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BIQUINONES—IV

ADDITION OF HYDROGEN HALIDES TO BIBENZOQUINONES[1]

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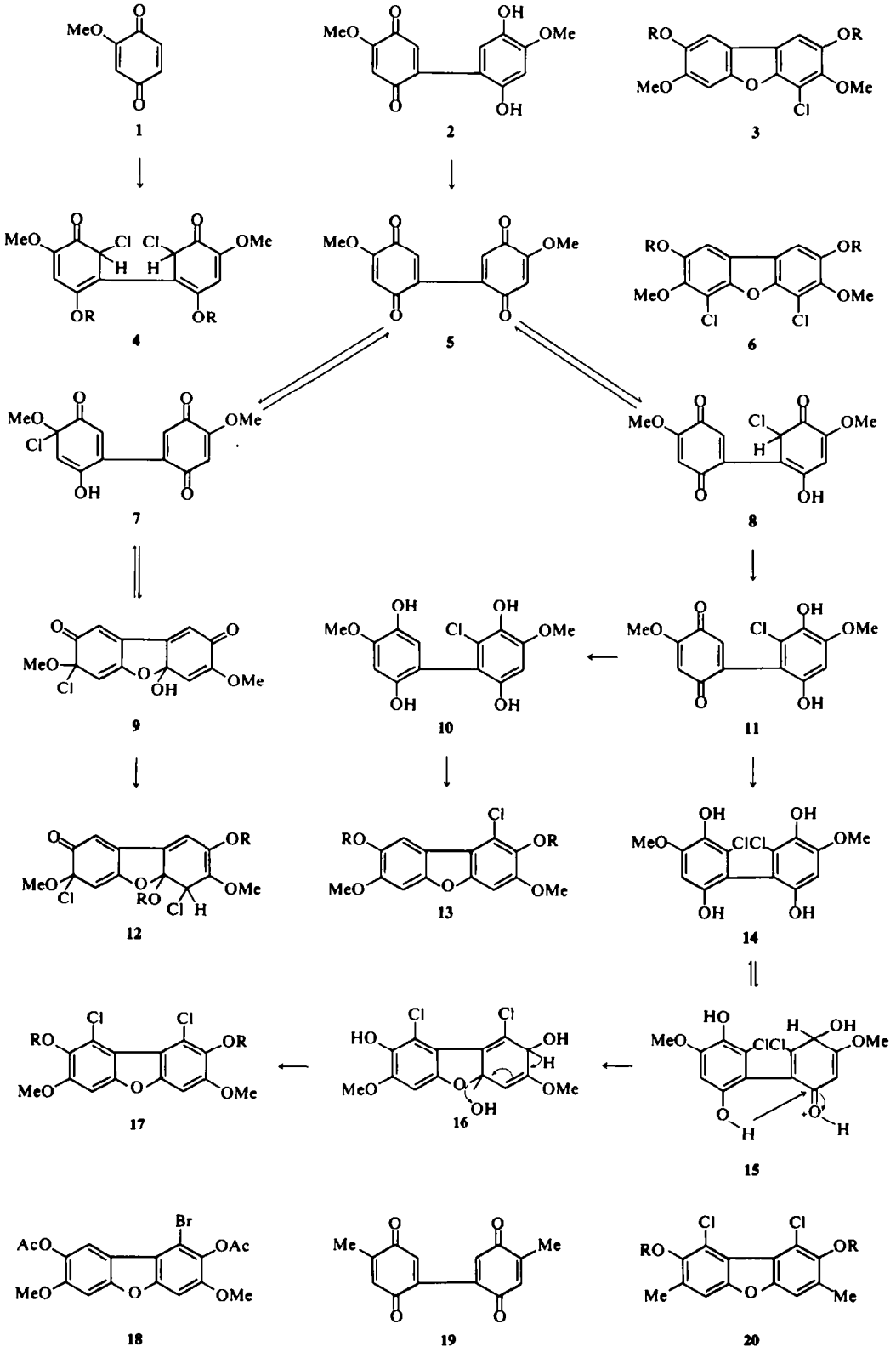
Abstract—The dienone structure (**12**; R = Ac) has been assigned to the diacetate of the product obtained by addition of hydrogen chloride to 4,4'-dimethoxy-2,5,2',5'-biquinone, in the cold, mainly on the basis of its ^{13}C NMR spectrum. The structures of a number of halogenodibenzofurans derived from this biquinone, and from the corresponding dimethylbiquinone, by reaction with hydrogen halide have also been determined.

