6-Methoxy-3-methylbenzofurano-4,7-quinone; Dimers of 3-Methylbenzofurans; and Tautomerism in 2-Acetyl-3-hydroxy-5-methoxy-1,4-benzoquinone

By **B. D. Cavell** and **J. MacMillan**, The Department of Organic Chemistry, The University, Woodland Road, Bristol 8

The synthesis of 6-methoxy-3-methylbenzofurano-4,7-quinone is described. Structures are deduced for the dimers, obtained in the preparation of 4,6,7-trimethoxy- and 4-hydroxy-6-methoxy-3-methylbenzofurans, and also for the trimer obtained in the cyclisation of 3,5-dimethoxyphenoxyacetone.

2-Acetyl-3-hydroxy-5-methoxy-1,4-benzoquinone, prepared in several ways, is shown by nuclear magnetic resonance spectroscopy to be in equilibrium with its 1,2-quinonoid tautomer in deuteriochloroform.

In another connection, 6-methoxy-3-methylbenzofurano-4,7-quinone (I) was required as a model for nuclear magnetic resonance (n.m.r.) and mass spectroscopic studies. The parent quinone [1] and the 2-methoxycarbonyl-,[1] the 5-hydroxy-,[2] and the 5-acetyl-6-hydroxy-[3] derivatives have been prepared but only their u.v. spectra were recorded. We now report a synthesis of the quinone (I) and some points of interest arising from unsuccessful routes to it.

2,6-Dihydroxy-4-methoxyacetophenone,[4] prepared by an improved procedure, was converted into the phenoxyacetic ester (II; R = Et). The corresponding acid (II; R = H) was cyclised, with acetic anhydride and sodium acetate, to the acetoxybenzofuran (III; R = Ac) which was hydrolysed with aqueous sodium hydroxide to the phenol (III; R = H). It was found that even brief exposure of the phenol (III; R = H) to dilute acid caused polymerisation (see below). Oxidation of (III; R = H) with potassium nitrosodisulphonate gave the required benzofuranoquinone (I). The n.m.r. spectrum of (I) showed the same allylic coupling (J = 1·5 c./sec.) between the 2- and the 3-methyl protons as the benzofurans described in this Paper (see Table 1). The mass spectrum consisted mainly of fragmentation routes which proceeded by successive loss of CO and CHO until all oxygen was lost. In one of these routes, loss of a methyl group also occurred.

TABLE 1

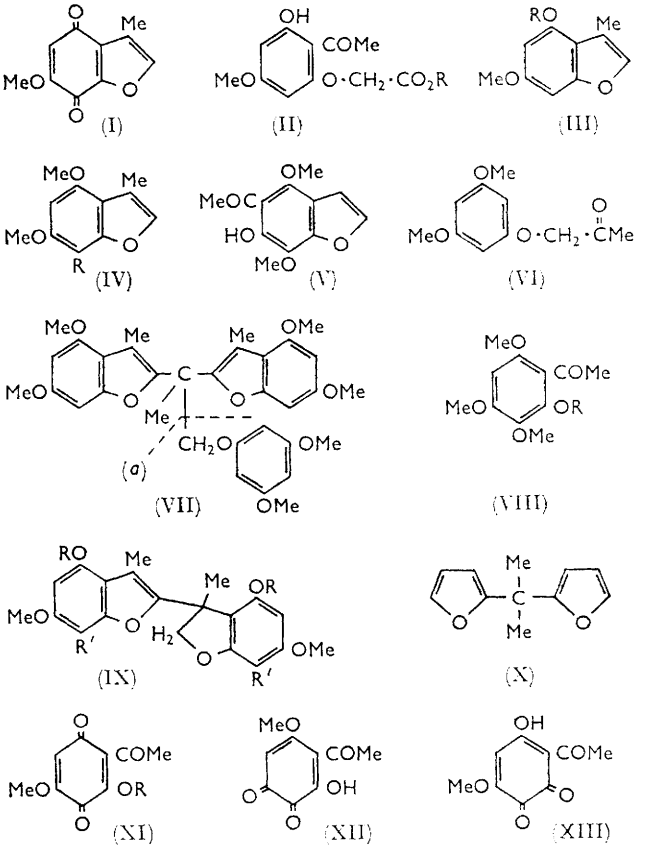
Approximate chemical shift (τ values) of 3-methylbenzofurans

