Synthesis and Some Reactions of 4-Hydroxy-2-methoxycarbonylquinoline-5,8-quinone

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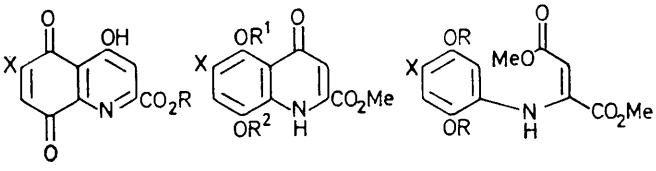
The title quinone was prepared by oxidation of 5,8-dihydroxy-2-methoxycarbonyl-4(1*H*)-quinolone with cerium(IV) ammonium nitrate. Addition of hydrogen chloride, toluene-*p*-sulphinic acid, and hydrazoic acid to the quinone yielded the corresponding 6-substituted hydroquinones. Attempted Diels–Alder addition of cyclohexa-1,3-diene to the quinone gave a low yield of the expected adduct but 1,3-dimethoxycyclohexa-1,3-diene gave a product tentatively formulated as a derivative of benzofuro[3,2-*h*]quinoline.

In connection with model experiments related to a synthesis of the naturally occurring aza-anthraquinone, phomazarin,[1] we have prepared the quinoline-5,8-quinone (Ia) and investigated its reactions with certain conjugated dienes and nucleophiles. The related ethyl ester (Ib) has been prepared by Butenandt and his co-workers [2] in connection with a structural investigation of xanthommatin but its chemistry has not been investigated.



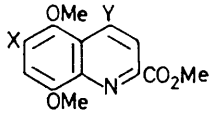
(I)
a; R = Me, X = H
b; R = Et, X = H
c; R = Me, X = Cl

(II)
a; $R^1 = R^2$ = Me, X = H
b; $R^1 = R^2$ = Me, X = NO_2
c; R^1 = X = H, R^2 = Me
d; R^1 = H, R^2 = Me, X = NO_2
e; $R^1 = R^2$ = X = H
f; $R^1 = R^2 = CH_2Ph$, X = H
g; $R^1 = R^2$ = H, X = Cl
h; $R^1 = R^2$ = Me, X = Cl
i; $R^1 = R^2$ = H, X = N_3
j; $R^1 = R^2$ = H, X = *p*-$MeC_6H_4 \cdot SO_2$
k; $R^1 = R^2$ = Me, X = NH_2

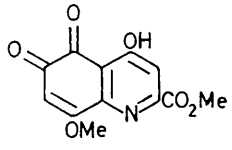
(III)
a; R = Me, X = H
b; R = Me, X = NO_2
c; R = CH_2Ph, X = H
d; R = Me, X = Cl

The syntheses of a number of 4-hydroxyquinoline-5,8-quinones, unsubstituted or possessing a methyl or phenyl substituent at position 2, have also been reported.[3]

We chose as the starting material the quinolone (IIa) which was, by analogy with the previous work, available through a modified Conrad–Limpach reaction. Thus 2,5-dimethoxyaniline added to dimethyl acetylenedicarboxylate to give the enamine (IIIa), which cyclised smoothly on heating for a short time in diphenyl ether to give the quinolone (IIa).[4] Prolonged reaction gave, in addition to the quinolone (IIa), the trimethoxyquinoline (IVa), identified on the basis of spectral evidence and by comparison with material synthesised from the quinolone (IIa) and diazomethane.



(IV)
a; X = H, Y = OMe
b; X = Cl, Y = OMe



(V)

Attempted oxidative demethylation of the quinolone (IIa) with silver(II) oxide and dilute nitric acid [5] failed. Nitric acid in acetic acid, the reagent normally used for oxidative demethylation,[6] is known to cause nitration at position 6 in compounds of type (II),[7] and when it was applied to quinolone (IIa) it yielded the nitro-compound (IIb), even with short reaction times.

Boron trichloride reacted with the quinolone (IIa) to give the hydroxy-compound (IIc).[8] Attempted oxidation of this quinolone (IIc) with nitric acid gave the mononitro-compound (IId), whose structure was con-

[1] F. Kogl and J. Sparenburg, *Rec. Trav. chim.*, 1940, **59**, 1180; A. J. Birch, D. N. Butler, and R. W. Rickards, *Tetrahedron Letters*, 1964, 1853.

[2] A. Butenandt, U. Schiedt, E. Biekert, and R. I. T. Cromartie, *Annalen*, 1954, **590**, 75.

[3] A. Cipriano, *Gazzetta*, 1961, **91**, 926; E. Biekert and W. Schäfer, *Chem. Ber.*, 1960, **93**, 642; Y. S. Tsizin and M. V. Rubtsov, *Khim. geterotsikl. Soedinenii*, 1969, 682, 687; Y. S. Tsizin, I. V. Persianova, and M. V. Rubtsov, *ibid.*, p. 690.

[4] *Cf.* N. D. Heindel, T. A. Brodof, and J. E. Kogelschatz, *J. Heterocyclic Chem.*, 1966, **3**, 222.

[5] C. D. Snyder and H. Rapoport, *J. Amer. Chem. Soc.*, 1972, **94**, 227.

[6] G. Schill, *Annalen*, 1966, **691**, 79.

[7] A. Butenandt, E. Biekert, and E. Harle, *Chem. Ber.*, 1964, **97**, 285.

[8] *Cf.* F. M. Dean, J. Goodchild, L. E. Houghton, and J. A. Martin, *Tetrahedron Letters*, 1966, 4153; W. Schäfer and B. Franck, *Chem. Ber.*, 1966, **99**, 160.

