J. Electroanal. Chem., 81 (1977) 171—187

ELECTROCHEMICAL OXIDATION OF 2,6-DI-tert-BUTYL-4-ISOPROPYLPHENOL

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(Received 28th June 1976)

ABSTRACT

The anodic oxidation of 2,6-di-tert-butyl-4-isopropylphenol, Ia, as well as the 4-ethyl (Ib) and 4-methyl (Ic) derivatives, has been studied in acetonitrile using carbon electrodes. Depending upon solution conditions and electrode potential, products derived from intermediate phenoxy radicals or phenoxonium ions are found. Oxidation of the phenoxides, IIa—c, leads to phenoxy radicals. Disproportionation of phenoxy radicals to form quinone methides is important for all three phenols, and in the case of IIa the quinone methide so formed, 2,6-di-tert-butyl-4-isopropylidene-2,5-cyclohexadienone, is susceptible to tautomerization followed by oxidation to a bis-quinone methide. The phenoxy radicals formed by oxidation of IIb are known to take part in a reversible dimerization to form a *para*-quinol ether and this reaction affects the cyclic voltammetry in a particularly interesting manner. Oxidation of Ia (or oxidation of its phenoxy radical) gives principally 2,6-di-tert-butyl-4-hydroxy-4-isopropyl-2,5-cyclohexadienone, a product formally derived from a phenoxonium ion intermediate. 2,6-Di-tert-butyl-4(2-hydroxy-2-propyl)phenol can also be formed on oxidation of Ia. The electrochemical behavior of these phenols is discussed in relation to chemical and electrochemical data of other phenols.

INTRODUCTION

In an earlier study the electrochemical oxidation of 2,4,6-tri-tert.-butylphenol was investigated [1]. The presence of the bulky tert.-butyl groups at the *ortho* and *para* positions limits the types of reactions which can occur upon anodic oxidation. As these tert.-butyl groups are removed or replaced by other alkyl groups, it is to be expected that new reaction pathways will be opened. The present investigation concerns 2,6-di-tert.-butyl-4-isopropylphenol and other phenols containing a 4-substituent with hydrogen atom(s) alpha to the ring.

The general framework of electrochemical reactivity which was found for 2,4,6-tri-tert.-butylphenol persists for the phenols studied in this work. This pattern is summarized below. The presumed intermediate phenoxonium ions IV are not detected but products derived from them by attack of water or other nucleophiles are obtained.

Two new reactions can be of importance with the phenols studied in this work. The phenoxy radicals III may disproportionate giving the original phenol

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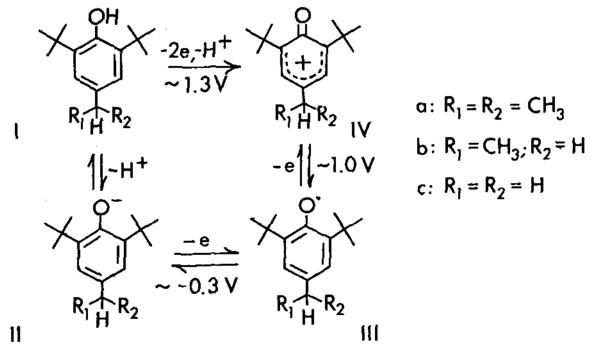
and the quinone methide V (reaction 2). In addition, when the 4-substituent is small, a reversible dimerization of phenoxy radicals can be detected (reaction 3). Both of these reactions were found to be of importance in the present work.



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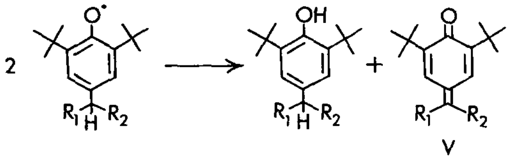

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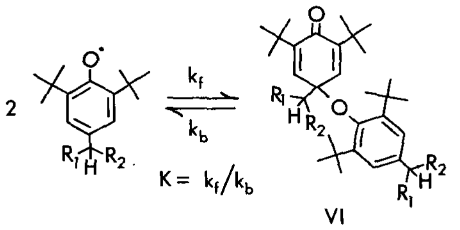

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The oxidation of 2,6-di-tert.-butyl-4-isopropylphenol (Ia) and similar phenols by means of chemical reagents has been the subject of several reports [2—5].

EXPERIMENTAL

Reagents

Dimethylsulfoxide was Matheson, Coleman and Bell spectroquality. Tetramethylammonium hydroxide, 10% in water (Eastman) was used as received, usually after a 10 : 1 dilution with water. Sources and preparations of other reagents have been described [1].

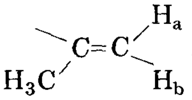
2,6-Di-tert.-butyl-4-isopropylphenol, Ia, was prepared by the acid catalyzed reaction of 4-isopropylphenol (Aldrich) with isobutene (Matheson Gas) in benzene. The phenol was first obtained as an oil, but three recrystallizations from cold 50% ethanol-water afforded pure white Ia, m.p. 39—41°C (lit. [3] 38—42°C). N.m.r. (CCl_4, TMS), δ 1.19 (d, J = 6.8 Hz, 6 H, $-CH(C\underline{H}_3)_2$), 1.42 (s, 18 H, tert.-butyl), 2.80 (h, J = 6.8 Hz, 1 H, $-C\underline{H}(CH_3)_2$), 4.77 (br s, 1 H, $-OH$), 6.97 (s, 2 H, arom).

2,6-Di-tert.-butyl-4-hydroxy-4-isopropyl-2,5-cyclohexadienone, XIIa, was prepared electrochemically by the oxidation of Ia. 93 mg of Ia in 75 ml AN (5% water) containing 0.10 M TEAP was exhaustively oxidized ($E = 1.40$ V, $n = 2.10$) at a carbon cloth electrode. 200 ml of water was added and the solution extracted three times with 25 ml portions of diethyl ether. The ether was evaporated and the residue recrystallized from a small amount of n-heptane to give 92.3 mg of white crystals (93% yield) of XIIa, m.p. 88—89°C. Low resolution mass spectrum: molecular ion at m/e 264. N.m.r. (CCl_4, TMS), δ 0.85 (d, J = 7 Hz, 6 H, $-CH(C\underline{H}_3)_2$), 1.22 (s, 18 H, tert.-butyl), 1.86 (h, J = 7 Hz, 1 H, $-C\underline{H}(CH_3)_2$), 2.3 (br, s, 1 H, $-O\underline{H}$), 6.40 (s, 2 H, olefinic).

