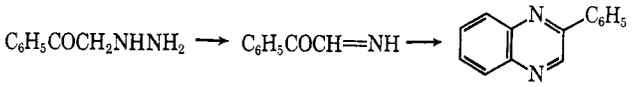
has also been obtained from the thermal decomposition of phenacyl azide *via* the nitrene and phenylglyoxal imine.[15] In discussing the formation of the dimeric product from **14**, Busch specifically rejected the possibility that imidazole **16** (in his view the pyrazine) arose from the hydrazino ketone by elimination to the aldimine, and invoked instead an initial dimerization to a tetrazocine followed by a double ring contraction.[5]

It was of interest to us to determine whether phenacylhydrazine, as a simple prototype of the diazepine systems, does in fact undergo elimination to phenylglyoxal imine, particularly in view of the diverse suggestions that have been made concerning this and related reactions. The base was obtained as described[5] and as previously observed, underwent rapid decomposition in methanol solution, with or without the addition of sodium methoxide.

The decomposition of **14** was also carried out in methanol solution in the presence of *o*-phenylenediamine. This reagent has been successfully used to trap phenylglyoxal imines formed in the pyrolysis of azides.[16] A product corresponding in melting point to 2-phenylquinoxaline (**17**) was isolated in 50% yield; the presence of the imidazole was detected by tlc. The yield was much lower when sodium methoxide was added.



17

It is thus clear that decomposition of the α-hydrazino ketone gives rise to the imine by elimination of ammonia, and that excess hydrazine or strong base is not required in the case of a simple hydrazine. It seems quite possible that the other reactions mentioned above also occur by this process, and that this elimination will be found to be characteristic for compounds containing a hydrazinomethyl system attached to a negative group such as carbonyl or the α position of an azine. Similar reactions of hydroxylamino ketones[17] and α-chloromethylpyridines with hydroxylamines[18] have also recently been described.

Registry No.—**7**, 4084-21-3; **1**, 1706-26-9; α-hydrazinoacetophenone, 10137-56-1.

(15) J. H. Boyer and D. Straw, *J. Am. Chem. Soc.*, **74**, 4506 (1952).
(16) J. H. Boyer and D. Straw, *ibid.*, **75**, 1642 (1953).
(17) S. C. Bell, R. J. McCaully, and S. J. Childress, *Tetrahedron Letters* 2889 (1965).
(18) H. Daniher, B. E. Hackley, and A. B. Ash, *J. Org. Chem.*, **31**, 2709 (1966).

Heterocyclic Studies. XXIV. The Formation and Reactions of the 1,6-Diazabicyclo[3.2.0]-3-hepten-2-one System[1]

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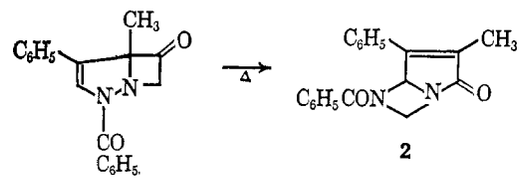
Compound **2**, the first example of the title system, is obtained by thermal isomerization of the bicyclic ketone (**1**). The reaction of **2** with alcohols or water leads to 1-alkoxymethyl-5-benzamido-3-pyrrolin-2-ones (**7**). Structure **7** was established by conversion to the 1-alkoxymethylmaleimide (**6**) and the pyrrolinones (**8** and **10**). A number of other derivatives of 5-benzamido-3-methyl-4-phenyl-3-pyrrolin-2-one are described. Isomerization of **2** with weak base gives the bicyclic oxadiazine (**14**). Synthetic efforts toward the 5-benzamidopyrrolinone (**8**) and the possible interconvertibility of succinimide and pyrrolinone tautomers are discussed.

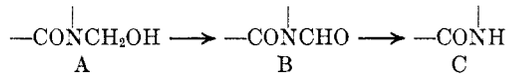
Among the diverse transformations of the bicyclic ketone (**1**),[3] one of the more interesting reactions that has been encountered is the conversion of the compound, on heating in benzene or other inert solvents, to an isomer in 77% yield. In this paper we present evidence leading to the 1,6-diazabicyclo[3.2.0]heptenone structure (**2**) for the thermal isomerization product. The nature of this unusual rearrangement is discussed in the following paper.[4]



1 **2**

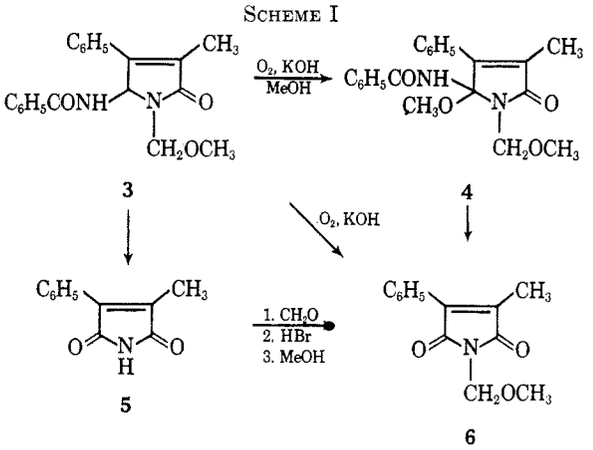
The main lines of evidence for the structure of the "thermal isomer" were developed from the products of a general acid catalyzed reaction with alcohols, water, or acetic acid to give addition products in excellent yield. These adducts, which will be shown to have structure **7**, had sharp infrared bands (data are for the methanol adduct) for CONH (ν^{CHCl_3} 3440 cm^{-1}, ν^{KBr} 3360 cm^{-1}) and two carbonyl groups (ν^{CHCl_3} 1680 and 1710 cm^{-1}, ν^{KBr} 1670 and 1700 cm^{-1}). The nmr spectra contained peaks for $CH_3C{=}$ (δ^{CDCl_3} = 1.98 ppm), nonequivalent CH_2 (δ_A = 4.70 ppm, δ_B = 4.98 ppm, J_{AB} = 10.5 cps) and a highly deshielded tertiary CH (δ = 7.0 ppm). The compounds were readily interconvertible, suggesting the functionality CON-CH_2OR, which is compatible with the nmr values. This grouping was characterized by mild chromic acid oxidation[5] of the hydroxy compound (A) to a formyl derivative (B, δ = 9.10 ppm) which was deformylated in acidic methanol to give methyl formate and a product (C), corresponding to the sequence shown.

(1) Supported in part by Grant DA-CML-18-108-61-G-24 from the Army Chemical Corps.
(2) National Science Foundation Cooperative Graduate Fellow, 1962–1963.
(3) J. A. Moore, F. J. Marascia, R. W. Medeiros, and R. L. Wineholt, *J. Org. Chem.*, **31**, 34 (1966).
(4) J. A. Moore, R. L. Wineholt, F. J. Marascia, R. W. Medeiros, and F. C. Creegan, *ibid.*, **32**, 1353 (1967).
(5) A similar chromic acid oxidation of a N-methylolamide has been reported by A. Einhorn, *Ann.*, **243**, 207 (1905).



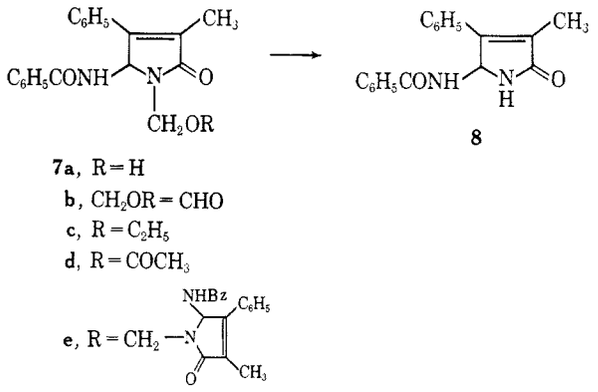
The presence of a pyrrole ring as the main structural unit in products A–C was revealed by vigorous oxidation of the hydroxymethyl, methoxymethyl, or formyl compounds to 3-methyl-4-phenylmaleimide (**5**).[6] A more informative degradation was encountered in an attempted hydrolysis of the methoxymethyl compound (**3**). The substance was quite stable to base in the absence of oxygen, but exposure to air in 5% methanolic alkali led to a mixture from which benzamide and 1-methoxymethyl-3-methyl-4-phenylmaleimide (**6**) were isolated (see Scheme I). An authentic sample of **6** was obtained from imide **5** *via* the methylol and bromomethyl derivatives. In another experiment in more dilute base, a compound containing an additional methoxyl group was isolated. This product on acid hydrolysis gave imide **6** and is assigned structure **4**. The aerial oxidation of **3** to **4** and **6** is similar to autoxidations that have been observed previously with pyrrole[7] and pyrazolones.[8]

