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Stereochemical Studies. XVIII.[1] Nitrous Acid Deaminations of *threo*- and *erythro*-Phenylserine and Their Methyl Esters in Acetic Acid[2]

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Nitrous acid deaminations of *threo*-(Ia) and *erythro*-phenylserine methyl ester (Ib) gave methyl benzoylacetate (II) and methyl phenylmalonaldehydate (IX) by hydrogen migration and phenyl migration, respectively. Further reaction of IX afforded methyl α-hydroximinophenylacetates (IIIa—b) and N-nitrosooxazolidines (VIa—g).

Deaminations of *threo*-(XIIIa) and *erythro*-phenylserine (XIIIb) were, however, highly specific and gave the corresponding α-acetoxy acid as the sole product with retention of configuration.

The reaction paths involved in this study were discussed.

Previous reports[4,5] from this laboratory showed that nitrous acid deamination of α-amino acid esters, *i.e.* L-phenylalanine ethyl ester and L-valine benzyl ester, in acetic acid gave various migration and elimination products as well as a substitution product (α-acetoxy ester) with net inversion in configuration. The reaction of the corresponding α-amino acid in acetic acid gave a substitution product (α-acetoxy acid) as the sole product, which retained its configuration owing to the participation of the neighbouring carboxylate group.[5-7]

The present paper is concerned with nitrous acid deaminations of diastereomeric phenylserines and their methyl esters in acetic acid for the investigation of the effects of neighbouring carboxylic acid or ester and hydroxyl groups on the reaction.

Deamination of *threo*-phenylserine methyl ester (Ia) was carried out with sodium nitrite in glacial acetic acid, then the mixture of deamination products was chromatographed in benzene–CH_2Cl_2 (1:1) on silica gel to give ten compounds (II, IIIa—b, IV, Va, VIa—d, and VII) as shown in Table I.

IIIa and IIIb are *syn*- and *anti*-isomers of methyl α-hydroximinophenylacetate. VIa—d are four diastereoisomers of the N-nitrosooxazolidine derivative with two additional asymmetric carbon formed during cyclization, but their stereochemistries were not examined. Methyl β-phenylglycerate (X) and its acetate (XI), a possible product of intermolecular substitution, and methyl β-phenylglycidate (XII), a possible epoxide by intramolecular substitution, were absent from the deamination products.

Products are assumed to be formed both by hydrogen migration and phenyl migration as shown in Fig. 1. Thus, a hydride shift of I′ with a subsequent splitting off of a proton will give methyl benzoylacetate (II). The possibility of the formation of II due to isomerization of methyl β-phenylglycidate (XII) was excluded experimentally by treating the syn-

1) Part XVII: M. Kobayashi, K. Koga, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **20**, 1898 (1972).
2) Part of this work was presented at the 89th Annual Meeting of the Pharmaceutical Society of Japan at Nagoya, April, 1969.
3) Location: *Hongo, Bunkyo-ku, Tokyo.*
4) S. Yamada, T. Kitagawa, and K. Achiwa, *Tetrahedron Letters*, **1967**, 3007.
5) S. Yamada, M. Taniguchi, and K. Koga, *Tetrahedron Letters*, **1969**, 25.
6) P. Brewster, *Nature*, **166**, 179 (1950).
7) We reported, however, that nitrous acid deaminations of L-phenylalanine and *p*-methoxy-L-phenylalanine in trifluoroacetic acid mainly afforded phenyl migration products (K. Koga, C.C. Wu, and S. Yamada, *Tetrahedron Letters*, **1971**, 2287).

TABLE I

Ia			Ib		
No.	Structures	Yields (%)	No.	Structures	Yields (%)
II	C_6H_5-CO-CH_2-$COOCH_3$	23%	II	C_6H_5-CO-CH_2-$COOCH_3$	18%
IIIa—b	C_6H_5-C(=N(OH))-$COOCH_3$	9%	IIIa—b	C_6H_5-C(=N(OH))-$COOCH_3$	9%
IV	C_6H_5-C(=O)-$COOCH_3$	<2%	IV	C_6H_5-C(=O)-$COOCH_3$	<2%
Va	C_6H_5-C(=CH-NH-CH(C_6H_5)-CH(OH)-$COOCH_3$)-$COOCH_3$	5%	Vb	C_6H_5-C(=CH-NH-CH(C_6H_5)-CH(OH)-$COOCH_3$)-$COOCH_3$	<2%
VIa—d	C_6H_5-CH(-CH(-O-N-NO-)-C_6H_5)-$COOCH_3$	35%	VIe—g	C_6H_5-CH(-CH(-O-N-NO-)-C_6H_5)-$COOCH_3$	35%
VII	C_6H_5-CH(OH)-CH(NH-CHO)-$COOCH_3$	3%	VIII	C_6H_5CHO	<2%

