572. *Muscarufin. Part III.* The Action of Diazotised Anthranilic Acid on Quinols.*

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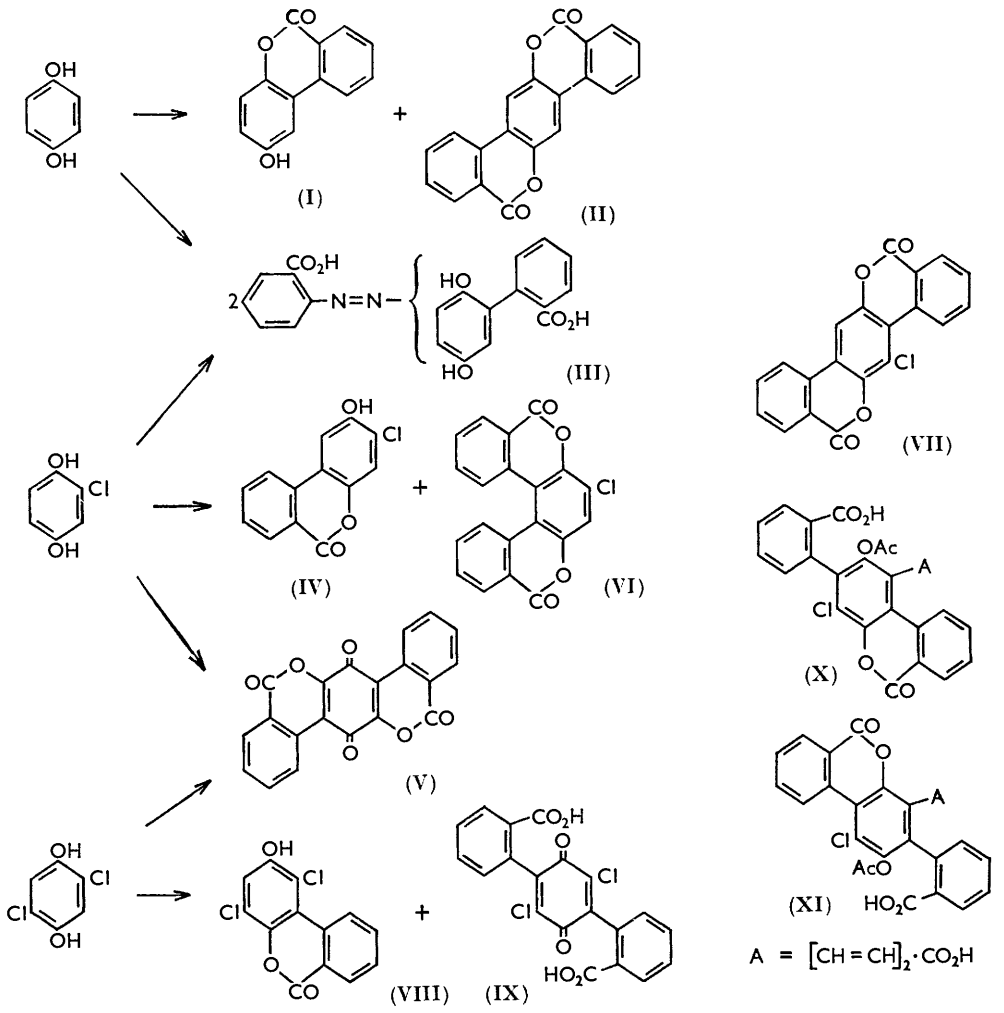
The products obtained by the action of diazotised anthranilic acid on quinol, chloroquinol, 2,5-dichloroquinol, and 2-(4-carboxybuta-1,3-dienyl)-5-chloroquinol are described.

In Part I [1] it was reported that 2,5-dichloro-1,4-benzoquinone underwent arylation, on treatment with diazotised anthranilic acid, in an abnormal manner and with loss of chlorine; hence this reaction was not appropriate to a synthesis of muscarufin. The products obtained by subjecting quinols to the action of the same reagent have now been investigated. Quinol fails to couple with diazonium compounds. Orton and Everatt [2] reported that alkaline solutions of diazonium compounds oxidise quinol to 1,4-benzoquinone; also, Betollo, Polla, and Abril,[3] and Dobas,[4] have shown that mono- and di-aryl derivatives of quinol are produced. Betollo *et al.* carried out their reactions in an acid solution and used *para*-substituted anilines. In experiments in acid solution, with quinol and diazotised *o*-, *m*-, and *p*-aminobenzoic acid, we found that reaction proceeded with the *para*-compound, but that little obvious change occurred with the *ortho*- and the *meta*-compound. On making the solutions of the latter slightly alkaline, however, evolution of

* Part II, *J.*, 1959, 3254.

[1] Edwards and Lewis, *J.*, 1959, 3250.
[2] Orton and Everatt, *J.*, 1908, **93**, 1021.
[3] Betollo, Polla, and Abril, *Gazzetta*, 1950, **80**, 76.
[4] Dobas, *Chem. Listy*, 1952, **46**, 277.

nitrogen commenced, and signs of arylation appeared; accordingly, the reactions with anthranilic acid described below were carried out under weakly alkaline conditions (procedure A, sodium acetate buffer; procedure B, an excess of sodium hydrogen carbonate; these are the conditions used by Kvalnes [5] and Schimmelschmidt,[6] respectively, in arylations of 1,4-benzoquinones by means of diazonium compounds).