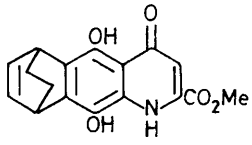
firmed by comparison with material synthesised from the quinolone (IIb) and boron trichloride. Oxidation of the quinolone (IIc) with Fremy's salt gave a low yield of a quinone tentatively formulated as compound (V) on the basis of spectroscopic evidence. Its i.r. spectrum showed the presence of a hydrogen bonded hydroxy-group as well as ester and quinone carbonyls. The n.m.r. spectrum showed, in addition to two methoxy-singlets at τ 5·96 and 5·99, two one-proton singlets at τ 2·15 and 3·82 attributed to protons 3 and 7 and a broad one-proton signal at τ −1·9 due to hydrogen-bonded OH.

Treatment of compound (IIa) with hydrobromic acid and subsequent re-esterification with methanolic hydrogen chloride gave the quinolone (IIe) in good yield, characterised as its tri-*O*-acetate. A possible alternative route to the quinolone (IIe) *via* the dibenzyl ether (IIf) was investigated but had to be abandoned. Thus 2,5-bisbenzyloxyaniline, prepared by reduction of 2,5-bis-benzyloxynitrobenzene [9] with iron(II) sulphate and ammonium hydroxide, reacted readily with dimethyl acetylenedicarboxylate to form the enamine (IIIc), but all attempts to cyclise this product failed.

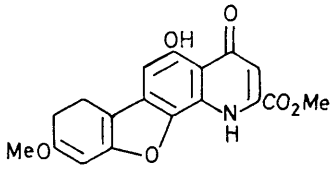
Oxidation of the quinolone (IIe) with cerium(IV) ammonium nitrate [10] rapidly gave the quinone (Ia) in good yield. This oxidation was also achieved with iron-(III) chloride and Fremy's salt but in both cases the product was difficult to purify. Evidence for the existence of the quinone in the 4-hydroxyquinoline form rather than as the 4(1*H*)-quinolone comes from the n.m.r. spectrum, which contained a signal at τ −1·92, readily removed by deuteriation, consistent with the presence of hydrogen-bonded OH.

Addition of nucleophiles to quinoline-5,8-quinone occurs preferentially at position 6. This preference has been ascribed to electron withdrawal by the ring nitrogen atom.[11] Juglone usually undergoes nucleophilic attack at position 3, an observation which may be rationalised by invoking electron donation from the hydroxy-group.[12] The quinone (Ia), at least formally, embodies the structural units related to both quinoline-5,8-quinone and juglone and consequently from the above observations might be expected to yield mainly 6-substituted products on reaction with nucleophiles. However, the presence of the 2-methoxycarbonyl residue and the fact that the hydroxy-group and ring nitrogen atom are conjugated may affect the electron withdrawing ability of the nitrogen atom.

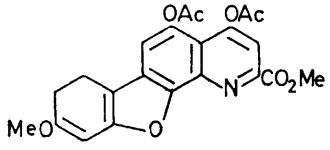
Addition of hydrogen chloride to the quinone (Ia) gave the 6-chloroquinolone (IIg) in good yield. Treatment of this compound with diazomethane gave compound (IVb), identical with the compound obtained by methylation of the quinolone (IIh). The latter was prepared from 4-chloro-2,5-dimethoxyaniline *via* the enamine (IIId). The addition of hydrazoic acid and of toluene-*p*-sulphinic acid to the quinone (Ia) gave the 6-substituted quinolones (IIi) and (IIj), respectively, which were also prepared from the chloroquinone (Ic).



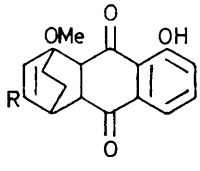
(VI)



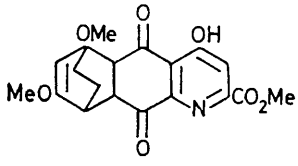
(VII)



(VIII)



(IX)
R = H or OMe



(X)

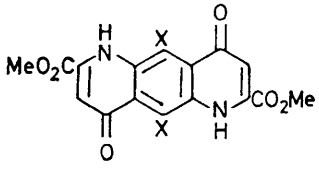
We have investigated the reactions of the quinone (Ia) with two conjugated dienes in the hope that they would provide a route to 1-aza-anthraquinone derivatives.[13] Cyclohexa-1,3-diene added to the quinone (Ia) to give the quinolone (VI) but in only 7% yield. When the quinone (Ia) reacted with 1,3-dimethoxycyclohexa-1,3-diene in refluxing benzene it gave the quinolone (IIe) and a compound to which structure (VII) is tentatively assigned. The i.r. spectrum of the latter confirmed the presence of the 2-methoxycarbonyl-4(1*H*)-quinolone nucleus ($\nu_{max.}$ 3340, 1725, and 1650 cm^{-1}) but its u.v. spectrum indicated a modified chromophore. The n.m.r. spectrum (Experimental section) confirmed the presence of the various structural units and showed that attachment of the diene system was at either position 6 or 7 of the original quinone: only two one-proton singlets were observed in the aromatic region (τ 3·18 and 3·43). On acetylation compound (VII) gave a diacetate formulated as (VIII). Evidence for the presence of the furo[3,2-*h*]quinoline nucleus rather than the isomeric furo[2,3-*f*]quinoline was obtained from two sources. The n.m.r. spectrum of the quinoline (IIc) shows in the aromatic region a singlet at τ 3·18 due to the C-3 proton and a pair of *ortho*-split doublets centred at τ 2·99 and 3·41, assigned to the C-7 and C-6 protons, respectively, in view of the observation that on acid-catalysed deuterium exchange the signal at τ 3·41 diminishes in intensity while that at τ 2·99 is unaffected. As noted above, compound (VII), like (IIc), shows signals at

