The Behavior of Some 2-Acetamido-2-deoxy-furanoses in the Presence of Alkaline Ion-exchange Resin

Hiroyuki OKUMURA,* Makoto KISO and Akira HASEGAWA**

*Department of Agricultural Chemistry, Gifu University,
Yanagido, Gifu 501-11, Japan*

Received October 12, 1982

In the presence of an alkaline ion-exchange resin (Amberlite IRA-410), 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-3-*O*-methyl- and -3-*O*-(tetrahydropyran-2-yl)-D-glucofuranoses, and 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-D-allofuranose, as well as 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-D-glucofuranose were converted into 2-acetamido-2,3-dideoxy-5,6-*O*-isopropylidene- α -D-erythro-hex-2-enofuranose. The β -elimination was also observed in the case of 2,5-diacetamido-2,5-dideoxy-D-xylo- and -D-ribo-furanoses, to give 2,5-diacetamido-2,3,5-trideoxy-D-glycero-pent-2-enofuranose. C-3-Deoxy-furanoses, such as 2-acetamido-2,3-dideoxy-5,6-*O*-isopropylidene-D-arabino- and -D-ribo-hexofuranoses, and 2,3,5-triacetamido-2,3,5-trideoxy-D-ribofuranose, however, did not give β -eliminated compounds under the same condition.

It is known that 2-acetamido-2-deoxy-D-glucose is converted into chromogens (unsaturated amino sugars) in an alkaline solution. The chemical structures of chromogens have been postulated by Kuhn *et al.*¹⁾

Previously, we have reported^{2,5)} that reactions of 2-acetamido- or 2-(benzyloxycarbonylamino)-2-deoxy-D-glucoses with 2,2-dimethoxy- or 2,2-dibenzoyloxy-propane — *p*-toluenesulfonic acid — *N,N*-dimethylformamide yielded many kinds of isopropylidene derivatives as kinetically controlled products, *e.g.*, methyl or benzyl 2-acetamido- or 2-(benzyloxycarbonylamino)-2-deoxy-5,6-*O*-isopropylidene- β -D-glucofuranoside. These isopropylidene derivatives are effective to synthesize biologically active compounds. For example, Prumycin,⁴⁾ (+)-biotin⁶⁾ and some analogs⁷⁾ of *N*-acetylmuramoyl-L-alanyl-D-isoglutamine were synthesized from benzyl 2-(benzyloxycarbonylamino)-2-deoxy-5,6-*O*-isopropylidene- β -D-glucofuranoside.

On the other hand, the treatment of 2-acetamido-2-deoxy-D-glucose with the reagents described above and subsequent removal of the acid with an alkaline ion-

exchange resin (Amberlite IRA-410) afforded an unsaturated compound in addition to many kinds of isopropylidene derivatives. This compound was also obtained⁸⁾ from 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-D-glucofuranose with the same resin. In the previous papers,^{5,8)} we presumed the structure of the unsaturated compound to be 2-acetamido-1,4-anhydro-2-deoxy-5,6-*O*-isopropylidene-D-arabino-hex-1-enitol (2). Recently, Beau *et al.* have reported⁹⁾ that an alkaline treatment of 2-acetamido-2-deoxy-3,4:5,6-di-*O*-isopropylidene-aldehyde-D-glucose gave 2-acetamido-2,3-dideoxy-5,6-*O*-isopropylidene- α -D-erythro-hex-2-enofuranose (1). Therefore, in this paper, we have reinvestigated the unsaturated compound described above and examined the behavior of some 2-acetamido-2-deoxy-furanoses in the presence of alkaline ion-exchange resin.

* Present address: Institute of Immunological Science, Hokkaido University, Sapporo 060, Japan.

** To whom inquiries should be addressed.

RESULTS AND DISCUSSION

Previously, we have reported⁸⁾ that treatment of 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-D-glucufuranose with Amberlite IRA-410 afforded an unsaturated compound as a crystalline material. Hydrogenation of this compound in methanol gave two derivatives (**3**, **5**), in the ratio of 1:2, after isolation by column chromatography. Both compounds reduced the Fehling solution. De-*O*-isopropylidenation of **3** and **5** by 60% acetic acid and subsequent acetylation at 0°C respectively gave 2-acetamido-1,4,6-tri-*O*-acetyl-2,3-dideoxy- α - and - β -D-*arabino*-hexopyranoses (**7a**, **7b**), and 2-acetamido-1,4,6-tri-*O*-acetyl-2,3-dideoxy- α -D-*ribo*-hexopyranose (**8**), which was identical with the acetylated Lividosamine.¹¹⁾ These results indicate that compound **5** is 2-acetamido-2,3-dideoxy-5,6-*O*-isopropylidene-D-*ribo*-hexofuranose, that **3** is 2-acetamido-2,3-dideoxy-5,6-*O*-isopropylidene-D-*arabino*-hexofuranose, and that the initial unsaturated compound is identical with **1** reported by Beau *et al.* Acetylation of **3** and **5** afforded 2-acetamido-1-*O*-acetyl-2,3-dideoxy-5,6-*O*-isopropylidene- β -D-*arabino*-hexofuranose (**4**; $[\alpha]_D -94^\circ$) and 2-acetamido-1-*O*-acetyl-2,3-dideoxy-5,6-*O*-isopropylidene- α -D-*ribo*-hexofuranose (**6**; $[\alpha]_D +109^\circ$) as the main products, respectively.

