

Notes

Oxidative Substitution on Halophenols

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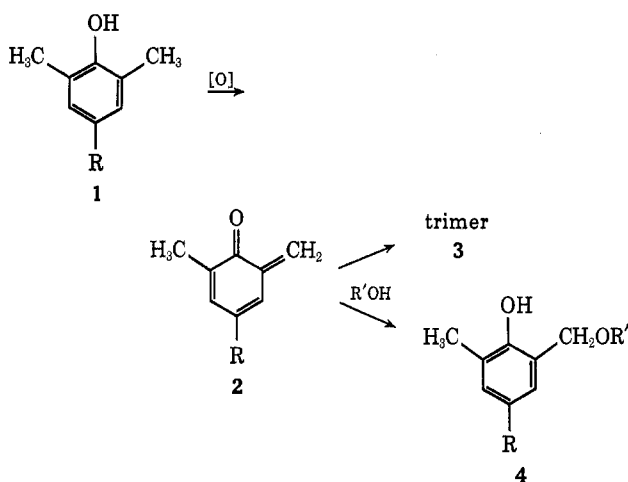
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Organic acids or phenols replace the halogen in 4-halogen substituted phenols when one-electron oxidizing agents oxidize the substituted phenol in the presence of the acid or phenol. Such a reaction allows the synthesis of a variety of substituted phenols, under mild conditions, which are difficult to make by other means.

Hunter^{1,2} and Price³ observed halogen replacement reactions in the oxidation of 4-bromo-2,6-xyleneol to polyphenylene oxide with concurrent loss of halogen. More highly halogen substituted phenols such as pentachlorophenol, when oxidized, yield quinol ethers, with no loss of halogen, instead of polymers.^{4,5} In certain cases the coupling occurs with carbon-carbon bond formation (diphenoquinones) rather than with carbon-oxygen bond formation as in quinol ethers.⁶ These couplings are free-radical dimerizations.

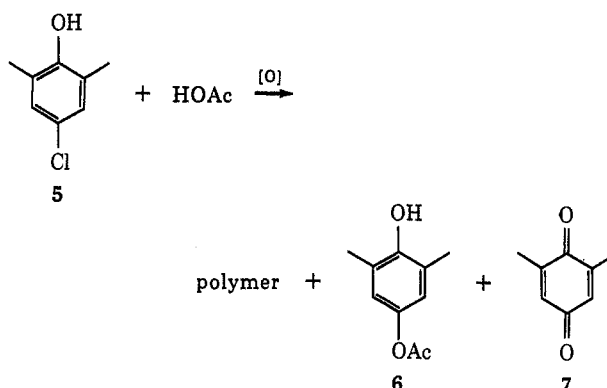
One-electron oxidation of phenols without 4-halogen substituents, particularly 4-substituted 2,6-xyleneol (**1**), can give an *o*-quinone methide **2** which can react with itself to give a trimer **3** or with another hydroxyl-containing group to give a benzyl ether **4**.^{7,8} When R



is a halogen this sequence is not followed. No trimer or benzyl ether is found; the observed products result from substitution of the halogen by some other group.

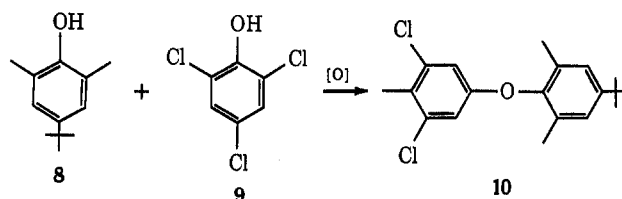
- (1) W. H. Hunter and A. A. Levine, *J. Amer. Chem. Soc.*, **48**, 1608 (1926).
- (2) W. H. Hunter and M. Morse, *J. Amer. Chem. Soc.*, **48**, 1615 (1926).
- (3) G. Staffin and C. C. Price, *J. Amer. Chem. Soc.*, **82**, 3632 (1960).
- (4) E. Muller, A. Rieker, and W. Beckert, *Z. Naturforsch. B*, **17**, 567 (1962).
- (5) H. D. Becker, *J. Org. Chem.*, **29**, 3068 (1964).
- (6) C. J. R. Adderley and F. R. Hewgill, *J. Chem. Soc. C*, 2770 (1968), and earlier papers.
- (7) D. A. Bolon, *J. Org. Chem.*, **35**, 715 (1970).
- (8) D. A. Bolon, *J. Org. Chem.*, **35**, 3666 (1970).

When 4-chloro-2,6-xyleneol (**5**) is oxidized with either silver oxide or potassium permanganate in acetic acid, two products are formed in addition to the expected polymer. The material present in larger amount was identified as 4-acetoxy-2,6-xyleneol by comparison of its mass spectrum, infrared spectrum, and retention time of its trimethylsilyl ether⁹ with those of authentic **6**.¹⁰ The second material is 2,6-xyloquinone (**7**).



