present. A sample of **23** isolated by gas chromatography had the same retention time as that of the crude **23**, proving no change in the column, and had $n^{25}D$ 1.4974 (lit.[16b] b.p. 61° at 0.25 mm., $n^{27}D$ 1.4970) and infrared spectrum identical with that of the authentic *anti* sample.

The other peaks were not identified. Their appearance may be due to the rearranged products on the deamination, to the isomerization products of **22** HCl salt, or to the by-products on the hydrolysis step.[36]

The gas chromatographic analyses were carried out at 180° with 6 mm. × 3 m. stainless steel tube in a Shimadzu gas chromatograph Model GC-1B and with a flow rate of 100 ml./min. of helium. Retention times on a column of 15 wt.% of diethylene glycol succinate polyester on acid-washed, 30–60-mesh Chromosorb W were for 2-norbornene-*syn*-7-methanol, 11.9 min., and for the *anti*-7-methanol **23**, 14.4 min.

Kinetic Measurements of the Reaction of *anti*-7-chloronorbornene (2) with Sodium Cyanide.—As a solvent for kinetics, 50% aqueous ethanol was prepared by mixing equal parts by volume of absolute ethanol and water. Samples of approximately 0.04 mole each of **2** were weighed into eight 10-ml. volumetric flasks. Then each of the flasks was filled with a solution of 49.40 mmoles of sodium cyanide in 10 ml. of 50% aqueous ethanol, already equibrated thermally in a thermostat at 24.9°. The dissolution of **2** was facilitated by shaking. The flasks were kept in the thermostat, and at recorded times the contents of each flask were drained into a titration flask containing 20 ml. of cold acetone. The amount of remaining sodium cyanide, and thereby the amount of remaining **2**, was determined by titrating with 0.01 *N* silver nitrate solution according to the Liebig–Dènigés method.[38]

A plot of ln $a/(a - x)$ *vs.* time was a straight line; a was the initial concentration of **2**, and x was the amount of **2** that had reacted. The rate constant, $(1.54 \pm 0.12) \times 10^{-4}$ sec.$^{-1}$ at 24.9°, was obtained from the slope of the linear plot. A plot of

$$\frac{1}{b - a} \ln \frac{a(b - x)}{b(a - x)}\ vs.\ t$$

resulted in upwards curvature; a and b were the initial concentrations of **2** and sodium cyanide, respectively, x was the amount of the substrates that had reacted, and t was time.

Acknowledgment.—We are indebted to Mr. T. Misumi, who performed much of the laboratory work.

---

[36] Since the submission of our first draft, Berson and Gajewski[37] noticed the formation of various kinds of the rearranged products on the deamination of **22**. Their observation does not contrast with our results.

[37] J. A. Berson and J. J. Gajewski, *J. Am. Chem. Soc.*, **86**, 5020 (1964).

[38] Refer to F. P. Treadwell and W. T. Hall, "Analytical Chemistry," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1935, p. 657.

Quinone Dehydrogenation. I. The Oxidation of Monohydric Phenols

HANS-DIETER BECKER

General Electric Research Laboratory, Schenectady, New York

Received October 9, 1964

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) is found to be a powerful oxidizing agent for phenols. The high yield reaction proceeds smoothly at room temperature in methanol solution and, depending on the structure of the phenol, leads to oxidative dimerization by either C–C or C–O coupling, oxidative debromination, or oxidative cleavage of hydroquinone monoethers and *p*-hydroxybenzyl ethers, as well as to benzylic oxidation. 2,4,6-Tri-*t*-butylphenol reacts with DDQ to yield 4-(2,3-dichloro-5,6-dicyano-4-hydroxyphenoxy)-2,4,6-tri-*t*-butyl-2,5-cyclohexadien-1-one which easily dissociates into radicals as demonstrated by an interesting aryloxy exchange reaction. 2,6-Di-*t*-butyl-4-methylphenol upon treatment with DDQ yields a crystalline dimer of 2,6-di-*t*-butyl-4-methylphenoxy radical, which in solution dissociates into the blue-colored monomer. Its disproportionation into 2,6-di-*t*-butyl-4-methylphenol and 2,6-di-*t*-butyl-1,4-quinone methide has been studied by spectroscopic and chemical means. The mechanism for the oxidation of phenols by DDQ is discussed.

Numerous papers, including several recent review articles, published during the last 15 years on the oxidation of natural and synthetic antioxidants reflect the general interest in this field of organic chemistry.[1–3] A large number of oxidizing agents of both heterolytic and homolytic nature have been employed in the oxidation of phenols. Quinones, however, apparently have not been used previously for the oxidation of monohydric phenols since "the scope of quinone dehydrogenation has not been fully established."[4] In this study 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (abbreviated henceforth DDQ) is introduced as an oxidizing agent for phenols.

DDQ was first synthesized almost 60 years ago by Thiele and Günther,[5] but only during the last decade was its usefulness in the dehydrogenation of hydroaromatic systems recognized.[6] The oxidation potential of DDQ is *ca.* 1.0 compared with 0.71 v. for chloranil.[4] In the dehydrogenation of tetraline, for instance, DDQ reacts 5500 times faster than chloranil that is commonly used in dehydrogenation reactions.[4] DDQ was employed successfully in dehydrogenating steroids,[7,8] the selective oxidation of steroidal allylic[9] alcohols, and also recently in the cleavage of steroidal enol ethers.[10]

When DDQ was applied earlier in the selective oxidation of benzyl alcohols, it was found to convert secondary *p*-hydroxybenzyl alcohols smoothly into the corresponding *p*-hydroxyphenyl alkyl ketones, a reaction in which the phenolic group appeared unattacked.[11] It has now been found that phenols are easily oxidized by DDQ. The present paper deals with the oxidation of substituted monohydric phenols and some reactions observed on highly reactive quinol ethers prepared in the course of this study.

---

[1] V. V. Ershov, A. A. Volod'kin, and G. N. Bogdanov, *Russ. Chem. Rev.* **32**, 75 (1963).

[2] H. Musso, *Angew. Chem.*, **75**, 965 (1963).

[3] K. U. Ingold, *Chem. Rev.*, **61**, 563 (1961).

[4] L. M. Jackman in "Advances in Organic Chemistry: Methods and Results," Vol. II, Interscience Publishers, Inc., New York, N. Y., 1960, p. 329.

[5] J. Thiele and F. Günther, *Ann.*, **349**, 45 (1906). For an improved synthesis of DDQ, see P. W. D. Mitchell, *Can. J. Chem.*, **41**, 550 (1963).

[6] L. M. Jackman and D. T. Thompson, *J. Chem. Soc.*, 4794 (1960), and earlier papers.

[7] D. Burn, D. N. Kirk, and V. Petrow, *Proc. Chem. Soc.*, 14 (1960); G. Muller, J. Martel, and C. Huynh, *Bull. soc. chim. France*, 2000 (1961); B. Berkoz, L. Cuellar, R. Grezemkovsky, N. V. Avila, and A. D. Cross, *Proc. Chem. Soc.*, 215 (1964).

[8] See also H. O. House, R. W. Magin, and H. W. Thompson, *J. Org. Chem.*, **28**, 2403 (1963).

[9] D. Burn, V. Petrow, and G. O. Weston, *Tetrahedron Letters*, **No. 9**, 14 (1960).

[10] S. K. Pradham and H. J. Ringold, *J. Org. Chem.*, **29**, 601 (1964).

[11] H.-D. Becker and E. Adler, *Acta Chem. Scand.*, **15**, 218 (1961).