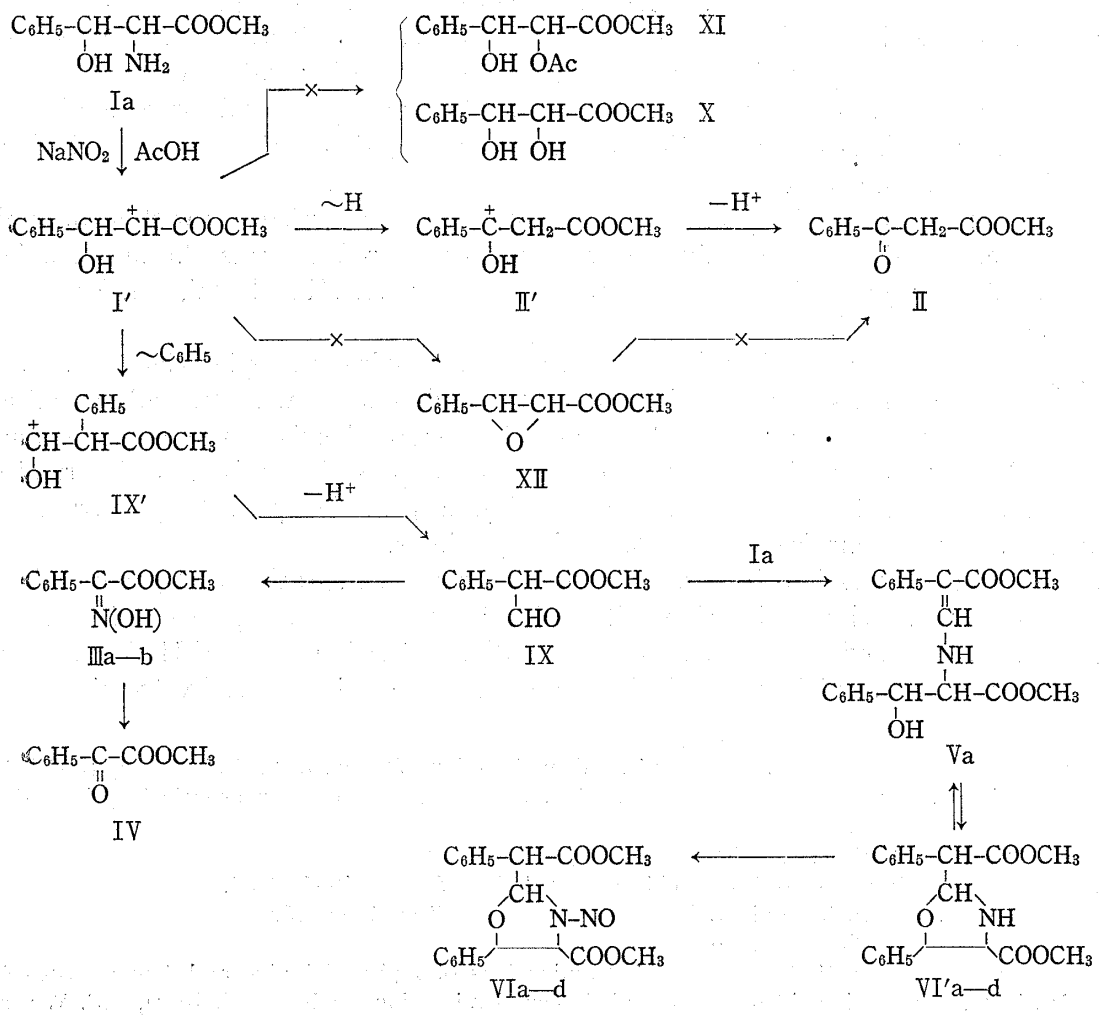

Fig. 1

thesized XII with sodium nitrite in acetic acid. The path to VIa—d may involve the formation of methyl phenylmalonaldehydate (IX) by phenyl migration, the condensation of which with unreacted Ia gives an equilibrium mixture of oxazolidines (VI'a—d) and enamine (Va). Evidence for this route was obtained by treating the enamine (Va), prepared by the condensation of IX and Ia, with sodium nitrite in acetic acid to give products identical with VIa—d. IIIa and IIIb should also be formed by the nitrosation of IX followed by elimination of a formyl group (Fig. 2). Their hydrolysis gives a small amount of methyl phenylglyoxylate (IV). N-Formyl-*threo*-phenylserine methyl ester (VII) is thought to be formed by the action of formic acid or its mixed anhydride with acetic acid, which are liberated in the formation of IIIa—b from IX (Fig. 2), on Ia.

