524. *Oxidation of Alkoxyphenols. Part III.*[1] *2-Methoxy-6-t-butylphenol, 2-Methoxy-5-t-butylphenol, and 2-Methoxy-4-t-butylphenol*

By F. R. Hewgill and B. S. Middleton

Oxidation with ferricyanide or lead dioxide gave 3,3′-dimethoxy-5,5′-di-t-butyl-4,4′-diphenoquinone in quantitative yield from 2-methoxy-6-t-butylphenol, and only polymers from 2-methoxy-5-t-butylphenol. 2-Methoxy-4-t-butylphenol gave 2,2′-dihydroxy-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl when oxidised in sodium acetate solution with ferricyanide, and the dioxepin (IV) when oxidised with lead dioxide or alkaline ferricyanide. Acid hydrolysis of the dioxepin gave acetone, 2,2′-dihydroxy-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl (VI), and a small quantity of the phenoxy-biphenyl (V).

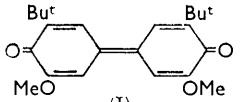
The efficiency of the three most accessible 2-methoxy-t-butylphenol isomers as antioxidants has been shown by Rosenwald and Chenicek [2] to be much less than that of the 4-methoxy-t-butylphenols, and as this function depends in part on the structures of the oxidation products we have examined the latter from these 2-methoxy-t-butylphenols. We were also interested in the possibility of obtaining similar oxidation products to the somewhat unusual ones described [3,4] for the 4-methoxy-t-butylphenols.

Oxidation of *oo*′-disubstituted phenols produces *pp*′-bonded dimers in high yield, and if the oxidation potential of the oxidising agent is sufficiently high the products are *pp*′-diphenoquinones.[5] It was, therefore, not surprising that the oxidation of 2-methoxy-6-t-butylphenol with both lead dioxide and alkaline ferricyanide produced 3,3′-dimethoxy-5,5′-di-t-butyl-4,4′-diphenoquinone in quantitative yield. A molecular weight determination indicated that the product involved two molecules of the original phenol, and the infrared carbonyl absorption frequencies in chloroform of 1623 and 1608 cm.$^{-1}$ correspond, although not closely, to those of 3,3′-dimethyl-5,5′-di-t-butyldiphenoquinone in carbon

[1] Part II, F. R. Hewgill, B. R. Kennedy, and D. Kilpin, preceding Paper.
[2] R. H. Rosenwald and J. A. Chenicek, *J. Amer. Oil Chemists' Soc.*, 1951, **28**, 185.
[3] J. Baltes and F. Volbert, *Fette u. Seifen*, 1955, **57**, 660.
[4] F. R. Hewgill, *J.*, 1962, 4987.
[5] H. Musso, *Angew. Chem. Internat. Ed.*, 1963, **2**, 723.

tetrachloride at 1607 and 1593 cm.$^{-1}$.[6] Catalytic hydrogenation resulted in the uptake of one mole of hydrogen and the product, 4,4′-dihydroxy-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl, gave a diacetate on acetylation. Dealkylation with hydrobromic acid gave the known [7] 3,3′,4,4′-tetrahydroxybiphenyl, which was readily methylated with diazomethane to the known tetramethyl ether.[8]

From its method of preparation the diphenoquinone might be expected to be a mixture of geometrical isomers and the nuclear magnetic resonance spectrum, measured at 60 Mc./sec. with tetramethylsilane as internal reference, indicated this, with a slight preponderance of *trans*-configuration.



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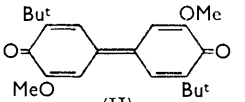

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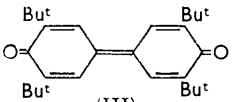


(III)

Apart from t-butyl (τ, 8·60) and methoxyl (τ, 6·08) signals, the spectrum exhibited four doublets in the vinylic proton region, at τ 3·18, 3·10, 2·31, and 2·20, the central two doublets possessing the lesser intensity. The separations between adjacent doublet pairs were 0·08 and 0·11 p.p.m., and the doublets had J 2·3, 2·2, 2·6, and 2·8 c./sec., respectively. While these J values are compatible with a splitting due to a *meta*-proton on the same ring, it seemed unlikely that the doublet pairs were related and arose from a further splitting, as this would have involved an interaction, through five bonds, of at least 0·08 p.p.m. Further, the doublet (τ, 2·31) corresponded exactly to the signal reported [9] for the vinylic protons of 3,3′,5,5′-tetra-t-butyl-4,4′-diphenoquinone (III). It was not possible to measure the spectrum of 3,5,3′,5′-tetramethoxy-4,4′-diphenoquinone, because of the very slight solubility of this compound. Thin-layer chromatography failed to separate the isomers.

