Oxidation of Alkoxyphenols. Part XVIII.[1] Further Examples of Epoxide Formation on Autoxidation of Moderately Hindered Phenols

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Autoxidation of 4,6-di-t-butylguaiacol (I) yields mainly 5,6-epoxy-4-hydroxy-2-methoxy-4,6-di-t-butylcyclohex-2-enone (III) and 2,5-dihydro-5-oxo-2,4-di-t-butylfuran-2-acetic acid (IV), and autoxidation of 5-methoxy-2,4-di-t-butylphenol (II) gives some 5,6-epoxy-4-hydroxy-3-methoxy-4,6-di-t-butylcyclohex-2-enone (XIX) as well as 4-hydroxy-5-methoxy-2,4-di-t-butylcyclohexa-2,5-dienone (XX).

E.s.r. examination of these oxidations reveals the formation of 6-hydroxy-2-t-butyl-1,4-benzosemiquinone during autoxidation of phenol (I), and of 2-hydroxy-3,5-di-t-butyl-1,4-benzosemiquinone during autoxidation of phenol (II). The transformation of compound (XX) into 2,5-di-t-butyl-1,4-benzosemiquinone is also observed by this method.

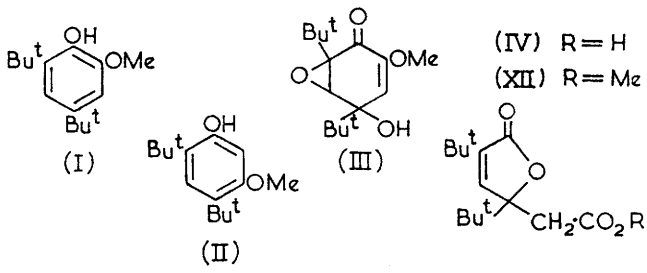
THE unexpected formation of epoxides of 2,5-di-t-butyl-1,4-benzoquinone by autoxidation of 4-methoxy-2,5-di-t-butylphenol was described in Part XV.[2] To see whether the formation of a quinone is a necessary preliminary we have now subjected 4,6-di-t-butylguaiacol (I) and 5-methoxy-2,4-di-t-butylphenol (II) to similar autoxidation. While oxidative demethylation of phenol (I) will give rise to an *ortho*-quinone, no such reaction is available to phenol (II).

Autoxidation of 4,6-di-t-butylguaiacol (I) in t-butyl alcohol-1,2-dimethoxyethane (1 : 1) containing potassium t-butoxide, or in ethanolic sodium hydroxide gave the epoxide (III) and the lactone (IV). In dimethyl sulphoxide containing potassium t-butoxide the epoxide (III) was the only product (*ca.* 90%).

The structure of epoxide (III) was indicated by its n.m.r. spectrum, which contained two t-butyl resonances at high field (τ 8·99 and 8·90), a hydroxy-resonance (τ 7·73) consistent with the presence of a tertiary alcoholic group, a methoxy-resonance at τ 6·45 and also a methine and a vinylic proton resonance at τ 6·38 and

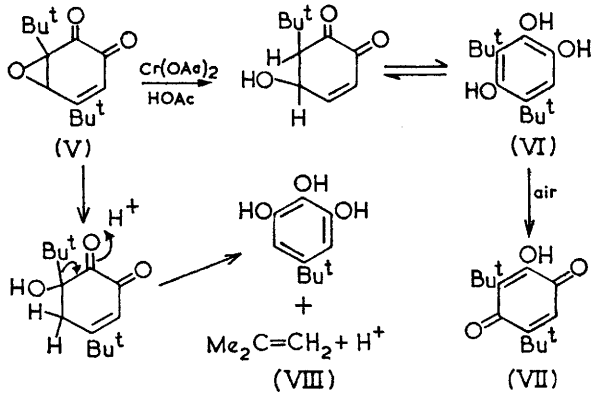
[1] Part XVII, C. J. R. Adderley and F. R. Hewgill, *J. Chem. Soc.* (*C*), 1968, 2770.
[2] F. R. Hewgill and S. L. Lee, *J. Chem. Soc.* (*C*), 1968, 1549.

4·94 respectively, both doublets with J 3·0 c./sec. The chemical shift of the methine proton is comparable to that of the similar proton in 2,5-di-t-butyl-1,4-benzoquinone monoepoxide [2] at τ 6·45. The i.r. spectrum was



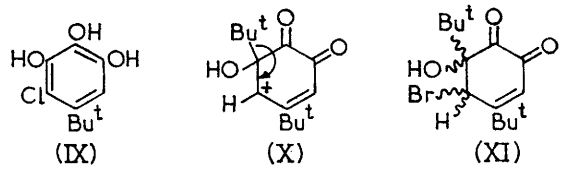
also compatible with structure (III). An analogous system occurs in the recently reported natural product Epoxydon.[3]

The vinylogous hemiacetal system in the epoxide (III) was hydrolysed on treatment with naphthalene-2-sulphonic acid giving a quantitative yield of the *ortho*-quinone epoxide (V). Reduction of this by chromium(II) acetate gave chiefly the hydroxy-quinone (VII) and a little 5-t-butylpyrogallol (VIII). It seems likely that the hydroxy-quinone (VII) is produced by adventitious aerial oxidation of the expected hydroxy-hydroquinone (VI), while the debutylation observed in the formation of 5-t-butylpyrogallol (VIII) is presumably the result of cleaving the epoxide ring in the alternative direction (Scheme 1).



