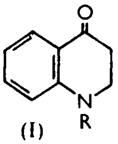
682. *The Structure and Properties of Certain Polycyclic Indolo- and Quinolino-derivatives. Part X.* Some Applications of the Friedländer Reaction, and Further Studies of the Quinolino-bases Prepared from Cyclic Keto-amines.*

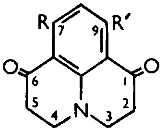
By John T. Braunholtz and Frederick G. Mann.

Certain cyclic keto-amines, previously studied, react with *o*-aminobenzaldehyde under very mild conditions to give the corresponding quinolino-derivatives in good yields. New evidence is adduced to support the structures assigned earlier to these compounds when obtained under the more vigorous conditions of the Pfitzinger reaction, followed by decarboxylation. The rather difficult allylic rearrangement of 1 : 2-dihydro-1-phenylquinolino-(3′ : 2′-3 : 4)quinoline has been shown to proceed similarly to that of its 1-methyl analogue. The structures of the two allylic isomers, 1 : 2- and 1 : 4′-dihydro-1-methylquinolino(3′ : 2′-3 : 4)quinoline, have been placed beyond doubt by measurements of infrared and nuclear magnetic resonance spectra. 1 : 2-Dihydro-1-toluene-*p*-sulphonylquinolino(3′ : 2′-3 : 4)quinoline and 3′ : 4′-dihydronaphtho(1′ : 2′-2 : 3)quinoline do not undergo the allylic rearrangement.

Earlier papers in this series [1,2,3] describe the reaction of keto-amines such as 1 : 2 : 3 : 4-tetrahydro-1-methyl-4-oxoquinoline (I; R = Me) and 1 : 6-dioxojulolidine (II; R = R′ = H) with isatin in ethanolic alkali to give quinolino-4′-carboxylic acids, from which the quinolino-bases (*e.g.*, III; R = Me; and IV; R = R′ = H) were obtained by decarboxylation. The allylic isomerisation which these bases undergo when heated with acids, and the ready oxidation to cyclic amides which both isomers derived from the quinoline (I; R = Me) undergo, have also been discussed.[2]



(I)



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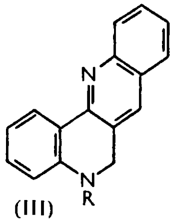

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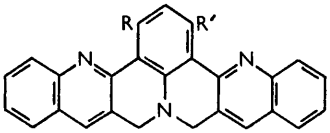

(IV)

The carboxylic acid (VI; R = CO_2H) obtained similarly by the Pfitzinger reaction from the tetrahydro-4-oxoarsinoline (V) resisted decarboxylation, however, and the corresponding quinolino-base (VI; R = H) was obtained by the reaction of the ketone (V) with *o*-aminobenzaldehyde.[4] The Friedländer reaction has now been applied to a number of ketones of types (I) and (II), with the object of preparing their derivatives (III) and (IV) under the mildest possible conditions, and therefore with the least risk of allylic rearrangement. In addition, the Friedländer reaction provides a very convenient method for the rapid preparation of these quinolino-bases on a larger scale and in a higher degree of initial purity than hitherto.

7 : 9-Dimethyl-1 : 6-dioxojulolidine (II; R = R′ = Me) with an excess of *o*-aminobenzaldehyde at room temperature gives 7 : 9-dimethyl-6-oxoquinolino(2′ : 3′-1 : 2)-juloline (VII; R = R′ = Me); the base gives a 2 : 4-dinitrophenylhydrazone, and its infrared spectrum contains the C=O absorption band at 1672 cm.$^{-1}$, close to that at

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* Part IX, *J.*, 1957, 3352.

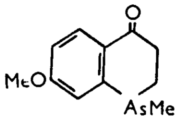
[1] Mann, *J.*, 1949, 2816.

[2] Braunholtz and Mann, *J.*, 1955, 381.

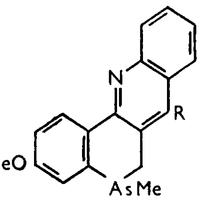
[3] *Idem*, *J.*, 1955, 393.

[4] Mann and Wilkinson, *J.*, 1957, 3346.

1668 cm.$^{-1}$ of its 7-methyl analogue [5] (VII; R = Me, R′ = H). Whereas we find no evidence of the formation of the diquinolino-compound (IV; R = R′ = Me) from the diketone (II; R = R′ = Me), 7-methyl-1 : 6-dioxojulolidine (II; R = Me, R′ = H) reacts readily with two molecules of *o*-aminobenzaldehyde, yielding 7-methyldiquinolino(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)juline (IV; R = Me, R′ = H), an intensely yellow base; and 1 : 6-dioxojulolidine similarly gives the bright orange diquinolino(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)juline [3] (IV; R = R′ = H). In both these cases, however, the initial ethanol-insoluble crude products show strong infrared absorption in the region of 1670 cm.$^{-1}$, close to the bands recorded above for the bases (VII; R = Me, R′ = Me or H); furthermore, both crude products, when heated in pyridine change markedly in appearance, and the compound (IV; R = R′ = H) when thus purified is identical with that described earlier.[3] It is possible that in the initial product one or both of the dioxojulolidine carbonyl groups are free and finally condense with ring-closure only at a higher temperature.



