XII.—*The Cyanine Dyes. Part X. The Constitution of the* apo*Cyanines.*

By William Hobson Mills and Henry Geoffrey Ordish.

The action of alcoholic potash on a mixture of a quinoline alkyliodide and a quinaldine alkyliodide leads, as is well known, to the formation of an *iso*cyanine. Very similar dyes, the *apo*cyanines, are, however, formed by the action of alcoholic potash on a quinoline alkyliodide alone (D.R.-P., 154448). In this condensation, two molecules of quinoline alkyliodide condense with the loss of the elements of one molecule of hydrogen iodide, and two isomeric dyes, one yellow—the xantho*apo*cyanine—and the other red—the erythro*apo*cyanine—result. On the probable assumption that the alkyl groups remain intact, the reaction may be represented as follows:

$$2(C_9H_7NR)I - HI = (C_{18}H_{13}N_2R_2)I,$$

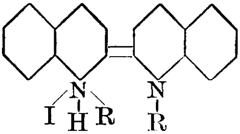
where R represents the alkyl group.

These compounds were investigated by Kaufmann and Strübin (*Ber.*, 1911, **44**, 690), who suggested formula (I) for the erythro*apo*cyanines. This, however, cannot be regarded as a satisfactory representation of these compounds, as it accords neither with their intense colour nor with their stability towards alkalis. We have therefore undertaken an investigation of these dyes and have selected the erythro*apo*cyanine derived from quinoline ethiodide for this purpose, as it is formed in better yield and, on account of its greater solubility, is more easily handled than the isomeric xantho*apo*cyanine.

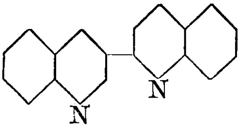
We first tried the method of oxidation with potassium permanganate which had proved successful in fixing the constitution of the *iso*cyanines (Mills and Wishart, J., 1920, **117**, 579). The chief product was a diquaternary ammonium compound, which was isolated as a dichromate, and the corresponding iodide proved to be identical with the iodide obtained by Kaufmann and Strübin by oxidising the *apo*cyanine with iodine. This oxidation, which was effected smoothly either by potassium permanganate or by iodine, brought about the removal of one hydrogen atom per molecule and the addition of an equivalent of an acid radical :

$$(C_{18}H_{13}N_2Et_2)I + I_2 = (C_{18}H_{12}N_2Et_2)I_2 + HI.$$

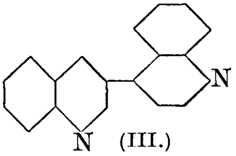
The nature of this product was easily inferred, for its composition and molecular weight, considered together with its ultimate origin from quinoline ethiodide, indicated that it was the diethiodide of a diquinolyl, $C_{18}H_{12}N_2$. Further, by heating the corresponding *diethochloride* in a vacuum, two molecules of ethyl chloride were eliminated and the diquinolyl itself was isolated. *Ethylerythro*-apo*cyanine* so clearly resembles the other classes of cyanine dyes that it seemed certain that its colour must be due to an analogous cause. It must consequently be associated with the presence of two NEt groups, in one of which the nitrogen is in the ammonium form, and in the other tervalent, connected by a chain of conjugated linkages. In order that the two nitrogen atoms may have this different function there must necessarily be an odd number of carbon atoms in the connecting chain. The molecules of the diquinolyl diethiodide and the erythro*apo*cyanine, being so readily interconvertible by the simple elimination or introduction of a hydrogen atom with the addition or removal of an ionic charge, must have the same carbon skeleton. The diethiodide must therefore be derived from a diquinolyl in which the two nitrogen atoms are separated by an odd number of carbon atoms. This condition is satisfied by the diquinolyls (II) and (III), in which the 3-position of one nucleus is linked to the 2- and to the 4-position respectively of the other.



(I.)



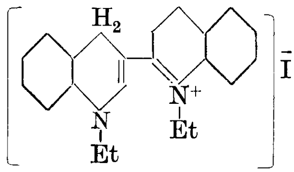
(II.)



(III.)

The probability that the *apo*cyanines are derived from a 3-quinolylquinoline is increased when it is remembered that the diquinolyl most easily prepared (by heating quinoline with sodium; Weidel, *Monatsh.*, 1881, **2**, 491) has been shown to have the constitution (II) (Carlier and Einhorn, *Ber.*, 1890, **23**, 2895). From diethiodides of diquinolyls of this constitution, the dyes will be obtained by the addition of one atom of hydrogen and the removal of one atom of iodine per molecule. There is only one possible position for the added hydrogen, which will leave a conjugated chain of unsaturated linkages between the two nitrogen atoms; namely the 4-position. These conditions, therefore, lead to the view that the *apo*cyanines are to be represented by the following formulæ :

(IV.)



