Research Article **ISSN: 2349 – 7106**

Asian Journal of Research in Chemistry and Pharmaceutical Sciences

Journal home page: www.ajrcps.com

https://doi.org/10.36673/AJRCPS.2024.v12.i02.A06

DESIGNED AND A NOVEL SYNTHESIS AND BIOEVALUATION OF 1, 3, 4 OXADIAZOLES DERIVATIVES FROM BENZIMIDAZOLES

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ABSTRACT

The present investigate and an efficient synthesis of a novel derivatives of 2-((5-bromo-2-(p-tolyl)-1H-benzo [d] imidazol-1-yl) methyl)-5-phenyl-1, 3, 4-oxadiazole is obtained by the prepared by 2-(5-bromo-2-(p-tolyl)-1H-benzo [d] imidazol-1-yl) acetohydrazide with benzoic acid in the presence of $POCl_3$. 2-(5-bromo-2-(p-tolyl)-1H-benzo [d] imidazol-1-yl) acetohydrazide is obtained by the mixture of ethyl 2-(5-bromo-2-(p-tolyl)-1H-benzo [d] imidazol-1-yl) acetate with hydrazine in the presence of ethanol. Ethyl 2-(5-bromo-2-(p-tolyl)-1H-benzo [d] imidazol-1-yl) acetate is prepared from -bromo-2-(p-tolyl)-1H-benzo [d] imidazole with bromoester in presence of K2CO3 IH acetone, 5-bromo-2-(p-tolyl)-1H-benzo [d] imidazole can be obtained from 4-bromobenzene-1, 2-diamine with 4-methyl benzaldehyde in the presence of $ZrOCl_2$.

KEYWORDS

2-((5-bromo-2-(p-tolyl)-1H-benzo [d] imidazol-1-yl) methyl)-5-phenyl-1, 3, 4-oxadiazole, substituted benzoic acid, POCl3, 4-bromobenzene-1, 2-diamine and Methyl benzaldehyde $ZrOCl_2$.

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INTRODUCTON

Oxadiazoles are the heterocyclic compounds having one oxygen and two nitrogen atoms in a five membered ring[1,2] and containing a diversity of useful pharmacological effects[3]. Oxadiazoles is considered to be resultant from furan by replacement of two methane (–CH=) groups by two pyridine type nitrogen atoms (–N=)[2]. The various methods have been reported in the literature for the synthesis of 1, 3, 4-oxadiazoles and the commonly used synthetic route for 1, 3, 4-oxadiazoles includes reactions of acid hydrazides (or hydrazine) with acid chlorides/carboxylic acids and direct cyclization of diacylhydrazines using a variety of

dehydrating agents such as phosphorous oxychloride[3], thionyl chloride[4], phosphorous pentoxide[5], triflic anhydride[6], Polyphosphoric acid[7] and direct reaction of acid with (N-isocyanimino-) triphenylphosphorane[8].

In recent time, benzofused heterocycles having nitrogen/ oxygen heteroatoms such as derivatives of benzimidazoles as starting moieties have been achieved an excellent reputation due to their numerous pharmaceutical activities. These moieties are anticancer[9], antimicrobial[10] and anti-inflammatory and clinically effective drugs[11].

The resistance of gram negative bacteria towards antibacterial substances is due to more lipophilic nature of membrane, which acts as a barrier for various antimicrobial compounds. It was expected that hydrophilic compounds are unable to penetrate the cell membranes of these bacteria. Gram positive bacteria do not have such outer membrane and complex cell wall structure. Antibacterial substances can easily destroy the bacterial cell wall and cytoplasmic membrane of gram positive bacteria, which results in leakage of the cytoplasm

Our progress work, the synthesis of designed bio active synthesis of 1, 3, 4 –Oxadiazoles derivatives from benzimidazoles which are prepared from 5-bromo -o-phenyl demine and 4-mrthyl benzaldehyde are starting materials and also studied for antimicrobial activity (Scheme-No.1) and also continued further investigation.

