[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

A Study of Some 2,3-Dioxopyrrolidines and Derived Bipyrrolidines[1]

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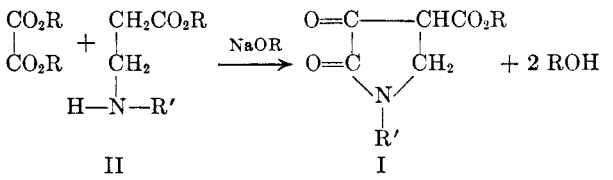
A one-step procedure is described for the preparation of 1-substituted-4-carbethoxy-2,3-dioxopyrrolidines from ethyl acrylate, a primary aliphatic amine, and ethyl oxalate as starting materials. Three of the products so obtained have been acetylated to yield 3-acetoxy-4-carbethoxy-2-oxo-3-pyrrolines, and seven have been hydrolyzed and decarboxylated to yield 1-substituted-2,3-dioxopyrrolidines. Among the latter substances four have been reduced to 3-hydroxy-2-oxopyrrolidines and two further reduced to 3-hydroxypyrrolidines. All of these conversions can be achieved in fair to good yield and may be considered of preparative value.

The 1-substituted-2,3-dioxopyrrolidines are readily converted into a variety of derivatives by reaction with carbonyl reagents. They also undergo self-condensations of the aldol type with great facility to yield products which contain the 3,3′-bipyrrolidine system.

Recent investigations in this laboratory have led to the development of a new and convenient method of synthesis for 4-carboalkoxy-2,3-dioxopyrrolidines (I) from readily available starting materials. The method is based upon the condensation of alkyl oxalates with esters of N-alkyl- or N-aryl-β-aminopropionic acids (II) in the presence of sodium alkoxides.[3,4] In the present work the application of



II I

this method to the synthesis of those members of the series which have aliphatic substituents in position 1 and the carbethoxy group in position 4 has been simplified and improved. In addition, a number of aspects of the chemistry of these easily accessible pyrrolidine derivatives have been studied. The simplified procedure for the preparation of the 4-carbethoxy-2,3-dioxopyrrolidines (I, R = C_2H_5) and the results of the investigation of the reactions of these compounds and of other pyrrolidines derived from them will be considered below under separate headings.

Preparation of 4-carbethoxy-2,3-dioxopyrrolidines (I, R = C_2H_5). An excellent method of preparing esters of N-alkyl- or N-aryl-β-aminopropionic acids is available through the addition of primary amines to alkyl acrylates.[5] In the case of primary amines of the aliphatic type the addition often proceeds in very satisfactory yield when the amine is mixed with ethyl acrylate in absolute ethanol solution, and no catalyst is required. The 4-carbethoxy-2,3-dioxopyrrolidines (I, R = C_2H_5) can then be obtained by simply adding ethyl oxalate and sodium ethoxide to the ethanol solutions in which the ethyl β-aminopropionates have been formed in this manner. The intermediate β-aminopropionates need not be isolated, and the over-all yields obtained from this one-step process (56–86%) were often markedly superior to those secured by the use of the somewhat more laborious procedures described previously.[4] The simplified procedure was used for the preparation of the ten 4-carbethoxy-2,3-dioxopyrrolidines having one of the following substituents in position 1: methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *tert*-butyl, cyclohexyl, benzyl, and β-phenylethyl.

Preparation and investigation of 3-acetoxy-4-carbethoxy-2-oxo-3-pyrrolines (IV). The acidity of 4-carbethoxy-2,3-dioxopyrrolidines due to enolization is comparable to that of carboxylic acids.[4] Both their titration behavior[6] and the strong, broad infrared band which they show at 3.18 μ suggest that these compounds exist largely, if not entirely, in the enolic form, *i.e.*, as 4-carbethoxy-3-hydroxy-2-oxo-3-pyrrolines (III). It was previously shown that these compounds react with diazomethane to give enol ethers in high yield,[4] and it has now been found that they react with ketene to yield 3-acetoxy-4-carbethoxy-2-oxo-3-pyrrolines (IV). Three

(1) This work was supported in part by a research grant (RG-4371) from the National Institutes of Health, U. S. Public Health Service. Most of it is described in the thesis submitted by E. Herbert Carlson in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the Carnegie Institute of Technology, September, 1955.

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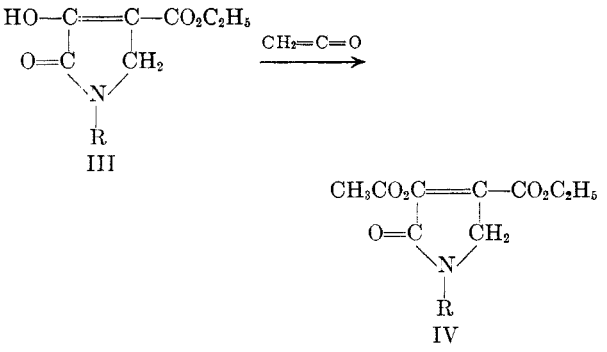
(3) Southwick and Seivard, *J. Am. Chem. Soc.*, **71**, 2532 (1949).

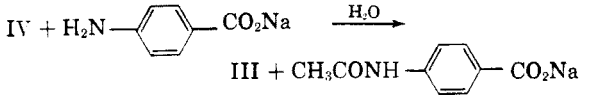
(4) Southwick and Crouch, *J. Am. Chem. Soc.*, **75**, 3413 (1953).

(5) Riddle, *Monomeric Acrylic Esters*, Reinhold Publishing Corp., New York, N. Y., 1954, p. 154.

(6) A potentiometric titration (glass electrode) of 1-benzyl-4-carbethoxy-2,3-dioxopyrrolidine performed in an aqueous ethanol solution showed a sharp *p*H rise at the equivalence point and indicated a pK_a for this compound of approximately 4.25. There was no delay in the consumption of base in this titration such as was observed by Vaughan and Peters, *J. Org. Chem.*, **18**, 405 (1953), in their titration of a 1,5-diaryl-2,3-dioxopyrrolidine. Thus there was no indication of incomplete enolization or of an attack by the base on the ester or lactam functions in the molecule.

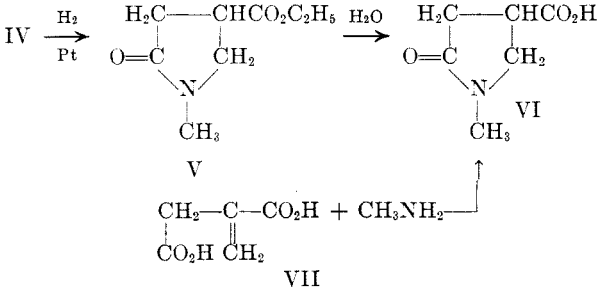


such compounds (IV, R = H, CH_3, or $(CH_3)_2CH$) have been prepared. Investigation has shown that, as would be expected, this type of substance can serve as an acetylating agent. The 1-methyl derivative (IV, R = CH_3), for example, was dissolved in water to yield an aqueous solution which was capable of acetylating sodium *p*-aminobenzoate. The same compound (IV, R = CH_3) was also readily converted back into the parent enol (III,

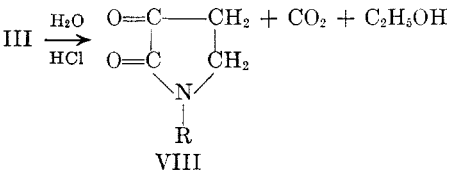


R = CH_3) by heating with ethanol containing a trace of sulfuric acid. However, an attempted saponification with sodium hydroxide in ethanol led to an altogether unexpected result; the compound (IV, R = CH_3) was immediately converted into an intensely dark-blue pigment, which could be precipitated by dilution of the solution with water. The pigment melted with decomposition above 350°, and efforts to crystallize it were unsuccessful.

