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

2,3-PYRROLIDINEDIONES. IV. FURTHER STUDIES ON TAUTOMERISM

WYMAN R. VAUGHAN AND DONALD I. McCANE[1]

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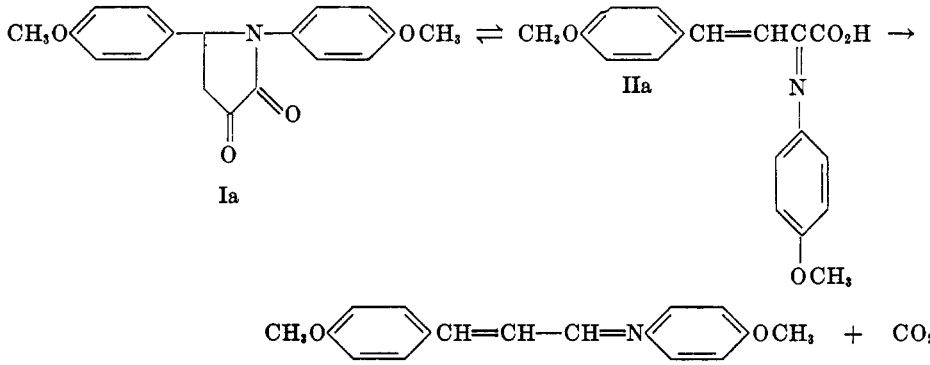
In a previous report from this laboratory (1), evidence of a kinetic character was presented for the hypothesis that 1,5-diaryl-2,3-pyrrolidinediones (I) are tautomeric with 3-arylidene-2-aryliminopropionic acids (II). The evidence consisted chiefly in the identity of rates of carbon dioxide evolution from the 1,5-*bis*-*p*-methoxyphenyl-2,3-pyrrolidinedione (Ia) and the corresponding arylidenearyliminopropionic acid (IIa) coupled with kinetic data showing that Ia is converted into IIa at a rate appreciably greater than the rate of carbon dioxide evolution.



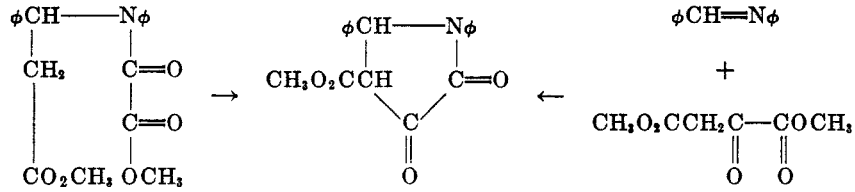
The structure of the pyrrolidinedione system (I) has been considered in the first paper in this series, but it seems advisable to record such additional structural information as is presently available before discussing the question of tautomerism in greater detail.

A lactonic structure has been proposed by Garzarolli-Thurnlackh (2) and by others. In confutation of such arguments the reaction of 3-anisylidene-2-anisyliminopropionic acid with hydrogen to give two reduction products, α-anisylamino-γ-anisylbutyric acid and 1,5-dianisyl-3-hydroxy-2-pyrrolidone, appears conclusive and at the same time establishes the intimate relationship between the 1,5-diaryl-2,3-pyrrolidinedione and α-arylimino-β-arylidenepropionic acid systems (1).

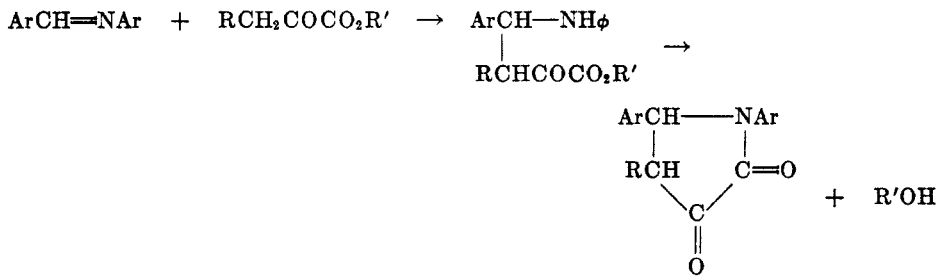
The conversion of 4-carbomethoxy-1,5-diphenyl-2,3-pyrrolidinedione to 1,5-diphenyl-2,3-pyrrolidinedione previously cited (3) can be taken as indicative but not entirely conclusive, because the reaction in its present state is not at all satisfactory from the yield standpoint and because the very conditions necessary for the hydrolysis of the carbomethoxy group appear to promote the tautomeric rearrangement, since the carbomethoxypyrrolidinedione is readily soluble in warm alkali and even in warm bicarbonate. Obviously if a rearrange-

[1] Abstracted in the main from a portion of the Ph.D. Dissertation of Donald I. McCane, University of Michigan, 1953.

ment occurs during the desired conversion, the value of any conclusions based on subsequent product formation is diminished. However, more secure support for the presently accepted structure is adducible from the identity of the Dieckmann cyclization product from methyl 3-phenyl-3-(N-methoxalyl-N-phenylamino)propionate and the addition-cyclization product from benzylideneaniline (*cf.* 4) and methyl methoxalylacetate.



