

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Dibenzofuran. XV. 1,4- and 1,4,6-Derivatives¹

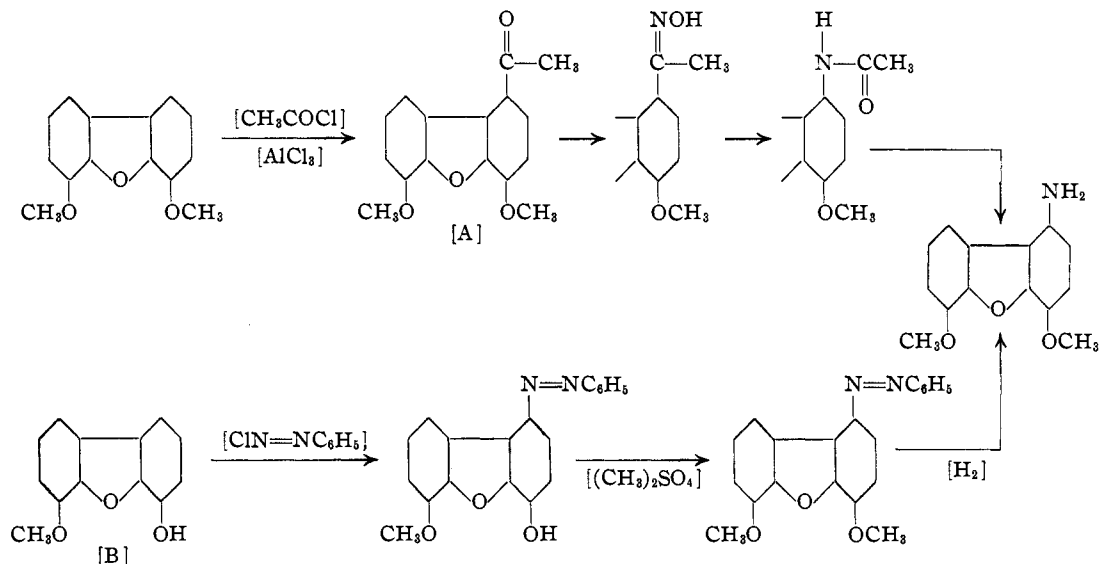
BY HENRY GILMAN AND LEE C. CHENEY

Introduction

Bridging of the 1,9-positions in dibenzofuran undoubtedly will be facilitated by the presence in the 4- and 6-positions of strong ortho-para direct-

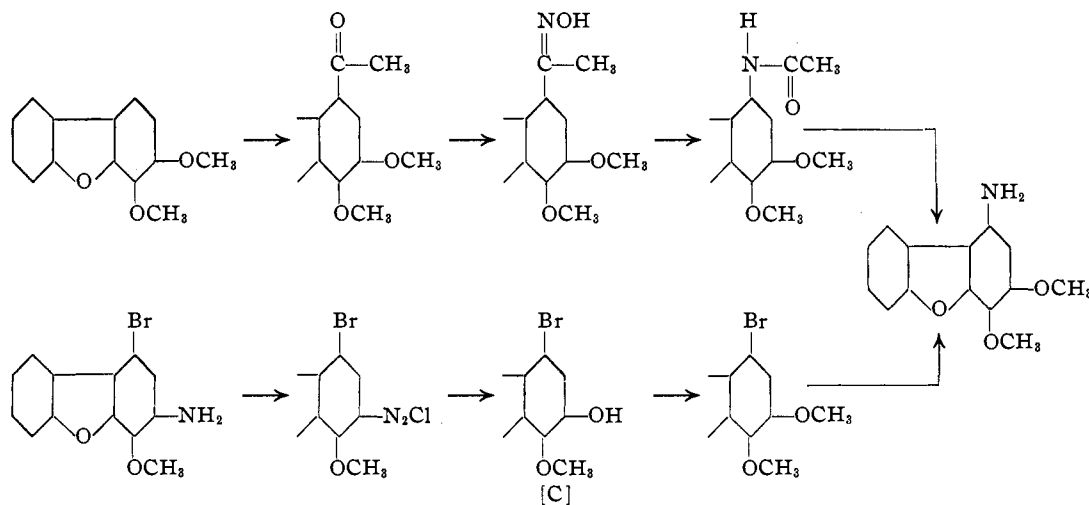
Friedel-Crafts Acylations.

—Acetylation of 4,6-dimethoxydibenzofuran gave 1-acetyl-4,6-dimethoxydibenzofuran, the structure of which was established by the following sequence of reactions



ing groups. The recent availability of procedures for the introduction of such substituents, as well as some authentic reference compounds having a substituent in the 1-position,² now permits the synthesis of desirable 1,4- and 1,4,6-derivatives.

The diazo coupling reaction with 4-hydroxy-6-methoxydibenzofuran [B] undoubtedly involved the nucleus containing the phenolic hydroxyl group. It was shown recently¹ that diazo coupling with 4-hydroxydibenzofuran goes para to the



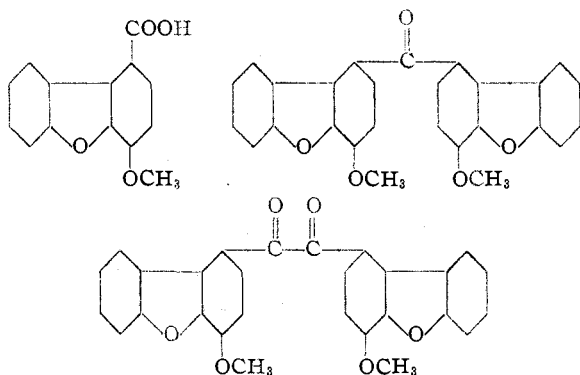
(1) Paper XIV is Gilman and M. W. Van Ess, *THIS JOURNAL*, **61**, 3146 (1939).

(2) Gilman and P. R. Van Ess, *ibid.*, **61**, 1365 (1939).

hydroxyl to yield 1-benzene-azo-4-hydroxydibenzofuran.