SCHEME 1

These same products, (VII) and (VIII), were obtained in the ratio 3 : 2 on reaction of the *ortho*-quinone epoxide (V) with hydrobromic acid. The formation of product (VIII) under these conditions was unexpected, particularly as reaction of epoxide (V) with hydrochloric acid gave the chlorophenol (IX) and the hydroxy-quinone (VII); the latter was isolated as the acetoxy-quinone after acetylation. The result of hydrochloric acid treatment recalls the similar reaction of 2,5-di-t-butyl-1,4-benzoquinone monoepoxide with hydrogen chloride or bromide.[2] The assigned structure of the chlorophenol (IX) is in accord with the spectroscopic evidence, and



was confirmed by formation of the chlorotriacetate, and by dechlorination with hydrazine to give 5-t-butylpyrogallol (VIII). Formation of compound (VIII) by reaction of (V) with hydrobromic acid appears to require either that the addition of bromide has been sterically suppressed and that the protonated epoxide has debutylated as in (X), or that t-butyl bromide has been eliminated from an intermediate bromohydrin such as (XI), in which considerable opportunity for tautomeric epimerisation exists. Though the present evidence does not permit a definite decision, our failure to isolate any product with sulphuric acid argues against the former possibility

Reaction of the original epoxide (III) with hydrobromic acid gave the same products, (VII) and (VIII), as that of epoxide (V), which is presumably an intermediate. On the other hand reduction by chromium(II) acetate in acetic acid gave a high yield of 4,6-di-t-butylguaiacol (I), and reductive acetylation gave in addition some 2-acetoxy-3,5-di-t-butylanisole. In accord with these results it was established that epoxide (III) is unaffected by acetic acid at 100°.

Since it has not proved possible to open the epoxide ring without loss of the hydroxy-group, no chemical evidence for the stereochemistry of (III) has been obtained. Models suggest that the t-butyl groups bear a *trans*-relationship to each other.

Spectroscopic evidence proved most valuable in determining the structure of the second autoxidation product, the lactone (IV). The n.m.r. spectrum showed two t-butyl resonances at τ 9·00 and 8·76, two non-equivalent methylene proton resonances at τ 7·14 and 7·10, one vinylic proton resonance at τ 3·03 and one carboxy-proton resonance at τ 1·76, removed on exchange with deuterium. The i.r. spectrum showed carbonyl absorption at 1700 and 1760 cm.$^{-1}$, and the u.v. spectrum had $\lambda_{max.}$ 213 mμ (ε 8652), compatible with figures quoted for other butenolides.[4] Both the carbonyl absorption at 1760 cm.$^{-1}$ and the large chemical shift of the vinylic proton suggest a γ-lactone rather than the alternative δ-lactone structure. The presence of a carboxy-group was demonstrated by formation of the methyl ester (XII).

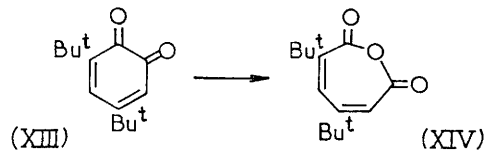
The structure of the lactone (IV) was proved by synthesis. An observation by Karrer, Schwyzer, and Neuwirth[5] that Baeyer-Villiger oxidation of *ortho*-quinones results in anhydrides suggested a simple route

[3] A. Closse, R. Mauli, and H. P. Sigg, *Helv. Chim. Acta*, 1966, **49**, 204.

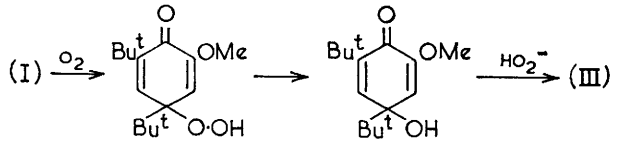
[4] A. I. Scott, 'Interpretation of the Ultraviolet Spectra of Natural Products,' Pergamon, Oxford, 1964, p. 79.

[5] P. Karrer, R. Schwyzer, and A. Neuwirth, *Helv. Chim. Acta*, 1948, **31**, 1210.

to (IV). Thus, oxidation of 3,5-di-t-butyl-1,2-benzoquinone (XIII) with monoperphthalic acid gave the anhydride (XIV), which was converted directly into the lactone (IV) by boiling water, and into the ester (XII) by acidified methanol.



It appears that the epoxide (III) and the lactone (IV) are the final products of two different processes involved in the autoxidation of 4,6-di-t-butylguaiacol. The origin of the epoxide can be explained by a course of events such as that shown in Scheme 2, while the lactone is presumably the result of further oxidation of 3,5-di-t-butyl-1,2-benzoquinone formed by oxidative demethylation of phenol (I).



SCHEME 2

To obtain more evidence for these suggestions we have examined the autoxidation of phenol (I) by e.s.r. spectrometry. When the guaiacol (I) was shaken with air in dimethyl sulphoxide containing potassium t-butoxide, a blue solution resulted, from which a spectrum, analysed as an overlapping doublet of doublets of decets, was obtained (Figure 1). An identical spectrum was obtained

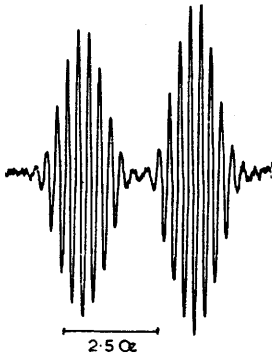


FIGURE 1 Initial e.s.r. spectrum from 4,6-di-t-butylguaiacol

when 3,5-di-t-butylcatechol was oxidised under the same conditions. Splitting constants were assigned as follows: a_{H-4} 2·90, a_{H-6} 0·56, and $a_{H\text{-}Bu^t-5}$ 0·28 Oe. The calculated intensities of the half spectrum, based on these splitting constants, were 1 : 9 : 37 : 93 : 162 : 210 : 210 : 162 : 93 : 37 : 9 : 1, in excellent agreement with the observed intensities, 0 : 10 : 34 : 91 : 157 : 210 : 210 : 157 : 91 : 34 : 10 : 0 (± 0·5% for the largest and ±10% for the smallest measured lines); the outside lines were too weak to be detected. Trapp, Tyson, and Giacometti[6] have reported the e.s.r. spectrum of this semiquinone, produced by oxidation of 3,5-di-t-butylcatechol in alkaline aqueous methanol, and assigned the splitting constants a_{H-4} 2·67, a_{H-6} 0·30 and $a_{H\text{-}Bu^t-5}$ 0·31 Oe. on the basis of Hückel molecular orbital calculations.

