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NOTES

Potential Antitubercular Agents, Part II: 4-Thiazolidinone Derivatives

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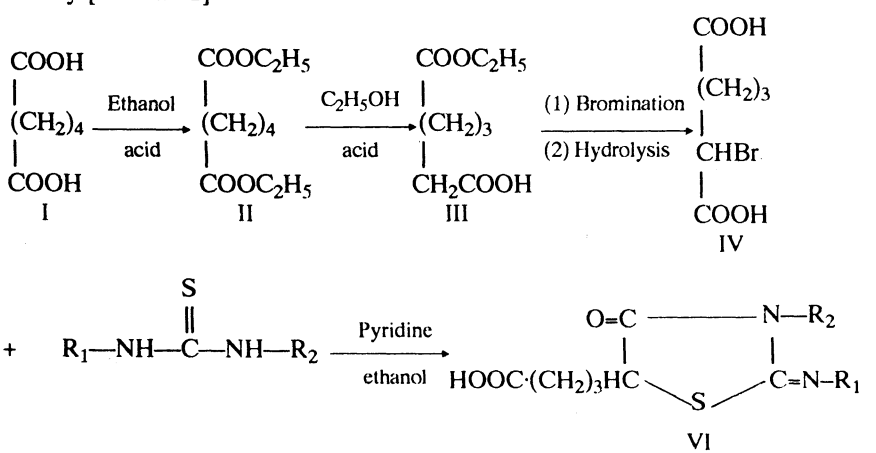
4-Thiazolidinones have been synthesised by the condensation of thiourea with 2-bromo-adipic acid using ethanol in presence of pyridine as catalyst. The compounds have been screened for antitubercular activity using $H_{37}Rv$ strain of bacteria. Their spectral studies are also included.

In continuation of our earlier work[1] on 2-phenyl-imino-5-(ω-carboxy propyl)-4-thiazolidinones and their antitubercular activity, we are reporting the synthesis of some new 2-phenyl-imino-3-phenyl-5-(ω-carboxy propyl)-4-thiazolidinones and their antitubercular activity.

For the preparation of 2-phenyl-imino-3-phenyl-5-(ω-carboxy propyl)-4-thiazolidinones [VI], the substituted thioureas [V] have been prepared. The thioureas were then condensed with 2-bromo-adipic acid in ethanol in presence of pyridine as catalyst. When tested, these compounds showed antitubercular activity [Scheme 1].



Scheme I

Melting points were taken in open capillaries in an electric melting point apparatus and are uncorrected. Infra-red spectra of the compounds were recorded on Perkin Elmer 237 grating spectrophotometer.

Preparation of diester of adipic acid[2] (II), monoester of adipic acid[3] (III), 2-bromo-adipic acid[4] (IV), thiourea (V)

Symmetrical 1,3-diaryl -2-thoureas are prepared by heating substituted aryl isothiocyanates and appropriately substituted aryl amine in absolute alcohol[5].

Preparation of 2-phenylimino-3-phenyl-5-(ω-carboxy propyl] -4-thiazolidinones (VI)[6]

2-Bromoadipic acid (0.021 mole), appropriate 1,3-disubstituted thiourea (0.02 mole), pyridine (AR grade, 0.025 mole) and 30 ml absolute ethyl alcohol were refluxed on a water bath for 4 hrs. The excess of solvent was evaporated. The residue was dissolved in sodium bicarbonate solution (50 ml) and filtered. The solution was adjusted to pH 3.0 by hydrochloric acid (AR grade). 4-Thiazolidinones thus obtained were either in liquid or semisolid state but they solidified on standing for 2 hrs to 2–3 days. The products were recrystallised from ethanol (Table 1).

TABLE 1
PHYSICAL DATA OF 2-PHENYL-IMINO-3-PHENYL-5-[ω-CARBOXY PROPYL] -4-THIAZOLIDINONES [VI]

S. No.	R_1	R_2	M. pt. °C	Molecular Formula	Analysis %: Found (Calc)	
					N	S
1.	$-C_6H_5$	$-C_6H_5$	202	$C_{19}H_{18}O_3N_2S$	7.85 (7.90)	9.00 (9.04)
2.	$-o-C_6H_4CH_3$	$-o-C_6H_4CH_3$	138	$C_{21}H_{22}O_3N_2S$	7.36 (7.32)	8.32 (8.38)
3.	$-m-C_6H_4CH_3$	$-m-C_6H_4CH_3$	112	$C_{21}H_{22}O_3N_2S$	7.25 (7.32)	8.29 (8.38)
4.	$-p-C_6H_4CH_3$	$-p-C_6H_4CH_3$	90	$C_{21}H_{22}O_3N_2S$	7.29 (7.32)	8.36 (8.38)
5.	$-m-C_6H_4Cl$	$-m-C_6H_4Cl$	158	$C_{19}H_{16}O_3N_2SCl_2$	6.58 (6.61)	7.41 (7.53)
6.	$-p-C_6H_4Cl$	$-p-C_6H_4Cl$	160	$C_{19}H_{16}O_3N_2SCl_2$	6.50 (6.61)	7.41 (7.53)
7.	$-o-C_6H_4OCH_3$	$-o-C_6H_4OCH_3$	117	$C_{21}H_{22}O_5N_2S$	6.69 (6.75)	7.69 (7.73)
8.	$-m-C_6H_4OCH_3$	$-m-C_6H_4OCH_3$	105	$C_{21}H_{22}O_5N_2S$	6.65 (6.75)	7.80 (7.73)
9.	$-p-C_6H_4OCH_3$	$-p-C_6H_4OCH_3$		$C_{21}H_{22}O_5N_2S$	— (6.75)	— (7.73)
10.	$-p-C_6H_4OC_2H_5$	$-p-C_6H_4OC_2H_5$	116	$C_{21}H_{26}O_5N_2S$	6.25 (6.33)	7.19 (7.25)

Screening for antitubercular activity

Compounds 2, 3, 4, 6, 7 and 10 were screened for their antitubercular activity

against $H_{37}Rv$ strain of bacteria. Out of six compounds, compounds 2, 6 and 7 are inactive, where as compounds 3, 4 and 10 showed activity at 100 mcg/ml. Isonicotinic acidhydrazide and streptomycin were used as standard drugs.

The IR spectra of the compound 1 exhibit characteristic bands at 1590 cm^{-1} (–C=C– stretching of aromatic ring), 1480 cm^{-1} (thioureid band) and 1700 cm^{-1} (–C=O of the ring).

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