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Synthesis of novel *N*,*N*-dimethyl-1-(5-methyl-2-arylimidazo[1,2-*a*]pyridin-3-yl) methanamine derivatives as potential antimicrobial agents

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The title compounds *N*,*N*-dimethyl-1-(5-methyl-2-arylimidazo[1,2-*a*]pyridin-3-yl)methanamines have been synthesized by reaction of α-haloketones with 6-methylpyridin-2-amine followed by a series of multistep reactions giving the targeted compounds **(4a-l)**. All the synthesized compounds have been screened for their *in vitro* antibacterial activity against *E. coli*, *S. aureus*, *P. aeruginosa*, *S. pyogenes* and antifungal activity against *C. albicans*, *A. niger* and *A. clavatus*. The structures of the synthesized compounds have been confirmed by spectral data IR, ^{1}H and ^{13}C NMR and mass spectra. Investigation of antimicrobial activity reveals that the compounds **4b**, **4c**, **4d**, **4e** and **4j** show significant activities against tested organisms as compared to standard drugs like ampicillin and griseofulvin.

Keywords: Imidazo[1,2-*a*]pyridine, phenacyl bromides, antibacterial activity, antifungal activity, SAR study, MIC

Among the nitrogen heterocycles, imidazo[1,2-*a*] pyridine skeleton represents an important class of organic molecules that attract the interest of both synthetic and medicinal chemists, which have been shown to possess a wide range of useful pharmacological properties[1]. Imidazo[1,2-*a*]pyridine ring system have been shown to possess useful biological activities, such as antibacterial[2], antiviral[3,4], anti-inflammatory[5], antiulcer[6], antifungal[7], analgesic[8] and anti-HIV[9] activities. This imidazo[1,2-*a*]pyridine skeleton also exhibits some unusual disease resistance activity like antiprotozoal[10], antiherpes[11] and treatment of hepatitis C[12]. In addition, this scaffold is present in a large number of compounds showing a variety of therapeutic properties such as agonist of benzodiazepine receptor and GABA[13], melatonin receptor ligands[14], β-amyloid formation inhibitor[15] and cardiotonic agents[16]. Indeed, the Mannich base encompassing bridged *N*-atom revealed diverse pharmacological action like antimicrobial[17], antimalarial[18] and anticancer[19].

It can be further considered that imidazopyridines are the major class of non-benzodiazepines, acting upon various central nervous systems (CNS) disorders. Several drugs like Alpidem (anxiolytic)[20], Zolimidine (antiulcer)[21], Olprinone (PDE-3 inhibitor or cardiotonic agent)[22], Necopidem (sedative and anxiolytic) and Zolpidem (hypnotic drug)[23] containing imidazo[1,2-*a*]pyridine nucleus are currently in the market. Alpidem and Zolpidem, have both proved higher affinity for benzodiazepine-1 than for benzodiazepine-2 receptors and their interaction with numerous receptors have been reported.

For the purpose of preliminary structure activity relationship studies (SAR), the structures of newly synthesized final compounds had resemblance with available pharmaceutical drugs like Zolpidem. Encouraged by the above mentioned findings, and our previous work for antimicrobial agents[24-26], we anticipated that the synthesized compounds would show higher *in vitro* antimicrobial activity against different strains of bacteria and fungi like *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes*, *Candida albicans*, *Asperigillus niger* and *Asperigillus clavatus* (Figure 1).

Results and Discussion

Initially various derivatives of phenacyl bromides **2a-l** were prepared by the bromination of acetophenones using anhydrous $AlCl_3$ in catalytic amount. 5-Methyl-2-arylimidazo[1,2-*a*]pyridines **3a-l** were synthesized by the reaction of 6-methyl-2-amino pyridine **1** and substituted phenacyl bromides **2a-l** in 3 h at 60-70°C. The targeted molecule *N*,*N*-dimethyl-1-(5-methyl-2-arylimidazo[1,2-*a*]pyridin-3-yl)

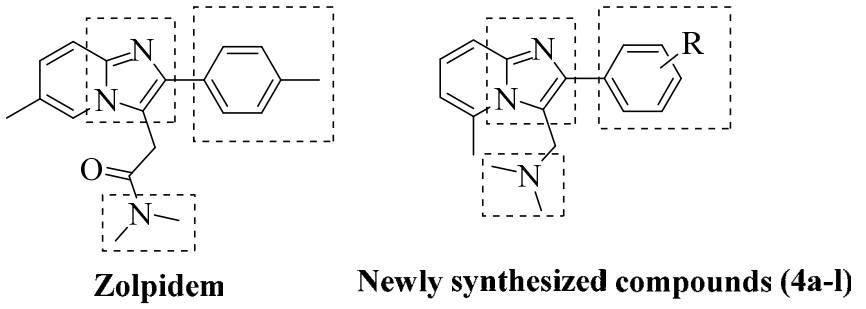
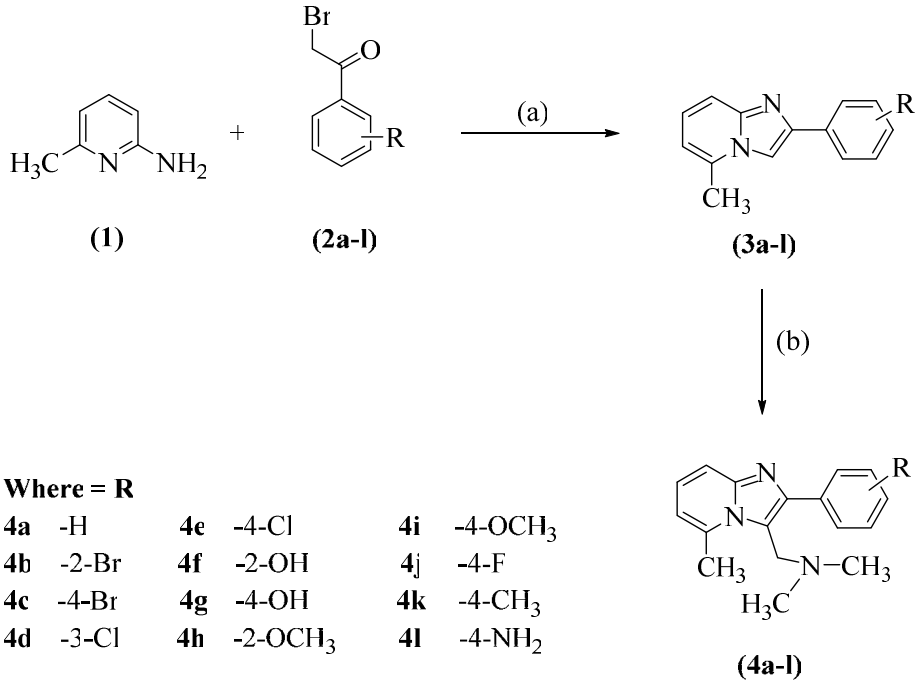


