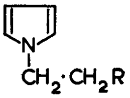
844. *The Structure and Properties of Certain Polycyclic Indolo- and Quinolino-derivatives. Part XIV.** *Derivatives of* 2,3-*Dihydro*-1-*oxo*-1H-*pyrrolizine.*

By John T. Braunholtz, Keith B. Mallion, and Frederick G. Mann.

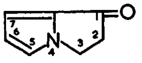
An improved synthesis of 2,3-dihydro-1-oxo-1*H*-pyrrolizine has been developed, and several reactions of this ketone investigated. The phenylhydrazone could not be converted into an indolo-derivative. Condensations of the ketone with *o*-aminobenzaldehyde to give ultimately 3′*H*-pyrrolizino-(1′,2′-2,3)quinoline, and with alkaline isatin to give the corresponding 4-carboxylic acid, have been investigated. The structure and properties of these compounds, and of the neutral isomer which the 4-carboxylic acid furnishes on being heated, have been studied.

In extension of earlier work[1] on the structure and properties of the products obtained by the application of the Fischer indolisation reaction and the Friedländer reaction to heterocyclic keto-amines, we have investigated the properties of 2,3-dihydro-1-oxo-1*H*-pyrrolizine (II).

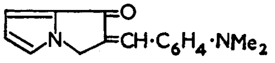
Clemo and Ramage[2] prepared, by the interaction of potassium pyrrole and ethyl β-chloropropionate, the ester (I; $R = CO_2Et$), and thence by hydrolysis the 1-2′-carboxyethylpyrrole (I; $R = CO_2H$), which they failed to cyclise to the ketone (II). The interaction of potassium pyrrole and 2-cyanoethyl toluene-*p*-sulphonate gave 1-2′-cyanoethylpyrrole (I; R = CN), which in ether with zinc chloride and hydrogen chloride gave the ketone (II) in moderate yield.



(I)



(II)



(III)

We find that the nitrile (I; R = CN), readily prepared by the direct cyanoethylation of pyrrole,[3] can be converted into the ketone (II) in high yield by treatment with a molten aluminium chloride–potassium chloride–sodium chloride mixture, although the experimental conditions are highly critical, as in the similar cyclisation of *N*-2-cyanoethyl-*N*-methylaniline.[4]

The carbonyl group in the ketone (II) shows normal chemical reactivity, and in the infrared spectrum appeared as a band at 1670 cm.$^{-1}$, characteristic of an αβ-unsaturated ketone.

The methylene group linked to the carbonyl group in the ketone (II) also shows normal reactivity, and readily combined with *p*-dimethylaminobenzaldehyde in alkaline ethanolic solution to give the benzylidene derivative (III).

The basic properties of the nitrogen atom in the ketone (II) are reduced both by its participation in the pyrrole ring and by steric hindrance at the bridgehead position. It does not form stable salts with acids or with quaternising agents, and thus resembles the amine group in 1,6-dioxojulolidine.[5] In the ketone (II) there is very little electronic interaction between the amino- and the carbonyl group, as the ultraviolet spectra (see Table) indicate.

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* Part XIII, Mann, Prior, and Willcox, *J.*, 1959, 3830.

[1] Mann, *J.*, 1949, 2816 and subsequent papers in this series.

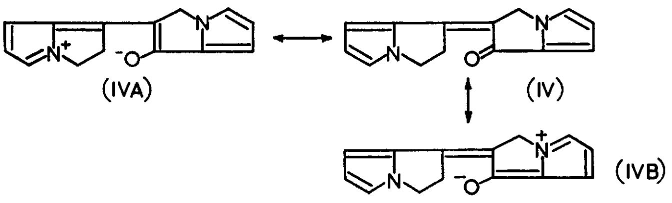
[2] Clemo and Ramage, *J.*, 1931, 49.

[3] Blume and Lindwall, *J. Org. Chem.*, 1945, **10**, 255; Corse, Bryant, and Shonle, *J. Amer. Chem. Soc.*, 1946, **68**, 1911.

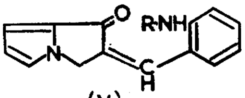
[4] Allison, Braunholtz, and Mann, *J.*, 1954, 403.

