

## ACKNOWLEDGMENT

We thank Joseph P. Bingham, Jeanne C. Zufall, Mildred E. Chapman, and Leo Schubert for valuable assistance. We gratefully acknowledge the suggestions of E. L. Becker and L. S. Hafner.

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RECEIVED for review February 25, 1966. Accepted September 9, 1966. Winter Meeting, ACS, Phoenix, Ariz., Division of Agricultural and Food Chemistry, January 1966.

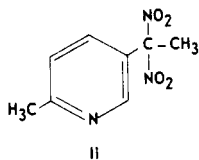
# 5-(1,1-Dinitroethyl)-2-picoline from the Reaction of 5-Ethyl-2-picoline with Nitric Acid

HARRY RUBINSTEIN,<sup>1</sup> GEORGE HAZEN, and RICHARD ZERFING

Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., Danville, Pa.

Investigation of the nitric acid oxidation of 5-ethyl-2-picoline revealed the presence of a new substance, 5-(1,1-dinitroethyl)-2-picoline. The latter may be an intermediate in the preparation of nicotinic acid. The substantial yield at moderate temperatures makes this a useful preparative method.

DURING the course of an investigation of the oxidation of 5-ethyl-2-picoline, I, with nitric acid, the authors discovered that a new compound, 5-(1,1-dinitroethyl)-2-picoline, II, was formed also in respectable yields. This reaction product was obtained



from the reaction of 5-ethyl-2-picoline and nitric acid in an autoclave, a tubular reactor, and in simple laboratory glassware. Although these three modes of preparation give different yields of II along with the expected pyridine carboxylic acids, they are similar in that the *gem* dinitro compound is the only

significant nitration product. This is shown by an almost quantitative product accountability as described in the experimental section.

There are several methods in the literature for the preparation of *gem* dinitro compounds (4, 13, 17). The most useful of these employ the nitro halogen moiety as the starting material as in the Ter Meer reaction (5, 14) or the oxidative nitration (6, 8) and electrolytic coupling (1). Other methods involving the nitration of esters (3, 9), conversion of  $\alpha$ -oximino esters (18), aldoximes (10), and olefins (7, 13) are reported also for the preparation of *gem* dinitro compounds.

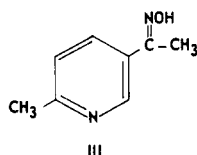
The work of Titov (15, 16) and McIntyre (12) illustrate two of the few cases reported where the direct nitration of alkyl groups gives *gem* dinitro compounds. The yields for this reaction vary widely and a mixture of nitration products are isolated. Pertinent results from the reaction of 5-ethyl-2-picoline with nitric acid are recorded in Table I.

The authors' data indicate that prolonged residence times at elevated temperatures in the tubular reactor—compare 4, 5, 6 and 8, 9, Table I—in the autoclave—

<sup>1</sup> Present address: Department of Chemistry, Lowell Institute of Technology, Lowell, Mass.

10 and 11, Table I—and in glassware—15 and 16, Table I—lead to lower yields of *gem* dinitro compound. Higher concentrations of nitric acid give higher yields of II—compare 12 and 13, Table I. Pressure has little effect upon the yield of II—compare 4 and 8, also 5 and 9, Table I. Probably, slight variations of the reaction conditions chosen would lead to better yields of II.

The structural assignment for compound II is based upon the following data: The ultraviolet spectrum showed two major bands at 205.6 and 265  $m\mu$  similar to 5-ethyl-2-picoline. The NMR spectrum was typically that of 2,5-disubstituted pyridine showing two C—CH<sub>3</sub> resonances both being singlets. The infrared spectrum shows two strong absorption bands at 1567 and 1314  $\text{cm}^{-1}$ , respectively, which is consistent with the *gem* dinitro group (2). The elemental analysis is consistent with the proposed structure. The known oxime, III, was produced by reduction of II.



## EXPERIMENTAL

**Safety Precautions.** Reaction of concentrated nitric acid with organic substances is potentially violent, especially in closed systems. The tubular reactor system and the autoclave were located behind a concrete barrier and operated remotely. Personnel were not exposed until the reactor product had been collected in a vented container and cooled. Glassware reactions were carried out behind ordinary laboratory shields. The authors considered 5-(1,1-dinitroethyl)-2-picoline an explosive and handled the pure substance in gram quantities.

