potassium permanganate and dried over potassium carbonate), solutions containing excess solute were held at the specified temperatures with frequent shaking for at least one hour, after which measured volumes of clear supernatant were withdrawn, evaporated to dryness at 100° and the residues weighed. A different approach was necessary with I ethyl ester hydrochloride in dioxane at 95°, since its solubility was so great that high viscosity of the solution precluded accurate volumetric transfer. In this case, weighed portions were added to a measured volume of solvent until a trace of undissolved material still remained one hour later. Results are shown in Table III.

Effect of Phenylserine Ethyl Ester Hydrochloride on Solubility of Allophenylserine Ethyl Ester Hydrochloride in Acetone.—I ethyl ester hydrochloride (1.000 g.) was dissolved in 8.0 ml. of dry acetone by refluxing. II ethyl ester hydrochloride (0.100 g.) was added, and refluxing was continued for five minutes. The hot mixture was filtered, 1.0 ml. of cold dry acetone being used to complete transfer of the undissolved allo compound to the filter funnel. Drying gave 0.026 g. and 0.030 g. of II ethyl ester hydrochloride undissolved in two such runs, m.p. 176° (dec.).

AMES, IOWA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Stereochemistry of the β-Phenylserines: Improved Preparation of Allophenylserine[1]

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Paper chromatography was used to study preparation of phenylserine and allophenylserine by condensation of benzaldehyde and glycine. The isomers were produced in comparable quantities with a one-hour condensation period; the proportion of allophenylserine decreased sharply with longer reaction time. Allophenylserine forms a hemihydrate, and a poorly soluble addition compound with dioxane. The latter was used to separate allophenylserine from phenylserine. The hydrochlorides, the methyl, ethyl, *n*-propyl and *i*-propyl ester hydrochlorides, and the corresponding esters of phenylserine and of allophenylserine were prepared. Threonine and allothreonine were separated on paper chromatograms under the same conditions as phenylserine and allophenylserine.

The main product from the condensation of benzaldehyde and glycine under alkaline conditions is ordinarily phenylserine (I): some allophenylserine (II) is also formed.[3] Paper chromatography has been studied as a means of controlling preparation of the latter. A typical papergram prepared by the ascending technique[4] is illustrated in Fig. 1.

The upper layer from a mixture, by volume, of 50% *n*-butanol, 6.25% acetone, 6.25% concentrated ammonium hydroxide and 37.5% water was used for development. The difference between R_F values of I and II diminished when other levels of acetone or concentrated ammonia were used. I and II were not separated when either acetone or ammonia was omitted, when 5% sodium hydroxide or pyridine was substituted for ammonium hydroxide, or *n*-butyl ethyl ketone for acetone. A less satisfactory separation was obtained using the upper layer from a mixture of equal parts of *n*-butanol and 5% hydrochloric acid.[5]

The solvent mixture used to resolve I and II also proved effective for the separation of threonine and allothreonine. In this case, no attempt was made to vary the ratio of solvent constituents in order to attain maximum difference in R_F values. Slow separation of these diastereomers on paper by *n*-butanol–diethylamine–water has been described.[6]

Paper chromatography was qualitatively useful for solutions containing 0.01–2.5% (w./v.) of I or II. One part (0.2γ) of one diastereomer could be detected in the presence of 250 parts (50γ) of the other. The range 0.05–0.2% was preferred for quantitative estimates, which were obtained by visually comparing spot areas from solutions of unknown with those of known concentration.

