potassium carbonate, and distilled. In no experiment was any methyl *s*-octyl ether found. (The ether was prepared independently from methyl iodide and sodium *s*-octoxide; b.p. 78–82° (42 mm.), n_D^{21} 1.4108.)

The aqueous carbonate solution was acidified to permit isolation of any organic acid. No significant amount of acid could be found in these experiments.

1. (−)*s-Octyl trimethylacetate* gave a 57% yield of methyl trimethylacetate (n_D^{20} 1.3894) and a 92% yield of (−)2-octanol (α_D^{20} −6.46°, n_D^{20} 1.4260).

2. (−)*s-Octyl t-butylacetate* gave a 61% yield of methyl *t*-butylacetate (n_D^{20} 1.3996) and a 93% yield of (−)2-octanol (α_D^{20} −6.44°, n_D^{20} 1.4255). The infrared spectrum of the alcohol indicated slight contamination by ester.

3. *s-Octyl diisopropylacetate*, even after 20 days, was recovered in 88% yield. Small amounts (less than 0.2 g.) of methyl diisopropylacetate and 2-octanol were also obtained.

4. *Methyl t-butylacetate* was recovered unchanged after 14 days refluxing. No attempt to trap methyl ether was made, but no *t*-butylacetic acid could be detected.

(*C*) *2-Propoxide in 2-propanol.* A solution prepared from 0.18 g.-atom of sodium metal, 275 ml. of anhydrous 2-propanol, and 0.13 mole of isopropyl *t*-butylacetate was refluxed for 5 days while being protected from atmospheric moisture. From the organic material extracted from the acidified mixture, no isopropyl ether nor *t*-butylacetic acid could be obtained. The unreacted ester was recovered.

(*D*) *Acid hydrolyses. 1.* (+)*s-Octyl trimethylacetate* (5.32 g., 0.025 mole) was dissolved in 60 ml. of aqueous 90% methanol which was 0.6*M* in HCl. The solution was refluxed for 4 days, diluted with water, and extracted with petroleum ether. The extract was washed with dilute carbonate solution and with water. Drying and distillation gave, in addition to about 6% recovery of *s*-octyl ester, a 12% yield of methyl trimethylacetate[24] and a 90% yield of (+)2-octanol (α_D^{20} +7.88°, n_D^{20} 1.4257).

2. (+)*s-Octyl t-butylacetate* (6.2 g., 0.027 mole) was treated in a similar fashion. There were obtained about 7% recovery of starting ester, 76% yield of methyl *t*-butylacetate and 83% yield of (+)2-octanol (α_D^{20} +7.77°, slight recemization).

3. When a solution of (+)*s-octyl diisopropylacetate* (4.7 g., 0.018 mole) in 60 ml. of aqueous 90% acetone, 0.6*M* in HCl, was refluxed for 12 days, no detectable reaction occurred.

Acknowledgment. We have appreciated helpful discussions with Dr. Harold Shechter about this study before experiments were begun, and with Dr. H. C. Brown and Dr. Samuel Siegel near its completion.

BATON ROUGE, LA.

(24) Some loss resulting from the difficulty of cleanly separating ester and petroleum ether may account for this low yield.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MICHIGAN]

1,5-Diaryl-2,3-pyrrolidinediones. VIII. Synthesis and Structure Proof

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1,5-Diphenyl-2,3-pyrrolidinedione (XI) has been synthesized and its structure has been proven. This material was found o be identical with the previously unidentified thermal decarboxylation product of 1,5-diphenyl-4-carbethoxy-2,3-pyrolidinedione, and distinctly different from the substance previously assigned this structure, which is now known to be 5-phenyl-3-anilino-2(5*H*)-furanone.

Many reports of 1,5-diaryl-2,3-pyrrolidinediones as the products of the reaction of a benzylideneaniline with pyruvic acid or of a benzylidenepyruvic acid with an aromatic amine have appeared in the literature since Schiff and Gigli[2] first reported 1,5-diphenyl-2,3-pyrrolidinedione itself. Although the formulation of these compounds has been accepted almost without question,[3] several curious aspects of their chemical behavior[4] and dissimilarities in properties and infrared spectra between these and 2,3-pyrrolidinediones with other types of substitution[4–6] suggested that a critical examination of the structure of the supposed 1,5-diaryl-2,3-pyrrolidinediones was in order.[7,8]

Previous investigators[9,10] have attempted degradative studies on the presumed 1,5-diphenyl-2,3-pyrrolidinedione (I) without conclusive results.

(1) National Science Foundation Predoctoral Fellow, 1954–1957. Abstracted from a portion of the Ph.D. dissertation of Walter L. Meyer, University of Michigan, 1957.

(2) R. Schiff and L. Gigli, *Ber.*, **31**, 1306 (1898).

(3) *Cf.*, however, K. Garzarolli-Thurnlackh, *Monatsh.*, **20**, 480 (1899).

(4) (a) W. R. Vaughan and L. R. Peters, *J. Org. Chem.*, **18**, 393 (1953); (b) W. R. Vaughan and L. R. Peters, *J. Org. Chem.*, **18**, 405 (1953); (c) W. R. Vaughan and D. I. McCane, *J. Org. Chem.*, **20**, 143 (1955); (d) W. R. Vaughan, *J. Org. Chem.*, **20**, 1619 (1955).

(5) (a) P. L. Southwick and L. L. Seivard, *J. Am. Chem. Soc.*, **71**, 2532 (1949); (b) P. L. Southwick and R. T. Crouch, *J. Am. Chem. Soc.*, **75**, 3413 (1953); (c) P. L. Southwick, E. P. Previc, J. Casanova, Jr., and E. H. Carlson, *J. Org. Chem.*, **21**, 1087 (1956).

(6) (a) R. Schiff and C. Bertini, *Ber.*, **30**, 601 (1897); (b) L. J. Simon and A. Conduché, *Ann. chim. phys.*, [8] **12**, 5 (1907).

