390. *Cinnolines. Part XXVIII.* The Nature of the $C_{(3)}$-position. Part I. The Neber–Bossel Synthesis of 3-Hydroxycinnoline.*

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Conditions have been devised under which *o*-nitromandelic acid can be converted into 3-hydroxycinnoline in 60% yield by cyclising in acid solution the derived *o*-hydrazinomandelic acid, a synthesis devised by Neber and Bossel (Bossel, "Inaugural Dissertation," Tübingen, 1925). This synthesis has been generalised with moderate success, and 6-chloro- and 3 : 6-dihydroxycinnoline are described. *o*-Aminomandelic acid and its derivatives are converted by hot acetic anhydride into *ON*-diacetyldioxindoles.

From the standpoint of comparative heterocyclic chemistry it is particularly interesting to study the nature of the $C_{(3)}$-position in cinnoline and its derivatives, but so far no cinnoline carrying an amino-, halogeno-, or methyl substituent at $C_{(3)}$ and lacking a complicating substituent at $C_{(4)}$ has been described. It is the purpose of this and subsequent papers to fill this gap, and to establish the nature of the cinnoline 3-position.

Neber, Knöller, Herbst, and Trissler (*Annalen*, 1929, **471**, 113) mentioned 3-hydroxycinnoline (VII; R = H) and described its reduction by phosphorus and hydriodic acid to oxindole (I; R = R′ = H), referring for its preparation to Bossel's work ("Inaugural Dissertation," Tübingen, May 1925). We have not been able to consult Bossel's thesis, but Dr. H. Hellmann of Tübingen kindly noted from it the essential reactions used in the synthesis

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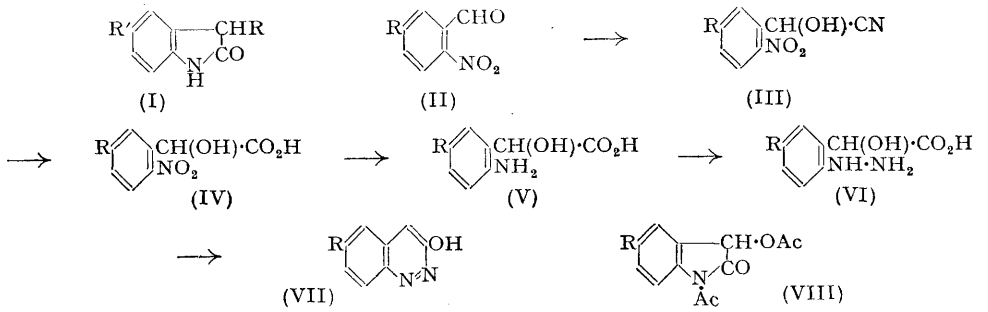
of 3-hydroxycinnoline, with which knowledge we have been able to devise satisfactory preparative conditions for this compound. Bossel obtained 3-hydroxycinnoline by adding an aqueous solution of sodium *o*-aminomandelate and sodium nitrite to hydrochloric acid [*o*-aminomandelic acid could not of course be diazotised directly in acid solution because of the rapidity with which it is converted into dioxindole (I; R = OH, R′ = H) under such conditions (Heller, *Ber.*, 1904, **37**, 938)], reducing the resulting diazonium salt with stannous chloride, and, after removing the tin, cyclising the *o*-hydrazinomandelic acid so formed in



boiling acid solution (V ⟶ VII; R = H). He described the preparation of a benzoyl derivative, and the reduction of (VII; R = H) to a dihydro-derivative by means of zinc dust and sulphuric acid.

