Design, synthesis and Anti microbial screening of 1,3,4-oxadizole ring clubbed s-triazine derivatives

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Abstract:
A Series of compounds 2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(arylamino)-s-triazine were synthesized and structures of these compound were elucidated by spectral (IR, ^{1}H NMR, Mass spectra) analysis synthesized compound were screened for in vitro antibacterial activity against the representative panel of Gram The title compounds were then examined for their in vitro microbial activity against 2 gram +Ve bacteria (S. Aerues, B. subtilis) 2 gram –Ve bacteria (E. Coli, P. Aeruginosa) bacteria. These compounds were also tested for their inhibitory action against strain of 2 fungal species (C. Albicans and A. niger). The synthesized compound showed potent inhibitory action against the test organisms.

Keywords: *1,3,4-oxadiazol, 2,4,6-trichloro-1,3,5-triazine, morpholine, antimicrobial activity*

Introduction

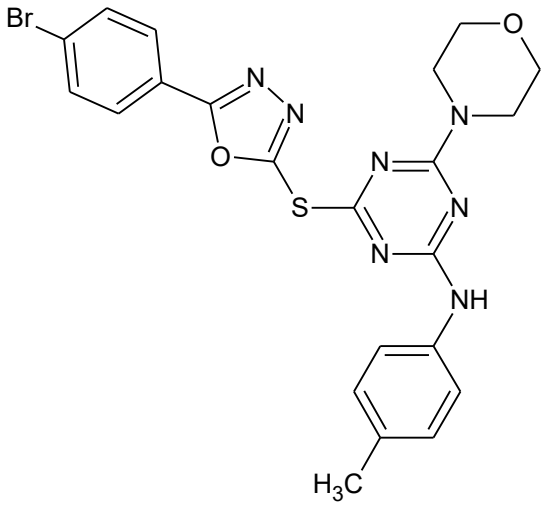
The rapidly expanding population of immune compromised patient results in a corresponding increase of diseases caused by bacteria, fungi and other yeast. Infection caused by these microorganisms pose a serious challenge to the medical community and highlight the importance and urgent need for new, more potent and selective non-traditional antimicrobial agent. The incidence of bacterial infections has increased dramatically in recent years [1]. The widespread use of antibacterial and antifungal drugs and their resistance against bacterial and fungal infections has led to serious health hazards. The resistance of wide spectrum antibacterial agents has prompted discovery and modification towards new antifungal and antibacterial drugs [2, 3].

Substituted 1,3,4-oxadiazoles are of considerable pharmaceutical importance, which is documented by several number of publications and patents. A large number of drugs used clinically have oxadiazole ring as a structural building block.
Literature survey reveals that 1,3,4-oxadiazoles have wide range of biological activities ranging from antibacterial,[4–9] antifungal[10,11] to anti-inflammatory.[12] Derivatives of 1,3,4-oxadiazole with suitable substitution at 2,5-position have been reported to possess considerable pharmacological activities, such as Anti Oxidatant[13] and Anticonvulsant. [14]

Having an unique importance in heterocyclic compounds due to its wide range of therapeutic activities [15-20], 2,4,6-trichloro-1,3,5-triazine exhibited biological importance such as anti microbial, antiprotozoal, anticancer, antimalarial and antiviral. 2,4,6-trichloro-1,3,5-triazine is an inexpensive, commercially available reagent and the different reactivities of the substituent chlorine atoms, which are controlled by temperature makes its use more attractive. In a view of its adaptable chemistry, we are promoted for sequential introduction of various amine into the 1,3,5- triazine ring.

