236. *The Benzoyl Derivatives of Indigotin.*

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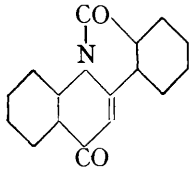
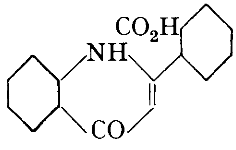
A method which has been used to elucidate the structure of Ciba Yellow (Indigo Yellow 3G Ciba) (Hope and Richter, J., 1932, 2783), *viz.*, degradation by heating with aqueous alkalis, has been applied to the closely related substances called in the patent literature Höchst Yellow R (isomeric with dibenzoylindigotin, $C_{30}H_{18}O_4N_2$) and Höchst Yellow U.

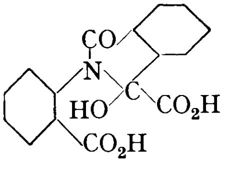
Höchst Yellow R is very easily attacked (when in a state of fine division) by boiling aqueous potassium hydroxide (10%), forming approximately equimolecular quantities of benzoic acid, anthranilic acid, and a *substance*, $C_{16}H_9O_2N$, to which we assign the structure (I). A clue to the structure of the original dye is afforded by a study of the last substance, which is without doubt the *lactam* of an *amino-acid*, $C_{16}H_{11}O_3N$ (II), into which it is convertible by heating with aqueous potassium hydroxide (15%) in an autoclave at 140°; similar treatment of the original dye, of course, yields this amino-acid directly.

(I.)



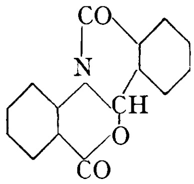


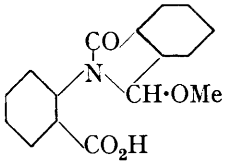
(II.)



(III.)

(IV.)





(V.)

The properties of the amino-acid (II) are in consonance with the view that it is a quinolone, in that the NH group is difficult to acylate. Methylation with methyl sulphate and alkali effects successive replacement of hydrogen first on the NH group and then in the carboxyl group.

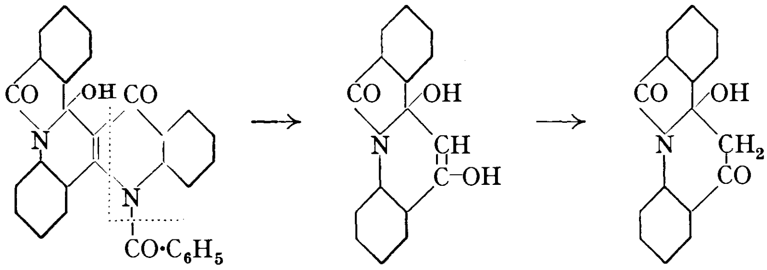
Further evidence for the proposed structure (I) is provided by a study of the product of oxidation. Oxidation by means of warm alkaline permanganate readily yields the product, $C_{16}H_{11}O_6N$ (III), which is a dibasic acid, forming a *disilver* salt and a *dimethyl* ester. Phthalic acid also is produced, in larger quantity the longer the oxidation is continued. The *acid* (III) loses water between 125° and 145°, and on continued heating at 170—190°, carbon dioxide is given off copiously. The solid residue has the formula

$C_{15}H_9O_3N$, and has been proved to be a *lactone* (IV). The formulæ proposed for (III) and (IV) are supported by the following evidence.

The lactone (IV) is readily hydrolysed by warming with aqueous sodium hydroxide (10%) to a hydroxy-acid, which can be methylated by methyl sulphate and alkali, yielding a *methoxy-acid* (V) (the lactam linkage being unaffected) and this when maintained at its melting point loses methyl alcohol, reverting to the lactone. Further, Zeisel determinations indicate the presence of one methoxyl group per molecule. When (IV) is oxidised in aqueous alkali at 40° with a limited quantity of permanganate, it yields phthalylanthranilic acid (m. p. and mixed m. p. 218—219°).

On the basis of the above evidence, it is possible to advance a structural formula for Höchst Yellow R. The formula (VI) appears to be the only reasonable one to account for the production of benzoic and anthranilic acids in equivalent amounts, leaving the residue represented by (I). If hydrolysis occurs at the dotted lines, and if the substance thereby formed loses water, the compound $C_{16}H_9O_2N$ is left.

(VI.)



If Höchst Yellow R is to be represented by (VI), then, since the Dessoulavy compound is convertible into it by simple hydrolysis, it becomes necessary to assign a like structure to this substance, *i.e.*, (VI) with Cl instead of OH. It is clear that this view of the structure of the Dessoulavy compound implies a new view of the mechanism of its conversion into Ciba Yellow 3G, and our former view (*loc. cit.*) concerning the mode of this conversion must be revised.

