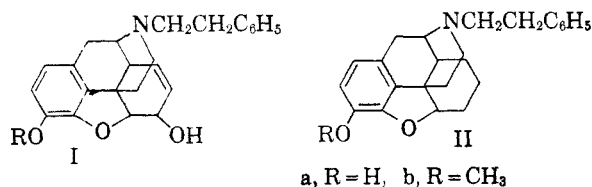


the ether was filtered and dried. The base left from evaporation of the ether was acidified (in acetone) with about 3.0 ml. of 33% HBr-AcOH to give 3.0 g. of IIb hydrobromide, m.p. 243–245°; plates from acetone, m.p. 245–246°,  $[\alpha]_D^{20} -77.2^\circ$  (c 1.0 in MeOH).

Anal. Calcd. for  $C_{25}H_{30}BrNO_2$ : C, 65.79; H, 6.63. Found: C, 65.93; H, 6.60.

*N*-Phenethylhydrosesoxymorphine-*D* hydrobromide (IIa). Refluxing 2.0 g. of IIb hydrobromide and 12 ml. of 48% HBr for 15 min., cooling and filtering gave a quantitative yield of the IIa hydrobromide, m.p. 285–290°. It crystallized from methanol in plates, m.p. 297–298° (dec.),  $[\alpha]_D^{20} -74.2^\circ$  (c 1.0 in MeOH), which analyzed for the hemihydrate; there was, however, no loss in weight of a sample dried for 5 hr. at 135° without vacuum.

Anal. Calcd. for  $C_{24}H_{28}BrNO_2 + \frac{1}{2} H_2O$ : C, 63.85; H, 6.48. Found: C, 63.92; H, 6.47.



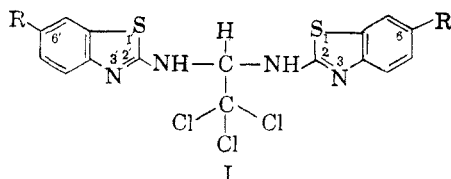
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## 2-Amino-6-substituted Benzothiazoles as Potential Anthelmintics

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In an earlier communication Mackie, Stewart and Misra<sup>2</sup> reported the paralyzant and lethal action of some benzothiazole compounds toward *Ascaris lumbricoides* and *Fasciola hepatica*. In view of the important physiological properties<sup>3a,b,c</sup> possessed by the 2-amino-6-substituted benzothiazoles, it appeared of interest to prepare the condensation products of these compounds with chloral, of the general structure (I), incorporating a lipoid-solubilizing group (trichloromethyl) which might assist



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the penetration of the compounds through the cuticle of *Ascaris lumbricoides* and thereby have a deleterious effect on the neuromuscular system of the intestinal nematodes and on other trematodes.

Condensation products of aromatic and heterocyclic amines with chloral had previously been reported by Sumerford and Dalton<sup>4</sup> and Nelson *et al.*<sup>5</sup> but no work in this respect seems to have been done with the 2-amino-6-substituted benzothiazoles.

The 1,1-bis(2-benzothiazolylamino)-2,2,2-trichloroethanes of the structure I were prepared by refluxing a benzene solution of the 2-amino-benzothiazole with an excess of freshly distilled chloral for 1.5 hr. on a water bath. The precipitate was filtered, washed with a small volume of dry benzene and recrystallized from a suitable solvent. Under the conditions of the experiment, the condensation did not take place with the 6-nitro, 6-carboxy or 6-carbomethoxy-2-aminobenzothiazoles. In the case of 6-chloro-2-aminobenzothiazole, a small amount of its hydrochloride was obtained during reflux along with the unreacted base, while with 2-amino-4,5,6,7-tetrahydrobenzothiazole, the hydrochloride of the base was isolated in good yield. This was presumably due to the partial photochemical decomposition of chloral and the liberation of hydrochloric acid.<sup>6</sup>

The details of the *in vivo* biological activity of these compounds toward the dog hookworms and the ascarid infections in poultry and dogs will be reported later.

## EXPERIMENTAL

The 2-aminobenzothiazole and its 6-substituted derivatives were prepared by the known methods.<sup>7–11</sup> The data concerning the new 1,1-bis(2-benzothiazolylamino)-2,2,2-trichloroethanes are listed in Table I. 2-Amino-4,5,6,7-tetrahydrobenzothiazole<sup>12</sup> gave its hydrochloride, which recrystallized in colorless rhomboids from benzene. Yield 50%, m.p. 236–237° (dec.).

