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Syntheses of Methyl α- and β-DL-Tetronitrosides (or Kijanosides)

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Methyl α- and β-DL-2,3,4,6-tetradeoxy-4-(methoxycarbonylamino)-3-*C*-methyl-3-nitro-*xylo*-hexopyranosides (**13a**, **b**) were synthesized from methyl α- and β-DL-2,3,4,6-tetradeoxy-hex-3-enopyranosides (**2**). The key step in the syntheses involved regio- and stereospecific addition of iodine isocyanate to the starting unsaturated sugar.

Keywords——amino sugar; carbamate sugar; nitro sugar; tetronitrose; kijanose; tetrocarcin; kijanimicin; iodine isocyanate addition

Tetronitrose (or kijanose) (**1**),[1] which is a component of the antitumor antibiotics tetrocarcins A and B,[2] and kijanimicin,[3] is an unusual sugar in that it has a branched-chain and has two nitrogen-containing functional groups, *i.e.*, nitro and carbamate groups at C_3 and C_4, respectively. In a preliminary communication,[4] we assigned the D-configuration to this novel sugar through the synthesis of methyl α-D-tetronitroside from D-mannose. This paper describes in detail the synthetic study of methyl α- and β-glycosides of the DL-sugar which had been performed as a preliminary investigation for the synthesis of the optically active sugar.

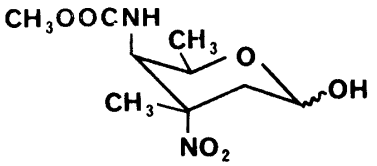
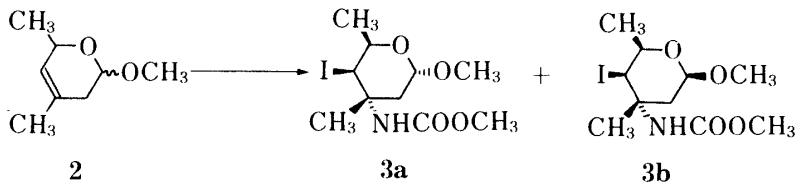


Chart 1

2-Methoxy-4,6-dimethyl-3,6-dihydro-2*H*-pyrane (**2**), a *ca.* 1:1 mixture of *cis* and *trans* isomers,[5] was reacted with iodine isocyanate after the procedure of Hassner[6] and the addition product was directly treated with methanol in the presence of sodium methoxide. The resulting products, which on TLC showed essentially two spots, were readily separated by silica gel chromatography to obtain two crystalline iodo-carbamate isomers: **3a** (20% yield) and **3b** (30% yield). Their structures were assigned as depicted in Chart 2 on the basis of ^{1}H-nuclear magnetic resonance (NMR) spectral data, among which the most informative were the spin-spin coupling constant (J=1.5 Hz) between C_4–H and C_5–H (the same in both isomers) and the coupling patterns for the anomeric C_1 protons: **3a**, δ 4.75 (dd, J=4, <1Hz); **3b**, δ 4.63 (dd, J=10, 2 Hz). Thus, addition of iodine isocyanate to **2** occurred with high regio- and stereoselectivities leading to the expected diaxial addition products.

Transformation of each anomer to the corresponding title compound *via* the 3,5-imino-intermediate is described in the following sections.



2 **3a** **3b**

Chart 2

Methyl α-DL-Tetronitroside (13a)

The iodo-carbamate **3a** was treated with refluxing methanolic potassium hydroxide to give the 3,4-imino sugar **4a** in high yield. The aziridine **4a** was then treated with excess sodium azide in the presence of ammonium chloride in refluxing aqueous ethanol to afford two hydrazoic acid addition products **5a** and **6a** in a ratio of 4.2: 1 with a combined yield of **70%**. The structures of **5a** and **6a** were deduced examination of their ^{1}H-NMR spectra. While C_4–H in **6a** appeared at δ 2.55 as a doublet ($J_{4ax',5ax'}=10$ Hz), the isomer **5a** showed C_4–H at a more deshielded position (δ 2.79) with $J_{4eq',5ax'}=<1$ Hz, as expected for the $C_{4ax'}$–N_3 structure. Further evidence for the structures was obtained by leading them to the corresponding *N*-methoxycarbonyl derivatives (**7a** and **8a**) and observing the splitting of the C_4–H signals in the ^{1}H-NMR spectra (see Experimental section).

