chem., in press.
(37) Since the submission of this manuscript a strong correlation has been reported for the quenching in acetonitrile of the triplet states of acetone and four aromatic ketones by tetramethylethylene.[28]
(38) Cf., for example, R. G. Brown and D. Phillips, *J. Am. Chem. Soc.*, **96**, 4784 (1974).
(39) T. Kubota, K. Shima, and H. Sakurai, *Chem. Lett.*, 343 (1972); A. A. Gorman and R. L. Leyland, *Tetrahedron Lett.*, 5345 (1972).

Base-Catalyzed Oxygenation of *tert*-Butylated Phenols. 1. Regioselectivity in the Base-Catalyzed Oxygenation of *tert*-Butylphenols[1]

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Abstract: In the oxygenation of 4-alkyl-2,6-di-*tert*-butylphenols (**1**) catalyzed by potassium *tert*-butoxide, molecular oxygen is added to the phenolates regioselectively depending on the solvent. In aprotic solvents the para position of the phenolates is oxygenated exclusively, and the resulting *p*-hydroperoxy anion intermediates (**5'**) are converted to the corresponding epoxy-*p*-quinols (**2**). In *tert*-butyl alcohol, the ortho position is oxygenated predominantly, resulting in *o*-hydroperoxy anion intermediates (**16'**) which are converted to epoxy-*o*-quinols (**11**). The oxygenation of 2,6-di-*tert*-butyl-4-methylphenol in *N,N*-dimethylformamide in the presence of a large amount of potassium *tert*-butoxide results in the selective oxidation of the methyl group to give 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde. In the *tert*-butoxide-catalyzed oxygenation of 2,4-di-*tert*-butylphenols (**6**) in aprotic solvents, epoxy-*p*-quinols (**7, 8**) are formed. In *tert*-butyl alcohol epoxy-*o*-quinols (**11**) as well as products (**14, 15**) resulting from ring cleavage are formed. The solvent-dependent regioselectivity may be interpreted in terms of the stability of the peroxy anion intermediates to which the counter cation (K^+) contributes depending on the solvent.

Base-catalyzed oxygenation of phenols involves oxidation of carbanions generated on the phenolic ring through resonance structures of the phenolate anions. The oxidizability of phenolates depends on their redox potential which, in turn, depends on the nature of the substituents on the aromatic ring. Electron-releasing groups lower the potential which results in an increase of the reactivity, whereas electron-withdrawing groups raise it.[2-5] The oxygenation of phenolates generally leads to a complex reaction mixture resulting from the introduction of oxygen as well as from oxidative coupling of the phenolic ring.[6-8] If, however, *tert*-butyl groups are in the ortho and para positions, a less complex reaction mixture is obtained since no or little oxidative coupling takes place owing to steric hindrance by the bulky *tert*-butyl groups. Base-catalyzed oxygenation of 2,6-di-*tert*-butylphenols in alcoholic alkaline solutions mainly gives 2,6-di-*tert*-butyl-4-hydroperoxy-2,5-cyclohexadienones.[9-14] Semiquinone radicals have been detected in the oxygenation of 4-alkyl-2,6-di-*tert*-butylphenols in aqueous acetone containing potassium hydroxide.[15] Recently, the oxygenation of 4-alkyl-2,6-di-*tert*-butylphenols in diethylamine containing sodium amide has been shown to provide a convenient method for the synthesis of 2,6-di-*tert*-butyl-4-hydroxy-2,5-cyclohexadienones (*p*-quinols).[16]

The present paper deals with the oxygeantion of 2,6- and 2,4-di-*tert*-butylphenols (**1, 6**) catalyzed by potassium *tert*-butoxide. A regioselectivity depending on the solvent used was observed. In aprotic solvents such as *N,N*-dimethylformamide (DMF), dimethyl sulfoxide (Me_2SO), and hexamethyl phosphoric triamide (HMPT), both phenols are oxygenated exclusively at the para position to give epoxy-*p*-quinols (**2, 7, 8**) in good yields. In *tert*-butyl alcohol, an ortho position is oxygenated predominantly resulting in the formation of epoxy-*o*-quinols (**11**). Both epoxyquinols are formed via hydroperoxy anion intermediates. In the case of 2,4-di-*tert*-butylphenol (**6b**), the hydroperoxy anion intermediate is converted not only to the epoxy-*o*-quinol, but also to products resulting from oxidative ring cleavage. The formation of the epoxy-*p*-quinols is of particular interest in connection with the biosynthesis of the naturally occurring epoxy-*p*-quinols such as epoxidone (**10**), a fungal metabolite.[17] Interestingly, the use of a large amount of potassium *tert*-butoxide in DMF in the oxygenation of 2,6-di-*tert*-butyl-4-methylphenol (**1d**) leads to the selective oxidation of the methyl group with formation of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (**1e**). The regioselective oxygenation of *tert*-butylphenols can be exploited for the synthesis of new compounds.[18-22] This regioselectivity may be interpreted in terms of the stability of the hydroperoxy anion intermediates.

Results

Formation of Epoxy-*p*-quinols. When 4-alkyl-2,6-di-*tert*-butylphenols (**1a–d,** Chart I) and 2,4-di-*tert*-butylphenols (**6a, 6b,** Chart II) are oxygenated (oxygen bubbling at ambient temperature) in aprotic solvents such as DMF, Me_2SO, and

