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Research Article

Synthesis, characterization and antimicrobial activity of novel 2,5-substituted aryl-7-phenyl-1,3,4-oxadiazolo-[3,2-a]-1,3,5-triazine derivatives

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Abstract

Synthesized fused heterocyclic compounds 1,3,4-oxadiazolo[3,2-a]-s-triazine derivatives based on microwave mediate multi-component reaction (MCRs). In general, multi-component reactions (MCRs) are economically and environmentally very advantageous because multi-step syntheses produce considerable amounts of waste mainly due to complex isolation procedures often involving expensive, toxic and hazardous solvents after each step. Simpler procedures, equipment, lower costs, time and energy and environmentally friendly.

All the synthesized compounds were characterized using physical and spectral analysis. Antimicrobial activity of synthesized compounds was carried out by cup-plate method. All the synthesized compounds show a moderate biological activity. The compound 1c, 1e, 1i, 2b, 2d, 2i and 1b, 1e, 1j, 2a, 2d shows better significant antibacterial and antifungal activity respectively.

Keywords: s-triazine, Semicarbazone, Schiff's base, Antimicrobial agent, microwave mediate multi-component reaction (MCRs)

1. Introduction

Heterocyclic compounds bearing a symmetrical s-triazine or 1,3,5-triazine moietie, represent an interesting class of compounds possessing a wide spectrum of biological activities such as anti-cancer[1-5], antiviral[6,7], bactericidal[8-14], fungicidal[15-17], antimalarial agents[18-20], herbicidal[21] and anti-tuberculosis[22]. 1,3,4-oxadiazole ring is also associated with various biological activities. A number of condensed ring system incorporating 1,3,4-oxadiazole nucleus is reported as potential fungicides, bactericides, herbicides and anticancer activity. In continuous of our works on synthesized fused heterocyclic compounds 1,3,4-oxadiazole [3,2-a]-s-triazine derivatives and Both the nuclei i.e. 1,3,4-oxadiazole and 1,3,5-triazine might be show enhanced potency activity[23-25].

The present study report the synthesis of 2,5-substituted aryl-7-phenyl-[1,3,4]-oxadiazolo- [3,2-a][1,3,5]-triazine (fig 1). Required semicarbazones were prepared by using the reported method as a reaction between aldehyde and semicarbazide (Vogel's,1996). Starting compound 2-amino-5-aryl-1,3,4-oxadiazole were synthesized by using Semicarbazone (0.01 M) and sodium acetate (0.02 M) were dissolved in 30–40 ml of glacial acetic acid taken in a round-bottomed flask equipped with a separating funnel for the addition of bromine. Bromine (0.7 ml in 5ml glacial acetic acid) was added slowly to it, while stirring magnetically. After half an hour stirring, the solution was poured on crushed ice. The resulting solid was separated, dried and recrystallized from aldehyde free ethanol (Vogel's, 1996). Respective Schiff's base were synthesized reaction between 2-amino-5-aryl-1,3,4-oxadiazole and aromatic aldehyde [26]. By considering the above facts a novel series of 2,5-substituted aryl-7-phenyl-[1,3,4]-oxadiazole-[3,2-a][1,3,5]-triazine derivatives have been synthesized and screened for antimicrobial activity. The structures of the compounds were assigned on the basis of IR, ^{1}HNMR and Mass spectral data.

