

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Dibenzofuran. XI. Substituents in the 1-Position*

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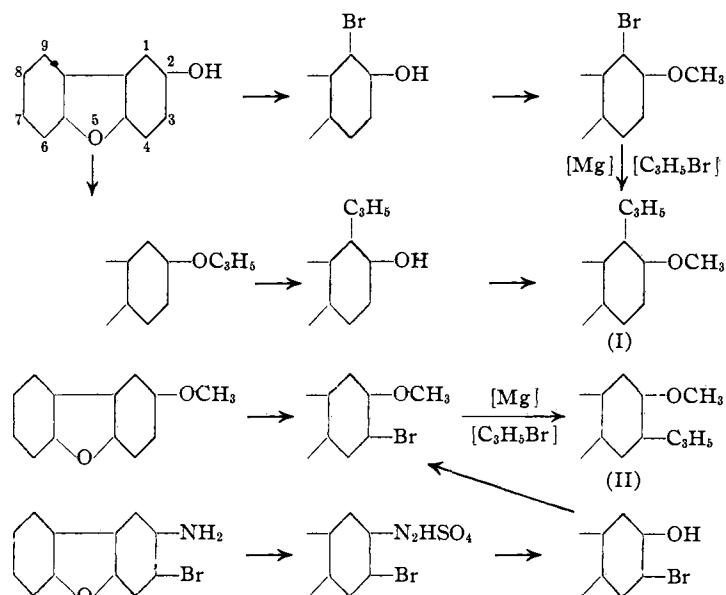
Introduction

Direct nuclear substitution of dibenzofuran permits introduction of mono-substituents in the 2-, 3- and 4-positions, but not in the 1-position. No ring-closure synthesis of a mono-1-substituted type has so far been successful.¹ We are now reporting syntheses of a number of simple and poly-functional dibenzofurans having a substituent in the 1-position.

Bromination of 2-hydroxydibenzofuran gives a bromo-2-hydroxydibenzofuran which might have the bromine in the 8-position, by analogy with the formation of 2,8-dibromodibenzofuran from 2-bromodibenzofuran,² or in the 1- or 3-position, in consideration of the strong ortho-para orienting influence of the hydroxyl group. First, 2-methoxy-8-bromodibenzofuran was synthesized by a reliable ring closure method (see Experimental Part for details), and shown to be unlike the methyl ether of bromo-2-hydroxydibenzofuran. Second, 2-hydroxy-3-bromodibenzofuran, prepared from authentic 2-amino-3-bromodibenzofuran,³ was shown to be different from the bromination product of 2-hydroxydibenzofuran. Accordingly, by a process of exclusion, the bromo-phenol must be 1-bromo-2-hydroxydibenzofuran.

Because some additional evidence seemed desirable, another series of reactions was examined. The allyl ether of 2-hydroxydibenzofuran was rearranged to an allyl-2-hydroxydibenzofuran. In accordance with Claisen's rule⁴ the allyl group must have rearranged to one of the available ortho positions to give either 1-allyl-2-hydroxydibenzofuran or 3-allyl-2-hydroxy-

dibenzofuran. The possibility of any para rearrangement is excluded because of the absence of a para hydrogen in 2-hydroxydibenzofuran.⁵ By another process of elimination, it was demonstrated that the allylphenol must be 1-allyl-2-hydroxydibenzofuran. This was accomplished by synthesizing 3-allyl-2-methoxydibenzofuran (II) by reliable reactions on compounds of established structure, and showing it to be unlike the methyl ether of the allylphenol (I) obtained by rearrangement. The following series of reactions indicate the several transformations correlating the rearrangement of the allyl ether of 2-hydroxydibenzofuran with the bromination of 2-hydroxydibenzofuran.



The simple 1-substituted dibenzofurans were prepared from 1-bromodibenzofuran which was synthesized by the following reactions.

Neither 2- nor 3-acetaminodibenzofuran directs bromine to the 1-position.^{6a} The structure of the

(5) See, Kawai, *Sci. Papers Inst. Phys. Chem. Res. (Tokyo)*, **3**, 263 (1926), for the formation of a mixture of 3-allyl- and 4-allyl catechol from the monoallyl ether of catechol. Even in this unusual case where there was not only an ortho-blocking group but also an available para-position, about one-half of the rearrangement took place ortho to one of the hydroxyls.

(6) (a) Bromination of 2-acetaminodibenzofuran gives 2-acetamino-3-bromodibenzofuran; and bromination of 3-acetaminodibenzofuran gives 2-bromo-3-acetaminodibenzofuran (see ref. 3); (b) bromination of 2-methoxydibenzofuran gives predominantly 2-methoxy-3-bromodibenzofuran.

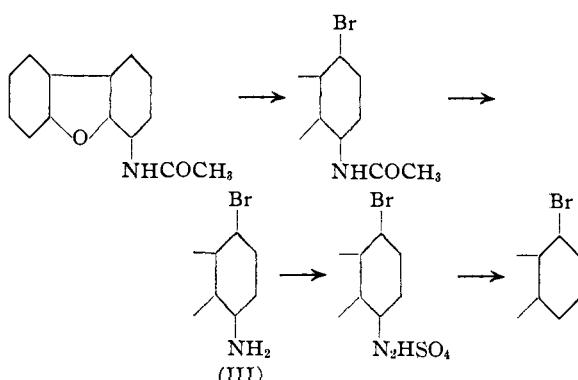
(*) Paper X, *THIS JOURNAL*, **61**, 954 (1939).

