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Research Article

Synthesis and characterization of some novel indole based 1, 3, 4-oxadiazoles with antimicrobial activity

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Abstract

A novel series of various 1-[5-(1*H*-indol-3-ylmethoxymethyl)-2-phenyl-[1,3,4]oxadiazol-3-yl]-ethanone and its derivatives **(5a-f)** were synthesized from (1*H*-indol-3-ylmethoxy)-acetic acid-benzylidene-hydrazide and its derivatives **(4a-f)** by using (1*H*-indol-3-yl)-methanol **(1)** as raw material and including (1*H*-indol-3-ylmethoxy)-acetic acid ethyl ester **(2)** and (1*H*-indol-3-ylmethoxy)-acetic acid hydrazide **(3)** as intermediates. The chemical structures of all these compounds have been entrenched by IR, ^{1}H & ^{13}C-NMR, mass spectral data and elemental analysis. The newly synthesized compounds have been used to find their potential in order to achieve the antibacterial and antifungal activities.

Keywords: Indole, 1, 3, 4-Oxadiazole, Antimicrobial activity

1. Introduction

1, 3, 4-Oxadiazoles are biologically active, synthetically useful and important heterocyclic compounds and investigation of their chemical and biological behaviors have gained more importance in recent decades. Different classes of oxadiazoles possess an extensive spectrum of pharmacological activities such as antimalarial[1], anti-inflammatory[2], anticonvulsant[3], analgesic[4], antimicrobial[5], antimycobacterial[6], antitumor[7], herbicidal[8], vasodialatory[9], cytotoxic[10], hypolipidemic[11], and antiedema[12]. Inspired by the biological profile of 1,3,4-oxadiazoles and their increasing importance in pharmaceutical and biological fields and in continuation of our research on biologically active heterocycles, we have inserted 1,3,4-oxadiazole moiety into the indole ring which leads to the presence of both active pharmacophores in a single molecular frame work for the intensified biological activities.

2. Experimental Section

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.

(1*H*-Indol-3-ylmethoxy)-acetic acid ethyl ester (2)
A mixture of (1*H*-indol-3-yl)-methanol **(1)** (0.01 mole), ethyl bromoacetate (0.01 mole) and anhydrous K2CO3 (0.01 mole) in dry acetone was refluxed on a water bath for 8 h. After realization of the reaction (monitored by TLC), the mixture was then filtered and solvent was removed under reduced pressure. The resulting solid was recrystallised from ethanol to afford compound **2** in pure form.

(1*H*-Indol-3-ylmethoxy)-acetic acid hydrazide (3)
A mixture of compound **2** (0.01 mole) and hydrazine hydrate (0.02 mole) in methanol was stirred constantly at ambient temperature for 8 h. After accomplishment of the reaction (scanned by TLC), the mixture was cooled and the solid that separated was washed with water, dried and recrystallized from ethanol to get pure compound **3**.

(1*H*-Indol-3-ylmethoxy)-acetic acid benzylidene-hydrazide (4a-f)
A mixture of compound **3** 0.01 mole) in ethanol (20 ml), aromatic aldehyde (0.01 mole) and glacial acetic acid (1 ml) was refluxed on water bath for 5-6 h. After achievement of the reaction (examined by TLC), the solvent was removed under reduced pressure and the separated solid was crystallized from methanol to achieve **4a-f** in pure form.

1-[5-(1*H*-Indol-3-ylmethoxymethyl)-2-phenyl-[1,3,4]oxadiazol-3-yl]-ethanones (5a-f)
The clear solution of compound **4a-f** in acetic anhydride was refluxed on water bath with constant stirring for 9-10 h. After completion of the reaction (observed by TLC), the solvent was removed under pressure and obtained solid was felted, dried and re crystallized from ethyl acetate to offered **5a-f** in pure form.

