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Research Article

Synthesis, characterization and biological evaluation of some novel substituted-(6*h*-thiazolo [4, 5-*e*] indol-2-yl)-amines and substituted benzylidene-(1*h*-indol-4-yl)-amines

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Abstract

A series of various novel substituted-(6*H*-thiazolo[4,5-*e*]indol-2-yl)-amines **(4a-d)** and substituted benzylidene-(1*H*-indol-4-yl)-amines **(5a-f)** have been synthesized by involving 4-nitro-1*H*-indole **(1)** as starting compound and 4-amino-1*H*-indole **(2)** and 1-(1*H*-indol-4-yl)-3-substituted-thioureas **(3a-d)** as intermediates. After structural confirmation, the title compounds were screened for their antibacterial activity.

Key words: Thiazolyl amines, Benzylidene amines, antimicrobial activity

1. Introduction

A ranula A literature search revealed that, thiazolidinone derivatives may exhibit antibacterial,[1] antituberculosis,[2] antiviral[3] and anticancer[4] properties. In addition, some thiazolidinones were recently reported as novel inhibitors of mycobacterial rhamnose synthetic enzymes.[5] Small ring heterocycles containing nitrogen, sulfur and oxygen have been under investigation for a long time because of their important medicinal and biological properties. Thiazole derivatives are an important class of heterocyclic compounds and they occupy a significant position in medicinal chemistry presenting a wide range of biological activities such as antibacterial[6], antifungal[7], anti-HIV[8], hypertension[9], anti-inflammatory[10], anticancer[11] and anti-convulsant[12] activities.

2. Materials and methods

All reagents and solvents were used as purchased without further purification. Melting points were determined on a Fisher–Johns melting point apparatus and are uncorrected. Crude products were purified by column chromatography on silica gel of 60–120 mesh. IR spectra were obtained on a Perkin-Elmer BX serried FTIR 5000 spectrometer using KBr pellet. NMR spectra were recorded on a varian 300 MHz spectrometer for ^{1}H NMR and 100 MHz spectrometer ^{13}C NMR. The chemical shifts were reported as ppm down field using TMS as an internal standard. Mass spectra were recorded on a VG-Micromass 7070H spectrometer operating at 70 eV.

2.1 General procedure for the preparation of 4-amino-1*H*-indole (2)

A solution of 4-nitro-1*H*-indole **(1)** (0.01 mol) in ethyl alcohol (20 ml) containing $SnCl_2.2H_2O$ (10 mmol) was refluxed on steam-bath for 30 min. A usual work-up, followed by crystallization of the product from dichloro methane furnished compound **2**.

2.2 General procedure for the preparation of 1-(1*H*-indole-4-yl)-3-substituted-thioureas (3a-d)

A solution of 4-amino-1*H*- indole **(2)** (0.01 mol) in methanol (10 ml) containing thioisocyanate (0.01 mol) was refluxed for 8-10 h, the solution was concentrated on steam-bath, allowed to cool down to room temperature and the resulting crystals filtered under suction and recrystallized to form compounds **3a-d**.

2.3 General procedure for the preparation of 6*H*-thiazolo[4,5-*e*]indole-2-yl-amines (4a-d)

A solution of Br_2 (0.01 mol) in acetic acid (1 ml) is added to the solution of 1-(1*H*-indole-4-yl)-3-substituted-thiourea **(3)** (0.01 mol) and acetic acid (3 ml) and the resulted reaction mixture was constantly stirred at room temperature for 1-2 h the reaction mixture was poured into crushed ice. The solid separated was filtered, dried and purified by recrystallization with hot methanol to yield **4a-d**.

2.4 General procedure for the preparation of benzylidene-(1*H*-indole-4-yl)-amines (5a-f)

A mixture of suitable aromatic aldehyde (0.01 mol) and 4-amino-1*H*-indole **(2)** (0.01 mol) in ethanol (20 ml) was refluxed for 2-3 h, the mixture was cooled and the solvent evaporated. The formed crude product was washed with cold aq. ethanol and then the product was purified by recrystallization from ethanol to afford the corresponding **5a-f**.