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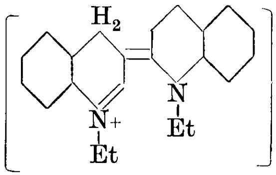
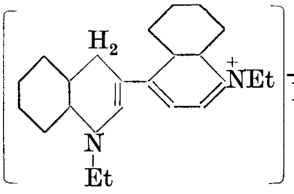


(V.)

(VI.)



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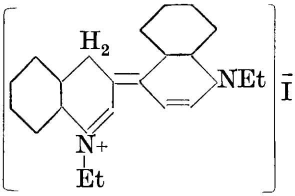
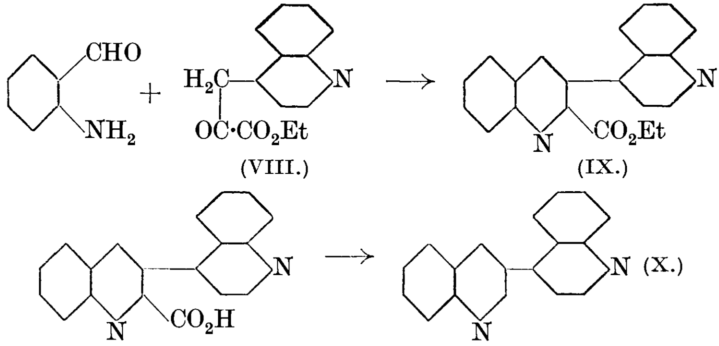


(VII.)

If these conclusions are correct, the tautomeric formulæ (IV) and (V), having a conjugated chain of three carbon atoms, represent the xantho*apo*cyanine, and the formulæ (VI) and (VII), with the longer chain of five atoms (as in the *iso*cyanines), represent the more deeply coloured red erythro*apo*cyanine.

Formulæ corresponding with (V) and (VII) were proposed by König five years ago (*Ber.*, 1922, **55**, 3293), but without proof. In the present paper, an experimental demonstration is given that the erythro*apo*cyanine has a constitution shown by formula (VI) (or VII). This was effected by synthesising the diquinolyl (III), and showing that its diethiodide was identical with that obtained by oxidising the dye with iodine.

This synthesis was carried out in the following manner. Ethyl 4-quinolylpyruvate (lepidineoxalate) (VIII) (Wislicenus, *Ber.*, 1909, **42**, 1141) was heated with *o*-aminobenzaldehyde, two molecules of water being eliminated and *ethyl* 3 : 4′-*diquinolyl*-2-*carboxylate* (IX) formed, a synthesis of the Friedländer type having evidently occurred. The corresponding *acid* lost carbon dioxide on heating, giving the 3 : 4′-diquinolyl (X), and the diethiodide of this was found to be identical with that obtained from the dye by oxidation with iodine.



(VIII.) (IX.) (X.)

By means of a similar series of reactions starting with ethyl 2-quinolylpyruvate and *o*-aminobenzaldehyde we have synthesised the 2 : 3′-diquinolyl, which is identical with that obtained by heating quinoline with sodium. A proof of the constitution of this diquinolyl is thus afforded which confirms that given by Carlier and Einhorn (*loc. cit.*).

EXPERIMENTAL.

*Diethylerythro*apo*cyanine Iodide.*—For the preparation of this compound we followed closely the details given in D.R.-P. (*loc. cit.*). Pure quinoline ethiodide (14 g.) was dissolved in the smallest possible quantity of boiling methyl alcohol, and two equal volumes (each of 7 c.c.) of a 10% solution of potassium hydroxide in methyl alcohol were added, one at the beginning and the other after an interval of about 10 minutes. The mixture was boiled for about 4 hours and, after dilution with methyl alcohol (50 c.c.), allowed to stand over-night. Crystals of both the erythro- and the xantho-*apo*cyanine were deposited (yield, about 30%), and separation was effected by recrystallisation from ethyl alcohol, in which the xantho-*apo*cyanine is the less soluble. A further small quantity of the mixed dyes could be obtained by evaporating the mother-liquor to two-thirds of the original bulk. The diethylerythro*apo*cyanine iodide formed reddish-brown needles with a green reflex. The analogous xantho*apo*cyanine was obtained as an orange, crystalline powder in a yield of 5%.

*Oxidation of Erythro*apo*cyanine Chloride.*—An aqueous solution of erythro*apo*cyanine chloride, prepared from the corresponding iodide (2 g.) by the action of silver chloride, was diluted with water (to 100 c.c.) and cooled to 0°, and a 2% solution of potassium permanganate added drop by drop to the well-stirred solution. The clear filtrate was extracted twice with chloroform and evaporated to dryness, and the residue extracted with absolute alcohol. The oil obtained on evaporation of the alcohol yielded a crystalline dichromate, m. p. 211°, having a composition the same as that of the dichromate obtained by Kaufmann and Strübin by the direct oxidation of the dye with sodium dichromate (Found: Cr, 19·1. Calc. for $C_{22}H_{22}O_7N_2Cr_2$: Cr, 19·0%). The dichromate obtained as described by Kaufmann and Strübin (*loc. cit.*) gave Cr, 19·1%.

