Carbohydrate Research, 81 (1980) 23–33

SYNTHESIS OF 2,5-DIACETAMIDO-2,5-DIDEOXY- AND 2,3,5-TRIACETAMIDO-2,3,5-TRIDEOXY-D-ALDOPENTOFURANOSE DERIVATIVES*

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(Received September 26th, 1979; accepted for publication, October 22nd, 1979)

ABSTRACT

2,5-Diacetamido-1,3-di-*O*-acetyl-2,5-dideoxy-α-D-xylofuranose, 2,5-diacetamido-1,3-di-*O*-acetyl-2,5-dideoxy-D-ribofuranose, 2,3,5-triacetamido-1-*O*-acetyl-2,3,5-trideoxy-α-D-xylofuranose, and 2,3,5-triacetamido-1-*O*-acetyl-2,3,5-trideoxy-α(and -β)-D-ribofuranose were synthesized from benzyl 2-(benzyloxycarbonylamino)-2-deoxy-β-D-xylofuranoside (**1**). The derived *p*-toluenesulfonate or methanesulfonate underwent displacement with azide ion, to yield, after reduction and acetylation, benzyl 2,5-diacetamido-3-*O*-acetyl-2,5-dideoxy-β-D-xylofuranoside, or benzyl 2,3,5-triacetamido-2,3,5-trideoxy-β-D-ribofuranoside (**20**), respectively. Treatment with sodium acetate of benzyl 2-acetamido-5-azido-3-*O*-mesyl-β-D-xylofuranoside (**10**), prepared from **1** in four steps, gave benzyl 2-acetamido-5-azido-2,5-dideoxy-β-D-ribofuranoside (**14**). Reduction of **14**, followed by acetylation, afforded the corresponding 2,5-diaminoribofuranoside derivative. Benzyl 2,3,5-triacetamido-2,3,5-trideoxy-β-D-xylofuranoside (**13**) was synthesized by way of an azide-exchange reaction on benzyl 2-acetamido-5-azido-2,5-dideoxy-3-*O*-mesyl-β-D-ribofuranoside, derived from **14**. Hydrogenation of benzyl 2,5-diacetamido-2,5-dideoxy-β-D-xylofuranoside and **13**, and benzyl 2,5-diacetamido-2,5-dideoxy-β-D-ribofuranoside and **20**, followed by acetylation, gave the title compounds in good yields. Treatment of **10**, or benzyl 2-acetamido-2-deoxy-3,5-di-*O*-mesyl-β-D-xylofuranoside, derived from benzyl 2-(benzyloxycarbonylamino)-2-deoxy-3,5-di-*O*-mesyl-β-D-xylofuranoside, with sodium azide afforded 2-methyl-(benzyl 5-azido-2,3,5-trideoxy-β-D-ribofuranosido)-[2,3-*d*]-2-oxazoline in good yield. Evidence in support of the structures assigned to the new derivatives is presented.

INTRODUCTION

In previous papers[2–5] in this series, we have shown that various *N*-substituted 2-amino-2-deoxyaldohexoses react with 2,2-dialkoxypropane–*N*,*N*-dimethylformamide–*p*-toluenesulfonic acid to give 5,6-*O*-isopropylidene furanosides. The potential

*The Behavior of Some Aldoses with 2,2-Dialkoxypropane–*N*,*N*-dimethylformamide–*p*-Toluenesulfonic acid, Part IX. For Part VIII, see ref. 1.

utility of this reagent for syntheses in the field of amino sugars was emphasized. The present paper describes the synthesis of two 2,5-diamino- and two 2,3,5-triamino-pentofuranose derivatives, undertaken as part of a program aimed at the synthesis of hetero sugars, and in view of the chemical properties of 5-amino-5-deoxypentofuranose derivatives.

RESULTS AND DISCUSSION

Benzyl 2-(benzyloxycarbonylamino)-2-deoxy-β-D-xylofuranoside[6] (**1**), derived from benzyl 2-(benzyloxycarbonylamino)-2-deoxy-5,6-*O*-isopropylidene-β-D-glucofuranoside[3,4], served as a convenient starting-material for the synthesis of all of the amino furanose derivatives described herein. Treatment of **1** with *p*-toluenesulfonyl chloride gave benzyl 2-(benzyloxycarbonylamino)-2-deoxy-5-*O*-tosyl-β-D-xylofuranoside (**2**), which was converted, *via* hydrogenation, *N*-acetylation, and a displacement reaction with sodium azide, into benzyl 2-acetamido-5-azido-2,5-dideoxy-β-D-xylofuranoside (**6**) according to the method reported[7] earlier.

Selective reduction of the azide group in compound **6** with hydrogen in the presence of 10% Pd–C catalyst gave the amino derivative, which was isolated as the acetic acid salt **7**; the 5-*N*-acetyl derivative (**8**) was formed by *N*-acetylation of **7**, and the peracetate (**9**) by *O*-acetylation of **8**. The structure of **9** was based on elemental analysis, and i.r. and n.m.r. spectroscopy. The n.m.r. spectrum (in chloroform-*d*) revealed the presence of two acetamido and one *O*-acetyl groups at δ 1.86, 1.97, and 2.08, benzyl methylene at δ 4.70 (s), H-1 as a doublet at δ 5.11 (1.1 Hz), H-3 as a doublet of doublets at δ 5.31 ($J_{2,3}$ 2.9 Hz, $J_{3,4}$ 6.5 Hz), and phenyl protons at δ 7.38 (s), and these data were consistent with structure **9**.

