SUPPORTING INFORMATION

SUPPORTING INFORMATION

Ring Closing Alkyne Metathesis. Application to the Total Synthesis of Sophorolipid Lactone

Alois Fürstner*, Karin Radkowski, Jaroslaw Grabowski, Conny Wirtz and Richard Mynott

Max-Planck-Institut für Kohlenforschung, D-45470 Mülheim/Ruhr, Germany

e-mail: fuerstner@mpi-muelheim.mpg.de

General. All reactions were carried out under Ar in pre-dried glassware using Schlenk techniques unless stated otherwise. The solvents were dried by distillation over the drying agents indicated and were stored and transferred under Ar: CH_2Cl_2 (CaH_2), toluene, benzene (Na/K), Et_2O, THF (magnesium/anthracene), EtOH, MeOH (Mg), HMPA (CaH_2), pyridine, Et_3N (KOH). Flash chromatography: Merck silica gel (230-400 mesh). Mp: Gallenkamp apparatus (uncorrected). NMR: Chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. IR: wavenumbers in cm^{-1}. Elemental analyses: Dornis & Kolbe, Mülheim. Commercially available reagents (Aldrich, Fluka, Lancaster) were used as received.

Alcohol 8. A solution of 1-bromo-6-octyne (1.40 g, 7.40 mmol)[19] in THF (3 ml) is added to a suspension of magnesium turnings (200 mg, 8.23 mmol; activated with a crystal of I_2) in THF (3 mL) at such a rate as to maintain gentle reflux. After the exothermic reaction has ceased, the reaction mixture is heated for another 2.5h. After cooling to ambient temperature, the supernatant liquid containing the Grignard reagent **6** is slowly added to a cooled (−78°C) suspension of CuCl(COD) (175 mg, 0.845 mmol) and (*S*)-propene oxide **7** (0.43 g, 7.40 mmol) in THF (10 mL). After slowly reaching ambient temperature overnight, the mixture is stirred for another 3.5h prior to the addition of aq. sat. NH_4Cl (15 mL) and HCl (2N, 4 mL). The aqueous layer is extracted with Et_2O (3x30 mL), the combined organic phases are washed with brine, dried (Na_2SO_4) and evaporated. A careful short path distillation followed by flash chromatography (pentane/Et_2O, 3:1→1:1) affords analytically pure alcohol **8** as a colorless liquid (783 mg, 63%). $[\alpha]_D^{20}$ = +7.4° (c 0.89, $CHCl_3$). The optical purity (ee ≥ 99.5%) was determined by GC on a chiral column (25m, 30% per-Me-β-cyclodextrin/70% OV61/3076)

by comparison with (±)-**8**. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 3.72-3.77 (m, 1H), 2.04-2.10 (m, 2H), 1.73 (t, 3H, *J* = 6.5 Hz), 1.51 (bs, 1H, -OH), 1.27-1.43 (m, 10H), 1.14 (d, 3H, *J* = 6.2 Hz); ^{13}C NMR (75 MHz, CD_2Cl_2): δ 79.3, 75.3, 68.0, 39.2, 29.1, 28.9, 28.8, 25.6, 23.4, 18.6, 3.4; IR: 3355, 2965, 2931, 2857, 1462, 1374, 1127, 1100, 1055, 1018, 936, 839 cm^{-1}. MS (EI) *m/z* (rel. intensity) 168 ([M$^+$], <1), 135 (21), 121 (34), 111 (16), 110 (11), 109 (14), 108 (28), 107 (29), 96 (13), 95 (48), 94 (37) 93 (82), 91 (13), 82 (20), 81 (61), 80 (18), 79 (71), 77 (13), 71 (13), 69 (28), 68 (87), 67 (78), 66 (22), 57 (13), 55 (84), 54 (30), 53 (29), 45 (100).

Tri-O-(p-methoxybenzyl)-D-glucal (10). To a solution of D-glucal **9** (1.06 g, 7.25 mmol) in DMF (10 mL) at 0°C is added NaH (60% dispersion in mineral oil, 960 mg, 24.0 mmol) in small portions. After the evolution of gas has ceased (ca. 30 min), p-methoxybenzyl chloride (3.3 mL, 24.3 mmol) and (n-Bu)$_4$NI (134 mg, 0.36 mmol) are added and the resulting mixture is stirred at ambient temperature for 16h. The reaction is quenched by careful addition of EtOAc (50 mL) and water (10 mL), the organic phase is washed with brine, dried (Na_2SO_4) and evaporated, and the crude product is purified by flash chromatography (pentane/EtOAc, 3:1) affording the title compound as a syrup which solidifies upon storage in the refrigerator (2.80 g, 76%). $[\alpha]_D^{20}$ = +8.1° (c 1.59, $CHCl_3$). ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.28 (d, 4H, *J* = 8.2 Hz), 7.20 (d, 2H, *J* = 8.6 Hz), 6.87-6.90 (m, 6H), 6.41 (d, 1H, *J* = 6.1 Hz), 4.89 (dd, 1H, *J* = 5.9, 2.7 Hz), 4.74 (d, 1H, *J* = 10.9 Hz), 4.47-4.60 (m, 5H), 4.14 (bd, 1H, *J* = 4.6 Hz), 4.02-4.05 (m, 1H), 3.80 (s, 9H, 3x -OMe), 3.73-3.80 (m, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ 159.7 (2x), 159.6, 144.7, 131.1, 131.0, 130.7, 129.9, 129.8, 129.7, 77.2, 75.5, 74.5, 73.5, 73.3, 70.4, 68.7, 55.5 (3x); IR: 3064. 3035, 2999, 2934, 2908, 2863, 2836, 1648, 1612, 1586, 1514, 1464, 1302, 1249, 1174, 1099, 1035, 820 cm^{-1}. MS (EI) *m/z* (rel. intensity) 385 (4), 122 (12), 121 (100). Anal. *calcd.* for $C_{30}H_{34}O_7$ (506.61) C 71.13, H 6.77; *found* C 71.19, H 6.64.

[(10*S*)-2-Undecyn-10-yl] 3,4,6-tri-O-(p-methoxybenzyl)-β-D-glucopyranoside (12). A solution of dimethyldioxirane (≈ 0.1M in acetone, 4 mL, 0.4 mmol)[30] is added over a period of 20 min to a solution of glucal **10** (165 mg, 0.326 mmol) in CH_2Cl_2 (1.6 mL) at −25°C. As soon as TLC indicates complete conversion of the substrate (1-2h), all volatiles are evaporated and the residue is dried in vacuo (10^{-3} mbar).

