fied by filtration, and the product thus obtained weighed 11.35 g. and was insoluble in water. A portion (5.2 g.) of the above crude diethylacetal of γ-acetamido-γ,γ-dicarbethoxybutyraldehyde was suspended in 15 cc. of water and 3.5 cc. of 1 *N* sulfuric acid was added. The resulting reaction mixture was warmed over a steam-bath for five to six minutes with vigorous swirling. The insoluble acetal hydrolyzed rapidly to yield a clear, light yellow solution. This solution was treated with 0.5 g. of sodium acetate and concentrated *in vacuo* to a volume of 11 cc. The addition of 33 cc. of ethanol caused an immediate precipitate which was removed by filtration and proved to be inorganic. The clear filtrate was mixed with one cc. of acetic acid and 4.8 cc. of phenylhydrazine. The resulting reaction mixture was heated to 55° and after cooling and diluting with water a crystalline product (0.4 g.) was collected by filtration. The filtrate was further diluted with water and yielded an additional crop of crystals (0.53 g.). The crude phenylhydrazone of the aldehydo compound I thus obtained melted at 128–132° and after crystallization from dilute ethanol it melted at 138–140°. The melting point was not depressed when mixed with the phenylhydrazone prepared by the first method.

Reduction of Ethyl α-Acetamido-α-carbethoxy-γ-cyanobutyrate.—The ethyl α-acetamido-α-carbethoxy-γ-cyanobutyrate was prepared in accordance with the directions given by Albertson and Archer.[1]

Anhydrous stannous chloride (41.6 g.) was suspended in anhydrous ether (320 cc.) and anhydrous hydrogen chloride was passed into the reaction mixture until the formation of two layers was noted. The substituted cyanobutyrate (26.8 g.) was dissolved in 125 cc. of chloroform and the resulting solution was added slowly over a ninety-minute period as the reaction mixture was stirred, and dry hydrogen chloride was passed in for four hours with vigorous stirring. The introduction of the hydrogen chloride was then interrupted; however, the stirring was continued overnight. The following day the introduction of hydrogen chloride was continued for an additional period of eighteen hours at which time a few crystals had appeared. The reaction mixture was then permitted to stand at room temperature for a period of five days. After this total reaction time of one week the aldimine complex had precipitated as a white crystalline product. The complex was collected by filtration, washed with ether and dried *in vacuo* (weight, 65 g.). The odor of hydrogen chloride was noted. A portion of the above complex VI (15 g.) was mixed with 100 cc. of water and warmed to 50°. The clear, aqueous solution which resulted was extracted twice with 100 cc. portions of chloroform. The chloroform extracts were combined and dried over anhydrous sodium sulfate. After filtration the chloroform was removed by distillation *in vacuo* and a viscous oil remained which partially crystallized on standing. This residue was dissolved in a small quantity of ethanol, and a few drops of acetic acid were added together with a slight excess of phenylhydrazine. The resulting reaction mixture was warmed on a steam-bath and after cooling and diluting with water a crystalline product was obtained. The crude phenylhydrazone of the aldehydo compound I melted at 133–137°. After crystallization from dilute ethanol it melted at 138–140°.

The above aqueous solution was again extracted with chloroform. After drying, the chloroform was removed under reduced pressure and a crystalline residue remained. This crude product melted at 135–155° and after crystallization from dilute ethanol it melted at 181–182°. The analysis of this product indicated that it was probably ethyl α-acetamido-α-carbethoxy-γ-carbamylbutyrate.

Anal. Calcd. for $C_{12}H_{20}O_6N_2$: C, 49.97; H, 6.99; N, 9.72. Found: C, 49.84; H, 7.07; N, 9.58.

Summary

1. The 1,4-addition of acylamidomalonates such as ethyl acetamidomalonate, ethyl phthalimidomalonate and ethyl acetamidocyanoacetate to acrolein has been reported.

2. The resulting aldehydo compounds have been characterized as the phenylhydrazones.

3. The structure of γ-acetamido-γ,γ-dicarbethoxybutyraldehyde (resulting from the 1,4-addition of ethyl acetamidomalonate to acrolein) has been proved by two independent synthetic routes.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES, GENERAL MILLS, INC.]

