The Structure and Properties of Certain Polycyclic Indolo- and Quinolino-derivatives. Part VI.* Derivatives of 1 : 2 : 3 : 4-Tetrahydro-1-methyl-4-oxoquinoline.

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The phenylhydrazone of the above ketone, when subjected to the Fischer indolisation, gives a ψ-indoloquinoline : the diphenylhydrazone gives a true indoloquinoline, in which the ·NMe·CH$_2$· group is readily oxidised to the ·NMe·CO· group, a novel type of oxidation in this series.

The parent ketone, when subjected to the Pfitzinger reaction with alkaline isatin, gives the scarlet quinolinoquinolinecarboxylic acid (IX) which on decarboxylation gives the yellow base (X). Conditions necessary for the " allylic rearrangement " of both compounds have been determined, and the isomeric acids, bases, and monohydrochlorides of each have thus been isolated. This type of isomerism has not previously been detected in such simple compounds.

Both isomeric bases undergo an oxidation similar to that noted above, with the formation of the same product (XVI).

In view of these results, the structure of certain analogous compounds has been briefly reinvestigated.

IN Part I (Mann, *J.*, 1949, 2816) it was shown that 1 : 2 : 3 : 4-tetrahydro-4-oxo-1-phenyl-quinoline (as IV) gave a phenylhydrazone which on Fischer cyclisation gave a yellow ψ-indole, which underwent aromatisation with acids to give colourless salts; further, the oxo-quinoline reacted with isatin in alkaline solution to give a carboxylic acid (as IX), which by decarboxylation gave an amine (as X) in which the ·NPh·CH$_2$· group underwent very ready oxidation to the –NPh·CO– group. In Part II (Mann and Smith, *J.*, 1951, 1898), a novel feature in these reactions appeared : it was shown that 1-oxojulolidine, similarly treated with alkaline isatin, gave an acid undergoing decarboxylation to quinolino-(2′ : 3′-1 : 2)juloline (I), which, however, when heated with acids gave the isomeric base (II), reconverted by heat into (I). Both isomers readily gave the same oxidation product (III).
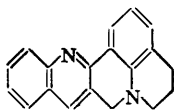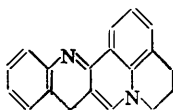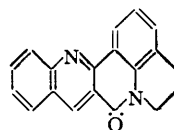
(I)   (II)   (III)

We have now investigated in some detail the comparable reactions of 1 : 2 : 3 : 4-tetra-hydro-1-methyl-4-oxoquinoline (IV) (Allison, Braunholtz, and Mann, *J.*, 1954, 403), as being the simplest *N*-substituted member of this series, and a considerable amplification and extension of these reactions has resulted.

The phenylhydrazone of the 4-oxoquinoline (IV), when boiled with ethanolic hydrogen chloride, undergoes cyclisation to form the yellow 1-methyl-ψ-indolo(3′ : 2′-3 : 4)quinoline (V). The considerable evidence for the identity of (V) as a ψ-indole rests on the following points. (i) The composition and the colour differ from those expected of the corresponding indoloquinoline, which should be colourless. (ii) The compound (V) very readily forms a stable colourless monohydrochloride having, it is suggested, the structure (VI; X = Cl); by this process the molecule undergoes aromatisation, and the structure (VI) would undoubtedly require loss of colour. The compound (V) also readily forms a colourless methiodide and ethiodide, similar to (VI; X = I) but with the ·NH· group replaced by ·NMe· and ·NEt· respectively. (iii) The compound (V), when crystallised from aqueous

* Part V, *J.*, 1952, 1870.

ethanol, forms a pale yellow hydrate, whose colour deepens on dehydration, although sublimation at 0·1 mm. is necessary to obtain the anhydrous (V) : this colour change is rapidly reversed by shaking a suspension of (V) in water, or more slowly by exposing the powdered (V) to the atmosphere.   It is highly probable that the ψ-compound (V), which is clearly an " anhydronium base " (cf. Robinson and Thornley, *J.*, 1924, **125**, 2169 ; Armit and Robinson, *J.*, 1925, **127**, 1604 ; Robinson, *J.*, 1929, 2947), exists in the hydrated form largely as (VI ; X = OH).   Strong evidence for this is obtained from the absorption spectra of (V) in anhydrous light petroleum, in 95% ethanol, and in 0·1N-hydrochloric acid [Fig. 1, in which the intensities in petroleum have been arbitrarily selected, because of the very low solubility of (V) in this solvent].   The spectrum of (V) in petroleum is markedly different from that in the acid, to which, however, the spectrum in ethanol shows considerable resemblance.   (iv) The infra-red spectrum of the ψ-indole (V) shows no bands below 6 μ, and hence the ·NH· group must be absent ; between 6 and 10 μ the spectrum is rather complex, but there are strong bands at 6·10 and 6·25 μ [cf. (XV), p. 384] : the hydrochloride (VI ; X = Cl) was too hygroscopic to allow the presence of the ·NH· band to be

FIG. 1.   FIG. 2.
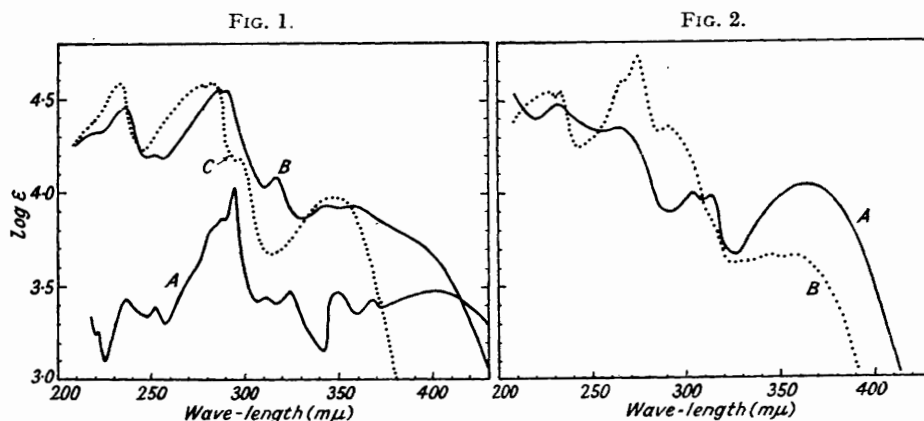
FIG. 1.   1-*Methyl-ψ-indolo*(3′ : 2′-3 : 4)*quinoline* (V) *in* (A) *light petroleum* (ε *values arbitrary*),
(B) *in* 95% *ethanol*, (C) *in* 0·1N-HCl.

FIG. 2.   A, 1 : 2-*Dihydro*-1-*methyl*-1′-*phenylindolo*(3′ : 2′-3 : 4)*quinoline* (VII) *in* 95% *ethanol*.
B, 1 : 2-*Dihydro*-1-*methyl*-2-*oxoquinolino*(3′ : 2′-3 : 4)*quinoline* (XVI) *in* 95% *ethanol*.

decisively determined.   (v) Kermack and Storey's entirely different synthesis (*J.*, 1950, 607) of the ψ-indole (V) affords strong support for the above structure.

