

at 110° for several hours over phosphorus pentoxide under reduced pressure.

An alcoholic solution of the product shows no coloration with ferric chloride and it does not reduce Fehling's solution. A chloroform solution of the substance absorbs bromine and it shows a yellow coloration in acetic acid on the addition of a few drops of sulfuric acid. The product was recovered unchanged after refluxing with acetic anhydride and sodium acetate for two hours. It was not affected by cold 20% potassium hydroxide but dissolved slowly on boiling to produce a light yellow solution.

Anal. Calcd. for $C_{25}H_{21}O_3(OCH_3)_3$: C, 72.7; H, 6.57; OCH_3 , 20.1; mol. wt., 462.4. Found: C, 72.9; H, 6.69; OCH_3 , 20.06; mol. wt. (Rast), 420, 437.

The same product was obtained by application of the same methylation procedure to pomiferin dimethyl ether. The identity of the products was established by melting point and mixed melting point.

Absorption Spectra.⁷—The absorption spectra of osajin, iso-osajin, pomiferin and iso-pomiferin were observed in absolute ethanol. The data are shown in Fig. 2 and Fig. 3. A single band spectrum was obtained for each compound.

Acknowledgment is gratefully made to the National Youth Administration for assistance rendered in this investigation.

Summary

1. A second yellow pigment has been isolated

(7) The absorption spectra measurements were made by Miss J. Appleton of this Laboratory, according to the method described in Brode, "Chemical Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1939, p. 273.

from the fruit of the osage orange tree (*Machura pomifera* Raf.). The name pomiferin is assigned to this substance and it is shown that the experimental data so far obtained harmonize with a provisional formula of $C_{25}H_{21}O_6$.

2. The basicity of osajin is shown to be more in harmony with an acidic phenolic structure than with a lactone structure.

3. The substance previously described as osajic acid di-*p*-toluenesulfonate² is shown to be pomiferin di-*p*-toluenesulfonate.

4. Osajin forms a mono-*p*-toluenesulfonate (m. p. 152°).

5. The melting point of osajin diacetate is established as 164°.

6. A diacetate, triacetate, dimethyl ether, trimethyl ether, and dimethyl ether monoacetate of pomiferin have been prepared.

7. Both osajin and pomiferin are isomerized by sulfuric acid-glacial acetic acid mixtures to high-melting, colorless, crystalline substances.

8. Pomiferin di-*p*-toluenesulfonate is isomerized under the same conditions and the product is identical with the reaction product formed between iso-pomiferin and *p*-toluenesulfonyl chloride.

9. The absorption spectra of osajin, iso-osajin, pomiferin and iso-pomiferin have been observed.

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Dibenzofuran. XIII. Orientation and Substituted Amines¹

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Introduction

Incidental to the determination of structure of substituted amines, it is now shown that the generalizations on orientation postulated previously² are adequate for the predominant products which result from polysubstitution of the dibenzofuran nucleus.

Nitration.—Nitration of a monosubstituted dibenzofuran having a strongly meta-orienting group proceeded heteronuclearly and the entering nitro group went largely to the 7-position, and the 8-position was involved only to a subordinate extent. The nitro acid obtained from nitration of 2-

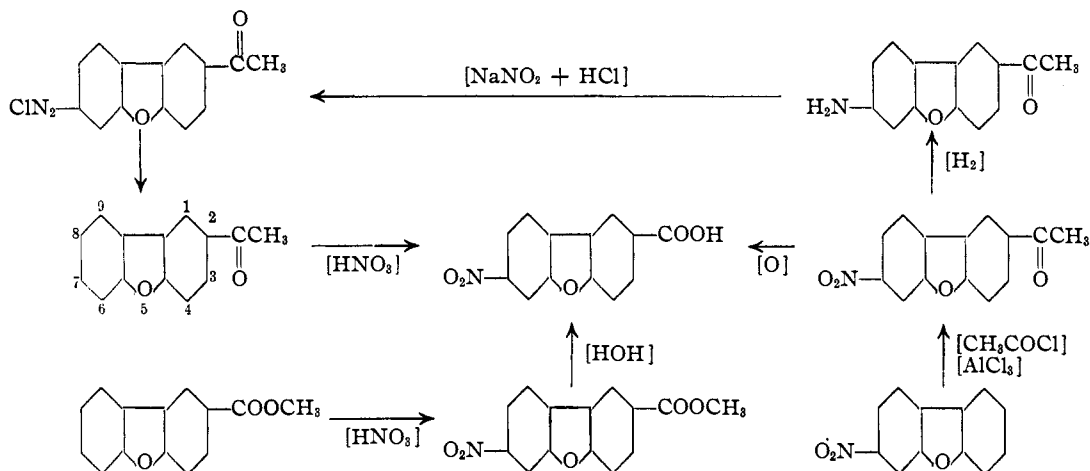
acetyldibenzofuran was identical with that obtained from nitration of methyl 2-dibenzofurancarboxylate. The same acid resulted by oxidation of the acetyl-3-nitrodibenzofuran prepared by a Friedel-Crafts reaction with 3-nitrodibenzofuran.

The chief nitro ester obtained by nitration of methyl 3-dibenzofurancarboxylate was methyl 2-nitro-7-dibenzofurancarboxylate. The position of the nitro group was shown by hydrolysis to a nitro acid which on decarboxylation yielded 2-nitrodibenzofuran.

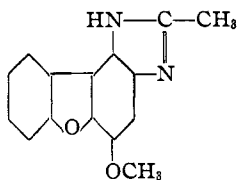
Nitration of 1-acetamino-4-methoxydibenzofuran took place homonuclearly, as might have been predicted, and the nitro group was directed ortho to the acetamino group. The structure of

(1) Paper XII, THIS JOURNAL, 61, 1371 (1939).

(2) Gilman, Brown, Bywater and Kirkpatrick, *ibid.*, 56, 2473 (1934); Gilman, Van Ess and Hayes, *ibid.*, 61, 643 (1939). See, also, Cullinane, *J. Chem. Soc.*, 2365 (1932).



the 1-acetamino-2-nitro-4-methoxydibenzofuran was established by reduction and cyclization to a methoxy-imidazole. Incidentally, it was shown



that the nitro group did not go ortho to the methoxy group, for the replacement of the original acetamino group by hydrogen gave a nitro-4-methoxydibenzofuran unlike the known 3-nitro-4-methoxydibenzofuran.³

The nitration product of 1-bromo-4-methoxydibenzofuran was shown to be 1-bromo-3-nitro-4-methoxydibenzofuran, for debromination and reduction gave a quantitative yield of the known 3-amino-4-methoxydibenzofuran.³

Nitration of 2-acetyl-7-acetaminodibenzofuran must have introduced a nitro group ortho to the acetamino group because reduction and cyclization gave an acetyl-imidazole. The nitro group undoubtedly entered the 8-position rather than the 6-position, for there is no case of direct nuclear substitution (other than metalation) into the 4- or the 6-position.⁴

Nitration of 4-bromo- and 4-iododibenzofuran would be expected to go heteronuclearly to a predominant extent, for nitration of 2-bromodibenzofuran gave 2-bromo-7-nitrodibenzofuran.⁵ Fur-

(3) Gilman, Jacoby and Swislowky, *THIS JOURNAL*, **61**, 954 (1939).

(4) In the preparation of pyridodibenzofurans by the Skraup synthesis with 3-aminodibenzofuran, one of the isomers involves a ring closure in the 4-position. See Mosettig and Robinson, *ibid.*, **57**, 902 (1935), and Kirkpatrick and Parker, *ibid.*, **57**, 1123 (1935). It is understood that a suitable accumulation of groups might force a direct nuclear substitution to the 4- or 6-position.

