The Reaction between Quinones and Anthranilic Acids.

By R. M. ACHESON and B. F. SANSOM.

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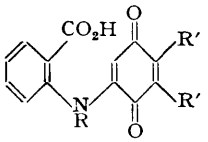
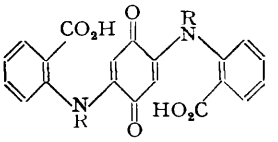
Quinone reacted with two mols. of anthranilic acid and its derivatives to give the corresponding 2 : 5-dianilinoquinones, some of which were cyclised by sulphuric acid. Monoanilinoquinones were not isolable from these reactions but one was obtained from 2 : 3-dimethoxyquinone.

DESCRIPTIONS of the reactions between anthranilic acid and benzoquinone (Ville and Astre, *Bull. Soc. chim. France*, 1895, **13**, 746; Astre, *ibid.*, 1896, **15**, 1025) and toluquinone (Suchanek, *J. prakt. Chem.*, 1914, **90**, 467), and of these quinones with *N*-ethylanthranilic acid (Linke, *ibid.*, 1920, **101**, 265) suggest that mono- and di-addition compounds (I and II; R = R′ = H) are formed under similar conditions, the quinol formed initially being oxidised by excess of quinone. The dimethoxy- and dihydroxy-derivatives of the quinone

(I) 

 (II)

(II; R = H) but no monoaddition products are reported as obtained (Lewicka, *Roczniki Chem.*, 1926, **6**, 881) from 2-amino-5-methoxy- and 2-amino-5-hydroxy-benzoic acid and benzoquinone. Compounds of type (I) have also been prepared from 1 : 4-naphthaquinone and anthranilic acid (Lesnianski, *Ber.*, 1918, **51**, 695; cf. Hauschka, *J. prakt. Chem.*,

1914, **90**, 447; Yakushevskii, *J. Gen. Chem. U.S.S.R.*, 1939, **9**, 1877; *Chem. Abs.*, 1940, **34**, 4070) and 2-amino-5-methoxybenzoic acid (Lewicka, *loc. cit.*), and the products have been cyclised to acridones with sulphuric acid.

Cyclisation of the benzoquinone (I; R = R′ = H), preceded or followed by reduction, appeared to offer an interesting route to hydroxyacridone derivatives. According to the earlier papers the compounds mentioned were little purified black solids with fairly high decomposition points. No derivatives were prepared, and identifications were often based only on poor analytical data, which did not differentiate, for example, between the two possible products from *p*-benzoquinone and anthranilic acid.

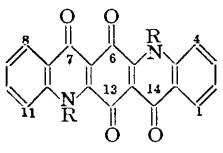
The only product we were able to obtain from anthranilic acid and a large excess of benzoquinone in boiling ethanol was 2 : 5-di-(*o*-carboxyanilino)-*p*-benzoquinone (II; R = H) (contrast Ville and Astre, *loc. cit.*). This crystallised from ***m***-cresol and gave the dimethyl ester with diazomethane, also obtained directly from the quinone and methyl anthranilate. Reduction of the quinone (II; R = H) by sodium dithionite gave the quinol which was slowly oxidised to the quinone by air.

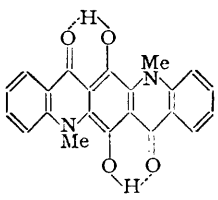
p-Benzoquinone and *N*-methylanthranilic acid similarly gave the diaddition product (II; R = Me) (characterised as the methyl ester), but *N*-ethylanthranilic acid did not give a crystalline product (contrast Linke, *loc. cit.*), nor did toluquinone with anthranilic acid (contrast Suchanek, *loc. cit.*).