(V)



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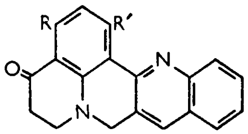
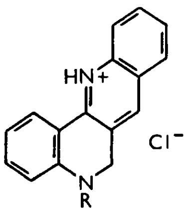


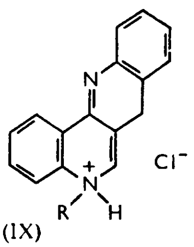
(VII)

It is noteworthy that the quinolino-bases (VII; R = R′ = Me) and (IV; R = Me, R′ = H) cannot be obtained from the corresponding dioxojulolidines by the Pfitzinger route, which gives no product with the diketone (II; R = R′ = Me), and only the mono-quinolino-derivative (VII; R = Me, R′ = H) with the 7-methyl-diketone [5] (II; R = Me, R′ = H). It therefore appears that, under the conditions of these experiments, the nuclear methyl groups exert a markedly greater steric obstruction to the Pfitzinger than to the Friedländer reaction. It is noteworthy that Buu-Hoï and Cagniant have shown that, although 1-acetyl-2-methylnaphthalene reacts with alkaline isatin, its 2-ethyl analogue does not.[6]

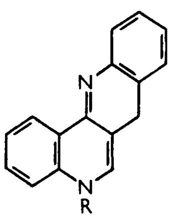
The 1 : 2 : 3 : 4-tetrahydro-4-oxoquinolines (I; R = Me [7] and Ph [1,8]) also react readily with *o*-aminobenzaldehyde at room temperature, giving 1 : 2-dihydro-1-methyl-quinolino(3′ : 2′-3 : 4)quinoline [2] (III; R = Me) and its 1-phenyl analogue [1] (III; R = Ph). The quinolinoquinolines obtained are identical with those prepared earlier by decarboxylation of the 4′-carboxylic acids obtained by the reaction between the keto-amines (I; R = Me or Ph) and alkaline isatin. Their formation in good yield under the very mild conditions of the Friedländer reaction gives strong supporting evidence for the structures originally assigned to the bases (III; R = Me or Ph), and in particular for the position of the sole cyclic methylene group which they both contain.



(VIII)



(IX)



(X)

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[5] Ittyerah and Mann, *J.*, 1958, 467.

[6] Buu-Hoï and Cagniant, *Bull. Soc. chim. France*, 1946, 123.

[7] Allison, Braunholtz, and Mann, *J.*, 1954, 403.

[8] R. C. Cookson and Mann, *J.*, 1949, 67.

The rather difficult conversion of 1 : 2-dihydro-1-phenylquinolino(3′ : 2′-3 : 4)quinoline[1] (III; R = Ph), *via* its deep red monohydrochloride (VIII; R = Ph), into the yellow monohydrochloride (IX; R = Ph) of the allylic isomeric base (X; R = Ph) was briefly recorded earlier.[2] It is now found that this isomerisation proceeds satisfactorily in boiling concentrated hydrochloric acid containing a small quantity of dioxan; the yellow salt (IX; R = Ph) is thus readily available, and the 1-phenylquinolino-series of compounds clearly undergoes a cycle of changes of the same nature as those in the 1-methylquinolino-series;[2] these may be summarised as in the annexed scheme.

FIG. 1. FIG. 2.

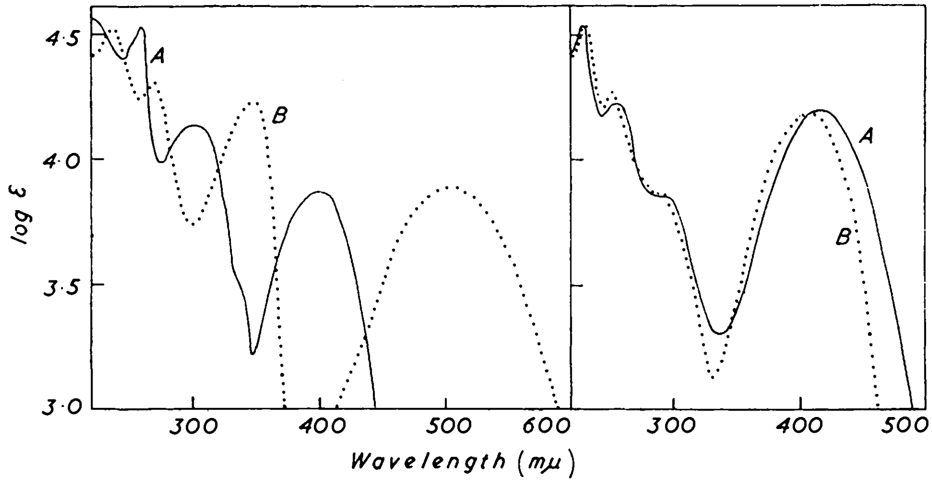
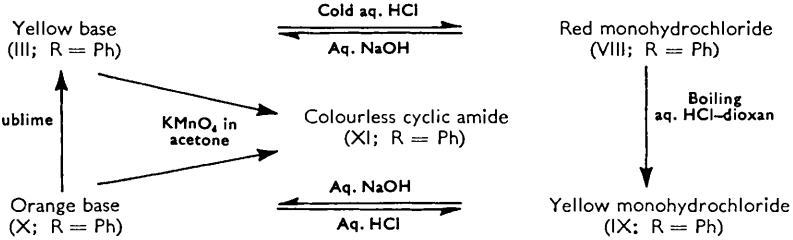


