Synthesis and antimicrobial evaluation of new 1,4-dihydro-4-pyrazolylpyridines and 4-pyrazolylpyridines

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Abstract
Background: Dialkyl 1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylates (1,4-DHP) have now been recognized as vital drugs. Some of these derivatives such as amlodipine, felodipine, isradipine, etc. have been commercialized. In view of wide range of biological properties associated with 1,4-DHP and owing to the biological importance of the oxidation step of 1,4-DHP, we carried out the synthesis and antimicrobial evaluation of new diethyl 1,4-dihydro-2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl)pyridine-3,5-dicarboxylates (2a-g) and diethyl 2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl)pyridine-3,5-dicarboxylates (3a-g).

Results: Synthesis of a series of new diethyl 1,4-dihydro-2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl)pyridine-3,5-dicarboxylates (2a-g) has been accomplished by multicomponent cyclocondensation reaction of ethyl acetoacetate, 3-aryl-1-phenyl pyrazole-4-carboxaldehyde (1a-g) and ammonium acetate. The dihydropyridines 2a-g were smoothly converted to new diethyl 2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl)pyridine-3,5-dicarboxylates (3a-g) using HTIB ([Hydroxy(tosyloxy)iodo]benzene, Koser’s reagent) as the oxidizing agent. The antimicrobial studies of the title compounds, 2a-g & 3a-g, are also described.

Graphical abstract
Synthesis of a series of new diethyl 1,4-dihydro-2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl)pyridine-3,5-dicarboxylates (2a-g), their aromatization using HTIB ([Hydroxy(tosyloxy)iodo]benzene, Koser’s reagent) to afford new diethyl 2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl)pyridine-3,5-dicarboxylates (3a-g), and antimicrobial studies of 2a-g and 3a-g are reported.

Keywords: 1,4-Dihydro-4-pyrazolylpyridines, 4-pyrazolylpyridines, HTIB, oxidation, antibacterial activity, antifungal activity
antiatherosclerotic, hepatoprotective, antitumour, antimutagenic, geroprotective, antidiabetic and antiplatelet aggregation agents [5-9]. In a recent article, 4-[5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl]-dihydropyridines have been shown to possess significant antimicrobial activity [10].

In addition to above, aromatization of 1,4-DHP has also attracted considerable attention in recent years as Böcker has demonstrated that metabolism of the above drugs involves a cytochrome P-450 catalysed oxidation in the liver [11].

In view of wide range of biological properties associated with 1,4-DHP and the biological importance of the oxidation step of 1,4-DHP, we carried out the synthesis and antimicrobial evaluation of new diethyl 1,4-dihydro-2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl)pyridine-3,5-dicarboxylates (2a-g) and diethyl 2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl)pyrrole-3,5-dicarboxylates (3a-g).

Results and discussion
Chemistry
The synthetic scheme used for the synthesis of diethyl 1,4-dihydro-2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl)pyridine-3,5-dicarboxylates (2a-g) is outlined in Scheme 1. Synthesis of the title compounds 2a-g was accomplished by multicomponent cyclocondensation reaction of ethyl acetoacetate, 3-aryl-1-phenyl-pyrazole-carboxaldehyde (1a-g) and ammonium acetate in ethanol. The purity of the compounds was checked by TLC and elemental analysis. Spectral data (IR, 1H NMR (see additional files 1, 2, 3, 4 and 5, mass) of the newly synthesized compounds 2a-g were in full agreement with their proposed structures. The IR spectra of compounds 2a-g exhibited characteristic peak at approximately 1697 cm⁻¹ because of the presence of ester group (-COOEt), and peak due to -N-H stretch appeared in the region 3300-3317 cm⁻¹. In 1H NMR of compounds 2a-g, the protons of C₅-H and -NH of the dihydropyridine ring resonate between δ 5 and 6 ppm.

Hypervalent iodine (III) and iodine (V) reagents have been used as green-oxidants for a variety of substrates [12-17]. Amongst the various reagents used, HTIB has been reported to serve as a mild, fast and efficient oxidant for the aromatization of Hantzsch 1,4-dihydropyridines to pyridines [18].

