683. *The Structure and Properties of Certain Polycyclic Indolo- and Quinolino-derivatives. Part XI.* Derivatives of* 4 : 5 : 6 : 7-*Tetrahydro*-1-*methyl*-4-*oxo*-2 : 3-*benzazepine.*

By JOHN T. BRAUNHOLTZ and FREDERICK G. MANN.

4 : 5 : 6 : 7-Tetrahydro-1-methyl-4-oxo-2 : 3-benzazepine in its simple reactions resembles 1 : 2 : 3 : 4-tetrahydro-1-methyl-4-oxoquinoline, but its indolo- and quinolino-derivatives differ markedly from those of the oxoquinoline. The Fischer reaction with the phenylhydrazone yields a true indole instead of a ψ-indole: the quinolino-acid obtained by the Pfitzinger reaction does not show the marked resonance and deep colour of the oxoquinoline derivative, and the corresponding base, obtained by decarboxylation of the acid or by direct application of the Friedländer reaction, does not undergo acid-catalysed allylic rearrangement or ready oxidation to a cyclic amide.

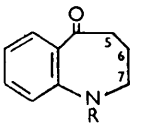
WE have investigated the preparation of 4 : 5 : 6 : 7-tetrahydro-1-methyl-4-oxo-2 : 3-benzazepine (I; R = Me) in order to compare the properties of this seven-membered ketoamine and certain of its polycyclic derivatives with those of 1 : 2 : 3 : 4-tetrahydro-1-methyl-4-oxoquinoline (II) and its corresponding derivatives.[1,2]

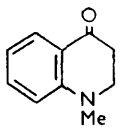
1-Arylsulphonyl-4 : 5 : 6 : 7-tetrahydro-4-oxo-2 : 3-benzazepines (*e.g.*, I; R = SO_2Ph) cannot be prepared by Friedel–Crafts cyclisation of γ-arylsulphonamidobutyryl chlorides (*e.g.*, III; R = SO_2Ph),[3,4,5] although the corresponding propionyl chlorides readily give the six-membered derivatives (as II).[6] Compounds such as (I; R = $SO_2{\cdot}C_6H_4Me$-*p*)

* Part X, preceding paper.

[1] Allison, Braunholtz, and Mann, *J.*, 1954, 403.
[2] Braunholtz and Mann, *J.*, 1955, 381.
[3] Astill and Boekelheide, *J. Amer. Chem. Soc.*, 1955, **77**, 4079.
[4] Proctor and Thomson, *J.*, 1957, 2302.
[5] Braunholtz and Mann, *J.*, 1957, 4174.
[6] Clemo and Perkin, *J.*, 1924, **125**, 1608; cf. also Johnson, Woroch, and Buell, *J. Amer. Chem. Soc.*, 1949, **71**, 1901.

have, however, recently been obtained by Proctor and Thomson [7] by a Dieckmann-type cyclisation, using intermediates such as (IV; R = $SO_2 \cdot C_6H_4Me$, R′ = R″ = alkyl), and


(I)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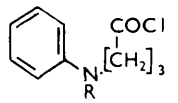
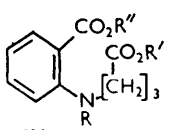
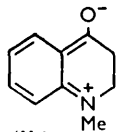
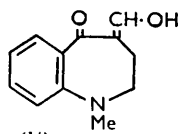

(III)

the 1-methyl derivative (I; R = Me) has similarly been obtained by Astill and Boekelheide [3] by cyclisation of the diester (IV; R = R′ = R″ = Me), followed by hydrolysis and decarboxylation. We have found that Dieckmann cyclisation of the diester (IV; R = R″ = Me, R′ = Et) under various conditions also gives the 1-methyl derivative (I; R = Me) in *ca.* 50% yield, and have briefly recorded that this compound shows both ketonic and basic properties,[8] contrary to earlier statements.[3]


(IV)


(IIA)


(V)

The infrared spectrum of this keto-amine is normal and resembles that of the quinolone (II), showing absorption bands [9] due to >NMe at 2820 cm.$^{-1}$ and to C=O at 1665 cm.$^{-1}$, with weak absorption at 3480 cm.$^{-1}$ (broad) possibly due to an enolic hydroxyl group; the corresponding bands in the spectrum of the keto-amine (II) are at 2835, 1677, and 3580 (broad) cm.$^{-1}$ respectively.

The ultraviolet spectra of the keto-amines (I; R = Me) and (II) are also closely similar (Fig. 1); the relative position of the long-wavelength absorption maxima suggests, however, that there is in the former compound slightly less interaction between the nitrogen atom and the carbonyl group, of type (IIA).[10] * This is probably due to loss of coplanarity caused by the steric requirements of the saturated seven-membered ring.[11]

