## 876. *The Synthesis and Rearrangement of* 3-*Vinyl*-2-*pyrrolidone.*

By W. A. W. Cummings and A. C. Davis.

3-2′-Hydroxyethyl-2-pyrrolidone (IV, R = H) has been synthesised in two stages via α-2-aminoethyl-γ-butyrolactone (not isolated) from ethyl γ-butyrolactone-α-carboxylate. Pyrolysis of the acetate of the alcohol (IV, R = H) yielded 3-vinyl-2-pyrrolidone and *cis*-3-ethylidene-2-pyrrolidone. The vinyl compound was rearranged by bases to the *trans*-isomer of the ethylidene-pyrrolidone, also obtained by other dehydrations of the alcohol. Treatment of 3-2′-chloroethyl-2-pyrrolidone with potassium t-butoxide gave 2,3,4,5-tetrahydro-3*a*-*H*-furo[2,3-*b*]pyrrole (XV). 3-2′-Hydroxyethyl-2-perhydroazepinone was also prepared. Unsuccessful attempts to obtain α-1-hydroxyethyl-lactams are reported.

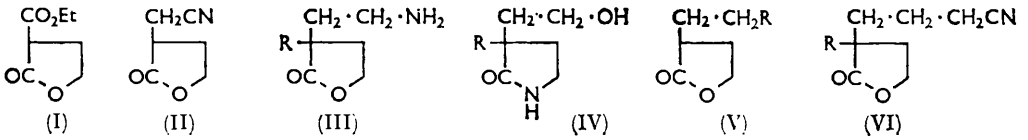
Hitherto only *N*-vinyl-lactams have been recorded, and these are prepared by direct vinylation [1] or via the *N*-β-hydroxyethyl or -chloroethyl derivatives.[2] For the synthesis

[1] Copenhaver and Bigelow, "Acetylene and Carbon Monoxide Chemistry," Reinhold Publishing Co., New York, 1947, p. 163; Labine, *Chem. Eng.*, 1960, **67**, 112.

[2] Puetzer, Katz, and Horwitz, *J. Amer. Chem. Soc.*, 1952, **74**, 4959; Shostakovskii and Sidel'kovskaya, *Bull. Acad. Sci. U.S.S.R.*, 1958, 109; *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1959, 892.

of a *C*-vinyl-lactam, 3-vinyl-2-pyrrolidone (X, R = H), the intermediate 3-2′-hydroxyethyl-2-pyrrolidone (IV, R = H) was required. A phenyl derivative (IV, R = Ph) was obtained by Walton and Green[3] by neutralisation of the hydrochloride of α-2-aminoethyl-α-phenyl-γ-butyrolactone (III, R = Ph). The hydroxyethyl-lactams (IV, R = H) and (VIII) have now been prepared by analogous rearrangements, the aminoalkyl-lactones not normally being isolated. Dehydration of (IV, R = H) by various methods yielded either 3-vinyl-2-pyrrolidone or one of its isomers.

α-Cyanomethyl-γ-butyrolactone (II) was prepared by alkaline condensation of chloroacetonitrile and ethyl γ-butyrolactone-α-carboxylate (I), the carbethoxyl group being simultaneously removed by ethanolysis. The ease of removal of an α-acyl group from fully α-substituted derivatives of butyrolactone has been previously observed by Stepanov.[4] Hydrogenation of the nitrile (II) gave up to 90% yield of 3-2′-hydroxyethyl-2-pyrrolidone (IV, R = H), in which the isomeric lactone (III, R = H) was not detected.




(I) (II) (III) (IV) (V) (VI)

In a less convenient synthesis of the hydroxyethyl-pyrrolidone, ethyl γ-butyrolactone-α-carboxylate, or α-acetyl-γ-butyrolactone, was first alkylated with acrylonitrile in the presence of sodium ethoxide to α-2-cyanoethyl-γ-butyrolactone (V, R = CN). In these alkylations, as in the preparation of the nitrile (II), the carbethoxyl group or acetyl group was eliminated simultaneously. Attempts to obtain the nitrile (V, R = CN) by cyanoethylation of γ-butyrolactone gave only resinous products and α-2′-tetrahydrofurfurylidene-γ-butyrolactone. The cyanoethyl-lactone was hydrated with 85% sulphuric acid to α-2-carboxamidoethyl-γ-butyrolactone (V, R = $CONH_2$), but Hofmann degradation of the latter failed to yield the pure lactam (IV, R = H). After hydrolysis of the nitrile to α-2-carboxyethyl-γ-butyrolactone (V, R = $CO_2H$), Schmidt degradation gave 3-2′-hydroxethyl-2-pyrrolidone (IV, R = H) in 65% yield.

The lactone (VI, R = H), unlike the lower homologues (II) and (V, R = CN), could not be obtained directly from ethyl γ-butyrolactone-α-carboxylate, since alkaline condensation with γ-bromobutyronitrile produced only the ester (VI, R = $CO_2Et$). The latter was hydrolysed with aqueous calcium carbonate, and, after acidification, decarboxylation occurred during working up, giving α-3-cyanopropyl-γ-butyrolactone (VI, R = H). Hydrogenation of the latter gave 3-2′-hydroxyethyl-2-perhydroazepinone (VIII).

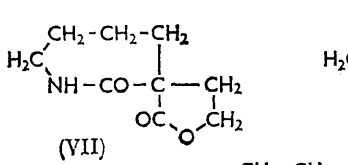
In an alternative route, the ester (VI, R = $CO_2Et$) was hydrogenated to produce the spiro-lactone-lactam (VII). The yield was low, apparently owing to further reduction of the lactam ring. The spiro-lactam was hydrolysed and decarboxylated with sulphuric acid to give poor yields of the lactam (VIII).

Treatment of 3-2′-hydroxyethyl-2-pyrrolidone with excess of acetic anhydride gave the *ON*-diacetyl derivative (IX, R = Ac), but the *O*-monoacetyl derivative (IX, R = H) was obtained on using one molar proportion of acetic anhydride in pyridine. The acetate was pyrolysed at 580°, giving 3-vinyl-2-pyrrolidone (X, R = H) together with isomer " A," m. p. 98—99·5°, of 3-ethylidene-2-pyrrolidone (XI, R = H), and other, unidentified, side-products. The positions of the double bond in the two products were established by ozonolysis.

3-Vinyl-2-pyrrolidone was unaffected by benzoyl peroxide, αα′-azobisisobutyronitrile, aqueous potassium persulphate/bisulphite mixture, or boron trifluoride–diethyl ether complex. The double bond therefore seems insufficiently activated for polymerisation.

[3] Walton and Green, *J.*, 1945, 315.
[4] Stepanov, *J. Gen. Chem.* (*U.S.S.R.*), 1955, **25**, 2369.

Treatment with butyl-lithium or lithium aluminium hydride in catalytic quantities in inert solvents converted the vinyl-lactam into high-melting forms of 3-ethylidene-2-pyrrolidone (XI, R = H). Upon sublimation these yielded isomer " B " (m. p. 176—177·5°) of the ethylidene-lactam. Isomers " A " and " B," which both yielded acetaldehyde upon ozonolysis, had slightly different infrared and ultraviolet spectra. The large difference in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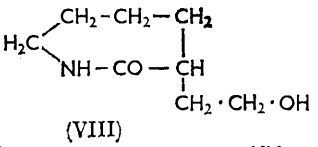
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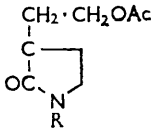
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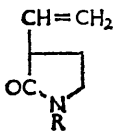
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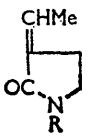

(XI)

melting point suggests that they are probably the *cis* and *trans* forms, respectively, of compound (XI, R = H). Treatment of the vinyl-lactam (X, R = H) with aqueous potassium carbonate at 100° also gave the supposed *trans*-isomer of the ethylidene-lactam. Except that acid-catalysed rearrangement has not been observed, the rearrangement is thus similar to the vinylacetic ⟶ crotonic acid system, in which chemically catalysed rearrangement yields *trans*-crotonic acid, but thermal rearrangement yields the *cis*-form also. The melting points of the isomeric vinyl- and *cis*- and *trans*-ethylidene-lactams (61, 98—99·5, 176—177·5°) are in the same relation as those of the amides of vinylacetic and *cis*- and *trans*-crotonic acid (74, 102, 159·5—160°). 3-Ethylidene-pyrrolidone could not be rearranged to the vinyl derivative.

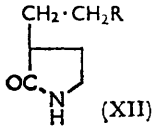
1-Acetyl-3-vinyl-2-pyrrolidone (X, R = Ac), obtained by acetylation of the vinyl-lactam with acetic anhydride, was unchanged by boron trifluoride treatment, but was rearranged by butyl-lithium to 1-acetyl-3-ethylidene-2-pyrrolidone (XI, R = Ac), also prepared by acetylation.

