

**2-Bromo-4-dibenzofurancarboxylic Acid.**—Five hundredths mole of *n*-butyllithium, prepared in the usual manner,<sup>11</sup> was added to 12.4 g. (0.05 mole) of 2-bromodibenzofuran dissolved in 50 cc. of ether. After refluxing this solution for one hour, an equal volume (150 cc.) of benzene was added and the refluxing continued, with stirring, for nine hours. Subsequent to carbonation and crystallization from acetic acid there was obtained 3.5 g. (24% yield) of 2-bromo-4-dibenzofurancarboxylic acid, m. p. 285–286°.

*Anal.* Calcd. for C<sub>13</sub>H<sub>7</sub>O<sub>3</sub>Br: neut. equiv., 291.1. Found: neut. equiv., 291.6.

In addition, dibenzofuran was isolated. The weight of crude product was 2.1 g., and from this was obtained 1 g. or a 12% yield of pure dibenzofuran.

The authors are grateful to W. Langham for suggestions concerning this metalation reaction.

**Methyl 2-Bromo-4-dibenzofurancarboxylate.**—Fifteen-tenths gram of 2-bromo-4-dibenzofurancarboxylic acid, dissolved in 100 cc. of dry ether, was methylated with an excess of diazomethane. Crystallization from glacial acetic acid gave 0.45 g. (87%) of methyl 2-bromo-4-dibenzofurancarboxylate which melted at 189–189.5°.

*Anal.* Calcd. for C<sub>14</sub>H<sub>9</sub>O<sub>3</sub>Br: Br, 26.11. Found: Br, 26.13. Methyl 2-bromo-6-dibenzofurancarboxylate melts at 165–166°.<sup>7</sup>

**Debromination of 2-Bromo-4-dibenzofurancarboxylic Acid.**—One-tenth gram of 2-bromo-4-dibenzofurancarboxylic acid, suspended in 20 cc. of absolute ethanol with 1 g. of palladium-calcium carbonate catalyst,<sup>12</sup>

(11) Gilman, Zoellner and Selby, *THIS JOURNAL*, **55**, 1252 (1933).

(12) Busch and Stöve, *Ber.*, **49**, 1063 (1916).

was allowed to stand at room temperature under hydrogen at a gage pressure of 30 pounds for twelve hours. The dehalogenation was quantitative, and the 4-dibenzofurancarboxylic acid obtained melted at 106–107°. A mixed melting point determination with an authentic specimen of 4-dibenzofurancarboxylic acid showed no depression.

**2-Bromo-4-methyldibenzofuran.**—One-tenth mole (12.6 g.) of dimethyl sulfate was added dropwise to a cooled reaction mixture obtained from the metalation of 0.05 mole of 2-bromodibenzofuran by *n*-butyllithium. After thirty minutes of refluxing the excess dimethyl sulfate was destroyed by sodium hydroxide and, following removal of the solvent, the product was subjected to fractional distillation under reduced pressure. From the fraction which boiled at 145–180° at 6 mm. (6 g.), there was obtained after repeated crystallizations from petroleum ether, 0.1 g. (0.8%) of 2-bromo-4-methyldibenzofuran melting at 105–106°. A mixed melting point determination with an authentic sample showed no depression.

### Summary

Metalation of dibenzofurans invariably takes place ortho to an ether linkage, but need not involve an available 4- or 6-position.

Homonuclear metalation occurs with 2-bromodibenzofuran to give 2-bromo-4-dibenzofuryllithium.

Oxidation of some aryllithium compounds gives coupling or biaryl products.

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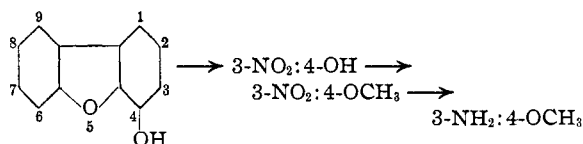
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

## Dibenzofuran. X. Aminohydroxy Derivatives

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### Introduction

The 3-amino-4-methoxydibenzofuran necessary to establish the structure of 3-hydroxy-4-methoxydibenzofuran described in the preceding paper<sup>1</sup> was synthesized as follows



3-Nitro-4-hydroxydibenzofuran was also prepared by means of a diazo reaction of 3-nitro-4-aminodibenzofuran which, in turn, was synthesized by the following sequence of reactions:

(1) Paper IX, Gilman, Cheney and Willis, *THIS JOURNAL*, **61**, 951 (1939).

