Chemistry of Quinones. Part IV.[1] Synthesis of Anthraquinones *via* Friedel–Crafts Reaction between 3,4-Dimethoxyphthalic Anhydride and *o*-Cresol: a Re-investigation

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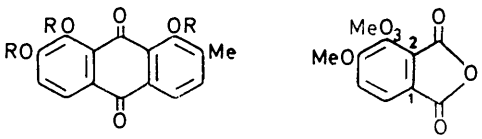
Contrary to previous reports, the Friedel–Crafts reaction between 3,4-dimethoxyphthalic anhydride and *o*-cresol gives a mixture of four benzoylbenzoic acids. After cyclisation and methylation, the major and minor products were 1,2,6- and 1,2,8-trimethoxy-7-methylanthraquinone respectively. The latter quinone and its demethylation product differ from cladofulvin trimethyl ether and cladofulvin respectively, thus indicating that the fungal pigment cladofulvin is not 1,2,8-trihydroxy-7-methylanthraquinone as was previously suggested.

An anthraquinone pigment, cladofulvin, was isolated by Agosti *et al.* from a strain of the fungus *Cladosporium fulvum* Cooke [syn. *Fulvia fulvum* (Cooke) Ciferri] and on the basis of classical degradations and spectroscopic (i.r. and u.v.–visible) data was assigned structure (Ia);[2] this has since been disputed by Chari *et al.*[3] Following the procedure of Simonsen[4] these workers treated 3,4-dimethoxyphthalic anhydride (II) with *o*-cresol and cyclised the resulting benzoylbenzoic acid.[4] Methylation of the product gave a trimethoxy(methyl)-anthraquinone which they believed had structure (Ib). Comparison of this synthetic product with cladofulvin trimethyl ether showed that they were different † and Chari *et al.* therefore concluded that cladofulvin did not have structure (Ia). However, neither Simonsen[4] nor Chari *et al.*[3] proved that their synthetic product had structure (Ib). We have re-investigated this synthetic work and now present the results.‡ We find that these reactions afford two quinones, the major product being that described previously, which is, in fact, quinone (IIIb), and the minor product being quinone (Ib). Comparison of the latter quinone and its demethylation product with cladofulvin trimethyl ether and cladofulvin respectively indicates that cladofulvin does not have structure (Ia).

Simonsen treated the anhydride (II) with *o*-cresol in the presence of aluminium trichloride in *sym*-tetrachloroethane at 120—130° and isolated an acidic product, m.p. 250—251°, to which he assigned structure (IVa).[4] By using the reported procedure[4] we obtained four acidic products in a combined yield of 24%. Acid A (12%), m.p. 145° (decomp.), contained one methoxy-group and two phenolic groups and on treatment with diazomethane gave a fully *O*-methylated ester. Cleavage of this ester with the butoxide–water reagent[5] gave 3,4-dimethoxybenzoic acid and 4-methoxy-3-methylbenzoic acid and as it was prepared using anhydride (II) it follows that the ester has structure (Va). The fact that both phenolic groups in acid A readily reacted with diazomethane suggests that neither group was intramolecularly hydrogen-bonded to the ketone group, and in agreement with this the ketone band in the i.r. spectrum of the methyl ester of acid A (prepared using sulphuric acid in methanol) appeared at 1655 cm^{-1},

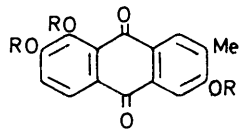


(I)

a, R = H

b, R = Me

(II)



(III)

a, R = H

b, R = Me

a value too high for a chelated diaryl ketone. This suggests acid A has structure (Vb). This is not the expected isomer as methoxy-groups *ortho* to carbonyl groups are usually demethylated preferentially in the presence of aluminium trichloride.[6] Acid B (8%), m.p. 260—262°, contained two methoxy-groups and a phenolic group and differed from acid A only in the extent of *O*-methylation, since it also reacted with diazomethane to give ester (Va). It follows that acid B has structure (Vc). Acid C (1·5%), m.p. 240—242°, contained one methoxy-group and two phenolic groups and acid D (2·5%), m.p. >320°, contained two methoxy-groups and one phenolic group. These acids differed only in the extent of *O*-methylation as both gave the same phenolic ester [subsequently shown to be (IVb)]