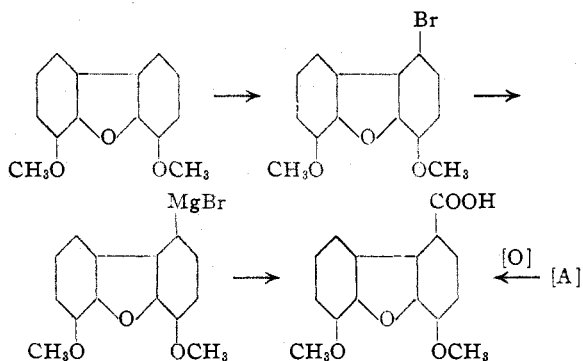
The recent proof of structure of 1-bromo-3-amino-4-methoxydibenzofuran³ provided the essential compound for establishing the constitution of the acetylation product of 3,4-dimethoxydibenzofuran by the transformations shown.

Oxalyl chloride, aluminum chloride and 4-methoxydibenzofuran gave the following three products: 4-methoxy-1-dibenzofurancarboxylic acid, di-(4-methoxy-1-dibenzofuryl) ketone, and bi-(4-methoxy-1-dibenzofuroyl), all of which owe their formation to initial acylation in the 1-position.



The same three types (acid, ketone and benzil analog) resulted from interaction of 4,6-dimethoxydibenzofuran with oxalyl chloride.

Bromination.—The structure of the monobromination product of 4,6-dimethoxydibenzofuran was established as follows



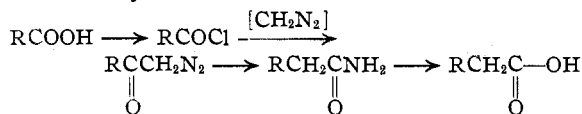
Dibromination of 4,6-dimethoxydibenzofuran gave 1,9-dibromo-4,6-dimethoxydibenzofuran. The same dibromo compound resulted on dibromination of 4,6-dihydroxydibenzofuran with subsequent methylation. However, dibromination of 4-hydroxy-6-methoxydibenzofuran followed by methylation produced a dibromo-4,6-dimethoxydibenzofuran which, unexpectedly, proved to be unlike the compound obtained by dibromination

(3) Gilman, Parker, Bailie and Brown, *THIS JOURNAL*, **61**, 2836 (1939).

of 4,6-dimethoxydibenzofuran. This isomer is probably 1,3-dibromo-4-hydroxy-6-methoxydibenzofuran. It would be interesting to establish the course of dibromination of 1-hydroxy-8-methoxy-naphthalene.

Bromination of 3,4-dimethoxydibenzofuran yielded 1-bromo-3,4-dimethoxydibenzofuran. The proof of structure of this product was established by first preparing 1-bromo-3-hydroxy-4-methoxydibenzofuran [C] from the authentic 1-bromo-3-amino-4-methoxydibenzofuran by means of the diazo reaction. Then the 3-hydroxy-4-methoxydibenzofuran was brominated to give the same 1-bromo-3-hydroxy-4-methoxydibenzofuran, and this on methylation yielded 1-bromo-3,4-dimethoxydibenzofuran, identical with the product of bromination of 3,4-dimethoxydibenzofuran.

4,6-Dimethoxy-1-dibenzofurylacetic Acid.—In the synthesis of this compound, 4,6-dimethoxy-1-dibenzofurancarboxylic acid (used as the starting material) was prepared by two procedures: oxidation of 1-acetyl-4,6-dimethoxydibenzofuran, and carbonation of the Grignard reagent prepared from 1-bromo-4,6-dimethoxydibenzofuran. The transformations of the acid were as follows, where R = 4,6-dimethoxy-1-dibenzofuryl.



1, 2, 3, 4 - Tetrahydro - 6 - aminodibenzofuran.—Reduction of 4-aminodibenzofuran by sodium and alcohol was shown to involve the unsubstituted nucleus, for the resulting tetrahydro-6-aminodibenzofuran formed no carbonate, but did undergo diazotization and subsequent coupling with β -naphthol.

Experimental Part

4,6-Dihydroxydibenzofuran.—Refluxing a solution of 8.56 g. (0.04 mole) of 4-hydroxy-6-methoxydibenzofuran with 20 ml. of hydrobromic acid (sp. gr. 1.49) in 50 ml. of acetic acid gave a 91.6% yield of 4,6-dihydroxydibenzofuran. The compound crystallized in needle form from dilute methanol, and melted at 200–202°. This melting point is higher than that reported for the dihydroxy compound obtained by two other procedures.⁴

4,6-Dimethoxydibenzofuran.—Methylation was effected by an adaptation of the procedure of Stevens and Tucker.⁵ From 24.5 g. (0.115 mole) of 4-hydroxy-6-methoxydibenzofuran, 0.345 mole of dimethyl sulfate, 39 ml. of 60%

(4) Gilman and Young, *ibid.*, **57**, 1121 (1935).

(5) Stevens and Tucker, *J. Chem. Soc.*, **123**, 2140 (1923).

potassium hydroxide, and acetone as a solvent, the yield of 4,6-dimethoxydibenzofuran was practically quantitative. The compound crystallized from petroleum ether (b. p. 60–68°) as pearly plates melting at 128–129°.

Anal. Calcd. for $C_{14}H_{12}O_3$: methoxy], 27.2. Found: methoxy], 26.4.

The picrate of 4,6-dimethoxydibenzofuran was obtained as deep yellow needles, melting at 161–162° after crystallization from alcohol. Under corresponding conditions of preparation, the isomeric 3,4-dimethoxy compound did not form a picrate.

Anal. Calcd. for $C_{14}H_{12}O_8 \cdot C_6H_3O_7N_3$: N, 9.19. Found: N, 9.11.

1-Acetyl-4,6-dimethoxydibenzofuran.—Admixture of reagents was effected in the cold between 17.35 g. (0.0761 mole) of 4,6-dimethoxydibenzofuran, 5.97 g. (0.0761 mole) of acetyl chloride, and 10.18 g. (0.0761 mole) of aluminum chloride in 100 ml. of nitrobenzene. When addition of aluminum chloride was complete, the contents of the flask were allowed to come slowly to room temperature, and stirring was continued for twenty hours. Subsequent to hydrolysis, and removal of the nitrobenzene by steam distillation, there was isolated 12.35 g. (a 60% yield) of 1-acetyl-4,6-dimethoxydibenzofuran which melted at 178.5–179.5° after crystallization from alcohol or dilute acetone.

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.18 and 71.30; H, 4.93 and 5.08.

