SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME 1,4-DIHYDROPYRIDINES DERIVATIVES

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ABSTRACT

A series of 1, 4-dihydropyridine derivatives were prepared from three compounds condensation reaction of ethylacetoacetate, aromatic aldehyde and ammonium hydroxide. A new series of compounds (2a-f) were prepared from compounds (1a-f) via reaction with α-naphthyl amine using the condensation method. The synthesized compounds were confirmed by IR, ¹H NMR, ¹³C-NMR and elemental analyses. The synthesized compounds (1e-f) and (2a-f) were also screened for antimicrobial properties.

Key words: Synthesis of 1,4-dihydropyridines, Antimicrobial activity.

INTRODUCTION

1, 4-Dihydropyridines (1, 4-DHPs) are important class of compounds in the field of drugs and pharmaceuticals.¹⁻³ Hantzsch 1,4-dihydropyridines (di alkyl 1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylates) are widely used clinically as calcium channel blockers for the treatment of cardiovascular diseases, such as, nifedipine and nitrendipine are used for the treatment of hypertension and angina pectoris, nislodipine is a potent vasodilator and nimodipine exhibits selectivity for cerebral vasculature.⁴ DHP derivatives are employed as potential drug candidates for the treatment of congestive heart failure.⁵ The success of those calcium antagonists has led to the development of novel synthetic strategies to improve their classical methods of preparation.

1,4-DHPs are generally synthesized by classical Hantzsch reaction, which involves the condensation of an aldehyde, -ketoester and ammonia or ammonium acetate in refluxing ethanol or other lower alcohols. A number of improved methods have been reported in the literature to modify this reaction.⁶ In recent years, clay catalysts, particularly montmorillonite have received considerable attention in chemical synthesis.⁷ They are inexpensive, non-corrosive and recyclable. Thus the montmorillonite-catalysed procedures have many advantages, such as environmental compatibility and easy handling. Recently, we reported the Hantzsch synthesis of 1, 4-dihydropyridine derivatives catalysed by montmorillonite K10.

Now a days there is an increasing awareness of urgent necessity to limit, as far as possible, any source of pollution. Facing up to these facts, chemists have to dedicate numerous efforts to the development...
of clean technologies. This new challenge has led to growing interest in the displacement of organic reaction in aqueous media\textsuperscript{11,12} and solvent free conditions\textsuperscript{13,14}.

Thus, development of an efficient and convenient synthetic methodology in aqueous medium is an important area of research. In this field, the synthesis of 1,4-dihydropyridine derivatives in aqueous media has been reported by using phase-transfer catalysts or hydro tropes under microwave irradiation or normal thermal conditions\textsuperscript{15-17}

\[
2 \text{CH}_3\text{COOCH}_2\text{COC}_2\text{H}_5 + \text{NH}_3 + \text{R-CHO} \rightarrow \text{HNN(C}_6\text{H}_4\text{)(C}_6\text{H}_4\text{)(CH}_3\text{O)OCH}_3}
\]

1a, 2a : R = 2-Furyl
1b, 2b : R = -Ph
1c, 2c : R = 4-Cl-C\(_6\)H\(_4\)
1d, 2d : R = 4-OH-C\(_6\)H\(_4\)
1e, 2e : R = 4-NO\(_2\)-C\(_6\)H\(_4\)
1f, 2f : R = 4-CH\(_3\)O-C\(_6\)H\(_4\)

\textbf{Scheme}

\textbf{EXPERIMENTAL}

\textbf{1,4 dihydro-2,6-dimethyl-4-(aryl substituted ) pridine-3,5-dicarboxylic acid dimethyl ester (1a-f)}

To a solution of aromatic aldehyde in ethanol (0.03 mol), methyl acetoacetate (0.06 mol) and liquid ammonia (5 mL) were added. The mixture was refluxed for 4 hours and the solid of tained was collected and filtered. It was washed with cold ethanol and recrystallised from ethanol.

\textbf{1,4 -di hydro-2,6-di methyl-4-aryl substituted pyridine-3,5-die-\textgreek{alpha}-napthal amide (2a-f)}

A mixture of 1,4 hydro-2,6-dimethyl-4-aryl substututed pyridine-3,5 dicarboxili acid dimethyl exter
(I) (0.01 mol) and α-napthal amine (0.02 mol) in 1,4 dioxane (25 mL) were refluxed for 7 hours over crushed ice. The soiled formed is recrystallised from methanol.

