

**926.** *The Structure and Properties of Certain Polycyclic Indolo- and Quinolino-derivatives. Part XVI.<sup>1</sup> Derivatives of 1,2,3,4-Tetrahydro-4-oxo-1-phenylphosphinoline.*

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1,2,3,4-Tetrahydro-4-oxo-1-phenylphosphinoline gives a phenylhydrazone which on indolisation affords the colourless indolo(3',2'-3,4)phosphinoline. It also condenses with *o*-aminobenzaldehyde to give the colourless quinolino-(3',2'-3,4)phosphinoline, which forms a yellow monohydrochloride, which with hot acid does not undergo allylic rearrangement. These reactions are similar to those of the analogous 4-oxoarsinoline and markedly different from those of the 4-oxo-quinolines. They confirm previous views regarding the conditions required for  $\psi$ -indoloquinoline formation, and the probable mechanism of the acid-catalysed allylic rearrangement of the 1,2-dihydro-quinolino(3',2'-3,4)quinolines.

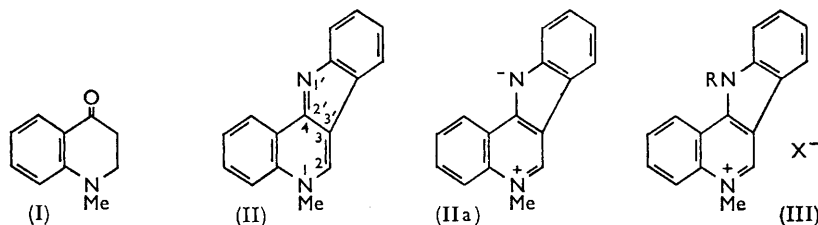
In extensive earlier studies in this series it had been shown that many polycyclic oxoamines having the general structural features of, for example, 1,2,3,4-tetrahydro-1-methyl-4-oxoquinoline (I), when converted into their phenylhydrazones and subjected to Fischer indolisation, gave yellow  $\psi$ -indoles (II).<sup>2,3</sup> The polar form (IIa) undoubtedly made a considerable contribution to the structure of these  $\psi$ -indoles, for they readily combined with acids or with methyl iodide to give colourless salts having the cation (III; R = H or Me). Further, compounds such as (I) when condensed with *o*-aminobenzaldehyde, or condensed with alkaline isatin and decarboxylated, gave the deep yellow 1,2-dihydro-1-methylquinolino(3',2'-3,4)quinoline (IV), which gave a deep red monohydrochloride in which the proton was linked to the 1'-nitrogen atom. This salt in boiling

<sup>1</sup> Part XV, Gallagher and Mann, *J.*, 1962, 5110.

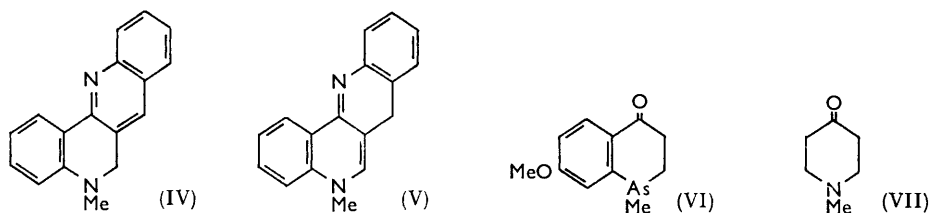
<sup>2</sup> Mann, *J.*, 1949, 2816.

<sup>3</sup> Brauholtz and Mann, *J.*, 1955, 381.

hydrochloric acid was converted into the yellow hydrochloride of the isomeric orange 1,4'-dihydro-1-methylquinolino(3',2'-3,4)quinoline (V) by an allylic rearrangement.



Considerable evidence has accumulated regarding the structural requirements and the probable mechanism of formation of these  $\psi$ -indoles, and of the isomerism (IV  $\rightarrow$  V) in the quinoline series.<sup>3</sup> The formation of the  $\psi$ -indoles is dependent on (a) an initial conjugation in the keto-amine between the C=O group and the 1-nitrogen atom, for example,



through an *o*-phenylene group as in (I), and the consequent conjugation between the 1-nitrogen atom and the =N- atom of the phenylhydrazone, and (b) an orientation of the two fused heterocyclic rings in the indolo-system such that dehydrogenation will further conjugate the 1- and the 1'-nitrogen atom in the  $\psi$ -indole (II). It is noteworthy that 1,2,3,4-tetrahydro-7-methoxy-1-methyl-4-oxoarsinoline (VI) gives a normal indole,<sup>4</sup> for the arsenic atom very rarely accepts an "internal" positive charge (as in II and III) to become part of an aromatic ring. On the other hand, 1-methyl-4-oxopiperidine (VII) gives a normal indole<sup>5</sup> because the above conjugation cannot occur.

