[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Preparation and Stereochemistry of the 1-Benzyl-2-carboisopropoxy-3-methylethylenimines[1]

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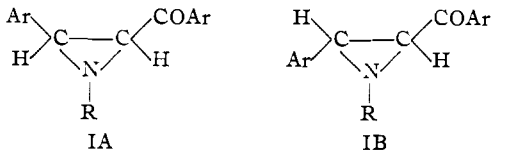
The reaction of the isopropyl ester of α-bromocrotonate, α-bromoisocrotonate or α,β-dibromobutyrate with benzylamine yields a mixture of the *cis* and *trans* isomers of 1-benzyl-2-carboisopropxy-3-methylethylenimine. The mixture has been separated chromatographically. One of the isomers is readily converted to DL-threonine, the other to DL-allothreonine by hydrolysis of the imine ring with perchloric acid and catalytic debenzylation of the product. The stereochemical configuration of the two isomers is discussed in the light of these data.

The preparation of the *cis* and *trans* forms of several 2-aryl-3-aroylethylenimines has been reported by Cromwell, *et al.*[4,5] In the *cis* form (IA) the aryl and aroyl groups lie on the same side of the plane of the ethylenimine ring; in the *trans* form on opposite sides.



In each isomeric pair one form was found to have the infrared carbonyl band displaced toward the lower frequencies and to show a bathochromic and hyperchromic shift in the ultraviolet as contrasted with the second isomer. On the basis of these data and a study of the phenylhydrazine reaction products, Cromwell and co-workers have tentatively assigned the *trans* configuration to the first isomer and the *cis* structure to the second. The *cis* forms of the ethylenimine ketones showed a strong band at 9.2μ which was absent in the *trans* forms.

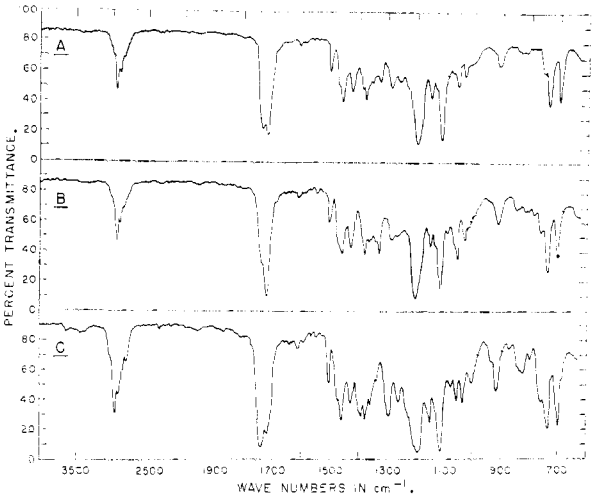


Fig. 1.—Infrared absorption spectra: A, mixture of *cis*- and *trans*-1-benzyl-2-carboisopropoxy-3-methylethylenimine; B, 1718 cm.$^{-1}$ ethyleneimine; C, 1736 cm.$^{-1}$ ethyleneimine, all as pure liquids.

Recently Stolberg, *et al.*,[6] reported the preparation of 1-benzyl-2-methyl-3-carbomethoxyethylenimine by the reaction of benzylamine with methyl α,β-dibromobutyrate. The product (obtained in 50% yield) did not give the 9.2 μ band and hence was tentatively assigned the *trans* configuration. No data were given for the infrared carbonyl absorption of this material.

We have investigated independently the reaction of isopropyl α,β-dibromobutyrate, isopropyl α-bromocrotonate and isopropyl α-bromoisocrotonate with benzylamine. Each of the three esters gave the same product (b.p. 0.5 mm., 125–127°; yield 65–85%). This material was identified as the ethylenimine (III) on the basis of chemical behavior, analytical data and absence of an NH stretching band at 3300 cm.$^{-1}$ in the infrared. Of particular interest was the observation that each of the products showed two bands in the infrared carbonyl region, one at 1736 cm.$^{-1}$ and the other at 1718 cm.$^{-1}$ (Fig. IA). The band at 1736 cm.$^{-1}$ is normal for an ester carbonyl while the 1718 cm.$^{-1}$ band is somewhat displaced toward the lower frequencies. The most logical interpretation of these data is that III consists of a mixture of the *cis* and *trans* forms of the ethylenimine. In view of the ready availability of III it seemed worthwhile to attempt the separation of the two isomers and to determine their configurations by conversion to the known aminohydroxybutyric acids. Such a study might provide a new approach to the synthesis of threonine and at the same time afford an unequivocal basis for assigning *cis* and *trans* structures to the two isomers.

