was allowed to stand overnight, filtered and evaporated. By ether extraction and separation into neutral and acid fractions there was obtained 75 g. of crude acids.

The crude acids were then dissolved in 200 cc. of chloroform, ozonized at −10°, and the ozonide decomposed with silver oxide and sodium hydroxide by the method of Asinger.[8] There was obtained a mixture of acids, 55 g., which was esterified with methanol and sulfuric acid in the usual manner.

Fifty grams of the mixture of methyl esters so obtained was fractionated through a 24 × 0.5 inch column packed with single-turn glass helices. Three main fractions were obtained.

Fraction I, 8 g., b. p. 84–90° at 1.3 mm.; $n^{22}D$ 1.4315, consisted mostly of methyl undecylate. Saponification and redistillation of the free acid gave impure undecylic acid, m. p. 24°, equivalent weight by titration 174. This material apparently originated from partial reduction of the double bond during the Rosenmund process.

Fraction II, 11 g., b. p. 92° at 1.6 mm. to 98° at 0.9 mm.; $n^{22}D$ 1.4335–1.4348. This fraction was saponified and the crude acids so obtained extracted twice with hot chloroform to remove some azelaic acid. After one recrystallization from water there was obtained 5 g. of suberic acid, m. p. 138–140°, equivalent weight 87.4. Attempts to recover lower dibasic acids from the mother liquors failed to yield any pure products.

Fraction III, 21 g., b. p. 104° at 0.9 mm.; $n^{22}D$ 1.4360. This fraction was almost pure azelaic acid methyl ester. Saponification of 2.0 g. of this fraction yielded 1.68 g. of azelaic acid, m. p. 106° without purification. Equivalent weight by titration was 94.3. This product gave no depression of m. p. with an authentic sample of azelaic acid. A separate hydrolysis of the top 0.5 g. of this fraction, obtained by distillation from a smaller apparatus, gave an acid, m. p. 102°, equivalent weight 94.2, which was nearly pure azelaic acid, indicating little if any sebacic acid was present in the mixture. A non-volatile residue, 3–4 g., was not identified.

Undecyne-10-al-1 Diethyl Acetal.—Undecylenoyl chloride, 30 g., dissolved in 90 cc. of dry xylene was treated at 0° with 24 g. of bromine. From the amount of hydrogen bromide evolved during this reaction it was evident that substitution had taken place to the extent of about 10% of the amount of bromine used. Palladium–barium sulfate catalyst, 1 g., was then added and the reduction carried out as usual. The addition of thiourea "poison" made no difference in the final product in this case. Hydrogen chloride corresponding to 75% of the theoretical amount was evolved as before in the course of three hours, after which time the reaction had almost stopped. After filtration of the catalyst and evaporation of the solvent *in vacuo* there was added 20 g. of ethyl orthoformate and 35 cc. of absolute ethanol containing 3 drops of concentrated sulfuric acid. The mixture was refluxed for half an hour on the steam-bath. A solution of 60 g. of potassium hydroxide in 200 cc. of 95% ethanol was then added and the mixture allowed to stand overnight at room temperature.[5] After refluxing for eight hours to complete the elimination of hydrogen bromide, the alcohol was evaporated and the undecyne-10-al-1 diethyl acetal isolated by distillation through a small fractionating column.[9] There was obtained 8.5–9.0 g. of undecyne-10-al-1 diethyl acetal, b. p. 104° at 1.2 mm.; $n^{22}D$ 1.4410.

Anal. Calcd. for $C_{15}H_{28}O_2$: C, 74.90; H, 11.64; C_2H_5O, 37.5. Found: C, 74.30; H, 11.90; C_2H_5O, 38.9. 0.0226 g. gave 2.03 cc. of methane at 24°, 760 mm.; calcd. for one active H, 2.27 cc. 0.1090 g. absorbed 22.0 cc. hydrogen at 22°, and 770 mm. in ethanol; calcd. 22.0 cc.

(8) F. Asinger, *Ber.*, **75**, 658 (1942).

(9) S. F. Velick, *J. Biol. Chem.*, **152**, 533 (1944).

Summary

It has been shown that the double bond of undecylenoyl chloride migrates during Rosenmund reduction.

Ozonolysis of the unsaturated aldehyde so obtained yielded suberic and azelaic acids but no detectable sebacic acid.

Undecyne-10-al-1 diethyl acetal has been prepared.

NEW HAVEN, CONN. RECEIVED MAY 23, 1945

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF MANN FINE CHEMICALS, INC.]

A New Synthesis of β-Alanine

BY ALEXANDER GALAT

In view of the importance of β-alanine in the synthesis of pantothenic acid, various new syntheses of this amino acid have been proposed. The starting material which attracted most attention in this connection was the inexpensive and now readily available acrylonitrile.[1] Unfortunately, the most promising method, that involving the interaction of acrylonitrile with ammonia, suffers from the disadvantage of relatively low yields (the highest reported is 39%), the necessity of separating large amounts of secondary amine and the instability of the crude β-amino-propionitrile. These drawbacks complicate this process considerably, particularly in its application to the large scale production of β-alanine.

The conversion of β-amino-propionitrile to the free amino-acid also presents certain difficulties. Hydrolysis with hydrochloric acid yields β-alanine hydrochloride which is treated with lead or silver oxide in order to obtain the free acid. A less tedious method which involves the use of ion exchange resins has been recently described.[2] Its chief disadvantage lies in the high dilutions employed. A more recent method uses alkaline hydrolysis with barium hydroxide.[3] However, considerable amounts of alkali are necessary for good yields and their subsequent removal in the form of barium carbonate is inconvenient on a large scale.