The ethylidene-lactam (XI, R = H) (and in one case the vinyl-lactam also) was obtained in some other dehydrations of 3-2′-hydroxyethyl-2-pyrrolidone. The chloride (XII, R = Cl), obtained by reaction of lactam (IV, R = H) with thionyl chloride, when treated with methanolic potassium hydroxide gave impure 3-2′-methoxyethyl-2-pyrrolidone (XII, R = OMe), but the corresponding iodide gave a low yield of the ethylidene compound. The chloride was treated with dimethylamine to give the tertiary base (XII, R = $NMe_2$) which when degraded by Cope's amine-oxide route [5] gave 64% of the ethylidene-lactam and approximately 5% of 3-vinyl-2-pyrrolidone. Reaction of the chloride with potassium t-butoxide gave 2,3,4,5-tetrahydro-3*a*-*H*-furo[2,3,*b*]pyrrole (XIII), a low-melting crystalline base. The reaction is analogous to the preparation of 1-oxa-4,7-diazabicyclo[3,3,0]oct-7-ene (XV) by McKay and Kreling,[6] and of the hexahydrodifuropyrazine (XVI) by Goering,[7] in each case by dehydrochlorination of a cyclic amide having 2-chloroethyl substituent(s) α to the carbonyl group. The tetrahydro-furopyrrole (XIII) showed the infrared absorption near 1680 $cm.^{-1}$ established by Goering [7] as characteristic of the α-alkylimino-ether group. It was hydrated by water to 3-2′-hydroxyethyl-2-pyrrolidone (XII, R = OH) and was hydrogenated to a liquid base, apparently 3-2′-hydroxyethylpyrrolidine (XIV). These reactions are analogous to those reported [7] for compound (XVI) with the same reagents.

Hofmann degradation of the quaternary base (XII, R = $NMe_3OH$), obtained via the

[5] Cope, Foster, and Fowle, *J. Amer. Chem. Soc.*, 1949, **71**, 3929; Cope and Ciganek, *Org. Synth.*, 1959, **39**, 40.
[6] McKay and Kreling, *Canad. J. Chem.*, 1959, **37**, 427.
[7] Goering, *J. Amer. Chem. Soc.*, 1951, **73**, 4737.

iodide, gave a mixture containing 3-ethylidene-2-pyrrolidone, 3-2′-dimethylaminoethyl-2-pyrrolidone, and other products apparently formed by *N*-methylation of the ring. Chugaev dehydration gave a crystalline xanthate, apparently the required ester (XVII), but pyrolysis of this gave unidentified sulphur-containing products. Direct dehydration of the alcohol (XII, R = OH) with toluene-*p*-sulphonic acid yielded 3-ethylidene-2-pyrrolidone;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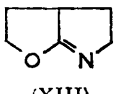
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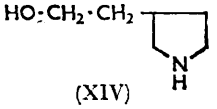
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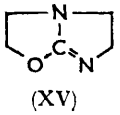
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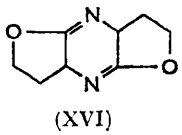
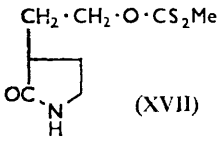

(XVI)

vapour-phase dehydration on alumina gave an unsaturated lactam isomeric with vinylpyrrolidone. The unsaturation in the latter could not be detected spectroscopically. Since a $\Delta^3$-pyrrolinone (XVIII) has been found by Plieninger and Decker [8] to show an absorption maximum at 2150 Å, and structure (XI, R = H) is eliminated by the present work, the alumina-dehydration product may be the non-conjugated 3-ethyl-4-pyrrolin-2-one (XIX). The preparation of 3-vinyl-2-perhydroazepinone by dehydration of 3-2′-hydroxyethyl-2-perhydroazepinone was not attempted, since 3-vinylpyrrolidone had yielded no polymers.

Unsuccessful attempts were made to produce *C*-(1-hydroxyethyl)-lactams by the reductive cyclisation of β-cyanoesters. In the case of ethyl α-cyanomethyl-acetoacetate (XX) (synthesised from acetoacetic ester and bromoacetonitrile), ring closure occurred preferentially to the keto-group. The product was a mixture of ethyl 2-methylpyrrole-3-carboxylate (XXI), previously obtained by Benary [9] from acetoacetic ester, α,β-dichlorodiethyl ether, and ammonia, and a base believed to be one of the corresponding pyrrolines. Hydrogenation of ethyl α-3-cyanopropyl-acetoacetate (XXIII) gave mainly resin, but some evidence was obtained of cyclisation partly to the keto-group and partly to the ester group.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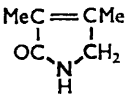
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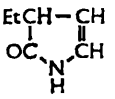
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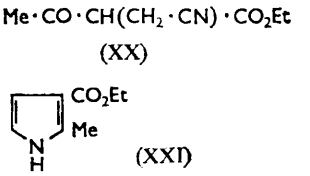
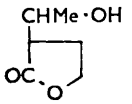

(XX)

(XXI)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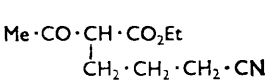
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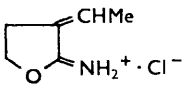
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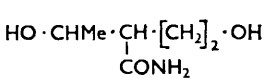
(XXV)

α-1-Hydroxyethyl-γ-butyrolactone (XXII) was obtained by hydrogenation of α-acetyl-γ-butyrolactone. Treatment of this lactone with ammonia at room temperature gave 1,4-dihydroxypentane-3-carboxamide (XXV), but attempts to dehydrate the latter to a lactam were unsuccessful. Heating the amide under atmospheric pressure gave ammonia and lactone (XXII). Treatment of the amide with thionyl chloride in benzene caused cyclisation probably to 2-imino-3-ethylidenetetrahydrofuran hydrochloride (XXIV). The structure of the latter followed from the easy elimination of ammonia under acidic or basic conditions, and from the infrared spectrum. Reaction of α-1-hydroxyethyl-γ-butyrolactone with ammonia under pressure at 180° led to only partial conversion to the amide

[8] Plieninger and Decker, *Annalen*, 1956, **598**, 198.
[9] Benary, *Ber.*, 1911, **44**, 493.

(XXV), but at 260° the lactone was decomposed, presumably by a retro-aldol change accompanying ammonolysis, to 2-pyrrolidone.

It was proposed to synthesise 3-acetyl-2-pyrrolidone by alkaline ring-closure of the unknown *N*-2-chloroethyl-acetoacetamide, $Me{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}NH[CH_2]_2Cl$. This was abandoned when an attempt to obtain *N*-2-hydroxyethyl-acetoacetamide, from acetoacetic ester and ethanolamine at 160°, gave instead an unidentified substance of empirical formula $C_6H_9NO_2$. This was not the required acetoacetamide, but was a feebly basic, non-ketonic substance which was not studied further.

## Experimental

Ultraviolet spectra were determined on $10^{-4}$M solutions in water.

*Ethyl γ-Butyrolactone-α-carboxylate* (I).—This was prepared by a modification of the method of Traube and Lehmann,[10] and had b. p. 102°/0·1 mm., $n_D^{20}$ 1·4468.

*α-Cyanomethyl-γ-butyrolactone* (II).—Sodium (43·5 g.) was dissolved in ethanol (650 c.c.) dried by calcium oxide, and the solution was added during 30 min. to a boiling stirred solution of ethyl γ-butyrolactone-α-carboxylate (255 g.) and chloroacetonitrile (121·7 g.) in dry ethanol (600 c.c.), and the mixture boiled under reflux for a further 1 hr. Acetic acid (31 c.c.) was added and the solvent was evaporated under reduced pressure. The product was treated with chloroform, washed (water, then $NaHCO_3$ solution) and dried ($Na_2SO_4$). After evaporation of the solvent the crude product was distilled at 130—140° (air-bath)/0·05—0·1 mm., to give a colourless oil (168 g.). This was diluted with ethyl acetate (125 c.c.) and after cooling to −15° yielded the crystalline *lactone* (112·4 g., 56%), m. p. 46—49°, which after recrystallisation (ethyl acetate) had m. p. 45·5—47·5° (Found: C, 57·5; H, 5·45; N, 11·3%. $C_6H_7NO_2$ requires C, 57·6; H, 5·6; N, 11·2%).

*3-2′-Hydroxyethyl-2-pyrrolidone* (IV, R = H).—α-Cyanomethyl-γ-butyrolactone (100·1 g.) in methanol (800 c.c.) was hydrogenated (Raney Co) at 1600 lb./in.$^2$ (initially) for 4 hr. at 120°. The solution was filtered and concentrated under reduced pressure and the product was distilled at 130—135° (air-bath)/0·04 mm. The *lactam* (88·4 g., 85%) formed an intensely hygroscopic colourless crystalline solid, m. p. 40—41° (Found: C, 55·6; H, 8·9; N, 10·7%. $C_6H_{11}O_2N$ requires C, 55·8; H, 8·6; N, 10·85%). Treatment with benzoyl chloride (1 equiv.) in pyridine at 40—60° converted the compound into *3-2′-benzoxyethyl-2-pyrrolidone*, m. p. 108—109·5° (from ethyl acetate) (Found: C, 67·2; H, 6·6; N, 5·8%. $C_{13}H_{15}NO_3$ requires C, 66·9; H, 6·5; N, 6·0%). The position of the benzoyl group was established by the absence of OH absorption between 3300 and 3200 cm.$^{-1}$.