Several examples of the cleavage of the ethylenimine ring with dilute acid to yield the vicinal aminohydroxy compound have been reported.[7,8] When III was treated with dilute perchloric acid it was converted to a product giving correct analytical data for the isopropyl ester of N-benzylaminohydroxybutyric acid (yield 73%). The cleavage of the imine ring was effected while the ester group remained intact. This unexpected stability of the ester was of considerable interest in connection with the mechanism of ring opening.

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(3) Part of the material in this paper is taken from the thesis submitted by Norman P. Salzman to the Graduate College of the University of Illinois in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry.

(4) N. H. Cromwell and H. Hoeksema, THIS JOURNAL, **71**, 708 (1949).

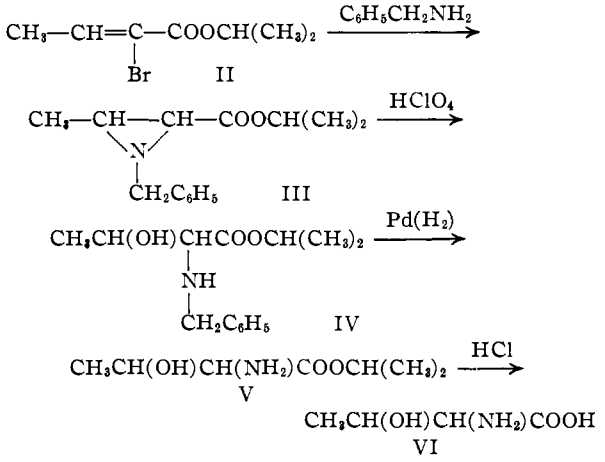
(5) N. H. Cromwell, *et al.*, *ibid.*, **73**, 1044 (1951).

(6) M. A. Stolberg, J. J. O'Neill and T. Wagner-Jauregg, *ibid.*, **76**, 5045 (1953).

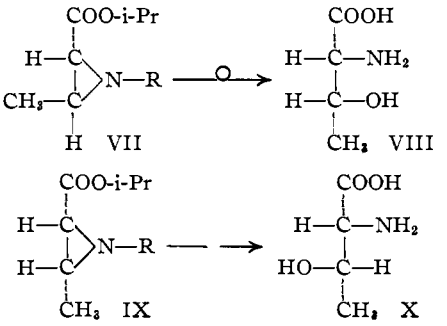
(7) O. E. Paris and P. E. Fanta, *ibid.*, **74**, 3007 (1952).

(8) F. H. Dickey, W. Fickett and H. J. Lucas, *ibid.*, **74**, 944 (1952).

Since opening of the ethylenimine ring may give a mixture of α-amino and β-amino isomers[9] it was necessary to determine the nature of the N-benzylaminohydroxybutyric acid mixture thus obtained. To establish this point, the reaction product was debenzylated by hydrogenolysis over palladium on charcoal and the resulting ester was hydrolyzed to a mixture of aminohydroxybutyric acids. This mixture gave identical values for total (Kjeldahl) and α-amino (ninhydrin-CO_2) nitrogen. Furthermore, on paper chromatography by the procedure of Hardy and Holland[10] the mixture behaved exactly as did a known mixture of DL-threonine and DL-allothreonine. Pure N-benzoyl-DL-allothreonine was readily obtained from the crude reaction mixture. No evidence for the presence of a β-amino isomer was obtained in any of these experiments. These data establish conclusively that ring cleavage occurred at the β-carbon to yield the α-N-benzylamino-β-hydroxy ester. The reactions involved are summarized in the equations



