2,3-PYRROLIDINEDIONES. VI. REACTIONS WITH PHENYLHYDRAZINE

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While the reaction between phenylhydrazine and 1,5-diphenyl-2,3-pyrrolidinedione (I) was first reported by Bodforss (1), the essential character of the reaction was first remarked by Bucherer and Russischwili (2) who observed that two products were obtained, one of which was assigned the structure, II. Their



investigations suggested that the reaction proceeded with the elimination of aniline, although explicit evidence on this point was not presented. Aniline was observed in the mother liquors of a number of runs, and a run in which phenylhydrazine was replaced by phenylhydrazine-4-sulfonic acid permitted isolation of aniline in substantial amounts. However, these authors make no mention of their isolation of aniline or of the sulfonic acid experiment in their experimental report but only in their discussion; and the sulfonic acid of II was not isolated. Consequently the reaction was investigated with the aid of nitrogen-15, and their suggestions were confirmed explicitly (3).

Inasmuch as II is readily prepared from benzylidenepyruvic acid and phenylhydrazine, and the infrared spectra of samples prepared in this manner and from I with phenylhydrazine are identical, the tautomeric interconversion



appears to be similar to the reaction $I \rightleftharpoons \phi CH = CHC(=N\phi)CO_2H$ (IV). Spectroscopic data already reported (3) indicate a preference for III in the solid state and II in chloroform solution, suggesting that the II \rightleftharpoons III is more facile than $I \rightleftharpoons IV$.¹

The foregoing points having been established with reasonable certainty, attention was next focused on the unidentified second product from the reaction of I with phenylhydrazine, m.p. $124-125^{\circ}$ dec. (2). It has been observed (3) that

¹A chance observation in which a second spectrum of IV was desired some months after its initial preparation, at which time a spectrum had been obtained, revealed that even in the dry solid state IV was completely transformed into I at room temperature.

a similar if not identical product, m.p. 132° dec., was earlier obtained from I and phenylhydrazine by Bodforss (1). The analytical data of both groups of investigators check well with each other, but neither group made a reasonable structural assignment, nor did the later investigators (2) recognize the similarity of their compound with that of Bodforss (1). Consequently, both sets of experiments were repeated and found to afford identical products, m.p. $131-132^{\circ}$ dec., from absolute ethanol. Subsequent study revealed that this substance, Va, is in fact a monoethanolate $C_{22}H_{19}N_3O \cdot C_2H_5OH$ which loses ethanol at its melting point to give V, $C_{22}H_{19}N_3O$, m.p. $204.0-204.5^{\circ}$ (from xylene). The molecular formula of V suggested that the compound might well be a phenylhydrazone anilide, and, accordingly, benzylidenepyruvanilide (2, 4) was treated with phenylhydrazine in ethanol and the Va which crystallized from the mixture was identified by mixture melting point and the identity of the infrared spectra.

In a subsequent experiment benzylidenepyruvanilide was treated with phenylhydrazine in a mildly acidic medium and a substance, VI, melting slightly lower than V was produced. VI depressed the melting point of V somewhat and possessed a strikingly different infrared spectrum, although it proved to be isomeric when analyzed. Consequently, V was subjected to prolonged heating above its melting point (in xylene) in one experiment and to refluxing in acetic acid in a second, and in both cases VI was produced. Inasmuch as refluxing II (III) with acid isomerizes it to 1,5-diphenyl- Δ^2 -pyrazoline-3-carboxylic acid (5, 6) it seemed reasonable to suppose that an analogous isomerization had occurred with $V \rightarrow VI$. Since VI gave an intense Knorr color reaction (7), characteristic of pyrazolines, the supposition appeared to be justified, and, hence, 1,5-diphenyl- Δ^2 -pyrazoline-3-carboxanilide was synthesized from the acid by use of thionyl chloride and aniline. The substance thus obtained was identical with VI, as shown by mixture melting point and identity of the infrared spectra. Thus, the low-melting compounds of Bodforss and of Bucherer and Russischwili have been proven to be identical and may be considered to be the monoethanolate of benzylidenepyruvanilide phenylhydrazone (Va). The possibility that Va, or V, may in fact have the 3-anil structure derived from II will be considered in the sequel.