In the present work we have used, besides *o*-aminomandelic acid itself, 2-amino-5-chloro- and 2-amino-5-methoxy-mandelic acid (V; R = Cl or OMe). Comments on the preparation of the necessary intermediates, 2-nitro-, 5-chloro-2-nitro-, and 5-methoxy-2-nitro-benzaldehyde, will be found in the Experimental section. The method described by McKenzie and Stewart (*J.*, 1935, 104) for the formation of *o*-nitromandelonitrile proved to be satisfactory for use on the large scale when applied with minor modifications, and Heller's procedure (*Ber.*, 1910, **43**, 2892) was used in the case of 5-chloro-2-nitromandelonitrile (III; R = Cl). This method was unsuccessful when applied to 5-methoxy-2-nitrobenzaldehyde, but 5-methoxy-2-nitromandelonitrile (III; R = OMe) was isolated in almost quantitative yield under conditions similar to those described by Robinson and Robinson (*J.*, 1915, **107**, 1755) for 3 : 4-dimethoxy-6-nitromandelonitrile. The three cyanohydrins were readily hydrolysed to the corresponding mandelic acids (IV; R = H, Cl, or OMe) by standard methods.

Free *o*-aminomandelic acid does not appear to have been described before McKenzie and Stewart (*loc. cit.*) prepared it by reducing the nitro-compound by means of ferrous sulphate and barium hydroxide. The resulting barium salt was converted into the sodium salt which, when treated with slightly less than the calculated quantity of sulphuric acid provided 43% of the free amino-acid. The source of the solution of sodium *o*-aminomandelate used by Bossel (*loc. cit.*) is not known to us. More recently Grimsell [*Arkiv Kemi, Mineral., Geol.*, 1942, **15***B*, No. 17; cf. Fredga and Andersson, *ibid.*, 1940, **14***B*, No. 18] described the more convenient preparation of *o*-aminomandelic acid by catalytic reduction of sodium *o*-nitromandelate in aqueous solution. We have found this method particularly useful because of its rapidity and the purity of the product. In one experiment it was found possible to isolate the free amino-acid in 85% yield by careful neutralisation of the reduction solution, but normally we used the latter directly in the next step towards 3-hydroxycinnoline. The same method also proved to be highly convenient for the preparation of 2-amino-5-methoxymandelic acid (V; R = OMe). This acid was previously described by Halberkann (*Ber.*, 1921, **54**, 3079) who acidified a cold alkaline solution of 5-methoxydioxindole (I; R = OH, R′ = OMe) with acetic acid, a procedure not suited to preparative ends. Not unexpectedly, attempts to reduce catalytically solutions of sodium 5-chloro-2-nitromandelate resulted in simultaneous elimination of the halogen atom, and we were obliged to resort to McKenzie and Stewart's chemical method of reduction mentioned above. Conversion of the resulting barium salt into the sodium salt

followed by careful acidification provided only 41% of 2-amino-5-chloromandelic acid. Excess of mineral acid precipitated 5-chloroisatin from the reaction solution, and there separated more slowly a white solid which was not further examined. It was presumably 5-chlorodioxindole or the related isatide.

To characterise 2-amino-5-chloro- and 2-amino-5-methoxy-mandelic acid these compounds were treated with hot acetic anhydride. In each case a crystalline product was obtained, and analysis suggested that these products were the diacetyl derivatives (VIII; R = Cl and OMe). Under the same conditions *o*-aminomandelic acid gave what is evidently the analogous substance (VIII; R = H). It is interesting to note that Suida (*Ber.*, 1879, **12**, 1326), by treating dioxindole with hot acetic anhydride, obtained only a monoacetyl derivative, later proved by Heller and Lauth (*Ber.*, 1929, **62**, 350) to be *O*-acetyldioxindole. It follows that very probably the present diacetyl derivatives arise by *N*-acetylation of the aminomandelic acids, followed by *O*-acetylation and cyclisation in undetermined order. This is supported by the observation that *o*-acetamidomandelic acid, which McKenzie and Stewart (*loc. cit.*) obtained by treating *o*-aminomandelic acid with acetic anhydride in cold aqueous suspension is converted by hot acetic anhydride into the diacetyldioxindole.*