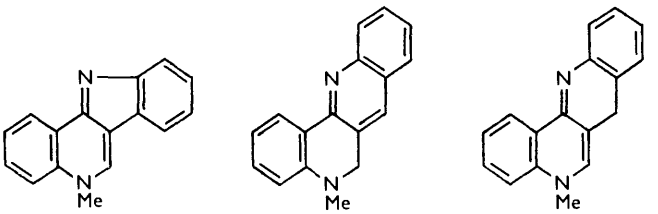
The keto-amine (I; R = Me), in conformity with its spectroscopic similarity to (II), shows normal ketonic reactivity towards phenylhydrazine, 2 : 4-dinitrophenylhydrazine, and semicarbazide. Our efforts to condense the 5-methylene group of the keto-amine with *p*-dimethylaminobenzaldehyde and with *p*-nitrosodimethylaniline have failed, in contrast to the results obtained [13] with the oxoquinoline (II); Astill and Boekelheide [3] have, however, introduced an exocyclic double bond at the 5-position by conversion of the ketone (I; R = Me) into the formyl derivative (V). The basic strength of the keto-amine (I; R = Me), although low, is greater than that of the oxoquinoline (II), for the keto-amine forms a colourless hydrochloride which can be recrystallised from ethanol; in the infrared spectrum of this salt, the >NMe absorption band of its parent is absent, but the $\geq NH^+$ band is present at 2190 cm.$^{-1}$ and the C=O band at 1685 cm.$^{-1}$, close to its position in the 1-acyltetrahydro-4-oxoquinolines.[10]

The tetrahydro-4-oxoquinolines (*e.g.*, II) are converted by the Fischer and the

* In ref. 10 we misquoted the position of the long-wavelength absorption band of β-tetralone, which should be at 292 mμ (ε 1710) (Fig. 1).

[7] Proctor and Thomson, *J.*, 1957, 2312.
[8] Braunholtz and Mann, *Chem. and Ind.*, 1957, 266.
[9] Braunholtz, Ebsworth, Mann, and Sheppard, *J.*, 1958, 2780.
[10] Braunholtz and Mann, *J.*, 1957, 4166.
[11] Hedden and Brown, *J. Amer. Chem. Soc.*, 1953, **75**, 3744.
[12] Biquard, *Bull. Soc. chim. France*, 1941, **8**, 55.
[13] Ittyerah and Mann, *J.*, 1958, 467.

Pfitzinger (or Friedländer) reaction respectively into ψ-indolo- (*e.g.*, VI) and quinolino- (*e.g.*, VII and VIII) derivatives, which have been extensively investigated.[2,14] 4 : 5 : 6 : 7-Tetrahydro-1-methyl-4-oxo-2 : 3-benzazepine (I; R = Me) is a particularly interesting



(VI) (VII) (VIII)

compound for an extension of these reactions; the mechanisms suggested,[2,14] on the basis of earlier work, to account for the formation of ψ-indoles rather than normal indoles, and for the allylic interconversion (VII ⇌ VIII), are not applicable to the corresponding

FIG. 1. FIG. 2.

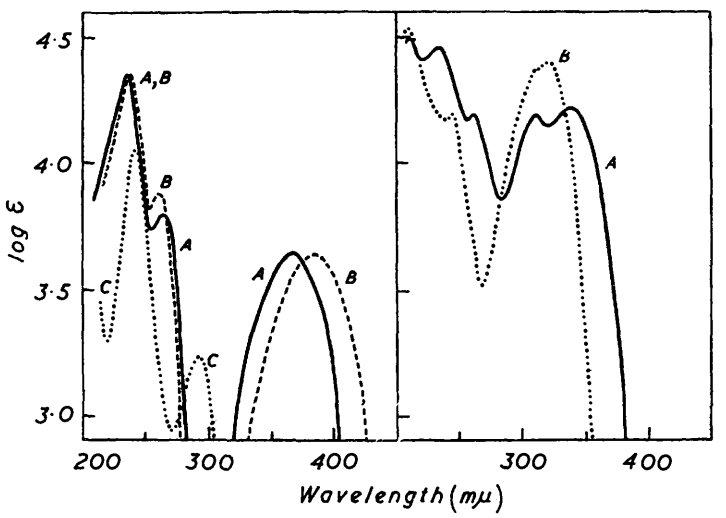
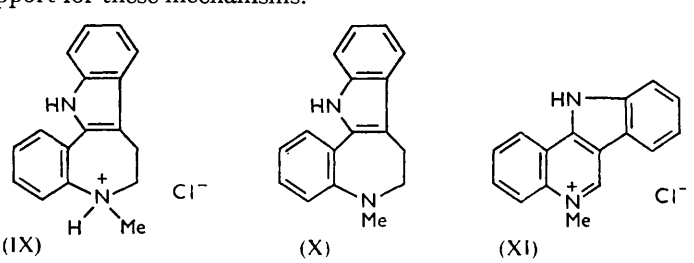


FIG. 1. *Ultraviolet spectra of ethanolic solutions of* (*A*) 4 : 5 : 6 : 7-*tetrahydro*-1-*methyl*-4-*oxo*-2 : 3-*benzazepine* (I; R = Me), (*B*) 1 : 2 : 3 : 4-*tetrahydro*-1-*methyl*-4-*oxoquinoline* (II), *and* (*C*) β-*tetralone* (*see also Biquard* [12]). *Curves* (*A*) *and* (*B*) *have minima at* 294 mμ (log ε 2·556) *and* 288 mμ (log ε 1·740) *respectively, which are not shown.*

FIG. 2. *Ultraviolet spectra of* 6 : 7-*dihydro*-1-*methyl*-2 : 3-*benzindolo*(2′ : 3′-4 : 5)*azepine* (X), (*A*) *in ethanol,* (*B*) *in* 1 : 1 *ethanol–*N*-hydrochloric acid.*

derivatives of the benzazepine system (I; R = Me). The results described below now give strong support for these mechanisms.