A similar attempt at preparation of XIIa in DMSO (5% water) solvent gave a tarry residue from which only a small amount of XIIa was obtained.

The addition of water to the AN was suggested by the results of coulometry. Rapid coulometric analysis in nominally dry AN was performed with a glassy carbon porous flow-through electrode. Aliquots from 1 to 10 μl of a 2.10 mM solution of Ia in AN containing 0.10 M TEAP were injected into a flowing stream (0.20 ml min^{-1}) of AN (containing 0.10 M TEAP) directly at the top of the electrode bed. A plot of coulombs passed (obtained by integrating the current-time curves) vs. volume of solution injected was linear. The data yielded an average n-value of 2.63. The effluent was slightly yellow. This, together with the high (>2) n-value indicates that some 2,6-di-tert.-butyl-1,4-benzoquinone may have been formed (reaction 7). Addition of 5% water to the AN lowered the n-value to 2.08, and the effluent was colorless.

2,6-Di-tert.-butyl-4-isopropylidene-2,5-cyclohexadienone, Va, was prepared by ferricyanide oxidation. Thus, 8.15 g of $K_3Fe(CN)_6$ (24.8 mmoles), and 1.21 g NaOH (24.8 mmoles), was added to 20 ml H_2O. 20 ml of n-heptane was then added and both phases were purged with nitrogen. Then 3.10 g of phenol Ia (12.4 mmoles) was added all at once and the mixture stirred under N_2 until the bright blue color of the phenoxy radical disappeared, ca. 45 min. The yellow n-heptane layer which contains Va was separated and washed three times with 20 ml portions of water. The heptane solution volume was reduced to ca. 10 ml by passing air over the solution, and crystals of Va began to form. After refrigerating overnight the first crystals of Va were removed. These were essentially pure Va, with a melting point of 103.5—104.5°C (lit. [3,4] 102—104°C). Recrystallization is best effected from acetonitrile, from which large single crystals up to 1 cm in length may be grown with care. Heptane may also be used. N.m.r. (CCl_4, TMS), δ 1.26 (s, 18 H, tert.-butyl), 2.15 (s, 6 H, $=C(C\underline{H}_3)_2$), 7.25 (s, 2 H, olefinic).

2,6-Di-tert.-butyl-4(2-propenyl)phenol, VIIa, was prepared by tautomerization of Va. 0.30 g of Va was dissolved in 10 ml AN and the solution was purged with N_2. 0.50 ml of 1.24 M $(CH_3)_4NOH$ (~1 mole per mole of Va) was then added. After 10 min 60 ml of water was added, precipitating VIIa. The white precipitate is quite pure and may be used as obtained. Recrystallization as for an occasional batch which was discolored, can be accomplished from 95% ethanol. Care must be exercised to keep the material from decomposing further; this is best accomplished by performing the recrystallization with room temperature or cooler solutions. Water is added to the ethanol dropwise after cooling to initiate precipitation, which should be done so that the needle shaped crystals form slowly, m.p. 77—78°C (lit. [6] 77—78°C). Low resolution mass spectrum: molecular ion at *m/e* 246. N.m.r. (CCl_4, TMS) δ 1.43 (s, 18 H, tert.-butyl), 5.00 (br s, 1 H, phenolic), 7.17 (s, 2 H, arom), AMX_3 pattern for  $\overset{}{\underset{H_3C}{>}}C{=}C\overset{H_a}{\underset{H_b}{<}}$: H_a = 5.12 (hept.), H_b = 4.87 (pent.), H_c = 2.08 (quart.), J_{ab} = 1.6 Hz, J_{bc} = 1.6 Hz, J_{ac} = 0.8 Hz.

VIIa is unstable in air and/or light. Solid material left on the lab reagent shelf rapidly decomposed to unknown materials giving many peaks in the n.m.r. spectrum. Kahovek et al. [7] observed that VIIa polymerized readily on standing.

A 1.00 m*M* solution of VIIa in deoxygenated AN is stable for hours, even in the presence of several m*M* $(CH_3)_4NOH$. The solid material is best kept refrigerated in a closed container in the dark.

bis-Quinone methide, IXa, was prepared by chemical oxidation of VIIa. Thus 6.0 g of VIIa was oxidized using 16 g $K_3Fe(CN)_6$, 2.4 g NaOH, 40 ml H_2O and 40 ml n-heptane. The mixture was stirred under N_2 for 1 hour. The heptane layer was separated, washed three times with 50 ml portions of water, and then evaporated. About two grams of yellow-orange crystals slowly precipitated as the heptane was removed. When recrystallized once from AN, IXa softened at 175°C and melted completely, 207—209°C. Low resolution mass spectrum: molecular ion at *m/e* 490. N.m.r. (CCl_4, TMS), δ 1.23 (s, 18 H, tert.-butyl), 1.28 (s, 18 H, tert.-butyl), 2.76 (s, 4 H, methylene), 2.22 (s, 6 H, methyl), 7.13 (center, AB quartet, J = 2.7 Hz, $\Delta\nu_{AB}$ = 5.6 Hz, 4 H, olefinic).

2,6-Di-tert.-butyl-4(2-hydroxy-2-propyl)phenol, XIIIa, may be prepared electrochemically, but the yield is poor. Fortunately a more convenient synthesis for larger quantities of XIIIa is available by the acid-catalyzed addition of water to the quinone methide Va. Thus 0.30 g of Va was dissolved in 10 ml of AN containing 10% water. A drop of 12 *M* HCl was added and after 10 min the new phenol XIIIa could be precipitated by adding 60 ml water. After one recrystallization from ethanol-water, the compound had a melting point of 65—66°C and gave a mass spectrum molecular ion peak at *m/e* 264. N.m.r. (CCl_4, TMS), δ 1.45 (s, 18 H, tert.-butyl), 1.50 (s, 6 H, $-COH(C\underline{H}_3)_2$), 3.65 (br s, 1 H, $-CO\underline{H}(CH_3)_2$), 4.95 (br s, 1 H, phenolic), 7.19 (s, 2 H, arom).