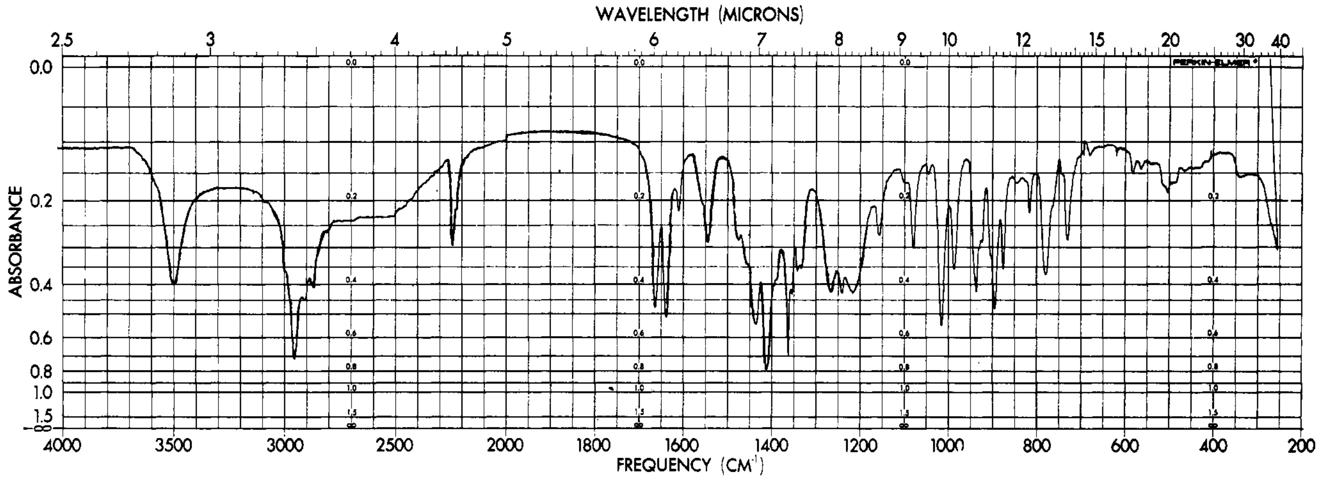
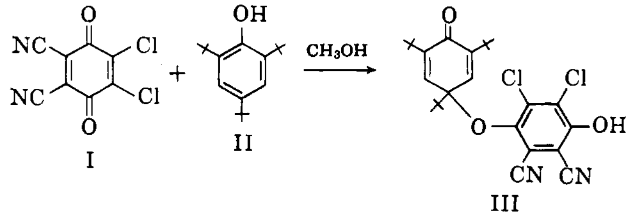


Figure 1.—The infrared spectrum of 4-(2,3-dichloro-5,6-dicyano-4-hydroxyphenoxy)-2,4,6-tri-*t*-butyl-2,5-cyclohexadien-1-one (III).

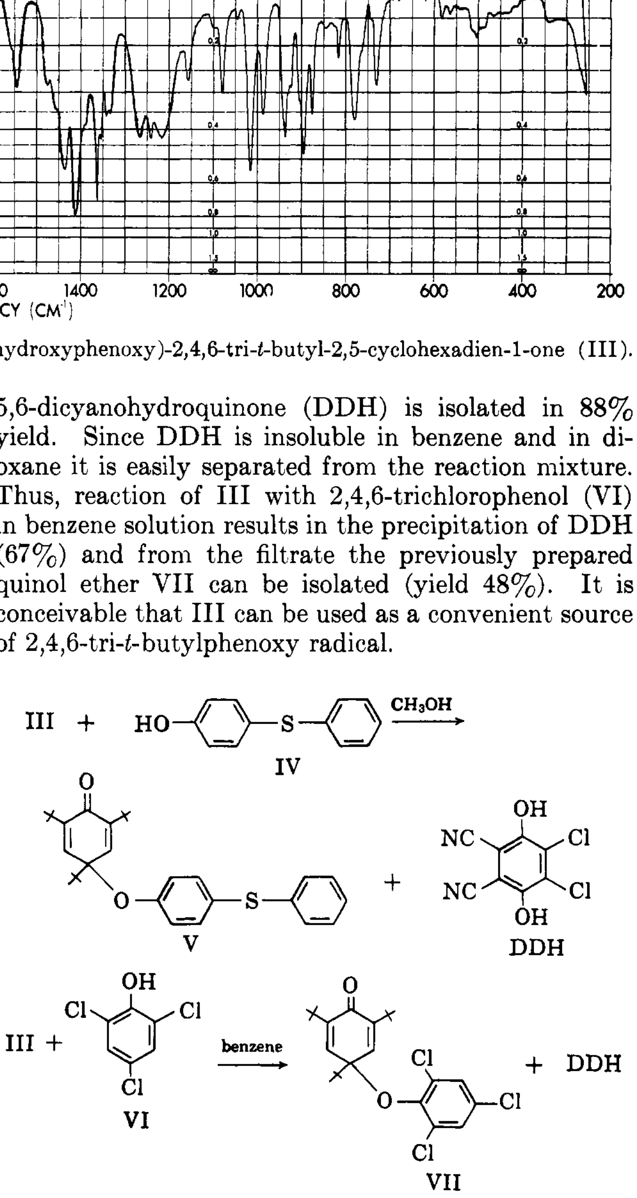
Results

A. Oxidation of Sterically Hindered Phenols. 2,4,6-Tri-*t*-butylphenol.—The oxidation of sterically hindered phenols to yield stable free radicals has received much attention ever since the isolation of 2,4,6-tri-*t*-butylphenoxy radical in crystalline form was reported.[12] Alkaline potassium ferricyanide, lead dioxide, or active manganese dioxide have been used as oxidizing agents.

DDQ (I) reacts instantaneously with 2,4,6-tri-*t*-butylphenol (II) in methanol solution at room temperature to yield 4-(2,3-dichloro-5,6-dicyano-4-hydroxyphenoxy)-2,4,6-tri-*t*-butyl-2,5-cyclohexadien-1-one (III). The compound precipitates during the oxidation and is easily removed by filtration. The structure of III is fully supported by analytical and spectroscopic data. The infrared spectrum (Figure 1) exhibits a double peak in the carbonyl region, typical for compounds with quinolid structure.[13,14] It is worth noting that monoquinol ethers of hydroquinones have not been prepared earlier since the normal procedure (reaction of 2,4,6-tri-*t*-butylphenoxy radical with hydroquinones) leads to quinones and 2,4,6-tri-*t*-butylphenol.[13]



More revealing than the analytical and spectroscopic data is the chemical reactivity of III. In methanol solution, III exhibits a blue color indicating dissociation into free radicals. In the presence of phenols the 2,3-dichloro-5,6-dicyano-4-hydroxyphenoxy moiety is readily exchanged. Addition of III to a solution of 4-hydroxydiphenyl thio ether (IV) leads to precipitation of 4-(4-phenylthiophenoxy)-2,4,6-tri-*t*-butyl-2,5-cyclohexadien-1-one (V, yield 84%), a quinol ether recently prepared from 2,4,6-tri-*t*-butylphenol and IV in the presence of active manganese dioxide.[14] 2,3-Dichloro-5,6-dicyanohydroquinone (DDH) is isolated in 88% yield. Since DDH is insoluble in benzene and in dioxane it is easily separated from the reaction mixture. Thus, reaction of III with 2,4,6-trichlorophenol (VI) in benzene solution results in the precipitation of DDH (67%) and from the filtrate the previously prepared quinol ether VII can be isolated (yield 48%). It is conceivable that III can be used as a convenient source of 2,4,6-tri-*t*-butylphenoxy radical.



2,6-Di-*t*-butyl-4-methylphenol.—The results obtained in the oxidation of 2,4,6-tri-*t*-butylphenol with DDQ suggested further investigation of sterically hindered phenols. The oxidation of 2,6-di-*t*-butyl-4-methylphenol (ionol, VIII) has received considerable attention, but earlier attempts to isolate 2,6-di-*t*-butyl-4-methylphenoxy radical have been unsuccessful.[15] Since the products previously obtained in the oxidation of VIII are 1,2-di-(3,5-di-*t*-butyl-4-hydroxyphenyl)-ethane and 3,3′,5,5′-tetra-*t*-butylstilbene-4,4′-quinone, a rearrangement of the phenoxy radical into a benzyl radical was suggested.[16] Recently, however, this rearrangement reaction was disproved since the bibenzyl derivative and the stilbene-4,4′-quinone were

---

[12] E. Müller and K. Ley, *Ber.*, **87**, 922 (1954); see ref. 1 and 2 for further references.

