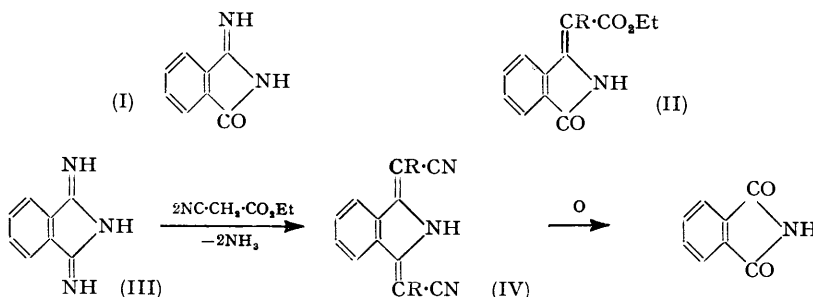


50. Heterocyclic Imines and Amines. Part VI.* Condensation Products from Di-iminoisoindoline and Succinimidine with Cyanoacetates.

By J. A. ELVIDGE, JOHN S. FITT, and R. P. LINSTAED.

Di-iminoisoindoline (III) condenses with 2 mols. of ethyl cyanoacetate with elimination of 2 mols. of ammonia to give the isoindoline (IV; R = CO₂Et). Succinimidine (V) condenses with only 1 mol. of cyanoacetate to yield the pyrrolidine (VI), but in the presence of sodium ethoxide, it yields the di-condensation product (IX). Degradations and ozonolyses are described, light absorptions are given, and the structures of the compounds are discussed with particular reference to their unexpected properties.

THE studies on imidines and their condensations with amines (previous papers * and forthcoming publications) have led to new syntheses of azaporphin pigments and related nitrogen-linked macrocycles (Elvidge and Linstead, *J.*, 1955, 3536; 1952, 5008; Linstead and Whalley, *J.*, 1955, 3530; Clark, Elvidge, and Linstead, *J.*, 1954, 2490). With the aim, ultimately, of preparing similar compounds containing carbon links, the condensation reactions of imidines with active methylene compounds are being investigated. Linstead and Rowe (*J.*, 1940, 1070) showed that the imine (I) condensed with acetoacetic and malonic ester, with elimination of ammonia, to yield the products (II; R = Ac and CO₂Et). The present paper is concerned mainly with analogous products from the reaction of cyanoacetates with di-iminoisoindoline (III) and with succinimidine (V).



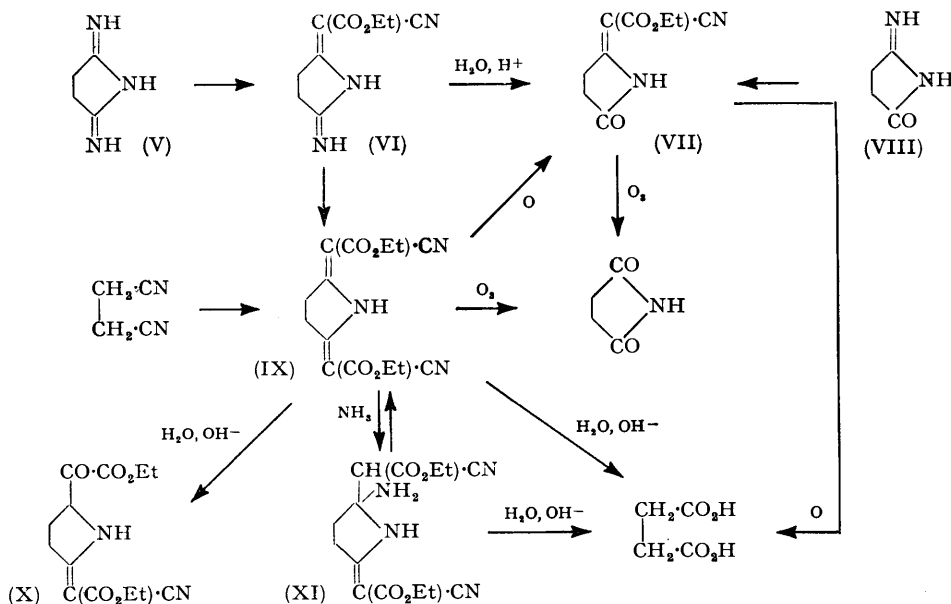
isoIndoline Derivatives.—Interaction of di-iminoisoindoline (III) with ethyl cyanoacetate in boiling ethanol produced ammonia and a yellow, dicondensation product, C₁₈H₁₅O₄N₃. That this (potentially tautomeric) compound had the structure (IV; R = CO₂Et) was confirmed by oxidation with permanganate to phthalimide in good yield. Incidentally, compound (IV; R = CO₂Et) was identified with a product prepared from phthalonitrile, guanidine, and ethyl cyanoacetate (Banfield, Thesis, Melbourne, 1950). Treatment of this compound (IV; R = CO₂Et) with alkali at once gave a red substance, presumably the resonance anion derived by deprotonation; this soon became hydrolysed, and after acidification the yellow dicarboxylic acid (IV; R = CO₂H) was isolated. Decarboxylation of the latter with pyridine and copper yielded 1:3-di(cyanomethylene)isoindoline (IV; R = H). This gave phthalimide in good yield on oxidation in conformity with the structure shown. The new isoindoline derivatives (IV) resisted acid hydrolysis and catalytic reduction. Their light absorptions are recorded in the Table.