Compound	Position of protons: 2 [a]	5	7	3-Me [a]	OMe
(IV; R = H) [b]	2·92	3·53	3·84	7·73	6·19, 6·26
(III; R = Ac) [b]	2·87	3·24	3·49	7·84	6·25
(III; R = H) [c]	2·81	3·40	3·80	7·67	6·22
(IV; R = OMe) [b]	2·93		3·84	7·79	6·14, 6·20, 6·23
(I) [c]	2·53	4·22		7·74	6·14

[a] $J_{1,3\text{-Me}}$ = 1·5 c./sec. in all cases. [b] In carbon tetrachloride. [c] In deuteriochloroform.

Oxidative demethylation of the benzofurans (IV; R = H) and (IV; R = OMe) to the benzofuranoquinone (I) failed under a variety of conditions. This failure was unexpected since the benzofuran (V) has been oxidised [3] smoothly to the corresponding 4,7-benzofuranoquinone.

Although these two routes and a third approach (described below) were unsuccessful, each provided points of interest. In the first route, 4,6-dimethoxy-3-methylbenzofuran (IV; R = H), prepared [5] by cyclisation of the phenoxyacetone (VI) with concentrated sulphuric acid at 0°, was accompanied by a trimer for which structure (VII) is suggested on the following spectroscopic evidence. In the n.m.r. spectrum, the presence of two 2- substituted 3-methyl-4,6-dimethoxybenzofuran systems was indicated by the absence of a signal between τ 2·5 and 3·0 (cf. Table 1); by two equivalent aromatic AB systems at τ 3·41 and 3·72 (J = 2·0 c./sec.); and by two equivalent olefinic methyl signals at τ 7·94. A three-proton singlet at τ 3·91 provided evidence for the phloroglucinol ring. A three-proton singlet at



[1] G. Rodghiero and U. Fornasiero, *Gazzetta*, 1961, **91**, 90.
[2] C. J. P. Spruit, *Rec. Trav. chim.*, 1962, **81**, 810.
[3] E. Späth and W. Gruber, *Chem. Ber.*, 1938, **71***B*, 106.
[4] A. Sonn and W. Bülow, *Chem. Ber.*, 1925, **58**, 1691.
[5] H. F. Birch and A. Robertson, *J. Chem. Soc.*, 1938, 300.

τ 8·06 and a two-proton singlet at τ 5·48, were assigned to the saturated methyl and methylene protons, respectively (see below). The methoxyl groups were of two types, four occurring at τ 6·19 and two at τ 6·27. The mass spectrum of the trimer showed a transition from parent peak to base peak ($P - C_9H_{11}O_3$) with an associated metastable ion. This fragmentation corresponds to cleavage at (*a*) in compound (VII).

