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Electrochemical Oxidation of 2,6-Di-*tert*-butyl-4-methylphenol in Basic Methanol

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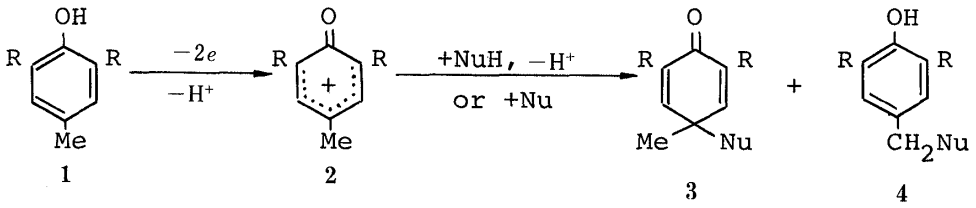
Electrochemical oxidation of 2,6-di-*tert*-butyl-4-methylphenol (**1**) in methanol containing sodium methoxide gave side-chain-oxidized phenols, $ArCH_2OMe$, ArCHO, and ArCOOMe (Ar = 3,5-di-*tert*-butyl-4-hydroxyphenyl), together with 2,6-di-*tert*-butylbenzoquinone and 3,5,3′,5′-tetra-*tert*-butyl-4,4′-diphenoquinone. The product distribution varied with the electricity consumption. Based on the results obtained, a simple electrochemical transformation of **1** to the hydroxybenzaldehyde ArCHO was effected.

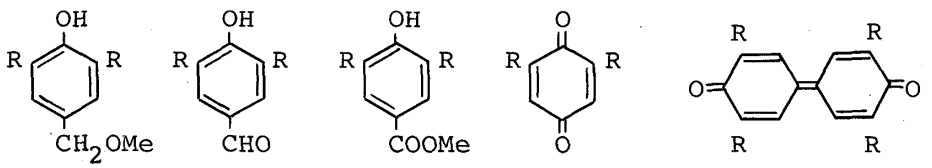
Keywords——electrochemical oxidation; cyclic voltammetry; controlled potential electrolysis; 2,6-di-*tert*-butyl-4-methylphenol; 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde

2,6-Di-*tert*-butyl-4-methylphenol (**1**), as well as 2,4,6-tri-*tert*-butylphenol, has often been employed as a model compound for studies on the electrochemical oxidation of phenols.[1] Electrolysis of **1** in acetonitrile or in methanol predominantly gave the cyclohexadienones **3** (Chart 1).[2–5] The side-chain-substituted phenols **4** were usually minor products, except in acetonitrile with added pyridine.[5] However, most of the products were obtained under acidic, neutral, or weakly basic conditions, where the phenoxonium ion **2** was suggested to be the intermediate yielding the products. There seems to be no report on the selective side-chain substitution of **1** by electrochemical oxidation. This paper reports the results of electrolysis of **1** in methanol containing sodium methoxide. The products **4a** and **5**—**8** were obtained.



1 2 3 4

R=*tert*-Bu; Nu=OH^-, MeO^-, AcO^-, pyridine, *etc.*



4a **5** **6** **7** **8**

Chart 1

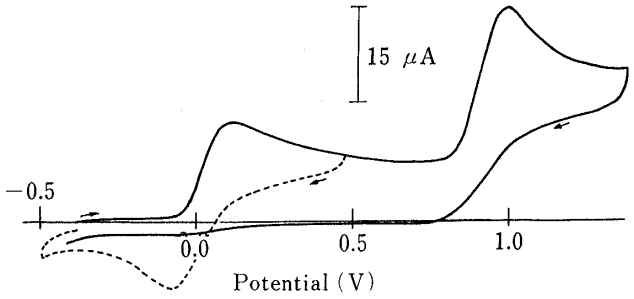


Fig. 1. Cyclic Voltammetry of **1**

In MeOH containing NaOMe equimolar with **1** (2.38 mM) and 0.1 M $NaClO_4$, at 25 °C; glassy carbon anode (area, 0.071 cm^2); voltage sweep rate, 50 $mV\,s^{-1}$. Arrows represent the direction of the voltage sweep. The dashed line represents the voltammogram observed when the sweep was reversed at a potential between the first and the second anodic peaks.

