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The Synthesis of Cyclic α-Amino Acids. III. The Synthesis of Methyl (+)- and (−)-3-Amino-3-*C*-carboxy-3-deoxypentopyranosides

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Cyclization of D'-methoxy-diglycolaldehyde, prepared by periodate cleavage of methyl β-L-arabinopyranoside, with ethyl nitroacetate gave a mixture of stereoisomers of cyclic α-nitro ester, *i.e.* methyl (+)-3-deoxy-3-*C*-ethoxycarbonyl-3-nitropentopyranoside. Catalytic reduction of the cyclic α-nitro ester afforded an isomeric mixture of cyclic α-amino esters, from which, on column chromatography, there could be isolated four diastereoisomers of methyl (+)-3-amino-3-deoxy-3-*C*-ethoxycarbonylpentopyranoside. Hydrolysis of each diastereoisomer gave the corresponding cyclic (+)-α-amino acid having a skeleton of pentopyranoside. The stereochemistry of the isomeric amino acids was studied by NMR spectroscopy and chemical degradation. On the other hand, three enantiomeric cyclic (−)-α-amino acids were also obtained from methyl β-D-xylopyranoside by the analogous route as that from methyl β-L-arabinopyranoside.

In a previous paper[1] one of the authors and others reported the synthesis of a cyclic amino acid, *i. e.* 1-amino-2,6-dihydroxycyclohexane-1-carboxylic acid by condensation of glutardialdehyde with ethyl nitroacetate, followed by reduction and hydrolysis. The present paper is concerned with an extension of this work and presents the synthesis of methyl (+)- and (−)-3-amino-3-*C*-carboxy-3-deoxypentopyranosides (VI-d, VI-1) which are the first synthetic examples of cyclic α-amino acid having a pyranoside-skeleton.

Details of the synthesis are summarized in Scheme 1. The starting materials, D'- and L'-diglycolaldehyde (III-d. III-1) were prepared from methyl β-L-arabinopyranoside (I) and β-D-xylopyranoside (II) respectively, by periodate oxidation as was reported by Bear and Fischer[2].

The condensation reaction of III-d with ethyl nitroacetate was carried out in the presence of potassium acetate and potassium carbonate to give a dextrorotatory methyl (+)-3-deoxy-3-*C*-ethoxycarbonyl-3-nitropentopyranoside (IV-d) in 81% yield. The purification of IV-d was accomplished by silica gel chromatography, although the diastereoisomeric separation of IV-d was unsuccessful in this step. The acetylation of IV-d with acetic anhydride in pyridine gave a diacetyl derivative of IV-d, the NMR spectrum (in $CDCl_3$) of which showed the presence of two *O*-acetyl groups at about τ 7.84 and 7.92.

The condensation reaction of III-1 with ethyl nitroacetate gave a levorotatory nitro ester (IV-1).

The catalytic hydrogenation of the nitro esters IV-d and IV-1 with Raney Ni T-4 gave methyl (+)- and (−)-3-amino-3-deoxy-3-*C*-ethoxycarbonylpentopyranosides (V-d and V-1) as a syrup, respectively.

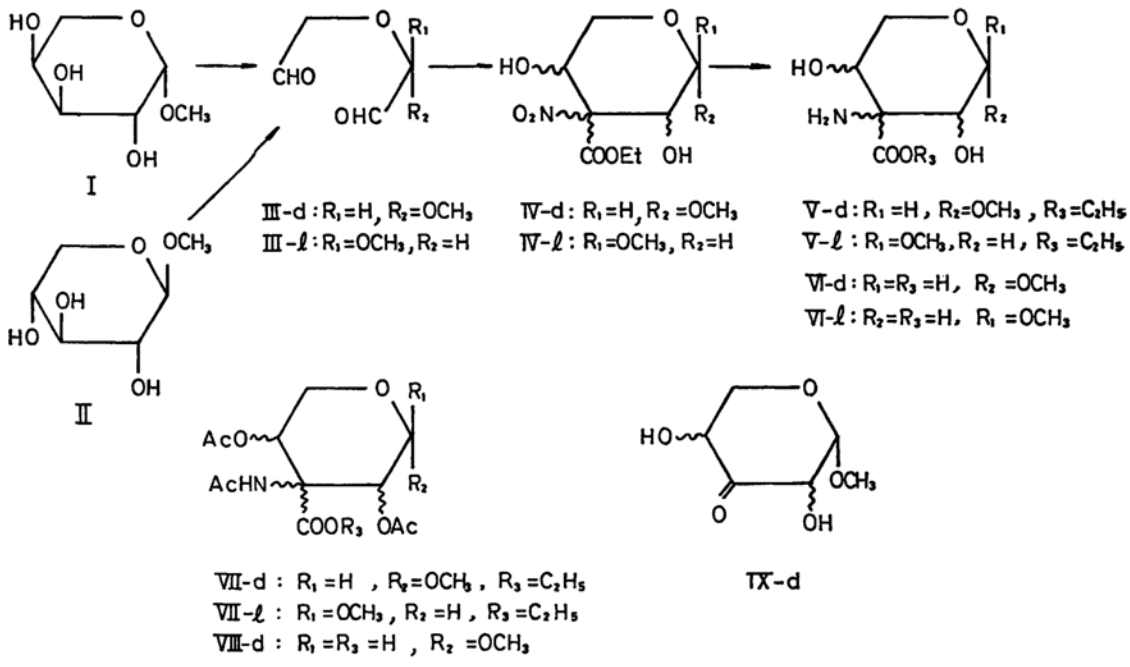
The amino ester V-d was shown by thin-layer chromatography to contain four ninhydrin positive components, VA-d (R_f 0.73), VB-d (R_f 0.55), VC-d (R_f 0.36) and VD-d (R_f 0.23). These components were separated from each other by silica gel column chromatography. The major component VB-d and minor one VD-d were obtained in crystalline states. The components, VA-d, VB-d, VC-d and VD-d were acetylated to give dextrorotatory crystalline triacetates, VIIA-d, VIIB-d, VIIC-d and VIID-d, respectively. These acetates were characterized as the fully acetylated diasteroisomeric amino esters on the basis of elemental and NMR analysis (Tables 1, 3 and 4).