Oxime of 1-Acetyl-4,6-dimethoxydibenzofuran and its Beckmann Rearrangement Product.—By using the procedure for the preparation of the oxime of 1-acetyl-4-methoxydibenzofuran,³ there was obtained an 88% yield of the oxime of 1-acetyl-4,6-dimethoxydibenzofuran which crystallized from alcohol as plates melting at 203–204°.

Anal. Calcd. for $C_{16}H_{16}O_4N$: N, 4.91. Found: N, 5.02.

Rearrangement of a benzene suspension of the oxime by phosphorus pentachloride gave a 76.4% yield of 1-acetamino-4,6-dimethoxydibenzofuran, which crystallized from benzene as fine needles melting at 244–245°.

Anal. Calcd. for $C_{16}H_{16}O_4N$: N, 4.92. Found: N, 4.93.

Hydrolysis of the acetamino compound by heating an alcohol-concd. hydrochloric acid solution gave a 94.5% yield of 1-amino-4,6-dimethoxydibenzofuran hydrochloride, obtained as needles melting at 286–287°. The hydrochloride and ammonium hydroxide gave 1-amino-4,6-dimethoxydibenzofuran melting at 162–162.5° after crystallization from methanol, and identical (mixed m. p.) with the amine obtained by reduction of 1-benzeneazo-4,6-dimethoxydibenzofuran.

1-Benzeneazo-4-hydroxy-6-methoxydibenzofuran.—The extreme insolubility of the potassium salt of 4-hydroxy-6-methoxydibenzofuran necessitated a modification of the procedure used for the coupling of 4-hydroxydibenzofuran.¹

The alkaline solution of the phenol prepared from 4.28 g. (0.02 mole) of 4-hydroxy-6-methoxydibenzofuran, 15 ml. of 15% potassium hydroxide solution, and 385 ml. of water, was placed in a one-liter three-necked flask equipped with stirrer, low-temperature thermometer

and dropping funnel. The diazonium salt solution was prepared from 2.58 g. (0.02 mole) of aniline hydrochloride in 15 ml. of water, 15–25 g. of cracked ice, 3.4 ml. of concd. hydrochloric acid, and 1.46 g. (0.021 mole) of sodium nitrite in 15 ml. of water. This ice-cold benzenediazonium chloride solution was added to the cold, stirred, alkaline solution of the phenol at such a rate that the temperature did not rise above 3°. A beautiful orange precipitate formed at once. After addition was complete, the reaction mixture was stirred for forty-five minutes, and the coupling product filtered off and dried. Two crystallizations from alcohol yielded rust-colored needles of 1-benzeneazo-4-hydroxy-6-methoxydibenzofuran, m. p. 175°. The yield was 3.6 g. or 56.6%.

Anal. Calcd. for $C_{19}H_{14}O_3N_2$: N, 8.84. Found: N, 8.89.

1-Benzeneazo-4,6-dimethoxydibenzofuran and its Reduction to 1-Amino-4,6-dimethoxydibenzofuran.—Methylation of 1.59 g. (0.005 mole) of 1-benzeneazo-4-hydroxy-6-methoxydibenzofuran by dimethyl sulfate and potassium hydroxide in acetone gave an 88% yield of deep orange prisms, melting at 170° when crystallized from benzene.

Anal. Calcd. for $C_{20}H_{16}O_3N_2$: N, 8.44. Found: N, 8.51.

The 1-benzeneazo-4,6-dimethoxydibenzofuran (1 g.) was reduced in essential accordance with the procedure described for the reduction of 1-benzeneazo-4-hydroxydibenzofuran.¹ The yield of 1-amino-4,6-dimethoxydibenzofuran was 0.24 g. (32.8%).

Anal. Calcd. for $C_{14}H_{16}O_3N$: N, 5.77. Found: N, 5.88.

Friedel-Crafts Reaction with 4-Methoxydibenzofuran and Oxalyl Chloride.—Into a solution of 9.90 g. (0.05 mole) of 4-methoxydibenzofuran and 7.0 g. (10% excess over 0.05 mole) of oxalyl chloride in 75 ml. of nitrobenzene contained in a three-necked flask equipped with stirrer and condenser topped with a calcium chloride tube, was gradually added 14.7 g. (10% excess) of anhydrous aluminum chloride. Throughout the addition an ice-bath cooled the reaction mixture, which was then allowed to come slowly to room temperature. After twenty-eight hours, the red-brown mixture was hydrolyzed with ice and hydrochloric acid, the nitrobenzene was removed with steam, and the amorphous solid boiled with 5% sodium hydroxide solution and filtered. The dried acidification product from the filtrate (0.7 g.), after crystallization from acetic acid, melted at 276–277° and was shown to be 4-methoxy-1-dibenzofurancarboxylic acid by mixed melting point.

The dried, amorphous, alkali-insoluble solid was extracted with 100 ml. of acetic acid. From the cold filtrate was obtained 1.9 g. (18%) of di-(4-methoxy-1-dibenzofuryl) ketone in the form of colorless needles, m. p. 234°.

Anal. Calcd. for $C_{27}H_{18}O_6$: C, 76.8; H, 4.29. Found: C, 76.1; H, 4.37.

The acetic acid insoluble residue, which proved to be bi-(4-methoxy-1-dibenzofuroyl), crystallized from nitrobenzene in the form of pale yellow needles, m. p. 329°. The yield was 3.9 g. or 34.6%.

Anal. Calcd. for $C_{29}H_{22}O_7$: C, 72.2; H, 4.62. Found: C, 72.3; H, 4.68.

Friedel-Crafts Reactions of 4-Methoxydibenzofuran with Chloroacetyl Chloride and Ethyl Chloroglyoxalate.—From 12.5 g. (0.063 mole) of 4-methoxydibenzofuran, 7.9 g. (0.07 mole) of chloroacetyl chloride, 8.5 g. (0.0635 mole) of aluminum chloride and 60 ml. of nitrobenzene there was obtained 6.3 g. or a 53.2% yield of 1-chloroacetyl-4-methoxydibenzofuran which crystallized from alcohol as needles melting at 165–166°.

Anal. Calcd. for $C_{15}H_{11}O_3Cl$: Cl, 12.92. Found: Cl, 13.12 and 13.05.

From a corresponding reaction between 9.9 g. (0.05 mole) of 4-methoxydibenzofuran, 7.5 g. (10% excess) of ethyl chloroglyoxalate, 8.0 g. (20% excess) of aluminum chloride and 60 ml. of nitrobenzene there resulted 6.4 g. (43%) of 1-ethoxalyl-4-methoxydibenzofuran which melted at 113° after crystallization from alcohol.