[13] E. Müller, K. Ley, and G. Schlechte, *ibid.*, **90**, 2660 (1957).

[14] H.-D. Becker, *J. Org. Chem.*, **29**, 3068 (1964).

[15] C. D. Cook, *ibid.*, **18**, 261 (1953); R. F. Moore and W. A. Waters, *J. Chem. Soc.*, 243 (1954); see ref. 1 and 2 for further references.

[16] C. D. Cook, N. G. Nash, and H. R. Flanagan, *J. Am. Chem. Soc.*, **77**, 1783 (1955).

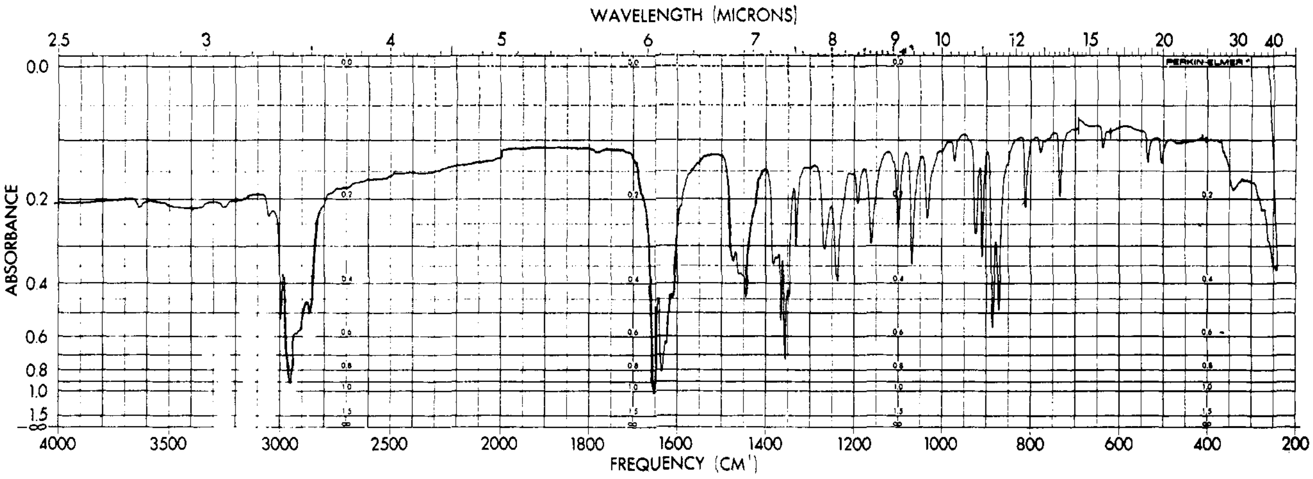


Figure 2.—The infrared spectrum of 4-(2,6-di-*t*-butyl-4-methylphenoxy)-2,6-di-*t*-butyl-4-methyl-2,5-cyclohexadien-1-one (IX).

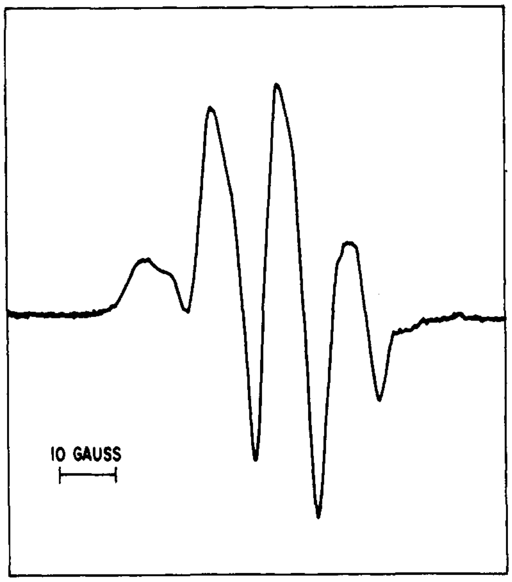
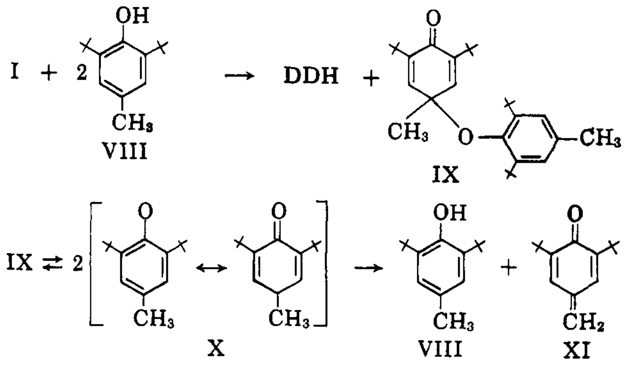


Figure 3.— The e.s.r. spectrum of IX.

found to be formed by dimerization of 2,6-di-*t*-butyl-1,4-quinone methide.[17]

DDQ (1 mole) reacts instantaneously with ionol (2 moles) at room temperature in methanol solution to form a colorless crystalline precipitate. The compound formed in 75–85% yield analyzes for $C_{15}H_{23}O$ and is rather unstable in the solid state and in solution. When dissolved in ether or methanol where it is only sparingly soluble, the solution exhibits a light blue color that rapidly turns yellow. The infrared spectrum (Figure 2) of the substance exhibits strong split absorption in the carbonyl region, typical for compounds with quinolid structure, but does not show any hydroxyl absorption. However, even in the KBr pellet chemical reactions proceed since a (phenolic) hydroxyl is detectable when the spectrum is rerun after 2 hr., and reexamination of the original KBr pellet after 1 week indicates disappearance of the quinolid structure. The compound in the solid state gives an e.s.r. spectrum[18] (Figure 3) consisting of a quadruplet as expected for an unpaired electron interacting with three equivalent protons.[19] These data establish that the oxidation of ionol by DDQ results in the formation of 4-(2,6-di-*t*-butyl-4-methylphenoxy)-2,6-di-*t*-butyl-4-methyl-2,5-cyclohexadien-1-one (IX) which even in the solid state is partially dissociated into the monomer phenoxy radicals (X). Dimer IX also is obtained in 55% yield by treating ionol with the quinol ether III according to this equation.



III + VIII → II + IX + DDH

Recently debromination of 4-bromo-2,6-di-*t*-butyl-4-methyl-2,5-cyclohexadien-1-one in isooctane by mercury to yield equimolar amounts of 2,6-di-*t*-butylmethylphenol and 2,6-di-*t*-butyl-1,4-quinone methide (XI) *via* 2,6-di-*t*-butyl-4-methylphenoxy radical has been studied by ultraviolet spectroscopic means.[17] It, therefore, was interesting to investigate the dissociation of IX and thus disproportionation of X.

The disproportionation of 2,6-di-*t*-butyl-4-methylphenoxy radical must be quite rapid. The course of the disproportionation of X in isooctane was hard to measure, the reaction being complete within the time that elapsed (about 3–5 min.) between dissolving IX and measuring the spectrum at an appropriate concentration. However, as shown in Figure 4, the position of the maximum at 285 mμ and the ε-value of 27,000 are in excellent agreement with the data reported for the quinone methide prepared by dehydrohalogenation of the corresponding benzyl halide,[20]

---

(17) R. H. Bauer and G. M. Coppinger, *Tetrahedron*, **19**, 1201 (1963).