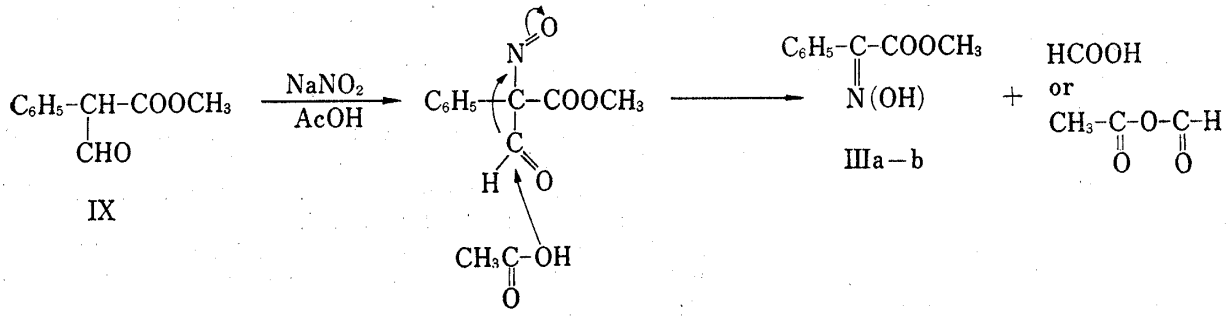

Fig. 2

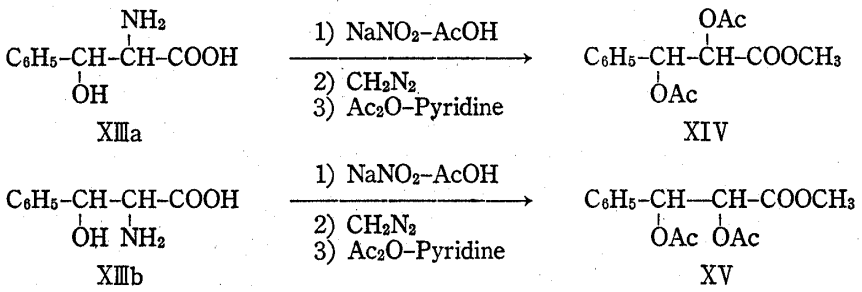

Fig. 3

Similarly, nine products (II, IIIa—b, IV, Vb, VIe—g, and VIII) were present in the deamination products of *erythro*-phenylserine methyl ester as shown in Table I.

On the other hand, nitrous acid deaminations of *threo*- and *erythro*-phenylserine were highly specific (Fig. 3). Thus, as reported previously,[8] nitrous acid deamination of *threo*-phenylserine (XIIIa) in acetic acid afforded the corresponding substitution product only, which was characterized as methyl *threo*-β-phenylglycerate diacetate (XIV). The deamination of *erythro*-phenylserine (XIIIb) in acetic acid followed by esterification and acetylation also afforded methyl *erythro*-β-phenylglycerate diacetate (XV) as the sole product.

In many nitrous acid deaminations of β-amino alcohols, products have been reported to be analogous to those of pinacol rearrangement.[9] It has been shown that this general rule is applicable in the present deaminations of *threo*- and *erythro*-phenylserine methyl ester. However, the results of deaminations of *threo*- and *erythro*-phenylserine clearly indicate that the carboxylate group exhibits a strong neighbouring effect, a "configuration holding effect,"[6] even in β-hydroxy-α-amino acids.

8) D. Billet, *Compt. Rend.*, **230**, 1074 (1950).
9) H. Zollinger, "Azo and Diazo Chemistry," Interscience Publ., New York, 1961, p. 101.

Experimental[10]

Starting Materials——*threo*-(XIIIa) and *erythro*-Phenylserine (XIIIb) and their methyl esters (Ia and Ib) were prepared by the published procedure.[11]

Deamination of *threo*-Phenylserine Methyl Ester (Ia)——Sodium nitrite (6.2 g, 0.090 mole) was added to a solution of Ia (17.0 g, 0.087 mole) in acetic acid (350 ml) over a 5 hr period with stirring at 20—23°, then the resulting solution was allowed to stand at room temperatures overnight. After *in vacuo* evaporation of the solvent to dryness, the residue was treated with 40 ml of water, then the whole was extracted with three 100 ml portions of benzene. Organic layers were combined, washed successively with 10% *aq.* Na_2CO_3, 10% aq. HCl, and sat. aq. NaCl, then dried over anhyd. Na_2SO_4. The solvent was removed under reduced pressure to give 16.0 g of a mixture of products, which showed the presence of at least nine components on thin-layer chromatography (TLC) (silica gel, benzene–CH_2Cl_2 (1:1)). A mixture of products was chromatographed on silica gel (600 g), and was eluted successively with benzene–CH_2Cl_2 (2:1), CH_2Cl_2, and finally 5% methanol in CH_2Cl_2 to give ten compounds (II, IIIa—b, IV, Va, VIa—d, and VII) as follows.

i) Methyl Phenylglyoxylate (IV) (*Rf* 0.66): This compound was eluted first and was shown, by its IR and NMR spectra, to be identical with the authentic sample described below. 2,4-Dinitrophenylhydrazone: mp 171—173° (lit.[12] mp 173°).