† The trihydroxyquinone obtained by demethylating the synthetic product differed (by t.l.c. and u.v. spectroscopy) from a sample of cladofulvin.[3] This result is of doubtful significance, however, as the u.v spectrum of their sample of the pigment differs from that reported previously.[2]

‡ A fuller account of this work is given in the Ph.D. Theses of D. G. Davies and P. Yates, University of Lancaster, 1970 and 1974, respectively.

[1] Part III, D. G. Davies, P. Hodge, and P. Yates, *J.C.S. Perkin I*, 1973, 2299.

[2] G. Agosti, J. H. Birkinshaw, and P. Chaplen, *Biochem. J.*, 1962, **85**, 528.

[3] V. M. Chari, S. Neelakantan, and T. R. Seshadri, *Tetrahedron Letters*, 1967, 999.

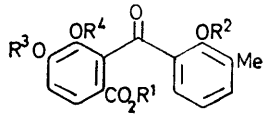
[4] J. L. Simonsen, *J. Chem. Soc.*, 1924, 721.

[5] D. G. Davies, M. Derenberg, and P. Hodge, *J. Chem. Soc.* (*C*), 1971, 455.

[6] G. A. Olah, 'Fridel–Crafts and Related Reactions,' vol. III, Interscience, New York, 1964, pp. 9 and 590.

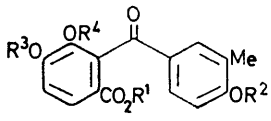
on treatment with diazomethane. The failure of the phenolic group in acid D to react with diazomethane suggested that it was chelated to the ketone group, and in agreement with this the ketone band in the i.r. spectrum of the methyl ester of acid D (prepared using sulphuric acid in methanol) appeared at 1635 cm^{-1}. As described below, cyclisation of acids C and D and methylation of the product gave quinone (Ib). It follows that acid D has structure (IVa). The ease with which the extra phenolic group in acid C reacted with diazomethane suggests that it was not chelated to the ketone group and, therefore, acid C probably has structure (IVc).

The Friedel–Crafts reaction has also been carried out in the absence of a solvent, but with a large excess of *o*-cresol. Simonsen [4] and also Jacobson and Adams [7] report that under these conditions the acidic product is the same as that obtained before, *i.e.* acid (IVa). We repeated the reaction and obtained acid (Vc) (8·5%) and acid (IVa) (2%): very little demethylation occurred. These reaction conditions also afford considerable quantities of a phthalein to which Jacobson and Adams [7] assigned structure (VI). The ^1H n.m.r. spectrum of the



(IV)

a; $R^1 = R^2 = H$, $R^3 = R^4 = Me$
b; $R^1 = R^3 = R^4 = Me$, $R^2 = H$
c; $R^1 = R^2 = R^3 = H$, $R^4 = Me$
d; $R^1 = R^4 = Me$, $R^2 = R^3 = H$



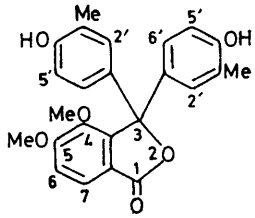
(V)

a; $R^1 = R^2 = R^3 = R^4 = Me$
b; $R^1 = R^2 = R^3 = H$, $R^4 = Me$
c; $R^1 = R^2 = H$, $R^3 = R^4 = Me$
d; $R^1 = H$, $R^2 = R^3 = R^4 = Me$
e; $R^1 = R^4 = Me$, $R^2 = R^3 = H$
f; $R^1 = R^3 = R^4 = Me$, $R^2 = H$

phthalein supports this assignment. The magnitudes of the coupling constants between the protons in the phenolic rings indicate that they are in 1,2,4-relationship. One methoxy-group appeared at δ 3·27, an unusually high field for such a group, and the most probable explanation for this is that the methoxy-group is at C-4 and is shielded by one or both of the phenolic rings.