2. Results and Discussion

2-(4-fluoropheny l-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(arylamino)-s-triazine(6) were obtained in 62-75% yield by converting 4-bromo benzoic acids to the methyl 4-bromo benzoate(1) and An ester intermediate was hydrazinolyzed with 99% hydrazine hydrate to afford 4-bromo benzohydrazide(2). which reacted with carbon disulfide and potassium hydroxide in ethanol followed by acidification furnished the corresponding 5-(4-bromopheneyl)-1,3,4-oxadiazole-2-thiol (3). Compound(4) 2-(4-bromophenyl-1,3,4-oxadiazolyl)-5-thio-4,6-dichloro-s-triazine was prepared by the condensation of cyanuric chloride and 5-(4-bromopheneyl)-1,3,4-oxadiazole-2-thiol (3) in THF at 0–5°C, which reacts with morpholin in THF at 40–45°C gave compound 2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-chloro-s-triazine (5). Which reacts with aryl amino in 1,4-dioxane at reflux temperature gave final compound 2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(arylamino)-s-triazine 6 (a-j)



Mass spectral data support the proposed structures. The mass spectrum showed various characteristic peaks. A peak at *m/z* 527 (m+1) was assigned to the molecular ion.

The FTIR spectrum showed absorption bands at 838 cm^{-1}(C=N stretching in s-triazine), 3328 cm^{-1} (-NH- stretching in amide), 1278 cm^{-1} (C-O stretching in oxadiazole), 1529 cm^{-1}(C=N stretching in oxadiazole), 1160 cm^{-1}(C-O) stretching in morpholine), 1115 cm^{-1}(C-N) stretching in morpholine), 1385 cm^{-1} (C-CH_3 stretching in aromatic ring) ,1235 cm^{-1}(C-O-C) stretching in alkanyl ether) respectively.

The ^{1}H-NMR spectrum of (6c) showed characteristic signals at 6.70 to 8.27 ppm which were assigned to the aromatic protons. A signal at 3.36-3.70 ppm was assigned to the morpholine proton. A signal at 2.29 ppm was assigned to the methyl proton, The singlet 9.89 ppm were assigned to the amino protons, respectively.

3. Conclusions

A series of trisubstituted s-triazine derivatives has been successfully synthesized and tested for their anti microbial activity. S-triazine nucleus is one of the active constituents present in many standard drugs, and is known to increase in pharmacological activity of the molecules as we have already reported its significant activity. The presence of morpholine moiety is also an instrumental in contributing the net biological activity. Herein, we have combined all these three potential unit, that is s-triazine nucleus, 1,3,4-oxadiazole, morpholine and various substituted aniline and moieties in one core and studied biological behavior of the resultant systems. Hence, it is concluded that, trisubstituted S-triazine are more active than mono and di-substituted S-triazine and thus, there is enough scope for

further study in developing such compounds as a good lead activity. Overall conclusion placed for synthesized compounds is that most of the compounds shown very good promising activity as compared to standard drug for all representative panel of bacterial anf fungal strains.

4. Experimental

All the melting points were recorded on Cintex melting point apparatus and are uncorrected. IR spectra in KBr were recorded on Schimadzu FTIR spectrophotometer in cm-1. 1HNMR spectra were recorded in CDCl3 or DMSO on a Bruker DRX-400 MHZ NMR instrument. Chemical shifts were reported in ppm using TMS as internal standard on δ scale. Mass spectra of compounds were recorded on mass spectrometer (Agilant 1100 series). Completion of the reactions was monitored time to time by TLC using E-Merck 0.25 mm silica gel plates and toluene: acetone (9:1) as solvent system.

General procedure to synthesis of 2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(arylamino)-s-triazine :

Step – I

(i) Synthesis of methyl 4-bromo benzoate (1)

p- Bromo benzoic acid (0.1 mol) in 200 ml methanol and 5.0 ml con.sulfuric acid was refluxed for 12 hrs. Excess solvent distilled off and collect the product. Recrystallized from alcohol. The progress of reaction was monitored by TLC using toluene : acetone (8:2) as eluent.

