org lett 2002;4(10):1691-1694.
21. Handy ST, Zhang X. Organic synthesis in ionic liquids the stille coupling. Org let 2002;3(2):233-236.