The reaction of hydrogen chloride with 1,4-benzoquinones does not invariably yield the corresponding chloroquinol. For example, 2,6-di-t-butyl-3-chloro-1,4-benzoquinone[2a] undergoes dealkylation while with 2-methoxy-6-n-propyl-1,4-benzoquinone[2b] the products are a biquinone and a dibenzofuran. Similarly, methoxy-1,4-benzoquinone (**1**) yields[3] initially the blue dimeric "quinhydrone" (**2**), and subsequently a chlorodibenzofuran formulated as **3** (R = H), while the dimethoxybiquinone (**5**) can give, depending on the conditions, either a dichlorodibenzofuran[3,4] or a non-aromatic adduct[4] with two molecules of hydrogen chloride which were formulated as **6** (R = H) and **4** (R = H), respectively. The adduct, which arises by treatment of the biquinone (**5**) with hydrogen chloride in the cold, readily reverts to the biquinone either on heating or in presence of base, and can only be obtained pure as its diacetate[4] or dimethyl ether.[5] The proposed structure **4** (R = H) is of particular interest since it contains two apparently non-enolisable keto groups.

We have now re-examined these methoxyquinone reactions, ascribed new structures to the products previously formulated as **3**, **4** and **6** which are fully consistent with their spectroscopic properties, and compared the reactions of the dimethoxybiquinone (**5**) and the corresponding dimethylbiquinone with hydrogen chloride.

Product analysis. Elemental analysis and mass spectral measurements confirmed the molecular formulae, $C_{16}H_{16}Cl_2O_6$ and $C_{18}H_{16}Cl_2O_8$, originally allotted[4,5] to the dimethyl ether and diacetate, respectively, of the adduct of the biquinone (**5**) with hydrogen chloride, and both derivatives displayed IR absorption bands near 1685 and 1620 cm^{-1} strongly indicative of a cyclohexa-2,4-dienone structure. However, the ^1H NMR spectrum of the dimethyl ether showed signals from four non-equivalent, uncoupled protons at τ 3·05, 3·47, 4·42 and 5·34 as well as from four OMe groups, of which two were equivalent (τ 6·17) and two were not (τ 6·20 and 6·25). Obviously, such a spectrum is not consistent with structure **4** (R = Me) and indicates that unsymmetrical addition of the hydrogen chloride to the biquinone has occurred. The ^1H NMR spectrum of the diacetate was similar with singlets at τ 2·75, 3·40, 4·38, 4·58 (each 1H), 6·17 (OMe), 6·20 (OMe) and 7·73 (2 OAc). Further chemical evidence supporting an unsymmetrical structure for the adduct, was provided by the partial hydrolysis of the diacetate to a monoacetate with sulphuric acid-acetic acid. The product showed OH absorption at 3480 cm^{-1} in its IR spectrum and a pattern of four 1-proton singlets in its NMR spectrum similar to that shown by the diacetate. Although the above results clearly disprove structures **4** (R = Me and Ac) they do not, by themselves, distinguish decisively between several other possible structures for the adduct, all of which can be derived from the biquinone (**5**) by unsymmetrical addition of two moles of hydrogen chloride in such a way that two enolisable keto groups are not formed.