Chart I

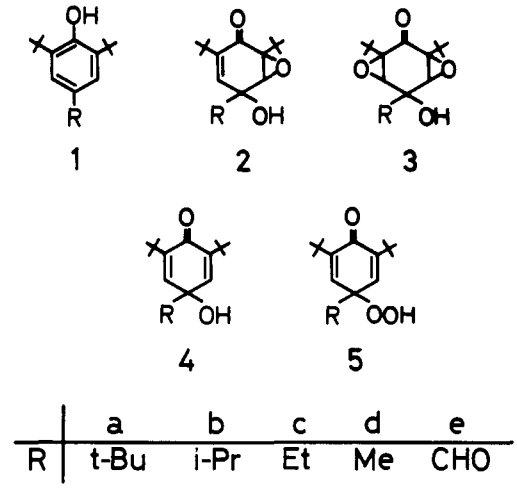

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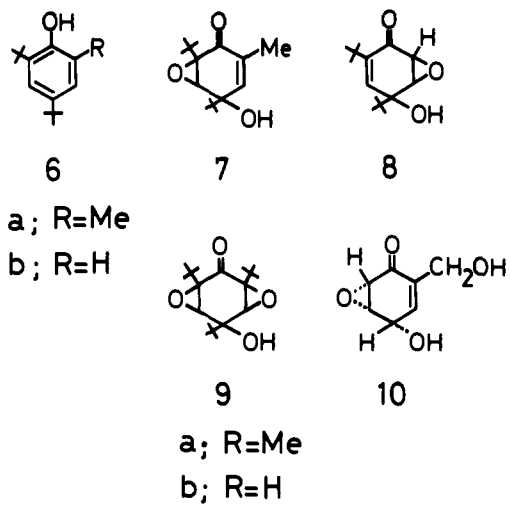
Table I. Base-Catalyzed Oxygenation of **1a–d** in Aprotic Solvent[a]

Run	Phenol	Base	Base/phenol mol/mol	Solvent	Product, (% yield[b])
1	**1a**	*t*-BuOK	0.5	DMF	**2a** (52), **3a** (14), **4a** (26)
2		*t*-BuOK	4.5	DMF	**2a** (100)
3		*t*-BuONa	4.0	DMF	**2a** (85), **3a** (15)
4		*t*-BuOK	4.5	Me_2SO	**2a** (100)
5		*t*-BuOK	4.5	HMPT	**2a** (100)
6		MeOK	4.5	HMPT	**2a** (90)
7	**1b**	*t*-BuOK	4.5	DMF	**2b** (89), **1** (R = COMe) (trace)
8	**1c**	*t*-BuOK	4.5	DMF	**2c** (59), **1e** (10)
9		*t*-BuOK	4.5	HMPT	**2c** (94)
10	**1d**	*t*-BuOK	4.5	DMF	**2d** (9), **3d** (6), **4d** (9), **1e** (58)
11		*t*-BuOK	2.0	DMF	**2d** (22), **3d** (18), **4d** (30), **1e** (4)
12		*t*-BuOK	10.0	DMF	**1e** (100)
13		*t*-BuOK	2.0	Me_2SO	**2d** (67)
14		*t*-BuOK	9.0	HMPT	**3d** (91)

[a] Oxygen was bubbled through the solutions at 40 °C for 1 h. [b] Yields were determined by NMR.

Chart II



HMPT containing *t*-BuOK, the corresponding 5,6-epoxy-4-hydroxy-2-cyclohexenones (epoxy-*p*-quinols) **2, 7,** and **8** are obtained. The oxygenation was completed normally in 1 h for DMF and Me_2SO, but required a longer time for HMPT. The products were isolated as crystalline solids. The structures of **2a–d** were confirmed on the basis of analytical and spectral data. The oxidation of **2a–d** with *tert*-butyl hydroperoxide in DMF containing *t*-BuOK quantitatively gave diepoxides **3a–d,** which provides additional evidence for the structures of **2a–d.** Yields of **2** are dependent on the nature of the solvent and the amount of base used (Table I). The best yield of **2** was obtained in HMPT, where the yield of **2** is independent of the size of the 4-alkyl group, whereas in DMF the yield decreases with decreasing size of the 4-alkyl group. In the latter case, oxidation of the 4-alkyl group takes place to some extent (Table I). The use of a smaller amount of base makes the reaction complex (Table I, run 1). The oxygenation of **1d** with a larger amount of *t*-BuOK in DMF, on the other hand, gave 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (**1e**) in quantitative yield.

A kinetic investigation of the reaction of **1a** indicates that the reaction is first order with respect to **1a** and nearly ten times faster at 35 °C than at 0 °C (the pseudo-first-order rate constants estimated under the reaction conditions depicted in Figure 1 are 9.9×10^{-2} min^{-1} (35 °C) and 8.9×10^{-3} min^{-1} (0 °C)). The rate of formation of **2a** is identical with that of the disappearance of **1a** (Figure 1). Total oxygen uptake was 1 mol/mol of **1a.**

The oxygenation of 2,6-di-*tert*-butylphenol (**1,** R = H) with *t*-BuOK in DMF gave 2,6-di-*tert*-butyl-*p*-benzoquinone in nearly quantitative yield, whereas in Me_2SO two products, $C_{14}H_{22}O_3$,[23] mp 74–76 °C (25%) and 2,6-di-*tert*-butyl-*p*-benzoquinone (50%) were obtained.

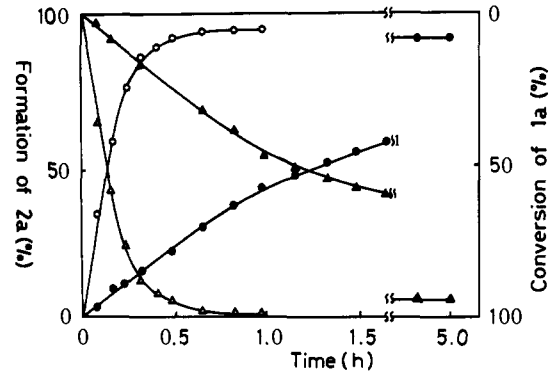
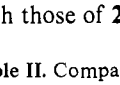
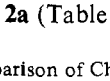


Figure 1. Oxygenation of **1a** in DMF with *t*-BuOK: [**1a**] 40 mM, [*t*-BuOK] 0.18 M. Conversion of **1a**: △ (35 °C), ▲ (0 °C). Formation of **2a**: ○ (35 °C), ● (0 °C).

