Synthesis of G_{M4} and G_{M3} Intermediates via Alkylation and Subsequent Intramolecular Glysodiation of 2-Alkoxy-2-phenylthioacetate

T. Takahashi, H. Tsukamoto, and H. Yamada
Department of Chemical Engineering, Tokyo Institute of Technology

Supporting Information

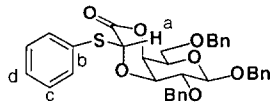
Lactone derivative of benzyl 2,6-di-*O*-benzyl-3-*O*-[(*R*)-1-carboxyl-1-(phenylthio)-methyl]-β-D-galactopyranoside (**6a**) and lactone derivative of benzyl 2,6-di-*O*-benzyl-3-*O*-[(*S*)-1-carboxyl-1-(phenylthio)-methyl]β-D-galactopyranoside(**7a**)

To a stirred solution of isopropyl (phenylthio)acetate (6.4 mL, 33.5 mmol) in dry carbon tetrachloride (16 mL) was added *N*-chlorosuccinimide (8.9 g, 66.7 mmol) at room temperature under argon. After being stirred for 12 h, the reaction mixture was filtered through Celite and the filtrate was concentrated to give the crude isopropyl 2-chloro-2-(phenylthio)-acetate, which was used for the next reaction without further purification.

Benzyl 2,6-di-*O*-benzyl-β-D-galactopyranoside (**5a**) (5.2 g, 11.6 mmol) was refluxed in dry toluene (50 mL) with dibutyltinoxide (3.0 g, 12.1 mmol) in a Dean-Stark apparatus for 8 h. Then, the mixture was cooled to room temperature and a solution of the crude isopropyl 2-chloro-2-(phenylthio)-acetate in dry toluene (50 mL) and tetrabutylammonium bromide (3.9 g, 12.1 mmol) were added. After being refluxed for 6 h, the mixture was concentrated and the residue was subjected to flash chromatography, eluting with 90:10-85:15 hexane:ethyl acetate to afford **6a** (4.73 g, 7.91 mmol, 69%) as a white solid (Rf 0.46 in 2:1 hexane:ethyl acetate) and **7a** (0.95 g, 1.59 mmol, 14%) as an amorphous mass (Rf 0.34 in 2:1 hexane:ethyl acetate).

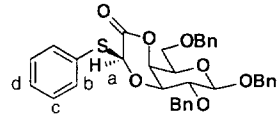
Lactone derivative of benzyl 2,6-di-*O*-benzyl-3-*O*-[(*R*)-1-carboxyl-1-(phenylthio)-methyl]β-D-galactopyranoside(**6a**)

$[\alpha]_D^{25}$ +18.4 ° (c 0.90 in $CHCl_3$); IR (KBr): 2876, 1735, 1452, 1234, 1085, 736, 694; ^{1}H NMR (270 MHz, $CDCl_3$): δ 3.48 (dd, $J_{1,2}$=7.8, $J_{2,3}$=9.6 Hz, 1H; H-2), 3.67-3.73 (m, 3H; H-5,6,6'), 4.01 (dd, $J_{3,4}$=4.0 Hz, 1H; H-3), 4.46 (d, 1H; H-1), 4.51 (dd, $J_{4,5}$<1 Hz, 1H; H-4), 4.54 (s, 1H; Bn), 4.64, 4.93 (2d, J_{gem}=11.9 Hz, 2H; Bn), 4.67, 4.84 (2d, J_{gem}=11.4 Hz, 2H; Bn), 4.99 (s, 1H; H-a), 7.31-7.34 (m, 9H; H-c,d,Bn), 7.54-7.56 (m, 2H; H-b); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 67.0, 71.1, ,71.5, 72.7, 72.9, 73.7, 74.5, 75.6, 79.2, 102.1, 127.8, 127.9x2, 128.0, 128.1, 128.39, 128.46, 128.50, 128.62, 129.3, 129.4, 130.6, 134.6, 136.9, 137.6, 137.7, 164.9.



Lactone derivative of benzyl 2,6-di-*O*-benzyl-3-*O*-[(*S*)-1-carboxyl-1-(phenylthio)-methyl]β-D-galactopyranoside(**7a**)

