

Experimental

Samples of I, II and III, each of 25 mg., were dissolved in distilled water (250 ml.), and 20-ml. aliquots were diluted to 100 ml. with appropriate solvents to give working solutions containing uniformly 20 mcg. per ml. The diluents were 0.1 and 0.0001 *N* hydrochloric acid, phosphate buffer (*pH* approx. 7.0) and 0.0002, 0.0001 and 0.1018 *N* NaOH. The *pH* values of the working solutions, with the exception of the most alkaline, were measured with a Beckman, model G, meter. The most alkaline value was calculated (*pH* 12.88). Absorption measurements on solutions in 1-cm. cells were made in the usual manner with a Beckman spectrophotometer.

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α,α -Diethylhydracrylic Acid

By B. J. LUDWIG

In connection with a study of the metabolic products of 2,2-diethyl-1,3-propanediol when administered orally to humans in the clinical treatment of certain forms of epilepsy, a compound was obtained from urine which was believed to be α,α -diethylhydracrylic acid.¹ The identity of this substance was established on the basis of its elementary analysis and neutral equivalent. Since no reference to this compound could be found in the literature it was of interest to prepare this hydroxy acid for comparison with the substance isolated.

Experimental

2,2-Diethyl-1,3-propanediol was prepared from 2-ethylbutyraldehyde and formaldehyde following the procedure of Shortridge, *et al.*² To a solution of 15 g. of 2,2-diethyl-1,3-propanediol and 3.0 g. of sodium hydroxide in 150 ml. of water there was added with stirring over a period of 90 minutes a solution of 30.3 g. of potassium permanganate in 500 ml. of water. The mixture was heated to boiling and refluxed until the permanganate color disappeared. After cooling, it was acidified, filtered to remove manganese dioxide and extracted with ether. The acidic portion of this extract was separated using sodium bicarbonate solution. The crude acid obtained as a thick oil was distilled, giving a clear viscous liquid which solidified on standing, b. p. 110–112° (5 mm.). Crystallization of the acid from petroleum ether–benzene gave 8 g. of white needles; m. p. 62–62.5°, n_D^{20} 1.4458.

Anal. Calcd. for $C_7H_{14}O_3$: C, 57.50; H, 9.65; neut. equiv., 146.2. Found: C, 57.43; H, 9.50; neut. equiv., 145.

Further confirmation of the identity of this acid as α,α -diethylhydracrylic acid was gained from its conversion to diethylmalonic acid by alkaline permanganate oxidation. The product obtained was shown by its physical constant and analysis to be diethylmalonic acid.

The acidic substance isolated from urine possessed a refractive index and melting point identical to those of the synthesized α,α -diethylhydracrylic acid, and a mixture of the two substances gave no depression in melting point.

(1) F. M. Berger and B. J. Ludwig, *J. Pharmacol. Exptl. Therap.*, **100**, 27 (1950).

(2) R. W. Shortridge, R. A. Craig, K. W. Greenlee, J. M. Derfer and C. E. Boord, *This Journal*, **70**, 946 (1948).

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2,2,2-Trinitroethanol: Preparation and Properties¹

By N. S. MARANS AND R. P. ZELINSKI

2,2,2-Trinitroethanol has not been reported in the literature, but its synthesis, according to a method essentially like that reported below, was accomplished in 1941 by C. D. Hurd and A. C. Starke of Northwestern University.² They found these properties: b. p. 77–80° (4 mm.), n_D^{20} 1.4578, m. p. about 27°.

Investigation of the acid strength of this compound seemed attractive, since it contained three strongly electronegative groups attached to one carbon. It was prepared by a non-catalyzed type aldol condensation of nitroform and paraformaldehyde. This alcohol gave typical esterification reactions with both acetyl chloride and propionyl chloride to form 2,2,2-trinitroethyl acetate and propionate. Nine-tenths of the trinitroethanol was recovered after heating at 100° with an excess of concentrated hydrochloric acid for two hours, but the compound was decomposed in mildly alkaline solution at 25°.

Determination of the acid ionization constant of 2,2,2-trinitroethanol indicated that it was a relatively strong acid, K_a 4.3×10^{-3} . The high acidity is readily explained by the strong electron attracting properties of the nitro group.

Experimental

Nitroform was prepared by a modification of the procedures in the literature³ starting with tetranitromethane.

To a solution of 30 g. of potassium hydroxide in 40 g. of 1:1 glycerol–water mixture there was added with continual shaking 25 g. of tetranitromethane. The potassium salt of nitroform was separated by filtration. The air dried salt was added slowly with stirring to concentrated sulfuric acid, the temperature being maintained below 50°. The upper organic layer, 3 g. of nitroform, was separated and the sulfuric acid layer added to water. Ethereal extracts of the aqueous layer were combined with the separated nitroform layer. Distillation of this material gave 11 g. of nitroform, b. p. 50° (50 mm.), 57% yield based on tetranitromethane.

