Summary

1. A new synthetic method for the preparation of hexachlorocyclopentadiene based on the pyrolysis of octachlorocyclopentene has been described.

2. The Prins reaction has been extended to include a member of the alicyclic series.

3. Three new compounds derived from hexachlorocyclopentadiene were synthesized.

4. Physical properties for the above substances and some of their intermediates are given.

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[CONTRIBUTION FROM THE WM. H. CHANDLER CHEMISTRY LABORATORY, LEHIGH UNIVERSITY]

Studies in the Sulfone Series. I. The Preparation of 2,8-Diaminodibenzothiophene-5-dioxide

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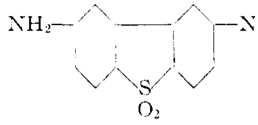
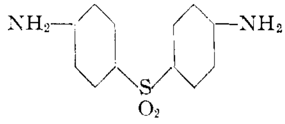
During the past few years numerous attempts have been made to improve the therapeutic index of the potent but toxic antibiotic, 4,4'-diaminodiphenyl sulfone. From these investigations have come such materials as diasone,[2,3] promin, the formaldehyde-bisulfite derivative,[3] certain carboxylic acid derivatives,[4] and the unsymmetrical diacyl compounds.[5] The work reported in this present paper was likewise designed to yield materials of more favorable therapeutic index but was directed along different lines.

2,8-Diamino-dibenzothiophene-5-dioxide (I) may be considered to be derived from 4,4'-diaminodiphenyl sulfone (II) by direct union of the 2,2'-positions.



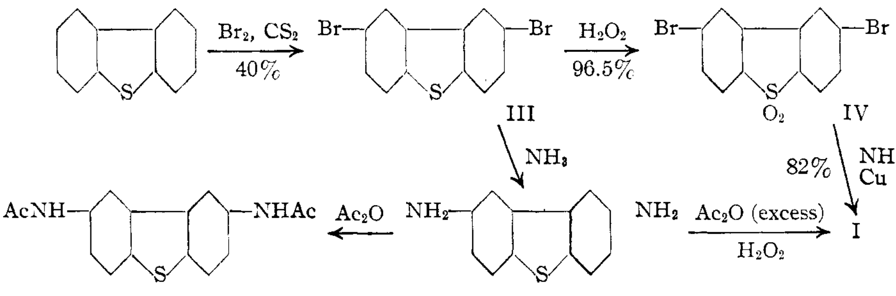
I



II

An investigation of the preparation of the compound and some of its derivatives has been made.

In most of its mono- and di-substitution reactions dibenzothiophene is attacked at the 2- and the 2,8-positions. Thus it has been shown that the product of mono-bromination is the 2-bromo derivative,[6] and in dibromination the 2,8 compound. Gilman has reported[7] the successful substitution of the halogen of 2-bromodibenzothiophene by the amino group. The following reaction sequence[8] was adapted to obtain (I).



The 2,8-dibromo derivative (III) was obtained in 40% yield by long refluxing of a carbon bisulfide[9] solution of bromine and dibenzothiophene. The conversion to the dioxide (IV) was accomplished in almost quantitative yield by refluxing the sulfide with hydrogen peroxide in glacial acetic acid. Amination of the dibromo sulfone with concentrated aqueous ammonia and a trace of copper powder at 175–220° afforded the corresponding diamine.

We also carried out the diamination of 2,8-dibromodibenzothiophene and obtained in this way the corresponding diamino compound which melted at 199.5–201.5°. Burger and his coworkers reported a melting point of 193–194° for the same compound while Courtot and Pomonis[10] found the compound to melt at 178°. Our diamine also yielded a diacetyl derivative which melted at 304–305.5° as compared to 253–255° for Burger's sample of the same material, and 237–239° (dec.) for Courtot's substance.

All attempts to oxidize the 2,8-diacetamidodibenzothiophene to the dioxide were fruitless, only colored materials of indefinite melting ranges being obtained. After the diamine had been refluxed

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[2] Raiziss, Clemence and Freifelder, *J. Am. Pharm. Assocn.*, **33**, 43 (1944).

[3] Bauer, THIS JOURNAL, **61**, 617 (1939).

[4] Gray and Platt, *J. Chem. Soc.*, 42 (1942).

[5] Shonle and Van Arendonk, THIS JOURNAL, **65**, 2375 (1943).

[6] Cullinane, Davies and Davies, *J. Chem. Soc.*, 1435 (1935).

[7] Gilman and Jacoby, *J. Org. Chem.*, **3**, 108 (1938).

[8] A second synthetic approach *via* the Beckmann rearrangement of the dioxime of 2,8-diacetyldibenzothiophene (Burger, Wartman and Lutz, THIS JOURNAL, **60**, 2628 (1938)) was discarded after preliminary experiments indicated that the method was not applicable to the preparation of reasonable quantities of material.

[9] The use of acetic acid as a solvent served to shorten the time required for the reaction, but the product was difficult to purify.

