The Formation of Dibenzofurans in Acid-catalysed Quinone–Phenol Reactions and Quinone Oligomerisations: Evidence for Quinone Hemiacetal Intermediates

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The acid-catalysed reductions of (2,4-dihydroxyphenyl)-1,4-naphthoquinone (1) and the quinone hemiacetal (7) by tetramethylhydroquinone furnish the 2-hydroxydibenzofurans (3) and (9), respectively. The quinone (1) reacts with 2-methylresorcinol and 2,4-dihydroxy-5-methylphenyl-1,4-naphthoquinone (2) reacts with resorcinol, giving two different methyl substituted dihydroxy(dihydroxyphenyl)benzonaphthofurans (6) and (5), respectively. The hemiacetal (7) and resorcinol give the dihydroxyphenyldibenzofuran (10). These results provide support for the participation of quinone hemiacetals in the acid-catalysed condensation reactions of quinones with phenols to form dibenzofurans.

THE acid-catalysed reactions of 1,4-naphthoquinones and 1,4-benzoquinones usually give mixtures of quinonoid hydroxybiaryls, teraryls, and higher polymers.[1-4] In some cases, however, products containing dibenzofuran systems are formed.[4,5] Such products are also obtained when certain quinones undergo oligomerisation in acidic media.[6]

Erdtman and I recently proposed that the formation of dibenzofurans in these reactions proceeds *via* hydroxyphenylquinones, *e.g.* (1), which isomerise to hemiacetals such as (11).[6] The former compounds are derived from polyhydroxybiaryls which are the primary 1,4-addition products, by oxidation effected by the starting quinone.

In some cases the hydroxyphenyl-quinones can be isolated. 1,4-Naphthoquinone, for example, couples with resorcinol, yielding at room temperature the dihydroxyphenylnaphthoquinone (1), whereas reaction at 118 °C affords a 4 : 1 mixture of the dihydroxybenzonaphthofuran (3) and the dihydroxyphenylbenzonaphthofuran (4).[4] The latter compound is also formed when quinone (1) reacts with resorcinol.[4] Some alkylquinones also behave similarly to naphthoquinone.[5]

In order to obtain further insight into the mechanism of the aforementioned formation of dibenzofurans I have now compared some reactions of the dihydroxyphenylnaphthoquinones (1) and (2) with those of the known stable hemiacetal (7) [7,8] which is obtained from the *o*-diphenoquinone (8) when this is treated gently with acid.

When refluxed in acetic acid containing a trace of sulphuric acid the dihydroxyphenylnaphthoquinone (1) was reduced by tetramethylhydroquinone to give the dihydroxybenzonaphthofuran (3) (65%, isolated as the acetate) along with tetramethyl-1,4-benzoquinone. 1,4-Dihydroxy-2-(2,4-dihydroxyphenyl)naphthalene, the hydroquinone corresponding to the quinone (1), was stable under the reaction conditions (as was tetramethyl-1,4-benzoquinone and -hydroquinone). Ring closure must therefore take place prior to reduction.

Similar treatment of the hemiacetal (7) and tetramethylhydroquinone yielded the hydroxydibenzofuran (9) (75%, isolated as the acetate).

Addition of the dihydroxymethylphenylnapthoquinone (2) (prepared from 1,4-naphthoquinone and 2-methylresorcinol) to a refluxing solution of resorcinol in acetic acid containing a trace of sulphuric acid resulted in the formation of the dihydroxyphenyl(methyl)-benzonaphthofuran (5) (87%) and a small amount of the isomeric compound (6) (6%).

Compound (1) and 2-methylresorcinol, however, gave the dihydroxymethylphenylbenzonaphthofuran (6) (71%) together with much less of the isomeric compound (5) (24%).

In a similar way, the hemiacetal (7) and resorcinol furnished the dihydroxyphenyldibenzofuran (10) in 75% yield. The possible isomeric product, 2,7-dihydroxy-1-2-hydroxy-5-methoxy-3-t-butylphenyl)-4-t-butyldibenzofuran, was not detected in the reaction mixture.