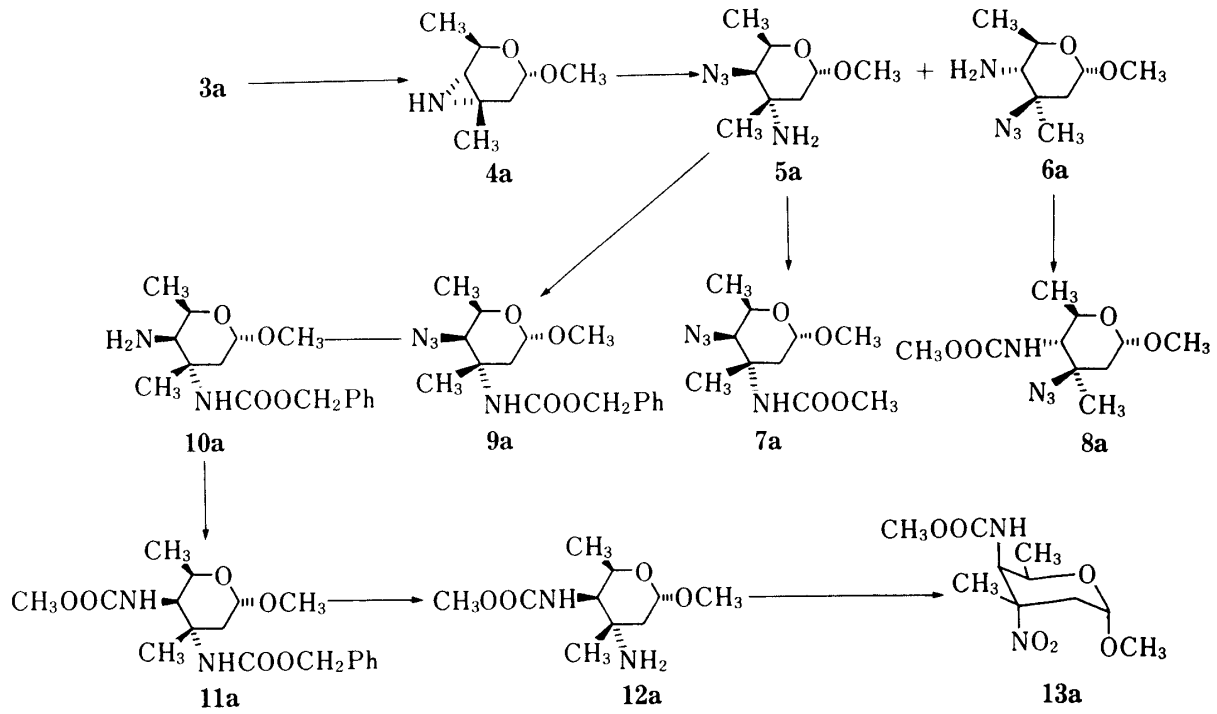


Chart 3

Methyl α-DL-2,3,4,6-tetradeoxy-3-amino-4-azido-3-*C*-methyl-*xylo*-hexopyranoside (**5a**) obtained above was subjected to *N*-benzyloxycarbonylation for protection of the 3-amino group, and the product **9a** was reduced with sodium borohydride and nickel chloride[7] to afford methyl α-DL-2,3,4,6-tetradeoxy-4-amino-3-(benzyloxycarbonylamino)-3-*C*-methyl-*xylo*-hexopyranoside (**10a**). The 4-amino compound **10a** was then processed for *N*-methoxycarbonylation in the usual manner and the dicarbamate product **11a** was subjected to catalytic debenzylation using triethylsilane in the presence of palladium carbon[8] to give methyl α-DL-2,3,4,6-tetradeoxy-3-amino-4-(methoxycarbonylamino)-3-*C*-methyl-*xylo*-hexopyranoside (**12a**) in an overall yield of 58% from **5a**. The final step leading to methyl α-DL-tetronitroside (**13a**), which involved conversion of the tertiary 3-amino group to the nitro group, was carried out by oxidation with *m*-chloroperbenzoic acid in dichloromethane.[9] Methyl α-DL-tetronitroside, obtained in 75% yield, was fully characterized by spectral data. The ^{1}H-NMR spectral data were essentially the same as those published for natural methyl α-kijanoside[3] and the EI mass spectrum showed a base peak at $m/e=128$ corresponding to the ion $[O{=}C{=}N{-}CH{=}C(NO_2)CH_3]^+$, which is diagnostic for the structure. Finally, conclusive evidence for the structure was obtained by direct comparison of the ^{1}H-NMR spectrum of our racemic compound with that of optically active methyl α-tetronitroside.

