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

Organic Chemistry

Elixir Org. Chem. 54A (2013) 12781-12783

ISSN: 2229-712X

Synthesis and antimicrobial activity of some 4 - oxo – thiazolidines-5-acetic acids

Parimal M. Chatrabhuji[1], Kartik B. Vyas[2], Kiran S. Nimavat[2] and Navinchandra K. Undavia[1]*

[1]Department of Chemistry, Kadi Science College – Kadi (N.G.) Gujarat, India.

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

ARTICLE INFO

Article history:

Received: 14 July 2012;

Received in revised form:

15 March 2013;

Accepted: 18 March 2013;

Keywords

Schiff's base,

Thiazolidinones

Antibacterial activity.

ABSTRACT

4- Oxo- thiazolidines substituted in 2 and 3 positions exhibit a wide range of biological activities. A series of 4-oxo-thiazolidine (4 a-o) have been obtained by cyclisation of various Schiff's base (3) with thiomalic acid. The Schiff's bases (3) are obtained by the reaction of 4 – Methyl cinnamoyl hydrazine with appropriate benzaldehyde. The product is characterized by spectral and analytical data. Most of the tested compounds show promising antibacterial activity.

Introduction

4- Thiazolidinones are associated with anticancer[1] and versatile pharmacological activities[2,3] like Anti-tubercular[4] Anti–inflammatory[5] antimicrobial[6], Anti - HIV [7], antioxidant[8], etc. Some thiazolidines are reported as analgesic and ulcerogenic[9]. Moreover anils are reported to have significant anticancer[10] and antibacterial[11] activity. All these observations and important role of anils and 4- thiazolidinones in certain biological reactions prompted us to synthesize some 4- Thiazolidinones incorporating styryl moiety and to study their antibacterial activity.

4 - Oxo - thiazolidines are synthesized either by cyclisation of acyclic compounds or by interconversion among appropriately substituted thiazolidinone derivatives by the action of thioglycolic acid on Schiff ' s bases. The reaction undergoes by the 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. 1 – benzylidine – 2 – [(4 – methyl cinnamoyl)] hydrazine on condensation with thiomalic acid gives 4-thiazolidinone-5-acetic acid. The steps involved in the synthesis are shown in scheme 1(Page-8).

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 reagents used were of A R grade. Melting point of all the compounds 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 analysis.

PREPARATION OF 2 – PHENYL - 3 - [(4 - METHYL CINNAMOYL AMINO) - 4 - OXO – THIAZOLIDINES-5-ACETIC ACID

Different methods for the preparation of 4-thiazolidinone s have been reported[12,13].

Preparation of 1 – benzylidine– 2 – [(4 – methyl cinnamoyl)] hydrazine (Type -III)(Compound3a):

4 – Methyl cinnamoyl hydrazine (1.76 g; 0.01 M) was dissolved in methanol (30 ml) and benzaldehyde (0.92 g; 0.01 M) in methanol (10 ml) 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 %). Compound(3a): Yield : 87.12 % ; m.p. : 182^{o}C; Anal. Calcd. For $C_{17}H_{16}N_2O$: C 72.27; H 6.06; N 10.60 . Found : C 72.10; H 5.96; N 10.50 . IR (KBr, cm^{-1}) : 1646 (C=O stretching of cinnamoyl group), 814 (para substituted Pheyl ring), 3221 (N-H stretching) , 1445(C=N stretching), 1375, 2850(C-H sym. and asym. stretching of –CH_3 group). ^{1}H NMR(200M Hz,DMSO-d_6, δ/ ppm): 1.65 (3H , s, Ar - CH_3), 8.5 (1H, s, NH) , 8.7- 7.5 (9H, m, Aromatic protons) , , 6.4(1H, m, Ar-CH), 2. 26 (2H , dd, - CH = CH -).

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

To a solution of 1 – 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 un reacted mercapto acetic acid. The solid product thus separated was filtered and washed with water. Recrystallized from ethanol (95 %). Compound(4a): Yield: 73.23% ; m.p.: 73^o C; m.w.: 396.46 ; Anal. Calcd. For $C_{21}H_{20}N_2O_4S$;C 63.62; H 5.04; N 7.06; S, 8.09. Found : C 63.59; H 5.01; N , 7.01 ; S, 8.02. TLC solvent

Tele:

E-mail addresses: kirankartik@yahoo.com

system: Acetone: Benzene (4:6). IR (KBr, cm^{-1}) : 1639 , 1655 (C=O stretching of acyclic and cyclic carbonyl respectively), 690 (C-S-C- linkage stretching of thiazolidine ring), 814 (para substituted Phenyl ring), 1150 (-C-O str.); 3209 (N-H stretching) .