Treatment of **6** with methanesulfonyl chloride in pyridine afforded the 3-*O*-mesyl derivative **10**, which was converted, in 90% yield, into benzyl 2-acetamido-5-azido-2,5-dideoxy-β-D-ribofuranoside (**14**) by heating with sodium acetate in 90% aqueous ethanol. Acetylation of **14** afforded the 3-acetate **15**; its n.m.r. spectrum (in chloroform-*d*) showed the presence of one *N*-acetyl and one *O*-acetyl group, at δ 1.97 and 2.05, H-4 as a quartet at δ 4.30 ($J_{3,4} = J_{4,5} = J_{4,5'} = 6.0$ Hz), H-1 as a doublet at δ 5.06 ($J_{1,2}$ 2.0 Hz), and H-3 as a triplet at δ 5.27 ($J_{2,3} = J_{3,4} =$ 6.0 Hz), indicating the structure shown for the β-D-ribofuranoside derivative **15**.

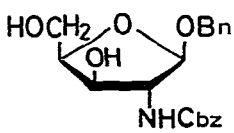
Reduction of the azide group in compound **14** with hydrogen in the presence of 10% Pd–C catalyst in ethanol gave the corresponding 5-amino-ribofuranoside derivative in good yield; this was also isolated as the acetic acid salt (**16**), the 5-*N*-acetyl derivative (**17**), and the peracetate (**18**). Significant signals in the n.m.r. spectrum of the peracetate **18** were a one-proton quartet at δ 4.20 ($J_{3,4} = J_{4,5} = J_{4,5'} =$ 6.0 Hz), a one-proton doublet at δ 5.10 ($J_{1,2}$ 1.8 Hz, H-1), and one-proton triplet at δ 5.31 ($J_{2,3} = J_{3,4} = 6.0$ Hz, H-3). Other n.m.r. data are given in the Experimental section, and are consistent with structure **18**.

Benzyl 2-acetamido-5-azido-2,5-dideoxy-β-D-ribofuranoside (**14**) was used as the starting material for the synthesis of a 2,3,5-triacetamido-2,3,5-trideoxy-D-xylose

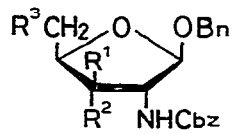
derivative. Methanesulfonylation of **14** gave the 3-mesylate **19**, which was treated with an excess of sodium azide in *N*,*N*-dimethylformamide for 2 days at 120°, to afford benzyl 2-acetamido-3,5-diazido-2,3,5-trideoxy-β-D-xylofuranoside (**12**). Reduction of the azide groups in compound **12**, and subsequent acetylation, yielded benzyl 2,3,5-triacetamido-2,3,5-trideoxy-β-D-xylofuranoside (**13**) in good yield.

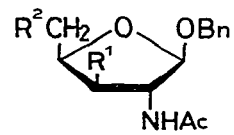
Treatment of benzyl 2-(benzyloxycarbonylamino)-2-deoxy-3,5-di-*O*-mesyl-β-D-xylofuranoside (**3**), derived from compound[7] **2**, with sodium azide gave the azide derivative **4** (whose i.r. and n.m.r. spectra were consistent with structure **4**). Hydrogenation of **4** with hydrogen in the presence of 10% Pd–C catalyst in 90% aqueous methanol, and subsequent acetylation, gave benzyl 2,3,5-triacetamido-2,3,5-trideoxy-β-D-ribofuranoside (**20**); the n.m.r. spectrum (in methanol-*d*) showed the presence of three acetamido groups, at δ 1.90, 1.96, and 1.99, H-1 as a singlet at δ 5.02, and phenyl protons at δ 7.40, indicating structure **20**.

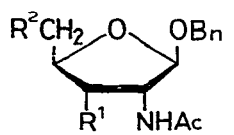
On the other hand, on treatment with sodium azide in *N*,*N*-dimethylformamide for 5 h at 90°, compound **10** or benzyl 2-acetamido-2-deoxy-3,5-di-*O*-mesyl-β-D-xylofuranoside (**11**), derived from **3** by hydrogenation and subsequent acetylation, afforded crystalline 2-methyl-(benzyl 5-azido-2,3,5-trideoxy-β-D-ribofuranosido)-[2,3-*d*]-2-oxazoline (**21**) in good yield, but none of the diazide compound was isolated. The structure of **21** was determined by elemental analysis, and i.r. and n.m.r. spectroscopy; its i.r. spectrum showed characteristic absorptions at 2070 (N_3) and 1660 cm^{-1} (C=N), and its n.m.r. spectrum revealed the presence of a methyl group (s, 3 H) at δ 1.99, H-1 as a singlet at δ 5.18, and phenyl protons (s, 5 H) at δ 7.33. Mild hydrolysis of **21** gave the β-D-ribofuranoside derivative **14**, and, on hydrogenation and subsequent acetylation, compound **21** afforded benzyl 2,5-diacetamido-3-*O*-acetyl-2,5-dideoxy-β-D-ribofuranoside (**18**) in 79% yield. These results supported the assignment of structure **21**.



1



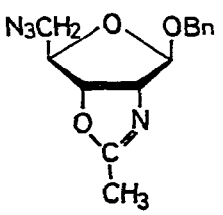




2 R^1 = OH, R^2 = H, R^3 = OTs
3 R^1, R^3 = OMs, R^2 = H
4 R^1 = H, R^2, R^3 = N_3

5 R^1 = OH, R^2 = OTs
6 R^1 = OH, R^2 = N_3
7 R^1 = OH, R^2 = NH_2.AcOH
8 R^1 = OH, R^2 = NHAc
9 R^1 = OAc, R^2 = NHAc
10 R^1 = OMs, R^2 = N_3
11 R^1, R^2 = OMs
12 R^1, R^2 = N_3
13 R^1, R^2 = NHAc