*α-2-Cyanoethyl-γ-butyrolactone* (V, R = CN).—(*a*) Ethyl-γ-butyrolactone-α-carboxylate (61·2 g.) was added to a sodium ethoxide solution prepared from sodium (4·0 g.) and dried (calcium oxide) ethanol (400 c.c.). The suspension of the sodio-lactone was treated with acrylonitrile (21·2 g.) in dry ethanol (20 c.c.), with cooling to keep the temperature below 40°. The resulting solution was kept for 1 hr. at 60° and then boiled for 30 min. under reflux. Acetic acid (12 c.c.) was added and the solvent was evaporated under reduced pressure. Water (100 c.c.) was added and the crude product was obtained by chloroform extraction as an oil (55 g.). This was twice distilled from an air-bath to give the pure *nitrile* (48·8 g., 90%) as a colourless oil, b. p. 140°/0·04 mm., $n_D^{24}$ 1·4654 (Found: C, 60·1; H, 6·8; N, 10·4%. $C_7H_9NO_2$ requires C, 60·4; H, 6·5; N, 10·1%).

(*b*) α-Acetyl-γ-butyrolactone (101·5 g.) was added with ice-cooling to a sodium ethoxide solution prepared from sodium (4 g.) and dry ethanol (600 c.c.). Acrylonitrile (42·0 g.) was added and the reaction mixture was kept for 30 min. at 30—40° (exothermic reaction) and for 1 hr. at 60°. Acetic acid (12 c.c.) was added and the crude product isolated as in (*a*), as a reddish-brown oil (110 g.). Fractional distillation of the product gave 79·4 g. (73%) of almost pure nitrile, b. p. 135—145° (air-bath)/0·05—0·3 mm., $n_D^{22}$ 1·4650. This material was sufficiently pure for hydration to the amide. The cyanoethyl-butyrolactone prepared by this method in some experiments could not be distilled without partial decomposition and was less pure.

*α-2-Carbamylethyl-γ-butyrolactone* (V, R = $CONH_2$).—α-2-Cyanoethyl-γ-butyrolactone (46 g.) was stirred in a water-bath at 60—70° while sulphuric acid (85% w/w) (24·6 c.c.) was added gradually during 10 min., and the solution was kept for 3 hr. at 70°. After being cooled to

[10] Traube and Lehmann, *Ber.*, 1901, **34**, 1976.

room temperature the solution was neutralised by addition of 10% sodium hydroxide (301 c.c.) with stirring and cooling, and was then evaporated to dryness at 100° under reduced pressure. The product (53·6 g.), isolated by extraction with hot absolute alcohol, was recrystallised from ethyl acetate to give α-2-*carbamylethyl-γ-butyrolactone* (29·9 g., 57·5%), m. p. 78·5—80·5°. An analytical sample (from benzene) had m. p. 81—82° (Found: C, 53·6; H, 7·2; N, 9·1%. $C_7H_{11}NO_3$ requires C, 53·5; H, 7·1; N, 8·9%).

Hofmann degradation of the amide with bromine and sodium methoxide or hydroxide, or with sodium hypochlorite, caused loss of ammonia. The reaction products were partly resinous and the distillable fractions yielded no pure product.

α-2-*Carboxyethyl-γ-butyrolactone* (V, R = $CO_2H$). α-Cyanoethyl-γ-butyrolactone (20·2 g.) and 20% aq. sodium hydroxide (80·0 c.c.) were boiled together under reflux in a slow stream of nitrogen for 6 hours. After cooling, the solution was washed with ether to remove unsaponified material, and treated with sufficient sulphuric acid (approx. 30% solution) to neutralise the inorganic base. The solution was evaporated to dryness under reduced pressure at 100° and the product was isolated by extraction with ethyl acetate. Upon distillation, the *carboxylic acid* (22·5 g., 98%) was obtained as a colourless hygroscopic crystalline solid, b. p. 145° (air-bath)/0·05 mm., m. p. 36—37·5° (Found: C, 52·6; H, 6·9%. $C_7H_{10}O_4$ requires C, 53·15; H, 6·4%).

*Schmidt Reaction of α-2-Carboxyethyl-γ-butyrolactone.*—The lactone (15·8 g., 0·1 mole) was dissolved in conc. sulphuric acid (32·0 c.c.) at 40°. A benzene solution of hydrazoic acid (0·14 mole in 106 c.c.) was added gradually with stirring at 40—45° during 1 hr. After a further 1 hr. the solution was concentrated under reduced pressure at 50° to remove unchanged hydrazoic acid and most of the benzene. The residue was neutralised by adding, with stirring and cooling, enough 20% aq. sodium hydroxide (230 c.c.) to neutralise the sulphuric acid. Aniline was removed by steam distillation and the residue was evaporated to dryness at 100° under reduced pressure. The crude product, obtained by ethanol–acetone extraction, was a viscous oil (12·2 g.), giving a crystalline solid (8·63 g., 67% yield) upon vacuum distillation at 110—125° (air-bath)/0·5 mm. Upon fractional redistillation this yielded almost pure 3-2′-hydroxyethyl-2-pyrrolidone (5·0 g.), b. p. 115° (air-bath)/0·05 mm., m. p. 36—39°, slightly coloured but showing no m. p. depression with pure material obtained by hydrogenation of α-cyanomethyl-γ-butyrolactone.

*Ethyl α-3-Cyanopropyl-γ-butyrolactone-α-carboxylate* (VI, R = $CO_2Et$).—Ethyl γ-butyrolactone-α-carboxylate (231 g.), γ-bromobutyronitrile (270 g.) and dry ethanol (750 c.c.) were boiled and stirred together under reflux while a solution prepared from sodium (33·7 g.) and dry ethanol (750 c.c.), was added slowly. The reaction mixture was boiled under reflux for a further 1 hr., acetic acid (26·5 c.c.) was added, and the solvent was evaporated under reduced pressure at 60°. Water was added to the residue, and the crude product was isolated as for α-cyanomethyl-γ-butyrolactone. It was twice distilled in vacuum, the main product forming a pale yellow oil, b. p. 155—165° (air-bath)/0·05 mm., $n_D^{18}$ 1·4662 (224·6 g., 68%) which crystallised upon storage, and was sufficiently pure for further reaction. After two recrystallisations (from ethyl acetate–cyclohexane at −15°) the *lactone* was obtained in colourless crystals, m. p. 41—41·5° (Found: C, 58·7; H, 7·0; N, 5·6%. $C_{11}H_{16}NO_4$ requires C, 58·4; H, 7·1; N, 6·2%). The same product was obtained, in good yield, when the alkaline reaction mixture was boiled under reflux for 18 hours before acidification and working up.

α-3-*Cyanopropyl-γ-butyrolactone* (VI, R = H).—Ethyl α-3-cyanopropyl-γ-butyrolactone-α-carboxylate (62 g.), calcium carbonate (27·5 g.) and water (500 c.c.) were heated together under reflux for 36 hr. The solution was filtered from unchanged $CaCO_3$ (15·2 g.), concentrated to a vol. of 150 c.c. and acidified to pH 4 with 25% sulphuric acid (29 c.c.). Calcium sulphate was removed by filtration and the product was obtained by continuous extraction with ethyl acetate, followed by concentration of the extract under reduced pressure below 60°. The infra-red spectrum of the crude product (32·1 g.) indicated that no carboxyl groups were present. After two distillations the pure *cyanopropyl-butyrolactone* (28·8 g., 68%) was obtained as a colourless oil, b. p. 138°/0·15 mm., $n_D^{21·5}$ 1·4661 (Found: C, 62·5; H, 7·1; N, 9·1%. $C_8H_{11}NO_2$ requires C, 62·7; H, 7·2; N, 9·1%).

The starting ester (VIII, R = $CO_2Et$) was recovered unchanged after being kept overnight in solution in conc. $H_2SO_4$ and precipitated with water. Attempted hydrolysis with aqueous sodium hydroxide (2 mols.) caused rapid formation of ammonia.

3-2′-*Hydroxyethyl-2-perhydroazepinone* (VIII).—α-3-Cyanopropyl-γ-butyrolactone (24 g.) was hydrogenated over Raney Co in ethanol (300 c.c.) for 2 hr. at 100°, with an initial hydrogen pressure of 100 atm. After filtration, the solution was concentrated under reduced pressure,

and the partly crystalline product (25·8 g.) was distilled at 160° (air-bath)/0·4 mm. The distillate (17·7 g.) was crystallised from twice its bulk of acetone at −15° to yield the lactam (6·2 g., 22%) in colourless crystals, m. p. 90—92°. Further recrystallisation from acetone gave the pure *azepinone*, m. p. 89·5—91·5° (Found: C, 61·1; H, 9·55; N, 9·15%. $C_8H_{15}NO_2$ requires C, 61·1; H, 9·6; N, 8·9%). The compound was neutral in aqueous solution but the mother-liquors were strongly basic.

*Perhydroazepin-2-one-3-spiro-3′-tetrahydrofuran-2′-one* (VII).—Ethyl α-3-cyanopropyl-γ-butyrolactone-α-carboxylate (51·5 g.) was hydrogenated (Raney Co) in methanol (800 c.c.) for 4 hr. at 120° with an initial hydrogen pressure of 120 atm. After filtration from catalyst, the solution was concentrated to low bulk, and the product collected by filtration and washed with methanol, yielding a white crystalline solid (24·9 g., 59·5%), m. p. 180·5—181·5°. After recrystallisation from ethanol the *spiro-tetrahydrofuranone* had m. p. 181—183° (Found: C, 58·9; H, 7·4; N, 8·1%. $C_9H_{13}NO_3$ requires C, 59·0; H, 7·15; N, 7·65%. The spiro-lactone-lactam was neutral in aqueous solution, but the hydrogenation by-product was strongly basic. The latter was separated by distillation into a resin and a liquid base (1·0 g.), b. p. 140°/0·7 mm., $n_D^{23}$ 1·4669 (Found: C, 64·5; H, 8·9; N, 8·8%. $C_9H_{15}NO_2$ requires C, 63·9; H, 8·9; N, 8·3%). This may be a bicyclic secondary amine resulting from reduction of the lactam ring in compound (VII).