2.5 Physical and spectral data

2.5.1 4-Amino-1H-indole (2)

Greenish gray solid, yield: 76%, mp: 107-109 °C; IR (KBr): 3112 (N-H), 3024 (C-H, Ar), 1580 (C=C, Ar) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.12 (s, 1H, NH), 7.36 (d, 1H, J = 6.8 Hz, CH), 7.32-7.15 (m, 3H, Ar-H), 6.52 (d, 1H, J = 6.8 Hz, CH), 3.87 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ 139.2, 136.7, 126.7, 122.6, 116.3, 110.5, 104.2; MS: *m/z* 132 (M^+); Elemental analysis: Calculated for $C_8H_8N_2$: C-72.70, H-6.10, N-21.20. Found: C-71.69, H-5.98, N-20.10.

2.5.2 1-(1*H*-Indol-4-yl)-3-methyl-thioureas (3a)

Gray solid, yield: 77%, mp: 130-132 °C; IR (KBr): 3163 (N-H), 3029 (C-H, Ar), 1581 (C=C, Ar) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.82 (s, 1H, NH), 9.75 (s, 1H, NH), 9.29 (s, 1H, NH-CH_3), 7.54 (d, 1H, J = 6.8 Hz, CH), 7.52-7.21 (m, 3H, Ar-H), 6.51 (d, 1H, J = 6.8 Hz, CH), 2.89 (d, 3H, J = 4

Hz, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.6, 135.7, 131.2, 125.6, 124.7, 119.7, 118.2, 107.3, 102.5, 43.6; MS: 205 *m/z* (M^+); Elemental analysis: Calculated for $C_{10}H_{11}N_3S$: C-58.51, H-5.40, N-20.47, S-15.62. Found: C-57.23, H-4.89, N-19.64, S-14.36.

2.5.3 1-Ethyl-3-(1*H*-indol-4-yl)-thiourea (3b)

Yellow solid, yield: 77%, mp: 121-123 °C; IR (KBr): 3155-3395 (N-H), 3035 (C-H, Ar), 1588 (C=C, Ar) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 10.88 (s, 1H, NH), 9.69 (s, 1H, NH), 9.31 (s, 1H, NH-CH_3), 7.58 (d, 1H, J = 6.5 Hz, CH), 7.52-7.21 (m, 3H, Ar-H), 6.35 (d, 1H, J = 6.5 Hz, CH), 4.31 (q, 2H, J = 7.2 Hz, CH_2), 1.41 (t, 3H, *J* = 7.2 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.6, 136.7, 130.2, 127.6, 125.7, 121.7, 117.2, 105.3, 104.5, 41.6, 17.6; MS: 219 *m/z* (M^+); Elemental analysis: Calculated for $C_{11}H_{13}N_3S$: C-60.24, H-5.97, N-19.16, S-14.62. Found: C-59.36, H-5.21, N-18.65, S-13.54.

2.5.4 1-(1*H*-Indol-4-yl)-3-propyl-thiourea (3c)

Brown solid, yield: 73%, mp: 155-157 °C; IR (KBr): 3168 (N-H), 3025 (C-H, Ar), 1565 (C=C, Ar) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 10.95 (s, 1H, NH), 9.80 (s, 1H, NH), 9.35 (s, 1H, NH-CH_3), 7.47 (d, 1H, J = 6.3 Hz, CH), 7.43-7.28 (m, 3H, Ar-H), 6.42 (d, 1H, J = 6.3 Hz, CH), 2.48 (m, 2H, NH-CH_2), 2.28 (m, 2H, CH_2-CH_3), 1.54 (t, 3H, *J* = 6.8 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.2, 138.5, 132.6, 128.2, 126.3, 122.7, 119.8, 107.2, 103.4, 52.3, 24.8, 13.6; MS: 233 *m/z* (M^+); Elemental analysis: Calculated for $C_{12}H_{12}N_3S$: C-61.77, H-6.48, N-18.01, S-13.74. Found: C-60.12, H-5.84, N-17.23, S-12.65.