Hydrogenation of 3-acetoxy-4-carbethoxy-1-methyl-2-oxo-3-pyrroline (IV, R = CH_3) in acetic acid solution over a platinum oxide (Adams) catalyst resulted in the removal of the 3-acetoxy group as well as saturation of the double bond. Saponification of the resulting 4-carbethoxy-1-methyl-2-pyrrolidone (V) yielded 1-methyl-2-pyrrolidone-4-carboxylic acid (VI), identical with a comparison sample made by means of the reaction between methyl amine and itaconic acid (VII).[7]

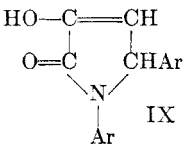


Preparation and characterization of 1-substituted-2,3-dioxopyrrolidines. The preparation of 1-benzyl-2,3-dioxopyrrolidine (VIII, R = $CH_2C_6H_5$) by means of the acid hydrolysis and decarboxylation of 4-carbethoxy-1-benzyl-2,3-dioxopyrrolidine (more properly regarded as 4-carbethoxy-1-benzyl-3-hydroxy-2-oxo-3-pyrroline (III, R = $CH_2C_6H_5$)) has been described previously.[4] The method has



since been used successfully for the preparation of other simple 2,3-dioxopyrrolidines (VIII) in which the 1-substituent, R, has been *n*-butyl, isobutyl, *tert*-butyl, cyclohexyl, phenyl, or β-phenylethyl. However, the isopropyl derivative (VIII, R = $(CH_3)_2CH$), was obtained only in the crude form or in the form of derivatives, and the method has thus far failed when attempts have been made to apply it to the preparation of 2,3-dioxopyrrolidine itself (VIII, R = H) or the 1-methyl derivative (VIII, R = CH_3). Seemingly other types of hydrolysis products were produced in these latter cases, but the nature of these products has not been determined.

The 1-substituted-2,3-dioxopyrrolidines (VIII), as obtained by the acid hydrolysis and decarboxylation of corresponding 4-carbethoxy derivatives (III), exhibited infrared spectra which lacked any indication of a band due to a hydroxyl group, but showed strong carbonyl absorption at 5.67 μ and at 5.86–5.89 μ, presumably due to the ketonic and lactam carbonyl groups respectively.[8] All of a number of 1,5-diaryl-2,3-dioxopyrrolidines examined by Vaughan and Peters,[9] on the other hand, displayed an hydroxyl band at 2.93 μ in chloroform or 3.04 μ in dioxane, and hence were presumed to exist at least in part in the enol form IX. The



simple 2,3-dioxopyrrolidines substituted only in the 1-position which are described here may be the first true (*i.e.*, unenolized) 2,3-dioxopyrrolidines ever prepared. They give no ferric chloride test.

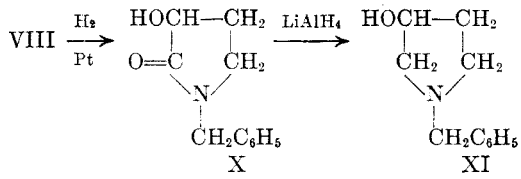
Verification of the presence of the pyrrolidine ring in these compounds was provided by the

(7) *Cf.* Paytash, Thompson, and Fykes, *J. Am. Chem. Soc.*, **74**, 4549 (1952).

(8) In the case of 1-phenyl-2,3-dioxopyrrolidine the strong absorption at *ca.* 5.86μ resulted from two closely spaced but distinct bands at 5.84 and 5.88μ, and the band at 5.67μ had a slight shoulder at *ca.* 5.65μ. Infrared data mentioned here and elsewhere in this paper were obtained with a Perkin-Elmer Model 21 spectrophotometer. Measurements were made on Nujol mulls unless otherwise indicated.

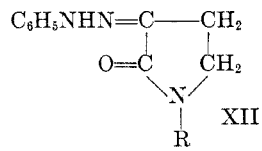
(9) Vaughan and Peters, *J. Org. Chem.*, **18**, 382 (1953).

results of a stepwise reduction of 1-benzyl-2,3-dioxopyrrolidine (VIII, R = $C_6H_5CH_2$). Hydrogenation over an Adams' platinum oxide catalyst in ethanol gave a 77% yield of 1-benzyl-3-hydroxy-2-oxopyrrolidine (X), which then was converted into 1-benzyl-3-hydroxypyrrolidine (XI) in 61% yield by lithium aluminum hydride reduction. The de-

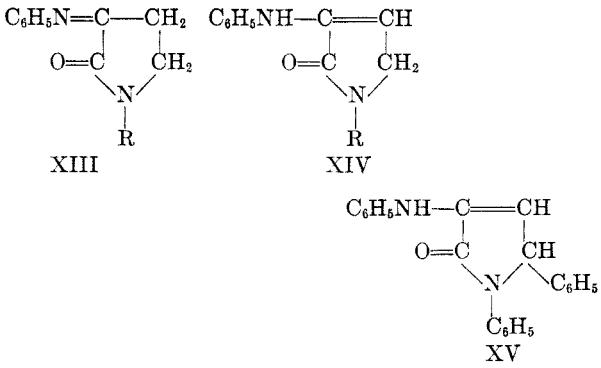


rivative formed from the latter substance with 3,5-dinitrobenzoyl chloride retained the basic nitrogen; thus the amino function in the final reduction product (XI) was tertiary and evidently incorporated into the assumed pyrrolidine ring. There is no reason to doubt the presence of the same ring in the precursors X and VIII (R = $C_6H_5CH_2$), and hence in the other 2,3-dioxopyrrolidines (VIII), three of which, the 1-*n*-butyl, 1-cyclohexyl, and 1-β-phenylethyl derivatives, were also reduced to the stage of 3-hydroxy-2-oxopyrrolidines, and one of which, the 1-β-phenylethyl derivative, was further reduced to the 3-hydroxypyrrolidine.

Most of the 1-substituted-2,3-dioxopyrrolidines examined in the course of the present investigation reacted with phenylhydrazine to give products corresponding in composition (although not necessarily in structure) to the formulas of the expected phenylhydrazones (XII). This is in contrast to the re-



sults reported with the 1,5-diaryl-2,3-dioxopyrrolidines, which react in a complex manner with phenylhydrazine.[10] In the case of 1-cyclohexyl-2,3-dioxopyrrolidine (VIII, R = *cyclo*-C_6H_{11}), however, the product of reaction with phenylhydrazine differed from the expected composition by the addition of the elements of a molecule of water. Oximes (of the expected composition) were formed from the only 2,3-dioxopyrrolidines tested, the 1-benzyl and 1-β-phenylethyl derivatives, and a semicarbazone was obtained from the 1-benzyl derivative. All of the 2,3-dioxopyrrolidines reacted with aniline to give products corresponding in composition to anils of the type XIII. However, the infrared spectrum of the "anil" of the 1-cyclohexyl derivative, the only such compound for which the spectrum was deter-



mined, contains a band at 3.02 μ probably due to an N—H structure, and this observation suggests that the structure of the "anils" may be that indicated by formula XIV. Vaughan[11] had proposed an analogous structure (XV) for Doebner's "anil-anilide," an apparently similar derivative of 1,5-diphenyl-2,3-dioxopyrrolidine.