In the oxygenation of 2,4-di-*tert*-butyl-6-methylphenol (**6a**) with *t*-BuOK in DMF or HMPT, 4,6-di-*tert*-butyl-5,6-epoxy-4-hydroxy-2-methyl-2-cyclohexenone (**7**) and 4,6-di-*tert*-butyl-2,3,5,6-diepoxy-4-hydroxy-2-methyl-2-cyclohexenone (**9a**) were isolated in 66 and 20% yield, respectively. The oxygenation of 2,4-di-*tert*-butylphenol (**6b**) under similar conditions gave 2,4-di-*tert*-butyl-5,6-epoxy-4-hydroxy-2-cyclohexenone (**8**) in 56 (in DMF) or 60% (in HMPT) yield and the diepoxide **9b** in 28 (in DMF) or 20% (in HMPT) yield.

Formation of 2,4,6-Tri-*tert*-butyl-6-hydroxy-4,5-epoxy-2-cyclohexenone (Epoxy-*o*-quinol). When the oxygenation of **1a** was carried out in *tert*-butyl alcohol with *t*-BuOK at 40 °C, the reaction stopped after an equimolar amount of oxygen had been taken up (1 h). The product was isolated as a crystalline solid. Elemental analysis showed the same composition as that of **2a.** The structure **11a** (epoxy-*o*-quinol) for the product can be deduced from a comparison of its NMR and UV spectra with those of **2a** (Table II). Epoxy-*o*-quinol **11a** (Chart III)

Table II. Comparison of Characteristic Spectral Data of **2a** and **11a**

	^{1}H NMR ($CDCl_3$), δ (ppm)			
Compd	OH			UV (MeOH), λ_{max}, nm (ε)
2a	4.02	3.80[a]	6.98[a]	255 (7100)
11a	2.22	3.65[b]	5.98[b]	244 (7800)

[a] Doublet, J = 3 Hz. [b] Doublet, J = 1 Hz.

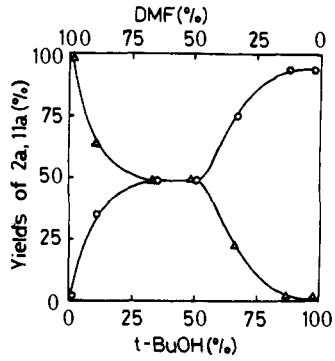
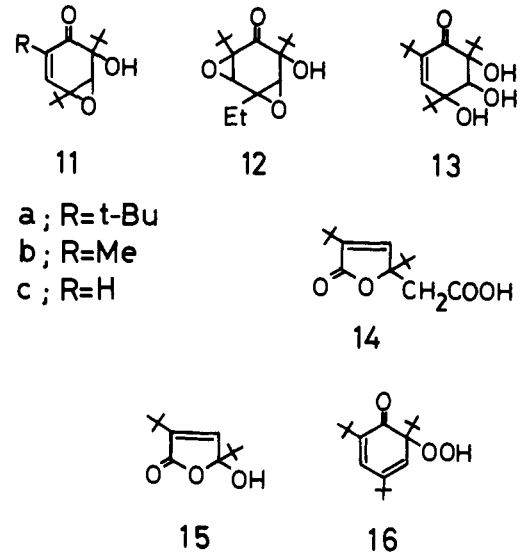


Figure 2. Formation of **2a** and **11a** in the oxygenation of **1a** in the mixture of *t*-BuOH and DMF containing *t*-BuOK.

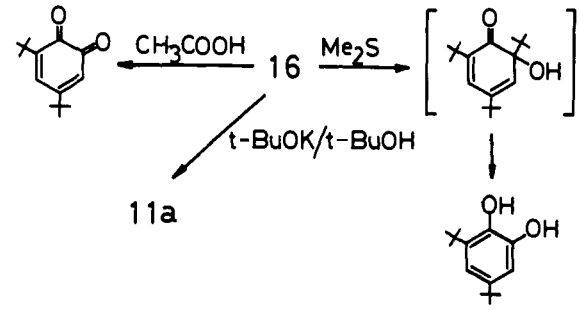
Chart III



was also obtained in the oxygenation of **1a** with *t*-BuOK or *t*-BuONa in *tert*-pentyl alcohol or *tert*-butylamine. The yield of **11a** as determined by NMR depends on the reaction system: 91% in *tert*-butyl alcohol with *t*-BuOK, 90% in *tert*-butyl alcohol with *t*-BuONa, 68% in *tert*-pentyl alcohol with *t*-BuOK, and 93% in *tert*-butylamine with *t*-BuOK. In the oxygenation of **1a** with *t*-BuOK in a mixture of DMF and *tert*-butyl alcohol, **2a** and **11a** are formed. The yield of **2a** and **11a** depends on the proportion of the solvents and are nearly equal in a 1:1 mixture of DMF and *tert*-butyl alcohol (Figure 2). This indicates that the formation of these products is controlled by the nature of the solvents.

6-Hydroperoxy-2,4,6-tri-*tert*-butyl-2,4-cyclohexadienone (16). When the oxygenation of **1a** with *t*-BuOK in *tert*-butyl alcohol was carried out below 20 °C (if necessary, a small amount of petroleum ether was added to avoid freezing of the solvent), 6-hydroperoxy-2,4,6-tri-*tert*-butyl-2,4-cyclohexadienone (**16**) was obtained in 70% yield. The structure **16** was confirmed by the liberation of iodine from potassium iodide, the formation of 3,5-di-*tert*-butyl-*o*-benzoquinone with trifluoroacetic acid, and the formation of 3,5-di-*tert*-butylcatechol with dimethyl sulfide. The di-*tert*-butylcatechol was formed by de-*tert*-butylation of the corresponding *o*-quinol, the primary reduction product. When a solution of **16** and *t*-BuOK in *tert*-butyl alcohol was heated at 60 °C for 3 min the epoxy-*o*-quinol **11a** was obtained in 90% yield (Scheme I), whereas treatment in DMF at room temperature for 5 min gave **1a** and **11a** in 60 and 40% yield, respectively. When the oxygenation was carried out at ~30 °C, a mixture of **11a** and **16** was obtained. These results strongly suggest that the hydroperoxide anion (**16'**) is an intermediate in the formation of