Methyl β-DL-Tetronitroside (13b)

Synthesis of methyl β-DL-tetronitroside (**13b**) from the iodo-carbamate **3b** was carried out by the same procedures as employed for the α-anomer (**13a**) as shown in Chart 4. The aziridine intermediate (**4b**) obtained by base treatment of **3b** was reacted with sodium azide to give a 6 : 1 mixture of regioisomeric azides **5b** and **6b** again, though some increase in the relative amount of the desired isomer **5b** was obtained. Their stereochemistries at C_3 and C_4 were determined by ^{1}H-NMR spectra as described for the corresponding α-anomers. The desired isomer **5b** was successively subjected to *N*-benzyloxycarbonylation and reduction with sodium borohydride and nickel chloride to give the 4-amino-3-benzyloxycarbonylamino compound (**10b**). *N*-Methoxycarbonylation of **10b** followed by catalytic debenzylation provided methyl β-DL-2,3,4,6-tetradeoxy-3-amino-4-(methoxycarbonylamino)-3-*C*-methyl-*xylo*-hexopyranoside (**12b**). The final step, oxidation of the 3-amino group in **12b**, proceeded smoothly to afford methyl β-DL-tetronitroside (**13b**). The structure of **13b** was confirmed comparison of its ^{1}H-NMR spectrum with that of natural methyl β-tetronitroside.

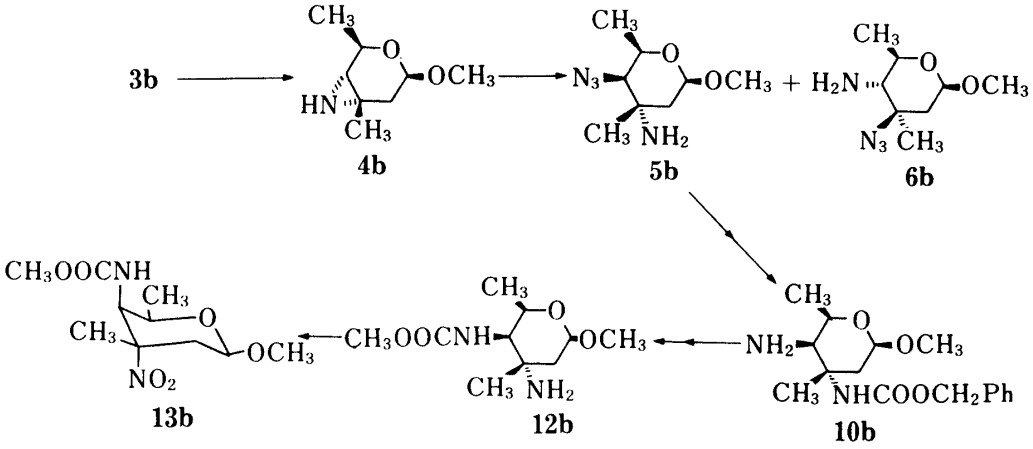


Chart 4

Experimental

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Jasco IRA-1 grating spectrophotometer. ^{1}H-NMR spectra were recorded on a Varian EM-390 or XL-200 spectrometer. Chemical shifts are reported in units ppm downfield from internal tetramethylsilane. Low- and high-resolution mass spectra were obtained on a Jeol JMS D-300 spectrometer at an ionization potential of 70 eV. Combustion analyses were carried out at the Microanalytical Laboratory of this university. Column chromatography was carried out with Merck silica gel (70—230 mesh). Merck precoated silica gel 60 F plates and Merck silica gel 60 PF were used for analytical and preparative thin-layer chromatography (TLC), respectively. All organic solvent extracts were dried over anhydrous magnesium sulfate and concentrated with a rotary evaporator at reduced pressure.

Methyl 2,3,4,6-Tetradeoxy-4-iodo-3-methoxycarbonylamino-3-*C*-methyl-α-DL-*xylo*-hexopyranoside (3a) and Methyl 2,3,4,6-Tetradeoxy-4-iodo-3-methoxycarbonylamino-3-*C*-methyl-β-DL-*xylo*-hexopyranoside (3b) ——A mixture of freshly prepared AgNCO (9.94 g, 64.6 mmol), iodine (12.63 g, 49.7 mmol) and dry ether (100 ml) was stirred under an Ar atmosphere in the dark for 30 min. A solution of **2** (7.06 g, 49.7 mmol) in dry ether (several ml) was then introduced dropwise over a 40 min period. After the reaction mixture had been vigorously stirred at room temperature for 5 h, it was filtered through a layer of Celite. The filtrate was mixed with dry MeOH (100 ml), and, after addition of MeONa (27 mg, 0.5 mmol), the mixture was stirred overnight under an Ar atmosphere at room temperature. The brown-colored reaction mixture was concentrated under reduced pressure, and the residue was dissolved in ether (200 ml). The ether solution was washed with 10% sodium sulfite and brine, dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 300 g) eluting with mixtures of AcOEt and hexane (1 : 7 to 1 : 1) to afford **3a** (3.4 g, 20%) and **3b** (5.1 g, 30%). **3a**: mp 100—101°C (colorless cubes from chloroform–petroleum ether). IR (KBr): 3420, 1715, 1500 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.20 (3H, d, J=6.5 Hz, 6-H), 1.63 (1H,