In the conversion of III to VI there is only one step in the sequence of reactions that affects the configuration of the groups around carbon atoms 2 and 3 of the final product. This occurs during the perchloric acid hydrolysis of the ethylenimine ring. During hydrogenolysis and the subsequent hydrolysis of the ester the configuration of the groups is not affected. Paris and Fanta,[7] and Dickey, *et al.*,[8] have studied the mechanism of opening of the ethylenimine ring in acidic media. Both groups of workers have established that the opening goes with a single Walden inversion. In the cases studied there were no reactive functional groups adjacent to the carbon atoms of the ring. However, Cromwell, *el al.*,[9b] have shown that the reaction of ethylenimine ketones with hydrogen chloride involves a single Walden inversion at the carbon atom undergoing bond change. Moreover, it has been shown that the ester group does not exert a neighboring group effect.[11] It seems valid, therefore, to assume that the ring opening of III to yield IV goes by the same mechanism, namely, a single inversion. Thus, the *trans*-1-benzyl-2-carboisopropoxy-3-methylethylenimine (VII) in its conversion to 2-amino-3-hydroxybutyric acid would be expected to undergo a single inversion and give rise to allothreonine (VIII). The *cis*-ethylenimine (IX) on the other hand by undergoing a single inversion would give rise to threonine (X). Since



the absolute configurations of allothreonine and threonine have been established this conversion makes it possible to assign absolute configurations to the two forms of the ethylenimine provided the two forms can be obtained in a reasonably pure state and converted to allothreonine and threonine, respectively.

These considerations made it important to fractionate the imine mixture. For this purpose, chromatography over acid-washed alumina was investigated. In order to determine the degree of enrichment of the isomers obtained, the infrared spectra of the various fractions were determined and the relative intensities of the bands at 1736 and 1718 cm.$^{-1}$ were noted. It was found that a fraction richer in the ethylenimine showing carbonyl absorption at 1718 cm.$^{-1}$ in the infrared (the 1718 cm.$^{-1}$ ethylenimine) was eluted from the column first by a less polar solvent. By changing to a more polar solvent a fraction richer in the ethylenimine whose carbonyl absorbs at 1736 cm.$^{-1}$ (the 1736 cm.$^{-1}$ ethylenimine) was then obtained. When the peak fraction richer in the 1718 cm.$^{-1}$ ethylenimine was rechromatographed, a material was obtained which was almost completely free of the 1736 cm.$^{-1}$ imine (Fig. 1B).

When the mixture of *cis*- and *trans*-ethylenimines was chromatographed on unwashed (basic) alumina, a poorer material balance resulted. But again a fraction significantly richer in the 1736 cm.$^{-1}$ ethylenimine (Fig. 1C) was eluted from the column with the more polar eluent.[12] These materials were used in the following experiments.

The 1718 cm.$^{-1}$ ethylenimine was converted to 2-amino-3-hydroxybutyric acid by the previously described series of reactions. The product analyzed correctly for aminohydroxybutyric acid and was shown to be essentially pure DL-allothreonine by paper chromatography, infrared

(9) (a) N. H. Cromwell and R. A. Wankel, THIS JOURNAL, **71**, 711 (1949); (b) N. H. Cromwell, G. V. Hudson, R. A. Wankel and P. S. Vanderborst, *ibid.*, **75**, 5384 (1953).

(10) T. L. Hardy and D. O. Holland, *Chemistry & Industry*, **35**, 855 (1952).

(11) W. A. Cowdrey, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 1208 (1937).

(12) It has not been possible to obtain a 1736 cm.$^{-1}$ imine fraction showing no absorption at 1718 cm.$^{-1}$. In view of the data discussed below on the conversion of the 1736 cm.$^{-1}$ imine fractions to essentially pure DL-threonine it seems probable that the pure imine gives a double carbonyl peak (1736 and 1718 cm.$^{-1}$). It is possible but less likely that the 1718 cm.$^{-1}$ peak resulted from contamination by the second isomer.

spectrum, and microbiological analysis (maximum content of DL-threonine, 5%).

The 1736 cm.$^{-1}$ fraction was also converted to 2-amino-3-hydroxybutyric acid. The product analyzed correctly and gave an infrared spectrum similar to that of DL-threonine and differing significantly from that of DL-allothreonine. Microbiological analyses showed that this product contained 90 to 100% of DL-threonine.

The conversion of the ethylenimines to the 2-amino-3-hydroxybutyric acids proceeded smoothly and in good yields. The crude unfractionated intermediates were used in subsequent steps in order to avoid possible fractionation of isomers. Yet the final products from the 1718 cm.$^{-1}$ and the 1736 cm.$^{-1}$ imine were essentially pure DL-allothreonine and DL-threonine, respectively. On the basis of these results the *trans* structure can be assigned to the 1718 cm.$^{-1}$ imine and the *cis* structure to the 1736 cm.$^{-1}$ imine. These results confirm in an unequivocal manner the assignments arrived at by Cromwell, *et al.*,[4,5] on the basis of less direct evidence.