FIG. 1. *Ultraviolet spectra of* 1 : 2-*dihydro*-1-*phenylquinolino*(3′ : 2′-3 : 4)*quinoline* (III; R = Ph) *in* (*A*) *ethanol*, (*B*) 1 : 1 *ethanol*–N-*hydrochloric acid*: *there is a minimum in* (*B*) *at* 380 mμ (log ε 2·255) *not shown.*

FIG. 2. *Ultraviolet spectra of* 1 : 4′-*dihydro*-1-*phenylquinolino*(3′ : 2′-3 : 4)*quinoline* (X; R = Ph) *in* (*A*) *ethanol*, (*B*) 1 : 1 *ethanol*–N-*hydrochloric acid.*

[*For the above spectra, and those in Figs.* 4 *and* 5, *the ethanol used contained* 5% *of water.*]



Three particular differences between the 1-methyl and 1-phenyl series may be noted: (*a*) The quinolino-base (III; R = Me) readily forms a colourless, rather unstable, dihydrochloride,[2] but the analogous 1-phenyl compound (III; R = Ph) forms only the red mono-salt under the corresponding conditions, owing to the reduced basic strength of the 1-amino-group. (*b*) When the conversion of the salt (VIII; R = Ph) into its isomer (IX; R = Ph) is attempted in ethanolic hydrochloric acid, an insoluble plum-coloured monohydrochloride is obtained. This salt is probably a dimorphic form of the yellow hydrochloride (IX; R = Ph), for their infrared spectra are almost identical, whereas that of the former differs markedly from that of the red hydrochloride (VIII; R = Ph). Basification of the intermediate hydrochloride gives the crude orange base (X; R = Ph). An analogous example of apparent dimorphism occurring during the acid-catalysed rearrangement of the Pfitzinger acids derived from 1 : 2 : 3 : 4-tetrahydro-1-methyl-4-oxoquinoline (I; R = Me) has been noted earlier.[2] (*c*) The orange quinolino-base (X; R = Ph) differs from the corresponding 1-methyl compound (X; R = Me) in being amorphous instead of highly crystalline, and its purification by recrystallisation has proved impossible, possibly owing to rapid atmospheric oxidation. The base (X; R = Ph) is also unusual in that its m. p. is below that of its precursor (III; R = Ph), into which it is converted by vacuum-sublimation (cf. X; R = Me).

The close analogy between the 1-methyl and the 1-phenyl series of interconvertible quinolino-derivatives (*e.g.*, III and X) is, however, emphasised by a comparison of the ultraviolet absorption curves for the latter (III and X; R = Ph) in ethanolic and acidic solution (Figs. 1 and 2), with those for the 1-methyl compounds recorded earlier,[2] when the structural evidence derived from these spectra was discussed.

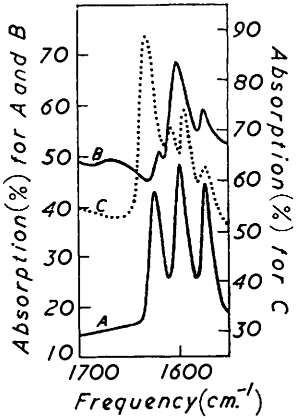


FIG. 3. *Infrared spectra of* (*A*) *quinoline* (*in liquid film*) *and of the quinolino-bases* (III; R = Me) (*B*) *and* (X; R = Me) (*C*), *in Nujol mull, in the region* 1550—1700 *cm.*$^{-1}$.

Infrared spectra (*cm.*$^{-1}$) *of certain polycyclic derivatives of quinoline in the region* 1570—1650 *cm.*$^{-1}$ (*in Nujol mull, unless otherwise stated*).

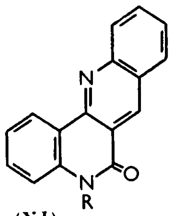
Quinoline *	1623(m)	1598 (s)	1574 (m)	
(III; R = Me)	1620 (w)	1602 (m)	1574 (w)	
(III; R = Ph)	1620 (w)	1598 (m)	1576 (w)	
(III; R = $SO_2 \cdot C_6H_4 \cdot Me$)	1618 (w)	1600 (m)	1580 (w)	
(XIII; R = H)	1620 (w)	1601 (m)	1578 (w)	
(IV; R = R′ = H)	1618 (m)	1601 (s)	1577 (m)	
(XII)	1639 (s)	1600 (s)		
(X; R = Me)	1631 (s)	1607 (m)	1593 (m)	1574 (w)
(X; R = Ph)	1632 (s)	1608 (w)	1593 (m)	1577 (w)
(III or X; R = H) †	1629 (m)	1618 (m)	1575 (s)	
Isomer of (IV; R = R′ = H)	1647 (m)	1626 (w)	1600 (m)	1575 (w)

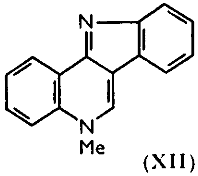
* Liquid film. † There is some uncertainty concerning the structure of this base; although the positions of the bands are similar to those in the first group, their relative intensities show a markedly different distribution.

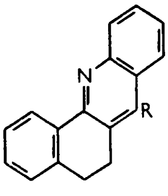
Further evidence for the structures of the quinolino-bases (III), (IV), and (X) has been obtained from their infrared spectra and, of particular importance in the case of the isomeric compounds (III; R = Me) and (X; R = Me), from their nuclear magnetic resonance spectra also.

The absorption bands between 1570 and 1650 cm.$^{-1}$ in the infrared spectra of the quinolino-bases are summarised in the Table, with those of quinoline and of 1-methyl-ψ-indolo(3′ : 2′-3 : 4)quinoline [2] (XII); the significant features are illustrated (Fig. 3) by a comparison of the infrared spectrum of quinoline with those of the isomeric quinolino-bases (III; R = Me) and (X; R = Me).