Anal. Calcd. for $C_{17}H_{14}O_5$: C, 68.4; H, 4.73. Found: C, 68.0; H, 4.82.

Hydrolysis of 1 g. of 1-ethoxalyl-4-methoxydibenzofuran by refluxing with 15% sodium hydroxide gave (subsequent to acidification) 0.43 g. of 4-methoxy-1-dibenzofuryl- α -oxoacetic acid which crystallized from alcohol as pale yellow needles melting at 187°.

Anal. Calcd. for $C_{15}H_{10}O_5$: C, 66.64; H, 3.73. Found: C, 66.39; H, 3.75.

Concentrated sulfuric acid colored the keto acid deep red. Oxidation of the keto acid by alkaline permanganate gave 4-methoxy-1-dibenzofurancarboxylic acid (mixed m. p.). The semicarbazone of 4-methoxy-1-dibenzofuryl- α -oxoacetic acid melted at 211.5–212° with decomposition after crystallization from alcohol.

Anal. Calcd. for $C_{16}H_{13}O_5N_3$: N, 12.84. Found: N, 12.83.

Friedel-Crafts Reaction with 4,6-Dimethoxydibenzofuran and Oxalyl Chloride.—The procedure described for the reaction of 4-methoxydibenzofuran and oxalyl chloride was used. Into an ice-cold solution of 4.56 g. (0.02 mole) of 4,6-dimethoxydibenzofuran and 2.8 g. (10% excess over 0.02 mole) of oxalyl chloride in 50 ml. of nitrobenzene, was slowly added 6.42 g. (20% excess over 0.04 mole) of powdered, anhydrous aluminum chloride. Addition required one and three-fourths hours, after which the reaction mixture was allowed to come to room temperature, stirring being continued for twenty hours. Hydrolysis was effected with ice and hydrochloric acid, after which the nitrobenzene was removed with steam. The remaining gray solid was extracted with 200 ml. of 10% sodium hydroxide solution to remove any acids. Acidification of the filtrate furnished 0.37 g. of 4,6-dimethoxy-1-dibenzofurancarboxylic acid, m. p. 297–298°.

The gray solid residue was extracted (Soxhlet apparatus) with 100 ml. of acetic acid to yield 0.5 g. (10.4%) of di-(4,6-dimethoxy-1-dibenzofuryl) ketone, m. p. 254–255°.

Anal. Calcd. for $C_{23}H_{22}O_7$: C, 72.17; H, 4.62. Found: C, 72.31 and 71.54; H, 4.93 and 4.68.

The pale yellow, extremely insoluble residue from the acetic acid extraction crystallized from nitrobenzene in the form of very small needles, m. p. above 300°. Analysis showed the compound to be bi-(4,6-dimethoxy-1-dibenzofuroyl). The yield was 3.1 g. (60.7% of the theoretical).

Anal. Calcd. for $C_{30}H_{22}O_8$: C, 70.65; H, 4.35. Found: C, 70.94 and 70.63; H, 4.60 and 4.69.

3,4-Dihydroxydibenzofuran and 3,4-Diacetoxydibenzofuran.—An 88% yield of 3,4-dihydroxydibenzofuran was obtained by refluxing an acetic acid solution of 8.56 g. (0.04 mole) of 3-hydroxy-4-methoxydibenzofuran with hydrobromic acid (sp. gr. 1.49). Recrystallization from hot water gave needles melting at 164–164.5°.

Anal. Calcd. for $C_{12}H_8O_3$: C, 71.98; H, 4.03. Found: C, 71.56; H, 4.21.

From 3,4-dihydroxydibenzofuran (1.95 g.), acetic anhydride and a drop of concd. sulfuric acid was obtained a 74.1% yield of 3,4-diacetoxydibenzofuran which melted at 104–105° after crystallization from methanol.

Anal. Calcd. for $C_{16}H_{12}O_6$: C, 67.5; H, 4.28. Found: C, 67.6; H, 4.21.

3,4-Dimethoxydibenzofuran.—Methylation of 49.2 g. (0.39 mole) of 3-hydroxy-4-methoxydibenzofuran by dimethyl sulfate and 10% sodium hydroxide gave an 81% yield of 3,4-dimethoxydibenzofuran, which crystallized from petroleum ether (b. p. 28–38°) as needles melting at 60–61°.

Anal. Calcd. for $C_{14}H_{12}O_3$: methoxyl, 27.2. Found: methoxyl, 26.8.

1-Acetyl-3,4-dimethoxydibenzofuran.—Acetylation of 13.7 g. (0.06 mole) of 3,4-dimethoxydibenzofuran by the procedure used with the 4,6-dimethoxy compound gave a 55.5% yield of 1-acetyl-3,4-dimethoxydibenzofuran which crystallized from alcohol as needles melting at 90.5–91°.

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.11 and 70.54; H, 5.41 and 5.42.

Some demethylated phenol also was isolated.

Oxime of 1-Acetyl-3,4-dimethoxydibenzofuran and its Rearrangement to 1-Acetamino-3,4-dimethoxydibenzofuran.—The oxime of 1-acetyl-3,4-dimethoxydibenzofuran (84% yield) was crystallized from alcohol as needles melting at 156–157°.

Anal. Calcd. for $C_{18}H_{18}O_4N$: N, 4.91. Found: N, 5.11.

A Beckmann rearrangement of a benzene solution of the oxime by phosphorus pentachloride gave a 94% yield of 1-acetamino-3,4-dimethoxydibenzofuran which crystallized from alcohol (to which several drops of acetic anhydride were added) as needles melting at 196–196.5°.

Anal. Calcd. for $C_{16}H_{18}O_4N$: N, 4.92. Found: N, 5.02.

Hydrolysis of 1 g. of 1-acetamino-3,4-dimethoxydibenzofuran by alcoholic potash gave a 48% yield of 1-amino-3,4-dimethoxydibenzofuran (m. p., 162.5–163°) which showed no depression in a mixed m. p. determination with the compound obtained by amination of 1-bromo-3,4-dimethoxydibenzofuran.