To a solution of crude epoxide **11** thus formed and alcohol **8** (90 mg, 0.535 mmol) in THF (3.2 mL) is added anhydrous $ZnCl_2$ (88 mg, 0.646 mmol) at −78°C. After stirring for 14h at ambient temperature, the reaction mixture is diluted with EtOAc (10 mL), the organic layer is washed with brine, dried (Na_2SO_4) and evaporated, and the crude product is purified by flash chromatography (pentane/EtOAc, 3/1) affording product **12** (95 mg, 42%) as a colorless syrup and unreacted alcohol **8** (ca. 45 mg, 50%) which can be recovered. Data of product **12**: $[\alpha]_D^{20}$ = −13.8° (c 1.14, CH_2Cl_2); ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.30 (t, 4H, *J* = 9.0 Hz), 7.12 (d, 2H, *J* = 8.7 Hz), 6.80-6.90 (m, 6H), 4.73-4.86 (m, 3H), 4.44-4.56 (m, 3H), 4.30 (d, 1H, *J* = 7.6 Hz), 3.79 (s, 9H), 3.65-3.80 (m, 3H), 3.39-3.52 (m, 4H), 2.37 (d, 1H, *J* = 1.9 Hz), 2.09-2.14

(m, 2H), 1.77 (t, 3H, J = 2.6 Hz), 1.34-1.65 (m, 10H), 1.26 (d, 3H, J = 6.3 Hz); ^{13}C NMR (75 MHz, CD_2Cl_2): δ 159.6 (2x), 159.5, 131.5, 131.0, 130.8, 129.9, 129.8, 129.7, 114.0, 113.9, 113.8, 102.8, 84.5, 79.5, 77.7, 77.1, 75.5, 75.3 (2x), 75.0, 74.8, 74.7, 73.3, 69.1, 55.5 (3x), 37.0, 30.0, 29.6, 29.4, 29.2, 25.7, 21.8, 19.0, 3.5; IR: 3484, 3065, 3033, 2998, 2932, 2857, 1613, 1586, 1514, 1464, 1442, 1357, 1302, 1248, 1173, 1098, 1061, 1036, 848, 821 cm^{-1}. MS (EI) *m/z* (rel. intensity) 569 (8), 401 (2), 137 (5), 122 (13), 121 (100). Anal. *calcd.* for $C_{41}H_{54}O_9$ (690.89) C 71.28, H 7.88; *found* C 71.35, H 7.90.

4,6-O-(p-Methoxybenzylidene)-D-glucopyranose (13). A suspension of D-glucose (5.0 g, 27.75 mmol), p-methoxybenzaldehyde dimethylacetal (5.2 mL, 30.54 mmol) and p-TsOH·H_2O (4.4 mg, 0.023 mmol) in DMF (20 mL) is stirred for 30 min at 60°C in vacuo (ca. 250 mbar) while a gentle stream of Ar is bubbled through the mixture in order to remove liberated methanol. The reaction is then quenched by addition of Et_3N (0.15 mL), all volatiles are removed in vacuo and the residue is purified by flash chromatography (EtOAc containing 0.1% of Et_3N). This affords product **13** as a colorless solid (4.25 g, 51%). IR: 3431, 2935, 2866, 2838, 1657, 1616, 1590, 1519, 1465, 1383, 1305, 1254, 1177, 1145, 1083, 1032, 984, 821 cm^{-1}. MS (EI) *m/z* (rel. intensity) 298 (20), 209 (16), 137 (100), 136 (29), 135 (50), 109 (12). Anal. *calcd.* for $C_{14}H_{18}O_7$ (298.30) C 56.37, H 6.08; *found* 56.18, H 5.96. For a compilation and an unambiguous assignment of the NMR data see below.

1,2,3-Tri-O-acetyl-4,6-O-(p-methoxybenzylidene)-α,β-D-glucopyranose (14). To a suspension of compound **13** (4.20 g, 14.1 mmol) in pyridine (10 mL) is slowly added Ac_2O (5 mL) and the resulting mixture is stirred for 19h at ambient temperature. All volatiles are then removed in vacuo, the remaining crude product is carefully rinsed with Et_2O (50 mL in two portions) and pentane (10 mL), and dried in vacuo, thus affording analytically pure **14** as a colorless solid (5.70 g, 95%). IR: 2940, 2873, 2842, 1758, 1746, 1616, 1519, 1441, 1374, 1248, 1223, 1101, 1082, 1070, 1056, 1033, 971, 935, 835, 822 cm^{-1}. MS (EI) *m/z* (rel. intensity) 424 ([M$^+$], 37), 423 (20), 245 (13), 179 (17), 137 (52), 136 (59), 135 (62), 115 (19), 43 (100). Anal. *calcd.* for $C_{20}H_{24}O_{10}$ (424.42) C 56.60, H 5.70; *found* C 56.75, H 5.72. For a compilation and an unambiguous assignment of the NMR data see below.

2,3-Di-O-acetyl-4,6-O-(p-methoxybenzylidene)-α,β-D-glucopyranose (15). A solution of compound **14** (1.045 g, 2.46 mmol) and benzylamine (392 mg, 3.66 mmol) in THF (10 mL) is stirred for 22 h at ambient temperature. The reaction is quenched upon addition of aq. HCl (0.25 M, 5 mL), the organic phase is quickly separated, washed with aq. sat. $NaHCO_3$ and brine, dried over Na_2SO_4 and evaporated. The crude product is purified by flash chromatography (hexane/EtOAc, 2/1→1.5/1) affording compound **15** as a colorless solid (720 mg, 76%). mp = 196-197°C. IR: 3504, 2967, 2942, 2875, 2844, 1745, 1616, 1521, 1437, 1374, 1315, 1250, 1222, 1173, 1096, 1063, 1031, 988, 934, 834, 821 cm^{-1}. MS (EI) *m/z* (rel.

intensity) 382 ([M^+], 30), 381 (15), 203 (8), 152 (4), 137 (100), 136 (47), 135 (65), 43 (96). Anal. *calcd.* for $C_{18}H_{22}O_9$ (382.38) C 56.54, H 5.80; *found* C 56.43, H 5.89. For a compilation and an unambiguous assignment of the NMR data see below.

2,3-Di-O-acetyl-4,6-O-(p-methoxybenzylidene)-α-D-glucopyranosyl bromide (16). A solution of $(PhO)_3P$ (327 mg, 1.05 mmol) in CH_2Cl_2 (1.5 mL) is added to a solution of Br_2 (180 mg, 1.13 mmol) in CH_2Cl_2 (4 mL) at 0°C and the resulting mixture is stirred for 25 min at ambient temperature. A solution of compound **15** (310 mg, 0.81 mmol) in CH_2Cl_2 (2.5 mL) and pyridine (0.1 mL) is then introduced and stirring is continued until TLC shows complete conversion (ca. 1.5h). The reaction is quenched with aq. sat. $NaHCO_3$ (8 mL), the aqueous phase is extracted with EtOAc (50 mL in several portions), the combined organic layers are washed with brine, dried (Na_2SO_4) and evaporated, and the crude product is purified by flash chromatography (pentane/EtOAc, 3:1) thus affording bromide **16** as a colorless solid (216 mg, 60%) which is stored under Ar in a freezer. $[\alpha]_D^{20}$ = +157.9° (c 0.57, CH_2Cl_2). ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.27 (d, 2H, *J* = 8.5 Hz), 6.81 (d, 2H, *J* = 8.5 Hz), 6.55 (d, 1H, *J* = 4.1 Hz), 5.50 (t, 1H, *J* = 7.1 Hz), 5.40 (s, 1H), 4.77 dd, 1H, *J* = 9.7, 4.1 Hz), 4.19-4.25 (m, 2H), 3.70 (s, 3H), 3.65-3.73 (m, 2H), 2.00 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (75 MHz, CD_2Cl_2): δ 170.2, 169.9, 160.7, 129.6, 127.9, 114.0, 102.2, 88.1, 78.4, 71.8, 69.1, 68.2, 67.5, 55.7, 20.9, 20.8. IR: 2964, 2936, 2858, 1750, 1617, 1518, 1372, 1304, 1240, 1222, 1124, 1098, 1074, 1035, 1008, 971, 821, 646, 604, 548 cm^{-1}. MS (EI) *m/z* (rel. intensity) 446/444 ([M^+], 21), 445 (16), 443 (12), 263 (13), 179 (12), 137 (30), 136 (100), 135 (61), 43 (72). Anal. *calcd.* for $C_{18}H_{21}BrO_8$ (445.26) C 48.56, H 4.75; *found* C 48.73, H 4.70.