By analogous chromatography four diastereoisomers of levorotatory amino esters, VA-1 (R_f 0.73), VB-1 (R_f 0.55), VC-1 (R_f 0.36) and VD-1 (R_f 0.23) were obtained from the mixed amino ester V-1. The crystalline major and minor isomers, VB-1 and VD-1 were characterized as the enantiomers of VB-d and VD-d, respectively (Table 1). Furthermore, the crystalline triacetates, VIIA-1, VIIB-1, and VIID-1 were also obtained from VA-1, VB-1 and VD-1, respectively (Table 1). The IR and NMR spectra of VIIA-1, VIIB-1 and VIID-1 were completely identical with those of VIIA-d, VIIB-d and VIID-d, respectively.

The hydrolysis of VA-d, VB-d, VC-d and VD-d afforded the isomeric methyl (+)-3-amino-3-*C*-carboxy-3-deoxypentopyranosides, VIA-d, VIB-d, VIC-d and VID-d, respectively, in good yields. Analogously, the enatiomeric (−)-amino acids,

1) S. Zen, Y. Takeda, A. Yasuda and S. Umezawa, This Bulletin, **40**, 431 (1967).

2) H. H. Bear and H. O. Fischer, *J. Am. Chem. Soc.*, **81**, 5184 (1959).



Scheme 1

TABLE 1. ISOMERIC AMINO ESTERS AND THEIR ACETYL DERIVATIVES

Compound	Mp °C	$[\alpha]_D^\circ$ (Temp. °C, Concn. %, Solv.*)	Formula	Calcd C, %	Calcd H, %	Calcd N, %	Found C, %	Found H, %	Found N, %
VB-d	133—4	+135 (23, 0.7, A)	$C_9H_{17}NO_6$	45.95	7.28	5.96	46.28	7.54	5.64
VD-d	161—2	+ 39 (23, 0.7, A)					46.44	7.39	5.70
VB-l	132—3	−133 (21, 0.5, A)					46.20	7.40	6.03
VD-l	161—2	− 37 (21, 0.5, A)					46.24	7.37	5.96
VIIA-d	174—5	+ 98 (22, 0.7, E)	$C_{15}H_{23}NO_9$	49.86	6.42	3.88	50.26	6.60	3.88
VIIB-d	118—20	+166 (22, 0.7, E)					50.06	6.63	3.69
VIIC-d	151—2	+ 55 (22, 0.7, B)					50.21	6.62	3.65
VIID-d	115—6	+ 49 (22, 0.7, E)					50.13	6.45	3.74
VIIA-l	174—5	−100 (29, 1.0, B)					50.16	6.62	3.89
VIIB-l	118—20	−171 (29, 1.0, E)					49.99	6.58	3.97
VIID-l	116—6.5	− 43 (18, 0.7, E)					50.08	6.46	3.89

* A=ethanol; E=ethyl acetate

TABLE 2. ISOMERIC AMINO ACIDS

Compound	Mp[a] °C (Dec.)	$[\alpha]_D^{21}$ (Conc. %) in water		R_f[b]	Formula	Calcd C, %	Calcd H, %	Calcd N, %	Found C, %	Found H, %	Found N, %
VIA-d	250	+ 51	(0.4)	0.13	$C_7H_{13}NO_6$	40.58	6.32	6.76	41.09	6.50	6.37
VIB-d	230	+193	(0.4)	0.18					41.07	6.47	6.28
VIC-d	180	+121	(0.3)	0.27					40.72	6.50	6.69
VID-d	160	+ 28*	(0.4)	0.16					40.41	6.58	6.43
VIA-l	250	− 41	(0.9)	0.13					40.44	6.97	6.34
VIB-l	230	−204**	(0.9)	0.18					40.92	6.79	6.67
VID-l	160	− 30	(0.7)	0.16					40.77	6.87	6.51

a) Determined on a Yanagimoto micro hot stage.
b) Solvent system; *n*-butanol - acetic acid - water (4 : 1 : 1).
* At 16°C, ** At 26°C

VIA-1, VIB-1 and VID-1 were also obtained from the amino esters, VA-1,VB-1 and VD-1, respectively (Table 2).