B.P = 260-263^{o}C

(ii) Synthesis of 4- Bromo benzohydrazide -(2)

A mixture of methyl ester of 4-bromo benzoate (0.1 mol) and hydrazine hydrate (0.2 mol) in methanol was heated for 14 hrs. and poured into ice. The product was filtered and washed with cold water. Crystallized from ethanol. The progress of reaction was monitored by TLC using toluene . acetone (8.2) as eluent.

M.P = 161-163^{o}C

(iii) Synthesis of 5-(4-bromopheneyl)-1,3,4-oxadiazole-2-thiol-(3)

The mixture of 4-bromo benzohydrazide (0.1 mol), CS_2 (0.1 mol) and KOH solution (0.05 mol) in methanol (82 ml) was refluxed for 8 to 10 hours. After the completion of reaction the resultant mixture was poured in to crushed ice. Product was filtered, washed with water and recrystallized from alcohol. The progress of reaction was monitored by TLC using toluene : acetone (7:3) as eluent.

M.P = 195-197^{o}C

Step – II: Synthesis of 2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4,6-dichloro-s-triazine-(4)

To a stirred solution of cyanuric chloride (0.1 mol) in THF 100 ml at 0-5°c, The solution of 5-(4-bromopheneyl)-1,3,4-oxadiazole-2-thiol (0.1 mol) in THF (100 ml) was added drop-wise and pH was maintained neutral by the addition of 10 % $NaHCO_3$ solution. The stirring was continued at 0-5°C for 2 hours. After the completion of reaction the stirring was stopped and the solution was treated with crushed ice. The solid product obtained was filtered and dried. The progress of reaction was monitored by TLC using ethyl acetate. hexane (6.4) as eluent. The crude product was purified by crystallization from absolute alcohol.

M.P = 120-122^{o}C

Step – III: Synthesis of 2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-chloro- s-triazine: (5)

The solution of Morpholine (0.1 mol) in THF (100 ml) was added drop-wise to well stirred suspension of 2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4,6-dichloro-s-triazine. (0.1 mol) in THF (100 ml) maintaining the temp 40°C the pH was kept neutral by the addition of 10 % $NaHCO_3$ solution .

The temperature was gradually raised to 45°C during 2 hours and futher maintained for 2 hr. After the completion of reaction the solution was poured in ice-cold water. The solid product was filtered and dried. The crude was purified by recrystalization from absolute alcohol.

M.P = 210-212ºC

Step – IV: Synthesis of 2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(arylamino)-s-triazine: 6(a-j)

A mixture of 2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-chloro-s-triazine (0.005 mol) and aryl amine (0.005 mol) in dioxane (50.0 ml) was refluxed on heating mental with stirring at 100-110°C for 5 hours. The pH was adjusted to neutral by addition of 10 % $NaHCO_3$ solution. After the completion of reaction the content was added to ice-cold water. The product was filtered and dried the progress of reaction was monitored by TLC using ethylacetate . hexane (4.6) eluent.

Purificaton of all the synthesized compounds was achieved by recrystallization and purity of each compound was monitored by thin layer TLC.

2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(2-chloro-phenyl-amino)-s-triazine (6a)

FTIR (KBr,cm^{-1}): 3321 cm^{-1} (-NH- in amide), 1527 cm^{-1} (C=N in oxadiazole), 1422 cm^{-1}(C-CH_3 in aromatic ring), 1264 cm^{-1} (C-O in oxadiazole), 1237 cm^{-1} (C-O-C in alkanyl ether), 1160 cm^{-1} (C-O in morpholine), 1129 cm^{-1} (C-N in morpholine), 830 cm^{-1}(C=N in s-triazine), ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.33(s, 3H, CH_3), 3.34-3.67 (m, 8H, morpholine), 6.54-7.47 (m, 3H, Ar-H), 7.37-8.13 (m, 4H, Ar-H), 9.57(s, 1H, NH_2). mass(m/z); 547.2

2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(4-acetoxy-phenyl-amino)-s-triazine (6b)