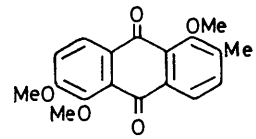
Cyclisation of the acid (Vb) using concentrated sulphuric acid, and exhaustive methylation of the product gave quinone (IIIb) (10%). Similarly acid (Vc) gave quinone (IIIb) (20%). The spectral data were as expected and the structure of the quinone has been confirmed by a cleavage reaction.[1] Demethylation of the quinone gave the hydroxyquinone (IIIa).

Cyclisation of a mixture of acids (IVa and c), and methylation of the product gave a second trimethoxy(methyl)anthraquinone in 4% overall yield. The ^1H n.m.r. spectrum of this quinone contained signals due to



(VI)

a β-methyl group and two pairs of aromatic protons *ortho* to each other. Hence the product is either quinone (Ib) or morindone trimethyl ether (VII). Comparison of the synthetic product and an authentic sample of the latter quinone showed they were different and structure (Ib) for the synthetic product was confirmed by a cleavage reaction which, as expected,[1] yielded 2,3-dimethoxy-, 3,4-dimethoxy-, 2-methoxy-3-methyl-, and 3-methoxy-4-methyl-benzoic acids. Demethylation of the quinone (Ib) gave the hydroxyquinone (Ia).



(VII)

In our experiments the overall yield of quinone (IIIb) was *ca.* 16 times that of quinone (Ib). Comparison (see the Table) of our m.p.s for quinones (Ib) and (IIIb) with those of the synthetic products of Simonsen [4] and Chari *et al.*[3] leaves little doubt that these workers actually obtained quinone (IIIb). Chari *et al.* demethylated their product to the hydroxyquinone and comparison of the m.p. and u.v. spectrum which they obtained for this hydroxyquinone with those which we obtained for quinones (Ia) and (IIIa) confirms that their synthetic quinone was in fact compound (IIIb). Hence the non-identity of the product obtained by Chari *et al.* with cladofulvin trimethyl ether proves that the latter compound does not have structure (IIIb).

A closely related Friedel–Crafts reaction was carried out by Bistrzycki and Krauer.[8] They treated the anhydride (II) with *o*-cresol methyl ether in the presence of aluminium trichloride and obtained an acid to which they assigned structure (Vd). The acid was converted, in several steps, into a trimethoxy(methyl)anthraquinone to which they assigned structure (IIIb). Demethylation gave a trihydroxyquinone. In this case the assignments appear to be correct as the m.p.s they quote for their quinones agree well (see Table) with those

[7] R. A. Jacobson and R. Adams, *J. Amer. Chem. Soc.*, 1925, **47**, 283.
[8] A. Bistrzycki and K. Krauer, *Helv. Chim. Acta*, 1923, **6**, 750.

which we obtained for quinones (IIIa) and (IIIb). Hence, in all the reactions between the anhydride (II) and *o*-cresol or *o*-cresol methyl ether described in this paper the major products result from the attack of the carbonyl group at C-2 in the anhydride (II) at the position *para* to the oxygen function in *o*-cresol or its methyl ether.

Finally, comparison (see the Table) of our m.p. and

M.p.s and u.v.–visible spectra of various quinones

Compound	M.p. (°C)	$\lambda_{max.}$/nm (log ε)
(Ia)	233—235	233, 261, 435 (4·42, 4·42, 3·97
(IIIa)	320 (decomp.)	225, 278, 308infl, 410
Trihydroxy-compound of Chari *et al.*[a]	310 (decomp.)	225, 278, 308infl [b]
Trihydroxy-compound of Bistryzcki and Krauer [c]	318—320	
Cladofulvin [d]	310 (decomp.)	235, 270, 449 (4·43, 4·43, 4·05)
(Ib)	154—155	
(IIIb)	218—219	
Trimethoxy-compound of Chari *et al.*[a]	209—210	
Trimethoxy-compound of Simonsen [e]	209—210	
Trimethoxy-compound of Bistryzcki and Krauer [e]	218	
Cladofulvin trimethyl ether [d]	212—214	

