Branched-chain Sugars. XI. Synthesis of 2,3,6-Trideoxy-3-*C*,4-*O*-dimethyl-3-nitro-D-*arabino*-hexopyranose (D-Evernitrose)[1]

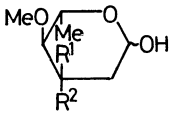
Juji YOSHIMURA,* Masafumi MATSUZAWA, and Masuo FUNABASHI

Laboratory of Chemistry for Natural Products, Faculty of Science, Tokyo Institute of Techgnology, Nagatsuta, Midori-ku, Yokohama 227

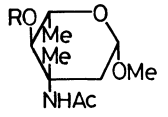
(Received October 31, 1977)

2,3,6-Trideoxy-3-*C*, 4-*O*-dimethyl-3-nitro-D-*arabino*-hexopyranose was synthesized by the oxidation of methyl α-glycoside of the corresponding 3-amino derivative with *m*-chloroperbenzoic acid followed by hydrolysis. The 3-amino derivative was synthesized from methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose by introduction of the amino-branching function according to the method of Bourgeois, followed by 6-deoxygenation and 4-*O*-methylation.

Evernitrose (**1**) is a natural nitro-sugar first found by Ganguly *et al.* in oligosaccharide antibiotics, everninomicin B, C, and D.[2] The structure of **1** was deduced from spectroscopic evidence and chemical degradation[3] to be 2,3,6-trideoxy-3-*C*,4-*O*-dimethyl-3-nitro-L-*ribo*-hexophyranose (**2**). However, this was revised to L-*arabino* configuration by X-ray analysis of methyl β-glycoside of the corresponding 3-acetamido derivative (**3**).[4] Brimacombe and Doner attempted the sysnthesis of **1** by the nitroethane cyclization of dialdehyde obtained from methyl α-L-rhamnopyranoside, the product with the revised configuration at nitro-branching position being converted into 4-*epi*-vancosaminide (**4**).[5] However, this process is unsuitable for the synthesis of **1**, because of the poor yield (12%) and the difficulty of selective 4-*O*-methylation of the cyclization product, and the inevitable reduction of the nitro group in the subsequent 2-deoxygenation. Bourgeois reported a new method for the introduction of methyl and amino groups into C-3 position of 1,2 : 5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose by subsequent reactions of cyano-mesylation, reduction into spiro-aziridine and hydrogenolysis of the aziridine ring.[6] The steric course of the aziridine ring formation was proved by Brimacombe *et al.* to proceed by the intramolecular S_N2 mechanism[7] from the fact that identical amino-branched derivative was obtained by addition of azide to the corresponding 3-methylene derivative followed by hydrogenation.



(**1**) R^1=Me, R^2=NO_2
(**2**) R^1=NO_2, R^2=Me

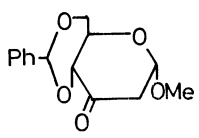


(**3**) R=Me
(**4**) R=Ac

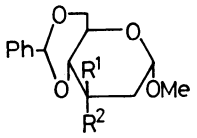
We have synthesized the enantiomer (**27**) of **1** from methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranoside-3-ulose (**5**)[9] *via* the oxidation of the amino group of the corresponding amino-branched derivative into a nitro group. Since the method of Brimacombe *et al.*[7] was unsuccessful for the pyranoside ring, the amino-branched sugar was synthesized by that of Bourgeois.

Results and Discussion

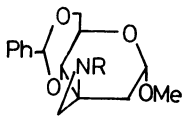
Reaction of **5** with hydrogen cyanide in pyridine gave cyanohydrin (**6**) in *ca.* 50% yield. However, subsequent addition of trimethylsilyl chloride to the reaction mixture gave the corresponding ether (**7**) quantitatively. The configuration of **7** was determined to be D-*ribo* from the fact that the hydrogenation of **7** with lithium aluminium hydride(LAH) gave the corresponding 3-aminomethyl derivative (**8**) which was identical with the product obtained from known methyl 4,6-*O*-benzylidene-2-deoxy-3-*C*-nitromethyl-α-D-*ribo*-hexopyranoside[9] by hydrogenation. This indicates that cyanide anion attacks the carbonyl function of **5** from the upper side of the pyranoside ring selectively.