2. Material and Methods

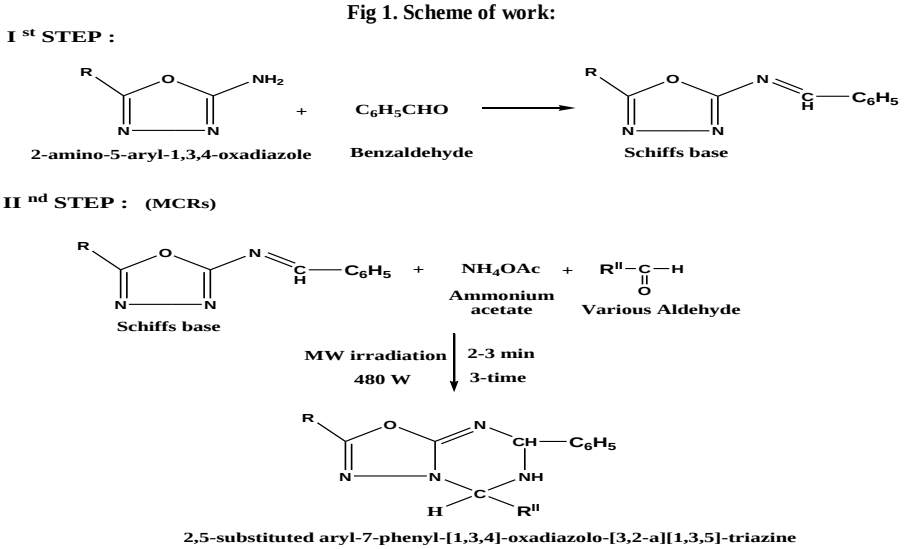
All the chemicals used were that of laboratory grade. Melting points were determined in open capillary tubes and were found uncorrected. The progresses of reactions were monitored by TLC. All compounds were purified by recrystallization with suitable organic solvents. The Purity of all the compounds was checked on Precoated silica gel-G plates using iodine vapour as detecting agent. IR spectra were recorded on FT-IR Spectrometer (Perkin Elmer) using KBr disc method. ^{1}H-NMR spectra were recorded on Bruker avance-400 MHz NMR spectrometer in DMSO, $CDCl_3$. Mass spectra were recorded on LC-MSD-Tranp-SL2010A Shimadzu.

2.1 Chemistry

2.1.1 Synthesis of Schiff's base: A solution of 2-amino-5-aryl-1,3,4-oxadiazole (0.01 M) was prepared in 30 ml alcohol in a round-bottomed flask. Benzaldehyde (0.01 M) then added to it. The mixture was refluxed for 5–6 hr. The volume of alcohol was reduced to half by distillation under reduced pressure. The resulting solution was poured on crushed ice. The precipitate which got separated was dried and recrystallized from alcohol. (Compound-1)

2.1.2 Synthesis of 2,5-substituted aryl-7-phenyl-[1,3,4]-oxadiazole-[3,2-a][1,3,5]-triazine (1a-1n) and (2a-2n). Schiff's base (compound-1) (0.01mol) was mix with ammonium acetate and various aromatic aldehyde treated in MW irradiation at 480 W for three times with minimum 2 min of intervals. Step-2 based on microwave mediate multi-component reaction (MCRs).[27]

Fig 1. Scheme of work:



2,5,7-triphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine(1a): M.P.-145°C, IR(KBr): 3370.23(N-H str.), 3068.65(=C-H str.), 2917.59(C-H str.), 1445.26 (C=C str.), 1657.18(C=N str.), 1047.94(C-O-C str.), 1308.17(N-N=C str.), ^{1}H-NMR(DMSO, δ ppm): 2.31(s,1H, NH), 3.80(s, 1H, CH), 5.17(s, 1H, CH), 7.025–7.7726(m, 15H, Ar-H), MS: m/z-354.12

5-(2-hydroxyphenyl)-2,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine (1b) : M.P.-180°C, IR(KBr):3432.66(O-H str.), 3162.62(N-H str.), 2907.73(C-H str.), 1445.38 (C=C str.), 1591.20(C=N str.), 1064.01(C-O-C str.), 1265.91(N-N=C str.),^{1}H-NMR(DMSO, δ ppm): 2.14(s, 1H, NH), 3.71(s, 1H, CH), 5.19(s, 1H, OH), 5.37(s, 1H, CH), 7.24–7.64(m, 14H, Ar-H), MS: m/z-370.24

5-(3-hydroxyphenyl)-2,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine (1c): M.P.-210°C, IR(KBr): 3313.59(O-H str.), 3062.14(C-H str.), 1433.91(C=C str.), 1676.01 (C=N str.), 1044.37(C-O-C str.), 1242.34(N-N=C str.), MS: m/z-370.04

5-(4-hydroxyphenyl)-2,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine (1d): M.P.-222°C, IR(KBr):3347.52(O-H str.), 3158.99(N-H str.), 2968.28(=C-H str.), 2882.07 (C-H str.), 1472.52(C=C str.), 1543.38(C=N str.), 1125.52(C-O-C str.), 1212.27(N-N=C str.), MS: m/z-370.24