XIIIa may be synthesized electrochemically in dry AN by the oxidation of Ia if the oxidation is carried out near the foot of the wave and electrolysis carried only to partial conversion. This is required because the oxidative peak potentials of Ia and XIIIa are quite close, 1.32 V and 1.38 V, respectively. Thus 75 ml of a 1.00 m*M* solution of Ia in nominally dry AN containing 0.10 *M* TEAP was electrolyzed at 1.25 V at a carbon cloth anode to approximately 50—60% completion of electrolysis. The n.m.r. spectrum of the extracted products showed peaks for Ia, XIIa and XIIIa. XIIa and XIIIa were present in approximately a 2 : 1 ratio. Such a synthesis does not have attractive features for making large quantities of XIIa. Nevertheless, Ronlán and Parker [8] were able to obtain up to 45% yield of 2,6-di-tert.-butyl-4-hydroxymethylphenol in their oxidation of 2,6-di-tert.-butyl-4-methylphenol.

2,6-Di-tert.-butyl-4-ethylphenol, Ib, was donated by the Ethyl Corporation, m.p. 43—44°C.

2,6-Di-tert.-butyl-4-methylphenol, Ic, was obtained from Aldrich Chemical Co., m.p. 69—71°C.

2,6-Di-tert.-butyl-4-ethylidene-2,5-cyclohexadienone, Vb, was prepared from Ib by the same procedure used in the preparation of quinone methide Va. M.p. 89—91°C (lit. [4] 92—93.5°C). N.m.r. (CCl_4, TMS), δ 1.23, 1.26 (s, 18 H, tert.-butyls), 2.10 (d, $J = 7$ Hz, 3 H, methyl), 6.18 (q, $J = 7$ Hz, 1 H, $=C\underline{H}CH_3$), 6.98 (center of AB pattern, $J = 3$ Hz, $\Delta\nu_{AB} = 29.6$ Hz, 2 H, ring protons).

2,3-Dimethyl-2,3-bis(3,5-di-tert.-butyl-4-hydroxyphenyl)butane, XVI, was prepared by electrolytic reduction of the quinone methide Va at −1.40 V at a carbon cloth cathode. Acetonitrile containing 10% water and 0.10 *M* TEAP was deaerated and the quinone methide was added slowly, a few crystals at a time, to keep its concentration fairly low (<0.25 m*M*) at all times during the electrolysis. The water is required to prevent formation of VIIa. 50 mg of Va was added in this manner over the course of an hour. The dimer began to precipitate during electrolysis and was recovered by filtration. When additional water was added to the solution, further dimer was recovered. Approximate yield was 30 mg. Recrystallization was accomplished using 95% ethanol to which a further small amount of water was added. The white crystalline compound so obtained had a melting point of 191—193°C. The mass spectrum showed a molecular ion peak at $m/e = 494$. N.m.r. (CCl_4, TMS), δ 1.27 (s, 12 H, $-C(CH_3)_2-$), 1.38 (s, 36 H, tert.-butyl), 4.84 (br s, 2 H, phenolic), 6.90 (s, 4 H, arom).

2,6-Di-tert.-butyl-3-isopropyl-5-cyclohexene-1,4-dione, XVII, was prepared by base induced rearrangement of XIIa in DMSO. To 0.1 g of XIIa in 10 ml deaerated DMSO was added 0.26 ml of 1.24 *M* $(CH_3)_4NOH$ in water (0.8 mole per mole of XIIa). After 2 min 50 ml of water was added and the solution was extracted four times with 25 ml portions of diethyl ether. Evaporation of the ether and recrystallization of the residue from 50% ethanol-water gave a 70% yield of XVII, m.p. 74—75°C, mass spectrum molecular ion peak at *m/e* 264. N.m.r. (CCl_4, TMS), δ 0.90, 1.24 (s, 18 H, tert.-butyls), 0.87 (d, $J = 6.5$ Hz, 6 H, $-CH(C\underline{H}_3)_2$), 1.90 (h, $J = 6.5$ Hz, 1 H, $-C\underline{H}(CH_3)_2$), 2.4—2.6 (m, 2 H, methine protons), 6.41 (d, $J = 1.2$ Hz, 1 H, olefinic proton).

2,3,6-Tri-tert.-butyl-5-cyclohexene-1,4-dione was produced from 2,4,6-tri-tert.-butyl-4-hydroxy-2,5-cyclohexadienone in the same way as XVII. M.p. 88—89°C (lit. [9] 85—87°C). N.m.r. (CCl_4, TMS), δ 0.92, 0.92, 1.25 (s, 27 H, tert.-butyls), 2.54 (d, 1 H, $J \sim 1$ Hz, methine proton), 2.65 (d, 1 H, $J \sim 1$ Hz, methine proton), 6.40 (d, 1 H, $J \sim 1$ Hz, olefinic).

2,6-Di-tert.-butyl-1,4-benzoquinone was obtained from Aldrich Chemical Co.

Apparatus and procedures

Electrochemical instrumentation, cells and glassy carbon electrodes as well as procedures for cyclic voltammetry and coulometry were the same as were employed in earlier work [1]. The flow-through electrodes which were used have been described elsewhere [10,11]. Usually a three electrode design was employed [11].

Cyclic voltammetry was performed at 21 ± 1°C using solutions which had been deaerated with solvent-saturated nitrogen. If base was to be added to the solution, this was done after deaeration to prevent air oxidation of the phenoxides [3]. The base, added by syringe, was 0.15 *M* tetramethylammonium hydroxide in water. Since peak potentials in AN were found to be dependent on water concentration, the amount of water added to the nominally dry AN is reported with each voltammogram. Unless indicated otherwise, 0.10 *M* TEAP was the electrolyte. All potentials are with respect to the aqueous saturated calomel electrode.

Melting points were obtained with a Fisher-Johns melting point apparatus. The n.m.r. spectrometers were Varian A-60, A-60A or T-60 instruments and mass spectra were obtained with an AEI MS-902 spectrometer.

