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Synthesis, Antibacterial and Antifungal Evaluation of Novel 3-(5-Phenyl[1,3,4]oxadiazol-2-yl]-3,4-dihydro-2*H*-benzo[e][1,3]oxazines

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Various novel 3-(5-phenyl[1,3,4]oxadiazol-2-yl]-3,4-dihydro-2*H*-benzo[e][1,3]oxazines (**5a-g**) have been synthesized from 5-phenyl-[1,3,4]oxadiazol-2-ylamine (**1**) and different salicylaldehydes (**2a-g**) as starting materials and 2-[(5-phenyl[1,3,4]oxadiazol-2-ylimino)methyl]phenols (**3a-g**) and 2-[(5-phenyl[1,3,4]oxadiazol-2-ylamino)methyl]phenols (**4a-g**) as intermediates. The newly synthesized compounds after structural confirmation were used to screen their antibacterial, antifungal and nematicidal activities and some of these compounds have been found as potential antimicrobial agents.

Keywords: 1,3,4-Oxadiazoles, 1,3-Oxazines, Antimicrobial activity, Nematicidal activity.

INTRODUCTION

1,3,4-Oxadiazoles are biologically active, synthetically useful and important heterocyclic compounds and investigation of their chemical and biological behavior have gained more importance in recent decades. Different classes of oxadiazoles possess an extensive spectrum of pharmacological activities such as antimalarial[1], antiinflammatory[2], anticonvulsant[3], analgesic[4], antimicrobial[5], antimycobacterial[6], antitumor[7], herbicidal[8], vasodialatory[9], cytotoxic[10], hypolipidemic[11] and antiedema[12].

Nitrogen heterocycles are of special interest because they constitute an important class of natural and nonnatural products, many of which exhibite useful biological activities. Investigation of the 1,3-oxazines has shown that they possess varied pharmacological properties such as analgesic, anticonvulsant, antitubercular, antibacterial and anticancer[13], anti HIV-1[14] and therapeutic activity[15]. The biological significance of these compounds impelled us to continue the work on the synthesis of some new and novel oxadiazoles and 1,3-oxazines.

EXPERIMENTAL

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 PerkinElmer 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 for ^{1}H NMR. The chemical shifts were reported as ppm down field using TMS as an internal standard. Mass spectra were recorded on a VG-Micromass 7070 H spectrometer operating at 70 eV.

2-[(5-Phenyl[1,3,4]oxadiazol-2-ylimino)methyl]phenols (3a-g): A mixture of 5-phenyl-[1,3,4]-oxadiazol-2-ylamine (**1**) (0.01 mol) and suitable salicylaldehyde (**2**) (0.01 mol) was refluxed in ethanol (10 mL) for 2-3 h. The resultant solution was cooled and the separated solid was filtered, dried and recrystallized from pet-ether.

2-[(5-Phenyl[1,3,4]oxadiazol-2-ylamino)methyl]phenols (4a-g): $NaBH_4$ (1.52 g, 0.04 mol) was added to a solution of 2-[(5-phenyl-[1,3,4]-oxadiazol-2-ylimino)-methyl] phenol (3) (0.01 mol) in ethanol (10 mL) and the mixture was stirred for 30-45 min room temperature. The solid separated, on pouring the mixture into ice-cold water, was filtered, dried and purified by column chromatography using a gradient of hexane-EtOAc (9:1-7:3).

3-(5-Phenyl[1,3,4]oxadiazol-2-yl]-3,4-dihydro-2*H*-benzo[*e*][1,3]oxazines (5a-g): Compound 2-[(5-phenyl-[1,3,4]-oxadiazol-2-ylamino)-methyl]-phenol 4 (0.01 mol) and formalin (37 %, 2 mL) were refluxed on a water bath for 5-6 h in $CHCl_3$ (10 mL). The solvent was evaporated *in vacuo* and the residue on purification by column chromatography using hexane-EtOAc (9:1) gave the desired product.

2-[(5-Phenyl[1,3,4]oxadiazol-2-ylimino)methyl] phenol (3a): White solid; Yield : 70 %, m.p. 125-127 °C; IR (KBr, ν_{max}, cm^{-1}): 3392 (O-H), 3073 (C-H, Ar), 1665 (C=N), 1623, 1582 (C=C, Ar); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.10-8.29 (m, 4H, Ar-H), 7.21-7.89 (m, 5H, Ar-H), 8.29 (s, 1H,CH), 11.69 (s, 1H,OH); MS: *m/z* (%) 265 (M^+).

