523. *Oxidation of Alkoxyphenols. Part II.*[1] *Reactions of 4-Methoxy-2- and -3-t-butylphenols with Various Oxidising Agents*

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Oxidation products of these phenols with metal ions vary with the acidity of the solution, the formation of dimers and trimers in alkaline solution giving place to oxidative demethylation as the acidity is increased. Lead tetra-acetate in acetic acid converts the phenols to mixtures of *o*- and *p*-quinones, and in benzene to unstable diacetoxycyclohexadienones. The structures of the monoacetates obtained on hydrogenolysis of the diacetates are proved. Oxidation of 4-methoxy-2-t-butylphenol with benzoyl peroxide leads to an unrearranged catechol monobenzoate, while traces of demethylated products are obtained from 4-methoxy-3-t-butylphenol.

Oxidation of 4-methoxy-2-t-butylphenol (I) and 4-methoxy-3-t-butylphenol (II) with alkaline ferricyanide, lead dioxide, or silver oxide has already been reported, the products being the 2,2′-biphenoquinone [2] (V) and the spiran [1] (IV), respectively. Intrigued by the unusual nature of these oxidation products, and to see how general is their formation, we have examined the effect of other oxidants on these phenols. The products that we were able to isolate are shown in Table 1, and where necessary their structures were proved as follows.

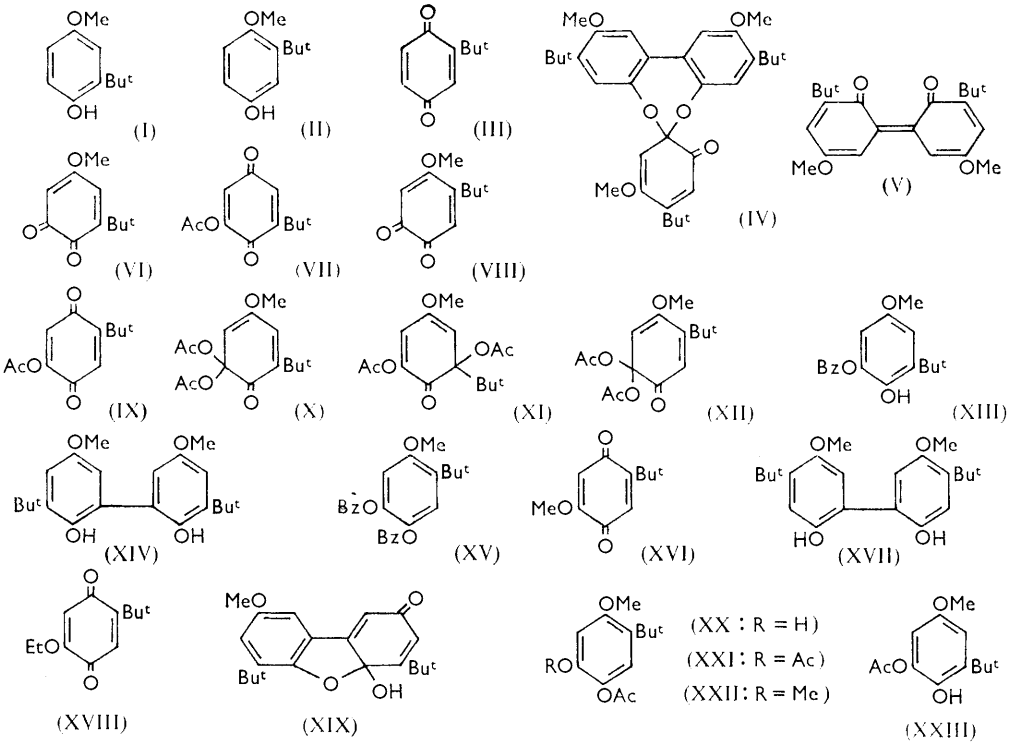
The biphenoquinone (V) cannot be isolated as such [2] and its presence was inferred by the deep blue colour of the solution, by reduction to the biphenol (XIV), and by conversion on silica into the hemiacetal (XIX). Proof of the hemiacetal's structure will form the substance of a later part of this series. As previous reports [2,3] of the biphenol (XIV) have mentioned only its analysis, and insolubility in alkali, as evidence of structure, we have carried out the following reactions, which are in agreement with the proposed structure. The 2,2′-arrangement of the hydroxyl groups was confirmed by formation of a cyclic sulphite with thionyl chloride. Dealkylation of compound (XIV) with hydrobromic acid followed by acetylation gave a mixture of 2,5,2′,5′-tetra-acetoxybiphenyl and 2,8-diacetoxydibenzofuran, both of which are known compounds, while demethylation with pyridinium chloride gave 2,8-diacetoxy-4,6-di-t-butyldibenzofuran. This last result was unexpected,

[1] Part I, F. R. Hewgill, *J.*, 1962, 4987.
[2] J. Baltes and F. Volbert, *Fette u. Seifen*, 1955, **57**, 660.
[3] R. H. Rosenwald and J. A. Chenicek, *J. Amer. Oil Chemists' Soc.*, 1951, **28**, 185.

TABLE 1

Oxidation products

Oxidant	Solvent	Products from (I)	Products from (II)
Ceric sulphate (2 moles)	Aqueous acetone containing sulphuric acid	t-Butyl-*p*-benzoquinone (III)	(III)
Sodium bismuthate (excess)	Acetic acid	(III)	(III) and 2,5′,10-Trimethoxy-3,4′,9-tri-t-butyldibenzo-[d,f]-dioxepin-6-spiro-2′-cyclohexa-3′,5′-dienone (IV)
	Cyclohexane	5,5′-Dimethoxy-3,3′-di-t-butyl-2′,2′-biphenoquinone (V) (not isolated)	(IV) (IV)
Lead tetra-acetate (2 moles)	Acetic acid	(VI) and (VII)	(VIII) and (IX)
	Benzene	(X) and (XI)	(XII)
Benzoyl peroxide (2 moles)	Chloroform	(XIII) and (XIV)	(XV) (trace only, after benzoylation)
	Methanol	Not investigated	(XVI) (trace only) and (XVII) (trace only)
	Ethanol	Not investigated	(XVIII) (trace only)



as similar treatment of 2,2′-dihydroxy-4,4′-di-t-butylbiphenyl resulted only in demethylation and not in cyclisation.[1] The ultraviolet spectra of the dibenzofuran derivatives were almost identical, and closely resembled that of dibenzofuran.

