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SYNTHESIS, SPECTRAL AND BIOLOGICAL EVOLUTION OF 2 -(4 -FLUOROPHENYL -1, 3, 4 -OXADIAZOL -2 –YL -5 -SULFANYL) -4 -(CYCLOHEXYLAMINO) -6 -(ARYLAMINO) -S -TRIAZINE.

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ABSTRACT

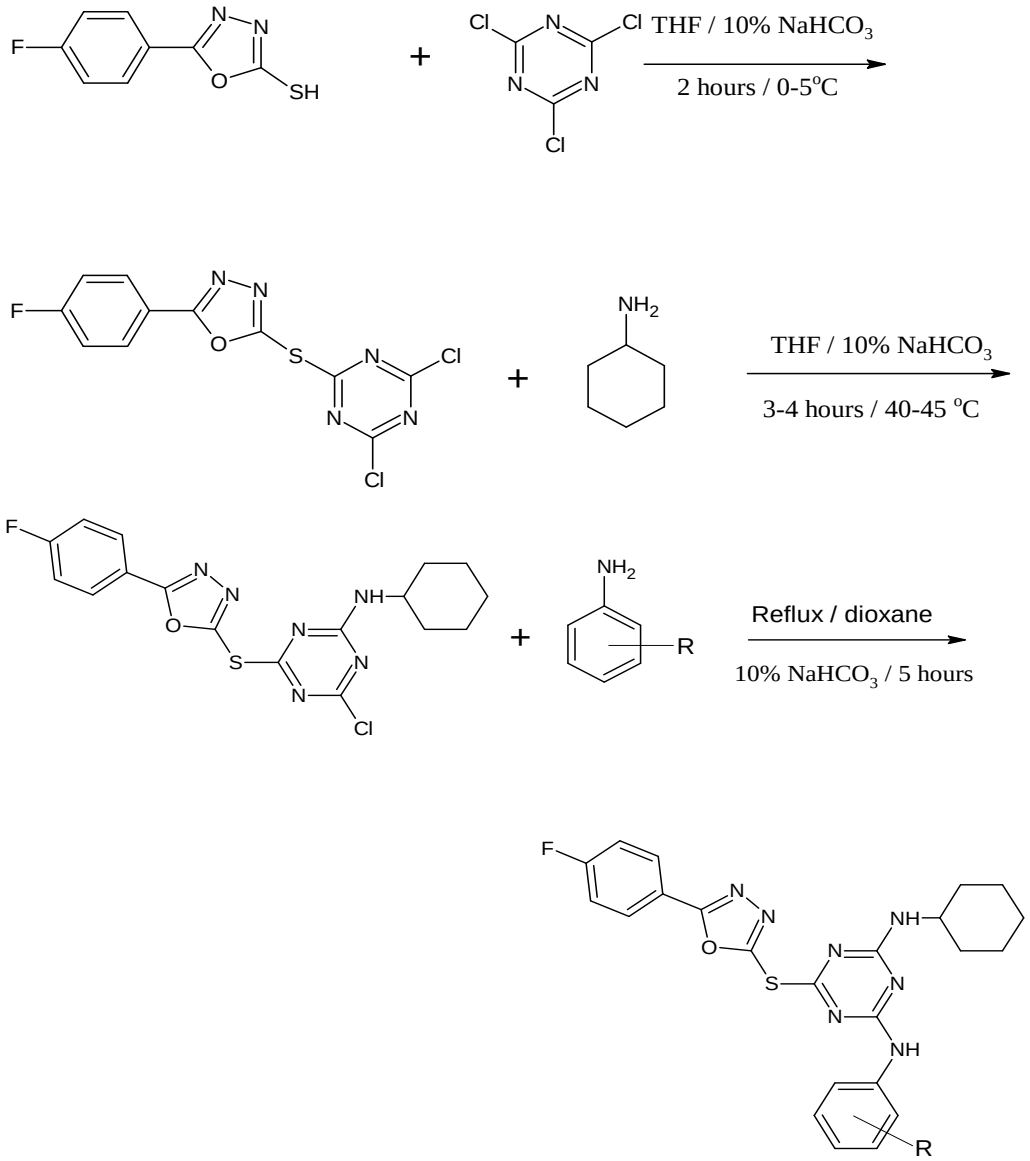
The s-triazine and their derivatives are important intermediates in organic synthesis and widespread application in medical sciences. The title s- triazine derivatives were synthesised with different substituted aryl amine. The synthesis derivatives were characterised by FTIR, ^{1}HNMR and LCMS. Synthesised compound were screened for their microbial activity against standard drugs.

KEYWORDS: fluorophenyl, oxadiazol, arylamino, sulfanyl, s-triazine.

