431. *Michael Additions to Methoxy*-p-*benzoquinone.*

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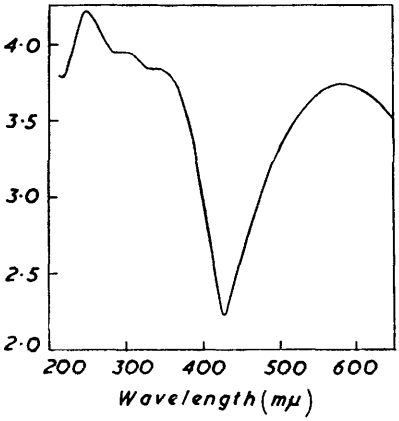
Methoxy-*p*-benzoquinone undergoes Michael additions to give compounds of type (I; R, R′ = CO_2Alk, CN, Ac); displacement of the methoxyl group can also occur. The products readily cyclise, giving a lactone or a furan. In alkaline solution, compounds of type (I) are readily oxidised by air to the blue anion of the corresponding quinone.

METHOXY-*p*-BENZOQUINONE was prepared from methoxyquinol by use of dichromate[1a] in weakly acid solution.[1b] Michael additions of diethyl and dimethyl malonate, ethyl cyanoacetate, malonodinitrile, and ethyl acetoacetate to this quinone were made with an alkoxide ion as catalyst (method 1). In addition, diethyl malonate and ethyl cyanoacetate were added with ammonia as catalyst (method 2). Primary products of type (I; R and R′ = CO_2Alk, CN, or Ac) were isolated, except that the product from ethyl acetoacetate was unstable. These dissolved in weak alkali (*e.g.*, sodium hydrogen carbonate solution) with the production of an intense blue colour, which was stable for several hours but was rapidly destroyed in 2N-sodium hydroxide.

TABLE 1. *Absorption maxima* (mμ; *approx.*) *in the visible spectrum of the anions of some Michael addition products derived from* p-*benzoquinone.*

Product from	$\lambda_{max.}$[a]	Product from	$\lambda_{max.}$
p-*Benzoquinone and*:		*Methoxy*-p-*benzoquinone and*:	
Et_2 malonate	585	Et benzoylacetate	540
Methoxy-p-*benzoquinones and*:		Acetylacetone	530[b]
Et_2 malonate	585	Dimedone	530[c]
Et cyanoacetate	605	Nitromethane	580[d]
Malonodinitrile	605	(Quinone alone)	None[e]
Et acetoacetate	530		

[a] Solutions blue. [b] Solution blue, rapidly becoming purple. [c] Very weak; solution purple. [d] Very weak; solution pink. [e] Solution green, becoming brown.



Absorption spectrum of the anion of 5-(*diethoxycarbonylmethyl*)-2-*methoxybenzo*-1 : 4-*quinone in* N/1000-NaOH *containing* 8% *by volume of* 95% *ethanol.*

Oxidation of the adduct (I; R = R′ = CO_2Et) with acidified dichromate gave the corresponding quinone as an oil. Like the parent quinol, this dissolved in alkali to a deep blue solution which, after acidification, showed ultraviolet absorption maxima at the same wavelengths as a solution of the pure quinone, but with ε values decreased by about 10%. Thus, the blue colour is that of the anion of the quinone (II); the two chief canonical structures of the resonance hybrid are shown. That similar quinones form stable anions

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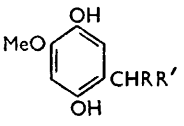
[1] (*a*) Dimroth, Eber, and Wehr, *Annalen*, 1926, **446**, 147; (*b*) Erdtmann, *Proc. Roy. Soc.*, 1934, *A*, **143**, 191.

