593. *Structure and Colour in the Indolo*(3′ : 2′-3 : 4)*quinoline and the 1 : 2-Dihydroquinolino*(3′ : 2′-3 : 4)*quinoline Series.*

By Frederick G. Mann.

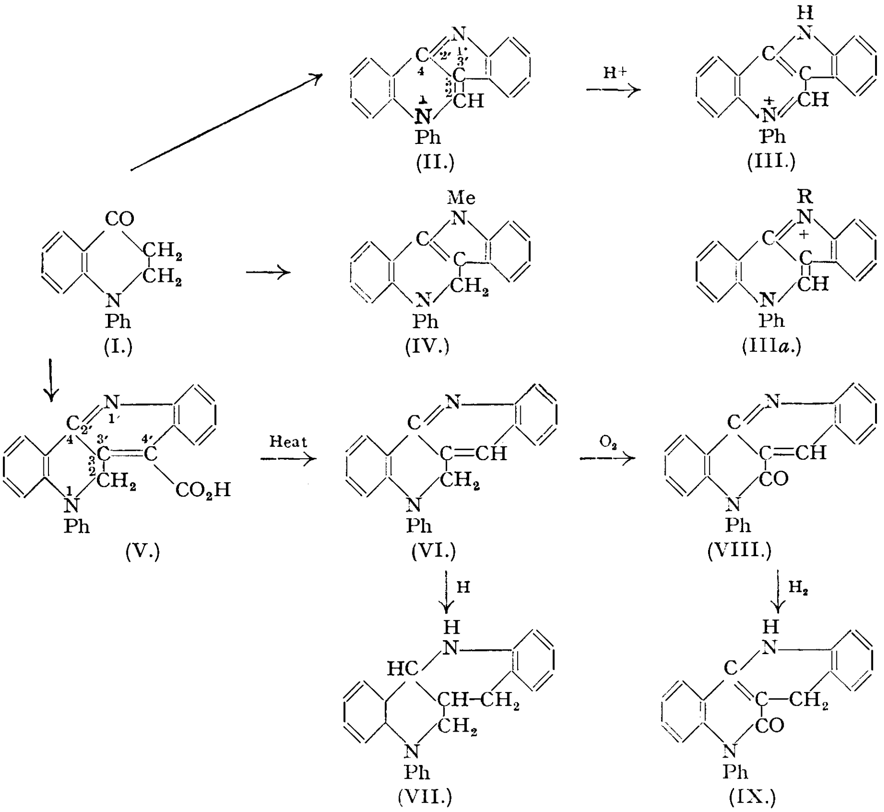
Further evidence is adduced to show that the formation of an indole from the phenylhydrazone of 4-keto-1-phenyl-1 : 2 : 3 : 4-tetrahydroquinoline (I) is accompanied by dehydrogenation to form the yellow 1-phenyl-*ψ*-indolo(3′ : 2′-3 : 4)quinoline (II), which however on salt formation gives the colourless 1-phenylindolo(3′ : 2′-3 : 4)quinolinium cation (III).

4-Keto-1-phenyl-1 : 2 : 3 : 4-tetrahydroquinoline condenses with isatin in alkaline solution to give the deep-red 1-phenyl-1 : 2-dihydro-quinolino(3′ : 2′-3 : 4)quinoline-4′-carboxylic acid (V), which however gives yellow salts and esters; there is little doubt that the free acid has a resonance zwitter-ion structure fundamentally different to that of its salts. The acid on heating undergoes decarboxylation to the yellow 1-phenyl-1 : 2-dihydroquinolino(3′ : 2′-3 : 4)-quinoline (VI), which forms deep-red salts with acids. These salts have a structure parallel to that of the previous acid (V), whilst that of the free base (VI) is analogous to that of the previous salts and esters: hence the similar colours of the two sets of derivatives.

The above base (VI) undergoes a remarkably ready oxidation to the cream-coloured 2-keto-1-phenyl-1 : 2-dihydroquinolino(3′ : 2′-3 : 4)quinoline (VIII), which gives orange-yellow salts. The structure of this compound and its derivatives has been investigated chemically and spectroscopically.

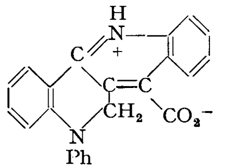
It has already been briefly noted by Cookson and Mann (this vol., p. 67) that the phenylhydrazone of 4-keto-1-phenyl-1 : 2 : 3 : 4-tetrahydroquinoline (I), when subjected to the Fischer indole condensation by boiling with alcoholic hydrogen chloride, gives bright greenish-yellow crystals of 1-phenyl-*ψ*-indolo(3′ : 2′-3 : 4)quinoline (II). The evidence that this compound has the structure (II), *i.e.*, that indole formation has been accompanied by loss of two hydrogen atoms, can be briefly summarised. (*a*) Analytical data indicate consistently that the compound has the formula $C_{21}H_{14}N_2$ in accordance with (II), and not $C_{21}H_{16}N_2$. (*b*) The yellow base gives a colourless hydrochloride, to the cation of which the structure (III) was attributed. It will be noted that the base (II) has a structure which would almost certainly cause colour, but proton addition allows both the indole and the quinoline system to re-establish their normal "aromatic" structure (III) and loss of colour would undoubtedly accompany this structural change to the 1-phenylindolo(3′ : 2′-3 : 4)quinolinium cation. There would clearly be a strong tendency to form this aromatic structure whenever conditions permitted. (*c*) It is known that in similar compounds dehydrogenation may accompany indolisation. Clemo and Perkin (*J.*, 1924, **125**, 1608) have shown that the phenylhydrazone of 4-keto-1 : 2 : 3 : 4-tetrahydroquinoline when boiled with dilute sulphuric acid undergoes a similar change to form the indolo(3′ : 2′-3 : 4)quinoline; in this case the dehydrogenation allows the aromatic structure to be retained and the product is colourless.

