

# Regioselective Synthesis of Difluorinated C-furanosides Involving a Debenzylative Cycloetherification

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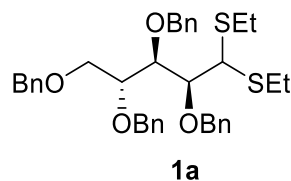
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## Materials and methods:

**Materials and methods:** All reactions were carried out under an argon atmosphere. Yields refer to chromatographically and spectroscopically homogeneous materials. Reagents and chemicals were purchased from Sigma-Aldrich or Acros at ACS grade and were used without purification. All reactions were performed using purified and dried solvents: tetrahydrofuran (THF) was refluxed over sodium-benzophenone, dichloromethane (CH<sub>2</sub>Cl<sub>2</sub>), triethylamine (NEt<sub>3</sub>), and pyridine were refluxed over calcium hydride (CaH<sub>2</sub>). All reactions were monitored by thin-layer chromatography (TLC) carried out on Merck aluminum roll silica gel 60-F254 using UV light and a phosphomolybdic acid solution as revelator. Merck silica gel (60, particle size 40-63 μm) was employed for flash column chromatography and preparative thin layer chromatography using technically solvent distilled prior to use as eluting solvents. NMR spectra were recorded on a JEOL ECX 400 or 500 with solvent peaks as reference. All compounds were characterized by <sup>1</sup>H and <sup>13</sup>C NMR as well as by <sup>1</sup>H-<sup>1</sup>H and <sup>1</sup>H-<sup>13</sup>C correlation experiments when necessary. The following abbreviations are used to describe the multiplicities: s= singlet, d= doublet, t= triplet, q= quartet, m= multiplet, br= broad. The numbering of the protons and carbons is illustrated in the Scheme below. Aromatic, benzyl and methyl (carbons and protons) are respectively labeled with “Arom”, “CH<sub>2</sub>Bn”, quaternary carbons are indicated with a “q” superscript. Chemical shifts (δ) are reported in ppm and referenced indirectly to residual solvent signals. High-resolution mass spectra (HRMS) were performed on a Bruker maXis mass spectrometer with an accuracy tolerance of 2 ppm by the "Fédération de Recherche" ICOA/CBM (FR2708) platform.

## Dithioacetal

### 2,3,4,5-Tetra-*O*-benzyl diethyl dithioacetal *D*-arabinose (**1a**).



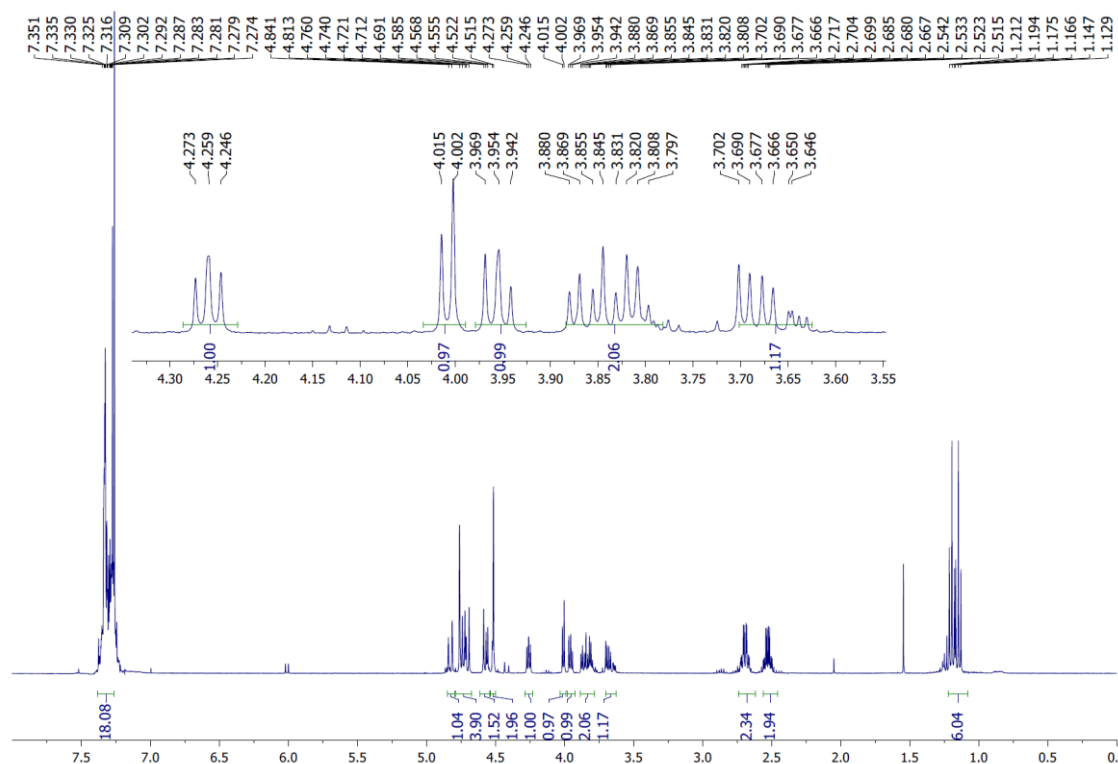
An aqueous solution of concentrated hydrochloric acid (37%, 60 ml, 724 mmol, 1.8 equiv.) was added to *D*-arabinose (60.1 g, 400 mmol) at room temperature. Then, ethanethiol (60 ml, 810 mmol, 2.0 equiv.) was added dropwise at 0 °C and the product was crystallized after 10 min of stirring at 0 °C. Then, the solid was washed with ice water and cooled diethyl ether to give diethyl dithioacetal *D*-arabinose as a white powder (73.5 g, 72%).

To a solution of diethyl dithioacetal *D*-arabinose (36.3 g, 142 mmol) in dry DMF (345 ml) under argon atmosphere was added benzyl bromide (74.6 ml, 624 mmol, 4.4 equiv.) at room temperature. The solution was cooled at 0 °C and NaH (60% in mineral oil, 23.8 g, 595 mmol, 4.2 equiv.) was added portionwise and the reaction was stirred for 48 h. Ice water was added carefully and the mixture was diluted with Et<sub>2</sub>O and the aqueous phase was extracted with Et<sub>2</sub>O (2 times). The combined organic phases were washed with saturated aqueous solution of NH<sub>4</sub>Cl (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated. Purification by chromatography on silica gel (Cy/EtOAc 95:5) gave molecule **1a** (79.9 g, 91%).

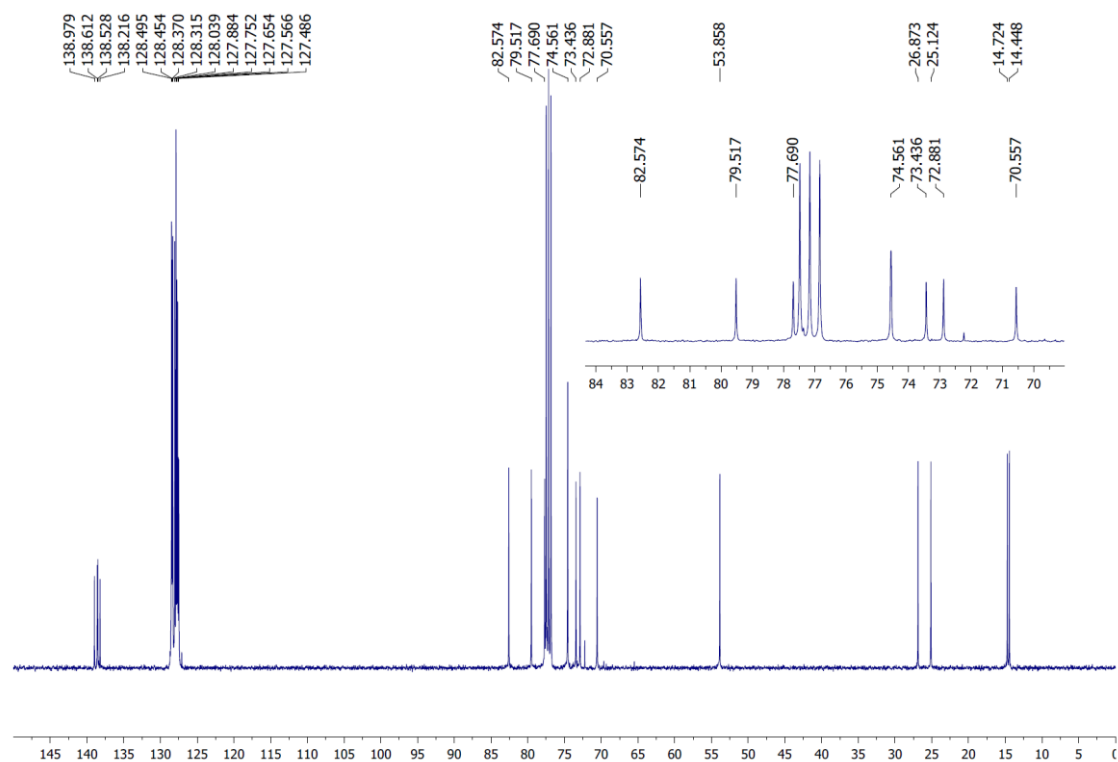
[ $\alpha$ ]<sub>D</sub><sup>20</sup>: +5.5 (*c* 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.38-7.26 (m, 20H, H<sup>arom</sup>), 4.83 (AB, 1H, *J*<sub>A-B</sub> = 11.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.78 (AB, 1H, *J*<sub>A-B</sub> = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.75 (AB, 1H, *J*<sub>A-B</sub> = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.73 (AB, 1H, *J*<sub>A-B</sub> = 11.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.71 (AB, 1H, *J*<sub>A-B</sub> = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.57 (AB, 1H, *J*<sub>A-B</sub> = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.53 (AB, 1H, *J*<sub>A-B</sub> = 12.4 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.50 (AB, 1H, *J*<sub>A-B</sub> = 12.4 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.26 (dd, 1H, *J*<sub>2-3</sub> = 5.7 Hz, *J*<sub>3-4</sub> = 5.0 Hz, H-3), 4.01 (d, 1H, *J*<sub>1-2</sub> = 4.8 Hz, H-1), 3.96 (dd, 1H, *J*<sub>1-2</sub> = 4.8 Hz, *J*<sub>2-3</sub> = 5.7 Hz, H-2), 3.88-3.85 (m, 2H, H-4, H-5a), 3.69 (ABX, 1H, *J*<sub>5a-5b</sub> = 9.9 Hz, *J*<sub>4-5b</sub> = 4.6 Hz, H-5b), 2.70 (dq, 2H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 2.3 Hz, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 2.53 (dq, 2H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 3.4 Hz, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 1.19 (t, 3H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 1.15 (t, 3H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 139.0 (C<sub>q</sub><sup>arom</sup>), 138.9 (C<sub>q</sub><sup>arom</sup>), 138.6 (C<sub>q</sub><sup>arom</sup>), 138.3 (C<sub>q</sub><sup>arom</sup>), 128.6-127.4 (CH<sup>arom</sup>), 83.1 (C-2), 80.5 (C-3), 79.0 (C-4), 75.4 (CH<sub>2</sub><sup>Bn</sup>), 74.9 (CH<sub>2</sub><sup>Bn</sup>), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 71.8 (CH<sub>2</sub><sup>Bn</sup>), 69.3 (C-5), 54.0 (C-1), 25.4 (SCH<sub>2</sub>CH<sub>3</sub>), 25.2 (SCH<sub>2</sub>CH<sub>3</sub>), 14.6 (SCH<sub>2</sub>CH<sub>3</sub>), 14.5 (SCH<sub>2</sub>CH<sub>3</sub>) ppm. These analytical data correspond to published ones.<sup>1</sup>

<sup>1</sup> Delbrouck J. A., Abdellatif Tikad A., Vincent S. P. *Chem. Commun.* **2018**, 54, 9845.

