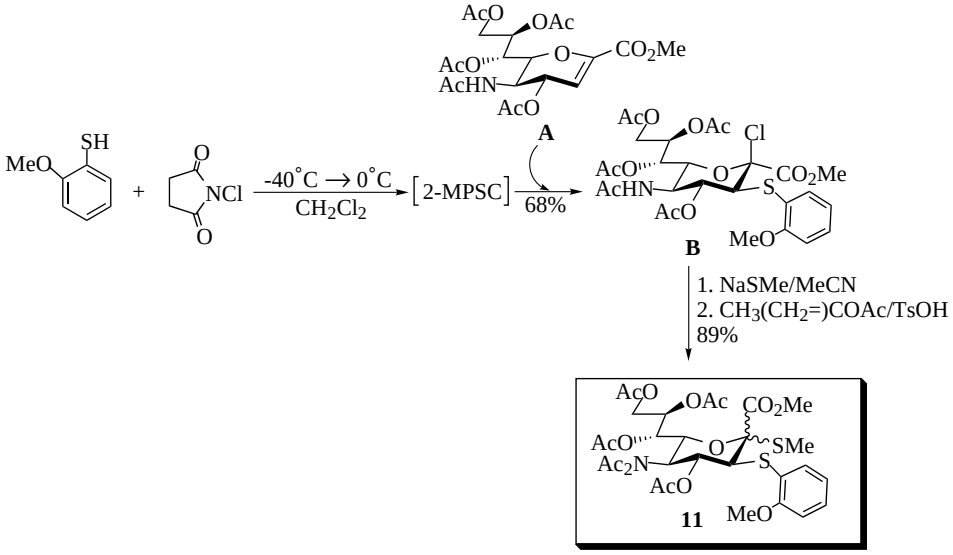
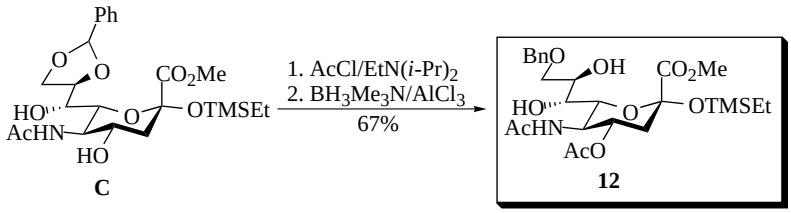
Supplementary Material

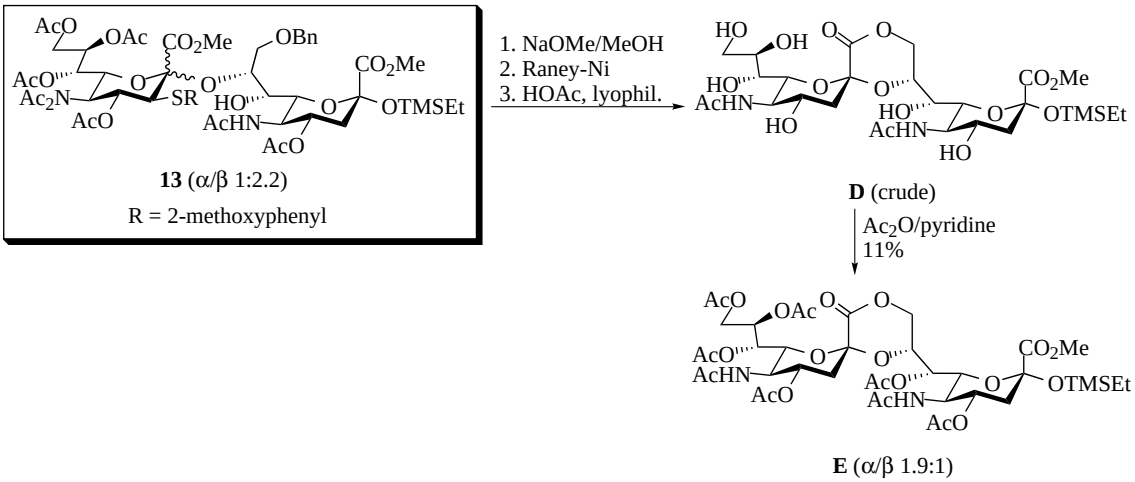
Preparation of the Donor 11:



Preparation of the Acceptor 12:

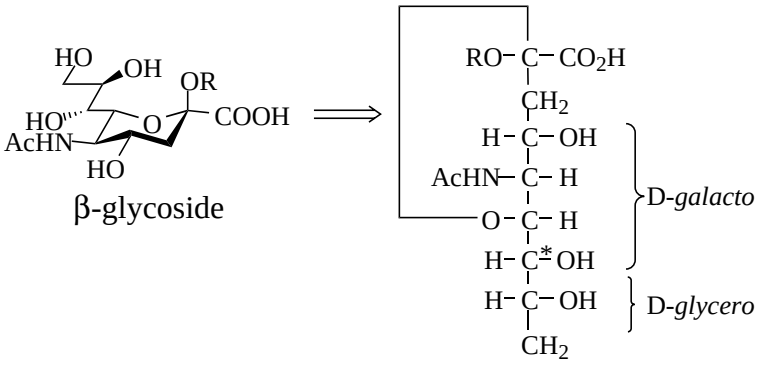


Deprotection and Structure Verification of the *bis*-Sialoside 13:



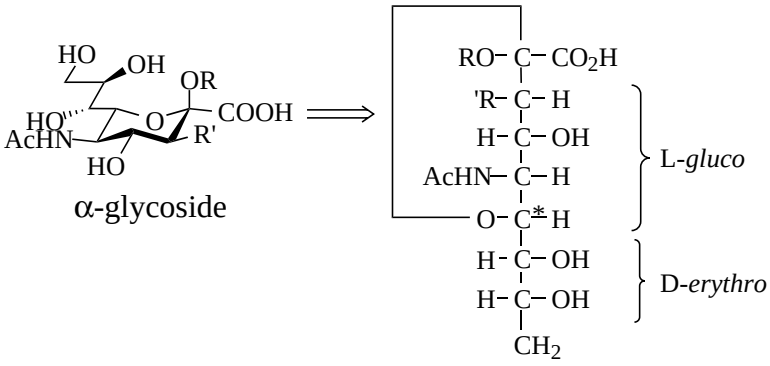
The nomenclature of Neu5Ac residues is deduced in accordance with the following Fischer projections:

Normal Neu5Ac:



* = reference carbon for the anomeric configuration

3-(*S*)-Substituted Neu5Ac:



Experimental

General. ^{1}H NMR spectra were recorded at 300, 400 or 500 MHz and assigned using 2D-methods (COSY, HETCOR). Optical rotations were measured at 22˚C. Chemical shifts are expressed in ppm using residual $CHCl_3$ as reference. Reactions were monitored by TLC using alumina plates coated with silica gel 60 F254 (Merck) and visualised using either UV light or charring with H_3PO_4 (aqueous 5% dip solution). The Al_2O_3 used was of Activity II-III (Merck). Preparative chromatography was performed with Amicon silica gel (35-70 μm, 60Å). CH_2Cl_2 and toluene were dried over 4Å molecular sieves. MeCN was distilled over CaH_2 immediately before use. Compounds obtained as white powders were precipitated with *n*-hexane from a chloroform/diethyl ether (~1:2) solution. All reactions were carried out under an argon atmosphere. Anomeric configurations of Neu5Ac residues were determined in accordance with Hori, H.; Nakajima, T.; Nishida, Y.; Ohrui, H.; Meguro, H. *Tetrahedron Lett.* **1988**, *29*, 6317-6320.

Methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-2-chloro-3-(2-methoxyphenyl)thio-3,5-dideoxy-D-*erythro*-α-L-*gluco*-2-nonulopyranosonate (B). To a stirred suspension of *N*-chlorosuccinimide (1.222 g, 9.15 mmol) in dichloromethane (8.0 mL) cooled to -40˚C was dropwise added 2-methoxybenzenethiol (1.120 mL, 9.18 mmol) over 5 min. After 1 h, the stirring was disrupted and the reaction mixture was kept 0˚C over night, thereby allowing the *N*-succinimide formed to sediment. Of the obtained ~1.0 M solution of 2-methoxyphenyl-sulfenyl chloride, 4.0 mL (~4 mmol) was added to the solid glycal **A**[1] (0.617 g, 1.30 mmol), and the reaction mixture was kept at room temperature for seven days in a dark place. Addition of aqueous 0.1 M $NaHCO_3$ (50 mL), transfer to a separatory funnel, extraction with CH_2Cl_2 (4 × 50 mL), concentration and chromatography (toluene/acetone, 6:1 → 3:1, gradient) on a silica gel column having a top layer (~1 cm) of Al_2O_3 afforded **B** (0.576 g, 68%) as a white powder: $[\alpha]_D$ ±0˚ (*c* 0.99, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48-6.83 (m, 4 H, Ph), 5.45 (dd, 1 H, $J_{6,7}$ 2.2 Hz, $J_{7,8}$ 8.2 Hz, H-7), 5.43 (d, 1 H, $J_{5,NH}$ 10.5 Hz, NH), 5.39 (dd, 1 H, $J_{4,5}$ 10.1 Hz, $J_{3,4}$ 10.6 Hz, H-4), 5.13 (ddd, 1 H, $J_{8,9A}$ 2.7 Hz, $J_{8,9B}$ 5.4 Hz, H-8), 4.40 (dd, 1 H, $J_{5,6}$ 10.9 Hz, H-6), 4.35 (m, 1 H, H-5), 4.28 (dd, 1 H, $J_{9A,9B}$ 12.5 Hz, H-9A), 4.21 (d, 1 H, H-3), 4.01 (dd, 1 H, H-9B), 3.88 (s, 3 H, PhOCH_3), 3.83 (s, 3 H, CO_2Me), 2.13, 2.10, 2.05, 1.88, 1.72 (s, 3 H each, 4OAc, NAc); ^{13}C NMR ($CDCl_3$): δ 171.3, 170.8, 170.5, 170.1, 169.7, 164.4 ($J_{C1,H3}$ 1.5 Hz, C-1), 158.6, 133.8, 129.7, 121.4, 121.2, 111.2, 102.9, 74.7, 73.9, 69.3, 66.7, 62.2, 55.9, 54.3, 54.2, 49.2, 23.2, 21.2, 21.0, 20.9, 20.6. HR FAB-MS for $C_{27}H_{34}ClNO_{13}SNa$ (M + Na): Calcd 670.1337. Found 670.1337.

[1] Meindl, P.; Tuppy, H. *Monatsch. Chem.* **1969**, *100*, 1295-1306.

Methyl [methyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*-acetylacetamido)-2-thio-3-(2-methoxyphenyl)thio-3,5-dideoxy-D-*erythro*-β-L-*gluco*-2-nonulopyranosid]onate (11). To a stirred mixture of **B** (0.509 g, 0.785 mmol) and sodium methanethiolate (0.091 g, 1.3 mmol) cooled to 0˚C was added acetonitrile (2.5 mL), and the mixture was stirred vigorously for 4 h at this temperature. Addition of acetic acid (0.2 mL), filtration through a short (<10 cm) column of silica gel, washing with toluene/acetone 1:1, concentration and chromatography on silica gel (toluene/acetone, 5:1 → 3:1, gradient) afforded methyl [methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-2-thio-3-(2-methoxyphenyl)thio-3,5-dideoxy-D-*erythro*-β-L-*gluco*-2-nonulopyranosid]onate (0.464 g, 90%, α/β 1:15) as a white powder: $[\alpha]_D$ +94˚ (*c* 0.49, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51-6.85 (m, 4 H, Ph), 5.38 (ddd, 1 H, $J_{7,8}$ 8.2 Hz, $J_{8,9A}$ 2.6 Hz, $J_{8,9B}$ 5.2 Hz, H-8), 5.31 (dd, 1 H, $J_{6,7}$ 2.2 Hz, H-7), 5.27 (d, 1 H, $J_{5,NH}$ 10.2 Hz, NH), 5.18 (dd, 1 H, $J_{3,4}$ 11.1 Hz, $J_{4,5}$ 10.2 Hz, H-4), 4.33 (dd, 1 H, $J_{9A,9B}$ 12.5 Hz, H-9A), 4.14 (q, 1 H, *J* 10.4 Hz, H-5), 4.11 (dd, 1 H, H-9B), 3.91, 3.90 (s, 3 H each, CO_2Me, PhOCH_3), 3.88 (dd, 1 H, $J_{5,6}$ 11.0 Hz, H-6), 3.72 (d, 1 H, H-3), 2.20, 2.17, 2.13, 2.04, 1.85, 1.80 (s, 3 H each, 4OAc, NAc, SMe); ^{13}C NMR ($CDCl_3$): δ 171.2, 170.9, 170.4, 170.3, 170.2, 167.3 ($J_{C1,H3}$ 7.7 Hz, C-1), 158.5, 133.5, 129.4, 124.3, 121.1, 111.3, 87.3, 74.8, 74.3, 69.0, 67.5, 62.3, 55.8, 54.9, 53.2, 50.6, 23.3, 21.4, 21.0, 21.0, 20.8, 12.5. HR FAB-MS for $C_{28}H_{37}NO_{13}S_2Na$ (M + Na): Calcd 682.1604. Found 682.1616.