Amino Acids. I. New Syntheses of DL-Tryptophan, DL-Ornithine and DL-Glutamic Acid*

BY DONALD T. WARNER AND OWEN A. MOE

Several syntheses for DL-tryptophan have been reported.[1] Most of these methods employ gramine as the starting material. A different approach was recently disclosed by Hegedus[2] wherein acetoacetic ester was used as the starting material. The present report concerns a new and convenient synthesis of DL-tryptophan employing the phenylhydrazone III of γ-acetamido-γ,γ-dicarbethoxybutyraldehyde I.[3]

The phenylhydrazone III readily underwent cyclization to yield IV, the same product as that obtained by the reaction between gramine and ethyl acetamidomalonate.[1a] The cyclized product IV was converted to DL-tryptophan in the usual way[1a]; the over-all yield based on III was 50%.

Recently, Albertson and Archer[4] published an excellent synthesis of DL-ornithine monohydrochloride in which the cyanoethylation product of ethyl acetamidomalonate was used as an intermediate. The synthesis of DL-ornithine monohydrochloride reported in the present paper involves the phenylhydrazone III as an intermediate. Reduction of III in the presence of Raney nickel gave β-

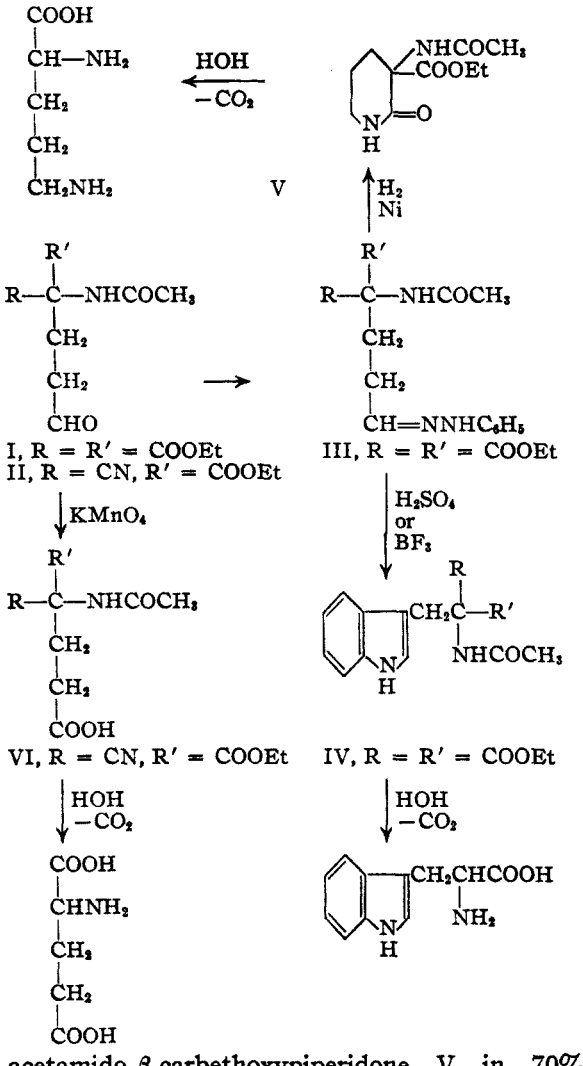
(*) Paper No. 90, Journal Series, Research Laboratories, General Mills, Inc.

(1) (a) Snyder and Smith, THIS JOURNAL, 66, 350 (1944); (b) Albertson, Archer and Suter, *ibid.*, 66, 500 (1944); 67, 36 (1945); (c) Howe, Zambito, Snyder and Tishler, *ibid.*, 67, 38 (1945); (d) Elks, Elliott and Hems, *J. Chem. Soc.*, 624, 626, 629 (1944).

(2) Hegedus, *Helv. Chim. Acta*, 29, 1499 (1946).

(3) Moe and Warner, THIS JOURNAL, 70, 2763 (1948).