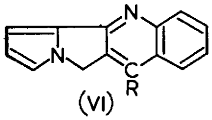
[5] Braunholtz and Mann, *J.*, 1953, 1817.

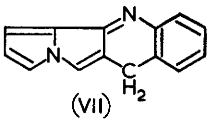
The ketone (II), m. p. 53·5—54°, when treated with boiling aqueous-ethanolic potassium hydroxide, gives rise to another crystalline yellow ketone (IV), m. p. 208°, identical with that which Clemo and Melrose [6] obtained by the action of zinc wool and methyl iodide on the ketone (II). The compound (IV) has some importance, for it may occur as a by-product in any reaction of the ketone (II) in a basic medium. It almost certainly has the structure indicated: this is confirmed by its mode of formation [essentially an aldol condensation comparable with that of the benzylidene compound (III)], its composition, molecular weight, and infrared spectrum, which shows a C=O band at 1670 cm.$^{-1}$, a weak band at 1563 attributed to the $C{:}C$ portion of the pyrrole ring, and an intense band at 1606 cm.$^{-1}$, attributed to a $C{:}C$ group other than those present in pyrrole rings, the last band being intensified by the conjugation with the carbonyl group. Unlike the ketone (II), the compound (IV) shows no normal ketonic properties and apparently does not form an oxime, a semicarbazone, or a phenyl- or 2,4-dinitrophenyl-hydrazone. No quaternary salts have been isolated. These properties are not unexpected, for the polar forms (IVA) and (IVB) might make substantial contributions to the structure. The compound (IV) formed a deep purple hydrochloride, an unstable red perchlorate, and a scarlet picrate. Addition of the proton to the negative oxygen atom in (IVA–B) would explain the colour of these compounds, for structurally they would be cyanine salts. The infrared spectrum of the hydrochloride showed no C=O or –NH– band, but also gave no indication of a hydroxyl group.


(IVA) (IV) (IVB)

The compound (IV) resisted catalytic reduction and was very slightly affected by cold ethanolic permanganate. Acetone–permanganate, however, afforded the ketone (II), which supports the structure (IV): no other product could be isolated, the remainder of the molecule having been apparently completely oxidised. The compound (IV) with chromium trioxide in acetic acid at room temperature underwent extensive oxidation and no product could be isolated. Ozonolysis gave a similar result.


(V)


(VI)


(VII)

Attempts to convert the phenylhydrazone of the ketone (II) by the Fischer reaction into the indolo-derivative failed, tars being formed.

Condensation of the ketone (II) with *o*-aminobenzaldehyde in weakly alkaline solutions (the Friedländer reaction) proved of particular interest, for the initial product was the 2-aminobenzylidene derivative (V; R = H). The infrared spectrum of this compound shows a band at 1671 cm.$^{-1}$, attributed to a conjugated $>$CO group and two bands at 3210 and 3310 cm.$^{-1}$, characteristic of the aromatic NH_2 group, the presence of which was confirmed by the preparation of crystalline acetamido- and toluene-*p*-sulphonamido-derivatives (V; R = $\cdot CO\cdot CH_3$ and $\cdot SO_2\cdot C_6H_4\cdot Me$). Although the amino-compound (V; R = H) was stable at its melting point, it was partly converted into the 3'*H*-pyrrolizino-(1',2',-2,3)quinoline (VI; R = H) when boiled in alkaline ethanolic solution. This cyclisation was readily and completely effected when the base (V; R = H) was heated

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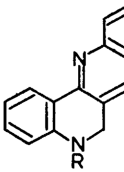
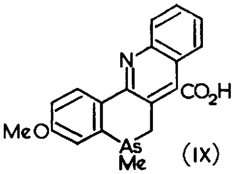
[6] Clemo and Melrose, *J.*, 1942, 424.

in a high vacuum. It is unusual for a stable intermediate compound to be formed in the Friedländer reaction, which normally yields the cyclised quinolino-derivative directly.