(5) Gilman, Brown, Bywater and Kirkpatrick, *ibid.*, **56**, 2473 (1934).

thermore, the nitrobromo compound obtained by nitration of 3-bromodibenzofuran⁵ has now been shown to be 3-bromo-7-nitrodibenzofuran because catalytic reduction replaced the bromine by hydrogen and reduced the nitro group to give 3-aminodibenzofuran. A similar reduction of the nitro-4-iododibenzofuran did not reduce the nitro group appreciably, and the chief product was 3-nitrodibenzofuran.

Bromination and Thiocyanogenation.—Bromination of ethyl 2-dibenzofurancarboxylate gave ethyl 2-bromo-8-dibenzofurancarboxylate. This structure followed from the fact that the bromo acid obtained by hydrolysis of the bromo ester was identical with the bromo acid obtained by oxidation of the Friedel-Crafts acetylation product of 2-bromodibenzofuran.

Thiocyanogenation of 3-aminodibenzofuran introduced the thiocyanogen group either into the 2- or the 4-position because the aminothiocyanogen compound could be rearranged to a thiazole. The thiocyanogen group undoubtedly entered the 2-position. Thiocyanogenation is like halogenation, and it is known that bromination of 3-acetaminodibenzofuran gives 2-bromo-3-acetaminodibenzofuran.⁵ In addition, we already have mentioned the improbability of direct substitution into a 4- or 6-position.

Friedel-Crafts Reactions.—Diacylation of dibenzofuran⁶ and acetylation of 2-acetyldibenzofuran gave 2,8-diacetyldibenzofuran, identified by oxidation to the corresponding dibasic acid. Acetylation of methyl 4-dibenzofurancarboxylate gave methyl 2-acetyl-6-dibenzofurancarboxylate, the structure of which was established by hydrolysis and then decarboxylation to yield 2-acetyl-di-

(6) Borsche and Schacke, *Ber.*, **56**, 2498 (1923).

benzofuran, and by making the reasonable assumption that heteronuclear substitution occurs when a strongly meta-orienting group is present. This assumption has great validity because bromine, which has a less marked heteronuclear orientation effect than a carbomethoxy group, directs acylation heteronuclearly. For example, acetylation of 2-bromodibenzofuran gave 2-acetyl-8-bromodibenzofuran, the structure of which was established by oxidation to a 2-bromodibenzofurancarboxylic acid, which on debromination yielded 2-dibenzofurancarboxylic acid.

Acetylation of 2,8-dibromodibenzofuran gave 2,8-dibromo-3-acetyldibenzofuran. The structure of this product was proved by debromination and then oxidation of the resulting 3-acetyldibenzofuran to the known 3-dibenzofurancarboxylic acid.

Other Friedel-Crafts reactions have been mentioned in the discussion of nitration, and the Experimental Part describes additional reactions of this kind leading to amino derivatives of the brazan and other types. A miscellany of reactions other than those concerned with direct nuclear substitution are also contained in the Experimental Part.

Experimental Part

Nuclear Substitutions of 4-Derivatives

1-Bromo-4-methoxydibenzofuran.—A solution of 27.5 g. (0.17 mole) of bromine in 170 cc. of acetic acid was added in several portions to a solution of 34 g. (0.17 mole) of 4-methoxydibenzofuran in 340 cc. of acetic acid at room temperature with shaking. Decolorization was immediate. After standing overnight the product was thrown out of solution by diluting with water. Crystallization from ethanol gave 42 g. (88%) of material melting at 96–97°. A second recrystallization gave the pure product melting at 97–97.5° which showed no depression in melting point when mixed with an authentic specimen prepared by the methylation of 1-bromo-4-hydroxydibenzofuran.⁷

4-Methoxy-1-dibenzofurancarboxylic Acid.—The Grignard reagent prepared from 5 g. (0.018 mole) of 1-bromo-4-methoxydibenzofuran and 0.5 g. (0.02 g. atom) of magnesium in a mixture of 25 cc. of ether and 10 cc. of benzene was carbonated in the customary manner. A yield of 2.7 g. (62%) of the pure compound (crystallization from ethanol) was obtained melting at 279–280° with decomposition.

Anal. Calcd. for $C_{14}H_{10}O_4$: C, 69.40; H, 4.13. Found: C, 69.67 and 69.00; H, 4.61 and 4.90.

1- β -Hydroxyethyl-4-methoxydibenzofuran.—To an ice-cold solution of the Grignard reagent prepared from 22.2 g. (0.08 mole) of 1-bromo-4-methoxydibenzofuran was added 8.0 g. (0.18 mole) of ethylene oxide. The solution was allowed to warm to room temperature and then re-

fluxed for one hour. After standing overnight, most of the ether was distilled off and replaced by dry benzene, and refluxing was continued for one hour. The resulting mixture was hydrolyzed by ice and 30% sulfuric acid, and the benzene layer was washed with sodium carbonate solution, dried and distilled under reduced pressure. The material, 11.5 g. (59%), distilled between 195–206° (2 mm.). Recrystallization from petroleum ether (b. p., 60–68°) gave crystals melting at 96–96.5°.

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 74.35; H, 5.83. Found: C, 74.42; H, 6.03.

1- β -Diethylaminoethyl-4-methoxydibenzofuran Hydrochloride.—Dry hydrogen bromide was bubbled through 8.8 g. (0.028 mole) of molten 1- β -hydroxyethyl-4-methoxydibenzofuran for two and one-half hours at 100°. After washing with water and recrystallizing twice from ethanol, the product weighed 2.0 g. and melted at 91–91.5°. The 1- β -bromoethyl-4-methoxydibenzofuran was mixed with 2.0 g. (0.016 mole) of diethylamine and 2 cc. of ethanol and heated for six hours at 100°. When cool the reaction product was treated with 5% sodium hydroxide solution and extracted with ether. The ether solution was evaporated and the residue warmed to drive off the excess diethylamine. Saturating an ether solution of the residual oil with dry hydrogen chloride precipitated the salt which was purified by recrystallizing from an acetone-ether mixture. The yield was 1.5 g. (68%) of hydrochloride melting at 187° with decomposition.

Anal. Calcd. for $C_{18}H_{24}O_2NCl$: N, 4.20. Found: N, 4.26 and 4.43.

1-Acetyl-4-methoxydibenzofuran.—A Friedel-Crafts reaction was effected with 10 g. (0.05 mole) of 4-methoxydibenzofuran in 50 cc. of carbon disulfide, 6.8 g. (0.05 mole) of aluminum chloride and 4.0 g. (0.05 mole) of acetyl chloride. One recrystallization of the crude material from ethanol gave 8.0 g. (66%) of product melting at 132–133°. A second recrystallization raised the melting point to 134–134.5°.

Anal. Calcd. for $C_{15}H_{12}O_3$: C, 74.97; H, 5.04. Found: C, 74.66 and 75.30; H, 5.42 and 5.39.

Oxidation of 1 g. (0.004 mole) of the 1-acetyl-4-methoxydibenzofuran in 130 cc. of water containing 2 g. of sodium hydroxide with 3 g. (0.019 mole) of potassium permanganate gave a 90% yield of 4-methoxy-1-dibenzofurancarboxylic acid (mixed m. p.).

The oxime of 1-acetyl-4-methoxydibenzofuran was obtained in an 88% yield, and melted at 176–177.5° after crystallization from ethanol.

Anal. Calcd. for $C_{15}H_{13}O_2N$: N, 5.49. Found: N, 5.44.

Beckmann Rearrangement of the Oxime from 1-Acetyl-4-methoxydibenzofuran.—The rearrangement was effected in 95% yield by treating a suspension of the oxime in benzene with phosphorus pentachloride. The resulting 1-acetamino-4-methoxydibenzofuran melted at 222–223° after crystallization from ethanol.