14 R^1 = OH, R^2 = N_3
15 R^1 = OAc, R^2 = N_3
16 R^1 = OH, R^2 = NH_2.AcOH
17 R^1 = OH, R^2 = NHAc
18 R^1 = OAc, R^2 = NHAc
19 R^1 = OMs, R^2 = N_3
20 R^1, R^2 = NHAc

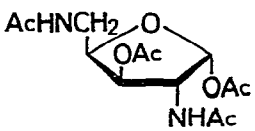


21

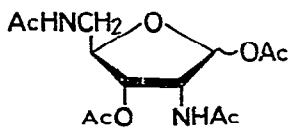
Hydrogenation of the benzyl group in compound **8** (in 90% aqueous methanol) with Pd-black catalyst afforded the free sugar, which gave a single spot in t.l.c. Acetylation gave the desired 2,5-diacetamido-1-*O*-acetyl-2,5-dideoxy-α-D-xylofuranose (**22**) in 82% yield. The structure of **22** was based on elemental analysis and n.m.r. spectroscopy. The n.m.r. spectrum (in methanol-d_4) exhibited two singlets, indicating twelve protons, at δ 1.94 and 2.07, which showed the presence of two *N*-acetyl and two *O*-acetyl groups. A low-field doublet appearing at δ 6.26 (5.2 Hz) was assigned to the anomeric proton of the α-acetate. The proton on C-3 appeared at δ 5.35 (7.0 Hz) as a triplet, indicating a gluco- or xylo-furanose derivative[8-10] having a 1-*O*-acyl or -alkyl group *cis* to the group on C-2.

Hydrogenation of the 2,5-diamino-β-D-ribofuranoside **17**, and subsequent acetylation, gave **23** as an anomeric mixture in 91% yield. In the n.m.r. spectrum of **23** (in methanol-d_4) at low-field, H-1 of the two anomers appeared as a doublet, at δ 6.02 (H-1β, 2.1 Hz) and 6.25 (H-1α, 5.0 Hz), and their intensity ratio indicated a mixture of the α and β anomers in the ratio of ~1 : 2. The proton on C-3 appeared as a doublet of doublets at δ 5.09 ($J_{2,3}$ 6.6, $J_{3,4}$ 2.2 Hz), and that of the β anomer as a triplet at δ 5.18 (5.2 Hz).

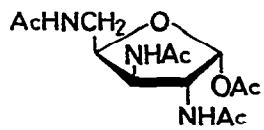
In the same way, hydrogenation and subsequent acetylation of the 2,3,5-triacetamido-β-D-xylofuranoside **13** and the 2,3,5-triacetamido-β-D-ribofuranoside **20** yielded the corresponding tetraacetyl furanose derivatives, **24** and **25a,b**, respectively, in excellent yields. On removal of the 1-*O*-benzyl group of the 5-acetamido-pentofuranosides by hydrogenation with Pd-black catalyst in neutral solution, only the furanose derivatives were isolated (in almost quantitative yields), and formation of sugars having nitrogen in the ring was not observed.



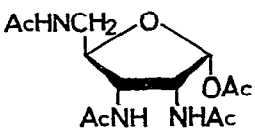
22



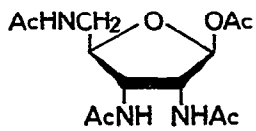
23



24



25a



25b

EXPERIMENTAL

General methods. — Melting points were determined with a Yanagimoto micro melting-point apparatus and are uncorrected. Specific rotations were deter-

mined with a Yanagimoto OR-50 polarimeter, and i.r. spectra were recorded with a Jasco IRA-1 spectrophotometer. N.m.r. spectra were recorded at 60 and 90 MHz with Hitachi R-24 and R-22 spectrometers. N.m.r. data were confirmed by use of decoupling techniques. Preparative chromatography was performed on silica gel (Waco Co.; 300 mesh) with the solvent systems specified. Evaporations were conducted *in vacuo*.

*Benzyl 2-acetamido-5-amino-2,5-dideoxy-β-*D*-xylofuranoside monoacetate* (**7**). — Benzyl 2-acetamido-5-azido-2,5-dideoxy-β-D-xylofuranoside[6] (**6**, 300 mg) was dissolved in ethanol (40 mL); 10% Pd–C catalyst (200 mg) was added, and hydrogen was bubbled through for 1 h while the solution was stirred at room temperature. The catalyst was filtered off, and acetic acid (1 mL) was added. The solution was evaporated, to give a crystalline product that was recrystallized from ethanol–ether, affording compound **7** (275 mg, 83%), m.p. 159°, $[\alpha]_D^{20}$ −59° (*c* 0.3, methanol); ν_{max}^{Nujol} 3320 (OH), 3180 and 1570 (NH), 2730–2400 (OH), 1660 (C=O), 1635 and 1540 (amide), and 740 and 690 cm^{-1} (phenyl).

Anal. Calc. for $C_{16}H_{24}N_2O_6$: C, 56.46; H, 7.11; N, 8.23. Found: C, 56.36; H, 7.28; N, 8.15.

*Benzyl 2,5-diacetamido-2,5-dideoxy-β-*D*-xylofuranoside* (**8**). — To a solution of **7** (600 mg) in methanol (10 mL) was added acetic anhydride (2 mL); after being kept for 30 min at room temperature, the solution was evaporated, to give a crystalline product. Recrystallization from ethanol gave **8** (550 mg, 97%) as needles, m.p. 249° (dec.), $[\alpha]_D^{20}$ −62° (*c* 0.3, methanol); ν_{max}^{Nujol} 3380 (OH), 3340 and 3270 (NH), 1650, 1600, 1570, and 1560 (amide), and 730 and 690 cm^{-1} (phenyl).

Anal. Calc. for $C_{16}H_{22}N_2O_5$: C, 59.61; H, 6.88; N, 8.69. Found: C, 59.35; H, 6.86; N, 8.71.

