[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF VERMONT]

Oxidation of Hindered Phenols. V. The 2,6-Di-*t*-butyl-4-isopropyl and -4-*sec*-Butylphenoxy Radicals

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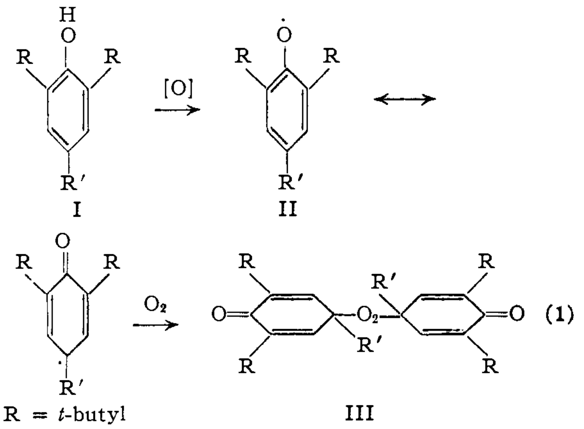
Oxidation of 2,6-di-*t*-butyl-4-isopropylphenol and 2,6-di-*t*-butyl-4-*sec*-butylphenol with alkaline ferricyanide produces the corresponding phenoxy radicals. These radicals react further to produce stable quinone methides. Alcohols can be added to the quinone methides producing *p*-alkoxydialkylmethylphenols which can be oxidized to produce stable phenoxy radicals. All of the phenoxy radicals react with oxygen to produce bis-cyclohexadienone peroxides.

It has been shown[1-6] that oxidation of 2,4,6-trisubstituted phenols produces stable phenoxy radicals when the substituents have sufficient bulk and have no hydrogen alpha to the nucleus. When one or more of the substituents is a methyl group, dimeric products, linked through the side chains, are frequently formed upon oxidation. In one case it has been shown[3] that the 2,6-di-*t*-butyl-4-methylphenoxy radical rearranges to the corresponding benzyl radical and dimerizes. In this case, the evidence for free radical formation was the appearance of an extremely transient blue color, the reaction conditions and the nature of the products. A number of other examples of dimerization through methyl groups are known.[7] In view of this, it was of interest to examine the effects of side chains, other than methyl or *t*-alkyl groups, on the stability of phenoxy radicals. A case of a tertiary α-hydrogen was of particular interest since it might shed some light on the mechanism of the rearrangement and because of the possibility of demonstrating more clearly the intervention of a phenoxy radical in the oxidation process.

Oxidation of 2,6-di-*t*-butyl-4-isopropylphenol (Ia) and 2,6-di-*t*-butyl-4-*sec*-butylphenol (Ib) by alkaline ferricyanide or lead dioxide produces a deep blue color similar to that of 2,4,6-tri-*t*-butylphenoxy.[1,2] This blue color must be due to the presence of the 2,6-di-*t*-butyl-4-*sec*-alkylphenoxy radicals (IIa, IIb). In the presence of oxygen these radicals react rapidly to produce the corresponding bis-cyclohexadienone peroxides (III, eq. 1).



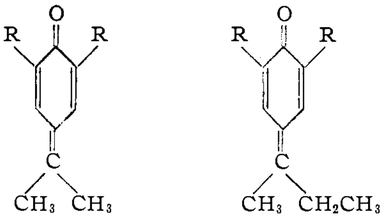
I II III

R = *t*-butyl

a, R' = isopropyl c, R' = dimethylmethoxymethyl

b, R' = *sec*-butyl d, R' = dimethylethoxymethyl

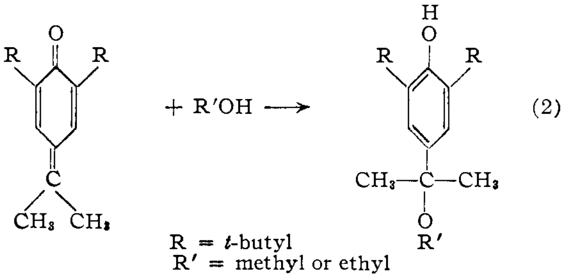
On standing under an inert atmosphere or on continued oxidation, the blue color fades over a period of a few minutes to produce yellow solutions. The chief products of this further reaction are the quinone methides (V and VI) rather than the dimeric products resulting when one substituent is a methyl group.