[9] H. Schiff and G. Pellizzari, *Annalen*, 1883, **221**, 369.
[10] T. L. Ho, T. W. Hall, and C. M. Wong, *Chem. and Ind.*, 1972, 729.
[11] Y. T. Pratt and N. L. Drake, *J. Amer. Chem. Soc.*, 1960, 82, 1155; Y. T. Pratt, *J. Org. Chem.*, 1962, **27**, 3905.
[12] R. H. Thomson, *J. Org. Chem.*, 1951, **16**, 1082; J. W. McLeod and R. H. Thomson, *ibid.*, 1960, **25**, 36.
[13] *Cf.* A. J. Birch, D. N. Butler, and J. B. Siddall, *J. Chem. Soc.*, 1964, 2941.

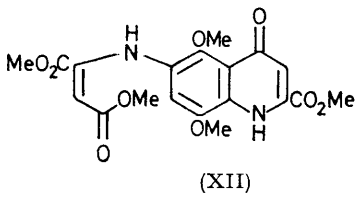
τ 3·18 and 3·43, suggesting the presence of the 8-alkoxy-5-hydroxy-4(1*H*)-quinolone unit. Boroacetic anhydride has been used in a colour test for the detection of hydroxy-groups *peri* to a carbonyl in the quinone series [14] and we have found that this reagent can be used with quinolones. Thus no colour reaction was observed with the quinolone (IIa), but an orange colour was obtained with the quinolone (IIc) and a red colour with (IIe). Compound (VII) gave an orange colour.

It has been established that the products of addition of 1-methoxycyclohexa-1,3-dienes to juglone are of the type (IX), in which C-1 of the diene is attached to C-3 of the quinone. This orientation, it has been suggested, is consistent with polarisation of the quinone by hydrogen-bonding involving the *peri*-hydroxy-group.[15] Adducts of type (IX) are unstable and rearrange to give products of cleavage of the C–C bond initially formed between C-1 of the diene and C-3 of the quinone.[15,16] Thus it seems probable that the furoquinoline (VII) arose by rearrangement of the initial adduct (X), cyclisation, and subsequent loss of methanol.

The nitroquinolone (IIb) was converted into the tricyclic compound (XIa) required in connection with other studies.[17] Thus, catalytic reduction of compound (IIb) gave the amine (IIk) which reacted with dimethyl acetylenedicarboxylate to give (XII). Cyclisation of the latter in diphenyl ether gave (XIa). The analogous formation of compound (XIb) from dimethyl acetylenedicarboxylate and *p*-phenylenediamine has been described previously.[18]



(XI)
a; X = OMe
b; X = H



(XII)

EXPERIMENTAL

Unless otherwise stated i.r. spectra were measured for Nujol mulls and u.v. and visible spectra for solutions in chloroform. N.m.r. spectra were measured at 100 MHz for solutions in trifluoroacetic acid with tetramethylsilane as internal reference. All integrations gave results consistent with the structural assignments. Column chromatography was performed on silicAR CC-7.

2,5-*Bisbenzyloxyaniline*.—To a solution of aqueous ammonia (s.g. 0·88; 60 ml) were added, simultaneously with stirring, solutions of 2,5-bisbenzyloxynitrobenzene [11] (2·2 g) in acetone (36 ml) and iron(II) sulphate (11·6 g) in hot water (40 ml). More aqueous ammonia (20 ml) was added and the mixture was heated on a steam-bath for 30 min, cooled, and filtered. The collected solid was extracted with chloroform and the dried extract ($MgSO_4$) was evaporated to dryness. Chromatography of the residue gave, on elution with benzene, the *aniline* (1·1 g), m.p. 99—100° (from ethanol) (Found: C, 78·6; H, 6·4; N, 4·8. $C_{20}H_{19}NO_2$ requires C, 78·7; H, 6·2; N, 4·6%), $\nu_{max.}$ (KBr) 3460, 3360, and 1620 cm^{-1}.

Dimethyl 2,5-*Bisbenzyloxyanilinofumarate* (IIIc).—A mixture of the foregoing aniline (0·332 g), dimethyl acetylenedicarboxylate (0·156 g), and methanol (5 ml) was refluxed for 24 h, and evaporated to dryness. Chromatography of the residue (elution with benzene) gave the *fumarate* (0·30 g), m.p. 59—60° (from ethanol–ether) (Found: C, 69·6; H, 5·7; N, 3·3. $C_{26}H_{25}NO_6$ requires C, 69·8; H, 5·6; N, 3·1%), $\lambda_{max.}$ 245, 270, and 345 nm (log ε 4·00, 3·89, and 4·09), $\nu_{max.}$ (KBr) 3300, 3080, 2880, 1740, 1680, and 1620 cm^{-1}, τ ($CDCl_3$) 0·24 (s, NH), 2·65 (s, Ph), 3·20 (d, *J* 9 Hz, 3-H), 3·46 (dd, *J* 9 and 3 Hz, 4-H), 3·52 (d, *J* 3 Hz, 6-H), 4·62 (s, vinyl H), 4·99 and 5·07 (2s, OCH_2Ph), and 6·32 and 6·40 (2s, OMe).