In the second unsuccessful route to the benzofuranoquinone (I), 4,6,7-trimethoxy-3-methylbenzofuran (IV; R = OMe) was prepared from 1,2,3-trimethoxybenzene which was converted, by published procedures,[6] into the acetophenone (VIII; R = H). We found that the oxidation of 1,2,3-trimethoxybenzene to 2,6-dimethoxy-1,4-benzoquinone with nitric acid produced 5-nitro-1,2,3-trimethoxybenzene in 25% yield. We also found that the Friedel–Crafts acetylation of 1,2,3,5-tetramethoxybenzene, derived from 2,6-dimethoxybenzoquinone by reduction and methylation, afforded the acetophenone (VIII; R = H) containing 10% of an ethoxyl-containing compound. This by-product was not isolated but is probably an ethoxy-homologue of the acetophenone (VIII; R = H), the ethyl group coming from cleavage of diethyl ether used as solvent. Cyclisation of the phenoxyacetic acid (VIII; R = CH_2CO_2H) gave 4,6,7-trimethoxy-3-methylbenzofuran (IV; R = OMe) and polymeric material from which a crystalline dimer was isolated by column chromatography. Structure (IX; R = Me, R′ = OMe) for this dimer is suggested on the basis of the known [7] mode of polymerisation of benzofurans and on the following n.m.r. evidence. The spectrum showed two unsplit aromatic protons at τ 3·71 and 3·98; an AB system at τ 5·28 and 5·58 (J = 8·5 c./sec.) assigned to the non-equivalent methylene protons; six methoxyl proton signals between τ 6·0 and 6·35, two of which were equivalent; and two three-proton singlets at τ 8·04 and 8·11 which are assigned to the allylic methyl protons and to the tertiary methyl group (see below).

The analogous structure (IX; R = R′ = H) is suggested for a non-crystalline dimer, isolated from the polymeric material (see above), obtained in the preparation of the hydroxybenzofuran (III; R = H). The n.m.r. spectrum of the dimer showed: two AB systems of aromatic protons at τ 3·49 and 3·87, and at τ 3·91 and 4·02, each with J = 2·0 c./sec.; an AB system of non-equivalent methylene protons at τ 3·33 and 5·56 (J = 8 c./sec.); two equivalent methoxyl groups at τ 6·26; and two methyl singlets at τ 7·83 and 8·21 assigned to the allylic methyl protons and to the tertiary methyl protons, respectively (see below). The n.m.r. spectrum of the derived, non-crystalline acetate (IX; R = Ac, R′ = H) was very similar to that of the parent phenol except that the two broad signals of phenolic protons at τ 4·12 and 4·35 were replaced by two acetyl methyl signals at τ 8·09 and 8·22.

The assignment of three-proton singlets at τ 8·06, 8·21, and 8·11 to the respective tertiary methyl protons in the trimer (VII), the dimer (IX; R = R′ = H), and the dimer (IX; R = Me, R′ = OMe) requires comment. Inspection of models shows that, in the most favourable conformation of these compounds, the methyl group lies in the deshielding cone of a benzofuran ring. Similarly, the methylene protons in (VII) are deshielded by the second benzofuran ring. Support for this interpretation is provided by the n.m.r. spectrum of the furan derivative (X) in which the methyl groups have been shown [8] to occur at τ 8·4.

A third projected synthesis of the furanoquinone (I) envisaged the cyclisation of the benzoquinone (XI; R = CH_2CO_2H) whose preparation from the phenoxyacetic acid (VIII; R = CH_2CO_2H) was attempted. However, oxidation of (VIII; R = CH_2CO_2H) or (VIII; R = CH_2CO_2Et) with nitric acid gave an orange-red quinone, $C_9H_8O_5$, with a sharp but variable m. p. in the range 127—140°. The assignment of structure to this quinone presented difficulties. First, the most likely structure (XI; R = H) had been allocated to an oxidation product, m. p. 156—158°, of the acetophenones (VIII; R = H) [9,10] and (VIII; R = Me) [9] and of 2-hydroxy-4,5,6-trimethoxy acetophenone.[9] Secondly, although this quinone appeared to be homogeneous, its n.m.r. spectrum (Table 2) indicated a 4 : 1 mixture of

TABLE 2

N.m.r. spectra of 2-acetyl-3-hydroxy-6-methylbenzoquinone.

Solvent	Chemical shift (τ values) of protons: Quinonoid	OMe	–COMe
$CDCl_3$ * at 20°	4·04 (4·16)	6·13 (6·19)	7·35 (7·28)
$CDCl_3$ + CF_3CO_2H ...	3·91	6·18	7·33
$(CD_3)_2CO$	3·99	6·18	7·47

* Signals in parentheses one-quarter intensity

two quinones, for example, (XI; R = H) and (XII). The formation of a quinoxaline derivative in high yield was not helpful in view of the known [11] formation of such derivatives from the tautomeric form of hydroxy-1,4-quinones.