(7) For a preliminary report on the results of this study see W. L. Meyer and W. R. Vaughan, *J. Org. Chem.*, **22**, 98 (1957).

(8) Since the publication of our preliminary report,[7] results of a study which reached the same conclusions have appeared, see H. H. Wasserman and R. C. Koch, *Chemistry & Industry*, 428 (1957).

(9) H. Bücherer and R. Russischwili, *J. Prakt. Chem.*, **128**, 89 (1930).

(10) S. Bodforss, *Ann.*, **455**, 41 (1927).

Thus it was determined that for a structure proof of I, unequivocal synthesis offered the most promising procedure.

For synthesis of the 2,3-pyrrolidinedione structure (Chart I), the starting materials of choice were the butyrolactams (II). Since a convenient procedure was available for the preparation of 1-phenyl-2-pyrrolidinone (IIb) from available starting materials,[11] pilot experiments on the introduction of a 3-keto function were carried out on this model.

For the introduction of functionality at the 3-position of the pyrrolidinone ring, the base-catalyzed formylation of an activated methylene position with ethyl formate was utilized. In spite of the weak activating influence of the amide carbonyl,[12] low yields of a crude semi-solid substance having properties expected of the desired 1-phenyl-3-hydroxymethylene-2-pyrrolidinone (III) could be obtained from this reaction. Although we were unable to purify this product, *O*-acyl derivatives were readily prepared and purified, serving

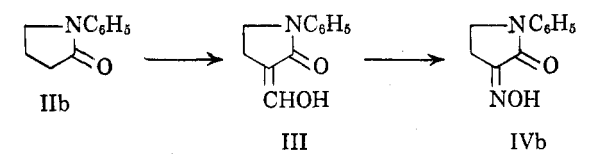
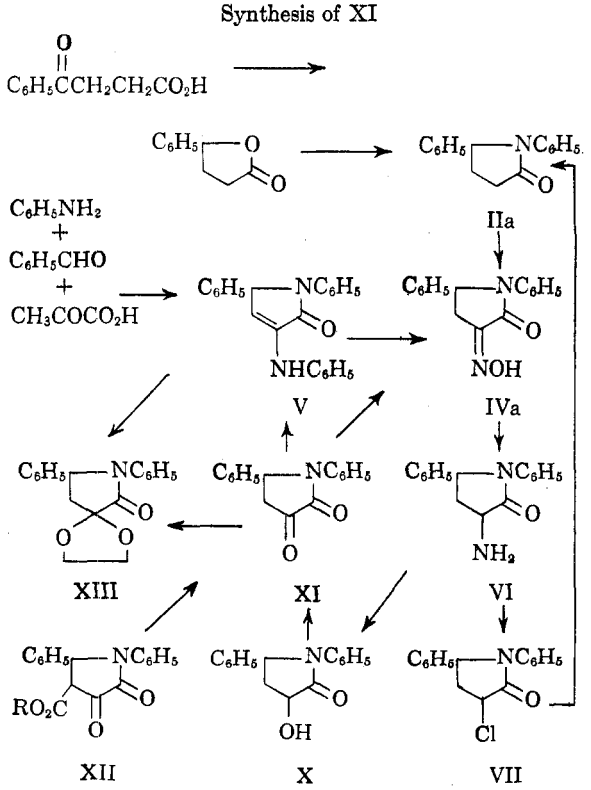


Chart I
Synthesis of XI



(11) E. Späth and J. Lintner, *Ber.*, 69, 2727 (1936).

(12) Other reagents designed to attack the 3-methylene group of IIb, *e.g.*, selenium dioxide, bromine, or amyl nitrite, failed to react, indicating the lactam methylene group to be very inactive.

further to characterize the hydroxymethylene compound (III).

Nitrosation of crude III at the reactive α-position with simultaneous cleavage of the formyl group afforded the 2,3-pyrrolidinedione-3-oxime (IVb). With the 1-phenyl compound, either aqueous nitrous acid or ethanolic amyl nitrite and base produced this conversion. In contrast to the hydroxymethylene compound III, 1-phenyl-3-oximino-2-pyrrolidinone (IVb) is a high-melting stable material, readily purified. However, even under the most fruitful reaction conditions employed, the yield of this oxime was very poor, 8.4% from the lactam IIb. Since all attempted hydrolysis experiments on IVb failed, attention was turned to the 1,5-diphenyl series, from which larger amounts of the corresponding oxime were available.

For the synthesis of 1,5-diphenyl-2-pyrrolidinone (IIa), γ-phenyl-γ-butyrolactone was conveniently prepared on a large scale by sodium borohydride reduction of β-benzoylpropionic acid. Application of our modified technique for reaction of a lactone with aniline afforded good yields of the desired lactam IIa.

In view of the difficulties encountered in the isolation and purification of the 1-phenyl-3-hydroxymethylene compound, reaction conditions were modified in such a manner as to obviate the isolation of the 1,5-diphenyl analog. Following the formylation step, the crude mixture was treated with sufficient alcohol to hydrolyze any excess sodium hydride, and butyl nitrite was added to effect the nitrosation. In this manner there was obtained a low yield of 1,5-diphenyl-3-oximino-2-pyrrolidinone (IVa). On treatment with acetic acid and acetic anhydride, an acetate, which was easily reconverted to the parent oxime, was readily obtained.

Bodforss[10] reported the preparation of an oxime by treatment of 1,5-diphenyl-3-anilino-2(5*H*)-pyrrolone (the pyrrolidinedione anil, V) with hydroxylamine hydrochloride and sodium ethoxide. His oxime was assigned the structure IVa, assuming replacement of the anil by oxime. However, Bodforss reported a rather ill-defined melting behavior for his material, which was incompletely characterized, whereas the IVa obtained in this work melted quite sharply with decomposition in a very reproducible manner. On repetition of Bodforss' procedure with some modification, we found it possible to obtain his oxime in excellent yields on a large scale. This material was found to be identical with the IVa produced by the formylation-nitrosation route, apparently confirming the structure assignment.