Although 2-methoxy-5-t-butylphenol possesses unsubstituted positions *ortho* and *para* to the hydroxyl group, both are hindered by the t-butyl substituent in the 5-position, and oxidation of this phenol with both lead dioxide and in alkaline solution with ferricyanide gave only polymeric products with molecular weights of the order of 700 to 900. Oxidation with ferricyanide of a suspension of the phenol in sodium acetate solution gave a small yield of amorphous, apparently polymeric material, plus unchanged phenol. Nuclear magnetic resonance spectroscopy showed a variety of methoxyl and t-butyl resonances in spectra of the polymers. Oxidation with potassium nitrosodisulphonate (Frémy's salt) gave the expected 2-methoxy-5-t-butyl-1,4-benzoquinone, a known compound.[10,11]

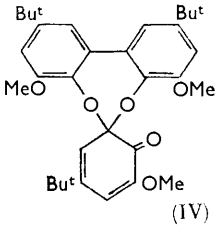
The oxidation of 2-methoxy-4-t-butylphenol with lead dioxide gave two major products, readily separated by chromatography on alumina; a colourless polymer (M, 3000) representing 22% of the total eluate, and a yellow solid (78% of the eluate) which was shown to be 4,6′,8-trimethoxy-2,4′,10-tri-t-butyldibenzo[*d*,*f*][1,3]dioxepin-6-spiro-2′-cyclohexa-3′,5′-dienone (IV). The same dioxepin was obtained without polymeric adulteration and in 70% yield from oxidation of the phenol with alkaline ferricyanide. The oxidation of 2-methoxy-4-t-butylphenol with these reagents was thus a second illustration of the type of oxidative coupling recently reported [4] for 4-methoxy-3-t-butylphenol, although in the case of the 2-methoxyphenol no blue intermediate was observed during the oxidation.

A molecular weight determination on the dioxepin (IV) indicated that it involved three molecules of the original phenol, and the nuclear magnetic resonance spectrum was of the same type as that of the dioxepin from oxidation of 4-methoxy-3-t-butylphenol,[4] with the

[6] J. M. Gordon and J. W. Forbes, *Appl. Spectroscopy*, 1961, **15**, 19.
[7] G. C. Forsyth and V. C. Quesnel, *Biochim. Biophys. Acta*, 1957, **25**, 155.
[8] F. H. Howell and D. A. H. Taylor, *J.*, 1956, 4252.
[9] S. Brownstein and K. U. Ingold, *J. Amer. Chem. Soc.*, 1962, **84**, 2258.
[10] M. S. Carpenter, W. M. Easter, and T. F. Wood, *J. Org. Chem.*, 1951, **16**, 586.
[11] W. Flaig, T. Ploetz, and A. Küllner, *Z. Naturforsch.*, 1955, **10***b*, 668.

exception that the aromatic and vinylic protons showed *meta*-splitting. The infrared spectrum showed absorption at 1710 cm.$^{-1}$ compatible with an αβ-unsaturated ketone, but no hydroxyl absorption, while the ultraviolet spectrum was similar to but more intense than that of the other dioxepin.

Catalytic hydrogenation of the dioxepin (IV) resulted in the uptake of one mole of hydrogen, and gave 2-hydroxy-2′-(2-hydroxy-3-methoxy-5-t-butylphenoxy)-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl (V). The infrared carbonyl absorption of the dioxepin had now been replaced by hydroxyl absorption at 3540 cm.$^{-1}$, while the nuclear magnetic



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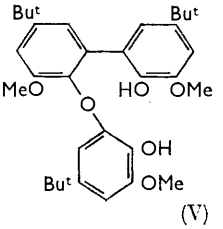

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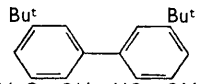

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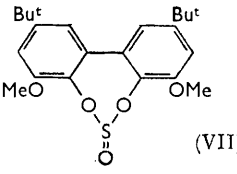

(VII)

resonance spectrum showed three non-equivalent t-butyl signals and a broad singlet corresponding to two protons and exchanging out with deuterium oxide. The dihydroxy-phenoxybiphenyl (V) gave a diacetate on acetylation, and the dioxepin (IV) on oxidation with alkaline ferricyanide.

Treatment of the dihydroxy-phenoxybiphenyl (V) with hydrobromic acid, under conditions which resulted in the dealkylation of 4,4′-dihydroxy-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl, demethylated the compound but left the t-butyl groups intact, and methylation of the product gave 2′-(2,3-dimethoxy-5-t-butylphenoxy)-2,3,3′-trimethoxy-5,5′-di-t-butylbiphenyl. Five distinct methoxyl groups were indicated in the nuclear magnetic resonance spectrum.