5-Methyl-2-[(5-phenyl[1,3,4]oxadiazol-2-ylimino) methyl]phenol (3b): Pale yellow solid; Yield: 78 %, m.p. 145-147 °C; IR (KBr, ν_{max}, cm^{-1}): 3385 (O-H), 3065 (C-H, Ar), 2972 (C-H, CH_3), 1662 (C=N), 1605, 1585 (C=C, Ar); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.29 (s, 3H, CH_3), 7.10 (s, 1H, Ar-H), 7.14-7.69 (m, 5H, Ar-H), 7.89 (d, 1H, *J* = 7.8 Hz), 8.02 (s, 1H, CH), 8.12 (d, 1H, *J* = 7.8 Hz), 11.58 (s, 1H, OH); MS: *m/z* (%) 279 (M^+).

2-[(5-Phenyl[1,3,4]oxadiazol-2-ylimino)methyl]-6-trifluoromethoxy phenol (3c): White solid; Yield: 72 %, m.p. 160-162 °C; IR (KBr, ν_{max}, cm^{-1}): 3402 (O-H), 3056 (C-H, Ar), 1658 (C=N), 1632, 1565 (C=C, Ar), 1318 (C-F), 1158 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.15-8.08 (m, 3H, Ar-H), 7.12-7.80 (m, 5H, Ar-H), 8.12 (s, 1H, CH), 11.25 (s, 1H, OH); MS: *m/z* (%) 349 (M^+).

2-[(5-Phenyl[1,3,4]oxadiazol-2-ylimino)methyl]-4-trifluoromethoxy phenol (3d): Yellow solid; Yield: 76 %, m.p. 140-142 °C; IR (KBr, ν_{max}, cm^{-1}): 3385 (O-H), 3069 (C-H, Ar), 1654 (C=N), 1625, 1578 (C=C, Ar), 1325 (C-F), 1145 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.16 (s, 1H,Ar-H), 7.25-7.92 (m, 5H, Ar-H), 7.75 (d, 1H, *J* = 7.5 Hz), 8.16 (d, 1H, *J* = 7.5 Hz), 7.98 (s, 1H, CH), 11.21 (s, 1H, OH); MS: *m/z* (%) 349 (M^+).

4-Chloro-2-[(5-phenyl[1,3,4]oxadiazol-2-ylimino) methyl] phenol (3e): Pale yellow solid; Yield: 73 %, m.p. 165-167 °C; IR (KBr, ν_{max}, cm^{-1}): 3378 (O-H), 3071 (C-H, Ar), 1661 (C=N), 1625, 1582 (C=C, Ar), 1210 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.26 (s, 1H, Ar-H), 7.15-7.78 (m, 5H, Ar-H), 7.84 (d, 1H, *J* = 7.6 Hz, Ar-H), 7.85 (s, 1H, CH), 8.06 (d, 1H, *J* = 7.6 Hz), 10.98 (s, 1H,OH); MS: *m/z* (%) 299 (M^+).

4-Amino-2-[(5-phenyl[1,3,4]oxadiazol-2-ylimino) methyl]phenol (3f): White solid; Yield: 71 %, m.p. 150-152 °C; IR (KBr, ν_{max}, cm^{-1}): 3452 (N-H), 3374 (O-H), 3066 (C-H, Ar), 1672 (C=N), 1619, 1565 (C=C, Ar); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.73 (s, 2H, NH_2), 7.23 (s, 1H, , Ar-H), 7.15-7.75 (m, 5H, Ar-H, Ar-H), 7.78 (d, 1H, *J* = 7.4 Hz, Ar-H), 7.85 (s, 1H, CH), 7.98 (d, 1H, *J* = 7.4 Hz, Ar-H), 10.85 (s, 1H, OH); MS: *m/z* (%) 280 (M+).