EXPERIMENTAL.

The Höchst Yellow R used in this work was made from indigo, benzoic anhydride, and zinc chloride (G.P. 270943). To ensure removal of accompanying Höchst Yellow U, the crude product was boiled twice with acetone, to remove excess benzoic anhydride, and then with xylene, the first dye being insoluble in these solvents. Before treatment with aqueous alkalis, the dye was obtained in fine division by solution in concentrated sulphuric acid and reprecipitation by water.

Action of 15% *Potassium Hydroxide.*—The Höchst Yellow R (damp, corresponding to 10 g. dry material) was heated for 6 hours in a steel autoclave with 100 c.c. of 15% potassium hydroxide. After cooling, the red-brown reaction liquid, which had strong green fluorescence, was treated with excess dilute hydrochloric acid (15%). The gummy precipitate was extracted with hot ligroin to remove benzoic acid, about one-third of the solid dissolving. The solute was proved to be benzoic acid by mixed m. p. The residual pale brown solid was crystallised from alcohol and had then m. p. 237° [Found : C, 72·91; H, 3·96; N, 5·34; *M* (Rast), 275. $C_{16}H_{11}O_3N$ requires C, 72·5; H, 4·15; N, 5·28%; *M*, 265]. The hydrochloric acid liquors were shown to contain anthranilic acid by isolating this through its copper salt. The employment of less concentrated alkalis in the above reaction had no influence on the nature of the products.

An experiment with 58 g. of Höchst Yellow R, using the above conditions, gave benzoic acid (10 g.), anthranilic acid (12 g.), and $C_{16}H_{11}O_3N$ (25 g.); theoretical amounts, according to the equation $C_{30}H_{18}O_4N_2 + 3H_2O = C_6H_5{\cdot}CO_2H + C_6H_4(NH_2){\cdot}CO_2H + C_{16}H_{11}O_3N$, are 15 g., 16·5 g., and 32·5 g., respectively.

Höchst Yellow R is also degraded by boiling (60 g.) at ordinary pressure with 10% caustic potash (500 c.c.) for 5 hours. In this case, accompanying benzoic and anthranilic acids, there is produced the *lactam*, $C_{16}H_9O_2N$ [*i.e.*, the dehydration product of the amino-acid (II)], which appears in the reaction liquid as an insoluble yellow suspension. Crystallised from toluene, ethyl acetate, or acetic acid, it has m. p. 232° [Found : C, 77·84; H, 3·73; N, 5·31; *M* (Rast), 253. $C_{16}H_9O_2N$ requires C, 77·4; H, 3·62; N, 5·6%; *M*, 247]. This lactam is converted into the amino-acid, $C_{16}H_{11}O_3N$, under the conditions described on p. 1000. It is evident that in the degradation carried out at ordinary pressure that part of the ring structure of Höchst Yellow R represented in formula (I) remains intact.

The Amino-acid $C_{16}H_{11}O_3N$ (II).—Acetylation is achieved by boiling with acetic anhydride and a drop of concentrated sulphuric acid or a little zinc chloride. Addition of water precipitates a white solid, which, recrystallised from alcohol, has m. p. 199° (Found : C, 70·38; H, 4·24. $C_{16}H_{10}O_3N{\cdot}COMe$ requires C, 70·36; H, 4·23%). Benzoylation was not possible by the Schotten–Baumann reaction, but when heated with four times its weight of benzoic anhydride (1 hour at 165°) (excess of anhydride being removed by warm ether), the amino-acid yields a *monobenzoyl* derivative, m. p. 236° from acetic acid [Found : C, 74·62; H, 4·12. $C_{16}H_{10}O_3N(CO{\cdot}C_6H_5)$ requires C, 74·8; H, 4·07%]. These acyl derivatives regenerate the amino-acid on warming with dilute sodium hydroxide solution.

Methylation. The amino-acid (1 g.) was dissolved in 100 c.c. of 5% sodium hydroxide, and 4 g. of methyl sulphate gradually added at room temperature. The *product*, precipitated by hydrochloric acid and crystallised from methyl alcohol, had m. p. 183—184° [Found : C, 68·85; H, 5·42; N, 4·34; *M* (Rast), 325. $C_{16}H_{10}O_3N(CH_3),H_2O$ requires C, 68·6; H, 5·5; N, 4·7%; *M*, 297] and was acidic.