Pyrrolidine Derivatives.—Succinimidine (V) differed from di-iminoisoindoline (III) in that it formed only a monocondensation product with ethyl cyanoacetate alone. The product, C₉H₁₁O₂N₃, was assigned the structure (VI) because of its light absorption (see

* Parts I—V, *J.*, 1952, 5000; 1953, 3593; 1954, 442; 1955, 3530.

Table) and its hydrolysis to the pyrrolidone (VII). This was synthesised from ethyl sodio-cyanoacetate and iminosuccinimide (VIII), a compound of established constitution (Elvidge and Linstead, *J.*, 1954, 442). The imino-group of (VI) was unreactive to aniline, as well as to cyanoacetate, although it was readily hydrolysed. Attempts to oxidise the pyrrolidone (VII) with permanganate to succinimide produced gross decomposition. Ozonolysis, however, gave a 44% yield of succinimide.

The finding that iminosuccinimide (VIII) condensed with ethyl cyanoacetate only when the latter was presented as the sodio-derivative, prompted us to treat the imine (VI) with ethyl sodiocyanoacetate. This reaction yielded the 2 : 5-di(cyanoethoxycarbonylmethylene)pyrrolidine (IX), which was also obtained by a Thorpe condensation of succinonitrile with ethyl cyanoacetate in the presence of sodium ethoxide. The imine (VI) was not detected as an intermediate in this condensation.

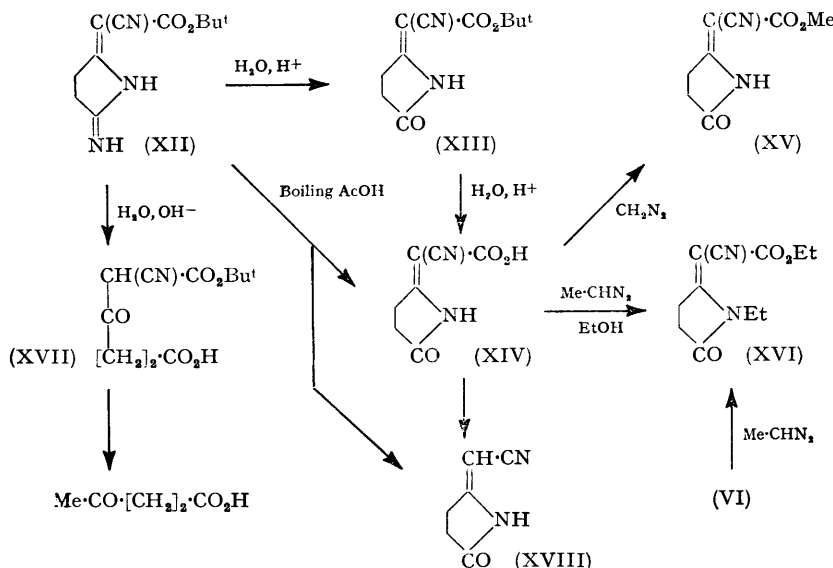


The disubstituted pyrrolidine (IX) was obtained in two forms, m. p. 150° and 205°. These were interconvertible by crystallisation (see Experimental section) and had identical light absorptions: they may be polymorphs or, less probably, *cis-trans*-isomers. The compound (IX) was weakly acidic, being sparingly soluble in concentrated aqueous ammonia, and it gave a monopotassium-derivative with potassium hydroxide in aqueous dioxan. The potassium-derivative decomposed when heated with water; clean hydrolysis to a carboxylic acid, as in the *isoindoline* series, was not obtained. Treatment of the potassium-derivative with dilute acid regenerated (IX) as a mixture of the two forms, m. p. ca. 171°. Attempted reaction of the potassium-derivative with ethyl iodide failed.

Like the monomethylenepyrrolidine (VI), the di(cyanoethoxycarbonylmethylene) compound (IX) resisted acid hydrolysis and proved troublesome to oxidise. From one oxidation of the latter, the pyrrolidone (VII) was isolated, whilst, more reliably, ozonolysis afforded some 6% of succinimide. Towards alkaline hydrolysis, the compound (IX) was unstable and tar was formed. Prolonged treatment with concentrated sodium hydroxide afforded succinic acid. Brief treatment, however, produced a crystalline product, C₁₃H₁₆O₅N₂, evidently derived by the replacement of a cyano- by a hydroxyl group. A possible structure is (X) or, perhaps better, the derived enol. The compound was acidic, gave a red colour with ferric chloride, and like simpler, highly enolised ketones failed to form ketonic derivatives (cf. Eisner, Elvidge, and Linstead, *J.*, 1951, 1501). It resisted mild acid hydrolysis and catalytic hydrogenation.

Treatment of the compound (IX) with dry ammonia afforded a 1:1 addition product, $C_{14}H_{18}O_4N_4$. This crystallised from acetic acid, and its light absorption, which differed from that of the potassio-derivative of (IX), indicated that the conjugation had been shortened (see Table). The preferred structure, therefore, is (XI); in agreement, the adduct was hydrolysed to succinic acid in good yield with aqueous alkali and was reconverted into the dimethylene compound (IX) when heated with benzoic anhydride. An adduct resembling (XI) was formed from the pyrrolidine (IX) and methylamine.