The pH dependence of the ferricyanide oxidation of 2-methoxy-4-t-butylphenol was illustrated by oxidising the phenol in aqueous sodium acetate (pH 7·8) as described by Haynes, Turner, and Waters [12] in their oxidation of 2-methoxy-4-methylphenol, and gave 2,2′-dihydroxy-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl (VI) in 12% yield.

A cyclic sulphite (VII) of the 2,2′-dihydroxy-biphenyl (VI) was produced by treatment with thionyl chloride, demonstrating the *oo*′-dihydroxy-grouping on the biphenyl skeleton. Treatment of the dihydroxy-biphenyl (VI) with hydrobromic acid in acetic acid under the conditions previously used for the dihydroxy-phenoxybiphenyl (V) resulted in demethylation, giving 2,3,2′,3′-tetrahydroxy-5,5′-di-t-butylbiphenyl. When the reaction was repeated using a fourfold increase in hydrobromic acid concentration complete dealkylation occurred, the product being 2,3,2′,3′-tetrahydroxybiphenyl; [7] methylation with dimethyl sulphate gave the known [7] 2,3,2′,3′-tetramethoxybiphenyl. As found [4] for 2,2′-dihydroxy-5,5′-dimethoxy-4,4′-di-t-butylbiphenyl, treatment of the dihydroxy-biphenyl (VI) with excess of diazomethane only resulted in methylation of one hydroxyl group. Methylation of the product, 2-hydroxy-2′,3,3′-trimethoxy-5,5′-di-t-butylbiphenyl, or of 2,3,2′,3′-tetrahydroxy-5,5′-di-t-butylbiphenyl, with dimethyl sulphate gave 2,3,2′,3′-tetramethoxy-5,5′-di-t-butylbiphenyl.

2-Methoxy-4-t-butylphenol was also oxidised with potassium nitrosodisulphonate, the product being 3-methoxy-5-t-butyl-1,2-benzoquinone. Infrared absorption at 1708 and 1667 cm.$^{-1}$, and ultraviolet absorption at 467 mμ (log ε, 3·16) corresponded to those of 3-methoxy-1,2-benzoquinone at 1690 and 1659 cm.$^{-1}$, and at 468 mμ (log ε, 3·23).[13] In

[12] C. G. Haynes, A. H. Turner, and W. A. Waters, *J.*, 1956, 2823.
[13] E. Adler, R. Magnusson, and B. Berggren, *Acta Chem. Scand.*, 1960, **14**, 515.

addition, the t-butyl-1,2-benzoquinone formed 1-methoxy-3-t-butylphenazine with *o*-phenylenediamine. Ultraviolet absorption of the phenazine at 267 and 368 mμ (log ε, 5·05 and 4·15) was similar to that of 1-methylphenazine at 255 and 362 mμ (log ε, 5·13, and 4·47).[14]

As was the case with its isomer,[4] the dioxepin (IV) was readily hydrolysed with acid. A solution of the dioxepin in methanol was briefly refluxed with dilute hydrochloric acid, then steam-distilled into a solution of 2,4-dinitrophenylhydrazine in 10% sulphuric acid. Acetone 2,4-dinitrophenylhydrazone was isolated in a yield corresponding to 1·4 moles of acetone per mole of dioxepin hydrolysed. The mean of six such reactions, including ones in which diglyme or ethanol solutions were hydrolysed with acetic acid, indicated the production of 1·7 moles of acetone from every mole of dioxepin hydrolysed. In an attempt to account for this surprising product, we have chromatographed the hydrolysis products on alumina and by reversed-phase paper chromatography. The only other products that could be identified were 2,2′-dihydroxy-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl (VI; $\frac{2}{3}$ mole per mole of dioxepin) and a small amount of the phenoxy-biphenyl (V). The latter can only arise by reduction of compound (IV). Isolation of compound (VI) in this ratio suggests that the bulk of the acetone is derived from the cyclohexadienone portion of the dioxepin, but further work is necessary before the mechanism can be established. The possibility of aerial oxidation being involved was eliminated by the isolation of a similar quantity of acetone when the reaction was carried out under nitrogen.

Experimental

Alumina for chromatography was acid-washed and standardised by the method of Brockmann and Schodder.[15] Infrared and ultraviolet spectra were measured using Perkin-Elmer 137, 137G, and 137UV instruments on carbon disulphide and ethanol solutions, respectively, unless otherwise indicated. Nuclear magnetic resonance spectra were measured on deuterochloroform solutions unless otherwise indicated, a Varian A60 spectrometer operating at 60 Mc./sec. being used with tetramethylsilane as internal reference. These spectra are reported as (D), (Q) and (D × D) meaning doublet, quartet and doublet of doublets respectively, with *J* values in c./sec. included in parentheses. M. p.s were determined on a Kofler hot-stage apparatus and are uncorrected, and b. p.s are uncorrected. Light petroleum had b. p. 55—60°.