To a stirred solution of methyl [methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-2-thio-3-(2-methoxyphenyl)thio-3,5-dideoxy-D-*erythro*-β-L-*gluco*-2-nonulopyranosid]onate (0.458 g, 0.694 mmol) in *iso*-propenylacetate (5.0 mL) was added *p*-toluenesulfonic acid monohydrate (4.7 mg, 0.025 mmol) and the reaction was kept at 65˚C for 14 h. Addition of triethylamine (0.2 mL), concentration with toluene and chromatography on silica gel (toluene/acetone, 15:1 → 8:1, gradient) afforded **11** (0.484 g, 99%, α/β 1:15) as a white powder: $[\alpha]_D$ +83˚ (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56-6.83 (m, 4 H, $C_6H_4OCH_3$), 5.81 (dd, 1 H, $J_{3,4}$ 10.7 Hz, $J_{4,5}$ 9.7 Hz, H-4), 5.33 (ddd, 1 H, $J_{7,8}$ 8.6 Hz, $J_{8,9A}$ 2.9 Hz, $J_{8,9B}$ 4.8 Hz, H-8), 5.12 (dd, 1 H, $J_{6,7}$ 1.9 Hz, H-7), 4.85 (dd, 1 H, $J_{5,6}$ 10.5 Hz, H-6), 4.35 (dd, 1 H, H-5), 4.27 (dd, 1 H, $J_{9A,9B}$ 12.6 Hz, H-9A), 4.13 (dd, 1 H, H-9B), 3.95, 3.89 (s, 3 H each, $C_6H_4OCH_3$, CO_2Me), 3.64 (d, 1 H, H-3), 2.35, 2.27, 2.24, 2.17, 2.11, 2.02, 1.71 (s, 3 H each, 4OAc, Ac_2N, SMe); ^{13}C NMR ($CDCl_3$): δ 174.1, 174.0, 170.9, 170.4, 170.3, 170.2, 167.0, 158.3, 133.0, 128.9, 125.1, 121.2, 111.2, 86.9, 72.2, 71.9, 68.5, 67.2, 61.9, 57.2, 56.5, 55.8, 53.2, 28.3, 26.8, 21.3, 21.2, 21.0, 20.6, 12.5. HR FAB-MS for $C_{30}H_{39}NO_{14}S_2Na$ (M + Na): Calcd 724.1710. Found 724.1702.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-4-*O*-acetyl-9-*O*-benzyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosid]onate (12). To a stirred solution of **C**[2] (0.331 g, 0.648 mmol) in dichloromethane (2.5 mL) was added *N*-ethyldiisopropylamine (0.23 mL, 1.3 mmol) and the temperature was lowered to -40˚C. Acetyl chloride (0.050 mL, 0.70 mmol) was added dropwise, and the reaction mixture was kept at -30˚C for 7 h, after which *t*-butanol (0.10 mL) was added. Filtration through a short column of silica gel, washing with toluene/acetone 2:1 and concentration afforded a residue which was dried *in vacuo* over night. To a vigorously stirred solution of the dried residue in tetrahydrofuran (3.5 mL) cooled to 0˚C was then added borane trimethylamine (0.200 g, 2.75 mmol) and $AlCl_3$ (0.37 g, 2.78 mmol). After 25 min, dichloromethane (50 mL) and aqueous 0.1 M $NaHCO_3$ (50 mL) was added, and the mixture was transferred to a separatory funnel. Extraction with dichloromethane (3 × 100 mL), concentration and