Thus, diethyl 1,4-dihydro-2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl) pyridine-3,5-dicarboxylates (2a-g) were further oxidized by treating with HTIB (Koser’s reagent) in dichloromethane (CH₂Cl₂) at room temperature to afford new diethyl 2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl)pyridine-3,5-dicarboxylates (3a-g) in good-to-excellent yields (Scheme 1). All the compounds 3a-g were unambiguously characterized on the basis of their spectral (IR, 1H NMR (see additional files 6, 7, 8, 9, 10, 11 and 12) and mass) and elemental data.

A plausible mechanism for the oxidation of dihydropyridines 2 to 3 is outlined in Scheme 2. The probable mechanism might involve the attack by N-H on PhI(OH)OTs, leading to the formation of intermediate 4. The intermediate 4 finally loses a molecule of iodobenzene (PhI) to give 3.
Pharmacology
All the synthesized compounds, 2a-g and 3a-g, were evaluated in vitro for their antibacterial activity against two gram-positive bacterial strains, Staphylococcus aureus & Bacillus subtilis and two gram-negative bacteria, namely, Escherichia coli and Pseudomonas aeruginosa and their activities were compared with a well-known commercial antibiotic, ciprofloxacin. In addition, the synthesized compounds were also evaluated for their antifungal activity against Aspergillus niger & Aspergillus flavus and their antifungal potential was compared to reference drug, fluconazole. Compounds possessed variable antibacterial activities against Gram-positive bacteria, S. aureus, B. subtilis. However, the compounds in this series were not effective against any Gram-negative bacteria, neither against E. coli nor against P. aeruginosa. Results of antibacterial evaluation are summarized in Table 1.

Compounds 2a-g and 3a-g showed zones of inhibition ranging between 14 and 20 mm. On the basis of the zones of inhibition produced against the test bacteria, compounds 2b and 3a were found to be most effective against S. aureus, showing the maximum zones of inhibition at 18 and 20 mm, respectively, and compounds 3a, 3e and 3g were found to be most effective against B. subtilis. The remaining compounds showed fair activity against gram-positive bacterial strains (Table 1). In the whole series, the MIC (minimum inhibitory concentration) values of various tested chemical compounds ranged between 64 and 256 μg/mL against gram-positive bacteria. Compounds 2b and 3a displayed good antibacterial activity with the lowest MIC value, 64 μg/mL against S. aureus. Three compounds, 3a, 3e and 3g possessed antibacterial activity with MIC value of 64 μg/mL against B. subtilis (Table 2).

Amongst the synthesized compounds, six compounds 2a, 2d, 2g, 3a, 3c and 3d showed more than 50% mycelial growth inhibition against A. niger whereas compounds, 2a, 2e, 2f, 3a, 3d and 3f were found to be active against A. flavus (Table 3). From the overall result it is evident that compound 3a could be identified as the most biologically active member within this study with good antifungal and antibacterial profile.

Conclusions
A series of diethyl 1,4-dihydro-2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl)pyridine-3,5-dicarboxylates (2a-g) and diethyl 2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl)pyridine-3,5-dicarboxylates (3a-g) has been synthesized with the hope of discovering new structure leads. Compounds 2b and 3a were found to be most effective against S. aureus showing the maximum zones of inhibition of 18 and 20 mm, respectively, and compounds 3a, 3e and 3g were found to be most effective against B. subtilis. Moreover, six compounds 2a, 2d, 2g, 3a, 3c and 3d showed more than 50% mycelial growth inhibition against A. niger whereas compounds, 2a, 2e, 2f, 3a, 3d and 3f were found to be active against A. flavus; however, no compound was found superior over the reference drug.