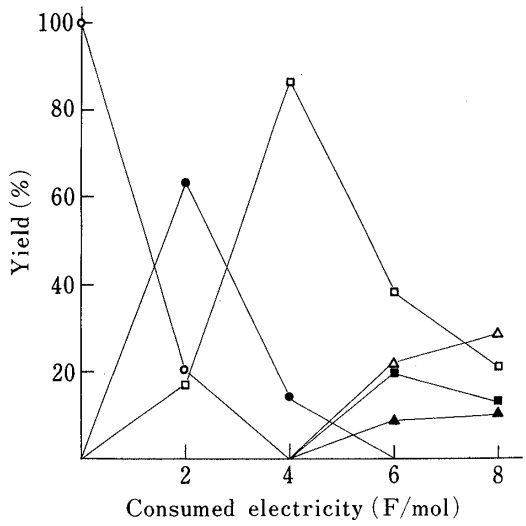


Fig. 2. Change of Product Distribution with Amount of Electricity Consumed in the Controlled Potential Electrolysis of **1**

In MeOH containing NaOMe equimolar with **1** (0.145 mmol) and 0.1 M $NaClO_4$, at 0.5 V: —○—, **1**; —●—, **4a**; —□—, **5**; —■—, **6**; —△—, **7**; —▲—, **8**. The results are averages of two or three runs. The lines connecting the experimental points are shown for convenience, and have no physical significance except for the intercepts at the abscissa.

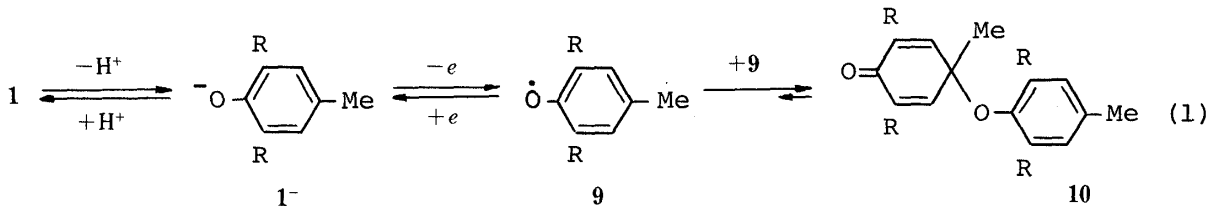
Results and Discussion

Figure 1 shows a typical voltammogram of **1** in methanol containing sodium methoxide. All potentials were measured against an aqueous saturated calomel electrode (S.C.E.). The voltammetric behavior of **1** is similar to those reported for 2,6-di-*tert*-butyl-4-alkylphenols in acetonitrile containing tetramethylammonium hydroxide[6] and essentially the same as that for 2,4,6-tri-*tert*-butylphenol in aqueous solution at pH 10.[6a] The first anodic peak has been ascribed to one-electron transfer from phenoxide ions to give phenoxy radicals (*cf.* Chart 2, Eq. 1). In the MeOH–NaOMe system, the phenols **4a**, **5**, and **6** showed voltammograms similar to that of **1**: the first and the second anodic peak potentials are 0.12 and 1.00 V for **1**, 0.14 and 1.13 V for **4a**, 0.35 and 1.25 V for **5**, and 0.29 and 1.27 V for **6**. The other two products **7** and **8** showed no anodic peak under these conditions.

