

TABLE I

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

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

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

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

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

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

Summary

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

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

AMES, IOWA

RECEIVED MARCH 2, 1939

{CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE}

Dibenzofuran. XII. Metalation of Some Bromo Derivatives

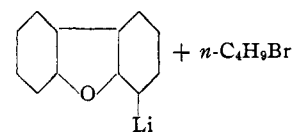
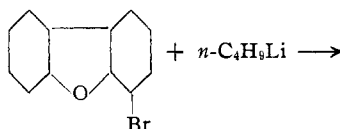
BY HENRY GILMAN, H. B. WILLIS AND JACK SWISLOWSKY

Introduction

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

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

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



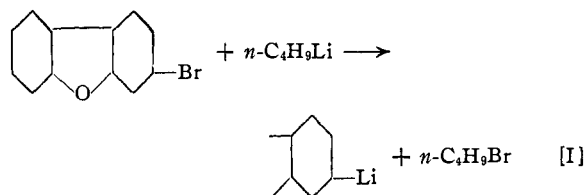
(1) (a) Gilman and Young, *THIS JOURNAL*, **56**, 1415 (1934); **57**, 1121 (1935); (b) Gilman and Bebb, *ibid.*, **61**, 109 (1939); (c) Gilman and Jacoby, *J. Org. Chem.*, **3**, 108 (1938); Wittig, Pockels and Dröge, *Ber.*, **71**, 1903 (1938); Gilman, Langham and Jacoby, *THIS JOURNAL*, **61**, 106 (1939); Wittig and Pockels, *Ber.*, **72**, 89 (1939); (d) Gilman, Cheney and Willis, *THIS JOURNAL*, **61**, 951 (1939).

This replacement reaction was not wholly ex-

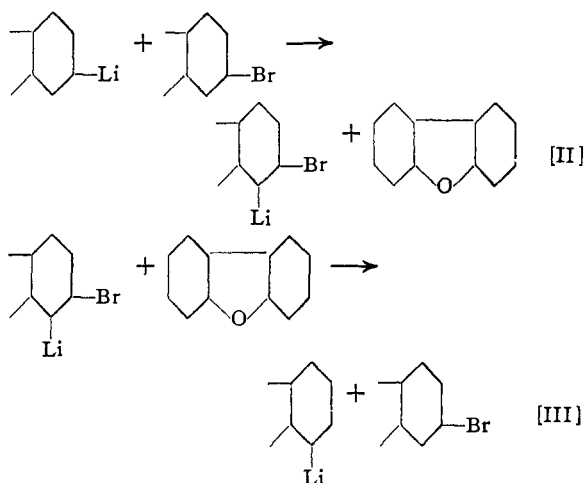
pected. Although halogen ortho to an ether linkage is replaceable by metal,^{1c} some metalation in the 6-position might have been predicted. The ease of this reaction suggested that a Grignard reagent might effect a related replacement. However, there was no evidence of such a reaction when methylmagnesium iodide was used under corresponding conditions.²

We are also reporting a reaction with 2,8-dibromodibenzofuran which took a completely unexpected course, and gave 2,8-dibenzofurylenedilithium. Inasmuch as 2-bromodibenzofuran reacted smoothly to give 2-bromo-4-dibenzofuryllithium, a related reaction with 2,8-dibromodibenzofuran should have given 2,8-dibromo-4,6-dibenzofurylenedilithium. The observed reaction is anomalous not only because the halogen replaced was not ortho to an ether linkage, but also because there was no metalation of the available positions ortho to the ether bridge. It is significant that the parent nucleus, dibenzofuran, cannot be dimetalated under the experimental conditions followed; the more reactive RNa and RK compounds have been used for dimetalation.^{1a} Incidentally, the reaction appears to be one of choice for the preparation of 2,8-dibenzofurancarboxylic acid by carbonation of the dilithium compound.