2.5.5 1-Benzyl-3-(1*H*-indol-4-yl)-thiourea (3d)

Yellow solid, yield: 77%, mp: 141-142 °C; IR (KBr): 3152 (N-H), 3027 (C-H, Ar), 1582 (C=C, Ar) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 10.92 (s, 1H, NH), 9.78 (s, 1H, NH), 9.32 (s, 1H, NH-CH_3), 7.68-7.23 (m, 8H, Ar-H), 7.58 (d, 1H, J = 6.4 Hz, CH), 6.38 (d, 1H, J = 6.4 Hz, CH); 2.36 (d, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.5, 142.3, 135.7, 131.0, 128.6, 128.3, 127.7, 127.2, 126.3, 124.5, 124.0, 119.9, 118.2, 107.2, 102.3, 55.6; MS: 281 *m/z* (M^+); Elemental analysis: Calculated for $C_{16}H_{15}N_3S$: C-68.30, H-5.37, N-14.93, S-11.40. Found: C-67.23, H-4.98, N-13.65, S-10.23.

2.5.6 Methyl-(6*H*-thiazolo[4,5-*e*]indol-2-yl)-amine (3a)

Pale yellow solid, yield: 71%, mp: 131-133 °C; IR (KBr): 3118 (N-H), 3016 (C-H, Ar), 1565 (C=C, Ar) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 10.84 (s, 1H, NH), 9.21 (s, 1H, NH), 7.52 (d, 1H, J = 7.1 Hz, Ar), 7.49 (d, 1H, J = 6.9 Hz, CH), 7.15 (d, 1H, J = 7.1 Hz, Ar), 6.38 (d, 1H, J = 6.9 Hz, CH), 2.51 (d, 3H, J = 4 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.3, 146.5, 126.3, 125.7, 124.2, 123.7, 122.7, 121.4, 103.6, 35.8; MS: 203 m/z (M^+); Elemental analysis: Calculated for $C_{10}H_9N_3S$: C-59.09, H-4.46, N-20.67, S-15.78. Found: C-58.12, H-4.21, N-19.32, S-14.21.

2.5.7 Ethyl-(6*H*-thiazolo[4,5-*e*]indol-2-yl)-amine (4b)

Gray solid, yield: 75%, mp: 151-153 °C; IR (KBr): 3168 (N-H), 3038 (C-H, Ar), 1572 (C=C, Ar) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 11.07 (s, 1H, NH), 9.35 (s, 1H, NH), 7.55 (d, 1H, J = 6.5 Hz, CH), 7.39 (d, 1H, J = 7.3 Hz, Ar-H), 7.25 (d, 1H, J = 7.3 Hz, Ar-H), 6.45 (d, 1H, J = 6.5 Hz, CH); 4.12 (q, 2H, J = 7.2 Hz, CH_2), 1.39 (t, 3H, J = 7.2 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.6, 145.2, 127.7, 126.6, 123.0, 122.4, 121.1, 120.2, 105.5, 44.2, 16.8; MS: 217 m/z (M^+); Elemental analysis: Calculated for $C_{11}H_{11}N_3S$: C-60.80, H-5.10, N-19.34, S-14.76. Found: C-58.36, H-4.69, N-18.84, S-13.68.