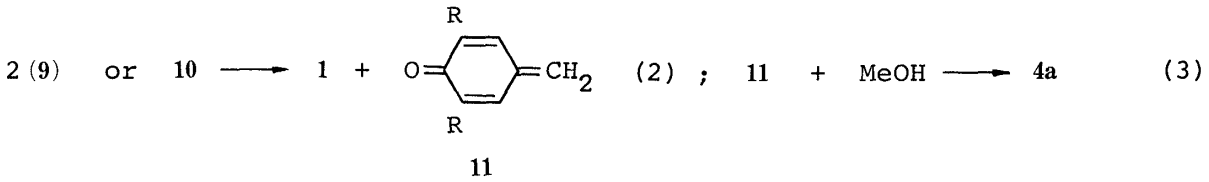
Controlled potential electrolysis of **1** in the MeOH–NaOMe system was carried out at 0.5 V in an undivided cell. As expected from the voltammetric results on **1**, **4a**, **5**, and **6**, the electrolysis current under these conditions did not converge to the background value even when 10 F per mol of **1** had been passed. The product distribution depended on the quantity of electricity consumed, as illustrated in Fig. 2, where the yields of the products were determined after acidification of the electrolysis solution with hydrochloric acid. If the acidification was omitted, the yields of the phenols **5** and **6** were considerably smaller than those shown in Fig. 2, indicating that some species other than **5** and **6**, probably the acetal **13** and the ortho ester **15** (see Chart 2), are the primary products in the electrolysis solution.

The scheme shown in Chart 2 is proposed for the electrolysis in the MeOH–NaOMe system. The process **1** to the quinone methide **11** (Eqs. 1 and 2) has been well documented in the chemical[7,8] and electrochemical[6b] one-electron oxidation of **1**. Formation of **4a**, **5**, and **6** *via* the corresponding intermediates **11**—**15** has been suggested in the oxidation of **1** with 2,3-dichloro-5,6-dicyanobenzoquinone[7] and tetrabutylammonium hexacyanoferrate (III).[9]

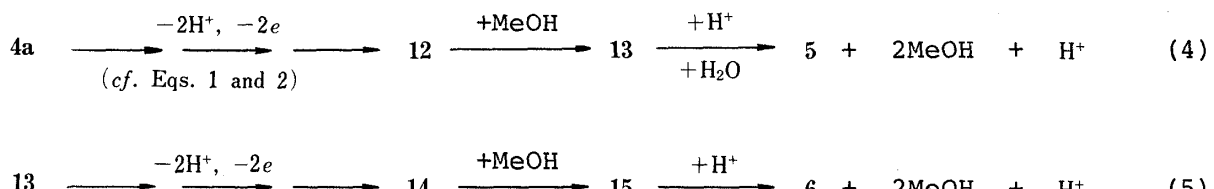
When the phenol **5** was subjected to electrolysis in the presence of sodium methoxide (twice the amount of **5**) at 0.5 V in a divided cell, the diphenoquinone **8** and methylformate were formed in 93 and 63% yields, respectively; 1.9 F per mol of **5** had been consumed. These results support the reactions in Eqs. 6 and 7. The diphenoquinone **8** has been obtained by I_2 oxidation of **5** in alkaline methanol.[10]



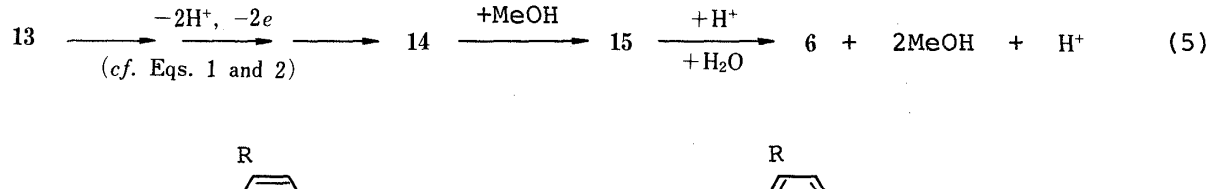
(1)