Dimethyl 2,5-*Dimethoxyanilinofumarate* (IIIa).—Prepared similarly from 2,5-dimethoxyaniline (6·12 g), dimethyl acetylenedicarboxylate (5·68 g), and methanol (70 ml), the *fumarate* (10·0 g) had m.p. 72—73° (from methanol) (Found: C, 56·8; H, 5·9; N, 5·0. $C_{14}H_{17}NO_6$ requires C, 57·0; H, 5·8; N, 4·8%), $\lambda_{max.}$ 279, 301, and 342 nm (log ε 3·73, 3·67, and 3·87), $\nu_{max.}$ (KBr) 3320, 1750, and 1680 cm^{-1}, τ ($CDCl_3$) 0·25 (s, NH), 3·17 (d, *J* 9 Hz, 3-H), 3·43 (dd, *J* 9 and 3 Hz, 4-H), 3·56 (d, *J* 3 Hz, 6-H), 4·56 (s, vinyl H), and 6·20 and 6·26 (2s, OMe).

5,8-*Dimethoxy*-2-*methoxycarbonyl*-4(1H)-*quinolone* (IIa).—A mixture of the foregoing fumarate (2·9 g) and diphenyl ether (29 g) was heated under reflux for 20 min, cooled, and diluted with a large volume of light petroleum. The precipitate was recrystallised from methanol to give the *quinolone* (1·94 g), m.p. 170—171° (Found: C, 59·5; H, 5·1; N, 5·2. $C_{13}H_{13}NO_5$ requires C, 59·3; H, 4·9; N, 5·3%), $\nu_{max.}$ (KBr) 3520, 3400, 1730, and 1630 cm^{-1}, τ ($CDCl_3$) 2·93 (s, 3-H), 3·00—3·41 (ABq, *J* 10 Hz, 6- and 7-H), and 6·03, 6·06, and 6·08 (3s, OMe).

Methyl 4,5,8-*Trimethoxyquinoline*-2-*carboxylate* (IVa).—(*a*) When the heating in the previous reaction was continued for 3 h a mixture of products was obtained. The major component was isolated by preparative t.l.c. (chloroform–ethanol, 19 : 1) and shown to be the *trimethoxy-ester*, m.p. 175—176° (from methanol) (Found: C, 60·4; H, 5·5; N, 5·0. $C_{14}H_{15}NO_5$ requires C, 60·7; H, 5·4; N, 5·1%), $\lambda_{max.}$ 257, 336, and 370 nm (log ε 4·46, 3·64, and 3·57), $\nu_{max.}$ (KBr) 3010, 2990, 2845, 1730, and 1620 cm^{-1}, τ ($CDCl_3$) 2·36 (s, 3-H), 2·96—3·16 (ABq, *J* 9 Hz, 6- and 7-H), and 5·94, 6·02, and 6·13 (3s, 4 × OMe).

(*b*) To a suspension of the quinolone (IIa) (0·410 g) in dry ether (40 ml) was added an excess of ethereal diazomethane. Methanol was added dropwise until all the solid had dissolved. The solution was kept for 24 h and evaporated to dryness. Chromatography of the residue gave unchanged quinolone (0·097 g) and the title quinoline (0·258 g), m.p. 175—176°, identical with the product obtained in (*a*).

Reaction between the Quinolone (IIa) *and Nitric Acid*.—To a solution of the quinolone (0·2 g) in glacial acetic acid (2 ml) concentrated nitric acid (1 ml) was added dropwise. After

[14] L. F. Fieser and M. Fieser, ' Reagents for Organic Synthesis,' Wiley, New York, 1967, p. 63.
[15] A. J. Birch and V. H. Powell, *Tetrahedron Letters*, 1970, 3467.
[16] (*a*) V. H. Powell, *Tetrahedron Letters*, 1970, 3463; (*b*) A. J. Birch, D. N. Butler, and J. B. Siddall, *J. Chem. Soc.*, 1964, 2932.
[17] D. B. Baird, I. Baxter, D. W. Cameron, and W. R. Phillips, *J.C.S. Perkin I*, 1973, 832.
[18] S. K. Khetan and M. V. George, *Canad. J. Chem.*, 1969, **47**, 3545.

2 min the mixture was neutralised with dilute aqueous ammonium hydroxide to give 5,8-*dimethoxy*-2-*methoxycarbonyl*-6-*nitro*-4(1H)-*quinolone* (IIb) (0·05 g), m.p. 216—218° (from ethanol) (Found: C, 50·9; H, 4·1; N, 8·8. $C_{13}H_{12}N_2O_7$ requires C, 50·7; H, 3·9; N, 9·1%), $\lambda_{max.}$ 342 and 376 nm (log ε 4·03 and 3·94), $\nu_{max.}$ (KBr) 3430, 1755, 1650, and 1625 cm^{-1}; τ 2·02 (s, 7-H), 2·03 (s, 3-H), and 5·74 and 5·78 (2s, OMe).

This compound was also obtained as follows: a mixture of 2,5-dimethoxy-4-nitroaniline [19] (3 g) and dimethyl acetylenedicarboxylate (2·13 g) in methanol (35 ml) was heated under reflux for 24 h. On cooling *dimethyl* 2,5-*dimethoxy*-4-*nitroanilinofumarate* (4 g), m.p. 146—147° (from methanol), was obtained (Found: C, 49·3; H, 4·7; N, 8·4. $C_{14}H_{16}N_2O_8$ requires C, 49·4; H, 4·7; N, 8·2%), $\lambda_{max.}$ 262, 328, and 395 nm (log ε 3·82, 3·97, and 4·28), τ ($CDCl_3$) 0·14br (s, NH), 2·42 (s, 3-H), 3·61 (s, 6-H), 4·34 (s, vinyl H), and 6·12, 6·15, 6·21 and 6·22 (4s, OMe). This product (1·4 g) was heated in diphenyl ether (40 g), as described previously, to give 5,8-dimethoxy-2-methoxycarbonyl-6-nitro-4(1*H*)-quinolone (0·9 g).