Analytic and spectral data

**Diethyl 4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1a)**

Yield: 75%; m.p.158°C; Anal. Calcd. for C_{17}H_{21}NO_{5}: C, 63.94; H, 6.63; N, 4.39%. Found: C, 63.98; H, 6.67; N, 4.35%. IR (KBr, cm^{-1}): 3352 (N–H str), 3030 (Ar–H), 2940 (C–H str of CH3), 1745 (C=O, ester), 810 (Ar–H). 1H-NMR (300 MHz, DMSO-\textit{d}6, \delta / ppm): 8.30 (1H, s, NH of pyridine ring), 7.37 (1H, s, furyl ring), 6.10–6.47 (2H, d, furyl ring), 4.22 (1H, s, C4–H), 4.20 (4H, q, C3–OCH2CH3 and C5–OCH2CH3), 2.31 (6H, s, C2–CH3 and C6–CH3), 1.34 (6H, t, C2–OCH2CH3 and C6–OCH2CH3). 13C-NMR (300 MHz, DMSO-\textit{d}6, \delta / ppm): 142.1, 109.6, 107.7, 152.5 (furyl ring), 151.8 (C2,6), 33.2 (C4), 102.3 (3,5--COOCH2CH3), 62.1 (3,5-COOCH2CH3), 15.9 (3,5-COOCH2CH3), 18.3 (2,6--CH3).

**Diethyl 2,6-dimethyl-4-phenyl-1,4-dihydropyridine-3,5-dicarboxylate (1b)**

Yield: 66%; m.p. 253°C; Anal. Calcd. for C_{19}H_{23}NO_{4}: C, 69.28; H, 7.04; N, 4.25 %. Found: C, 69.24; H, 7.07; N, 4.28 %. IR (KBr, cm –1): 3350 (N–H str), 3034 (Ar–H), 2953 (C–H str of CH3), 1755 (C=O, ester), 802 (Ar–H). 1H-NMR (300 MHz, DMSO-\textit{d}6, \delta / ppm): 8.25 (1H, s, NH of pyridine ring), 7.33–7.27 (5H, m, Ph-ring), 4.70 (2H, s, C4–H), 4.22 (4H, q, C3–OCH2CH3 and C5–OCH2CH3), 2.28 (6H, s, C2–CH3 and C6-CH3), 1.32 (6H, t, C2–OCH2CH3 and C6–OCH2CH3). 13C-NMR (300 MHz, DMSO-\textit{d}6, \delta / ppm): 125.1, 128.4, 127.1, 144.8 (phenyl ring), 150.7 (C2,6), 101.9 (3,5-COOCH2CH3), 62.1 (3,5--COOCH2CH3), 44.1 (C4), 19.1 (2,6-CH3), 15.4 (3,5-COOCH2CH3).

**Diethyl 4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1c)**

Yield: 57%; m.p. 240°C. Anal. Calcd. for C_{19}H_{22}ClNO_{4}: C, 62.72; H, 6.09; N, 3.85%. Found: C, 62.75; H, 6.07; N, 3.81%. IR (KBr, cm–1): 3334 (N–H str), 3084 (Ar–H), 2944 (C–H str of CH3), 1746 (C=O, ester), 832 (Ar–H), 616 (C–Cl), 787 (Ar–H). 1H-NMR (300 MHz, DMSO-\textit{d}6, \delta / ppm): 8.41 (1H, s, NH of pyridine ring), 7.36–7.20 (5H, m, Ph-ring), 4.77 (1H, s, C4–H), 4.20 (4H, q, C3–OCH2CH3 and C5–OCH2CH3), 2.19 (6H, s, C2–CH3 and C6–CH3), 1.33 (6H, t, C2–OCH2CH3 and C6–OCH2CH3). 13C-NMR (300 MHz, DMSO-\textit{d}6, \delta / ppm): 131.4, 128.1, 130.8, 142.5 (Ph–Cl), 152.5 (C2,6), 34.7 (C4), 19.1 (2,6-CH3), 15.5 (3,5-COOCH2CH3).

