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Catalyst and Solvent Free Synthesis and Biological Activities of Imidazo[1,2-*a*]pyridine

Gangadhar B. Gundlewad[1,✉], S.S. Wagh[2] and Bhagwan. R. Patil[3]

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ABSTRACT

A series of imidazo[1,2-*a*]pyridines were synthesized by the reaction of α-chloroacetophenone and 2-aminopyridine under catalyst and solvent free condition. The synthesized compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. These imidazo[1,2-*a*]-pyridines were screened for anti-inflammatory activity by carrageenan induced rat hind paw edema model. Good anti-inflammatory activity was shown by few compounds. The antibacterial activity was studied against two Gram-positive bacteria *S. aureus* and *B. subtilis*, two Gram-negative bacteria *E. coli* and *S. typhi* and antifungal activity against *P. chrysogenum*, *F. moneliforme*, *A. flavus* and *A. niger*. All the synthesized compounds were desplayed good antimicrobial and antifungal activities. Some of the compounds were shown higher anti-bacterial activity than reference drug penicillin.

KEYWORDS

α-Chloroacetophenone, 2-Aminopyridine, Imidazo[1,2-*a*]pyridine, Anti-inflammatory activity, Antimicrobial activity.

INTRODUCTION

Imidazo[1,2-*a*]pyridine is an important nucleus, its derivatives has wide range of applications in medicinal [1], material science [2], organometallics [3], *etc*. Various clinical drugs like SCH28080, zolimidine, zolipdem, olprinone and alpidem contain imidazo[1,2-*a*]pyridine basic skeleton [4]. Imidazo[1,2-*a*] has been found to exhibit variety of biological activities like antipsychotic [5], anticancer [6], antitubercular [7], anti-inflammatory [8], anti-HIV [9], antifungal [10], anti-bacterial [11], antileishmanial [12]. In addition, it was proved that 2-(2-hydroxyphenyl)imidazo[1,2-*a*]pyridine exhibit excellent excited state intramolecular proton transfer [13], imidazo[1,2-*a*]-pyridine based radio ligands have been widely used for positron emission tomography (PET) [14].

The wide applicability of imidazo[1,2-*a*]pyridine, inspired researchers to develop number of methods for its synthesis. These methods involves condensation of 2-aminopyridine with ketone using various catalysts like CuI [15], $KHCO_3$ [16], ZnI_2 [17]. By the reaction of 2-aminopyridine, aldehyde and isocyanate catalyzed by $ZnCl_2$ [18], from 1,1,1-trifluoro-4-(phenylsul-fonyl)but-3-ene-2,2-diols and various 2-aminopyridines [19] oxidative coupling of ketoxime acetates with simple pyridines catalyzed by copper(I) [20], from aminopyridines and 2-methyl-nitroolefins [21], A^3-coupling of heterocyclic amidine with

Author affiliations:

[1]Department of Chemistry, Shri Shivaji College, Parbhani-431401, India
[2]Department of Chemistry, Adarsh Mahavidyalaya, Hingoli-431531, India
[3]Department of Chemistry, Sharda Mahavidyalaya, Parbhani-431401, India

✉To whom correspondence to be addressed:

E-mail: gbgundlewad@rediffmail.com

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aldehyde and alkyne [22] the condensation of *o*-hydroxyacetophenone with 2-aminopyridine [13]. The most common method involves the condensation of 2-aminopyridine with α-halocarbonyl compounds in presence of some catalyst [23-26].

Though these methods are effective, few of them have some disadvantages like, hazardous solvents, low yield, long reaction time, excess amount of catalyst, *etc*. which leaves some space to development new environmentally clean syntheses. The present paper report the synthesis of imidazo[1,2-*a*]pyridine from 2-aminopyridine and α-chloroacetophenone under catalyst and solvent free condition.