EXPERIMENTAL METHODS

The synthetic grade reagents, solvents, chemicals and desired raw materials are procured from Merck chemical Private Limited and also used for without purification. The melting points of the newly obtained derivatives were measured by a Thermo Scientific Fluke 51 II, melting point instrument and uncorrected was reported. The newly synthesized derivatives were evaluated by advanced spectroscopic methods such as 1H NMR (400 MHz) and ^{13}C NMR (100MHz) spectra of the synthesized compounds were recorded values by an instrument Bruker Ultra Shield at room temperature Ultra Shield using tetramethylsilanes (TMS) as the internal standard and deuterated chloroform ($CDCl_3$) as the solvent. The molecular weights of the derivatives were measured by LCMS instrument were run on a Shimadzu spectrometer instrument, which was operating at 70 eV in positive mode. The progress of the reactions was examined by thin layer chromatography (TLC) analyses using (Merck 60 F254 silica gel).

5-bromo-2-(p-tolyl)-1H-benzo [d] imidazole

Take clean and dry four necks 50 ml RBF.25mL ethanol taken by this RBF and a mixture of 5-bromo, O-phenyl diamine (1mol) and p-methyl benzoic acid (1.15mol) aldehyde (1.154mol) is introduced in an RBF.A Lew's acid catalyst such as $ZrOCl_2$gradually added above mixture .The total set up arranged on magnetic stirrer and continued the reaction at reflux for 4 hrs. The progress of the reaction was monitored by TLC (5: 5- EtOH: n-hexane) and after completion of the reaction cooled at RT. The reaction mixture added with ice water and also addition with ethylacetae as solvent .The reaction mixture was washed with Braine solution and separated the organic solvent and also distilled out. The compounds get after purified by columns chromatography.

Pale yellow; Yield-91%; m.p: 214-216^{o}C; R_f: 0.45(EtOH: n-hexane: 5:5); IR(KBr, cm-1): 3448, 3048, 2945, 1569, 1512, 1502, 1485, 698; ^{1}HNMR (400MHz, $CDCl_3$) δppm: 11.496 (s, 1H, N-H), 8.246 (d, J=8.8Hz, Ar-H), 7.717 (s, 1H, Ar-H), 7.482-7.414 (m, 3H, Ar-H), 1.176 (s, 3H, CH_3); ^{13}CNMR (100MHz, $CDCl_3$): 146.74, 139.61, 137.36, 130.76, 129.46, 128.84, 128.46, 126.66, 119.08, 117.44, 115.64, 24.78; LCMS (m/z): 288.22 (M+2); Molecular formulae: $C_{14}H_{11}BrN_2$; Elemental analysis: Calculated: C-58.56, H-3.86, N-9.76; Obtained: C-58.49, H-3.84, N- 9.83.

1-(5-bromo-2-(p-tolyl)-1H-benzo[d]imidazol-1-yl)-3-chloropropan-2-one

5-bromo-2-(p-tolyl)-1H-benzo[d]imidazole is dissolved in 25mL of methylene dichloride in 50mL four neck RBF and triethylamine was added .The slowly add the chloroacetyl chloride by using dropping funnel. The total mixture setup on the magnetic stirrer and continued the reaction for 5hrs at reflux. The progress of the reaction was monitored by TLC (5:5 = EtOH: n-hexane). After

completion of the reaction, unconsumed chloroacetyl chloride can be evaporated and the crude was taken in a ethylacetae and washed with saturated solution of sodium bi carbonate and separated the organic solvent. The organic solvent distilled off under vacuum distillation final compounds obtained.