5-(2-nitrophenyl)-2,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine(1e): M.P.-188°C, IR(KBr):3234.02(N-H str.), 2916.75(C-H str.), 1452.66(C=C str.), 1677.95 (C=N str.), 1090.14(C-O-C str.), 1281.76(N-N=C str.), 1360.55(C-NO_2 str.), ^{1}H-NMR (DMSO, δ ppm): 2.35(s, 1H, NH), 4.25(s, 1H, CH), 5.27(s, 1H, CH), 7.01–7.77(m, 14H, Ar-H), MS: m/z-399.11

5-(3-nitrophenyl)-2,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine(1f): M.P.-178°C, IR(KBr): 3234.19(N-H str.), 2884.14(C-H str.), 1452.46(C=C str.), 1677.45(C=N str.), 1077.77(C-O-C str.), 1284.56(N-N=C str.), 1348.05(C-NO_2 str.), MS: m/z-399.35

5-(4-nitrophenyl)-2,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine(1g): M.P.-200°C, IR(KBr): 3332.62(N-H str.), 2916.03(C-H str.), 1451.81(C=C str.), 1673.96 (C=N str.), 1083.95(C-O-C str.), 1300.73(N-N=C str.), 1505.17(C-NO_2 str.), MS: m/z-399.33

5-(2-chlorophenyl)-2,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine(1h): M.P.- 206°C, IR(KBr): 3323.34(N-H str.), 2950.07(C-H str.), 1462.76(C=C str.), 1627.20(C=N str.), 1037.18(C-O-C str.), 1268.39(N-N=C str.), 744.23(C-Cl str.),^{1}H-NMR(DMSO,δ ppm): 2.39(s, 1H, NH), 3.89(s, 1H, CH), 5.18(s, 1H, CH), 7.01–7.94(m, 14H, Ar-H), MS: m/z-388.21

5-(4-chlorophenyl)-2,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine(1i): M.P.-190°C, IR(KBr): 3294.77(N-H str.), 2982.07(C-H str.), 1492.08(C=C str.), 1612.73 (C=N str.), 1100.68(C-O-C str.), 1237.91(N-N=C str.), 745.24(C-Cl str.), MS: m/z-388.82

5-(4-dimethylaminophenyl)-2,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5] triazine(1j): M.P.-169°C, IR(KBr): 3352.09(N-H str.), 2916.42(C-H str.), 1451.78(C=C str.), 1615.73(C=N str.), 1093.14(C-O-C str.), 1300.27(N-N=C str.),^{1}H-NMR(DMSO,δ ppm): 2.28 (s, 1H, NH), 3.23(s, 6H, CH_3), 4.14(s, 1H, CH), 5.37(s, 1H, CH), 7.24 – 8.25(m, 14H, Ar-H), MS: m/z-397.17

5-(3,4,5-trimethoxyphenyl)-2,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5] triazine(1k): M.P.-245°C, IR(KBr): 3309.56(N-H str.), 3134.02(=C-H str.), 2923.09(C-H str.), 1496.82(C=C str.), 1597.39(C=N str.), 1032.28(C-O-C str.), 1200.02(N-N=C str.),MS: m/z-444.03

5-(4-methoxyphenyl)-2,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine (1l): M.P.-156°C, (KBr): 3317.17(N-H str.), 3062.99(=C-H str.), 1514.03(C=C str.), 1596.65 (C=N str.), 1107.21(C-O-C str.), 1293.59(N-N=C str.), MS: m/z-384.21

5-(3-methoxy-4-hydroxyphenyl)-2,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2a][1,3,5] triazine(1m): M.P.-196°C, IR(KBr): 3440.03(O-H str.), 2979.48(=C-H str.), 1443.91(C=C str.), 1671.37(C=N str.), 1070.61(C-O-C str.), 1266.89(N-N=C str.), MS: m/z-400.23

5-(2,5-dichlorophenyl)-2,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine (1n): M.P.-237°C, IR(KBr): 3458.08(N-H str.), 3192.00(=C-H str.), 1477.37(C=C str.), 1660.43 (C=N str.), 1104.08(C-O-C str.), 1251.42(N-N=C str.), 771.92(C-Cl str.), MS: m/z-423.17