It is clear that in this region of the infrared spectrum, characterising the C=C and C=N– groups, the bases (*e.g.*, III, IV, XIII) initially obtained by Friedländer or Pfitzinger reactions give rise to a band pattern which is remarkably constant in position and distribution of intensities. This constancy emphasises the structural similarities between the bases, and the pattern itself, which appears to arise from the true (unhydrogenated) quinolino-portion of the compounds, provides a diagnostic test whereby they may be distinguished from their allylic isomers. The spectra of the latter derivatives (*e.g.*, X; R = Me or Ph) also show a characteristic pattern in the 1570—1650 cm.$^{-1}$ region; the major band is now considerably above 1600 cm.$^{-1}$, and the similarities with the infrared spectrum of the ψ-indole (XII) are in accordance with the proposed structures of the quinolino-bases.


(XI)


(XII)


(XIII)

It has been shown that the free $>$NMe group gives rise to an infrared absorption band of moderate strength close to 2800 cm.$^{-1}$, which disappears or becomes extremely weak when structural modifications involving the nitrogen lone pair of electrons occur.[9] This band is accordingly present in the spectra of the isomeric bases (III; R = Me) (at 2790 cm.$^{-1}$) and (X; R = Me) (at 2795 cm.$^{-1}$) but absent from that of their common oxidation product (XI; R = Me), thus confirming its cyclic amide structure. Further, it is present in the spectrum of the red monohydrochloride (VIII; R = Me) of the base (III; R = Me) (at 2790 cm.$^{-1}$), and thus confirms that salt formation has not occurred at the $>$NMe group; on the other hand, it is absent from the spectrum of the yellow monohydrochloride (IX; R = Me) of the isomeric base (X; R = Me), showing that in this salt protonation has occurred on the $>$NMe group and not at position 1′.

Hitherto there has been no physical method available by which the structures of our isomeric bases could be decisively differentiated with respect to the location of the solitary methylene group at position 2 in one base (*e.g.*, III; R = Me) and at position 4′ in the other (*e.g.*, X; R = Me), or *vice versa*. Dr. Sheppard has kindly investigated the nuclear magnetic resonance spectra of these bases in pyridine solution, and reports:

" The high-resolution hydrogen nuclear magnetic resonance spectra of the two compounds were taken in " AnalaR " pyridine solution, with *cyclo*hexane as an external standard; a Varian Associates 4300 B spectrometer was used with a frequency of 40 Mc., and the resonances of the hydrogen atoms in the saturated groupings $>CH_2$ and $-CH_3$ were studied. In each case, two sharp peaks were observed, of relative intensities 3 : 2, which could clearly be assigned to the $>$N–Me group and the methylene group respectively. The chemical shifts were measured relative to *cyclo*hexane, assumed to be +3·9 parts per million relative to water. The chemical shifts in the case of base (III; R = Me) were 2·9 for the $>$N–Me group and 1·6 for the methylene group. In the case of base (X; R = Me), the corresponding chemical shifts were 2·5 and 1·8 respectively. The relative values of these chemical shifts agree well with expectations based on the two formulæ given. In particular, the lower value of the $>$N–Me chemical shift of base (X; R = Me) is to be expected because of the extra double bond immediately adjacent to the nitrogen atom." [10]

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[9] Braunholtz, Ebsworth, Mann, and Sheppard, *J.*, 1958, 2780.
[10] Wertz, *Chem. Rev.*, 1955, **55**, 829.

It is especially noteworthy that this confirmation of the structures (III and X; R = Me) is extended, by the interrelations between the infrared spectra of the quinolino-derivatives discussed above, to all the bases of types (III) and (X), whose structures are thereby confirmed.

Further evidence for the factors which determine the interannular allylic isomerisation in compounds such as (III; R = Me or Ph) has been obtained by investigating the quinolino-bases (III; R = $\cdot SO_2\cdot C_6H_4Me$) and (XIII; R = H).[11]

1 : 2 : 3 : 4-Tetrahydro-4-oxo-1-toluene-*p*-sulphonylquinoline[12] (I; R = $SO_2\cdot C_6H_4Me$) reacts readily with *o*-aminobenzaldehyde to give 1 : 2-dihydro-1-toluene-*p*-sulphonyl-quinolino(3′ : 2′-3 : 4)quinoline (III; R = $SO_2\cdot C_6H_4Me$). This cream-coloured base forms a rather unstable yellow hydrochloride; treatment with boiling dilute hydrochloric acid, a process which causes rapid isomerisation of the 1-methyl base (III; R = Me), leaves the derivative (III; R = $SO_2\cdot C_6H_4Me$) unchanged, but prolonged boiling with concentrated hydrochloric acid removes the toluene-*p*-sulphonyl group, and the monohydrochloride (probably IX; R = H)[2] of the base (III, R = H; or X, R = H), first prepared by Clemo and Perkin,[13] is obtained.

FIG. 4.

FIG. 5.

