[Contribution from the Chemistry Department, University of Missouri]

PHENOXYQUINONES. II. THE DIPHENOXYQUINONES

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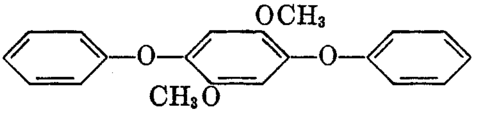
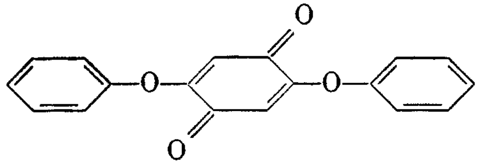
Considerable difficulties have been experienced in attempts to introduce two phenoxyl groups into dimethoxybenzene derivatives, due to the tendency of their dibromo derivatives to lose bromine. Thus 2,5-dibromo-1,4-dimethoxybenzene yields 1,4-dimethoxy-2-phenoxybenzene under the usual conditions of the Ullmann reaction. The dehalogenation reaction in this case can be prevented largely when phenol is used as a solvent in the reaction. The resulting 1,4-dimethoxy-2,5-diphenoxybenzene (I) is demethylated in quantitative yield by aluminum bromide. The diphenoxyhydroquinone is converted to 2,5-diphenoxyquinone (II) by oxidation with nitric acid.

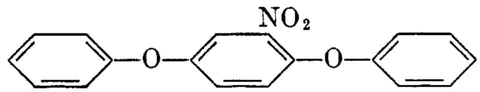


I



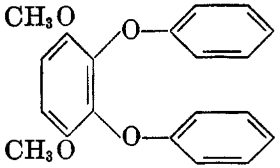
II

An alternate synthetic route for the preparation of II from 5-bromo-2-chloronitrobenzene has led to the preparation of 2,5-diphenoxynitrobenzene (III).

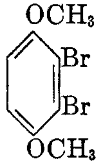


III

All attempts to obtain 1,4-dimethoxy-2,3-diphenoxybenzene (IV) from 2,3-dibromo-1,4-dimethoxybenzene (V) have resulted in the loss of one atom of



IV



V

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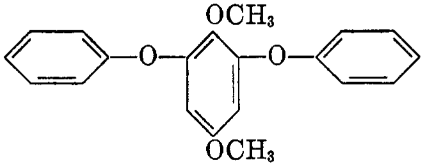
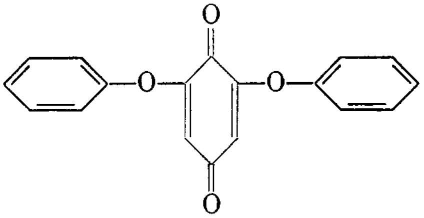
bromine. 1,4-Dimethoxy-2-phenoxybenzene (1) is the only product of the reaction regardless of whether the Ullmann reaction is run with solvents or without.

The isomeric 1,4-dimethoxy-2,6-diphenoxybenzene (VI) has been prepared by condensation of 2,6-dibromo-1,4-dimethoxybenzene with potassium phenoxide in phenol solution. The corresponding quinone (VII) is obtained by demethylation of VI followed by oxidation of the hydroquinone.



VI



VII

Loss of bromine in the Ullmann reaction was observed by Ullmann in the case of 1,2,3,5-tetrabromobenzene which yielded 1,3,5-triphenoxybenzene (2).

Because of unfavorable solubilities, the normal potentials of the phenoxyquinones (I) and (II) and 5-methyl-2-phenoxy-*p*-benzoquinone have been determined polarographically in dioxane-buffer mixtures. While the absolute values are considerably affected by the change in solvent, potential differences remain essentially unaltered and the potential-lowering effects of 0.126, 0.132, and 0.135 v.[3] for the phenoxyl groups in the three compounds compare favorably with the value of 0.131 v. determined from the normal potential of 2-phenoxybenzoquinone in alcoholic solution (1).

The observed potential-lowering for the phenoxyl group is of the same order of magnitude as the values for methoxyl (0.117 v.), ethoxyl (0.128 v.), and hydroxyl (0.103 v.) groups (3) in benzoquinone and the corresponding values (0.131, 0.131, 0.127 v.) (4, 5) in 1,4-naphthoquinone but differs from the value reported by Conant and Fieser (3) for the lowering of the phenoxyl group in 2,3-diphenoxy-1,4-naphthoquinone (0.019 v. per group). The authors' conclusion that the phenoxyl group is distinctly different from alkoxyl radicals (6) must be revised in view of the present data. The abnormal lowering in this naphthoquinone is presumably a characteristic of its structure.[4]

The absorption curves of the phenoxyquinones show two of the three quinone bands which have been designated A, B, and C bands by Braude (7). The A and B bands of the phenoxyquinones have been measured carefully and have been compared with the corresponding bands of *p*-benzoquinone in the same solvent.