EXPERIMENTAL

Melting points were determined by open capillary methods & are uncorrected. The compounds were purified by column chromatography using silica gel (60-120 mesh) eluted with ethyl acetate-petroleum ether (1:3) as eluent. IR spectra were recorded using KBr pallet on 'Shimadzu' IR spectrophotometer. ^{1}H NMR & ^{13}C NMR were recorded on 'Avance-300' in DMSO-*d* & TMS as internal standard. Mass spectra were recorded in electron impact mode.

General procedure

Synthesis of imidazo[1,2-*a*]pyridine: The mixture of corresponding α-chloroacetophenone (1.0 mmol) and 2-aminopyridine (1.0 mmol) was stirred under vigorous magnetic stirring for specified time. The progress of reaction was monitored by TLC; the mixture turned to liquid state and finally solidifies as yellow mass. This was washed with ethyl acetate (3 × 10 mL) and the solvent was evaporated in vacuum to obtain crude solid product. It was further purified on silica gel column using ethyl acetate-petroleum ether (1:3) as eluent.

Anti-inflammatory activity: Carrageenan induced paw edema method [27] was used to perform anti-inflammatory activity studies in rat. The experiments were carried out as per guidelines of Institutional Animal Ethics Committee (Animal Ethics Committee AISSMS College of Pharmacy, Pune. Protocol No. CPCSEA/IAEC/OP-10/01-2K18). Edema was induced in the right hind paw of the male Wistar rats (100-150 g) by subplantar injection of 0.1 mL of freshly prepared 1% carrageenan. The animals were starved 12 h before experiment. The test compounds were administered orally as a suspension in 1% carboxyl methyl cellulose 0.5 h prior to carrageenan injection.

The animals were divided into 26 groups (n = 3).

Group 1 - served as control and given carrageenan (1% W/V in saline).

Group 2 - served as standard and received Diclofenac sodium (25 mg/kg p.o)

Group 3 to 26 - received the test compounds (100 and 200 mg/kg p.o), respectively.

The volume of paw edema was measured at 0.5, 1, 2, 3 and 5 h after above treatments using plethysmograph. The values for edema volume are as mean ± SEM of seven observations and ANOVA followed by post hoc test. The groups were compared by Dunnet test.

Antimicrobial activity: The agar cup method [28] was employed to study antibacterial activity. Sterile agar was seeded with turbid suspension of selected bacteria and poured in sterile Petri dish. With the help of sterile cork borer, cups of 10 mm diameter were made and 100 µL solution of test compound in DMF was added in the cup under septic condition. DMF and penicillin were used as negative and positive control, respectively. The plates were incubated for 24 h at 37 ºC. Zone of inhibition was recorded in millimeters using zone reader.

Antifungal activity: Poison plate method [29] was used to study antifungal activity using sterile potato dextrose agar as medium. The test samples were added to the sterile medium so as to get final concentration as 1%. DMF was used as negative control and gresiofulvin as positive control. The fungal suspension was spot inoculated on the plates prepared using compounds with the help of nicrome wire loop. The plates were incubated at room temperature for 48 h.

Incubated plates were observed for the growth of inoculated fungi. Results were noted as growth of fungi (no antifungal activity), reduced growth of fungi (moderate antifungal activity) and no growth of fungi (antifungal activity).

