Available online at www.elixirpublishers.com (Elixir International Journal)

Organic Chemistry

Elixir Org. Chem. 77 (2014) 29365-29367

ISSN: 2229-712X

Synthesis of some new 2 – aryl - 3 - [(4 - methyl cinnamoyl) –amino] – 5 – methyl - 4 - oxothiazolidines and evaluation for their antimicrobial activity

P. M.Chatrabhuji[1], K.S.Nimavat[2], K.B.Vyas[2] and N. K.Undavia[1,*]

[1]Department of Chemistry, Bahauddin Science College – Junagadh-362 001, Gujarat, India.

[2]Department of Chemistry, Government Science College – Gandhinagar-382 015, Gujarat, India.

ARTICLE INFO

Article history:

Received: 17 June 2011;

Received in revised form:

10 December 2014;

Accepted: 24 December 2014;

Keywords

Schiff Base,

Thiazolidinones and

Antimicrobial activity.

ABSTRACT

4-Oxothiazolidines(1a-o) have been synthesized by cyclisation of various Schiff bases with thiolactic acid. The schiff bases are obtained by the condensation reaction of 4-methyl cinnamoyl hydrazine with different benzaldehydes. The synthesized compounds are identified on the basis of spectral and elemental analysis. All the products have been evaluated for their *in vitro* antimicrobial activity against various strains of bacteria.

Introduction

The chemistry of 4-thiazolidinone ring system was reviewed in depth[1]. 4-thiazolidinone derivatives play a vital role owing to their wide range of biological activities[2]. Compounds containing thiazolidinone ring exhibit variety of biological activities such as anti-HIV[3],

antitubercular [4], antioxidant [5] and antimicrobial [6,7] etc. 4 - Oxothiazolidines are synthesized either by cyclisation of thiolactic acid and schiff bases or by interconversion among appropriately substituted thiazolidinone derivatives by the action of thiolactic acid on Schiff bases. The reaction undergoes an attack of the mercapto acetic acid upon the C = N group, with the - S - CH_2 - COOH adding to the carbon atom followed by the capture of a proton by nitrogen and subsequent cyclisation. The nucleophilic attack of mercaptoacetic acid anion on carbon of azomethene, which has got positive character while nitrogen has negative character, is evidenced [8]. Simultaneous removal of water as it forms in reaction helps in condensation and determination of the reaction time. 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.

Material and Method

Chemistry

All the reagents used were of A R grade. All the melting points were 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 – (4-methoxy Phenyl) - 3 - [(4 - methyl cinnamoyl)-amino] – 5-methyl-4 - oxothiazolidines:

General procedure to the preparation of 4-thiazolidinones have been reported [9,10].

1 – (4-Methoxy benzylidine)– 2 – [(4 – methyl cinnamoyl)] hydrazine :

4 – Methyl cinnamoyl hydrazine (0.01 M) was dissolved in methanol (30 mL) and 4-methoxy benzaldehyde (0.01 M) in methanol (10 mL) was slowly added to it. The reaction mixture refluxed for 3 hours on water bath. The temperature was allowed to cool at room temperature and the resulting precipitated was filtered and washed with ice cold methanol, dried and recrystallised from ethanol (95 %). Yield : 81%(2.1 g) ; M.P. : 170^{o}C.

2 – (4-methoxy phenyl) – 3 – [(4 – methyl cinnamoyl)-amino]– 5 – methyl - 4 - oxo thiazolidine(Compd. 1f):

To a solution of 1 – (4-methoxy benzylidine) – 2 – [(4 – methyl cinnamoyl)] hydrazine (0.01 M) in 1, 4 dioxane (25 mL), thiolactic acid (0.01 M) was added. 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 product formed was filtered, washed with water and recrystallised from ethanol (95 %). Compd.1f : (m.w. 382.47gm, 87%), M.P.: 77^o C. ^{1}H NMR($CDCl_3$) δ ppm : 9.6 (s, 1H, - NH) , 7.2 – 6.8 (m, 8H, Aromatic protons) , 3.85 (3H, -OCH_3) 3.5 (2H , - CH_2 , Thiazolidine ring) , 3.33 (m, 1H , N – CH – Ar), 2.50 (s, 3H , Ar - CH_3), 2.4 (s, 3H, -CH_3) , 2.3 (dd, 2H , - CH = CH -). Elemental analysis; found : N , 7.28 %. S, 8.38% for $C_{21}H_{22}N_2O_3S$ required : N , 7.32 % , S, 8.10 %. IR bands υ max (KBr cm^{-1}): 1599 , 1663 (acyclic and cyclic carbonyl respectively). 697 (C-S-C- linkage of thiazolidine ring), 811 (para substituted Phenyl ring), 1152 (-C-O str.); 3210 (N-H str.); 955 (di substituted alkene).