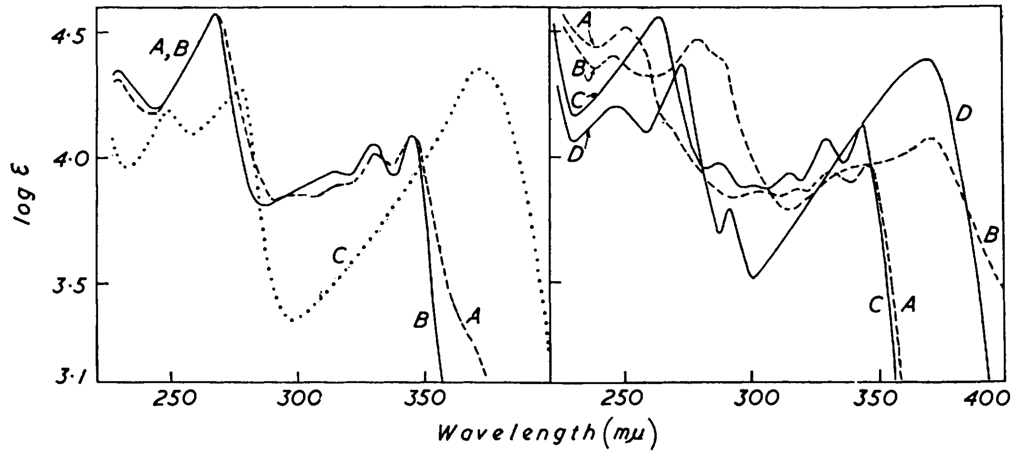

FIG. 4. *Ultraviolet spectra of 3′ : 4′-dihydronaphtho(1′ : 2′-2 : 3)quinoline-4-carboxylic acid* (XIII; R = CO_2H) (*A*) *in ethanol,* (*B*) *in* 1 : 1 *ethanol*–0·1N-NaOH *and* (*C*) *in* 1 : 1 *ethanol*–N-*hydrochloric acid.*

FIG. 5. *Ultraviolet spectra of* 1 : 2-*dihydro*-1-*toluene*-p-*sulphonylquinolino*(3′ : 2′-3 : 4)*quinoline* (III; R = $SO_2\cdot C_6H_4Me$) (*A*) *in ethanol and* (*B*) *in* 1 : 1 *ethanol*–0·1N-*hydrochloric acid, and of* 3′ : 4′-*dihydro-naphtho*(1′ : 2′-2 : 3)*quinoline in* (*C*) *ethanol and* (*D*) 1 : 1 *ethanol*–N-*hydrochloric acid.*

3′ : 4′-Dihydronaphtho(1′ : 2′-2 : 3)quinoline-4-carboxylic acid (XIII; R = CO_2H), prepared from α-tetralone by the Pfitzinger reaction,[11] differs in the following respects from the analogous carboxylic acids which are derived from the keto-amines (I; R = H, Me or Ph) and contain a basic nitrogen atom in the 1-position [corresponding to the 4′-position in the acid (XIII; R = CO_2H)].

(*a*) The acid (XIII; R = CO_2H) resembles the acid (VI; R = CO_2H) prepared from the 1 : 2 : 3 : 4-tetrahydro-4-oxoarsinoline[4] in being pale yellow, whereas the acids from the oxoquinolines are red: contribution by a canonical form similar in type to (XIV), which by stabilising a zwitterion structure might well give rise to an intense colour,[1,2] is in the first two acids impossible and improbable respectively.

(*b*) The ultraviolet spectra of the acid (XIII; R = CO_2H) in various media (Fig. 4) show that absorptions by the acid and its anion are almost identical, and closely resemble

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[11] von Braun and Wolff, *Ber.*, 1922, **55**, 3675.

[12] Johnson, Woroch, and Buell, *J. Amer. Chem. Soc.*, 1949, **71**, 1901.

[13] Clemo and Perkin, *J.*, 1924, **125**, 1608.

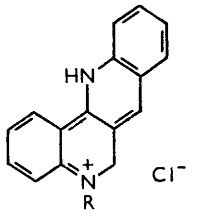
that of the derived base (XIII; R = H) (Fig. 5), whereas a slight shift to longer wavelength occurs on passing into an acidic medium. This evidence suggests strongly that the free acid is not a zwitterion.

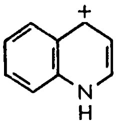
(*c*) Evidence from the infrared spectrum of the acid is indecisive. Although there are strong bands present in the regions 1610—1550 and 1400—1300 cm.$^{-1}$,[14] there are also three broad regions of absorption centred at 3310, 2450, and *ca.* 2000 cm.$^{-1}$ which indicate an analogy with cinchoninic acid and quinaldinic acid which apparently exist as a non-zwitterionic structure exhibiting powerful hydrogen-bonding.[15]

(*d*) The acid (XIII; R = CO_2H) sublimes unchanged when strongly heated at very low pressures; in this it again resembles the quinolino-acid (VI; R = CO_2H) derived from the oxoarsinoline,[4] but differs from those obtained from the oxoquinolines (III). Smooth decarboxylation is, however, effected by heating the acid at 14 mm.

The low-melting almost colourless dihydronaphthoquinoline (XIII; R = H) forms a pale yellow hydrochloride, which is unchanged even when boiled with concentrated hydrochloric acid for ten hours, and an allylic rearrangement analogous to the change (III $\longrightarrow$ X) could not be achieved. Further, the base is unaffected by an excess of permanganate in hot acetone, whereas the bases (III and X; R = Me or Ph) are rapidly converted into the keto-amines (XI; R = Me or Ph), even at room temperature, by this reagent.