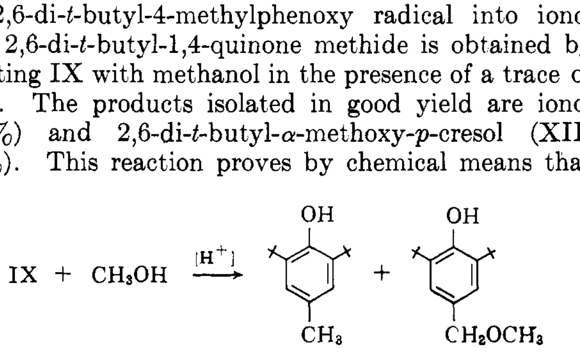
(18) Thanks are due to Drs. C. M. Huggins and J. H. Lupinski for recording and interpreting the spectrum.

(19) J. K. Becconsall, S. Clough, and G. Scott, *Trans. Faraday Soc.*, **56**, 459 (1960); G. N. Bogdanov, M. S. Postnikova, and N. M. Emanuel, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 173 (1963) [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 154 1963].

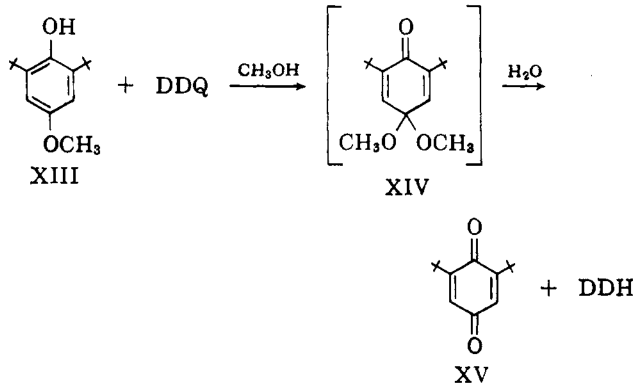
(20) L. J. Filar and S. Winstein, *Tetrahedron Letters*, **No. 25**, 9 (1960).

oxidation of ionol with lead dioxide,[20] or dehalogenation of the corresponding bromocyclohexadienone.[17] (The ultraviolet spectrum of the amount of ionol formed in the disproportionation reaction of IX is shown as the dashed line in Figure 4.) In ether solution, however, the disproportionation of X can be followed and the results (Figure 5) are in complete agreement with those obtained in the debromination reaction with mercury.[17]

Finally, chemical evidence for the disproportionation of 2,6-di-*t*-butyl-4-methylphenoxy radical into ionol and 2,6-di-*t*-butyl-1,4-quinone methide is obtained by treating IX with methanol in the presence of a trace of acid. The products isolated in good yield are ionol (96%) and 2,6-di-*t*-butyl-α-methoxy-*p*-cresol (XII, 70%). This reaction proves by chemical means that 2,6-di-*t*-butyl-4-methylphenoxy radical disproportionates into the parent phenol and the quinone methide XI. Addition reactions of methanol to quinone methides are known,[21] and the methyl ether XII has previously been obtained as a by-product in the oxidation of ionol with 2,6-di-*t*-butyl-4-cyanophenoxy radical in methanol solution.[22]



2,6-Di-*t*-butyl-4-methoxyphenol.—2,6-Di-*t*-butyl-4-methoxyphenol (XIII) is known to form a stable free radical when rapidly oxidized with lead dioxide or alkaline potassium ferricyanide.[23] Oxidation of XIII with DDQ in methanol gives a yellow oil whose infrared and n.m.r. spectra are suggestive of 2,6-di-*t*-butyl-1,4-benzoquinone dimethyl ketal (XIV). Its hydrolysis leads to the formation of 2,6-di-*t*-butyl-1,4-benzoquinone (XV). It has been reported earlier that extensive oxidation of XIV does not give the phenoxy radical but results in the formation of XV.[23]



2,6-Di-*t*-butyl-4-bromophenol.—The oxidation of 2,6-di-*t*-butyl-4-bromophenol (XVI) is readily accomplished with active manganese dioxide to yield 3,3′,5,5′-tetra-*t*-butyldiphenoquinone,[14] but XVI is also known to react with phenoxy radicals to give *p*-quinol ethers.[24] Co-oxidation of XVI and pentachlorophenol yields 4,4-bis(pentachlorophenoxy)-2,6-di-*t*-butyl-2,5-cyclohexadien-1-one, an aromatic quinone ketal.[14]

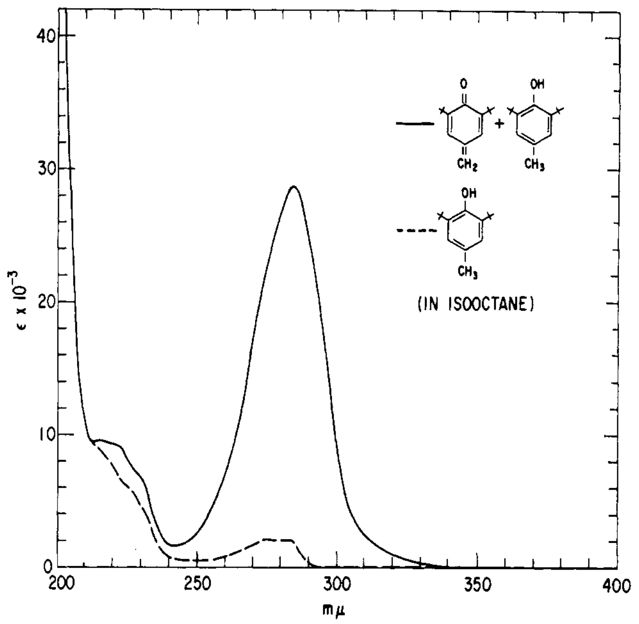
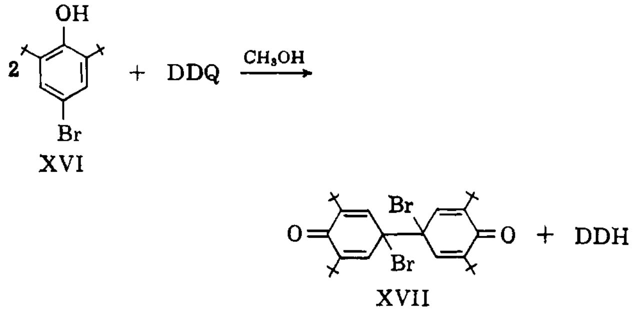


Figure 4.—The ultraviolet spectrum of the products of the disproportionation of 2,6-di-*t*-butyl-4-methylphenoxy radical (X).

The addition of DDQ to a solution of 4-bromo-2,6-di-*t*-butylphenol in methanol leads to immediate precipitation of bis(1-bromo-3,5-di-*t*-butyl-4-oxo-2,5-cyclohexadienyl-1) (XVII, 79%). Previously XVII has been obtained by oxidation of 2,6-di-*t*-butyl-4-bromophenol with 2,4,6-tri-*t*-butylphenoxy radical.[25] However, for preparative purposes the oxidation with DDQ is advantageous because the reaction is fast and XVII can simply be removed from the reaction mixture by filtration. As reported earlier,[25] XVII loses bromine upon heating, thus giving rise to 3,3′,5,5′-tetra-*t*-butyldiphenoquinone.



4-Bromotetramethylphenol.—Oxidation of durophenol by peroxidase has been reported to give 4,4′-dihydroxyoctamethylbiphenyl, but it could not be oxidized to the corresponding diphenoquinone probably owing to steric hindrance.[26] It appeared worth investigating 4-bromotetramethylphenol (XVIII) in order to compare its behavior toward DDQ with that of 4-bromo-2,6-di-*t*-butylphenol (XVI). Treatment of XVIII with DDQ in methanol results in the liberation of HBr. After separation of DDH (91%) and hydrolysis of the oily residue, duroquinone (XXI) is

---

(21) E. Adler and B. Stenemur, *Ber.*, **89**, 291 (1956); C. D. Cook and B. F. Norcross, *J. Am. Chem. Soc.*, **78**, 3797 (1956); K. Freudenberg and H.-K. Werner, *Ber.*, **97**, 579 (1964).

