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An Abnormal Hydrolysis of γ-Nitro-γ,γ-Disubstituted Butyric Acid Derivatives

BY J. C. WESTFAHL

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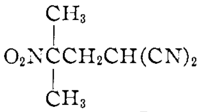
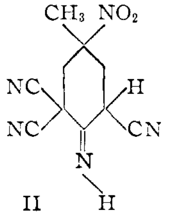
Refluxing γ-nitro-γ,γ-disubstituted butyric acid derivatives with concentrated hydrochloric acid was shown to produce γ,γ-disubstituted-γ-butyrolactones. Five examples and a plausible mechanism of this unusual reaction are given.

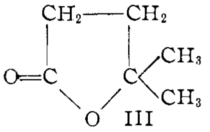
In two recent papers a series of compounds prepared from active hydrogen compounds and low molecular weight polyvinylidene cyanide were reported.[1,2] The structures of these compounds were established by hydrolysis and identification of the acids produced and by infrared spectroscopy. For the compounds derived from 2-nitropropane and from nitroethane, and assigned structures I and II, the hydrolyses proceeded abnormally. The hydrolysis of I and II will be discussed in this paper.

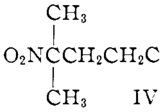

$O_2NC(CH_3)_2CH_2CH(CN)_2$

I



Hydrolysis of I by refluxing with hydrochloric acid gave a neutral, nitrogen-free hydrolysis product which was shown to be γ-isocaprolactone (III). Refluxing the cyanoethylation product of

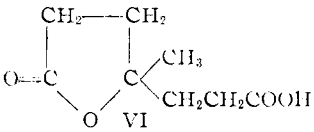



$O_2NC(CH_3)_2CH_2CH_2CN$

IV

2-nitropropane (IV)[3] as well as the corresponding acid, γ-nitroisocaproic acid (V), with concentrated hydrochloric acid also gave III. The conversion of V to III showed that the nitrile group is not necessary for lactone formation.

Hydrolysis of II with hydrochloric acid produced a liquid, nitrogen-free acid shown to have structure VI.



Acid VI also was formed in the hydrolysis of the dicyanoethylation product of nitroethane, $CH_3C(NO_2)(CH_2CH_2CN)_2$ (VII).[3] Structure VI was established by comparing the *p*-phenylphenacyl ester of VI derived from II and VII with the *p*-phenylphenacyl ester of VI synthesized as shown in Chart I.

A plausible mechanism for this unusual reaction is shown in Chart II.

The hydrolysis of nitrile groups and then decarboxylation produces a γ-nitro-γ,γ-disubstituted

CHART I

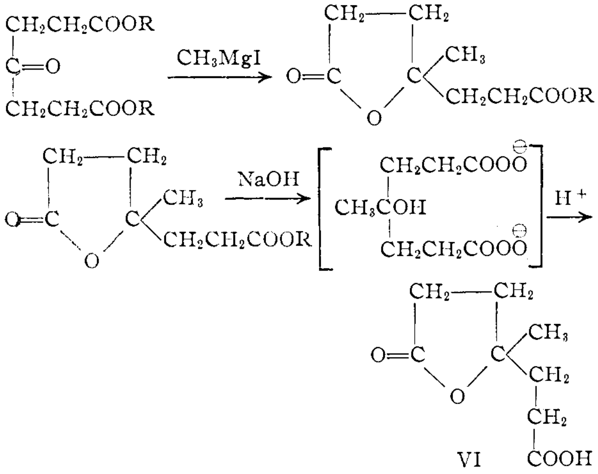
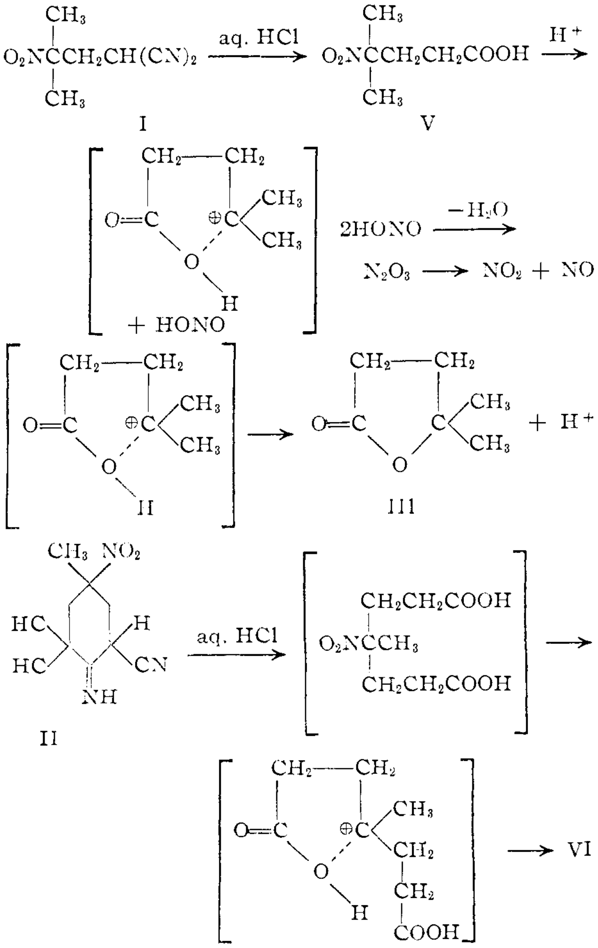