In order to examine behaviors of 2-acetamido-2-deoxy-furanoses in the presence of an alkaline ion-exchange resin, we prepared 9 kinds of furanoses (**3**, **5**, **13**~**15**, **18** and **22**~**24**). The synthetic method for 2-acet-

amido-2-deoxy-5,6-*O*-isopropylidene-D-glucufuranose (**13**) has been described previously.⁵⁾ 2-Acetamido-2-deoxy-5,6-*O*-isopropylidene-3-*O*-methyl- and -3-*O*-(tetrahydropyran-2-yl)-D-glucufuranoses (**14**, **15**) were synthesized from benzyl 2-acetamido-2-deoxy-5,6-*O*-isopropylidene- β -D-glucufuranoside³⁾ (**9**), *via* 3-*O*-methyl and 3-*O*-(tetrahydropyran-2-yl) compounds, respectively. For the preparation of 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-D-allofuranose (**18**), compound **9** was first 3-*O*-methanesulfonylated with methanesulfonyl chloride to give compound **12**, which was then converted by treatment with potassium acetate—aqueous 90% ethanol into benzyl 2-acetamido-2-deoxy-5,6-*O*-isopropylidene- β -D-allofuranoside (**16**) in a high yield. The configuration of **16** was confirmed by ¹H-NMR with the acetylated compound **17**. The chemical shift of the H-3 proton (δ 5.47) and the coupling constant between H-2 and H-3 ($J_{2,3}=6.0$ Hz) were different from those of benzyl 2-acetamido-3-*O*-acetyl-2-deoxy-5,6-*O*-isopropylidene- β -D-glucufuranoside (H-3; δ 5.37, $J_{2,3}=2.4$ Hz). The results indicate that the configuration of **16** and **17** is a D-*allo* form. Hydrogenolitic

9	R=H	13	R=H
10	R=Me	14	R=Me
11	R=THP	15	R=THP
12	R=Ms		

Bn-PhCH₂
THP=tetrahydropyran-2-yl

removal of the benzyl group in **16** gave the desired compound **18**.

Recently, we have reported¹⁰⁾ that the hydrogenolysis of benzyl 2,5-diacetamido-2,5-dideoxy- β -D-xylo- or - β -D-ribo-furanoside (**19**, **20**) or benzyl 2,3,5-triacetamido-2,3,5-trideoxy- β -D-ribofuranoside (**21**) in a neutral condition, with subsequent acetylation afforded only the corresponding furanose derivatives. Therefore, in this study, we have used these 5-acetamido furanoses (**22**~**24**).

These furanoses (**3**, **5**, **13**~**15**, **18** and **22**~**24**) thus synthesized were each treated with Amberlite IRA-410 (OH⁻) resin in methanol. The 3-*O*-alkylated compounds (**14**, **15**), as well as compound **13**, were easily converted into 2-enofuranose **1**. The β -elimination was also observed in the case of the *D*-allo isomer **18**, to give compound **1**. However, the C-3-unsubstituted compounds (**3**, **5**) did not change under the same condition.

TABLE I. ¹H-NMR DATA^a FOR 2,3-UNSATURATED FURANOSIDES

Compound ^b	Chemical shifts (δ)			Coupling constants (Hz)			
	H-1	H-3	H-4	$J_{1,3}$	$J_{1,4}$	$J_{1,OH}$	$J_{3,4}$
25 (α)	5.71	5.99	4.75	0	4.3	8.0	1.0
25 (β)	5.66	6.04	4.59	0	1.8	8.2	1.0
1 (α)	5.68	6.03	4.65	0	4.0	8.0	1.0

^a Measured at 90 MHz in DMSO-*d*₆.

^b α or β indicates a glycosidic linkage.

When compound **22** was treated with Amberlite IRA-410 ion-exchange resin in methanol at room temperature, 2,5-diacetamido-2,5-dideoxy-D-xylopyranose (**26**) was at first detected and the ratio of **26** to **22** reached 1:1 on TLC. Compound **26** was isolated from the reaction mixture as a crystalline product and then acetylated, to afford 2,5-diacetamido-1,3,4-tri-*O*-acetyl-2,5-dideoxy- α -D-xylopyranose (**27**). The coupling constants of each proton in **27** at ¹H-NMR ($J_{1,2}=3.8$, $J_{2,3}=10.7$, $J_{3,4}=9.1$, $J_{4,5a}=10.2$ and $J_{4,5e}=5.7$) indicate the compound is a α -D-xylopyranose form.^{12,13)} On continuation of the reaction of **22** in an alkaline solution, **22** and **26** gradually disappeared and 2,5-di-acetamido-2,3,5-trideoxy-D-*glycer*o-pent-2-enofuranose (**25**) was produced. After chromatographic purification, compound **25** was isolated as crystals in a good yield. The ¹H-NMR data of **25** are shown in Table I. The presence of two kinds of NH protons (δ 7.75; m, NH at C-5 and δ 9.64; s, NH at C-2) indicates that this compound is a furanoid form, and similar chemical shifts of H-1, H-3 and H-4 to those of compound **1** show that the compound is a 2,3-unsaturated sugar. The anomeric configurations were determined from the observed $J_{1,4}$ values, as the coupling between H-1 and H-4 is large ($\sim$ 4 Hz) when the proton is *trans*-related, and small ($\sim$ 1 Hz) when the relationship is *cis*.¹⁴⁾ The data given in Table I are also comparable to those of the 3-deoxy-pent-enose derivatives reported by Ferrier and Hurford,¹⁵⁾ and the anomeric ratio (α : β) in **25** was estimated at $\sim$ 1:1. When **26** was

treated with Amberlite IRA-410 in methanol, the equilibrium between **26** and **22** was observed at first, and then only compound **25** was detected after the disappearance of both of **26** and **22** on TLC. Similarly, treatment of **23** with IRA-410 in methanol gave compound **25**. In this case, a pyranose material corresponding to **26** was also detected on TLC at the initial stage of the reaction, although it was not isolated. On the other hand, the treatment of the triacetamido compound **24** in the same condition afforded 2,3,5-triacetamido-2,3,5-trideoxy-D-ribofuranose (**28**) exclusively, and no unsaturated compound was detected. The $^1\text{H-NMR}$ spectrum of the acetylated compound **29** revealed the presence of five acetyl groups (15 protons) at δ 1.97~2.12, H-1 of the α -anomer as a doublet at δ 6.00 (2.2 Hz) and H-1 of the β -anomer as a doublet at δ 6.16 (4.3 Hz), and these data were consistent with a D-ribofuranose form.¹²⁾

