'Cap-Tag' – Novel Methods for the Rapid Purification of Oligosaccharides Prepared by Automated Solid-Phase Synthesis

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Supplementary Material

General Methods. All chemicals used were reagent grade and used as supplied except where noted. Dichloromethane (CH_2Cl_2) and tetrahydrofuran (THF) used for washing cycles were purchased from Mallinckrodt (HPLC Grade) and used without further purification. CH_2Cl_2 and THF used for reagent preparation were purchased from J.T. Baker (Cycletainer^{TM}) and passed through a neutral alumina column prior to use. Pyridine was refluxed over calcium hydride and distilled prior to use. Trimethylsilyl trifluoromethanesulfonate (TMSOTf) was purchased from Acros Chemicals. Sodium methoxide (25% w/v in MeOH), glacial acetic acid (AcOH) and hydrazine acetate (98%) were purchased from Aldrich Chemicals. Fluorous silica (0.77 mmol/g, 230 – 400 mesh) and isocyanate-3 scavenging resin (1.4 mmol/g, 230 – 400 mesh) was purchased from Silicycle Inc. Analytical thin-layer chromatography was performed on E. Merck silica gel 60 F_{254} plates (0.25 mm). Compounds were visualized by dipping the plates in a cerium sulfate-ammonium molybdate solution followed by heating. Liquid column chromatography was performed using forced flow of the indicated solvent on Silicycle 230 - 400 mesh (60 Å pore diameter) silica gel. ^{1}H NMR spectra were obtained on a Varian VXR-500 (500 MHz) or a Bruker-400 (400 MHz) spectrometer and are reported in parts per million (δ) relative to $CHCl_3$ (7.27 ppm). Coupling constants (*J*) are reported in Hertz. ^{13}C NMR spectra were obtained on a Varian VXR-500 (125 MHz) or a Bruker-400 (100 MHz) spectrometer and are reported in δ relative to $CDCl_3$ (77.23 ppm) as an internal reference.

General Procedure A: Installation of the A-Tag ester (Solution phase). Alcohol (1.0 equiv.) was dissolved in CH_2Cl_2 (10 mL/mmol) and pyridine (1.0 equiv.). 4-Dimethylaminopyridine (DMAP) (0.1 equiv.) and 2-azido-2-methylpropionic acid (A-Tag) anhydride **2** (1.5 equiv.) were added. The resulting mixture was stirred at ambient temperature for 1 h, after which time the reaction mixture was diluted with CH_2Cl_2, washed with 1% aqueous HCl and water and the organic layer was dried over Na_2SO_4. After filtration and removal of solvents, the product was purified by passing through a plug of silica (eluent: 3:1 hexanes:EtOAc).

General Procedure B: Incorporation of the A-Tag cycle (Automated solid-phase).

The resin (25 μmol) was swelled in CH_2Cl_2 (3 mL) and the A-Tag anhydride **2** (30.0 mg, 5 equiv., loaded into cartridges) was dissolved in CH_2Cl_2 (2 mL) and added to the reaction vessel. After vortexing for 5 s, 1 mL of a 0.01 M solution of DMAP in pyridine was added. Mixing of the suspension was performed (10 s vortex, 50 s rest) for 15 min.

General Procedure C: Oligosaccharide cleavage from the polymer support and purification (A-Tag Method). The glycosylated resin (25 μmol) was dried *in vacuo* over phosphorous pentoxide for 12 h and transferred to a solid-phase round bottom flask. The resin was swelled in THF (3 mL) and tributyl phosphine (112 μL, 18 equiv.) and water (13 μL, 30 equiv.) were added and the reaction mixture was shaken for 30 min. The resin was washed with THF (8 x 5 mL) and CH_2Cl_2 (8 x 5 mL) and dried *in vacuo* over phosphorous pentoxide for 2 h. The resin was transferred to a 10 mL round bottom flask, purged with ethylene and Grubbs' catalyst (bis(tricyclohexylphosphine)benzylidine ruthenium (IV) dichloride, 4.1 mg, 20 mol %) was added. The reaction mixture was diluted with CH_2Cl_2 (3 mL) and stirred under 1 atm ethylene for 36 h. Triethylamine (100 μL, 160 equiv.) and tris hydroxymethylphosphine (50 mg, 80 equiv.) were added and the resulting solution was stirred at room temperature for 1 h. The pale yellow reaction mixture was diluted with CH_2Cl_2 (5 mL) and washed with water (3 x 5 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL) and the combined organics were dried over Na_2SO_4, filtered and concentrated. The crude mixture was dissolved in CH_2Cl_2 (1 mL) and Silicycle Inc. isocyanate-3 resin (50.0 mg, 1.4 mmol/g loading, 3.0 equiv.) was added. The reaction mixture was stirred for 3 h, filtered and the solvents were removed *in vacuo*. The product was then either isolated by chromatography or analyzed by HPLC and compared to a pure trisaccharide standard.