The conversion of the phenylhydrazone of (IV) into the ψ-indole (V) involves a dehydrogenation, which could not occur if, for example, the diphenylhydrazone were used. We find that the latter gives 1 : 2-dihydro-1-methyl-1′-phenylindolo(3′ : 2′-3 : 4)quinoline (VII), which, as expected, is colourless, does not form a stable hydrochloride, and forms a methiodide only under " forcing " conditions.   The ultra-violet absorption spectrum of (VII) (Fig. 2) is markedly different from that of (V).

It is noteworthy that the indole (VII), when treated with potassium permanganate in acetone, readily gave the colourless 1 : 2-dihydro-1-methyl-2-oxo-1′-phenylindolo(3′ : 2′-3 : 4)quinoline (VIII), the first example recorded of this type of oxidation in indoloquinolines, although several examples in dihydroquinolinoquinolines are known (cf. Parts I—V).   The oxoquinoline (VIII), being a cyclic acid amide, is weakly basic and did not give a 2 : 4-dinitrophenylhydrazone ; its infra-red spectrum showed a strong band at 6·06 μ, due to the amide CO group [cf. (XVI) below].

When the oxoquinoline (IV) was condensed with isatin in hot alkaline solution, acidification then gave 1 : 2-dihydro-1-methylquinolino(3′ : 2′-3 : 4)quinoline-4′-carboxylic acid (IX) as deep scarlet very slightly soluble crystals, which underwent decarboxylation by heat to form the vividly yellow crystalline 1 : 2-dihydro-1-methylquinolino(3′ : 2′-3 : 4)-quinoline (X), m. p. 98—100°.

It is significant that the scarlet acid (IX) gave a yellow potassium salt (XI), whereas the yellow base (X) gave a stable purplish-red monohydrochloride (XII). There is no doubt therefore that the acid (IX) exists as a zwitterion, receiving contributions from the forms (XIII*A*, *B*, *C*; R = CO$_2$⁻): this zwitterion formation is destroyed in the potassium salt (XI), the colour of which therefore resembles that of the base (X). The hydrochloride (XII) of this base has a cation receiving similar contributions by the forms (XIII*A*, *B*, *C*; R = H) and hence has a colour resembling that of the zwitterion acid (IX).
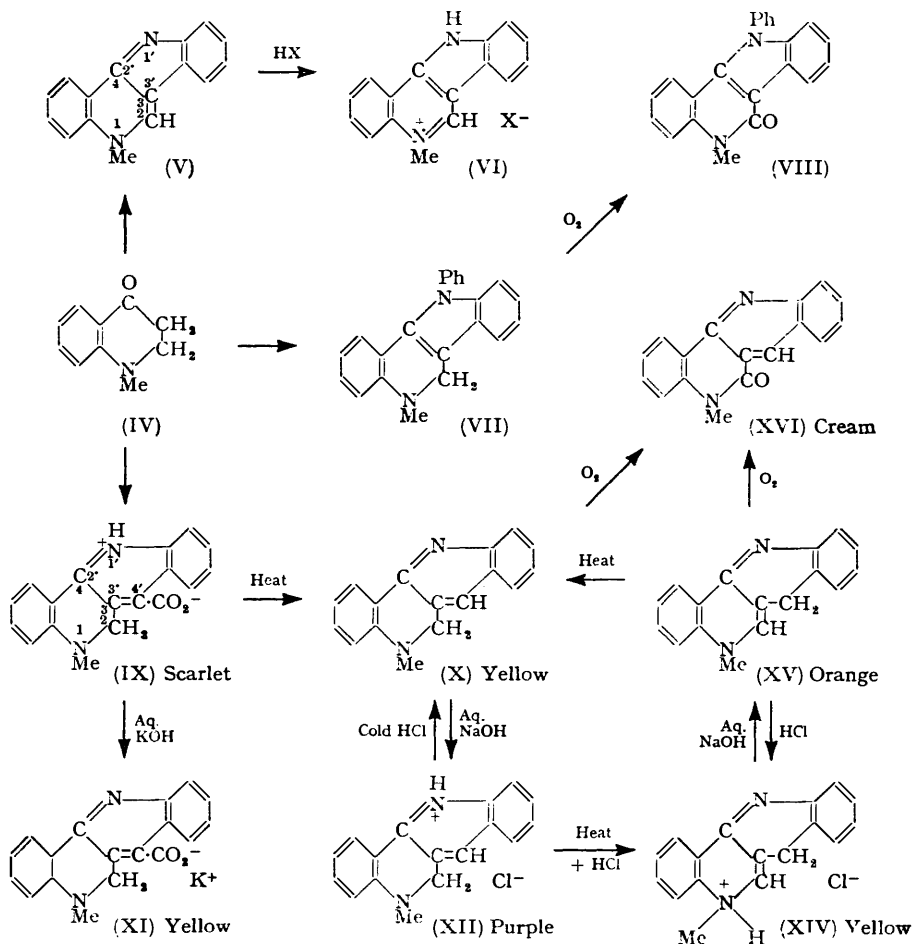
Further confirmation of these structural changes is provided by an acetone solution of the base (X), which when treated with hydrogen chloride rapidly acquired a deep red colour which faded as the passage of chloride continued, and ultimately the colourless solution deposited fine colourless needles, undoubtedly of the dihydrochloride of (X), in which the above resonance could not occur; this salt was so unstable that it reverted to the red monohydrochloride (XII) immediately on removal from the acid solution. Similarly the base dissolved in concentrated hydrochloric acid to a colourless solution, which on dilution with water, ethanol, or acetone immediately became deep reddish-purple. By the use of concentrated solutions of chloroplatinic and chloroauric acid, however, unstable salts corresponding to the dihydrochloride have been isolated.

The acid (IX) and the base (X) both show an isomerism comparable with that of quinolino(2′ : 3′-1 : 2)juloline (I), and which has not hitherto been detected in these simpler compounds. The isomerism of the base (X) will be discussed first.

When a solution of the yellow base (X) in an excess of dilute hydrochloric acid, or an aqueous solution of the purple monohydrochloride (XII), was boiled under nitrogen, the purple colour rapidly changed to reddish-orange and finally to yellow, with a greenish