Anal. Calcd. for $C_{15}H_{13}O_2N$: N, 5.49. Found: N, 5.43 and 5.47.

Refluxing a solution of 2 g. (0.008 mole) of the 1-acetamino-4-methoxydibenzofuran in 200 cc. of 95% ethanol with 50 cc. of concd. hydrochloric acid gave a 91% yield

(7) Gilman and Van Ess, *This Journal*, **61**, 1365 (1939).

of 1-amino-4-methoxydibenzofuran hydrochloride. The free base melting at 103–104° showed no depression in melting point with the 1-amino-4-methoxydibenzofuran obtained by reduction of 1-nitro-4-methoxydibenzofuran.⁹

1-Acetamino-2-nitro-4-methoxydibenzofuran.—Nitration of 0.8 g. (0.003 mole) of 1-acetamino-4-methoxydibenzofuran in glacial acetic acid with 1 cc. of fuming nitric acid gave a 74% yield of the nitro compound which melted at 244° after recrystallization from acetic acid.

Anal. Calcd. for C₁₃H₁₂O₅N₂: N, 9.33. Found: N, 9.30 and 9.69.

The acetamino compound was hydrolyzed in essentially quantitative yield by refluxing with concd. hydrochloric acid in ethanol. The 1-amino-2-nitro-4-methoxydibenzofuran melted at 206–207° after crystallization from toluene.

Anal. Calcd. for C₁₃H₁₀O₄N₂: N, 10.85. Found: N, 10.36 and 10.70.

2-Nitro-4-methoxydibenzofuran.—The 1-amino-2-nitro-4-methoxydibenzofuran could not be diazotized by usual procedures; however, diazotization was effected in essential accordance with the directions of De Milt and Van Zandt.⁸

A mixture of 15 cc. of concd. sulfuric acid and 7.5 cc. of water was cooled to 5° in an ice-bath. Six-tenths of a gram (0.009 mole) of sodium nitrite was added and the mixture was warmed gently on the steam-bath until a clear solution resulted. This solution was cooled to 5–10° and a solution of 0.6 g. (0.0023 mole) of the 1-amino-2-nitro-4-methoxydibenzofuran in 12 cc. of pyridine was added dropwise over a period of forty-five minutes with continuous shaking. The temperature was maintained below 10° at all times. Following the addition of the pyridine solution the mixture was allowed to stand at this temperature for one-half hour and then stirred into 50 g. of ice. To remove the excess of nitrous acid, 0.6 g. of urea was added and the mixture stirred until foaming had ceased. Fifteen cc. of ethanol was added and the clear solution was refluxed for five minutes on the hot plate. When cool, the red-brown precipitate was recrystallized repeatedly from methanol, and there resulted a 35% yield of the 2-nitro-4-methoxydibenzofuran as light yellow, feathery needles melting at 185–186°.

Anal. Calcd. for C₁₃H₉O₄N: N, 5.76. Found: N, 5.72 and 5.66.

2-Amino-4-methoxydibenzofuran.—A suspension of 0.1 g. of the 2-nitro-4-methoxydibenzofuran in 25 cc. of ethanol was reduced at room temperature under forty-five pounds (4 atm.) gage pressure of hydrogen using Raney nickel as a catalyst. The amine was obtained in fine, slightly colored crystals melting at 127–127.5° after crystallization from ethanol.

Anal. Calcd. for C₁₃H₁₁O₂N: N, 6.57. Found: N, 6.74.

3-Dibenzofurylurea.—A solution of 9.15 g. (0.05 mole) of 3-aminodibenzofuran and 6.0 g. (0.057 mole) of nitro-urea in 150 cc. of ethanol was allowed to stand at room temperature. A pearly, crystalline precipitate of pure 3-dibenzofurylurea had settled at the end of two days, weighing 7.5 g. (66.5% yield). In a capillary tube the material

shows signs of softening at 215–220°, but does not melt up to 325°. On a nickel block the substance melts and re-solidifies immediately at 222–223°.

Anal. Calcd. for C₁₃H₁₀O₂N₂: N, 12.38. Found: N, 12.65 and 12.52.

Buck and Ferry⁹ have observed that ethanol is a better medium than water for the reaction between amines and nitro-urea.

4-Bromodibenzofuran.—An ether solution of 4-dibenzofuryllithium was prepared by metalating 42 g. (0.25 mole) of dibenzofuran with *n*-butyllithium. To the cooled solution was admitted a slow stream of bromine vapor obtained by bubbling nitrogen through 40 g. (0.25 mole) of bromine. The yield of 4-bromodibenzofuran melting at 70–71° was 40.5%.

Anal. Calcd. for C₁₂H₇OBr: Br, 25.05. Found: Br, 25.19.

4-Bromo-7-nitrodibenzofuran.—An acetic acid solution of 4-bromodibenzofuran was nitrated by fuming nitric acid to give 4-bromo-7-nitrodibenzofuran which melted at 205° after crystallization from acetic acid.

Anal. Calcd. for C₁₂H₆O₃NBr: N, 4.79. Found: N, 5.10 and 5.18. The residues are being examined for isomers.

4-Iodo-7-nitrodibenzofuran.—To a solution of 10 g. (0.034 mole) of 4-iododibenzofuran in 50 cc. of glacial acetic acid was added 8 cc. of fuming nitric acid, and the mixture was warmed and stirred for three hours. The yellow 4-iodo-7-nitrodibenzofuran was obtained in 32.4% yield, and melted at 223° after crystallization from acetic acid.

Anal. Calcd. for C₁₂H₆O₃NI: N, 4.13. Found: N, 4.13 and 4.14.

Reduction of 4-Iodo-7-nitrodibenzofuran and 3-Bromo-7-nitrodibenzofuran.—An absolute ethanol solution of 0.25 g. of 4-iodo-7-nitrodibenzofuran was reduced in essential accordance with the directions of Busch and Stöve¹⁰ using the palladium catalyst and shaking for one and one half hours under a 15-pound gage pressure of hydrogen. A 32% yield of 3-nitrodibenzofuran (mixed m. p.) was obtained.

Under corresponding conditions, 3-bromo-7-nitrodibenzofuran⁵ gave a 40% yield of 3-aminodibenzofuran (mixed m. p.).

Methyl 2-Acetyl-6-dibenzofurancarboxylate.—To a suspension of 13.5 g. (0.06 mole) of methyl 4-dibenzofurancarboxylate and 10.6 g. (0.08 mole) of aluminum chloride in 100 cc. of carbon disulfide was added 4.7 g. (0.06 mole) of acetyl chloride. After refluxing for eight hours and then allowing to stand overnight, there was obtained 2.5 g. (15.5%) of methyl 2-acetyl-6-dibenzofurancarboxylate which melted at 174–175° subsequent to recrystallization from ethanol. In addition there was recovered 9.6 g. of the initial ester.

Anal. Calcd. for C₁₆H₁₂O₄: C, 71.64; H, 4.48. Found: C, 71.47 and 71.38; H, 4.65 and 4.56.

Hydrolysis of the acetyl ester by heating with 20% sodium hydroxide gave 2-acetyl-6-dibenzofurancarboxylic acid, which when crystallized from dilute ethanol melted

(8) De Milt and Van Zandt, *THIS JOURNAL*, **58**, 2044 (1936).

(9) Buck and Ferry, *ibid.*, **58**, 854 (1936).

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

at 262–265°. This acetyl acid was decarboxylated by heating with copper bronze and quinoline for one-half hour at 235–240° to give 2-acetyldibenzofuran (mixed m. p.).