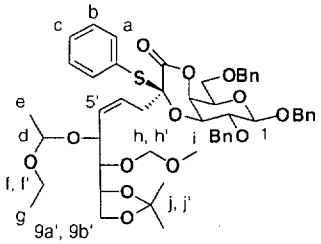
$[\alpha]_D^{25}$ -141 ° (c 1.2 in $CHCl_3$); IR (KBr): 2868, 1736, 1452, 1365, 1252, 1168, 1102, 957, 747, 691; ^{1}H NMR (270 MHz, $CDCl_3$): δ 3.74-3.91 (m, 3H; H-5,6,6'), 4.05 (dd, $J_{1,2}$=6.6, $J_{2,3}$=9.7 Hz, 1H; H-2), 4.11 (dd, $J_{3,4}$=2.8 Hz, 1H; H-3), 4.48 (d, 1H; H-1), 4.56, 4.61 (2d, J_{gem}=11.9 Hz, 2H; Bn), 4.79 (dd, $J_{4,5}$<1 Hz, 1H; H-4), 4.65, 4.95 (2d, J_{gem}=11.7 Hz, 2H; Bn), 4.83, 5.02 (2d, J_{gem}=10.9 Hz, 1H; Bn), 5.88 (s, 1H; H-a), 7.28-7.34 (m, 9H; H-c,d,Bn), 7.59-7.62 (m, 2H; H-b); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 67.0, 71.3, ,71.7, 73.1, 73.9, 74.3, 74.7, 76.2, 79.5, 102.8, 127.5, 127.7, 127.9, 128.02, 128.06, 128.10, 128.19, 128.3, 128.5, 128.6, 129.1, 132.6, 133.0, 136.9, 137.7, 138.3, 165.1.



Lactone derivative of benzyl 2,6-di-*O*-benzyl-3-*O*-[(1*S*)-(3*Z*)-1-carboxy-2,3,4-trideoxy-5-*O*-(1-ethoxyethyl)-7,8-*O*-isopropylidene-6-*O*-methoxymethyl-1-(phenylthio)-D-arabino-oct-3-enityl]β-D-galactopyranoside(**10a**)

To a stirred solution of diisopropylamine (0.59 mL, 4.21 mmol) in dry THF (2.5 mL) was added 1.53 M solution of nBuLi in haxane (2.6 mL, 3.98 mmol) at 0 °C under argon. After being stirred for 20 min, the mixture was cooled to -78 °C and **6a** (1.60 g, 2.68 mmol), azeotroped three times from toluene, in dry THF (5 mL) was added. After 15 min, to the mixture was added HMPA (2 mL, 11.5 mmol) at -40 °C, followed by **9** (0.80 g, 2.02 mmol). After being stirred at the same temperature for 1 h, the mixture was diluted with ether and poured into saturated aq. NH_4Cl with cooling, and the layers were separated. The aqueous layer was extracted with ethyl acetate (200 mL) and the combined extracts were washed with water and brine, dried over $MgSO_4$, filtered and evaporated *in vacuo*. The residue was subjected to flash chromatography, eluting with 85:15 hexane:ethyl acetate to afford **10a** (1.52 g, 1.66 mmol, 83%) as an amorphous mass (Rf 0.19 and 0.23 in 2:1 hexane:ethyl acetate).

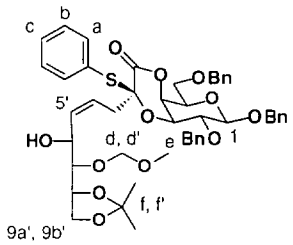
IR (KBr): 2976, 2926, 2878, 1745, 1204, 1155, 1111, 1079, 1024; ^{1}H NMR (270 MHz, $CDCl_3$): δ 0.99-1.34 (m, 12H; H-e,g,j,j'), 2.51-2.88 (m, 2H; H-3a',3b'), 3.17-4.22 (m, 14H; H-3,5,6a,6b,6',7',8',9a',9b',f,f',i), 4.39-5.19 (m, 12H; H-1,2,4,d,h,h',Bn), 5.47-5.73 (m, 2H; H-4',5'), 7.17-7.35 (m, 18H; H-b,c,Bn), 7.69-7.73 (m, 2H; H-a).



Lactone derivative of benzyl 2,6-di-*O*-benzyl-3-*O*-[(1*S*)-(3*Z*)-1-carboxy-2,3,4-trideoxy-7,8-*O*-isopropylidene-6-*O*-methoxymethyl-1-(phenylthio)-D-arabino-oct-3-enitityl]β-D-galactopyranoside(**11a**)

To a stirred solution of **10a** (1.50 g, 1.64 mmol) in ethanol (8 mL) was added PPTS (0.12 g, 0.477 mmol) at room temperature. After being stirred for 10 h, the reaction mixture was neutralized with triethylamine (0.06 mL, 0.430 mmol) and concentrated. The residue was partitioned between chloroform (100 mL) and 1 M HCl (50 mL), and the layers were separated. The aqueous layer was extracted with further chloroform (50 mL) and the combined extracts were washed with saturated aq. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and evaporated *in vacuo*. The residue was subjected to flash chromatography, eluting with 4:1 hexane:ethyl acetate to afford **11a** (1.05 g, 1.25 mmol, 76%) as an amorphous mass (Rf 0.15 in 3:2 hexane:ethyl acetate).

