557. Preparation of p-Benzoquinones.

By M. F. ANSELL, B. W. NASH, and D. A. WILSON.

The preparation of thirteen new *p*-benzoquinones is reported. Nitric acid in ether is useful for oxidising the more substituted quinols to the corresponding quinones.

FOR our work on the Diels–Alder reaction [1] we required a wide range of substituted *p*-benzoquinones. The most usual precursor of a quinone is the corresponding quinol, *p*-aminophenol, or the related phenol or amine.[2] For example, amines, phenols, and *p*-aminophenols are usually oxidised by sodium or potassium dichromate or manganese dioxide in dilute sulphuric acid; ferric chloride and sulphate have been widely used to oxidise aminophenols and quinols. As well as these reagents, silver oxide and nitric acid fumes can be used to oxidise quinols. However, many quinones are not very stable to light, heat, and moisture, and stability cannot readily be correlated with structure; in these circumstances, oxidation of the quinol with freshly prepared [2b] silver oxide, in benzene suspension, is generally advised. Some quinones, particularly tri- and tetra-substituted ones, can be prepared from the corresponding quinols by oxidation with concentrated nitric acid in ether at low temperatures (see Experimental) in good yield. This is an extension of the use of oxides of nitrogen as an oxidising agent, which is suitable for fairly stable quinones but sometimes yields a nitroquinol.[3] Nitric acid has previously been used to prepare *p*-benzoquinones from quinol mono- and di-ethers, *p*-halogenophenols, and, in isolated cases, from quinols.[4] Quinols can be prepared from the usually readily

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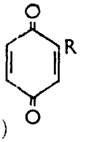
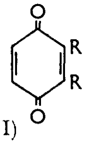
[1] Ansell, Nash, and Wilson, preceding papers.
[2] Cason, *Org. Reactions*, 1948, **4**, (*a*) 305; (*b*) 354.
[3] Ansell and Culling, *J.*, 1961, 2908.
[4] Edwards and Lewis, *J.*, 1959, 3250; Nield and Tatlow, *Tetrahedron*, 1960, **8**, 38.

accessible phenol (there are, of course, two possible starting phenols for most quinols) either by coupling with a diazonium salt (usually from sulphanilic acid), followed by reduction of the azo-compound and conversion of the amino-phenol into the quinol, or directly by Elbs persulphate oxidation.[5] Although the latter method rarely gives yields greater than 40%, and usually about 30%, as a general method (see Experimental) it is reliable, and the product is uncontaminated with starting material. In this paper we report the preparations of the thirteen new quinones, and some comments on the published methods of preparation of other quinones where this seems desirable.

The only new monosubstituted quinone prepared was the fairly unstable cyanobenzoquinone (Ia), obtained by oxidation of 2,5-dihydroxybenzonitrile[6] with silver oxide. 2,3-Dimethoxycarbonylbenzoquinone (IIb) was prepared by oxidation of methyl 3,6-dihydroxyphthalate.[7] The first step in this synthesis is the addition of hydrogen cyanide to benzoquinone. Jackman[8] gives a detailed account of this reaction and gives a 60% yield of 3,6-dihydroxyphthalonitrile. Careful temperature control throughout the addition of the potassium cyanide solution (18—23°) and removal of the alcohol by distillation, followed by extraction of the diluted residue with ethyl acetate and crystallisation of the product from water (charcoal), gives consistent yields of 75—80%. This quinol was oxidised to 2,3-dicyanobenzoquinone (IIa) by oxides of nitrogen.[9] This quinone (IIa) with boiling methanolic acid, gave the corresponding quinol in about a 40% yield, and a scheme has been suggested[10] for this kind of reaction; with hot 50% aqueous alkali, 2,5-dihydroxybenzoic acid is formed from the quinone in about 50% yield. Hydrolysis of 3,6-dihydroxyphthalonitrile to the diacid by boiling 50% aqueous alkali is accompanied by a slower decarboxylation so that the product, 3,6-dihydroxyphthalic acid, may be contaminated with 2,5-dihydroxybenzoic acid; prolonged hydrolysis affords only the latter. Similarly, vigorous alkaline hydrolysis[11] of 3,6-dihydroxy-4-methylphthalonitrile gives 2,5-dihydroxy-4-methylbenzoic acid. 3,6-Dihydroxyphthalic acid can be esterified by methanol-acid in good yield (Newman's method[12] gives a low yield), and the diester quinol affords the stable quinone (IIb) with oxides of nitrogen or silver oxide. The isomeric methyl 2,5-dihydroxyterephthalate gives a dinitro-compound with the former reagent, and affords only a quinhydrone with the latter.[3]



(I)



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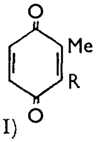

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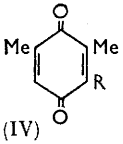

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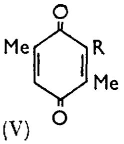

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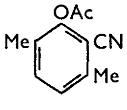

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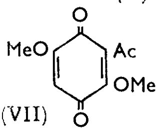

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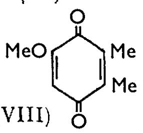

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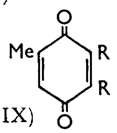

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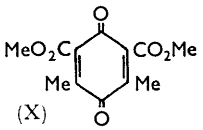

(X)

(a: R = CN; b: R = CO_2Me; c: R = NO_2; d: R = Ac)

2-Cyano-3-methylbenzoquinone (IIIa) was prepared by oxidising the previously unknown 2,5-dihydroxy-6-methylbenzonitrile with silver oxide. This quinol was obtained by persulphate oxidation of 3-hydroxy-2-methylbenzonitrile.[13] This intermediate was

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[5] Sethna, *Chem. Rev.*, 1951, **49**, 91.

