and then with water followed by saturated brine and dried over anhydrous sodium sulfate. The residue obtained on removal of the solvent at reduced pressure amounted to 0.021 g of yellow oily material, $\lambda_{max}^{CHCl_3}$ 5.77 μ (ketone C=O). This material was chromatographed on 7.5 g of basic alumina. The major fraction, eluted with 20% ether in petroleum ether, amounted to 0.013 g of an oil which was evaporatively distilled at 155–160° (10^{-5} mm) to afford 0.012 g of a colorless oil which crystallized on standing. This material was rinsed with a few drops of ether–petroleum ether to give a sample, mp 65–68°, $[\alpha]D$ +342° (*c* 0.075, MeOH). This material was recrystallized from the same solvent pair to give 0.004 g (17% yield) of colorless prisms: mp 71.8–74°; $\lambda_{max}^{CHCl_3}$ 5.79 μ (C=O); λ_{max}^{EtOH} 286 mμ (shoulder, ϵ 2000) and 278 (2280). Vapor phase chromatographic analysis at 255° and coinjection studies demonstrated the presence of a single component which differed from the hitherto known isomers of estrone methyl ether.

Anal. Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.1; H, 8.5.

A similar preparation of 8α,9β-isoestrone methyl ether, in which potassium *t*-butoxide was employed for the Dieckmann cyclization, gave a sample, mp 62–64°. The mass spectrum of this substance is reproduced in Figure 2. Recrystallization of this material from ether–petroleum ether afforded a sample melting at 73.5–74°. The infrared spectrum of this specimen is reproduced in Figure 1.

Registry No.—I, 15983-67-2; IV (R = CH_3), 15983-68-3.

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3-Aryl-2-methylserines. I. A New Synthesis

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The controlled addition of an aryl Grignard reagent to a 4-carboalkoxy-2,4-dimethyloxazol-5-one **6** provides alkyl 2-acetamido-2-aroylpropionates **7** which can be reduced to give derivatives of the title class of compounds. The dominant reduction product is the *erythro* isomer. The synthesis of both isomers of 3-(3,4-dihydroxyphenyl)-2-methylserine is reported.

While β-arylserines have been much studied, in particular over the past 20 years,[1] the corresponding α-methyl derivatives have received scant attention. In 1959, the Japanese workers Kameda and Kimura[2] described the synthesis of two isomeric α-methyl-β-(*p*-nitrophenyl)serines by Bergmann's[3] modification of the Erlenmeyer reaction. The stereochemistry of the isomers was not defined. More recently, Tristram and coworkers[4] have accomplished a stereoselective synthesis of two of the optically active isomers of 3-(3-hydroxyphenyl)-2-methylserine. They were able to assign the absolute stereochemistry to each by virtue of having started with an optically active acyloin of known absolute configuration. Tristram's serines have since been inverted[5] at the 3 position to provide the other two enantiomers.

In this paper, we report a new synthesis which we believe is more generally suited for the preparation of various substituted 3-aryl-2-methylserines. This route is shown schematically in Scheme I. The requisite azlactone **6** can be synthesized from readily attainable starting materials.

Condensation of phenylmagnesium bromide with **6a** at −70° provided the α-acylamino-β-keto ester **7a** in over-all yields above 30%. Others[6,7] have reported reactions of organometallics with oxazolones. Excess reagent was invariably used, however, and a carbinol was usually isolated. Our procedure appears to be the first example of a selective Grignard addition to an oxazolone **6** to provide α-acylamino-β-keto esters.

Reduction of **7a** with buffered sodium borohydride produced two isomeric alcohols, **8a** and **9a**, in a ratio of *ca.* 2–3:1. The major product was assigned the *erythro*[8] configuration on the basis of Cram's rule[9] and other more demonstrable evidence presented later.[10]

A variety of other reductions (diborane, disiamylborane, diisopropylaluminum chloride–isopropyl alcohol, calcium borohydride, and catalytic methods) were examined in order to achieve a higher proportion of **9a**. Only in the case of calcium borohydride was a significant change noted; an approximate 1:1 ratio prevailed, albeit with some sacrifice in the over-all yield.[11]

Hydrolysis of both **8a** and **9a** with hydrochloric acid provided two different amino acids, **10a** and **11a**, respectively. The former, *erythro*, possessed the lower decomposition point and exhibited a strong band in

(1) For a leading reference, see J. P. Greenstein and M. Winitz, "Chemistry of the Amino Acids," John Wiley and Sons, Inc., New York, N. Y., 1961, Chapter 49.