4-Nitro-2-[(5-phenyl[1,3,4]oxadiazol-2-ylimino) methyl]phenol (3g): Yellow solid; Yield: 75 %, m.p. 154-156 °C; IR (KBr, ν_{max}, cm^{-1}): 3384 (O-H), 3062 (C-H, Ar), 1658 (C=N), 1619, 1562 (C=C, Ar), 1365 (N=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.12 (s, 1H, , Ar-H), 7.26-7.95 (m, 5H, Ar-H), 7.72 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.84 (s, 1H, CH), 8.06 (d, 1H, *J* = 7.8 Hz, Ar-H), 11.06 (s, 1H, OH); MS: *m/z* (%) 310 (M^+).

2-[(5-Phenyl[1,3,4]oxadiazol-2-ylamino)methyl]phenol (4a): Yellow solid; Yield: 70 %, m.p. 130-132 °C; IR (KBr, ν_{max}, cm^{-1}): 3452 (N-H), 3385 (O-H), 3054 (C-H, Ar), 2954 (C-H, CH_2), 1662 (C=N), 1605, 1545 (C=C, Ar); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.55 (s, 2H, CH2), 6.05 (s, 1H, NH), 7.24-8.12 (m, 4H, Ar-H), 7.32-7.89 (m, 5H, Ar-H), 11.12 (s, 1H, OH); MS: *m/z* (%) 267 (M^+).

5-Methyl-2-[(5-phenyl[1,3,4]oxadiazol-2-ylamino) methyl]phenol (4b): Pale yellow solid; Yield: 74 %, m.p. 144-146 °C; IR (KBr, ν_{max}, cm^{-1}): 3462 (N-H), 3358 (O-H), 3065 (C-H, Ar), 2965 (C-H, CH_2), 1654 (C=N), 1621, 1575 (C=C, Ar); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.26 (s, 3H, CH_3), 2.62 (s, 2H, CH_2), 6.15 (s, 1H, NH), 7.71 (d, 1H, *J* = 7.2 Hz, Ar-H), 7.75 (d, 1H, *J* = 7.2 Hz, Ar-H), 7.26 (s, 1H, Ar-H), 7.15-7.76 (m, 5H, Ar-H), 11.21 (s, 1H, OH),; MS: *m/z* (%) 281 (M^+).

2-[(5-Phenyl[1,3,4]oxadiazol-2-ylamino)methyl]-6-trifluoromethoxy phenol (4c): White solid; Yield: 77 %, m.p. 175-177 °C; IR (KBr, ν_{max}, cm^{-1}): 3415 (N-H), 3385 (O-H), 3058 (C-H, Ar), 2945 (C-H, CH_2), 1658 (C=N), 1628, 1575 (C=C, Ar), 1328 (C-F), 1165 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.42 (s, 2H, CH_2), 6.12 (s, 1H, NH), 7.20-8.04 (m, 3H, Ar-H), 7.15-7.98 (m, 5H, Ar-H), 10.93 (s, 1H, OH); MS: *m/z* (%) 351 (M^+).

2-[(5-Phenyl[1,3,4]oxadiazol-2-ylamino)methyl]-4-trifluoromethoxy phenol (4d): Pale yellow solid; Yield: 71 %, m.p. 156-158 °C; IR (KBr, ν_{max}, cm^{-1}): 3448 (N-H), 3365 (O-H), 3045 (C-H, Ar), 2952 (C-H, CH_2), 1654 (C=N), 1618, 1574 (C=C, Ar), 1315 (C-F), 1146 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.56 (s, 2H, CH_2), 5.98 (s, 1H, NH), 7.18 (s, 1H, Ar-H), 7.12-7.96 (m, 5H, Ar-H), 7.73 (d, 1H, *J* = 7.8 Hz), 7.86 (d, 1H, *J* = 7.4 Hz), 11.12 (s, 1H,OH); MS: *m/z* (%) 351 (M^+).

4-Chloro-2-[(5-phenyl[1,3,4]oxadiazol-2-ylamino) methyl]phenol (4e): Yellow solid; Yield: 73 %, m.p. 168-170 °C; IR (KBr, ν_{max}, cm^{-1}): 3445 (N-H), 3365 (O-H), 3045 (C-H, Ar), 2963 (C-H, CH_2), 1651 (C=N), 1645, 1568 (C=C, Ar), 1225 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.49 (s, 2H, CH_2), 5.96 (s, 1H, NH), 7.21 (s, 1H, Ar-H), 7.25-7.90 (m, 5H, Ar-H), 7.74 (d, 1H, *J* = 7.6 Hz, Ar-H), 7.84 (d, 1H, *J* = 7.6 Hz, Ar-H), 11.01 (s, 1H, OH); MS: *m/z* (%) 301 (M^+).