5-*Hydroxy*-8-*methoxy*-2-*methoxycarbonyl*-4(1H)-*quinolone* (IIc).—To a stirred, cold solution of the quinolone (IIa) (1·12 g) in dichloromethane (150 ml) was added a solution of boron trichloride (12·5 g) in dichloromethane (50 ml). After 1·5 h aqueous 10% sodium acetate was added and the organic phase was collected, dried (Na_2SO_4), and evaporated to dryness to give the *quinolone* (0·90 g), m.p. 175—176° (from ethanol) (Found: C, 58·0; H, 4·6; N, 5·5. $C_{12}H_{11}NO_5$ requires C, 57·8; H, 4·4; N, 5·6%), $\lambda_{max.}$ 262, 300, and 339 nm (log ε 4·28, 3·51, and 3·48) $\lambda_{max.}$ (0·1N-HCl) 236, 259, 281, 334, and 388 nm (log ε 4·27, 4·17, 3·72, 3·59, and 3·40), $\lambda_{infl.}$ 290 and 327 nm (log ε 3·43 and 3·38), $\nu_{max.}$ (KBr) 3390, 1730, 1660, and 1620 cm^{-1}, τ ($CDCl_3$) 0·53 (s, NH), 2·99, 3·41 (ABq, *J* 9 Hz, 6-H and 7-H), 3·18 (s, 3-H), and 6·00 and 6·10 (2s, OMe).

Reaction between the Quinolone (IIc) *and Nitric Acid*.—To a solution of the quinolone (0·20 g) in glacial acetic acid (4 ml) was added concentrated nitric acid (1 ml). After 25 s, water was added and the precipitate collected. Recrystallisation from chloroform–light petroleum gave 5-*hydroxy*-8-*methoxy*-6-*nitro*-4(1H)-*quinolone* (0·07 g), m.p. 246—248°. This compound was also prepared as follows: to a solution of the quinolone (IIb) (0·31 g) in dichloromethane was added boron trichloride (2·5 g) in dichloromethane (10 ml). The mixture was worked up as before to give the quinolone (0·23 g), m.p. 248—249° (from chloroform–light petroleum) (Found: C, 48·8; H, 3·6; N, 9·3. $C_{12}H_{10}N_2O_7$ requires C, 49·0; H, 3·4; N, 9·5%), $\lambda_{max.}$ 249 and 368 nm (log ε 4·31 and 3·94), λ_{infl} 295 nm (log ε 3·70), $\nu_{max.}$ 3395, 2800—2300, 1755, 1655, 1620, and 1535 cm^{-1}, τ 1·82 (s, 7-H), 2·03 (s, 3-H), and 5·71 (s, 2 × OMe).

1,4-*Dihydro*-8-*methoxy*-2-*methoxycarbonyl*-4-*oxoquinoline*-5,6-*quinone* (V).—To a stirred solution of the hydroxyquinolone (IIc) (0·393 g) in acetone (180 ml) was added Fremy's salt (1·38 g) in aqueous buffer (pH 7; 100 ml). After 1 h the mixture was filtered, diluted with water (300 ml), and extracted first with dichloromethane and then with chloroform. Evaporation of the dried dichloromethane extract gave unchanged starting quinolone (0·263 g); evaporation of the chloroform extract gave the *quinone* (V) (30 mg), m.p. 235—238° (from methanol) (Found: C, 55·3; H, 3·8; N, 5·7. $C_{12}H_9NO_6$ requires C, 54·8; H, 3·5; N, 5·3%), *m/e* 263 (M^+) and 265 (M + 2), $\lambda_{max.}$ (EtOH) 260 and 360 nm (log ε 4·33 and 3·48), $\nu_{max.}$ 3400—3300w,br, 1730, and 1655 cm^{-1}, τ ($CDCl_3$) —1·9br (s, OH), 2·15 (s, 3-H), 3·82 (s, C*H*=C), and 5·96 and 5·99 (2s, OMe).

5,8-*Dihydroxy*-2-*methoxycarbonyl*-4(1H)-*quinolone* (IIe).—A mixture of 5,8-dimethoxy-2-methoxycarbonyl-4(1*H*)-quinolone (15 g) and 48% hydrobromic acid (200 ml) was heated under reflux for 2 h. Addition of water to the cooled solution precipitated a solid (10 g) which was collected, dried, and dissolved in anhydrous methanol (200 ml) containing hydrogen chloride. The solution was refluxed for 2 h, and then kept for 12 h at room temperature. Evaporation gave a solid which was washed with water, dried, and recrystallised from methyl acetate to give the *quinolone* (10·1 g), m.p. 280—281° (Found: C, 55·9; H, 4·1; N, 5·8. $C_{11}H_9NO_5$ requires C, 56·2; H, 3·9; N, 6·0%), $\lambda_{max.}$ (EtOH) 237, 260, 290, 340, and 400 nm (log ε 4·30, 4·16, 3·79, 3·72, and 3·39), $\nu_{max.}$ (KBr) 3400, 2700—2600, 1745, and 1650 cm^{-1}, τ 2·28 (s, 3-H), 2·48 and 2·80 (2d, *J* 8 Hz, 6-H and 7-H), and 5·75 (s, OMe). The *tri*-O-*acetate* had m.p. 199° (from benzene) (Found: C, 56·1; H, 4·2; N, 3·8. $C_{17}H_{15}NO_8$ requires C, 56·5; H, 4·2; N, 3·9%), $\nu_{max.}$ 1780sh, 1765, 1720, and 1627w cm^{-1}, τ ($CDCl_3$) 8·58, 8·56, and 8·43 (3s, Ac), 5·96 (s, OMe), 2·66 and 2·44 (2d, *J* 8 Hz, 6-H and 7-H), and 2·04 (s, 3-H).