### Table 1 Antibacterial activity of chemical compounds through agar well diffusion method

| Compound | Diameter of growth of inhibition zone (mm) | S. aureus | Bacillus Subtilis | E. coli | P. aeruginosa |
|----------|------------------------------------------|-----------|------------------|--------|--------------|
| 2a       | 15.6                                     | 16.3      | -                | -      | -            |
| 2b       | 186                                      | 156       | -                | -      | -            |
| 2c       | 163                                      | 156       | -                | -      | -            |
| 2d       | 176                                      | 163       | -                | -      | -            |
| 2e       | 16                                       | 15.3      | -                | -      | -            |
| 2f       | 156                                      | 14        | -                | -      | -            |
| 2g       | 15.3                                     | 16.6      | -                | -      | -            |
| 3a       | 20                                       | 193       | -                | -      | -            |
| 3b       | 15                                       | 15.6      | -                | -      | -            |
| 3c       | 15.3                                     | 166       | -                | -      | -            |
| 3d       | 166                                      | 146       | -                | -      | -            |
| 3e       | 166                                      | 18.3      | -                | -      | -            |
| 3f       | 15.3                                     | 166       | -                | -      | -            |
| 3g       | 163                                      | 18.6      | -                | -      | -            |
| Ciprofloxacin | 27.6                          | 26.3      | 25.0             | 25.3   |              |

*No activity

*Values, including diameter of the well (8 mm), are means of three replicates

### Table 2 MIC (in μg/mL) of compounds obtained using macrodilution method

| Compound | S. aureus | Bacillus Subtilis | Compound | S. aureus | Bacillus Subtilis |
|----------|-----------|------------------|----------|-----------|------------------|
| 2a       | 128       | 128              | 3a       | 64        | 64               |
| 2b       | 64        | 128              | 3b       | 128       | 128              |
| 2c       | 128       | 128              | 3c       | 128       | 128              |
| 2d       | 128       | 128              | 3d       | 128       | 256              |
| 2e       | 128       | 128              | 3e       | 128       | 64               |
| 2f       | 128       | 256              | 3f       | 128       | 128              |
| 2g       | 128       | 128              | 3g       | 128       | 64               |
| Ciprofloxacin | 5            | 5                 |          |           |                  |
Finally, compound 3a could be identified as the most biologically active member within this study with an interesting antibacterial and antifungal profile.

**Experimental**

**Chemical synthesis**

Melting points were taken in open capillaries and are uncorrected. IR spectra were recorded on Perkin-Elmer IR spectrophotometer. The 1H NMR spectra were recorded on Brucker 300 MHz instrument. The chemical shifts are expressed in ppm units downfield from an internal TMS standard. 3-Aryl-1-phenylpyrazole-4-carboxaldehydes (1a-h), needed for the present study, were synthesized by Vilsmeier-Haack reaction according to the literature procedure [19].

**Synthesis of diethyl 1,4-dihydro-2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl) pyridine-3,5-dicarboxylates (2a-g)**

General procedure: A mixture of appropriate 3-aryl-1-phenylpyrazole-4-carboxaldehyde (1, 10 mmol), ethyl acetoacetate (20 mmol) and ammonium acetate (22 mmol) in ethanol was allowed to reflux on water bath for 25-30 min. After completion of the reaction, the reaction mixture was cooled to room temperature to give pure diethyl 1,4-dihydro-2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl) pyridine-3,5-dicarboxylates (2a-g).

**Characterization data of diethyl 1,4-dihydro-2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl) pyridine-3,5-dicarboxylates (2a-g)**

| Compound | A. niger | A. flavus | Compound | A. niger | A. flavus |
|----------|----------|-----------|----------|----------|-----------|
| 2a       | 51.1     | 58.8      | 3a       | 52.5     | 51.1      |
| 2b       | 50       | 44.4      | 3b       | 48.8     | 45.5      |
| 2c       | 48.8     | 50        | 3c       | 51.1     | 50        |
| 2d       | 52.5     | 48.8      | 3d       | 55.5     | 52.5      |
| 2e       | 45.5     | 51.1      | 3e       | 45.5     | 44.4      |
| 2f       | 47.7     | 52.5      | 3f       | 50       | 51.1      |
| 2g       | 51.1     | 48.8      | 3g       | 48.8     | 44.4      |

Fluconazole 81.1 77.7

Table 3 Antifungal activity of chemical compounds through poisoned food method (mycelial growth inhibition) (%)

Finally, compound 3a could be identified as the most biologically active member within this study with an interesting antibacterial and antifungal profile.