2-Methoxy-6-t-butylphenol and 2-methoxy-5-t-butylphenol were prepared as described by Rosenwald.[16]

2-Methoxy-4-t-butylphenol.—2-Methoxyphenol (124 g.) was treated with t-butyl alcohol (82 g.) as described by Rosenwald,[16] and acidification of the combined solutions obtained by extraction with 3 and 10% aqueous sodium hydroxide solutions gave a yellow oil (141 g.). Distillation in a Todd precise fractionating assembly, using a 12 mm. helix-packed vacuum-jacketed column, gave an oil (60 g.), b. p. 81·5—85·5°/4 mm., crystallisation from pentane giving 2-methoxy-4-t-butylphenol (20 g.), m. p. 51—52° (lit.,[16] 50—51·5°).

Oxidation of 2-Methoxy-6-t-butylphenol.—(*a*) *By lead dioxide.* 2-Methoxy-6-t-butylphenol (500 mg.) was dissolved in benzene (10 ml.) and shaken at room temperature with lead dioxide (5·0 g.) in the presence of 0·1N-sodium hydroxide solution (2 drops), for 1 hr. The suspension was filtered and the precipitate extracted with boiling benzene. The combined filtrates were evaporated to give a brick-red residue (489 mg.), crystallisation from benzene giving *3,3′-dimethoxy-5,5′-di-t-butyl-4,4′-diphenoquinone* (54 mg.) as red prisms, m. p. 247—248° (Found: C, 74·1; H, 7·7%; *M* (by *X*-ray), 356·4. $C_{22}H_{28}O_4$ requires C, 74·1; H, 7·9%; *M*, 356·4); $\lambda_{max.}$ 219, 261 (infl.) and 449 mμ (log ε, 4·29, 3·84 and 4·43); $\nu_{max.}$ (in CCl_4) 1623 and 1608 cm.$^{-1}$ (diphenoquinone); τ 8·60 (Bu^t), 6·08 (OMe), then 3·18 (D, 2·3), 3·10 (D, 2·2), 2·31 (D, 2·6) and 2·20 (D, 2·8) (C=CH–C). Thin-layer chromatography on silica gel in chloroform–methanol (2 : 1) gave only one spot.

(*b*) *By ferricyanide in aqueous alkaline solution.* 2-Methoxy-6-t-butylphenol (2·0 g.) was dissolved in benzene (150 ml.) and shaken for 30 min. with a solution of potassium ferricyanide (9·1 g.) and sodium hydroxide (2·2 g.) in water (100 ml.). The benzene layer was separated

[14] L. Birkofer, *Chem. Ber.*, 1952, **85**, 1023.
[15] H. Brockmann and H. Schodder, *Ber.*, 1941, **74**, 73.
[16] R. H. Rosenwald, *J. Amer. Chem. Soc.*, 1952, **74**, 4602.

and evaporated, and the residue crystallised from benzene to give the diphenoquinone (768 mg.), m. p. and mixed m. p. 252·5—253·5°.

Reduction of 3,3′-Dimethoxy-5,5′-di-t-butyl-4,4′-diphenoquinone.—The quinone (38·0 mg.) was hydrogenated in ethanol over 10% palladium charcoal. Uptake ceased when 2·65 ml. at 24°/771 mm. (1·03 mole) had been absorbed, the solution becoming colourless. Evaporation of the filtered solution gave a brown glass. The product (296 mg.) of a larger-scale hydrogenation was dissolved in light petroleum–benzene (4 : 1) and filtered through alumina (5 g., neutral). The residue (273 mg.) obtained on evaporation was crystallised from light petroleum giving *4,4′-dihydroxy-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl* (181 mg.) as needles, m. p. 174·5—175° (Found: C, 73·5; H, 8·5. $C_{22}H_{30}O_4$ requires C, 73·7; H, 8·4%), $\lambda_{max.}$ 218, 272, and 289 (infl.) mμ (log ε, 4·63, 4·22, and 4·15); $\nu_{max.}$ 3520 cm.$^{-1}$ (bonded OH).

Oxidation of this compound by ferricyanide in aqueous alkaline solution gave the diphenoquinone in high yield, while acetylation with acetic anhydride–pyridine gave the *diacetate* as granules, m. p. 167·5—168° (Found: C, 70·9; H, 7·7. $C_{26}H_{34}O_6$ requires C, 70·6; H, 7·7%), $\nu_{max.}$ 1770 cm.$^{-1}$ (acetate).

