tion boiling at 140–144° was collected. Redistillation of this fraction gave 2.0 g. (10%) of (−)-α-methylvaleronitrile, b.p. 145–147°, $n^{25}D$ 1.3938, $\alpha^{25}D$ −28.0° (lit.[39] b.p. 146.6°, $n^{30}D$ 1.3959 for racemic material). Capillary g.c.[36] showed this product to be homogeneous.[22]

(39) C. de Hoffmann and E. Barbier, *Bull. soc. chim. Belges*, **45**, 565 (1936).

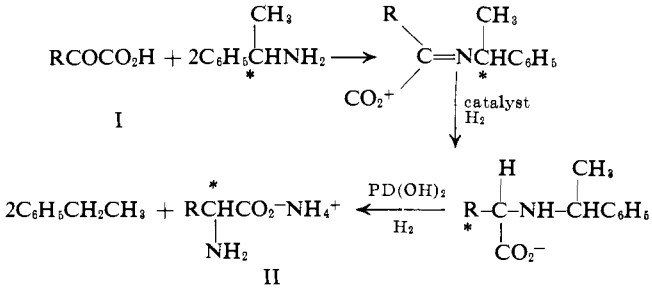
Azomethine Chemistry. III. Reduction of N-Pyruvylamino Acid Azomethines[1,2]

Richard G. Hiskey and Ralph C. Northrop[3]

Contribution from the Venable Chemical Laboratory, The University of North Carolina, Chapel Hill, North Carolina. *Received July 13, 1964*

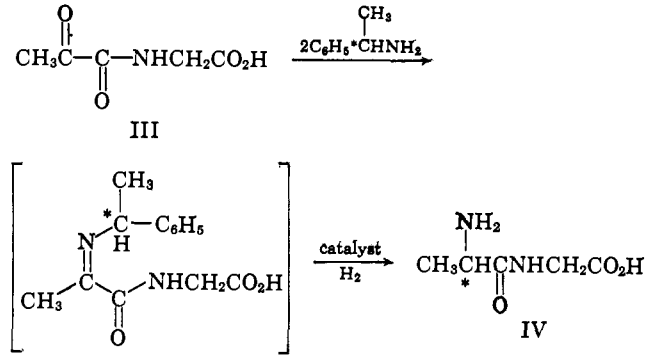
Reductive amination of N-pyruvylglycine with D-(+)- *and* L-(−)-*α-methylbenzylamine provided* D- *and* L-*alanylglycine in optical yields of approximately 50%. When the procedure was applied to N-pyruvyl-*L-*alanine using* D-(+)-*α-methylbenzylamine the ratio of* D-*alanyl-*L-*alanine to the* LL-*isomer was 74:26; with benzylamine the ratio was 67:33; with* L-(−)-*α-methylbenzylamine the ratio was 36:64. These results are discussed in terms of the Prelog rule of asymmetric induction.*

An earlier report[4] on the formation of optically active α-amino acids, by catalytic hydrogenation of the azomethines derived from resolved α-methylbenzylamine and various α-keto acids, described several features of the over-all process. The most striking aspect of the conversion of I to II was the fact that the configuration of the α-amino acid produced depended on the configuration of α-methylbenzylamine employed, *i.e.*, L-amine gave L-amino acid; D-amine gave D-amino acid. The yield and optical purity of the α-amino acids prepared by this route were compared with the size of the side chain, R, present in I. In general the yield of II was found to decrease as the size of R increased from methyl to *t*-butyl. The reduction



also became less selective as the size of the side chain increased, *i.e.*, the optical yield[5] decreased from 82% for alanine (II, R = CH_3–) to 63% for butyrine (II, R = CH_3CH_2–), to 28% for valine (II, R = $(CH_3)_2CH$–). A logical extension of this reaction sequence would involve a study of the hydrogenation of several N-pyruvylamino acids in the presence of optically active α-methylbenzylamine. The present report concerns the results of such an investigation.

The reductive amination of N-pyruvylglycine (III), by analogy with the previous experiments,[4] would be expected to provide alanylglycine (IV). The optical yields of IV should be similar to those previously obtained with α-keto acids. Thus, any asymmetry observed in IV would arise from the influence of the asymmetric center in the α-methylbenzyl portion of



the molecule on the hydrogenation.