Characterisation

White solid; Yield-86%: m.p: 256-258^{o}C; Rf; 0.45 (EtOH: n-hexane-4: 6); IR (KBr, cm-1): 3047, 2978, 2847, 1745, 1598, 1543, 1508, 1478, 1346, 714; 1HNMR (400MHz, $CDCl_3$) δppm: 8.214 (d, J=7.2Hz, 2H, Ar-H), 7.704 (s, 1H, Ar-H); 7.518-7.428 (m, 4H, Ar-H), 3.874 (s2H, -CH_2-), 2.248-1.849 (m, 2H, -CH_2-), 1.158 (s, 3H, -CH_3), 0.975 (t, 3H, -CH_3); 13CNMR (100MHz, $CDCl_3$): 195.74, 150.34, 138.37, 134.76, 130.40, 128.84, 128.04, 127.66, 125.67, 119.09, 118.44, 117.74, 60.76, 33.61, 22.46, 11.72; LCMS (m/z): 358.54 (M+2); Molecular formulae: $C_{18}H_{17}BrN_2O$; Elemental analysis: Calculated C- 60.52, H- 4.80, N- 7.84; Obtained: C-60.45, H-4.78, N-7.88.

2-(5-bromo-2-(p-tolyl)-1H-benzo [d] imidazol-1-yl) acetohydrazide

Take clean and dry the four neck 50mL RBF and poured 25mL ethanol in a RBF. The 1-(5-bromo-2-(p-tolyl)-1H-benzo [d] imidazol-1-yl)-3-chloropropan-2-one was dissolved in ethanol and addition with hydrazine hydrate. The reaction mixture was continued for 6-7 hrs. The progress of the reaction was checked by TLC and after completion of the reaction and solvent can be removed. The final compound can be obtained.

Characterisation

White solid; Yield-90%: m.p: 215-217^{o}C; Rf; 0.40 (EtOH: n-hexane-6:4); IR (KBr, cm-1): 3641, 3475, 3054, 2954, 2889, 1787, 1594, 1548, 1507, 1497, 698; ^{1}HNMR (400MHz, $CDCl_3$) δppm: 9.047 (s, 1H, NH); 8.184 (d, J=9.2Hz, 2H, Ar-H), 7.715 (s, 1H, Ar-H); 7.504-7.412 (m, 4H, Ar-H), 3.854 (s, 2H, -CH_2-), 3.647 (s, 2H, -NH_2), 1.158 (s, 3H, -CH_3); 13CNMR (100MHz, $CDCl_3$): 163.45, 150.55, 138.18, 134.07, 130.40, 129.47, 128.98, 128.44, 127.22, 126.47, 125.06, 119.12, 118.32, 116.75, 38.55, 22.68.; LCMS (m/z): 360.21 (M+2); Molecular formulae: $C_{16}H_{15}BrN_4O$; Elemental analysis: Calculated: C- 53.50, H- 4.21, N-15.60; Obtained: C-53.42, H-4.19, N-15.68.

Genera procedure of 2-((5-bromo-2-(p-tolyl)-1Hbenzo [d] imidazole-1-yl) methyl)-5-phenyl-1 3, 4-oxidiazole

The mixture of 2-(5-bromo-2-(p-tolyl)-1H-benzo [d] imidazol-1-yl) acetohydrazide and substituted benzoic acid taken in 50mL RBF and slowly addition with $POCl_3$. The reaction mixtures was fitted on the magnetic stirrer and check the reaction and poured in ice cold water and addition of organic solvent. The crude was washed with a solution of NaHCO3 and get final product after purified by the chromatography.

2-((5-bromo-2-(p-tolyl)-1Hbenzo [d] imidazole-1-yl) methyl)-5-phenyl-13, 4-oxidiazole (7a)

