Regio- and Stereo-Selective Transformation of Glycosides to Amino-glycosides[1]: Practical Synthesis of Amino-sugars, 4-Amino-4-deoxy-D-galactose, 4-Amino-4-deoxy-L-arabinose, 3-Amino-3-deoxy-D-allose, 3-Amino-3-deoxy-D-glucose, 3-Amino-3-deoxy-D-ribose, 3-Amino-3-deoxy-D-xylose, 2-Amino-2-deoxy-D-mannose, and 5-Amino-5-deoxy-D-glucose (Nojirimycin)[2]

Yoshisuke TSUDA,* Yukihiro OKUNO, Minoru IWAKI, and Kimihiro KANEMITSU[3]

Faculty of Pharmaceutical Sciences, Kanazawa University, 13-1 Takara-machi, Kanazawa 920, Japan. *Received March 27, 1989*

One of the hydroxyl groups in glycosides was regio- and stereo-selectively converted to an amino group as follows. A glycoside was regioselectively converted to an oxo-glycoside by bis-tributyltin oxide–bromine oxidation. Oximation of this and reduction of the resulting oxime in a stereoselective manner gave an amino-glycoside in a satisfactory yield.

By application of this method, 4-amino-4-deoxy-D-galactose, 4-amino-4-deoxy-L-arabinose, 3-amino-3-deoxy-D-allose, 3-amino-3-deoxy-D-glucose, 3-amino-3-deoxy-D-ribose, 3-amino-3-deoxy-D-xylose, and 2-amino-2-deoxy-D-mannose were synthesized in satisfactory yields from D-xylose or D-glucose as their α- or β-methyl glycosides. The method also provided a practical synthetic route to nojirimycin (5-amino-5-deoxy-D-glucose), a glucosidase-inhibitory antibiotic, from D-glucose.

Keywords oxo-glycoside; amino-glycoside; regioselective oxidation; stereoselective reduction; oximation; amino-sugar; nojirimycin; ^{13}C-NMR

In a preceding paper[1] we reported that glycosides were smoothly oxidized by bis-tributyltin oxide and bromine to give oxo-glycosides, usually in high yields, in which a particular hydroxyl group had been oxidized selectively. Regioselectivity in this oxidation can be predicted by simple rules: anomeric control (the glycosides with an axial glycosidic linkage are oxidized at C-4 and those with an equatorial glycosidic linkage are oxidized at C-3) and axial oxidation of a *cis*-1,2-glycol. The implication is that when the oximes derived from the oxo-glycosides are reduced to amino compounds in a stereoselective manner, the overall process provides a new method converting a glycoside-hydroxyl group to an amino group, thus opening a new route to hardly available amino-sugars from easily available glycosides. With the hope of exploiting this practical route to amino-sugars, we examined the reactions on various glycosides.

Results and Discussion

Oxidation of glycosides was done as described in a previous paper.[1] Since the resulting oxo-glycoside and its dimers are known to give the same oxime on oximation, the products were used without further purification.

Oximation was done with *O*-methylhydroxylamine for the product analysis (and with hydroxylamine for preparative purposes), since the resulting *O*-methyloximes are easily separable from the unchanged oxo-glycosides (and the dimers) on chromatography. The yield was satisfactory in every case. The results are shown in Table I.

3- and 4-Amino-glycosides The *O*-methyloximes, **1** and **2**, derived from 3-oxo-glycosides were mixtures of *E* and *Z* forms. This fact was suggested by their proton nuclear magnetic resonance (^{1}H-NMR) spectra, although thin layer chromatography (TLC) and gas chromatography (GC) of the trimethylsilyl (TMS) derivatives often gave only one spot or one peak, and was conclusively indicated by their carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectra (Table II), which showed pairs of the peaks for the mixtures. The others were single isomers.

Most of the *O*-methyloximes except for **3** had *C1* confor-

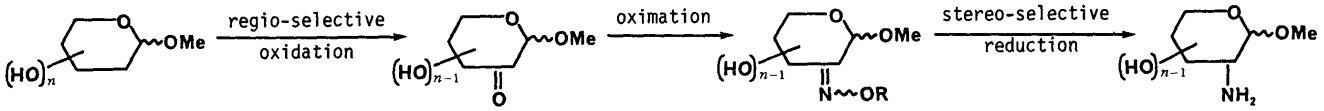

Chart 1. Amino-glycosides from Glycosides (General Scheme)

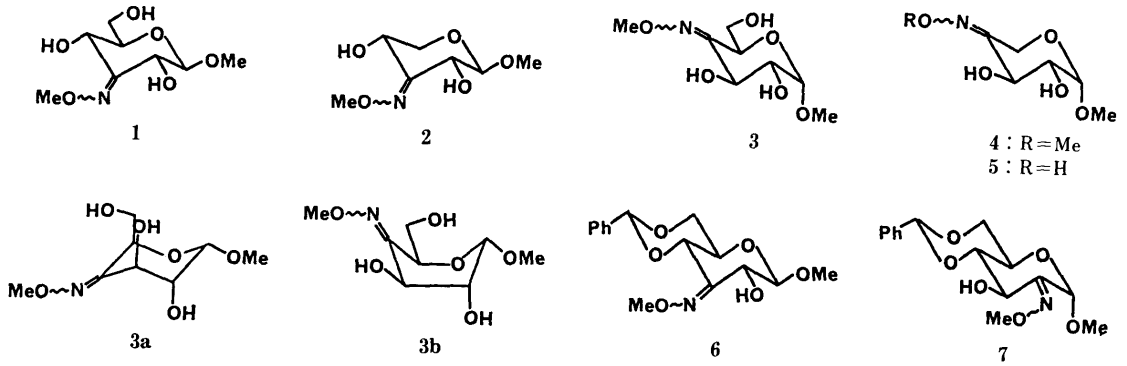

Chart 2

TABLE I. *O*-Methyloximes, Yield and Characterization

Compd.	Yield (%)	mp (°C)	TLC	GC[a]	C–OMe[b]	N–OMe[b]
1	86	Syrup	Two spots	One peak	3.45, 3.49	3.77, 3.80
2	73	Syrup	One spot	Two peaks	3.33, 3.34	3.79
3	79	78—80	One spot	One peak	3.53	3.79
4	68	Syrup	One spot	One peak	3.45	3.86
6	93	166—171	One spot	One peak	3.42	3.78
7	95	178—180	One spot	One peak	3.45	3.94

a) TMS derivative. *b*) ^{1}H-NMR in pyridine-d_5.