Scheme 1

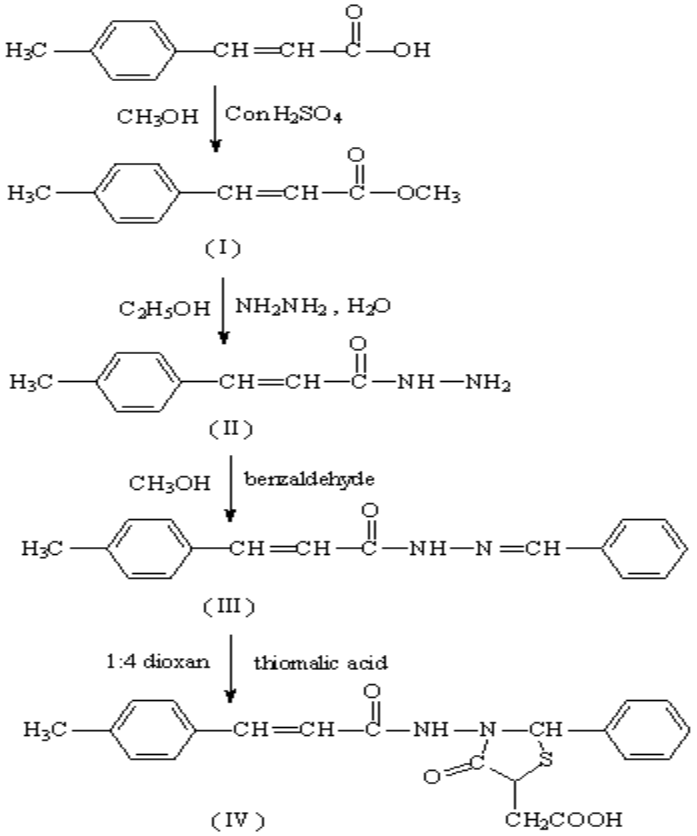

Table I : Physical Constants of the compounds 4a-o

Comp. No.	AR	MOLECULAR FORMULA	M.W.	M.P. °C	% OF YIELD	% OF CARBON		% OF HYDROGEN		% OF NITROGEN	
						Cal.	*FFound*	Cal.	*FFound*	Cal.	*FFound*
4a	C_6H_5-	$C_{21}H_{20}N_2O_4S$	396.46	73	75	63.62	63.59	5.04	5.01	7.06	7.01
4b	4(OH)C_6H_4-	$C_{21}H_{20}N_2O_5S$	412.46	104	77	61.15	61.11	4.85	4.81	6.79	6.75
4c	2(OH)C_6H_4-	$C_{21}H_{20}N_2O_5S$	412.46	154	67	61.15	61.12	4.85	4.81	6.79	6.76
4d	3(OH)C_6H_4-	$C_{21}H_{20}N_2O_5S$	412.46	91	59	61.15	61.10	4.85	4.82	6.79	6.77
4e	2,4$(OH)_2C_6H_3$-	$C_{21}H_{20}N_2O_6S$	428.45	122	68	58.87	58.83	4.67	4.64	6.54	6.51
4f	4$(OCH_3)C_6H_4$-	$C_{22}H_{22}N_2O_5S$	426.48	89	66	61.95	61.91	5.16	5.13	6.57	6.54
4g	2$(OCH_3)C_6H_4$-	$C_{22}H_{22}N_2O_5S$	426.48	82	78	61.95	61.91	5.16	5.12	6.57	6.54
4h	3,4$(OCH_3)_2C_6H_3$-	$C_{23}H_{24}N_2O_6S$	456.51	132	80	60.51	60.49	5.26	5.22	6.13	6.10
4i	3,4,5$(OCH_3)_3C_6H_2$-	$C_{24}H_{26}N_2O_7S$	486.53	114	79	59.24	59.20	5.34	5.30	5.76	5.72
4j	4(OH),3$(OCH_3)C_6H_3$-	$C_{22}H_{22}N_2O_6S$	442.48	104	69	59.71	59.68	4.97	4.93	6.33	6.30
4k	4$(CH_3)C_6H_4$-	$C_{22}H_{22}N_2O_4S$	410.48	62	75	64.37	64.33	5.36	5.33	6.82	6.79
4l	4(Cl)C_6H_4-	$C_{21}H_{19}N_2O_4SCl$	430.90	68	73	58.53	58.50	4.41	4.39	6.50	6.47
4m	4$(NO_2)C_6H_4$-	$C_{21}H_{19}N_3O_6S$	441.45	110	77	57.13	57.10	4.30	4.28	9.51	9.49
4n	3,4,-O-(CH_2)-O-C_6H_3-	$C_{22}H_{20}N_2O_6S$	440.47	59	67	59.99	59.96	4.54	4.50	6.36	6.33
4o	C_6H_5-CH=CH-	$C_{23}H_{22}N_2O_4S$	422.49	87	80	65.38	65.34	5.21	5.19	6.63	6.60