**Diethyl 4-(4-hydroxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1d)**

Yield: 56%; m.p. 240°C; Anal. Calcd. for C_{19}H_{23}NO_{5}: C, 69.07; H, 6.71; N, 4.06%. Found: C, 69.03; H, 6.75; N, 4.01%. IR (KBr, cm−1): 3342 (N–H str), 3027 (Ar–H), 2944 (C–H str of CH3), 1746 (C–O, ester), 832 (Ar–H), 116 (C–Cl), 787 (Ar–H). 1H-NMR (300 MHz, DMSO-\textit{d}6, \delta / ppm): 9.44 (1H, s, C–OH), 8.43 (1H, s, NH of pyridine ring), 7.36–7.20 (5H, m, Ph-ring), 4.77 (1H, s, C4–H), 4.20 (4H, q, C3–OCH2CH3 and C5–OCH2CH3), 2.19 (6H, s, C2–CH3 and C6–CH3), 1.33 (6H, t, C2–OCH2CH3 and C6–OCH2CH3). 13C-NMR (300 MHz, DMSO-\textit{d}6, \delta / ppm): 155.6, 116.2, 131.2, 139.2 (Ph–OH), 151.4 (C2,6), 45.9 (C4), 103.9 (3,5-COOCH2CH3), 60.4 (3,5-COOCH2CH3), 15.5 (3,5-COOCH2CH3), 18.8 (2,6-CH3).

**Diethyl 2, 6-dimethyl-4-(4-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (1e)**

Yield: 69%; m.p. 240°C; Anal. Calcd. for C_{19}H_{22}N_{2}O_{6}: C, 60.95; H, 7.48; N, 7.48 %. Found: C, 60.91; H, 7.42; N, 7.41%. IR (KBr, cm−1): 3364 (N–H str), 3047 (Ar–H), 2944 (C–H str of CH3), 1762 (C–O, ester), 1445 (C–OH), 819 (Ar–H). 1H-NMR (300 MHz, DMSO-\textit{d}6, \delta / ppm): 8.13–7.44 (4H, m, Ph-ring), 4.78 (1H, s, C4–H), 4.28 (4H, q, C3–OCH2CH3 and C5–OCH2CH3), 2.33 (6H, s, C2–CH3 and C6–CH3), 1.31 (6H, t, C2–OCH2CH3 and C6–OCH2CH3). 13C-NMR (300 MHz,
**Diethyl-(4-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1f)**

Yield: 72%; m.p. 197°C; Anal. Calcd. for C20H25NO5: C, 66.83; H, 7.01; N, 3.90%. Found: C, 66.87; H, 7.07; N, 3.97%. IR (KBr, cm⁻¹): 3355 (N–H str), 3033 (Ar–H), 2861 (C–H str of CH₃), 1733 (C=O, ester), 819 (Ar–H). ¹H--NMR (300 MHz, DMSO-d₆, δ / ppm): 8.25 (1H, s, NH of pyridine ring), 5.76–6.17 (5H, m, Ph-ring), 4.70 (1H, s, C4–H), 4.22 (4H, q, C3–OCH₂CH₃ and C5–OCH₂CH₃), 3.78 (3H, s, –OCH₃), 2.21 (6H, s, C2–CH₃ and C6–CH₃), 1.23 (6H, t, C2–OCH₂CH₃ and C6–OCH₂CH₃). ¹³C-NMR (300 MHz, DMSO-d₆, δ / ppm): 153.1, 112.6, 128.3, 134.9 (Ph), 158.3 (C2, 6), 101.2 (3,5-COOCH₂CH₃), 61.3 (3,5-COOCH₂CH₃), 54.7 (Ph–OCH₃), 44.6 (C4), 13.8 (3,5-COOCH₂CH₃), 18.4 (2,6-CH₃).

**1,4-dihydro-2,6-dimethyl-4-(2'-furyl) pyridine 3,5-di-α-naphthamide (2a)**

Yield: 63%; m.p. 161°C; Anal. Calcd. for C33H26O₃N₃: C, 77.34; H, 5.07; N, 8.20%. Found: C,77.30; H, 4.25; N, 7.99. IR (KBr, cm–¹): 3372 (N–H), 3200 (NH–C=O), 3021 (Ar–H), 1091 (N–C–N), 828 (Ar–H). ¹H--NMR (300 MHz, CDCl₃, δ / ppm):  8.43 (1H, s, NH of pyridine ring), 8.09 (1H, d, C3–CONH and C5–CONH), 7.51 (1H, d, 5'-H-furyl) 6.24 (1H, d, 4'-H-furyl), 6.24 (1H, d, 3'-H-furyl); 5.17 (2H, s, C4–H), 2.28 (6H, s, C2–CH₃ and C6–CH₃), 2.02 (1H, d, –NHCS). ¹³C-NMR (300 MHz, CDCl₃, δ / ppm): 111.8, 108.3, 143.2, 152.8 (C₄ in furyl ring), 105.3 (C₃,5 in pyridine ring), 166.2 (C=O), 148. 9 (C₂,6 in pyridine ring), 35.3 (C₄ in pyridine ring), 18.2 (C₂,6–CH₃ in pyridine ring).

