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SHORT COMMUNICATION

Discovery of novel methanone derivatives acting as antimycobacterial agents

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Abstract

A series of pyrazoline derivatives were synthesized and *in vitro* activity against *Mycobacterium tuberculosis* H37Rv was carried out. Among the synthesized compounds, compounds (**4d**) and (**4f**) 4-aminophenyl-3-(3,4-dimethoxyphenyl)-6,7-dimethoxy-2,3,3a,4-tetrahydroindeno[1,2-*c*]pyrazol-2-ylmethanone and 4-aminophenyl-6,7-dimethoxy-3-phenyl-2,3,3a,4-tetrahydroindeno[1,2-*c*]pyrazol-2-ylmethanone were found to be the most active agent against *M. tuberculosis* H37Rv with a minimum inhibitory concentration of 10 µg/mL.

Keywords: Mycobacterial agents, pyrazoline, indanone, *Mycobacterium tuberculosis*

Introduction

Mycobacterium tuberculosis (MTB) is a genus of one of the major health issues worldwide, that is, tuberculosis (TB)[1]. According to WHO statistical reports, about 1.3 million people died from TB in 2008 and a new person is infected every second in the world[1]. Until 50 years ago, there were no medicines available for the treatment of TB. Streptomycin was the first antibiotic used in TB, and nowadays the standard TB treatment includes rifampicin, isoniazid, ethambutol, and pyrazinamide[2]. These are responsible for the development of multidrug-resistant TB (MDR-TB, i.e. resistant to both isoniazid and rifampicin) and more recently of extremely drug-resistant TB (XDR-TB, i.e. MDR-TB also resistant to fluoroquinolones and to one of the following second-line anti-TB injectable drugs: kanamycin, capreomycin, or amikacin), which are nearly untreatable, especially in HIV-infected patients[3–5]. A medication for TB still remains as an unresolved problem and the need of new potent drugs that are highly effective in eradicating the disease deep.

This need lead us to focus our research in the development of novel drugs for TB. Literature survey of novel chemotherapeutic agents reveals that the substituted pyrazoline derivatives are proved to be active against many mycobacterial species[3–15]. In the present work, we have synthesized novel heterocyclic molecules and tested the compounds against the tubercle bacterium. Two of the compounds showed a moderate activity against MTB.

Results and discussion

Chemistry

Pyrazoline derivatives **4a**–**4u** described in this study are shown in Table 1 and a reaction sequence for the preparation is outlined in Scheme 1. In the initial step, 5,6-dimethoxy-2-[(*E*)-1-phenylmethylidene]-1-indanone

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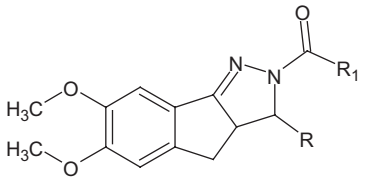
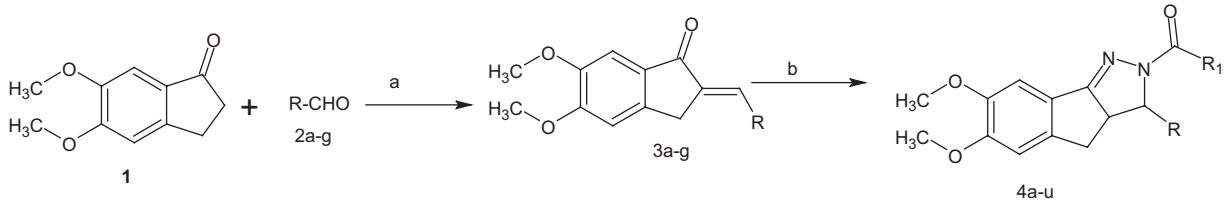
Table 1. Physicochemical characteristics and antimycobacterial activity of compounds **4a**–**4u**.