A similar experiment using N-pyruvyl-L-alanine (V) as a substrate would present a somewhat different stereochemical situation. That is, the azomethine VII derived from V and optically active α-methylbenzylamine contains two asymmetric centers, both of which would be expected to influence the stereochemistry of the reduction.

The effect of the asymmetric center in the L-alanine portion of V, on the reduction of the azomethine, can be evaluated in the following manner. The structure of the azomethine VII is formally analogous to the substrates studied by Prelog, *et al.* Catalytic hydrogenation of α-keto esters of optically active alcohols has been discussed[6] and adherence to the "Prelog rule" was found, provided the substrate contained a single asymmetric center in the alcohol portion of the molecule.

(1) Supported in part by a grant from the Petroleum Research Fund administered by the American Chemical Society and in part by grant A-3416 from the National Institute of Arthritis and Metabolic Diseases of the National Institutes of Health, U. S. Public Health Service.

(2) Part II of this series: R. G. Hiskey and J. M. Jung, *J. Am. Chem. Soc.*, **85**, 578 (1963).

(3) Abstracted in part from a dissertation submitted by R. C. Northrop to the University of North Carolina in partial fulfillment of the requirements for the Ph.D. Degree, Dec. 1963.

(4) R. G. Hiskey and R. C. Northrop, *J. Am. Chem. Soc.*, **83**, 4798 (1961).

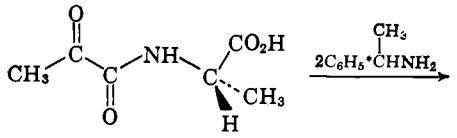
(5) Defined as ($[\alpha]^{25}D$ observed/$[\alpha]^{25}D$ literature) × 100.

(6) V. Prelog, *Bull. soc. chim. France*, 987 (1956).

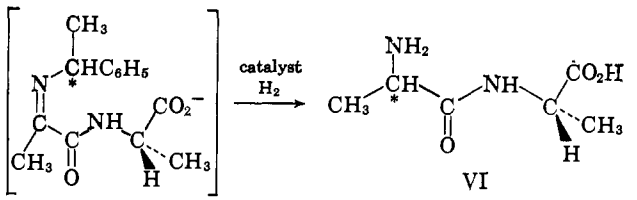
Table I. Preparation of Peptides by Reductive Amination

Expt. no.	Substrate[a]	Configuration of amine	Yield of dipeptide, %	$[\alpha]^{25}D$ obsd.	Optical yield,[b] %	Ala₂OH,[c] % Direct DL, %	Direct LL, %	Enzymic DL, %	Enzymic LL, %
1	Pyr·GlyOH	L	30	+27.5[d,e]	53.5				
2	Pyr·GlyOH	D	33	−30[f]	58				
3	Pyr-L-AlaOH	D	24			74	26	81	19
4	Pyr-L-AlaOH	[g]	36			67	33	67	33
5	Pyr-L-AlaOH	L	20			36	64	28	72

[a] Pyr = CH_3COCO—; other abbreviations are standard. [b] Optical yield = ($[\alpha]D$ obsd./$[\alpha]D$ lit.) × 100. [c] Per cent composition of dipeptide in the mixture. [d] $[\alpha]^{17}D$ +51.44°: W. Grassmann and E. Wunsch, *Ber.*, **91**, 449 (1958). [e] C-1, H_2O. [f] C-2, H_2O. [g] Benzylamine.

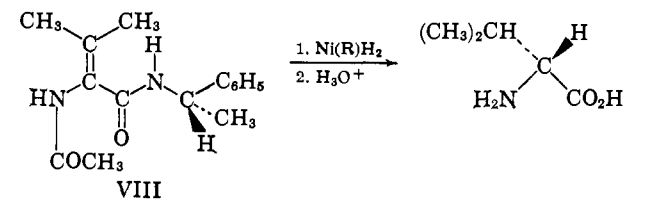


V



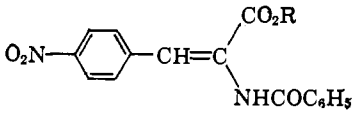
VII VI

Several literature reports have utilized the "Prelog rule" for the synthesis of optically active α-amino acids. Sheehan and Chandler[7] employed the method of Akabori[8] to prepare valine and phenylalanine (*via* VIII) in optical yields of 18–39 and 6%, respectively. Pedrazzoli[9] has demonstrated that the catalytic reduction of the *l*-menthyl ester of IX also exhibited "Prelog