The German patent[7] method of condensing glycine and benzaldehyde was then reinvestigated. The condensation cakes obtained from various batches were allowed to stand at room temperature for different periods of time prior to acidification. The proportions of I and II in the resulting crude products, aqueous filtrates and ethanol washings were determined by paper chromatography. Typical results are presented in Table I. With a one hour condensation period, II was formed to an extent comparable to I, but with increasing condensation time, the level of II declined sharply. With a 24-hour interval, combined yield of I and II was maximal, but the small quantity of II present remained in the aqueous filtrate, or was eluted during hot ethanol washing of the crude product. On the basis of these findings, II can now be prepared readily.[8]

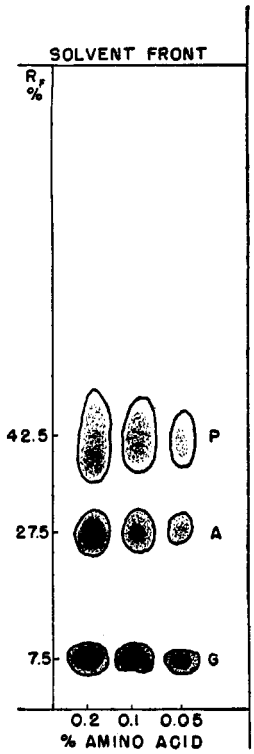

Fig. 1.—P, Phenylserine; A, allophenylserine; G, glycine.

(1) Work supported by the Industrial Science Research Institute of Iowa State College. Presented at the Northwest Regional Meeting of the American Chemical Society, Corvallis, Ore., June 20, 1952.

(2) From the Ph.D. dissertation of Kenneth N. F. Shaw, 1951.

(3) K. N. F. Shaw and S. W. Fox, THIS JOURNAL, **75**, 3417 (1953).

(4) R. J. Williams and H. Kirby, *Science*, **107**, 481 (1948).

(5) Separation of the *p*-nitrophenylserines on paper by *n*-butanol–formic acid was reported recently: D. O. Holland and P. A. Jenkins, *Chemistry and Industry*, 1092 (1951).

(6) T. L. Hardy and D. O. Holland, *ibid.*, 855 (1952).

(7) Ges. für Kohlentechnik, m.b.H., German Patent 632,424 (July 8, 1936).

(8) Since this work was completed, preparation of II has been reported from ethyl benzoylacetate[9] and its α-oximino derivative.[10,11]

(9) W. A. Bolhofer, THIS JOURNAL, **74**, 5459 (1952).

(10) Y. Chang and W. H. Hartung, *ibid.*, **75**, 89 (1953).

(11) I. Elphimoff-Felkin and H. Felkin, *Compt. rend.*, **232**, 241 (1951).

TABLE I

YIELD AND PHENYLSERINE DIASTEREOMER CONTENT IN GLYCINE–BENZALDEHYDE CONDENSATION

Condensation time, hr.[a]	Glycine recovered,[b] %	Yield Wt., g.[c]	Yield %[d]	Diastereomer fraction[e] I	Diastereomer fraction[e] II
1	15–25	33.4	46	0.55–0.60	0.40–0.45
4	5–10	44.3	61	0.80–0.85	0.15–0.20
24	2–4	52.7	73	1.00	0
60	1–2	49.0	68	1.00	0

[a] Period elapsing between benzaldehyde addition and acidification. [b] Material in aqueous filtrate and ethanol washings. [c] Ethanol-washed crude product from 30.0 g. of glycine. [d] If (b) is included, these values are raised 10–20%. [e] Based on (c). With (b) included, diastereomer ratio was essentially unchanged for 1 and 4 hours, but was 0.96–0.98 I; 0.02–0.04 II for both 24 and 60 hours.

The disappearance of II is associated with several distinct reaction stages. When the reactants were mixed vigorously, a hitherto unreported primary product precipitated. It redissolved rapidly and the resulting homogeneous thin sirup then yielded the usual solid condensation cake, which has been regarded as the sodium salt of N-benzalphenylserine.[12] When this cake was acidified, benzaldehyde was liberated in quantities which varied markedly with condensation time. Further study is required to determine the number and nature of the intermediates involved, and their relation to the changing ratio of I to II.

Originally,[3] II was freed from I by conversion to the ethyl ester hydrochlorides. Fractionation of the sodium salts with ethanol[13] was unsuccessful, but more promising results (Table II) were obtained by recrystallizing a crude condensation product from other solvents. The first crop from water was mainly I, but in 50% aqueous dioxane, II was precipitated almost quantitatively as a stable addition compound with dioxane.[14] This has made possible direct separation of I and II. The crude product from a one-hour condensation was crystallized from water to give one-half of the I, which contained very little II. Dioxane was added to the filtrate to precipitate II substantially free of I. The remaining I was collected by concentrating the dioxane filtrate and adding ethanol.