1-Amino-3,4-dimethoxydibenzofuran.—A mixture of 7.5 g. (0.0244 mole) of 1-bromo-3,4-dimethoxydibenzofuran, 15 g. of powdered cuprous bromide, and 130 ml. of concd. ammonium hydroxide was heated in a bomb for fourteen and one-half hours at 220–230°. After working up in a customary manner there was obtained a 10% yield of 1-amino-3,4-dimethoxydibenzofuran which crystal-

lized from dilute methanol as needles melting at 162.5–163°.

Anal. Calcd. for $C_{14}H_{13}O_3N$: N, 5.76. Found: N, 5.94.

Bromination of 4,6-Derivatives.—Bromination of 22.8 g. (0.1 mole) of 4,6-dimethoxydibenzofuran in 600 ml. of acetic acid by the dropwise addition of 100 ml. of a molar solution of bromine in acetic acid gave a 73% yield of 1-bromo-4,6-dimethoxydibenzofuran which crystallized from a large volume of alcohol as plates melting at 152°. In addition, 3.7 g. (12%) of product melting at 144–147° was isolated.

Anal. Calcd. for $C_{14}H_{11}O_3Br$: Br, 26.01. Found: Br, 26.23.

From 3.0 g. (0.0132 mole) of 4,6-dimethoxydibenzofuran in 120 ml. of acetic acid and 52.7 ml. of a 0.5 molar solution of bromine in acetic acid was obtained a 74% yield of 1,9-dibromo-4,6-dimethoxydibenzofuran which crystallized from acetic acid as needles melting at 167–168°.

Anal. Calcd. for $C_{14}H_{10}O_3Br_2$: Br, 41.42. Found: Br, 41.60.

Instantaneous decolorization was noted when 40 ml. of a 0.5 molar solution of bromine in acetic acid was added to a solution of 2.0 g. (0.01 mole) of 4,6-dihydroxydibenzofuran in 20 ml. of acetic acid. The yield of 1,9-dibromo-4,6-dihydroxydibenzofuran was essentially quantitative. The melting point after crystallization from xylene was 239–240° (with decomposition).

Anal. Calcd. for $C_{12}H_8O_3Br_2$: Br, 44.66. Found: Br, 44.77.

Methylation by dimethyl sulfate converted the dibromodihydroxy compound quantitatively to 1,9-dibromo-4,6-dimethoxydibenzofuran, identical with the dibromination product of 4,6-dimethoxydibenzofuran.

Decolorization was less rapid when 40 ml. of a 0.5 molar solution of bromine in acetic acid was added to 2.14 g. (0.01 mole) of 4-hydroxy-6-methoxydibenzofuran in 20 ml. of acetic acid. The dibromo compound, probably 1,3-dibromo-4-hydroxy-6-methoxydibenzofuran, crystallized from acetic acid as needles melting at 177–178°; yield, 2.17 g. (58.6%).

Anal. Calcd. for $C_{13}H_9O_3Br_2$: Br, 42.98. Found: Br, 43.10.

The dibromo-4-hydroxy-6-methoxydibenzofuran was methylated in the usual manner (using acetone as part of the medium) to give a quantitative yield of what is probably 1,3-dibromo-4,6-dimethoxydibenzofuran. This compound crystallized from acetic acid as needles melting at 173.5–174°.

Anal. Calcd. for $C_{14}H_{10}O_3Br_2$: Br, 41.42. Found: Br, 41.68.

Bromination of 3,4-Derivatives.—Decolorization proceeded rapidly when 13.4 ml. of a 0.5 molar solution of bromine in acetic acid was added slowly and with shaking to 1.5 g. (0.0066 mole) of 3,4-dimethoxydibenzofuran in 15 ml. of acetic acid. Crystallization from alcohol gave an 88.5% yield of 1-bromo-3,4-dimethoxydibenzofuran in the form of fine needles which melted at 108°.

Anal. Calcd. for $C_{14}H_{11}O_3Br$: Br, 26.03. Found: Br, 26.11.

To a stirred solution of 4.28 g. (0.02 mole) of 3-hydroxy-4-methoxydibenzofuran in 50 ml. of acetic acid was slowly introduced 40 ml. of a 0.5 molar solution of bromine in acetic acid. The decolorization was almost instantaneous. Dilution of the reaction mixture, followed by filtration, furnished 5.65 g. of substance which melted at 130–149°, indicating that isomers were probably present. After one crystallization from 30% alcohol and three recrystallizations from benzene, white fluffy needles of 1-bromo-3-hydroxy-4-methoxydibenzofuran, m. p. 161–162°, were obtained. The yield was 3.1 g. or 54.6% of the theoretical. No attempt was made to isolate the more soluble isomer.

Anal. Calcd. for $C_{13}H_9O_3Br$: Br, 27.28. Found: Br, 27.32.

An intimate mixture of this compound and authentic 1-bromo-3-hydroxy-4-methoxydibenzofuran prepared from the known 1-bromo-3-amino-4-methoxydibenzofuran showed no melting point depression.

1-Bromo-3,4-dimethoxydibenzofuran, m. p. 108°, was prepared by methylating 0.5 g. of 1-bromo-3-hydroxy-4-methoxydibenzofuran at room temperature with 3 ml. of dimethyl sulfate and 5 ml. of 10% sodium hydroxide solution. The compound obtained by direct bromination of 3,4-dimethoxydibenzofuran was proved identical with this by a mixed melting point determination.

Conversion of 1-Bromo-3-amino-4-methoxydibenzofuran to 1-Bromo-3-hydroxy-4-methoxydibenzofuran.—An iced diazonium solution prepared from 0.95 g. (0.00325 mole) of 1-bromo-3-amino-4-methoxydibenzofuran, sodium nitrite and sulfuric acid was added dropwise to a boiling solution of 75 g. of copper sulfate in 250 ml. of water contained in a distilling flask fitted with a condenser. The white solid which steam-distilled was dissolved in 5% sodium hydroxide solution, treated with Norite, filtered, and acidified. The white needles of authentic 1-bromo-3-hydroxy-4-methoxydibenzofuran thus obtained, m. p. 161–162°, weighed 0.2 g. (21% yield). No depression in melting point was observed when this compound was mixed with the bromination product of 3-hydroxy-4-methoxydibenzofuran.