A similar substitution is obtained with benzoic acid where dimethylformamide is needed as a solvent. This oxidation yields 4-benzoyloxy-2,6-xyleneol when 4-chloro-2,6-xyleneol is oxidized with silver oxide.

In addition to organic acids, phenols will replace the halogen on a chlorophenol. The oxidation with silver oxide of a mixture of 4-*tert*-butyl-2,6-xyleneol (**8**) and

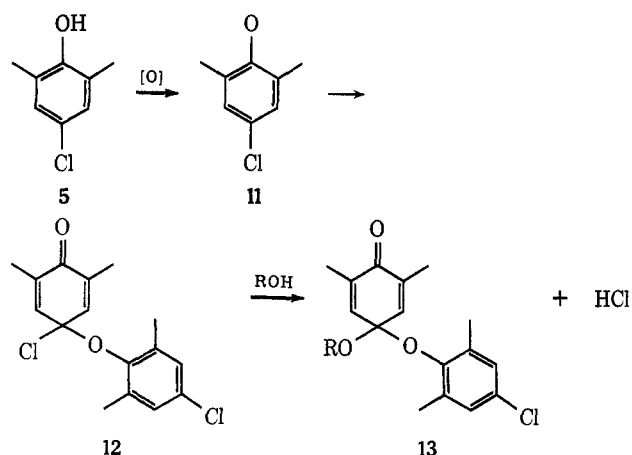


2,4,6-trichlorophenol (**9**) in a 1:1 ratio gives the phenoxy phenol **10** as the chief product. An nmr and mass spectrum identified **10** as the illustrated para isomer.

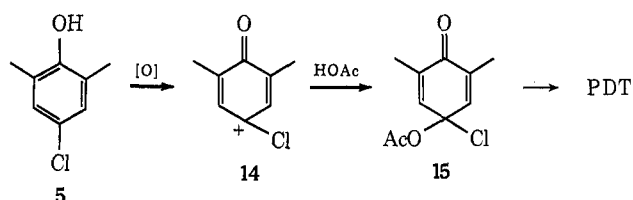
These reactions probably all occur by a similar mechanism. One mechanism that accounts for these results involves oxidation of **5** to the radical **11**, which then dimerizes to the quinol ether **12**, a well-known reaction. This intermediate solvolyzes, perhaps by some sort of ionic reaction, with the attendant organic acid or phenol to yield the quinone ketal **13**, which can then separate and abstract a hydrogen to yield 4-acetoxy-2,6-xyleneol (R = AcO) or solvolyze to 2,6-xyloquinone.

Although this work uses typical one-electron oxidizing agents, there appears to be mounting evidence that in certain cases the two electrons can be removed with equal ease.¹¹ If this should occur in these reactions,

- (9) J. F. Klebe, H. Finkbeiner, and D. M. White, *J. Amer. Chem. Soc.*, **88**, 3390 (1966).
- (10) E. Zbiral, F. Wessely, and E. Lahrmann, *Monatsh. Chem.*, **91**, 331 (1960).
- (11) M. Chanham, F. M. Dean, K. Kindley, and M. Robinson, *J. Chem. Soc. D*, **19**, 1141 (1971).



the phenol **5** could be oxidized directly to **14** and subsequently yield the products by a solvolysis mechanism.



In all of the reactions a polymeric material forms which is probably a polyphenylene oxide polymer but which was not characterized.

This reaction offers a method of making some substituted phenols which would be difficult to make by other means. The conditions are mild and the reaction easy to run.

The reaction is general in the sense that a wide variety of oxidants yield identical results. Lead dioxide, silver oxide, and potassium permanganate all give the same distribution of products. Phenols that fulfill the conditions of blocked ortho positions also will work. Alcohols do not give a similar product distribution and an investigation of this reaction is under way.

Experimental Section

4-Chloro-2,6-xyleneol and 2,4,6-Trichlorophenol.—These materials were used as obtained from Aldrich Chemical Co.