RESULTS AND DISCUSSION

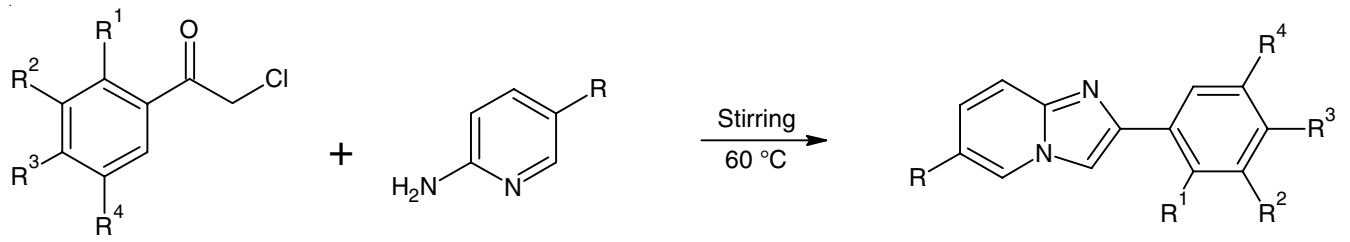
In present study, a new series of imidazo[1,2-*a*]pyridine was synthesized (**Scheme-I**). The mixture of α-chloroacetophenone and 2-aminopyridine (1:1) in solid state was stirred vigorously for 20-40 min at 60 ºC, the mixture was turned to liquid state during the process of stirring, finally solidified to a light yellow solid mass. This crude product was purified by column chromatography and characterized by spectral data. In IR spectra shows the absorption band between 1620-1635 cm^{-1} for C=N stretching in imidazole ring; 1600-1420 cm^{-1} for C=C stretching. In ^{1}H NMR spectra, singlet between δ 7.88-7.40 corresponds to hydrogen on imidazole ring. ^{13}C NMR spectra shows bands at δ 111, δ 140 and δ 145 ppm corresponds to C_3, C_2 and C_9, respectively. The results obtained from mass spectral analysis were in accordance to their molecular weight.

Spectral data

2-(*H*-Imidazo[1,2-*a*]pyridin-2-yl)-4-iodo-6-methylphenol (3a): m.f.: $C_{14}H_{11}N_2OI$: yield: 78%; m.p.: 175 °C; IR (KBr, ν_{max}, cm^{-1}): 3390 (-OH *str.*), 3012 (Ar-H *str.*), 1563 (C=N *str.*), 1615, 1470 (C=C *str.*), 1298 (C-N *str.*); ^{1}H NMR (DMSO-d_6): δ 13.15 (s, 1H), 8.62 (s, 1H), 8.40 (d, 1H), 8.07 (d, 1H), 7.81 (s, 1H), 7.73 (t, 1H), 7.49 (s, 1H), 7.22 (t, 1H), 2.32 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 161.12, 150.83, 142.84, 141.09, 136.16, 135.28, 131.88, 127.72, 127.29, 118.65, 112.49, 110.59, 102.11, 26.15; mass *m/z* 350 M$^+$.

2-(*H*-Imidazo[1,2-*a*]pyridin-2-yl)-6-iodo-4-methylphenol (3b): m.f.: $C_{14}H_{11}N_2OI$; yield: 75%; m.p.: 162 °C; IR (KBr, ν_{max}, cm^{-1}): 3430 (-OH *str.*), 3022 (Ar-H *str.*), 1564 (C=N *str.*), 1612, 1475 (C=C *str.*), 1290 (C-N *str.*); ^{1}H NMR (DMSO-d_6): δ 12.15 (s, 1H), 8.67 (s, 1H), 8.42 (d, 1H), 8.04 (d, 1H), 7.80 (s, 1H), 7.73 (t, 1H), 7.50 (s, 1H), 7.22 (t, 1H), 2.31 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 165.07, 151.83, 142.94, 140.99, 136.26, 135.18, 131.84, 127.92, 128.19, 118.60, 112.19, 110.49, 102.91, 25.15; mass *m/z* 350 M$^+$.