SCHEME I



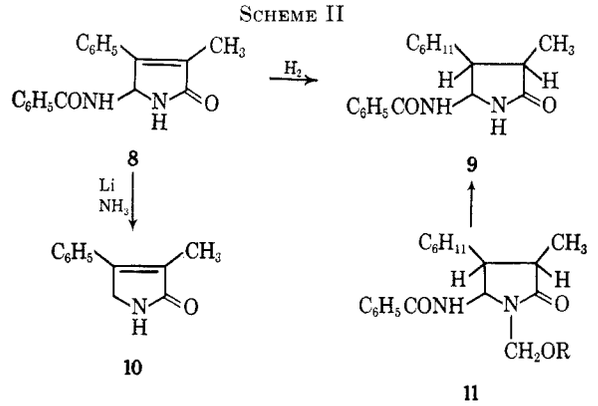
The properties and facile acid-catalyzed interconversions of the alkoxy, hydroxy, and acetoxy compounds (**7**) are in keeping with the chemistry of N-methylolamide derivatives.[9] In addition to the stepwise degradation of methylol compound **7a** to the parent benzamidopyrrolone (**8**) *via* formyl derivative **7b**, controlled oxidation of **7a** or the methoxy compound (**3**) with chromic acid gave **8** in useful yield. Hydrolytic removal of the side chain was not a practical reaction; pyrrolone **8** was isolated in low yield, together with acetate **7d**, on prolonged refluxing of methyl ether **3** with acetic acid. An attempt to effect conversion of **7a** to **8** by pyrolytic removal of formaldehyde gave a small amount of **8** and, as the main product, bimolecular ether **7e**. The latter was also obtained from the methoxy derivative on treatment with trifluoroacetic acid in chloroform.

The foregoing data define a 1-substituted 5-benzamido-3-pyrrolin-2-one structure for the addition products (**7**). Information on the final structural question,



namely the location of the methyl and phenyl substituents relative to C-2 and C-5, was first sought in the hydrogenation products of the methoxymethyl derivative (**3**) and the unsubstituted compound (**8**), since it was hoped that the multiplicity of the ring protons in the pyrrolidinones would resolve the point. Dihydro products could not, however, be isolated. Compound **8** was recovered unchanged after hydrogenation with nickel. With palladium catalyst an inseparable mixture was obtained which may have contained the desired pyrrolidinone. More vigorous hydrogenation of **8** using platinum gave in 65% yield the cyclohexylpyrrolidinone (**9**). Similarly, the methoxymethyl and hydroxymethyl derivatives were converted to saturated cyclohexylpyrrolidinones (**11**); these compounds could be oxidized to **9**. Hydrogenation of the phenyl ring without hydrogenolysis of the N-methylol group seems noteworthy (see Scheme II).

SCHEME II



A solution to the orientation question was finally achieved by reduction of unsubstituted pyrrolinone **8** to 3-methyl-4-phenyl-3-pyrrolin-2-one (**10**).[4,10] Both this compound and the 4-methyl-3-phenyl isomer[6] had previously been prepared and characterized. Removal of the benzamido group was based on the well-known metal–ammonia hydrogenolysis of negative substituents that are activated by adjacent carbonyl or sulfonyl groups. Treatment of **8** with lithium in liquid ammonia produced a complex mixture, but the pyrrolinone was isolated in low yield; the crystalline material was identical with an authentic sample of **10**. This transformation provides conclusive evidence for the structures of pyrrolinone **8** and, together with the other interconversions and degradations, for the addition products **7** arising from solvolysis of the thermal isomer.

(6) R. L. Wineholt, E. Wyss, and J. A. Moore, *J. Org. Chem.*, **31**, 48 (1966)

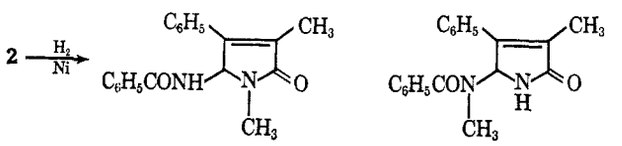
(7) P. de Mayo and S. T. Ried, *Chem. Ind.* (London), 1576 (1962).

(8) S. Viebel and S. C. Linholt, *Acta Chem. Scand.*, **9**, 963, 970 (1955).

(9) H. Hellman, "Neuere Methoden der Präparativen Organischen Chemie," Vol. 2, W. Foerst, Ed., Verlag Chemie, Weinheim/Bergstr., Germany, 1960, p 190.

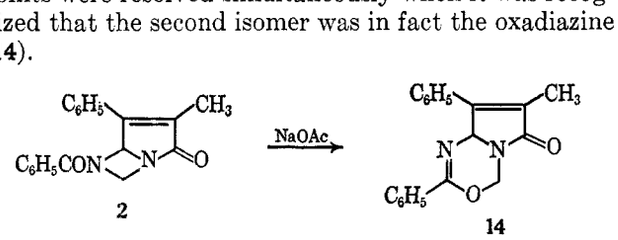
(10) J. A. Moore and J. Binkert, *J. Am. Chem. Soc.*, **81**, 6029 (1959).

Hydrogenation of the thermal isomer itself with nickel gave a dihydro compound in which the pyrrolinone ring remained intact. Spectra showed that CONH and NCH_3 (δ_{DMSO} = 2.88 ppm) groups were present. This compound was not correlated directly with the other pyrrolinones (**7**), but it was assigned the 1-methyl structure (**12**) rather than the isomeric **13** from ultraviolet evidence. The spectrum [λ_{max}^{EtOH} 234 mμ (ε 20,000) and 271 mμ (ε 8000)] was essentially identical with those of the 1-substituted pyrrolinones (**7**), and, like the spectra of **7**, was unaffected by base. The spectrum of **13** would be expected to resemble that of the 1-unsubstituted pyrrolinone (**8**), which is quite similar to that of the 1-substituted series in neutral solution but shows a new maximum at 284 mμ (ε 11,000) an addition of base.



12 **13**

The addition of hydrogen or the elements HX to the thermal isomer, with creation of C_6H_5CONH and NCH_3 or NCH_2X groups, requires the opening of a ring in the isomer, and moreover a ring containing a highly electrophilic disubstituted methylene group. The methoxy compound (**3**) was obtained in good yield simply by refluxing in methanol. The diacyl uretidine system in **2**, a functional system that has not previously been reported, satisfies this requirement; the bis(acylaminomethane) unit in a small ring should be an excellent substrate for solvolysis. One other structure, however, is admissable on the evidence thus far presented, this is the oxadiazine (**14**). An additional problem that remained at this point was the structure of another isomeric compound which was obtained from the thermal rearrangement product on treatment with alcoholic sodium carbonate or sodium acetate. These points were resolved simultaneously when it was recognized that the second isomer was in fact the oxadiazine (**14**).



2 **14**

The spectral properties of **2** and **14** were very similar, as noted in Table I. The most notable differences are seen in the nmr signals for CH_3 and CH_2 protons in the two compounds. The smaller value of $\delta_A - \delta_B$ for the methylene protons in **14** is expected for the larger ring. The diamagnetic shift of the methyl peak in **14** is larger than would be anticipated from any effect on the pyrrolinone ring owing to the difference in ring fusion; ν_{CO} is nearly the same in both compounds. The additional shielding in the CH_3 protons of **14** may be due to its proximity to the shielding cone of the phenyl group in the oxadiazine ring.

TABLE I

Compd	λ_{max}^{EtOH}, mμ (ε)	ν_{max}^{KBr}, cm^{-1}	δ_{CH_3}, ppm	δ_{CH_2}, ppm	δ_{CH}, ppm
2	245 (24,000)	1710 1650	2.07 (d, J = 1.2 cps)	H_A 6.02 H_B 5.23 (J_{AB} = 9.6 cps)	6.00[a]
14	250 (28,000)	1730 1640	1.80	H_A 5.86 H_B 5.73 (J_{AB} = 8.9 cps)	7.2

[a] Apparent doublet; quartet not resolved.