(XIII*A*)   (XIII*B*)   (XIII*C*)
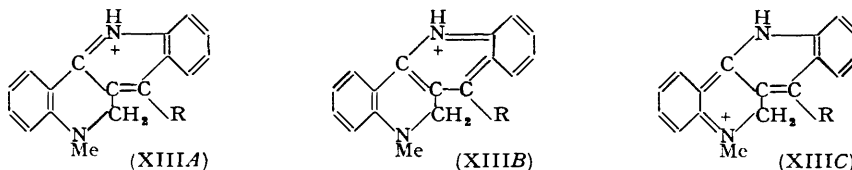
fluorescence. If the solution was then basified, the isomeric 1 : 4'-dihydro-1-methyl-quinolino(3' : 2'-3 : 4)quinoline (XV) separated as bright orange plates, m. p. 155°, considerably less soluble in most solvents than the yellow base (X) : if, however, the solution were set aside, the monohydrochloride (XIV) of the base (XII) separated as bright yellow needles. This salt was also obtained directly by the action of hydrochloric acid on the orange base (XV). There is thus a very marked and significant difference in the colour changes which occur when the yellow base (X) and the orange base (XV)
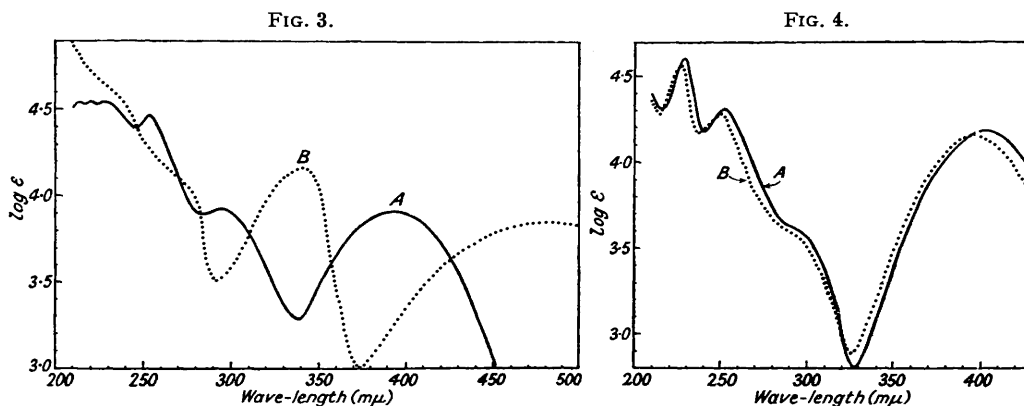

FIG. 3.   FIG. 4.

FIG. 3. 1 : 2-*Dihydro-1-methylquinolino*(3' : 2'-3 : 4)*quinoline* (X) *in* (*A*) 95% *ethanol*, (*B*) *in* 0·1N-HCl.

FIG. 4. 1 : 4'-*Dihydro-1-methylquinolino*(3' : 2'-3 : 4)*quinoline* (XV) *in* (*A*) 95% *ethanol*, (*B*) *in* 0·1N-HCl.

are converted into their respective monohydrochlorides. Furthermore, the base (XV) does not apparently act as a diacidic base : it forms a monochloroaurate under conditions where the yellow base (X) forms a dichloroaurate. This difference in the acidity of the two bases may be due to the fact that the two nitrogen atoms in (X) and (XV) are linked through one and two conjugated systems respectively : in both compounds salt formation on either nitrogen atom would thus tend to deactivate the other, but this effect would be stronger in (XV) than in (X). Finally, the orange base (XV) when heated in a vacuum distilled with conversion into the yellow base (X), the greater thermal stability of which is probably due to its higher degree of aromatic character [cf. (I) and (II)].

Neither the infra-red spectrum of (X) nor that of (XV) shows any significant band below 6 μ, and the ·NH· group is therefore absent in both. Whereas that of (X) shows a moderately strong band at 6·23 μ with weaker bands at 6·16 and 6·34 μ, that of (XV) shows a strong and very sharp band at 6·1 μ, which also appears in that of the ψ-indole (V) : it is probable that this band is due to the conjugated ·N:C·C:C·N· system present in both compounds.

The ultra-violet spectra (Fig. 3) of the base (X) and of its hydrochloride (XII) differ of course very considerably, indicating a marked difference in their fundamental structures. By contrast, the spectra (Fig. 4) of the base (XV) and its hydrochloride (XIV) are almost identical, indicating that salt formation has occurred without structural change: conse-

quently the cation must have been formed by proton addition to the ·NMe· group and not to the 1'-N atom, since the latter addition would allow resonance comparable in character with (XIIIA, B, and C) and thus give a deeply coloured salt.

Oxidation of the base (X) or the base (XV) in acetone with potassium permanganate or in benzene with air readily yielded the cream-coloured 1 : 2-dihydro-1-methyl-2-oxo-quinolino(3' : 2'-3 : 4)quinoline (XVI) : however, the base (X) in acetone containing a large excess of hydrogen peroxide underwent no oxidation during 1 week, a result unaffected by making the solution weakly basic or acidic (a similar result is recorded in Part I).

The infra-red spectrum of (XVI) shows no band below 6 μ, but a strong band at 6·04 μ, ascribed to the carbonyl absorption of the cyclic amide, and apparently identical with that at 6·06 μ shown by the indole derivative (VIII); in the region 6—10 μ the spectrum of (XVI) is considerably simpler than those of the bases (X) and (XV). The ultra-violet absorption spectrum of (XVI) (Fig. 2) is also markedly different from those of (X) and (XII).

The elucidation of the isomerism of the bases (X) and (XV) simplifies that shown by the scarlet acid (IX). When the powdered acid (IX) was ground with cold 20% hydrochloric acid, the latter became intense purple and the former was converted into an even more insoluble deep blackish-purple monohydrochloride. This salt is comparatively unstable, and in warm water or ethanol readily regenerates the acid (IX); when treated with aqueous sodium hydroxide or carbonate, it gives a yellow solution of the sodium salt (as XI), which on the addition of acetic acid deposits again the scarlet acid (IX). The colour and low solubility of this hydrochloride, and its ready regeneration of the acid (IX), all indicate that it has the structure (XVII), in which the resonance cation would again receive contributions from (XIIIA, B, C; R = CO₂H).

When a suspension of the purple monohydrochloride (XVII) in hydrochloric acid was boiled for 30 min., the colour of the solution faded to a pale yellowish-brown, and a highly crystalline insoluble deep green isomeric hydrochloride was deposited. When, however, the mixture was boiled for 7 hr., the solution became very pale and the deep green crystals became yellow without change in composition. It appeared initially that the hot acid treatment had again caused the allylic transformation [as in (XII) ⟶ (XIV)], and that the green and the yellow crystals were the monohydrochlorides (XVIII) and (XIX)
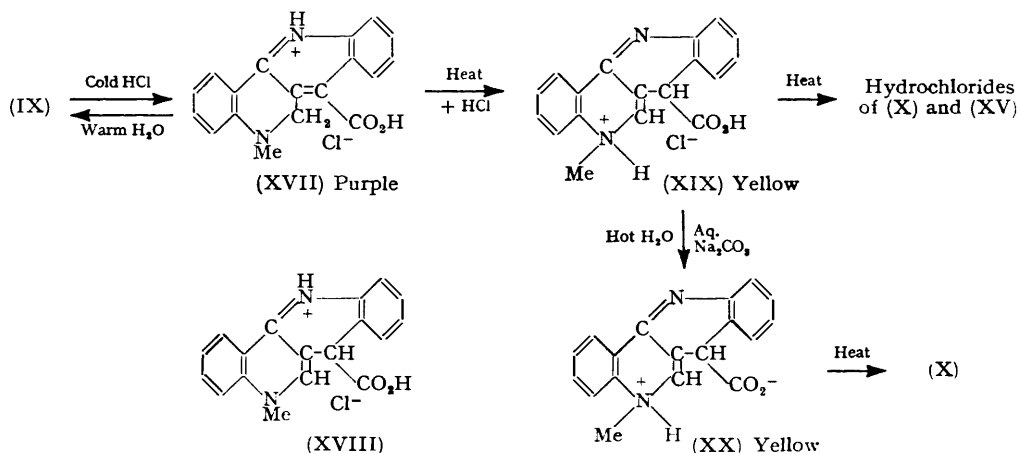
respectively. The following evidence indicates strongly, however, that the green and the yellow crystals represent solely dimorphic forms of the monohydrochloride (XIX). (i) The yellow crystals have m. p. 250°. The green crystals, when heated, become progressively more yellow between 160° and 200° and ultimately melt at 250°; when immersed even at 240°, the colour change occurs before melting. A mixture of the two forms has m. p. 250°. (ii) The green crystals, heated at 200°/0·01 mm., are transformed completely into