**1,4-dihydro-2,6-dimethyl-4-(4'-chloro phenyl) pyridine 3,5-di-α-naphthamide (2c)**

Yield: 75%; m.p. 180°C; Anal. Calcd. for C35H27O₂N₃Cl: C, 75.47; H, 4.85; N, 7.54%. Found: C, 74.00; H, 4.44; N, 7.33%. IR (KBr, cm⁻¹): 3323 (N–H), 3233 (NH₂), 3188 (NH–C=O), 3014 (Ar–H), 1767(C=O), 1057 (N–C–N), 803 (Ar–H), 625 (C–Cl). ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 8.44 (1H, s, NH of pyridine ring), 8.10 (1H, d, C₃–CONH and C₅–CONH), 7.38–7.14 (5H, m, Ph-ring), 5.11 (2H, s, C₄–H), 2.35 (6H, s, C₂–CH₃ and C₆–CH₃), 2.18 (1H, d, –NHCS). ¹³C-NMR (300 MHz, CDCl₃, δ / ppm): 129.7, 109.3, 144.4, 152.8 (C₄ in furyl ring), 106.3 (C₃, 5 in pyridine ring), 166.2 (C=O), 148.9 (C₂,6 in pyridine ring), 35.6 (C₄ in pyridine ring), 19.9 (2,6-CH₃ in pyridine ring).

**1,4-dihydro-2,6-dimethyl-4-(4'-hydroxy phenyl) pyridine 3,5-di-α-naphthamide (2d).**

Yield: 74%; m.p. 201°C; Anal. Calcd. for C₃₅H₂₈N₃O₃: C, 83.39; H, 5.79; N, 8.10%. Found: C, 83.30; H, 5.49; N, 8.03%. IR (KBr, cm⁻¹): 3332 (N–H), 3182 (NH–C=O), 3014 (Ar–H), 1767(C=O), 1057 (N–C–N), 803 (Ar–H), 625 (C–Cl). ¹H-NMR (CDCl₃, δ / ppm): 9.31 (1H, s, OH), 8.10 (1H, d, C₃–CONH and C₅–CONH), 7.38–7.14 (5H, m, Ph-ring), 5.11 (2H, s, C₄–H), 2.35 (6H, s, C₂–CH₃ and C₆–CH₃), 2.18 (1H, d, –NHCS). ¹³C-NMR (300 MHz, CDCl₃, δ / ppm): 129.7, 109.3, 144.4, 152.8 (C₄ in furyl ring), 106.3 (C₃, 5 in pyridine ring), 166.2 (C=O), 147.9 (C₂, 6 in pyridine ring), 38.3 (C₄ in pyridinering), 19.2 (2,6–CH₃ in pyridine ring).
4-OH-phenyl ring), 103.9 (3,5-C in pyridine ring), 165.9 (C=O), 143.1 (C2, 6 in pyridine ring), 44.8 (C4 in pyridine ring), 19.2 (2,6–CH3 in pyridine ring).

**1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl) pyridine3,5-di-α-naphthamide (2e)**

Yield: 76%; m.p. 190°C; Anal. Calcd. for C35H27N4O4: C, 83.39; H, 5.79; N, 8.10%. Found: C, 83.33; H, 5.33; N, 8.00%. IR (KBr, cm–1): 3310 (N–H), 3218 (NH–C=O), 3041 (Ar–H), 1710 (C=O), 1530 (C–NO2), 1094 (N–C–N). 1H-NMR (300 MHz, CDCl3, δ ppm): 8.60 (1H, s, NH of pyridine ring), 8.15 (1H, d, C3–CONH and C5–CONH), 7.42–7.18 (5H, m, Ph-ring), 5.17 (2H, s, C4–H), 2.31 (6H, s, C2–CH3 and C6–CH3), 2.08 (1H, d, –NHCS). 13C-NMR (300 MHz, CDCl3, δ ppm): 143.2, 123.7, 126.7 (C4 in 4--NO2-phenyl ring), 102.9 (3,5-C in pyridine ring), 164.9 (2,6-C in pyridine ring), 44.5 (4-C in pyridine ring), 19.7 (2,6-C–CH3 in pyridine ring).