TABLE II. ^{13}C-NMR of *O*-Methyloximes in Pyridine-d_5

Compd.	C-1	C-2	C-3	C-4	C-5	C-6	OMe	N–OMe
1	104.5	71.4	156.0	65.1	81.1	62.5	56.0	61.6
	103.5	68.4	155.3	66.6	79.0	62.5	55.7	61.6
2	103.1	70.9	153.4	66.1	63.3		54.6	61.5
	102.7	68.9	153.4	64.9	61.4		54.6	61.5
3	98.3	73.8	72.0	156.5	71.6	62.0	56.3	61.8
4	101.1	74.2	70.5	156.2	55.9		55.7	61.8
6	105.5	75.7	146.8	71.3	67.2	69.3	57.1	63.4
7	92.1	151.4	68.5	83.6	62.3	68.5	55.3	62.7

TABLE III. Stereoselectivity in Reduction of *O*-Methyloximes

Substrate	Hydrogenation		AlH_3 reduction	
	Yield (%)	Ax. Eq.	Yield (%)	Ax. Eq.
1	67[a]	7:1	61	1:2
2	87[a]	7:3	52	Eq. only
6	53[b]	Ax. only	51	4:1
3	90[a]	6:1	66	2:1
4	77[a,b,c]	7:1	59	5:1
5	76[a]	7:1		
7	63[b]	3:1	87	5:1

a) Over PtO_2 in acetic acid. *b*) Over Raney Ni in EtOH. *c*) Contaminated with an unidentified compound.

mations, as expected. The 4-*O*-methyloxime **3** derived from methyl α-D-glucoside was suggested unexpectedly to have either $_4C^1$ (**3a**) or $^4B^1$ (**3b**) conformation, since the coupling constant between H_2 and H_3 was 3.4 Hz.

The oximes (without separation of *E* and *Z* forms) were reduced by two methods; a) aluminum hydride reduction and b) catalytic hydrogenation over PtO_2 in acetic acid, and the product was analyzed by GC (as the TMS derivative)

TABLE IV. ^{13}C-NMR of Amino-glycosides (*N*-Acetate) in Pyridine-d_5

Compd.	C-1	C-2	C-3	C-4	C-5	C-6	OMe	–CO–CH_3
8b	103.3	70.5	51.3	68.8	78.7	62.8	56.1	172.5 23.1
9b	105.5	73.1	59.1	69.5	78.9	62.0	56.5	174.3 23.2
10b	102.3	70.5	47.1	69.0	64.8		54.8	172.2 23.2
11b	106.3	72.3	59.2	70.0	67.6		56.5	173.5 23.3
12b	101.3	71.0	69.6	52.4	70.6	61.9	55.1	172.7 22.8
13b	101.3	73.7	72.6	53.3	71.8	62.4	55.1	174.0 23.1
14b	101.3	70.6	69.6	50.7	62.1		55.5	172.0 23.2

TABLE V. ^{13}C-NMR of Amino-glycosides (Peracetate) in Chloroform-*d*

Compd.	C-1	C-2	C-3	C-4	C-5	C-6	OMe	C-7[a]
8c	99.5	69.3	44.7	67.4	72.1	63.1	56.5	
9c	102.0	71.7	53.4	68.7	72.7	62.1	57.0	
10c	97.9	69.5	43.5	68.7	60.4		55.3	
11c	101.0	70.3	50.7	68.6	61.8		56.5	
12c	97.0	68.5	68.1	48.4	66.3	62.6	55.4	
13c	96.8	70.9	70.0	50.6	69.0	63.1	55.3	
14c	97.5	68.7	67.8	48.0	60.9		55.6	
15c	97.0	70.9	70.0	50.6	59.7		55.3	
16c	100.2	50.3	69.1	66.1	67.9	62.5	55.3	
17c	98.3	51.9	71.3	68.2	67.6	62.0	55.3	
18c	100.0	70.5	48.4	75.6	64.9	69.2	57.0	101.4
19c	101.6	72.7	52.8	78.6	67.8	68.6	57.1	102.4
20c	101.2	50.8	68.8	76.8	63.4	68.3	55.2	102.2
21c	99.0	52.6	70.3	79.0	62.8	68.9	55.3	101.6

a) Benzylidene carbon.

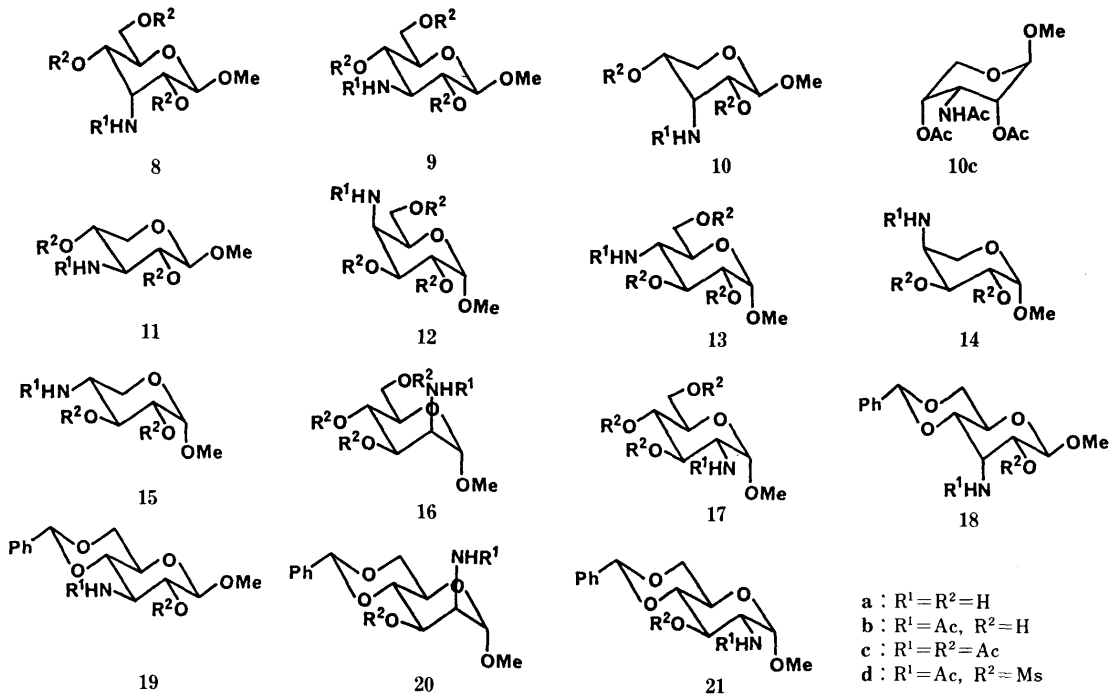

Chart 3

and ^{13}C-NMR after conversion to the *N*-acetates. The structure of each product was further confirmed by isolation as the peracetate. Table III shows the results.

As expected, method a) yielded an equatorial and method b) gave an axial amino group preferentially for the 3-oximes, while the 4-oximes gave axial isomers preferentially in either reduction, although the ratio was different depending on the reduction method. This is consistent with the fact that 4-oxo-glycosides gave 4-axial hydroxy isomers equally or preferentially to the 4-equatorial isomers on $NaBH_4$ reduction and exclusively gave 4-axial hydroxy isomers on hydrogenation over PtO_2 in acetic acid.[1]

In the GC of *N*-acetyl derivatives (TMS derivatives) the axial isomers always moved faster than the corresponding equatorial isomers except for the pair of **14** and **15**, where the equatorial isomer **15** moved faster than the axial isomer **14**. The stereochemistries of this pair therefore required chemical proof.

This was done as follows. Similar hydrogenation of the 4-oxime **5** gave **14a** in 7-fold preference over **15a**. Compound **14a** was converted to the *N*-acetyl-*O*,*O*-dimesylate **14d** by *N*-acetylation followed by methanesulfonylation. The resulting product was identical with an authentic sample prepared from methyl α-D-xylopyranoside by the known procedure,[4] thus proving the stereochemistry of **14**.