6-(*H*-Imidazo[1,2-*a*]pyridin-2-yl)-2,4-diiodo-3-methylphenol (3c): m.f.: $C_{14}H_{10}N_2OI_2$; yield: 77%; m.p.: 145 °C; IR (KBr, ν_{max}, cm^{-1}): 3420 (-OH *str.*), 3020 (Ar-H *str.*), 1574 (C=N *str.*), 1610, 1480 (C=C *str.*), 1295 (C-N *str.*); ^{1}H NMR (DMSO-



Compd.	R	R^1	R^2	R^3	R^4	Time (min)	Compd.	R	R^1	R^2	R^3	R^4	Time (min)
3a	H	OH	CH_3	H	I	30	**3g**	CH_3	OH	CH_3	H	I	20
3b	H	OH	I	H	CH_3	30	**3h**	CH_3	OH	I	H	CH_3	25
3c	H	OH	I	CH_3	I	30	**3i**	CH_3	OH	I	CH_3	I	20
3d	H	H	I	Br	H	45	**3j**	CH_3	H	I	Br	H	35
3e	H	H	I	Cl	H	50	**3k**	CH_3	H	I	Cl	H	40
3f	H	Cl	I	Cl	H	60	**3l**	CH_3	Cl	I	Cl	H	40

Scheme-I

d_6): δ 12.12 (s, 1H), 8.77 (s, 1H), 8.32 (d, 1H), 7.94 (d, 1H), 7.83 (s, 1H), 7.73 (t, 1H), 7.60 (s, 1H), 7.29 (t, 1H), 2.35 (s, 3H). ^{13}C NMR (DMSO-*d_6*): δ 164.52, 150.83, 143.04, 141.09, 136.16, 134.98, 132.24, 128.12, 128.10, 118.80, 112.12, 105.42, 100.91, 25.25; mass *m/z* 476 M^+.

2-(4-Bromo-3-iodophenyl)*H*-imidazo[1,2-*a*]pyridine (3d): m.f.: $C_{13}H_8N_2BrI$; yield: 72%; m.p.: 120 °C; IR (KBr, ν_{max}, cm^{-1}): 3023 (Ar-H *str.*), 1584 (C=N *str.*), 1615, 1488 (C=C *str.*), 1315 (C-N *str.*); ^{1}H NMR (DMSO-*d_6*): δ 8.85 (d, 1H), 8.81 (s, 1H), 7.7-7.9 (m, 5H), 7.42 (s, 1H); ^{13}C NMR (DMSO-*d_6*): δ 153.83, 144.04, 140.59, 135.76, 135.08, 132.84, 131.96, 128.82, 127.90, 118.87, 112.32, 111.42, 101.91; mass *m/z* 398 M^+.

2-(4-Chloro-3-iodophenyl)*H*-imidazo[1,2-*a*]pyridine (3e): m.f.: $C_{13}H_8N_2ClI$; yield: 71%; m.p.: 130 ºC; IR (KBr, ν_{max}, cm^{-1}): 3090 (Ar-H *str.*), 1634 (C=N *str.*), 1615, 1489 (C=C *str.*), 1319(C-N *str.*) 826 (C-Cl *str.*); ^{1}H NMR (DMSO-*d_6*): δ 8.77 (d, 1H), 8.75 (s, 1H), 8.30 (d, 1H), 7.92 (d, 1H), 7.88 (d, 1H), 7.70 (t, 1H), 7.52 (*s*, 1H), 7.29 (t, 1H). ^{13}C NMR (DMSO-*d_6*): δ 153.12, 142.57, 138.23, 135.92, 133.42, 131.23, 129.90, 129.14, 127.90, 127.50, 116.23, 111.21, 99.70; mass *m/z* 354 M^+.

2-(2,4-Dichloro-3-iodophenyl)*H*-imidazo[1,2-*a*]pyridine (3f): m.f.: $C_{13}H_8N_2ClI$; yield: 70%; m.p.: 154 °C; IR (KBr, ν_{max}, cm^{-1}): 3080 (Ar-H *str.*), 1624 (C=N *str.*), 1613, 1484 (C=C *str.*), 1315(C-N *str.*) 827 (C-Cl *str.*); ^{1}H NMR (DMSO-*d_6*): δ 8.76 (d, 1H), 8.65 (d, 1H), 8.20 (d, 1H), 7.92 (d, 1H), 7.70 (t, 1H), 7.49 (s, 1H), 7.29 (t, 1H). ^{13}C NMR (DMSO-*d_6*): δ 153.12, 142.57, 140.23, 135.92, 133.42, 131.23, 129.90, 129.14, 127.90, 127.50, 116.23, 111.21, 99.70; mass *m/z* 389 M^+.