Decisive proof that the quinone had indeed structure (XI; R = H) was obtained by its preparation from 2,6-dihydroxy-4-methoxyacetophenone and Fremy's salt. In our hands, the same quinone was obtained by oxidation of the acetophenones (VIII; R = H) and (VIII; R = Me) and the cause of the difference between the present m. p. and the earlier values [9,10] is not known.

Further n.m.r. studies clearly indicated that the quinone (XI; R = H) exists in deuteriochloroform solutions as a tautomeric mixture of (XI; R = H) and (XIII). Varying the temperature from −20°

[6] W. Baker, *J. Chem. Soc.*, 1941, 666.
[7] W. E. Sheehan, H. E. Kelly, and W. H. Carmody, *Ind. Eng. Chem.*, 1937, **29**, 576.
[8] P. H. Boyle, W. Cocker, T. B. H. McMurry, and A. C. Pratt, unpublished work.
[9] G. S. Krishna Rao and T. R. Seshadi, *Proc. Indian Acad. Sci.*, 1948, **27***A*, 245.
[10] P. D. Gardner, W. J. Horton, and R. E. Pincock, *J. Amer. Chem. Soc.*, 1956, **78**, 2541.
[11] Y. T. Pratt and N. L. Drake, *J. Amer. Chem. Soc.*, 1955, **77**, 37.

to +50° caused a progressive increase in the ratio of intensities of minor to major component from 1 : 8 to 1 : 2. The spectrum of the minor component is assigned to the (presumably) less-stable 1,2-quinone (XIII). A single spectrum was obtained in deuterioacetone and on the addition of trifluoroacetic acid to a deuteriochloroform solution (Table 2).

EXPERIMENTAL

Melting points are corrected. Unless otherwise stated, i.r. spectra were obtained for chloroform solutions on a Unicam SP 200 spectrometer and u.v. spectra for ethanolic solutions on a Unicam SP 800 spectrometer. N.m.r. spectra were obtained on a Varian A60 spectrometer for deuteriochloroform or carbon tetrachloride solutions with tetramethylsilane as internal standard. For t.l.c., Kieselgel layers (0·3 mm.) were used. Light petroleum had b. p. 60—80°.

2,6-Dihydroxy-4-methoxyacetophenone.[4]— Alcohol-free [12] diazomethane [6·0 g., from *N*-methyl-*N*-nitrosotoluene-*p*-sulphonamide (43 g.)] in dry, ice-cold ether (350 ml.) was added rapidly at 0° to a stirred solution of 2,4,6-trihydroxyacetophenone (20 g.).[13] After 1 day at 0° and 1 day at 25°, the solution was extracted with 5% aqueous sodium hydrogen carbonate (2 × 100 ml.), then with *N*-sodium carbonate (11 × 100 ml.), to give 13 fractions which were monitored by t.l.c. with benzene–ethyl acetate (2 : 1) as solvent. Fractions 1—5 contained starting material (9·0 g.), fraction 6 contained a mixture (2·37 g.) of starting material and the required monomethyl ether, fractions 7—12 consisted of the required product (8·4 g.), and fraction 13 was a mixture of the mono- and dimethyl-ethers. Recrystallisation of the combined fractons 7—12 from benzene gave 2,6-dihydroxy-4-methoxyacetophenone (6·0 g.), m. p. 138—140°, and pure by t.l.c.; a further 2·0 g. from the mother-liquor contained (t.l.c.) a trace of starting material and dimethyl ether.