the yellow crystals. (iii) The green crystals when finely crushed give a greenish-yellow powder. (iv) The two forms, suspended as a mull in paraffin, give identical infra-red spectra. (v) In no circumstances did the green or the yellow hydrochloride regenerate the scarlet acid (IX) : both dissolved in aqueous sodium hydroxide to give a bright yellow solution, which underwent no appreciable change on treatment with acetic acid [cf. the behaviour of (XVI)]. (vi) A solution of either form in warm dilute sodium carbonate, or in hot water, on cooling, deposited the bright yellow crystalline 1 : 4'-dihydro-1-methyl-quinolino(3' : 2'-3 : 4)quinoline-4'-carboxylic acid (XX) : this acid was also obtained when solutions of the hydrochlorides in aqueous sodium hydroxide were treated with an excess of carbon dioxide.

The above evidence shows almost conclusively that the colour of the green crystals is due solely to surface reflexion and thus has no fundamental constitutional significance. The insolubility (without chemical change) in all liquids prevents observation of the true colour by transmitted light : the properties of the salt are, however, in marked contrast to those of the scarlet acid (IV), which when finely crushed still retains its deep red colour, and, although also insoluble in almost all liquids, gives in boiling acetic acid a very dilute saturated solution which is still deeply red. Examples of compounds existing in two crystalline forms of different colour are not rare. Huang-Hsinmin and Mann (*J.*, 1949, 2908) have recorded two cyanine dyes, each of which exists in two crystalline forms which are markedly different in colour but have the same m. p. and give identical solutions in cold solvents; in one case the particular crystalline form obtained depended solely on the solvent employed for crystallisation.

The constitution (XIX) is allocated to the yellow monohydrochloride, for the alternative structure (XVIII) would possess marked resonance and cause the salt to show intense colour in the solid state and in solution. There is strong evidence that the yellow acid (XX) has the zwitterion structure indicated. The infra-red spectrum of the yellow monohydro-chloride (XIX) shows a strong band at $5 \cdot 85 \mu$, which must be attributed to the carbonyl function of the non-ionised carboxyl group; in phenylacetic acid, of which (XIX) may be regarded as a derivative, the corresponding band occurs at $5 \cdot 87 \mu$. The infra-red spectrum of the acid (XX), shows broad absorption centred at $3 \cdot 05 \mu$, due to $\equiv NH^+$, and has two bands at $6 \cdot 11$ and $6 \cdot 24 \mu$; the latter, which is appreciably the stronger, is attributed to the carboxylate ion of the zwitterion (XX). This band is characteristic of amino-acids having a zwitterion structure and occurs between the limits $6 \cdot 21$—$6 \cdot 38 \mu$; the values for the acid (XX) and its hydrochloride (XIX) may be compared with the corresponding bands shown by phenylglycine and its hydrochloride at $6 \cdot 38$ and $5 \cdot 78 \mu$ respectively. The colour of the acid indicates that the proton has become linked to the ·NMe· group as in (XX).

The yellow acid (XX), when heated at 15 mm., underwent decarboxylation, the yellow base (X) distilling : in these circumstances, the orange base (XV), if initially formed, would of course be converted into (X). The green or the yellow hydrochloride (XIX), when heated in a narrow tube at 250—300°/0·003 mm., gave a sublimate consisting of two zones. The more volatile zone was reddish-purple and when purified gave the hydro-chloride (XII) of the yellow base (X); the less volatile crystalline yellow zone afforded the isomeric hydrochloride (XIV) of the orange base (XV).

The above very full elucidation of the isomerism of indolo- and quinolino-derivatives of 1 : 2 : 3 : 4-tetrahydro-4-oxoquinolines invites a re-examination of earlier examples. It is noteworthy that in the present series four ketones of the 4-oxoquinoline type have given ψ-indoles, the formation of which is apparently dependent structurally on (*a*) an initial conjugation of the ketonic and the amino-group, for example, through an *o*-phenylene group, so that the amino-group and the ·N: group in the phenylhydrazone are also conjugated [1-methyl-4-oxopiperidine phenylhydrazone, which lacks this factor, gives a normal indole (Cook and Read, *J.*, 1945, 399)], and (*b*) an orientation of the two fused heterocyclic rings in the indolo-system such that dehydrogenation will further conjugate the two nitrogen atoms [as in (V)].

The compound obtained by Clemo and Perkin (*J.*, 1924, **125**, 1608) from 1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline is structurally unique, however, since the ketone has the unsubstituted ·NH· group. Although on indolisation two hydrogen atoms were lost, the

properties of the indolo-derivative (colourless crystals) show that the mobile hydrogen has now allowed aromatisation by giving the structure (XXI) and that, as expected, a ψ-indole has not been formed.

(XXI) (XXIIA) (XXIIB) (XXIII)
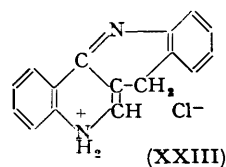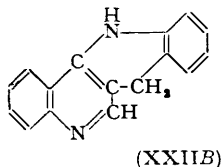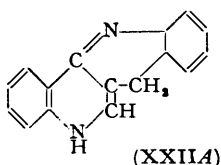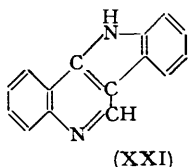
The properties of the red 1 : 2-dihydroquinolino(3′ : 2′-3 : 4)quinoline-4′-carboxylic acid which Clemo and Perkin (*loc. cit.*) obtained by the action of alkaline isatin on their ketone show that its constitution is as (IX). We find, however, that when the purple-red solution of this acid in hydrochloric acid is boiled, the colour rapidly fades and the precipitated yellow material, when suitably crystallised, affords the isomeric 1 : 4-dihydroquinolino(3′ : 2′-3 : 4)quinoline-4′-carboxylic acid (as XX); the same isomerisation is readily induced by heating the red acid at 170—175°/15 mm., and therefore always occurs before the acid melts.

On the other hand, the yellow base obtained by Clemo and Perkin by decarboxylation of their red acid, dissolves in hot hydrochloric acid to a yellow solution, which deposits a bright yellow crystalline monohydrochloride, from which the yellow base can readily be regenerated. These properties indicate strongly that the allylic transformation has already occurred in this base. This is confirmed by the fact that the ultra-violet spectra of this base and our orange base (XV) in ethanol show some resemblance, but in 0·1N-hydrochloric acid are almost identical. Although Clemo and Perkin's base may thus have structure (XXIIA or B), the former is more probable, the monohydrochloride then having the structure (XXIII).