$[\alpha]_D^{25}$ -127 ° (c 0.53 in MeOH); IR (KBr): 3460, 2924, 1743, 1204, 1155, 1109, 1076, 1025, 750, 697; ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.32, 1.36 (2s, 6H; H-f,f'), 2.51 (dd, J_{gem}=14.2, $J_{3a',4'}$=7.6 Hz, 1H; H-3a'), 2.53 (d, $J_{6',OH}$=5.4 Hz, 1H; OH), 2.88 (dd, $J_{3b',4'}$=8.1 Hz, 1H; H-3b'), 3.30 (s, 3H; H-e), 3.59 (dd, $J_{6',7'}$=4.0, $J_{7',8'}$=4.3 Hz, 1H; H-7'), 3.73-3.94 (m, 5H; H-5,6a,6b,9a',9b'), 4.03-4.10 (m, 2H; H-3,8'), 4.19 (ddd, $J_{5',6'}$=8.9 Hz, 1H; H-6'), 4.52 (dd, $J_{1,2}$=6.9, $J_{2,3}$=7.6 Hz, 1H; H-2), 4.53 (d, 1H; H-1), 4.58, 4.60 (2d, J_{gem}=5.6 Hz, 2H; H-d,d'), 4.61, 4.68 (2d, J_{gem}=6.9 Hz, 2H; Bn), 4.76 (dd, $J_{3,4}$=3.6, $J_{4,5}$<1 Hz, 1H; H-4), 4.66, 4.96 (2d, J_{gem}=11.7 Hz, 2H; Bn), 4.91, 5.19 (2d, J_{gem}=10.9 Hz, 2H; Bn), 5.52 (ddd, $J_{4',5'}$=11.2 Hz, 1H; H-4'), 5.68 (dd, 1H; H-5'), 7.17-7.39 (m, 18H; H-b,c,Bn), 7.68-7.71 (m, 2H; H-a); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 25.3, 26.4, 40.1, 56.1, 65.6, 67.0, 67.5, 71.2, 71.9, 72.8, 73.7, 73.8, 74.5, 74.9, 76.2, 80.1, 86.9, 97.7, 103.3, 108.7, 124.5, 127.5, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.5x2, 128.8, 129.5, 129.6, 134.8, 136.6, 136.7, 137.7, 138.4, 167.2; MS (ESI) $C_{47}H_{54}O_{12}SNa$: m/z=865 (M+Na).



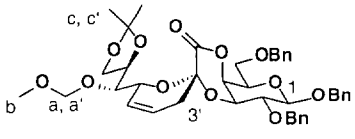
Benzyl 2,6-di-*O*-benzyl-3-*O*-[3,4,5-trideoxy-8,9-*O*-isopropylidene-7-*O*-methoxymethyl-α-D-arabino-non-4-en-2-ulopyranosylono-1',4-lactone]-β-D-galactopyranoside (**12a**) and benzyl 2,6-di-*O*-benzyl-3-*O*-[3,4,5-trideoxy-8,9-*O*-isopropylidene-7-*O*-methoxymethyl-β-D-arabino-non-4-en-2-ulopyranosylono-1',4-lactoneβ-D-galactopyranoside(**13a**)

To powdered MS-4A were added a solution of **11a** (1.02 g, 1.21 mmol), azeotroped three times from toluene, in dry dichloromethane (30 mL) and DTBP (0.44 mL, 1.96 mmol) at room temperature and the mixture was stirred for 15 min under argon. Then, AgOTf (0.47 g, 1.83 mmol) was added and the mixture was cooled to -78 °C. To the cooled mixture was added 2 M solution of phenylsulfenyl chloride in dichloromethane (0.85 mL, 1.70 mmol) and the mixture was allowed to warm to -40 °C for 2 h. The mixture was neutralized with triethylamine and filtered through Celite. The filtrate was concentrated and the residue was subjected to flash chromatography, eluting with 4:1 hexane:ethyl acetate to afford **12a** and **13a** (0.70 g, 0.956 mmol, 79%, **12a**:**13a**=4.0:1) as an amorphous mass.

The diastereoisomers of the product were separated by HPLC (Lichrosorb Si60-5, 7.5x300 mm, eluted with 35% ethyl acetate in hexane, 2.96 ml/min). The first eluent (Rt=8-11 min) was **12a** (Rf 0.32 in 3:2 hexane:ethyl acetate) and the second (Rt=11-14 min) was **13a** (Rf0.24 in 3:2 hexane:ethyl acetate).