ii) Methyl 2-(α-methoxycarbonylbenzyl)-3-nitroso-5-phenyloxazolizine-4-carboxylate (VIa) (*Rf* 0.53): This compound was obtained as a mixture with methyl benzoylacetate (II), and was purified by recrystallization from MeOH to give colorless plates of mp 126—126.5°. IR ν_{max}^{KBr} cm^{-1}: 1740 (ester). NMR (τ, $CDCl_3$): 2.65 (10H, m, aromatic protons), 3.10 and 5.52 (2H, AB q, methine proton on C-2 and C_6H_5-C<u>H</u>-$COOCH_3$), 4.47 and 5.45 (2H, AB q, methine protons on C-4 and C-5), 6.20 and 6.25 (6H, s, -$COOC\underline{H}_3$). *Anal.* Calcd. for $C_{20}H_{20}O_6N_2$: C, 62.49; H, 5.24; N, 7.29. Found: C, 62.72; H, 5.23; N, 7.45.

iii) Methyl Benzoylacetate (II) (*Rf* 0.50): This compound was obtained as a liquid, and was identified with an authentic prepared sample.[13] 2,4-Dinitrophenylhydrazone: mp 166—169°. (lit.[14] mp 169—170°). *Anal.* Calcd. for $C_{16}H_{14}O_6N_4$: N, 15.64. Found: N, 15.87.

iv) Methyl 2-(α-Methoxycarbonylbenzyl)-3-nitroso-5-phenyloxazolidine-4-carboxylate (VIb and VIc) (*Rf* 0.43): These compounds were obtained as a mixture with II. Repeated recrystallizations from MeOH gave VIb as colorless needles of mp 134.5—137.5°. IR ν_{max}^{KBr} cm^{-1}: 1750, 1740 (ester). NMR (τ, $CDCl_3$): 2.70 (10H, m, aromatic protons), 3.13 and 5.52 (2H, AB q, methine proton on C-2 and C_6H_5-C<u>H</u>-$COOCH_3$), 4.68 and 5.30 (2H, AB q, methine protons on C-4 and C-5), 6.28 (6H, s, -$COOC\underline{H}_3$). *Anal.* Calcd. for $C_{20}H_{20}O_6N_2$: C, 62.49; H, 5.24; N, 7.29. Found: C, 62.76; H, 5.28; N, 7.59. VIc was obtained from the mother liquor as colorless prisms of mp 158.0—160.0°. IR ν_{max}^{KBr} cm^{-1}: 1740 (ester). NMR (τ, $CDCl_3$): 2.70 (10H, s, aromatic protons), 3.80 and 5.23 (2H, AB q, methine proton on C-2 and C_6H_5-C<u>H</u>-$COOCH_3$), 4.95 and 5.72 (2H, AB q, methine protons on C-4 and C-5), 6.30 and 6.35 (6H, s, -$COOC\underline{H}_3$).

v) Methyl 2-(α-Methoxycarbonylbenzyl)-3-nitroso-5-phenyloxazolidine-4-carboxylate (VId) (*Rf* 0.38); This compound was isolated as a solid and was recrystallized from MeOH to give colorless needles, mp 161.0—162.5°. IR ν_{max}^{Nujol} cm^{-1}: 1740 (ester). NMR (τ, $CDCl_3$): 2.70 (10H, m, aromatic protons), 3.50 and 5.35 (2H, AB q, methine proton on C-2 and C_6H_5-C<u>H</u>-$COOCH_3$), 4.89 and 5.88 (2H, AB q, methine protons on C-4 and C-5), 6.22 and 6.25 (6H, s, -$COOC\underline{H}_3$). *Anal.* Calcd. for $C_{20}H_{20}O_6N_2$: C, 62.49; H, 5.24; N, 7.29. Found: C, 62.44; H, 5.60; N, 7.61.

vi) Methyl α-Hydroximinophenylacetate (IIIa) (*Rf* 0.17): This compound was isolated as a liquid, and was identified spectrally with an authentic sample.

vii) N-(α-Methoxycarbonylstyryl)-*threo*-phenylserine Methyl Ester (Va) (*Rf* 0.06): This compound was obtained as a liquid, and was identified with the authentic sample described below.

viii) Methyl α-Hydroximinophenylacetate (IIIb) (*Rf* 0.06): This compound was eluted just after Va and was recrystallized from benzene to give colorless prisms, mp 133.0—139.0°, which were identical with the authentic IIIb described below.

ix) N-Formyl-*threo*-phenylserine Methyl Ester (VII) (*Rf* 0.00): Elution with 5% MeOH in CH_2Cl_2 gave VII. VII also separated from the aqueous layers during extraction. Recrystallization of crude VII from $CHCl_3$–hexane gave colorless prisms, mp 151°. This melting point was not depressed by admixture with an authentic sample prepared from *threo*-phenylserine methyl ester (Ia) and methyl formate.

Deamination of *erythro*-Phenylserine Methyl Ester (Ib)——Sodium nitrite (7.0 g, 0.010 mole) was added

10) All melting and boiling points are uncorrected. Infrared (IR) spectra were measured with a spectrometer, Model DS-402G, Japan Spectroscopic Co., Ltd. Nuclear magnetic resonance (NMR) spectra were measured with a spectrometer, Model 3H-60, Japan Electron Optics Lab., using TMS as the internal standard. The following abbreviations are used: d=doublet, q=quartet, m=multiplet, s=singlet.