As described above, when OH or *O*-alkyl groups are present at the C-3 position, 2-acetamido-2-deoxy-furanoses were converted into 2,3-unsaturated-furanose derivatives in the presence of an alkaline ion-exchange resin, and this conversion didn't occur in the case of 2-acetamido-2,3-dideoxy-furanose (**3**, **5**) or 2,3,5-triacetamido-2,3,5-trideoxy-furanose (**24**). On the other hand, the configurational change at the C-3 position such as compounds **18** and **23** didn't affect the β -elimination. These results indicate that the oxygen atom at the C-3 position is required for this β -elimination. Formula **30** illustrates the mechanism proposed for the reaction. The existence of the

enolic form, which is probably stabilized by the 2-acetamido group in the alkaline solution, is considered to be responsible for causing the β -elimination. In the case of the 2,5-diacetamido-furanoses (**22**, **23**), although the furanose-pyranose equilibrium (**22** **26**) was observed at the initial stage, the final product was the β -eliminated compound (in furanoid form). This result shows that the 2,3-unsaturated amino sugar is favorable for the furanoid structure.

EXPERIMENTAL

Melting points were determined with a Yanagimoto micro melting-point apparatus and are uncorrected. Specific rotations were determined with a Union PM-201 polarimeter and IR spectra were recorded with a Jasco IRA-1 spectrophotometer. NMR spectra were recorded at 60 MHz and 90 MHz with Hitachi R-24BS and R-22 spectrometers in CDCl_3 and with TMS as an internal standard unless otherwise noted. Preparative chromatography was performed on silica gel (Wako Co.; 300 mesh) with the solvent systems specified. Evaporations were conducted *in vacuo*.

2-Acetamido-2,3-dideoxy-5,6-*O*-isopropylidene-D-arabino-hexofuranose (**3**) and 2-acetamido-2,3-dideoxy-5,6-*O*-isopropylidene-D-ribo-hexofuranose (**5**). A solution of 2-acetamido-2,3-dideoxy- α -D-erythro-hex-2-enofuranose^{8,9)} (**1**) (500 mg) in MeOH (30 ml) was kept for 24 hr at room temperature, and the solution was then hydrogenated, with stirring, in the presence of 10% Pd-C catalyst (250 mg) for 5 hr at room temperature. After removal of the catalyst and evaporation of the solvent, the residue was chromatographed on a column of silica gel (40 g) with (a) 50:1, and (b) 20:1 CHCl_3 -MeOH. The eluant (a) gave compound **3** (150 mg, 30%) as a syrup, $[\alpha]_D^{15} -12^\circ$ ($c=0.68$, MeOH; 24 hr).

Eluant (b) afforded compound **5** (310 mg, 61%) as

crystals, mp 142~143°C, $[\alpha]_D^{23} + 34.5^\circ$ ($c=0.4$, DMSO; 24 hr); $\nu_{\max}^{\text{Nujol}} \text{ cm}^{-1}$: 3330 (OH), 3230 (NH), 1610 and 1570 (amide), and 840 (Me_2C); NMR δ (90 MHz, DMSO- d_6): 1.25 and 1.32 (6H, 2s, Me_2C), 1.79 and 1.81 (3H, 2s, AcN), 1.60~2.15 (2H, m, H-3,3'), 4.79 (d, $J_{1,2}=0$, $J_{1,\text{OH}}=4.8$ Hz, H-1 of β -anomer), 5.10 (t, $J_{1,2}=J_{1,\text{OH}}=4.5$ Hz, H-1 of α -anomer), 6.26 (d, $J_{1,\text{OH}}=4.8$ Hz, OH of β -anomer), 6.35 (d, $J_{1,\text{OH}}=4.5$ Hz, OH of α -anomer), 7.59 (d, $J_{2,\text{NH}}=8.0$ Hz, NH of α -anomer) and 7.90 (d, $J_{2,\text{NH}}=6.0$ Hz, NH of β -anomer). *Anal.* Found: C, 53.77; H, 7.96; N, 5.69. Calcd. for $\text{C}_{11}\text{H}_{19}\text{NO}_5$: C, 53.86; H, 7.81; N, 5.71%.

2-Acetamido-1-O-acetyl-2,3-dideoxy-5,6-O-isopropylidene- β -D-arabino-hexofuranose (4). Acetylation of **3** (150 mg) with acetic anhydride (1 ml) in pyridine (3 ml) at 0°C gave the product. It was purified by chromatography on a column of silica gel (15 g) with 100:1 CHCl_3 -MeOH, to give compound **4** (120 mg, 68%) as a syrup, $[\alpha]_D^{22} - 94^\circ$ ($c=0.9$, CHCl_3); $\nu_{\max}^{\text{film}} \text{ cm}^{-1}$: 3240 (NH), 1740 (C=O), 1650 and 1540 (amide), and 840 (Me_2C); NMR δ (90 MHz): 1.33 and 1.40 (6H, 2s, Me_2C), 1.98 (3H, s, AcN), 2.10 (3H, s, AcO), 1.60~1.97 and 2.28~2.64 (2H, H-3,3'), 4.60 (1H, m, $J_{1,2}=4.2$, $J_{2,3}=7.8$, $J_{2,3'}=11.3$, $J_{2,\text{NH}}=8.0$ Hz, H-2), 6.10 (1H, d, $J_{1,2}=4.2$ Hz, H-1), and 6.29 (1H, d, $J_{2,\text{NH}}=8.0$ Hz, NH). *Anal.* Found: C, 54.55; H, 7.30; N, 4.72. Calcd. for $\text{C}_{13}\text{H}_{21}\text{NO}_6$: C, 54.34; H, 7.37; N, 4.88%.