(1) A number of disubstituted dibenzofurans having one substituent in the 1-position have been prepared by ring closures of biphenyl derivatives. See, for example, Sugii and Shindo, *J. Pharm. Soc. (Japan)*, **54**, 829 (1934) [C. A., **29**, 790 (1935)]; I. G. Farbenind. A.-G., British Patent, 470,021, Aug. 9, 1937 [C. A., **32**, 1487 (1938)] and French Patent, 816,719, Aug. 16, 1937 [C. A., **32**, 2145 (1938)].

(2) McCombie, Macmillan and Scarborough, *J. Chem. Soc.*, 529 (1931).

(3) Gilman, Brown, Bywater and Kirkpatrick, *THIS JOURNAL*, **56**, 2473 (1934).

(4) Claisen and Eisleb, *Ann.*, **401**, 23 (1913).



1-bromodibenzofuran was established by first debrominating to prove an intact dibenzofuran nucleus, and then showing that the bromo compound was unlike the other three possible and known monobromodibenzofurans. In like manner the other 1-substituted dibenzofurans derived from 1-bromodibenzofuran were shown to differ from their corresponding isomers. It is now possible to compare the melting points of all isomeric monobromo, -hydroxy, -amino, -acetamino, -carboxy, and -carbomethoxy compounds, and a table in the Experimental Part gives this information.

Although 4-acetaminodibenzofuran is the only acetaminodibenzofuran which brominates in the 1-position, both 2-hydroxydibenzofuran and 4-hydroxydibenzofuran (as well as their methyl ethers) direct bromine to the 1-position.^{6b} No isomers were isolated from the monobromination of 4-acetamino-, 4-hydroxy-, and 4-methoxydibenzofuran; but bromination of 2-hydroxydibenzofuran gave a very small quantity of the corresponding 3-bromo isomer, and bromination of 2-methoxydibenzofuran gave principally the 3-bromo compound and only a very small amount of the 1-bromo isomer. It is interesting that nitration differs in a number of respects from bromination. For example, nitration of 4-hydroxydibenzofuran gives 3-nitro-4-hydroxydibenzofuran, whereas nitration of 4-methoxydibenzofuran yields 1-nitro-4-methoxydibenzofuran.^{7a} And nitration of 4-acetaminodibenzofuran in acetic anhydride at low temperatures gives 3-nitro-4-acetaminodibenzofuran, but nitration in acetic acid at 60° gives 1-nitro-4-acetaminodibenzofuran.^{7b} Both bromination and nitration of a compound like methyl 4-dibenzofurancarboxylate, in which a meta director is present, lead to

(7) (a) Gilman, Jacoby and Swislawsky, THIS JOURNAL, **61**, 954 (1939); (b) unpublished studies.

heteronuclear substitution⁸ as is the case with all monosubstituted dibenzofurans having a group which orients meta.

The problem of homo- and heteronuclear substitutions in dibenzofuran is intimately associated with the structures of the intermediate compounds used in the synthesis of the simple 1-substituted dibenzofurans. For example, the bromo-4-aminodibenzofuran (Formula III) used in the synthesis of 1-bromodibenzofuran might be either 1-bromo-4-aminodibenzofuran or 9-bromo-4-aminodibenzofuran, for each compound would give 1-bromodibenzofuran on deamination. The Experimental Part describes steps leading to an unsuccessful attempt to prepare an authentic 1,4-disubstituted dibenzofuran by ring closure. This is additional evidence⁹ for the difficulty, if not impossibility, of effecting syntheses of 4-substituted dibenzofurans by phenyl ether ring closures if the nitro group through which the ring is ultimately closed by reduction and diazotization is not in the same nucleus with the group which is to be the 4-substituent in the dibenzofuran product. However, because strong ortho-para directing groups (like amino and hydroxy) have always given homonuclear substitution, whereas meta directors have always given heteronuclear substitution, it is extremely probable that the bromine, for example, in the bromination product of 4-acetamino- and of 4-hydroxydibenzofuran, is in the homo 1-position and not in the hetero 9-position. An indication that substitution of 4-acetaminodibenzofuran goes homonuclearly is the behavior of 1,4-diaminodibenzofuran (prepared from 1-bromo-4-aminodibenzofuran^{7b}) to air. This diamine, like the 2,3- and 3,4-diaminodibenzofurans, colors rapidly in air. The heterosubstituted 2,7-, 3,7- and 2,8-diaminodibenzofurans are very stable in air. These several observations conform with the general principle that ortho or para diamines are more sensitive to air than other isomeric diamines.

Experimental Part

2-Hydroxydibenzofuran.—The method used previously for this synthesis (oxidation of 2-dibenzofurylmagnesium bromide¹⁰) was found to be less satisfactory than a procedure adapted from a recent patent.¹¹ No catalyst was mentioned in the abstract of the patent, and we were successful in getting any 2-hydroxydibenzofuran only after

(8) Gilman, Van Ess and Hayes, *ibid.*, **61**, 643 (1939).

(9) See Ref. 8. Also unpublished observations by Paul T. Parker.

(10) Gilman, Bywater and Parker, THIS JOURNAL, **57**, 885 (1935).

