The monopicrate formed immediately in ethanol and after recrystallization from this solvent melted at 204–208°.

Anal. Calcd. for $C_{21}H_{25}O_7N_5$: C, 54.90; H. 5.49. Found: C, 55.20; H, 5.46.

9-Methyl-3,9-diazabicyclo[3.3.1]nonane Dihydrochloride.—A solution of IX (4.7 g.) in ethanol (200 ml.) was acidified with hydrochloric acid and shaken with hydrogen (30 lb.) in the presence of 5% palladium-on-charcoal (1 g.). The hydrogenolysis product was completely absorbed on the surface of the catalyst and could be washed off only with several portions of boiling water. The aqueous solution was evaporated to a sufficiently small volume to cause crystallization of the product, yield 3.3 g. (70%). Further recrystallization followed by sublimation produced a sample which sublimed unchanged on the hot-stage beginning at 260°.

Anal. Calcd. for $C_8H_{18}N_2Cl_2$: C, 45.08; H, 8.51. Found: C, 45.09; H, 8.53.

A portion of the hydrochloride was treated with sodium hydroxide and steam distilled. An aqueous solution of picric acid was added to the distillate. A dark yellow extremely insoluble picrate separated. This substance could be recrystallized only from a large amount of hot 80% acetic acid, m.p. 239–242° (dec.).

Anal. Calcd. for $C_{20}H_{22}O_{14}N_8$: C, 40.14; H, 3.17. Found: C, 40.82; H, 3.68.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF DELAWARE]

On the Structure of Pyrrolidinetriones and Oxazolidinediones

BY GLENN S. SKINNER AND CHARLES B. MILLER, JR.

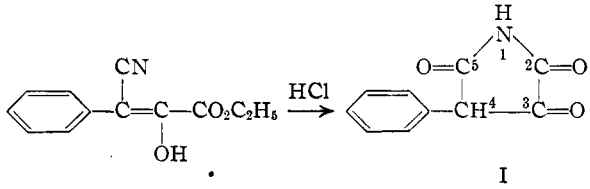
RECEIVED AUGUST 4, 1952

The condensation of ethyl oxalate with phenylacetamide yields 4-phenylpyrrolidinetrione identical with the product obtained by cyclization of ethyl β-cyano-α-hydroxycinnamate. Oxalyl chloride yields the isomeric oxazolidinedione. These isomers are further distinguished by their behavior toward alcohol, aniline and urea. The "pyrrolidinetriones" from oxalyl chloride (*vide infra*) are oxazolidinediones.

A series of compounds[1] made by the action of oxalyl chloride[2] on derivatives of acetamide has been reported. The assignment of the pyrrolidinetrione (I) structure[3] was accepted and no structural evidence was given beyond the infrared absorption studies which seemed to substantiate the structure previously assigned. Our studies of structure have not been completed but in view of interruptions and the seriousness of the question it is desirable to report the progress which shows them to be oxazolidinediones.

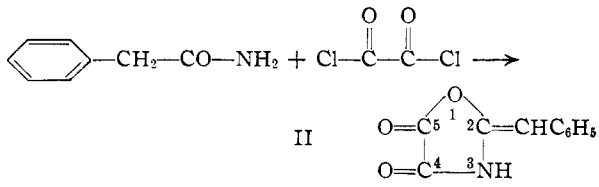
The above structure was questioned by Stolle and Luther[4] because the product from oxalyl chloride and acetanilide reacted with water to give acetic acid and oxanilic acid. It also failed to give a deep green color with dilute ferric chloride solution. Their assignment of the oxazolidinedione structure was supported by Spielman[5] especially on account of the cleavage of the ring by alcohol to the oxamic ester. Sheehan and Corey[6] have converted an oxazolidinedione through ring cleavage and condensation in an alkaline medium to an isomeric compound which was assigned the pyrrolidinetrione structure. These investigators conclude that the infrared data of the compounds from oxalyl chloride agree better with the oxazolidinedione structure.