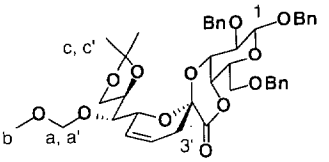
Benzyl 2,6-di-*O*-benzyl-3-*O*-[3,4,5-trideoxy-8,9-*O*-isopropylidene-7-*O*-methoxymethyl-α-D-arabino-non-4-en-2-ulopyranosylono-1',4-lactone]-β-D-galactopyranoside(**12a**)

$[\alpha]_D^{25}$ +7.6 ° (c 0.26 in MeOH) ; IR (KBr): 2920, 1763, 1156, 1076, 1028, 739, 699; ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.25, 1.33 (2s, 6H; H-c,c'), 2.24-2.32 (m, 1H; H-3a'), 2.44-2.50 (m, 1H; H-3b'), 3.33 (s, 3H; H-b), 3.46 (dd, $J_{1,2}$=7.8, $J_{2,3}$=9.1 Hz, 1H; H-2), 3.75-3.85 (m, 4H; H-5,6a,6b,7'), 3.94 (dd, $J_{8',9a'}$=6.3, J_{gem}=8.3 Hz, 1H; H-9a'), 3.99 (dd, $J_{8',9b'}$=6.3 Hz, 1H; H-9b'), 4.16 (dd, $J_{3,4}$=4.5 Hz, 1H; H-3), 4.20 (ddd, $J_{7',8'}$=6.3 Hz, 1H; H-8'), 4.40 (m, 1H; H-6'), 4.47 (d, 1H; H-1), 4.54-4.98 (m, 8H; H-a,a',Bn), 5.29 (dd, $J_{4,5}$<1 Hz, 1H; H-4), 5.67-5.71 (m, 1H; H-5'), 5.87-5.95 (m, 1H; H-4'), 7.26-7.36 (m, 15H; Bn); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 25.3, 26.6, 31.4, 56.0, 66.3, 68.2, 71.0, 71.9, 72.1, 73.66, 73.73x2, 74.8x2, 78.3, 78.8, 94.6, 97.5, 101.6, 108.8, 124.1, 124.5x2, 127.7, 127.87, 128.92, 128.2, 128.3, 128.4, 128.5, 137.2, 137.8, 138.0, 164.8; MS (ESI) $C_{41}H_{48}O_{12}$: m/z=733 (M+H).

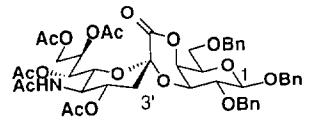


Benzyl 2,6-di-*O*-benzyl-3-*O*-[3,4,5-trideoxy-8,9-*O*-isopropylidene-7-*O*-methoxymethyl-β-D-arabino-non-4-en-2-ulopyranosylono-1',4-lactone]-β-D-galactopyranoside(**13a**)

$[\alpha]_D^{25}$ +2.8 ° (c 0.14 in MeOH) ; IR (KBr): 2920, 1758, 1104, 1076, 1041, 738, 698; ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.25, 1.27 (2s, 6H; H-c,c'), 2.21-2.28 (m, 1H; H-3a'), 2.74-2.82 (m, 1H; H-3b'), 3.21 (s, 3H; H-b), 3.71-4.18 (m, 9H; H-2,3,5,6a,6b,7',8',9a',9b'), 4.43 (d, $J_{1,2}$=6.9 Hz, 1H; H-1), 4.53-5.07 (m, 10H; H-4,6',a,a',Bn), 5.87-5.88 (m, 2H; H-4',5'), 7.23-7.37 (m, 15H; Bn); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 25.4, 26.3, 34.3, 55.9, 65.5, 67.0, 71.1, 71.3, 72.0, 72.5, 73.4, 73.8, 75.3x2, 78.4, 93.8, 97.8, 103.1, 108.3, 121.2, 125.3, 126.6, 127.3, 127.9, 128.0, 128.16, 128.23, 128.4, 128.5, 136.8, 137.7, 138.8, 165.9; MS (ESI) $C_{41}H_{48}O_{12}$: m/z=733 (M+H).