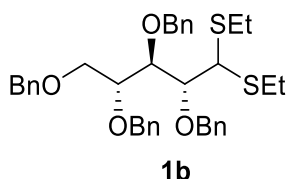
# <sup>1</sup>H NMR



# <sup>13</sup>C NMR



*2,3,4,5-Tetra-O-benzyl diethyl dithioacetal D-ribose (1b).*



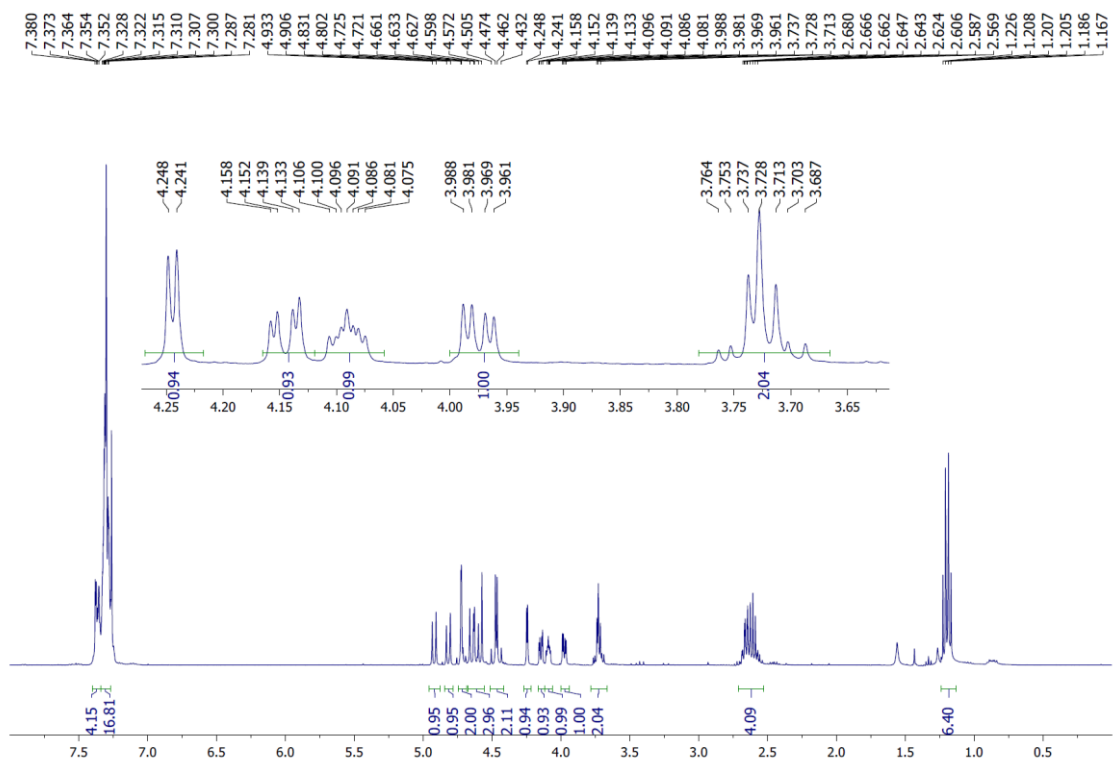
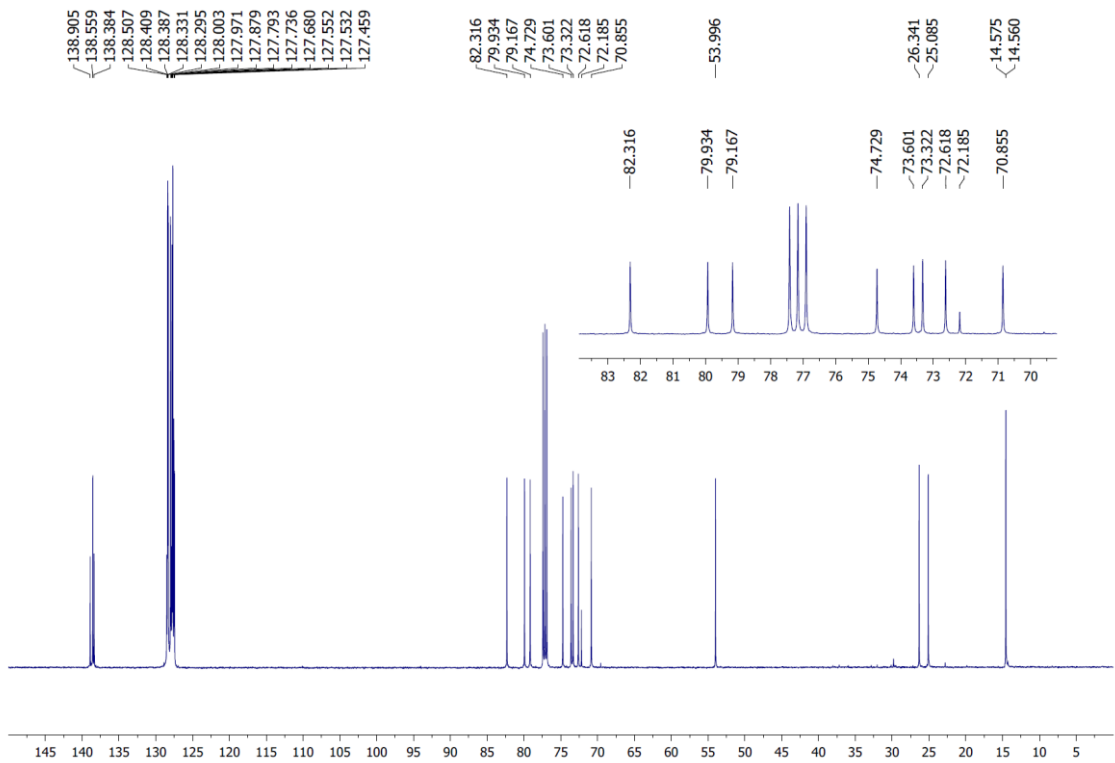
An aqueous solution of concentrated hydrochloric acid (37%, 52.0 ml, 627 mmol, 1.8 equiv.) was added to D-ribose (52.6 g, 350 mmol) at 0 °C and the mixture was stirred for 10 min at 0 °C. Then, ethanethiol (52.0 ml, 702 mmol, 2.0 equiv.) was added and the solution was stirred for 20 min at 0 °C and 18 h at room temperature. Methanol (700 ml) was added and the solution was neutralized with Na<sub>2</sub>CO<sub>3(s)</sub> to pH=7. Filtration on celite<sup>®</sup>, concentration of the filtrate under reduced pressure and recrystallization from hot toluene (50 °C) afforded diethyl dithioacetal D-ribose as an orange powder (32.3 g, 36%).

To a solution of diethyl dithioacetal D-ribose (15.9 g, 62 mmol) in dry DMF (210ml) under argon atmosphere was added benzyl bromide (32.6 ml, 273 mmol, 4.4 equiv.) at room temperature. The solution was cooled at 0 °C and NaH (60% in mineral oil, 12.9 g, 312 mmol, 5.0 equiv.) was added portionwise and the reaction was stirred for 20 h. Ice water was added carefully and the mixture was diluted with Et<sub>2</sub>O and the aqueous phase was extracted with Et<sub>2</sub>O (2 times). The combined organic phases were washed with saturated aqueous solution of NH<sub>4</sub>Cl (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated. Purification by chromatography on silica gel (Cy/EtOAc 95:5) gave compound **1b** (37.7 g, 98%).

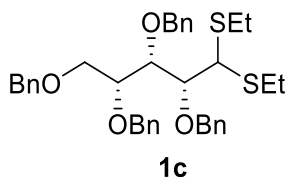
[ $\alpha$ ]<sub>D</sub><sup>20</sup>: +42.3 (*c* 0.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.37-7.26 (m, 20H, H<sup>arom</sup>), 4.91 (AB, 1H, *J*<sub>A-B</sub> = 11.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.81 (AB, 1H, *J*<sub>A-B</sub> = 11.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.73 (AB, 1H, *J*<sub>A-B</sub> = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.70 (AB, 1H, *J*<sub>A-B</sub> = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.64 (AB, 1H, *J*<sub>A-B</sub> = 11.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.61 (AB, 1H, *J*<sub>A-B</sub> = 11.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.48 (AB, 1H, *J*<sub>A-B</sub> = 12.1 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.44 (AB, 1H, *J*<sub>A-B</sub> = 12.1 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.24 (d, 1H, *J*<sub>1-2</sub> = 3.0 Hz, H-1), 4.14 (dd, 1H, *J*<sub>2-3</sub> = 7.8 Hz, *J*<sub>3-4</sub> = 2.5 Hz, H-3), 4.08 (m, 1H, H-4), 3.97 (dd, 1H, *J*<sub>1-2</sub> = 3.0 Hz, *J*<sub>2-3</sub> = 7.8 Hz, H-2), 3.74 (ABX, , 1H, *J*<sub>4-5a</sub> = 4.4 Hz, *J*<sub>5a-5b</sub> = 10.5 Hz, H-5a), 3.70 (ABX, , 1H, *J*<sub>4-5b</sub> = 6.2 Hz, *J*<sub>5a-5b</sub> = 10.5 Hz, H-5b), 2.67-2.55 (m, 4H, 2 SCH<sub>2</sub>CH<sub>3</sub>), 1.20 (q, 6H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.6 Hz, 2 SCH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 138.9 (C<sub>q</sub><sup>arom</sup>), 138.6 (2x C<sub>q</sub><sup>arom</sup>), 138.4 (C<sub>q</sub><sup>arom</sup>), 128.6-127.4 (CH<sup>arom</sup>), 82.3 (C-2), 79.9 (C-3), 79.2 (C-4), 74.7 (CH<sub>2</sub><sup>Bn</sup>), 73.6 (CH<sub>2</sub><sup>Bn</sup>), 73.3 (CH<sub>2</sub><sup>Bn</sup>), 72.6 (CH<sub>2</sub><sup>Bn</sup>), 70.9 (C-5), 54.0 (C-1), 26.4 (SCH<sub>2</sub>CH<sub>3</sub>), 25.1 (SCH<sub>2</sub>CH<sub>3</sub>), 14.6 (2 SCH<sub>2</sub>CH<sub>3</sub>) ppm. These analytical data correspond to published ones.<sup>1</sup>