(2) Y. Kameda and Y. Kimura, *Kanazawa Daigaku Yakugakubu Kenkyu Nempo*, **9**, 23 (1959); *Chem. Abstr.*, **54**, 3237 (1960).

(3) E. D. Bergmann, H. Bendas, and W. Taub, *J. Chem. Soc.*, 2673 (1951).

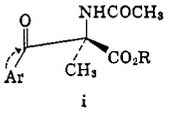
(4) E. W. Tristram, B. F. Powell, D. E. Williams, R. J. Tull, and J. M. Chemerda, presented at the meeting of the New York–New Jersey Section of the American Chemical Society, Jan 1962.

(5) S. H. Pines, S. Karady, M. A. Kozlowski, and M. Sletzinger, *J. Org. Chem.*, **33**, 1762 (1968).

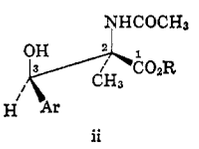
(6) J. W. Cornforth, "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, pp 738, 792.

(7) W. I. Awad and M. S. Hafez, *J. Org. Chem.*, **25**, 1180 (1960).

(8) For the sake of clarity, we are defining the *erythro* isomers of this system as those in which the disposition of the heteroatoms and "aliphatic" (CH_3 and C_3–H) portions are similar (ii).