[2] Demchenko, A.V.; Boons, G.J. *Chem. Eur. J.* **1999**, *5*, 1278-1283.

chromatography on silica gel (toluene/acetone, 4:1 → 2:1, gradient) afforded **12** (0.242 g, 67%) as a white powder: $[\alpha]_D$ -32˚ (*c* 0.99, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.24 (m, 5 H, Ph), 5.90 (d, 1 H, $J_{5,NH}$ 7.8 Hz, NH), 4.92 (ddd, 1 H, $J_{3e,4}$ 4.9 Hz, $J_{4,5}$ 10.4 Hz, $J_{3a,4}$ 12.2 Hz, H-4), 4.64 (d, 1 H, $J_{HA,HB}$ 12.2 Hz, OCH_2Ph), 4.60 (d, 1 H, OCH_2Ph), 4.59 (d, 1 H, $J_{7,OH}$ 4.5 Hz, OH-7), 4.09 (m, 1 H, H-8), 4.03-3.90 (m, 2 H, H-5, OCH_2CH$_2$Si), 3.85 (m, 1 H, H-9A), 3.84 (s, 3 H, CO_2Me), 3.66 (dd, 1 H, $J_{8,9B}$ 6.0 Hz, $J_{9A,9B}$ 10.2 Hz, H-9B), 3.56 (m, 1 H, H-7), 3.55 (d, 1 H, $J_{8,OH}$ 4.1 Hz, OH-8), 3.51 (dd, 1 H, $J_{6,7}$ 1.7 Hz, $J_{5,6}$ 10.5 Hz, H-6), 3.40 (m, 1 H, OCH_2CH$_2$Si), 2.68 (dd, 1 H, $J_{3a,3e}$ 13.0 Hz, H-3e), 2.11 (s, 3 H, OAc), 2.01 (t, 1 H, *J* 12.7 Hz, H-3a), 1.97 (s, 3 H, NAc), 0.88 (t, 2 H, *J* 7.8 Hz, OCH$_2$CH_2Si), 0.00 (s, 9 H, $SiMe_3$); ^{13}C NMR ($CDCl_3$): δ 172.9, 172.5, 169.5, 138.7, 128.5, 127.9, 127.7, 98.6, 74.2, 73.6, 71.8, 70.3, 69.3, 68.9, 62.3, 53.3, 52.0, 37.7, 23.3, 21.3, 18.1, -1.1. HR FAB-MS for $C_{26}H_{41}NO_{10}SiNa$ (M + Na): Calcd 578.2397. Found 578.2408.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-4-*O*-acetyl-9-*O*-benzyl-3,5-dideoxy-8-*O*-[methyl [4,7,8,9-tetra-*O*-acetyl-5-(*N*-acetylacetamido)-3-(2-methoxyphenyl)thio-3,5-dideoxy-D-*erythro*-β-L-*gluco*-2-nonulopyranosid]onate]-D-*glycero*-α-D-*galacto*-2-nonulopyranosid]onate (13). To a stirred solution of **11** (0.108 g, 0.154 mmol), **12** (0.132 g, 0.238 mmol) and 3 Å molecular sieves (0.25 g) in acetonitrile (0.9 mL) was added a solution of AgOTf (0.054 g, 0.21 mmol) in acetonitrile (0.2 + 0.2 mL). After cooling to -40˚C, a 1.0 M solution (0.21 mL, 0.21 mmol) of ICl in dichloromethane was added dropwise over 10 min. After 2 h, diisopropylamine (0.070 mL, 0.50 mmol) was added. Filtration (Celite), washing with chloroform/acetone 1:1, concentration and chromatography (toluene/acetone, 5:1 → 3:1, gradient) afforded recovered **12** (0.066 g) and **13** (0.103 g, 56%, α/β 1:2.2), both as white powders.