While these arguments are very compelling and the initial error in not considering the possible oxazolidinedione structure is freely acknowledged, it is also true that the formation of isomers having different reaction characteristics is not absolute proof of the structure of either. We have therefore sought to compare the two isomers to a compound prepared in such manner that its ring structure has not been questioned. Such a reference pyrrolidinetrione (I) is provided by the reaction[7]



I

The compound (m.p. 217°) prepared by condensation of ethyl oxalate and phenylacetamide with the aid of sodium ethoxide in toluene was found to be identical with the pyrrolidinetrione (I). The product (II) from oxalyl chloride and phenylacetamide was obtained as brilliant yellow scales (dec. p. 166–167°) when crystallized from tetrahydrofuran.



II

The compound (I) when refluxed in absolute alcohol for 51 hours was recovered unchanged. The compound II after refluxing in absolute alcohol for 13.5 hours gave an almost colorless solution from which phenylacetamide (m.p. 156–157°) was isolated. With a trace of pyridine in alcohol (II) gave phenylacetyloxamic ester, m.p. 72–73°.

The compound (I) yielded a stable salt with aniline while (II) readily suffered aminolysis at room temperature to give N-phenyl-N′-phenylacetyloxamide. The aniline salt of (I) was dehydrated to 4-phenyl-3-phenyliminopyrrolidine-2,5-dione by heating at 185°.

(1) G. S. Skinner and J. F. Perkins, THIS JOURNAL, **72**, 5569 (1950).
(2) T. Figee, *Rec. trav. chim.*, **34**, 289 (1915).
(3) *Beilstein*, Vol. 4, p. 21 (436).
(4) R. Stolle and M. Luther, *Ber.*, **53**, 314 (1920).
(5) M. A. Spielman in "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, p. 239.
(6) J. C. Sheehan and E. J. Corey, THIS JOURNAL, **74**, 360 (1952).
(7) V. Harlay, *C. A.*, **31**, 6226[1] (1937); *J. pharm. chim.*, **26**, 537 (1936).

The compound (I) when heated with urea just above its melting point gave 3-imino-4-phenylpyrrolidine-2,5-dione. Similar treatment of compound (II) resulted in extensive breakdown to a mixture of products that were difficult to separate. One of these products was identified as phenylacetylurea.

The infrared absorption for 2-benzylidene-4,5-oxazolidinedione (A) shows no evidence for O–H. 4-Phenylpyrrolidinetrione (B) shows strong absorption for OH at 3.1 μ indicating that it is in the enol form. It is to be noted also that the absorption for (A) is very similar to that of the previously described trialkyl derivatives[1] in which the possibility of enolization in either structures does not exist. It would appear from this that the three bands at 5.6, 5.8 and 6.0 μ should be ascribed to two C=O and one C=C. Both 3-phenylimino-4-phenylpyrrolidine-2,5-dione (C) and 3-imino-4-phenylpyrrolidine-2,5-dione (D) give strong absorption at 6.1 μ which may be ascribed to the C=N linkage.[8] Also the absorption at 2.9 μ ascribable to N–H (D) disappears when hydrogen is replaced by phenyl (C).[9]

The identity of the authentic pyrrolidinetrione (hydroxymaleimide) with the product of the basic condensation of phenylacetamide with ethyl oxalate and the sharp distinction in the chemical behavior of the substances prepared by the use of oxalyl chloride provide definite evidence that the previously described[1] compounds possess the oxazolidinedione structure. The synthesis of the isomeric pyrrolidinetriones is under way. So far, the alkaline condensation has yielded only the pyrrolidinetrione.

Experimental

4-Phenylpyrrolidinetrione (I).—To a stirred suspension of 4.83 g. (0.21 mole) of powdered sodium in 300 cc. of toluene at 60° there was added during a half-hour 23.5 g. (0.30 mole) of absolute alcohol. After all of the sodium had reacted the mixture was distilled to remove the excess of alcohol. When the reaction mixture had cooled to 80°, 13.5 g. (0.10 mole) of phenylacetamide was added. After the mixture had cooled to 60°, 16.0 g. (0.11 mole) of ethyl oxalate was added during 10 minutes. An orange-red solid separated. The alcohol of reaction was slowly distilled with some of the toluene during a period of three hours. The residue was rapidly mixed with a large excess of concentrated hydrochloric acid (42 cc.) and 100 g. of finely crushed ice until the lumps had completely disintegrated. The yellow solid was filtered from the ice-cold toluene and washed alternately with iced water and toluene, yield 15 g. (79%), m.p. 213–215°. When recrystallized from alcohol it had m.p. 217°. The melting point was unchanged when mixed with a sample prepared from ethyl β-cyano-α-hydroxycinnamate.