2-(4-hydroxyphenyl)-5,7-diphenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine (2a): M.P.-190°C, IR(KBr): 3418.08(O-H str.), 3386.30(N-H str.), 2985.50(=C-H str.), 2919.23 (C-H str.), 1470.12(C=C str.), 1634.03(C=N str.), 1047.78(C-O-C str.), 1256.58(N-N=C str.), ^{1}H-NMR (DMSO,δ ppm): 2.30(s, 1H, NH), 4.40(s, 1H, CH), 5.28(s, 1H, OH), 5.63(s, 1H, CH), 7.61– 8.04(m, 14H, Ar-H), MS: m/z-370.33

2-(4-hydroxyphenyl)-5-(2-hydroxyphenyl)]7-phenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine(2b): M.P.-275°C, IR(KBr): 3455.02(O-H str.), 3324.07(N-H str.), 2970.74 (C-H str.), 1468.48(C=C str.), 1689.93(C=N str.), 1091.81(C-O-C str.), 1198.93(N-N=C str.), ^{1}H-NMR (DMSO,δ ppm): 2.11(s, 1H, NH), 5.10(s, 1H, OH), 5.20(s, 1H, OH), 4.30(s, 1H, CH), 5.51(s, 1H, CH), 7.22-7.81(m, 14H, Ar-H), MS: m/z-386.35

2-(4-hydroxyphenyl)-5-(3-hydroxyphenyl)-7-phenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine(2c): M.P.-263°C, IR(KBr): 3399.89(O-H str.), 3334.67(N-H str.), 2849.31 (C-H str.), 1597.36(C=C str.), 1693.03(C=N str.), 1108.63(C-O-C str.), 1201.86(N-N=C str.), MS: m/z-386.23

2,5-bis(4-hydroxyphenyl)-7-phenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a][1,3,5]triazine (2d): M.P.-254°C, IR(KBr): 3404.06(O-H str.), 3329.86(N-H str.), 2971.58(C-H str.), 1468.98 (C=C str.), 1688.33(C=N str.), 1091.99(C-O-C str.), 1252.14(N-N=C str.), MS: m/z-386.14

2-(4-hydroxyphenyl)-5-(2-nitrophenyl)-7-phenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a] [1,3,5]triazine(2e): M.P.-262°C, IR(KBr): 3434.67(O-H str.), 3312.78(N-H str.), 3117.92 (=C-H str.), 3048.93(C-H str.), 1547.56(C=C str.), 1608.26(C=N str.),1097.62(C-O-C str.), 1254.04(N-N=C str.), 1629.41(C-NO_2 str.),^{1}H-NMR(DMSO,δ ppm): 2.45(s, 1H, NH), 4.10 (s, 1H, CH), 5.27(s, 1H, OH), 5.6(s, 1H, CH), 7.01–7.78(m, 14H, Ar-H), MS: m/z-415.26

2-(4-hydroxyphenyl)-5-(3-nitrophenyl)-7-phenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a] [1,3,5]triazine(2f): M.P.-296°C, IR(KBr): 3434.65(O-H str.), 3370.23(N-H str.), 3068.65 (=C-H str.), 2917.59(C-H str.), 1531.55(C=C str.), 1657.18(C=N str.), 1075.56(C-O-C str.), 1202.31(N-N=C str.), 1603.97(C-NO_2 str.), MS: m/z-415.04

2-(4-hydroxyphenyl)-5-(4-nitrophenyl)-7-phenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a] [1,3,5]triazine(2g): M.P.-279°C, IR(KBr): 3454.10(O-H str.), 3268.22(N-H str.), 2970.71(C-H str.), 1443.51(C=C str.), 1619.66(C=N str.), 1095.42(C-O-C str.), 1242.24(N-N=C str.), 1536.60(C-NO_2 str.), MS: m/z-415.18

2-(4-hydroxyphenyl)-5-(2-chlorophenyl)-7-phenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a] [1,3,5]triazine(2h): M.P.-307°C, IR(KBr): 3452.04(O-H str.), 3335.98(N-H str.), 2968.97 (C-H str.), 1467.73(C=C str.), 1615.89(C=N str.), 1037.88(C-O-C str.), 1249.27(N-N=C str.), 769.09 (C-Cl str.), ^{1}H-NMR(DMSO,δ ppm): 2.56(s, 1H, NH), 4.12(s, 1H, CH), 5.18(s, 1H, OH), 5.47 (s, 1H, CH), 6.63 – 7.75(m, 14H, Ar-H), MS: m/z-404.36