Although the isomerisation of the acid and the base is thus far more rapid in the ·NH· series than in the ·NMe· series, a brief reinvestigation of the ·NPh· series (Mann, *loc. cit.*) indicates great stability. The red 1-phenyl acid (as IX) in ethanolic hydrochloric acid gave a solution which was reddish-purple, with a purplish fluorescence, and was unaffected by 4 hours' boiling under reflux. The yellow 1-phenyl base (as X) in hydrochloric acid gave a deep red solution, which was unaffected by 15 minutes' boiling and on cooling deposited the highly crystalline deep red hydrochloride (as XII). When, however, the deep red solution was boiled for 6 hr., the colour faded to yellowish-brown and, on cooling, the isomeric yellow monohydrochloride (as XIV) crystallised. This salt on treatment with alkali liberated an orange base, which again gave a bright yellow solution in hydrochloric acid.

The mechanism of the allylic rearrangement in the above compounds remains uncertain. Consideration of all the known cases indicates that a hetero-atom in position 1, sufficiently basic for salt formation, is essential for the change. It is tentatively suggested that this change occurs essentially in two steps : (i) proton migration from the 1′- to the 1-nitrogen atom : the positive pole on the latter atom, being adjacent to the allylic methylene group, renders the hydrogen atom of this group more mobile, and catalyses step (ii), in which a proton from position 2 migrates to position 4′. This is supported by the very sluggish isomerisation in the ·NPh· series, where the 1-nitrogen atom is very feebly basic.

EXPERIMENTAL

Certain compounds gave consistent m. p.s only in evacuated sealed tubes, noted as (E.T.) ; in certain cases the tubes had to be immersed in a preheated bath, and the immersion temperature is noted as (I.T. $x°$). Molecular weights were determined ebullioscopically in acetone.

1-*Methyl-ψ-indolo*(3′ : 2′-3 : 4)*quinoline* (V).—Ethanol, saturated with hydrogen chloride (35 c.c.), was added to a mixture of 1 : 2 : 3 : 4-tetrahydro-1-methyl-4-oxoquinoline phenyl-hydrazone (3·2 g.) and ethanol (15 c.c.), which was then boiled under reflux for 5·5 hr., the initial deep orange colour fading considerably. The solution was set aside at 5° overnight, and the

colourless precipitate collected. This was dissolved in water and the solution was basified. The precipitated yellow ψ-indole (V) was recrystallised from aqueous ethanol and finally purified by sublimation at 210—230°/0·1 mm., and obtained as lemon-yellow crystals, m. p. 193·5—194° (Found : C, 82·9; H, 4·9; N, 12·1%; M, 228. Calc. for $C_{16}H_{12}N_2$: C, 82·7; H, 5·2; N, 12·1%; M, 232). Kermack and Storey (*J.*, 1950, 607) give m. p. 195°.

The avidity of the indole for water, presumably with the formation of the hydroxide (VI; X = OH), is shown by the fact that the crude material, even after five recrystallisations from aqueous ethanol, was obtained as pale yellow crystals, which, when dried at 70°/0·1 mm. for 5 hr. or in a vacuum over phosphoric anhydride for several days, darkened in colour with loss of weight and crystal shape, but could not thus be obtained anhydrous (Found, in 3 preparations : C, 81·6, 82·0, 81·5; H, 5·2, 5·35, 4·9%). This material, immersed at 50°, melted at 105—125°, resolidified at 125—150°, and remelted at 195°; immersed at 150°, it immediately melted with effervescence and without resolidification. The sublimed material, exposed to the air for 10 days, became pale and, immersed at 155°, melted with effervescence, resolidified, and remelted at 190—192°.

The colourless precipitate in the above preparation, when recrystallised from ethanol containing 10% of water, afforded colourless hygroscopic needles, m. p. 297° (I.T. 285°), of the *hydrochloride hemihydrate* (VI; X = Cl) (Found : C, 68·8; H, 5·3; N, 10·0. $C_{16}H_{12}N_2,HCl,0·5H_2O$ requires C, 69·2; H, 5·1; N, 10·1%).

The indole gave a *picrate*, yellow needles, m. p. 325° (decomp.), from aqueous dimethyl-formamide (Found : C, 57·4; H, 3·4; N, 15·0. $C_{16}H_{12}N_2,C_6H_3O_7N_3$ requires C, 57·3; H, 3·3; N, 15·2%); it also gave a colourless crystalline sulphate which could not be purified.

A methanolic solution of (V), when boiled with methyl iodide under reflux for 30 min., deposited a cream-coloured solid which, twice recrystallised from methanol, gave 1-*methyl-ψ-indolo*(3' : 2'-3 : 4)*quinoline methiodide*, colourless needles, m. p. 315—320° (E.T., I.T. 307°) (Found : C, 54·4; H, 4·3; N, 7·6. $C_{17}H_{15}N_2I$ requires C, 54·55; H, 4·05; N, 7·5%). The *ethiodide*, similarly prepared with 3 hours' boiling and recrystallised from methanol, formed a methanol *solvate*, colourless plates, m. p. 298° (effervescence, E.T.) (Found : C, 54·1; H, 3·8; N, 6·7. $C_{18}H_{17}N_2I,CH_4O$ requires C, 54·2; H, 5·0; N, 6·65%); when recrystallised from aqueous ethanol and rigorously dried, it formed an ethanol *solvate* of identical m. p. (Found : C, 55·1; H, 4·7. $C_{18}H_{17}N_2I,0·5C_2H_6O$ requires C, 55·4; H, 4·9%). This salt gave the *ethopicrate*, intensely yellow crystals, m. p. 200—260° (E.T., I.T. 155), from aqueous ethanol (Found : C, 58·6; H, 3·8; N, 14·0. $C_{24}H_{19}O_7N_5$ requires C, 58·9; H, 3·9; N, 14·3%).

1 : 2-*Dihydro*-1-*methyl*-1'-*phenylindolo*(3' : 2'-3 : 4)*quinoline* (VII).—A solution of the crude ketone (3 g.) and as.-diphenylhydrazine (5·6 g.) in ethanol (25 c.c.) containing acetic acid (0·3 c.c.) was boiled under reflux for 6 hr. and then diluted with water (*ca.* 5 c.c.). Cooling and vigorous stirring gave the *diphenylhydrazone* (4·5 g.) which after crystallisation from ethanol formed bright yellow crystals, m. p. 112—113° (Found : C, 80·8; H, 6·2; N, 13·1. $C_{22}H_{21}N_3$ requires C, 80·7; H, 6·45; N, 12·85%).

This diphenylhydrazone, when indolised as described above, gave a reaction mixture which was filtered whilst hot and diluted with water; the precipitated solid, when recrystallised from ethanol, afforded 1 : 2-*dihydro*-1-*methyl*-1'-*phenylindolo*(3' : 2'-3 : 4)*quinoline* (VII), cream-coloured plates, m. p. 152—153° (E.T.) (Found : C, 84·8; H, 5·8; N, 9·0%; M, 302. $C_{22}H_{18}N_2$ requires C, 85·15; H, 5·85; N, 9·0%; M, 310). The indole, when slowly heated in an open tube, had m. p. 210—215°, showing that almost complete atmospheric oxidation to (VIII) (see below) had occurred. Ethanolic solutions of the pure indole had a marked blue fluorescence.