The latter reaction was first realized by Simon and Conduché (4) who used the ethyl ester, and a sample of the ethyl ester prepared according to their directions proved to have an infrared spectrum generally resembling that of the methyl ester prepared under similar conditions. The reaction is obviously a variant of the synthesis of 1,5-diaryl-2,3-pyrrolidinediones from pyruvic acid or substituted pyruvic acids (3, 5) and is reasonably formulated as a Michael type addition with subsequent cyclization:

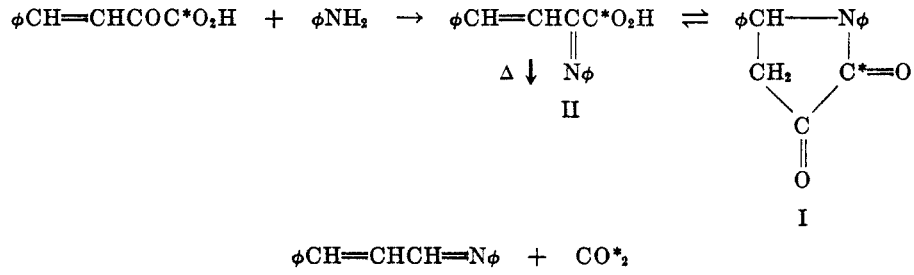


R	R′
$CO_2C_2H_5$	C_2H_5 (36)
CO_2CH_3	CH_3
ϕ (37)	H (37)
H (2)	H (2)

It should be noted that the infrared spectra of the 4-substituted-1,5-diphenyl-2,3-pyrrolidinediones prepared in this manner clearly resemble the spectra of the simpler 1,5-diaryl-2,3-pyrrolidinediones; and in addition, 4-carbethoxy-1,5-diphenyl-2,3-pyrrolidinedione may be thermally decomposed in boiling nitrobenzene to give one mole of carbon dioxide per mole of compound, as do the previously studied 1,5-diaryl-2,3-pyrrolidinediones (6). Thus, when all of the available evidence is considered, there is little if any reason for not accepting the 1,5-diaryl-2,3-pyrrolidinedione structure as established.

Because of the unique character of the rearrangement it seemed desirable to obtain additional evidence in support of the tautomeric hypothesis. Accordingly,

the isotope tracer technique suggested itself. It seemed reasonable, in view of the large body of evidence (3, 6) that is at hand showing that II can be converted smoothly into I, that a preparation of I from benzylidenepyruvic acid-1-C^{14} by way of its 2-phenylimino derivative would afford a sample of I which should yield radioactive carbon dioxide upon thermal decomposition, if, and only if, I rearranged to II:



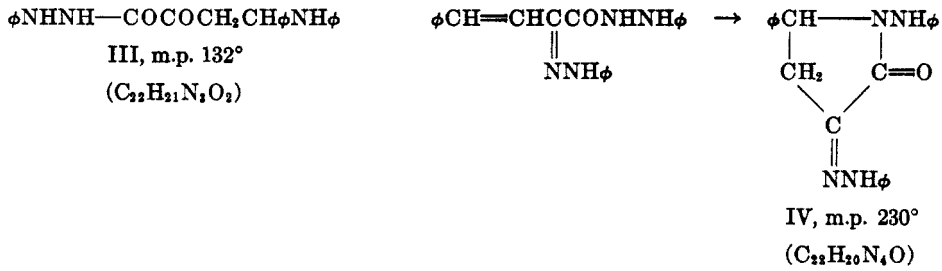
It has been pointed out that the conversion of I to II has been realized only in the one specific case of Ia (1) whereas the reverse reaction constitutes the best general method for the preparation of the analogs of I (3). The reaction, II → I, may be carried out directly, or more conveniently, without actually isolating II, from benzylidenepyruvic acid and aniline (3).

Accordingly, cuprous cyanide-C^{14}, was prepared from barium carbonate-C^{14} (7) and then was allowed to react with acetyl bromide to give pyruvonitrile-1-C^{14} which was hydrolyzed to pyruvic acid-1-C^{14} [*cf.* the preparation of pyruvic acid-2-C^{14} by Calvin and Lemmon (8)]. Next, the labelled pyruvic acid was condensed with benzaldehyde to give the desired benzylidenepyruvic acid-1-C^{14} which reacted with aniline in absolute ethanol (3) to give I-2-C^{14}.