4-Amino-2-[(5-phenyl[1,3,4]oxadiazol-2-ylamino) methyl]phenol (4f): Pale yellow solid; Yield: 76 %, m.p. 142-144 °C; IR (KBr, ν_{max}, cm^{-1}): 3418 (N-H), 3363 (O-H), 3069 (C-H, Ar), 2945 (C-H, CH_2), 1672 (C=N), 1632, 1564 (C=C, Ar); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.42 (s, 2H, CH_2), 5.70 (s, 2H, NH_2), 6.12 (s, 1H, NH), 7.23 (s, 1H, Ar-H), 7.12-7.75 (m, 5H, Ar-H), 7.80 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.95 (d, 1H, *J* = 7.8 Hz, Ar-H), 10.85 (s, 1H, OH); MS: *m/z* (%) 282 (M^+).

4-Nitro-2-[(5-phenyl[1,3,4]oxadiazol-2-ylamino) methyl]phenol (4g): White solid; Yield : 74 %, m.p. 135-137 °C; IR (KBr, ν_{max}, cm^{-1}): 3428 (N-H), 3374 (O-H), 3062 (C-H, Ar), 2965 (C-H, CH_2), 1654 (C=N), 1632, 1575 (C=C, Ar), 1348 (N=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.45 (s, 2H, CH_2), 6.09 (s, 1H, NH), 7.16 (s, 1H, Ar-H), 7.12-7.98 (m, 5H, Ar-H), 7.69 (d, 1H, *J* = 7.6 Hz, Ar-H), 7.75 (d, 1H, *J* = 7.6 Hz, Ar-H), 10.98 (s, 1H,OH); MS: *m/z* (%) 312 (M^+).

3-(5-Phenyl[1,3,4]oxadiazol-2-yl]-3,4-dihydro-2*H*-benzo[*e*][1,3]oxazine (5a): Pale yellow solid; Yield: 70 %, m.p. 154-156 °C; IR (KBr, ν_{max}, cm^{-1}): 3065 (C-H, Ar), 2945 (C-H, CH_2), 1658 (C=N), 1612, 1548 (C=C, Ar), 1146 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.98 (s, 2H, OCH_2), 4.23 (s, 2H, NCH_2), 7.12-8.02 (m, 4H, Ar-H), 7.19-7.82 (m, 5H, Ar-H); MS: *m/z* (%) 279 (M^+).

7-Methyl-3-(5-phenyl[1,3,4]oxadiazol-2-yl]-3,4-dihydro-2*H*-benzo[*e*][1,3]oxazine (5b): Yellow solid; Yield: 74 %, m.p. 180-182 °C; IR (KBr, ν_{max}, cm^{-1}): 3052 (C-H, Ar), 2948 (C-H, CH_2), 1654 (C=N), 1614, 1538 (C=C, Ar), 1142

(C-O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.32 (s, 3H, CH_3), 4.02 (s, 2H, OCH_2), 4.32 (s, 2H, NCH_2), 7.18 (s, 1H, Ar-H), 7.23-7.81 (m, 5H, Ar-H), 7.78 (d, 1H, *J* = 7.4 Hz, Ar-H), 7.95 (d, 1H, *J* = 7.4 Hz, Ar-H); MS: *m/z* (%) 293 (M^+).

3-(5-Phenyl[1,3,4]oxadiazol-2-yl]-8-trifluoromethoxy-3,4-dihydro-2*H*-benzo[*e*][1,3]oxazine (5c): Pale yellow solid; Yield: 76 %, m.p. 170-172 °C; IR (KBr, ν_{max}, cm^{-1}): 3038 (C-H, Ar), 2942 (C-H, CH_2), 1668 (C=N), 1645, 1538 (C=C, Ar), 1328 (C-F), 1142 (C-O), 1154 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.85 (s, 2H, OCH_2), 4.19 (s, 2H, NCH_2), 7.15-7.98 (m, 3H, Ar-H), 7.25-7.79 (m, 5H, Ar-H); MS: *m/z* (%) 363 (M^+).