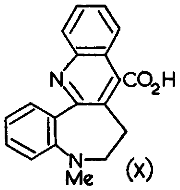
It is noteworthy that the quinolino-base (VI; R = H) could not be converted into the isomer (VII) by acid-catalysed allylic rearrangement which occurs so readily with analogous compounds such as 1,2,3,4-tetrahydro-1-methyl(and phenyl)-4-oxoquinoline (VIII; R = Me or Ph).[1,7] Further, the methylene group in the base (VI; R = H) resists oxidation to a carbonyl group, a process which occurs spontaneously at room temperature when the compound (VIII; R = Me) and its allylic isomer, and also the compound (VIII; R = Ph), are exposed in benzene solution to the air. These differences were not unexpected, however, for earlier studies in this series have shown that the properties of the dihydroquinolinoquinolines (VIII) and similar compounds, particularly their susceptibility to isomerisation and oxidation, are largely determined by the basic properties of the cyclic keto-amine from which they are prepared.[7-9]



(VIII)



(IX)



(X)

The ketone (II), when boiled with a solution of isatin in aqueous-ethanolic alkali, with subsequent acidification (the Pfitzinger reaction), afforded the yellow 3′*H*-pyrrolizino-(1′,2′-2,3)quinoline-4-carboxylic acid (VI; R = CO_2H); this formed a yellow sodium salt. The infrared spectrum of the free acid showed (*a*) a band at 1675 cm.$^{-1}$ corresponding to the C=O portion of a carboxyl group conjugated to a quinoline ring, (*b*) two of a trio of broad bands [10] expected from acids of this type at 2400 and 1990 cm.$^{-1}$, the third band, usually at *ca.* 1690 cm.$^{-1}$, being presumably obscured by the carbonyl band, and (*c*) no evidence of the acid's existing as a zwitterion. The absence of zwitterion formation, which was also strongly indicated by the closely similar colours of the acid and its sodium salt, and by its ultraviolet spectrum (see Table), is characteristic of analogous acids, such as (IX) [8] and (X),[11] in which interaction between the two heterocyclic atoms is greatly reduced.

The acid (VI; R = CO_2H), m. p. *ca.* 320°, when heated at 280—345°/14 mm., gave a sublimate which consisted mainly of the base (VI; R = H), with a small proportion of the unchanged acid and of an isomeric non-acidic compound, m. p. 226—227°. When the acid was heated at 340°/5 × 10^{-4} mm., it sublimed with only faint traces of the base and of the isomer.

To determine whether the isomer was formed during the Pfitzinger reaction or during the subsequent sublimation, the acid (VI; R = CO_2H) was extracted from the mixture of the above three components with warm aqueous sodium hydrogen carbonate solution, which was filtered, cooled, and acidified; the precipitated acid, when extracted with boiling ethanol, was pure. The undissolved mixture of base and isomer, after repeated recrystallisation from ethanol, gave the pure isomer. The highly pure acid (VI; R = CO_2H), when again sublimed at 280—345°/14 mm., afforded the three components as before, and the neutral isomer is therefore formed during the sublimation.

Investigation of the structure of the isomer was rendered difficult by its great stability. The compound was unaffected by boiling acetic acid–acetic anhydride, by diazomethane

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[7] Braunholtz and Mann, *J.*, 1955, 381.
[8] Mann and Wilkinson, *J.*, 1957, 3346.
[9] Braunholtz and Mann, *J.*, 1958, 3368.
[10] Braunholtz, Hall, Mann, and Sheppard, *J.*, 1959, 868.
[11] Braunholtz and Mann, *J.*, 1958, 3377.

Ultraviolet spectra (λ in mμ).

Compound	$\lambda_{max.}$	ε	$\lambda_{min.}$	ε
(II) In ethanol (3·196 mg./25 c.c.)	288	21,400	222	393
,, water (1·094 mg./25 c.c.)	293	20,420	224	420
,, 0·1N-NaOH (1·377 mg./25 c.c.)	294	18,920	229	920
,, 0·1N-HCl (1·618 mg./25 c.c.)	293	18,380	225	537

(IV) In ethanol (1·545 mg./25 c.c.):

$\lambda_{max.}$ ...	399	312	246	218	$\lambda_{min.}$ ...	337	269	236	214	$\lambda_{infl.}$ ...	319—326
ε	34,820	7835	4935	11,410	ε	5710	2740	4645	11,200	ε	7065