4-*Hydroxy*-2-*methoxycarbonylquinoline*-5,8-*quinone* (Ia).—A mixture of the foregoing quinolone (0·235 g), cerium(IV) ammonium nitrate (1·1 g), methyl cyanide (6 ml), and water (2 ml) was shaken for 3 min, poured into saturated brine (150 ml), and extracted with dichloromethane. Evaporation of the dried extract ($MgSO_4$) gave the *quinone* (0·16 g), m.p. 151—155° (from methyl acetate) [Found: C, 56·7; H, 3·3; N, 5·9%; M^+, 233, (M + 2)$^+$, 235. $C_{11}H_7NO_5$ requires C, 56·7; H, 3·0; N, 6·0%; *M*, 233], $\lambda_{max.}$ 360 nm (log ε 3·30), $\nu_{max.}$ 3200—2900, 1720, 1685, and 1655 cm^{-1}, τ 1·72 (s, 3-H), 2·62 (s, 6-H and 7-H), and 5·77 (s, OMe), τ ($CDCl_3$) —1·92br (s, OH), 2·08 (s, 3-H), 2·81 and 2·95 (ABq, *J* 10 Hz, 6-H and 7-H), and 5·98 (s, OMe).

4-*Acetoxy*-2-*methoxycarbonylquinoline*-5,8-*quinone*.— A mixture of the foregoing quinone (160 mg) and acetic anhydride (5 ml) was refluxed for 30 min, and evaporated to dryness to give the *quinone* (50 mg) as a partial solvate, m.p. 165—167° (from benzene) [Found: C, 58·0, 57·9; H, 3·5, 3·5; N, 4·4, 4·7%; M^+, 275, (M + 2)$^+$, 277. $C_{13}H_9NO_6$,0·5C_6H_6 requires C, 58·2; H, 3·7; N, 4·3%; $C_{13}H_9NO_6$ requires *M*, 275], $\nu_{max.}$ 1775, 1720, 1685, and 1665 cm^{-1}, τ ($CDCl_3$) 1·89 (s, 3-H), 2·83 and 3·05 (ABq, *J* 10 Hz, 6-H and 7-H), 5·94 (s, OMe), and 7·51 (s, COMe). The presence of benzene of solvation was confirmed by a singlet at τ 2·66.

Addition Reactions of the Quinone (Ia).—(i) *Hydrogen chloride*. Dry hydrogen chloride was passed through a solution of the quinone (0·18 g) in benzene (20 ml) for 5 min. The precipitate was collected and recrystallised from methanol to give 6-*chloro*-5,8-*dihydroxy*-2-*methoxycarbonyl*-4(1H)-*quinolone* (IIg) (0·16 g), m.p. >300° (Found: C, 49·0; H, 3·1; N, 5·4. $C_{11}H_8ClNO_5$ requires C, 49·0; H, 3·0; N, 5·2%), $\nu_{max.}$ 3350, 1735, and 1645 cm^{-1}, $\lambda_{max.}$ (MeOH) 243, 263, and 345 nm (log ε 4·33, 4·22, and 3·81), $\lambda_{infl.}$ 290 and 397 nm (log ε 3·81 and 3·52), τ 2·19 and 2·34 (2s, 3-H and 7-H) and 5·73 (s, OMe).

(ii) *Toluene*-p-*sulphinic acid*. To a solution of the quinone (0·15 g) in glacial acetic acid (5 ml) was added sodium toluene-*p*-sulphinate dihydrate (0·16 g) and the

[19] J. Gulland and R. Robinson, *J. Chem. Soc.*, 1929, 2930; L. Rubenstein, *ibid.*, 1925, 2003.

mixture was stirred for 15 min. The precipitate gave 5,8-*dihydroxy*-2-*methoxycarbonyl*-6-p-*tolylsulphonyl*-4(1H)-*quinolone* (IIj) (0·15 g), m.p. 267—268° (decomp.) (from methyl acetate) (Found: C, 55·5; H, 4·1; N, 3·5. $C_{18}H_{15}NO_7S$ requires C, 55·5; H, 3·9; N, 3·6%), $\nu_{max.}$ 3360, 1735, and 1640 cm^{-1} $\lambda_{max.}$ (EtOH) 245 and 343 nm (log ε 4·41 and 3·95), $\lambda_{infl.}$ 262, 290, and 392 nm (log ε 4·30, 3·73, and 3·58), τ 2·08 and 2·58 (ABq, *J* 8 Hz), 2·12 and 2·39 (2s, 3-H and 7-H), 5·81 (s, OMe), and 7·56 (s, ArMe).

(iii) *Hydrazoic acid*. To a solution of the quinone (0·15 g) in glacial acetic acid (5 ml) was added sodium azide (0·065 g). The mixture was kept for 2 h, and filtered to give 6-*azido*-5,8-*dihydroxy*-2-*methoxycarbonyl*-4(1H)-*quinolone* (IIi) (0·15 g), m.p. *ca.* 204° (with darkening and decomp.) (from methanol–methyl acetate, 1 : 1) (Found: C, 48·2; H, 3·0; N, 20·1. $C_{11}H_8N_4O_5$ requires C, 47·8; H, 2·9; N, 20·3%), $\nu_{max.}$ 3350, 2100, 1730, and 1645 cm^{-1}, τ 1·84 (s, 3-H), 3·34 (s, 7-H), and 5·78 (s, OMe).