We have thus opened a practical synthetic route to 3-amino-3-deoxy-D-allose, 3-amino-3-deoxy-D-glucose, 3-amino-3-deoxy-D-ribose, 3-amino-3-deoxy-D-xylose, 4-amino-4-deoxy-D-galactose, and 4-amino-4-deoxy-L-arabinose as their α- or β-methyl glycosides. Most of these amino-sugars are found in antibiotics[5] or lipopolysaccharide of micro-organisms[6] and are usually not readily accessible synthetically.

A comment should be made on the conformation of methyl 3-amino-3-deoxy-β-D-riboside **10**, whose triacetate exhibited an anomeric proton signal at δ 4.73 as a broad singlet, thus suggesting that it adopts the *1C* conformation **10c**. The 400 MHz NMR spectra of the other amino-glycosides (as the acetates) are consistent with *C1* conformations.

2-Amino-2-deoxy-D-mannose (Mannosamine) Oxidation of methyl 4,6-*O*-benzylidene β- or α-D-glucopyranoside gave the 3-oxo or 2-oxo derivative, respectively, in high yield, as a sigle product.[1] These were converted to single *O*-methyloximes, **6** and **7**, respectively, in excellent yields.

Reduction of the 4,6-*O*-benzylidene 3- or 2-*O*-methyloximes, **6** or **7**, with AlH_3 or catalytic hydrogenation over Raney Ni in ethanol always produced the axial isomer, **18** or **20**, preferentially over the corresponding equatorial isomer, **19** or **21**, though the stereoselectivity was different depending on the method and the substrate (Table III). The structure of each product was confirmed by converting them into the acetates, **8c**, **9c**, **16c**, and **17c**, after removal of the benzylidene group.

Hydrogenation of the 3-*O*-methyloxime **6** gave the *allo* derivative. **18** as a single product. Interestingly and rather unexpectedly, aluminum hydride reduction of the 2-*O*-methyloxime **7** gave the axial (*manno*) derivative **20** more stereoselectively (5 : 1) than the hydrogenation. Since the total yield of oxidation, oximation, and AlH_3 reduction of methyl 4,6,-*O*-benzylidene-α-D-glucopyranoside is satisfactory, this transfomation provides an efficient route to mannosamine.

5-Amino-5-deoxy-D-glucose (Nojirimycin)[7] The 5-amino-5-deoxy derivatives of D-glucose and L-idose, **24** and **25**, were stereoselectively synthesized as follows.

Oxidation of 1,2-*O*-isopropylidene-α-D-glucofuranose gave the 5-oxo derivative **22** in 92% yield.[1] Treatment of **22** with *O*-methylhydroxylamine hydrochloride in the presence of $NaHCO_3$ gave two *O*-methyloximes, **23a** (mp 74—76 °C) and **23b** (oil), in a ratio of 1 : 2.5. On the other hand, a similar oximation in the presence of 5 mol eq of Na_2CO_3 gave **23a** and **23b** in a ratio of 1.6 : 1. Each oxime gave the same equilibrium mixture (**23a**/**23b** = 1 : 3.5), on treatment with a catalytic amount of *p*-TsOH in methanol, indicating that **23a** is a kinetically controlled and **23b** is a thermodynamically controlled product. Their configurations were determined by the X-ray analysis of the crystalline isomer **23a** (Fig. 1), which indicated that this isomer **23a** is of *E*-configuration, existing in two forms (A and B in Fig. 1)[8] in the crystalline state. Therefore, the other isomer **23b** must be the *Z*-isomer.

These oximes behaved differently in reductions. The stereoselectivity in reductions (*gluco*/*ido* ratio) relative to

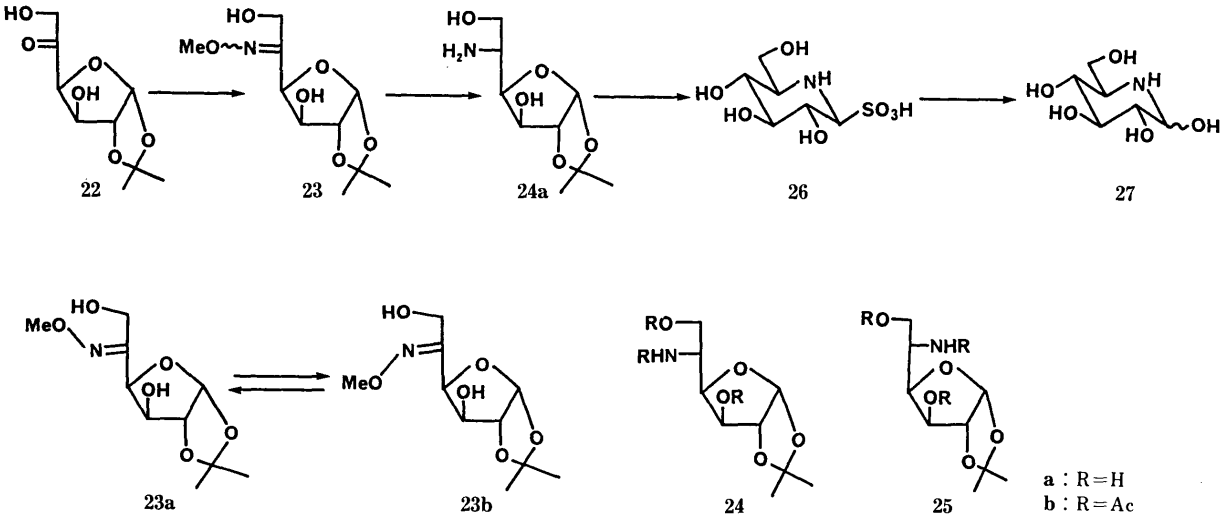

Chart 4

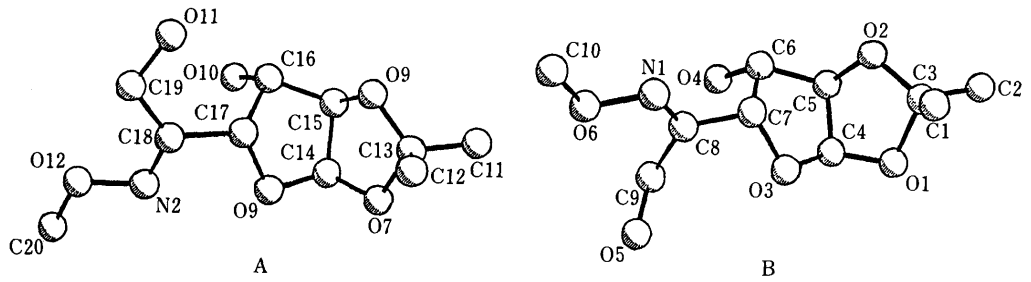

Fig. 1. The Crystal Structures of the *E*-*O*-Methyloxime **23a**

TABLE VI. Stereoselectivity in Reduction of **23** (*gluco***24**/*ido***25** Ratio)[a]

Substrate	Reducing agent					
	$Me_2S \cdot BH_3$	LAH/ ether	LAH/ THF	LAH/ DME	AlH_3/ THF	H_2/Raney Ni
23a (*E*)	1.0	0.33	0.45	1.0	0.43	—
23b (*Z*)	1.0	1.5	1.0	3.0	4.0	1.7

a) Determined by GC after conversion to the triacetates.