4a-u

Compound	R	R_1	Yield (%)	Melting point (°C)	MIC-MTB[a] (μg/mL)
4a	Pyridyl-	4-Aminophenyl	84	144	>10.0
4b	2-Chlorophenyl-	4-Aminophenyl	60	162	>10.0
4c	4-Fluorophenyl-	4-Aminophenyl	67	143	>10.0
4d	3,4-Dimethoxyphenyl-	4-Aminophenyl	72	141	10.0
4e	4-Methoxyphenyl-	4-Aminophenyl	80	128	>10.0
4f	Phenyl-	4-Aminophenyl	62	103	10.0
4g	4-Cyanophenyl-	4-Aminophenyl	71	176	>10.0
4h	Pyridyl-	3,4-Dimethoxyphenyl-	66	145	>10.0
4i	2-Chlorophenyl-	3,4-Dimethoxyphenyl-	67	164	>10.0
4j	4-Fluorophenyl-	3,4-Dimethoxyphenyl-	72	184	>10.0
4k	3,4-Dimethoxyphenyl-	3,4-Dimethoxyphenyl-	80	198	>10.0
4l	4-Methoxyphenyl-	3,4-Dimethoxyphenyl-	80	168	>10.0
4m	Phenyl-	3,4-Dimethoxyphenyl-	74	144	>10.0
4n	4-Cyanophenyl-	3,4-Dimethoxyphenyl-	68	162	>10.0
4o	Pyridyl-	4-Methoxyphenyl-	89	153	>10.0
4p	2-Chlorophenyl-	4-Methoxyphenyl-	74	151	>10.0
4q	4-Fluorophenyl-	4-Methoxyphenyl-	64	128	>10.0
4r	3,4-Dimethoxyphenyl-	4-Methoxyphenyl-	78	153	>10.0
4s	4-Methoxyphenyl-	4-Methoxyphenyl-	92	166	>10.0
4t	Phenyl-	4-Methoxyphenyl-	67	165	>10.0
4u	4-Cyanophenyl-	4-Methoxyphenyl-	70	174	>10.0

[a]Mycobacterium tuberculosis H37Rv.



Scheme 1. Protocol for synthesis. (a) Reagents: NaOH/EtOH and (b) $R_1CONHNH_2$.

analogues were synthesized by condensing 5,6-dimethoxy-1-indanone with appropriate aldehyde in dilute methanolic sodium hydroxide solution at room temperature. The product 5,6-dimethoxy-2-[(*E*)-1-phenylmethylidene]-1-indanone was then treated with appropriate acid hydrazide in the presence of glacial acetic acid to get methanone derivatives in 62–84% yield after recrystallization with ethanol. The purity of the compounds was checked by thin-layer chromatography (TLC) and elemental analyses. Both analytical and spectral data (^{1}H NMR, IR) of all the synthesized compounds were in full agreement with the proposed structures. The elemental analysis results were within ±0.4% of the theoretical values.

Antimycobacterial activity

Among the 12 compounds synthesized, most of the compounds were found below-to-moderate active with minimum inhibitory concentration of <10 μg/mL against MTB. Compounds with electron-donating groups substituted on the phenyl ring were shown to have higher activity potentials. Among the 21 newly synthesized compounds, compounds (**4d**) and (**4f**), 4-aminophenyl-3-(3,4-dimethoxyphenyl)-6,7-dimethoxy-2,3,3a,4-tetrahydroindeno[1,2-*c*] pyrazol-2-ylmethanone and 4-aminophenyl-6,7-dimethoxy-3-phenyl-2,3,3a,4-tetrahydroindeno[1,2-*c*] pyrazol-2-ylmethanone, were found to have highest activity against MTB H37Rv. The minimum inhibitory concentration of this compound (**4d**) and (**4f**) were found to be 10 μg/mL. However, the compounds substituted with electron-withdrawing groups such as 4-cyanophenyl, 2-chlorophenyl, 4-flurophenyl, and pyridyl produced low inhibitory activity against MTB. On the other hand, the compounds like 4-methoxyphenyl

also showed low antitubercular activity. Out of all the substitutions of the phenyl ring, the results indicate that the amino with 3,4-dimethoxyphenyl substitution and amino with phenyl substitution cause remarkable improvement in antimycobacterial activity.

The present investigation describes the synthesis of pyrazoline analogues and evaluation of antimycobacterial activity. The heterocycles synthesized in the present work display low-to-moderate activity against MTB. The synthesis and screening for biological activity of further series of compounds and molecular docking simulation for possible action on *InhA* are currently under investigation.