(**5**)



(**6**) R^1=CN, R^2=OH
(**7**) R^1=CN, R^2=OTMS
(**8**) R^1=CH_2NH_2, R^2=OH
(**9**) R^1=CN, R^2=OMs
(**10**) R^1=OMs, R^2=CN
(**13**) R^1=NH_2, R^2=Me
(**14**) R^1=NHAc, R^2=Me
(**25**) R^1=NO_2, R^2=Me

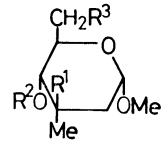


(**11**) R=H (**12**) R=Ac

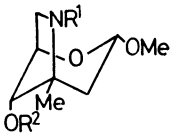
Cyano-mesylation of **5** in a similar manner afforded the corresponding 3-*C*-cyano-3-*O*-mesyl derivative of D-*ribo* (**9**) and D-*arabino* (**10**) configuration in 64% and 3% yields, respectively. Compound **9** was converted into the corresponding spiro-aziridine (**11**) in 81% yield by reduction with LAH, which was then characterized as the *N*-acetyl derivative (**12**). Catalytic hydrogenation of **11** in the presence of Raney nickel gave the amino-branched derivative (**13**) in 93% yield, which was also characterized as the *N*-acetyl derivative (**14**). The two characteristic singlets (δ 2.24 and 2.70) of the methylene protons of aziridine ring in the NMR spectrum of **12** turned into a singlet of methyl protons (δ 1.59) in that of **14**. Treatment of **14** with *N*-bromosuccinimide and barium carbonate gave methyl 3-acetamido-4-*O*-benzoyl-6-bromo-2,3,6-trideoxy-3-*C*-methyl-α-D-*arabino*-hexopyranoside (**15**) in 60% yield, 6-bromine atom of which was hydrogenolyzed with Raney nickel to give the corresponding 6-deoxy derivative (**16**) as a sirup.

On the other hand, attempted dehydrobromination of **15** with silver fluoride[10] in pyridine or with 1,8-diazabicyclo[5.4.0]undec-7-ene in boiling benzene

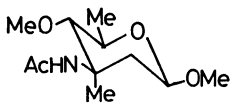
unexpectedly gave a bicyclo pyrrolidine (**17**) quantitatively. The structure of **17** was distinguished from the possible seven-membered oxazolidine derivative by de-*O*-benzoylation with methanolic ammonia, followed by successful de-*N*-acetylation with aqueous potassium hydroxide. The 1C conformation of the pyranoside ring was confirmed by the NMR spectrum of de-*O*-benzoylated prodect (**18**: $J_{1,2a}=9.0$, $J_{1,2e}=4.0$ Hz). The conversion confirmed the configuration of the branching point of **15**—**16**, and also the steric course of the aziridine formation.



(**15**) R^1=NHAc, R^2=Bz, R^3=Br
(**16**) R^1=NHAc, R^2=Bz, R^3=H
(**20**) R^1=NHAc, R^2=H, R^3=H
(**21**) R^1=NHAc, R^2=Me, R^3=H
(**23**) R^1=NH_2, R^2=Me, R^3=H
(**26**) R^1=NO_2, R^2=Me, R^3=H

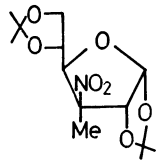


(**17**) R^1=Ac, R^2=Bz
(**18**) R^1=Ac, R^2=H
(**19**) R^1=H, R^2=H

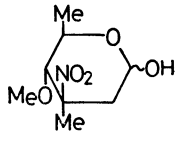


(**22**)

Compound **16** was de-*O*-benzoylated and then methylated with equimolar sodium hydride and methyl iodide to give 4-*O*-methyl derivative (**21**) in 93% yield. It is interesting that **21** anomerized to the β-anomer (**22**) by treatment with cation exchanger (IR-120) in boiling methanol for 17 h, due to the 1,3-diaxial interaction between 3-*C*-Me and 1-OMe groups. Treatment of **21** with potassium hydroxide in hot aqueous ethanol gave a sirupy de-*N*-acetyl derivative (**23**) in 52% yield. In order to examine the oxidation of an amino group at the branching point, potassium permanganate and magnesium sulfate[11] were used for 3-amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methyl-α-D-*gluco*-hexofuranose[5] and **13** in aqueous acetone, but the yields of the corresponding 3-nitro derivatives (**24** and **25**) were very poor (18% and 7.6%, respectively). However, *m*-chloroperbenzoic acid oxidation[12] of **13** in chloroform improved the yield (41%) of **25**. Thus, **23** in dichloromethane was successfully oxidized into the corresponding 3-nitro derivative (**26**) in 77% yield. The final hydrolysis of **26** with 0.05M sulfuric acid in aqueous dioxane at 90—95 °C gave D-evernitrose (**27**) in 72% yield.



