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One-pot two-step facile synthesis of new 6,7-dihydro-1*H*—pyrazolo [3,4-*b*] pyridine-5- carbonitrile hybrids as antimicrobial agents

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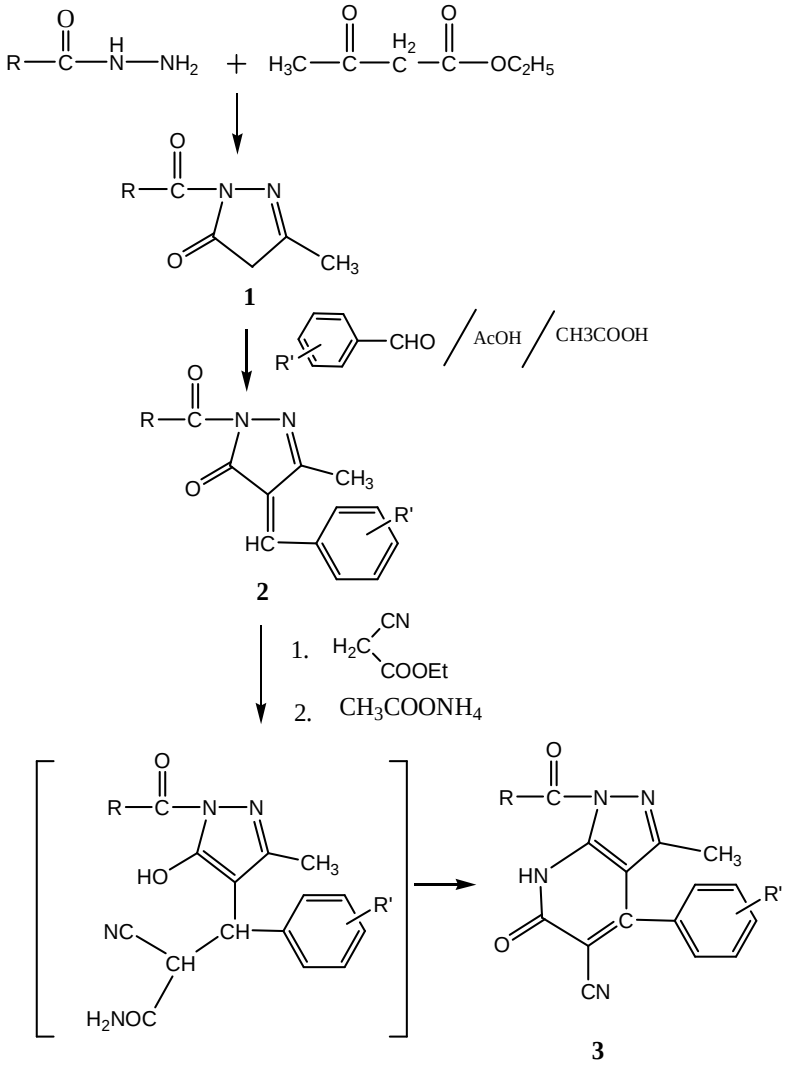
A new series of novel 1-benzoyl-4-(4-aroyl/aroyloxy methyl)-3-methyl-6-oxo-6,7-dihydro-*1H*-pyrazolo [3,4-*b*] pyridine-5-carbonitrile have been synthesized from a common intermediate, in good yields. These compounds have been screened for their antibacterial and antifungal activity against different pathogenic strains of bacteria and fungi. The minimum inhibitory concentration (MBC) and minimum fungicidal concentration (MFC) have been determined for the test compounds as well as for reference standards. Compounds **3c**, **3f**, **3h**, **3i**, **3n**, **3o**, **3p** have shown good antibacterial activity where as compounds **3b**, **3e**, **3g**, **3i**, **3p** have displayed better antifungal activity.