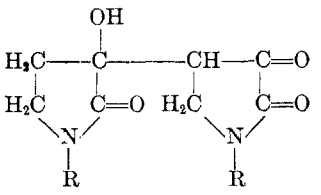
A reaction which clearly did not follow the expected course was observed when 1-benzyl-2,3-dioxopyrrolidine (VIII, R = $C_6H_5CH_2$) was subjected to the conditions of the Leuckart reaction. When refluxed in formamide solution this compound gave in rather poor yield a compound which crystallized from the reaction mixture as nearly black crystals with a greenish-bronze metallic lustre. This product melted at 351–352° with decomposition after recrystallization from dimethylformamide, the only solvent in which it was found to be appreciably soluble. No information regarding the structure of this product has been obtained as yet.

Self-condensation of 1-substituted-2,3-dioxopyrrolidines. Perhaps the most remarkable characteristic of the 1-substituted-2,3-dioxopyrrolidines is the extreme ease with which some members of this class undergo self-condensation. The 1-cyclohexyl derivative was on several occasions observed to undergo this change upon standing in the solid state, and did so reproducibly and in nearly quantitative yield upon being allowed to stand for a minute or two in an ethanol solution containing pyridine. The 1-*tert*-butyl derivative, the other member of the series which was studied in this regard, was best converted into the initial self-condensation product by a short period of heating in refluxing toluene.

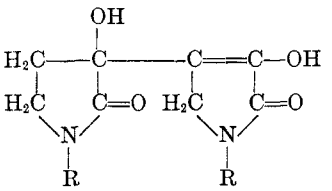
Molecular weight data indicated that self-condensation had occurred, and the preponderance of evidence suggests a condensation of the aldol type. The composition of the initial condensation products corresponded to the formula (XVI) of a 1,1′-disubstituted-2,4′,5′-trioxo-3-hydroxy-3,3′-bipyrrolidine (or to its enolic modification XVII). Bands attributable to the hydroxyl group were found at 3.01 μ for the *tert*-butyl compound and at 3.02 μ for the cyclohexyl derivative when the infrared spectra were measured in Nujol mulls. The *tert*-

(10) See Vaughan, *J. Org. Chem.*, **20**, 1619 (1955), for a discussion of the literature and a reinvestigation of reactions of 1,5-diaryl-2,3-dioxopyrrolidines with phenylhydrazine. Because of the possibilities for isomerism in phenylhydrazine derivatives of 2,3-dioxopyrrolidines, we assign structure XII to our products only on a tentative basis.

(11) Vaughan, *J. Org. Chem.*, **20**, 1613 (1955).

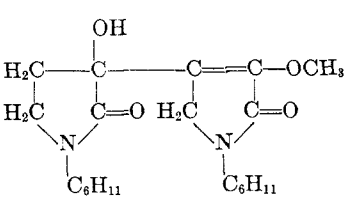


XVI



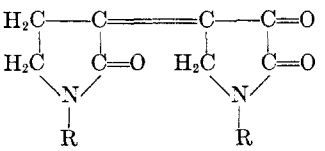
XVII

butyl derivative also showed a band of lower intensity at 3.14 μ. The fact that the spectrum of neither compound contained a band in the range appropriate to a ketonic carbonyl group suggested that the enolic formula XVII best represents these compounds as they exist in the solid state. This interpretation would require that the bands due to two different lactam carbonyls and the enolic carbon to carbon double bond be accounted for in the case of the *tert*-butyl compound by an intense and broad absorption with a maximum at 6.00 μ and in the case of the cyclohexyl compound by an intense absorption at 5.91 μ plus a less intense band at 6.01 μ. The curve of the *tert*-butyl compound showed irregularities on the lower wave-length side of the 6.00 μ maximum which suggested that it was formed from overlapping bands. In chloroform solution, on the other hand, both compounds showed a rather weak band at the proper position for a ketonic carbonyl in a ring of five members.[12] (5.68 μ for the *tert*-butyl compound, 5.69 μ for the cyclohexyl compound), and there was also a considerable weakening of the hydroxyl bands, which now appeared at 2.89 μ in the *tert*-butyl compound and at 2.88 μ in the cyclohexyl compound. Thus there is evidence of tautomerism when these substances are in solution. The presence of an enolic form was also indicated by the very characteristic purple color given with ferric chloride, and by the reaction, studied only with the cyclohexyl compound, in which diazomethane reacted to give a product corresponding in composition to the enol methyl ether, 1-cyclohexyl-2-oxo-3-methoxy-4-(1-cyclohexyl-2-oxo-3-hydroxy-3-pyrrolidyl)-3-pyrroline (XVIII).

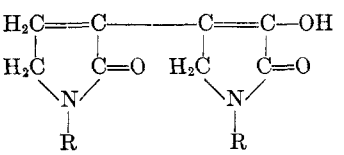


XVIII

Both of the self-condensation products which were studied underwent dehydration readily to give high yields of products which appeared to be 1,1′-disubstituted-2,4′,5′-trioxo-3,3′-bipyrrolidylidenes (XIX). The dehydrated condensation product



XIX

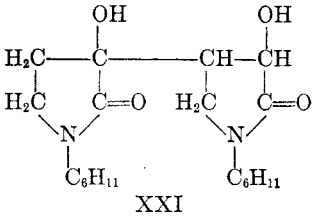


XX

was, in fact, formed directly in 95% yield when 1-*tert*-butyl-2,3-dioxopyrrolidine (VIII, R = *tert*-butyl) was treated with pyridine in ethanol solution; under these conditions the initial aldol (XVI, R = *tert*-butyl) evidently dehydrated rapidly. The cyclohexyl aldol (XVI or XVII, R = cyclohexyl) underwent dehydration when repeatedly crystallized from ethanol, when sublimed under reduced pressure, or when suspended in refluxing 20% hydrochloric acid. The ultraviolet absorption spectrum was measured for the cyclohexyl dehydration product and found to show bands at 247 mμ, ϵ = 10,800, and at 295 mμ, ϵ = 11,400, which clearly indicated conjugation such as would be present in formula XIX. Infrared spectra for the two compounds of this type which were studied were determined in Nujol mulls and found to be very similar to each other. Both lacked any bands in the hydroxyl region and were characterized by bands at 5.92 μ, 5.98 μ, and 6.12 μ for the *tert*-butyl compound and correspondingly at 5.94 μ, 6.01 μ, and 6.15 μ for the cyclohexyl compound. It seemed likely that the bands in the 6.12–6.15 μ range corresponded to a carbon-carbon double bond. The only property of these compounds which is clearly not in accord with formula XIX is the characteristic green to green-blue color produced with ferric chloride. This color test may perhaps indicate the possibility of tautomerism with a form represented by formula XX. The test color is reminiscent of that given by 1,4,5-triphenyl-2,3-dioxopyrrolidine with ferric chloride.

The possibility of reducing the ketonic carbonyl (or enolic) function in the initial condensation products of the type XVI or XVII was investigated in the case of the cyclohexyl compound. Hydrogenation over an Adams' platinum oxide catalyst in absolute ethanol gave a new compound having the composition and properties expected for 1,1′-dicyclohexyl-3,4′-dihydroxy-2,5′-dioxo-3,3′-bipyrrolidine (XXI). The hydrogenation product differed from the starting material in producing no

(12) Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, Inc., New York, N. Y., 1954.



