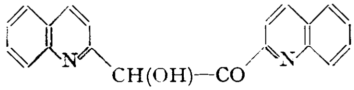
121. *Cyclic Meso-ionic Compounds derived from Quinoline.*

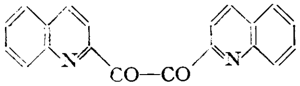
By B. R. Brown and D. Ll. Hammick.

A new class of compound, produced by the action of cyanide or cyanide-type ions on aldehydes of the quinoline and *iso*quinoline series, is described. The evidence for regarding them as possessing meso-ionic structures (IV) is reviewed. We propose to call them quinocolls, a systematic name for them being 3 : 6-dihydroxydiquinolino(1′ : 2′-1 : 2)(1″ : 2″-4 : 5)-pyrazinium dihydroxide bisanhydro-salts. A mechanism for their production is suggested.

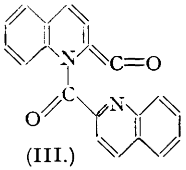
Henze (*Ber.*, 1934, **67**, 753) reports that quinaldoin (I), m. p. 261°, is produced by the action of aqueous-alcoholic potassium cyanide on quinoline-2-aldehyde. No analysis or chemical properties of the compound are given. Kaplan (*J. Amer. Chem. Soc.*, 1941, **63**, 2654) confirmed this work and recorded an analysis. He also obtained the compound (very pale brown needles, m. p. 269—271°) by the action of old selenium dioxide on quinaldine in dioxan. By analogy with the formation of benzoin from benzaldehyde and potassium cyanide, Kaplan assumed that the compound was quinaldoin (I), but recorded no chemical properties. Later Linsker and Evans (*ibid.*, 1946, **68**, 947) obtained a compound, m. p. 175°, which they formulated as quinaldil (II), from the reaction of selenium dioxide with quinaldine. This reacted with urea in the same way as does benzil, and on reduction yielded a compound, m. p. 135°, which had the chemical properties expected for quinaldoin (I).



(I.)



(II.)



(III.)

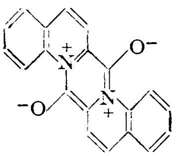
By the decarboxylating action of picolinic or quinaldinic acid on quinoline-2-aldehyde we have obtained a compound in the form of colourless needles, m. p. 266—267°, which proved to be identical with the compound produced from quinoline-2-aldehyde and potassium cyanide. This is a further example of the analogous chemical behaviour of the cyanide ion and the ions resulting from the decarboxylation of picolinic and quinaldinic acids (Dyson and Hammick, *J.*, 1937, 1724; Ashworth, Daffern, and Hammick, *J.*, 1939, 809; Brown and Hammick, *J.*, 1949, 173).

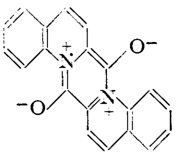
The compound dissolves in concentrated hydrochloric acid and in 30% sulphuric acid to a yellow solution. It forms a yellow *diperchlorate*. Oxidation with potassium permanganate in hot aqueous pyridine yields 77% of quinaldinic acid. The compound reacts vigorously with hot concentrated aqueous potassium hydroxide to yield 60% of potassium quinaldinate. This reaction proceeds with simultaneous reduction of added methylene-blue. Boiling aniline converts the compound into the anilide of quinaldinic acid. The compound is inert towards carbonyl or hydroxyl group reagents under a variety of conditions, and is unaffected by cold potassium permanganate solution or by bromine water.

Elementary analysis of the compound agrees better with the empirical formula $C_{20}H_{12}O_2N_2$ than with $C_{20}H_{14}O_2N_2$ [cf. Kaplan (*loc. cit.*) whose analysis also agrees better with $C_{20}H_{12}O_2N_2$].

A molecular-weight determination proved impossible owing to insolubility of the compound in suitable solvents. However, a dimethyl analogue produced from 3-*methylquinoline*-2-*aldehyde* and potassium cyanide is more soluble, and a molecular-weight determination in camphor indicates that its molecular formula is $C_{22}H_{16}O_2N_2$, *i.e.*, that it corresponds with a molecular formula of $C_{20}H_{12}O_2N_2$ for the original compound. Thus in its formation from two molecules of quinoline-2-aldehyde two hydrogen atoms must be lost: $2C_{10}H_7ON = C_{20}H_{12}O_2N_2 + 2H$. This was established by the observations that added methylene-blue is reduced and the compound produced when an aqueous-alcoholic solution of quinoline-2-aldehyde is treated with aqueous potassium cyanide.