Keywords: Substituted aroyl/aroyloxymethyl, Schiff base, pyrazolin, pyridine, carbonitrile, antimicrobial, antibacterial activity, antifungal activity

Efficient synthesis of drug-like small molecules has been the focus of the research for medicinal chemists and chemical biologists because they play a very important role in drug discovery processes[1]. These different drug-like bioactive compounds are broadly used to modulate enzyme or receptor function and can serve as important leads for drug development[2-4]. Pyrazoles represent a key structural motif in heterocyclic chemistry and occupy a significant position in medicinal and pesticide chemistry because of their capability to exhibit a wide range of biological activities including antibacterial[5-8], antifungal[9], antidiabetic[10] herbicidal[11], analgecic[12], antitumor[13], anti-anxiety[14] and antihyperglycemic activity[15]. The use of pyrazole derivative as potential antimicrobial agents has received considerable attention following the discovery of the natural pyrazole C-glycoside, pyrazofurin that demonstrated a broad spectrum of antimicrobial activity[16]. Prazolo [3,4-*b*] pyridine skeleton have proven to be interesting classes of heterocycles due to diverse biological properties including antitubercular, antibacterial and antioxidant activities[17-19]. Recently, many authors[20] synthesized pyrazolo [3,4-*b*] pyridine by novel methods. J Quiroga and coworkers[21,22] have been prepared pyrazolo [3,4-*b*] pyridine by the reaction of 5-amino-3-methyl/phenyl-1-phenyl/H-1*H*-pyrazole and chalcones of benzoyl acetonitrile/malononitrile with some aromatic aldehydes. The cyano group is a stable and useful functional group that can be transformed to various other functional groups such as acyl, carboxy, formyl, carbamoyl, *etc*.[23] The past seven decades has witnessed the transition of organic nitriles from a position of laboratory curiosities to that of large tonnage chemicals of commercial importance. On the other hand, reactions involving C-C bond formation are one of the mainstays in synthetic organic chemistry. The use of nitrile function for C-C bond formation reactions occupies an important position in organic chemistry[24-26].

In light of the above literature and abundance on bio-potentials of pyrazolo and pyridine analogues, we designed the synthesis of titled compounds having carbonitrile as one of the appendages and were confident that these frame work would provide the important structural motifs for the discovery of new antimicrobial agents. In continuation of our research on efficient synthesis of biologically active small molecules[27], we developed one-pot synthesis of pyrazolo [3,4-*b*] pyridine carbonitrile derivatives and demonstrated their antimicrobial activity. The structure of these compunds was established by the IR, ^{1}H NMR spectral data and elemental analysis (Scheme I).



a	$R = C_6H_5$	$R' = 4\text{-}OCH_3$	**i**	$R = 4\text{-}NO_2C_6H_4$	$R' = 4\text{-}Cl$
b	$R = C_6H_5$	$R' = 3,4\text{-}(OCH_3)_2$	**j**	$R = 4\text{-}NO_2C_6H_4$	$R' = 3,4\text{-}(OCH_3)_2$
c	$R = 4\text{-}ClC_6H_4$	$R' = 4\text{-}OCH_3$	**k**	$R = C_6H_4OCH_2$	$R' = 4\text{-}OCH_3$
d	$R = 4\text{-}ClC_6H_4$	$R' = 4\text{-}Cl$	**l**	$R = C_6H_4OCH_2$	$R' = 3, 4\text{-}(OCH_3)_2$
e	$R = 4\text{-}ClC_6H_4$	$R' = 3,4\text{-}(OCH_3)_2$	**m**	$R = C_6H_4OCH_2$	$R' = 4\text{-}Cl$
f	$R = 2,4\text{-}Cl_2C_6H_3$	$R' = 4\text{-}OCH_3$	**n**	$R = 4\text{-}ClC_6H_4OCH_2$	$R' = 4\text{-}Cl$
g	$R = 2\text{-}OHC_6H_4$	$R' = 4\text{-}OCH_3$	**o**	$R = 4\text{-}ClC_6H_4OCH_2$	$R' = 4\text{-}OCH_3$
h	$R = 2\text{-}OHC_6H_4$	$R' = 3,4\text{-}(OCH_3)_2$	**p**	$R = 4\text{-}ClC_6H_4OCH_2$	$R' = 3,4\text{-}(OCH_3)_2$

Scheme I

The required starting material 1-aroyl/ aroyloxymethyl-4-arylideno-3-methyl-pyrazolin-5-ones was prepared by the following known methods[28]. A mixture of 1-aroyl/aroyloxymethyl-3-methyl-pyrazolin-5-one, fused sodium acetate and an araldehyde in glacial acetic acid was refluxed for 2-3 h. The reaction mixture was poured into cold water, filtered, dried and recrystallized from methanol to furnish the corresponding pyrazolin derivatives.