(**24**)



(**27**)

Experimental

All the melting points are uncorrected. The solutions were evaporated under reduced pressure at a bath temperature not exceeding 45 °C. Specific rotations were measured in a 0.5-dm tube with a Carl Zeiss LEP-Al polarimeter with use of chloroform as the solvent unless otherwise stated. The IR spectra were recorded with a Hitachi Model EPI-G2 spectrometer. The NMR spectra were taken with a JEOL PS-100 spectrometer using tetramethylsilane as an internal standard in deuteriochloroform unless otherwise stated. Chemical shifts and coupling constants were recorded in δ and Hz units and IR frequencies in cm^{-1}.

*Methyl 4,6-O-Benzylidene-3-C-cyano-2-deoxy-α-D-ribo-hexopyranoside (**6**).* Hydrogen cyanide (1 ml, 25 mmol) was added to an ice-cooled solution of methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose (**5**: 5 g, 18.9 mmol) in anhydrous pyridine (40 ml), and the resulting solution was kept at room temperature for one day. Appearance of a new spot was detected on TLC. Evaporation of the reaction mixture gave crystals which were fractionally recrystallized to give **6** in 50% (2.7 g) yield. Mp 156—159 °C, $[\alpha]_D^{22}$ +55.2° (*c* 1.0), IR: 3450 (OH), 2240 (CN), NMR: 7.64—7.24 (Ph; m), 5.65 (PhCH, s), 4.78 (H_1: q, $J_{1,2e}=1.6$, $J_{1,2a}=4.0$), 4.40—3.60 (H_4, H_5, H_6, H_6': m), 3.40 (OMe), 2.53 (H_{2e}: q, $J_{gem}=15.0$), 2.26 (H_{2a}: q).

Found: C, 61.73; H, 5.88; N, 4.86%. Calcd for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81%.

*Methyl 4,6-O-Benzylidene-3-C-cyano-2-deoxy-3-O-trimethylsilyl-α-D-ribo-hexopyranoside (**7**).* Trimethylsilyl chloride (0.37 g, 3.4 mmol) was added to a reaction mixture of **5** (0.5 g, 1.9 mmol) and hydrogen cyanide (1 ml, 25 mmol) in pyridine (5 ml) as described above, and the resulting solution was kept at room temperature for one day. After evaporation of the mixture, the residue was extracted with toluene. Evaporation of the extracts gave pure crystals (0.65 g, 95%). Mp 88—91 °C, $[\alpha]_D^{22}$ +67.6° (*c* 1.0), IR: 2250 (CN), NMR: 0.24 (Me_3Si: s).

Found: C, 59.46; H, 6.86; N, 3.71%. Calcd for $C_{18}H_{25}NO_5Si$; C, 59.48; H, 6.93; N, 3.85%.

*Methyl 3-Aminomethyl-4,6-O-benzylidene-2-deoxy-α-D-ribo-hexopyranoside (**8**).* A suspension of **7** (0.5 g, 1.4 mmol) and excess LAH (75 mg) in ether was stirred at room temperature for 2 h, then poured gradually into ice-water containing acetic acid. The resulting mixture was extracted with chloroform and then worked up in the usual way to give **8** as crystals in 60% (0.24 g) yield. Mp 138—139 °C (ethanol–hexane), $[\alpha]_D^{22}$ +94.0° (*c* 1.0), IR: 3500—3000 (NH and OH), NMR: 7.6—7.1 (Ph: m), 5.57 (PhCH), 4.82 (H_1; q, $J_{1,2e}=1.0$, $J_{1,2a}=4.3$), 4.62—3.5 (H_4, H_5, H_6, and H_6': m), 3.36 (OMe), 2.96 and 2.62 (CH_2: each d, $J_{gem}=13.5$), 2.35 (OH), 2.12 (NH_2), 2.03 (H_{2e}: q, $J_{gem}=14.0$), 1.84 (H_{2a}: q).

Found: C, 60.81; H, 7.17; N, 4.54%. Calcd for $C_{15}H_{21}NO_5$: C, 61.00; H, 7.17; N, 4.74%.

The same compound was also obtained from methyl 4,6-*O*-benzylidene-2-deoxy-3-nitromethyl-α-D-*ribo*-hexopyranoside by catalytic reduction with Raney nickel.