Tele:

E-mail addresses: kirankartik@yahoo.com

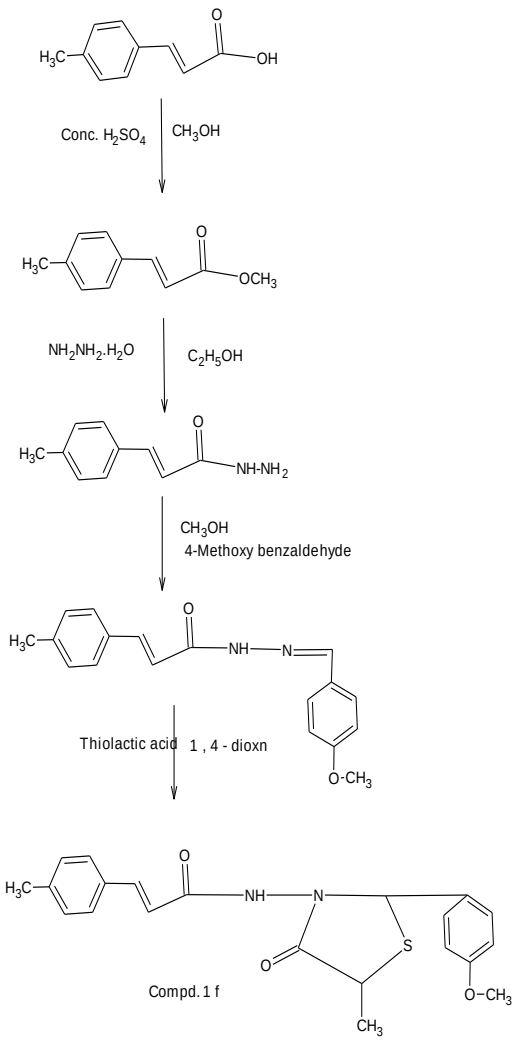
Similarly other 4 - oxothiazolidines were prepared using the general procedure. The physical data are recorded in **Table -1.**

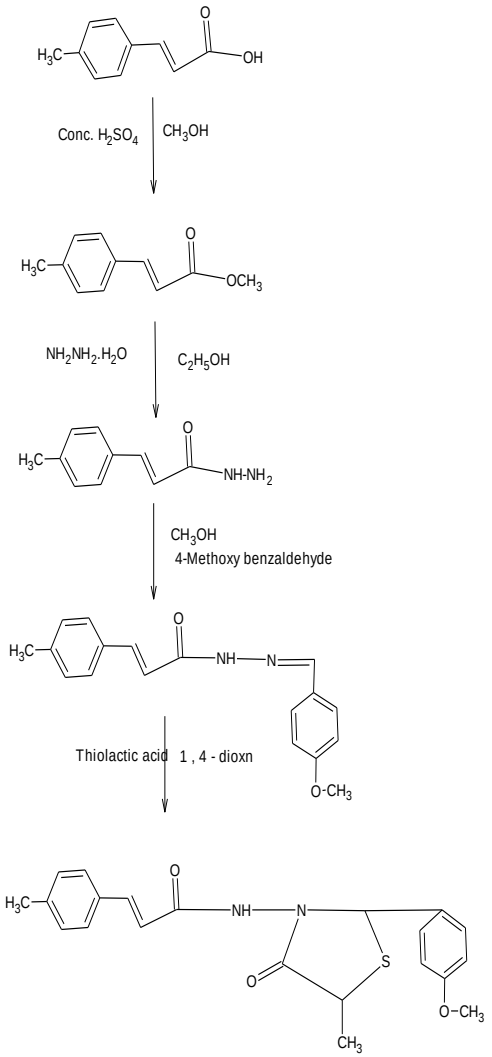
Compounds **1a - o** were screened for their *in vitro* antibacterial activity using cup-plate agar diffusion method[11] at a concentration of 40 µg/ml using gram positive bacterial strains such as *Staphylococcus aureus* and gram negative bacterial strain such as *Escherichia coli*. Known antibiotic Chloramphenicol was 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.

Result and Discussion

All the compounds gave satisfactory elemental analysis and spectral results. The introduction of a methoxy group or methyl group increases antibacterial activity against *S. aureus*. Compounds **1b. 1e, 1g**, and 1l have good activity against *S.aureus* and compoundsno.**1a, 1c, 1d, 1h, 1i,** 1n and 1o have also possess good activity against *E. coli*. Where as compounds **1d, 1i, 1j,** 1n and 1o exhibit excellent activity against *S.aureus* . Antimicrobial results of all compounds are given in **Table-2.**

Scheme 1





Acknowledgement

The authors are thankful to Head of the Department, Department of Chemistry, Bhavnagar University, Bhavnagar for providing research facility and CSMCRI Bhavnagar for providing instrumental facilities. Authors are also thankful to Dr. R. P. Bhatt, Principal, Bahauddin Science College – Junagadh. Saurashtra University, Rajkot. .

