83. *Cyclic Keto-amines. Part III.* The Reactions of Substituted 1 : 2 : 3 : 4-Tetrahydro-4-oxoquinolines and of 1 : 6-Dioxojulolidines.*

By P. I. Ittyerah and Frederick G. Mann.

Earlier studies of the reactions of the above two types of keto-amines have been extended. The structures of the derivatives formed by the action of *p*-nitrosodimethylaniline, by bromination, and by dehydrogenation have been elucidated. The action of hydrazine and of nitric acid, and the application of the Mannich and the Schmidt reaction, have also been investigated.

The properties of 1 : 6-dioxo*iso*julolidine are of particular interest.

The preparation of 1 : 2 : 3 : 4-tetrahydro-4-oxo-1-phenylquinoline [1,2] (I; R = Ph) and its 1-methyl analogue [3] (I; R = Me), and that of the allied 1 : 6-dioxojulolidine [4] (II; R = R′ = H), with certain of their properties,[5–8] have been described. The most noteworthy properties of these cyclic keto-amines at present recorded concern the reactivity of the carbonyl groups. In the oxoquinoline derivatives (I; R = Ph or Me), this group reacts readily with appropriate amino-groups: it therefore forms a phenylhydrazone, and, in conjunction with the adjacent 3-methylene group, it undergoes the Pfitzinger reaction with alkaline isatin.[2,9] On the other hand, although the carbonyl group will readily condense with malononitrile to give a scarlet derivative,[10] no similar condensation has been achieved with other compounds having reactive methyl or methylene groups, such as quinaldine methiodide and 2-methylbenzothiazole ethiodide.

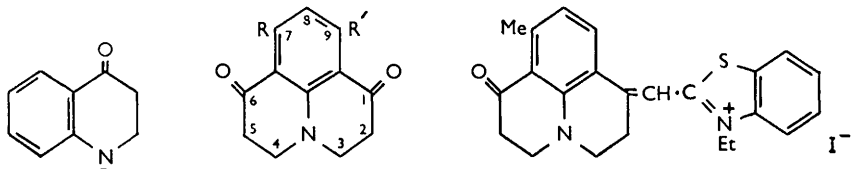
Similar properties are shown by the diketo-amine (II; R = R′ = H),[11] but, whereas this compound will condense with one or two equivalents of malononitrile, 7-methyl-1 : 6-dioxojulolidine (II; R = Me, R′ = H) will condense with only one equivalent, and the 7 : 9-dimethyl member (II; R = R′ = Me) does not condense.[10] The 7- and 9-methyl groups, in addition to showing this steric hindrance, can also activate the carbonyl groups. For example, the dioxojulolidines (II; R = R′ = H or Me) do not react with 2-methylbenzothiazole ethiodide under most rigorous conditions, but the 7-methyl member reacts with one equivalent of the ethiodide to give the cyanine iodide [12] (III).

In the present paper, a number of other reactions of these keto-amines are described.

* Part II, Braunholtz and Mann, *J.*, 1957, 4166.

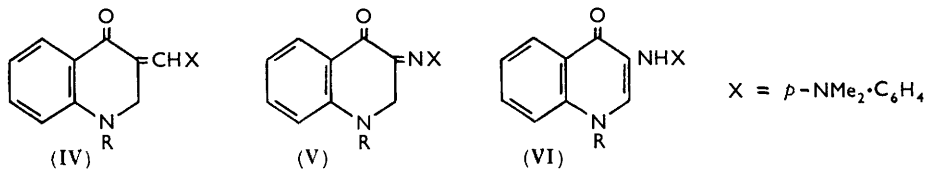
[1] R. C. Cookson and Mann, *J.*, 1949, 67.
[2] Mann, *ibid.*, p. 2816.
[3] Allison, Braunholtz, and Mann, *J.*, 1954, 403.
[4] Mann and Smith, *J.*, 1951, 1898.
[5] Braunholtz and Mann, *J.*, 1952, 3046.
[6] *Idem*, *J.*, 1953, 1817.
[7] *Idem*, *J.*, 1954, 651.
[8] *Idem*, *J.*, 1957, 4166.
[9] *Idem*, *J.*, 1955, 381.
[10] Ittyerah and Mann, *J.*, 1956, 3179.
[11] Braunholtz and Mann, *J.*, 1955, 393.
[12] *Idem*, *ibid.*, p. 398.

1 : 2 : 3 : 4-Tetrahydro-1-methyl-4-oxoquinoline (I; R = Me) with *p*-dimethylaminobenzaldehyde in boiling ethanol containing piperidine gives the bright red 3-(*p*-dimethylaminobenzylidene) derivative (IV). The oxoquinoline (I; R = Me) also condenses with



(I) (II) (III)

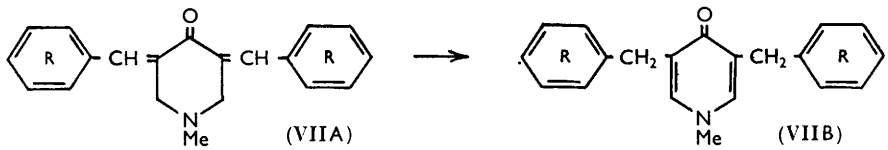
p-nitrosodimethylaniline in ethanol containing sodium hydroxide, apparently to give the analogous 3-(*p*-dimethylaminophenylimino)-derivative (V). This compound however forms deep yellow crystals, but in general compounds having the :N·C_6H_4·NMe_2 group are markedly deeper in colour than the analogous compounds having the :CH·C_6H_4·NMe_2



(IV) (V) (VI) X = *p*-NMe_2·C_6H_4

group. The infrared spectrum of the yellow crystals revealed two sharp strong bands at 3280 and 1627 cm.$^{-1}$, indicating an :NH group and a highly conjugated :CO group respectively, and there is little doubt that the imino-derivative (V) has isomerised to 3-(*p*-dimethylaminoanilino)-1 : 4-dihydro-1-methyl-4-oxoquinoline (VI; R = Me). The dark yellow 1-phenyl homologue has therefore the same structure (VI; R = Ph).

It is noteworthy that Leonard and Locke [13] have adduced evidence that various 1-methyl-4-oxo-3 : 5-dibenzylidenepiperidines (VIIA, where R is a *p*- or *m*-substituent),



(VIIA) (VIIB)

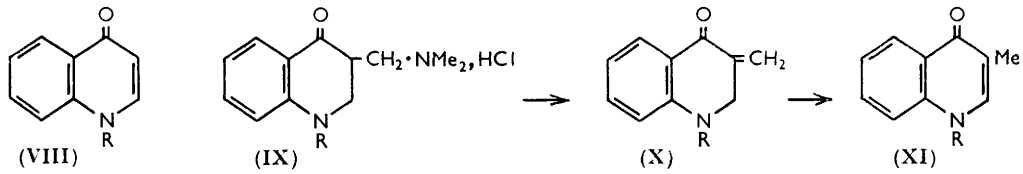
when heated with palladium–charcoal, preferably in ethylene glycol, undergo a similar conversion into the colourless 1 : 4-dihydro-pyridine isomers (VIIB). It is clear that under the far milder conditions of our condensations, the imino-compound (V) undergoes this isomerisation, whereas the highly coloured methylene compound (IV) does not.

Dehydrogenation of the oxoquinolines (I; R = Me and Ph) has been investigated both by attempted bromination in the 3-position with subsequent loss of hydrogen bromide, and by the action of palladised charcoal. The direct bromination of the oxoquinoline (I; R = Me) proved however to be unsatisfactory and a pure derivative was not isolated. *N*-Bromosuccinimide (1 or 2 equivalents) reacted with the oxoquinoline in cold carbon tetrachloride solution, to give the 6-bromo- and the 6 : 8-dibromo-derivative respectively, and no decisive evidence of bromination of the heterocyclic ring was obtained. The constitution of the lemon-yellow 6-bromo-derivative is confirmed by the following evidence: (*a*) it is unaffected by hot aqueous or ethanolic potassium hydroxide; (*b*) it forms a phenylhydrazone, and reacts with *p*-dimethylaminobenzaldehyde and with *p*-nitrosodimethylaniline to give a deep orange benzylidene derivative (as IV) and a yellow anilino-derivative (as VI) respectively; (*c*) its infrared spectrum shows a strong band at 813 cm.$^{-1}$ (12·30 μ) characteristic of 1 : 2 : 4-trisubstituted benzenes, and a band at 1672 cm.$^{-1}$ which

[13] Leonard and Locke, *J. Amer. Chem. Soc.*, 1955, **77**, 1852.

is normal for a :CO group directly conjugated to a benzene ring. The deep yellow 6 : 8-dibromo-derivative also has the chemical properties noted in (*a*) and (*b*).