2-Acetamido-1-O-acetyl-2,3-dideoxy-5,6-O-isopropylidene- α -D-ribo-hexofuranose (6). Acetylation of **5** (150 mg) was performed in the same way as described above. Recrystallization of the product from ether gave **6** (145 mg, 83%) as needles, mp 118°C, $[\alpha]_D^{22} + 109^\circ$ ($c=0.4$, CHCl_3); $\nu_{\max}^{\text{Nujol}} \text{ cm}^{-1}$: 3310 (NH), 1725 (C=O), 1640 and 1520 (amide), and 850 (Me_2C); NMR δ (90 MHz): 1.33 and 1.43 (6H, 2s, Me_2C), 1.73~2.00 (1H, m, H-3), 1.99 (3H, s, AcN), 2.10 (3H, s, AcO), 2.41 (1H, m, $J_{3,3'}=12.5$, $J_{2,3'}=8.3$, $J_{3',4}=2.5$ Hz, H-3'), 4.72 (1H, m, $J_{1,2}=4.2$, $J_{2,3}=11.0$, $J_{2,3'}=8.3$, $J_{2,\text{NH}}=8.3$ Hz, H-2), 5.77 (1H, d, $J_{2,\text{NH}}=8.3$ Hz, NH), and 6.15 (1H, d, $J_{1,2}=4.2$ Hz, H-1). *Anal.* Found: C, 54.30; H, 7.42; N, 4.80. Calcd. for $\text{C}_{13}\text{H}_{21}\text{NO}_6$: C, 54.34; H, 7.37; N, 4.88%.

2-Acetamido-1,4,6-tri-O-acetyl-2,3-dideoxy- α -D-arabino-hexopyranose (7a) and 2-acetamido-1,4,6-tri-O-acetyl-2,3-dideoxy- β -D-arabino-hexopyranose (7b). A solution of **3** (150 mg) in 60% aqueous acetic acid (5 ml) was heated for 2 hr at 45°C, and evaporated. The syrupy residue was acetylated with acetic anhydride (1 ml) in pyridine (5 ml) at 0°C. After evaporation, the residue was chromatographed on a column of silica gel (15 g) with CHCl_3 and 70:1 CHCl_3 -MeOH. With the latter eluate, compound **7a** (120 mg, 59%) was obtained as the faster-moving component, mp 172°C, $[\alpha]_D^{25} - 36.7^\circ$ ($c=0.65$, CHCl_3); $\nu_{\max}^{\text{Nujol}} \text{ cm}^{-1}$: 3290 (NH), 1740 (C=O), and 1640 and 1530 (amide); NMR δ (90 MHz): 2.01 (3H, s, AcN), 2.07 and 2.10 (9H, 2s, 3AcO), 5.82 (1H, d, $J_{2,\text{NH}}=8.0$ Hz,

NH), and 5.90 (1H, d, $J_{1,2}=3.0$ Hz, H-1). *Anal.* Found: C, 50.86; H, 6.26; N, 4.22. Calcd. for $\text{C}_{14}\text{H}_{21}\text{NO}_8$: C, 50.75; H, 6.39; N, 4.23%.

Compound **7b** appeared as the slower-moving component, and was obtained as a syrup (35 mg, 17%), $[\alpha]_D^{22} - 51^\circ$ ($c=0.35$, CHCl_3); $\nu_{\max}^{\text{film}} \text{ cm}^{-1}$: 3250 (NH), 1740 (C=O), and 1650 and 1540 (amide); NMR δ (90 MHz): 1.99, 2.05, 2.09 and 2.13 (12H, 4s, AcN and 3AcO), 5.05 (1H, m, $J_{3a,4}=J_{4,5}=6.7$, $J_{3e,4}=3.0$ Hz, H-4), 6.04 (1H, d, $J_{2,\text{NH}}=8.0$ Hz, NH), and 6.13 (1H, d, $J_{1,2}=4.3$ Hz, H-1). *Anal.* Found: C, 50.51; H, 6.44; N, 4.04. Calcd. for $\text{C}_{14}\text{H}_{21}\text{NO}_8$: C, 50.75; H, 6.39; N, 4.23%.

2-Acetamido-1,4,6-tri-O-acetyl-2,3-dideoxy- α -D-ribo-hexopyranose (8). Hydrolysis of **5** (150 mg) and subsequent acetylation were carried out as described above. Crystallization of the product from ether gave compound **8** (135 mg, 67%) as needles, mp 146~147°C, $[\alpha]_D^{15} + 108.5^\circ$ ($c=0.3$, CHCl_3); lit.⁽¹¹⁾ mp 151~152°C, $[\alpha]_D^{23} + 107.4^\circ$ ($c=0.5$, CHCl_3).

Benzyl 2-acetamido-2-deoxy-5,6-O-isopropylidene-3-O-methyl- β -D-glucofuranoside (10). To a solution of benzyl 2-acetamido-2-deoxy-5,6-O-isopropylidene- β -D-glucofuranoside⁽⁹⁾ (**9**) (500 mg) in dry 1,4-dioxane (5 ml) were added methyl iodide (950 mg) and silver oxide (1.6 g). The mixture was stirred in the dark overnight at room temperature, and the insoluble materials were then removed by filtration. The filtrate was evaporated to a syrup which was chromatographed on a column of silica gel (20 g) with CHCl_3 and 100:1 CHCl_3 -MeOH. The latter eluate gave compound **10** (510 mg, 98%) as a syrup, $[\alpha]_D^{26} - 98.1^\circ$ ($c=0.7$, CHCl_3); $\nu_{\max}^{\text{film}} \text{ cm}^{-1}$: 3250 (NH), 1640 and 1530 (amide), 850 (Me_2C), and 740 and 690 (phenyl); NMR δ (60 MHz): 1.30 and 1.38 (6H, 2s, Me_2C), 1.88 (3H, s, AcN), 3.47 (3H, s, MeO), 5.00 (1H, s, H-1), 6.52 (1H, broad s, NH), and 7.30 (5H, s, Ph). *Anal.* Found: C, 62.23; H, 7.37; N, 3.70. Calcd. for $\text{C}_{19}\text{H}_{27}\text{NO}_6$: C, 62.45; H, 7.45; N, 3.83%.