2.1 Physical and Spectral Data

(1*H*-Indol-3-ylmethoxy)-acetic acid ethyl ester (2) White solid, Yield: 75 %, M.P: 112-114 °C, IR (KBr): 3224 (N-H), 3035 (C-H, Ar), 2975 (C-H, CH_3), 1740 (C=O), 1592 (C=C, Ar), 1210 (C-O) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 11.02 (s, 1H, NH), 7.75 (s, 1H, CH), 7.28-7.56 (m, 4H, Ar-H), 4.12 (q, 2H, J = 5.4 Hz, CH_2), 3.45 (s, 2H, CH_2CO), 3.18 (s, 2H, CH_2O), 1.24 (t, 3H, J = 5.4 Hz, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.4, 136.5, 131.7, 122.8, 121.7, 120.5, 119.6, 113.0, 112.7, 73.1, 68.8, 59.5, 13.6. MS: *m/z* 233 (M^+). Anal. Calcd. for $C_{13}H_{15}NO_3$: C-66.94, H-6.48, N-6.00, O-20.58. Found: C-65.89, H-6.32, N-5.89, O-19.84.

(1*H*-Indol-3-ylmethoxy)-acetic acid hydrazide (3) Yellow solid, Yield: 72 %, M.P: 122-124 °C, IR (KBr): 3320 (N-H), 3030 (C-H, Ar), 2985 (C-H, CH_2), 1670 (C=O), 1585 (C=C, Ar), 1220 (C-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 10.98 (s, 1H, NH), 8.04 (s, 1H, NH), 7.68 (s, 1H, CH), 7.28-7.62 (m, 4H, Ar-H), 4.68 (s, 2H, CH_2), 4.42 (s, 2H, NH_2), 3.29 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.2, 135.1, 130.8, 123.4, 120.4, 119.8, 117.6, 110.8, 109.4, 75.5, 69.8. MS: *m/z* 219 (M^+). Anal. Calcd. for $C_{11}H_{13}N_3O_2$: C-60.26, H-5.98, N-19.17, O-14.60. Found: C-59.26, H-5.21, N-18.74, O-13.64.

(1*H*-Indol-3-ylmethoxy)-acetic acid benzylidene-hydrazide (4a) Pale yellow solid, Yield: 70 %, M.P: 145-147 °C, IR (KBr): 3326 (N-H), 3028 (C-H, Ar), 2978 (C-H, CH_2), 1672 (C=O), 1630 (C=N), 1575 (C=C, Ar), 1224 (C-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 11.08 (s, 1H, NH), 8.15 (s, 1H, NH), 7.65 (s, 1H, CH), 7.41 (s, 1H, CH), 7.32-7.78 (m, 9H, Ar-H), 4.74 (s, 2H, CH_2), 3.32 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.0, 156.7, 137.8, 133.2, 131.5, 130.8, 129.4, 127.4, 124.7, 123.2, 121.4, 117.8, 114.1, 112.3, 73.7, 67.4. MS: *m/z* 307 (M^+). Anal. Calcd. for $C_{18}H_{17}N_3O_2$: C-70.34, H-5.58, N-13.67, O-10.41. Found: C-69.85, H-5288, N-12.89, O-9.84.

(1*H*-Indol-3-ylmethoxy)-acetic acid (4-methyl-benzylidene-hydrazide (4b) White solid, Yield: 74 %, M.P: 153-155 °C, IR (KBr): 3318 (N-H), 3022 (C-H, Ar), 2982 (C-H, CH_2), 1674 (C=O), 1634 (C=N), 1590 (C=C, Ar), 1228 (C-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 11.12 (s, 1H, NH), 8.07 (s, 1H, NH), 7.78-7.35 (m, 4H, Ar-H), 7.70 (d, 2H, *J* = 7.4 Hz, Ar-H), 7.58 (s, 1H, CH), 7.38 (s, 1H, CH), 7.32 (d, 2H, *J* = 7.4 Hz, Ar-H), 4.67 (s, 2H, CH_2), 3.18 (s, 2H, CH_2), 2.15 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.3, 156.7, 143.7, 138.4, 133.6, 131.7, 128.4, 127.2, 125.4, 124.2, 122.4, 117.8, 115.4, 113.0, 73.8, 67.8, 23.4. MS: *m/z* 321 (M^+). Anal. Calcd. for $C_{19}H_{19}N_3O_2$: C-71.01, H-5.96, N-13.08, O-9.96. Found: C-70.12, H-5.52, N-12.48, O-9.24.