Antibacterial Activity

The synthesized pure compounds were sereened for their anti bacterial activities adopting standard protocols[29]. The antibacterial activity, of prepared

final pure compounds was performed against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Klebsiella pneumoniae* using Ciprofloxacin as positive and DMSO as negative control. Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were determined and the activity was reported in μg/mL. The nutrient broth, which contained logarithmic serially two fold diluted amount of test compounds and controls were inoculated with approximately 5×10^5 c.f.u/mL of activity dividing bacteria cells. The cultures were incubated for 24 h at 37°C and the growth was monitored visually and spectrophotometerically. The antibacterial results are summarized in Table I, only for those compounds which were found active against any tested strain of bacteria. It is inferred from Table I that compounds **3g**, **3i** and **3j** showed moderate activity against gram-positive bacteria *S.aureus* and *B.subtilis* where as **3n**, **3o** and **3p** were active against gram-negative *K. pneumoniae* ranging from 30 to 50 μg/mL concentration and only one compound **3l** was found active against *E.coli* 25 μg/mL Concentration (Table I). MBC/MIC ratio of all active compounds is ranging from 2.0 to 3.3 suggesting these compounds are bactericidal not bacteriostatic. Antimicrobial agent is considered bacteriostatic when the minimal MBC/MIC ratio is greater than or equal to 8 where as it is considered bactericidal if MBC/MIC ratio is less than or equal to 4.

Fungicidal Activity

The antifungal activity of the prepared pure compounds was performed against *Pyricularia oryzae Pseudoperonospora cubensis*, *Sphaerotheca fuliginea* and *phytophthora infestans* using Griseofulvin as positive and DMSO as negative control. Minimum inhibitory concentration (MIC) was determined and reported in μg/mL. Antifungal activity was carried out through disk diffusion method[30,31]. All fungal cultures were routinely maintained on sabouraud dextrose (SDA) and incubated at 28°C. The Antifungal activities are summarized in Table II, only for those compounds which were found active against any of these strains of fungi. It is inferred from Table II that compounds **3d**, **3d**, **3e** and **3h** showed antifungal activity against *P.oryzae P. cubensis*, *S.fuliginea* and *P. infestans* strain of fungi ranging from 10 to 20 μg/mL in concentration which is comparable to Griseofulvin. The structure-activity relationship (SAR) of the tested compounds for antifungal as well as antibacterial activity can be summarized as follow:

(i) In the series of the substituted pyrazolo [3, 4-*b*] pyridine -5- carbonitrile derivatives has shown better antibacterial activity than the *o*-substituted groups.

(ii) Presence of one or more polar groups in phenyl ring with phenoxy moiety is an important scaffold for better antibacterial activity.

(iii) Most of the antibacterial compounds have MBC/MIC ratio below 4, it means they are bactericidal not bacteriostatic.

Antifungal activity of these compounds was similar or even better in some cases as compare to Griseofulvin a known antifungal agent. the possible meachanism for the antibacterial activity of examined

Table I — Antibacterial activity of Compounds possess promising biological activity

Compd	Gram-positive bacteria				Gram-negative bacteria			
	S.aureus		*B.subtilis*		*E.coli*		*K.pneumonie*	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
3g	40	100	30	50	n.a.	n.a.	n.a.	n.a.
3i	30	100	20	50	n.a.	n.a.	n.a.	n.a.
3j	30	50	40	100	n.a.	n.a.	n.a.	n.a.
3l	n.a.	n.a.	n.a.	n.a.	25	50	n.a.	n.a.
3n	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	25	50
3o	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	25	50
3p	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	50	100
Ciprofloxacin	6.5	12.5	10.0	25	6.25	25	6.25	10.25
DMSO	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