*Benzyl 2,5-diacetamido-3-*O*-acetyl-2,5-dideoxy-β-*D*-xylofuranoside* (**9**). — Compound **8** (150 mg) was acetylated by heating with acetic anhydride–pyridine for 2.5 h at 45°. The product was crystallized from ether; wt. 150 mg (88%), m.p. 182–183°, $[\alpha]_D^{20}$ −43° (*c* 0.3, methanol); ν_{max}^{Nujol} 3280 (NH), 1740 and 1235 (ester), 1650 and 1550 (amide), and 730 and 680 cm^{-1} (phenyl); n.m.r. data at 60 MHz (in chloroform-*d*): δ 1.86, 1.97, 2.08 (3 s, 9 H, 2 AcN, AcO), 3.38–3.53 (m, 2 H, H-5,5'), 4.25–4.50 (m, 2 H, H-2,4), 4.70 (s, 2 H, benzyl methylene), 5.11 (d, 1 H, $J_{1,2}$ 1.0 Hz, H-1), 5.31 (d of d, 1 H, $J_{2,3}$ 2.9, $J_{3,4}$ 6.5 Hz, H-3), 6.06 (near t, 1 H, NH), 7.18 (d, 1 H, $J_{2,NH}$ 7.5 Hz, NH), and 7.38 (s, 5 H, Ph).

Anal. Calc. for $C_{18}H_{24}N_2O_6$: C, 59.33; H, 6.64; N, 7.69. Found: C, 59.28; H, 6.51; N, 7.68.

*Benzyl 2-acetamido-5-azido-2,5-dideoxy-3-*O*-mesyl-β-*D*-xylofuranoside* (**10**). — To an ice-cooled solution of **6** (6.0 g) in dry pyridine (40 mL) was added methanesulfonyl chloride (4.8 g), and the mixture was kept for 3 h at 0°. The mixture was evaporated, the residue extracted with chloroform, and the extract successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried (sodium sulfate), and evaporated to give a crystalline product. Recrystallization from ethanol–ether afforded **10** (6.2 g, 82%) as needles, m.p. 128°, $[\alpha]_D^{20}$ −81° (*c* 0.3, chloroform);

ν_{max}^{Nujol} 3280 (NH), 2090 (azide), 1660 and 1540 (amide), 1180 (SO_2), and 735 and 690 cm^{-1} (phenyl).

Anal. Calc. for $C_{15}H_{20}N_4O_6S$: C, 46.86; H, 5.24; N, 14.58. Found: C, 46.83; H, 5.18; N, 14.70.

*Benzyl 2-acetamido-5-azido-2,5-dideoxy-β-*D*-ribofuranoside* (**14**). — (*A*) *From compound* **10**. To a solution of **10** (1.8 g) in 90% aqueous ethanol (65 mL) was added sodium acetate (3.6 g), and the mixture was refluxed for 8 h. The mixture was evaporated, the residue extracted with chloroform, and the extract successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried (sodium sulfate), and evaporated, to give a syrup which was crystallized from ether. The product was obtained as needles, wt. 1.3 g (91%), m.p. 128–130°, $[\alpha]_D^{20}$ −56° (*c* 0.3, chloroform); ν_{max}^{Nujol} 3300 (OH, NH), 2080 (azide), 1650 and 1540 (amide), and 750 and 690 cm^{-1} (phenyl).

Anal. Calc. for $C_{14}H_{18}N_4O_4$: C, 54.89; H, 5.92; N, 18.29. Found: C, 54.77; H, 5.81; N, 18.26.

(*B*) *From compound* **21**. To a solution of **21** (250 mg) in acetic acid (30 mL) was added 2M hydrochloric acid (1 mL). The mixture was heated for 4 h at 50°, cooled, and treated with Amberlite IRA-45 ion-exchange resin to remove hydrochloric acid; the resin was filtered off and washed with acetic acid. The filtrate and washings were combined, and evaporated to a syrup which was chromatographed on a column of silica gel (15 g) with chloroform and then with 50:1 chloroform–methanol. The latter eluate gave compound **14** (160 mg, 68%).

*Benzyl 2-acetamido-3-*O*-acetyl-5-azido-2,5-dideoxy-β-*D*-ribofuranoside* (**15**). — Acetylation of **14** (150 mg) with acetic anhydride–pyridine, by heating for 2.5 h at 45°, gave **15** (150 mg, 88%), m.p. 81°, $[\alpha]_D^{20}$ −63° (*c* 0.3, chloroform); ν_{max}^{Nujol} 3280 (NH), 2100 (azide), 1730 and 1230 (ester), 1660 and 1560 (amide), and 750 and 700 cm^{-1} (phenyl); n.m.r. data at 60 MHz (in chloroform-*d*): δ 1.98, 2.05 (2 s, 6 H, AcN, AcO), 4.30 (q, 1 H, $J_{3,4} = J_{4,5} = J_{4,5'} = 6.0$ Hz, H-4), 4.50, 4.79 (2 d, 2 H, J_{gem} 12.0 Hz, benzyl methylene), 4.55–4.82 (m, 1 H, H-2), 5.06 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1), 5.27 (t, 1 H, $J_{2,3} = J_{3,4} = 6.0$ Hz), 6.46 (d, 1 H, $J_{2,NH}$ 8.2 Hz, NH), and 7.30 (s, 5 H, Ph).

Anal. Calc. for $C_{16}H_{20}N_4O_5$: C, 55.16; H, 5.79; N, 16.08. Found: C, 55.28; H, 5.76; N, 16.30.