2-(4-hydroxyphenyl)-5-(4-chlorophenyl)-7-phenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo[3,2-a] [1,3,5]triazine(2i): M.P.-284°C, IR(KBr): 3454.08(O-H str.), 3091.93(=C-H str.), 2938.27 (C-H str.), 1531.02(C=C str.), 1693.49(C=N str.), 1037.38(C-O-C str.), 1303.62(N-N=C str.), 719.82(C-Cl str.), MS: m/z-404.39

2-(4-hydroxyphenyl)-5-(4-dimethylaminophenyl)-7-phenyl-6,7-dihydro-5H-[1,3,4]oxadia zolo[3,2-a][1,3,5]triazine(2j): M.P.-236°C, IR(KBr): 3433.34(O-H str.), 3370.23(N-H str.), 3068.65(=C-H str.), 2917.59(C-H str.), 1445.26(C=C str.), 1470.73(C=N str.), 1075.56(C-O-C str.), 1202.31(N-N=C str.),^{1}H-NMR(DMSO,δ ppm): 2.38(s, 1H, NH), 2.99(s , 6H, CH_3), 3.80 (s, 1H, CH), 5.23(s, 1H, OH), 5.63(s, 1H, CH), 6.74-7.71(m, 14H, Ar-H), MS: m/z-413.23

2-(4-hydroxyphenyl)-5-(3,4,5-trimethoxyphenyl)-7-phenyl-6,7-dihydro-5H-[1,3,4]oxadia zolo[3,2-a][1,3,5]triazine(2k): M.P.-310°C, IR(KBr): 3391.90(O-H str.), 3054.47(=C-H str.), 2970.64(C-H str.), 1493.62(C=C str.), 1573.84(C=N str.), 1082.15(C-O-C str.), 1229.27(N-N=C str.), MS: m/z-460.04

2-(4-hydroxyphenyl)-5-(4-methoxyphenyl)-7-phenyl-6,7-dihydro-5H-[1,3,4]oxadiazolo [3,2-a][1,3,5]triazine(2l): M.P.-223°C, IR(KBr): 3417.82(O-H str.), 3055.16(=C-H str.), 2981.81(C-H str.), 1560.09(C=C str.), 1643.39(C=N str.), 1036.90(C-O-C str.), 1333.39 (N-N=C str.), MS: m/z-400.14

2-(4-hydroxyphenyl)-5-(3-methoxy-4-hydroxyphenyl)-7-phenyl-6,7-dihydro-5H-[1,3,4]oxa diazolo[3,2-a][1,3,5]triazine(2m): M.P.-231°C, IR(KBr): 3444.06(O-H str.), 2979.75(=C-H str.), 1424.75(C=C str.), 1681.92(C=N str.), 1027.79(C-O-C str.), 1267.26(N-N=C str.), MS: m/z-416.12

2-(4-hydroxyphenyl)-5-(2,5-dichlorophenyl)-7-phenyl-6,7-dihydro-5H-1,3,4]oxadiazolo[3,2-a][1,3,5]triazine(2n): M.P.- 215°C, IR(KBr): 3208.14(O-H str.), 2938.62(C-H str.), 1451.85 (C=C str.), 1692.98(C=N str.), 1071.64(C-O-C str.), 1264.72(N-N=C str.), 673.85(C-Cl str.), MS: m/z-439.07

2.2 Antimicrobial activity

The compounds were tested against bacterial strains i.e. *Escherichia coli* (Gram-ve), *Klebsiella pneumonia* (Gram–ve), *Staphylococcus aureus* (Gram+ve), *Bacillus subtilis* (Gram+ve) and fungal strains i.e. *Aspergillus niger* by using Cup-Plate method. Ciprofloxacin and Ketoconazole were used as standards for antibacterial and antifungal studies respectively. The stock solutions of the compounds were prepared in dimethyl sulfoxide (DMSO). The solutions of all the test compounds prepare at three different concentration 100µg/ml, 200µg/ml and 300µg/ml. Nutrient agar (beef extract 3 gm, Agar 15 g, Peptic Digest of Animal Tissue 5 g, sodium chloride 5 g and distilled water-q.s. to 1,000 ml) was employed as culture media for antimicrobial activity**.**