MIC (μg/mL) minimum inhibitory concentration *i.e.* the lowest concentration of the compound to inhibit growth of bacteria completely, MBC (μg/mL) minimum bacterial concentration *i.e.* the lowest concentration of the compound for killing the bacteria completely, MBC/MIC ratio are against-*S.aureus* (**3g** 2.5, **3i** 3.3, **3j** 1.6), *B. subtilis* (**3g** 1.6, **3i** 2.0, **3o** 2.0, **3p** 2.0), *E.coli* (**3l** 2.0) and *K.pneumoniae aureus* (**3n** 2.0, **3o** 2.0, **3p** 2.0) n.a. - no activity detected.

Table II — Antifungal activity of compounds **3b, 3d, 3e** and **3h**

Compd	Fungal species and MIC (μg/mL)			
	P.oryzae	*P.cubensis*	*S.fuliginea*	*P.infestans*
3b	20	16	12	14
3d	18	14	12	16
3e	12	10	10	10
3h	14	12	16	16
Griseofulvin	20	18	16	18
DMSO	n.a.	n.a.	n.a.	n.a.

MIC (μg/mL), minimum inhibitory concentration *i.e.* the lowest concentration of the compound to inhibit the growth of fungi. n.a. – no activity detected.

compounds is not known at the moment and investigations are being done to investigate the mechanism of antibacterial action, and to synthesize more effective compounds.

Experimental Section

Melting points were recorded in Richerf-Thermover instrument and are uncorrected. The IR spectra were recorded on Perkin-Elmer RXI spectrometer in KBr. ^{1}H and ^{13}C NMR spectra were recorded on Bruker 300 and Bruker Avance II 400 spectrometer using tetra methylsilane (TMS) as an internal standard and DMSO-d_6/$CDCl_3$ as solvent. The micro analytical data were collected on Elemental Vario EL III elemental analyzer. All chemicals used were purchased from Merck and Fluka Chemicals. The homogeneity of compounds was checked by thin layer chromatography (TLC) on glass plates coated with silica gel G_{254} (Merck, Mumbai, India) using chloroform-methanol (3:1) mixture as mobile phase.

General procedure for synthesis of 1-substituted aroyl/substituted aroyloxymethyl-4-substituted aryl -3- methyl –6- oxo-6,7-dihydro-*1H*-pyrazolo [3,4-*b*] pyridine-5-carbonitrile

A mixture of ethylcyanoacetate (0.01 mol), 1-aroyl/aroyloxymethyl-4-arylideno-3-methyl pyrazolin -5-one (0.01 mo1) and ammonium acetate (0.08 mo1) was heated at 150-170°C in an oil bath for 2-3 h. The resulting solution was cooled and poured into water. The solid product obtained was filtered and washed with water, dried and purified by recrystallization from ethanol to get crystalline solid products **3a-p**.

3a: Yield 68%. m.p.165°C. IR (KBr): 3200 (NH stretching) 3035 (C-H aromatic stretching), 2100 (C ≡ N Stretching) 1720, 1760 (C= O stretching), 1620 (C= N stretching) and 1470 cm^{-1} (C = C Stretching); ^{1}H NMR (DMSO-d_6): δ 8.0 (s, NH proton), 7.8-6.7 (m, 9H, H-aromatic), 3.5 (s, 3H, methoxy proton); ^{13}C NMR (DMSO-d_6): δ 11.3, 55.2, 92.0, 114.5, 115.5, 127.7, 129.3, 129.3, 130.5, 132.5, 133.4, 144.2, 165.5, 168.0, 168.6.