*Methyl 4,6-O-benzylidene-3-C-cyano-2-deoxy-3-O-methylsulfonyl-α-D-ribo- (**9**) and D-arabino-Hexopyranoside (**10**).* Methylsulfonyl chloride (70 ml, 0.9 mol) was added dropwise at 0 °C to a reaction mixture of **5** (40 g, 0.15 mol) and hydrogen cyanide (10 ml, 0.25 mol) in pyridine, and the resulting solution was kept at 0 °C for 2 days. The mixture was poured into ice–water and extracted with chloroform. The usual work-up of the extract gave a half-crystalline mass which was triturated with ethanol to give crystals (34 g, 62%). **9**: Mp

161—162 °C (from dichloromethane-hexane), $[\alpha]_D^{22}$ +38.1° (*c* 1.0), IR: 2230 (CN), 1370 and 1190 (OMs), NMR: 7.56—7.24 (Ph: m), 5.66 (PhCH), 4.81 (H_1: q, $J_{1,2e}=1.0$, $J_{1,2a}=4.0$), 4.42—3.60 (H_4, H_5, H_6, and $H_{6'}$: m), 3.46 (OMs), 3.41 (OMe), 3.20 (H_{2e}: q, $J_{gem}=15.0$), 2.28 (H_{2a}: q).

Found: C, 51.92; H, 5.19; N, 3.65; S, 8.52%. Calcd for $C_{16}H_{19}NO_7S$: C, 52.03; H, 5.19; N, 3.79; S, 8.66%.

Chromatographic separation of the sirup obtained from the mother liquor of the above experiment gave **9** (0.2 g, 0.5%) and the 3-epimer, **10** (1.13 g, 3%). **10**: Mp 151—151.5 °C, $[\alpha]_D^{22}$ +102.1° (*c* 1.0), IR: 1360 and 1180 (OMs).

Found: C, 52.03; H, 5.18; N, 3.76; S, 8.50%. Calcd for $C_{16}H_{19}NO_7S$: C, 52.03; H, 5.19; N, 3.79; S, 8.60%.

*Spiro[aziridine-2,3'-(methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-*D*-arabino-hexopyranoside)] (**11**) and Its* N*-Acetyl Derivative (**12**).* A suspension of **9** (30 g, 82 mmol) and LAH (4.6 g, 121 mmol) in ether (500 ml) was stirred at room temperature for 4 h, and then poured into water containing ethyl acetate to decompose excess LAH. The usual work-up of the resulting mixture gave unstable **11** in 81% (18.42 g) yield. Base-catalyzed acetylation of a part of this sirup gave **12** quantitatively. Mp 112—113 °C, $[\alpha]_D^{22}$ +34.6° (*c* 1.0), IR: 1680 (amido), NMR: 7.32 (Ph: s), 5.54 (PhCH), 4.82 (H_1: q, $J_{1,2e}=1.0$, $J_{1,2a}=4.0$), 4.36—3.64 (H_4, H_5, H_6, and $H_{6'}$: m), 3.35 (OMe), 2.70 and 2.24 (CH_2: each s), 2.56 (H_{2a}: q), 2.03 (NAc), 1.62 (H_{2e}: q, $J_{gem}=14.0$).

Found: C, 63.48; H, 6.65; N, 4.15%. Calcd for $C_{17}H_{21}NO_5$: C, 63.93; H, 6.63; N, 4.39%.

*Methyl 3-Amino-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-methyl-α-*D*-arabino-hexopyranoside (**13**) and Its* N*-Acetyl Derivative (**14**).* Hydrogenation of a suspension of **11** (18 g, 65 mmol) and Raney nickel (30 g) in methanol (400 ml) in an autoclave at 40 °C under 100 kg/cm² hydrogen atmosphere, and then the usual work-up gave a sirupy **13** in 93% (16.8 g) yield. Base-catalyzed acetylation of **13** and purification of the sirupy product on a silica gel column (benzene–acetone) gave pure **14** as an amorphous solid. The yield from **9** was 49%. $[\alpha]_D^{22}$ +38.6° (*c* 1.0), IR: 3300 (NH), 1650 and 1540 (amide), NMR: 7.60—7.28 (Ph: m), 5.56 (PhCH), 5.50 (NH: broad s), 4.72 (H_1: q, $J_{1,2a}=4.0$), 4.40—3.60 (H_4, H_5, H_6, and $H_{6'}$: m), 2.69 (H_{2a}: q), 2.35 (H_{2e}: q, $J_{gem}=14.0$), 1.93 (NAc), 1.59 (Me).

