

### 23. $\alpha\gamma$ -Diaminobutyric Acid.

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$\alpha\gamma$ -Diaminobutyric acid has certain properties distinct from those of the higher homologues, ornithine and lysine: (a) this diamino-acid forms three characteristic hydrochlorides, (b) treatment of  $\alpha\gamma$ -dicarbobenzyloxyaminobutyric acid with phosphorus pentachloride gives 1-carbobenzyloxy-3-(carbobenzyloxyamino)pyrrolid-2-one and not  $\gamma$ -(carbobenzyloxyamino)- $\alpha$ -carboxyaminobutyric acid anhydride, which one might expect by analogy with ornithine and lysine.

Our present interest in  $\alpha\gamma$ -diaminobutyric acid arises from its presence in acid hydrolysates of the antibiotic polypeptides, the polymyxins, from which both the DL-form (Catch and Jones, *Biochem. J.*, 1948, **42**, lii) and the L-form (Catch, Jones, and Wilkinson, *Ann. N.Y. Acad. Sci.*, 1949, **51**, 917) have been isolated. We now report some reactions of  $\alpha\gamma$ -diaminobutyric acid which differ from those of the higher homologues, ornithine and lysine.

It was found that  $\alpha\gamma$ -diaminobutyric acid gave not only the expected mono- and di-hydrochlorides, but also formed a third, stable hydrochloride of characteristic crystalline form, in which the amino-acid and hydrogen chloride were present in the molecular ratio, 2 : 3. This corresponds to Synge's observations (*Biochem. J.*, 1939, **33**, 671) that  $\alpha\gamma$ -diaminobutyric acid forms three crystalline oxalates in which the proportions of oxalic acid are 0.5, 1.0, and 1.5 moles to each mole of amino-acid, whilst Carter, Abeele, and Rothrock's findings (*J. Biol. Chem.*, 1949, **178**, 325) that DL- $\alpha\gamma$ -diaminobutyric acid dihydrochloride, on repeated crystallisation from alcohol-water, was converted into the monohydrochloride, confirm, in part, our experiments.

The polypeptide structure of the polymyxins, and the presence of a new, naturally-occurring amino-acid, stimulated attempts to prepare polypeptides containing  $\alpha\gamma$ -diaminobutyric acid residues. It was intended to polymerise  $\gamma$ -(carbobenzyloxyamino)- $\alpha$ -carboxyaminobutyric acid anhydride following the procedures described for the preparation of polylysine (Katchalski, Grossfeld, and Frankel, *J. Amer. Chem. Soc.*, 1947, **69**, 2565; 1948, **70**, 2095) and polyornithine (Katchalski and Spitnik, *Nature*, 1949, **164**, 1092).

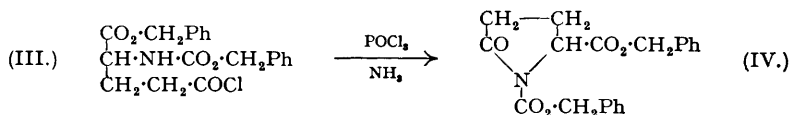
Following the method for the synthesis of  $\epsilon$ -carbobenzyloxy- $\alpha$ -carboxy-L-lysine anhydride (Bergmann, Zervas, and Ross, *J. Biol. Chem.*, 1935, **111**, 245), L- $\alpha\gamma$ -diaminobutyric acid (I) was converted into the dicarbobenzyloxy-derivative and treated in cold ethereal solution with

phosphorus pentachloride. On storage, a crystalline, optically active solid separated. This was apparently not the required anhydride but 1-carbobenzyloxy-3-(carbobenzyloxyamino)-