2,2,2-Trinitroethanol.—To 11 g. of nitroform there was added 5 g. of paraformaldehyde with a slight exothermic reaction occurring. The mixture was allowed to stand for 12 hours and then poured into water. From the mixture material boiling below 70° was distilled. The undistilled portion was cooled to room temperature, the organic layer was separated and the aqueous layer extracted with ether. The combined organic layers gave on distillation (oil-bath temperature kept below 150°) 10 g. of trinitroethanol, b. p. 103° (14 mm.), m. p. 30°, a 75% yield based on nitroform, a 41% yield based on tetranitromethane.

Anal. Calcd. for $C_2H_3N_3O_7$: C, 13.27; H, 1.67. Found: C, 13.20; H, 1.80.

Explosions were encountered during distillation of both nitroform and trinitroethanol. Careful control of temperature in all operations is extremely important.

(1) This work was performed with the aid of U. S. Navy funds under Sub-contract number 2, Contract NOrd 9709, and Sub-contract number 1, Contract NOrd 10431, both prime contracts being with the Hercules Powder Company, Allegany Ballistics Laboratory.

(2) Private communication from C. D. Hurd.

(3) "Organic Syntheses," Vol. 21, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 105; Macbeth and Orr, *J. Chem. Soc.*, 538 (1932); Hantzsch and Rinckenberger, *Ber.*, **22**, 685 (1899); and Andrew and Hammick, *J. Chem. Soc.*, 244 (1934).

2,2,2-Trinitroethyl Acetate.—To 14 g. of redistilled acetyl chloride in a round-bottom flask fitted with a condenser, there was added 6 g. of trinitroethanol in 10 cc. of ether. After removal of the ether by heating, an additional 7 g. of acetyl chloride was added. On heating at 100° copious fumes of hydrogen chloride were evolved. After two hours at 100° the reaction solution was cooled and added to water. The organic layer was separated and then distilled to give 5.5 g. of 2,2,2-trinitroethyl acetate, b. p. 118° (4 mm.), n_{20}^D 1.4478, d_{25}^{25} 1.474, 75% yield.

Anal. Calcd. for $C_4H_5N_3O_8$: C, 21.53; H, 2.26. Found: C, 21.30; H, 2.23.

2,2,2-Trinitroethyl Propionate.—The above experiment was repeated with the substitution of propionyl chloride for acetyl chloride. Quantities used were 4 g. of trinitroethanol and 20 g. of propionyl chloride. Final distillation gave 4.7 g. of 2,2,2-trinitroethyl propionate, b. p. 125° (6 mm.), n_{20}^D 1.4452, d_{25}^{25} 1.403, 90% yield.

Anal. Calcd. for $C_6H_7N_3O_8$: C, 25.32; H, 2.98. Found: C, 25.80; H, 3.32.

Reaction with Alkali.—Mixtures of weighed samples (0.3 g.) of the 2,2,2-trinitroethyl esters and a measured excess of 0.1 *N* aqueous sodium hydroxide were shaken until they became homogeneous (5 minutes). Back-titration with standard hydrochloric acid gave for the equivalent weight of 2,2,2-trinitroethyl acetate a value of 85.8 (calcd. for three equivalents per molecular weight, 77.4; for two equivalents, 111.6); for the equivalent weight of 2,2,2-trinitroethyl propionate, 90.2 (calcd. for three equivalents per molecular weight, 79.1; for two equivalents per molecular weight, 118.6). Trinitroethanol by direct titration with standard aqueous sodium hydroxide gave an equivalent weight of 182.6 (calcd. for one equivalent per molecular weight, 181.2). However, trinitroethanol on the addition of excess of sodium hydroxide and back-titration with hydrochloric acid gave an equivalent weight of 176 with a fading end-point. Use of 0.2 *N* alcoholic potassium hydroxide gave a neutral equivalent of 165 with a fading end-point.

Saponification equivalents for the above compounds were determined in the usual manner, using an excess of alcoholic potassium hydroxide, heating for 30 minutes, and back-titration with standard hydrochloric acid. Equivalent weights obtained were 77.0 for 2,2,2-trinitroethyl acetate (calcd. for three equivalents per molecular weight, 74.4); 81.7 for 2,2,2-trinitroethyl propionate (calcd. 79.1); and 95 to 134 for trinitroethanol (calcd. for two equivalents per molecular weight, 90.6).