(VI; R = H) In ethanol (1·361 mg./50 c.c.):

$\lambda_{max.}$ ...	370	360	311	299	284	218
ε	15,800	16,600	10,900	11,800	15,100	35,150
$\lambda_{min.}$ ...	365	320	307	294	247	
ε	15,700	3660	9300	11,100	4910	

In 0·1N-HCl (1·649 mg./50 c.c.):

$\lambda_{max.}$ ...	399	288	221	$\lambda_{min.}$ ...	330—329	258
ε	32,350	11,710	35,000	ε	2620	3200

(VI; R = CO_2H) In ethanol (1·392 mg./25 c.c.):

$\lambda_{max.}$ ...	395	295—296		$\lambda_{min.}$ ...	332	261
ε	14,720	17,840		ε	4040	7960

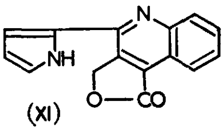
In 0·1N-NaOH (1·100 mg./25 c.c.):

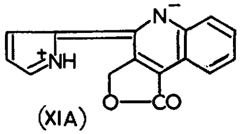
$\lambda_{max.}$ ...	366	386	226	$\lambda_{min.}$ ...	324—325	254—256
ε	20,050	21,000	33,100	ε	6550	10,380

In 0·1N-HCl (2·365 mg./100 c.c.):

$\lambda_{max.}$ ...	409	294	221	$\lambda_{min.}$ ...	337	265	211
ε	28,950	14,040	33,700	ε	3433	4560	29,820

in benzene solution, by 2,4-dinitrophenylhydrazine, by acrylonitrile in acetic acid at 100°, by methyl toluene-*p*-sulphonate at 90° or in boiling acetone, by saturated ammonia–ethanol during 4 hours at room temperature, by boiling ethanolic iodine, or by dissolution in boiling acetone–permanganate for 10 minutes (longer boiling gave a dark tar). It is insoluble in cold aqueous sodium carbonate [unlike the acid (VI; R = CO_2H)], but dissolves slowly in boiling aqueous 5% potassium hydroxide and is reprecipitated when this solution is cooled and acidified.


(XI)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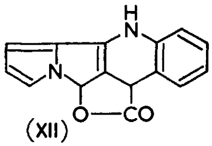
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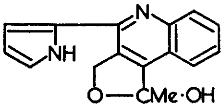
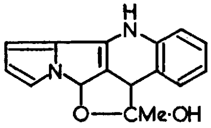

(XIII)

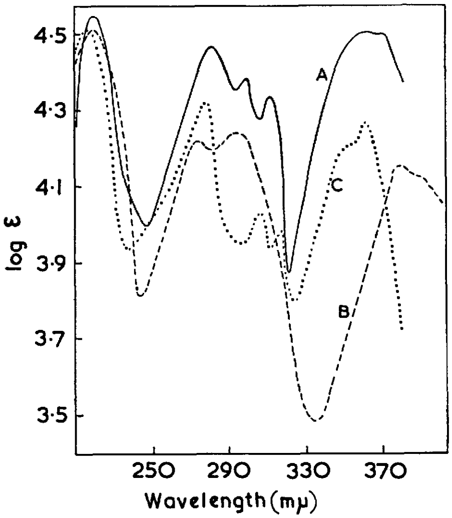

(XIV)

The most probable structures of this isomer appeared to be (XI) or (XII). The infrared spectrum of the isomer shows an –NH– band at 3355 cm.$^{-1}$ and a C=O band at 1757 cm.$^{-1}$, this value being normal for an αβ-unsaturated five-membered lactone and thus supporting structure (XI). However, attempts to detect in the alkaline solution of the compound by chemical means an OH or a CO_2^- group formed by opening of the lactone ring failed.

The stability towards boiling acetone–permanganate makes the 1,4-dihydroquinoline structure (XII) unlikely.