[a] Ref. 3. [b] Values taken from an illustration of spectrum for the range 225—330 nm. The band at 225 nm could be a maximum or a point of inflexion. [c] Ref. 8. [d] Ref. 2. [e] Ref. 4.

u.v.–visible spectral data for quinones (Ia) and (Ib) with the data reported [2] for cladofulvin and its trimethyl ether leaves no doubt that cladofulvin does not have structure (Ia).

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were measured for Nujol mulls and u.v. spectra for solutions in ethanol. Unless indicated otherwise ^{1}H n.m.r. spectra were recorded at 60 MHz for *ca.* 10% solutions in deuteriochloroform containing tetramethylsilane as internal reference. Petroleum was the fraction b.p. 40—60°. Organic solutions were dried with magnesium sulphate. Preparative t.l.c. (p.l.c.) was carried out using plates coated with silica gel (Merck Kieselgel HF_{254}).

Reaction of 3,4-*Dimethoxyphthalic Anhydride with* o-*Cresol.*—(a) sym-*Tetrachloroethane as solvent.* Aluminium trichloride (28 g) was added to a vigorously stirred solution of the anhydride (II) (13·9 g) and *o*-cresol (14·0 g) in *sym*-tetrachloroethane (100 ml) at 55° and the mixture was stirred at 120—130° for 2 h. Ice (50 g) and N-hydrochloric acid (100 ml) were added to the cold reaction mixture and the excess of *o*-cresol was removed by steam distillation. The residue was filtered off and exhaustively extracted with 5% sodium carbonate solution. The combined extracts were washed with ethyl acetate and then acidified with conc. hydrochloric acid. The acidic products were extracted into ethyl acetate and the extracts were washed, dried, and evaporated to dryness. P.l.c. (ether–glacial acetic acid, 19 : 1) of the residue (6·6 g) afforded four acids. These were not readily purified and were, therefore, characterised as their methyl esters, prepared by treating the acids for 7 days with a 4% solution of concentrated sulphuric acid in methanol at 21°.

Acid A, R_F 0·37, was 4-hydroxy-2-(4-hydroxy-*m*-toluoyl)-3-methoxybenzoic acid (Vb) (2·6 g, 12%), m.p. 145° (decomp.) (ethyl acetate), $\nu_{max.}$ 3300—2500, 1685, and 1650 cm^{-1}, $\lambda_{max.}$ 292 nm. The *methyl ester* (Ve) (98%) had m.p. 106—107° (petroleum), $\nu_{max.}$ 3400—3100, 1710, and 1655 cm^{-1}, δ [$(CD_3)_2CO$] 2·25 (3H, s, CMe), 3·64 (3H, s, OMe), 4·05 (3H, s, OMe), 6·93 (1H, d, *J* 8·5 Hz, H-5′),* 7·20 (1H, d, *J* 8·5 Hz, H-5), 7·58 (1H, q, *J* 8·5 and 2 Hz, H-6′), 7·65 (1H, d, *J* 2 Hz, H-2′), and 7·72 (1H, d, *J* 8·5 Hz, H-6) (Found: C, 64·2; H, 4·8. $C_{17}H_{16}O_6$ requires C, 64·5; H, 5·1%).