br d, J=15 Hz, 2-H$_{eq}$), 1.69 (3H, s, 3-CH$_3$), 2.18 (1H, dd, J=15, 4 Hz, 2-H$_{ax}$), 3.32 (1H, qd, J=6.5, 1.5 Hz, 5-H), 3.38 (3H, s, OCH$_3$), 3.63 (3H, s, OCH$_3$), 4.75 (1H, dd, J=4, <1 Hz, 1-H), 4.78 (1H, br s, 4-H), 6.50 (1H, br s, NH). MS *m/e*: 343 (M$^+$), 312, 311, 280, 237, 216, 158, 141, 115. *Anal.* Calcd for $C_{10}H_{18}INO_4$: C, 35.00; H, 5.29; N, 4.08. Found: C, 34.93; H, 5.11; N, 4.11. **3b**: mp 145—146°C (colorless needles from CH_2Cl_2–hexane). IR (KBr): 3340, 1690, 1530 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.26 (3H, d, J=6 Hz, 6-H), 1.68 (3H, s, 3-CH$_3$), 1.70 (1H, dt, J=15, 2 Hz, 2-H$_{eq}$), 2.09 (1H, dd, J=15, 10 Hz, 2-H$_{ax}$), 3.14 (1H, qd, J=6, 1.5 Hz, 5-H), 3.52 (3H, s, OCH$_3$), 3.66 (3H, s, OCH$_3$), 4.63 (1H, dd, J=10, 2 Hz, 1-H), 4.74 (1H, br s, 4-H), 4.96 (1H, br s, NH). MS *m/e*: 343 (M$^+$), 312, 311, 216, 141, 115, 114. *Anal.* Calcd for $C_{10}H_{18}INO_4$: C, 35.00; H, 5.29; N, 4.08. Found: C, 34.92; H, 5.18; N, 3.99.

Methyl 3-Amino-4-azido-2,3,4,6-tetradeoxy-3-*C*-methyl-α-DL-*xylo*-hexopyranoside (5a) and Methyl 4-Amino-3-azido-2,3,4,6-tetradeoxy-3-*C*-methyl-α-DL-*arabino*-hexopyranoside (6a)——A stirred solution of **3a** (550 mg, 1.60 mmol) in MeOH (4.4 ml) was treated with 30% KOH (1.2 ml), and the mixture was refluxed for 19.5 h. After evaporation of MeOH, the residue was thoroughly extracted with ether. The ether extract was dried and concentrated to give the aziridine **4a** (232 mg, 92%) as an oil, which showed essentially a single spot on TLC and was used for the next step without purification. IR (neat): 3310 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.27 (3H, s, 3-CH$_3$), 1.40 (3H, d, J=6.5 Hz, 6-H), 1.64 (1H, br s, 4-H), 1.92 (1H, diffused d, J=15 Hz, 2-H), 2.10 (1H, diffused d, J=15 Hz, 2-H), 3.35 (3H, s, OCH$_3$), 4.05 (1H, q, J=6.5 Hz, 5-H), 4.70 (1H, t, J=3.5 Hz, 1-H), MS *m/e*: 157.1059 (M$^+$, calcd for $C_8H_{15}NO_2$: 157.1101), 126.0937 (M$^+$−OCH$_3$, calcd 126.0919).

Sodium azide (2.093 g, 32.2 mmol) and ammonium chloride (1.722 g, 32.2 mmol) were added to a stirred solution of **4a** (1.248 g, 7.95 mmol) in 75% EtOH (40 ml), and the solution was heated under reflux for 15 h. The cooled reaction mixture was diluted with ether (300 ml) and the ether solution was washed with brine, dried, and concentrated. The residue was subjected to column chromatography (silica gel, 80 g) with AcOEt–MeOH (9: 1) to give the more polar **5a** (958 mg, mp 35—36°C after crystallization from chloroform–petroleum ether) and the less polar **6a** (228 mg, oil). **5a**, IR (neat): 3400, 2100 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.23 (3H, s, 3-CH$_3$), 1.35 (3H, d, J=6.5 Hz, 6-H), 1.53 (1H, d, J=13.5 Hz, 2-H), 1.73 (1H, dd, J=13.5, 4 Hz, 2-H), 1.98 (2H, br s, NH$_2$), 2.79 (1H, br s, 4-H), 3.38 (3H, s, OCH$_3$), 4.35 (1H, q, J=6.5 Hz, 5-H), 4.77 (1H, d, J=4 Hz, 1-H). *Anal.* Calcd for $C_8H_{16}N_4O_2$: C, 47.98; H, 8.05; N, 27.98. Found: C, 48.22; H, 8.05; N, 27.90. **6a**, IR (neat): 3380, 3320, 2105 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.20 (2H, br s, NH$_2$), 1.27 (3H, d, J=6.5 Hz, 6-H), 1.45 (3H, s, 3-CH$_3$), 1.90 (1H, dd, J=15, 4 Hz, 2-H), 2.08 (1H, dd, J=15, 2 Hz, 2-H), 2.55(1H, d, J=10 Hz, 4-H), 3.35 (3H, s, OCH$_3$), 3.57 (1H, dq, J=10, 6.5 Hz, 5-H), 4.76 (1H, dd, J=4, 2 Hz, 1-H).