3-(5-Phenyl[1,3,4]oxadiazol-2-yl]-6-trifluoromethoxy-3,4-dihydro-2*H*-benzo[*e*][1,3]-oxazine (5d): Pale yellow solid; Yield: 78 %, m.p. 154-156 °C; IR (KBr, ν_{max}, cm^{-1}): 3054 (C-H, Ar), 2954 (C-H, CH_2), 1662 (C=N), 1605, 1545 (C=C, Ar), 1321 (C-F), 1146 (C-O), 1138 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.85 (s, 2H, OCH_2), 4.15 (s, 2H, NCH_2), 7.25 (s, 1H, Ar-H), 7.12-7.65 (m, 5H, Ar-H), 7.75 (d, 1H, *J* = 7.6 Hz, Ar-H), 8.05 (d, 1H, *J* = 7.6 Hz, Ar-H); MS: *m/z* (%) 363 (M^+).

6-Chloro-3-(5-phenyl[1,3,4]oxadiazol-2-yl]-3,4-dihydro-2H-benzo[e][1,3]oxazine (5e): Pale yellow solid; Yield: 72 %, m.p. 160-162 °C; IR (KBr, ν_{max}, cm^{-1}): 3036 (C-H, Ar), 2942 (C-H, CH_2), 1652 (C=N), 1625, 1565 (C=C, Ar), 1234 (C-Cl), 1132 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.05 (s, 2H, OCH_2), 4.36 (s, 2H, NCH_2), 7.18 (s, 1H, Ar-H), 7.14-7.85 (m, 5H, Ar-H), 7.82 (d, 1H, *J* = 7.8 Hz, Ar-H), 8.08 (d, 1H, J = 7.8 Hz, Ar-H); MS: *m/z* (%) 313 (M^+).

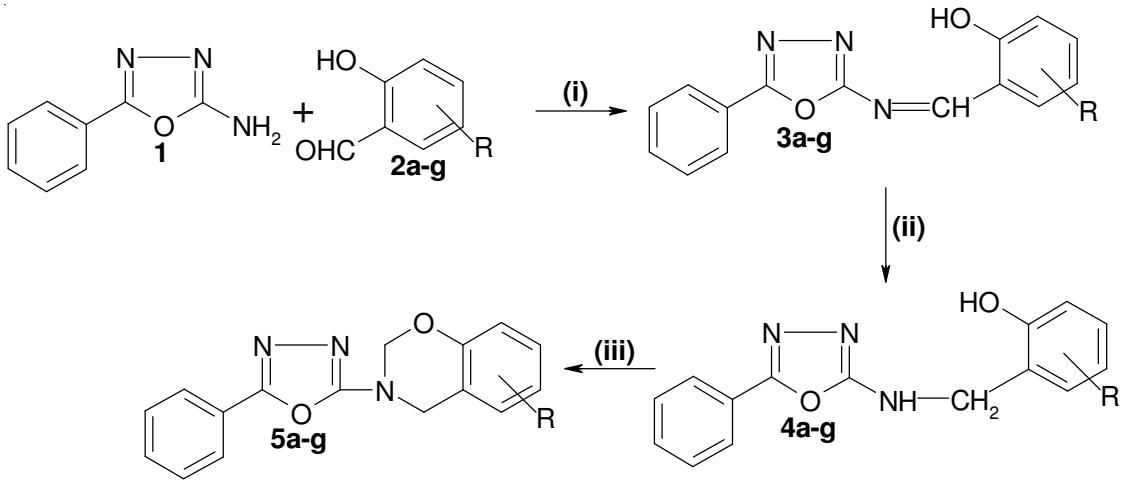
6-Amino-3-(5-phenyl[1,3,4]oxadiazol-2-yl]-3,4-dihydro-2*H*-benzo[*e*][1,3]oxazine (5f): White solid; Yield: 75 %, m.p. 166-168 °C; IR (KBr, ν_{max}, cm^{-1}): 3426 (N-H), 3045 (C-H, Ar), 2958 (C-H, CH_2), 1654 (C=N), 1628, 1536 (C=C, Ar), 1148 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.84 (s, 2H, OCH_2), 4.12 (s, 2H, NCH_2), 5.85 (s, 2H, NH_2), 7.15 (s, 1H, Ar-H), 7.25-8.02 (m, 5H, Ar-H), 7.95 (d, 1H, *J* = 7.4 Hz, Ar-H), 8.06 (d, 1H, *J* = 7.4 Hz, Ar-H); MS: *m/z* (%) 294 (M^+).