4-Iodo-2-methyl-6-(6-methyl-*H*-imidazo[1,2-*a*]pyridin-2-yl)phenol (3g): m.f.: $C_{15}H_{13}N_2OI$; yield: 80%; m.p.: 164 °C; IR (KBr, ν_{max}, cm^{-1}): 3340 (-OH *str.*), 3014 (Ar-H *str.*), 1560 (C=N *str.*), 1610, 1465 (C=C *str.*), 1290 (C-N *str.*); ^{1}H NMR (DMSO-*d_6*): δ 13.25 (s, 1H), 8.62 (s, 1H), 8.42 (d, 1H), 8.05 (d, 1H), 7.80 (s, 1H), 7.75 (t, 1H), 7.48 (s, 1H), 7.21 (t, 1H), 2.39 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (DMSO-*d_6*): δ 163.95, 151.83, 142.84, 139.09, 136.06, 134.28, 130.88, 127.02, 126.29, 118.65, 112.49, 110.59, 101.11, 35.15, 27.15; mass *m/z* 364 M^+.

2-Iodo-4-methyl-6-(6-methyl-*H*-imidazo[1,2-*a*]pyridin-2-yl)phenol (3h): m.f.: $C_{15}H_{13}N_2OI$; yield: 75%; m.p.: 165 °C; IR (KBr, ν_{max}, cm^{-1}): 3340 (-OH *str.*), 3014 (Ar-H *str.*), 1560 (C=N *str.*), 1610, 1465 (C=C *str.*), 1290 (C-N *str.*); ^{1}H NMR (DMSO-*d_6*): δ 13.22 (s, 1H), 8.63 (s, 1H), 8.40 (d, 1H), 8.09 (d, 1H), 7.82 (s, 1H), 7.76 (t, 1H), 7.46 (s, 1H), 7.22 (t, 1H), 2.37 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (DMSO-*d_6*): δ 165.32, 150.83, 141.84, 139.19, 136.26, 134.38, 130.80, 127.22, 126.69, 118.62, 112.50, 110.49, 101.01, 35.25, 27.19; mass *m/z* 364 M^+.

2,4-Diiodo-3-methyl-6-(6-methyl-*H*-imidazo[1,2-*a*]-pyridin-2-yl)phenol (3i): m.f.: $C_{15}H_{12}N_2OI_2$; yield: 78%; m.p.: 177 °C; IR (KBr, ν_{max}, cm^{-1}): 3425 (-OH *str.*), 3022 (Ar-H *str.*), 1570 (C=N *str.*), 1611, 1483 (C=C *str.*), 1285 (C-N *str.*); ^{1}H NMR (DMSO-*d_6*): δ 14.12 (s, 1H), 8.87 (s, 1H), 8.42 (d, 1H), 7.91 (d, 1H), 7.81 (s, 1H), 7.75 (t, 1H), 7.61 (s, 1H), 7.22 (t, 1H), 3.15 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (DMSO-*d_6*): δ 164.02, 150.23, 142.94, 141.04, 136.26, 134.92, 132.20, 129.12, 128.10, 118.90, 111.12, 103.42, 100.91, 31.25, 22.25; mass *m/z* 489 M^+.