4-tert-Butyl-2,6-xyleneol.—This material was prepared by butylation of 2,6-xyleneol.⁷

Oxidation of 4-Chloro-2,6-xyleneol (5) in Acetic Acid.—The slow addition of powdered potassium permanganate (1.58 g, 0.05 equiv) to 4-chloro-2,6-xyleneol (2.34 g, 0.015 mol) in glacial acetic acid (75 ml) produced a bright yellow solution which was poured into water and the organics were extracted with ether. The ether was washed with sodium bicarbonate solution and water and dried, and the ether was distilled, which left a yellow gum. Upon treatment with bis(trimethylsilyl)acetamide⁹ the sample became sufficiently volatile so that it could be analyzed by vapor phase chromatography (vpc) and the major product was collected. This material is 4-acetoxy-2,6-xyleneol trimethylsilyl ether, as shown by mass spectra (molecular weight and fragmentation pattern), infrared spectrum, and vpc retention time when compared with those of an authentic material.¹²

The residual oil gave pale yellow crystals (0.4 g, 8%) when dissolved in hexane and cooled to -20° . These crystals, mp $65-67^\circ$, are 2,6-xyloquinone, as shown by the mixture melting point and a comparison of infrared spectra with those of an authentic material.⁶

Oxidation of 4-Chloro-2,6-xyleneol and Benzoic Acid.—Silver oxide (6.96 g, 0.03 mol) was stirred with a mixture of 4-chloro-

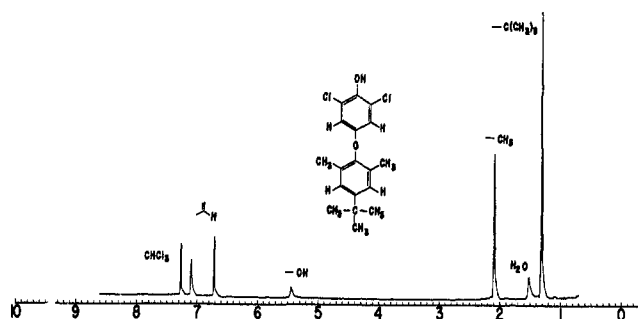


Figure 1.

2,6-xyleneol (4.68 g, 0.03 mol), benzoic acid (3.66 g, 0.03 mol), magnesium sulfate, and dimethylformamide over an 18-hr period. The solid silver salts were filtered and the filtrate was placed in water. Ether extraction removed the organic materials, after which sodium bicarbonate and water washes removed contaminants. The dried ether was distilled, leaving a red, gummy residue. The gum was dissolved in hexane and cooled to -20° . Tan crystals formed in a yield of 12%. Recrystallization of these crystals gave a yellow solid which was 4-benzoyloxy-2,6-xyleneol, mp $139-141^\circ$. The infrared spectrum shows a hydroxyl at 3430 , carbonyl at 1725 , and phenyl absorptions at 710 and 735 cm^{-1} which support the assigned structure **6** (OAc = OBz).

Anal. Calcd for $\text{C}_{15}\text{H}_{14}\text{O}_3$: C, 74.4; H, 5.8; mol wt, 242. Found: C, 74.5; H, 5.7; mol wt, 245.

Oxidation of 4-tert-Butyl-2,6-xyleneol and 2,4,6-Trichlorophenol.—4-tert-Butyl-2,6-xyleneol (1.78 g, 0.01 mol) and 2,4,6-trichlorophenol (1.97 g, 0.01 mol) in benzene were stirred with silver oxide (2.3 g, 0.01 mol) for 0.5 hr and then filtered. A vpc of the silylated reaction mixture showed that the products were 80% phenoxy phenol **10** and 20% mixed monomers. A sample of silylated **10** was collected from the vpc and gave the correct mass spectrum for the trimethylsilyl derivative of **10**; major peaks at m/e 412, 410, and 177 (phenoxy) were found along with no evidence for three chlorines on the molecule.

Chromatography of the residue after filtration and benzene removal, and elution by hexane followed by 20% benzene-hexane, gave several fractions. One consisted of 0.16 g of solids which a vpc analysis showed was 90% **10**. This fraction, when separated by preparative thin layer chromatography, gave 0.102 g of a gum which crystallized at -30° , giving white plates, mp $105-106^\circ$.

Anal. Calcd as $\text{C}_{15}\text{H}_{20}\text{O}_2\text{Cl}_2$: C, 63.7; H, 5.9. Found: C, 63.7; H, 6.2.

The nmr spectrum of this material (Figure 1) clearly shows that the structure of **10** is the assigned 4 isomer.

Registry No.—**5**, 1123-63-3; **6** trimethylsilyl ether, 38645-01-1; **8**, 879-97-0; **9**, 88-06-2; **10**, 38645-02-2; 4-benzoyloxy-2,6-xyleneol, 38645-03-3.

The Mechanism of the Cope Elimination

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The Cope elimination¹ involves the thermal decomposition of an amine oxide by a five-membered cyclic transition state. This reaction has been extensively used as a "reference reaction" for syn elimination, since its mechanism has been considered to be essentially

(12) H. Finkbeiner and A. Toothaker, *J. Org. Chem.*, **33**, 4347 (1968).

(1) A. C. Cope and E. R. Trumbull, *Org. React.*, **11**, 317 (1960).