All attempts to isolate a hydrochloride of (VII) failed. The indole gave a *picrate*, bright orange needles (from methanol), m. p. 208·5—209° (Found : C, 62·6; H, 4·0; N, 12·85. $C_{22}H_{18}N_2,C_6H_3O_7N_3$ requires C, 62·35; H, 3·9; N, 13·0%); exposure to the air caused the colour to become dull yellowish-brown. When a solution of the indole in an excess of methyl iodide was boiled under reflux for 2 hr., the indole was recovered unchanged. When this solution was diluted with nitromethane and similarly boiled under nitrogen, evaporation gave a solid deposit, which, recrystallised from aqueous methanol, afforded the *methiodide*, colourless needles, m. p. 141° (effervescence) (Found : C, 60·9; H, 4·4; N, 5·95. $C_{23}H_{21}N_2I$ requires C, 61·1; H, 4·7; N, 6·2%).

Oxidation. A solution of the indole (VII) (0·3 g.) in acetone (25 c.c.) was boiled under reflux for 3 hr. during which potassium permanganate in acetone was periodically added to maintain a slight excess. The solution, when filtered, concentrated, and cooled, deposited 1 : 2-*dihydro*-1-*methyl*-2-*oxo*-1'-*phenylindolo*(3' : 2'-3 : 4)*quinoline* (VIII) (0·25 g., 80%), colourless needles,

m. p. 218·5°, from acetone (Found : C, 81·7; H, 5·1; N, 9·0. $C_{22}H_{16}ON_2$ requires C, 81·5; H, 5·0; N, 8·65%). The oxidation also occurred in cold acetone solution, but the product (VIII) was then difficult to free from unchanged material.

The oxo-indole (VIII) is very weakly basic : in ethanolic solution it formed a picrate, pale orange needles, which partly dissociated on attempted recrystallisation.

1 : 2 : 3 : 4-*Tetrahydro*-1-*methyl*-4-*oxoquinoline methylphenylhydrazone*, similarly prepared to the diphenyl analogue, formed bright yellow crystals, m. p. 78—79°, from aqueous ethanol (Found : C, 77·2; H, 7·3; N, 15·9. $C_{17}H_{19}N_3$ requires C, 76·95; H, 7·2; N, 15·85%) : its indolisation was not investigated.

1 : 2-*Dihydro*-1-*methylquinolino*(3′ : 2′-3 : 4)*quinoline*-4′-*carboxylic Acid* (IX).—A solution of the crude ketone (IV) (3 g.) in ethanol (20 c.c.) and water (5 c.c.), to which isatin (3 g.) and potassium hydroxide (3·6 g.) were added, was boiled under reflux in nitrogen for 9 hr., cooled, filtered into 10% aqueous acetic acid (100 c.c.) and set aside overnight. The finely divided precipitated scarlet *acid* (IX) (5 g.) when collected, washed with much water and ethanol, and dried, had m. p. 172° (effervescence) (E.T., I.T. 160°) before and after heating at 60°/0·1 mm. for 5 hr., but was still impure (Found : C, 73·4; H, 5·1. Calc. for $C_{18}H_{14}O_2N_2$: C, 74·5; H, 4·9%). The acid is almost insoluble in all the usual liquids, but a small quantity, recrystallised from boiling acetic acid by using a filter-stick immersed in the heated solvent vapour, and then dried at 60°/0·1 mm. for 6 hr., had m. p. 175° (E.T., I.T. 160°); nevertheless it still retained acetic acid (Found : C, 72·8; H, 5·0; N, 9·5. $C_{18}H_{14}O_2N_2$,0·25$C_2H_4O_2$ requires C, 72·8; H, 4·95; N, 9·2%); stronger heating was not practicable without risk of decarboxylation. The presence of this solvent prevented detection of an ·NH· band in the infra-red spectrum.

The crystals of the acid were apparently stable in air, and after one week showed no darkening, unlike the phenyl analogue (cf. Part I). The acid readily dissolved in concentrated aqueous potassium hydroxide or carbonate to give a yellow solution, but the potassium salt (XI) was isolated only as an uncrystallisable yellow gum.

The preparation and properties of the hydrochlorides of this acid will be described after those of the amines.

The Yellow Base (X).—The powdered acid (IX) (2 g.) was heated in a glass tube (3 cm. in diameter) at 180° rising to 230°/0·01 mm. for 1 hr., during which a straw-coloured liquid distilled and formed a viscous glass. The latter was removed under nitrogen and dissolved in boiling ethanol to which a small amount of water was then added; cooling deposited 1 : 2-*di-hydro*-1-*methylquinolino*(3′ : 2′-3 : 4)*quinoline* (X) (1·25 g., 74%), vivid yellow crystals, m. p. 98—100° (E.T., I.T. 95°) after further recrystallisation from aqueous ethanol (Found : C, 82·9; H, 6·1; N, 11·5%; *M*, 239. $C_{17}H_{14}N_2$ requires C, 82·9; H, 5·75; N, 11·4%; *M*, 246). In ethanol or acetone, the base gives a bright yellow solution with a greenish-yellow fluorescence. The crystals apparently undergo slow oxidation in air, without change of colour : a sample so exposed for 48 hr. had m. p. 95·5—100° (E.T., I.T. 93°).

Action of Hydrogen Chloride on the Yellow Base (X).—(*A*) A stream of dry hydrogen chloride was passed into a dilute solution of the base in acetone; the bright yellow colour changed rapidly to deep red, which then faded until the solution was colourless. Addition of ether precipitated fine colourless needles, undoubtedly of the dihydrochloride, which, however, on removal from the acid solution rapidly dissociated and became deep red.

(*B*) Just sufficient hydrogen chloride was passed into a more concentrated acetone solution of the base to precipitate a mass of deep reddish-purple needles of the *monohydrochloride* (XII), m. p. 240—245° (E.T.) after crystallisation from acetone containing *ca.* 5% of ethanol (Found : C, 72·0; H, 5·4; N, 9·7. $C_{17}H_{14}N_2$,HCl requires C, 72·2; H, 5·35; N, 9·9%). Heating caused the colour of the compound to show the changes : dark green (*ca.* 140°) ⟶ olive-green ⟶ greenish-yellow (*ca.* 200°). The finely powdered salt on exposure to the air passed slowly through the same changes and after 72 hr. had become yellow; in a vacuum the salt was stable indefinitely. A solution of the salt (XII) when treated with aqueous sodium hydroxide regenerated the base (X). The infra-red spectrum of the salt shows rather complex absorption at 3—4 μ, the main bands occurring at 3·6 and 3·85 μ.

The yellow base dissolves in concentrated hydrochloric acid to give a colourless solution, which on dilution immediately becomes reddish-purple.

The base gave a *monopicrate*, deep purple-red needles, m. p. 233° (decomp.), from aqueous ethanol (Found : C, 58·3; H, 3·7; N, 14·4. $C_{17}H_{14}N_2$,$C_6H_3O_7N_3$ requires C, 58·1; H, 3·6; N, 14·7%); this is stable at 70°, but at *ca.* 160° becomes dark olive-green, and darkens considerably from 220° to 233°.