The unusual results with 2,8-dibromodibenzofuran suggested a metalation of 3-bromodibenzofuran. The two acids isolated, subsequent to carbonation, were 3-dibenzofurancarboxylic acid and 4-dibenzofurancarboxylic acid. The 3-acid probably resulted by a replacement or interconversion. It is more difficult to account for the formation of the 4-acid. A possible explanation is one involving intramolecular metalation, or essentially rearrangement of the 3-lithium compound to the 4-lithium compound which would have the metal ortho to an ether linkage. A more probable interpretation is illustrated by the following transformations:



(2) Challenger and Miller, *J. Chem. Soc.*, **894**, (1938), have shown that anisole and phenetole can be metalated under forced conditions by some Grignard reagents to yield the corresponding *o*-methoxyphenyl- and *o*-ethoxyphenylmagnesium bromides.



That is, the initially formed 3-dibenzofuryllithium [I] metalated 3-bromodibenzofuran to give 3-bromo-4-dibenzofuryllithium and dibenzofuran [II]. Then a second metalation took place, and the unsubstituted dibenzofuran underwent metalation as it does with all metalating agents to give the 4-dibenzofuryllithium [III].

Some of the apparently anomalous results now reported with bromine derivatives of dibenzofuran are not peculiar to this heterocycle. Mr. Wright Langham³ has observed that the three bromotoluenes when treated with *n*-butyllithium and then followed by carbonation give the three corresponding toluic acids; the *p*-bromo- and *p*-iodotoluenes under related conditions give *p*-toluic acid; and that *p*-chloroanisole and *p*-fluoroanisole give the 2-methoxy-5-halogenobenzoic acids. Apparently, the so-called positive alkoxy or alkyl groups are not necessary for smooth replacement reactions, inasmuch as excellent yields of *p*-chlorobenzoic acid and *p*-iodobenzoic acid are obtained from *p*-chloriodobenzene in only thirty minutes with no external application of heat.

Experimental Part

4-Bromodibenzofuran.—To 10 g. (0.041 mole) of 4-bromodibenzofuran in ether was added a solution of *n*-butyllithium (0.06 mole) in ether. After refluxing one hour, an equal volume (150 cc.) of dry benzene was added. The solution was refluxed six hours, then cooled, diluted with ether and carbonated by pouring upon solid carbon dioxide. After extraction with several portions of 5% potassium hydroxide, the alkaline solution was acidified and yielded 7.4 g. (81%) of crude 4-dibenzofurancarboxylic acid melting at 197–200°. Crystallization from alcohol gave 5 g. (57.5%) of pure acid, melting at 207–208°, and free of bromine. A mixed melting point determination with an authentic specimen showed no depression.

(3) Private communication.

Anal. Calcd. for $C_{13}H_8O_3$: neut. equiv., 212.6. Found: 212.2.

The 4-dibenzofurancarboxylic acid was then converted to the corresponding methyl ester, by means of diazomethane, and the methyl 4-dibenzofurancarboxylate was identified by the method of mixed melting points.

A solution of 5 g. of 4-bromodibenzofuran in 50 cc. of ether and 30 cc. of a 2 molar (excess) solution of methylmagnesium iodide in *n*-butyl ether was heated for sixteen hours at 50°. Subsequent to carbonation and hydrolysis by the usual procedures there was recovered 4 g. or 80% of 4-bromodibenzofuran.

2,8-Dibromodibenzofuran.—To a solution of 10.7 g. (0.033 mole) of 2,8-dibromodibenzofuran in 150 cc. of benzene was added a filtered solution of 0.066 mole of *n*-butyllithium in 75 cc. of ether. A clear greenish solution resulted upon mixing, and after a few minutes the solution turned opaque and a white precipitate started to form. This precipitate became quite heavy before one hour had passed. Heating was begun as soon as the two solutions were mixed, and stirring and gentle refluxing (reflux temperature, 60–65°) were continued for seven and one-half hours. In carbonating, by pouring upon crushed solid carbon dioxide, it was necessary to rinse the flask several times with dry ether in order to wash out the heavy, grayish sludge which settled to the bottom.

Subsequent to removal of the solvent there was obtained 4.4 g. (52.1%) of 2,8-dibenzofurandicarboxylic acid which melted above 350°.

Anal. Calcd. for $C_{14}H_8O_5$: neut. equiv., 128. Found: neut. equiv. 127.7, 128.5.

The dimethyl ester, prepared from the acid and diazomethane, melted at 165–166° and showed no depression with a sample⁴ prepared from 2,8-dibromodibenzofuran via cuprous cyanide fusion, hydrolysis and diazomethane esterification.

