The Reaction of Cyclic Monoacetals of *o*-Benzoquinones with Hydroxylamine

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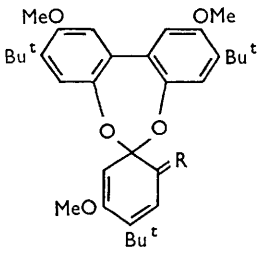
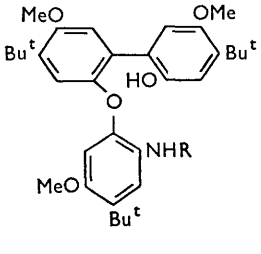
The trimeric spiroacetals obtained by oxidation of 4-methoxy-3-t-butylphenol and 4-t-butylguaiacol react with hydroxylamine hydrochloride to give (aminophenoxy)hydroxybiphenyls. The oxidation of such a compound is examined.

The product of the reaction between hydroxylamine hydrochloride and 2,5′,10-trimethoxy-3,4′,9-tri-t-butyldibenzo[*d*,*f*][1,3]dioxepin-6-spirocyclohexa-3′,5′-dien-2′-one (I) has been briefly described by one of us.[1] We now find that it is not the expected oxime (II).

Its n.m.r. spectrum shows the presence of three t-butyl groups, two of which are equivalent, three non-equivalent methoxy-groups, and six aromatic protons. A broad three-proton signal at τ 5·8 was removed on exchange with deuterium. I.r. bands at 3360 and 3440 cm.$^{-1}$ indicate a primary amino-group, and that at 3550 cm.$^{-1}$ a bonded hydroxy-group. The u.v. absorption maximum at 302 mμ in ethanol exhibited a bathochromic shift in base, and a hypsochromic shift in acid. Such shifts are characteristic of phenols and amines respectively.[2] Structure (III) is consistent both with these spectral data and with the analytical results, and is further supported by the formation of a diacetate, which was hydrolysed by base to the acetamidophenol (IV), and by acid to the aminophenol (III). The reaction of an isomeric dibenzodioxepin with hydroxylamine hydrochloride was entirely analogous, and gave the aminophenol (V).



(I) R = O
(II) R = NOH
(VI) R = NH

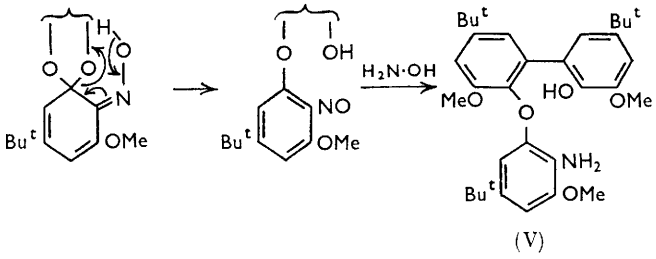


(III) R = H
(IV) R = Ac

To explain the formation of these aminophenols we suggest the mechanism of the Scheme, involving aromatisation of the ring bearing the oximino-substituent, and subsequent reduction of the resulting nitroso-group by hydroxylamine. The rearrangement has an obvious analogy in the well known tautomerism of quinone mono-oximes.

The structure of these aminophenols suggest the pos-

[1] F. R. Hewgill, *J. Chem. Soc.*, 1962, 4987.
[2] A. I. Scott, 'Interpretation of the Ultra Violet Spectra of Natural Products,' Pergamon Press, London, 1964.



(V)

SCHEME

sibility of their oxidation to iminodibenzodioxepins, *e.g.* (VI). Silver oxide will oxidise the corresponding dihydroxyphenoxybiphenyls to dioxepins,[1] but oxidation of the aminophenol (III) with either silver oxide or alkaline ferricyanide gave only a purple gum, which could not be characterised, either directly or by reductive acetylation. However, when lead tetra-acetate was used as the oxidant the dioxepin (I) was obtained. The imino-compound (VI) is probably formed first, and subsequently hydrolysed to the ketone. Attempts to bring about the crossed oxidative coupling of 2,2′-dihydroxy-5,5′-dimethoxy-4,4′-di-t-butylbiphenyl with 4-methoxy-3-t-butylaniline were unsuccessful; the only identifiable oxidation products were those of the individual reactants.