**Experimental**

**Chemical synthesis**

Melting points were taken in open capillaries and are uncorrected. IR spectra were recorded on Perkin-Elmer IR spectrophotometer. The 1H NMR spectra were recorded on Brucker 300 MHz instrument. The chemical shifts are expressed in ppm units downfield from an internal TMS standard. 3-Aryl-1-phenylpyrazole-4-carboxaldehydes (1a-h), needed for the present study, were synthesized by Vilsmeier-Haack reaction according to the literature procedure [19].

**Synthesis of diethyl 1,4-dihydro-2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl) pyridine-3,5-dicarboxylates (2a-g)**

General procedure: A mixture of appropriate 3-aryl-1-phenylpyrazole-4-carboxaldehyde (1, 10 mmol), ethyl acetoacetate (20 mmol) and ammonium acetate (22 mmol) in ethanol was allowed to reflux on water bath for 25-30 min. After completion of the reaction, the reaction mixture was cooled to room temperature to give pure diethyl 1,4-dihydro-2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl) pyridine-3,5-dicarboxylates (2a-g).

**Characterization data of diethyl 1,4-dihydro-2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl) pyridine-3,5-dicarboxylates (2a-g)**

| Compound | A. niger | A. flavus | Compound | A. niger | A. flavus |
|----------|----------|-----------|----------|----------|-----------|
| 2a       | 51.1     | 58.8      | 3a       | 52.5     | 51.1      |
| 2b       | 50       | 44.4      | 3b       | 48.8     | 45.5      |
| 2c       | 48.8     | 50        | 3c       | 51.1     | 50        |
| 2d       | 52.5     | 48.8      | 3d       | 55.5     | 52.5      |
| 2e       | 45.5     | 51.1      | 3e       | 45.5     | 44.4      |
| 2f       | 47.7     | 52.5      | 3f       | 50       | 51.1      |
| 2g       | 51.1     | 48.8      | 3g       | 48.8     | 44.4      |

Fluconazole 81.1 77.7
HTIB (12 mmol) and the mixture was stirred at room temperature. The progress of the reaction was monitored by TLC. Reaction was completed in 4-5 min. After the completion of reaction, the reaction mixture was washed with aqueous NaHCO₃ solution. Organic phase was then separated, dried and concentrated on water bath. Crude product, thus obtained, was purified by silica gel column chromatography using Pet ether/ EtOAc (20:1) as eluent to afford pure diethyl 2,6-dimethyl-4-(3-aryl-1-phenyl-4-pyrazolyl)pyridine-3,5-dicarboxylates (3a-g).

**Characterization data of dimethyl 2,6-dimethyl-4-pyrazolylpyridine-3,5-dicarb oxylates (3a-g)**

**3a:** M.p.: 111°C; yield: 68%; IR (νmax cm⁻¹, KBr): 1736, 1233; ¹H NMR (CDCl₃, δ, ppm): 0.911-0.997 (t, 6 H), 2.613 (s, 6 H), 3.910-4.07 (m, 4 H), 7.110-7.313 (m, 4 H), 7.817 (s, 1 H), 7.581-7.690 (m, 6 H); mass: m/z 470.20 (M⁺ + 1, 100%).

Anal. Calcd for C₂₈H₂₆N₃O₄: C 61.31, H 4.79, N 7.69.

**3b:** M.p.: 105°C; yield: 69%; IR (νmax cm⁻¹, KBr): 1720, 1234; ¹H NMR (CDCl₃, δ, ppm): 0.913-0.960 (t, 6 H), 2.611 (s, 6 H), 2.468 (s, 3 H), 3.923-4.072 (q, 4 H), 6.839-6.868 (d, 2H, J = 8.7 Hz), 7.280-7.501 (m, 5 H), 7.732-7.759 (d, 2 H, J = 8.7 Hz), 7.905 (s, 1 H); mass: m/z 484.40 (M⁺ + 1, 100%).

Anal. Calcd for C₂₉H₂₉N₃O₅: C 72.05, H 6.00, N 8.70; found: C 72.68, H 6.05, N 8.70.