(1*H*-Indol-3-ylmethoxy)-acetic acid (4-methoxy-benzylidene-hydrazide (4c) Brown solid, Yield: 70 %, M.P: 165-167 °C, IR (KBr): 3338 (N-H), 3034 (C-H, Ar), 2988 (C-H, CH_2), 1676 (C=O), 1642 (C=N), 1610 (C=C, Ar), 1236 (C-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 11.14 (s, 1H, NH), 8.10 (s, 1H, NH), 7.65 (d, 2H, *J* = 7.1 Hz, Ar-H), 7.61 (s, 1H, CH), 7.54-7.35 (m, 4H, Ar-H), 7.31 (s, 1H, CH), 7.30 (d, 2H, *J* = 7.1 Hz, Ar-H), 4.58 (s, 2H, CH_2), 3.78 (s, 3H, CH_3), 3.31 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.3, 166.5, 158.4, 138.3, 134.2, 133.7, 127.4, 125.6, 123.7, 122.4, 120.1, 117.4, 113.6, 112.8, 77.4, 70.6, 58.3. MS: *m/z* 337 (M^+); Anal. Calcd. for $C_{19}H_{19}N_3O_3$: C-67.64, H-5.68, N-12.46, O-14.23. Found: C-66.36, H-4.98, N-11.28, O-13.87.

(1*H*-Indol-3-ylmethoxy)-acetic acid (4-chloro-benzylidene-hydrazide (4d) White solid, Yield: 76 %, M.P: 132-134 °C, IR (KBr): 3340 (N-H), 3036 (C-H, Ar), 2974 (C-H, CH_2), 1680 (C=O), 1624 (C=N), 1620 (C=C, Ar), 1242 (C-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 10.85 (s, 1H, NH), 8.12 (s, 1H, NH), 7.78-7.34 (m, 4H, Ar-H), 7.74 (d, 2H, *J* = 7.2 Hz, Ar-H), 7.48 (s, 1H, CH), 7.36 (s, 1H, CH), 7.35 (d, 2H, *J* = 7.2 Hz, Ar-H), 4.59 (s, 2H, CH_2), 3.29 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.5, 153.6, 139.7, 138.4, 133.2, 131.7, 130.5, 127.6, 124.7, 123.6, 121.0, 117.4, 115.6, 113.4, 77.4, 67.5. MS: *m/z* 341 (M^+); Anal. Calcd. for $C_{18}H_{16}ClN_3O_2$: C-63.25, H-4.72, Cl-10.37, N-12.29, O-9.36. Found: C-62.74, H-4.21, Cl-9.68, N-11.84, O-8.67.

(1*H*-Indol-3-ylmethoxy)-acetic acid (4-bromo-benzylidene-hydrazide (4e) Yellow solid, Yield: 69 %, M.P: 125-127 °C, IR (KBr): 3335 (N-H), 3042 (C-H, Ar), 2980 (C-H, CH_2), 1678 (C=O), 1646 (C=N), 1620 (C=C, aromatic), 1232 (C-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 11.10 (s, 1H, NH), 8.09 (s, 1H, NH), 7.72 (s, 1H, CH), 7.68 (d, 2H, *J* = 7.3 Hz, Ar-H), 7.54-7.21 (m, 4H, Ar-H), 7.36 (d, 2H, *J* = 7.3 Hz, Ar-H), 7.30 (s, 1H, CH), 4.74 (s, 2H, CH_2), 3.21 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.8, 156.3, 138.7, 134.6, 133.0, 132.7, 131.0, 128.7, 126.4, 123.7, 122.7, 120.4, 118.4, 116.1, 72.7, 68.7. MS: *m/z* 386 (M^+); Anal. Calcd. for $C_{18}H_{16}BrN_3O_2$: C-55.97, H-4.18, Br-20.69, N-10.88, O-8.28. Found: C-54.85, H-4.07, Br-19.86, N-10.21, O-8.03.

(1*H*-Indol-3-ylmethoxy)-acetic acid (4-nitro-benzylidene-hydrazide (4f) Pale yellow solid, Yield: 71 %, M.P: 140-142 °C, IR (KBr): 3325 (N-H), 3042 (C-H, Ar), 2990 (C-H, CH_2), 1685 (C=O), 1642 (C=N), 1625 (C=C, Ar), 1236 (C-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 11.08 (s, 1H, NH), 8.06 (s, 1H, NH), 7.92 (s, 1H, CH), 7.65 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.54-7.36 (m, 4H, Ar-H), 7.38 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.42 (s, 1H, CH), 4.65 (s, 2H, CH_2), 3.28 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.3, 156.3, 153.4, 138.7, 137.4, 133.1, 132.7, 125.7, 123.7, 124.7, 123.7, 121.4, 114.7, 113.1, 71.7, 68.4. MS: *m/z* 352 (M^+); Anal. Calcd. for $C_{18}H_{16}N_4O_4$: C-61.36, H-4.58, N-15.90, O-18.16. Found: C-60.84, H-4.23, N-15140, O-17.68.