Dealkylation of 4,4′-Dihydroxy-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl.—The dihydroxybiphenyl (303 mg.) was dissolved in acetic acid (20 ml.) and the solution refluxed for 6 hr. with hydrobromic acid (6·0 ml. of 48% acid). Evaporation under reduced pressure in a nitrogen atmosphere, and crystallisation from water, gave 3,4,3′,4′-tetrahydoxybiphenyl (71 mg.), m. p. 229—230° (lit.,[7] 229°). Methylation in ether–methanol with diazomethane gave 3,4,3′,4′-tetramethoxybiphenyl, m. p. 133—134° (lit.,[8] 133—134°), after three crystallisations from ethanol.

Oxidation of 2-Methoxy-5-t-butylphenol.—(*a*) *By lead dioxide.* A solution of 2-methoxy-5-t-butylphenol (2·53 g.) in light petroleum (40 ml.) and benzene (5 ml.) was shaken at room temperature for 10 hr. with lead dioxide (20 g.) in the presence of 0·1N-sodium hydroxide solution (8 drops). The solid was centrifuged out and extracted with boiling benzene, and the extracts combined, centrifuged, decanted, and evaporated to give a brown solid (2·28 g.). Chromatography on alumina (50 g.) gave two fractions: (i) A white amorphous solid (1·88 g.), which was eluted with benzene and was twice reprecipitated from benzene–light petroleum. A molecular weight determination (freezing-point depression of benzene) showed the solid to be a polymer (*M*, 860); (ii) An orange-brown amorphous solid (0·35 g.), which was eluted with benzene–chloroform (1 : 1), and similarly shown to be a polymer (*M*, 830).

(*b*) *In aqueous alkaline solution by ferricyanide.* 2-Methoxy-5-t-butylphenol (3·0 g.) was added to a solution of sodium hydroxide (2·3 g.) in water (25 ml.), precipitating an insoluble sodium salt. The suspension was shaken for 1 hr. with a solution of potassium ferricyanide (4·5 g.) in water (25 ml.), then extracted into ether. The extract was washed with water, dried, and evaporated giving an amorphous, yellow solid which could not be crystallised but which was reprecipitated from benzene–light petroleum giving polymeric material (*M*, 730). A variety of methoxyl and t-butyl resonances were evident in the nuclear magnetic resonance spectrum.

(*c*) *By potassium nitrosodisulphonate.* A solution of 2-methoxy-5-t-butylphenol (3·0 g.) in acetone (200 ml.) was added to a stirred mixture of crushed ice (200 g.) and potassium nitrosodisulphonate (20·0 g.) in M/6 potassium dihydrogen phosphate solution (800 ml.) at 0°. Stirring was continued at 0° for 1 hr., then at room temperature for 1 hr., and the product was extracted into chloroform. After being washed with water and dried, the chloroform solution was evaporated at 40°, and the residue crystallised from methanol giving 2-methoxy-5-t-butyl-1,4-benzoquinone (1·6 g.), m. p. 162—163° (lit.,[10] 162—163°); $\lambda_{max.}$ (in CCl_4) 263 and 354 mμ (log ε, 2·86 and 4·20; cf. Flaig, Ploetz and Küllner [11]); $\nu_{max.}$ 1672 and 1637 cm.$^{-1}$.

Oxidation of 2-Methoxy-4-t-butylphenol.—(*a*) *By lead dioxide.* A solution of 2-methoxy-4-t-butylphenol (7·6 g.) in benzene (150 ml.) was refluxed for 3½ hr. with lead dioxide (20 g.) in the presence of 0·1N-sodium hydroxide solution (2·0 ml.). The mixture was filtered and the filtrate extracted with boiling benzene. The combined filtrates gave a brown glass (8·4 g.) on evaporation, and this was chromatographed on alumina to give two major fractions: (i) A colourless glass (1·0 g.), which was eluted with benzene, and shown to be a polymer (*M*, 2940; by freezing-point depression of cyclohexane); (ii) A yellow glass (3·5 g.), m. p. 217—221°, which was eluted with benzene–chloroform. Crystallisation from cyclohexane gave *4,6′,8-trimethoxy-2,4′,10-tri-t-butyldibenzo*[d,f][1,3]*dioxepin-6-spiro-2′-cyclohexa-3′,5′-dienone* (151 mg.) as yellow crystals, m. p. 226·5—227° (Found: C, 74·5; H, 8·0%; *M*, 445. $C_{33}H_{42}O_6$ requires C, 74·1; H, 7·9%; *M*, 535); $\lambda_{max.}$ 220, 255, and 287 mμ (log ε, 4·82, 4·27, and 3·71); $\nu_{max.}$

1710 cm.$^{-1}$ (C=O), τ (in $CHCl_3$) 8·82 (Bu^t), 8·63 (2 × Bu^t), 6·23 (OMe), 6·18 (2 × OMe), 4·10 (D, 1·8, C=CH–C), 3·99 (D, 1·6, C=CH–C), 3·07 (D, 2·0, 2 × ArH), and 2·90 (D, 2·2, 2 × ArH).