*Hydrolysis and Decarboxylation of Perhydroazepin-2-one-3-spiro-3′-tetrahydrofuran-2-one.*—The spiro-tetrahydrofuranone (9·15 g.) was dissolved in 70% w/w $H_2SO_4$ (b. p. 150°) (40·0 c.c.) and the solution was boiled under reflux for 3 hr. Carbon dioxide was evolved during the first 45 min. Sufficient 20% aqueous sodium hydroxide (161·3 c.c.) was added to bring the solution to pH 9. Water was removed by distillation under reduced pressure and the crude product obtained by ethanol extraction from the residue as a viscous yellow oil (10·4 g.). Distillation from an air-bath at 160° under 0·06 mm. pressure gave a colourless liquid (2·26 g.) and a glassy hygroscopic residue (5·7 g.). The liquid was redistilled and the fraction of b. p. 120—130° (air-bath)/0·04 mm. was collected as an oil (1·34 g.) which crystallised to a solid, m. p. 74—84°. Recrystallisation from acetone gave 3-2′-hydroxyethyl-2-perhydroazepinone, m. p. 89—91°, undepressed by admixture with the sample prepared by hydrogenation of α-3-cyanopropyl-γ-butyrolactone (above). When the neutralisation of the sulphuric acid decarboxylation mixture was carried only to pH 8, working up as above but without distillation produced in low yield *di-*[*4-(tetrahydrofuran-2′-on-3′-yl)-butylammonium*]*sulphate*, m. p. 222—224° (Found: C, 46·3; H, 7·55; N, 6·9; S, 7·9%. $C_{16}H_{32}N_2O_8S$ requires C, 46·6; H, 7·8; N, 6·8; S, 7·8%).

*Acetylation of 3-2′-Hydroxyethyl-2-pyrrolidone.*—The pyrrolidone (43 g.), acetic anhydride (34 g.) and pyridine (80 c.c.) were heated together on the steam-bath for 2 hr. The solvent was removed under reduced pressure and the residue was dissolved in water. The crude product, obtained by chloroform extraction, was distilled once from an air-bath to give the almost pure ester (48 g.) as a fraction of b. p. 125—134°/0·04 mm., solidifying to a crystalline mass of m. p. 55—57°. An analytical sample (from cyclohexane) of the *3-2′-acetoxyethyl-2-pyrrolidone* was obtained with m. p. 59—59·5° (Found: C, 56·6; H, 8·05; N, 8·25%. $C_8H_{13}NO_3$ requires C, 56·1; H, 7·65; N, 8·2%).

Excess of acetic anhydride at the b. p. for 2 hr. gave *1-acetyl-3-2′-acetoxyethyl-2-pyrrolidone*, an oil, b. p. 100—110°/0·03 mm., $n_D^{18}$ 1·4827 (Found: C, 56·4; H, 7·1; N, 6·5%. $C_{10}H_{15}NO_4$ requires C, 56·3; H, 7·1; N, 6·6%).

*Pyrolysis of 3-2′-Acetoxyethyl-2-pyrrolidone* (IX, R = H).—Pyrolyses were carried out in Pyrex apparatus under 200 mm. nitrogen pressure. The ester, introduced into the pyrolysis tube at 1 g./min., passed through a pre-heating zone at 250° and then a reaction zone (3 cm. × 38 cm.) at 550—580°. Little reaction occurred below 540°. In a typical experiment, the acetoxyethyl-pyrrolidone (32 g.) yielded 30·6 g. of pyrolysate, which, after distillation of acetic acid, was separated into a partially crystalline " olefinic fraction " (14·45 g.), b. p. 80—100°/0·02 mm., and a fraction of b. p. 100—130°/0·02 mm. (6·7 g.). The latter after one recrystallisation gave impure 3-2′-acetoxyethyl-2-pyrrolidone with m. p. 52—55°.

The " olefinic fractions " from several pyrolyses (107·5 g.) were combined and recrystallised twice from ethyl acetate–cyclohexane (1 : 10), yielding the crude vinyl compound (40·5 g.), m. p. 51—51·5°. This was distilled, and the fraction of b. p. 88—94°/0·08 mm. recrystallised (light petroleum, b. p. 60—80°) to give *3-vinyl-2-pyrrolidone* (20·7 g., 17% yield based on non-recovered acetate), m. p. 60—61·5° (Found: C, 64·6; H, 8·2; N, 12·5%. $C_6H_9NO$ requires C, 64·8; H, 8·2; N, 12·6%), $\lambda_{max.}$ 196 mμ (ε 5000) [cf. 2-pyrrolidone, $\lambda_{max.}$ 192 mμ (ε 6000) and

3-ethyl-2-pyrrolidone, $\lambda_{max.}$ 192 mμ (ε 6800)], $\nu_{max.}$ 3180 (>NH), 1669 (C=O) and a shoulder (C=C) at 1640 cm.$^{-1}$. Weaker bands (assigned to CH in the vinyl group) occurred at 986 and 910 cm.$^{-1}$. The sample was quantitatively hydrogenated in methanol over palladium–charcoal (Found: hydrogen uptake 200·4 c.c./g. at S.T.P.; one double bond in $C_6H_9ON$ requires 202 c.c./g.). Ozonolysis of the vinyl compound in ethyl acetate at −30°, followed by hydrogenation, gave formaldehyde (isolated as the 2,4-dinitrophenylhydrazone) in poor yield. Acetylation in acetic anhydride at the b. p. gave the 1-*acetyl derivative*, b. p. 54°/0·1 mm., $n_D^{20}$ 1·5070 (Found: C, 62·4; H, 7·4; N, 9·0%. $C_8H_{11}NO_2$ requires C, 62·7; H, 7·25; N, 9·15%).

An impure crystalline sample of 3-vinyl-2-pyrrolidone (5·0 g.), m. p. 48—53°, obtained by the acetate pyrolysis, was chromatographed in benzene on " neutral alumina " (Hopkin and Williams, acid-washed grade). Elution with ethyl acetate gave several crystalline fractions with m. p. in the range 90—95° (total 0·81 g.), which were combined and after two crystallisations from light petroleum (b. p. 60—80°) yielded cis-3-*ethylidene*-2-*pyrrolidone* (0·2 g.), m. p. 98—99·5° (Found: C, 65·1; H, 8·0; N, 12·8%. $C_6H_9NO$ requires C, 64·8; H, 8·1; N, 12·6%), $\lambda_{max.}$ 227 mμ (ε 11,200), $\nu_{max.}$ 3190 (>NH), 1682 (>C=O) and 1658 (C=C) cm.$^{-1}$; there was a band of medium intensity at 776 cm.$^{-1}$, not found in the spectrum of the *trans*-isomer (see below). Silica-gel columns were also used successfully to extract the *cis*-ethylidene-pyrrolidone from crude vinyl-lactam, but from normal-grade alumina only the *trans*-isomer could be eluted. The compound was ozonised in ethyl acetate–acetic acid at −35° and the product was hydrogenated to give acetaldehyde, identified as the 2,4-dinitrophenylhydrazone. Hydrogenation of *cis*-3-ethylidene-2-pyrrolidone over palladium–charcoal yielded 3-ethyl-2-pyrrolidone, m. p. 42—45°, undepressed by admixture with 3-ethyl-2-pyrrolidone prepared as described below.

3-2′-*Chloroethyl*-2-*pyrrolidone* (XII, R = Cl).—Thionyl chloride (28 g.) was added slowly to a mixture of 3-2′-hydroxyethyl-2-pyrrolidone (30·4 g.) and benzene (28 c.c.) with stirring and sufficient cooling to keep the reaction temperature at 35—40°. The reaction mixture was kept for a further 3 hr. at 40° and was kept overnight at room temperature. The solvent was distilled under reduced pressure at 50° and the product was dissolved in chloroform and washed ($Na_2CO_3$ solution). Charcoal treatment, drying ($Na_2SO_4$) and concentration of the extract left a grey solid which was recrystallised from benzene (60 c.c.) and cyclohexane (600 c.c.) to give the product (31·5 g., 91%) with m. p. 101·5—102·5°, which was pure enough for use. Sublimation, followed by recrystallisation from cyclohexane, gave the pure *chloroethyl-pyrrolidone* in needles, m. p. 102—102·5° (Found: C, 48·7; H, 6·9; N, 9·7; Cl, 24·1%. $C_6H_{10}ClNO$ requires C, 48·8; H, 6·8; N, 9·5; Cl, 24·0%). The compound was hydrolysed rapidly to chloride ion by water at 100°.