Found: C, 63.25; H, 7.22; N, 4.14%. Calcd for $C_{17}H_{23}NO_5$: C, 63.52; H, 7.21; N, 4.36%.

*Methyl 3-Acetamido-4-*O*-benzoyl-6-bromo-3-*C*-methyl-2,3,6-trideoxy-α-*D*-arabino-hexopyranoside (**15**).* A suspension of **14** (10 g, 31 mmol), *N*-bromosuccinimide (6.6 g, 37 mmol) and barium carbonate (7.3 g, 37 mmol) in dried carbon tetrachloride (400 ml) was refluxed for 4—5 h under normal room light until the colour changed from red to yellow, and then filtered. The filtered mass was washed with dichloromethane. The filtrate and washings were combined and washed in turn with aqueous sodium hydrogensulfite (5%), sodium hydrogencarbonate and water, and then dried. Evaporation of the solution gave a sirup (9.86 g) which was purified on a silica gel column (benzene–acetone) to give pure **15** in 60% (7.4 g) yield. The sirup gradually crystallized in a desiccator. Mp 71—72 °C, $[\alpha]_D^{22}$ +81.0° (*c* 1.0), IR: 3400 (NH), 1720 (ester), 1650 and 1530 (amide), NMR: 8.2—7.3 (Ph: m), 6.26 (NH: broad s), 5.48 (H_4: d, $J_{4,5}=10.0$), 4.85 (H_1: t, $J_{1,2e}=J_{1,2a}=3.0$), 4.18 (H_5: dt, $J_{5,6}=3.0$), 3.64—3.44 (H_6 and $H_{6'}$: m), 3.42 (OMe), 2.56 (H_{2e} and H_{2a}: d), 1.85 (NAc), 1.64 (Me).

Found: C, 50.55; H, 5.99; N, 3.08%. Calcd for $C_{17}H_{22}NO_5Br$: C, 51.01; H, 5.54; N, 3.50%.

*Methyl 3-Acetamido-4-*O*-benzoyl-3-*C*-methyl-2,3,6-tridoxy-α-*D*-arabino-hexopyranoside (**16**).* Catalytic hydrogenation of a suspension of **15** (0.36 g, 0.9 mmol) and triethylamine (0.11 g, 1.1 mmol) and Raney nickel (0.83 g) in methanol (100 ml) in an autoclave under 95 kg/cm² hydrogen atmosphere for 2 days and the usual work-up for the separation of the product from the amine salt gave sirupy **16** in 95% (0.28 g) yield. IR: 3400 (NH), 1720 (ester), 1650 and 1540 (amide), NMR: 8.18—7.30 (Ph: m), 6.20 (NH: s), 5.14 (H_4: d, $J_{4,5}=10.0$), 4.71 (H_1: q, $J_{1,2e}=1.6$, $J_{1,2a}=4.0$), 4.05 (H_5: dq, $J_{5,6}=7.2$), 3.37 (OMe), 2.68 (H_{2e}: q, $J_{gem}=15.0$), 2.36 (H_{2a}: q), 1.86 (NAc), 1.66 (Me), 1.24 (H_6: d).

Found: C, 62.94; H, 7.02; N, 4.41%. Calcd for $C_{17}H_{23}NO_5$: C, 63.53; H, 7.21; N, 4.36%.

Methyl N*-Acetyl-3,6-epimino-4-*O*-benzoyl-2,3,6-trideoxy-3-*C*-methyl-α-*D*-arabino-hexopyranoside (**17**) and Its De-*O*-benzoyl Derivative (**18**).* A solution of **15** (4.4 g, 11.0 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (1.84 g, 12.1 mmol) in dried benzene (70 ml) was refluxed for 3 h, and the crystals deposited were filtered off. A sirup obtained by evaporation of the filtrate was purified on a silica gel column to give **17** in 82% (2.9 g) yield. Mp 169—174 °C, $[\alpha]_D^{22}$ −111.3° (*c* 1.0), IR: 1720 (ester), 1622 (amide).

Found: C, 63.49; H, 6.49; N, 4.16%. Calcd for $C_{17}H_{21}NO_5$: C, 63.93; H, 6.63; 4.39%.

