

Reactions of Quinones with Aromatic Ethers. Part IV.¹ Dibenzofurans from the Cyclisation of Arylbenzoquinones

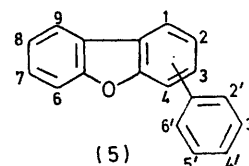
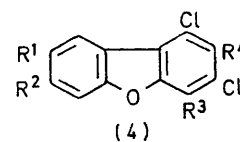
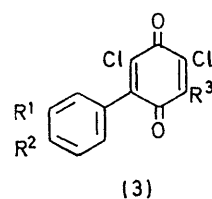
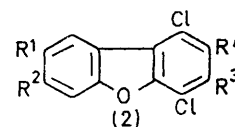
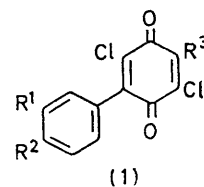
By Oliver C. Musgrave * and Colin J. Webster, Chemistry Department, The University, Old Aberdeen AB9 2UE

2,5- and 2,6-Dichlorobenzoquinone react with diazotised 3-methoxy-4-methyl- and 4-methoxy-3-methyl-aniline to form the expected monoaryl- and diaryl-dichlorobenzoquinones which undergo cyclisation on treatment with aluminium chloride to give the corresponding dichlorodibenzofurans.

CERTAIN dichloro-3-(3,4-dimethoxyphenyl)benzoquinones, *e.g.* (1; $R^1 = R^2 = \text{MeO}$, $R^3 = \text{H}$), cyclise in the presence of 70% v/v aqueous sulphuric acid to give the corresponding hydroxydibenzofurans, *e.g.* (2; $R^1 = R^2 = \text{MeO}$, $R^3 = \text{H}$, $R^4 = \text{OH}$).¹ To learn more about the scope of this reaction we have examined the cyclisation of a number of related monoaryl- and diarylbenzoquinones each containing one methoxy and one methyl group at C-3 and C-4 on the aromatic nucleus.

Treatment of 2,5- and 2,6-dichlorobenzoquinone with buffered solutions of diazotised 3-methoxy-4-methyl- and 4-methoxy-3-methyl-aniline gave the monoarylbenzoquinones (1; $R^1 = \text{MeO}$, $R^2 = \text{Me}$, $R^3 = \text{H}$), (1; $R^1 = \text{Me}$, $R^2 = \text{MeO}$, $R^3 = \text{H}$), and (3; $R^1 = \text{Me}$, $R^2 = \text{MeO}$, $R^3 = \text{H}$) together with the diaryl compounds (1; $R^1 = \text{MeO}$, $R^2 = \text{Me}$, $R^3 = 3\text{-MeO-4-MeC}_6\text{H}_3$), (1; $R^1 = \text{MeO}$, $R^2 = \text{MeO}$, $R^3 = 4\text{-MeO-3-MeC}_6\text{H}_3$), (3; $R^1 = \text{MeO}$, $R^2 = \text{Me}$, $R^3 = 3\text{-MeO-4-MeC}_6\text{H}_3$), and (3; $R^1 = \text{Me}$, $R^2 = \text{MeO}$, $R^3 = 4\text{-MeO-3-MeC}_6\text{H}_3$). 70% v/v Aqueous sulphuric acid¹ proved to be unsuitable for the cyclisation of most of these quinones. At room temperature it had no effect while above 60° it usually caused decomposition. Only one quinone (3; $R^1 = \text{Me}$, $R^2 = \text{OMe}$, $R^3 = \text{H}$), was converted into the corresponding dibenzofuran under the latter, more vigorous, conditions. We had previously observed that anhydrous aluminium chloride also effected the cyclisation of the (dimethoxyphenyl)quinone (1; $R^1 = R^2 = \text{MeO}$, $R^3 = \text{H}$) in boiling benzene but caused partial demethylation of the resulting dibenzofuran. After methylation, however, the product was identical with a specimen of the trimethoxydibenzofuran (2; $R^1 = R^2 = R^4 = \text{MeO}$, $R^3 =$

H) prepared from the hydroxydimethoxy-compound (2; $R^1 = R^2 = \text{MeO}$, $R^3 = \text{H}$, $R^4 = \text{OH}$).¹ Both the monoaryl- and the diarylbenzoquinones behaved in a similar manner on being heated with aluminium chloride. The



products isolated (see Table 1) were either the fully methylated dibenzofurans or, in two cases, the 2-hydroxy-compounds. Their structures follow from the resemblance of their u.v. absorption data to those¹ of the hydroxydimethoxydibenzofurans (2 and 4; $R^1 = R^2 = \text{MeO}$, $R^3 = \text{H}$, $R^4 = \text{OH}$) (see Table 2) and, more

¹ Part III, O. C. Musgrave and C. J. Webster, preceding paper.