2-Benzylideneoxazolidine-4,5-dione (II).—Oxalyl chloride (15.8 g., 0.125 mole) was added during three hours to a stirred mixture of 13.5 g. of phenylacetamide and 300 cc. of dry benzene at 55–60°. The mixture was then heated eight hours longer at this temperature. The brilliant yellow crystals were washed with dry benzene, then with dry ether and dried *in vacuo;* yield 17.5 g. (95%). The crude product sintered at 164° and melted with decomposition at 166–167°. It was purified by recrystallization of 8 g. from 170 cc. of pure boiling tetrahydrofuran from which 4.0 g. separated on gradual cooling, finally in ice, as glistening yellow scales, m.p. 166–167° (dec.). Three grams more was obtained by concentrating the filtrate. *Anal.* Calcd. for $C_{10}H_7O_3N$: N, 7.40. Found: N, 7.44.

Reaction with Alcohol.—In an apparatus with glass connections 0.3 g. of (I) was refluxed 51 hours in 12 cc. of absolute alcohol. From this solution there was isolated 0.26 g. of the original material, m.p. 216–217°. Similar treatment of (II) caused almost complete loss of color after 13.5 hours. Concentration of the solution to a volume of 3 cc. caused the separation of 0.20 g. of white crystals, m.p. 156–157°, identical with phenylacetamide as determined by the mixed melting point.

The intermediate ethyl phenylacetyloxamate was obtained by heating 3.0 g. (0.0157 mole) of (II), 45 cc. of alcohol and two drops of pyridine at gentle reflux for 20 minutes at which time all had dissolved. The solution was concentrated to a volume of 10 cc., then cooled in ice, at which white felt-like needles appeared; yield 2.38 g. (63.5%), m.p. 71–73°. From the evaporated filtrate there was obtained by recrystallization from tetrahydrofuran 0.24 g. (11%) of phenylacetamide, m.p. 156–157°. The filtered solution of the material (m.p. 71–73°) in 70 cc. of absolute ether was mixed with 70 cc. of petroleum ether and cooled in ice for two hours, at which 1.93 g. of white felt-like needles separated, m.p. 72–73°. *Anal.* Calcd. for $C_{12}H_{13}O_4N$: N, 5.95. Found: N, 6.03.

Reaction with Aniline.—Three grams (0.0159 mole) of (I) in 30 cc. of tetrahydrofuran was treated with 3 cc. of freshly distilled aniline. After cooling in an ice-bath the brown-yellow solid was filtered and washed with petroleum ether; 2.25 g., m.p. 144° (dec.). More (1.75 g.) was obtained from the filtrate by the addition of 50 cc. of petroleum ether. The combined solids were dissolved in 24 cc. of absolute alcohol with slight heating. The brown-yellow salt was precipitated by mixing with 20 cc. of water; 2.8 g., m.p. 146° (dec.). It was reconverted to (I) by dissolution in a minimum of alcohol, followed by the addition of a drop of concentrated hydrochloric acid and dilution with water; m.p. 217°.

One gram of the above salt was heated in an oil-bath at 170° for one hour and then at 185° for 10 minutes. The product was dissolved in 12 cc. of hot alcohol and then filtered while hot to remove a small amount of deep red granular material. Brown crystals were obtained by cooling the filtrate in an ice–salt-bath; 0.63 g., m.p. 175–180°. Concentration of the mother liquor gave 0.2 g. more. Recrystallization from carbon tetrachloride and from 50% alcohol gave 0.42 g. (47%) of yellow crystals, m.p. 179–180°. *Anal.* Calcd. for $C_{16}H_{12}O_2N_2$: N, 10.52. Found: N, 10.25.

