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Synthesis of Some New Heterocyclic Compounds with Potential Biological Activity

D.P. Bhoot, R.C. Khunt,* V.K. Shankhavara, and H.H. Parekh

Department of Chemistry, Saurashtra University, Rajkot-360 005, India

Abstract

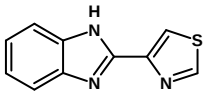
A series of new 2-arylimino-3-aryl-5-[5′-(3,4-dichlorophenyl)-2′-furylidene]-4-thiazolidinones (3a-l) have been synthesised by the condensation of 5-(3,4-dichlorophenyl)-2-furaldehyde 1 with 2-arylimino-3-aryl-5H-4-thiazolidinones 2 in glacial acetic acid. The physical and spectral data of the synthesised compounds are determined. The synthesised compounds have been screened for their in vitro antimicrobial activity against various strains of bacteria and fungi.

Keywords: Thiazolidinone; Antimicrobial activity

Introduction

Amongst different heterocycles, a major impetus for research on thiazolidinone [1-3] derivatives has stemmed from the significant physiological function of this ring system. Moreover, furan containing heterocyclic compounds have also been shown to have deep impact on biological activities like antitumor [4], anti-inflammatory [5], antimicrobial [6], antiviral [7], *etc*.

The presence of N-C-S linkage in the compounds has been shown to have nematocidal and antifungal activity. The compounds which possess N-C-S linkage like omizole (a) possess nematocidal activity. Hence, it was subject of interest to synthesise and study some new derivatives.



(a)

The target compound 3a-l have been synthesised by the condensation of 5-(3,4-dichlorophenyl)-2-furaldehyde 1 with 2-arylimino-3-aryl-5H-4-thiazolidinone 2 in glacial acetic acid. The 2 was obtained by the reaction of N^1, N^3-bisaryl thiourea and chloroacetic acid. The reaction between diazonium salt of 3,4-dichloroaniline and furfural yielded 1.

The constitution of the products has been supported by elemental analyses, IR and ^{1}H NMR spectral study. All the products have been screened *in vitro* for their antimicrobial activity against different strain of bacteria and fungi.

Antimicrobial Activity

The antimicrobial activity was assayed by using the cup-plate agar diffusion method [8] by measuring the inhibition zone in mm. All the compounds were screened *in vitro* for their antimicrobial activity towards variety of bacterial strains such as *B. mega, S. aureus, E. coli, P. vulgaris* and fungi such as *Aspergillus niger* at a concentration of 40 μg. Known antibiotics such as Ampicillin, Amoxycillin, Norfloxacin and Penicillin showed zones of inhibition at 17-22 mm, 18-24 mm, 19-

*E-mail: drrckhunt12@yahoo.com

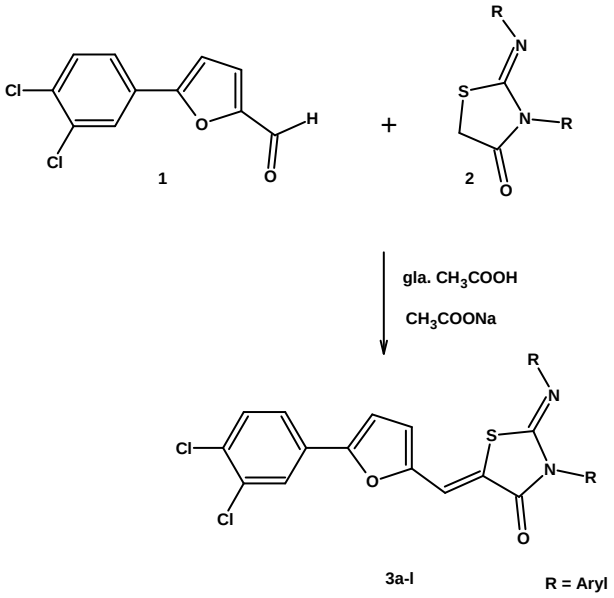
23 mm and 22-25 mm respectively towards bacterial strains and greseofulvin showed zones of inhibition of 26 mm towards fungi *A. niger*.

Experimental

Melting points were determined in an open capillary tubes and are uncorrected IR spectra (KBr) were recorded on Shimadzu FT-IR-8400-spectropheotometer ^{1}H NMR spectra on BRUKER spectrometer (300 MHz) using TMS as an internal standard. Purity of the compounds was checked by TLC using silica gel G layer.

Synthesis of 5-(m,p-dichlorophenyl)-2-furaldehyde (1)

A mixture of 3,4-dichloroaniline (16.2 g, 0.1 M) dil HCl (15%, 60 ml) and water (90 ml) was heated to get a clear solution. The solution was cooled to 0°C and diazotized with $NaNO_2$ solution (30%, 24 ml). The diazonium salt solution was filtered and to the filtrate, water (50 ml) and freshly distilled furfural (11.1 ml, 0.1 M) and aqueous cupric chloride (2.5 g in 10 ml of water) were added with stirring. The stirring was continued for 4 h and kept overnight. The separated solid was collected by filtration and washed with cold ethanol, crystallised from a mixture of ethanol-DMF. (Yield 80%, m.p. 270°C.)



Scheme

Synthesis of 2-arylimino-3-aryl-5H-4-thiazolidinone (2)

A solution of N^1, N^3, bisaryl thiourea (0.01 M) and chloroacetic acid (0.94 g, 0.01 M) in glacial acetic acid (15 ml) was refluxed with fused sodium acetate (1.25 g, 0.015 M) for 5 h. The reaction product was poured in water; kept overnight crude product was isolated and crystallised from methanol.

