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Research Article

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Synthesis, characterization and biological evaluation of 2-(4-methyl-7-hydroxycoumarin)-4-(4-flouro-3-chloroamino)-6-(arylamino)-*s*-triazine

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ABSTRACT

A simple and efficient synthesis of 2-(4-methyl-7-hydroxy-coumarin) -4-(4-Flouro-3-Choro-amino)-6-(arylamino)-s-triazine have been synthesized. The novel compounds structure has been established on the basis of their substituted aryl amine derivatives. All the compounds were characterized by FT-IR, and ^{1}H-NMR spectroscopy as well as elemental analysis. These new compounds were evaluated for their in vitro antibacterial activity.

Key words: s-triazine, Spectral data, Elemental analysis and bacterial activity.

INTRODUCTION

The chemistry of s-Triazine has been extensively studied because many drugs include this ring.Number of derivatives containing s-triazine ring have been reported as hetrocyclic compounds [1-3]. They are applicable mostly as reactive dyes and some are used as polymers and drugs [4]. *s*-triazine derivatives were reported for their antitubercular, anti-AIDS and anti cancer activities[5-7]. Among them 1,3,5-triazines represent a widely used lead structure with multitude of interesting applications in numerous fields [8] Several derivatives of *s*-triazine show antibacterial [9], antimicrobial [10], and herbicidal activities [11].

General procedure for synthesis of 2-(4-methyl-7-hydroxy-coumarin)-4-(4-flouro-3-choro-amino)-6-(arylamino)-s-triazine

Step – 1 Synthesis of 4-methyl -7-hydroxy-coumarin

Take cons. H_2SO_4 in a round bottle flask and cool it to 5^{o}C by stirring the flask in an icebath. Prepare a soln. of resorcinol in ethylacetoacetate in a test tube add this soln. drop by drop to the cold H_2SO_4 by maintaining the temperature of the mix below 10^{o}C continue stirring for 30 min. Pour the reaction mixture in to 25 gm crushed ice. Filter the separated product. And wash several time with cold water.

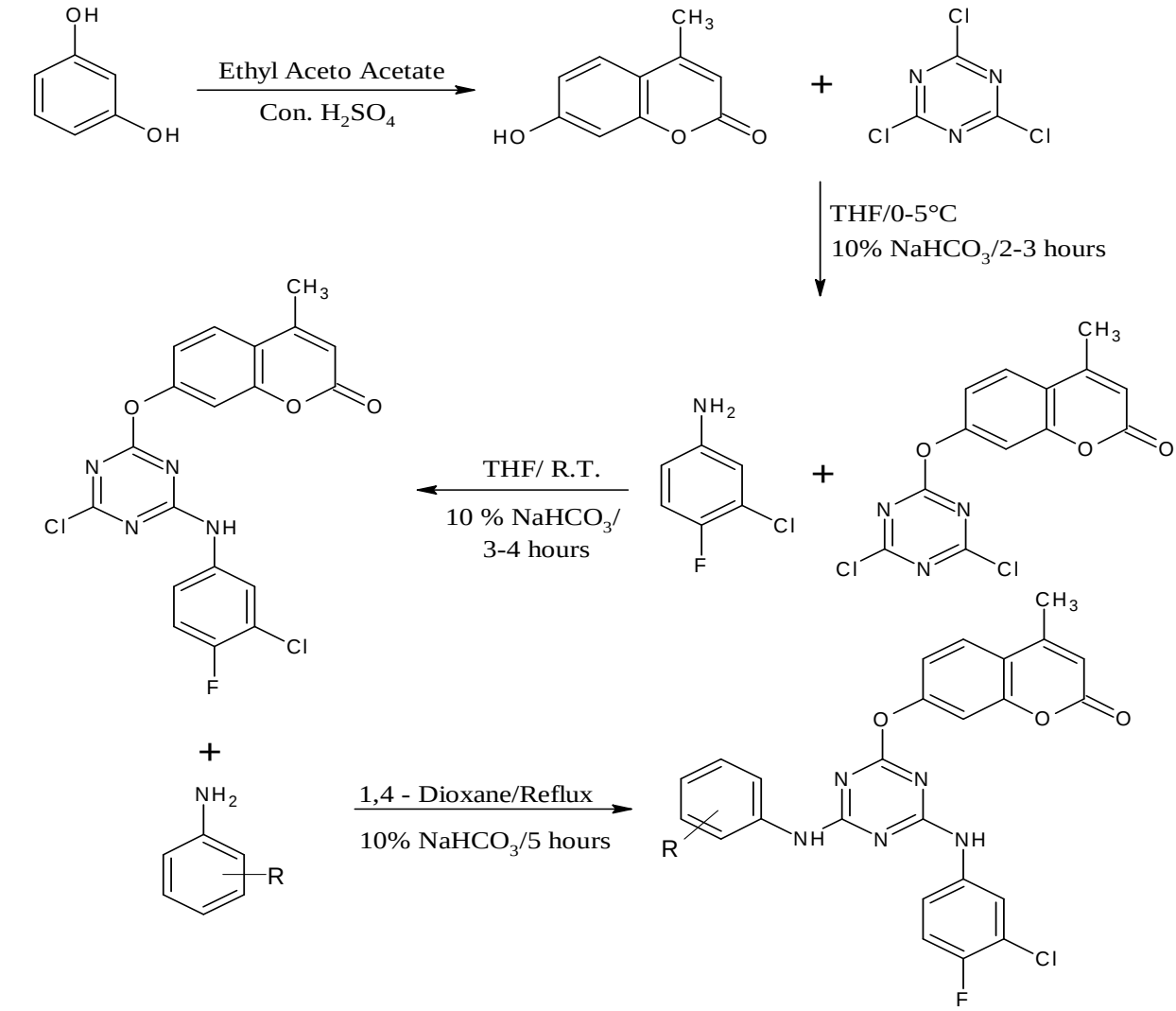
Dissolve the product in cold 10% NaOH soln. reppt. Product by adding 10% aq. HCl till the soln. becomes acidic to litmus paper. Filter the product wash with cold water and crystallization from alcohol using activated charcoal.