Treatment of **17** with methanolic ammonia in the usual manner gave **18** in 66% yield. Mp 109—111 °C, $[\alpha]_D^{22}$ −74° (*c* 1.0), IR: 3300 (OH), 1640 (amide), NMR (in CD_3OD): 4.62 (H_1: q, $J_{1,2e}=4.0$, $J_{1,2a}=9.0$), 4.23 (H_5: dt, $J_{5,6}=J_{5,6'}=2.0$), 3.50 (H_4: d, $J_{4,5}=3.0$), 3.46 (OMe), 3.67 (H_6 and $H_{6'}$: d, $J_{gem}=0$), 3.50 (H_4: d, $J_{4,5}=3.0$), 3.46 (OMe), 2.08 (H_{2a}: q), 2.05 (NAc), 1.74 (H_{2e}: q, $J_{gem}=13.0$), 1.52 (Me).

Found: C, 55.56; H, 7.93; N, 6.53%. Calcd for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96; N, 6.51%.

*Methyl 3,6-Epimino-3-*C*-methyl-2,3,6-trideoxy-α-*D*-arabino-hexopyranoside (**19**).* A solution of **18** (60 mg, 0.28 mmol) in 2 M potassium hydroxide (4 ml) was refluxed for 4 days. The starting material was still detected on TLC, but the solution was neutralized with acetic acid and evaporated. The residue was extracted with chloroform and the product obtained was separated on TLC to give sirupy **19** (15 mg, 31%). NMR: 4.24 (H_5: q, $J_{5,6}=2.7$), 4.88 (H_1: q, $J_{1,2e}=5.0$, $J_{1,2a}=8.1$), 3.51 (OMe), 3.45 (H_4: d, $J_{4,5}=3.8$), 3.19 (H_6 and $H_{6'}$: d, $J_{gem}=0$), 2.51 (NH and OH: s), 1.99 (Me), 1.80 (H_{2a}: q), 1.61 (H_{2e}: q, $J_{gem}=14.0$).

Found: C, 55.02; H, 8.16; N, 8.00%. Calcd for $C_8H_{15}NO_3$: C, 55.47; H, 8.73; N, 8.09%.

*Methyl 3-Acetamido-3-*C*-methyl-2,3,6-trideoxy-α-*D*-arabino-hexopyranoside (**20**).* A solution of **16** (120 mg, 0.37 mmol) in saturated methanolic ammonia (5 ml) was kept at room temperature overnight, evaporated, and the residual sirup was purified on TLC to give pure **20** (60 mg, 72%). $[\alpha]_D^{22}$ +73.8° (*c* 1.0, 50% MeOH–H_2O), IR: 3700—3150 (OH and NH), 1650 and 1540 (amide), NMR: 6.05 (OH), 5.84 (NH: broad s), 4.66 (H_1: q, $J_{1,2e}=1.6$, $J_{1,2a}=4.0$), 3.61 (H_5: dq, $J_{5,6}=6.0$), 3.38 (H_4: d, $J_{5,4}=9.4$), 3.32 (OMe), 2.01 (H_{2e}: q, $J_{gem}=15.8$), 2.00 (NAc), 1.85 (H_{2a}: q), 1.52 (Me), 1.31 (H_6: d).

Found: C, 56.08; H, 8.87; N, 6.16%. Calcd for $C_{10}H_{19}NO_4$: C, 55.28; H, 8.82; N, 6.45%.

The positive rotational change of this compound in cuprammonium solution ($[M]_{436}^{22}$ +254° → $[M]_{436}^{cupraA}$ +296°) also supports the configuration.

*Methyl 3-Acetamido-2,3,6-trideoxy-3-*C*,4-*O*-dimethyl-α-*D*-arabino-hexopyranoside (**21**).* To a solution of **20** (1.2 g, 5.4 mmol) in *N*,*N*-dimethylformamide (20 ml) was subsequently added equimolar sodium hydride (0.27 g) and methyl iodide (0.8 g) with stirring at room temperature. After

30 min, the reaction mixture was poured into ice-water and extracted with ether. The usual work-up of the extracts gave crystals (1.18 g, 93%), a part of which was recrystallized from hexane. Mp 136—138 °C, $[\alpha]_D^{22}$ +73° (*c* 1.0), NMR: 5.36 (NH: broad s), 4.68 (H_1: d, $J_{1,2a}$=4.5), 3.90 (H_4: d, $J_{4,5}$=10.0), 3.64 (H_5: dq, $J_{5,6}$=6.0), 3.49 and 3.28 (2×OMe), 2.97 (H_{2a}: q, J_{gem}=13.6), 1.94 (NAc), 1.77 (H_{2e}: d), 1.35 (Me), 1.28 (H_6: d).