CHART II



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(1) J. C. Westfahl, THIS JOURNAL, **80**, 871 (1958).

(2) J. C. Westfahl, *ibid.*, **80**, 874 (1958).

(3) H. A. Bruson, U. S. Patent 2,361,259.

butyric acid. Ionization of the protonated nitro group (SN1), gives an acid containing a γ-tertiary carbonium ion which cyclizes and loses a proton to give a γ,γ-disubstituted butyrolactone. The nitrous acid decomposes in acid solution to oxides of nitrogen.

Experimental[4]

Hydrolysis of α-Cyano-γ-nitroisocapronitrile (I).—A mixture consisting of 8.00 g. (47.9 millimoles) of I and 25 ml. (29.8 g., 302 millimoles) of concentrated hydrochloric acid was refluxed for 17 hours and cooled. Ether was added and the mixture was shaken and filtered with suction. The white solid (NH_4Cl) was discarded. The filtrate was separated and the aqueous layer was extracted five times with ether. Two extractions with saturated aqueous sodium bicarbonate removed acids from ether extract. After drying the solution with magnesium sulfate and filtering off the magnesium sulfate, the ether solution was freed of ether to leave 3.21 g. (58.8%) of crude III. Distillation gave 1.95 g. (35.7%) of III having b.p. 91–92° (15 mm.), d^{25}_{4} 1.000 and n^{25}D 1.4315; reported for III[5] b.p. 95° (20 mm.) and n^{25}D 1.4312.

In a "crown cap" Pyrex tube was placed 2 ml. of 28% aqueous ammonia which had been saturated at 0° with gaseous ammonia and 0.99 g. of distilled III. The tube was capped and shaken mechanically at room temperature for 17 hours and 40 minutes. After cooling the tube in ice, the tube was opened and water and ammonia were removed *in vacuo* to leave 1.18 g. of colorless amide. One recrystallization from chloroform gave 0.89 g. (78%) of γ-hydroxyisocaproamide of m.p. 99–101°. Further recrystallization raised the m.p. to 100.7–101.7°; reported melting points of γ-hydroxyisocaproamide are 99°[5] and 101°.[6]

Hydrolysis of γ-Nitroisocapronitrile (IV).—A mixture consisting of 5.00 g. (35.2 millimoles) of IV (b.p. 97° at 1.0 mm., n^{25}D 1.4480, d^{25}_{4} 1.095) prepared by the method of Bruson[3] and 25 ml. (29.8 g., 302 millimoles) of concentrated hydrochloric acid was refluxed for 23 hours and 40 minutes. The reaction mixture was worked up as described for the hydrolysis of I to give 1.43 g. (35.7%) of crude III. Distillation gave 0.53 g. of III of b.p. 92° (15 mm.), n^{25}D 1.4312 and d^{25}_{4} 1.002. This liquid was shown to be identical with the III prepared from I by comparison of their infrared spectra.

Preparation of γ-Nitroisocaproic Acid (V).—A mixture consisting of 10.00 g. (0.070 mole) of γ-nitroisocapronitrile,[3] 100 ml. of water and 10 g. (0.25 mole) of sodium hydroxide was refluxed for 3 hours. The cooled solution was acidified with concentrated hydrochloric acid and extracted three times with ether. The combined ether extract was extracted with three portions of saturated aqueous sodium bicarbonate solution. After washing the combined sodium bicarbonate extract once with ether, the extract was acidified with concentrated hydrochloric acid and extracted three times with ether. The ether extract was dried with magnesium sulfate, filtered, and freed of ether to leave 6.31 g. (55.6%) of impure, liquid V. When cooled and stirred, the acid crystallized. Three recrystallizations from benzene–hexane gave V of m.p. 47.5–48.5°. This material was not pure as suggested by its neutral equivalent of 153; calcd. neutral equivalent of V, 161.