Acid B, R_F 0·53, was 2-(4-hydroxy-*m*-toluoyl)-3,4-dimethoxybenzoic acid (Vc) (1·7 g, 8%), m.p. 260—262° (ethyl acetate), $\nu_{max.}$ 3300—2500, 1685, and 1670 cm^{-1}, $\lambda_{max.}$ 290 nm. The *methyl ester* (Vf) (98%) had m.p. 159—160° (petroleum ether), $\nu_{max.}$ 3300—3100, 1710, and 1658 cm^{-1}, δ 2·25 (3H, s, CMe), 3·78 (3H, s, OMe), 3·83 (3H, s, OMe), 4·10 (3H, s, OMe), 6·88 (1H, d, *J* 8·5 Hz, H-5′), 7·27 (1H, d, *J* 8·5 Hz, H-5), 7·73 (1H, q, *J* 8·5 and 2 Hz, H-6′), 7·88 (1H, d, *J* 2 Hz, H-2′), and 8·16 (1H, d, *J* 8·5 Hz, H-6) (Found: C, 65·1; H, 5·2. $C_{18}H_{18}O_6$ requires C, 65·45; H, 5·45%).

Acid C, R_F 0·71, was 4-hydroxy-2-(2-hydroxy-*m*-toluoyl)-3-methoxybenzoic acid (IVc) (0·37 g, 1·5%), m.p. 240—242°, $\nu_{max.}$ 3300—2500, 1685, and 1615 cm^{-1}, $\lambda_{max.}$ 259 nm. The *methyl ester* (IVd) (35%) had m.p. 164—166° (petroleum), δ (100 MHz) 2·17 (3H, s, CMe), 3·54 (1H, s, OMe), 3·86 (3H, s, OMe), 6·96 (1H, d, *J* 8·5 Hz, H-5), 7·72 (1H, d, *J* 8·5 Hz, H-6), and 6·5—7·4 p.p.m. (3H, complex m, H-4′—6′) (Found: C, 64·4; H, 5·0. $C_{17}H_{16}O_6$ requires C, 64·5; H, 5·1%).

Acid D, R_F 0·83, was 2-(2-hydroxy-*m*-toluoyl)-3,4-dimethoxybenzoic acid (IVa) (0·58 g, 2·5%), m.p. >320°, $\nu_{max.}$ 3300—2500, 1680, and 1630 cm^{-1}, $\lambda_{max.}$ 257 nm. The *methyl ester* (IVb) (40%) had m.p. 170—171° (petroleum), $\nu_{max.}$ (CCl_4) 3300—2800, 1730, and 1635 cm^{-1}, δ (100 MHz) 2·20 (3H, s, CMe), 3·56 (3H, s, OMe), 3·62 (3H, s, OMe), 3·87 (3H, s, OMe), 7·02 (1H, d, *J* 8·5 Hz, H-5), 7·87 (1H, d, *J* 8·5 Hz, H-6), and 6·5—7·4 (3H, complex m, H-4′—6′) (Found: C, 65·4; H, 5·7. $C_{18}H_{18}O_6$ requires C, 65·45; H, 5·45%).

(b) *No solvent and a large excess of* o-*cresol.* Aluminium trichloride (8 g) was added to a stirred mixture of the anhydride (II) (5·0 g) and *o*-cresol (20 ml) and the mixture was heated at 70° for 6 h. The reaction was worked up as described by Jacobson and Adams.[7] P.l.c. of the acidic fraction (1·03 g) as above gave acid (Vc) (0·64 g, 8·5%) and acid (IVa) (0·16 g, 2%). T.l.c. indicated the presence of only traces of acids (Vb) and (IVc). 3,3-Bis-(4-hydroxy-*m*-tolyl)-4,5-dimethoxyphthalide (VI) (1·3 g, 26%) had m.p. 239—241° (glacial acetic acid) (lit.,[4] 237—238°; lit.,[7] 238—239·5°), $\nu_{max.}$ 3260br and 1720 cm^{-1}, $\lambda_{max.}$ 263·5 nm (log ε 4·09), after addition of ethanolic sodium hydroxide 256 and 575 nm (log ε 4·26 and 4·09), δ [220 MHz, $(CD_3)_2CO$] 2·15 (6H, s, 2 CMe), 3·27 (3H, s, 4-OMe), 3·96 (3H, s, 5-OMe), 6·77 (2H, d, *J* 8·5 Hz, 2 H-5′), 6·95 (2H, q, *J* 8·5 and 2 Hz, 2 H-6′), 7·05 (2H, d, *J* 2 Hz, 2 H-2′), 7·31 (1H, d, *J* 8 Hz, H-6), and 7·61 (1H, d, *J* 8 Hz, H-7).