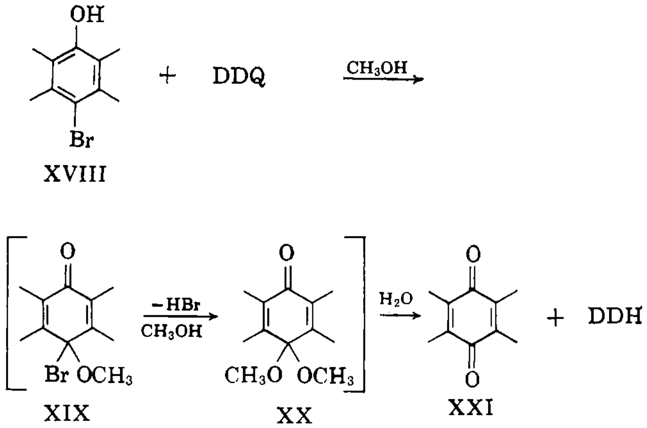
(22) E. Müller, A. Rieker, K. Ley, R. Mayer, and K. Scheffler, *ibid.*, **92**, 2278 (1959).

(23) E. Müller and K. Ley, *ibid.*, **88**, 601 (1955).

(24) E. Müller, A. Rieker, and A. Schick, *Ann.*, **673**, 40 (1964).

(25) K. Ley, E. Müller, R. Mayer, and K. Scheffler, *Ber.*, **91**, 2670 (1958).

(26) H. Booth and B. C. Saunders, *J. Chem. Soc.*, 940 (1956).



XVIII

XIX

XX

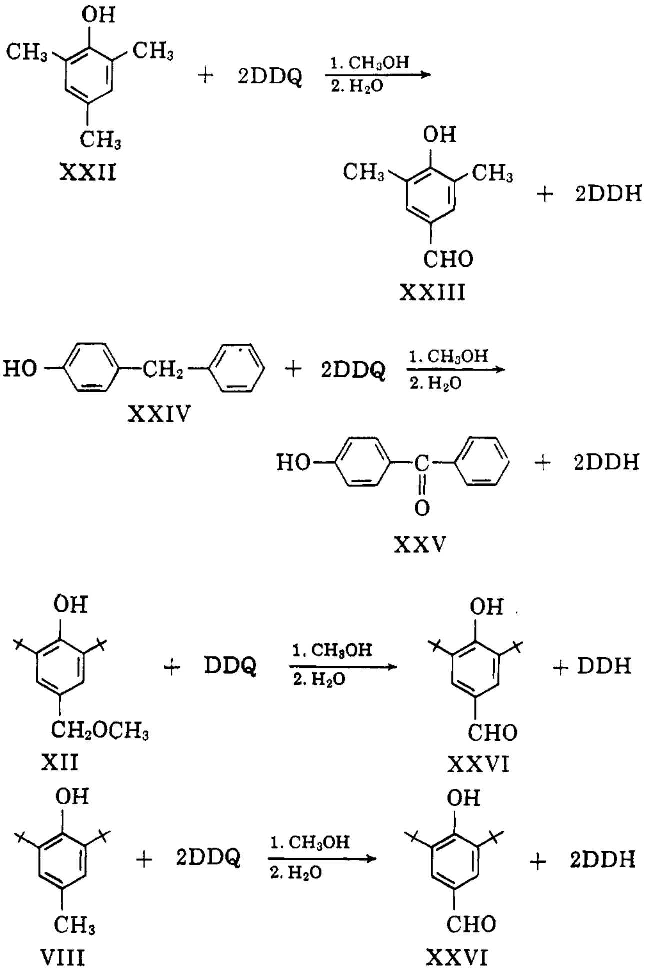
XXI

isolated (91%). A possible route of this reaction could involve a 4-bromoquinol ether XIX that reacted with methanol to yield HBr and a hydrolyzable quinone ketal, XX.

B. Benzylic Oxidation. Mesitol, 4-Hydroxydiphenylmethane, 2,6-Di-*t*-butyl-α-methoxy-*p*-cresol, and Ionol.—Oxidation of mesitol (XXII) has been carried out with a variety of oxidizing agents leading to benzylic oxidation of the *p*-methyl group.[27] Potassium nitrosodisulfonate, for instance, reacts with mesitol to yield 3,5-dimethyl-4-hydroxybenzyl alcohol, 2,6-dimethyl-1,4-benzoquinone, and 3,5-dimethyl-4-hydroxybenzyl-2,4,6-trimethylphenyl ether.[27]

The reaction of mesitol with DDQ in methanol leads to a deep blue-colored solution, but the color rapidly changes to light yellow. After separation of DDH (96%) from the reaction mixture, the oxidation product is easily hydrolyzed to yield 3,5-dimethyl-4-hydroxybenzaldehyde (XXIII, 83%). Similarly, 4-hydroxydiphenylmethane (XXIV) reacts with 2 moles of DDQ to yield 4-hydroxybenzophenone (XXV, 91%) (see Scheme I).

SCHEME I



XXII

XXIII

XXIV

XXV

XII

XXVI

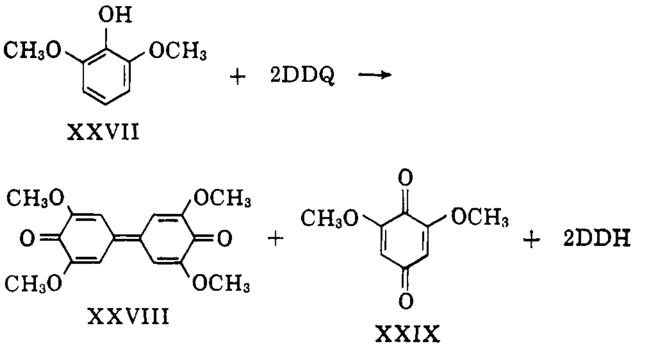
VIII

XXVI

Since it is known that benzyl ethers can undergo oxidative cleavage, it appeared interesting to oxidize a phenolic benzyl ether. Indeed, 2,6-di-*t*-butyl-α-methoxy-*p*-cresol (XII) is readily converted into 3,5-di-*t*-butyl-4-hydroxybenzaldehyde (XXVI, 94%) upon treatment with DDQ in methanol solution.

It appeared unlikely that ionol (VIII), which was described above forming a dimer, would show an exceptional behavior in the benzylic oxidation with DDQ. Therefore, the oxidation of VIII was studied in dilute solution, thus preventing precipitation of the dimer of 2,6-di-*t*-butyl-4-methylphenoxy radical. By this procedure ionol in methanol solution is easily oxidized with DDQ to give 3,5-di-*t*-butyl-4-hydroxybenzaldehyde (86%); however, 2 moles of oxidizing agent are required. The formation of XXVI from VIII or XII has been found earlier to occur upon oxidation with bromine.[28]

C. 2,6-Dimethoxyphenol.—All the reactions described above were carried out with *para*-substituted phenols. When the oxidation with DDQ was extended to 2,6-dimethoxyphenol (XXVII) in methanol, 3,3′,5,5′-tetramethoxydiphenoquinone (XXVIII, cerulignone) precipitated immediately from the reaction mixture (62%). As a by-product, however, 13% of 2,6-dimethoxy-1,4-benzoquinone (XXIX) was isolated after addition of water to the filtrate.



XXVII

XXVIII

XXIX

Discussion

DDQ is known to be a strong electron acceptor readily forming complexes with suitable electron donors.[29] The reaction of DDQ with phenols often leads to deep-colored intermediates of varying stability. Therefore, it is suggested that the primary step in the oxidation of phenols by DDQ is the formation of a charge-transfer complex. The question then arises, if charge

---

[27] R. Magnusson, *Acta Chem. Scand.*, **18**, 759 (1964).