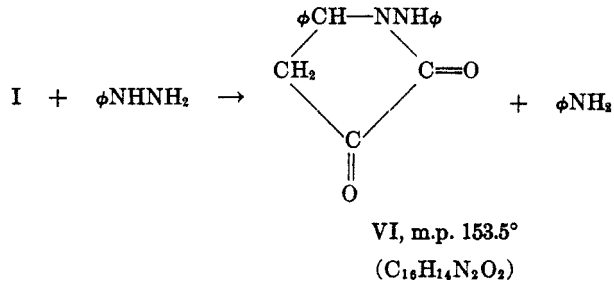
The labelled sample of I was dissolved in *o*-dichlorobenzene and the solution was heated to effect evolution of carbon dioxide which was absorbed in alkali and precipitated as barium carbonate. The absolute specific activity of the barium carbonate thus obtained was 94.9 ± 2.1 % that of the barium carbonate with which the synthesis was started. Thus, it is clear that even though II cannot be obtained from I in isolable quantities, it must be the intermediate involved in the thermal decomposition of I to cinnamylideneaniline and carbon dioxide. In the light of this evidence and the evidence afforded by the previous kinetic study (1) it now may be stated unequivocally that 1,5-diaryl-2,3-pyrrolidinediones are invariably decomposed thermally to cinnamylideneanilines and carbon dioxide by initial rearrangement to the isomeric 3-arylidene-2-aryliminopropionic acids.

In view of the general tautomeric behavior of I and its analogs, it is of considerable interest to re-examine some of the earlier work on the chemistry of this system. It has been reported that two products are obtained when I is allowed to react with phenylhydrazine (9): one substance melted at 132° dec. and the other at 230°.

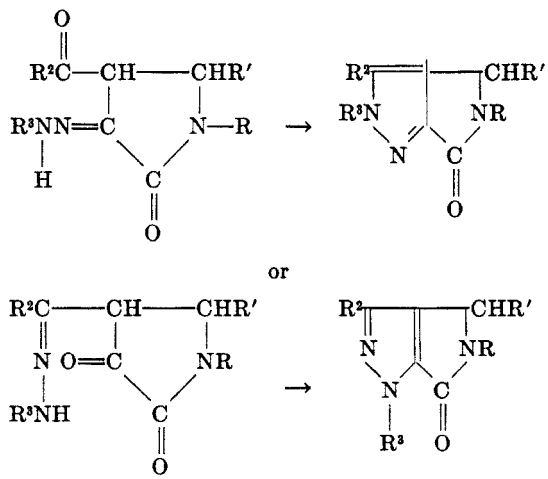
The following structures were assigned:



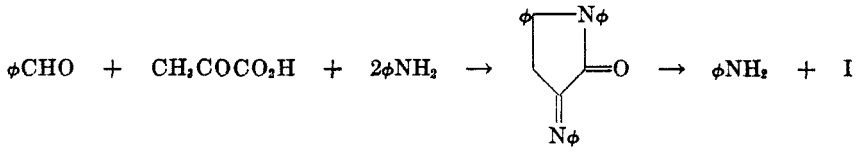
Subsequently, others carried out the same reaction and obtained two different products (10): one melting at 124–125° dec., $C_{16}H_{14}N_2O$, (V) was uncharacterized, and the other melting at 153.5° was assigned the structure VI, with the reaction formulated as:



However, they failed to isolate and identify the aniline. These investigators were unable to prepare the simple 3-phenylhydrazone of I, notwithstanding the fact that the 3-anil was known (11). Others subsequently reported a series of 3-phenylhydrazones of 4-acyl-2,3-pyrrolidinediones (12), but reasonable doubt exists as to whether these substances were in fact 3-phenylhydrazones or were phenylhydrazones derived from the 4-acyl group, since the pyrazopyrrolidones to which the phenylhydrazones were cyclized were not characterized:

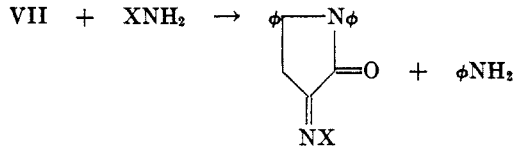


The literature abounds in examples of reactions wherein I or its analogs or their tautomers afford 3-anils, *e.g.*, VII, on treatment with amines (2, 9–11, 13–24):