As indicated above, the aqueous solution of sodium *o*-aminomandelate produced by catalytic reduction was used directly in the next stage of the synthesis. To it was added sodium nitrite, and diazotisation was effected by adding the solution to cold hydrochloric acid. The resulting diazonium salt was reduced to the hydrazine (VI; R = H) by stannous chloride. According to Bossel (*loc. cit.*) separation of a "tin salt," presumably that of the hydrazine, occurred at this stage. We did not observe this in early experiments on the small or medium scale, but subsequently the substance was always encountered. Yields of 3-hydroxycinnoline realised by processing the total reaction solution from which the "tin salt" had not separated were less satisfactory than those resulting when the salt was treated separately. The "tin salt" was soluble in water as stated by Bossel, and removal of the tin as sulphide left a colourless solution. When this solution was acidified and boiled it became golden-yellow, and neutralisation precipitated 3-hydroxycinnoline. The process ultimately adopted yielded 61·2% of crude product, or 59·5% of once-crystallised material, based on the amount of *o*-nitromandelic acid used.

Results obtained in attempts to convert 2-amino-5-chloromandelic acid into 6-chloro-3-hydroxycinnoline were not so satisfactory. A small yield of product, undoubtedly that required, was isolated under conditions described below, but we have been unable to standardise the reaction in the preparative sense.

More interesting was the behaviour of 2-amino-5-methoxymandelic acid. The essential step of cyclisation of the intermediate hydrazine in the present type of reaction is effected, as already mentioned, by boiling it in acid solution, and the possibility of demethylation occurring was appreciated. There was obtained a moderate yield of product, soluble in alkali, but not in the usual organic solvents, showing no definite melting point. It probably consisted of 3 : 6-dihydroxycinnoline, and a pure specimen of this compound was isolated through the monobenzoyl derivative. Analysis and the strong yellow colour of the latter (3-benzoyloxycinnoline is colourless) support its formulation as 6(3?)-benzoyloxy-3(6?)-hydroxycinnoline. Acid hydrolysis of this derivative readily provided 3 : 6-dihydroxycinnoline.

3-Hydroxycinnoline and its 6-chloro- and 6-hydroxy-derivatives are bright yellow compounds with ability to retain water strongly. Anhydrous 3-hydroxycinnoline was obtained by vigorous drying of the hydrated form, but even this was insufficient with 6-chloro-3-hydroxycinnoline.

The properties and reactions of 3-hydroxycinnoline and their bearing on the nature of the $C_{(3)}$-position will be discussed in a forthcoming publication. We propose to make a more general examination of the synthesis of cinnolines by the cyclisation of hydrazines.

* Halberkann (*loc. cit.*) obtained a compound, m. p. 225—226°, supposedly *ON*-diacetyl-5-methoxydioxindole, by treating 5-methoxydioxindole with acetic anhydride and sodium acetate on the water-bath. The high melting point disqualifies such a formulation, and the substance was probably a monoacetyl derivative.

Since this paper was written, Hellmann and Renz (*Chem. Ber.*, 1951, **84**, 901) have described *ON*-diacetyldioxindole, the properties of which agree with those of our preparation.

Experimental

M.p.s are uncorrected.

Nitro-aldehydes.—(i) The method for preparing *o*-nitrobenzaldehyde described in *Org. Synth.*, **24**, 75, is unsuitable when large quantities of the compound are required. In numerous experiments in this laboratory the overall yield of the aldehyde obtained by this method from *o*-nitrotoluene rarely exceeded 18%. Far more convenient is Reissert's procedure (*Ber.*, 1907, **50**, 4216; D.R.P., 152,218; 186,881; 182,217) which from 0·6 mole of *o*-nitrotoluene gave 62% of the aldehyde.

(ii) 5-Chloro-2-nitrobenzaldehyde was obtained by nitrating *m*-chlorobenzaldehyde (obtained in undiminished yield from experiments on twice the scale of that described in *Org. Synth.*, *Coll. Vol.* **2**, 130. The chloro-compound (111·7 g.) was added during 20 minutes to a stirred mixture of nitric acid (53 c.c., *d* 1·42) and concentrated sulphuric acid (607 c.c.) at 0—5°. After a further hour's stirring at room temperature the solution was poured on ice (4 l.), and the product (141 g., 95%; m. p. 70—72°) was collected, washed, and dried *in vacuo*. A specimen crystallised from ethanol had m. p. 78° (Mettler, *Ber.*, 1905, **38**, 2809, gives m. p. 76°; Eichengrun and Einhorn, *Annalen*, 1891, **262**, 137, give m. p. 77·5°). The uncrystallised product was pure enough for further use.