[6] Seebeck, *Helv. Chim. Acta*, 1947, **30**, 149.

[7] Helferich, *Ber.*, 1921, **54**, 155.

[8] Jackman, *Adv. Org. Chem.*, 1960, **2**, 360.

[9] Braude, Brook, and Linstead, *J.*, 1954, 3569.

[10] Braude, Fawcett, and Webb, *J.*, 1954, 1049 (footnote, p. 1051).

[11] Hickinbottom, " Reactions of Organic Compounds," Longmans, Green and Co., London, 1957, p. 382.

[12] Newman, *J. Amer. Chem. Soc.*, 1941, **63**, 2431.

[13] Noelting, *Ber.*, 1904, **37**, 1015.

prepared from 2,6-dinitrotoluene: reduction of one nitro-group [14] (the yield on this stage was 84%) was followed by conversion of the amine into 2-methyl-3-nitrobenzonitrile [13] rather than into 2-methyl-3-nitrophenol [15] since reduction of the latter [13] then gave 3-amino-2-methylphenol which could not be diazotised. 2,6-Dinitrotoluene was also used in the synthesis of 2-methyl-3-nitrobenzoquinone (IIIc). This quinone had previously been prepared [16] by a two-stage synthesis from the same dinitrotoluene; the first stage, however, gave only a 1% yield of 4-amino-3-methyl-2-nitrophenol. The present synthesis followed more conventional steps and had an overall yield of 6%.

3-Cyano-2,5-dimethylbenzoquinone (Va) was prepared from 2-hydroxy-3,6-dimethylbenzaldehyde.[17] The derived oxime was dehydrated with acetic anhydride and the acetoxy-cyanide (VI) was hydrolysed to the corresponding phenol which was then oxidised to 2,5-dihydroxy-3,6-dimethylbenzonitrile, and thence to the quinone (Va). 2-Cyano-3,5-dimethylbenzoquinone (IVa) was similarly prepared, from 2-hydroxy-4,6-dimethylbenzaldehyde,[18] in which sequence the cyano-phenol and its precursors are all known compounds.[19] These two cyano-quinones were unstable to aqueous sodium hydrogen carbonate. The C≡N stretching frequency absorption (*ca.* 4·48 μ) was strong for the cyano-phenols and cyano-quinols, but was very weak for the cyano-quinones. The absorption was stronger for the Diels–Alder adducts [1] of the quinones than for the quinones themselves, but was still quite weak.*

The two ester-quinones (IVb and Vb) were prepared by carboxylation of 3,5- and 2,5-dimethylphenol, respectively (both phenols react *ortho*- to the phenolic group), and treatment of the resulting phenol acids with, first, methanolic acid, then potassium persulphate, and finally nitric acid in ether. In these preparations, as in a number of others, the Elbs persulphate oxidation was performed on the phenol esters. This was possible because in all these cases the esters were di-*ortho*-substituted, and thus not hydrolysed under mild conditions. Similar oxidations of phenolic ester not thus substituted usually afford the corresponding quinol acids as products, since the reaction involves keeping the ester in aqueous alkaline solution for several hours and then heating it in aqueous acid for about an hour.

3,5-Dimethyl-2-nitrobenzoquinone (IVc) was prepared from 3,5-dimethyl-2-nitrophenol [21] by oxidation with ammonium persulphate and then nitric acid. 2-Acetyl-3,5-dimethylbenzoquinone (IVd) was obtained only as a liquid for which no satisfactory analysis was obtained. However, the Diels–Alder product [1] from the liquid and 2,3-dimethylbutadiene confirmed the assumption that the liquid consisted mainly of the quinone

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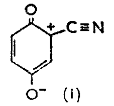
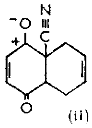
* Sensi and Gallo [20] have shown that the intensity of the C≡N stretching frequency absorption depends on the electron density of the carbon atom to which the group is attached. Electron-withdrawing groups reduce the intensity by decreasing the contribution of the dipolar $-\overset{+}{C}=\overset{-}{N}$ form; electron-donating groups increase the intensity. The resonance forms (i), (ii), and (iii) show how this $-\overset{+}{C}=\overset{-}{N}$


(i)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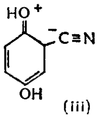
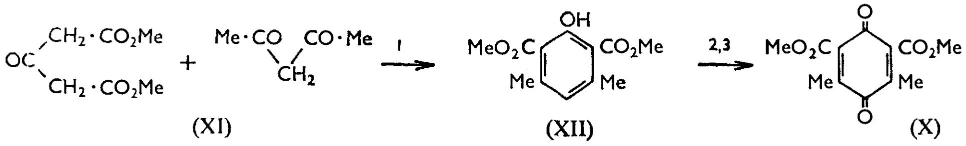

(iii)

contribution will be greatly reduced in (i), reduced to some extent in (ii) where the positive charge will act inductively, but increased in (iii). The C≡N absorption is stronger for *o*-, *m*-, and *p*-hydroxybenzonitrile than for benzonitrile, in the order $p > o > m >$ H.[20]

[14] Gibson and Johnson, *J.*, 1929, 1244.
[15] Ullmann, *Ber.*, 1884, **17**, 1957.
[16] Cohen and Marshall, *J.*, 1904, **85**, 527.
[17] Grünager and Cardani, *Gazzetta*, 1953, **83**, 664.
[18] Duff, *J.*, 1941, 547.
[19] von Auwers and Saurwein, *Ber.*, 1922, **55**, 2372.
[20] Sensi and Gallo, *Gazzetta*, 1955, **85**, 224, 235.
[21] Adams and Stewart, *J. Amer. Chem. Soc.*, 1941, **63**, 2859.