(11) I. G. Farbenind. A.-G., German Patent 606,350 [C. A., **29**, 1434 (1935)].

experimenting with several catalysts. In a typical preparation, 100 g. (0.405 mole) of 2-bromodibenzofuran, 85 g. of sodium hydroxide in 100 cc. of water, 30 g. of copper sulfate in 150 cc. of water, 100 g. of copper turnings, and 10 g. of copper bronze were heated in a steel bomb¹² for twelve hours at 240°. The phenol was isolated by acidification with hydrochloric acid, and the yield of crude brown solid melting at 117–120° varied between 56–75%. Distillation was found to be the most convenient method of purification; 100 g. of the crude was distilled at 175–180° (5 mm.) to give 78 g. of colorless product melting at 125–130°. One crystallization from water was sufficient to raise the melting point to 134°.

Bromination of 2-Hydroxydibenzofuran.—To a solution of 18.4 g. (0.10 mole) of 2-hydroxydibenzofuran in 300 cc. of glacial acetic acid was added 100 cc. of a molar solution of bromine in glacial acetic acid, dropwise and with shaking, at room temperature. After precipitation by water and crystallization from hot ethanol and then from a mixture of 180 cc. of benzene and 90 cc. of petroleum ether (b. p. 60–68°) there was obtained a 43% yield of 1-bromo-2-hydroxydibenzofuran melting at 123–123.5°.

Anal. Calcd. for $C_{12}H_7O_2Br$: Br, 30.39. Found: Br, 30.74 and 30.58.

Treatment of the bromophenol with dimethyl sulfate and sodium hydroxide gave a 76% yield of 1-bromo-2-methoxydibenzofuran which melted at 117–118° after crystallization from ethanol.

Anal. Calcd. for $C_{13}H_9O_2Br$: Br, 28.85. Found: Br, 29.12 and 29.35.

Bromination of 2-Methoxydibenzofuran.—First, 2-methoxydibenzofuran was prepared from 14.6 g. (0.08 mole) of 2-hydroxydibenzofuran by dimethyl sulfate and sodium hydroxide. The yield was 10.1 g. of compound distilling at 164–165° (6 mm.) and melting at 46–47° after crystallization from petroleum ether.

Anal. Calcd. for $C_{13}H_{10}O_2$: C, 78.76; H, 5.09. Found: C, 79.18; H, 5.15.

Bromination of 10 g. of 2-methoxydibenzofuran in glacial acetic acid gave 4.6 g. or a 33% yield of 2-methoxy-3-bromodibenzofuran which crystallized from benzene as needles melting at 171–172°. The same bromomethoxy compound was isolated in very small quantities by methylating the mother liquors from which 1-bromo-2-hydroxydibenzofuran was obtained by bromination of 2-hydroxydibenzofuran. The methylation by dimethyl sulfate was carried out after several unsuccessful attempts to isolate the 2-hydroxy-3-bromodibenzofuran.

Anal. Calcd. for $C_{13}H_9O_2Br$: Br, 28.85. Found: Br, 28.94 and 29.05.

The mother liquors (from the bromination of 2-methoxydibenzofuran) gave a solid which when dissolved in a mixture of benzene and petroleum ether deposited, after slow evaporation, large prismatic and small needle crystals. The prismatic crystals were separated mechanically and were found to melt at 117–118° and to be identical with 1-bromo-2-methoxydibenzofuran (see below).

2 - Hydroxy - 3 - bromodibenzofuran.—2 - Acetamino - 3 - bromodibenzofuran was prepared previously by the

bromination of 2-diacetaminodibenzofuran.³ We observed that the more conveniently prepared 2-acetamino-dibenzofuran also could be used. First, 2-aminodibenzofuran was prepared by the high temperature amination of 2-bromodibenzofuran.³ Then 2-acetamino-dibenzofuran was synthesized in accordance with W. G. Bywater's directions by treating the amine in benzene with acetic anhydride. Bromination of the acetamino compound in glacial acetic acid gave a 16.4% yield of 2-acetamino-3-bromodibenzofuran. Alcoholic potassium hydroxide, rather than alcoholic hydrochloric acid,³ was used for hydrolysis; the yield of 2-amino-3-bromodibenzofuran was 96%.

Diazotization of the amino-bromo compound was effected in accordance with the procedure of Misslin,¹³ used for other amines; and the diazonium group was replaced by hydroxyl by adding to a boiling aqueous solution of copper sulfate.¹⁴ The 2-hydroxy-3-bromodibenzofuran was obtained in a 13% yield as needles melting at 143–144° after crystallization from 50% ethanol.

Anal. Calcd. for $C_{12}H_7O_2Br$: Br, 30.39. Found: Br, 30.66 and 30.71.

Methylation by dimethyl sulfate and sodium hydroxide gave 2-methoxy-3-bromodibenzofuran (m. p. 172°), identical with the 172° melting bromination product of 2-methoxydibenzofuran.

2-Allyloxydibenzofuran.—In accordance with Claisen's⁴ general procedure for the synthesis of allyl ethers, a mixture of 21.7 g. (0.118 mole) of 2-hydroxydibenzofuran, 0.13 mole of anhydrous potassium carbonate, 0.130 mole of allyl bromide and 30 cc. of acetone was heated at gentle reflux for six hours. In two preparations, the yields of 2-allyloxydibenzofuran were 72 and 82%. The ether distilled at 178–180° (4 mm.), without rearrangement as evidenced by insolubility in dilute sodium hydroxide; n^{25}_{D} 1.6248 and d^{25}_4 1.1553.