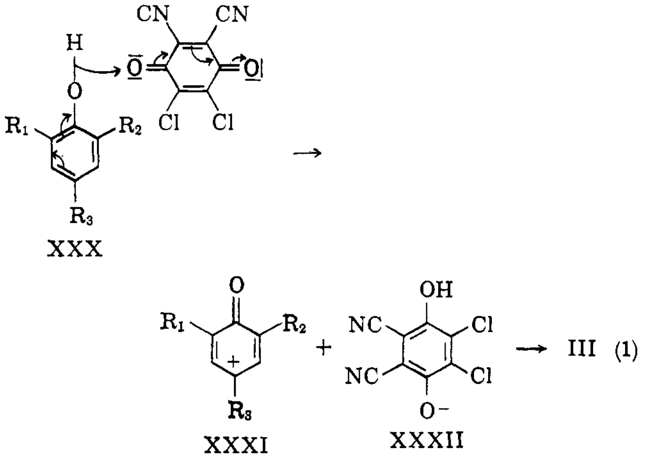
[28] G. N. Coppinger and T. W. Campbell, *J. Am. Chem. Soc.*, **75**, 734 (1963); V. V. Ershov and A. A. Volod'kin, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 2150 (1962); 893 (1963) [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 2057 (1962); 805 (1963)].

[29] A. Ottenberg, R. L. Brandon, and M. E. Browne, *Nature*, **201**, 1119 (1964).

separation occurs in a one-electron or a two-electron process.

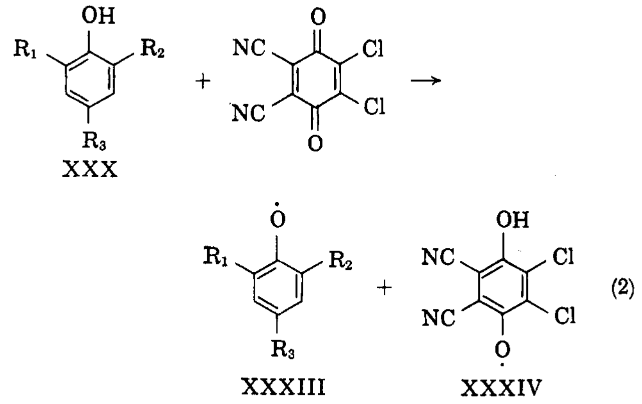
The mechanism of the dehydrogenation of hydroaromatic systems by quinones has been extensively studied by Braude, Linstead, Jackman, and co-workers.[4] Evidence was presented for a two-stage ionic process involving a hydride ion transfer from the substrate to the quinone. Indeed, such a step (eq. 1) appeared to be possible in the oxidation of phenols as exemplified by the formation of III *via* the intermediates XXXI (R_1, R_2, R_3 = *t*-butyl) and XXXII. Application of this ionic mechanism to the formation of the quinol ether IX from ionol would then have to involve the reaction of the intermediate XXXI (R_1, R_2 = *t*-butyl; R_3 = methyl) with the parent phenol. However, it has been demonstrated in this study that IX is obtained from ionol in a radical reaction by using the quinol ether III as oxidizing agent. Furthermore, the hydride ion transfer reaction would not explain the formation of C–C coupled products from phenols such as bis(1-bromo-3,5-di-*t*-butyl-4-oxo-2,5-cyclohexadienyl-1) (XVII) unless one assumes dissociation of a C–O coupled product formed by an ionic mechanism, and recombination under C–C coupling by a radical mechanism. However, there is no proof for such a mechanism, and all C–O-coupled products in the oxidation of phenols are more likely formed by a one-electron transfer from the phenol (XXX) to the quinone giving the phenoxy radical XXXIII (reactions 2 and 3). Formation of III would involve radical combination of XXXIII with XXXIV (R_1, R_2, R_3 = *t*-butyl). Formation of IX from ionol would proceed by dimerization of radical XXXIII (R_1, R_2 = *t*-butyl; R_3 = methyl). This dimerization reaction is suggestive of a reaction 4 in which two phenol molecules are dehydrogenated by one quinone molecule in a single process, giving rise to radical XXXIII and DDH thus bypassing formation of semiquinone radical XXXIV (reaction 2). It also appears possible that the semiquinone radical, formed in reaction 2, can undergo a disproportionation according to

$$\text{XXXIV} \longrightarrow \text{DDQ} + \text{DDH}$$

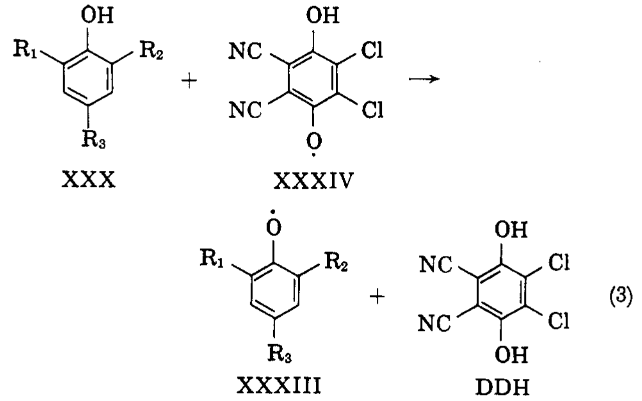


(1)

The oxidative demethylation of XIII or the oxidative debromination of XVIII as well as the formation of 2,6-dimethoxy-1,4-benzoquinone from XXVII probably involves 1,4-quinone dimethyl ketals. However, this does not necessarily require an ionic mechanism in the oxidation step. It is known that aromatic quinone ketals formed in a radical reaction easily do exchange their aryloxy moiety for an alkoxy moiety.[30] Thus, not even an isolated aliphatic quinone ketal would prove an ionic oxidation because the primary step is obscured.



(2)



(3)

$$2\text{XXX} + \text{DDQ} \longrightarrow 2\text{XXXIII} + \text{DDH} \qquad (4)$$

Comparison of the dehydrogenation of phenols by DDQ with oxidation of phenols involving carbonium ions reveals the difference between these reactions. Adler and co-workers have studied extensively the oxidations of phenols by periodate involving ionic intermediates.[31] For instance, the oxidation of mesitol by periodate leads to 2,4,6-trimethyl-1,4-quinol and 2,4,6-trimethyl-1,2-quinol (dimer),[32] as opposed to the oxidation by potassium nitrosodisulfonate leading to 3,5-dimethyl-4-hydroxybenzyl 2,4,6-trimethylphenyl ether and 3,5-dimethyl-4-hydroxybenzyl alcohol.[27] The benzylic oxidation observed in the reaction of 4-alkyl-substituted monohydric phenols with DDQ presumably proceeds in a reaction sequence XXXV through XL involving addition of methanol to 1,4-quinone methide intermediates XXXVI and XXXVIII (R_1, R_2 = CH_3 in the case of mesitol). Compounds of type XXXVII indeed are easily oxidized by DDQ to yield the corresponding aldehyde as described in the case of 2,6-di-*t*-butyl-α-methoxy-*p*-cresol (XII, R_1, R_2 = *t*-butyl in XXXVII). (See Scheme II.)

All results presented in this paper are best interpreted by a one-electron transfer reaction from the phenol to the quinone. It has been demonstrated recently that the dehydrogenation of hydroaromatic

---

(30) C. Martius and H. Eilingsfeld, *Ann.*, **607**, 159 (1957).

(31) E. Adler, I. Falkehag, and B. Smith, *Acta Chem. Scand.*, **16**, 529 (1962), and earlier papers.

(32) E. Adler, J. Dahlen, and G. Westin, *ibid.*, **14**, 1580 (1960).

