Potential Antiviral and Antituberculous Compounds. II

N-(2-Dibenzothiophenyl)-N'-alkyl and N'-aryl Thioureas, N-(2-Dibenzothiophenyl) and N-(2-Dibenzothiophenyl-5-dioxide) Amidines

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Summary

Seventeen new condensation products of 2-amino dibenzothiophene with several alkyl and aryl isothiocyanates and eight new substituted amidines with 2-dibenzothiophenyl and 2-dibenzothiophenyl-5-dioxide substituents have been prepared with a view to study their antiviral and tuberculostatic activity.

It has been observed that several heterocyclic compounds like N-thiazolyl nicotinamide[1]), isonicotinic acid hydrazide[2]), N-4-phenyl-α-pyridyl-p-tolyl amidine[3]) exhibited promising antitubercular activity in vitro and 2-amino dibenzothiophene[4]) showed potent activity against Mycobacterium tubercle also in vivo. Moreover, thiourea derivatives have been reported as effective antiviral agents[5]). These observations have prompted us to synthesise a series of N-(2-dibenzothiophenyl) and N-(2-dibenzothiophenyl-5-dioxide) amidines and thiourea derivatives of the biologically active 2-amino dibenzothiophene moiety as potential antitubercular and antiviral compounds. It is expected that the thioureas will exhibit the dual property of antiviral and antitubercular activity as has been reported by Buu Hoi et al. in such compounds.

N-(2-Dibenzothiophenyl)-N'-alkyl and N'-aryl thioureas have been prepared by the condensation of 2-amino dibenzothiophene with various alkyl and aryl isothiocyanates. It may be mentioned here that 2-amino dibenzo-

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[1]) S. Kushner et al., J. org. Chem. **13**, 834 (1948).
[2]) Bernstein et al., Amer. Rev. Tuberc. **65**, 357 (1952).
[3]) Misra et al., J.I.C.S. **31**, 918 (1954).
[4]) Doub and Youmans, Amer. Rev. Tuberc. **61**, 407 (1950).
[5]) Buu Hoi et al., J. chem. Soc. London **1956**, 2160.

thiophene-5-dioxide did not yield the corresponding thioureas, inspite of our repeated attempts.

2-Amino dibenzothiophene, one of the starting materials, was obtained by the method of GILMAN and NOBIS[6]) by the nitration and catalytic reduction of dibenzothiophene. The other starting material, 2-amino dibenzothiophene-5-dioxide, was prepared by the oxidation of 2-nitro dibenzothiophene with hydrogen peroxide to 2-nitro dibenzothiophene-5-dioxide and then its subsequent reduction to 2-amino dibenzothiophene-5-dioxide[7]).

The amidines were obtained by following the method of OXLEY and SHORT[8]) and as adopted by MISRA et al.[9]). N-(2-Dibenzothiophenyl)-N'-butyl amidine, however, could not be liberated from its amidine benzene sulphonate by shaking with alkali.

The antiviral and antitubercular activity of these compounds will be reported later on.

Experimental

N-(2-Dibenzothiophenyl) ammonium benzene sulphonate (A)

It was obtained according to the method of BAUER and CYMERMAN[10]). 2-Amino dibenzothiophene (0.99 g, 0.005 mol) was suspended in 50 ml of dry ether and benzene sulphonic acid (0.79 g, 0.005 mol) dissolved in methanol, was added to it slowly under stirring. A pinkish white solid separated out which was filtered, dried and crystallised from hot water. Yield 78.6% of theory (1.4 g), m.p. 200 °C. (Found N, 3.81%, $C_{18}H_{15}NO_3S_2$ requires N, 3.92%.)

N-(2-Dibenzothiophenyl-5-dioxide) ammonium benzene sulphonate (B)

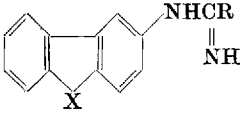
To 2-amino dibenzothiophene-5-dioxide (1.15 g, 0.005 mol), stirred in dry ether, benzene sulphonic acid (0.79 g, 0.005 mol) dissolved in methanol, was added dropwise. The benzene sulphonate separated out as a pale yellow solid which was filtered and crystallised from hot water. Yield 72% of theory (1.4 g), m.p. above 275 °C. (Found N, 3.59%, $C_{18}H_{15}NO_5S_2$ requires N, 3.60%.)

N-(2-Dibenzothiophenyl) and N-(2-dibenzothiophenyl-5-dioxide) amidines

Either of the compounds A or B prepared above (1 mol) was mixed with excess ortho, meta, para toluo, benzo, n-capronitriles (only with A) in a round bottom flask, fitted with a reflux condenser and a calcium chloride guard tube. The mixture was heated at 220 to 245 °C (external bath temperature) for 4 hours. The resulting paste was repeatedly triturated with acetone or ether when an amorphous powder of the amidine benzene sulpho-

[6]) H. GILMAN and J. F. NOBIS, J.A.C.S. **71**, 274 (1949).
[7]) K. BROWN, N. A. NELSON and J. CHARLES WOOD, J.A.C.S. **74**, 1165 (1952).
[8]) OXLEY and SHORT, J. chem. Soc. London **1946**, 147.
[9]) MISRA et al., J.I.C.S. **39**, 109 (1962).
[10]) BAUER and CYMERMAN, J. chem. Soc. London **1950**, 1826.