White solid; Yield: 87%; m.p-213-215^{o}C: Rf -0.45(EtOH: n-hexane: 6: 4); IR (KBr, cm-1): 3047, 2972, 2868, 1601, 1569, 1528, 1502, 1486, 696; ^{1}HNMR (400MHz, $CDCl_3$) δppm: 8.204 (d, J=6.4Hz, 2H, Ar-H), 7.708 (s, 1H, Ar-H), 7.498-7.272 (m, 7H, Ar-H), 3.914 (s, 2H, -CH2-), 1.164 (s, 3H, -CH3); ^{13}CNMR (100MHz, $CDCl_3$): 163.62, 161.09, 149.66, 138.84, 130.09, 129.78, 129.17, 128. 91,128.08, 127.64, 127.15, 126.44, 125.39, 119.14, 118.07, 117.84, 50.35, 22.66; LCMS (m/z): 444.15 (M+2); Molecular formulae: $C_{23}H_{17}BrN_4O$; Elemental analysis: Calculated: C-62.01, H-3.85, N-12.56; Obtained: C-61.95, H-3.83, N- 12.63.

2-((5-bromo-2-(p-tolyl)-1H benzo [d] imidazol-1-yl) methyl)-1, 3, 4-oxidiazol-2-yl)-2-ethoxyphenol (7b)

White solid; Yield: 90%; m.p–208-210^{o}C: Rf-0.45 (EtOH: n-hexane 6: 4); IR (KBr, cm-1): 3048, 2982, 2844, 1602, 1572, 1541, 1513, 1486, 1149, 715, 647; 1HNMR (400MHz, CDCl3) δppm: 9.173 (s, 1H, -OH); 8.226 (d, J=5.8Hz, 2H, Ar-H), 7.712 (s, 1H, Ar-H), 7.513-7.275 (m, 7H, Ar-H), 3.942 (s, 2H, -CH2-), 2.136-1.473 (m, 2H, -CH2-); 1.189 (s, 3H, -CH3); 0.947 (t, 3H, -CH3); ^{13}CNMR (100 MHz, CDCl3): 163.91, 161.69, 150.08, 139.77, 138.04, 131.35, 129.74, 128.95, 128.53, 128.12, 127.36, 126.36, 12644, 125.11, 119.08, 118.29, 116.96, 51.65, 28.46, 22.64, 22.64, 11.36. LCMS (m/z): 506.31 (M+2); Molecular formulae: $C_{25}H_{21}BrN_4O_3$; Elemental Analaysis: Calculated: C-

59.42, H-4.19, N-11.09; Obtained: C- 59.35, H-4.17, N- 11.18.

2-((5-bromo-2-(p-tolyl)-1hbenzo [d] imidazole-1-yl) methyl)-5-(4-methoxyphenyl)-1, 3, 4-oxidiazole (7c)

White solid; Yield: 92%m.p-221-223^{o}C; Rf-0.45 (EtOH: n-hexane: 6:4); IR (KBr, cm-1): 3061, 2956, 2896, 1602, 1567, 1537, 1501, 1482, 1184, 704, 636; 1HNMR (400MHz, CDCl3) δppm: 8.124 (d, J=7.8Hz, 2H, Ar-H), 7.886 (d, J=9.2Hz, 2H, Ar-H), 7.677 (s, 1H, Ar-H), 7.517-7.274 (m, 6H, Ar-H), 3.967 (s, 2H, -CH2-), 3.616 (s, 3H, -OCH3), 1.096 (s, 3H, -CH3),13CNMR (100MHz, $CDCl_3$): 162.76, 160.37, 149.14, 139.23, 130.84, 129.56, 128.67, 128.39, 128.02, 127.64, 126.18, 125.64, 119.16, 118.09, 117.69, 54.62, 50.16, 22.04; LCMS (m/z): 476.16 (M+2); Molecular formulae: $C_{24}H_{19}BrN_4O_2$; Elemental analysis: Calculated: C-60.64, H-4.03, N-11.79; Obtained : C-60.58, H-4.01, N-11.86.