The *o*-quinones (VI) and (VIII) were identified with known [1,4] compounds, as was the *p*-quinone (IX).[4] The structure of the *p*-quinone (VII) follows from its reduction and subsequent acetylation to the known [4] 2,3,5-triacetoxy-1-t-butylbenzene. The *o*-quinones (VI) and (VIII) are also produced in high yield by oxidation of phenols (I) and (II) with Frémy's salt.

[4] W. Flaig, T. Ploetz, and H. Biergans, *Annalen*, 1956, **597**, 196.

Turning now to the diacetoxycyclohexadienones, hydrogenolysis [5] of compound (XII) gave a mixture of monoacetates, of which (XX) is one isomer. Acetylation of the product gave only the known [1] diacetate (XXI). Chromatography of the monoacetate mixture on alumina gave one isomer only, compound (XX), identical with that obtained by hydrolysis [1] of the dioxepin (IV). The position of the acetyl group was established by methylation with diazomethane in ether, the product (XXII) differing from the isomeric material obtained by reaction of 2,5-dimethoxy-4-t-butylphenyldiazonium acetate with acetic anhydride. It is interesting that methylation of compound (XX) with diazomethane in ether-methanol gave only 2,4,5-trimethoxy-1-t-butylbenzene. This facile methanolysis of the acetoxy-group is in agreement with recent observations [6,7] of the ease of hydrolysis and methanolysis of catechol monoesters.

Of the two diacetoxycyclohexadienones, (X) and (XI), produced from phenol (I), the *gem*-diacetoxy-compound (X) on hydrogenolysis gave a mixture of monoacetates, which on acetylation gave a diacetate identical with that obtained on reductive acetylation of the *o*-quinone (VI). The single monoacetate obtained on chromatography of the hydrogenolysis product was assigned structure (XXIII), as the same monoacetate is the sole product of hydrogenolysis of compound (XI). The production in the latter case of a single monoacetate on hydrogenolysis is more consistent with structure (XI) than with that of possible alternatives.

Further evidence for the structure of the three diacetoxycyclohexadienones is provided by their nuclear magnetic resonance spectra (Table 2). It will be seen that the vinylic protons in compounds (X) and (XI) are *meta*-coupled, and that the two acetoxyl groups in (XI) are in different environments. The t-butyl group in the last spectrum is moved upfield, consistent with its situation on a tetrahedral carbon atom. The similarity of the methoxyl chemical shifts argues against compound (XI) possessing a *gem*-acetoxymethoxy-grouping.

TABLE 2

Chemical shifts (τ units) and coupling constants (c./sec.) for diacetoxycyclohexadienones (" D " indicates a doublet) determined on a Varian A60 spectrometer at 60 Mc./sec. in carbon tetrachloride with tetramethylsilane as internal reference

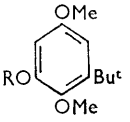
Compound	Vinylic H	OMe	OAc	Bu^t
(X)	3·62D(3·5), 5·00D(3·0)	6·40	Both 8·00	8·80
(XI)	3·73D(3·0), 5·17D(3·0)	6·45	7·85, 8·05	9·05
(XII)	4·02, 4·73	6·33	Both 7·99	8·71

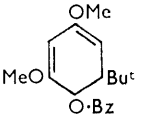
The position of the benzoyl group in the monobenzoate (XIII) was determined by methylation with diazomethane to compound (XXIV), which was identical with the benzoate prepared by methylation, hydrolysis, and benzoylation of the catechol monoacetate (XXIII). The isomeric 2-benzoyloxy-3,5-dimethoxy-1-t-butylbenzene (XXVI) was prepared by butylation of 2,4-dimethoxyphenol, followed by benzoylation, and was found to be different. Further evidence was provided by the ultraviolet spectrum of phenol (XXV) obtained by hydrolysis of compound (XXIV). Coggeshall and Glessner [8] have shown that 0·1N-ethanolic sodium hydroxide will suffice to ionise unhindered phenols completely, whereas a partially hindered phenol (*e.g.*, one with an *o*-t-alkyl group) is only fully ionised in 0·5N-alkali. Thus for phenol (XXV) $\lambda_{max.}$ in ethanol at 270 mμ was replaced by $\lambda_{max.}$ 297 mμ in 0·02N-ethanolic sodium hydroxide. By comparison, 6-t-butylguaiacol and phenol (I), $\lambda_{max.}$ in ethanol 278 and 290 mμ, respectively, were not completely ionized in 0·1N-ethanolic sodium hydroxide, but were ($\lambda_{max.}$ 297 and 308 mμ, respectively) in 1·0N-alkali. An attempt to prove the position of the hydroxyl group in (XXV) by

[5] F. Wessely, E. Schinzel, H. Vilcsek, and W. Mettesics, *Monatsh.*, 1957, **88**, 1069.
[6] B. Hamsen, *Acta Chem. Scand.*, 1963, **17**, 1375.
[7] R. Biggins, T. Cairns, G. Eglington, E. Haslam, and R. D. Haworth, *J.*, 1963, 1750.
[8] N. D. Coggeshall and A. S. Glessner, *J. Amer. Chem. Soc.*, 1949, **71**, 3150.

Claisen rearrangement of its allyl ether was unsuccessful, heating giving rise to loss of the allyl group rather than rearrangement.

(XXIV : R = Bz)
(XXV : R = H)





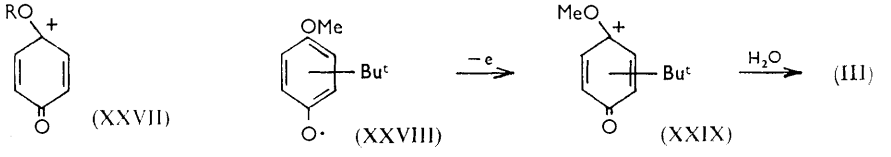
(XXVI)

In each of the three solvents tried, the reaction of phenol (II) with benzoyl peroxide led chiefly to intractable gums. The structures of the few products isolated were established as follows. The dibenzoate (XV), isolated after benzoylation of the reaction mixture, was identical with material prepared by benzoylation of the known [4] catechol. The biphenol (XVII) is known.[1] The *p*-quinone (XVI) is also known,[4] but was prepared in larger quantity by oxidation of 5-t-butylguaiacol with Frémy's salt. Reduction of compound (XVI) gave 2-methoxy-5-t-butylquinol, which was extremely susceptible to atmospheric oxidation, attempts to recrystallise the quinol giving a purple quinhydrone unless carried out in a reducing atmosphere. The nuclear magnetic resonance spectrum of the quinhydrone in deuterochloroform indicated that no association between the components occurred in this solvent. The structure of the ethoxy-quinone (XVIII) follows from its nuclear magnetic resonance spectrum.