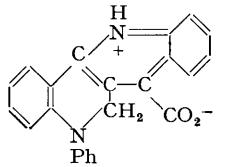
Further evidence for structures (II) and (III) has now been obtained. The base (II) gives a crystalline *hydrogen sulphate* and *hydrogen oxalate*, both of which are colourless; furthermore the addition of even weak acids such as acetic acid to an alcoholic solution of (II) causes an immediate decolorisation, which, it is thus clear, is the normal result of proton addition. It should be noted however that the base (II) gives a *monomethiodide* and a *monoethiodide*, both of which form fine buff-coloured crystals, markedly less intensely coloured than the parent base. The significance of the colour of these quaternary salts is not certain. The formation of quaternary alkyl iodides from similar cyclic amines may be accompanied by colour formation when no fundamental structural change has occurred : for example, the methiodides and ethiodides of quinoline, quinaldine, and *iso*quinoline are yellow. On the other hand, whereas salt formation from the base (II) by addition of acids gives almost solely the colourless quinolinium cation (III), the salt obtained by addition of alkyl halides may possibly have some proportion of the cation (III*a*) in addition to that corresponding to (III), and it is thus the resonance hybrid of these forms which possesses the pale buff colour. These arguments are based on the assumption that quaternary salt formation has occurred on the indole nitrogen atom, for the quinoline nitrogen atom bearing the phenyl group must be markedly inert.

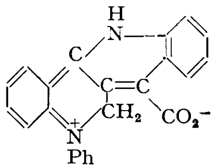


Indirect evidence for the structure of the base (II) comes from the fact that the quinolone (I) readily gives a *phenylmethylhydrazone*, which on indolisation gives 1-*phenyl*-1′-*methyl*-1 : 2-*dihydroindolo*(3′ : 2′-3 : 4)*quinoline* (IV). The structure of this compound is certain, since dehydrogenation cannot now accompany indole formation, and it is significant that this crystalline compound is white, in accordance with structural considerations. Unlike the ψ-derivative (II), it did not form a methiodide : this property again is to be expected of a true *N*-alkylindole.

The compounds obtained from the quinolone (I) by a Pfitzinger condensation present several features of considerable interest. When the quinolone and isatin are boiled together in alkaline solution, subsequent acidification gives 1-*phenyl*-1 : 2-*dihydroquinolino*(3′ : 2′-3 : 4)-*quinoline*-4′-*carboxylic acid* (V) as deep-red crystals (m. p. 210°), which when heated in a vacuum undergo decarboxylation, and the distillate then affords yellow crystals of 1-*phenyl*-1 : 2-*dihydroquinolino*(3′ : 2′-3 : 4)*quinoline* (VI), m. p. 139—141°. Now it is clear that the formal structure (V) should not cause the intense red colour of this carboxylic acid. Furthermore, a solution of the acid when made alkaline becomes yellow, and the slightly soluble yellow *potassium* salt, for example, can be readily isolated; this salt on acidification regenerates the unchanged red acid. When the potassium salt is boiled with methyl iodide, the yellow crystalline *methyl* ester is formed, the nitrogen atom being apparently too inert for quaternary salt formation.

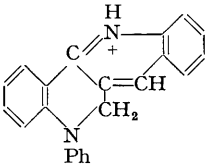

(V*a*.)

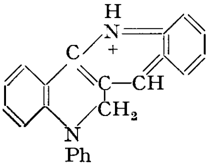

(V*b*.)

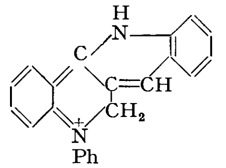

(V*c*.)

These facts indicate strongly that the free acid cannot have the structure (V), but must be a zwitter-ion, which would exist as a resonance hybrid of the canonical forms (V*a*), (V*b*), and (V*c*). The structure of these forms would certainly cause the hybrid to possess a marked colour. The metallic salt and the esters have however the formal structure as (V) and hence possess the much paler colour.

Confirmation of these structural deductions is given by the yellow base (VI), which reverses the above colour changes, *i.e.*, acidification gives a deep-red colour, and the hydrochloride, for example, can be readily isolated as garnet-red crystals. Here there is no doubt that the structure (VI) is correctly assigned to the free base, but that the cation formed by proton addition is a resonance hybrid of the canonical forms (VI*a*), (VI*b*), and (VI*c*) parallel in type to those of the zwitter-ion form of the acid (V).


(VI*a*.)


(VI*b*.)


(VI*c*.)

Further evidence for the above structural changes can also be obtained from the reduction and the oxidation products of the yellow base (VI). The reduction products, although less important than the oxidation products, are described first because their discussion is simpler.

When the base (VI) is hydrogenated, either by the action of sodium and alcohol or by catalytic reduction, 1-*phenyl*-1 : 2 : 1′ : 2′ : 3′ : 4′-*hexahydroquinolino*(3′ : 2′-3 : 4)*quinoline* (VII) is obtained; the crude product has m. p. 105—108°, but recrystallisation ultimately gives a product of m. p. 117°, and it is probable therefore that the initial product is a mixture of *cis*- and *trans*-isomers, from which one isomer is ultimately completely removed by recrystallisation. The notable fact is however that the hexahydro-base (VII) and its hydrochloride are colourless crystalline compounds. This is to be expected, since the base has no structural features that could cause colour, and its salts cannot possess resonance of the type depicted above (VI*a*—*c*). It is noteworthy that the colourless hydrochloride of the hydrogenated base (VII) on exposure to air slowly becomes red, which may indicate atmospheric dehydrogenation to the more stable hydrochloride of the base (VI).

