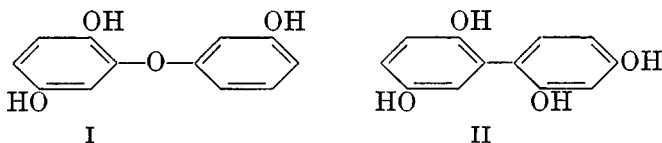


2,3',5-TRIHYDROXYDIPHENYL ETHER¹

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According to Blumenfeld and Friedlander, *p*-benzoquinone and resorcinol react when heated with acid (1) or under the influence of heat alone (2) to give 2,3',5-trihydroxydiphenyl ether (I). The condensation reaction is supposedly fairly general and applicable to naphthoquinones and various polyhydric phenols.

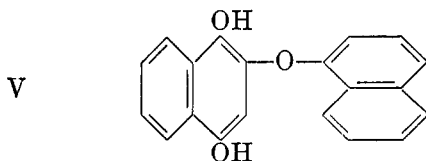


The alternative structure (II) has been proposed for the product of the reaction between benzoquinone and resorcinol by Pummerer and Huppman (3). Both the hydroxydiphenyl and hydroxydiphenyl ether structures, however, appear somewhat doubtful because phenoxy and hydroxyphenyl groups would tend to lower the normal potential of *p*-benzoquinone (4, 5) and thus the formed hydroquinone would be susceptible to oxidation by the original quinone.

Various attempts to repeat the described preparation (1, 2) of (I) have failed to give this substance. It has been possible, however, to isolate hydroquinone in yields of 31% from the reaction mixture, which may be regarded as evidence that the reaction product was at least partially oxidized by the quinone.

In order to obtain further evidence concerning the compounds involved, (I) has been prepared synthetically. 2,3',5-Trimethoxydiphenyl ether (III) is obtainable through the Ullmann reaction from bromohydroquinone dimethyl ether and the potassium salt of resorcinol monomethyl ether or from *m*-bromoanisole and the potassium salt of hydroxyhydroquinone dimethyl ether. The demethylation of the product with the usual reagents has failed to yield (I). Even hydriodic acid gives only a dihydroxymethoxydiphenyl ether (IV). The complete demethylation of (III) has been effected by the use of aluminum bromide. Since the product and its derivative have physical constants differing from those reported previously (1, 2, 3), the product of Blumenfeld and Friedlander cannot be represented by (I).

Attempts to prepare synthetically another one of the compounds (V) reported by the same authors have failed. The Ullmann reaction of 2-bromo-1,4-

¹ From the Master's thesis of Harold Hein.

dimethoxynaphthalene with potassium 1-naphthoxide yields largely 1,4-dimethoxynaphthalene, while the reaction of 1-bromonaphthalene with the potassium salt of 2-hydroxy-1,4-dimethoxynaphthalene yields naphthalene.

EXPERIMENTAL

All temperatures uncorrected. Analyses by Karl Zilch.

Condensation of quinone and resorcinol. Resorcinol (10 g.), mixed with quinone (10 g.) was dissolved in 100 cc. of acetic acid. One cc. of concentrated sulfuric acid was added and the solution was heated at 130° for one hour. The sulfuric acid was neutralized with an equivalent amount of solid sodium bicarbonate. The acetic acid was removed by distillation *in vacuo* and the residue was sublimed from a molecular still in a high vacuum. The sublimate (3.2 g.) melted at 167–169° and did not depress the melting point of a sample of hydroquinone.

Bromohydroquinone dimethyl ether. Hydroquinone dimethyl ether (66 g.) was brominated in 400 cc. of chloroform with 82 g. of bromine dissolved in 30 cc. of chloroform in the presence of 2 g. of iron. The product boiling at 140–144° (16 mm.) weighed 45.2 g.

2,3',5-Trimethoxydiphenyl ether (III). The potassium salt of resorcinol monomethyl ether prepared from 20.8 g. of the phenol was heated with 0.3 g. of copper powder and 44.3 g. of bromohydroquinone dimethyl ether as described previously (6). The steam-distillate of the reaction mixture contained 2.6 g. of hydroquinone dimethyl ether. The non-volatile residue yielded 13.0 g. of trimethoxydiphenyl ether boiling at 160° (1 mm.).

Anal. Calc'd for $C_{15}H_{16}O_4$: C, 69.23; H, 6.20.

Found: C, 68.97; H, 6.44.

The substance was also prepared from *m*-bromoaniline and 2-aminohydroquinone dimethyl ether. *m*-Bromoaniline was diazotized and converted to *m*-bromophenol in 60% yield (7). Methylation of this substance with dimethyl sulfate gave 53% of *m*-bromoanisole, b.p. 73–75° (5 mm.). Commercial aminohydroquinone dimethyl ether² was diazotized in the usual way. The diazonium sulfate solution was decomposed with sulfuric acid at 130–135° (7), special care being taken to keep the solution ice-cold before it was decomposed. The steam-distillate was extracted with ether. The extract was dried and distilled. 2-Hydroxyhydroquinone dimethyl ether was obtained; b.p. 93–95° (7 mm.). The Ullmann reaction with the potassium salt of this phenol and *m*-bromoanisole gave a 12.6% yield of 2,3',5-trimethoxydiphenyl ether, b.p. 160° (1 mm.).