In view of the excellent yields in the oximation of V, and the ready availibility of V from pyruvic acid, benzaldehyde, and aniline,[13] there was at

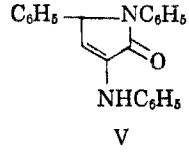
(13) W. R. Vaughan, *J. Org. Chem.*, 20, 1613 (1955).

hand a useful synthetic route to IVa. Although extensive research was undertaken toward its hydrolysis to the ketone, many common and several obscure methods for oxime cleavage being attempted, we were unable to find suitable conditions for this conversion. It would seem that 3-carbonyl derivatives of 1,5-diphenyl-2,3-pyrrolidinedione are extremely resistant to hydrolysis, for although the anil V may be converted to an ethylene ketal, it likewise has resisted cleavage; and the derived ethylene ketal is similarly unaltered under various hydrolytic conditions.

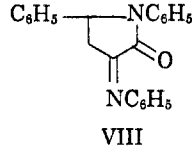
Catalytic hydrogenation of the oxime IVa over a platinum catalyst in acetic acid gave good yields of the primary amine VI. This amine, on treatment with nitrosyl chloride, smoothly afforded 1,5-diphenyl-3-chloro-2-pyrrolidinone (VII), which on catalytic hydrogenolysis in alcoholic base over palladium on calcium carbonate[14] yielded 1,5-diphenyl-2-pyrrolidinone (IIa). The identity of this substance with the sample previously prepared was confirmed by mixture melting point and identity of the infrared spectra of the two samples.

Thus it is assured that the pyrrolidinone skeleton has not been altered in any of the intermediates II through VII, and at the same time the structure IVa is confirmed.

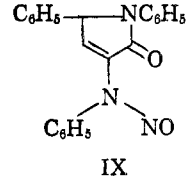
The arguments may now be extended to the anil V. Since this substance contains a replaceable anilino group, in the oxidation state of the anil, which is replaced by hydroxylamine to yield IVa, the anil function must also be at the 3-position of the lactam ring. Only two possible formulations allow this, V and VIII; and



V



VIII



IX

the infrared spectrum, as pointed out by Vaughan,[13] is inconsistent with VIII, since it contains a strong sharp absorption at 3300 cm.$^{-1}$ (NH).

Bodforss[10] reported the conversion of the anil to a derivative by treatment with sodium nitrite in hot glacial acetic acid. For unexplained reasons he postulated this compound to be a nitro derivative, although the sole analytical figure reported, (nitrogen) is in better agreement with the nitroso derivative. Since it was insoluble in sodium hydroxide, he postulated the "nitro" group to have entered one of the aromatic rings. The derivative was described as a yellow compound of melting point 143°.

We have been unable to duplicate this result. Rather, when the anil was subjected to Bodforss' conditions, a red mono*nitroso* derivative (IX) which melted with decomposition at 271–272° was obtained.[15] The nitroso derivative is transparent in the high frequency (3000-4000 cm.$^{-1}$) region of the infrared, but otherwise has a spectrum which resembles that of the anil V. Thus it must be formulated as the *N*-nitroso derivative, chemically confirming the presence of an NH function in V. It was not found possible to obtain a positive Liebermann test for the *N*-nitroso group of IX, although the formation of the various colors characteristic of the test may easily have been masked by the intense color of IX itself. Thus both chemical and physical evidence demand an NH group in the anil, and the formulation of Vaughan[13] (V) is confirmed.

On treatment of the hydrochloride of VI with aqueous sodium nitrite, VI afforded the corresponding alcohol X in nearly quantitative yield.[16] Under rigidly controlled conditions, similar to those of Bruce[17] for the oxidation of dihydrocholesterol, chromic acid in aqueous acidic solution oxidized the alcohol in benzene solution to a ketonic product. This substance, the pyrrolidinedione XI, was difficult to separate from starting material and a second contaminant, but the characteristic nature of its infrared spectrum (as described below) and the preparation of pure derivatives, an anil identical with the intermediate V (of proven structure) and an ethylene ketal (*vide infra*) served for its characterization.

The formation of these derivatives confirms the hypothesis drawn from the infrared spectrum that the oxidation product is 1,5-diphenyl-2,3-pyrrolidinedione (XI). They demonstrate the presence of a ketonic carbonyl group in the material by their very formation, and the position of this new carbonyl must be *3*, since V has been shown to have the anil function at the *3* position.

1,5-Diphenyl-4-carbethoxy-2,3-pyrrolidinedione (XII) is known to decarboxylate on heating in nitrobenzene, but the organic product of this pyrolysis was not identified.[4c] This substance has now been isolated and purified, and was found to have an infrared spectrum similar to that of the XI obtained by oxidation of X.[18] We have determined

(14) M. Busch and H. Stöve, *Ber.*, **49**, 1063 (1916).

(15) Since it was found in the present work that at lower reaction temperatures significant amounts of anil were recovered, lowering the melting point and decreasing the intensity of the color of the product, it is suspected that Bodforss' material was the same as ours, but highly contaminated with unreacted anil.

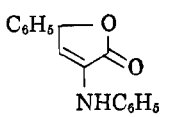
(16) A compound for which the structure X was offered was reported by Wasserman and Koch, *cf.* ref. 8, who oxidized it to what appears to be XI. While their compound melted 50° above our X, we have found our X and that of Wasserman and Koch to have *very similar* (but not identical) infrared spectra and to be monomeric. It is possible that they are epimers.

(17) W. F. Bruce, *Org. Syntheses*, **Coll. Vol. II**, 139 (1943).

(18) A pure product from the thermal decomposition of XII was first obtained by Mrs. I. S. Covey in independent work in these laboratories. We are indebted to Mrs. Covey for communication of her results and observations to us prior to publication. [W. R. Vaughan and I. S. Covey, paper in preparation].

that this "decarbethoxylation"[19] product of XII is in fact 1,5-diphenyl-2,3-pyrrolidinedione (XI). A sample of XI prepared in this manner readily affords an anil (V), an oxime (IVa), and an ethylene ketal (XIII). The first two of these derivatives are identical with our synthetic intermediates of proven structure, confirming the assignment of structure XI to the ketone; and the ethylene ketal XIII is identical with that obtained from the oxidation product XI. This confirms the structure of XIII as assigned and the identity of the two samples of XI.