TABLE II

RECRYSTALLIZATION OF CRUDE ONE-HOUR CONDENSATION PRODUCT[a]

Solvent[b]	Crystalline product Recy., %	Crystalline product Isomer content[c]	Filtrate Isomer content[c]
Water	28	*ca.* 95% I	I < II
50% Methanol	54	I > II	I < II
50% Ethanol	75	I > II	I < II
50% Acetone	65	I < II	I > II
50% Dioxane	67	*ca.* 65% II	*ca.* 95% I

[a] 55–60% I, 40–45% II. [b] 1.000 g. samples of crude product dissolved in 10.0 ml. of hot water; organic solvent added as indicated. [c] > or < indicates only small difference in isomer content, as checked by paper chromatography.

(12) E. Erlenmeyer, Jr., and E. Früstück, *Ann.*, **284**, 36 (1895).

(13) Threonine and allothreonine have been separated in this manner: K. Pfister, 3rd, C. A. Robinson, A. C. Shabica and M. Tishler, THIS JOURNAL, **71**, 1101 (1949).

(14) This may be an oxonium salt; its infrared absorption spectrum, although similar to those of anhydrous I and II, lacks the broad absorption bands characteristic of dioxane.

For final purification of I (first plus third crops), aqueous ethanol proved to be most suitable. Aqueous acetone was preferred for recovering pure II from its dioxane compound. I was obtained as the monohydrate: II crystallized in anhydrous form or as a hemihydrate, depending upon temperature and solvent. The purity of each diastereomer was established as 99.5% or better by paper chromatography. It should be noted that the decomposition points of I, II, their solvates and various mixtures (183–197°, varying with initial bath temperature and heating rate) showed differences too small to be useful for identification. The results of a typical fractionation are summarized in Table III.

TABLE III

SEPARATION OF PHENYLSERINE (I) AND ALLOPHENYLSERINE (II) FROM A CRUDE ONE-HOUR CONDENSATION PRODUCT[a]

Fraction	Total wt., g.	I[b] Wt., g.	I[b] Recy., %	II[b] Wt., g.	II[b] Recy., %
Pure I	36.5	36.5	41	..	..
Pure II	24.0	..	..	24.0	27
Residual crops	15.2	9.1	10	6.1	7
	5.4	3.2	4	2.2	3
Residual filtrate	2.4	1.2	1	1.2	1
Totals	83.5	50.0	56	33.5	38

[a] 89.2 g. crude product (55–60% I, 40–45% II). [b] Individual weights of I and II given for mixed crops were estimated by paper chromatography.

The hydrochlorides of I and II were prepared by treating suspensions in dioxane with hydrogen chloride. These derivatives showed the same order of solubility as their parent amino acids (I < II), and hence seemed of little value for separating mixtures. Pertinent data are presented in Table IV.

TABLE IV

PHENYLSERINE (I) AND ALLOPHENYLSERINE (II) HYDROCHLORIDES

Series	Yield, %	M.p., °C.[a] Crude	M.p., °C.[a] Recryst.[a]	Cl,[b] % Calcd.	Cl,[b] % Found	N, % Calcd.	N, % Found
I	88	163	160[c]	16.29	16.15	6.44	6.31
					16.22		6.39
II	93	163	159[d]	16.29	15.99	6.44	6.43
					16.10		6.43
Mixture	159						

[a] All with decomposition: initial bath temperature 150–155°, 4–5 minutes heating. [b] Mercurimetric. [c] M.p. 157°,[15] 164–166°.[3] [d] M.p. 212°.[15]

Preparation of I methyl, I ethyl and II ethyl ester hydrochlorides, and the corresponding esters was described in an earlier paper.[3] These and other ester hydrochlorides (Table V) were obtained in almost quantitative yield by use of anhydrous starting materials and higher temperatures during hydrogen chloride treatment.