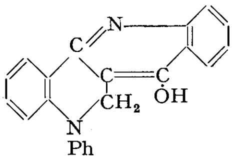
The most remarkable property of the base (VI) is however the extraordinary ease with which it undergoes oxidation. When the crystalline base is heated in a stream of air even at 120° it undergoes complete oxidation to give cream-coloured crystals of a base, m. p. 259°, which has been identified as 2-*keto*-1-*phenyl*-1 : 2-*dihydroquinolino*(3′ : 2′-3 : 4)*quinoline* (VIII). The same oxidation occurs when the base (VI) is treated with a cold acetone solution of potassium permanganate, but not with a cold aqueous-acetone solution of hydrogen peroxide. The oxidised base (VIII) gives an orange-yellow crystalline *monohydrochloride*, in sharp contrast to the deep-red salt of the parent base (VI). This change in colour is not unexpected because, although the cation produced by proton addition to the keto-base (VIII) would probably exist also as a resonance hybrid of three canonical forms corresponding to (VI*a*), (VI*b*), and (VI*c*), the contribution of the last form, having a positive charge on the phenyl-substituted nitrogen atom, would now be very small in view of the fact that the compound (VIII) is really a cyclic amide; hence the colours of such salts should be less intense than those of the base (VI).

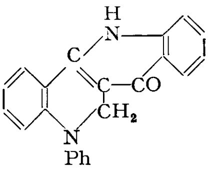
The allocation of the structure (VIII) to this oxidation product receives strong support from the chemical evidence, but is placed beyond doubt by an infra-red spectroscopical examination kindly undertaken by Dr. G. B. B. M. Sutherland. The chemical evidence will be briefly summarised first :

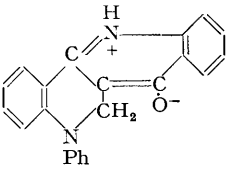
(1) Analytical data for the oxidised base and its salts indicate consistently that it has the formula $C_{22}H_{14}ON_2$, *i.e.*, that oxidation has occurred by addition of one atom of oxygen and the removal of two atoms of hydrogen. Nevertheless the possibility that the two hydrogen atoms have not been removed and that the formula is therefore $C_{22}H_{16}ON_2$ cannot be ignored. If this were the case, three possibilities for the oxidation of the base (VI) would arise : (i) Formation of the ⁚C(OH)· group in the 4′-position giving the compound (X-*A*), which would be tautomeric with the imino-keto-form (X-*B*), and the latter in addition might exist as a stable zwitter-ion (X-*C*). All three forms would of course give the same hydrochloride (X-*D*). (ii) Formation of the ⁚CH·OH group in the 2-position giving the compound (XI). (iii) Formation of the ⁝N → O group in the 1′-position, giving the quinoline 1′-oxide (XII).

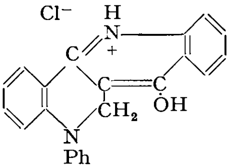
(2) Had oxidation according to (X) or (XI) occurred, the hydrochloride of the oxidised base would have been merely that of the 4′-hydroxy- or 2-hydroxy-derivative respectively of the base (VI), and the colour of these salts should have been closely similar.

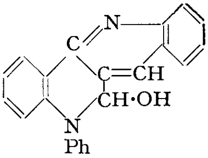
(3) The base (VIII) is unaffected by boiling acetic anhydride or by 2 : 4-dinitrophenylhydrazine. This eliminates (XI) and makes (X-*A*) unlikely.

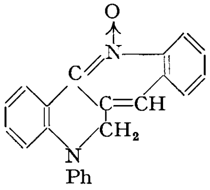

(X-*A*.)


(X-*B*.)


(X-*C*.)


(X-*D*.)


(XI.)


(XII.)

(4) The base (VIII) is unaffected by sodium in boiling ethanol solution, but when subjected to catalytic hydrogenation under vigorous conditions gives a colourless dihydro-derivative without loss of oxygen. It is exceedingly unlikely that the tertiary amine oxide (XII) would not have been reduced to the tertiary amine under these conditions, whereas the amide CO group in (VIII) would almost certainly have remained unchanged. Evidence is given below that this dihydro-derivative has the structure (IX) and hence is 1-*phenyl*-2-*keto*-1 : 2 : 1′ : 4′-*tetrahydroquinolino*(3′ : 2′-3 : 4)*quinoline*.

(5) The increase in m. p. of 119° is in harmony with the oxidation of the cyclic amine group in (VI) to the cyclic amide group in (VIII).