Methylation at 40° with twice the proportion of methyl sulphate gives as main product a neutral compound, separating during reaction; recrystallised from methyl alcohol, this had m. p. 98° (Found : C, 70·0; H, 5·71; N, 4·4; *M*, 338. $C_{16}H_9O_3NMe_2,H_2O$ requires C, 69·45; H, 5·5; N, 4·5%; *M*, 311). That the second methyl group has produced an ester is shown by hydrolysing the second methylation product to the first by means of boiling dilute alkali. Formula (II) accounts for this behaviour.

The Substance $C_{16}H_9O_2N$ (I).—This was obtained as described on p. 1001. It is neutral, being insoluble in dilute acids or alkalis, but dissolves in concentrated sulphuric acid, giving a reddish solution with green fluorescence. It resists the action of benzoic anhydride at 150° and also boiling acetic anhydride.

Oxidation. The substance (20 g.) (in finely divided condition produced by the usual method) was stirred vigorously in suspension in 500 c.c. of 5% aqueous sodium hydroxide, finely pulverised potassium permanganate (25 g.) being added in small portions during 2½ hours, and the reaction vessel being in a water-bath at 40—50°. Finally, the temperature was raised to 70°, and the warm solution filtered. Hydrochloric acid (12%) was added to the filtrate, which was then left for at least 24 hours. Slow separation of colourless crystals occurred, which, after being collected, washed, and dried in air, melted with effervescence at 135—138° (Found, in material crystallised from ethyl acetate and dried at 100° : C, 61·53; H, 3·73. $C_{16}H_{11}O_6N$ requires C, 61·34; H, 3·52%). The substance readily loses one mol. of water (Loss in 2 hrs. at 125° in a vacuum : 5·9. $C_{16}H_9O_5N,H_2O$ requires $1H_2O$, 5·75%) (Found in dehydrated specimen : N, 4·99. $C_{16}H_9O_5N$ requires N, 4·75%). This *acid* forms a *disilver* salt when its ammoniacal solution is treated with silver nitrate (Found : Ag, 41·4. $C_{16}H_9O_6NAg_2$ requires Ag, 40·99%). This salt reacted with methyl iodide in boiling benzene and the resulting *dimethyl* ester was crystallised from ethyl acetate and dried at 100° (Found : C, 63·45; H, 4·75. $C_{18}H_{15}O_6N$ requires C, 63·35; H, 4·69%).

Action of Heat on the Hydroxy-acid, $C_{16}H_{11}O_6N$ (III).—When this acid is heated in a wide test-tube fitted with a delivery tube, two stages of decomposition are observed (see p. 1000), and the product finally solidifies, then melts at 210—212°; m. p. 216—217° from alcohol or ethyl acetate (Found : C, 71·9; H, 3·67; N, 5·3. $C_{15}H_9O_3N$ requires C, 71·7; H, 3·6; N, 5·6%). This *lactone* (IV) is insoluble in cold sodium carbonate or hydroxide, but dissolves slowly on continued heating with dilute alkalis. Confirmation of its structure follows from examination of the effects of methylation. The lactone (3 g.) is dissolved in hot dilute sodium hydroxide (50 c.c.) and stirred vigorously at 15° while methyl sulphate (12 g.) is gradually dropped in from a burette. Addition of dilute hydrochloric acid precipitates the product (Found, in specimen, m. p. 172—173°, recrystallised from ethyl alcohol–water : C, 67·91; H, 4·84; MeO, 9·8. $C_{16}H_{13}O_4N$ requires C, 67·85; H, 4·6; MeO, 10·9%), which is clearly a *methoxy-monobasic acid.* It decomposes at its m. p. (see p. 1001) to give the lactone $C_{15}H_9O_3N$.

The *hydroxy-acid* corresponding to this lactone was isolated (2·5 g.) by refluxing the latter (5 g.) for a short time with 10% sodium hydroxide and acidifying with acetic acid. The acid (Found : C, 66·75; H, 4·33; loss on heating at 130°, 6·76. $C_{15}H_{11}O_4N$ requires C, 66·9, H, 4·1; loss of $1H_2O$, 6·69%) is soluble in sodium carbonate solution and reverts to the lactone readily on heating. The silver salt could not be obtained entirely free from silver oxide; when it was dried and warmed gently with a benzene solution of methyl iodide, it afforded the *methyl* ester, m. p. 207° from methyl alcohol (Found : C, 67·58; H, 4·67. $C_{16}H_{13}O_4N$ requires C, 67·85; H, 4·6%).

This isomeride of the substance prepared by the use of methyl sulphate does not lose methyl alcohol when heated at the m.p. or above.

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