VII

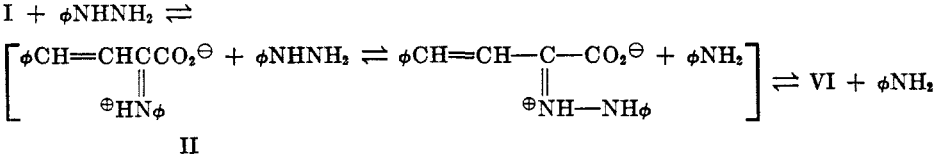
Furthermore, it has been shown that VII will react with amines to give analogs (9):



VIII

However, only the two papers cited above (9, 10) consider the reaction of either I or VII with phenylhydrazine; the former reports the same product, III, from VII and phenylhydrazine as from I and phenylhydrazine, but states that from VII, III is the sole product. Similarly, the latter reports the same product, V, from VII and phenylhydrazine as from I and phenylhydrazine but states that from VII, V is the sole product. It would appear that III and V are the same substance in spite of the discrepancy in decomposition temperature and ascribed molecular formulae, since the analytical data reported for III are: C, 73.9; H, 6.4; N, 11.0 and for V: C, 74.18; H, 6.38; N, 10.97. Neither set of data is satisfactorily in accord with the proposed molecular formulae, but the agreement *inter se* is good.

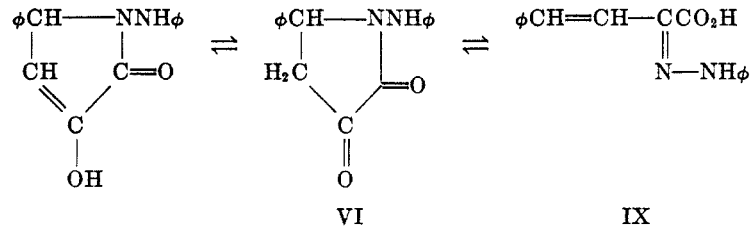
If one accepts as a working hypothesis the identity of III and V, it becomes possible to consider the behavior of I with phenylhydrazine in a rational manner. Two facts militate against the probability that the 3-carbonyl of I reacts directly with phenylhydrazine: one is that the oxygen function in this position appears to be an enolic hydroxyl (3) and the other is that the phenylimino group of the isomeric form II, since it is zwitterionized (1), is accordingly a more attractive site for such a reaction. Thus, the initial reaction with phenylhydrazine should lead to VI:



II

Evidence for the assigned structure of VI is sketchy at the very best. It is reported to melt at 153.5°, to form salts readily and to be sufficiently acidic to

dissolve in dilute aqueous ammonia (10). We have found that it melts, with subsequent decomposition and the evolution of a gas, at 154–155°, gives a strong greenish blue-violet color with alcoholic ferric chloride thus ruling out IX as its principal structure, dissolves readily in 5% sodium bicarbonate, especially on warming, and may be reprecipitated from bicarbonate solution with acid (unaltered), thus arguing against a 3,4-pyridazinedione structure (10). Since the color of VI is light orange, it obviously possesses a strong chromophore; thus, the dicarbonyl structure is favored over the enolic structure or the isomeric analog of II. The presence of bands in the infrared spectrum at 5.74 μ and 5.97 μ (chloroform) confirm the presence of the two carbonyl groups suggested by the color, and the absence of any distinctly resolvable band near 6.02 μ, which is present in the spectrum of I, points to little or no carbon-carbon double bond. Likewise, the absence of a clearly defined band in the 2.93 μ region, which is present in the spectrum of I, indicates a correspondingly low concentration of hydroxyl. A broad band peaking at 3.29 μ confirms the presence of the nitrogen-hydrogen bond, and owing to its width, it may mask any weak hydroxyl absorption. That there is some enolic hydroxyl is demonstrated by the positive ferric chloride test, however. Consequently, it would appear that VI correctly represents the structure of this compound, which is slightly enolized and whose distinctly acidic character may be attributed to facile isomerization to IX. The system is thus completely analogous to the 1,5-diaryl-2,3-pyrrolidinedione-benzylidenepyruvic acid anil system:



VI IX

The alternative 1,5-diphenyl-Δ^2-pyrazoline-3-carboxylic acid structure need not be considered since this substance, which can be formed by heating IX (VI) in acetic acid has been fully characterized and melts with loss of carbon dioxide at 192–193° (25, 26).

The spectrum of VI in the solid state indicates that the isomeric change into IX is far more facile than with the system I → II, for the spectrum of VI in Nujol resembles that of II under similar conditions more closely than it does that of I. There is little or no indication of absorption between the 3 μ and 6 μ regions, the first strong band appearing at 6.13 μ; thus, an ionized carboxyl is strongly suggested, and IX (zwitterionized) would account for this.