1,5-Diphenyl-2,3-pyrrolidinedione (XI) exhibits properties expected of a compound of its structure. The infrared spectrum contains strong carbonyl absorptions at 1760 and 1700 cm.$^{-1}$, and no evidence of any (enolic) hydroxyl group. The compound gives no color reaction with aqueous or alcoholic ferric chloride solution and affords carbonyl derivatives with great ease, in complete analogy with the other authentic 2,3-pyrrolidinediones examined by Southwick.[5b,c] It bears no similarity to the material formerly assigned this structure, which on consideration of the evidence of Meyer and Vaughan[7] is now known to be 5-phenyl-3-anilino-2(5*H*)-furanone (XIV). Thus this



XIV

must be considered the first *true* 1,5-diaryl-2,3-pyrrolidinedione not containing other substituents which has been prepared (*cf.* ref 8).

The pyrrolidinedione XI apparently also exhibits the aldol dimerization behavior observed by Southwick for his simple 1-substituted compounds.[5c] Such a dimer is presumed to be the contaminant in the XI produced by the chromic acid oxidation of the alcohol X, from consideration of the infrared spectrum of the crude oxidation product. Although it was not purified and analyzed in the course of this work, the spurious bands in the infrared agree quite well with those reported by Southwick for the 1,1′-disubstituted-2,4′,5′-trioxo-3-hydroxy-3,3′-bipyrrolidines,[5c] and a high melting compound with a similar spectrum is obtained in the thermal preparation of XI from the β-keto ester XII if the solution is too concentrated or the thermal treatment is prolonged. Further work on this presumed dimer will be reported at a later date.

(19) This curious thermal "decarbethoxylation" of XII appears to be similar to the thermal decarbomethoxylation of *dl*-3-ethylenedioxy-16-carbomethoxy-5-androsten-17-one reported by W. S. Johnson, B. Bannister, R. Pappo, and J. E. Pike, *J. Am. Chem. Soc.*, **78**, 6354 (1956). Additional observations concerning this reaction will be published separately, W. R. Vaughan and I. S. Covey, paper in preparation.

EXPERIMENTAL

All melting and boiling points are uncorrected. Infrared spectra, unless otherwise noted, were obtained from Nujol mulls by means of a Perkin-Elmer Model 21 Infrared Spectrophotometer. Microanalyses are by Spang Microanalytical Laboratory, Ann Arbor, Mich.

1-Phenyl-2-pyrrolidinone (IIb). The method of Späth and Lintner[11] was modified for the preparation of IIb. A mixture of 86 g. (1.0 mole) of γ-butyrolactone (General Aniline and Film Corp.) and 165 ml. of aniline was heated at reflux with azeotropic removal of water for 3 days. After this period, 17 ml. (95%) of water had been collected and the pot temperature reached 220°. The mixture was distilled at reduced pressure, the fraction boiling 195–200°/21 mm. being collected as IIb. In this manner there was obtained 137 g. (85%) of product which solidified in the receiver. On recrystallization from petroleum ether (b.p. 60–75°) or ethyl acetate, the compound melts at 68–69° (reported[11] 68–69°).

1-Phenyl-3-hydroxymethylene-2-pyrrolidinone (III). The procedure of Tracy and Elderfield[20] for the formylation of γ-ethoxypropylmethyl ketone was modified for this reaction. In a four-neck, round-bottom flask, fitted with a mercury sealed stirrer, dropping funnel, reflux condenser, and inlet for dry nitrogen, was placed 100 ml. of dry toluene and 4.6 g. (0.10 g.-atom) of a 50% dispersion of sodium in toluene.[21] Under a dry nitrogen atmosphere with cooling in ice there was added dropwise a solution of 16.1 g. (0.100 mole) of IIb and 18 ml. of ethyl formate in 50 ml. of toluene. After the addition was complete, the mixture was allowed to rise to room temperature and was stirred for 12 hr. The tan gelatinous suspension was poured onto a mixture of ice and 5% hydrochloric acid, the layers were separated, and the aqueous layer was extracted twice with ether. After washing the combined organic layers three times with 100 ml. portions of 5% sodium bicarbonate solution, they were dried with Drierite and the solvent was removed at reduced pressure to leave 17.0 g. of a yellow oil. The oil gave a blue-green color with ferric chloride and was instantly oxidized by 1% potassium permanganate solution, but on distillation it was found to consist mainly of starting material. No procedure was found for purifying III. In one experiment it was separated from the starting lactam with dilute sodium hydroxide, which allowed isolation of a crude sample of III. This gave the above described positive tests with ferric chloride and potassium permanganate, and an infrared spectrum which contained strong absorptions at 3160, 1700, 1645, and 1620 cm.$^{-1}$ was obtained. This sample was also found incapable of purification. However, derivatives were prepared from the crude yellow oil as follows:

Acetate. A sample of the oil was treated with 5 ml. of acetic anhydride and heated on the steam bath for 1.5 hr. Cooling and partial evaporation produced fine white cottony needles of 1-phenyl-3-acetoxymethylene-2-pyrrolidinone. After several recrystallizations from methanol, the material melted at 162.0–162.5°.

Anal. Calcd. for $C_{13}H_{13}NO_3$: C, 67.53; H, 5.67; N, 6.06. Found: C, 67.53; H, 5.69; N, 6.11.

Benzoate. A 3.0 g. sample of the oil was dissolved in a few ml. of pyridine and treated with benzoyl chloride. After warming on the steam bath for 30 min., the solution was cooled, methanol was added, and 0.6 g. (12% based on IIb) of the benzoate of III was filtered off; m.p. 182–184°. After two recrystallizations from ethanol, the analytical sample was obtained as white cottony needles, m.p. 183.0–183.5°.