The ester hydrochlorides were converted to the corresponding esters (Table VI) by treatment in ether with ammonia.[3] Yields were slightly lower than in earlier runs where second crops were recovered by concentration of filtrates.

(15) G. Carrara and G. Weitnauer, *Gazz. chim. ital.*, **79**, 856 (1949).

TABLE V

PHENYLSERINE (I) AND ALLOPHENYLSERINE (II) ESTER HYDROCHLORIDES

Ester hydrochloride	Yield[a] Wt., g.	%	M.p., °C.[b]	Cl,[b] % Calcd.	Found	N,[b] % Calcd.	Found
I Methyl	4.360	94	160 (dec.)[c]	15.30	14.99, 15.03	6.05	6.00, 6.01
I Ethyl	4.796	98	140[c]	14.43	14.61, 14.71	5.70	5.61, 5.66
I *n*-Propyl	4.679	90	131[d]	13.65	13.30, 13.62	5.39	5.18, 5.21
I *i*-Propyl	4.947	95	164	13.65	13.34, 13.51	5.39	5.31, 5.35
II Methyl	4.485	97	180 (dec.)	15.30	14.98, 15.00	6.05	5.98, 6.05
II Ethyl	4.783	96	178 (dec.)[c,e]	14.43	14.54, 14.71	5.70	5.63, 5.64
II *n*-Propyl	5.031	97	160	13.65	13.32, 13.45	5.39	5.21, 5.27
II *i*-Propyl	5.069	98	159 (dec.)	13.65	13.60	5.39	5.24, 5.28

[a] Total yield of crude product, first and second crops from 3.624 g. of I or II. [b] Values determined with first crop from recrystallization out of ether–parent alcohol (92–97% recovery for I series, 82–94% recovery for II series). [c] Other reported values were cited in an earlier paper.[3] [d] M.p. 129°.[15] [e] M.p. 180–181°,[9] 170°.[10]

TABLE VI

PHENYLSERINE (I) AND ALLOPHENYLSERINE (II) ESTERS

Ester	Yield,[a] %	M.p., °C.[b]	N,[b] % Calcd.	Found	Crystal form
I Methyl	75	62[c]	7.17	7.09, 7.15	Needles
I Ethyl	77	84[c]	6.69	6.54, 6.58	Mica plates
I *n*-Propyl	85	59[d]	6.27	6.18, 6.22	Needles, blades
I *i*-Propyl	89	75	6.27	6.21, 6.25	Needles, blades
II Methyl	89	110	7.17	7.15, 7.15	Mica plates
II Ethyl	92	86[c,e]	6.69	6.50, 6.57	Needles
II *n*-Propyl	89	63	6.27	6.23, 6.24	Needles
II *i*-Propyl	85	75	6.27	6.27, 6.30	Needles

[a] From recrystallization of crude product out of ether–Skelly D. [b] Values determined after a second recrystallization from ether–Skelly B (71–91% recovery for single crops). [c] Other reported values were cited in an earlier paper.[3] [d] M.p. 57°.[15] [e] M.p. 85–86°.[11]

Experimental[16]

Paper Chromatography of Phenylserine (I) and Allophenylserine (II).—Aqueous solutions were applied by means of 2.0 λ micropipets to points 1.4 cm. apart along a line 3.0 cm. from the narrow side of a 20 × 27 cm. rectangle of No. 4 Whatman filter paper. The resulting spots were allowed to dry at room temperature, then the rectangle was cylinderized by stapling, with the long sides not quite touching. The cylinder was stood upright, sample spots near the bottom, in a screw-capped wide-mouthed glass chemical jar (5 in. diameter, 12 in. high) which contained 125–150 ml. of the upper water-poor layer from a mixture of 200 ml. of *n*-butanol, 150 ml. of water, 25 ml. of acetone and 25 ml. of concentrated ammonium hydroxide. The solvent was clarified initially in the jar by addition of a few ml. of acetone with thorough shaking to equilibrate liquid and vapor phases. The liquid was allowed to ascend for 3–6 hours at room temperature. The solvent front was penciled and the cylinder was dried in air at room temperature. The opened sheet was sprayed uniformly with 0.2% (w./v.) ninhydrin solution in *n*-butanol saturated with water and dried at 80° for 10–15 minutes. The resulting orange-brown spots darkened to violet within 24 hours.