One gram (0.0053 mole) of (II), partially soluble in 30 cc. of tetrahydrofuran, completely dissolved through the addition of 0.98 g. of freshly distilled aniline. White needle-like crystals began to separate in 15 minutes. After standing overnight the crystals were filtered, washed with ether; 0.6 g., m.p. 204–205°. A second fraction was obtained from the mother liquor by distillation of the solvent and slurrying with ether; 0.63 g., m.p. 197–200°. Crystallization of the combined product from tetrahydrofuran gave 0.9 g. (61.5%) of white needles, m.p. 204.5–205°. *Anal.* Calcd. for $C_{16}H_{14}O_3N_2$: N, 9.85. Found: N, 10.05.

Reaction with Urea.—A mixture of 3.78 g. (0.020 mole) of (I) and 2.64 g. (0.044 mole) of dry urea was finely ground in a mortar. As the mixture was heated gradually it was observed that the vapor was acid to litmus in the range 106–120° during 15 minutes. Evidence of carbon dioxide was first obtained at 138°. After maintaining the mixture at 135° for 25 minutes longer at which the evolution of carbon dioxide ceased the melt was poured from the heated tube, the spongy solid was triturated in a mortar with 20 cc. of water and the solid was filtered; yield 2.24 g. (59%), m.p. 243–246°. The crude product was crystallized from boiling alcohol (60%); 1.68 g., m.p. 248–249°. *Anal.* Calcd. for $C_{10}H_8O_2N_2$: N, 14.88. Found: N, 14.60. This is identical with the melting point of 3-imino-4-phenylpyrrolidine-2,4-dione.[10]

A mixture of 6.44 g. (0.036 mole) of (II) and 6.48 g. (0.108 mole) of fused urea was ground in a mortar and then heated similarly. After 20 minutes when the temperature had reached 109° the mixture melted slightly and the acidic vapor gave a test for carbon dioxide. As it melted much foaming ensued so that the bath was kept at 100° for 15 minutes. The mixture was then heated at 124° for one hour. The brown tacky mass was triturated with 45 cc. of water. The insoluble portion weighed 2.88 g. Repeated crystallization from a mixture of dioxane and alcohol (5:2)

(8) L. W. Daasch, THIS JOURNAL, 73, 4524 (1951).

(9) The infrared measurements were supervised by Dr. Harold C. Beachell.

(10) "Beilstein," Vol. 4, 21, 566.

gave 0.4 g. of white crystalline material, m.p. 211–213°. The melting point was not lowered by mixing with an authentic sample of phenylacetylurea (m.p. 211–213°) prepared from phenylacetyl chloride and urea. *Anal.* Calcd. for $C_9H_{10}O_2N_2$: N, 15.73. Found: N, 15.51.

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[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

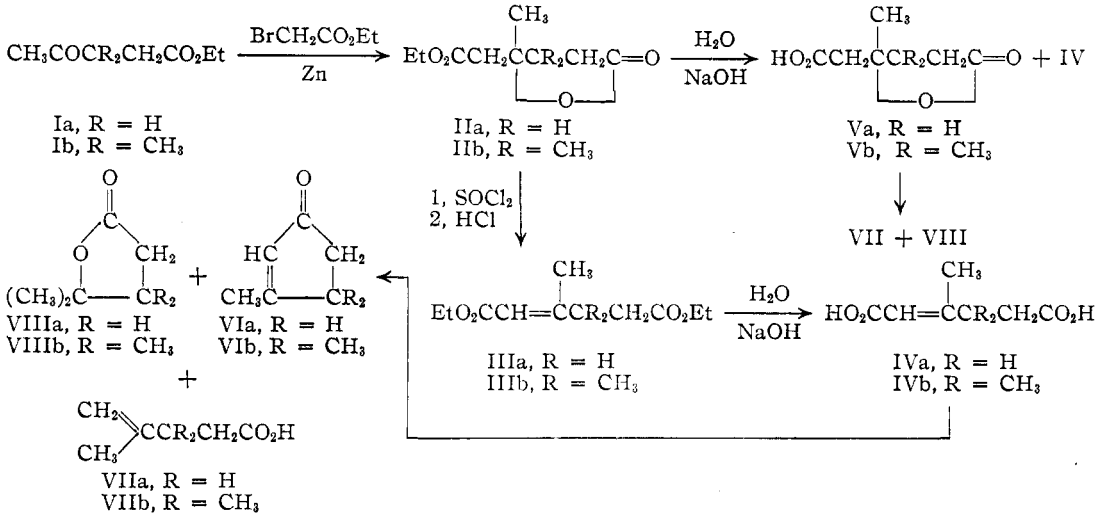
Cyclization and Decarboxylation of α-Hydromuconic Acids

