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Synthesis and antibacterial activity of some new thiazolidines

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ABSTRACT

4-oxo-thiazolidine have been synthesized by cyclisation of acyclic compounds and thioglycolic acid on Schiff 's bases. All the products have been evaluated for their in vitro antimicrobial activity against various strains of bacteria.

Introduction

In recenty decades, problems of multy-drug resistant microorganisms have reached on alarming level in many countries around the world, and also infection caused by those microorganisms pose a serious challenge to the medical community and the need for an effective therapy has led to a search for novel antibacterial agents. The development of bacterial resistant of existing drugs is a major problem in antibacterial and necessitates continuing research in to new classes of antibacterial [1].

Compounds containing thiazolidinone ring exhibit variety of biological activities such as anti-HIV3, antitubercular 4, antioxidant5, antiviral activity 6,. Anticancer7.

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 activity against 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. 1H 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 - METHOXY CINNAMOYL AMINO) - 4 - OXO – THIAZOLIDINES-5-ACETIC ACID:

Different methods for the preparation of 4-thiazolidinone s have been reported8,9

Preparation of 1 – benzylidine– 2 – [(4 – methoxy cinnamoyl)] hydrazine (III):

4 – Methoxy cinnamoyl hydrazine (1.92 g; 0.01 M) was dissolved in methanol (30 ml) and benzaldehyde (1.06 g; 0.01 M) in methanol (10 ml) was slowly added. The reaction mixture was refluxed for 3 hours on waterbath. 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 : 2.12 g;(75.71 %) ; M.P. : 105^{O}C

Preparation of 2–(2-chloro phenyl)– 3 – [(4 – methyl cinnamoyl) amino] 4 - oxo – thiazolidine-5-acetic acid (IV):

To a solution of 1 – (2-choloro benzylidine) – 2 – [(4 – methyl cinnamoyl)] hydrazine (2.64 g; 0.01 M) in 1: 4 dioxane (25 ml) was added thiomalic acid (1.6 g; 0.01 M). The mixture was refluxed at 110 - 115^{O}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: 2.8 g; (72.17%); M.P.: 83^O C. M.F. : $C_{19}H_{17}ClN_2O_3S$; M.W.: 388.87 ; Required : N , 7.20 % Found : N , 6.88 %. S,8.25 % S , 8.02 %. TLC solvent system: Acetone: Benzene (4:6). IR (KBr) in u max cm^{-1} : 1260 (Ar-OCH_3)1639 & 1655 (acyclic and cyclic carbonyl respectively). 812 (para di substituted ring), 670 (C-S-C- linkage of thiazolidine ring), 814 (para substituted Pheyl ring), 1599, 1624 and 1725 (-C-O str.); 3209 (N-H str.) . 1H NMR in d ppm ; 9.2 δ (1H, - NH) , 8.8 d – 8.5 δ (8H, Aromatic protons) , 3.4 δ (3H , - OCH_3), 2.4 δ (2H , - CH = CH -).

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

Results and discussion

Antibacterial activity

Compounds 1a – o were screened for their in vitro antibacterial activity using cup-plate agar diffusion method[9] at a concentration of 40 µg/ml using gram positive bacterial strains such as Staphylococcus aureus and gram negative bacterial strain such as Escherichia coli. Known antibiotics like ampicillin, amoxycillin, norfloxacin, penicillin were used for comparison purpose. By visualizing the antimicrobial data, these compounds have noteworthy activity as observed in Table-2. Interestingly some of these have remarkable zone of inhibition as compared to solvent These compounds also do not exhibit any activity against E.coli. However they show moderate to good activity against S.aureus. Six compounds have zone of inhibition 20 mm. or more. Where as non of these compounds have activity against E.coli all of them are

