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Synthesis and Antimicrobial Activity of 4-Thiazolidinones

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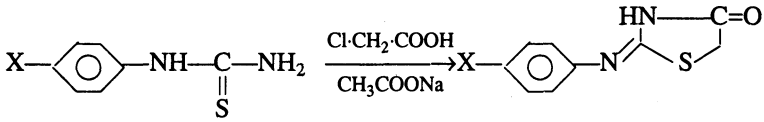
Twelve new 2-substituted 4-thiazolidinones have been synthesised and evaluated for antimicrobial activity. Some of them were found to be effective.

INTRODUCTION

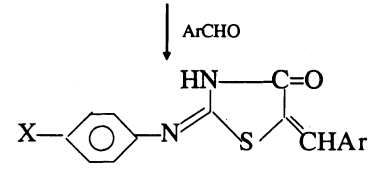
4-Thiazolidinones, the heterocyclic nucleus of the present work, is a versatile pharmacophore, which exhibits a wide variety of biological activities. A few of them which are worthy of mention are antibacterial[1], antiviral[2], antitumour[3] and CNS depressant.[4]

Chemistry[5, 6]

The reaction followed the given path:



I II



Ia X = —OH
Ib X = —NO_2

III and IV

EXPERIMENTAL

The structures of the compounds were established on the basis of nitrogen analysis report, done on Carlo Erba 1108 and IR spectral data, using Perkin-Elmer 1800. The melting points were determined by using open capillaries and are uncorrected.

Synthesis of Phenyl Thiourea(I)

Aromatic amine (0.1 M) was dissolved in minimum amount of dil. HCl in a

round-bottomed flask. Ammonium thiocyanate (0.2 M) was then added and the mixture refluxed for 5–6 h. After cooling the product separated out as crystals, which were separated and washed several times with cold distilled water and dried. Recrystallisation was effected from rectified spirit.

Ia X = —OH, m.p. 215–218°C, yield 75%

Ib X = —NO_2, m.p. 204–206°C, yield 65%

Synthesis of 2-(substituted)phenylimino 4-thiazolidinone(II)

A mixture of I (0.1 M) and fused sodium acetate (0.2 M) was taken in absolute alcohol (300 mL) and refluxed for 8 h. The bulk of the solvent was reduced to about one-third by distilling off the solvent under reduced pressure. Ice-cold water was then added to the content. The precipitate so obtained was filtered and washed with distilled water. Rectified spirit was used for recrystallisation.

IIa X = —OH, m.p. 230–232°C, yield 86%

IIb X = —NO_2, m.p. 225°C (dec), yield 85%

Synthesis of the compounds III and IV

A mixture of II (0.01 M), required aldehyde (0.01 M) and anhydrous sodium acetate (0.01 M) was made in glacial acetic acid and refluxed for 5–7 h. After cooling the solution was poured on crushed ice to precipitate the product. Warm water was used to wash the precipitate. The product was recrystallised from rectified spirit.

The synthesised compounds were characterised by adsorption: 3350–3300 cm^{-1} ν(—N—H str.), 1680–1670 cm^{-1} ν(C=O str), 1510–1500 cm^{-1} ν(C=N str.) and 690 cm^{-1} ν(C—S—C str. of the ring). The physical constants of the title compounds are given in Table-1.

Evaluation of Antimicrobial Activity

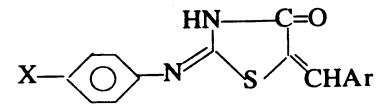
All the synthesised compounds were subjected to antimicrobial activity on agar plates using cup-plate[7] technique. The bacterial cultures used were *Staphylococcus aureus*, *Bacillus subtilis* (gram +ve); *Escherichia coli* and *Salmonella typhi* (gram –ve). The standard drug, used for the present study was Norfloxacin.

For antifungal activity study *Aspergillus flavus*, *Aspergillus niger* and *Alternaria alternata* cultures were chosen. The standard drug used was Clotrimazole. The concentration of the compounds synthesized and the standard drugs were taken as 100 μg/mL for ease of the compound. All the drugs taken were dissolved in DMF. In order to account for the effect due to DMF a blank was also performed.

RESULTS AND DISCUSSION

A perusal of the Table-1 shows that compared to the standard drug, five compounds namely IIIc, IIIe, IVb, IVe and IVf are effective against *E. coli*. So far as *S. aureus* is concerned only one compound *i.e.* IVf is effective. Against *B. subtilis* one compound *i.e.* IIId is effective whereas IIId and IVf are effective against *S. typhi*.

TABLE-1
ANTIMICROBIAL ACTIVITY OF 4-THIAZOLIDINONES



Comp. No.	Ar (m.f.)	X	m.p. (°C)	N% found (calcd.)	Antibacterial activity Zone of inhibition (mm)				Antifungal activity Zone of inhibition (mm)		
					E. coli	*S. aureus*	*B. subtilis*	*S. typhi*	*A. niger*	*A. flavus*	*Altarnaria alternata*
III_a	Phenyl $C_{16}H_{12}N_2O_2S$	—OH	256	9.40 (9.45)	16	16	20	16	16	16	35
III_b	*o*-Hydroxy-phenyl $C_{16}H_{12}N_2O_3S$	—OH	265 (dec.)	8.85 (8.97)	25	25	20	16	20	16	30
III_c	*p*-Hydroxy phenyl $C_{16}H_{12}N_2O_3S$	—OH	266 (dec.)	8.85 (8.97)	30	20	20	25	16	16	25
III_d	*p*-Methyl phenyl $C_{17}H_{14}N_2O_2S$	—OH	268 (dec.)	9.00 (9.03)	16	20	30	30	20	16	20
III_e	Cinnamyl $C_{18}H_{14}N_2O_2S$	—OH	260 (dec.)	9.01 (9.06)	30	16	20	20	16	20	35
III_f	*p*-Dimethylamino phenyl $C_{18}H_{17}N_3O_2S$	—OH	270 (dec.)	12.02 (12.38)	20	25	20	16	16	25	25
IV_a	Phenyl $C_{16}H_{11}N_3O_3S$	$—NO_2$	258–260	12.90 (12.92)	25	16	20	16	16	16	30
IV_b	*o*-Hydroxy-phenyl $C_{16}H_{11}N_3O_4S$	$—NO_2$	265–268 (dec.)	12.20 (12.31)	30	16	25	20	25	20	35
IV_c	*p*-Hydroxy phenyl $C_6H_{11}N_3O_4S$	$—NO_2$	270–274 (dec.)	12.08 (12.31)	25	20	20	16	25	16	30
IV_d	*p*-Methyl phenyl $C_{17}H_{13}N_3O_3S$	$—NO_2$	275 (dec.)	12.19 (12.38)	20	25	25	20	20	25	25
IV_e	Cinnamyl $C_{18}H_{13}N_3O_3S$	$—NO_2$	266 (dec.)	12.02 (12.42)	30	20	20	16	16	16	25
IV_f	*p*-Dimethylamino phenyl $C_{18}H_{16}N_4O_3S$	$—NO_2$	255	15.17 (15.21)	35	30	25	30	16	16	30
	Standard	—	—	—	30	35	30	50	20	30	30

% yield varied from 64 to 84.

Similarly, in the antifungal activity study it is observed that only IIIa, b, e and IVa, b, c and f are effective against *A. niger*. However, these compounds are ineffective against *A. flavus*.

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