Nuclear Substitutions of 3-Derivatives

2-Acetyl-7-nitrodibenzofuran.—A Friedel-Crafts reaction was carried out with a suspension of 56 g. (0.26 mole) of 3-nitrodibenzofuran in 400 cc. of nitrobenzene, 53 g. (0.40 mole) of powdered aluminum chloride, and 33 g. (0.42 mole) of acetyl chloride. Subsequent to hydrolysis the aqueous layer was decanted from the resulting gelatinous precipitate and nearly all of the nitrobenzene was removed by steam distillation. Complete removal of the solvent was effected by shaking the residue with methanol, filtering, and washing the material with an additional small quantity of methanol. The crude product weighed 62 g. (93.5%) and melted at 208–210°. Crystallization from acetic acid gave the pure compound melting at 212–213°.

Anal. Calcd. for $C_{14}H_9O_4N$: N, 5.49. Found: N, 5.58 and 5.62.

When carbon disulfide was used as the medium, the 3-nitrodibenzofuran was recovered unchanged after heating for eight hours.

2-Acetyl-7-aminodibenzofuran.—If the nitro compound used in this preparation was washed with dilute ammonium hydroxide and thoroughly dried, it was hydrogenated easily with Raney nickel catalyst. Twenty grams (0.079 mole) of 2-acetyl-7-nitrodibenzofuran suspended in 150 cc. of absolute ethanol was reduced with hydrogen at steam temperature under forty-five pounds gage pressure using approximately 10 cc. of an alcoholic suspension of Raney nickel catalyst. Reduction required about an hour and gave practically a quantitative yield of the crude amine melting at 156°. After recrystallization from ethanol the 2-acetyl-7-aminodibenzofuran melted at 158–159°.

Anal. Calcd. for $C_{14}H_{11}O_2N$: N, 6.22. Found: N, 6.26 and 6.54.

2-Acetyl-7-acetaminodibenzofuran and Its Oxime.—A nearly quantitative yield of the crude monoacetamino compound was obtained, at room temperature, by adding 8.7 g. (0.08 mole) of acetic anhydride to a well-stirred solution of 15.3 g. (0.068 mole) of the 2-acetyl-7-aminodibenzofuran in 150 cc. of acetic acid diluted with 35 cc. of water. The acetamino compound, which precipitated immediately, was recrystallized from ethanol and finally from benzene to yield cotton-like needles melting at 203°.

Anal. Calcd. for $C_{16}H_{15}O_3N$: N, 5.24. Found: N, 5.32.

A portion of this compound was converted to the oxime to make certain that reduction of the ketone group had not occurred in the preceding hydrogenation. A solution of 0.5 g. of potassium hydroxide in 5 cc. of water was added to a solution of 1.35 g. (0.005 mole) of the 2-acetyl-7-acetaminodibenzofuran and 0.5 g. (0.007 mole) of hydroxylamine hydrochloride in 75 cc. of ethanol. After four and one-half hours of refluxing the solution was poured into water and the precipitate filtered off. Crystallization from ethanol gave a 64% yield of colorless crystals of 1-acetyl-7-acetaminodibenzofuran oxime melting at 203°. A mixed melting point with the starting material was 176–178°.

Anal. Calcd. for $C_{16}H_{14}O_3N_2$: N, 9.92. Found: N, 9.92.

Replacement of Amino Group in 2-Acetyl-7-amino-dibenzofuran by Hydrogen.—The acetyl-amino compound was diazotized, and by customary procedures, using ethanol, the diazonium group was replaced by hydrogen. The resulting 2-acetyldibenzofuran was identified by mixed melting point.

Oxidation of 2-Acetyl-7-nitrodibenzofuran.—A solution of 16 g. of the acetyl-nitro compound in 150 cc. of acetic acid was oxidized by heating for three hours with 80 g. of chromic acid in 150 cc. of acetic acid. The resulting 3-nitro-7-dibenzofurancarboxylic acid, purified through the sodium salt, was obtained in a yield of 11.5 g. (72%) and was observed to soften at 295° and decompose at 300°.

Anal. Calcd. for $C_{13}H_7O_6N$: N, 5.45; neut. equiv., 256. Found: N, 5.53 and 5.51; neut. equiv., 251 and 252.

The following oxidizing agents were not satisfactory: acid or neutral potassium permanganate, bromine, sodium dichromate and sulfuric acid, and "Perchloron" (70% calcium hypochlorite).

Nitration of Methyl 3-Dibenzofurancarboxylate.—The 3-dibenzofurancarboxylic acid (m. p. 270°) was prepared in an 84% yield by carbonation of 3-dibenzofurylmagnesium bromide. Esterification by methanol and hydrogen chloride gave a quantitative yield of methyl 3-dibenzofurancarboxylate.

Nitration of 6 g. (0.0265 mole) of methyl 3-dibenzofurancarboxylate by a mixture of 32.5 cc. of concd. nitric acid and 5 cc. of fuming nitric acid gave 2.5 g. (34.8%) of methyl 2-nitro-7-dibenzofurancarboxylate which melted at 235–236° after recrystallization from acetic acid.

Anal. Calcd. for $C_{14}H_9O_6N$: N, 5.17. Found: N, 5.28 and 5.13.

In addition to some unaltered ester, there was isolated another nitro ester which melted at 202–203° and which was probably methyl 3-nitro-7-dibenzofurancarboxylate.

Hydrolysis of the methyl 2-nitro-7-dibenzofurancarboxylate by heating with a mixture of acetic and hydrochloric acids gave 2-nitro-7-dibenzofurancarboxylic acid which did not melt at 330°. This nitro acid was decarboxylated, by heating with quinoline and copper, to yield 2-nitrodibenzofuran (mixed m. p.).

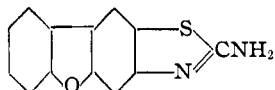
3-Amino-2-dibenzofurylthiocyanate.—Five grams (0.027 mole) of 3-aminodibenzofuran and 8.5 g. (0.11 mole) of ammonium thiocyanate were dissolved in 400 cc. of 95% acetic acid and cooled to 1–3°. A solution of 4.3 g. of bromine in 25 cc. of acetic acid was then added dropwise over a period of fifteen minutes to the vigorously stirred mixture. Despite the addition of 100 cc. more of 95% acetic acid a complete solution could not be maintained at this temperature. The crude material was recrystallized from hot ethanol to yield 2.8 g. (43%) of slightly crude 3-amino-2-dibenzofurylthiocyanate. Further recrystallization gave the pure product melting at 175° with immediate resolidification.

Anal. Calcd. for $C_{18}H_9OSN_2$: N, 11.66. Found: N, 11.88 and 11.62.

The compound gave the characteristic yellow precipitate always formed when an alkaline lead tartrate solution is

added to an ethanolic solution of a thiocyanate.¹¹ Rearrangement had not taken place to the thiazole, for the thiazole compound (described below) gave a white precipitate under corresponding conditions.

2 - Aminobenzofuro[2,3-f]benzothiazole.—A rearrangement of the 3-amino-2-dibenzofurylthiocyanate to the thiazole compound was effected by refluxing an ethanolic



solution with hydrochloric acid for one-half hour. A quantitative yield of the crude compound was obtained which was recrystallized several times from benzene to give the pure product melting at 268–269°.

Anal. Calcd. for $C_{13}H_9OSN_2$: N, 11.66. Found: N, 11.64 and 11.62.

The hydrochloride, precipitated from an ether solution of the base by dry hydrogen chloride, decomposed above 300°.