Scheme I



11a from **1a** and that the oxygenation in *tert*-butyl alcohol containing *t*-BuOK occurs predominantly at an ortho position of **1a.**

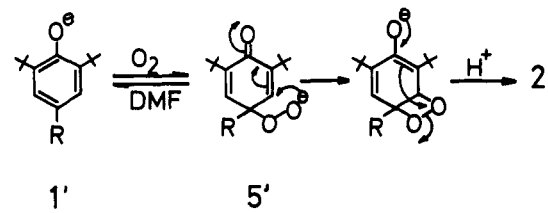
Oxygenation of 2,4-Di-*tert*-butylphenol (6b). The oxygenation of 2,4-di-*tert*-butylphenol (**6b**) with *t*-BuOK in *tert*-butyl alcohol at room temperature gave 2,4-di-*tert*-butyl-4-carboxymethyl-2-buten-4-olide (**14**)[24] and 2,4-di-*tert*-butyl-4-hydroxy-2-buten-4-olide (**15**)[25] in 51 and 10% yield, respectively, and 4,6-di-*tert*-butyl-5,6-epoxy-4-hydroxy-2-cyclohexenone (**11c**) in 17% yield. Lactones **14** and **15** have been shown to result from the base-catalyzed oxygenation of 3,5-di-*tert*-butyl-*o*-benzoquinone.[25] It is therefore reasonable to assume that these lactones have been formed from **6b** via the 3,5-di-*tert*-butyl-*o*-benzoquinone intermediate. This provides additional evidence that the oxygenation of the *tert*-butylated phenols in *tert*-butyl alcohol containing *t*-BuOK occurs predominantly at the ortho position.

Oxygenation of Other Phenols with *t*-BuOK in *tert*-Butyl Alcohol. The preferential ortho oxygenation in the *tert*-butyl alcohol/*t*-BuOK system becomes less pronounced with decreasing size of the *p*-alkyl group in **1a.** Thus, **1c** gave 2,6-di-*tert*-butyl-4-ethyl-6-hydroxy-2,4-cyclohexadienone diepoxide (**12**) and *p*-quinol **4c,** both in 30% yield. With **1d** no ortho hydroperoxylation but only para hydroperoxylation took place. From the oxygenation of **6a** epoxy-*o*-quinol **11b** was isolated in 10% yield and 2,4-di-*tert*-butyl-6-methyl-4,5,6-trihydroxy-2-cyclohexenone (**13**) in 30% yield.

Discussion

The oxygenation at 0 °C of **1** in methanol, ethanol, or 2-propanol containing potassium hydroxide gives rise to the corresponding *p*-hydroperoxides **5** in nearly quantitative yield. This is apparently due to the stabilization of the peroxy anion **5'** through hydrogen bonding with the hydroxy group of the solvents. No epoxy-*p*-quinol is formed from the reaction of *p*-quinols **4** with hydroperoxides **5** or *tert*-butyl hydroperoxide. When hydroperoxide **5a** was dissolved in DMF containing *t*-BuOK, most of **5a** (~90%) reverted instantaneously to **1a** with the liberation of O_2 and the remainder was quantitatively converted to **2a.** Similar reactions were observed with the other hydroperoxides **5.** These results strongly suggest that the dioxygen addition takes place reversibly at the para position and the peroxy anions **5'** are quite unstable unless they are solvated. They undergo an intramolecular decomposition and give in an oxygen atmosphere epoxy-*p*-quinols as shown in Scheme II. The intermediacy of **5'** is also supported by the facts

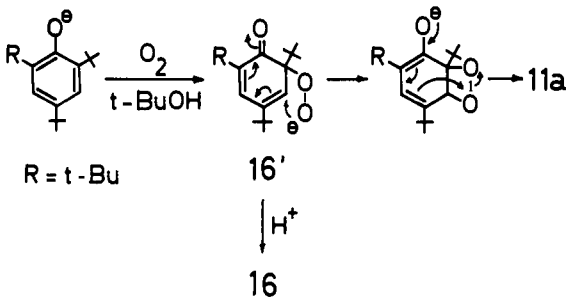
Scheme II



that the rates of oxygen uptake, disappearance of the starting phenol, and formation of the product **2a** in the oxygenation of **1a** are identical and that only **1a** and **2a** are detectable during the course of the reaction. The kinetic study and the decomposition of **5'** also indicate that the intramolecular decomposition of **5'** is the rate-determining step and that the equilibrium between **1'** and **5'** is shifted very much toward **1'** so that the hydroperoxide **5** cannot be detected during the reaction. Since the mechanism for the formation of **2** should be the same as that operating in the oxygenation which gives rise to the epoxy-*o*-quinols, it is reasonable to assume an intramolecular Michael addition of **5'** followed by an unusual asymmetric decomposition of the resulting dioxetane intermediate. Association of the potassium cation with DMF destabilizes the peroxy anion and enhances its nucleophilicity.[26] This, therefore, strongly suggests a cis configuration for the hydroxy and epoxy groups in **2.**