Anal. Calcd. for $C_{18}H_{15}NO_3$: C, 73.70; H, 5.16; N, 4.78. Found: C, 73.75; H, 5.23; N, 4.69.

(20) A. H. Tracy and R. C. Elderfield, *J. Org. Chem.*, **6**, 63 (1941).

(21) The sodium dispersion had an average particle size 6μ; this reagent was kindly supplied by the Ethyl Corp., Detroit, Mich.

1-Phenyl-3-oximino-2-pyrrolidinone (IVb). The preparation of III was carried out as described above to the point of hydrolysis. After the 12 hr. reaction period, there was added to the gelatinous suspension a solution of 11.7 g. (0.100 mole) of amyl nitrite (Merck & Co., Inc., U.S.P.) in toluene. After stirring an additional 4 hr., the mixture was poured onto ice. The layers were separated and the organic layer washed with two 200-ml. portions of 5% sodium hydroxide solution. The combined aqueous layers were acidified with hydrochloric acid and extracted with benzene. The solution was dried with Drierite and the solvent was evaporated in an air stream. After one recrystallization of the residue from ethanol there was obtained 1.6 g. (8.4%) of IVb, m.p. 200–205° dec. Three further recrystallizations produced white needles of analytical purity, m.p. 210.5–212.0° dec.

Anal. Calcd. for $C_{10}H_{10}N_2O_2$: C, 63.14; H, 5.30; N, 14.73. Found: C, 63.31; H, 5.36; N, 14.79.

This compound could also be obtained by treatment of a basic aqueous solution of the crude hydroxymethylene compound III with sodium nitrite, followed by slow acidification.

The oxime IVb is soluble in 5% sodium hydroxide solution, produces no color with ferric chloride, and gives a negative test with Tollens' reagent. It dissolves in concentrated sulfuric acid affording a yellow solution which turns blood-red immediately on addition of concentrated nitric acid (Bodforss'[10] test for the pyrrolidinedione anil). It was not hydrolyzed by ethanolic-aqueous hydrochloric acid.

γ-Phenyl-γ-butyrolactone. To a filtered solution of 89 g. (0.50 mole) of crude β-benzoylpropionic acid[22] in 500 ml. of ethanol was added slowly with stirring a solution of 30 g. (0.79 mole) of commercial sodium borohydride (Metal Hydrides Inc.) in 500 ml. of ethanol. Following the addition, the reaction mixture was stirred at room temperature for 3 hr. After acidification with 10% hydrochloric acid, most of the ethanol was distilled off at atmospheric pressure on the steam bath. The resulting mixture was cooled to room temperature, extracted with benzene, and the benzene extracts dried with Drierite. The benzene was removed at reduced pressure on the steam bath and the residue distilled at 106–113°/0.5 mm. (reported 171–172°/11 mm.,[23] 123°/2 mm.[24]). This yielded 68.2 g. (84%) of product which solidified and melted at 34–36° (reported[24] 38°) and was sufficiently pure for further use.

1,5-Diphenyl-2-pyrrolidinone (IIa). The preparation of IIa was carried out by the procedure devised for the synthesis of IIb. A mixture of 68.2 g. (0.421 mole) of γ-phenyl-γ-butyrolactone and 80 ml. of aniline was refluxed with azeotropic removal of water for 3 days, 4.5 ml. of water being collected. When no further azeotroping occurred, excess aniline was distilled at water pump pressure and the residue dissolved in benzene. After washing thoroughly with 10% hydrochloric acid, the benzene solution was dried with Drierite and evaporated to dryness in an air stream. The crystalline residue was recrystallized from ethyl acetate to yield 61.5 g. (62%) of IIa. Two further recrystallizations from ethyl acetate or isopropyl alcohol yielded 52.0 g. (52%) of white product, m.p. 110–112°.

Anal. Calcd. for $C_{16}H_{15}NO$: C, 80.99; H, 6.37; N, 5.90. Found: C, 81.11; H, 6.41; N, 5.98.

1,5-Diphenyl-3-anilino-2(5H)-pyrrolone (V). The procedure of Vaughan[13] was used for the reaction between benzaldehyde, aniline, and pyruvic acid to produce V.

1,5-Diphenyl-3-oximino-2-pyrrolidinone (IVa). (a) *From 1,5-Diphenyl-2-pyrrolidinone* (IIa). A one-liter, four-neck, round-bottom flask was fitted with a reflux condenser, dropping funnel, mercury sealed stirrer, and thermometer, charged with 100 ml. of sodium dried reagent benzene and 2.0 g. (0.085 mole) of sodium hydride, and filled with a dry nitrogen atmosphere. While stirring and passing through a slow stream of dry nitrogen, there was added at room temperature a solution of 6.3 g. (0.0085 mole) of ethyl formate (dried over phosphoric anhydride and redistilled, b.p. 53.0–53.2°) in 25 ml. of dry benzene. The resulting suspension was warmed to 55–60°, and a solution of 10.0 g. (0.0422 mole) of IIa in 125 ml. of dry benzene was added dropwise over a 1-hr. period. Following this addition, the reaction mixture was stirred at 55–60° under dry nitrogen for 24 hr.

After cooling the mixture to 6°, 20 ml. of absolute ethanol was added dropwise and the temperature was allowed to rise to about 25° with stirring to decompose residual sodium hydride. A solution of 4.4 g. (0.043 mole) of *n*-butyl nitrite[25] in 25 ml. of benzene was added and the mixture was then stirred for 8 hr. at 40–50°. After cooling to 10°, 100 ml. of water was added, the resulting mixture was stirred for 15 min., poured into a separatory funnel, and the layers were separated. The organic phase was washed with two 50-ml. portions of 10% sodium hydroxide. The combined aqueous phase and basic wash solutions were cooled, treated with Norit, filtered, and acidified with hydrochloric acid. The resinous yellow-orange suspension was cooled in the refrigerator overnight and then filtered. Recrystallization from ethanol produced 0.50 g. (4.5%) of IVa which melted at 219–222° dec. after darkening near 210°. After two further recrystallizations from ethanol, there was obtained analytically pure product in the form of white needles, m.p. 229–230° dec. (heated at 3°/min. after immersion in the bath at 200°).