The sterilization of the nutrient broth, culture tubes, pipette and other glassware was done by autoclaving. For antibacterial studies, incubation was carried out at 37°C for 24 h and for antifungal studies, incubation was carried out at 25±2°c for 72 h. Diameters of zone of inhibition were measured for the plates in which the zones of inhibition in mm for each organism. The zone of inhibition were measured for all synthesized compounds.[28-29]

2.3 Statistical Analysis

The results of the study were expressed as mean ± SEM. All the data is analyzed by one way ANOVA was used to analyze and compare the data, test for multiple comparisons. The value of probability less than 5% ($P < 0.05$) was considered statistically significant.[30-31]

3. Results and discussion

The present study report the synthesis of 2,5-substituted aryl-7-phenyl-[1,3,4]-oxadiazolo-[3,2-a] [1,3,5]-triazine derivatives. The first step involve synthesized the Schiff's base as reaction between 2-amino-5-aryl-1,3,4-oxadiazole and aromatic aldehyde.

In Step -2 Schiff's base (compound-1) was mix with ammonium acetate and various aromatic aldehyde treated in MW irradiation at 480 W for three times with minimum 2 min of intervals. The step -2 Reaction based on microwave mediate multi-component reaction (MCRs). Series of compounds 1a-1n and 2a-2n synthesized by respected scheme.

The synthesized compounds were recrystallized and identified by TLC. The melting point were found uncorrected. The difference in the R_f value and melting point show the change in the structure between the molecules. All Physical data of the compounds are recorded in table-01 and table-02.

IR Spectra were recorded in KBr on Perkin FT-IR instrument. All the compounds show the presence of N-H stretching vibration in amine between 3458.08 to 3370.23 cm^{-1}, Aromatic C-H stretching between 3068.65-2985.50 cm^{-1}. Aliphatic C-H stretching between 2917.12 to 2849.23 cm^{-1}, C=N in ring between 1657.18-1591.20 cm^{-1} and C-O-C stretching between 1047.94-1037.88 cm^{-1} presence of cyclic ring system in [1,3,4] oxadiazoline. All the compounds show C=C stretching vibration at 1531.02-1424.75 cm^{-1}. Compound 2a-2n show 0-H stretching vibration of 3452.04 to 3404.06

In compound 1j and 2j show C-H str. due to CH_3 at 2917.59 and 2916.42 cm^{-1}. Compounds 1e, 1f, 1g and Compounds 2e, 2f, 2g show characteristic C-NO_2 stretching vibration between 1505.17- 1348.05 cm^{-1} and 1629.41- 1536.60 cm^{-1} respectively may be due to nitro group in compounds. Compound1h,1i,1n and 2h,2i,2n show C-Cl stretching vibration at 771.92-745.24 cm^{-1} and 719.82-769.09 cm^{-1} presence of chlorine substitution in respective compounds .

^{1}NMR was recorded on Bruker avance-400 MHz NMR spectrometer, chemical shift was measured at part per million downfield from tetra methyl silane. All compounds show sharp singlet near δ 2.4 to 2.1 might be due to NH proton and sharp singlet near δ 5.3 to 5.1 might be due to CH proton in C-5 position in ring. Multiple between δ 6.6 to 7.8 showed the presence of aromatic proton (Ar-H). The singlet formed between δ 5.1 to 5.2 might be due to presence of OH in compounds. Compound 1j and 2j show sharp singlet at δ 3.2 and 2.9 respectively due to presence of CH_3 in dimethylamine. All compounds show sharp singlet near δ 3.8 to 4.1 might be due to CH proton in C-7 position in ring.

Mass spectra were recorded on LC-MSD-Trap-SL which show characteristic molecular ion and base peak and further confirmed the compounds.