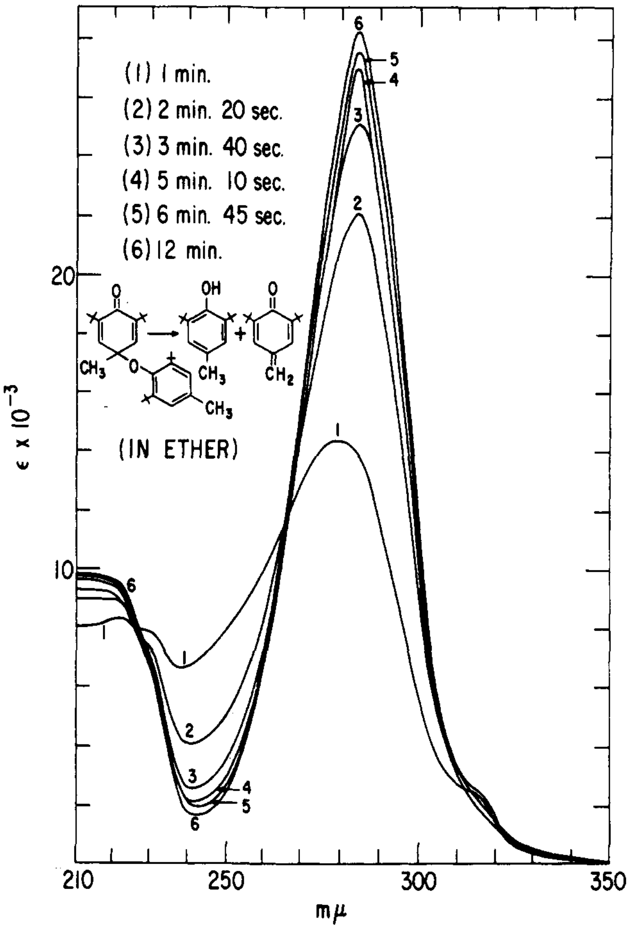


Figure 5.—Ultraviolet spectra showing the disproportionation of X in ether.

systems by quinones is dependent on the nature of the substrate and can lead either to carbonium ions or to carbon radicals.[33]

Experimental

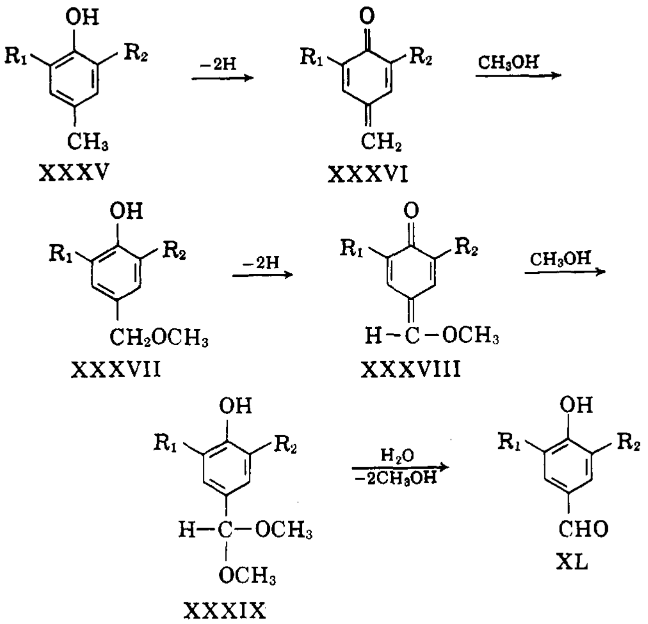
2,3-Dichloro-5,6-dicyano-1,4-benzoquinone was recrystallized from methylene chloride. Absolute methanol was commercial grade. Oxidation reactions were carried out in screw-cap bottles under nitrogen. All melting points were taken on a Fisher-Johns melting point apparatus and are not corrected.

4-(2,3-Dichloro-5,6-dicyano-4-hydroxy phenoxy)-2,4,6-tri-*t*-butyl-2,5-cyclohexadien-1-one (III).—DDQ (454 mg., 2 mmoles) was added at one time to a solution of 524 mg. (2 mmoles) of 2,4,6-tri-*t*-butylphenol in 5 ml. of absolute methanol that was agitated by a stream of nitrogen. As the DDQ dissolved a colorless precipitate was formed. After 10 min. of agitation by nitrogen, the reaction mixture was filtered, and the residue was quickly washed with a few milliliters of cold methanol, yielding 610–800 mg. (62–82%) of III as colorless crystals that slowly turned greenish upon standing at room temperature. Upon heating, the substance turned red at about 135°, then almost colorless above 160°, and melted with decomposition around 265°.

Anal. Calcd. for $C_{26}H_{30}Cl_2N_2O_3$ (489.43): C, 63.80; H, 6.18; Cl, 14.49; N, 5.72. Found: C, 63.02; H, 6.43; Cl, 13.61; N, 5.56.

Attempts to improve the analytical data of C and Cl by recrystallization from methanol were unsuccessful.

SCHEME II



Reaction of III with 4-Hydroxydiphenyl Sulfide.—Compound III (245 mg., 0.5 mmole) was added to a solution of 101 mg. (0.5 mmole) of 4-hydroxydiphenyl sulfide in 8 ml. of absolute methanol, agitated by a stream of nitrogen. As III dissolved, a crystalline substance precipitated. After 10 min. the solution was partly concentrated *in vacuo* and filtered, yielding 195 mg. (84%) of 4-(4-phenylthiophenoxy)-2,4,6-tri-*t*-butyl-2,5-cyclohexadien-1-one, m.p. 110°. The mixture melting point with authentic[14] material gave no depression.

Evaporation of the filtrate and treatment of the solid residue with benzene yielded 100 mg. (88%) of DDH.

Reaction of III with 2,4,6-Trichlorophenol.—Compound III (245 mg., 0.5 mmole) was added to a solution of 99 mg. (0.5 mmole) of 2,4,6-trichlorophenol in 5 ml. of benzene. The solution was shaken under nitrogen for 17 hr. The reaction mixture was filtered, yielding 76 mg. (67%) of benzene-insoluble DDH. The filtrate was evaporated *in vacuo* and the residue obtained was treated with a little methanol, yielding 120 mg. (48%) of 4-(2,4,6-trichlorophenoxy)-2,4,6-tri-*t*-butyl-2,5-cyclohexadien-1-one. Its infrared spectrum was identical with that of authentic material.[14]

4-(2,6-Di-*t*-butyl-4-methylphenoxy)-2,6-di-*t*-butyl-4-methyl-2,5-cylohexadien-1-one (IX).—DDQ (908 mg., 4 mmoles) was added at one time to a solution of 1.76 g. (8 mmoles) of 2,6-di-*t*-butyl-4-methylphenol in 10 ml. of absolute methanol, agitated by a stream of nitrogen. The solution turned first dark, then after a few seconds turned light colored as a colorless substance precipitated. The reaction mixture was filtered after about 3 min. The residue was washed quickly with a little cold methanol and dried by pressing on filter paper: yield, 1.3–1.5 g. (75–85%) of IX as colorless or very light blue-greenish crystals that turned yellow at room temperature. The substance turned yellow upon heating and melted between 85 and 90°, depending on the rate of heating, forming a red-brown melt.

Anal. Calcd. for $C_{30}H_{46}O_2$ (438.67): C, 82.13; H, 10.57. Found: C, 82.28; H, 10.60.

Oxidation of 2,6-di-*t*-butyl-4-methylphenol with III.—Compound III (245 mg., 0.5 mmole) was added to a solution of 220 mg. (1 mmole) of 2,6-di-*t*-butyl-4-methylphenol in 3 ml. of absolute methanol, agitated with a stream of nitrogen. As III dissolved, the reaction mixture turned yellow and cloudy. After 3 min. it was filtered and the residue was washed with little methanol, yielding 120 mg. (55%) of 4-(2,6-di-*t*-butyl-4-methylphenoxy)-2,6-di-*t*-butyl-4-methyl-2,5-cyclohexadien-1-one. Its infrared spectrum was identical with that of the substance obtained by oxidation of 2,6-di-*t*-butyl-4-methylphenol with DDQ. From the filtrate 86 mg. (75%) of DDH were isolated.