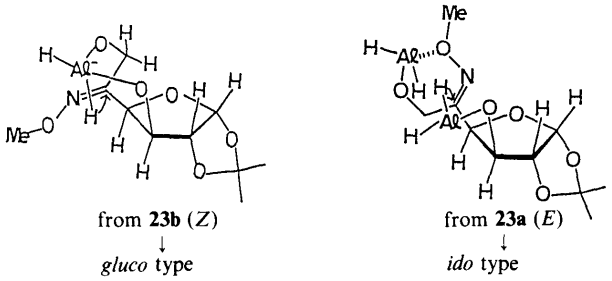

Fig. 2. Supposed Stereochemical Paths in Reduction of the *O*-Methyloximes **23**

the stereochemistry of oximes and the nature of reducing agents is summarized in Table VI. In particular, reduction of **23b** with AlH_3 in tetrahydrofuran (THF) gave the *gluco*-isomer **24** over the *ido*-isomer **25** with a 4 : 1 stereoselectivity, while reduction of **23a** with lithium aluminum hydride (LAH) in ether gave the *ido*-isomer **25** in 3-fold excess over the *gluco*-isomer **24**. This high *gluco*-selectivity in the reduction of the *Z*-isomer **23b** may be explained by an intramolecular hydride attack from the aluminum-chelated species adopting the most stable conformation as depicted in Fig. 2. On the other hand, in LAH reduction of **23a**, 2 mol of aluminum may participate, and an intramolecular hydride attack may occur from the less hindered face of the nitrogen-containing ring.

Thus, reduction of the equilibrium mixture of **23a** and **23b** with LAH in dimethoxyethane gave the 5-amino derivatives with a *gluco* (**24**)/*ido* (**25**) ratio of 2 : 1.

The ratio of the reduction product was determined by GC of the triacetate, and their configurations were determined as follows. i) **24** gave a positive Cotton effect in circular dichroism (CD) at 310 nm when measured in the presence of salicylaldehyde.[9] ii) The triacetate **24b**, mp 150—151 °C, gave a smaller retention time in GC than the isomer **25b**, mp 92—96 °C, in accordance with the relative mobilities of the triacetates of 1,2-*O*-isopropylidene-α-D-*gluco*- and β-L-*ido*-furanose. This assignment was finally confirmed by actual transformation of **24** to nojirimycin.

On keeping the above *gluco*/*ido* mixture in methanol saturated with sulfur dioxide, a precipitate appeared of the crystalline bisulfite adduct, which was identical with nojirimycin bisulfite adduct **26**.[9,10] The overall yield of **26** from the starting 1,2-*O*-isopropylidene-α-D-glucofuranose was *ca.* 50%. Since the bisulfite adduct **26** is quantitatively convertible to 5-amino-5-deoxy-D-glucose (nojirimycin) **27**,[9] the present investigation opened a practical route to a biologically important antibiotic, nojirimycin **27**, from 1,2-*O*-isopropylidene-α-D-glucofuranose without requiring chromatographic separation of stereoisomers at any synthetic stage.[11]

Experimental

Unless otherwise stated, the following procedures were adopted. Melting points were determined on a Yanaco micro hot stage melting point apparatus and are uncorrected. Infrared (IR) spectra were taken in KBr disks, recorded on a Jasco IRA-2 spectrometer, and the data are given in cm^{-1}. ^{1}H-NMR spectra (400 MHz) were taken with a JEOL GX-400 and ^{13}C-NMR spectra (25 MHz) with a JEOL FX-100 spectrometer in chloroform-*d* solution with tetramethylsilane as an internal standard, and the chemical shifts are given in δ values. GC analyses were carried out with a Shimadzu GC4CM-PF gas chromatograph with an FID detector, using a column (2 m × 3 mm i.d.) packed with 1.5% OV-1 on Shimalite W (80—100 mesh) and N_2 (50—80 ml/min) as a carrier gas. The TMS derivatives were prepared by the method of Sweeley *et al.*[12] Mass spectra (MS) were taken with a Hitachi M-80 machine and peaks are indicated as *m/z*. Column chromatography was performed on Fuji-Davison Silica gel BW-820MH and medium pressure liquid chromatography (MPLC) on Merck LiChroprep Si 60. For TLC, Macherey-Nagel precoated TLC plates G25 UV_{254} were used and spots were developed by spraying 1% $Ce(SO_4)_2$ in 10% H_2SO_4 and heating the plates at 100 °C until coloration took place.

***O*-Methyloximation of Oxo-glycosides (General Procedure)** Oxo-glycosides (0.5—1.0 g), *O*-methylhydroxylamine hydrochloride (1.5 mol eq), and $NaHCO_3$ (1.5 mol eq) in methanol (20—40 ml) were heated under reflux for 1—2 h. After filtration to remove inorganic salts and evaporation of the solvent from the filtrate, the residue was extracted with hot ethyl acetate and the extract was passed through a short silica gel column to yield the *O*-methyloximes.

(1) Methyl α-D-*xylo*-4-Hexulopyranoside *O*-Methyloxime 3 Colorless needles from ethyl acetate–ether, mp 78—80 °C. ^{1}H-NMR: 4.20 (1H, dd, *J*=2.7, 11.6 Hz, H-6), 4.40 (1H, dd, *J*=5.8, 11.6 Hz, H-6), 4.47 (1H, dd, *J*=3.1, 3.4 Hz, H-2), 4.86 (1H, d, *J*=3.4 Hz, H-3), 5.38 (1H, d, *J*=3.1 Hz, H-1), 5.44 (1H, dd, *J*=2.7, 5.8 Hz, H-5). MS: 222 (M^++1), 191 (M^++1 −OMe), 74 (100%). *Anal.* Calcd for $C_8H_{15}NO_6$: C, 43.43; H, 6.84; N, 6.63. Found: C, 43.14; H, 6.96; N, 6.31.

(2) Methyl 4,6-*O*-Benzylidene-β-D-*ribo*-3-hexulopyranoside *O*-Methyloxime 6 Colorless needles from ethyl acetate–hexane, mp 166—171 °C. MS: 310 (M^++1), 278 (M^+−OMe), 107 (100%). *Anal.* Calcd for $C_{15}H_{19}NO_6$: C, 58.24; H, 6.19; H, 4.53. Found: C, 58.17; H, 6.17; N, 4.02.

(3) Methyl 4,6-*O*-Benzylidene-α-D-*arabino*-2-hexulopyranoside *O*-Methyloxime 7 Colorless needles from ethyl acetate–hexane, mp 178—180 °C. MS: 308 (M^+−1), 278 (M^+−OMe), 131 (100%). *Anal.* Calcd for $C_{15}H_{19}NO_6$: C, 58.24; H, 6.19; N, 4.53. Found: C, 58.24; H, 6.14; N, 4.57.

Hydrogenation of *O*-Methyloximes over PtO_2 in Acetic Acid (General Procedure) *O*-Methyloxime (0.2—0.3 g) in acetic acid (20 ml) was hydrogenated over platinic oxide (0.1 g) under hydrogen (4—5 kg/cm^2) for 24 h at room temperature. Removal of the catalyst and the solvent left a gum, a

part of which was dissolved in *tert*-BuOH–H_2O (10:1) and treated with acetic anhydride for 12 h at room temperature. The product obtained by concentration was dissolved in $CHCl_3$–MeOH (4:1) and purified by passing it through a silica gel column. The resulting *N*-acetate was analyzed by GC (as the TMS-derivative) and by ^{13}C-NMR.