Dimethyl 4-*Chloro*-2,5-*dimethoxyanilinofumarate* (IIId).—Prepared as described for compound (IIIa), from dimethyl acetylenedicarboxylate (7·1 g) and 4-chloro-2,5-dimethoxyaniline (9·1 g) in methanol (100 ml), the *fumarate* (11 g) had m.p. 101—102° (from methanol) (Found: C, 51·4; H, 5·0; N, 4·0. $C_{14}H_{16}ClNO_6$ requires C, 51·0; H, 4·9; N, 4·3%), τ ($CDCl_3$) 0·4br (s, NH), 3·15 and 3·45 (2s, ArH), 4·58 (s, CH=C), and 6·23 and 6·27 (2s, OMe).

6-*Chloro*-5,8-*dimethoxy*-2-*methoxycarbonyl*-4(1H)-*quinolone* (IIh).—Prepared from the foregoing compound (5 g) and diphenyl ether (50 ml) as described for the quinolone (IIa), *compound* (IIh) (4 g) had m.p. 227—229° (from methanol) (Found: C, 52·4; H, 4·1; N, 4·6. $C_{13}H_{12}ClNO_5$ requires C, 52·4; H, 4·1; N, 4·7%), $\nu_{max.}$ 3410, 1750, and 1630 cm^{-1}, τ 2·13 and 2·42 (2s, 3-H and 7-H) and 5·68 and 5·76 (2s, OMe).

6-*Chloro*-4,5,8-*trimethoxy*-2-*methoxycarbonylquinoline* (IVc).—(*a*) To a suspension of the foregoing quinolone (160 mg) in methyl acetate (10 ml) was added an excess of ethereal diazomethane and the mixture was kept for 3 days. Acetic acid (1 drop) was added and the mixture was evaporated to dryness. The residue gave the *quinoline* (80 mg), m.p. 191—192° (from methanol–methyl acetate, 1 : 1) (Found: C, 54·2; H, 4·7; N, 4·6. $C_{14}H_{14}ClNO_5$ requires C, 53·9; H, 4·5; N, 4·5%), τ ($CDCl_3$) 2·34 (s, 3-H), 2·96 (s, 7-H), 5·88 (3H, s, OMe), 5·98 (6H, s, OMe), and 6·14 (3H, s, OMe).

(*b*) Prepared from quinolone (IIg) (110 mg) as described in (*a*), the quinoline (IVc) (65 mg) had m.p. and mixed m.p. 189—191° and was identical (i.r. and n.m.r. spectra) with the compound obtained in (*a*).

6-*Chloro*-4-*hydroxy*-2-*methoxycarbonylquinoline*-5,8-*quinone* (Ic).—Prepared from the quinolone (IIg) (160 mg) and cerium(IV) ammonium nitrate (750 mg) as described for the quinone (Ia), the quinone (Ic) (100 mg) had m.p. 178—179° (with darkening) (from methyl acetate) (Found: C, 49·2; H, 2·5; N, 5·3. $C_{11}H_6ClNO_5$ requires C, 49·4; H, 2·3; N, 5·2%), $\nu_{max.}$ 3150—2600, 1730, 1673, and 1650 cm^{-1}, τ ($CDCl_3$) −1·7 (s, OH), 2·06 (s, 3-H), 2·62 (s, 7-H), and 5·98 (s, OMe).

Reactions of the Quinone (Ic).—(i) With *toluene*-p-*sulphinic acid*. A mixture of the quinone (65 mg) and sodium toluene-*p*-sulphinate dihydrate (65 mg) in acetic acid (2·5 ml) was kept for 1 h and filtered to give the quinolone (IIj) (15 mg), m.p. 267—268° (decomp.), identical with the material obtained earlier.

(ii) *With hydrazoic acid*. A mixture of the quinone (60 mg), sodium azide (20 mg), and acetic acid (2·5 ml) was kept for 2 h and filtered to give the quinolone (IIi) (15 mg), m.p. *ca.* 204° (decomp.), identical with the material obtained earlier.

6,9-*Dihydro*-5,10-*dihydroxy*-2-*methoxycarbonyl*-6,9-*ethanonaphtho*[2,3-b]*pyridin*-4(1H)-*one* (VI).—A mixture of the quinone (Ia), (0·30 g) benzene (170 ml), and chloroform (170 ml) was refluxed until most of the solid had dissolved and filtered hot. Cyclohexa-1,3-diene (0·90 g) was added and the mixture was refluxed for 18 h and filtered hot. On cooling the filtrate deposited *compound* (VI) (26 mg), m.p. 255—258° (from methanol–methyl acetate) (Found: C, 64·8; H, 4·9; N, 4·5. $C_{17}H_{15}NO_5$ requires C, 65·2; H, 4·8; N, 4·5%), $\lambda_{max.}$ 265, 305, and 398 nm (log ε 3·91, 3·66, 3·13), $\lambda_{infl.}$ 330 nm (log ε 3·47), $\nu_{max.}$ 3380, 3300—3100, 1740, and 1670 cm^{-1}, τ 2·29 (s, 3-H), 3·38 (m, vinyl H), 5·42 (s, bridge CH), 5·77 (s, OMe), and 8·34 (m, CH_2·CH_2).