XXI

color with ferric chloride. The infrared spectrum showed no band corresponding to a ketonic carbonyl, but had a broad band in the hydroxyl region (max. at 3.03 μ with a slight shoulder at 3.15 μ) and a strong band in the carbonyl region at 5.93 μ (shoulder at *ca.* 6.01 μ) which is presumably due to the lactam carbonyls. It seems evident that condensation products of the type XVI (or XVII) can serve as starting materials for the synthesis of a variety of 3,3′-bipyrrolidine derivatives.[13]

EXPERIMENTAL[14]

1-Substituted-4-carbethoxy-2,3-dioxopyrrolidines (I or III). In a typical run, equimolecular quantities of an aliphatic primary amine and freshly distilled ethyl acrylate were dissolved in absolute ethyl alcohol (0.5- to 1.0-mole amounts in 250 ml. of absolute ethyl alcohol). After the mixture had been allowed to stand for 24 hours, there were added equivalent amounts of diethyl oxalate and an ethanolic sodium ethoxide solution prepared by dissolving 0.5- to 1.0-g.-atom of freshly cut metallic sodium in 250 ml. of absolute ethyl alcohol. The reaction mixture was refluxed for one hour on a steam-cone, and then the solvent was removed by distillation. The solid residue was taken up in water (usually 250 ml.) by heating on a steam-cone, and the resulting solution was acidified with 20% hydrochloric acid. The *n*-butyl, β-phenylethyl, and cyclohexyl derivatives usually began to precipitate at once, but in the case of the other compounds clear yellow solutions resulted which were filtered while hot to remove small amounts of suspended solid impurities. The solutions were usually allowed to stand overnight in the refrigerator to complete the crystallization of the products, which were removed by filtration and air-dried. All of the products gave a red color with ferric chloride solution. Minor variations in the procedure are indicated in the sections devoted to the individual compounds.[15] The quantity of alcohol used was the same in all runs unless otherwise indicated.

1-Methyl-4-carbethoxy-2,3-dioxopyrrolidine. Yield, 57.8 g. (60%) of colorless needles, m.p. 155–157°, from 16.2 g. (0.52 mole) of gaseous methylamine, 70.5 g. (0.7 mole) of ethyl acrylate, 76 g. (0.52 mole) of diethyl oxalate, and 12 g. (0.52 g.-atom) of sodium. Crystallization from 95% ethanol raised the m.p. to 156–157°.

Anal. Calc'd for $C_8H_{11}NO_4$: C, 51.88; H, 5.99; N, 7.56. Found: C, 51.80; H, 5.82; N, 7.91.

1-Ethyl-4-carbethoxy-2,3-dioxopyrrolidine. Yield, 66.5 g. (60%) of fine, short, colorless needles, m.p. 97–98°, from 25 g. (0.555 mole) of gaseous ethylamine, 80 g. (0.8 mole) of ethyl acrylate, 81 g. (0.555 mole) of diethyl oxalate, and 12.8 g. (0.555 g.-atom) of sodium. Crystallization from a high-boiling petroleum ether-benzene mixture (5:1) raised the m.p. to 105.5–106.5°.

Anal. Calcd. for $C_9H_{13}NO_4$: C, 54.26; H, 6.58; N, 7.03. Found: C, 54.50; H, 6.87; N, 7.05.

1-n-Propyl-4-carbethoxy-2,3-dioxopyrrolidine. Yield, 80.5 g. (69.5%) of long, fine, colorless needles, m.p. 114–116°, from 32 g. (0.545 mole) of *n*-propylamine, 54.5 g. (0.545 mole) of ethyl acrylate, 80 g. (0.55 mole) of diethyl oxalate, and 12.5 g. (0.545 g.-atom) of sodium. The volume of absolute ethyl alcohol used in the ethyl acrylate-*n*-propylamine reaction was 200 ml., and the mixture was allowed to stand for 30 hours. Crystallization from a cyclohexane-benzene mixture (10:1) raised the m.p. to 119–119.5°.

Anal. Calc'd for $C_{10}H_{15}NO_4$: C, 56.32; H, 7.09; N, 6.57. Found: C, 56.20; H, 7.26; N, 6.22, 6.25.

1-Isopropyl-4-carbethoxy-2,3-dioxopyrrolidine. Yield, 135 g. (63.5%) of light-yellow needles, m.p. 132–134°, from 59 g. (1 mole) of isopropylamine, 100 g. (1 mole) of ethyl acrylate, 146 g. (1 mole) of diethyl oxalate, and 23 g. (1 g.-atom) of sodium. The recorded yield was the combined weight of three crops of crystals after the third crop obtained from the mixture had been crystallized twice from a cyclohexane-benzene mixture. Further crystallization from a cyclohexane-benzene mixture (10:1) produced colorless needles, m.p. 135–136°.

Anal. Calc'd for $C_{10}H_{15}NO_4$: C, 56.32; H, 7.09; N, 6.57. Found: C, 56.20; H, 6.96; N, 6.75.

1-n-Butyl-4-carbethoxy-2,3-dioxopyrrolidine. Yield, 98 g. (78.5%) of colorless needles, m.p. 133–134°, from 40 g. (0.55 mole) of *n*-butylamine, 55 g. (0.55 mole) of ethyl acrylate, 80 g. (0.55 mole) of diethyl oxalate, and 13 g. (0.55 g.-atom) of sodium. Crystallization from 50% ethanol raised the m.p. to 136.5–137.5°.

Anal. Calc'd for $C_{11}H_{17}NO_4$: C, 58.13; H, 7.54; N, 6.16. Found: C, 58.00, H, 7.48; N, 6.19.

1-Isobutyl-4-carbethoxy-2,3-dioxopyrrolidine. Yield, 75 g. (65.5%) of long, flat, colorless needles, m.p. 142–144°, from 37 g. (0.505 mole) of isobutylamine, 50.5 g. (0.505 mole) of ethyl acrylate, 74 g. (0.505 mole) of diethyl oxalate, and 11.6 g. (0.505 g.-atom) of sodium. Crystallization from a high-boiling petroleum ether-benzene mixture (10:1) raised the m.p. to 155–156°.

Anal. Calc'd for $C_{11}H_{17}NO_4$: C, 58.13; H, 7.54; N, 6.16. Found: C, 58.45, 58.50; H, 7.69, 7.61; N, 6.20.

1-tert-Butyl-4-carbethoxy-2,3-dioxopyrrolidine. Yield, 64 g. (56.5%) of very light-yellow needles, m.p. 120–121°, from 36.5 g. (0.5 mole) of *tert*-butylamine, 50 g. (0.5 mole) of ethyl acrylate, 73 g. (0.5 mole) of diethyl oxalate, and 11.5 g. (0.505 g.-atom) of sodium. The mixture of *tert*-butylamine, ethyl acrylate, and 200 ml. of absolute ethyl alcohol was refluxed for one hour on a steam-cone, and then was allowed to stand for 24 hours. Crystallization from high-boiling petroleum ether produced stout colorless needles, m.p. 126.5–127.5°.

Anal. Calc'd for $C_{11}H_{17}NO_4$: C, 58.13; H, 7.54; N, 6.16. Found: C, 57.94; H, 7.46; N, 6.12.

1-β-Phenylethyl-4-carbethoxy-2,3-dioxopyrrolidine. Yield, 191 g. (69%) of colorless crystalline flakes, m.p. 159°, from 122 g. (1.01 mole) of β-phenylethylamine, 101.3 g. (1.01 mole) of ethyl acrylate, 148 g. (1.01 mole) of diethyl oxalate, and 23.2 g. (1.01 g.-atoms) of sodium in 400 ml. of absolute ethyl alcohol. Crystallization from 95% ethanol produced long, narrow colorless plates, m.p. 159–159.5°.

Anal. Calc'd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.40; H, 6.13; N, 5.35.

Preparation of 3-acetoxy-4-carbethoxy-2-oxo-3-pyrrolines

(13) Few compounds of established structure related to 3,3′-bipyrrolidine are described in the literature. For examples, mainly of unsaturated derivatives, for which correct structural assignments have probably been made, see Knott, *J. Chem. Soc.*, 1196 (1947) and Gabriel, *Ber.*, **47**, 3033 (1914).