(IVd). 3,5-Dimethylphenol was acetylated and treated with aluminium chloride, to give 2-acetyl-3,5-dimethylphenol.[22] The usual sequence of persulphate and nitric acid oxidation afforded the crude quinone (Vd), which slowly decomposed at room temperature.

3-Acetyl-2,5-dimethoxybenzoquinone (VII) was prepared by oxidation of the known quinol.[23] 5-Methoxy-2,3-dimethylbenzoquinone [24] (VIII) has been prepared by an improved route, directly from 2,3-dimethylbenzoquinone. 2,3-Dicyano- and 2,3-dimethoxycarbonyl-5-methylbenzoquinone (IXa and b) were prepared by oxidation of the known dicyano-quinol.[25] Alkaline hydrolysis of 3,6-dihydroxy-4-methylphthalonitrile gives concomitant decarboxylation (see above), so the dimethyl ether was prepared which, with sulphuric acid, gave crude 3,6-dimethoxy-4-methylphthalic anhydride.[25] With methanolic acid this anhydride gave methyl 3,6-dimethoxy-4-methylphthalate, which was then oxidised to the quinone (IXb).



(XI) (XII) (X)

Reagents: 1, NaOMe. 2, $K_2S_2O_8$. 3, HNO_3–Et_2O.

The tetrasubstituted quinone (X) was prepared by the sequence (XI $\longrightarrow$ XII $\longrightarrow$ X). The reaction (XI $\longrightarrow$ XII) followed the analogous reaction reported by Prelog *et al.*[26] with the ethyl ester. The diester phenol was converted into the quinone (X) by the usual reactions and was also hydrolysed to the known diacid,[26] which was converted into the new 2,5-dihydroxy-4,6-dimethylisophthalic acid by persulphate.

Preparation of 2,6-dimethylbenzoquinone-3,5-dicarboxylic acid was unsuccessfully attempted by oxidation of this diacid quinol with nitric acid. The infrared spectrum of the product suggested that the diacid quinone had been formed. An unsuccessful attempt was also made to carboxylate 2,5-dimethoxybenzoquinol by the Marassé method.

EXPERIMENTAL

Ultraviolet absorption spectra are recorded for ethanol (95%) solutions.

Oxidation of Phenols to Quinols.—Baker and Brown's method [27] was followed. The phenol (1 mole) was dissolved in 5N-sodium hydroxide (1 l.) (pyridine being added to effect complete solution if necessary); an aqueous solution of potassium or ammonium persulphate (1·1 moles, minimum volume) was slowly added to the stirred solution at 0° (the more soluble ammonium salt allowed up to 1 mole of phenol to be used). The solution was left for 1—3 days, then acidified to Congo Red with concentrated hydrochloric acid and extracted with ether (with prior filtration if necessary) to remove starting phenol. The solution was then made strongly acid with more hydrochloric acid and was heated on the water-bath for 1—2 hr. The cooled solution was extracted with ether; the dried extracts afforded the crude quinol in 20—40% yield.

Oxidation of Quinols to Quinones.—(*a*) *With silver oxide.* The quinol (1 g.) was dissolved or suspended in sodium-dried benzene (*ca.* 50 ml.), and anhydrous potassium carbonate (3 g.) and freshly prepared silver oxide [2b] (3 g.) were added. The mixture was shaken at *ca.* 45° for 5—30 min. with light excluded. The mixture was filtered on to anhydrous potassium carbonate, and the residue was washed with solvent. The dried solution was filtered and evaporated at <35°/18 mm. in the dark and the residue was crystallised, to afford the quinone.

(*b*) *With oxides of nitrogen.* The finely powdered quinol (1 g.) was suspended in carbon

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[22] Smith and Opie, *J. Org. Chem.*, 1941, **6**, 427.
[23] Ramage and Stead, *J.*, 1953, 1393.
[24] Fieser and Ardao, *J. Amer. Chem. Soc.*, 1956, **78**, 774.
[25] Anslow and Raistrick, *Biochem. J.*, 1940, **34**, 1124.
[26] Prelog, Metzler, and Jeger, *Helv. Chim. Acta*, 1947, **30**, 675.
[27] Baker and Brown, *J.*, 1948, 2303.

tetrachloride (*ca.* 20 ml.) and oxides of nitrogen [9] were added dropwise, with vigorous stirring, until present in excess. Stirring was continued for 5 min., then filtration and crystallisation of the residue gave the quinone.