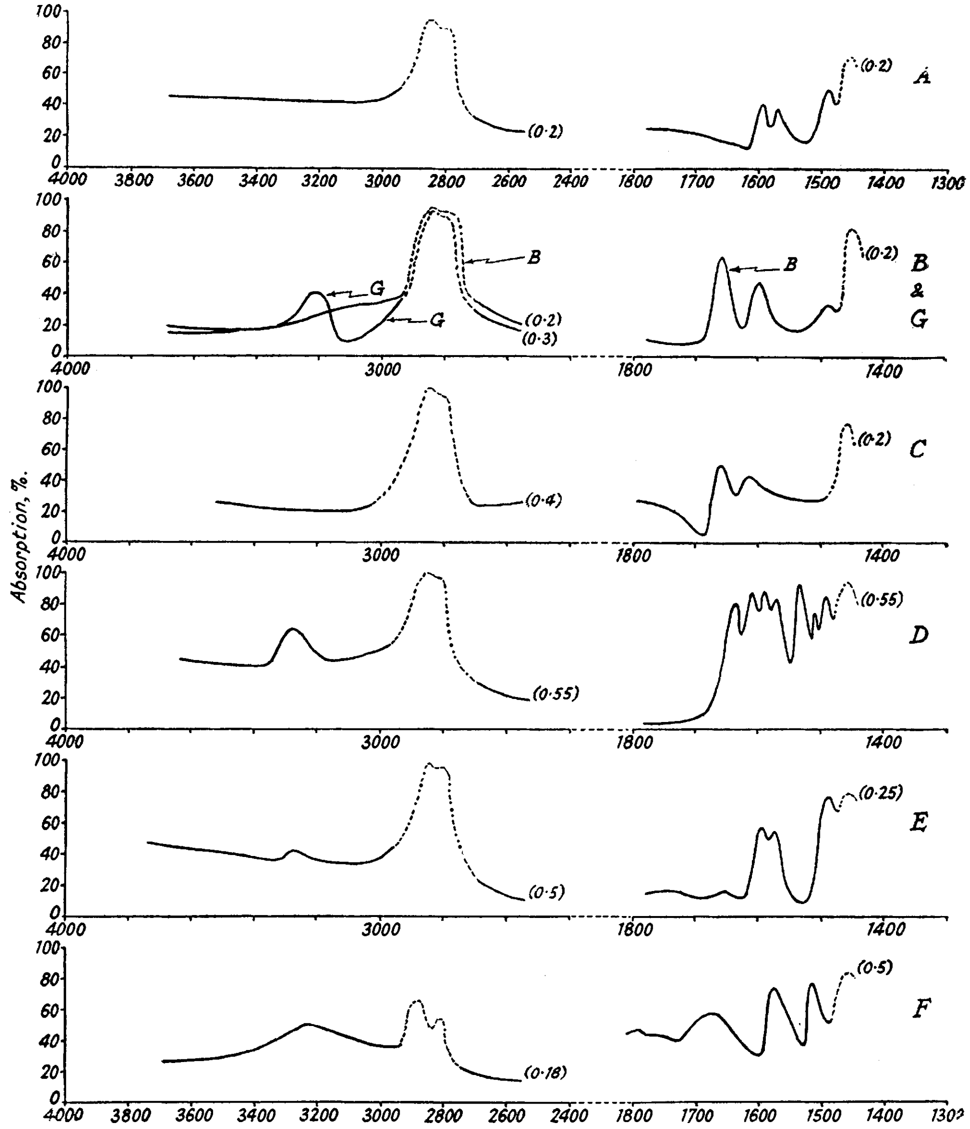
Dr. Sutherland reports : " In order to determine whether infra-red methods would provide evidence from which it might be possible to decide between structures (VIII), (X-*A*), (X-*B*), (X-*C*), (XI), and (XII) for the oxidation product, the infra-red spectra of the following compounds were obtained by Mr. T. S. Robinson, using a Perkin Elmer Model 12 B recording infra-red spectrometer :

(A) The base (VI).
(B) The oxidation product of this base.
(C) The hydrochloride of the oxidation product.
(D) The dihydro-derivative of the oxidation product.
(E) The tetrahydro-derivative (VII) of the base (VI).
(F) Quinoline oxide.
(G) Cholesterol, which was selected as a hydroxy-compound of comparable molecular weight to that of the oxidation product.

" The samples were all used as suspensions in liquid paraffin between rock-salt plates, and the resulting curves are shown in the figure, A—G.

" Comparison of the spectra of the oxidation product (B) and its hydrochloride (C) with that of the base (A) shows that (B) and (C) each possess a strong band at 1660 cm.$^{-1}$ which is absent in (A). The position and intensity of this band indicate that it is most probably due to a CO group, thus favouring structures (VIII) and (X-*B*) as against (X-*A*), (X-*C*), (XI), and (XII). The structures (X-*A*) and (XI) are however completely eliminated by the comparison of (B) and (G), since for roughly equivalent path-lengths the OH group is readily detected in

Infra-red absorption spectra of the following compounds in the regions 1500—1700 *cm.*$^{-1}$ *and* 2600—3600 *cm.*$^{-1}$ *:* (*A*) *The base* (*VI*). (*B*) *The oxidation product of this base.* (*C*) *The hydrochloride of the oxidation product.* (*D*) *The dihydro-derivative of the oxidation product.* (*E*) *The tetrahydro-derivative* (*VII*) *of the base* (*VI*). (*F*) *Quinoline oxide.* (*G*) *Cholesterol.*



Numerals recorded on each curve give the approximate thickness (*mm.*) *of the layer of paraffin suspension of the compound. The fraction, by weight, of compound in the suspension lies between* $\frac{1}{6}$ *and* $\frac{1}{4}$ *in all cases except* (*F*) (*quinoline oxide*) *where it is* $\frac{1}{3}$. *Regions of paraffin absorption are shown thus* - - - - - -. *The broad band in* (*F*) *centred on* 3210 *cm.*$^{-1}$ *probably arises from water due to the hygroscopic nature of quinoline oxide.*

cholesterol (G) by the band at 3210 cm.$^{-1}$, of which no sign is found in the spectrum of (B), the oxidation product. Independently of this, however, the three structures (X-*A*), (X-*B*), and (X-*C*) are eliminated, because no sign of any OH frequency is found in the spectrum of the hydrochloride (C) of the oxidation product, whereas the hydrochloride of the above three structures must have the hydroxy-structure (X-*D*).

" Next, the structure (XII) is eliminated by comparing spectra of (B) and (F). The 1660-cm.$^{-1}$ band has been shown to be associated with the oxidation product (*i.e.*, it cannot arise from the benzene rings or from $C{=}C$ or $C{=}N$ bonds); consequently if the structure (XII) were correct, this band must arise from the $N \rightarrow O$ link. It would therefore be expected to appear in the spectrum of quinoline oxide (F), but although the latter does show some absorption in this neighbourhood the shape and intensity of the band are entirely different from the sharp intense absorption shown here by the oxidation product.