Synthesis of 2-(p-tolylimino)-3-(4-tolyl)-5-[5'-(3,4-dichlorophenyl)-2'-furylidene]-4-thiazolidinone (3)

A mixture of 2-(4-tolylimino)-3-(4-tolyl)-5H-4-thiazolidinone (2.96 g, 0.01 M), 5-(3,4-dichlorophenyl)-2-furaldehyde (2.41 g, 0.01 M) and fused sodium acetate (1.25 g, 0.015 M) was refluxed in glacial acetic acid (15 ml) for 4-5 h, cooled and poured into water. The solid thus obtained was filtered, washed, dried and crystallised from DMF. Yield 72%, m.p. 182°C.

Analysis: for $C_{28}H_{20}Cl_2N_2O_2S$

Calculated: C, 64.74; H, 3.88; N, 5.39%;

Found: C, 64.50; H, 3.71; N, 5.15%.

IR (KBr) cm^{-1}: 2948 (C-H str.): 1710 (C=O str.); 1629 (S-C=N str.); 1490 (C=C str.); 790 (C-Cl str.)

^{1}H NMR ($CDCl_3$) δ ppm: 2.37 (s, 3H, Ar-CH_3); 2.41 (s, 3H, Ar-CH_3); 6.76-7.64 (m, 13H, Ar-H); 7.55 (s, 1H, =CH).

Other 4-thiazolidinones were prepared. The physical constants are recorded in Table 1.

Results and Discussion

By visualizing the antimicrobial data it could be observed that compounds 3a and 3h were highly active towards *B. megaterium*. The compounds 3a, 3b, 3g and 3l were significantly active towards *S. aureus*. In case of *E. coli,* compounds 3a, 3g and 3h have displayed maximum activity. The compounds 3a, 3g and 3h showed comparable activity towards *P. vulgaris*. The compounds 3a, 3e and 3f were highly active towards fungi *A. niger* (Table 2).

Looking to the structure activity relationship it can be concluded that remarkable inhibition was observed in compounds bearing R=phenyl, 2-methoxyphenyl, 2-methylphenyl, 3-methylphenyl 4-nitrophenyl substituents.

Acknowledgement

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Table 1. Physical data constants of compounds 3a-l

Sr. No.	R	Molecular formula	M.P. (°C)	Rf* value	Yield (%)	% of Nitrogen	
						Calculated	*Found*
3a	C_6H_5-	$C_{26}H_{16}Cl_2N_2O_2$	225	0.78	74	5.70	5.45
3b	4-Cl-C_6H_4-	$C_{26}H_{14}Cl_4N_2O_2S$	205	0.72	65	5.00	5.32
3c	3,4-$(Cl)_2$-C_6H_3-	$C_{26}H_{12}Cl_6N_2O_2S$	190	0.48	72	4.45	4.10
3d	4-F-C_6H_4-	$C_{26}H_{14}Cl_2F_2N_2O_2S$	240	0.84	68	5.31	5.62
3e	2-OCH_3-C_6H_4-	$C_{28}H_{20}Cl_2N_2O_4S$	280	0.82	60	5.08	4.92
3f	4-OCH_3-C_6H_4-	$C_{28}H_{20}Cl_2N_2O_4S$	180	0.51	62	5.08	5.20
3g	2-CH_3-C_6H_4-	$C_{28}H_{20}Cl_2N_2O_2S$	252	0.78	69	5.39	5.05
3h	3-CH_3-C_6H_4-	$C_{28}H_{20}Cl_2N_2O_2S$	198	0.72	71	5.39	5.65
3i	4-CH_3-C_6H_4-	$C_{28}H_{20}Cl_2N_2O_2S$	182	0.55	72	5.39	5.72
3j	2-NO_2-C_6H_4-	$C_{26}H_{14}Cl_2N_4O_6S$	152	0.81	70	9.64	10.00
3k	3-NO_2-C_6H_4-	$C_{26}H_{14}Cl_2N_4O_6S$	200	0.67	63	9.64	9.44
3l	4-NO_2-C_6H_4-	$C_{19}H_{14}Cl_2N_4O_6S$	228	0.68	66	9.64	9.40

Table 2. Biological activities of the compounds 3a-l

Sr. No.	R	Zone of inhibition (mm)				
		Antimicrobial activity				Antifungal activity
		B. mega	*S. aureus*	*E. coli*	*P. vulgaris*	*A. niger*
3a	C_6H_5-	22	20	17	19	20
3b	4-Cl-C_6H_4-	20	19	16	14	14
3c	3,4-$(Cl)_2$-C_6H_3-	14	14	14	14	15
3d	4-F-C_6H_4-	13	13	13	15	16
3e	2-OCH_3-C_6H_4-	19	21	17	13	22
3f	4-OCH_3-C_6H_4-	20	18	16	16	20
3g	2-CH_3-C_6H_4-	18	21	18	19	19
3h	3-CH_3-C_6H_4-	22	12	19	17	21
3i	4-CH_3-C_6H_4-	17	15	14	16	17
3j	2-NO_2-C_6H_4-	12	16	12	14	16
3k	3-NO_2-C_6H_4-	16	14	15	13	14
3l	4-NO_2-C_6H_4-	15	19	16	12	18
a	ampicilin	22	20	17	19	–
b	amoxicillin	24	22	20	18	–
c	norfloxacin	23	19	21	20	–
d	penicillin	25	24	23	22	–
e	greseofulvin	–	–	–	–	26

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