Because the ethyl ester groups of the pyrrolidine derivatives could not be hydrolysed selectively—there was either no attack or general decomposition—other esters were investigated. From methyl cyanoacetate and succinimidine, the methyl esters analogous to compounds (VI) and (VII) were prepared but these also were resistant to hydrolysis. Condensation of *tert.*-butyl cyanoacetate with succinimidine afforded the analogue (XII) which with hydrochloric acid in aqueous acetone gave the expected pyrrolidone (XIII). When the latter was boiled in aqueous acetic acid, *isobutene* was evolved and the oxo-



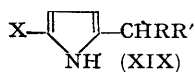
pyrrolidinecarboxylic acid (XIV) was formed. The structure of the acid was confirmed by the reaction with ethereal diazomethane which afforded the methyl ester (XV), identical with that from the condensation of methyl cyanoacetate with succinimidine. With diazoethane, the acid (XIV) reacted only when in solution (in ethanol) and then afforded a diethylated product. Since this was unaffected by primary amines it presumably has the structure (XVI) and is not the isomeric *O*-ether: less probably it has a *C*-Et structure. The same derivative (XVI) was obtained from the oxopyrrolidine ethyl ester (VII) and diazoethane in ethanol.

Attempts to remove only the *tert.*-butyl ester grouping of the parent imino-compound (XII) failed. Thus mild alkaline hydrolysis (cf. Barrett, Linstead, Leavitt, and Rowe, *J.*, 1940, 1076) effected more extensive degradation to an acid (XVII), $C_{11}H_{15}O_5N$, with loss of ammonia. The compound gave *isobutene* when heated in water, behaved as a dibasic acid on titration, gave an orange colour with ferric chloride, and was degraded to lævulic acid by acid hydrolysis. The acyclic keto-acid structure (XVII), doubtless highly enolised, therefore seemed most likely. In any case, the ultimate degradation product, lævulic acid, provided a confirmation of the carbon skeleton taken as present in the succinimidine-cyanoacetate condensation product (XII). Treatment of the imine (XII) with boiling acetic acid caused hydrolysis of the imino-group concomitantly with elimination of *isobutene* and some carbon dioxide: 5-cyanomethylene-2-pyrrolidone (XVIII) was isolated

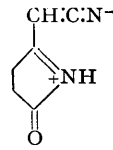
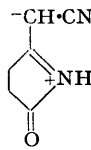
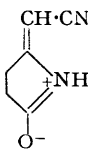
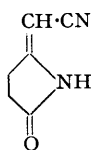
in every experiment, and sometimes also the acid (XIV). The oxopyrrolidine acid (XIV), best obtained from the ester (XIII), as mentioned above, was a little decomposed by sublimation but was decarboxylated satisfactorily to 5-cyanomethylene-2-pyrrolidone (XVIII) by boiling pyridine containing copper acetate.

Discussion of Structures.—The simple pyrrolidone (XVIII) gave succinimide in 79% yield on ozonolysis, a result which strongly supports the assigned bond structure, and thence of course the structures (XIV), (XIII), and (XII) for the precursors. This result is important because it excludes for these compounds the pyrrole structures (XIX). The evidence of light absorption (see Table) is not in disagreement (cf. Cookson, *J.*, 1953, 2789) though it is less clear-cut because of a lack of data for comparison.

The properties of the compounds to which pyrrolidine structures have been given were unexpected. It seems that these might be accounted for (at least qualitatively) by regarding the compounds as resonance hybrids. Including bond structures which involve dipolar charge separations, there are for example four electronic isomers of 5-cyanomethylene-2-pyrrolidone (XVIII) :

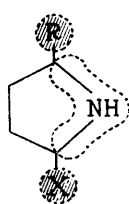


(X = NH₂, OH)

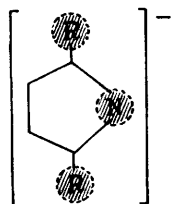


Hence the best representation of this molecule is perhaps (XX; R = CH·CN, X = O). Similarly, there are five canonical forms of the oxopyrrolidine ester (VII) and no less than seven of the dicondensation product (IX). The difficulty of effecting oxidation cleanly may then be attributed to the delocalisation of the double bonds. Ozone, however, will attack resonance systems as if they were simply mixtures of the canonical structures. On ozonolysis of the compound (IX)—which is mesomerised to the greatest extent—the lowest yield (6.5%) of succinimide was obtained, whilst the pyrrolidone (VII) gave 44% and the simplest, least degenerate derivative (XVIII) gave 79% of succinimide. These results are in qualitative agreement with the suggested fine structures.

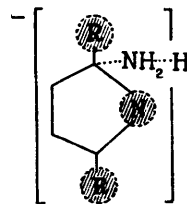
Evidently because the ester groups of the derivatives (VI), (VII), (IX), and (XV) participate in the mesomerism, these esters are not easily hydrolysed. The ready acid hydrolysis of the exocyclic nitrogen function of the compounds (VI) and (XII), which contrasts with the usual stability of amidines to acids, is indicative of electron deficiency at the adjacent carbon atom (position 2 of the ring). The resonance picture of the structures [see (XX)] shows there is such electron deficiency.



(XX)




(XXI)



(XXII)

 Region of electron excess.

 Region of electron deficiency.