3b: Yield 65%. m.p 170°C. IR (KBr): 3150 (NH stretching), 3025 (C-H aromatic stretching), 2075 (C ≡ N stretching), 1740, 1700 (C = O stretching), 1620 (C = N stretching) and 1450 cm^{-1} (C = C stretching); ^{1}H NMR (DMSO-d_6): δ 8.2 (s, NH proton), 7.8-6.6 (m. 7H, H-aromatic), 3.7 (s, 6H, methoxy proton), 2.7 (s, 3H, methyl proton); ^{13}C NMR (DMSO -d_6): δ 11.3, 56.2, 92.0, 97.3, 111.6, 114.5, 115.5, 119.7, 127.7, 129.3, 130.5, 132.5,133.4, 134.6, 144.2, 149.2, 149.7, 165.5, 168.0, 168.7.

3c: Yield 70%. m.p.167°C. IR (KBr): 3160 (NH stretching), 3010 (C-H aromatic stretching) 2166 (C ≡ N stretching) 1690, 1720 (C=O stretching) 1610 (C=N stretching) and 1450 cm^{-1} (C=C stretching); ^{1}H NMR (DMSO-d_6): δ 8.0(s, NH proton), 7.7-6.7 (m, 8H, H-aromatic), 3.7 (s, 3H, methoxy proton), 2.7 (s, 3H, methyl proton); ^{13}C NMR (DMSO-d_6): δ 11.3, 55.9, 92.0, 97.7, 111.6, 114.5, 127.5, 128.7, 129.7, 132.5, 140.0, 144.2, 159.2, 165.7, 168.9.

3d: Yield 69%. m.p.198°C. IR (KBr): 3140 (NH stretching), 3015 (C-H aromatic stretching), 2176 (C ≡ N stretching), 1680, 1700 (C=O stretching), 1615 (C=N stretching) and 1470 cm^{-1} (C=C stretching); ^{1}H NMR (DSMO-d_6): δ 8.3 (s, NH proton), 7.7-7.2 (m, 8H, H-aromatic), 2.7 (s, NH methyl proton); ^{13}C NMR (DMSO-d_6): δ 11.5, 92.0, 97.7, 115.6, 127.5, 128.1, 128.7, 129.2, 131.3, 133.5, 138.4, 140.5, 140.6, 144.2, 165.7, 168.5.

3e: Yield 63%. m.p.178°C. IR (KBr): 3090 (NH stretching), 3005 (C-H aromatic stretching), 2210 (C ≡ N stretching), 1690, 1710 (C=O stretching), 1620 (C=N stretching) and 1490 cm^{-1} (C=C stretching); ^{1}H NMR (DSMO-d_6): δ 8.2 (s, NH proton), 7.6-6.8 (m, 8H, H-aromatic), 3.7 (s, 3H, methyl proton); ^{13}C NMR (DMSO-d_6): δ 11.3, 55.9, 92.0, 97.7, 114.6, 115.9, 127.1, 130.2, 132.3, 132.8, 135.4, 136.1, 140.6, 141.7, 144.5, 159.9, 165.2, 168.7.

3f: Yield 67%. m.p.200°C. IR (KBr): 3150 (NH stretching), 3010 (C-H aromatic stretching), 2215(C≡N stretching), 1680, 1715 (C=O stretching), 1630 (C=N stretching) and 1500 cm^{-1} (C=C stretching); ^{1}H NMR (DMSO-d_6): δ 8.2 (s, NH proton), 7.6-6.8 (m, 7H, H-aromatic), 3.7 (s, 3H

methyl proton); ^{13}C NMR (DMSO-d_6): δ 11.0, 55.9, 92.0, 97.7, 114.6, 115.9, 127.1, 127.7, 130.2, 132.3, 132.8, 135.4, 136.1, 140.6, 141.7, 144.5, 159.9, 165.2, 168.7.