Figure 1 — Structural correlation of marketed drug and newly synthesized compounds



(a) Ethanol, 60-70° C, 3 h; (b) $(CH_3)_2NH$, $(HCHO)_n$, HCl, Toluene, 80-90° C, 3-5 h.

Scheme I — Synthetic pathway of imidazo[1,2-*a*]pyridine derivatives

methanamines **4a-l** were obtained by performing Mannich reaction on 5-methyl-2-arylimidazo[1,2-*a*]pyridines **3a-l** with formaldehyde, dimethyl amine and 50% con HCl at 80-90°C for 3-5 h in toluene as a solvent (Scheme I).

All the newly synthesized compounds were characterized by using IR, ^{1}H and ^{13}C NMR, and mass spectra. IR spectrum of title compound **4j** (molecular formula $C_{17}H_{18}N_3F$) has given stretching vibration at 2975 cm^{-1}, which showed strong peak corresponding to -N$(CH_3)_2$. The intense absorption peaks at 2804 and 2727 cm^{-1} were obtained due to -CH_2- and -CH_3 group respectively. Compound **4j** showed characteristic peak at 1123 cm^{-1} assignable to C-F bond. From the ^{1}H NMR spectrum, the structure of compound **4j** was confirmed by the appearance of singlet signal at δ 2.56 for -CH_2 group on imidazo[1,2-*a*]pyridine ring system. Methyl groups of Ar-CH_3 and -CH_2-N$(CH_3)_2$ proved its appearance as singlet peaks at δ 1.85 and 3.44. Meanwhile, ^{13}C NMR spectrum showed signals at δ 21.3, 46.6, 57.7, 116.0, 117.3, 117.5, 122.1, 128.7, 130.6, 134.8, 139.8, 144.8, 145.5, 162.9 (aromatic) and mass spectrum authenticated the molecular formula of compound **4j** by displaying a molecular ion peak at *m/z* 283.15 (M^+).

Amongst the synthesized compounds **4a-l**, many of them had proven their antimicrobial potency which

varies from good to excellent. From antibacterial activity results (Table I), it was observed that compounds **4c** (-4-Br) and **4d** (-3-Cl) possess very good activity against *E. coli*. Further, replacement of hydrogen in **4a** by 4-Cl and 4-F groups gave **4e** and **4j** compounds respectively, which possessed excellent activity against *E. coli*. It was observed that halogen containing compounds are highly active against *E. coli*. It is noteworthy that compounds **4c** (-4-Br), **4d** (−3-Cl) and **4b** (-2-Br), **4e** (-4-Cl) possess good to very good activity against *P. aeruginosa*, respectively. It is observed that if in **4a** the fourth position on phenyl ring is replaced with fluorine atom, the activity is amplified and shows highest inhibition at MIC = 25 μg mL^{-1} against *P. aeruginosa*. Moreover compounds **4d** (-3-Cl), **4e** (-4-Cl) and **4j** (-4-F) possess very good activities against *S. aureus* and substitution of bromo group at *ortho* and *para* positions enhance activity to the MIC = 25 μg mL^{-1} against *S. aureus*. Further, compound **4c** (-4-Br) has shown very good MIC value (50 μg mL^{-1}) against *S. pyogenes* while substitution applied in the form of -Cl and -F groups gave **4e** and **4j** compounds respectively, which possessed excellent activities (25 μg mL^{-1} and 12.5 μg mL^{-1} respectively) against *S. pyogenes*.

From the antifungal activity it is seen that compound **4d** (-3-Cl) influenced very good activity against *C. albicans*. Excellent activity at MIC = 100 μg mL^{-1} against *C. albicans* is shown by 4-Cl (**4e**) and 4-F (**4j**) derivatives. Compound **4c** exhibited activity similar to that of the standard drug griseofulvin (MIC 500 μg mL^{-1}) against *C. albicans*. Another fungi, *A. niger* was employed to check the activity of the series of compounds synthesized. Compounds **4c** (-4-Br) and **4e** (-4-Cl) show good activity against *A. niger* and when we apply derivatization on **4a** by 3-Cl and 4-F substituents, the activity is improved, and it has furnished excellent activity against *A. niger*. Furthermore, compound **4c** (-4-Br) possesses very good activity against *A. clavatus* and excellent activity against *A. clavatus* is shown by compounds **4d** (-3-Cl) and **4j** (-4-F) as compared to other compounds.