In estimating the proportion of I and II present in various condensation products, three mixed standard solutions were used. Each contained I, II and glycine, at levels of 0.20, 0.10 and 0.05% (w./v.), respectively. Several different dilutions of an unknown were used when amino acid content was uncertain; otherwise, concentrations were set to give developed spots of approximately the same area as the 0.1% standard. Single spots from each standard were spaced uniformly across the sheet of filter paper, together with non-adjacent duplicates of five unknown samples.

Papergrams of products from separation experiments were made with 2.5% solutions. Absence of a barely visible spot, corresponding to that obtained with a 0.01% solution of I or II, was taken to indicate diastereomeric purity of 99.5% or better.

Paper Chromatography of Threonine and Allothreonine.—A papergram was prepared as described above with three spots each of 0.1% (w./v.) solutions of threonine and allothreonine. Ascent proceeded for 5.5 hours. Respective R_F values were 0.18–0.19 and 0.13–0.14. Separation occurred to the same extent on another papergram prepared with four spots of a mixed solution containing 0.1% of each isomer. The ninhydrin-treated blue-violet spots were sharply bordered and of smaller area than I and II run at the same concentration.

Condensation of Benzaldehyde with Glycine.—A solution of 30.0 g. (0.40 mole) of glycine and 24.0 g. (0.60 mole) of sodium hydroxide in 100 ml. of water was chilled to 15°. With cooling maintained at 15° (water-bath), and rapid agitation with a Hershberg stirrer, 84.9 g. (0.80 mole) of benzaldehyde was added all at once. The emulsified reaction mixture suddenly set to a particulate paste after 2–3 minutes, and abruptly halted the agitator. This transitory product, which was not encountered if impure benzaldehyde was used, or if the reactants were mixed slowly, redissolved when stirred by hand. The stirring motor was turned on again at high speed after 5–6 minutes. At this point, the temperature reached a maximum of 25–26° and then declined gradually. The reaction mixture was a transparent light sirup after 12–13 minutes. Precipitation commenced anew in 25–28 minutes, followed by rapid and complete solidification.

The condensation cake was allowed to stand at room temperature for different periods of time with various batches. Concentrated hydrochloric acid (50.0 ml., *ca.* 0.6 mole) was then added dropwise during 30 minutes to the fragmented cake with water-bath cooling at 15°. Mechanical agitation was continued for one hour after addition of acid.

Two batches which stood only one hour (from the time of benzaldehyde addition) gave a thin slurry at the close of acidification. Further agitation caused thickening to a smooth paste, then large solid lumps formed, leaving a clear pale yellow supernatant. The mixture was suction-filtered as dry as possible after being chilled at 5° for two hours. The aqueous filtrate (*p*H 3.1) contained only a few ml. of supernatant benzaldehyde.

Three batches acidified after four hours showed different behavior. The reaction mixture thickened to a stiff paste, without lumping, during subsequent agitation. The paste was suction-filtered after refrigeration at 5° for 1–24 hours. No supernatant benzaldehyde was visible in the pale yellow transparent filtrate (*p*H 4–4.7) and its odor in the filter cake was weak. Similarly, no appreciable liberation of benzaldehyde occurred with one batch acidified to *p*H 2.8 and then treated with sodium hydroxide solution to *p*H 5.8.

Two condensation cakes acidified after 24 hours were fragmented with more difficulty. Small oily pellets formed which smelled strongly of benzaldehyde. One batch was stored overnight at 5°; the other was treated with 100 ml. of ether, which gave a thick paste surrounded by aqueous supernatant upon further agitation. In both runs, suction-filtration proceeded slowly and yielded a clear aqueous layer surmounted by a substantial quantity of benzaldehyde.