Disaccharide 17. To a cooled (–5°C) suspension of bromide **16** (102 mg, 0.229 mmol), MS 4Å (powdered, 300 mg), compound **12** (106 mg, 0.153 mmol) and 2,6-di-*tert*-butylpyridine (0.11 mL, 0.49 mmol) in CH_2Cl_2 (4.6 mL) is added AgOTf (70 mg, 0.27 mmol). After stirring the reaction mixture at that temperature until TLC indicates complete conversion (ca. 3h), insoluble residues are filtered off through a pad of Kieselgur and are rinsed with anhydr. EtOAc (30 mL). The combined filtrates are adsorped on Celite and added on top of a silica column. Standard flash chromatography (pentane/EtOAc, 3/1 containing 0.1% of Et_3N) affords disaccharide **17** as a colorless syrup (144 mg, 89%). Note that the product is fairly unstable if kept in CH_2Cl_2 solution. $[\alpha]_D^{20}$ = –38.1° (c 0.53, CH_2Cl_2). IR: 2997, 2920, 2859, 1752, 1615, 1586, 1515, 1465, 1442, 1383, 1303, 1240, 1171, 1094, 1021, 933, 904, 884, 824 cm^{-1}. MS (EI) *m/z* (rel. intensity) 933 (1), 765 (2), 365 (10), 229 (2), 169 (4), 135 (3), 121 (100). Anal. *calcd.* for $C_{59}H_{74}O_{17}$ (1055.25) C 67.16, H 7.07; *found* C 67.04, H 6.89. For a compilation and an unambiguous assignment of the NMR data see below.

Disaccharide 19. A solution of disaccharide **17** (175 mg, 0.166 mmol) in MeOH (15 mL) is treated with NaOMe (11 mg, 0.204 mmol) at ambient temperature until TLC shows complete

conversion (ca. 20 h). All volatiles are removed in vacuo. EtOAc (10 mL) and Et_2O (20 mL in two portions) are then distilled off the crude material in order to remove any residual methanol. Product **18** thus obtained (160 mg, 99%) is used in the next step without further purification.

To a solution of diol **18** (101 mg, 0.104 mmol) in DMF (1.6 mL) is added NaH (60% dispersion in mineral oil, 20.7 mg, 0.518 mmol) at 0°C and the resulting mixture is stirred for 30 min at that temperature until the evolution of gas has ceased. p-Methoxybenzyl chloride (70 μL, 0.516 mmol) and $(n\text{-}Bu)_4NI$ (4.0 mg, 0.011 mmol) are introduced and the resulting mixture is stirred at ambient temperature for 22h. A standard extractive work-up followed by flash chromatography (pentane/EtOAc, 4:1→2:1, containing 0.1% of Et_3N) affords disaccharide **19** as a colorless syrup which slowly solidifies upon standing (115 mg, 91%). The product is stored under Ar in a freezer. $[\alpha]_D^{20} = -4.7°$ (c 1.11, CH_2Cl_2). IR: 2999, 2962, 2927, 2856, 1631, 1614, 1586, 1515, 1463, 1369, 1302, 1254, 1173, 1089, 1033, 962, 819. MS (ESI-pos.) *m/z* (rel. intensity) 1233 ([M+Na^+], 100). Anal. *calcd.* for $C_{71}H_{86}O_{17}$ (1211.5) C 70.39, H 7.16; *found* C 70.24, H 7.08. For a compilation and an unambiguous assignment of the NMR data see below.

Disaccharide 20. A solution of trifluoroacetic acid (0.55 mL, 7.1 mmol) in DMF (1.5 mL) is added dropwise at 0°C to a suspension containing compound **19** (340 mg, 0.28 mmol), $NaBH_3CN$ (176 mg, 2.8 mmol) and MS 4Å (powdered, 1.05 g) in DMF (6 mL). After stirring the resulting mixture for 3 d at ambient temperature, all insoluble residues are filtered off though a short pad of Kieselgur and are carefully rinsed with EtOAc (100 mL). The combined filtrates are extracted with aq. sat. $NaHCO_3$ (30 mL in three portions) and brine (40 mL in two portions), the organic layer is dried (Na_2SO_4) and evaporated, and the residue is purified by flash chromatography (pentane/EtOAc, 2:1 containing 0.1% of Et_3N) affording product **20** as a colorless syrup (300 mg, 88%). $[\alpha]_D^{20} = -10.3°$ (c 0.7, CH_2Cl_2); IR: 3438, 3000, 2931, 2857, 1613, 1514, 1465, 1359, 1303, 1249, 1174, 1066, 1035, 820 cm^{-1}. MS (ESI-pos.) *m/z* (rel. intensity) 1235 ([M+Na^+], 100); Anal. *calcd.* for $C_{71}H_{88}O_{17}$ (1213.5) C 70.28, H 7.31; *found* C 70.38, H 7.34. For a compilation and an unambiguous assignment of the NMR data see below.

Disaccharide 21. A mixture of compound **20** (85 mg, 0.070 mmol), DCC (17.2 mg, 0.083 mmol) and DMAP (4.8 mg, 0.039 mmol) in CH_2Cl_2 (2.5 mL) is stirred for 5 min until a clear solution has formed. 9-Undecynoic acid (14.8 mg, 0.081 mmol) is then added and the resulting mixture is stirred for 3 d at ambient temperature. For work-up, the mixture is filtered through a short pad of Kieselgur which is carefully washed with CH_2Cl_2 (5 mL in several portions), the combined filtrates are evaporated and the crude product is purified by flash chromatography (hexane/EtOAc, 4/1→3/1) affording product **21** as a colorless syrup (90 mg, 93%). $[\alpha]_D^{20} = +3.8°$ (c 1.58, CH_2Cl_2); IR: 3439, 2997, 2930, 2857, 1744, 1612, 1586, 1514,

1464, 1358, 1302, 1248, 1173, 1065, 1035, 820, 760 cm^{-1}. MS (MALDI-pos.) *m/z* (rel. intensity) *calcd.* for $C_{82}H_{104}O_{18}$+Na 1399.7115; *found* 1399.7101; Anal. *calcd.* for $C_{82}H_{104}O_{18}$ (1377.75) C 71.49, H 7.61; *found* C 71.56, H 7.73. For a compilation and an unambiguous assignment of the NMR data see below.