4-NHCOCH<sub>3</sub> → 3-NO<sub>2</sub>:4-NHCOCH<sub>3</sub> → 3-NO<sub>2</sub>:4-NH<sub>2</sub>. The nitro group in the nitro-4-aminodibenzofuran was shown to be in the 3-position by replacing the amino group by hydrogen via diazotization and establishing the identity of the resulting 3-nitrodibenzofuran. Obviously, this does not tell whether the nitro group was in the same ring with the amino group or in the other benzenoid nucleus. This question was answered by reducing the nitro-amine to the diamine and then forming the phenazine derivative with phenanthraquinone.

Although 4-hydroxydibenzofuran directs the entering nitro group to the ortho or 3-position, the related 4-methoxydibenzofuran orients the nitro group to the para or 1-position to give 1-nitro-

4-methoxydibenzofuran. However, bromination of 4-hydroxydibenzofuran and 4-alkoxydibenzofurans gives the 1-bromo-4-hydroxy(or alkoxy)-dibenzofurans.<sup>2</sup> The different orientation effects of hydroxy and alkoxy groups in nitration and in bromination find their counterparts in some nuclear substitution reactions of related benzene types. For example, nitration of *o*-methoxyphenol introduces the nitro group ortho to the hydroxyl<sup>3</sup>; but nitration of *o*-dimethoxybenzene introduces the nitro group para to one of the methoxy groups.<sup>4</sup> Bromination of *o*-methoxyphenol, unlike nitration, introduces the bromine para to the hydroxyl group.<sup>5</sup>

### Experimental Part

**3-Nitro-4-acetaminodibenzofuran.**—To a suspension of 2 g. (0.0089 mole) of 4-acetaminodibenzofuran in 10 cc. of acetic anhydride cooled to  $-10^{\circ}$  was added slowly 1 cc. (0.0238 mole) of fuming nitric acid (sp. gr. 1.49). Two crystallizations from glacial acetic acid and one from ethanol gave pale yellow needles, melting at  $238^{\circ}$ ; yield 35%.

*Anal.* Calcd. for  $C_{14}H_{10}O_4N_2$ : N, 10.35. Found: N, 10.50 and 10.52.

Under other conditions, the principal product in the nitration of 4-acetaminodibenzofuran is 1-nitro-4-acetaminodibenzofuran, the preparation of which will be described in a subsequent paper.

**3-Nitro-4-aminodibenzofuran.**—One-half gram of 3-nitro-4-acetaminodibenzofuran was refluxed for three hours with a mixture of 15 cc. of concd. hydrochloric acid and 15 cc. of ethanol. The free nitroamine, which was liberated by ammonium hydroxide, was obtained as deep yellow needles melting at  $185-186^{\circ}$  after crystallization from ethanol.

*Anal.* Calcd. for  $C_{12}H_8O_3N_2$ : N, 12.28. Found: N, 12.28 and 12.42.

The amino group was replaced by hydrogen, by diazotization of a solution of the nitroamine in sulfuric acid and ethanol, to give 3-nitrodibenzofuran.

**3-Amino-4-acetaminodibenzofuran.**—Catalytic reduction of 3-nitro-4-acetaminodibenzofuran gave a quantitative yield of silvery, transparent plates melting at  $236-237^{\circ}$  after crystallization from methanol.

*Anal.* Calcd. for  $C_{14}H_{12}O_2N_2$ : N, 11.68. Found: N, 11.60 and 11.77.

**3,4-Diacetaminodibenzofuran.**—Acetylation of 3-amino-4-acetaminodibenzofuran by refluxing a benzene solution with the calculated quantity of acetic anhydride gave colorless needles of the diacetamino compound which melted at  $257^{\circ}$  after crystallization from glacial acetic acid.

*Anal.* Calcd. for  $C_{16}H_{14}O_4N_2$ : N, 9.93. Found: N, 9.92 and 9.89.

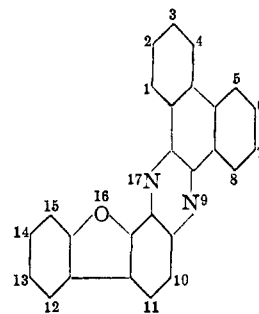
(2) Studies by P. R. Van Ess and P. T. Parker.

(3) Kauffmann and Franck, *Ber.*, **39**, 2725 (1906).

(4) Cardwell and Robinson, *J. Chem. Soc.*, **107**, 256 (1915).

(5) Robertson, *ibid.*, **93**, 791 (1908).