The experiments of Linsker and Evans (*loc. cit.*) together with the chemical evidence which we have obtained (lack of carbonyl or hydroxyl group reactivity) indicate that the compound is neither quinaldoin (I) nor quinaldil (II). Furthermore, Mr. B. H. Thewlis working in this laboratory has independently synthesised quinaldil (II), which is identical with the compound of Linsker and Evans, from 1 : 2-di-2′-quinolylethane. Another possibility, the keten structure (III), is eliminated on account of the stability of the compound towards reagents such as alcohol. The oxidation of the substance to quinaldinic acid necessitates the conclusion that only the α-carbon atoms and possibly the nitrogen atoms are involved in the fusion of the two quinoline nuclei which the molecular weight indicates. The physical properties of the substance (insolubility in common solvents and high m. p.) indicate that it has a salt-like structure. This, together with the fact that the obvious structures have been eliminated, leads us to suggest that the compound has the structure of a zwitterion. A few of the contributing canonical forms, (IV), (V), (VI), and (VII), are shown below. This structure, though revoluntionary, is of the type called " meso-ionic " by Baker, Ollis, and Poole (*J.*, 1949, 307), and is analogous to the formulæ which they have proposed for the sydnones. A much closer parallel is the zwitterion formula (VIII)—(IX), suggested by Krollpfeiffer and Schneider (*Annalen*, 1937, **530**, 34) for Besthorn's red, a compound produced by the decarboxylation of quinaldinic acid in acetic anhydride (Besthorn and Ibele, *Ber.*, 1904, **37**, 1236; 1905, **38**, 2127). Since in the resonance hybrid of the new structure, comprising (IV), (V), (VI), and (VII), there is no actual shift of electronic charge the compound is expected to be colourless. Besthorn's red provides an interesting contrast, since in the molecule of this compound the positive charge is asymmetrically distributed across a conjugated system. On reaction with a strong acid (*e.g.*, sulphuric or perchloric) the compound (IV) can act as a diacidic base yielding a cation capable of formulation in terms of canonical forms such as (X) and (XI). Consequently, on account of the asymmetry and mobility of the positive charge, it is not surprising that this cation is yellow.


(IV.)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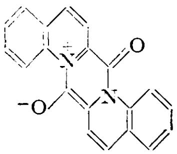
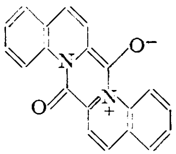
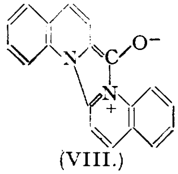
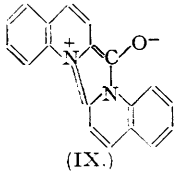
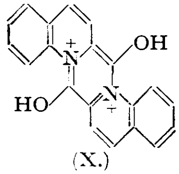
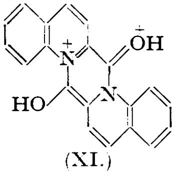

(VI.)


(VII.)

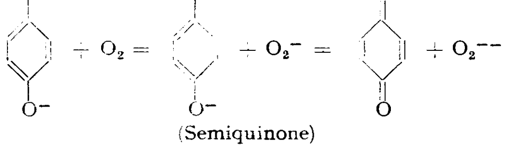

(VIII.)


(IX.)

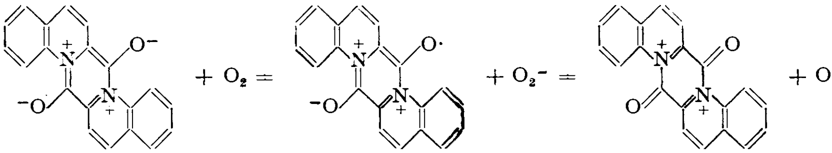

(X.)


(XI.)