The other part of the hydrogenation product was fully acetylated on treatment with pyridine–acetic anhydride overnight and worked up in the usual way. The resulting peracetate was purified by MPLC to yield the axial and equatorial isomers.

Reduction of *O*-Methyloximes with Aluminum Hydride (General Procedure) Aluminum hydride in THF solution was prepared by addition of concentrated H_2SO_4 to $LiAlH_4$ in THF at 0 °C and stirred for 30 min.[13] This solution (5 mol eq) was added dropwise to a stirred THF solution of an *O*-methyloxime and the stirring was continued overnight at room temperature. After decomposition of the excess reagent with water, $NaHCO_3$ was added, the mixture was filtered, and the filtrate was concentrated. A part of the product was *N*-acetylated and the other part was fully acetylated, and analyzed as described above.

(1) Methyl 3-Acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-β-D-allopyranoside 8c Colorless plates from ethyl acetate–hexane, mp 180—183 °C. IR: 1739, 1647. ^1H-NMR: 2.03, 2.08, 2.10, 2.11 (each 3H, s, Ac), 3.48 (3H, s, OMe), 4.03 (1H, q, J=5.5 Hz, H-5), 4.28 (1H, dd, J=5.5, 11.7 Hz, H-6), 4.32 (1H, dd, J=5.5, 11.7 Hz, H-6), 4.65 (1H, d, J=4.4 Hz, H-1), 4.86—4.90 (2H, H-2), 5.01 (1H, m, H-4), 5.79 (1H, d, J=8.1 Hz, NH). MS: 362 (M^++1), 101 (100%). *Anal.* Calcd for $C_{15}H_{23}NO_9$: C, 49.86; H, 6.42; N, 3.88. Found: C, 49.71; H, 6.62; N, 3.81.

(2) Methyl 3-Acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-β-D-glucopyranoside 9c Colorless needles from ethyl acetate–hexane, mp 163—164 °C (lit. mp 160 °C).[14] IR: 1742, 1655. ^1H-NMR: 1.90, 2.04, 2.07, 2.08 (each 3H, s, Ac), 3.52 (3H, s, OMe), 3.76 (1H, ddd, J=2.2, 4.8, 10.3 Hz, H-5), 4.14 (1H, dd, J=2.2, 12.1 Hz, H-6), 4.32 (1H, dd, J=4.8, 12.1 Hz, H-6), 4.36 (1H, q, J=10.3 Hz, H-3), 4.47 (1H, d, J=7.7 Hz, H-1), 4.75 (1H, dd, J=7.7, 10.3 Hz, H-2), 4.88 (1H, t, J=10.3 Hz, H-4), 5.57 (1H, d, J=10.3 Hz, NH). MS: 362 (M^++1), 330 (M^+−OMe), 101 (100%). *Anal.* Calcd for $C_{15}H_{23}NO_9$: 49.86; H, 6.42; N, 3.88. Found: C, 49.60; H, 6.43; N, 3.67.

(3) Methyl 3-Acetamido-2,4-di-*O*-acetyl-3-deoxy-β-D-ribopyranoside 10c Colorless prisms from ethyl acetate–hexane, mp 152—154 °C. IR: 1740, 1714, 1671. ^1H-NMR: 1.99, 2.17, 2.18 (each 3H, s, Ac), 3.40 (3H, s, OMe), 3.82 (1H, dd, J=1.5, 13.2 Hz, H-5), 3.95 (1H, dd, J=1.8, 13.2 Hz, H-5), 4.69 (1H, dt, J=3.7, 8.8 Hz, H-3), 4.73 (1H, br s, H-1), 4.83 (1H, d, J=3.7 Hz, H-2), 4.94 (1H, m, H-4), 5.81 (1H, d, J=8.8 Hz, NH). MS: 290 (M^++1), 186 (100%). *Anal.* Calcd for $C_{12}H_{19}NO_7$: C, 49.82; H, 6.62; N, 4.84. Found: C, 50.00; H, 6.76; N, 4.90.

(4) Methyl 3-Acetamido-3-deoxy-β-D-xylopyranoside 11b mp 205—208 °C (lit. mp 201—202 °C)[15]

(5) Methyl 3-Acetamido-2,4-di-*O*-acetyl-3-deoxy-β-D-xylopyranoside 11c Colorless needles from ethyl acetate–hexane, mp 179—182 °C. IR: 1736, 1659. ^1H-NMR: 1.96, 2.08, 2.10 (each 3H, s, Ac), 3.49 (3H, s, OMe), 3.57 (1H, dd, J=6.6, 12.5 Hz, H-5), 4.01 (1H, dd, J=4.0, 12.5 Hz, H-5), 4.33 (1H, dt, J=7.3, 9.2 Hz, H-3), 4.52 (1H, d, J=5.1 Hz, H-1), 4.69 (1H, dd, J=5.1, 7.3 Hz, H-2), 4.79 (1H, m, H-4), 6.04 (1H, d, J=9.2 Hz, NH). MS: 290 (M^++1), 186 (100%). *Anal.* Calcd for $C_{12}H_{19}NO_7$: C, 49.82; H, 6.62; N, 4.84. Found: C, 49.64; H, 6.75; N, 4.94.

(6) Methyl 4-Acetamido-2,3,6-tri-*O*-acetyl-4-deoxy-α-D-galactopyranoside 12c Colorless syrup (lit. syrup).[16] IR($CHCl_3$): 1739, 1681. ^1H-NMR: 1.99, 2.05, 2.07, 2.10 (each 3H, s, Ac), 3.40 (3H, s, OMe), 4.06 (1H, dd, J=5.2, 11.6 Hz, H-6), 4.17 (1H, dd, J=7.3, 11.6 Hz, H-6), 4.26 (1H, ddd, J=1.8, 5.2, 7.3 Hz, H-5), 4.73 (1H, ddd, J=1.8, 4.3, 9.8 Hz, H-4), 4.93 (1H, dd, J=4.0, 10.7, H-2), 4.98 (1H, d, J=4.0 Hz, H-1), 5.27 (1H, dd, J=4.3, 10.7 Hz, H-3), 5.99 (1H, d, J=9.8 Hz, NH). MS: 362 (M^++1, 100%), 330 (M^+−OMe).

(7) Methyl 4-Acetamido-2,3,6-tri-*O*-acetyl-4-deoxy-α-D-glucopyranoside 13c Colorless prisms from ether, mp 144—145 °C (lit. mp 140—141 °C).[17] ^1H-NMR: 1.86, 1.97, 2.01, 2.03 (each 3H, s, Ac), 3.32 (3H, s, OMe), 3.73 (1H, dt, J=3.7, 10.6 Hz, H-5), 4.12 (1H, m, H-4), 4.13 (2H, d, J=3.7 Hz, H-6), 4.84 (1H, dd, J=3.7, 10.3 Hz, H-2), 4.90 (1H, d, J=3.7 Hz, H-1), 5.23 (1H, t, J=10.3 Hz, H-3), 5.63 (1H, d, J=9.5 Hz, NH).