1-[5-(1*H*-Indol-3-ylmethoxymethyl)-2-phenyl-[1,3,4]oxadiazol-3-yl]-ethanone (5a) Yellow solid, Yield: 74 %, M.P: 122-124 °C, IR (KBr): 3344 (N-H), 3061 (C-H, Ar), 2984 (C-H, CH_2), 1674 (C=O), 1652 (C=N), 1647 (C=C, Ar), 1241 (C-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 10.95 (s, 1H, NH), 7.84 (s, 1H, CH), 7.69-7.38 (m, 9H, Ar-H), 7.36 (s, 1H, CH), 4.58 (s, 2H, CH_2), 3.36 (s, 2H, CH_2), 2.61 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.3, 156.3, 142.6, 137.4, 132.7, 128.7, 125.7, 123.7, 124.7, 123.7, 121.4, 119.6, 114.7, 113.1, 76.3, 71.7, 69.7, 18.3. MS: *m/z* 349 (M^+); Anal. Calcd. for $C_{20}H_{19}N_3O_3$: C-68.75, H-5.48, N-12.03, O-13.74. Found: C-67.36, H-5.12, N-11.75, O-12.98.

1-[5-(1*H*-Indol-3-ylmethoxymethyl)-2-(4-methyl-phenyl)-[1,3,4]oxadiazol-3-yl]-ethanone (5b) Pale yellow solid, Yield: 70 %, M.P: 135-137 °C, IR (KBr): 3352 (N-H), 3054 (C-H, Ar), 2972 (C-H, CH_2), 1681 (C=O), 1647 (C=N), 1642 (C=C, Ar), 1249 (C-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 10.78 (s, 1H, NH), 7.84 (s, 1H, CH), 7.58 (d, 2H, *J* = 7.4 Hz, Ar-H), 7.50-7.28 (m, 4H, Ar-H), 7.30 (s, 1H, CH), 7.29 (d, 2H, *J* = 7.4 Hz, Ar-H), 4.59 (s, 2H, CH_2), 3.31 (s, 2H, CH_2), 2.69 (s, 3H, CH_3), 2.58 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.3, 157.4, 144.6, 139.4, 131.0, 127.6, 126.1, 124.7, 122.1, 121.2, 120.5, 118.4, 116.3, 115.1, 79.7, 76.3, 66.3, 23.1, 20.1. MS: *m/z* 363 (M^+); Anal. Calcd. for $C_{21}H_{21}N_3O_3$: C-69.41, H-5.82, N-11.56, O-13.21. Found: C-68.65, H-5.36, N-11.02, O-12.98.

1-[5-(1*H*-Indol-3-ylmethoxymethyl)-2-(4-methoxy-phenyl)-[1,3,4]oxadiazol-3-yl]-ethanone (5c) Brown solid, Yield: 75 %, M.P: 149-151 °C, IR (KBr): 3349 (N-H), 3065 (C-H, Ar), 2988 (C-H, CH_2), 1670 (C=O), 1643 (C=N), 1640 (C=C, Ar), 1235 (C-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 10.84 (s, 1H, NH), 7.79 (s, 1H, CH), 7.61 (d, 2H, *J* = 7.0 Hz, Ar-H), 7.54-7.31 (m, 4H, Ar-H), 7.36 (s, 1H, CH), 7.31 (d, 2H, *J* = 7.0 Hz, Ar-H), 4.51 (s, 2H, CH_2), 3.37 (s, 2H, CH_2), 2.89 (s, 3H, OCH_3), 2.45 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.7, 159.6, 144.7, 139.7, 133.0, 129.4, 127.4, 126.3, 125.0, 124.7, 124.2, 120.1, 113.6, 112.0, 78.7, 76.1, 68.1, 56.7, 21.7. MS: *m/z* 379 (M^+); Anal. Calcd. for $C_{21}H_{21}N_3O_4$: C-66.48, H-5.58, N-11.08, O-16.87. Found: C-65.23, H-5.21, N-10.84, O-16.12.