(14) Melting points are corrected. Microanalyses are by Micro Tech Laboratories, Skokie, Illinois; Drs. G. Weiler and F. B. Strauss, Oxford, England; Geller Laboratories, Hackensack, New Jersey; and O. E. Harris, University of Pittsburgh, Pittsburgh, Pennsylvania.

(15) This procedure gave 1-benzyl-4-carbethoxy-2,3-dioxopyrrolidine in 79% yield and 1-cyclohexyl-4-carbethoxy-2,3-dioxopyrrolidine in 65% yield. Since the properties of these two compounds were described previously (Ref. 4), no further details concerning them are given below.

(IV). The stream of gas from a ketene generator[16] was passed for 40–45 minutes through a solution of 2–5 g. of the 4-carbethoxy-2,3-dioxopyrrolidine in 75 ml. of chloroform which had been warmed initially to dissolve at least a part of the starting material. During this period any suspended starting material dissolved and the color of the solution changed from yellow to pale green. Concentration of the mixture at room temperature under reduced pressure left a solid residue. This material was washed with 50 ml. of cold ether and purified by recrystallization or sublimation as described below for the individual compounds.

3-Acetoxy-4-carbethoxy-2-oxo-3-pyrroline. Yield, 2 g. (80%), m.p. 148–149°, from 2 g. of 4-carbethoxy-2,3-dioxopyrrolidine; this compound was obtained as flat, colorless needles, m.p. 152–154°, following crystallization from toluene.

Anal. Calc'd for $C_9H_{11}NO_5$: C, 50.70; H, 5.20; N, 6.57. Found: C, 50.87; H, 5.33; N, 6.60.

3-Acetoxy-4-carbethoxy-1-isopropyl-2-oxo-3-pyrroline. Yield, 3.5 g. (58%) from 5 g. of 4-carbethoxy-1-isopropyl-2,3-dioxopyrrolidine; the substance was obtained as colorless prisms, m.p. 55.5–57.5°, following crystallization from a 3:1 mixture of low-boiling petroleum ether and toluene.

Anal. Calc'd for $C_{12}H_{17}NO_5$: C, 56.46; H, 6.71; N, 5.49. Found: C, 56.64; H, 6.54; N, 5.44.

3-Acetoxy-4-carbethoxy-1-methyl-2-oxo-3-pyrroline. Yield, 5 g. (81%) from 5 g. of 4-carbethoxy-1-methyl-2,3-dioxopyrrolidine; this material was obtained as stout colorless prisms, m.p. 91.5–93.5°, following crystallization from water. The compound is also readily purified by vacuum sublimation.

Anal. Calc'd. for $C_{10}H_{13}NO_5$: C, 52.86; H, 5.77; N, 6.17. Found: C, 52.87; H, 5.59; N, 6.23.

When a 0.9-g. sample of this compound was heated in 10 ml. of refluxing 95% ethanol containing one drop of concentrated sulfuric acid, 4-carbethoxy-1-methyl-2,3-oxopyrrolidine was obtained. The ethanolysis did not proceed in the absence of the sulfuric acid.

Attempted saponification of 3-acetoxy-4-carbethoxy-1-methyl-2-oxo-3-pyrroline with one equivalent of aqueous ethanolic potassium hydroxide resulted in the immediate formation of a deep-blue pigment. Acidification of the basic solution with hydrochloric acid did not alter the deep blue color. The pigment was partially precipitated by diluting the solution with water and allowing the mixture to stand in a refrigerator. When dried, the blue material failed to melt below 350°.

Anal. Found: C, 55.70; H, 5.37; N, 7.50.

Acetylation of sodium p-aminobenzoate by 3-acetoxy-4-carbethoxy-1-methyl-2-oxo-3-pyrroline (IV, R = CH_3). A solution prepared from 1.5 g. (0.011 mole) of *p*-aminobenzoic acid and 1.9 g. (0.022 mole) of sodium bicarbonate in 15 ml. of water was mixed with a solution of 2.5 g. (0.011 mole) of 3-acetoxy-4-carbethoxy-1-methyl-2-oxo-3-pyrroline in 10 ml. of hot water. The mixture turned dark red. It was swirled until the evolution of carbon dioxide ceased, then allowed to cool in a refrigerator. Acidification to *p*H 3 with 30% hydrochloric acid precipitated 2.8 g. of a grey-green solid, m.p. *ca.* 205°. Recrystallization from water with charcoal decolorization yielded 0.5 g. (a 25.5% yield) of *p*-acetylaminobenzoic acid, m.p. 260–261°, which did not depress the m.p. of an authentic sample.

Conversion of 3-acetoxy-4-carbethoxy-1-methyl-2-oxo-3-pyrroline (IV, R = CH_3) *into 1-methyl-2-pyrrolidone-4-carboxylic acid* (VI). A 6.2-g. (0.027 mole) sample of 3-acetoxy-4-carbethoxy-1-methyl-2-oxo-3-pyrroline was dissolved in 50 ml. of glacial acetic acid and hydrogenated for 13 hours over an Adams' platinum oxide catalyst (*ca.* 50 mg.) using an initial hydrogen pressure of 46 lbs./sq. in. After removal of the catalyst and concentration of the solution by distillation, the residual oil was distilled under reduced pressure. The product, 4-carbethoxy-1-methyl-2-pyrrolidone, was collected at 110–112° (1 mm.).[17] The yield was 3.7 g. (79%).

A 1.5-g. (0.009 mole) sample of this ester was saponified by dissolving it in a solution prepared from 0.75 g. (0.013 mole) of potassium hydroxide, 2 ml. of water, and 10 ml. of 95% ethanol and allowing the mixture to stand in a refrigerator for several days. Following acidification to Congo Red with 20% hydrochloric acid, the precipitated potassium chloride was removed by filtration and the solution was evaporated to yield a solid product, which was obtained as colorless needles, m.p. 153–154° following crystallization from ethyl acetate.

Anal. Calc'd for $C_6H_9NO_3$: C, 50.34; H, 6.34; N, 9.79. Found: C, 50.13, 50.39; H, 6.25, 6.34; N, 9.72.

For purposes of comparison a sample of this compound was also made by means of the reaction of itaconic acid with methylamine.[7] A mixture of 10 g. (0.077 mole) of itaconic acid and 10 g. (0.0805 mole) of 25% aqueous methylamine was heated under reflux for 40 minutes. The water was removed by distillation under reduced pressure. The residue, which solidified upon cooling, was recrystallized from ethyl acetate to yield 7 g. (63.5% yield) of colorless needles, m.p. 152–153.5°. Further crystallization gave a product melting at 153–154° which did not depress the m.p. of the product prepared by the other method.

Preparation of 1-substituted-2,3-dioxopyrrolidines (VIII). The 1-substituted-4-carbethoxy-2,3-dioxopyrrolidines were refluxed with hydrochloric acid at least until the solution no longer gave a ferric chloride test. In some cases ethanol was added in the beginning to aid in dissolving the starting material. At the end of the heating period a clear solution had usually been obtained, but sometimes small amounts of suspended solids were present. The solutions were cooled to room temperature, filtered if necessary, and extracted with chloroform, using two to three 50-ml. portions of chloroform when there was *ca.* 200 ml. of acid solution to be extracted. The combined chloroform extracts were concentrated under reduced pressure to yield the crude 1-substituted-2,3-dioxopyrrolidine, which usually crystallized at once or after a short period of standing.