Nuclear Substitutions of 2-Derivatives

2,8-Diacetyldibenzofuran.—This diacetyl derivative was prepared by Friedel–Crafts reactions starting with either dibenzofuran or 2-acetyldibenzofuran. To a solution of 67.2 g. (0.4 mole) of dibenzofuran and 80 g. (0.6 mole) of aluminum chloride in 200 cc. of carbon disulfide was added 31.4 g. (0.4 mole) of acetyl chloride. The reaction products were fractionated under reduced pressure. The yield of pure 2-acetyldibenzofuran ranged from 46 to 57%, and the yield of 2,8-diacetyldibenzofuran was about 8%. With acetic anhydride, the yield of diacetyl compound increased somewhat at the expense of the monoacetyl compound. Nitrobenzene appeared less satisfactory as a medium, for the yield of monoacetyl compound was 40% and the mixture was worked up with greater difficulty.

Under essentially corresponding conditions, 18 g. (0.086 mole) of 2-acetyldibenzofuran, 22.8 g. (0.17 mole) of aluminum chloride, 7.3 g. (0.09 mole) of acetyl chloride and 100 cc. of carbon disulfide yielded 7 g. (32%) of 2,8-diacetyldibenzofuran. The diacetyl compound melted in all cases at 160° and not at 140° as reported previously.⁶ The identity of our diacetyl compound was established by oxidation to 2,8-dibenzofurandicarboxylic acid. Incidentally this dibasic acid was also synthesized in a low yield by carbonation of the di-Grignard reagent prepared from 2,8-dibromodibenzofuran. It was, however, best prepared by carbonation of the dilithium compound obtained by interaction of *n*-butyllithium and 2,8-dibromodibenzofuran. Metalation of 2,8-dibromodibenzofuran by means of phenylcalcium iodide, and then carbonation yielded 2,8-dibromo-4,6-dibenzofurandicarboxylic acid.¹²

The oxime of 2-acetyldibenzofuran was obtained in a 97% yield, and melted after crystallization from ethanol at 139–140°.

Oxidation of 10 g. (0.03 mole) of 2-acetyldibenzofuran by an alkaline solution of "Perchloron" gave a 97% yield of 2-dibenzofurancarboxylic acid melting at 236–242°. Recrystallization from ethanol raised the melting point to 247–248°. The procedure described was less satisfactory

when larger quantities of reactants were used. 2-Acetyldibenzofuran was first oxidized to 2-dibenzofurancarboxylic acid by means of calcium hypochlorite.¹³

2,8-Dibromo-3-acetyldibenzofuran.—From reaction between 22.8 g. (0.07 mole) of 2,8-dibromodibenzofuran, 13.3 g. (0.1 mole) of aluminum chloride and 5.5 g. (0.07 mole) of acetyl chloride in 150 cc. of carbon disulfide was obtained 10 g. (35%) of 2,8-dibromo-3-acetyldibenzofuran melting at 157–157.5° after crystallization from acetic acid.

Anal. Calcd. for $C_{14}H_9O_2Br_2$: Br, 43.48. Found: Br, 43.67 and 43.72.

The structure of the dibromo-acetyl compound was established by first replacing the bromines by hydrogen (palladium–calcium carbonate catalyst) to get a relatively pure 3-acetyldibenzofuran which melted at 120–122° after crystallization from ethanol; and then oxidizing the acetyl compound by alkaline permanganate to 3-dibenzofurancarboxylic acid, which was compared with an authentic specimen.

Nitration of 2-Acetyldibenzofuran.—The nitro-acetyl compound obtained by earlier workers⁶ was not isolated by us; instead, a nitro acid was obtained which melted at 290°.

Methyl 3-Nitro-8-dibenzofurancarboxylate.—A 95% yield of methyl 2-dibenzofurancarboxylate, melting at 73–74° after crystallization from petroleum ether (b. p. 60–68°), was obtained by the rapid addition of hydrogen chloride to a heated suspension of 2-dibenzofurancarboxylic acid in methanol. When the ester was nitrated in essential accordance with the directions described recently¹⁴ for the nitration of methyl 4-dibenzofurancarboxylate, one of the products isolated melted at 239–240°.

Acetylation of 2-Bromodibenzofuran.—A 32% yield of 2-bromo-8-acetyldibenzofuran distilling at 205° (4 mm.) was obtained by a Friedel–Crafts reaction between 2-bromodibenzofuran and acetyl chloride in carbon disulfide. Oxidation of the bromo-acetyl compound by means of hypochlorite gave 2-bromo-8-dibenzofurancarboxylic acid melting at 328°. Debromination of the bromo acid by means of hydrogen and the palladium–calcium carbonate catalyst gave 2-dibenzofurancarboxylic acid (mixed m. p.).

Ethyl 2-Bromo-8-dibenzofurancarboxylate.—Ethyl 2-dibenzofurancarboxylate, prepared by the addition of absolute ethanol to the reaction mixture of 2-dibenzofurancarboxylic acid and thionyl chloride, melted at 54°. To 5 g. (0.02 mole) of this ester in 30 cc. of glacial acetic acid was added 3.33 g. (0.02 mole) of bromine. The mixture was heated for eight hours at 70° and finally for four hours at 115° before bromine vapors ceased refluxing. A part of the product was 2-bromo-8-dibenzofurancarboxylic acid. The main fraction (28% yield) was ethyl 2-bromo-8-dibenzofurancarboxylate which melted at 130°.

Anal. Calcd. for $C_{15}H_{11}O_3Br$: Br, 32.36. Found: Br, 32.53 and 32.40.

The ester was hydrolyzed quantitatively, by refluxing with a mixture of acetic and concd. hydrochloric acids, to 2-bromo-8-dibenzofurancarboxylic acid which melted with decomposition at 328°.

Neutralization equivalent. Calcd. for $C_{15}H_{11}O_3Br$: 291.

(11) Soderbach, *Ann.*, **443**, 156 (1925).

(12) Studies by R. E. Dickey.

(13) Mayer and Krieger, *Ber.*, **55**, 1659 (1922).

(14) Gilman, Van Ess and Hayes, *This Journal*, **61**, 643 (1939).

Found: 290. A comparison of this bromo acid with that obtained from the Friedel-Crafts reaction with 2-bromodibenzofuran showed them to be the same.

1-Bromo-3-nitro-4-methoxydibenzofuran and its Reduction to 3-Amino-4-methoxydibenzofuran.—A mixture of 10 g. (0.036 mole) of 1-bromo-4-methoxydibenzofuran, 10 cc. of fuming nitric acid (sp. gr. 1.50) and 75 cc. of glacial acetic acid was heated with stirring for one and one-half hours at 90–95°. The yield of 1-bromo-3-nitro-4-methoxydibenzofuran, melting at 160–161°, was 47.5%. The acetic acid filtrate from the nitration contains the initial compound which can be recovered readily and used in a second nitration.

Anal. Calcd. for $C_{12}H_9O_4NBr$: N, 4.35. Found: N, 4.31.

When an ethanolic solution of the bromonitromethoxy compound was reduced using the palladium-calcium carbonate catalyst, there resulted a quantitative yield of 3-amino-4-methoxydibenzofuran (mixed m. p.).

1-Bromo-3-amino-4-methoxydibenzofuran.—Reduction of an acetic acid solution of the bromonitromethoxy compound by stannous chloride and hydrochloric acid gave a practically quantitative yield of 1-bromo-3-amino-4-methoxydibenzofuran which melted at 135–136° after crystallization from ethanol.

Anal. Calcd. for $C_{13}H_{10}O_2NBr$: N, 4.79. Found: N, 4.95.

1-Bromo-3-acetamino-4-methoxydibenzofuran prepared by acetylation of the corresponding amine melted at 178–179° after crystallization from ethanol.

Anal. Calcd. for $C_{15}H_{12}O_3NBr$: N, 4.19. Found: N, 4.50.