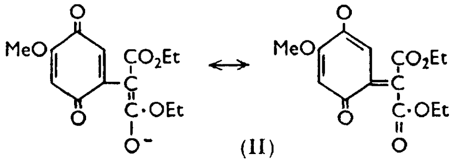
has long been known, and it has been stated[2] that the quinone (III) is a stronger acid then diethyl malonate. Attempts to prepare quinones from the quinols (I; R = CO_2Et or CN, R′ = CN) failed, but solutions of these quinols in N/1000-sodium hydroxide, of such a concentration that the dissolved oxygen would be enough for complete oxidation to the quinones, had absorption spectra that were qualitatively very similar to that of the anion (II) (Figure), compound (I; R = CO_2Et, R′ = CN) having $\lambda_{max.}$ 236, 302, 350, and 605 mμ, and (I; R = R′ = CN) 242, 300, 363, and 605 (inflection at 490) mμ. Table 1 shows the dependence of the position of maximum absorption in the visible spectrum on the nature of the methylene component. Dialkylaminovinylquinones[3] (*e.g.*, IV), the structure of whose resonance hybrid resembles that of the anion (II), show light absorption similar to that of this anion.

TABLE 2. *Infrared bands* (*cm.*$^{-1}$) *between* 1650 *and* 2500 *cm.*$^{-1}$ (recorded by a Grubb–Parsons Type 54 instrument, with the samples in KCl discs).

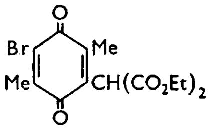
Compound	Band	Assignment	Compound	Band	Assignment
(I; R = R′ = CO_2Et) ...	1739	CO (Ester)	(X)	1675	CO (Amide)
(V)	1739	CO (Ester)		1745	CO (Ester)
	1815	CO (Lactone)		2273	CN
(I; R = CO_2Et, R′ = CN	1736	CO (Ester)		2353	Not known
	2273	CN	2 : 5 : 1 : 4-		
(VII)	1667 (infl.)	CO (Amide)	$(HO)_2C_6H_2(CH_2{\cdot}CO_2Et)$	1715	CO (Ester)
(IX)	1672	CO (Amide)		2310	Not known
	2358	Not known		2420	



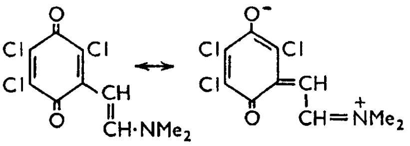
(I)



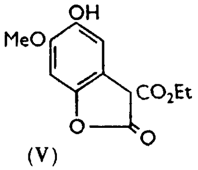
(II)



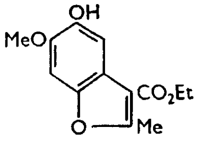
(III)



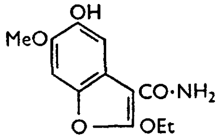
(IV)



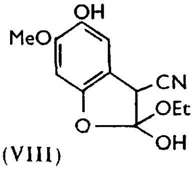
(V)



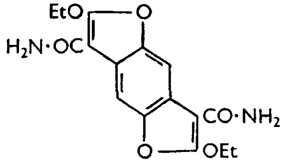
(VI)



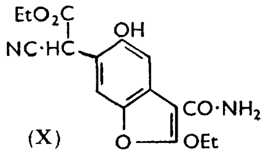
(VII)



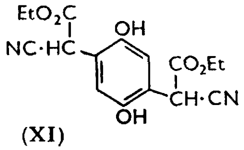
(VIII)



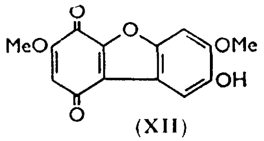
(IX)



(X)



(XI)



(XII)

On treatment with acid, the primary adducts readily underwent ring-closure; the quinol (I; R = R′ = CO_2Et) gave the lactone (V), and the chief crystalline product isolated from the reaction of methoxy-*p*-benzoquinone with ethyl acetoacetate was the benzofuran (VI). The quinol (I; R = CO_2Et, R′ = CN) gave an isomer formulated as

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[2] Smith, Arnold, and Nichols, *J. Amer. Chem. Soc.*, 1943, **65**, 2131.
[3] Buckley, Henbest, and Slade, *J.*, 1957, 4891.

(VII), since the compound has no ester-carbonyl or nitrile band in the infrared spectrum (the parent quinol has both bands), nor has it a lactone-carbonyl band; however, it has a band at 1667 cm.$^{-1}$, suggesting an amide group. If structure (VII) is correct, it is possible that it is formed by rearrangement of the ortho-ester (VIII).