Reaction of the Acids (Vb), (Vc), (IVc), *and* (IVa) *with Diazomethane.*—(a) *Acid* (Vb). The acid was treated for

* Primed numbers for the acids and esters refer to positions in the toluoyl substituent.

24 h with an excess of diazomethane in ether at 21°. Excess of diazomethane was destroyed with acetic acid, the solvent was evaporated, and the residue was purified by p.l.c. (ether) to give *methyl* 3,4-*dimethoxy*-2-(4-*methoxy*-m-*toluoyl*)-*benzoate* (Va) (98%), m.p. 122—123° (carbon tetrachloride), $\nu_{max.}$ (CCl_4) 1730 and 1675 cm^{-1}, δ 2·20 (3H, s, CMe), 3·63 (s), 3·68 (s), 3·82 (s), and 3·90 (s) (12H, 4 OMe), 6·76 (1H, d, *J* 8·5 Hz, H-5′), 6·98 (1H, d, *J* 8·5 Hz, H-5), 7·57 (1H, q, *J* 8·5 and 2 Hz, H-6′), 7·64 (1H, d, *J* 2 Hz, H-2′), and 7·84 (1H, d, *J* 8·5 Hz, H-6), *m/e* 344 (M^+) (Found: C, 66·4; H, 5·85. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8%).

(b) *Acid* (Vc). The product (98%) was identical (mixed m.p., i.r., and ^1H n.m.r. spectra) with (Va) prepared as in (a).

(c) *Acid* (IVc). The product (38%) was identical (mixed m.p., i.r. and ^1H n.m.r. spectra) with (IVb) prepared above by methylation of acid D.

(d) *Acid* (IVa). The product (45%) was identical (mixed m.p., i.r. and ^1H n.m.r. spectra) with (IVb) prepared above.

Cleavage of Ester (Va).—The ester (15 mg) was cleaved using the procedure described previously,[1] the reaction mixture being heated under reflux for 2 h. The acid products (40%) were 3,4-dimethoxy- and 4-methoxy-3-methyl-benzoic acids in the ratio 47 : 53.

Conversion of Acids (Vb) *and* (Vc) *into* 1,2,6-*Trimethoxy*-7-*methylanthraquinone* (IIIb).—(a) *Acid* (Vb). The acid (500 mg) was treated with conc. sulphuric acid (5 ml) at 150° for 30 min. The cooled mixture was added to ice (50 g) and the mixture was extracted with ethyl acetate (3 × 50 ml). The combined extracts were washed with 5% sodium carbonate, then water, and dried. The solvent was evaporated off and the residue (190 mg) methylated first with diazomethane in ether, and then with dimethyl sulphate and potassium carbonate in acetone. The crude product was subjected to p.l.c. (chloroform–glacial acetic acid, 95 : 1) to give 1,2,6-trimethoxy-7-methylanthraquinone (IIIb) (53 mg, 10%), m.p. 218—219° (ethanol), $\nu_{max.}$ 1670 cm^{-1}, $\lambda_{max.}$ 220, 276, 298, and 356 nm (log ε 4·61, 4·73, 4·38, and 4·05), δ 2·34 (3H, s, CMe), 3·95 (9H, s, 3 OMe), 7·20 (1H, d, *J* 9 Hz, H-4), 7·55 (1H, s, H-5), 8·00 (1H, s, H-8), and 8·10 (1H, d, *J* 9 Hz, H-3), *m/e* 312 (M^+).

(b) *Acid* (Vc). The acid (Vc) (320 mg) was converted into 1,2,6-trimethoxy-7-methylanthraquinone (IIIb) (66 mg, 20%) using a procedure similar to that above.