(*b*) *By ferricyanide in aqueous alkaline solution.* 2-Methoxy-4-t-butylphenol (6·0 g.) was oxidised by ferricyanide in aqueous alkaline solution as described for 2-methoxy-6-t-butylphenol. Chromatography of the orange product (5·9 g.) on alumina (50 g.) gave a yellow solid (3·5 g.) by elution with light petroleum–benzene (2 : 1). The dioxepin (1·9 g.), m. p. and mixed m. p. 225—226°, was obtained on crystallisation from benzene.

(*c*) *In sodium acetate solution by ferricyanide.*[12] A solution of potassium ferricyanide (12 g.) in water (80 ml.) was added in 15 min. to a stirred suspension of 2-methoxy-4-t-butylphenol (1·92 g.) in a solution of sodium acetate (5·1 g.) in water (180 ml.). Vigorous stirring was continued for 4½ hr., when the precipitate was collected, washed with water, and crystallised from petrol, forming granules (0·87 g.), m. p. 165—170°. Two further crystallisations from benzene–light petroleum followed by two from methanol gave *2,2′dihydroxy-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl* (0·23 g.) as prisms, m. p. 184° (Found: C, 74·1; H, 8·3. $C_{22}H_{30}O_4$ requires C, 73·7; H, 8·4%); $\lambda_{max.}$ 218 and 281 mμ (log ε, 4·73 and 3·70); $\nu_{max.}$ 3530 cm.$^{-1}$ (bonded OH); τ 8·67 (Bu^t), 6·07 (OMe), 3·90 (OH), and 3·00 (2 × ArH), τ (in acetone) 8·67 (Bu^t), 6·09 (OMe), 2·97 (D × D, 2·2 × 5·1, 2 × ArH), and 2·72 (OH). After several days in a stoppered container the m. p. had dropped to a constant 169—170°, while another fresh sample had m. p. 157·5—158°. The m. p. 157·5—158° was not depressed on admixture with the form of m. p. 184°, nor was m. p. 169—170° on admixture with the form of m. p. 184°. The nuclear magnetic resonance spectra of all three samples were identical, indicating the existence of at least two polymorphs.

(*d*) *By potassium nitrosodisulphonate.* 2-Methoxy-4-t-butylphenol (2·00 g.) was oxidised by potassium nitrosodisulphonate as previously described. The residue (1·73 g.) obtained on evaporation of the solvent, after crystallisation from benzene–light petroleum gave *3-methoxy-5-t-butyl-1,2-benzoquinone* (0·55 g.) as deep red needles, m. p. 86—88° (Found: C, 68·1; H, 7·3. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·3%); $\lambda_{max.}$ (in $CHCl_3$) 246 and 467 mμ (log ε, 3·70 and 3·16); $\nu_{max.}$ 2845 (OMe), 1708 and 1667 cm.$^{-1}$ (*o*-benzoquinone); τ 8·76 (Bu^t), 6·23 (OMe), 3·99 (D, 1·7, C=CH–C), and 3·89 (D, 1·9, C=CH–C).

The *o*-benzoquinone with *o*-phenylenediamine in chloroform over sodium sulphate gave *1-methoxy-3-t-butylphenazine* as yellow needles, m. p. 77—80°, from benzene–light petroleum (Found: C, 76·6; H, 6·7; N, 10·7. $C_{17}H_{18}N_2O$ requires C, 76·7; H, 6·8; N, 10·5%); $\lambda_{max.}$ 215, 267, 368, and 402 mμ (log ε, 4·45, 5·05, 4·15, and 3·66).

