Syntheses of Some Amino Acids and Amino Aldehydes. IV.
(+)-4-Amino-2, 3-dihydroxybutyric Acid

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(Received August 28, 1961)

The present authors have synthesized (+)-4-amino-2, 3-dihydroxybutyric acid from L-(+)-tartaric acid (I), which failed in crystallization, as reported in the first paper[1] of this series. Ethyl 3-aminocarbonyl-2, 3-dihydroxypropionate (II), obtained from commercial L-(+)-tartaric acid (I) by Weermann's method[2], was acetylated to give ethyl 3-aminocarbonyl-2, 3-diacetyloxypropionate (III). Dehydration of III yielded ethyl 3-cyano-2, 3-diacetyloxypropionate (IV), which was subjected to catalytic reduction over a platinum oxide catalyst in an acetic acid solution containing sulfuric acid to afford (+)-4-amino-2, 3-dihydroxybutyric acid (4-amino-4-desoxy-L-threonic acid) (V), m. p. 221~222°C (decomp.) (picrolonate, m. p. 198~200°C (decomp.)) and a compound of m. p. 195~196°C (decomp.) (picrolonate, m. p. 182~182.5°C (decomp.) ; phenylhydrazine salt, m. p. 128~129°C), was assumed to be 4-amino-2-hydroxybutyric acid acid (VI)[3]. On being heating above the melting point, V changed into 3,4-dihydroxy-2-oxopyrrolidine (VII), m. p. 139~142°C, which reformed into V by hydrolysis. In the same way, VI gave 3-hydroxy-2-oxopyrrolidine (VIII), b. p. 159~160°C/1 mmHg, and this reformed into VI.

Experimental

Ethyl 3-Aminocarbonyl-2, 3-dihydroxypropionate (II).—A solution of 200 g. of diethyl L-(+)-tartarate in 400 g. of absolute ethanol was saturated with dry ammonia at 0~3°C for less than 2 hr. After having been left standing for 2 hr. at 10°C, the solvent was removed at as low a temperature as possible under reduced pressure. The crystals formed were collected, washed with ethanol and then with ether. The crystals were heated with a smaller amount of absolute ethanol, and the insoluble diamide was filtered off. The ethanolic solution, on standing, gave 95 g. of crystals, m. p. 134~137°C.

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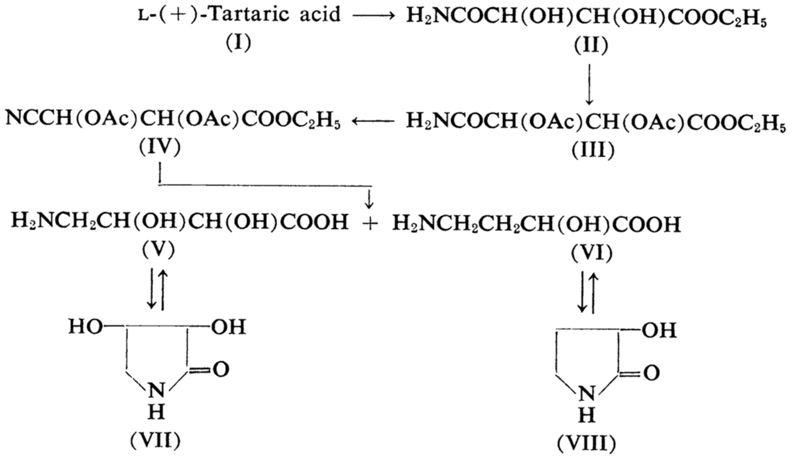
[1] A. Yokoo, *Bull. Tokyo Inst. Technol.*, **13**, 13 (1948), (*Chem. Abstr.*, **45**, 553).

[2] R. A. Weermann, *Rec. trav. chim.*, **37**, 46 (1918).

[3] E. Fischer, *Ber.*, **42**, 4880 (1909), **43**, 3272 (1910) ; A. Mori, *J. Biochem.* (*Japan*), **46**, 59 (1959).



Ethyl 3-Aminocarbonyl-2,3-diacetyloxypropionate (III).—To a solution of 43 g. of II in 60 cc. of pyridine was added 70 g. of acetic anhydride. After having been left standing overnight, the pyridine was removed under reduced pressure and ether was added. The crystals formed were collected and washed with ether. The crystals were heated with 80 cc. of absolute ethanol, and some insoluble materials were removed by filtration. To the ethanolic solution was added twice the volume of ether, and any insoluble material was filtered off. The solution was concentrated to a smaller volume under reduced pressure. The crystals formed on standing were filtered and washed with a small amount of ethanol to yield 33 g. of III, m. p. 95~96°C.

Found: N, 4.47. Calcd. for $C_{10}H_{15}O_7N\cdot C_2H_5OH$: N, 4.56%.

After being heated for 2 hr. at 150°C, the nitrogen content was 5.17% (calcd. for $C_{10}H_{15}O_7N$: N, 5.36%).

Ethyl 3-Cyano-2, 3-diacetyloxypropionate (IV).—To 20 g. of cooling III was gradually added 80 g. of phosphorous oxychloride. After the resulting mixture had been heated for 30 min. on a water bath, the remaining oxychloride was removed almost completely under reduced pressure. Ice was added to cool the residue, which was then extracted with ether. The ethereal solution was washed with a sodium carbonate solution and dried over anhydrous sodium sulfate. The ether was removed, and vacuum distillation gave 11 g. of a colorless viscous oil, b. p. 172~174°C/21 mmHg.

Found: N, 5.48. Calcd. for $C_{10}H_{13}O_6N$: N, 5.76%.