2.5.8 Propyl-(6*H*-thiazolo[4,5-*e*]indol-2-yl)-amine (4c)

Orange solid, yield: 74%, mp: 130-132 °C; IR (KBr): 3162 (N-H), 3036 (C-H, Ar), 1582 (C=C, Ar) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 10.85 (s, 1H, NH), 9.30 (s, 1H, NH), 7.58 (d, 1H, J = 6.3 Hz, CH), 7.32 (d, 1H, J = 7.5 Hz, Ar), 7.12 (d, 1H, J = 7.5 Hz, Ar), 6.52 (d, 1H, J = 6.3 Hz, CH); 2.41 (m, 2H, NH-CH_2), 2.32 (m, 2H, CH_2-CH_3), 1.39 (t, 3H, J = 6.8 Hz, CH_3), ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.0, 148.8, 127.5, 125.4, 122.0, 121.6, 120.1, 119.6, 104.0, 54.3, 25.6, 14.3; MS: 231 m/z (M^+); Elemental analysis: Calculated for $C_{12}H_{13}N_3S$: C-62.31, H-5.66, N-18.17, S-13.86. Found: C-60.98, H-4.98, N-17.12, S-12.84.

2.5.9 Phenyl-(6*H*-thiazolo[4,5-*e*]indol-2-yl)-amine (4d)

Brown solid, yield: 74%, mp: 128-130 °C; IR (KBr): 3304, 3150 (N-H), 3021 (C-H, Ar), 1624 (C=C, Ar) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 11.08 (s, 1H, NH), 9.28 (s, 1H, NH), 7.54-7.13 (m, 5H, Ar-H), 7.51 (d, 1H, J = 7.6 Hz, Ar), 7.49 (d, 1H, J = 6.5 Hz, CH), 7.19 (d, 1H, J = 7.6 Hz, Ar), 6.38 (d, 1H, J = 6.5 Hz, CH); 2.15 (s, 2H, CH_2), ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.7, 151.9, 137.5, 133.6, 129.4, 129.4, 128.4, 128.4, 125.1, 125.1, 125.0, 124.1, 122.7, 122.1, 102.3, 38.3; MS: 279 m/z (M^+); Elemental analysis: Calculated for $C_{16}H_{13}N_3S$: C-72.70, H-4.58, N-10.60, S-12.13. Found: C-71.02, H-4.07, N-9.68, S-11.65.

2.5.10 Benzylidene-(1*H*-indol-4-yl)-amine (5a)

White solid, yield: 70%, mp: 113-137 °C; IR (KBr): 3328 (N-H), 3025 (C-H, Ar), 1564 (C=C, Ar) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 11.08 (s, 1H, NH), 7.86-7.17 (m, 8H, Ar-H), 7.65 (d, 1H, J = 7.0 Hz, CH), 7.48 (s, 1H, CH), 6.49 (d, 1H, J = 7.0 Hz, CH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.7, 145.2, 136.8, 131.2, 130.8, 129.0, 129.0, 128.6, 128.6, 124.1, 121.1, 120.9, 115.2, 109.5, 102.1; MS: 220 m/z (M^+); Elemental analysis: Calculated for $C_{15}H_{12}N_2$: C-81.79, H-5.49, N-12.72. Found: C-80.23, H-5.21, N-11.65.

2.5.11 (1*H*-Indol-4-yl)-(4-nitro-benzylidene)-amine (5b)

Gray solid, yield: 70%, mp: 151-153 °C; IR (KBr): 3318 (N-H), 3028 (C-H, Ar), 1614 (C=C, Ar) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 11.12 (s, 1H, NH), 7.62-7.12 (m, 3H, Ar-H), 7.78 (d, 2H, J = 7.5 Hz, Ar-H), 7.65 (d, 1H, J = 6.0 Hz, CH), 6.42 (d, 1H, J = 6.0 Hz, CH), 7.56 (s, 1H, CH), 7.50 (d, 2H, J = 7.5 Hz, Ar); ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.3, 149.8, 146.2, 137.5, 136.4, 130.2, 130.2, 125.6, 124.3, 124.3, 122.1, 121.5, 116.3, 110.8, 103.7; MS: 265 m/z (M^+); Elemental analysis: Calculated for $C_{15}H_{11}N_3O_2$: C-67.92, H-4.18, N-15.84, O-12.06. Found: C-66.58, H-3.98, N-14.68, O-11.45.