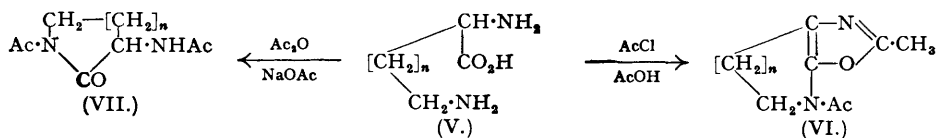
pyrrolid-2-one (II; R = R' = CO<sub>2</sub>·CH<sub>2</sub>Ph). Hydrogenation of the product in ethanol in the presence of platinum oxide gave a product to which the 3-carbobenzyloxyamino-structure (II; R = H, R' = CO<sub>2</sub>·CH<sub>2</sub>Ph) rather than the 1-carbobenzyloxyamino-structure (II; R = CO<sub>2</sub>·CH<sub>2</sub>Ph, R' = H) was assigned, because of its inability to react with acetic anhydride and of the non-production of colour with ninhydrin. Both (II; R = R' = CO<sub>2</sub>·CH<sub>2</sub>Ph) and (II; R = H, R' = CO<sub>2</sub>·CH<sub>2</sub>Ph) were hydrogenated in glacial acetic acid in the presence of platinum oxide to 3-aminopyrrolid-2-one (II; R = R' = H), which was isolated as a crystalline solid, m. p. 98—99°, by sublimation *in vacuo*. The product was optically active ( $[\alpha]_D^{25} = -64.4^\circ$  in water), gave a strong purplish-blue with ninhydrin, and was readily hydrolysed by hydrochloric acid to L- $\alpha\gamma$ -diaminobutyric acid. 3-Aminopyrrolid-2-one gave a picrate, m. p. 180—184°, and a mono-acetyl derivative, m. p. 191°,  $[\alpha]_D^{25} = -97.3^\circ$  in water. These physical constants were obviously different from those recorded by Adamson (*J.*, 1943, 39); the explanation was found in the partial racemisation which occurred under the relatively drastic condition employed by Adamson [cf. the racemisation when 2-ketopyrrolidine-4-carboxylic acid is prepared by heating glutamic acid (Arnew and Opsahl, *J. Biol. Chem.*, 1940, 134, 649)]. L- $\alpha\gamma$ -Diaminobutyric acid was therefore converted into the ethyl ester dihydrochloride by Akabori and Numano's method (*Bull. Chem. Soc. Japan*, 1936, 11, 214). The free ester on liberation in the cold cyclised on being kept, even at room temperature to give L-3-aminopyrrolid-2-one, identical with that obtained by hydrogenation of the dicarbobenzyloxy-pyrrolidone (II; R = R' = CO<sub>2</sub>·CH<sub>2</sub>Ph). Further proof of identity was shown by its conversion into L-3-acetamidopyrrolid-2-one, m. p. 191°,  $[\alpha]_D^{25} = -97.3^\circ$  in water. The ease of racemisation of L-3-aminopyrrolid-2-one was shown by heating a sample in a sealed tube at 155—160° for five hours (shorter times of heating caused only partial racemisation), whereupon DL-3-aminopyrrolid-2-one was isolated; this gave DL-3-acetamidopyrrolid-2-one, hydrolysed by hydrochloric acid to DL- $\alpha\gamma$ -diaminobutyric acid. On the paper chromatogram the behaviour of DL- and L-3-aminopyrrolid-2-one was identical.

The course of the cyclisation of  $\alpha\gamma$ -di(carbobenzyloxyamino)butyric acid has an analogy in Berenbom and White's observation (*J. Amer. Chem. Soc.*, 1949, 71, 2246) that, unless the phosphorus oxychloride formed during the conversion of  $\alpha$ -benzyl hydrogen *N*-carbobenzyloxy-



oxyglutamate into the acid chloride (III) was removed, treatment of (III) with ammonia did not give the desired amide but intramolecular cyclisation occurred to give 1:5-dicarbobenzyloxy-pyrrolid-2-one (IV).

The ease of cyclisation of ethyl  $\alpha\gamma$ -diaminobutyrate led to an investigation of the cyclisation of the acid itself. When L- $\alpha\gamma$ -diaminobutyric acid (V;  $n = 1$ ) monohydrochloride, acetic anhydride, and anhydrous sodium acetate were heated on the steam-bath racemisation occurred and from the reaction mixture DL-1-acetyl-3-acetamidopyrrolid-2-one (VII;  $n = 1$ ) was isolated.



This is in contrast to Wrede's observation (*Z. physiol. Chem.*, 1932, 206, 146) that treatment of lysine (V;  $n = 3$ ) or ornithine (V;  $n = 2$ ) with acetyl chloride and acetic acid at 100° caused racemisation and gave a compound, formulated as (VI;  $n = 3$ ) or (VI;  $n = 2$ ), respectively.