TABLE 1
Dichlorodibenzofurans

	M.p. (°)	Formula	Found (%)		Required (%)	
			C	H	C	H
1,4-Dichlorodibenzofurans						
(2; R ¹ = R ² = R ⁴ = MeO, R ³ = H)	201.5—203.5 ^a	C ₁₅ H ₁₂ Cl ₂ O ₄	55.1	3.8	55.05	3.7
(2; R ¹ = MeO, R ² = Me, R ³ = H, R ⁴ = OH)	178—179 ^b	C ₁₄ H ₁₀ Cl ₂ O ₃ ^d	56.6	3.6	56.6	3.4
(2; R ¹ = R ⁴ = MeO, R ² = Me, R ³ = 3-MeO-4-MeC ₆ H ₃)	206—207 ^c	C ₂₃ H ₂₀ Cl ₂ O ₄	64.3	4.6	64.05	4.65
(2; R ¹ = Me, R ² = R ⁴ = MeO, R ³ = 4-MeO-3-MeC ₆ H ₃)	218—219 ^a	C ₂₃ H ₂₀ Cl ₂ O ₄	63.9	4.5	64.05	4.65
1,3-Dichlorodibenzofurans						
(4; R ¹ = R ⁴ = MeO, R ² = Me, R ³ = 3-MeO-4-MeC ₆ H ₃)	213—215 ^c	C ₂₃ H ₂₀ Cl ₂ O ₄	64.0	4.8	64.05	4.65
(4; R ¹ = Me, R ² = MeO, R ³ = H, R ⁴ = OH)	208—212 ^b (decomp.)	C ₁₄ H ₁₀ Cl ₂ O ₃	56.8	3.3	56.6	3.4
(4; R ¹ = Me, R ² = R ⁴ = MeO, R ³ = 4-MeO-3-MeC ₆ H ₃)	205—208 ^c	C ₂₃ H ₂₀ Cl ₂ O ₄	64.2	4.8	64.05	4.65
^a From chloroform-ethanol. ^b From methanol. ^c From nitromethane. ^d Found: OMe, 10.9. Required: OMe, 10.45%.						

^a From chloroform-ethanol. ^b From methanol. ^c From nitromethane. ^d Found: OMe, 10.9. Required: OMe, 10.45%.TABLE 2
U.v. absorption * of dichlorodibenzofurans

Compound	$\lambda_{\max.}/\text{nm}$ (log ϵ) in CHCl ₃	
	$\lambda_{\max.}/\text{nm}$ (log ϵ)	$\lambda_{\max.}/\text{nm}$ (log ϵ)
(2; R ¹ = R ² = MeO, R ³ = H, R ⁴ = OH) † ¹	233 (4.36)	245i (4.17), 256i (3.99), 298i (4.24), 308 (4.35), 318i (4.21), 327i (4.03)
(2; R ¹ = R ² = R ⁴ = MeO, R ³ = H)	260i (4.08), 268 (4.03)	311 (4.38), 332 (4.09)
(2; R ¹ = MeO, R ² = Me, R ³ = H, R ⁴ = OH)	266 (4.06)	298i (4.10), 307 (4.29), 321i (3.92), 336 (3.77)
(2; R ¹ = R ⁴ = MeO, R ² = Me, R ³ = 3-MeO-4-MeC ₆ H ₃)	265i (4.17)	308 (4.35), 317i (4.28), 333i (4.00)
(2; R ¹ = Me, R ² = R ⁴ = MeO, R ³ = 4-MeO-3-MeC ₆ H ₃)	257 (4.26), 267i (4.15)	313i (4.45), 319 (4.47), 351 (3.66)
(4; R ¹ = R ² = MeO, R ³ = H, R ⁴ = OH) † ¹	223 (4.45), 243i (4.22)	315 (4.37), 322i (4.30), 345i (3.43)
(4; R ¹ = R ⁴ = MeO, R ² = Me, R ³ = 3-MeO-4-MeC ₆ H ₃)	263 (4.38)	311 (4.29), 332i (3.98)
(4; R ¹ = Me, R ² = MeO, R ³ = H, R ⁴ = OH) †	234 (4.35)	305 (4.37), 310 (4.38), 317 (4.44), 324i (4.15)
(4; R ¹ = Me, R ² = R ⁴ = MeO, R ³ = 4-MeO-3-MeC ₆ H ₃)	259i (4.33), 266 (4.33), 282 (4.19)	312i (4.36), 320 (4.41)

* The symbol i denotes an inflection. † In ethanol.