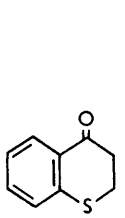


(IX) (X) (XI)

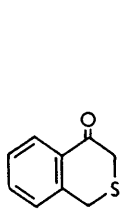
[14] Braunholtz and Mann, preceding paper.

When a solution of the syrupy phenylhydrazone of the oxobenzazepine (I; R = Me) in ethanol saturated with hydrogen chloride is boiled under reflux, the stable colourless monohydrochloride (IX) is obtained in high yield. The indole >NH group and the $\geqslant NH^+$ group give rise to infrared absorption at 3210 and 2420 cm.$^{-1}$ respectively; >NMe absorption in the 2800 cm.$^{-1}$ region is absent, as in the spectrum of the hydrochloride of the parent keto-amine (I; R = Me). Basification of the solution of the salt (IX) yields the cream-coloured indolobenzazepine (X), the structure of which as a true indole is beyond doubt. Its infrared spectrum shows >NH absorption maxima at 3420 and 3380 cm.$^{-1}$ and a shoulder (2800 cm.$^{-1}$) corresponding to the >NMe group;[9] further, the similarity between the ultraviolet spectra of the base (X) in ethanol and in ethanolic hydrochloric acid (Fig. 2) accords with the protonation of the benzazepine-nitrogen atom rather than that of a ψ-indole, such as (VI), where a marked hypsochromic shift occurs.[2]

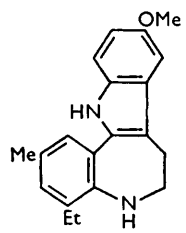
It is thus clear that when the driving force of aromatisation is excluded, the ready abnormal Fischer reaction, described in earlier papers in this series,[2,15] leading to salts (*e.g.*, XI) of ψ-indoles such as (VI), is replaced by normal indolisation. Conjugation of the nitrogen atom of the keto-amine with the potential indolo-nitrogen atom, as in (I; R = Me) and in (II), is, therefore, not a sufficient factor alone for ψ-indole formation, although we believe that it is a necessary one; for example, 1-thiochroman-4-one (XII) and 2-thio-*iso*chroman-4-one (XIII) both give true indolo-derivatives,[16] although in each case the salt of a ψ-indolo-form would have enhanced aromatic character.



(XII)



(XIII)



(XIV)

It is noteworthy that the selenium dehydrogenation of the alkaloid ibogaine is reported [17] to give two heterocyclic bases, to one of which is assigned the structure (XIV), closely related to the indolobenzazepine (X); the ultraviolet spectra of this base (XIV), in ethanolic and hydrochloric acid solution, are very similar to those of the base (X) (Fig. 2).

Attempts to oxidise the indole (X) to a keto-indole derivative yielded mixtures from which pure products could not be isolated; unsuccessful attempts have also been made to dehydrogenate the saturated 6 : 7-linkage, by reagents such as palladium–charcoal or chloranil.

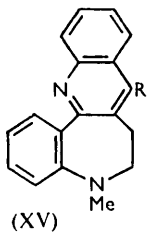
The oxobenzazepine (I; R = Me) reacts with alkaline isatin similarly to the oxoquinoline (IV), giving 6 : 7-dihydro-1-methyl-2 : 3-benzoquinolino(2′ : 3′-4 : 5)azepine-4′-carboxylic acid (XV; R = CO_2H) in moderate yield. This acid, in contrast to the scarlet quinolino-acid [2] (XVII), is pale yellow, melts without immediate effervescence and sublimes unchanged at very low pressures; a slow decarboxylation can be effected at *ca.* 300°/15 mm. These indications that the acid is not zwitterionic (as XVI; R = CO_2^-) are supported by spectroscopic evidence:

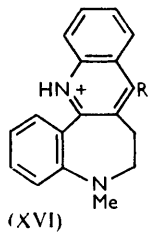
(*a*) The infrared spectrum of the acid (XV; R = CO_2H) does not contain the dominant pair of absorption bands in the regions 1610—1550 and 1400—1300 cm.$^{-1}$ which are characteristic of the carboxylate ion,[18] but resembles that [19] of cinchoninic acid (XVIII) and of

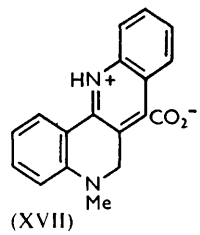
[15] Mann, *J.*, 1949, 2816.
[16] Kiang and Mann, *J.*, 1957, 1909.
[17] Bartlett, Dickel, and Taylor, *J. Amer. Chem. Soc.*, 1958, **80**, 126; see also Taylor, *ibid.*, 1957, **79**, 3298.
[18] Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 1956, p. 149.
[19] Braunholtz, Hall, Mann, and Sheppard, unpublished work.