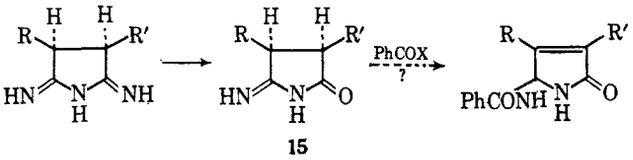
Treatment of **14** under the conditions used for the solvolysis of **2** resulted in complex mixtures, but the acetoxymethyl pyrrolinone (**7d**) was obtained in low yield on treatment with acetic acid. Vigorous oxidation gave imide **5**. The assignment of the oxadiazine structure is based mainly on the intermediate position which the compound occupies between **2** and the pyrrolinone.

The isomerization of **2** to **14**, as indicated, occurs in the presence of very weak bases. With strong base, **2** gives a bright red solution from which only a very small amount of the oxadiazine can be recovered. The optimum conditions, in effect, appear to be the use of just enough base to suppress the solvolysis to **7**. Precedent for this type of ring expansion is found in the isomerization of 1-acylaziridines to oxazolines with acid or with sodium iodide.[11] The latter reagent did not affect **2**. More closely related to the present case are the recently reported isomerizations of 1-acylazetidines to 1,3-oxazines,[12] in which the acid of a weakly nucleophilic base such as picrate is the most effective catalyst. It appears that the isomerization of **2** may be mechanistically quite unrelated to these other reactions.

Since the 5-benzamidopyrrolone structures were a crucial issue in this work, some efforts were directed to the synthesis of the parent compound (**8**). Preliminary attempts to utilize pyrrolinone **10** as a starting point were unsuccessful. Nitrosation gave the N-nitroso derivative, while azo coupling gave a mixture of dyes which was unpromising for futher study.

Attention was then turned to the preparation and cyclization of a suitable acyclic precursor of the 5-aminopyrrolinone. This approach raises a point that has been ignored in the preceding discussion, namely the plurality of tautomeric structures possible for **7** and **8**. The presence of a methyl singlet at $\delta \sim 2.0$ ppm in the nmr spectra of all the pyrrolinones in this series obviates the need to consider tautomeric forms other than the Δ^3 structures for these benzoyl derivatives. Moreover there were no indications in any of the transformations of these pyrrolinones of the formation of isomers, and the Δ^3 tautomers were therefore considered to be the stable form, in keeping with the usual behavior of 2-oxygenated pyrroles.[10,13] In the limited literature on pyrroles with 2-oxygen and 5-nitrogen substituents, however, the 5-imino-2-pyrrolidinone structures have generally been preferred. Thus Linstead and co-workers[14,15] assigned structure **15** to the hydrolysis products of succinimidines; acyl derivatives were not described. Although the pyrrolinones seem clearly to be the stable tautomeric form in the acylamido compounds, there is no clear

(11) H. W. Heine, *Angew. Chem.*, **74**, 772 (1962).
(12) Y. Iwakura, A. Nabeya, T. Nishiguchi, and Y. Ichikawa, *J. Org. Chem.*, **30**, 3410 (1965).
(13) J. H. Atkinson, R. S. Atkinson, and A. W. Johnson, *J. Chem. Soc. Suppl.*, 5999 (1964).
(14) R. P. Linstead and M. Whalley, *ibid.*, 3530 (1955).
(15) J. A. Elvidge, J. S. Fitt, and R. P. Linstead, *ibid.*, 235 (1956).



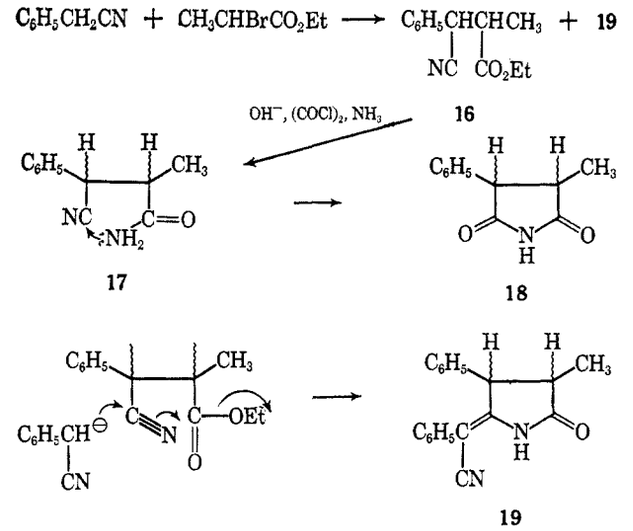
15

precedent for the isomerization of a succinimide tautomer to a pyrrolinone.

Our synthetic approach to **8** was based on the cyclization of an α-methyl-α'-phenylsuccinic acid derivative to a product which would, presumably, be **15** (R = C_6H_5, R′ = CH_3), with the premise that conversion to the Δ^3-pyrrolinone structure would occur on benzoylation. In order to maintain the correct orientation of substituents, cyanoamide **17** appeared to be the most suitable precursor. Cyclizations of this type, leading to 4,4-disubstituted 5-iminopyrrolidinones, have been accomplished with α,α'-disubstituted cyanoamides.[16]

The cyano ester (**16**) was prepared as described[17] by alkylation of sodiophenylacetonitrile with ethyl α-bromopropionate. A crystalline by-product was obtained in this reaction and found to be the 5-(cyanobenzylidene)pyrrolidinone (**19**). Oxidation of **19** gave the succinimide (**18**). This by-product was shown to arise from attack of the nitrile anion on cyano ester **16** by its formation in 44% yield from the ester (see Scheme III). Compounds of this type have been obtained previously by condensation of the iminopyrrolidinones (**15**) with active methylene compounds.[15] This rather facile reaction suggested the possibility that a suitable nitrogen anion might lead in the same way to the desired 5-aminopyrrolidinone derivative, but attempts in this direction with N-benzoylurethan were unsuccessful.

SCHEME III



The cyanoamide (**17**) was prepared by conversion of the cyano ester to the acid and then treatment with oxalyl chloride and ammonia. Several attempts were made to obtain a product related to **15**. Treatment of **17** under the alkaline conditions used successfully by Foucaud[16] gave the imide (**18**). A reaction occurred in anhydrous ethanolic hydrogen chloride, and the crude product was then benzoylated. No pure compound could be isolated, and the pyrrolinone (**8**) was not detected. The work was discontinued at this point, and it cannot be stated from these inconclusive results if the iminopyrrolidinone (**15**) was produced. If cyclization of the cyanoamide in this sense did occur, as might be inferred from the formation of **18** in one case, the assumption of a facile tautomerization to the aminopyrrolinone is evidently erroneous.

(16) A. Foucaud, *Bull. Soc. Chim. France*, 123 (1964).

(17) F. W. Upson and T. J. Tompson, *J. Am. Chem. Soc.*, **44**, 181 (1922).

Experimental Section[18]

6-Benzoyl-3-methyl-4-phenyl-1,6-diazabicyclo[3.2.0]hept-3-en-2-one (2).—A solution of 7.5 g (0.025 mole) of the 2-benzoyl-1,2-diazabicyclic ketone (**1**) in 350 ml of benzene was heated at reflux for 7 hr. Evaporation of benzene *in vacuo*, dilution of the concentrated solution with ether, and chilling furnished 5.2 g of white, crystalline solid, mp 150–152°. Concentration of the filtrate furnished an additional 0.6 g of product, mp 149–151° (total yield 77%). Recrystallization from ethyl acetate furnished fine, white needles, mp 153–154°. For spectral data, see Table I.

Anal. Calcd for $C_{19}H_{16}N_2O_2$ (304.34): C, 74.98; H, 5.30; N, 9.21. Found: C, 75.29; H, 5.20; N, 9.09; mol wt (osmometric), 293 (by mass spectrum, 304).

5-Benzamido-1-methoxymethyl-3-methyl-4-phenyl-3-pyrrolin-2-one (3). A.—To a suspension of 2.00 g (6.5 moles) of the bicyclic pyrrolinone (**2**) in 30 ml of methanol was added 15 drops of concentrated hydrochloric acid. The reaction mixture was swirled; within 1 min, the solid had dissolved. The clear solution was diluted with 100 ml of water to furnish a thick, white oil which crystallized on scratching. Filtration, washing with water, and air drying furnished 2.10 g (95% yield) of **3** as a colorless, crystalline solid: mp 156.5–158°; after recrystallization from methanol, mp 157.5–158.5°; λ_{max}^{EtOH} 224 mμ (ϵ 19,000), 234 (19,000), 270 (11,000) (no change on addition of dilute acid or base); for infrared, see text; nmr δ ($CDCl_3$) 1.98 (s, 3), 3.33 (s, 3), 4.84 (center of AB, J = 10.5 cps, $\delta_A - \delta_B$ = 16.4 cps), 7.0–7.9 ppm (m, 12, one proton exchangeable with acidic D_2O).

