[Contribution from the Chemistry Department, University of Missouri]

PHENOXYQUINONES. III. 2-(HYDROXYPHENOXY)-*p*-BENZOQUINONES

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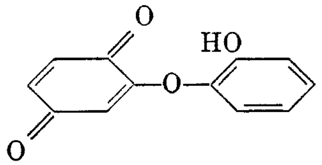
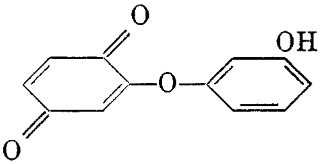
Received July 3, 1950

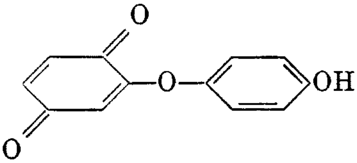
An improved method of cleaving trimethoxydiphenyl ethers (1) has made available a series of trihydroxydiphenyl ethers. By suitable methods of oxidation it has become possible to convert these substances to phenoxyquinones with hydroxyl substituents in the phenoxy group. The present investigation describes successful methods for the preparation of the three monohydroxyphenoxy-*p*-benzoquinones (I–III).



I



II



III

The hydroxyphenoxy quinones are of interest because of their increased water solubility as compared to simple phenoxyquinones (2), and for reasons of the two physiologically active functional groups, *viz.* the α,β-unsaturated carbonyl (3) and the phenolic hydroxyl group (4). The results of the bacteriological tests with the compounds will be published elsewhere.

The normal potentials of the three quinones (I, II, III) have been determined at the dropping mercury electrode in aqueous ethanol, and are found to be 0.618, 0.625, and 0.604 v. (25°). The potential-lowering of the hydroxyl-substituted phenoxyl group is therefore somewhat smaller (90–111 mv.) than that of the unsubstituted group (131 mv.).

The substances (I–III) have been characterized by derivatives and absorption spectra.

EXPERIMENTAL

Analyses by R. Carpenter, J. Finney, and Felix H. Otey. All temperatures uncorrected.

2,2′,5-Trimethoxydiphenyl ether. The customary procedure for methoxydiphenyl ethers

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(5) gave only a small yield (24.7%) of the desired product. A far better yield was obtained as follows (6): A mixture of 9.3 g. of guaiacol, 15 g. of 2-bromo-1,4-dimethoxybenzene (1), 0.5 g. of copper powder, 7 g. of anhydrous potassium carbonate, and 1 g. of pyridine was heated at 190–200° for two hours. Dilute hydrochloric acid was added and the mixture was extracted with ether. Fractional distillation of the product gave a large fraction boiling at 160–190° (4 mm.). This viscous oil was crystallized from aqueous methanol. The yield of colorless crystalline ether was 11.7 g. (60%), m.p. 70–70.8°.[3]

Anal. Calc'd for $C_{15}H_{16}O_4$: C, 69.19; H, 6.19.

Found: C, 69.12, 68.95; H, 6.24, 6.19.

2,2′,5-Trihydroxydiphenyl ether. 2,2′,5-Trimethoxydiphenyl ether (0.6 g.) was demethylated with aluminum bromide as described previously (1). The crude product was purified by vacuum distillation at 200° (17 mm.). The residue solidified after standing for a few hours. It was crystallized from benzene; m.p. 148–149° (in a sealed tube). The substance sublimed at 145°, yield 0.35 g. (45%).

Anal. Calc'd for $C_{12}H_{10}O_4$: C, 66.05; H, 4.62.

Found: C, 66.31; H, 4.64.

2-(o-Hydroxyphenoxy)-p-benzoquinone. A mixture of 0.5 g. of 2,2′,5-trihydroxydiphenyl ether, 25 cc. of water, and 1 cc. of concentrated sulfuric acid was heated to boiling and poured into a filtered solution of 0.8 g. of potassium dichromate in 12 cc. of cold water with stirring. The mixture was cooled in an ice-bath and the quinone was extracted with ether. The tan compound was crystallized from benzene and Skellysolve A; m.p. 126.5–127.5°, yield 0.3 g.; λ max$_1$ 250 mμ (log ϵ 3.95), λ max$_2$ 325 mμ (log ϵ 3.53), λ min 285 mμ (log ϵ 3.29).

Anal. Calc'd for $C_{12}H_8O_4$: C, 66.66; H, 3.73.

Found: C, 66.91; H, 3.93.

Dioxime. Oximation of 0.5 g. of this quinone with 1 g. of hydroxylamine hydrochloride in aqueous alcohol yielded 0.3 g. of yellow dioxime, m.p. 160–165° (dec.) (from ether-petroleum ether).