**1,4-dihydro-2,6-dimethyl-4-(4’-methoxy phenyl) pyridine3,5-di-α-naphthamide (2f)**

Yield: 67%; m.p. 185°C; Anal. Calcd. for C36H30O3N3: C, 78.26; H, 5.74; N, 8.04%. Found: C, 78.23; H, 5.09; N, 8.01%. IR (KBr, cm–1): 3323 (N–H), 3251 (NH–C=O), 3034 (Ar–H), 1717 (C=O), 1091 (N–C–N), 808 (Ar–H). 1H-NMR (300 MHz, DMSO-d6, δ ppm): 8.57 (1H, s, N–H of pyridine ring), 8.05 (1H, d, C3–CONH and C5–CONH), 7.33–7.27 (5H, m, Ph-ring), 5.21 (2H, s, C4–H), 3.81 (3H, s, –OCH3), 2.25 (6H, s, C2–CH3 and C6–CH3), 2.10 (1H, d, –NHCS). 13C-NMR (300 MHz, CDCl3, δ ppm): 111.8, 108.3, 143.2, 152.8 (C4 in 4-CH3O-phenyl ring), 105.3 (3,5-C in pyridine ring), 166.2 (3,5-C=O), 147.7 (2,6-C in pyridine ring), 44.7 (C4 in pyridine ring), 18.8 (2,6-CH3 in pyridine ring), 55.9 (–OCH3).

**Spectroscopy**

The IR spectra of compounds 1a–f showed an absorption band at 3332 to 3354 cm–1 due to N–H stretching, another absorption band at 1741–1764 cm–1 due to the keto group in the ester groups. Compound 1c showed an absorption band at 610 cm–1 corresponding to the Cl–C bonds, compound 1d showed an absorption band at 1447 cm–1 corresponding to the HO–C bonds and compound 1e showed an absorption band at 1536 cm–1 corresponding to the O2N–C groups. The 1H-NMR spectra of compounds 1a–f showed a singlet at δ 8.11–8.41 ppm, attributable to the NH protons present in the 1,4-dihydropyridine ring, and another important singlet at δ 4.67–4.79 ppm, which was attributable to the 1,4-dihydropyridine ring. The 1H-NMR spectra of compounds 2a–f showed a singlet at δ 8.41–8.64 ppm, attributable to the NH protons present in the 1,4-dihydropyridine ring. The C4–H, CONH, and NHCS protons resonated as singlets at δ 5.10–5.21, 8.01–8.15, and 2.02–2.12 respectively. The IR spectra of compounds 1a–f showed an absorption band at δ 33.2–44.9 ppm, corresponding to the C4–H proton present in the 1,4-dihydropyridine ring and another absorption band at 3118–3200 cm–1, which was due to NH–C=O stretching. An absorption band for the C=S group was observed at 1242–1272 cm–1. The 13C-NMR spectra of compounds 2a–f showed as a singlet a band at δ 8.41–8.64 ppm, attributable to the NH protons present in the 1,4-dihydropyridine ring, and another absorption band at 3181–3200 cm–1, which was due to NH–C=O stretching. An absorption band for the C=S group was observed at 1242–1272 cm–1.

**Antibacterial screening**

The bacterial zones of inhibition values (mm) are given in Table I. The antimicrobial activities of compounds 1a–f and 2a–f were screened. The structure activity relationship (SAR) analysis of the base compounds 1a–f was compared with that of the thiosemicarbazone-containing compounds 2a–f.
Ciprofloxacin was used as a standard at 100 µg mL⁻¹. Compounds 1a–f showed low activity compared with compounds 2a–f towards all the tested organisms.

Table 1: Antibacterial activity of the synthesized compounds 1a–f and 2a–f (disk diameter: 7 cm)

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Compounds 2a–f were screened for *Staphylococcus aureus* and compound 2c was found to be highly active compared with the standard ciprofloxacin because it contained an amide group in the 3,5-position with 4-chloro-phenyl group in the fourth position. On the other hand, compounds 2a, 2b and 2d–f had low activities compared with the standard ciprofloxacin.

