[CONTRIBUTION FROM THE RESEARCH LABORATORIES, EASTMAN KODAK COMPANY]

THE SYNTHESIS OF 4-PHENOXYCATECHOL AND 2-PHENOXYHYDROQUINONE[1]

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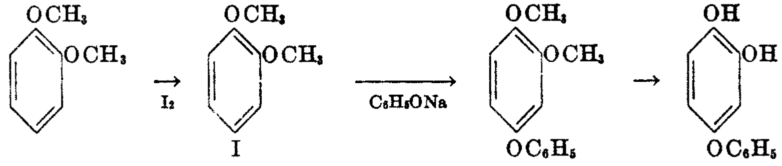
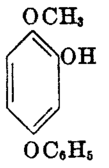
As a part of a study of the developing action of certain substituted catechols and hydroquinones, it was necessary to prepare 4-phenoxycatechol (III) and 2-phenoxyhydroquinone (X). The methods used to prepare these compounds are described here.

The synthesis of 4-phenoxycatechol was achieved by the following sequence of reactions: Veratrol was iodinated in carbon tetrachloride solution in the presence of a molar equivalent of silver trifluoroacetate to 4-iodoveratrol (I) in a yield of 91%. The reaction also proceeds in the absence of a solvent but the yield is somewhat lower. When the silver trifluoroacetate is replaced by silver acetate, the yield is decreased to 77%. These iodination procedures have a decided advantage over the mercuric oxide-catalyzed iodinations, not only because of better yields, but also because mercuric salts are difficult to remove. 4-Iodoveratrol was treated with sodium phenoxide in the presence of copper to give 4-phenoxycatechol dimethyl ether (II). Complete demethylation of the latter to give 4-phenoxycatechol was effected by adding the ether to a sodium chloride-aluminum chloride melt. Insofar as we are aware, this is the first time that this mixture has been used as a demethylating agent. It offers the advantage of a broad temperature range (110–225°) and may be of use where demethylation proceeds with difficulty.

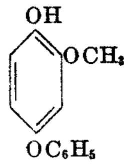


I II III

If the demethylation of the dimethyl ether II is carried out with aluminum chloride in benzene, a mixture of the monomethyl ethers, IV and V, results. Separation of the mixture into a low melting (63–64°) and a high melting (105°) isomer is accomplished with petroleum ether in which the latter has the lower solubility. Assignment of structure IV to the low-melting isomer and V to the



IV



V

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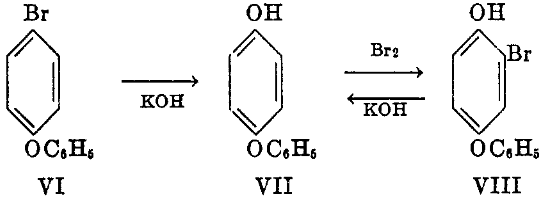
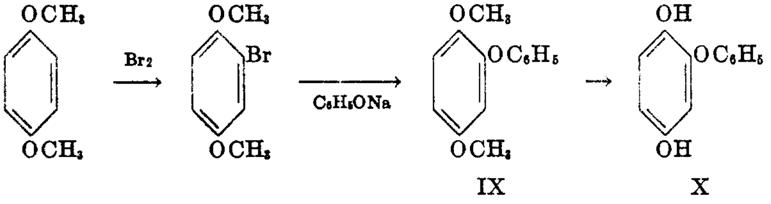
[1] Communication No. 1725 from the Kodak Research Laboratories.

high-melting product is based upon the fact that oxidized *p*-phenylenediamines will couple with phenols only if the *p*-position is open, unless the *p*-substituent couples off (1). In actual test, the lower-melting isomer (IV) couples with oxidized 4-amino-N,N-diethyl-3-methylaniline to give an intense blue dye, while the higher-melting compound fails to couple under the same conditions. In tests with a large number of phenols, no case of *ortho* coupling has been observed (1). The test was carried out as previously described (2).

An alternate route to 4-phenoxycatechol, which started with 4-bromodiphenyl ether (VI), was unsuccessful. The latter was converted to 4-hydroxydiphenyl ether (VII) by alkaline hydrolysis in a yield of 81.6%. This method of preparation is much superior to the decomposition of the diazonium salt of 4-aminodiphenyl ether (3, 4), a method which gives a poor yield. 4-Hydroxydiphenyl ether was brominated in carbon disulfide to give an 83% yield of 3-bromo-4-hydroxydiphenyl ether (VIII), b.p. 180–182°/2 mm. The alkaline hydrolysis of 3-bromo-4-hydroxydiphenyl ether gave a 27% yield of 4-hydroxydiphenyl ether and a large amount of highly colored amorphous products. This is another example of the replacement of a halogen by hydrogen under alkaline conditions (5).