N-Methoxycarbonyl derivatives (prepared in the usual manner): **7a** (oil), ^{1}H-NMR ($CDCl_3$) δ: 1.35 (3H, d, J=6 Hz, 6-H), 1.59 (3H, s, 3-CH$_3$), 1.67 (1H, d, J=15 Hz, 2-H), 1.90 (1H, dd, J=15, 4 Hz, 2-H), 3.40 (3H, s, OCH$_3$), 3.67 (3H, s, OCH$_3$), 3.84 (1H, br s, 4-H), 4.24 (1H, diffused q, J=6 Hz, 5-H), 4.75 (1H, d, J=4 Hz, 1-H), 6.34 (1H, br s, NH). MS *m/e*: 227.1132 (M$^+$−OCH$_3$, calcd 227.1143). **8a**, (mp 113—115°C). ^{1}H-NMR (C_6D_6) δ: 1.13 (3H, s, 3-CH$_3$), 1.17 (3H, d, J=6 Hz, 6-H), 1.65 (2H, 2-H), 3.01 (3H, s, OCH$_3$), 3.18 (1H, dq, J=10, 6 Hz, 5-H), 3.55 (3H, s, OCH$_3$), 3.86 (1H, dd, J=10, 2 Hz, 4-H), 4.35 (1H, t, J=3 Hz, 1-H). MS *m/e*: 227 (M$^+$−OCH$_3$), 184, 128, 111. *Anal.* Calcd for $C_{10}H_{18}N_4O_4$: C, 46.50; H, 7.02; N, 21.69. Found: C, 46.50; H, 6.91; N, 21.72.

Methyl 3-Amino-4-azido-2,3,4,6-tetradeoxy-3-*C*-methyl-β-DL-*xylo*-hexopyranoside (5b) and Methyl 4-Amino-3-azido-2,3,4,6-tetradeoxy-3-*C*-methyl-β-DL-*arabino*-hexo pyranoside (6b)——After the procedure described in the preceding section, these β-anomers were obtained in a ratio of **5b**: **6b**=6: 1 in a combined overall yield of 76% from **3b**. The spectral data including those of the aziridine intermediate (**4b**) and the *N*-methoxycarbonyl derivative of **6b** are given below.

4b, IR (neat): 3290 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.57 (1H, br s, NH), 1.38 (3H, s, 3-CH$_3$), 1.43 (3H, d, J=6.5 Hz, 6-H), 1.55 (1H, dd, J=13.5, 9 Hz, 2-H$_{ax}$), 1.97 (1H, br s, 4-H), 2.08 (1H, dd, J=13.5, 3 Hz, 2-H$_{eq}$), 3.48 (3H, s, OCH$_3$), 3.92 (1H, q, J=6.5 Hz, 5-H), 4.33 (1H, dd, J=9, 3 Hz, 1-H). MS *m/e*: 156 (M$^+$−1), 149, 142, 126, 110, 98, 97, 84, 82. **5b**, IR (neat): 3400, 2120 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.25 (2H, s, NH$_2$), 1.33 (3H, s, 3-CH$_3$), 1.40 (3H, d, J=6.5 Hz, 6-H), 1.47 (1H, dd, J=15, 3.5 Hz, 2-H$_{eq}$), 1.70 (1H, dd, J=15, 9 Hz, 2-H$_{ax}$), 2.78 (1H, br s, 4-H), 3.53 (3H, s, OCH$_3$), 4.33 (1H, dq, J=6.5, 1 Hz, 5-H), 4.67 (1H, dd, J=9, 3.5 Hz, 1-H). MS *m/e*: 200.1303 (M$^+$, calcd for $C_8H_{16}N_4O_2$: 200.1273), 169, 141, 101, 86, 70, 58, 43, 42. **6b**, IR (neat): 3400, 3340, 2100 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.32 (3H, d, J=6 Hz, 6-H), 1.35 (3H, s, 3-CH$_3$), 1.78 (1H, dd, J=12, 9 Hz, 2-H$_{ax}$), 2.06 (1H, dd, J=12, 2 Hz, 2-H$_{eq}$), 2.57 (1H, d, J=10 Hz, 4-H), 3.35 (1H, dq, J=10, 6 Hz, 5-H), 3.52 (3H, s, OCH$_3$), 4.50 (1H, dd, J=9, 2 Hz, 1-H). *N*-Methoxycarbonyl derivative of **6b**, (mp 97—98°C), IR (KBr): 3365, 2105, 1695 cm^{-1}. MS *m/e*: 257 (M$^+$−1), 227, 216, 215, 199, 183, 172. *Anal.* Calcd for $C_{10}H_{18}N_4O_4$: C, 46.50; H, 7.02; N, 21.69. Found: C, 46.50; H, 7.14; N, 21.77.