3 : 4′-*Diquinolyl*-2-*carboxylic Acid.*—Ethyl 4-quinolylpyruvate (4·6 g.) was mixed with *o*-aminobenzaldehyde (2·4 g.) and heated in a vacuum (12—15 mm.) at 150—160° until water vapour ceased to be evolved. The dark-coloured product, consisting of the crude ethyl diquinolylcarboxylate, was dissolved in alcohol and hydrolysed by warming with an excess of 10% aqueous sodium hydroxide. The solution of the resulting sodium salt was extracted twice with ether to remove impurities, filtered, and made acid with acetic acid. 3 : 4′-*Diquinolyl*-2-*carboxylic acid* separated on standing as a brown, crystalline deposit which was purified by boiling in alcohol with animal charcoal. The pure acid was obtained as a colourless, crystalline powder from alcohol, or as prisms containing 1½ molecules of water from 30% acetic acid (Found: H_2O, 8·4. $C_{19}H_{12}O_2N_2,1\frac{1}{2}H_2O$ requires H_2O, 8·3%). The anhydrous acid melts and decomposes at 204° (Found: C, 75·9; H, 3·9. $C_{19}H_{12}O_2N_2$ requires C, 76·0; H, 4·0%).

3 : 4′-*Diquinolyl.*—By heating 3 : 4′-diquinolyl-2-carboxylic acid to 205° carbon dioxide was eliminated; the impure diquinolyl, after being washed with sodium carbonate solution, was obtained as a white, apparently amorphous powder by allowing its solution in light petroleum to evaporate slowly; m. p. 83—84° (Found: C, 84·3; H, 4·7; N, 10·0. $C_{18}H_{12}N_2$ requires C, 84·4; H, 4·7; N, 10·9%). A crystalline *picrate* was prepared, m. p. 243°.

Preparation of 3 : 4′-*Diquinolyl from Erythro*apo*cyanine Iodide.*—The diethiodide, obtained by oxidising the dye with iodine as described by Kaufmann and Strübin (*loc. cit.*), was converted by silver chloride into the corresponding water-soluble diethochloride (deliquescent crystals, m. p. 121°). By heating this compound in a vacuum (1—2 mm.), ethyl chloride was removed and a dark red sublimate formed in the cooler parts of the tube. This was extracted with benzene and yielded a white powder, which, like the synthetic product, could not be induced to crystallise. It gave, however, the same crystalline picrate, m. p. 244°, mixed m. p. 244°, and could also be converted into the original diethiodide, m. p. 198°, mixed m. p. 198°.

3 : 4′-*Diquinolyl Diethiodide.*—3 : 4′-Diquinolyl was boiled with an excess of ethyl iodide for 4 hours, and the resulting solid was recrystallised from dilute alcohol, giving the pure salt as orange-

yellow crystals, m. p. 198° (Found : I, 44·9. $C_{22}H_{22}N_2I_2$ requires I, 44·7%). This compound was identical with that prepared directly from the dye by oxidation with iodine as described by Kaufmann and Strübin. There was exact correspondence in the appearance and behaviour of these two products in the melting-point tube; moreover the synthetical product did not dissolve in a saturated solution of the other.

2′ : 3-*Diquinolyl*-2-*carboxylic Acid*.—Ethyl 2-quinolylpyruvate (Wislicenus, *loc. cit.*) (4·8 g.) and *o*-aminobenzaldehyde (2·4 g.) were dissolved in 50% alcohol (15 c.c.), 10% potassium hydroxide solution (30 c.c.) was added, and the mixture kept for 24 hours. An excess of alkali was then added and the whole steam-distilled to remove any unchanged *o*-aminobenzaldehyde and quinaldine. The residue, after filtration, was made almost neutral with hydrochloric acid, and an excess of acetic acid added. The diquinolylcarboxylic acid separated as a very sparingly soluble, brown powder; this was precipitated from boiling glacial acetic acid by water as a white powder, m. p. 175° (decomp.) (Found : C, 75·8; H, 4·2. $C_{19}H_{12}O_2N_2$ requires C, 76·0; H, 4·0%).

2′ : 3-*Diquinolyl*.—When 2′ : 3-diquinolylcarboxylic acid was heated to 175°, carbon dioxide was given off. The residue crystallised from alcohol or benzene in small, colourless prisms, m. p. 175°.

We desire to thank the Chemical Society for a grant to one of us (H. G. O.), which defrayed most of the cost of this research.

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[*Received, December* 1*st*, 1927.]