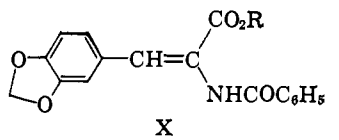


VIII

rule" type asymmetric induction. Yamada, *et al.*,[10] report, however, that catalytic reduction of X (R = *l*-menthyl) provided nearly equal amounts of the diastereoisomeric esters. From these data the L-alanyl

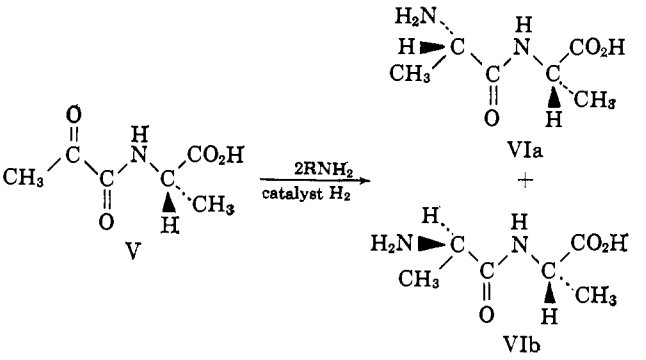


IX



X

portion of VII would be expected to induce predominately the L-configuration; therefore L-alanyl-L-alanine (VIa) should be obtained in larger amounts than D-alanyl-L-alanine (VIb) by reductive amination of V using ammonia or an optically inactive amine such as benzylamine. This prediction is based on the

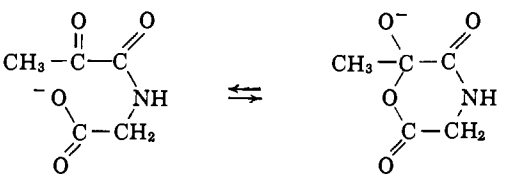


V VIa + VIb

assumption that the *carboxylate* group in V is larger than the methyl group.

With this general background in mind three sets of reductive amination experiments on N-pyruvylamino acids were performed. These included: (a) the reduction of N-pyruvylglycine (III) with the resolved α-methylbenzylamines, (b) the reduction of N-pyruvyl-L-alanine (V) with the resolved α-methylbenzylamines, and (c) the reduction of V with benzylamine. The results of these experiments are summarized in Table I.

The reduction of III in the presence of 2 equiv. of L-(−)- or D-(+)-α-methylbenzylamine provided alanylglycine (IV) in only about 30% yield. The low product yields may reflect an unfavorable keto–imine equilibrium. This situation could arise from a decrease in the electrophilicity of the keto group, owing to the interaction of the latter with the carboxylate anion.



The optical yields (about 55%) of IV in expt. 1 and 2 (Table I) were also somewhat lower than those previously obtained[4] with pyruvic acid (82%) or benzyl pyruvate (74%). This result might be explained by an increase in the bulk of the substrate and hence a decrease in stereospecificity of hydrogen transfer or by an unfavorable catalyst–substrate interaction due to the presence of an additional polar group in the latter. When a related substrate containing a carboxyl group, α-ketoglutaric acid (I, R = $CH_2CH_2CO_2H$), was reduced in the presence of 3 equiv. of L-(−)-α-methylbenzylamine the optical yield

(7) J. C. Sheehan and R. E. Chandler, *J. Am. Chem. Soc.*, **83**, 4795 (1961).
(8) S. Akabori, *KagaKu* (Tokyo), **25**, 54 (1955).
(9) A. Pedrazzoli, *Helv. Chim. Acta*, 40, 80 (1957).
(10) S. Yamada, T. Fujii, and T. Shioiri, *Chem. Pharm. Bull.* (Tokyo), 10, 680 (1962).

of L-(+)-glutamic acid was also low (35%). However, despite the decrease in the optical yields of the alanylglycine samples obtained from III, the over-all stereochemical course of the reductive amination remained the same as previously observed with ketones and α-keto acids; L-amine gave L-peptide and D-amine, D-peptide.