3-2′-*Dimethylaminoethyl*-2-*pyrrolidone* (XII, R = $NMe_2$).—3-2′-Chloroethyl-2-pyrrolidone (40 g.) and 26% aqueous dimethylamine (150 g.) were heated together in a closed 250-c.c. bottle for 7 hr. at 40—50° and then for 24 hr. at 45—55°. The solution was treated with $K_2CO_3$ (19 g.) and evaporated to dryness. The crude product, obtained by extraction with ethyl acetate–ethanol mixture, formed a hygroscopic solid (48·6 g.), purified by distillation at 90—100° (air-bath)/0·02 mm. to give the base as a white crystalline mass (39·9 g., 94%), m. p. 60—63°. An analytical sample of the *dimethylaminoethyl-pyrrolidone*, obtained by crystallisation from benzene–cyclohexane followed by resublimation, formed rods, m. p. 65—67° (Found: C, 61·4; H, 10·45; N, 17·6%. $C_8H_{16}N_2O$ requires C, 61·5; H, 10·3; N, 17·9%).

*Preparation and Pyrolysis of the Oxide of* 3-2′-*Dimethylaminoethyl*-2-*pyrrolidone*.—30% Aqueous hydrogen peroxide (26·5 c.c.) was added to a solution of 3-β-dimethylaminoethyl-2-pyrrolidone (35·6 g.) in methanol (30 c.c.) at 0°. The solution was kept for 30 min, in an ice-bath, then overnight at room temperature. More hydrogen peroxide solution (26·5 c.c.) was added and the solution was kept for 7 hr. longer. Unchanged hydrogen peroxide was decomposed by stirring with platinum black for 24 hr. at room temperature. The solution was filtered and concentrated under reduced pressure at 55°, and the residual amine oxide hydrate was pyrolysed by heating gradually to 160° under 17 mm. pressure. The distillate was treated with ethyl acetate and filtered, giving residue " A " (14·8 g.), m. p. 175—177°. The filtrate was concentrated to small bulk and the partially crystalline residue was distilled at 60—100° (air-bath)/0·04 mm. to remove traces of tarry matter. The distillate was freed from some 3-2′-dimethylaminoethyl-2-pyrrolidone by solution in hydrochloric acid, and extraction with chloroform. The neutral extract (4·5 g.) was crystallised from ethyl acetate to give product " B " (1·4 g.), m. p. 173—175°. Products " A " and " B " were identical, and consisted of crude trans-3-*ethylidene*-2-*pyrrolidone* (16·2 g., 64%): an analytical sample (from ethyl acetate)

had m. p. 176—177·5° (Found: C, 64·9; H, 8·1; N, 12·75. $C_6H_9NO$ requires C, 64·8; H, 8·2; N, 12·6%), $\lambda_{max.}$ 222 mμ (ε 13,000), $\nu_{max.}$ 3125 (>NH), 1680 (C=O), and 1650 cm.$^{-1}$ (C=C). The longer wavelength region contained a sharp weak band at 870 cm.$^{-1}$, not observable in the spectrum of the *cis*-ethylidene compound (above). This compound was ozonised by the same technique as for the *cis*-ethylidene compound, and gave acetaldehyde 2,4-dinitrophenylhydrazone in good yield. The compound decolourised bromine in chloroform slowly, and reduced aqueous potassium permanganate rapidly. The filtrate from product "B" yielded 5% of 3-vinyl-2-pyrrolidone.

The pyrolysis was also carried out with acetic acid as a diluent for the amine oxide hydrate, but the yield of vinyl-pyrrolidone was not increased.

3-*Ethyl*-2-*pyrrolidone*.—The *trans*-ethylidene compound (1·00 g.) was quantitatively hydrogenated in methanol (10 c.c.) over palladium–charcoal catalyst. The product, b. p. 60—62° (air-bath)/0·02 mm. was almost pure 3-ethyl-2-pyrrolidone (0·99 g., 97%), a white, crystalline, strongly hygroscopic solid, m. p. 47—48·5°. An analytical sample, sublimed at 45°/0·02 mm., formed leaflets, m. p. 47·5—49° (Found: C, 63·7; H, 10·1; N, 12·2%. Calc. for $C_6H_{11}NO$: C, 63·7; H, 9·8; N, 12·4%), $\lambda_{max.}$ 192 mμ (ε 6800). The ethyl-pyrrolidone did not reduce potassium permanganate solution. It was also obtained by hydrogenation of 3-2′-chloroethyl-2-pyrrolidone over Raney nickel at room temperature. 3-Ethyl-2-pyrrolidone has previously been obtained by Brunner and Heck-Bleckmann,[11] who gave m. p. 37—38°, from α-ethyl-γ-butyrolactone and ammonia.

*Rearrangement of* 3-*Vinyl*-2-*pyrrolidone*.—(a) *With butyl-lithium*. A solution of the vinyl-lactam (1·0 g.) in dry toluene (25 c.c.) was treated with a solution of butyl-lithium in heptane (0·3 c.c. of 1·6M solution: 5 mole % based on the vinyl compound) and kept under nitrogen for 48 hr. at room temperature. After neutralisation with acetic acid the crude product (0·37 g.), m. p. 238—243°, was collected by filtration. After two recrystallisations from ethyl acetate the *substance* formed colourless crystals, m. p. 242—243·5° (Found: C, 64·4; H, 8·1; N, 13·1%. $C_6H_9NO$ requires C, 64·8; H, 8·2; N, 12·6%). Evaporation of the original filtrate to dryness gave a crystalline residue of m. p. 225—229° (234—238° after recrystallisation) indicating that rearrangement was almost complete.

(*b*) *With lithium aluminium hydride*. The previous experiment was repeated, using in place of butyl-lithium a 5 mole % quantity of lithium aluminium hydride (as 1·13M solution in tetrahydrofuran). In this case the crystals separating during the rearrangement (0·84 g.) and the residue after concentration of the filtrate had m. p. 166—173 and 167·5—172°, respectively. After recrystallisation from ethyl acetate, however, these two samples had m. p. 232—234 and 228—232°, respectively, and showed no depression of m. p. when mixed with the product of the butyl-lithium rearrangement. The infrared spectra and *X*-ray powder photograph of this high-melting substance were indistinguishable from those of normal *trans*-3-ethylidene-2-pyrrolidone of m. p. 176—177·5°. Sublimation of the substance (0·180 g.) yielded a normal sample of the *trans*-ethylidene-lactam (0·158 g.) of m. p. 173·5—177·5°. Attempted re-conversion to the high-melting substance with lithium aluminium hydride in tetrahydrofuran was unsuccessful.

(*c*) *With potassium carbonate*. 3-Vinyl-2-pyrrolidone (0·1 g.), dissolved in 1% aqueous potassium carbonate (1 c.c.), was kept for 20 min. at 100° and then overnight at room temperature. The thick white needles (0·04 g.) which separated were collected and after being washed with water and dried at room temperature had m. p. 174—175°, undepressed by admixture with *trans*-3-ethylidene-2-pyrrolidone.

From experiments on its synthesis it was evident that 3-vinyl-2-pyrrolidone is not rearranged by acetic acid or dilute hydrochloric acid at room temperature. It was also unaffected by boron trifluoride–acetic acid complex in 2% concentration at 100°.

The reverse rearrangement of *trans*-3-ethylidene-2-pyrrolidone to the vinyl-pyrrolidone was tried unsuccessfully, under conditions in which the vinyl compound could have been distilled from the equilibrium mixture, (*a*) without catalyst, (*b*) with toluene-*p*-sulphonic acid, and (*c*) with potassium hydroxide, at temperatures up to 210° in each case.

*Rearrangement of* 1-*Acetyl*-3-*vinyl*-2-*pyrrolidone*.—The acetyl-lactam (1·0 g.) in dry toluene (2 c.c.) was treated under nitrogen at −20° with butyl-lithium in heptane (0·04 c.c. of 1·5M solution; 1 mole %). The solution was kept for 16 hr. at room temperature and neutralised with acetic acid. After evaporation of the solvent the liquid residue was distilled at 68°/1·4 mm. to give an oil (0·39 g.) solidifying to colourless needles, m. p. 44·5—47°. After sublimation at

[11] Brunner and Heck-Bleckmann, *Monatsh.*, 1951, **82**, 371.

45°/0·04 mm. and recrystallisation from light petroleum (b. p. 60—80°) this yielded an almost pure sample of 1-*acetyl*-3-*ethylidene*-2-*pyrrolidone*, of m. p. 45—47·5° (Found: C, 62·6; H, 7·2; N, 9·0%. $C_8H_{11}NO_2$ requires C, 62·7; H, 7·25; N, 9·15%).

Acetylation of *trans*-3-ethylidene-2-pyrrolidone with acetic anhydride at the b. p. gave the same acetyl derivative, m. p. 48—50° (Found: C, 62·4; H, 7·3; N, 9·15%). A mixture of the two samples melted at 47·5—50°, and the infrared spectra were identical.

*Reaction of* 3-2′-*Chloroethyl*-2-*pyrrolidone with Potassium Hydroxide and other Bases.*—The chloroethyl compound (5·9 g., 0·04 mole) and potassium hydroxide (0·04 equiv.) were kept together in boiling absolute methanol (120 c.c.) for 46 hr. After neutralisation to pH 8 with acetic acid (0·1 c.c.) the solvent was evaporated under reduced pressure and the residue was treated with ethyl acetate, filtered from inorganic matter, and re-concentrated. The syrupy residue (5·6 g.) was distilled and the fraction (2·7 g.) of b. p. 90—100°/0·03 mm., $n_D^{21\cdot5}$ 1·4814 was re-fractionated to give a colourless liquid *product*, b. p. 94—97°/0·03 mm., $n_D^{21}$ 1·4810 (Found: C, 58·8; H, 9·1; N, 10·5%. $C_7H_{13}NO_2$ requires C, 58·7; H, 9·15; N, 9·8%). From its analysis and infrared spectrum this is probably 3-2′-methoxyethyl-2-pyrrolidone.