## EXPERIMENTAL.

*Hydrochlorides of  $\alpha$ -Diaminobutyric Acid.*—The *dihydrochlorides* were prepared by recrystallisation from concentrated hydrochloric acid or glacial acetic acid-concentrated hydrochloric acid. The DL-salt, m. p. 202—205° (decomp.), was isolated as beautiful hexagonal prisms (Found : N, 14.6; Cl, 37.1.  $C_4H_{10}O_2N_2 \cdot 2HCl$  requires N, 14.7; Cl, 37.2%), whilst the L-form gave unsymmetrical quadrilateral prisms, m. p. 197—198° (decomp.),  $[\alpha]_D^{21} + 13.3^\circ$  ( $c = 0.25$  in water),  $[\alpha]_{5461}^{21} + 16.2^\circ$  ( $c = 0.8$  in water) (Found : C, 25.2; H, 6.3; N, 14.5; Cl, 37.2.  $C_4H_{10}O_2N_2 \cdot 2HCl$  requires C, 25.1; H, 6.3; N, 14.7; Cl, 37.2%).

On careful crystallisation of the dihydrochlorides from aqueous alcohol, the respective *sesquihydrochlorides* were obtained in rosettes of slender prisms. The sesquihydrochlorides were also obtained on drying the dihydrochlorides *in vacuo* at 100°. The DL-salt had m. p. 194—196° (decomp.) (Found : N, 16.4; Cl, 30.5.  $C_4H_{10}O_2N_2 \cdot 1\frac{1}{2}HCl$  requires N, 16.2; Cl, 30.8%); the L-form had m. p. 211—212° (decomp.),  $[\alpha]_D^{21} + 13.5^\circ$  ( $c = 0.8$  in water),  $[\alpha]_{5461}^{21} + 16.2^\circ$  ( $c = 0.8$  in water),  $[\alpha]_{5461}^{21} + 26.9^\circ$  ( $c = 0.8$  in 5N-hydrochloric acid) (Found : C, 27.8; H, 6.4; N, 15.9; Cl, 30.8.  $C_4H_{10}O_2N_2 \cdot 1\frac{1}{2}HCl$  requires C, 27.8; H, 6.6; N, 16.2; Cl, 30.8%).

The *monohydrochlorides* were prepared from the dihydrochlorides on treatment with pyridine in aqueous alcohol. Recrystallisation from aqueous alcohol gave shallow rectangular prisms: DL-form, m. p. 229° (decomp.) (Found : C, 31.3; H, 7.0; N, 17.9; Cl, 22.7.  $C_4H_{10}O_2N_2 \cdot HCl$  requires C, 31.1; H, 7.1; N, 18.1; Cl, 23.0%); L-form, m. p. 225° (decomp.),  $[\alpha]_D^{21} + 23.8^\circ$  ( $c = 1.2$  in 6N-hydrochloric acid),  $[\alpha]_{5461}^{21} + 28.6^\circ$  ( $c = 1.2$  in water),  $[\alpha]_{5461}^{21} + 10.0^\circ$  ( $c = 1.7$  in N-KOH) (Found : N, 18.2; Cl, 23.0); D-form, m. p. 223—224°,  $[\alpha]_D^{21} - 11.4^\circ$  ( $c = 0.25$  in water) (Found : N, 18.0; Cl, 22.8%).

*Dipicrates of  $\alpha$ -Diaminobutyric Acid.*—The *dipicrates* were isolated as yellow, long fine prisms by crystallisation from water: DL-form, m. p. 189° (decomp.) (Found : C, 33.1; H, 2.5; N, 19.5.  $C_4H_{10}O_2N_2 \cdot 2C_6H_4O_7N_3$  requires C, 33.3; H, 2.8; N, 19.5%); L-form, m. p. 187° (decomp.) (Found : C, 33.7; H, 2.6; N, 19.5%); D-form, m. p. 187° (Found : N, 19.6%).

The D-glutamic acid used in the synthesis of D- $\alpha$ -diaminobutyric acid was prepared by hydrolysis of the D-glutamylpeptide from the capsule of *Bacillus anthracis* (cf. Bruckner and Ivanovics, *Z. physiol. Chem.*, 1937, **247**, 281).