(*c*) *With nitric acid.* The quinol (1 g.) was dissolved or suspended in ether (25—50 ml.) at between 0° and −20°. Concentrated nitric acid (up to 10 ml.) was added, with stirring, until it formed a separate layer or until the ether layer did not deepen further in colour. The ether layer was separated from any nitric acid layer, and sodium hydrogen carbonate was added until the effervescence just ceased. The ethereal solution was then washed with dilute sodium hydrogen carbonate solution to remove any nitro-quinols [this step was omitted with the two cyanodimethylbenzoquinones (IVa and Va) which were unstable to bicarbonate solution], then with water, and dried ($MgSO_4$). Evaporation to dryness gave a residue that crystallised to yield the quinone.

Cyano-1,4-*benzoquinone* (Ia).—2,5-Dihydroxybenzonitrile [6] (500 mg.) was oxidised with silver oxide (the mixture was boiled for 45 min.), affording *cyanobenzoquinone* (250 mg., 50%), m. p. 124—125° (yellow-brown needles from benzene), $\lambda_{max.}$ 4·47vw (CN), 6·01, 6·07 (C=O), 6·18, 6·29 μ (C=C) (Found: C, 63·45; H, 2·7; N, 10·35. $C_7H_3NO_2$ requires C, 63·2; H, 2·3; N, 10·5%).

2,3-*Dicyanobenzoquinone* (IIa).—3,6-Dihydroxyphthalonitrile [8] was oxidised with oxides of nitrogen, to afford 2,3-dicyanobenzoquinone, m. p. 178—180° (lit.,[9] 178—180°). This quinone (IIa) (2 g.) was heated under reflux with methanol (25 ml.) containing concentrated sulphuric acid (1·5 ml.) for 54 hr. Dilution with water and extraction with ether afforded a solid (1·8 g.) which crystallised from water (charcoal), to give 3,6-dihydroxyphthalonitrile (580 mg.).

The quinone (IIa) (2 g.) was heated under reflux with water (50 ml.) containing sodium hydroxide (50 g.) for 15 hr. The cooled solution was acidified (effervescence) and extracted with ether. The ethereal solution was extracted with sodium hydrogen carbonate solution which, on acidification and extraction, afforded a solid (1·02 g.), m. p. 180—185° (decomp.). Crystallisation from water (charcoal) gave 2,5-dihydroxybenzoic acid, m. p. 206—208° (decomp.) [lit.,[28] 206—208° (decomp.)].

2,3-*Dimethoxycarbonylbenzoquinone* (IIb).—3,6-Dihydroxyphthalonitrile (20 g.) was heated under reflux with water (160 ml.) containing potassium hydroxide (160 g.) under nitrogen for 75 min. The cooled solution was poured into an excess of dilute sulphuric acid, and the solution was extracted with ethyl acetate (6 × 160 ml.) to afford, on removal of the solvent, a light brown solid (16·5 g.), m. p. 185—195° (decomp.). Crystallisation from a small volume of water (charcoal) afforded 3,6-dihydroxyphthalic acid (10·7 g., 52%), m. p. 219—225° (decomp.), raised to m. p. 224—225° (decomp.) on further crystallisation [lit.,[29] 213° (decomp.)]. Prolonged hydrolysis (45 hr.) under the same conditions afforded 2,5-dihydroxybenzoic acid (50%) as the only isolable product. The diacid was esterified with methanol–sulphuric acid, to give methyl 3,6-dihydroxyphthalate (63%), m. p. 140—143° (from water) (lit.,[7] 141—142°), $\lambda_{max.}$ 218, 244infl., 348 mμ (ε 19,500, 6700, and 7700). Esterification by Newman's method [12] gave the diester (16%) and unchanged diacid.

The diester quinol was oxidised with oxides of nitrogen, to afford 2,3-*dimethoxycarbonylbenzoquinone* (IIb) (60%), m. p. 155·5—157° [orange needles from benzene–light petroleum (b. p. 60—80°)], $\lambda_{max.}$ 5·78 (ester), 6·02 (quinone C=O), 6·15, 6·28 μ (C=C) (Found: C, 53·9; H, 3·65. $C_{10}H_8O_6$ requires C, 53·6; H, 3·6%). Oxidation of the quinol by silver oxide also gave the quinone (30%).

2-*Cyano*-3-*methylbenzoquinone* (IIIa).—3-Hydroxy-2-methylbenzonitrile [13] (23·5 g.) was oxidised with potassium persulphate, to afford 2,5-*dihydroxy*-6-*methylbenzonitrile* (6 g., 23%), m. p. 200—210°; when purified by crystallisation from water (charcoal) this had m. p. 218—220°, $\lambda_{max.}$ 217, 245, 333 mμ (ε 20,000, 6600, and 5200), 3·07 (OH), 4·48s (CN), 6·20, 6·67 μ (C=C) (Found: C, 64·4; H, 4·6; N, 10·0. $C_8H_7NO_2$ requires C, 64·4; H, 4·7; N, 9·4%). This quinol was oxidised with silver oxide, to afford 2-*cyano*-3-*methylbenzoquinone* (IIIa) (45%), m. p. 99—101° (decomp.) [from benzene–light petroleum (b. p. 80—100°)], $\lambda_{max.}$ 4·47vw (CN), 6·03 (C=O), 6·28 μ (C=C) (Found: C, 65·6; H, 3·6; N, 9·3. $C_8H_5NO_2$ requires C, 65·3; H, 3·4; N, 9·5%).

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[28] Fichter, *Helv. Chim. Acta*, 1921, **4**, 930, gives m. p. 200°, but Dr. G. C. Culling (personal communication) found m. p. 206—208° (decomp.).

[29] Thiele and Günther, *Annalen*, 1906, **349**, 45.