2-((5-bromo-2-(p-tolyl)-1hbenzo [d] imidazole-1-yl) methyl)-5-(3, 5-dichloro phenyl) -1, 3, 4-oxidiazole (7d)

White solid; Yield-88%: m.p-207-209^{o}C: Rf-0.47 (EtOH: n-hexane: 5: 5); IR (KBr, cm-1): 3051, 2966, 2884, 1597, 1552, 1524, 1501, 1496, 742, 696; 1HNMR (400MHz, $CDCl_3$) δppm: 8.226 (d, J=7.0Hz, 2H, Ar-H), 7.792-7.596 (m, 3H, Ar-H), 7.542 (s, 1H, Ar-H), 7.461-7.354 (m, 4H, Ar-H), 3.946 (s, 2H, -CH_2-), 1.096 (s, 3H, -CH3); ^{13}CNMR (100MHz, $CDCl_3$) δppm: 163.87, 161.08, 150.17, 139.44, 132. 63, 129.86, 128.28, 128.07, 127.77, 127.38, 126.74, 125.88, 124.64, 119.09, 118.36, 117.64, 50.39, 22.06; LCMS (m/z): 513.44 (M+H); Molecular formulae: $C_{23}H_{15}BrCl_2N_4O$; Elemental analysis: Calculated: C-53.72, H-2.94, N-10.90; Obtained: C-53.65, H-2.92, N-10.98.

2-((5-bromo-2-(p-tolyl)-1hbenzo [d] imidazole-1-yl) methyl)-5-(3, 4, 5-trimethoxy phenyl) -1, 3, 4-oxidiazole (7e)

White solid; Yield-92%; m.p-218-220^{o}C: Rf-0.42 (EtOH: n-hexane: 4: 6); IR (KBr, cm-^{1}): 3046, 2956, 2897, 1602, 1574, 1538, 1510, 1196, 710, 649; 1HNMR (400MHz, $CDCl_3$) δppm: 8.118 (d, J=7.2HZ, 2H, Ar-H), 7.716 (s, 1H, Ar-H), 7.467-7.289 (m, 6H, Ar-H), 3.975 (s, 2H,-CH_2-), 3.617 (s, 3H, -OCH_3), 3.567 (s, 3H, OCH_3), 1.015 (s, 3H, -CH_3); ^{13}CNMR (100MHz, $CDCl_3$): 163.09, 160.76, 150.37, 145. 66, 139.11, 135.09, 129.17, 128.69, 128.06, 127.74, 126.68, 125.19, 124.38, 118.57, 117.31, 116.34, 58.38, 54.06, 50.09, 22.46. LCMS (m/z): 536.11 (m/z); Molecular formulae: $C_{26}H_{23}BrN_4O_4$; Elemental analysis: Calculated: C-58.33, H-4.33, N-10.46; Obtained: C-58.25, H-4.31, N-10.52.

2-((5-bromo-2-(p-tolyl)-1hbenzo [d] imidazole-1-yl) methyl)-5-(4, -nitro phenyl) -1, 3, 4-oxidiazole (7e)

Whiteb solid; Yield-86%; m.p-198-200^{o}C Rf-0.45 (EtOH: n-hexane: 6:4); IR (KBr, cm-1): 3051, 2966, 2872, 1595, 1547, 1512, 1496, 714, 684; 1HNMR (400MHz, CDCl3) δppm: 8.218 (d, J=8.0 HZ, 2H, Ar-H), 8.065 (d, J=6.4HZ, 2H, Ar-H), 7.884 (d, J=8.8HZ, 2H, Ar-H), 7.715 (s, 1H, Ar-H), 7.486-7.214 (m, 8H, Ar-H), 4.125 (s, 1H, -CH2-), 1.126 (s, 3H, -CH3); 13CNMR (100MHz, CDCl3): 164.08, 161.96, 150.88, 143.46, 139.37, 131.28, 130.54, 129.18, 128.46, 127.09, 126.84, 125.39, 118.92, 116.84, 51.09, 22.46; LCMS (m/z): 491.14; Molecular formulae: $C_{23}H_{16}BrN_5O_3$; Elemental analysis: Calculated: C- 56.34, H-3.29, N-14.28; Obtained: C-56.28, H-3.28, N- 14.34.