After some time the initial spectrum (Figure 1) obtained from 4,6-di-t-butylguaiacol decayed, and was replaced by a doublet of doublets (Figure 2). Reduction

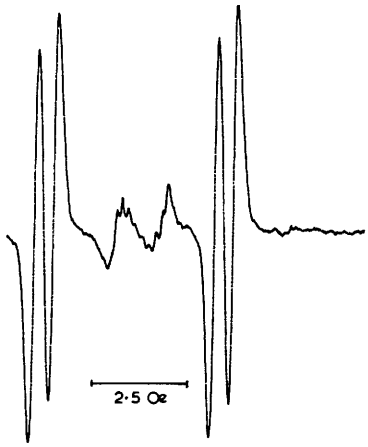


FIGURE 2 Secondary e.s.r. spectrum from 4,6-di-t-butylguaiacol

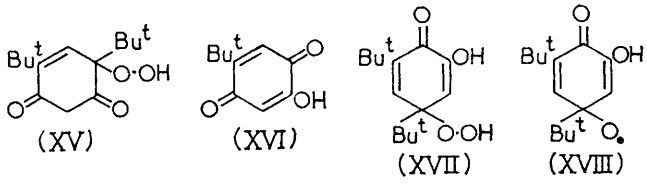
of 5-methoxy-3-t-butyl-1,2-benzoquinone or oxidation of 2,3,5-triacetoxy-t-butylbenzene in dimethyl sulphoxide gave spectra identical with that of Figure 2.[7] Clearly, the common radical obtainable from these last two compounds is 6-hydroxy-2-t-butyl-1,4-benzosemiquinone; this implies replacement of the 5-t-butyl group by a hydroxy-group. The splitting constants assigned to the doublet of doublets on this basis are a_{H-4} 4·75 and a_{H-6} 0·50 Oe. The absence of t-butyl splitting in the spectrum in Figure 2 suggests that its origin in that of Figure 1 is the group at C-5; this supports the assignment made by Trapp, Tyson, and Giacometti. The spectrum later became more complex and could not be interpreted.

As no mono-t-butyl compounds could be isolated from the autoxidation of 4,6-di-t-butylguaiacol, one must assume that debutylation occurs only to a limited extent. This emphasizes the need for care in drawing conclusions about reaction pathways solely from e.s.r. measurements; trace amounts of long-lived radicals may dominate the spectrum.

As regards the mechanism of debutylation a careful study of the autoxidation of 4,6-di-t-butylresorcinol has recently been made by Musso and his co-workers,[8-10] who have isolated the hydroperoxide (XV) as the chief product of low-temperature oxidation, and have provided evidence to show that its thermal decomposition involves cleavage of the O–O bond and formation of

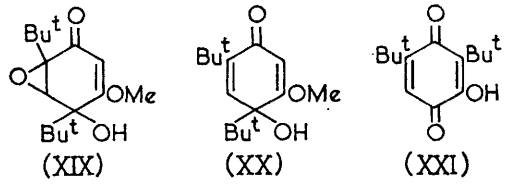
[6] C. Trapp, C. A. Tyson, and G. Giacometti, *J. Amer. Chem. Soc.*, 1968, **90**, 1394.
[7] I. J. Barns and F. R. Hewgill, unpublished work.
[8] H. Musso and D. Maassen, *Annalen*, 1965, **689**, 93.
[9] H. Musso and R. Zunker, *Annalen*, 1968, **717**, 64.
[10] R. Zunker and H. Musso, *Annalen*, 1968, **717**, 73.

three products, one of which is the debutylated quinone (XVI). A similar reaction may operate here. The necessary hydroperoxide (XVII) could be formed by attack of a hydroperoxy-radical on 3,5-di-t-butyl-1,2-benzosemiquinone, or by addition of hydroperoxide anion to the quinone (XIII). Cleavage of the peroxide linkage would then give (XVIII), from which 6-hydroxy-2-t-butyl-1,4-benzosemiquinone could be derived *via* the quinone.



Although no information was gained concerning the mechanism of formation of epoxide (III), the e.s.r. spectra clearly demonstrate that oxidative demethylation of the guaiacol (I) does occur under conditions of autoxidation, and that quinone (XIII) is therefore the most likely precursor of the lactone (IV). This was further confirmed when autoxidation of 3,5-di-t-butylcatechol under the same conditions gave the *ortho*-quinone and the lactone (IV).

The autoxidation of 5-methoxy-2,4-di-t-butylphenol (II) gave small amounts of the epoxide (XIX) as well as the cyclohexadienone (XX) previously obtained by Musso and Maassen.[8] The yields of these two com-



pounds (XIX) and (XX) were not reproducible; several repetitions of the autoxidation gave only traces of the epoxide, detected by t.l.c. Assignment of structure (XIX) is based on the similarity of the n.m.r. spectrum of this compound to that of epoxide (III), the only significant difference being the absence of coupling in the ring-proton resonances of (XIX).