References and Notes

1. Khusli, E. and Sonita, S. *Gazz. Chem. Ital*., 1949, 79, 621.
2. Vashi , B . S . Mehta , D . S . Shah , V . H . *Indian J . Chem* . ; 1995, 34 (B) , 802 – 803 , Chem. Abstr. 1995, 123 , 339793 z .
3. Abdel Rehman, R. M. *Boll Chim. Fama*., 2001, 140(6), 401.
4. Babaoglu, K. Page, M. A. And Lee, R. E. *Bioorg. Med. Chem*., 2003, 13, 3227.
5. Sinh, M. H. And Ke, F. Y., *Bioorg. Med. Chem.*, 2004, 12, 4633.
6. Bondock, S., Khalifa, W. And Fadda, A.A., *Eur. J. Med. Chem*., 2007, 42(7), 948. Chem. Abstr. 2007, 147, 257687z.
7. Solankee, A., Patel, G. And Solankee, S., *Oriental J. Chem.* , 2008, 25(1), 245-258.
8. Fenech, G. , Monforte, P. , *Ann. Chim.(Rome)* ; 1958, 48 , 975 , Chem. Abstr. 1959, 53, 8121i .
9. Surrey, A . R., *J . Am . Chem . Soc* . ; 1948, 70 , 4262 .
10. Patel C. L. and parekh H. , *J. Indian Chem. Soc*., 1988, 65, 282.
11. Barry A. L., The Antimicrobial Susceptibility test; Principle and practice, edited by Illus. Lea and Febiger, (Philadelphia Pel USA) 180, (*Bio. Abstr*., 1977, 64, 25183).

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.	% OF NITROGEN FOUND
1a	C_6H_5-	$C_{20}H_{20}N_2O_2S$	352.45	44	85	7.94	7.90
1b	4(OH)C_6H_4-	$C_{20}H_{20}N_2O_3S$	368.45	48	68	7.60	7.58
1c	2(OH)C_6H_4-	$C_{20}H_{20}N_2O_3S$	368.45	62	81	7.60	7.57
1d	3(OH)C_6H_4-	$C_{20}H_{20}N_2O_3S$	368.45	129	64	7.60	7.58
1e	2,4$(OH)_2C_6H_3$-	$C_{20}H_{20}N_2O_4S$	384.44	118	73	7.28	7.25
1f	4$(OCH_3)C_6H_4$-	$C_{21}H_{22}N_2O_3S$	382.47	86	77	7.32	7.28
1g	2$(OCH_3)C_6H_4$-	$C_{21}H_{22}N_2O_3S$	382.47	175	67	7.32	7.29
1h	3,4$(OCH_3)_2C_6H_3$-	$C_{22}H_{24}N_2O_4S$	412.50	194	78	6.79	6.75
1i	3,4,5$(OCH_3)_3C_6H_2$-	$C_{23}H_{26}N_2O_5S$	442.52	213	56	6.33	6.30
1j	4(OH),3$(OCH_3)C_6H_3$-	$C_{21}H_{22}N_2O_4S$	398.47	110	67	7.03	6.98
1k	4$(CH_3)C_6H_4$-	$C_{21}H_{22}N_2O_2S$	366.47	130	61	7.64	7.60
1l	4(Cl)C_6H_4-	$C_{20}H_{19}N_2O_2SCl$	386.89	104	74	7.24	7.21
1m	4$(NO_2)C_6H_4$-	$C_{20}H_{19}N_3O_4S$	397.44	100	73	10.57	10.53
1n	3,4,-O-(CH_2)-O-C_6H_3-	$C_{21}H_{20}N_2O_4S$	396.46	131	75	7.06	7.01
1o	C_6H_5-CH=CH-	$C_{22}H_{22}N_2O_2S$	378.48	79	79	7.40	7.38

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

Compd. No.	Aryl	Zone of inhibition in mm. *E. coli*	Zone of inhibition in mm. *S. aureus*
1a	C_6H_5-	17	14
1b	4(OH)C_6H_4-	16	19
1c	2(OH)C_6H_4-	16	-
1d	3(OH)C_6H_4-	17	20
1e	2,4$(OH)_2C_6H_3$-	15	17
1f	4$(OCH_3)C_6H_4$-	15	17
1g	2$(OCH_3)C_6H_4$-	15	18
1h	3,4$(OCH_3)_2C_6H_3$-	17	13
1i	3,4,5$(OCH_3)_3C_6H_2$-	17	20
1j	4(OH),3$(OCH_3)C_6H_3$-	14	21
1k	4$(CH_3)C_6H_4$-	15	13
1l	4(Cl)C_6H_4-	14	18
1m	4$(NO_2)C_6H_4$-	16	18
1n	3,4,-O-(CH_2)-O-C_6H_3-	17	20
1o	C_6H_5-CH=CH-	17	20
Solvent DMF	-	15	12
Chloram--phenicol	-	23	27