BY HENRY E. BAUMGARTEN

RECEIVED SEPTEMBER 27, 1952

The thermal decarboxylation of β-methyl-α-hydromuconic acid (IVa) yields 4-methyl-4-pentenoic acid (VIIa) and γ-methyl-γ-valerolactone (VIIIa). Thermal decarboxylation of β,γ,γ-trimethyl-α-hydromuconic acid (IVb) yields largely β,β,γ-trimethyl-γ-valerolactone (VIIIb). Thermal cyclization and decarboxylation of the barium salts of the foregoing α-hydromuconic acids yields 3-methyl-2-cyclopentenone (VIa) and 3,4,4-trimethyl-2-cyclopentenone (VIb), respectively. A mechanistic interpretation of some of these reactions is suggested.

In an earlier communication[1] we described an apparently general procedure for the synthesis of certain alkylcyclopentanones which included as an important part the sequence I → V, illustrated in the flow sheet. Hydrogenation of the α-hydromuconic acid (IV) to the substituted adipic acid and cyclization of the latter constituted the remainder of the synthesis. We acknowledged at that time that a similar procedure, differing in that cyclization to a cyclopentenone preceded hydrogenation, had been utilized earlier by Okazaki.[2,3] Even earlier Ruzicka[4] had shown that distillation of the anhydrides of 3-heptenedioic acids (or treatment of their esters with sodium) gave low yields of cyclohexenones, and Merejkowsky[5] had reported that, although slow distillation of β-hydromuconic acid gave a good yield of 2-pentenoic acid and no cyclopentenone, distillation of the calcium salt of the acid gave a low yield of cyclopentenone (accompanied by 1,3-butadiene, carbon monoxide and condensation products of the ketone). This communication reports, as an extension of our earlier work, the results of a study of the cyclization and decarboxylation of β-methyl-α-hydromuconic acid (IVa) and β,γ,γ-trimethyl-α-hydromuconic acid (IVb).



The acids IVa and IVb were prepared as indicated in the flow sheet. The procedure was described in detail (for IVb) in the earlier report.[1] In that report it was stated that the direct alkaline hydrolysis of the lactonic ester IIb gave a mixture of products, the solid acid IVb and a liquid assumed but not proved to be the lactonic acid Vb, in roughly equal amounts. In this work the similar hydrolysis of IIa gave at most 15% of the solid acid IVa, the remainder of the product being a non-crystallizable liquid. Fortunately, in this later work it was possible to distil the liquid under reduced pressure with only slight decomposition. Elementary analysis and neutralization equivalent data on the distilled liquid support fairly well the lactonic acid structure, Va.

When the acid IVa was heated with a trace of manganous carbonate, a trace of barium hydroxide, or an equivalent amount of either (conditions usually conducive to the cyclization of adipic acids), decarboxylation began at about 220° accompanied by distillation of a liquid product containing only a trace of 3-methyl-2-cyclopen-

(1) H. E. Baumgarten and D. C. Gleason, *J. Org. Chem.*, **16**, 1658 (1951).

(2) K. Okazaki, *J. Pharm. Soc. Japan*, **63**, 629 (1943); *C. A.*, **45**, 188 (1951).

(3) The original paper of Okazaki is not currently available to us and, unfortunately, the abstract (ref. 2) of his work is both so unusually brief and so garbled by typographical errors that it is not clear to us whether Okazaki cyclized the equivalent of IV or of V (as the barium salt).

(4) L. Ruzicka, *Helv. Chim. Acta*, **2**, 144 (1919).

(5) B. K. Merejkowsky, *Bull. soc. chim.*, [4], **37**, 1174 (1925).