The autoxidation and alkaline hydrolysis of the compound are particularly suggestive of the meso-ionic formula advanced. The structure suggested for the compound is similar to that of a quinol ion, and it is well known (Weissberger, Thomas, and Valle, *J. Amer. Chem. Soc.*, 1943, **65**, 1489) that in alkaline solution quinols readily undergo autoxidation to yield the corresponding quinones :


(Semiquinone)

A similar autoxidation of our compound would proceed as follows :

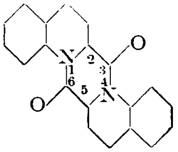


(XII.) (XIII.)

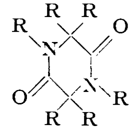
The product (XIII) is the cation of an acylquinolinium hydroxide, and hence would be expected to hydrolyse readily to quinaldinic acid. The formation of a semiquinone type of ion (XII) as an intermediate is suggested by the deep colour which appears and then fades as the reaction with alkali proceeds. The reaction with aniline producing the anilide of quinaldinic acid possibly involves a similar oxidative attack.

We have given the trivial name quinocoll to the structure, by analogy with the compound pyrocoll (XVIII) (Weidel and Ciamician, *Monatsh.*, 1880, **1**, 279; Ciamician and Silber, *Ber.*, 1884, **17**, 106) which has almost the same central ring fused to two pyrrole nuclei. The quinoline rings are numbered in the normal manner, so that the compounds (XXIII) and (XXIV) are respectively 3 : 3′-dimethyl- and 6 : 6′-dimethylquinocoll. We feel that for convenience it is desirable to have such a name, though it is also clearly necessary to have a systematic description. The Editor has suggested that the parent compound (IV) be called 3 : 6-dihydroxydiquinolino-(1′ : 2′-1 : 2)(1″ : 2″-4 : 5)pyrazinium dihydroxide bisanhydro-salt, and that the numbering be as indicated (XIV). Thus the compound is regarded as the internal salt resulting from the dehydration of a phenolic ammonium hydroxide.

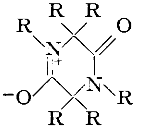
It is of interest to compare the central ring in this new structure with that in the diketopiperazines (XV), (XVI), and (XVII), and in the compound called pyrocoll (XVIII), (XIX), and (XX) (*idem, ibid.*). The difference is to be found in the fact that the new structure is completely aromatic, the central ring containing six non-localised electrons. In the diketopiperazines and in pyrocoll the central ring contains only four non-localised electrons. This difference is reflected in the alkaline hydrolysis of these compounds, pyrocoll yielding pyrrole-2-carboxylic acid directly, but quinocoll undergoing simultaneous autoxidation and hydrolysis to yield quinoline-2-carboxylic acid.



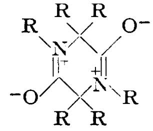
(XIV.)



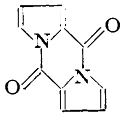
(XV.)



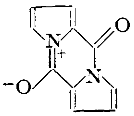
(XVI.)



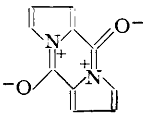
(XVII.)



(XVIII.)

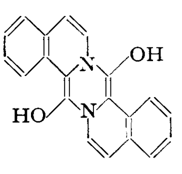


(XIX.)

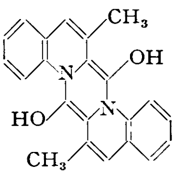


(XX.)

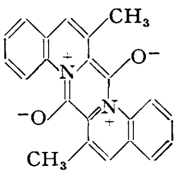
The reaction of quinoline-2- and *iso*quinoline-1-aldehydes with potassium cyanide to yield quinocolls appears to be quite general. Under these conditions *iso*quinoline-1-aldehyde and 3-methylquinoline-2-aldehyde yield the *dihydro*-derivatives (XXI) and (XXII), which exhibit none of the reactions of keto-compounds. Both these compounds are thermochromic, being



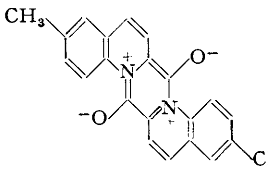
(XXI.)



(XXII.)



(XXIII.)