By procedure A, quinol gave in poor yield a red crystalline compound, $C_{27}H_{18}O_8N_4$, apparently a product from two mols. of anthranilic acid and one of 2′,5′-dihydroxybiphenyl-2-carboxylic acid. The ultraviolet spectrum ($\lambda_{max.}$ 3150 Å) resembles that of azobenzene ($\lambda_{max.}$ 3190 Å). The positions of attachment of the azo-groupings have not been found. Procedure B yielded a mixture of the monolactone (I) and the less soluble dilactone (II), separated by solvent extraction. The dilactone (II) was made by Nilsson [7] by reduction of 2,5-di-*o*-carbomethoxyphenyl-1,4-benzoquinone.

Procedure A, carried out on chloroquinol, gave three identifiable products, all in poor yield—the azo-compound (III), the chloro-lactone (IV) and the quinone dilactone (V).

[5] Kvalnes, *J. Amer. Chem. Soc.*, 1934, **56**, 2478.
[6] Schimmelschmidt, *Annalen*, 1950, **566**, 184.
[7] Nilsson, *Acta Chem. Scand.*, 1956, **10**, 1377.

Procedure B gave the chloro-lactone (IV), together with the chloro-dilactone (VI). The latter is more soluble and has a higher m. p. than the known isomer (VII).[7]

Procedure A, applied to 2,5-dichloroquinol, gave the quinone dilactone (V) and the dichloro-lactone (VIII), both in poor yield. Procedure B gave 2,5-di-*o*-carboxyphenyl-3,6-dichloro-1,4-benzoquinone (IX), together with some dichloro-lactone (VIII).

It became clear that procedure B results in arylation at unsubstituted positions; it was therefore applied to 2-(4-carboxybuta-1,3-dienyl)-5-chloroquinol.[8] Treatment of the product with acetic anhydride yielded a crystalline diarylated product containing chlorine, in which one carboxyl group had lactonised, *i.e.*, either (X) or (XI). Either of these compounds offers the prospect of preparing the compound stated by Kögl and Erxleben [9] to be muscarufin by two simple stages, *viz.*, alkaline hydrolysis and mild oxidation. We were unable to complete the synthesis from the small quantity of (X) or (XI) available; work is proceeding.

Experimental

Reaction of Quinol.—Procedure A. Anthranilic acid (27·4 g.) was diazotised in the usual way.[1] Saturated sodium acetate solution was added until the liquid was alkaline to Congo Red. The resulting solution was added all at once to a stirred solution of quinol (22 g.) in water (300 ml.) at 5°; stirring was continued for 90 min. The solution was filtered, set aside overnight, and filtered again. Acidification with hydrochloric acid precipitated an orange solid, which crystallised from acetic acid–ethanol (1 : 1) as orange needles (0·8 g.) of an *azo-compound*, m. p. 244° (Found: C, 61·8; H, 3·7; N, 10·1. $C_{27}H_{18}O_8N_4$ requires C, 61·6; H, 3·4; N, 10·6%), $\lambda_{max.}$ 315 mμ (log ε 3·10). These and other spectroscopic data refer to ethanol solutions.

Procedure B. A diazonium chloride solution prepared from anthranilic acid (27·4 g.) was added dropwise in 4 hr. to a stirred solution of quinol (22 g.) in water (300 ml.) containing sodium hydrogen carbonate (50 g.). The mixture was acidified with dilute sulphuric acid, and the precipitate was separated and extracted under reflux successively with ethanol (100 ml.) and acetic acid (100 ml.). The ethanol extract yielded 2-o-*carboxyphenylquinol lactone* (I) (6·5 g.), m. p. 225°, needles (from ethanol) (Found: C, 73·7; H, 3·85. $C_{13}H_8O_3$ requires C, 73·6; H, 3·8%), $\lambda_{max.}$ 3310 and 2630 Å (log ε 3·79 and 4·08). The *acetate* formed needles (from ethanol), m. p. 138° (Found: C, 71·0; H, 3·9. $C_{15}H_{10}O_4$ requires C, 70·9; H, 3·9%). The acetic acid extract furnished 2,5-*di*-o-*carboxyphenylquinol dilactone* (II) (1·6 g.), m. p. above 400° (Found: C, 76·5; H, 3·3. $C_{20}H_{10}O_4$ requires C, 76·4; H, 3·2%).