6-Nitro-3-(5-phenyl[1,3,4]oxadiazol-2-yl]-3,4-dihydro-2H-benzo[e][1,3]oxazine (5g): Yellow solid; Yield: 73 %, m.p. 148-150 °C; IR (KBr, ν_{max}, cm^{-1}): 3048 (C-H, Ar), 2965 (C-H, CH_2), 1646 (C=N), 1626, 1534 (C=C, Ar), 1356 (N=O), 1142 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.84 (s, 2H, OCH_2), 4.19 (s, 2H, NCH_2), 7.04 (s, 1H, Ar-H), 7.22-7.85 (m, 5H, Ar-H), 7.65 (d, 1H, *J* = 7.6 Hz, Ar-H), 7.89 (d, 1H, *J* = 7.6 Hz, Ar-H); MS: *m/z* (%) 324 (M^+).

RESULTS AND DISCUSSION

On the basis of these findings and as a part of our ongoing research involving the synthesis of biologically active compounds, we have reported this work on synthesis and biological properties of various novel 3-(5-phenyl[1,3,4]oxadiazol-2-yl]-3,4-dihydro2*H*-benzo[*e*][1,3]oxazines (**5a-g**). Accordingly, the synthetic route leading to the title compounds (**5a-g**) is summarized in **Scheme-I**. The key intermediates, 2-[(5-phenyl[1,3,4]-oxadiazol-2-ylimino)methyl]phenols (**3a-g**) have been prepared from the condensation reaction between commercially available 5-phenyl[1,3,4]oxadiazol-2-ylamine (**1**) and different salicylaldehydes (**2a-g**) in ethanol under reflux for 2-3 h. The reduction of compounds **3a-g** with sodium borohydride in ethanol at room temperature for 30-45 min afforded the subsequent intermediates 2-[(5-phenyl[1,3,4]oxadiazol-2-ylamino)-methyl]phenols (**4a-g**). Further, the target compounds **5a-g** were prepared in good to excellent yields through Mannich type condensation followed by cyclization of compounds **4a-g** with formaldehyde in chloroform at reflux temperature for 5-6 h. The chemical structures of all the newly synthesized compounds were confirmed by their IR, ^{1}H, ^{13}C NMR, mass spectral data and elemental analysis. Further these compounds have been screened for their antibacterial, antifungal and nematicidal activities. On the other hand, there is no report on the synthesis of 3-(5-phenyl[1,3,4]oxadiazol-2-yl]-3,4-dihydro-2*H*-benzo[*e*][1,3]-oxazines (**5a-g**) from any compound including 5-phenyl[1,3,4]oxadiazol-2-ylamine (**1**) and salicylaldehyde (**2**).

Antibacterial activity: The newly synthesized novel compounds **5a-g**, were assayed for their antibacterial activity against three Gram-positive bacteria *viz*., *Bacillus subtilis*, *Staphylococcus aureus* and *Micrococcus luteus* and three Gram-negative bacteria *viz*., *Proteus vulgaris*, *Salmonella typhimurium* and *Escherichia coli* by the broth dilution method[16]. The minimum inhibitory concentration (MIC, µg/mL) was determined for all the compounds and standard control ampicillin. The investigation of antibacterial screening data revealed that the compound containing 3-trifluoro methoxy



Scheme-I: (i) EtOH, Reflux, 2-3 h; (ii) $NaBH_4$, EtOH, RT, 30-45 min; (iii) Formalin, $CHCl_3$, Reflux, 5-6 h, 3-5 R (a) = H, (b) = 4-CH_3, (c) = 3-OCF_3, (d) = 5-OCF_3, (e) = 5-Cl, (f) = 5-NH_2, (g) = 5-NO_2

group on salicylaldehyde ring **5c** is highly active against all the microorganisms employed except *E. coli* at 1.56 µg/mL concentration which is equal to the standard. Compound **5g** with nitro moiety on same ring is also exhibited high active against *M. luteus* and *P. vulgaris* at the same concentration as **5c**. The compound having 5-trifluoro methoxy substituent on salicylaldehyde ring **5d** also showed good antibacterial activity against all the organisms tested. Compound **5a** is almost inactive towards *M. luteus* and *E. coli*. The remaining compounds showed moderate to good activity (Table-1).