The chloroethyl-compound when treated with methanolic sodium methoxide was partly recovered, together with a small yield of impure methoxyethyl-pyrrolidone. It was not affected by anhydrous potassium carbonate in boiling t-butanol or by sodamide in liquid ammonia at the b. p.

3-2′-*Iodoethyl*-2-*pyrrolidone* (XII, R = I).—A solution of 3-2′-chloroethyl-2-pyrrolidone (14·8 g.) and sodium iodide (15·5 g.) in acetone (75 c.c.) was boiled under reflux for 30 hr. The solution was filtered hot and the residual sodium chloride (6·0 g.) was washed with acetone (25 c.c.). The filtrate and washings were combined and diluted with cyclohexane (50 c.c.) and cooled to −20°, giving pale yellow needles (16·3 g., 68%), m. p. 90—96°. After two re-crystallisations from acetone the *iodoethyl-pyrrolidone* had constant m. p. 99—102°, but did not give correct analytical figures (Found: C, 30·9; H, 4·4; N, 5·85; I, 50·35%. $C_6H_{10}INO$ requires C, 30·1; H, 4·2; N, 5·9; I, 53·1%). For the reaction with trimethylamine (see below) the use of the iodoethyl-pyrrolidone in acetone solution as prepared above, without isolation, was satisfactory.

2-(*Pyrrolid*-2′-*on*-3′-*yl*)-*ethyl Trimethylammonium Iodide* (XII, R = $NMe_3I$).—The above preparation of 3-2′-iodoethyl-2-pyrrolidone was repeated as far as the removal of sodium chloride. The filtrate was concentrated to low bulk and transferred to a heavy-walled 100-c.c. glass bottle in which it was diluted with acetone to a bulk of 60 c.c. Trimethylamine (10·0 g.) was added and the bottle was closed and kept for 22 hr. at room temperature. The separated product (23·5 g., 79%) after collection, washing with acetone, and vacuum drying, had m. p. 203—210°. An analytical sample (from ethanol) of the *quaternary iodide* had m. p. 220—222° (Found: C, 36·15; H, 6·6; N, 9·5; I, 42·6%. $C_9H_{19}IN_2O$ requires C, 36·2; H, 6·4; N, 9·3; I, 42·6%).

*Pyrolysis of* 2-(*Pyrrolid*-2′-*on*-3-*yl*)-*ethyl Trimethylammonium Hydroxide.*—The hydroxide was liberated by reaction of the corresponding iodide (15·0 g.) in methanol (150 c.c.) with silver oxide (10 g.) with exclusion of light for 18 hr. The solution was filtered and concentrated under reduced pressure to a syrup, which was pyrolysed at 0·1—0·5 mm. pressure in a 250-c.c. flask heated slowly from 80° to 160° (air-bath). The distilled pyrolysate (5·1 g.), a colourless oil, $n_D^{21}$ 1·4872, upon re-distillation gave the following fractions: (i) (1·86 g.) 60—70°/0·07 mm.; an oil, $n_D^{20}$ 1·4888: (ii) (1·7 g.) 70—90°/0·07 mm.; crystalline solid, m. p. 51—58°: (iii) (0·6 g.) 90—160°/0·07 mm.; cryst. solid, m. p. 175—177°. Fraction (i) was separated by two more distillations into a further quantity (0·3 g.) of product (ii) and a difficulty separable mixture of liquid bases. The infrared spectrum and microanalysis of the main fraction (0·49 g.), b. p. 50—54°/0·02 mm., $n_D^{22}$ 1·4950, suggested that it was an impure sample of 1-methyl-3-ethylidene-2-pyrrolidone (Found: C, 66·3; H, 9·3; N, 11·0%. $C_7H_{11}NO$ requires C, 67·2; H, 8·9; N, 11·2%). Fraction (ii) after recrystallisation from benzene–cyclohexane and sublimation at 56—63°/0·02 mm. yielded an almost pure specimen of 3-2′-dimethylaminoethyl-2-pyrrolidone, m. p. 62—64°, identified by its infrared spectrum and absence of m. p. depression with the authentic base obtained from 3-2′-chloroethyl-2-pyrrolidone and dimethylamine. Fraction (iii) upon recrystallisation from ethyl acetate yielded *trans*-3-ethylidene-2-pyrrolidone, m. p. 175—177°, identified by its infrared spectrum and absence of m. p. depression with the authentic compound obtained by pyrolysis of the oxide of 3-2′-dimethylaminoethyl-2-pyrrolidone.

*Reaction of* 3-2′-*Iodoethyl*-2-*pyrrolidone with Potassium Hydroxide.*—The iodoethyl-compound

(15·0 g., 0·063 mole) was kept for 2½ hr. at 50—55° with potassium hydroxide (0·063 equiv.) in methanol (12·9 c.c.). The solvent was evaporated under reduced pressure at 60° and the crude product (1·6 g., 23%), m. p. 169—173°, was isolated by chloroform extraction. Recrystallisation from ethyl acetate gave *trans*-3-ethylidene-2-pyrrolidone, m. p. 175—177° (Found: C, 64·7; H, 8·0; N, 12·7%. Calc. for $C_6H_9NO$: C, 64·8; H, 8·2; N, 12·6%), which did not depress the m. p. of a sample obtained by the amine oxide pyrolysis method. The filtrate from this product yielded more of the ethylidene-lactam and an unidentified liquid base.

*Preparation and Reactions of* 2,3,4,5-*Tetrahydro*-3a-H-*furo*[2,3-b]*pyrrole* (XIII).—Potassium (15·6 g., 0·4 g. atom) was dissolved in dry t-butanol (600 c.c.) under dry nitrogen. The solution was added during 80 min. to a boiling stirred solution of 3-2′-chloroethyl-2-pyrrolidone (59 g., 0·4 mole) in dry t-butanol (600 c.c.) under reflux. The reaction mixture was boiled for 20 min. longer and the solvent was distilled under reduced pressure at 40—60°. The residue was treated with kieselguhr (10 g.) and a solution of hydroquinone (0·1 g.) in ethyl acetate (225 c.c.), and the inorganic material was removed by filtration and washed with ethyl acetate. The filtrates were concentrated under reduced pressure at 90° to leave the crude product (44·1 g.) as a brown oil, crystallising on cooling. Upon distillation at 50—56°/0·04 mm. the *furopyrrole* was obtained in white, intensely hygroscopic platelets (32·5 g., 73%), m. p. 44—49° (Found: C, 64·4; H, 8·1; N, 12·1%. $C_6H_9NO$ requires C, 64·8; H, 8·2; N, 12·6%). Infrared spectrum: doublet at 1684 (strong) and 1718 (weak) cm.$^{-1}$; $\nu_{max.}$ 1230 and 1023 cm.$^{-1}$; doublet at 948 and 921 cm.$^{-1}$. The residue (10·4 g.) was a glassy fusible resin. Re-sublimation of the furopyrrole raised the m. p. to a constant value of 49·5—51·5°, but the analytical results were still imperfect. The compound resinified gradually when exposed to air, even over $P_2O_5$. Treatment of 3-2′-iodoethyl-2-pyrrolidone with potassium t-butoxide, in more concentrated solution, gave a 26% yield of the furopyrrole, together with a larger quantity of a high-boiling product. The latter formed a viscous pale yellow liquid, b. p. 120—125°/0·08 mm., $n_D^{21}$ 1·5166, and its infrared spectrum suggested that it was possibly the bimolecular iminoether, 2-[2-(pyrrolid-2′-on-3′-yl)-ethoxy]-3-2′-hydroxyethyl-1-pyrroline (Found: C, 59·7; H, 8·5; N, 11·7%. $C_{12}H_{20}N_2O_3$ requires C, 60·0; H, 8·4; N, 11·7%).

The furopyrrole was highly alkaline in aqueous solution (pH >10·5) but no crystalline salt could be obtained from any solvent. Upon acetylation with boiling acetic anhydride, the base (0·62 g.) yielded a pitch (0·5 g.) and a liquid acetate (0·53 g. after re-distillation), b. p. 90—100°/0·03 mm., $n_D^{21}$ 1·4814, identical with the *ON*-diacetyl derivative of 3-2′-hydroxyethyl-2-pyrrolidone.

The furopyrrole reduced cold aqueous potassium permanganate solution very rapidly 3-2′-Hydroxyethyl-2-pyrrolidone did not show this reaction.

A solution of the furopyrrole (5 g.) in water (25 c.c.) was heated on the steam-bath for 2 hr. The solvent was evaporated and the residue was distilled in vacuum, yielding fractions (i) b. p. 80—110°/0·04 mm. (25 mg.) partially crystalline, and (ii) b. p. 120—130°/0·04 mm. (4·96 g.), $n_D^{21}$ 1·5060, crystalline, m. p. 36—39°, and a glassy undistillable resin. The infrared spectrum of fraction (ii) was identical with that of 3-2′-hydroxyethyl-2-pyrrolidone.

