

CCCLIV.—Preparation of Hydroxybenzophenones and Hydroxyxanthenes.

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NISHIKAWA and ROBINSON have shown (J., 1922, **121**, 839) that the Hoesch reaction, applied to the condensation of phloroglucinol with salicylonitrile, leads to 2:4:6:2'-tetrahydroxydiphenyl ketimine hydrochloride, which, on boiling with water, gives the free base. The ketimine is readily hydrolysed by aqueous sodium hydroxide, yielding 1:3-dihydroxyxanthone, no tetrahydroxybenzophenone being produced (compare Karrer, *Helv. Chim. Acta*, 1921, **4**, 992). Hydroxyxanthenes, however, are not invariably formed by this method, since Shoesmith and Haldane (J., 1924, **125**, 113) isolated only 2:4:2':4'-tetrahydroxybenzophenone by the condensation of resorcinol with diacetyl- β -resorcylnitrile and subsequent hydrolysis of the ketimine hydrochloride with 25% sulphuric acid. These authors found that the compound described by Marcus (*Ber.*, 1891, **24**, 3652) as β -resorcylnitrile would not condense with resorcinol; hence their use of the diacetyl derivative. With a view to obtain several hydroxyxanthenes for spectrographic examination, the applicability of the Hoesch reaction to (a) salicylonitrile and resorcinol, (b) salicylonitrile and pyrogallol, and (c) β -resorcylnitrile and pyrogallol has now been tested, and the work of Nishikawa and Robinson has been repeated. We are able to confirm the data of these investigators in all details, but, except in the case of 1:3-dihydroxyxanthone, we find that no reaction takes place unless the hydroxy-groups of the aromatic nitrile are protected. When the acetyl derivatives are employed, the reaction takes the usual course; the presence of the acetyl group, however, gives rise to various side reactions which complicate the isolation of the required products and also considerably reduce the yield. In the synthesis carried out by Shoesmith and Haldane (*loc. cit.*), resacetophenone and β -resorcyamide also were isolated, the production of the former compound being attributed to the formation of acetyl chloride during the reaction. Analogously, when pyrogallol is condensed with diacetyl- β -resorcylnitrile, gallacetophenone

is formed together with a red colouring matter seemingly identical with that obtained when acetyl chloride reacts with pyrogallol (compare Knoll & Co., *Centralbl.*, 1900, I, 270).

In none of the condensations were we able to isolate the intermediate product (ketimine hydrochloride or free ketimine) in a condition giving analytical values reconcilable with those demanded by the respective compounds. This failure may be attributed to the partial removal of acetyl groups during the condensation, for it has been found that, in addition to the direct evidence of the production of gallacetophenone, on boiling the condensation products with water, the hydroxy- and not the acetoxy-benzophenones are produced. Moreover, in the reaction between *o*-acetoxybenzocyanide and pyrogallol, 3:4-dihydroxyxanthone has been obtained directly. This can be attributed only to the formation of 3:4-dihydroxyxanthyl ketimine hydrochloride, $O \left\langle \begin{array}{c} C_6H_4 \\ C_6H_2(OH)_2 \end{array} \right\rangle C:NH, HCl$, during the initial condensation, since treatment of 2:3:4:2'-tetrahydroxybenzophenone with water alone at 100° does not bring about ring closure.

EXPERIMENTAL.

3-Hydroxyxanthone.—Through a solution of *o*-acetoxybenzocyanide (7.5 g.) and dry resorcinol (10 g.; 2 mols.) * in pure dry ether (100 c.c.) containing freshly-fused zinc chloride (2 g.), dry hydrogen chloride was passed for 6 hours; a viscous syrup began to be deposited after about 4 hours. The mixture was kept at 0° for a week, more syrup being precipitated. The ether was then decanted, the residue twice triturated with dry ether, and all solvent removed under reduced pressure. Attempts to isolate a pure ketimine hydrochloride having failed, the gummy condensate was dissolved in hot water (100 c.c.) and treated with an excess of potassium acetate, which caused immediate precipitation of an amorphous, yellow solid, presumably the free ketimine. This compound crystallised from dilute alcohol in orange needles (m. p. 150—153°) the nitrogen content of which did not agree with that of 2:4-dihydroxy-2'-acetoxydiphenyl ketimine (Found: N, 3.5. $C_{13}H_{15}O_4N$ requires N, 5.2%). The precipitate was therefore boiled with an excess of *N*/2-sodium hydroxide, until the evolution of ammonia had ceased, and the cooled solution was acidified with dilute hydrochloric acid. The yellow, amorphous precipitate was dried, and repeatedly extracted with boiling xylene; 3-hydroxyxanthone, which separated from the xylene solution, crystallised from dilute alcohol in colourless needles (yield, 1.8 g.), m. p. 246°, giving a blue

* The use of 2 mols. of the phenol to 1 mol. of the nitrile increased the yield.

fluorescence in alkaline solution. Kostanecki and Nessler (*Ber.*, 1891, **24**, 3981) and Ullmann and Denkler (*Ber.*, 1906, **39**, 4332) give m. p. 242°.