In order to account for the observed regioselectivity, the major pathway leading to the dihydroxyphenylbenzonaphthofurans (6) and (5) must involve the transformation of the dihydroxyphenylnaphthoquinones (1) and (2) to furanoid intermediates before these react with the relevant resorcinols. The hemiacetal (7) which already possesses a furan ring reacts in exactly the same manner.

A reaction sequence analogous to that proposed [6] for the closely related quinone oligomerisations provides a satisfactory explanation for the experimental results. The dihydroxyphenylquinone (1), for example, is first transformed into the hemiacetal (11) which on protonation followed by dehydration affords the cation (12). On reduction this yields the benzonaphthofuran (3), whereas reaction with methylresorcinol furnishes the dihydroxy(methyl)phenylbenzonaphthofuran (6).

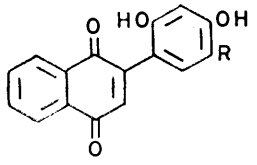
It may be noted that products containing two furan rings are not obtained when resorcinols react with a hydroxyphenylquinone such as (1). By contrast, the benzobisbenzofuran (13) is the major product obtained from the oligomerisation of 1,4-benzoquinone.[6] It is probably formed from the dibenzofuranylhydroquinone (14) (also isolated in trace amounts) by dehydrogenation to the corresponding dibenzofuranylquinone followed by hemiacetal formation, protonation, and reduction.[6] However, compounds like (4), (5), (6), and (10) which possess a 2,4- rather than a 2,5-dihydroxyphenyl group

cannot be dehydrogenated to 1,4-quinones. Hence they are incapable of forming the hemiacetals required for the formation of an additional furan ring.

Some previously reported reactions closely resemble those mentioned here. For example, 2-methoxy-6-n-propyl-1,4-benzoquinone, when treated with hydrogen chloride, undergoes dimerisation to give an equimolar mixture of a dibenzofuran and a diquinone,[9] and similar treatment of 5,5′-dimethoxy-2,2′-bi-1,4-benzoquinone gives a dichlorodibenzofuran.[10] The formation of furan rings in these reactions probably proceeds *via* a mechanism similar to that discussed here rather than *via* the classical mechanism involving dehydration of dihydroxybiphenyls.

The validity of the proposed mechanism is dependent on correct structural assignments. These were based on the spectral properties of the new compounds and their modes of formation. The mass spectra of the dihydroxyphenylbenzonaphthofurans (5) and (6) are informative, a dominant fragmentation for which was the loss of the dihydroxyphenyl groups. Thus compound (5) cleanly gave the ion (15) (*m/e* 263) whereas compound (6) gave the ion (16) (*m/e* 249). These facts and the mode of formation (*cf.* ref. 4) of compounds (5) and (6) prove their structures.

The n.m.r. spectra of the acetates of the phenols (5), (6), and (10) supply further structural information. In aryldibenzofurans of type (17) the H_A-protons show



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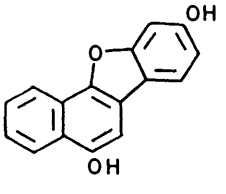
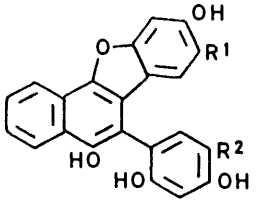
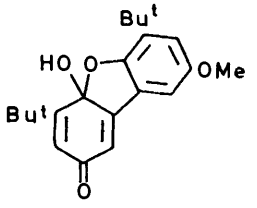


(3)



(4) $R^1 = R^2 = H$
(5) R^1 = Me; R^2 = H
(6) R^1 = H; R^2 = Me



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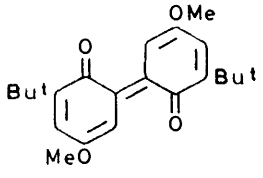

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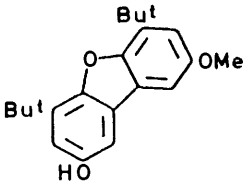
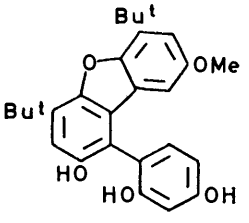