Experimental

The entire chemicals were supplied by E. Merck (India) and S.D. Fine Chemicals (India). Melting points were determined by open tube capillary method and are uncorrected. Purity of the compounds was checked on TLC plates (silica gel G) in the solvent system toluene–ethyl formate–formic acid (5:4:1) and benzene–methanol (8:2), the spots were located under iodine vapours or UV light. IR spectra were obtained on a Perkin-Elmer 1720 FT-IR spectrometer (KBr pellets). ^{1}H NMR spectra were recorded or a Bruker AC 300 MHz spectrometer using TMS as internal standard in DMSO/$CDCl_3$. Mass spectra were recorded on a Bruker Esquire LCMS using ESI and elemental analyses were performed on a Carlo Erba 1106 elemental analyzer. Column chromatography was performed on silica gel (230–400 mesh) using petroleum ether–ethyl acetate as eluent.

General procedure

Synthesis of 2-[(E)-1-(substituted phenyl)methylidene]-5, 6-dimethoxy-1-indanone (3a–3g)[10,11]

5,6-Dimethoxy-1-indanone (1.92 g, 0.01 mol), appropriate aldehyde (1.02 g, 0.01 mol), dissolved in ethanol and sodium hydroxide (30%, 5 mL) with 10 mL of petroleum ether, was stirred under room temperature for 4 h. The resulting solution allowed to stand overnight and then poured into cold water and neutralize with HCl. The solid separate was filtered, dried and purified by ethanol.

General procedure

Synthesis of pyrazol-2-ylmethanone

To a 2-[(*E*)-1-(substituted phenyl)methylidene]-5,6-dimethoxy-1-indanone (**3a**–**3o**) (0.001 mol) in 15 mL of glacial acetic acid, 0.002 mol of appropriate aromatic acid hydrazide was added and the reaction mixture was refluxed for 15 h and cooled. Excess of solvent was removed under reduced pressure and the reaction mixture was cooled poured on to crushed ice (20 g). The product obtained was filtered, washed with water, and recrystallized from methanol.

4-Aminophenyl-6,7-dimethoxy-3-(4-pyridyl)-2,3,3a, 4-tetrahydroindeno[1,2-c]pyrazol-2-ylmethanone (4a) IR: (KBr) cm^{-1}: 3320 (NH_2), 3042 (CH), 1590 (C=N), 1680 (C=O), 1320 (C-N). ^{1}H NMR (DMSO-d_6) ppm: 2.48 (2H, m, CH_2), 3.09 (1H, m, CH), 3.82 (6H, s, OCH_3), 5.16 (1H, d, CH), 5.4 (2H, s, CO=NH_2), 6.6–7.5 (6H, m, aromatic), 6.6–7.5 (4H, m, pyridine). EI-MS (*m*/*z*): 415 (M^{+1}); Cal/Ana: [C (69.55) 69.54, H (5.35) 5.37, N (13.52) 13.54].

4-Aminophenyl-3-(2-chlorophenyl)-6,7-dimethoxy-2,3,3a, 4-tetrahydroindeno[1,2-c]pyrazol-2-ylmethanone (4b) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N), 786 (C-Cl). ^{1}H NMR (DMSO-d_6) ppm: 2.38 (2H, m, CH_2), 3.81 (6H, s, OCH_3), 3.08 (1H, m, CH), 5.16 (1H, d, CH), 5.4 (2H, s, CO=NH_2), 6.6–7.75 (10H, m, aromatic), EI-MS (*m*/*z*): 448 (M^{+1}); Cal/Ana: [C (67.04) 67.08, H (4.95) 4.93, N (9.38) 9.37].

4-Aminophenyl-3-(4-fluorophenyl)-6,7-dimethoxy-2,3,3a, 4-tetrahydroindeno[1,2-c]pyrazol-2-ylmethanone (4c) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N), 776 (C-F). ^{1}H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (6H, s, OCH_3), 3.09 (1H, m, CH), 5.16 (1H, d, CH), 5.4 (2H, s, CO=NH_2), 6.6–7.65 (10H, m, aromatic), EI-MS (*m*/*z*): 432 (M^{-1}); Cal/Ana: [C (69.59) 69.57, H (5.14) 5.12, N (9.74) 9.72].