Structure-activity relationship

SAR study helped in enlightening the effect of different substitutions and their electronic effect on various microbial strains. From the results of antimicrobial activity data it may be concluded that the substitution pattern on the phenyl ring and lipophilic profile of the compounds affected the antibacterial as well as antifungal activities. Compounds having electron-withdrawing groups like -F, -Cl and -Br exhibited superior activity as compare to the compounds with electron-donating

Table I — Antimicrobial screening of the compounds **4a-l**

Compd	-R	Minimum inhibitory concentrations for bacteria (MIC) in μg mL^{-1}				Minimum inhibitory concentrations for fungi (MIC) in μg mL^{-1}		
		Gram-negative		Gram-positive		Fungi		
		E. coli	*P. aeruginosa*	*S. aureus*	*S. pyogenes*	*C. albicans*	*A. niger*	*A. clavatus*
4a	-H	250± 1.15^{c}	500± 2.35^{a}	500± 2.21^{c}	500±2.63^{b}	1000± 2.75	500± 1.33^{a}	500± 4.08^{c}
4b	-2-Br	250± 0.78^{b}	50± 1.45^{b}	25± 3.12^{a}	250± 2.75^{b}	1000± 3.66	500± 3.15^{a}	250± 3.68^{b}
4c	-4-Br	50± 2.45^{c}	100± 1.34^{b}	25± 1.12^{a}	50± 1.66^{b}	500± 0.89^{c}	100± 2.11^{c}	100± 2.10^{c}
4d	-3-Cl	50± 1.45^{b}	100± 2.23^{b}	100± 2.22^{a}	250± 3.26^{c}	250± 2.89^{b}	50± 3.08^{b}	50± 1.19^{b}
4e	-4-Cl	12.5± 1.56^{c}	50± 1.19^{c}	100± 2.11^{b}	25± 1.83^{b}	100± 2.23^{c}	100± 1.44^{b}	250± 2.38^{a}
4f	-2-OH	500± 3.15^{a}	1000± 3.26	1000± 1.35	500± 4.30^{a}	1000± 1.02	500± 2.25^{b}	500± 3.78^{b}
4g	-4-OH	250± 2.78^{b}	250± 2.85^{b}	1000± 2.35	250± 3.04^{b}	1000± 1.62	250± 1.02^{b}	250± 2.66^{a}
4h	-2-OCH_3	500± 2.78^{a}	500± 2.15^{b}	500± 2.17^{c}	500± 3.57^{a}	1000± 3.45	500± 3.03^{a}	1000± 2.12
4i	-4-OCH_3	500± 2.25^{a}	500± 1.78^{b}	1000± 1.42	250± 4.15^{b}	1000± 2.78	250± 2.82^{a}	500± 2.76^{a}
4j	-4-F	25± 3.12^{b}	25± 0.85^{c}	100± 2.59^{c}	12.5± 1.00^{b}	100± 1.12^{b}	25± 1.10^{b}	50± 2.35^{c}
4k	-4-CH_3	250± 3.47^{b}	250± 0.99^{c}	250± 3.56^{a}	500± 2.35^{b}	1000± 2.44	250± 1.48^{b}	500± 1.12^{b}
4l	-4-NH_2	250± 3.34^{c}	500± 2.95^{b}	1000± 1.47	250± 2.09^{b}	1000± 1.21	500± 3.44^{a}	250± 1.08^{a}
Ampicillin		100± 2.15	100± 0.98	250± 1.52	100± 2.08	–	–	–
Griseofulvin		–	–	–	–	500± 0.58	100± 1.16	100± 1.10

All values are presented as mean of six experiments (n = 6). All significant differences are considered from control value (0.00).
±SD standard deviation ^{a} P<0.05 significant, ^{b} P<0.01 moderately significant, ^{c} P<0.001 extremely significant
Escherichia coli MTCC 443; *Pseudomonas aeruginosa* MTCC 1688, *Staphylococcus aureus* MTCC 96; *Staphylococcus pyogenes* MTCC 442; *Candida albicans* MTCC 227; *Aspergillus niger* MTCC 282; *Aspergillus clavatus* MTCC 1323.

groups like -OH, -NH_2, -CH_3 and -OCH_3. Compounds **4c**, **4d**, **4e** and **4j** possessing halogen groups show excellent activity against the bacterial and fungal strains. It is also observed that the compounds **4f**, **4g, 4k** and **4l** possessing strongly activating groups and compounds **4h** and **4i** possessing moderately activating groups display poor activity against all type of microbial strains. SAR study also revealed that the presence of fluorine substitution at *para* position in the phenyl ring has induced the antimicrobial potency to an excellent level across the panel of gram-positive, gram-negative and fungal strains. Overall, the presence of electron-withdrawing groups like -F, -Cl and -Br in the heterocyclic skeletons is responsible for the increase in the antimicrobial influence.