Brazan Derivatives

β -[2-Dibenzofuroyl]-propionic Acid.—This compound was originally prepared by Mayer and Krieger^{15,16} but the method by which it was obtained was not described. The following procedure is based on the one used by Fieser and Hershberg¹⁶ for the Friedel-Crafts reaction of succinic anhydride with phenol ethers.

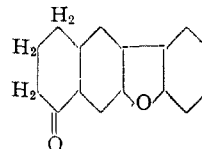
Dibenzofuran, 84.0 g. (0.5 mole), and succinic anhydride, 55.0 g. (0.55 mole), were suspended in a mixture of 400 cc. of tetrachloroethane and 200 cc. of nitrobenzene. With the temperature of the mixture held at 0–5°, 147.0 g. (1.1 moles) of powdered aluminum chloride was added in small portions with vigorous stirring. Subsequent to hydrolysis and steam distillation, the residue was filtered and extracted several times with hot sodium carbonate solution. The combined filtrates were acidified with dilute hydrochloric acid and the dried precipitate recrystallized from ethyl acetate to give 111 g. (83%) of the purified compound which melted at 185–186° in agreement with the value reported by Mayer and Krieger.¹⁵

β -[2-Dibenzofuryl]-*n*-butyric Acid.—For the reduction of the dibenzofuroylpropionic acid, the modified Clemmensen method reported by Martin¹⁷ was employed.

Fifty-five grams of β -[2-dibenzofuroyl]propionic acid was suspended in a mixture of 100 cc. of toluene, 75 cc.

of water and 175 cc. of concd. hydrochloric acid, and refluxed for twenty-five hours with 100 g. of amalgamated zinc. Three additional 50-cc. portions of concd. hydrochloric acid were added at approximately six-hour intervals. Crystallization from petroleum ether (b. p. 80–100°) gave 43.6 g. (83%) of the pure compound melting at 112–113°, in agreement with the melting point reported.¹⁵

7-Keto-7,8,9,10-tetrahydrobenzo[*b*]naphtho[2,3-*d*]furan.—Five grams (0.02 mole) of β -[2-dibenzofuryl]-*n*-



butyric acid was stirred into 100 g. of 88% sulfuric acid and the mixture allowed to stand at room temperature for fifteen minutes. The resulting deep red solution was poured on ice and the dilute acid decanted from the precipitate. The crude material was washed by decantation and warmed with 50 cc. of 10% sodium carbonate solution. The insoluble product was filtered off and recrystallized from ethanol to give 2.0 g. (45%) of pure compound melting at 137°.

Anal. Calcd. for $C_{16}H_{12}O_2$: C, 81.32; H, 5.12. Found: C, 81.53; H, 5.56.

Using sulfuric acid as the cyclizing agent none of the isomeric keto compound was isolated.¹⁸ Later, Robinson and Mosettig¹⁵ used phosphoric acid as the condensing agent and obtained a 3–4% yield of the isomer, and also established the structure of the 137° compound by conversion to brazan (benzo[*b*]naphtho[2,3-*d*]furan).

The oxime of 7-keto-7,8,9,10-tetrahydrobenzo[*b*]naphtho[2,3-*d*]furan, obtained in 85% yield, melted at 212–213° after crystallization from ethanol.

Anal. Calcd. for $C_{16}H_{12}O_2N$: N, 5.58. Found: N, 5.48.

7-Amino-7,8,9,10-tetrahydrobenzo[*b*]naphtho[2,3-*d*]furan Hydrochloride.—Fifty grams of freshly prepared 2% sodium amalgam was added in small portions to a well-stirred solution of 1.7 g. (0.007 mole) of the oxime of 7-keto-7,8,9,10-tetrahydrobenzo[*b*]naphtho[2,3-*d*]furan in 65 cc. of absolute ethanol at a temperature of 55–60°. The solution was constantly maintained slightly acid by the dropwise addition of acetic acid. When reduction was complete the solution was decanted away from the mercury into several times its volume of water. The solution was made acid to litmus with acetic acid and extracted once with ether. The ether extract was discarded and the aqueous layer was made alkaline with dilute sodium hydroxide solution and extracted twice with ether. The ether extracts were dried, and dry hydrogen chloride passed into the solution. The amine hydrochloride was obtained in a 54% yield and melted at 266–267° after crystallization from an ethanol-ether mixture.

Anal. Calcd. for $C_{16}H_{16}ONCl$: N, 5.12. Found: N, 4.95 and 5.23.

7-Keto-8-dimethylaminomethyl-7,8,9,10-tetrahydrobenzo[*b*]naphtho[2,3-*d*]furan Hydrochloride.—The

(15) See, also, Robinson and Mosettig, *THIS JOURNAL*, **61**, 1148 (1939).

(16) Fieser and Hershberg, *ibid.*, **58**, 2314 (1936).

(17) Martin, *ibid.*, **58**, 1438 (1936).

(18) Parker, *Iowa State Coll. J. Sci.*, **12**, 148 (1937) [*C. A.*, **32**, 2987 (1938)].

method of Mannich and Braun,¹⁹ as modified by Burger and Mosettig,²⁰ for the preparation of amino ketones was used in this synthesis.

A suspension of 2.4 g. (0.01 mole) of the 7-keto-7,8,9,10-tetrahydrobenzo[*b*]naphtho[2,3-*d*]furan, 1.0 g. (0.012 mole) of dimethylamine hydrochloride and 0.9 g. (0.03 mole) of trioxymethylene in 25 cc. of amyl alcohol was refluxed for five minutes. The hydrochloride was purified by carefully reprecipitating it several times from an absolute ethanolic hydrogen chloride solution with ether. The salt formed lustrous prisms melting at 185–186°. The yield of pure compound was 0.45 g. (14.3%).

Anal. Calcd. for C₁₈H₁₈O₂NCl: N, 4.43. Found: N, 4.39.

A repetition of this procedure with a longer time of refluxing gave no improvement in the yield.

Lateral Amino Derivatives

2- α -Aminoethylidibenzofuran Hydrochloride.—Interaction of 10.5 g. (0.05 mole) of 2-acetyldibenzofuran, 20 g. of ammonium formate and 5 cc. of acetic acid gave 2- α -aminoethylidibenzofuran hydrochloride which melted at 222–223° after crystallization from an acetone-ethanol mixture.

Anal. Calcd. for C₁₄H₁₃ONCl: N, 5.66. Found: N, 5.57 and 5.92.

2- α -Diethylaminoethylidibenzofuran Picrate.—Methyl-2-dibenzofurylcarbinol was prepared from 2-dibenzofurylmagnesium bromide and acetaldehyde.²¹ The corresponding bromide, prepared by means of dry hydrogen bromide, was treated with diethylamine to give the highly hygroscopic diethylamino salt. The picrate of the amine melted at 173–174° after crystallization from aqueous acetone.

Anal. Calcd. for C₂₄H₂₄O₃N₄: N, 11.29. Found: N, 11.45.

2- β -Dimethylaminopropionylidibenzofuran.—A mixture of 20.0 g. (0.095 mole) of 2-acetyldibenzofuran, 7.8 g. (0.096 mole) of dimethylamine hydrochloride and 3.0 g. (0.096 mole) of trioxymethylene suspended in 40 cc. of absolute ethanol was heated on the steam-bath for twelve hours. When cool the precipitate was filtered off and the filtrate evaporated. The combined residues were shaken with ether to remove unchanged 2-acetyldibenzofuran. The ether-insoluble crude 2- β -dimethylaminopropionylidibenzofuran hydrochloride weighing 21.4 g. (74%) was purified by recrystallizing from ethanol to give crystals melting at 194–195°. The free base, obtained by adding dilute ammonium hydroxide to an aqueous solution of the salt, was recrystallized from petroleum ether (b. p. 60–68°) and melted at 88–89°.