Anal. Calc'd for $C_{12}H_{10}N_2O_4$: C, 58.54; H, 4.09.

Found: C, 58.84; H, 4.54.

2-(m-Hydroxyphenoxy)-p-benzoquinone. 2,3′,5-Trihydroxydiphenyl ether (1) (0.43 g.) was oxidized with chromic acid as described for the *o*-isomer. The precipitated quinone was washed, dried, and recrystallized from benzene. The pure substance (0.34 g.) began to decompose at 158° and melted completely at 165°. It was soluble in alcohol and ether but only slightly soluble in water and insoluble in Skellysolve. Absorption characteristics, λ max$_1$ 275 mμ (log ϵ 4.12), λ max$_2$ 365 mμ (log ϵ 2.55), λ min 330 mμ (log ϵ 2.30).

Anal. Calc'd for $C_{12}H_8O_4$: C, 66.66; H, 3.73.

Found: C, 66.42; H, 3.70.

Dioxime. The oximation procedure used for the *o*-isomer yielded 70% of yellow dioxime, m.p. 185–195° (dec.) (from ether-petroleum ether).

Anal. Calc'd for $C_{12}H_{10}N_2O_4$: C, 58.54; H, 4.09.

Found: C, 58.81; H, 4.37.

2,4′,5-Trimethoxydiphenyl ether. The customary Ullmann procedure furnished 30% of the ether from 2-bromo-1,4-dimethoxybenzene, whereas the above described pyridine method (6) yielded 52.5% of product boiling at 153–154° (3 mm.), m.p. 44.5–45.5° (from aqueous methanol).

Anal. Calc'd for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20.

Found: C, 69.24; H, 6.39.

2,4′,5-Trihydroxydiphenyl ether. The trimethyl ether (0.57 g.) was smoothly demethylated by refluxing with aluminum bromide (6.5 g.) and benzene (35 cc.). The product after purification by sublimation under reduced pressure melted at 191–192° (dec.), yield 0.23 g.

Anal. Calc'd for $C_{12}H_{10}O_4$: C, 66.05; H, 4.62.

Found: C, 66.21; H, 4.75.

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[3] The first sample of this compound was prepared by John Hobaugh.

2-(p-Hydroxyphenoxy)-p-benzoquinone. 2,4′,5-Trihydroxydiphenyl ether (1 g.) on oxidation with chromic acid gave 0.5 g. of pure quinone, m.p. 136–142° (from benzene-petroleum ether). Its solubilities were analogous to those of the *meta*-isomer; λ $\max_1$ 252.5 mμ (log ϵ 4.21), λ $\max_2$ 365 mμ (log ϵ 3.11), λ min 302 mμ (log ϵ 2.59).

Anal. Calc'd for $C_{12}H_8O_4$: C, 66.66; H, 3.73.

Found: C, 66.73; H, 3.93.

Dioxime. The dioxime from 0.6 g. of quinone weighed 0.4 g. and decomposed at 160°.

Anal. Calc'd for $C_{12}H_{10}N_2O_4$: C, 58.53; H, 4.09.

Found: C, 58.24; H, 4.03.

Normal potentials. Half wave potentials for the quinones (I–III) were determined polarographically in buffers made up by dissolving buffer tablets in aqueous 10% alcohol over the *p*H range 2–8. The *p*H of each solution was determined accurately with a Beckman *p*H meter. The determinations were carried out under nitrogen as described previously (7). The half wave potentials were plotted against the *p*H values and extrapolated to *p*H 0.

Absorption spectra.[4] The ultraviolet absorption spectra of the quinones were determined in 95% alcohol (0.0003 molar solutions) in the range of 220–500 mμ. A and B maxima (8) of the substances were observed in this region.

The A bands of I and III were found at wavelengths close to the corresponding band in phenoxybenzoquinone (250 mμ) (2). The bathochromic shifts are therefore similar for phenoxyl and *o*- or *p*-hydroxy substituted phenoxyl groups. The high intensity absorption band of II, however, was found to be clearly out of line. The unusually large shift in this case can be explained by independent absorption of the phenol and phenoxyquinone chromophores without appreciable resonance between them. Addition of the absorption curves for phenol and phenoxyquinone gives the following composite values: λ max 270 mμ, log ϵ 3.96 (A) and 355 mμ, log ϵ 2.90 (B) and λ min 330 mμ, log ϵ 2.82. These are found to be in reasonable agreement with the observed figures.

SUMMARY

Physical and chemical properties have been described for the three isomeric 2-(hydroxyphenoxy)-*p*-benzoquinones.

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[4] Absorption spectra by Dr. E. E. Pickett, University of Missouri.