11) K.N.F. Shaw and S.W. Fox, *J. Am. Chem. Soc.*, **75**, 3417, 3421 (1953).

12) P.G. Sergeev and A.M. Sladkov, *Zh. Obshch. Khim.*, **27**, 819 (1957) [*C. A.*, **51**, 16348 (1957)].

13) R.L. Shriner, "Organic Syntheses," Coll. Vol. II, ed. by A.H. Blatt, John Wiley and Sons, Inc., New York, 1943, p. 266.

to a solution of Ib (17.5 g, 0.090 mole) in acetic acid (290 ml) over a 5 hr period with stirring at 20—23°. After standing overnight, the reaction mixture was worked up as in the deamination of Ia, giving a mixture of products (16.5 g), which showed the presence of at least nine components on TLC (silica gel, benzene–CH_2Cl_2 (1:1)). A mixture of products was chromatographed in benzene–CH_2Cl_2 (1:1) on silica gel (550 g) to give nine compounds (II, IIIa—b, IV, Vb, VIe—g, and VIII) as follows.

i) Methyl Phenylglyoxylate (IV) and Benzaldehyde (VIII) (*Rf* 0.66): The initially eluted part was recognized as a mixture of IV and VIII based on NMR and IR spectra. Repeated recrystallization of the 2,4-dinitrophenylhydrazones from $CHCl_3$–methanol gave orange needles, which were identical with the 2,4-dinitrophenylhydrazone of benzaldehyde (VIII).

ii) Methyl Benzoylacetate (II) and Methyl 2-(α-methoxycarbonylbenzyl)-3-nitroso-5-phenyloxazolidine -4-carboxylate (VIe and VIf) (*Rf* 0.50): The mixture obtained was triturated and gave a pale yellow solid which consisted of 2 compounds, VIe and VIf, based on the NMR spectrum. No further separation was successful, but the NMR spectrum of pure VIe obtained by alternative synthesis showed the presence of VIe in the mixture. Pure VIf could not be obtained in this experiment, however, the characteristic two pairs of doublet showed that VIf was also present in the mixture.

NMR VIe: (τ, $CDCl_3$): 3.45 and 5.32 (2H, AB q, methine proton on C-2 and C_6H_5-C<u>H</u>-$COOCH_3$), 4.67 and 4.78 (2H, AB q, methine protons on C-4 and C-5), 6.20 and 6.80 (6H, s, -$COOC\underline{H}_3$), VIf: (τ, $CDCl_3$) 3.15 and 5.50 (2H, AB q, methine proton on C-2 and C_6H_5-C<u>H</u>-$COOCH_3$), 4.50 and 5.10 (2H, AB q, methine protons on C-4 and C-5), 6.25 and 6.85 (6H, s, -$COOC\underline{H}_3$).

The residue obtained from evaporation of the mother liquor was again chromatographed in benzene on silica gel to give pure methyl benzoylacetate (II). NMR and IR spectra were identical with those of an authentic sample. 2,4-Dinitrophenylhydrazone. mp 167° (lit.[14] mp 169—170°).

iii) Methyl 2-(α-Methoxycarbonylbenzyl)-3-nitroso-5-phenyloxazolidine-4-carboxylate (VIg) (*Rf* 0.34): Crude VIg isolated from the deamination mixture was recrystallized from MeOH to give colorless needles mp 153.5—155.0°. IR ν_{max}^{KBr} cm^{-1}: 1740 (ester). NMR (τ, $CDCl_3$): 2.65 (10H, m, aromatic protons), 3.50 and 5.10 (2H, AB q, methine proton on C-2 and C_6H_5-C<u>H</u>-$COOCH_3$), 4.70 and 5.40 (2H, AB q, methine protons on C-4 and C-5), 6.25 and 6.85 (6H, s, -$COOCH_3$). *Anal.* Calcd. for $C_{20}H_{20}O_6N_2$: C, 62.49; H, 5.24; N, 7.29. Found: C, 62.28; H, 5.16; N, 7.46.

iv) Methyl α-Hydroximinophenylacetate (IIIa) (*Rf* 0.17): Isolated crude IIIa was recrystallized from benzene–hexane to give colorless plates, mp 76—80°, which was identified with the authentic IIIa described below.

v) N-(α-Methoxycarbonylstyryl)-*erythro*-phenylserine Methyl Ester (Vb) (*Rf* 0.12): This compound was obtained as a liquid, and was identified with an authentic sample by its IR and NMR spectra.

vi) Methyl α-Hydroximinophenylacetate (IIIb) (*Rf* 0.06): Isolated crude IIIb was recrystallized from $CHCl_3$ to give colorless prisms, mp 131.0—138.5°. This melting point was identical with that of an authentic sample.