The amide prepared by a standard method[7] and recrystallized from benzene had m.p. 80.5–81.5°. *Anal.* Calcd. for $C_6H_{12}N_2O_3$: C, 45.01; H, 7.55; N, 17.49. Found: C, 45.13, 45.00; H, 7.48, 7.57; N, 17.47, 17.51.

The *p*-bromophenacyl ester prepared by a standard method[8] and recrystallized from ethanol–water had m.p. 70.5–71.5°. *Anal.* Calcd. for $C_{14}H_{16}BrNO_5$: C, 46.94; H, 4.50; N, 3.91. Found: C, 46.91, 46.90; H, 4.46, 4.39; N, 3.89, 4.03.

Formation of Lactone from γ-Nitroisocaproic Acid (V).—A solution of 0.52 g. (3.2 millimoles) of V (m.p. 47.5–48.5°) in 10 ml. (11.9 g., 121 millimoles) of concentrated hydrochloric acid was refluxed for 18 hours, cooled and extracted six times with ether. The combined ether solution was extracted twice with a saturated aqueous sodium bicarbonate solution, dried with magnesium sulfate, filtered, and freed of ether to leave 0.19 g. (51.6%) of III. This sample of III was shown, by means of infrared spectra, to be identical with the III prepared from I and IV.

Hydrolysis of 2,2,6-Tricyano-4-methyl-4-nitrocyclohexanonimine (II).—A mixture of 0.63 g. (2.7 millimoles) of II (m.p. 216–217° dec.) and 10 ml. (11.9 g., 121 millimoles) of concentrated hydrochloric acid was refluxed for 17 hours, cooled, and extracted five times with chloroform. The combined chloroform extracts was extracted with two portions of saturated aqueous sodium bicarbonate solution. After washing the bicarbonate solution once with ether, it was acidified with concentrated hydrochloric acid and extracted five times with ether. The combined ether extract was dried with magnesium sulfate, filtered, and freed of ether to leave 0.06 g. of light brown liquid VI. The chloroform extracted reaction mixture was freed of water and hydrogen chloride *in vacuo* and the residue was boiled with ether and the hot ether decanted. This was repeated for a total of five extractions. The ammonium chloride residue weighed 0.53 g. (91.4%). After drying the ether solution with magnesium sulfate and filtering off the magnesium sulfate, the ether was removed to leave 0.235 g. of yellow VI. The infrared spectra of the two samples of VI suggested that the material differed only in purity; total crude VI, 0.295 g. (62.8%).

A solution of 0.19 g. (1.1 millimoles) of crude VI in 2.5 ml. of water was neutralized with 5% sodium hydroxide solution and adjusted to just acid to litmus. Fifteen ml. of ethanol and 0.27 g. (0.98 millimole) of *p*-phenylphenacyl bromide were added and the solution was refluxed for one hour, diluted slightly with water and cooled in an ice-bath. The solid which separated was filtered and recrystallized three times from ethanol to give colorless crystals of m.p. 125–126.5°.

Hydrolysis of γ-Methyl-γ-nitropimelonitrile (VII).—A mixture of 5.00 g. (27.6 millimoles) of crude VII[9] and 20 ml. (23.8 g., 242 millimoles) of concentrated hydrochloric acid was refluxed for 17 hours, cooled, and most of the water and hydrogen chloride were removed *in vacuo*. The wet salt residue was extracted with five portions of warm ether as previously described. The salt residue was dried further *in vacuo* at 60° and the residue was extracted with a further five portions of boiling ether. The combined ether solution was dried with magnesium sulfate, filtered, and freed of ether to leave 4.40 g. (92.6%) of crude VI. The dried ammonium chloride residue weighed 3.13 g. (106%). A sample of VI was distilled several times using an apparatus such as described by Conolly and Oldham[10]; b.p. 134–140° (0.01 mm.), n^{25}D 1.4712.

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.81; H, 7.01. Found: C, 55.39; H, 7.12.