3g: Yield 72%. m.p.185°C. IR (KBr): 3120 (NH stretching), 3015 (C-H aromatic stretching), 2220 (C≡N stretching), 1690, 1710 (C=O stretching), 1625 (C=N stretching) and 1495 cm^{-1} (C=C stretching); ^{1}H NMR (DMSO-d_6): δ 8.4 (s, NH proton), 7.7-6.7 (m, 8H, H-aromatic), 5.0 (s, OH proton), 3.7 (s, 3H, methoxy proton), 2.8 (s, 3H, methyl proton); ^{13}C NMR (DMSO-d_6): δ 11.6, 55.9, 92.0, 97.7, 114.0, 116.0, 127.0, 129.0, 131.0, 132.8, 140.6, 144.7, 159.9, 165.2, 168.3.

3h: Yield 64%. m.p.178°C. IR (KBr): 3260 (OH stretching): 3150 (NH stretching), 3020 (C-H aromatic stretching), 2210 (C≡N stretching), 1685, 1705 (C=O stretching), 1610 (C=N stretching) and 1470 cm^{-1} (C=C stretching); ^{1}H NMR (DMSO-d_6): δ 7.8 (s, NH, proton), 7.6-6.6 (m, 7H, H- aromatic), 5.3 (s, OH proton), 3.7 (s, 6H, methoxy proton), 2.7 (s, 3H, methyl proton); ^{13}C NMR (DMSO-d_6): δ 11.6, 56.2, 92.0, 98.0, 111.0, 115.2, 116.0, 119.2, 122.0, 131.2, 133.3, 136.3, 140.6, 144.7, 149.0, 161.8, 165.2, 168.3.

3i: Yield 66%. m.p.205°C. IR (KBr): 3250 (NH stretching), 3025 (C-H aromatic stretching), 2200 (C≡N stretching), 1680, 1700 (C=O stretching), 1620 (C=N stretching) and 1490 cm^{-1} (C=C stretching); ^{1}H NMR (DMSO-d_6): δ 8.0 (s, NH proton), 7.4-7.2 (m, 8H, H-aromatic), 2.8 (s, 3H, methyl proton); ^{13}C NMR (DMSO-d_6): δ 11.6, 92.0, 97.7, 115.2, 121.2, 127.7, 128.1, 130.2, 133.5, 136.6, 138.2, 140.3, 144.6, 154.7, 161.8, 165.2, 168.3.

3j: Yield 63%. m.p.185°C. IR (KBr): 3190 (NH stretching), 3015 (C-H aromatic stretching), 2228 (C≡N stretching), 1690, 1715 (C=O stretching), 1610 (C=N stretching) and 1510 cm^{-1} (C=C stretching); ^{1}H NMR (DMSO-d_6): δ 8.2 (s, NH proton), 7.4 - 6.6 (m, 7H, H-aromatic), 3.7 (s, 6H, methoxy proton), 2.8 (s, 3H, methyl proton); ^{13}C NMR (DMSO-d_6): δ 11.8, 56.4, 92.0, 97.7, 111.3, 115.2, 115.7, 119.1, 121.2, 130.5, 133.6, 136.2, 140.5, 144.3, 149.0, 149.8, 154.7, 165.7, 168.6.

3k: Yield 65%. m.p.176°C. IR (KBr): 3210 (NH stretching), 3028 (C-H aromatic stretching), 2206 (C≡N stretching), 1680, 1710 (C=O stretching), 1590 (C=N stretching) and 1490 cm^{-1} (C=C stretching); ^{1}H NMR (DMSO-d_6): δ 8.0 (s, NH proton), 7.1-6.7 (m, 9H, H-aromatic), 5.0 (s, 2H, OCH_2 proton), 3.7 (s, 3H, methoxy proton), 2.7 (s, 3H, methyl proton); ^{13}C NMR (DMSO-d_6): δ 11.7, 55.8, 71.5, 92.1, 97.9, 114.3, 114.9, 115.7, 121.1, 127.2, 129.5, 132.6, 140.5, 144.3, 159.0, 160.8, 168.6, 201.0.