Alkyne Metathesis. To a stirred solution of the molybdenum complex **5** (2 mg, 0.003 mmol) in toluene (3 mL) are successively added CH_2Cl_2 (100 μL) and diyne **21** (51 mg, 0.037 mmol) dissolved in toluene (1 mL). The resulting mixture is stirred at 80°C for 24 h. For work-up, the solvent is evaporated in vacuo and the residue is purified by flash chromatography with hexane/ethyl acetate (3:1) as the eluent. This affords cycloalkyne **22** as a colorless syrup (38 mg, 78%). $[\alpha]_D^{20}$ = +4.5° (c 0.75, CH_2Cl_2); IR (neat) 2998, 2929, 2856, 1743, 1612, 1586, 1513, 1463, 1442, 1359, 1302, 1249, 1173, 1076, 1035, 819, 760 cm^{-1}. MS (ESI pos): *m/z* (rel intensity) 1345 ([M+Na^+], 100). Anal. *calcd.* for $C_{78}H_{98}O_{18}$ (1323.65) C 70.78, H 7.46; *found* C 70.84, H 7.38. For a compilation and an unambiguous assignment of the NMR data see below.

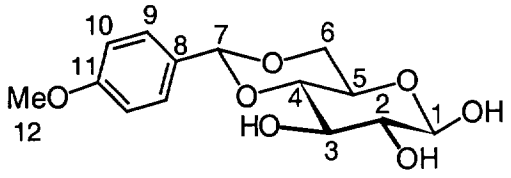
Lactone 23. A suspension of cycloalkyne **22** (64 mg, 0.048 mmol), quinoline (0.15 mL of a stock solution containing 57 mg of quinoline in 10 mL of hexane), and commercially available Lindlar catalyst (33.5 mg, 5 % *w/w* Pd poisoned with Pb on $CaCO_3$,) in CH_2Cl_2 (10 mL) is stirred under an atmosphere of H_2 (1 atm) for 5.5 h at ambient temperature. For work-up, all insoluble residues are filtered off through a short pad of Kieselgur and the filtrate is evaporated. This affords analytically pure lactone **23** (64 mg, quant.) which is used in the next step without any further purification. For a compilation and an unambiguous assignment of its NMR data see below.

Sophorolipid Lactone 1. A solution of compound **23** (64 mg, 0.048 mmol) and DDQ (67.3 mg, 0.30 mmol) in water (0.2 mL) and CH_2Cl_2 (3.6 mL) is stirred at ambient temperature for 8h until TLC shows complete disappearance of the starting material. The reaction is diluted with EtOAc (10 mL) and filtered through a pad of Celite, the filtrate is evaporated and the residue is purified by flash chromatography (EtOAc; then EtOAc/MeOH, 20/1) to afford the title compound as a syrup (27 mg, 93%). This material contains trace impurities and was further purified by preparative HPLC (Shimadzu LC-8A; column: 250/20 mm BIAX, eluent: MeCN/H_2O, 7/3) giving analytically pure material (64%) as a waxy solid. IR: 3422, 3004, 2927, 2856, 1741, 1636, 1457, 1404, 1377, 1347, 1241, 1198, 1167, 1081, 1041 cm^{-1}. MS (ESI pos): *m/z* (rel intensity) 627 ([M+Na^+], 100). Anal. *calcd.* for $C_{30}H_{52}O_{12}$ (604.73) C 59.58 H 8.67; *found* C 59.54, H 8.73. For a compilation and an unambiguous assignment of the NMR data see below.

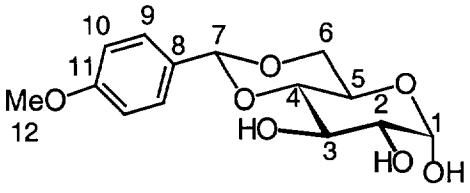
Compilation and Analysis of the NMR Data of Selected Compound

The NMR spectra were measured on a Bruker DMX-600 NMR spectrometer at 303 K. The chemical shifts were recorded relative to the solvent signals and the chemical shifts converted to the TMS scale (Conversion factors: CD_2Cl_2, $\delta_C \equiv 53.8$, $\delta_H \equiv 5.32$; d_6-DMSO, $\delta_C \equiv 39.5$, $\delta_H \equiv 2.49$; d_5-pyridine, $\delta_C(\alpha\text{-CD}) \equiv 149.9$, δ_H (α-CH) $\equiv 8.71$; d_4-methanol, $\delta_C(CD_3) \equiv 49.0$, $\delta_H(CHD_2) \equiv 4.78$). Although the ^{13}C chemical shifts are accurate to no better than ±0.1 ppm, they have been given to two decimal places in order to show better the relative differences between α- and β-anomers or rotamers in the same sample.

The signal assignments are unambiguous unless stated otherwise. They are based upon 1D and 2D spectra recorded using the following pulse sequences from the Bruker standard pulse program library: DEPT; COSY (*cosygs* and *cosydqtp*); HSQC (*invietgssi*) optimized for $^1J(C,H)$ = 145 Hz; HMBC (*inv4gslplrnd*) for correlations via $^nJ(C,H)$; HSQC-TOCSY (*invietgsml*) using an MLEV17 mixing time of 120 ms.



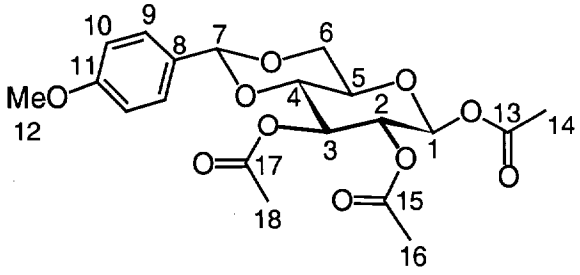
β–**13**



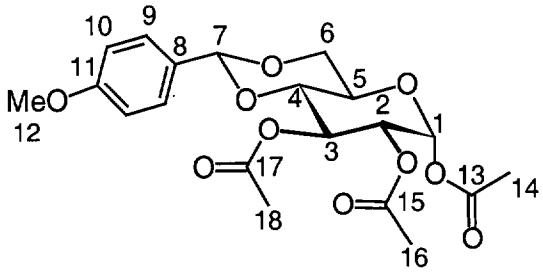
α-**13**

Solvent: DMSO-d_6. Arbitrary numbering as shown. Ratio of anomers, α : β ≈ 40 : 60.

position	β-anomer		α-anomer	
	δ ^{13}C (ppm)	δ ^{1}H (ppm)	δ ^{13}C (ppm)	δ ^{1}H (ppm)
1	97.57	4.44 (7.9 Hz)	93.13	4.97 (3.2 Hz)
2	75.75	3.01	72.85	3.25
3	72.90	3.38	69.63	3.61
4	80.84	3.31	81.67	3.29
5	65.74	3.31	61.95	3.76
6	67.98	3.63, 4.13	68.35	3.62, 4.06
7	100.59	5.49	100.74	5.48
8	130.23		130.29	
9	127.62	7.35	127.66	7.35
10	113.25	6.90	113.25	6.90
11	159.47		159.47	
12	55.08	3.74	55.08	3.74