In view of the extraordinary nature of the 2,3-pyrrolidinedione system, it seemed advisable to obtain additional evidence in support of the direct exchange between phenylhydrazine and aniline and for the formation of VI from IX by a reaction analogous to the formation of I from II. Accordingly, spectroscopic evidence was obtained by comparing the infrared spectra of the reaction prod-

ucts from (a) 1-(4′-anisyl)-5-phenyl-2,3-pyrrolidinedione and phenylhydrazine and (b) benzylidenepyruvic acid and phenylhydrazine with the spectrum of VI. These three spectra were identical except for small differences attributable to minor impurities and slight differences in concentration.

Since isolation of anisidine from reaction 1 (above) presented some difficulty, and because the methoxyl group has been shown to influence the position and rate of establishing equilibrium in the reaction I $\rightleftarrows$ II, it was decided to use a tracer technique to confirm the spectroscopic evidence. Accordingly, aniline-N^{15} was prepared from potassium phthalimide-N^{15} (2%) by way of the Hofmann reaction and decarboxylation of the anthranilic acid (27); and phenylhydrazine-β-N^{15} was prepared from aniline by the Emil Fischer (28) method using potassium nitrite-N^{15} (29). From the labelled aniline, I-1-N^{15} was prepared, and from the labelled phenylhydrazine VI-1-N^{15} was prepared. Table I summarizes the mass-spectrometric data.

The labelled I was treated with ordinary phenylhydrazine, the aniline was recovered and deaminated (30, 31), and the nitrogen thus obtained was analyzed (sample 2, Table I) and found to be of the same order enrichment as the original aniline (sample 1, Table I). The sample of VI from the same reaction (sample 3) was burned to nitrogen by the Dumas procedure (31–33) and shown to contain no enrichment in N^{15}. The sample of VI (sample 6) which was obtained from the

TABLE I

ISOTOPE ANALYSIS[a]

Sample	Compound	Source	Method of Generating Nitrogen Sample	Excess-% N^{15} in Compound Obs.	Expected Excess N^{15}, %	Obs. Excess N^{15}, %
1	Aniline	Std.	A	3.44	Std.	100
2	Aniline hydrochloride	I	A	3.40	100	98.9
3	VI	I	B	0.00	0	0.0
4	KNO_2	Std.	C	2.02	Std.	100
5	Phenylhydrazine hydrochloride	II	B	2.00	100	99.0
6	VI	III	B	1.94	100	96.0

Key to Table I:

Source: I Product from the reaction of phenylhydrazine and 1,5-diphenyl-2,3-pyrrolidinedione-1-N^{15}.

II Prepared from standard enriched potassium nitrite.

III Product from the reaction of 1,5-diphenyl-2,3-pyrrolidinedione and phenylhydrazine-β-N^{15}.

Method of Generating Nitrogen Samples:

A. Deamination.

B. Dumas Combustion.

C. Reaction between potassium nitrite and ammonium chloride.

[a] Consolidated-Nier instrument, model 21-201 of the Department of Chemical and Metallurgical Engineering of the University of Michigan. Values are correct to $\pm 1.0\%$ of the recorded values.

reaction of labelled phenylhydrazine and ordinary I was burned to nitrogen by the Dumas procedure (31–33) and was shown to contain essentially the same enrichment of N^{15} as the labelled phenylhydrazine (sample 5) from which it was prepared.

It is clear from the analytical data thus obtained that the aniline isolated from the reaction between I and phenylhydrazine does in fact come from I rather than from reduction of phenylhydrazine, and hence there must be an exchange between the aniline and phenylhydrazine. The N^{15}-enrichment observed in VI prepared from ordinary I and β-labelled phenylhydrazine confirms this conclusion.

In view of these findings, and the fact that the preparation of IX from benzylidenepyruvic acid and phenylhydrazine affords a product indistinguishable from VI, it would seem reasonable to propose that the anil of benzylidenepyruvic acid is in fact the key intermediate in the preparation of VI from I and phenylhydrazine.

EXPERIMENTAL[2a, b]

Methyl β-phenyl-β-N-methoxalyl-N-phenylaminopropionate (34). Methyl β-phenyl-β-phenylaminopropionate was prepared from 14.4 g. of 1,4-diphenylazetidinone (35) by refluxing overnight in 125 ml. of hydrogen chloride-saturated methanol, which was subsequently removed *in vacuo*. The residue was ground in water and rendered slightly alkaline with sodium bicarbonate, whereupon the ester was extracted with ether and recovered by evaporation: 14.13 g., m.p. 90–95° (86.5%). It was recrystallized from methanol to yield white needles, m.p. 105–106°. The product is the same subsequently reported by Burgstahler (36) who prepared his product by esterification of the acid.