Both A and B bands are shifted to longer wavelengths when a phenoxyl group is introduced, the A-band shift amounting to 8.5–15.5 $m\mu$ per phenoxyl group.

In view of the similarity between the quinone A-band and the high intensity

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[3] If the potential lowering due to methyl (0.075 v.) is deducted from the total lowering of 0.210 v.

[4] The lowering *per* methoxyl group in 2,3-dimethoxy-1,4-naphthoquinone amounts to only 0.048 v. (5).

band in C═C—C═O (7) it is to be expected that quinones will show regular bathochromic shifts of the A-bands when substituents are introduced. A survey of published ultraviolet absorption spectra (1, 7) shows A-band shifts per substituent for *p*-benzoquinones containing nucleophilic substituents which are roughly proportional to the potential-lowering of the substituents. Only the values due to phenoxyl constitute an exception. There is no explanation at present for the small A-band shift in this case.

EXPERIMENTAL[5]

2,5-Dibromo-1,4-dimethoxybenzene. The bromination of 1,4-dimethoxybenzene (35 g.) in glacial acetic acid with 140 g. of bromine yielded 64 g. of product, m.p. 142–143° (from acetone).

1,4-Dimethoxy-2,5-diphenoxybenzene. Potassium phenoxide, prepared by adding potassium hydroxide (3.8 g.) to phenol (6.4 g.), was heated *in vacuo* for three hours at 150°. 2,5-Dibromo-1,4-dimethoxybenzene (10 g.), copper powder (0.3 g.), and phenol (35 cc.) were added to the salt and the mixture was refluxed for two hours at 195–200°. After extraction with two 100-cc. portions of water and three 50-cc. portions of ether the combined extracts were steam-distilled with superheated steam to remove 1,4-dimethoxy-2-phenoxybenzene (1.6 g.). The nonvolatile material was extracted with benzene and the extract was washed with 10% sodium hydroxide solution. Distillation of the benzene solution gave a solid brown residue which was crystallized from aqueous methanol and ligroin-benzene. The yield of 1,4-dimethoxy-2,5-diphenoxybenzene, m.p. 145° was 3.8 g.

Anal. Calc'd for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63.

Found: C, 74.62; H, 5.84.

2,5-Diphenoxyhydroquinone. A mixture of 1,4-dimethoxy-2,5-diphenoxybenzene (4.22 g.), aluminum bromide (35 g.), and benzene (100 cc.) was refluxed for four hours. The mixture was cooled and poured into 200 cc. of cold water. The benzene layer was separated and the water layer was extracted twice with benzene. The combined benzene extracts were evaporated, leaving a solid brown residue which was crystallized from a mixture of toluene and Skellysolve B (8:2). The yield of 2,5-diphenoxyhydroquinone was 3.31 g.; m.p. 127–127.7°.

Anal. Calc'd for $C_{18}H_{14}O_4$: C, 73.46; H, 4.90.

Found: C, 73.62; H, 4.85.

2,5-Diphenoxy-p-benzoquinone. Concentrated nitric acid (15 cc.) was added with stirring to a solution of 2,5-diphenoxyhydroquinone (1.96 g.) in 100 cc. of acetic acid at 25°. A yellow flaky precipitate separated immediately. An additional amount of solid precipitated on the addition of cold water. The solid was filtered, dried, and crystallized from xylene. The pure 2,5-diphenoxy-*p*-benzoquinone weighed 1.25 g., m.p. 228–229°; λ $\max_1$ 265 mμ (log ϵ 4.12), λ $\max_2$ 375 mμ (log ϵ 2.70); E_0 0.542 v.

Anal. Calc'd for $C_{18}H_{12}O_4$: C, 73.96; H, 4.14.

Found: C, 74.02; H, 4.34.

An attempt to prepare this quinone by an alternative sequence of reactions led to the preparation of 2,5-diphenoxynitrobenzene as follows:

5-Bromo-2-chloronitrobenzene. A mixture of *o*-chloronitrobenzene (53 g.) and iron powder (1 g.) was refluxed with bromine (20 cc.). The crude reaction product was recrystallized from ethanol; m.p. 71–72° (8), yield 32 g.