4-Bromo-6-hydroxydibenzofuran.—A suspension of 0.5 g. of 4-bromo-6-methoxydibenzofuran in 5 ml. of hydriodic acid (sp. gr. 1.67) was heated to give a 19% yield of 4-bromo-6-hydroxydibenzofuran which crystallized from water as needles melting at 138–139°. An alcoholic solution of this phenol gave a green color with ferric chloride solution.

Anal. Calcd. for $C_{12}H_7O_2Br$: Br, 30.39. Found: Br, 30.47.

4-Amino-6-methoxydibenzofuran and 4-Amino-6-hydroxydibenzofuran.—An intimate mixture of 5 g. (0.018 mole) of 4-bromo-6-methoxydibenzofuran and 6 g. of freshly prepared cuprous bromide was placed in a large test-tube, covered with 150 ml. of concd. ammonium hydroxide, and electrically heated in a steel bomb at 100° for ten hours. The temperature was then raised to 215° and held constant for eight hours. The hydrochloride of 4-amino-6-methoxydibenzofuran, isolated in a 51% yield by customary procedures, crystallized from water as fine needles melting at 235–236° with discoloration. The 4-amino-6-methoxydibenzofuran, m. p. 109°, was obtained

in the form of needles by adding ammonium hydroxide to a hot solution of the hydrochloride.

Anal. Calcd. for $C_{12}H_{11}O_2N$: N, 6.57. Found: N, 6.53.

To 2.35 g. (0.0094 mole) of 4-amino-6-methoxydibenzofuran, dissolved in 25 ml. of glacial acetic acid, was added 25 ml. of hydrobromic acid (sp. gr. 1.49), and the mixture was refluxed for nine hours. The hydrobromide, which precipitated on cooling, was dissolved in hot water and the hydrochloride, in the form of small plates melting at 265–266° dec., was precipitated from this solution by passing in dry hydrogen chloride. The free 4-amino-6-hydroxydibenzofuran, crystallizing as needles which melted at 191.5–192.5°, was not discolored by atmospheric oxygen.

Anal. Calcd. for $C_{12}H_9O_2N$: N, 7.03. Found: N, 7.15.

4,6-Diaminodibenzofuran and 4,6-Diacetoxydibenzofuran.—In each of four Carius tubes, a mixture of 1.0 g. (0.005 mole) of 4,6-dihydroxydibenzofuran, 7.5 g. of sodium bisulfite dissolved in 15 ml. of water, and 15 ml. of concd. ammonium hydroxide was sealed. The tubes were then heated at 185–195° in an electric furnace for twenty hours. The cooled mixtures were combined and extracted thrice with a total volume of 400 ml. of ether. The ether solution was washed thoroughly with 10% sodium hydroxide solution and then with water. The **4,6-diaminodibenzofuran dihydrochloride**, m. p. 297–298° with decomposition, was precipitated from the dried ether solution by the introduction of dry gaseous hydrogen chloride. The yield was 4.4 g. or 81% of the theoretical. The hydrochloride was dissolved in about 25 ml. of hot water, digested with Norite, filtered and precipitated again with gaseous hydrogen chloride to give needles which melted at 298° with decomposition.

Anal. Calcd. for $C_{12}H_{12}ON_2Cl_2$: N, 10.33. Found: N, 10.52.

The free **4,6-diaminodibenzofuran**, liberated by the addition of ammonium hydroxide to a solution of the hydrochloride, crystallized from the methanol in the form of colorless prisms, m. p. 152°. This compound has been obtained recently by the reduction of 4,6-dinitrodibenzofuran, which in turn was prepared by a biphenyl ring closure.^{6a}

The picrate of **4,6-diaminodibenzofuran** crystallized from alcohol as shiny, red-brown plates which melted at 213° with pronounced decomposition.

Anal. Calcd. for $C_{12}H_{10}ON_2 \cdot C_6H_3O_7N_3$: N, 16.40. Found: N, 16.28.

The **4,6-diacetaminodibenzofuran**, prepared in quantitative yield from the 4,6-diamino compound and acetic anhydride, crystallized from acetic acid as needles melting at 297–298°.

Anal. Calcd. for $C_{16}H_{14}O_2N_2$: N, 9.93. Found: N, 9.92.

Yamasiro^{6a} has reported a melting point of 322.5–323.5° for this compound. In the same paper are reported 4-aminodibenzofuran, m. p. 118–119°, and 4-

acetaminodibenzofuran, m. p. 235–236°. The melting points observed in this Laboratory for these two compounds were 84.5–85.5° and 172.5°, respectively.^{6b}

4,6-Diacetoxydibenzofuran (prepared in 53% yield from 4,6-dihydroxydibenzofuran, acetic anhydride and a drop of concd. sulfuric acid) crystallized from methanol as small, shiny plates melting at 177°.

Anal. Calcd. for $C_{16}H_{12}O_6$: C, 67.5; H, 4.28. Found: C, 67.4; H, 4.31.

Coupling of Benzenediazonium Chloride with 4,6-Dihydroxydibenzofuran.—A cold benzenediazonium chloride solution prepared from 7.75 g. (0.06 mole) of aniline hydrochloride was added to a cold solution of 6.0 g. (0.03 mole) of 4,6-dihydroxydibenzofuran in aqueous potassium hydroxide to give 5.1 g. of a very dark brown microcrystalline product which melted at about 224° with decomposition. Recrystallization from acetic acid raised the melting point to 228° with decomposition. The product dissolved in acetone with a brilliant red color and, because the nitrogen analyses were nearly one per cent. low for 1,3,9-tribenzeneazo-4,6-dihydroxydibenzofuran, the impurity may be a dibenzeneazo derivative. Methylation imparted stability to the molecule, and a pure compound was isolated by methylating in acetone to give a 77% yield of what is probably 1,3,9-tribenzeneazo-4,6-dimethoxydibenzofuran. Crystallization from acetic acid gave a red-orange product melting at 191–193°. The structure assigned the compound is based largely on our present knowledge of diazo coupling of hydroxydibenzofurans.

Anal. Calcd. for $C_{22}H_{22}O_2N_6$: N, 15.56. Found: N, 15.52.

4,6-Dimethoxy-1-dibenzofurancarboxylic Acid. A.—Oxidation of 1 g. of 1-acetyl-4,6-dimethoxydibenzofuran by the procedure of Fuson and Tullock⁷ (iodine-potassium iodide, sodium hydroxide and dioxane) gave a 55.2% yield of 4,6-dimethoxy-1-dibenzofurancarboxylic acid which melted at 297–298° after crystallization from acetic acid.