Ionization Constant of Trinitroethanol.—The method used required that the sodium salt of the acid should be formed during the titration with sodium hydroxide. The formation of the sodium salt was indicated by the following experiment. To an aqueous solution of 1.5 g. of 2,2,2-trinitroethanol there was added 6 ml. of 5% aqueous sodium hydroxide. This solution was just basic to phenolphthalein. The mixture was reacidified with concentrated hydrochloric acid and extracted with ether. The ethereal extracts on distillation gave 1.3 g. of trinitroethanol, b. p. 108° (16 mm.), 87% recovery.⁴

Determination of the acid strength was made by a potentiometric method using a Coleman model 3 *pH* electrometer.⁵ The ionization constant of benzoic acid determined by this method was 6.9×10^{-5} (lit. value 6.6×10^{-5}). The ionization constant determined for 2,2,2-trinitroethanol was $4.3 \pm 0.2 \times 10^{-5}$.

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(4) Use of a large excess of base and allowing the solution to stand for 72 hours before working up gave no recovery of trinitroethanol.

(5) For a recent application of this method see Newman, Taylor, Hodgson and Garrett, *This Journal*, **69**, 1784 (1947).

2-Nitratoethyl Esters of Acrylic, Crotonic and Methacrylic Acids¹

BY N. S. MARANS AND R. P. ZELINSKI

In continuation² of the investigation of nitrogen compounds containing acrylic, methacrylic or crotonic acid radicals we have synthesized 2-nitratoethyl acrylate, crotonate and methacrylate. These compounds were prepared by the reaction of 2-nitratoethanol with the corresponding acid chloride in the presence of cuprous chloride, a polymerization inhibitor. Both the 2-nitratoethyl acrylate and methacrylate were polymerized in the presence of benzoyl peroxide. 2-Nitratoethyl crotonate did not polymerize under the same conditions.

In aqueous sodium hydroxide at room temperature these esters reacted rapidly with an equivalent of base to yield 2-nitratoethanol and the sodium salt of the organic acid. In alcoholic potassium hydroxide they reacted with only about one-fifth of an equivalent. However, at reflux temperature in alcoholic potassium hydroxide, saponification was complete; *i. e.*, two equivalents of base were consumed.

Experimental

Acrylyl, methacrylyl and crotonyl chlorides were prepared by reaction of phosphorus trichloride³ with the corresponding acids. The 2-nitratoethanol was prepared by the reaction of silver nitrate and ethylene chlorohydrin or bromohydrin.⁴ The 2-nitratoethanol was purified by either distillation or fractionation, both under reduced pressure. In both cases the physical constants obtained were, b. p. 75° (5 mm.), n_{20}^D 1.4362, d_{25}^{25} 1.333.

2-Nitratoethyl Acrylate.—A mixture of 5.5 g. of 2-nitratoethanol, 16 g. of acrylyl chloride, and 1 g. of cuprous chloride was heated at 50° with considerable evolution of hydrogen chloride occurring. The mixture after having been washed with water was distilled to give 4.1 g. of 2-nitratoethyl acrylate, b. p. 100–103° (8 mm.), n_{20}^D 1.4500, d_{25}^{25} 1.246, 49% yield.

Anal. Calcd. for $C_4H_7NO_6$: C, 37.27; H, 4.38. Found: C, 36.87; H, 4.45.

2-Nitratoethyl Methacrylate.—A mixture of 10 g. of 2-nitratoethanol, 20 g. of methacrylyl chloride and 1 g. of cuprous chloride was heated at 50° for 30 minutes, and then was washed with 2% aqueous sodium hydroxide and finally with water. Distillation gave 8.7 g. of 2-nitratoethyl methacrylate, b. p. 90–95° (3 mm.), n_{20}^D 1.4518, d_{25}^{25} 1.207, 53% yield. Other attempts to purify this compound using fractionation in the presence of cuprous chloride gave extensive polymerization.

Anal. Calcd. for $C_6H_9NO_6$: C, 41.14; H, 5.18. Found: C, 40.50; H, 5.16.

2-Nitratoethyl Crotonate.—In the same manner a mixture of 9 g. of 2-nitratoethanol, 16 g. of crotonyl chloride and 1 g. of cuprous chloride yielded, after two distillations, 10 g. of 2-nitratoethyl crotonate, b. p. 122–125° (12 mm.), n_{20}^D 1.4580, d_{25}^{25} 1.191, 58% yield. In another preparation in which fractionation was used extensive decomposition of 2-nitratoethyl crotonate occurred.

(1) This work was performed with the aid of U. S. Navy funds under Subcontract number 2, Contract NOrd 9709 and Subcontract number 1, Contract NOrd 10431, both prime contracts being with the Hercules Powder Company, Alligany Ballistics Laboratory.

(2) N. S. Marans and R. P. Zelinski, *This Journal*, **72**, 2125 (1950).

(3) Rehberg, Dixon and Fletcher, *ibid.*, **67**, 208 (1945).

(4) *Wenry. Ann. chim.*, [4] **27**, 243 (1872).