The e.s.r. spectrum (Figure 3) obtained from an autoxidising solution of phenol (II) in dimethyl sulphoxide is an overlapping doublet of decets, corresponding to splitting by one ring proton (a_H 1·05 Oe) and nine t-butyl protons ($a_{H\text{-}Bu^t}$ 0·16 Oe). Further oxygenation of phenol (II) is obviously necessary for the production of a stable semiquinone, and the absence of methoxy-splitting implies that demethylation has also occurred. In the light of the recent studies of the autoxidation of 4,6-di-t-butylresorcinol by Musso and Zunker,[9] it appeared that the semiquinone of the decomposition product (XXI) of hydroperoxide (XV) would be most likely to give rise to the spectrum of Figure 3. This indeed proved to be the case: reduction of the acetate of (XXI) by sodium dithionite in dimethyl sulphoxide containing potassium t-butoxide gave the same spectrum.

When the hydroxy-dienone (XX) was shaken with air in dimethyl sulphoxide containing potassium t-butoxide the only e.s.r. signal observed was that of 2,5-di-t-butyl-1,4-benzosemiquinone, a triplet with a_H 2·14 Oe. The presence of 2,5-di-t-butyl-1,4-benzoquinone (XXII) was also shown by t.l.c. The formation of this quinone can be nicely explained (Scheme 3) by a variation of the base-catalysed acyloin rearrangement,[11] involving elimination of methoxide rather than dienone–phenol rearrangement as the final step.

As the autoxidation of phenols (I) and (II) indicates that epoxidation is most likely where either *para*-quinones or 2,5-cyclohexadienones are produced, we have

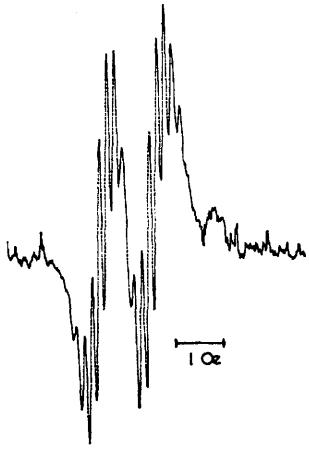
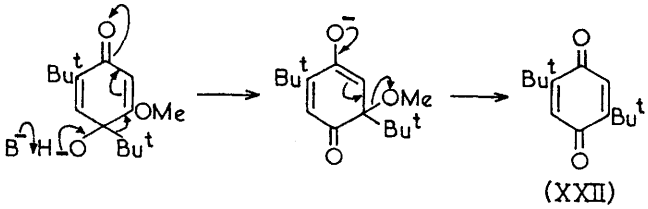


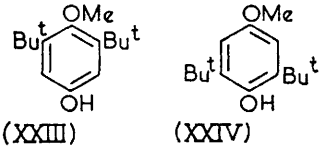
FIGURE 3 E.s.r. spectrum from 5-methoxy-2,4-di-t-butylphenol

also examined phenols (XXIII) and (XXIV), which should give *para*-quinonoid autoxidation products.



SCHEME 3

Phenol (XXIII) was prepared by monobenzoylation of 2,6-di-t-butylhydroquinone, followed by methylation and hydrolysis, but no measurable autoxidation occurred



under the conditions described for phenols (I) and (II). Phenol (XXIV) gave 2,6-di-t-butyl-1,4-benzoquinone in *ca.* 70% yield on autoxidation, but no epoxide. Gers-

[11] S. Goodwin and B. Witkop, *J. Amer. Chem. Soc.*, 1957, **79**, 179.

mann and Bickel [12] have also autoxidised phenol (XXIV) and found that the initial hydroperoxide is converted into the quinone. If an epoxide is formed it may be unstable in alkaline solution, as no pure material could be isolated on attempted epoxidation of the quinone under conditions which gave good yields of the epoxides of 2,5-di-t-butyl-1,4-benzoquinone. The only e.s.r. signal observed in the autoxidation of phenol (XXIV) was the triplet (a_H 1·9 Oe) of 2,6-di-t-butyl-1,4-benzosemiquinone.

In no case during the autoxidation of the t-butylphenols described here or in our previous paper [2] were the e.s.r. spectra of simple aryloxy-radicals observed, although those from the more hindered phenols such as 2,5-di-t-butyl-4-methoxyphenol are relatively stable.[13] Whether this can be construed as evidence for the phenoxide anion–oxygen mechanism put forward for phenol autoxidation by Gersmann and Bickel,[12,14] is debatable, as the bisphenol products of autoxidation of the less hindered phenols, such as 2- and 3-t-butyl-4-methoxyphenol,[2] are clearly the result of radical coupling. While it is therefore not possible to make generalisations about the initial reaction in phenol autoxidation, some trends in the type of final product obtained from these alkoxyphenols are observable. Thus, increasing substitution appears to decrease the likelihood of irreversible oxidative coupling, but to favour the formation of epoxides, especially from *para*-quinonoid intermediates.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. N.m.r. spectra were obtained with a Varian spectrometer at 60 Mc./sec. and i.r. and u.v. spectra with Perkin-Elmer 137G and 137UV instruments. Carbon tetrachloride and carbon disulphide solutions were used for n.m.r. and i.r. measurements respectively unless stated to the contrary. Light petroleum had b.p. 56—60°.

Autoxidation was conducted by shaking alkaline solutions of the phenols in oxygen until oxygen (1 mol. measured volumetrically) had been absorbed. In some cases external cooling was necessary to keep the solutions at room temperature.

E.s.r. examination of autoxidising solutions was made by allowing a briefly shaken alkaline solution of the phenol to remain in contact with a limited amount of oxygen in the cavity of a Varian V 4502 spectrometer for up to 3 days.