i



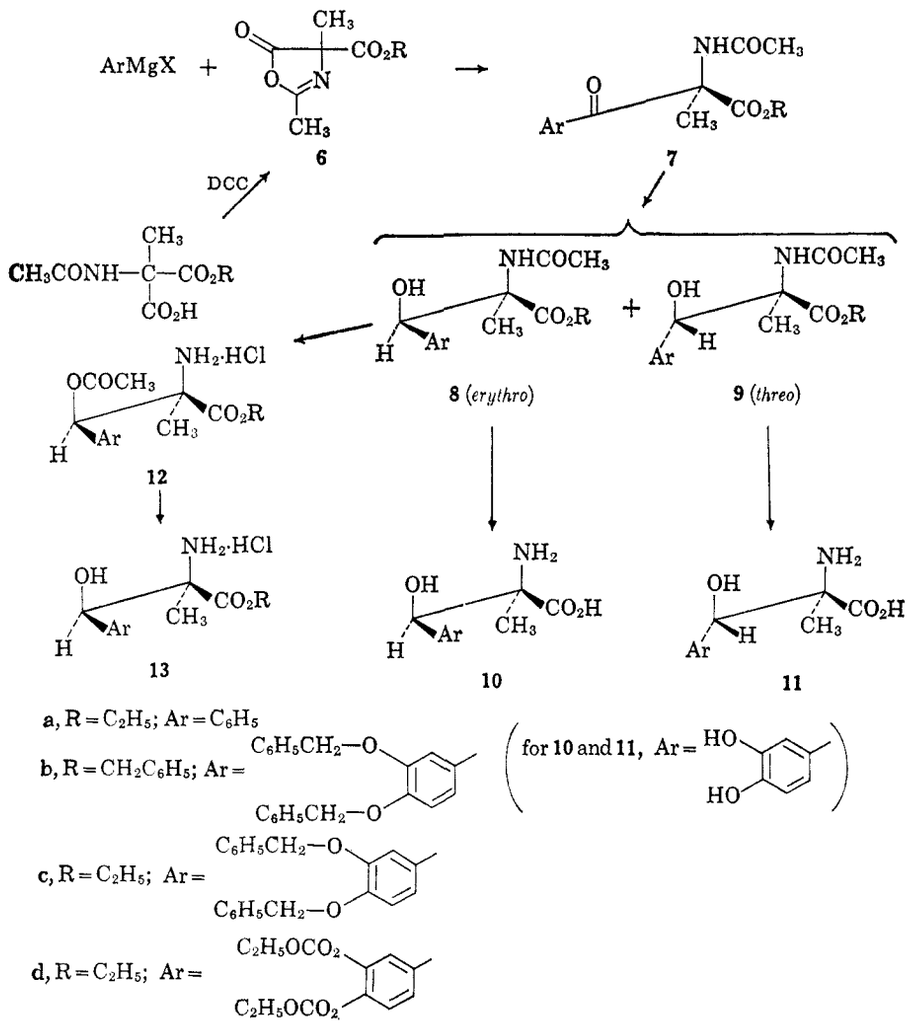
ii

(9) D. J. Cram and F. A. A. Elhafez, *J. Amer. Chem. Soc.*, **74**, 5828 (1952); D. J. Cram and K. R. Kopecky, *ibid.*, **81**, 2748 (1959).

(10) For characterization *via* nmr spectroscopy, see ref 5.

(11) Benzaldehyde was noted as a by-product in this reduction. It could have been produced by retroaldolization of the *erythro* product.

SCHEME I



the infrared region at 835 cm^{-1}.[12] The two acids were not separated by thin layer chromatography but could be clearly distinguished by ion-exchange chromatography (Spinco),[13] the *threo* isomer being eluted first with pH 2.75 buffer.

The synthesis of 3-(3,4-dihydroxyphenyl)-2-methylserine (**10b** and **11b**), in reality the primary goal of this undertaking, was attempted along the same lines as those described above for the parent compound. A Grignard reaction of 3,4-dibenzyloxyphenylmagnesium bromide with **6a** provided **7c** in 39% yield. Borohydride reduction proceeded normally to give the amido alcohols **8c** and **9c** in the expected manner. However, we were unable to accomplish the desired hydrolysis (represented in Scheme I by **8** → **10**, **9** → **11**) by means of hydrochloric acid.[14]

Carboethoxyl protective groups[14,15] were tried and found wanting. Reaction of **8d** with ethanolic hydrogen chloride gave the product of N → O acyl migration, **12d**, which could be transformed to **13d** under more vigorous conditions. Acid hydrolysis of either **8d** or **13d** led to unidentifiable mixtures. Mild treatment of **13d** with stoichiometric quantities of dilute alkali gave only *ca.* 5% of the desired **10b**. The major product found was 3,4-dihydroxybenzaldehyde. Similar mild base hydrolysis of **13c** gave 3,4-dibenzyloxybenzaldehyde. Similar mild base hydrolysis of **13c** gave 3,4-dibenzyloxybenzaldehyde. Carbonate saponification of N-chloroacetyl-2-methyl-3-(*p*-nitrophenyl)serine methyl ester has also given the retroaldolization product.[2]

The final ester hydrolysis was eliminated as a problem by repeating the synthesis using the azlactone benzyl ester **6b** for the Grignard reaction. During the two-stage deacylation, we were able to show the intermediacy of an O-acetate, **12b**, by reconversion back to **8b** with sodium bicarbonate. Hydrogenolysis removed the three benzyl groups, and the free amino acids **10b** and **11b** were obtained in crystalline form. The *erythro* isomer again possessed the lower melting point; the *threo* isomer was the more mobile in ion-exchange chromatography.

(12) W. A. Bolhofer [*J. Amer. Chem. Soc.*, **76**, 1322 (1954)] has published spectra of diastereomeric pairs of β-substituted serines and shown empirically that this band is characteristic of *erythro* isomers. This distinction does not hold for all α-methylserines. See also J. P. Greenstein and M. Winitz, "Chemistry of the Amino Acids," Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1961, p 2599.

(13) Spinco amino acid analyzer, Beckman Instruments, Inc., Palo Alto, Calif.

(14) W. A. Bolhofer [*J. Amer. Chem. Soc.*, **75**, 4469 (1953)] was unable to hydrolyze *erythro*-N-acetyl-3-(*p*-hydroxyphenyl)serine methyl ester under similar conditions.

(15) K. W. Rosenmund and H. Dornsaft, *Ber.*, **52**, 1734 (1919).