Lactones usually react with Grignard reagents to give substituted diols, but the isomer when treated with an excess of methylmagnesium iodide at room temperature gave a pale yellowish-green compound $C_{16}H_{14}N_2O_2$ in 70—82% yield. This introduction of only one hydroxyl group into a lactone structure by a Grignard reagent is rare.[12] The infrared spectrum of the compound $C_{16}H_{14}N_2O_2$ shows an –NH– band at 3340 cm.$^{-1}$, an OH band at 3130 cm.$^{-1}$, and no C=O band; the compound could therefore have the structure (XIII) or (XIV).

The ultraviolet spectra of the lactone and (more particularly) the alcohol $C_{16}H_{14}N_2O_2$ in ethanolic solution, however, closely resemble that of the base (VI; R = H) (see Figure) and thus provide strong evidence for the structures (XI) and (XIII); the presence of a 1,4-dihydroquinoline system, as in (XII) and (XIV), would almost certainly be incompatible with this close resemblance of the three spectra.



Absorption spectra, in ethanol, of: (A) 3′*H*-pyrrolizino(1′,2′-2,3)quinoline (VI; R = H) (1·361 mg. in 50 c.c.); (B) the lactone (?XI) (1·834 mg. in 50 ml.); and (C) the alcohol (?XIII) (1·264 mg. in 100 ml.).

The chemical inactivity of the pyrrole ring in the compound (XI) would be explained if the polar form (XIA) made a significant contribution to the structure: this factor would also explain the inertness of the quinoline-nitrogen atom towards quaternising agents, coupled with its ready salt formation under the more powerful influence of mineral acids.

EXPERIMENTAL

Consistent m. p.s for some compounds were obtained only if the material was immersed in a preheated bath: in such cases the immersion temperature is noted as (I.T. —°).

1-2′-*Cyanoethylpyrrole* (I; R = CN).—Redistilled vinyl cyanide (44·3 g., 1·6 mol.) was added during 1 hr. to a stirred mixture of pyrrole (35·5 g.) and 40% aqueous benzyltrimethylammonium hydroxide (" Triton B ") (3·5 c.c.) at 0°. The reaction, which had an induction period, was highly exothermic. The complete mixture was heated at 35—40° for 1 hr., and on distillation gave 1-2′-cyanoethylpyrrole, b. p. 132—136°/14 mm. (lit.,[3] 135—150°/8—10 mm.) (56 g., 88%).

A mixture of this product and 50% aqueous potassium hydroxide, when boiled under reflux for 1½ hr., diluted, cooled, and acidified, deposited 1-2′-carboxyethylpyrrole (I; R = CO_2H), b. p. 114°/0·4 mm., m. p. 57—58° (lit.,[2] 59—60°) from ether–light petroleum (b. p. 40—60°).

2,3-*Dihydro*-1-*oxo*-1H-*pyrrolizine* (II).—Careful attention to the conditions of this preparation is essential. A finely ground mixture of fresh aluminium chloride (28 g.), sodium chloride (5·6 g.), and potassium chloride (5·6 g.) was heated in a boiling-tube to form a clear

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[12] Barnett, Cook, and Nixon, *J.*, 1927, 504.

straw-brown melt, which was thoroughly stirred by the vertical movement of a glass rod flattened at the base. When the temperature fell to 120°, 1-2′-cyanoethylpyrrole (I; R = CN) (7 g.) was rapidly added, and the mixture, after vigorous stirring for 35—40 sec., was poured quickly into stirred ice-water (400 c.c.). Concentrated aqueous potassium hydroxide was added to the stirred mixture until the initial gelatinous precipitate had almost completely dissolved. The mixture was heated at 75—80° for 30 min. and then filtered, the inorganic residue being washed with water. The united filtrate and washings were extracted with chloroform (5 × 500 c.c.). The dried extract, on evaporation, gave the oxo-pyrrolizine (II) as a brown oil which rapidly solidified (4·9 g., 70%); recrystallisation from ether–light petroleum (b. p. 40—60°) afforded the pure ketone, m. p. 53·5—54° (lit.,[6] 54°) (Found: N, 11·6. Calc. for C_7H_7NO: N, 11·6%).

Attempts to cyclise the acid (I; R = CO_2H) to the ketone (II) by polyphosphoric acid at 100° and 150° gave only unchanged acid and tar.