" The following points provide further evidence in favour of the structure (VIII) and against the structure (X-*B*). First the position of the CO frequency at 1660 cm.$^{-1}$ is characteristic of cyclic amides, whereas a CO group such as that in (X-*B*) would be expected to have a frequency in excess of 1700 cm.$^{-1}$. Secondly the structure (X-*B*) should show an NH frequency in the spectrum near 3280 cm.$^{-1}$, and this is not observed. Finally, the spectrum (E) of the tetrahydro-derivative (VII) of the base (VI) shows an NH band at 3280 cm.$^{-1}$; the dihydro-derivative of the oxidation product also has this NH band in its spectrum (D) in this position, but shows no indication of an OH band which if present should have appeared close to 3200 cm.$^{-1}$ (cf. cholesterol). This is strong evidence that this dihydro-derivative has the structure (IX), whereas (X-*B*) on hydrogenation would almost certainly have produced an OH group on the C atom in position 4′.

" There is therefore very powerful positive spectroscopic evidence in favour of the structure (VIII) for the oxidation product, and equally strong independent spectroscopic evidence against all the other structures."

In view of these results, the structures of the compounds obtained by the application of the Fischer indole reaction and the Pfitzinger reaction to a number of other cyclic keto-amines, *e.g.*, 4-keto-1-methyl-1 : 2 : 3 : 4-tetrahydroquinoline and 4-ketojulolidine, have been investigated and will be described later.

EXPERIMENTAL.

Salts of 1-*Phenyl*-ψ-*indolo*(3′ : 2′-3 : 4)*quinoline*.—(i) *Hydrogen sulphate*. A cold concentrated aqueous solution of the hydrochloride of (II), prepared as described by Cookson and Mann (*loc. cit.*), was treated with dilute sulphuric acid, and the colourless crystalline precipitate of the *hydrogen sulphate monohydrate* which soon appeared was collected, washed with water, dried in a vacuum, and analysed without delay (Found : C, 61·75; H, 4·6; N, 6·55. $C_{21}H_{14}N_2,H_2SO_4,H_2O$ requires C, 61·5; H, 4·4; N, 6·8%). The crystals, m. p. 284—290° (decomp.), slowly became pale yellow on exposure to light.

(ii) *Hydrogen oxalate*. This was prepared similarly to the above, with however a cold saturated aqueous solution of oxalic acid. The white crystals of the *hydrogen oxalate* which rapidly separated were treated as above, and had m. p. 237—238° (effervescence) (Found : C, 67·2; H, 4·45; N, 7·0. $C_{21}H_{14}N_2,C_2H_2O_4,1\frac{1}{2}H_2O$ requires C, 67·1; H, 4·6; N, 6·8%). The salt was unchanged by rapid recrystallisation from water; it also became pale yellow on exposure to light.

(iii) *Methiodide*. A solution of (II) (0·5 g.) in methyl iodide (5 c.c.) deposited yellow crystals in a few minutes. The mixture was set aside overnight, and the crystals, when collected and recrystallised from methanol, furnished the *methiodide monomethanolate* as yellowish-buff crystals, m. p. 286° when immersed in a preheated bath (Found : C, 58·8; H, 4·3; N, 6·0. $C_{22}H_{17}N_2I,CH_4O$ requires C, 59·0; H, 4·5; N, 6·0%). This compound, when heated at 100°/1 mm. for 3 hours, gave the pure *methiodide* of unchanged m. p. (Found : C, 60·5; H, 4·3; N, 6·6. $C_{22}H_{17}N_2I$ requires C, 60·55; H, 3·9; N, 6·4%).

(iv) *Ethiodide*. A solution of (II) (0·5 g.) in ethyl iodide (5 c.c.) formed two layers in the cold (unlike the methyl analogue) and when set aside for 48 hours deposited only a few crystals. The mixture was therefore heated under reflux for 1 hour and then cooled. The crystals of the *ethiodide* which separated were recrystallised from ethanol, had m. p. 293° (decomp.), and were almost indistinguishable in appearance from those of the methiodide (Found : C, 61·3; H, 4·4; N, 5·6. $C_{23}H_{19}N_2I$ requires C, 61·3; H, 4·25; N, 5·8%).

1-*Phenyl*-1′-*methyl*-1 : 2-*dihydroindolo*(3′ : 2′-3 : 4)*quinoline* (IV).—Solutions of the quinolone (I) in ethanol (30 c.c.) containing a few drops of acetic acid and of *as*-phenylmethylhydrazine (5 g.) in ethanol (5 c.c.) were mixed and boiled under reflux for 1 hour. The solution on cooling deposited the solid 4-*keto*-1-*phenyl*-1 : 2 : 3 : 4-*tetrahydroquinoline phenylmethylhydrazone*, which when recrystallised from methanol afforded bright orange-yellow crystals, m. p. 102—102·5° (Found : C, 81·2; H, 6·7; N, 12·6. $C_{22}H_{21}N_3$ requires C, 80·7; H, 6·45; N, 12·8%). A solution of this hydrazone (6 g.) in ethanol previously saturated with hydrogen chloride (50 c.c.) was heated under reflux for 5 hours, the initial deep-red colour of the solution slowly fading. The cold solution was poured into 10% aqueous sodium carbonate solution, and the mixture extracted with chloroform. The extract was dried (Na_2SO_4) and evaporated, leaving a viscous residual gum. A solution of this gum in methanol containing *ca.* 1% of water was set aside for several days, during which period crystallisation proceeded slowly. The collected crystals were repeatedly recrystallised from ethanol until the above *indolo*(3′ : 2′-3 : 4)*quinoline*

(IV) was obtained as white crystals, m. p. 191° (Found : C, 85·3; H, 6·2; N, 9·0. $C_{22}H_{18}N_2$ requires C, 85·1; H, 5·8; N, 9·0%). These recrystallisations had to be performed rapidly, otherwise the initial deposit of crystals became contaminated with a more soluble impurity which separated more slowly. The residual gum was also distilled at 0·1 mm. presure : the distillate rapidly formed white crystals, which on recrystallisation from ethanol gave (IV), m. p. 189—190°, but the yield was smaller.