β–**14**

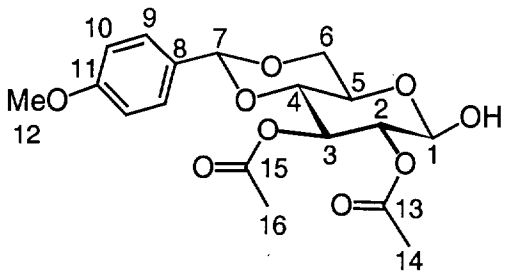


α-**14**

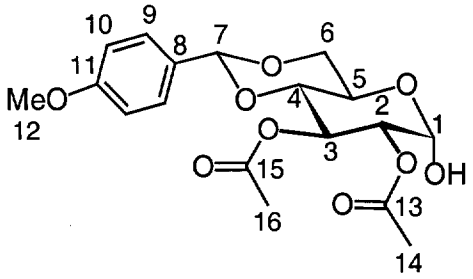
Solvent: CD_2Cl_2. Arbitrary numbering as shown. Ratio of anomers, α : β ≈ 50 : 50.

position	β-anomer		α-anomer	
	δ ^{13}C (ppm)	δ ^{1}H (ppm)	δ ^{13}C (ppm)	δ ^{1}H (ppm)
1	92.60	5.79 (8.1 Hz)	89.91	6.28 (3.9 Hz)
2	71.48	5.10	70.32	5.08
3	72.03	5.33	69.09	5.53
4	78.44	3.74	79.02	3.72
5	67.42	3.67	65.29	4.03
6	68.61	4.34, 3.75	68.82	4.28, 3.73
7	101.96	5.47	102.01	5.48
8	129.82*		129.75*	
9	127.87	7.35*	127.82	7.36*
10	113.89°	6.89°	113.88°	6.88°
11	160.67^		160.65^	
12	55.62	3.80^	55.62	3.79^
13	169.17		169.48	
14	20.93	2.09	21.07	2.17
15	169.69		170.19	
16	20.74	2.03	20.67	2.02
17	170.20		170.20	
18	20.88	2.03	20.93	2.05

Signals marked *,°,^ have not been unambiguously assigned to one of the anomers and may be pairwise interchanged.



β–**15**

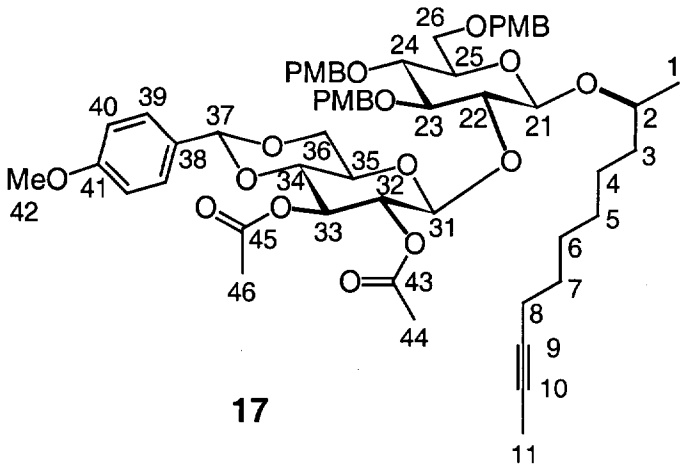


α-**15**

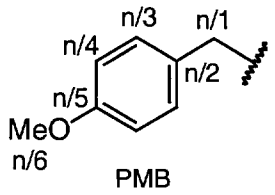
Solvent: DMSO-d_6. Arbitrary numbering as shown. Ratio of anomers, α : β ≈ 50 : 50.

position	β-anomer		α-anomer	
	δ ^{13}C (ppm)	δ ^{1}H (ppm)	δ ^{13}C (ppm)	δ ^{1}H (ppm)
1	94.56	4.88 (7.7 Hz)	89.96	5.23 (3.6 Hz)
2	73.45	4.71	71.66	4.73
3	71.63	5.23	68.48	5.37
4	77.73	3.74	78.14	3.77
5	65.32	3.64	62.00	3.92
6	67.60	4.19, 3.72	67.85	4.14, 3.72
7	100.33	5.56	100.52	5.56
8	129.65*		129.67*	
9	127.44	7.29	127.48	7.30
10	113.40	6.90	113.40	6.90
11	159.59		159.56	
12	55.08	3.74	55.08	3.74
13	169.12		169.83	
14	20.51	2.01	20.44	1.98
15	169.55		169.57	
16	20.46	1.96	20.47	1.99
1-OH		7.28		7.18

Signals marked * have not been unambiguously assigned to one of the anomers.

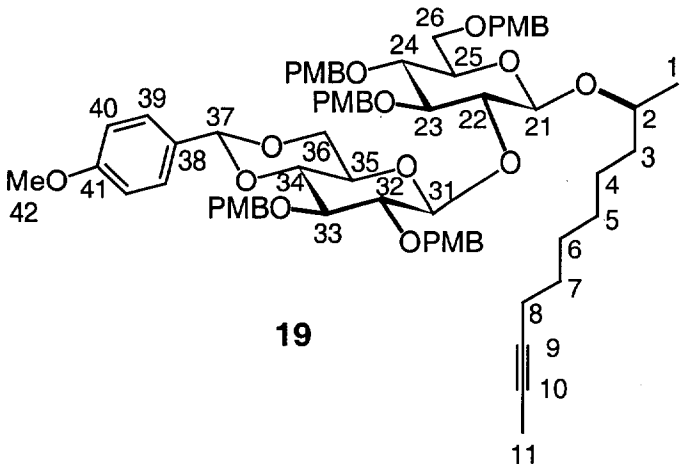


17

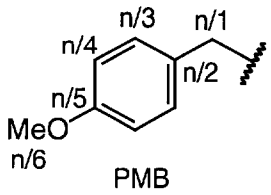


Solvent: CD_2Cl_2. Arbitrary numbering as shown.

position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	position	δ ^{13}C (ppm)	δ ^{1}H (ppm)
1	21.69	1.24	**37**	101.86	5.48
2	77.21	3.73	**38**	130.01	
3	37.05	1.60, 1.42	**39**	127.87	7.36
4	25.50	1.42	**40**	113.85	6.89
5	29.83	1.36	**41**	160.61	
6	29.47	1.44	**42**	55.62	3.80
7	29.63	1.51	**43**	169.72	
8	19.06	2.15	**44**	21.00	1.99
9	79.60		**45**	170.39	
10	75.56		**46**	20.94	2.02
11	3.49	1.75	**23/1**	75.35	4.75, 4.71
21	101.7	4.37 (7.5 Hz)	**23/2**	131.00	
22	79.49	3.62	**23/3**	129.94	7.33
23	85.06	3.53	**23/4**	114.10	6.90
24	78.51	3.52	**23/5**	159.71	
25	75.04	3.37	**24/1**	74.68	4.68, 4.48
26	69.01	3.65, 3.64	**24/2**	130.82	
31	100.59	5.15 (7.9 Hz)	**24/3**	129.79	7.10
32	73.66	4.95	**24/4**	113.99	6.82
33	72.58	5.23	**24/5**	159.70	
34	78.85	3.72	**26/1**	73.33	4.53, 4.46
35	66.74	3.43	**26/2**	130.81	
36	68.98	4.33, 3.77	**26/3**	129.73	7.27
			26/4	114.03	6.87
			26/5	159.66	
			n/6	55.58, 55.56, 55.55	3.80, 3.78(2)