*L- $\alpha$ -Di(carbobenzyloxyamino)butyric Acid.*—To a solution of L- $\alpha$ -diaminobutyric acid monohydrochloride (18.9 g.) in sodium hydroxide solution (122.4 ml.; 2N.) maintained at 0°, benzyl chloroformate (41.7 g.) and sodium hydroxide solution (183.6 ml.; 2N.) were added in four equal portions at intervals of thirty minutes and with vigorous stirring. After being stirred for a further two hours the mixture was acidified with hydrochloric acid and extracted with chloroform. The chloroform solution was washed with water, dried ( $Na_2SO_4$ ), and concentrated under reduced pressure. The residue crystallised from ethyl acetate-light petroleum (b. p. 60—80°) in micro-needles, m. p. 91—92° (33 g.) (Found : C, 62.2; H, 5.7; N, 7.2.  $C_{20}H_{22}O_6N_2$  requires C, 62.2; H, 5.7; N, 7.25%). The acid was insoluble in water, readily soluble in alcohol, somewhat soluble in ether, and did not produce any characteristic colour with ninhydrin.

*L-1-Carbobenzyloxy-3-(carbobenzyloxyamino)pyrrolid-2-one.*— $\alpha$ -Di(carbobenzyloxyamino)butyric acid (73.9 g.) was dissolved in dry ether (500 ml.), cooled to -5° and phosphorus pentachloride (44 g.) added, with stirring. After a further twenty minutes a clear solution was obtained and then on more prolonged cooling a crystalline mass separated, which was filtered off and washed several times with cold ether. Recrystallisation from ethyl acetate-light petroleum (b. p. 60—80°) or ethyl acetate-ether gave prisms, m. p. 113—114° (45 g.) [Found : C, 65.2; H, 5.3; N, 7.7%; *M* (Rast), 358.  $C_{20}H_{20}O_6N_2$  requires C, 65.2; H, 5.4; N, 7.6%; *M*, 350]. The *pyrrolidone* was optically active,  $[\alpha]_{5461}^{21} = -35.1^\circ$  ( $c = 0.8$  in ethyl acetate), and did not produce any characteristic colour with ninhydrin. A further crop (12 g.) was isolated from the original ether solution by concentration *in vacuo*, trituration with light petroleum, and crystallisation from ethyl acetate-ether.

*Ethyl L- $\alpha$ -Diaminobutyrate Dihydrochloride.*—L- $\alpha$ -Diaminobutyric acid monohydrochloride (35 g.) was suspended in dry absolute ethanol (1000 ml.) and dry hydrogen chloride passed into the boiling mixture until a clear solution was obtained. The solution was refluxed for 6 hours and concentrated to dryness *in vacuo*, and any residual hydrochloric acid removed by reconcentration *in vacuo* after the addition of ethanol and then benzene. The resinous mass slowly crystallised after prolonged drying in a vacuum desiccator over phosphoric oxide and was twice recrystallised, first from ethanol-benzene and then from ethanol-ether, giving prisms, m. p. 172° (decomp.) (29 g.), very soluble in water and ethanol and somewhat hygroscopic (Found : N, 12.6.  $C_8H_{16}O_2N_2Cl_2$  requires N, 12.7%). The product gave a purplish-blue colour with ninhydrin.

*L-3-Aminopyrrolid-2-one.*—The ester dihydrochloride (28 g.) was dissolved in absolute ethanol (100 ml.), cooled to -5°, and a solution of sodium ethoxide [from sodium (5.9 g.)] in absolute alcohol (100 ml.) added, with vigorous stirring. After a few minutes the mixture was diluted with twice the volume of dry ether, the precipitated sodium chloride filtered off, and the filtrate concentrated to dryness *in vacuo*. On being set aside at ca. 0° the residue crystallised, and was recrystallised from benzene-acetone giving plates, m. p. 98—99° (18 g.). The product could also be purified by sublimation at 80°/10<sup>-2</sup> mm. giving needles, m. p. 99°,  $[\alpha]_D^{21} = -64^\circ$  ( $c = 1.8$  in water) [Found : C, 48.0; H, 7.9; N, 27.9%; *M* (Rast), 105.  $C_4H_8ON_2$  requires C, 48.0; H, 8.0; N, 28.0%; *M*, 100].