The problem was resolved by means of the ^{13}C NMR spectra of the diacetate (Figs 1–3) which we have interpreted in terms of structure **12** (R = Ac). The position, multiplicity and assignment of the observed resonances are given in Table 1 together with the shifts estimated by assuming the additivity of substituent effects.[6] One of the key factors lead-



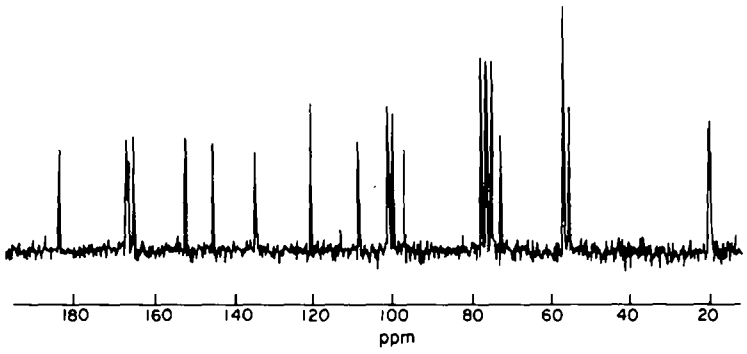


Fig 1. Proton noise-decoupled ^{13}C Fourier transform spectrum of **12** (R = Ac) in $CDCl_3$ solution; 6000 transients.

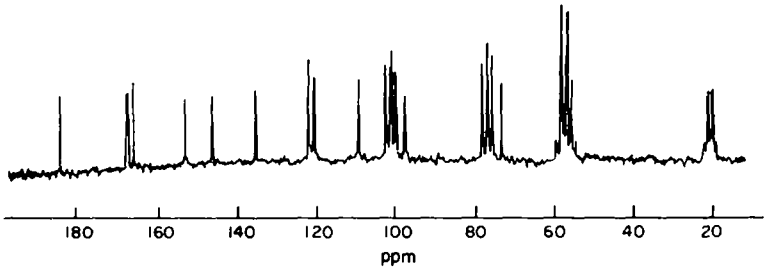


Fig 2. Off-resonance decoupled ^{13}C spectrum of **12** (R = Ac) in $CDCl_3$ solution; 50 × 1000 transients.

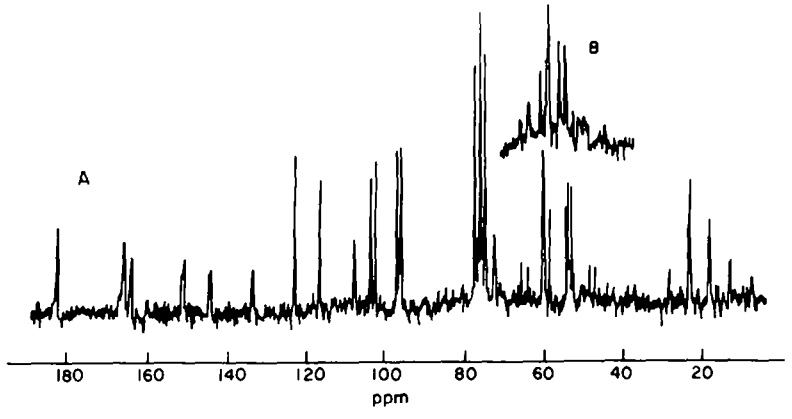
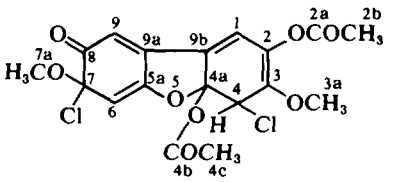


Fig 3. (A) Undecoupled ^{13}C spectrum of **12** (R = Ac) in $CDCl_3$ solution; 50 × 1000 transients. (B) ^{13}C spectrum of **12** (R = Ac) with specific decoupling of H-4.

ing to this structural assignment was the discernment of a doublet at 57·5 ppm (partly obscured by one of the OMe resonances) in the off-resonance decoupled[8] spectrum (Fig 2) attributable to an sp^3 hybridised carbon bearing a H atom. This doublet, which is more obvious in the undecoupled spectrum (Fig 3A), was collapsed to a singlet (Fig 3B) by irradiating near the resonance frequency of the proton signal at τ 4·58. The fortuitous chemical shift equivalence of C-4 and one of the OMe resonances was not observed in C_5D_5N solution, where separate signals were seen. A further guide to structure **12** (R = Ac) was provided by the detection of only three resonances attributable to CO carbon atoms, two of which, near 168 ppm, were clearly due to acetate carbonyls, and the third at 185·3 ppm to that of an α,β-unsaturated ketone. The singlet at 166·7 ppm is assigned to the