Anal. Calcd. for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.30; H, 5.39; N, 10.53.

The benzene layer, after being washed with sodium hydroxide solution, was dried with Drierite and evaporated under an air stream. This produced 7.7 g. (77%) of starting material, identified by melting point and infrared spectrum.

(b) *From 1,5-diphenyl-3-anilino-2(5H)-pyrrolone* (V). This procedure is essentially that of Bodforss.[10] To a refluxing solution of sodium ethoxide prepared from 17.0 g. (0.739 g.-atom) of sodium and 800 ml. of absolute alcohol was added with stirring 42.0 g. (0.610 mole) of hydroxylamine hydrochloride. After stirring at reflux for 20 min., 40.0 g. (0.122 mole) of V was added. The suspension was stirred and refluxed for 18 hr. and then filtered while hot, affording 41.0 g. of inorganic salts. An equal volume of water was added to the filtrate, and after chilling in the refrigerator for 3 hr., this was filtered from a trace of insoluble material through a pad of Celite on a sintered glass funnel. The clear solution was acidified with glacial acetic acid and cooled for 1.5 hr. The copious white precipitate was filtered and washed with 50% ethanol to yield 24.4 g. of IVa. By chilling the filtrate overnight, an additional 2.5 g. was obtained. The total yield of nearly pure material by this procedure was 26.9 g. (82.9%), m.p. 230–231° dec. (reported[10] darkening at 195°, liquefaction by 245°). The analytical sample was recrystallized twice from ethanol, m.p. 230–231° dec. (heated at 3°/min. after immersion in the bath at 200°), and m. p. 238–240° dec. (heated at 16°/min.).

Anal. Calcd. for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.12; H, 5.31; N, 10.51.

This product has an infrared spectrum identical with that of the compound obtained by procedure (a), the main absorptions being at 3180 (broad), 1695, and 1660 cm.$^{-1}$ On admixture of the two samples there is no depression of the melting point (mixture m.p. 229–230° dec., heated at 3°/min. after immersion in the bath at 200°).

An acetate was prepared with acetic anhydride and acetic acid, m.p. 190–192° dec. (heated at 8°/min.) after three recrystallizations from ethanol.

(22) L. F. Somerville and C. F. H. Allen, *Org. Syntheses*, **Coll. Vol. II**, 81 (1943).

(23) N. H. Cromwell, P. L. Creger, and K. E. Cook, *J. Am. Chem. Soc.*, **78**, 4412 (1956).

(24) I. Heilbron, *Dictionary of Organic Compounds*, Oxford University Press, New York, 1953, Vol. 2, p. 809.

(25) W. A. Noyes, *Org. Syntheses*, **Coll. Vol. II**, 108 (1943).

Anal. Calcd. for $C_{18}H_{16}N_2O_3$: C, 70.11; H, 5.23; N, 9.09. Found: C, 70.16; H, 5.31; N, 9.09.

Samples of this acetate prepared from the IVa obtained by procedures (a) and (b) were identical, having an undepressed mixture m.p. and superimposable infrared spectra.

A sample of the acetate was treated with sodium methoxide in methanol. After filtration, dilution with water, and acidification, the oxime IVa was obtained and identified by m.p. and infrared spectrum.

1,5-Diphenyl-3-amino-2-pyrrolidinone (VI). A 2.0 g. (0.0075 mole) sample of the oxime IVa was hydrogenated in 100 ml. of glacial acetic acid with 100 mg. of platinum dioxide (Baker & Co., Inc.) and 43 p.s.i.g. of hydrogen. After shaking for 3 days, the catalyst was filtered off and the tan filtrate was evaporated nearly to dryness in an air stream. Approximately 150 ml. of water and 5 ml. of hydrochloric acid were added to dissolve most of the oil. Three extractions with 50 ml. portions of benzene removed all non-basic material, and after filtration of the aqueous solution 20% potassium hydroxide was added until the mixture was basic. The suspension was cooled to 0° and extracted with a total of 200 ml. of benzene in three portions. The benzene was dried with magnesium sulfate and evaporated to dryness in an air stream. This left 1.6 g. (85%) of white crystalline VI, which after one recrystallization from ethyl acetate-petroleum ether (b.p. 60–75°) melted at 139–142°. Two further recrystallizations produced white plates of analytically pure material, m.p. 140.5–142.0°.

Anal. Calcd. for $C_{16}H_{16}N_2O$: C, 76.17; H, 6.39; N, 11.11. Found: C, 76.13; H, 6.31; N, 11.01.

A hydrochloride was prepared and recrystallized from aqueous hydrochloric acid, m.p. 243–245° dec.

Anal. Calcd. for $C_{16}H_{17}ClN_2O$: C, 66.55; H, 5.93; Cl, 12.28; N, 9.70. Found: C, 66.47; H, 6.04; Cl, 12.25; N, 9.74.

1,5-Diphenyl-3-chloro-2-pyrrolidinone (VII). A 0.5 g. (2.0 mmole) sample of VI was dissolved in 50 ml. of chloroform and cooled to the freezing point in a Dry Ice–acetone bath. To this was added a solution of nitrosyl chloride in chloroform until the yellowish color persisted for some time. After a few minutes shaking, colorless needles started to precipitate, and after 4 hr. a clear yellow solution was obtained. The solvent was evaporated in an air stream, leaving a tan oil. This was dissolved in 25 ml. of benzene and passed through a small chromatographic column packed with alumina. Elution was continued with benzene. The first 100 ml. to come through the colum was collected and evaporated to dryness. The yellowish crystals were recrystallized from carbon tetrachloride-petroleum ether (b.p. 60–75°) to yield 0.26 g. (48%) of VII as fine white needles, m.p. 95–99°. Two further recrystallizations gave the analytical sample, m.p. 102.5–103.5°.