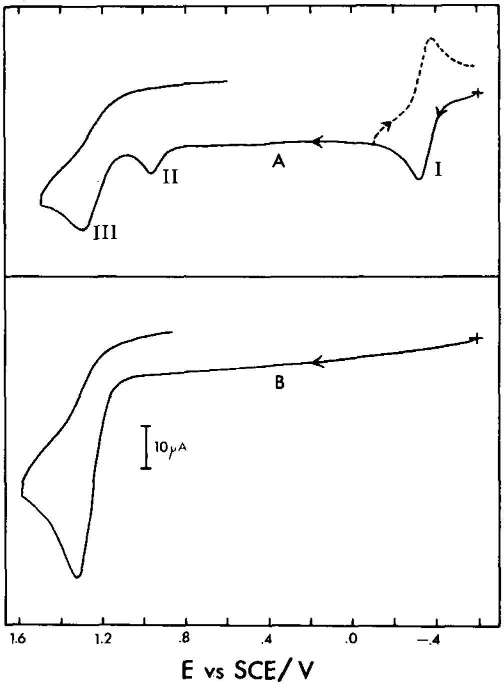
RESULTS

Voltammetric oxidation of phenoxide, IIa

The phenoxides are very easily oxidized to the phenoxy radicals and it is these latter species whose altered reactivity is of principal interest. As shown earlier [1], and verified in the present work by means of photometric titrations, the phenoxides may be prepared quantitatively in situ by addition of an equivalent amount of tetraalkylammonium hydroxide. A cyclic voltammogram of a solution of IIa is shown in Fig. 1A. Anodic peak I (—0.32 V) is due to the reversible oxidation to the phenoxy radical IIIa. Peak II is due to the further one electron oxidation of the radical to the phenoxonium ion IVa followed by rapid attack by water producing a hydroxydienone and liberating protons. These protons neutralize incoming IIa causing peak II to be smaller than expected, in exact parallel with the behavior of 2,4,6-tri-tert.-butylphenol [1]. Peak III is due to oxidation of phenol Ia produced during the preceding peak. For comparison, a voltammogram of the phenol is presented in Fig. 1B.

The large cathodic peak associated with peak I persisted at the slowest scan rates employed indicating that phenoxy radical IIIa was not disproportionating on the voltammetric time scale. The addition of excess hydroxide in nominally dry AN caused the reduction peak associated with peak I to disappear. The process responsible for the destruction of the radical in excess hydroxide is not known but it was observed that the addition of a few tenths per cent water was sufficient to stabilize the radical even with a hydroxide/phenoxide ratio of 2—3. It is well known that anions like hydroxide are highly reactive in dipolar aprotic solvents such as AN and the addition of a hydrogen-bonding cosolvent like water will make the anion less reactive by increasing the activation energies for nucleophilic attack [12].

The addition of water has one other interesting effect which is presented in Fig. 2. The peak potential becomes more positive as the water concentration is increased. (Changes in the reference electrode/test solution liquid junction potential are not a major contributing factor as evidenced by the fact that the



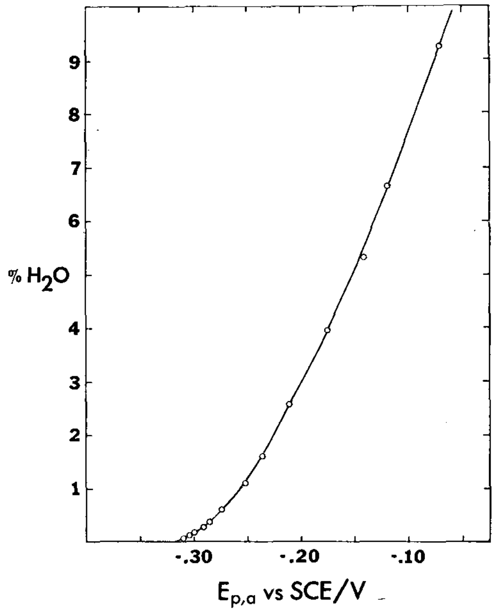


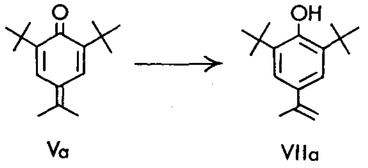
Fig. 1. Voltammograms of 2,6-di-tert.-butyl-4-isopropylphenol, Ia, in acetonitrile. Glassy carbon electrode. 0.050 V s^{-1}. (A) 1.00 m*M* phenoxide IIa. 134 µl of 0.149 *M* tetramethylammonium hydroxide (in water) was added to 20 ml of 1.00 m*M* Ia. (B) 1.00 m*M* solution of Ia.

Fig. 2. Dependence of anodic peak potential of 2,6-di-tert.-butyl-4-isopropylphenoxide, IIa, on concentration of water added to acetonitrile. Glassy carbon electrode. 0.050 V s^{-1}. 1.00 m*M* IIa.

ferrocinium/ferrocene potential changes only about 40 mV over the same range of water concentrations [13].) This shift has been attributed to protonation of the phenoxide [14] but is more probably caused by stabilization of the phenoxide by increased solvation via hydrogen bonding in the partially aqueous media.

Controlled potential electrolysis of phenoxide, IIa

Disproportionation of the radical IIIa (reaction 2) has been shown to be unimportant on the voltammetric time scale. This is not surprising in view of the fact that the disproportionation rate constant is only 5 M^{-1} s^{-1} (in benzonitrile at 25°C [4]). The reaction is important on the time scale of controlled potential electrolysis and one would expect that one-electron oxidation of IIa should give equal quantities of phenol and quinone methide Va. However, Va is unstable in the presence of base (such as IIa or hydroxide) and it slowly tautomerizes to 2,6-di-tert.-butyl-4(2-propenyl)phenol, VIIa. For example, the Va to VIIa conversion catalyzed by hydroxide was monitored by observing the decrease in peak height for the voltammetric reduction of Va at −1.54 V. The reaction was first order in hydroxide and Va and the rate constant was 60 M^{-1}



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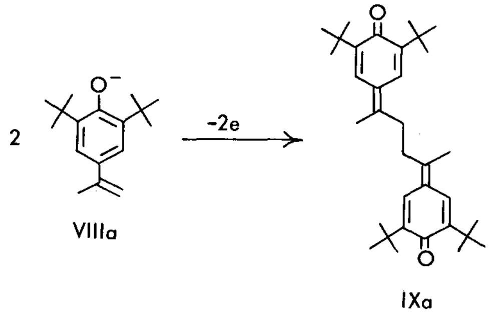
s^{-1} (base: tetramethylammonium hydroxide; solvent: AN containing ca. 0.06% water; 20°C). In 2.3% water/AN the rate constant was reduced to 4.3 M^{-1} s^{-1}.

If the phenoxide VIIIa forms during the electrolysis, it will be oxidized (E_p = −0.28 V) to the bis-quinone methide, IXa. It has been found that the sequence



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of reactions (2), (4) and (5) adequately explains the product mixture formed upon electrolysis of IIa.

Electrolysis of 1.0 m*M* IIa in nominally dry AN at a carbon cloth anode at 0.00 V gave a bright blue solution of IIIa. The color slowly disappeared giving a yellow fully electrolyzed solution. The current-time curve exhibited a normal exponential decay giving n = 0.94. (These oxidations are normally limited by the amount of base present so n-values were always near unity (with respect to initial base concentration) regardless of product distribution.)