Stereochemical Considerations. The anomeric carbon atom C-1 in each of the isomers of the (+)-amino acid (VI-d) apparently has the same configuration as that of the anomeric carbon atom in the methyl β-L-arabinopyranoside (I) used as a starting substance. The other asymmetric carbon atoms (C-2, C-3 and C-4), however, have unknown configurations, because they are new asymmetric centers which have been formed by the condensation reaction of the dialdehyde (II-d) with ethyl nitroacetate. The steric configurations

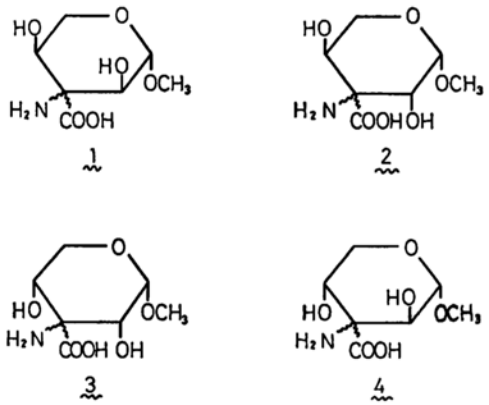


Fig. 1

of the isomeric (+)-amino acids, VIA-d, VIB-d, VIC-d and VID-d, therefore, must be assigned to any of the eight possible configurations. When the configuration at C-3 is let aside, the four formulas shown in Fig. 1 are possible for the isomeric (+)-amino acids.

Conformational and configurational studies based on the NMR (in $CDCl_3$) analysis[3] of the fully acetylated amino esters, VIIA-d, VIIB-d, VIIC-d and VIID-d, served to deduce the configurations at the two carbon atoms (C-2 and C-4) of the above-mentioned three unknown asymmetric carbon atoms in the amino acid isomers. The spectral features were assigned on the basis of chemical shifts, integrated area, magnitudes of splittings and decoupling splitting patterns (Fig. 2). The assigned chemical shifts and coupling constants are listed in the Tables 3 and 4. From the following results partial conformations for VIIA-d, VIIB-d, VIIC-d and VIID-d could be deduced on the assumption that most pyranoside sugars and their derivatives may exist in the chair conformations (*C1*, *1C*)[4].

The ring proton coupling constants ($J_{1,2}=1.8$, $J_{4,5e}=J_{4,5a}=2.0$ Hz) observed in the spectrum (Fig. 2, A) of VII-d indicate that the pair of H-1 and H-2 protons is in equatorial-axial or equatorial-equatorial orientation and H-4 proton is not antiparallel to H-5 axial proton. Decoupling reveals that the long range coupling of 1.5 Hz is found between H-2 proton and H-4 proton. Therefore, H-2 proton may be located on equatorial as well as

Table 3. Chemical shifts (τ) in $CDCl_3$ at 100 MHz

Compound	NH	H-1	H-2	H-4	H-5a	H-5e	O-Ac	NAc	CH_2	CH_3	OCH_3
VIIA-d	3.96	5.26	4.92	4.28	5.65 or 6.20		7.79, 7.88	8.08	5.75	8.71	6.68
VIIB-d	3.21	5.29	4.72	4.18	5.52 or 6.27		7.78, 7.87	8.12	5.75	8.71	6.63
VIIC-d	3.22	5.10	4.17	4.07	5.79	6.24	7.93, 8.00	8.04	5.69	8.68	6.62
VIID-d	3.27	5.18	4.33	4.09	6.22	5.91	7.96, 7.96	8.03	5.68	8.67	6.52
VIIID-d	—*	4.88 or 5.14		4.88	5.9 — 6.2		8.01, 8.03	7.83	—	—	6.55

* Not observed.

Table 4. Coupling constants (*J*, Hz)

Compound	$J_{1,2}$	$J_{4,5a}$	$J_{4,5e}$	$J_{5a,5e}$	$J_{2,4}$	J_{CH_2,CH_3}
VIIA-d	1.8	2.0	2.0	13.2	1.5	7.2
VIIB-d	3.1	2.0 or 1.4		13.2	0	7.2
VIIC-d	4.7	10.1	6.2	11.5	0	7.5
VIID-d	5.7	7.3	5.0	12.5	0	7.1
VIIID-d	8.3	10	3	12	0	—

3) R. U. Lemieux and J. D. Stevens, *Can. J. Chem.*, **43**, 2059 (1965).
4) N. S. Bhacca and D. Horton, *J. Am. Chem. Soc.*, **89**, 5993 (1967); L. D. Hall, *Advan. Carbohydrate Chem.*, **19**, 51 (1964).