The furopyrrole (2·2 g.) and cyclohexylamine (2·1 g.) were heated together for 16 hr. at 50° in methanol (10 c.c.). After evaporation of the solvent, the viscous oily residue (4·1 g.) partially crystallised. The product was collected by dilution with cyclohexane, filtration and washing with ether, forming colourless needles (1·4 g.), m. p. 112—122°. Sublimation at 116°/0·02 mm., followed by recrystallisation from toluene gave the *substance* with constant m. p. 119·5—121·5° (Found: C, 68·25; H, 10·6; N, 12·8%. $C_{12}H_{22}N_2O$ requires C, 68·5; H, 10·5; N, 13·3%). The substance thus proved to be an equimolar adduct. It was basic, but did not show the infrared spectrum (in particular, hydroxyl absorption) required by the expected product, 2-cyclohexylamino-3-2′-hydroxyethyl-1-pyrroline.

The furopyrrole (4·5 g.) in methanol (15 c.c.) was hydrogenated at atmospheric pressure over Adams's catalyst. Reduction was stopped after 19 days when 1·9 mol. of hydrogen had been absorbed per mol. of base. After removal of the catalyst and evaporation of the solvent, the residual oil (4·7 g.) was distilled at 70—80°/0·02 mm., yielding 3-2′-*hydroxyethylpyrrolidine*, a colourless viscous oil (3·3 g., 74%), $n_D^{19}$ 1·4862, and an undistillable resinous residue (Found: C, 62·7; H, 11·3; N, 12·1%. $C_6H_{13}NO$ requires C, 62·6; H, 11·4; N, 12·2%). The picrate and benzoyl derivative of the compound were obtained only as oils.

*Chugaev Dehydration of* 3-2′-*Hydroxyethyl*-2-*pyrrolidone*.—The hydroxyethyl-lactam (59·9 g.), dried xylene (330 c.c.) and potassium (18·1 g.) were stirred together under dry nitrogen for 3 hr.

at 70—90°. The suspension of the potassio-derivative was treated with dried ether (350 c.c.) and carbon disulphide (45 g.) and boiled under reflux for 3 hr. and left overnight. Methyl iodide (73 g.) was added slowly at the b. p. and the mixture was boiled under reflux for 6 hr. after the exothermic reaction had ceased. Part of the solvent was distilled under reduced pressure and the residual mixture (about 500 c.c.) was treated under nitrogen with water (100 c.c.) followed by chloroform (300 c.c.). The aqueous layer was separated, washed with chloroform (3 × 50 c.c.) and discarded. The combined organic layers were washed with water (50 c.c.) and concentrated under reduced pressure at 60° to 400 c.c. After being cooled to 0° the product was collected, washed with light petroleum (b. p. 60—80°) and dried at room temperature. It formed a creamy-white powder (55·7 g., 55%), m. p. 108—110°. An analytical sample (from ethyl acetate) of the *xanthate* had m. p. 109—110° (Found: C, 44·0; H, 5·9; N, 6·25; S, 26·5%. $C_8H_{13}NO_2S_2$ requires C, 43·8; H, 6·0; N, 6·4; S, 29·2%). Infrared absorption at 3214 cm.$^{-1}$ suggested that the ester contained a hydroxyl group. The latter could not however be detected by hydroxyl determination with acetic anhydride/pyridine or by reaction with thionyl chloride.

Samples of the xanthate ester prepared as above were pyrolysed at various pressures, and temperatures in the range 90—160°, but yielded much undistillable tar and only 15—30% of their weight of pyrolysate. The pyrolysates appeared to be complex mixtures, with two unidentified sulphur-containing main components, an oil, b. p. 80—90°/0·02 mm., $n_D^{24}$ 1·5062, and a crystalline solid, m. p. 57—59°.

*Dehydration of* 3-2′-*Hydroxyethyl*-2-*pyrrolidone with Toluene*-p-*sulphonic Acid*.—The hydroxyethyl compound (5·0 g.) and toluene-*p*-sulphonic acid (0·5 g.) were kept together under 12 mm. pressure while the temperature was increased gradually to 160°. A crystalline distillate was obtained. Upon further increase in temperature to 280° a small quantity of tarry oil distilled and the residue resinified. The distillate after filtration and washing with ethyl acetate (3 c.c.) yielded crude *trans*-3-ethylidene-2-pyrrolidone (0·5 g., 12%), m. p. 160—163°. One recrystallisation from ethyl acetate yielded a sample of m. p. 171—174°, undepressed by mixing with a sample obtained by the amine-oxide pyrolysis.

*Pyrolysis of* 3-2′-*Hydroxyethyl*-2-*pyrrolidone on Alumina*.—The apparatus was the same as for the pyrolysis of the corresponding acetate (see above), but the tube was packed with Spence-type " W " activated alumina (4—8 mesh). While the tube was heated at 440° and the pressure was kept at 100 mm., water (100 c.c.) was introduced, followed by a solution of the hydroxyethyl compound (25 g.) in water (20 c.c.) added during 20 min., and finally more water (20 c.c.) (during 10 min.). Concentration of the pyrolysate left a viscous brown oil (5·8 g.). Vacuum-distillation gave a light-yellow partially crystalline fraction, (2·8 g.), b. p. 60—80°/0·02 mm., which was treated with cyclohexane (5 c.c.) yielding a beige crystalline solid (1·1 g.), m. p. 74—82°. Sublimation at 78°/0·02 mm., followed by two recrystallisations from cyclohexane, gave the *substance* in colourless needles, m. p. 81·5—84·5° (Found: C, 64·5; H, 8·1; N, 13·1%. $C_6H_9NO$ requires C, 64·8; H, 8·2; N, 12·6%), $\lambda_{max.}$ 194 mμ (ε 7000); λ(infl.) 233 mμ (ε 500). The substance was neutral, and failed to yield a picrate. The infrared spectrum indicated the presence of the pyrrolidone ring and of a methyl group. The substance reduced cold aqueous potassium permanganate rapidly, but decolorised bromine solutions only slowly and could not be hydrogenated at atmospheric pressure. It gave a liquid *monoacetyl derivative*, b. p. 40—45°/0·02 mm., $n_D^{23}$ 1·5011 (Found: C, 62·8; H, 7·5; N, 8·9%. $C_8H_{11}NO_2$ requires C, 62·7; H, 7·2; N, 9·1%), the infrared spectrum of which closely resembled that of 1-acetyl-2-pyrrolidone.

Pyrolysis at 400° gave the same product in smaller yield, together with some unchanged starting material. The mother liquor of the crystalline product contained a substance which reduced bromine very rapidly. From the product of a further pyrolysate, at 370°, this was isolated in an impure state as a yellow oil (0·5 g. from 27·5 g. of hydroxyethyl compound), b. p. 40—50°/0·01 mm., $n_D^{21}$ 1·5309, apparently stable at −80° but darkening rapidly at room temperature (Found: C, 77·7; H, 10·0; N, 7·8%). Addition of bromine to a chloroform solution gave at first a colourless and then a brownish-purple solution, darkening when kept. The infrared spectrum indicated the presence of the pyrrolidone ring and of the −CH=CH−(*cis*) grouping.

*Ethyl* α-*Cyanomethylacetoacetate* (XX).—Sodium (33·2 g.) was dissolved in absolute alcohol (600 c.c.) and the excess of ethanol was distilled under reduced pressure to leave dry sodium ethoxide. Dry ether (300 c.c.) and acetoacetic ester (375 g.) were added and bromoacetonitrile (173·4 g.) was added slowly with stirring during 20 min. The reaction mixture was kept overnight at room temperature and then boiled under reflux for 7 hr. The reaction mixture was neutralised with tartaric acid (30 g.) in water (250 c.c.) and the product was extracted with ether

and washed ($NaHCO_3$). After evaporation of the solvent, unchanged acetoacetic ester (193 g.) was distilled at 36—40°/0·1 mm. The residue was distilled and the fraction of boiling range 100—150°/0·2 mm. was redistilled. The crude ester formed a fraction of b. p. 82—92°/0·1 mm., a pale yellow oil (149 g., 61%), $n_D^{20}$ 1·4441. Upon redistillation the ethyl *α-cyanomethyl-acetoacetate* had b. p. 85—86°/0·1 mm., $n_D^{20}$ 1·4471 (Found: C, 56·7; H, 6·8; N, 8·0%. $C_8H_{11}NO_3$ requires: C, 56·8; H, 6·55; N, 8·3%). Condensation of chloro- or bromo-acetonitrile and ethyl acetoacetate using sodium ethoxide in anhydrous ethanol gave a maximum yield of 13% of the cyanomethyl-acetoacetic ester.