(iii) 5-Methoxy-2-nitrobenzaldehyde was prepared as described by Mason (*J.*, 1925, 1195). The following is a satisfactory procedure for the methylation of the intermediate 5-hydroxy-2-nitrobenzaldehyde. To the phenolic aldehyde (12·5 g.) suspended in water (40 c.c.) was added half of a solution of sodium hydroxide (4·5 g.) in water (5 c.c.). The resulting solution was heated and stirred on the steam-bath while methyl sulphate (8·9 c.c.) and the remainder of the alkali were added simultaneously, drop by drop, during 15 minutes. The reaction mixture was stirred for 10 minutes more without heating, and the product (10·7 g.; m. p. 82·5—84°) was collected. Acidification of the filtrate precipitated unchanged starting material (1·9 g.; m. p. 159—161°).

Nitromandelonitriles.—(i) (Cf. McKenzie and Stewart, *loc. cit.*). The following method avoids the separation of *o*-nitrobenzaldehyde during the initial cooling, a very troublesome occurrence in large-scale experiments. A stirred suspension of *o*-nitrobenzaldehyde (100 g.) in acetic acid (200 c.c.) was cooled to 10° by iced-water, and slow addition of potassium cyanide (66 g. in 132 c.c. of water) begun. After the addition of about one third of the cyanide solution the temperature was maintained at 0—5° by an ice–salt bath, whilst the remainder of the addition was made more quickly and with vigorous stirring. All of the cyanide was added during ½ hour, after which the solution was stirred for 4—5 hours at room temperature, diluted with water (900 c.c.), and set aside overnight. The product (107·4 g., 91·2%; m. p. 92—93°) was collected, washed with water, and dried *in vacuo*.

(ii) (Cf. Heller, *Ber.*, 1910, **43**, 2892). 5-Chloro-2-nitrobenzaldehyde (50 g.; finely powdered) was stirred for a few minutes with acetic acid (200 c.c.) at room temperature, the mixture was cooled to about 10°, and a solution of potassium cyanide (40 g.) in water (80 c.c.) was added dropwise. The temperature fell and was kept during most of the addition at 0—5°. The mixture was then stirred for 1 hour at room temperature, water (800 c.c.) was added, and the precipitated oil, which soon crystallised, was collected next morning. The crude product (45·7 g., 76·5%; m. p. 66—71°) was satisfactory for further use. A specimen crystallised from chloroform–light petroleum (b. p. 40—60°) had m. p. 81—83° (Heller, *loc. cit.*, gives m. p. 85°).

(iii) Potassium cyanide (52·5 g.) was added with shaking to 5-methoxy-2-nitrobenzaldehyde (35 g.) in acetic acid (560 c.c.) cooled in ice. The mixture was set aside for 5 days at room temperature and the resulting solution was then diluted with water (3·5 l.) and extracted with ether, and the extract was washed thoroughly with sodium carbonate solution. Removal of the solvent from the dried (Na_2SO_4) solution gave an oil which slowly solidified (37·4 g.; m. p. 92—93·5°). Crystallisation from benzene gave white needles, m. p. 93·5—95°. The nitrile (which was not analysed) gave a red solution in sulphuric acid.

Nitromandelic Acids.—(i) Crude *o*-nitromandelonitrile (107·4 g.) and concentrated hydrochloric acid (537 c.c.) were refluxed for ½ hour and the solution was then evaporated to half the volume. When the solution cooled crystals (112·5 g.; m. p. 139—142°) separated; they were suitable for further use. This procedure gave a cleaner product than was obtained by evaporation to dryness and subsequent crystallisation from water.

(ii) Crude 5-chloro-2-nitromandelonitrile (45·7 g.) was hydrolysed as above with concentrated hydrochloric acid (900 c.c.). The solid remaining when the solution was evaporated to dryness was extracted with boiling benzene, and the solution filtered from ammonium chloride. The granular product (38·8 g., 78%; m. p. 134—135°) separated on cooling (Heller, *Ber.*, 1910, **43**, 2892, gives m. p. 134°).