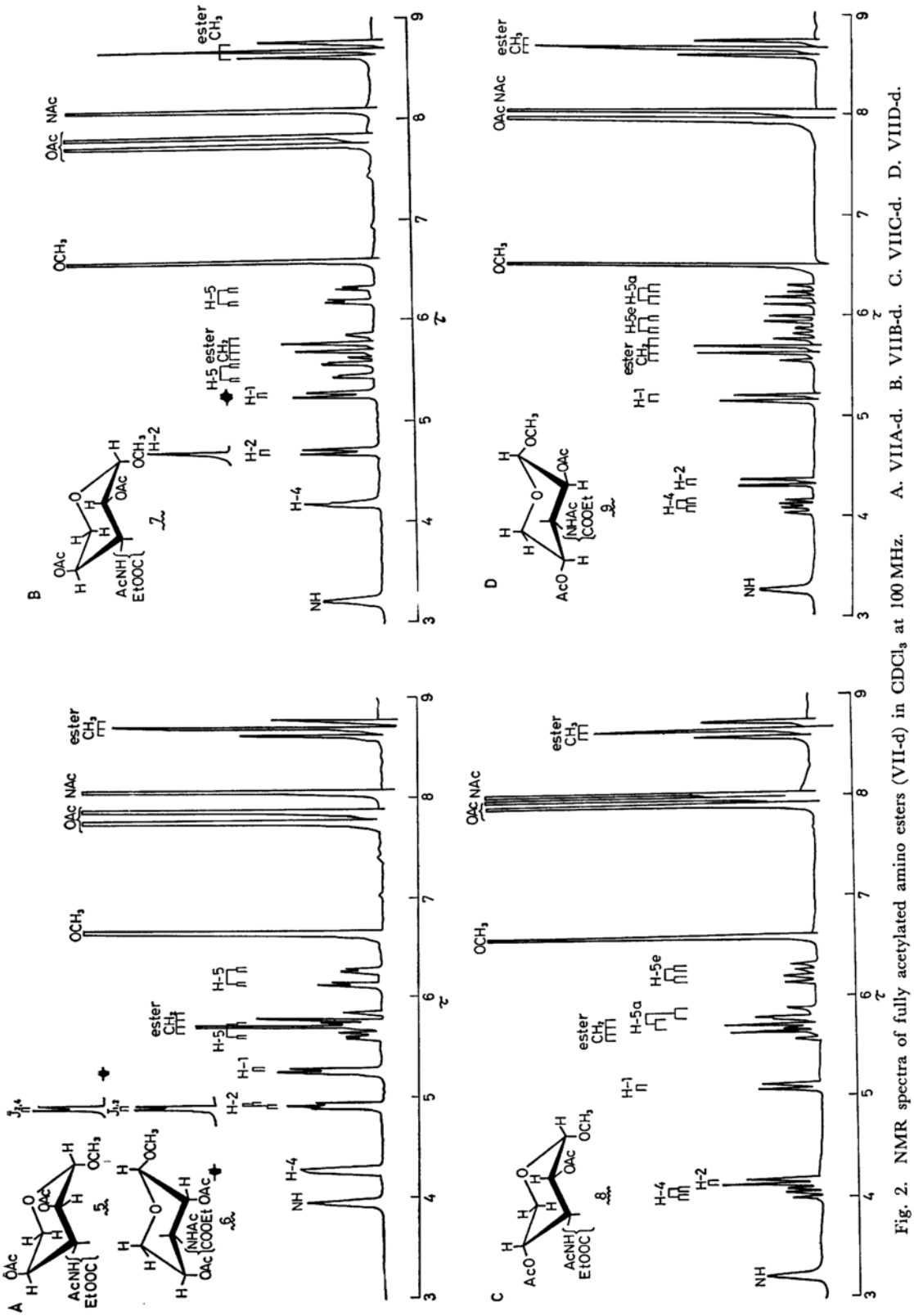


Fig. 2. NMR spectra of fully acetylated amino esters (VII-d) in $CDCl_3$ at 100 MHz. A. VIIA-d. B. VIIB-d. C. VIIC-d. D. VIID-d.