2-*Methyl*-3-*nitrobenzoquinone* (IIIc).—2-Methyl-3-nitrophenol[15] (11 g.) was oxidised with potassium persulphate to give 2-methyl-3-nitroquinol (3·2 g., 29%), m. p. 100—112°, raised only slowly to m. p. 115° by crystallisation from benzene (lit.,[16] 117—118°). This quinol (3 g.) was oxidised with silver oxide; the crude product was purified by sublimation at 50—55°(bath)/0·5 mm., affording bright yellow 2-methyl-3-nitrobenzoquinone (IIIc) (1·1 g., 37%), m. p. 65—67° [lit.,[16] ruby-red prisms (from ether), m. p. 64—65°]. The overall yield of this quinone from 2,6-dinitrotoluene was 6%.

3-*Cyano*-2,5-*dimethylbenzoquinone* (Va).—2,5-Dimethylphenol was converted into 2-hydroxy-3,6-dimethylbenzaldehyde[17] by Duff's method.[18] The derived *oxime* had m. p. 131—132° (from aqueous ethanol) (Found: C, 65·05; H, 7·05; N, 8·55. $C_9H_{11}NO_2$ requires C, 65·45; H, 6 7; N, 8·5%). The oxime (30 g.) was heated under reflux in acetic anhydride (180 ml.) containing anhydrous sodium acetate (15 g.) for 3 hr. The cooled mixture was poured into water (1 l.), then filtration and crystallisation of the residue from light petroleum (b. p. <40°) afforded 2-*acetoxy*-3,6-*dimethylbenzonitrile* (VI) (23·7 g., 71%), m. p. 36—37° (Found: C, 69·95; H, 5·8; N, 7·55. $C_{11}H_{11}NO_2$ requires C, 69·8; H, 5·85; N, 7·4%). This acetoxy-nitrile (VI) (30 g.) was stirred with 5N-sodium hydroxide (300 ml.), containing sufficient ethanol to give a homogeneous solution, at 70° for 15 min., then the solution was acidified and cooled. Filtration and crystallisation of the residue from aqueous acetic acid gave 2-*hydroxy*-3,6-*dimethylbenzonitrile* (21·8 g., 95%), m. p. 100—101°, $\lambda_{max.}$ 3·04 (OH), 4·49s μ (CN) (Found: C, 73·0; H, 6·05; N, 9·1. C_9H_9NO requires C, 73·45; H, 6·15; N, 9·5%). This cyano-phenol (14·7 g.) was oxidised with potassium persulphate to 2,5-*dihydroxy*-3,6-*dimethylbenzonitrile* (5·8 g., 36%), m. p. 219—220° (from acetic acid), $\lambda_{max.}$ 2·93, 3·01 (OH), 4·49s μ (CN) (Found: C, 66·4; H, 5·85; N, 8·75. $C_9H_9NO_2$ requires C, 66·25; H, 5·55; N, 8·6%). This quinol (5 g.) was oxidised with nitric acid in ether at −10° to 3-*cyano*-2,5-*dimethylbenzoquinone* (Va) (4·8 g., 96%), m. p. 123—124° [from light petroleum (b. p. 100—120°)], $\lambda_{max.}$ 4·49vw (CN), 6·02 (C=O), 6·20 μ (C=C) (Found: C, 66·95; H, 4·3; N, 8·75. $C_9H_7NO_2$ requires C, 67·05; H, 4·4; N, 8·7%).

2-*Cyano*-3,5-*dimethylbenzoquinone* (IVa).—2-Hydroxy-4,6-dimethylbenzonitrile[19] (14·7 g.) was oxidised with potassium persulphate to 3,6-*dihydroxy*-2,4-*dimethylbenzonitrile* (8·5 g., 52%), m. p. 186—188° [from water (charcoal)], $\lambda_{max.}$ 3·00br (OH), 4·49s μ (CN) (Found: C, 66·3; H, 5·5; N, 9·0. $C_9H_9NO_2$ requires C, 66·25; H, 5·55; N, 8·6%). This quinol (10 g.) was oxidised with nitric acid in ether at 0° to 2-*cyano*-3,5-*dimethylbenzoquinone* (IVa) (9·3 g., 93%), m. p. 124—126° [from light petroleum (b. p. 100—120°)], $\lambda_{max.}$ 4·48vw (CN), 6·02 (C=O), 6·20 μ (C=C) (Found: C, 67·25; H, 4·55; N, 8·9. $C_9H_7NO_2$ requires C, 67·05; H, 4·4; N, 8·7%). This cyano-quinone decomposed slowly on storage.