In the reaction of I with phenylhydrazine as carried out by Bodforss (1) no II was reported, but instead there was obtained still another compound, $C_{22}H_{20}N_4O$, m.p. 229–230°, VII (along with Va). Similarities in the infrared spectra of VII and V suggested to the present investigator, in agreement with Bodforss, that VII might well be the phenylhydrazide phenylhydrazone of benzylidenepyruvic acid. Consequently, II was treated with excess phenylhydrazine as described (1) for the reaction of I with phenylhydrazine, and VII was obtained. The substance gave a Knorr test (7), but the color was not permanent; so in order to check the possibility that VII was not the phenylhydrazide of 1,5-diphenyl- Δ^2 -pyrazoline-3-carboxylic acid, the latter acid was converted to its phenylhydrazide by refluxing in phenylhydrazine. The resulting phenylhydrazide (VIII), which gave a lasting color on applying the Knorr test (7), was in no way similar to VII nor, surprisingly, could VII be converted into it as V had been converted to VI. A profound change occurred in VII, but no characteristic product was obtained either on prolonged heating or on refluxing in glacial acetic acid. Since the reaction of benzylidenepyruvic acid with phenylhydrazine also produced VII, in this reaction as the only product (1), VII would appear to be the phenylhydrazide phenylhydrazone of benzylidinepyruvic acid.

Bucherer and Russischwili (2) reported that Va was the only product when the 3-anil of I,

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was allowed to react with phenylhydrazine. Thus, the question as to how Va (V) is formed, either from I or X, arises. Since exchanges between X and aromatic amines have been observed, with the structures assigned in such a manner to indicate that the exchange involves only the anil (2) or anilino (8) structure, it seems reasonable to suppose that V likewise is formed by replacement of the anil or anilino structure by a phenylhydrazone or phenylhydrazino structure. In any other system of compounds this would be taken for granted, and the structure for V would be written:



However, the production of Va (V) from benzylidenepyruvanilide would seem to preclude Vb as the correct structure, the more especially so, since no one has successfully prepared phenylhydrazones corresponding to Vb from 1,5-diaryl-2,3-pyrrolidinediones, as noted in a previous paper of this series (3).

The preceding paper in this series (8) has established the correctness of X as the structure for Doebner's "anil-anilide" (9), and as in that study the infrared

spectrum of the "anil-anilide" could not be used to differentiate X from Doebner's structure,



since both possess N—H groups, so in the present study the existence of two N—H absorption bands in the infrared spectrum is of no help in differentiating between the structures,



Nor is the presence of a weak band at 6.04 μ a useful diagnostic aid, since either structure possess a carbon-carbon double bond (conjugated) which should absorb in this region. Likewise, the carbonyl absorption observed at 5.98 μ permits no distinction since this is the position observed for the conjugated lactam carbonyl of X. It might be argued that the hydrazone bond conjugated with the amide carbonyl should lengthen the wave-length of the absorption due to the latter, but there is no conclusive evidence on this point (10). It is only arguable, on the basis of the facile transformation $V \rightarrow VI$ and from the presence of two bands in the N—H stretching region of the infrared spectrum, that V or XII are in fact more probable structures than the alternative phenylhydrazone structure (Vb).

Much the same type of argument applies to VII where two clear bands with a shoulder on one of them are to be observed in the N—H stretching region of the infrared spectrum. For VII, however, three resolvable bands (5.87 μ , 5.92 μ , 5.98 μ) and a distinct shoulder (6.04 μ) are to be found. But while this and the appearance of the spectrum suggest a mixture, the sharp melting point (232.0-232.5°) indicates a single compound. Thus nothing can be said with certainty about the structure. Since the strongest band in the carbonyl region appears at 5.98 μ it is tentatively suggested that VII is structurally related to V and that both are related to X, the parent system being