Phenylhydrazones[18] and *oximes*[19] were made by standard procedures and were purified by crystallization from 95% ethanol. *Anils* were obtained by heating *ca.* 0.5 g. of the 2,3-dioxopyrrolidine with an equivalent quantity of aniline in 10–25 ml. of 95% ethanol for 15 minutes to 1 hour on a steam-cone. The anils separated when the solutions were cooled, and were recrystallized from 95% ethanol.

Individual compounds are described below:

1-Cyclohexyl-2,3-dioxopyrrolidine. Yield, 5.1 g. (71%) from 10 g. (0.04 mole) of 1-cyclohexyl-4-carbethoxy-2,3-dioxopyrrolidine heated for 2 hours with 200 ml. of 20% hydrochloric acid and 35 ml. of ethanol; obtained as colorless flakes, m.p. 93.5–95° after several crystallizations from a 2.5:1 ether-petroleum ether (b.p. 30–60°) mixture.

Anal. Calc'd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73. Found: C, 66.28; H, 8.43; N, 7.54.

The anil was obtained as white flakes, m.p. 221°.

Anal. Calc'd for $C_{16}H_{20}N_2O$: C, 75.00; H, 7.57; N, 10.52. Found: C, 74.85; H, 7.80; N, 10.94.

The phenylhydrazine derivative was obtained as light-yellow flakes, m.p. 213–214°.

Anal. Calc'd for $C_{16}H_{21}N_3O \cdot H_2O$: C, 66.41; H, 8.01; N, 14.52. Found: C, 66.20; H, 8.20; N, 14.90.

1-n-Butyl-2,3-dioxopyrrolidine. Yield, 3 g. (88%), m.p. 47–52°, from 5 g. of 1-*n*-butyl-4-carbethoxy-2,3-dioxopyrrolidine heated for 1 hour with 200 ml. of 10% hydrochloric acid; obtained as thin colorless plates, m.p. 56.5–57° follow-

(16) Hanford and Sauer, *Org. Reactions*, **3**, 132 (1946).

(17) This ester was prepared previously by another method. See Uhle, *J. Am. Chem. Soc.*, **73**, 2402 (1951).

(18) Shriner and Fuson, *Identification of Organic Compounds*, 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 116.

(19) Ref. 18, p. 202.

ing recrystallization by diluting a concentrated benzene solution of the compound with cyclohexane at room temperature.

Anal. Calc'd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 62.01, 61.94; H, 7.94, 8.81; N, 9.33, 8.82.

The anil was obtained as colorless needles, m.p. 150.5–151.5°.

Anal. Calc'd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.17. Found: C, 72.65, 72.90; H, 7.77, 7.97; N, 11.84, 12.40.

The phenylhydrazone was obtained as thin colorless plates, m.p. 195–196°.

Anal. Calc'd for $C_{14}H_{19}N_3O$: C, 68.54; H, 7.81; N, 17.13. Found: C, 68.50; H, 7.94; N, 16.90.

1-Isobutyl-2,3-dioxopyrrolidine. Yield, 2.6 g. (76%) from 5 g. of 1-isobutyl-4-carbethoxy-2,3-dioxopyrrolidine heated for 90 min. with 200 ml. of 10% hydrochloric acid; obtained as colorless plates, m.p. 59–60°, by diluting a concentrated toluene solution of the compound with low-boiling petroleum ether at room temperature.

Anal. Calc'd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 62.05; H, 8.37; N, 9.05.

The anil was obtained as colorless needles, m.p. 170–171°.

Anal. Calc'd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.17. Found: C, 72.80; H, 7.98; N, 12.30.

1-tert-Butyl-2,3-dioxopyrrolidine: Yield, 4.7 g. (69%), m.p. 94–97°, from 10 g. of 1-*tert*-butyl-4-carbethoxy-2,4-dioxopyrrolidine heated for 2 hours with 250 ml. of 10% hydrochloric acid; obtained by crystallization from toluene as needles, m.p. 103.5–104°, with a light-tan discoloration.

Anal. Calc'd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 62.30, 62.25, 62.09; H, 8.58, 8.47, 8.56; N, 9.20.

The anil was obtained as colorless flakes, m.p. 185.5–186.5°.

Anal. Calc'd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.17. Found: C, 72.90; H, 7.79; N, 11.90.

The phenylhydrazone was obtained as yellow rectangular plates, m.p. 203–205°.

Anal. Calc'd for $C_{14}H_{19}N_3O$: C, 68.54; H, 7.81; N, 17.13. Found: C, 68.40; H, 7.80; N, 17.20.

1-Phenyl-2,3-dioxopyrrolidine. Yield, 1.5 g. (41%), m.p. 128–138°, from 5 g. (0.022 mole) of 1-phenyl-4-carbethoxy-2,3-dioxopyrrolidine[4] heated for 4 hours with 250 ml. of 10% HCl to which 25 ml. of 95% ethanol had been added; obtained as colorless thin sheets, m.p. 154–155° (red melt) after recrystallization from toluene.

Anal. Calc'd for $C_{10}H_9NO_2$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.30; H, 5.13; N, 8.35.

The anil was obtained as plates with a light-pink coloration, m.p. 188–190° (red melt).

Anal. Calc'd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.41; H, 5.49; N, 11.22.

1-β-Phenylethyl-2,3-dioxopyrrolidine. Yield, 12 g. (81%), m.p. 159–160°, from 20 g. (0.073 mole) of 1-β-phenylethyl-4-carbethoxy-2,3-dioxopyrrolidine heated for 70 minutes with 500 ml. of 20% hydrochloric acid; obtained as tiny white prisms, m.p. 161–162°.

Anal. Calc'd for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.45; N, 6.89. Found: C, 70.90; H, 6.46; N, 6.93.

The phenylhydrazone was obtained as short yellow needles, m.p. 214–215°.

Anal. Calc'd for $C_{18}H_{19}N_3O$: C, 73.80; H, 6.53; N, 14.33. Found: C, 73.80; H, 6.82; N, 13.90, 14.10.

The oxime was obtained as colorless needles, m.p. 189–190°.

Anal. Calc'd for $C_{12}H_{14}N_2O_2$: C, 66.03; H, 6.47; N, 12.84. Found: C, 66.08; H, 6.02; N, 13.11.

1-Benzyl-2,3-dioxopyrrolidine. This compound has been described before,[4] but the following derivatives are new:

The anil was obtained as colorless needles or granules, m.p. 154–155°.

Anal. Calc'd for $C_{17}H_{16}N_2O$: C, 77.20; H, 6.11; N, 10.61. Found: C, 77.59; H, 6.24; N, 10.78.

The phenylhydrazone was obtained as light yellow needles, m.p. 187–188°.

Anal. Calc'd for $C_{17}H_{17}N_3O$: C, 73.20; H, 6.09; N, 15.05. Found: C, 73.05; H, 6.16; N, 14.80.

The oxime was obtained as colorless needles, m.p. 219°.

Anal. Calc'd for $C_{11}H_{12}N_2O_2$: C, 64.75; H, 5.88; N, 13.72. Found: C, 64.63; H, 6.01; N, 13.30, 13.33.

1-Isopropyl-2,3-dioxopyrrolidine. This substance was not obtained in completely purified form. However, crystalline derivatives were prepared from the oil obtained when 5 g. (0.024 mole) of 1-isopropyl-4-carbethoxy-2,3-dioxopyrrolidine was hydrolyzed by heating for 90 minutes with 200 ml. of 10% hydrochloric acid using the usual procedure. On one occasion a small amount of solid was obtained, m.p. 42–48°, which may have represented a fairly pure sample of the 2,3-dioxopyrrolidine.

The anil was obtained as colorless plates, m.p. 130.5–131.5°.

Anal. Calc'd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found: C, 71.80, 72.20; H, 7.13, 7.47; N, 13.22.