Found: C, 56.50; H, 8.98; N, 5.90%. Calcd for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.06%.

Anomerization of ***21***. A suspension of **21** (0.1 g) and IR-120 (0.3 g) in absolute methanol (10 ml) was refluxed for 17 h and filtered, the filtrate then being evaporated to give a sirup (65 mg). Separation of the sirup on TLC (benzene: acetone=4:1) gave the β-anomer (**22**, 35 mg). Mp 159—160 °C, $[\alpha]_D^{22}$ −57° (*c* 1.0), NMR: 5.54 (NH: s), 4.50 (H_1: q, $J_{1,2e}$=2.5, $J_{1,2a}$=8.9), 3.75 (H_4: d, $J_{4,5}$=8.8), 3.54 (H_5: dq, $J_{5,6}$=6.0), 3.49 and 3.44 (2×OMe), 2.55 (H_{2a}: q, J_{gem}=13.5), 1.95 (H_{2e}: q), 1.93 (NAc), 1.34 (H_6: d), 1.30 (Me).

Found: C, 56.76; H, 9.00; N, 5.95%. Calcd for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.06%.

*Methyl 3-Amino-2,3,6-trideoxy-3-*C*,4-*O*-dimethyl-α-*D*-arabino-hexopyranoside (****23****).* A solution of **21** (630 mg, 2.73 mmol) and potassium hydroxide (612 mg) in 70% aqueous ethanol (3 ml) was refluxed under nitrogen atmosphere at 100—105 °C (bath temperature) for 4 days, neutralized with acetic acid, and then extracted with chloroform. The usual work-up of the extracts gave a sirup which was separated on a silica gel column to give sirupy **23** (113 mg) and the starting material (360 mg). NMR: 4.65 (H_1: q, $J_{1,2e}$=1.5, $J_{1,2a}$=4.0), 3.64 (H_5: dq, $J_{5,6}$=6.4), 3.57 and 3.29 (2×OMe), 2.67 (H_4: d, $J_{4,5}$=9.6), 1.82 (H_{2e}: q, J_{gem}=13.5), 1.70 (H_{2a}: q), 1.69 (NH_2: s), 1.28 (H_6: d), 1.24 (Me).

Found: C, 56.85; H, 10.22; N, 7.15%. Calcd for $C_9H_{19}NO_3$: C, 57.11; H, 10.12; N, 7.40%.

*3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methyl-3-nitro-α-*D*-glucofuranose (****24****) and Methyl 2,3-Dideoxy-4,6-*O*-benzylidene-3-*C*-methyl-3-nitro-α-*D*-arabino-hexopyranoside (****25****). By Permanganate Oxidation*: A suspension of 3-amino-3-deoxy-1,2 : 5,6-di-*O*-isopropylidene-3-*C*-methyl-α-D-glucofuranose[5] (150 mg, 0.55 mmol), potassium permanganate (0.6 g, 3.8 mmol), and magnesium sulfate 7 hydrate (0.18 g) in acetone (4 ml) and water (1 ml) was stirred at room temperature for 29 h. Inorganic substances were precipitated by addition of acetone, and then filtered. The filtrate was evaporated and the residual sirup was extracted with chloroform. The usual work-up of the extract gave a sirup which was purified on a silica gel column to give **24** (30 mg, 18%). Mp 58—60 °C, $[\alpha]_D^{22}$ +52.6° (*c* 1.0), IR: 1550 (NO_2).

Found: C, 50.90; H, 6.86; N, 4.42%. Calcd for $C_{13}H_{21}NO_7$: C, 51.48; H, 6.98; N, 4.62%.

In a similar manner, **13** was oxidized to give **25** in 7.6% yield. Mp 131—132 °C (from ethanol), $[\alpha]_D^{22}$ +57.9° (*c* 1.0), IR: 1540 (NO_2).

Found: C, 57.95; H, 6.02; N, 4.23%. Calcd for $C_{15}H_{19}NO_6$: C, 58.24; H, 6.19; N, 4.53%.

By Peroxide Oxidation: A solution of **13** (0.2 g, 0.72 mmol) in chloroform (10 ml) was added dropwise over a period of 20 min to a refluxing solution of *m*-chloroperbenzoic acid (0.98 g, 5.7 mmol) in chloroform (10 ml). Heating was continued for 30 min. The resulting solution was then washed thoroughly with aqueous sodium sulfite (10%), saturated potasium hydrogencarbonate and water. Evaporation of the organic layer gave crystals which were fractionated on a silica gel column to give **25** in 41% (91 mg) yield.