Step – II Synthesis of 2-(4-methyl -7-hydroxy-coumarin)-4,6-dichloro-s-triazine

To a stirred solution of cyanuric chloride (0.1 M) in THF 100 ml at 0-5^{o}C, The solution of 5-(4-methyl-7-hydroxy-coumarin) (0.1 M) 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^{o}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^{o}C

REACTION SCHEME



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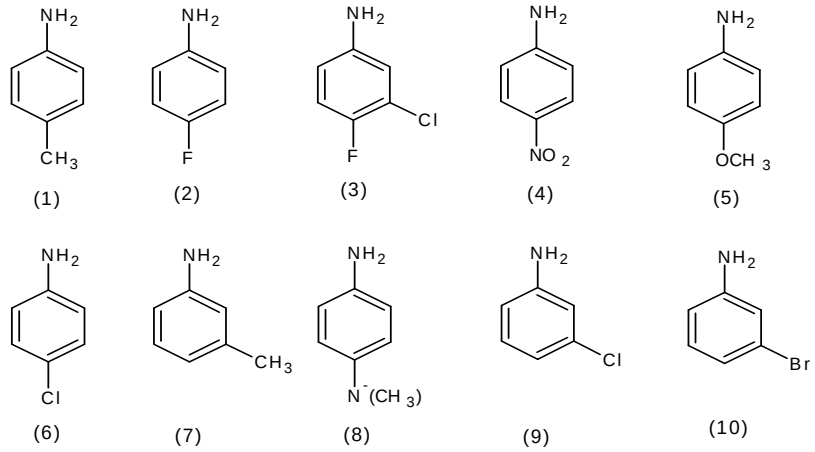

Step – III Synthesis of 2-(4-methyl-7-hydroxy-coumarin)-4-(cyclohexylamino)-6-chloro-s-triazine

The solution of cyclohexylamine (0.1 M) in THF was added drop-wise to well stirred suspenension of 2-(4-methyl-7-hydroxy-coumarin)-4,6-dichloro-s-triazine (0.1 M) in THF (100 ml) maintaining the temp 40^{o}C the pH was kept neutral by the addition of 10% $NaHCO_3$ solution. The temp. was gradually raised to 45^{o}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^{o}C

Step – IV Synthesis of 2-(4-methyl-7-hydroxy-coumarin)-4-(4-flouro-3-choro-amino)-6-(arylamino)s-triazine
A mixture of 2-(4-methyl-7-hydroxy-coumarin)-4-(4-flouro-3-choro-amino)-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^{o}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.

RESULTS AND DISCUSSION

Table 1: Physical properties of 2-(4-methyl-7-hydroxy-coumarin)-4-(4-flouro-3-choro-amino)-6-(arylamino)s-triazine