**3c:** M.p.: 136°C; yield: 72%; IR (νmax cm⁻¹, KBr): 1740, 1034; ¹H NMR (CDCl₃, δ, ppm): 0.913-0.998 (t, 6 H), 2.612 (s, 6 H), 3.808 (s, 3 H), 3.924-4.08 (q, 4 H), 6.835-6.864 (d, 2 H, J = 8.7 Hz), 7.311-7.501 (m, 5 H), 7.732-7.759 (d, 2 H, J = 8.7 Hz), 7.905 (s, 1 H); mass: m/z 500.29 (M⁺ + 1, 100%).

Anal. Calcd for C₂₉H₂₉N₄O₆: C 64.37, H 4.98, N 10.73; found: C 64.34, H 5.08, N 10.87.

**3d:** M.p.: 121°C; yield: 70%; IR (νmax cm⁻¹, KBr): 1728, 1236, 1037; ¹H NMR (CDCl₃, δ, ppm): 0.924-0.971 (t, 6 H), 2.615 (s, 6 H), 3.905-4.105 (q, 4 H), 6.987-7.044 (m, 2 H), 7.280-7.365 (m, 1 H), 7.469-7.622 (m, 4 H), 7.733-7.759 (d, 2 H, J = 7.8 Hz), 7.923 (s, 1 H); mass: m/z 488.36 (M⁺ + 1, 100%).

Anal. Calcd for C₂₉H₂₉N₄O₇: C 69.73, H 5.81, N 8.41; found: C 69.71, H 5.83, N 8.40.

**3e:** M.p.: 101-102°C, lit [20] M.p.: 101-102°C; yield: 65%.

**3f:** M.p.: 115°C; yield: 70%; IR (νmax cm⁻¹, KBr): 1734, 1030; ¹H NMR (CDCl₃, δ, ppm): 0.940-0.962 (t, 6 H), 2.617 (s, 6 H), 3.957-4.039 (q, 4 H), 7.200-7.495 (m, 7 H), 7.732-7.756 (d, 2 H, J = 7.2 Hz), 7.921 (s, 1 H); mass: m/z 548.20, 550.20.

Anal. Calcd for C₂₈H₂₆N₃O₄Br: C 61.42, H 4.75, N 7.68; found: C 61.31, H 4.79, N 7.69.

**3g:** M.p.: 172°C; yield: 68%; IR (νmax cm⁻¹, KBr): 1728, 1234, 1034; ¹H NMR (CDCl₃, δ, ppm): 0.895-0.941 (t, 6 H), 2.632 (s, 6 H), 3.923-4.039 (m, 4 H), 7.279-7.410 (m, 3 H), 7.499-7.769 (m, 4 H), 7.960 (s, 1 H), 8.178-8.207 (d, 2 H, J = 7.5 Hz); mass: m/z 515.26 (M⁺ + 1, 100%).

Anal. Calcd for C₂₈H₂₆N₄O₅: C 65.34, H 5.08, N 10.73; found: C 65.34, H 5.08, N 10.87.

**Pharmacology**

**Test microorganisms**

Total six microbial strains were selected on the basis of their clinical importance in causing diseases in humans. Two Gram-positive bacteria (S. aureus MTCC 96 and B. subtilis MTCC 121); two Gram-negative bacteria (E. coli MTCC 1652 and P. aeruginosa MTCC 741) and two fungi (A. niger and A. flavus) the ear pathogens isolated from the patients of Kurukshetra [21], were used in the present study for the evaluation of antimicrobial activities of the chemical compounds. All the cultures were procured from Microbial Type Culture Collection (MTCC), IMTECH, Chandigarh. The bacteria and fungi were subcultured on Nutrient agar and Sabouraud's dextrose agar (SDA), respectively, and incubated aerobically at 37°C.

**In vitro antibacterial activity**

The antibacterial activities of compounds, 2a-g and 3a-g, were evaluated by the agar well diffusion method. All the cultures were adjusted to 0.5 McFarland standard, which is visually comparable to a microbial suspension of approximately 1.5 × 10⁸ cfu/mL. 20 mL of Mueller Hinton agar medium was poured into each Petri plate, and the agar plates were swabbed with 100 μL inocula of each test bacterium and kept for 15 min for adsorption. Using sterile cork borer of 8-mm diameter, wells were bored into the seeded agar plates, and these were then loaded with a 100 μL volume with concentration of 2.0 mg/mL of each compound reconstituted in the dimethyl sulfoxide (DMSO). All the plates were incubated at 37°C for 24 h. Antibacterial activity of each compound was evaluated by measuring the zone of growth inhibition against the test organisms with zone reader (Hi Antibiotic zone scale). DMSO was used as a negative control whereas ciprofloxacin was used as a positive control. This procedure was performed in three replicate plates for each organism [22,23].