FTIR (KBr,cm^{-1}): 3317 cm^{-1} (-NH- in amide), 1511 cm^{-1} (C=N in oxadiazole), 1391 cm^{-1}(C-CH_3 in aromatic ring), 1285 cm^{-1} (C-O in oxadiazole), 1253 cm^{-1} (C-O-C in alkanyl ether), 1173 cm^{-1} (C-O in morpholine), 1129 cm^{-1} (C-N in morpholine), 839 cm^{-1}(C=N in s-triazine),
^{1}H-NMR (DMSO-d_6, δ, ppm): 2.23(s, 3H, CH_3), 3.25-3.58 (m, 8H, morpholine), 6.57-7.52 (m, 4H, Ar-H), 7.39-8.15 (m, 4H, Ar-H), 9.61(s, 1H, NH_2). mass(m/z); 571.6

2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(4-methyl-phenyl-amino)-s-triazine (6c)

FTIR (KBr,cm^{-1}): 3328 cm^{-1} (-NH- in amide), 1529 cm^{-1} (C=N in oxadiazole), 1385 cm^{-1}(C-CH_3 in aromatic ring), 1278 cm^{-1} (C-O in oxadiazole), 1235 cm^{-1} (C-O-C in alkanyl ether), 1160 cm^{-1} (C-O in morpholine), 1115 cm^{-1} (C-N in morpholine), 838 cm^{-1}(C=N in s-triazine),
^{1}H-NMR (DMSO-d_6, δ, ppm): 2.29(s, 3H, CH_3), 3.36-3.70 (m, 8H, morpholine), 6.70-7.51 (m, 4H, Ar-H), 7.42-8.27 (m, 4H, Ar-H), 9.89(s, 1H, NH_2), mass(m/z); 527.9

2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(4-nitro-phenyl-amino)-s-triazine (6d)

FTIR (KBr,cm^{-1}): 3327 cm^{-1} (-NH- in amide), 1556 cm^{-1} (C=N in oxadiazole), 1365 cm^{-1}(C-CH_3 in aromatic ring), 1282 cm^{-1} (C-O in oxadiazole), 1223 cm^{-1} (C-O-C in alkanyl ether), 1137 cm^{-1} (C-O in morpholine), 1119 cm^{-1} (C-N in morpholine), 827 cm^{-1}(C=N in s-triazine),
^{1}H-NMR (DMSO-d_6, δ, ppm): 2.38(s, 3H, CH_3), 3.32-3.61 (m, 8H, morpholine), 6.70-7.39 (m, 4H, Ar-H), 7.31-8.37 (m, 4H, Ar-H), 9.35(s, 1H, NH_2). mass(m/z); 558.6

2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(4-chloro-phenyl-amino)-s-triazine (6e)

FTIR (KBr,cm^{-1}): 3310 cm^{-1} (-NH- in amide), 1521 cm^{-1} (C=N in oxadiazole), 1403 cm^{-1}(C-CH_3 in aromatic ring), 1269 cm^{-1} (C-O in oxadiazole), 1249 cm^{-1} (C-O-C in alkanyl ether), 1171 cm^{-1} (C-O in morpholine), 1129 cm^{-1} (C-N in morpholine), 843 cm^{-1}(C=N in s-triazine),
^{1}H-NMR (DMSO-d_6, δ, ppm): 2.23(s, 3H, CH_3), 3.37-3.76 (m, 8H, morpholine), 6.58-7.37 (m, 4H, Ar-H), 7.38-8.23 (m, 4H, Ar-H), 9.75(s, 1H, NH_2). mass(m/z); 547.4

2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(3-methyl-phenyl-amino)-s-triazine (6f)