The oxoquinoline (I; R = Ph) under the above conditions also gave the 6-bromo-derivative, having similar properties.



(VIII) (IX) (X) (XI)

The oxoquinolines (I; R = Me and Ph) were readily dehydrogenated by palladised charcoal in boiling ethylene glycol to 1 : 4-dihydro-1-methyl-4-oxoquinoline (echinopsine) (VIII; R = Me) and the 1-phenyl analogue (VIII; R = Ph) respectively. It is noteworthy that the 6-bromo-derivative of the oxoquinoline (I; R = Me) when similarly treated also gave the compound (VIII; R = Me).

The stability of the 1 : 4-dihydro-4-oxo-quinoline system is further emphasised by the application of the Mannich reaction to the oxoquinolines (I; R = Me and Ph). The

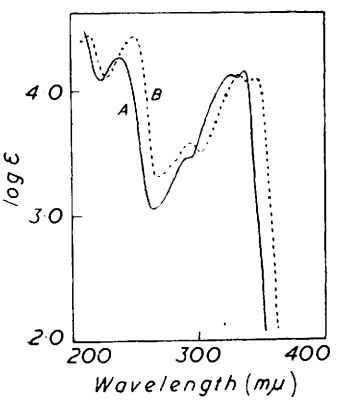


FIG. 1. *Absorption spectra in ethanol of* (*A*) 1 : 4-*dihydro*-1-*methyl*-4-*oxoquinoline* (VIII; R = Me) *and* (*B*) 1 : 4-*dihydro*-1 : 3-*dimethyl*-4-*oxoquinoline* (XI; R = Me).

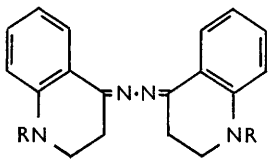
oxoquinoline (I; R = Me), when dissolved in ethanol containing paraformaldehyde, dimethylamine hydrochloride, and a trace of hydrochloric acid, was recovered unchanged after the solution had been boiled for 4 hr. A similar mixture in *iso*pentyl alcohol gave a vigorous reaction on boiling, and deposited the pale yellow 1 : 4-dihydro-1 : 3-dimethyl-4-oxoquinoline (XI; R = Me). The evidence for this structure is summarised: (*a*) analysis and molecular-weight determination; (*b*) the compound shows no ketonic reactions, in common with the compound (VIII; R = Me); (*c*) the infrared spectrum shows a band at 1625 cm.$^{-1}$, indicating a highly conjugated :CO group joined to a benzene ring, but there is no band in the 890 cm.$^{-1}$ region and hence a :CH_2 group is absent; (*d*) the ultraviolet spectra of this compound and of (VIII; R = Me) are almost identical (Fig. 1).

The oxoquinoline (I; R = Ph), similarly treated, gave the 1 : 4-dihydro-3-methyl-1-phenyl derivative (XI; R = Ph), which was also obtained when diethylamine hydrochloride was used in the reaction. There is little doubt therefore that the initial product in this reaction is the tertiary amine hydrochloride (IX), which breaks off the dialkylamine hydrochloride to form the 3-methylene derivative (X), which then isomerises to the stable 3-methyl derivative (XI).

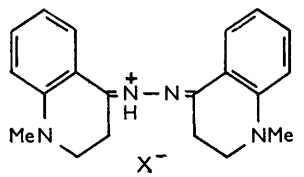
The amines (I; R = Me and Ph) reacted readily with hydrazine in ethanolic solution to give the ketazines (XII; R = Me), orange plates, and (XII; R = Ph), golden-yellow crystals, respectively.

When the ketazine (XII; R = Me) was added to an excess of picric acid, both in cold

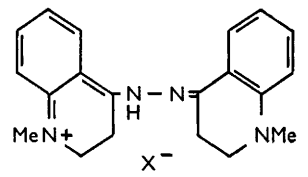
ethanolic solution, deep red crystals of the stable monopicrate were deposited. A chilled ethanolic suspension of the ketazine, when treated with hydrogen chloride, gave first a clear deep red solution which then deposited deep red crystals of a hydrochloride. The addition of cold concentrated hydrochloric acid to the red solution, before separation of the hydrochloride, immediately gave a colourless solution which then deposited crystalline



(XII)



(XIIIA)

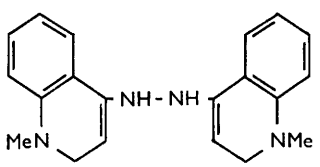


(XIIIB)

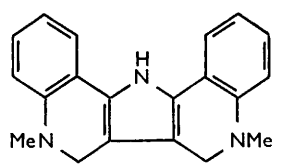
hydrazine dihydrochloride, demonstrating the ready hydrolysis of the ketazine in the presence of an excess of aqueous acid. The red crystalline hydrochloride of the ketazine was not obtained pure, for it could not be recrystallised, and was highly deliquescent, giving a red liquid which on exposure to air slowly evaporated, depositing the crude, dry yellow ketazine. Analysis indicated that the red crystals were probably a dihydrochloride.

If salt formation with the ketazine occurred by protonation of the MeN: group, no fundamental change in structure or colour would result. Consequently protonation must occur on the nitrogen of the azine chain, and the picrate will therefore be a cyanine salt, having the canonical forms (XIIIA—B). In the dihydrochloride this process may be duplicated, or, if the positive charge on the first nitrogen of the azine group tends to inactivate the second,[14] protonation may occur on this first nitrogen atom and on the more distant MeN: group.

Many unsuccessful attempts to convert the ketazine (XII; R = Me) into the indole (XV) have been made. The ketazine in boiling ethanolic hydrogen chloride or ethanolic acetic acid again underwent hydrolysis to the parent amine (I; R = Me). When hydrogen chloride was passed through the molten ketazine[15] at 190—200°, the almost colourless dihydrochloride of the isomeric *s*-bis-(1 : 2-dihydro-1-methyl-4-quinolyl)hydrazine (XIV) was obtained, and was further characterised by conversion into the yellow dipicrate.



(XIV)



(XV)

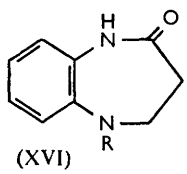
The oxoquinoline (I; R = Me) when subjected to the Schmidt reaction, by the addition of sulphuric acid and then sodium azide to its chilled chloroform solution, gave the colourless lactam (XVI; R = Me): the amine (I; R = Ph) behaved similarly. The precise structure of these lactams has not been determined, but by analogy with the results obtained by Briggs and De Ath[16] the structure (XVI) is more probable than the isomeric structure (XVII).

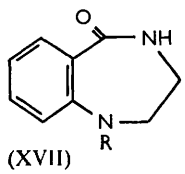
The oxoquinoline (I; R = Me), when treated with nitric acid–acetic acid below 15°, readily gave the 6-nitro-derivative (XVIII) in high yield.

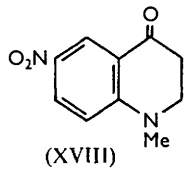
The chemistry of 1 : 6-dioxojulolidine (II; R = R′ = H) and its derivatives has been investigated on similar lines.

[14] Mann and Watson, *J. Org. Chem.*, 1948, **13**, 502.
[15] Robinson and Robinson, *J.*, 1918, **113**, 639.
[16] Briggs and De Ath, *J.*, 1937, 456.