### <sup>1</sup>H NMR

<sup>13</sup>C NMR

*2,3,4,5-Tetra-O-benzyl diethyl dithioacetal D-xylose (1c).*

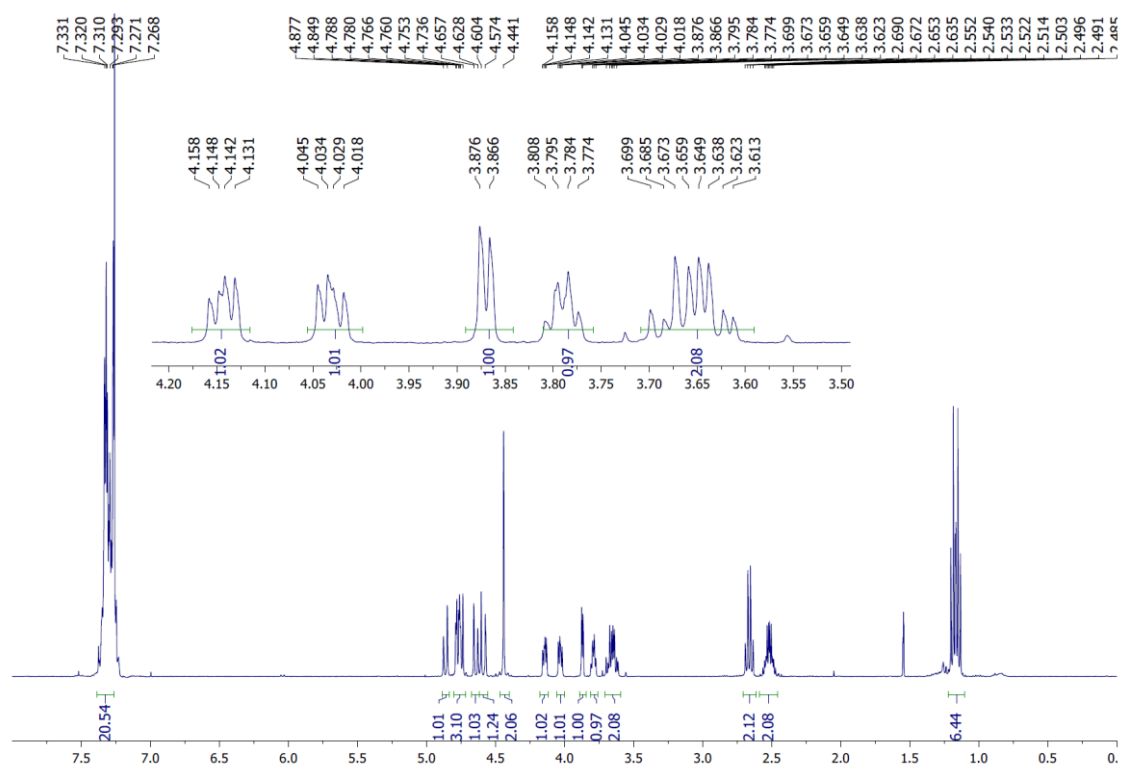


D-xylose (30.0 g, 200 mmol) was dissolved in an aqueous solution of concentrated hydrochloric acid (37%, 25 ml, 302 mmol, 1.5 equiv.) at 0 °C under argon atmosphere. Then, ethanethiol (35 ml, 472 mmol, 2.4 equiv.) was added dropwise at 0 °C over 15 min and the reaction was stirred for 30 min at r.t. The mixture was cooled again to 0 °C and neutralized with NH<sub>4</sub>OH solution (28-30 wt%, 35 ml, 14.5 M). The crude was extracted with hexane (4 times) to remove unreacted ethanethiol. The aqueous layer was concentrated to give an impure yellow oil, which was dissolved in a mixture of (acetone/ethyl acetate, 2:1, 700 ml), filtered through a celite<sup>®</sup> pad and concentrated. The yellow oil was recrystallized from dichloromethane/diethyl ether to yield **1c** as a white solid (42.0 g, 82%).

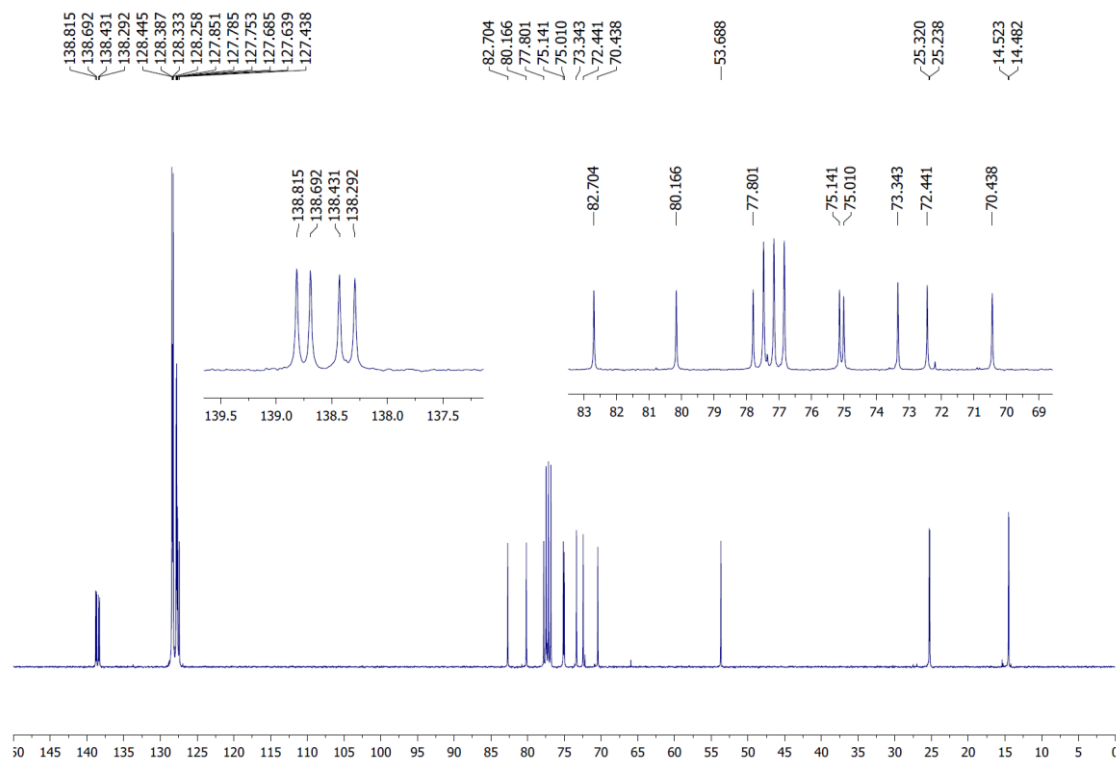
To a solution of diethyl dithioacetal D-xylose (15.7 g, 61 mmol) in dry DMF (210 ml) under argon atmosphere was added benzyl bromide (32.3 ml, 270 mmol, 4.4 equiv.) at r.t. The solution was cooled at 0 °C and NaH (60% in mineral oil, 12.2 g, 306 mmol, 5.0 equiv.) was added portionwise and the reaction was stirred for 24 h. Ice water was added carefully and the mixture was diluted with Et<sub>2</sub>O and the aqueous phase was extracted with Et<sub>2</sub>O (2 times). The combined organic phases were washed with saturated aqueous solution of NH<sub>4</sub>Cl (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated. Purification by chromatography on silica gel (Cy/EtOAc 95:5) gave molecule **1c** (33.6 g, 89%).

[ $\alpha$ ]<sub>D</sub><sup>20</sup>: -9.2 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.38-7.26 (m, 20H, H<sup>arom</sup>), 4.86 (AB, 1H,  $J_{A-B}$  = 11.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.77 (AB, 1H,  $J_{A-B}$  = 11.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.76 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.75 (AB, 1H,  $J_{A-B}$  = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.64 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.59 (AB, 1H,  $J_{A-B}$  = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.46 (AB, 1H,  $J_{A-B}$  = 11.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.43 (AB, 1H,  $J_{A-B}$  = 11.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.14 (dd, 1H,  $J_{2-3}$  = 6.6 Hz,  $J_{3-4}$  = 4.1 Hz, H-3), 4.03 (dd, 1H,  $J_{1-2}$  = 4.4 Hz,  $J_{2-3}$  = 6.6 Hz, H-2), 3.87 (d, 1H,  $J_{1-2}$  = 4.4 Hz, H-1), 3.79 (m, 1H, H-4), 3.68 (ABX, 1H,  $J_{4-5a}$  = 5.5 Hz,  $J_{5a-5b}$  = 10.3 Hz, H-5a), 3.64 (ABX, 1H,  $J_{4-5b}$  = 4.1 Hz,  $J_{5a-5b}$  = 10.3 Hz, H-5b), 2.66 (q, 2H,  $J$  = 7.6 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 2.55-2.49 (m, 2H, SCH<sub>2</sub>CH<sub>3</sub>), 1.18 (t, 3H,  $J_{CH_2CH_3}$  = 7.6 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 1.15 (t, 3H,  $J_{CH_2CH_3}$  = 7.6 Hz, SCH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):  $\delta$  = 138.8 (C<sub>q</sub><sup>arom</sup>), 138.7 (C<sub>q</sub><sup>arom</sup>), 138.4 (C<sub>q</sub><sup>arom</sup>), 138.3 (C<sub>q</sub><sup>arom</sup>), 128.5-127.4 (CH<sup>arom</sup>), 82.7 (C-2), 80.2 (C-3), 77.8 (C-4), 75.1 (CH<sub>2</sub><sup>Bn</sup>), 75.0 (CH<sub>2</sub><sup>Bn</sup>), 73.4 (CH<sub>2</sub><sup>Bn</sup>), 72.4 (CH<sub>2</sub><sup>Bn</sup>), 70.4 (C-5), 53.7 (C-1), 25.3 (SCH<sub>2</sub>CH<sub>3</sub>), 25.2 (SCH<sub>2</sub>CH<sub>3</sub>), 14.5 (2 x SCH<sub>2</sub>CH<sub>3</sub>) ppm. These analytical data correspond to published ones.<sup>1</sup>