Deamination of *threo*-Phenylserine——Sodium nitrite (4.3 g, 0.062 mole) was added to the suspension of *threo*-phenylserine (10.0 g, 0.055 mole) in acetic acid (400 ml) during a 6 hr period with stirring at 20°, then the reaction mixture was left at room temperature overnight. After evaporation of the solvent, the residue was treated with 150 ml of ether. The whole was washed with 10% aq. HCl and sat. aq. NaCl, then extracted with three 30 ml portions of 10% aq. Na_2CO_3. Combined aqueous layers were acidified with conc. HCl under cooling, then extracted with three 100 ml portions of ether. Organic layers were washed with sat. aq. NaCl and dried over anhyd. Na_2SO_4. Treatment of the carboxylic acid obtained above with ethereal diazomethane gave 6.7 g of ester. The mixture of ester (3.5 g), acetic anhydride (3.0 g), and pyridine (35 ml) was stirred at room temperature for 2 days. After evaporation of the solvent, the residue was treated with 120 ml of ethyl acetate, then washed successively with 10% aq. HCl, 10% aq. Na_2CO_3, and sat. aq. NaCl, after which it was dried over anhyd. Na_2SO_4. Removal of the solvent left 3.9 g of oil, which solidified on standing. IR and NMR spectra of the acetylated product were identical with those of authentic *threo*-β-phenylglycerate diacetate (XIV).

Deamination of *erythro*-Phenylserine——Sodium nitrite (4.4 g, 0.064 mole) was added to a suspension of *erythro*-phenylserine (XIIIb) (10.5 g, 0.058 mole) in acetic acid (450 ml) during a 4 hr period with stirring at 20°.

The working up of the reaction mixture followed by esterification similar to procedures for *threo*-phenylserine, gave 5.5 g of ester.

The mixture of ester (1.7 g), acetic anhydride (1.5 g), and pyridine (15 ml) was stirred at room temperature for 2 days, then treated as usual to give 2.0 g of an oil which solidified on standing. The NMR of the product was identical with that of authentic *erythro*-β-phenylglycerate diacetate (XV).

Syntheses of Authentic Samples

Methyl Phenylglyoxylate (IV)——$C_6H_5COCOCl$ (2.5 g, 0.015 mole) was added dropwise at 0° to a solution of MeOH (0.70 g, 0.019 mole) and pyridine (1.42 g, 0.018 mole) in ether (20 ml), then the mixture

14) W.J. Croxall, J.O. Van Hook, and H.J. Schneider, *J. Am. Chem. Soc.*, **73**, 2713 (1951).

was stirred for 4 hr at room temperature. The reaction mixture was filtered from pyridine hydrochloride and the filtrate was washed successively with 10% aq. HCl, sat. aq. NaCl, 10% aq. Na_2CO_3, and sat. aq. NaCl, then dried over anhyd. Na_2SO_4. Removal of the solvent afforded IV as a pale yellow oil (2.07 g, 84.1% yield). IR ν_{max}^{film} cm^{-1}: 1745 (ester), 1695 (ketone). NMR (τ, $CDCl_3$): 2.00—2.65 (5H, m, aromatic protons), 6.10 (3H, s, -COOC<u>H</u>$_3$). 2,4-Dinitrophenylhydrazone mp 171.5—173.5° (lit.[12] mp 173°).

Methyl α-Hydroximinophenylacetate (IIIa and IIIb[15])——a) From Methyl Phenylglyoxylate (IV): A mixture of IV (1.64 g, 0.010 mole), hydroxylamine hydrochloride (0.90 g, 0.013 mole), pyridine (2 ml), and ethanol (10 ml) was refluxed for 3 hr. The resulting solution was combined with 70 ml of ether. The whole was washed successively with 10% aq. HCl, sat. aq. NaCl, 10% aq. Na_2CO_3, and sat. aq. NaCl then dried over anhyd. Na_2SO_4.

Evaporation of the solvent gave a mixture of IIIa and IIIb, which was chromatographed in CH_2Cl_2 on silica gel (160 g) to give IIIa (0.84 g) and IIIb (0.40 g).

Recrystallization of crude IIIa from benzene–hexane gave colorless plates, mp 75—80°. Recrystallization of crude IIIb from $CHCl_3$–hexane gave colorless prisms melting at 131—138°.

b) From Methyl Phenylmalonaldehydate[16] (IX): Sodium nitrite (3.20 g, 0.044 mole) was added in portions to a solution of IX (7.24 g, 0.041 mole) in acetic acid (70 ml). The resulting solution was left at room temperature overnight. After evaporation of the solvent the residue was worked up in the usual manner to afford the crude products, which showed the presence of three products, IV, IIIa, and IIIb on TLC. Crude products were chromatographed in CH_2Cl_2 on silica gel (150 g) to give IV (1.31 g), IIIa (1.44 g), and IIIb (2.00 g).