In the course of this investigation the action of aqueous hydrochloric acid on III was investigated. The main product of the reaction was identified as N-benzylglycine hydrochloride by comparison with an authentic sample prepared by the procedure of Granacher, *et al.*[13] It is possible that this unexpected result may be due to hydrolysis of the isopropyl ester, preceding ring opening. Further study of this reaction will be required to settle this point.

In conclusion, it should be noted that these reactions provide a good over-all yield of amino-hydroxybutyric acids from dibromobutyric acid. If the proportion of *cis*-imine could be increased by altering the reaction conditions a satisfactory method for the preparation of DL-threonine might result.

Experimental

Preparation of Intermediates.—α,β-Dibromobutyric acid, prepared by the method of Michael and Norton,[14] was readily converted to α-bromoisocrotonic acid. To a solution of 316 g. (1.28 moles) of α,β-dibromobutyric acid in 427 ml. (1.28 moles) of 3 *N* sodium hydroxide was added 1400 ml. of 1 *N* sodium hydroxide. The reaction proceeded at room temperature for 105 minutes. The reaction mixture was then made strongly acid with concentrated hydrochloric acid. The mixture was cooled and the crystalline solid was filtered giving 156 g. (74%) of α-bromoisocrotonic acid (m.p. 91–92°). α-Bromocrotonic acid was prepared from α,β-dibromobutyric acid by the action of pyridine using the procedure of Pfeiffer.[15]

Each of the acids was converted to the isopropyl ester by refluxing for 4 hr. in anhydrous isopropyl alcohol containing 5–8% of anhydrous hydrogen chloride. The esters were purified by fractionation *in vacuo*. Isopropyl α,β-dibromobutyrate, b.p. 116–118° (19 mm.), yield 65%; isopropyl α-bromocrotonate, b.p. 95–96° (22 mm.), yield 60%; isopropyl α-bromoisocrotonate, b.p. 97–101° (23 mm.), yield 65%.

Preparation of 1-Benzyl-2-carboisopropoxy-3-methylethylenimine. Reaction of Isopropyl α-Bromoisocrotonate with Benzylamine.—To a solution of 74 g. (0.69 mole) of benzylamine in 250 ml. of benzene was added dropwise 60 g. (0.29 mole) of isopropyl α-bromoisocrotonate. The solution stood at room temperature 2 hr. and then was refluxed overnight. The mixture was cooled and filtered to remove the benzylamine hydrobromide. Benzene was removed *in vacuo* and anhydrous ether was added to the residue causing additional benzylamine hydrobromide to separate. The ether-soluble material was fractionated *in vacuo* giving 58.4 g. (87%) yield of a yellow oil (b.p. 126–129° (0.6 mm.). This material is a mixture of the *cis* and *trans* forms of the ethylenimine (III).

Anal. Calcd. for $C_{14}H_{19}O_2N$ (233.3): C, 72.07; H, 8.21; N, 6.0. Found: C, 72.24; H, 8.04; N, 5.98.

The infrared absorption curve, determined on the pure oil, is shown in Fig. 1A.

When the reaction of isopropyl α-bromoisocrotonate and benzylamine was carried out in the absence of a solvent the main product was a resinous mass which decomposed during distillation.

Reaction of Isopropyl α,β-Dibromobutyrate with Benzylamine.—To a solution of 10.5 g. (0.098 mole) of benzylamine in 70 ml. of benzene was added dropwise 9.0 g. (0.031 mole) of isopropyl α,β-dibromobutyrate. Benzylamine hydrobromide separated during the course of the reaction. The reaction mixture was heated on the steam-cone overnight. The crystals of benzylamine hydrobromide were filtered off and the benzene was removed *in vacuo*. The oil that remained was distilled *in vacuo*, giving 4.65 g. (64%) of III as a pale yellow liquid distilling at 125–130° at 0.5 mm.