One batch was allowed to stand 60 hours after benzaldehyde addition; 150 ml. of ether was added during acidification and subsequent agitation to facilitate disintegration of the hard condensation cake. Further processing and behavior were otherwise similar to the ether-treated 24-hour batch.

The filter cakes obtained after acidification were thoroughly mixed with three 200–250 ml. volumes of boiling 95% ethanol, and the resulting slurry was filtered each time.

(16) All melting points are uncorrected and were taken in open capillary tubes.

The cake from one four-hour batch was initially stirred with only 100 ml. of boiling 95% ethanol to give a thin slurry which quickly solidified. A further 150 ml. of boiling alcohol was added to furnish a filtrable slurry again. When the cake from a 24-hour run was treated similarly with portions of boiling 95% ethanol, mere slurrying occurred and no sudden solidification. Subsequent alcohol washing of these two batches was effected as with the others. Each alcohol-washed crude product was dried to constant weight over Anhydrone at 50–60° and 10–15 mm. The proportion of I and II present was determined by paper chromatography. Data for typical runs are collected in Table I.

Ethanol washings were concentrated under reduced pressure. All cleaved benzaldehyde was present in the washings from four hour batches. With others, the amount corresponded to that retained within the filter cake prior to hot ethanol washing.

Phenylserine Monohydrate.—A 2.500-g. sample of I was recrystallized from 30 ml. of boiling water; 30 ml. of boiling ethanol was added after solution. The resulting layered hexagonal plates (microscope) were dried over Anhydrone at 50–60° and *ca.* 20 mm. during 18 hours to give 2.175 g. (87% recovery) of anhydrous I.

Anal. Calcd. for $C_9H_{11}O_3N \cdot H_2O$: H_2O, 9.05. Found: H_2O, 9.01, 9.05, 9.10. Calcd. for $C_9H_{11}O_3N$: N, 7.73; neut. equiv., 181.2. Found: N, 7.72, 7.85; neut. equiv. (formol), 181, 182, 183.

Allophenylserine–Dioxane Addition Compound.—A solution of 2.500 g. of II in 35 ml. of boiling water was treated with 35 ml. of boiling dioxane. Rapid crystallization of blunt needles ensued. Overnight storage at 5°, filtration, washing with cold 50% dioxane and drying in air at room temperature gave 3.001 g. of II–dioxane addition compound. Desiccation over Anhydrone at *ca.* 20 mm. and 50–60° during 18 hours decreased the weight to 2.998 g. (97%), unchanged by heating at 77° and *ca.* 0.1 mm. over phosphorus pentoxide for two hours.

Anal. Calcd. for $(C_9H_{11}O_3N)_2 \cdot C_4H_8O_2$: N, 5.96; neut. equiv., 235. Found: N, 6.05, 6.21, 5.93, 5.94; neut. equiv. (formol), 229, 231.

Allophenylserine Hemihydrate.—A solution of 11.124 g. of II–dioxane compound in 100 ml. of boiling water was gently simmered for 5–10 minutes. The vessel was scratched, with cold water cooling. The resulting hexagonal microprisms of II-hemihydrate weighed 5.972 g. (63% yield) after drying in air at room temperature. The material was recrystallized for analysis from hot water with ice-bath cooling, ice-water washing and drying in air at room temperature. A sample was desiccated over phosphorus pentoxide at 77° and *ca.* 0.1 mm. during 10 hours. Slow evaporation of aqueous solutions of II at room temperature also gave the hemihydrate.

Anal. Calcd. for $(C_9H_{11}O_3N)_2 \cdot H_2O$: N, 7.36; H_2O, 4.74. Found: N, 7.34; H_2O, 4.85. Calcd. for $C_9H_{11}O_3N$: N, 7.73. Found: N, 7.70.

The filtrate from the crude hemihydrate was raised to the boiling point and treated with an equal volume of boiling dioxane. This led to 2.856 g. (26% recovery) of II–dioxane compound.