Autoxidation of 4,6-*Di-t-butylguaiacol* (I).—This guaiacol was prepared by the method of Ley and Müller.[15] The guaiacol (6·00 g.) in t-butyl alcohol and 1,2-dimethoxyethane (1 : 1; 60 ml.) containing potassium t-butoxide (5·00 g.) was autoxidised. The dark green solution was poured into water, neutralised with dilute hydrochloric acid, and extracted with ether. The washed (water) and dried (Na_2SO_4) extract was evaporated to leave a pale yellow gum (6·40 g.) which was adsorbed on alumina. Elution with light petroleum gave starting material (0·65 g.) and 5,6-*epoxy*-4-*hydroxy*-2-*methoxy*-4,6-*di-t-butylcyclohex*-2-*enone* (III) (3·20 g.) as prisms, m.p. 103—104° (from light petroleum) (Found: C, 67·5; H, 9·1. $C_{15}H_{24}O_4$ requires C, 67·1; H, 9·0%), $\nu_{max.}$ ($CHCl_3$) 3560 (OH) and 1690 and 1640 (C=O) cm.$^{-1}$, τ 8·99 and 8·90 (2 × Bu^t), 7·73 (OH, exchangeable), 6·45 (OMe), 6·38 and 4·94 (each d, J 3·0 c./sec., 1 methine and 1 vinylic H).

Elution with ether gave an uncharacterised mixture 0·40 g.) and 2,5-*dihydro*-5-*oxo*-2,4-*di-t-butylfuran*-2-*acetic acid* (IV) (0·60 g.) as needles, m.p. 132—133° (from benzene–light petroleum) (Found: C, 66·5; H, 8·6. $C_{14}H_{22}I_4$ requires C, 66·1; H, 8·7%), $\nu_{max.}$ 1700 (carboxy C=O) and 1760 (lactone C=O), $\lambda_{max.}$ 213 mμ (ε 8652), τ 9·00 and 8·76 (2 × Bu^t), 7·14 and 7·10 (2 methylene H), 3·03 (vinylic H), and 1·76 (CO_2H).

When the guaiacol (2·40 g.) was autoxidised in ethanol (70 ml.) containing M-aqueous sodium hydroxide (30 ml.), the epoxide (III) (0·20 g.), the lactone (IV) (0·18 g.), starting material (1·00 g.), and an unidentified mixture of oils (0·27 g.) were isolated.

When the guaiacol (3·00 g.) was autoxidised in dimethyl sulphoxide (100 ml.) containing potassium t-butoxide (3·00 g.), the epoxide (III) (*ca.* 90%, by n.m.r. spectroscopy) and starting material (*ca.* 10%) were obtained. The lactone (IV) was not detected.

Reaction of 5,6-*Epoxy*-4-*hydroxy*-2-*methoxy*-4,6-di-t-*butylcyclohex*-2-*enone* (III) *with Naphthalene*-2-*sulphonic Acid*.—The epoxide (III) (270 mg.) and naphthalene-2-sulphonic acid (15 mg.) in ethyl acetate (10 ml.) were heated under reflux for 10 min. The solvent was then evaporated off to leave a yellow residue which was taken up in benzene. The insoluble naphthalenesulphonic acid was filtered off, and the filtrate was evaporated to give a quantitative yield of 3,4-*epoxy*-3,4-*dihydro*-3,5-*di-t-butyl*-1,2-*benzoquinone* (V) as yellow needles, m.p. 72—74° (from light petroleum) (Found: C, 71·2; H, 8·4. $C_{14}H_{20}O_3$ requires C, 71·2; H, 8·5%), $\nu_{max.}$ 1740 and 1690 cm.$^{-1}$ (C=O), τ 8·87 and 8·71 (2 × Bu^t) and 6·20 and 4·02 (each d, J 3·0 c./sec., 1 methine and 1 vinylic H).

Reactions of 3,4-*Epoxy*-3,4-*dihydro*-3,5-*di-t-butyl*-1,2-*benzoquinone* (V).—(a) *With chromium*(II) *acetate*. The *ortho*-quinone epoxide (V) (170 mg.) in glacial acetic acid (10 ml.) was reduced by excess of chromium(II) acetate (500 mg.) as described for 2,5-di-t-butyl-*p*-benzoquinone monoepoxide.[2] Extraction with ether and evaporation of the dried (Na_2SO_4) solution gave an orange oil (165 mg.). Recrystallisation from carbon tetrachloride gave 5-t-butylpyrogallol (VIII) (18 mg.) as plates, m.p. and mixed m.p. 137—139°. The mother liquor was evaporated to dryness and the residue adsorbed on alumina. Elution with benzene gave an orange oil (100 mg.), $\nu_{max.}$ 3340 (bonded OH) and 1660 (C=O) cm.$^{-1}$, τ 8·70 and 8·63 (2 × Bu^t), 3·55 (vinylic H), and 2·82 (OH, exchangeable). Acetylation of this orange oil in acetic anhydride–pyridine at room temperature for 16 hr. gave a quantitative yield of 2-*acetoxy*-3,5-*di-t-butyl*-1,4-*benzoquinone*, as yellow prisms, m.p. 82—83° (from n-pentane) (Found: C, 68·7; H, 8·0. $C_{16}H_{22}O_4$ requires C, 69·0; H, 8·0%), $\nu_{max.}$ 1660 (C=O) and 1775 (OAc) cm.$^{-1}$, τ 8·69 and 8·64 (2 × Bu^t), 7·73 (OAc), and 3·56 (vinylic H).