Reaction of Isopropyl α-Bromocrotonate with Benzylamine.—Isopropyl α-bromocrotonate (8.0 g., 0.39 mole) was added dropwise to a solution of 9.1 g. (0.085 mole) benzylamine dissolved in 30 ml. benzene. The mixture was allowed to stand at room temperature for 2 hr. and then was heated on the steam-cone 10 hr. The benzylamine hydrobromide was filtered off, the benzene was removed *in vacuo*, and the oil that remained was distilled *in vacuo* giving 7.0 g. (77%) of a pale yellow liquid, b.p. 125–127° (0.5 mm.).

Conversion of 1-Benzyl-2-carboisopropoxy-3-methylethylenimine to Threonine and Allothreonine. Preparation of Isopropyl-2-Benzylamino-3-hydroxybutyrate.—A solution of 47.7 g. (0.025 mole) of 1-benzyl-2-carboisopropoxy-3-methylethylenimine (III) and 60 ml. of 72% perchloric acid in 1100 ml. of water was heated at 100° for 4 hr. After cooling, a small amount of an insoluble oil was extracted with ether. The aqueous layer was then made basic with solid sodium bicarbonate and the oil that separated was extracted with ether. After drying with magnesium sulfate, the ether was removed *in vacuo* and the oily residue was fractionated *in vacuo*, giving a colorless, viscous liquid (37.7 g., 73% yield) distilling at 145–147° at 0.1 mm.

Anal. Calcd. for $C_{14}H_{21}O_3N$ (251.3): C, 66.90; H, 8.42; N, 5.57. Found: C, 67.59; H, 8.26; N, 5.76.

Preparation of Isopropyl 2-Amino-3-hydroxybutyrate.—Isopropyl 2-benzylamino-3-hydroxybutyrate (5.0 g., 0.020 mole) dissolved in 50 ml. of isopropyl alcohol was reduced catalytically in the presence of 1 g. of 10% palladium on charcoal catalyst at atmospheric pressure and at 35°. After 5 hr. 1.05 moles of hydrogen was absorbed per mole of compound. The catalyst was filtered off and the filtrate evaporated to dryness *in vacuo*. The residue consisted of 3.20 g. (100% yield) of a colorless basic oil.

Preparation of 2-Amino-3-hydroxybutyric Acid.—A solution of 3.2 g. (0.02 mole) of isopropyl 2-amino-3-hydroxybutyrate in 20 ml. of 5 *N* hydrochloric acid was refluxed for 5 hr. The resulting solution was taken to dryness *in vacuo* giving 3.0 g. of a colorless, hard resin. The hydrochloride was dissolved in water and the *p*H was adjusted to 5 by stirring with IR-45 in the hydroxyl phase. The resin was filtered off and the filtrate was taken to dryness *in vacuo*, giving a colorless crystalline product (2.2 g., 93% yield). When this material was chromatographed on paper in phenol–water (75:25) it behaved exactly as did a mixture of DL-threonine and DL-allothreonine. This crude solid prior to any fractional crystallization was submitted for total nitrogen (Kjeldahl) and an α-amino acid nitrogen (ninhydrin–CO_2 procedure) determination.[16]

Kjeldahl nitrogen, found: 10.9, 11.0%; α-Amino nitrogen, found: 10.8, 10.9%.

Thus the crude product had a purity of 93% based on Kjeldahl nitrogen (theory 11.9% for 2-amino-3-hydroxy-

(13) C. Granacher, G. Wolf and A. Weidinger, *Helv. Chim. Acta*, **11**, 1229 (1928).

(14) A. Michael and L. M. Norton, *Am. Chem. J.*, **2**, 11 (1880).

(15) P. Pfeiffer, *Ber.*, **48**, 1048 (1915).

(16) These analyses were performed by Mrs. P. Wiegand.

butyric acid) and all of the nitrogen was present as α-amino nitrogen.