Methyl 4-Azido-3-benzyloxycarbonylamino-2,3,4,6-tetradeoxy-3-*C*-methyl-α-DL-*xylo*-hexopyranoside (9a)——Benzyl chloroformate (1.64 ml, 8.42 mmol) was added to a stirred solution of **5a** (560 mg, 2.8 mmol) in dry pyridine (8.4 ml) at room temperature over a 5 min period. After continued stirring overnight, the reaction mixture was concentrated under reduced pressure and the residue was partitioned between AcOEt and brine. The organic layer was dried and concentrated to give **9a** (869 mg), which was used for the next step without further purification. The analytical sample was obtained as an oil by column chromatography of a portion of the crude product eluting with AcOEt–hexane (1: 5). IR (neat): 3410, 2100, 1720,

1505 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.30 (3H, d, J=6 Hz, 6-H), 1.58 (1H, diffused d, J=15 Hz, 2-H_{ax}), 1.58 (3H, s, 3-CH_3), 1.90 (1H, dd, J=15, 4.5 Hz, 2-H_{eq}), 3.38 (3H, s, OCH_3), 3.83 (1H, diffused s, 4-H), 4.22 (1H, qd, J=6, 1 Hz, 5-H), 4.73 (diffused d, J=4.5 Hz, 1-H), 5.02 (1H, d, J=13.5 Hz, Ar–CH<u>H</u>), 5.20 (1H, d, J=13.5 Hz, Ar–CH<u>H</u>), 6.37 (1H, diffused s, NH), 7.42 (5H, s, Ar–H). MS *m/e*: 277.1533 (M^+-OCH_3, calcd 277.1551), 252.1221 ($M^+-C_3H_6N$, calcd 252.1234).

Methyl 4-Amino-3-benzyloxycarbonylamino-2,3,4,6-tetradeoxy-3-*C*-methyl-α-DL-*xylo*-hexopyranoside (10a)——Anhydrous nickel chloride (1.28 g, 9.9 mmol) was added to a stirred solution of **9a** (815 mg, 2.44 mmol) in EtOH (60 ml), and then a solution of $NaBH_4$ (1.25 g, 33 mmol) in water (20 ml) was introduced dropwise at room temperature, leading to an exothermic reaction. After 20 min, the reaction mixture was filtered with the aid of Celite and the filtrate was concentrated. The residue was extracted with chloroform, and the chloroform solution was dried and concentrated to give **10a** (610 mg). This crude product was used for the next step without further purification. The analytical sample was obtained as an oil by column chromatography of a portion of the crude product eluting with AcOEt–MeOH (9: 1). IR (neat): 3400, 1720, 1505 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.20 (3H, d, J=6 Hz, 6-H), 1.52 (3H, s, 3-CH_3), 1.53 (1H, diffused d, J=15 Hz, 2-H_{ax}), 1.87 (1H, dd, J=15, 4.5 Hz, 2-H_{eq}), 3.08 (1H, br s, 4-H), 3.38 (3H, s, OCH_3), 4.25 (1H, qd, J=6, 1 Hz, 5-H), 4.72 (1H, diffused d, J=4.5 Hz, 1-H), 6.35 (1H, diffused s, NH), 5.00 (1H, d, J=13.5 Hz, Ar–CH<u>H</u>), 5.17 (1H, d, J=13.5 Hz, Ar–CH<u>H</u>), 7.41 (5H, s, Ar–H). MS *m/e*: 308.1662 (M^+, calcd for $C_{16}H_{24}N_2O_4$: 308.1735), 277.1533 (M^+-OCH_3, calcd 277.1551), 252.1221 ($M^+-C_3H_6N$, calcd 252.1234).