Discussion of Results

Stone and Waters [9] have recently shown that electron spin resonance spectra obtained under steady state conditions, when both phenols (I) and (II) are oxidised by alkaline ferricyanide or acidified ceric sulphate, correspond to the simple aryloxy-radicals only. It is therefore clear that the products of radical coupling obtained with alkaline ferricyanide, and the oxidative demethylation observed with ceric sulphate, represent different ultimate fates of each aryloxy-radical.

Oxidative dealkylation by Ce^{IV} appears to be a general reaction of *o*- and *p*-alkoxyphenols, and was introduced by Smith, Ruoff, and Wawzonek [10] to split the chroman ring of tocopherol. Adler and his co-workers have found that monoethers of catechol and quinol are oxidatively dealkylated by sodium periodate in acidic or neutral solution,[11] and have shown [12] that the mechanism involves nucleophilic displacement by water of the alkoxy-group in the intermediate carbonium ion (XXVII). Thus it seems probable that in acid solution Ce^{IV}, being a much stronger oxidant than ferricyanide, can remove a



(XXVII) (XXVIII) (XXIX) (III)

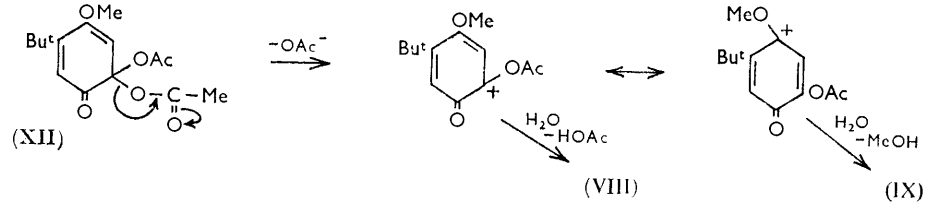
second electron from the aryloxy-radical (XXVIII) before coupling can occur. The resulting carbonium ion (XXIX) is then equivalent to intermediate (XXVII).

Though Haynes, Turner, and Waters [13] have shown that in the ferricyanide oxidation of phenols coupling appears to be less extensive in solutions of low basicity, it is not clear at present whether the rate of radical coupling is decreased, or whether the rate of oxidative demethylation is increased with increasing acidity of the solution. Both effects may operate. But that the acidity of the solution does influence the ultimate fate of the aryloxy-radical can be seen from the products of sodium bismuthate oxidation. Thus in

[9] T. J. Stone and W. A. Waters, *J.*, 1964, 213.
[10] L. I. Smith, P. M. Ruoff, and S. Wawzonek, *J. Org. Chem.*, 1941, **6**, 237.
[11] E. Adler and S. Hernestam, *Acta Chem. Scand.*, 1955, **9**, 319.
[12] E. Adler, I. Falkehag, and B. Smith, *Acta Chem. Scand.*, 1962, **16**, 529.
[13] C. G. Haynes, A. H. Turner, and W. A. Waters, *J.*, 1956, 2823.

neutral solution only radical coupling was observed, while in acetic acid both phenols were oxidatively demethylated, and in the case of phenol (II) concurrent radical coupling was also observed, the acetal (IV) unexpectedly being isolated.

There is evidence [5,14,15] that the oxidation of phenols by lead tetra-acetate proceeds by the reaction of acetoxy-radicals with the aryloxy-radicals formed initially, and solvent effects have been discussed,[16] acetic acid favouring acetoxylation and non-polar solvents dimerisation. The absence of di- or tri-meric products from phenols (I) and (II) in benzene is therefore surprising, and it appears that the reaction of *p*-alkoxy-phenols with acetoxy-radicals is more rapid than that of the alkylphenols examined so extensively by Wessely. The *gem*-diacetoxycyclohexadienones (X) and (XII), produced in benzene, were found to be particularly unstable compounds. So unstable was compound (XII) that attempts to



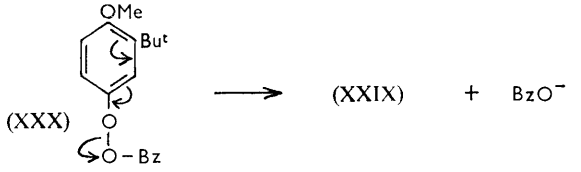
to obtain a combustion analysis gave only values required by the acetoxy-*p*-quinone (IX). In fact, solid (XII) is converted into compound (IX) merely by being kept at room temperature for several days.

The reason for the production of quinones (VI)—(IX), under conditions described by Wessely and his colleagues [5] for the production of acetoxycyclohexadienones from alkyl-substituted phenols, became apparent when it was observed that compound (XII) was converted into a mixture of the quinones (VIII) and (IX) by cold acetic acid. Assuming the initial formation of the *gem*-diacetate, loss of acetate can lead to both products as shown below.

The oxidation of phenols with benzoyl peroxide to catechol monobenzoates has been shown [17,18] to proceed by an ionic mechanism. However, there are many instances [19] of the isolation of phenol dimers from this reaction, and there is less evidence that these are the products of ionic rather than radical dimerisation. The formation of the biphenols (XIV) and (XVII) is not unexpected. In the catechol monobenzoate (XIII) it will be seen that the benzoyl group has entered at the expected position, which is the reverse in all previously recorded catechol monobenzoates obtained from *p*-substituted phenols in this reaction. Acyl migration, presumably catalysed by the benzoic acid produced in the reaction, has been suggested [20] to explain the situation of the benzoyl group in these cases, and in the present case it is likely to be prevented by the bulk of the t-butyl group.