2.5.12 (1*H*-Indol-4-yl)-(4-bromo-benzylidene)-amine (5c)

Pale yellow solid, yield: 74%, mp: 123-125 °C; IR (KBr): 3345 (N-H), 3032 (C-H, Ar), 1616 (C=C, Ar) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 10.95 (s, 1H, NH), 7.64 (d, 2H, J = 7.6 Hz, Ar-H), 7.52 (d, 1H, J = 6.6 Hz, CH), 7.39 (s, 1H, CH), 7.36-7.06 (m, 3H, Ar-H), 7.14 (d, 2H, J = 7.6 Hz, Ar-H), 6.41 (d, 1H, J = 6.6 Hz, CH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.8, 144.6, 137.4, 132.6, 132.6, 130.5, 130.5, 129.7, 126.4, 125.7, 120.7, 119.4, 116.2, 109.7, 103.5; MS: 299 m/z (M^+); Elemental analysis: Calculated for $C_{15}H_{11}BrN_2$: C-60.22, H-3.71, Br-26.71, N-9.36. Found: C-59.23, H-3.12, Br-25.45, N-9.01.

2.5.13 (1*H*-Indol-4-yl)-(4-methoxy-benzylidene)-amine (5d)

Brown solid, yield: 77%, mp: 120-122 °C; IR (KBr): 3308 (N-H), 3025 (C-H, Ar), 1615 (C=C, Ar) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 10.84 (s, 1H, NH), 7.74 (d, 2H, J = 7.6 Hz, Ar-H), 7.47 (d, 1H, J = 7.2 Hz, CH), 7.42-7.16 (m, 3H, Ar-H), 7.36 (s, 1H, CH), 7.31 (d, 2H, J = 7.6 Hz, Ar-H), 6.52 (d, 1H, J = 7.2 Hz, CH), 3.72 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2, 161.0, 146.8, 137.2, 131.2, 131.2, 124.1, 123.5, 121.1, 120.9, 115.2, 114.2, 114.2, 109.5, 102.1, 56.8; MS: 250 m/z (M^+); Elemental analysis: Calculated for $C_{16}H_{14}N_2O$: C-76.78, H-5.64, N-11.19, O-6.39. Found: C-75.23, H-4.98, N-10.58, O-5.69.

2.5.14 Benzo[1,3]dioxol-5-yl-methylene-(1*H*-indol-4-yl)-amine (5e)

Orange solid, yield: 74%, mp: 125-127 °C; IR (KBr): 3368 (N-H), 3028 (C-H, Ar), 1588 (C=C, Ar) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 11.14 (s, 1H, NH), 7.65-7.15 (m, 3H, Ar-H), 7.49 (d, 1H, J = 7.3 Hz, Ar), 7.25 (d, 1H, J = 7.3 Hz, Ar), 7.21 (s, 1H, Ar-H), 6.87 (s, 1H, CH), 6.80 (d, 1H, J = 7.8 Hz, CH), 6.55 (d, 1H, J = 6.8 Hz, CH), 5.81 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.8, 149.8, 147.2, 145.6, 136.8, 124.5, 124.1, 122.3, 121.4, 120.9, 115.6, 115.2, 115.2, 108.1, 101.0, 91.3; MS: 264 m/z (M^+); Elemental analysis: Calculated for $C_{16}H_{12}N_2O_2$: C-72.72, H-4.58, N-10.60, O-12.11. Found: C-71.02, H-4.12, N-9.68, O-11.06.