(b) *With hydrobromic acid*. The *ortho*-quinone epoxide (V) (90 mg.) in glacial acetic acid (5 ml.) containing 48% hydrobromic acid (0·5 ml.) was heated at 100° for 5 min. The mixture was poured into water and extracted with ether. The extract was washed with aqueous sodium

[12] H. R. Gersmann and A. F. Bickel, *J. Chem. Soc.*, 1962, 2356.
[13] C. J. R. Adderley and F. R. Hewgill, *J. Chem. Soc.* (*C*), 1968, 1443.
[14] H. R. Gersmann and A. F. Bickel, *J. Chem. Soc.*, 1959, 2711.
[15] K. Ley and E. Müller, *Chem. Ber.*, 1956, **89**, 1402.

hydrogen carbonate and water, and then dried (Na_2SO_4). Evaporation gave an orange oil (85 mg.), and crystallization from carbon tetrachloride gave 5-t-butylpyrogallol (VIII) (30 mg.), m.p. and mixed m.p. 137—139°. The mother liquor was evaporated to dryness and the residue adsorbed on alumina. Elution with benzene gave an orange oil (45 mg.), which was acetylated to give 2-acetoxy-3,5-di-t-butyl-1,4-benzoquinone (48 mg.), shown by n.m.r. and i.r. spectra to be identical with the sample already described.

When the *ortho*-quinone (V) was treated with concentrated sulphuric acid under the same conditions an unidentified mixture was obtained.

(c) *With hydrochloric acid.* The *ortho*-quinone epoxide (V) (200 mg.) in glacial acetic acid (10 ml.) containing concentrated hydrochloric acid (1 ml.) was heated at 100° for 30 min. The products were extracted with ether, and evaporation of the washed (water) and dried (Na_2SO_4) solution gave an orange gum. Recrystallisation from benzene–light petroleum gave 4-chloro-5-t-butylpyrogallol (IX) (120 mg.), as needles, m.p. 114—115°, $\nu_{max.}$ 3550 and 3520 cm.$^{-1}$ (bonded OH), τ 8·58 (Bu^t), 5·00—4·50 (3 × OH, exchangeable), and 3·41 (ArH).

The mother liquor was evaporated to leave an orange gum which was acetylated to give 2-acetoxy-3,5-di-t-butyl-1,4-benzoquinone (50 mg.). The m.p. was not depressed on admixture with the sample already described.

The chloropyrogallol (IX) was acetylated in acetic anhydride–pyridine at room temperature for 10 hr. to give a quantitative yield of 1,2,3-*triacetoxy*-4-*chloro*-5-*t*-*butylbenzene* as prisms, m.p. 119—120° (from benzene–light petroleum) (Found: C, 56·0; H, 5·7. $C_{16}H_{19}ClO_6$ requires C, 56·1; H, 5·6%), $\nu_{max.}$ 1775 cm.$^{-1}$ (OAc), τ 8·50 (Bu^t), 7·82 (2 × OAc), 7·74 (OAc), and 2·34 (ArH).

Dechlorination of 4-*Chloro*-5-*t*-*butylpyrogallol* (IX).—A solution of the chloropyrogallol (IX) (160 mg.) in ethanol (50 ml.) containing 10% palladium–charcoal (80 mg.) and 98% hydrazine hydrate (2 ml.) was heated under reflux with stirring for 20 min. The palladium–charcoal was filtered off, and the filtrate was evaporated to leave a residue which was taken into ether. Evaporation of the washed (water) and dried (Na_2SO_4) solution, and recrystallisation from carbon tetrachloride gave 5-t-butylpyrogallol (VIII) (90 mg.), m.p. and mixed m.p. 137—139°.

Reactions of 5,6-*Epoxy*-4-*hydroxy*-2-*methoxy*-4,6-*di*-*t*-*butylcyclohex*-2-*enone* (III).—(a) *Reductive acetylation.* The epoxide (III) (100 mg.) was reductively acetylated as described for the 2,5-di-t-butyl-1,4-benzoquinone monoepoxide,[2] to give a pale yellow oil (95 mg.). Adsorption on alumina and elution with light petroleum gave 4,6-di-t-butylguaiacol (I) (60 mg.), and elution with benzene–light petroleum (1 : 1) gave 2-*acetoxy*-3,5-*di*-*t*-*butylanisole* (20 mg.) as prisms, m.p. 88—89° (from aqueous ethanol) (Found: C, 73·7; H, 9·6. $C_{17}H_{26}O_3$ requires C, 73·3; H, 9·4%), $\nu_{max.}$ 1760 cm.$^{-1}$ (OAc), τ 8·68 (2 × Bu^t), 7·79 (OAc), 6·25 (OMe), and 3·25 and 3·13 (each d, J 2·0 c./sec., 2 × ArH). An authentic sample was prepared by acetylation of 4,6-di-t-butylguaiacol (I). The i.r. and n.m.r. spectra of the samples were identical.

(b) *With chromium*(II) *acetate.* The epoxide (III) (240 mg.) in acetic acid (20 ml.) was reduced by excess of chromium(II) acetate (800 mg.) as already described, to give 4,6-di-t-butylguaiacol (I) (*ca.* 100%, by n.m.r. spectroscopy.)

(c) *With hydrobromic acid.* The epoxide (III) (530 mg.) in glacial acetic acid (20 ml.) and 48% hydrobromic acid (2 ml.) was heated at 100° for 5 min. The products were extracted as already described, and evaporation of the ether extract gave an orange oil. Recrystallisation from carbon tetrachloride gave 5-t-butylpyrogallol (VIII) (190 mg.), m.p. and mixed m.p. 137—139°. The mother liquor was evaporated to dryness, and the residue was adsorbed on alumina. Elution with benzene gave an orange oil (250 mg.), which was acetylated to give 2-acetoxy-3,5-di-t-butyl-1,4-benzoquinone (240 mg.), identical (i.r. and n.m.r. spectra) with the sample already described.