2-((5-bromo-2-(p-tolyl)-1Hbenzo [d] imidazol-1-yl) methyl)-1, 3, 4-oxidiazol-2-yl) benzonitrile (7f)

White solid; Yield: 87%; m.p: Rf-0.45 (EtOH: n-hexane: 6: 4); IR(KBr, cm-1): 3049, 2946, 2877, 2156, 1601, 1574, 1538, 1502, 715, 696; 1HNMR (400MHz, CDCl3) δppm: 8.134 (d, J=8.0HZ, 2H, Ar-H), 7.810 (s, 1H, Ar-H), 7.775-7.417 (m, 8H, Ar-H), 2.830 (s, 1H, -CH2-), 1.126 (s, 3H, -CH_3). ^{13}CNMR (100MHz, $CDCl_3$): 163.88, 161.15, 150.08, 139.74, 131.19, 130.03, 129.49, 128.94, 128.26, 127.52, 126.45, 125.37, 124.68, 119.09, 117.64, 116.66, 51.39, 22.46. LCMS (m/z): 471.24 (M+2); Molecular formulae: $C_{24}H_{16}BrN_5O$; Elemental analysis: Calculated: C- 61.29, H-3.43, N-14.89; Obtained: C-61.22, H- 3.42, N-14.95.

BIOLOGICAL ACTIVITY

ANTIBACTERIAL ACTIVITY

In vitro antibacterial activity of the titled derivatives (9a-g) enhanced have being examined against

bacterial strains such *S.aureus, E.coli, S. typhi, B.substills*. The *in vitro* activities of the test derivatives were examined using agar plates containing in nutrient broth for bacteria. The test compounds were tested against each microbial species. The antibacterial potent of the test compounds have being compared with Streptomycin as standard drug. The antimicrobial inhibitions of the derivatives are determined as the area of zone of inhibition and summarized in Table No.1. This representation reveals that the marked and antibacterial activity may be due to the presence of high hydrophobic content of these titled derivatives. The titled compounds possesses derivatives segments are more active against bacteria strains. Consequently, due to the strong interaction of the later with the agar medium, this hinders their diffusion in agar medium.

Antifungal Activity

In vitro antifungal determination against *A.ngier* and *Candida albicans* was used as test strains. The tested compounds were dissolved in dimethyl sulfoxide (DMSO) and prepare to concentration of 10 mg/mL. Antifungal activity of these derivatives was determined by broth micro dilution method. The tested fungal culture was prepared from the stock fungal culture, a 1:1000 dilution with broth (e.g. 10μL stock fungal culture: 10 μL broth) was prepared. Sabouraud maltose broth was used as the growth medium and modified antimicrobial susceptibility testing is based on references drug. Finally all the wells were filled with 100 μL of working fungal culture. Fluconazole were used as a reference drug in the antifungal test. Wells containing serial dilution of DMSO and broth were prepared as control tests. The plate was covered and incubated at 37°C for 24 to 30 h. The minimum inhibitory concentration (MIC) values of tested derivatives were determined by reading the lowest concentration of compound in the well showing no growth.

RESULTS AND DISCUSSION

2-((5-bromo-2-(p-tolyl)-1H-benzo [d] imidazol-1-yl)methyl)-5-phenyl-1, 3, 4-oxadiazole is obtained by the prepared by 2-(5-bromo-2-(p-tolyl)-1H-benzo [d] imidazol-1-yl) acetohydrazide with benzoic acid in the presence of $POCl_3$ .2-(5-bromo-2-(p-tolyl)-1H-benzo [d] imidazol-1-yl) acetohydrazide is obtained by the mixture of ethyl 2-(5-bromo-2-(p-tolyl)-1H-benzo[d]imidazol-1-yl)acetate with hydrazine in the presence of ethanol. Ethyl 2-(5-bromo-2-(p-tolyl)-1H-benzo [d] imidazol-1-yl)acetate is prepared from -bromo-2-(p-tolyl)-1H-benzo [d] imidazole with bromoester in presence of K_2CO_3 IH acetone, 5-bromo-2-(p-tolyl)-1H-benzo[d]imidazole can be obtained from 4-bromobenzene-1,2-diamine with 4-methyl benzaldehyde in the presence of $ZrOCl_2$.