A solution of (IV) in methyl iodide was heated under reflux for 3 hours, but the compound (IV) was then recovered unchanged.

4-*Keto*-1-*phenyl*-1 : 2 : 3 : 4-*tetrahydroquinoline Phenylethylhydrazone*.—This *compound* was prepared as the above hydrazone, and after recrystallisation from ethanol formed yellow crystals, m. p. 95° (Found : C, 80·7; H, 7·0; N, 12·5. $C_{23}H_{23}N_3$ requires C, 80·9; H, 6·8; N, 12·3%). Many attempts were made to prepare an indole from this compound under a variety of conditions, but indefinite products were always obtained.

4-*Keto*-1-*phenyl*-1 : 2 : 3 : 4-*tetrahydroquinoline Diphenylhydrazone*.—Similarly prepared from *as*-diphenylhydrazine, this *hydrazone* was obtained as yellow crystals from ethanol, m. p. 160° (Found : C, 83·3; H, 6·2; N, 10·4. $C_{27}H_{23}N_3$ requires C, 83·3; H, 5·95; N, 10·8%). Again no definite products could be obtained on attempted preparation of an indole from this compound.

1-*Phenyl*-1 : 2-*dihydroquinolino*(3′ : 2′-3 : 4)*quinoline*-4′-*carboxylic Acid* (V).—Isatin (3 g.) and the quinolone (I) (4 g.) were added in turn to a solution of potassium hydroxide (3·6 g.) in water (4 c.c.) and ethanol (20 c.c.), which was then heated under reflux for 15 hours. The dark green fluorescent solution was cooled and poured into an excess of dilute acetic acid, a dark red precipitate immediately forming. This precipitate was collected, washed with much water and then ethanol, and was finally recrystallised from boiling ethanol in which it was only sparingly soluble; it was only very slightly soluble in the other usual organic solvents. The 4′-*carboxylic acid* (V) was thus obtained as deep-red needles, m. p. 210° (effervescence) (Found : C, 78·2; H, 5·0; N, 8·1. $C_{23}H_{16}O_2N_2$ requires C, 78·4; H, 4·55; N, 8·0%). This compound undergoes a slow decomposition on storage, particularly on exposure to light. Thus a sample in a securely stoppered tube was kept in the dark for 5 weeks, by which time its brilliant red colour had not appreciably changed, but its m. p. had dropped to 195—197°. Another finely-powdered sample, similarly secured, was exposed to bright daylight for 12 days with occasional shaking; its colour had by then faded to a dull brownish-orange, and on heating it softened at 176° and melted at 188—192°.

The deep-red alcoholic solution of the acid when treated with an excess of alkali immediately changed to bright yellow, this change being reversed on acidification. To prepare the pure *potassium* salt, the powdered, freshly crystallised acid was dissolved in a concentrated aqueous solution of potassium carbonate with gentle warming, a clear yellow solution being ultimately obtained. On cooling, slender yellow crystals of the potassium salt separated; these were collected and twice recrystallised from very dilute potassium carbonate solution. After drying in a vacuum, they softened slightly at 80° and melted at 295—300° (Found: N, 7·0. $C_{23}H_{15}O_2N_2K$ requires N, 7·2%). These crystals when exposed to light darkened slowly in colour to a dull orange. The potassium salt was moderately soluble in warm water, and acidification of the aqueous solution immediately precipitated the original red acid.

When ethanolic solutions of the acid (V) and of a considerable excess of *p*-toluidine were mixed, the solution immediately became yellow. When however in an attempt to isolate the *p*-toluidine salt this experiment was repeated with equimolecular quantities of the acid and amine, the mixed solution remained red and on concentration at room temperature deposited crystals of the unchanged acid (V).

To obtain the *methyl* ester of (V), a mixture of the powdered potassium salt and methyl iodide was heated under reflux for 6 hours, cooled, filtered, and allowed to evaporate. The yellowish-brown residue, when twice recrystallised from methanol, gave bright yellow crystals of the methyl ester, m. p. 139—140°, the m. p. and composition being unchanged by further recrystallisation. These crystals were apparently a *monomethanolate*, although they were unchanged by heating at 60°/0·1 mm. (Found : C, 75·9; H, 5·1; N, 7·3. $C_{24}H_{18}O_2N_2,CH_4O$ requires C, 75·4; H, 5·5; N, 7·0%).

When a mixture of the acid (V) and methyl iodide was boiled under reflux for 6 hours and then allowed to evaporate, the unchanged acid was recovered. No indication was therefore obtained that either the free acid or its methyl ester forms a methiodide.

1-*Phenyl*-1 : 2-*dihydroquinolino*(3′ : 2′-3 : 4)*quinoline* (VI).—The acid (V) was heated cautiously at 0·1 mm. pressure. Vigorous effervescence occurred, and a yellow oil distilled and rapidly solidified. Recrystallisation from ethanol (charcoal) gave the *base* (VI) as magnificent bright yellow crystals, m. p. 139—141° (Found : C, 85·5; H, 5·2; N, 9·2. $C_{22}H_{16}N_2$ requires C, 85·8; H, 5·2; N, 9·1%). If the m. p. of this compound is determined in an acid-bath, the capillary tube should be sealed to protect the substance from acid fumes. An alcoholic solution of the base was yellow with a marked green fluorescence.