The mechanism of the allylic transformation apparently contains two major steps: (a) proton migration in the hydrochloride of the base (IV) from the 1'-atom to the 1-nitrogen atom, for which there is strong evidence; and (b) the positive pole on the 1-nitrogen atom, being then adjacent to the allylic CH<sub>2</sub> group, apparently renders a hydrogen atom of this group more mobile, and thus promotes its migration from the 2- to the 4'-carbon atom to give the more stable salt of the base (V).<sup>3</sup> This mechanism accounts for the very sluggish isomerisation of the 1-phenyl member (as IV) in which the 1-nitrogen atom is only weakly basic, and its non-occurrence in 1,2-dihydro-7-methoxy-1-methylquinolino(3',2'-3,4)arsinoline (VIII), in which the arsenic atom is neutral.<sup>4</sup>

These considerations give great interest to the reactions of 1,2,3,4-tetrahydro-4-oxo-1-phenylphosphinoline (IX),<sup>6</sup> in view of its intermediate position between the keto-amine (I) and the keto-arsine (VI).

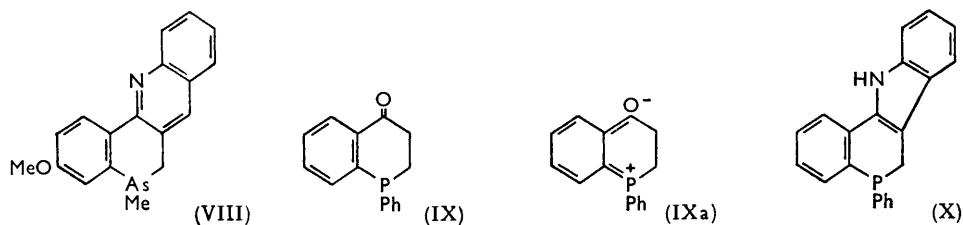
We find that the keto-phosphine (IX) gives a phenylhydrazone which is converted in hot ethanolic hydrogen chloride into the colourless 1,2-dihydro-1-phenylindolo(3',2'-3,4)phosphinoline (X). The structure of this compound is shown by its infrared spectrum, which has a sharp >NH band at 3420 cm.<sup>-1</sup>, and by the formation of a methiodide, which must have occurred normally at the phosphorus atom. This formation of a normal

<sup>4</sup> Mann and Wilkinson, *J.*, 1957, 3346.

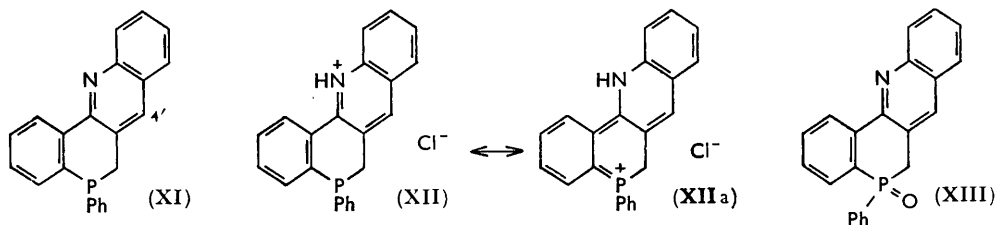
<sup>5</sup> Cook and Reid, *J.*, 1945, 399.

<sup>6</sup> Gallagher, Kirby, and Mann, preceding paper.

indole was to be expected, for no evidence of charge-separation of type (IXa) could be detected in the keto-phosphine (IX).<sup>6</sup>



The oxo-phosphine (IX) reacted with *o*-aminobenzaldehyde in alkaline ethanolic solution to give the colourless 1,2-dihydro-1-phenylquinolino(3',2'-3,4)phosphinoline (XI), which formed a bright yellow hydrochloride (XII). This salt, in contrast to the colourless



base (XI), by its colour indicates strongly that the form (XIIa) makes some contribution to the structure of the cation (XII). This is confirmed by the difference in the absorption spectra of the base (XI) in ethanol and in ethanol-hydrochloric acid (Fig. 1): moreover,

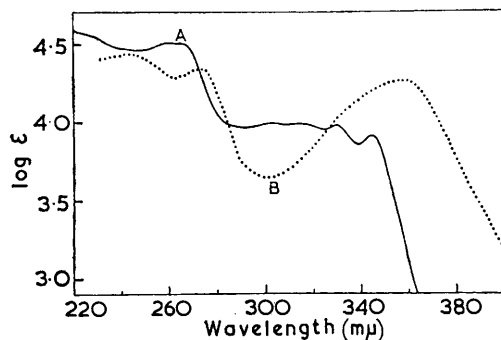


FIG. 1. Ultraviolet spectra of (A) the quinolinophosphinoline (XI) (2.242 mg. in 100 ml. of ethanol) and (B) the same solution diluted with 2% of concentrated hydrochloric acid.