FTIR (KBr,cm^{-1}): 3340 cm^{-1} (-NH- in amide), 1519 cm^{-1} (C=N in oxadiazole), 1368 cm^{-1}(C-CH_3 in aromatic ring), 1291 cm^{-1} (C-O in oxadiazole), 1247 cm^{-1} (C-O-C in alkanyl ether), 1164 cm^{-1} (C-O in morpholine), 1093 cm^{-1} (C-N in morpholine), 829 cm^{-1}(C=N in s-triazine),
^{1}H-NMR (DMSO-d_6, δ, ppm): 2.31(s, 3H, CH_3), 3.29-3.64 (m, 8H, morpholine), 6.67-7.68 (m, 3H, Ar-H), 7.48-8.19 (m, 4H, Ar-H), 9.59(s, 1H, NH_2). mass(m/z); 527.6

2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(4-fluoro-phenyl-amino)-s-triazine (6g)

FTIR (KBr,cm^{-1}): 3340 cm^{-1} (-NH- in amide), 1542 cm^{-1} (C=N in oxadiazole), 1370 cm^{-1}(C-CH_3 in aromatic ring), 1261 cm^{-1} (C-O in oxadiazole), 1250 cm^{-1} (C-O-C in alkanyl ether), 1167 cm^{-1} (C-O in morpholine), 1113 cm^{-1} (C-N in morpholine), 830 cm^{-1}(C=N in s-triazine),
^{1}H-NMR (DMSO-d_6, δ, ppm): 2.18(s, 3H, CH_3), 3.31-3.59 (m, 8H, morpholine), 6.73-7.59 (m, 4H, Ar-H), 7.63-8.21 (m, 4H, Ar-H), 9.70(s, 1H, NH_2). mass(m/z); 531.4

2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(3-chloro-4-fluoro-phenyl-amino)-s-triazine (6h)

FTIR (KBr,cm^{-1}): 3329 cm^{-1} (-NH- in amide), 1530 cm^{-1} (C=N in oxadiazole), 1387 cm^{-1}(C-CH_3 in aromatic ring), 1289 cm^{-1} (C-O in oxadiazole), 1227 cm^{-1} (C-O-C in alkanyl ether), 1161 cm^{-1} (C-O in morpholine), 1117 cm^{-1} (C-N in morpholine), 839 cm^{-1}(C=N in s-triazine), ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.32(s, 3H, CH_3), 3.47-3.79 (m, 8H, morpholine), 6.69-7.51 (m, 3H, Ar-H), 7.40-8.37 (m, 4H, Ar-H), 9.87(s, 1H, NH_2). mass(m/z); 564.1

2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(3-bromo-phenyl-amino)-s-triazine (6i)

FTIR (KBr,cm^{-1}): 3328 cm^{-1} (-NH- in amide), 1539 cm^{-1} (C=N in oxadiazole), 1389 cm^{-1}(C-CH_3 in aromatic ring), 1259 cm^{-1} (C-O in oxadiazole), 1222 cm^{-1} (C-O-C in alkanyl ether), 1141 cm^{-1} (C-O in morpholine), 1126 cm^{-1} (C-N in morpholine), 847 cm^{-1}(C=N in s-triazine),
^{1}H-NMR (DMSO-d_6, δ, ppm): 2.21(s, 3H, CH_3), 3.16-3.43 (m, 8H, morpholine), 6.60-7.72 (m, 4H, Ar-H), 7.38-8.21 (m, 4H, Ar-H), 9.93(s, 1H, NH_2). mass(m/z); 592.6