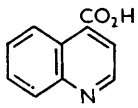
certain other related quinoline-4-carboxylic acids (see preceding paper). Three rather ill-defined regions of absorption are centred at 2450, 1950, and 1700 cm.$^{-1}$, and probably arise from strongly hydrogen-bonded hydroxyl groups.

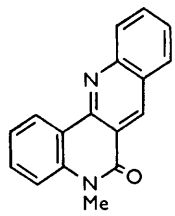
(*b*) The ultraviolet spectra of the acid (XV; R = CO_2H) in neutral and alkaline media are shown in Fig. 3. The similarity between the spectra of the acid and its anion (XV; R = CO_2^-) strongly suggests that the acid does not have the zwitterion structure (XVI;

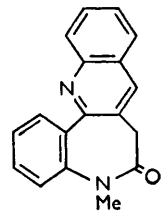

(XV)


(XVI)


(XVII)


(XVIII)


(XIX)


(XX)

R = CO_2^-), which would have additional resonance not possible in the anion (XV; R = CO_2^-). It is noteworthy that the spectrum of the quinolino-acid (XVII), derived from the keto-amine (II), on the other hand, undergoes a very marked hypsochromic shift on passing from neutral to alkaline solution.[2]

These properties (*a*) and (*b*) differ markedly from those of the acid (XVII); it is probable that the formation of the zwitterion occurs only when favoured by additional resonance stabilisation, which apparently cannot occur in the non-planar seven-membered ring.

The Friedländer reaction [14,20] between the oxobenzazepine (I; R = Me) and *o*-aminobenzaldehyde readily gives 6 : 7-dihydro-1-methyl-2 : 3-benzoquinolino(2′ : 3′-4 : 5)azepine (XV; R = H), identical with the product of decarboxylation of the acid (XV; R = CO_2H). The relationship of the base to the analogous quinolino-derivative (VII) may be summarised:

(*a*) The base (XV; R = H) sublimes unchanged; it forms fine cream-coloured needles, whereas the analogous quinolinoquinoline (VII) is intensely yellow. The formulation of the base (XV; R = H) as a true quinoline derivative is supported by the infrared spectrum, which shows the characteristic trio of absorption bands at 1617 (w), 1598 (m), and 1572 cm.$^{-1}$ (w), which have been observed with compounds of type (VII) but not with the allylic isomers (as VIII) (see preceding paper). The expected >NMe absorption band [9] at 2810 cm.$^{-1}$ is also observed.

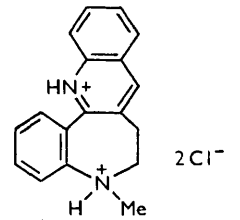
(*b*) The base (XV; R = H) is unchanged after exposure to the atmosphere in benzene solution for a week, or in the solid state for several weeks, and is not appreciably affected by a cold saturated solution of potassium permanganate. This stability is in marked contrast to that of the bases (VII) and (VIII), which in similar circumstances oxidise readily to the cyclic amide (XIX).

The oxo-derivative (XX) is obtained only when the base (XV; R = H) is boiled in acetone with permanganate for an hour. The disappearance of the *N*-methyl infrared absorption band, the lack of ketonic properties and the very low basic strength show that this oxidation product is the 7-oxo- and not the 6-oxo-isomer, which should be ketonic and

[20] Mann and Wilkinson, *J.*, 1957, 3336.

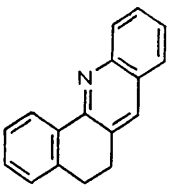
should absorb in the 2800 cm.$^{-1}$ region. Infrared absorption due to the carbonyl group occurs at 1660 cm.$^{-1}$, very close to that [2] in the 2-oxoquinolinoquinoline (XIX) (1656 cm.$^{-1}$).

(*c*) Treatment of an acetone solution of the benzoquinolinoazepine with dry hydrogen chloride readily affords either an orange monohydrochloride having the cation (XVI;

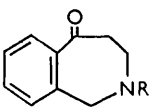


(XXI)

2Cl$^-$



(XXII)



(XXIII)

R = H), or a rather unstable colourless dihydrochloride (XXI), according to the quantity of gas employed. The NMe absorption band is present at 2807 cm.$^{-1}$ in the infrared spectrum of the first salt (XVI; R = H), but is absent from that of the second (XXI).

FIG. 3.

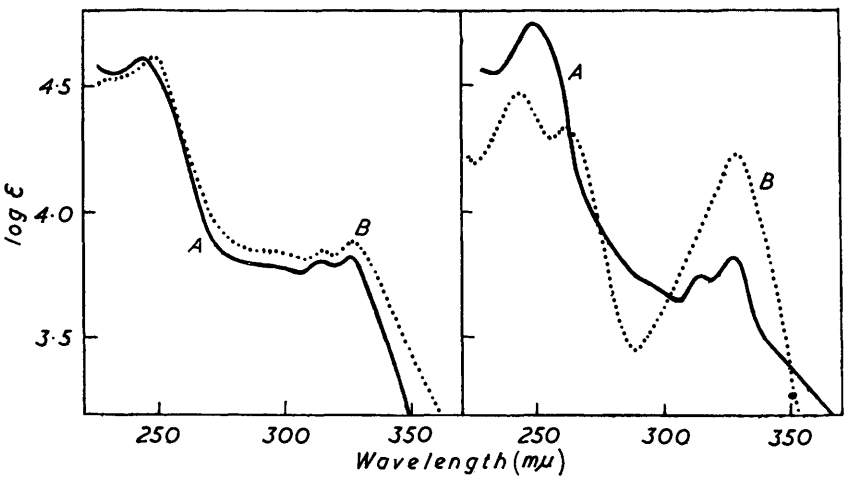


FIG. 4.