5-Bromo-2-phenoxynitrobenzene. Potassium hydroxide (9.5 g.) was dissolved in Butyl Cellosolve (200 cc.). Purified phenol (16 g.) was added. The resultant solution was heated to boiling and was treated with 20 g. of 5-bromo-2-chloronitrobenzene. After refluxing for four hours, the solution was filtered and the filtrate was poured into 1.5 l. of water. The

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[5] All temperatures uncorrected.

brown oil which separated was extracted with ether. The extract was washed twice with water and twice with 10% aqueous sodium hydroxide. The ether was evaporated and the residual red oil was distilled under reduced pressure. The pure product, b.p. 189–190° (3 mm.), weighed 6.0 g.

Anal. Calc'd for $C_{12}H_8BrNO_3$: C, 49.00; H, 2.74.
Found: C, 49.12; H, 2.85.

2,5-Diphenoxynitrobenzene. The dry potassium salt of phenol (from 3.0 g. of phenol), mixed with 9.3 g. of 5-bromo-2-phenoxynitrobenzene, 20 g. of phenol, and 0.1 g. of copper powder was heated for two hours at 230–240°. The mixture was allowed to cool and was extracted with benzene. The benzene solution was washed twice with 10% aqueous sodium hydroxide, the solvent removed, and the red oily residue distilled under reduced pressure. The largest fraction, b.p. 230–235° (1 mm.), weighed 4.5 g.

Anal. Calc'd for $C_{18}H_{13}NO_4$: C, 70.35; H, 4.26.
Found: C, 70.24; H, 4.37.

Tribromophenol bromide. A solution of bromine (41.5 g.) in water (1300 cc.) was added to phenol (4.7 g.) dissolved in water (150 cc.). Recrystallization of the yellow precipitate from chloroform yielded 18 g. of product, m.p. 118–119° [lit. 118° (9)].

2,6-Dibromo-p-benzoquinone. Tribromophenol bromide (8 g.) was oxidized with fuming nitric acid (20 cc.) at 0–20°. The yield of crude quinone was 5.6 g. Recrystallization from ethanol yielded 3.2 g. of pure quinone, m.p. 131–132° [lit., 131° (10)].

2,6-Dibromohydroquinone. The above quinone (1 g.) suspended in 25 cc. of water was reduced with sulfur dioxide. The white precipitate was taken up in ether, the solution was decolorized with charcoal and evaporated. The residual product, m.p. 163–164° weighed 0.89 g. [lit., m.p. 163° (11)].

2,6-Dibromo-1-methoxyphenol. A sodium methoxide solution prepared from 1 g. of sodium and 15 cc. of methanol was added to a mixture of 2,6-dibromohydroquinone (8.7 g.), methanol (80 cc.), and methyl iodide (9.2 g.). The mixture was refluxed for three hours, the excess methanol removed, and the residue shaken with a dilute sodium hydroxide solution and ether. When the aqueous layer was acidified a white precipitate appeared which was crystallized from Skellysolve C. The mono ether, m.p. 139.5–140.2°, weighed 5.9 g.

Anal. Calc'd for $C_7H_6Br_2O_2$: C, 29.82; H, 2.14.
Found: C, 29.58; H, 2.19.

2,6-Dibromo-1,4-dimethoxybenzene. Methyl sulfate (23.2 cc.) was added slowly with stirring to a solution of 2,6-dibromohydroquinone in 61 cc. of 15% aqueous sodium hydroxide. Aqueous 10% sodium hydroxide (50 cc.) was added and the mixture was heated at 100° for one hour. The dimethyl ether separated on cooling. After recrystallization from aqueous methanol it melted at 37.1–37.4°[6] [lit., m.p. 56° (12)] and gave a negative Folin test.

1,4-Dimethoxy-2,6-diphenoxybenzene. Potassium phenoxide, prepared from 3.5 g. of phenol, was heated for two hours with 2,6-dibromo-1,4-dimethoxybenzene (5 g.), copper powder (0.3 g.), and phenol (30 cc.). The reaction mixture was extracted with three 50-cc. portions of benzene and the combined benzene extracts were decolorized with charcoal and the benzene removed. The brown oily residue was chromatographed on alumina from benzene solution. The benzene eluate (flowing chromatogram) gave a light yellow oil (0.4 g.), b.p. 178–189° (1 mm.).

Anal. Calc'd for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63.
Found: C, 74.71; H, 5.99.