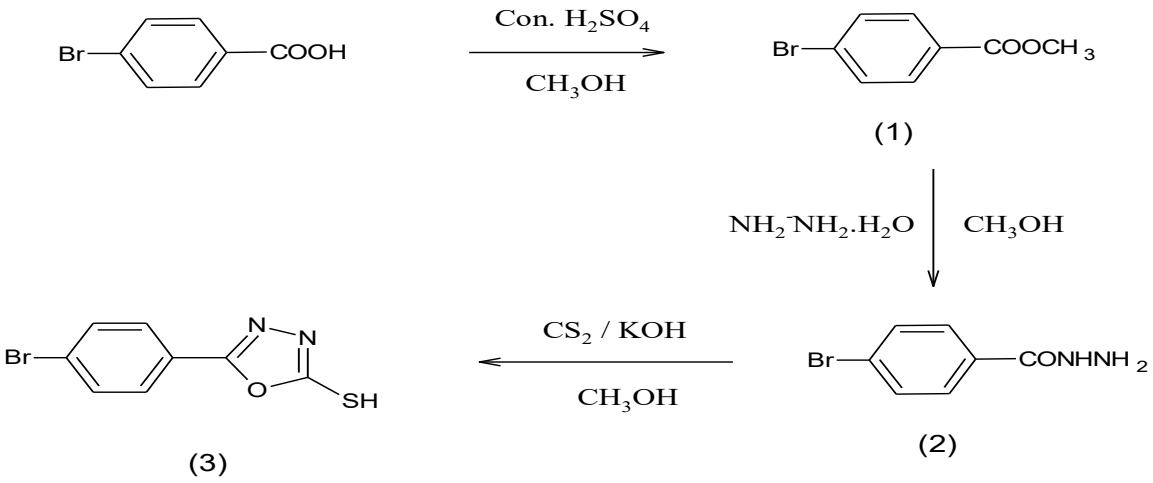
2-(4-bromophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(morpholino)-6-(4-methoxy-phenyl-amino)-s-triazine (6j)

FTIR (KBr,cm^{-1}): 3311 cm^{-1} (-NH- in amide), 1529 cm^{-1} (C=N in oxadiazole), 1375 cm^{-1}(C-CH_3 in aromatic ring), 1259 cm^{-1} (C-O in oxadiazole), 1229 cm^{-1} (C-O-C in alkanyl ether), 1145 cm^{-1} (C-N in morpholine), 1137 cm^{-1} (C-O in morpholine), 812 cm^{-1}(C=N in s-triazine),
^{1}H-NMR (DMSO-d_6, δ, ppm): 2.29(s, 3H, CH_3), 3.29-3.47 (m, 8H, morpholine), 6.41-7.29 (m, 4H, Ar-H), 7.22-8.37 (m, 4H, Ar-H), 9.73(s, 1H, NH_2). mass(m/z); 543.5

Scheme

Synthesis of 2-(4-bromophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(arylamino)-s-triazine.

Step - I



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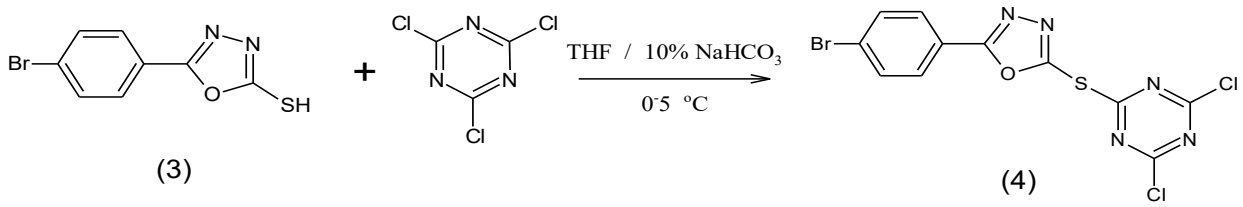