Experimental Section[16]

o-Dibenzyloxybenzene.—To a solution of 55 g (0.5 mol) of pyrocatechol in 750 ml of acetone under a nitrogen atmosphere was added 172.5 g (1.25 mol) of anhydrous potassium carbonate and 158 g (1.25 mol) of benzyl chloride. The slurry was stirred under reflux for 4 days. After cooling, the solids were removed by filtration, and the filtrate and acetone washes concentrated. The residue was partitioned between benzene and 1 *N* sodium hydroxide and the organic layer further washed with saturated sodium chloride solution. The dried benzene layer was concentrated and the residue crystallized from 200 ml of petroleum ether (bp 30–60°). There was obtained 119 g (82%), mp 60.5–61.5° (lit.[17] mp 61.5°), of the desired ether.

3,4-Dibenzyloxybromobenzene.—The procedure was adapted from the preparation of 4-bromoveratrole.[18] A solution of 103 g (0.355 mol) of *o*-dibenzyloxybenzene and 69.4 g (0.39 mol) of N-bromosuccinimide was refluxed in 350 ml of carbon tetrachloride. The reaction initiated after a few moments and boiled vigorously for 5–10 min without heating. After the reaction subsided, the reflux period was continued for 1 hr with application of heat. The solution was cooled and washed with two 150-ml portions of water, 150 ml of 1 *N* sodium hydroxide, and then water. The carbon tetrachloride solution was evaporated and the residue crystallized from 200 ml of methanol. The slurry was stirred 2 hr at 0–5°, filtered, and washed with cold methanol. There was obtained 71.6 g of product, approximately 95% pure by bromine analysis, mp 59–64°. This represented a 52% yield, corrected for purity. Thin layer chromatography (C) showed the product to be slightly contaminated with starting material. An analytical sample was obtained by preparative chromatography in the same system, mp 65.5–66.5° from methanol.

Anal. Calcd for $C_{20}H_{17}BrO_2$: C, 65.05; H, 4.64. Found: C, 65.21; H, 4.4.

Benzyl Acetamidomethylmalonate (4).—Ethyl acetamidomethylmalonate[19] (**1**, 231 g, 1 mol) was slurried in 1.2 l. of ice and water and to it was added 2.03 equiv of 4 *N* KOH solution. After 4 hr, the solvent was removed by lyophilization. The crude salt **3** (265.4 g) was ground to a reasonably fine powder and stirred in 1 l. of dimethylformamide and 100 ml of *t*-butyl alcohol with 392 g (2.3 mol) of benzyl bromide at 60° overnight. The suspended potassium bromide was removed by filtration and washed with benzene (which was held for the extractions). The original filtrate was concentrated under high vacuum to an oil. This oil, dissolved in the benzene above, was washed with water and sodium bicarbonate, dried, and again concentrated to a residue which crystallized from a mixture of hexane–ether (500:150). The crystals were filtered, washed with hexane, and dried, yield 271 g, mp 71–73°. Recrystallization from ether–hexane provided an analytical sample, mp 73.5–75°.

Anal. Calcd for $C_{20}H_{21}NO_5$: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.75; H, 5.92; N, 3.69.

A crystalline modification melting at 89–90° could be obtained from ether.

Benzyl Hydrogen Acetamidomethylmalonate (5).—The above diester was converted into the half-ester **5** by the method reported for the diethyl ester.[19] The yield was 61%, mp 143.5–144° (with gas evolution, from ethanol–water).

Anal. Calcd for $C_{13}H_{15}NO_5$: C, 58.86; H, 5.70; N, 5.28. Found: C, 58.80; H, 5.87; N, 5.37.

Azlactonization of Half-Ester 4-Carboethoxy-2,4-dimethyloxazol-5-one (6a).—Ethyl hydrogen acetamidomethylmalonate (100 g, 0.494 mol) was dissolved by warming to *ca.* 50° in 1400 ml of peroxide-free, dry dioxane. The solution was rapidly cooled to 30° and 102 g (0.494 mol) of dicyclohexylcarbodiimide in 100 ml of the same solvent was added over a 15-min period with stirring and external cooling to maintain a 25–30° temperature range. After 2 hr, the precipitated urea was removed by filtration. The filtrate was distilled *in vacuo*. The product boiled at 72–75° (0.25 mm), providing 80.5 g (88%), $n^{25}D$ 1.4365, a center cut of which was used for analysis.