A dilute red solution of the base in hydrochloric acid when treated with dilute aqueous

chloroplatinic acid deposited a deep red chloroplatinate, which on being heated became green and finally greenish-yellow, like the monohydrochloride. A colourless solution of the base in concentrated hydrochloric acid, treated with highly concentrated chloroplatinic acid, deposited a colourless amorphous *chloroplatinate*, which was collected, washed with hydrochloric acid, and dried in a vacuum (Found : C, 30·2; H, 2·6; Pt, 30·1. $C_{17}H_{14}N_2,H_2PtCl_6$ requires C, 31·1; H, 2·45; Pt, 29·8%). The salt rapidly became red in contact with hot solvents. The *di(chloroaurate)*, similarly prepared and isolated, formed a very pale yellow powder (Found : C, 21·9; H, 1·8; Au, 43·0. $C_{17}H_{14}N_2,2HCl_4Au$ requires C, 22·05; H, 1·75; Au, 42·6%), m. p. 235—240° (decomp.); in dilute solution, a red salt was obtained, and underwent the usual colour changes on heating.

A solution of the yellow base in methanolic methyl iodide, when heated, acquired an orange-red colour, but boiling under reflux in nitrogen for 4 hr. followed by concentration furnished the unchanged base. The base was also recovered unchanged when its ethanolic solution was boiled under reflux in nitrogen for 2 hr. with (*a*) *p*-dimethylaminobenzaldehyde (1·24 mols.) and a trace of alkali, or (*b*) diphenylformamidine (1·25 mols.).

The Orange Base (XV).—A solution of the yellow base (X) (0·65 g.) in dilute hydrochloric acid (25 c.c.) was boiled under reflux in nitrogen for 15 min., the deep purple solution becoming reddish-orange and finally yellow with a pale green fluorescence. On cooling, yellow needles (0·73 g., 100%) of the monohydrochloride (XIV) of 1 : 4'-dihydro-1-methylquinolino(3' : 2'-3 : 4)quinoline (XV) separated, and on recrystallisation from ethanol under nitrogen gave the *monohydrate* as bright yellow hygroscopic needles, m. p. 243·5—244·5° (decomp.) (E.T., I.T. 230°) (Found : C, 68·3; H, 5·9; N, 9·3. $C_{17}H_{14}N_2,HCl,H_2O$ requires C, 67·9; H, 5·7; N, 9·3%). The m. p. is markedly affected by the rate of heating.

When the above hot yellow solution was transferred under nitrogen to an excess of dilute aqueous sodium hydroxide, the mixture on cooling deposited the *base* (XV) (92%), which, recrystallised from acetone, formed bright orange plates, m. p. 155° (E.T., I.T. 130°) (Found : C, 82·5, 82·55; H, 5·85, 5·6; N, 11·2%; M, 240. $C_{17}H_{14}N_2$ requires C, 82·9; H, 5·75; N, 11·4%; M, 246). In organic solvents it gives orange solutions having a slight orange fluorescence. It gives a bright yellow solution in both dilute and concentrated hydrochloric acid, in marked contrast to the yellow base (X).

The above yellow monohydrochloride (XIV) was also obtained (*a*) by boiling a suspension of the purple monohydrochloride (XII) in water under nitrogen, the above colour changes again occurring, and (*b*) by warming the orange base with dilute hydrochloric acid.

The base (XV) gave a *monopicrate*, dull yellow needles, m. p. 230° (decomp.) (I.T. 225°), from aqueous acetone (Found : C, 58·4; H, 3·65; N, 14·8. $C_{17}H_{14}N_2,C_6H_3O_7N_3$ requires C, 58·1; H, 3·6; N, 14·7%).

Addition of a solution of the base (XV) to one of an excess of chloroauric acid, each in concentrated hydrochloric acid, deposited the monochloroaurate as an orange-brown amorphous powder, m. p. 205° (decomp., shrinking at 155—165°) : it was too unstable for purification (Found : C, 33·2; H, 2·5; Au, 34·9. Calc. for $C_{17}H_{14}N_2,HCl_4Au$: C, 34·9; H, 2·6; Au, 33·6%).

Oxidation of the Yellow Base (X).—(*a*) A saturated acetone solution of potassium permanganate was added dropwise in slight excess to one of the base (0·4 g.) in cold acetone (25 c.c.), decolorisation of the permanganate and precipitation of manganese dioxide rapidly occurring. The mixture was shaken for 1 hr., colourless needles separating. The mixed precipitate was collected and extracted with boiling acetone (100 c.c.), and the extract added to the filtrate, which on concentration deposited 1 : 2-*dihydro*-1-*methyl*-2-*oxoquinolino*(3' : 2'-3 : 4)*quinoline* (XVI) (0·35 g., 83%), very pale cream needles, m. p. 218°, from acetone (Found : C, 78·4; H, 4·8; N, 10·6. $C_{17}H_{12}ON_2$ requires C, 78·4; H, 4·65; N, 10·75%).

(*b*) A solution of the base (50 mg.) in benzene (25 c.c.) was exposed to the air for 7 days, evaporation losses being replaced daily. The initial fluorescence was rapidly lost and precipitation of a cream-coloured solid occurred within 12 hr. The solution was then allowed to evaporate completely and the residue, recrystallised from acetone, yielded the amide (XVI) in almost theoretical yield and of m. p. 216·5—217·5°, alone and mixed.

An acetone solution of the amide (XVI), when treated with an excess of ethanol saturated with hydrogen chloride, deposited the hydrated *hydrochloride* as bright orange-yellow needles, m. p. 217—218°, when collected, washed with much acetone and dried over calcium chloride (Found: C, 62·9; H, 4·9; N, 8·6. $C_{17}H_{12}ON_2,HCl,1·5H_2O$ requires C, 63·1; H, 5·0; N, 8·65%). The hydrochloride readily dissociated on attempted recrystallisation, or at 60°/0·1 mm.; its m. p. indicates that dissociation to the free base is complete before fusion. The picrate was too unstable for purification.

Oxidation of the Orange Base (XV).—This was performed with permanganate precisely as above, and yielded the oxo-compound (XVI), m. p. and mixed m. p. 217°. A solution of the base (XV) in benzene also gave the same product on exposure to air. There was no obvious difference in the speed of oxidation of the bases (X) and (XV) in benzene solution, unlike that of (I) and (II).

The base (XV) was stable in a desiccator for 14 days or a specimen-tube for 10 days (unchanged in colour and m. p.).

Conversion of the Base (XV) *into the Base* (X).—The orange base (XV) (50 mg.) was heated in a small sublimation tube at 200—230°/0·1 mm. Rapid distillation occurred, giving a straw-coloured glass, which was extracted with hot ethanol under nitrogen. The yellow extract, when diluted with a small amount of water and allowed to cool, deposited the highly crystalline bright yellow base (X), m. p. and mixed m. p. 96—98°.

The Isomerism of the Acid (IX) *and its Monohydrochloride* (XVII).—(a) When a mixture of the finely powdered acid (IX) and 20% hydrochloric acid was vigorously shaken, the latter immediately became intense purple in colour, and the acid (IX) was immediately transformed into the deep blackish-purple monohydrochloride (XVII), m. p. 170—172° (effervescence) (E.T.), the salt becoming reddish-brown before melting. The very low solubility of both the acid (IX) and the monohydrochloride (XVII), and the instability of the latter to heat, prevented the isolation of the salt free from traces of unchanged (IX) (Found : C, 68·8; H, 5·4; N, 9·0. Calc. for $C_{18}H_{14}O_2N_2$,HCl : C, 66·2; H, 4·65; N, 8·6%); the infra-red spectrum of (XVII) was therefore not investigated.