General Procedure D: Installation of the F-Tag cap (Solution phase). Alcohol (1.0 equiv.) was dissolved in CH_2Cl_2 (10 mL/mmol) and 2,6-lutidine (6.0 equiv.) was added. The solution was stirred for 5 min, then a 0.1 M solution of F-Tag triflate **11** (4.0 equiv.) was added dropwise. After 10 min the clear solution was diluted with CH_2Cl_2 (20 mL), washed with sat. $NaHCO_3$ (2 X 25 mL) and brine (25 mL). Following drying (Na_2SO_4), filtration and concentration the crude material was purified by silica gel column chromotography (10% EtOAc/hexanes).

General Procedure E: Incorporation of the F-Tag cap cycle (Automated solid-phase). The resin (50 μmol) was swelled in a 0.1 M solution of 2,6-lutidine in CH_2Cl_2 (4 mL, 8.0 equiv.). After vortexing for 5 s, a 0.1 M solution of the F-Tag triflate **11** in CH_2Cl_2 (2.5 mL, 5.0 equiv., loaded into cartidges) was delivered to the reaction vessel. Mixing of the suspension was performed (10 s vortex, 50 s rest) for 15 min.

General Procedure F: Oligosaccharide cleavage from the polymer support and purification (F-Tag Method). The glycosylated resin (50 μmol) was dried *in vacuo* over phosphorous pentoxide for 12 h and transferred to a round bottom flask. After purging with ethylene, Grubbs' catalyst (bis(tricyclohexylphosphine)benzylidine ruthenium (IV) dichloride, 8.2 mg, 20 mol %) was

added. The reaction mixture was diluted with CH_2Cl_2 (1 mL) and stirred under 1 atm ethylene for 36 h. Triethylamine (100 μL, 160 equiv.) and tris hydroxymethylphosphine (50 mg, 80 equiv.) were added and the resulting solution was stirred at room temperature for 1 h. The pale yellow reaction mixture was diluted with CH_2Cl_2 (5 mL) and washed with water (3 x 5 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL) and the combined organics were dried over Na_2SO_4, filtered and concentrated. The crude mixture was dissolved in CH_2Cl_2/MeOH (1 mL, 1:1) and added to a column of tridecafluoro (Si-$(CH_2)_2$-$(CF_2)_5$-$CF_3)_3$) functionalized silica gel (Silicycle) equilibrated in 80% MeOH/20% H_2O. One column length of 80% MeOH/20% H_2O was eluted, and the solvent was changed to 100% MeOH. Non-fluorinated material typically eluted in fractions 1-4, while fluorinated material remained on the column until the gradient was increased to 100% MeOH. The desired non-fluorinated fractions were concentrated and analyzed by HPLC. Recycling of the fluorous silica gel was possible after washing with 3 column lengths MeOH, 4 column lengths CH_2Cl_2 and drying with N_2.