Benzyl 2-acetamido-2-deoxy-5,6-O-isopropylidene-3-O-(tetrahydropyran-2-yl)- β -D-glucofuranoside (11). To a solution of **9** (400 mg) in dry 1,4-dioxane (5 ml) were added dihydropyran (200 mg) and *p*-toluenesulfonic acid monohydrate (5 mg). The mixture was stirred for 4 hr at room temperature, treated with Amberlite IR-45 (OH^-) resin to remove the acid, and evaporated to a syrup which was chromatographed on a column of silica gel (20 g), firstly with CHCl_3 , and then with 100:1 CHCl_3 -MeOH. The latter eluant gave compound **11** (480 mg, 97%) as a syrup, $[\alpha]_D^{26} - 50.3^\circ$ ($c=0.32$, CHCl_3); $\nu_{\max}^{\text{film}} \text{ cm}^{-1}$: 3250 (NH), 1640 and 1540 (amide), 840 (Me_2C) and 740, 730, and 690 (phenyl). *Anal.* Found: C, 63.38; H, 7.71; N, 3.06. Calcd. for $\text{C}_{23}\text{H}_{33}\text{NO}_7$: C, 63.43; H, 7.64; N, 3.22%.

Benzyl 2-acetamido-2-deoxy-5,6-O-isopropylidene-3-O-mesyl- β -D-glucofuranoside (12). To an ice-cooled solution

of **9** (1.0 g) in dry pyridine (10 ml) was added methanesulfonyl chloride (500 mg), and the mixture was kept for 5 hr at 0°C. After evaporation of the solvent, the mixture was extracted with CHCl_3 , and the extract was successively washed with 2 M HCl, M Na_2CO_3 and H_2O , dried (Na_2SO_4), and evaporated to a syrup. The product was purified by chromatography on a column of silica gel (25 g) with 100:1 CHCl_3 -MeOH. Recrystallization from ether-hexane afforded **12** (810 mg, 66%) as needles, mp 110°C, $[\alpha]_D^{18} - 70.5^\circ$ ($c=0.5$, CHCl_3); $\nu_{\text{max}}^{\text{Nujol}} \text{ cm}^{-1}$: 3240 (NH), 1650 and 1545 (amide), 1340 and 1180 (SO_2), 840 (Me_2C), and 740 and 695 (phenyl); NMR δ (60 MHz): 1.31 and 1.42 (6H, 2s, Me_2C), 1.95 (3H, s, AcN), 3.15 (3H, s, MeSO_2), 5.07~5.18 (2H, H-1 and H-3), 6.60 (1H, broad s, NH) and 7.34 (5H, s, Ph). *Anal.* Found: C, 53.30; H, 6.48; N, 3.23. Calcd. for $\text{C}_{19}\text{H}_{27}\text{NO}_8\text{S}$: C, 53.13; H, 6.34; N, 3.26%.

2-Acetamido-2-deoxy-5,6-O-isopropylidene-3-O-methyl-D-glucofuranose (14). To a solution of **10** (350 mg) in MeOH (15 ml) was added 10% Pd-C catalyst (700 mg), and the mixture was hydrogenated, with stirring, for 3 hr at 40°C. The catalyst was filtered off and washed with MeOH. The filtrate and washings were combined, and evaporated to a syrup which was chromatographed on a column of silica gel (20 g) firstly with CHCl_3 and then 50:1 CHCl_3 -MeOH. The latter eluate afforded compound **14** (215 mg, 82%) as crystals. Recrystallization from EtOH-Et₂O gave needles, mp 106~107°C, $[\alpha]_D^{26} - 9.5^\circ$ ($c=0.6$, MeOH; 24 hr); NMR δ (60 MHz): 1.29 and 1.35 (6H, 2s, Me_2C), 2.00 (3H, s, AcN), 5.20 (d, $J_{1,2}=0$, $J_{1,\text{OH}}=10.0$ Hz, H-1 of β -anomer), 5.57 (dd, $J_{1,2}=5.5$, $J_{1,\text{OH}}=4.0$ Hz, H-1 of α -anomer), 5.78 (1H, OH) and 6.60 (1H, d, $J_{2,\text{NH}}=7.0$ Hz, NH). *Anal.* Found: C, 52.41; H, 7.80; N, 4.98. Calcd. for $\text{C}_{12}\text{H}_{21}\text{NO}_6$: C, 52.35; H, 7.69; N, 5.09%.

2-Acetamido-2-deoxy-5,6-O-isopropylidene-3-O-(tetrahydropyran-2-yl)-D-glucofuranose (15). To a solution of **11** (220 mg) in MeOH (10 ml) was added 10% Pd-C catalyst (400 mg), and the mixture was hydrogenated, with stirring, for 4 hr at room temperature. After removal of the catalyst and evaporation of the solvent, the product was purified by chromatography on a column of silica gel (15 g) with 50:1 CHCl_3 -MeOH to give **15** (121 mg, 69%) as a syrup, $[\alpha]_D^{28} + 9.8^\circ$ ($c=1.2$, CHCl_3 ; 24 hr); $\nu_{\text{max}}^{\text{film}} \text{ cm}^{-1}$: 3340~3260 (OH and NH), 1640 and 1520 (amide), and 840 (Me_2C). *Anal.* Found: C, 55.35; H, 7.96; N, 3.99. Calcd. for $\text{C}_{16}\text{H}_{27}\text{NO}_7$: C, 55.64; H, 7.88; N, 4.06%.

