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SYNTHESIZES AND ANTIMICROBIAL EVALUATION OF SOME NOVEL HETEROCYCLIC COMPOUNDS

TARUN M. PATEL and AMIT M. PATEL*

Department of Applied Science, Singhania University, PACHERI BARI, Jhunjhunu (Raj.) INDIA

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ABSTRACT

4-(1H-naphtho[1,8-de][1,2,3]triazin-1-ylsulfonyl)aniline (1) undergoes facile condensation with aromatic aldehydes to afford the corresponding 4-(1H-naphtho[1,8-de] [1,2,3]triazin-1-ylsulfonyl)-N-arylideneaniline (2a-d) in good yields. cyclocondensation of compounds (2a-d) with thioglycolic acid 3-(4-(1H-naphtho[1,8-de][1,2,3]triazin-1-ylsulfonyl)phenyl)-2-arylthiazolidin-4-one (3a-d). The structures of these compounds were established on the basis of analytical and spectral data. All the newly synthesized compounds were evaluated for their antibacterial and antifungal activities.

Key words: 4-(1H-naphtho[1,8-de][1,2,3] Triazin-1-ylsulfonyl) Aniline, Thiazolidine, Antibacterial activity.

INTRODUCTION

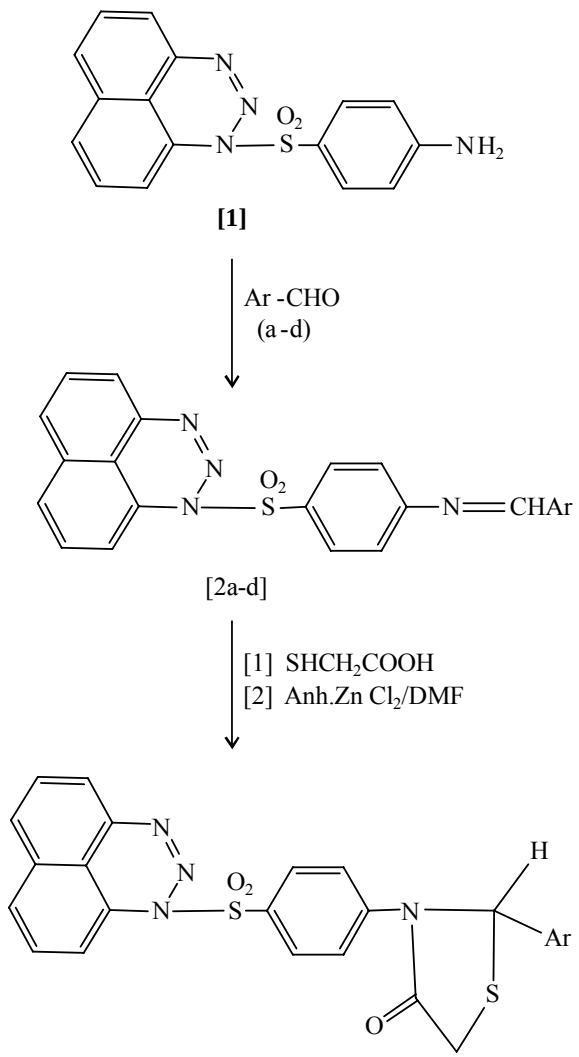
The heterocyclic compounds such as,4-thiazolidinones[1,2], fused thiazolidinones[3,4], 2-pyrrole and 2-pyrrolidinones[4,5], 1,3,5-oxadiazine[1] and tetrazole[6] have prominent role in pharmaceutical. Literature assessment reveals that Schiff bases indicate that they have coordinating behavious with the transition metal ions. Schiff bases also display biochemical and physiochemical effects[7-10]. The another moiety triazoles and their derivatives are found to be associated with various biological activities, such as anticonvulsant, antifungal, anticancer and antibacterial properties[11-13]. If both these moiety clubbed into one molecule, it will be afford as good bioactive compound. 4-thiazolidinones are also known to exhibit antitubercular[14], antibacterial[15], antifungal[16] and anticonvulsant activities. Hence, it was thought of interest to merge both of thiazolidinone and triazine moieties which may enhance the drug activity of compounds to some extent or they might possess some of the above mentioned biological activities. Hence the present communication comprises the synthesis of 3-(4-(1H-naphtho[1,8-de][1,2,3]triazin-1-ylsulfonyl)phenyl)-2-aryl thiazolidin-4-one (3a-d). The synthetic approach is shown in Scheme 1.

EXPERIMENTAL

Materials

Naphthotriazine was purchased from local market. 4-aminobenzene-1-sulfonyl chloride was prepared by reported method[17].