The major product of the reaction of phenol (II) with benzoyl peroxide remains an enigma, though isolation of the dibenzoate (XV) after benzoylation suggests that some monobenzoate may have been formed. The origin of the *p*-quinone (XVI) must be by nucleophilic attack of methanol on t-butyl-*p*-benzoquinone. The latter could arise by loss of benzoate from the intermediate perbenzoate (XXX). A similar mechanism has been suggested [21] to account for the formation of quinones during the reaction of aromatic ethers with perbenzoic acid. That the methoxyl group in compound (XVI) is derived

[14] F. Wessely and E. Schinzel, *Monatsh.*, 1953, **84**, 425.
[15] G. N. Bogdanov, M. S. Postnikova, and N. M. Emanuel, *Izvest. Akad. S.S.S.R., Otdel Khim. Nauk*, 1963, 173 (*Chem. Abs.*, 1963, **58**, 12391).
[16] H. E. Barron, G. W. K. Cavill, E. R. Cole, P. T. Gilham, and D. H. Solomon, *Chem. and Ind.*, 1954, 76.
[17] C. Walling and R. B. Hodgdon, *J. Amer. Chem. Soc.*, 1958, **80**, 228.
[18] D. B. Denney and D. Z. Denney, *J. Amer. Chem. Soc.*, 1960, **82**, 1389.
[19] *E.g.*, S. L. Cosgrove and W. A. Waters, *J.*, 1951, 388.
[20] S. L. Cosgrove and W. A. Waters, *J.*, 1949, 3189.
[21] S. L. Friess, A. H. Soloway, B. K. Morse, and W. C. Ingersoll, *J. Amer. Chem. Soc.*, 1952, **74**, 1305.



from the solvent was shown by carrying out the oxidation in ethanol, which gave the corresponding ethoxy-quinone (XVIII). Moreover, t-butyl-*p*-benzoquinone gave compound (XVI) when heated in dry methanol. It is interesting that the addition of anhydrous zinc chloride to this reaction produced 2-methoxy-6-t-butyl-1,4-benzoquinone. Perhaps the zinc chloride forms a complex with the unhindered carbonyl group, thus directing nucleophilic attack to the 6-position. The structure of 2-methoxy-6-t-butyl-1,4-benzoquinone was proved by its formation on oxidising 6-t-butylguaiacol with Frémy's salt.

To summarise the more interesting conclusions of this study: (*a*) Oxidation of *p*-methoxy-phenols in acid solution is likely to result in oxidative demethylation. (*b*) It appears that with cerium(IV) this process involves the consecutive removal of two electrons from the phenol. (*c*) 3-t-Butylcatechol monoesters exist preferentially in the form with the ester group remote from the t-butyl.

Experimental

Ultraviolet and infrared spectra were determined by using Perkin-Elmer 137G and Unicam S.P. 700 instruments. Nuclear magnetic resonance spectra were determined at 60 Mc./sec. with a Varian A60 spectrometer, with tetramethylsilane as internal reference, and are reported as τ values with coupling constants (c./sec.) included in parentheses. Melting points were determined on a Kofler hot-stage apparatus. Light petroleum had b. p. 55—60° unless otherwise stated.

Oxidations with Ceric Sulphate.—Ceric sulphate (5 g.) in aqueous sulphuric acid (500 ml. of 5%) was added to a stirred solution of 4-methoxy-2-t-butylphenol (I) (1·2 g.) in acetone (300 ml.) containing aqueous sulphuric acid (100 ml. of 5%). After 1 hr. the solution was extracted with chloroform; the extract was washed with water, dried ($MgSO_4$), and evaporated under reduced pressure. The resulting oil was chromatographed on alumina, elution with and recrystallisation from light petroleum giving t-butyl-*p*-benzoquinone (0·83 g.), m. p. 58—59°. A similar result was obtained using 4-methoxy-3-t-butylphenol (II). Potentiometric titration in the presence of a little osmic acid showed that 2 moles of ceric sulphate were required in each case.

Oxidations with Sodium Bismuthate.—(*a*) *In acetic acid.* Sodium bismuthate (4 g.) was shaken with 4-methoxy-2-t-butylphenol (I) (0·9 g.) in acetic acid (25 ml.). After 20 min. the mixture was poured into water and extracted with chloroform. The dried ($MgSO_4$) extract was evaporated and the residue chromatographed on alumina, giving t-butyl-*p*-benzoquinone (100 mg.). No other product could be isolated.

The same procedure applied to 4-methoxy-3-t-butylphenol (II) gave t-butyl-*p*-benzoquinone (80 mg.) and 2,5′,10-trimethoxy-3,4′,9-tri-t-butyldibenzo[d,f]dioxepin-6-spiro-2′-cyclohexa-3′,5′-dienone (IV) (220 mg.), m. p. and mixed m. p. 208—209°.

(*b*) *In cyclohexane.* 4-Methoxy-2-t-butylphenol (I) (1·8 g.) in cyclohexane was stirred for 2 hr. with sodium bismuthate (8 g.). The resulting blue solution was filtered, and half the filtrate was reduced by shaking it with a solution of potassium iodide in aqueous acetic acid. The organic layer was separated, washed with aqueous sodium thiosulphate, then water, dried ($MgSO_4$), and concentrated. When this material was cooled, 2,2′-dihydroxy-5,5′-di-methoxy-3,3′-di-t-butylbiphenyl (XIV) (250 mg.) was deposited, m. p. 228—229° after recrystallisation from light petroleum (lit.,[2] 228°).

The remainder of the blue solution was run through silica gel, and the eluate recycled till colourless. Elution with chloroform and recrystallisation from cyclohexane gave 2,4a-*dihydro*-4a-*hydroxy*-8-*methoxy*-2-*oxo*-4,6-*di-t-butyldibenzofuran* (XIX), m. p. 130—145° (decomp.) (Found: C, 73·2; H, 7·6. $C_{21}H_{26}O_4$ requires C, 73·7; H, 7·7%).

An identical oxidation of 4-methoxy-3-t-butylphenol (II) (1·8 g.) gave the dioxepin (0·6 g.), m. p. and mixed m. p. 208—209°. Some 2,2′-dihydroxy-5,5′-dimethoxy-4,4′-di-t-butylbiphenyl (XVII) was detected by thin-layer chromatography on silica gel.

Reactions of 2,2′-Dihydroxy-5,5′-dimethoxy-3,3′-di-t-butylbiphenyl (XIV).—Acetylation with acetic anhydride in pyridine gave the *diacetate* as prisms, m. p. 149—149·5° (from benzene–light petroleum) (Found: C, 70·9; H, 7·7. $C_{26}H_{34}O_6$ requires C, 70·6; H, 7·8%). With 3,5-dinitrobenzoyl chloride in pyridine compound (XIV) gave a *mono-3,5-dinitrobenzoate* as yellow needles, m. p. 182·5—183·5°, from ethanol (Found: C, 63·3; H, 5·8; N, 5·1. $C_{29}H_{32}N_2O_9$ requires C, 63·0; H, 5·8; N, 5·1%).