TABLE 3
N.m.r. signals of dichlorodibenzofurans

	Chemical shift (δ) in CDCl ₃ *,†						
	9-H	6-H	3- or 4-H	2'-H	7-, 8-, 3'-, and 4'-MeO	2-MeO (or 2-HO)	7-, 8-, 3'-, and 4'-Me
1,4-Dichlorodibenzofurans							
(2; R ¹ = R ² = MeO, R ³ = H, R ⁴ = HO) ¹	7.66	7.09	7.15		4.00, 3.98	(5.48)	
(2; R ¹ = R ² = R ⁴ = MeO, R ³ = H)	7.69	7.08	6.93		3.98, 3.96	3.93	
(2; R ¹ = MeO, R ² = Me, R ³ = H, R ⁴ = HO)	7.58	7.36	7.11		3.93	(5.53)	2.37
(2; R ¹ = R ⁴ = MeO, R ² = Me, R ³ = 3-MeO-4-MeC ₆ H ₃)	7.72	7.41		6.88	3.97, 3.84	3.53	2.39, 2.31
(2; R ¹ = Me, R ² = R ⁴ = MeO, R ³ = 4-MeO-3-MeC ₆ H ₃)	8.06	7.11		7.18	3.94, 3.91	3.50	2.37, 2.29
1,3-Dichlorodibenzofurans							
(4; R ¹ = R ² = MeO, R ³ = H, R ⁴ = HO) ¹	7.67	7.04	7.42		3.98, 3.96	(5.75)	
(4; R ¹ = Me, R ² = MeO, R ³ = H, R ⁴ = HO)	7.99	6.99	7.44		3.91	(5.75)	2.34
(4; R ¹ = R ⁴ = MeO, R ² = Me, R ³ = 3-MeO-4-MeC ₆ H ₃)	7.71	7.26		6.98	4.00, 3.96	3.86	2.34, 2.32
(4; R ¹ = Me, R ² = R ⁴ = MeO, R ³ = 4-MeO-3-MeC ₆ H ₃)	8.05	6.97		7.30	3.99, 3.92	3.86	2.36, 2.32

* Positions numbered as in formula (5). † All the signals are singlets except those of the C-5' and C-6' protons which appear essentially as AB quartets between δ 7.4 and 6.8.

specifically, from their n.m.r. spectra. The assignments of the proton resonances given in Table 3 are based on comparison of the spectra and on data for related dibenzofurans.² They indicate that in each case cyclisation involves the position in the aromatic ring *para* to the methoxy or methyl substituent.

EXPERIMENTAL

Details of the general methods and of the instruments used were given in Part I.³ U.v. absorption spectra were measured in chloroform solution unless stated otherwise.

Arylation of 2,5-Dichlorobenzoquinone.—(a) Using diazotised 3-methoxy-4-methylaniline. The solution of the diazonium salt prepared from 3-methoxy-4-methylaniline⁴ (276 mg) in 2M-hydrochloric acid (5 ml) and sodium nitrite (170 mg) in water (2 ml) at 5° was added together with a solution of sodium acetate (500 mg) in water (5 ml) to a

² S. Forsén and N. E. Stjernström, *Arkiv Kemi*, 1964, **21**, 65; C. Brown, A. R. Forrester, and R. H. Thomson, *Tetrahedron*, 1973, **29**, 3059.

³ O. C. Musgrave and C. J. Webster, *J. Chem. Soc. (C)*, 1971, 1393.