The acidity of the pyrrolidones and of the dicondensation product (IX) is presumably a result of the localisation of positive charge in the neighbourhood of the pyrrolidine nitrogen [see (XX)]. This would facilitate the loss of a proton. In particular, the anion of the dicondensation product would have a lower energy content than the neutral molecule

(IX) because there are still seven canonical forms for the anion and none of these involves a formal separation of charges.

The resistance of the compounds to hydrogenation may result not only from the resonance stabilisation but also from steric hindrance. In acetic acid, with an active platinum catalyst, the compound (IX) was much more slowly hydrogenated than was benzene.

In contrast, ammonia added readily to the compound (IX). Under the reaction conditions, the disubstituted pyrrolidine (IX) was presumably present as the anion, and in this the negative charge would tend to have the distribution shown in (XXI) (derived by superposition of the seven hypothetical canonical forms). Interaction with ammonia, polarised in the sense $\overset{\delta-}{\text{N}}\text{H}_2\text{-}\overset{\delta+}{\text{H}}$, would give the anionic transition complex (XXII) from which the adduct (XI) would be derived.

Compound	Solvent	λ_{max} (Å)	ϵ	Compound	Solvent	λ_{max} (Å)	ϵ
(IV; R = CO ₂ Et)	CHCl ₃	2800	13,600	(VI)	EtOH	3100	38,600
		3630 *	22,900	(XII)	"	3100	34,300
		3960 }	30,300	(VII)	"	2740	23,300
		4150 }		(XIII)	"	2770	21,700
(IV; R = CO ₂ H)	Dioxan	2550	16,300	(XIV)	"	2730	25,200
		3450	9,800	(XVIII)	"	2510	21,300
		3950 }	30,000	(IX) (both forms)	EtOH, hexane	3220	41,000
		4150 }			3320	43,000	
		(IV; R = H)	Dioxan	2880	11,400	K deriv. of (IX)	H ₂ O
3590	28,400					3350	12,900
3740	26,500					3710	11,000
				(XI)	AcOH	2830	30,600
		(X)	EtOH	2600	21,500		
		(XVII)	"	2570	13,500		

* Inflection.

The light-absorption characteristics of the compounds (see Table) support the idea that the formal unsaturation and the functional groups are involved together in mesomerism. No one of the possible classical bond structures can account for the observed high-intensity maxima.

EXPERIMENTAL

Analyses are by Mr. F. H. Oliver and his staff of the microanalytical laboratory, and light-absorption measurements by Mrs. A. I. Boston of the spectroscopic laboratory of this Department.

1 : 3-Di(cyanoethoxycarbonylmethylene)isoindoline (IV; R = CO₂Et).—(a) *Preparation*. (i) Di-iminoisoindoline (Elvidge and Linstead, *J.*, 1952, 5000) (21 g.) in methanol (1 l.) was heated under reflux with ethyl cyanoacetate (34 g.) overnight. The mixture was cooled and the yellow solid (44 g., 84%) collected. From ethyl methyl ketone, 1 : 3-di(cyanoethoxycarbonylmethylene)isoindoline formed long yellow needles, m. p. 231°, which showed a greenish fluorescence (Found : C, 64.0; H, 4.6; N, 12.2. C₁₈H₁₅O₄N₃ requires C, 64.1; H, 4.5; N, 12.5%).

(ii) [With MARGARET WHALLEY] Guanidine (2.26 g.) was added to phthalonitrile (4 g.) in ethanol (40 c.c.), and the solution kept at 37° overnight. Ethyl cyanoacetate (8.7 g.) was added and the mixture warmed on the steam-bath for several minutes to start the reaction. Next day, the greenish solid product was extracted with ethanol. A trace of phthalocyanine (3 mg.) remained and from the extract di(cyanoethoxycarbonylmethylene)isoindoline (5 g.) was obtained as yellow crystals, m. p. 228—231° undepressed by the product from the preparation above (cf. Banfield, Thesis, Melbourne, 1950).

(b) *Oxidation*. A solution of di(cyanoethoxycarbonylmethylene)isoindoline (0.5 g.) in acetone (45 c.c.) was treated with potassium permanganate (1.5 g.) in water (20 c.c.) and, next day, with sulphur dioxide. The clear solution was evaporated to remove acetone, and the aqueous residue was cooled. Phthalimide (0.15 g., 80%) separated, m. p. and mixed m. p. 228°.

(c) *Hydrolysis to the di-acid* (IV; R = CO₂H). Addition of potassium hydroxide (10 g.) in water (750 c.c.) to di(cyanoethoxycarbonylmethylene)isoindoline (20 g.) dissolved in dioxan (1 l.)

afforded a dark red precipitate. This dissolved on warming of the mixture. The solution was then heated under reflux for 1 hr. and cooled, and the solid product was dissolved in the minimum of water. Acidification of the aqueous solution with hydrochloric acid precipitated 1 : 3-*di*-(*carboxycyanomethylene*)*isoindoline* (11 g., 66%; no characteristic m. p.) (Found : C, 60.0; H, 2.7; N, 15.0%; equiv., 139. $C_{14}H_7O_4N_3$ requires C, 59.8; H, 2.5; N, 14.9%; equiv., 140.6).

A solution of the potassium salt (0.25 g.) in water (30 c.c.) was kept overnight with potassium permanganate (1.5 g.). The mixture was then treated with acetone (30 c.c.) and sulphur dioxide, and the clear solution was evaporated, yielding phthalic acid (0.13 g., 90%), which was identified by mixed m. p. and by conversion into the *S*-benzylthiuronium salt.