The crude unfractionated 2-amino-3-hydroxybutyric acid (2.1 g., 0.018 mole) was benzoylated in 150 ml. of 2 *N* sodium hydroxide with 7.7 g. (0.055 mole) of benzoyl chloride. The clear solution was acidified with concentrated hydrochloric acid to *p*H 2 at 0°, the benzoic acid was filtered off, and the filtrate concentrated *in vacuo* until crystals began to separate. After standing overnight at 0°, the solid was filtered, dried and extracted with hot high boiling petroleum ether. The crystalline residue was dissolved in boiling water and after standing at −10° for 2 hr. the crystals were filtered (350 mg., m.p. 155–165°). When the mother liquor was concentrated slightly *in vacuo* a second crop of crystals (750 mg., m.p. 165–170°) was obtained. By successive concentration three additional solid fractions of crystals were obtained. The third weighed 300 mg. and melted at 135–140°. The fourth weighed 850 mg. and melted at 130–140°. The last weighed 800 mg. The total yield of crystalline benzoyl derivative was 3.05 g. (78%).

The first and second fractions were combined and crystallized from water. After one recrystallization the material melted at 165–172° and after the second recrystallization at 176–177°. This material is benzoyl-DL-allothreonine. The third, fourth and fifth fractions were combined and crystallized from water. After the first recrystallization 1.0 g. of material was obtained melting at 134–146°. The second recrystallization from water yielded 700 mg. of material, m.p. 135–140°. A third recrystallization from ethyl acetate still yielded solid that melted at 135–140°. This solid appears to be a mixture of benzoyl-DL-threonine (m.p. 143–144°) and benzoyl-DL-allothreonine (m.p. 176–177°).

Separation of the *cis* and *trans*-Isomers of III.—The mixture of imines obtained by reaction of isopropyl α-bromoisocrotonate and benzylamine was used in these experiments. The infrared spectrum of this material is shown in Fig. 1A. The imine mixture (5.02 g.) was dissolved in 20 ml. of a 1:1 mixture of low boiling petroleum ether and benzene. The solution was applied to a 20 × 363 mm. column containing 100 g. of acid-washed alumina and the column was developed with the 1:1 petroleum ether–benzene mixture (total of 320 ml.) and then with benzene (390 ml.). The first petroleum ether–benzene fractions were enriched in the 1718 cm.$^{-1}$ imine, the benzene fractions in the 1736 cm.$^{-1}$ imine. Refractionation of the first petroleum ether–benzene fraction (1.57 g.) through two additional acid-washed alumina columns using petroleum ether as the sole solvent gave 400 mg. of pure 1718 cm.$^{-1}$ (*trans*) imine, showing no 1736 cm.$^{-1}$ absorption (Fig. 1B).

The purified 1736 cm.$^{-1}$ imine was obtained by fractionation over alkaline alumina (Harshaw Activated Alumina, Grade Al-0109P). Ten grams of the imine mixture was dissolved in 100 ml. of low boiling petroleum ether and applied to a 31 × 248 mm. column containing 200 g. of alumina. Development with 950 ml. of petroleum ether gave a sharp peak containing 3.4 g. of 1718 cm.$^{-1}$ imine. Subsequent development with benzene (500 ml.) gave a second sharp peak fraction (2.5 g.) which was greatly enriched in the 1736 cm.$^{-1}$ imine. Although this fraction still showed 1718 cm.$^{-1}$ absorption (Fig. 1C), it gave essentially pure threonine on hydrolysis, indicating that this fraction consisted mainly, if not entirely, of the *cis* imine. This material was used in the hydrolysis studies described below.

Conversion of the 1718 cm.$^{-1}$ Ethylenimine to DL-Allothreonine.—The methods used to effect the conversion of 1-benzyl-2-carboisopropoxy-3-methylethylenimine to 2-amino-3-hydroxybutyric acid have already been described in detail. Only those points in the procedure which differ significantly will be given here.