2,3',5-Dihydroxymethoxydiphenyl ether (IV).³ Acetic anhydride (10 cc.) and hydriodic acid (2.7 cc., *d.* 1.5) were added to a solution of 1 g. of 2,3',5-trimethoxydiphenyl ether dissolved in 18 cc. of acetic acid. The mixture was refluxed for 1.5 hours and poured into 60 cc. of cold water. The precipitated product (0.5 g.) was crystallized from acetic acid and sublimed at 1×10^{-4} mm. It melted at 150° (*dec.*).

Anal. Calc'd for $C_{13}H_{12}O_4$: C, 67.24; H, 5.17.

Found: C, 67.80; H, 5.32.

Dibenzoate. Benzoylation of this product (0.15 g.) with benzoyl chloride (0.6 cc.) and 10% aqueous sodium hydroxide gave 0.2 g. of dibenzoate melting at 135–137° (from alcohol).

Anal. Calc'd for $C_{27}H_{20}O_6$: C, 73.64; H, 4.54.

Found: C, 73.67; H, 4.65.

2,3',5-Trihydroxydiphenyl ether. (I). Attempts to demethylate 2,3',5-trimethoxydiphenyl ether with 48% hydrobromic acid and acetic acid or with aluminum chloride in benzene yielded intractable mixtures. Methylmagnesium iodide at 240° effected a demethylation but slightly less than two thirds of the theoretical amount of methane was evolved and the product could not be purified.

² The authors wish to thank the Tennessee Eastman Corporation for a sample of this substance.

³ It has not been possible to ascertain which methoxyl groups have been cleaved in this compound.

The compound (1 g.) was successfully demethylated by refluxing with aluminum bromide (4.6 g.) and benzene (75 cc.) for four hours. The reaction mixture was decomposed with ice and hydrochloric acid and was extracted with benzene. The product was purified through its sodium salt, regenerated, extracted with ether, dried, and freed from solvent. It solidified on standing and was crystallized from benzene, m.p. 116–118°, yield 0.3 g.

Anal. Calc'd for $C_{12}H_{10}O_4$: C, 66.05; H, 4.59.

Found: C, 65.81; H, 4.85.

Tribenzoate. Benzoylation of the trihydroxy compound (0.1 g.) yielded 0.1 g. of tribenzoate, m.p. 49–51° (from alcohol).

Anal. Calc'd for $C_{33}H_{22}O_7$: C, 74.71; H, 4.15.

Found: C, 74.56; H, 4.24.

2-Bromo-1,4-dimethoxynaphthalene. 1,4-Dimethoxynaphthalene (20 g.) was brominated with 17.0 g. of bromine in chloroform (230 cc.) at room temperature. Iron nails were used as catalyst. The crude bromination product was washed, dried, freed from solvent, and distilled. The distillate boiling at 150° (3 mm.) solidified on cooling. It was crystallized from aqueous alcohol. The colorless crystals melted at 54–55° and weighed 17.2 g.

Anal. Calc'd for $C_{12}H_{11}BrO_2$: C, 53.95; H, 4.43.

Found: C, 53.73; H, 4.54.

1,4-Dimethoxy-2-naphthol. The Grignard reagent from 2-bromo-1,4-dimethoxynaphthalene was oxidized essentially according to Kharasch (8). A solution of 10.7 g. of the bromo-compound and 10 g. of isopropyl bromide in 40 cc. of dry ether and 24 cc. of dry benzene was added to 2.9 g. of magnesium, 5 cc. of ether, and a crystal of iodine. After complete addition, the mixture was stirred for thirty minutes. It was oxygenated during twenty minutes, was allowed to stand overnight, and decomposed with aqueous sulfuric acid. The naphthol was removed from the combined ether extracts with 10% aqueous potassium hydroxide containing a small amount of sodium hydrosulfite. The basic solution was acidified with hydrochloric acid, diluted with water (40 cc.), brought to boiling, and allowed to cool. The precipitate was crystallized from Skellysolve B. It melted at 90.5–92.5°, yield 3.1 g.

Anal. Calc'd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.94.

Found: C, 70.70; H, 6.28.

Ullmann reaction. The reaction between potassium 1-naphthoxide (from 3.4 g. of 1-naphthol), 4.2 g. of 2-bromo-1,4-dimethoxynaphthalene, and copper powder at 230° gave 0.4 g. of 1,4-dimethoxynaphthalene (from the steam-distillate). The non-volatile fraction was a tar.

The volatile product from the reaction of 1-bromonaphthalene (0.78 g.) and potassium 1,4-dimethoxy-2-naphthoxide (from 1.53 g. of 1,4-dimethoxy-2-naphthol) proved to be naphthalene (0.1 g.). The non-volatile fraction (0.4 g.) was sublimed at 150° (1 mm.). The viscous oil possibly represents an oxidation product of 1,4-dimethoxy-2-naphthol.

Anal. Calc'd for $C_{12}H_{12}O_4$: C, 65.44; H, 5.49.

Found: C, 66.73; H, 5.53.

SUMMARY

Authentic 2,3',5-trihydroxydiphenyl ether has been prepared and characterized by a derivative. It is not identical with the product previously assigned this structure.

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