*Methyl 2,3,6-Trideoxy-3-*C*,4-*O*-dimethyl-3-nitro-α-*D*-arabino-hexopyranoside (****26****).* Oxidation of **23** (112 mg) in dichloromethane with *m*-chloroperbenzoic acid in a similar way gave sirupy **26** in 77% (99 mg) yield. $[\alpha]_D^{22}$ +95.4° (*c* 1.9), IR: 1540 (NO_2), NMR: 4.74 (H_1: q, $J_{1,2e}$=1.5, $J_{1,2a}$=4.5), 3.78 (H_4: d, $J_{4,5}$=9.5), 3.64 (H_5: dq, $J_{5,6}$=5.4), 3.40 and 3.31 (2×OMe), 2.46 (H_{2a}: q, J_{gem}=13.5), 2.14 (H_{2e}: q), 1.75 (Me), 1.34 (H_6: d).

Found: C, 49.05; H, 7.78; N, 6.02%. Calcd for $C_9H_{17}NO_5$ C, 49.30; H, 7.82; N, 6.39%.

*2,3,6-Trideoxy-3-*C*,4-*O*-dimethyl-3-nitro-α-D-arabino-hexopyranose (D-Evernitrose) (****27****).* A solution of **26** (97 mg, 0.44 mmol) in 0.05 M sulfuric acid of dioxane-water (50%, 3 ml) was heated at 90—95 °C for 8 h, neutralized with excess barium carbonate and then filtered. The filtrate was evaporated to give a sirup which was purified on TLC. The sirup thus obtained (65 mg, 72%) was crystallized from benzene-hexane. Mp 84—88 °C, $[\alpha]_D^{22}$ +23.6° (*c* 0.9, ethanol) [lit,[3] the enantiomer: mp 88—93 °C, $[\alpha]_D$ −19.4°], IR: 3400 (OH), 1550 (NO_2). NMR spectrum showed the presence of α-(H_1: δ 5.33, q, $J_{1,2e}$=1.5, $J_{1,2a}$=4.0) and β-anomers (H_1: δ 4.88, q, $J_{1,2e}$=4.4, $J_{1,2a}$=7.2) in the ratio 1:1.

Found: C, 46.68; H, 7.33; N, 6.65%. Calcd for $C_8H_{15}NO_5$: C, 46.82; H, 7.37; N, 6.83%.

The authors are indebted to Mr. H. Matsumoto for NMR measurements and to the members of the Laboratory of Organic Analysis for microanalysis.

References

1) Part X. Submitted to *Carbohydr. Res.*

2) A. K. Ganguly and A. K. Saksena, *J. Antibiot.*, **28**, 707 (1975); A. K. Ganguly and S. Szmulewicz, *ibid.*, **28**, 710 (1975); A. K. Ganguly, O. Z. Sarre, D. Greeves, and J. Morton *J. Am. Chem. Soc.*, **97**, 1982 (1975).

3) A. K. Ganguly, O. Z. Sarre, and H. Reimann, *J. Am. Chem. Soc.*, **90**, 7129 (1968).

4) A. K. Ganguly, O. Z. Sarre, A. T. Mcphail, and K. D. Onan, *J. Chem. Soc., Chem. Commun.*, **1977**, 313.

5) J. S. Brimacombe and L. W. Doner, *J. Chem. Soc., Perkin Trans. 1*, **1974**, 62.

6) J. M. Bourgeois, *Helv. Chim. Acta*, **57**, 2553 (1974); **58** 363 (1975); **59**, 2214 (1976).

7) J. S. Brimacombe, J. A. Miller, and U. Zakir, *Carbohydr. Res.*, **41**, C3 (1975); **44**, C9 (1975); **49**, 233 (1976).

8) A. Klemer and G. Rodemeyer, *Chem. Ber.*, **107**, 2612 (1974); A. Rosenthal and P. Catsoulacos, *Can. J. Chem.*, **46**, 2868 (1968).

9) A. Rosenthal, K.-S. Ong., *Can. J. Chem.*, **48**, 3034 (1970).

10) D. Horton and W. Weckerle, *Carbohydr. Res.*, **44**, 227 (1975).

11) N. Kornblum, R. J. Clutter, and W. J. Jones, *J. Am. Chem. Soc.*, **78**, 4003 (1956).

12) C. H. Robinson, L. Milewich, and P. Hofer, *Tetrahedron*, **31**, 524 (1966).