**Preparation of II. TUBULAR REACTOR.** This reactor is a 100-foot section of spiralled titanium tubing— $1\frac{1}{4}$  inch O.D. and 0.049 inch wall thickness—immersed in a circulating oil bath. The reactor feed was pumped into the tubular reactor, using a Milton Roy positive displacement pump, the desired pressure was maintained by a pressure controlling device—Fisher Gismo Valve—and suitable instrumentation. The reactor effluent was collected in a glass or stainless steel vessel. Thus, for Experiment 1 a feed blend of 1162 ml.—1500 grams—of a solution containing 276 grams of I, 867 grams of nitric acid, and the rest water was passed through the reactor at 1500 p.s.i.g. at a rate of 2.7 ml. per minute and 114° C. This feed was followed by 700 ml. of water. The resulting reactor effluent was assayed for nicotinic acid, 6-methylnicotinic, and pyridine-2,5-dicarboxylic acid and unreacted I by gas-liquid chromatography. This accounted for 79.6% of the charge. Infrared assay procedures showed that 21.6% of I charged had been converted to II. Thus the material balance was 101.2% of theory.

**AUTOClave REACTION.** A 1-liter Recipromix Autoclave—Pressure Products Industries—was used for these reactions. For Experiment 12, a feed blend consisting of 17.6 grams of I, 110 grams of HNO<sub>3</sub>, and 150.2 grams of water was charged to the autoclave. The autoclave was sealed and heated to 120° C. for 240 minutes and developed 125 p.s.i.g. of pressure during this time. The autoclave then was cooled, discharged, and an aliquot was assayed. Nicotinic acid, 6-methylnicotinic acid, pyridine-2,5-dicarboxylic acid, and recovered I constituted 86.1% of the yield based upon the I charged and the dinitro component constituted 15.9% of the yield based on the I charged. Thus the material balance was 101.0% of theory.

**GLASSWARE REACTION.** A solution containing 3 liters of 70% nitric acid and 363 grams of I was placed in a three-necked 5-liter flask containing an efficient reflux condenser and a thermometer temperature controlling device—Thermocap Relay. The solution was heated to 110° C. and maintained at this tempera-

Table I. Data from the Reaction of 5-Ethyl-2-picoline with Nitric Acid

| Expt. No.       | HNO <sub>3</sub> <sup>a</sup> % | Ratio Moles HNO <sub>3</sub> to Moles I | Residence <sup>b</sup> Time, Minutes | Pressure, p.s.i.g. | Temp., ° C. | Yield II <sup>c</sup> % of Theory |
|-----------------|---------------------------------|-----------------------------------------|--------------------------------------|--------------------|-------------|-----------------------------------|
| 1 <sup>d</sup>  | 57.8                            | 6.05/1                                  | 63.2                                 | 1500 <sup>g</sup>  | 114         | 21.6                              |
| 2 <sup>d</sup>  | 56.4                            | 5.98/1                                  | 22.6                                 | 1500 <sup>g</sup>  | 121         | 8.2                               |
| 3 <sup>d</sup>  | 57.8                            | 6.05/1                                  | 21.5                                 | 1500 <sup>g</sup>  | 129         | 10.3                              |
| 4 <sup>d</sup>  | 56.4                            | 5.98/1                                  | 11.5                                 | 1500 <sup>g</sup>  | 140         | 11.9                              |
| 5 <sup>d</sup>  | 56.4                            | 5.98/1                                  | 26.8                                 | 1500 <sup>g</sup>  | 140         | 4.1                               |
| 6 <sup>d</sup>  | 56.4                            | 5.98/1                                  | 41.2                                 | 1500 <sup>g</sup>  | 140         | 3.3                               |
| 7 <sup>d</sup>  | 56.4                            | 5.98/1                                  | 11.2                                 | 1500 <sup>g</sup>  | 160         | 0                                 |
| 8 <sup>d</sup>  | 58                              | 6/1                                     | 12.8                                 | 300 <sup>g</sup>   | 143         | 10.8                              |
| 9 <sup>d</sup>  | 58                              | 6/1                                     | 27.8                                 | 300 <sup>g</sup>   | 143         | 5.8                               |
| 10 <sup>e</sup> | 57.8                            | 6.05/1                                  | 360                                  | 900 <sup>g</sup>   | 120         | 21.3                              |
| 11 <sup>e</sup> | 57.8                            | 6.05/1                                  | 1320                                 | 900 <sup>g</sup>   | 120         | 17.5                              |
| 12 <sup>e</sup> | 40                              | 12/1                                    | 240                                  | 125 <sup>h</sup>   | 120         | 15.9                              |
| 13 <sup>e</sup> | 50                              | 12/1                                    | 240                                  | 175 <sup>h</sup>   | 120         | 21.3                              |
| 14 <sup>e</sup> | 50                              | 12/1                                    | 120                                  | 275                | 140         | 22.4                              |
| 15 <sup>f</sup> | 62                              | 11/1                                    | 4200                                 | Atmospheric        | 110         | 16.3                              |
| 16 <sup>f</sup> | 62                              | 11/1                                    | 7200                                 | Atmospheric        | 110         | 10.5                              |

<sup>a</sup> Per cent by weight determined by titration of reactor feed.

<sup>b</sup> In tubular reactor determined from reactor volume, volume fed, and time for run, in autoclave determined by time at specified temperature.