2 : 3-Dimethoxy-*p*-benzoquinone combined with anthranilic acid, but not with its methyl ester or *N*-methyl derivative, to give 5-(*o*-carboxyanilino)-2 : 3-dimethoxy-*p*-benzoquinone (I; R = H, R′ = OMe). The hydroxyl groups of the quinol, obtained on catalytic reduction, did not react with diazomethane and the product was the quinone ester because of aerial oxidation. Reductive methylation of the quinone gave a black tar containing a trace of 2′ : 3′ : 4′ : 5′-tetramethoxydiphenylamine-2-carboxylic acid.

Treatment of the quinone (II; R = H) with concentrated sulphuric acid at 150—180° gave a dark brown product, which was insoluble in all solvents examined except concentrated sulphuric acid; it could not be obtained analytically pure. As it did not dissolve in dilute aqueous sodium hydroxide it is probably largely 5 : 6 : 7 : 12 : 13 : 14-hexahydro-6 : 7 : 13 : 14-tetraoxo-5 : 12-diazapentacene (III; R = H), in agreement with Scharwin, Bonderewski and Januschewski (*J. Russ. Phys. Chem. Soc.*, 1915, **47**, 1260; *Chem. Zentr.*, 1916, II, 16) and not 2-(*N*-*o*-carboxyanilino)-1 : 4 : 5 : 10-tetrahydro-1 : 4 : 5-trioxoacridine as claimed by Suchanek (*loc. cit.*).

(III)





(IV)

Similar cyclisation of the *N*-methyl-quinone (II; R = Me) gave the diazapentacene (III; R = Me) which on reduction gave a blue quinol (IV). This formulation is supported by infrared absorption data: the quinone (III; R = Me) shows a maximum at 5·96 μ, similar to that shown by anthraquinone (5·97 μ; Flett, *J.*, 1948, 1441), corresponding to the 6 : 13-carbonyl groups and there is no evidence of hydroxyl groups or hydrogen bonding. This peak is absent in the quinol (IV) but a new maximum, at 3·75 μ, indicates the presence of a hydrogen-bonded hydroxyl group; there is no maximum at *ca.* 3·0 μ which would be expected from an ordinary phenolic hydroxyl group in this type of compound. These results are in agreement with the infrared absorption spectra of the four 1 : 2 : 3 : 4-monohydroxy-trimethoxy-10-methylacridones (Crow and Price, *Austral. J. Sci. Res.*, 1949, *A*, **2**, 282): the quinone (III; R = Me) and 10-methylacridone (Acheson, Burstall, Jefford, and Sansom, *J.*, 1954, 3742) showed sharp maxima at 6·17 and 6·23 μ, and 6·13 and 6·26 μ, respectively, the first of each pair corresponding to the acridone-carbonyl group, while there is a single much broader maximum at 6·26 μ (with a shoulder at 6·22 μ) in the case of the quinol (IV) which confirms the postulate of hydrogen bonding.

Experimental

2 : 5-*Di*-(o-*carboxyanilino*)-p-*benzoquinone* (II; R = H).—Anthranilic acid (7·0 g.) and *p*-benzoquinone (freshly steam-distilled; 8·0 g.) in ethanol (75 ml.) were heated at 50—55° for 6 hr. After 3 days at room temperature a black solid (7·1 g.) was collected from the red-black mixture and washed with water and ethanol. Recrystallisation from *m*-cresol gave the *amino-benzoquinone* (II; R = H) as an orange microcrystalline powder, m. p. 335° (decomp.) (Found : C, 63·1; H, 4·0; N, 6·9. $C_{20}H_{14}O_6N_2$ requires C, 63·5; H, 3·7; N, 7·4%).

2 : 5-*Di*-(o-*methoxycarbonylanilino*)-p-*benzoquinone* was obtained from the acid with ethereal diazomethane and separated from pentyl alcohol in red needles, m. p. 265—267° (Found : C, 65·5; H, 4·7; N, 6·9. $C_{22}H_{18}O_6N_2$ requires C, 65·0; H, 4·4; N, 6·9%). The same ester (2·0 g.), m. p. and mixed m. p. 265—267°, separated on cooling a mixture of methyl anthranilate (4·0 g.), *p*-benzoquinone (4·0 g.), and ethanol (50 ml.) which had been refluxed for 5 hr.