2-*Methoxycarbonyl*-3,5-*dimethylbenzoquinone* (IVb).—3,5-Dimethylphenol was carboxylated by the Marassé procedure given by Wessely *et al.*[30] and Baine *et al.*[31] on a 1·33-molar scale (thirteen times greater than that used by Baine, and with half the minimum amount of potassium carbonate recommended by Wessely), to give 2-hydroxy-4,6-dimethylbenzoic acid (88%), m. p. 166—167° (lit.,[32] 164—165°). It was essential to use very dry reactants to obtain good yields of acid. The acid was heated under reflux in methanol containing concentrated sulphuric acid (3% v/v) for 40 hr., giving *methyl* 2-*hydroxy*-4,6-*dimethylbenzoate* (82%), m. p. 79·5—80° (from methanol), $\lambda_{max.}$ 3·00br (OH), 6·07 (ester), 6·15, 6·20sh, 6·31, 6·38, 6·50 μ (C=C) (Found: C, 66·6; H, 6·7. $C_{10}H_{12}O_3$ requires C, 66·65; H, 6·7%). This ester was oxidised with potassium persulphate to *methyl* 2,5-*dihydroxy*-4,6-*dimethylbenzoate* (31%), m. p. 129·5—130° [from water (charcoal)], $\lambda_{max.}$ 2·86 (OH), 6·07 (ester), 6·19, 6·37 μ (C=C) (Found: C, 61·3; H, 6·2. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·15%). This ester-quinol (10 g.) was oxidised with nitric acid in ether at 0° to 2-*methoxycarbonyl*-3,5-*dimethylbenzoquinone* (IVb) (8·4 g., 84%), m. p. 54·5—55·5° (from carbon disulphide), $\lambda_{max.}$ 5·78 (ester), 6·01sh, 6·06 (quinone C=O), 6·10sh, 6·18 μ C=C) (Found: C, 62·1; H, 5·3. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%).

3-*Methoxycarbonyl*-2,5-*dimethylbenzoquinone* (Vb).—2,5-Dimethylphenol was carboxylated as described by Palfrey and Metayer[33] to give 2-hydroxy-3,6-dimethylbenzoic acid (52%). This acid was heated under reflux in methanol containing concentrated sulphuric acid (3% v/v) for 70 hr., giving unchanged acid (61%) and *methyl* 2-*hydroxy*-3,6-*dimethylbenzoate* (22%), m. p. 34—35° (from aqueous methanol), $\lambda_{max.}$ 3·00w (OH), 6·08 (ester), 6·22, 6·33 μ (C=C) (Found:

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[30] Wessely, Benedikt, Benger, Friedrich, and Prillinger, *Monatsh.*, 1950, **81**, 1071.

[31] Baine, Adamson, Barton, Fitch, Swayampati, and Jesky, *J. Org. Chem.*, 1954, **19**, 510.

[32] Fuson, Corse, and Welldon, *J. Amer. Chem. Soc.*, 1941, **63**, 2645.

[33] Palfrey and Metayer, *Bull. Soc. chim. France*, 1948, 956.

C, 66·25; H, 6·45. $C_{10}H_{12}O_3$ requires C, 66·65; H, 6·7%). This ester was oxidised with potassium persulphate to *methyl 2,5-dihydroxy-3,6-dimethylbenzoate* (29%), m. p. 133·5—134° [from water (charcoal)], $\lambda_{max.}$ 2·97 (OH), 6·08 (ester), 6·16sh, 6·27 μ (C=C) (Found: C, 61·35; H, 6·2. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·15%). This ester-quinol was oxidised with nitric acid in ether at 0° to *3-methoxycarbonyl-2,5-dimethylbenzoquinone* (Vb) (87%), m. p. 66—68° (from carbon disulphide), $\lambda_{max.}$ 5·77 (ester), 6·04sh, 6·09 (quinone C=O), 6·19 μ (C=C) (Found: C, 62·05; H, 5·55. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%).

3,5-Dimethyl-2-nitrobenzoquinone (IVc).—3,5-Dimethyl-2-nitrophenol [21] (41·7 g.) was oxidised with ammonium persulphate (starting material removed by steam-distillation of the acidified reaction mixture) to *3,5-dimethyl-2-nitroquinol* (22·5 g., 50%), m. p. 113—117°, raised to m. p. 118—120° (from carbon tetrachloride), $\lambda_{max.}$ 2·93 (OH), 6·17, 6·29 (C=C), 6·53 μ (NO_2) (Found: C, 51·95; H, 4·95; N, 7·5. $C_8H_9NO_4$ requires C, 52·45; H, 4·95; N, 7·65%). If the quinol was left in contact with carbon tetrachloride after crystallisation, the orange crystals changed to red-brown crystals of the same m. p. The quinol (10 g.) was oxidised with nitric acid in ether at −10° to *3,5-dimethyl-2-nitrobenzoquinone* (IVc) (8·0 g., 80%), m. p. 69—71° [from light petroleum (b. p. 80—100°)], $\lambda_{max.}$ 6·01, 6·04sh (C=O), 6·16 (C=C), 6·53 μ (NO_2) (Found: C, 53·15; H, 4·15; N, 7·5. $C_8H_7NO_4$ requires C, 53·05; H, 3·9; N, 7·75%).

2-Acetyl-3,5-dimethylbenzoquinone (IVd).—2-Acetyl-3,5-dimethylphenol [22] (164 g.) was oxidised with ammonium persulphate to the yellow *3,6-dihydroxy-2,4-dimethylacetophenone* (60·4 g., 34%), m. p. 135—136° [from light petroleum (b. p. 80—100°)], $\lambda_{max.}$ 3·10 (OH), 6·10 (C=O?), 6·16, 6·27 μ (C=C) (Found: C, 66·6; H, 6·65. $C_{10}H_{12}O_3$ requires C, 66·65; H, 6·7%). This quinol (10 g.) was oxidised with nitric acid in ether at −20° to afford an oil (7·9 g.), $\lambda_{max.}$ 5·85 (acetyl C=O), 6·00, 6·10sh (quinone C=O), 6·19, 6·45 μ (C=C). The oil was distilled at 100°(bath)/2 mm., but the yellow distillate slowly decomposed and no satisfactory analysis was obtained. The Diels–Alder reaction of this oil [1] showed that it consisted mainly of the expected 2-acetyl-3,5-dimethylbenzoquinone (IVd).

