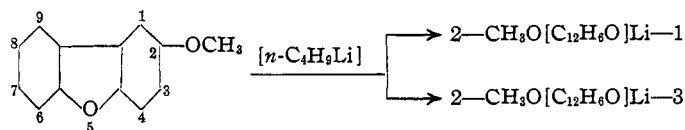


[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

**Dibenzofuran. XVIII. Isomeric Metalation Products of Some Phenols and their Methyl Ethers<sup>1</sup>**

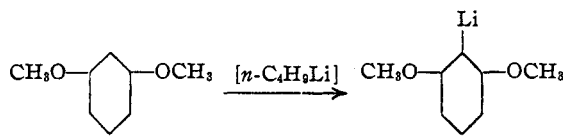
BY HENRY GILMAN, H. B. WILLIS, T. H. COOK, F. J. WEBB AND R. N. MEALS

Metalation in an ortho position is a general reaction not only of ethers but also of the corresponding phenols.<sup>2</sup> However, where isomeric metalation products are possible, the phenols of dibenzofuran appear to form a lesser number of isomers than do the corresponding methyl ethers. For example, metalation of 2-methoxydibenzofuran<sup>3</sup> takes place in the 1- and the 3-positions, whereas metalation of 2-hydroxydibenzofuran apparently involves the 1-position exclusively, for



the only acid isolated subsequent to carbonation is 2-hydroxy-1-dibenzofurancarboxylic acid. Similarly, metalation of 4-methoxydibenzofuran, followed by carbonation, gives both 4-methoxy-6-dibenzofurancarboxylic acid and 4-methoxy-3-dibenzofurancarboxylic acid; and metalation of 4-hydroxydibenzofuran gives, subsequent to carbonation, only 4-hydroxy-6-dibenzofurancarboxylic acid.

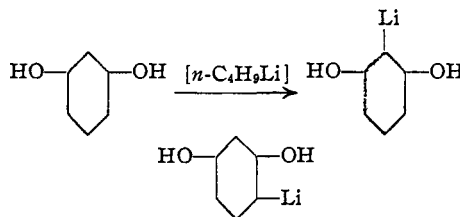
This more highly selective metalation of phenols is of particular interest in problems of orientation concerned with the dibenzofuran nucleus. However, because metalations of phenols and their ethers are of increasing diagnostic significance in establishing structures of compounds having nuclei other than dibenzofuran, it seemed of interest to examine some simple benzene types. Metalation of resorcinol dimethyl ether by phenyllithium gives 2,6-dimethoxyphenyllithium.<sup>4</sup> We have found that the same product is formed when *n*-butyllithium is used as the metalating agent.

(1) Paper XVII; *THIS JOURNAL*, **62**, 348 (1940).

(2) Gilman, "Metalation and Related Interconversion Reactions," Eighth National Organic Chemistry Symposium, St. Louis, Dec. 30, 1939.

(3) Gilman and Bebb, *THIS JOURNAL*, **61**, 109 (1939).(4) Wittig and Pockels, *Ber.*, **72**, 89 (1939).

However, metalation of resorcinol by *n*-butyllithium gives the two isomers: 2,6-dihydroxyphenyllithium and 2,4-dihydroxyphenyllithium.<sup>5</sup>



Accordingly there is a complete reversal here, the phenol giving more isomers than the ether. Inasmuch as the ratio of isomers that may result from particular phenols and their ethers might vary markedly, it becomes necessary to establish in each case the structure of the metalation product and not to carry over analogies from phenols to ethers or from ethers to phenols.