(4) Albertson and Archer, *ibid.*, 67, 2043 (1945).



acetamido-β-carbethoxypiperidone V in 70% yield. This piperidone V is the same product as that obtained by the reduction of ethyl α-acetamido-α-carbethoxy-γ-cyanobutyrate in the presence of Raney nickel. Hydrolysis of V essentially as described by Albertson and Archer[4] yielded DL-ornithine monohydrochloride in nearly quantitative yield.

Glutamic acid has been synthesized by the 1,4-addition of phthalimidomalonic and acetamidomalonic esters to methyl acrylate[5,6] and acrylonitrile.[4] In the present work, oxidation by permanganate of γ-acetamido-γ-carbethoxy-γ-cyanobutyraldehyde yielded γ-acetamido-γ-carbethoxy-γ-cyanobutyric acid VI which was converted to DL-glutamic acid by the action of concentrated hydrochloric acid.

Experimental[7]

Cyclization of III Using Sulfuric Acid as Catalyst.—The phenylhydrazone III (50 g.) was mixed with 300 cc. of water containing 14 cc. of concentrated sulfuric acid. The reaction mixture was heated to the reflux temperature with very vigorous stirring. The phenylhydrazone liquefied at the reflux temperature, and after approximately one hour the suspended liquid had solidified. The reflux temperature was maintained for a period of four and one-half hours. After cooling, the solid reaction product was then mixed with water in a Waring blendor, collected, washed with water and dried *in vacuo*. The yield of product melting at 145–149° was 42.5 g. (approximately 90%). Recrystallization from aqueous ethanol (50–50) gave 35 g. (73%) of product IV melting at 156–157°.

Anal. Calcd. for $C_{18}H_{22}N_2O_5$: C, 62.44; H, 6.40; N, 8.01. Found: C, 62.55; H, 6.51; N, 8.05.

Cyclization of III in absolute ethanol using sulfuric acid as the catalyst gave the cyclized product in 40–50% yield. When the cyclization reaction was carried out in 50 volume per cent. aqueous ethanol the yield of IV was 55–65%.

Ethyl α-acetamido-α-carbethoxy-β-(3-indole)-propionate was also prepared by the reaction between gramine and ethyl acetamidomalonate, as described by Howe, Zambito, Snyder and Tishler.[16] The resulting product melted at 157–158° and no depression in the mixed melting point was observed with the above described sample.

Cyclization of the Phenylhydrazone III Using Boron Trifluoride[8] as the Catalyst.—To a suspension of the phenylhydrazone III (36.3 g.) in 100 cc. of glacial acetic acid there was added with swirling boron trifluoride etherate (14.2 g.) and the resulting reaction mixture was heated cautiously in an oil-bath. The reflux temperature was maintained for a period of thirty minutes. A copious precipitate of the boron trifluoride–ammonia complex was noted and after cooling was removed by filtration. Water was added to the filtrate to yield a slight turbidity, and the mixture was cooled in the refrigerator overnight. The precipitated product (amorphous in appearance) was collected and dried *in vacuo*. The dry product weighed 13.8 g. (40%) and melted at 137–142°. Recrystallization from 50 volume per cent. aqueous ethanol yielded 8.8 g. (25%) melting at 153–155°.

DL-Tryptophan.—The hydrolysis and decarboxylation of the cyclized product IV to yield DL-tryptophan (m. p. 281–283°) were carried out as described by Snyder and Smith.[16]

Anal. Calcd. for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92. Found: C, 64.70; H, 6.01.

Preparation of Piperidone V.—The phenylhydrazone III (54.48 g.) was suspended in 350 cc. of 95% ethanol and reduced in the presence of Raney nickel catalyst at 1400 pounds of hydrogen at 100°. After approximately six hours, the reduction was complete. The catalyst was removed by filtration and the filtrate was concentrated *in vacuo*. The residual pasty solid (amine odor) was suspended in 250 ml. of ether. The suspended solid had the appearance of shiny leaflets.