Spectrum data of **19a**. $[\alpha]_D^{25}$ -5.5 ° (c 0.44 in MeOH); IR (KBr): 3442, 1745, 1665, 1370, 1223, 1086, 1044, 745, 699; ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.82 (dd, J_{gem}=13.9, $J_{3ax.',4'}$=10.9 Hz, 1H; H-3ax.'), 2.01-2.07 (m, 1H; H-3eq.'), 1.88, 1.98x2, 2.04, 2.14 (5s, 15H; Ac), 3.38 (dd, $J_{1,2}$=7.8, $J_{2,3}$=9.2 Hz, 1H; H-2), 3.64 (dd, $J_{5',6'}$=10.6, $J_{6',7'}$=2.0 Hz, 1H; H-6'), 3.73-4.00 (m, 4H; H-5,6a,6b,9a'), 4.16 (ddd, $J_{4',5'}$=$J_{5',NH}$=10.9 Hz, 1H; H-5'), 4.16 (dd, $J_{3,4}$=4.0 Hz, 1H; H-4), 4.37 (dd, $J_{8',9b'}$=2.8, J_{gem}=12.5 Hz, 1H; H-9b'), 4.49 (d, 1H; H-1), 4.59, 4.65 (2d, J_{gem}=12.2 Hz, 2H; Bn), 4.67, 4.83 (2d, J_{gem}=11.4 Hz, 2H; Bn), 4.92 (dd, $J_{4,5}$<1 Hz, 1H; H-4), 4.69, 4.97 (2d, J_{gem}=11.9 Hz, 2H; Bn), 5.11 (ddd, $J_{7',8'}$=7.6, $J_{8',9a'}$=6.6 Hz, 1H; H-8'), 5.23 (dd, 1H; H-7'), 5.32 (d, 1H; NH), 5.45 (ddd, $J_{3eq.',4'}$=5.3 Hz, 1H; H-4'), 7.27-7.36 (m, 15H; Bn); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 20.6, 20.7, 20.8, 20.9, 23.2, 38.2, 49.3, 62.0, 67.3, 68.4, 69.3, 69.5, 71.2, 72.4, 72.9x2, 73.3, 73.7, 74.8, 77.9, 95.0, 101.6, 127.7, 127.8, 128.0, 128.35, 128.44, 137.0, 137.8, 138.0, 163.9, 170.1x2, 170.4, 170.6, 170.9; MS (ESI) $C_{46}H_{54}NO_{17}$: m/z = 892 (M+H).



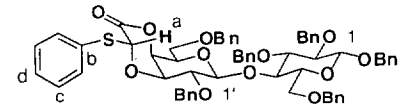
The satisfactory mass spectra could not be obtained on the following intermediates.

Lactone derivative of benzyl 2,3,6-tri-*O*-benzyl-*O*-[2,6-di-*O*-benzyl-3-*O*-[(*R*)-1-carboxyl-1-(phenylthio)-methyl]-β-D-galactopyranosyl]-β-D-glucopyranoside (**6b**) and lactone derivative of benzyl 2,3,6-tri-*O*-benzyl-*O*-[2,6-di-*O*-benzyl-3-*O*-[(*S*)-1-carboxyl-1-(phenylthio)-methyl]β-D-galactopyranosyl]β-D-glucopyranoside(**7b**)

Compound **6b** and **7b** were prepared from **5b** (4.8 g, 5.44 mmol) as described for the preparation of **6a** and **7a**, yielding **6b** (2.62 g, 2.54 mmol, 47%) as a white solid (Rf 0.46 in 2:1 hexane:ethyl acetate) and 7**b** (0.92 g, 0.89 mmol, 16%) as an amorphous mass (Rf 0.36 in 2:1 hexane:ethyl acetate).

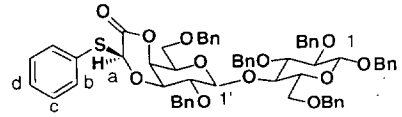
Lactone derivative of benzyl 2,3,6-tri-*O*-benzyl-*O*-[2,6-di-*O*-benzyl-3-*O*-[(*R*)-1-carboxyl-1-(phenylthio)-methyl]-β-D-galactopyranosyl]-β-D-glucopyranoside(**6b**)

$[\alpha]_D^{25}$ +2.4 ° (c 1.3 in $CHCl_3$); IR (KBr): 2916, 2866, 1753, 1452, 1361, 1245, 1094, 738, 698; ^{1}H NMR (270 MHz, $CDCl_3$): δ 3.30-3.57 (m, 7H; H-2,3,5,2',5',6a',6b'), 3.72 (dd, $J_{5,6a}$<1, J_{gem}=10.9 Hz, 1H; H-6a), 3.85 (dd, $J_{5,6b}$=3.6 Hz, 1H; H-6b), 3.86 (dd, $J_{2',3'}$=9.4, $J_{3',4'}$=4.0 Hz, 1H; H-3'), 3.96 (dd, $J_{3,4}$= $J_{4,5}$=9.1 Hz, 1H; H-4), 4.30-4.96 (m, 15H; H-1,1',4',Bn), 5.09 (s, 1H; H-a), 7.22-7.35 (m, 33H; H-c,d,Bn), 7.54-7.58 (m, 2H; H-b); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 66.2, 68.0, 71.0, 71.2, 72.2, 73.2, 73.3, 73.4, 74.8, 75.0x2, 7.56, 76.8, 77.0, 79.4, 81.9, 82.6, 102.3, 102.5, 127.4, 127.6, 127.7, 127.8, 127.9, 128.01, 128.08, 128.14, 128.2, 128.3, 128.4, 129.3, 130.8, 134.4, 137.5, 137.6, 137.9, 138.3, 138.5, 138.7, 165.1.