The dihydroxybiphenyl (XIV) (0·5 g.) in anhydrous pyridine (2 ml.) was stirred with thionyl chloride (1 ml.) on a steam-bath for 4 hr. After cooling, the solution was taken up in ether and successively washed with aqueous hydrochloric acid, aqueous sodium hydrogen carbonate, and water. Removal of the ether from the dried (Na_2SO_4) extract left brown crystals (0·4 g.). Recrystallisation from heptane gave the *cyclic sulphite* as colourless prisms, m. p. 153·5—154° (Found: C, 65·2; H, 6·8; S, 7·9%; *M* (Rast) 373. $C_{22}H_{28}O_5S$ requires C, 65·5; H, 7·0; S, 7·9%; *M*, 404). Hydrolysis of the cyclic sulphite by ethanolic sodium hydroxide gave the dihydroxybiphenyl (XIV).

Dealkylation was achieved by heating the dihydroxybiphenyl (XIV) (0·5 g.) in acetic acid (50 ml.) under reflux, and adding hydrobromic acid (46%) till precipitation was imminent. After 6 hr. heating the solution was evaporated to dryness *in vacuo*, and the residue acetylated with acetic anhydride and pyridine. Recrystallisation from aqueous acetic acid gave 2,5,2′,5′-tetra-acetoxybiphenyl, m. p. 168—169°, undepressed on admixture with an authentic sample. Under otherwise identical conditions, heating for 18 hr. gave some 2,8-diacetoxydibenzofuran, m. p. 152—153°, undepressed on admixture with an authentic sample; $\lambda_{max.}$ (in cyclohexane) 227, 237 (infl.), 245, 284, 298 (infl.), and 301 (infl.) mμ (log ε 4·35, 4·12, 4·23, 4·26, 3·89, and 3·65).

The dihydroxybiphenyl (XIV) (300 mg.) was heated at 220° for 2 hr. with pyridinium chloride (1 g.) and then with acetic anhydride and pyridine. The crystals produced on pouring the mixture into water were crystallised from aqueous acetic acid giving 2,8-*diacetoxy-4,6-di-t-butyldibenzofuran* as plates (140 mg.), m. p. 134—135° (Found: C, 72·6; H, 7·1. $C_{24}H_{28}O_5$ requires C, 72·7; H, 7·1%); $\lambda_{max.}$ (in cyclohexane) 228, 240 (infl.) 248, 282, 296 (infl.), and 302 (infl.) mμ (log ε 4·50, 4·17, 4·23, 4·24, 3·89, and 3·73).

Oxidations with Lead Tetra-acetate.—(*a*) *In acetic acid.* 4-Methoxy-2-t-butylphenol (I) (10·8 g.) in acetic acid was added to a stirred slurry of lead tetra-acetate (60 g.) in the same solvent, at such a rate that the temperature did not rise above 50°. After 2 hr. the red solution was poured into water. Three extractions with chloroform and evaporation of the washed (H_2O) and dried ($MgSO_4$) extract left a red oil which did not crystallise and was therefore distilled at 0·6 mm. Three fractions were collected: (1) 3·5 g., b. p. 75—110°; (2) 2·8 g., b. p. 112—126°; (3) 2·2 g., b. p. 126—130°. Fraction (3) crystallised; recrystallisation from light petroleum gave 5-methoxy-3-t-butyl-1,2-benzoquinone (VI) (1·5 g.), m. p. 74—75° (lit.,[11] 72—73°) (Found: C, 67·9; H, 7·2. Calc. for $C_{11}H_{14}O_3$ C, 68·0; H, 7·3%). This quinone was also prepared in 95% yield by oxidation of phenol (I) with Frémy's salt as described for 4-methoxy-5-t-butyl-1,2-benzoquinone in Part I. Reductive acetylation gave 2,3-*diacetoxy-5-methoxy-t-butylbenzene*, prisms, m. p. 59—60°, from light petroleum (Found: C, 64·3; H, 7·3. $C_{15}H_{20}O_5$ requires C, 64·3; H, 7·2%). Fraction (2) was chromatographed on alumina. Elution with light petroleum gave a yellow oil (2 g.) which, after recrystallisation from light petroleum (b. p. <40°), gave 2-*acetoxy-6-t-butyl-1,4-benzoquinone* (VII) as yellow prisms, m. p. 36—37° (Found: C, 64·4; H, 6·3. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·4%), τ (in deuterochloroform) 3·46D (2·5), 3·60D (2·5), (2 vinylic protons *meta*-coupled), 7·68 (–OMe), 8·70 (Bu^t). Hydrogenation of compound (VII), requiring one mole of hydrogen, followed by acetylation gave 2,3,5-triacetoxy-t-butylbenzene, m. p. 107—108° (lit.,[4] 105·5—106·5°). Elution with benzene–light petroleum, 5 : 1, gave quinone (VI) (200 mg.). Fraction (1) could not be purified.

4-Methoxy-3-t-butylphenol (II) (1·8 g.) was similarly oxidised. Though each addition of the phenol to the lead tetra-acetate produced a local, blue colour, this rapidly faded. The resulting residue (1·8 g.) crystallised. Recrystallisation from light petroleum gave 4-methoxy-5-t-butyl-1,2-benzoquinone (VIII) (0·6 g.), m. p. and mixed m. p. with an authentic sample 99—100°. The mother-liquors were concentrated and cooled giving yellow plates. Sublimation of these at 100°/20 mm. gave 2-acetoxy-5-t-butyl-1,4-benzoquinone (IX) (160 mg.) m. p. 94—95° (lit.,[4] m. p. 93—94°). Hydrogenation, requiring 1 mole of hydrogen, followed by acetylation, gave 2,4,5-triacetoxy-t-butylbenzene, m. p. and mixed m. p. with an authentic sample 121—123°.

(*b*) *In benzene.* 4-Methoxy-2-t-butylphenol (I) (6·5 g.) in benzene was added to a stirred

solution of lead tetra-acetate (35 g.) in benzene. After 30 min. the mixture was filtered, and the benzene washed with water, dried ($MgSO_4$), and evaporated under reduced pressure. Recrystallisation of the residue from benzene–light petroleum gave 2,2-*diacetoxy*-4-*methoxy*-6-*t*-*butylcyclohexa*-3,5-*dienone* (X) (3·6 g.) as almost colourless needles, m. p. (decomp.) 119—122° (Found: C, 60·8; H, 6·7. $C_{15}H_{20}O_6$ requires C, 60·8; H, 6·8%); $\lambda_{max.}$ (in cyclohexane) 242 and 330 mμ (log ε 3·94, 3·44).