**Dibenzo[*a,c*]benzofuro[2,3-*b*]phenazine.**—A suspension of 0.5 g. of 3-nitro-4-aminodibenzofuran in 50 cc. of ethanol was reduced, using the Raney nickel catalyst. The alcoholic solution of the diamine, which was colorless, was filtered from the catalyst and concentrated to 3 cc. During the heating, the solution turned yellow, then green and finally a deep purple. To this solution was added a hot solution of 0.1 g. of phenanthraquinone in 3 cc. of glacial acetic acid. The greenish-yellow precipitate which formed at once was filtered; the filtrate was treated with more phenanthraquinone; the precipitates were combined, and then crystallized successively from toluene, xylene and glacial acetic acid to give a yellow crystalline powder melting at  $277-278^{\circ}$ .



*Anal.* Calcd. for  $C_{22}H_{14}ON_2$ : N, 7.57. Found: N, 7.54 and 7.70.

**3-Nitro-4-hydroxydibenzofuran. A.** From 4-hydroxydibenzofuran.—To a solution of 2 g. of 4-hydroxydibenzofuran in 15 cc. of acetic anhydride, cooled to  $-12^{\circ}$ , was added dropwise and with vigorous stirring a mixture of 0.5 cc. of fuming nitric acid (sp. gr. 1.5) and 5 cc. of acetic anhydride. Crystallization from acetic acid followed by dilute ethanol gave a 25% yield of light yellow needles, m. p.  $193^{\circ}$ .

*Anal.* Calcd. for  $C_{12}H_7NO_4$ : N, 6.1. Found: N, 5.9.

**B. From 3-Nitro-4-aminodibenzofuran.**—The diazonium solution from 0.5 g. of the nitroamine hydrochloride was added to a boiling solution of 75 g. of copper sulfate and 5 cc. of concd. sulfuric acid in 300 cc. of water to give the 3-nitro-4-hydroxydibenzofuran.

**3-Nitro-4-methoxydibenzofuran.**—Diazomethane and 3-nitro-4-hydroxydibenzofuran gave a 65% yield of yellow nitromethoxy compound melting at  $129.5^{\circ}$  after crystallization from petroleum ether (b. p.  $60-68^{\circ}$ ).

*Anal.* Calcd. for  $C_{13}H_9O_4N$ : N, 5.76. Found: N, 5.58.

**3-Amino-4-methoxydibenzofuran.**—Alcohol solutions of the nitromethoxy compound were reduced (Raney nickel catalyst) in 80% yields to the aminomethoxy compound which melted at  $75.5^{\circ}$  after crystallization from petroleum ether (b. p.  $60-68^{\circ}$ ).

*Anal.* Calcd. for  $C_{13}H_{11}O_2N$ : N, 6.57. Found: N, 6.41 and 6.53.

The hydrochloride crystallizes from dilute hydrochloric acid as fine colorless needles which do not melt below  $230^{\circ}$ .

**3,8-Dinitro-4-hydroxydibenzofuran.**—A mixture of 5 cc. of concd. nitric acid and 5 cc. of glacial acetic acid was added rapidly with stirring to 2 g. of 4-hydroxydibenzofuran in 25 cc. of glacial acetic acid at about  $60^{\circ}$ . The orange-red crystals melted at  $225^{\circ}$  (dec.) after crystallization from glacial acetic acid; yield 77%.

*Anal.* Calcd. for  $C_{12}H_6O_6N_2$ : N, 10.2. Found: N, 10.3.

An approximately theoretical yield of the same dinitrophenol was obtained when 3-nitro-4-hydroxydibenzofuran

was nitrated under corresponding conditions. This reaction establishes the position of the 3-nitro group in the dinitro compound, and the 8-position is assigned to the other nitro group on the basis of general observations on heteronuclear nitrations.<sup>6</sup>

**3,8-Dinitro-4-methoxydibenzofuran.**—The dinitrophenol was methylated in 83% yield by diazomethane to give orange colored crystals melting at 177° after crystallization from a mixture of chloroform and petroleum ether.

*Anal.* Calcd. for  $C_{13}H_9O_5N_2$ : N, 9.72. Found: N, 9.80.

**Dinitro-2-hydroxydibenzofuran.**—Addition, with stirring, of a mixture of 7.5 cc. of concd. nitric acid and 7.5 cc. of glacial acetic to 3 g. of 2-hydroxydibenzofuran in 35 cc. of glacial acetic acid warmed to 60° gave an 80% yield of yellow dinitrophenol melting at 240° (dec.) after crystallization from a mixture of ethanol and glacial acetic acid. By analogy with other nuclear substitution reactions the compound is probably 3,8-dinitro-2-hydroxydibenzofuran.