1 : 3-*Di*-(*cyanomethylene*)*isoindoline* (IV; R = H).—(a) *Preparation*. The di-acid (5 g.) and copper bronze (0.5 g.) were boiled together in pyridine (75 c.c.) for 1 hr. The filtrate was evaporated under reduced pressure, and the residue was powdered, mixed with charcoal, and extracted with ethanol in a Soxhlet apparatus. From ethanol, the 1 : 3-*di*-(*cyanomethylene*)*isoindoline* (1.81 g., 53%) crystallised as long yellow needles (no m. p.) (Found : C, 74.4; H, 3.8; N, 21.8. $C_{12}H_7N_3$ requires C, 74.6; H, 3.65; N, 21.75%).

(b) *Oxidation*. Di-(*cyanomethylene*)*isoindoline* (100 mg.) in acetone (40 c.c.), and potassium permanganate (0.6 g.) in water (5 c.c.), were shaken together overnight. The mixture was decolorised with sulphur dioxide, filtered, evaporated under reduced pressure to a small bulk, and cooled. The white solid (50 mg., 72%) which separated was identified as phthalimide by m. p. and mixed m. p.

5-*Cyanoethoxycarbonylmethylene-2-iminopyrrolidine* (VI).—Ethyl cyanoacetate (23.5 c.c.) was added to a boiling solution of succinimide (Elvidge and Linstead, *J.*, 1954, 442) (19.7 g.) in ethanol (1 l.), and after 45 min. the mixture was cooled. Extractive crystallisation of the solid product (30 g., 76%) from pyridine afforded 5-*cyanoethoxycarbonylmethylene-2-iminopyrrolidine* as a microcrystalline powder with no characteristic m. p. (Found : C, 55.9; H, 5.9; N, 21.7. $C_9H_{11}O_2N_3$ requires C, 55.95; H, 5.7; N, 21.75%). The imine dissolved in aqueous hydrochloric acid and was precipitated by ammonia or sodium hydroxide.

5-*Cyanoethoxycarbonylmethylene-2-pyrrolidone* (VII).—(a) *Preparation*. (i) A solution of the preceding imino-pyrrolidine (10 g.) in 3% hydrochloric acid (50 c.c.) was boiled until no more solid separated (6.3 g., 60%). Several crystallisations from ethanol afforded needles of 5-*cyanoethoxycarbonylmethylene-2-pyrrolidone*, m. p. 140—150° unchanged by sublimation at 20 mm. (Found : C, 56.0; H, 5.4; N, 14.4. $C_9H_{10}O_3N_2$ requires C, 55.7; H, 5.2; N, 14.4%).

(ii) Ethyl cyanoacetate (1 g.) and iminosuccinimide (1 g.) were added successively to a cold solution of sodium ethoxide (from 0.3 g. of sodium) in ethanol (15 c.c.). The mixture was heated under reflux for 1 hr., cooled and poured into hydrochloric acid and ice. Recrystallisation of the precipitate from ethanol afforded 5-*cyanoethoxycarbonylmethylene-2-pyrrolidone* (0.8 g., 35%), m. p. 140—150° alone and in admixture with the previous preparation.

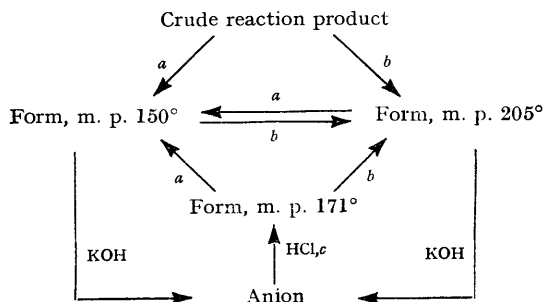
(b) *Oxidation*. Ozonised oxygen (1—3%) was bubbled slowly through a solution of 5-*cyanoethoxycarbonylmethylene-2-pyrrolidone* (286 mg.) in acetic acid for 17 hr. Water (5 c.c.) was added and the solution evaporated on the steam-bath. The residue, which crystallised when rubbed with a glass rod, was drained on porous tile : the solid was identified as succinimide (65 mg., 44%) by mixed m. p.

2 : 5-*Di*-(*cyanoethoxycarbonylmethylene*)*pyrrolidine* (IX).—(a) *Preparation*. (i) Ethyl cyanoacetate (3 g.) was added to cold ethanolic sodium ethoxide, prepared from sodium (1.2 g.) and ethanol (45 c.c.). 5-*Cyanoethoxycarbonylmethylene-2-iminopyrrolidine* (3 g.) was added, and the mixture was heated under reflux for 1 hr., cooled, and poured into ice (24 g.) and hydrochloric acid (12 g.). Recrystallisation of the greenish precipitate (3.7 g., 80%) from ethanol [charcoal or, better, brief treatment with permanganate, as in (d) (ii) below, to destroy impurities] afforded colourless needles, m. p. 205°, of 2 : 5-*di*-(*cyanoethoxycarbonylmethylene*)*pyrrolidine* (Found : C, 58.1; H, 5.5; N, 14.3; OEt, 32.6. $C_{14}H_{15}O_4N_3$ requires C, 58.1; H, 5.2; N, 14.5; OEt, 31.1%). The compound was sparingly soluble in cold aqueous potassium hydroxide and in concentrated ammonia.