Anal. Calcd. for $C_{13}H_{12}O_2$: C, 80.32; H, 5.40. Found: C, 80.32; H, 5.45.

1 - Allyl - 2 - hydroxydibenzofuran.—2 - Allyloxydibenzofuran (0.164 mole) was rearranged by heating (metal bath) to 220°, when an exothermic reaction took place which rapidly raised the inner temperature to 230°. The outer temperature was raised to 230° and held there for fifteen minutes. All of the product was soluble in dilute alkali, and recrystallization from petroleum ether (b. p. 60–68°) gave a 34% yield of needles melting at 83°. In another experiment, the crude product was first purified by distillation (b. p. 173° at 5 mm.). No isomers were isolated.

Anal. Calcd. for $C_{15}H_{12}O_2$: C, 80.32; H, 5.40. Found: C, 80.51; H, 5.50.

1-Allyl-2-methoxydibenzofuran was prepared from the allylphenol by means of dimethyl sulfate. The yield was quantitative, and the product crystallized from petroleum ether (b. p. 28–38°) as prisms melting at 67–68°.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.64; H, 5.93. Found: C, 80.42; H, 5.62.

The same allyl-methoxy compound was synthesized

(13) Misslin, *Helv. Chim. Acta*, **3**, 626 (1910).

(14) Tatematsu and Kubota, *Bull. Chem. Soc. Japan*, **9**, 448 (1934).

(12) The authors are grateful to Dr. F. E. Brown for the use of the bomb and assistance in its operation.

in 74% yield by the reaction of allyl bromide with the Grignard reagent prepared from 1-bromo-2-methoxydibenzofuran.

1-Propenyl-2-hydroxydibenzofuran was prepared by heating 1-allyl-2-hydroxydibenzofuran in methyl alcoholic potassium hydroxide. Crystallization from petroleum ether, followed by crystallization from dilute methanol, gave needles melting at 14–95°.

Anal. Calcd. for $C_{10}H_{10}O$: C, 80.32; H, 5.40. Found: C, 80.27; H, 5.37.

2-Methoxy-3-allyldibenzofuran.—The Grignard reagent of the 172° melting 2-methoxy-3-bromodibenzofuran was treated with an excess of allyl bromide. The yield of 2-methoxy-3-allyldibenzofuran was 60%; b. p., 158–159° (4 mm.); n^{25}_{D} 1.6261; d^{25}_{4} 1.1488.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.64; H, 5.93. Found: C, 80.03 and 79.90; H, 5.79 and 5.75.

1-Hydroxy-2-methoxydibenzofuran.—A mixture of Grignard reagents of 1-bromo-2-methoxydibenzofuran and *n*-butyl bromide was prepared by the reaction of 42.4 g. (0.15 mole) of the former halide in 75 cc. of ether and 75 cc. of benzene, 20.6 g. (0.15 mole) of the latter halide in 100 cc. of dry ether, and 10 g. of magnesium turnings. Oxygen was then slowly passed over the surface of the mixture which was stirred and cooled to 0°. The 71% yield of 1-hydroxy-2-methoxydibenzofuran is unusually good for a procedure of this kind.¹⁵ Recrystallization from 30% ethanol followed by crystallization from petroleum ether gave needles melting at 111–111.5°.

Anal. Calcd. for $C_{13}H_{10}O_3$: C, 72.87; H, 4.71. Found: C, 72.88; H, 4.61.

1-Hydroxy-2-methoxydibenzofuran is rather unstable in alkaline solution: a deep brown color is developed and a dark brown insoluble substance is deposited slowly.¹⁶ 1-Hydroxy-4-methoxydibenzofuran does not show this instability in alkali. In an orienting experiment, hydroiodic acid with 1-hydroxy-2-methoxydibenzofuran gave an alkali insoluble purple resin.

1,2-Dimethoxydibenzofuran.—A mixture of 1.75 g. (0.0077 mole) of 1-hydroxy-2-methoxydibenzofuran, anhydrous potassium carbonate, methyl iodide and acetone was refluxed on a water-bath for eight hours. The yield of 1,2-dimethoxydibenzofuran was 83%, and the compound melted at 79° after crystallization from petroleum ether (b. p. 28–38°).

Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.65; H, 5.30. Found: C, 73.23; H, 5.13.

2-Methoxy-1-dibenzofurancarboxylic Acid.—The Grignard reagent of 1-bromo-2-methoxydibenzofuran was carbonated by solid carbon dioxide to yield 70% of the methoxy acid which melted at 156–157°, and crystallized as needles from benzene.

Anal. Calcd. for $C_{14}H_{10}O_4$: C, 69.40; H, 4.16. Found: C, 69.37; H, 4.05.

The corresponding methyl 2-methoxy-1-dibenzofurancarboxylate, prepared¹⁷ from the methoxy acid and diazomethane, melted at 99.5–100°.

(15) Ivanoff, *Bull. soc. chim.*, **39**, 47 (1926).

(16) Bezdík and Friedländer, *Monatsh.*, **30**, 283 (1909), have reported a related behavior with 2-methoxy-1-naphthol.

