[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Rearrangement with 4-Iododibenzothiophene in Amination by Sodamide

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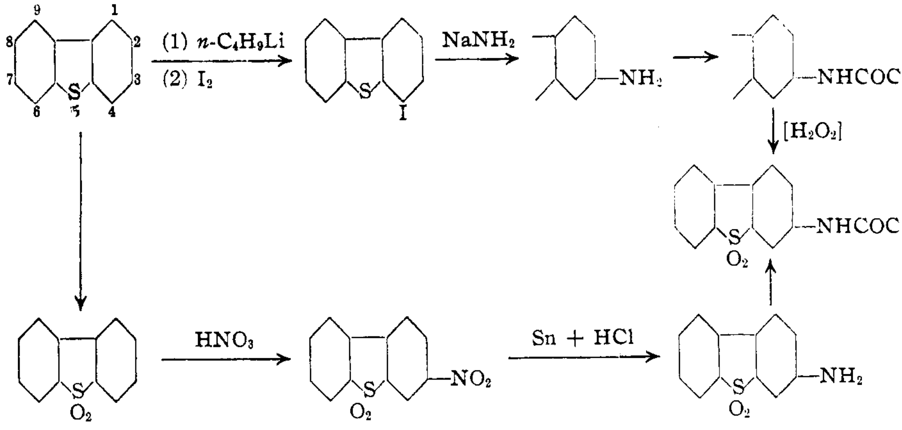
The recent report[1] on the rearrangement of *ortho*-halogenated ethers by sodamide in liquid ammonia to give *meta*-amino ethers suggested an examination of the reaction between 4-iododibenzothiophene and sodamide in liquid ammonia. If a corresponding rearrangement occurred with the sulfur-heterocycle, a way would be opened to the preparation of 3-substituted dibenzothiophenes desired in connection with studies on pharmacological action. The direct introduction of a substituent in the 3-position by means of the anomalous metalation of dibenzothiophene by phenylcalcium iodide[2] is of little preparative value because of the very low yields. Other direct nuclear substitution reactions involve the 2-position and the 4-position,[3] the latter position being made accessible by metalations with organometallic compounds other than phenylcalcium iodide.

We have found that the sodamide reaction in liquid ammonia with 4-iododibenzothiophene gives the rearrangement product, 3-aminodibenzothiophene. The following sequence of reactions was used to establish the structure of the amine.



The 4-iododibenzothiophene is a new compound. In order to reduce the possibility of a rearrangement occurring during its formation, it was treated with metallic lithium to give an organolithium compound which on carbonation gave the known 4-dibenzothienylcarboxylic acid. Incidentally, hydrogen peroxide appears to be a reagent of choice for converting dibenzothiophene to dibenzothiophene-5-dioxide.

It is quite probable that *ortho*-halogenated sulfides, in general, will undergo the rearrangement with metallic amides. Other studies have shown the reaction to be rather broad in scope. For example, *ortho*-halogenated sulfones undergo the rearrangement, and liquid ammonia is not always necessary, for the rearrangement is shown with types like lithium diethylamide in ether.

Experimental

Dibenzothiophene.—Dibenzothiophene was prepared in essential accordance with the earlier directions.[3] However, it was observed that the crude yield could be checked by the use of two instead of eight extractions with one liter portions of boiling absolute ethanol. The yield of pure dibenzothiophene (not reported previously) was 47%.

4-Iododibenzothiophene.—A solution of 0.88 mole of n-butyllithium[4,5] in 1500 cc. of ether was refluxed with 134 g. (0.73 mole) of dibenzothiophene for nineteen hours. At the end of this time, a negative color test II[6] was observed and this showed that the alkyllithium compound had been used up. The reaction mixture was cooled in ice, and 190 g. (0.75 mole) of powdered iodine was added slowly. The mixture was then refluxed for one hour, and a negative color test I[7] at the end of this time showed the absence of any organometallic compound. The solution was poured into water; and the ether layer was separated, washed with sodium bisulfite, and dried over sodium sulfate. After removal of the ether, the residual oil was distilled under reduced pressure to give 100 g. or a 44% yield of a crude product which distilled over the range 160–170° (1 mm.), and melted over the range 90–100°. Recrystallization from petroleum ether (b. p. 63–78°) to a constant melting point of 101–102° reduced the yield to 50 g. (22%).