3-Acetyl-2,5-dimethoxybenzoquinone (VII).—2,5-Dihydroxy-3,6-dimethoxyacetophenone [23] (10 g.) was slowly added to stirred concentrated nitric acid (180 ml.). The yellow solution was left for 2 min. and then diluted with water (200 ml.). The precipitate was collected and sublimed at 270°(bath), giving *3-acetyl-2,5-dimethoxybenzoquinone* (VII) (8·7 g., 87%), m. p. 324—324·4° (with sublimation), $\lambda_{max.}$ 5·78 (acetyl C=O), 5·95sh, 6·01 (quinone C=O), 6·28 μ (C=C) (Found: C, 57·6; H, 4·5. $C_{10}H_{10}O_5$ requires C, 57·15; H, 4·8%). The quinone (VII) was also prepared, but in poorer yield, by oxidising the quinol with silver oxide. Aqueous and methanolic solutions of the quinol deposited a red solid, as previously reported,[23] which was shown (by infrared spectra) to be impure quinone. The quinone (1·6 g.) was heated with zinc powder (10 g.) in acetic acid (60 ml.) and acetic anhydride (60 ml.) for 15 hr. on the water-bath. Filtration and dilution with water (500 ml.) gave a precipitate of 2,5-diacetoxy-3,6-dimethoxyacetophenone (1·2 g., 53%), m. p. 188—190° (from ethanol), identical with an authentic specimen,[23] m. p. 187—189°.

5-Methoxy-2,3-dimethylbenzoquinone (VIII).—Anhydrous zinc chloride (40 g.) was added to a solution of 2,3-dimethylbenzoquinone [34] (33·5 g.) in dry methanol (160 ml.) at 50°, and the mixture was shaken until it was homogeneous. It was kept at 50° for 24 hr. in the dark, and then at 0° for 5 hr. The brown solid was filtered off and extracted with cold benzene (5 × 50 ml.). The residue was impure 2,3-dimethylquinol. The solvent was removed from the extracts, and the residue crystallised from methanol, affording 5-methoxy-2,3-dimethylbenzoquinone (10·1 g., 50%), m. p. 113—115°, $\lambda_{max.}$ 6·00, 6·09 (C=O), 6·16, 6·24 μ (C=C), in agreement with Flaig *et al.*[35] (lit.,[24] 110—111°).

2,3-Dicyano-5-methylbenzoquinone (IXa).—3,6-Dihydroxy-5-methylphthalonitrile was prepared by the method of Anslow and Raistrick.[25] It was best to keep the reaction temperature between 20° and 30° and to ensure that the mixture was only slightly acid throughout the reaction by adding the acid at the same time as the cyanide solution. This quinol (2 g.) was oxidised with nitric acid in ether at −20° to *2,3-dicyano-5-methylbenzoquinone* (IXa) (1·6 g., 80%), m. p. 161—162° [from benzene–light petroleum (b. p. 80—100°)], $\lambda_{max.}$ 4·50vw (CN), 6·00sh, 6·03 (C=O), 6·23 μ (C=C) (Found: C, 62·4; H, 2·55; N, 16·55. $C_9H_4N_2O_2$ requires C, 62·8; H, 2·35; N, 16·3%).

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[34] Smith and Austin, *J. Amer. Chem. Soc.*, 1942, **64**, 528.

[35] Flaig and Salfeld, *Annalen*, 1959, **626**, 215.

2,3-*Dimethoxycarbonyl*-5-*methylbenzoquinone* (IXb).—Hydrolysis of 3,6-dihydroxy-5-methylphthalonitrile with sulphuric acid (90% v/v) at 100° gave only tars; hydrolysis with boiling 50% w/w potassium hydroxide solution for 20 hr. gave 2,5-dihydroxy-4-methylbenzoic acid (isolated as the methyl ester,[36] m. p. 123—125°). The quinol was converted into its dimethyl ether,[25] m. p. 188—190° (lit.,[25] 182°), and thence, in 2-g. batches, into the crude 3,6-dimethoxy-4-methylphthalic anhydride [25] which was not purified. The anhydride (from 14 × 2 g. of nitrile) was heated under reflux in methanol (500 ml.) containing concentrated sulphuric acid (15 ml.) for 15 hr. The non-acidic product was crystallised from methanol, giving two substances—large crystals and thin needles. Hand-sorting and crystallisation of the former from methanol gave *methyl* 3,6-*dimethoxy*-4-*methylphthalate* (13·8 g., 37%), m. p. 83·5—84·5°, $\lambda_{max.}$ 5·74, 5·81 (C=O), 6·25 μ (C=C) (Found: C, 58·35; H, 6·05. $C_{13}H_{16}O_6$ requires C, 58·2; H, 6·0%). The dimethoxy-ester (1 g.) was ground with concentrated nitric acid (10 ml.) at 0°, ether (50 ml.) was added as soon as the solution became yellow, and the general procedure was then followed. The product was crystallised from carbon disulphide, affording 2,3-*dimethoxycarbonyl*-5-*methylbenzoquinone* (IXb) (910 mg., 91%), m. p. 91—92°, $\lambda_{max.}$ 5·70, 5·76 (ester C=O), 6·03, 6·08sh (quinone C=O), 6·19 μ (C=C) (Found: C, 55·35; H, 4·3. $C_{11}H_{10}O_6$ requires C, 55·45; H, 4·25%).