Synthesis of 2-azido-2-methylpropionic acid anhydride 2. 2-Azido-2-methylpropionic acid was synthesized using known procedures from the commercially available 2-bromo-2-methylpropionic acid.[i] 2-Azido-2-methylpropionic acid (4.8 g, 37.3 mmol) was dissolved in dry diethyl ether (50 mL) and dicyclohexylcarbodiimide (DCC) (3.8 g, 18.7 mmol) was added. The reaction mixture was stirred overnight, filtered through a pad of celite and washed with saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered and the solvents were removed *in vacuo* to afford **2** (5.93 g, 24.7 mmol, 66%) with no further purification. ^{1}H-NMR (400 MHz) δ 1.58 (s, 6H); ^{13}C-NMR (100 MHz) δ 167.7, 63.8, 24.1.

Synthesis of 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-heptadecafluorodecyldiisopropylsilyl triflate 11. Triflate **11** was prepared according to the following procedure obtained from Fluorous Technologies Inc., 970 William Pitt Way, Pittsburgh PA 15238, www.fluorous.com.

1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-Heptadecafluorodecyldiisopropylsilane. To a dry round bottom flask charged with Et_2O (16 mL) was added a 1.7 M solution of *tert*-butyllithium in pentane (6.15 mL, 10.5 mmol). The yellow solution was cooled to –78°C, stirred for 5 min, and a solution of 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-heptadecafluoro-10-iodo-decane (2.0 g, 3.48 mmol) in Et_2O (20 mL) was added dropwise by cannula. The resulting solution was stirred at –78°C for 1 h, after which diisopropylchlorosilane (505 μL, 2.96 mmol) was added. The mixture was warmed to room temperature over 2 h, quenched with saturated aqueous NH_4Cl and washed with CH_2Cl_2 (3 x 50 mL). The combined organics were washed with brine (1 x 50 mL), dried (Na_2SO_4), filtered and concentrated. The crude oil was purified by vacuum distillation (b.p. 78°C at 0.04 mm) to give the silane as a clear oil (1.4 g, 80%). ^{1}H NMR (500 MHz) δ 3.49 (br s, 1H), 2.21-2.03 (m, 2H), 1.06 (s, 12H), 0.89-0.82 (m, 2H); ^{13}C-NMR (125 MHz) δ 27.2 (t, J = 24.2 Hz), 18.8, 18.4, 10.4, -2.16.

1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-Heptadecafluorodecyldiisopropylsilyl triflate 11. The above silane (2.03 g, 3.61 mmol) was dissolved in CH_2Cl_2 (36 mL) and dry trifluoromethanesulfonic acid

(479 μL, 5.41 mmol) was added. The resulting pale yellow solution was stirred at room temperature for 3 h, then transferred and stored in dry vials. Triflate **11** was stable for up to 2 months when stored under N_2 in a dessicator.

Automated synthesis of β-glucoside 14 using the A-Tag method. Octenediol functionalized resin **12** (25 μmol, 90 mg, 0.30 mmol/g loading) was loaded into a reaction vessel equipped with a cooling jacket and inserted into a modified ABI-433A peptide synthesizer. The resin was glycosylated using donor **13** (5 equiv., 0.125 mmol, 90 mg loaded into cartridges) delivered in CH_2Cl_2 (3 mL) and TMSOTf (5 equiv., 1 mL, 0.125 M TMSOTf in CH_2Cl_2) at –15°C. Mixing of the suspension was performed (10 s vortex, 50 s rest) for 15 min. The resin was then washed with CH_2Cl_2 (6 x 4 mL each), warmed to 15°C, and the unglycosylated sites were capped using General Procedure B. Deprotection of the levulinoyl ester was carried out by treating the glycosylated resin with hydrazine acetate (20 equiv., 4 mL, 0.25 M N_2H_4-HOAc in pyridine:acetic acid 3:2) for 15 min. The resin was subjected to the deprotection conditions a second time for 15 min followed by the washing cycle. The deprotected polymer-bound C6-OH β-monosaccharide was then elongated by reiteration of the above glycosylation/capping/deprotection protocol using donor **13**. The final trisaccharide was not deprotected, thereby simplifying the analysis of the products. The product was liberated from the resin and purified by General Procedure C.