Biological assay

Antimicrobial assay

The newly synthesized compounds **4a-l** have been screened for their antibacterial activity against Gram-negative bacteria *E. coli* (MTCC-443), *P. aeruginosa* (MTCC-1688) and Gram-positive *S. aureus* (MTCC-96), *S. pyogenes* (MTCC-442). All MTCC cultures were collected from the Institute of Microbial Technology, Chandigarh. Antibacterial activity was carried out by serial broth dilution method[27-29]. The standard strains used for the antimicrobial activity were procured from Institute of Microbial Technology, Chandigarh. The drugs which were found to be active in primary screening were similarly diluted to obtain 100, 50, 25, 12.5 µg mL^{-1} concentrations. 10 µg mL^{-1} suspensions were further inoculated on appropriate media and growth was noted after 24 and 48 h. The lowest concentration preventing appearance of turbidity was considered as minimum inhibitory concentration (MIC, µg mL^{-1}) *i.e.*, the amount of growth from the control tube before incubation (which represents the original inoculum) was compared. A set of tubes containing only seeded broth and solvent controls were maintained under identical conditions so as to make sure that the solvent had no influence on strain growth. The standard drug used in this study was 'ampicillin' for evaluating antibacterial activity which showed 100, 100, 250, and 100 µg mL^{-1} MIC against *E. coli*, *P. aeruginosa*, *S. aureus* and *S. pyogene*, respectively in Table I.

The newly synthesized compounds **4a-l** were screened for their antifungal activity in six sets against *C. albicans*, *A. niger* and *A. clavatus* at various concentrations of 1000, 500, 250, and 100 µg mL^{-1}. Results were recorded in the form of primary and secondary screening. The compounds found to be active in primary screening were similarly diluted to obtain 200, 125, 100, 62.5, 50 and 25 µg mL^{-1} concentrations for secondary screening to test in a second set of dilution against all microorganisms. 'Griseofulvin' was used as a standard drug for antifungal activity, which shows 500, 100 and 100 µg mL^{-1} MIC against *C. albicans*, *A. niger* and *A. clavatus*, respectively. For fungal growth, in the present protocol, we have used Sabourauds dextrose broth at 28°C in aerobic condition for 48 h. Results of antimicrobial evaluation of derivatives **4a-l** are shown in Table I.

Statistical analysis

Standard deviation value was expressed in terms of ±SD. On the basis of calculated value by using one-way ANOVA method followed by independent two sample *t* test, it was observed that differences below 0.001 level was considered as statistically significant.

Experimental Section

Melting points were determined on an electro thermal melting point apparatus and are reported uncorrected. The progress of reaction and the homogeneity of all compounds was checked on aluminum-coated TLC plates $_{60}F^{245}$ (E. Merck) using various solvent systems as mobile phase and visualized under ultraviolet (UV) light, or iodine vapor. Elemental analysis (% C, H, N) was carried out by a Perkin-Elmer 2400 CHN analyzer. IR spectra were also recorded on Perkin-Elmer FT-IR spectrophotometer in KBr. ^{1}H NMR spectra were recorded on Varian Gemini 400 MHz and ^{13}C NMR spectra on Varian Mercury-400, 100 MHz in DMSO-d_6 as solvent and tetramethylsilane (TMS) as an internal standard. Mass spectra were scanned on a Shimadzu LCMS 2010 spectrometer. Büchi Rotavapor was used for distillation.

General procedure for the preparation of 2-bromo-1-arylethan-1-one (phenacyl bromides), 2a-l

Compound 2-bromo-1-arylethan-1-one (phenacyl bromide) **2a-l** is prepared according to the literature method[30]. Further, all derivatives of the series were prepared by same method and reactions monitored by thin layer chromatography.

General procedure for the preparation of 5-methyl-2-arylimidazo[1,2-*a*]pyridines, 3a-l

To a solution of 6-methylpyridin-2-amine **1** (0.01 mol) in 100 mL of ethanol, different derivative

of phenacyl bromides **2a-l** (0.01 mol) was added at RT. The reaction was heated at 60-70°C and stirred for 3 h. Obtained crystalline solid was filtered, washed with warm ethanol and crystallized from 50% HCl.

5-Methyl-2-phenylimidazo[1,2-*a*]pyridine, 3a: Yield 65%. m.p.169-71°C. IR (KBr): 2736 (C-H, -CH_3), 2973 cm^{-1} (C-H, aromatic ring); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.86 (s, 3H, Ar-CH_3), 6.85-8.49 (m, 9H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 113.1, 117.3, 117.6, 123.9, 127.5, 128.8, 129.3, 130.1, 133.0, 139.8, 145.2; LCMS: *m/z* 208.10 (M^+). Anal. Calcd for $C_{14}H_{12}N_2$: C, 80.72; H, 5.81; N, 13.65. Found: C, 80.66; H, 5.75; N, 13.45%.

2-(2-Bromophenyl)-5-methylimidazo[1,2-*a*]pyridine, 3b: Yield 68%. m.p.176-78°C. IR (KBr): 2734 (C-H, -CH_3), 2973 (C-H, aromatic ring), 831 cm^{-1} (C-Br, stretching); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.82 (s, 3H, Ar-CH_3), 6.82-8.47 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 113.2, 117.3, 117.6, 120.2, 123.9, 128.8, 129.7, 130.9, 132.1, 139.8, 145.2; LCMS: *m/z* 286.01 (M^+). Anal. Calcd for $C_{14}H_{11}BrN_2$: C, 58.72; H, 4.81; N, 9.86. Found: C, 58.56; H, 3.86; N, 9.76%.