After cooling, the piperidone V was collected by filtration and dried *in vacuo*. The yield of the white crystalline product was 24.1 g. (70%) melting at 136.5–138°. The melting point was not depressed when mixed with the piperidone prepared as described by Albertson and Archer.[4]

DL-Ornithine Monohydrochloride.—The piperidone V was converted to DL-ornithine monohydrochloride (m. p. 218°) by refluxing with concentrated hydrochloric acid as described in the literature.[4] The dipicrate (m. p. 196°) and the dibenzoate (ornithuric acid) (m. p. 186°) of ornithine were prepared.

Permanganate Oxidation of γ-Acetamido-γ-carbethoxy-γ-cyanobutyraldehyde, II.—Crude γ-acetamido-γ-carbethoxy-γ-cyanobutyraldehyde II (22.6 g., m. p. 109–112°), was dissolved in 400 cc. of water. The resulting solution was cooled to 8° and a solution of potassium permanganate (10.6 g. of permanganate in 400 cc. of water) was added in portions. The temperature was maintained at 8–12° and the *p*H at approximately 8. When the oxidation was complete, the reaction mixture

(5) Marvel and Stoddard, *J. Org. Chem.*, **3**, 198 (1938).

(6) Snyder, Skeleton and Lewis, THIS JOURNAL, **67**, 310 (1945).

(7) Micro analyses by Mr. Harold Boyd and Miss Katherine Tullot.

(8) Snyder and Smith, THIS JOURNAL, **66**, 2452 (1945).

was allowed to stand at room temperature overnight. After removal of the manganese dioxide, the solution was acidified with 10 cc. of concentrated hydrochloric acid. Concentration *in vacuo* to a volume of approximately 100 cc. yielded a turbid emulsion. After saturation with sodium chloride the reaction mixture was extracted with two 100-cc. portions of ethyl acetate. After drying over anhydrous sodium sulfate the ethyl acetate was removed by distillation. The solid residue was macerated with ether, and filtration yielded 15.9 g. of a white solid. Purification by crystallization from ethyl acetate yielded the γ-acetamido-γ-carbethoxy-γ-cyanobutyric acid melting at 154–154.5°.

Anal. Calcd. for $C_{10}H_{14}O_5N_2$: C, 49.99; H, 5.87; N, 11.66; neut. equiv., 240. Found: C, 49.68; H, 6.06; N, 11.55; neut. equiv., 241.7.

DL-Glutamic Acid.—The γ-acetamido-γ-carbethoxy-γ-cyanobutyric acid (5 g.) was mixed with 25 cc. of concentrated hydrochloric acid. The resulting reaction mixture was refluxed for a period of sixteen hours and then concentrated *in vacuo*. The residual solid was dissolved in 12 cc. of water. After filtration the filtrate was neutralized by addition of 10% aqueous sodium hydroxide solution to a *p*H of 3.2. When cooled, the resulting solution yielded a crystalline product (2.3 g.) which melted at 193–194° with decomposition after drying *in vacuo*. The melting point was not depressed when mixed with an authentic sample. The N-benzoyl derivative was prepared and it melted at 156–157.5°.

Summary

1. New syntheses of DL-tryptophan, DL-ornithine and DL-glutamic acid have been reported.

2. These amino acids result from the aldehydo intermediates prepared by the 1,4-addition of acylamidomalonates to acrolein.

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Some Free Radical Reactions of Hydrogen Chloride

BY JOHN H. RALEY, FREDERICK F. RUST AND WILLIAM E. VAUGHAN

Although the chain addition of hydrogen bromide to ethylenic linkages is readily brought about by peroxides (the well known Kharasch "peroxide effect")[1] or actinic radiation,[2] it has been generally recognized that the analogous reaction with hydrogen chloride is much less likely. In fact, at the time the present study was begun, there was no report of a free radical hydrogen chloride–olefin combination.[3]

In this paper the vapor phase addition of hydrogen chloride to ethylene, as initiated by ultraviolet light or di-*t*-butyl peroxide, is described. Evidence for the corresponding, but much slower, reaction with propylene, is presented. Hydrogen chloride sensitizes the vapor phase decomposition of di-*t*-alkyl peroxides. This reaction, apparently a chain process involving chlorine atoms, is related to the photochlorination of di-*t*-butyl peroxide which is also described.