Anhydrous Allophenylserine.—A solution of 2.500 g. of II in 50 ml. of hot water was treated with 50 ml. of boiling acetone. Overnight storage at 5°, filtration, washing with 50% acetone, acetone, then ether and drying over Anhydrone for 12 hours at 50–60° and 10–15 mm., yielded 1.818 g. (73% recovery) of anhydrous II as long fibrous needles (microscope). Desiccation of air-dried samples obtained similarly caused no appreciable weight loss. A further recrystallization from water–acetone was carried out for analysis. Recrystallization from hot water alone also yielded anhydrous II, if the solution was allowed to cool slowly to room temperature with frequent swirling.

Anal. Calcd. for $C_9H_{11}O_3N$: N, 7.73; neut. equiv., 181.2. Found: N, 7.54, 7.62; neut. equiv. (formol), 181, 181.

Separation of Phenylserine (I) and Allophenylserine (II). The crude product from a one-hour condensation (89.2 g., 55–60% I, 40–45% II by paper chromatography) was recrystallized from 890 ml. of boiling water to give 26.7 g. (30% recovery) of I containing less than 5% II. The aqueous filtrate was heated to the boiling point and an equal volume of boiling dioxane was added. This treatment yielded 43.0 g. (39% recovery) of II–dioxane compound containing *ca.* 5% I. The 50% dioxane filtrate was concentrated under reduced pressure to 170 ml., heated to the boiling point, and treated with an equal volume of boiling ethanol. This led to 18.9 g. (21% recovery) of I in which only traces of II were detected. The 50% ethanol filtrate contained about 6.5 g. (7% of original starting material) of I + II (paper chromatography); slightly more I than II was present.

The two high I fractions were combined and twice recrystallized from 50% ethanol in the usual manner to give isomerically pure I. The II–dioxane compound middle fraction was recrystallized once from 50% dioxane and then converted to isomerically pure II by recrystallization from 50% acetone. All filtrates were combined, concentrated under reduced pressure and treated with ethanol to give two residual crops. Over-all results are summarized in Table III.

Phenylserine and Allophenylserine Hydrochlorides.—Anhydrous I or II (1.812 g., 0.0100 mole), suspended in 18 ml. of anhydrous dioxane, was treated with a brisk stream of dry hydrogen chloride for 15 minutes. The clear solutions were diluted with equal volumes of dioxane, and ether was added until cloudiness developed. After refrigerating, 1.918 g. of I hydrochloride and 2.030 g. of II hydrochloride were collected. The hydrochlorides were poorly soluble in fresh boiling dioxane. For analysis, each was recrystallized from methanol–ether. Further recrystallization from ether–acetic acid did not change decomposition points (Table IV). Each compound had the form of blunt needles or blades.

Phenylserine (I) and Allophenylserine (II) Ester Hydrochlorides.—Dry hydrogen chloride was vigorously introduced into a suspension of 3.624 g. (0.0200 mole) of anhydrous I or II in the appropriate alcohol (36 ml.) under reflux. After the amino acid had dissolved (usually in five minutes, 45 minutes with II in *n*-propyl alcohol, 150 minutes and also 24 ml. more solvent with II in *i*-propyl alcohol), this treatment was continued for 2.5–3 hours. The clear solutions of the methyl, ethyl and *n*-propyl derivatives of I were concentrated almost to dryness, the residual oil or paste was taken up in a small volume of hot parent alcohol, and ether was added to the point of incipient crystallization. The other ester hydrochlorides listed in Table V, which precipitated during hydrogen chloride treatment, were just redissolved by addition of hot parent alcohol. The products were filtered after overnight refrigeration, washed with ether and dried at 50°. Small second crops were worked up from the filtrates. The ester hydrochlorides of each series formed as hexagonal or diamond plates.

Phenylserine (I) and Allophenylserine (II) Esters.—Each ester hydrochloride (0.0100 mole) noted in the preceding section was converted to the corresponding ester by suspension in ether and treatment with ammonia gas.[3] Data concerning the products are collected in Table VI.

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