FIG. 3. *Ultraviolet spectra of* 6 : 7-*dihydro*-1-*methyl*-2 : 3-*benzoquinolino*(2′ : 3′-4 : 5)*azepine*-4′-*carboxylic acid* (XV; R = CO_2H), (*A*) *in* 0·1N-NaOH, (*B*) *in ethanol.*

FIG. 4. *Ultraviolet spectra of* 6 : 7-*dihydro*-1-*methyl*-2 : 3-*benzoquinolino*(2′ : 3′-4 : 5)*azepine* (XV; R = H), (*A*) *in ethanol*, (*B*) *in* 1 : 1 *ethanol*–N-*hydrochloric acid.*

This behaviour is similar to that of the corresponding quinolinoquinoline (VII); the ultraviolet spectra of the base (XV; R = H) in neutral and acid solution (Fig. 4) show, however, that the bathochromic shift accompanying salt formation is much less marked with (XV; R = H) than with (VII),[2] and the long-wave absorption intensities are much lower. This is presumably due to the diminished importance of structures in which the positive charge on the 1′-nitrogen atom is borne by the azepine-nitrogen. The observed small shift may in fact be due to contributions of a different type altogether, since an analogous displacement, to longer wavelength, of less than 20 mμ, accompanied by a marked increase in the intensity of absorption, has been found to accompany salt formation in the case of 3 : 4-dihydronaphtho(1′ : 2′-2 : 3)quinoline (XXII) (see preceding paper) and certain related bases in which " classical " cyanine-type resonance is impossible or improbable.

(*d*) The benzoquinolinoazepine (XV; R = H) differs strikingly from the quinolinoquinoline (VII) in its behaviour in hot hydrochloric acid. Although the latter base is thus

rapidly converted into the hydrochloride of the isomeric compound (VIII),[2] the azepine derivative does not undergo rearrangement even on prolonged boiling in concentrated acid, and this treatment yields only the unchanged monohydrochloride (XVI; R = H) and thence the original base (XV; R = H).

The marked differences in behaviour between the derivatives of the ketones (I; R = Me) and (II), brought about solely by the insertion of one additional methylene group into the keto-amine ring of the compound (II), are particularly interesting in connection with the structural features required to facilitate the allylic transformation (*e.g.*, VII ⇌ VIII): these differences emphasise that this allylic system should be directly joined to an atom readily protonated,[2,14] for the interposition of one " insulating " methylene group is sufficient to destroy the activating effect of such a basic centre. It is hoped later to describe indolo- and quinolino-derivatives of an isomeric keto-amine of type (XXIII).

Experimental

Ethyl γ-Bromobutyrate (cf. ref. 4).—Dry hydrogen bromide was bubbled into absolute ethanol (500 c.c.) at 0° until 100 g. had been absorbed. γ-Butyrolactone (67 g.) was added, and the mixture was boiled under reflux for 4·5 hr.; fractional distillation under reduced pressure gave the crude ethyl γ-bromobutyrate (100 g., 77%), b. p. 85—87°/14 mm., n_D^{20} 1·451, sufficiently pure for subsequent use.

Attempts to prepare the methyl ester by an analogous procedure were unsuccessful.

Methyl N-(3-*Ethoxycarbonylpropyl*)*anthranilate* (IV; R = H, R′ = Et, R″ = Me) (cf. ref. 3).—Ethyl γ-bromobutyrate (100 g.) and methyl anthranilate (200 g., 2·2 mol.) were heated together at 100° for 12 hr.; the pasty crystalline mass was then shaken with water (400 c.c.) to which an excess of sodium hydrogen carbonate was gradually added. The mixture was extracted with ether, which when dried and distilled yielded (*a*) unchanged methyl anthranilate (150 g.), b. p. 115—120°/0·4 mm., and (*b*) *methyl*-N-(3-*ethoxycarbonylpropyl*)*anthranilate* (IV; R = H, R′ = Et, R″ = Me) (75 g., 85% based on unrecovered methyl anthranilate), b. p. 176—180°/0·07 mm., forming colourless crystals, m. p. 43·5°, from light petroleum (b. p. 40—60°) (Found: C, 63·65; H, 7·5; N, 5·35. $C_{14}H_{19}O_4N$ requires C, 63·4; H, 7·2; N, 5·3%).

A solution of this diester (5 g.) in aqueous ethanol (25 c.c.: 10 c.c.) containing potassium hydroxide (7 g.), when boiled under reflux for 1 hr., cooled, and acidified to pH 6, deposited the colourless microcrystalline *diacid* (IV; R = R′ = R″ = H) (3·9 g., 95%), m. p. 190° (effervescence) (from ethanol) (Found: C, 59·3; H, 5·75; N, 6·5. $C_{11}H_{13}O_4N$ requires C, 59·2; H, 5·85; N, 6·3%).