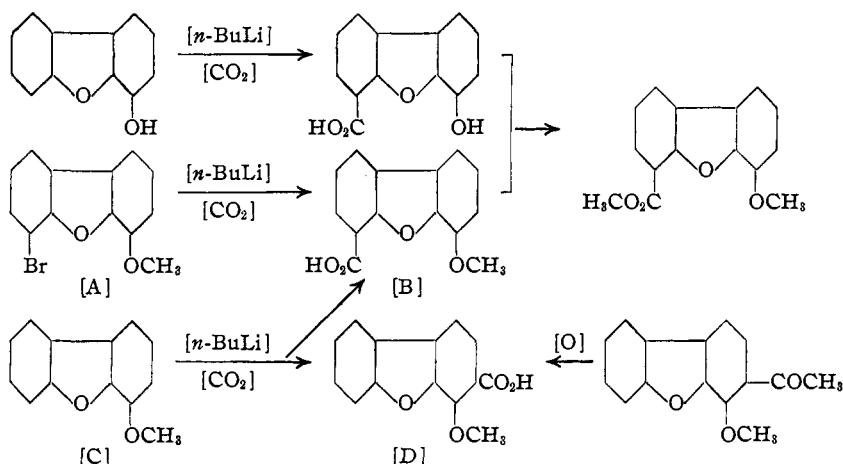
**Carbonation of Organolithium Compounds.**—In the first experiments<sup>4</sup> on the carbonation of 2,6-dimethoxyphenyllithium gaseous carbon dioxide was used, and there was obtained a 14% yield of 2,6-dimethoxybenzoic acid, accompanied by a 25% yield of 2,2',6,6'-tetramethoxybenzophenone. However, we used solid carbon dioxide which gave a 55% yield of the acid and only traces of the ketone. Gaseous carbon dioxide also can be used under special conditions<sup>6</sup> to give improved yields of carboxylic acids from organolithium compounds, but solid carbon dioxide is more convenient, more rapid and more effective.<sup>6</sup>

**Structure Determinations.**—For convenience, the products of metalation were carbonated. The resulting acids obtained from resorcinol and its dimethyl ether were compared with previously described compounds. The structures of the dibenzofuran compounds were established by the following sequence of reactions.

The halogen-metal interconversion indicated by the transformation of [A] to [B] was reported

(5) Actually, of course, the active hydrogens of the phenolic groups react first, and the true products are the —OLi salts of the organolithium compounds.

(6) Gilman and Van Ess, *THIS JOURNAL*, **55**, 1258 (1933).



recently<sup>7a</sup> starting with authentic 4-methoxy-6-bromodibenzofuran [A]. Such halogen-metal interconversions appear to be not only general, but also reliable when an equivalent or more of *n*-butyllithium is used.<sup>7b</sup> Additional supporting evidence for the formation of [B] and [D] from [C] is to be had in the preparation of 4-methoxy-6-hydroxydibenzofuran and 4-methoxy-3-hydroxydibenzofuran by oxidation of the metalation products of 4-methoxydibenzofuran.<sup>7c</sup>

**Correlation with Bromination.**—It is interesting to note that bromination of 2-hydroxydibenzofuran and of 2-methoxydibenzofuran parallels metalation of these compounds: 2-hydroxydibenzofuran yields 1-bromo-2-hydroxydibenzofuran, whereas 2-methoxydibenzofuran yields the isomeric 1- and 3-bromo-2-methoxydibenzofurans.<sup>7d</sup>

### Experimental Part

**Metalation of 2-Hydroxydibenzofuran.**—A solution of approximately 0.034 mole of *n*-butyllithium in 75 cc. of ether was added slowly with constant stirring to 3.1 g. (0.0168 mole) of 2-hydroxydibenzofuran dissolved in 75 cc. of benzene. The reaction mixture was stirred and heated for four hours and then carbonated by pouring it upon crushed solid carbon dioxide. Following carbonation, the solvent was removed by distillation and the residue was extracted with hot, dilute alkali; then carbon dioxide was passed into the alkaline solution to precipitate the phenol. The bicarbonate solution was extracted three times with 100-cc. portions of ether to remove last traces of the phenol. The acid was precipitated by the addition of hydrochloric acid. The yield of 2-hydroxy-1-dibenzofurancarboxylic acid was 0.830 g. (21.5%); m. p. 209–214° (dec.).

Three-tenths gram of the acid was methylated with

alkali and dimethyl sulfate, followed by treatment with diazomethane, to yield the known methyl 2-methoxy-1-dibenzofurancarboxylate, which melted at 98–99° after crystallization from methyl alcohol. A mixed m. p. with an authentic specimen<sup>7d</sup> showed no depression.

**Metalation of 4-Hydroxydibenzofuran.**—A solution of 0.031 mole of *n*-butyllithium in 35 cc. of ether was added slowly to a solution of 1.84 g. (0.01 mole) of 4-hydroxydibenzofuran dissolved in 35 cc. of dry benzene. During the addition there was a vigorous evolution of gas and a

heavy white precipitate formed. The resulting mixture was refluxed with stirring for four hours, after which it was carbonated by pouring it upon crushed solid carbon dioxide. The carbonation mixture was extracted with dilute sodium hydroxide and then carbon dioxide was bubbled through the alkaline solution to precipitate the unchanged phenol, of which 1.22 g. (65%) was recovered. The bicarbonate solution after filtration was acidified to yield a precipitate which was recrystallized from a benzene-acetone solution (4:1). The resulting crystals of 4-hydroxy-6-dibenzofurancarboxylic acid (0.1 g. or 4.4% yield) melted at 251–253° (dec.).