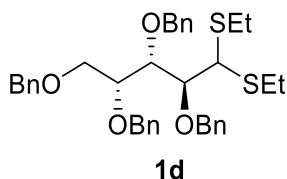
# <sup>1</sup>H NMR



# <sup>13</sup>C NMR



*2,3,4,5-Tetra-O-benzyl diethyl dithioacetal D-lyxose (1d).*

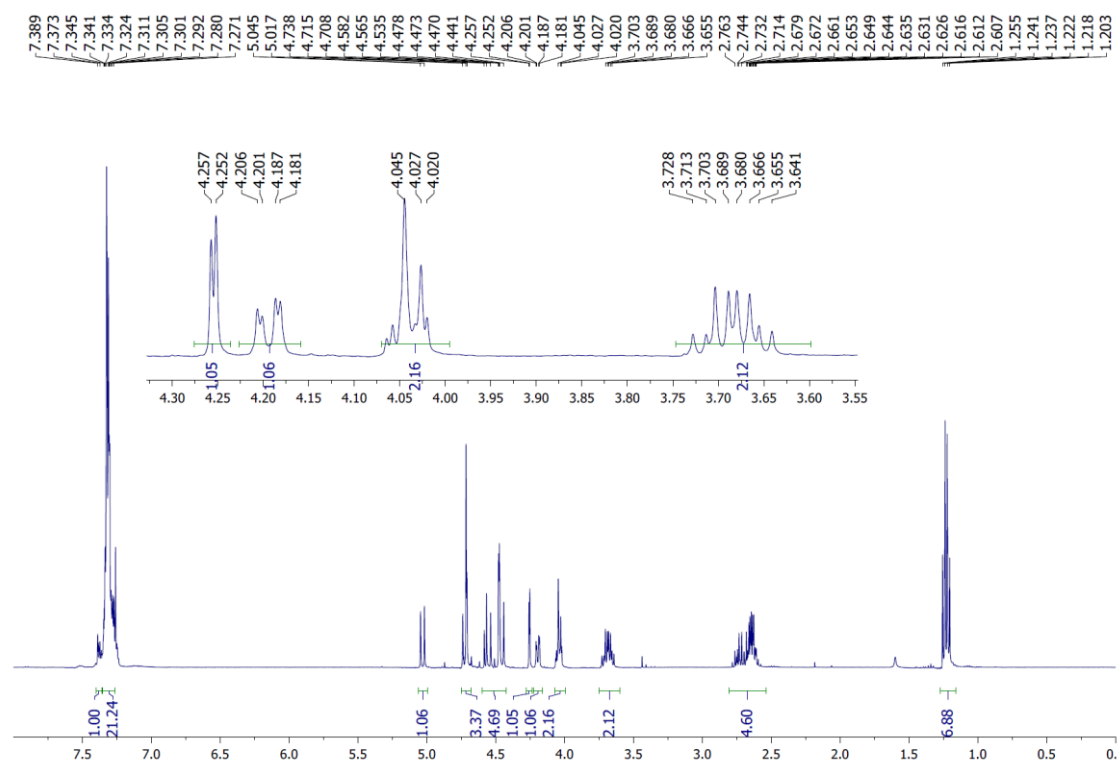


An aqueous solution of concentrated hydrochloric acid (37%, 23.1 ml, 279 mmol, 1.81 equiv.) was added to D-lyxose (23.1 g, 154 mmol) at room temperature. Then, ethanethiol (23.1 ml, 312 mmol, 2.0 equiv.) was added dropwise at 0 °C and the solution was stirred 2 h at 0 °C without solid formation. The mixture was neutralized carefully with potassium carbonate to reach pH 7 and stirred for 16 h at room temperature. The white solid was filtered, washed with Et<sub>2</sub>O (3 times) and the filtrate was stirred with decolorizing carbon for 1 h at r.t. After filtration on celite<sup>®</sup>, evaporation of solvents, the product was recrystallized in ethanol (95%, 125 ml) at 0 °C. Diethyl dithioacetal D-lyxose was obtained as a white powder (12.8 g, 33%).

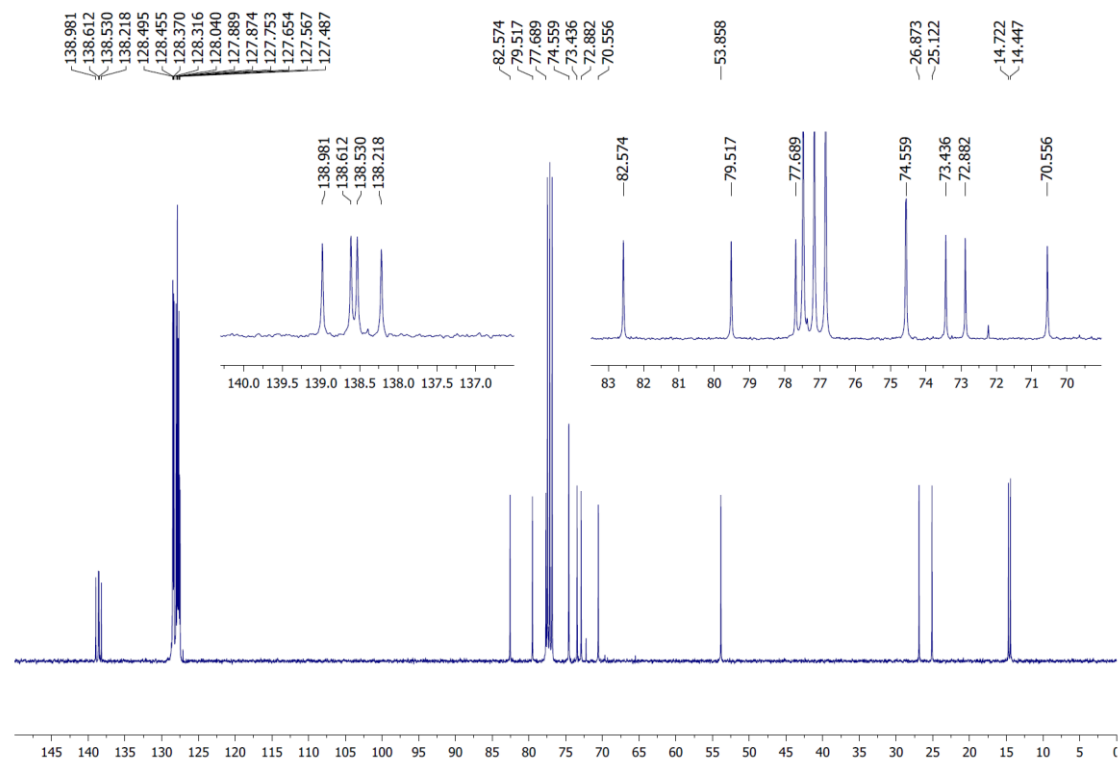
To a solution of diethyl dithioacetal D-lyxose (5.3 g, 21 mmol) in dry DMF (80ml) under argon atmosphere was added benzyl bromide (10.9 ml, 91 mmol, 4.4 equiv.) at r.t. The solution was cooled at 0 °C and NaH (60% in mineral oil, 4.1 g, 103 mmol, 5.0 equiv.) was added portionwise and the reaction was stirred for 24 h. Ice water was added carefully and the mixture was diluted with Et<sub>2</sub>O and the aqueous phase was extracted with Et<sub>2</sub>O (2 times). The combined organic phases were washed with saturated aqueous solution of NH<sub>4</sub>Cl (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated. Purification by chromatography on silica gel (Cy/EtOAc 95:5) gave compound **1c** (11.8 g, 92%).

[ $\alpha$ ]<sub>D</sub><sup>20</sup>: +22.7 (*c* 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.39-7.26 (m, 20H, H<sup>arom</sup>), 5.03 (AB, 1H, *J*<sub>A-B</sub> = 11.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.74-4.70 (m, 3H, CH<sub>2</sub><sup>Bn</sup>), 4.56 (AB, 1H, *J*<sub>A-B</sub> = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.50-4.44 (m, 3H, CH<sub>2</sub><sup>Bn</sup>), 4.26 (d, 1H, *J*<sub>1-2</sub> = 2.3 Hz, H-1), 4.20 (dd, 1H, *J*<sub>2-3</sub> = 8.0 Hz, *J*<sub>3-4</sub> = 2.0 Hz, H-3), 4.06-4.02 (m, 2H, H-2, H-4), 3.71 (ABX, 1H, *J*<sub>4-5a</sub> = 5.7 Hz, *J*<sub>5a-5b</sub> = 9.9 Hz, H-5a), 3.67 (ABX, 1H, *J*<sub>4-5b</sub> = 5.7 Hz, *J*<sub>5a-5b</sub> = 9.9 Hz, H-5b), 2.77-2.60 (m, 4H, 2x SCH<sub>2</sub>CH<sub>3</sub>), 1.24 (t, 3H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 1.22 (t, 3H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):  $\delta$  = 139.0 (C<sub>q</sub><sup>arom</sup>), 138.6 (C<sub>q</sub><sup>arom</sup>), 138.5 (C<sub>q</sub><sup>arom</sup>), 138.2 (C<sub>q</sub><sup>arom</sup>), 128.5-127.5 (CH<sup>arom</sup>), 82.6 (C-3), 79.5 (C-2), 77.7 (C-4), 74.6 (2 x CH<sub>2</sub><sup>Bn</sup>), 73.4 (CH<sub>2</sub><sup>Bn</sup>), 72.9 (CH<sub>2</sub><sup>Bn</sup>), 70.6 (C-5), 53.9 (C-1), 26.9 (SCH<sub>2</sub>CH<sub>3</sub>), 25.1 (SCH<sub>2</sub>CH<sub>3</sub>), 14.7 (SCH<sub>2</sub>CH<sub>3</sub>), 14.5 (SCH<sub>2</sub>CH<sub>3</sub>) ppm. These analytical data correspond to published ones.<sup>1</sup>

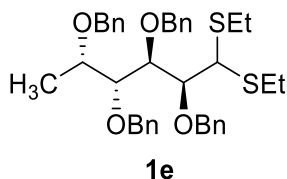
# <sup>1</sup>H NMR



# <sup>13</sup>C NMR



*2,3,4,5-Tetra-O-benzyl diethyl dithioacetal L-fucose(1e).*

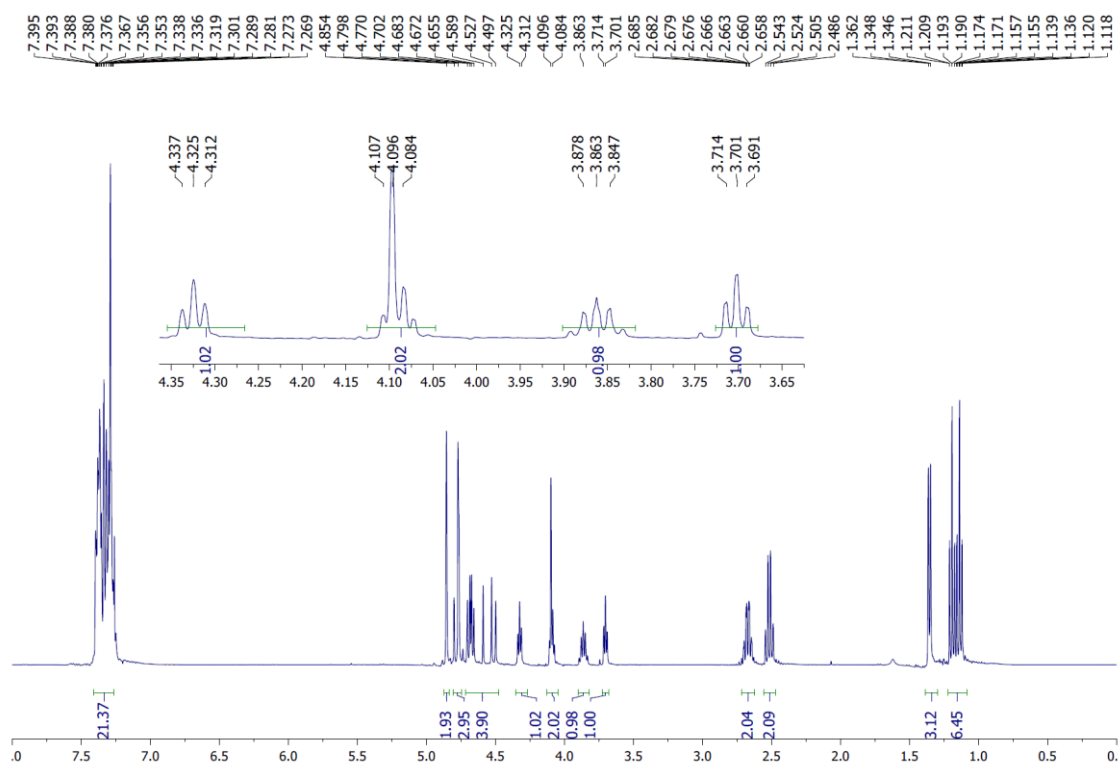


L-Fucose (15.9 g, 97 mmol) was dissolved in an aqueous solution of concentrated hydrochloric acid (37%, 16 ml, 193 mmol, 2.0 equiv.) at r.t. under argon atmosphere. Then, ethanethiol (16 ml, 216 mmol, 2.2 equiv.) was added dropwise at r.t. and the product was crystallized after 10 min of vigorous stirring. Then, the solid was filtered, washed with ice water and cooled diethyl ether (2 times) and dried under reduced pressure to give diethyl dithioacetal L-fucose (17.3 g, 64 mmol, 66%) as a white powder.