Optimization of the synthesis of 1, 3, 4-oxidiazoles reaction conditions were performed by choosing substituted benzoic acid as model substrate. The reaction was previously investigated under catalytic conditions. Our result was particularly good and interesting, as the product was recovered pure in short times and in excellent yield without requiring the use of complex purification procedures and encouraged by the success of this preliminary study, the adopted procedure was applied for the preparation of a series of 1, 3, 4 –Oxadiazoles derivatives from benzimidazoles. The different substituted aromatic carboxylic acid were tested under the developed reaction conditions using aniline, the amine component, as a constant (Scheme-1).

The maximum yield of the compounds obtained in presence of phosphorus oxychloride ($POCl_3$) catalyst than oxidative related catalyst such as sulphuric acid (H2SO4), phosphorus pentoxide (PCl5), Polyphosphoric acid (PPA) and phosphorus oxychloride (POCl3) whereas various amount of catalyst utilized during the reaction (Table No.1).

The various solvents were used during the reaction that were evaluated (DMF, acetonitrile, ethanol, methanol) in the model reaction. It was identified to be the best medium for the reaction, with 94% product yield and therefore used as the solvent for subsequent reactions on the merits of higher yield, green nature and easy work-up.

Biological activity

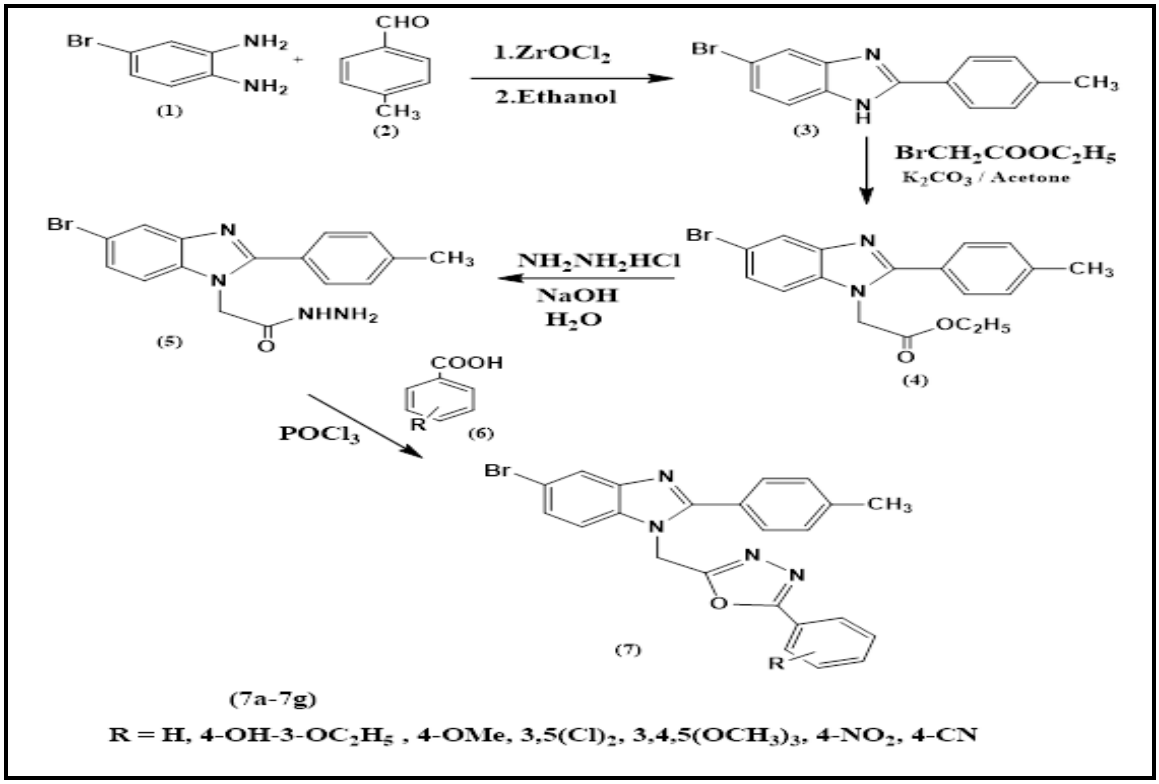
Anti-Bacterial Activity

The anti-bacterial activities of new derivatives were examined against 4 pathogenic bacteria strains. The gram negative bacteria screened were *E. coli*, *P. aeruginosa*. The gram positive bacteria screened were S-aureas and Bacillus .The desired derivatives were used at the concentration of 250µglml and 500µglml using DMSO as a solvent the streptomycin 10µglml disc were used as a standard drug. The reaming of the derivatives was identified to be moderate active against the tested microorganism. The result of antibiotic activity studies for the compounds as shown in Table No.1.

Anti-Fungal Activity

Anti-fungal activities of newly derivatives compounds were examined by disc diffusion method against the organism of aspergillusniger and Candida albicans. Compared were treated at the concentrations of 500µglml and 1000µglml using DMSO as a solvent. The standard drug was used as ketoconazole 50µglml against both organisms.