INTRODUCTION

1,3,4- Oxadiazole is biologically active, synthetically useful and important heterocyclic compound. For this reasons the chemistry of 1,3,4- oxadiazole has been the subject of many synthesis of oxadizolidine[1], indol[2], 2-mercapto[3] and semicarbazide cyclization[4] based investigation. Like that the chemistry of s-triazine has been extensively studied because many drugs compounds[5-7] include this ring system in polymers[8], antibacterial[9-10], antimicrobial.[11] With an aim to synthesis this mention compound as under and all derivatives characterised by spectral, physico-chemical and biological evolution.

Reaction Scheme



Where –'R' = Substituted Aryl Amine.

Experimental

All compounds were routinely checked for their homogeneity by TLC on silica gel-G aluminium plates. IR spectra were recorded in KBr on a Perkin-Elmer BX series FT-IR spectrophotometer, ^{1}H NMR spectra on a 400 MH_Z using TMS as internal standard and satisfactory C, H, and N analysis were obtained for all the compounds. The biological evolution data obtained from the National Chemical Laboratory (NCL) Pune, India.

General procedure for synthesis of 2-(4-fluorophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(cyclohexylamino)-6-(arylamino) -s-triazine.

Step – 1 Synthesis of 2-(4-fluorophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4,6-dichloro-s-triazine: To a stirred solution of cyanuric chloride (0.1 M, 18.4 gm) in THF 100 ml at 0-5 c, The solution of 5-(4-flourophenyl)-1,3,4-oxadiazole-2-thiol (0.1M, 19.2 gm) in THF (100 ml) was added dropwise and PH was maintained neutral by the addition of 10% $NaHCO_3$ solution. The stirring was continued at 0-5^{0}C for 2-3 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 = 110-115 ^{0}C.

Step – 2 Synthesis of 2-(4-fluorophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(cyclohexylamino)-6-chloro-s-triazine: The solution of cyclohexylamine (0.1 M) in THF was added drop-wise to well stirred suspenension of 2-(4-fluorophenyl-1,3,4-oxadiazol-2yl-5-sulfanyl)-4,6-dichloro-s-triazine (0.1 M) in THF (100 ml) maintaining the temp 40^{0}C the PH was kept neutral by the addition of 10% $NaHCO_3$ solution. The temp. Was gradually raised to 45^{0}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 = 225-230^{0}C.

Step – 3 Synthesis of 2-(4-fluorophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(cyclohexylamino)-6-(arylamino)-s-triazine: A mixture of 2-(4-fluorophenyl-1,3,4-oxadiazol-2yl-5-sulfanyl)-4-(cyclohexylamino)-6-chloro-s-triazine (0.005 M) and aryl amine (0.005 M) in dioxane (50.0 ml) was refluxed on heating mental with stirring at 100-110^{0}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 ethyl acetate: hexane (4: 6) eluent. M.P = 148-151^{0}C.

RESULT AND DISCUSSION

Spectral data of 2-(4-fluorophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(cyclohexylamino)-6-(4-methyl phenyl amino)-s-triazine(KE-1).

IR (KBr): 1265 cm^{-1} (<C=O - Streching in oxadiazole), 1529 cm^{-1} (<C=N – Streching in oxadiazole), 821 cm^{-1} (-C=N- Streching in S-triazine), 3408 cm^{-1} (-NH- Stretching in amide), 3255 cm^{-1} (-NH- Stretching in amide), 1209 cm^{-1} (-C-O-C Stretching (asym.) in alkanyl ether), 1053 cm^{-1} (-C-O-C Stretching (sym.) in alkanyl ether), 2850 cm^{-1} (-C-H- Stretching in

methelene),1384 cm^{-1} (-C-CH_3- Stretching in aromatic ring), 1084 cm^{-1} - (-C-F- Stretching in aromatic ring).

1H NMR(δ ppm)**:** δ 1.68-2.10 (10 H, m, Ar-H), δ 2.32 (3H, s, -CH_3), δ 7.22-7.27 (4H, m, Ar-H), δ 7.35-7.39 (4H, m, Ar-H), δ 9.29(1H, s, -NH), δ 9.52(1H, s, -NH).

MS: m/z 300, 330, 389, 417,477, 478(M+1)

Physical properties of 2-(4-fluorophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(cyclohexylamino)-6-(arylamino)-s-triazine.

Table-1.

