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NOTES

Synthesis and Antitubercular Activity of 2, 3-Disubstituted -5-[ω-Carboxyheptyl]-4-Thiazolidinones

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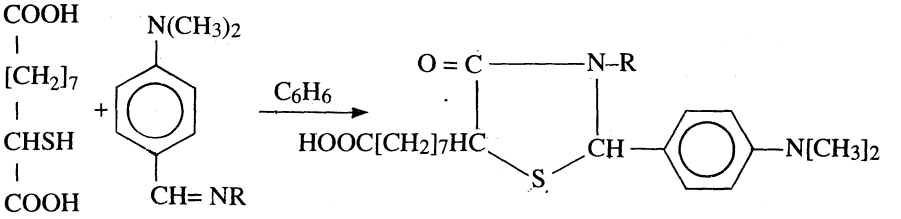
2, 3-Disubstituted-4-thiazolidinones have been synthesised by refluxing Schiff bases with 2-mercaptosebacic acid using benzene as solvent. The compounds have been screened for their antitubercular activity against $H_{37}R_v$ strain of Mycobacterium tuberculosis.

In continuation of our earlier work on 4-thiazolidinone[1], we herein report the synthesis and antitubercular activity of 2, 3-disubstituted 5-(ω-carboxyheptyl)-4-thiazolidinones. For the preparation of 2, 3-disubstituted –5-(ω-carboxyheptyl)-4-thiazolidinones, Schiff's bases were prepared. Schiff's bases were then refluxed with 2-mercaptosebacic acid in dry benzene (scheme–1). 4-Thiazolidinones thus obtained were screened for antitubercular activity.



Scheme–I

Preparation of monoester of sebacic acid and diester of sebacic acid was carried out by reported method[2, 3]. 2-Bromosebacic was prepared by reported method[4].

Preparation of Schiff bases: A mixture of aryl aldehyde (0.01 mole) and arylamine (0.01 mole) and dry benzene (100 ml) was refluxed for 4 h using Dean-Stark water separator. After evaporation of benzene, Schiff base was obtained.

Preparation of 2-mercaptosebacic acid

A mixture of 2-bromosebacic acid (0.2 mole), freshly distilled thiolacetic acid and dry ethyl acetate (20 ml) was refluxed for 2 h and then concentrated under reduced pressure. Crude acetyl derivative thus obtained was hydrolysed with HCl (30 ml) to give the product which was purified by benzene treatment, (70%).

Preparation of 2-phenyl-3-substituted phenyl –5(ω-carboxyheptyl)-4-thiazoli-

dinones (I): A mixture of the Schiff base (0.01 mole), 2-mercaptosebacic acid (0.01 mole) and dry benzene (100 ml) was refluxed for 3 h using Dean-Stark water separator. After the theoretical quantity of water was separated, the mixture was poured into evaporating dish. The residue after removal of benzene was washed in saturated solution of sodium bicarbonate and filtered. The filterate was acidified with hydrochloric acid at pH 3.0. the resulting solid was washed with water, dried and crystallised from acetone.

TABLE 1
ANALYTICAL AND SPECTRAL DATA OF 2-PHENYL-3-SUBSTITUTED PHENYL -5-(ω-CARBOXYHEPTYL)-4-THIAZOLIDINONES : (I): *

Compd. No.	R	M.p. °C	Yield %	Molecular formulae	IR bands (cm^{-1})
1.	$-C_6H_5$	119	70	$C_{25}H_{32}O_3N_2S$	2680[OH], 1690[C = O], 1305[C–N]
2.	$-CH_2C_6H_5$	127	72	$C_{26}H_{34}O_3N_2S$	2680[OH], 1700[C = O], 1310[C–N]
3.	$-o-C_6H_4CH_3$	126	67	$C_{26}H_{34}O_3N_2S$	2680[OH], 1680[C = O], 1300[C–N]
4.	$-m-C_6H_4CH_3$	123	75	$C_{26}H_{34}O_3N_2S$	2640[OH], 1710[C = O], 1350[C–N]
5.	$-p-C_6H_4CH_3$	134	70	$C_{26}H_{34}O_3N_2S$	2650[OH], 1705[C = O], 1340[C–N]
6.	$-o-C_6H_4Cl$	123.5	68	$C_{25}H_{31}O_3N_2SCl$	2650[OH], 1700[C = O], 1330[C–N]
7.	$-m-C_6H_4Cl$	121.2	65	$C_{25}H_{31}O_3N_2SCl$	2670[OH], 1720[C = O], 1330[C–N]
8.	$-p-C_6H_4Cl$	125	78	$C_{25}H_{31}O_3N_2SCl$	2680[OH], 1710[C = O], 1320[C–N]
9.	$-o-C_6H_4OCH_3$	120	80	$C_{26}H_{34}O_4N_2S$	2680[OH], 1700[C = O], 1315[CN]
10.	$-m-C_6H_4OCH_3$	124	80	$C_{26}H_{34}O_4N_2S$	2670[OH], 1690[C = O], 1300[CN]
11.	$-p-C_6H_4OCH_3$	121	69	$C_{26}H_{34}O_4N_2S$	2660[OH], 1690[C = O], 1360[C–N]
12.	$-p-C_6H_4OC_2H_5$	129	74	$C_{27}H_{36}O_4N_2S$	2650[OH], 1700[C = O], 1360[C–N]
13.	$-p-C_6H_4Br$	118	77	$C_{25}H_{31}O_3N_2SBr$	2670[OH], 1710[C = O], 1330[C–N]
14.	$-1-C_{10}H_7$	126	72	$C_{29}H_{34}O_3N_2S$	2670[OH], 1710[C = O], 1310[C–N]
15.	$-2-C_{10}H_7$	130	70	$C_{29}H_{34}O_3N_2S$	2680[OH], 1720[C = O], 1310[C–N]

*All the compounds gave satisfactory C, H, N and S analysis.

Screening for antitubercular activity

Compounds 2, 7, 9, 11, 12 and 15 were screened for antitubercular activity against $H_{37}R_v$ strain of Mycobacterium tuberculosis in Lowenstein-Jensen egg media at 3 and 30 μg ml^{-1}. The retardation of growth was studied upto 6 weeks at 37°C. The antitubercular activity was compared with standard isonicotinic acid hydrozide (INH). Compound 12, where R = $-p-C_6H_4OC_2H_5$ showed activity at 30 μg ml^{-1} whereas the others revealed low inhibitory effect.

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