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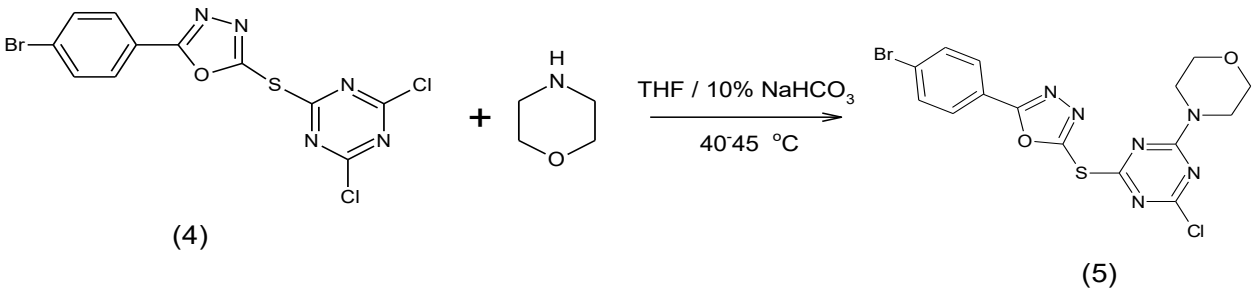
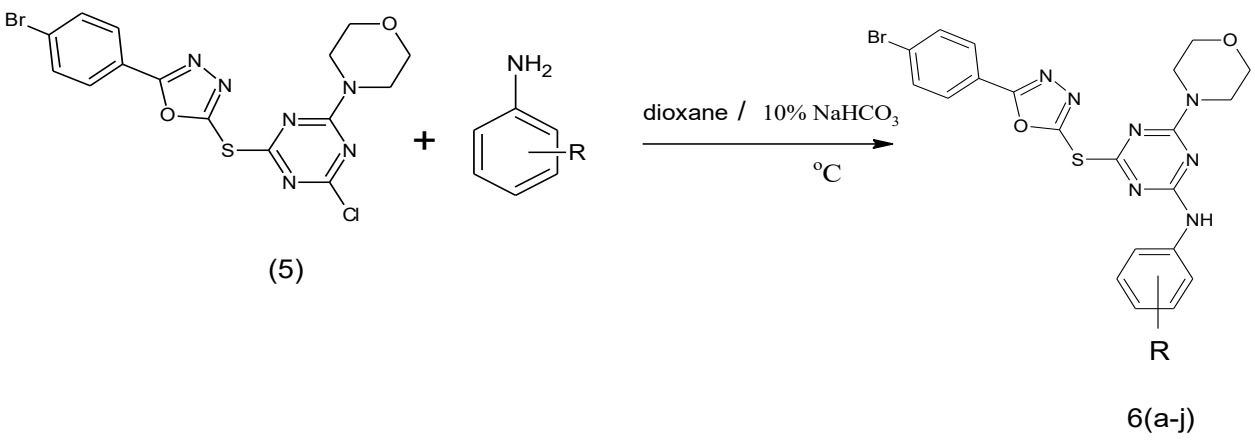


Step - IV



Sr. No.	Compound	Molecular Formula	Appearance	M.W	M.P. (°C)	% Of Yeild	R_f Value	% of Carbon Found (Calc.)	% of Hydrogen Found (Calc.)	% of Nitrogen Found (Calc.)
1	6a- 2 Cl	$C_{21}H_{17}BrClN_7O_2S$	White	547.2	176-178	62	0.62	46.08 (46.13)	3.07 (3.13)	17.87 (17.93)
2	6b- 4 acetoxy	$C_{23}H_{20}BrN_7O_4S$	White	571.6	176-178	64	0.59	48.39 (48.43)	3.49 (3.53)	17.14 (17.19)
3	6c- 4 CH3	$C_{22}H_{20}BrN_7O_2S$	Light Yellow	527.9	167-169	65	0.64	50.14 (50.20)	3.81 (3.83)	18.59 (18.63)
4	6d- NO2	$C_{21}H_{17}BrN_8O_4S$	Yellow	558.6	191-193	69	0.56	45.21 (45.25)	3.04 (3.07)	20.06 (20.10)
5	6e- 4 Cl	$C_{21}H_{17}BrClN_7O_2S$	White	547.4	170-172	60	0.62	46.10 (46.13)	3.10 (3.13)	20.23 (20.29)
6	6f- 3 CH3	$C_{22}H_{20}BrN_7O_2S$	White	527.6	171-173	71	0.65	50.17 (50.20)	3.76 (3.83)	18.61 (18.63)
7	6g- 4 F	$C_{21}H_{17}FBrN_7O_2S$	Brown	531.4	182-184	67	0.68	47.52 (47.56)	3.18 (3.23)	18.45 (18.49)
8	6h- 3 Cl,4 F	$C_{21}H_{16}FBrClN_7O_2S$	Pale Yellow	547.5	165-167	70	0.63	44.61 (44.66)	2.83 (2.86)	17.30 (17.36)
9	6i- 3 Br	$C_{21}H_{17}Br_2N_7O_2S$	Brown	592.6	179-181	67	0.67	42.63 (42.66)	2.86 (2.90)	16.52 (16.58)
10	6j- 4 OCH3	$C_{22}H_{20}BrN_7O_3S$	White	543.5	174-177	66	0.66	48.68 (48.72)	3.70 (3.72)	18.03 (18.08)