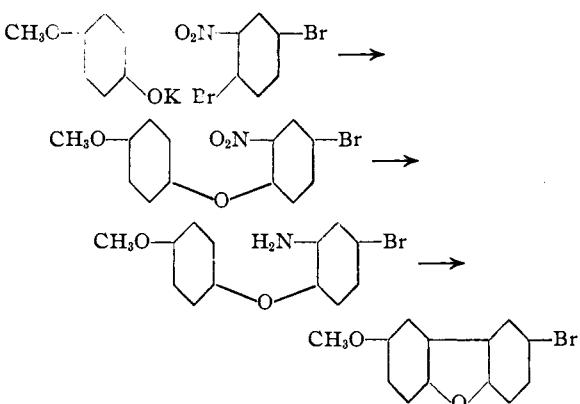
(17) By R. L. Bebb. See also, Gilman and Bebb, *THIS JOURNAL*, **61**, 109 (1939).

2-Methoxy-3-dibenzofurancarboxylic Acid.—A 60% yield of this acid was prepared from the Grignard reagent of 2-methoxy-3-bromodibenzofuran and solid carbon dioxide. Crystallization from a large volume of ethanol gave needles melting at 206–207°.

Anal. Calcd. for $C_{14}H_{10}O_4$: C, 69.40; H, 4.16. Found: C, 69.22; H, 4.05.

The corresponding methyl 2-methoxy-3-dibenzofurancarboxylate¹⁷ prepared from the acid and diazomethane melted at 122.5°.

2-Methoxy-8-bromodibenzofuran.—This compound was prepared by a ring closure synthesis used by McCombie and co-workers² for some other 2,8-disubstituted dibenzofurans. The sequence of reactions is



To the monomethyl ether of hydroquinone¹⁸ in ethanol was added the calculated quantity of potassium hydroxide, and the potassium salt was thrown out by diluting with ether. The potassium *p*-methoxyphenoxide (8.8 g., 0.054 mole) and 1,4-dibromo-2-nitrobenzene (15.26 g., 0.054 mole) were heated at 170° for two hours. The resulting crude 2-nitro-4-bromo-4'-methoxydiphenyl ether (12.9 g.) was reduced by stannous chloride to the corresponding amine, and the hydrochloride of the amine was diazotized. Ring closure was then effected in the customary manner by adding the diazonium chloride solution dropwise to 200 cc. of boiling 50% sulfuric acid. The yield of 2-methoxy-8-bromodibenzofuran was 0.94 g. or 8%, and the compound melted at 92.5° after crystallization from ethanol.

*Anal.*¹⁹ Calcd. for $C_{12}H_8OBr$: Br, 28.85; OCH_3 , 11.19. Found: Br, 29.21 and 29.25; OCH_3 , 11.10 and 10.90.

The formation of a dibenzofuran system and the position of the methoxy group were established by debromination, using palladium–calcium carbonate as the catalyst.²⁰ The resulting 2-methoxydibenzofuran was shown to be identical with an authentic specimen.

1-Bromo-4-hydroxydibenzofuran was prepared by bromination of an acetic acid solution of 4-hydroxydibenzofuran. The yield of purified bromophenol was 35%, and the compound crystallized as needles from benzene; m. p. 151.5–152°.

(18) Tiemann and Müller, *Ber.*, **14**, 1989 (1881).

(19) The authors are grateful to W. M. Hoehn for the micro-Zeisel analysis.

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

Anal. Calcd. for $C_{12}H_7O_2Br$: Br, 30.39. Found: Br, 30.71 and 30.80.

1-Bromo-4-methoxydibenzofuran.—Methylation of the bromophenol by dimethyl sulfate gave an 81% yield of 1-bromo-4-methoxydibenzofuran which melted at 97-97.5° after crystallization from ethanol.

Anal. Calcd. for $C_{13}H_9O_2Br$: Br, 28.85. Found: Br, 29.10 and 29.15.

The same bromomethoxy compound was prepared²¹ in 86% yield by bromination of 4-methoxydibenzofuran in acetic acid, and melted at 97-98°. The high yield and ease of purification indicate little, if any, isomer formation in the bromination of 4-methoxydibenzofuran.

1-Hydroxy-4-methoxydibenzofuran.—A mixture of the Grignard reagent of 1-bromo-4-methoxydibenzofuran and *n*-butylmagnesium bromide was oxidized at 0° to give a 39% yield of 1-hydroxy-4-methoxydibenzofuran. The compound crystallized as needles from 10% alcohol, and melted at 155°.

Anal. Calcd. for $C_{13}H_{10}O_3$: C, 72.87; H, 4.71. Found: C, 72.75; H, 4.73.

1,4-Dihydroxydibenzofuran was formed by refluxing 0.2 g. of 1-hydroxy-4-methoxydibenzofuran for two hours with 5 cc. of constant boiling hydriodic acid in the presence of a small amount of red phosphorus. The light tan colored compound melted at 217-218° with decomposition, after crystallization from water.

Anal. Calcd. for $C_{12}H_8O_3$: C, 71.96; H, 4.03. Found: C, 72.20; H, 4.18.

1,4-Dimethoxydibenzofuran was prepared in 54% from 5 g. of 1-hydroxy-4-methoxydibenzofuran, dimethyl sulfate and sodium hydroxide. Recrystallization from petroleum ether (b. p. 60-68°) gave prisms melting at 78.5°.

Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.65; H, 5.30. Found: C, 73.96; H, 5.24.