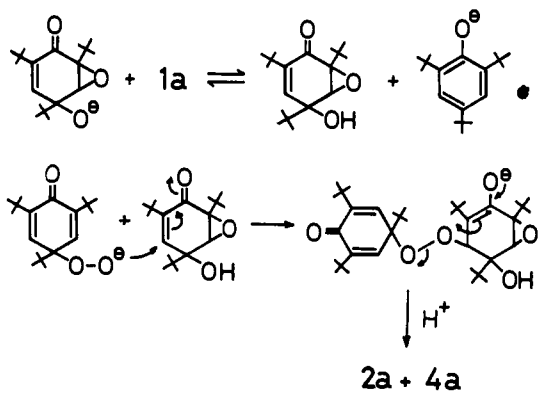
In the oxygenation of **1a** in the *tert*-butyl alcohol/*t*-BuOK system, the hydroperoxide anion **16'** has been demonstrated to be an intermediate in the formation of **11a.** In addition, both **2a** and **11a** are quite stable in the DMF/*t*-BuOK system as well as in the *tert*-butyl alcohol/*t*-BuOK system so that **2a** and **11a** are not interconvertible. This eliminates the possibility that one of these may be an intermediate for the other. Furthermore, the conversion of **16** to **11a** follows first-order kinetics with a rate constant of 6.7×10^{-2} min^{-1} (40 °C). It is therefore obvious that the conversion is an intramolecular reaction. From these findings, Scheme III has been derived for the formation of **16** and **11a** from **1a.**

Scheme III



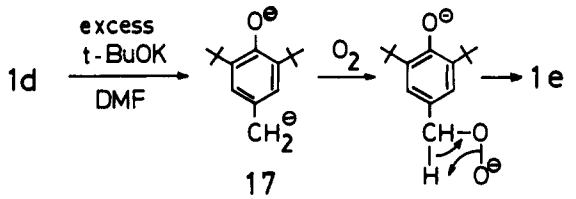
The complexity in the oxygenation of **1** with a lesser amount of base may result from proton transfer equilibrium between undissociated **1a** and the anionic form of the product. Thus, the formation of a mixture of **2a, 3a,** and **4a** from **1a** (Table I, run 1) may be interpreted as shown in Scheme IV.

Scheme IV



It is, however, particularly noteworthy that in DMF with a large excess of *t*-BuOK th oxygenation of **1d** does not result in ring oxidation, but in side-chain oxidation to give the aldehyde **1e.** The mechanism of this reaction is not clear but the assumption can be made that with a large excess of *t*-BuOK the *p*-methyl group of **1d** undergoes deprotonation to form the dianion **17.** The benzylic carbanion hinders further carbanion formation on the aromatic ring because of electronic repulsion, so that the phenolate is fixed in the phenoxide form which is not susceptible to oxygenation. Consequently, only the benzylic anion can now be oxygenated with the formation of **1e,** as shown in Scheme V. This assumption is supported by the fact

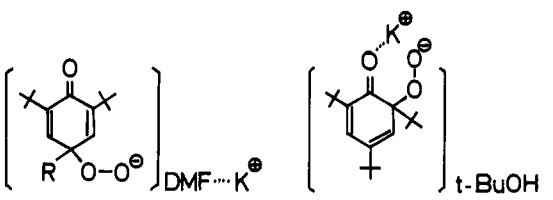
Scheme V



that the yield of **1e** increases with an increasing amount of base (Table I, runs 10-12), although the possibility that **5d** is an intermediate cannot be excluded entirely. The selective oxygenation of the methyl group in *p*-cresols is due to the nature of the substituent: electron-releasing groups accelerate the oxidations.[27]

The solvent-dependent regioselectivity observed in the oxygenation of **1** may be rationalized in terms of the stability of the peroxy anion intermediates. Since the potassium ion associates with polar solvents such as DMF, Me_2SO, and HMPT more strongly than with alcohols,[26,28] the peroxy anion intermediates **5'** will be in a free state in these solvents. Electronic repulsion between the resulting free peroxy anion and the carbonyl group of the cyclohexadienone intermediates results in the preferential addition of the peroxy anion in the para position.

The peroxy anion intermediate in *tert*-butyl alcohol, on the other hand, seems to undergo stabilization by association with the counter cation K^+ and partly also by solvation through hydrogen bonding. With a smaller R group in **1** steric hindrance is minimized so that the peroxy anion intermediate formed from **1d** is stabilized at the para position, which results in the formation of the hydroperoxide **5d.** In the case of the peroxy anion intermediate from **1a** the magnitude of the steric hindrance is about the same at the ortho and para positions. In that case, the stabilization of the peroxy anion is at the ortho position appears to be due to chelate formation with the carbonyl group of the intermediate. Direct attack of molecular oxygen at the ortho position of **1a** in *tert*-butyl alcohol cannot



be ruled out since association of the 4-alkyl-2,6-di-*tert*-butylphenolate anion with potassium ion has been demonstrated.[29]

Experimental Section

General. All melting points are uncorrected. Elemental analyses were performed by the Analytical Center of Kyoto University. Infrared spectra were recorded with a Jasco IRA-1 spectrometer. Ultraviolet spectra were recorded with a Shimazu UV 200 spectrophotometer. Proton magnetic resonance spectra were recorded with a Varian T-60 spectrometer using Me_4Si as the internal reference.

Starting Phenols. Phenols **1a, 1d, 6b,** and 2,6-di-*tert*-butylphenol are commercially available and were purified by repeated recrystallization from methanol, if necessary. Phenols **1b, 1c,** and **6a** were synthesized according to published methods[30,31] and purified by repeated recrystallization from methanol.

Base-Catalyzed Oxygenation of 4-Alkyl-2,6-di-*tert*-butylphenols (1a–d) in HMPT. Oxygen was bubbled for 1 h at room temperature through the solutions of **1a–d** (1 mmol) in HMPT (25 mL) containing *t*-BuOK (1.0 g). The resulting yellow solutions were poured into ice-cooled water to give **2a–d** as crystalline products, which were collected by suction and recrystallized from hexane. Spectral and analytical data are given below.

2a: colorless prisms; mp 133–134 °C; IR (Nujol) 3520 (OH), 1690 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.98 (s, 9 H), 1.12 (s, 9 H), 1.16 (s, 9 H), 2.22 (s, 1 H, OH), 3.65 (d, J = 3 Hz, 1 H), 5.98 (d, J = 3 Hz, 1 H). Anal. Calcd for $C_{18}H_{30}O_3$: C, 73.43; H, 10.27. Found: C, 73.24; H, 10.35.