The aqueous filtrate from which the xanthone had been separated slowly deposited pale yellow needles (0.5 g.), m. p. 133—134°, which had all the properties of 2 : 4 : 2'-trihydroxybenzophenone (compare Michael, *Ber.*, 1881, **14**, 658).

2 : 3 : 4 : 2'-*Tetrahydroxybenzophenone*.—This compound was prepared from pyrogallol (10 g.) and *o*-acetoxybenzoxynitrile (7.5 g.) by the method described above. The syrupy condensate, after removal of all the ether, was dissolved in cold water, and the solution strongly acidified with hydrochloric acid; bright yellow needles, m. p. 182—184°, then separated. These were boiled with water for 1 hour; the solution, on cooling, deposited glistening, bronze plates mixed with a red dye. From an ethereal solution of the mixture, light petroleum precipitated a deep red, semi-solid material, which was removed; the filtrate was evaporated to dryness and after a preliminary purification by means of alcohol and animal charcoal the residue was crystallised from hot water. 2 : 3 : 4 : 2'-*Tetrahydroxybenzophenone* was thus obtained in lustrous, yellow plates, m. p. 100°, which, after drying in the steam-oven, melted at 149° (compare Graebe and Eichengrün, *Ber.*, 1891, **24**, 969). Yield, 18.5%.

The oily dye previously mentioned, further quantities of which were obtained on boiling the acid filtrate from which the supposed ketimine salt had crystallised, was extracted with boiling xylene, and from the extract, on cooling, a yellow, crystalline solid was deposited. Treatment of this with boiling water removed a further quantity of tetrahydroxybenzophenone and left a very small, insoluble residue which, on crystallisation from dilute alcohol, deposited yellow needles, m. p. 238—240°, agreeing in properties with the 3 : 4-dihydroxyxanthone obtained by Graebe and Eichengrün (*loc. cit.*). In addition to these two substances, gallacetophenone, m. p. 168°, was isolated in minute quantity by repeated extraction of the boiled aqueous filtrate, after separation of the red oil, by means of ether. It yielded a semicarbazone, m. p. 224°, in agreement with that found by Fischer (*Ber.*, 1909, **42**, 1015).

2 : 3 : 4 : 2' : 4'-*Pentahydroxybenzophenone*.—Pyrogallol (12 g.) and diacetyl- β -resorcyloxynitrile (10 g.) were dissolved in dry ether (150 c.c.) together with freshly-fused zinc chloride (2 g.), and the whole was treated with dry hydrogen chloride. The solution became turbid after 7 hours and a yellow, crystalline solid separated. After standing in the ice-chest for 4 days, the ether was decanted and the residual mixture of crystalline solid and syrup freed from ether and

boiled for 2 hours with water. On cooling, a red, crystalline mass separated and this, after drying, was extracted with boiling xylene. The pink, crystalline solid (2.7 g.) which separated on cooling was recrystallised from dilute alcohol; the pentahydroxybenzophenone then separated in yellow needles which softened at 180° and melted at 187°. The compound contains 2 mols. H₂O which are removed by heating at 110°. The alkaline solution of the compound is bright yellow and exhibits no fluorescence, but on keeping the colour changes to greenish-yellow and finally to dark olive-green (Found : C, 52.6, 52.3; H, 4.7, 4.7; H₂O, 11.6. Calc. for C₁₃H₁₀O₆.2H₂O : C, 52.4; H, 4.7; H₂O, 12.1%). The melting point given for this substance in the patent specifications (Badische Anilin- und Soda-Fabrik, D.R.-PP. 49149, 50451) is 168—170°. After removal of the pentahydroxybenzophenone, the aqueous solution, on extraction with ether, yielded a small quantity of gallacetophenone.

3 : 6-Dihydroxyxanthone.—The condensation of resorcinol and diacetyl-β-resorcyronitrile was carried out as detailed by Shoesmith and Haldane (*loc. cit.*), but *N*/2-sodium hydroxide was used to hydrolyse the ketimine hydrochloride. On acidification, a solid separated from which 2 : 4 : 2' : 4'-tetrahydroxybenzophenone was removed with boiling water, leaving a brown, amorphous residue; this crystallised from alcohol, after charcoal treatment, in faintly brown needles. The substance, which did not melt below 300° and was only formed in 1% yield, showed all the properties of 3 : 6-dihydroxyxanthone, the alkaline solution of which is characterised by an intense violet fluorescence (compare Meyer and Conzetti, *Ber.*, 1897, 30, 969).

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