2.5.15 Furan-2-yl-methylene-(1*H*-indol-4-yl)-amine (5f)

Yellow solid, yield: 71%, mp: 124-126 °C; IR (KBr): 3342 (N-H), 3024 (C-H, Ar), 1618 (C=C, Ar) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 11.10 (s, 1H, NH), 7.56 (s, 1H, CH), 7.54 (d, 1H, J = 7.0 Hz, CH), 7.52-7.19 (m, 3H, Furan-H), 7.45-7.21 (m, 3H, Ar-H), 6.51 (d, 1H, J = 7.0 Hz, CH); ^{13}C

NMR (100 MHz, DMSO-d_6): δ 165.3, 143.7, 143.7, 141.0, 136.8, 124.1, 121.0, 120.9, 115.7, 110.8, 111.4, 111.4, 101.8; MS: 210 m/z (M^+); Elemental analysis: Calculated for $C_{13}H_{10}N_2O$: C-74.27, H-4.79, N-13.33, O-7.61. Found: C-72.34, H-4.02, N-12.98, O-7.12.

3. Results and Discussion

Inspired by the biological profile of thiazoles and their derivatives and in continuation of our research on biologically active heterocycles, we have introduced thiazole moiety into the indole ring that leads to the synthesis of target compounds with both active pharmacophores in a single molecular frame work for the intensified biological activities. The synthetic route leading to the target compounds is summarized in Scheme 1. In this chapter, we have designed and synthesized a series of novel substituted-(6*H*-thiazolo[4,5-*e*]indol-2-yl)-amines **(4a-d)** and substituted benzylidene-(1*H*-indol-4-yl)-amines **(5a-f)** by using commercially available 4-nitro-1*H*-indole **(1)** as starting compound and 4-amino-1*H*-indole **(2)** and 1-(1*H*-indol-4-yl)-3-substituted-thioureas **(3a-d)** as intermediates.

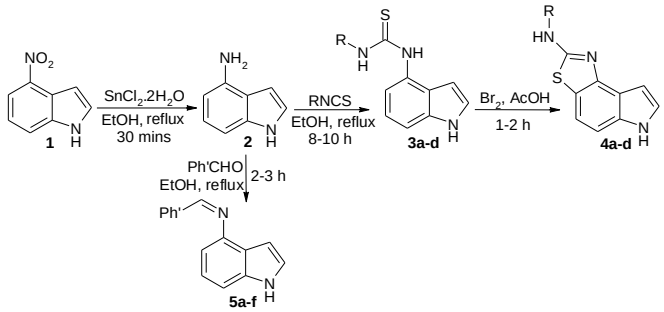

Figure 1. 4 R = (a) = CH_3, (b) = C_2H_5, (c) = C_3H_7, (d) = CH_2-C_6H_5. **5** Ph' = (a) = C_6H_5, (b) = 4-NO_2-C_6H_4, (c) = 4-Br-C_6H_4, (d) = 4-CH_3O-C_6H_4, (e) = 3,4-(O-CH_2-O)C_6H_3, (f) = 2-furyl

Thus the first intermediate 4-amino-1*H*-indole **(2)** has been prepared from 4-nitro-1*H*-indole **(1)** in ethanol on reduction with $SnCl_2$ under reflux with constant stirring for 30 minutes. The intermediate **2** was converted into 1-(1*H*-indol-4-yl)-3-substituted-thioureas **(3a-d)** on reaction with different alkyl isothiocyanides in refluxing methanol for 8-10 h.. Subsequently, cyclization of compounds **3a-d** with Br_2 in acetic acid at room temperature with constant stirring for 1-2 h gave substituted-(6*H*-thiazolo[4,5-*e*]indol-2-yl)-amines **(4a-d)**. Finally compound **2** on condensation with various aromatic aldehydes in presence of refluxing ethanol for 2-3 h yielded corresponding benzylidene-(1*H*-indol-4-yl)-amines **(5a-f)**. The chemical structures of all the newly synthesized compounds were confirmed by their IR, ^{1}H NMR, ^{13}C NMR, mass spectra data and elemental analysis. Further the compounds were screened for their antibacterial activity.