2-(4-Bromophenyl)-5-methylimidazo[1,2-*a*]pyridine, 3c: Yield 72%. m.p.172-74°C. IR (KBr): 2733 (C-H, –CH_3), 2975 (C-H, aromatic ring), 833 cm^{-1} (C-Br, stretching); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.83 (s, 3H, Ar-CH_3), 6.86-8.42 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 113.2, 117.3, 117.6, 123.2, 123.9, 128.8, 130.0, 132.0, 132.1, 139.8, 145.2; LCMS: *m/z* 286.01 (M^+). Anal. Calcd for $C_{14}H_{11}BrN_2$: C, 58.72; H, 4.81; N, 9.86. Found: C, 58.56; H, 3.86; N, 9.76%.

2-(3-Chlorophenyl)-5-methylimidazo[1,2-*a*]pyridine, 3d: Yield 74%. m.p.175-77°C. IR (KBr): 2738 (C-H, –CH_3), 2977 (C-H, aromatic ring), 836 cm^{-1} (C-Cl, stretching); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.88 (s, 3H, Ar-CH_3), 6.85-8.46 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 113.2, 117.3, 117.6, 123.9, 125.6, 128.8, 129.5, 129.6, 130.0, 134.4, 134.8, 139.8, 145.2; LCMS: *m/z* 242.06 (M^+). Anal. Calcd for $C_{14}H_{11}ClN_2$: C, 69.70; H, 4.62; N, 11.84. Found: C, 69.28; H, 4.55; N, 11.54%.

2-(4-Chlorophenyl)-5-methylimidazo[1,2-*a*]pyridine, 3e: Yield 79%. m.p.166-68°C. IR (KBr): 2732 (C-H, –CH_3), 2974 (C-H, aromatic ring), 835 cm^{-1} (C-Cl, stretching); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.87 (s, 3H, Ar-CH_3), 6.82-8.49 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 113.2, 117.3, 117.6, 123.9, 128.9, 129.3, 130.0, 131.1, 134.3, 139.8, 145.2; LCMS: *m/z* 242.06 (M^+). Anal. Calcd for $C_{14}H_{11}ClN_2$: C, 69.70; H, 4.62; N, 11.84. Found: C, 69.28; H, 4.54; N, 11.54%.

2-(5-Methylimidazo[1,2-*a*]pyridin-2-yl)phenol, 3f: Yield 69%. m.p.164-66°C. IR (KBr): 2732 (C-H, –CH_3), 2974 (C-H, aromatic ring), 3191 cm^{-1} (C-OH, stretching); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.88 (s, 3H, Ar-CH_3), 5.35 (s, H, Ar-OH), 6.82-8.42 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 113.2, 117.3, 117.6, 117.8, 120.5, 121.8, 123.9, 130.1, 131.5, 139.8, 140.1, 145.2, 155.2; LCMS: *m/z* 224.09 (M^+). Anal. Calcd for $C_{14}H_{12}ON_2$: C, 74.70; H, 5.62; N, 12.94. Found: C, 74.98; H, 5.39; N, 12.49%.

4-(5-Methylimidazo[1,2-*a*]pyridin-2-yl)phenol, 3g: Yield 72%. m.p.169-70°C. IR (KBr): 2733 (C-H, –CH_3), 2974 (C-H, aromatic ring), 3193 cm^{-1} (C-OH, stretching); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.88 (s, 3H, Ar-CH_3), 5.35 (s, H, Ar-OH), 6.85-8.43 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 113.2, 116.4, 117.3, 117.6, 123.9, 125.6, 128.9, 130.1, 139.8, 145.2, 158.5; LCMS: *m/z* 224.09 (M^+). Anal. Calcd for $C_{14}H_{12}ON_2$: C, 74.70; H, 5.62; N, 12.94. Found: C, 74.98; H, 5.39; N, 12.49%.

2-(2-Methoxyphenyl)-5-methylimidazo[1,2-*a*] pyridine, 3h: Yield 65%. m.p.165-67°C. IR (KBr): 2733 (C-H, -CH_3), 2974 (C-H, aromatic ring), 2925 cm^{-1} (C-OCH_3, stretching); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.86 (s, 3H, Ar-CH_3), 3.83 (s, 3H, –OCH_3), 6.85-8.45 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 56.1, 111.1, 113.2, 117.3, 118.9, 121.5, 123.9, 129.7, 131.1, 139.8, 140.1, 145.2, 157.3; LCMS: *m/z* 238.11 (M^+). Anal. Calcd for $C_{15}H_{14}ON_2$: C, 75.70; H, 5.99; N, 11.94. Found: C, 75.61; H, 5.92; N, 11.76%.

2-(4-Methoxyphenyl)-5-methylimidazo[1,2-*a*] pyridine, 3i: Yield 72%. m.p.164-66°C. IR (KBr): 2732 (C-H, -CH_3), 2974 (C-H, aromatic ring), 2927 cm^{-1} (C-OCH_3, stretching); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.88 (s, 3H, Ar-CH_3), 3.83 (s, 3H, -OCH_3), 6.84-8.42 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 55.8, 113.2, 114.8, 117.3, 117.5, 125.3, 128.5, 130.1, 139.8, 145.2, 160.6; LCMS: *m/z* 238.11 (M^+). Anal. Calcd for $C_{15}H_{14}ON_2$: C, 75.70; H, 5.99; N, 11.94. Found: C, 75.61; H, 5.92; N, 11.76%.