Anal. Calcd for $C_8H_{11}NO_4$: C, 51.88; H, 5.99; N, 7.56. Found: C, 51.85; H, 5.85; N, 7.66.

The identical procedure was used with benzyl (half-) ester, providing 4-carbobenzyloxy-2,4-dimethyloxazol-5-one (**6b**), bp 133–135° (0.2 mm).

Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.67. Found: C, 63.71; H, 5.34; N, 5.83.

Ethyl 2-Acetamido-2-benzoylpropionate (7a).—A well-stirred solution of azlactone **6a** (6 g, 0.032 mol) in 100 ml of ether was cooled in a Dry Ice–acetone bath and to it was added over a period of 1.5 hr a solution of phenylmagnesium bromide (0.03 mol) in 20 ml of ether. The mixture was allowed to warm to room temperature and was decomposed by addition of 30 ml of 3 *N* hydrochloric acid. The ether layer was washed with water, 10% sodium carbonate, then water again. After removal of the solvent, the residue crystallized from ether–hexane to yield 2.6 g (28%) of **7a** as colorless crystals. Chromatography of the mother liquor provided additional product. The material was a single spot on tlc (R_f 0.5, A.). An analytical sample was prepared by recrystallization from ether: mp 80–81°; λ_{max}^{EtOH} 245 and shoulder at 275 mμ (ε 10,800 and 900, respectively); $\nu_{max}^{CCl_4}$ 3600, 1760, 1740, 1700, and 1690 cm^{-1}.

Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.86; H, 6.51; N, 5.32. Found: C, 63.76; H, 6.26; N, 5.29.

Benzyl 2-Acetamido-2-(3,4-dibenzyloxybenzoyl)propionate (7b).—The Grignard reagent was prepared by refluxing 76 g (0.206 mol) of 3,4-dibenzyloxybromobenzene in 200 ml of tetrahydrofuran with 5.35 g (0.22 g-atom) of magnesium turnings. After *ca.* 3 hr most of the magnesium was dissolved and tlc (C) showed the virtual absence of starting material.

The Grignard reagent was added over a 2-hr period to a solution of 58 g (0.235 mol) of 4-carbobenzyloxy-2,4-dimethyloxazol-5-one **6b** in 900 ml of anhydrous ether at −70° in a Dry Ice–acetone bath. The mixture was allowed to come to room temperature as the coolant evaporated overnight. The reaction was quenched by pouring it into 500 ml of ice and water containing 30 ml of acetic acid. The organic layer was combined with an ethyl acetate (150 ml) extract of the aqueous phase and washed with 500 ml of saturated sodium bicarbonate and 100 ml of salt solution. After drying, the solvent was removed and the residue crystallized from 250 ml of ether over a weekend.[20] There was obtained 39.5 g (36%) of the keto ester, mp 106–108°. An analytical sample was prepared by recrystallization from ethanol: mp 110.5–111.5°; λ_{max}^{EtOH} 234, 283, 308 mμ (ε 16,100, 20,200, and 28,200, respectively).

Anal. Calcd for $C_{33}H_{31}NO_6$: C, 73.72; H, 5.81; N, 2.61. Found: C, 73.80; H, 5.75; N, 2.66.

The ethyl ester (**7c**) was made in an identical fashion from the azlactone **6a**: 39% yield, mp 114–118° (ethanol).

Anal. Calcd for $C_{28}H_{29}NO_6$: C, 70.72; H, 6.15; N, 2.95. Found: C, 70.90; H, 6.00; N, 3.21.

Differential thermal analysis showed a melting point endotherm at 123° with gas evolution.

N-Acetyl-2-methyl-3-phenylserine Ethyl Ester. Buffered Sodium Borohydride.—A solution of 7.9 g (0.03 mol) of keto ester **7a** in 100 ml of dioxane was stirred while bubbling carbon dioxide through it. To it was added over a 5-min period 25 ml of 10% aqueous sodium borohydride. After 30 min, the reaction was acidified with dilute hydrochloric acid and the product extracted with ether. The washed extracts were evaporated to provide 7.8 g of an oil, which showed (tlc, A) two major products. Separation was achieved by dry column chromatography on 150 g of silica gel H, system A. The *erythro* isomer, **8a** was eluted first to give 4.9 g of crude alcohol which, after crystallization from ether, yielded 4.2 g of colorless crystals. Recrystallization from isopropyl ether provided an analytical sample, mp 129–130°.