Compounds 2a–f were screened for *Bacillus subtilis*, whereby compounds 2b and 2f showed equipotent activity with the standard ciprofloxacin. On the other hand, compounds 2a, 2d–e and 2f had low activities compared with the standard ciprofloxacin.

Compounds 2a–f were screened for *Escherichia coli* and the compound 2d was found to have an equipotent activity compared with the standard ciprofloxacin. On the other hand, compounds 2a–c and 2e–f had low activities compared with the standard ciprofloxacin.

Compounds 2a–f were screened for *Vibreocholerae*, whereby the compound 2a exhibited equipotent activity compared with the standard ciprofloxacin, while the other compounds 2b–f had low activities compared with the standard ciprofloxacin.

**Antifungal screening**

The fungacidal zones of inhibition, mm, values are given in Table 2. Compounds 2a–f were screened for *Aspergillus niger*; the compounds 2b–f were less active compared with the standard clotrimazole, while compound 2a had no activity. Compounds 2a–f were screened for *Candida albicans*. Compound 2d was highly active compared with the standard clotrimazole because it contained an amide group in the 3,5-position and 4-hydroxyphenyl in the fourth position, while the other compounds 2a–c and 2e–f had lower activities than the standard clotrimazole.
Table 2: Antifungal activity of the synthesized compounds 1a–f and 2a–f (disk diameter: 7 cm)

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<td>8</td>
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<tr>
<td>2b</td>
<td>11</td>
<td>-</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>2c</td>
<td>14</td>
<td>21</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>2d</td>
<td>15</td>
<td>26</td>
<td>18</td>
<td>15</td>
</tr>
<tr>
<td>2e</td>
<td>9</td>
<td>12</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>2f</td>
<td>10</td>
<td>16</td>
<td>19</td>
<td>23</td>
</tr>
<tr>
<td>Clotrimazole</td>
<td>26</td>
<td>23</td>
<td>26</td>
<td>24</td>
</tr>
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</table>

Compounds 2a–f were screened for Microsporum audouinii. The compounds 2a and 2e–f had lower activity than the standard clotrimazole, while compound 2b was inactive.

Compounds 2a–f were screened for Cryptococcus neoformans, the compound 2f had equipotent activity with the standard clotrimazole, while the other compounds 2a–d and 2e had lower activities compared with the standard clotrimazole and compound 2f exhibited no activity.

Chemistry

The melting points were recorded in open capillary tubes and are reported uncorrected. The IR spectra were recorded in KBr on a Shimadzu 8201pc FTIR spcrometer (4000–400 cm⁻¹). The ¹H-NMR and ¹³C-NMR spectra were recorded on a Bruker DRX-300 MHz instrument. The mass spectra (EI) were obtained on a Jeol JMS D-300 spectrometer operating at 70 eV. Elemental analyses (C, H, N and S) were realized using an Element Analyzer, Model Vario EL III. The purity of the compounds was checked by thin layer chromatography (TLC).

In vitro antibacterial screening

The compounds la–f and 2a–f were evaluated for their in vitro antibacterial activity against S. aureus (ATCC-25923), b.Subtilus (recultured), E. coli (ATCC-25922) and Vibrocholerae (ATCC-27853) by the agar diffusion method¹⁸,¹⁹ using Mueller-Hinton agar (Hi--Media) medium. Each compound was tested at a concentration of 100 ug mL⁻¹ in DMSO. Ciprofloxacin was used as the standard. The zone of inhibition (mm) was measured after 24 h incubation at 37°C.

In vitro antifungal screening

The compounds la–f and 2a–f were evaluated for their in vitro antifungal activity against Trichoderma Sp, A. niger, A. Parasitica and Chrysosporium Sp (recultured) using an agar diffusion method²⁰,²¹ with Sabouraud’s dextrose agar (Hi-Media). Each compound was tested at a concentration of
100 µg mL\(^{-1}\) in DMSO. Clotrimazole was used as the standard. The zone of inhibition (mm) was measured after 24 h incubation at 37°C.

**CONCLUSION**

A new series of 1,4-dihydropyridine derivatives 2a-f was synthesized. The synthesized compounds were screened for their antibacterial activity, whereby compound 2c was more active than ciprofloxacin against *B. Subtilius* organism. When the synthesized compounds were screened for their antifungal activity, a compound 2d showed higher activity than clotrimazole against *A. Parasitica*. These findings could be of importance for further studies in this field.

**REFERENCES**