2-(4-Fluorophenyl)-5-methylimidazo[1,2-*a*]pyridine, 3j: Yield 76%. m.p.176-79°C. IR (KBr): 2733 (C-H,

$-CH_3$), 2974 (C-H, aromatic ring), 1125 cm^{-1} (C-F, stretching); ^1H NMR (400 MHz, DMSO-d_6): δ 1.88 (s, 3H, Ar-CH_3), 6.85-8.46 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 113.2, 116.5, 117.3, 117.5, 123.9, 127.5, 130.1, 139.8, 145.2, 162.9; LCMS: *m/z* 226.09 (M^+). Anal. Calcd for $C_{14}H_{11}FN_2$: C, 74.70; H, 4.99; N, 12.94. Found: C, 74.31; H, 4.90; N, 12.38%.

5-Methyl-2-*p*-tolylimidazo[1,2-*a*]pyridine, 3k: Yield 70%. m.p.171-72°C. IR (KBr): 2733 (C-H, $-CH_3$), 2974 (C-H, aromatic ring), 2738 cm^{-1} (C-H, Ar-CH_3); ^1H NMR (400 MHz, DMSO-d_6): δ 1.84 (s, 6H, Ar-CH_3), 6.85-8.46 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 113.2, 117.3, 117.5, 123.9, 125.7, 129.5, 130.0, 131.7, 139.8, 145.2; LCMS: *m/z* 222.12 (M^+). Anal. Calcd for $C_{15}H_{14}N_2$: C, 81.70; H, 6.99; N, 12.95. Found: C, 81.05; H, 6.35; N, 12.60%.

4-(5-Methylimidazo[1,2-*a*]pyridin-2-yl)aniline, 3l: Yield 74%. m.p.177-79°C. IR (KBr): 2733 (C-H, $-CH_3$), 2974 (C-H, aromatic ring), 3252 cm^{-1} (N-H, 2° amine); ^1H NMR (400 MHz, DMSO-d_6): δ 1.86 (s, 3H, Ar-CH_3), 6.27 (s, 2H, Ar-NH_2), 6.85-8.48 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 115.2, 117.3, 117.5, 123.0, 123.9, 128.3, 130.0, 139.8, 145.2, 145.6; LCMS: *m/z* 223.11 (M^+). Anal. Calcd for $C_{14}H_{13}N_3$: C, 75.70; H, 5.99; N, 18.95. Found: C, 75.31; H, 5.87; N, 18.82%.

General procedure for the preparation of *N*,*N*-dimethyl-1-(5-methyl-2-arylimidazo[1,2-*a*]pyridin-3-yl)methanamines, 4a-l

Compounds **3a-l** (0.01 mol) in dry toluene (80 mL) was taken in round bottom flask. Formaldehyde (0.01 mol) was added to the reaction flask at a temperature below 35°C. The mixture was stirred for 1 h at RT. Dimethyl amine (0.01 mol) in 50% conc. HCl (20 mL) was then added drop-wise to the reaction mixture at RT and heated at 80-90°C for 3-5 h with constant stirring (care was taken to see that the temperature did not rise above 90°C). The solvent was removed under reduced pressure and the product obtained was washed with 1% aqueous solution of sodium carbonate.

***N*,*N*-Dimethyl-1-(5-methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)methanamine, 4a**: Yield 78%. m.p.251-53°C. IR (KBr): 2723 (C-H, -CH_3), 2809 (C-H, -CH_2-), 2978 cm^{-1} (C-H, -$N(CH_3)_2$); ^1H NMR (400 MHz, DMSO-d_6): δ 1.86 (s, 3H, Ar-CH_3), 2.58 (s, 2H, -CH_2-$N(CH_3)_2$), 3.43 (s, 6H, -CH_2-$N(CH_3)_2$), 6.83-8.40 (m, 8H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 46.6, 57.7, 117.3, 117.5, 122.1, 123.9, 127.5, 129.3, 133.0, 134.8, 139.8, 144.8, 145.5; LCMS: *m/z* 265.16 (M^+). Anal. Calcd for $C_{17}H_{19}N_3$: C, 76.51; H, 7.56; N, 15.73. Found: C, 76.40; H, 7.45; N, 15.65%.

1-(2-(2-Bromophenyl)-5-methylimidazo[1,2-*a*]pyridin-3-yl)-*N*,*N*-dimethylmethanamine, 4b: Yield 68%. m.p.150-52°C. IR (KBr): 2725 (C-H, $-CH_3$), 2805 (C-H, -CH_2-), 2975 (C-H, -$N(CH_3)_2$), 831 cm^{-1} (C-Br, stretching); ^1H NMR (400 MHz, DMSO-d_6): δ 1.83 (s, 3H, Ar-CH_3), 2.55 (s, 2H, -CH_2-$N(CH_3)_2$), 3.47 (s, 6H, -CH_2-$N(CH_3)_2$), 6.85-8.35 (m, 7H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 46.6, 57.7, 117.3, 117.5, 120.1, 122.2, 128.2, 129.7, 133.0, 130.9, 134.8, 139.8, 144.8, 145.5; LCMS: *m/z* 343.07 (M^+). Anal. Calcd for $C_{17}H_{18}BrN_3$: C, 59.14; H, 5.54; N, 12.17. Found: C, 58.05; H, 5.13; N, 12.02%.