A-Tag/Phosphate/ Levulinate Cycle

Step	Function	Reagent	Time (Min)
1	Glycosylation	5 equiv. Donor and 5 equiv. TMSOTf	20
2	Wash	Dichloromethane	9
3	Capping	5 equiv. **2**, cat DMAP	18
4	Wash	Tetrahydrofuran	9
5	Wash	0.2 M AcOH/MeOH/THF	9
6	Deprotection	2 x 20 equiv. Hydrazine (NH_2NH_2)	40
7	Wash	Tetrahydrofuran	9
8	Wash	0.2 M AcOH/MeOH/THF	9
9	Wash	Tetrahydrofuran	9
10	Wash	Dichloromethane	9

Automated synthesis of β-glucoside 14 using the F-Tag method. Octenediol functionalized resin **12** (50 μmol, 50 mg, 1.0 mmol/g loading) was loaded into a reaction vessel equipped with a cooling jacket and inserted into a modified ABI-433A peptide synthesizer. The resin was glycosylated using donor **13** (5 equiv., 0.250 mmol, 180 mg loaded into cartridges) delivered in CH_2Cl_2 (3 mL) and TMSOTf (5 equiv., 2 mL, 0.125 M TMSOTf in CH_2Cl_2) was added to the reaction vessel at –15°C. Mixing of the suspension was performed (10 s vortex, 50 s rest) for 15 min. The resin was then washed with CH_2Cl_2 (6 x 4 mL each), the reaction vessel warmed to 15°C, and the unglycosylated sites were capped using General Procedure E. Deprotection of the levulinoyl ester was carried out by treating the glycosylated resin with hydrazine acetate (20 equiv., 4 mL, 0.25 M N_2H_4-HOAc in pyridine:acetic acid 3:2) for 15 min. The resin was subjected

to the deprotection conditions a second time for 15 min followed by the washing cycle. The deprotected polymer-bound C6-OH β-disaccharide was then elongated by reiteration of the above glycosylation/capping/deprotection protocol using donor **13**. The final trisaccharide was not deprotected, thereby simplifying the analysis of the products. The product was liberated from the resin and purified by General Procedure F.

F-Tag/Phosphate/ Levulinate Cycle

Step	Function	Reagent	Time (Min)
1	Glycosylation	5 equiv. Donor and 5 equiv. TMSOTf	20
2	Wash	Dichloromethane	9
3	Capping	5 equiv. **11**, 8 equiv. Lutidine	18
4	Wash	Tetrahydrofuran	9
5	Deprotection	2 x 20 equiv. NH_2NH_2	40
6	Wash	0.2 M AcOH/MeOH/THF	9
7	Wash	Tetrahydrofuran	9
8	Wash	Dichloromethane	9

***n*-Pentenyl 3,4-di-*O*-benzyl-6-*O*-levulinoyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-6-*O*-levulinoyl-2-*O*-pivaloyl-β-D-glucopyranosyl-(1→6)-3,4-di-*O*-benzyl-6-*O*-levulinoyl-2-*O*-pivaloyl-β-D–glucopyranoside 14.** ^{1}H-NMR (500 MHz) δ 7.34 – 7.18 (m, 30H), 5.84 – 5.76 (m, 1H), 5.09 – 4.95 (m, 5H), 4.79 – 4.65 (m, 10H), 4.62 – 4.55 (m, 3H), 4.52 (d, *J* = 10.6 Hz, 1H), 4.47 (d, *J* = 7.6 Hz, 1H), 4.35 (d, *J* = 7.9 Hz, 1H), 4.34 – 4.31 (m, 1H), 4.22 (dd, *J* = 5.2, 11.9 Hz, 1H), 4.03 – 3.96 (m, 2H), 3.88 – 3.83 (m, 1H), 3.76 – 3.55 (m, 10H), 3.46 – 3.42 (m, 3H), 2.67 – 2.63 (m, 2H), 2.53 – 2.50 (m, 2H), 2.14 (s, 3H), 2.13 – 2.06 (m, 2H), 1.69 – 1.63 (m 2H), 1.20 (s, 9H), 1.19 (s, 9H), 1.18 (s, 9H); ^{13}C-NMR (125 MHz) δ 206.6, 177.0, 176.9, 176.8, 172.8, 138.3, 138.2, 138.1, 138.0, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 115.3, 101.3, 101.0, 100.9, 83.4, 78.4, 78.2, 76.0, 75.4, 75.2, 73.6, 73.4, 73.3, 69.1, 68.4, 67.5, 63.5, 39.3, 38.2, 30.4, 30.2, 29.2, 28.6, 28.0; ESI-MS *m/z* (M + Na^+): Calcd 1485.7119, obsd 1485.7073.