The phenylhydrazone was obtained as broad, colorless needles, m.p. 187–188°.

Anal. Calc'd for $C_{13}H_{17}N_3O$: C, 67.50; H, 7.41; N, 18.17. Found: C, 67.35; H, 7.47; N, 17.90.

1-Substituted-3-hydroxy-2-oxopyrrolidines. The 1-substituted-2,3-dioxopyrrolidines were dissolved in 95% ethanol or glacial acetic acid and hydrogenated over an Adams' platinum oxide catalyst. After removal of the catalyst and distillation of the solvent, the products were purified by crystallization or vacuum sublimation. These substances sublime very readily. Data on individual compounds are given below:

1-*n-Butyl-3-hydroxy-2-oxopyrrolidine.* Yield, 1.5 g. (87%) after a 2.5-hour hydrogenation of 1.7 g. (0.011 mole) of 1-*n*-butyl-2,3-dioxopyrrolidine in 25 ml. of ethanol over 50 mg. of catalyst; obtained as a colorless oil, b.p. 105–107° (1–2 mm.). The compound was characterized as a *phenylurethan* by treating a 0.5 g.-sample of the oil with 0.4 g. of phenyl isocyanate as in the procedure of Shriner and Fuson.[20] The yield was 0.9 g. (quantitative) of a white derivative, m.p. 93–97°. Further recrystallization from a 5:1 high-boiling petroleum ether-benzene mixture gave small colorless prisms, m.p. 98.5–100°.

Anal. Calc'd for $C_{15}H_{20}N_2O_3$: C, 65.19; H, 7.30; N, 10.14. Found: C, 65.48; H, 7.60; N, 10.26.

1-Cyclohexyl-3-hydroxy-2-oxopyrrolidine. Yield, 2.9 g. (83%) after a 5.5-hour hydrogenation of 3.4 g. (0.019 mole) of 1-cyclohexyl-2,3-dioxopyrrolidine in 100 ml. of ethanol over 40 mg. of catalyst; obtained as colorless crystals, m.p. 117–119° after purification by vacuum sublimation.

Anal. Calc'd for $C_{10}H_{17}NO_2$: C, 65.54; H, 9.35; N, 7.64. Found: C, 65.70; H, 9.31; N, 7.68.

1-Benzyl-3-hydroxy-2-oxopyrrolidine (X). Yield, 4.3 g. (77.5%) after a 2-hour hydrogenation of 5.5 g. (0.29 mole) of 1-benzyl-2,3-dioxopyrrolidine in 200 ml. of ethanol over 50 mg. of catalyst; obtained as an oil which solidified to a tan solid, m.p. 67.5–69° when a concentrated solution in toluene was diluted with high-boiling petroleum ether and allowed to stand in a refrigerator overnight. Purification by recrystallization from cyclohexane, or more readily by vacuum sublimation, gave colorless needles, m.p. 69–70°.

Anal. Calc'd for $C_{11}H_{13}NO_7$: C, 69.09; H, 6.85; N, 7.33. Found: C, 68.75; H, 6.87; N, 7.11.

The acetate. Treatment of 5 g. (0.026 mole) of 1-benzyl-3-hydroxy-2-oxopyrrolidine with 20 g. of acetyl chloride, concentration of the mixture under reduced pressure, and crystallization of the product from high-boiling petroleum ether yielded 5.5 g. (91%) of thin colorless plates, m.p. 67–68°.

Anal. Calc'd for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.48; N, 6.01. Found: C, 66.88; H, 6.68; N, 6.35.

The phenylurethan. This derivative was prepared in 74% yield using a procedure of Shriner and Fuson;[20] obtained as

(20) Ref. 18, pp. 163–164.

fine, short, colorless needles, m.p. 149–150° following crystallization from carbon tetrachloride.

Anal. Calc'd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.45; H, 5.66; N, 9.31.

1-β-Phenylethyl-3-hydroxy-2-oxopyrrolidine. Yield, 5.6 g. (77%), m.p. 126–127°, after a 2-hour hydrogenation of 8.7 g. (0.043 mole) of 1-β-phenylethyl-2,3-dioxopyrrolidine in 200 ml. of acetic acid over 50 mg. of catalyst. Purification by crystallization from a 1:1 benzene-cyclohexane mixture gave colorless needles, m.p. 128–129°.

Anal. Calc'd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.27; H, 7.44; N, 6.89.

1-Substituted-3-hydroxypyrrolidines. Somewhat different procedures were used in the preparation of two compounds of this type.

1-Benzyl-3-hydroxypyrrolidine (XI). An ethereal solution of 4.4 g. (0.023 mole) of 1-benzyl-3-hydroxy-2-oxopyrrolidine was added over a period of one hour to 170 ml. of an approximately 1 *molar* ethereal solution of lithium aluminum hydride. The mixture then was heated under reflux for one hour. The excess lithium aluminum hydride was destroyed by cautious addition of water, 500 ml. of 10% sodium hydroxide was added, and the mixture was extracted with 850 ml. of ether used in 4 separate portions. The combined ether extracts were filtered, dried over calcium sulfate, and concentrated by distillation. Distillation of the residual oil yielded 2.5 g. (61%) of a colorless product, b.p. 113–115° (2 mm.). The same product was obtained in 65% yield by a similar reduction of the acetate of 1-benzyl-3-hydroxy-2-oxopyrrolidine.

The product was characterized in the form of the *3,5-dinitrobenzoate hydrochloride.* The 3,5-dinitrobenzoate was prepared according to a procedure of Shriner and Fuson[21] using 0.8 g. (0.0045 mole) of 1-benzyl-3-hydroxypyrrolidine, 1 g. (0.0045 mole) of 3,5-dinitrobenzoyl chloride, and 6 ml. of dry pyridine. The yield was 1.5 g. (89%) of a product melting at 110–112° which proved difficult to recrystallize. It was dissolved in ether and precipitated as the hydrochloride by addition of dry hydrogen chloride. Following recrystallization from absolute ethanol, short, nearly colorless needles were obtained, m.p. 230–231° (decomposition).

Anal. Calc'd for $C_{18}H_{18}ClN_3O_6$: C, 53.01; H, 4.42; N, 10.30. Found: C, 53.21; H, 4.47; N, 9.94, 10.26.

1-β-Phenylethyl-3-hydroxypyrrolidine. 1-β-phenylethyl-3-hydroxy-2-oxopyrrolidine (7.5 g., 0.036 mole) was extracted from the thimble of a Soxhlet extractor during a period of 22 hours into a solution prepared from 3.5 g. (0.1 mole) of lithium aluminum hydride in 200 ml. of ether. The reaction mixture was treated with 100 ml. of 20% sodium potassium tartrate, and the layers were separated. The aqueous layer was extracted 3 times with 150 ml. portions of ether and the combined ether solutions were dried over Drierite and concentrated by distillation. The residual oil distilled at 145° (2 mm.) to yield 6.4 g. (94%) of a colorless oil which solidified to a waxy white solid, m.p. 30–35°.

The compound was not easily crystallized as the free base, and was characterized as the *p-toluenesulfonate,* prepared by adding an equivalent of *p*-toluenesulfonic acid to the free base in a small volume of ethanol, removing the solvent by distillation, and recrystallizing the residue from ethyl acetate to yield colorless needles, m.p. 137–138.5°.

Anal. Calc'd for $C_{19}H_{25}NO_4S$: C, 62.79; H, 6.93; N, 3.85. Found: C, 62.35; H, 6.89; N, 3.52.