2b: colorless prisms; mp 62–63 °C; IR (Nujol) 3520 (OH), 1690 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.11 (s, 9 H), 1.17 (s, 9 H), 0.97 (d, J = 7 Hz, 6 H), 1.90 (sept, J = 7 Hz, 1 H), 2.35 (s, 1 H, OH), 3.52 (d, J = 3 Hz, 1 H), 5.98 (d, J = 3 Hz, 1 H). Anal. Calcd for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 72.53; H, 10.13.

3c: colorless prisms; mp 86–87 °C; IR (Nujol) 3350 (OH), 1690 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.11 (s, 9 H), 1.17 (s, 9 H), 0.84 (t, J = 8 Hz, 3 H), 1.74 (q, J = 8 Hz, 2 H), 2.79 (s, 1 H, OH), 3.48 (d, J = 3 Hz, 1 H), 5.98 (d, J = 3 Hz, 1 H). Anal. Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 71.88; H, 9.95.

2d: colorless prisms; mp 102–103 °C; IR (Nujol) 3350 (OH), 1690 (C=O) cm^{-1}; NMR ($CDCl_3$) 1.11 (s, 9 H), 1.15 (s, 9 H), 1.35 (s, 3 H), 2.30 (s, 1 H, OH), 3.53 (d, J = 3 Hz, 1 H), 6.05 (d, J = 3 Hz, 1 H). Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.14; H, 9.80.

Kinetics. A DMF (20 mL) solution containing **1a** (40 mM) and *t*-BuOK (0.18 M) was stirred at temperatures given in Table I under an atmospheric pressure of oxygen. Aliquot was taken up at 10-min intervals and the amounts of **1a** and **2a** in the aliquot were determined by NMR during the course of the reaction. In a separate experiment, oxygen uptake was determined by gas volumetry with a gas buret at the given temperatures under the constant atmospheric pressure of oxygen.

4-Alkyl-2,6-di-*tert*-butyl-2,3,5,6-diepoxy-4-hydroxycyclohexanones (3a–d). To solutions of **2a–d** (1 mmol) in DMF (10 mL) containing *t*-BuOK (4.5 mmol) was added *tert*-butyl hydroperoxide (5 mmol). The solutions were allowed to stand at room temperature for 30 min. The reaction mixtures were poured into ice-cooled water to give the diepoxides **3a–d** as crystalline solids, which were collected by suction and recrystallized from petroleum ether. Spectral and analytical data are given below.

3a: colorless prisms; mp 87–88 °C; IR (Nujol) 3540, 3480, 3440 (OH), 1710 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.06 (s, 18 H), 1.13 (s, 9 H), 2.67 (s, 1 H, OH), 3.60 (s, 2 H). Anal. Calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.64; H, 9.89.

3b: colorless prisms; mp 75–76 °C; IR (Nujol) 3530, 3450 (OH), 1710 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.07 (s, 18 H), 1.09 (d, J = 8 Hz, 6 H), 2.06 (sept, J = 8 Hz, 1 H), 2.83 (s, 1 H, OH), 3.38 (s, 2 H). Anal. Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 68.75; H, 9.67.

3c: colorless prisms; mp 109–110 °C; IR (Nujol) 3300 (OH), 1710 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.05 (s, 18 H), 1.00 (t, J = 8 Hz, 3 H), 1.79 (q, J = 8 Hz, 2 H), 2.28 (s, 1 H, OH), 3.35 (s, 2H). Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.05; H, 9.28. Found: C, 67.83 H, 9.37.

3d: colorless prisms; mp 141–142 °C; IR (Nujol) 3530 (OH), 1710 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.04 (s, 18 H), 1.37 (s, 3 H), 3.13 (s, 1 H, OH), 3.41 (s, 2 H). Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02. Found: C, 66.89; H, 9.01.

Oxygenation of 4-Alkyl-2,6-di-*tert*-butylphenols (1b–d) in DMF Containing *t*-BuOK. Oxygen was bubbled through solutions of **1b–d** in DMF (25 mL) containing *t*-BuOK (1.0 g) at room temperature for 1 h. The resulting solutions were poured into ice-cooled water, acidified with dilute hydrochloric acid, and extracted with ether. The extracts were washed with water, dried (Na_2SO_4), and evaporated to leave pale yellow residues. The products were separated by silica gel chromatography. A thin layer chromatographic separation of the products from **1b** developing with benzene gave **2b** (0.49 g) and 3,5-di-*tert*-butyl-4-hydroxyacetophenone (**1**, R = $COCH_3$) (0.01 g) which was identical with an authentic sample[32] (IR and NMR). The products from **1c** were chromatographed on a silica gel column eluting with a mixture of petroleum ether and benzene (1:1) to give **2c** (0.47 g) and 2,6-di-*tert*-butyl-4-hydroxybenzaldehyde (**1e**, 0.02 g) which was identical with an authentic sample[33] (IR and NMR). The products from **1d** were chromatographed on a silica gel column. Eluting with a mixture of petroleum ether and benzene (1:1) gave **1e** (0.05 g) and 2,6-di-*tert*-butyl-4-hydroxy-4-methyl-2,5-cyclohexadienone (**4d**, 0.17 g) which was identical with an authentic sample[16] (IR and NMR). Elution with a mixture of petroleum ether and benzene (1:2) gave **2d** (0.11 g).

Similar procedures were applied for the oxygenation of phenols **6** in DMF with *t*-BuOK and products were isolated by means of silica gel column chromatography.

7: colorless prisms; mp 98–99 °C; IR (Nujol) 3540 (OH), 1675 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.03 (s, 9 H), 1.13 (s, 9 H), 1.83 (d, J = 2 Hz, 3 H), 2.16 (s, 1 H, OH), 3.38 (d, J = 3 Hz, 1 H), 6.10 (d d, J = 2, 3 Hz, 1 H). Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.45; H, 9.71.