Anal. Calcd for $C_{20}H_{20}N_2O_3$ (336.4): C, 71.41; H, 5.99; N, 8.33. Found: C, 71.17; H, 6.02; N, 8.37.

The compund did not react with semicarbazide reagent and was recovered unchanged after treatment with acetic anhydride–pyridine.

B.—A solution of 500 mg (1.6 mmoles) of **2** in 50 ml of methanol was refluxed for 2 hr and then evaporated *in vacuo* to a yellowish white solid. This residue was slurried with 5 ml of 10% sodium carbonate, and the mixture was extracted with methylene chloride. Neutralization of the sodium carbonate layer and extraction with ether furnished 5 mg of tar. Evaporation of the methylene chloride extracts and trituration with a minimum volume of ether furnished 476 mg (88%) of **3**, mp 155–156°.

5-Benzamido-1-ethoxymethyl-3-methyl-4-phenyl-3-pyrrolin-2-one (7c).—A suspension of 1.00 g of **2** in 20 ml of ethanol was treated with 15 drops of hydrochloric acid and the product was isolated as described for **3** to give 1.00 g (95%) of **7c** as white needles: mp 175–177°; after recrystallization from ethanol, mp 178–179°; λ_{max}^{EtOH} 223 mμ (ϵ 20,000), 234 (21,000), 271 (12,000); ν^{KBr} 3360, 1715, 1640 cm^{-1}.

Anal. Calcd for $C_{21}H_{22}N_2O_3$ (350.41): C, 71.98; H, 6.33; N, 8.00. Found: C, 72.24; H, 6.26; N, 7.83.

1-Acetoxymethyl-5-benzamido-3-methyl-4-phenyl-3-pyrrolin-2-one (7d).—A solution of 500 mg of **2** in 5 ml of glacial acetic acid was heated on the steam bath for 45 min. The colorless solution was then diluted with 60 ml of ether, washed with sodium bicarbonate solution and water, and evaporated to give 460 mg (77% yield) of white, crystalline solid: mp 158–162°; λ_{max}^{EtOH} 224 mμ (ϵ 19,000), 233 (19,000), 273 (11,000); (d, 3, J = 2 cps), ν^{KBr} 3360, 1762, 1724, 1645 cm^{-1}; δ (CCl_4) 1.97 (s, 3), 2.12 (s, 3), 5.45 (center of AB, J = 10.3, $\delta_A - \delta_B$ 17.5 cps), 6.91 (s, broad 2), 7.3–7.75 ppm (m, 10).

Anal. Calcd for $C_{21}H_{20}N_2O_4$ (364.39): C, 69.21; H, 5.53; N, 7.69. Found: C, 68.83; H, 5.54; N, 7.45.

(18) General procedures are given in paper XXII of this series: J. A. Moore, R. W. Medeiros, and R. L. Williams, *J. Org. Chem.*, **31**, 52 (1966). Nmr peak positions are given in ppm downfield from internal tetramethylsilane; the multiplicity is designated as singlet (s), doublet (d), etc.; numerals refer to whole number(s) of protons from integral curve.

5-Benzamido-1-hydroxymethyl-3-methyl-4-phenyl-3-pyrrolin-2-one (7a). A.—To a solution of 500 mg of **2** in 14 ml of dioxane was added 13 ml of water. The solution became cloudy; addition of 12 drops of concentrated hydrochloric acid, followed by rapid swirling, caused the solution to become clear again. After standing for several minutes, the reaction mixture was diluted with 50 ml of water and chilled to give 487 mg (92%) of white, crystalline solid, mp 193–195°. Some preparations exhibited a double melting point (190–192° and 234–236° dec). Thin layer chromatography showed a persistent small impurity which could not be isolated by column chromatography, but which led to erratic analytical data. Analytically pure material was obtained by suspending 500 mg (1.6 mmoles) of the compound in 4 ml of acetone and adding dropwise a solution of 113 mg (1.13 mmoles) of chromic anhydride in 0.9 ml of water and 0.1 ml of concentrated sulfuric acid. After stirring for a total of 2 hr the mixture was diluted with water and extracted with methylene chloride. The residue remaining after the evaporation of the methylene chloride was recrystallized repeatedly from ethanol to furnish **7a** as a white, crystalline solid: mp 187–188°; with untreated material, mmp 187–190°; tlc identical with that of untreated compound, but without minor impurities; λ_{max}^{EtOH} 224 mμ (ε 18,000), 234 (18,000), 270 (9800); no change on addition of dilute acid or dilute base; ν^{KBr} 3670, 3360, 1700, 1670 cm^{-1}.

Anal. Calcd for $C_{19}H_{18}N_2O_3$ (322.35): C, 70.79; H, 5.63; N, 8.69. Found: C, 70.84; H, 5.59; N, 8.81.

B.—A solution of 100 mg of **2** in 1.5 ml of tetrahydrofuran was saturated with dry hydrogen chloride gas and then diluted with 10 ml of water. Chilling and scratching furnished 81 mg (76%) of white, crystalline solid, mp 245–255° dec; after recrystallization from ethyl acetate, a double mp (197–198° and 238–240° dec). The infrared spectrum was identical with that of sample prepared in A.

Other Conversions of 3 and 7.—Treatment of **7a**, **7c**, or **7d** with boiling methanol containing a few drops of concentrated H_2SO_4 gave methoxymethyl derivative **3** in 70–90% yields. Hydrolysis of **3** or acetate **7d** in boiling aqueous acetic acid gave hydroxymethyl compound **7a**, mp 187–190° and 225–230° dec in 60–70% yields. Treatment of **3** with hot glacial acetic acid gave **8** in 11% yield and **7d** in 50% yield. Identifications were made by melting point and infrared comparisons in each case.

5-Benzamido-1-formyl-3-methyl-4-phenyl-3-pyrrolin-2-one (7b).—A suspension of 500 mg (1.55 mmoles) of the 1-hydroxymethylpyrrolinone (**7a**) in 10 ml of glacial acetic acid was treated with a solution of 115 mg (1.15 mmole) of chromic anhydride in 0.1 ml of water and 0.9 ml of glacial acetic acid. The chromic anhydride solution was added dropwise during 45 min; the 1-hydroxymethylpyrrolinone slowly went into solution and the reaction mixture became quite dark. After stirring for an additional 45 min, the reaction mixture was diluted with 100 ml of water, and extracted repeatedly with methylene chloride. After washing with sodium bicarbonate solution and with water, the dried methylene chloride extracts were evaporated to furnish 356 mg of fluffy, white solid, mp 195–197°; further concentration of the mother liquid furnished an additional 63 mg of solid, mp 188–193°; total yield was 419 mg (84%). Repeated recrystallization from ethanol furnished fine, white needles: mp 198.5–199.5°; λ_{max}^{EtOH} 225 mμ (ε 19,000), 283 mμ (ε 14,000); no change with dilute acid; $\lambda_{max}^{EtOH + base}$ 223 mμ (ε 17,000), 233 (17,000), 271 (7900); ν^{KBr} 3330, 1745, 1700, 1660 cm^{-1}; δ^{CDCl_3} 2.16 (s, 3), 7.0–7.7 (m, 12), 9.10 ppm (s, broadened, 1).

Anal. Calcd for $C_{19}H_{16}N_2O_3$ (320.34): C, 71.24; H, 5.03; N, 8.75. Found: C, 71.09; H, 5.21; N, 9.02.

5-Benzamido-3-methyl-4-phenyl-3-pyrrolin-2-one (8). A.—A solution of 100 mg (0.31 mmole) of the 1-formylpyrrolinone (**7b**) in 20 ml of methanol containing 3 drops of 6 *N* sulfuric acid was refluxed for 1 hr under a slow stream of nitrogen. A trap cooled with Dry Ice–acetone was used to collect volatile material. After 1 hr, the condenser was turned downward and approximately 2 ml of liquid was distilled and collected. The remainder of the reaction mixture was then evaporated and diluted with water to furnish 67 mg (74%) of white, crystalline solid: mp 238–241°; after recrystallization from ethanol, mp 242–243°; λ_{max}^{EtOH} 224 mμ (ε 20,000), 233 (21,000), 266 (inflection, 11,000); no change with dilute acid; $\lambda_{max}^{EtOH + base}$ 223 mμ (ε 17,000), 236 (18,000), 284 (11,000); ν^{KBr} 3390, 3240, 1700, 1670, cm^{-1}.