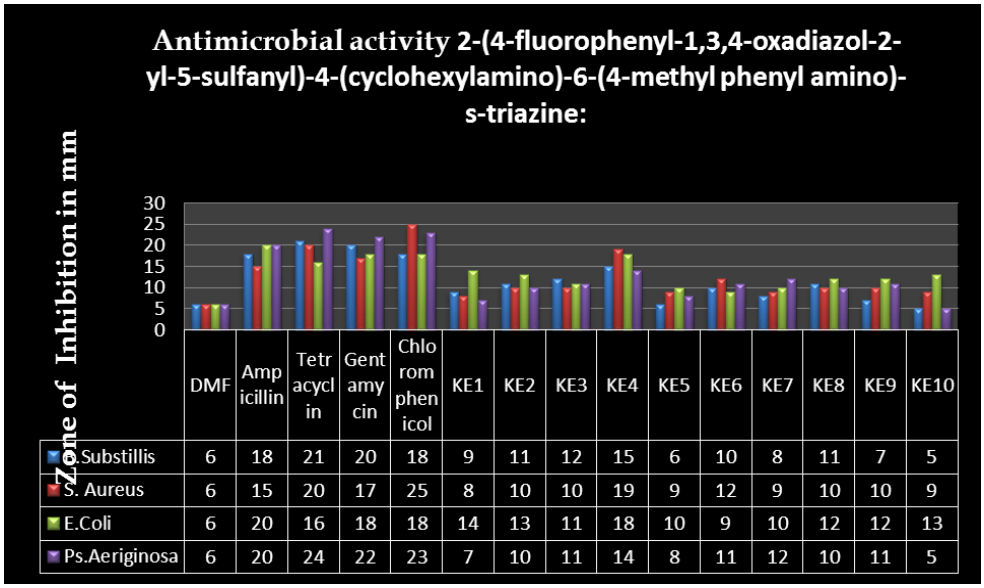
Comp.	Mol. formula	Mol. Weight	% of Yield	M.P (^{0}C)	Elemental Analysis					
					% C		% H		% N	
					Cal.	Found	Cal.	Found	Cal.	Found
K-E1	$C_{24}H_{24}FN_7OS$	477.5	73	165-167	60.36	60.39	5.07	5.09	20.53	20.58
K-E2	$C_{23}H_{21}F_2N_7OS$	481.5	64	188-190	57.37	57.41	4.40	4.44	20.36	20.39
K-E3	$C_{23}H_{20}ClF_2N_7OS$	515.9	69	214-216	53.54	53.59	3.91	3.95	19.00	19.01
K-E4	$C_{23}H_{21}FN_8O_3S$	508.5	58	202-204	54.32	54.38	4.16	4.19	22.03	22.07
K-E5	$C_{24}H_{24}FN_7O_2S$	493.5	66	167-169	58.40	58.43	4.90	4.95	19.87	19.89
K-E6	$C_{23}H_{21}ClFN_7OS$	497.9	71	143-145	55.47	55.51	4.25	4.29	19.69	19.72
K-E7	$C_{24}H_{24}FN_7OS$	477.5	65	158-160	60.36	60.40	5.07	5.09	20.53	20.58
K-E8	$C_{24}H_{27}FN_8OS$	506.5	62	233-235	59.27	59.31	5.37	5.40	22.12	22.15
K-E9	$C_{23}H_{21}ClFN_7OS$	497.9	69	178-180	55.47	55.51	4.25	4.26	19.69	19.71
K-E10	$C_{23}H_{21}BrFN_7OS$	542.4	58	199-201	50.93	50.96	3.40	3.44	18.06	18.09

Antimicrobial Activity

Antimicrobial activity of 2-(4-fluorophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(cyclohexylamino)-6-(4-methyl phenyl amino)-s-triazine.

Ampicillin, Tetracycline, Gentamycin, and Chloramphenicol were used as standard drugs and a solvent control was also run to know the activity of solvent. Activity of standards and inhibition due to DMF (solvent) are given in graphs. Among Antimicrobial activity of 2-(4-fluorophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(cyclohexylamino)-6-(4-methyl phenyl amino)-s-triazine. Compounds KE-2, KE-3 and KE-4 shows good antimicrobial activity. Other prepared compounds shows moderate activity compared to standard drugs against all four bacterial strains *B. subtillis, S. aureus, E. coli and Ps. aeruginosa.*

Graphical Chart ofAntimicrobial activity of 2-(4-fluorophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(cyclohexylamino)-6-(4-methyl phenyl amino)-s-triazine.



	DMF	Ampicillin	Tetracycl in	Gentamycin	Chloromphenicol	KE1	KE2	KE3	KE4	KE5	KE6	KE7	KE8	KE9	KE10
B.Substillis	6	18	21	20	18	9	11	12	15	6	10	8	11	7	5
S. Aureus	6	15	20	17	25	8	10	10	19	9	12	9	10	10	9
E.Coli	6	20	16	18	18	14	13	11	18	10	9	10	12	12	13
Ps.Aeriginosa	6	20	24	22	23	7	10	11	14	8	11	12	10	11	5

CONCLUSION

In conclusion, we have describe simple method for the synthesis of 2-(4-fluorophenyl-1,3,4-oxadiazol-2-yl-5-sulfanyl)-4-(cyclohexylamino)-6-(arylamino)-s-triazine. The newly synthesised s-triazine derivatives were conformed and by the spectral, physico-chemical analysis and evaluated for their microbiological activity. The microbial activity shows that most of derivatives give good to moderate results.

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