Figure 3A is a voltammogram of the final electrolysis solution showing reduction peaks for quinone methide Va (E_p = −1.54 V) and the bis-quinone methide IXa (E_p = −1.46 V). The peak potentials are in agreement with those found for independently synthesized samples of Va and IXa. These products were also identified in the electrolysis solution by thin layer chromatography.

Thus the reaction sequence operating during controlled potential oxidation of IIa is proposed to be formation of phenoxy radicals IIIa followed by disproportionation giving the quinone methide Va which in turn suffers base-catalyzed tautomerization (the principal base is unreacted IIa) to VIIIa which can be oxidized to the bis-quinone methide IXa. The concentrations of products indicated by the voltammogram in Fig. 3A account for approximately all of the base initially added so Va and IXa appear to be the major products though others are undoubtedly formed.

If high yields of quinone methide Va are to be achieved, the reaction sequence must be interrupted at the point where Va is lost by tautomerization. Two methods of achieving this have been found. In the first, the electrolysis of IIa is performed in AN containing 10% water (n = 0.96). As indicated above, the base-catalyzed tautomerization is slower in this mixed solvent and a larger yield of Va is produced. A voltammogram of the electrolysis solution is shown in Fig. 3B

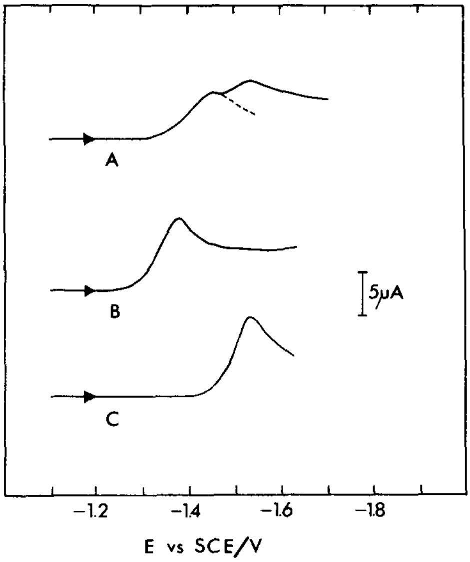


Fig. 3. Voltammograms of electrolyzed solutions of 2,6-di-tert.-butyl-4-isopropylphenoxide, IIa. 1.00 m*M* IIa electrolyzed in each case. Glassy carbon electrode used for voltammetry. 0.050 V s^{-1}. (A) Controlled potential oxidation of IIa in acetonitrile at carbon cloth electrode. First reduction peak is due to bis-quinone methide IXa while second is due to quinone methide Va. (B) Controlled potential oxidation of IIa in acetonitrile containing 10% water. Single reduction peak is due to Va. (C) Electrolysis of IIa using porous bed flow-through electrode. Flow rate was 0.50 ml min^{-1} with a current of 0.84 mA. Solvent: acetonitrile. Single reduction peak is due to Va.

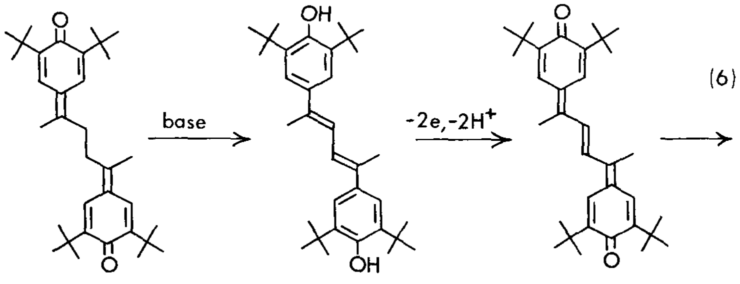
showing a single reduction peak which has been shifted to −1.38 V presumably for the same reason that the phenoxy radical/phenoxide potential is shifted by the addition of water. The peak current corresponds to a 95% yield.

The second method employs a porous bed flow-through electrode [9,10] in which IIa was oxidized quantitatively to the phenoxy radical IIIa during the few seconds' passage through the bed. The bright blue effluent contained no unreacted IIa so the quinone methide Va formed by disproportionation encounters no base. The effluent was collected under nitrogen and after disproportionation the voltammogram of Fig. 3C was obtained showing a good yield (>95% based on voltammetric peak current) of the quinone methide Va. In a separate experiment, 0.05 *M* IIa was oxidized and the effluent was examined by n.m.r. (after disproportionation) and equal quantities of quinone methide Va and phenol Ia were found.

Other investigations of IXa

The oxidation of the 2,6-di-tert.-butyl-4(2-propenyl)phenoxide VIIIa (reaction 5) presumably proceeds through an intermediate radical which dimerizes to IXa. Cyclic voltammetry of VIIIa reveals an irreversible oxidation peak (E_p = −0.28 V). No reduction peak for the radical is detected up to scan rates of 200 V s^{-1} so the dimerization must be extremely rapid. The preparation and characterization of other bis-quinone methides has been reported by other workers [15].

Because IXa is also a quinone methide, it is likely that it will also tautomerize and undergo further oxidation with the possibility of more than one isomer at each state of oxidation. Oxidations similar to Xa → XIa have been reported [16].



IXa Xa XIa

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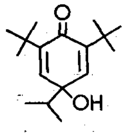
The AB quartet for the ring protons of IXa, centered at 7.13 ppm, collapses into a sharp singlet at 7.23 ppm when a few crystals of $(CH_3)_4NOH \cdot 5\ H_2O$ are added to IXa in AN under nitrogen. Other changes in the spectrum, though less striking, were also consistent with the IXa to Xa transformation. Treatment of IXa with base also causes the development of an irreversible anodic voltammetric peak with $E_p = -0.33$ V, characteristic of a phenoxide, and a new reduction peak at −1.60 V. Attempts to isolate Xa from this reaction mixture failed.

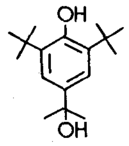
Controlled potential coulometry of VIIIa (AN; carbon cloth anode; −0.10 V) gave n-values near unity and large reduction peaks for the bis-quinone methide IXa ($E_p = -1.48$ V) as well as presumed Xa ($E_p = -1.6$ V). Presence of IXa was confirmed by thin layer chromatography and, in agreement with earlier observations concerning the effect of water on the rate of base-catalyzed tautomerizations, it was found that the voltammetric peak for IXa was much larger than that of Xa when the electrolysis was performed in AN containing 10% water. Unfortunately, no conditions could be found which permitted a reasonable electrochemical synthesis of IXa or Xa from VIIIa though chemical oxidation of VIIIa to IXa was successful (cf. Experimental section).

