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Synthesis and antimicrobial study of some new 2-aryl-3-[(4-methoxy cinnamoyl amino)-4-oxo-thiazolidines

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ABSTRACT

New anils were synthesized in good yield from 4-Methoxy cinnamoyl hydrazine and various benzaldehydes. Further these anils were converted into 4-thiazolidines by the action of mercapto acetic acid. All the products have been evaluated for their *in vitro* antimicrobial activity against various strains of bacteria.

KEYWORDS

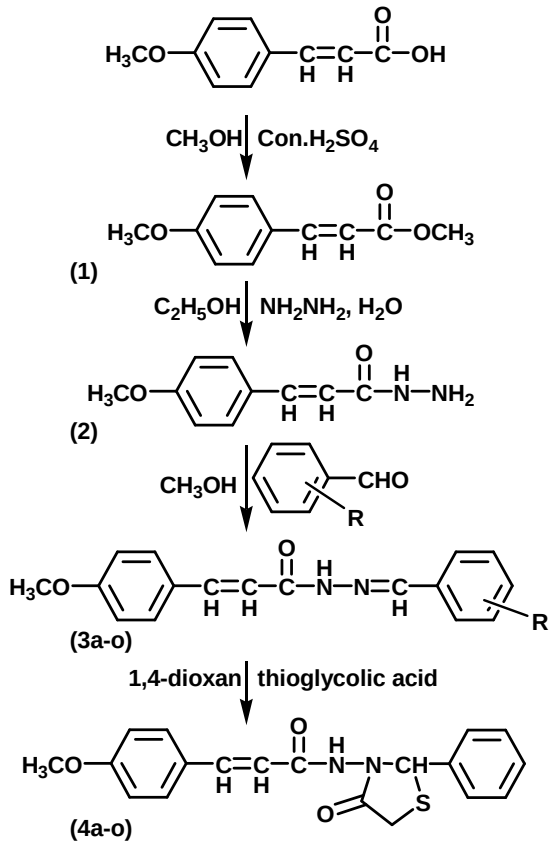
Schiff base;
Thiazolidines;
Antimicrobial activity.

INTRODUCTION

Schiff bases have diverse physiological and pharmacological activities such as anticancer[1], antipyretic[2], Anti-tubercular activity[3], anti-inflammatory[4] and antitumor[5]. 4-oxo-thiazolidines play a vital role in pharmaceutical sciences owing to wide biological applications[6,7]. 4-oxo-thiazolidines have been reported for their antibacterial, antiparkinsonian and anticonvulscant[8] activities. 4-oxo-thiazolidines find their application as local anesthetics and also as moderate tuberculostic agent[9].

Moreover, 4-oxo-thiazolidine with styryl moiety has shown antibacterial[10], anti-HIV and anticancer activities. These interesting biological activities have attracted our attention to the chemistry of nitrogen and sulfur containing heterocycles. Hence it was thought of interest that 4-oxo-thiazolidine, if coupled to styryl moiety; the resulting compounds may possess significant biological potency.

Keeping in view of these varied pharmacological activities, we have planned to synthesize new 2-aryl - 3-[(4-methoxy cinnamoyl) amino] 4-oxo-thiazolidine



Scheme

TABLE 1 : Physical constants of the compounds (4a-o)

Comp. No.	R	Molecular formula	M.W.	M.P.°C	% of yield	% of nitrogen	
						Req.	Found
4a	C_6H_5-	$C_{19}H_{18}N_2O_2S$	338.42	60	76	8.27	8.22
4b	4(OH)C_6H_4-	$C_{19}H_{18}N_2O_3S$	354.42	236	77	7.90	7.89
4c	2(OH)C_6H_4-	$C_{19}H_{18}N_2O_3S$	354.42	194	81	7.90	7.89
4d	3(OH)C_6H_4-	$C_{19}H_{18}N_2O_3S$	354.42	176	80	7.90	7.88
4e	2,4$(OH)_2C_6H_3$-	$C_{19}H_{18}N_2O_4S$	370.42	160	74	7.56	7.50
4f	4$(OCH_3)C_6H_4$-	$C_{20}H_{20}N_2O_3S$	368.45	135	76	7.60	7.56
4g	2$(OCH_3)C_6H_4$-	$C_{20}H_{20}N_2O_3S$	368.45	75	76	7.60	7.57
4h	3,4$(OCH_3)_2C_6H_3$-	$C_{21}H_{22}N_2O_4S$	398.47	119	75	7.03	7.00
4i	3,4,5$(OCH_3)_3C_6H_2$-	$C_{22}H_{24}N_2O_5S$	428.50	151	80	6.53	6.50
4j	4(OH),3$(OCH_3)C_6H_3$-	$C_{20}H_{20}N_2O_4S$	384.44	126	65	7.28	7.24
4k	4$(CH_3)C_6H_4$-	$C_{20}H_{20}N_2O_2S$	352.45	82	64	7.94	7.91
4l	4$(Cl)C_6H_4$-	$C_{19}H_{17}N_2O_2SCl$	372.86	86	72	7.51	7.46
4m	4$(NO_2)C_6H_4$-	$C_{19}H_{17}N_3O_4S$	383.42	120	78	10.95	10.90
4n	3,4,-O-(CH_2)-O-C_6H_3-	$C_{20}H_{18}N_2O_4S$	382.42	243	71	7.32	7.30
4o	C_6H_5-CH = CH-	$C_{21}H_{20}N_2O_2S$	364.46	108	77	7.68	7.61