Methyl N-*Benzoyl*-N-(3-*ethoxycarbonylpropyl*)*anthranilate* (IV; R = Bz, R′ = Et, R″ = Me).—A solution of the diester (IV; R = H, R′ = Et, R″ = Me) (5 g.) in dry pyridine (20 c.c.) was treated with benzoyl chloride (4·2 g., 1·6 mols.) gradually with shaking and cooling. The pasty mixture was then heated at 50° for 1 hr., cooled, and poured into water (300 c.c.). The heavy oil which separated was collected, washed with water by decantation, and fractionally distilled, giving an almost quantitative yield of *methyl* N-*benzoyl*-N-(3-*ethoxycarbonylpropyl*)-*anthranilate* (IV; R = Bz, R′ = Et, R″ = Me), b. p. 215—225°/0·05 mm. (Found: C, 68·0; H, 6·6; N, 3·85. $C_{21}H_{23}O_5N$ requires C, 68·3; H, 6·3; N, 3·8%); the ester solidified when set aside for 3 months, and then formed colourless needles, m. p. 46°, after crystallisation from ether–light petroleum (b. p. 40—60°).

This diester (1 g.) was quantitatively hydrolysed by boiling it in 50% aqueous ethanol (20 c.c.) containing potassium hydroxide (2 g.) for 45 min.; the cold mixture on acidification gave N-*benzoyl*-N-(3-*carboxypropyl*)*anthranilic acid* (IV; R = Bz, R′ = R″ = H), m. p. 175° (from aqueous ethanol) (Found: C, 66·15; H, 5·3; N, 4·35. $C_{18}H_{17}O_5N$ requires C, 66·1; H, 5·25; N, 4·3%).

Unsuccessful attempts to form the seven-membered ring of the benzazepine system (*e.g.*, I) were made as follows: (*a*) The dicarboxylic acid (IV; R = R′ = R″ = H) was treated with acetic anhydride and potassium acetate under a variety of conditions.[21] Black amorphous solids were the only products isolated. (*b*) The diester (IV; R = Bz, R′ = Et, R″ = Me) in xylene solution, when boiled under reflux with sodium for 9 hr. and then worked up in the usual way (cf. ref. 7), gave no ketonic product.

[21] Uhle, *J. Amer. Chem. Soc.*, 1949, **71**, 761; see also Bekhli, *Doklady Akad. Nauk S.S.S.R.*, 1955, **101**, 679; *Chem. Abs.*, 1956, **50**, 3441[a].

Methyl N-(3-*Ethoxycarbonylpropyl*)-N-*methylanthranilate* (IV; R = R″ = Me, R′ = Et) (cf. ref. 3).—The secondary amine (IV; R = H, R′ = Et, R″ = Me) (30 g.) and methyl iodide (45 g., 2·8 mol.) were heated together at 90° for 4 hr. in a stainless-steel autoclave. The cold product was added to a mixture of water (100 c.c.) and ether (50 c.c.) and treated with an excess of sodium hydrogen carbonate. The mixture was extracted with ether (400 c.c., portionwise), which was dried and evaporated. Fractional distillation gave a very small fore-run, b. p. 80—115°/0·01 mm., and then the *methyl* N-(3-*ethoxycarbonylpropyl*)-N-*methylanthranilate* (IV; R = R″ = Me, R′ = Et), b. p. 127—133°/0·01 mm. (18 g., 57%); redistillation gave the pure amine, b. p. 139°/0·03 mm. (Found: C, 64·8; H, 7·75; N, 5·25. $C_{15}H_{21}O_4N$ requires C, 64·5; H, 7·6; N, 5·0%).

4 : 5 : 6 : 7-*Tetrahydro*-1-*methyl*-4-*oxo*-2 : 3-*benzazepine* (I; R = Me).—In a typical Dieckmann cyclisation, a solution of the diester (IV; R = R″ = Me, R′ = Et) (6 g.) in dry xylene (35 c.c.) was added during 45 min. to a supension of " molecular " sodium (1 g., 2 g.-atoms) in vigorously stirred, boiling xylene (120 c.c.) under a slow stream of nitrogen, the boiling being then continued with stirring for 7—12 hr. The cold mixture was treated with sufficient methanol to decompose the excess of sodium. The xylene solution was extracted with 6N-hydrochloric acid (3 × 40 c.c.), and the aqueous extract was boiled under reflux in nitrogen for 45 min.; the mixture was cooled, treated with an excess of sodium hydrogen carbonate, and extracted with ether. Fractional distillation of the dried extract under nitrogen gave 4 : 5 : 6 : 7-tetrahydro-1-methyl-4-oxo-2 : 3-benzazepine (I; R = Me) (1·8 g., 48%), b. p. 112°/0·2 mm. (Found: N, 8·25. Calc. for $C_{11}H_{13}ON$: N, 8·0%) (lit.,[3] b. p. 112°/0·07 mm.). The pale yellow liquid ketone did not crystallise; it was stable for several weeks under normal conditions.