Experimental

Photochemical Experiments.—The cell was a fused quartz cylinder (22 mm. o.d. × 150 mm.) provided with plane windows. The body of the cell was wrapped with metal foil and jacketed by an aluminum pipe which was heated electrically. A thermocouple imbedded in the foil gave an approximate measure of the reaction temperature.

The light source was a hydrogen discharge tube of the Kistiakowsky type[4] (Hanovia Mfg. Co.) operated from a 2.5-kw. transformer. Since mercury vapor (from the vacuum line) could be present in the cell, radiation absorbable by this element was excluded to prevent the occurrence of mercury-sensitized reactions. The filter was a quartz cylinder dimensionally identical with the cell, containing carbon dioxide saturated with mercury vapor at room temperature. Ethylene absorbs appreciably only below the quartz region[5] but continuous absorption by hydrogen chloride begins at about 2500 Å. and increases rapidly below 2200 Å.[6]

The pressure change was measured with a quartz spiral manometer[7] sealed to the cell. After irradiation, the cell contents were transferred directly to a bulb by means of a Toepler pump, measured, and subsequently analyzed mass spectrometrically.

Experiments with Di-*t*-alkyl Peroxides.—The closed system apparatus used has been described in an earlier communication.[8] For certain experiments the 500-cc. reaction vessel was packed with 2-mm. Pyrex rods to effect an increase in the surface:volume ratio from 0.61 to 7.0 cm.$^{-1}$.

After reaction, the vessel contents were condensed with Dry Ice–acetone and the volatile products, excepting a portion of the dissolved ethyl chloride, pumped into a sample bulb for mass spectrometric analysis. The cold trap contents were dissolved in water containing a little isopropyl alcohol and aliquots taken for carbonyl[9] and chloride ion (Volhard) determinations.

Larger scale runs with a flow type apparatus provided material for product identification. This apparatus also has been described previously.[10] Because of the complexity of the effluent, particularly when the peroxide content of the feed was high, product yields could be determined only very roughly. However, isobutylene chlorohydrin was isolated (in *ca.* 10% yield) from the products of both the di-*t*-butyl peroxide–hydrogen chloride and di-*t*-butyl peroxide–hydrogen chloride–ethylene re-

(1) For literature review, see Mayo and Walling, *Chem. Rev.*, **27**, 351 (1940).

(2) Vaughan, Rust and Evans, *J. Org. Chem.*, **7**, 477 (1942).

(3) In a recent patent (U. S. 2,418,832, April 15, 1947), Hanford and Harmon report the preparation of a homologous series of primary alkyl chlorides by a high pressure reaction between ethylene and hydrogen chloride. Catalysts employed include oxygen, peroxides, and lead tetraphenyl. This work was presented as Paper No. 57 before the Organic Division of the American Chemical Society, 113th National Meeting, Chicago, Ill., April 19–23, 1948.

(4) Kistiakowsky, *Rev. Sci. Instruments*, **2**, 549 (1931).

(5) Noyes and Leighton, "The Photochemistry of Gases," Reinhold Publishing Corp., New York, N. Y., 1941, p. 331; also, Price, *Phys. Rev.*, **47**, 444 (1935).

(6) H. Trivedi, *Proc. Nat. Acad. Sci. India*, **6**, 18 (1936).

(7) Vaughan, *Rev. Sci. Instruments*, **18**, 192 (1947).

(8) Raley, Rust and Vaughan, THIS JOURNAL, **70**, 88 (1948).

(9) This procedure, based on reaction with hydroxylamine hydrochloride, is a modification of the method of Marasco (*Ind. Eng. Chem.*, **18**, 701 (1926)), and is described in "Methyl Ethyl Ketone, Its Uses and Data on Its Properties," Shell Chemical Co., San Francisco, Calif., 1938, p. 45.

(10) Rust, Seubold and Vaughan, THIS JOURNAL, **70**, 95 (1948).