TABLE 2 : Antimicrobial activity of the compounds (4a-o)

Comp. No.	R	Zone of inhibition in mm.	
		E.coli	*S.aureus*
4a	C_6H_5-	11	10
4b	4$(OH)C_6H_4$-	13	10
4c	2$(OH)C_6H_4$-	13	11
4d	3$(OH)C_6H_4$-	12	11
4e	2,4$(OH)_2C_6H_3$-	11	14
4f	4$(OCH_3)C_6H_4$-	11	12
4g	2$(OCH_3)C_6H_4$-	14	13
4h	3,4$(OCH_3)_2C_6H_3$-	11	10
4i	3,4,5$(OCH_3)_3C_6H_2$-	12	12
4j	4(OH),3$(OCH_3)C_6H_3$-	12	14
4k	4$(CH_3)C_6H_4$-	13	13
4l	4$(Cl)C_6H_4$-	11	11
4m	4$(NO_2)C_6H_4$-	14	11
4n	3,4,-O-(CH_2)-O-C_6H_3-	11	10
4o	C_6H_5-CH = CH-	14	10

(4)[11] by condensation of anils of aromatic system by the action of the mercaptoacetic acid. The constitution of all the products has been characterized using elemental analyses, IR, ^{1}H NMR and mass spectral study. All the compounds were screened for their *in vitro* antimicrobial activityagainst different strains of bacteria.

EXPERIMENTAL

All the melting points are determined in open capillary tubes and are uncorrected. Thin layer chromatography was used for monitoring the reaction and to check purity. IR spectra recorded on Bio-Rad FTS-40 spectrophotometer on KBr disc. ^{1}H NMR spectra were recorded on a model DPX-200 Brucker FT-NMR instrument using TMS as an internal standard, FAB mass spectra were recorded on JEOL SX 102/DA 6000 spectrophotometer. All the compounds gave satisfactory elemental analyses.

Preparation of 2-phenyl-3-[(4-methyl cinnamoyl amino)-4-oxo-thiazolidines

Preparation of 1-benzylidine-2-[(4-methoxy cinnamoyl)] hydrazine (3)

4-methoxy cinnamoyl hydrazine (1.92g; 0.01 M) was dissolved in methanol (30ml) and benzaldehyde (1.06g; 0.01 M) in methanol (10ml) was slowly added. The reaction mixture was refluxed for 3 hours on water bath. The resulting mass was allowed to cool at room temperature; product separated was filtered and washed with ice cold methanol, dried and recrystallised from ethanol (95 %). Yield : 2.12g;(75.71 %) ; m.p. : 105°C.

Preparation of 2-phenyl-3-[(4-methoxy cinnamoyl) amino]-4-oxo-thiazolidine (4)

To a solution of 1-benzylidine-2-[(4-methoxy cinnamoyl)] hydrazine (2.80g; 0.01 M) in 1: 4 dioxane (25ml) was added thioglycolic acid (0.925g; 0.01 M). The mixture was refluxed at 110-115°C for 8 hours. The reaction mixture was allowed to cool at room temperature and triturated with 10 % sodium bicarbonate solution to remove unreacted mercaptoacetic acid. The solid product thus separated was filtered and washed with water. Recrystallised from ethanol (95%). Yield: 2.67g; (75.42%); m.p.: 154°C. M.F.: $C_{19}H_{18}N_2O_3S$; M.W.: 354.42; Required: N, 7.90%, S, 9.05%; Found: N, 7.65 %, S, 8.80 %. TLC solvent system: Acetone: Benzene (4:6). IR (KBr) in ν max cm^{-1}: 1249 (aryl alky ether), 755 (mono substituted bezene ring), 831 (di substituted benzene ring); 1671 & 1619 (acyclic and cyclic carbonyl respectively); 692 (di substituted alkene); 3450 (N-H str.); 698 (C-S-C-linkage of thiazolidine ring); ^{1}H NMR in ‰ ppm; 8.2 ‰ (s, 1H, -NH), 6.9-7.8 ‰ (m, 9H, Aromatic protons), 3.8 ‰ (s, 3H, Ar- OCH_3), 3.68 ‰ (s, 2H, -CH_2 Thiazolidine

ring), 3.12 ‰ (s, 1H, N-CH-Ar), 2.4 ‰ (d, d 2H, -CH = CH-).

Similarly other 4-oxo-thiazolidines were prepared. The physical data are recorded in TABLE 1.

RESULTS AND DISCUSSION

Compounds **(1a-o)** were screened for their *in vitro* antibacterial activity using cup-plate agar diffusion method[12] at a concentration of 40μg/ml using gram positive bacterial strains such as Staphylococcus and gram negative bacterial strain such as *Escherichia coli*. Known antibiotics like ampicillin, amoxycillin, norfloxacin, penicillin and greseofulvin were used for comparison purpose. By visulizing the antimicrobial data, these compounds have no noteworthy activity as observed in TABLE 2. Only compounds **(1e)**, **(1g)**, **(1j)** and **(1k)** have good activity against *S.aureus*. While compounds **(1b)**, **(1c)**, **(1g)**, **(1k)** and **(1o)** possess very good activity against *E. coli*.

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