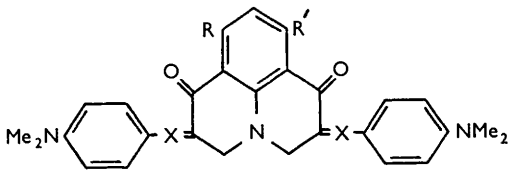
Braunholtz and Mann [12] have shown that this diketo-amine with *p*-dimethylaminobenzaldehyde and *p*-nitrosodimethylaniline gives the bright orange 2 : 5-bis-(*p*-dimethylaminobenzylidene) derivative (XIX; R = R′ = H, X = :CH·) and the bluish-purple

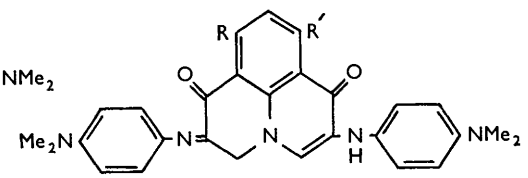

(XVI)


(XVII)


(XVIII)

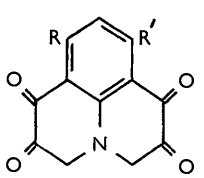
2 : 5-bis-(*p*-dimethylaminophenylimino)-derivative (XIX; R = R′ = H, X = :N·) respectively. We find that 7 : 9-dimethyl-1 : 6-dioxojulolidine (II; R = R′ = Me) condenses with these reagents to give the pale yellow derivative (XIX; R = R′ = Me, X = :CH·) and the dark purple derivative (apparently XIX; R = R′ = Me, X = :N·) respectively. These differences in colour between the two methin compounds (X = :CH·) on the one hand

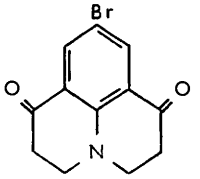

(XIX)

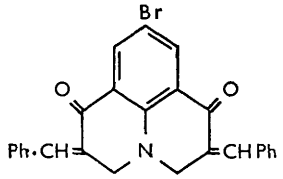

(XIXA)

and the two azomethin compounds (X = :N·) are to be expected on the basis of the above structures. We find however that the infrared spectra of the two azamethin compounds (XIX; R = R′ = H and Me, X = :N·) show marked absorption bands at 3280 and 3370 cm.$^{-1}$ respectively, and each compound must therefore have an :NH group. Hence there is little doubt that each compound has undergone isomerisation on one side only, to give the structure (XIXA), which is that of an *iso*julolidine * derivative. The evidence for this limitation of the isomerisation is the intense, dark colours of the two compounds, for which, had the isomerisation occurred on both sides, there would have been no adequate structural basis: the reason for the limitation is the fact (discussed below) that the 1 : 6-dioxojulolidine structure can accept a double bond in the 2 : 3- or 4 : 5-position, but cannot accept this bond in both these positions, which of course is what the double isomerisation would entail.

The isomerisation is readily reversible, for the two azamethin compounds readily undergo acid hydrolysis to the brown 1 : 2 : 5 : 6-tetraoxojulolidine [12] (XX; R = R′ = H) and its 7 : 9-dimethyl homologue (XX; R = R′ = Me).


(XX)


(XXI)


(XXII)

The diketo-amine (II; R = R′ = H) also gave indefinite products on direct bromination. *N*-Bromosuccinimide in cold solution gave the yellow 8-bromo-1 : 6-dioxojulolidine (XXI). The position of the bromine atom is shown by the evidence: (*a*) the

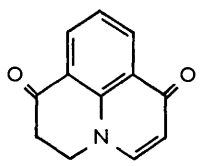
* For the nomenclature of unsaturated derivatives of julolidine, see refs. 4, 12.

compound is unaffected by hot aqueous-ethanolic potassium hydroxide; (*b*) it gives a yellow bisphenylhydrazone and with benzaldehyde a 2 : 5-dibenzylidene derivative (XXII); (*c*) its infrared spectrum is very similar to that of 8-chloro-1 : 6-dioxojulolidine, prepared by Braunholtz and Mann by cyclisation of *p*-chloro-*NN*-di-2-cyanoethylaniline.[7]

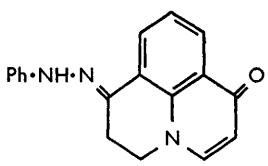
When however the yellow diketo-amine (II; R = R′ = H), m. p. 146°, was treated with palladised charcoal in boiling *p*-cymene, dehydrogenation occurred to give the colourless 1 : 6-dioxo*iso*julоline (XXIII), m. p. 202°, in 60% yield. Although the conditions of the experiment were varied over wide limits, no further dehydrogenation could be effected.

The properties of the *iso*juloline (XXIII) may be summarised.

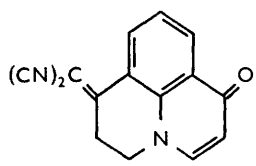
(i) Unlike the diketo-amine (II; R = R′ = H), which does not form stable salts with acids or apparently undergo quaternisation, the *iso*juloline (XXIII) forms a stable hydrobromide, picrate, and methotoluene-*p*-sulphonate. With perchloric acid, it forms a pale yellow salt of unusual composition, $(C_{12}H_9O_2N)_2,HClO_4$, which when treated with an excess of the acid gives the colourless normal salt, $C_{12}H_9O_2N,HClO_4$.



(XXIII)



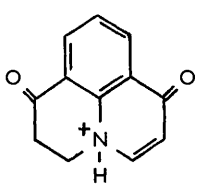
(XXIV)



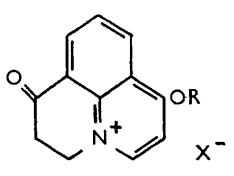
(XXV)

(ii) Only one of the carbonyl groups in the *iso*juloline has normal reactivity. For example, in the presence of an excess of reagent the *iso*juloline forms a scarlet monophenylhydrazone (XXIV), and a bright yellow condensation product (XXV) with one equivalent of malononitrile, whereas the diketo-amine (II; R = R′ = H) gives a yellow bisphenylhydrazone and a deep red product with two equivalents of malononitrile. The infrared spectra confirm this difference: the spectrum of the dioxojulolidine shows only one sharp band, at 1681 cm.$^{-1}$ (5·95 μ) associated with the :CO group, this value being normal for a carbonyl group joined to a benzene ring, but that of the dioxo*iso*juloline shows two such bands, at 1695 cm.$^{-1}$ (5·90 μ) and 1631 cm.$^{-1}$ (6·13 μ), the second being that of a carbonyl group joined to a benzene ring and having additional conjugation. Moreover the identity of the reactive carbonyl group is not in doubt, for the spectra of the monophenylhydrazone of the dioxo*iso*juloline and of the malononitrile derivative show only one carbonyl band at 6·16 and 6·12 μ respectively, which also confirms the structures (XXIV) and (XXV).

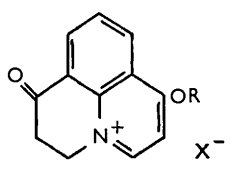
In spite of this clear spectral differentiation between the two :CO groups in the *iso*juloline (XXIII), the precise structure of its salts, such as the hydrobromide and the methotoluene-*p*-sulphonate, remains uncertain. Direct protonation of the nitrogen atom, to give salts such as (XXVI), appears chemically unlikely and might entail some strain on the nitrogen valencies: protonation of the (probably markedly negative) oxygen atom at



(XXVI)



(XXVIIA)



(XXVIIB)

the 1-position would give salts stabilised by the two forms (XXVIIA—B), of which form (B) has moreover acquired an extra aromaticised ring. Similar considerations apply to the quaternary salts. The infrared spectrum of the hydrobromide shows a broad band at 2690 cm.$^{-1}$, which might indicate a :NH$^+$ group or a heavily bonded OH group, and the

normal :CO band at 1710 cm.$^{-1}$, but the second :CO band is either absent or represented by a shoulder at 1625 cm.$^{-1}$, although this is almost overlaid by the conjugated aromatic band. The spectrum of the methotoluene-*p*-sulphonate gives no definite evidence for the :NMe$^+$ group, and shows the normal :CO band at 1708 cm.$^{-1}$, and again a faint shoulder at 1627 cm.$^{-1}$ largely obscured by the strong toluene-*p*-sulphonate absorption in this region.

FIG. 2. FIG. 3.