2-(4-Bromo-3-iodophenyl)-6-methyl-*H*-imidazo[1,2-*a*]-pyridine (3j): m.f.: $C_{14}H_{10}N_2BrI$; yield: 75%; m.p.: 136 °C; IR (KBr, ν_{max}, cm^{-1}): 3023 (Ar-H *str.*), 1584 (C=N *str.*), 1615, 1488 (C=C *str.*), 1315 (C-N *str.*); ^{1}H NMR (DMSO-*d_6*): δ 8.88 (*d,* 1H), 8.81 (*s,* 1H), 7.7-7.9 (*m,* 5H), 7.45 (*s,* 1H), 3.15 (*s*, 3H). ^{13}C NMR (DMSO-*d_6*): δ 153.73, 144.14, 140.19, 136.76, 135.38, 132.94, 131.96, 128.92, 127.90, 118.87, 112.52, 111.42, 103.91, 31.35; Mass *m/z* 413 M^+.

2-(4-Chloro-3-iodophenyl)-6-methyl-*H*-imidazo[1,2-*a*]-pyridine (3k): m.f.: $C_{14}H_{10}N_2ClI$; yield: 72%; m.p.: 152 °C; IR (KBr, ν_{max}, cm^{-1}): 3070 (Ar-H *str.*), 1639 (C=N *str.*), 1619, 1487 (C=C *str.*), 1339(C-N *str.*) 828 (C-Cl *str.*); ^{1}H NMR (DMSO-*d_6*): δ 8.77 (d, 1H), 8.71 (s, 1H), 8.31 (d, 1H), 7.91 (d, 1H), 7.85 (d, 1H), 7.71 (t, 1H), 7.52 (s, 1H), 7.39 (t, 1H), 3.17 (s, 3H). ^{13}C NMR (DMSO-*d_6*): δ 153.14, 142.52, 138.21, 135.95, 133.40, 131.21, 129.94 129.14, 127.90, 127.55, 116.23, 111.22, 99.70, 30.25; mass *m/z* 368 M^+.

2-(2,4-Dichloro-3-iodophenyl)-6-methyl-*H*-imidazo-[1,2-*a*]pyridine (3l): m.f.: $C_{14}H_9N_2Cl_2I$; yield: 74%; m.p.: 139 °C; IR (KBr, ν_{max}, cm^{-1}): 3040 (Ar-H *str.*), 1622 (C=N *str.*),