When the above procedure was repeated, with toluene in place of xylene, a yield of *ca.* 42% was obtained; when 1 g.-atom of sodium was used, in xylene containing a trace of methanol,[22] with heating under reflux for 10 hr., the yield was 40%. The Dieckmann reaction employing sodium in anhydrous benzene containing a trace of methanol gave a 27% yield, and the use of sodium hydride in dry benzene gave only traces of ketonic material. Repetition of the procedure of Astill and Boekelheide,[3] with boiling dry toluene with potassium *tert.*-butoxide as catalyst, gave the same yield (48%) as in the above experiment.

Derivatives of the Benzazepine (I; R = Me).—(*a*) A solution of the ketone (I; R = Me) (0·5 g.) in ethanol (5 c.c.) containing water (2 c.c.) was treated with semicarbazide hydrochloride (0·35 g.) and sodium acetate; the solution was boiled under reflux in nitrogen for 2 hr. and on cooling deposited 4 : 5 : 6 : 7-*tetrahydro*-1-*methyl*-4-*oxo*-2 : 3-*benzazepine semicarbazone* (0·5 g., 75%), colourless platelets, m. p. 198° (from ethanol) (Found: C, 61·8; H, 6·8; N, 24·4%; *M*, ebullioscopic in ethanol, 244. $C_{12}H_{16}ON_4$ requires C, 62·0; H, 6·95; N, 24·1%; *M*, 232). (*b*) An ethanolic solution of the ketone (I; R = Me) when briefly warmed with a solution of 2 : 4-dinitrophenylhydrazine in ethanolic hydrochloric acid, deposited the stable orange microcrystalline 2 : 4-*dinitrophenylhydrazone*, m. p. 202—203° (Found: N, 19·85. $C_{17}H_{17}O_4N_5$ requires N, 19·6%). (*c*) The phenylhydrazone of the ketone (I; R = Me), prepared in the usual way, formed a viscous syrup which did not crystallise. (*d*) Treatment of an acetone–ether solution of the base (I; R = Me) with dry hydrogen chloride precipitated the colourless *hydrochloride*, m. p. 160—161° (decomp.) after crystallisation from ethanol (Found: C, 62·4; H, 6·6; N, 6·45; Cl, 17·0. $C_{11}H_{13}ON$,HCl requires C, 62·4; H, 6·65; N, 6·6; Cl, 16·75%). (*e*) The picrate was precipitated from aqueous-ethanolic solution by aqueous picric acid but has not been obtained pure.

Reactions of the 5-*Methylene Group*.—All attempts to isolate crystalline products of condensation between the 5-methylene group of the ketone (I; R = Me) and *p*-dimethylaminobenzaldehyde or *p*-nitrosodimethylaniline [13] have failed: the former reagent gave no reaction, and the latter gave intractable tars.

6 : 7-*Dihydro*-1-*methyl*-2 : 3-*benzindolo*(2′ : 3′-4 : 5)*azepine* (X).—A solution of the syrupy phenylhydrazone (from 1·4 g. of ketone) in a mixture of saturated ethanolic hydrogen chloride (50 c.c.) and ethanol (10 c.c.) was boiled under reflux for 8 hr. The deep orange solution became first ruby-red, then slowly yellow-brown while a colourless solid separated. The solution was cooled to 0° for 2 hr., and the solid deposit then collected, washed with cold water, and recrystallised from ethanol containing a trace of water, yielding 6 : 7-*dihydro*-1-*methyl*-2 : 3-*benzindolo*-(2′ : 3′-4 : 5)*azepine hydrochloride* (IX) (2·1 g., 92%), m. p. 235° (effervescence) (Found: C,

[22] Openshaw and Robinson, *J.*, 1946, 912.

71·65; H, 6·25; N, 9·95; Cl, 12·3. $C_{17}H_{16}N_2$,HCl requires C, 72·0; H, 6·0; N, 9·85; Cl, 12·5%).

An aqueous-ethanolic solution of the hydrochloride (IX), when basified with 10% aqueous sodium hydroxide, yielded the *indole* (X), which formed cream-coloured needles, m. p. 119°, from aqueous ethanol in which it formed a colourless solution with a vivid violet fluorescence (Found: C, 82·2; H, 6·9; N, 11·2. $C_{17}H_{16}N_2$ requires C, 82·2; H, 6·5; N, 11·3%).

The indole (X) is completely stable when exposed to the atmosphere; a slow and partial oxidation apparently occurs in hot acetone–permanganate, but no pure derivative has been isolated.

6 : 7-*Dihydro*-1-*methyl*-2 : 3-*benzoquinolino*(2′ : 3′-4 : 5)*azepine*-4′-*carboxylic Acid* (XV; R = CO_2H).—Isatin (1·4 g., 1·2 mols.) and potassium hydroxide (1·7 g., 3·8 mols., in 5 c.c. of water) were added to a solution of the ketone (I; R = Me) (1·4 g.) in ethanol (10 c.c.) which was then boiled under reflux for 10 hr. in a nitrogen atmosphere, cooled, and filtered into an excess of a 10% solution of acetic acid in water. The crude yellow precipitate, when collected and recrystallised from dioxan, yielded 6 : 7-*dihydro*-1-*methyl*-2 : 3-*benzoquinolino*(2′ : 3′-4 : 5)-*azepine*-4′-*carboxylic acid* (XV; R = CO_2H) (0·75 g., 31%), a pale yellow microcrystalline powder, m. p. 295° (slow effervescence, in evacuated tube, immersion temp. 260°) (Found: C, 74·55; H, 5·6; N, 9·1. $C_{19}H_{16}O_2N_2$ requires C, 74·95; H, 5·3; N, 9·2%).