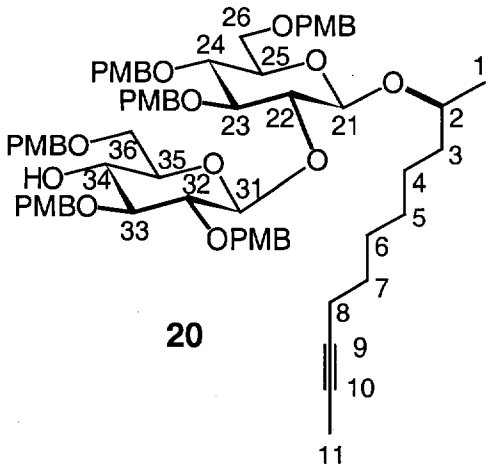


19

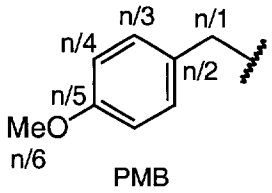


Solvent: CD_2Cl_2. Arbitrary numbering as shown.

position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	position	δ ^{13}C (ppm)	δ ^{1}H (ppm)
1	21.84	1.24	**23/1**	75.15	4.75, 4.71
2	77.52	3.72	**23/2**	131.15	
3	37.21	1.59, 1.43	**23/3**	130.00	7.24
4	25.43	1.50, 1.41	**23/4**	113.98	6.79
5	29.84	1.33	**23/5**	159.58	
6	29.46	1.42	**24/1**	74.76	4.74, 4.51
7	29.67	1.49	**24/2**	130.90	
8	19.07	2.12	**24/3**	129.85	7.14
9	79.56		**24/4**	114.02	6.83
10	75.58		**24/5**	159.71	
11	3.49	1.73	**26/1**	73.32	4.55, 4.47
21	102.13	4.38 (7.5 Hz)	**26/2**	130.92	
22	78.02	3.70	**26/3**	129.69	7.28
23	86.02	3.60	**26/4**	114.02	6.88
24	78.25	3.52	**26/5**	159.64	
25	75.20	3,43	**32/1**	75.20	4.84, 4.72
26	69.20	3.69, 3.65	**32/2**	131.25	
31	102.52	5.03 (7.5 Hz)	**32/3**	130.09	7.27
32	89.95	3.35	**32/4**	113.83	6.82
33	81.04	3.64	**32/5**	159.56	
34	82.10	3.64	**33/1**	74.61	4.82, 4.74
35	66.25	3.25	**33/2**	131.38	
36	69.20	4.28, 3.73	**33/3**	129.91	7.27
37	101.38	5.53	**33/4**	113.89	6.83
38	130.60		**33/5**	159.58	
39	127.73	7.41	**n/6**	55.57	3.79(3),
40	113.78	6.91		55.55(2),	3.77(2)
41	160.41			55.52(2)	
42	55.61	3.82			



20



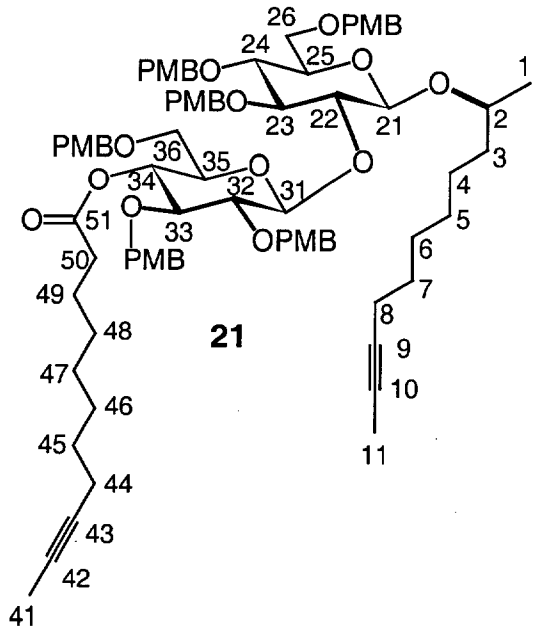
Solvent: CD_2Cl_2. Arbitrary numbering as shown.

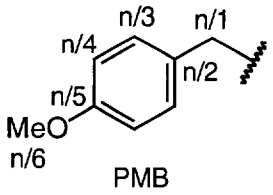
position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	position	δ ^{13}C (ppm)	δ ^{1}H (ppm)
1	21.89	1.21	**23/1**	75.10	4.76, 4.72
2	77.49	3.71	**23/2**	131.21	
3	37.17	1.55, 1.39	**23/3**	129.98	7.26
4	25.44	1.47, 1.38	**24/1**	74.74	4.73, 4.50
5	29.76	1.26	**24/2**	130.92	
6	29.43	1.35	**24/3**	129.85	7.13
7	29.66	1.45	**26/1**	73.31	4.55, 4.47
8	19.03	2.08	**26/2**	130.92	
9	79.59		**26/3**	129.70	7.28
10	75.50		**32/1**	74.81	4.91, 4.70
11	3.49	1.73	**32/2**	131.33	
21	102.16	4.40 (7.5 Hz)	**32/3**	130.08	7.30
22	77.55	3.71	**33/1**	74.88	4.85, 4.69
23	86.32	3.63	**33/2**	131.49	
24	78.50	3.52	**33/3**	129.88	7.25
25	75.18	3.43	**36/1**	73.75	4.53
26	69.23	3.68, 3.64	**36/2**	130.81	
31	102.35	4.91 (7.5 Hz)	**36/3**	129.81	7.28
32	82.57	3.29			
33	84.08	3.31			
34	72.36	3.52			
35	74.54	3.23			
36	70.34	3.67			
34-OH		2.55			

Signals of the **n/4** positions of the PMB ether groups: ^{13}C NMR: 114.07, 114.05, 114.02(2), 113.97, 113.89; ^{1}H NMR: 6.87(2), 6.86, 6.83(2), 6.81

Signals of the **n/5** positions of the PMB ether groups: ^{13}C NMR: 159.70, 159.66, 159.65, 159.63, 159.56(2)

Signals of the **n/6** positions of the PMB ether groups: ^{13}C NMR: 55.57, 55.56, 55.55(2), 55.54, 55.53; ^{1}H NMR: 3.79(2), 3.78(3), 3.76.