TABLE-1
ANTI-INFLAMMATORY ACTIVITY OF IMIDAZO[1,2-*a*]PYRIDINES

Compound	Dose (mg/kg)	0.5#	1 h#	2 h#	3 h#	5 h#
Control		1.53±0.26	1.70±0.09	1.82±0.09	1.78±0.16	1.77±0.15
3a	100	1.39±0.21 (09.10%)	1.60±0.12** (05.88%)	1.65±0.11* (09.34%)	1.67±0.18* (06.10%)	1.67±0.21 (05.64%)
	200	1.37±0.09 (10.44%)	1.55±0.22 (08.82%)	1.67±0.13 (08.21%)	1.70±0.31 (04.08%)	1.65±0.15 (06.77%)
3b	100	1.32±0.19 (13.71%)	1.51±0.19 (11.17%)	1.60±0.21* (12.08%)	1.56±0.12 (12.35%)	1.51±0.31 (14.68%)
	200	1.21±0.18 (20.91%)	1.28±0.16 (24.70%)	1.37±0.26** (24.72%)	1.59±0.29** (10.67%)	1.52±0.32 (14.12%)
3c	100	1.37±0.31 (10.45%)	1.47±0.21 (13.52%)	1.64±0.27* (09.89%)	1.59±0.19** (10.67%)	1.47±0.22 (16.94%)
	200	1.42±0.29 (07.18%)	1.64±0.31 (03.50%)	1.73±0.21* (04.94%)	1.61±0.19 (09.55%)	1.53±0.18(13.55.74%)
3d	100	1.49±0.31 (02.6%)	1.68±0.17 (01.17%)	1.82±0.13** (00.00%)	1.75±0.16** (01.68%)	1.68±0.02 (05.08%)
	200	1.44±0.07 (05.88%)	1.65±0.15 (02.94%)	1.76±0.19 (04.90%)	1.7±0.14 (00.56%)	1.72±0.06 (02.82%)
3e	100	1.49±0.31 (02.6%)	1.68±0.17* (01.17%)	1.82±0.13** (00.00%)	1.75±0.26* (01.68%)	1.71±0.02 (03.38%)
	200	1.47±0.69 (03.92%)	1.63±0.43** (04.11%)	1.77±0.59** (02.74%)	1.75±0.55* (01.68%)	1.76±0.27 (00.50%)
3f	100	1.43±0.41 (06.53%)	1.70±0.36* (00.00%)	1.73±0.39 (04.94%)	1.78±0.29 (00.00%)	1.68±0.18 (05.08%)
	200	1.37±0.39 (10.45%)	1.54±0.22 (09.41%)	1.73±0.19** (04.94%)	1.69±0.42** (05.05%)	1.53±0.38 (13.55%)
3g	100	1.21±0.13 (20.91%)	1.31±0.31 (22.94%)	1.53±0.03* (15.93%)	1.42±0.28* (20.22%)	1.25±0.11 (29.37%)
	200	1.19±0.23 (22.22%)	1.32±0.13 (22.35%)	1.43±0.23* (21.42%)	1.50±0.18* (15.73%)	1.45±0.21 (18.05%)
3h	100	1.20±0.33 (21.56%)	1.21±0.23 (28.82%)	1.23±0.37 (32.41%)	1.51±0.13***(15.16%)	1.48±0.23** (16.38%)
	200	1.13±0.23 (26.14%)	1.03±0.32 (39.41%)	1.35±0.23 (25.82%)	1.38±0.21** (22.47%)	1.36±0.19** (23.16%)
3i	100	1.38±0.26 (09.80%)	1.55±0.15 (08.82%)	1.54±0.12* (15.38%)	1.49±0.15 (16.29%)	1.42±0.14 (19.77%)
	200	1.29±0.13 (15.68%)	1.39±0.11 (18023%)	1.55±0.19 (14.83%)	1.63±0.17** (08.42%)	1.53±0.23 (13.55%)
3j	100	1.16±0.23 (24.18%)	1.35±0.16* (20.58%)	1.39±0.03* (23.62%)	1.40±0.23* (21.34%)	1.27±0.02 (28.24%)
	200	0.97±0.16 (36.60%)	1.23±0.27* (27.64%)	1.26±0.12* (30.76%)	1.19±0.22** (33.14%)	1.09±0.12 (38.41%)
3k	100	1.37±0.18 (10.45%)	1.42±0.16 (16.47%)	1.62±0.34* (10.98%)	1.71±0.17** (03.93%)	1.55±0.18 (12.42%)
	200	1.28±0.24 (16.33%)	1.33±0.19 (21.76%)	1.42±0.21 (21.97%)	1.63±0.01* (08.42%)	1.51±0.23 (14.68%)
3l	100	1.32±0.16 (13.72%)	1.43±0.19 (15.88%)	1.52±0.13 (16.48%)	1.57±0.15* (11.79%)	1.42±0.18 (19.77%)
	200	1.27±0.22 (16.99%)	1.42±0.11* (16.47%)	1.63±0.18* (10.43%)	1.32±0.21* (25.84%)	1.30±0.19 (26.55%)
Diclofenac	25	1.25±0.31 (18.30%)	1.04±0.32 (38.82%)	1.00±0.2 (95.32%)	1.52±0.096 (37.08%)	1.7±0.34 (03.95%)

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$; #Mean ± SEM (% REV)

1623, 1481 (C=C *str.*), 1335 (C-N *str.*) 829 (C-Cl *str.*); ^{1}H NMR (DMSO-d_6): δ 8.74 (d, 1H), 8.64 (d, 1H), 8.21 (d, 1H), 7.91 (d, 1H), 7.70 (t, 1H), 7.49 (s, 1H), 7.29 (t, 1H), 3.17 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 153.12, 142.57, 140.23, 135.92, 133.42, 131.23, 129.90, 129.14, 127.90, 127.50, 116.23, 111.21, 99.70, 30.25; mass *m/z* 403 M^+.