*Benzyl 2-acetamido-5-amino-2,5-dideoxy-β-*D*-ribofuranoside monoacetate* (**16**).— A solution of **14** (1.1 g) in ethanol (80 mL) was hydrogenated in the presence of 10% Pd–C catalyst (150 mg) for 20 min at 40°. The same procedure as used for the preparation of **7** gave **16** (900 mg, 74%) as needles, m.p. 105–108° (dec.), $[\alpha]_D^{20}$ −37° (*c* 0.3, methanol); ν_{max}^{Nujol} 3300 (OH), 3180 and 1580 (NH), 2730–2400 (OH), 1650 (C=O), 1640 and 1540 (amide), and 730 and 680 cm^{-1} (phenyl).

Anal. Calc. for $C_{16}H_{24}N_2O_6$: C, 56.46; H, 7.11; N, 8.23. Found: C, 56.55; H, 7.30; N, 8.19.

*Benzyl 2,5-diacetamido-2,5-dideoxy-β-*D*-ribofuranoside* (**17**). — *N*-Acetylation of **16** (310 mg) with acetic anhydride (2 mL) in methanol (10 mL) by the same

procedure as described in the preparation of **8** afforded compound **17** (280 mg, 95%), m.p. 135°, $[\alpha]_D^{20}$ −52° (*c* 0.5, methanol); ν_{max}^{Nujol} 3400 (OH), 3340 and 3300 (NH), 1650, 1620, 1560, and 1550 (amide), and 730 and 690 cm^{-1} (phenyl).

Anal. Calc. for $C_{16}H_{22}N_2O_5$: C, 59.61; H, 6.88; N, 8.69. Found: C, 59.58; H, 6.83; N, 8.75.

*Benzyl 2,5-diacetamido-3-*O*-acetyl-2,5-dideoxy-β-*D*-ribofuranoside* (**18**). — (*A*) *From compound* **17**. Acetylation of **17** (150 mg) with acetic anhydride–pyridine gave **18** (140 mg, 83%) as needles, m.p. 160°, $[\alpha]_D^{20}$ −48° (*c* 0.2, methanol); ν_{max}^{Nujol} 3300 and 3280 (NH), 1740 and 1240 (ester), 1655, 1640, 1560, and 1540 (amide), and 735 and 690 cm^{-1} (phenyl); n.m.r. data at 60 MHz (in chloroform-*d*): δ 1.81, 2.01, 2.07 (3 s, 9 H, 2 AcN, AcO), 3.37–4.08 (m, 2 H, H-5,5'), 4.20 (q, 1 H, $J_{3,4} = J_{4,5} = J_{4,5'} =$ 6.0 Hz, H-4), 4.41–4.90 (m, 1 H, H-2), 4.68 (s, 2 H, benzyl methylene), 5.10 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 5.31 (t, 1 H, $J_{2,3} = J_{3,4} = 6.0$ Hz, H-3), 5.86–6.27 (m, 2 H, 2 NH), and 7.38 (s, 5 H, Ph).

Anal. Calc. for $C_{18}H_{24}N_2O_6$: C, 59.33; H, 6.64; N, 7.69. Found: C, 59.35; H, 6.58; N, 7.69.

(*B*) *From compound* **21**. Compound **21** (390 mg) was dissolved in 90% aqueous ethanol (30 mL); 10% Pd–C catalyst (100 mg) was added, and hydrogen was bubbled through for 1 h while the solution was stirred at 30°. The catalyst was filtered off, and the filtrate was evaporated to a syrup which was acetylated with acetic anhydride (1 mL) in pyridine (7 mL) by heating for 2 h at 40°. The mixture was evaporated, and the residue crystallized from ether–hexane, to give 390 mg (79%) of **18**.

*Benzyl 2-acetamido-5-azido-2,5-dideoxy-3-*O*-mesyl-β-*D*-ribofuranoside* (**19**). — To an ice-cooled solution of **14** (1.3 g) in dry pyridine (20 mL) was added methanesulfonyl chloride (1.3 g), and the mixture was kept for 3 h at 0°. Processing in the usual way gave the 3-mesylate **19** (1.3 g, 80%) as needles, m.p. 134° (dec.), $[\alpha]_D^{20}$ −75° (*c* 0.3, chloroform); ν_{max}^{Nujol} 3240 (NH), 2070 (azide), 1655 and 1550 (amide), 1180 (SO_2), and 740 and 690 cm^{-1} (phenyl).

Anal. Calc. for $C_{15}H_{20}N_4O_6S$: C, 46.86; H, 5.24; N, 14.58. Found: C, 46.59; H, 5.20; N, 14.46.

*Benzyl 2-acetamido-3,5-diazido-2,3,5-trideoxy-β-*D*-xylofuranoside* (**12**). — To a solution of **19** (1.3 g) in dry *N*,*N*-dimethylformamide (20 mL) was added sodium azide (3.0 g), and the mixture was heated, with stirring, for 48 h at 120°. It was then cooled, the salts were filtered off, and the filtrate was evaporated to a syrup which was extracted with chloroform. The extract was successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried (sodium sulfate), and evaporated, to give a crystalline mass. Recrystallization from ether–hexane afforded the diazide **12**, wt. 630 mg (56%), m.p. 151°, $[\alpha]_D^{20}$ −103° (*c* 0.3, methanol); ν_{max}^{Nujol} 3260 (NH), 2110 and 2090 (azide), 1655 and 1560 (amide), and 750 and 690 cm^{-1} (phenyl); n.m.r. data at 60 MHz (in chloroform-*d*): δ 1.99 (s, 3 H, AcN), 3.41–3.57 (m, 2 H, H-5,5'), 4.14–4.95 (m, 3 H, H-2,3,4), 4.55, 4.88 (2 d, 2 H, J_{gem} 12.0 Hz, benzyl methylene), 5.08 (d, 1 H, $J_{1,2}$ 1.4 Hz, H-1), 5.78 (d, 1 H, $J_{2,NH}$ 7.8 Hz, NH), and 7.38 (s, 5 H, Ph).