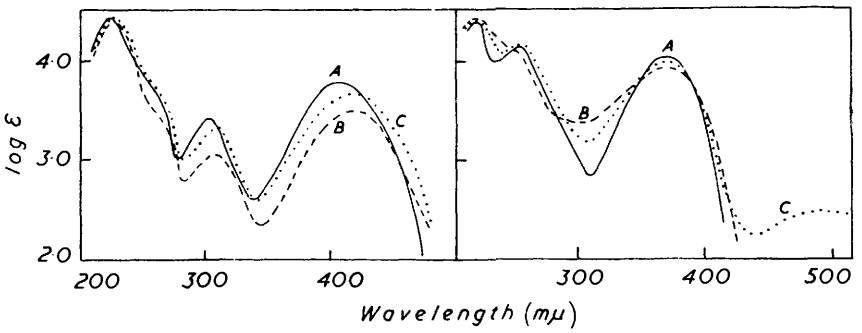


FIG. 2. *Absorption spectra of* 1 : 6-*dioxojulolidine* (II; R = R′ = H) *in* (*A*) *ethanol*, (*B*) 0·1N-*hydrochloric acid, and* (*C*) 0·1N-*aqueous potassium hydroxide.*

FIG. 3. *Absorption spectra of* 1 : 6-*dioxoisojuloline* (XXIII) *in* (*A*) *ethanol*, (*B*) 0·1N-*hydrochloric acid, and* (*C*) 0·1N-*aqueous potassium hydroxide.*

(iii) The *iso*juloline has, as expected, only one reactive methylene group, and hence with *p*-dimethylaminobenzaldehyde gives the 5-(*p*-dimethylaminobenzylidene) derivative.

(iv) The pale yellow colour of ethanolic solutions of the dioxojulolidine becomes rather darker on the addition of acids, but is unaffected by alkali, and the ultraviolet absorption spectra in the three types of solvent are very closely similar (Fig. 2). An ethanolic solution of the dioxo*iso*juloline is unaffected in colour by the addition of acids, but becomes intensely purple on the addition of concentrated aqueous potassium hydroxide.

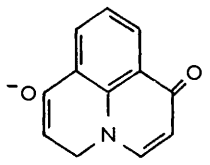
The ultraviolet spectra of the *iso*juloline (XXIII) in ethanolic and in acid and alkaline solution are shown in Fig. 3. The main absorption centred at 410 mμ shown by the dioxojulolidine is now shifted to 370 mμ for the *iso*juloline, but the spectrum of the latter in the alkaline solution shows a broad and novel band centred about 495 mμ which is responsible for the deep colour. The pure potassium derivative has not been isolated and its constitution remains uncertain: the purple derivative crystallises from cold concentrated aqueous-ethanolic potassium hydroxide, but is too deliquescent for collection. An ethanolic solution of the equimolecular mixture of the *iso*juloline and potassium hydroxide, when evaporated to dryness in a vacuum, gave a purple solid, the infrared spectrum of which indicated a mixture of the unchanged dioxo-compound and its potassium derivative: the use, in a similar experiment, of an excess of sodium methoxide in methanol to ensure complete conversion into the sodium derivative gave a solid hygroscopic purple deposit which was difficult to handle, and the infrared spectrum of which gave no decisive structural information.

It is unlikely that the anion (XXVIII) can produce this deep colour. Fission of the aryl–nitrogen bond in this anion to give the highly conjugated isomeric anion (XXIX) having marked resonance would almost certainly do so, but no evidence for this change could be obtained. The deep purple aqueous-ethanolic solution of the potassium derivative, when chilled and acidified, deposited the original dioxo*iso*juloline. Further, the anion (XXIX) on oxidation should give *iso*phthalic acid, but a solution of the *iso*juloline in aqueous sodium hydroxide, when oxidised with aqueous potassium permanganate, did not afford this acid.

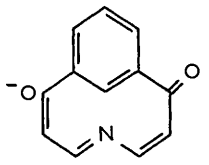
Addition of ethanolic ferric chloride to an ethanolic solution of the *iso*juloline

precipitated an unstable brown crystalline iron complex which redissolved in an excess of the chloride.

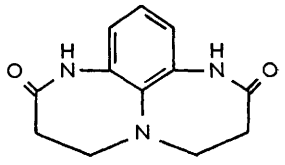
The dioxojulolidines (II; R = R′ = H and Me), unlike the oxo-amines (I), reacted with hydrazine to give amorphous stable, insoluble products which were probably complex. When suspensions of these products in ethylene glycol containing potassium hydroxide were heated, julolidine and its 7 : 9-dimethyl derivative respectively were formed in very low yield and isolated as their picrates.



(XXVIII)



(XXIX)

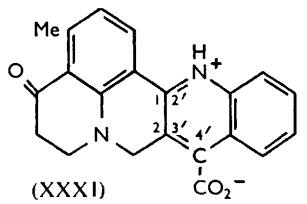


(XXX)

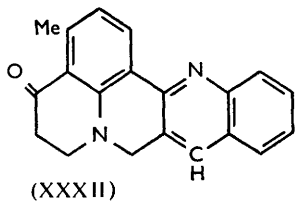
In the Schmidt reaction the dioxo-amine (II; R = R′ = H) gave the dilactam, most probably of structure (XXX), but no similar product was isolated from the dioxo-amine (II; R = R′ = Me), almost certainly because of the steric obstruction of the two methyl groups.

This steric obstruction arises also in the application of the Pfitzinger reaction to the 1 : 6-dioxojulolidines. Braunholtz and Mann [11] have shown that the parent compound (II; R = R′ = H) reacts with two equivalents of isatin in boiling alkaline solution, and the structures of the resulting zwitterionic dicarboxylic acid, and of the amine produced by its decarboxylation, have been extensively studied. 7-Methyl-1 : 6-dioxojulolidine, when similarly treated, afforded solely 7-methyl-6-oxoquinolino(2′ : 3′-1 : 2)juloline-4′-carboxylic acid, the deep purple colour of which showed that it had formed the zwitterion (XXXI). This condensation parallels that of 7-methoxy-1 : 6-dioxoarsulolidine, which with an excess of *o*-aminobenzaldehyde gave solely 7-methoxy-6-oxoquinolino(2′ : 3′-1 : 2)arsuloline.[17] 7 : 9-Dimethyl-1 : 6-dioxojulolidine, on the other hand, was unaffected by isatin in boiling alkaline solution, the two methyl groups completely obstructing the normal reaction.

The monocarboxylic acid (XXXI), when heated in a vacuum, underwent decarboxylation to the yellow crystalline 7-methyl-6-oxoquinolino(2′ : 3′-1 : 2)juloline (XXXII), which formed a deep red hydrochloride. The colour and structure of the acid (XXXI) and the base (XXXII) and its salts are clearly therefore strictly analogous to those of the corresponding unmethylated derivatives.[11]



(XXXI)



(XXXII)

1 : 6-Dioxojuloline (II; R = R′ = H) on nitration readily gave the 9-nitro-derivative. The reactions of this compound, and of the 6-nitro-oxoquinoline (XVIII) and its 1-phenyl analogue, are now being studied, particularly with regard to their reduction products.

Experimental

3-p-*Dimethylaminobenzylidene*-1 : 2 : 3 : 4-*tetrahydro*-1-*methyl*-4-*oxoquinoline* (IV; R = Me). —A solution of the oxoquinoline (I; R = Me) (0·3 g.) and *p*-dimethylaminobenzaldehyde (0·3 g., 2 mols.) in ethanol (15 c.c.) containing piperidine (0·1 c.c.), when boiled under reflux for 4 hr. and cooled, deposited the above *compound* as scarlet crystals (0·2 g., 36%), m. p. 145° after

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

crystallisation from ethanol (Found: C, 78·2; H, 6·8; N, 9·5. $C_{19}H_{20}ON_2$ requires C, 78·1; H, 6·85; N, 9·6%). The use of sodium hydroxide in place of piperidine gave only a sticky product in low yield.

A solution of the oxoquinoline (I; R = Ph) (0·3 g.) and the aldehyde (0·3 g.) in ethanol (5 c.c.) containing 10% aqueous sodium hydroxide (0·2 c.c.), when boiled for 1 hr. and set aside overnight, deposited the 1-*phenyl analogue* (IV; R = Ph) (0·4 g.), pale yellow crystals, m. p. 148—150° (from acetone) (Found: C, 80·7; H, 6·3; N, 8·0. $C_{24}H_{22}ON_2$ requires C, 81·35; H, 6·2; N, 7·9%). The use of piperidine in place of sodium hydroxide in this experiment gave only unchanged oxoquinoline.