A solution of 5.1 g. (0.02 mole) of the ester in 50 ml. of phosphorus pentoxide-dried ethylene chloride containing 15 ml. of dry pyridine was treated dropwise with 3.0 ml. of methoxalyl chloride. The temperature rose and the solution became red, and almost at once there appeared a precipitate of pyridine hydrochloride. After standing 3 hr. at room temperature, the mixture was diluted with 50 ml. of ether and washed with 100 ml. of water, 100 ml. of 5% hydrochloric acid (in three portions), and finally with 100 ml. of water. The organic layer then was dried with magnesium sulfate, treated with a little Norit, filtered, and evaporated *in vacuo* on the steam-bath to leave a viscous oil which crystallized slowly to give 6.5 g. (95%) of methyl β-phenyl-β-N-methoxalyl-N-phenylaminopropionate, m.p. 71.5–75.0°. Recrystallization from benzene-petroleum ether (60–75°) afforded an analytically pure material, m.p. 75.5–76.0°.

Anal. Calc'd for $C_{19}H_{19}NO_5$: C, 66.87; H, 5.61; N, 4.10.

Found[2b]: C, 67.20; H, 5.91; N, 4.13.

4-Carbomethoxy-1,5-diphenyl-2,3-pyrrolidinedione (37). *A. By Dieckmann cyclization.* To a solution of sodium methoxide prepared from 0.07 g. of sodium and 20 ml. of absolute methanol was added 0.90 g. of methyl β-phenyl-β-N-methoxalyl-N-phenylaminopropionate. An orange color appeared and in a few minutes the mixture set to an almost colorless gel. It was allowed to stand for 4 hr., with occasional shaking, and then it was neutralized with the calculated quantity of acetic acid in 50 ml. of water. The resulting mixture was extracted with ether, and the extract was washed with water, 5% bicarbonate, and water, and was dried over magnesium sulfate, filtered, and evaporated to dryness at room temperature. The residue was triturated with hot ligroin, leaving 0.5 g., m.p. 174–178° dec.

[2a] Melting points are uncorrected.

[2b] Microanalyses by Microtech Laboratories, Skokie, Illinois.

Recrystallization from methanol at 0° afforded a pure product which melted constantly at 196–199° dec. It gave a deep red color with alcoholic ferric chloride.

Anal. Calc'd for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.89; N, 4.53.

Found[2b]: C, 69.81; H, 5.04; N, 4.98.

The ligroin extracts invariably were found to contain methyl cinnamate and some methoxalylanilide, both identified by mixture melting points. It was noted that longer reaction times and continuous shaking appeared to diminish the yield of Dieckmann product and favor the formation of the two observed decomposition products.

B. From benzylideneaniline and methyl methoxalylacetate. The method of Simon and Conduché (4) for the ethyl ester was used. Upon adding 2 g. of methyl methoxalylacetate to 50 ml. of ether containing 2 g. of benzylideneaniline, an immediate precipitate formed and was filtered off. Evaporation of the filtrate afforded a white solid which was insoluble in water but soluble in warm 5% sodium bicarbonate. It gave a deep red color with alcoholic ferric chloride and melted at 193–195° dec. The reaction was repeated in methanol, and the crude product was dissolved in warm 5% sodium bicarbonate, filtered, and reprecipitated with dilute hydrochloric acid. The precipitate was recrystallized from methanol at 0°, m.p. 196–199° dec.; no depression when mixed with the sample from (*A*).

Anal. Calc'd for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.89; N, 4.53.

Found[2b]: C, 69.80; H, 4.90; N, 4.94.

The infrared spectrum is identical with that of the product from (*A*) and generally resembles that of Simon and Conduché's ethyl analog, and closely resembles those of other 1,5-diaryl-2,3-pyrrolidinediones. A sample of the ethyl analog (4) was decomposed in nitrobenzene at the reflux temperature and the gas was collected as described for 1,5-diphenyl-2,3-pyrrolidinedione, one mole of carbon dioxide being collected per mole of compound decomposed.

Pyruvonitrile-1-C^{14} (8). Cuprous cyanide-C^{14} was prepared from barium carbonate-C^{14} by a procedure we have reported elsewhere (7). To 22.5 g. (0.125 mole) of the labelled cuprous cyanide contained in a 100-ml. flask fitted with a stirrer and reflux condenser, protected from moisture with a calcium chloride drying tube, was added 37 g. (0.3 mole) of freshly distilled acetyl bromide. The mixture was heated to 70–80° with stirring for two hours. The reaction flask was cooled and fitted with a small fractionating column, and the pyruvonitrile-1-C^{14} was distilled at 87–91°; yield, 9.5 g. (54.3%).[3]

Pyruvic acid-1-C^{14} (5). To 9 g. (0.13 mole) of pyruvonitrile-1-C^{14} was added 12.5 ml. of concentrated hydrochloric acid (*sp. gr.* 1.18) dropwise with cooling (ice-bath) and shaking. To the resulting crystalline mass was added 40 ml. of water, and the mixture was heated for two hours at 70° on a water-bath. The reaction mixture was cooled and extracted ten times with 20-ml. portions of ether. The combined ether extracts were dried over sodium sulfate.