The present paper describes a method which gives high yields of β-alanine hydrochloride from acrylonitrile and phthalimide by a combination of a Michael condensation and the Gabriel synthesis. It also describes a simple procedure for

(1) U. S. Patents 1,992,615; 2,334,163; 2,335,605; 2,335,653; 2,335,997; 2,336,067; THIS JOURNAL, **66**, 725 (1944).

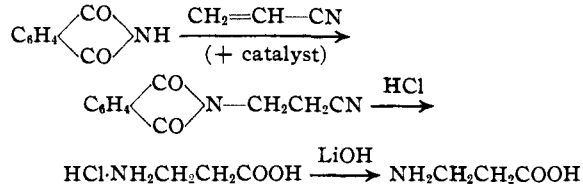
(2) Buc, Ford and Wise, *ibid.*, **67**, 72 (1945).

(3) Ford, *ibid.*, **67**, 876 (1945).

converting the hydrochloride to the free β-alanine.

It was found that the condensation between acrylonitrile and phthalimide in the presence of alkaline catalysts takes place under mild conditions and with nearly quantitative yields. Both acrylonitrile and phthalimide are inexpensive and readily available and are thus suitable for a practical process. It was also found that the phthalimide thus obtained is readily hydrolyzed by strong acids to yield β-alanine and phthalic acid. This hydrolysis can be run directly on the crude product of the Michael condensation without the isolation or the purification of the intermediate phthalimido-propionitrile.

A convenient method was also found for the conversion of the hydrochloride of β-alanine to the free amino acid. The hydrochloride was treated with an equimolecular amount of lithium hydroxide in the presence of a small quantity of water and the mixture was evaporated to dryness. On the addition of methanol the free amino acid crystallized out in a yield of over 90%, while lithium chloride remained in solution.



Large amounts of β-alanine can be rapidly and conveniently prepared by the present method.

Experimental

β-Phthalimido-propionitrile.—Twenty-nine and four-tenths grams (0.2 mole) of phthalimide was refluxed with 100 cc. of acrylonitrile. Two and five-tenths cc. of a 40% solution of trimethylbenzylammonium hydroxide was added slowly through the condenser. The catalyst must be added with a long pipet in order that it drops directly into the reaction mixture, instead of flowing along the walls of the condenser. Otherwise, the catalyst comes in contact with the vapors of acrylonitrile and polymerization takes place. After all the catalyst has been added, which should require about ten minutes, the reaction mixture is refluxed for another ten minutes. By that time all of the phthalimide is usually in solution and the reaction is complete. It occasionally occurs that not all is dissolved, in which case a few more drops of the catalyst are added and the mixture is refluxed for another five to ten minutes. The resulting solution is somewhat turbid due to the presence of a small amount of amorphous material which can be removed by filtration if pure product is desired. This last operation is not necessary for the subsequent steps.

The excess of acrylonitrile is removed on the steam-bath under reduced pressure and the unreacted amount is recovered quantitatively. The residue in the flask is a yellow crystalline product; yield, 40 g. (quantitative).

The product recrystallized from water or alcohol is colorless and melts at 154–155.5° (uncor.).

Anal. Calcd. for $C_{11}H_8O_2N_2$: N, 14.0. Found: N, 13.8.

β-Alanine Hydrochloride.—Three hundred and forty cc. of 20% hydrochloric acid was added to the crude β-phthalimido-propionitrile (40 g.) and the mixture refluxed. After about one hour the solid went into solution. The refluxing was continued until phthalic acid separated out, which usually occurred after four hours with a characteristic suddenness. The mixture was refluxed for another half hour (the total time of reaction was thus about four and one-half hours) and then allowed to cool to room temperature. When the separation of phthalic acid appeared complete, it was filtered off, washed with water and dried at 100°. There was obtained 31.6 g. of acid, which represents a yield of 95%. The material was white and melted at 207° with decomposition.

The colorless filtrate was evaporated under reduced pressure on a steam-bath and dried *in vacuo* of 15 mm. for one hour. The residue was refluxed with 240 cc. of isopropanol and the ammonium chloride was filtered off. The crystals were washed with 80 cc. of boiling isopropanol and the combined filtrates were allowed to cool. The β-alanine hydrochloride crystallized out, was filtered off, washed with a little isopropanol and dried at 70–80°. The filtrate was evaporated under reduced pressure to a small volume and on cooling a second crop of crystals was obtained. The combined yield was 19.9–20.0 g. (80%), m. p. 115–118°. One recrystallization from boiling alcohol brings the melting point to 118–120°.

β-Alanine.—Twelve and forty-five hundredths grams (0.1 mole) of β-alanine hydrochloride was dissolved in 10 cc. of water and 4.2 g. (0.1 mole) of lithium hydroxide monohydrate was added in small portions with stirring. The mixture was evaporated to dryness on a steam-bath and the pasty residue was stirred with methanol. At first, complete solution took place and the crystallization of β-alanine was induced by rubbing or seeding. The crystals were filtered off, washed with methanol and dried at 90°; yield, 8–8.5 g. (90–95%), m. p. 195–200° (dec.).

Another procedure consists of hydrolyzing the β-phthalimido-propionitrile with 25% sulfuric acid, removing the excess acid with calcium hydroxide and evaporating to dryness. β-Alanine crystallizes on rubbing or the addition of methanol.

Summary

A convenient and inexpensive method for preparing β-alanine is described. It involves the condensation of acrylonitrile with phthalimide, followed by an acid hydrolysis of the β-phthalimido-propionitrile. A simple procedure for converting the β-alanine hydrochloride to β-alanine by the use of lithium hydroxide is also described.

22 SHERMAN AVE.
YONKERS, N. Y.

RECEIVED JUNE 6, 1945