V R = *t*-butyl VI

The rate of disproportionation of 2,6-di-*t*-butyl-4-isopropylphenoxy was followed spectrophotometrically at 625 mμ. A plot of the reciprocal of optical density against time gave a linear plot over a threefold concentration range, indicating that disproportionation is second order with respect to the phenoxy radicals. This kinetic study is being continued.

Isopropenylquinonemethide (V) adds hydrogen bromide to produce an unstable and rather insoluble addition product. Alcohols add to produce *p*-alkoxymethylphenols (eq. 2), the reaction being acid catalyzed. The resulting phenols can be oxidized to produce radicals having stabilities comparable with that of 2,4,6-tri-*t*-butylphenoxy. They react with oxygen to produce the appropriate bis-cyclohexadienone peroxides.



R = *t*-butyl

R' = methyl or ethyl

Reduction of 2,6-di-*t*-butyl-4-isopropenylquinonemethide with lithium aluminum hydride regenerates the original phenol; reduction with

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(1) C. D. Cook, *J. Org. Chem.*, **18**, 261 (1953).

(2) C. D. Cook and R. C. Woodworth, THIS JOURNAL, **75**, 6242 (1953).

(3) C. D. Cook, N. G. Nash and H. R. Flanagan, *ibid.*, **77**, 1783 (1955).

(4) C. D. Cook, D. A. Kuhn and P. Fianu, *ibid.*, **78**, 2002 (1956).

(5) I. E. Muller and K. Ley, *Ber.*, **87**, 922 (1954); **88**, 601 (1955).

(6) I. E. Muller, K. Ley and W. Kiedaisch, *ibid.*, **87**, 1605 (1954); **88**, 1819 (1955).

(7) See reference 3 for a partial list.

zinc and acetic acid produces a dimeric product believed to be 1,2-bis-(3,5-di-*t*-butyl-4-hydroxyphenyl)-1,1,2,2-tetramethylethane.

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Experimental

Preparation of 2,6-Di-*t*-butyl-4-isopropylphenol (Ia).—A solution of 60 g. (0.44 mole) of *p*-isopropylphenol in 50 ml. of benzene was alkylated with isobutylene at 50–60° using 2 ml. of concd. sulfuric acid as the catalyst.[8] After a weight gain of 60–65 g. (1.07–1.15 moles) of isobutylene the solution was washed once with water, once with 10% sodium hydroxide and three times with Claisen solution (a 50% potassium hydroxide solution diluted with an equal volume of methanol). After evaporation of the benzene, the straw-colored oil was vacuum distilled through a 24″ Vigreux column. The product, boiling from 105–106° at 0.3 mm. and melting at 38–42° was obtained in 50–60% yields.

Anal. Calcd. for $C_{17}H_{28}O$: C, 82.11; H, 11.36. Found: C, 82.01; H, 11.47.

Preparation of 2,6-Di-*t*-butyl-*p*-*sec*-butylphenol (Ib).—The preparation of this compound was carried out in exactly the same way as above except for the substitution of *p*-*sec*-butylphenol for the *p*-isopropylphenol. The product boiled at 110–112° at a pressure of approximately 0.2 mm. and was liquid at room temperature, $n^{25}D$ 1.4959.[9]

Anal. Calcd. for $C_{18}H_{30}O$: C, 82.38; H, 11.52. Found: C, 82.18; H, 11.01.

Preparation of Quinonemethides V and VI.—A solution of 12.4 g. (approx. 0.05 mole) of 2,6-di-*t*-butyl-4-isopropyl- or -4-*sec*-butylphenol in 50 ml. of benzene or *n*-hexane was stirred under a nitrogen atmosphere with 50 ml. of a solution of 50 g. of sodium hydroxide and 65.8 g. (0.20 mole) of potassium ferricyanide in 500 ml. of water. After two hours, all traces of the brilliant blue of the phenoxy radical had disappeared, leaving a bright yellow solution. After evaporation of the solvent, the gummy residue was recrystallized. For the ultraviolet spectra of the two products, see Fig. 1.