Table 1. ^{13}C NMR spectrum of diacetate (**12a**) of the dienone adduct



(12a)

Carbon Atom	Estimated Shift	Observed Shift*
	(ppm)	(ppm)
1	100	102·2(d)†[a]
2	146	146·8(s)
2a	168	168·2(s)[b]
2b	20	20·4(q)[c]
3	157	153·7(s)
3a	55	55(q)[d]
4	54	57·5(d)
4a	100	98·2(s)
4b	168	168·5(s)[b]
4c	20	20·7(q)[c]
5a	139	136·0(s)
6	100	101(d)[a]
7	80	73·5(s)
7a	55	56·1(q)[d]
8	187	185·3(s)
9	120	121·8(d)
9a	170	166·7(s)
9b	120	109·7(s)

*Lettered pairs could be reversed.
†s = singlet, d = doublet and q = quartet.

olefinic carbon C_{9a} which has a β-oxygen substituent. Agreement between the observed and estimated values in Table 1 is generally good considering the present availability of reliable substituent shifts, and it was particularly gratifying to derive concordant values for the acetal carbon C_{4a}. The largest discrepancy is for C_{9b} but it is important to note that the calculated values take no account of molecular conformation which is known[9] to have a substantial effect on ^{13}C shifts. The available data are insufficient to allow assignment of the stereochemistry at C_4, C_{4a} and C_7.

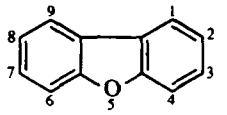
Comparison of the proton spectra of the diacetate and dimethyl ether **12** (R = Ac and Me), and reference to known proton shifts of 2,4-cyclohexadienones[10] leads us to make tentative assignment of the lowest field signal in each spectrum to the proton attached to C_1, and the signals near τ 3·43 and 4·40 to protons attached to C_6 and C_9, respectively. A surprising consequence of this interpretation and of the similarity of the spectra of the mono- and di-acetates (which differ significantly only in the position of the H_9 proton signal) is that it is the acetate group at C_{4a} which is removed on hydrolysis. However, the monoacetate was obtained in low yield and there was evidence of much biquinone (**5**) being regenerated (following hydrolysis of the ketal acetate).

Spectroscopic comparison of (a) the diacetate of the product obtained by Ioffe and Sukhina[3] by treatment of the biquinone (**5**) with concentrated hydrochloric acid in boiling acetic acid, and (b) the diacetate ("Erdtman's anhydride"[4]) produced from the adduct **12** (R = H) with hot acetic anhydride in a current of air, confirmed that these are identical dichlorodibenzofurans. Both showed ν_{CO} at 1750 cm^{-1} and an aromatic proton singlet (2H) at τ 2·92 (in addition to methoxyl and acetoxyl signals). Normally the H_1 and H_9 protons in dibenzofurans resonate at relatively low field[11] (examples in Table 2) and the observed shift (τ 2·92) corresponds more closely with that of the H_4 (H_6) protons. Hence we ascribe structure **17** (R = Ac) rather than **6** (R = Ac) to this product. Corroboration of this reassignment was gained by comparing the NMR spectrum of this dichlorodibenzofuran with that of the monochlorodibenzofuran formed either from the "quinhydrone" (**2**) and cold concentrated hydrochloric acid, followed by acetylation, or from the adduct **12** (R = H) and hot acetic anhydride. This product showed two aromatic proton signals at τ 2·88 and 2·95, and one at τ 2·14, and hence must be the 1-chlorodibenzofuran derivative **13** (R = Ac) rather than the 4-chloro isomer previously suggested for this compound.