Anal. Calcd. for $C_{12}H_{12}O_5$: C, 66.45; H, 4.45. Found: C, 66.21; H, 4.53.

B.—The filtered Grignard reagent prepared from 22.5 g. (0.073 mole) of 1-bromo-4,6-dimethoxydibenzofuran in a 1:1 ether-benzene solution, was carbonated by solid carbon dioxide to give the same 4,6-dimethoxy-1-dibenzofurancarboxylic acid (m. p. 297–298°). Mixed melting point determinations were made not only with the two acids from (A) and (B), but also with the methyl esters from each of these acids.

The methyl 4,6-dimethoxy-1-dibenzofurancarboxylate, prepared in a quantitative yield from the acid and diazomethane, melted at 163°.

Anal. Calcd. for $C_{16}H_{14}O_6$: C, 67.11; H, 4.93. Found: C, 67.2; H, 5.11.

Diazomethyl 4,6-Dimethoxy-1-dibenzofuryl Ketone.—The directions used were those of Arndt and Eistert,⁸ adapted to dibenzofurans. The required acid chloride was prepared by refluxing 11.5 g. (0.042 mole) of 4,6-dimethoxy-1-dibenzofurancarboxylic acid with 80.0 g.

(6) (a) Yamasiro, *J. Chem. Soc. Japan*, **59**, 945 (1938) [*C. A.*, **33**, 603 (1939)]; (b) Kirkpatrick and Parker, *This Journal*, **57**, 1123 (1935).

(7) Fuson and Tullock, *ibid.*, **56**, 1638 (1934).

(8) Arndt and Eistert, *Ber.*, **68**, 200 (1935); see, also, ref. 3.

(0.672 mole) of thionyl chloride for two and one-half hours, during which time the solid acid slowly dissolved to produce a clear red solution. The excess thionyl chloride was distilled off at diminished pressure at a temperature of 100° (water-bath). The crude pink acid chloride, after crystallization from dry benzene, melted over a wide, indefinite range which indicated incomplete conversion. Purification was effected by boiling the substance with petroleum ether (b. p. 77–115°). The acid chloride dissolved and 5.2 g. of impure, unconverted acid was removed by filtration. The colorless product which separated from the cooled solution melted at 147–150°. The yield was 6.2 g. or 50.5% of the theoretical.

To a stirred solution of diazomethane prepared from 20 ml. of ethyl N-nitroso-N-methylcarbamate was introduced, in several portions, 6.2 g. (0.0213 mole) of 4,6-dimethoxy-1-dibenzofurancarboxylic acid chloride. After five minutes of stirring, 100 ml. of anhydrous dioxane was added to effect solution. The ice-bath was removed and the clear yellow reaction mixture was allowed to stand overnight. The pale yellow crystals of diazomethyl 4,6-dimethoxy-1-dibenzofuryl ketone, melting at 151° with gas evolution, were filtered from solution. The yield was 1.34 g. or 21.2% of the theoretical.

*Anal.*⁹ Calcd. for C₁₆H₁₂O₄N₂: N, 9.46. Found: N, 9.51.

4,6-Dimethoxy-1-dibenzofurylacetylamide.—A solution of 1.25 g. (0.0042 mole) of diazomethyl 4,6-dimethoxy-1-dibenzofuryl ketone in 75 ml. of dioxane was placed in a 250-ml. flask fitted with reflux condenser and mechanical stirrer. With efficient stirring, 15 ml. of concd. ammonium hydroxide was added followed by 5 ml. of 10% silver nitrate solution. Heating on the steam-bath and stirring were continued for forty-five minutes. Then 5 ml. more of concd. ammonium hydroxide was added, and the stirred solution was heated for thirty minutes longer.

The hot solution was filtered and diluted to a volume of 300 ml. with water. Cooling in the refrigerator precipitated 0.82 g. (66% yield) of the gray amide, m. p. 206–207°. Pure 4,6-dimethoxy-1-dibenzofurylacetylamide crystallized from alcohol, after digestion with Norite, in the form of needles, m. p. 210–211°. The yield of pure compound was 0.62 g. or 51.6%.

Anal. Calcd. for C₁₆H₁₅O₄N: N, 4.91. Found: N, 4.86.

4,6-Dimethoxy-1-dibenzofurylacetic Acid.—A mixture of 0.5 g. (0.00175 mole) of 4,6-dimethoxy-1-dibenzofurylacetylamide, 25 ml. of 15% sodium hydroxide solution and 5 ml. of alcohol was refluxed for thirteen hours before a clear solution was realized. The reaction mixture was diluted with 50 ml. of water, gently boiled with a pinch of Norite, and filtered. Acidification of the solution precipitated the crude acid in nearly quantitative yield, m. p. 204–205°. Two crystallizations from alcohol gave colorless needles of 4,6-dimethoxy-1-dibenzofurylacetic acid, m. p. 205.5–206.5°. The yield was 0.36 g. or 71.7%.

Anal. Calcd. for C₁₆H₁₄O₆: C, 67.11; H, 4.93. Found: C, 67.0; H, 4.98.

(9) The authors are grateful to Messrs. L. D. Apperson and T. H. Cook for help with some of the nitrogen analyses.

3-Hydrazinodibenzofuran.—In essential accordance with the directions of Fischer,¹⁰ 9.2 g. (0.05 mole) of 3-aminodibenzofuran was diazotized, and the suspension of diazonium chloride was reduced by stannous chloride.

The white 3-hydrazinodibenzofuran hydrochloride was filtered off and crystallized from a large volume of water. It melted with decomposition at 242–243°. The yield was 10.3 g. or 87.3%.

Anal. Calcd. for C₁₂H₁₁ON₂Cl: N, 11.94. Found: N, 11.98.

The free 3-hydrazinodibenzofuran was obtained by decomposing a hot solution of the hydrochloride with sodium acetate. The base readily dissolved in hot alcohol, crystallizing from this solvent in the form of small pale yellow needles, m. p. 174–175°, which turned orange in color in contact with the atmosphere.

Anal. Calcd. for C₁₂H₁₀ON₂: N, 14.14. Found: N, 14.09.