(9)



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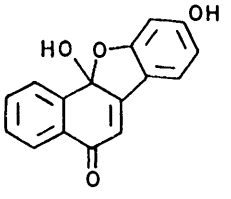

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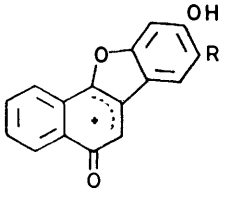

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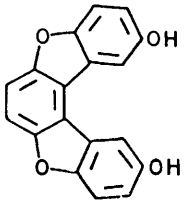

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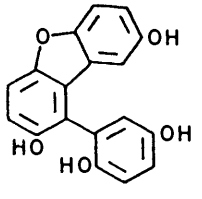

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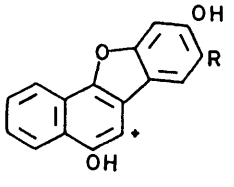
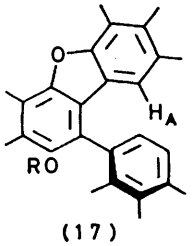
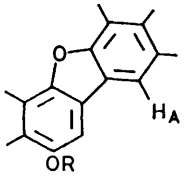


(15) R = Me
(16) R = H



(17)



(18)

large upfield shifts of *ca.* 0.8—1.0 p.p.m. relative to the shifts of the analogous H_A-protons in the corresponding dibenzofurans of type (18) [see Experimental section and compare with the n.m.r. spectra [6] of the compound (14, OMe for OH) and the corresponding 2,8-dimethoxydibenzofuran]. This effect is due to deshielding by the phenyl group which probably adopts a conformation in which the phenyl ring is not in the same plane as the dibenzofuran unit. The n.m.r. spectrum of the acetate of the dibenzofuran (9) shows the H_A resonance at δ 7.04 whereas that of the triacetate of compound (10) shows the H_A resonance at δ 6.25. This proves that the structure assigned to compound (10) is correct.

The composition of the products obtained from the quinones (1) and (2) and resorcinol and methylresorcinol, respectively, were determined by n.m.r. spectroscopy. The methyl groups of the addition products (6) and (5) resonate at different frequencies and the molar ratios of these compounds in the products were easily obtained by integration.

EXPERIMENTAL

5,9-*Diacetoxybenzo*[b]*naphtho*[2,1-d]*furan* (3, OAc *instead of* OH).—2-(2,4-Dihydroxyphenyl)-1,4-naphthoquinone (1) (100 mg) was added in small portions to a refluxing solution of tetramethylhydroquinone (0.5 g) and sulphuric acid (2M; 3 ml) in acetic acid (12 ml). After refluxing for an additional 10 min the mixture was cooled and the excess of tetramethylhydroquinone precipitated. The filtered solution was mixed with saturated sodium hydrogencarbonate and the resulting mixture was evaporated to dryness whereupon most of the tetramethyl-1,4-benzoquinone formed sublimed off. The residue was treated with pyridine (5 ml) and acetic anhydride (10 ml) and then warmed to reflux. After cooling and pouring into water a solid precipitated which was collected by filtration. Sublimation of the solid under reduced pressure gave a trace of tetramethyl-1,4-benzoquinone followed by small amounts of tetramethylhydroquinone diacetate and then the diacetate of compound (3) (83 mg, 65%). The latter was identical with an authentic sample;[4] δ (200 MHz; $CDCl_3$) 2.08, 2.38 (6 H, 2s, 2 COMe), 7.14 (1 H, dd, *J* 2.2 and 8.5 Hz, 8-H), 7.48 (1 H, d, *J* 2.2 Hz, 10-H), 7.76 [1 H, d, *J* 8.5 Hz, 7-H, corresponding to H_A in (18)], 7.50—7.72, 7.94—8.00, and 8.40—8.45 (4 H, several m, 1- to 4-H).

