Asian Journal of Chemistry Vol. 10, No. 4 (1998), 1009–1010

NOTE

Study of Some Anti-tubercular Agents

ASHVIN N. MODI*, BHADRESH NAIK†, PRATIBHA DESAI‡,
C.M. DESAI† and DINESH PATEL†
Junior Laboratory Technician
G.N.F.C. Ltd., Bharuch-392 015, India

The anti-TB activity of some benzylidene derivatives of sulfathiazole and sulfa-phenazole against $H_{37}R_v$ is inhibitory at 5 μ/mL, while that for pyridine derivatives is nil.

Tibione is a thiosemicarbazone of *p*-acetamido benzaldehyde having both —C=N and NHCSNH grouping contributing to antimicrobial activity. Tibione, an anti-TB drug, is also a benzylidene derivative. In our earlier work[1], it has been observed that groups such as $—OCH_3$, —Cl, $—OC_2H_5$ contribute to anti-TB activity of substances and, further, sulfathiazole and sulfaphenazole quinolinyl derivatives have proved effective against $H_{37}R_v$ at 5 μg/mL.

Hence it has been planned to prepare benzylidene derivatives of sulfathiazole and sulfa-phenazole by condensing them with 2-chloro-, 4 methoxy and 2,4,5-trimethoxy benzaldehydes. Isoniazid, niacinamide and thionicotinamide are pyridine derivatives having tuberculostatic activity; hence some pyrimidithiones have been prepared by condensing aryl aldehydes, ethyl acetoacetate and urea, thiourea or ammonia.

A mixture of 2-chloro or 4-methoxy or 3,4,5-trimethoxy benzaldehyde (0.04 M) and sulfathiazole or sulfaphenazole (0.04 M) was refluxed in pyridine (20 mL) for 6 h. After cooling, the product obtained on acidification was crystallized from ethanol. The purity was established by TLC and then tested for anti-TB activity by the known method[1].

4-Substituted phenyl-6-methyl-5-carbethoxy-1,3,4-trihydro-2-pyrimidone or -2-pyrimidithione

It is obtained by refluxing the mixture of substituted aryl aldehyde (0.075 M), ethyl acetoacetate (0.112 M) and urea (0.085 M) or thiourea (0.085 M) in methanol (25 mL) with 7.5 mL of conc. hydrochloric acid. After cooling the mixture, the product obtained was washed with methanol and crystallized from ethanol. The purity was checked by TLC.

†Artemis Research Center, Themis Chemicals Ltd., Vapi-396 195, India.
‡Department of Microbiology, B.P. Baria Institute, Navsari (Gujarat), India.

When the benzaldehyde (0.1 M) was refluxed with ethyl acetoacetate (0.2 M) in presence of ammonium hydroxide (0.2 M) for 15 to 20 h, 4-substituted phenyl-3,5-dicarbethoxy-2,6-dimethyl-1-4-dihydropyridine is obtained. The reaction mixture after cooling gave a product which was filtered, washed and crystallized from aqueous ethanol. The purity was checked by TLC. Details are given in Tables.

PYRIMIDONE

X	Yield %	m.w. found/calcd.	m.p. (°C)	I.R. (cm^{-1})
—H	78	254/259	204	—NH stretching 3350, ν(C=O) 1710
-2—Cl	52	290/294.5	222	ν(C—Cl) 750
-4—OCH_3	60	285/289	202	—OCH_3 2840

PYRIMIDITHIONE

X	Yield %	m.w. Found/Calcd.	m.p. (°C)	I.R. (cm^{-1})
—H	46	270/275	200	—NH stretching 3315, ν(C=S) 1210
-4—OCH_3	44	298/305	105	—OCH_3 2840, α : β unsaturated ester 1690

4-PHENYL-3,5-DICARBETHOXY-2,6-DIMETHYL-1-4-DIHYDROPYRIMIDINE

X	Yield %	m.w. Found/Calcd.	m.p. (°C)	I.R. (cm^{-1})
—H	43	323/328	162–163	—NH stretching 3390 α : β unsaturated ester 1700 cm^{-1}
-4—OCH_3	40	352/358	161	—OCH_3 2835 C—CH_3 stretching 2990

It was observed that 2-chloro or 4-methoxy or 3,4,5-benzylidene sulfa thiazole or phenazole (six products) inhibit growth of $H_{37}R_v$ at 5 μg/mL. However, all the pyridine derivatives did not show any inhibitory activity at 5 μg/mL or even 10 μg/mL.

ACKNOWLEDGEMENTS

The authors thank Dr. P.K. Desai, Directory Span Research Center for anti-TB data and Shantibhai Patel, President, Themis Chemicals Ltd. for providing research facilities.

REFERENCES

1. P.K. Desai, Pratibha Desai, Dilip Machhi, C.M. Desai and Dinesh Patel, *Indian J. Chem.*, **35B**, 871 (1996).

(*Received:* 1 March 1998; *Accepted*: 15 June 1998) AJC-1535