2,6-Diphenoxyhydroquinone. A mixture of 1,4-dimethoxy-2,6-diphenoxybenzene (1 g.), aluminum bromide (9 g.), and benzene (25 cc.) was refluxed for four hours, and then poured into 100 cc. of water. The benzene layer was separated and the aqueous layer was extracted with benzene. When the combined benzene solutions were evaporated, a dark solid residue remained. This was crystallized from benzene-Skellysolve F (1:10). The light tan solid was

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[6] Fisher-Johns block.

recrystallized from Skellysolve C; yield, 0.63 g. of 2,6-diphenoxyhydroquinone, m.p. 107–108°.

Anal. Calc'd for $C_{18}H_{14}O_4$: C, 73.46; H, 4.90.

Found: C, 73.55; H, 4.98.

2,6-Diphenoxy-p-benzoquinone. Concentrated nitric acid (5 cc.) was added with stirring to a solution of 2,6-diphenoxyhydroquinone (0.23 g.) in acetic acid (20 cc.) at 25°. A fluffy, light yellow solid separated when the solution was diluted with cold water. The solid was recrystallized from Skellysolve C and yielded 0.21 g. of 2,6-diphenoxy-*p*-benzoquinone, m.p. 158–159°; λ $\max_1$ 265 mμ (log ϵ 3.86), λ $\max_2$ 375 mμ (log ϵ 2.84); E_0 0.529 v.

Anal. Calc'd for $C_{18}H_{12}O_4$: C, 73.96; H, 4.14.

Found: C, 74.02; H, 4.34.

2,5-Dimethoxynitrobenzene. 1,4-Dimethoxybenzene (10 g.) dissolved in 40 cc. of glacial acetic acid was nitrated with 40 cc. of nitric acid (sp. gr. 1.41) at 30°. Crystallization of the material from methanol gave 13.15 g. of pure product, m.p. 72–73° [lit., 71–72° (13)].

3-Bromo-2,5-dimethoxynitrobenzene. 2,5-Dimethoxynitrobenzene (60 g.) was brominated with dry bromine (60 g.) at 70–75° at a rate of one drop every half minute. Upon cooling, a solid mass of 3-bromo-2,5-dimethoxynitrobenzene was formed. The mass was stirred with 50 cc. of methanol, cooled below 0°, and the resultant solid crystallized successively from aqueous acetic acid and methanol. The pure product, m.p. 152–153°, weighed 42 g.

Anal. Calc'd for $C_8H_8BrNO_4$: C, 36.66; H, 3.08.

Found: C, 36.54; H, 3.25.

2-Amino-6-bromo-1,4-dimethoxybenzene. Concentrated hydrochloric acid (60 cc.) was added to a mixture of granulated tin (18 g.) and 3-bromo-2,5-dimethoxynitrobenzene (10 g.) dissolved in 200 cc. of ethanol. The mixture was refluxed on a steam-bath until the solution became colorless. The solution was poured onto 100 g. of ice and placed in a freezing mixture. It was made strongly alkaline by adding a cold saturated solution of sodium hydroxide containing a small amount of sodium hydrosulfite. The mixture was extracted with ether and the combined extracts decolorized with charcoal and evaporated. The solid residue, after crystallization from aqueous methanol, had m.p. 79–80°; yield 6.8 g.

Anal. Calc'd for $C_8H_{10}BrNO_2$: C, 41.39; H, 4.34.

Found: C, 41.30; H, 4.56.

2-Acetamino-6-bromo-1,4-dimethoxybenzene. Acetylation of the above amine (6 g.) with acetic anhydride (30 g.) gave 5 g., m.p. 90–91° (from Skellysolve B-benzene).

Anal. Calc'd for $C_{10}H_{12}BrNO_3$: C, 43.81; H, 4.41.

Found: C, 43.74; H, 4.60.

2-Acetamino-5,6-dibromo-1,4-dimethoxybenzene. The above amide (8 g.), dissolved in 100 cc. of chloroform, was brominated over a period of one hour with 4.2 g. of bromine dissolved in 15 cc. of chloroform. Distillation of the chloroform gave a pink residue which was decolorized with charcoal in benzene solution. After removal of the benzene, the substance was crystallized from Skellysolve C, yield, 6.8 g., m.p. 124–125°.

Anal. Calc'd for $C_{10}H_{11}Br_2NO_3$: C, 34.01; H, 3.14.

Found: C, 33.93; H, 3.31.

2-Amino-5,6-dibromo-1,4-dimethoxybenzene hydrochloride. The dibromo compound (4 g.) was refluxed for three hours with 60 cc. of absolute ethanol and 70 cc of concentrated hydrochloric acid. The amine hydrochloride crystallized when the mixture was cooled in a freezing mixture. It was washed with cold alcohol and dried. Yield, 3.3 g.; m.p. 130° (dec.).