Crude IIIa was recrystallized from CCl_4–hexane to afford colorless plates melting at 79.5—81.0°. IR ν_{max}^{KBr} cm^{-1}: 3300 (OH), 1725, 1710 (C=O), 1628 (C=N). NMR (τ, $CDCl_3$): 0.45 (1H, s, OH), 2.50 (5H, m, aromatic protons), 6.00 (3H, s, -COOC<u>H</u>$_3$). *Anal.* Calcd. for $C_9H_9O_3N$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.71; H, 5.22; N, 7.99.

Recrystallization of crude IIIb from $CHCl_3$–hexane gave colorless prisms melting at 133.0—139.0°. IR ν_{max}^{KBr} cm^{-1}: 3240 (OH), 1740 (C=O). NMR (τ, $CDCl_3$): 2.58 (5H, s, aromatic protons), 6.15 (3H, s, -COOC<u>H</u>$_3$). The NMR spectrum showed no signal for OH above τ −5.0. *Anal.* Calcd. for $C_9H_9O_3N$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.73; H, 4.88; N, 7.96.

Methyl Benzoylacetate (II)——II was prepared from methyl acetoacetate following the published procedure for the preparation of ethyl benzoylacetate.[13] 2,4-Dinitrophenylhydrazone mp 167.0—168.5° (lit.[14] 169.0—170.0°).

N-(α-Methoxycarbonylstyryl)-*threo*-phenylserine Methyl Ester (Va)——A mixture of methyl phenylmalonaldehydate[16] (3.6 g, 0.020 mole) and *threo*-phenylserine methyl ester (Ia) (4.0 g, 0.021 mole) in benzene (60 ml) was refluxed for 2 hr. Liberated water was removed azeotropically by a Dean and Stark distilling receiver. Evaporation of the solvent gave a syrup, which solidified on scratching. Recrystallization from benzene–hexane afforded Va, 4.3 g, mp 118.5—121.0°. Repeated recrystallizations from benzene–hexane gave colorless prisms, mp 122.5—124.0°. IR ν_{max}^{KBr} cm^{-1}: 3400, 3340 (NH, OH), 1745, 1655 (C=O), 1590 (C=C). NMR (τ, $CDCl_3$): 1.30 (1H, q, NH), 2.80 (10H, m, aromatic protons), 3.70 (1H, d, >C=C<u>H</u>-), 4.83 (1H, d, C_6H_5-C<u>H</u>-C), 6.07 (1H, q, -C<u>H</u>-COOCH$_3$), 6.32 and 6.38 (6H, s, -COOC<u>H</u>$_3$), 6.60 (1H, broad, OH). *Anal.* Calcd. for $C_{20}H_{21}O_5N$: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.29; H, 6.05; N, 4.15.

N-(α-Methoxycarbonylstyryl)-*erythro*-phenylserine Methyl Ester (Vb)——The solution of IX (5.4 g, 0.030 mole) and *erythro*-phenylserine methyl ester (Ib) (6.0 g, 0.031 mole) in benzene (100 ml) was refluxed for 1 hr. Liberated water was removed azeotropically by a Dean and Stark distilling receiver. The resulting solution was allowed to stand overnight, then the precipitate was filtered off and dried giving a white powder (A), 1.75 g, mp 137—145°. Although its structure was not established, compound A seems to be a isomer of enamine (Vb), as it changed gradually to enamine (Vb) in CH_2Cl_2.

The filtrate was evaporated to dryness, then the residual solid was recrystallized from benzene–hexane (1:1) to give enamine Vb, 7.45 g, as colorless prisms of mp 97.0—102°. The enamine Vb obtained contained a small amount of compound A, on TLC, and no further purification was successful. However, the structure of Vb is evident judging from its NMR and IR spectra which were similar to those of enamine Va. IR ν_{max}^{KBr} cm^{-1}: 3460, 3320 (NH, OH), 1740, 1665 (C=O), 1595 (C=C). NMR (τ, $CDCl_3$): 1.55 (1H, q, NH), 2.85 (10H, m, aromatic protons), 3.56 (1H, d, >C=C<u>H</u>-), 5.00 (1H, d, C_6H_5-C<u>H</u>-C), 5.95 (1H, q, -C-C<u>H</u>-COOCH$_3$), 6.27 and 6.35 (6H, s, -COOC<u>H</u>$_3$), 6.70 (1H, broad, OH).

Methyl 2-(α-Methoxycarbonylbenzyl)-3-nitroso-5-phenyloxazolidine-4-carboxylate (VIa—d) from Enamine

15) *a*) Methyl α-hydroximinophenylacetate with a mp of 138—139° is reported in the literature. This compound is thought to correspond to IIIb (Müller, *Chem. Ber.*, **16**, 2987 (1833)); *b*) IIIa and IIIb were in a state of equilibrium in CH_2Cl_2 solution.

16) Wilhelm Wislicenus, *Ann.*, **413**, 206 (1917).