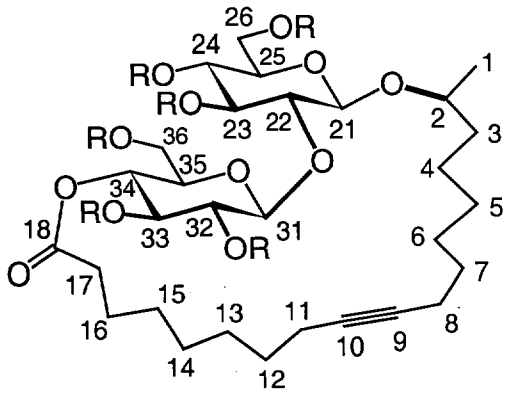
Solvent: CD_2Cl_2. Arbitrary numbering as shown.

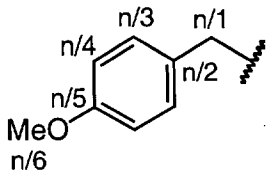
position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	position	δ ^{13}C (ppm)	δ ^{1}H (ppm)
1	21.89	1.21	**23/1**	75.14	4.77, 4.74
2	77.44	3.72	**23/2**	131.30	
3	37.15	1.57, 1.39	**23/3**	129.97	7.27
4	25.46	1.48, 1.38	**23/4**	114.03	6.83
5	29.75	1.28	**24/1**	74.74	4.74, 4.51
6	29.44	1.37	**24/2**	130.93	
7	29.67	1.46	**24/3**	129.86	7.14
8	19.01	2.08	**24/4**	113.95	6.83
9	79.66		**26/1**	73.32	4.56, 4.48
10	75.43		**26/2**	130.93	
11	3.50	1.73	**26/3**	129.70	7.29
21	102.08	4.42 (7.6 Hz)	**26/4**	114.03	6.87
22	77.86	3.72	**32/1**	74.93	4.9, 4.69
23	86.29	3.64	**32/2**	131.18	
24	78.54	3.53	**32/3**	130.16	7.29
25	75.19	3.43	**32/4**	113.90	6.82
26	69.22	3.69, 3.65	**33/1**	74.83	4.73, 4.54
31	102.26	4.92	**33/2**	131.17	
32	82.72	3.35	**33/3**	129.68	7.15
33	81.97	3.46	**33/4**	113.93	6.84
34	71.07	4.91	**36/1**	73.75	4.51, 4.45
35	74.03	3.34	**36/2**	130.99	
36	69.59	3.50, 3.45	**36/3**	129.84	7.27
41	3.50	1.75	**36/4**	113.95	6.85
42	75.52				
43	79.49				
44	18.97	2.09			

45	29.47	1.44		
46	29.08	1.33		
47	29.22	1.25		
48	29.46	1.25		
49	25.08	1.5		
50	34.54	2.11		
51	172.62			

Signals of the **n/5** positions of the PMB ether groups: ^{13}C NMR: 159.71, 159.64, 159.60, 159.58, 159.56(2).

Signals of the **n/6** positions of the PMB ether groups: ^{13}C NMR: 55.56, 55.54, 55.53, 55.52, 55.5; ^{1}H NMR: 3.79(3), 3.78, 3.77(2).





R = PMB

22

^{1}H NMR (600 MHz, CD_2Cl_2). Arbitrary numbering as shown.

position	Rotamer A		Rotamer B
1	1.25		1.24
2	3.84		3.67
8		2.10-2.16	
17	2.19		2.23
21	4.34 (7.6 Hz)		4.70 (7.0 Hz)
22	3.72		3.77
23	3.61		3.78
24	3.50		3.54
25	3.44		3.41
26	3.70, 3.65		3.65, 3.62
31	4.92 (7.5 Hz)		4.99 (7.7 Hz)
32	3.29		3.41
33	3.54		3.57
34	4.85		5.05
35	3.45		3.53
36	3.54, 3.52		3.56, 3.47
n/1		4.91-4.42	
n/3		7.29-7.12	
n/4		6.88-6.77	
n/6		3.81-3.74	

^{13}C NMR (150 MHz, CD_2Cl_2). Arbitrary numbering as shown.

position	Rotamer A	Rotamer B	position	Rotamer A	Rotamer B
1	21.99	21.46	**23/1**	75.16	75.53
2	79.54	76.99	**23/2**	131.29	131.49
3	38.20	37.20	**24/1**	74.75	74.73
4	25.85	25.08	**24/2**	130.93	131.06
8	19.30*	18.81*	**26/1**	73.30	73.30
9	81.47°	80.85°	**26/2**	130.95	130.90
10	80.34°	80.01°	**32/1**	74.83	74.37
11	18.90*	18.69*	**32/2**	130.99	131.37
16	23.81	25.11	**33/1**	74.80	75.00
17	33.74	35.19	**33/2**	131.19	131.15
18	172.95	172.52	**36/1**	73.72	73.65
21	103.20	101.59	**36/2**	131.15	130.50
22	77.64	81.34			
23	86.43	84.84			
24	78.51	78.17			
25	75.23	74.90			
26	69.29	69.36			
31	102.14	101.19			
32	82.73	83.23			
33	81.49	82.52			
34	71.88	70.33			
35	73.82	73.65			
36	70.45	69.21			

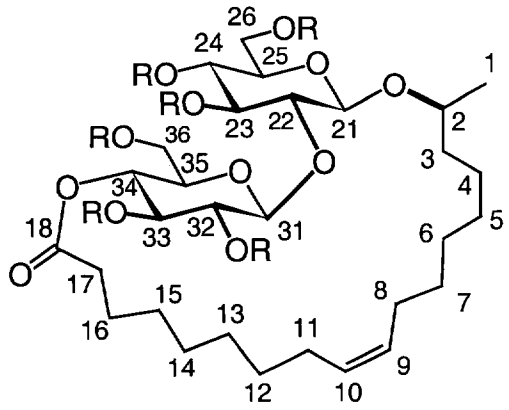
Signals of the C-atoms **5, 6, 7, 12, 13, 14, 15** not rigorously assigned to the individual rotamers: 30.71, 30.49, 30.07, 29.79, 29.64, 29.47, 29.35, 28.91, 28.76, 28.72, 28.49, 28.35, 27.61, 27.51.

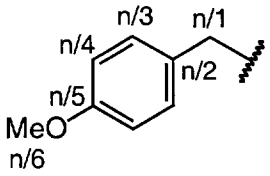
Signals of the **n/3** positions of the PMB ether groups not rigorously assigned to the individual rotamers: 130.30, 130.10, 129.98, 129.93, 129.88(2), 129.71, 129.69, 129.67(2) 129.64, 129.54.

Signals of the **n/4** positions of the PMB ether groups not rigorously assigned to the individual rotamers: 114.02(5), 113.98, 113.94(3), 113.88, 113.85, 113.77.

Signals of the **n/5** positions of the PMB ether groups not rigorously assigned to the individual rotamers: 159.72, 159.68, 159.65, 159.64, 159.62(2), 159.58, 159.57, 159.55, 159.51, 159.48, 159.41.

Signals of the **n/6** positions of the PMB ether groups not rigorously assigned to the individual rotamers: 55.56, 55.54, 55.53, 55.51, 55.49.





R = PMB

23

^{13}C NMR (150 MHz, CD_2Cl_2). Arbitrary numbering as shown.