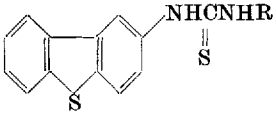
Table 1
N-(2-Dibenzothiophenyl)/
N-(2-Dibenzothiophenyl-5-dioxide) amidines



No.	R =	X =	M.P. °C	% Yield (of theory)	Formula	% Nitrogen Found	Calcd.
1.	C_6H_5-	S	140	12.3	$C_{19}H_{14}N_2S$[a]	8.95	9.27
2.	p-$CH_3 \cdot C_6H_4$-	S	166	47.0	$C_{20}H_{16}N_2S$[a]	8.42	8.86
3.	m-$CH_3 \cdot C_6H_4$-	S	165	56.5	$C_{20}H_{16}N_2S$[a]	8.88	8.86
4.	o-$CH_3 \cdot C_6H_4$-	S	207	50.0	$C_{20}H_{16}N_2S$[b]	8.72	8.86
5.	C_6H_5-	SO_2	162	70.3	$C_{19}H_{14}N_2O_2S$[a]	8.86	8.38
6.	o-$CH_3 \cdot C_6H_4$-	SO_2	165	62.5	$C_{20}H_{16}N_2O_2S$[b]	8.07	8.04
7.	m-$CH_3 \cdot C_6H_4$-	SO_2	162	40.3	$C_{20}H_{16}N_2O_2S$[a]	8.01	8.04
8.	p-$CH_3 \cdot C_6H_4$-	SO_2	210	63.6	$C_{20}H_{16}N_2O_2S$[c]	7.90	8.04

Crystallised from (a) Methyl ethyl ketone-petrol ether; (b) Methyl ethyl ketone; (c) Acetone-ether.

Table 2
N-(2-Dibenzothiophenyl)-N′-alkyl and N′-aryl thioureas



No.	R =	M.P. °C	% Yield (of theory)	Formula	% Nitrogen Found	Calcd.
1.	C_6H_5-	142—143	82	$C_{19}H_{14}N_2S_2$	8.01	8.38
2.	$C_6H_5 \cdot CH_2$-	169—170	80	$C_{20}H_{16}N_2S_2$	7.69	8.04
3.	o-$CH_3 \cdot C_6H_4$-	166	68	$C_{20}H_{16}N_2S_2$	7.57	8.04
4.	p-$CH_3 \cdot C_6H_4$-	131	72	$C_{20}H_{16}N_2S_2$	7.92	8.04
5.	m-$CH_3 \cdot C_6H_4$-	165	70	$C_{20}H_{16}N_2S_2$	7.58	8.04
6.	p-$C_2H_5O \cdot C_6H_4$-	141	75	$C_{21}H_{18}N_2OS_2$	7.16	7.40
7.	n-C_6H_{11}-	175—176	79	$C_{19}H_{20}N_2S_2$	7.89	8.23
8.	m-$CH_3O \cdot C_6H_4$-	168	72	$C_{20}H_{16}N_2OS_2$	7.26	7.69
9.	o-$CH_3O \cdot C_6H_4$-	107	68	$C_{20}H_{16}N_2OS_2$	7.48	7.69
10.	p-Br · C_6H_4-	145	72	$C_{19}H_{13}N_2S_2Br$	6.81	6.77
11.	m-Br · C_6H_4-	166	79	$C_{19}H_{13}N_2S_2Br$	6.62	6.77
12.	o-Cl · C_6H_4-	165	82	$C_{19}H_{13}N_2S_2Cl$	7.90	7.60
13.	p-$NO_2 \cdot C_6H_4$-	168—170	82	$C_{19}H_{13}N_3O_2S_2$	11.12	11.08
14.	n-C_3H_7-	132	65	$C_{16}H_{16}N_2S_2$	8.91	9.33
15.	iso-C_3H_7-	183	68	$C_{16}H_{16}N_2S_2$	8.87	9.33
16.	n-C_4H_9-	142—143	72	$C_{17}H_{18}N_2S_2$	8.50	8.91
17.[11]	H-	185—186	65	$C_{13}H_{10}N_2S_2$	10.63	10.85

[11]) Ammonium thiocyanate was used with the hydrochloride of amine.

nate was obtained. This was converted to the appropriate amidine by shaking with 100 ml of 5N-NaOH for 5—6 hours. The liberated amidine was filtered and crystallised from a suitable solvent (vide Table 1).

N-(2-Dibenzothiophenyl) thioureas

Equimolar quantities of 2-amino dibenzothiophene and the appropriate alkyl or aryl isothiocyanates were refluxed in the presence of ethanol for 2—3 hours. On cooling, the condensation products separated out, which were filtered after distilling off the excess ethanol, and then crystallised from ethanol (vide Table 2).

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