8 (this was not purified completely because of a sticky contamination of diepoxide **9b** but characterized by its IR and NMR spectra): IR (Nujol) 3500 (OH), 1690 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.00 (s, 9 H), 1.53 (s, 9 H), 2.10 (s, 1 H, OH), 3.70 (d d, J = 3, 4 Hz, 1 H), 3.46 (d, J = 4 Hz, 1 H), 6.08 (d, J = 3 Hz, 1 H).

The structures **7** and **8** were further confirmed by the epoxidation of these compounds to give diepoxides **9** quantitatively according to the method using *tert*-butyl hydroperoxide described above.

9a: colorless prisms; mp 60–62 °C; IR (Nujol) 3540, 3460 (OH), 1715 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.03 (s, 9 H), 1.07 (s, 9 H), 1.85 (s, 3 H), 2.93 (s, 1 H, OH), 3.47 (d, J = 4 Hz, 1 H), 3.64 (d, J = 4 Hz, 1 H). Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02. Found: C, 66.72; H, 9.20.

9b: colorless prisms; mp 99–100 °C; IR (Nujol) 3490 (OH), 1710 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.04 (s, 9 H), 1.11 (s, 9 H), 3.06 (s, 1 H, OH), 3.70–3.23 (m, 3 H). Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72. Found: C, 65.86; H, 8.86.

Oxygenation of 2,6-Di-*tert*-butylphenol (1, R = H) in Me_2SO Containing *t*-BuOK. Oxygen was bubbled through a solution of **1** (R = H) (1.03 g, 5 mmol) and *t*-BuOK (1.12 g, 10 mmol) for 40 min at room temperature. The reaction mixture was poured into ice-cooled dilute hydrochloric acid and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on a silica gel column (100 g). Elution with benzene gave colorless crystalline product (0.3 g), which was recrystallized from petroleum ether to give colorless needles: mp 74–76 °C; IR (Nujol) 1706, 1655, 1645 cm^{-1} (no OH band); NMR ($CDCl_3$) δ 1.18 (s, 9 H), 1.24 (s, 9 H), 4.1–4.7 (m, 3 H), 5.50 (s, 1 H). Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.55; H, 9.31. Found: C, 70.54; H, 9.60.

Further elution with benzene gave 2,6-di-*tert*-butyl-*p*-benzoquinone (0.55 g), which was identical with an authentic sample (melting point, NMR, and IR).

Similar oxygenation of **1** (R = H) in DMF afforded only 2,6-di-*tert*-butyl-p-benzoquinone.

Selective Formation of 3,5-Di-*tert*-butyl-4-hydroxybenzaldehyde (1e) from 1d. Oxygen was bubbled through a solution of **1d** (2 mmol) in DMF (20 mL) containing *t*-BuOK (20 mmol) at room temperature for 12 h. The reaction mixture was poured into ice-cooled water and acidified with dilute hydrochloric acid to give 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (**1e**) as a crystalline solid which was collected by suction, yield 90%. TLC showed a single spot for the aldehyde and the product was identical with an authentic sample (IR and NMR).

Oxygenation of 2,4,6-Tri-*tert*-butylphenol (1a) in *t*-BuOH Containing *t*-BuOK. Oxygen was bubbled through a solution of **1a** (0.52 g) and *t*-BuOK (1.0 g) in *t*-BuOH (25 mL) at 40 °C for 1 h. The solution turned yellow. The resulting yellow solution was poured into ice-cooled water, acidified with dilute hydrochloric acid, and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to leave a pale yellow crystalline residue. Recrystallization of the residue from hexane gave 4,5-epoxy-6-hydroxy-2,4,6-tri-*tert*-butyl-2-cyclohexenone (**11a**, 0.54 g), colorless prisms: mp 59–60 °C; IR (Nujol) 3520 (OH), 1680 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.89 (s, 9 H), 1.08 (s, 9 H), 1.23 (s, 9 H), 4.02 (s, 1 H, OH), 3.80 (d, J = 1 Hz, 1 H), 6.98 (d, J = 1 Hz, 1H). Anal. Calcd for $C_{18}H_{30}O_3$: C, 73.43; H, 10.27. Found: C, 73.22, H, 10.51.

Oxygenation of 2,6-Di-*tert*-butyl-4-ethylphenol (1c) in *t*-BuOH Containing *t*-BuOK. Oxygen was bubbled through a solution of **1c** (0.48 g) and *t*-BuOK (1.0 g) in *t*-BuOH (25 mL) at 40 °C for 1 h. The reaction mixture was poured into ice-cooled water, acidified with dilute hydrochloric acid, and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to give a semicrystalline mass. Trituration of the mass with hexane gave colorless prisms, which

were recrystallized from hexane to give 2,5-di-*tert*-butyl-2,3,4,5-diepoxy-4-ethyl-6-hydroxycyclohexanone (**12**) (0.1 g): colorless prisms; mp 116–118 °C; IR (Nujol) 3570 (OH), 1710 (CO) cm^{-1}; NMR ($CDCl_3$) δ 1.10 (t, J = 8 Hz, 3 H). 1.12 (s, 18 H), 1.90 (q, J = 8 Hz, 2 H), 3.34 (s, 1 H), 3.42 (s, 1 H), 3.77 (s, 1 , OH). Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.05; H, 9.28. Found: C, 67.91; H, 9.21. The mother liquor was submitted to a silica gel chromatography. Elution with petroleum ether containing benzene (3:1) gave **4c** (0.15 g) and with benzene gave **12** (0.07 g).