Anal. Calc. for $C_{14}H_{17}N_7O_3$: C, 50.75; H, 5.17; N, 29.59. Found: C, 50.53; H, 5.28; N, 29.30.

*Benzyl 2,3,5-triacetamido-2,3,5-trideoxy-β-*D*-xylofuranoside* (**13**). — A solution of **12** (760 mg) in ethanol (70 mL) was hydrogenated with hydrogen in the presence of 10% Pd–C catalyst (100 mg) for 1 h at 35°. The mixture was filtered, and acetic anhydride (5 mL) was added to the filtrate; t.l.c. indicated complete reaction within 30 min, and the solvent was evaporated to give a syrupy product. Crystallization from ethanol–ether afforded **13** (650 mg, 78%), m.p. 228°, $[\alpha]_D^{20}$ −54° (*c* 0.3, methanol); ν_{max}^{Nujol} 3270 (NH), 1650, 1560, and 1540 (amide), and 730 and 690 cm^{-1} (phenyl).

Anal. Calc. for $C_{18}H_{25}N_3O_5$: C, 59.49; H, 6.93; N, 11.56. Found: C, 59.38; H, 6.88; N, 11.41.

*Benzyl 2-(benzyloxycarbonylamino)-2-deoxy-3,5-di-*O*-mesyl-β-*D*-xylofuranoside* (**3**). — To an ice-cooled solution of **1** (1.0 g) in dry pyridine (10 mL) was added methanesulfonyl chloride (600 mg), and the mixture was kept for 3 h at 0°. The same procedure as described in the preparation of **10** gave compound **3** (1.21 g, 85%), m.p. 128°, $[\alpha]_D^{20}$ −54° (*c* 0.3, chloroform); ν_{max}^{Nujol} 3230 (NH), 1690 and 1540 (amide), 1180 (SO_2), and 740 and 690 cm^{-1} (phenyl).

Anal. Calc. for $C_{22}H_{27}NO_{10}S_2$: C, 49.89; H, 5.14; N, 2.65. Found: C, 50.08; H, 5.23; N, 2.68.

*Benzyl 3,5-diazido-2-(benzyloxycarbonylamino)-2,3,5-trideoxy-β-*D*-ribofuranoside* (**4**). — To a solution of **3** (5.0 g) in dry *N,N*-dimethylformamide (70 mL) was added sodium azide (4.3 g), and the mixture was heated, with stirring, for 12 h at 80–85°; t.l.c. then revealed the formation of a single product. The solution was cooled, and filtered, insoluble material was washed with methanol, and the filtrate and washings were combined, and evaporated, to give a syrup which was extracted with chloroform. The extract was successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried (sodium sulfate), and evaporated. The residue was chromatographed on a column of silica gel (100 g) with 200:1 chloroform–methanol, to give the diazide **4** (3.7 g, 93%), m.p. 64°, $[\alpha]_D^{20}$ −4.8° (*c* 0.5, chloroform); ν_{max}^{Nujol} 3250 (NH), 2080 (azide), 1680 and 1540 (amide), and 690 cm^{-1} (phenyl); n.m.r. data at 60 MHz (in chloroform-*d*): δ 3.28–3.36 (m, 2 H, H-5,5′), 3.83–4.41 (m, 3 H, H-2,3,4), 4.42, 4.75 (2 d, 2 H, J_{gem} 11.5 Hz, benzyl methylene), 5.10 (s, 2 H, benzyloxycarbonyl methylene), 5.03 (s, 1 H, H-1), 5.49 (d, 1 H, $J_{2,NH}$ 7.0 Hz, NH), and 7.30 (s, 5 H, Ph).

Anal. Calc. for $C_{20}H_{21}N_7O_4$: C, 56.73; H, 5.00; N, 23.16. Found: C, 56.59; H, 4.95; N, 23.45.

*Benzyl 2,3,5-triacetamido-2,3,5-trideoxy-β-*D*-ribofuranoside* (**20**). — A solution of **4** (3.0 g) in methanol (100 mL) was hydrogenated with 10% Pd–C catalyst (500 mg) for 3 h at 35°. The catalyst was removed by filtration, acetic anhydride (10 mL) was added to the filtrate, and, after being kept for 30 min at room temperature, the solution was evaporated to a syrup which was crystallized from ethanol–ether, to afford **20** (1.96 g, 76%), m.p. 166°, $[\alpha]_D^{20}$ −74° (*c* 0.3, methanol); ν_{max}^{Nujol} 3350 (NH),

1650, 1570, and 1530 (amide), and 730 and 690 cm^{-1} (phenyl); n.m.r. data at 60 MHz (in methanol-d_4): δ 1.90, 1.95, 1.99 (3 s, 9 H, 3 AcN), 3.35–3.75 (m, 2 H, H-5,5'), 4.00–4.80 (m, 5 H, H-2,3,4, benzyl methylene), 5.02 (s, 1 H, H-1), and 7.39 (s, 5 H, Ph).

Anal. Calc. for $C_{18}H_{25}N_3O_5$: C, 59.49; H, 6.93; N, 11.56. Found: C, 59.52; H, 6.88; N, 11.39.