Methyl 4-Amino-3-benzyloxycarbonylamino-2,3,4,6-tetradeoxy-3-*C*-methyl-β-DL-*xylo*-hexopyranoside (10b)——This compound was prepared from **5b** by employing the same procedures as described for the corresponding α-anomer: mp 104.5—105.5°C (colorless colonies from chloroform–hexane). IR (KBr): 3200, 1705, 1530 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.23 (3H, d, J=6 Hz, 6-H), 1.47 (3H, s, 3-CH_3), *ca.* 1.8 (1H, dd, J=*ca.* 15, 10 Hz, 2-H_{ax}), *ca.* 2.0 (1H, dd, J=*ca.* 15, 3 Hz, 2-H_{eq}), 3.47 (3H, s, OCH_3), 3.84 (1H, br m, 4-H), 3.98 (1H, q, J=6 Hz, 5-H), 4.47 (1H, dd, J=10, 3 Hz, 1-H), 4.70 (1H, br s, NH), 5.07 (2H, s, Ar–CH_2), 7.38 (5H, s, Ar–H). MS *m/e*: 309 (M^++1), 308 (M^+), 307 (M^+−1), 277, 252, 236, 190, 178. *Anal.* Calcd for $C_{16}H_{24}N_2O_4$: C, 62.31; H, 7.85; N, 9.09. Found: C, 62.40; H, 8.08; N, 9.04.

Methyl 3-Benzyloxycarbonylamino-2,3,4,6-tetradeoxy-4-methoxycarbonylamino-3-*C*-methyl-α-DL-*xylo*-hexopyranoside (11a)——A solution of crude **10a** (355 mg) in dry pyridine (3.5 ml) was treated with methyl chloroformate (0.18 ml, 2.3 mmol) at room temperature overnight. Pyridine was evaporated off under reduced pressure, and the residue was partitioned between AcOEt and brine. The organic layer was dried and concentrated to give **11a** (378 mg, 90%), which was essentially homogeneous on TLC, and was used for the next step without further purification. IR (neat): 3410, 1720 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.16 (3H, d, J=6 Hz, 6-H), 1.46 (3H, s, 3-CH_3), 1.57 (1H, br d, J=18 Hz, 2-H), 1.80 (1H, br d, J=18 Hz, 2-H), 3.37 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 4.07—4.43 (2H, m, 4-H and 5-H), 4.72 (1H, diffused t, 1-H), 6.03 (1H, d, J=12 Hz, Ar–CH<u>H</u>), 6.22 (1H, d, J=12 Hz, Ar–CH<u>H</u>), 6.16 (1H, br s, NH), 7.41 (5H, br s, Ar–H). MS *m/e*: 335.1645 (M^+-OCH_3, calcd 335.1607).

Methyl 3-Amino-2,3,4,6-tetradeoxy-4-methoxycarbonylamino-3-*C*-methyl-α-DL-*xylo*-hexopyranoside (12a)——Triethylsilane (0.67 ml, 4.15 mmol) and 10% Pd–C (300 mg) were added to a solution of the crude **11a** (305 mg, 0.83 mmol) obtained above in dry MeOH (5 ml). The mixture was stirred and heated under reflux for 1.5 h. Removal of the catalyst followed by evaporation of the MeOH afforded an oil, which was subjected to column chromatography (silica gel, 15 g) to give essentially homogeneous oily **12a** (166 mg, 86%). IR (neat): 1725, 1530 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.11 (3H, s, 3-CH_3), 1.17 (3H, d, J=6 Hz, 6-H), 1.02 (2H, br s, 2-H), 2.04 (2H, br s, NH_2), 3.38 (3H, s, OCH_3), 3.74 (3H, s, OCH_3), 4.42 (1H, qd, J=6, 1 Hz, 5-H), 4.73 (1H, diffused t, 1-H), 4.97 (1H, diffused d, J=*ca.* 10 Hz, NH). MS *m/e*: 232.1424 (M^+, calcd for $C_{10}H_{20}N_2O_4$: 232.1423), 201.1253 (M^+-OCH_3, calcd 201.1240), 157.1012 ($M^+-C_3H_7O_2$, calcd 157.0977), 118.0856 ($M^+-C_5H_8NO_2$, calcd 118.0866).