Similar treatment of 2-(2,4-dihydroxyphenyl)-1,4-naphthohydroquinone in refluxing acetic acid containing sulphuric acid gave only recovered starting material (isolated as the acetate).

2-*Acetoxy*-8-*methoxy*-4,6-*di-t-butyldibenzofuran* (9, OAc *instead of* OH).—The hemiacetal (7) [7] (100 mg) and tetramethylhydroquinone (0.5 g) were treated as in the preceding experiment (sulphuric acid: 1M; 0.1 ml). In this case the product was separated by chromatography on silica gel (CH_2Cl_2 as eluant) to give the desired acetate of compound (9) (84 mg, 75%) as needles, m.p. 124.5—125 °C (from EtOH) (lit.,[8] 105—108 °C, from aqueous MeOH); δ (60 MHz; CCl_4) 1.54, 1.56 (18 H, 2s, 2 Bu^t), 2.22 (3 H, s, COMe), 3.78 (3 H, s, OMe), 6.82 (1 H, d, *J* 2.6 Hz, 7-H), 6.91 (1 H, d, *J* 2.4 Hz, 3-H), 7.04 [1 H, d, *J* 2.6 Hz, 9-H, corresponding to H_A in (18)], and 7.41 (1 H, d, *J* 2.4 Hz, 1-H). Hydrolysis of the acetate (MeOH, H_2SO_4; 2 h reflux) gave the dibenzofuranol (9), m.p. 159—161 °C (lit.[7] 160—161 °C).

2-(2,4-*Dihydroxy*-5-*methylphenyl*)-1,4-*naphthoquinone* (2).—This compound was prepared from 2-methylresorcinol and 1,4-naphthoquinone as described for the dihydroxyphenylnaphthoquinone (1).[4] The *naphthoquinone* (2) gave red-brown needles (from EtOH), m.p. 206—208 °C (decomp. sealed evacuated capillary tube) (Found: C, 72.7; H, 4.3. $C_{17}H_{12}O_4$ requires C, 72.9; H, 4.3%).

5,9-*Diacetoxy*-6-(2,4-*diacetoxyphenyl*)-8-*methylbenzo*[b]*naphtho*[2,1-d]*furan* (5, OAc *instead of* OH).—The preceding quinone (2) (140 mg) was added during 10 min to a refluxing solution of resorcinol (620 mg) and sulphuric acid (2M; 0.4 ml) in acetic acid (10 ml). After refluxing for an additional 10 min the mixture was poured into water and the solid collected by filtration (184 mg). Its n.m.r. and mass spectra (see below) showed that it was a 93 : 7 mixture of compounds (5) and (6). Recrystallisation of the crude product from acetic acid–water gave the essentially pure phenol (5) (170 mg, 90%); δ [200 MHz; $(CD_3)_2CO$] 2.51 (3 H, s, Ar*Me*), 2.8—3.2br (4 H, OH), and 6.55—8.50 (9 H, several m, ArH); *m/e* 372 (100%, M^+), 354(7), 343(6), and 263(17). The purified phenol gave a *tetra-acetate* (from Ac_2O–pyridine), m.p. 204—205 °C (from AcOH) (Found: C, 68.6; H, 4.4. $C_{31}H_{24}O_9$ requires C, 68.9; H, 4.5%); δ (200 MHz; $CDCl_3$) 1.86, 2.17, 2.37, 2.37, 2.52 (15 H, 5s, 4 COMe and 1 ArMe), 6.78 [2 H, s, 10- and 7-H, corresponding to H_A in (17)], 7.11, 7.16, 7.44 (3 H, 2 d, 1 dd, $J_{3,5}$ 2.3, $J_{3,6}$ 8.6 Hz, 5-, 3-, and 6-H, respectively, of the 2,4-diacetoxyphenyl group), and 7.63—8.55 (4 H, several m, 1- to 4-H).