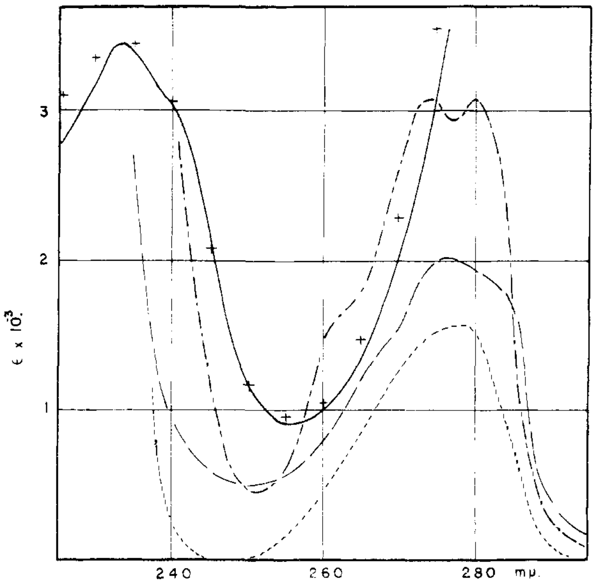

Fig. 1.—Spectra, measured at concentrations of approx. 10^{-4} *M* in cyclohexane, of: —, 2,6-di-*t*-butyl-4-*sec*-butenylquinonemethide (VI); +, 2,6-di-*t*-butyl-4-isopropenylquinonemethide (V); -----, 2,6-di-*t*-butyl-4-dimethylethoxy methylphenol; — – —, 1,2-bis-(3,5-di-*t*-butyl-4-hydroxyphenyl)-1,1,2,2-tetramethylethane; — — —, 2,6-di-*t*-butyl-4-isopropylphenol (Ia).

(a) 2,6-Di-*t*-butyl-4-isopropenylquinonemethide (V).—After three recrystallizations from *n*-hexane, 7.5 g. (60%) of yellow crystals, m.p. 103.5–105.5° were obtained. *Anal.* Calcd. for $C_{17}H_{26}O$: C, 82.86; H, 10.65; mol. wt., 246. Found: C, 82.66; H, 10.44; mol. wt. (cryoscopic, benzene), 247.

(b) 2,6-Di-*t*-butyl-4-*sec*-butenylquinonemethide (VI).—After two recrystallizations from *n*-hexane the yield was approx. 30%, m.p. 56–57°. *Anal.* Calcd. for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 83.32; H, 10.75.

Reaction of 2,6-Di-*t*-butyl-4-isopropenylquinonemethide with Methanol and Ethanol.—When the yellow quinonemethide was dissolved in methanol or ethanol and a drop or two of concd. sulfuric acid added, the system immediately turned colorless. Water was added and the addition product immediately extracted with petroleum ether (E.K. #P950). The petroleum ether was evaporated and the residue recrystallized from the appropriate alcohol. Yields were in the order of 80–90%. Both products reacted readily with alkaline ferricyanide to produce blue phenoxy radicals. The ultraviolet spectra of the phenols were very similar to that of 2,4,6-tri-*t*-butylphenol (see Fig. 1). The infrared spectra showed only the characteristic hindered hydroxyl band.[10]

(a) 2,6-Di-*t*-butyl-4-dimethylmethoxymethylphenol.—This compound melted at 106.5–108.5°. *Anal.* Calcd. for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found: C, 77.36; H, 10.70.

(b) 2,6-Di-*t*-butyl-4-dimethylethoxymethylphenol.—This compound melted at 79–80°. *Anal.* Calcd. for $C_{19}H_{32}O_2$: C, 78.03; H, 11.03; mol. wt., 292. Found: C, 78.66; H, 10.82; mol. wt. (cryoscopic, benzene), 295.

Preparation of Peroxides.—A solution of 5 g. of the appropriate phenol in 50 ml. of benzene was added dropwise over a four-hour period to a solution of 10 g. of sodium hydroxide and 30 g. of potassium ferricyanide in 200 ml. of water. A stream of oxygen was bubbled slowly into the vigorously stirred solution. Benzene lost by evaporation was replaced periodically. When the reaction was complete (all trace of blue coloration gone) the benzene layer was separated, washed with water and evaporated to dryness. The yellow residue was taken up in hot solvent, filtered and cooled quickly.