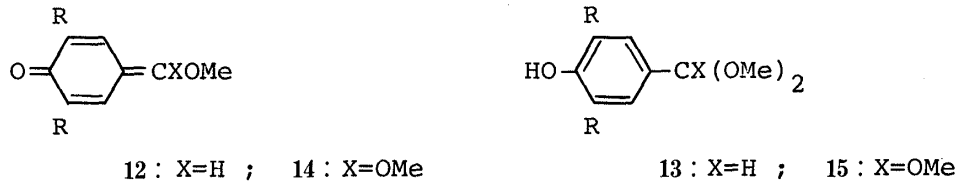
(2) ; (3)



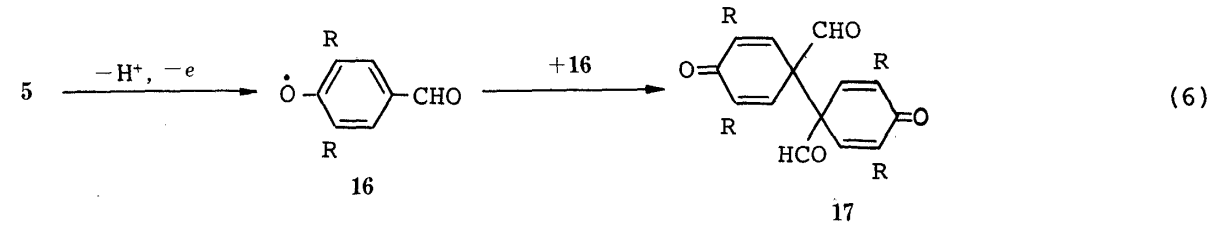
(4)



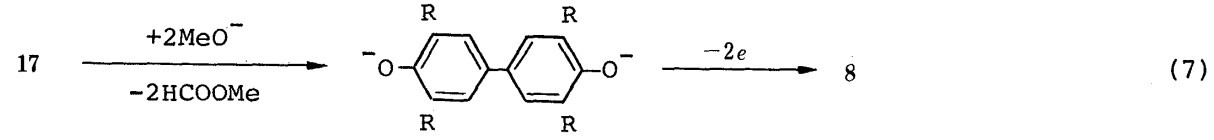
(5)



12 : X=H ; 14 : X=OMe 13 : X=H ; 15 : X=OMe



(6)



(7)

Chart 2

Formation of the benzoquinone **7** along with the cyclohexadienone **3** (Nu=OMe) has been demonstrated in the electrolysis of **1** in acetonitrile buffered by adding methanol and tetraethylammonium hydroxide concomitantly with the current flow.[2] A reaction process has been suggested which involves a stepwise oxidation of **1** to 3,5-di-*tert*-butyl-4-hydroxybenzoic

acid followed by oxidative decarboxylation and reaction with water (an overall ten-electron process). In the present system, however, the benzoic acid may not be a necessary intermediate. When the phenol **6** was electrolyzed under the conditions described in Fig. 2, **7** was formed in 47% yield; 7.5 F per mol of **6** had been consumed.

Based on the results in Fig. 2, together with the voltammetric results on **1** and the products obtained, the preparation of the phenols **4a** and **5** was examined. At least the phenol **5** was expected to be obtainable in a good yield. Electrolysis of **1** in methanol–ether (4:1, v/v)[11] at 0.12 V (2 F per mol of **1**) gave **4a** in 61% yield; column chromatography was required to isolate the product. The phenol **5** was obtained by similar electrolysis (at 0.12 V, 4 F per mol of **1**) in 68% yield, without the chromatographic work-up. Details of the procedures are described in the experimental section. The electrochemical method for the preparation of **5** is comparable with that which involves oxidation of **1** with metal acetates in acetic acid,[12] but the former does not require heating of the reaction mixture.

Experimental

Cyclic voltammetry was carried out essentially as described previously.[13] Controlled potential electrolysis was performed in an undivided cylindrical cell (diameter, 35 mm; height, 75 mm) unless otherwise noted, using a Hokuto Denko HA-104 potentiostat-galvanostat with a Hokuto Denko HF-201 coulometer and a Toa Dempa EPR-108 electronic recorder. A glassy carbon plate, a platinum foil, and an S.C.E. separated by an agar bridge were used as the anode, cathode, and reference electrode, respectively.