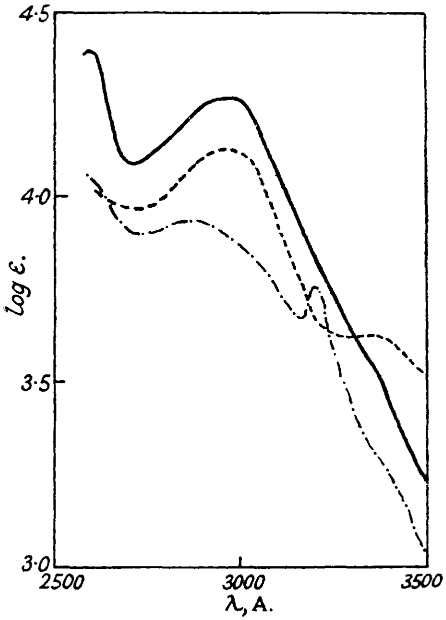


(XXIV.)

colourless in cold alcoholic solution and passing reversibly on being heated through yellow and orange to deep red. Both readily reduce methylene-blue, and (XXII) is oxidised by air to 3 : 3′-*dimethylquinocoll* (XXIII). This compound does not readily undergo autoxidation and hydrolysis with alkali, possibly owing to a steric effect of the methyl groups adjacent to the central ring. 6-*Methylquinoline*-2-*aldehyde* reacts with potassium cyanide to yield 6 : 6′-*dimethylquinocoll* (XXIV) directly.

The isolation of dihydro-compounds which are readily oxidised to quinocolls indicates that the formation of the meso-ionic structure occurs by dimerisation of the quinoline-2-aldehyde under the influence of cyanide-type ions, followed by atmospheric oxidation of the resulting dihydro-derivative. The processes involved are illustrated in a simple manner by the following tentative mechanism. An analogy for the initial addition is provided by the reaction between quinoline and benzaldehyde in sunlight, which yields 1-benzoyl-1 : 2-dihydroquinoline (Benrath, *J. pr. Chem.*, 1906, **73**, 384).

FIG. 1.

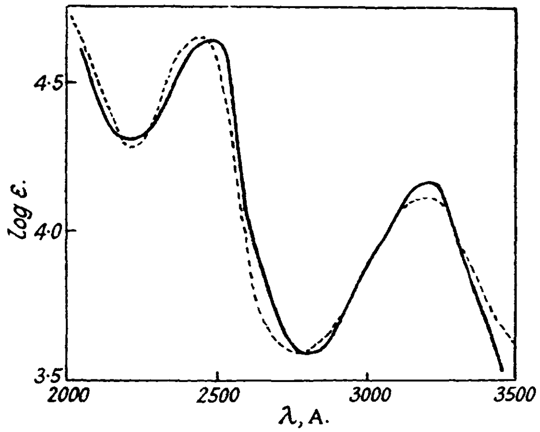


——— *Absorption spectrum of quinocoll in dioxan.*

- - - - *Absorption spectrum of* 3 : 3′-*dimethylquinocoll in dioxan.*

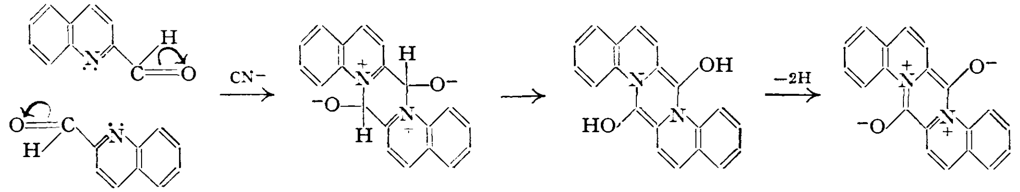
— · — · *Absorption spectrum of* 3 : 3′-*dimethyldihydroquinocoll in dioxan.*

FIG. 2.