Available online at www.sadgurupublications.com
*Author for correspondence; E-mail: tarunpatel16185@yahoo.in



Where Ar = -C_6H_5, 4-Cl-C_6H_4, 4-Br-C_6H_4, 4-OCH_3-C_6H_4

Scheme 1

Measurement

Melting points were determined in open capillary tubes and were uncorrected. The IR spectra were recorded in KBr pellets on a Nicolet 400D spectrometer and ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO with TMS as internal standard on a Bruker spectrometer at 400 MHz and 100 MHz, respectively.

Preparation of 4-(1H-naphtho[1,8-de][1,2,3]triazin-1-ylsulfonyl)aniline (1)

The solution of 4-aminobenzene-1-sulfonyl chloride (0.01 mole) in methanol was treated with naphthotraizine (0.01 mole) in methanol at room temperature. The resultant product hydrolysed in acidic condition. The product was filtered and hydrolyzed by 50 : 50 HCl: Ethanol mixture.

Preparation of 4-(1H-naphtho[1,8-de] [1,2,3]triazin-1-ylsulfonyl)-N-arylideneaniline (2a-d)

General procedure: An equimolecular mixture of 4-(1H-naphtho[1,8-de][1,2,3]triazin-1-ylsulfonyl) aniline (1), (0.01 mole) and the aromatic aldehydes (a-d) in ethanol (15 mL) was refluxed on a water bath for

1-2 hrs. The solid separated was collected by filtration, dried and recrystallized from ethanol. The yields, melting points and other characterization data of these compounds are given in Table 1.

Preparation 3-(4-(1H-naphtho[1,8-de][1,2,3]triazin-1-ylsulfonyl)phenyl)-2-aryl thiazolidin -4-one (3a-d)

General procedure: A mixture 4-(1H-naphtho[1,8-de] [1,2,3]triazin-1-ylsulfonyl)-N-arylideneaniline (2a-d) (0.01 mole) in THF (30 mL) and mercapto acetic acid (thioglycolic acid) (0.01 mole) with a pinch of anhydrous $ZnCl_2$ was refluxed for 12 hrs. The solvent was then removed to get a residue, which was dissolved in benzene and passed through a column of silica gel using benzene: chloroform (8:2; v/v) mixture as eluent. The eluate was concentrated and the product crystallized from alcohol to give 3-(4-(1H-naphtho[1,8-de][1,2,3]triazin-1-ylsulfonyl)phenyl)-2-arylthiazolidin-4-one (3a-d), which were obtained in 62-66% yield. The yields, melting points and other characterization data of these compounds are given in Table 2.

Table 1: Analytical data and elemental analysis of compounds (2a-d)

Compd.	Molecular formula (Mol. wt.)	LC-MS Data	Yield	M.P.* ^{0}C	Elemental Analysis							
					%C		%H		%N		%S	
					Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
2a	$C_{23}H_{16}N_4O_2S$ (412)	438	86	248-249	66.95	66.97	3.88	3.91	13.56	13.58	7.75	7.77
2b	$C_{23}H_{15}ClN_4O_2S$ (446)	457	84	242-244	61.80	61.81	3.36	3.38	12.52	12.54	7.15	7.17
2c	$C_{23}H_{15}BrN_4O_2S$ (490)	502	85	239-241	56.21	56.22	3.05	3.08	11.38	11.40	6.51	6.53
2d	$C_{24}H_{18}N_4O_3S$ (442)	459	87	242-243	65.12	65.14	4.07	4.10	12.65	12.66	7.23	7.25

***** Uncorrected

Table 2: Analytical data and elemental analysis of compounds (3a-d)

Compd.	Molecular formula (Mol. wt.)	LC-MS Data	Yield	M.P.* ^{0}C	Elemental Analysis							
					%C		%H		%N		%S	
					Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
3a	$C_{25}H_{18}N_4O_3S_2$ (486)	503	75	223-224	61.69	61.71	3.72	3.73	11.49	11.51	13.16	13.18
3b	$C_{25}H_{17}ClN_4O_3S_2$ (520)	539	72	216-218	57.61	57.63	3.27	3.29	10.72	10.75	12.30	12.31
3c	$C_{25}H_{17}BrN_4O_3S_2$ (563)	577	71	210-212	53.08	53.10	3.01	3.03	9.90	9.91	11.32	11.34
3d	$C_{26}H_{20}N_4O_4S_2$ (516)	529	73	211-213	60.42	60.45	3.88	3.90	10.84	10.85	12.39	12.41

*****Uncorrected

Biological screening

Antibacterial activities

The antibacterial activities of all the compounds were studied against gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*) and gram-negative bacteria (*E. coli*, and *Klebsiella promioe*) at a concentration of 50 µg/mL by agar cup plate method. A methanol system was used as control in this method. Similar conditions using tetracycline as a control was used standard for comparison. The area of inhibition of zone measured in mm. Compounds 3b and 3d were found more toxic for microbes. Other compounds found to be less or moderate active than tetracycline Tables 3.