(a) **Bis-(3,5-di-*t*-butyl-1-isopropyl-2,5-cyclohexadiene-4-one) Peroxide (IIIa).**—The yield of this compound was 5 g. (93%), m.p. 122–125° dec. after one recrystallization from ethanol; after three recrystallizations, m.p. 124–126° dec. *Anal.* Calcd. for $C_{34}H_{54}O_4$: C, 77.52; H, 10.33; mol. wt., 526.7. Found: C, 77.36; H, 10.39; mol. wt. (benzene, cryoscopic), 520.

(b) **Bis-(3,5-di-*t*-butyl-1-*sec*-butyl-2,5-cyclohexadiene-4-one) Peroxide (IIIb).**—After one recrystallization from ethanol the yield of this compound was 2.6 g. (50%), m.p. 90–92° dec. *Anal.* Calcd. for $C_{36}H_{58}O_4$: C, 77.93; H, 10.54. Found: C, 77.73; H, 10.28.

(c) **Bis-(3,5-di-*t*-butyl-1-dimethylmethoxymethyl-2,5-cyclohexadiene-4-one) Peroxide.**—After one recrystallization from *n*-hexane the yield was 5 g. (95%), m.p. 135–137°; after two more recrystallizations, m.p. 137–138° dec. *Anal.* Calcd. for $C_{36}H_{58}O_6$: C, 73.68; H, 9.96. Found: C, 74.08; H, 10.34.

Preparation of 1,1,2,2-Tetramethyl-1,2-bis-(3,5-di-*t*-butyl-4-hydroxyphenyl)-ethane.—A *n*-hexane solution of the isopropenylquinonemethide (V) was reduced with zinc and acetic acid to a nearly colorless solution. Extraction with *n*-hexane gave a white product which after three recrystallizations from *n*-hexane melted at 205–220° dec. The ultraviolet spectrum was very much like those of other hindered phenols (see Fig. 1) and the infrared spectrum showed only the presence of the hindered hydroxyl group.

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[8] For details of this technique see G. H. Stilson, D. W. Sawyer and C. K. Hunt, THIS JOURNAL, **67**, 303 (1945); B. G. Somers and C. D. Cook, *J. Chem. Ed.*, **23**, 312 (1955).

[9] (a) W. C. Sears and L. J. Kitchen, THIS JOURNAL, **71**, 4110 (1949) (no data); (b) G. E. P. Smith and H. E. Alpert, U. S. Patent 2,581,907, b.p. 141–141.5° (10 mm.); (c) J. I. Wasson and W. M. Smith, *Ind. Eng. Chem.*, **45**, 197 (1953) (no data).

[10] W. C. Sears and L. J. Kitchen, THIS JOURNAL, **71**, 4110 (1949); C. D. Cook, R. G. Inskeep, A. S. Rosenberg and E. C. Curtis, Jr., *ibid.*, **77**, 1672 (1955).

Anal. Calcd. for $C_{34}H_{54}O_2$: C, 82.53; H, 11.00; mol. wt., 495. Found: C, 82.39; H, 10.89; mol. wt. (Rast, micro), 486.

Lithium Aluminum Hydride Reduction of the Isopropenylquinonemethide.—A five-gram sample of the quinonemethide V was reduced with lithium aluminum hydride according to the procedure of Brown.[11] After vacuum distillation the melting point and infrared spectrum were identical with a sample of 2,6-di-*t*-butyl-4-isopropylphenol.

Addition of Hydrogen Bromide to the Isopropenylquinonemethide (VII).—Anhydrous hydrogen bromide was bubbled through a petroleum ether solution of the quinone methide. On cooling a copious precipitate of white crystals, m.p. 102–111° dec., was formed. On standing in the air the crystals rapidly decomposed.

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(11) W. G. Brown, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MICHIGAN]

Arylation of Unsaturated Systems by Free Radicals. VI.[1] The Meerwein Reaction. IV.[2] The Stereochemistry of the Arylation of Maleic and Fumaric Acid Derivatives

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The Meerwein arylation of the methyl and butyl esters and nitriles of maleic and fumaric acid with *p*-chlorobenzenediazonium chloride gave mixtures of the corresponding derivatives of *p*-chlorophenylmaleic acid and *p*-chlorophenylfumaric acid in a ratio of 1:2. The ratio was independent of the geometry of the starting material. This result is explained by suggesting that the intermediate formed by the attack of the aryl radical on the double bond is incapable of retaining its configuration. A mechanism for the Meerwein reaction is proposed.