Attempts to widen the scope of this novel addition reaction leading to the dienone (**12**) have been unsuccessful. Thus, treatment of the biquinone (**5**) with hydrogen bromide in the cold, followed by cold acetylation, gave only a dibenzofuran derivative. This monobromo compound showed three aromatic proton signals in its NMR spectrum at τ 1·98, 2·86 and 2·88, and hence is the 1-bromodibenzofuran (**18**). As described by Erdtman[4] addition of hydrogen chloride to the dimethylbibenzoquinone (**19**) gave an unstable adduct (ν_{max} 3350, 1680, 1615 cm^{-1}) whose behaviour on heating, or with alkali, was similar to that of the adduct of **5**. However, methylation with diazomethane, or acetylation with cold acetic anhydride gave only dichlorodibeezofuran derivatives. The NMR spectrum of the diacetate showed a singlet at τ 2·68 and that of the dimethyl ether one at τ 2·79. Consideration of the spectra of the foregoing dibenzofurans and those in Table 2, and the known effects of Me and OMe substituents on the chemical shifts of adjacent aromatic protons,[12] allows the unequivocal structural assignments **20** (R = Me and Ac) to be made for these products.

Product formation. We account for the formation of these dibenzofuran derivatives in terms of the reversibility of the hydrogen halide addition processes and the relative solubilities of the various possible adducts in the reaction medium. The instability of the hemiketal **12** (R = H) with respect to biquinone and hydrogen chloride is self-evident.

Table 2. ^{1}H NMR spectra of dibenzofuran derivatives



Dibenzofuran	Chemical Shift (τ) H_1	H_4	H_6	H_9
Dimethyl ether (**12**; R = Me)	3·03	5·35	3·47	4·42
Diacetate (**12**; R = Ac)	2·75	4·58	3·40	4·38
Monoacetate (**12**; R = H and Ac)	2·85	4·58	3·42	4·36
Unsubstituted[11]	2·20	–	–	2·20
2,8-Diacetoxy-1,9-dichloro-3,7-dimethoxy (**17**; R = Ac)	–	2·92	2·92	–
2,8-Diacetoxy-1-chloro-3,7-dimethoxy (**13**; R = Ac)	–	2·88	2·95	2·14
2,8-Diacetoxy-1,9-dichloro-3,7-dimethyl (**20**; R = Ac)	–	2·68	2·68	–
1,9-Dichloro-2,8-dimethoxy-3,7-dimethyl (**20**; R = Me)	–	2·79	2·79	–
2,8-Diacetoxy-1-bromo-3,7-dimethoxy (**18**)	–	2·86	2·88	1·98
1,2-Dimethoxy[11]	–	2·90	2·90	1·94
1,8-Dimethoxy[11]	–	–	–	2·53
3-Methoxy[11]	2·29	–	–	–
1,4,8,9-Tetramethoxy[11]	–	–	2·86	–
1,2,8,9-Tetramethoxy[11]	–	2·91	2·91	–

If it is assumed that addition of hydrogen chloride, in ways which give enolisable dienones such as **8**, is also reversible, then in cold chloroform solution, in which the dienone **12** (R = H) is sparingly soluble, equilibration will lead to the observed product. Under homogeneous conditions, e.g., in hot acetic acid, enolisation of adducts such as **8** to give aromatic products such as **11** (and **10** by a redox reaction) will prevail and chlorodibenzofurans will result. Cyclisation of 2,2′,5,5′-tetrahydroxybiphenyls (*e.g.* **14**) to dibenzofurans presumably proceeds by protonation of one ring followed by nucleophilic attack by an adjacent hydroxyl in the other ring, *i.e.* **14** → **15** → **16** → **17**. Hence, formation of the monochlorodibenzofuran (**13**) from the dienone adduct **12** (R = H) in hot acetic acid must proceed by an indirect route involving regeneration of biquinone and hydrogen chloride. The different behaviour of the dimethoxybiquinone (**5**) with hydrogen bromide and of the dimethylbiquinone (**19**) with hydrogen chloride we attribute simply to the greater solubility of the adducts corresponding to **12** (R = H) in chloroform solution. The reason why only a monobromodibenzofuran (**18**) is formed under circumstances which produced a dichlorodibenzofuran with hydrogen chloride is not obvious.