Table 3: Antibacterial activity of compounds (3a-d)

Compounds	Gram +ve		Gram -ve	
	Staphylococcus aureus	***Bacillus subtilis***	***E. coli***	***Klebsiella promioe***
3a	59	62	69	56
3b	72	65	73	73
3c	64	60	61	64
3d	73	74	82	55
Tetracycline	55	79	74	84

Antifungal activities

The fungicidal activity of all the compounds was studied at 1000 ppm concentration *in vitro*. Plant pathogenic organisms used were *Nigrospora Sp, Aspergillus niger, Botrydepladia thiobromine,* and *Rhizopus nigricum***,** *Fusarium oxyporium*. The antifungal activities of all the compounds (3a-d) were measured on each of these plant pathogenic strains on a potato dextrose agar (PDA) medium. Such a PDA medium contained potato 200 g, dextrose 20 g, agar 20 g and water 1c. Five days old cultures were employed. The compounds to be tested were suspended (1000 ppm) in a PDA medium and autoclaved at 120^{o}C for 15 min. at 15 atm. pressure. These media were poured into sterile petri plates and the organisms were inoculated after cooling the petri plates. The percentage inhibition for fungi was calculated after five days using the formula given below:

Percentage of inhibition = 100 (X-Y) / X

Where, X = Area of colony in control plate

Y = Area of colony in test plate

The fungicidal activity displayed by various compounds (3a-d) is shown in Tables-4.

Table 4: Antifungal activity of compounds (3a-d)

	Zone of inhibition at 1000 ppm (%)				
Compounds	***Nigrospora Sp.***	***Aspergillus Niger***	***Botrydepladia Thiobromine***	***Rhizopus Nigricum***	***Fusarium oxyporium***
3a	70	68	66	61	68
3b	77	71	76	67	80
3c	65	56	65	63	69
3d	72	73	70	76	71

RESULTS AND DISCUSSION

It was observed that 4-(1H-naphtho[1,8-de][1,2,3]triazin-1-ylsulfonyl)aniline (1) undergoes facile condensation with aromatic aldehydes to afford the corresponding 4-(1H-naphtho[1,8-de] [1,2,3]triazin-1-ylsulfonyl)-N-arylideneaniline (2a-d). The structures of (2a-d) were confirmed by elemental analysis and IR spectra showing an absorption band at 1630-1660 cm^{-1} (C=N), 3030-3085 cm^{-1} (C-H, of Ar.), 2815-2850 cm^{-1} (-OCH_3). ^{1}H NMR : 7.30 – 8.20 (10H, m) (Ar - H), 8.43-8.80 (1H, s) (-N=CH), 4d; 3.90 (3H, s) (-OCH_3). ^{13}C NMR: 163.2-115.6 (Ar-22C), 160.3 (-N=CH); (4b): 55.5-56.7 (-OCH_3). The C, H, N analysis data of all compounds are presented in Table 1.

The structures assigned to 3-(4-(1H-naphtho[1,8-de][1,2,3]triazin-1-yl sulfonyl) phenyl)-2-arylthiazolidin-4-one (3a-d) were supported by the elemental analysis and IR spectra showing an absorption bands at 1690 cm^{-1} (C=O of thiazolidinone ring), 718 cm^{-1} (C-S-C of thiazolidinone ring), 3075-3095 cm^{-1} (CH_2 of thiazolidinone ring), 3030-3080 cm^{-1} (C-H of Ar.). ^{1}H NMR: 7.40 – 8.20 (10H, m) (Ar - H), 6.50 (1H, s) (CH), 3.89 (2H,s) (-CH_2CO-), 4d; 3.90 (3H, s) (-OCH_3). ^{13}C NMR: 163.2-114.4 (Ar-22C), 195.4, 171.6 (-CO), 72.6 (CH), 34.2 (CH_2); (4b): 55.5-56.7 (-OCH_3). The C, H, N, S analysis data of all compounds are presented in Table 2.

The examination of elemental analytical data reveals that the elemental contents are consistence with the predicted structure shown in Scheme 1. The IR data also direct for assignment of the predicted structure. The final structure of all compounds is confirmed by LC-MS. LC-MS data of all compounds are presented in Tables 1, 2.

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