4-Aminophenyl-3-(3,4-dimethoxyphenyl)-6,7-dimethoxy-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-ylmethanone (4d) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N). ^{1}H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (12H, s, OCH_3), 3.09 (1H, m, CH), 5.16 (1H, d, CH), 5.4 (2H, s, CO=NH_2), 6.6–7.65 (9H, m, aromatic), EI-MS (*m*/*z*): 474 (M^{+1}); Cal/Ana: [C (68.48) 68.47, H (5.75) 5.72, N (8.87) 8.85].

4-Aminophenyl-6,7-dimethoxy-3-(4-methoxyphenyl)-2,3,3a, 4-tetrahydroindeno[1,2-c]pyrazol-2-ylmethanone(4e) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N). ^{1}H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (9H, s, OCH_3), 3.09 (1H, m, CH), 5.16 (1H, d, CH), 6.4 (2H, s, CO=NH_2), 6.6–7.65 (10H, m, aromatic), EI-MS (*m*/*z*): 444 (M^{+1}); Cal/Ana: [C (70.41) 70.42, H (5.68) 5.67, N (9.47) 9.48].

4-Aminophenyl-6,7-dimethoxy-3-phenyl-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-ylmethanone (4f) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N). ^{1}H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (6H, s, OCH_3), 3.09 (1H, m, CH), 5.16 (1H, d, CH), 6.4 (2H, s, CO=NH_2), 6.6–7.65 (11H, m, aromatic), EI-MS (*m*/*z*): 415 (M^{+2}); Cal/Ana: [C (72.62) 72.64, H (5.61) 5.62, N (10.16) 10.18].

4-[2-(4-Aminobenzoyl)-6,7-dimethoxy-2,3,3a, 4-tetrahydroindeno[1,2-c]pyrazol-3-yl]benzonitrile(4g) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N). ^{1}H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (6H, s, OCH_3), 3.09 (1H, m, CH), 5.16 (1H, d, CH), 6.4 (2H, s, CO=NH_2), 6.6–7.65 (10H, m, aromatic),

EI-MS (*m/z*): 439 (M^{+1}); Cal/Ana: [C (71.22) 71.20, H (5.06) 5.07, N (12.78) 12.80].

3,4-Dimethoxyphenyl-6,7-dimethoxy-3-(4-pyridyl)-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-ylmethanone (4h) IR: (KBr) cm^{-1}: 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N), 788 (C-Cl). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (12H, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6–7.25 (5H, m, aromatic), 7.6–8.35 (4H, m, pyridine), EI-MS (*m/z*): 460 (M^{+1}); Cal/Ana: [C (67.96) 67.98, H (5.48) 5.46, N (9.14) 9.16].

3-(2-Chlorophenyl)-6,7-dimethoxy-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-yl-3,4-dimethoxyphenylmethanone (4i) IR: (KBr) cm^{-1}: 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N), 788 (C-Cl). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (12H, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6–7.55 (9H, m, aromatic), EI-MS (*m/z*): 493 (M^{+1}); Cal/Ana: [C (65.79) 65.80, H (5.11) 5.13, N (5.68) 5.66].

3,4-Dimethoxyphenyl-3-(4-fluorophenyl)-6,7-dimethoxy-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-ylmethanone (4j) IR: (KBr) cm^{-1}: 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N), 770 (C-F). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (12H, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6–7.55 (9H, m, aromatic), EI-MS (*m/z*): 477 (M^{+1}); Cal/Ana: [C (68.06) 68.08, H (5.29) 5.27, N (5.88) 5.86].

3,4-Dimethoxyphenyl-3-(3,4-dimethoxyphenyl)-6,7-dimethoxy-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-ylmethanone (4k) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (18H, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6–7.55 (8H, m, aromatic), EI-MS (*m/z*): 519 (M^{+1}); Cal/Ana: [C (67.17) 67.18, H (5.83) 5.84, N (5.40) 5.41].

6,7-Dimethoxy-3-(4-methoxyphenyl)-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-yl-3,4-dimethoxyphenylmethanone (4l) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (15H, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6–7.55 (9H, m, aromatic), EI-MS (*m/z*): 489 (M^{+1}); Cal/Ana: [C (68.84) 68.82, H (5.78) 5.76, N (5.73) 5.71].