Anal. Calcd. for $C_{16}H_{14}ClNO$: C, 70.73; H, 5.19; Cl, 13.05; N, 5.16. Found: C, 70.73; H, 5.24; Cl, 13.09; N, 5.20.

1,5-Diphenyl-2-pyrrolidinone (IIa). A 220-mg. (0.81 mmole) sample of crude VII was dissolved in 50 ml. of absolute alcohol. To this solution was added 3.2 ml. of a solution of 170 mg. of 85% potassium hydroxide in 100 ml. of absolute ethanol (0.82 mmole of KOH) and 1 g. of a palladium on calcium carbonate catalyst.[14] The suspension was stirred at room temperature under one atmosphere of hydrogen for 6 hr., until the reduction had stopped and 88% of the theoretical amount of hydrogen had been absorbed. The catalyst was filtered and washed with ethanol and the solvent evaporated in an air stream. The residue was taken up in 10 ml. of benzene, dried with magnesium sulfate, filtered, and the solution again evaporated to dryness. The total yield of crude product from evaporation of the benzene was 180 mg. (94%). Recrystallization of the residue from isopropyl alcohol yielded 20 mg. (10%) of IIa, m.p. 107–110°. Infrared spectra of this material and the authentic sample were identical, and on admixture the m.p. was undepressed.

1,5-Diphenyl-3-(phenylnitrosamino)-2(5H)-pyrrolone (IX). The conditions of Bodforss[10] were modified for the nitrosation.[26] To a stirred suspension of 2.0 g. (0.0061 mole) of 1,5-diphenyl-3-anilino-2(5*H*)-pyrrolone (V) in 50 ml. of hot acetic acid on the steam bath was added dropwise over a 20 min. period of solution of 0.5 g. (0.0072 mole) of sodium nitrite in 10 ml. of water. On addition of the first drop, the reaction mixture became deep yellow, and by the end of addition it was deep red. Complete solution occurred near the end of addition, and shortly afterward red needles began to precipitate from the solution. The heating was maintained for 10 min. after the end of addition and the mixture was then allowed to reach room temperature over a 2-hr. period. The suspension was chilled and the solid filtered off. In this manner there was obtained 0.4 g. (18%) of IX. An analytical sample was prepared by four recrystallizations from acetic acid, fine bright red needles, m.p. 271–272° dec.

Anal. Calcd. for $C_{22}H_{17}N_3O_2$: C, 74.35; H, 4.82; N, 11.84. Found: C, 74.42; H, 4.72; N, 11.84.

The infrared spectrum of this material was transparent in the high frequency region, the only absorptions above 1600 cm.$^{-1}$ (except the weak CH band at 3040 cm.$^{-1}$ observed in a hexachlorobutadiene mull) being at 1655 and 1692 cm.$^{-1}$

1,5-Diphenyl-3-hydroxy-2-pyrrolidinone (X). A solution of 2.0 g. (0.0079 mole) of 1,5-diphenyl-3-amino-2-pyrrolidinone (VI) in 73.5 ml. (0.00793 mole) of 0.1083 *N* hydrochloric acid (or an equivalent amount of the solid amine hydrochloride) was diluted to 300 ml. and filtered. Over a period of 3 days there was added a solution of 0.65 g. (0.0094 mole) of sodium nitrite in 50 ml. of water. White crystals were slowly deposited, and bubbles of gas slowly evolved. After 2 more days, 1.6–2.0 g. (80–100%) of X was filtered off. This melted at 140–145°, with prior shrinking, to form a red melt. Three recrystallizations from isopropyl alcohol-water gave the analytical sample, m.p. 148–150°, with shrinking at 145°.

Anal. Calcd. for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53, Mol. Wt., 253. Found: C, 75.78; H, 5.89; N, 5.54, Mol. Wt., 255, 258 (f.p. in camphor).

A benzoate was prepared by the use of benzoyl chloride and pyridine, m.p. 181–185°. After several recrystallizations from methanol, m.p. 188–189°.

Anal. Calcd. for $C_{23}H_{19}NO_3$: C, 77.29; H, 5.36; N, 3.92. Found: C, 77.17; H, 5.43; N, 3.92.

1,5-Diphenyl-2,3-pyrrolidinedione (XI). (a) *From* X. The chromic acid oxidation of the alcohol X was carried out in a manner similar to that used by Bruce[17] for the oxidation of dihydrocholesterol. A solution of 1.0 g. (4.0 mmoles) of X in 20 ml. of benzene was shaken with a solution of 0.3 g. (3.0 mmoles) of chromium trioxide in 30 ml. of water containing 2.0 ml. of sulfuric acid and 2.0 ml. of acetic acid for 24 hr. At the end of this period, the layers were separated and the aqueous layer was washed with 50 ml. of benzene. The combined benzene solutions were dried with magnesium sulfate, treated with Norit, filtered, and evaporated in an air stream. A small amount of toluene was added to the resulting sirup and the crystalline material was filtered. The infrared spectrum of this product contained strong sharp absorption bands at 1760 and 1700 cm.$^{-1}$ in addition to weaker bands from a contaminant. It melted at 159–162°, but could not be completely purified by recrystallization from any solvent tried nor by chromatography on alumina. It was characterized as the following derivatives:

Anil (V). Treatment of an ethanolic solution of the product with aniline produced white crystals after a day at room temperature, m.p. 215–217° dec. after recrystallization from ethanol. This had an infrared spectrum identical with authentic V, and on admixture there was no depression of m.p.

Ethylene ketal (XIII). The oxidation product was refluxed in benzene containing ethylene glycol and methane-

(26) The product obtained by Bodforss in this manner was not well characterized.

sulfonic acid for 4 hr., the solution was dried with sodium carbonate, and chromatographed on alumina. The second 25-ml. fraction to come through the column on elution with benzene was evaporated and the solid was fractionally crystallized from ethanol. After one further recrystallization from ethanol, the solid melted at 143–146°, and on admixture with an authentic sample of the ketal (*vide infra*) this was undepressed. The infrared spectrum of this sample and that of the authentic ketal were identical.