Comparison of the ultraviolet spectra of the quinolino-derivatives (III; R = $SO_2{\cdot}C_6H_4Me$) and (XIII; R = H) in neutral and acidic solution (Fig. 4) shows that protonation of each base is accompanied by a small but significant bathochromic shift and by a marked increase in the intensity of the long-wave absorption band. In the case of the quinolino-bases (III; R = Me or Ph), any similar effect would be masked by the more striking spectroscopic changes caused by the marked resonance (VIII) $\longleftrightarrow$ (XIV) of their cations. This effect was noted previously[4] for the analogous quinolino(3′ : 2′-3 : 4)-arsinoline (VI; R = H), in which again only the 1′-quinolino-nitrogen atom has basic properties. The conversion of quinoline into its cation is also accompanied by an intensification of ultraviolet absorption,[16, 17] and by a small shift to longer wavelength, which has been attributed to participation of structures such as (XV) in the resonance hybrid of the cation;[16] forms analogous to (XV) are presumably also responsible for the corresponding spectroscopic effects in the bases (III; R = $SO_2{\cdot}C_6H_4Me$) and (XIII; R = H).


(XIV)


(XV)

A comparison of the above properties of the bases (III; R = ${\cdot}SO_2{\cdot}C_6H_4Me$) and (XIII; R = H) with those of the 1-methyl- and 1-phenyl-quinolino-analogues (III; R = Me or Ph) provides strong confirmation for our earlier suggestion[2] that the interannular allylic system of these polycyclic quinoline derivatives shows highly reactive tautomeric properties only if it is directly joined to a basic nitrogen atom. Other examples will be discussed later.[18]

Whereas this allylic rearrangement occurs in the direction (III) $\longrightarrow$ (X) under the influence of acids, the reverse change (X) $\longrightarrow$ (III) occurs when the free bases of type (X)

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[14] Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 1956, pp. 206 ff.

[15] Braunholtz, Hall, Mann, and Sheppard, unpublished work

[16] Ewing and Steck, *J. Amer. Chem. Soc.*, 1946, **68**, 2181.

[17] Albert, Brown, and Cheeseman, *J.*, 1951, 474.

[18] Braunholtz and Mann, following paper.

sublime at low pressure and is presumably determined by the greater stability of the more highly aromatised isomer (III).

EXPERIMENTAL

To obtain consistent m. p.s, certain substances were heated in evacuated tubes (indicated as E.T.) with the immersion temperature noted as (I.T.).

The Ketones.—α-Tetralone was a purified technical sample. The preparative sources of the keto-amines are given in the references in the following section.

The Friedländer Reaction.—(*a*) In a typical reaction, a solution of 1 : 2 : 3 : 4-tetrahydro-1-methyl-4-oxoquinoline [7] (I; R = Me) (0·3 g.) in ethanol (3 c.c.) was treated with *o*-aminobenzaldehyde [4] (0·25 g., 1·1 mol.) and 10% aqueous sodium hydroxide (0·3 c.c.); the mixture was set aside at room temperature for 36 hr. under nitrogen, then diluted with water (1 c.c.); the crystalline deposit of 1 : 2-dihydro-1-methylquinolino(3′ : 2′-3 : 4)quinoline [2] (III; R = Me) (0·4 g., 87%) had m. p. 98—100° after crystallisation from ethanol (Found: N, 11·6. Calc. for $C_{17}H_{14}N_2$: N, 11·4%).

(*b*) The following Friedländer conversions were similarly effected, *ca.* 1·1 mol. of *o*-aminobenzaldehyde being used for each keto-methylene group: 1 : 2 : 3 : 4-Tetrahydro-4-oxo-1-phenylquinoline [8] (I; R = Ph) into 1 : 2-dihydro-1-phenylquinolino(3′ : 2′-3 : 4)quinoline [1] (III; R = Ph) (96%), m. p. 139—142° (from ethanol) (lit.,[1] 139—141°) (Found: N, 9·15. Calc. for $C_{22}H_{16}N_2$: N, 9·1%); 1 : 2 : 3 : 4-tetrahydro-4-oxo-1-toluene-*p*-sulphonylquinoline [19] (I; R = $SO_2{\cdot}C_6H_4Me$) into 1 : *2-dihydro-1-toluene-*p*-sulphonylquinolino*(3′ : 2′-3 : 4)*quinoline* (III; R = $SO_2{\cdot}C_6H_4Me$) (47%), pale cream needles, m. p. 179° (from ethanol) (Found: C, 71·7; H, 4·85; N, 7·15. $C_{23}H_{18}O_2N_2S$ requires C, 71·5; H, 4·7; N, 7·25%); 1 : 6-dioxojulolidine [20, 21] (II; R = R′ = H) into diquinolino(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)juline [3] (IV; R = R′ = H) (81%), m. p. 327° (E.T., I.T. 320°) (lit.,[3] m. p. 320°) (from pyridine) (Found: N, 11·15. Calc. for $C_{26}H_{17}N_3$: N, 11·3%); 7-methyl-1 : 6-dioxojulolidine [5, 21, 22] (II; R = Me, R′ = H) into *7-methyldiquinolino*(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)*juline* (cf. ref. 5) (IV; R = Me, R′ = H) (83%), intensely yellow needles, m. p. 275° (E.T., I.T. 265°) (from pyridine) (Found: C, 84·45; H, 4·95; N, 11·1. $C_{27}H_{19}N_3$ requires C, 84·2; H, 4·9; N, 10·9%); 7 : 9-dimethyl-1 : 6-dioxojulolidine [5] (II; R = R′ = Me) into 7 : *9-dimethyl-6-oxoquinolino*(2′ : 3′-1 : 2)*juloline* (VII; R = R′ = Me) (cf. ref. 5) (50%), bright yellow platelets, m. p. 195° (E.T., I.T. 175°) (from ethanol) (Found: C, 80·4; H, 6·0; N, 9·05. $C_{21}H_{18}ON_2$ requires C, 80·3; H, 5·75; N, 8·9%).