3l: Yield 64%. m.p.185°C. IR (KBr): 3190 (NH stretching), 3030(C-H aromatic stretching), 2200 (C≡N stretching), 1680, 1710 (C=O stretching), 1590 (C=N stretching) and 1480 cm^{-1} (C=C stretching); ^{1}H NMR (DMSO-*d*): δ 8.0 (s, NH proton), 7.1-6.6 (m, 8H, H-aromatic), 5.1 (s, 2H, OCH_2 proton), 3.7 (s, 6H, methoxy proton), 2.8 (s, 3H, methyl proton); ^{13}C NMR (DMSO-d_6): δ 11.6, 56.8, 71.6, 92.1, 97.9, 111.3, 114.9, 115.7, 119.1, 121.2, 129.5, 133.6, 140.5, 144.3, 149.0, 160.5, 168.3, 201.0.

3m: Yield 73% m.p.155°C. IR (KBr): 3210 (NH stretching), 3020 (C-H aromatic stretching), 3020 (C-H aromatic stretching), 2190 (C≡N Stretching), 1690, 1715 (C=O stretching), 1585 (C=N stretching), and 1475 cm^{-1} (C=C Stretching); ^{1}H NMR (DMSO-d_6); δ 8.0 (s, NH proton), 7.3-6.6 (m, 9H, H-aromatic), 5.1 (s, 2H, OCH_2 proton), 2.8 (s, 3H, methyl proton); ^{13}C NMR (DMSO-d_6): δ 11.6, 71.6, 92.3, 97.7, 114.3, 115.7, 121.6, 127.5, 128.3, 133.5, 138.4, 140.5, 114.3, 160.5, 168.3, 201.3.

3n: Yield 62%. m.p.165°C. IR (KBr): 3190 (NH stretching), 3028 (C-H aromatic stretching), 2215 (C≡N sretching), 1680, 1700 (C=O Stretching), 1590 (C=N stretching) and 1468 cm^{-1} (C=C stretching), ^{1}H NMR (DMSO-d_6): δ 8.2 (s, NH proton), 7.4-6.8 (m, 8H, H=aromatic), 5.1 (s, 2H, OCH_2 proton), 2.8 (s, 3H, methyl proton); ^{13}C NMR (DMSO-d_6): δ 14.6, 71.6, 97.3, 98.7, 115.3, 117.3, 126.6, 128.5, 130.3, 133.8, 138.2, 140.5, 145.3, 156.5, 168.3).

3o: Yield 67%. m.p.165°C. IR (KBr): 3210 (NH stretching), 3015 (C-H aromatic stretching), 2205 (C≡N stretching), 1690, 1720 (C=O stretching), 1580 (C=N stretching), and 1465 cm−1 (C=C stretching); 1H NMR (DMSO-d6): δ 8.0 (s, NH proton), 7.4-7.0 (m, 8H, H-aromatic), 5.0 (s, 2H, Methyl proton); 3.8 (s, 3H, methoxy proton), 2.7 (s, 3H, methyl proton); 13C NMR (DMSO-d6): δ 14.5, 55.8, 71.6, 97.3, 98.7, 114.3, 115.7, 117.2, 126.5, 129.8, 132.4, 140.2, 145.5, 156.2, 159.0, 168.3.

3p: Yield 69%. m.p.177°C. IR (KBr): 3205 (NH stretching), 3005 (C-H aronatic stretching), 2200 (C≡N stretching), 1695, 1715 (C=O streteching),1590 (C=N stretching), and 1468 cm−1 (C=C stretching);

1H NMR (DMSO-d6): δ 8.0 (s, NH proton), 7.4-6.8 (m, 7H, H-aromatic), 5.0 (s, 2H, OCH2 proton), 3.8 (s, 6H, methoxy proton), 2.4 (s, 3H, Methyl proton); 13C NMR (DMSO-d6): δ 14.3, 56.8, 71.6, 97.2, 98.5, 108.8, 111.7, 115.4, 117.3, 121.8, 126.4, 130.2, 133.5, 140.7, 145.5, 149.3, 156.6, 159.0, 168.3.

Conclusion

In the present investigation, a series of new heterocycles have been synthesized and screened for their antifungal and antibacterial activity. The activity results reveal that the synthesized compounds possess moderate to good activity profiles. The insights gained in this study will be useful for development of newer anti-infective agents.

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