Anal. Calcd. for  $C_7H_{10}N_2S \cdot HCl$ , C, 44.09%, H, 5.70%, N, 14.60%. Found C, 43.98%, H, 5.80%, N, 14.89%.

Sprague and Kissinger<sup>13</sup> gave the melting point of the hydrochloride, 249–250°.

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TABLE I  
1,1-Bis(2-BENZOTHAZOLYLAMINO)-2,2,2-TRICHLOROETHANES

R	M.P.	Formula	% C		% H		% N		% Cl		Yield, %
			Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	
(a) H	203° (dec.)	C <sub>16</sub> H <sub>11</sub> Cl <sub>3</sub> N <sub>4</sub> S <sub>2</sub>	44.70	45.20	2.56	2.66	13.03	13.00	24.79	24.65	80
(b) CH <sub>3</sub>	180-181° (dec.)	C <sub>18</sub> H <sub>15</sub> Cl <sub>3</sub> N <sub>4</sub> S <sub>2</sub>	47.21	47.60	3.27	3.34	12.24	12.50	23.27	22.89	51
(c) OCH <sub>3</sub>	196-197° (dec.)	C <sub>19</sub> H <sub>15</sub> Cl <sub>3</sub> N <sub>4</sub> O <sub>2</sub> S <sub>2</sub>	44.12	44.30	3.06	3.06	11.44	11.56			82
(d) OC <sub>2</sub> H <sub>5</sub>	168-169° (dec.)	C <sub>20</sub> H <sub>19</sub> Cl <sub>3</sub> N <sub>4</sub> O <sub>2</sub> S <sub>2</sub>	46.37	46.73	3.67	3.67	10.82	10.73			85
(e) .COO.(CH <sub>2</sub> ) <sub>2</sub> -N<C <sub>2</sub> H <sub>5</sub> C <sub>2</sub> H <sub>5</sub>	102-103°	C <sub>30</sub> H <sub>37</sub> Cl <sub>3</sub> N <sub>6</sub> O <sub>4</sub> S <sub>2</sub> .2HCl	45.70	45.93	4.94	4.97	10.65	10.00			75

The analytical samples were: (a) recrystallized in colorless needles from benzene; (b, c, d) recrystallized in colorless needles from absolute ethanol-light petroleum (40-60°); (e) recrystallized from dry benzene, hygroscopic, decomposes if crystallized from hydroxylic solvents.

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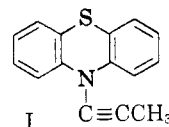
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### An Unusual Reaction of Propargyl Bromide

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When an attempt to alkylate phenothiazine with propargyl bromide failed using the customary conditions of sodamide in xylene, the procedure was changed to one using sodium hydride in dimethylformamide. Under these conditions, alkylation occurred to give a 70% yield of product which turned out to be *N*-(1-propynyl)phenothiazine (I) instead of the desired isomeric *N*-(2-propynyl)phenothia-



zine. Support for the assigned structure includes the presence of disubstituted acetylenic absorption at 4.48 microns in the infrared, and the absence of  $\equiv\text{C}-\text{H}$  and  $>\text{C}=\text{C}=\text{C}<$  absorption in the 3 and 5.1 micron regions, respectively. However, a disturbing feature of the infrared spectrum is the absence of C-methyl absorption at 7.25 $\mu$ . Instead, two strong bands appear at 6.87 $\mu$  and 6.96 $\mu$ , more characteristic of *N*-methyl absorption. In view of the chemical evidence, it is assumed, nevertheless, that this shift is caused by attachment of methyl to the polar  $\text{N}-\text{C}\equiv\text{C}-$  system.

Chemical evidence for structure I was obtained by hydrogenation to known *N*-(*n*-propyl)phenothiazine and by hydrolytic cleavage to unsubstituted phenothiazine.

The anomalous course of this reaction can be rationalized by postulating involvement of the dipolar ion,  $\text{CH}_2\text{C}\equiv\text{C}^-$ , of the type proposed by Hennion and co-workers<sup>1-3</sup> to explain some of the hydrolytic and aminolytic reactions of certain

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