A *p*-phenylphenacyl ester prepared from 0.57 g. (3.3 millimoles) of the above crude VI, 5 ml. of water, 0.82 g. (3.0 millimoles) of *p*-phenylphenacyl bromide and 20 ml. of ethanol as previously described gave solid ester of m.p. 121–124°. Three recrystallizations from ethanol raised the m.p. to 125–126.5°. The melting point of a mixture of this solid ester with that derived from II was not depressed. The infrared spectra of the two samples were identical.

Anal. Calcd. for $C_{22}H_{22}O_5$: C, 72.11; H, 6.05. Found: C, 72.08, 72.16; H, 6.11, 6.27.

Preparation of VI from Di-2-ethylhexyl γ-Ketopimelate.[11]—A Grignard reagent prepared from 14.2 g. (0.1 mole) of methyl iodide, 2.43 g. (0.1 atom) of magnesium and 40 ml. of ether was added dropwise over a 15-minute interval with stirring to a solution of 35.8 g. (0.09 mole) of di-2-ethylhexyl γ-ketopimelate[12] in 50 ml. of ether and 50 ml. of benzene at 0°. The ether was distilled from the reaction mixture (to a vapor temperature of 75°) and the benzene solution was refluxed for 3 hours, cooled in ice, and hydrolyzed by the

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(4) All melting points and boiling points are uncorrected.

(5) S. A. Glickman and A. C. Cope, THIS JOURNAL, **67**, 1014 (1945).

(6) T. Strom, *J. prakt. Chem.*, [2] **48**, 220 (1893).

(7) S. M. McElvain, "The Characterization of Organic Compounds," The Macmillan Co., New York, N. Y., 1945, p. 141.

(8) Reference 7, p. 185.

(9) Prepared according to example 4 of reference 3 except that two equivalents of acrylonitrile were used thus favoring dicyanoethylation.

(10) J. M. Conolly and G. Oldham, *Analyst*, **76**, 52 (1951).

(11) This preparation is based on the preparation of isocaprolactone (III) by J. S. Buckley, Jr., and J. Richter, THIS JOURNAL, **69**, 2323 (1947).

(12) This compound was kindly furnished by J. T. Gregory of this Laboratory.

dropwise addition of a solution prepared from 100 ml. of water and 5.5 ml. of concentrated sulfuric acid. The aqueous layer was separated and extracted once with ether. The combined ether–benzene solution was washed once with water and freed of ether and benzene *in vacuo*. Refluxing the brown liquid residue for 2 hours with 10 g. (0.25 mole) of sodium hydroxide in 100 ml. of water gave an upper brown 2-ethylhexanol layer and a lower dark-reddish aqueous layer. Ether was added, the layers were separated, and the aqueous layer was extracted three times with ether. After boiling the aqueous solution to reduce its volume by one-half, the solution was acidified with 22 ml. of concentrated hydrochloric acid and refluxed for one hour. The cooled mixture was filtered to remove a brown, insoluble viscous liquid. The yellow aqueous filtrate was freed of water *in vacuo* and the salt residue was extracted with ten 10-ml. portions of warm ether. After drying the ether with magnesium sulfate and filtering off the magnesium sulfate, the ether was removed *in vacuo* to leave 7.90 g. of reddish-brown liquid. The color was due to free iodine as shown by adding water and sodium sulfite to a drop of the liquid.

Preliminary distillation of 4.94 g. of the crude product at 0.01 mm. gave a forerun (1.48 g.) containing iodine and a pale yellow fraction weighing 2.70 g. Redistillation of the main fraction gave a pale yellow VI of b.p. 141–144° (0.1 mm.) and $n^{25}D$ 1.4731.

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.81; H, 7.01. Found: C, 55.23; H, 7.19.

The *p*-phenylphenacyl ester prepared as previously described was not obtained pure by recrystallization. The purest material prepared had m.p. 122–125.5°. The melting point of a mixture of this solid with the pure derivative of m.p. 125–126.5° was 123–125.5°. The infrared spectrum of this sample of ester was identical with those of the samples derived from II and VII. Comparison of the infrared spectra of the purest VI derived from II, VII and that synthesized by the Grignard route indicated that the samples differed only in purity.

Acknowledgments.—The author is indebted to T. L. Gresham for his interest and encouragement, to J. R. Kubik for analyses and to J. J. Shipman, J. P. Kiehl and A. Hawthorne for the determination and interpretation of infrared spectra.