Methyl 3-Amino-2,3,4,6-tetradeoxy-4-methoxycarbonylamino-3-*C*-methyl-β-DL-*xylo*-hexopyranoside (12b)——This compound was obtained from **10b** in an overall yield of 77% by essentially the same procedures as described for the α-anomer: mp 93.5—94°C (colorless cubes from chloroform–hexane). IR (KBr): 3340, 3260, 1720, 1595, 1520 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.20 (3H, s, 3-CH_3), 1.23 (3H, d, J=6 Hz, 6-H), 1.45 (2H, m, 2-H_{ax}, 2-H_{eq}), 3.22 (1H, br d, J=10 Hz, 4-H), 3.51 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 4.35 (1H, qd, J=6, *ca.* 1 Hz, 5-H), 4.67 (1H, dd, J=9, 4.5 Hz, 1-H), 5.22 (1H, br d, J=10 Hz, NH). *Anal.* Calcd for $C_{10}H_{20}N_2O_4$: C, 51.70; H, 8.68; N, 12.06. Found: C, 51.74; H, 8.86; N, 12.09.

Methyl α-DL-Tetronitroside (13a)——A solution of **12a** (74 mg, 0.319 mmol) in dry CH_2Cl_2 (4.4 ml) was added with a syringe over a 35 min period to a refluxing and stirred solution of *m*-chloroperbenzoic acid (435 mg, 2.52 mmol) in dry CH_2Cl_2 (4.4 ml). After continued refluxing for 30 min, the reaction mixture was allowed to cool and diluted with chloroform. The organic solution was successively washed with 10% Na_2SO_3, saturated $NaHCO_3$ and water, and dried. Evaporation of the solvent afforded **13a** (70.2 mg), which was subjected to column chromatography (silica gel, 3.5 g) with AcOEt–hexane (1: 1) to give crystals (62.7 mg, 75%). An analytical sample was obtained by recrystallization from chloroform–petroleum ether, mp 140—142°C (colorless needles). IR (KBr): 3320, 1690, 1535 cm^{-1}. MS *m/e*: 263 (M^++1), 261 (M^+−1), 231, 199, 184, 172, 156. ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.20 (3H, d, J=6.5 Hz, 6-H), 1.54 (3H, s, 3-CH_3), 1.79 (1H, dd, J=15.6, 4.0 Hz, 2-H), 2.77 (1H, d, J=15.6 Hz, 2-H_{eq}), 3.24 (3H, s, OCH_3), 3.73 (3H, s, OCH_3), 4.27

(1H, q, J=6.5 Hz, 5-H), 4.49 (1H, d, J=9.5 Hz, 4-H), 4.65 (1H, d, J=4.0 Hz, 1-H), 5.00 (1H, br d, J=9.5 Hz, NH). *Anal.* Calcd for $C_{10}H_{18}N_2O_6$: C, 45.79; H, 6.92; N, 10.68. Found: C, 45.77; H, 6.92; N, 10.89.

Methyl β-DL-Tetronitroside (13b)——This compound was obtained from **12b** by essentially the same procedure as described above for **12a**: 27 mg of **12b** afforded 22 mg (71%) of homogeneous solid **13b** after column chromatography (silica gel, 1.2 g; solvent, AcOEt–hexane=2: 3). The analytical sample was obtained by recrystallization of the solid product from chloroform–petroleum ether: mp 120.5—121.5°C (colorless needles). IR (KBr): 3360, 1690, 1545 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.22 (3H, d, J=6.3 Hz, 6-H), 1.52 (1H, dd, J=15.1, 9.8 Hz, 2-H_{ax}), 1.59 (3H, s, 3-CH_3), 2.68 (1H, br d, J=15.1 Hz, 2-H_{eq}), 3.50 (3H, s, OCH_3), 3.59 (1H, q, J=6.3 Hz, 5-H), 3.73 (3H, s, OCH_3), 4.42 (1H, d, J=*ca.* 10 Hz, 4-H), 4.45 (1H, dd, J=15.1, 2.3 Hz, 1-H), 5.14 (1H, br d, J=*ca.* 10 Hz, NH). MS *m/e*: 261 (M^+-1), 184, 172, 156, 140, 128. *Anal.* Calcd for $C_{10}H_{18}N_2O_6$: C, 45.79; H, 6.92; N, 10.68. Found: C, 45.79; H, 6.90; N, 10.58.

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References and Notes

1) We prefer the trivial name "tetronitrose" for this particular sugar, rather than kijanose, in view of the history of this compound, *i.e.*, tetronitrose was first discovered and its structure determined, and more importantly, the suffix "nitrose" is apparently in current use for nitro group-containing sugars of natural origin. Evernitrose and rubranitrose are examples of this usage. Evernitrose: A.K. Ganguly, O.Z. Sarre, and H. Reimann, *J. Am. Chem. Soc.*, **90**, 7129 (1968); Rubranitrose: S.A. Mizsak, H. Hoeksema, and L.M. Pschigoda, *J. Antibiot.*, **32**, 771 (1979).
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