EXPERIMENTAL

The ^{13}C spectra of **12** (R = Ac) were obtained at 25·15 MHz using a JEOL PS-100 NMR spectrometer operating in the Fourier transform (F.T.) mode. Spectra were run in $CDCl_3$ or C_5D_5N solution using the deuterium signals from the solvents to provide a field-frequency lock. 8 mm O.D. tubes were employed, and the samples were subjected to 5 μsec (*ca* 30°) pulses at 1 sec intervals. The spectral width was 6·25 KHz and 4096 data points were used. Noise modulated proton decoupling was carried out at a nominal power level of *ca* 40 watts. For the off-resonance experiments, the noise modulation was turned off, without changing the decoupler power, and the proton frequency lowered by approximately 3 KHz. Specific decoupling of H-4 was achieved using low decoupler power levels around 1 watt.

IR spectra were measured as Nujol mulls and ^{1}H NMR spectra in deuterochloroform solution.

4,7-*Dichloro*-2,4a-*dihydroxy*-3,7-*dimethoxy*-8-*oxo*-4,4a,-6,7-*tetrahydrodibenzofuran* ("*Erdtman's adduct*" **12**; R = H) was prepared, acetylated and methylated as described by Erdtman[4] and Lindberg.[5]

Hydrolysis of diacetate (**12**; R = Ac). The diacetate (0·2 g) was dissolved in warm H_2SO_4–HOAc (1:9) (10 ml) and left for 3 days at room temp. The resulting green soln was poured into water and the ppt (0·12 g) which separated was collected. TLC on silica in $CHCl_3$–Me_2CO (19:1) gave 4a-*acetoxy*-4,7-*dichloro*-2-*hydroxy*-3,7-*dimethoxy*-8-*oxo*-4,4a,6,7-*tetrahydrodibenzofuran*, m.p. 234–235° (from $CHCl_3$-petrol). (Found: C, 49·4; H, 3·9; Cl, 17·2. $C_{16}H_{14}Cl_2O_7$ requires: C, 49·4; H, 3·6; Cl, 18·2%); ν_{max} 3480, 1740, 1680(w), 1650 and 1600 cm^{-1}, τ 7·7 (3H, s, Ac), 6·2 (3H, s, OMe), 6·1 (3H, s, OMe)—see also Table 2.

2,8-*Diacetoxy*-1,9-*dichloro*-3,7-*dimethoxydibenzofuran* (**17**; R = Ac), m.p. 252–253°, ν_{max} 1750 cm^{-1}, τ 7·58 (6H, s, 2Ac), 4·05 (6H, s, 2MeO) and see Table 2, was prepared as described by Ioffe and Sukhina[3] and was identical (IR, NMR, m.p.) with an authentic specimen of "Erdtman's anhydride" supplied by Professor Erdtman.

2,8-*Diacetoxy*-1-*chloro*-3,7-*dimethoxydibenzofuran* (**13**; R = Ac). The adduct **12** (R = H; 8 g) in Ac_2O (40 ml) was heated for 10 min in a current of air, and then allowed to cool. The dimethoxybiquinone (3·8 g) which precipitated was collected, and the red filtrate was poured into water After 16 hr the water was decanted and the yellow residue was crystallised from aqueous Me_2CO to give the product (0·2 g), m.p. 229–230°, ν_{max} 1753 cm^{-1}, τ 7·65 (3H, s, Ac), 7·60 (3H, s, Ac), 6·1 (6H, s, 2MeO) and see Table 2. This

product was identical (IR, NMR) with that obtained from the "internal quinhydrone" (2) and HCl as described by Ioffe and Sukhina.[3]