Forty milligrams of the hydroxy acid was treated with diazomethane and the resulting product was recrystallized from alcohol to yield a compound melting at 122.5–124°. This same methyl 4-methoxy-6-dibenzofurancarboxylate (mixed m. p.) was prepared from authentic 6-bromo-4-methoxydibenzofuran by halogen-metal interconversion, followed by methylation.<sup>7a</sup>

**Metalation of 4-Methoxydibenzofuran.**—A solution of 0.06 mole of *n*-butyllithium in 40 cc. of ether was added to a solution of 10 g. (0.05 mole) of 4-methoxydibenzofuran dissolved in 40 cc. of dry ether and the resulting mixture was refluxed with stirring for four hours, after which it was carbonated in the usual manner. The ether was removed by distillation and the solid residue was extracted with hot dilute sodium hydroxide. Acidification of the hot alkaline solution yielded 3 g. of crude acidic product.

This crude product was dissolved in hot 10% potassium hydroxide solution, filtered, and cooled. The white silky needles were filtered off and the filtrate was acidified with dilute hydrochloric acid. The precipitate was recrystallized several times from glacial acetic acid to yield 0.65 g. (5.3%) of 4-methoxy-3-dibenzofurancarboxylic acid melting at 182–183°. The same 4-methoxy-3-dibenzofurancarboxylic acid (mixed m. p.) was prepared by permanganate oxidation of authentic 3-acetyl-4-methoxydibenzofuran.

*Anal.* Calcd. for  $\text{C}_{14}\text{H}_{10}\text{O}_4$ : neut. equiv., 242. Found: neut. equiv., 238, 240.

The white needles obtained from the alkaline solution were dissolved in hot water and the acid was precipitated by addition of hydrochloric acid. Recrystallization from

(7) (a) Gilman, Swislow and Brown, *THIS JOURNAL*, **62**, 348 (1940); (b) Gilman, Langham and Willis, *ibid.*, **62**, 346 (1940); (c) Gilman, Cheney and Willis, *ibid.*, **61**, 951 (1939); (d) Gilman and Van Ess, *ibid.*, **61**, 1365 (1939).

glacial acetic acid gave 1.12 g. or a 9.2% yield of 4-methoxy-6-dibenzofurancarboxylic acid melting at 240–242°.

*Anal.* Calcd. for  $C_{14}H_{10}O_4$ : neut. equiv., 242. Found: neut. equiv., 237.

The methyl 4-methoxy-6-dibenzofurancarboxylate prepared by means of diazomethane from the methoxy acid melting at 240–242° was proved identical with both the methoxy ester of the single acid obtained from metalation of 4-hydroxydibenzofuran and an authentic sample of methyl 4-methoxy-6-dibenzofurancarboxylate.

*Anal.* Calcd. for  $C_{16}H_{12}O_4$ : methoxyl, 24.20. Found: methoxyl, 24.25.

**Metalation of Resorcinol.**—To an ice-cold solution of approximately 0.3 mole *n*-butyllithium in 400 cc. of ether was added dropwise with stirring 11.0 g. (0.1 mole) of resorcinol in 75 cc. of ether. Gas was evolved but no precipitate formed during the ensuing twenty-one hour period of refluxing. Carbonation, in the usual manner, was followed by acidification with iced dilute hydrochloric acid and extraction with ether. The crude acid obtained from the ether layer<sup>8</sup> was recrystallized from water to give 3.3 g., m. p. 145–147°, and 0.8 g., m. p. 192–195°. An additional 0.7 g., m. p. 150°, was obtained from the filtrate; combined yield, 31.1%.

The 3.3-g. portion, melting at 150–152° after recrystallization from water, was treated with dimethyl sulfate and sodium hydroxide to form 2,6-dimethoxybenzoic acid,<sup>9</sup> m. p. 183–184°, identified by a mixed melting point determination with a reference sample.

The 0.8-g. portion, m. p. 206–207° after recrystallization from water, was converted with diazomethane to methyl 2-hydroxy-4-methoxybenzoate<sup>10</sup> melting at 49° alone or mixed with an authentic specimen. Hydrolysis of the

ester with alcoholic potassium hydroxide gave 2-hydroxy-4-methoxybenzoic acid, m. p. 153–154°. The mixed melting point with a known sample showed no depression.