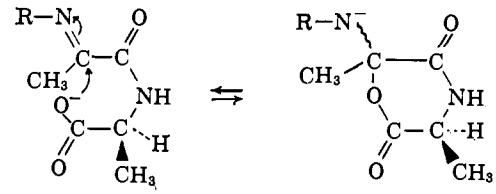
With these results available, the hydrogenation of V in the presence of L-(−)- and D-(+)-α-methylbenzylamine was considered. Since both optically active diastereomeric dipeptides VIa and VIb would probably be present in the reaction mixture, isolation of either dipeptide by crystallization would lead to partial resolution and therefore uncertainity as to the magnitude of the asymmetric induction. Thus an analytical method which did not involve actual isolation of either VIa or VIb was desirable. Automatic ion exchange chromatography provided a convenient tool for the determination of VIa and VIb in the reaction mixture. The results of these determinations are reported in Table I (expt. 3 and 5).

In order to check the analytical results obtained by the direct determination of VIa and VIb, a second method was developed. A portion of the stock solution containing the reaction mixture was hydrolyzed with 6 *N* hydrochloric acid; aliquots were then analyzed for total alanine by ion-exchange chromatography. Separate aliquots of the hydrolysate were incubated with hog kidney D-amino acid oxidase[11]; the resulting solution was then analyzed for alanine. This series of analyses provided the amount of L-alanine and by difference the amount of D-alanine present in the peptide hydrolysate. The agreement between the direct and enzymic methods (Table I) was reasonable although the direct method is considered the more reliable of the two. From these determinations the relative amounts of VIa and VIb and the amount of free alanine present in the reaction mixture could be calculated.

The free alanine content was found to be less than 1% of the total alanine content present after hydrolysis. Thus, the low yields of VIa and VIb (expt. 3, 4, and 5, Table I) are not the result of hydrolysis, ethanolysis, or aminolysis of the amide bond. A reasonable explanation for the low yields of VIa and VIb could, therefore, involve reduction of V prior to azomethine formation. Presumably then, a considerable quantity of lactyl-L-alanine was present in the reaction mixture. An enzymic microdetermination for L-(+)-lactic acid (performed on the hydrolyzed reaction mixture from exp. 4, Table I) indicated an amount of L-lactic acid roughly equivalent to the amount of excess L-alanine was present. From these data approximately 80% of V can be accounted for in each run.

The results of the hydrogenation of V in the presence D-(+)- and L-(−)-α-methylbenzylamine (Table I, expt. 3 and 5) indicate approximately the same degree of asymmetric induction as was observed with III (Table I, expt. 1 and 2). The configuration of the new asymmetric center was again dependent on the configuration of α-methylbenzylamine employed. Thus, reduction with D-(+)-amine (expt. 3) provided VIb in excess while L-(−)-amine (expt. 5) afforded predominantly VIa. These data suggest that the asymmetric center present in the L-alanyl portion of V plays virtually no part in determining the stereochemistry at the new asymmetric center.

In order to determine the effect of the L-alanyl portion of V *in the absence* of another asymmetric center, V was reduced in the presence of benzylamine (Table I, expt. 4). Contrary to expectation, D-alanyl-L-alanine (VIb) was found to predominate over the LL-isomer VIa. No definative explanation of this unexpected observation is presently available. If the reduction of V, using benzylamine, follows the "Prelog rule" the correct isomer VIa is predicted only if the methyl group is larger than the carboxylate group. Alternatively some other feature, such as the reduction of a cyclic form similar to XIb, may be directing the stereochemical course of the reaction. A more detailed investigation of this system is currently in progress.



XIa XIb

Experimental[12]

N-Pyruvylglycine Benzyl Ester. A stirred solution of 10.12 g. (0.03 mole) of glycine benzyl ester *p*-toluenesulfonate[13] and 2.64 g. (0.03 mole) of pyruvic acid in 150 ml. of tetrahydrofuran was cooled to −15° and treated with 2.75 ml. (0.03 mole) of phosphorus oxychloride. Pyridine (7.5 ml., 0.09 mole) was then added over 10 min. The mixture was allowed to stand for 30 min. at −15° and for 1 hr. at room temperature. Dilution with 30 ml. of water and removal of the tetrahydrofuran gave an emulsion which was extracted with ethyl acetate. The extracts were washed with water, 2 *N* hydrochloric acid, 5% sodium bicarbonate, and water. The extract was dried and evaporated to yield a yellow solid which after three recrystallizations from ethyl acetate–petroleum ether (b.p. 60–90°) provided 1.60 g. (23% of ester, m.p. 100–101° (lit.[14] m.p. 100°).