(+)-4-Amino-2, 3-dihydroxybutyric Acid (V) and 4-Amino-2-hydroxybutyric Acid (VI).—A solution of 10 g. of IV in 60 cc. of gacial acetic acid containing 2 g. of concentrated sulfuric acid was reduced for 2 hr. at 60°C in an autoclave in the presence of 1 g. of platinum oxide at an initial pressure of hydrogen 62 atm. The catalyst was filtered off and the acetic acid was removed under reduced pressure. After dilution of the residue with 130 cc. of water, 15 g. of lead acetate was added and the mixture was heated and filtered. The filtrate was treated with hydrogen sulfide, filtered and concentrated to a syrup under reduced pressure. The syrup was refluxed with 100 cc. of 6 N hydrochloric acid for 6 hr. and evaporated to dryness under reduced pressure. Water was added to the residue, which was then treated hot with silver oxide and filtered. The filtrate was again treated with hydrogen sulfide and evaporated to dryness as before. The residue was dissolved in a small amount of water and left to stand in order to deposit crystalline V. This was collected and recrystallized from water to yield 0.8 g. of colorless crystals, m. p. 221~222°C (decomp.), $[\alpha]_D^{27}=+42°$ (water).

Found: C, 35.35; H, 6.77; N, 10.13. Calcd. for $C_4H_9O_4N$: C, 35.55; H, 6.71; N, 10.37%.

Picrolonate of V.—A solution of V and picrolonic acid in water was heated and left to stand. The crystals formed were recrystallized from dilute ethanol to give orange yellow crystals, m. p. 198~200°C (decomp.).

Found: N, 16.50. Calcd. for $C_4H_9O_4N\cdot C_{10}H_8O_5N_4\cdot H_2O$: N, 16.78%.

The mother liquor of V was evaporated to dryness under reduced pressure, and the residue was dissolved in a small amount of water. Ethanol was added until turbidity took place. The crystals deposited on standing were collected and dissolved in a small amount of water. Methanol was added while hot until the solution became turbid, and the solution was then left to stand. The solution, together with the formed crystals, was warmed for a while, the insoluble crystals of V were filtered off, and again the solution was left to stand. The crystals finally formed were recrystallized from dilute methanol to give 1.05 g. of VI, m. p. 195~196°C (decomp.).

Found: C, 40.20; H, 7.67; N, 12.02. Calcd. for $C_4H_9O_3N$: C, 40.33; H, 7.62; N, 11.76%.

Picrolonate of VI. was obtained, as in the case of V, and recrystallized from water in the form of orange yellow crystals, m. p. 182~182.5°C (decomp.).

Found: N, 18.53. Calcd. for $C_4H_9O_3N\cdot C_{10}H_8\cdot O_5N_4$: N, 18.27%.

The picrolonates have shown a melting point depression on admixture with 4-amino-3-hydroxybutyric acid prepared by Tomita's method[4].

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[4] M. Tomita, *Z. physiol. Chem.*, **124**, 253 (1923).

3, 4-Dihydroxy-2-oxopyrrolidine (VII).—After heating 0.7 g. of V in an oil bath at 230°C for 30 min. under diminished pressure (water pump), water was added, treated with decolorizing carbon and evaporated to dryness under reduced pressure. The residue was taken up in ethanol, and a little ether was added. The crystals formed were recrystallized from ethanol to give 0.25 g. of VII, m. p. 139~142°C.

Found: C, 40.99; H, 6.27; N, 12.19. Calcd. for $C_4H_7O_3N$: C, 41.02; H, 6.03; N, 11.96%.

2,4-Dinitrophenylhydrazone of VII.—The crude 2,4-dinitrophenylhydrazone of VII was recrystallized from ethanol to give orange plates, m. p. 163~165°C.

Found: N, 23.95. Calcd. for $C_{10}H_{11}O_6N_5$: N, 23.56%.

Hydrolysis of VII. — A mixture of 0.2 g. of VII and 5 cc. of 6 N hydrochloric acid was refluxed for 2 hr. and evaporated to dryness under reduced pressure. The residue was dissolved in water, treated with silver oxide and then with hydrogen sulfide. The filtrate was evaporated to dryness and dissolved in a small amount of water. A little methanol was added, and the solution was left to stand to deposit crystals, which were recrystallized as before. The crystals, m. p. 219~220°C (decomp.), did not depress the melting point on mixed fusion with V.

3-Hydroxy-2-oxopyrrolidine (VIII).—After 0.5 g. of VI had been heated in a tiny Claisen flask at 215~220°C for 20 min., vacuum distillation gave 0.25 g. of VIII, b. p. 159~160°C/1 mmHg, which on standing solidified as strongly hygroscopic crystals.

Found: N, 13.89. Calcd. for $C_4H_7O_2N$: N, 13.86%.

VIII did not give 2,4-dinitrophenylhydrazone.

Phenylhydrazine Salt of VI.—A mixture of 0.1 g. of VIII, 0.3 g. of phenylhydrazine and 0.3 g. of commercial glacial acetic acid was heated at 130~135°C for 30 min. The crystals deposited on standing were recrystallized from ethanol to form colorless crystals, m. p. 128~129°C.

Found: N, 18.56. Calcd. for $C_4H_9O_3N \cdot C_6H_8N_2$: N, 18.49%.

This salt did not depress the melting point on admixture with that derived from VI.

The authors take this opportunity to express their sincere gratitude to the Ministry of Education for its grant-in-aid for Scientific Research and also to Dr. A. Kondo (the Department of Organic Chemistry of Tokyo Institute of Technology) for carrying out the carbon and hydrogen microanalyses.

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