⁴ F. Ullmann and R. Fitzenkam, *Ber.*, 1905, **38**, 3787.

solution of 2,5-dichlorobenzoquinone (390 mg) in acetone (30 ml) at 5°. The solution was warmed to 10–15° and stirred for 1 h, water (20 ml) was added, and the mixture was cooled to 0° and filtered. Digestion of the red residue with ethanol (3 × 15 ml) gave an insoluble orange solid (A) (50 mg). Evaporation of the ethanol washings afforded 2,5-dichloro-3-(3-methoxy-4-methylphenyl)-1,4-benzoquinone which crystallised from ethanol in red crystals (240 mg), m.p. 162–163° (Found: C, 56.6; H, 3.6; Cl, 22.4. $C_{14}H_{10}Cl_2O_3$ requires C, 56.6; H, 3.4; Cl, 23.85%), ν_{\max} 1675 cm^{-1} (quinone C=O), λ_{\max} (EtOH) 275 (log ϵ 4.13) and 435 nm (3.01), λ_{infl} 254 (log ϵ 3.97), 267 (4.09), and 321 nm (3.05). The solid (A) crystallised from nitromethane to give 2,5-dichloro-3,6-bis-(3-methoxy-4-methylphenyl)-1,4-benzoquinone as orange-red crystals (45 mg), m.p. 295–297° (Found: C, 63.2; H, 4.1; Cl, 18.1. $C_{22}H_{18}Cl_2O_4$ requires C, 63.3; H, 4.35; Cl, 17.0%), ν_{\max} 1664 cm^{-1} (quinone C=O), λ_{\max} 282 (log ϵ 4.16), 312 (3.82), and 377 nm (3.27), λ_{infl} 334 (log ϵ 3.62) and 425 nm (3.25).

(b) *Using diazotised 4-methoxy-3-methylaniline.* A similar reaction using 4-methoxy-3-methylaniline (for preparation, see below) yielded 2,5-dichloro-3-(4-methoxy-3-methylphenyl)-1,4-benzoquinone (120 mg) as deep red crystals, m.p. 148–149° (from ethanol) (Found: C, 56.8; H, 3.2; Cl, 23.6. $C_{14}H_{10}Cl_2O_3$ requires C, 56.6; H, 3.4; Cl, 23.85%), ν_{\max} 1676 cm^{-1} (quinone C=O), λ_{\max} (EtOH) 264 (log ϵ 4.21) and 470 nm (3.24), λ_{infl} 325 nm (log ϵ 2.90), and 2,5-dichloro-3,6-bis-(4-methoxy-3-methylphenyl)-1,4-benzoquinone (17 mg) as deep brown needles, m.p. 265–267° (from nitromethane) (Found: C, 63.1; H, 4.2. $C_{22}H_{18}Cl_2O_4$ requires C, 63.3; H, 4.35%), ν_{\max} 1670 cm^{-1} (quinone C=O), λ_{\max} 272 (log ϵ 4.41) and 456 nm (3.64), λ_{infl} 318 nm (log ϵ 3.14).

Arylation of 2,6-Dichlorobenzoquinone.—(a) *Using diazotised 3-methoxy-4-methylaniline.* A reaction similar to that described above for 2,5-dichlorobenzoquinone gave 2,6-dichloro-3,5-bis-(3-methoxy-4-methylphenyl)-1,4-benzoquinone as deep brown needles (115 mg), m.p. 183–186°, which crystallised from ethanol and sublimed at 210° and 0.2 mmHg (Found: C, 63.4; H, 4.3; Cl, 17.8. $C_{22}H_{18}Cl_2O_4$ requires C, 63.3; H, 4.35; Cl, 17.0%), ν_{\max} 1680 and 1660 cm^{-1} (quinone C=O), λ_{\max} 258 (log ϵ 4.11), 284 (4.26), 318 (3.55), and 465 nm (3.31), λ_{infl} 365 nm (log ϵ 3.29). None of the monoarylated product was obtained and an examination of the rest of the reaction mixture by t.l.c. on silica gel using ether–hexane showed the presence of unchanged 2,6-dichlorobenzoquinone and the diarylated product only.

(b) *Using diazotised 4-methoxy-3-methylaniline.* A similar reaction was performed with 4-methoxy-3-methylaniline using ethanol in place of acetone as the solvent for the quinone. The mixture was stirred for 4 h, and the resulting brown solid (A) was collected. The filtrate was diluted with water and extracted with ether. The resulting syrup was separated by column chromatography on silica gel using ether–hexane into 2,6-dichlorobenzoquinone (53 mg) and 2,6-dichloro-3-(4-methoxy-3-methylphenyl)-1,4-benzoquinone which crystallised from ethanol in deep blue crystals (88 mg), m.p. 130–131° (Found: C, 56.8; H, 3.4; Cl, 23.8. $C_{14}H_{10}Cl_2O_3$ requires C, 56.6; H, 3.4; Cl, 23.85%), ν_{\max} 1685 and 1665 cm^{-1} (quinone C=O), λ_{\max} (EtOH) 223 (log ϵ 3.96), 266 (4.27), 332 (3.16), and 475 nm (3.37). The solid (A) crystallised from chloroform–ethanol to give 2,6-dichloro-3,5-bis-(4-methoxy-3-methylphenyl)-1,4-benzoquinone as deep brown crystals (38 mg) which sublimed at 210° and 0.2