Ethyl (2-Acetyl-3-hydroxy-5-methoxyphenoxy)acetate (II; R = Et).—Ethyl bromoacetate (1·1 g.) in dry acetone (15 ml.) was stored overnight over potassium iodide, then added during 0·5 hr. to a stirred, refluxing solution of the above monomethyl ether (1·19 g.) in dry acetone (10 ml.) containing anhydrous potassium carbonate (1·93 g.). The reaction mixture was heated under reflux for 9 hr. and worked up as usual to give the *acetate* (1·79 g.) which, after sublimation at 85° and 0·2 mm., then crystallisation from methanol, was obtained as needles, m. p. 106—107° (Found: C, 58·3; H, 6·1. $C_{13}H_{14}O_6$ requires C, 58·2; H, 6·0%), $\nu_{max.}$ 1755 (ester carbonyl) and 1625 (bonded carbonyl) cm.$^{-1}$; τ values ($CDCl_3$); 3·95 and 4·27 (Ar–H), 5·40 (OCH_2), 6·22 (OMe), and 7·28 (COMe).

2-Acetyl-3-hydroxy-5-methoxyphenoxyacetic Acid (II; R = H).—The above ester (1·2 g.) in 2N-sodium hydroxide (7·5 ml.) was boiled for 15 min. under nitrogen. Working up in the usual way gave the crude *acetic acid* (1·04 g.) m. p. 178—183°; $\nu_{max.}$ (mull) 1762 (acid carbonyl) and 1625 (bonded carbonyl) cm.$^{-1}$. A portion, sublimed at 160° and 0·1 mm., was crystallised from ethyl acetate in needles, m. p. 208—208·5° (Found: C, 54·9; H, 5·0. $C_{12}H_{12}O_6$ requires C, 55·0; H, 5·0%), $\nu_{max.}$ (Nujol) 1740 and 1625 cm.$^{-1}$.

4-Acetoxy-6-methoxy-3-methylbenzofuran (III; R = Ac).—The above acid (1·0 g.), acetic anhydride (10 ml.), and anhydrous sodium acetate (2·0 g.) were heated under reflux for 2 hr., then water (25 ml.) was added to the cooled solution. The precipitated oil which solidified overnight was recovered in ether (sodium hydrogen carbonate washing) to yield the *benzofuran* (940 mg.), purified by sublimation at 85° and 0·1 mm., and crystallised from light petroleum as needles (740 mg.), m. p. 76—77° (Found: C, 65·6; H, 5·5. $C_{12}H_{12}O_4$ requires C, 65·45; H, 5·5%), $\lambda_{max.}$ 248, 253, and 285 mμ (ε 11,000, 10,760, and 4125); $\nu_{max.}$ 1750 cm.$^{-1}$ (acetate carbonyl).

4-Hydroxy-6-methoxy-3-methylbenzofuran (III; R = H).—(*a*) The above acetate (184 mg.) and 2N-sodium hydroxide (9 ml.) were heated under reflux under nitrogen until solution occurred (6·5 hr.). The solution was extracted with ether, acidified to pH 6, and *rapidly* re-extracted with ether. The latter extract was washed with 2% aqueous sodium hydrogen carbonate and recovered to give the *hydroxybenzofuran*, purified by sublimation at 50° and 0·1 mm., and crystallised from aqueous ethanol as needles (143 mg.), m. p. 95° (Found: C, 67·4; H, 5·65. $C_{10}H_{10}O_3$ requires C, 67·45; H, 5·7%), $\lambda_{max.}$ 254 mμ (ε 12,400); $\lambda_{infl.}$ 287 mμ (ε 623); (plus NaOH) 267 and 298 mμ (ε 11,610 and 5343); $\nu_{max.}$ 3400 cm.$^{-1}$ (sharp, hydroxyl).