1-(2-(4-Bromophenyl)-5-methylimidazo[1,2-*a*]pyridin-3-yl)-*N*,*N*-dimethylmethanamine, 4c: Yield 64%. m.p.167-69°C. IR (KBr): 2725 (C-H, $-CH_3$), 2807 (C-H, -CH_2-), 2979 (C-H, -$N(CH_3)_2$), 831 cm^{-1} (C-Br, stretching); ^1H NMR (400 MHz, DMSO-d_6): δ 1.84 (s, 3H, Ar-CH_3), 2.56 (s, 2H, -CH_2-$N(CH_3)_2$), 3.46 (s, 6H, -CH_2-$N(CH_3)_2$), 6.83-8.38 (m, 7H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 46.6, 57.7, 117.3, 117.5, 122.2, 123.1, 128.3, 132.0, 132.1, 134.8, 139.8, 144.8, 145.5; LCMS: *m/z* 343.07 (M^+). Anal. Calcd for $C_{17}H_{18}BrN_3$: C, 59.14; H, 5.54; N, 12.17. Found: C, 58.56; H, 5.20; N, 12.02%.

1-(2-(3-Chlorophenyl)-5-methylimidazo[1,2-*a*]pyridin-3-yl)-*N*,*N*-dimethylmethanamine, 4d: Yield 55%. m.p.160-62°C. IR (KBr): 2727 (C-H, $-CH_3$), 2808 (C-H, -CH_2-), 2976 (C-H, -$N(CH_3)_2$), 836 cm^{-1} (C-Cl, stretching); ^1H NMR (400 MHz, DMSO-d_6): δ 1.86 (s, 3H, Ar-CH_3), 2.52 (s, 2H, -CH_2-$N(CH_3)_2$), 3.48 (s, 6H, -CH_2-$N(CH_3)_2$), 6.85-8.37 (m, 7H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 46.6, 57.7, 117.3, 117.5, 122.2, 123.1, 125.6, 128.8, 129.5, 129.7, 134.4, 134.8, 139.8, 144.8, 145.5; LCMS: *m/z* 299.12 (M^+). Anal. Calcd for $C_{17}H_{18}ClN_3$: C, 75.00; H, 5.80; N, 14.29. Found: C, 74.10; H, 5.50; N, 14.01%.

1-(2-(4-Chlorophenyl)-5-methylimidazo[1,2-*a*]pyridin-3-yl)-*N*,*N*-dimethylmethanamine, 4e: Yield 59%. m.p.260-62°C. IR (KBr): 2726 (C-H, $-CH_3$), 2806 (C-H, -CH_2-), 2976 (C-H, -$N(CH_3)_2$), 835 cm^{-1} (C-Cl, stretching); ^1H NMR (400 MHz, DMSO-d_6): δ 1.85 (s, 3H, Ar-CH_3), 2.51 (s, 2H, -CH_2-$N(CH_3)_2$), 3.48 (s, 6H, -CH_2-$N(CH_3)_2$), 6.85-8.39 (m, 7H, Ar-H);

^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 46.6, 57.7, 117.3, 117.5, 122.2, 128.9, 129.3, 131.1, 134.3, 134.8, 139.8, 144.8, 145.5; LCMS: *m/z* 299.12 (M^+). Anal. Calcd for $C_{17}H_{18}ClN_3$: C, 67.87; H, 6.36; N, 13.96. Found: C, 66.05; H, 6.15; N, 13.03%.

2-(3-((Dimethylamino)methyl)-5-methylimidazo [1,2-*a*]pyridin-2-yl)phenol, 4f: Yield 78%. m.p.143-45°C. IR (KBr): 2724 (C-H, -CH_3), 2806 (C-H, -CH_2-), 2976 (C-H, -N(CH_3)$_2$), 3190 cm^{-1} (C-OH, stretching); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.88 (s, 3H, Ar-CH_3), 2.53 (s, 2H, -CH_2-N(CH_3)$_2$), 3.44 (s, 6H, -CH_2-N(CH_3)$_2$), 5.35 (s, H, Ar-OH), 6.82-8.42 (m, 7H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 46.6, 57.7, 117.3, 117.5, 117.8, 120.5, 121.9, 130.1, 131.5, 134.8, 139.8, 144.8, 145.5, 155.2; LCMS: *m/z* 281.35 (M^+). Anal. Calcd for $C_{17}H_{19}N_3O$: C, 61.51; H, 5.53; N, 15.37. Found: C, 61.23; H, 5.40; N, 15.20%.

4-(3-((Dimethylamino)methyl)-5-methylimidazo 1,2-*a*]pyridin-2-yl)phenol, 4g: Yield 66%. m.p.176-78°C. IR (KBr): 2726 (C-H, -CH_3), 2807 (C-H, -CH_2-), 2977 (C-H, -N(CH_3)$_2$), 3192 cm^{-1} (C-OH, stretching); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.86 (s, 3H, Ar-CH_3), 2.54 (s, 2H, -CH_2-N(CH_3)$_2$), 3.46 (s, 6H, -CH_2-N(CH_3)$_2$), 5.37 (s, H, Ar-OH), 6.85-8.44 (m, 7H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 46.6, 57.7, 116.4, 117.3, 117.5, 125.6, 128.9, 134.8, 139.8, 144.8, 145.5, 158.5; LCMS: *m/z* 281.35 (M^+). Anal. Calcd for $C_{17}H_{19}N_3O$: C, 72.31; H, 7.13; N, 14.88. Found: C, 72.04; H, 7.02; N, 14.70%.