——— *Absorption spectrum of quinocoll in* 30% *sulphuric acid.*

- - - - *Absorption spectrum of* 3 : 3′-*dimethylquinocoll in* 30% *sulphuric acid.*



The ultra-violet absorption spectra of quinocoll and its 3 : 3′-dimethyl analogue in dioxan and in 30% sulphuric acid (Figs. 1 and 2) leave little doubt that the compounds have analogous structures. The spectrum of 3 : 3′-dimethyldihydroquinocoll in dioxan (Fig. 1) is very similar to those of ordinary quinoline derivatives, and differs markedly from the spectra of the quinocolls.

EXPERIMENTAL.

(M. p.s are uncorrected. Analyses are by Mr. F. C. Hall. Absorption spectra are by Dr. F. B. Strauss of Oxford.)

ωω-Dibromoquinaldine *.—ωωω-Tribromoquinaldine (48·0 g.) was heated in tetralin (80 ml.) at 100° for 12 hours. The resulting brown crystalline mass was diluted with light petroleum, and the light-brown crystals (34·4 g.) were recrystallised from alcohol. ωω-Dibromoquinaldine was obtained as colourless needles, m. p. 119—120°. Hammick (*J.*, 1926, 1302) records m. p. 120°.

Quinocoll [3 : 6-*Dihydroxydiquinolino*(1′ : 2′-1 : 2)(1″ : 2″-4 : 5)*pyrazinium Dihydroxide Bisanhydrosalt*] (IV).—(a) *By the action of potassium cyanide on quinoline-2-aldehyde* (Henze, *loc. cit.*; Kaplan, *loc. cit.*). The compound separated from pyridine as pale yellow needles, m. p. 266—267°. After treatment of a hot pyridine solution with a drop of acetic anhydride the compound crystallised as colourless needles, m. p. 266—267°. Henze (*loc. cit.*) gives m. p. 261°; Kaplan (*loc. cit.*) gives m. p. 269—271°.

(b) *By the decarboxylation of picolinic or quinaldinic acid in quinoline-2-aldehyde.* A mixture of picolinic or quinaldinic acid (0·2 g.) and quinoline-2-aldehyde (1·0 g.) was heated at 150—165° for 10 minutes. Carbon dioxide was evolved and a vigorous reaction occurred, during which the mixture darkened and completely solidified. The mass of dark brown needles was collected, washed with alcohol, and recrystallised several times from pyridine (plus a drop of acetic anhydride to remove the colour). The compound (0·7 g.) was thus obtained as colourless needles, m. p. 266—267°, unchanged on admixture with the compound obtained from the action of potassium cyanide on quinoline-2-aldehyde (Found: C, 76·9; H, 4·0; N, 9·2. Calc. for $C_{20}H_{12}O_2N_2$: C, 76·9; H, 3·85; N, 9·0%). The compound is slightly soluble in hot ethyl alcohol, glacial acetic acid, benzene, or chloroform, but almost insoluble in water, acetone, or light petroleum. It crystallises well from dioxan or from 2-methoxyethanol. It is soluble in concentrated hydrochloric or sulphuric acid with production of a yellow colour. It is insoluble in cold dilute alkalis.

The compound is unaffected under a variety of conditions by acetic anhydride, acetyl chloride, benzoyl chloride, phenylhydrazine, 2 : 4-dinitrophenylhydrazine, or bromine. It forms no picrate.

The *perchlorate* separated from a mixture of acetic and 60% perchloric acid as small yellow prisms, m. p. (rapid heating) 222—223° (decomp.), which were dried at 50° in a vacuum (Found: Cl, 14·4. $C_{20}H_{12}O_2N_2,2HClO_4$ requires Cl, 13·8%).

Permanganate Oxidation of Quinocoll.—A solution of quinocoll (0·5 g.) in a mixture of pyridine and water (20 ml. each) was treated at 90° during 2 hours with potassium permanganate (2·0 g.) in water (10 ml.). The precipitated manganese dioxide was collected and washed with hot water, and the colourless filtrate made just acid and again filtered. Treatment with excess of copper sulphate solution yielded a greyish-blue precipitate of copper quinaldinate, which was washed with hot water and dried at 100° (0·5 g., 77%). The copper salt was converted into the crystalline sodium salt from which the hydrochloride of quinaldinic acid was obtained as colourless needles (from alcohol), m. p. 192—196° (decomp.).