**Determination of minimum inhibitory concentration**

Minimum inhibitory concentration (MIC) is the lowest concentration of an antimicrobial compound that will inhibit the visible growth of a microorganism after overnight incubation. MIC of the compounds against bacterial strains was tested through a macrodilution tube
method as recommended by NCCLS [24]. In this method, various test concentrations of chemically synthesized compounds were made from 256 to 1 μg/mL in sterile tubes, 1–10. 100 μL sterile Mueller Hinton Broth was poured in each sterile tube, and followed by addition of 200 μL test compound in tube 1. Twofold serial dilutions were carried out from tubes 1 to 10, and excess broth (100 μL) was discarded from the tube 10. To each tube, 100 μL of standard inoculum (1.5 × 10^8 cfu/mL) was added. Ciprofloxacin was used as control. Turbidity was observed after incubating the inoculated tubes at 37°C for 24 h.

**In vitro antifungal activity**

The antifungal activity of the synthesized chemical compounds was evaluated by poison food technique. The moulds were grown on SDA at 25°C for 7 days and used as inocula. 15 mL of molten SDA (45°C) was poisoned by the addition of 100 μL volume of each compound having concentration of 4.0 mg/mL, reconstituted in the DMSO, poured into a sterile Petri plate and allowed to solidify at room temperature. The solidified poisoned agar plates were inoculated at the centre with fungal plugs (8-mm diameter), obtained from the actively growing colony and incubated at 25°C for 7 days. DMSO was used as the negative control whereas fluconazole was used as the positive control. The experiments were performed in triplicates. Diameter of the fungal colonies was measured and expressed as percent mycelial inhibition determined by applying the following formula [25]:

\[
\text{Inhibition of mycelial growth} \% = \frac{(dc - dt)}{dc} \times 100
\]

where \( dc \) is the average diameter of fungal colony in negative control plates, and \( dt \) the average diameter of fungal colony in experimental plates.

**Additional material**

- Additional file 1: 1HNMR spectrum of compound 2b
- Additional file 2: 1HNMR spectrum of compound 2c
- Additional file 3: 1HNMR spectrum of compound 2e
- Additional file 4: 1HNMR spectrum of compound 2f
- Additional file 5: 1HNMR spectrum of compound 2g
- Additional file 6: 1HNMR spectrum of compound 3a
- Additional file 7: 1HNMR spectrum of compound 3b
- Additional file 8: 1HNMR spectrum of compound 3c
- Additional file 9: 1HNMR spectrum of compound 3d
- Additional file 10: 1HNMR spectrum of compound 3e
- Additional file 11: 1HNMR spectrum of compound 3f
- Additional file 12: 1HNMR spectrum of compound 3g

**Abbreviations**

- 1,4-DHP: dialkyl 1,4-dihydropyridine-2,6-dicarboxylates
- DMSO: dimethylsulfoxide
- HTPB: hydroxy (tosyloxy)iodobenzene
- MTC: microfungal type culture collection
- SDA: Sabouraud dextrose agar

**Acknowledgements**

We are thankful to the CSIR, New Delhi (Grant no. CSIR 01 (2816)/07/EMR-II) for providing financial assistance to accomplish this research. The authors are also grateful to the CSIR for the award of junior research fellowship to Khalid Hussain.

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**Competing interests**

The authors declare that they have no competing interests.

**Received:** 21 March 2011  **Accepted:** 3 August 2011  **Published:** 3 August 2011

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Cite this article as: Prakash et al.: Synthesis and antimicrobial evaluation of new 1,4-dihydro-4-pyrazolylpyridines and 4-pyrazolylpyridines. Organic and Medicinal Chemistry Letters 2011, 1:5.