4-Aminodibenzofuran.—Several methods have been examined for the preparation of the important 4-aminodibenzofuran. Amination of 4-hydroxydibenzofuran with zinc chloride and ammonium chloride gave a 16% yield; and the Hofmann degradation of the amide 4-dibenzofurancarboxylic acid gave yields between 30-65% (based on amide actually used).²² The amine has also been prepared²³ in yields between 50-60% by heating 4-bromodibenzofuran with ammonium hydroxide and cuprous bromide at 190-200°.

In this work, the amine was prepared in yields averaging 56.7% by a modified Hofmann reaction adapted from Jeffreys' procedure for the preparation of *p*-nitroaniline.²⁴ To 10.6 g. (0.05 mole) of the amide in methanol was added 0.1 mole of sodium methylate; then 0.05 mole of bromine was added, and the resulting solution of methyl urethan was treated with calcium hydroxide. To the dry lime mixture was added the 2.1 g. of the urea that precipitated earlier, and the mixture was pulverized and then heated at 200-210° for one and one-half hours.

(21) Studies by P. T. Parker.

(22) Studies by W. G. Bywater. See also, Kirkpatrick and Parker, THIS JOURNAL, 57, 1126 (1935).

(23) Studies by L. C. Cheney.

(24) Jeffreys, Am. Chem. J., 22, 14 (1899).

After extracting with ether, the amine was precipitated as the hydrochloride (by hydrogen chloride), and the free amine was obtained finally by addition of ammonium hydroxide.

1 - Bromo - 4 - aminodibenzofuran.—4 - Acetaminodibenzofuran (0.1 mole), prepared by acetylating the amine in benzene with acetic anhydride, was brominated in acetic acid by an equivalent of bromine, to give 31.1 g. of **1-bromo-4-acetaminodibenzofuran** which melted at 228° after crystallization from toluene.

Anal. Calcd. for $C_{14}H_{10}O_2NBr$: Br, 26.26. Found: Br, 26.23 and 26.41.

Hydrolysis of 1-bromo-4-acetaminodibenzofuran (0.07 mole) by refluxing for two hours with a solution of 40 g. of potassium hydroxide in 400 cc. of ethanol gave an 89% yield of 1-bromo-4-aminodibenzofuran which crystallized as needles (m. p. 119-120°) from a mixture of benzene and petroleum ether (b. p. 60-68°).

Anal. Calcd. for $C_{12}H_8ONBr$: Br, 30.51. Found: Br, 30.82.

1-Bromo-4-hydroxydibenzofuran.—The diazonium solution from 0.6 g. (0.0025 mole) of 1-bromo-4-aminodibenzofuran was added slowly to a boiling solution of copper sulfate. The resulting 1-bromo-4-hydroxydibenzofuran (m. p. 152°) was shown to be identical with the bromination product of 4-hydroxydibenzofuran.

1-Bromodibenzofuran.—The diazotized solution from 13.1 g. (0.05 mole) of 1-bromo-4-aminodibenzofuran was treated with hypophosphorous acid in accordance with the procedure described by Mai²⁵ for the replacement of the diazonium group by hydrogen. The yield of 1-bromodibenzofuran was 78%, and the compound crystallized as prisms melting at 67° after recrystallization from petroleum ether (b. p. 28-38°). A mixed melting point determination with 4-bromodibenzofuran (m. p. 72°) showed a depression.

Anal. Calcd. for $C_{12}H_7OBr$: Br, 32.35. Found: Br, 32.30 and 32.11.

1-Aminodibenzofuran.—Amination of 2 g. of 1-bromodibenzofuran was effected by heating with 2 g. of cuprous bromide and 10 cc. of concd. ammonium hydroxide at 230-240° for ten hours. The yield of crude amine (obtained from the hydrochloride) was 24%, and the melting point (72-73°) was raised to 74° by one crystallization from dilute methanol. The amine crystallizes as needles.

Anal. Calcd. for $C_{12}H_9ON$: N, 7.65. Found: N, 7.84 and 7.86.

Whereas the 2-, 3-, and 4-aminodibenzofurans are without odor, the 1-amine has a slight odor similar to that of α -naphthylamine.

1-Acetaminodibenzofuran was prepared from the 1-amine by the action of acetic anhydride in petroleum ether (b. p. 60-68°). The fine needles melted at 205° after recrystallization from 70% ethanol.

Anal. Calcd. for $C_{14}H_{11}O_2N$: N, 6.22. Found: N, 6.38 and 6.40.

1-Hydroxydibenzofuran was prepared by oxidizing a mixture of 1-dibenzofurylmagnesium bromide and *n*-butylmagnesium bromide (prepared simultaneously in a

(25) Mai, Ber., 35, 162 (1902).

mixture of ether and benzene). Prior to oxidation, one cc. of the mixture was hydrolyzed to yield a small quantity of dibenzofuran. The yield of 1-hydroxydibenzofuran was 31%, and the compound (2.42 g.) melted at 140–140.5° after crystallization from about one liter of water.

Anal. Calcd. for $C_{12}H_8O_2$: C, 78.24; H, 4.38. Found: C, 78.54; H, 4.53.

Of the 2-, 3-, and 4-hydroxydibenzofurans, the one melting closest to the 1-hydroxy compound is the 3-hydroxydibenzofuran (m. p. 137–138°); however, a mixed m. p. determination of the 1- and 3-compounds showed a depression of 10°.

Bromination of 1-Hydroxydibenzofuran.—Bromination in acetic acid of 2.4 g. (0.013 mole) of 1-hydroxydibenzofuran gave fine needles of a bromo-1-hydroxydibenzofuran melting at 178°, after repeated recrystallizations from benzene.