<sup>c</sup> Based upon quantitative infrared assay as described in experimental section.

<sup>d</sup> Tubular reactor.

<sup>e</sup> Autoclave.

<sup>f</sup> Glassware.

<sup>g</sup> Imposed with N<sub>2</sub> and generated.

<sup>h</sup> Generated by reaction.

ture for 70 hours. A sample was withdrawn, and the reaction mixture was heated again for an additional 50-hour period. Analysis of the reaction mixture after 70 hours showed 71.8% of the usual carboxylic acids, 16.3% of II, and 10.8% of unreacted I. Material balance 98.9%. Analysis after 120 hours showed 87.6% of oxidized material, 10.5% of II, and 4.1% of unreacted I. Material balance 102.2%.

**Isolation of 5-(1,1-Dinitroethyl)-2-picoline, II.** A 200-ml. aliquot of the reactor effluent was stirred with 200 grams of ice, and the pH was adjusted exactly to a phenolphthalein end point using sodium hydroxide. The resulting solution was distilled, and the turbid azeotropic fraction was isolated and exhaustively extracted with methylene chloride. The methylene chloride was removed using a steam bath and the residue distilled in vacuo. Compound II had a boiling point of 112° C. at 1 mm. Hg and a boiling point of 138° C. at 4 mm. Hg. In an alternate method of isolation, an aliquot of the glassware reaction mixture was exhaustively extracted with methylene chloride after the pH was adjusted to 8.0. The methylene chloride layer was treated then as above.

Anal. Calcd. for  $C_8H_9N_3O_4$ : C, 45.50; H, 4.30; N, 19.90; Found: C, 45.92; H, 4.08; N, 19.73.

**Infrared Determinations.** A weighed sample of purified II was dissolved in methylene chloride, and solutions of concentrations of 0.02 gram per 25 ml. to 0.25 gram per ml. were scanned—Perkin-Elmer Infracord, Model 137—from 4 to 8 microns using 0.2 mm. fixed thickness sodium chloride liquid cells. The absorbance of these solutions, determined at 6.4 microns, adhered to the Beer-Lambert law. In practice, if I is present, a compensating blank containing a known amount of I in methylene chloride based on vapor phase assay, is used in the determination.

**Reduction of II.** A 2-gram sample of II was reduced using an aqueous solution of tin and hydrochloric acid. The reduction product was extracted with methylene chloride and recrystallized from methylene chloride-hexane giving 0.95 gram of 5(1-oximinoethyl)-2-picoline as a white solid. Melting point 183–185° C. uncorrected; literature (11) 182° C. The infrared and NMR spectra of this material was consistent with III.

Anal. Calcd for  $C_8H_{10}N_2O$ : C, 64.0; H, 5.66; N, 18.66. Found: C, 64.16; H, 6.47; N, 18.95.

## ACKNOWLEDGMENT

The authors are indebted to Nelson J. Trenner of Merck & Co., Inc., Rahway, N. J., and his staff for carrying out the NMR and analytical work and their helpful interpretation of these data. The authors also express gratitude to Ronald Harnetz of Merck & Co., Danville, Pa., for his aid in supplying some of the experimental data.

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RECEIVED for review March 24, 1966. Accepted October 12, 1966.

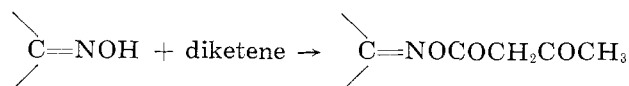
## Reactions of Oximes with Diketene

ERICH MARCUS, JOHN K. CHAN, and JOHN L. HUGHES<sup>1</sup>

Research and Development Department, Chemical Division, Union Carbide Corp., South Charleston, W. Va.

The reaction of diketene with oximes in the presence of 1,4-diazabicyclo[2.2.2]octane gave good yields of new derivatives of oximes, the O-acetoacetyl derivatives. Attempted O-acetoacetylation of N-phenylpyruvamide oxime led to 4-acetyl-3-methyl-1-phenyl-3-pyrroline-2,5-dione 2-oxime, and the O-acetoacetylation of the oxime of dehydroacetic acid gave 3,6-dimethyl-4H-pyrano[3,4-d]isoxazol-4-one.

THE present paper describes the reaction of diketene with oximes leading to novel O-acetoacetyl derivatives.



<sup>1</sup> Present address: Armour Pharmaceutical Co., Kankakee, Ill.

The reaction proceeded in an inert solvent without catalyst but was accelerated by tertiary amines. For benzaldoxime, under identical conditions an uncatalyzed reaction gave 56% yield, while trimethylamine and 1,4-diazabicyclo[2.2.2]octane (DABCO) in a concentration of 1% by weight with respect to diketene gave 86 and 90%, respectively. The general scheme for the reaction was to add diketene slowly to a mixture of the oxime and the catalyst in the presence