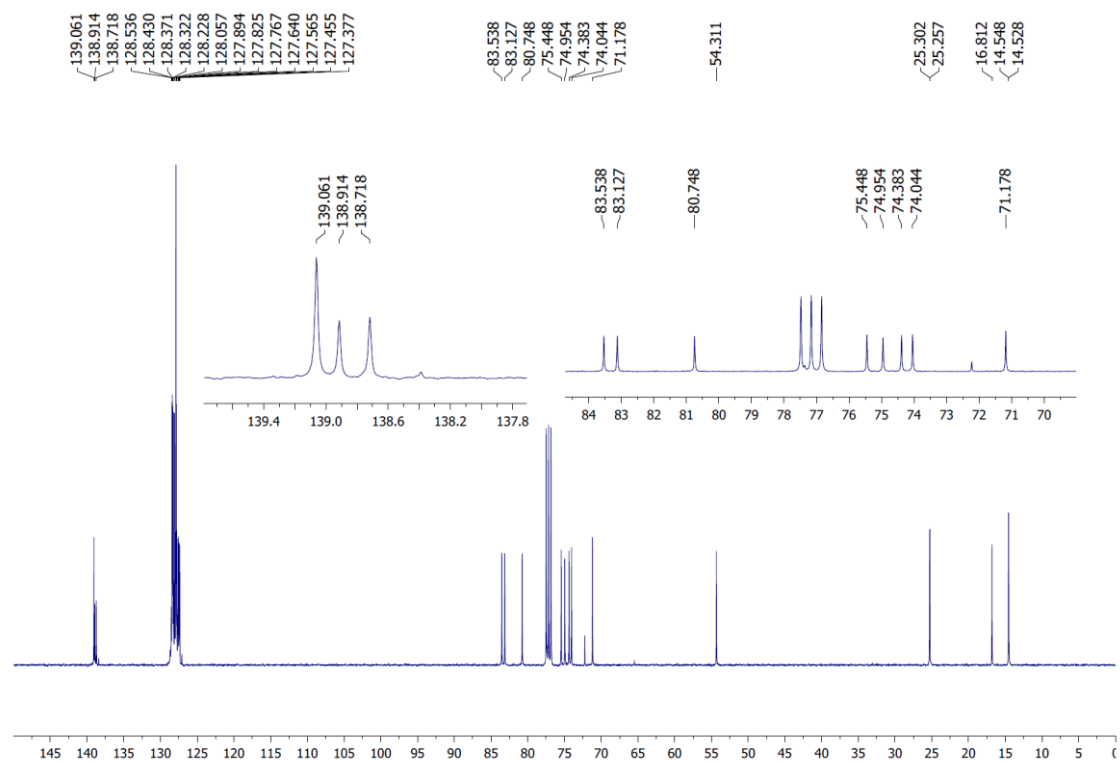
To a solution of diethyl dithioacetal L-fucose (16.0 g, 59 mmol) in dry DMF (210 ml) under argon atmosphere was added benzyl bromide (31.1 ml, 260 mmol, 4.4 equiv.) at room temperature. The solution was cooled at 0 °C and NaH (60% in mineral oil, 11.8 g, 296 mmol, 5.0 equiv.) was added portionwise and the reaction was stirred for 24 h. Ice water was added carefully and the mixture was diluted with Et<sub>2</sub>O and the aqueous phase was extracted with Et<sub>2</sub>O (2 times). The combined organic phases were washed with saturated aqueous solution of NH<sub>4</sub>Cl (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated. Purification by chromatography on silica gel (Cy/EtOAc 95:5) gave molecule **1e** (36.0 g, 97%).

$[\alpha]^{20}_{\text{D}}$ : +7.6 (*c* 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.38-7.23 (m, 20H, H<sup>arom</sup>), 4.83 (AB, 2H, *J*<sub>A-B</sub> = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.77-4.71 (m, 3H, CH<sub>2</sub><sup>Bn</sup>), 4.66 (AB, 1H, *J*<sub>A-B</sub> = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.65 (AB, 1H, *J*<sub>A-B</sub> = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.49 (AB, 1H, *J*<sub>A-B</sub> = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.29 (t, 1H, *J*<sub>2-3</sub> = *J*<sub>3-4</sub> = 5.3 Hz, H-3), 4.06 (m, 2H, H-1, H-2), 3.84 (m, 1H, H-5), 3.67 (dd, 1H, *J*<sub>3-4</sub> = 5.3 Hz, *J*<sub>4-5</sub> = 5.0 Hz, H-4), 2.65 (qd, 2H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 2.3 Hz, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 2.49 (q, 2H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 1.33 (d, 3H, *J*<sub>5-6</sub> = 6.4 Hz, CH<sub>3</sub>), 1.18 (t, 3H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 1.11 (t, 3H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  = 139.1 (2 C<sub>q</sub><sup>arom</sup>), 138.9 (C<sub>q</sub><sup>arom</sup>), 138.7 (C<sub>q</sub><sup>arom</sup>), 128.5-127.4 (CH<sup>arom</sup>), 83.5 (C-4), 83.1 (C-2), 80.8 (C-3), 75.4 (C-5), 75.0 (CH<sub>2</sub><sup>Bn</sup>), 74.4 (CH<sub>2</sub><sup>Bn</sup>), 74.0 (CH<sub>2</sub><sup>Bn</sup>), 71.2 (CH<sub>2</sub><sup>Bn</sup>), 54.3 (C-1), 25.3 (SCH<sub>2</sub>CH<sub>3</sub>), 25.2 (SCH<sub>2</sub>CH<sub>3</sub>), 16.8 (C-6), 14.6 (SCH<sub>2</sub>CH<sub>3</sub>), 14.5 (SCH<sub>2</sub>CH<sub>3</sub>) ppm. These analytical data correspond to published ones.<sup>1</sup>

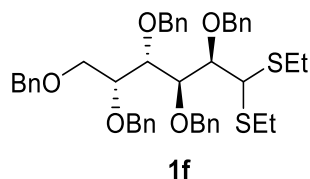
# <sup>1</sup>H NMR



# <sup>13</sup>C NMR



*2,3,4,5-Tetra-O-benzyl diethyl dithioacetal D-galactose (1f).*



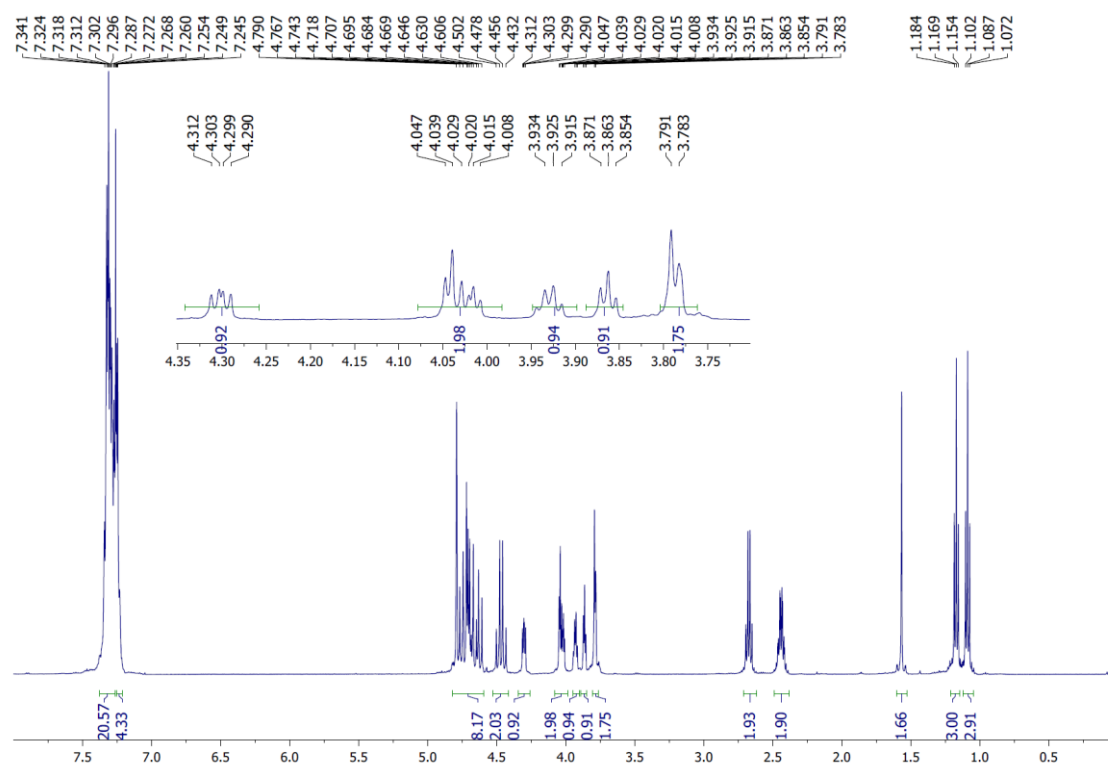
D-galactose (50.0 g, 278 mmol) was dissolved in an aqueous solution of concentrated hydrochloric acid (37%, 75 ml, 905 mmol, 3.25 equiv.) at r.t. under argon atmosphere. Then, ethanethiol (50 ml, 675 mmol, 2.4 equiv.) was added and the mixture was stirred vigorously at r.t. while the pressure was released occasionally. After a few minutes, an increase of the temperature was observed and a small amount of ice were added, which caused almost instantaneously solidification of the reaction mixture. The solid was filtered and washed with ice water (50 ml) and small amount of acetone to afford diethyl dithioacetal D-galactose as a white solid (69.9 g, 88%).

To a solution of diethyl dithioacetal D-galactose (15.5g, 54 mmol) in dry DMF (150 ml) under argon atmosphere was added benzyl bromide (38.8 ml, 325 mmol, 6.0 equiv.) at r.t. The solution was cooled at 0 °C and NaH (60% in mineral oil, 11.9 g, 298 mmol, 5.5 equiv.) was added portionwise and the reaction was stirred for 24 h. Ice water was added carefully and the mixture was diluted with Et<sub>2</sub>O and the aqueous phase was extracted with Et<sub>2</sub>O (2 times). The combined organic phases were washed with saturated aqueous solution of NH<sub>4</sub>Cl (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated. Purification by chromatography on silica gel (Cy/EtOAc 95:5) gave compound **1f** (34.5 g, 86%).