(8) Methyl 4-Acetamido-2,3-di-*O*-acetyl-4-deoxy-β-L-arabinopyranoside 14c Colorless prisms from ethyl acetate–hexane, mp 72—75 °C. IR: 1734, 1666. ^1H-NMR: 2.01, 2.05, 2.10 (each 3H, s, Ac), 3.40 (3H, s, OMe), 3.52 (1H, dd, J=2.2, 12.1 Hz, H-5), 4.01 (1H, dd, J=1.8, 12.1 Hz, H-5), 4.60 (1H, m, H-4), 4.94 (1H, d, J=4.0 Hz, H-1), 4.97 (1H, dd, J=3.7, 10.6 Hz, H-3), 5.27 (1H, dd, J=4.0, 10.6 Hz, H-2), 6.27 (1H, d, J=8.8 Hz, NH). MS: 290 (M^++1), 258 (M^+−OMe), 170 (100%). *Anal.* Calcd for $C_{12}H_{19}NO_7 \cdot 1/2H_2O$: C, 48.32; H, 6.76; N, 4.70. Found: C, 48.68; H, 6.70; N, 4.71.

Transformation of Methyl 4-Amino-4-deoxy-β-L-arabinopyranoside 14a to the *N*-Acetyl-di-*O*-mesyl Derivative 14d The oxime **5**[1] (0.1 g) was hydrogenated over PtO_2 in AcOH and the product was converted to the *N*-acetate as described in the general procedure. The resulting *N*-acetate **14b** was mesylated in pyridine with an excess of methanesulfonyl chloride overnight at room temperature. The product was purified by chromatography to give **14d** (60 mg), as colorless prisms from pentane, mp 162—163 °C. IR: 3440, 1655, 1548. ^1H-NMR (100 MHz): 2.09 (3H, s, OAc), 3.16 (6H, s, $SO_2Me \times 2$), 3.47 (3H, s, OMe), 3.56 (1H, dd, J=2, 12.5 Hz, H-5), 4.02 (1H, dd, J=2, 12.5 Hz, H-5), 4.48—4.60 (1H, m, H-4), 4.67 (1H, dd, J=3.5, 10 Hz, H-2), 5.00 (1H, d, J=3.5 Hz, H-1), 5.12 (1H, dd, J=4.1, 10 Hz, H-3), 6.36 (1H, d, J=8.8 Hz, NH). The identity with the authentic sample (lit. mp 158—159 °C)[4] was confirmed by mixed melting point determination and spectral comparisons.

Reduction of Methyl 4,6-*O*-Benzylidene-α-D-*arabino*-2-hexulopyranoside *O*-Methyloxime 7 i) Hydrogenation over Raney Ni: The *O*-methyloxime **7** (100 mg) in EtOH (20 ml) was hydrogenated (H_2, 4 kg/cm^2) over an excess of Raney Ni for 20 h at room temperature. Removal of the catalyst and the solvent left a gummy residue, which was acetylated with pyridine and acetic anhydride, and the product (63%) was analyzed by GC (**20c**/**21c** = 3/1), then separated by MPLC to yield the diacetates, **20c** and **21c**.

ii) AlH_3 reduction: The *O*-methyloxime **7** (100 mg) was reduced with AlH_3 as described in the general procedure and the product was acetylated as above to give a mixture of **20c** and **21c** (87%, GC: **20c**/**21c** = 5/1), which were separated by MPLC.

(1) Methyl 2-Acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-α-D-mannopyranoside 20c Colorless prisms from $CHCl_3$–hexane, mp 219—221 °C. IR: 1718, 1675. ^1H-NMR: 2.02, 2.06 (each 3H, s, Ac), 3.40 (3H, s, OMe), 3.79 (1H, t, J=10.4 Hz, H-6), 3.81 (1H, t, J=10.4 Hz, H-4), 3.97 (1H, dt, J=4.9, 10.4 Hz, H-5), 4.29 (1H, dd, J=4.9, 10.4 Hz, H-6), 4.64 (1H, br s, H-1), 4.70 (1H, ddd, J=1.2, 4.6, 9.2 Hz, H-2), 5.27 (1H, dd, J=4.6, 10.4 Hz, H-3), 5.56 (1H, s, H-7), 5.74 (1H, d, J=9.2, NH), 7.35—7.47 (5H, Ar-H). MS: 366 (M^++1), 156 (100%). *Anal.* Calcd for $C_{18}H_{23}NO_7$: C, 59.18; H, 6.33; N, 3.83. Found: C, 59.25; H, 6.37; N, 3.80.

(2) Methyl 2-Acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside 21c Colorless needles from chloroform–hexane, mp 220 °C. IR: 1740, 1649. ^1H-NMR: 1.19, 2.05 (3H, s, Ac), 3.40 (3H, s, OMe), 3.71 (1H, t, J=9.5 Hz, H-6), 3.78 (1H, t, J=9.5 Hz, H-4), 3.87 (1H, dt, J=4.6, 9.5 Hz, H-5), 4.29 (1H, dd, J=4.6, 9.5 Hz, H-6), 4.34 (1H, dt, J=3.7, 9.5 Hz), 4.71 (1H, d, J=3.7 Hz, H-1), 5.29 (1H, t, J=9.5 Hz, H-3), 5.52 (1H, s, H-7), 5.86 (1H, d, J=9.5 Hz, NH), 7.34—7.45 (5H, Ar-H). MS: 366 (M^++1), 156 (100%). *Anal.* Calcd for $C_{18}H_{23}NO_7$: C, 59.18; H, 6.33; N, 3.83. Found: C, 59.30; H, 6.38; N, 4.01.

Conversion of 20c and 21c to Methyl *N*,*O*-Tetraacetyl-α-D-mannosaminide 16c and Methyl *N*,*O*-Tetraacetyl-α-D-glucosaminide 17c A 3:1 mixture of the diacetate **20c** and **21c** (74 mg) in ethanol (15 ml) was shaken with hydrogen (4.5 kg/cm^2) over 10% Pd–C (100 mg) for 10 h at room temperature. The product obtained by removal of the catalyst and the solvent was acetylated to the peracetates (57 mg, 78%) which gave one spot on TLC; analysis by ^{13}C-NMR showed that it is a mixture of **16c** and **17c**.

Methyl Tetraacetyl-D-glucosaminide *N*-Acetylglucosamine (100 mg) and Amberlite CG-120 (H^+) (59 mg) in MeOH (10 ml) were heated under reflux for 3 h, and filtered. Concentration of the filtrate and acetylation of the residue gave an anomeric mixture of methyl tetraacetyl-D-glucosaminide (143 mg, 88%; α/β ratio 1.4/1), which was separated on MPLC to give the α anomer **17c** (syrup) and the β anomer (mp 168—169 °C).

Methyl Tetraacetyl-D-mannosaminide *N*-Acetylmannosamine (50 mg) was methylated and acetylated as above to give **16c** (63 mg, 76%, syrup, α anomer exclusively).

Reduction of Methyl 4,6-*O*-Benzylidene-β-D-*ribo*-3-hexulopyranoside *O*-Methyloxime 6 i) Hydrogenation over Raney Ni: The *O*-methyloxime **6** (100 mg) was hydrogenated and the product was acetylated as described above to give the *allo* isomer **18c** (62 mg, 53%) as a single product.

ii) AlH_3 reduction: The *O*-methyloxime **6** (150 mg) was reduced with AlH_3 as described in the general procedure and the product was acetylated to give the *N*,*O*-diacetate (88 mg, 51%) as a mixture of the *allo* and *gluco* isomers, **18c** and **19c** (GC: 4:1). MPLC resulted in isolation of **18c** and ^{13}C-NMR of the mother liquor from **18c** indicated the presence of the *gluco* isomer **19c**.