Benzyl 2-acetamido-2-deoxy-3,5-di-O-mesyl-β-D-xylofuranoside (**11**). — A solution of **3** (4.0 g) in 1,4-dioxane (30 mL) and methanol (100 mL) was hydrogenated with 10% Pd–C catalyst (500 mg) for 2.5 h at room temperature. The catalyst was removed by filtration, and the filtrate was evaporated. To a solution of the residue in methanol (50 mL) was added acetic anhydride (4 mL), and, after being kept for 30 min at room temperature, the mixture was evaporated to give a syrup. Crystallization from ethanol–ether afforded **11** (2.5 g, 76%) as needles, m.p. 129°, $[\alpha]_D^{20}$ −70° (*c* 0.3, methanol); ν_{max}^{Nujol} 3240 (NH), 1650 and 1540 (amide), 1180 (SO_2), and 730 and 690 cm^{-1} (phenyl); n.m.r. data at 60 MHz (in chloroform-*d*): δ 1.98 (s, 3 H, AcN), 3.04, 3.25 (2 s, 6 H, MeS), 4.35–4.84 (m, 4 H, H-2,4,5,5'), 4.55, 4.88 (2 d, 2 H, J_{gem} 11.5 Hz, benzyl methylene), 5.15 (d, 1 H, $J_{1,2}$ 1.0 Hz, H-1), 5.18 (d of d, 1 H, $J_{2,3}$ 2.0, $J_{3,4}$ 6.8 Hz, H-3), 6.28 (d, 1 H, $J_{2,NH}$ 8.0 Hz, NH), and 7.37 (s, 5 H, Ph).

Anal. Calc. for $C_{16}H_{23}NO_9S_2$: C, 43.92; H, 5.30; N, 3.20. Found: C, 43.99; H, 5.36; N, 3.29.

2-Methyl-(benzyl 5-azido-2,3,5-trideoxy-β-D-ribofuranosido)-[2,3-d]-2-oxazoline (**21**). — (*A*) *From compound* **10**. To a solution of **10** (1.0 g) in dry *N*,*N*-dimethylformamide (10 mL) was added sodium azide (700 mg), and the mixture was heated, with stirring, for 5 h at 50°, cooled, and evaporated; the residue was extracted with chloroform, and the extract washed successively with 2M hydrochloric acid, M sodium carbonate, and water, dried (sodium sulfate), and evaporated to a syrup which was crystallized from ether–hexane to give the oxazoline **21** (570 mg, 76%), m.p. 80–81°, $[\alpha]_D^{20}$ −85° (*c* 0.3, chloroform); ν_{max}^{Nujol} 2070 (azide), 1660 (C=N), and 740 and 690 cm^{-1} (phenyl); n.m.r. data at 60 MHz (in chloroform-*d*): δ 1.99 (s, 3 H, Me), 3.15–3.76 (m, 2 H, H-5,5'), 4.32 (d, 1 H, $J_{2,3}$ 7.0 Hz, H-2), 4.50, 4.80 (2 d, 2 H, J_{gem} 12.0 Hz, benzyl methylene), 4.56–4.95 (m, 2 H, H-3,4), 5.18 (s, 1 H, H-1); and 7.33 (s, 5 H, Ph).

Anal. Calc. for $C_{14}H_{16}N_4O_3$: C, 58.32; H, 5.59; N, 19.44. Found: C, 58.26; H, 5.58; N, 19.38.

(*B*) *From compound* **11**. The dimesylate **11** (3.6 g) in dry *N*,*N*-dimethylformamide (50 mL) containing sodium azide (3.0 g) was heated, with stirring, for 5 h at 90°. The same procedure as described in (*A*) gave compound **21** (1.78 g, 75%).

2,5-Diacetamido-1,3-di-O-acetyl-2,5-dideoxy-α-D-xylofuranose (**22**). — Compound **8** (150 mg) was dissolved in 90% aqueous methanol (15 mL); Pd-black catalyst (100 mg) was added, and hydrogen was bubbled through for 2.5 h while the solution was stirred at 35°. The catalyst was filtered off, and the solution evaporated. The residue was acetylated with acetic anhydride (1 mL) in pyridine (5 mL) for 12 h at 0°. The product was obtained as needles (120 mg, 82%), m.p. 198–200° (dec.), $[\alpha]_D^{20}$ +108° (*c* 0.3, methanol); ν_{max}^{Nujol} 3320 and 3280 (NH), 1740, 1730, 1250, and

1230 (ester), and 1640, 1540, and 1530 cm^{-1} (amide); n.m.r. data at 90 MHz (in methanol-d_4): δ 1.94, 2.07 (2 s, 12 H, 2 AcN, 2 AcO), 3.32–3.38 (m, 2 H, H-5,5'), 4.42 (d of d, 1 H, $J_{1,2}$ 5.2, $J_{2,3}$ 7.0 Hz, H-2), 4.48–4.70 (m, 1 H, H-4), 5.34 (t, 1 H, $J_{2,3} = J_{3,4} = 7.0$ Hz, H-3), and 6.26 (d, 1 H, $J_{1,2}$ 5.2 Hz, H-1).

Anal. Calc. for $C_{13}H_{20}N_2O_7$: C, 49.36; H, 6.37; N, 8.86. Found: C, 49.28; H, 6.35; N, 8.80.

*2,5-Diacetamido-1,3-di-*O*-acetyl-2,5-dideoxy-*D*-ribofuranose* (**23**). — Compound **17** (140 mg) in 90% aqueous methanol (15 mL) was hydrogenated with hydrogen in the presence of Pd-black catalyst (100 mg) for 1 h at 35°. After removal of the catalyst, the solvent was evaporated, and the residue was acetylated as in the preparation of **22**. The product was purified by chromatography on a column of silica gel (10 g) with chloroform and then 30:1 chloroform–methanol. The latter eluate yielded **23** (120 mg, 96%) as a syrup; ν_{max}^{film} 3370 (NH), 1750 and 1230 (ester), and 1650 and 1540 (amide); n.m.r. data at 90 MHz (in methanol-d_4): δ 5.09 (d of d, $J_{2,3}$ 6.6, $J_{3,4}$ 2.2 Hz, H-3α), 5.18 (t, $J_{2,3} = J_{3,4} = 5.2$ Hz, H-3β), 6.02 (d, $J_{1,2}$ 2.1 Hz, H-1β), and 6.25 (d, $J_{1,2}$ 5.0 Hz, H-1α); the anomeric ratio (α:β) was estimated as ~1:2 from the ratio of the intensities of H-1α and H-1β.