Reactions of 2,5-*Dihydro*-5-*oxo*-2,4-*di*-*t*-*butylfuran*-2-*acetic Acid* (IV).—(a) *Attempted hydrolysis.* The lactone (IV) (100 mg.) in M-aqueous sodium hydroxide (7 ml.) was heated under reflux for 30 min. The solution was poured into water, neutralised with dilute hydrochloric acid, and extracted with ether. Evaporation of the dried (Na_2SO_4) solution gave starting material (89 mg.).

(b) *Esterification.* The lactone (IV) (60 mg.) was heated for 2 hr. in refluxing dry methanol (10 ml.) containing a catalytic amount of conc. sulphuric acid. The mixture was poured into water, and extracted with ether. Evaporation of the dried solution (Na_2SO_4) gave an oil (70 mg.). Recrystallisation from light petroleum gave *methyl* 2,5-*dihydro*-5-*oxo*-2,4-*di*-*t*-*butylfuran*-2-*acetate* (XII) (52 mg.) as needles, m.p. 68—69° (Found: C, 67·1; H, 9·0. $C_{15}H_{24}O_4$ requires C, 67·1; H, 9·0%), $\nu_{max.}$ 1750 (lactone C=O) and 1730 (ester) cm.$^{-1}$, τ 9·00 and 8·75 (2 × Bu^t), 7·23 and 7·21 (2 methylene H), 6·43 (OMe), and 3·10 (vinylic H).

Synthesis of Lactone (IV).—(a) 3,5-*Di*-*t*-*butyl*-1,2-*benzoquinone.* A solution of cerium(IV) sulphate monohydrate (35 g.) in water (700 ml.) and conc. sulphuric acid (50 ml.) was added dropwise to a stirred solution of 4,6-di-t-butylguaiacol (10 g.) in acetone (400 ml.). After 10 hr. the mixture was poured into water and extracted with ether to give 3,5-di-t-butyl-1,2-benzoquinone (*ca.* 80%), m.p. 114—115° (lit.,[15] 113—114°).

(b) 2,4-*Di*-*t*-*butylmuconic Anhydride* (XIV).—A cold solution of monoperphthalic acid in ether (0·34M; 30 ml.) was added to 3,5-di-t-butyl-1,2-benzoquinone (2·2 g.) in ether (50 ml.), and the mixture was left at room temperature for 24 hr. The ether was removed and the residue taken into chloroform. The phthalic acid (1·7 g.) was filtered off; evaporation of the filtrate gave pale red oil (2·1 g.). Crystallisation from light petroleum gave 2,4-*di*-*t*-*butylmuconic anhydride* (XIV) (1·7 g.) as prisms, m.p. 97—98° (Found: C, 71·0; H, 8·4. $C_{14}H_{20}O_3$ requires C, 71·2; H, 8·5%), $\nu_{max.}$ 1780 and 1730 cm.$^{-1}$ (anhydride), τ 8·81 and 8·72 (2 × Bu^t) and 3·95 and 3·62 (each d, J 2·0 c./sec., 2 vinylic H).

(c) *Hydrolysis of* 2,4-*di*-*t*-*butylmuconic Anhydride* (XIV). The anhydride (XIV) (120 mg.) in water (25 ml.) was heated under reflux for 1 hr. Extraction with ether gave the lactone (IV) (100 mg.), identical (n.m.r. and i.r. spectra) with the sample already described.

When the anhydride (XIV) was treated under the conditions for autoxidation of 4,6-di-t-butylguaiacol (I), a quantitative yield of the lactone (IV) was obtained.

When the anhydride (XIV) was heated in refluxing methanol containing a catalytic amount of conc. sulphuric acid, the methyl ester (XII) was obtained quantitatively.

Autoxidation of 3,5-*Di*-*t*-*butylcatechol.*—The catechol (280 mg.) in t-butyl alcohol and 1,2-dimethoxyethane (1 : 1;

15 ml.) containing potassium t-butoxide (300 mg.) was autoxidised as already described. Extraction with ether gave a red oil (300 mg.), which was adsorbed on alumina. Elution with light petroleum gave a mixture of 3,5-di-t-butyl-1,2-benzoquinone (*ca.* 80%, by n.m.r. spectroscopy) and an unidentified mixture (*ca.* 20%). Elution with ether gave an oil which was recrystallised from benzene–light petroleum to give the lactone (IV) (20 mg.), i.r. and n.m.r. spectra identical with those of the sample already described.

Autoxidation of 5-Methoxy-2,4-di-t-butylphenol (II).—The phenol [16] (1·2 g.) was autoxidised in t-butyl alcohol and 1,2-dimethoxyethane (1 : 1; 40 ml.) containing potassium t-butoxide (1·1 g.). Extraction with ether gave a pale yellow gum, which was recrystallised from light petroleum to give *5,6-epoxy-4-hydroxy-3-methoxy-4,6-di-t-butylcyclohex-2-enone* (XIX) (100 mg.) as needles, m.p. 174—175° (Found: C, 67·1; H, 9·0. $C_{15}H_{24}O_4$ requires C, 67·1; H, 9·0%), $\nu_{max.}$ ($CHCl_3$) 3560 (OH), 1620, and 1660 cm.$^{-1}$, τ 9·03 and 8·93 (2 × Bu^t), 7·42 (OH, exchangeable), 6·50 (methine H), 6·42 (OMe), and 5·06 (vinylic H).

The mother liquor was evaporated to dryness and the residue adsorbed on alumina. Elution with light petroleum gave starting material (180 mg.), and elution with benzene–light petroleum (1 : 1) gave 4-hydroxy-5-methoxy-2,4-di-t-butylcyclohexa-2,5-dienone (XX) (210 mg.) as needles, m.p. 93—95° (lit.,[8] 93—95°). The n.m.r. spectrum was identical with that reported.[8] Elution with benzene–ether (1 : 1) gave an unidentified mixture (120 mg.).