*Hydrogenation of Ethyl α-Cyanomethylacetoacetate.*—The ester (29·8 g.) was hydrogenated in methanol (150 c.c.) over Raney nickel for 3 hours at 70°, at an initial hydrogen pressure of 100 atm. After filtration from catalyst the solvent was distilled to leave a dark oil (26 g.) which partially crystallised. The crude product (23·1 g.) was fractionally distilled to give products " A " (8·3 g.), b. p. 52—56°/0·04 mm., $n_D^{26}$ 1·4958, and " B " (10·6 g.), b. p. 56—108° (mainly at 100—102°)/0·04 mm., crystallising to a solid m. p. 74—77°. Upon recrystallisation from cyclohexane, product " B " gave needles, m. p. 78·5—80°, of ethyl 2-methylpyrrole-3-carboxylate (XXI) (Found: C, 62·2; H, 7·3; N, 8·8%. Calc. for $C_8H_{11}NO_2$: C, 62·7; H, 7·2; N, 9·1%). Benary [9] gives m. p. 78—79° (from aq. alcohol). The pyrrole failed to give a picrate or hydrochloride, and was resinified by hot conc. HCl.

Product " A " upon redistillation had a narrow boiling range, 39—45°/0·04 mm., but fractions of varying refractive index were collected. A centre fraction (2 g.), b. p. 43—43·5°/0·04 mm., $n_D^{25}$ 1·4980, was obtained, which from its analysis and infrared spectrum was apparently impure ethyl 2-methylpyrroline-3-carboxylate (Found: C, 61·2; H, 9·0; N, 8·2%; *M* (Rast), 137,162. $C_8H_{13}NO_2$ requires C, 61·9; H, 8·4; N, 9·0%; *M*, 155). With acetic anhydride this yielded a *monoacetyl derivative*, b. p. 110—120°/0·04 mm., m. p. 76—78° (from cyclohexane) (Found: C, 60·9; H, 7·6; N, 7·6%. $C_{10}H_{15}NO_3$ requires: C, 60·9; H, 7·7; N, 7·1%).

*Hydrogenation of Ethyl α-3-Cyanopropylacetoacetate* (XXIII).—Reduction of the nitrile (49·5 g.) (prepared according to Derick and Hess [12]) on nickel or cobalt catalysts gave products which easily resinified. The following experiment gave the highest yield of distillable products. The nitrile (32·6 g.) was hydrogenated in methanol (200 c.c.) over Raney cobalt for 4 hr. at 60°. After filtration and concentration, the product was distilled to give two main liquid products: (*a*) b. p. 60—65° (9·1 g.), $n_D^{27}$ 1·4651 (Found: C, 64·7; H, 10·6; N, 8·3%: $C_{10}H_{19}NO_2$ requires C, 64·8; H, 10·3; N, 7·6%): the infrared spectrum of this fraction was consistent with the structure ethyl 2-methylperhydroazepin-3-carboxylate, suggested by the microanalysis; (*b*) b. p. 93—115° (12·6 g.); upon redistillation, b. p. 97°/0·03 mm., $n_D^{26}$ 1·4953 (Found: C, 60·9; H, 9·8; N, 8·6%. $C_8H_{15}NO_2$ requires C, 61·1; H, 9·6; N, 8·9%); the microanalysis was in agreement with the structure 3-1′-hydroxyethylperhydroazepin-2-one; the infrared spectrum also suggested this structure, but showed that an ester impurity was present. The material (*b*) resinified slowly upon storage.

*α-1-Hydroxyethyl-γ-butyrolactone* (XXII).—α-Aceto-γ-butyrolactone (Knunyantz *et al.*[13]) (47·5 g.) was hydrogenated in methanol (150 c.c.) over Raney nickel for 2 hr. at 120°. After filtration from catalyst and distillation of the solvent the crude product was fractionally distilled, yielding the required lactone (34·3 g., 71%), a pale yellow oil, $n_D^{23}$ 1·4641, as the fraction of b. p. 93—96°/0·05 mm. Further fractionation yielded the *hydroxyethyl-lactone* as a colourless oil, b. p. 76—77°/0·1 mm., $n_D^{18}$ 1·4635 (Found: C, 55·0; H, 7·5%. $C_6H_{10}O_3$ requires C, 55·4%; H, 7·75).

*1,4-Dihydroxypentane-3-carboxamide* (XXV).—α-1-Hydroxyethyl-γ-butyrolactone (34·3 g.) was dissolved in aqueous ammonia (s.g. 0·880) (120 c.c.) and the solution was kept for 28 hr. at room temperature. Water and ammonia were distilled under reduced pressure at 100° to leave a viscous oil (37·6 g.) which was stirred with acetone (175 c.c.) at the boiling point. After cooling, the crude crystalline product (16·3 g., 42%), m. p. 125—128°, was collected by filtration and washed with acetone. Further crystallisation from acetone gave the pure *dihydroxy-amide* in colourless needles, m. p. 135—137° (Found: C, 49·3; H, 8·8; N, 9·3%. $C_6H_{13}NO_3$ requires C, 49·0; H, 8·9; N, 9·5%).

When heated above the m. p. the compound evolved ammonia rapidly. A small sample kept for 30 min. at 180° under 15 mm. pressure distilled completely. The infrared spectrum of

[12] Derick and Hess, *J. Amer. Chem. Soc.*, 1918, **40**, 537.
[13] Knunyantz, Chelintzev, and Osetrova, *Compt. rend. Acad. Sci. U.R.S.S.* [N.S.], 1934, **1**, 312; (*Chem. Abs.*, 1934, **28**, 4382).

the oily distillate was that expected from α-1-hydroxyethyl-γ-butyrolactone containing a trace of the primary amide (XXV).

Reaction of α-1-hydroxyethyl-γ-butyrolactone (26 g.) with ammonia (10 g.) in methanol (100 c.c.) in a sealed autoclave for 4½ hr. at 180° produced 2·65 g. (9%) of impure 1,4-dihydroxypentane-3-carboxamide, m. p. 120—125°, and 18·1 g. (69%) of recovered hydroxyethyl-lactone, b. p. 95—105°/0·1 mm., $n_D^{24}$ 1·4660, the remainder of the product being resinous.

The hydroxyethyl-lactone (15·0 g.) and ammonia (5 g.) were heated together in a sealed autoclave for 2 hr. at 200°, followed by 4 hr. at 260°. Ammonia and the more volatile reaction products were removed by distillation under reduced pressure at 60° Upon fractional distillation of the syrupy residue (11·2 g.), crude 2-pyrrolidone (4·7 g., 48%), b. p. 86—92°/0·05 mm., $n_D^{20}$ 1·4840, was obtained in addition to a viscous oil (0·9 g.), boiling range 92—152°/0·05 mm., $n_D^{20}$ 1·5226, and a pitch (3·4 g.). Upon further fractionation the pyrrolidone was obtained with b. p. 67—68°/0·05 mm., $n_D^{20}$ 1·4845. It gave a picrate, m. p. 100—102° (from benzene). A commercial sample of 2-pyrrolidone had $n_D^{22}$ 1·4854 after redistillation. Its picrate had m. p. 101—103·5°. A mixture of the two picrates had m. p. 101—103·5°.

*Reaction of* 1,4-*Dihydroxypentane-3-carboxamide with Thionyl Chloride.*—The amide (3·0 g.), benzene (10 c.c.) and thionyl chloride (5·4 g.) were kept together at room temperature for 16 hr. and then heated for 1 hr. at 100°. Thionyl chloride was evaporated under reduced pressure at 60° and the residue was treated with benzene and filtered from ammonium chloride (0·32 g.). Removal of benzene and treatment of the partially solid residue with acetone gave strongly deliquescent fawn needles of *3-ethylidene-2-iminotetrahydrofuran hydrochloride* (XXIV) (0·55 g.), m. p. 144—147° (Found: C, 48·4; H, 6·8; N, 9·5; Cl, 24·1%. $C_6H_{10}ClNO$ requires C, 48·8; H, 6·8; N, 9·5; Cl, 24·0%). The imine hydrochloride in ethanol gave the yellow crystalline *iminotetrahydrofuran picrate*, m. p. 192—194°, (Found: C, 42·45; H, 3·6; N, 16·9%. $C_{12}H_{12}N_4O_8$ requires C, 42·35; H, 3·6; N, 16·5%).

The imine hydrochloride in aqueous solution decolourised bromine water rapidly. Treatment of the hydrochloride with boiling acetic anhydride gave acetamide as the only identifiable product. Ammonia was evolved when the imine hydrochloride was warmed with aqueous sodium hydroxide.

*Reaction of Ethanolamine and Ethyl Acetoacetate.*—Ethanolamine (24·4 g.) and ethyl acetoacetate (52 g.) were heated together under reflux for 3 hr. in an oil-bath at 150°. The bath temperature was raised slowly to 160° during 4 hr. while aqueous ethanol (21·0 g.), b. p. 78—84°, $n_D^{23}$ 1·3653, was allowed to distil. The residue (52·3 g.) was mixed with ethanol (10 c.c.) followed by acetone (100 c.c.) and after crystallisation was complete the crude product (9·0 g.), m. p. 169·5—175°, was collected and washed with acetone. Recrystallisation from ethanol–ethyl acetate and then from ethanol gave the *substance* with m. p. 187—187·5° (Found: C, 56·65; H, 7·4; N, 11·1%. $C_6H_9NO_2$ requires C, 56·7; H, 7·1; N, 11·0%), $\nu_{max.}$ 1656, 1637, 1574, 1565, 1540, 3371, and 3261 $cm.^{-1}$. The substance did not yield a phenylhydrazone or 2,4-dinitrophenylhydrazone. It was neutral, and could not be titrated, in aqueous solution. Titration with perchloric acid in acetic acid indicated that it was a base (equiv. wt. 368).

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