(*b*) The above experiment was repeated with the acetate (670 mg.) except that the acidified reaction mixture was left overnight. The precipitated oil (550 mg.) was recovered in ether and shown by t.l.c. to consist of a major component (R_f values 0·0 in benzene and 0·05 in chloroform) and traces of the hydroxybenzofuran (III; R = H) (R_f values, 0·16 in benzene and 0·21 in chloroform). Acetylation of the oil gave a gummy acetate shown by t.l.c. in chloroform to contain a little of the acetoxybenzofuran (III; R = Ac) (R_f value 0·64) and a major component (R_f value 0·44). The n.m.r. evidence for the structures (IX; R = R′ = H) and (IX; R = OAc, R′ = H) for the major components of the oil and acetate is detailed in the discussion.

6-Methoxy-3-methylbenzofuro-4,7-quinone (I).—A solution of potassium nitrosodisulphonate (201 mg.) in water (17 ml.) and *N*-sodium acetate (1 ml.) was added in one portion to a stirred solution of the above phenol (65 mg.) in methanol (2 ml.). The precipitated *quinone* was collected after 30 min. and recrystallised from methanol as yellow needles, m. p. 211° (sealed tube; uncorrected) (Found: C, 62·6; H, 4·3. $C_{10}H_8O_5$ requires C, 62·5; H, 4·2%), $\lambda_{max.}$ 268·5, 315, and 403 mμ (ε 10,480, 6384, and 656); $\nu_{max.}$ (mull) 1690 and 1650 (quinone carbonyl), 1605, 845, and 830 cm.$^{-1}$.

3,5-Dimethoxyphenoxyacetone (VI).—Prepared from 3,5-dimethoxyphenol and chloroacetone, the phenoxyacetone was obtained as an oil, b. p. 128—130° and 0·4 mm. (lit.,[5] b. p. 127—132° and 0·1 mm.); $\nu_{max.}$ (liquid film) 1725 (carbonyl), 1600 (olefinic str.), and 825 cm.$^{-1}$ (o.o.p. Ar–H); τ values (CCl_4): 4·04 (Ar–H), 5·68 (OCH_2), 6·28 (2 OMe), and 7·82 ($COCH_3$).

The *2,4-dinitrophenylhydrazone* crystallised from ethyl acetate as needles, m. p. 158—163° (Found: C, 51·9; H, 4·9; N, 14·25. $C_{17}H_{18}N_4O_7$ requires C, 52·3; H, 4·65; N, 14·4%)

4,6-Dimethoxy-3-methylbenzofuran (IV; R = H).—Cold concentrated sulphuric acid (1 ml.) was added, with stirring and over 10 min., to the above ketone (880 mg.). The solution which has been kept below 0° was allowed to warm to 5° and ice (25 g.) was added. An ethereal extract, washed with 5% aqueous sodium hydrogen carbonate, was re-

[12] T. J. De Boer and H. J. Bacher, *Org. Synth.*, Coll. Vol. 4, p. 250.

[13] A. I. Vogel, "Practical Organic Chemistry," Longmans, 3rd edn., p. 736.

covered to yield an oil which rapidly solidified. The solid was washed with ether (4 × 5 ml.) then crystallised from acetone–light petroleum to give the *trimer* as prisms (340 mg.), m. p. 162—164° (Found: C, 68·6; H, 6·2%; *M/e* 576. $(C_{11}H_{12}O_3)_3$ requires C, 68·7; H, 6·4%; *M/e* 576).

Evaporation of the ether washings from the trimer gave an oil (430 mg.) which formed a picrate (see below). The purified picrate was decomposed on a column of alumina; the benzofuran (IV; R = H) was eluted with benzene and purified by molecular distillation at 100° and 0·5 mm. to give needles, m. p. 34—35° (Found: C, 68·7; H, 6·3%; *M/e* 192. Calc. for $C_{11}H_{12}O_3$: C, 68·7; H, 6·4%; *M/e* 192), $\nu_{max.}$ (liquid film) 1620 and 1600 cm.$^{-1}$; $\lambda_{max.}$ 255, 261, and 287·5 mμ (ε 11,300, 10,140, and 742).