3-p-*Dimethylaminoanilino*-1 : 4-*dihydro*-1-*methyl*-4-*oxoquinoline* (VI; R = Me).—A solution of *p*-nitrosodimethylaniline (0·3 g., 2 mols.) in ethanol (5 c.c.) was added dropwise to a stirred solution of the oxoquinoline (I; R = Me) (0·3 g.) in ethanol (5 c.c.), diluted with 10% aqueous sodium hydroxide (2 c.c.), both solutions at 60°. The mixture when set aside deposited the *compound* (VI; R = Me), deep yellow needles, m. p. 215° (from ethanol) (Found: C, 73·6; H, 6·4; N, 14·2. $C_{18}H_{19}ON_3$ requires C, 73·7; H, 6·5; N, 14·3%): 0·5 g., 92%.

A similar experiment, with the oxoquinoline (I; R = Ph), deposited the 1-*phenyl analogue*, a second crop being obtained by diluting the filtrate with water: the united crops, recrystallised from ethanol, afforded mustard-yellow crystals (0·6 g., 75%), m. p. 175° (Found: C, 77·6; H, 6·3; N, 11·5. $C_{23}H_{21}ON_3$ requires C, 77·7; H, 5·9; N, 11·8%).

A solution of the oxoquinoline (I; R = Ph) (0·7 g.), quinoline-2-aldehyde (0·5 g.), and potassium hydroxide (0·1 g.) in ethanol (15 c.c.), when boiled for 2 hr. and cooled, deposited the pale yellow 1-*phenyl*-3-2′-*quinolylmethylene*-4-*oxo-derivative* (1 g.), m. p. 205° (Found: C, 83·1; H, 5·0; N, 7·6. $C_{25}H_{18}ON_2$ requires C, 82·9; H, 5·0; N, 7·7%).

Action of N-*Bromosuccinimide*.—(i) This reagent (1·7 g., 1 mol.) was added to a solution of the oxoquinoline (I; R = Me) (1·6 g.) in carbon tetrachloride (30 c.c.), which was vigorously shaken for 2 hr., filtered to remove deposited succinimide, and then evaporated under reduced pressure. The cold syrupy residue, which solidified when stirred, gave lemon-yellow 6-*bromo*-1 : 2 : 3 : 4-*tetrahydro*-1-*methyl*-4-*oxoquinoline*, m. p. 85° (from ethanol) (1·9 g., 78%) (Found: C, 50·3; H, 4·1; N, 5·7. $C_{10}H_{10}ONBr$ requires C, 50·0; H, 4·1; N, 5·8%). A solution of this compound in aqueous-ethanolic potassium hydroxide was boiled for 1 hr., and when poured into water deposited the unchanged compound.

This compound, treated with *p*-dimethylaminobenzaldehyde in ethanol containing piperidine as described above, gave the deep orange 3-p-*dimethylaminobenzylidene-derivative* (as IV), m. p. 165° (from benzene) (Found: C, 61·8; H, 4·8; N, 7·85. $C_{19}H_{19}ON_2Br$ requires C, 61·45; H, 5·1; N, 7·55%). A similar experiment, using *p*-nitrosodimethylaniline in ethanol containing 10% aqueous sodium hydroxide, afforded the yellow 3-p-*dimethylaminoanilino-derivative* (as VI), m. p. 281° (Found: C, 58·1; H, 4·5; N, 11·4. $C_{18}H_{18}ON_3Br$ requires C, 58·1; H, 4·8; N, 11·3%).

(ii) The oxoquinoline (I; R = Ph), similarly treated, gave the yellow 6-*bromo*-1 : 2 : 3 : 4-*tetrahydro*-1-*phenyl*-4-*oxoquinoline*, m. p. 95—100° (from ethanol) (Found: C, 59·3; H, 4·2; N, 4·8. $C_{15}H_{12}ONBr$ requires C, 59·6; H, 4·0; N, 4·6%), unaffected by boiling aqueous potassium hydroxide. It gave a pale orange 3-p-*dimethylaminoanilino-derivative* (as VI), m. p. 210° (from ethanol) (Found: C, 62·4; H, 4·8; N, 9·4. $C_{23}H_{20}ON_3Br$ requires C, 63·6; H, 4·6; N, 9·6%): low carbon values were obtained for this compound.

(iii) Experiment (i) was repeated, but *N*-bromosuccinimide (3·4 g., 2 mols.) and benzoyl peroxide (5 mg.) were used, the mixture being shaken for 4 hr. and set aside overnight. The residue from the filtered evaporated solution, when recrystallised from ethanol, gave the 6 : 8-*dibromo*-1-*methyl*-4-*oxo-derivative* (2·8 g., 88%), yellow needles, m. p. 126° (Found: C, 38·0; H, 3·0; N, 4·6. $C_{10}H_9ONBr_2$ requires C, 37·6; H, 2·8; N, 4·4%).

It gave a 3-p-*dimethylaminobenzylidene-derivative*, bright red plates, m. p. 190° (from benzene or methanol) (Found: C, 50·9; H, 3·75; N, 6·3. $C_{19}H_{18}ON_2Br_2$ requires C, 50·7; H, 4·0; N, 6·2%), and a bright yellow 3-p-*dimethylaminoanilino-derivative* (as VI), m. p. 225° (Found: C, 48·3; H, 3·9; N, 9·25. $C_{18}H_{17}ON_3Br_2$ requires C, 47·9; H, 3·8; N, 9·3%).

Dehydrogenation.—(i) A mixture of the oxoquinoline (I; R = Me) (1 g.), 10% palladised charcoal (0·1 g.) and ethylene glycol (10 c.c.) was boiled under reflux for 30 min. and filtered, the catalyst being then washed with the hot solvent. The combined filtrate and washings, when evaporated under reduced pressure, gave a brown viscous residue which readily crystallised. Its solution in ethanol, when treated with ethanolic picric acid, deposited the

yellow crystalline picrate[3] of 1 : 4-dihydro-1-methyl-4-oxoquinoline (VIII; R = Me), m. p. and mixed m. p. 226° (1·95 g., 80%).

(ii) Repetition of experiment (i), but using the 6-bromo-1-methyl-4-oxoquinoline, gave a brown viscous residue which readily solidified. It was soluble in water and contained ionic bromine. A portion, treated with picric acid, both in ethanol, afforded the above picrate, m. p. and mixed m. p. 226° (Found: C, 49·4; H, 3·0; N, 14·25. Calc. for $C_{10}H_9ON,C_6H_3O_7N_3$: C, 49·5; H, 3·1; N, 14·4%).

(iii) A similar experiment, using the oxoquinoline (I; R = Ph), afforded the pale greenish-yellow *picrate* of the 1-phenyl compound (VIII; R = Ph), m. p. 136° (from ethanol) (Found: C, 56·1; H, 2·85; N, 12·6. $C_{15}H_{11}ON,C_6H_3O_7N_3$ requires C, 56·0; H, 3·1; N, 12·45%).

The Mannich Reaction.—(i) A mixture of the oxoquinoline (I; R = Me) (0·8 g.), dimethylamine hydrochloride (0·6 g.), paraformaldehyde (0·2 g.), and *iso*pentyl alcohol (15 c.c.) was boiled under reflux for 15 min., and the clear yellow solution then treated with more aldehyde (0·3 g.), boiled for a further 30 min., and cooled. The yellow solid (0·8 g.) which separated was washed with hot ethanol, and when recrystallised from *iso*pentyl alcohol afforded the almost colourless crystalline 1 : 4-*dihydro*-1 : 3-*dimethyl*-4-*oxoquinoline* (XI; R = Me), m. p. 320° (decomp.) (Found: C, 76·6; H, 6·4; N, 8·2. $C_{11}H_{11}ON$ requires C, 76·3; H, 6·4; N, 8·1%). It was very sparingly soluble in boiling ethanol, acetone, and benzene. The ultraviolet spectrum is shown in Fig. 1.

(ii) Repetition of this experiment, but using the oxoquinoline (I; R = Ph) (1·1 g.), gave 1 : 4-*dihydro*-3-*methyl*-4-*oxo*-1-*phenylquinoline* (XI; R = Ph) which, on recrystallisation from *iso*pentyl alcohol, formed pale yellow crystals (1·0 g.) which when slowly heated darkened at 295° and slowly decomposed at 320—340°, but when immersed at 310° had m. p. 325° to a clear yellow liquid (Found: C, 82·0; H, 5·85; N, 6·2%; *M*, in boiling ethylene dibromide, 195. $C_{16}H_{13}ON$ requires C, 81·7; H, 5·5; N, 6·0%; *M*, 235).