The bright yellow crystals of this base on exposure to bright light slowly acquired a dull yellowish-brown colour, and the m. p. fell and became indefinite. When, on the other hand, samples of the crystals were kept in securely stoppered tubes in the dark for many weeks, the bright colour remained apparently unchanged, but the m. p. varied considerably, *e.g.*, for different samples, m. p. 137—144°, 142—147°, 143—149°. One such sample after repeated recrystallisation from ethanol had m. p. 143—147° and its composition was unchanged; another after similar treatment had m. p. 136—143° unchanged by further crystallisation, and had changed slightly in composition (Found : C, 84·4; H, 4·6%). The significance of these changes is still uncertain; they may be due to slow and slight atmospheric oxidation, as it is extremely difficult to remove traces of the less soluble oxidation product (VIII) from (VI) by recrystallisation.

The crystalline base (VI) was dissolved by gentle warming in ethanol previously saturated with hydrogen chloride. The deep-red solution when moderately concentrated in a vacuum deposited garnet-red crystals of the *hydrochloride* which, when recrystallised from ethanolic hydrogen chloride, had m. p. 280° (decomp.) (Found : C, 76·2; H, 5·2; N, 8·2; Cl, 10·0. $C_{22}H_{16}N_2,HCl$ requires C, 76·7; H, 5·0; N, 8·1; Cl, 10·3%).

Many attempts were made to prepare quaternary salts of the base (VI). When a solution of the base in an excess of methyl iodide was heated under reflux for 3 hours, the pale fluorescent yellow colour of the solution slowly turned red—an indication of salt formation. When however the solution was allowed to evaporate spontaneously, the residue on recrystallisation from methanol deposited a small amount of the almost colourless oxidation product (VIII), m. p. 256—258°, described later, the remainder being very soluble. Similarly when a mixture of equimolecular quantities of the base (VI) and methyl toluene-*p*-sulphonate was heated with a solvent at 100—120° for 7 hours, it rapidly developed a deep-red colour, but subsequent recrystallisation of the cold dark sticky product from methanol gave only a small quantity of the compound (VIII), m. p. 257—258°. To suppress this oxidation, a solution of the base (VI) in a mixture of methanol and methyl iodide was sealed in a tube under an atmosphere of nitrogen, and then heated at 80° for 8 hours. The cold deep-red solution was evaporated at room temperature in a vacuum, giving an oily residue which subsequently solidified. One recrystallisation from methanol gave deep-red crystals, which on heating decomposed over a range of temperature, becoming green and finally black at 300—325°; analysis indicated however that the crystals were probably the *hydriodide* of the base (Found : C, 60·1; H, 4·0; N, 6·25. $C_{22}H_{16}N_2$,HI requires C, 60·5; H, 3·8; N, 6·4. $C_{22}H_{16}N_2$,CH_3I requires C, 61·3; H, 4·3; N, 6·2%). The small quantity available and the high solubility prevented further recrystallisation and hence complete identification.

Reduction to 1-*Phenyl*-1 : 2 : 1′ : 2′ : 3′ : 4′-*hexahydroquinolino*(3′ : 2′-3 : 4)*quinoline* (VII).—(*a*) A solution of the base (VI) in ethanol was boiled under reflux while an excess of sodium was added in portions, until the yellow colour of the solution had almost completely faded. The solution was then poured into much distilled water that had been previously boiled and cooled. The cloudy solution was extracted with chloroform, and the extract dried (Na_2SO_4) and evaporated. The crystalline residue of the *hexahydro*-base (VII) after one recrystallisation from ethanol had m. p. 105—108°, but after five such crystallisations had a constant m. p. 117°, and separated as very slender colourless needles (Found : C, 84·5; 84·3; H, 6·3, 6·6; N, 9·0. $C_{22}H_{20}N_2$ requires C, 84·6; H, 6·5; N, 9·0%).

(*b*) An ethanolic solution of the base (VI) containing a platinum catalyst underwent no reduction when treated with hydrogen at atmospheric pressure. When however a solution of the base (VI) (0·267 g.) in ethanol (120 c.c.) with the catalyst was hydrogenated at 75—85°/50 atmospheres for 6 hours, and the cold solution then filtered and evaporated to *ca.* 25 c.c., cream-coloured crystals separated. These had m. p. 110—113°, and after two recrystallisations from ethanol furnished the above colourless hexahydro-base (VII), m. p. 117—117·5° (Found : C, 84·5; H, 6·4%).

When ethanolic solutions of the base (VII) and of hydrogen chloride were mixed and stirred, slender colourless crystals of the *hydrochloride* separated (Found : C, 75·9; H, 6·35; N, 7·95. $C_{22}H_{20}N_2$,HCl requires C, 75·7; H, 6·1; N, 8·0%). These crystals on heating decomposed over an indefinite range of temperature; when exposed to air, they slowly became faintly pink. The mother-liquor when set aside developed a red colour.

Oxidation to 2-*Keto*-1-*phenyl*-1 : 2-*dihydroquinolino*(3′ : 2′-3 : 4)*quinoline* (VIII).—(*a*) The finely powdered base (VI) (1 g.) was heated at 100—120° for 4 hours in a conical flask through which a stream of air was gently sucked, the powdered material being meanwhile gently shaken from time to time. A sample withdrawn from the main bulk had m. p. 215—248°. The heating was next increased to 175° for a further 4 hours, and the product then had m. p. 254—256°. This material, when twice recrystallised from ethanol (charcoal), furnished the pure cream-coloured 2-*keto*-base (VIII), m. p. 259° (Found : C, 81·8; H, 4·6; N, 8·8. $C_{22}H_{14}ON_2$ requires C, 82·0; H, 4·4; N, 8·7%). A mixture of this compound and the original base (VI) when heated began to shrink at 135° and to melt at 162°, and ultimately gave a clear melt at 254°.

The above conditions of oxidation were unnecessarily vigorous in order to ensure complete oxidation. A small sample of the base (VI) was heated in a stream of air at 120° for 2 hours, and the product had then m. p. 250—254°, increased to 258—259° by ethanolic recrystallisation. Another sample was similarly heated in a stream of air so that the temperature rose steadily to 175° and was then maintained there for 2 hours. No fusion was detectable as the temperature approached the m. p. of the base (VI), and the final product on recrystallisation had m. p. 259°. For the oxidation of larger quantities, however, the preliminary heating at 100—120° is advisable, followed by heating at *ca.* 175°.