Benzyl 2-acetamido-2-deoxy-5,6-O-isopropylidene- β -D-allofuranoside (16). To a solution of **12** (780 mg) in 90% aqueous EtOH (8 ml) was added AcOK (500 mg), the mixture being boiled under reflux, with stirring, for 5 hr. After being cooled, the insoluble materials were removed by filtration and the filtrate was evaporated to a syrup which was chromatographed on a column of silica gel

(20 g) with CHCl_3 and 100:1 CHCl_3 -MeOH. The latter eluate afforded compound **16** (630 mg) as a syrup which crystallized from ether-hexane to give plates (570 mg, 89%), mp 90°C, $[\alpha]_D^{18} - 42^\circ$ ($c=0.6$, CHCl_3); $\nu_{\text{max}}^{\text{Nujol}} \text{ cm}^{-1}$: 3340 (OH), 3270 (NH), 1610 and 1530 (amide), 850 (Me_2C), and 750 and 695 (phenyl); NMR δ (60 MHz): 1.31 and 1.41 (6H, 2s, Me_2C), 1.98 (3H, s, AcN), 5.06 (1H, d, $J_{1,2}=1.3$ Hz, H-1), 6.49 (1H, d, $J_{2,\text{NH}}=6.0$ Hz, NH), and 7.30 (5H, s, Ph). *Anal.* Found: C, 61.48; H, 7.14; N, 4.03. Calcd. for $\text{C}_{18}\text{H}_{25}\text{NO}_6$: C, 61.52; H, 7.17; N, 3.99%.

Benzyl 2-acetamido-3-O-acetyl-2-deoxy-5,6-O-isopropylidene- β -D-allofuranoside (17). Acetylation of **16** (60 mg) with acetic anhydride (0.5 ml) in pyridine (2 ml) at room temperature gave the product. Recrystallization from ether-hexane gave **17** (60 mg, 90%) as needles, mp 88.5~89°C, $[\alpha]_D^{21} - 66^\circ$ ($c=0.5$, CHCl_3); $\nu_{\text{max}}^{\text{Nujol}} \text{ cm}^{-1}$: 3240 (NH), 1750 and 1230 (ester), 1650 and 1540 (amide), 840 (Me_2C), and 740 and 695 (phenyl); NMR δ (60 MHz): 1.30 and 1.40 (6H, 2s, Me_2C), 1.95 (3H, s, AcN), 2.02 (3H, s, AcO), 4.00 (1H, m, H-4), 4.26 (1H, m, H-2), 5.03 (1H, d, $J_{1,2}=2.3$ Hz, H-1), 5.47 (1H, t, $J_{2,3}=J_{3,4}=6.0$ Hz, H-3), 6.67 (1H, d, $J_{2,\text{NH}}=7.0$ Hz, NH), and 7.28 (5H, s, Ph). *Anal.* Found: C, 61.27; H, 6.80; N, 3.51. Calcd. for $\text{C}_{20}\text{H}_{27}\text{NO}_7$: C, 61.05; H, 6.92; N, 3.56%.

2-Acetamido-2-deoxy-5,6-O-isopropylidene-D-allofuranose (18). To a solution of **16** (350 mg) in MeOH (25 ml) was added 10% Pd-C catalyst (400 mg), the mixture being hydrogenated, with stirring, for 5 hr at 30°C. After removal of the catalyst and evaporation of the solvent, the product was purified by chromatography on a column of silica gel (15 g) with 50:1 and then 20:1 CHCl_3 -MeOH. The latter eluate gave compound **18** (211 mg, 81%) as crystals. Recrystallization from EtOH-Et₂O gave needles, mp 133~134°C, $[\alpha]_D^{20} - 10^\circ$ ($c=0.5$, MeOH; 24 hr); $\nu_{\text{max}}^{\text{Nujol}} \text{ cm}^{-1}$: 3400 (OH), 3240 (NH), 1610 and 1540 (amide), and 840 (Me_2C). *Anal.* Found: C, 50.68; H, 7.46; N, 5.29. Calcd. for $\text{C}_{11}\text{H}_{19}\text{NO}_6$: C, 50.56; H, 7.33; N, 5.36%.

2,5-Diacetamido-2,5-dideoxy-D-xylofuranose (22). To a solution of benzyl 2,5-diacetamido-2,5-dideoxy- β -D-xylofuranoside¹⁰⁾ (**19**) (1.1 g) in 60% aqueous MeOH (70 ml) and AcOH (0.7 ml) was added 10% Pd-C catalyst (300 mg). The mixture was hydrogenated, with stirring, for 3 hr at room temperature. The catalyst was removed by filtration, and the filtrate was evaporated to give crystals which recrystallized from EtOH-Et₂O. Compound **22** was obtained as needles, yield 610 mg (77%), mp 171°C, $[\alpha]_D^{26} + 64^\circ$ ($c=0.5$, MeOH; 24 hr); $\nu_{\text{max}}^{\text{Nujol}} \text{ cm}^{-1}$: 3410~3260 (OH and NH), 1635, 1620 and 1560 (amide). *Anal.* Found: C, 46.41; H, 6.89; N, 11.75. Calcd. for $\text{C}_9\text{H}_{16}\text{N}_2\text{O}_5$: C, 46.54; H, 6.94; N, 12.06%.

2,5-Diacetamido-2,5-dideoxy-D-ribofuranose (23) To a solution of benzyl 2,5-diacetamido-2,5-dideoxy- β -D-

ribofuranoside¹⁰) (**20**) (480 mg) in 80% aqueous MeOH (15 ml) and AcOH (0.15 ml) was added 10% Pd-C catalyst (500 mg), and the mixture was hydrogenated for 3.5 hr at room temperature. After the same treatment as described above, compound **23** (245 mg, 71%) was obtained as needles, mp 151~153°C, $[\alpha]_D^{20} -16^\circ$ ($c=0.5$, MeOH; 24 hr); $\nu_{\text{max}}^{\text{Nujol}} \text{ cm}^{-1}$: 3380, 3340, 3290 and 3260 (OH, NH), and 1640, 1610, 1560 and 1540 (amide); NMR δ (60 MHz, CD₃OD): 1.93, 1.99 and 2.01 (6H, 3s, 2AcN), 5.13 (d, $J_{1,2}=2.1$ Hz, H-1 of β -anomer), and 5.30 (d, $J_{1,2}=4.3$ Hz, H-1 of α -anomer). *Anal.* Found: C, 46.18; H, 6.80; N, 11.81. Calcd. for C₉H₁₆N₂O₅: C, 46.54; H, 6.94; N, 12.06%.