The 1718 cm.$^{-1}$ ethylenimine (363 mg.) was suspended in 20 ml. of water and 2 ml. of 72% perchloric acid was added. On addition of the imine to the acid solution a crystalline mass formed. This is assumed to be the perchlorate salt of the imine. The mixture was heated on the steam-cone for 4 hr. The acid solution was extracted with ether to remove the acid insoluble material present. This ether extract when dried and taken to dryness *in vacuo* yielded 56 mg. of dark brown oil. The aqueous acid layer was made basic with saturated sodium bicarbonate. The basic solution was extracted with ether. The ether extract was dried and then it was taken to dryness *in vacuo*. A pale yellow oil (187 mg., 48%) was obtained. This oil partially crystallized on standing. This crude isopropyl 2-benzylamino-3-hydroxybutyrate was used in the following step. It was dissolved in 20 ml. of isopropyl alcohol and catalytically reduced at atmospheric pressure at 35° in the presence of 45 mg. of 10% palladium on charcoal. Theoretical hydrogen uptake was complete in 5 hr. The catalyst was filtered, and the filtrate was taken to dryness *in vacuo*. The residual colorless oil was refluxed with 20 ml. of 6 *N* hydrochloric acid for 10 hr. The hydrolysate was taken to dryness *in vacuo*. The residue was dissolved in 40 ml. of water and passed over a column containing 17 ml. of IR-45 in the hydroxyl phase. The column was washed until the washings were ninhydrin negative. The eluate and washings were combined. This solution was taken to dryness *in vacuo* and yielded 62 mg. of white solid. This material gave a value of 11.35% for nitrogen (theory for allothreonine, 11.76%). The infrared spectra of this material was identical with that of DL-allothreonine and differed significantly from that of DL-threonine. In order to determine the amount of DL-threonine present in this sample, it was assayed microbiologically[17] and was found to contain less than 5% of DL-threonine.

Conversion of the 1736 cm.$^{-1}$ Ethylenimine to DL-Threonine.—The 1736 cm.$^{-1}$ ethylenimine (2.305 g.) was suspended in 30 ml. of water and 3 ml. of 72% perchloric acid was added. On the addition of the imine to the acid solution, no crystalline material formed. The mixture was heated on the steam-cone 4 hr. The acid solution was extracted with ether to remove the acid insoluble material present. This ether extract was dried and then taken to dryness *in vacuo*. It yielded 618 mg. of dark brown oil. The aqueous acid layer was made basic and the oil that separated was extracted with ether. The ether extract was dried and then it was taken to dryness *in vacuo*. The residue was a pale yellow oil (1.788 g., 72%). A portion of this oil (388 mg.) was dissolved in 20 ml. of isopropyl alcohol. Hydrogenolysis of the benzyl group was carried out at atmospheric pressure at 35° in the presence of 75 mg. of 10% palladium on charcoal. Theoretical hydrogen uptake was complete in 3.5 hr. The catalyst was filtered, and the filtrate was taken to dryness *in vacuo*. The colorless oil that was obtained was dissolved in 20 ml. of 6 *N* hydrochloric acid and refluxed for 12 hr. The hydrolysate was taken to dryness *in vacuo*, and the residue was taken up in 30 ml. of water. The solution was passed over a column containing 17 ml. of IR-45 in the hydroxyl phase. The resin was washed with water until the washings were ninhydrin negative. The combined eluate and washings gave a negative halogen test with silver nitrate. This solution was taken to dryness *in vacuo* yielding 131 mg. of white solid giving analytical data in agreement with those for threonine. The infrared spectrum of this material was identical with that of DL-threonine. Microbiological assay showed this material to contain 90–100% of DL-threonine.

Conversion of 1-Benzyl-2-carboisopropoxy-3-methylethylenimine to N-Benzylglycine Hydrochloride.—A solution of 6.18 g. (0.027 mole) of III in 25 ml. of 6 *N* hydrochloric acid was heated 5 hr. in a water-bath at 80°. The hydrolysate was cooled at 5° overnight giving 1.86 g. of pink solid. The mother liquor was taken to dryness *in vacuo*. The residue was taken up in absolute alcohol and upon the addition of high boiling petroleum ether an additional 0.62 g. of solid was obtained. The combined yield of crude N-benzylglycine hydrochloride was 2.48 g. (45%). The remainder of the material which could not be crystallized was a brown resinous material. A portion of the solid was recrystallized two times from absolute alcohol giving white plates melting at 226–228° with effervescence.

Anal. Calcd. for $C_8H_{11}O_2N\cdot HCl$ (201.6): C, 53.60; H, 6.00; N, 6.95. Found: C, 53.75; H, 5.59; N, 6.70.

The hydrochloride was converted to N-benzylglycine over IR-45 in the hydroxyl phase. The crude product was recrystallized from methanol giving pure N-benzylglycine melting at 201–203°.

Anal. Calcd. for $C_9H_{11}O_2N$ (165.2): C, 65.44; H, 6.71; N, 8.48. Found: C, 64.85; H, 6.54; N, 8.46.

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(17) The microbiological assays were performed by Dr. Owen J. Koeppe. His help is gratefully acknowledged.