Anal. Calc'd for $C_8H_{10}Br_2ClNO_2$: C, 27.65; H, 2.91.

Found: C, 27.60; H, 2.99.

2-Amino-5,6-dibromo-1,4-dimethoxybenzene. The hydrochloride (3.3 g.), dissolved in 25 cc. of water, was stirred vigorously while 10% aqueous sodium hydroxide was added until the solution was just neutral to litmus. The amine separated on cooling the mixture in an ice-bath. It was recrystallized from aqueous methanol containing a small amount of sodium hydrosulfite. The pure amine, m.p. 114–115° weighed 1.87 g.

Anal. Calc'd for $C_8H_9Br_2NO_2$: C, 30.89; H, 2.32.

Found: C, 30.70; H, 2.45.

2,3-Dibromo-1,4-dimethoxybenzene. The above amine (1.87 g.) was added to a hot solution of 20 cc. of water and 1.55 cc. of concentrated hydrochloric acid. The solution was cooled to 15°, 1.75 cc. of concentrated hydrochloric acid was added, and the mixture was placed in an ice-bath. It was diazotized with 1.15 g. of sodium nitrite in 25 cc. of water and rapidly filtered. The clear filtrate was reduced with 30% hypophosphorous acid. The ether solution of the oily product was washed with 20% aqueous sodium hydroxide, then with water, dried over sodium sulfate, and distilled. The residual bromo compound (0.8 g.) was used without further purification.

Ullmann reaction. 2,3-Dibromo-1,4-dimethoxybenzene (0.94 g.) was heated with potassium phenoxide (from 0.7 g. of phenol), 0.1 g. of copper powder, and 3 cc. of phenol at 170–200° for two hours. The product, taken up in benzene, was washed with 20% aqueous sodium hydroxide, decolorized with charcoal, and freed from solvent. Crystallization of the brown residual solid from Skellysolve F gave 0.20 g. of 1,4-dimethoxy-2-phenoxybenzene, m.p. and mixed m.p. 46–47°, as the only alkali-insoluble product.

Normal potentials. Half wave potentials of the quinones were determined in 50% dioxane-buffer solutions from *p*H 5.2 to 8 with a Sargent polarograph. The *p*H of the buffer solutions was determined with a Beckman *p*H meter using a glass electrode. Gelatin (0.5% solution) was added to give a concentration of 0.01% of gelatin to suppress maxima in the polarograms. The measurements were carried out in an atmosphere of purified nitrogen at 23 ± 2° with a standard calomel electrode as reference electrode. The capillary for the dropping mercury electrode had a drop time of 3.5 seconds and an m-value of 1.908 mg. of mercury per second measured on open circuit in 50% dioxane-buffer solutions.

The half wave potentials, measured from the well defined waves in this *p*H range, were plotted against *p*H and interpolated for *p*H 0. The normal potentials for *p*-benzoquinone and 2-methyl-5-phenoxy-*p*-benzoquinone amounted to 0.794 v. and 0.584 v. respectively.

Absorption spectra. The ultraviolet absorption spectra of the phenoxyquinones were determined in dioxane solution in concentrations of 0.00024 moles per liter in the range of 240–460 mμ.[7]

SUMMARY

Two diphenoxy-*p*-benzoquinones have been prepared. Their normal potentials and ultraviolet absorption spectra have been determined and correlated with similar compounds.

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REFERENCES

(1) UNGNADE AND ZILCH, *J. Org. Chem.*, **15**, 1108 (1950).
(2) ULLMANN AND SPONAGL, *Ann.*, **350**, 83 (1906).
(3) CONANT AND FIESER, *J. Am. Chem. Soc.*, **46**, 1858 (1924).
(4) FIESER AND FIESER, *J. Am. Chem. Soc.*, **57**, 492 (1935).
(5) FIESER, *J. Am. Chem. Soc.*, **50**, 442 (1928).
(6) CONANT AND FIESER, *J. Am. Chem. Soc.*, **46**, 1871 (1924).
(7) BRAUDE, *J. Chem. Soc.*, 490 (1945).
(8) HOLLEMAN, *Rec. trav. chim.*, **34**, 204 (1915).
(9) BENEDICKT, *Ann.*, **199**, 127 (1879).
(10) HODGSON AND NIXON, *J. Chem. Soc.*, 1085 (1930).
(11) KOHN AND BENCZER, *Ann.*, **433**, 305 (1923).
(12) ANDERSON, *Nature*, **140**, 583 (1927).
(13) ALBRECHT, *Ann.*, **348**, 31 (1906).

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