2,3,5-Triacetamido-2,3,5-trideoxy-D-ribofuranose (24). To a solution of benzyl 2,3,5-triacetamido-2,3,5-trideoxyl- β -D-ribofuranoside¹⁰) (**21**) (520 mg) in 70% aqueous MeOH (30 ml) and AcOH (0.3 ml) was added 10% Pd-C catalyst (500 mg), and the mixture was hydrogenated for 2 hr at 40°C. After the same procedure as described in the preparation of **22**, compound **24** (350 mg, 89%) was obtained as prisms, mp 187~188°C, $[\alpha]_D^{15} -10.5^\circ$ ($c=0.3$, MeOH; 24 hr); $\nu_{\text{max}}^{\text{Nujol}} \text{ cm}^{-1}$: 3360 (OH), 3240 (NH), and 1640, 1550 and 1510 (amide). *Anal.* Found: C, 48.16; H, 6.90; N, 15.15. Calcd. for C₁₁H₁₉N₃O₅: C, 48.34; H, 7.01; N, 15.38%.

2-Acetamido-2,3-dideoxy-5,6-O-isopropylidene- α -D-erythro-hex-2-enofuranose (1).

(A) From **14**. To a solution of **14** (60 mg) in MeOH (2 ml) was added Amberlite IRA-410 (OH⁻) ion-exchange resin (2 g), and the mixture was stirred for 6 hr at room temperature. The suspension was filtered and the resin was washed with MeOH. The filtrate and washings were combined, and evaporated to a syrup which was chromatographed on a column of silica gel (12 g) with CHCl₃ and then 50:1 CHCl₃-MeOH. The latter eluate afforded a homogeneous syrup which crystallized from benzene, to give compound **1** (35 mg, 66%).

(B) From **15**. Alkaline ion-exchange resin treatment of **15** (120 mg) in MeOH was performed according to the procedure as described above. The title compound was obtained as crystals (50 mg, 59%).

(C) From **18**. To a solution of **18** (100 mg) in MeOH (3 ml) was added Amberlite IRA-410 (2 g), and the mixture was stirred for 24 hr at 50°C. After the same treatment as already described, the title compound (40 mg, 43%) was obtained, mp 152°C, $[\alpha]_D^{25} -21^\circ$ (2 min) $\rightarrow -5^\circ$ (5 hr) $\rightarrow +0.7^\circ$ ($c=1.0$, MeOH; 17 hr), $[\alpha]_D^{25} -35^\circ$ (2 min) $\rightarrow -33^\circ$ ($c=0.5$, CHCl₃; 2 hr), $[\alpha]_D^{25} -58^\circ$ (2 min) $\rightarrow -57^\circ$ ($c=0.5$, DMSO; 2 hr); lit.⁹) mp 156~158°C, $[\alpha]_D^{20} -3.7^\circ$ (7 min) $\rightarrow +11.3^\circ$ ($c=0.99$, 4:1 MeOH-H₂O; 20 hr).

2,5-Diacetamido-2,3,5-trideoxy-D-glycero-pent-2-enofuranose (25).

(A) From **22**. To a solution of **22** (300 mg) in MeOH (15 ml) was added Amberlite IRA-410 (3 g), and the

mixture was stirred for 14 hr at room temperature. The resin was filtered and washed with MeOH. The filtrate and washings were combined and evaporated below 40°C. The syrupy residue was chromatographed on a column of alumina gel (10 g) with 20:1 CHCl₃-MeOH to afford a syrup (230 mg), which was crystallized from acetone-ether to give compound **25** (200 mg, 67%), mp 105~115°C (dec.), $[\alpha]_D^{28} -5^\circ$ ($c=0.2$, MeOH; 24 hr); $\nu_{\text{max}}^{\text{Nujol}} \text{ cm}^{-1}$: 3480~3240 (OH and NH), 1680 (C=C), and 1610 and 1570 (amide); NMR δ (90 MHz, DMSO-*d*₆): 1.80 and 1.94 (6H, 2s, 2AcN), 3.12 (2H, m, $J_{4,5}=6.8$, $J_{4,5'}=5.8$, $J_{5,\text{NH}}=12.8$, $J_{5',\text{NH}}=11.8$ Hz, H-5 and H-5'), 6.42 and 6.58 (1H, 2d, OH), 7.75 (1H, m, NH at C-5), and 9.64 (1H, s, NH at C-2). Other NMR data are given in Table I. *Anal.* Found: C, 46.58; H, 6.90; N, 11.82. Calcd. for C₉H₁₄N₂O₄·H₂O: C, 46.54; H, 6.94; N, 12.06%.

(B) From **23**. To a solution of **23** (150 mg) in MeOH (3 ml) was added Amberlite IRA-410 (1.5 g), and the mixture was stirred for 20 hr at 40°C. After the same treatment as described above, compound **25** (65 mg, 43%) was obtained as crystals.

2,5-Diacetamido-2,5-dideoxy-D-xylopyranose (26). To a solution of **22** (300 mg) in MeOH (15 ml) was added Amberlite IRA-410 (3 g), and the mixture was stirred at room temperature. After 20 min, the ratio of the product to the starting material reached ~1:1 on TLC, but compound **25** had not yet been detected. The resin was filtered off and washed with MeOH. The filtrate and washings were combined, and evaporated. The solid mass thus obtained was crystallized from MeOH to give compound **26** as needles (70 mg, 24%), mp 190~192°C (dec.), $[\alpha]_D^{20} +17^\circ$ ($c=0.38$, MeOH; 24 hr); $\nu_{\text{max}}^{\text{Nujol}} \text{ cm}^{-1}$: 3400, 3300 and 3250 (OH and NH), and 1610 and 1540 (amide). *Anal.* Found: C, 46.31; H, 6.84; N, 11.96. Calcd. for C₉H₁₆N₂O₅: C, 46.54; H, 6.94; N, 12.06%.