Concentration of the mother-liquors gave 2,6-*diacetoxy*-4-*methoxy*-2-*t*-*butylcyclohexa*-3,5-*dienone* (XI) as pale yellow needles, m. p. (decomp.) 115—123° (Found: C, 60·8; H, 6·9. $C_{15}H_{20}O_6$ requires C, 60·8; H, 6·8%); $\lambda_{max.}$ (in cyclohexane) 234 and 330 mμ (log ε 4·00, 3·45).

4-Methoxy-3-t-butylphenol (II) (3 g.) similarly oxidised with lead tetra-acetate (15 g.) gave 2,2-*diacetoxy*-4-*methoxy*-5-*t*-*butyl*-*cyclohexa*-3,5-*dienone* (XII) as colourless prisms (1·93 g.), m. p. (decomp.) 114—116° (from light petroleum) (Found: C, 64·5; H, 6·6. $C_{15}H_{20}O_6$ requires C, 60·8; H, 6·8; $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·4%); $\lambda_{max.}$ (in cyclohexane) 244 and 330 mμ (log ε 4·12, 3·46).

Reactions of 2,2-*Diacetoxy*-4-*methoxy*-5-*t*-*butyl*-*cyclohexa*-3,5-*dienone* (XII).—Hydrogenation in acetic acid over palladium-charcoal required 1 mole of hydrogen. The product, an oil which could not be crystallised, was acetylated with acetic anhydride in pyridine giving 4,5-diacetoxy-2-methoxy-t-butylbenzene (XXI), m. p. 86—87°, undepressed on admixture with an authentic sample.

Chromatography of the reduction product (1 g.) on alumina and elution with benzene–light petroleum (1 : 4) gave 2-acetoxy-5-methoxy-4-t-butylphenol (XX) (0·26 g.) m. p. 136—137°, undepressed on admixture with the monoacetate described in Part I. Elution with stronger solvents gave only some quinone (VIII).

Methylation of this monoacetate (XX) (100 mg.) in ether with diazomethane gave 5-*acetoxy*-2,4-*dimethoxy*-*t*-*butylbenzene* (XXII) (60 mg.) as plates, m. p. 122—123°, from light petroleum (Found: C, 66·9; H, 8·1. $C_{14}H_{20}O_4$ requires C, 66·6; H, 8·0%). Methylation of compound (XX) with diazomethane in ether–methanol gave 2,4,5-*tri*-*methoxy*-*t*-*butylbenzene*, needles, m. p. 54—55° (from light petroleum) (Found: C, 69·7; H, 8·6. $C_{13}H_{20}O_3$ requires C, 69·6; H, 9·0%).

Solutions of the cyclohexadienone (XII) in acetic acid rapidly became orange. Removal of the acetic acid *in vacuo* from a solution of compound (XII) (100 mg.) left overnight, and crystallisation from light petroleum, gave 4-methoxy-5-t-butyl-1,2-benzoquinone (VIII) (25 mg.). Sublimation of the mother-liquor at 100°/20 mm. and crystallisation of the sublimate from light petroleum gave 2-acetoxy-5-t-butyl-1,4-benzoquinone (IX) (20 mg.).

The solid cyclohexadienone (XII) could be stored satisfactorily in the dark at 0°. However, samples left in the laboratory became yellow overnight. Crystallisation from light petroleum of such a sample two weeks old gave 2-acetoxy-5-t-butyl-1,4-benzoquinone (IX) and none of the *o*-quinone (VIII).

Preparation of 4-*Acetoxy*-2,5-*dimethoxy*-*t*-*butylbenzene*.—2,5-Dimethoxy-4-t-butylaniline (2·1 g.) in chilled acetic acid (50 ml.) was diazotised by the addition of sodium nitrite (1 g.) in portions with stirring. The resulting green solution was boiled under reflux with acetic anhydride (20 ml.) for 30 min. The cooled solution was poured into water, extracted with chloroform, the extract washed with aqueous sodium hydrogen carbonate, then water, dried ($MgSO_4$), and evaporated leaving a red oil. Distillation gave material, b. p. 119—122°/0·5 mm., from which, after crystallisation from methanol, *the acetate* was obtained as plates, m. p. 75—76° depressed to 60—65° on admixture with the isomer (XXII) (Found: C, 67·0; H, 8·0. $C_{14}H_{20}O_4$ requires C, 66·6; H, 8·0%).

Reactions of 2,2-*Diacetoxy*-4-*methoxy*-6-*t*-*butylcyclohexa*-3,5-*dienone* (X).—Hydrogenation of compound (X) (0·5 g.) in acetic acid over palladium–charcoal required 1 mole of hydrogen, giving an oil which would not crystallise. Chromatography of the oil on alumina and elution with light petroleum gave 2-*acetoxy*-4-*methoxy*-6-*t*-*butylphenol* (XXIII) (130 mg.) as prisms, m. p. 119—120° (from light petroleum) (Found: C, 65·6; H, 7·5. $C_{13}H_{18}O_4$ requires C, 65·5; H, 7·6%). Acetylation of the monoacetate (XXIII) with acetic anhydride in pyridine gave 2,3-diacetoxy-5-methoxy-t-butylbenzene, m. p. and mixed m. p. 59—60°.

Methylation of the monoacetate (XXIII) (350 mg.) with diazomethane in ether and distillation of the product at 0·6 mm. (bath temp. 170°) gave 3-*acetoxy*-2,5-*dimethoxy*-*t*-*butylbenzene*, n_D^{20} 1·507 (Found: C, 66·7; H, 8·1. $C_{14}H_{20}O_4$ requires C, 66·6; H, 8·0%). This material was hydrolysed by dissolving it in concentrated sulphuric acid, and after 5 min. pouring the solution

into iced water. Extraction with ether and evaporation of the washed (H_2O) and dried ($MgSO_4$) extract gave a residue, which was benzoylated with benzoyl chloride in pyridine. Recrystallisation from methanol gave *3-benzoyloxy-2,5-dimethoxy-t-butylbenzene* (XXIV) as granular crystals, m. p. 126—127° (Found: C, 72·7; H, 7·0. $C_{14}H_{22}O_4$ requires C, 72·6; H, 7·0%).

Reactions of 2,6-Diacetoxy-4-methoxy-2-t-butylcyclohexa-3,5-dienone (XI).—Hydrogenation of compound (XI) (63 mg.) in acetic acid over palladium–charcoal required 1 mole of hydrogen. Filtration and evaporation of the filtrate left a crystalline residue. Recrystallisation from light petroleum gave 2-acetoxy-4-methoxy-6-t-butylphenol (XXIII) (25 mg.), m. p. and mixed m. p. 119—120°.