(iii) 5-Methoxy-2-nitromandelonitrile (37·4 g.) and concentrated hydrochloric acid (400 c.c.) were refluxed for ½ hour, and the red-brown solution was filtered whilst still hot. On partial evaporation and then cooling of the filtrate, light brown crystals (38·5 g., m. p. 118—122°) separated. The acid could be crystallised from water or benzene. *5-Methoxy-2-nitromandelic acid* formed prisms, m. p. 122—125° (Found: C, 47·6; H, 4·2. $C_9H_9O_6N$ requires C, 47·6; H, 4·0%), when crystallised from benzene containing a little alcohol. The compound slowly became brown when exposed to light.

Aminomandelic Acids.—(i) (Cf. Grimsell, *loc. cit.*). *o*-Nitromandelic acid (100 g.) was neutralised with standard sodium hydroxide (2·1N; 240 c.c.), and the volume of the solution was made up to 800 c.c. (more concentrated solutions were reduced more slowly). When shaken with palladium–charcoal (5%; 10 g.) the solution absorbed about 37 l. of hydrogen in 4 hours. The filtered solution was used for the preparation of 3-hydroxycinnoline as described below.

In one experiment, the filtered reduction solution (from 5 g. of the nitro-acid) was evaporated to about two-thirds of its original volume, cooled in ice, and treated with 85% of the theoretical amount of sulphuric acid (4N). There separated 3·6 g. (85%) of *o*-aminomandelic acid, m. p. 142—145° (rapid heating). McKenzie and Stewart (*loc. cit.*) give m. p. 144°.

(ii) When 5-chloro-2-nitromandelic acid was treated as above, hydrogen absorption continued beyond the amount required for reduction of the nitro-group, precipitation occurred, the mixture became acidic, and a positive test for chloride ion was obtained.

To ferrous sulphate (31 g.) in boiling water (30 c.c.) was added a solution prepared from chloronitromandelic acid (4 g.), barium hydroxide octahydrate (8 g.), and boiling water (200 c.c.), and then a second barium hydroxide solution (40 g. in 120 c.c. of boiling water). The resulting sludge was stirred for 1 hour without further heating and then boiled for ½ hour under reflux. The mixture was filtered, the residue was extracted several times with boiling water, and the combined filtrate and washings were saturated with carbon dioxide and then again filtered and evaporated to half volume. After the addition of sodium carbonate (0·92 g. in a small volume of water) and filtration, the solution was evaporated further (to *ca.* 60 c.c.) and treated with sulphuric acid (4N; 3·6 c.c.) whilst being cooled in ice, whereupon 2-amino-5-chloromandelic acid (1·43 g., 41%) separated. This compound melted with effervescence at 138—140°, the melt becoming red above this temperature. A further 1 c.c. of sulphuric acid precipitated from the filtrate more solid (0·15 g.), m. p. 128—130°, and finally excess of sulphuric acid (5 c.c.) with warming on the steam-bath caused the separation of red crystals of 5-chloroisatin, m. p. 249° (Found: C, 53·3; H, 2·4. Calc. for $C_8H_4O_2NCl$: C, 52·9; H, 2·2%). When kept at room temperature the filtrate from the isatin deposited a white solid (0·72 g.), m. p. 217°. This was not further examined but was probably the isatide formed by oxidation of the intermediate dioxindole.

(iii) 5-Methoxy-2-nitromandelic acid (1 g.) in sodium hydroxide solution (2·1N; 2·1 c.c.) and water (5 c.c.) was hydrogenated as usual with 5% palladium–charcoal (0·1 g.). Reduction was complete in about 2 hours. After removal of the catalyst the solution was evaporated to half volume, then cooled in ice and treated with sulphuric acid (4·09N; 1 c.c.). After some time at 0° the amino-acid (0·71 g.) separated as a light-brown solid, m. p. 153—155° (Halberkann, *Ber.*, 1921, **54**, 3079, gives m. p. 160°).