3′ : *4′-Dihydronaphtho*(1′ : 2′-2 : 3)*quinoline* (XIII; R = H).—(*a*) A solution of α-tetralone (3 g.) in aqueous ethanol (5 c.c./20 c.c.) containing potassium hydroxide (3·6 g.) was treated with isatin (3 g., 1 mol.), and boiled under reflux for 4·5 hr. The cold mixture, when poured into an excess of 10% aqueous acetic acid, deposited the crystalline 3′ : 4′-dihydronaphtho-(1′ : 2′-2 : 3)quinoline-4-carboxylic acid [11] (XIII; R = CO_2H) (4·25 g., 75%), very pale yellow crystals, m. p. 253° (effervescence) (from ethanol) (lit.,[11] m. p. 252°) (Found: N, 5·05. Calc. for $C_{18}H_{13}O_2N$: N, 5·1%).

(*b*) The acid (XIII; R = CO_2H) when heated at 250—280°/14 mm. underwent smooth decarboxylation without residue, giving 3′ : 4′-dihydronaphtho(1′ : 2′-2 : 3)quinoline [11] (XIII; R = H), m. p. 60° (from aqueous ethanol) (lit.,[11] m. p. 60°) (Found: N, 5·75. Calc. for $C_{17}H_{13}N$: N, 6·0%).

(*c*) The acid (XIII; R = CO_2H) sublimed unchanged at 210—220°/0·0001 mm.; the identity of the pale yellow crystalline sublimate, m. p. and mixed m. p. 253° (effervescence) was confirmed by infrared spectroscopy.

Action of Hydrochloric Acid on the Quinolino-derivatives.—(A) *The* 1-*methyl bases* (III and X; R = Me).[8] (*a*) Pure samples of the isomeric monohydrochlorides (VIII; R = Me), deep red crystals, m. p. 240—245° (E.T.) (from ethanol–acetone) (Found: Cl^-, 12·7. Calc. for $C_{17}H_{14}N_2,HCl$: Cl^-, 12·6%) and (IX; R = Me), bright yellow hydrated needles, m. p. 243—245° (decomp.) (E.T., I.T. 230°) (from ethanol) (Found: Cl^-, 11·9. Calc. for $C_{17}H_{14}N_2,HCl,H_2O$: Cl^-, 11·9%), were prepared for infrared examination.

(*b*) Basification of a solution of the pure hydrochloride (IX; R = Me) gave the isomeric

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[19] Braunholtz and Mann, *J.*, 1957, 4166.
[20] Mann and Smith, *J.*, 1951, 1898.
[21] Braunholtz and Mann, *J.*, 1952, 3046.
[22] *Idem, J.*, 1954, 651.

orange base (X; R = Me), m. p. 159—160° (E.T.) (lit.,[2] m. p. 155°) (from acetone), with infra-red spectrum identical with that recorded earlier.[2] This sample was used for the nuclear magnetic resonance investigation.

(B) *The* 1-*phenyl bases* (III and X; R = Ph). (*a*) A solution of the base (III; R = Ph), when treated with dry hydrogen chloride, precipitated the deep red monohydrochloride [1] (VIII; R = Ph), m. p. 285—290° (E.T.; colour change to yellow-brown before melting) [lit.,[1] m. p. 280° (decomp.)] (from ethanol containing a small quantity of hydrogen chloride) (Found: C, 76·65; H, 5·2; Cl^-, 10·1. Calc. for $C_{22}H_{16}N_2$,HCl: C, 76·7; H, 5·0; Cl^-, 10·3%). Prolonged treatment with hydrogen chloride did not furnish a colourless dihydrochloride (cf. III; R = Me[2]).

(*b*) A suspension of the base (III; R = Ph) in concentrated hydrochloric acid–ethanol (3 : 1 by vol.) was boiled under reflux for 8 hr. in nitrogen, very little colour change occurring in the dark red solution. The mixture when set aside overnight deposited a *monohydrochloride*, plum-coloured plates with a metallic sheen, m. p. 285—290° (E.T., I.T. 275°; colour change to yellow-brown before melting) (Found: Cl^-, 9·95. $C_{22}H_{16}N_2$,HCl,H_2O requires Cl^-, 9·75%). This hydrochloride, which was probably dimorphous with (IX; R = Ph) (see p. 3370), could not be obtained free from traces of its precursor (VIII; R = Ph), which coloured its solutions red-brown; on basification it yielded the crude orange base (X; R = Ph).

(*c*) When the purple solution of the base (III; R = Ph) (300 mg.) in concentrated hydrochloric acid (12 c.c.) containing dioxan (1—2 c.c.) was boiled under reflux for 4 hr., its colour gradually changed to bright yellow, with a greenish fluorescence; on cooling, the solution deposited almost quantitatively the bright yellow *monohydrochloride monohydrate* [2] (IX; R = Ph), m. p. 290—295° (E.T., I.T. 250°) (lit.,[2] 228—230° from room temperature) (from water containing a trace of ethanol) (Found: C, 73·1; H, 5·4; Cl^-, 9·85. Calc. for $C_{22}H_{16}N_2$,HCl,H_2O: C, 72·9; H, 5·25; Cl^-, 9·75%). (The composition of the sample briefly recorded earlier [2] was incorrectly shown as $C_{22}H_{18}N_2$,HCl.) It is noteworthy that both the " isomeric " yellow hydrochlorides (IX; R = Me or Ph) differ from their red precursors (VIII; R = Me or Ph) in the tenacity with which they retain one molecule of water of crystallisation.