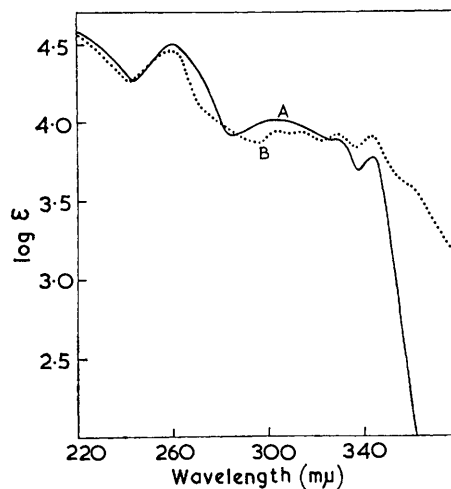


FIG. 2. Ultraviolet spectra of (A) the quinolinophosphinoline oxide (XIII) (2.394 mg. in 100 ml. of ethanol) and (B) the same solution diluted with 2% of concentrated hydrochloric acid.

the corresponding phosphine oxide (XIII), whose hydrochloride cannot show a structure of type (XIIa), gives spectra in ethanol and ethanol-hydrochloric acid which are closely similar both to one another (Fig. 2) and to that of the base (XI). Hence the spectral changes which occur on salt formation of the base (XI) are not simply those observed when simple quinolines are protonated.

It is noteworthy that the absorption spectra of the quinolinophosphinoline (XI) in ethanol and ethanolic hydrochloric acid closely resemble those of the quinolinoarsinoline (VIII) in these solvents.<sup>4</sup> Since the hydrochlorides of the compounds (XI) and (VIII) are bright and pale yellow, respectively, whereas those of the quinolinoquinoline (IV) and its 1-phenyl analogue are deep red, it is probable that the cation of type (XIIa) makes a very limited contribution to the salts of these phosphorus and arsenic compounds. This would almost certainly apply to all quinolinoarsinolines of type (VIII); but a keto-phosphine of type (IX), having however a *P*-methyl (and therefore more strongly basic) group, might give a quinolinophosphinoline which came in respect to charge-separation more emphatically between the nitrogen and the arsenic analogue (IV) and (VIII). Such a keto-phosphine might also give a  $\psi$ -indole of type (II).

The keto-phosphine (IX) reacted with a boiling alkaline solution of isatin to give the 4'-carboxylic acid of the quinolinophosphinoline (XI). This acid could not be purified, but when heated at 220—240°/0.0005 mm. gave a sublimate of the phosphinoline (XI) and an unidentified colourless solid.

The hydrochloride (XII) of the quinolinophosphinoline was unaffected by vigorous boiling in dioxan-hydrochloric acid, and gave no indication of an allylic transformation into an isomer (as V). In view of the weak basic strength of the *P*-phenyl group both in the oxo-phosphine (IX) and in the compound (XI), this supports the suggested mechanism of this isomerisation.<sup>3</sup>

In the nitrogen series, one striking property of both isomers (IV) and (V) is their rapid atmospheric oxidation in cold benzene solution to a derivative of the isomer (IV) having the 2-methylene group converted into carbonyl.<sup>3</sup> No similar behaviour is shown by the quinolinophosphinoline (XI), in which oxidation of the tertiary phosphine group to the very stable phosphine oxide is the over-riding reaction.

#### EXPERIMENTAL

All operations involving tertiary phosphines, including their recrystallisations, had to be carried out under nitrogen to obtain pure products.

1,2-Dihydro-1-phenylindolo(3',2'-3,4)phosphinoline (X).—The oxo-phosphine<sup>6</sup> (IX) gave a yellow phenylhydrazone, m. p. 55—60°, which rapidly decomposed. A solution of the crude hydrazone (0.56 g.) in ethanol (10 ml.) was added to saturated ethanolic hydrogen chloride (10 ml.), which was then boiled under reflux for 1 hr., cooled, and poured into water (160 ml.). The precipitated yellow solid, when collected and recrystallised from ethanol, gave the indole (X) (0.19 g., 37%), m. p. 191—192° (Found: C, 79.8; H, 5.4; N, 4.4. C<sub>21</sub>H<sub>16</sub>NP requires C, 80.1; H, 5.1; N, 4.5%).

The indole gave a pale yellow *methiodide monohydrate* that had m. p. 278—280° (decomp.) with marked contraction at 170—180°, after crystallisation from methanol: the monohydrate was unaffected when heated at 100°/0.1 mm. for 6 hr. (Found: C, 56.0; H, 4.6; N, 3.1. C<sub>22</sub>H<sub>19</sub>INP, H<sub>2</sub>O requires C, 55.6; H, 4.4; N, 3.0%). It gave a yellow *methopicate*, m. p. 214° (from ethanol) (Found: C, 59.9; H, 4.0; N, 9.9. C<sub>28</sub>H<sub>21</sub>N<sub>4</sub>O<sub>7</sub>P requires C, 60.4; H, 3.8; N, 10.1%).