Anal. Calcd for $C_{18}H_{16}N_2O_2$ (292.32): C, 73.95; H, 5.52; N, 9.58. Found: C, 73.56; H, 5.64; N, 9.52.

The distillate from the reaction mixture above was combined with the liquid collected in the Dry Ice–acetone trap, and redistilled through a 6-in. column packed with glass helices. Vapor phase chromatography of the first 0.5 ml of distillate was carried out using a 5-ft Ucon Polar column at 55°; the presence of methyl formate in the distillate was demonstrated by peak enhancement. Comparison with known methyl formate–methanol mixtures indicated that the distillate contained 14–16 μl of methyl formate; the theoretical yield of methyl formate is 18.6 mg (20 μl).

B.—A solution of 500 mg (1.49 mmoles) of the 1-methoxymethylpyrrolinone (**3**) and 600 mg (6.0 mmoles) of chromic anhydride in 20 ml of 50% aqueous acetic acid was heated overnight on the steam bath. The usual isolation procedure gave 98 mg of white, crystalline solid, mp 236–238°; mixture melting point with a sample of the 1-unsubstituted pyrrolinone from A showed no depression; the infrared spectra were identical.

Further concentration of the mother liquors furnished 95 mg of colorless, crystalline solid, mp 153–165°; tlc showed that this material was a mixture of the 1-unsubstituted pyrrolinone (**8**) and 3-methyl-4-phenylmaleimide (**5**) in a ratio of about 1:2.

Chromic Acid Oxidation of 5-Benzamido-1-formyl-3-methyl-4-phenyl-3-pyrrolin-2-one (7b).—A solution of 50 mg (0.16 mmole) of the 1-formylpyrrolinone (**7b**) and 60 mg (0.60 mmole) of chromic anhydride in 2 ml of 50% aqueous acetic acid was heated for 24 hr on the steam bath. After adding a few drops of methanol to quench unreacted chromic anhydride, the mixture was diluted with 5 ml of water and extracted with methylene chloride. The methylene chloride extracts were washed with sodium bicarbonate solution and with water, dried, and evaporated to furnish 32 mg of yellowish white, semicrystalline solid. Recrystallization from methanol furnished white crystals, mp 176–177°; mixture melting point with an authentic sample of 3-methyl-4-phenylmaleimide (**5**)[6] showed no depression; the infrared spectra were identical.

1,1′-Bis[1-(5-benzamido-3-methyl-2-oxo-4-phenyl-3-pyrrolinyl)] Methyl Ether (7e). A.—A solution of 250 mg (0.74 mmole) of the 1-methoxymethylpyrrolinone (**3**) in a minimum volume of chloroform was treated with 12 drops of trichloroacetic acid, and allowed to evaporate slowly at room temperature. The residue was a pinkish oil which was soluble in chloroform. On further standing, 83 mg of white, crystalline solid slowly precipitated, mp 250–260° dec. Dilution of the filtrate with a small volume of acetone furnished an additional 88 mg of white, crystalline solid, mp 270–274° dec, total yield was 171 mg (73%). The compound was very sparingly soluble in organic solvents, but could be recrystallized by dissolving in a large volume of boiling chloroform, concentrating the chloroform solution to approximately half-volume, and chilling: mp 297° dec; ν^{KBr} 3330, 1725, 1700 (sh), 1660 cm^{-1}. The carbon analysis was unsatisfactory.

Anal. Calcd for $C_{35}H_{34}N_4O_5$ (628.70): C, 72.59; H, 5.77; N, 8.91. Found: C, 71.83; H, 5.59; N, 8.71.

B.—A 100-mg sample of the methylol compound (**7a**) was placed in a short-path sublimer at 0.6 mm and heated slowly to 230°. After heating for several minutes, the apparatus was cooled and the material on the coldfinger was recovered by dissolving in methylene chloride; evaporation furnished 9 mg of white, crystalline solid, mp 230–234°. The infrared spectrum and mixture melting point showed that this material was 5-benzamido-3-methyl-4-phenyl-3-pyrrolin-2-one (**8**). The residue remaining in the sublimer was washed with ether and filtered to furnish 67 mg of white, crystalline solid, mp 250–252° dec; the infrared spectrum was identical with that of the bimolecular ether (**7e**) obtained in A.

1-Methoxymethyl-3-methyl-4-phenylmaleimide (6).—A solution of 500 mg (1.5 mmoles) of the 1-methoxymethylpyrrolinone (**3**) in 25 ml of 5% methanolic potassium hydroxide was agitated in contact with air at room temperature for 55 min. The solution rapidly became bright yellow. The methanol was then removed *in vacuo* at room temperature, and a few milliliters of water was added to the residual syrup. A small amount of the syrup dissolved, but most remained as a bright yellow gum. Extraction with four portions of ether removed all the water-insoluble material. Concentration of the dried ether extracts to small volume furnished 203 mg of unreacted starting material, mp and mmp 150–153°.

Evaporation of the ethereal mother liquor gave 195 mg of yellow oil, which was chromatographed on 6 g of alumina. Elution with 500 ml of benzene–hexane (1:1) furnished 93 mg (46% based on unrecovered starting material) of an oily, white solid which showed only one spot in tlc. Trituration with heptane

furnished a white, crystalline solid: mp 82–84°; after recrystallization from heptane, mp 83.5–84.5°; λ_{max}^{EtOH} 224 mμ (ε 14,000), 258 (4800), 329 (3100); no change with dilute acid; $\lambda_{max}^{EtOH + base}$ 220 mμ (ε 12,000), 247 mμ (inflection, ε 8200); ν^{KBr} 3050, 1790, 1720, plus five extremely sharp strong bands at 800, 778, 748, 723, and 700 cm^{-1}; δ^{CDCl_3} 2.20 (s, 3), 3.38 (s, 3), 4.95 (s, 2), 7.51 ppm (s, 5).

Anal. Calcd for $C_{13}H_{13}NO_3$ (231.24): C, 67.52; H, 5.67; N, 6.06. Found: C, 67.39; H, 5.51; N, 5.84.

The chromatogram from above was eluted further with solvent mixtures of increasing polarity. Elution with 600 ml of 10% chloroform in benzene furnished 103 mg (theory, 107 mg; based on unrecovered starting material) of slightly waxy, white solid. Trituration with ether furnished white, almost transparent, plates, mp 127–128°; mixture melting point with an authentic sample of benzamide was 127–128°; the infrared spectra were identical.

Alternative Synthesis of Methoxymethylmaleimide 6. A. 1-Hydroxymethyl-3-methyl-4-phenylmaleimide.—A solution of 50 mg (0.27 mmole) of the maleimide (**5**) in 0.5 ml of hot 37% formalin was allowed to cool to room temperature, and was then concentrated *in vacuo* until a mass of white crystals separated. The mixture was filtered and washed with water to furnish 30 mg of white, crystalline solid, mp 113–116°; after recrystallization from carbon tetrachloride, mp 124–125°. Upon standing, the filtrate deposited 17 mg more of material: mp 110–113°; total yield 82%; λ_{max}^{EtOH} 224 mμ (ε 14,000), 257 (inflection, 4100), 330 (2700); ν^{KBr} 3560, 3010, 1780, 1720 cm^{-1}.

Anal. Calcd for $C_{12}H_{11}NO_3$ (217.22); C, 66.35; H, 5.10; N, 6.45. Found: C, 66.60; H, 5.10; N, 6.31.

B.—A mixture of 47 mg (0.22 mmole) of the above 1-(hydroxymethyl)maleimide with 0.2 ml of 48% hydrobromic acid and 0.05 ml of concentrated sulfuric acid was heated for 2 hr in a 50–60° bath. The reaction mixture was then chilled, diluted with water, and filtered to furnish 44 mg (72%) of the 1-(bromomethyl)imide, mp 130–132°. This compound was dissolved in 1.2 ml of methanol and refluxed for 1.5 hr. Evaporation of the methanol *in vacuo* furnished 29 mg of yellow oil which dissolved partially in hot heptane, leaving a reddish tar. On chilling, the heptane solution furnished 14 mg (41%) of white, crystalline solid, mp 79–81°; mixture melting point with a sample of the 1-methoxymethyl maleimide **6** prepared by autoxidation of **3** showed no depression; the infrared spectra were identical.