2,5-Dimethoxydiphenyl ether (IX) was obtained from bromohydroquinone dimethyl ether and sodium phenoxide in the presence of copper powder. The complete demethylation of 2,5-dimethoxydiphenyl ether to 2-phenoxyhydroquinone (X) was effected by use of aluminum chloride in benzene. After recrystallization from acetic acid, it melted at 155°, as previously reported by Ungnade and Zilch (6).



In agreement with Ungnade and Zilch (6), it was not possible to prepare 2-phenoxyhydroquinone directly from benzoquinone and phenol in the presence of an acid catalyst (7–9); some reaction of undetermined nature must have taken place, but the only product isolated was hydroquinone in 52% yield. The phenoxy group tends to lower the normal potential of benzoquinone so that the phenoxyhydroquinone (or phenoxycatechol) would be susceptible to oxidation by the original quinone.

In general, these reactions should be applicable to the preparation of substituted phenoxycatechols and phenoxyhydroquinones.

EXPERIMENTAL

4-Iodoveratrol (I). Silver trifluoroacetate was prepared by reacting a suspension of 187 g. (1.5 moles) of silver hydroxide in 500 ml. of water with 177 g. (1.5 moles) of trifluoroacetic acid. The water was removed on a steam-bath under a vacuum and the crude product was placed in a Soxhlet thimble and extracted with ether. After removal of the ether, 300 g. (89%) of the purified silver trifluoroacetate was obtained.

A mixture of 110 g. (0.5 mole) of silver trifluoroacetate and 69 g. (0.5 mole) of dry veratrol was placed in a dry, 1-l. flask equipped with stirrer and dropping-funnel. A solution of 127 g. (0.5 mole) of iodine dissolved in about 750 ml. of carbon tetrachloride was added during a half hour. Any undissolved iodine was added as the solid. After stirring for two hours, the mixture was filtered and the precipitate was washed with 100 ml. of carbon tetrachloride. The solvent was removed and the residue distilled. The yield of product boiling at 152–155°/15 mm. was 112 g. (91%).[3]

4-Phenoxycatechol dimethyl ether (III). A mixture of 75 g. (0.3 mole) of iodoveratrol, 70 g. (0.6 mole) of sodium phenoxide, and 1 g. of copper powder was placed in a 500-ml. flask equipped with stirrer, thermometer, and reflux condenser. The stirred mixture was heated to 200° for four hours and then was poured into 500 ml. of water. The water solution was extracted with 1 l. of benzene in three portions. The benzene was removed under a vacuum and the fraction boiling at 150–152°/1.5 mm. was collected. The yield was 36 g. (60%). This material solidified on standing and a small sample was recrystallized from petroleum ether; m.p. 43–44°.

Anal. Calc'd for $C_{14}H_{14}O_3$: C, 73.0; H, 6.1.

Found: C, 73.0; H, 6.4.

4-Phenoxycatechol (III). To a melt prepared by heating a mixture of 72 g. (0.53 mole) of anhydrous aluminum chloride and 12 g. (0.2 mole) of sodium chloride in a 250-ml. beaker to 120° was added, over a period of one-half hour, 15 g. (0.06 mole) of 4-phenoxycatechol dimethyl ether. The mixture then was poured into ice and hydrochloric acid and the resulting solution was extracted with three 500-ml. portions of benzene. The benzene was removed under a vacuum and the fraction boiling at 180–185°/1 mm. was collected. The yield was 11 g. (85%); n_D^{25} 1.6030.

Anal. Calc'd for $C_{12}H_{10}O_3$: C, 71.2; H, 4.9; Active H, 2.

Found: C, 71.6; H, 5.6; Active H, 1.9.

Monomethyl ethers of 4-phenoxycatechol. A solution of 10 g. (0.04 mole) of 4-phenoxycatechol dimethyl ether in 25 ml. of benzene was treated with 18 g. (0.13 mole) of anhydrous aluminum chloride. After the initial reaction subsided, the mixture was heated on a steam-bath for two hours. The solid mass then was decomposed with ice and hydrochloric acid, and the mixture was extracted with benzene. The benzene was removed and the product was distilled. The yield of product boiling at 165–170°/3 mm. was 5.5 g. (60%). The product solidified on standing and was separated into two parts by treatment with warm petroleum ether. The soluble portion crystallized from the petroleum ether on chilling and after recrystallization from the same solvent, melted at 64°. It coupled with an oxidized developer (2), and is, therefore, 4-hydroxy-3-methoxydiphenyl ether (IV).

Anal. Calc'd for $C_{13}H_{12}O_3$: C, 72.2; H, 5.5.

Found: C, 72.3; H, 5.7.

The insoluble portion was recrystallized twice from hexane. It melted at 105° and did not couple with an oxidized developer (2). It is, therefore, 4-hydroxy-3-methoxydiphenyl ether (V).