Oxygenation of 6a in *t*-BuOH Containing *t*-BuOK. Oxygen was bubbled through a solution of **6a** (0.44 g) and *t*-BuOK (1.0 g) in *t*-BuOH (25 mL) at 40 °C for 1 h. The reaction mixture was worked up in the usual manner and chromatographed on a silica gel column. Elution with a mixture of petroleum ether and benzene (2:1) gave **11b** (0.05 g) as colorless prisms from hexane: mp 57–60 °C; IR (Nujol) 3540 (OH), 1680 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.96 (s, 9 H), 1.06 (s, 9 H), 1.67 (d, J = 2 Hz, 3 H), 3.70 (s, 1 H, OH), 3.82 (d, J = 1 Hz, 1 H), 6.92 (dd, J = 2, 1 Hz, 1 H). Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.10; H, 9.85. Elution with a mixture of benzene and ether (1:1) gave **13** (0.18 g), colorless prisms from hexane: mp 125–127 °C; IR (Nujol) 3540 (OH), 3390 (OH), 1720 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.96 (s, 9 H), 1.24 (s, 9 H), 1.45 (s, 3 H), 3.43 (br, 2 H, OH), 4.13 (s, 1 H, OH), 4.48 (d, J = 2 Hz, 1 H), 5.85 (d, J = 2 Hz, 1 H). Anal. Calcd for $C_{15}H_{26}O_4$: C, 66.63; H, 9.69. Found: C, 66.35; H, 9.57.

Oxygenation of 6b in *t*-BuOH Containing *t*-BuOK. Oxygen was bubbled through a solution of **6b** (0.31 g) and *t*-BuOK (0.75 g) in *t*-BuOH (20 mL) at 40 °C for 24 h. The reaction mixture was poured into ice-cooled water, acidified with dilute hydrochloric acid, and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to leave a semicrystalline residue. Trituration of the residue with hexane gave lactone carboxylic acid **14** (0.10 g), which was identical with an authentic sample[25] (IR and NMR). The hexane solution after removal of **14** was submitted to a silica gel column chromatography. Elution with petroleum ether gave the starting phenol (0.07 g). Successive elution with a mixture of petroleum ether and benzene (1:1) gave epoxy-*o*-quinol **11c** (0.04 g) as colorless prisms from hexane: mp 80–81 °C; IR (Nujol) 3540 (OH), 1690 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.00 (s, 9 H), 1.18 (s, 9 H), 3.62 (s, 1 H, OH), 3.88 (d, J = 1 Hz, 1 H), 6.20 (d, J = 10 Hz, 1 H), 7.27 (dd, J = 10, 1 Hz, 1 H). Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.55; H, 9.53. Found: C, 70.62; H, 9.53. Further elution with a mixture of benzene and ether (5:1) gave the hydroxy lactone **15** (0.025 g), which was identical with an authentic sample (IR and NMR),[24] and then **14** (0.05 g).

6-Hydroperoxy-2,4,6-tri-*tert*-butyl-2,4-cyclohexadienone (16). Oxygen was bubbled through a solution of **1a** (0.53 g) and *t*-BuOK (4.0 g) in a mixture of *t*-BuOH and petroleum ether (2:1) (300 mL) at 0 °C for 2 h. The reaction mixture was poured into an excess of ice-cooled aqueous NH_4Cl solution and extracted with ether. The extract was dried (Na_2SO_4) and evaporated in vacuo to leave a pale yellow semicrystalline residue. Crystallization and recrystallization of the residue from petroleum ether gave the *o*-hydroperoxide **16** (0.4 g): mp 109–110 °C; IR (Nujol) 3440, 3360 (OH), 1660, 1650 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.92 (s, 9 H), 1.21 (s, 9 H), 1.24 (s, 9 H), 6.13 (d, J = 3 Hz, 1 H), 6.73 (d, J = 3 Hz, 1 H), 9.14 (s, 1 H, OOH). Anal. Calcd for $C_{18}H_{30}O_3$: C, 73.43; H, 10.27. Found: C, 73.28; H, 10.55.

Reduction of 16 with Dimethyl Sulfide. Hydroperoxide **16** (0.2 g, 0.7 mmol) was dissolved in dimethyl sulfide (2 mL) (exothermic). The solution was allowed to stand at room temperatue for 30 min. Dimethyl sulfide was then evaporated and the residue was triturated with water to give 3,5-di-*tert*-butylcatechol as a crystalline solid (0.15 g), which was identical with an authentic sample (IR and NMR). When the reaction was carried out at 0 °C, a 2,4,5-tri-*tert*-butyl-6-hydroxy-2,4-cyclohexadienone (*o*-quinol) intermediate was temporally obtained as judged from its NMR spectrum which was quite similar to that of **16** except the signal position of OH group (δ 4.5). This intermediate was, however, very unstable at room temperature and decomposed to 3,5-di-*tert*-butylcatechol with liberation of isobutene during workup.

Acid Treatment of 16. Hydroperoxide **16** (0.2 g, 0.7 mmol) was dissolved in trifluoroacetic acid (2 mL) and the solution was heated to 50 °C for 5 min. The mixture was poured into ice-cooled water to give 3,5-di-*tert*-butyl-*o*-benzoquinone as orange yellow crystals (0.13 g), which was identical with an authentic sample (IR and NMR).

Reaction of 16 with *t*-BuOK. To a solution of **16** (0.1 g) in DMF (5 mL) was added *t*-BuOK (0.05 g) at room temperature under nitrogen atmosphere. The solution was allowed to stand for 5 min, poured into ice-cooled water, acidified with dilute hydrochloric acid, and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated. The NMR spectrum of the residue showed the formation of epoxy-*o*-quinol **11a** and phenol **1a** in 60 and 40% yield, respectively.

Acknowledgment. The present work was partially supported by the Japan Association for the Promotion of Science and a Grant-in-Aid for Scientific Research from the Ministry of Education.

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(23) Structure of the unidentified product may be tentatively assigned as i which

(i)

could result from an intramolecular rearrangement of **2** (R = H). Haynes and Musso reported that the oxygenation of **1** (R = H) in Me_2SO with *t*-BuOK gave 2,6-di-*tert*-butyl-*p*-benzoquinone and 2,2′,6,6′-tetra-*tert*-butyldiphenoquinone in 17 and 34% yield.[6] We, however, could not detect the latter product in our case.
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