Reactions with Hydrazine.—A solution of the oxoquinoline (I; R = Me) (0·8 g.) and pure hydrazine hydrate (0·12 g.) in ethanol (10 c.c.) containing acetic acid (0·1 c.c.) was boiled under reflux for 1 hr., crystals separating meanwhile. The deposit from the cold mixture, when collected and recrystallised from benzene, afforded NN′-*bis*-(1 : 2 : 3 : 4-*tetrahydro*-1-*methyl*-4-*quinolyl*)*diazine* (XII; R = Me) (0·75 g., 94%), bright orange plates, m. p. 198° (Found: C, 75·7; H, 6·8; N, 17·65. $C_{20}H_{22}N_4$ requires C, 75·5; H, 6·9; N, 17·6%).

Use of the oxoquinoline (I; R = Ph) in the above experiment afforded the golden-yellow 1-*phenyl analogue* (XII; R = Ph) (73%), m. p. 208° (from dioxan) (Found: N, 12·9. $C_{30}H_{26}N_4$ requires N, 12·7%).

Reactions of the Diazine (XII; R = Me).—(i) *Salt formation.* An ethanolic solution of the diazine, when added to a large excess of ethanolic picric acid, rapidly deposited the *monopicrate* (XIIIA–B; X = $C_6H_2O_7N_3$), very dark red needles, m. p. 165° (decomp.; immersed at 160°); the appearance and m. p. of the salt were unchanged by recrystallisation from hot ethanol (Found: C, 56·95; H, 5·0; N, 17·95. $C_{20}H_{22}N_4,C_6H_3O_7N_3$ requires C, 57·0; H, 4·6; N, 17·9%). An ethanolic suspension of the powdered diazine, when chilled to 0° and treated with a slow stream of dry hydrogen chloride, gave a clear deep red solution, from which red crystals separated. The mixture of solution and solute, when cautiously evaporated in an evacuated desiccator containing sodium hydroxide, gave fine deep red crystals of the hydrochloride. A portion of the red solution, before separation of the red crystals, was treated dropwise with cold concentrated hydrochloric acid; it became almost colourless and deposited hygroscopic crystals of hydrazine dihydrochloride, m. p. 198—200°, immersed at 180° (Found: H, 6·0; N, 27·5. Calc. for $H_4N_2,2HCl$: H, 5·8; N, 26·7%). Alternatively, a very fine suspension of the diazine in dry ether, when similarly treated with hydrogen chloride, was rapidly replaced by the deep red crystals, m. p. 85—87° (immersed at 60°) after decantation of the ether and rapid drying in a vacuum: analysis indicated these were apparently a dihydrochloride (Found: N, 14·3; Cl, 17·9. Calc. for $C_{20}H_{22}N_4,2HCl$: N, 14·3; Cl, 18·1%), but the composition varied with the age of the specimen. A sample when exposed to the air rapidly formed a red liquid which ultimately gave the crude dry ketazine, m. p. 180—189°.

(ii) *Attempted indolisation.* Hydrogen chloride was passed through the molten diazine initially at 200° and then at 190—200° for 30 min., the melt becoming red and viscous. An ethanolic solution of the cold product was filtered and diluted with considerable ether. The precipitated colourless crystals of the *dihydrochloride* of s-*bis*-(1 : 2-*dihydro*-1-*methyl*-4-*quinolyl*)-*hydrazine* (XIV), when collected, washed with ether–acetone, and dried had m. p. 295°

(decomp.), which varied with the rate of heating (Found: C, 60·7; H, 6·3; N, 13·9. $C_{20}H_{22}N_4,2HCl$ requires C, 61·4; H, 6·1; N, 14·3%).

This salt, treated in ethanol with picric acid, deposited the deep yellow *dipicrate*, m. p. 243° (decomp.) (from ethanol) (Found: C, 49·9; H, 3·4; N, 17·6. $C_{20}H_{22}N_4,2C_6H_3O_7N_3$ requires C, 49·6; H, 3·6; N, 18·0%).

Schmidt Reaction.—(i) Concentrated sulphuric acid (8 c.c.) was added dropwise to a stirred solution of the oxoquinoline (I; R = Me) (1·6 g.) in dry chloroform (10 c.c.) chilled in ice-water, and sodium azide (1·6 g., 2·5 mols.) was then added during 30 min. The solution was stirred for a further 15 min., diluted with ice-water (45 c.c.), neutralised with potassium carbonate, and extracted with ether. The extract, when dried (K_2CO_3) and evaporated, left a white residue, which on recrystallisation from benzene afforded the β-(N-o-*aminophenyl*-N-*methylamino*)-*propionic lactam* (XVI; R = Me) (1 g., 57%), needles, m. p. 170° (Found: C, 68·5; H, 6·7; N, 15·4. $C_{10}H_{12}ON_2$ requires C, 68·1; H, 6·8; N, 15·9%).

(ii) The oxoquinoline (I; R = Ph), similarly treated, afforded colourless β-(N-o-*aminophenylanilino*)*propionic lactam* (XVI; R = Ph), (91%), m. p. 221° after crystallisation from ethanol and then benzene (Found: C, 75·9; H, 6·1; N, 11·8. $C_{15}H_{14}ON_2$ requires C, 75·6; H, 5·9; N, 11·8%).

Nitration.—A mixture of concentrated nitric acid (1 c.c.) and acetic acid (10 c.c.) was added dropwise to a solution of the oxoquinoline (I; R = Me) (1 g.) in acetic acid (10 c.c.) at <15°. The mixture was set aside for 20 min. and then poured into water (50 c.c.). The crystalline precipitate afforded the 6-*nitro-derivative* (1·2 g., 93%), yellow needles, m. p. 169° (from ethanol) (Found: C, 58·5; H, 4·8; N, 13·6. $C_{10}H_{10}O_3N_2$ requires C, 58·25; H, 4·85; N, 13·6%). The compound gave a *phenylhydrazone*, bright red plates, m. p. 198° (decomp.) (from ethanol) (Found: C, 64·4; H, 5·2; N, 18·8. $C_{16}H_{16}O_2N_4$ requires C, 64·9; H, 5·4; N, 18·9%), and a 3-p-*dimethylaminobenzylidene derivative* (prepared in the presence of piperidine), red plates, m. p. 210° (from ethanol) (Found: C, 67·8; H, 5·4; N, 12·3. $C_{19}H_{19}O_3N_3$ requires C, 67·7; H, 5·6; N, 12·5%).

Cyanoethylation.—*p*-Chloroaniline on cyanoethylation gives a low yield of *p*-chloro-*NN*-bis-2-cyanoethylaniline,[5,6] which in turn on cyclisation gives a small yield of 8-chloro-1 : 6-dioxojulolidine.[7] This difficulty applies also to the bromo-analogues, but *p*-bromo-*NN*-bis-2-cyanoethylaniline and 8-bromo-1 : 6-dioxojulolidine can be readily prepared by direct bromination with *N*-bromosuccinimide.

p-*Bromo*-NN-*bis*-2-*cyanoethylaniline.*—(i) A mixture of *p*-bromoaniline (17 g.), vinyl cyanide (12 g., 2·25 mols), acetic acid (12 g.), and cuprous chloride (1·7 g.) was boiled gently under reflux for 12 hr. and then poured with stirring into ammonia (100 c.c.; *d* 0·88). The precipitated dark oil solidified when stirred and was collected and recrystallised from ethanol (charcoal), giving a crude almost colourless product, m. p. 75—90°. Fractional distillation gave p-*bromo*-N-2-*cyanoethylaniline*, b. p. 160°/5 mm., m. p. 96—98° (from ethanol) (Found: C, 47·9; H, 4·0; N, 12·3. $C_9H_9N_2Br$ requires C, 48·0; H, 4·0; N, 12·45%). The residue in the flask decomposed at higher temperatures.

This experiment, when repeated with boiling for 20 hr., gave on distillation a low-boiling fraction of the above compound (2 g.) and a crude higher fraction, b. p. 180—200°/0·5 mm., which after several laborious recrystallisations from ethanol gave p-*bromo*-NN-*bis*-2-*cyanoethylaniline* (4 g., 14%), m. p. 94—95° (Found: C, 51·8; H, 4·0; N, 15·1. $C_{12}H_{12}N_3Br$ requires C, 51·8; H, 4·3; N, 15·1%).