Position	Rotamer A	Rotamer B	position	Rotamer A	Rotamer B
1	21.98	21.38	**23/1**	75.21	75.72
2	79.32	77.46	**24/1**	74.77	74.74
3	38.19	37.35	**26/1**	73.28	73.31
4	25.86*	25.94*	**32/1**	74.93	74.32
8	27.86^	27.34^	**33/1**	74.79	74.93
9	130.98°	130.43°	**36/1**	73.72	73.65
10	129.79°	130.01°			
11	27.15^	26.94^			
16	23.95*	25.07*			
17	33.50	34.91			
18	172.85	172.39			
21	103.04	102.17			
22	77.16	81.42			
23	86.58	84.76			
24	78.54	78.12			
25	75.29	74.93			
26	69.26	69.32			
31	102.18	101.31			
32	82.66	83.35			
33	81.45	82.70			
34	71.68	70.05			
35	73.92	73.66			
36	70.24	69.04			

Signals marked *, °, ^ are not unambiguously assigned and may be pairwise interchanged

Signals of the C-atoms **5, 6, 7, 12, 13, 14, 15** not rigorously assigned to the individual rotamers: 31.36, 31.24, 30.49, 30.28, 30.08, 29.96, 29.25, 28.91, 28.56, 28.37, 28.31, 28.10, 27.58, 27.51.

Signals of the **n/2** positions of the PMB ether groups not rigorously assigned to the individual rotamers: 131.43, 131.38, 131.25, 131.24, 131.12, 131.11, 131.05, 130.99, 130.98, 130.97, 130.92, 130.90,

Signals of the **n/3** positions of the PMB ether groups not rigorously assigned to the individual rotamers: 130.08, 129.97, 129.93, 129.84, 129.86, 129.70, 129.68, 129.65, 129.86, 129.70, 129.68, 129.65, 129.60. 129.58.

Signals of the **n/4** positions of the PMB ether groups not rigorously assigned to the individual rotamers: 114.01(4), 113.99(2), 113.96, 113.95, 113.92, 113.89, 113.83, 113,75.

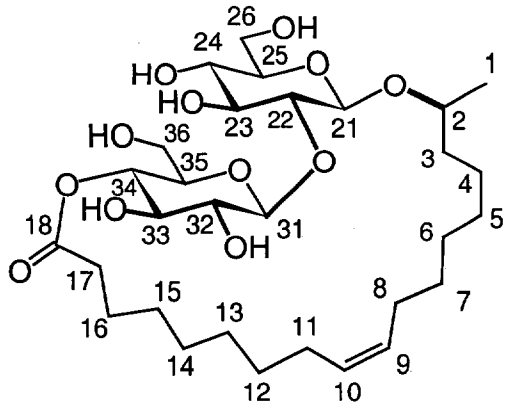
Signals of the **n/5** positions of the PMB ether groups not rigorously assigned to the individual rotamers: 159.72, 159.71, 159.66, 159.65, 159.62, 159.61(2), 159.59, 159.50(2), 159.43, 159.38.

Signals of the **n/6** positions of the PMB ether groups not rigorously assigned to the individual rotamers: 55.58(2), 55.55(7), 55.52, 55.51, 55.49.

^{1}H NMR (600 MHz, CD_2Cl_2). Arbitrary numbering as shown.

Position	Rotamer A	Rotamer B
1	1.22	1.21
2	3.67	3.79
3	1.48, 1.42	1.62, 1.40
8	2.11, 2.04°	2.00°
9	5.39*	5.34*
10	5.32*	5.30*
11	1.99, 1.93°	2.03°
17	2.17	2.17
21	4.29 (7.7 Hz)	4.63 (7.2 Hz)
22	3.69	3.74
23	3.60	3.69
24	3.47	3.53
25	3.42	3.40
26	3.68, 3.63	3.63, 3.61
31	4.89 (7.5 Hz)	5.02 (7.6 Hz)
32	3.34	3.37
33	3.49	3.55
34	4.84	5.04
35	3.36	3.49
36	3.49, 3.46	3.53, 3.42
4,5,6,7,12,13,14,15,16	1.70-1.25	
23/1	4.74, 4.70	4.78
24/1	4.72, 4.50	4.73, 4.48
26/1	4.55, 4.48	4.51, 4.44
32/1	4.87, 4.74	4.79, 4.43
33/1	4.74, 4.59	4.68, 4.50
36/1	4.56, 4.40	4.43, 4.38
n/3	7.27-7.08	
n/4	6.86-6.77	
n/6	3.79, 3.78, 3.77, 3.76, 3.75, 3.71	

Signals marked *, °, ^ are not unambiguously assigned and may be pairwise interchanged



1

NMR: Bruker DMX-600; two different solvents. Arbitrary numbering as shown.

position	δ ^{13}C (ppm) d_5-pyridine	δ ^{13}C (ppm) d_4-MeOH	position	δ ^{1}H (ppm) d_5-pyridine	δ ^{1}H (ppm) d_4-MeOH
1	21.51	21.77	**1**	1.34	1.25
2	78.59	80.32	**2**	3.85	3.79
3	37.87	28.60	**3**	1.82, 1.63	1.55, 1.47
4	25.60	26.40	**4**	1.43	1.54, 1.36
8	27.56*	27.88*	**8**	2.10°	2.06*
9	130.62°	131.25°	**9**	5.49*	5.33
10	130.03°	130.59°	**10**	5.44*	5.33
11	27.36*	28.34*	**11**	2.16°	2.02*
16	25.21	25.43	**16**	1.74, 1.58	1.68, 1.62
17	34.63	34.74	**17**	2.43, 2.35	2.39
18	173.02	174.76	**18**		
21	103.73	103.59	**21**	4.88 (7.7 Hz)	4.43 (7.7 Hz)
22	84.23	82.32	**22**	4.16	3.46
23	77.75	78.11	**23**	4.30	3.55
24	71.50	71.52	**24**	4.19	3.28
25	78.03	77.68	**25**	3.85	3.27
26	62.60	62.77	**26**	4.48, 4.32	3.84, 3.64
31	106.11	104.71	**31**	5.27 (7.7Hz)	4.67 (7.7)
32	77.57	76.57	**32**	4.09	3.29
33	75.12	75.22	**33**	4.30	3.57
34	71.81	72.23	**34**	5.82	4.80
35	76.39	76.32	**35**	3.93	3.43
36	61.61	62.53	**36**	4.23, 4.05	3.59, 3.52

Signals marked *, °, ^ are not unambiguously assigned and may be pairwise interchanged

Signals of **5, 6, 7, 12, 13, 14, 15** not rigorously assigned to the individual C-atoms: ^{13}C NMR (pyridine-d_5): 30.65, 30.45, 29.91, 29.33, 28.92, 28.68, 28.55. ^{13}C NMR (MeOH-d_4): 31.64, 31.54, 31.13, 29.84, 29.39, 29.16, 28.93. ^{1}H NMR (pyridine-d_5): 1.4-1.2; ^{1}H NMR (MeOH-d_4): 1.47-1.32.