(ii) Succinonitrile (20 g.) was added to cold ethanolic ethyl sodiocyanoacetate, prepared from ethanol (75 c.c.), sodium (6 g.), and ethyl cyanoacetate (52 c.c.). The mixture was boiled for 1 hr. (ammonia was evolved), then cooled, and poured into ice (4.0 g.) and hydrochloric acid (80 g.). Recrystallisation of the greenish product (49 g., 53%) from ethanol (charcoal) gave colourless prismatic needles, m. p. 205° undepressed by the preceding preparation of 2 : 5-*di*-(*cyanoethoxycarbonylmethylene*)*pyrrolidine*. Crystallisation of the crude reaction product from light petroleum (b. p. 60—80°) gave prismatic needles, m. p. 150° (Found : C, 58.3; H, 5.5; N, 14.8%). Another sample, obtained from the potassio-derivative (see below) and

hydrochloric acid, was repeatedly crystallised from benzene–light petroleum (b. p. 60–80°); it then formed prismatic needles, m. p. 171° (Found : C, 58.2; H, 5.3; N, 14.7%). Mixtures of these forms of 2 : 5-di(cyanoethoxycarbonylmethylene)pyrrolidine had intermediate m. p.s.

The forms were interconverted quantitatively as follows :



a, 17 Hours' boiling with light petroleum (b. p. 60–80°).

b, 5 Hours' boiling with ethanol.

c, Crystallisation from benzene–light petroleum (b. p. 60–80°).

(b) *Potassio-derivative*. A hot solution of the pyrrolidine (IX) (1 g.) in dioxan (5 c.c.) was poured into a cold solution of potassium hydroxide (0.4 g.) in water (3 c.c.). After 10 min., the mixture was cooled in ice, and the solid was collected and washed exhaustively with ethanol. From cold pyridine (0.1% solution) by addition of light petroleum (b. p. 60–80°) (4 vols.) the *potassio-derivative* was obtained as small yellowish-brown prisms (Found : C, 51.8; H, 4.6; N, 12.9; K, 11.9. $C_{14}H_{14}O_4N_3K$ requires C, 51.4; H, 4.3; N, 12.9; K, 12.0%). This was sparingly soluble in water : no definite product could be isolated after the aqueous solution had been boiled.

After an attempt to cause the potassio-derivative to react with an excess of ethanolic ethyl iodide at 100° overnight, 2 : 5-di(cyanoethoxycarbonylmethylene)pyrrolidine (68%) was isolated, having m. p. and mixed m. p. 204°.

(c) *Acid-hydrolysis experiments*. The pyrrolidine derivative (IX) was recovered in >90, 85, and 50% yield respectively, after being heated with concentrated hydrochloric or 20% sulphuric acid under reflux, with 90% sulphuric acid at 40° for 48 hr., and with 4 : 10 : 1 sulphuric acid–acetic acid–water under reflux for 3 hr. Tar was formed under the last two sets of conditions and was the only product from an attempted hydrolysis with boiling 75% sulphuric acid.

(d) *Oxidations*. (i) Treatment of the pyrrolidine (IX) in 80% sulphuric acid with chromic acid produced hydrogen cyanide, carbon dioxide, and tar.

(ii) Treatment of the pyrrolidine (305 mg.) in acetic acid (20 c.c.) containing sulphuric acid (0.05 c.c.) with 0.1N-potassium permanganate solution (4 c.c., 2 atoms of O) afforded, after subsequent addition of sulphur dioxide and water (20 c.c.), a white solid (255 mg., 84%) which did not depress the m. p. of the high-melting form of the starting material (m. p. 205°) (Found : C, 58.4; H, 5.5%).

(iii) The pyrrolidine (IX) (1 g.) in acetone (50 c.c.) was stirred and slowly treated with potassium permanganate (1.5 g.) dissolved in the minimum of 5 : 1 acetone–water. The filtrate from the manganese dioxide was acidified, filtered, and evaporated to dryness. The residue crystallised from ethanol, affording 5-cyanoethoxycarbonylmethylene-2-pyrrolidone (75 mg., 12%), identified by mixed m. p.

(iv) Ozonised oxygen (1–3%) was slowly bubbled for 15 hr. through a solution of the pyrrolidine (IX) (1 g.) in acetic acid (30 c.c.). Water (10 c.c.) was added, the solution evaporated on the steam-bath, and the oily residue dried under reduced pressure over potassium hydroxide. Trituration of the residue with ethyl acetate afforded crystals which, after being drained on porous tile, were identified as succinimide (22 mg., 6.5%) by mixed m. p.

(e) *Action of alkali*. (i) The pyrrolidine (IX) (2 g.) was heated under reflux for 2 hr. with a solution of potassium hydroxide (3 g.) in water (10 c.c.) and ethanol (25 c.c.). The ethanol was removed by distillation in steam, and the solution was acidified (sulphuric acid), boiled for several minutes, and then extracted continuously with ether for 16 hr. Evaporation of the extract and crystallisation of the residue from water afforded succinic acid (0.4 g., 36%).