(ii) *NN*-Bis-2-cyanoethylaniline, when treated in carbon tetrachloride with *N*-bromosuccinimide (1 mol.) and benzoyl peroxide (0·05 mol.) for 4 hr. and worked up as previously described, gave the above *p*-bromo-derivative (82%), m. p. and mixed m. p. 95° (Found: N, 15·45%).

Attempted Cyclisation.—*p*-Bromo-*NN*-bis-2-cyanoethylaniline was heated with aluminium chloride in chlorobenzene, and the mixture worked up as described earlier.[5] The crude yellow solid, m. p. 79—81°, was apparently 1-2′-cyanoethyl-1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline (I; R = $\cdot C_2H_4\cdot CN$) (lit.,[18] m. p. 79—79·5°), for it gave a pale yellow *phenylhydrazone*, m. p. 250° (Found: C, 75·25; H, 6·0; N, 19·4. $C_{18}H_{18}N_4$ requires C, 74·7; H, 5·9; N, 19·4%), and a 2 : 4-*dinitrophenylhydrazone*, m. p. >360° (Found: N, 22·15. $C_{18}H_{16}O_4N_6$ requires N, 22·1%). Under the conditions employed for this monocyclisation the nuclear bromine had therefore been removed.

[18] Johnson and DeAcetis, *J. Amer. Chem. Soc.*, 1953, **75**, 2766.

Derivatives of 1 : 6-*Dioxojulolidine.*—*Quinoline-2-aldehyde derivatives.* A mixture of the diketone (II; R = R′ = H), the aldehyde (0·6 g.), ethanol (15 c.c.), and potassium hydroxide (0·1 g.) was boiled under reflux for 1 hr., and on cooling deposited crystals and some tar. Recrystallisation of the deposit from benzene afforded pale yellow 1 : 6-*dioxo*-2 : 5-*di*-(2-*quinolylmethylene*)*julolidine* (0·3 g.), m. p. 185° (Found: N, 8·7. $C_{32}H_{21}O_2N_3$ requires N, 8·8%).

The 7 : 9-dimethyl diketone (II; R = R′ = Me), similarly treated, gave the pale yellow 7 : 9-*dimethyl homologue*, m. p. 225° (from benzene) (Found: C, 80·3; H, 5·1; N, 8·4. $C_{34}H_{25}O_2N_3$ requires C, 80·4; H, 4·9; N, 8·3%).

The 7 : 9-dimethyl diketone, when treated with *p*-dimethylaminobenzaldehyde (2·2 mols.) in boiling alkaline ethanol, as previously described, gave 2 : 5-*bis*-p-*dimethylaminobenzylidene*-7 : 9-*dimethyl*-1 : 6-*dioxojulolidine* (XIX; R = R′ = Me, X = :CH·), (93%), pale yellow needles, m. p. 245° (from ethanol) (Found: C, 78·5; H, 6·6; N, 8·7. $C_{32}H_{33}O_2N_3$ requires C, 78·2; H, 6·7; N, 8·55%).

The 7 : 9-dimethyl diketone, similarly treated with *p*-nitrosodimethylaniline (2·1 mols.), afforded 2-p-*dimethylaminoanilino*-5-(p-*dimethylaminophenylimino*)-7 : 9-*dimethyl*-1 : 6-*dioxojulolidine* (XIXA; R = R′ = Me) (83%), which formed dark purple crystals, m. p. 268° (decomp.), from much acetone (Found: C, 73·2; H, 6·3; N, 14·2. $C_{30}H_{31}O_2N_5$ requires C, 73·0; H, 6·3; N, 14·2%). A solution of this compound (0·5 g.) in concentrated hydrochloric acid (20 c.c.) was boiled under reflux for 30 min., the deep red solution becoming brown and depositing 7 : 9-*dimethyl*-1 : 2 : 5 : 6-*tetraoxojulolidine* (XX; R = R′ = Me) (1·25 g.) as bronze-coloured crystals, which when collected and washed with water and then with boiling ethanol, benzene, and acetone, slowly decomposed above 330° (Found: C, 66·5; 64·6; H, 4·3, 4·3; N, 5·5. $C_{14}H_{11}O_4N$ requires C, 65·4; H, 4·3; N, 5·45%. The carbon value varied with the temperature and time of the combustion). This compound resembles the parent member (XX; R = R′ = H) in that it is insoluble in all the usual boiling solvents, but dissolves in aqueous potassium hydroxide to give an intense purple solution from which it is reprecipitated on acidification, and it does not condense with *p*-phenylenediamine.

Bromination.—*N*-Bromosuccinimide (2 g., 2 mols.) and benzoyl peroxide (0·05 g.) were added to a solution of the diketone (II; R = R′ = H) (1 g.) in carbon tetrachloride, which was then shaken vigorously for 3 hr. The yellow precipitate, when twice recrystallised from ethanol to remove succinimide and bromosuccinimide, gave 8-*bromo*-1 : 6-*dioxojulolidine* (XXI) (1·2 g., 86%), golden-yellow plates, m. p. 208° (Found: C, 51·2; H, 3·3; N, 5·1. $C_{12}H_{10}O_2NBr$ requires C, 51·4; H, 3·6; N, 5·0%). The ultraviolet spectrum in ethanol gave the following values (ε values in parentheses): $\lambda_{max.}$ 421·5—425·5 (5130); 301—302·5 (4490); 227 (30,100); $\lambda_{min.}$ 338·5—340 (252); 276·5 (1650).

When the above reaction mixture was boiled under reflux, only a pale brown amorphous intractable material was obtained.

The compound (XXI) gave a yellow crystalline *bisphenylhydrazone*, m. p. 270° (Found: C, 62·5; H, 4·7; N, 15·3. $C_{24}H_{22}N_5Br$ requires C, 62·6; H, 4·8; N, 15·2%). A mixture of the compound (XXI) (0·28 g.) and benzaldehyde (0·22 g., 2 mols.) in ethanol (15 c.c.) and piperidine (0·1 c.c.), when boiled under reflux, deposited deep red crystals of 2 : 5-*dibenzylidene*-8-*bromo*-1 : 6-*dioxojulolidine* (XXII) (0·2 g.), m. p. 200° (from ethanol) (Found: C, 68·0; H, 4·2; N, 3·4. $C_{26}H_{18}O_2NBr$ requires C, 68·4; H, 3·9; N, 3·1%).

When the diketone (II; R = R′ = H) was treated with *N*-chlorosuccinimide (1 mol.) under the above conditions, no reaction occurred at room temperature, but when the mixture was boiled under reflux for 1 hr. a sticky solid was deposited and after repeated recrystallisation from ethanol afforded 8-chloro-1 : 6-dioxojulolidine (68%), m. p. and mixed m. p. 201°.

Dehydrogenation.—A mixture of the diketone (II; R = R′ = H) (1 g.), 10% palladised charcoal (0·1 g.) and *p*-cymene (25 c.c.) was boiled under reflux for 90 min., a slow stream of carbon dioxide being blown through the solution. The hot mixture when filtered and cooled deposited 1 : 6-*dioxo*isojuloline (XXIII), which recrystallised from dry benzene as colourless needles (0·6 g.), m. p. 202° (Found: C, 72·6, 72·3; H, 4·5, 4·5; N, 7·1%; *M* in boiling ethanol, 188. $C_{12}H_9O_2N$ requires C, 72·4; H, 4·5; N, 7·0%; *M*, 199). Lower yields were obtained in experiments on a larger scale.

Hydrobromic acid (1 c.c.; 48%) was added to a stirred solution of the *iso*juloline (0·1 g.) in ethanol (2 c.c.), which was then diluted with ether. The white crystalline precipitated *hydrobromide*, when collected and washed with ethanol–ether, had m. p. 270° (decomp.) (Found: C, 51·8; H, 3·7; N, 5·2. $C_{12}H_9O_2N$,HBr requires C, 51·4; H, 3·6; N, 5·0%).

The *iso*juloline and picric acid, when mixed in ethanolic solution, deposited the *picrate* as yellow needles, m. p. 202° after recrystallisation from ethanol (Found: C, 50·95; H, 3·0; N, 12·95. $C_{12}H_9O_2N,C_6H_3O_7N_3$ requires C, 50·5; H, 2·8; N, 13·1%). A mixture of the *iso*juloline and its picrate melted at *ca.* 170—175°.