(b) *From 1,5-diphenyl-4-carbethoxy-2,3-pyrrolidinedione* (XII). This procedure is due to the research of Covey.[18] A solution of 1.0 g. (0.0031 mole) of 1,5-diphenyl-4-carbethoxy-2,3-pyrrolidinedione (XII)[6b] in 80 ml. of nitrobenzene was heated until gas evolution commenced and for 12 min. thereafter. The nitrobenzene was then concentrated at the water pump, the resulting solution was evaporated nearly dry in an air stream, and ether was added. The solid was collected and washed with ether, 0.5 g. (65%), m.p. 163–168°. The analytical sample was recrystallized several times from toluene, m.p. 162–163° with softening at 158° (reported[8] 158–159°).

Anal. Calcd. for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.21; N, 5.57. Mol. Wt., 251. Found: C, 76.54; H, 5.35; N, 5.45. Mol. Wt., 268, 271 (f.p. in camphor).

This compound had an infrared spectrum with absorption bands at 1700 and 1760 cm.$^{-1}$ which were identical with the strong bands of the product obtained by procedure (a). It was further characterized by means of its derivatives: the anil (V), m.p. 223–225° dec. (heated at 5°/min.) (reported[13] 227–228° dec.), mixture m.p. undepressed by authentic V, and infrared spectrum identical with that of V; the oxime (IVa), m.p. 238–239° dec. (heated at 16°/min.), no depression of m.p. by authentic IVa, which had an identical infrared spectrum; and the ethylene ketal, m.p. 145–147° from ethanol (see next experiment).

1,5-Diphenyl-3-ethylenedioxy-2-pyrrolidinone (XIII). A suspension of 1.0 g. (0.0030 mole of 1,5-diphenyl-3-anilino-2(5*H*)-pyrrolone (V) in 10 ml. of ethylene glycol containing 0.3 ml. of methanesulfonic acid was heated on the steam bath for 4 hr., at which time all solid had dissolved. The solution was poured into three times its volume of water and extracted with benzene. After drying with magnesium sulfate, the solvent was evaporated, leaving 0.8 g. (90%) of the ethylene ketal, m.p. 144–146°. After three recrystallizations from ethanol the material was analytically pure, white needles, m.p. 145–146°.

Anal. Calcd. for $C_{18}H_{17}NO_3$: C, 73.21; H, 5.80; N, 4.74. Found: C, 73.36; H, 5.85; N, 4.75.

The melting point of this sample was undepressed on admixture with the ketal prepared from either sample of XI, and the infrared spectra of the samples were identical.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MICHIGAN]

1,5-Diaryl-2,3-pyrrolidinediones. IX. Reassignment of Structure[1]

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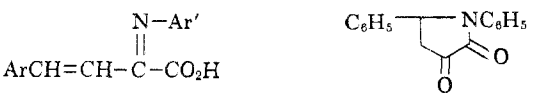
The compound previously described as 1,5-di(*p*-anisyl)-2,3-pyrrolidinedione has been shown to be 5-(*p*-anisyl)-3-(*p*-anisylamino)-2(5*H*)furanone through synthesis of its dihydro reduction product, α-(*p*-anisylamino)-γ-(*p*-anisyl)-γ-butyrolactone. This enamino lactone structure applies to all previously reported 1,5-diaryl-2,3-pyrrolidinediones having no other substitution in the heterocyclic ring.

The tautomerism between the enamino lactones (formerly the pyrrolidinediones) and α-arylimino-β-benzylidenepropionic acids is pointed out to be an example of lacto-enoic tautomerism, facilitated by the participation of the free electron pair on the amino nitrogen atom.

The observations that supposed 1,5-diaryl-2,3-pyrrolidinediones (I) underwent thermal decarboxylation to cinnamylideneanilines and were tautomeric with α-arylimino-β-benzylidenepropionic acids (II)[3] were unprecedented and thus may give rise to doubts concerning the validity of the structure assignment of I. When 1,5-diphenyl-2,3-pyrrolidinedione (III) was synthesized and found to be different from the substance (Ia) previously assigned this structure,[4] it was of interest to determine the correct structure of I unequivocally.



IIa: Ar = Ar′ = C_6H_5

IIb: Ar = Ar′ = *p*-$CH_3OC_6H_4$

III

Examination of the literature indicates that little concrete structural information is available for I. The diphenyl compound (Ia) was originally formulated as the 2,3-pyrrolidinedione by Schiff and Gigli[5] on the basis of an assumed analogy between the reactions of pyruvic acid and ethyl oxaloacetate with benzylideneaniline, ethyl oxaloacetate affording 1,5-diphenyl-4-carbethoxy-2,3-pyrrolidinedione (IV) under these conditions,[6] while pyruvic acid led to Ia. The compound IV behaved as was expected for its structure, and although at

(1) Preliminary communication, W. L. Meyer and W. R. Vaughan, *J. Org. Chem.*, 22, 98 (1957).

(2) National Science Foundation Predoctoral Fellow, 1954–57. Abstracted from a portion of the Ph.D. dissertation of W. L. Meyer, University of Michigan, 1957.

(3) (a) W. R. Vaughan and L. R. Peters, *J. Org. Chem.*, 18, 382 (1953); (b) W. R. Vaughan and L. R. Peters, *J. Org. Chem.*, 18, 393 (1953); (c) W. R. Vaughan and L. R. Peters, *J. Org. Chem.*, 18, 405 (1953); (d) W. R. Vaughan and D. I. McCane, *J. Org. Chem.*, 20, 143 (1955).

(4) W. L. Meyer and W. R. Vaughan, *J. Org. Chem.*, 22, 1554 (1957).

(5) R. Schiff and L. Gigli, *Ber.*, 31, 1306 (1898).

(6) (a) R. Schiff and C. Bertini, *Ber.*, 30, 601 (1897); (b) L. J. Simon and A. Conduché, *Ann. chim. et phys.*, [8] 12, 5 (1907).