Table II : Antimicrobial activity of the compounds 4a-o.

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

^{1}H NMR(200M Hz,DMSO-d_6, δ/ ppm): 1.68 (3H , s, Ar - CH_3), 8.7 (1H, s, NH) , 8.5 7.3 (9H, m, Aromatic protons) , 3.9 (2H , s, - CH_2 , Thiazolidine ring) , 6.3(1H, m, Ar-CH), 2. 2 (2H , dd, - CH = CH -).

Similarly other 4 - oxo - thiazolidines were prepared. The physical data are recorded in Table I(Page-9).

Results and Discussion

All the compounds gave satisfactory elemental analysis and spectral results are in well agreement with their theoretical values. For antibacterial activity compounds 4a - o were screened for their *in vitro* antibacterial activity using cup-plate agar diffusion method[14] 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 is used for comparison purpose. By visulizing the antimicrobial data, these compounds have noteworthy activity as observed in Table-II. Interestingly some of these have remarkable zone of inhibition as compared to solvent. Compounds no. 4f, 4g and 4i has good activity against *E. coli* and compounds 4n and 4o have also possess very good activity against *E. coli*. Compounds 4e, 4f, 4i, 4j, 4k, and 4m possess very good activity against *S.aureus*. Where as compounds 4b, 4c, 4g, 4h,4 and 4o exhibit excellent activity against *S.aureus* . Antimicrobial results of all compounds are given in Table-II(Page-10).

Conclusion

The introduction of a methyl group or a carboxy methyl group at position no. 4 or 5 –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.

Acknowledgements

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

1. R. P. Pawar, N. M. Andurkar and Y. B. Vibhute, *J. Ind. Chem. Soc*., 76 (1999) 271.
2. S. N. Thore et al. *Asian . J. Chem*. 8 (1996) 2.
3. L. Jaish and S. K. Srivastava, *J. Sci. Ind. Res*., 60 (2001) 33.
4. K.Babaoglu, M. A. Page And R. E. Lee, *Bioorg. Med. Chem*., 13(2003) 3227.
5. A. Kumar, S.Verma et al. *Orient J. Chem*., 22(2) (2006) 259.
6. A.Solankee, G. Patel and S. Solankee, *Orient J. Chem*, 25(1) (2008) 245.
7. R. M. Abdel Rehman, *Boll Chim. Fama*., 140(6) (2001) 401.
8. M. H. Sinh and F. Y. Ke, *Bioorg. Med. Chem*., 12 (2004) 4633.
9. A. Kumar, S.Verma et al. *Orient J. Chem*., 22(2) (2006) 259.
10. D. Modi, S. S. Sabia and C. V. Deliwati, *J. Med. Chem*. 3 (1970) 935.
11. N. Raman, S. Thalamuthu and S. Benerjee, *J. Chill Chem. Soc*., 53 (2008) 1450.
12. C. L. Patel and H. Parekh , *J. Indian Chem. Soc*., 65 (1988) 282.
13. A. R . Surrey, *J . Am . Chem . Soc* . , 70 (1948) 4262.
14. A. L. Barry The Antimicrobial Susceptibility test; Principle and practice, edited by Illus. Lea and Febiger, (Philadelphia Pel USA) 1977, p. 180 , Bio. Abstr., 64 (1977) 25183 .