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Potential Antibacterial Agents: 4-Thiazolidinone Derivatives

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The cycloaddition reaction of thioglycolic acid with Schiff bases gives the corresponding 4-thiazolidinones. 4-Thiazolidinone derivatives on condensation with 3,4,5-trimethoxy benzaldehyde resulted in benzylidene derivatives of 4-thiazolidinones. The synthesised compounds were characterised on the basis of elemental analysis and spectral studies and tested *in vitro* against *E. coli*, *S. aureus*, *S. thyphi* and *E. aerugenes* for their antibacterial activity.

INTRODUCTION

4-Thiazolidinone derivatives have been found to possess wide variety of physiological properties *viz.* anticonvulsant[1], sciatic nerve block[2], local anaesthetic[3], sedative[4] and choleretic[5]. Several methods for the synthesis of 4-thiazolidinones have been reported[6–9]. The chemistry of the 4-thiazolidinone ring system was reviewed in detail[10]. This paper decribes the synthesis of arylidene derivatives of 4-thiazolidinones, the characterisation of the compounds on the basis of spectral studies and antibacterial activity of the synthesised compounds.

The cycloaddition reaction of thioglycolic acid with Schiff bases, synthesised by condensing benzaldehyde with substituted anilines[11, 12] gives the corresponding 2,3-disubstituted-4-thiazolidinones[13, 14]. 2,3-Disubstituted-4-thiazolidinone derivatives on condensation with 3,4,5-trimethoxy benzaldehyde gave the corresponding benzylidene derivatives of 4-thiazolidinones, which were purified by recrystallisation from alcohol. The products have been identified on the basis of elemental analysis and spectral studies.

All melting points are uncorrected. The IR spectra were recorded on Perkin-Elmer 237 spectrophotometer. Elemental analysis was performed on Carlo Erba-1108 analyser. Purity of the compounds in addition to elemental analysis was checked by TLC.

EXPERIMENTAL

The general procedure for the preparation of 2-phenyl-3-substituted phenyl-4-thiazolidinone(I) is as follows:

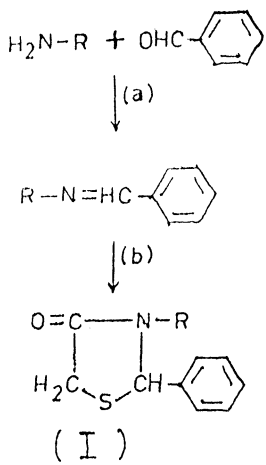
Thioglycolic acid (0.01 M) added to solution of Schiff base (0.01 M) in benzene (20 mL) was refluxed for 9 h. Excess solvent and thioglycolic acid was

removed under vacuum. The residue was washed thoroughly with $NaHCO_3$ solution and water, dried and the product crystallised from ethanol (95%).

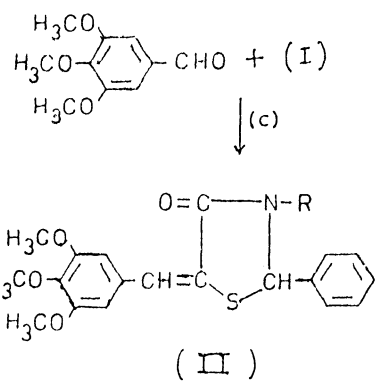
The general procedure for the preparation of benzylidene derivatives of 2,3-disubstituted 4-thiazolidinones(II) is as follows.

To a solution of 3,4,5-trimethoxybenzaldehyde (0.01 M) and 2-phenyl-3(2-ethoxyphenyl)-4-thiazolidinone (0.01 M) in glacial acetic acid (25 mL) was added anhydrous sodium acetate (0.015 M) and the reaction mixture was refluxed for 4–5 h with occasional shaking. It was then cooled and poured into crushed ice. The solid separated out was filtered, washed successively with water and recrystalised from alcohol.

Yield: *ca.* 65%, Compound (4), m.p. 110°C. IR (KBr): 1700 cm^{-1} ν(C=O), 1250 cm^{-1} ν_{asym}(C—O—C), 1020 cm^{-1} ν_{sym}(C—O—C), 1100 cm^{-1} ν(C—N), 690 cm^{-1} ν(C—S—C).



(I)



(II)

(a) = C_6H_6; (b) = $HSCH_2COOH$, C_6H_6; (c) = glacial CH_3COOH, Anhy. CH_3COONa

RESULTS AND DISCUSSION

The physical and analytical data of compounds are presented in Table-1.

TABLE-1
PHYSICAL AND ANALYTICAL DATA OF COMPOUNDS

Compd. No.	R	Molecular Formula	m.p. (°C)	Yield (%)	N (%) Found (Calcd.)
1.	4-Bromophenyl	$C_{25}H_{22}O_4NSBr$	90	58	2.76 (2.73)
2.	2-Methoxyphenyl	$C_{26}H_{25}O_5NS$	Limpid	67	3.05 (3.02)
3.	4-Methoxyphenyl	$C_{26}H_{25}O_5NS$	88	60	2.99 (3.02)
4.	2-Ethoxyphenyl	$C_{27}H_{27}O_5NS$	110	65	2.97 (2.93)
5.	4-Ethoxyphenyl	$C_{27}H_{27}O_5NS$	Limpid	45	2.91 (2.93)
6.	3-Acetamidophenyl	$C_{27}H_{26}O_5N_2S$	79	59	5.75 (5.71)
7.	4-Acetamidophenyl	$C_{27}H_{26}O_5N_2S$	Limpid	70	5.69 (5.71)
8.	2-Methoxy-5-acetamidophenyl	$C_{28}H_{28}O_6N_2S$	70	52	5.35 (5.38)
9.	3-propionamidophenyl	$C_{28}H_{28}O_5N_2S$	Limpid	64	5.58 (5.55)
10.	1-Naphthyl	$C_{23}H_{25}O_4NS$	75	56	3.39 (3.40)
11.	Benzyl	$C_{26}H_{25}O_4NS$	96	58	3.16 (3.13)

The antibacterial activity of the synthesised compound was screened against both gram +ve and gram –ve bacteria employing the disk diffusion technique[15]. The microorganisms employed were *S. aureus*, *E. coli*, *S. typhi* and *E. aerugenes*. Ampicillin and penicillin-G were used as the standard drugs.

The zones of inhibition in mm for compounds tested for antibacterial activity are given in Table-2.

Compound 5 has shown maximum activity towards *S. aureus*, *E. coli*, *S. typhi* and *E. aerugenes*. Compound 8 possesses good activity against *S. aureus* and *S. Typhi*, but it is inactive against *E. coli* and *E. aerugenes*. Compound are given 2, 3, 4, 6, 7 and 9 have shown good activity against *S. aureus* whereas compounds 1,10 and 11 are inactive against gram-positive bacteria, *i.e.*, against *S. aureus*. The rest of the compounds except compound 5 are inactive against *E. coli*, *S. typhi* and *E. aerugenes*.

TABLE-2
ANTIMICROBIAL ACTIVITY OF COMPOUNDS

Compd. No.	Diameter of zone of inhibition (in mm)			
	S. aureus	*E. coli*	*S. typhi*	*C. aerugenes*
1.	—	—	—	—
2.	7	—	—	—
3.	8	—	—	—
4.	7	—	—	—
5.	7	9	7	9
6.	7	—	—	—
7.	8	—	—	—
8.	10	—	10	—
9.	6	—	—	—
10.	—	—	—	—
11.	—	—	—	—

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