Several repeated autoxidations of this phenol gave only a small amount of the cyclohexadienone (XX). When the phenol was autoxidised in ethanol containing sodium hydroxide or in dimethyl sulphoxide containing potassium t-butoxide, again only a small quantity of the cyclohexadienone (XX) was isolated. The main product in both cases was starting material, and the epoxide (XIX) was not obtained.

The 2-acetoxy-3,5-di-t-butyl-1,4-benzoquinone required for e.s.r. examination was prepared by reaction of dipivaloyl peroxide with 2-acetoxy-5-t-butyl-1,4-benzoquinone as described by Musso and Zunker [9] for the corresponding reaction of the hydroxy-quinone. Its n.m.r. spectrum was identical with that described by them.

Synthesis of 4-Methoxy-3,5-di-t-butylphenol (XXIII).—(a) *2,6-Di-t-butyl-1,4-benzoquinone.* To a suspension of Frémy's salt (12·0 g.) in 0·04M-aqueous potassium dihydrogen phosphate (400 ml.) at 10°, 2,6-di-t-butylphenol (2·4 g.) in acetone (300 ml.) was added dropwise. Water (200 ml.) was then added, and the solution was stirred for 4 hr. The mixture was poured into water and extracted with chloroform. Evaporation of the washed and dried (Na_2SO_4) solution gave a red gum (2·2 g.) which was adsorbed on alumina. Elution with light petroleum gave 2,6-di-t-butyl-1,4-benzoquinone (1·55 g.), m.p. 66—67° (lit.,[17] 65—66°).

(b) *4-Benzoyl-2,6-di-t-butylphenol.* 2,6-Di-t-butylhydroquinone (prepared by hydrogenation of 2,6-di-t-butyl-1,4-benzoquinone over palladium–charcoal) (5·0 g.) in 10% aqueous sodium hydroxide (50 ml.) was shaken with benzoyl chloride (3·5 g.) under nitrogen. Extraction with ether gave a mixture (5·6 g.), which was adsorbed on alumina. Elution with light petroleum gave 2,6-di-t-butyl-1,4-benzoquinone (0·5 g.). Elution with benzene gave the desired *benzoate* (2·2 g.), as plates, m.p. 128—129° (from aqueous ethanol) (Found: C, 76·9; H, 7·9. $C_{21}H_{26}O_3$ requires C, 77·3; H, 8·0%), $\nu_{max.}$ 3620 (OH) and 1725 (C=O) cm.$^{-1}$, τ 8·54 (2 × Bu^t), 5·00 (OH, exchangeable), 3·08 (2 × ArH), and 2·35—2·60 and 1·70—1·90 (Ph).

(c) *Methylation of 4-Benzoyloxy-2,6-di-t-butylphenol.* The phenol (1·0 g.) in acetone (100 ml.) containing dimethyl sulphate (2 ml.) and anhydrous potassium carbonate (4·5 g.) was heated under reflux for 18 hr. The mixture was diluted with water, followed by conc. ammonia (8 ml.), and then extracted with ether. The extract was washed with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and then water. Evaporation of the dried solution gave a gum (1·1 g.). Crystallisation from aqueous ethanol gave *4-benzoyloxy-2,6-di-t-butylanisole* (0·8 g.) as plates, m.p. 72—74° (Found: C, 77·6; H, 8·2. $C_{22}H_{28}O_3$ requires C, 77·6; H, 8·3%), $\nu_{max.}$ 1725 cm.$^{-1}$ (C=O), τ 8·54 (2 × Bu^t), 6·29 (OMe), 2·98 (2 × ArH), and 2·42—2·65 and 1·75—2·00 (Ph).

(d) *Hydrolysis of 4-Benzoyloxy-2,6-di-t-butylanisole.* The benzoate (600 mg.) in methanol (50 ml.) containing potassium hydroxide (2·0 g.) was heated under reflux in an atmosphere of nitrogen for 3 hr. The cooled solution was poured into water, neutralized with dilute hydrochloric acid, and extracted with ether. Evaporation of the washed (water) and dried (Na_2SO_4) solution gave a quantitative yield of *4-methoxy-3,5-di-t-butylphenol*, as fine needles, m.p. 90—91° (from n-pentane) (Found: C, 76·1; H, 10·0. $C_{15}H_{24}O_2$ requires C, 76·2; H, 10·2%), $\nu_{max.}$ 3580 cm.$^{-1}$ (OH), τ 8·70 (2 × Bu^t), 6·43 (OMe), 4·50—4·70 (OH, exchangeable), and 3·43 (2 × ArH).

Attempted Autoxidation of 4-Methoxy-3,5-di-t-butylphenol.—This phenol was not autoxidised under the various conditions described above.

Autoxidation of 4-Methoxy-2,6-di-t-butylphenol.—This phenol [18] (800 mg.) was autoxidised in t-butyl alcohol and 1,2-dimethoxyethane (1 : 1; 50 ml.) containing potassium t-butoxide (1·0 g.) to give an orange oil (850 mg.). Chromatography on alumina and elution with light petroleum gave 2,6-di-t-butyl-1,4-benzoquinone (460 mg.), and elution with benzene gave a mixture of unidentified oils (150 mg.).

Attempted Epoxidation of 2,6-Di-t-butyl-1,4-benzoquinone.—To the quinone (300 mg.) in ethanol (20 ml.) containing 0·1M-aqueous sodium hydroxide (20 ml.), 30% hydrogen peroxide (1 ml.) was added. The mixture was left at room temperature for 20 hr.; extraction with ether then gave unidentified oil (290 mg.).

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