Antimicrobial activity

All the newly synthesized compounds were tested for their in vitro antibacterial and antifungal activity (MIC-minimum inhibitory concentration) by broth dilution method with two gram positive bacteria S. aureus and B. subtilis, 2 gram negative bacteria E. coli, P. aeruginosa and fungi species like C. albicans, A. niger organisms taking ciprofloxacin, ampicillin, chloramphenicol, norfloxacin, flucanazole, griseofulvin, and Nystatin as standard controll drug. Muller Hinton broth was used as nutrient medium to grow and dilute the drug suspension for test. DMSO was used as a diluent which is ineffective to the growth of microbes.

The above mentioned anti bacterial results revealed that the compound **6b, 6g, 6i and 6j** bearing 4-Acetoxy, 4-fluoro, 3-bromo and 4-methoxy aniline derivative to the basic s-triazine nucleus containing morpholine in addition to 5-(4-bromopheneyl)-1,3,4-oxadiazole-2-thiol linkage proved more beneficial compound compared to other analogues against both gram positive and gram negative bacteria.

The compound **6h** possessed 3-chloro-4-fluoro aniline substituent showed good activity against gram negative bacteria while moderate activity against *B.subtilis* gram negative bacteria where rest of the compounds showed good to moderate activity.

We made an attempt to increase the biological activity by increasing the volume of the substituent's attached to the ring system led to different biological potency, depending on the nature, position and number of the atoms or groups introduced, whereas, high potency has been observed in the final scaffolds due to the presence of aniline systems with halogen, fluoro atom(s), methoxy group(s) . Due to the highest electro negativity, high thermal stability and lipophilicity of F-atom, introduction of F substituent's to biologically active aniline ring can affect their biological properties associated with lipophilicity, absorption, and transportation.

Minimum inhibitory concentration Comp. no.	R	Gram negative		Gram positive		Fungal Species	
		E.coli	P.aeruginosa	S.aureus	B. subtilis	C. albicans	A.niger
6a	2-chloro-aniline	50	100	100	50	100	250
6b	4-acetoxy -aniline	50	50	50	100	250	100
6c	4-methyl-aniline	500	250	250	250	250	500
6d	4-nitro-aniline	100	100	250	250	500	250
6e	4-chloro-aniline	100	250	100	25	100	25
6f	3-methyl-aniline	100	100	50	100	250	500
6g	4-fluoro-aniline	50	50	100	50	25	50
6h	3-chloro-4-fluoro aniine	100	100	50	250	100	500
6i	3-bromo-aniline	50	100	50	50	50	100
6j	4-methoxy-aniline	100	50	50	100	100	50
Ampicillin		100	100	250	100	-	-
Ciprofloxacin		25	25	50	50	-	-
Chloramphenicol		50	50	50	50	-	-
Norfloxacin		10	10	10	10	-	-
Griseofulvin				500		100	
Nystatin				100		100	
Flucanazole				10		10	

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