Lactone derivative of benzyl 2,3,6-tri-*O*-benzyl-*O*-[2,6-di-*O*-benzyl-3-*O*-[(*S*)-1-carboxyl-1-(phenylthio)-methyl]-β-D-galactopyranosyl]-β-D-glucopyranoside(**7b**)

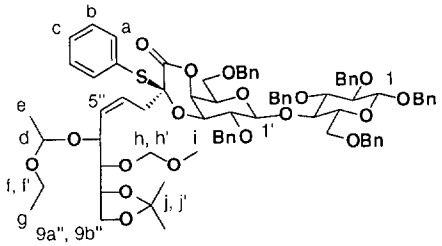
$[\alpha]_D^{25}$ –88.6 ° (c 1.4 in $CHCl_3$); IR (KBr): 2862, 1754, 1452, 1361, 1248, 1092, 1069, 738, 698; ^{1}H NMR (270 MHz, $CDCl_3$): δ 3.31-3.83 (m, 9H; H-2,3,5,6a,6b,2',5',6a',6b'), 3.93 (dd, $J_{2',3'}$=9.9, $J_{3',4'}$=3.6 Hz, 1H; H-3'), 3.99 (dd, $J_{3,4}$= $J_{4,5}$=8.8 Hz, 1H; H-4), 4.33-4.98 (m, 15H; H-1,1',4',Bn), 5.86 (s, 1H; H-a), 7.23-7.38 (m, 33H; H-c,d,Bn), 7.56-7.60 (m, 2H; H-b); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 66.2, 68.0, 71.0, 71.2, 73.1, 73.5, 73.6, 73.7, 74.90, 74.95, 75.1, 75.6, 76.9, 77.3, 79.5, 81.9, 82.5, 102.6, 102.7, 127.5, 127.6, 127.7, 127.83, 127.89, 128.08, 128.17, 128.28, 128.32, 128.41, 128.44, 129.1, 132.3, 132.9, 137.5, 137.8, 138.2x2, 138.5, 138.7, 165.5.



Lactone derivative of benzyl 2,3,6-tri-*O*-benzyl-*O*-[2,6-di-*O*-benzyl-3-*O*-[(1*S*)-(3*Z*)-1-carboxy-2,3,4-trideoxy-5-*O*-(1-ethoxyethyl)-7,8-*O*-isopropylidene-6-*O*-methoxymethyl-1-(phenylthio)-D-arabino-oct-3-enityl]β-D-galactopyranosyl]β-D-glucopyranoside (**10b**)

Compound **10b** was prepared from **6b** (3.45 g, 3.35 mmol) as described for the preparation of **10a**, yielding **10b** (2.72 g, 1.97 mmol, 68%) as an amorphous mass (Rf 0.28 and 0.24 in 2:1 hexane:ethyl acetate).

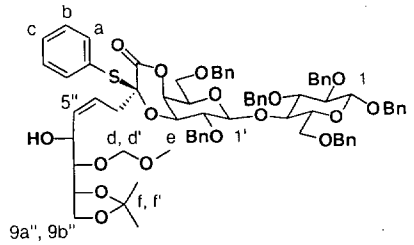
IR (KBr): 2872, 1745, 1452, 1365, 1206, 1094, 1026, 737, 698; ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.01-1.37 (m, 12H; H-d,g,j,j'), 2.53-2.90 (m, 2H; H-3a",3b"), 3.23-4.99 (m, 39H; H-1,2,3,4,5,6a,6b,1',2',3',4',5',6a',6b',6",7",8",9a",9b",e,f,f',h,h',i,Bn), 5.48-5.74 (m, 2H; H-4",5"), 7.12-7.42 (m, 33H; H-b,c,Bn), 7.63-7.66 (m, 2H; H-a).



Lactone derivative of benzyl 2,3,6-tri-*O*-benzyl-*O*-[2,6-di-*O*-benzyl-3-*O*-[(1*S*)-(3*Z*)-1-carboxy-2,3,4-trideoxy-7,8-*O*-isopropylidene-6-*O*-methoxymethyl-1-(phenylthio)-D-arabino-oct-3-enityl]β-D-galactopyranosyl]β-D-glucopyranoside (**11b**)

Compound **11b** was prepared from **10b** (2.67 g, 1.93 mmol) as described for the preparation of **11a**, yielding **11b** (1.96 g, 1.50 mmol, 77%) as an amorphous mass (Rf 0.21 in 3:2 hexane:ethyl acetate).