Anal. Calcd. for $C_{12}H_7O_2Br$: Br, 30.39. Found: Br, 30.24.

The quantity of pure product isolated was insufficient for conversion to the known 1,2- or 1,4-dimethoxydibenzofuran. However, it is highly probable that the bromine entered either the 2- or the 4-position.

1-Dibenzofurancarboxylic Acid.—1-Dibenzofurylmagnesium bromide was carbonated by solid carbon dioxide to give a 90% yield of 1-dibenzofurancarboxylic acid melting at 232–233° after crystallization from 50% ethanol.

Anal. Calcd. for $C_{13}H_8O_3$: C, 73.58; H, 3.82; neut. equiv., 212. Found: C, 73.76; H, 4.07; neut. equiv., 207.

Methyl 1-dibenzofurancarboxylate was prepared by saturating a methanol solution of the 1-acid with hydrogen chloride. The yield of methyl ester was 88%, and the compound crystallized from methanol as lustrous plates melting at 63°.

Anal. Calcd. for $C_{14}H_{10}O_3$: C, 74.31; H, 4.46. Found: C, 74.31; H, 4.48.

Nitration of Methyl 1-Dibenzofurancarboxylate.—Nitration of 2.5 g. of the methyl ester by concd. nitric acid (d. 1.42) gave a 33% yield of methyl nitro-1-dibenzofurancarboxylate which melted at 216° and crystallized as needles from acetic acid.

Anal. Calcd. for $C_{14}H_9O_6N$: N, 5.17. Found: N, 5.34 and 5.43.

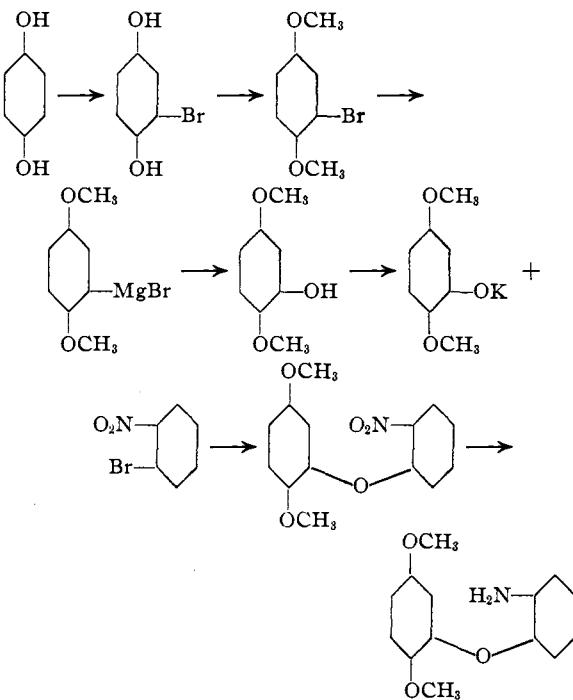
The nitro group is probably in either the 3-position or the 7-position, with the latter more likely.

Hydrolysis of 1 g. of the nitro ester by refluxing for three hours with 75 cc. of a 1:1 mixture of acetic acid and concd. hydrochloric acid gave a nitro acid which crystallized from acetic acid as fine, light yellow needles melting at 297–298°.

Anal. Calcd. for $C_{13}H_7O_6N$: N, 5.45. Found: N, 5.45 and 5.36.

The nitro acid must be either 3-nitro-1-dibenzofurancarboxylic acid or 7-nitro-1-dibenzofurancarboxylic acid because decarboxylation by heating at 230° with quinoline and copper bronze gave 3-nitrodibenzofuran.

2,5-Dimethoxy-2'-aminodiphenyl Ether.—In connection with the attempted preparation of 1,4-dimethoxydibenzofuran by ring closure, 2,5-dimethoxy-2'-aminodiphenyl ether was synthesized by the reactions



Bromohydroquinone,²⁶ obtained in 55% yield, was converted to 1,4-dimethoxy-2-bromobenzene²⁷ in 52% yield. A mixture of the Grignard reagent from 1,4-dimethoxy-2-bromobenzene and *n*-butylmagnesium bromide (prepared at one time from the two bromides and magnesium in ether) was oxidized to give a 43% yield of 2,5-dimethoxyphenol, obtained as a light yellow oil distilling at 134–135° (15 mm.).

Anal. Calcd. for $C_8H_{10}O_3$: C, 62.31; H, 6.54. Found: C, 62.41; H, 6.37.

The benzoate of 2,5-dimethoxyphenol, prepared by a Schotten-Baumann reaction with benzoyl chloride, melted at 73.5° after crystallization from ethanol.

Anal. Calcd. for $C_{10}H_{14}O_4$: C, 69.73; H, 5.48. Found: C, 69.33; H, 5.39.

Thirty-three grams (0.17 mole) of the potassium salt of 2,5-dimethoxyphenol (prepared in quantitative yield by the reaction of the phenol with potassium hydroxide in methanol solution and precipitation with ether) was mixed with 41.2 g. (0.204 mole) of *o*-bromonitrobenzene. Coupling was effected by heating in an oil-bath at 170° for two hours, to give a 38% yield of 2,5-dimethoxy-2'-nitrodi phenyl ether distilling at 190–193° (3 mm.).