(ii) To the pyrrolidine (IX) (1 g.), suspended in boiling ethanol (8 c.c.), potassium hydroxide

(0.9 g.) in water (2 c.c.) was added. After 8 min., the ethanol was distilled off in steam, the solution was cooled and acidified, and the precipitate (0.25 g., 26%) collected. From ethanol (charcoal), 2-cyanoethoxycarbonylmethylene-5-ethoxalyl (or 5-ethoxycarbonylhydroxymethylene)-pyrrolidine (X) formed long needles, m. p. 136° (Found : C, 55.8; H, 5.9; N, 10.2; OEt, 29.1. $C_{13}H_{16}O_5N_2$ requires C, 55.7; H, 5.75; N, 10.0; OEt, 32.1). It behaved on titration with sodium hydroxide against phenolphthalein as a dibasic acid, and gave a red colour with ferric chloride in aqueous ethanol.

(f) *Addition products from amines.* (i) From ammonia. The pyrrolidine (IX) (5 g.) was dissolved in dry dioxan (100 c.c.), and liquid ammonia (25 c.c.) was added cautiously. The product (3.1 g., 58%) was crystallised from hot acetic acid to give 2-amino-2-cyanoethoxycarbonylmethyl-5-cyanoethoxycarbonylmethylenepyrrolidine (XI), m. p. 232° (decomp.) (Found : C, 54.6; H, 6.1; N, 18.4; OEt, 30.1. $C_{14}H_{18}O_4N_4$ requires C, 54.9; H, 5.9; N, 18.3; OEt, 29.4%).

(ii) From methylamine. A solution of the pyrrolidine (1 g.) in dioxan (20 c.c.) was kept with methylamine (20 c.c.) overnight and then evaporated under reduced pressure. The dark product was taken up in chloroform, the solution treated with charcoal and evaporated, and the residue treated with light petroleum (b. p. 40—60°) and ethanol whereupon the *methylamine adduct* (20 mg.) crystallised; it had m. p. 241° (Found : C, 56.5; H, 6.5; N, 16.5. $C_{15}H_{20}O_4N_4$ requires C, 56.2; H, 6.3; N, 17.5%).

(iii) Alkaline hydrolysis of the ammonia product. A suspension of the compound (XI) (265 mg.) in 2N-sodium hydroxide (10 c.c.) was warmed on the steam-bath for 2 hr., during which ammonia was slowly evolved. Acidification of the solution and continuous extraction with ether for 24 hr. afforded succinic acid, which was crystallised from ethanol (yield, 70 mg., 68%; m. p. undepressed by an authentic specimen).

(iv) Action of benzoic anhydride on the ammonia product. The compound (XI) (255 mg.), mixed with benzoic anhydride (2 g.), was warmed on the steam-bath for 70 min., and the melt was then treated with 1 : 1 aqueous ammonia. From ethanol, the product afforded crystals (209 mg., 87%) of the high-melting form of 2 : 5-dicyanoethoxycarbonylmethylenepyrrolidine, identified by mixed m. p.

5-Cyanomethoxycarbonylmethylene-2-iminopyrrolidine.—(a) *Preparation.* Methyl cyanoacetate (1 c.c.) was added to a boiling solution of succinimidine (1 g.) in methanol (15 c.c.). After 1 hr., the mixture was cooled and the solid product (1.2 g., 60%) extractively crystallised from pyridine, to afford 5-cyanomethoxycarbonylmethylene-2-iminopyrrolidine (Found : C, 53.7; H, 5.2; N, 23.3. $C_8H_9O_2N_3$ requires C, 53.6; H, 5.1; N, 23.45%).

(b) *Hydrolysis to the pyrrolidone* (XV). The preceding imine (1 g.) was boiled in 2N-hydrochloric acid for 10 min. and the solution was cooled. The product (0.35 g., 35%) was crystallised from methanol and sublimed under reduced pressure. 5-Cyanomethoxycarbonylmethylene-2-pyrrolidone was obtained as needles, m. p. 167° (Found : C, 53.3; H, 4.3; N, 15.5. $C_8H_8O_3N_2$ requires C, 53.3; H, 4.5; N, 15.55%).

5-tert.-Butoxycarbonylcyanomethylene-2-iminopyrrolidine (XII).—*tert.-Butyl* cyanoacetate (Beech and Piggott, *J.*, 1955, 423) (10 g.) was added to a suspension of succinimidine (7.35 g.) in boiling *tert.-butyl* alcohol (350 c.c.). After 4 hr., the mixture was allowed to cool, and the product was collected, washed with methanol, and dried (yield, 13 g., 75%). The solid was extracted continuously with boiling pyridine and the solution treated with light petroleum (b. p. 80—100°). 5-*tert.-Butoxycarbonylcyanomethylene-2-iminopyrrolidine* was obtained as a microcrystalline powder, decomp. 238—240° (Found : C, 59.5; H, 7.1; N, 19.0. $C_{11}H_{15}O_2N_3$ requires C, 59.7; H, 6.8; N, 19.0%).

5-tert.-Butoxycarbonylcyanomethylene-2-pyrrolidone (XIII).—The preceding imine (1 g.) was boiled for 5 min. with a mixture of acetone (10 c.c.), water (9 c.c.), and concentrated hydrochloric acid (1 c.c.). When the mixture had cooled, the product (0.79 g., 78%) was filtered off. From aqueous ethanol, 5-*tert.-butoxycarbonylcyanomethylene-2-pyrrolidone* crystallised as needles, m. p. 174° (decomp.) (Found : C, 59.4; H, 6.5; N, 12.8. $C_{11}H_{14}O_3N_2$ requires C, 59.45; H, 6.35; N, 12.6%).