When made by method (1), the quinol (I; $R = CO_2Et$, $R' = CN$) was accompanied by several other compounds. Analyses of two of these indicated formula $C_{16}H_{16}O_6N_2$, and on the basis of their infrared spectra (see Table 2) these compounds are formulated as (IX) and (X). The former appears to be the same as the adduct from *p*-benzoquinone and ethyl cyanoacetate described by Wood *et al.*[4] as the quinol (XI). Acid hydrolysis of compound (IX) and then esterification gave 2 : 5-di(ethoxycarbonylmethyl)quinol, identical with a sample prepared by the method of Wood *et al.* Displacement of a methoxyl group by the anion of the methylene component was not noticed in any of the other cases; nucleophilic displacements of a similar type have, however, been described before.[3,5]

Although the quinols of type (I) were readily oxidised by air in weakly alkaline solution to the anions of the corresponding quinones, treatment of the quinol (I; $R = CO_2Et$, $R' = CN$) with acidified dichromate gave no simple quinone, but a very small yield of a red substance whose ultraviolet absorption resembles that of the dibenzofuran (XII) produced by acid-catalysed or thermal rearrangement of 4 : 4'-dimethoxydiphenyl-2 : 5 : 2' : 5'-diquinone.[6]

EXPERIMENTAL

Ultraviolet spectra were measured on a Unicam S.P. 500 spectrophotometer. Woelm acid alumina was used throughout, and the dry powder measured by volume; Roman numerals refer to the Brockmann grade, prepared according to the makers' instructions; before use, the alumina was exposed to sulphur dioxide. Unless otherwise stated, light petroleum had b. p. 40—60°.

Methoxy-p-*benzoquinone.*—Methoxyquinol was prepared from vanillin by a method prescribed [7] for the conversion of *ortho*-vanillin into pyrogallol monomethyl ether. The crude product (yield, 60—70%) distilled at 177°/16 mm., with no fore-run, but gave a precipitate with Brady's reagent. It was used without further purification. A cooled mixture of concentrated sulphuric acid (31 ml.) and water (50 ml.) was added to a solution of the crude quinol (53 g.) in water (250 ml.), and the whole run dropwise into a stirred solution of sodium dichromate (41 g.) in water (200 ml.) containing a little ice. More ice was added in small quantities during the oxidation. After all the methoxyquinol had been added, the solution (final volume *ca.* 800 ml.) was stirred for a further 15 min., then extracted with chloroform, and the extract dried (Na_2SO_4) and concentrated, to yield the yellow quinone (36 g., in two crops), m. p. 142° (lit., 145°).

Michael Additions to Methoxy-p-*benzoquinone.*—(a) *Diethyl malonate.* Method (1). Solutions of methoxy-*p*-benzoquinone (10 g.) in chloroform (100 ml.) dried by azeotropic distillation, and of diethyl sodiomalonate [made by dissolving sodium (1·6 g.) in anhydrous ethanol (100 ml.) and then adding malonic ester (7 ml.)] were separately cooled to −40°, mixed, and kept for 5—10 min. Liquid sulphur dioxide was sprayed in till the mixture became red and after 20 min., water (about 700 ml.) was added, and the mixture extracted with ether. The upper layer was separated and washed, first, with successive small quantities of sodium hydrogen carbonate solution until the washings, which were initially yellow, had changed through red, brown, and green, to blue, then with aqueous sulphur dioxide solution, finally repeatedly with water; it was then dried and evaporated, and a little benzene was added to the residue. Crystallisation was spontaneous and after recrystallisation from water, then from light petroleum (b. p. 100—102°), *diethyl* 2 : 5-*dihydroxy*-4-*methoxyphenylmalonate* had m. p. 137° (Found: C, 56·9; H, 6·1. $C_{14}H_{18}O_7$ requires C, 56·4; H, 6·0%). The yield was variable (0·5—3·5 g.), usually about 1·5 g.