(1) Methyl 3-Acetamido-2-*O*-acetyl-4,6-*O*-benzylidene-3-deoxy-β-D-allopyranoside 18c Colorless plates from chloroform–hexane, mp 217—221 °C. IR: 1734, 1648. ^1H-NMR: 2.03, 2.05 (each 3H, s, Ac), 3.52 (3H, s, OMe), 3.68 (1H, dt, J=4.9, 9.8 Hz, H-5), 3.78 (1H, t, J=9.8 Hz, H-

6), 3.84 (1H, dd, J=4.6, 9.8 Hz, H-4), 4.40 (1H, dd, J=4.9, 9.8 Hz, H-6), 4.59 (1H, d, J=8.6 Hz, H-1), 4.81 (1H, dd, J=4.3, 8.6 Hz, H-2), 5.00 (1H, m, H-3), 5.56 (1H, s, H-7), 5.69 (1H, d, J=7.9 Hz, NH), 7.30—7.44 (5H, Ar-H). MS: 366 (M^++1), 262 (100%). *Anal.* Calcd for $C_{18}H_{23}NO_7$: C, 59.18; H, 6.33; N, 3.83. Found: C, 57.40; H, 6.20; N, 3.59.

Methyloximation of the 5-Oxo Derivative 22 i) The 5-oxo derivative **22** (910 mg), *O*-methylhydroxylamine hydrochloride (526 mg, 1.5 mol eq), and $NaHCO_3$ (526 mg, 1.5 mol eq) in MeOH (25 ml) were heated under reflux for 1 h. The precipitated salt was filtered off and the filtrate was concentrated to give a residue, which was extracted with hot chloroform. The extract was chromatographed to give a mixture of *E*- and *Z*-*O*-methyloximes (1.02 g, 99%; GC of the TMS derivative: E/Z ratio=1/2) from ethyl acetate eluate. MPLC of this mixture (solvent: $CHCl_3$–MeOH=19:1) resulted in separation and purification of **23a** (*E*) and **23b** (*Z*).

ii) The above oximation with various bases gave the following results: sodium carbonate (0.75 mol eq), E/Z=1/2.7; sodium carbonate (1.0 mol eq), E/Z=1.3/1; sodium carbonate (5.0 mol eq), E/Z=1.6/1; lithium hydroxide (2.5 mol eq), E/Z=1.3/1.

(1) The *E*-Methyloxime 23a Colorless prisms from ether–hexane, mp 74—76 °C. IR: no CO absorption. ^{1}H-NMR (100 MHz): 1.33, 1.50 (each 3H, s, O_2CMe_2), 3.91 (3H, s, OMe), 4.38 (1H, d, J=2.7 Hz, H-4), 4.55 (2H, s, H-6), 4.56 (1H, d, J=3.7 Hz, H-2), 4.86 (1H, d, J=2.7 Hz, H-3), 5.99 (1H, d, J=3.7 Hz, H-1). ^{13}C-NMR: 105.0 (C-1), 84.7 (C-2), 79.2 (C-3), 76.2 (C-4), 156.6 (C-5), 56.8 (C-6), 62.5 (OMe), 26.2, 26.8 (each Me), 112.1 (O_2CMe_2). MS: 247 (M^+), 232 (M^+−Me), 59 (100%). *Anal.* Calcd for $C_{10}H_{17}NO_6$: C, 48.58; H, 6.93; N, 5.67. Found: C, 48.20; H, 7.07; N, 5.52.

(2) The *Z*-Methyloxime 23b Colorless oil. IR (film): no CO absorption. ^{1}H-NMR (100 MHz): 1.33, 1.50 (each 3H, s, O_2CMe_2), 3.90 (3H, s, OMe), 4.12, 4.36 (each 1H, d, J=13.5 Hz, H-6), 4.52 (1H, d, J=2.6 Hz, H-4), 4.54 (1H, d, J=3.5 Hz, H-2), 5.28 (1H, d, J=2.6 Hz, H-3), 5.98 (1H, d, J=3.5 Hz, H-1). ^{13}C-NMR: 104.4 (C-1), 84.9 (C-2), 78.3 (C-3), 74.5 (C-4), 155.4 (C-5), 60.6 (C-6), 62.2 (OMe), 26.2, 26.8 (Me), 112.0 (O_2CMe_2). MS: 247 (M^+), 59 (100%).

Acid Catalyzed Isomerization of the *O*-Methyloximes 23 i) The *E*-oxime **23a** (3 mg) in methanol (2 ml) was stirred with a catalytic amount of *p*-toluenesulfonic acid. After 3 and 4 h, GC (TMS derivative) of the product showed E/Z ratios of 1/2 and 1/3.5, respectively.

ii) The *Z*-oxime **23b** (3 mg) was isomerized as above. The E/Z ratio was found to be 1/3.

iii) A 1:2 mixture of **23a** (*E*) and **23b** (*Z*) (1.02 g) and *p*-toluenesulfonic acid (20 mg) in methanol (25 ml) were stirred for 2 h at room temperature. The mixture was concentrated and the residue was chromatographed to give, from the ethyl acetate eluate, a mixture of **23** (970 mg, 95%) with an E/Z ratio of 1/3.5.

Reduction of the *E*- and *Z*-*O*-Methyloximes An *O*-methyloxime (each 10 mg) was reduced with various reagents and, after evaporation of the solvent, the residue was acetylated with an excess of pyridine and acetic anhydride. The product was analyzed by GC. Conditions: N_2, 40 ml/min. Injection, 240 °C. Column temperature, 150 °C to 230 °C (10 °C/min). Relative retention times: *gluco* (**24b**) 0.95, *ido* (**25b**) 1.00. The results are shown in Table VI.

Reduction of the Equilibrium Mixture of the *O*-Methyloximes 23 with Lithium Aluminum Hydride in Dimethoxyethane A 1:3.5 mixture of *E*- and *Z*-*O*-methyloximes **23** (873 mg) and $LiAlH_4$ (670 mg, 5.0 mol eq) in dimethoxyethane (30 ml) were heated under reflux for 5 h. After decomposition of the reagent with water, the mixture was filtered and the residue was washed several times with hot chloroform–methanol. The combined filtrate and washings were concentrated *in vacuo* and the residue was chromatographed to give the 5-amino sugars (650 mg, 84%) from the chloroform–methanol (4:1—1:1) eluate. GC: *gluco* **24**/*ido* **25** ratio=2/1.

This mixture (4 mg) was treated with salicylaldehyde (10 mg) in EtOH (1 ml) for 2 h at room temperature. The resulting solution showed a positive Cotton effect at 310 nm in the CD spectrum.

The above mixture of amino-sugars was acetylated in a usual manner and the product was purified by MPLC (solvent: benzene–acetone 1:1) to yield **24b** (*gluco*) and **25b** (*ido*).