2 : 5-*Di*-(o-*carboxyanilino*)*quinol* was precipitated when a solution of the corresponding quinone in aqueous sodium hydroxide was decolourised with sodium dithionite (hydrosulphite) and acidified. It separated from ethanol in colourless needles, m. p. *ca.* 300° (decomp.) (Found : C, 63·0; H, 4·1; N, 7·3. $C_{20}H_{16}O_6N_2$ requires C, 63·2; H, 4·2; N, 7·4%). It was oxidised by air to the quinone slowly at room temperature and rapidly at 100°.

2 : 5-*Di*-(o-*carboxy*-N-*methylanilino*)-p-*benzoquinone* (II; R = Me).—*N*-Methylanthranilic acid (6·0 g.) and *p*-benzoquinone (6·5 g.) were refluxed in ethanol (50 ml.) for 6 hr. The *amino-benzoquinone* (2·7 g.) was collected from the deep red solution and separated from ethanol in red rhombs, m. p. 260° (decomp.) (Found : C, 65·1; H, 4·3; N, 6·7. $C_{22}H_{18}O_6N_2$ requires C, 65·0; H, 4·4; N, 6·9%). The *dimethyl ester*, prepared with diazomethane in methanol–ether, separated from ethanol in red needles, m p 225° (Found : C, 66·8; H, 5·4; N, 6·1 $C_{24}H_{22}O_6N_2$ requires C, 66·4; H, 5·1; N, 6·5%) Refluxing *p*-benzoquinone (2 g.) and methyl *N*-methyl-anthranilate (2 g.) in ethanol (50 ml.) gave a deep red solution from which none of the quinone ester could be isolated. Evaporation gave only *p*-benzoquinone and a black tar.

2 : 5-*Di*-(o-*carboxy*-N-*methylanilino*)*quinol*, obtained as above, separated from ethanol in colourless rhombs, decomp. *ca.* 300° (Found : C, 65·0; H, 5·3; N, 6·4. $C_{22}H_{20}O_6N_2$ requires C, 64·7; H, 4·9; N, 6·9%); it was oxidised rapidly to the quinone above 200°.

5 : 6 : 7 : 12 : 13 : 14-*Hexahydro*-5 : 12-*dimethyl*-6 : 7 : 13 : 14-*tetraoxo*-5 : 12-*diazapentacene* (III; R = Me).—2 : 5-Di-(o-carboxy-*N*-methylanilino)-*p*-benzoquinone (0·1 g.) was heated with concentrated sulphuric acid (2 ml.) for 2 hr. at 170—180° and then poured into boiling water. The precipitated *diazapentacene* was washed with water and dried. It was easily soluble in *m*-cresol, pentyl alcohol, and acetic acid, sparingly so in ethanol and ethyl acetate, and separated from butanol as a yellow microcrystalline powder, m. p. 342° (Found : C, 71·6; H, 3·8; N, 7·5. $C_{22}H_{14}O_4N_2$ requires C, 71·4; H, 3·8; N, 7·6%). Its infrared absorption spectrum (3·7—7 μ) in paraffin paste had max. at 5·96, 6·17, 6·23, 6·54, 6·72, and 6·83 μ.

5 : 7 : 12 : 14-*Tetrahydro*-6 : 13-*dihydroxy*-5 : 12-*dimethyl*-7 : 14-*dioxo*-5 : 12-*diazapentacene* (IV).—The above quinone (III; R = Me) (0·05 g.) gave a yellow solution in hot acetic acid (10 ml.), and sodium dithionite was added until the colour changed through green to royal blue. The *dihydroxydiazapentacene*, precipitated by pouring the mixture into water, crystallised from acetic acid in blue needles, m. p. 260° (Found : C, 70·4; H, 4·4; N, 7·4. $C_{22}H_{16}O_4N_2$ requires C, 71·0; H, 4·3; N, 7·5%); infrared absorption max. (paraffin paste) were at 3·75, 6·26 (shoulder at 6·2), 6·40, 6·66, and 6·83 μ.

