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NOTE

Synthesis and Antitubercular Activity of 4-Thiazolidinones

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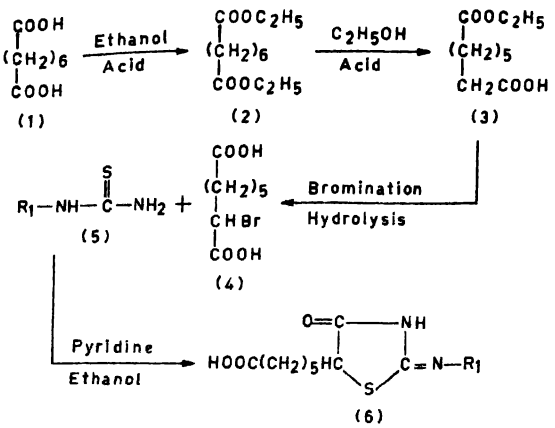
Many 4-thiazolidinones possess various pharmacological activities[1]. It has been known that the system –NHCSNH– contributes to tuberculostatic activity[2]. An interesting structural variation is the cyclisation of thiocarbenilides to thiazolines and thiazolidinones which are likely to show such activity[3,4]. Litvinchuk[5] reported antitubercular activity of a few derivatives of 2-imino-4-thiazolidinones. Kapustyak[6] studied structure-tuberculostatic activity relationship of some 4-thiazolidinones.

In view of the above facts, we have synthesised some 2-phenylimino-4-thiazolidinones (Table 1) and were tested for the antitubercular activity using $H_{37}R_v$ strain of bacteria.



Experimental

M.ps. are uncorrected. Ir spectra (KBr) were recorded on a Perkin-Elmer 237 spectrophotometer. Preparation of monoester and diester of suberic acid were carried out by reported method.

TABLE 1–PHYSICAL AND ANTITUBERCULAR ACTIVITY OF COMPOUNDS 6*

Compd. no.	R_1	M.p. °C	MIC**
6a	H	194	Inactive
b	C_6H_5	99	Inactive
c	*o*-C_6H_4Cl	122	200
d	*m*-C_6H_4Cl	110	100
e	*p*-C_6H_4Cl	152	100
f	*o*-$C_6H_4CH_3$	145	Inactive
g	*m*-$C_6H_4CH_3$	142	200
h	*p*-$C_6H_4CH_3$	137	100
i	*o*-$C_6H_4OCH_3$	95	–
j	*m*-$C_6H_4OCH_3$	112	100
k	*p*-$C_6H_4OCH_3$	135	–
l	*p*-$C_6H_4OC_2H_5$	133	40
m	*p*-$C_6H_4OC_3H_{7n}$	152	5
n	*p*-$C_6H_4OC_4H_{9n}$	140	–
o	2-$C_{10}H_7$	216	5

*All compounds gave satisfactory C, H, N and S analyses.
**MIC for isonicotinic acid hydrazide = 0.04 μg/ml and streptomycin = 1.00 μg/ml.

2-Bromosuberic acid[7] (**4**) : To a mixture of monoester of suberic acid (**3**; 0.3 mol) and dry red phosphorous (10 g), bromine (50 ml) was added dropwise and refluxed for 1 h. It was then hydrolysed to get the corresponding bromo derivative which was purified by alcohol, yield 70%.

The thiourea[8] (**5**) : Substitued phenyl thioureas were prepared by refluxing the hydrochlorides of substituted anilines with ammonium thiocyanate or potassium thiocyanate in absolute alcohol.

2-Phenylimino-5-(ω-carboxypentyl)-4-thiazolidinones (**6**) : A mixture of 2-bromosuberic acid (**4**; 0.021 mol) and the substituted thiourea (**5**; 0.02 mol) in absolute ethanol (30 ml) in presence of

sodium acetate (0.025 mol) was refluxed for 4 h. The solvent was then evaporated and the resulting solid was dissolved in sodium bicarbonate solution and precipitated at a definite pH. The products were recrystallised either from ethanol or benzene-petroleum ether (b.p. 60–80) mixture. Ir spectra of compounds showed bands at 1 560 (C=C stretch of aromatic ring), 1 700 (C=O of acid), 1 460–1 480 (thioureid band) and 1 630 cm^{1} (C=N).

Antitubercular activity : The activity of the compounds (Table 1) enhanced with lengthening of the side-chain in position-5, and in a few cases the activity was doubled. With 2-(chlorophenyl)imino derivatives the activity was retained. But in case of 2-(*m*/*p*-methylphenyl)imino compounds, some activity was observed. The activity of 2-(*p*-n-propioxyphenyl)imino and 2-(2-naphthyl)imino compounds, the activity was maximum amongst all the compounds tested.

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References

1. S. N. GOLUBOVA, *Ukr. Biokhim. Zh.*, 1953, **25**, 325; G SATZINGER, US Pat. 3 072 670/1963; K. ENRICO, *Gazz. Chim. Ital.*, 1949, **79**, 621; M. RAI, B. S. DHIR and P S. KALSI, *J. Indian Chem. Soc.*, 1986. **63**, 705; M P DAVE, J. M. PATEL, N. A. LANGLIA and K. A. THAKER, *J. Indian Chem. Soc.*, 1986, **63**, 320, H. D. TROUTMANN and L. M. LONG, *J. Am. Chem. Soc.*, 1948, **70**, 3436.
2. E. FROLICH, A. FRUACHAN, F. K. KRICHNER, E. J ALEXANDER and S. ARCHER, *J. Am. Chem. Soc.*, 1954, **76**, 3099.
3. P. C. EISMAN, E. A. KANOPKA and R. L. MAYER, *J. Am. Rev. Tuberc.*, 1954, **70**, 121.
4. P. C. EISMAN. E. A. KANOPKA, T. GISI, R. H. MIZZONI and R. L. MAYER, *Am Rev. Tuberc.*, 1958, **77**, 703 (*Chem. Abstr.*, 1959, **58**, 5494).
5. M. D. LITVINCHUK, *Farmacol.-Toksikol.*, 1963, **26**, 725 (*Chem. Abstr.*, 1964, **60**, 13761).
6. S. M. KAPUSTYAK. *Zb. Nauk. Prats. L'vivs'k Med Inst.*, 1963, **24**, 78 (*Chem. Abstr.*, 1965, **63**, 1077).
7. B. TEICHMANN, *Z. Chem.*, 1965, **5**, 18.
8. H. KRALL and R. D. GUPTA, *J. Indian Chem. Soc.*, 1935, **12**, 629.