The *pyrrolidone* was very soluble in water, ethanol, and acetone, very hygroscopic, and gave a strong purplish-blue colour with ninhydrin; it did not give the deep-red coloration characteristic of a diketopiperazine on being warmed with an alkaline solution of picric acid (Abderhalden, *Z. physiol. Chem.*, 1924, **139**, 181). Acetylation by means of acetic anhydride gave L-3-acetamidopyrrolid-2-one, crystallising from acetone in needles, m. p. 191°,  $[\alpha]_D^{21} = -97.3^\circ$  ( $c = 1.8$  in water) [Found : C, 51.0; H, 7.0; N,

19.6%; *M* (Rast), 119.  $C_6H_{10}O_2N_2$  requires C, 50.7; H, 7.0; N, 19.7%; *M*, 142]. The *hydrochloride*, precipitated when dry hydrogen chloride was passed through an alcoholic solution of the pyrrolidone, crystallised from ethanol-ether in needles, m. p. 186° (Found: C, 35.0; H, 6.6; N, 20.3; Cl, 25.9.  $C_6H_9ON_2Cl$  requires C, 35.2; H, 6.6; N, 20.5; Cl, 26.0%). The *hydrogen oxalate* crystallised from moist alcohol in needles, softening at 120° and decomposing vigorously at 140° (Found: N, 14.8.  $C_6H_{10}O_5N_2$  requires N, 14.7%). The *picrate* crystallised from aqueous alcohol in yellow prisms, m. p. 180—184° (decomp.) after darkening, softening at 170° (Found: C, 36.8; H, 3.4; N, 21.0.  $C_{10}H_{11}O_8N_3$  requires C, 36.48; H, 3.3; N, 21.3%).

Hydrolysis with 6*N*-hydrochloric acid gave *L*- $\alpha\gamma$ -diaminobutyric acid, which was isolated as its monohydrochloride, m. p. 225° (decomp.),  $[\alpha]_{D}^{25} = +27.0^\circ$  ( $c = 2.6$  in *N*-hydrochloric acid), and also identified by conversion into the dipicrate, which crystallised from water in yellow prisms, m. p. 187° (decomp.).

*L*-3-(*Carbobenzyloxyamino*)pyrrolid-2-one.—*L*-1-Carbobenzyloxy-3-(carbobenzyloxyamino)pyrrolid-2-one (2.6 g.) was dissolved in absolute alcohol (60 ml.) and hydrogenated in the presence of Adams's catalyst (0.8 g.). After the adsorption of 1 mol. of hydrogen the rate of hydrogenation was negligible. The catalyst was filtered off and, after evaporation of the alcohol *in vacuo*, the residue crystallised from ethanol-light petroleum (b. p. 60—80°) as plates, m. p. 178° (1.9 g.),  $[\alpha]_{D}^{25} = -52.3^\circ$  ( $c = 0.9$  in ethanol). (Alternatively the alcohol solution was concentrated *in vacuo* and the solid residue extracted with warm water, and filtered. When the filtrate was cooled a crystalline mass of *L*-3-(*carbobenzyloxyamino*)pyrrolid-2-one separated.) [Found: C, 61.3; H, 5.9; N, 11.9%; *M* (Rast), 270.  $C_{12}H_{14}O_5N_2$  requires C, 61.55; H, 6.0; N, 12.0%; *M*, 234]. The product was sparingly soluble in cold water but readily soluble in hot water; it did not produce any characteristic colour with ninhydrin.

The product was warmed on the steam-bath for 15 minutes with acetic anhydride; the mixture was concentrated to dryness *in vacuo* and the residue crystallised from acetone giving plates, m. p. 177° (undepressed on admixture with the starting material).