The third portion was not identified but was probably a mixture of the two acids contaminated with resorcinol.

**Metalation of Resorcinol Dimethyl Ether.**—A mixture of 0.1 mole of resorcinol dimethyl ether and 0.1 mole of *n*-butyllithium in ether was refluxed for twenty hours. Carbonation, by pouring the mixture jet-wise upon solid carbon dioxide, gave 10 g. (55% yield) of 2,6-dimethoxybenzoic acid melting at 186°. The methyl 2,6-dimethoxybenzoate, prepared by refluxing the silver salt of the dimethoxy acid with methyl iodide, melted at 87°.<sup>9</sup>

A small quantity (0.043 g.) of 2,2',6,6'-tetramethoxybenzophenone,<sup>4</sup> melting at 204°, was also isolated.

### Summary

Metalation by *n*-butyllithium of 2-methoxydibenzofuran gives 2-methoxy-1-dibenzofuryllithium and 2-methoxy-3-dibenzofuryllithium; and metalation of 4-methoxydibenzofuran gives 4-methoxy-6-dibenzofuryllithium and 4-methoxy-3-dibenzofuryllithium. However, metalation of the corresponding phenols gives but one product in each case: 2-hydroxydibenzofuran yielding 2-hydroxy-1-dibenzofuryllithium (as a lithium salt of the phenol); and 4-hydroxydibenzofuran yielding 4-hydroxy-6-dibenzofuryllithium.

In contrast, metalation of resorcinol dimethyl ether gives apparently but one product (2,6-dimethoxyphenyllithium), whereas resorcinol gives the two isomers, 2,6-dihydroxyphenyllithium and 2,4-dihydroxyphenyllithium.

AMES, IOWA

RECEIVED JANUARY 15, 1940

(8) Nierenstein and Clibbens, *Org. Syntheses*, **10**, 95 (1930).

(9) Mauthner, *J. prakt. Chem.*, [2] **121**, 259 (1929).

(10) Herzig, Henzel and Batscha, *Monatsh.*, **24**, 888 (1903).

## Tenth Report of the Committee on Atomic Weights of the International Union of Chemistry

By G. P. BAXTER (*Chairman*), M. GUICHARD, O. HÖNIGSCHMID AND R. WHYTLAW-GRAY

The following report of the Committee covers the twelve-month period September 30, 1938 to September 30, 1939.<sup>1</sup> Three changes in the table of atomic weights have been adopted:

Hydrogen, from 1.0081 to 1.0080, iron, from 55.84 to 55.85, lutecium, from 175.0 to 174.99.

**Hydrogen.**—Several investigations of the  $H^1/H^2$  ratio in certain natural waters during the last four years have given values higher than that

(1) Authors of papers bearing on the subject are requested to send copies to each of the four members of the Committee at the earliest possible moment: Prof. G. P. Baxter, Coolidge Laboratory, Harvard University, Cambridge, Mass., U. S. A.; Prof. M. Guichard, Faculté des Sciences, Sorbonne, Paris, France; Prof. O. Hönlgschmid, Sofienstrasse 9/2, Munich, Germany; Prof. R. Whytlaw-Gray, University of Leeds, Leeds, England.

used in computing the atomic weight of hydrogen for the Table, 5000 (see Eighth Report of this Committee).

Johnston, <i>THIS JOURNAL</i> , <b>57</b> , 484 (1935)	5900
Tronstad, Nordhagen and Brun, <i>Nature</i> , <b>136</b> , 515 (1935)	5840
Hall and Jones, <i>THIS JOURNAL</i> , <b>58</b> , 1915 (1936)	6550
Gabbard and Dole, <i>ibid.</i> , <b>59</b> , 181 (1937)	7020
Morita and Titani, <i>Bull. Chem. Soc. Japan</i> , <b>13</b> , 419 (1938)	6320
Tronstad and Brun, <i>Trans. Faraday Soc.</i> , <b>34</b> , 766 (1938)	5400
Voskuyl, Thesis, Harvard University (1938)	6700
Swartout and Dole, <i>THIS JOURNAL</i> , <b>61</b> , 2025 (1939)	6970
	6880

Since with  $H^1 = 1.00785$  (chemical scale) and even with  $H^1/H^2 = 6000$  the atomic weight of