All the desired compounds were evaluated by anti-bacterial activity as well as antifungal activity. The electron withdrawing group of compounds and electron releasing group compounds exhibited different potent activities against bacterial as well as fungal strains. Therefore, electron withdrawing group of compounds showed low biological potent activity compared with electron releasing groups. All halogen compounds exhibit well to excellent activity. The compound which possess electron donating group showed moderate activity as shown in Table No.3.



Scheme No.1

Table No.1: The reaction of aryl carboxylic acid and compound - (7b)

Entry	Catalyst	Time (hrs)	Yield (%)
1	H_2SO_4	4	55
2	PCl5	4	70
3	PPA	4	62
4	$POCl_3$	4	94

Table No.2: The reaction of aryl carboxylic acid and compound - (7b)

Entry	Catalyst	Time (hrs)	Yield (%)
1	DMF	4	44
2	CH_3CN	4	94
3	EtOH	4	54
4	MeOH	4	60

Table No.3: Antimicrobial activity assay of new synthesized scaffold

S.No	Compound Code	*Zone of inhibition in (mm)					
		Bacteria				Fungi	
		S.aureus	***E.coli***	***S. typhi***	***B.substill***	***A. Niger***	***C. albicans***
1	3a	04	06	08	06	05	05
2	3b	14	15	13	15	06	07
3	3c	20	19	15	18	14	12
4	3d	18	20	20	19	15	16
5	3e	12	11	13	11	10	09
6	3f	10	12	09	10	08	06
7	Streptomycin	25	25	22	22	NA	NA
8	Ketoconazole	NA	NA	NA	NA	20	20
9	DMSO	---	----	---	---	---	---

CONCLUSION

The structure of the newly synthesized derivatives was elucidated on the basis of elemental analysis and spectral data. When all analysis results of the synthesized compounds were examined, the presence of characteristic peaks proving the formation of imine was observed and the synthesis of the compounds was successful. Also, this synthesis has quite environmentally friendly synthesis method because ethanol and methane Sulphonic acid as a catalyst was used as solvent.

ACKNOWLEDGEMENT

The authors gratefully acknowledge to the management of PRISM PG and DG College Visakhapatnam, India, for laboratory support. The authors also gratefully thank both referees for their helpful critical suggestions.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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Please cite this article in press as: Krishnarao *et al*. Designed and a novel synthesis and bio-evaluation of 1, 3, 4 oxadiazoles derivatives from benzimidazoles, *Asian Journal of Research in Chemistry and Pharmaceutical Sciences*, 12(2), 2024, 35-42.