*L*-3-Aminopyrrolidone.—(a) *By catalytic hydrogenation of L*-1-carbobenzyloxy-3-(carbobenzyloxyamino)pyrrolid-2-one in glacial acetic acid. The dicarbobenzyloxy-pyrrolidone (2.85 g.) was hydrogenated in glacial acetic acid (50 ml.) in the presence of platinum oxide (1 g.). After the absorption of 2 mols. of hydrogen the reaction ceased. The catalyst was filtered off, the solvent removed *in vacuo*, the residue triturated several times with warm dry ether, and dried in a vacuum-desiccator over phosphoric oxide. A sample of the dried resinous material was dissolved in cold ethanol, and the solution made faintly alkaline with sodium methoxide and concentrated to dryness *in vacuo*. The residue was extracted with acetone and filtered, and the filtrate sublimed *in vacuo* at 90°/10<sup>-2</sup> mm. to give a crystalline sublimate, m. p. 98—99° not depressed on admixture with *L*-3-aminopyrrolid-2-one prepared as described previously (Found: N, 28.0. Calc. for  $C_6H_8ON_2$ : N, 28.0%). The product was optically active,  $[\alpha]_{D}^{25} = -64.4^\circ$  ( $c = 1.8$  in water), and gave a purplish-blue colour with ninhydrin but none with alkaline sodium picrate.

The hydrochloride crystallised from ethanol-ether in needles, m. p. 186° (undepressed on admixture with the pyrrolidone hydrochloride obtained previously) (Found: C, 35.2; H, 6.5. Calc. for  $C_6H_9ON_2Cl$ : C, 35.2; H, 6.8%). The hydrogen oxalate crystallised from ethanol in platelets which decomposed at 140° after softening at 120°.

The 2:4-dinitrophenyl derivative crystallised from aqueous alcohol in yellow needles, m. p. 205—206° (not depressed on admixture with a sample prepared from the 3-aminopyrrolidone obtained previously) (Found: N, 18.8.  $C_{10}H_{11}N_4O_7$  requires N, 18.7%).

The resin (0.6 g.) was gently warmed for a few minutes with acetic anhydride (2 ml.); the solution was cooled and diluted with ether, and the crystalline precipitate was filtered off and crystallised from acetone giving *L*-3-acetamidopyrrolidone (0.6 g.) as plates, m. p. 192° (alone or on admixture with the previous sample),  $[\alpha]_{D}^{25} = -96.5^\circ$  ( $c = 0.8$  in water) (Found: C, 51.0; H, 6.9; N, 20.0. Calc. for  $C_6H_{10}O_2N_2$ : C, 50.7; H, 7.0; N, 19.7%). The product may also be purified by sublimation at 140°/10<sup>-2</sup> mm.

The resin (0.5 g.) was also heated on the steam-bath for 30 minutes with hydrochloric acid (25 ml.; 6*N*). After being concentrated *in vacuo*, the residue was dried and dissolved in alcohol, and pyridine slowly added. The precipitate was filtered off and recrystallised from moist alcohol to give *L*- $\alpha\gamma$ -diaminobutyric acid monohydrochloride, m. p. 225° (decomp.),  $[\alpha]_{D}^{25} = +26.8^\circ$  ( $c = 2.5$  in *N*-hydrochloric acid).

(b) *By catalytic hydrogenation of L*-3-(*carbobenzyloxyamino*)pyrrolid-2-one in glacial acetic acid. *L*-3-(*Carbobenzyloxyamino*)pyrrolid-2-one (0.15 g.) in glacial acetic acid (15 ml.) was hydrogenated in the presence of platinum oxide (0.13 g.); after the absorption of 1 mol. of hydrogen, the reaction ceased. The catalyst was filtered off and the solvent removed *in vacuo*. The residual resin, after treatment as described above, was sublimed at 80—90°/10<sup>-2</sup> mm. to yield a crystalline sublimate, m. p. 98° (0.08 g.).

*L*-3-Acetamidopyrrolidone, prepared in the usual manner, was isolated as plates, m. p. 191—192°,  $[\alpha]_{D}^{25} = -96^\circ$  ( $c = 1$  in water).

The resin was distilled from a small distillation flask, and had b. p. 120—130°/10<sup>-2</sup> (oil-bath at 160—180°). The main bulk rapidly darkened in colour but a clear distillate (ca. 50%) was obtained which set to a crystalline mass, m. p. ca. 98—100°,  $[\alpha]_{D}^{25} = -27^\circ$  ( $c = 0.7$  in water).