The ether was distilled off at steam-bath temperature, and the residue was vacuum-distilled at 40–60°/18 mm. The yield of pyruvic acid-1-C^{14} was 4.38 g. (38%) and it titrated 93% pure acid with standard base.

Benzylidenepyruvic acid 1-C^{14}. This procedure is based in part on one described by Reimer (38) in the preparation of unlabelled benzylidenepyruvic acid. One gram (0.0113 mole) of pyruvic acid-1-C^{14} was added to 5 ml. of 10% sodium hydroxide and the solution cooled to 0°. To this was added with stirring 1.2 g. (0.0113 mole) of benzaldehyde followed by the dropwise addition over 10 minutes of 3 ml. of 10% sodium hydroxide. The mixture was stirred vigorously for 50 minutes. The temperature must not rise above 12° to insure good results. The sodium salt of the benzylidenepyruvic acid which precipitated was filtered, washed with a little methanol, and dried in a vacuum desiccator over calcium chloride; yield 0.9 g. (46%) of sodium salt.

The sodium salt was dissolved in 20 ml. of ice-water with vigorous shaking for two

[3] Yields of 85% or better were obtained in larger scale (0.5 mole) preparations of unlabelled pyruvonitrile by this method.

minutes and rapidly was filtered into 25 drops of concentrated hydrochloric acid in 10 g. of ice-water. The precipitated acid was filtered and dried; m.p. 68–69°; yield 0.37 g. (47% based on the sodium salt of the acid).

1,5-Diphenyl-2,3-pyrrolidinedione-2-C^{14} (3). To a solution of 0.67 g. (0.0038 mole) of benzylidenepyruvic acid-1-C^{14} in 15 ml. of absolute ethanol was added dropwise and with stirring a solution of 0.36 g. (0.0039 mole) of aniline in 5 ml. of absolute ethanol. The mixture was stirred for one-half hour at room temperature. To the resulting paste was added an additional 25 ml. of absolute ethanol. The solution was refluxed for one hour and then was cooled in an ice-bath. The pyrrolidinedione was filtered and dried; yield 0.77 g. (80%), m.p. 158–160° dec. (gas), reported m.p. 161° dec. (10).

Preparation of 1,5-diphenyl-2,3-pyrrolidinedione-1-N^{15}: *Aniline-N*^{15}. N^{15}-labelled potassium phthalimide was converted into aniline-N^{15} by the standard procedure of Holt and Bullock (27) who used the Hofmann rearrangement followed by decarboxylation of the anthranilic acid so obtained. A sample of the aniline so prepared was deaminated (30) and the nitrogen was subjected to mass-spectrometric analysis (31).

1,5-Diphenyl-2,3-pyrrolidinedione-1-N^{15}. The same procedure was used as for the unlabelled compound. The product was converted to nitrogen by the Dumas procedure and the gas was subjected to mass spectrometric analysis (31).

Reaction between phenylhydrazine and 1,5-diphenyl-2,3-pyrrolidinedione-N^{15}. To a solution of 2.51 g. (0.01 mole) of 1,5-diphenyl-2,3-pyrrolidinedione-N^{15} in 25 ml. of absolute ethanol were added 1.1 g. (0.0104 mole) of phenylhydrazine in 10 ml. of absolute ethanol and four drops of glacial acetic acid. The mixture was refluxed for one-half hour (red solution in 15 minutes). The solution stood for 12 hours at room temperature after which time it was refluxed for an additional hour.

The solution was cooled in an ice-bath and 70 ml. of water was added with stirring. The 1-anilino-5-phenyl-2,3-pyrrolidinedione (VI) was filtered and dried in a vacuum desiccator; yield 2.56 g., m.p. 144–148°. The compound was recrystallized from a mixture of chloroform-petroleum ether (60–75°); yield 2.06 g., (79%), m.p. 154–155° dec., reported m.p. 153.5° dec. (10).[4] The product was converted to nitrogen by the Dumas method and the gas was subjected to mass spectrometric analysis (31).

The filtrate from the above reaction was extracted with four 50-ml. portions of benzene. The combined benzene extracts were dried over potassium hydroxide. Anhydrous hydrogen chloride was passed into the benzene solution, and the aniline hydrochloride was filtered; yield 0.96 g. (74%), m.p. 197–199°. The aniline hydrochloride was sublimed twice at 100°/0.4 mm.; yield 0.85 g., m.p. 197–198°. This sample was deaminated (30) and the nitrogen (31) subjected to mass-spectrometric analysis.