Reaction of Chloroquinol.—Procedure A. Chloroquinol (14·5 g.) in water (600 ml.) was added with stirring to a diazonium chloride solution prepared from anthranilic acid (13·7 g.) containing an excess of sodium acetate. The whole was stirred for 2 hr. and set aside overnight. The dark brown precipitate was filtered off. Acidification of the filtrate with hydrochloric acid produced a brown tar which after several recrystallisations from ethanol gave colourless needles of 2-o-*carboxyphenyl-5-chloroquinol lactone* (0·8 g.), m. p. 242° (Found: C, 63·1; H, 3·0; Cl, 14·4. $C_{13}H_7O_3Cl$ requires C, 63·3; H, 2·8; Cl, 14·4%), $\lambda_{max.}$ 3340, 2680, and 2120 Å (log ε 3·67, 4·07, and 3·75). The *acetate* had m. p. 193° (needles from ethanol) (Found: C, 62·15; H, 3·3; Cl, 11·8. $C_{15}H_9O_4Cl$ requires C, 62·4; H, 3·1; Cl, 12·3%). The precipitate that separated after the initial reaction was extracted under reflux with acetic acid. The residue crystallised from anisole as yellow plates of 2,5-di-*o*-carboxyphenyl-3,6-dihydroxy-1,4-benzoquinone dilactone (0·4 g.), m. p. >400° (Found: C, 69·6; H, 2·3. Calc. for $C_{20}H_8O_6$: C, 69·8; H, 2·3%). After concentration, the acetic acid extract yielded orange needles (0·14 g.) of the azo-compound previously obtained from quinol, m. p. and mixed m. p. 244°.

Procedure B. Chloroquinol (14·5 g.) was treated with diazotised anthranilic acid (13·7 g. of acid) as previously described. On acidification of the resulting solution with hydrochloric acid, a yellow precipitate was obtained. From this, three recrystallisations from ethanol gave colourless needles of 2-*o*-carboxyphenyl-5-chloroquinol lactone (6·2 g.), m. p. and mixed m. p. 242°. A residue from the recrystallisation was crystallised from acetic acid, giving pale yellow needles (0·8 g.), m. p. 400°, of 2,3-*di*-o-*carboxyphenyl*-6-*chloroquinol dilactone* (Found: C, 68·8; H, 2·75; Cl, 10·45. $C_{20}H_9O_4Cl$ requires C, 68·9; H, 2·6; Cl, 10·2%).

[8] Edwards and Lewis, *J.*, 1959, 3254.
[9] Kögl and Erxleben, *Annalen*, 1930, **479**, 11.

Reaction of 2,5-*Dichloroquinol*.—Procedure A (2,5-dichloroquinol, 5·3 g.; anthranilic acid, 4·1 g.) led to a red-brown solution with a brown precipitate, which was filtered off. The solid was extracted under reflux with acetic acid; the extraction residue crystallised from anisole as yellow plates (0·5 g.), m. p. >400°, of 2,5-di-*o*-carboxyphenyl-3,6-dihydroxy-1,4-benzoquinone dilactone (Found: C, 69·6; H, 2·1%). The filtrate, after acidification with hydrochloric acid, deposited a solid which crystallised from ethanol in colourless needles of 2-o-*carboxyphenyl*-3,6-*dichloroquinol lactone* (0·6 g.), m. p. 279° (Found: C, 55·6; H, 2·1; Cl, 25·6. $C_{13}H_6O_3Cl_2$ requires C, 55·5; H, 2·1; Cl, 25·3%). Application of Procedure B (2,5-dichloroquinol, 8·9 g.; anthranilic acid, 6·8 g.) resulted in a brown suspension. The solid was separated and recrystallised several times from ethanol, to give yellow plates of 2,5-*di*-o-*carboxyphenyl*-3,6-*dichloro*-1,4-*benzoquinone* (0·4 g.), m. p. >400° (Found: C, 57·3; H, 2·55; Cl, 16·7. $C_{20}H_{10}O_6Cl_2$ requires C, 57·55; H, 2·4; Cl, 17·0%). (Hydrolysis of this quinone by cold alkali yielded 2,5-di-*o*-carboxyphenyl-3,6-dihydroxy-1,4-benzoquinone in almost quantitative yield.) Concentration of the mother-liquors yielded a solid which after four recrystallisations from ethanol gave colourless needles of 2-*o*-carboxyphenyl-3,6-dichloroquinol lactone (2·6 g.), m. p. and mixed m. p. 279°.

Reaction of 2-(4-*Carboxybuta*-1,3-*dienyl*)-5-*chloroquinol*.—Procedure B (the quinol, 1·2 g.; anthranilic acid, 1·5 g.) gave a dark red suspension. The solid was separated and then extracted under reflux with chloroform; removal of solvent from the extract left a red amorphous solid. This was dissolved in acetic anhydride (3 ml.) containing concentrated sulphuric acid (0·05 ml.) by warming the whole at 40° for 1 min. The mixture was poured into water, and the dark red solid that separated was extracted with benzene (25 ml.) under reflux. On cooling, the extract deposited crystals; these were recrystallised from benzene, to yield an *acetoxycarboxychloro-lactone* as yellow needles (10·5 mg.), m. p. 238° (decomp.) (Found: C, 64·5; H, 3·4; Cl, 6·7. $C_{27}H_{17}O_8Cl$ requires C, 64·2; H, 3·3; Cl, 7·0%).

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[*Received, February 10th*, 1960.]