Autoxidation and Alkaline Hydrolysis of Quinocoll.—Quinocoll (0·5 g.) in hot dioxan (20 ml.) was treated with a solution of potassium hydroxide (2·0 g.) in water (3 ml.). A vigorous reaction occurred and the solution became dark brown. The mixture was boiled under reflux for 30 minutes, during which the colour faded appreciably. The aqueous layer of potassium hydroxide was separated and proved to contain no potassium quinaldinate. The dioxan layer was evaporated under reduced pressure, and the resulting potassium quinaldinate (0·4 g., 60%) converted into the hydrochloride of quinaldinic acid, m. p. 189—194° (decomp.).

Action of Aniline on Quinocoll.—Quinocoll (0·5 g.) was heated under reflux with redistilled aniline (15 ml.) for 4 hours. Initially the solution became very dark brown, but finally it had a clear yellowish-brown colour. Distillation with steam removed aniline, and on cooling the residual brown oil solidified. Two crystallisations from alcohol yielded colourless silky needles (0·4 g., 50%), m. p. 138—139° (Found: C, 77·7; H, 4·8; N, 11·0. Calc. for $C_{16}H_{12}ON_2$: C, 77·4; H, 4·8; N, 11·3%). On admixture with an authentic specimen of the anilide of quinaldinic acid (Krollpfeiffer and Schneider, *loc. cit.*) the m. p. was unchanged.

3-*Methylquinoline*-2-*aldehyde*.—β-(3-Methyl-2-quinolyl)acrylic acid (16·0 g.) (Brown, Hammick, and Robinson, *J.*, in the press), sodium carbonate solution (150 ml. of 6%), and benzene (100 ml.) were cooled in ice, stirred vigorously, and treated during 1 hour with powdered potassium permanganate (25·3 g.). The mixture was filtered, the manganese dioxide washed with ether, and the ether–benzene layer separated from the filtrate, washed with water, and dried. Removal of the solvents yielded 3-*methylquinoline*-2-*aldehyde* (6·8 g.) as a slightly yellow crystalline solid. Recrystallisation from light petroleum (b. p. 80—100°) gave flat colourless needles, m. p. 114—115° (Found: C, 77·1; H, 5·3. $C_{11}H_9ON$ requires C, 77·2; H, 5·3%). The 2 : 4-*dinitrophenylhydrazone* separated from xylene–pyridine as fine orange-coloured needles, m. p. 261—262° (Found: N, 19·7. $C_{17}H_{13}O_4N_5$ requires N, 19·9%).

3 : 3′-*Dimethyldihydroquinocoll* (XXII). *Action of Potassium Cyanide on* 3-*Methylquinoline*-2-*aldehyde*.—A hot solution of 3-methylquinoline-2-aldehyde (1·5 g.) in alcohol (15 ml.) and water (15 ml.) was treated under nitrogen with a solution of potassium cyanide (0·2 g.). The solution immediately became dark brown and a crystalline solid separated. Several recrystallisations from alcohol yielded 3 : 3′-*dimethyldihydroquinocoll* (0·9 g.) as colourless rectangular prisms, m. p. 154—155° to a dark red melt (Found: C, 77·65; H, 5·45. $C_{22}H_{18}O_2N_2$ requires C, 77·2; H, 5·3%). The compound is thermochromic. Its cold alcoholic solution is colourless, but on being heated it passes slowly through yellow and orange to deep red. These colour changes are reversed as the solution cools. The compound is soluble in acids but not in alkalis. In air it slowly becomes light brown and falls to a powder. A hot alcoholic solution of the dihydro-compound quickly reduces and decolorises methylene-blue. It does not react with phenylhydrazine.

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* The free-radical mechanism of this reaction will be discussed in a later publication.