5,9-*Diacetoxy*-6-(2,4-*diacetoxy*-3-*methylphenyl*)*benzo*[b]*naphtho*[2,1-d]*furan* (6, OAc *instead of* OH). The dihydroxyphenylnaphthoquinone (1) (133 mg) and 2-methylresorcinol were treated as described for the preceding compound. The crude product (176 mg, 95%) was a 3 : 1 mixture of the phenols (6) and (5). Recrystallisation of the crude product from acetic acid and water gave the phenol (6) essentially pure; δ [200 MHz; $(CD_3)_2CO$] 2.23 (3 H, s, Ar*Me*), 2.8—3.2br (4 H, OH), and 6.55—8.50 (9 H, several m, ArH); *m/e* 372 (100%; M^+), 354(8), 343(6), and 249(18). Acetylation of the purified material gave the *tetra-acetate* of (6), m.p. 216.0—216.5 °C (from HOAc) (Found: C, 68.7, H 4.5. $C_{31}H_{24}O_9$ requires C, 68.9; H 4.5%); δ (200 MHz; $CDCl_3$) 1.80, 2.10, 2.11, 2.14, 2.15 (15 H, 5s, ArMe and 4 COMe), 6.88 (1 H, dd, *J* 8.5 and 2.4 Hz, 8-H), 6.96 [1 H, d, *J* 8.5 Hz, 7-H, corresponding to H_A in (17)], 7.16, 7.29 (2 H, 2 d, *J* 8.6 Hz, 5- and 6-H of the 2,4-diacetoxy-3-methylphenyl group), 7.46 (1 H, d, *J* 2.4 Hz, 10-H), and 7.6—8.5 (4 H, several me, 1- to 4-H).

Analysis of Mixtures of Compounds (5) *and* (6).—The crude dried phenolic products were analysed by n.m.r. spectroscopy [200 MHz; $(CD_3)_2CO$]. Comparisons of the areas under the two peaks at δ 2.51 and 2.23 [ArMe of compounds (5) and (6), respectively] gave the ratios of the two compounds in the products. Alternatively the mass spectra of the products were recorded (70 eV). The relative heights of the fragment ion peaks at *m/e* 263 and 249 corresponding to fragment ions (15) and (16), respectively, gave the molar ratios of the phenyls (5) and (6). Both methods gave results agreeing to within 5%.

1-(2,4-*Dihydroxyphenyl*)-2-*hydroxy*-8-*methoxy*-4,6-*di-t-butyldibenzofuran* (10).—The hemiacetal (7) (250 mg) was added in small portions during 20 min to a stirred solution of resorcinol (1.0 g) in acetic acid (5 ml) containing sulphuric

acid (4M; 0.2 ml) at room temperature. The solution was stirred for an additional 0.5 h and then poured into water, and the solid formed filtered off (0.3 g). Recrystallisation from xylene furnished the pure *dibenzofuran* (10) (238 mg, 75%), m.p. 271—272 °C (sealed evacuated capillary tube) (Found: C, 74.6; H, 7.0. $C_{27}H_{30}O_5$ requires C, 74.6; H, 7.0%); *m/e* 434(100%; M^+), 419(43), and 57(18).

Acetylation (Ac_2O, pyridine) gave the *triacetate* of (10), m.p. 173—174 °C (from EtOH) (Found: C, 70.3; H, 6.4. $C_{33}H_{36}O_8$ requires C, 70.7; H, 6.5%); δ (200 MHz; $CDCl_3$) 1.51, 1.61 (18 H, 2s, 2 Bu^t), 1.96, 2.06, 2.33 (9 H, 3s, 3 COMe), 3.58 (3 H, s, OMe), 6.25 [1 H, d, *J* 2.7 Hz, 9-H, corresponding to H_A in (17)], 6.93 (1 H, d, *J* 2.7 Hz, 7-H), 7.10 (1 H, s, 3-H), and 7.10—7.50 (3 H, complex pattern arising from the AA'X spin system of the 2,4-diacetoxyphenyl group. A computer simulated spectrum gave a good fit with shifts at δ 7.13, 7.15, and 7.44; 5-, 3-, and 6-H, respectively; $J_{3,5}$ 2.2, $J_{3,6}$ 0.1, and $J_{5,6}$ 8.8 Hz).

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