In another preparation the iodine was dissolved in ether before being added to the organolithium compound. This procedure is without any advantage, and actually involves the handling of an unnecessarily large volume of solvent. In this preparation, recrystallization was attempted before distillation. This procedure is impractical because it appears that any unreacted dibenzothiophene is more effectively separated from the 4-iododibenzothiophene by preliminary distillation under reduced pressure. The yield in this preparation was 20%.

Anal. Calcd. for $C_{12}H_7IS$: I, 41.0. Found: I, 41.1.

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[1] Gilman and Avakian, THIS JOURNAL, **67**, 349 (1945).

[2] Gilman, Jacoby and Pacevitz, *J. Org. Chem.*, **3**, 120 (1938).

[3] Gilman and Jacoby, *ibid.*, **3**, 108 (1938).

[4] Gilman and Stuckwisch, THIS JOURNAL, **65**, 1462 (1943).

[5] The titer of the n-butyllithium was determined by the analytical procedure of Gilman and Haubein, THIS JOURNAL, **66**, 1515 (1944).

[6] Gilman and Swiss, *ibid.*, **62**, 1847 (1940).

[7] Gilman and Schulze, *ibid.*, **47**, 2002 (1925).

3-Aminodibenzothiophene.—A solution of sodamide was prepared according to the directions of Vaughn, Vogt and Nieuwland[8] from 4.6 g. (0.2 g. atom) of sodium and 0.5 g. of ferric nitrate in 250 cc. of liquid ammonia. Then 18 g. (0.058 mole) of 4-iododibenzothiophene was added over a period of fifteen minutes. The reaction was not vigorous, and after stirring for thirty minutes the unreacted sodamide was decomposed by ammonium chloride. Subsequent to evaporation of the ammonia, the residue was extracted with benzene. The admission of hydrogen chloride to the benzene solution precipitated the amine-hydrochloride from which was liberated, by ammonium hydroxide, 8.5 g. (74%) of the crude amine. Purification was effected by dissolving in hot methanol, treating with charcoal, and then adding water to obtain a 50-50 mixture from which was obtained 5.7 g. (49.5%) of 3-aminodibenzothiophene melting at 114–119°. The analytical sample melted at 121.5–122° after recrystallization from 50% methanol.

Anal. Calcd. for $C_{12}H_9NS$: N, 7.05. Found: N, 7.22.

The melting point of 4-aminodibenzothiophene is 110°.[3]

3-Acetaminodibenzothiophene.—After refluxing for one hour 3 g. (0.015 mole) of 3-aminodibenzothiophene and 2 g. (0.019 mole) of acetic anhydride in 20 cc. of benzene, there was obtained 3 g. (83.5%) of the acetamino compound melting at 197–198°. Recrystallization from dilute ethanol of a sample for analysis raised the melting point to 199–200°.

Anal. Calcd. for $C_{14}H_{11}ONS$: N, 5.82. Found: N, 6.02.

Inasmuch as the melting point of the 3-acetaminodibenzothiophene is close to that reported[3] for the corresponding 4-acetaminodibenzothiophene (m. p. 198°), a mixed m. p. determination of the two compounds was made and found to be over the range 170–190°.

3-Acetaminodibenzothiophene-5-dioxide. A. From 3-Acetaminodibenzothiophene.—A mixture of 1.25 g. (0.005 mole) of 3-acetaminodibenzothiophene in 20 cc. of glacial acetic acid and 10 cc. (0.08 mole) of 30% hydrogen peroxide was heated for three hours on a boiling water-bath. The orange-colored solid that settled out was filtered after cooling the mixture, and the yield of product melting at 324–326° was one gram (70.5%). It was observed that the yield was reduced markedly if the reactants were refluxed. Also, pouring the reaction mixture into water rather than filtering directly makes recrystallization (from ethanol) necessary and reduces the yield to 61%.