Antimicrobial activity of synthesized compounds was evaluated by cup-plate method. All the synthesized compounds show a moderate biological activity. The compound 1c, 1e, 1i, 2b, 2d, 2i and 1b, 1e, 1j, 2a, 2d show better significant antibacterial and antifungal activity respectively. Antimicrobial activity of synthesized compounds are recorded in table-03, table-04 and table-05

Table-01: Physical Parameters

S. No.	Compound code	Molecular formula	Molecular weight	Melting point ^{0}C	R_f value	% yield	Appearance
1.	**1a**	$C_{22}H_{18}N_4O$	354.40	145°C	0.63	76	Light Yellow
2.	**1b**	$C_{22}H_{18}N_4O_2$	370.40	180°C	0.73	70	White
3.	**1c**	$C_{22}H_{18}N_4O_2$	370.40	210°C	0.71	63	Light Yellow
4.	**1d**	$C_{22}H_{18}N_4O_2$	370.40	222°C	0.75	59	Light brown
5.	**1e**	$C_{22}H_{17}N_5O_3$	399.40	188°C	0.65	73	White
6.	**1f**	$C_{22}H_{17}N_5O_3$	399.40	178°C	0.74	77	Yellow
7.	**1g**	$C_{22}H_{17}N_5O_3$	399.40	200°C	0.79	69	Dark brown
8.	**1h**	$C_{22}H_{17}N_4OCl$	388.84	206C	0.60	81	Yellow
9.	**1i**	$C_{22}H_{17}N_4OCl$	388.84	190°C	0.69	78	Light green
10.	**1j**	$C_{24}H_{23}N_5O$	397.47	169°C	0.78	65	Light brown
11.	**1k**	$C_{25}H_{24}N_4O_4$	444.48	245°C	0.59	79	Pink
12.	**1l**	$C_{23}H_{20}N_4O_2$	384.43	156°C	0.62	68	Dark Brown
13.	**1m**	$C_{23}H_{20}N_4O_3$	400.42	196°C	0.72	75	Light Pink
14.	**1n**	$C_{22}H_{16}N_4OCl_2$	423.29	237°C	0.56	84	Yellow

Table-02: Physical Parameters

S. No.	Compound code	Molecular formula	Molecular weight	Melting point ^{0}C	R_f value	% yield	Appearance
1.	**2a**	$C_{22}H_{18}N_4O_2$	370.40	190°C	0.71	81	Light Yellow
2.	**2b**	$C_{22}H_{18}N_4O_3$	386.40	275°C	0.76	76	Light Brown
3.	**2c**	$C_{22}H_{18}N_4O_3$	386.40	263°C	0.62	71	Light Yellow
4.	**2d**	$C_{22}H_{18}N_4O_3$	386.40	254°C	0.78	83	Yellow
5.	**2e**	$C_{22}H_{17}N_5O_4$	415.40	262°C	0.76	80	White
6.	**2f**	$C_{22}H_{17}N_5O_4$	415.40	296°C	0.62	72	Light Yellow
7.	**2g**	$C_{22}H_{17}N_5O_4$	415.40	279°C	0.69	80	Brown
8.	**2h**	$C_{22}H_{17}N_4O_2Cl$	404.84	307°C	0.74	70	Yellow
9.	**2i**	$C_{22}H_{17}N_4O_2Cl$	404.84	284°C	0.70	65	Yellow
10.	**2j**	$C_{24}H_{23}N_5O_2$	413.47	236°C	0.82	75	Brown
11.	**2k**	$C_{25}H_{24}N_4O_5$	460.48	310°C	0.73	65	Yellow
12.	**2l**	$C_{23}H_{20}N_4O_3$	400.42	223°C	0.79	75	White
13.	**2m**	$C_{23}H_{20}N_4O_4$	416.42	231°C	0.66	55	Brown
14.	**2n**	$C_{22}H_{16}N_4O_2Cl_2$	439.29	215°C	0.69	68	Yellow

Table-03 : Antimicrobial activities of the compounds (1a-1n)

Compound Code	Diameter of Zone of Inhibition in mm											
	E.coli			*K.pneumoniae*			*S.aureus*			*B.subtilis*		
	100 µg/ml	200 µg/ml	300 µg/ml	100 µg/ml	200 µg/ml	300 µg/ml	100 µg/ml	200 µg/ml	300 µg/ml	100 µg/ml	200 µg/ml	300 µg/ml
1a	12	14	16	14	15	16	12	14	16	11	13	14
1b	13	15	17	12	13	14	14	15	16	12	13	15
1c	15	17	19	16	17	19	15	16	18	14	15	17
1d	10	12	14	11	12	13	14	15	16	11	13	15
1e	14	16	18	16	18	20	16	17	18	13	15	17
1f	12	13	15	13	14	16	12	13	15	10	12	14
1g	11	12	14	12	14	16	14	15	16	11	13	15
1h	13	14	16	12	13	15	12	14	15	12	13	15
1i	15	17	19	15	17	18	15	17	18	13	15	17
1j	11	12	14	12	13	15	13	14	15	12	14	16
1k	11	13	15	12	14	16	12	14	15	11	13	15
1l	12	13	15	13	14	16	14	15	16	11	13	15
1m	12	14	16	11	13	15	13	14	15	12	13	14
1n	11	13	15	12	13	14	13	14	16	12	14	15
Std (10µg/ml)	22	22	22	23	23	23	21	21	21	20	20	20