The arylation by diazonium salts of a carbon-carbon double bond conjugated with an "activating" group, initiated by cupric chloride,[3] is known as the Meerwein reaction.[4,5] The product is usually a mixture of addition and substitution compounds (types A and B, eq. 1)

$$\mathrm{ArN_2Cl + RCH{=}CRZ \xrightarrow{CuCl_2} \underset{A}{ArCR{=}CRZ} + \underset{B}{ArCHRC(R)ClZ}} \quad (1)$$

Only a few observations on the stereochemistry of the Meerwein reaction have been recorded to date. Bergmann, Dimant and Japhe[6] found that the two stereoisomeric forms of β-phenyl-β-*p*-bromophenylacrylic acid were converted to the same 1-phenyl-1-*p*-bromophenyl-2-*p*-nitrophenylethene upon reaction with *p*-nitrobenzenediazonium chloride, the yields being 30 and 11%. Taylor and Strojny[7] obtained 6% of phenylmaleic anhydride and 12% of phenylfumaric acid from benzenediazonium chloride and methyl maleate, although the alkaline hydrolysis may have caused partial isomerization of one form to the other.[4] Meerwein, Büchner and van Emster[4] used *p*-chlorobenzenediazonium chloride with methyl fumarate, but they demonstrated that their alkaline hydrolysis conditions caused isomerization so that the sole product was *p*-chlorophenylfumaric acid. In their parallel experiment with methyl maleate, the saponification conditions were selected so as not to cause isomerization, and they obtained 28% of *p*-chlorophenylfumaric acid and 19% of *p*-chlorophenylmaleic anhydride.

Since none of these experiments provides conclusive evidence about the stereochemistry of the Meerwein reaction, we have investigated the reaction of *p*-chlorobenzenediazonium chloride with three *cis-trans* pairs, the methyl and butyl esters and the nitriles of maleic and fumaric acids. This diazonium salt was selected on the basis of preliminary experiments which showed that it gave good yields of products with convenient physical properties.

The reactions were conducted according to standardized conditions developed previously.[2] The crude products (mixtures of types A and B) were treated with 2,6-lutidine or 2,4,6-collidine to convert type B into type A. The amount of chlorine thus eliminated was determined by weighing the amine hydrochloride formed, and checked by hydrolysis with alcoholic alkali; approximately one-third mole of eliminatable chlorine per mole of *p*-chloroaniline was found in each example.[8] The small amount of tarry by-product was removed by filtration through a column of activated alumina, and the eluate was evaporated under high vacuum to remove volatile impurities. A small amount of diarylated material (resulting from further arylation of type A product) was not removed by this treatment. The stereoisomer ratio in the residue was determined by infrared spectroscopy. The stereochemical results are given in Table I.

The pure stereoisomeric esters required for infrared comparison were prepared from the available[5] *p*-chlorophenylmaleic anhydride and *p*-chlorophenylfumaric acid; different methods of esterification gave the same esters, indicating that isomerization had not occurred. The stereoisomeric nitriles were isolated from a large-scale arylation of fumaronitrile, and their configurations were es-

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(1) Paper V, C. S. Rondestvedt, Jr., and H. S. Blanchard, *J. Org. Chem.*, **21**, 229 (1956).

(2) Paper III, C. S. Rondestvedt, Jr., and O. Vogl, THIS JOURNAL, **77**, 3401 (1955).

(3) See, however, J. K. Kochi, *ibid.*, **77**, 5090 (1955).

(4) H. Meerwein, E. Büchner and K. van Emster, *J. prakt. Chem.*, **152**, 237 (1939).

(5) The literature has been reviewed by C. S. Rondestvedt, Jr., and O. Vogl, THIS JOURNAL, **77**, 2313 (1955). See also ref. 3.

(6) F. Bergmann, E. Dimant and H. Japhe, *ibid.*, **70**, 1618 (1948).

(7) E. C. Taylor, Jr., and E. J. Strojny, *ibid.*, **76**, 1872 (1954).

(8) It is tempting to seek some significance in the constancy of the amount of eliminatable chlorine. However, since the yield of arylation product (see below) varies widely, it seems unwise to attempt to explain this possibly fortuitous coincidence in the absence of further evidence.