TABLE-1
ANTIBACTERIAL ACTIVITY OF 3-(5-PHENYL-[1,3,4]-OXADIAZOL-2-YL]-3,4-DIHYDRO-2*H*-BENZO[*e*][1,3]-OXAZINES (**5a-g**) (ZONE OF INHIBITION IN mm AT 100 µg/mL)

S. No	*B. subtilis*	*S. aureus*	*M. luteus*	*P. vulgaris*	*S. typhi-murium*	*E. coli*
5a	12.5	12.5	–	12.5	12.5	25
5b	6.25	12.5	6.25	6.25	6.25	12.5
5c	1.56	1.56	1.56	1.56	1.56	12.5
5d	3.12	6.25	1.56	1.56	3.12	1.56
5e	6.25	6.25	6.25	–	12.5	6.25
5f	12.5	6.25	3.12	12.5	6.25	12.5
5g	6.25	12.5	1.56	1.56	12.5	12.5
Ampicillin	1.56	1.56	1.56	3.12	3.12	12.5

— Indicates bacteria are resistant to the compound > 50 µg/mL concentration.

Antifungal activity: Compounds **5a-g** were also screened for their antifungal activity against four fungal organisms *viz. Candida albicans, Aspergillus fumigatus, Trichophyton rubrum* and *Trichophyton mentagrophytes* in dimethyl sulfoxide by broth dilution method[16]. The minimum inhibitory concentration (MIC, µg/mL) were measured and compared with the standard drug amphotericin B. The MIC values of the screened compounds are given in Table-2. The antifungal screening data showed good activity of the tested compounds. Among the screened compounds **5c** is highly active against *T. rubrum, T. mentagrophytes*, **5e** is also active against only *C. albicans* and **5d** is highly active against *C. albicans, T. mentagrophytes*, the activity of these compounds are almost equal to the standard. It is interesting to note that **5d** and **5e** showed excellent antifungal activity towards *C. albicans* at the concentration of 3.12 µg/mL, which is less than the concentration of the standard. The remaining compounds performed moderate to good activity.

TABLE-2
ANTIFUNGAL ACTIVITY OF COMPOUNDS **5a-g**
(ZONE OF INHIBITION IN mm AT 100 µg/mL)

S. No.	*C. albicans*	*A. fumigatus*	*T. rubrum*	*T. mentagropytes*
5a	25.0	12.5	>50.0	25.0
5b	25.0	25.0	25.0	25.0
5c	12.5	6.25	3.12	3.12
5d	3.12	6.25	6.25	3.12
5e	3.12	12.5	12.5	25.0
5f	50.0	25.0	12.5	12.5
5g	25.0	25.0	12.5	3.12
Amphotericin B	6.25	3.12	3.12	3.12

Nematicidal activity: All the newly synthesized compounds **5a-g**, were also assayed for their nematicidal activity against *Ditylenchus myceliophagus* and *Caenorhabditis elegans* by aqueous *in vitro* screening technique[17] at various concentrations. The nematicidal activity of each tested compound was compared with the standard drug Levamisole. The results are expressed in terms of LD_{50} *i.e.* median lethal dose at which 50 % of nematodes became immobile (dead). The nematicidal screening data (Table-3) revealed that the compound **5e** is the most effective against *D. myceliophagus* and *C. elegans* with LD_{50} of 160 and 180 ppm, respectively and is almost equally active as the standard. Compounds **5f** and **5g** are also most active against *C. elegans* with LD_{50} of 190 ppm and *D. myceliophagus* with LD_{50} of 180 ppm, respectively. The other tested compounds showed moderate activity.

TABLE-3
MEDIAN LETHAL DOSE (LD_{50}, ppm) OF COMPOUNDS **5a-g**

S. No.	**5a**	**5b**	**5c**	**5d**	**5e**	**5f**	**5g**	**Levmisole**
Dm	780	840	550	260	160	420	180	160
Ce	750	760	350	210	180	190	760	170

Dm = *D. myceliophagus*; Ce = *C. elegans*

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