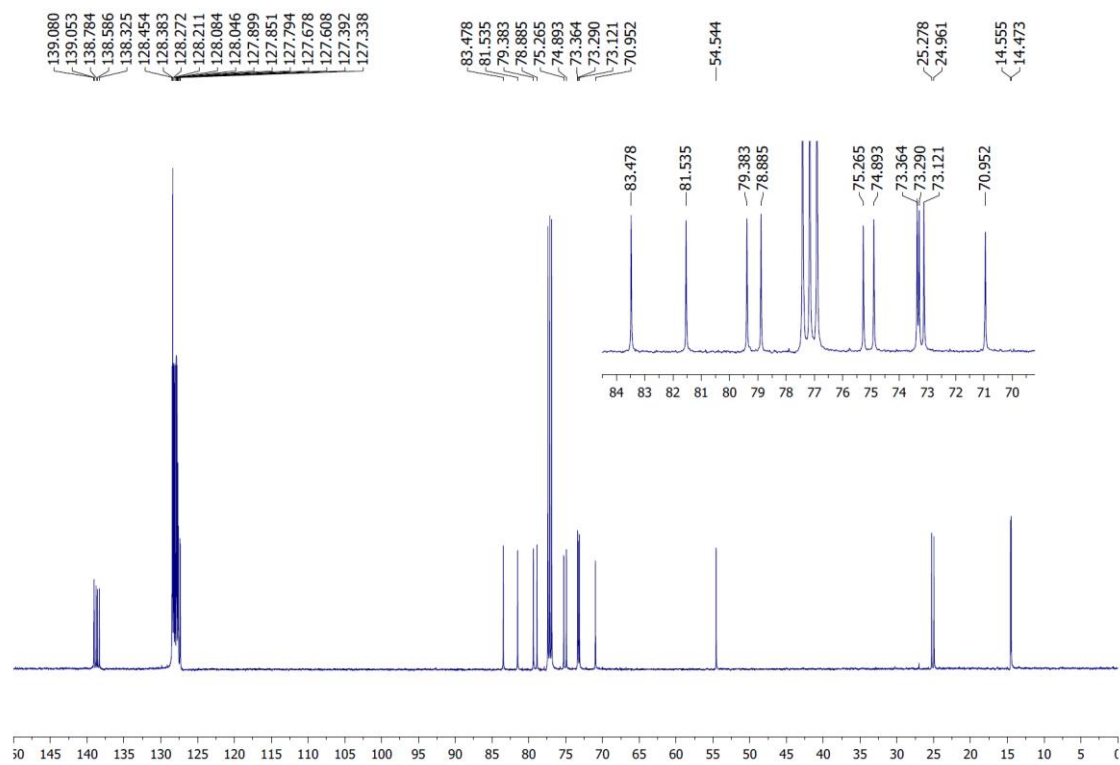
$[\alpha]^{20}_D$ : +12.0 (*c* 1.3, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ = 7.35-7.22 (m, 25H, H<sup>arom</sup>), 4.79 (s, 2H, CH<sub>2</sub><sup>Bn</sup>), 4.76 (AB, 1H, *J*<sub>A-B</sub> = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.71 (AB, 2H, *J*<sub>A-B</sub> = 11.5 Hz, *J*<sub>A-B</sub> = 10.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.70 (AB, 1H, *J*<sub>A-B</sub> = 10.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.66 (AB, 1H, *J*<sub>A-B</sub> = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.62 (AB, 1H, *J*<sub>A-B</sub> = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.49 (AB, 1H, *J*<sub>A-B</sub> = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.45 (AB, 1H, *J*<sub>A-B</sub> = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.31 (dd, 1H, *J*<sub>2-3</sub> = 6.3 Hz, *J*<sub>3-4</sub> = 4.6 Hz, H-3), 4.05-4.00 (m, 2H, H-1, H-2), 3.93 (dd, 1H, *J*<sub>4-5</sub> = 4.6 Hz, *J*<sub>5-6a,6b</sub> = 9.7 Hz, H-5), 3.86 (t, 1H, *J*<sub>3-4</sub> = *J*<sub>4-5</sub> = 4.6 Hz, H-4), 3.78 (m, 2H, H-6a, H-6b), 2.67 (q, 2H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.5 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 2.44 (dq, 2H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 2.3 Hz, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.5 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 1.17 (t, 3H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.5 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 1.09 (t, 3H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.5 Hz, SCH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 139.1 (C<sub>q</sub><sup>arom</sup>), 139.0 (C<sub>q</sub><sup>arom</sup>), 138.8 (C<sub>q</sub><sup>arom</sup>), 138.6 (C<sub>q</sub><sup>arom</sup>), 138.3 (C<sub>q</sub><sup>arom</sup>), 128.5-127.2 (CH<sup>arom</sup>), 83.5 (C-2), 81.6 (C-3), 79.4 (C-4), 78.9 (C-5), 75.3 (CH<sub>2</sub><sup>Bn</sup>), 74.9 (CH<sub>2</sub><sup>Bn</sup>), 73.4 (CH<sub>2</sub><sup>Bn</sup>), 73.3 (CH<sub>2</sub><sup>Bn</sup>), 73.1 (CH<sub>2</sub><sup>Bn</sup>), 71.0 (C-6), 54.6 (C-1), 25.3 (SCH<sub>2</sub>CH<sub>3</sub>), 25.0 (SCH<sub>2</sub>CH<sub>3</sub>), 14.6 (SCH<sub>2</sub>CH<sub>3</sub>), 14.5 (SCH<sub>2</sub>CH<sub>3</sub>) ppm. These analytical data correspond to published ones.<sup>1</sup>



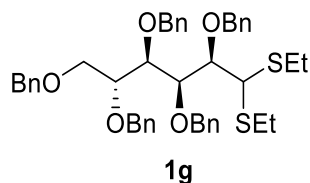
# <sup>1</sup>H NMR



# <sup>13</sup>C NMR



*2,3,4,5-Tetra-O-benzyl diethyl dithioacetal D-glucose (1g).*

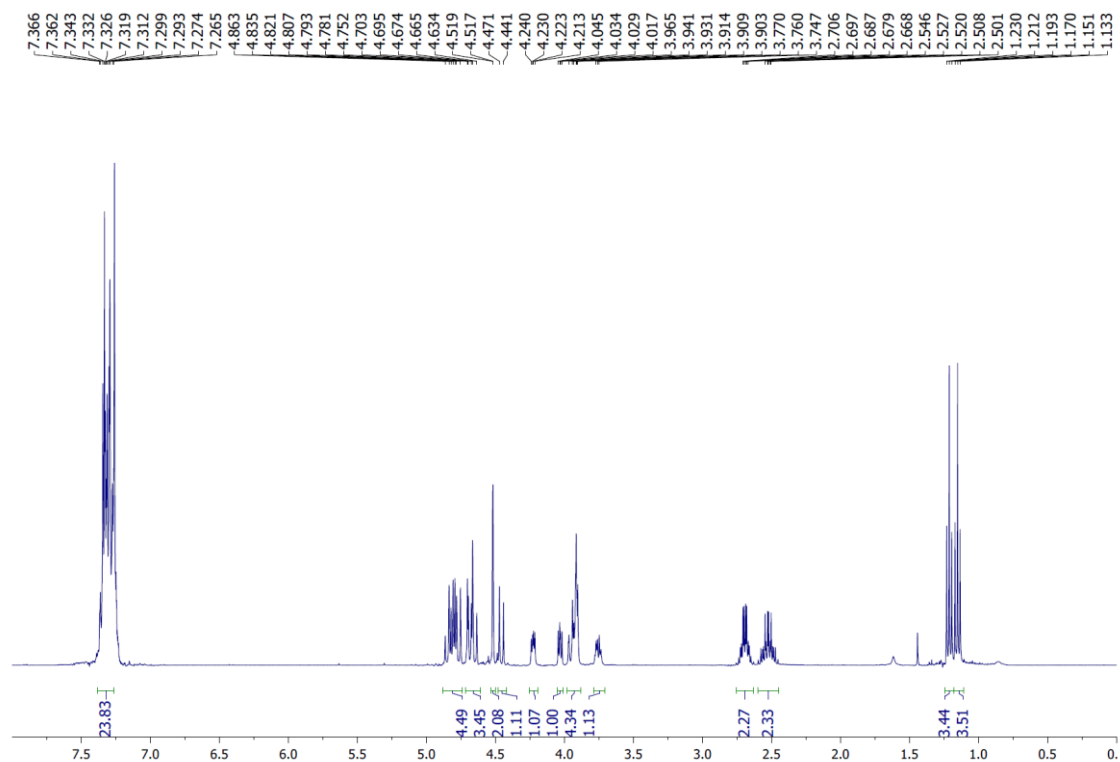


D-glucose (60.0 g, 333 mmol) was dissolved in an aqueous solution of concentrated hydrochloric acid (37%, 51 ml, 615 mmol, 1.85 equiv.) at r.t. under argon atmosphere. Then, ethanethiol (60 ml, 810 mmol, 2.4 equiv.) was added and the mixture was stirred vigorously at r.t. for 15 min. Temperature was maintained below 25 °C by adding small amount of ice and the stirring was continued until crystallization occurs. Then, the mixture was cooled for 30 min in an ice-salt bath, the white solid was filtered, subsequently washed with cold water and diethyl ether, dried under reduced pressure to afford diethyl dithioacetal D-glucose (83.8 g, 0.293 mol, 88%).

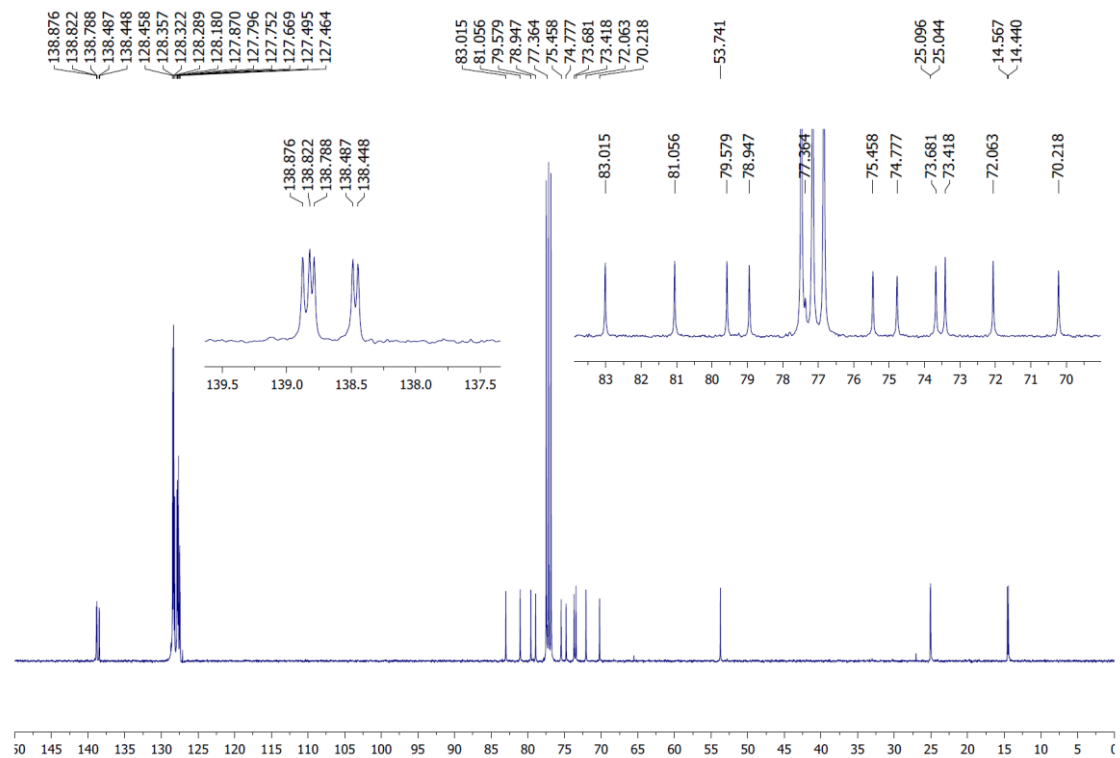
To a solution of diethyl dithioacetal D-glucose (21.3 g, 74 mmol) in dry DMF (250 ml) under argon atmosphere was added benzyl bromide (48.9 ml, 409 mmol, 5.5 equiv.) at room temperature. The solution was cooled at 0 °C and NaH (60% in mineral oil, 16.4 g, 409 mmol, 5.5 equiv.) was added portionwise and the reaction was stirred for 24 h. Ice water was added carefully and the mixture was diluted with Et<sub>2</sub>O and the aqueous phase was extracted with Et<sub>2</sub>O (2 times). The combined organic phases were washed with saturated aqueous solution of NH<sub>4</sub>Cl (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated. Purification by chromatography on silica gel (Cy/EtOAc 95:5) gave molecule **1g** (42.8 g, 78%).