B. From 3-Aminodibenzothiophene-5-dioxide.—After heating a mixture of 0.1 g. (0.004 mole) of 3-aminodibenzothiophene-5-dioxide[2] in 5 cc. of benzene with a few drops of acetic anhydride under reflux for one-half hour, there was obtained 0.1 g. (96%) of the 3-acetaminodibenzothiophene-5-dioxide melting at 325–327° and showing no depression in a mixed m. p. determination with the product obtained by oxidation of 3-acetaminodibenzothiophene.

Anal. Calcd. for $C_{14}H_{11}O_3NS$: N, 5.13. Found: N, 5.05.

Dibenzothiophene-5-dioxide.—Various procedures have been described[9a] for the preparation of this dioxide, but apparently no study was made of a hydrogen peroxide oxidation of the parent heterocycle.[9b]

To 18.4 g. (0.1 mole) of dibenzothiophene dissolved in 100 cc. of glacial acetic acid at 80° was added 30 cc. of 30% hydrogen peroxide. The solution was heated at 90° for one hour and then refluxed for thirty minutes. The dioxide soon started to separate, and an additional 10 cc. of hydrogen peroxide was added. The refluxing was continued another thirty minutes and the reaction mixture allowed to cool. The white solid was removed by filtration and washed well with water. The yield of product melting at 233–234° was 20.7 g. or 96%.[10]

It was found that a four-hour reflux period had no advantage and the yield of pure compound was 92%. Dilution of the filtrate, however, gives a small amount of the crude dioxide.

When the reactants were refluxed for one hour immediately after the addition of the hydrogen peroxide, and the reaction mixture allowed to stand overnight, the yield was 97.5%.

Methyl 4-Dibenzothiophenecarboxylate.—A mixture of 5 g. (0.0161 mole) of 4-iododibenzothiophene and 0.28 g. (0.04 g. atom) of finely cut lithium in 50 cc. of ether was refluxed under nitrogen. Color test I,[7] taken at the end of one hour, was positive; and an acid-titration analysis[11] made at the end of three hours of refluxing showed the yield of RLi compound to be 75%. The mixture was carbonated by pouring on Dry Ice to give a 55% yield of once crystallized acid melting in the range 245–250°. Recrystallization from dilute methanol raised the melting point to 248–251°, and sublimation under reduced pressure gave a melting point of 255–257°. The melting point previously reported[3] was 252–253°. The acid was converted to methyl 4-dibenzothiophenecarboxylate by means of diazomethane, and the ester was shown to be identical (mixed m. p.) with an authentic specimen.[3]

Summary

4-Iododibenzothiophene, prepared from 4-dibenzothienyllithium and iodine, has been shown to undergo rearrangement when treated with sodamide in liquid ammonia to give 3-aminodibenzothiophene. This rearrangement reaction provides a means for obtaining otherwise generally inaccessible 3-substituted dibenzothiophenes.

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[8] Vaughn, Vogt and Nieuwland, THIS JOURNAL, **56**, 2120 (1934).

[9] (a) Courtot and Rochebouet, *Bull. soc. chim.*, (5) **4**, 1972 (1937); see, also, ref. 6 in Gilman, Jacoby and Pacevitz, *J. Org. Chem.*, **3**, 120 (1938); (b) Courtot and Bastani, *Compt. rend.*, **203**, 197 (1936); see, also, Courtot, *ibid.*, **198**, 2260 (1934).

[10] This procedure was first used by G. A. Martin and the yield reported was 98.5%.

[11] Gilman, Wilkinson, Fishel and Myers, THIS JOURNAL, **45**, 150 (1923).