The partially racemised *acetyl* derivative, prepared from the above distillate, crystallised from acetone in needles, m. p. 176—177° (after some preliminary softening at 172°),  $[\alpha]_{D}^{25} = -62.0^\circ$  ( $c = 0.64$  in water) [Found: C, 50.9; H, 6.8; N, 20.1%; *M* (Rast), 117.  $C_6H_{10}O_2N_2$  requires C, 50.7; H, 7.0; N, 19.7%; *M*, 142]. Hydrolysis with 6*N*-hydrochloric acid gave a partially racemised *L*- $\alpha\gamma$ -diaminobutyric acid monohydrochloride,  $[\alpha]_{D}^{25} = +21.8^\circ$  ( $c = 2.7$  in *N*-hydrochloric acid).

The *picrate* crystallised from aqueous alcohol in yellow needles, m. p. 198—200° (decomp.) (Found : C, 36.8; H, 3.1.  $C_4H_8ON_2, C_6H_3O_7N_3$  requires C, 36.48; H, 3.3%).

*The Racemisation of L-3-Aminopyrrolidone.*—A sample of L-3-aminopyrrolidone (0.7 g.) was heated in a sealed tube in an atmosphere of nitrogen at 150° for 30 minutes, then at 170° for 15 minutes. The melt darkened and on cooling solidified; sublimation at 90°/10<sup>-2</sup> mm. gave a crystalline solid (0.48 g.), m. p. 93—96° (after softening at 92°),  $[\alpha]_D^{21} = -54.7^\circ$  ( $c = 1.8$  in water). The acetyl derivative, m. p. 177—178° (after softening at 168°),  $[\alpha]_D^{21} = -59^\circ$  ( $c = 1.1$  in water), on hydrolysis with 6*N*-hydrochloric acid gave a partially racemised L- $\alpha$ -diaminobutyric acid,  $[\alpha]_{5461}^{21} = +21.8^\circ$  ( $c = 2.6$  in water).

A sample of L-3-aminopyrrolidone (0.8 g.) was heated in a sealed tube in an atmosphere of nitrogen for 5 hours at 155—160°. The resulting brown solid was sublimed at 100°/10<sup>-1</sup> mm. to give DL-3-aminopyrrolidone (0.5 g.) [Found : N, 27.8%; *M* (Rast), 119.  $C_4H_8ON_2$  requires N, 28.0%; *M*, 100].

DL-3-Acetamidopyrrolidone, prepared from the above, crystallised from acetone in needles, m. p. 174—175°,  $[\alpha]_{5461}^{21} = 0.00^\circ$  ( $c = 0.8$  in water) [Found : C, 51.0; H, 7.0; N, 19.6%; *M* (Rast), 145.  $C_6H_{10}O_2N_2$  requires C, 50.7; H, 7.0; N, 19.7%; *M*, 142]. Hydrolysis of the DL-3-acetamidopyrrolidone with 6*N*-hydrochloric acid gave DL- $\alpha$ -diaminobutyric acid monohydrochloride, m. p. 228—229° (decomp.),  $[\alpha]_{5461}^{21} = 0.00^\circ$  ( $c = 1.2$  in *N*-hydrochloric acid).

DL-3-Acetamido-1-acetylpyrrolidone. L- $\alpha$ -Diaminobutyric acid monohydrochloride (4 g.) was heated on the steam-bath for 3 hours with acetic anhydride (25 ml.) and anhydrous sodium acetate (1 g.). The mixture was cooled, filtered, and concentrated to dryness *in vacuo*. The residue was extracted with hot acetone, and the solution filtered from the insoluble solid and concentrated *in vacuo*. The residual resin crystallised from acetone-ether in rosettes of prisms (2.8 g.), m. p. 132°,  $[\alpha]_{5461}^{21} = 0.00^\circ$  ( $c = 1.3$  in water) [Found : C, 52.2; H, 6.6; N, 15.3%; *M* (Rast), 220.  $C_8H_{12}O_3N_2$  requires C, 52.2; H, 6.5; N, 15.2%; *M*, 184]. The product was readily soluble in water and did not give any characteristic colour with ninhydrin.

Distillation in a micro-molecular still gave a clear resin, b. p. 120°/10<sup>-3</sup> mm., which set to a hard crystalline mass on being kept.

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