The nitro ether (18 g., 0.065 mole) was dissolved in ether, and 53 g. (0.234 mole) of stannous chloride dihydrate added. Hydrogen chloride was passed for two hours into the stirred ether solution, cooled by an ice-bath. The yield of 2,5-dimethoxy-2'-aminodiphenyl ether was 45%; b. p. 183–185° (4 mm.); m. p., 72° after recrystallization from petroleum ether (b. p. 60–68°).

Anal. Calcd. for $C_{14}H_{14}O_8N$: N, 5.74. Found: N, 5.73 and 5.99.

The 2,5-dimethoxy-2'-aminodiphenyl ether was diazo-

(26) Sarauw, *Ann.*, **209**, 105 (1881).

(27) Votocek and Köhler, *Ber.*, **46**, 1767 (1913).

TABLE I

	Br	OH	NH ₂	NHCOCH ₃	COOH	COOCH ₃
1-	67°	140-140.5°	74°	205°	232-233°	63°
2-	110°	134°	127-128°	162-163°	249°	73-74°
3-	120°	138-138.5°	101°	178°	271.5-272°	138.5°
4-	72°	102°	84.5-85.5°	172.5°	209-210°	93-94°

tized and the diazonium chloride solution was dropped slowly into a boiling solution of 50% sulfuric acid. Steam distillation gave an alkali soluble phenolic product. Apparently the diazonium group was replaced by hydroxyl, instead of coupling to give 1,4-dimethoxydibenzofuran.

Ferric Chloride Tests on Phenols.—To each of alcoholic solutions of the several phenols obtained in this study was added a drop of ferric chloride solution; water was then added to incipient turbidity. The results of these tests are assembled here.

1-Hydroxydibenzofuran.....	Light purple
2-Hydroxydibenzofuran	Green
3-Hydroxydibenzofuran	Green
4-Hydroxydibenzofuran.....	Green
1-Bromo-2-hydroxydibenzofuran	None
1-Allyl-2-hydroxydibenzofuran	None
1-Propenyl-2-hydroxydibenzofuran	None
1-Hydroxy-2-methoxydibenzofuran	Red
1-Bromo-4-hydroxydibenzofuran	None
1-Hydroxy-4-methoxydibenzofuran	Green
1,4-Dihydroxydibenzofuran	Deep yellow
Bromo-1-hydroxydibenzofuran.....	None
2,5-Dimethoxyphenol	Red brown

It is interesting that α -naphthol gives a violet color, and β -naphthol gives a green color.²⁸ However, although 1-allyl-2-naphthol and 2-allyl-1-naphthol both give a green color, 1-allyl-2-hydroxydibenzofuran gives no color. This may not be surprising, for some of Claisen's allyl phenols give "weak and little characteristic colors" with ferric chloride.⁴

Melting Points.—In Table I are assembled the melting points of all completed series of monosubstituted dibenzofurans. The information contained therein is of some diagnostic value.

Summary

The preparation of a series of 1-monosubstituted dibenzofurans, the first to be reported, has been described. The structures of these and related compounds have been established by several procedures including ring closure.

(28) Hans Meyer, "Analyse und Konstitutionsermittlung organischer Verbindungen," Verlag von Julius Springer, Berlin, 1931, pp. 301-302.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Dibenzofuran. XII. Metalation of Some Bromo Derivatives

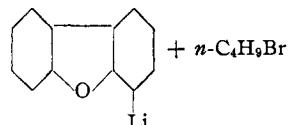
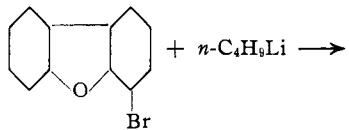
BY HENRY GILMAN, H. B. WILLIS AND JACK SWISLOWSKY

Introduction

The initial studies on the metalation of dibenzofuran showed that a metal invariably was introduced ortho to the ether linkage to give a 4-metalated or 4,6-dimetatalated product.^{1a} Subsequently, metalation of 2-methoxydibenzofuran by *n*-butyllithium was shown to give a mixture of 2-methoxy-1-dibenzofuryllithium and 2-methoxy-3-dibenzofuryllithium.^{1b} This confirmed the pronounced tendency of metalation to take place ortho to an ether linkage,^{1b,c,d} even to the exclusion of the 4- and 6-positions in dibenzofuran. The course of the recent metalation of 2-bromodibenzofuran to give 2-bromo-4-dibenzofuryllithium

ium,^{1d} might have been predicted for two reasons: first, it involved a position ortho to an ether linkage; and, second, a nucleus having a negative substituent is metalated in preference to a nucleus without a substituent.^{1c}

We now find that under conditions of metalation, 4-bromodibenzofuran proceeds quite smoothly to give 4-dibenzofuryllithium.



This replacement reaction was not wholly ex-

(1) (a) Gilman and Young, THIS JOURNAL, **56**, 1415 (1934); **57**, 1121 (1935); (b) Gilman and Bebb, *ibid.*, **61**, 109 (1939); (c) Gilman and Jacoby, *J. Org. Chem.*, **8**, 108 (1938); Wittig, Pockels and Dröge, *Ber.*, **71**, 1903 (1938); Gilman, Langham and Jacoby, THIS JOURNAL, **61**, 106 (1939); Wittig and Pockels, *Ber.*, **72**, 89 (1939); (d) Gilman, Cheney and Willis, THIS JOURNAL, **61**, 951 (1939).