Oxidation of phenol, Ia

Oxidation of the phenol Ia in AN ($E_p = 1.32$ V, Fig. 1B) parallels that observed for 2,4,6-tri-tert.-butylphenol [1]. The normal product is 2,6-di-tert.-butyl-4-hydroxy-4-isopropyl-2,5-cyclohexadienone, XIIa, presumably formed by attack of water on phenoxonium ion IVa, but at low water concentrations ($\leq 0.05\%\ H_2O$) and at a potential near the foot of the wave (1.25 V) some XIIIa is formed as well. This latter type of product was also found by Ronlån and



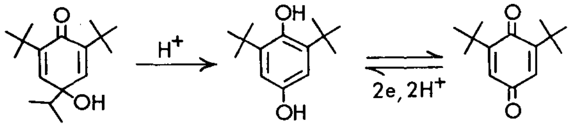
XIIa



XIIIa

Parker [8] for the anodic oxidation of 2,6-di-tert.-butyl-4-methylphenol. These authors found a similar dependence of product distribution on water concentration and they were able to produce alkoxy, and hydroxydienones from other phenols as well [8,17,18].

As with 2,4,6-tri-tert.-butylphenol [1,8] the hydroxydienone XIIa is susceptible to acid-catalyzed dealkylation giving hydroquinone XIV which is oxidized to the quinone XV. When starting with a neutral solution of Ia, the protons released on formation of XIIa serve as catalyst for the dealkylation which tends to proceed in the diffusion layer. The cyclic voltammograms nicely illustrate this reaction path (Fig. 4). In Fig. 4A the steady-state voltammogram of Ia after about 20 cycles is shown. The oxidation peak for the phenol may be seen at 1.3 V and the reduction peak for the primary product, hydroxydienone XIIa is at —2.0 V. The small set of peaks at 0.1 and 0.9 V are due to the quasireversible quinone XV/hydroquinone XIV couple as confirmed by the voltammogram of



XIIa XIV XV (7)

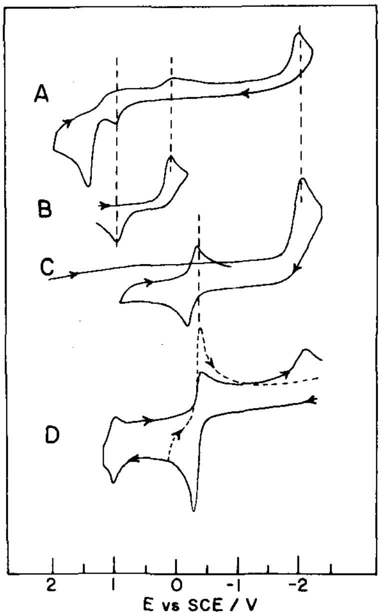


Fig. 4. Summary of cyclic voltammetric behavior of 2,6-di-tert.-butyl-4-isopropylphenol, Ia, and its major oxidation products in acetonitrile. Glassy carbon electrode. 20 V s^{-1}. (A) 5.0 m*M* Ia after about 20 cycles through the potential range —2.2 to +1.8 V. Solution contains 0.6% water. (B) Voltammogram of 2.5 m*M* 2,6-di-tert.-butyl-1,4-benzoquinone in acetonitrile with 0.1 *M* perchloric acid. (C) Voltammogram of 2,6-di-tert.-butyl-4-hydroxy-4-isopropyl-2,5-cyclohexadienone, XIIa. (D) Voltammograms of 5.0 m*M* 2,6-di-tert.-butyl-4-isopropylphenoxide, IIa, with two different switching potentials.

the quinone shown in Fig. 4B. Also shown in Fig. 4C is the voltammogram of the hydroxydienone XIIa which has an irreversible, two-electron reduction peak at −2.0 V the products of which are phenoxide IIa and hydroxide. The phenoxide is detected on the reverse scan through its reversible oxidation at about −0.2 V. The phenoxide is not detected in Fig. 4A because the diffusion layer is generally acidic due to protons released upon oxidation of the phenol. Figure 4D is a voltammogram for oxidation of the phenoxide IIa and it shows that the hydroxydienone XIIa (peak at −2.0 V) is also formed upon oxidation of the radical IIIa (small anodic peak at 1.0 V), an observation completely analogous to the behavior of 2,4-6-tri-tert.-butylphenol [1].

Oxidation of other phenols containing hydrogen atoms α to the ring

Controlled potential oxidation of 2,6-di-tert.-butyl-4-ethylphenoxide, IIb, (carbon cloth anode) gave an *n*-value of 1.12 and a nearly quantitative yield of the corresponding quinone methide Vb as judged by its voltammetric peak current ($E_p = -1.42$ V). Unlike the isopropyl derivative, there was no evidence for products arising from tautomerization of the quinone methide. This is partially due to its lower rate of tautomerization, the rate constant for hydroxide catalyzed tautomerization in AN at 20° being $37 \pm 2\ M^{-1}\ s^{-1}$ for Vb.

The rate of disproportionation of the phenoxy radicals IIIb is greater than for the isopropyl derivative, IIIa [5]. Both a bimolecular reaction of phenoxy radicals and a unimolecular decomposition of a *para*-quinol ether dimer VIb can be operative as mechanisms for quinone methide formation [4,5,19]. As the 4-substituent is made smaller, the possibility of *para*-quinol ether formation becomes important. No such derivatives are known for the 4-tert.-butyl and 4-isopropyl compounds but the *para*-quinol ether from 2,5-di-tert.-butyl-4-methylphenol has been characterized [20].