(1) 5-Acetamido-3,6-di-*O*-acetyl-5-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose 24b Colorless needles from ethyl acetate–hexane, mp 150—151 °C. IR: 1747, 1731, 1653. ^{1}H-NMR (100 Mz): 1.31, 1.50 (each 3H, s, O_2CMe_2), 1.93, 2.07, 2.11 (each 3H, s, Ac), 4.25 (1H, dd, J=2.8, 9.8 Hz, H-4), 4.27 (2H, d, J=4.1 Hz, H-6), 4.46 (1H, d, J=3.7 Hz, H-2), 4.57 (1H, tt, J=4.1, 9.8 Hz, H-5), 5.31 (1H, d, J=2.8 Hz, H-3), 5.85 (1H, d, J=9.8 Hz, NH), 5.91 (1H, d, J=3.7 Hz, H-1). ^{13}C-NMR: 105.0 (C-1), 83.3 (C-2), 77.9 (C-3), 74.7 (C-4), 46.1 (C-5), 64.6 (C-6), 20.8, 20.9, 23.2 (Ac), 26.2, 26.7 (Me), 112.2 (O_2CMe_2), 169.4, 169.8, 170.8 (CO). MS: 330 (M^+−Me), 143 (100%). *Anal.* Calcd for $C_{15}H_{23}NO_8$: C, 52.17; H, 6.71; N, 4.06. Found: C, 51.95; H, 6.87; N, 4.22.

(2) 5-Acetamido-3,6-di-*O*-acetyl-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose 25b Colorless crystals from ether, mp 92—96 °C. IR: 1737, 1651. ^{1}H-NMR (100 MHz): 1.31, 1.51 (each 3H, s, O_2CMe_2), 2.01, 2.05, 2.08 (each 3H, s, Ac), 4.11 (2H, d, J=5.8 Hz, H-6), 4.34 (1H, dd, J=3.1, 5.8 Hz, H-4), 4.50 (1H, d, J=3.9 Hz, H-2), 4.52 (1H, dq, J=5.8, 8.1 Hz, H-5), 5.23 (1H, d, J=3.1 Hz, H-3), 5.92 (1H, d, J=3.9 Hz, H-1), 6.06 (1H, d, J=8.1 Hz, NH). ^{13}C-NMR: 104.4 (C-1), 83.6 (C-2), 76.6 (C-3), 76.9 (C-4), 46.8 (C-5), 64.0 (C-6), 20.7, 20.8, 23.3 (Ac), 26.1, 26.6 (Me), 112.3 (O_2CMe_2), 169.8, 170.6 (Ac). MS: 330 (M^+−Me), 43 (100%). *Anal.* Calcd for $C_{15}H_{23}NO_8$: C, 52.17; H, 6.71; N, 4.06. Found: C, 51.88; H, 6.77; N, 4.09.

5-Amino-5-deoxy-D-glucose-1-sulfonic Acid (Nojirimycin Bisulfite Adduct) 26 A 2:1 mixture of **24a** and **25a** (268 mg) was dissolved in water (3 ml) saturated with SO_2 and kept for 3 days at room temperature, then MeOH (10 ml) was added and the mixture was kept in a refrigerator overnight. The precipitated crystals (160 mg, 75% from **24a**) were collected by filtration. mp 138—139 °C. The IR spectrum (in Nujol mull) was superimposable on that of the reported nojirimycin bisulfite adduct **26** (mp 145—147 °C).[9] *Anal.* Calcd for $C_6H_{15}NO_8S$: C, 27.59; H, 5.79; N, 5.36. Found: C, 27.56; H, 5.98; N, 5.22.

The mother liquor of **26** precipitated further crops of **26** (47 mg) when the cold methanolic solution was kept for long time (total yield, 207 mg) (47% from 1,2-*O*-isopropylidene-α-D-glucofuranose).

Acknowledgement We thank Mr. M. Nishimura for technical assistance in some experiments. This work was supported in part by a Grant-in-Aid for Scientific Research (62570935) from the Ministry of Education, Science and Culture, Japan.

References and Notes

1) Utilization of Sugars in Organic Synthesis. XXII. Part XXI: Y. Tsuda, M. Hanajima, N. Matsuhira, Y. Okuno, and K. Kanemitsu, *Chem. Pharm. Bull.*, **37**, 2344 (1989).
2) Parts of this work were reported as preliminary communications: *a*) Y. Tsuda, M. Hanajima, and K. Yoshimoto, *Chem. Pharm. Bull.*, **31**, 3778 (1983); *b*) Y. Tsuda, Y. Okuno, and K. Kanemitsu, *Heterocycles*, **27**, 63 (1988).
3) Present address: *Ishikawa-ken Red Cross Blood Centre, Ru-75 Minamishinbo, Kanazawa 920, Japan.*
4) A. J. Dick and J. K. N. Jones, *Can. J. Chem.*, **46**, 425 (1968).
5) *a*) H. Ogawa, T. Ito, S. Kondo, and S. Inoue, *J. Antibiot.*, **11A**, 169 (1958); *b*) C. W. Waller, P. W. Fryth, B. L. Hutchings, and H. Williams, *J. Am. Chem. Soc.*, **75**, 2025 (1953); *c*) H. Maehr and C. P. Schaffner, *ibid.*, **89**, 6789 (1967).
6) *a*) W. A. Volk, C. Galanos, and O. Luderitz, *FEBS Lett.*, **8**, 161 (1970); *b*) *Idem, Eur. J. Biochem.*, **17**, 223 (1970).
7) For biological activity of nojirimycin, see *a*) T. Niwa, T. Inouye, T. Turuoka, Y. Koaze, and T. Niida, *Agric. Biol. Chem.*, **34**, 966 (1970); *b*) E. T. Reese, F. W. Parrish, and M. Ettinger, *Carbohydr. Res.*, **18**, 381 (1971); *c*) G. Hanozet, H. P. Pircher, P. Vann, B. Oesch, and G. Semenza, *J. Biol. Chem.*, **256**, 3703 (1981).
8) We thank Rigaku Co., Ltd., Japan, and Molecular Structure Corporation, Texas, U.S.A., for the X-ray analysis.
9) S. Inouye, T. Tsuruoka, T. Ito, and T. Niida, *Tetrahedron*, **23**, 2125 (1968).
10) Y. Komada, T. Tsuruoka, T. Niwa, and S. Inouye, *J. Antibiot.*, **38**, 116 (1985).
11) Other syntheses: *a*) Ref. 9); *b*) H. Seki and E. Ohki, *Chem. Pharm. Bull.*, **16**, 2477 (1968); *c*) A. Klemer, U. Hofmeister, and R. Lemmes, *Carbohydr. Res.*, **31**, 391 (1979); *d*) A. Vassela and R. Voeffray, *Helv. Chim. Acta*, **65**, 1134 (1982).
12) C. C. Sweeley, R. Bentley, M. Makita, and W. W. Wells, *J. Am. Chem. Soc.*, **85**, 2497 (1963).
13) N. M. Yoon and H. C. Brown, *J. Am. Chem. Soc.*, **90**, 2927 (1968).
14) S. Peat and L. F. Wiggins, *J. Chem. Soc.*, **1938**, 1810.
15) R. E. Schaub and M. J. Weiss, *J. Am. Chem. Soc.*, **80**, 4683 (1958).
16) F. W. Lichtenthaler and P. Heidel, *Angew. Chem., Int. Ed. Engl.*, **7**, 458 (1968).
17) E. J. Reist, R. R. Spencer, D. F. Calkins, B. R. Baker, and L. Goodman, *J. Org. Chem.*, **30**, 2312 (1965).