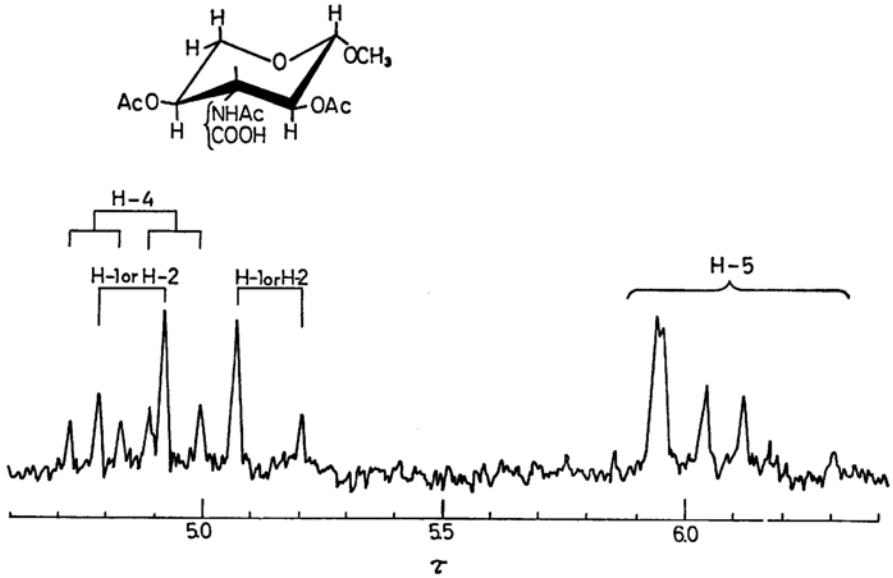


Fig. 3. NMR spectrum of VIIID-d in $CDCl_3$ at 60 MHz.

H-4 proton according to stereospecificity of the long-range coupling ("W"-conformation[5]). The chemical shifts (τ 7.79 and 7.88) for the ring-acetoxy protons at C-2 and C-4 also support this conformation, because they fall in the range of the chemical shifts (τ 7.80—7.90) reported for the axial orientation.[6] There must be then considered two possible partial conformations, **5** and **6** for VIIA-d (Fig. 2, A). The former is a *C1* conformation corresponding to the configuration **1** and the later is a *1C* conformation corresponding to the configuration **3**.

In the NMR spectrum (Fig. 2, B) of VIIB-d, the ring proton coupling constants ($J_{4,5a}=J_{4,5e}=1.4$—2.0 Hz) show that H-4 proton is not antiparallel to H-5 axial proton, therefore, H-4 proton is equatorial. The H-2 proton may be in axial orientation, because decoupling experiment shows no long-range coupling between H-2 and H-4 protons. The small coupling constant ($J_{1,2}=3.1$ Hz) shows that H-1 proron is gauche to the H-2 proton. Consequently, the H-1 proton thus may be located on equatorial orientation. The acetoxy signal at τ 7.78 indicates that one axial acetoxy group exists in VIIB-d. Conformation **7** is deduced as a possible partial conformation for VIIB-d and this is *C1* conformation corresponding to the configuration **2**.

The NMR spectrum (Fig. 2, C) of VIIC-d shows that the pair of H-1 and H-2 protons is in equatorial-axial or equatorial-equatorial orientation($J_{1,2}=4.7$ Hz), while H-4 proton is located on axial orientation ($J_{4,5e}=10.1$ Hz). The acetoxy signals at τ 7.93 and 8.00 indicate that VIIC-d has two equatorial ring-acetoxy groups.[6] Consequently, H-2 proton is located on axial orientation and H-1 proton is to be regarded as equatorial. A possible partial conformation for VIIC-d is deduced as **8** which is a *C1* conformation corresponding to the configuration **3**.

In the NMR spectrum (Fig. 2, D) of the last isomer VIID-d, the observed ring-proton coupling constants ($J_{1,2}=5.7$ and $J_{4,5a}=7.3$ Hz) reveal that H-1, H-2 and H-4 protons are all in axial orientation. The existence of two equatorial acetoxy groups is shown by the sharp singlet at τ 7.96, which is caused by overlapping of the two acetoxy signals. These results are confirmed by the NMR analysis for the triacetate (VIIID-d) of the free amino acid VID-d, which affords a spectrum of the AB and ABX type arising from the protons at the 1,2- and 4,5,5-positions, respectively (Fig. 3). Treating these protons as an isolated AB and ABX system, the following coupling constants are obtained; $J_{1,2}=8.3$, $J_{5a,5e}=12$, $J_{4,5e}=3.0$ and $J_{4,5a}=10.0$ Hz. From these results a possible partial conformation for VIID-d is to be considered as **9** which is a *1C* conformation corresponding to configuration **1**.

It is not possible to distinguish between the conformations **5** and **6** by the study of the ring proton resonances as described above. In other words, it remains unknown which of the configurations **1** and **3** is to be assigned for VIA-d. On the other hand, oxidation of the isomeric amino acids (VI-d) with chloramine-T yielded the corresponding methyl pentopyranosid-3-uloses (IX-d). They were isolated by preparative layer chromatography in the forms

5) L. D. Hall and L. Hough, *Proc. Chem. Soc.*, **1962**, 382; K. Heyns, J. Weyer and H. Paulsen, *Chem. Ber.*, **98**, 327 (1965); C. V. Holland, D. Horton and J. S. Jewell, *J. Org. Chem.*, **32**, 1818 (1967).