It was of interest to see if quinol ether formation would affect the cyclic voltammetric response. Figure 5 gives voltammograms for oxidation of phenoxide IIb at three scan rates. At the fastest scan rate employed, a reduction peak for phenoxy radical IIIb is not detected. Instead an irreversible peak at −2.0 V is found. This peak is attributed to the direct reduction of the *para*-quinol ether which is formed from the radical in a very fast bimolecular reaction ($k_f \sim 1.3 \times 10^7\ M^{-1}\ s^{-1}$, CCl_4, 20°C [21]). As the scan rate is decreased, a peak

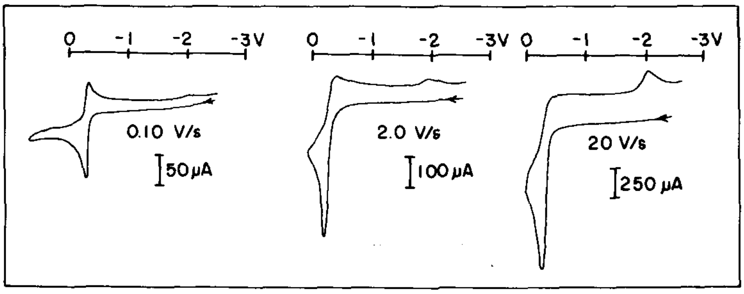


Fig. 5. Voltammograms of 2,6-di-tert.-butyl-4-ethylphenoxide, IIb. Glassy carbon electrode. 4.14 m*M* IIb.

for reduction of the radical begins to appear. This is explained by assuming that the quinol ether has sufficient time to dissociate ($k_b \sim 10$ s^{-1}, CCl_4, 20°C [21]) giving phenoxy radicals which in turn are reduced. Digital simulation [22] of this reaction scheme produced voltammograms in good agreement with Fig. 5 with the kinetic parameter $K\sqrt{k_f}$ (cf. reaction 3) equal to 10^8 $M^{-3/2}$ s$^{-1/2}$ compared to 4×10^9 $M^{-3/2}$ s$^{-1/2}$ calculated from the data of Land and Porter [21] for CCl_4 solvent at 20°C.

As described earlier, the eventual product of the oxidation of IIb is the quinone methide Vb but the disproportionation reaction is too slow to be important even at the slowest scan rate employed though of course it predominates under the longer time scale of controlled potential coulometry.

Voltammograms similar to those in Fig. 5 were obtained with 2,5-di-tert.-butyl-4-methylphenoxide IIc. For this compound, the dimerization rate constant for phenoxy radicals has been estimated [21] to be 1.5×10^8 M^{-1} s^{-1} and the dissociation rate constant for the quinol ether was 10^2 s^{-1} (carbon tetrachloride, 20°C).

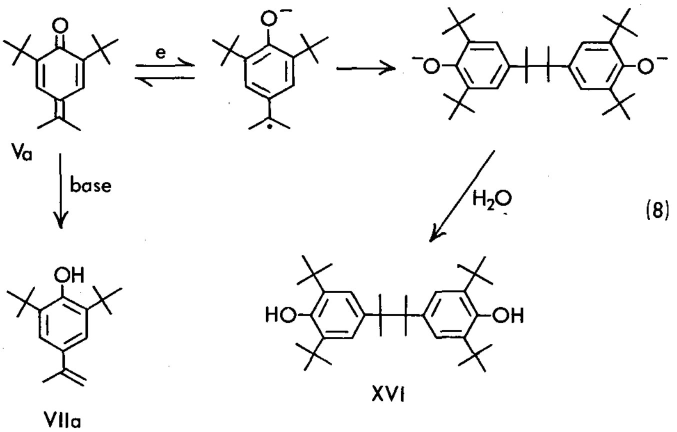
For the 4-isopropyl derivative, IIa, no evidence for a quinol ether reduction peak could be found on the return scan even at a scan rate of 500 V s^{-1} probably because the equilibrium constant for the formation of the highly hindered quinol ether is so small that no appreciable amount forms.

The overall scheme for the one-electron oxidation of these phenoxides is summarized in reactions (2) and (3). The initially formed phenoxy radicals enter into an equilibrium with the quinol ether with the equilibrium constant being very small for the isopropyl derivative. The radicals also undergo a slow disproportionation reaction giving the quinone methide and the original phenol and it is this latter process which is important at long times.

In a manner similar to that described for IIa, the effluents from porous bed electrolysis of 2.0 mM solutions of phenoxides IIb and IIc were collected and analyzed by cyclic voltammetry. A three electrode porous bed cell was used with a control potential of 0.25 V. In both cases a single reduction peak of appropriate peak current and potential corresponding to a quinone methide product was obtained. The peak potentials for the quinone methide reductions were respectively −1.56 V ($=C-(CH_3)_2$), −1.42 V ($=CHCH_3$), and −1.36 V ($=CH_2$). The solutions contained ca. 1.0% water added with the base used for phenoxide formation.

Reduction of quinone methide, Va

Cyclic voltammetry of Va in AN up to 500 V s^{-1} showed an irreversible reduction peak at −1.52 V. On the return half-cycle an oxidation peak was observed at −0.35 V due to oxidation of VIIa formed during the reduction. Reduction of Va forms basic substances which both catalyze the conversion of Va to VIIa, and provide base for converting VIIa to the oxidizable phenoxide VIIIa. This destruction of the reactant in the diffusion layer causes the plot of peak current for Va reduction vs. concentration to be non-linear, peak currents being relatively too small at high concentration. It was also observed that the peak current increases when water is added. As explained earlier, the rate of base-catalyzed conversion of Va to VIIa is lower when water is present. The only two products identified after constant potential electrolysis of Va in AN were VIIa (tautomerization) and the dimer XVI.



(8)

The presumed radical anion intermediate [23] apparently dimerizes more rapidly than it can be protonated and reduced to Ia. Coulometric *n*-values for reduction of Va in AN at −1.70 V ranged from 0.31 to 0.57 for concentrations of Va from 2.0 to 0.25 m*M* (Table 1). When 10% water was added to the solution, formation of VIIa was suppressed, the *n*-value was about one, and the only isolable product was the dimer XVI (cf. Experimental section).

Hydroxydienone rearrangement

Hydroxydienone XIIa was found to be base sensitive in dimethylsulfoxide (but not AN) forming first the isolable enedione XVII (cf. Experimental section) and then another product, probably a phenol.

This interesting reaction, a vinylogous α-ketol rearrangement [24], is evident in the cyclic voltammetric data of XIIa with base addition (Fig. 6). A small quantity of base causes rapid conversion of XIIa to XVII (Fig. 6B) but eventual-

TABLE 1

Coulometric *n*-values for the reduction of quinone methide Va in acetonitrile [a]

Initial concentration of Va/m*M*	*n* [b]
2.00	0.31, 0.39
1.00	0.42
0.50	0.47
0.25	0.57
2.00	0.81 (10% water)
0.25	1.07, 0.97, 0.99 (10% water)
0.50	0.65 [c]

[a] Nominally dry AN; 0.10 *M* tetraethylammonium perchlorate; carbon cloth electrode; −1.70 V.

[b] Calculated from area under current-time curve.

[c] Using porous flow-through electrode.