6 : 7-*Dihydro*-1-*methyl*-2 : 3-*benzoquinolino*(2′ : 3′-4 : 5)*azepine* (XV; R = H).—(A) *By the Friedländer reaction.* A solution of the ketone (I; R = Me) (0·7 g.) in warm ethanol (10 c.c.) was treated with *o*-aminobenzaldehyde [20] (0·5 g., 1 mol.) and aqueous 10% sodium hydroxide (0·2 c.c.), and set aside at room temperature under nitrogen for 1 week. The mixture on dilution with water deposited the crystalline 6 : 7-*dihydro*-1-*methyl*-2 : 3-*benzoquinolino*(2′ : 3′-4 : 5)*azepine* (XV; R = H) (0·8 g., 75%), colourless needles, m. p. 127° (from aqueous ethanol) (Found: C, 82·9; H, 6·3; N, 10·85. $C_{18}H_{16}N_2$ requires C, 83·0; H, 6·2; N, 10·8%). The base distils smoothly in the sublimation tube at *ca.* 300°/15 mm. without change (shown by m. p. and infrared spectrum).

(B) *By decarboxylation of the quinolino-acid* (XV; R = CO_2H). (*a*) The acid when heated in a tube at 0·002 mm. sublimed at 250—310° without residue. The yellow crystalline sublimate had m. p. and mixed m. p. 285—290°, and its infrared spectrum was identical with that of the original material.

(*b*) In a similar experiment at 15 mm. a clear viscous orange-yellow distillate was obtained at *ca.* 300°, and solidified to a glass on cooling. This product was shown, by infrared and chromatographic analysis to be the almost pure quinolino-base (XV; R = H) contaminated with traces of the acid (XV; R = CO_2H) which were readily removed by recrystallisation from aqueous ethanol.

Derivatives of the Quinolino-base (XV; R = H).—(*a*) The base reacted with boiling methyl iodide, to give the unstable *methiodide*, an orange microcrystalline powder, m. p. 210—211° (effervescence) (from acetone containing a trace of methanol) (Found: N, 7·05. $C_{19}H_{19}N_2I$ requires N, 7·0%).

(*b*) A dry ethereal solution of the pure base (XV; R = H) on cautious treatment with a slow stream of dry hydrogen chloride deposited the bright orange *monohydrochloride* (cation as XVI; R = H), m. p. 194—196° (Found: Cl^-, 12·3. $C_{18}H_{16}N_2$,HCl requires Cl^-, 12·0%). This salt could not be recrystallised satisfactorily; it dissolved readily in cold ethanol to give a stable deep orange solution, decolorised by additional hydrogen chloride (see below), whereas its solution in water slowly deposited the free base.

(*c*) A solution of the pure base in dry acetone, when treated with an excess of dry hydrogen chloride, became first orange, then colourless, and deposited the colourless *dihydrochloride* (XXI), m. p. 200—205° (giving a deep red liquid, and darkening and decomposing progressively before melting) after being washed with warm acetone (Found: Cl^-, 20·5. $C_{18}H_{16}N_2$,2HCl requires C, 21·0%). This salt was unstable; it gave orange solutions (*e.g.*, in ethanol), and became pink when exposed to the atmosphere or (rapidly) when heated.

(*d*) Several attempts were made to effect the acid-catalysed isomerisation of the base (XV; R = H). The unchanged base or its hydrochloride was recovered almost quantitatively after being boiled in solution in dilute hydrochloric acid (4 hr.), in concentrated hydrochloric acid (6 hr.), or in concentrated hydrochloric acid containing a small quantity of dioxan (6 hr.). Identification in each case was confirmed by infrared spectroscopy.

Permanganate Oxidation of the Base (XV; R = H).—A boiling solution of the

quinolino-base (XV; R = H) (50 mg.) in acetone (10 c.c.) was treated with an excess of saturated acetone–permanganate (in portions) during 2 hr.; the solution was further boiled under reflux until the purple colour disappeared, then cooled and filtered. The filtrate, when concentrated, filtered again, and cooled, deposited 6 : 7-*dihydro*-1-*methyl*-7-*oxo*-2 : 3-*benzo*-*quinolino*(2′ : 3′-4 : 5)*azepine* (XX) (50 mg., 95%), colourless needles, m. p. 192—193° (from aqueous ethanol) (Found: C, 78·65; H, 5·35; N, 10·45. $C_{18}H_{14}ON_2$ requires C, 78·8; H, 5·15; N, 10·2%). The cyclic amide (XX), which cannot be obtained at room temperature by atmospheric oxidation in benzene solution or by permanganate oxidation in acetone solution, does not form a stable hydrochloride and does not react with 2 : 4-dinitrophenylhydrazine.

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