Sr. No.	Compound	Molecular Formula	Molecular Weight	Appearance	M.P (^{0}C)	% Yield	% of C Cal/Found	% of H Cal/Found	% of N Cal/Found
1	1	$C_{26}H_{19}ClFN_5O_3$	503.5	Pale Yellow	188-190	72	61.97 (61.93)	3.80 (3.76)	13.90 (13.85)
2	2	$C_{25}H_{16}ClF_2N_5O_3$	507.8	White	211-212	65	59.12 (59.06)	3.18 (3.10)	13.79 (13.74)
3	3	$C_{25}H_{15}Cl_2F_2N_5O_3$	542.3	White	173-175	59	55.37 (55.33)	2.79 (2.72)	12.91 (12.84)
4	4	$C_{25}H_{16}ClFN_6O_5$	534.8	White	215-217	71	56.14 (56.06)	3.02 (2.95)	15.71 (15.66)
5	5	$C_{26}H_{19}ClFN_5O_4$	519.9	Light brown	188-190	64	60.06 (60.01)	3.68 (3.62)	13.47 (13.43)
6	6	$C_{25}H_{16}Cl_2FN_5O_3$	524.3	White	145-147	62	57.27 (57.22)	3.08 (3.02)	13.36 (13.28)
7	7	$C_{26}H_{19}ClFN_5O_3$	503.5	Light green	176-178	73	61.97 (61.88)	3.80 (3.71)	13.90 (13.86)
8	8	$C_{27}H_{22}ClFN_6O_3$	523.9	White	231-233	72	60.85 (60.80)	4.16 (4.06)	15.77 (15.68)
9	9	$C_{26}H_{16}Cl_2FN_5O_3$	524.3	White	134-136	70	57.27 (57.22)	3.08 (3.01)	13.36 (13.28)
10	10	$C_{25}H_{26}BrClFN_5O_3$	568.7	Light yellow	209-211	63	52.79 (52.72)	3.34 (3.30)	12.31 (12.25)

Spectral data of 2-(4-methyl-7-hydroxy-coumarin)-4-(4-flouro-3-choro-amino)-6-(arylamino)s-triazine.
858 cm^{-1} - (-C=N- Streching in s-triazine), 3416 cm^{-1} - (-NH- Stretching in amide), 3292 cm^{-1} - (-NH- Stretching in amide), 1213 cm^{-1} - (-C-O-C Stretching in coumarine), 1708 cm^{-1} - (-C=O Stretching in coumarine), 2852 cm^{-1} - (-C-H- Stretching in methelene), 1340 cm^{-1} - (-C-CH_3- Stretching in aromatic ring), 1383 cm^{-1} - (-C-CH_3- Stretching in aromatic ring), 798 cm^{-1} – (-C-Cl- Stretching in aromatic ring), 1078 cm^{-1} - (-C-F – Stretching in aromatic ring) δ 2.47 (3H, -CH_3), δ 2.89 (3H, -CH_3), δ 7.24-7.39 (4H, Ar-H), δ 7.45-7.70 (3H, -Ar-H), δ 7.85-7.95 (3H, -Ar-H), δ 9.75 (1H, -NH), δ 9.93 (1H, -NH) ppm.

Table-2: The antimicrobial activity of standard drugs.

No.	Name of compound	Zone of inhibition (in mm)			
		Gram positive		Gram negative	
		B. Subtillis	*S. Aureus*	*E. Coli*	*Ps. Aeruginosa*
1	DMF	6	6	6	6
2	Ampicillin	18	15	20	20
3	Tetracycline	21	20	16	24
4	Gentamycin	20	17	18	22
5	Chloramphenicol	18	25	18	23

Table-2.1: Antimicrobial activity of 2-(4-methyl-7-hydroxy-coumarin)-4-(4-Flouro-3-Chloro-amino)-6-(arylamino)-s-triazine.

Compound	Zone of Inhibition (in mm)			
	Gram positive		Gram negative	
	B. Subtillis	*S. Aureus*	*E. Coli*	*Ps. Aeruginosa*
1	12	14	13	11
2	11	15	11	09
3	12	12	11	11
4	10	10	09	10
5	12	11	08	14
6	17	16	11	18
7	18	20	12	16
8	12	11	09	13
9	15	14	16	17
10	16	08	13	12

The compounds tested for antimicrobial activity are listed in **Table 2 and 2.1** show size of zone of inhibition of bacterial growth procedure by test compounds for broad range of antimicrobial activity inhibiting growth of Gram-positive bacterial strains *B.Subtillis* and *S.Aureus*, and Gram-negative bacterial strains *E.Coli* and *Ps. Aeruginosa*.

Comparison of antimicrobial activity of produced compounds with that of standard antimicrobial drugs reveals that the produce compounds shows moderate to good activity against all four bacterial strains.

Among **2-(4-methyl -7-hydroxy-coumarin)-4-(4-Flouro-3-Choro-amino)-6-(arylamino)-s-triazine.** (1-10) **(Table-2)** compounds 6, 7 and 9 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*.

CONCLUSION

In summary, we have described a simple method for the synthesis of 2-(4-methyl-7-hydroxy-coumarin)-4-(4-Flouro-3-Chloro-amino)-6-(arylamino)-s-triazine. The newly synthesized compounds were confirmed by the spectral analysis and further evaluated for their antimicrobial activity. The antibacterial activity revealed that most of the compounds showed moderate to good activity.

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