The *picrate* crystallised from methanol as red needles, m. p. 105·5—107° (Found: C, 48·45; H, 3·8; N, 10·1. $C_{11}H_{12}O_3,C_6H_3N_3O_7$ requires C, 48·7; H, 3·6; N, 10·0%).

2-*Hydroxy*-3,4,6-*trimethoxyacetophenone* (VIII; R = H).—The acetophenone was prepared from 1,2,3-trihydroxybenzene in overall yield (36%) by the methods of W. Baker [6] with the following two modifications: (*a*) the oxidation product of 1,2,3-trimethoxybenzene contained 20% of 1,2,3-trimethoxy-5-nitrobenzene which was readily separated from 2,6-dimethoxy-*p*-benzoquinone by extraction (Soxhlet) with ether; and (*b*) the acetophenone (VIII; R = H) contained an ethoxy (n.m.r.) impurity from which it was separated by repeated crystallisation from methanol to give needles, m. p. 111·5—113·5° (Found: C, 58·4; H, 5·9. Calc. for $C_{11}H_{14}O_5$: C, 58·4; H, 6·2%), $\nu_{max.}$ 1620 (bonded carbonyl) cm.$^{-1}$; τ values ($CDCl_3$): 4·09 (Ar–H), 6·10, 6·15, and 6·22 (OMe), and 7·43 (COMe).

Ethyl (2-*Acetyl*-3,5,6-*trimethoxyphenoxy*)*acetate* (VIII; R = CH_2CO_2Et).—The above acetophenone (5·3 g.) in acetone (40 ml.) was treated with ethyl bromoacetate (7·8 g.) in acetone (10 ml.) in the presence of anhydrous potassium carbonate (6·5 g.) as described above for 2,6-dihydroxy-4-methoxyacetophenone. After heating for 24 hr. under reflux, the reaction mixture was worked up in the usual manner to give the *acetate* as an oil (6·62 g.), b. p. 172° at 0·5 mm. (Found: C, 58·0; H, 6·7. $C_{15}H_{20}O_7$ requires C, 57·7; H, 6·5%), $\nu_{max.}$ (liquid film) 1755 (ester carbonyl) and 1700 (ketone carbonyl) cm.$^{-1}$; τ values (CCl_4); 3·81 (Ar–H), 5·51 (OCH_2), 6·19, 6·28, and 6·32 (OMe), and 7·64 (COMe).

2-*Acetyl*-3,5,6-*trimethoxyphenoxyacetic Acid* (VIII; R = CH_2CO_2H).—The above ester (5·0 g.) and 2·5N-sodium hydroxide (35 ml.) were boiled for 45 min. and the solution was worked up in the usual way to give a quantitative yield of the *acetic acid* (VIII; R = CH_2CO_2H), needles, m. p. 129—131° from aqueous ethanol (Found: C, 55·1; H, 5·7. $C_{14}H_{18}O_7$ requires C, 54·9; H, 5·7%); $\nu_{max.}$ 1745 (carboxyl carbonyl) and 1658 cm.$^{-1}$ (ketone carbonyl); (mull) 1725 and 1640 cm.$^{-1}$; τ values ($CDCl_3$): 3·70 (Ar–H), 5·17 (OCH_2), 6·08, 6·12, and 6·25 (OMe), and 7·45 (COMe).

4,6,7-*Trimethoxy*-3-*methylbenzofuran* (IV; R = OMe).—The above acid (7·70 g.), anhydrous sodium acetate (15·6 g.), and acetic anhydride (46 ml.) were heated under reflux for 1·5 hr. Water was added to the cooled solution which was left overnight. Basification with saturated sodium carbonate solution and extraction with ether gave an oil (5·76 g.) which was chromatographed on grade 1 Woelm alumina (200 g.). Elution with benzene–light petroleum (7 : 3, 1 : 1, and 3 : 7), and then benzene, gave the *benzofuran* (IV; R = OMe) (1·4 g.) which, after molecular distillation at 115° and 0·05 mm., was obtained as needles, m. p. 45—47° (Found: C, 65·1; H, 6·3. $C_{12}H_{14}O_4$ requires C, 64·85; H, 6·35%), $\lambda_{max.}$ 261 mμ (ε 12,720) and $\lambda_{infl.}$ 290 mμ (ε 2295). The *picrate*, prepared in ethanol, crystallised from ethanol as needles, m. p. 108—110° (Found: C, 48·1; H, 4·0; N, 8·8. $C_{12}H_{14}O_4,C_6H_3N_3O_7$ requires C, 47·9; H, 3·8; N, 9·3%).