Oxidation of 4-Methoxy-2-t-butylphenol (I) *with Benzoyl Peroxide.*—(Cf. Cosgrove and Waters [20]). A solution of the phenol (I) (6 g.) in dry chloroform was added to benzoyl peroxide (8·1 g.) in the same solvent. The temperature rose and the solution was boiled under reflux for 4 hr. When cool, the solution was extracted with aqueous sodium hydrogen carbonate, the extract giving benzoic acid (5 g.) on acidification. The washed (H_2O) and dried ($MgSO_4$) chloroform solution was evaporated, and the residual red gum crystallised by boiling in light petroleum (50 ml.). The crystals were filtered off from the cold solution, and extracted with cold methanol (40 ml.). Crystallisation of the undissolved portion from benzene–light petroleum gave 2,2′-dihydroxy-5,5′-dimethoxy-3,3′-di-t-butylbiphenyl (XIV) (450 mg.), m. p. and mixed m. p. 228—229°. Removal of the methanol and recrystallisation of the residue from benzene–light petroleum gave *2-benzoyloxy-4-methoxy-6-t-butylphenol* (XIII) (4 g.) as prisms, m. p. 144—146° (Found: C, 72·1; H, 6·8. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7%). The same products in similar proportions were obtained on carrying out the reaction at room temperature for 4 days.

Reactions of 2-Benzoyloxy-4-methoxy-6-t-butylphenol (XIII).—Benzoylation with benzoyl chloride in pyridine gave *2,3-dibenzoyloxy-5-methoxy-t-butylbenzene* as prisms, m. p. 160—161°, from benzene–light petroleum (Found: C, 74·1; H, 5·9. $C_{25}H_{24}O_5$ requires C, 74·2; H, 6·0%).

Hydrolysis of the monobenzoate (XIII) was achieved by dissolving it (3 g.) in hot, boiled-out, aqueous sodium hydroxide (100 ml. of 10%) under nitrogen. After the solution had been boiled for 2 min. it was cooled and acidified. Extraction with ether, and extraction of the ethereal extract with aqueous sodium hydrogen carbonate, gave benzoic acid (1 g.) on acidification. The washed (H_2O) and dried ($MgSO_4$) ethereal extract was evaporated and the residue recrystallised from benzene–light petroleum giving 5-methoxy-3-t-butylcatechol (1·2 g.), m. p. 95—96° (lit.,[4] 94°). Methylation with ethereal diazomethane gave *2,3,5-trimethoxy-t-butylbenzene*, b. p. 108—110°/0·5 mm. (Found: C, 69·3; H, 9·0. $C_{13}H_{20}O_3$ requires C, 69·6; H, 9·0%).

Methylation of the monobenzoate (XIII) with ethereal diazomethane gave 3-benzoyloxy-2,5-dimethoxy-t-butylbenzene (XXIV), m. p. and mixed m. p. 126—127°. Hydrolysis of this with concentrated sulphuric acid as described above for the acetoxy-compound gave *2,5-dimethoxy-3-t-butylphenol* (XXV), b. p. 155—160°/1 mm., n_D^{18} 1·244 (Found: C, 69·0; H, 8·6. $C_{12}H_{18}O_3$ requires C, 68·5; H, 8·6%). Benzoylation reconverted the hydrolysis product into (XXIV).

Preparation of 2-Benzoyloxy-3,5-dimethoxy-t-butylbenzene (XXVI).—Orthophosphoric acid (1·6 g. of 100%), 2,4-dimethoxyphenol (0·5 g.), t-butyl alcohol (0·3 g.) and light petroleum (1 ml.) were heated under reflux for 2 hr., cooled, and poured into water. The mixture was extracted with ether, the extract washed with aqueous sodium hydroxide, then with water, dried (Na_2SO_4), and the solvent evaporated. The residual oil was distilled and the distillate (0·1 g., 140—150° (bath)/0·5 mm.) benzoylated with benzoyl chloride in pyridine. Recrystallisation from light petroleum then aqueous ethanol gave the *benzoate* (XXVI) as prisms (20 mg.), m. p. 122·5—124° (Found: C, 72·3; H, 7·0. $C_{19}H_{22}O_4$ requires C, 72·6; H, 7·1%).

Preparation and Attempted Claisen Rearrangement of 3-Allyloxy-2,5-dimethoxy-t-butylbenzene.—Allyl bromide (1 ml.) was added to 2,5-dimethoxy-3-t-butylphenol (XXV) (740 mg.) and sodium ethoxide (640 mg.) in ethanol (20 ml.). The solution was heated under reflux in an atmosphere of nitrogen for 6 hr.; the solvent was evaporated, and the residue poured into water and extracted with ether. The extract was dried (Na_2SO_4), the solvent evaporated, and the residue chromatographed on alumina. Elution with, then crystallisation from, light petroleum gave the *allyl ether* (250 mg.), m. p. 22·5° (Found: C, 72·2; H, 8·7. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·9%).

The allyl ether (350 mg.) and *NN*-dimethylaniline (5 ml.) were heated under reflux for

10 min., cooled, and diluted with ether. After being washed with aqueous sulphuric acid (2N), aqueous sodium hydrogen carbonate, and water, the dried (Na_2SO_4) ether solution was evaporated, and the residue benzoylated. Crystallisation from light petroleum gave 3-benzoyloxy-2,5-dimethoxy-t-butylbenzene, m. p. and mixed m. p. 125·5—126·5°.

Oxidation of 4-Methoxy-3-t-butylphenol (II) *with Benzoyl Peroxide.*—(*a*) *In chloroform.* The phenol (II) (2 g.) oxidised in boiling chloroform as described for phenol (I) gave no identifiable product. Plates, m. p. 193—194° (30 mg.) from light petroleum (Found: C, 73·8; H, 8·1) were deposited from a light petroleum solution of the product. Varying reaction times and chromatography of the products failed to yield crystalline material, though benzoic acid was obtained from the sodium hydrogen carbonate washings. Benzoylation of the crude product (1 g.) with benzoyl chloride in pyridine, followed by chromatography on alumina, gave *4,5-dibenzoyloxy-2-methoxy-t-butylbenzene* (XV) (40 mg.) as prisms, m. p. 110·5—112° (from aqueous methanol) (Found: C, 74·2; H, 5·9. $C_{25}H_{24}O_5$ requires C, 74·2; H, 6·0%). The same material (m. p. and mixed m. p. 110·5—112°) was obtained by benzoylation of 4-methoxy-5-t-butylcatechol. Alkaline hydrolysis of the crude benzoyl peroxide reaction product gave benzoic acid as the only identifiable material.