1-[5-(1*H*-Indol-3-ylmethoxymethyl)-2-(4-chloro-phenyl)-[1,3,4]oxadiazol-3-yl]-ethanone (5d) White solid, Yield: 74 %, M.P: 130-132 °C, IR (KBr): 3369 (N-H), 3065 (C-H, Ar), 2981 (C-H, CH_2), 1669 (C=O), 1652 (C=N), 1640 (C=C, Ar), 1235 (C-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 10.78 (s, 1H, NH), 7.71 (s, 1H, CH), 7.67 (d, 2H, *J* = 7.2 Hz, Ar-H), 7.62-7.36 (m, 4H, Ar-H), 7.32 (s, 1H, CH), 7.29 (d, 2H, *J* = 7.2 Hz, Ar-H), 4.62 (s, 2H, CH_2), 3.48 (s, 2H, CH_2), 2.65 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.7, 158.4, 143.6, 139.7, 134.2, 130.0, 127.4, 125.6, 124.3, 122.3, 120.7, 117.4, 116.2, 115.1, 78.6, 75.6, 66.7, 21.3. MS: *m/z* 383 (M^+); Anal. Calcd. for $C_{20}H_{18}ClN_3O_3$: C-62.58, H-4.73, Cl-9.24, N-10.95, O-12.51. Found: C-61.23, H-4.23, Cl-8.96, N-10.12, O-12.09.

1-[5-(1*H*-Indol-3-ylmethoxymethyl)-2-(4-bromo-phenyl)-[1,3,4]oxadiazol-3-yl]-ethanone (5e) Pale yellow solid, Yield: 77 %, M.P: 155-157 °C, IR (KBr): 3336 (N-H), 3068 (C-H, Ar), 2991 (C-H, CH_2), 1669 (C=O), 1648 (C=N), 1636 (C=C, Ar), 1232 (C-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 10.92 (s, 1H, NH), 7.84 (s, 1H, CH), 7.72 (d, 2H, *J* = 7.4 Hz, Ar-H), 7.68-7.37 (m, 4H, Ar-H), 7.32 (s, 1H, CH), 7.27 (d, 2H, *J* = 7.4 Hz, Ar-H), 4.71 (s, 2H, CH_2), 3.41 (s, 2H, CH_2), 2.51 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.0, 155.3, 141.7, 136.3, 133.7, 126.7, 124.6, 122.7, 121.0, 123.7, 121.4,

119.6, 114.7, 113.1, 76.3, 71.7, 69.7, 18.3. MS: *m/z* 428 (M^+); Anal. Calcd. for $C_{20}H_{18}BrN_3O_3$: C-56.09, H-4.24, Br-18.66, N-9.81, O-11.21. Found: C-55.12, H-4.04, Br-17.85, N-9.29, O-10.84.

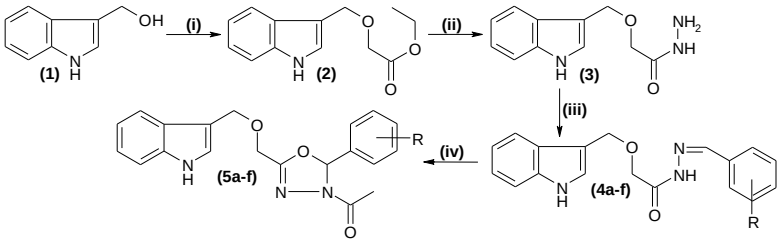
1-[5-(1*H*-Indol-3-ylmethoxymethyl)-2-(4nitro-phenyl)-[1,3,4]oxadiazol-3-yl]-ethanone (5f) White solid, Yield: 73 %, M.P: 161-163 °C, IR (KBr): 3362 (N-H), 3068 (C-H, Ar), 2978 (C-H, CH_2), 1684 (C=O), 1654 (C=N), 1639 (C=C, Ar), 1237 (C-O) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 10.70 (s, 1H, NH), 7.74 (s, 1H, CH), 7.68 (d, 2H, *J* = 7.3 Hz, Ar-H), 7.52-7.24 (m, 4H, Ar-H), 7.39 (s, 1H, CH), 7.28 (d, 2H, *J* = 7.3 Hz, Ar-H), 4.45 (s, 2H, CH_2), 3.41 (s, 2H, CH_2), 2.69 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.3, 156.3, 142.6, 137.4, 132.7, 128.7, 127.3, 125.7, 124.7, 123.0, 122.0, 116.3, 113.7, 111.0, 78.9, 70.1, 66.3, 22.0. MS: *m/z* 394 (M^+); Anal. Calcd. for $C_{20}H_{18}N_4O_5$: C-60.91, H-4.60, N-14.21, O-20.28. Found: C-59.98, H-4.23, N-13.87, O-19.68.