Table-04 : Antimicrobial activities of the compounds (2a-2n)

Compound Code	Diameter of Zone of Inhibition in mm											
	E.coli			*K.pneumoniae*			*S.aureus*			*B.subtilis*		
	100 µg/ml	200 µg/ml	300 µg/ml	100 µg/ml	200 µg/ml	300 µg/ml	100 µg/ml	200 µg/ml	300 µg/ml	100 µg/ml	200 µg/ml	300 µg/ml
2a	11	13	15	13	15	17	13	14	16	13	14	16
2b	14	17	19	15	17	19	14	15	18	14	16	18
2c	13	14	16	12	14	16	11	13	15	12	14	15
2d	13	16	18	16	18	20	15	17	19	13	15	18
2e	12	14	16	12	14	15	12	13	15	11	13	15
2f	11	13	15	14	15	17	13	15	17	13	14	15
2g	12	14	15	11	14	16	12	14	16	11	13	15
2h	12	14	16	12	15	16	13	15	17	12	14	15
2i	13	15	17	16	18	20	14	16	19	13	15	17
2j	12	13	15	13	15	17	13	15	17	11	13	15
2k	11	13	15	14	16	18	13	16	18	13	14	15
2l	12	13	15	12	15	17	12	14	16	12	13	15
2m	12	14	16	13	15	17	12	15	17	13	14	16
2n	13	15	16	14	16	18	13	15	17	12	14	16
Std (10µg/ml)	22	22	22	23	23	23	21	21	21	20	20	20

Antibacterial activity at 100µg/ml, 200µg/ml, 300µg/ml of test compounds against *(Gram+ve) and (Gram–ve)* bacterial strains, Ciprofloxacin 10µg/ml used as standard drug

Table-05 : Antifungal Activity of the Compounds Against *Aspergillus niger*

Concentration in µg/ml	Diameter of the Inhibition Zone (mm)														
	1a	**1b**	**1c**	**1d**	**1e**	**1f**	**1g**	**1h**	**1i**	**1j**	**1k**	**1l**	**1m**	**1n**	**Std(10µg/ml)**
100	11	16	12	14	15	13	14	14	14	16	11	10	11	13	24
200	13	18	14	16	17	15	15	15	16	18	12	13	13	14	24
300	14	20	16	18	19	17	17	16	17	20	14	15	15	16	24
Concentration in µg/ml	**Diameter of the Inhibition Zone (mm)**														
	2a	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2h**	**2i**	**2j**	**2k**	**2l**	**2m**	**2n**	**Std (10µg/ml)**
100	15	11	13	16	14	10	13	13	13	11	11	10	12	14	24
200	17	13	14	18	16	12	14	15	15	13	13	14	14	15	24
300	19	14	16	20	18	14	15	17	17	15	14	14	16	17	24

Antifungal activity at 100µg/ml, 200µg/ml, 300µg/ml of test compounds against *Aspergillus niger*, Ketoconazole 10µg/ml used as standard drug

4. Conclusion

A series of novel heterocyclic compounds 1,3,4-oxadiazolo-[3,2-a]-1,3,5-triazine derivatives has been successfully synthesized by bridging between bioactive heterocyclic rings 1,3,5-triazine and 1,3,4-oxadiazole. Synthesis reaction based on microwave mediate multi-component reaction (MCRs). Derivatives of 1,3,4-oxadiazolo-[3,2-a]-1,3,5-triazine shown very good promising activity as compared to standard drug for all representative panel of bacterial and fungal strains and thus, there is enough scope for further study in developing such compounds as a good bioactive molecules.

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