SELF-CONDENSATION PRODUCTS OF 1-SUBSTITUTED-2,3-DIOXOPYRROLIDINES

1,1'-Dicyclohexyl-2,4',5'-trioxo-3-hydroxy-3,3'-bipyrrolidine (XVI or XVII, R = cyclohexyl). To a solution of 2.5 g. (0.055 mole) of 1-cyclohexyl-2,3-dioxopyrrolidine in 10 ml. of warm 95% ethanol was added 1.1 g. (0.055 mole) of pyridine. The resulting mixture was diluted almost immediately with 100 ml. of water. A solid precipitated promptly, but the mixture was allowed to cool for several hours in the refrigerator before the precipitate (2.4 g., a 96% yield) was removed by filtration. The substance melted at *ca.* 232° (decomposition). It was crystallized by dissolving it in chloroform, filtering out traces of insoluble material, and adding high-boiling petroleum ether; tiny colorless needles were obtained, m.p. 268–269° when the temperature of the sample was raised slowly from 200°. However, when placed in a melting point block at 240–250° the solid collapsed immediately and resolidified before finally melting near 268°. (The upper melting point is probably actually that of the dehydration product described in the next section.)

Anal. Calc'd for $C_{20}H_{30}N_2O_4$: C, 66.27; H, 8.34; N, 7.73; Mol. Wt., 362.46. Found: C, 66.30; H, 8.63; N, 7.54; Mol. Wt., 437, 440 (Menzies-Wright ebullioscopic method, chloroform).

The compound gives a purple color with ferric chloride. It is soluble in 5% aqueous sodium hydroxide solution.

1,1'-Dicyclohexyl-2,4',5'-trioxo-3,3'-bipyrrolidylidene (XIX, R = cyclohexyl). A suspension of 1.3 g. of 1,1'-dicyclohexyl-2,4',5'-trioxo-3-hydroxy-3,3'-bipyrrolidine in 50 ml. of 20% hydrochloric acid was refluxed for 6 hours. The mixture was cooled, and 1 g. of a light-tan solid, m.p. 271–272° (decomposition), was collected by filtration. Another 0.1 g. of similar material was obtained by chloroform extraction of the acid filtrate, to bring the yield to 1.1 g. (92%). Crystallization from dioxane or 95% ethanol gave short, light-yellow needles, m.p. 273–274° with decomposition. The compound has also obtained from the same starting material simply by vacuum sublimation.

Anal. Calc'd for $C_{20}H_{28}N_2O_3$: C, 69.74; H, 8.19; N, 8.13; Mol. Wt., 344.44. Found: C, 69.72, 69.75; H, 7.69, 8.37; N, 8.00; Mol. Wt., 362 (Menzies-Wright ebullioscopic method, chloroform).

The substance gives a pale-green color with ferric chloride.

1-Cyclohexyl-2-oxo-3-methoxy-4-(1-cyclohexyl-2-oxo-3-hydroxy-3-pyrrolidyl)-3-pyrroline (XVIII). To a suspension of 1 g. (0.0028 mole) of 1,1'-dicyclohexyl-2,4',5'-trioxo-3-hydroxy-3,3'-bipyrrolidine in 60 ml. of chloroform was added an excess of ethereal diazomethane. The starting material dissolved as the reaction proceeded. The mixture was allowed to stand overnight before the excess of diazomethane was destroyed by addition of *ca.* 5 ml. of glacial acetic acid. The ethereal solution was washed successively with water, 5% sodium hydroxide and water, then was dried over magnesium sulfate. Evaporation of the solvent left a tan oil which crystallized from a 1:5 toluene-cyclohexane solution when the mixture was allowed to stand overnight in a refrigerator. The solid which separated was removed by filtration and was washed with a small amount of cold ether. The yield was 0.4 g. (38.5%) of a colorless crystalline powder, m.p. 101–103°. Recrystallization from cyclohexane raised the m.p. to 139–140°. The compound appeared to be hygroscopic, and the initial lower m.p. may be that of a hydrated or solvated form.

Anal. Calc'd for $C_{21}H_{32}N_2O_4$: C, 66.99; H, 8.57; N, 7.44; CH_3O, 8.24. Found: C, 67.06; H, 8.61; N, 7.49; CH_3O, 8.24.

1,1'-Dicyclohexyl-3,4'-dihydroxy-2,5'-dioxo-3,3'-bipyrrolidine (XXI). A suspension of 0.6 g. (0.00165 mole) of 1,1'-dicyclohexyl-2,4',5'-trioxo-3-hydroxy-3,3'-bipyrrolidine (XVI or XVII, R = cyclohexyl) in 50 ml. of absolute ethanol was hydrogenated over *ca.* 50 mg. of Adams' platinum oxide catalyst for 5 hours beginning at a pressure of 45 lbs./sq. in. After removal of the catalyst the filtrate was evaporated to leave 0.6 g. (95.5%) of a light-tan solid, m.p. 166–176° (dark melt). Crystallization from toluene produced short, colorless needles, m.p. 204–206° (dark-red, glassy melt). The compound does not give a color with ferric chloride.

Anal. Calc'd for $C_{20}H_{32}N_2O_4$: C, 65.90; H, 8.85; N, 7.69. Found: C, 66.34; H, 8.91; N, 7.67.

1,1'-Di-tert-butyl-2,4',5'-trioxo-3-hydroxy-3,3'-bipyrrolidine (XVI or XVII, R = *tert*-butyl). In an attempt to recrystallize

(21) Ref. 18, pp. 164–165.

a sample of 1-*tert*-butyl-2,3-dioxopyrrolidine from hot toluene the compound was quantitatively transformed into a white powdery solid, m.p. 165° (red melt) which was insoluble in hot toluene. The substance was recrystallized by dissolving it in a small amount of warm chloroform, removing a small amount of insoluble impurities by filtration, and diluting the filtrate with high-boiling petroleum ether. The compound was obtained as short, colorless needles, m.p. 165° (red melt) and further crystallization did not raise the m.p.

Anal. Calc'd for $C_{16}H_{26}N_2O_4$: C, 61.91; H, 8.44; N, 9.03. Found: C, 62.24; H, 8.46; N, 8.82.

The compound gives a purple color with ferric chloride.

1,1'-Di-tert-butyl-2,4',5'-trioxo-3,3'-bipyrrolidylidene (XIX, R = *tert*-butyl). To a solution of 1 g. (0.0065 mole) of 1-*tert*-butyl-2,3-dioxopyrrolidine in 10 ml. of warm 95% ethanol was added 0.51 g. (0.0065 mole) of pyridine. The resulting mixture was diluted with 200 ml. of water, then was allowed to stand for several days in the refrigerator. The precipitated light-tan needles (0.9 g., 95.5% yield) melted at 188–190° (dark melt). Crystallization from 50% ethanol produced short, almost colorless needles, m.p. 190–191° (orange, glassy melt).

Anal. Calc'd for $C_{16}H_{24}N_2O_3$: C, 65.72; H, 8.27; N, 9.58. Found: C, 65.25, 65.20; H, 8.30, 8.51; N, 9.08, 9.36.

The compound gave a blue-green color with ferric chloride.

Reaction of 1-benzyl-2,3-dioxopyrrolidine (VIII, R = *benzyl*) *with formamide.* A mixture of 3 g. (0.0159 mole) of 1-benzyl-2,3-dioxopyrrolidine and 80 ml. of formamide was heated at the reflux temperature for 2 hours. After the mixture had been cooled in a refrigerator for several hours, 0.8 g. of greenish-black crystals with a bronze lustre, m.p. 351°, had separated and were removed by filtration. Recrystallization from dimethylformamide left the appearance of the compound unchanged and raised the m.p. only to 351–352° (decomposition).

Anal. Found: C, 74.06; H, 5.45; N, 9.56, 9.90.

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