5-Carboxycyanomethylene-2-pyrrolidone (XIV).—(a) *Preparation.* The preceding pyrrolidone (XIII) (320 mg.) was boiled in 10% aqueous acetic acid (10 c.c.) until the evolution of *isobutene* slackened. When the solution was cooled, 5-*carboxycyanomethylene-2-pyrrolidone* (100 mg., 42%) crystallised; it was recrystallised extractively from ether and then had m. p. 210° (decomp.) (Found : C, 50.4; H, 3.8; N, 16.8. $C_7H_6O_3N_2$ requires C, 50.6; H, 3.6; N, 16.9%).

(b) *Methylation.* An excess of ethereal diazomethane was added to a suspension of 5-*carboxycyanomethylene-2-pyrrolidone* (20 mg.) in ether (10 c.c.). After 30 min., the solution was evaporated to dryness and the residue sublimed at 130°/20 mm. The sublimate (8 mg.,

31%) was identified as 5-cyanomethoxycarbonylmethylene-2-pyrrolidone (above) by mixed m. p.

(c) *Ethylation*. An excess of ethereal diazoethane (Arndt and Scholz, *Z. angew. Chem.*, 1933, 46, 47) was added to a solution of 5-carboxycyanomethylene-2-pyrrolidone (20 mg.) in ethanol (10 c.c.) and ether (10 c.c.). Evaporation of the solution and sublimation of the residue at 20 mm. afforded a white solid (23 mg., 86%), m. p. 65°, which did not depress the m. p. of material prepared as follows.

5-Cyanoethoxycarbonylmethylene-2-pyrrolidone (200 mg.), dissolved in ethanol (10 c.c.) and ether (10 c.c.), was treated with an excess of ethereal diazoethane. Subsequently, the solution was evaporated under reduced pressure and the residue sublimed at 20 mm. 5-Cyanoethoxycarbonylmethylene-1-ethyl-2-pyrrolidone (XVI) (?) (201 mg., 87%) had m. p. 70° (Found : N, 13.0. $C_{11}H_{14}O_3N_2$ requires N, 12.6%).

Action of Alkali on 5-tert.-Butoxycarbonylcyanomethylene-2-iminopyrrolidine.—The imine (1 g.) was boiled with 2*N*-sodium hydroxide (10 c.c.) until it had just dissolved. Cooling of the solution and acidification with concentrated hydrochloric acid, precipitated 5-tert.-butoxycarbonyl-5-cyano-4-oxopentanoic acid (XVII) (1 g., 92%), m. p. 130° (Found : C, 55.1; H, 6.4; N, 6.2. $C_{11}H_{15}O_5N$ requires C, 54.8; H, 6.3; N, 5.8%). It dissolved in aqueous sodium hydrogen carbonate with effervescence, gave an orange colour with ferric chloride in aqueous ethanol, behaved as a dibasic acid on titration with sodium hydroxide against phenolphthalein, evolved isobutene on prolonged boiling with water, and failed to form ketonic derivatives (cf. Eisner, Elvied, and Linstead, *J.*, 1951, 1501).

Degradation to Lævulic Acid.—When the acid (XVII) (1 g.) was boiled with concentrated hydrochloric acid, isobutene was evolved rapidly. After 3.5 hr., the solution was filtered from a little tar, cooled, and treated with an excess of a solution of 2 : 4-dinitrophenylhydrazine in concentrated hydrochloric acid. The dinitrophenylhydrazone of lævulic acid crystallised as orange-yellow needles (119 mg., 10%), m. p. and mixed m. p. 203°.

Action of Acetic Acid.—5-tert.-Butoxycarbonylcyanomethylene-2-iminopyrrolidine (0.7 g.) was boiled with 10% aqueous acetic acid (11 c.c.) until the evolution of isobutene became very slow. Tar was filtered off, and the solution was cooled.

(i) In two out of five runs, a white solid then separated (196 mg., 19%) which, after extractive crystallisation from ether, had m. p. 210° (decomp.) alone and when mixed with 5-carboxycyanomethylene-2-pyrrolidone (above).

(ii) Continuous extraction of the filtrate (charcoal) with ether and subsequent evaporation of the extract yielded crystals (55%), which were recrystallised from ethanol, and then sublimed at 150°/25 mm. The neutral, white, microcrystalline 5-cyanomethylene-2-pyrrolidone (XVIII) had m. p. 170° (Found : C, 58.8; H, 5.2; N, 23.2. $C_6H_6ON_2$ requires C, 59.0; H, 4.95; N, 22.9%).

Decarboxylation of 5-Carboxycyanomethylene-2-pyrrolidone.—The cyano-acid (24.5 mg.) was boiled for 5 min. in pyridine containing copper acetate, the solution was evaporated under reduced pressure, and the residue sublimed at 20 mm. The neutral sublimate (10 mg.) was identified as 5-cyanomethylene-2-pyrrolidone (above) by mixed m. p.

At 210°/26 mm. the cyano-acid (19.8 mg.) afforded a slightly discoloured sublimate (9.8 mg.), soluble with effervescence in aqueous sodium hydrogen carbonate and having m. p. 200° undepressed by the starting material.

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