1-(2-(2-Methoxyphenyl)-5-methylimidazo[1,2-*a*] pyridin-3-yl)-*N*,*N*-dimethylmethanamine, 4h: Yield 75%. m.p.199-201°C. IR (KBr): 2729 (C-H, -CH_3), 2809 (C-H, -CH_2-), 2978 (C-H, -N(CH_3)$_2$), 2925 cm^{-1} (C-OCH_3, stretching); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.84 (s, 3H, Ar-CH_3), 2.53 (s, 2H, -CH_2 -N(CH_3)$_2$), 3.43 (s, 6H, -CH_2-N(CH_3)$_2$), 3.83 (s, 3H, -OCH_3), 6.85-8.45 (m, 7H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 46.6, 56.1, 57.7, 111.2, 117.3, 117.5, 118.9, 121.5, 122.1, 129.8, 131.1, 134.8, 139.8, 144.8, 145.5, 157.3; LCMS: *m/z* 295.17 (M^+). Anal. Calcd for $C_{18}H_{21}N_3O$: C, 72.94; H, 7.48; N, 14.17. Found: C, 72.80; H, 7.55; N, 14.10%.

1-(2-(4-Methoxyphenyl)-5-methylimidazo[1,2-*a*] pyridin-3-yl)-*N*,*N*-dimethylmethanamine, 4i: Yield 71%. m.p.212-14°C. IR (KBr): 2729 (C-H, -CH_3), 2809 (C-H, -CH_2-), 2978 (C-H, -N(CH_3)$_2$), 2925 cm^{-1} (C-OCH_3, stretching); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.86 (s, 3H, Ar-CH_3), 2.54 (s, 2H, -CH_2-N(CH_3)$_2$), 3.45 (s, 6H, -CH_2-N(CH_3)$_2$), 3.85 (s, 3H, -OCH_3), 6.83-8.43 (m, 7H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 46.6, 55.8, 57.7, 114.8, 117.3, 117.5, 125.3, 128.5, 134.8, 139.8, 144.8, 145.5, 160.6; LCMS: *m/z* 295.17 (M^+). Anal. Calcd for $C_{18}H_{21}N_3O$: C, 72.94; H, 7.48; N, 14.17. Found: C, 72.70; H, 7.30; N, 14.09%.

1-(2-(4-Fluorophenyl)-5-methylimidazo[1,2-*a*] pyridin-3-yl)-*N*,*N*-dimethylmethanamine, 4j: Yield 77%. m.p.137-39°C. IR (KBr): 2727 (C-H, -CH_3), 2804 (C-H, -CH_2-), 2975 (C-H, -N(CH_3)$_2$), 1123 cm^{-1} (C-F, stretching); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.85 (s, 3H, Ar-CH_3), 2.56 (s, 2H, -CH_2-N(CH_3)$_2$), 3.44 (s, 6H, -CH_2-N(CH_3)$_2$), 6.85-8.49 (m, 7H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 46.6, 57.7, 116.0, 117.3, 117.5, 122.1, 128.7, 130.6, 134.8, 139.8, 144.8, 145.5, 162.9; LCMS: *m/z* 283.15 (M^+). Anal. Calcd for $C_{17}H_{18}N_3F$: C, 71.80; H, 6.73; N, 14.77. Found: C, 71.66; H, 6.60; N, 14.65%.

***N*,*N*-Dimethyl-1-(5-methyl-2-*p*-tolylimidazo[1,2-*a*] pyridin-3-yl)methanamine, 4k**: Yield 63%. m.p.120-22°C. IR (KBr): 2729 (C-H, -CH_3), 2809 (C-H, -CH_2-), 2978 (C-H, -N(CH_3)$_2$), 2738 cm^{-1} (C-H, Ar-CH_3); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.85 (s, 6H, Ar-CH_3), 2.55 (s, 2H, -CH_2-N(CH_3)$_2$), 3.46 (s, 6H, -CH_2-N(CH_3)$_2$), 6.85-8.42 (m, 7H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 46.6, 57.7, 117.3, 117.5, 122.1, 125.7, 129.5, 130.0, 131.7, 134.8, 139.8, 144.8, 145.5; LCMS: *m/z* 279.17 (M^+). Anal. Calcd for $C_{18}H_{21}N_3$: C, 72.94; H, 7.48; N, 14.17. Found: C, 72.88; H, 7.23; N, 13.89%.

4-(3-((Dimethylamino)methyl)-5-methylimidazo 1,2-*a*]pyridin-2-yl)aniline, 4l: Yield 75%. m.p.156-58°C. IR (KBr): 2729 (C-H, -CH_3), 2809 (C-H, -CH_2-), 2978 (C-H, -N(CH_3)$_2$), 3250 cm^{-1} (N-H, 2º amine); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.86 (s, 3H, Ar-CH_3), 2.52 (s, 2H, -CH_2-N(CH_3)$_2$), 3.49 (s, 6H, -CH_2-N(CH_3)$_2$), 6.27 (s, 2H, Ar-NH_2), 6.82-8.46 (m, 7H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.3, 46.6, 57.7, 115.1, 117.3, 117.5, 122.1, 123.0, 128.3, 134.8, 139.8, 144.8, 145.5, 145.7; LCMS: *m/z* 280.17 (M^+). Anal. Calcd for $C_{17}H_{20}N_4$: C, 72.94; H, 7.48; N, 14.17. Found: C, 72.80; H, 7.33; N, 14.05%.

Conclusion

On the basis of biological activity results and observation of SAR study, we may conclude that the introduction of various substituents in the

imidazo[1,2-*a*]pyridine framework plays a very important role in identifying the targeted compounds with electron withdrawing groups such as fluoro, chloro and bromo as effective microorganism growth inhibitors. These groups enhanced the antibacterial and antifungal activities and gave promising resultant compounds like **4b, 4c**, **4d**, **4e** and **4j**.

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