1,2-Dihydro-1-phenylquinolino(3',2'-3,4)phosphinoline (XI).—10% Aqueous sodium hydroxide (0.5 ml.) was added to a solution of the oxo-phosphine (IX) (200 mg.) and *o*-aminobenzaldehyde (100 mg., 1.1 mol.) in ethanol (5 ml.), which was set aside under nitrogen for 12 hr. The pure *quinolino-phosphinoline* (XI) (241 mg., 89%), m. p. 125—127° (Found: C, 80.9; H, 4.5; N, 4.5. C<sub>22</sub>H<sub>16</sub>NP requires C, 81.2; H, 4.9; N, 4.3%), after recrystallisation from ethanol, had m. p. 127.5—128.5°. It gave a lemon-yellow *picrate monohydrate*, m. p. 168—169° (from methanol) (Found: C, 58.9; H, 3.5; N, 9.6. C<sub>22</sub>H<sub>16</sub>NP, C<sub>6</sub>H<sub>3</sub>N<sub>3</sub>O<sub>7</sub>, H<sub>2</sub>O requires C, 58.7; H, 3.7; N, 9.8%). A solution of the base in warm concentrated hydrochloric acid deposited the bright yellow *monohydrochloride hydrate*, which effervesced at ca. 110°, solidified, and remelted at 218—219° without change in colour (Found: C, 67.7; H, 4.7; N, 3.5. C<sub>22</sub>H<sub>16</sub>NP, HCl, H<sub>2</sub>O requires C, 67.8; H, 4.6; N, 3.6%). The hydrate was unaffected by confinement over phosphoric anhydride at atmospheric pressure for 3 weeks: when heated at 90°/0.1 mm. it lost hydrochloric acid and water.

A solution of the phosphinoline (XI) (100 mg.) in concentrated hydrochloric acid (2 ml.) and

dioxan (0.5 ml.), when boiled under reflux for 6 hr. and cooled, deposited the monohydrated hydrochloride (107 mg.), m. p. and mixed m. p. 218—220°. Basification of the mother-liquor yielded the phosphinoline (15 mg.), m. p. and mixed m. p. 125—127°.

The phosphinoline (XI) was unaffected when its ethanolic solution was allowed to evaporate at room temperature during 48 hr., or when air was passed through the boiling solution for 6 hr. A solution in acetone, when treated with hydrogen peroxide (100-vol.), warmed, and evaporated to dryness, gave 1,2-dihydro-1-phenylquinolino(3',2'-3,4)phosphinoline oxide hemihydrate (XIII), forming cream-coloured crystals, m. p. 114—115° (effervescence), from benzene (Found: C, 75.3; H, 4.8.  $C_{22}H_{16}NOP, \frac{1}{2}H_2O$  requires C, 75.4; H, 4.85%),  $\nu_{max}$  3220 (OH) and 1170 (P=O)  $cm^{-1}$ . This water was difficult to remove, but 5 days' heating at 90°/0.1 mm. gave the hygroscopic oxide, m. p. 189—190° (Found: C, 77.6; H, 4.4; N, 4.2.  $C_{22}H_{16}NOP$  requires C, 77.4; H, 4.7; N, 4.4%). Evaporation of a solution of the oxide in hydrochloric acid in a desiccator afforded the very pale yellow monohydrochloride monohydrate, m. p. 198—199° with contraction at 135° (Found: C, 66.4; H, 4.7.  $C_{22}H_{16}NOP, HCl, H_2O$  requires C, 66.9; H, 4.8%).

The oxo-phosphine (IX) (360 mg.) and isatin (333 mg., 1.5 mol) were added to a solution of potassium hydroxide (360 mg.) in water (1 ml.) and ethanol (4 ml.), which was then boiled under reflux in nitrogen for 48 hr. The cold product was poured into freshly boiled, chilled 10% aqueous acetic acid (50 ml.), which was then warmed at 100° to convert the very finely divided precipitate into a gum. The latter was collected and dissolved in aqueous sodium hydrogen carbonate, which when filtered and acidified deposited a yellow solid (54 mg.). Shorter periods of boiling decreased this yield. The solid, which underwent partial melting between 130° and 200°, was cautiously heated at 220—240°/0.0005 mm. in a sublimation tube, giving a yellow glass and some colourless crystals. The glass, m. p. 118—120°, was the phosphinoline (XI), mixed m. p. 121—122°: the crystals were insufficient for accurate identification, but analysis and infrared spectra indicated an impure sample of the 4'-carboxylic acid of the quinolino-phosphinoline (XI).

We gratefully acknowledge the award of a University of Queensland Research Scholarship (to M. J. G.).