$[\alpha]_D^{25}$ –78.3 ° (c 1.2 in MeOH); IR (KBr): 3452, 2918, 1745, 1452, 1366, 1206, 1096, 1025, 736, 697; ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.33, 1.38 (2s, 6H; H-f,f'), 2.52 (d, $J_{6",OH}$=5.6 Hz, 1H; OH), 2.53 (dd, J_{gem}=14.5, $J_{3a",4"}$=6.6 Hz, 1H; H-3a"), 2.90 (dd, $J_{3b",4"}$=8.3 Hz, 1H; H-3b"), 3.31 (s, 3H; H-e), 3.24-4.12 (m, 14H; H-2,3,4,5,6a,6b,3',5',6a',6b',7",8",9a",9b"), 4.20-4.99 (m, 19H; H-1,1',2',4',6",d,d',Bn), 5.53 (ddd, $J_{4",5"}$=10.9 Hz, 1H; H-4"), 5.69 (dd, $J_{5",6"}$=8.9 Hz, 1H; H-5"), 7.13-7.41 (m, 33H; H-b,c,Bn), 7.64 (d, $J_{a,b}$=7.3 Hz, 2H; H-a); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 25.4, 26.5, 40.0, 56.1, 65.7, 66.3, 67.6, 68.0, 71.1, 71.6, 73.0, 73.3, 73.7, 73.8, 74.6, 74.9, 75.1, 75.5, 75.7, 76.2x2, 80.2, 82.0, 82.4, 87.0, 97.8, 102.6, 103.4, 108.8, 124.7, 127.1, 127.4, 127.6, 127.7, 127.8, 128.0, 128.1, 128.28, 128.38, 128.46, 128.49, 128.55, 128.8, 129.5, 129.6, 134.7, 136.6, 137.5, 137.9, 138.2, 138.54, 138.59, 138.64, 167.2.

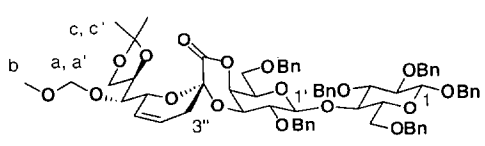


Benzyl 2,3,6-tri-*O*-benzyl-4-*O*-[2,6-di-*O*-benzyl-3-*O*-[3,4,5-trideoxy-8,9-*O*-isopropylidene-7-*O*-methoxymethyl-α-D-arabino-non-4-en-2-ulopyranosylono-1",4'-lactone]-β-D-galactopyranosyl]-β-D-glucopyranoside (**12b**) and benzyl 2,3,6-tri-*O*-benzyl-4-*O*-[2,6-di-*O*-benzyl-3-*O*-[3,4,5-trideoxy-8,9-*O*-isopropylidene-7-*O*-methoxymethyl-β-D-arabino-non-4-en-2-ulopyranosylono-1",4'-lactone]-β-D-galactopyranosyl]β-D-glucopyranoside (**13b**)

Compound **12b** and **13b** were prepared from **11b** (1.93 g, 1.47 mmol) as described for the preparation of **12a** and **13a**, yielding **12b** and **13b** (1.43 g, 1.19 mmol, 81%, **12b**:**13b** =2.8:1) as an amorphous mass.
The diastereoisomers of the product were separated by HPLC (Lichrosorb Si60-5, 7.5x300 mm, eluted with 32% ethyl acetate in hexane, 2.96 ml/min). The first effluent (Rt=7-10 min) was **12b** (Rf 0.36 in 3:2 hexane:ethyl acetate) and the second (Rt=11-14 min) was **13b** (Rf 0.27 in 3:2 hexane:ethyl acetate).

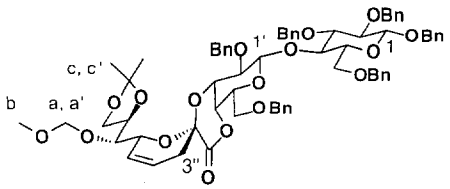
Benzyl 2,3,6-tri-*O*-benzyl-4-*O*-[2,6-di-*O*-benzyl-3-*O*-[3,4,5-trideoxy-8,9-*O*-isopropylidene-7-*O*-methoxymethyl-α-D-arabino-non-4-en-2-ulopyranosylono-1",4'-lactone]β-D-galactopyranosyl]β-D-glucopyranoside (**12b**)