Reaction of IX in Methanol.—Dimer IX (1 g., 2.3 mmoles) was added to 50 ml. of absolute methanol containing 1 drop of concentrated hydrochloric acid and the solution was refluxed for 80 min. (The reaction mixture first turned blue, but was colorless after 3 min.) Evaporation *in vacuo* gave a solid residue that was subjected to sublimation at 60° (1 mm.) for 20 min. yielding 480 mg. (96%) of 2,6-di-*t*-butyl-4-methylphenol (m.p. 66–68°) as sublimate. The residue was recrystallized from petroleum ether (b.p. 30–60°), yielding 400 mg. (70%) of 2,6-di-*t*-

---

[33] D. H. Reid, M. Fraser, B. B. Molloy, H. A. S. Payne, and R. G. Sutherland, *Tetrahedron Letters*, **No. 15**, 530 (1961).

Table I

Phenol (mmoles)	DDQ, mmoles	CH$_3$OH, ml.	Time	Product (% yield)	M.p., °C.	DDH, % yield
4-Hydroxydiphenylmethane (2)	4	5	16 hr	XXV (91)	133–134	94
2,6-Di-*t*-butyl-α-methoxy-*p*-cresol (2)	2	8	16 hr.	XXVI (94)	188–189	93
Ionol[a] (1)	2	50	40 min.	XXVI (86)	188–189	90
2,6-Di-*t*-butyl-4-methoxyphenol[b] (2)	2	15	12 hr.	XV (81)	66–68	90
4-Bromotetramethylphenol (2)	2	4	24 hr.	XXI (91)	109	91

[a] Ionol was added to the solution of DDQ in methanol. [b] Acetic acid could also be used as solvent.

butyl-α-methoxy-*p*-cresol, m.p. 98–99°. Its infrared spectrum was identical with that of authentic material.

Bis(1-bromo-3,5-di-*t*-butyl-4-oxo-2,5-cyclohexadien-yl-1) (XVII).—DDQ (227 mg., 1 mmole) was added to a solution of 570 mg. (2 mmoles) of 4-bromo-2,6-di-*t*-butylphenol in 5 ml. of absolute methanol, agitated by a stream of nitrogen. The reaction mixture turned deep brown, then after a few seconds very bright yellow as a light yellow crystalline substance precipitated. After 5 min., the reaction mixture was filtered and the residue was washed with little methanol, yielding 450 mg. (79%) of XVII as light yellow crystals. The yield can be increased to 85% if the reaction mixture is kept in the refrigerator for several hours before filtration. The substance turned red at about 90° (*cf.* ref. 25), losing bromine upon heating, thus forming 3,3′,5,5′-tetra-*t*-butyldiphenoquinone, m.p. 242–244°.

Anal. Calcd. for $C_{28}H_{40}Br_2O_2$ (568.43): C, 59.16; H, 7.09; Br, 28.1. Found: C, 59.13; H, 7.08; Br, 27.4.

Oxidation of 2,4,6-Trimethylphenol (Mesitol).—DDQ (908 mg., 4 mmoles) was added to a solution of 272 mg. (2 mmoles) of mesitol in 10 ml. of methanol, agitated by a stream of nitrogen. The solution turned deep blue with evolution of heat, then brown after 1 min., and finally yellow. The reaction mixture was kept standing under nitrogen for 12 hr. and then evaporated *in vacuo* yielding a solid, light yellow residue. Treatment with 50 ml. of boiling benzene left 875 mg. (95%) of 2,3-dichloro-5,6-dicyanohydroquinone undissolved. Evaporation of the filtrate left a light yellow solid that was washed with aqueous methanol and filtered, yielding 250 mg. of 3,5-dimethyl-4-hydroxybenzaldehyde (83%), m.p. 113–114°. Recrystallization from aqueous methanol raised the melting point to 114–115°.

Other oxidations involving a similar work-up as the oxidation of mesitol are summarized in Table I.

Oxidation of 2,6-Dimethoxyphenol.—DDQ (454 mg., 2 mmoles) was added to a solution of 308 mg. (2 mmoles) of 2,6-dimethoxyphenol in 3 ml. of absolute methanol. The solution turned warm and a dark violet-colored precipitate was formed. Filtration after 1 min. yielded 188 mg. (62%) of 3,3′,5,5′-tetramethoxydiphenoquinone. To the filtrate were added 2 drops of water, yielding a yellow crystalline precipitate. It was sublimed at 180° (10 mm.) yielding 43 mg. (13%) of 2,6-dimethoxy-1,4-benzoquinone, m.p. 255°.

Spectra.[34]—The infrared spectra were taken on a Perkin-Elmer grating infrared spectrophotometer, Model 521.

Ultraviolet spectra were obtained with a Cary recording spectrophotometer, Model 14. Figure 4 represents the spectrum obtained by dissolving 5.5 mg. of IX in 500 ml. of isooctane, corresponding to a 2.5 × 10^{-5} *M* solution. The spectrum of Figure 5 was obtained by dissolving an unweighed amount of IX in ether directly in the ultraviolet cell. The ϵ-scale given in Figure 5 is based on the ϵ-value calculated from the experiment given in Figure 4.

---

[34] All spectra were taken with the technical assistance of Miss D. V. McClung of this laboratory.

Quinone Dehydrogenation. II. The Oxidative Dimerization of Enols and Enolizable Ketones

Hans-Dieter Becker

General Electric Research Laboratory, Schenectady, New York

Received October 9, 1964

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) under mild conditions reacts smoothly with enols and enolizable ketones. Flavonol is readily oxidized by DDQ to give a C–O-coupled dehydro dimer. 2-Arylindane-1,3-diones are easily converted into 2,2′-diaryl-2,2′-biindane-1,1′,3,3′-tetrones. Treatment of 2-methylsulfonylindane-1,3-dione with DDQ gives the addition product, 2-(2,3-dichloro-5,6-dicyano-4-hydroxyphenoxy)-2-methylsulfonylindane-1,3-dione. A mechanism for the oxidation of enolizable ketones involving a one-electron transfer from the enolate ion to the quinone is discussed on the basis of an ultraviolet spectroscopic investigation.

In the preceding paper on quinone dehydrogenation it has been shown that 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (henceforth abbreviated DDQ) represents a powerful oxidizing agent for phenols.[1] The results obtained in the oxidation of phenols suggested the extension of the reaction to enols and ketones known to exist in a keto–enol equilibrium in solution.

Dehydrogenation of ketones by quinones has previously been applied in the preparation of $\Delta^{1,4}$ or $\Delta^{1,4,6}$ steroidal ketones from Δ^4 or $\Delta^{4,6}$ steroidal ketones. The reaction requires elevated temperature.[2] At room temperature the α,β-unsaturated steroidal ketones are stable toward quinones. They can be prepared by oxidation of the corresponding allylic alcohols with DDQ.[3]

This paper is concerned with the quinone dehydrogenation of enols and enolizable ketones for which α–β unsaturation is structurally not possible. Such enols and enolizable ketones are found to undergo oxidative dimerization in excellent yields.

Results

A. Flavonol.—DDQ reacts with flavonol (I) in dioxane solution at room temperature to give 2,3-dichloro-5,6-dicyanohydroquinone (henceforth abbreviated DDH) and a yellow crystalline compound (yield 64%) for which elemental analysis and molecular weight are in agreement with a flavonol dehydro dimer. The infrared spectrum of this dehydro dimer (in KBr; Figure 1) exhibits carbonyl peaks at 1740 and 1695

---

[1] H.-D. Becker, *J. Org. Chem.*, **30**, 982 (1965).

[2] D. Burn, D. N. Kirk, and V. Petrow, *Proc. Chem. Soc.*, 14 (1960).

[3] D. Burn, V. Petrow, and G. O. Weston, *Tetrahedron Letters*, **No. 9** 14 (1960).