(16) Melting and boiling points are uncorrected. Elemental analyses were performed by Mr. R. N. Boos and his associates of these laboratories. Ir spectra were obtained, in the main, with a Perkin-Elmer Infracord and are not routinely described; nmr spectra were obtained by Messrs. B. Singleton and R. Zerfing with a Varian A-60A. Unless otherwise stated, it may be assumed that all organic solutions were freed from water by drying over sodium sulfate; solvent was removed by vacuum evaporation in a rotating evaporator. Thin layer chromatography was carried out with silica gel G plates (Analtech Laboratories, 250 μ), used as received. The solvent systems were as follows (v/v): A, chloroform–acetone (15:1); B, chloroform–acetone (85:15); C, benzene–hexane (35:15); D, *n*-butyl alcohol–acetic acid–water (65:10:25). Developed plates were visualized by exposure to iodine vapor, charring after 10% sulfuric acid spray, or by spraying with a solution of potassium permanganate in concentrated sulfuric acid.

(17) H. Burton, P. F. G. Praill, *J. Chem. Soc.*, 523 (1951).

(18) R. A. B. Bannard and G. Latremouille, *Can. J. Chem.*, **31**, 469 (1953).

(19) See ref 6, p 840.

(20) The crystallization is slow. Some preparations unaccountably failed to crystallize, and we were forced to resort to chromatography (A). These runs gave lower yields, *ca.* 25%.

Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.42; H, 7.14; N, 5.24.

The *threo* isomer, **9a**, 2 g, was obtained by continued elution. The analytical sample (isopropyl ether) showed mp 128–129°.

Anal. Found: C, 63.27; H, 7.36; N, 5.28.

Reduction with Calcium Borohydride.—The reagent was prepared and used according to the general procedure of Kollonitsch *et al.*[21]

An ethanolic solution of calcium borohydride (6.6 mmol in 17 ml) was mixed at −30° with a solution of 1.73 g (1.6 mmol) of **7a** in 5 ml of ethanol. After 30 min at −30°, the reaction was decomposed with dilute hydrochloric acid. Most of the ethanol was removed by concentration and the residue extracted with methylene chloride. The washed and dried extracts provided 1.4 g of an oil smelling of benzaldehyde, containing approximately equal parts of *erythro* and *threo* alcohols, as estimated by tlc and nmr spectroscopy. Chromatography, as before, yielded 425 mg of pure **8a** and 510 mg of pure **9a**.

N-Acetyl-3-(3,4-dibenzyloxyphenyl)-2-methylserine Benzyl Ester.—The reduction of **7b** was performed in tetrahydrofuran at ice-bath temperature by means of the buffered sodium borohydride method above. The isomer ratio (after identical chromatography) was even higher, approximately 6:1, *erythro*/*threo*.

The *erythro* isomer, **8b**, more mobile, was crystallized from ethyl acetate–hexane. It showed mp 117.5–118.5°.

Anal. Calcd for $C_{33}H_{33}NO_6$: C, 73.45; H, 6.16; N, 2.6. Found: C, 73.43; H, 6.13; N, 2.81.

From later fractions was obtained the minor, *threo* isomer **9b** which was also crystallized from ethyl acetate–hexane, mp 109–110.5°. An analytical sample was prepared by recrystallization from ethanol, mp 108–110°.

Anal. Found: C, 73.47; H, 6.28; N, 2.57.

2-Methyl-3-phenylserine. *erythro* Isomer 10a.—A solution of 1.25 g of **8a** in 50 ml of methanol was cooled in ice and saturated with dry hydrogen chloride. The solution was refluxed 1 hr and evaporated and the residue taken up in 50 ml of 6 *N* hydrochloric acid and refluxed under an atmosphere of nitrogen overnight. Again, the solvent was removed, and the residue taken up in 10 ml of acetone. The free amino acid was precipitated with stirring upon addition of an excess of propylene oxide. Recrystallization from water provided pure **10a**, 600 mg, 65%. The analytical sample was recrystallized from methanol–water and showed mp 208–210° dec, single spot on tlc (D), single peak on Spinco analysis.[13]

Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.52; H, 6.71; N, 7.18. Found: C, 61.53; H, 6.51; N, 7.17.