EXPERIMENTAL

N.m.r. spectra were measured with a Varian A60 instrument for solutions in carbon tetrachloride. I.r. and u.v. spectra were measured with Perkin-Elmer 337 and 137 UV instruments. M.p.s were determined with a Kofler hot-stage apparatus. Light petroleum had b.p. 56—60°.

Aminophenols (III) *and* (V).—2,5′,10-Trimethoxy-3,4′,9-tri-t-butyldibenzo[*d*,*f*][1,3]dioxepin-6-spirocyclohexa-3′,5′-dien-2′-one (I) (300 mg.) and hydroxylamine hydrochloride (450 mg.) were heated in pyridine under reflux for 1·5 hr. The cooled mixture was poured into water and extracted with ether, and the extract was washed with dilute sulphuric acid and water. The solvent was evaporated off and the residue gave 2′-(2-*amino*-5-*methoxy*-4-t-*butylphenoxy*)-5,5′-*dimethoxy*-4,4′-*di*-t-*butylbiphenyl*-2-*ol* (III) (110 mg., 37%), m.p. 199—200° (from light petroleum) (lit.,[1] 195—196°) (Found: C, 74·2; H, 8·6; N, 2·8. $C_{33}H_{45}NO_5$ requires C, 74·0; H, 8·5; N, 2·6%), τ 8·73 (Bu^t), 8·66 (2Bu^t), 6·36, 6·24, and 6·11 (3OMe), 3·72, 3·46, 3·40, 3·24, 3·22, and 3·12 (6ArH), and 5·80 (OH and NH_2, removed on exchange with D_2O), $\nu_{max.}$ (CS_2) 3360 and 3440 (NH_2) and 3550 (bonded OH) cm.$^{-1}$, $\lambda_{max.}$ (ethanol) 208 and 303 mμ (log ε 4·72 and 4·08), $\lambda_{max.}$ (0·1M-ethanolic HCl) 295 mμ (log ε 3·95), $\lambda_{max.}$ (0·1M-ethanolic NaOH) 307 mμ (log ε 3·95).

When the reaction was carried out in ethanol (8 ml.) containing water (3 ml.) and sodium acetate (500 mg.) the yield was increased to 130 mg. (43%).

Similar reaction (in pyridine) of 3′,4,8-trimethoxy-2,5′,10-tri-t-butyldibenzo[*d*,*f*][1,3]dioxepin-6-spirocyclohexa-3′,5′-dien-2′-one (300 mg.) gave 2′-(2-*amino*-3-*methoxy*-5-*t*-*butylphenoxy*)-3,3′-*dimethoxy*-5,5′-*di*-t-*butylbiphenyl*-2-*ol* (V) as plates (120 mg., 40%), m.p. 180—181° (from aqueous ethanol) (Found: C, 74·0; H, 8·3; N, 2·9%), τ 8·86 (2Bu^t). 8·59 (Bu^t), 6·22 (2OMe), 6·16 (OMe), 5·75 (OH and NH_2), and 3·32 (2ArH); two AB quartets ν_A 2·96, ν_B 3·07 (*J* 1·8 c./sec.) and ν_A 3·67, ν_B 3·93 (*J* 1·8 c./sec.) were assigned to the two pairs of *meta*-protons of the biphenyl rings; $\nu_{max.}$ (CS_2) 3360, 3450, and 3520 cm.$^{-1}$, $\lambda_{max.}$ (ethanol) 215 and 285 mμ (log ε 4·70 and 3·73), $\lambda_{max.}$ (0·1M-ethanolic HCl), 281 mμ (log ε 3·71), $\lambda_{max.}$ (0·1M-ethanolic NaOH) 307 mμ (log ε 3·41).