The ketone (II) gave a colourless light-sensitive *phenylhydrazone*, m. p. 144—146° (decomp.) (from ethanol) (Found: C, 73·6; H, 6·15; N, 20·0. $C_{13}H_{13}N_3$ requires C, 73·9; H, 6·2; N, 19·9%), a deep red *2,4-dinitrophenylhydrazone*, m. p. 222—224° (Found: N, 23·3. $C_{13}H_{11}N_5O_4$ requires N, 23·3%), and a semicarbazone, m. p. 210° (lit.,[2] 211°) (from 97% ethanol).

A mixture of the ketone (II) (0·35 g.), *p*-dimethylaminobenzaldehyde (0·45 g., 1·1 mol.), and ethanol (5 c.c.) containing 10% aqueous potassium hydroxide (0·2 c.c.) was boiled for 10 min., and when cooled deposited orange *2-*p*-dimethylaminobenzylidine-2,3-dihydro-1-oxo-1*H* pyrrolizine* (III) (0·55 g., 76%), m. p. 234° (from ethanol containing dioxan) (Found: C, 76·2; H, 6·35; N, 11·0. $C_{16}H_{16}N_2O$ requires C, 76·2; H, 6·4; N, 11·1%).

The pale yellow dilute aqueous solution of the ketone (II) became pale orange on the addition of dilute hydrochloric acid. The colourless acetone solution became deep red when saturated with hydrogen chloride; addition of dry ether precipitated the flocculent red hydrochloride, which rapidly dissociated in the absence of free acid.

*2-(2,3-Dihydro-1*H*-pyrrolizin-1-ylidene)-2,3-dihydro-1-oxo-1*H*-pyrrolizine* (IV).—The ketone (II) (1·36 g.) was added to a solution of potassium hydroxide (2·4 g.) in aqueous ethanol (3 + 12 c.c.), which was boiled under reflux for 15 min. The bright yellow *product* (IV) (1·05 g., 83%), when collected from the cold mixture and crystallised from ethanol had m. p. 208·5° (decomp. I.T. 205°) (Found: C, 75·1; H, 5·6; N, 12·7%; *M*, in 0·6% boiling acetone, 233. $C_{14}H_{12}N_2O$ requires C, 75·0; H, 5·4; N, 12·5%; *M*, 224).

Hydrogen chloride, when passed through a chilled ethanolic solution of the ketone (IV), deposited in almost theoretical yield the purple *hydrochloride*, which was rapidly washed with chilled acetone–ether and collected, and dried over calcium chloride under reduced pressure; it had m. p. 181° (decomp., I.T. 175°) (Found: C, 65·4; H, 5·25; N, 10·7. $C_{14}H_{12}N_2O,HCl$ requires C, 64·4; H, 5·0; N, 10·8%). This salt on treatment with aqueous sodium hydroxide regenerated the ketone (IV). Addition of 60% aqueous perchloric acid to an ethanolic solution of the ketone (IV) gave deep red plates, which decomposed when collected from the solution. The ketone gave a bright scarlet *picrate*, m. p. 153° (decomp.) (from ethanol) (Found: C, 53·0; H, 4·0; N, 15·6. $C_{14}H_{12}N_2O,C_6H_3N_3O_7$ requires C, 52·8; H, 3·3; N, 15·5%).

Oxidation of the Ketone (IV).—Potassium permanganate (1 g., 1·1 mol.) was added to a solution of the ketone (0·979 g.) in boiling acetone, which was then heated under reflux for 35 min.; decolorisation of the permanganate appeared then to be complete. Addition of the permanganate with further boiling was repeated, with occasional filtration to follow the slow disappearance of the yellow colour, until this process was complete; boiling for 8 hr. and addition of 8·6 g. of permanganate were required. The filtered solution, on evaporation, yielded the ketone (II) (0·131 g.), m. p. and mixed m. p. 53—54°; its identity was confirmed by its infrared spectrum.

No compounds could be identified in the traces of organic material isolated from the precipitated manganese dioxide.

