[Contribution from the Department of Chemistry, University of California at Los Angeles]

The Reaction of Diazomethane with α-Cyanocrotonic Acid[1]

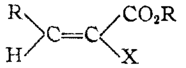
By William G. Young, Lawrence J. Andrews, Seymour L. Lindenbaum and Stanley J. Cristol

Among several methods considered for the preparation of the methyl ester of α-cyanocrotonic acid was the reaction of the acid with diazomethane. It was hoped that the diazomethane would methylate the carboxyl group much faster than it would attack the ethylenic linkage.[2] However, the product isolated had considerably different properties from those of methyl α-cyanocrotonate prepared by treatment of the silver salt of α-cyanocrotonic acid with methyl iodide or by the acid catalyzed esterification with methanol.

An investigation of the structure of the product of the reaction with diazomethane indicated that the compound isolated was methyl isopropylidenecyanoacetate. The presence of the isopropylidene linkage was demonstrated by the fact that the compound liberated acetone on heating with aqueous sodium hydroxide. This unsaturated compound, like others of its type,[3] was resistant to ozonization; and no acetone could be isolated when the product of its reaction with ozone was hydrolyzed. On the other hand, methyl α-cyanocrotonate gave small amounts of acetaldehyde both when it was ozonized and when it was heated with dilute alkali. The structure of the diazomethane reaction product was definitely established by a comparison of its absorption spectrum and melting point with those of a sample of methyl isopropylidenecyanoacetate prepared by condensing acetone with methyl cyanoacetate.[4]

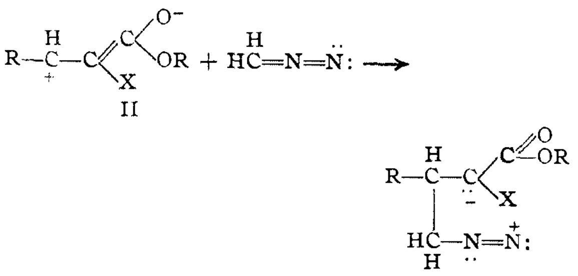
It previously has been shown that diazomethane reacts with the olefin bond of α,β-unsaturated esters[5] or ketones[6] producing a pyrazoline which loses nitrogen on heating, usually to form a mixture of a substituted cyclopropane and the β-methyl analog of the original olefin. Presumably the reaction of diazomethane with α-cyanocrotonic acid first gives a methyl ester which then reacts with a second molecule of diazomethane forming a pyrazoline. An attempt was made to isolate this pyrazoline intermediate by treatment of methyl α-cyanocrotonate with an ether solution of diazomethane, but the mixture gave off nitrogen at room temperature, and the only product isolated was methyl isopropylidenecyanoacetate.

It is interesting to note that in reactions of diazomethane with compounds of the type I the carbon atom of diazomethane attaches to the β-carbon of the ethylenic linkage. This is no doubt associated with the existence of resonance forms


I

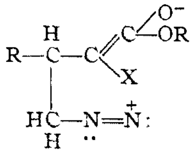
X = CH_3, CO_2R, or CN

of the type II which may allow the β-carbon atom to enter into an electrophilic attack on the carbon-nitrogen double bond of diazomethane to give the intermediate III which is stabilized by resonance


II

III

with the form IV. This normally leads to the production of the pyrazoline V. The thermal decom-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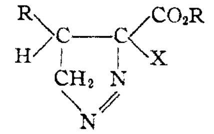
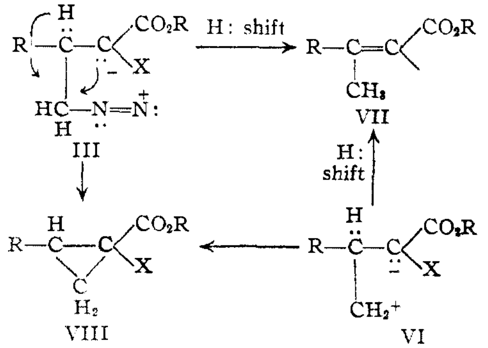

V

position of this pyrazoline undoubtedly involves the formation of the same intermediate III. At temperatures favoring the decomposition of the pyrazoline the intermediate III may dissociate spontaneously to give VI or react by displacement reactions involving an attack on the gamma carbon either by a Whitmore hydride shift or by the electron pair on the alpha carbon to give VII or VIII as follows:



If X is a cyano or carboalkoxy[5] group, the only product isolated is VII; while if X is a methyl[5] group both VII and VIII are obtained. When X is a cyano or carboalkoxy group the intermediates III and VI have a decreased electron density on

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(1) This work was made possible by a research grant from Sharp and Dohme, Inc.