The Action of Acetic Anhydride on o-*Aminomandelic Acids.*—(i) A suspension of *o*-aminomandelic acid (0·5 g.) in acetic anhydride (6 c.c.) was set aside at room temperature for 2 days and then heated on the steam-bath for ½ hour and poured into water. ON-*Diacetyldioxindole* (0·45 g.) which separated on cooling formed white needles, m. p. 88—89° (Found: C, 61·9; H, 5·0. $C_{12}H_{11}O_4N$ requires C, 61·8; H, 4·75%) from methanol.

This product also resulted from similar treatment of *o*-acetamidomandelic acid [prepared by shaking *o*-aminomandelic acid (0·5 g.) with water (3 c.c. containing a small amount of ice) and acetic anhydride (0·5 c.c.) until dissolution occurred, evaporating the solution to dryness in a vacuum desiccator, and crystallising the residue from water. The white product had m. p. 142—144°. McKenzie and Stewart (*loc. cit.*) give m. p. 142—143°].

(ii) 2-Amino-5-chloromandelic acid (0·5 g.) and acetic anhydride (5 c.c.) were left overnight, and the solution was then heated on the steam-bath for a few minutes and poured into water (50 c.c.). Crystallisation of the product (0·3 g.) from alcohol gave feathery white needles of ON-*diacetyl-5-chlorodioxindole*, m. p. 130·5—131·5° (Found: C, 53·5; H, 3·7; N, 5·1. $C_{12}H_{10}O_4NCl$ requires C, 53·8; H, 3·8; N, 5·2%).

(iii) In the same way 2-amino-5-methoxymandelic acid gave ON-*diacetyl-5-methoxydioxindole* which formed white prisms, m. p. 97·5—98° (Found: C, 58·7; H, 5·0; N, 5·5. $C_{13}H_{13}O_5N$ requires C, 59·3; H, 5·0; N, 5·3%).

3-*Hydroxycinnolines.*—(i) The solution obtained by reducing catalytically *o*-nitromandelic

acid (100 g.), as described above, was evaporated to *ca.* 400 c.c., and sodium nitrite (35 g.) was added. The resulting solution was added dropwise to stirred concentrated hydrochloric acid (650 c.c.) maintained at 0°. Stirring was continued for a few minutes after removal of the freezing bath, and the diazonium solution was then added slowly to stannous chloride (605 g.) and concentrated hydrochloric acid (650 c.c.), stirred at 0°. When the addition was almost complete, separation of the " tin salt " began, and on complete addition very slow stirring was continued for ¾ hour at room temperature. After remaining in the ice-chest overnight the " tin salt " was collected and dissolved in water (800 c.c.), giving a pale yellow solution which was treated with hydrogen sulphide. After removal of the tin sulphide concentrated hydrochloric acid (40 c.c.) was added to the filtrate, and this solution was boiled for ½ hour and became brownish-yellow. Neutralisation with solid sodium acetate precipitated 3-hydroxycinnoline as orange crystals (45·34 g., 62%), which after one crystallisation from water had m. p. 198—200° (yield, 44·1 g.). A specimen crystallised several times from water, and once from benzene, gave bright yellow needles, m. p. 201—203° (with preliminary sintering) (Found, in material dried at 70°/5 mm.: C, 61·1; H, 4·7. Calc. for $C_8H_6ON_2,\frac{1}{2}H_2O$: C, 61·9; H, 4·55. In material dried 120°/5 mm.: C, 64·7; H, 4·0; N, 19·6. Calc. for $C_8H_6ON_2$: C, 65·75; H, 4·1; N, 19·2%).

The benzoyl derivative was prepared according to Bossel (*loc. cit.*) as follows: 3-hydroxycinnoline (0·75 g.), sodium hydroxide (1N; 5·5 c.c.), benzoyl chloride (0·65 g.), and some ice chips were shaken for ½ hour. The product (0·8 g.; m. p. 140—145°) was collected, washed with dilute sodium carbonate solution, and crystallised from aqueous alcohol; it formed white crystals, m. p. 148—149° (Bossel gives m. p. 146°) (Found: C, 72·2; H, 4·15. Calc. for $C_{15}H_{10}O_2N_2$: C, 72·0; H, 4·0%).