Data for **13** (anomeric mixture): ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.90 (dd, 1 H, $J_{3',4'}$ 8.6 Hz, $J_{4',5'}$ 9.5 Hz, H-4'), 5.88 (d, 1 H, $J_{5,NH}$ 9.4 Hz, NH), 3.86, 3.81, 3.78 (s, 3 H each, 2CO_2Me, C_6H_4OCH_3), 3.68 (d, 1 H, H-3'), 2.61 (dd, 1 H, $J_{3a,3e}$ 12.8 Hz, $J_{3e,4}$ 5.0 Hz, H-3e), 2.39, 2.20, 2.12, 2.05, 2.04, 2.04, 1.93, 1.88 (s, 3 H each, 5OAc, Ac_2N, NAc), -0.05 (s, 9 H, Si$(CH_3)_3$). HR FAB-MS for $C_{55}H_{76}N_2O_{24}SSiNa$ (M + Na): Calcd 1231.4176. Found 1231.4180.

Data for α-anomer of **13** (<1 mg ~80% pure material isolated by silica gel chromatography): ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.13 (d, 1 H, $J_{5,NH}$ 7.6 Hz, NH), 5.92 (dd, 1 H, $J_{3',4'}$ 8.2 Hz, $J_{4',5'}$ 9.5 Hz, H-4'), 3.89, 3.85, 3.83 (s, 3 H each, 2CO_2Me, C_6H_4OCH_3), 2.70 (dd, 1 H, $J_{3a,3e}$ 12.6 Hz, $J_{3e,4}$ 4.8 Hz, H-3e), 2.40, 2.30, 2.12, 2.08, 2.02, 2.00, 1.89, 1.80 (s, 3 H each, 5OAc, Ac_2N, NAc), -0.03 (s, 9 H, Si$(CH_3)_3$).

Methyl {2-(trimethylsilyl)ethyl 5-acetamido-4,7-di-*O*-acetyl-3,5-dideoxy-8-*O*-[5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulo-pyranosyl]-D-*glycero*-α-D-*galacto*-2-nonulopyranosid}onate 1'→9-Lactone (E). To a stirred solution of **13** (0.071 g, 0.059 mmol) in methanol (0.5 mL) was added a 1.0 M solution (0.050 mL, 0.050 mmol) of sodium methoxide in methanol. After 13 h at room temperature, acetic acid (0.1 mL) was added, and the mixture was concentrated with toluene/ethanol 1:1 and dried *in vacuo* over night. Raney-Ni (1 g) in ethanol (10 mL) was added, and the mixture was stirred vigorously for 24 h at room temperature. The Raney-Ni was then washed with toluene/methanol 1:1 (6 × 15 mL), where each washing involved stirring for at least 10 min. After filtration (Celite) and concentration of the combined wash solutions, the residue was dissolved in acetic acid (8 mL) and freeze-

dried, thereby providing a residue[*] to which acetic anhydride (3.0 mL) and pyridine (1.5 mL) was added. After 13 h, the reaction mixture was concentrated with toluene and the residue was chromatographed on silica gel (toluene/acetone, 3:1 → 3:2 → 1:2, gradient) to provide **E** (5.9 mg, 11%, α/β 1.9:1) as a white powder: ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.84 (s, 3 H, CO_2Me), 2.65 (dd, 1 H, $J_{3e,4}$ 4.9 Hz, $J_{3a,3e}$ 12.8 Hz, H-3e), 2.45 (dd, 1 H, $J_{3'e,4'}$ 5.5 Hz, $J_{3'a,3'e}$ 13.5 Hz, H-3'e), 2.20, 2.13, 2.08, 2.05, 2.04, 2.03, 1.93, 1.91 (s, 3 H each, 6OAc, 2NAc), 0.03 (s, 9 H, $Si(CH_3)_3$). HR FAB-MS for $C_{40}H_{60}N_2O_{22}SiNa$ (M + Na): Calcd 971.3305. Found 971.3278.

[*] When this residue was purified by silica gel chromatography, only various monosaccharides and crude **D** (pure **D** is disclosed in Ercegovic, T.; Magnusson, G. *J. Org. Chem.* **1996**, *61*, 179-184) as an α/β mixture were isolated. Unexpectedly, extensive cleavage of the 2→8 glycoside bond occurred during the Raney-Ni reduction.