The *threo* isomer **11a** was obtained in the same fashion from **9a**. Recrystallization was effected from ethanol–water, mp 253° dec. Differential thermal analysis showed an endotherm at 122°, indicating bound solvent. After a sample was dried at 122° under vacuum, it showed mp 249° dec and gave a satisfactory analysis.

Anal. Found: C, 61.32; H, 6.77; N, 7.37.

(21) J. Kollonitsch, O. Fuchs, and V. Gabor, *Nature*, **173**, 125 (1954).

The two isomers were indistinguishable by tlc (D), but were clearly separated *via* Spinco analysis, the *threo* isomer being eluted first.

***erythro*-3-(3,4-Dihydroxyphenyl)-2-methylserine (10b).**—The corresponding amido ester (**8b**, 10 g, 0.0186 mol) was stirred in 240 ml of ethanol, cooled, and purged with nitrogen. While an inert atmosphere was maintained, 60 ml of 10 *N* ethanolic hydrogen chloride was added. The solids dissolved over the period of 1 hr and the reaction was allowed to stand 2 days at room temperature. The infrared region of a portion of the residue (in chloroform) showed the virtual absence of the amide band (1660 cm^{-1}). The solvent and excess hydrogen chloride were removed *in vacuo*; the residue was refluxed overnight in 200 ml of 0.1 *N* ethanolic hydrogen chloride. The ir region was not greatly changed in the carbonyl region; the last traces of amide had been removed. The solvent-free residue was hydrogenated in 200 ml of ethanol over 0.5 g of 5% Pd on carbon at 2–3 atm. Uptake ceased after the absorption of 94% of the theoretical amount of hydrogen. The catalyst was removed, the solvent again evaporated, and the residue dissolved in acetone (60 ml). Propylene oxide, 2.5 ml, was added under an inert atmosphere and the crude product allowed to crystallize at ice temperature. There was obtained 4.3 g of material which still showed some ester absorption (ir 1750 cm^{-1}).

Recrystallization from 7.5 ml of water and 12.5 ml of ethanol gave 2.4 g of single-spot material (tlc, D) which clung tenaciously to 1 mol of ethanol (nmr). Recrystallization from water gave, after drying over phosphorus pentoxide in a vacuum desiccator, the monohydrate, mp 162–163° dec.

Anal. Calcd for $C_{10}H_{15}NO_6$: C, 48.97; H, 6.17; N, 5.71. Found: C, 49.18; H, 5.95; N, 5.75.

Attempts to obtain a satisfactory analysis (calcd: C, 52.86; H, 5.77) after drying the ethanol solvate were not quite so rewarding. After drying at 65° (0.05 mm), we found C, 51.30, 51.22; H, 5.94, 6.13. At 75°, some decomposition was already evident on two different samples: C, 53.91, 53.42; H, 6.19, 5.86.

***threo*-3-(3,4-Dihydroxyphenyl)-2-methylserine (11b).**—The identical reaction scheme was used on the *threo*-amido ester (**9b**) to give, after the water–ethanol crystallization, the unsolvated title compound, mp 197–198° dec.

Anal. Calcd for $C_{10}H_{13}NO_5$: C, 52.86; H, 5.77; N, 6.17. Found: C, 53.05; H, 5.85; N, 6.12.

The **monohydrate**, obtained from water recrystallization, showed mp 172–173° dec.

Anal. Calcd for $C_{10}H_{15}NO_6$: C, 48.97; H, 6.17; N, 5.71. Found: C, 48.78; H, 6.25; N, 5.64.

Registry No.—3,4-Dibenzyloxybromobenzene, 16047-57-7; **4**, 16047-70-4; **5**, 16047-58-8; **6a**, 16047-59-9; **6b**, 16047-60-2; **7a**, 16047-61-3; **7b**, 16047-62-4; **7c**, 16047-63-5; **8a**, 16047-64-6; **8b**, 16047-65-7; **9a**, 16047-66-8; **9b**, 16047-67-9; **10a**, 16047-68-0; **10b**, 16047-71-5; **11a**, 16047-69-1; **11b**, 16047-72-6.