5-Benzamido-5-methoxy-1-methoxymethyl-3-methyl-4-phenyl-3-pyrrolin-2-one (4).—A solution of 1.002 g (3.0 mmoles) of **3** in 50 ml of methanolic potassium hydroxide was agitated overnight in contact with air. After removal of the methanol *in vacuo*, water was added to the resulting syrup, and the mixture was extracted with ether. Evaporation of the ether solution to small volume furnished 351 mg (35%) of unreacted **3**, mp and mmp 156–158°. Further concentration furnished 69 mg of the 5-methoxy-1-methoxymethylpyrrolinone (**4**), mp 137–141°. The ether solution was then evaporated to dryness to furnish 465 mg of yellow gum which was chromatographed on 15 g of alumina. Elution with benzene–hexane (1:1) furnished 222 mg of white, crystalline solid, mp 132–137°; after recrystallization from benzene–heptane, mp 148–149°. The total yield of **4** was 291 mg (41% based on unrecovered starting material); λ_{max}^{EtOH} 225 mμ (ε 18,000), 278 mμ (ε 8000); ν^{KBr} 3320, 1720, 1660 cm^{-1}; δ^{CDCl_3} 2.16 (s, 3), 3.22 (s, 3), 3.38 (s, 3), 4.83 (m, 2), 6.8 (s, broad, 1), 7.1–7.8 ppm (m, 12).

Anal. Calcd for $C_{21}H_{22}N_2O_4$ (366.40): C, 68.83; H, 6.05; N, 7.65. Found: C, 69.07; H, 6.11; N, 7.65.

A solution of 20 mg of **4** in 1 ml of 50% aqueous acetic acid was refluxed for 1 hr under a slow stream of nitrogen. After dilution with 10 ml of water, the acetic acid was neutralized with sodium bicarbonate, and the cloudy mixture was extracted with methylene chloride. Evaporation of the methylene chloride furnished 17 mg of yellow oil. Thin layer chromatography showed that this oil contained 1-methoxymethyl-3-methyl-4-phenylmaleimide (**6**), 3-methyl-4-phenylmaleimide (**5**), and 1-hydroxymethyl-3-methyl-4-phenylmaleimide in the approximate ratio 4:3:1, respectively. The positions of the components of the mixture were identical with those of authentic samples spotted on the same plate; all the imide spots, mixture, and authentic samples, showed the characteristic greenish fluorescence under ultraviolet light. Development of the plate in an iodine chamber showed an additional small spot with an R_f value corresponding to that of benzamide.

5-Benzamido-4-cyclohexyl-3-methyl-2-pyrrolidone (9). A.—A solution of 168 mg of the 1-unsubstituted pyrrolinone (**8**) in 100 ml of methanol was hydrogenated at 50 psi over platinum dioxide catalyst for 24 hr. Filtration of the catalyst and concentration of the filtrate to small volume furnished 60 mg of fine, white needles, mp 251–253°. Further evaporation gave an additional 51 mg of solid, mp 240–243°; total yield was 111 mg (64%). Recrystallization from methanol gave needles: mp 258.5–259°; ν^{KBr} 3330, 2960, 2900, 1715, 1650 cm^{-1}; ν^{CDCl_3} 3410, 2910, 2840 cm^{-1}; δ^{CDCl_3} 0.97 (d, J = 7.2 cps, CH_3), 0.95–2.0 (m, C$_6H_{11}$), 3.00 (six lines of doublet–quartet, CHCH$_3$), 3.76 (d, broadened J = 6 cps, C$_6$H$_{11}$CH), 5.4 (broad-exchangeable, NH), 5.87 (d, J = 6 cps, H-5), 6.4 (broad-exchangeable, NH), 7.4 ppm (m, 5).

Anal. Calcd for $C_{18}H_{24}N_2O_2$ (300.39): C, 71.97; H, 8.05; N, 9.33. Found: C, 71.45; H, 7.91; N, 9.09.

5-Benzamido-4-cyclohexyl-1-methoxymethyl-3-methyl-2-pyrrolidone (11, R = CH$_3$).—A solution of 400 mg of the 1-methoxymethylpyrrolinone (**3**) in 200 ml of methanol was hydrogenated at 50 psi over platinum dioxide catalyst for 24 hr. Filtration of the catalyst and evaporation of the filtrate furnished 454 mg of clear, viscous oil; trituration with isopropyl ether gave 255 mg (62% yield) of white, crystalline solid, mp 109–112°; after recrystallization from ether the melting point was 119–120°. Spectral data can be obtained from author.

Anal. Calcd for $C_{20}H_{28}N_2O_3$ (344.44): C, 69.74; H, 8.19; N, 8.13. Found: C, 69.92; H, 8.24; N, 7.84.

5-Benzamido-4-cyclohexyl-1-hydroxymethyl-3-methyl-2-pyrroline (11, R = H).—A solution of 400 mg of the 1-hydroxymethylpyrrolinone (**7a**) in 200 ml of methanol was hydrogenated at 50 psi over platinum dioxide catalyst for 24 hr. Filtration of the catalyst and evaporation of the filtrate gave 381 mg (92%) of a white, crystalline solid, mp 138–140°; after repeated recrystallization from ethanol, the double melting point was 164° and 250–251°. Spectral data can be obtained from author.

Anal. Calcd for $C_{19}H_{26}N_2O_3$ (330.41): C, 69.06; H, 7.93; N, 8.48. Found: C, 68.64; H, 7.83; N, 8.33.

A solution of 75 mg of the 1-methoxymethyl cyclohexylpyrrolidone (**11**, R = CH$_3$) and 44 mg (0.44 mole) of chromic anhydride in 4 ml of 75% acetic acid was heated on the steam bath for 10.5 hr. The reaction mixture was diluted with 20 ml of water and extracted repeatedly with methylene chloride; after washing with sodium bicarbonate solution and with water, the methylene chloride was evaporated to furnish 74 mg of smeary, white solid. Trituration with ether furnished 47 mg (71% yield) of white, crystalline solid, mp 248–250°; mixture melting point with an authentic sample of the 1-unsubstituted pyrrolidone **9** showed no depression. Similar oxidation of **11** (R = H) gave **9** in 48% yield.

3-Methyl-4-phenyl-3-pyrrolin-2-one (10).—A suspension of 146 mg (0.50 mmole) of the 5-benzamidopyrrolinone (**8**) in ether was added during 10 min to a solution of 60 mg (8.6 mg-atoms) of lithium in 25 ml of liquid ammonia. The reaction mixture was then stirred for an additional 30 min. During the final 5 min, the color changed from deep blue to bright orange-yellow. On addition of 800 mg (15 mmoles) of ammonium chloride, the color faded to pale yellow. The ammonia was allowed to evaporate; the residue was taken up in 1 *N* hydrochloric acid, and extracted repeatedly with methylene chloride. Evaporation furnished 91 mg of orange oil; trituration with methylene chloride–ether furnished 7 mg (8%) of the pyrrolinone **10**, mp 155–158°; mixture melting point with an authentic sample[10] was 155–158°; the infrared spectra were identical.

The mother liquor was evaporated, redissolved in methanol, and treated with charcoal to furnish 39 mg of pale yellow oil. Thin layer chromatography showed that this contained the pyrrolinone **10** and three or four other components. Nothing further could be crystallized from this oil.

5-Benzamido-1,3-dimethyl-4-phenyl-3-pyrrolin-2-one (12).—A solution of 200 mg of the bicyclic pyrrolinone (**2**) in 100 ml of methanol was hydrogenated for 5 hr at 50 psi over Raney nickel catalyst. After filtration, the methanol was evaporated to furnish 127 mg (63%) of slightly greenish white, crystalline solid. Tlc showed only one mobile spot; however, a small amount of material remained at the origin, and there appeared to be a trace amount of material traveling with the solvent front. The compound was chromatogaphed on a column of neutral alumina (Woelm) and recrystallized from methanol to furnish white crystals of **12**: mp 248–249°; λ_{max}^{EtOH} 225 mμ (ε

20,000), 234 (20,000), 271 (8200); no change on addition of dilute acid or dilute base; ν^{KBr} 3340, 1690, 1660 cm^{-1}; δ^{DMSO-d_6} 2.03 (d, J = 1.5 cps), 2.88 (s, 3), 6.66 (dd, 1, J = 9 and 1.5 cps; after D_2O addition and heating, 9-cps splitting disappeared, leaving a slightly split, poorly resolved band, 6.60 ppm, J = *ca.* 1 cps); 7.2–7.9 (m, 10), ppm (d, J = 9 cps, exchanges with D_2O and heat).

Anal. Calcd for $C_{19}H_{18}N_2O_2$ (306.35): C, 74.49; H, 5.92; N, 9.15. Found: C, 74.32; H, 6.26; N, 9.00.