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Scheme

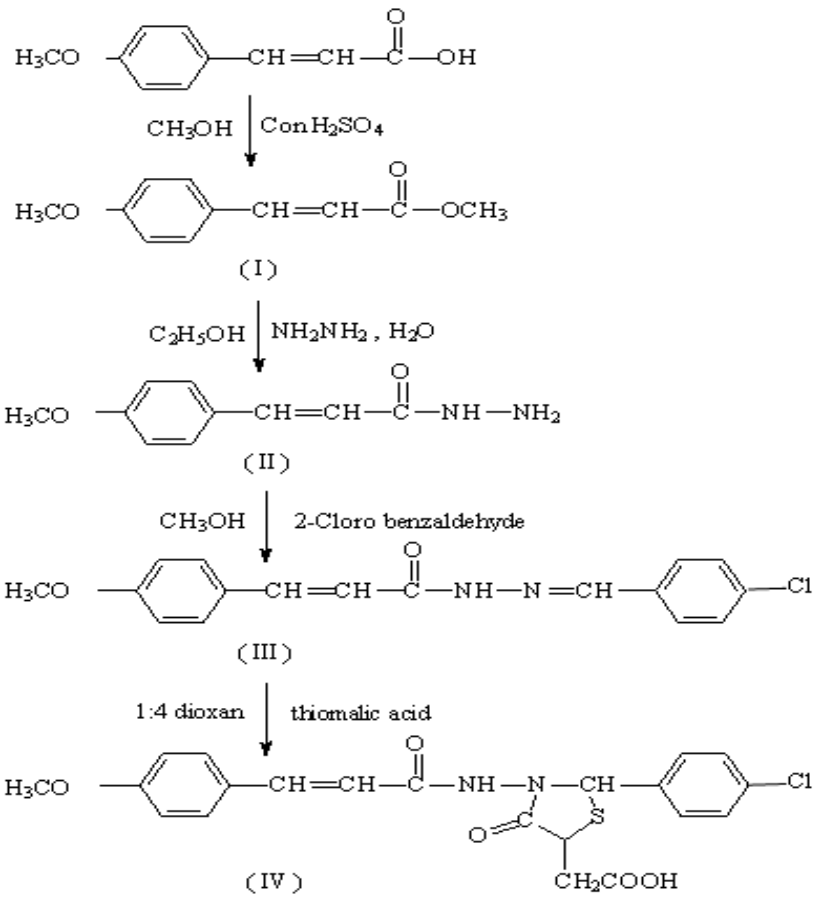

Table 1 : Physical Constants of the compounds 1a-o

Comp. No.	ARYL	MOLECULAR FORMULA	M.W.	M.P. ^{O}C	% OF YIELD	% OF NITROGEN	
						REQ.	FOUND
1a	C_6H_5-	$C_{21}H_{20}N_2O_5S$	412.46	50	87	6.79	6.71
1b	4(OH)C_6H_4-	$C_{21}H_{20}N_2O_6S$	428.45	165	68	6.54	6.46
1c	2(OH)C_6H_4-	$C_{21}H_{20}N_2O_6S$	428.45	152	70	6.54	6.46
1d	3(OH)C_6H_4-	$C_{21}H_{20}N_2O_6S$	428.45	58	77	6.54	6.47
1e	2,4$(OH)_2C_6H_3$-	$C_{21}H_{20}N_2O_7S$	444.45	255	69	6.3	6.28
1f	4$(OCH_3)C_6H_4$-	$C_{22}H_{22}N_2O_6S$	442.48	162	79	6.33	6.29
1g	2$(OCH_3)C_6H_4$-	$C_{22}H_{22}N_2O_6S$	442.48	84	65	6.33	6.29
1h	3,4$(OCH_3)_2C_6H_3$-	$C_{23}H_{24}N_2O_7S$	472.51	175	58	5.93	5.89
1i	3,4,5$(OCH_3)_3C_6H_2$-	$C_{24}H_{26}N_2O_8S$	502.53	112	82	5.57	5.52
1j	4(OH),3$(OCH_3)C_6H_3$-	$C_{22}H_{22}N_2O_7S$	458.48	98	74	6.11	6.09
1k	4$(CH_3)C_6H_4$-	$C_{22}H_{22}N_2O_5S$	426.48	106	76	6.57	6.46
1l	4(Cl)C_6H_4-	$C_{21}H_{19}N_2O_5SCl$	446.90	93	69	6.27	6.21
1m	4$(NO_2)C_6H_4$-	$C_{21}H_{19}N_3O_7S$	457.45	84	76	9.18	9.10
1n	3,4,-O-(CH_2)-O-C_6H_3-	$C_{22}H_{20}N_2O_7S$	456.46	104	78	6.13	6.02
1o	C_6H_5-CH=CH-	$C_{23}H_{22}N_2O_5S$	438.49	50	75	6.39	6.30

Table-2 : Antimicrobial activity of the compounds 1a-o.

Comp. No.	ARYL	Zone of inhibition in mm.	
		E.coli	S.aureus
1a	C_6H_5-	14	16
1b	4(OH)C_6H_4-	19	17
1c	2(OH)C_6H_4-	13	15
1d	3(OH)C_6H_4-	11	15
1e	2,4$(OH)_2C_6H_3$-	14	16
1f	4$(OCH_3)C_6H_4$-	18	14
1g	2$(OCH_3)C_6H_4$-	13	17
1h	3,4$(OCH_3)_2C_6H_3$-	15	17
1i	3,4,5$(OCH_3)_3C_6H_2$-	17	19
1j	4(OH),3$(OCH_3)C_6H_3$-	13	18
1k	4$(CH_3)C_6H_4$-	11	17
1l	4(Cl)C_6H_4-	12	16
1m	4$(NO_2)C_6H_4$-	14	16
1n	3,4,-O-(CH_2)-O-C_6H_3-	14	16
1o	C_6H_5-CH=CH-	14	15

active against S.aureus. A comparison of the anti- bacterial data of these three series leads to following conclusion. The introduction of a methyl group or a carboxymethyl group at position no.5 of 4-oxo-thiazolidine increases anti- bacterial activity. Particularly against S.aureus. These compounds have as such no activity against E.coli but zone of inhibition expands with the introduction of two above mentioned groups.

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