(ii) The solution obtained by reducing 5-chloro-2-nitromandelic acid (5 g.), as described above, was evaporated to 50—60 c.c., sodium nitrite (1·5 g.) was added, and the mixture was added slowly to hydrochloric acid (27·5 c.c.; *d* 1·16) and stirred below 0°. The cloudy diazonium solution was then added to the ice-cold reduction medium (25·7 g. of stannous chloride in 27·5 c.c. of concentrated hydrochloric acid), and the resulting suspension was stirred for ½ hour at room temperature and stored in the ice-chest overnight. Filtration of the suspension was slow and during the process the solid residue became yellow. It was extracted with cold water (500 c.c.; most of the material was insoluble), the extract was treated with hydrogen sulphide and filtered, and the filtrate then treated with concentrated hydrochloric acid (5 c.c.) and evaporated to small bulk. During the evaporation a yellow powder separated which redissolved when the volume decreased to about 30 c.c., and on cooling, white crystals were deposited. This suspension was neutralised with excess of sodium acetate, and the light yellow product (0·32 g.) was collected. *6-Chloro-3-hydroxycinnoline* crystallised from alcohol as yellow needles, m. p. 262—265° (with darkening) (Found: C, 50·25; H, 3·0. $C_8H_5ON_2Cl$ requires C, 53·2; H, 2·8. Found, in material dried at 120°/5 mm.: C, 51·3; H, 3·2. $C_8H_5ON_2Cl,\frac{1}{2}H_2O$ requires C, 50·7; H, 3·2%). Numerous attempts to raise the yield of the desired product in this reaction were unsuccessful.

(iii) To the solution obtained by reducing 5-methoxy-2-nitromandelic acid (5 g.) as described above was added sodium nitrite (1·5 g.), and the whole was slowly run into concentrated hydrochloric acid (40 c.c.) stirred at 0—5°. The diazonium solution was then added to stannous chloride (25·5 g.) in concentrated hydrochloric acid (40 c.c.) at 0°. After two days in the ice-chest the solution was diluted to 1 l. with water and treated with hydrogen sulphide. Filtration gave a clear solution which became yellow when boiled and was evaporated almost to dryness. Neutralisation with sodium acetate provided a greenish-yellow powder (1·4 g.) which darkened at about 300° but did not show a discernible m. p. Dissolution in hydrochloric acid and water (2 : 1 by volume) (charcoal) and re-precipitation by sodium acetate gave a yellow powder, practically insoluble in most solvents, slightly soluble in pyridine.

This product (1·15 g.) was dissolved in sodium hydroxide solution (1N; 11 c.c.) containing ice chips and treated with benzoyl chloride (3 c.c.). After being shaken for some time the product was collected (1·4 g.). Washing this with sodium hydroxide (2N; 30 c.c.) left a solid (0·93 g.) of vague m. p. Crystallisation from methanol, rejection of the most soluble and least soluble fractions, and recrystallisation of the middle fractions from the same solvent gave fluffy yellow crystals of *6(3?)-benzoyloxy-3(6?)-hydroxycinnoline*, m. p. 233—235° (after darkening) (Found: 67·9; H, 3·8; N, 10·5. $C_{15}H_{10}O_3N_2$ requires C, 67·7; H, 3·8; N, 10·5%).

The benzoyl derivative (0·15 g.) and hydrochloric acid (5 c.c. of a mixture containing 3 c.c. of concentrated acid and 2 c.c. of water) were refluxed together for ½ hour. Benzoic acid separated and was removed by ether. The acid layer was boiled (charcoal) and concentrated,

and the precipitate was washed with water. Recrystallisation from hydrochloric acid (roughly 5N) gave yellow nodules of **3 : 6-*dihydroxycinnoline*** (Found : C, 59·1; H, 3·6. $C_8H_6O_2N_2$ requires C, 59·3; H, 3·7%).

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