2,6-*Dimethoxycarbonyl*-3,5-*dimethylbenzoquinone* (X).—Methyl β-oxoglutarate [37] was prepared from citric acid by the method used by Baker *et al.*[38] for the ethyl ester. The ester (174 g.) and acetylacetone (100 g.) were added to a solution of sodium methoxide (from 24 g. of sodium) in methanol (600 ml.). The mixture was left for 20 hr. The sodium salt was filtered off, dissolved in hot water, and acidified with dilute sulphuric acid. Cooling, filtration, and crystallisation of the residue from light petroleum (b. p. 60—80°) afforded *methyl* 2-*hydroxy*-4,6-*dimethylisophthalate* (XII) (214 g., 91%), m. p. 105—106°, $\lambda_{max.}$ 2·95br (OH), 5·82, 6·04 (C=O), 6·21, 6·43 μ (C=C) (Found: C, 60·3; H, 5·85. $C_{12}H_{14}O_5$ requires C, 60·5; H, 5·9%). This diester phenol (79·3 g.) was oxidised with potassium persulphate to *methyl* 2,5-*dihydroxy*-4,6-*dimethylisophthalate* (38·8 g., 31%), m. p. 110—110·5° (from aqueous methanol), $\lambda_{max.}$ 2·93 (OH), 5·88, 6·03 (C=O), 6·23 μ (C=C) (Found: C, 56·95; H, 5·4. $C_{12}H_{14}O_6$ requires C, 56·7; H, 5·55%). This diester-quinol (10 g.) was oxidised with nitric acid in ether at 0° to 2,6-*dimethoxycarbonyl*-3,5-*dimethylbenzoquinone* (X) (9·5 g., 95%), m. p. 54—56° [from light petroleum (b. p. 60—80°)], $\lambda_{max.}$ 5·77sh, 5·80 (ester C=O), 6·00sh, 6·04 (quinone C=O), 6·11, 6·16 μ (C=C) (Found: C, 57·2; H, 5·0. $C_{12}H_{12}O_6$ requires C, 57·15; H, 4·8%). Silver oxide oxidation afforded no quinone.

Methyl 2-hydroxy-4,6-dimethylisophthalate (52·2 g.) was hydrolysed with aqueous alkali to 2-hydroxy-4,6-dimethylisophthalic acid (24·1 g., 41%), m. p. 225—226° (decomp.) (lit.,[26] 226°). This acid (69·4 g.) was oxidised with potassium persulphate to 2,5-*dihydroxy*-4,6-*dimethylisophthalic acid* (22·9 g., 31%), m. p. 216—217·5° (decomp.) (from glacial acetic acid) (Found: C, 53·1; H, 4·4. $C_{10}H_{10}O_6$ requires C, 53·1; H, 4·5%). This diacid-quinol (2 g.) was oxidised with nitric acid in ether at 0° to a yellow oil which slowly solidified. Crystallisation of this material [m. p. 170—175° (decomp.)] from ether at −70° gave a yellow powder, m. p. 147—149° (decomp.), $\lambda_{max.}$ 5·88, 5·92 (acid C=O), 6·00, 6·08 μ (quinone C=O). No satisfactory analysis was obtained, and the solid decomposed on being heated in the common organic solvents.

Attempted Preparation of 2,5-*Dihydroxy*-3,6-*dimethoxybenzoic Acid.*—A solution of sodium methoxide (from 46 g. of sodium) in dry oxygen-free methanol (300 ml.) was added to a suspension of 2,5-dimethoxyquinol (170 g.) in dry methanol (300 ml.). The mixture was heated under reflux for 1 hr. under nitrogen, and the solvent was then distilled off. The residue was dried at 100°, cooled to 0°, and ground to a fine powder which was mixed with anhydrous potassium carbonate (500 g., dried at 500°). The mixture, which quickly became warm on storage, was heated with carbon dioxide under 30 atm. at 220° for 4 hr. The cooled mixture was added to water (1 l.) and the black insoluble material was filtered off. The filtrate was acidified with concentrated hydrochloric acid and extracted with ether. The dried ($MgSO_4$) extracts afforded a solid which crystallised from acetic acid, to give an orange substance (3·6 g.), m. p. 230—231° (decomp.), $\lambda_{max.}$ 3·04, 3·23 (OH), 5·85, 6·07 (C=O), 6·11, 6·19 μ (C=C) (Found: C, 50·85; H, 2·95; MeO, 1·35%). The solid, which was not obtained when carboxylation was repeated at 150°, was insoluble in sodium hydrogen carbonate solution. This substance, with acetic anhydride–sulphuric acid, gave a pale yellow acetyl derivative, m. p. 157—159° (from

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[36] Ansell, Lown, Turner, and Wilson, following paper.

[37] Diels, Beckmann, and Tönnies, *Annalen*, 1924, **439**, 76.

[38] Baker, Schaub, Querry, and Williams, *J. Org. Chem.*, 1952, **17**, 97

ethanol), $\lambda_{max.}$ 3·25 (OH), 5·60, 5·63, 5·93, 5·98 (C=O), 6·17 μ (C=C) (Found: C, 53·8; H, 3·4%; *M*, 216). This substance was also insoluble in sodium hydrogen carbonate solution.

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