Method (2). A solution of the quinone (1 g.) in absolute ethanol (100 ml.) containing diethyl malonate (2 ml.) was run down a column (12 × ½") packed with glass beads, through which a current of ammoniacal air was drawn. The effluent was run into dilute acid (about

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[4] Wood, Colburn, Cox, and Garland, *J. Amer. Chem. Soc.*, 1944, **66**, 1540.
[5] Fieser, *J. Amer. Chem. Soc.*, 1926, **48**, 2936.
[6] Erdtman, *Proc. Roy. Soc.*, 1934, *A*, **143**, 223.
[7] Surrey, in " Organic Syntheses," John Wiley & Sons, Inc., New York, 1955, Vol. III, p. 759.

500 ml.) through which a stream of sulphur dioxide was passed. After extraction with ether, working up was as described above (yield, 0·1—0·25 g.).

Slow chromatography of this ester in ether over alumina (grade II or III) caused partial conversion into the more strongly adsorbed lactone, *ethyl 5-hydroxy-6-methoxy-2-oxobenzofuran-3-carboxylate* (V), which crystallised from ether as rhombs, collapsing in air, m. p. 204° (decomp. from 180°) (Found: C, 56·7; H, 5·1. $C_{12}H_{12}O_6$ requires C, 57·1; H, 4·8%).

(b) *Dimethyl malonate.* Method (1) was followed, on half the scale, with methanol in place of ethanol. After evaporation of the solvents, the crude product was extracted from the residue with boiling ether–light petroleum (1 : 5 v/v), which left tar undissolved. Two experiments gave (i) 30 mg., (ii) no yield. Recrystallisation from ether–light petroleum gave *dimethyl* 2 : 5-*dihydroxy*-4-*methoxyphenylmalonate*, m. p. 139° (m. p. 115—117° on admixture with the diethyl ester) (Found: C, 53·1; H, 5·1. $C_{12}H_{14}O_7$ requires C, 53·3; H, 5·2%).

(c) *Ethyl cyanoacetate.* Method (1) was followed, on half the scale described in (a). After evaporation the ether-soluble portion of the residue was chromatographed over alumina (65 ml.; grade II). Unchanged ethyl cyanoacetate was followed by a fraction giving a blue colour with sodium carbonate solution, then by one giving a pink colour with this reagent. From the latter two fractions were isolated: (*a*) an oil and (*b*) crystals (0·08 g.) of 3 : 7-*dicarbamoyl*-2 : 6-*diethoxybenzo*[1,2-*b* : 4,5-*b*]*difuran* (IX), m. p. 268° (decomp.) (Found: C, 58·3; H, 5·0; N, 8·5. $C_{16}H_{16}O_6N_2$ requires C, 57·8; H, 4·8; N, 8·4%). Acid-hydrolysis and then esterification with ethanolic hydrogen chloride gave 1 : 4-di(ethoxycarbonylmethyl)-2 : 5-dihydroxybenzene, m. p. 153° (Kofler block), identical (infrared spectrum) with an authentic sample, m. p. 153°. Treatment of the oil with ether–light petroleum gave (*inter alia*) crystals of *ethyl* α-(3-*carbamoyl*-2-*ethoxy*-5-*hydroxybenzo*[b]*fur*-6-*yl*)-α-*cyanoacetate* (X), m. p. 193—195°, solidifying and remelting at *ca.* 210° (decomp.) (Found: C, 58·3; H, 5·1; N, 8·7. $C_{16}H_{16}O_6N_2$ requires C, 57·8; H, 4·8; N, 8·4%). The compound gave an intense pink colour with 2N-sodium carbonate.

In another run, on the scale described, the ether-soluble products were chromatographed over alumina (40 ml.; grade III), and the fractions giving a blue colour with sodium carbonate solution collected and evaporated. The combined residues were recrystallised from ether–light petroleum (3 : 7, v/v), yielding *ethyl* α-(2 : 5-*dihydroxy*-4-*methoxyphenyl*)-α-*cyanoacetate* (Found: C, 57·7; H, 5·1; N, 5·7. $C_{12}H_{13}O_5N$ requires C, 57·5; H, 5·2; N, 5·6%). The compound had no definite m. p.; heated in a capillary tube, most of the crystals softened from about 110—120°, melting being complete between 140° and 150°, usually at 147°; however, isolated crystals on the wall of the tube melted completely at about 120°, resolidified at about 130°, and remelted at about 175°. Paper chromatography (acetic acid–butanol–water, 1 : 4 : 5) and exposure to ammonia vapour developed a single blue spot, R_F 0·92; spraying the alkaline paper with Folin–Ciocalteau reagent did not reveal any other spots, showing the absence of phenolic impurity.