N-Pyruvylglycine (III). A solution of 2.66 g. (0.0113 mole) of N-pyruvylglycine benzyl ester in 40 ml. of methanol was added dropwise to a stirred suspension of 0.1 g. of 10% palladium on charcoal in 30 ml. of methanol under 1 atm. of hydrogen. After 290 ml. of hydrogen was absorbed, the catalyst was filtered and the solvent was evaporated. The oily residue partially solidified on cooling and was extracted with ether. Removal of the ether and recrystallization of the residue from an ethyl acetate–petroleum ether (b.p. 60–90°) mixture provided 1.01 g. (77%) of III, m.p. 89.2–90.5° (lit.[14] m.p. 90°).

(11) S. Ishii and B. Witkop, *J. Am. Chem. Soc.*, **85**, 1832 (1963).

(12) Elemental analyses were performed by Micro-Tech Laboratories, Skokie, Ill. Ion-exchange chromatographic analyses were carried out on a Phoenix Model VG-6000-B instrument. Optical rotations were determined with a Rudolf polarimeter, Model 80, equipped with a Model 200 photoelectric attachment. The melting points and boiling points are uncorrected. Literature values of specific rotations are the highest reported, regardless of sign. Unless specified, amino acids and peptides were obtained from Mann Research Laboratories. The rotations were checked prior to use.

(13) L. Zervas, M. Winitz, and J. P. Greenstein, *J. Org. Chem.*, **22**, 1515 (1957).

(14) T. Wieland, K. H. Shin, and B. Heinke, *Ber.*, **91**, 483 (1958).

L-*Alanine benzyl ester p-toluenesulfonate* was prepared by the general method of Winitz, *et al.*,[15] in 86% yield, m.p. 113.5–114.5°, $[\alpha]^{25}D$ −6.73° (lit.[15] m.p. 114°, $[\alpha]^{27}D$ −6.9°.

N-Pyruvyl-L-Alanine (V). A solution of N-pyruvyl-L-alanine benzyl ester (3.86 g., 0.0155 mole), prepared by the procedure previously described for N-pyruvylglycine benzyl ester but not purified, was hydrogenated in methanol. The hydrogenation procedure was the same as previously used except that several portions of fresh catalyst were added to overcome a catalyst poison.

The reaction mixture was filtered and evaporated to a yellow solid. The material was washed with ether and the insoluble residue was recrystallized three times from an ethyl acetate–ethanol–hexane mixture to afford 1.20 g. (49%) of V, m.p. 168–169.5°, $[\alpha]^{25}D$ −4.2° (*c* 2.03, ethanol).

Anal. Calcd. for $C_6H_9NO_3$: C, 45.28; H, 5.70; N, 8.80. Found: C, 45.23; H, 5.71; N, 8.68.

Preparation of Alanylglycine (IV) by Reductive Amination of III. A solution of 400 mg. (2.75 mmoles) of III and 669 mg. (5.52 mmoles) of D-α-methylbenzylamine was prepared as previously described[4] and hydrogenated over 1.0 g. of 10% palladium-on-charcoal catalyst. The general work-up procedure described earlier[4] afforded 132 mg. (33%) of white crystalline solid IV, $[\alpha]^{25}D$ −30° (*c* 2.4, water) (lit.[16] $[\alpha]^{17}D$ +51.44°).

A 7.6-mg. sample of IV was hydrolyzed with 5 ml. of glass-distilled hydrochloric acid in a sealed tube at 110° for 24 hr. The solution was evaporated and the residue was diluted to 100 ml. with pH 2.2 citrate buffer. Ion-exchange analysis of an aliquot of the solution indicated the presence of alanine and glycine in a ratio of 1:1.

Preparation of Alanyl-L-alanine (VI) by Reductive Amination Using D-α-Methylbenzylamine. N-Pyruvyl-L-alanine (V) was hydrogenated in the presence of 2 equiv. of D-α-methylbenzylamine as previously described. The usual work-up provided an aqueous solution. A few milliliters of this solution were evaporated to dryness and the dry residue was examined in the infrared for phenyl absorption at 700 $cm.^{-1}$. If the infrared spectrum of the aliquot exhibited absorption at 700 $cm.^{-1}$, the aqueous solution was diluted with 50% ethanol, fresh palladium hydroxide catalyst was added, and the hydrogenation was resumed. Normally about 5 days was required for complete debenzylation. The reaction mixture was then concentrated to a sirup and diluted to 25 ml. with distilled water to give stock solution I-A.