Va——Sodium nitrite (0.50 g, 0.0070 mole) was added to the solution of Va (2.6 g, 0.0073 mole) in 80 ml of acetic acid during a 6 hr period with stirring at 20°. After standing overnight, the reaction mixture was worked up in the usual manner to give a red oil, 2.55 g. The crude products were chromatographed in benzene–CH_2Cl_2 (1:1) on silica gel to give VIa (0.28 g), a mixture of VIb and VIc (0.50 g), and VId (0.16 g) as the major products. Unreacted enamine (Va) and a small amount of methyl phenylglyoxylate (IV) were also isolated. Recrystallization of crude VIa from MeOH gave colorless plates, with a mp of 125.0—126.5°, which was identical with VIa isolated from the deamination mixture.

Recrystallization of crude VId from MeOH gave colorless needles with a mp of 157.5—160.5°, which also was identical with VId isolated from the deamination mixture.

Methyl 2-(α-Methoxycarbonylbenzyl)-3-nitroso-5-phenyloxazolidine-4-carboxylate (VIe—g) from Enamine Vb——Sodium nitrite (1.57 g, 0.023 mole) was added to the solution of Vb (7.4 g, 0.021 mole) in 150 ml of acetic acid during a 4 hr period at 20°. After standing overnight at room temperature, the reaction mixture was treated as usual to afford 7.4 g of curde products. Crude products were chromatographed in benzene–CH_2Cl_2 (1:1) on silica gel to give a mixture of VIe and VIf (1.67 g), and VIg (*ca.* 1.2 g) as the major products. Unreacted enamine (Vb) was also isolated. Repeated recrystallizations of a mixture of VIe and VIf from methanol gave colorless needles of VIe, mp 162.5—164.0°. IR ν_{max}^{KBr} cm^{-1}: 1750, 1735 (ester). NMR (τ, $CDCl_3$), 2.68 (10H, s, aromatic protons), 3.45 and 5.32 (2H, AB q, methine proton on C-2 and C_6H_5-C<u>H</u>-$COOCH_3$), 4.67 and 4.78 (2H, AB q, methine protons on C-4 and C-5), 6.20 and 6.80 (6H, s, -$COOC\underline{H}_3$). *Anal.* Calcd. for $C_{20}H_{20}O_6N_2$: C, 62.49; H, 5.24; N, 7.46. Found: C, 62.67; H, 5.33; N, 7.29. Recrystallization of crude VIg gave colorless needles which were identical with VIg isolated from the deamination mixture based on IR and NMR spectra.

N-Formyl-*threo*-phenylserine Methyl Ester (VII)——The solution of *threo*-phenylserine methyl ester (Ia) (1.0 g) in 20 ml of methyl formate was refluxed for 2 hr. After evaporation of the solvent, the residual solid was recrystallized from acetone–hexane to give colorless prisms, 0.92 g, mp 155°. IR ν_{max}^{KBr} cm^{-1}: 3320, 3260 (NH, OH), 1750 (ester), 1655 (amide). *Anal.* Calcd. for $C_{11}H_{13}O_4N$: C, 59.18; H, 5.87; N, 6.28. Found: C, 58.93; H, 5.86; N, 6.28.

Methyl *threo*-β-Phenylglycerate Diacetate (XIV)——A mixture of methyl *threo*-phenylglycerate[17] (0.90 g), acetic anhydride (2.0 g), and pyridine (10 ml) was refluxed for 3 hr. After working it up in the usual way, 1.02 g of an oil was obtained, which solidified on standing. Recrystallization from hexane gave colorless plates, mp 77—78°. IR ν_{max}^{Nujol} cm^{-1}: 1740 (ester). NMR (τ, $CDCl_3$): 2.70 (5H, s, aromatic protons), 3.75 and 4.67 (2H, AB q, methine protons), 6.30 (3H, s, -$COOC\underline{H}_3$), 7.85 and 7.90 (6H, s, -$OCOC\underline{H}_3$). *Anal.* Calcd. for $C_{14}H_{16}O_6$: C, 59.99; H, 5.75. Found: C, 60.17; H, 5.83.

Methyl *erythro*-β-Phenylglycerate Diacetate (XV)——A mixture of methyl *erythro*-β-phenylglycerate[17] (0.30 g), acetic anhydride (1.0 g), and pyridine (5 ml) was stirred at room temperature for 2 days, then treated as usual to give an oil (0.35 g) which solidified on standing. Recrystallization from hexane gave colorless needles, mp 66.0—66.5°. IR ν_{max}^{KBr} cm^{-1}: 1750 (ester). NMR (τ, $CDCl_3$): 2.73 (5H, s, aromatic protons), 3.83 and 4.56 (2H, AB q, methine protons), 6.25 (3H, s, -$COOC\underline{H}_3$), 7.90 (6H, s, -$OCOC\underline{H}_3$). *Anal.* Calcd. for $C_{14}H_{16}O_6$: C, 59.99; H, 5.75. Found: C, 59.91; H, 5.78.

17) R.P. Linstead, *J. Chem. Soc.*, 1953, 1222.