Reduction of the Dioxepin.—The dioxepin (37·1 mg.) was hydrogenated in ethanol over 10% palladium–charcoal. Uptake ceased when 1·69 ml. at 19°/769 mm. (1·00 mole) had been absorbed, the solution becoming colourless. Evaporation of the filtered solution gave a glass. The product (165 mg.) of a larger-scale hydrogenation on recrystallisation from benzene–light petroleum gave *2-hydroxy-2′-(2-hydroxy-3-methoxy-5-t-butylphenoxy)-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl* (36 mg.) as long prisms, m. p. 142·5—143° (Found: C, 74·1; H, 8·7. $C_{33}H_{44}O_6$ requires C, 73·8; H, 8·3%); $\lambda_{max.}$ 223, 252 (infl.), and 298 mμ (log ε, 4·87, 4·41, and 4·03); $\nu_{max.}$ 3540 cm.$^{-1}$ (bonded OH); τ 8·91 (Bu^t), 8·81 (Bu^t), 8·63 (Bu^t), 6·18 (2 × OMe), 6·12 (OMe), 4·32 (2 × OH), 3·78 (D, 2·3, ArH), 3·58 (D, 2·0, ArH), 3·17 (2 × ArH), and 2·95 (D × D, 2·4 × 4·7, 2 × ArH). Acetylation with acetic anhydride–pyridine afforded the *diacetate* as prisms, m. p. 188—189° (Found: C, 71·7; H, 8·0. $C_{37}H_{48}O_8$ requires C, 71·6; H, 7·8%); $\nu_{max.}$ 1770 cm.$^{-1}$ (acetate).

Treatment of the dihydroxy-compound (271 mg.) in refluxing acetic acid (20 ml.) with 48% hydrobromic acid (6·0 ml.) for 6 hr. gave a buff-coloured solid (239 mg.) with no absorption corresponding to a methoxyl group in either the infrared or nuclear magnetic resonance spectra. Methylation of this product with dimethyl sulphate over anhydrous potassium carbonate gave *2′-(2,3-dimethoxy-5-t-butylphenoxy)-2,3,3′-trimethoxy-5,5′-di-t-butylbiphenyl* (111 mg.) as a glass which could not be crystallised (Found: C, 74·9; H, 8·6%; *M*, 457. $C_{35}H_{48}O_6$ requires C, 74·4; H, 8·6%; *M*, 565); $\lambda_{max.}$ 217 and 280 mμ (log ε, 4·83 and 3·78); $\nu_{max.}$ 2830 cm.$^{-1}$ (OMe); τ 8·91 (Bu^t), 8·86 (Bu^t), 8·63 (Bu^t), 6·49 (OMe), 6·40 (OMe), 6·23 (OMe), 6·18 (OMe), 6·16 (OMe), 3·76 (D, 2·0, ArH), 3·50 (D, 2·0, ArH), 3·29 (D, 2·4, ArH), 3·18 (D, 2·2, ArH), 3·00 (D, 2·4, ArH), and 2·92 (D, 2·0, ArH).

Oxidation of the dihydroxy-compound (120 mg.) with alkaline ferricyanide as in (*a*) above gave the dioxepin (109 mg.), m. p. and mixed m. p. 218—220°. Infrared and nuclear magnetic resonance spectra were identical with those of the previous sample.

Derivatives of 2,2′-Dihydroxy-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl.—(*a*) *A cyclic sulphite* was prepared by treatment of the dihydroxy-biphenyl with thionyl chloride using the method described in Part II, and had m. p. 207—208° (from methanol) (Found: C, 65·3; H, 7·0; S, 8·1. $C_{22}H_{28}O_5S$ requires C, 65·3; H, 7·0; S, 7·9%); $\nu_{max.}$ 1195 cm.$^{-1}$ [O·S(:O)·O].

(*b*) Treatment of the dihydroxy-biphenyl (236 mg.) in refluxing acetic acid (16 ml.) with 48% hydrobromic acid (5·0 ml.) for 6 hr. gave *2,3,2′,3′-tetrahydroxy-5,5′-di-t-butylbiphenyl* as needles, m. p. 180—180·5° from methanol (Found: C, 72·5; H, 8·0. $C_{20}H_{26}O_4$ requires C, 72·7; H, 7·9%); $\lambda_{max.}$ 217 and 283 mμ (log ε, 4·54 and 3·51); $\nu_{max.}$ 3530 cm.$^{-1}$ (bonded OH); τ (in acetone) 8·71 (Bu^t), 3·11 (D × D, 2·3 × 6·8, 2 × ArH), and 2·25 (OH). However, when the dihydroxy-biphenyl (256 mg.) was treated for 6 hr. in refluxing acetic acid (30 ml.) with 48% hydrobromic acid (40 ml.), crystallisation of the product from water gave 2,3,2′,3′-tetrahydroxy-biphenyl as crystals, m. p. 220·5—221° (lit.,[7] 221°). Methylation of this product with dimethyl sulphate gave 2,3,2′,3′-tetramethoxy-biphenyl, m. p. 103—104° (lit.,[17] 104—105°).