Determination of the Product Distribution——The electrolysis cell contained stock solutions of the phenol **1** (10 ml, which contains 32 mg of **1**) and NaOMe (1.0 ml, equimolar with respect to **1**) both in methanol, 0.6 g of $NaClO_4$, and the necessary amount of methanol to make the volume 40 ml. The mixture was subjected to electrolysis at 0.5 V and at room temperature (>20 °C) until a predetermined quantity of electricity (2, 4, 6, or 8 F per mol of **1**) had been consumed. The solution after electrolysis was made just acid with 1 N HCl, and adjusted to 100.0 ml in a volumetric flask with methanol. The resulting solution was subjected to liquid chromatography to estimate the yields of products by using a Waters 6000-A solvent delivery system with a U6K universal injector and a JASCO UVID-EC-1 spectrophotometer [Bondapack C_{18}-Corasil; 60% (v/v) aqueous methanol].

The products, **4a**, **5**, **6**, **7**, and **8** are all known compounds. Authentic samples were obtained by electrolyzing larger amounts of **1**, **4a**, or **5**, and characterized by elemental analysis and infrared and nuclear magnetic resonance spectroscopy. Typical examples are described below. The phenol **4a** (205 mg) was subjected to electrolysis in the MeOH–NaOMe system (50 ml) containing 0.1 M $NaClO_4$ at 0.5 V until 875 C, which corresponded to 11 F per mol of **4a**, had been consumed. The electrolyzed solution, after being acidified with 1 N HCl, was evaporated to dryness under reduced pressure, and the residue was extracted with benzene. The benzene was removed under reduced pressure and the residue, after being washed with hexane, was recrystallized from hexane to give **6** (88 mg, 41%): mp, 166.5—167.5 °C (lit.,[14] 161—162 °C). Evaporation of the hexane washings under reduced pressure followed by recrystallization of the residue from acetone gave **8** (17 mg, 9%): mp, 251—252 °C (lit.,[15] 248 °C). The diphenoquinone **8** was also obtained on electrolysis of the phenol **5** in a divided cell as described in the text. The benzoquinone **7** was separated from the product mixture obtained by similar work-up of the electrolyzed solution of the phenol **1** (treatment with 1 N HCl, evaporation of the solvent, and extraction with benzene), by column chromatography on silica gel [benzene–petroleum ether (1:2, v/v)]: mp, 66.5—67.5 °C (lit.,[10] 66—68 °C).

Preparation of the Phenols 4a and 5——The phenol **1** (448 mg, *ca.* 2 mmol) was subjected to electrolysis in a mixture of MeOH (40 ml) and Et_2O (10 ml) containing NaOMe (equimolar with **1**) and 0.1 M $NaClO_4$ at 0.12 V at 25 °C until 2 F per mol of **1** had been consumed. The electrolyzed solution was evaporated to dryness under reduced pressure, 1 N HCl (30 ml) was added to the residue, and the mixture was extracted with Et_2O (3 × 30 ml). The extract, after being dried with Na_2SO_4, was evaporated to dryness under reduced pressure, and the residue was subjected to column chromatography on silica gel [*n*-hexane–AcOEt (15:1, v/v)]. The phenols **1** and **4a** were obtained in 16% (70 mg) and 61% (274 mg) yields, respectively.

The phenol **1** (435 mg, *ca.* 2 mmol) was electrolyzed similarly until 4 F per mol of **1** had been consumed. The solution after electrolysis was evaporated to dryness under reduced pressure, 1 N HCl (30 ml) was added to the residue, and the mixture was allowed to stand overnight. The precipitate was separated by filtration, washed with a small amount of water, dried, and recrystallized from benzene–*n*-hexane to give **5** in 68% yield (314 mg).

References and Notes

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