(C) *The* 1-*toluene*-p-*sulphonyl base* (III; R = $SO_2 \cdot C_6H_4Me$). (*a*) Treatment of an ethereal solution of the derivative (III; R = $SO_2 \cdot C_6H_4Me$) with dry hydrogen chloride in the usual way afforded the pale yellow monohydrochloride (VIII; R = $SO_2 \cdot C_6H_4Me$), m. p. 180—185°, which was too unstable to be completely purified for analysis.

(*b*) A solution of the base (III; R = $SO_2 \cdot C_6H_4Me$) (30 mg.) in ethanol (1 c.c.) mixed with dilute hydrochloric acid (2 c.c.) was boiled under reflux for 4 hr., and on cooling deposited the yellow crystalline hydrochloride (VIII; R = $SO_2 \cdot C_6H_4Me$) (30 mg.), which was identified by infrared analysis, and on basification yielded the starting material (III; R = $SO_2 \cdot C_6H_4Me$).

(*c*) When the bright yellow solution of the base (III; R = $SO_2 \cdot C_6H_4Me$) (120 mg.) in concentrated hydrochloric acid (5 c.c.) containing a few drops of ethanol was boiled under reflux for 2 hr., the colour changed to deep orange and the solution deposited the bright yellow 1 : 4'-dihydroquinolino(3' : 2'-3 : 4)quinoline monohydrochloride [2, 13] (X; R = H) (75 mg., 89%), m. p. 322—323° (decomp.) (E.T., I.T. 160°) (lit.,[2] m. p. 310—312°), yellow needles (from aqueous ethanol) (Found: Cl^-, 13·2. Calc. for $C_{16}H_{12}N_2$,HCl: Cl^-, 13·2%). The identity of this salt was confirmed by infrared spectroscopy.

(D) *The naphthoquinoline* (XIII; R = H). (*a*) A solution of the base (XIII; R = H) in ether–acetone, when treated with dry hydrogen chloride, afforded the unstable pale yellow hydrochloride, m. p. 223° (decomp.) (lit.,[11] m. p. 226°) (Found: Cl^-, 13·6. Calc. for $C_{17}H_{13}N$,HCl: Cl^-, 13·3%).

(*b*) No colour change occurred when a solution of the base (XIII; R = H) in concentrated hydrochloric acid was boiled under reflux for 6 hr.; the cooled solution furnished the above hydrochloride, which on basification regenerated the base (XIII; R = H), m. p. and mixed m. p. 58—59°, with infrared characteristics identical with those of the authentic material.

1 : 4'-*Dihydro*-1-*phenylquinolino*(3' : 2'-3 : 4)*quinoline* (X; R = Ph).—A solution of the yellow monohydrochloride (IX; R = Ph) in air-free water was filtered into a dilute solution of sodium carbonate in air-free water, in a nitrogen atmosphere. The orange amorphous precipitate was washed with cold water and dried under a vacuum at room temperature, affording 1 : 4'-*dihydro*-1-*phenylquinolino*(3' : 2'-3 : 4)*quinoline* (X; R = Ph), m. p. 89—90° (E.T., I.T. 85°) (Found: C, 83·6; H, 5·25; N, 8·9. $C_{22}H_{16}N_2$ requires C, 85·7; H, 5·2; N, 9·1%). The base could not be satisfactorily recrystallised, nor could a satisfactory carbon analysis be

obtained. Molecular-weight determination by the drop-evaporation method [23] ($0{\cdot}67 \times 10^{-2}$M in chloroform) gave values 291, 337 (calc., 308).

The base (X; R = Ph) (50 mg.) when heated at 200—250°/0·01 mm. afforded a clear yellow distillate which solidified, to give the " parent base," 1 : 2-dihydro-1-phenylquinolino(3' : 2'-3 : 4)quinoline (III; R = Ph) (40 mg., 80%), m. p. 138—140° (from ethanol), undepressed on admixture with the authentic material and having an identical infrared spectrum.

Atmospheric and Permanganate Oxidation of the Bases.—(*a*) An acetone solution of the orange base (X; R = Ph) was treated at room temperature with a cold saturated acetone solution of potassium permanganate in portions, until the initially rapid decolorisation had ceased. The mixture, when set aside for 1 hr., filtered, and concentrated, deposited 1 : 2-dihydro-2-oxo-1-phenylquinolino(3' : 2'-3 : 4)quinoline (XI; R = Ph) (yield quantitative), m. p. 255—256° (from ethanol), identical (m. p. and mixed m. p. and infrared spectrum) with the authentic material.[1] The same oxoquinoline (XI; R = Ph) was also obtained when benzene solutions of each isomeric base (III and X; R = Ph) were exposed to the atmosphere for 1 week.

(*b*) Neither of the above methods of oxidation affected the quinolino-bases (III; R = $SO_2{\cdot}C_6H_4Me$) and (XIII; R = H), which were recovered almost quantitatively.

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[23] Müller and Stolten, *Analyt. Chem.*, 1953, **25**, 1103; see also Taylor and Hall, *ibid.*, 1951, **23**, 947.