A melting point of 225° for the hydrochloride, and 152° for the free base, have been reported.¹¹

1,2,3,4-Tetrahydro-6-aminodibenzofuran.—Two and five-tenths grams (0.0136 mole) of 4-aminodibenzofuran was dissolved in 100 ml. of absolute alcohol contained in a three-necked flask equipped with stirrer and reflux condenser. A nitrogen atmosphere was used throughout the reduction. While the solution was stirred vigorously, the sodium (8.0 g.) was added in small pieces through the top of the condenser. After the addition, which required twenty-five minutes, the solution was boiled gently to dissolve the remaining sodium. A noticeable amount of ammonia was evolved during the reduction.

The hot reaction mixture was poured promptly into ice and hydrochloric acid in sufficient quantity to render the resulting solution acid to litmus. After removal of the alcohol by steam distillation, the mixture was immersed in a freezing mixture, made alkaline with 10% sodium hydroxide, and extracted thrice with a total volume of 400 ml. of ether. This red solution was dried over anhydrous sodium sulfate, and, following filtration, gaseous hydrogen chloride was introduced. The solid was filtered off and repeatedly washed with sodium-dried ether to remove a red resinous impurity adhering to the shiny pink plates of the hydrochloride. The yield was 1.9 g. or 62%. The salt was dissolved in water, digested with Norite, and filtered. Gaseous hydrogen chloride precipitated small pink plates which commenced to darken at 214° and melted at 228° with decomposition. Attempts to prepare a solid free base were unsuccessful, the product remained as an oil at 0°. The low hydrogen values indicated that some unreduced amine may have been present as an impurity.

Anal. Calcd. for C₁₂H₁₄ONCl: C, 64.4; H, 6.31. Found: C, 64.4 and 64.4; H, 6.06 and 5.99.

In experiments to determine which ring had been reduced, the observation was made that a dry ether solution of the tetrahydro-6-aminodibenzofuran would not form a carbonate, although carbon dioxide was bubbled into the solution for an hour.

The following coupling reaction definitely established the aromatic nature of the reduced amine. Five milli-

(10) Fischer, *Ann.*, **222**, 237 (1885).

(11) Borsche and Bothe, *Ber.*, **41**, 1940 (1908).

liters of dilute (6 *N*) hydrochloric acid was added to a solution of 0.1 g. (0.00045 mole) of the tetrahydro-6-aminodibenzofuran hydrochloride in 15 ml. of water. Diazotization was effected by cautiously adding a 5% solution of sodium nitrite to the ice-cold, well-stirred solution until cadmium iodide-starch paper immediately turned blue when moistened with the stirring rod. After the clear yellow diazonium solution had stood for thirty minutes, it was slowly added to a cold solution of 0.1 g. of β -naphthol in 25 ml. of 10% sodium hydroxide. A brilliant carmine red dye, m. p. 199–201°, immediately precipitated in quantitative yield (0.15 g.).

Summary

Incidental to studies concerned with the bridging of the 1- and 9-positions in dibenzofuran types, series of 1,4- and 1,4,6-derivatives have been synthesized. In these compounds the 4- and the 4,6-substituents are strong ortho-para directors. Among other compounds described are 4,6-dimethoxy-1-dibenzofurylacetic acid and 1,2,3,4-tetrahydro-6-aminodibenzofuran.

AMES, IOWA

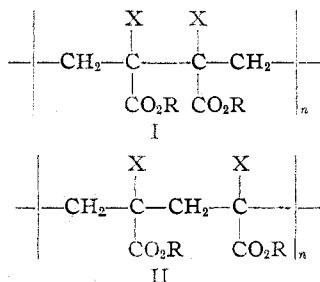
RECEIVED SEPTEMBER 1, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

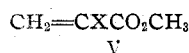
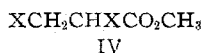
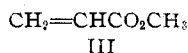
The Structure of Vinyl Polymers. IV.¹ The Polymers of the Methyl α -Haloacrylates

BY C. S. MARVEL AND JOHN CHARLES COWAN²

The polymers of the α -haloacrylates are especially suitable for a study of the arrangement of the structural units in the polymeric chain, since the reactions of the simple 1,2- and 1,3-dihalogen esters which correspond to the two most probable arrangements (I and II) of the structural units in these polymers are well known.



The polymer of methyl α -chloroacrylate has been described³ but the corresponding bromo compound apparently has not been prepared previously. In the present work the α,β -dihaloacrylates (IV) were treated with quinoline to give the α -haloacrylates (V).



The monomeric esters polymerized readily on standing or more rapidly on warming in the presence of peroxides. The polymers could be obtained either as clear, pale amber glassy solids or

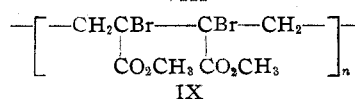
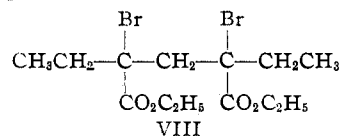
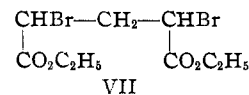
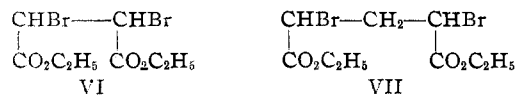
(1) For the third communication in this series, see *THIS JOURNAL*, **61**, 1682 (1939).

(2) Du Pont Special Research Assistant in Chemistry, 1937–1939.

(3) British Patent 411,860; *C. A.*, **28**, 6956 (1934).

as white powders. They were readily soluble in dioxane and acetone. Viscosity measurements on 0.606% (0.0368 molar, based on monomeric unit) solutions indicated a molecular weight of about 11,500. One sample of methyl α -chloroacrylate which polymerized slowly at room temperature over a period of nine months gave a polymer insoluble in acetone, benzene and dioxane; this insolubility indicates a very high molecular weight.

When either the chloro or bromo polymer was treated with potassium iodide in peroxide-free acetone or dioxane, iodine was liberated. This reaction is characteristic for 1,2-dihalogen compounds⁴ and indicates that the methyl α -haloacrylate polymers have structure I above and thus do not have the usual 1,3-distribution of the functional groups which has been accepted as the structural feature of most vinyl polymers. A comparison of the amount of iodine liberated from potassium iodide by ethyl α,α' -dibromosuccinate (VI), ethyl α,α' -dibromoglutarate (VII),



(4) Davis and Heggie, *J. Org. Chem.*, **2**, 470 (1937).