Method (2). This experiment was done as described in section (a). Isolation of the product with ether and chromatography of the crude extract over alumina (30 ml.; grade III) gave the quinol (I; $R = CO_2Et$, $R' = CN$) (0·24 g.). In a repetition of this experiment, in which the mixture was set aside overnight before extraction with ether, the only product isolated was 2-*ethoxy*-5-*hydroxy*-6-*methoxybenzofuran*-3-*carboxyamide* (VII) (0·33 g.), m. p. 173° (from benzene) (Found: C, 57·3; H, 5·2; N, 5·8. $C_{12}H_{13}O_5N$ requires C, 57·5; H, 5·2; N, 5·6%).

(d) *Malonodinitrile.* Using malonodinitrile (2·3 g.) and half quantities of the other reagents, as in (a), method (1), gave 0·6 g. of ether-soluble material. Chromatography of this in ether over alumina (60 ml.; grade III) gave 2 : 5-*dihydroxy*-4-*methoxyphenylmalonodinitrile*, needles (from methyl cyanide), m. p. 233° (decomp.) (Found: C, 59·35; H, 4·3. $C_{10}H_8O_3N_2$ requires C, 58·8; H, 3·9%). The compound is very readily oxidised.

(e) *Ethyl acetoacetate.* Method (1) in section (a) was followed. After evaporation of the solvents, the residue was extracted with boiling light petroleum, then with ether. Concentration of the ether gave *ethyl* 5-*hydroxy*-6-*methoxy*-2-*methylbenzofuran*-3-*carboxylate*, prisms (from 95% ethanol), m. p. 160—161° (Found: C, 62·0; H, 5·5. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·6%). After evaporation of the petroleum, the residue was dissolved in ether; this ethereal solution gave a deep blue colour to sodium carbonate solution. After passage through alumina (100 ml.; grade III) the eluates gave only a weak blue colour to alkali, and contained a small quantity of the benzofuran (VI).

5-(*Diethoxycarbonylmethyl*)-2-*methoxybenzoquinone*.—The quinol (I; $R = R' = CO_2Et$) (0·4 g.) was dissolved in warm water (200 ml.) containing 1 drop of 0·1N-sulphuric acid and, after being cooled, was added to a mixture of water (100 ml.), ice (300 g.), 0·1N-potassium dichromate (28 ml.), and N-sulphuric acid (4 ml.); after 40 min., the solution was extracted with ether, and the extract dried (Na_2SO_4), concentrated to about 20 ml., and run on a column of alumina (60 ml., grade II; this sample had not been exposed to sulphur dioxide). Development with ether caused a single, intensely purplish-brown band to move down the column, giving a yellow eluate. Evaporation of a portion of the eluate just behind the leading edge of the band left 5-(*diethoxycarbonylmethyl*)-2-*methoxybenzoquinone* as a pale yellow oil (Found, in material dried at 100°/16 mm. for 2 hr.: C, 56·6; H, 5·4. $C_{14}H_{16}O_7$ requires C, 56·8; H, 5·4%). Treatment of the quinone with aqueous sulphur dioxide gave white crystals, m. p. 138° (mixed with the parent quinol, m. p. 137°).

Measurement of the Spectra for Table 1.—In those cases in which the quinols of type (I) were not isolated, solutions of the quinone (0·2%; 4 ml.) in absolute ethanol, the reactive methylene component (4 ml. in 10 ml. of 50% ethanol), and 5% sodium hydrogen carbonate solution (1 ml.) were mixed, and the spectra examined an a 2 mm. cell; with dimedone, 4 ml. of a 10% solution in absolute ethanol were used, in a 10 mm. cell. Many experiments had to be made to determine the position of $\lambda_{max.}$, because of the speed with which the colour faded.

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