Automated synthesis of α-(1→2)-trimannoside[ii] 16 using the F-Tag method. Octenediol functionalized resin **12** (50 μmol, 50 mg, 1.0 mmol/g loading) was loaded into a reaction vessel and inserted into a modified ABI-433A peptide synthesizer. The resin was glycosylated using donor **15** (5 equiv., 0.25 mmol, 160 mg) delivered in CH_2Cl_2 (4mL) and TMSOTf (0.5 equiv., 1 mL, 0.0125 M TMSOTf in CH_2Cl_2). Mixing of the suspension was performed (10 s vortex, 50 s rest) for 30 min. The resin was then washed with CH_2Cl_2 (6 x 4 mL each) and the unglycosylated sites were capped using General Procedure E. Deprotection of the acetyl ester was carried out by treating the glycosylated resin with sodium methoxide (8 equiv., 0.5 mL, 0.75 M NaOMe in MeOH) in CH_2Cl_2 (5 mL) for 30 min. The resin was then washed with CH_2Cl_2 (1 x 4 mL) and subjected to the deprotection conditions a second time for 30 min. The deprotected polymer-bound C2-OH α-mannoside was then elongated by reiteration of the above glycosylation/capping/deprotection

protocol. The final trisaccharide was not deprotected, thereby simplifying the analysis of the products. The product was liberated from the resin and purified by General Procedure F.

F-Tag/Imidate/Acetate Cycle

Step	Function	Reagent	Time (Min)
1	Glycosylation	5 equiv. Donor and 0.5 equiv. TMSOTf	20
2	Wash	Dichloromethane	9
3	Capping	5 equiv. **11**, 8 equiv. Lutidine	18
4	Wash	Dichloromethane	9
5	Deprotection	2x10 equiv. NaOMe	60
6	Wash	0.2 M AcOH/MeOH/THF	9
7	Wash	Tetrahydrofuran	9
8	Wash	Dichloromethane	9

6-*O*-2'-Azido-2'-methylpropionoyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside 3. 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranoside (50.0 mg, 0.192 mmol) was subjected to General Procedure A to afford **3** (64.0 mg, 0.172 mmol) in 90% yield. $[\alpha]^{24}_{D}$: - 29.1° (*c* 2.75, CH_2Cl_2); IR (thin film) 2989, 2937, 2114, 1741, 1069 cm^{-1}; ^{1}H-NMR (500 MHz) δ 5.53 (d, *J* = 5.2 Hz, 1H), 4.62 (dd, *J* = 2.4, 7.9 Hz, 1H), 4.40 (dd, *J* = 4.0, 11.3 Hz, 1H), 4.32 – 4.27 (m, 2H), 4.24 (dd, *J* = 1.8, 7.9 Hz, 1H), 4.05 (ddd, *J* = 1.8, 4.0, 8.2 Hz, 1H), 1.50 (app s, 6H), 1.48 (s, 3H), 1.46 (s, 3H), 1.35 (s, 3H), 1.33 (s, 3H); ^{13}C-NMR (125 MHz) δ 173.0, 110.0, 109.0, 96.5, 71.1, 70.9, 70.6, 66.1, 64.8, 63.3, 26.1, 26.1, 25.1, 24.7, 24.6.