(*b*) Acetone solutions of the base (VI) (0·5 g.) and of potassium permanganate were shaken together at room temperature for 2 hours, and the brown sludge was removed by filtration. The filtrate, which was bright yellow and therefore still contained some unoxidised base (VI), was treated with more permanganate until no further change was perceptible. The product was evaporated to dryness by gentle heating and added to the previous dried sludge, and the whole thoroughly extracted with much boiling ethanol. The filtrate deposited the pure keto-base (VIII), m. p. 258—260° (0·35 g.) (Found : C, 81·5; H, 4·6%).

Concentrated aqueous hydrogen peroxide (" 20 vols.") was added to an acetone solution of the base (VI), and the clear solution set aside for 24 hours. The crystals which had then separated had m. p. 139—140°, unchanged by admixture with an authentic sample of (VI). An ethanolic solution of (VI) was boiled gently under reflux while the concentrated hydrogen peroxide was added dropwise during 1·5 hours. The solution was set aside overnight, and the crystals which separated proved again to be the unchanged base (VI), m. p. 138—145° (mixed and unmixed).

The keto-base (VIII) is markedly less soluble in boiling ethanol than the base (VI).

The following salts of the keto-base (VIII) were prepared.

Hydrochloride. A stream of hydrogen chloride was led into a boiling suspension of the keto-base (VIII) (0·4 g.) in ethanol (30 c.c.); bright yellow crystals rapidly appeared as the crystals of (VIII) dissolved—the process could be readily followed by eye. After 1 hour, the mixture was cooled, and the bright orange-yellow crystals of the *hydrochloride* collected and recrystallised from ethanol containing hydrogen chloride; they were collected and dried without washing. When heated the crystals became white at *ca.* 240° and then melted at 257—258°; it is probable therefore that dissociation to the base preceded melting (Found : C, 73·3; H, 4·7; N, 7·6; Cl, 9·5. $C_{22}H_{14}ON_2$,HCl requires C, 73·6; H, 4·2; N, 7·8; Cl, 9·9%).

Picrate. When almost saturated ethanolic solutions of the base (VIII) and of picric acid were mixed, well-formed bright yellow crystals of the *picrate* were rapidly deposited, m. p. 223—225° (Found : C, 60·7; H, 3·3; N, 13·0. $C_{22}H_{14}ON_2,C_6H_3O_7N_3$ requires C, 60·9; H, 3·1; N, 12·7%). Attempted recrystallisation of this picrate from ethanol caused dissociation, and the free base (VIII), m. p. 253—258°, was deposited.

Nitrate. A few drops of concentrated nitric acid were cautiously added to a warm aqueous-ethanolic solution of (VIII), and the mixture was then cooled. Bright yellow needles of the *nitrate* separated, m. p. 238—250° (Found : C, 68·65; H, 4·0; N, 10·6. $C_{22}H_{14}ON_2,HNO_3$ requires C, 68·55; H, 3·9; N, 10·9%). The m. p. of the nitrate indicates that considerable dissociation probably precedes melting.

When a solution of the base (VIII) in methyl iodide was heated under reflux for 12 hours and then allowed to evaporate, the residue consisted of unchanged (VIII), m. p. 253—255°. A solution of (VIII) in acetic anhydride was boiled under reflux for 4 hours, and on cooling deposited the unchanged (VIII), m. p. 256—258°. Ethanolic solutions of (VIII) and of 2 : 4-dinitrophenylhydrazine, containing a few drops of acetic acid, were mixed and heated under reflux for 1·5 hours; on cooling, the unchanged (VIII), m. p. 256—258°, was deposited.

Reduction to 2-*Keto*-1-*phenyl*-1 : 2 : 1′ : 4′-*tetrahydroquinolino*(3′ : 2′-3 : 4)*quinoline* (IX).—(*a*) An excess of sodium was added to a boiling solution of the keto-base (VIII), and the mixture then heated under reflux until all the sodium had dissolved (*ca.* 1 hour) and finally poured into previously-boiled distilled water. The unchanged base (VIII) was precipitated.

(*b*) A solution of the keto-base (VIII) (0·3 g.) in ethanol (180 c.c.) containing a platinum catalyst was hydrogenated at 100°/75 atmospheres for 6 hours. The cold filtered solution, which had a magnificent blue fluorescence but was otherwise colourless, was evaporated so that 2 consecutive crops were obtained. These had m. p. 238—257° and 241—258°, respectively, and were identical; they were united and twice recrystallised from ethanol, whereby the colourless *monoethanolate* of the 2-keto-tetrahydro-base (IX) was obtained, m. p. 238—257° (Found : C, 77·5; H, 6·2; N, 7·8. $C_{22}H_{16}ON_2,C_2H_6O$ requires C, 77·8; H, 6·0; N, 7·6%). A similar sample, prepared by hydrogenation for 5 hours, gave the monoethanolate, m. p. 239—256° (Found : C, 77·5; H, 6·1%); when heated at 120°/0·1 mm. for 4 hours, this lost ethanol and gave the pure *base* (IX), m. p. 238—257° (Found : C, 81·7; H, 4·8; N, 8·8. $C_{22}H_{16}N_2O$ requires C, 81·5; H, 5·0; N, 8·6%). A mixture of this base and the base (VIII) (m. p. 258—259°) had m. p. 230—253°. The wide but almost constant range of the m. p. of the base (IX), shown in the above fractions, appears to be a characteristic property; the fact that the ethanolate has the same m. p. indicates that the ethanol is almost certainly lost before the m. p. is reached.

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