2,8-Diacetoxy-1-bromo-3,7-dimethoxydibenzofuran (**18**). HBr was bubbled into a soln of **5** (1·0 g) in $CHCl_3$ (75 ml) for 30 min. The clear soln was evaporated to dryness at room temp, and the residue was washed successively with small amounts of cold MeOH and ether. The resulting solid, which showed no IR absorption between 1700–1600 cm^{-1} was treated with Ac_2O (5 ml) containing a trace of conc. H_2SO_4, and left for 24 hr. The soln was then diluted with water, and the ppt which separated was collected and crystallised from aqueous Me_2CO to give the product, m.p. 207–209°. (Found: C, 50·7; H, 3·3. $C_{18}H_{15}BrO_7$ requires: C, 51·1; H, 3·5%); ν_{max} 1750 cm^{-1}, τ 7·65 (3H, s, Ac), 6·6 (3H, s, Ac), 6·1 (6H, s, 2MeO) and see Table 2.

Reaction of 4,4'-dimethyl-2,5,2',5'-bibenquinone with hydrogen chloride. HCl was bubbled into a soln of the biquinone[13] (0·8 g) in $CHCl_3$ (50 ml) for 3 hr at room temp. The resulting soln was evaporated to dryness at room temp, and the residue was washed with small amounts of ether and MeOH. This product (ν_{CO} 3400, 1675 and 1615 cm^{-1}) was unstable on treatment with alkali. Acetylation with cold acetic anhydride gave *2,8-diacetoxy-1,9-dichloro-3,7-dimethyldibenzofuran*, m.p. 168–170° (from aqueous EtOH) (Found: C, 56·3; H, 3·6; Cl, 17·9. $C_{18}H_{14}Cl_2O_5$ requires: C, 56·7; H, 3·7; Cl, 18·6%); ν_{max} 1750 cm^{-1}, τ 7·68 (6H, s, 2Me), 7·58 (6H, s, 2Me) and see Table 2, and methylation with etherial diazomethane gave *1,9-dichloro-2,3,7,8-tetramethoxydibenzofuran*, m.p. 176° (from aqueous EtOH). (Found: C, 58·9; H, 4·2. $C_{16}H_{14}Cl_2O_5$ requires: C, 59·1; H, 4·3%), τ 7·58 (6H, s, 2Me), 6·17 (6H, s, 2MeO) and see Table 2.

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REFERENCES

[1]Part III, K. Chandrasenan and R. H. Thomson, *Tetrahedron* **27**, 2529 (1971)
[2a]H. W. Moore, D. L. Maurer, D. S. Pearce and M. S. Lee, *J. Org. Chem.* **37**, 1984 (1972);
[b]F. M. Dean, A. M. Osman and A. Robertson, *J. Chem. Soc.* 11 (1955)
[3]I. S. Ioffe and A. F. Sukhina, *J. Gen. Chem. U.S.S.R.* **23**, 1433 (1953)
[4]H. G. H. Erdtman, *Proc. Roy. Soc.* **143A**, 191 (1934)
[5]B. Lindberg, *Acta Chem. Scand.* **5**, 885 (1951)
[6]G. C. Levy and G. L. Nelson, ^{13}C *Nuclear Magnetic Resonance for Organic Chemists* Ch. 2. Wiley, N.Y. (1972)
[7]*cf.*, R. Hollenstein and W. von Philipsborn, *Helv. Chim. Acta* **55**, 2030 (1972)
[8]Ref. 6, p. 9
[9]D. M. Grant and B. V. Cheney, *J. Am. Chem. Soc.* **89**, 5315 (1967); D. K. Dalling and D. M. Grant, *Ibid.* **89**, 6612 (1967)
[10]W. Regel an W. von Philipsborn, *Helv. Chim. Acta* **51**, 867 (1968)
[11]S. Forsen and N. E. Stjernstrom, *Arkiv. Kemi* **21**, 65 (1964)
[12]L. M. Jackman and S. Sternhell, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry* p. 202. Pergamon, London (1969)
[13]Th. Posternak, W. Alcalay and R. Huguenin, *Helv. Chim. Acta* **39**, 1556 (1956)