***n*-Pentenyl 2-*O*-2'-Azido-2'-methylpropionoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside.** *n*-Pentenyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (61.6 mg, 0.199 mmol) was subjected to General Procedure A to afford product (66.5 mg, 0.106 mmol) in 89% yield. $[\alpha]^{24}_{D}$: - 20.4° (*c* 2.67, CH_2Cl_2); IR (thin film) 2924, 2870, 2112, 1743, 1092 cm^{-1}; ^{1}H-NMR (500 MHz) δ 7.38 – 7.21 (m, 15H), 5.84 – 5.75 (m, 1H), 5.40 (app t, *J* = 2.1 Hz, 1H), 5.06 – 4.95 (m, 2H), 4.86 (app s, 1H), 4.83 (d, *J* = 10.7 Hz, 1H), 4.70 (d, *J* = 11.3 Hz, 1H), 4.64 (d, *J* = 11.9 Hz, 1H), 4.56 (d, *J* = 11.6 Hz, 1H), 4.52 (d, *J* = 12.8 Hz, 1H), 4.50 (d, *J* = 11.0 Hz, 1H), 4.02 – 4.00 (m, 1H), 3.87 – 3.69 (m, 5H), 3.47 – 3.40 (m, 1H), 2.14 – 2.08 (m, 2H), 1.71 – 1.64 (m, 3H), 1.46 – 1.44 (m, 6H); ^{13}C-NMR (125 MHz) δ 172.5, 138.5, 138.3, 138.1, 138.1, 128.5, 128.5, 128.3, 128.2, 127.9, 127.9, 127.8, 127.7, 115.3, 97.5, 78.4, 75.5, 74.5, 73.5, 72.0, 71.5, 70.2, 69.1, 67.5, 63.4, 30.4, 28.7, 24.7, 24.6.

1,2-3,4-di-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranoside 7. 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranoside (187 mg, 0.73 mmol) was dissolved in CH_2Cl_2 (1 mL) and 2,6-lutidine (213 μL, 1.83 mmol) was added. The solution was stirred for 5 min and TBSOTf (250 μL, 1.09 mmol) was added dropwise. After 10 min the clear solution was diluted with CH_2Cl_2 (20 mL), washed with saturated $NaHCO_3$ (2 X 25 mL) and brine (25 mL). Following drying (Na_2SO_4), filtration and concentration, the crude product was purified by silica gel column

chromatography (10% EtOAc/hexanes) to afford **7** (238 mg, 87%) as a clear oil. Spectra are in accordance with the reported data.[iii]

1,2-3,4-di-*O*-isopropylidene-6-*O*-(1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-heptadecafluorodecyldiisopropyl)silyl-α-D-galactopyranoside 8. 1,2-3,4-di-*O*-isopropylidene (14 mg, 0.055 mmol) was subjected to General Procedure D to afford 114 mg of a mixture of **8** and 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-heptadecafluorodecyldiisopropylsilyl alcohol. ^{1}H NMR (500 MHz) δ 5.51 (d, *J* = 5.2 Hz, 1H), 4.61 (dd, *J* = 2.1, 7.9 Hz, 1H), 4.32 - 4.30 (m, 1H), 4.28 (d, *J* = 8.2 Hz, 1H), 3.87 - 3.79 (m, 3H), 2.23 - 2.06 (m, 7H), 1.53 (s, 3H), 1.42 (s, 3H), 1.33 (s, 3H), 1.32 (s, 3H), 1.05 - 0.97 (m, 42H), 0.89 - 0.82 (m, 7H); ^{13}C-NMR (125 MHz) δ 109.8, 109.2, 100.1, 97.0, 71.4, 71.3, 69.0, 63.0, 26.7, 26.5, 26.1, 25.9, 25.6, 24.9, 18.2, 18.1, 18.1, 17.9, 17.8, 13.5, 13.1, 13.1, 1.36, 0.41.