Phenylhydrazine-β-N^{15} *hydrochloride.* Phenylhydrazine-β-N^{15} hydrochloride was prepared by the Emil Fischer method (28) from aniline and N^{15}-enriched potassium nitrite (29). A sample of the product was converted to nitrogen by the Dumas method and the gas was subjected to mass spectrometric analysis (31).

Reaction between 1,5 diphenyl-2,3-pyrrolidinedione and phenylhydrazine-β-N^{15}. This procedure is the same as that for the unlabelled compound. Part (0.66 g.) of the 1-anilino-5-phenyl-2,3-pyrrolidinedione, isolated in 75% yield, m.p. 154.5–156° d., after recrystallization from a chloroform-petroleum ether (60–75°) mixture, was used to prepare a nitrogen sample for mass spectrometric analysis by a Dumas combustion (31).

Deamination procedure. There being no previous demonstration of this method of collecting nitrogen for mass spectrometric analysis, this operation is reported in detail (*cf.* ref. 30, 31). A mixture of 0.39 g. (0.003 mole) of aniline hydrochloride, 6.0 g. (50%, 0.045 mole) of hypophosphorous acid, and 10 ml. of water was placed in a 50-ml. flask fitted with a special adapter (31). The solution was cooled to 5° in an ice-bath. A dropping-funnel with a pressure equalizing arm, containing a solution of 0.21 g. (0.003 mole) of sodium nitrite in 10

[4] This product was found to be identical with the phenylhydrazone of benzylidenepyruvic acid in all respects (24, 25).

ml. of water, was inserted into the adapter. The whole system then was swept out with a stream of carbon dioxide until micro-bubbles were obtained in the gas collection burette (30 minutes).

The mixture was stirred (magnetic stirrer) while the sodium nitrite solution was added dropwise over a period of ten minutes. The mixture was allowed to warm up slowly to room temperature, and the nitrogen which was evolved was collected for mass-spectrometric analysis.

Decarboxylation procedure. A solution of 0.251 g. (0.001 mole) of 1,5-diphenyl-2,3-pyrrolidinedione-2-C^{14} in 20 ml. of *o*-dichlorobenzene was placed in a 50-ml. flask fitted with a special adapter which was connected to a sodium hydroxide trap (39) containing 30 ml. of 1 *N* sodium hydroxide (sodium carbonate-free) diluted to 125 ml. with freshly boiled distilled water.

The entire system was swept out with a stream of carbon dioxide-free nitrogen for 15 minutes. The pyrrolidinedione solution was heated for one hour at 180° (mantle temperature) and allowed to cool while nitrogen was swept through the system for an additional hour.

To the sodium hydroxide solution which was drained into a special precipitation flask (40) were added 1.6 g. of ammonium chloride and a solution of 1.2 g. of barium chloride dihydrate in 35 ml. of distilled water. The flask was swirled to mix its contents and most of the air was removed from the flask by attaching it to a vacuum line and opening the stopcock momentarily.

After standing for 15 minutes, the flask was opened and its contents were filtered through a weighed sintered-glass filter funnel of medium porosity. The precipitated barium carbonate was washed with 200 ml. of hot distilled water and dried at 120°; the weight of barium carbonate was 0.191 g. Blank determinations carried out under identical conditions gave 4.5 mg. of barium carbonate. A portion of the barium carbonate was "plated out" and counted according to the standard procedure (41). Absolute specific activity (c./min./mg.); 215 ± 3; 212 ± 3; 222 ± 3; 219 ± 3; 217 ± 3. Specific activity of barium carbonate from which cuprous cyanide was prepared: 230 ± 3 c./min./mg. Activity of product = 94.5% original.

SUMMARY

Additional evidence for the structure of the 1,5-diaryl-2,3-pyrrolidinedione system has been presented and the "decarboxylation" reaction has been examined with the assistance of carbon-14 tracer techniques. The evidence thus obtained is in agreement with the hypothesis that 1,5-diaryl-2,3-pyrrolidinediones are tautomeric with α-arylimino-β-arylidenepropionic acids and that it is the latter species which undergoes thermal decarboxylation.

The reaction of 1,5-diphenyl-2,3-pyrrolidinedione with phenylhydrazine has been investigated using nitrogen-15 tracer techniques, and the hypothesis that the resultant 1-anilino-5-phenyl-2,3-pyrrolidinedione is formed by an exchange between the tautomeric arylimino acid and phenylhydrazine is advanced and supported.

ANN ARBOR, MICHIGAN

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