Acetylation of the Aminophenols (III) *and* (V).—Reaction of the aminophenol (III) (150 mg.) with acetic anhydride in pyridine gave 2-*acetoxy*-2′-(2-*acetamido*-5-*methoxy*-4-*t*-*butylphenoxy*)-5,5′-*dimethoxy*-4,4′-*di*-t-*butylbiphenyl* (145 mg., 83%) as plates, m.p. 185—186·5° (from light petroleum) (Found: C, 71·8; H, 8·0; N, 2·4. $C_{37}H_{49}NO_7$ requires C, 71·7; H, 8·0; N, 2·3%), $\nu_{max.}$ (CS_2) 3360 (NH), 1690 (NAc), and 1750 (OAc) cm.$^{-1}$, τ 8·14 (NAc) and 8·04 (OAc).

When this diacetate (200 mg.) was heated under reflux for 5 hr. in ethanol (5 ml.) containing sulphuric acid (0·5 ml.), the aminophenol (III) (170 mg., 98%), m.p. and mixed m.p. 199—200°, was obtained. When the diacetate (150 mg.) was heated under reflux for 1 hr. in ethanol (7 ml.) containing 10% aqueous sodium hydroxide (5 ml.) the *acetamidophenol* (IV) (130 mg., 93%) was obtained as prisms, m.p. 246—247·5° (from benzene–light petroleum) (Found: C, 72·5; H, 8·0; N, 2·7. $C_{35}H_{47}NO_6$ requires C, 72·8; H, 8·2; N, 2·4%), $\nu_{max.}$ (CS_2) 1680 (NAc) and 3540 (bonded OH) cm.$^{-1}$; τ 8·17 (NAc).

Similar acetylation and hydrolyses of the aminophenol (V) gave the corresponding *diacetate* as plates, m.p. 167—168° (from benzene–light petroleum) (Found: C, 71·5; H, 8·3; N, 2·2%), $\nu_{max.}$ (CS_2) 1760 and 1670 cm.$^{-1}$; τ 8·20 (NAc) and 7·91 (OAc), the aminophenol (V), m.p. and mixed m.p. 178·5—180°, and the *acetamidophenol* as plates, m.p. 181—182° (from cyclohexane) (Found: C, 72·7; H, 8·1; N, 2·6%), $\nu_{max.}$ (CS_2) 1670 and 3510 cm.$^{-1}$; τ 8·33 (NAc).

Oxidation of the Aminophenol (III).—A solution of the aminophenol (III) (200 mg.) in dry ether (30 ml.) was added dropwise to a stirred suspension of lead tetra-acetate (200 mg.) in ether. After 2 hr. the dark purple mixture was poured into water and extracted with ether. The extract was washed with water, dried, and evaporated. Chromatography of the residue on alumina, and elution with benzene–light petroleum (2 : 5) gave the dibenzo[1,3]dioxepin (I) (98 mg., 49%), m.p. and mixed m.p. 208—209°. Elution with benzene gave a purple gum which could not be further purified.

Oxidation of the aminophenol (III) by silver oxide in ether, or by alkaline potassium ferricyanide, also gave intractable purple gums, which did not yield crystalline material on reductive acetylation.

Attempted Oxidative Coupling of 2,2′-*Dihydroxy*-5,5′-*dimethoxy*-4,4′-*di*-t-*butylbiphenyl with* 4-*Methoxy*-3-t-*butylaniline*.—When equimolar mixtures of the diol and amine in benzene were oxidised with alkaline potassium ferricyanide, the solution became reddish purple. Chromatography of the product on alumina gave a little 8-methoxy-3,7-di-t-butyldibenzofuran-1,4-quinone, m.p. and mixed m.p. 190—190·5° (ref. 3), as the only identifiable product. When silver oxide was used as the oxidant, both this quinone and various oxidation products of the amine (which will be described in a later publication) were isolated. Reductive acetylation of the purple chromatographic fractions from either oxidation produced no crystalline material.

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[3] F. R. Hewgill and D. G. Hewitt, *J. Chem. Soc.* (*C*), 1967, 723.