6) R. U. Lemieux, R. K. Kulling, H. J. Berstein and W. G. Schneider, *J. Am. Chem. Soc.*, **80**, 6098 (1958); F. W. Lichtenthaler and P. Emig, *Tetrahedron Letters*, **1967**, 577.

of their *p*-nitrophenylhydrazone derivatives which were characterized by IR spectra and mixed melting point determinations. The two same kinds of *p*-nitrophenylhydrazones, A_1 (mp 172°C dec., R_f 0.32) and A_2 (mp 174.5°C dec., R_f 0.43) were obtained from each of the oxidation products of VIA-d and VID-d. This indicates that the amino acids, VIA-d and VID-d are converted to a same methyl pentopyranosid-3-ulose by the chloramine-T oxidation and that VIA-d is the C-3 epimer of VID-d. The structures of the above-mentioned *p*-nitrophenylhydrazones can not be stated clearly at the present stage, because there must be considered the prototropy phenomenon which may be caused in the α-hydroxycarbonyl grouping[–(C=O)–CH(OH)–] of the oxidation products. However, the configuration **1** is to be assigned to VIA-d as well as to VID-d. The oxidation products of VIB-d and VIC-d afforded the *p*-nitrophenylhydrazones, B (mp 162—164°C dec., R_f 0.26) and C (mp 168°C dec., R_f 0.42), respectively, each of which was completely different from A_1 and A_2.

In conclusion, the above-mentioned experimental findings permit the assignment of the structural formulas **2** and **3** to VIB-d (major component)and VIC-d, respectively, and the formula **1** to VIA-d and VID-d, which are in epimeric relation with each other at C-3. The compound corresponding to the configuration **4** was not obtained.

Experimental

Paper chromatograms of amino acids were run with *n*-butanol - acetic acid - water (4 : 1 : 1) on Toyo Roshi No. 50 paper using an ascending technique, and spots were detected by means of a spray of a 0.5% pyridine solution of ninhydrin. Thin layer chromatography (TLC) and preparative layer chromatography (PLC) were conducted by the use of silica gel (Daiichi Pure Chemicals Co., Inc.). The prepared plates were activated at 110°C and the spray reagents used were 10% sulfuric acid and 0.5% pyridine solution of ninhydrin. Silica gel column chromatography was carried out by the use of silica gel (Kanto Chemical Co., Inc.) activated at 110°C before use. NMR spectra were taken with Japan Electron Optics JNM-4H-100 spectrometer and Varian A-60D spectometer at a frequency of 100 and 60 MHz by using about 10—20% solution of the sample in deuteriochloroform with tetramethylsilane as an internal standard.

Methyl (+)-3-Deoxy-3-*C*-ethoxycarbonyl-3-nitro-pentopyranoside (IV-d). Methyl β-L-arabinopyranoside[7] (I) (10.0 g, 0.061 mmol) was added in small portions to a stirred solution of periodic acid (27.8 g, 0.122 mmol based on H_5IO_6) in 500 m*l* of water at 20°C. The reaction mixture was allowed to stand for 20 hr at room temperature and was neutralized (pH 5) with hot 0.244 M strontium hydroxide solution (250 m*l*, 0.061 mol). The precipitate was removed by filtration and was washed with ethanol. The filtrate and washings were evaporated to afford the syrupy D'-methoxy-diglycolaldehyde (III-d), which was dissolved in ethanol (100 m*l*) and was filtered to remove a small amount of undissolved matter. The ethanolic solution of III-d was stirred under ice-cooling, while ethyl nitroacetate (8.1 g, 0.061 mol), 40% aqueous potassium acetate solution (14.2 m*l*) and 40% aqueous potassium carbonate solution (8.8 m*l*) were added successively. After the mixture was stirred in an ice bath for 3 hr, Amberlite IR-120 (100 m*l*) was added and was stirred for an additional one hour. The resin was removed by filtration and the filtrate (pH 4) was evaporated in a vacuum to afford a yellow syrup (14.6 g) of the title compound (IV-d). The product was purified through a silica gel (123 g) column. Elution with benzene-acetone (6 : 1) afforded 13.1 g (81%) of the pure nitro ester IV-d, $[\alpha]_D^{32}$ +157° (*c* 0.58, water), ν_{max}^{Film} 3455(OH), 1750 (ester C=O) and 1564 cm^{-1} (NO_2).

Found: C, 41.08; H, 5.91; N, 5.30%. Calcd for $C_9H_{15}NO_8$: C, 40.75; H, 5.70; N, 5.28%.