From the acidic fraction there was obtained also 0.5 g. of gummy material which softened at 90°, was not melted completely at 200° and which did not contain bromine. From the neutral residue (1.3 g.) there was obtained on steam distillation 25 mg. of dibenzofuran and about 1 g. of a colorless, oily liquid which may be 2,8-dibutyldibenzofuran. In two additional experiments in which the reactants were refluxed for 30 minutes and 10 minutes, the yields of di-acid were 68.7% and 72.2%.

In another experiment, 16.3 g. (0.05 mole) of 2,8-dibromodibenzofuran in 160 cc. of benzene was treated with 0.11 mole of *n*-butyllithium in 160 cc. of ether at the reflux temperature (about 50°) for seven hours. The color and precipitate formation were like those in the experiment having more benzene and heated at a higher temperature; however, the yield of 2,8-dibenzofurandicarboxylic acid was 1.9 g. or 14.8%, and more of the neutral oily liquid formed.

Incidentally, the preparation of 2,8-dibenzofurandicarboxylic acid by metalation at a reflux temperature of 60–65° is very probably a method of choice. Although a 62% yield is obtainable⁵ from the dicyanide, the hydroly-

sis is difficult and slow. The dibasic acid is formed in 10% yield by carbonation of the corresponding di-RMgBr compound. Sugii and Shindo⁶ obtained the acid by stepwise oxidation of 2,8-dimethyldibenzofuran, prepared by ring closure; and Tomita⁷ prepared the acid by oxidation of 2,8-dichloroacetyldibenzofuran. These authors also prepared the corresponding dimethyl ester (m. p. 167°).

3-Bromodibenzofuran.—Three and one-half grams (0.0142 mole) of 3-bromodibenzofuran in 60 cc. of benzene was refluxed for seven hours with 0.04 mole (determined by acid titration⁸) of *n*-butyllithium in 30 cc. of ether. Within a few minutes after mixing, a white precipitate formed which became heavier as the reaction progressed. Carbonation yielded 830 mg. (27.4%) of crude acid (m. p. 175–215°), which did not contain bromine. From 0.2 g. of this material, which was fractionally crystallized from dilute methanol, dilute acetic acid and glacial acetic acid, there was isolated 4-dibenzofurancarboxylic acid, m. p. 206–207°, and impure 3-dibenzofurancarboxylic acid, m. p. 245–260°. The 4-acid showed no depression in melting point when mixed with an authentic specimen. Four-tenths gram of the crude material was esterified by treatment with excess diazomethane in ether. The crude ester melted at 65–80°. After fractional crystallizations from dilute acetic acid and petroleum ethers (b. p. 30–40° and 60–68°), there was isolated 3-carbomethoxydibenzofuran, m. p. 137–138°, and 4-carbomethoxydibenzofuran, m. p. 92–94°. Both esters showed no depressions in mixed melting point determinations with authentic specimens. The ratio of 4-carbomethoxydibenzofuran to 3-carbomethoxydibenzofuran appeared to be about 5 to 1. From the neutral residue there was recovered by steam distillation 650 mg. (18.5%) of 3-bromodibenzofuran.

In a second experiment, some pure 3-dibenzofurancarboxylic acid was isolated in addition to an acid which did not melt at 350° and whose methyl ester melted at 140°. This new acid is very probably a bi-dibenzofurandicarboxylic acid formed as a result of coupling.

Summary

Interconversion but no metalation takes place when 4-bromodibenzofuran and 2,8-dibromodibenzofuran are treated with *n*-butyllithium. The products, subsequent to carbonation, are 4-dibenzofurancarboxylic acid and 2,8-dibenzofurandicarboxylic acid, respectively.

Both interconversion and metalation probably occur when 3-bromodibenzofuran is metalated, and the acids obtained are 3-dibenzofurancarboxylic acid and 4-dibenzofurancarboxylic acid.

AMES, IOWA

RECEIVED MARCH 29, 1939

(6) Sugii and Shindo, *J. Pharm. Soc. Japan*, **53**, 571 (1933).

(7) Tomita, *ibid.*, **56**, 901 (1936).

(8) Gilman, Wilkinson, Fishel and Meyers, *THIS JOURNAL*, **46**, 150 (1923).

(4) Kindly provided by E. W. Smith.

(5) Studies by E. W. Smith.