***n*-Pentenyl-3,4,6-tri-*O*-benzyl-2-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranoside 9.** *n*-Pentenyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (55 mg, 0.11 mmol) was dissolved in CH_2Cl_2 (1 mL) and 2,6-lutidine (26 μL, 0.22 mmol) was added. The solution was stirred for 5 min and TBSOTf (27 μL, 0.12 mmol) was added dropwise. After 10 min the clear solution was diluted with CH_2Cl_2 (20 mL), washed with saturated $NaHCO_3$ (2 X 25 mL) and brine (25 mL). Following drying (Na_2SO_4), filtration and concentration, the crude product was purified by silica gel column chromatography (10% EtOAc/hexanes) to afford **9** (52 mg, 75%) as a clear oil. $[\alpha]^{24}_{D}$: + 22.8° (*c* 4.56, CH_2Cl_2); IR (thin film) 2926, 2855, 1497, 1361, 1133 cm^{-1}; ^{1}H NMR (500 MHz) δ 7.41 - 7.18 (m, 15H), 5.87 - 5.79 (m, 1H), 5.07 - 4.98 (m, 4H), 4.84 (d, *J* = 10.7 Hz, 1H), 4.77 - 4.68 (m, 4H), 4.56 (d, *J* = 11.9 Hz, 1H), 4.53 (d, *J* = 11.0 Hz, 1H), 4.07 (t, *J* = 2.1 Hz, 1H), 3.99 - 3.95 (m, 1H), 3.85 - 3.83 (m, 1H), 3.80 - 3.77 (m, 4H), 3.46 - 3.42 (m, 1H), 2.16 - 2.11 (m, 2H), 1.72 - 1.65 (m, 2H), 0.93 (s, 9H), 0.11 (s, 3H), 0.08 (s, 3H); ^{13}C-NMR (125 MHz) δ 138.4, 138.3, 138.1, 137.8, 128.0, 127.9, 127.9, 127.5, 127.3, 127.2, 127.2, 127.1, 127.0, 127.0, 114.6, 100.3, 79.9, 74.7, 74.3, 72.8, 71.9, 69.5, 69.0, 66.5, 30.1, 28.4, 25.5, 17.9, -4.81, -5.10; ESI MS *m/z* (M + Na^{+}) calcd 655.3425, found 655.3449.

***n*-Pentenyl-3,4,6-tri-*O*-benzyl-2-*O*-(1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-heptadecafluorodecyldiisopropyl)silyl-α-D-mannopyranoside 10.** *n*-Pentenyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (54 mg, 0.10 mmol) was subjected to General Procedure D to afford 158 mg of a mixture of **10** and 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-heptadecafluorodecyldiisopropylsilyl alcohol. ^{1}H NMR (500 MHz) δ 7.39 - 7.19 (m, 9H), 5.86 - 5.79 (m, 1H), 5.05 (dd, *J* = 1.53, 17.1 Hz, 1H), 4.98 (dd, *J* = 1.2, 10.1 Hz, 1H), 4.85 (d, *J* = 10.7 Hz, 1H), 4.79-4.72 (m, 2H), 4.67 (d, *J* = 11.9 Hz, 1H), 4.58 (d, *J* = 12.2 Hz, 1H), 4.53 (d, *J* = 11.0 Hz, 1H), 4.12-4.11 (m, 1H), 3.98-3.93 (m, 1H), 3.87 (dd, *J* = 2.4, 9.5 Hz, 1H), 3.81 - 3.72 (m, 2H), 3.47 - 3.42 (m, 1H), 2.30-2.11 (m, 4H), 1.74-1.67 (m, 2H), 1.06 (s, 17H), 0.95-0.85 (m, 3H); ^{13}C-

NMR (125 MHz) δ 139.3, 139.2, 139.0, 139.0, 138.9, 138.7, 138.7, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.3, 128.3, 128.2, 128.1, 121-108 (m, CF_2, CF_3), 101.1, 101.1, 83.3, 80.6, 76.5, 75.8, 75.6, 74.0, 73.9, 73.8, 73.0, 72.6, 71.8, 71.6, 69.9, 67.6, 31.0, 30.4, 29.3, 26.2, 26.0, 26.0 (t, J = 21.9 Hz), 18.3, 18.3, 18.2, 18.2, 17.8, 17.8, 13.8, 13.7, 13.6, 13.5, 13.3, 1.5, 1.4.

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[i] For procedure see: Tornoe, CW, et al., *J. Peptide Sci.* **2000**, 6(7), 314.
[ii] For spectral data see: Andrade R.B. et al., *Org. Lett.* **1999**, 1, 1811.
[iii] Dahlhoff, K.M et al., *Synthesis* **1986**, 561.