2 : 3-*Dimethoxyquinone*.—This was prepared according to Baker (*J.*, 1931, 2542) with the following modifications. 3 : 4-Dimethoxysalicylic acid (122 g.; m. p. not less than 167°; less pure material gave low yields at the nitration stage) was heated under reflux at atmospheric pressure for 1 hr. Distillation gave 2 : 3-dimethoxyphenol (82 g.), b. p. 236—242° (on redistillation). 2 : 3 : 4-Trimethoxynitrobenzene was hydrogenated in methanol at room temperature and pressure over Raney nickel. Filtration into methanolic hydrogen chloride followed by evaporation gave 2 : 3 : 4-trimethoxyaniline hydrochloride quantitatively. 2 : 3-Dimethoxy-quinone was characterised as its *mono*-2 : 4-*dinitrophenylhydrazone*, which separated from ethyl acetate in orange needles, m. p. 196° (Found : C, 48·4; H, 3·5. $C_{14}H_{12}O_7N_4$ requires C, 48·2; H, 3·4%).

2-(o-*Carboxyanilino*)-5 : 6-*dimethoxy*-p-*benzoquinone* (I; R = H, R′ = OMe).—2 : 3-Dimethoxybenzoquinone (2·4 g.) and anthranilic acid (1·22 g.) were refluxed in methanol (50 ml.; lower yields were obtained by using ethanol or propanol) for 66 hr., and about half the solvent was evaporated. The red-black solution was cooled at 0° for 24 hr., and the precipitate collected, washed with a little methanol, and dried (1·34 g.). Recrystallisation by cooling a boiling

saturated methanol solution to −70° gave a 92% recovery of the quinone as dark orange-red needles, m. p. 217—218° (Found : C, 59·2; H, 4·5; N, 4·8. $C_{15}H_{13}O_6N$ requires C, 59·4; H, 4·3; N, 4·6%). Treatment in methanol with ethereal diazomethane gave the *methyl ester*, which separated from acetone in red needles, m. p. 124—125° (Found : C, 60·3; H, 4·8. $C_{16}H_{15}O_6N$ requires C, 60·6; H, 4·7%).

The deep red solution of the carboxyanilinoquinone (0·19 g.) in methanol or ether became pale yellow when one mol. of hydrogen had been absorbed at room temperature and pressure over Raney nickel. Filtration into excess of ethereal diazomethane followed by evaporation after 12 hr., during which the solution reddened greatly, gave only the methoxycarbonylanilinoquinone (0·1 g.) and a deep red gum.

The quinone (I; R = H, R′ = OMe) (0·29 g.) was dissolved in sodium hydroxide (0·56 g.) and water (3 ml.), and dithionite was added until the deep purple solution changed through red to yellow. Methyl sulphate (0·33 g.) was added and the mixture refluxed. Sodium dithionate was added occasionally to keep the solution yellow and refluxing continued (2 hr.) until a drop of the solution did not clearly redden in air. Acidification of the brown solution precipitated a black tar which was purified through aqueous potassium hydrogen carbonate (charcoal). Recrystallisation of the benzene-soluble fraction from benzene–light petroleum (b. p. 60—80°) gave <1 mg. of pale yellow needles, m. p. 157°. Hughes, Neill, and Ritchie (*Austral. J. Sci. Res.*, 1950, *A*, **2**, 282) report m. p. 159—160° for 2′ : 3′ : 4′ : 5′-tetramethoxydiphenylamine-2-carboxylic acid.

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THE LABORATORY OF HUMAN NUTRITION, DEPARTMENT OF BIOCHEMISTRY.
DYSON PERRINS LABORATORY, OXFORD. [*Received, July 18th*, 1955.]