The *in vitro* antimicrobial activity for the screening of the newly synthesized compounds **4a-d** and **5a-f** is carried out by the disc diffusion method[13]. The antibacterial activity of **4a-d** and **5a-f** was tested against three gram-positive bacteria *i.e. Staphylococcus aureus*, *Staphylococcus albus*, *Streptococcus faecalis* and against three gram-negative bacteria *i.e.*, *Escherichia coli*, *Proteus mirabilis*, *Salmonella typhi*. The antifungal activity of these compounds was screened against two fungal organisms namely *Candia albicans* and *Aspergillus fumigatus*. Amicacin and Fluconazole were used as reference compounds in antibacterial and antifungal studies respectively. The lowest concentration (highest dilution) of the compounds at which, there was no visually detectable bacterial growth was taken as minimum inhibitory concentration (MIC). The zone of inhibition caused by the various compounds on the micro organisms was measured and the activity was rated on the basis of the size of the inhibition zone. The observed zone of inhibition in mm is presented in Table 1.

Table 1 Antimicrobial activity of compounds 4a-d and 5a-f. Zone of inhibition in mm (activity index)*

Compound	Antibacterial activity					Antifungal activity		
	S. aureus	*S. albus*	*S. faecalis*	*E. coli*	*P. mirabilis*	*S. typhi*	*C. albicans*	*A. fumigatus*
4a/4b	18/16 (0.75)/(0.66)	16/19 (0.72)/(0.86)	18/17 (0.69)/0.65)	16/18 (0.80)/(0.90)	13/14 (0.62)/(0.66)	15/16 (0.83)/(0.88)	16/14 (0.69)/(0.60)	16/18 (0.64)/(0.72)
4c/4d	17/16 (0.83)/(0.70)	17/16 (0.79)/(0.72)	14/16 (0.53)/(0.61)	15/17 (0.75)/(0.85)	14/16 (0.66)/(0.76)	13/14 (0.72)/(0.77)	15/13 (0.65)/(0.56)	14/16 (0.56)/(0.64)
5a/5b	11/13 (0.46)/(0.54)	13/11 (0.59)/(0.50)	13/12 (0.50)/(0.46)	12/13 (0.60)/(0.65)	00/13 (0.00)/(0.62)	10/11 (0.55)/(0.61)	10/12 (0.43)/(0.52)	12/13 (0.48)/(0.52)
5c/5d	06/08 (0.25)/(0.33)	07/09 (0.31)/(0.75)	19/10 (0.73)/(0.38)	02/11 (0.01)/(0.55)	12/11 (0.57)/(0.52)	12/10 (0.66)/(0.55)	11/12 (0.48)/(0.52)	11/10 (0.44)/(0.40)
5e/5f	13/14 (0.54)/(0.58)	10/12 (0.45)/(0.54)	15/13 (0.57)/(0.50)	10/12 (0.50)/(0.60)	10/12 (0.47)/(0.57)	10/13 (0.55)/(0.72)	13/12 (0.56)/(0.52)	13/10 (0.52)/(0.40)
Amicacin	24	22	26	20	21	18	—	—
Fluconazole	—	—	—	—	—	—	23	25

Activity index = Zone of inhibition of the sample/ Zone of inhibition of the standard

The results of the antimicrobial screening of the tested compounds revealed that, all the tested compounds exhibited antimicrobial activity comparable with that of reference compounds. Most of the compounds showed significant activity against both bacteria and fungi. Compound **5a**, compare with other products was found to be totally inactive against *P. mirabilis*. Compound **5c** was good active only against *S. faecalis* and almost inactive towards *E. coli*. This compound exhibited moderate activity against the rest of organisms. The remaining compounds exhibited moderate to good activity. It can be concluded that the antimicrobial activity of such compounds may change by introduction or elimination of a specific group.

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