Reaction of the Ketone (II) *with* o-*Aminobenzaldehyde*.—The ketone (II) (0·3 g.) and the aldehyde (0·3 g., 1 mol.) were dissolved in turn in warm ethanol (7 c.c.), to which 10% aqueous sodium hydroxide (0·2 c.c.) was added. The solution, when set aside overnight at room temperature, deposited *2-*o*-aminobenzylidene-2,3-dihydro-1-oxo-1*H*-pyrrolizine* (V; R = H) (0·4 g., 54%), bright orange needles, m. p. 198—199° (from ethanol) (Found: C, 74·8; H, 5·9; N, 12·85. $C_{14}H_{12}N_2O$ requires C, 75·0; H, 5·4; N, 12·5%).

This compound gave the *acetamido-derivative* (V; R = Ac). m. p. 230° (from ethanol)

(Found: C, 71·65; H, 5·5; N, 10·25. $C_{16}H_{14}N_2O_2$ requires C, 72·1; H, 5·3; N, 10·5%), and the *toluene-*p*-sulphonamido-derivative* (V; R = $SO_2{\cdot}C_6H_4Me$), m. p. 248° (from dioxan) (Found: C, 66·5; H, 5·0; N, 7·4. $C_{21}H_{18}N_2O_3S$ requires C, 66·7; H, 4·8; N, 7·4%), both cream-coloured.

The oxo-amine (V; R = H) (0·5 g.), when heated in a tube at 300°/14 mm., gave a clear yellow distillate which readily solidified (0·45 g.), and after crystallisation from ethanol afforded the pale yellow *3'*H*-pyrrolizino*(1',2'-2,3)*quinoline* (VI; R = H), m. p. 146—147° (Found: C, 81·9; H, 5·0; N, 13·3. $C_{14}H_{10}N_2$ requires C, 81·6; H, 4·9; N, 13·6%).

An acetone solution of the base (VI; R = H) when treated with hydrogen chloride deposited a bright yellow *monohydrochloride*, m. p. 290—292° (decomp., I.T. 286°) (from ethanol–acetone) (Found: C, 69·0; H, 4·9; N, 11·75. $C_{14}H_{10}N_2$,HCl requires C, 69·3; H, 4·6; N, 11·55%). The base readily gave a bright orange *methiodide*, m. p. 294° (decomp., I.T. 285°) (from methanol) (Found: C, 51·7; H, 4·1; N, 7·85. $C_{15}H_{13}IN_2$ requires C, 51·7; H, 3·8; N, 8·0%).

Solutions of the base (VI; R = H) in ethanol–hydrochloric acid mixtures of various concentrations were boiled under reflux for 2 hr. The solutions, the initial deep red-brown colour of which did not change, deposited, on cooling, the above hydrochloride (identified by m. p. and infrared spectra), and basification afforded the unchanged base (VI; R = H). The latter was also recovered unchanged after its solution in acetone–permanganate had been boiled under reflux for 3 hr.

Reaction of the Ketone (II) *with Isatin and Alkali.*—Isatin (5·5 g., 1·1 mol.) and potassium hydroxide (6·7 g.) were added in this order to a solution of the ketone (II) (4·2 g.) in ethanol (30 c.c.) and water (30 c.c.). The dark solution was boiled under reflux for 9 hr., set aside overnight, and then filtered into water–acetic acid (7 : 3 v/v; 200 c.c.), leaving a residue of the compound (XI) (0·1 g.). The acidified filtrate deposited the *3'*H*-pyrrolizino*(1',2'-2,3)-*quinoline-*4*-carboxylic acid* (VI; R = CO_2H), a bright mustard-coloured powder (5·3 g., 61%), having m. p. *ca.* 320° (effervescence) after thorough washing with ethanol and acetone (Found: C, 72·1; H, 4·3; N, 11·4. $C_{15}H_{10}N_2O_2$ requires C, 72·0; H, 4·0; N, 11·2%). This gave a yellow *sodium salt* (Found: N, 10·0. $C_{15}H_9N_2NaO_2$ requires N, 10·3%), and an unstable yellow *hydrochloride*, m. p. indefinite above 300° (Found: C, 62·7; H, 4·05; N, 9·6. $C_{15}H_{10}N_2O_2$,HCl requires C, 62·8; H, 3·85; N, 9·75%).