3,4-Dimethoxyphenyl-6,7-dimethoxy-3-phenyl-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-ylmethanone (4m) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (12H, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6–7.55 (10H, m, aromatic), EI-MS (*m/z*): 459 (M^{+1}); Cal/Ana: [C (70.73) 70.72, H (5.72) 5.73, N (6.11) 6.13].

4-[2-(3,4-Dimethoxybenzoyl)-6,7-dimethoxy-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-3-yl]benzonitrile (4n) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (12H, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6-7.55 (9H, m, aromatic), EI-MS (*m/z*): 484 (M^{+1}); Cal/Ana: [C (69.55) 69.54, H (5.21) 5.22, N (8.69) 8.67].

6,7-Dimethoxy-3-(4-pyridyl)-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-yl-3-methoxyphenylmethanone (4o) IR: (KBr) cm^{-1}: 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N), 788 (C-Cl). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (9H, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6–7.25 (6H, m, aromatic), 7.6–8.45 (4H, m, pyridine), EI-MS (*m/z*): 430 (M^{+1}); Cal/Ana: [C (69.92) 69.94, H (5.40) 5.42, N (9.78) 9.76].

3-(2-Chlorophenyl)-6,7-dimethoxy-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-yl-3-methoxyphenylmethanone (4p) IR: (KBr) cm^{-1}: 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N), 788 (C-Cl). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (9H, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6–7.55 (10H, m, aromatic), EI-MS (*m/z*): 463 (M^{+1}); Cal/Ana: [C (67.46) 67.48, H (5.01) 5.03, N (6.05) 6.06].

3-(4-Fluorophenyl)-6,7-dimethoxy-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-yl-3-methoxyphenylmethanone (4q) IR: (KBr) cm^{-1}: 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N), 770 (C-F). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (9H, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6–7.55 (10H, m, aromatic), EI-MS (*m/z*): 447 (M^{+1}); Cal/Ana: [C (69.94) 69.02, H (5.19) 5.17, N (6.27) 6.26].

3-(3,4-Dimethoxyphenyl)-6,7-dimethoxy-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-yl-3-methoxyphenylmethanone (4r) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (15, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6–7.55 (9H, m, aromatic), EI-MS (*m/z*): 489 (M^{+1}); Cal/Ana: [C (68.84) 68.86, H (5.78) 5.80, N (5.73) 5.75].

6,7-Dimethoxy-3-(4-methoxyphenyl)-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-yl-3-methoxyphenylmethanone (4s) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (12H, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6–7.55 (10H, m, aromatic), EI-MS (*m/z*): 459 (M^{+1}); Cal/Ana: [C (70.73) 70.75, H (5.72) 5.74, N (6.11) 6.13].

6,7-Dimethoxy-3-phenyl-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-2-yl-3-methoxyphenyl methanone (4t) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (9H, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6–7.55 (11H, m, aromatic), EI-MS (*m/z*): 429 (M^{+1}); Cal/Ana: [C (72.88) 72.86, H (5.65) 5.63, N (6.54) 6.53].

4-[6,7-Dimethoxy-2-(3-methoxybenzoyl)-2,3,3a,4-tetrahydroindeno[1,2-c]pyrazol-3-yl]benzonitrile (4u) IR: (KBr) cm^{-1}: 3322 (NH_2), 3040 (CH), 1592 (C=N), 1672 (C=O), 1320 (C-N). ^1H NMR (DMSO-d_6) ppm: 2.36 (2H, m, CH_2), 3.82 (9H, s, OCH_3), 3.09 (1H, m, CH), 5.16-(1H, d, CH), 6.6–7.55 (10H, m, aromatic), EI-MS (*m/z*): 454 (M^{+1}); Cal/Ana: [C (71.51) 71.52, H (5.11) 5.12, N (9.27) 9.26].

Biology

Drug susceptibility

MTB H37Rv was grown on Loëwenstein-Jensen medium. Minimum inhibitory concentrations (MICs) were determined by the proportion method as described previously[16]. In brief, 10^3 and 10^5 colony-forming unit (CFU) were inoculated onto 7H11 agar supplemented with 10% oleic acid–albumin–dextrose–catalase, containing 1, 10 and 100 mg/L of the compound. Colonies were enumerated after 21 to 30 days of incubation at 37°C. The MIC was defined as the drug concentration at which the bacterial growth was reduced to 1% or less of that of the drug-free control culture[17].

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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