The formation of V from I under conditions comparable to the formation of the "anil-anilide" from I indicates that both reactions involve anilide formation at

some stage during the tautomeric process $I \leftrightarrows IV$ or $II \leftrightarrows V$. Since it has been argued (3) that II is formed from I by way of IV it would seem reasonable to propose that V (or XII) is formed from the "anil-anilide" (X) through the unisolable anil of benzylidenepyruvanilide (XI) by an analogous exchange at the α -carbon, *e.g.*,



especially since the following transformation is realizable:



In any case there is no precedent for the nitrogen transfer during rearrangement, the nearest related reaction being the unprecedented oxygen transfer considered in previous papers in this series (3, 11). The implication that the replacement of aniline by a substituted aniline leads to the 1-aryl-5-phenyl-3-anilino- Δ^{8} -2-pyrrolinone rather than to 1,5-diphenyl-3-arylamino- Δ^{8} -2-pyrrolinone is clear. However, detailed consideration of this hypothesis and further information on the general character of the formation of the "anil-anilide" system must await the results of further studies on this and the related I \leftrightarrows IV tautomerism now in progress in this laboratory.

EXPERIMENTAL²

1-ANILINO-5-PHENYL-2,3-PYRROLIDINEDIONE (II)

A. From 1,5-diphenyl-2,3-pyrrolidinedione (I). The procedure of Bucherer and Russischwili (2) as modified (3) was used. The product melted at $154-155^{\circ}$ dec.

B. From benzylidenepyruvic acid. The procedure of Ciusa (5) or the standard procedure for phenylhydrazone preparation was used: m.p. 154-155° dec. No depression when mixed

² Melting points are uncorrected.

with the product from (A). The infrared spectra of chloroform solutions of (A) and (B) were identical as were their Nujol mull spectra, the latter being characteristic of amino acids and the former appearing as previously reported (3).

FIRST BY-PRODUCT (VA) FROM THE REACTION OF I WITH PHENYLHYDRAZINE

A. By the procedure of Bucherer and Russischwili (2). The product was recrystallized from absolute ethanol, m.p. $131-132^{\circ}$ dec. Upon slow continued heating the substance resolidified and remelted at 198-200°.

B. By the procedure of Bodforss from I (1). The product was recrystallized from absolute ethanol, m.p. 131-132° dec. It did not depress the m.p. of the previous sample and possessed an identical infrared spectrum, both having bands at 3.0 μ (O—H) and 3.20 μ (N—H).

C. By the procedure of Bodforss (1) from IX (X) (8). As reported (1) the product is identical in all respects with that obtained in procedure (B), and hence in procedure (A) as well.

D. From benzylidenepyruvanilide. Benzylidenepyruvanilide (1, 4) was treated with phenylhydrazine in ethanol according to directions of Shriner and Fuson (12). The product was identical in all respects with the foregoing products. Microanalyses were obtained on all preparations and although the substance has been reported earlier (1, 2), it has not been compared with the correct molecular formula, data for which are here appended.

Anal. Cale'd for $C_{24}H_{25}N_{3}O_{2}$ ($C_{22}H_{19}N_{3}O \cdot C_{2}H_{5}OH$): C, 74.39; H, 6.50; N, 10.85.

Found: ³ C, 74.17; H, 6.43; N, 10.97.

E. Removal of ethanol. A sample of Va was recrystallized from xylene, m.p. 204.0-204.5°d.

Anal. Calc'd for C₂₂H₁₉N₃O: C, 77.39; H, 5.61; N, 12.31.

Found: C, 77.75;³ H, 5.85;³ N, 12.40.⁴

Isomerization of V. Samples of V and Va were refluxed briefly with glacial acetic acid or for a prolonged time in xylene. The products were identical upon recrystallization from ethanol, m.p. $202-203^{\circ}$ (VI). The melting point was depressed to $188-198^{\circ}d$. when V was added, and the infrared spectra of V and VI were markedly different.

Anal. Calc'd for C₂₂H₁₉N₃O: C, 77.39; H, 5.61; N, 12.31.