Di-*O*-acetyl Derivative of IV-d. A mixture of the nitro ester (IV-d) (136 mg), pyridine (6 m*l*) and acetic anhydride (2 m*l*) was allowed to stand overnight at room temperature. The reaction mixture was poured into ice-water and the liberated oil was extracted with four 10 m*l* portions of chloroform. The extracts were evaporated and the last trace of pyridine was removed by co-distillation with toluene. The residue was purified through a silica gel (20 g) column. Elution with benzene-acetone (10 : 1) afforded the title compound as a yellow syrup, yield 151 mg (84.5%), $[\alpha]_D^{32}$ +164° (*c* 0.9, ethyl acetate). The acetate was shown to be a mixture of diastereoisomers by its NMR spectrum. The NMR signals for the main isomer were observed at τ ($CDCl_3$): 7.84 and 7.92 (singlets, acetoxy protons); 6.62 (singlet, glycoside methyl protons); 5.60 (quartet, J=7.5 Hz, ester methylene protons); 8.67 (triplet, ester methyl protons); 6.06 and 5.62 (doublets, J=3.5 Hz, H-1 and H-2 proton); 6.19 (quartet, J=2.0 and 2.5 Hz, H-4 proton); 5.58 (quartet J=2.5 and 14.0 Hz, H-5 proton) and 6.12 (quartet J=2.0 and 14.0 Hz, H-5 proton).

Found: C, 44.95; H, 5.83; N, 4.13%. Calcd for $C_{13}H_{19}NO_{10}$: C, 44.69; H, 5.49; N, 4.01%.

Methyl (–)-3-Deoxy-3-*C*-ethoxycarbonyl-3-nitro-pentopyranoside (IV-1). Methyl β-D-xylopyranoside[8] (II) (9.0 g, 0.055 mol) was oxidized with a solution of periodic acid (25 g, 0.11 mol) in 300 m*l* of water by the same procedure as described for the preparation of III-d. A solution of the resulting L'-methoxy-diglycolaldehyde (III-l) in ethanol (120 m*l*) was stirred under ice-cooling, while ethyl nitroacetate (7.3 g, 0.055 mol), 40% aqueous potassium acetate solution (15 m*l*) and 40% aqueous potassium carbonate solution (10 m*l*) were added successively. The mixture was then worked up by the same procedure as described for the preparation of the nitro ester IV-d. The purified title compound IV-1 was obtained as a syrup, yield 13.7 g (94%), $[\alpha]_D^{20}$ –123° (*c* 1.14, water), ν_{max}^{Film} 3455 (OH), 1750 (ester C=O) and 1564 cm^{-1} (NO_2).

7) F. Smith and J. W. Cleve, *J. Am. Chem. Soc.*, **77**, 3159 (1955).

8) M. L. Wolfrom, J. W. Spoors and R. A. Gibbons, *J. Org. Chem.*, **22**, 1513 (1957).

Methyl (+)-3-Amino-3-deoxy-3-*C*-ethoxycarbonylpentopyranoside (V-d). A solution of methyl (+)-3-deoxy-3-*C*-ethoxycarbonyl-3-nitropentopyranoside (IV-d) (9.79 g) was hydrogenated in ethanol (45 m*l*) with Raney Ni T-4 (30 m*l*) for 4.5 hr under 120 kg/cm² of an initial hydrogen pressure at 20—25°C. The contents were then filtered to remove the catalyst and the filtrate was evaporated in a vacuum to afford the crude V-d (6.93 g) as a brown syrup. The sample was shown by TLC using ethyl acetate to contain four diastereoisomeric amino esters, each of which was ninhydrin positive.

Separation of Diastereoisomers of V-d. The brown syrup (6.92 g) in a small amount of ethyl acetate was placed on a silica gel column (300 g, 5×43 cm) and eluted with ethyl acetate - ethanol (6 : 1). Fractions (*ca.* 10 m*l*) were collected and examined by TLC. Fractions, 113—123, 127—135, 138—157 and 163—185 gave the isomers, VA-d (syrup, 0.92 g, R_f 0.73), VB-d (crystalline solid, 2.76 g, R_f 0.55), VC-d (syrup, 0.64 g, R_f 0.36) and VD-d (crystalline solid, 0.56 g, R_f 0.23), respectively. Total yield was 47.5% based on the original nitro ester IV-d. The analytical sample of VB-d was obtained by two recrystallizations from ethyl acetate, followed by sublimation (90—110°C/1.5 mmHg), while the analytical sample of VD-d was given by only two recrystallizations from ethyl acetate (Table 1).

Methyl (−)-3-Amino-3-deoxy-3-*C*-ethoxycarbonylpentopyranoside (V-l) and Its Diastereoisomeric Separation. The nitro ester (IV-l) (9.95 g) was hydrogenated with Raney Ni T-4 (30 m*l*) as described on the preparation of the antipode V-d. The obtained brown syrup (7.75 g) of the crude V-l was chromatographed on a silica gel column (250 g, 4.5×40 cm). Elution with ethyl acetate - ethanol (6 : 1) afforded four isomers, VA-l (syrup, 1.39 g, R_f 0.73), VB-l (crystalline solid, 2.45 g, R_f 0.55), VC-l (syrup, 1.30 g, R_f 0.36) and VD-l (crystalline solid, 1.19 g, R_f 0.23). The analytical sample of VB-l was obtained by two recrystallizations from ethyl acetate, followed by sublimation (110—120°C/3 mmHg), while the pure sample of VD-l was given by two recrystallizations from ethyl acetate (Table 1).