Perchloric acid (0·1 c.c.; 60%) when added to a solution of the *iso*juloline (0·1 g.) in ethanol (5 c.c.) gave a thick pale yellow curdy precipitate of the *bis*-(1 : 6-*dioxo*iso*juloline*) *perchlorate*, m. p. 240° (decomp.), unchanged by crystallisation from ethanol (diamond-shaped crystals) or from water (needles) (Found: C, 58·1; H, 3·7; N, 5·8; Cl, 7·0. $2C_{12}H_9O_2N,HClO_4$ requires C, 57·8; H, 3·8; N, 5·6; Cl, 7·1%). A cold aqueous suspension of this salt when treated with aqueous ammonia deposited the *iso*juloline. An ethanolic solution of the salt, when treated with an excess of perchloric acid and set aside at 0° overnight, deposited colourless hygroscopic needles of the normal *perchlorate*, m. p. 125° (Found: N, 4·3. $C_{12}H_9O_2N,HClO_4$ requires N, 4·7%): these crystals dissolved in hot ethanol to give yellow solution, which on cooling deposited pale yellow crystals, m. p. 240° (decomp.), of the first salt.

A mixture of the *iso*juloline (0·1 g.) and methyl toluene-*p*-sulphonate (0·1 g.) when heated at 150° for 30 min. formed a clear red liquid which solidified on cooling. An ethanolic solution of this product was diluted with ether, whereby the colourless crystalline *methotoluene*-p-*sulphonate* was precipitated, and when collected and washed with ether–acetone had m. p. 180° (decomp.) (Found: N, 3·5. $C_{20}H_{19}O_5NS$ requires N, 3·6%).

The *phenylhydrazone* (XXIV) crystallised from methanol as a *hemihydrate*, scarlet plates, m. p. 220° (Found: C, 72·4, 72·5; H, 5·45, 5·6; N, 14·2. $C_{18}H_{15}ON_3,\frac{1}{2}H_2O$ requires C, 72·5; H, 5·4; N, 14·1%). The crystals when crushed on a porous plate formed a reddish-brown powder. 2-p-*Dimethylaminobenzylidene*-1 : 6-*dioxo*iso*julolidine*, prepared in boiling ethanol with piperidine, formed deep red crystals, m. p. 230°, from dioxan (Found: C, 76·0; H, 5·4; N, 8·8. $C_{21}H_{18}O_2N_2$ requires C, 76·5; H, 5·45; N, 8·5%).

A mixture of the *iso*juloline (0·33 g.), malononitrile (0·22 g., 2 mols.), ammonium acetate (0·1 g.), dry benzene (10 c.c.), and acetic acid (1 c.c.) was boiled under reflux for 45 min. in a flask fitted with a constant water-separator,[10] bright yellow crystals separating after 15 min. The crystals from the cold mixture were collected and recrystallised from ethanol and then acetic acid, affording 1-*dicyanomethylene*-6-*oxo*iso*juloline* (XXV), deep yellow needles, m. p. 245° (decomp.) (Found: C, 73·3; H, 3·8; N, 16·5. $C_{15}H_9ON_3$ requires C, 72·9; H, 3·6; N, 17·0%).

Attempted application of the Mannich reaction to the diketone (II; R = R′ = H) under the conditions described above gave solely an intractable pale-brown amorphous powder of indefinite m. p.

Action of Hydrazine.—(i) An ethanolic solution of the diketone (II; R = R′ = H) (2 mols.), hydrazine hydrate (1 mol.), and a few drops of acetic acid, when heated, deposited a complex orange polymeric mixture, m. p. 280—320°, from which no pure constituent could be isolated. The diketone (II; R = R′ = Me) gave a deep yellow mixture having similar properties.

(ii) To investigate reduction under the Wolff–Kishner conditions, a mixture of the diketone (II; R = R′ = Me) (1 g.), 100% hydrazine hydrate (1 g.), potassium hydroxide (0·5 g.), and ethylene glycol was boiled under reflux for 2 hr. and then heated at 195—200° for 4 hr., during which much of the initial orange precipitate decomposed. The mixture was diluted with water, cooled, and filtered. The collected material was dried and extracted with ethanol. The extract when evaporated afforded a brown solid, which, when redissolved in ethanol and treated with picric acid, gave in small yield a yellowish-orange picrate, almost certainly julolidine picrate: after crystallisation from ethanol this salt had m. p. 165° on slow heating, and m. p. 172° when immersed at 160° (lit.,[19,20] 165°, 174°).

The diketone (II; R = R′ = Me), similarly treated, afforded also in small yield yellow-orange 7 : 9-*dimethyljulolidine picrate*, m. p. 160° after crystallisation from ethanol (Found: C, 55·6; H, 4·8; N, 13·0. $C_{14}H_{19}N,C_6H_3O_7N_3$ requires C, 55·7; H, 5·1; N, 13·0%).

Schmidt Reaction.—The diketone (II; R = R′ = H), when treated in chloroform with sulphuric acid and sodium azide, precisely as described above, gave the *dilactam* (XXX) of 2 : 6-diamino-*NN*-di-2′-carboxyethylaniline (81%), which formed colourless plates, m. p. 356° (decomp.), from acetic acid (Found: C, 62·6; H, 5·25; N, 17·6. $C_{12}H_{13}O_2N_3$ requires C, 62·3; H, 5·5; N, 18·2%).

[19] Pinkus, *Ber.*, 1892, **25**, 2802; von Braun, Heider, and Wyczatkowsa, *Ber.*, 1918, **51**, 1224.
[20] Smith and Yu, *J. Amer. Chem. Soc.*, 1952, **74**, 1096.

Pfitzinger Reaction.—A solution of 7-methyl-1 : 6-dioxojulolidine (II; R = Me, R′ = H) (2·1 g.), isatin (3·1 g., 2·1 mols.), and potassium hydroxide (3·6 g.) in methanol (25 c.c.) and water (5 c.c.) was boiled under reflux for 20 hr., and then filtered into a stirred solution of acetic acid (40 c.c.) in water (160 c.c.). The deep purple precipitated *7-methyl-6-oxoquinolino-(2′ : 3′-1 : 2)juloline-4′-carboxylic acid* (XXXI) (3 g., 87%), when collected, washed with hot ethanol, and dried, had m. p. 215° (decomp.) (Found: C, 73·3; H, 4·6. $C_{21}H_{16}O_3N_2$ requires C, 73·2; H, 4·65%. High nitrogen values were obtained). Its low solubility in boiling solvents precluded recrystallisation.

The acid, when heated in a tube at 210—220°/0·1 mm., underwent decarboxylation and gave a bright orange sublimate, which on crystallisation from ethanol afforded *7-methyl-6-oxoquinolino(2′ : 3′-1 : 2)juloline* (XXXII), bright yellow plates, m. p. 185°, unchanged by further crystallisation or sublimation (Found: C, 79·8; H, 5·2; N, 9·4, 9·45. $C_{20}H_{16}ON_2$ requires C, 80·0; H, 5·3; N, 9·3%).

Nitration.—Concentrated nitric acid (1 c.c.) was added dropwise to a solution of the diketone (II; R = R′ = H) (1 g.) in acetic acid (10 c.c.) at <20°; yellow crystals separated. The mixture was set aside for 20 min. and then poured into water (50 c.c.). The precipitate, after crystallisation from ethanol, afforded *8-nitro-1 : 6-dioxojulolidine* (1·2 g., 100%), golden-yellow needles, m. p. 250° (Found: C, 58·5; H, 4·2; N, 11·2. $C_{12}H_{10}O_4N_2$ requires C, 58·55; H, 4·1; 11·4%). The *bisphenylhydrazone*, prepared in the usual manner, formed deep red crystals, m. p. 270° (decomp.), insoluble in the common organic solvents (Found: C, 67·2; H, 5·0; N, 19·5. $C_{24}H_{22}O_2N_6$ requires C, 67·6; H, 5·2; N, 19·7%).

We gratefully acknowledge grants from the Asia Christian Colleges Association and the British Council (to P. I. I.), and also the gift of various intermediates from Imperial Chemical Industries Limited, Dyestuffs Division.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 23rd,* 1957.]