Found: ⁸ C, 77.60; H, 5.74; N, 11.98.

1,5-diphenyl- Δ^2 -pyrazoline-3-carboxanilide (vi)

A. 1,5-Diphenyl- Δ^2 -pyrazoline-3-carboxylic acid (6) was treated with thionyl chloride in benzene solution and then with a benzene solution of aniline in the usual manner to produce the anilide which was recrystallized from ethanol, m.p. 203-204°, with no depression on being mixed with VI produced in the preceding reaction. Infrared spectra of VI from both reactions were identical.

Anal. Calc'd for C₂₂H₁₉N₃O: C, 77.39; H, 5.61; N, 12.31.

Found: ⁴ C, 77.49; H, 5.64; N, 12.42.

B. Benzylidenepyruvanilide (1, 4) was allowed to react with phenylhydrazine in methanol to which a drop of acetic acid was subsequently added according to directions of Cheronis and Entrikin (13) for the preparation of phenylhydrazones. The product was recrystallized from ethanol and proved to be identical with VI from the previous reactions (m.p., mixture m.p., and infrared spectrum).

SECOND BY-PRODUCT (VII) FROM THE REACTION OF I WITH PHENYLHYDRAZINE

A. By Bodforss' procedure (1). A mixture of 0.4 g. of I and 0.45 g. of phenylhydrazine was heated for 10 min. at 100° and then was treated with glacial acetic acid. The product was isolated as described (1), m.p. $232.0-232.5^{\circ}$ (reported 232°).

³ Microanalysis by Anna B. Griffin, University of Michigan.

⁴ Microanalysis by Spang Microanalytical Laboratory, Plymouth, Michigan.

1,5-Diphenyl- Δ^2 -pyrazolinecarboxylic- β -phenylhydrazide (VIII). 1,5-Diphenyl- Δ^2 -pyrazolinecarboxylic acid (0.5 g.) was boiled with 1.0 ml. of phenylhydrazine for 30 min., diluted with benzene, cooled, and filtered. The product was recrystallized from aqueous ethanol, m.p. 179.7-180.5°. The infrared spectrum was strikingly different from that of the product of the previous reaction but possessed relatively strong bands attributable to N—H stretching at the same frequencies as for the previous compounds.

Anal. Cale'd for C₂₂H₂₀N₄O: C, 74.03; H, 5.66; N, 15.72.

Found: C, 74.03;⁸ H, 5.54;⁸ N, 15.42,⁴ 15.33.⁴

Knorr tests (7). The Knorr test for the pyrazoline system was carried out on the listed compounds as follows: 9 ml. of conc'd sulfuric acid was added to 1 ml. of water and a crystal of the substance was dissolved in the resulting solution. There was then added 1 drop of alcoholic ferric chloride solution. A positive test was indicated by the immediate development of an *intense* coloration which persisted after 12 hrs.

Compound	Color	Duration
II (III)	Crimson	Several hours ^a
Va	Greenish blue	Several hours ^a
v	Greenish blue	Several hours ^a
VI	Emerald green	Positive
VII	Brown-violet	Several hours ^o
VIII	Sapphire blue	Positive

^a The initial brilliant color changed to a muddy brown after several hours.

SUMMARY

The reactions of 1,5-diphenyl-2,3-pyrrolidinedione and of 1,5-diphenyl-3phenylamino- Δ^3 -2-pyrrolinone (Doebner's "anil-anilide") with phenylhydrazine have been examined and evidence for the structure of the resulting products has been presented. No conclusive decision is possible between the alternatives of the anilide (or phenylhydrazide) of benzylidenepyruvic acid phenylhydrazone and the isomeric 1-phenylamino-5-phenyl-3-phenylamino (or -3- β -phenylhydrazino)- Δ^3 -2-pyrrolinone structures. Transformation of the anilide phenylhydrazone (or the isomeric phenylaminopyrrolinone) to 1,5-diphenyl- Δ^2 -pyrazoline-3-carboxanilide has been demonstrated.

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