BRECKSVILLE, OHIO

[CONTRIBUTION FROM THE DEPARTMENT OF TEXTILE INDUSTRIES, BRADFORD INSTITUTE OF TECHNOLOGY]

The Reactions of N-Mercaptomethylpolyhexamethyleneadipamide Disulfide

BY CHRISTOPHER EARLAND AND DAVID J. RAVEN

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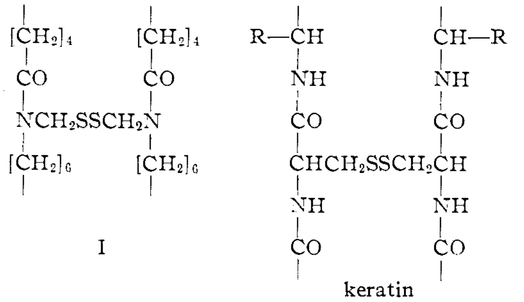
The properties and preparation of N-methylenepolyhexamethyleneadipamidesulfonic acid and N-mercaptomethylpolyhexamethyleneadipamide monosulfide from the corresponding disulfide are described. An alternative method for preparing N-alkylthiomethylpolyamides is given also.

The preparation of the disulfide of N-mercaptomethylpolyhexamethyleneadipamide[1] has been described by Cairns, *et al.*[2] Since this cross-linked polymer has a structure similar to that accepted for the keratins of animal hairs and horn, in that the $-CH_2SSCH_2-$ group forms a bridge between long-chain polyamide molecules

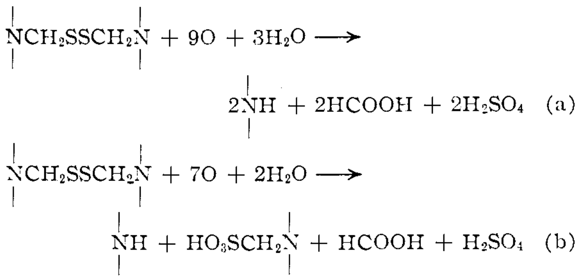


I

keratin

it was decided to investigate the reactions of N-mercaptomethyl-66 disulfide with particular emphasis on the use of reagents which react with the disulfide cross-linkage of keratin.[3]

It has been found that N-mercaptomethyl-66 disulfide (I) undergoes oxidation in two ways. Either the sulfur may be eliminated as sulfuric acid, or it may be converted to combined sulfonic acid groups to give N-methylene-66-sulfonic acid (II), according to the equations



$$NCH_2SSCH_2N + 9O + 3H_2O \longrightarrow 2NH + 2HCOOH + 2H_2SO_4 \quad (a)$$

$$NCH_2SSCH_2N + 7O + 2H_2O \longrightarrow NH + HO_3SCH_2N + HCOOH + H_2SO_4 \quad (b)$$

II

The only reagents which effect reaction (b) are aqueous solutions of peracetic acid[4] or alkaline potassium permanganate. Permanganate in acid solution, solutions of bromine, chlorine dioxide, sodium hypochlorite and hypochlorous acid bring about exclusively reaction a. Hydrogen peroxide in acid or alkaline solution fails to oxidize I, although I strongly catalyzes the decomposition of peroxide in alkaline solution, an effect which does not occur with polymer-66 itself in similar physical form. Solutions of permanganate, however, cause considerable weight loss and main-chain degradation of polymer-66 as shown by its number average molecular weight,[5] and only peracetic acid oxidizes

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(1) Polyhexamethyleneadipamide will be referred to as 66.

(2) T. L. Cairns, H. W. Gray, A. K. Schneider and R. S. Schreiber, THIS JOURNAL, **71**, 655 (1949).

(3) For a review of these reactions see P. Alexander and R. F. Hudson, "Wool. Its Chemistry and Physics," Chapman & Hall, London, 1954, pp. 244–283.

(4) Although performic acid may be used, it is not as convenient as peracetic acid since it is less stable and it swells or dissolves polyamides when they are not cross-linked.

(5) Determined from the specific viscosity in 88% formic acid. See M. L. Huggins, THIS JOURNAL, **64**, 2716 (1942); G. B. Taylor, *ibid.*, **69**, 635 (1947); and H. C. Haas, S. G. Cohen, A. C. Oglesby and E. R. Karlin, *J. Polymer Sci.*, **15**, 427 (1955). Thus under conditions which brought about reaction b, peracetic acid reduced $\overline{M}n$ from 13,250 for untreated polymer -66 to 12,350, whereas alkaline permanganate gave $\overline{M}n$ 4600.