mmHg, m.p. 208–209° (Found: C, 63.6; H, 4.4; Cl, 17.7. $C_{22}H_{18}Cl_2O_4$ requires C, 63.3; H, 4.35; Cl, 17.0%), ν_{\max} 1677 and 1660 cm^{-1} (quinone C=O), λ_{\max} 270 (log ϵ 4.37), 321 (3.30), and 480 nm (3.56), λ_{infl} 282 nm (log ϵ 4.26).

Cyclisation of the Monoaryl- and Diaryl-dichlorobenzoquinones.—A mixture of the quinone (200 mg), dry benzene (20 ml), and anhydrous aluminium chloride (250 mg) was heated under reflux for 1–2 h. The solvent was evaporated under reduced pressure and the dark residue was shaken with chloroform and 5M-hydrochloric acid. Evaporation of the dried (MgSO₄) chloroform layer gave the crude 2-hydroxydibenzofuran which was either crystallised or heated under reflux for 1 h with a mixture of acetone (10 ml), dimethyl sulphate (0.5 ml), and fused potassium carbonate (60 mg). The mixture was evaporated under reduced pressure and the residue was warmed with 2M-sodium hydroxide solution. Crystallisation of the resulting solid gave the 2-methoxydibenzofuran (27–76%) which could be sublimed near its m.p. at 0.2 mmHg. The compounds prepared in this way and their u.v. and n.m.r. data are recorded in Tables 1–3.

1,4-Dichloro-2,7,8-trimethoxydibenzofuran.—Prepared by the methylation of 1,4-dichloro-2-hydroxy-7,8-dimethoxydibenzofuran¹ using dimethyl sulphate and potassium carbonate in acetone, this (72%; m.p. 201–203°) was identical with the specimen prepared by the aluminium chloride-catalysed reaction.

Cyclisation of 2,6-Dichloro-3-(4-methoxy-3-methylphenyl)-1,4-benzoquinone using Sulphuric Acid.—A mixture of the powdered quinone (35 mg) and 70% v/v aqueous sulphuric acid (3 ml) was kept at 75° for 12 h and at room temperature for 2 days, diluted with water (5 ml), and filtered. The resulting solid crystallised from aqueous methanol to give 1,3-dichloro-2-hydroxy-7-methoxy-8-methyldibenzofuran as needles (22 mg), m.p. 207–210° (decomp.), identical with the specimen prepared by the aluminium chloride-catalysed reaction.

2-Methoxy-5-nitrotoluene.—2-Methoxytoluene (14 g) was added dropwise to a stirred mixture of concentrated nitric acid (75 ml) and water (75 ml). The mixture was heated at 50° for 1 h, poured into ice–water, filtered, and the residue was washed with aqueous 2M-sodium hydroxide. The solid crystallised from methanol to give 2-methoxy-5-nitrotoluene (8.6 g), m.p. 60–62° (lit.,⁵ 63°).

4-Methoxy-3-methylaniline.—A mixture of 2-methoxy-5-nitrotoluene (6 g), tin(II) chloride (27 g), concentrated hydrochloric acid (30 ml), and ethanol (60 ml) was heated at 80° for 30 min, concentrated to ca. 65 ml, and cooled to 0°. The resulting crystalline solid was washed with concentrated hydrochloric acid, dissolved in water, and the solution was made strongly alkaline by the addition of solid sodium hydroxide. Extraction with ether afforded an oily solid which crystallised from ether–light petroleum (b.p. 40–60°) giving 4-methoxy-3-methylaniline as plates (3.6 g), m.p. 58–59° (lit.,⁶ 59–59.5°) (Found: C, 70.0; H, 7.8. Calc. for $C_9H_{11}NO$: C, 70.05; H, 8.1%).

We thank the S.R.C. for a research studentship.

[4/890 Received, 6th May, 1974]

⁵ J. Kenner and M. Parkin, *J. Chem. Soc.*, 1920, **117**, 852.

⁶ E. Bamberger, *Annalen*, 1925, **443**, 192.