The acid (VI; R = CO_2H) was insoluble in the common solvents except dimethylformamide, from which it did not crystallise well. To ensure the absence of the isomer, the acid (1 g.) was heated at 5×10^{-4} mm. so that the temperature rose during 40 min. to 340° and then remained constant for 1·5 hr.; the m. p. of the yellow sublimed acid (0·89 g.) was unchanged. When a solution of this acid in hot aqueous sodium hydrogen carbonate was filtered into 30% acetic acid, the acid was precipitated as a bright lemon-yellow powder, which was collected, washed with water and ethanol, extracted with boiling ethanol (100 c.c.), and again collected and dried (Found: C, 71·7; H, 4·15; N, 11·15%). Although this high purification of the acid was unnecessary for most purposes, it ensured a higher and more constant yield of the lactone (XI) in the following preparation.

The Lactone (?XI).—The conversion of the acid (VI; R = CO_2H) into the lactone (?XI) proceeds best when only small quantities of the acid are heated. The pure acid (0·5 g.) was therefore placed in each of two parallel sublimation tubes which were evacuated to 14 mm. and then heated to 345° during 10—15 min., the tubes pointing slightly downwards meanwhile. The production of a yellow sublimate ceased when the temperature reached 345°. The cold sublimates were removed, united, and dissolved in boiling ethanol (20 c.c.). The filtered extract, on cooling, deposited the *lactone* (0·10 g., 10%), which formed bright lemon-yellow needles, m. p. 226—227°, after thorough washing with aqueous sodium hydrogen carbonate and water and recrystallisation from ethanol (Found: C, 72·0; H, 4·2; N, 11·2%; *M*, in boiling acetone, 240. $C_{15}H_{10}N_2O_2$ requires C, 72·0; H, 4·0; N, 11·2%; *M*, 250). Hydrogen chloride, when passed into an acetone solution of the lactone, deposited the bright yellow unstable *hydrochloride*, which, when collected, rapidly washed with acetone, and dried over calcium chloride, had m. p. 236—237° (decomp. I.T. 234°) (Found: N, 9·9. $C_{15}H_{10}N_2O_2$,HCl requires N, 9·8%). The base was liberated when this salt was added to water.

The cold ethanolic mother-liquor from the initial extraction of the lactone contained only traces of the latter and, when concentrated and diluted with water, deposited the crystalline base (VI; R = H), m. p. and mixed m. p. 146—147° (after recrystallisation from ethanol, followed by vacuum-distillation).

When an intimate mixture of the acid (VI; R = CO_2H) (250 mg.) and barium hydroxide was heated at 320—340°/5 × 10^{-5} mm., very slow decarboxylation occurred, with sublimation of the base (VI; R = H) (75 mg.).

Action of Methylmagnesium Iodide on the Lactone (?XI).—A large excess of this reagent, prepared from methyl iodide (1·35 g.) and magnesium (0·6 g.) in ether (15 c.c.), was added to a stirred solution of the lactone (228 mg.) in pure benzene (40 c.c.). A deep ruby-red product immediately separated, and the benzene developed an intense green fluorescence. After 10 min., the mixture was poured into saturated aqueous ammonium chloride (80 c.c.), which was vigorously shaken. The benzene layer, now colourless, when dried and distilled under reduced pressure, afforded the very pale greenish-yellow alcohol (?XIII) (166 mg., 70%), m. p. 202—204° (decomp., I.T. 195°) (from chloroform) (Found: C, 72·0; H, 5·3; N, 10·5. $C_{16}H_{14}N_2O_2$ requires C, 72·2; H, 5·3; N, 10·5%). In two repetitions of this preparation, the yields were 69% and 82%.

Action of Methyl Iodide on the Lactone (?XI).—A solution of the lactone (77 mg.) in acetone (10 c.c.) containing a trace of methanol was heated with methyl iodide (0·92 g., 11 mol.) in a sealed tube at 100° for 7 hr. Evaporation gave a dark red solid residue (102 mg.), which did not crystallise. Attempted crystallisation from ethanol–acetone gave a dark red and a deep purple powder, but the very small quantity and apparently amorphous nature of these products prevented purification.

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UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, March* 1*st*, 1962.]