*Anal.* Calcd. for  $C_{12}H_9O_6N_2$ : N, 10.2. Found: N, 10.0.

**1-Nitro-4-methoxydibenzofuran.**—To a solution of 7 g. of 4-methoxydibenzofuran in 40 cc. of acetic anhydride cooled to -15 to -20° was added slowly, and with stirring, a mixture of 2 cc. of fuming nitric acid and 40 cc. of acetic anhydride. The colorless product melted at 155° after crystallization from methanol; yield 18%.

*Anal.* Calcd. for  $C_{13}H_9O_4N$ : N, 5.76. Found: N, 5.75 and 5.76.

**1-Amino-4-methoxydibenzofuran.**—Reduction of the corresponding nitromethoxy compound using Raney nickel catalyst is almost quantitative. The amine is best purified through the hydrochloride or hydrobromide. The colorless hydrobromide does not melt at 250°, and when treated with ammonium hydroxide gives the free base which crystallizes from petroleum ether as pale lavender crystals melting at 104°.

*Anal.* Calcd. for  $C_{13}H_{11}O_2N$ : N, 6.57;  $OCH_3$ , 14.6. Found: N, 6.53 and 6.63;  $OCH_3$ , 14.4 and 14.5.

The structure of the aminomethoxy compound (as well as that of the nitromethoxy compound) was established by heating 2 g. of 1-bromo-4-methoxydibenzofuran<sup>7</sup> in a sealed tube with 15 cc. of concd. ammonium hydroxide and 2 g. of cuprous bromide for six hours at 230–240°. The 1-amino-4-methoxydibenzofuran obtained was identical with the reduction product of the nitromethoxy compound.

**1-Nitro-4-ethoxydibenzofuran.**—The 4-ethoxydibenzofuran prepared from 4-hydroxydibenzofuran, diethyl sul-

fate and sodium hydroxide distilled at 150–155° (3 mm.). Nitration of 2.8 g. in 10 cc. of acetic anhydride cooled to -19° was effected by the slow addition of 0.75 cc. of fuming nitric acid in 15 cc. of acetic anhydride. The fine yellow needles melted at 135–135.5° after crystallization from acetic acid; yield 28%.

*Anal.* Calcd. for  $C_{14}H_{11}O_4N$ : N, 5.45. Found: N, 5.37.

**1-Amino-4-ethoxydibenzofuran.**—The nitroethoxy compound was reduced in the presence of the Raney catalyst and purification of the amine was effected through the slightly soluble hydrochloride. The free aminoethoxy compound melts at 91°.

*Anal.* Calcd. for  $C_{14}H_{13}O_2N$ : N, 6.16. Found: N, 5.90.

The colorless needles of 1-acetamino-4-ethoxydibenzofuran, prepared by acetylating in benzene with acetic anhydride, melt at 218.5° after crystallization from ethanol.

*Anal.* Calcd. for  $C_{16}H_{15}O_2N$ : N, 5.20. Found: N, 5.50 and 5.50.

**3-Diethylaminodibenzofuran.**—This compound was prepared earlier,<sup>8</sup> but was analyzed as the hydrochloride because of difficulty in obtaining a solid diethylamino compound. To a mixture of 28.4 g. (0.182 mole) of ethyl iodide, 24 g. of sodium carbonate and 250 cc. of water was added 15 g. (0.082 mole) of 3-aminodibenzofuran. The mixture was refluxed for forty-eight hours, cooled, made definitely alkaline by the addition of a small quantity of potassium hydroxide, and extracted with ether. The amine hydrochloride was precipitated from the ether by hydrogen chloride, and after crystallization was treated with ammonium hydroxide to give the free base which melted at 68° after crystallization from ethanol; yield 70%.

*Anal.* Calcd. for  $C_{16}H_{17}ON$ : N, 5.86. Found: N, 6.00.

It is quite certain that the same compound can be prepared by the action of diethylaminolithium on 3-bromodibenzofuran, a procedure used subsequently for the synthesis of 4-diethylaminodibenzofuran.

### Summary

Nitration of 4-hydroxydibenzofuran and of 4-acetaminodibenzofuran introduces a nitro group into the ortho or 3-position. However, nitration of 4-methoxydibenzofuran goes para to yield 1-nitro-4-methoxydibenzofuran.

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(6) Gilman, Van Ess and Hayes, *THIS JOURNAL*, **61**, 643 (1939).

(7) Kindly provided by P. R. Van Ess.

(8) Kirkpatrick and Parker, *THIS JOURNAL*, **57**, 1123 (1935).