(2) Fieser, "Experiments in Organic Chemistry," Second edition, D. C. Heath and Company, Boston, Mass., 1941, p. 375.

(3) Scheiber and Meisel, *Ber.*, **48**, 238 (1915).

(4) Cope, This Journal, **59**, 2327 (1937).

(5) Auwers and König, *Ann.*, **496**, 252 (1932).

(6) Smith and Pings, *J. Org. Chem.*, **2**, 23 (1937).

the α-carbon atom due to increased resonance involving these groups. Consequently the hydride shift should be favored.

Experimental Part

α-Cyanocrotonic Acid.—Fifty grams (0.58 mole) of cyanoacetic acid,[7] 34 g. (0.77 mole) of acetaldehyde and 1.4 ml. of piperidine were placed in that order in a 125-ml. pressure bottle and the mixture was heated at 60–70° for ten hours. The product was cooled and excess acetaldehyde was removed under reduced pressure. The hygroscopic crude yellow crystalline product was filtered under a rubber dam. The weight of crude product was 36 g. For ordinary synthetic work the acid was purified by two recrystallizations from a carbon tetrachloride–ether solution using decolorizing carbon. To obtain an analytically pure sample a small quantity of the crude acid was recrystallized several times from carbon tetrachloride until the product no longer oiled out but crystallized from the solvent. The properties of a pure sample were: m. p. 96–99°.[8] *Anal.* Calcd. for $C_5H_5O_2N$: C, 54.06; H, 4.54; neut. eq., 111.1. Found: C, 53.84; H, 4.69; neut. eq., 113.2.

Methyl α-Cyanocrotonate.—The dried silver salt prepared from 11.1 g. (0.1 mole) of α-cyanocrotonic acid was refluxed and stirred for twenty-four hours with a solution of 21.3 g. (0.15 mole) of methyl iodide in 100 ml. of ether. The ether solution of the product was filtered from the silver residue. After removal of the ether the product was distilled under reduced pressure. Six grams of methyl α-cyanocrotonate having the following properties was obtained: b. p. 75.5–76.8° (4–5 mm.); m. p. 20.0–22.0°; n^{25}_D 1.4571; d^{25}_4 1.0687; M_D calcd. 30.85; M_D obs. 31.89; exalt., +1.04; absorption maximum in 95% ethanol 220 mμ (ε 8400). *Anal.* Calcd. for $C_6H_7O_2N$: C, 57.59; H, 5.64. Found: C, 57.71; H, 6.04.

This ester was also prepared by heating (80–95°) a mixture of 11 g. (0.1 mole) of α-cyanocrotonic acid, 80 ml. of anhydrous methanol and 0.4 ml. of concentrated sulfuric acid in a pressure bottle for ten hours. Excess methanol was removed under reduced pressure, and 150 ml. of water was added to the residue. The mixture was extracted several times with ether. The ether solution was washed with water and aqueous sodium carbonate, dried and distilled. The properties of the methyl α-cyanocrotonate (3.3 g.) thus obtained were essentially those given for the ester prepared from the silver salt of the acid.