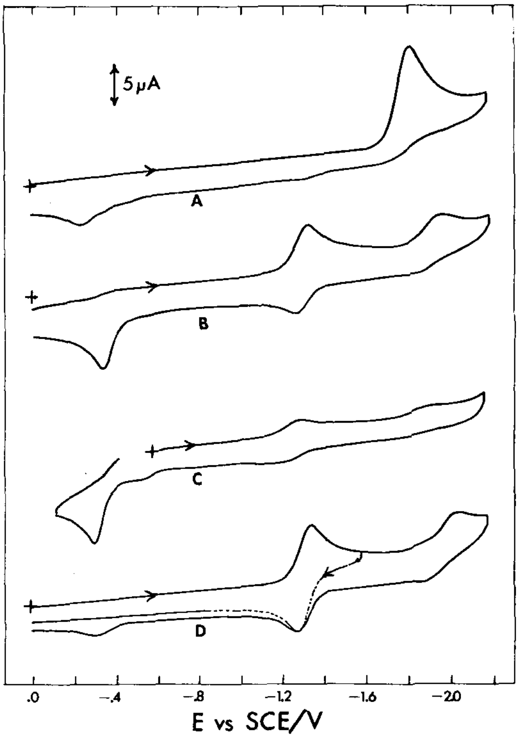
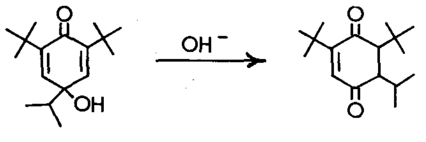


Fig. 6. Voltammograms showing rearrangement of 2,6-di-tert.-butyl-4-hydroxy-4-isopropyl-2,5-cyclohexadienone, XIIa. Glassy carbon electrode. 0.10 *M* TEAP in dimethylsulfoxide. 0.050 V s^{-1}. (A) 1.00 m*M* XIIa. (B) 1.00 m*M* XIIa after addition of 0.2 moles of tetramethylammonium hydroxide per mole of XIIa. New reduction peaks at −1.35 and −1.95 V are due to XVII. Oxidation peak at −0.30 V may be due to a phenoxide formed in the reaction. (C) Solution in B after 20 min has elapsed. (D) 1.00 m*M* 2,6-di-tert.-butyl-3-isopropyl-5-cyclohexene-1,4-dione, XVII.



(9)

XIIa XVII

ly XVII disappears (Fig. 6C). By a similar reaction 2,4,6-tri-tert.-butyl-4-hydroxy-2,5-cyclohexadienone is converted to 2,3,6-tri-tert.-butyl-5-cyclohexene-1,4-dione (cf. Experimental section).

DISCUSSION

From this and earlier work, a general pattern for the anodic oxidation of hindered trialkylphenols emerges. It remains to be seen to what extent this pattern will be valid for simpler phenols though recent data indicate some similarity exists [25,26]. The phenoxide form is readily oxidized (peak potentials typically a few tenths volt negative of SCE) to phenoxy radicals which either persist as stable entities or, when the 4-substituent is small such as ethyl or methyl, the radicals enter into a previously characterized reversible equilibrium with the dimeric *para*-quinol ether, VI. This equilibrium exerts an unusual though predictable effect on the cyclic voltammetry. In principle, at rapid scan rates it should be possible to see the reversible phenoxide/phenoxy radical couple but the dimerization of the radicals is sufficiently rapid that no radical reduction peak is observed at fast scan rates. Instead, a reduction peak for the dimer is detected at quite negative potentials. However, at slow scan rates the slow dissociation of the dimer becomes important and reversible cyclic voltammetric behavior is observed.

This type of carbon-oxygen coupling is of fundamental importance in phenol chemistry because many of the final products of phenol oxidation have new carbon-oxygen bonds suggesting reversible dimerization of phenoxy radicals to quinol ethers as an early step in the reaction sequence. It will be interesting to see if quinol ether formation can be detected in the anodic oxidation of other phenols, e.g., trialkylphenols with small 2-substituents or 2,6-dialkylphenols. In the latter case, of course, carbon-carbon dimerization is known to be important but the quinol ether may still play a role in the reaction scheme.

The disproportionation of phenoxy radicals giving quinone methides (reaction 2) has been shown to occur upon anodic oxidation of phenoxides but its rate is sufficiently low that it does not affect the voltammetric behavior but becomes important during controlled potential electrolysis. Evidence for quinone methide formation has been presented for all phenols studied in this work (4-isopropyl-, 4-ethyl- and 4-methyl-2,6-di-tert.-butylphenol).

The quinone methides derived from the isopropyl and ethyl derivatives (Va and Vb) are quite susceptible to base-catalyzed tautomerization and for Va it has been shown that this reaction opens up a complex sequence of additional oxidation reactions which was partially delineated. Throughout this work the rapidity of reactions involving bases like hydroxide in the solvents acetonitrile and dimethylsulfoxide has been noted and these reactions can introduce discomforting complications such as destruction of phenoxy radicals, the tautomerization cited above and other rearrangements. It has been found that the addition of quite small amounts of water to the solvents reduces the rate of these base-catalyzed reactions which actually simplifies the electrochemical behavior in contrast to the normal deleterious effect of water in electrochemistry in nonaqueous solvents due to its acidic and nucleophilic character.

In contrast to the phenoxide, the phenol form is much more difficult to oxidize (peak potentials ca. +1.3 V vs. SCE). This potential is more positive than the potential for oxidation of phenoxy radicals (ca. +1.0 V [1]) so the oxidation of the phenol leads to oxidation products formally derived from phenoxonium ions. Briefly, to obtain products derived from phenoxy radical intermediates, the phenoxide is oxidized at low potential (ca. 0.8--0.0 V vs. SCE). To obtain products derived from phenoxonium ion intermediates, the phenoxide is oxidized at high potential (>1.0 V) or the phenol form is oxidized. These conclusions are consistent with observations concerning oxidation of other phenols though Papouchado et al. [26] have shown that products derived from phenoxy radicals can be obtained near the foot of a phenol oxidation peak. (For naphthols the phenol peak actually splits into two separate peaks.) In the cases studied in the present work, the irreversible reactions available to the phenoxy radicals (disproportionation to quinone methides) are too slow to compete with oxidation of the radicals so two electron products are found whereas the phenoxy radicals of many other phenols [26] can undergo very rapid irreversible reactions (particularly C—C dimerization) which can compete with further oxidation particularly at low potentials near the foot of the wave.

ACKNOWLEDGMENTS

Support of this research by the National Science Foundation (CHE75-04930) is gratefully acknowledged. We also thank Dennis Corrigan who performed the digital simulations.

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