1,2,6-*Trihydroxy*-7-*methylanthraquinone* (IIIa).—1,2,6-Trimethoxy-7-methylanthraquinone (IIIb) (6 mg) was treated with aqueous hydrobromic acid (5 ml; 48%) and glacial acetic acid (10 ml) at reflux for 12 h. The mixture was then added to water (100 ml) and the quinones were extracted with chloroform (3 × 50 ml). The dried extracts were evaporated, and the residue was recrystallised from aqueous ethanol to give 1,2,6-trihydroxy-7-methylanthraquinone (IIIa) (3 mg, 60%), m.p. 320° (decomp.), $\lambda_{max.}$ see Table, *m/e* 270 (M^+, 100%).

Conversion of Acids (IVc) *and* (IVa) *into* 1,2,8-*Trimethoxy*-7-*methylanthraquinone* (Ib).—A mixture of the acids (IVc) and (IVa) (1·07 g; mole ratio, 2 : 3) was cyclised and the product methylated using the procedure described above. P.l.c. (chloroform–carbon tetrachloride, 1 : 1) of the crude product gave 1,2,8-*trimethoxy*-7-*methylanthraquinone* (Ib) (40 mg, 4%) as yellow needles, m.p. 154—155° (ethanol), $\nu_{max.}$ 1670 and 1655 cm^{-1}, $\lambda_{max.}$ 220, 270, and 366 nm (log ε 4·48, 4·40, and 3·90), δ (100 MHz) 2·32 (3H, s, CMe), 3·86 (s), 3·90 (s), and 3·95 (s) (9H, 3 OMe), 7·18 (1H, d, *J* 9 Hz, H-3), 7·50 (1H, d, *J* 8 Hz, H-6), 7·92 (1H, d, *J* 8 Hz, H-5), and 8·03 (1H, d, *J* 9 Hz, H-4), *m/e* 312 (M^+, 100%) (Found: C, 69·2; H, 5·15. $C_{18}H_{16}O_5$ requires C, 69·2; H, 5·2%).

A comparison (mixed m.p. and ^1H n.m.r. spectra) of the above product and a highly purified sample of morindone trimethyl ether (VII), m.p. 239—240°, kindly supplied by Professor L. H. Briggs, showed that they were different.

Cleavage of 1,2,8-*Trimethoxy*-7-*methylanthraquinone* (Ib).—The quinone (3·5 mg) was cleaved using the procedure described previously,[1] the reaction mixture being heated under reflux for 2 h. The cleavage yield was 50% and the proportions of the acidic products were: 2,3-dimethoxy- 33%, 3,4-dimethoxy- 29%, 2-methoxy-3-methyl- 13%, and 3-methoxy-4-methyl-benzoic acid 25%.

1,2,8-*Trihydroxy*-7-*methylanthraquinone* (Ia).—The trimethoxyanthraquinone (Ib) (18 mg) was demethylated using aqueous hydrobromic acid (5 ml; 48%) and glacial acetic acid (10 ml) at reflux for 24 h and the reaction was worked up using the procedure described for quinone (IIIb). The mass spectrum of the product (12 mg) indicated that it was a mixture of the desired product (M^+ 270) and a monobrominated derivative (M^+ 351/349). To remove the bromine the product in ethanol (5 ml) was treated with 10% palladium on charcoal (13 mg) and hydrazine hydrate (0·5 ml; 64% w/v) at reflux temperature for 1 h.[9] The cold mixture was filtered and the filtrate concentrated to small volume. The concentrate was added to dilute hydrochloric acid and the mixture was extracted with chloroform (3 × 60 ml). The dried extracts were evaporated to dryness. The absence of a peak at *m/e* 351/349 in the mass spectrum of the crude product indicated that the bromine had been removed. Sublimation (175° and 0·01 mmHg) of the crude product gave 1,2,8-*trihydroxy*-7-*methylanthraquinone* (Ia) (3 mg, 20%) as dark red needles, m.p. 233—235°, $\lambda_{max.}$ see Table [Found: M^+ (100%), 270·0513. $C_{15}H_{10}O_5$ requires *M*, 270·0528].

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