The Reaction of α-Cyanocrotonic Acid with Diazomethane.—Seven hundred ml. of an ether solution containing about 5 g. of diazomethane, prepared from 25 ml. of ethyl N-nitroso-N-methylcarbamate,[9] was treated with 11.6 g. of α-cyanocrotonic acid. Vigorous evolution of nitrogen took place, and the solution lost its yellow color. After the solution had stood for several hours, the ether was removed and the residue distilled under reduced pressure. The distillate (6.7 g.) had properties which were within experimental error identical with those of methyl isopropylidenecyanoacetate prepared according to Cope.[4] These properties and those of the sample prepared by the method of Cope (in parentheses) were: b. p. 90–91° (5 mm.) (88–90° (5 mm.)); m. p. 19.5–21.0° (21.5–22°) (mixed m. p. of the two samples 21.0–22.0°); n^{25}_D 1.4728 (1.4726); d^{25}_4 1.0605 (1.0632); M_D calcd. 35.45; M_D obs. 36.89; exalt., +1.44; absorption maximum in 95% ethanol 230 mμ, ε 11100 ($\lambda_{max.}$ 230 mμ, ε 10900). *Anal.* (diazomethane reaction product) Calcd. for $C_7H_9O_2N$: C, 60.42; H, 6.52. Found: C, 60.16, 59.74; H, 7.02, 6.57.

The Reaction of Methyl α-Cyanocrotonate with Diazomethane.—To an ice-cold solution of 1.9 g. of diazomethane in 500 ml. of ether was added a solution of 5 g. (0.04 mole) of methyl α-cyanocrotonate in 25 ml. of ether. The yellow color of the diazomethane immediately decreased in intensity. As the ether solution warmed to room temperature, nitrogen bubbled off vigorously and the solution became almost colorless. Three grams of methyl isopropylidenecyanoacetate, having the same physical properties as those previously given, was obtained after removing the ether and distilling the product.

The Reaction of Methyl α-Cyanocrotonate and Methyl Isopropylidenecyanoacetate with Dilute Aqueous Alkali.—Each ester (0.75 g.) was heated at 90° in a modified Claisen flask with 10 ml. of 3 *N* sodium hydroxide solution until the ester had completely dissolved. The bath temperature was then raised, and 2 ml. of distillate was collected in an ice-cooled receiver. A few drops of the distillate was tested for acetone by the use of sodium nitroprusside.[10] The product from methyl α-cyanocrotonate gave a negative test, while those from the methyl isopropylidenecyanoacetate samples gave a positive test. The remainder of the distillate was treated with a solution of 2,4-dinitrophenylhydrazine in acidified ethanol. The isopropylidene type ester gave 0.12 g. of acetone 2,4-dinitrophenylhydrazone (m. p. after one recrystallization from ethanol and mixed m. p. with an authentic sample 125.5–127.5°). The ethylidene type ester gave 0.038 g. of acetaldehyde 2,4-dinitrophenylhydrazone which after two recrystallizations from ethanol melted from 160.5–162.5° (mixed m. p. with an authentic sample 160.5–164.5°) with some softening below these temperatures.

Ozonization of Methyl α-Cyanocrotonate.—A solution of 1.0 g. (0.008 mole) of the ester in 6 ml. of methylene chloride was ozonized at dry-ice temperature for one hour. After removal of the solvent the ozonide was decomposed under reducing conditions,[11] and the aqueous solution of the product was tested with methone reagent for formaldehyde and acetaldehyde.[12] No formaldehyde derivative was obtained, but a small quantity of the methone derivative of acetaldehyde was isolated. After one recrystallization from ethanol this gave a m. p. and mixed m. p. with an authentic sample of 142–144°.

When methyl isopropylidenecyanoacetate was submitted to this ozonization procedure, no aldehyde or acetone could be detected after reductive decomposition procedures were applied.

The authors are indebted to Mr. J. W. Ralls for the combustion analyses reported.

Summary

The reaction of diazomethane with α-cyanocrotonic acid produces methyl isopropylidenecyanoacetate rather than methyl α-cyanocrotonate. The reaction is presumed to occur through the formation of a pyrazoline as an intermediate, and a mechanism for the decomposition of this pyrazoline has been proposed.

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(7) Purified by the method of Weissberger and Porter, This Journal, **65**, 52 (1943).

(8) The method described for preparing the acid is a modification of those of Auwers, *Ber.*, **56B**, 1172 (1923), who gave a m. p. of 80°, and of Fiquet, *Bull. soc. chim.*, [3] **7**, 767 (1892), who gave a m. p. of 92°.

(9) Pechmann, *Ber.*, **28**, 855 (1895).

(10) Huntress and Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1941, p. 374.

(11) Whitmore and Church, This Journal, **54**, 3710 (1932).

(12) Kimel and Cope, *ibid.*, **65**, 1992 (1943).