(*c*) Methylation of 2,2′-dihydroxy-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl with diazomethane afforded the *monomethyl ether* as plates, m. p. 122—123° (Found: C, 74·3; H, 8·7. $C_{23}H_{32}O_4$ requires C, 74·1; H, 8·7%); $\nu_{max.}$ 3525 cm.$^{-1}$ (bonded OH). Methylation of this compound or of 2,3,2′,3′-tetrahydroxy-5,5′-di-t-butylbiphenyl with dimethyl sulphate gave *2,3,2′,3′-tetramethoxy-5,5′-di-t-butylbiphenyl* as prisms, m. p. and mixed m. p. 110·5—111°, from light petroleum (Found: C, 74·9; H, 8·8%; *M*, 357. $C_{24}H_{34}O_4$ requires C, 74·6; H, 8·9%; *M*, 386); $\lambda_{max.}$ 218 and 281 mμ (log ε, 4·73 and 3·70).

Hydrolysis of the Dioxepin.—A solution of the dioxepin (203 mg.) in ketone-free methanol (20 ml.) was refluxed for 30 min. with hydrochloric acid (0·5 ml.), then diluted with water (100 ml.) and steam-distilled for 1 hr., the distillate being collected in a solution of 2,4-dinitrophenylhydrazine (504 mg.) in 10% aqueous sulphuric acid (30 ml.). The orange-red precipitate was collected and chromatographed on alumina (10 g.). Elution with benzene gave an orange solid (143 mg.) which was twice recrystallised from benzene–light petroleum to yield acetone 2,4-dinitrophenylhydrazone (34 mg.), m. p. and mixed m. p. 125—126°. The infrared and nuclear magnetic resonance spectra were identical with those of an authentic sample, and an identical reaction, from which the dioxepin was omitted, gave no hydrazone.

Acetone 2,4-dinitrophenylhydrazone was also obtained in equal yield when the reaction was carried out under purified nitrogen, using solvents previously refluxed under nitrogen.

The residues after steam-distillation of the hydrolysis products of the dioxepin (404 mg.) were extracted into ether, and the ether solution washed with sodium hydrogen carbonate solution and water, dried, and evaporated to yield a red oil (380 mg.). Chromatography on alumina (10 g.) gave a solid (141 mg.) eluted with benzene–chloroform (2 : 1), identified after two crystallisations from methanol as 2,2′-dihydroxy-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl, m. p. and mixed m. p. 184°. The infrared and nuclear magnetic resonance spectra were identical with those of the sample described earlier.

The residues (450 mg.) from another hydrolysis were dissolved in ether and extracted with 10% sodium hydroxide solution. The residual ether solution was evaporated, giving a residue (116 mg.) which was recrystallised four times from light petroleum to give 2-hydroxy-2′-(2-hydroxy-3-methoxy-5-t-butylphenoxy)-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl (4 mg.), m. p. and mixed m. p. 142—143°.

Application of the residues (300 mg.) from another hydrolysis in 50 mg. portions to the baselines of sheets of Whatman 3MM chromatography paper impregnated with paraffin oil was followed by development in the ascending direction with the solvent system chloroform–water–methanol–paraffin (10 : 6 : 10 : 4). The edge strips were sprayed with a mixture of M-ferric chloride solution–10% potassium ferricyanide solution (1 : 1), allowing detection of bands with R_F values of 0·91, 0·76, 0·55, 0·12, and 0·04. The band with R_F 0·91 was isolated and continuously extracted with ether for 16 hr., and the extract shaken with 10% sodium hydroxide solution. The alkaline solution was acidified, washed with aqueous sodium hydrogen carbonate solution and with water, dried, and evaporated to give a yellow oil (30 mg.), $\lambda_{max.}$ 214 and 274 mμ, which could not be crystallised. The band with R_F 0·76, treated in the same way, gave a brown oil (7 mg.), $\lambda_{max.}$ 214 and 277 mμ. Although treatment of the band with R_F 0·55 in the same way gave an insoluble sodium salt, both salt and solution gave a brown oil (total 66 mg.) on acidification, with $\lambda_{max.}$ 214 and 279 mμ. The insoluble sodium salt similarly

[17] H. Gilman, J. Swiss, and L. C. Cheney, *J. Amer. Chem. Soc.*, 1940, **62**, 1963.

obtained from the band with R_F 0·12 gave, on acidification, 2,2′-dihydroxy-3,3′-dimethoxy-5,5′-di-t-butylbiphenyl (30 mg.), m. p. and mixed m. p. 169·5—170° (from light petroleum). Sodium hydroxide extraction of the ether extract of the band with R_F 0·04 yielded the same product (21 mg.).

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