Anal. Calc'd for $C_{13}H_{12}O_3$: C, 72.2; H, 5.5.

Found: C, 71.7; H, 5.2.

4-Bromodiphenyl ether (VI). A solution of 340 g. (2.0 moles) of diphenyl ether in 200 g. of carbon tetrachloride was heated to 95–100° and treated dropwise, with stirring, with 320 g.

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[3] When the silver trifluoroacetate was replaced by silver acetate and the carbon tetrachloride with acetic acid, a 77% yield of 4-iodoveratrol was obtained.

(2.0 moles) of bromine over an eight-hour period. The carbon tetrachloride was removed under a vacuum and the residue fractionated. The fraction boiling at 120–167°/10 mm. was collected and redistilled. The fraction boiling at 158–160°/10 mm. was 4-bromodiphenyl ether. The yield was 287 g. (57%).

Anal. Calc'd for $C_{12}H_9BrO$: C, 57.9; H, 3.6.
Found: C, 58.0; H, 3.5.

4-Hydroxydiphenyl ether (VII). A mixture of 372 g. (1.5 moles) of 4-bromodiphenyl ether, 204 g. of potassium hydroxide, 4 g. of copper powder, and 700 ml. of water was placed in a stainless-steel autoclave and heated at 245–250° for 16 hours. After cooling, the contents of the bomb were removed. The light-brown alkaline solution was filtered and made acid with 200 ml. of concentrated hydrochloric acid. The oily precipitate, which quickly solidified, was filtered and dried. The product was distilled and the fraction boiling at 177–180°/9 mm. was collected. This material solidified on cooling, m.p. 81–82°. The yield was 228 g. (81.6%). One recrystallization from benzene-ligroin raised the melting point to 83°.

3-Bromo-4-hydroxydiphenyl ether (VIII). A solution of 93 g. (0.5 mole) of 4-hydroxydiphenyl ether in 300 ml. of carbon disulfide was treated slowly with 83 g. (0.5 mole) of bromine, with stirring, and at a temperature of 5–10°. The carbon disulfide was removed under a vacuum and the residue was distilled. The fraction boiling at 178–183°/2 mm. was collected. The yield was 127 g. (96%).

Anal. Calc'd for $C_{12}H_9BrO_2$: Br, 30.1. Found: Br, 29.8.

2,5-Dimethoxydiphenyl ether (IX). A mixture of 108.5 g. (0.5 mole) of bromohydroquinone dimethyl ether, 111 g. (1.0 mole) of sodium phenoxide, and 1 g. of copper powder was placed in a 500-ml. flask equipped with stirrer and thermometer. The stirred mixture was heated to 200° for four hours and then was poured into 500 ml. of water. The water solution was extracted with 1 l. of benzene in three portions. The benzene was removed and the residue was distilled. The yield of product boiling at 150–155°/2 mm. was 55 g. (33%). The product solidified on cooling, m.p. 44–45°.

Anal. Calc'd for $C_{14}H_{14}O_3$: C, 73.0; H, 6.1.
Found: C, 72.8; H, 6.3.

2-Phenoxyhydroquinone (X). A mixture of 28 g. of 2,5-dimethoxydiphenyl ether and 200 g. (1.4 moles) of anhydrous aluminum chloride in 100 ml. of benzene was heated under reflux on a steam-bath for two hours and then poured into ice and hydrochloric acid. The gray solid (20 g. 88%) was recrystallized from dilute acetic acid, m.p. 155°. When the method described for preparing 4-phenoxycatechol was applied to 2-phenoxyhydroquinone dimethyl ether, an 85% yield of the demethylated product was obtained.

SUMMARY

The syntheses of 4-phenoxycatechol and 2-phenoxyhydroquinone are described. A method of iodination is given that should have wide application. A new demethylation procedure is reported.

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REFERENCES

(1) VITTUM AND BROWN, *J. Am. Chem. Soc.*, **71**, 2287 (1949).
(2) WEISSBERGER AND PORTER, *J. Am. Chem. Soc.*, **65**, 52, 1502 (1943).
(3) HAUSSERMANN AND BAUER, *Ber.*, **29**, 2084 (1896).
(4) HAUSSERMANN AND MILLER, *Ber.*, **34**, 1070 (1901).
(5) ALLEN AND VANALLAN, *J. Org. Chem.*, **14**, 798 (1949).
(6) UNGNADE AND ZILCH, *J. Org. Chem.*, **15**, 1108 (1950).
(7) BLUMENFELD AND FRIEDLÄNDER, *Ber*, **30**, 1464, 2563 (1897).
(8) PUMMER AND HUPPMANN, *Ber.*, **60**, 1444 (1927).
(9) FRIEDLÄNDER AND BLUMENFELD, German Patent 96,565 (Jan. 24, 1898): *Frdl.*, **5**, 670 (1897–1900).