7-Methyl-2,8-diphenyl-4H-pyrrolo[1,2-*c*][1.3.5]oxadiazin-6-(8aH)-one (14). A.—To a solution of 500 mg of the bicyclic pyrrolinone (**2**) in 60 ml of methanol was added 10 ml of water, followed by 10 ml of 10% sodium bicarbonate solution. The solution immediately became bright orange. After evaporating slowly in a 75° bath for 3.5 hr, the solution was diluted with water, chilled, and filtered to furnish 123 mg (25%) of **14** as white crystals, mp 215–217° dec; after recrystallization from methanol, the melting point was 222–223° dec; for spectral data, see Table I.

Anal. Calcd for $C_{19}H_{16}N_2O_2$ (304.34): C, 74.98; H, 5.30; N, 9.21. Found: C, 74.91; H, 4.85; N, 9.18; mol wt (mass spectrum), 304.

Methylene chloride extraction of the aqueous filtrate from above furnished a yellow oil which showed at least six spots on a thin layer chromatogram.

B.—To a solution of 500 mg of **2** in 60 ml of methanol was added 10 ml of water followed by 10 ml of 10% sodium acetate solution. The solution slowly went from colorless to bright yellow. Isolation as in A gave 317 mg (63%) of very pale yellow, crystalline solid, mp 220–223° dec. Thin layer chromatogram showed only **14**. Extraction of the aqueous filtrate with methylene chloride furnished 143 mg of oily, yellow material. A thin layer chromatogram showed two major and two minor components in addition to a trace of **14**.

A solution of 100 mg of **14** and 120 mg of chromic anhydride in 8 ml of 50% acetic acid was heated on the steam bath for 24 hr. After cooling, the mixture was diluted with 20 ml of water and extracted repeatedly with methylene chloride. After washing with sodium bicarbonate solution and with water, the methylene chloride was evaporated to furnish 49 mg of white solid which was triturated with isopropyl ether to furnish 35 mg of white crystals, mp 158–161°; mixture melting point with an authentic sample of 3-methyl-4-phenylmaleimide was 160–165°. The thin layer chromatogram showed one minor spot in addition to the maleimide.

Acetoxymethylpyrrolinone 7d from 14.—A solution of 73 mg of **14** in 5 ml of glacial acetic acid was refluxed for 3 hr. During this time, a yellow color developed and then faded. The acetic acid was diluted with methylene chloride, and the solution was then washed with sodium bicarbonate solution and with water. Evaporation furnished a yellow-orange oil; trituration with ether–isopropyl ether furnished 12 mg (14% yield) of the 1-acetoxymethylpyrrolinone (**7d**), mp 158–163°; the infrared spectrum was identical with that of a sample prepared from **2**. Evaporation of the filtrate furnished 55 mg of yellow oil; tlc showed several spots. No further crystals were obtained.

Reaction of 14 with Methanolic Sulfuric Acid.—A solution of 50 mg of **14** in 20 ml of methanol containing 3 drops of concentrated sulfuric acid was refluxed for 12 hr, then concentrated *in vacuo* and diluted with 50 ml of water. A white precipitate slowly settled out; filtration furnished 16 mg of white solid, mp 95–100°. The tlc showed four minor spots in addition to a major spot corresponding to the 1-methoxymethylpyrrolinone (**3**).

1-Nitroso-3-methyl-4-phenyl-3-pyrrolin-2-one.—A slurry of 111 mg of 3-methyl-4-phenyl-3-pyrrolin-2-one (**10**) in 0.9 ml of water containing 187 mg of potassium hydroxide was cooled to 0° in an ice–salt bath. After addition of 78 mg of sodium nitrite, the mixture was treated dropwise with 0.8 ml of 40% sulfuric acid without allowing the temperature to rise above 7°. The mixture became yellow, was acidic to congo red paper, and turned starch–iodide paper blue. After standing overnight at 0°, a yellow solid was collected and dissolved in ether. The ether was washed with water, dried, and evaporated to furnish 93 mg of fine, yellow crystals: mp 157–160°; after recrystallization from ethanol, mp 164–164.5; ν^{KBr} 3100, 3010, 1740, 1690, 1630 cm^{-1}; δ^{CDCl_3} 2.24 (t, 3, J < 1 cps), 4.51 (q, 2, J < 1), 7.50 ppm (s, 5).

Anal. Calcd for $C_{11}H_{10}N_2O_2$ (202.21): C, 65.33; H, 4.98. Found: C, 65.18; H, 5.06.

Ethyl 3-Cyano-2-methyl-3-phenylpropionate (16).—A mixture of 11.7 g (0.10 mole) of phenylacetonitrile and 3.9 g (0.10 mole) of sodium amide in 125 ml of dry benzene was refluxed for 11.5 hr, and then allowed to cool. A solution of 18.1 (0.10 mole) of ethyl 2-bromopropionate in 25 ml of dry benzene was then added rapidly, and the mixture was warmed cautiously until a vigorous reaction ensued. When the reaction had subsided, heating was resumed, and the mixture was refluxed for a total of 16 hr, cooled, poured into water, and acidified with 6 *N* HCl. The benzene layer was separated, washed, dried, and evaporated to furnish 18.9 g of a red oil. The aqueous layer was extracted with ether; evaporation of the dried ether solution furnished 3.4 g of red oil and 693 mg of white, crystalline solid, mp 189–191°. Recrystallization gave prisms, mp 194–195°; the infrared spectrum was identical with that of **19** described below.

The 22.3 g of combined red oil was distilled at 0.35 mm; the fraction boiling at 104–120° was collected as the nitrile ester yielding 7.4 g (34%); ν^{neat} 3010, 2270, 1740 cm^{-1}.

4-Methyl-5-oxo-α,3-diphenyl-Δ²-α-pyrrolidineacetonitrile (19).—A mixture of 180 mg (4.6 mmoles) of sodium amide and 539 mg (4.6 mmoles) of phenylacetonitrile in 30 ml of dry benzene was refluxed for 11 hr and then cooled. After addition of 1.00 g (4.6 mmoles) of the cyano ester (**16**) in 20 ml of dry benzene, the mixture was refluxed for an additional 16 hr and then diluted with water and acidified with 6 *N* hydrochloric acid. Evaporation of the washed and dried benzene layer furnished 1.583 g of red slush; trituration with ether gave 362 mg of white, crystalline solid, mp 189–191°. The aqueous layer was extracted with ether; evaporation of the ether furnished 49 mg of white crystals, mp 191–193°. On standing, the combined mother liquors furnished an additional 12 mg of solid, mp 185–187°; total yield was 432 mg (44%). The combined solid fractions were recrystallized from ethanol to give **19**: mp 194–195°; λ_{max}^{EtOH} 277 mμ (ε 14,000); no change with dilute acid; $\lambda_{max}^{EtOH + base}$ 224 mμ (ε 10,000), 314 mμ (ε 19,000); ν^{KBr} 3240, 3140, 3080, 2230, 1760, 1630 cm^{-1}; δ^{CDCl_3} 1.38 (d, 3, J = 7.2 cps), 2.55–2.85 (m, 1), 3.95 (d, 1, J = 4.5 cps), 6.8–7.3 (m, 10), 9.0 ppm (broad, 1).

Anal. Calcd for $C_{19}H_{16}N_2O$ (288.33): C, 79.14; H, 5.59; N, 9.72. Found: C, 79.25; H, 5.82; N, 9.74.

A mixture of 250 mg of chromic anhydride and 500 mg of **19** in 14 ml of glacial acetic acid and 1 ml of water was heated for 12 hr on the steam bath. After dilution with 50 ml of water, the mixture was extracted with methylene chloride. Evaporation of the washed and dried methylene chloride extracts furnished 332 mg of yellow oil, which was dissolved in a minimum volume of ether and chilled to furnish 169 mg (51% yield) of white crystals of the succinimide **18**: mp 95–101°; after recrystallization from ether, mp 106° (lit.[19] mp 109°); ν^{KBr} (3.06 and 3.22 μ) 3270, 3100, 1785, 1725 cm^{-1}; δ^{CDCl_3} 1.41 (d, 2, J = 7.4), 3.00 (m, 1—six lines of ABX), 3.68 (d, 1, J = 6.6 cps), 7.4 ppm (s, 5).