The modified reduction procedure was applied to the reduction of V using benzylamine to give stock solution II-A and L-α-methylbenzylamine to give stock solution III-A. The stock solutions were frozen and stored until analyzed by the methods described below.

Analysis of Dipeptide Mixtures by Ion-Exchange Chromatography. Solutions I-A, II-A, and III-A were analyzed by the following procedure. A 1-ml. aliquot of the stock solution was evaporated to dryness and the residue was diluted to 50 ml. with pH 2.2 citrate buffer. Aliquots of this solution were chromatographed using the procedure of Piez and Morris.[17]

Analysis of standard solutions of authentic D-alanyl-L-alanine and L-alanyl-L-alanine showed the peak area to concentration ratios of the two dipeptides were nearly identical. Thus, a single average value was used for both substances. This value was determined as 38.2 area units (a.u.) per μmole of sample. A series of determinations on two different standard solutions of DL-alanine gave an average value of 19.5 a.u./μmole of sample. The peak areas of the stock solutions are reported in Table II.

Table II. Analysis of Dipeptide Mixtures by Ion-Exchange Chromatography

Solution	Peak area[a] DL	LL	AlaOH	Sum of dipeptide peak areas[a]
I	13.9	5.0	0.13	18.9
II	16.2	7.9	0.24	24.1
III	5.8	10.5	0.29	16.3

[a] In area units (a.u.).

Analysis of Dipeptide Mixtures by Enzymic Oxidation. A 1-ml. aliquot of solution I-A was hydrolyzed with 5 ml. of glass-distilled hydrochloric acid in a sealed tube at 110° for 26 hr. The hydrolysate was evaporated to dryness, diluted with water, and again evaporated to dryness. The residue was dried *in vacuo* over sodium hydroxide and diluted to 10 ml. with pH 8.2 pyrophosphate buffer (solution F). A 1-ml. aliquot of solution F was evaporated to dryness and the residue was diluted to 10 ml. with pH 2.2 citrate buffer (solution G). Aliquots (1 ml.) of solution G were analyzed for alanine.

The enzymic oxidation of D-alanine was performed on a 1-ml. aliquot of solution F using 1 ml. of a solution of hog kidney D-amino acid oxidase in pH 8.2 pyrophosphate buffer (6 mg. of enzyme/ml.). The mixture was incubated at 38° for 15 hr. The enzyme was precipitated by the addition of 6 drops of 12 *N* hydrochloric acid, the mixture was centrifuged, the supernant was withdrawn, and the precipitate was washed once with 6 *N* hydrochloric acid. The combined supernant and washings were evaporated to dryness and reconcentrated with water, and the residue was vacuum dried over sodium hydroxide.

The dried residue was taken up in a few milliliters of pH 2.2 citrate buffer and filtered through sintered glass into a 10-ml. volumetric flask. The solution was diluted to 10 ml. to give solution H. A control prepared from 1 ml. of enzyme solution and 1 ml. of pyrophosphate buffer solution was incubated at the same time as solution F and worked up in exactly the same manner.

Aliquots (1 ml.) of solutions G, H, and the control were analyzed by ion-exchange chromatography. The results are shown in Table III.

Enzymic Determination of L-(+)-Lactic Acid. Solution II-F was analyzed for L-lactic acid by the method of Friedland and Dietrich.[18] The concentration of L-(+)-

(15) M. Winitz, L. Bloch-Frankenthal, N. Izumiya, S. M. Birnbaum, C. G. Baker, and J. P. Greenstein, *J. Am. Chem. Soc.*, 78, 2423 (1956).
(16) A. Bothner-By, *ibid.*, 73, 846 (1951).
(17) K. A. Piez and L. Morris, *Anal. Biochem.*, 1, 187 (1960).
(18) I. M. Friedland and L. S. Dietrich, *ibid.*, 2, 390 (1961).

Table III. Enzymic Analysis of Dipeptide Hydrolysates

Solution	Area	Enzyme blank	Corr. area	Concn. of alanine[a] Total[b]	Free[c]	Bound[d]
I–G	21.1[e]		21.1	1.08	0.003	1.08
I–H	18.4[e]	1.3	17.1	0.88	0.003	0.88
II–G	19.9[f]		19.9	1.02	0.006	1.01
II–H	17.0[g]	1.3	15.7	0.81	0.006	0.80
III–G	21.2[h]		21.2	1.09	0.007	1.08
III–H	21.4[h]	1.3	20.1	1.03	0.007	1.02

[a] In μmoles/ml. [b] Calculated. [c] Taken from Table II; converted to concentration units and corrected for dilution by a factor of 10^{-2}. [d] Alanine present in some form other than the free amino acid. [e] Average of 2 runs. [f] Average of 8 runs. [g] Average of 4 runs. [h] Average of 3 runs.

lactic acid obtained from a standard curve was 4.2 μmoles/ml.