3 : 3′-*Dimethylquinocoll* [3 : 6-*Dihydroxy*-3′ : 3″-*dimethyldiquinolino*(1′ : 2′-1 : 2)(1″ : 2″-4 : 5)-*pyrazinium Dihydroxide Bisanhydro-salt*] (XXIII).—When 3 : 3′-dimethyldihydroquinocoll is kept in air for several days the colourless rectangular prisms gradually change into a light-brown powder, which is only very slightly soluble in boiling alcohol. Recrystallisation from alcohol–pyridine yields 3 : 3′-*dimethylquinocoll* as slightly brown needles, m. p. 220—221° [Found : C, 77·4; H, 4·8%; *M* (cryoscopic in camphor), 330. $C_{22}H_{16}O_2N_2$ requires C, 77·65; H, 4·7%; *M*, 340]. The compound is readily soluble in cold pyridine or dioxan. Its solution in propyl alcohol yields no colour or precipitate with 2 : 4-dinitrophenylhydrazine sulphate.

6-*Methyl-2-tribromomethylquinoline*.—Bromination of 2 : 6-dimethylquinoline (35·0 g.) (Doebner and Miller, *Ber.*, 1883, **16**, 2465) by the method of Hammick (*J.*, 1923, 2882) yielded 6-*methyl*-2-*tribromomethylquinoline* (54·7 g.), which separated from acetic acid as colourless narrow plates, m. p. 132—133° (Found : Br, 61·0. $C_{11}H_8NBr_3$ requires Br, 60·9%).

6-*Methyl-2-dibromomethylquinoline*.—The above tribromo-compound (50·0 g.) was heated at 100° with tetralin (85 ml.) for 12 hours. The mixture was diluted with light petroleum (b. p. 40—60°) and kept at 0° overnight. The light-brown crystals (24·9 g.) were recrystallised from alcohol. 6-*Methyl*-2-*dibromomethylquinoline* was thus obtained as colourless needles, m. p. 85—86° (Found : Br, 51·0. $C_{11}H_9NBr_2$ requires Br, 50·8%).

6-*Methylquinoline-2-aldehyde*.—6-Methyl-2-dibromomethylquinoline (6·0 g.) was hydrolysed by means of silver nitrate (method of Hammick, *J.*, 1926, 1302). Steam-distillation from slightly alkaline solution yielded a colourless oil which solidified in the distillate. The *aldehyde* (2·7 g.), which was isolated by means of ether, separated from light petroleum (b. p. 40—60°) as colourless elongated plates, m. p. 105—106° (Found : C, 77·5; H, 5·3. $C_{11}H_9ON$ requires C, 77·2; H, 5·3%).

6 : 6′-*Dimethylquinocoll* [3 : 6-*Dihydroxy*-6′ : 6″-*dimethyldiquinolino*(1′ : 2′-1 : 2)(1″ : 2″-4 : 5)-*pyrazinium Dihydroxide Bisanhydro-salt*] (XXIV).—6-Methylquinoline-2-aldehyde (1·7 g.) was treated in hot aqueous alcohol with an aqueous solution of potassium cyanide (0·2 g.), and the mixture heated under reflux for 15 minutes. The reddish-brown precipitate was collected, washed with water, and crystallised several times from pyridine or dioxan. 6 : 6′-*Dimethylquinocoll* was obtained as small slightly yellow plates, m. p. 250—251° (Found : C, 77·8; H, 4·9. $C_{22}H_{16}O_2N_2$ requires C, 77·65; H, 4·7%).

*Dihydro*iso*quinocoll* (XXI). *Action of Potassium Cyanide on* iso*Quinoline*-1-*aldehyde*.—A hot solution of *iso*quinoline-1-aldehyde (1·0 g.) (Barrows and Lindwall, *J. Amer. Chem. Soc.*, 1942, **64**, 2430) in aqueous alcohol (50 ml.) was treated with an aqueous solution of potassium cyanide (0·2 g.) and heated under reflux for 15 minutes. The mixture was cooled and the brown crystals (1·0 g.) were collected, washed, and dried. Several recrystallisations from alcohol yielded *dihydro*iso*quinocoll* as fine slightly brown needles, m. p. 163—164° to a dark red melt (Found : C, 76·5; H, 4·65; N, 8·9. $C_{20}H_{14}O_2N_2$ requires C, 76·4; H, 4·45; N, 8·9%). The compound shows thermochromism, its alcoholic solution passing reversibly on being heated through yellow and orange to deep red. The compound quickly reduces methylene-blue in aqueous alcohol. It yields no hydrazone with 2 : 4-dinitrophenylhydrazine sulphate in alcohol.

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