Methyl (+)-3-Acetamido-2,4-di-*O*-acetyl-3-deoxy-3-*C*-ethoxycarbonylpentopyranoside (VIIB-d). *(A Typical Example of the General Method for the Preparation of Isomeric Amino Ester Triacetate).* A mixture of the amino ester (VB-d) (297 mg), acetic anhydride (4 m*l*) and pyridine (12 m*l*) was allowed to stand for 2 days at room temperature. The mixture was evaporated in a vacuum. The semi-crystalline residue (498 mg) was purified through a silica gel (10 g) column. Elution with methyl ethyl ketone - *n*-hexane (1 : 1) afforded crystalline title compound (VIIB-d), yield 379 mg (83%), mp 115—117°C. Recrystallization from diisopropyl ether-acetone (20 : 1) yielded an analytically pure sample of VIIB-d, mp 118—120°C.

The other triacetates of the isomeric amino esters, VIIA-d, VIIC-d, VIID-d, VIIA-l, VIIB-l and VIID-l were prepared from the corresponding amino esters by the general procedure (Table 1).

Methyl (+)-3-Amino-3-*C*-carboxy-3-deoxypentopyranoside (VIB-d) *(A Typical Example of the General Procedure for the Preparation of the Isomeric Free Amino Acids).* The amino ester (VB-d) (230 mg, 0.98 mmol) was dissolved in a 0.457N barium hydroxide solution (2.32 m*l*, 0.53 mmol). After the solution had been allowed to stand for 20hr at 37°C in an incubator, the reaction mixture was treated with 1N sulfuric acid. The supernatant layer which was separated from barium sulfate by centrifuging was evaporated in a vacuum. The residual colorless powder was recrystallized from water-acetone to afford crystalline amino acid VIB-d (180 mg, 87.3%), from which an analytical sample was obtained by two recrystallizations from water-acetone, followed by drying over phosphorus pentoxide for 5 hr at 105—110°C/3 mmHg. (Table 2).

The other amino acid isomers, VIA-d, VIC-d and VID-d and their enantiomeric amino acids VIA-l, VIB-l and VID-l were prepared from the corresponding amino esters by the general procedure (Table 2).

Methyl (+)-3-Acetamido-2,4-di-*O*-acetyl-3-*C*-carboxy-3-deoxypentopyranoside (VIIID-d). The amino acid (VID-d) (40 mg) was acetylated with acetic anhydride (0.5 m*l*) and pyridine (1.5 m*l*) at room temperature overnight. After the mixture was evaporated in a vacuum, the crystalline residue was recrystallized from acetone - diisopropyl ether to afford a pure sample of VIIID-d, yield 25 mg (38.8%), mp 203—204°C, $[\alpha]_D^{26}$ +44° (*c* 0.7, Ethyl acetate).

Found: C, 46.85; H, 6.11; N, 4.11%, Calcd for $C_{13}H_{19}NO_9$: C, 46.83; H, 5.76; N, 4.20%.

Chloramine-T Oxidation *Oxidation of VIA-d.* To a solution of the amino acid (VIA-d) (80 mg 0.39 mmol) in water (1 m*l*) was added chloramine-T (109 mg, 0.39 mmol), and the mixture was shaken for 1 hr. The reaction mixture was filtered to remove an insoluble material. The filtrate was mixed with a solution of *p*-nitrophenylhydrazine hydrochloride (80 mg, 0.43 mmol) in methanol (1 m*l*) and was allowed to stand overnight. The orange-yellow precipitate was separated by centrifuging and was subjected to PLC [1 plate (20 cm×20 cm×0.8 mm), benzene - ethyl acetate (2 : 1)] and two kinds of *p*-nitrophenylhydrazones, A_1 (R_f 0.32) and A_2 (R_f 0.42) were obtained as crystals. They were recrystallized from ethyl acetate-ether: A_1, mp 172°C dec., ν_{max}^{KBr} 1593, 1538, 1501, 1470 and 1415 cm^{-2}; A_2 mp 174.5°C dec., ν_{max}^{KBr} 1595, 1504, and 1487 cm^{-1}.

Oxidation of VID-d was worked up by the same procedure as mentioned above. The oxidation product afforded the two kinds of crystalline *p*-nitrophenylhydrazone, which were identical with the above-mentioned *p*-nitrophenylhydrazones, A_1 and A_2 on the basis of melting points and IR spectra.

Oxidation of VIB-d and VIC-d were also carried out by the same procedure as described above to give crystalline *p*-nitrophenylhydrazones, B and C, respectively: B, mp 162—164°C dec. (from ethyl acetate), R_f 0.26, ν_{max}^{KBr} 1602, 1520, 1500, 1472, 1448 and 1407 cm^{-1}; Found: C, 49.26; 5.47; N, 13.71%. Calcd for $C_{12}H_{15}N_3O_6$: C, 48.48; H, 5.09; N, 14.14%; mp 168°C dec. (from ethyl acetate-ether), R_f 0.42, ν_{max}^{KBr} 1597, 1517, 1495 and 1468 cm^{-1}.

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