(b) The purple hydrochloride (XVII) was thoroughly ground with 20% hydrochloric acid, and the mixture then boiled under reflux in nitrogen for *ca.* 30 min., the colour of the liquid gradually fading to pale yellowish-brown as (XVII) completely dissolved and was replaced by the highly crystalline insoluble deep green *monohydrochloride.* A sample, when washed thoroughly with water and acetone and dried in a vacuum over phosphoric anhydride, had m. p. 250° (effervescence) (E.T., I.T. 230°) (Found : C, 66·1; H, 4·8; N, 8·9. $C_{18}H_{14}O_2N_2$,HCl requires C, 66·2; H, 4·65; N, 8·6%).

(c) When the boiling of the above mixture in (b) was continued for *ca.* 7 hr., the solution became very pale and the green crystals became dull yellow, remaining highly crystalline. The yellow *monohydrochloride* (XIX), collected as before, had m. p. 250° (effervescence) (E.T.) (Found : C, 66·4; H, 4·9; N, 8·9. $C_{18}H_{14}O_2N_2$,HCl requires C, 66·2; H, 4·65; N, 8·6%). The same salt was obtained when the pure green crystals were heated at 200°/0·01 mm. for 45 min.

(d) The green or the yellow monohydrochloride, when added to hot dilute aqueous sodium carbonate, gave a yellow solution which, on cooling, deposited the highly crystalline 1 : 4′-*dihydro-1-methylquinolino*(3′ : 2′-3 : 4)*quinoline-4′-carboxylic acid* (XX), yellow hygroscopic needles, m. p. 138° (E.T.) (effervescence, resolidifying and remelting at 205—220°), from water (Found : C, 74·3; H, 4·95; N, 9·9. $C_{18}H_{14}O_2N_2$ requires C, 74·4; H, 4·85; N, 9·7%). This acid forms a hydrate, which undergoes complete dehydration only on prolonged exposure in a vacuum to phosphoric anhydride [cf. the hydrochloride (XIV) of the corresponding base (XV)].

A solution of the acid (XX), or of either form of its monohydrochloride, in hot concentrated aqueous potassium hydroxide on cooling deposited the yellow hygroscopic potassium salt, which could not be obtained pure. The yellow sodium salt was similarly obtained.

Decarboxylation. (a) The green and the yellow monohydrochloride (XIX) of the acid (XX) ultimately behaved identically when heated up to 250—300°/0·003 mm., in a narrow tube, since the initial effect on the green salt was conversion into the yellow. The results are recorded on p. 386.

(b) The yellow acid (XX), when cautiously heated at 15 mm. in a similar tube, melted with effervescence and gave a distillate which condensed to a bright yellow glass, and on crystallisation from aqueous ethanol afforded the vivid yellow crystals of the yellow base (X), m. p. 97—99°, alone and mixed.

1 : 2-*Dihydroquinolino*(3′ : 2′-3 : 4)*quinoline-4′-carboxylic Acid* (as IX).—This acid was prepared as Clemo and Perkin direct, the alkaline reaction mixture being filtered into an excess of 10% aqueous acetic acid to precipitate the dull red microcrystalline acid (82%), which became bright yellow at 170—175° and melted at 185° : as Clemo and Perkin found, the acid could not be completely purified (Found : N, 9·4. Calc. for $C_{17}H_{12}O_2N_2$: N, 10·1%).

When a solution of this acid in hot hydrochloric acid was boiled, the purple-red colour soon faded and a pale yellow-buff precipitate (presumably of an unstable monohydrochloride) was deposited. The latter, recrystallised from a large volume of aqueous ethanol, afforded the yellow amorphous 1 : 4-*dihydroquinolino*(3′ : 2′-3 : 4)*quinoline-4′-carboxylic acid hemihydrate,*

m. p. 201° (effervescence) (E.T.) (Found : C, 71·9; H, 4·7; N, 9·7. $C_{17}H_{12}O_2N_2,0.5H_2O$ requires C, 71·6; H, 4·6; N, 9·8%). The ultra-violet spectrum of this acid in aqueous 0·1N-sodium hydroxide solution shows the characteristics :

| $\lambda_{max.}$ | ...... | 364—365 | 224 | $\lambda_{min.}$ | .... | 322—323 | $\lambda_{infl.}$ | .... | 324—329 | 246—250 |
| $\varepsilon_{max.}$ | ...... | 7980 | 35,400 | $\varepsilon_{min.}$ | .... | 3990 | $\varepsilon_{infl.}$ | .... | 4000 | 21,800 |

The red acid, when heated at 190—200°/0·1 mm., gave a yellow crystalline sublimate (XXII*A* or *B*), which when recrystallised from aqueous ethanol, ground thoroughly with aqueous sodium hydroxide, washed, and resublimed, had m. p. 227—228° (softening at 225°) (Found : N, 12·4. Calc. for $C_{16}H_{12}N_2$: N, 12·1%). The ultra-violet spectra in (*A*) ethanol, (*B*) 0·1N-hydrochloric acid gave the values :

(A)	$\lambda_{max.}$	...	360—363	301	296	253	243	225				
	$\varepsilon_{max.}$	...	12,300	3,140	3,000	19,000	18,000	44,800				
	$\lambda_{min.}$	...	308	297	294	245	240	211				
	$\varepsilon_{min.}$	...	2,890	2,980	2,960	18,450	18,300	32,500				
(B)	$\lambda_{max.}$	...	390	247	226	$\lambda_{min.}$	...	322	236	214—215	$\lambda_{infl.}$	... 285—289
	$\varepsilon_{max.}$	...	14,300	21,200	37,400	$\varepsilon_{min.}$	...	1,180	16,100	18,600	$\varepsilon_{infl.}$	... 5130

The yellow base in hot hydrochloric acid gave a yellow solution with a greenish fluorescence, and on cooling deposited the *monohydrochloride*, bright yellow needles, m. p. 310—312° (decomp., softening at *ca.* 305°) (E.T.), after crystallisation from aqueous ethanol (Found : N, 10·3. $C_{16}H_{12}N_2$,HCl requires N, 10·4%). Prolonged boiling of the above solution caused no colour change, and cooling and rendering alkaline precipitated the unchanged base. The latter shows no tendency to form a colourless solution in a large excess of cold concentrated hydrochloric acid : in this respect it resembles the orange base (XV) and differs strikingly from the yellow base (X).

Isomerism in the 1-*Phenyl Series.*—(i) A solution of the yellow 1-phenyl base (as X) in concentrated hydrochloric acid was boiled for 15 min., but the deep red colour remained unchanged, and the solution on cooling deposited the deep red crystalline monohydrochloride (as XII), m. p. 280° (decomp.) (cf. Part I). (ii) This solution was boiled under reflux for 6 hr.; the change in colour to yellowish-brown then appeared complete. The solution, on cooling, deposited the isomeric yellow crystalline *monohydrochloride* (as XIV), m. p. 228—230° (decomp.) (E.T.) (Found : N, 8·15. $C_{22}H_{18}N_2$,HCl requires N, 8·1%). This salt on treatment with aqueous sodium hydroxide yielded a dull orange base, but insufficient material precluded purification and investigation.

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