Preparation of N-Carbobenzoxy-D-alanyl-L-alanine Benzyl Ester. N-Carbobenzoxy-D-alanine *p*-nitrophenyl ester[19] (3.66 g., 0.0106 mole) and L-alanine benzyl ester *p*-toluenesulfonate (3.73 g., 0.0106 mole) were dissolved in 15 ml. of N,N-dimethylformamide. Triethylamine (1.48 ml., 0.0106 mole) was added and the solution was kept at room temperature for 38 hr. The reaction mixture was diluted with 40 ml. of ethyl acetate and washed twice with 1 *N* hydrochloric acid, once with water, five times with 5% sodium bicarbonate solution, and three times with water. The organic layer was dried and concentrated to a white solid. Recrystallization from ethyl acetate–petroleum ether (b.p. 30–60°) provided 3.14 g. (77%) of the protected dipeptide, m.p. 123.5–124.5, $[\alpha]^{25}D$ +9.8° (*c* 3.7, $CHCl_3$) (lit.[20] m.p. 114°, $[\alpha]^{25}D$ −2.9° (*c* 1, $CHCl_3$)).

Anal. Calcd. for $C_{21}H_{24}N_2O_5$: C, 65.61; H, 6.29; N, 7.29. Found: C, 65.47; H, 6.24; N, 7.28.

Preparation of D-Alanyl-L-alanine (XIV). N-Carbobenzoxy-D-alanyl-L-alanine benzyl ester (2.77 g., 7.22 mmoles) was suspended in 30 ml. of methanol and treated with ethyl acetate until solution was complete. After addition of a few milliliters of dilute acetic acid, the solution was hydrogenated at 50 p.s.i. in the presence of 300 mg. of palladium hydroxide-on-charcoal catalyst. The reduction was complete in 5 min. Removal of the solvent afforded a sirup which crystallized on addition of ethanol. Recrystallization was accomplished by dissolving the dipeptide in a few milliliters of water, adding 10 ml. of ethanol, seeding, and adding 1 drop of ethyl acetate. In this manner 1.00 g. (87%) of XIV was obtained, $[\alpha]^{25}D$ −71.0° (*c* 1.9, H_2O) (lit.[21] $[\alpha]^{25}D$ −71.1°).

The D-alanyl-L-alanine exhibited a purple ninhydrin spot and the same R_f (0.39) in the 1-butanol–water–acetic acid system (4:5:1) as an authentic sample of L-alanyl-L-alanine. The two dipeptides had slightly different retention times by ion-exchange chromatography.

Reductive Amination of α-Ketoglutaric Acid. Hydrogenation of α-ketoglutaric acid and 3 equiv. of L-α-methylbenzylamine in the manner previously described[4] provided a clear gum. The material was dissolved in a few milliliters of water and cooled. The crystalline solid amounted to 29% of theoretical.

The mother liquor was evaporated to a sirup and triturated with ether to provide a solid which was combined with the crystals obtained from water, total yield 79%, $[\alpha]^{25}D$ +11.1° (*c* 2, *N* HCl) (lit.[22] $[\alpha]^{25}D$ +31.8°).

The combined solids exhibited a single peak identical with pure glutamic acid when analyzed by ion-exchange chromatography.

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Optically Active Amines. III. The Optical Rotatory Dispersion Curves of the N-Salicylidene Derivatives of Some Open-Chain Primary Amines[1]

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The optical rotatory dispersion curves and electronic absorption spectra of the N-salicylidene derivatives of a series of optically active amines and amino acid esters were measured. The Schiff bases having an aryl group α or β to the salicylidenimino group display anomalous rotatory dispersion curves with a Cotton effect near 315 mμ of high amplitude, similar to some of those associated with inherently dissymmetric chromophores. The correlation of the absolute configuration of an α-arylalkylamine Schiff base with the shape of its dispersion curve is discussed.

(1) Paper II: H. E. Smith, S. L. Cook, and M. E. Warren, Jr., *J. Org. Chem.*, **29**, 2265 (1964).
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