Anal. Calc. for $C_{13}H_{20}N_2O_7$: C, 49.36; H, 6.37; N, 8.86. Found: C, 49.28; H, 6.33; N, 8.83.

*2,3,5-Triacetamido-1-*O*-acetyl-2,3,5-trideoxy-α-*D*-xylofuranose* (**24**). — Compound **13** (130 mg) was hydrogenated with Pd-black catalyst (100 mg) in 90% aqueous methanol (15 mL) for 1 h at 35°. The product was acetylated with acetic anhydride (1 mL) and pyridine (5 mL) for 12 h at 0°. Crystallization from ethanol afforded **24** (95 mg, 84%) as needles, m.p. 229–231° (dec.), $[\alpha]_D^{20}$ +132° (*c* 0.3, *N,N*-dimethylformamide); ν_{max}^{Nujol} 3300 (NH), 1740 and 1230 (ester), and 1650 and 1540 cm^{-1} (amide); n.m.r. data at 90 MHz (in methanol-d_4): δ 1.93, 1.94, 1.98 (3 s, 9 H, 3 AcN), 2.07 (s, 3 H, AcO), 4.32–4.75 (m, 5 H, H-2–5'), and 6.23 (d, 1 H, $J_{1,2}$ 4.2 Hz, H-1).

Anal. Calc. for $C_{13}H_{21}N_3O_6$: C, 49.51; H, 6.71; N, 13.33. Found: C, 49.55; H, 6.65; N, 13.28.

*2,3,5-Triacetamido-1-*O*-acetyl-2,3,5-trideoxy-α(and -β)-*D*-ribofuranose* (**25a**, **25b**). — Compound **20** (400 mg) was hydrogenated with Pd-black catalyst (250 mg) in 90% aqueous methanol (50 mL) for 2 h at 35°. The free sugar was acetylated with acetic anhydride (2 mL) in pyridine (10 mL) as already described. The resulting syrup was crystallized from ethanol, to give the β-acetate **25b** (130 mg, 37%). The α-acetate **25a** (160 mg, 46%) was isolated from the mother liquors after chromatography on a column of silica gel (15 g) with 50:1 chloroform–methanol. An inseparable, anomeric mixture (40 mg, 12%) was also obtained.

For **25a**: amorphous, $[\alpha]_D^{20}$ +78° (*c* 1.0, methanol); ν_{max}^{film} 3260 (NH), 1750 and 1230 (ester), and 1650 and 1540 cm^{-1} (amide); n.m.r. data at 90 MHz (in methanol-d_4): δ 2.01 (s, 6 H, 2 AcN), 2.06 (s, 3 H, AcN), 2.15 (s, 3 H, AcO), 3.40–3.51 (m, 2 H, H-5,5'), 4.11–4.28 (m, 1 H, H-4), 4.46 (d of d, 1 H, $J_{2,3}$ 8.0, $J_{3,4}$ 3.8 Hz, H-3), 4.73 (d of d, 1 H, $J_{1,2}$ 4.2, $J_{2,3}$ 8.0 Hz, H-2), and 6.27 (d, 1 H, $J_{1,2}$ 4.2 Hz, H-1).

For **25b**: m.p. 189°, $[\alpha]_D^{20}$ +13° (*c* 0.4, methanol); ν_{max}^{Nujol} 3320 and 3300 (NH),

1740 and 1235 (ester), and 1650 and 1540 cm^{-1} (amide); n.m.r. data at 90 MHz (in methanol-d_4): δ 1.95 (s, 6 H, 2 AcN), 1.98 (s, 3 H, AcN), 2.07 (s, 3 H, AcO), 3.10–3.65 (m, 2 H, H-5,5'), 3.95–4.18 (m, 1 H, H-4), 4.35–4.54 (m, 2 H, H-2,3), and 5.98 (s, 1 H, H-1).

Anal. Calc. for $C_{13}H_{21}N_3O_6$: C, 49.51; H, 6.71; N, 13.33. Found: For **25a**; C, 49.59; H, 6.65; N, 13.21. For **25b**; C, 49.39; H, 6.69; N, 13.26.

REFERENCES

1 A. HASEGAWA, E. TANAHASHI, AND M. KISO, *Carbohydr. Res.*, 79 (1980) 255–264.
2 A. HASEGAWA AND H. G. FLETCHER, JR., *Carbohydr. Res.*, 29 (1973) 223–237.
3 A. HASEGAWA, T. SAKURAI, AND N. HASEGAWA, *Carbohydr. Res.*, 45 (1975) 19–27.
4 A. HASEGAWA, N. ARITAKE, AND M. KISO, *Carbohydr. Res.*, 51 (1976) c10–c12.
5 A. HASEGAWA, N. ARITAKE, AND M. KISO, *Carbohydr. Res.*, 52 (1976) 137–149.
6 A. HASEGAWA, T. SAKURAI, AND M. KISO, *Agric. Biol. Chem.*, 42 (1978) 153–158.
7 A. HASEGAWA, N. ARITAKE, AND M. KISO, *Carbohydr. Res.*, 80 (1980) 277–283.
8 A. HASEGAWA, Y. KAWAI, H. KASUGAI, AND M. KISO, *Carbohydr. Res.*, 63 (1978) 131–137.
9 B. L. KAM, J.-L. BARASCUT, AND J.-L. IMBACH, *Carbohydr. Res.*, 69 (1979) 135–142.
10 A. MAGNANI AND Y. MIKURIYA, *Carbohydr. Res.*, 28 (1973) 158–164.