[10] Courtot and Pomonis, *Compt. rend.*, **182**, 893, 931 (1926).

for some time with an excess of acetic anhydride (and thereby probably converted to the tetracetyl derivative) treatment with hydrogen peroxide no longer gave difficulty. The oxidized material, after deacetylation (with dilute aqueous HCl) and purification proved to be identical (by the method of mixed melting points) with the diamino compound prepared from (IV).

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Experimental[11]

2,8-Dibromodibenzothiophene (III). **A.**—The procedure of Cullinane, Davies and Davies[6] for monobromination has been adapted for our use. A solution of 10 g. (0.0544 mole) of dibenzothiophene and 17.6 g. (0.11 mole) of bromine in 60 ml. of carbon bisulfide was refluxed for nine days, after which the solvent was removed by distillation on a water-bath. A first recrystallization of the residue from acetic acid did not effect much purification so the process was repeated using acetic anhydride. This afforded 7.4 g. (40%) of the dibromo compound melting at 225–228°. Courtot, *et al.*, reported[12] m. p. 229°.

B. To a suspension of 10 g. of dibenzothiophene in 200 ml. of glacial acetic acid was added 17.6 g. of bromine in 50 ml. of acetic acid over a period of thirty minutes after which the mixture was stirred for two hours. It was then refluxed for five hours, cooled and filtered. After washing with water and drying, the crude product weighed 5.8 g. (31%) and melted at 208–216° (uncor.). Recrystallization from 100 ml. of acetic anhydride yielded 4.4 g. (24%) of material melting at 226–228.5°.

2,8-Dibromodibenzothiophene-5-dioxide. (IV).—A suspension of 6.9 g. (0.02 mole) of 2,8-dibromodibenzothiophene in 77 ml. of glacial acetic acid was refluxed for two hours with 9.6 ml. of glacial acetic acid. Cooling and filtering yielded 7.3 g. (96.5%) of product which melted at 341.0–above 344°: reported[13] m. p. 361–362°.

2,8-Diaminodibenzothiophene-5-dioxide (I)[14] **From IV.**—A mixture of 21.5 g. (0.0585 mole) of IV, about 150 ml. of concentrated aqueous ammonia and about 1 g. of copper–bronze was heated for approximately eight hours at 200–220°. The crude solid diamino compound thus obtained weighed 11.5 g. (82.2%) and melted at 317–326°. Recrystallization from water with the aid of Norit yielded almost colorless crystals, m. p. 329–331° (dec.).

Anal. Calcd. for $C_{12}H_{10}O_2N_2S$: S, 13.01. Found: S, 13.22.

From V.—About 0.2 g. of V was converted to the tetraacetyl derivative by boiling in 10 ml. of acetic anhydride. The excess anhydride was removed on the hot-plate and the residue dissolved immediately in 15 ml. of glacial acetic acid. To the resulting hot solution was added 1 ml. of 30% hydrogen peroxide after which gentle refluxing was continued for about three hours. The solid which separated on cooling was removed and boiled for about one hour in 4% hydrochloric acid solution after which solution was complete. The solid which was then thrown down with sodium bicarbonate melted, after washing and drying, at 323–329° (dec.). The compound was purified by decolorization of a solution in 4% hydrochloric acid with charcoal and reprecipitation with sodium bicarbonate. After drying in a pistol, the compound melted at 331–333° (dec.), and in admixture with material prepared above (m. p. 329–331°) at 330–332°.

2,8-Diaminodibenzothiophene (V).—A mixture of 2 g. of 2,8-dibromodibenzothiophene, 15 ml. of concentrated ammonium hydroxide and a small amount of copper powder were heated in a sealed tube at 175–210° for twenty-one and one-half hours.[15] The crude product was recrystallized twice (as the hydrochloride) from about 4% hydrochloric acid solution after which it melted at 199.5–201.5°: reported,[8] m. p. 193–194°.

Anal. Calcd. for $C_{12}H_{10}N_2S$: S, 14.96. Found: S, 15.05.

A solution of 0.3 g. of the diamine (V) was refluxed in acetic acid with 0.6 ml. of acetic anhydride for three hours. After the crude product had been washed with aqueous sodium bicarbonate and recrystallized from alcohol, it melted at 304–305.5°: reported[8] for 2,8-diacetamidodibenzothiophene, m. p. 253–255°.

Anal. Calcd. for $C_{16}H_{14}O_2N_2S$: S, 10.75. Found: S, 10.86.

Summary

2,8-Diaminodibenzothiophene-5-dioxide has been prepared for the purpose of determining its possible value in the treatment of bacterial infections.

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(11) Unless otherwise noted, all melting points have been corrected for thermometer stem-emergence.

(12) Courtot, Nicholas and Liang, *Compt. rend.*, **186**, 1624 (1928).

(13) Courtot, *ibid.*, **198**, 2260 (1934).

(14) This amination was carried out in an Aminco bomb in the laboratories of the Wm. S. Merrell Co.

(15) The percentage yield in this preparation was low because a defect in the Carius furnace prevented the temperature from reaching the desired range (200–225°).