$[\alpha]_D^{25}$ +4.8 ° (c 0.37 in MeOH) ; IR (KBr): 2916, 1763, 1452, 1366, 1210, 1157, 1069, 1027, 737, 698; ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.25, 1.35 (2s, 6H; H-c,c'), 2.25-2.33 (m, 1H; H-3a"), 2.47-2.53 (m, 1H; H-3b"), 3.34 (s, 3H; H-b), 3.22-4.02 (m, 14H; H-2,3,4,5,6a,6b,2',3',5',6a',6b',7",9a",9b"), 4.19 (ddd, $J_{7",8"}$= $J_{8",9a"}$= $J_{8",9b"}$=6.0 Hz, 1H; H-8"), 4.29-4.97 (m, 17H; H-1,1',6",a,a',Bn), 5.20 (dd, $J_{3',4'}$=4.0, $J_{4',5'}$<1 Hz, 1H; H-4'), 5.69-5.73 (m, 1H; H-5"), 5.90-5.96 (m, 1H; H-4"), 7.20-7.36 (m, 30H; Bn); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 25.1, 26.5, 31.4, 56.0, 66.0, 67.1, 68.0, 71.0, 71.4, 71.6, 73.2, 73.5, 73.9, 74.1, 75.0x4, 75.2, 75.6, 78.5, 79.1, 81.9, 82.7, 94.6, 97.5, 101.7, 102.6, 108.7, 124.2, 124.4, 127.35, 127.58, 127.67, 127.73, 127.9, 128.1, 128.3, 128.4, 137.5, 138.1x2, 138.3, 138.5, 138.8, 165.0.



Benzyl 2,3,6-tri-*O*-benzyl-4-*O*-[2,6-di-*O*-benzyl-3-*O*-[3,4,5-trideoxy-8,9-*O*-isopropylidene-7-*O*-methoxymethyl-β-D-arabino-non-4-en-2-ulopyranosylono-1",4'-lactone]β-D-galactopyranosyl]β-D-glucopyranoside (**13b**)

$[\alpha]_D^{25}$ –9.6 ° (c 0.54 in MeOH) ; IR (KBr): 2866, 1760, 1452, 1365, 1263, 1210, 1098, 1059, 737, 698; ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.24, 1.26 (2s, 6H; H-c,c'), 2.23-2.31 (m, 1H; H-3a"), 2.72-2.78 (m, 1H; H-3b"), 3.14 (s, 3H; H-b), 3.13-3.16 (m, 1H; H-5), 3.39-4.03 (m, 13H; H-2,3,4,6a,6b,2',3',5',6a',6b',7",9a",9b"), 4.15-4.94 (m, 19H; H-1,1',4',6",8",a,a',Bn), 5.83-5.93 (m, 2H; H-4",5"), 7.19-7.40 (m, 30H; Bn); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 25.3, 26.3, 34.5, 55.8, 65.2, 66.3, 67.9, 71.0x2, 71.6, 72.7, 73.1, 73.5, 74.0, 74.7, 75.0x2, 75.2, 75.7, 76.4, 77.3, 78.1, 81.8, 82.5, 93.5, 97.7, 102.5, 103.0, 108.1, 121.1, 125.2, 126.6, 127.3, 127.4, 127.7, 127.8, 127.9, 128.08, 128.16, 128.25, 128.34, 128.37, 128.43, 137.4, 137.9, 138.1, 138.5, 138.7x2, 165.9.



Spectrum data of **19b**. $[\alpha]_D^{25}$ –1.9 ° (c 0.32 in MeOH); IR (KBr): 3390, 2920, 1748, 1683, 1452, 1367, 1221, 1094, 1071, 738, 699; ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.85 (dd, J_{gem}=13.5, $J_{3ax.",4"}$=10.9 Hz, 1H; H-3ax."), 2.15 (dd, $J_{3eq.",4"}$=5.3 Hz, 1H; H-3eq."), 1.89, 1.93, 2.01, 2.04, 2.15 (5s, 15H; Ac), 3.25 (dd, $J_{1',2'}$=7.9, $J_{2',3'}$=9.2 Hz, 1H; H-2'), 3.36-3.59 (m, 5H; H-2,3,5,5',6a'), 3.69-4.97 (m, 24H; H-1,4,6a,6b,1',3',4',6b',5",6",9a",9b",Bn), 5.06 (ddd, $J_{7",8"}$=6.3, $J_{8",9a"}$=6.4, $J_{8",9b"}$=2.5 Hz, 1H; H-8"), 5.25 (dd, $J_{6",7"}$=2.0 Hz, 1H; H-7"), 5.29 (d, $J_{5",NH}$=10.9 Hz, 1H; NH), 5.50 (ddd, $J_{4",5"}$=10.9 Hz, 1H; H-4"), 7.20-7.39 (m, 30H; Bn); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 20.7x2, 20.8, 20.9, 23.2, 38.2, 49.1, 62.0, 67.4, 67.8, 69.6, 70.3, 71.0, 72.2, 72.5, 73.2, 73.4, 73.6, 73.8, 75.0x4, 75.5, 76.8, 78.8, 81.8, 82.6, 95.1, 101.7, 102.5, 127.3, 127.60, 127.65, 127.74, 127.85, 127.89, 128.07, 128.10, 128.17, 128.3, 128.4, 137.5, 137.8, 138.2x2, 138.5, 138.9, 164.2, 170.1, 170.2, 170.4, 170.7, 170.8.