Anal. Calcd. for C₁₇H₁₇O₂N: N, 5.24. Found: N, 5.30.

3-Ethylaminodibenzofuran Hydrochloride.—The experiments in this section provide a new physical constant²² as

(19) Mannich and Braun, *Ber.*, **53**, 1874 (1920).

(20) Burger and Mosettig, *This Journal*, **58**, 1570 (1936).

(21) This compound was prepared earlier by Mosettig and Robinson, *ibid.*, **57**, 2186 (1935), by the catalytic hydrogenation of 2-acetyldibenzofuran.

(22) Kirkpatrick and Parker, *ibid.*, **37**, 1123 (1935).

well as some reactions of this compound. A mixture of 9.15 g. (0.05 mole) of 3-aminodibenzofuran and 10.5 g. (0.0525 mole) of ethyl *p*-toluenesulfonate was heated at 175–185° for one hour. After treatment with ammonium hydroxide and then with hydrogen chloride, the amine hydrochloride (3.5 g.) (33%) was found to melt at 228–229° with decomposition. Crystallization was from ethanol.

Anal. Calcd. for C₁₄H₁₄ONCl: N, 5.66. Found: N, 5.67.

The hydrochloride and sodium acetate in an ether-water medium gave a colorless oil which solidified to crystals melting at 69–70°.

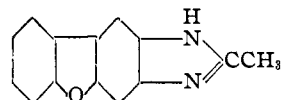
The **3-ethylnitrosoaminodibenzofuran** (prepared from the hydrochloride, sodium nitrite and dilute hydrochloric acid) crystallized from ethanol as bright orange crystals melting at 136–137°.

Anal. Calcd. for C₁₄H₁₂O₂N₂: N, 11.66. Found: N, 11.12.

Reduction of the nitrosoamine with stannous chloride and concd. hydrochloric acid gave the 3-ethylaminodibenzofuran hydrochloride (mixed m. p.).

Imidazoles

2-Methyl-1-benzofuro[2,3-*f*]benzimidazole.—3-Aminodibenzofuran was monoacetylated by adding 12 g. (0.12



mole) of acetic anhydride to a solution of 20 g. (0.11 mole) of 3-aminodibenzofuran in a mixture of 150 cc. of acetic acid and 200 cc. of water at a temperature between 40 and 50° with vigorous stirring. The thick, heavy precipitate which resulted in a few seconds was poured into water and filtered off to give a 97% yield of material suitable for nitration.

Nitration was effected by adding 3.5 cc. of fuming nitric acid (sp. gr. 1.50) to a solution of 10 g. (0.04 mole) of 3-acetaminodibenzofuran in 60 cc. of glacial acetic acid at 85–90°. The 2-nitro-3-acetaminodibenzofuran separated almost at once. The mixture was poured into an excess of water and filtered. Crystallization of the crude product from acetic acid yielded 9.2 g. (76%) of light yellow crystals melting at 196°.

To a hot solution of 2.0 g. (0.0074 mole) of 2-nitro-3-acetaminodibenzofuran in 25 cc. of acetic acid was cautiously added in several portions with shaking a solution of 8.0 g. (0.035 mole) of hydrated stannous chloride in 8.0 cc. of concd. hydrochloric acid and the solution heated for a few minutes. The crude imidazole was purified through its hydrochloride by recrystallizing from dilute hydrochloric acid. The hydrochloride (melting above 335°) was converted to the free base which melts at 270°, and was obtained in a yield of 0.9 g. (55%).²³

Anal. Calcd. for C₁₄H₁₀ON₂: N, 12.61. Found: N, 12.79 and 12.87.

2-Methyl-5-methoxy-1-benzofuro[3,2-*e*]benzimidazole.—To a hot solution of 3.0 g. (0.01 mole) of 1-

(23) Weidenhagen and Weeden, *Ber.*, **71**, 2347 (1938), have reported a melting point of 264.5° for the free base and a decomposition point at about 278° for the hydrochloride.

acetamino-2-nitro-4-methoxydibenzofuran in 75 cc. of glacial acetic acid was added in several portions a solution of 12.5 g. (0.055 mole) of hydrated stannous chloride in 13.5 cc. of concd. hydrochloric acid. The mixture was then refluxed for five and one-half hours on the hot-plate. After diluting with 200 cc. of water the solution was made alkaline with 33% sodium hydroxide solution and the precipitate filtered off. The crude material was purified by boiling its methanol solution with Norite and saturating the cooled solution with dry hydrogen chloride. The hydrochloride precipitated in fine needles melting at 306–307° with decomposition. From the hydrochloride was obtained the free base in a yield of 1.8 g. (72.5%), melting at 222–222.5°.

Anal. Calcd. for $C_{15}H_{12}O_2N_2$: N, 11.10. Found: N, 10.95 and 11.16.

2 - Methyl - 8 - acetyl - 1 - benzofuro[2,3-*f*]benzimidazole.—First, **2-acetyl-7-acetamino-8-nitrodibenzofuran** was prepared. A solution of 5.4 g. (0.02 mole) of 2-acetyl-7-acetaminodibenzofuran in 120 cc. of glacial acetic acid was heated on the steam-bath with stirring, and 6 cc. of fuming nitric acid (sp. gr. 1.50) was added in one portion. The practically pure material thus obtained weighed 4.0 g. (64%) and melted at 269–270°. Crystallization from acetic acid raised the melting point to 270–271°.

Anal. Calcd. for $C_{16}H_{17}O_5N_2$: N, 8.97. Found: N, 9.19 and 9.00.

Four grams (0.013 mole) of 2-acetyl-7-acetamino-8-nitrodibenzofuran was suspended in 80 cc. of ethanol and reduced with hydrogen at 100° for one-half hour under a gage pressure of forty-five pounds using Raney nickel catalyst. The crude 2-acetyl-7-acetamino-8-aminodibenzofuran was refluxed one hour with 50 cc. of glacial acetic acid. The crude imidazole was obtained by diluting the acetic acid solution with water and making alkaline with ammonium hydroxide. The product was dissolved in hot methanol, boiled with Norite, and the solution saturated with dry hydrogen chloride. The pure hydrochloride precipitated in fine needles melting with decomposition at about 325°. From the hydrochloride was obtained the free base melting at 298° in a yield of 2.3 g. (55%).

Anal. Calcd. for $C_{16}H_{12}O_2N_2$: N, 10.59. Found: N, 10.73 and 10.96.

4-Dibenzofuryl Derivatives

1-(4-Dibenzofuryl)-isoquinoline.—This compound was prepared in essential accordance with the directions of Ziegler and Zeiser²⁴ for 1-*n*-butylisoquinoline, and the method is being extended to other dibenzofurylnitrogen heterocycles.

A solution of *n*-butyllithium prepared from 27.4 g. (0.2 mole) of *n*-butyl bromide and 2.8 g. (0.4 g. atom) of lithium in 300 cc. of ether was refluxed with 30 g. (0.18 mole) of dibenzofuran under a nitrogen atmosphere for four and one-half hours. The resulting solution of 4-dibenzofuryllithium was cooled to 0–5° in an ice-bath and 19.3 g. (0.15 mole) of isoquinoline in 50 cc. of dry ether was added with stirring. Subsequent to hydrolysis and treatment with

ammonium hydroxide, several recrystallizations from ethanol gave 5.0 g. (a 11.3% yield based on isoquinoline) of the free base melting at 137–138°.

Anal. Calcd. for $C_{21}H_{19}ON$: N, 4.74. Found: N, 4.83 and 4.82.

The hydrochloride is immediately hydrolyzed in water.