$[\alpha]_D^{20}$ : -2.0 (*c* 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.36-7.24 (m, 25H, H<sup>arom</sup>), 4.85 (AB, 1H, *J*<sub>A-B</sub> = 11.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.81 (AB, 1H, *J*<sub>A-B</sub> = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.79 (AB, 1H, *J*<sub>A-B</sub> = 11.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.77 (AB, 1H, *J*<sub>A-B</sub> = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.69 (AB, 1H, *J*<sub>A-B</sub> = 11.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.68 (AB, 1H, *J*<sub>A-B</sub> = 12.1 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.65 (AB, 1H, *J*<sub>A-B</sub> = 12.1 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.53 (AB, 1H, *J*<sub>A-B</sub> = 12.4 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.50 (AB, 1H, *J*<sub>A-B</sub> = 12.4 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.46 (AB, 1H, *J*<sub>A-B</sub> = 11.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.22 (dd, 1H, *J*<sub>2-3</sub> = 4.1 Hz, *J*<sub>3-4</sub> = 6.4 Hz, H-3), 4.03 (dd, 1H, *J*<sub>3-4</sub> = 6.4 Hz, *J*<sub>4-5</sub> = 4.6 Hz, H-4), 3.97-3.90 (m, 4H, H-1, H-2, H-5, H-6a), 3.78-3.73 (m, 1H, H-6b), 2.69 (dq, 2H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 3.2 Hz, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 2.58-2.47 (m, 2H, SCH<sub>2</sub>CH<sub>3</sub>), 1.21 (t, 3H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 1.15 (t, 3H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):  $\delta$  = 138.9 (C<sub>q</sub><sup>arom</sup>), 138.8 (C<sub>q</sub><sup>arom</sup>), 138.7 (C<sub>q</sub><sup>arom</sup>), 138.5 (C<sub>q</sub><sup>arom</sup>), 138.4 (C<sub>q</sub><sup>arom</sup>), 128.5-127.5 (CH<sup>arom</sup>), 83.0 (C-4), 81.1 (C-3), 79.6 (C-2), 78.9 (C-5), 75.5 (CH<sub>2</sub><sup>Bn</sup>), 74.8 (CH<sub>2</sub><sup>Bn</sup>), 73.7 (CH<sub>2</sub><sup>Bn</sup>), 73.4 (CH<sub>2</sub><sup>Bn</sup>), 72.1 (CH<sub>2</sub><sup>Bn</sup>), 70.2 (C-6), 53.7 (C-1), 25.1 (SCH<sub>2</sub>CH<sub>3</sub>), 25.0 (SCH<sub>2</sub>CH<sub>3</sub>), 14.6 (SCH<sub>2</sub>CH<sub>3</sub>), 14.4 (SCH<sub>2</sub>CH<sub>3</sub>) ppm. These analytical data correspond to published ones.<sup>1</sup>

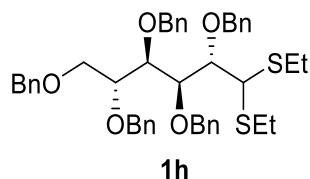
# <sup>1</sup>H NMR



# <sup>13</sup>C NMR



*2,3,4,5-Tetra-O-benzyl diethyl dithioacetal D-mannose (1h).*

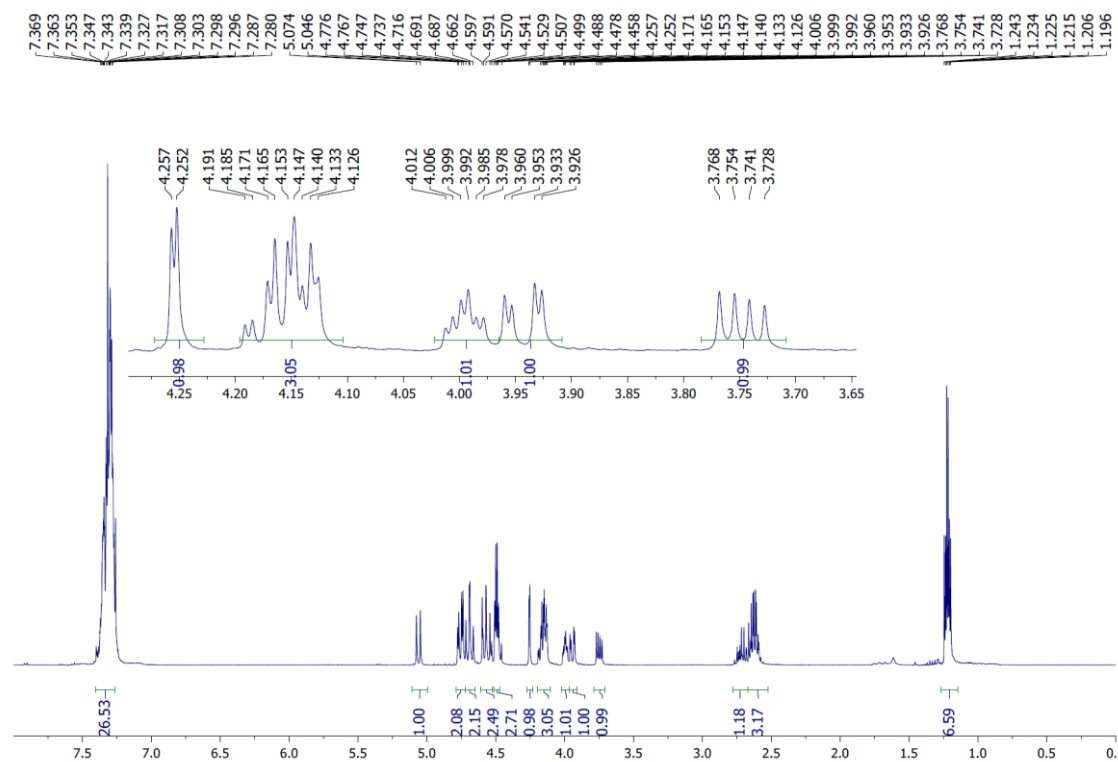


D-Mannose (26.1 g, 145 mmol) was dissolved in an aqueous solution of concentrated hydrochloric acid (37%, 39 ml, 470 mmol, 3.24 equiv.) at r.t. under argon atmosphere. Then, ethanethiol (26 ml, 351 mmol, 2.4 equiv.) was added and the mixture was stirred vigorously at r.t. for 1h. A small amount of ice was added, which causes almost instantaneously solidification of the reaction mixture. The solid was filtered and washed with cold water and cooled diethyl ether to give diethyl dithioacetal D-mannose as a white crystalline solid (28.8 g, 70%).

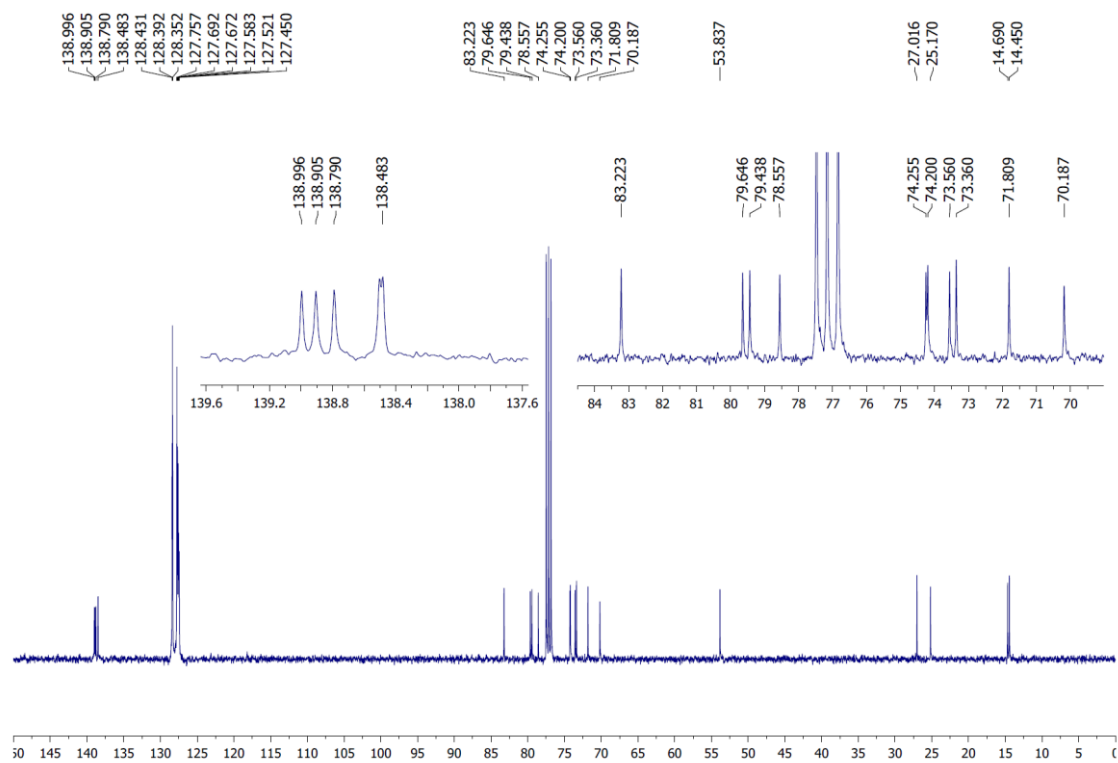
To a solution of diethyl dithioacetal D-mannose (14.5 g, 51 mmol) in dry DMF (250 ml) under argon atmosphere was added benzyl bromide (33.3 ml, 278 mmol, 5.5 equiv.) at r.t. The solution was cooled at 0 °C and NaH (60% in mineral oil, 11.1 g, 278 mmol, 5.5 equiv.) was added portionwise and the reaction was stirred for 24 h. Ice water was added carefully and the mixture was diluted with Et<sub>2</sub>O and the aqueous phase was extracted with Et<sub>2</sub>O (2 times). The combined organic phases were washed with saturated aqueous solution of NH<sub>4</sub>Cl (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated. Purification by chromatography on silica gel (Cy/EtOAc 95:5) gave compound **1h** (26.3 g, 71%).