2,5-Diacetamido-1,3,4-tri-O-acetyl-2,5-dideoxy- α -D-xylopyranose (27). Compound **26** (40 mg) was acetylated with acetic anhydride (0.5 ml) in pyridine (5 ml) overnight at 0°C. After the usual treatment, the product was obtained as prisms (50 mg, 81%), mp 178~179°C, $[\alpha]_D^{20} +30^\circ$ ($c=0.25$, CHCl₃); $\nu_{\text{max}}^{\text{Nujol}} \text{ cm}^{-1}$: 3250 (NH), 1750 and 1220 (ester), and 1650 and 1550 (amide); NMR δ (90 MHz): 1.95, 2.06, 2.07, 2.16, 2.29 (15H, 5s, 2AcN and 3AcO), 2.78 (1H, t, $J_{\text{gem}}=J_{4,5a}=10.2$ Hz, H-5a), 4.28 (1H, m, H-2), 4.75 (1H, m, H-5e), 4.94 (1H, m, $J_{3,4}=9.1$, $J_{4,5a}=10.2$, $J_{4,5e}=5.7$ Hz, H-4), 5.27 (1H, dd, $J_{2,3}=10.7$, $J_{3,4}=9.1$ Hz, H-3), 6.04 (1H, d, $J_{2,\text{NH}}=8.0$ Hz, NH) and 6.52 (1H, d, $J_{1,2}=3.8$ Hz, H-1). *Anal.* Found: C, 50.16; H, 6.13; N, 7.80. Calcd. for C₁₅H₂₂N₂O₈: C, 50.27; H, 6.19; N, 7.82%.

2,3,5-Triacetamido-2,3,5-trideoxy-D-ribofuranose (28). To a solution of **24** (200 mg) in MeOH (5 ml) was added Amberlite IRA-410 (2 g), and the mixture was stirred overnight at room temperature. The starting material was

no longer detectable on TLC. The resin was removed by filtration and the filtrate was evaporated to afford a crystalline product; it was recrystallized from EtOH to give needles (120 mg, 60%), mp 251°C, $[\alpha]_D^{20} + 36.5^\circ$ ($c = 0.5$, MeOH; 24 hr); $\nu_{\max}^{\text{Nujol}} \text{ cm}^{-1}$: 3350–3270 (OH, NH), and 1640 and 1540 (amide). *Anal.* Found: C, 48.18; H, 6.93; N, 14.98. Calcd. for $\text{C}_{11}\text{H}_{19}\text{N}_3\text{O}_5$: C, 48.34; H, 7.01; N, 15.38%.

2,3,5-Triacetamido-1,4-di-O-acetyl-2,3,5-trideoxy-D-ribofuranose (29). Compound **28** (50 mg) was acetylated with acetic anhydride (1 ml) in pyridine (5 ml) overnight at 0°C. Compound **29** was obtained as an amorphous mass (65 mg, quantitative); $\nu_{\max}^{\text{Nujol}} \text{ cm}^{-1}$: 3260 (NH), 1750 (C=O), and 1650 and 1540 (amide); NMR δ (90 MHz, CD_3OD): 1.97, 1.98, 2.10 and 2.12 (15H, 4s, 3AcN and 2AcO), 6.00 ($J_{1,2} = 2.2 \text{ Hz}$, H-1 of α -anomer), and 6.16 (d, $J_{1,2} = 4.3 \text{ Hz}$, H-1 of β -anomer). *Anal.* Found: C, 50.29; H, 6.28; N, 11.47. Calcd. for $\text{C}_{15}\text{H}_{23}\text{N}_3\text{O}_7$: C, 50.42; H, 6.49; N, 11.76%.

Acknowledgments. We thank Professor Ichiro Azuma for his encouragement and Miss Mutsuko Araki for typing the manuscript.

REFERENCES

- 1) R. Kuhn and G. Krüger, *Chem. Ber.*, **89**, 1473 (1956).
- 2) A. Hasegawa and H. G. Fletcher, Jr., *Carbohydr. Res.*, **29**, 223 (1973).
- 3) A. Hasegawa, T. Sakurai and N. Hasegawa, *Carbohydr. Res.*, **45**, 19 (1975).
- 4) A. Hasegawa, N. Aritake and M. Kiso, *Carbohydr. Res.*, **52**, 137 (1976).
- 5) A. Hasegawa and M. Kiso, *Carbohydr. Res.*, **63**, 91 (1978).
- 6) H. Ohru, N. Sueda and S. Emoto, *Agric. Biol. Chem.*, **42**, 865 (1978).
- 7) A. Hasegawa, H. Okumura, K. Nishibori, Y. Kaneda, M. Kiso and I. Azuma, *Carbohydr. Res.*, **97**, 337 (1981).
- 8) A. Hasegawa and M. Kiso, *Carbohydr. Res.*, **74**, 341 (1979).
- 9) J.-M. Beau, P. Rollin and P. Sinaÿ, *Carbohydr. Res.*, **53**, 187 (1977).
- 10) A. Hasegawa, N. Aritake and M. Kiso, *Carbohydr. Res.*, **81**, 23 (1980).
- 11) A. Hasegawa, E. Tanahashi and M. Kiso, *Carbohydr. Res.*, **79**, 255 (1980).
- 12) P. L. Durette and D. Horton, *J. Org. Chem.*, **36**, 2658 (1971).
- 13) H. Paulsen, *Angew. Chem.*, **78**, 501 (1966).
- 14) R. V. Lemieux, K. A. Watanabe and A. A. Pavia, *Can. J. Chem.*, **47**, 4413 (1969).
- 15) R. J. Ferrier and J. R. Hurford, *Carbohydr. Res.*, **38**, 125 (1974).