3. Results and Discussion

Thus, we have designed and synthesized various novel 1-[5-(1*H*-indol-3-ylmethoxymethyl)-2-phenyl-[1,3,4]oxadiazol-3-yl]-ethanone and its derivatives **(5a-f)**. The target compounds were synthesized by using commercially available (1*H*-indol-3-yl)-methanol **(1)** as starting material. The initial intermediate, (1*H*-indol-3-ylmethoxy)-acetic acid ethyl ester **(2)** has been prepared from compound **1** on reaction with bromo ethylacetate and K_2CO_3 in acetone solvent under reflux for 8 h. The next intermediate, (1*H*-indol-3-ylmethoxy)-acetic acid hydrazide **(3)** was afforded from the reaction between compound **2** and hydrazine hydrate in methanol solvent at room temperature for 8 h. Then compound **3** is turned into final intermediate, (1*H*-indol-3-ylmethoxy)-acetic acid-benzylidene-hydrazides **(4a-f)** on reaction with different aromatic aldehydes in presence of acetic acid in ethanol solvent under reflux for 5-6 h. Finally the target compounds, **5a-f** were synthesized from the reaction of compounds **4a-f** in acetic anhydride on reflux for 9-10 h. The chemical structures of the newly prepared compounds were confirmed by their IR, ^{1}H & ^{13}C NMR, mass spectral data and elemental analysis. Further the compounds have been used to evaluate their antimicrobial activity.

3.1 Antimicrobial Activity

All the newly synthesized target compounds, 1-[5-(1*H*-indol-3-ylmethoxymethyl)-2-phenyl-[1,3,4]oxadiazol-3-yl]-ethanone and its derivatives **(5a-f)** have been screened for their antibacterial activity against three representative bacteria like *Escherichia coli*, *Micrococus luteus* and *Staphylococcus aureus* and antifungal activity against three representative fungi such as *Aspergellius flavus*, *Aspergillus niger* and *Curvuliaria lunata*. The *in vitro* antimicrobial activity was carried out by using cup-plate method (13). Chloramphenicol (0.001 mole/ml) and Flucanazole (0.001 mole/ml) were used as standard drugs for the study of antibacterial and antifungal activity respectively. Inhibition was recorded by measuring the diameter of the inhibition zone at the end of 24 hr for bacteria and 48 hr for fungi. Each experiment was repeated thrice and the average of the three independent determinations was recorded. The results of the biological screening of these compounds are reported in Table 1. Among the screened compounds for antibacterial activity, compound **5a** was found to display considerable activity against all the bacteria, where as compound **5c** was found to exhibit promising activity against *E. coli* and *M. luteus*. Compound **5d** performed more antifungal activity than the bacterial activity and the compound **5f** exhibited almost equipotent activity against *A. flaves* and *A. niger* and was found to be more active than the standard against *C. lunata*.



Scheme 1: (i) $BrCH_2CO_2Et$, acetone, K_2CO_3, reflux, 8 h; (ii) NH_2NH_2, MeOH, RT, 8 h; (iii) ArCHO, EtOH, AcOH, reflux, 5-6 h; (iv) Ac_2O, reflux, 9-10 h.
R = (a) = H, (b) = 4-CH_3, (c) = 4-OCH_3, (d) = 4-Cl, (e) = 4-Br, (f) = 4-NO_2

Table 1: *In vitro* antimicrobial activity of compounds 5a-f (Zone of inhibition in mm)

Compound	Antibacterial activity			Antifungal activity		
	E. coli	*M. luteus*	*S. aureus*	*A. flavus*	*A. niger*	*C. lunata*
5a	34	33	36	14	12	15
5b	16	18	20	11	13	10
5c	34	32	30	14	16	15
5d	28	26	17	24	20	21
5e	18	20	19	11	13	12
5f	21	34	20	16	20	20
Chloramphenicol	40	38	44	-	-	-
Flucanazole	-	-	-	18	22	18

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