(*b*) *In methanol.* Phenol (II) (2·1 g.) and benzoyl peroxide (2·9 g.) were heated under reflux in methanol (80 ml.) for 4 hr. The cooled solution was diluted with water and extracted with ether. Benzoic acid (2·3 g.) was obtained after acidifying sodium hydrogen carbonate washings of the extract. Evaporation of the dried ($MgSO_4$) ether extract left a dark orange residue (2·2 g.). This was washed with methanol which on cooling deposited yellow crystals (200 mg.). Recrystallisation from light petroleum gave 2-methoxy-5-t-butyl-1,4-benzoquinone (XVI), m. p. 162—163° (lit.,[22] 162—163°) (Found: C, 67·9; H, 7·1. Calc. for $C_{11}H_{14}O_3$: C, 68·0; H, 7·3%); τ (in deuterochloroform) 3·56, 4·24 (2 × vinylic H), 6·26 (OMe) 8·73 (Bu^t). Chromatography of the methanol-washed residue on alumina and elution with benzene gave 2,2′-dihydroxy-5,5′-dimethoxy-4,4′-di-t-butylbiphenyl (XVII) (60 mg.), m. p. 167·5—168·5° undepressed on admixture with an authentic sample.

(*c*) *In ethanol.* Conditions similar to those used in (*b*), and extraction of the residue with ethanol, gave *2-ethoxy-5-t-butyl-1,4-benzoquinone* (XVIII) (3% yield) as yellow needles, m. p. 154·5—155°, from light petroleum (Found: C, 68·9; H, 7·8. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·7%); τ (in deuterochloroform), 3·58, 4·26 (2 × vinylic H), 6·08 quartet (7·2) (CH_2), 8·58 triplet (7·2) (CH_3), 8·74 (Bu^t).

Preparation and Reactions of 2-Methoxy-5-t-butyl-1,4-benzoquinone (XVI).—2-Methoxy-5-t-butylphenol (100 mg.) in methanol (10 ml.) was added to a stirred solution of Frémy's salt (0·4 g.) in aqueous potassium dihydrogen phosphate (20 ml. of M/24) at 10°. After 15 min. water (10 ml.) was added and stirring continued at room temp. for 1·5 hr. Extraction with chloroform and evaporation of the dried ($MgSO_4$) extract under reduced pressure left a residue which on crystallisation from light petroleum gave the quinone (XVI), m. p. and mixed m. p. 162—163°.

Reaction with 2,4-dinitrophenylhydrazine in acetic acid gave the *2,4-dinitrophenylazophenol* as yellow needles, m. p. 263—264°, from aqueous ethanol [Found: C, 54·2; H, 4·7; N, 14·9%; *M* (Rast), 334. $C_{17}H_{18}N_4O_6$ requires C, 54·5; H, 4·9; N, 15·0%; *M*, 374].

Hydrogenation of the quinone (XVI) in ethanol over palladium–charcoal was quantitative. It was necessary to filter the solution under sulphur dioxide, and to evaporate the filtrate in a desiccator. Crystallisation from light petroleum gave *2-methoxy-5-t-butylquinol* as hexagonal plates, m. p. 110—110·5° (Found: C, 67·1; H, 8·3. $C_{11}H_{16}O_3$ requires C, 67·3; H, 8·2%), τ (in deuterochloroform) 3·20, 3·74 (ArH) 4·95, 5·49 (–OH), 6·24 (–OMe), 8·65 (–Bu^t). Acetylation gave *2,5-diacetoxy-4-methoxy-1-t-butylbenzene*, plates, m. p. 146·5° (from aqueous ethanol) (Found: C, 64·3; H, 7·2. $C_{15}H_{20}O_5$ requires C, 64·3; H, 7·2%). Benzoylation gave *2,5-dibenzoyloxy-4-methoxy-1-t-butylbenzene*, prisms, m. p. 180—182° (from benzene–light petroleum) (Found: C, 74·7; H, 6·2. $C_{25}H_{24}O_5$ requires C, 74·2; H, 6·0%). Admixture of quinone (XXIV) with its quinol, equal quantities in light petroleum, and evaporation, gave the *quinhydrone*, purple crystals, m. p. 135—136·5 (sealed, evacuated tube) [Found: C, 68·3; H, 8·2%; *M* (Rast), 392. $C_{22}H_{30}O_6$ requires C, 67·7; H, 7·7%; *M*, 390]. The n.m.r. spectrum (in deuterochloroform) perfectly combined those of the two components.

Reaction of t-Butyl-1,4-benzoquinone with Methanol.—(*a*) The quinone (0·84 g.) was heated under reflux in dry methanol for 1·5 hr. Evaporation left a residue containing purple crystals.

[22] M. S. Carpenter, W. M. Easter, and T. F. Wood, *J. Org. Chem.*, 1951, **16**, 586.

Chromatography on alumina and elution with benzene–light petroleum (1 : 9) gave the starting material (200 mg.). Elution with benzene–light petroleum (1 : 1) gave 2-methoxy-5-t-butyl-1,4-benzoquinone (XVI) (0·13 g.) m. p. and mixed m. p. 162—163°.

(*b*) t-Butyl-1,4-benzoquinone (0·8 g.) was dissolved in dry methanol and anhydrous zinc chloride (3 g.) added. After being boiled under reflux for 1·5 hr. the solution was poured into water and extracted with chloroform. Chromatography of the residue on alumina after evaporation of the solvent, and elution with benzene–light petroleum (1 : 9) gave 2-*methoxy*-6-*t*-*butyl*-1,4-*benzoquinone* as yellow plates (0·16 g.) m. p. 84—85° (Found: C, 68·3; H, 7·3. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·3%).

Oxidation of 6-*t*-*Butylguaiacol with Frémy's Salt.*—Frémy's salt (7·2 g.) in aqueous potassium dihydrogen phosphate (400 ml. of 0·04M) was added to a stirred solution of 6-t-butylguaiacol (1·8 g.) in acetone (200 ml.) at 10°. After 45 min. water (200 ml.) was added and stirring continued for 1 hr. Extraction with chloroform and evaporation of the dried (Na_2SO_4) and washed extract under reduced pressure gave 2-methoxy-6-t-butyl-1,4-benzoquinone (1·4 g.) from light petroleum, m. p. and mixed m. p. 84—85°.

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