3-Cyano-2-methyl-3-phenylpropionamide (17).—A mixture of 2.0 g (9.2 mmoles) of the 3-cyanopropionic ester **16** in 25 ml of 20% ethanol containing 655 mg (1 equiv) of potassium hydroxide was heated on the steam bath for 35 min. Acidification of the resulting clear solution with 6 *N* HCl caused the separation of a pale yellow oil, which was extracted into methylene chloride. Evaporation of the dried methylene chloride solution furnished 1.9 g of crude 3-cyanopropionic acid. A solution of 1.4 g (7.6 mmoles) of the acid in 25 ml of ether was treated with 0.8 ml (9.5 mmoles) of oxalyl chloride and then refluxed overnight. The yellow-orange syrup remaining after evaporation of the ether was then treated with 1.5 ml of cold, concentrated ammonia, and the resulting solution was filtered to remove a few milligrams of oxamide. After dilution with water, the solution was extracted with ether; evaporation of the dried ether furnished 313 mg of viscous, yellow oil which, upon trituration with isopropyl ether, gave the crystalline amide **17**: mp 108–115°; after recrystallization from ether, mp 131–132°; δ^{CDCl_3} 1.42 (d, 3, J = 7.5 cps), 2.50–2.95 (m, 1), 4.25 (d, 2, J = 8.1 cps), 5.7 (broad, 2), 7.37 ppm (s, 5).

Anal. Calcd for $C_{11}H_{12}N_2O$ (188.22): C, 70.18; H, 6.43; N, 14.88. Found: C, 70.02; H, 6.54; N, 14.95.

Acidification of the aqueous ammonia layer from above and extraction with methylene chloride gave 631 mg of unreacted 3-cyanopropionic acid.

Attempted Cyclization of 17. A.—A solution of 50 mg (0.27 mmole) of the amide (**17**) in 1.5 ml of cold, aqueous alcoholic

(19) C. A. Miller, H. I. Scholl, and L. M. Long, *J. Am. Chem. Soc.*, **73**, 5608 (1951).

(1:1) 1.5 *N* sodium hydroxide was allowed to stand for 3 hr in an ice bath. A pale yellow color slowly developed. The mixture was then treated with 0.04 ml (0.36 mmole) of benzoyl chloride, allowed to stand for an additional 25 min, and acidified with 6 *N* HCl. Benzoic acid precipitated from the solution, and then on prolonged standing, white needles slowly formed. These were collected to give 41 mg of 3-methyl-4-phenylsuccinimide, (**18**), mp 107–108°; the infrared spectrum was identical with that of a sample prepared from **19**.

B.—A suspension of 100 mg (0.54 mmole) of the amide (**17**) in 2 ml of chloroform was chilled in an ice–salt bath and saturated with dry hydrogen chloride gas; the solid rapidly went into solution. After standing for several days at 0°, the mixture solidified. Trituration with ether furnished a white solid which was collected; this material became an oil on contact with air. This product was immediately dissolved in 4 ml of pyridine and treated with 0.08 ml (0.72 mmole) of benzoyl chloride. The reaction mixture became warm, and a precipitate slowly settled. Filtration gave **18** mg of white solid which was insoluble in water and in methylene chloride, and which did not melt when heated to 300°. Dilution of the pyridine solution with 50 ml of water caused precipitation of 2 mg of brownish solid; thin layer chromatography showed two components. Acidification of the solution with 1 *N* hydrochloric acid and extraction with methylene chloride furnished 106 mg of sticky, red-brown solid; tlc showed that this was mainly benzoic acid.

Registry No.—**2**, 10137-20-9; **14**, 10137-21-0; **3**, 10137-22-1; **7c**, 10137-23-2; **7d**, 10137-24-3; **7a**, 10137-25-4; **7b**, 10137-26-5; **8**, 10137-27-6; **5**, 5109-46-6; **7e**, 10137-28-7; **6**, 10137-29-8; 1-hydroxymethyl-3-methyl-4-phenylmaleimide, 10137-30-1; **4**, 10137-31-2; **9**, 10137-32-3; **11** (R = CH_3), 10137-33-4; **11** (R = H), 10137-34-5; **10**, 10137-07-2; **12**, 10137-36-7; 1-nitroso-3-methyl-4-phenyl-3-pyrrolin-2-one, 10137-37-8; **16**, 10137-38-9; **19**, 10137-39-0; **18**, 10137-40-3; **17**, 10147-14-5.

Heterocyclic Studies. XXV. Rearrangements of 2-Acyl-1,2-diazabicyclo[3.2.0]-3-hepten-6-ones in Methanol and in Base[1]

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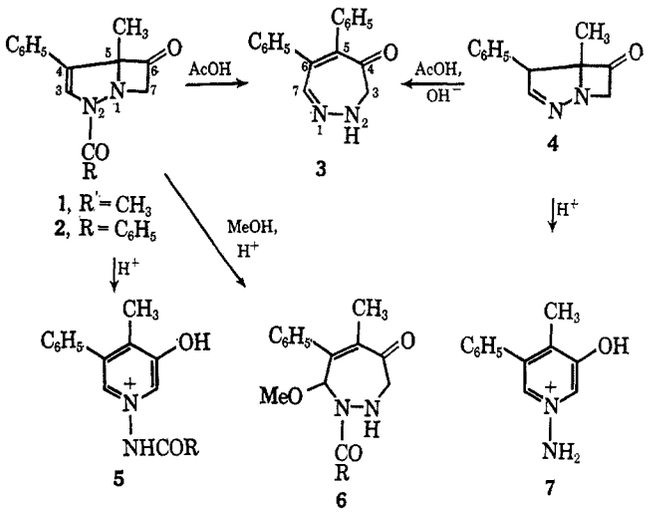
The unsaturated acyldiazabicyclic ketones (**1** and **2**) are converted by heating in methanol to the acylpyrrolinones (**8**) and 6-acylamidopyridines (**9**). In aqueous base the acetyl ketone (**1**) and the methoxy ketone (**10**) give the 4-aminopiperidines (**11** and **12**), respectively, which are readily converted to the pyridone (**13**). The benzoyl ketone (**2**) in aqueous base gives predominately the enamino ketone (**15**), with a small amount of **13**. Mechanisms for these reactions and for the thermal conversion of **2** to the uretidine (**17**) are proposed. Initial fragmentation of **1** and **2** is suggested to give the azetinone (**18**) which is then attacked by water or methanol to give intermediates that undergo cyclizations or fragmentations leading to **8**, **9**, **11**, and **15**. Recyclization of **18** leads to **17**.

The 2-acyl-Δ^3-bicyclic ketones (**1** and **2**) are converted under acidic conditions to the diazepinones (**3** or **6**) or the 1-acylamidopyridine (**5**).[2] In these reactions, the chemistry of **1** and **2** closely resembles that of the Δ^2-ketone (**4**). The latter compound gives the diazepine (**3**) or the pyridine (**7**) in acid solution; treatment of **4** with base also causes rapid isomerization to **3**[2] (see Scheme I). Under neutral or basic conditions, however, a different spectrum of products is obtained from the 2-acyl ketones (**1** and **2**); these transformations are described in this paper.[3]

On brief warming in methanol solution, the 2-acyl ketones (**1** and **2**) give rise to mixtures containing two principal products in each case. From the acetyl ketone (**1**) the 1-acetylpyrrolinone (**8a**) and 6-acetamidopyridine (**9a**) were obtained as the major and minor products, respectively. Traces of **3** and probably **6** (R = CH_3) were also detected. Under comparable conditions, (somewhat longer heating), the correspondbenzoyl compounds (**8b** and **9b**) were isolated from the methanolysis of **2**, but the pyridine (**9b**) predominated. The structures of these products were deduced from spectral and chemical properties and confirmed by conversion to known compounds. Mild alkaline hydrolysis of the pyrrolinones (**8**) gave the parent compound (**8c**) which has been described previously.[4] Likewise, hydrolysis of the 6-acylamidopyridines (**9**) under vigorous acid conditions led to the free 6-aminopyridine, the synthesis of which has been reported.[5]

SCHEME I



Qualitatively similar results were observed in solutions of **1** and **2** in methanolic sodium methoxide; under these conditions, however, the yield of the pyrrolines (**8**) was somewhat higher than in neutral solution. An increase in the yield of **8b** at the expense

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(2) J. A. Moore, F. J. Marascia, R. W. Medeiros, and R. L. Wineholt, *J. Org. Chem.*, **31**, 34 (1966).

(3) A preliminary account of part of this work has been presented: J. A. Moore, F. J. Marascia, R. W. Medeiros, and E. Wyss, *J. Am. Chem. Soc.*, **84**, 3022 (1962).

(4) J. A. Moore and J. Binkert, *ibid.*, **31**, 6029 (1959).

(5) J. A. Moore and F. J. Marascia, *ibid.*, **31**, 6049 (1959).