Attempted Addition of 1,3-*Dimethoxycyclohexa*-1,3-*diene to the Quinone* (Ia).—A mixture of the quinone (0·80 g), the crude diene [16b] (1·2 g), and dry benzene (60 ml) was refluxed for 2 h and cooled. The precipitate of 5,8-dihydroxy-2-methoxycarbonyl-4(1*H*)-quinolone (IIe) (0·19 g) was collected. The filtrate was evaporated to dryness and the residue stirred with ether (2 × 100 ml); the supernatant liquid was decanted. Recrystallisation of the residue from benzene gave more quinolone (IIe) (0·5 g). The ethereal supernatant liquid was evaporated to dryness and the residue tritiated with light petroleum. The insoluble portion was chromatographed on silicAR CC-7. Elution with chloroform gave 7,8-*dihydro*-5-*hydroxy*-9-*methoxy*-2-*methoxycarbonylbenzofuro*[3,2-h]*quinolin*-4(1H)-*one* (VII) (0·13 g), m.p. 202—203° (from methyl acetate) (Found: C, 63·3; H, 4·8; N, 3·9%; M^+, 341. $C_{18}H_{15}NO_6$ requires C, 63·3; H, 4·4; N, 4·1%; *M*, 341), $\lambda_{max.}$ 338 nm (log ε 4·46), $\lambda_{infl.}$ 385 nm (log ε 3·85), $\nu_{max.}$ 3340, 1725, 1650, and 1618 cm^{-1}, τ ($CDCl_3$) 0·9br (NH), 3·18 and 3·43 (2s, 3-H and 6-H), 4·46br (s, CH=C), 5·95 and 6·27 (2s, OMe), and 7·24 (m, CH_2·CH_2). A solution of compound (VII) (60 mg) in acetic anhydride (5 ml) was refluxed for 30 min, and evaporated to dryness. Crystallisation of the residue gave *methyl* 4,5-*diacetoxy*-7,8-*dihydro*-9-*methoxybenzofuro*[3,2-h]*quinoline*-2-*carboxylate* (VIII) (25 mg), m.p. 259—260° (decomp.) (from chloroform–light petroleum) (Found: C, 61·9; H, 4·7; N, 3·3%; M^+, 425. $C_{22}H_{19}NO_8$ requires C, 62·1; H, 4·5; N, 3·3%; *M*, 425), $\lambda_{max.}$ 318 and 347 nm (log ε 4·42 and 4·44), $\lambda_{infl.}$ 332 nm (log ε 4·41), $\nu_{max.}$ 1765, 1718, and 1620 cm^{-1}, τ ($CDCl_3$) 2·21 (s, 3-H), 2·69 (s, 6-H), 4·26br (s, CH=C), 5·94 (s, CO_2Me), 6·26 (s, MeO), 7·24 (m, CH_2·CH_2), and 7·56 and 7·60 (2s, Ac).

6-*Amino*-5,8-*dimethoxy*-2-*methoxycarbonyl*-4(1H)-*quinolone* (IIk).—A solution of 5,8-dimethoxy-2-methoxycarbonyl-6-nitro-4(1H)-quinolone (0·60 g) in ethanol (250 ml) was hydrogenated over 5% palladium–charcoal (0·10 g) until uptake ceased. The filtered solution was evaporated to dryness to give the *aminoquinolone* (0·45 g), m.p. 194—195° (from chloroform–light petroleum) (Found: C, 56·1; H, 4·9; N, 10·3. $C_{13}H_{14}N_2O_5$ requires C, 56·1; H, 5·1; N, 10·1%), $\lambda_{max.}$ 269, 347, and 395 nm (log ε 4·42, 3·80, and 3·66), $\nu_{max.}$ (KBr) 3500, 3400, 1735, and 1615 cm^{-1}, τ 2·00 (s, 7-H), 2·31 (s, 3-H), and 5·75 and 5·82 (9H, 2s, 3 × Me).

6-(1,2-*Bismethoxycarbonylvinylamino*)-5,8-*dimethoxy*-2-*methoxycarbonyl*-4(1H)-*quinolone* (XII).—A mixture of the quinolone (IIk) (0·37 g), dimethyl acetylenedicarboxylate (0·19 g), and methanol (25 ml) was refluxed for 24 h, concentrated, and set aside to yield *compound* (XII) (0·24 g), m.p. 174—175° (from chloroform–light petroleum) (Found:

C, 54·5; H, 4·9; N, 6·5. $C_{19}H_{20}N_2O_9$ requires C, 54·3; H, 4·8; N, 6·7%), $\lambda_{max.}$ 291 and 360 nm (log ε 4·23 and 4·18), $\nu_{max.}$ (KBr) 3400, 1740, 1680, and 1620 cm^{-1}, τ ($CDCl_3$) 0·29 (s, 2NH), 2·85 and 3·25 (2s, 3- and 7-H), 4·42 (s, vinyl H), and 5·99, 6·03, 6·22, 6·24, and 6·28 (5s, OMe).

5,10-Dimethoxy-2,7-bismethoxycarbonylpyrido[2,3-g]*quinoline-4,9-dione* (XIa).—*Compound* (XIa) (0·292 g), prepared from the foregoing enamine (0·375 g) and diphenyl ether (5 g) as described for the quinolone (IIa), had m.p. 290—291° (from chloroform–light petroleum) (Found: C, 55·6; H, 4·1; N, 7·0%; M^+, 388. $C_{18}H_{16}N_2O_8$ requires C, 55·7; H, 4·2; N, 7·2%; *M*, 388), $\lambda_{max.}$ 265, 298, 356, 443, and 465 nm (log ε 4·66, 4·08, 3·89, 4·01, and 4·08), $\nu_{max.}$ (KBr) 3400, 1735, and 1635 cm^{-1}, τ 2·24 (s, ArH) and 5·66 and 5·78 (2s, OMe).

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