4-Dibenzofurylacetylacetamide.—This synthesis was based on the general procedures of Arndt and Eistert.²⁵ 4-Dibenzofurancarboxylic acid chloride was prepared by treating the acid with thionyl chloride in the usual manner. A more convenient purification was effected, however, by recrystallizing the acid chloride from petroleum ether (b. p. 60–68°).

To a diazomethane solution in ether, prepared from 50 g. (0.485 mole) of nitrosomethylurea was added 25 g. (0.11 mole) of 4-dibenzofurancarboxylic acid chloride in several portions. The crude diazomethyl 4-dibenzofuryl ketone was obtained in a quantitative yield, and a portion recrystallized once from petroleum ether (b. p. 60–68°) melted at 72–75°. This material was used directly in the following procedure.

Conversion of the diazo compound to the 4-dibenzofurylacetylacetamide is accomplished in a better yield if too large a run is not made. A solution of 5.0 g. (0.02 mole) of the diazomethyl 4-dibenzofuryl ketone in 100 cc. of dioxane was heated on the steam-bath, and 25 cc. of concd. ammonium hydroxide was added followed by 5 cc. of a 10% solution of silver nitrate. The precipitated crude 4-dibenzofurylacetylacetamide was obtained in a 67% yield. Recrystallization from ethanol gave the pure compound melting at 211–212°.

Anal. Calcd. for $C_{14}H_{11}O_2N$: N, 6.22. Found: N, 6.10 and 5.98.

4-Dibenzofurylacetic Acid.—Five grams (0.022 mole) of the 4-dibenzofurylacetylacetamide suspended in 150 cc. of 15% sodium hydroxide solution was refluxed for five hours. Acidification of the solution with dilute hydrochloric acid precipitated the crude 4-dibenzofurylacetic acid in an 82% yield, which melted at 213.5–214.5° after crystallization from ethanol.

Anal. Calcd. for $C_{14}H_{10}O_3$: C, 74.31; H, 4.46. Found: C, 74.57; H, 4.66.

3,4-Dimethoxy- α -(4-dibenzofurylacetylacetamino)-acetophenone.—Two grams (0.009 mole) of 4-dibenzofurylacetic acid and 10 cc. of thionyl chloride were gently refluxed together for three hours. The excess thionyl chloride was removed under reduced pressure and the residual oil dissolved in petroleum ether (b. p. 60–68°) and filtered to remove a slight amount of insoluble residue. Evaporation of the petroleum ether left the 4-dibenzofurylacetyl chloride as a viscous oil which was dissolved in 95 cc. of ether and added to 20 cc. of an aqueous solution of 1.5 g. (0.0065 mole) of 3,4-dimethoxy- α -aminoacetophenone hydrochloride.²⁶ A solution of 2.5 g. of potassium hydroxide in 15 cc. of water was added, and the mixture shaken for ten minutes and allowed to stand overnight. The emulsion which had formed was filtered, leaving a residue of 2.6 g. of the crude amide. Acidification of the

(25) Arndt and Eistert, *Ber.*, **68**, 200 (1935).

(26) Prepared according to the procedure of Pictet and Gams, *ibid.*, **42**, 2943 (1909).

(24) Ziegler and Zeiser, *Ann.*, **485**, 174 (1931).

filtrate yielded 0.3 g. of crude 4-dibenzofurylacetic acid. The crude amide was recrystallized from benzene to yield 1.5 g. (57% yield based on amine) of the pure amide melting at 186–187°.

Anal. Calcd. for $C_{24}H_{21}O_5N$: N, 3.47. Found: N, 3.71 and 3.72.

3,4 - Dimethoxy - α - (4 - dibenzofuroylamino) - acetophenone.—The reaction between 0.1 g. of 4-dibenzofurancarboxylic acid chloride and 0.1 g. of 3,4-dimethoxy- α -aminoacetophenone hydrochloride was carried out by the same procedure as that just given. The product was recrystallized from ethanol and melted at 178–179°.

Anal. Calcd. for $C_{28}H_{19}O_5N$: N, 3.71. Found: N, 3.68.

Acknowledgment.—The authors are grateful to H. B. Willis for assistance.

Summary

Experiments are described concerning the preparation and proof of structure of some substituted amines and other derivatives of dibenzofuran. The generalizations on orientation postulated previously have been shown to be adequate for the predominant products which result from polysubstitution of the dibenzofuran nucleus.

AMES, IOWA

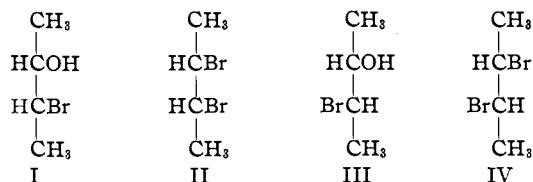
RECEIVED JUNE 26, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 724]

The Loss of Optical Activity in the Reaction of the Optically Active erythro- and threo-3-Bromo-2-butanols with Hydrobromic Acid

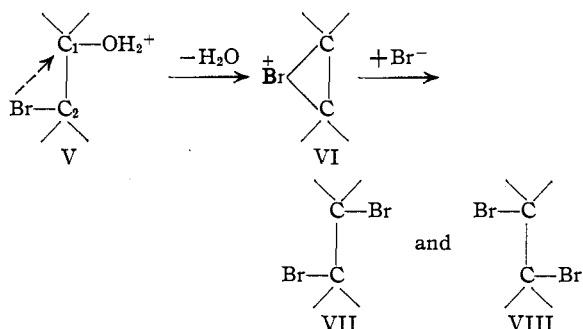
BY S. WINSTEIN¹ AND H. J. LUCAS

Recently it was shown² that *dl*-erythro-3-bromo-2-butanol I is converted into *meso*-2,3-dibromobutane II, and *dl*-threo-3-bromo-2-butanol III, is converted into *dl*-2,3-dibromobutane IV, by the action of fuming hydrobromic acid, with complete retention of configuration.^{3,4}



In order to account for this unusual behavior, it was assumed that the replacement of the hydroxyl group by the bromine atom took place by a mechanism involving attack by the bromine atom on the adjacent carbon atom of the bromohydrin. This bromine atom, simultaneously with the removal of the OH_2^+ group V (which is formed from the OH group and a proton), forms a bond with the carbon atom on the face away from the OH_2^+ group, thus leading to the formation of the positively charged cyclic intermediate, VI,⁵ of

Roberts and Kimball⁶ which then reacts with bromide ion to produce the two possible dibromides VII and VIII.



On the basis of this mechanism two inversions take place, for the formation of the intermediate, VI, is accompanied by an inversion of carbon atom C_1 , and the reaction of this with bromide ion is accompanied by a second inversion. If VII is the product, C_1 is inverted twice, while if VIII is the product C_1 and C_2 are each inverted once. This explains the formation of *meso*-2,3-dibromobutane from the *erythro*-bromohydrin, and of *dl*-2,3-dibromobutane from the *threo*-bromohydrin. In fact, each of the active forms of the *threo*-bromohydrin is predicted by this mechanism to give *dl*-2,3-dibromobutane, since VII and VIII would be formed in equal amounts.

It was pointed out that this feature could be used as a test for the mechanism by starting

(1) At present National Research Fellow in Chemistry at Harvard University.

(2) Winstein and Lucas, *THIS JOURNAL*, **61**, 1576 (1939).

(3) Only one of the two antipodes of the *dl*-compounds is shown.

(4) By retention of configuration in these cases is meant merely that an *erythro*-bromohydrin gives rise to a *meso*-dibromide and a *threo*-bromohydrin to a *dl*-dibromide. Strictly speaking, configuration is not retained.

(5) We propose to call the simplest ion having this structure, ethylenebromonium ion.

(6) Roberts and Kimball, *THIS JOURNAL*, **59**, 947 (1937).