Anti-inflammatory activity: All the synthesized compounds were screened for anti-inflammatory activity by carrageenan induced rat hid paw edema method using diclofenac as standard. The values of paw edema are given as Mean ± SEM of seven observations and ANOVA followed by post hoc test. Dunnet test was used to compare the groups and the percentage protection (or inhibition) was calculated by using the formula:

$$\text{Protection } (\%) = \left(1 - \frac{V_t}{V_c}\right) \times 100$$

V_t = increase the paw volume in the test animal; V_c = increase the paw volume in the control group.

Result obtained from antiinflammatory studies (Table-1) revealed that compounds **3b**, **3g**, **3h**, **3j**, **3k** were shown good activity at 100 mg/kg as well as 200 mg/kg body weght dose while **3f** and **3l** were desplayed more activity at 200 mg/kg body weight dose. It was observerd that compounds with hydroxy and methyl substituents has higher anti-inflammatory activity than other compounds of the series.

Antimicrobial activity: The antimicrobial activity was assessed *in vitro* against two Gram-positive bacteria *S. aureus* and *B. subtilis*, two Gram-negative bacteria *E. coli* and *S. typhi* by disc dufussion method (Table-2) and antifungal activity against *P. chrysogenum*, *F. moneliforme*, *A. flavus* and *A. niger* using poison plate (Table-3). Compounds **3d**, **3e**, **3f** and **3g** displayed good antibacterial activity and it was clear that compounds having halogen substituents show good antibacterial activities. All the compounds exhibited good antifungal activity.

TABLE-2
ANTIBACTERIAL ACTIVITY OF IMIDAZO[1,2-*a*]PYRIDINES

Compound	Zone of inhibition (mm)			
	E. coli	*S. typhi*	*S. aureus*	*B. subtilis*
3a	15	17	28	31
3b	16	18	31	29
3c	15	16	25	23
3d	20	14	30	22
3e	32	30	45	12
3f	25	23	40	32
3g	20	14	36	12
3h	16	13	22	23
3i	12	14	24	12
3j	14	16	22	19
3k	11	12	21	18
3l	15	13	20	19
DMSO	-ve	-ve	-ve	-ve
Penicillin	14	14	34	22

Conclusion

A series of imidazo[1,2-*a*]pyridine was synthesized under catalyst and solvent free condition and evaluated for anti-inflammatory and antimicrobial activities. It was observerd that compounds exhibited good anti-inflammatory activity,

TABLE-3
ANTIFUNGAL ACTIVITY OF IMIDAZO[1,2-*a*]PYRIDINES

Comp.	*P. chrysogenum*	*F. moneliforme*	*A. flavus*	*A. niger*
3a	-ve	-ve	-ve	-ve
3b	-ve	-ve	-ve	-ve
3c	-ve	-ve	-ve	-ve
3d	-ve	-ve	-ve	-ve
3e	-ve	-ve	-ve	-ve
3f	-ve	-ve	-ve	-ve
3g	-ve	-ve	-ve	-ve
3h	-ve	-ve	-ve	-ve
3i	-ve	-ve	-ve	-ve
3j	-ve	-ve	-ve	-ve
3k	-ve	-ve	-ve	-ve
3l	-ve	-ve	-ve	-ve
DMSO	+ve	+ve	+ve	+ve
Griseofulvin	-ve s	-ve	-ve	-ve

- ve = No growth of fungi (antifungal activity present); RG = Reduced growth (more than 50% reduction in growth); + ve = Growth of fungi (antifungal activity absent).

compounds with hydroxy and methyl substituents has higher anti-inflammatory activity. All the compounds were exhibited good antibacterial as well as antifungal activity.

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