After benzene and benzene–chloroform (1 : 1) had removed an oil (0·96 g.), chloroform eluted the *dimer* (IX; R = Me, R′ = OMe) which crystallised from acetone or methanol as prisms, m. p. 123° (Found: C, 64·5; H, 6·2%; *M/e*, 444. $(C_{12}H_{24}O_4)_2$ requires C, 64·85; H, 6·35%; *M/e*, 444).

2-*Acetyl*-3-*hydroxy*-5-*methoxybenzo*-1,4-*quinone* (XI; R = H).—(a) *From the phenoxyacetic acid* (VIII; R = CH_2CO_2H). Nitric acid (5 ml., *d* 1·2) was added to a stirred solution of the acid (500 mg.) in ethanol (3 ml.). The solution, stirred overnight at room temperature, deposited the quinone (170 mg.) which was combined with a further 170 mg. obtained by extraction of the mother-liquors. The quinone was crystallised from acetone–light petroleum, benzene, or ethyl acetate to give orange plates, m. p. 127—130°, unchanged after sublimation at 115° and 1 mm. (Found: C, 55·6; H, 4·1. $C_9H_8O_5$ requires C, 55·1; H, 4·1%), $\nu_{max.}$ 1705, 1670 (quinonoid carbonyl), and 1628 (bonded carbonyl) cm.$^{-1}$; $\lambda_{max.}$ 241·5 and 281 mμ (ε 13,330 and 13,720); $\lambda_{infl.}$ 345 mμ (ε 3920).

The *quinoxaline*, obtained from the quinone (250 mg.) and *o*-phenylene diamine (261 mg.), was purified by chromatography on silica in chloroform–ethyl acetate and crystallised from ethanol as needles (203 mg.), m. p. 246—249° (decomp.) (Found: C, 67·1; H, 4·7; N, 10·6. $C_{15}H_{12}N_2O_3$ requires C, 67·2; H, 4·5; N, 10·4%).

(b) *From* 2,6-*dihydroxy*-4-*methoxyacetophenone*. A solution of potassium nitrosodisulphonate (7·5 g.) in water (270 ml.) and *N*-sodium acetate (30 ml.) was added in one portion to a stirred solution of the acetophenone (1·4 g.) in methanol (135 ml.). After 5 min., water (220 ml.) and *N*-sodium acetate (20 ml.) were added to the reaction mixture which was stirred for a further 2·5 hr. then extracted with chloroform. Recovery gave the *quinone* (1·14 g.), m. p. 131—135 (Found: C, 55·0; H, 4·1%).

(c) *From the ethyl phenoxyacetate* (VIII; R = CH_2CO_2Et). The ester, oxidised as for the acid (VIII; R = CH_2CO_2H) in (a) gave the quinone, m. p. 127—130° in 35—50% yield.

(d) *From* 2-*hydroxy*-3,4,6-*trimethoxyacetophenone* (VIII; R = H).[9,10] The acetophenone, oxidised as in (a) or with fuming nitric acid in ether at 25° for 24 hr., gave the quinone, m. p. 134—136°, in 35—50% yield.

(e) *From* 2,3,4,6-*tetramethoxyacetophenone* (VIII; R = Me).[9] The acetophenone (240 mg.), oxidised either as in (a) or with fuming nitric acid in ether, gave the quinone (185 mg.), m. p. 137—140°.

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