$[\alpha]_D^{20}$ : -8.9 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.38-7.26 (m, 25H, H<sup>arom</sup>), 5.06 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.76 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.75 (AB, 1H,  $J_{A-B}$  = 12.1 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.70 (AB, 1H,  $J_{A-B}$  = 10.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.68 (AB, 1H,  $J_{A-B}$  = 10.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.58 (AB, 1H,  $J_{A-B}$  = 11.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.56 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.52 (AB, 1H,  $J_{A-B}$  = 12.1 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.49 (AB, 1H,  $J_{A-B}$  = 11.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.47 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.26 (d, 1H,  $J_{1-2}$  = 1.8 Hz, H-1), 4.19-4.12 (m, 3H, H-2, H-3, H-4), 4.00 (td, 1H,  $J_{4-5}$  =  $J_{5-6a}$  = 2.5 Hz,  $J_{5-6b}$  = 5.5 Hz, H-5), 3.95 (ABX, 1H,  $J_{5-6a}$  = 2.5 Hz,  $J_{6a-6b}$  = 10.8 Hz, H-6a), 3.75 (ABX, 1H,  $J_{5-6b}$  = 5.5 Hz,  $J_{6a-6b}$  = 10.8 Hz, H-6b), 2.75-2.58 (m, 4H, 2 SCH<sub>2</sub>CH<sub>3</sub>), 1.22 (t, 3H,  $J_{CH_2CH_3}$  = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>), 1.21 (t, 3H,  $J_{CH_2CH_3}$  = 7.3 Hz, SCH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):  $\delta$  = 139.0 (C<sub>q</sub><sup>arom</sup>), 138.9 (C<sub>q</sub><sup>arom</sup>), 138.8 (C<sub>q</sub><sup>arom</sup>), 138.5 (2 C<sub>q</sub><sup>arom</sup>), 128.5-127.5 (CH<sup>arom</sup>), 83.2 (C-4), 79.6 (C-2), 79.4 (C-5), 78.6 (C-3), 74.3 (CH<sub>2</sub><sup>Bn</sup>), 74.2 (CH<sub>2</sub><sup>Bn</sup>), 73.6 (CH<sub>2</sub><sup>Bn</sup>), 73.4 (CH<sub>2</sub><sup>Bn</sup>), 71.8 (CH<sub>2</sub><sup>Bn</sup>), 70.2 (C-6), 53.8 (C-1), 27.0 (SCH<sub>2</sub>CH<sub>3</sub>), 25.2 (SCH<sub>2</sub>CH<sub>3</sub>), 14.7 (SCH<sub>2</sub>CH<sub>3</sub>), 14.5 (SCH<sub>2</sub>CH<sub>3</sub>) ppm. These analytical data correspond to published ones.<sup>1</sup>

# <sup>1</sup>H NMR

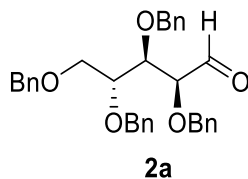


# <sup>13</sup>C NMR



## Aldehydes

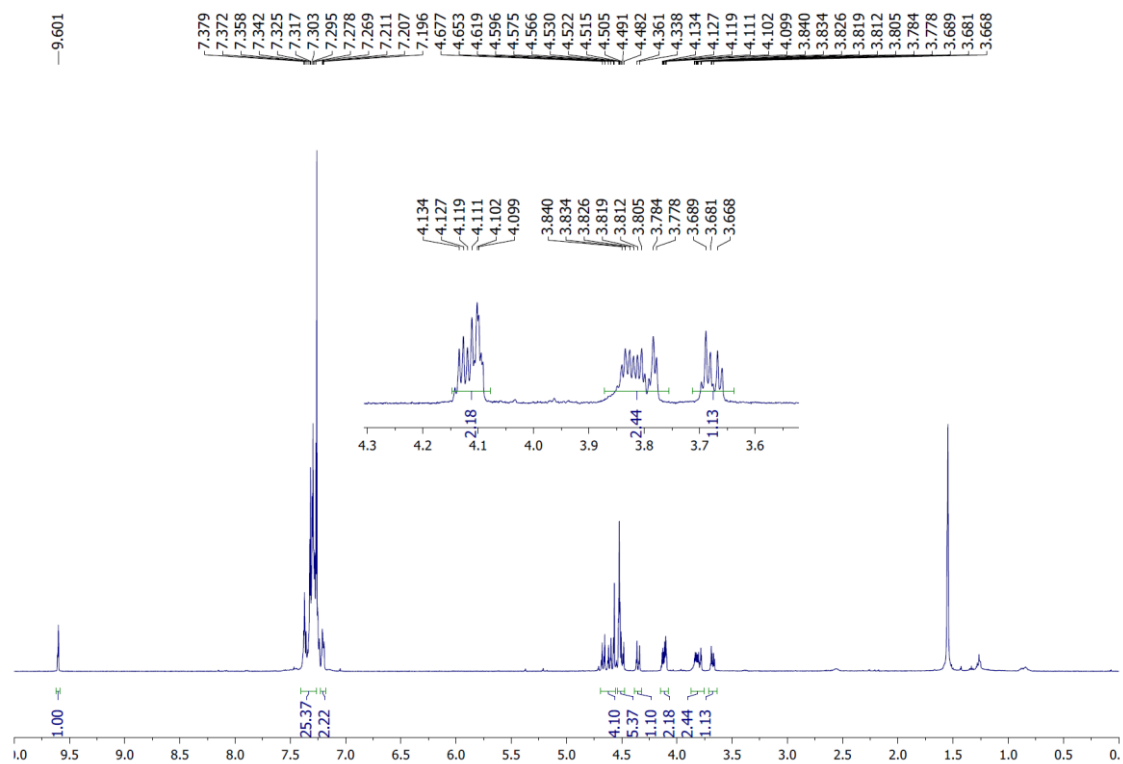
2,3,4,5-Tetra-*O*-benzyl aldehydo *D*-arabinose (**2a**).



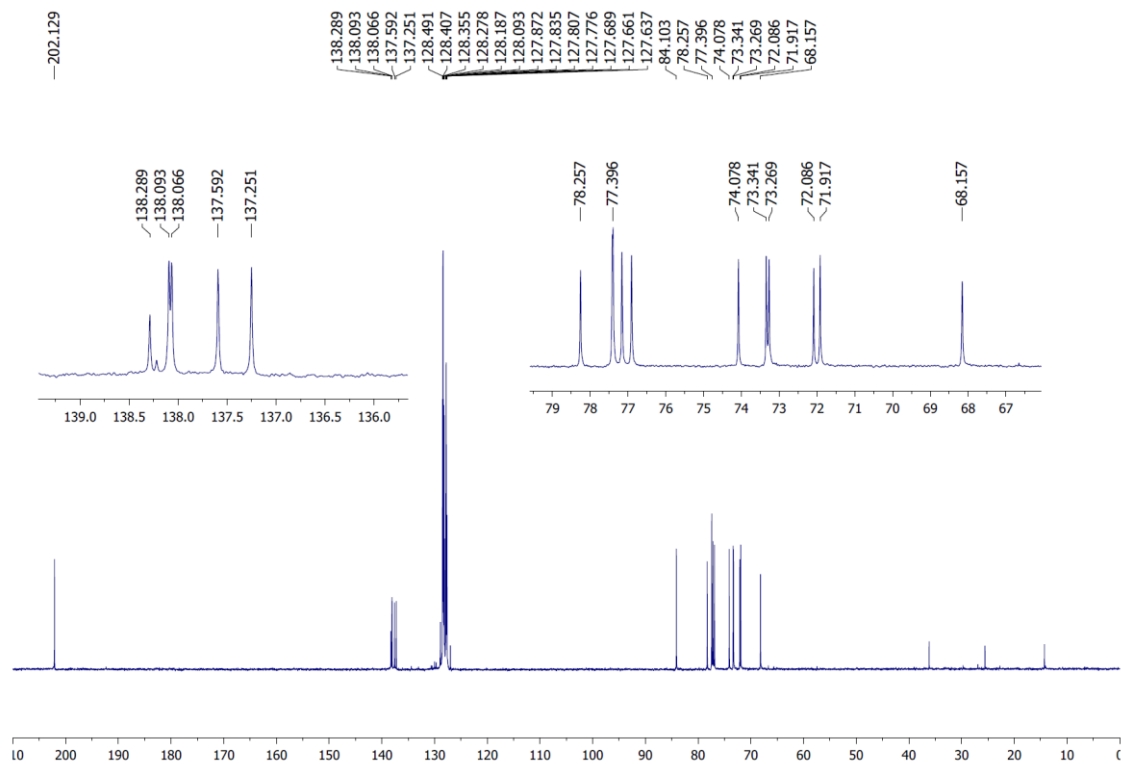
2,3,4,5-Tetra-*O*-benzyl diethyl dithioacetal *D*-arabinose **1a** (11.14 g, 43.2 mmol) was dissolved in an acetone/water mixture (4/1, 440 ml). Sodium bicarbonate (8.0 g, 95 mmol, 2.2 equiv.) and iodine (24.1 g, 95 mmol, 2.2 equiv.) were subsequently added at r.t. The mixture was stirred vigorously for 1h at room temperature. Then, saturated solution of sodium bicarbonate (100 ml) and saturated solution of sodium thiosulfate (100 ml) were added and acetone was removed under reduced pressure. The mixture was dissolved in Et<sub>2</sub>O, saturated solution of sodium thiosulfate (100 ml) was added and the solution was stirred for 15 min. (until formation of a clear solution). The aqueous phase was extracted with Et<sub>2</sub>O and the combined organic layer were washed with brine (2 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 95:5) gave compound **2a** (74.4 g, 81%) as a colorless oil.

$[\alpha]_{\text{D}}^{20}$ : -2.6 (*c* 0.9, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 9.60 (d, 1H, *J*<sub>1-2</sub> = 1.4 Hz, H-1), 7.32-7.26 (m, 18H, H<sup>arom</sup>), 7.21-7.19 (m, 2H, H<sup>arom</sup>), 4.67 (AB, 1H, *J*<sub>A-B</sub> = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.61 (AB, 1H, *J*<sub>A-B</sub> = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.53-4.8 (m, 5H, CH<sub>2</sub><sup>Bn</sup>), 4.35 (AB, 1H, *J*<sub>A-B</sub> = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.14-4.09 (m, 2H, H-2, H-3), 3.84-3.78 (m, 2H, H-4, H-5<sub>a</sub>), 3.67 (ABX, 1H, *J*<sub>4-5b</sub> = 3.9 Hz, *J*<sub>5a-5b</sub> = 10.5 Hz, H-5<sub>b</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 202.3 (C-1), 138.2 (2 C<sub>q</sub><sup>arom</sup>), 137.7 (C<sub>q</sub><sup>arom</sup>), 137.4 (C<sub>q</sub><sup>arom</sup>), 128.6-127.8 (CH<sup>arom</sup>), 84.2 (C-2), 78.4 (C-3), 77.5 (C-4), 74.2 (CH<sub>2</sub><sup>Bn</sup>), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 73.4 (CH<sub>2</sub><sup>Bn</sup>), 72.1 (CH<sub>2</sub><sup>Bn</sup>), 68.3 (C-5) ppm. HRMS (ESI<sup>+</sup>): *m/z* calculated for C<sub>33</sub>H<sub>34</sub>O<sub>5</sub>Na [M+Na]<sup>+</sup>: calc. 533.2298; found: 533.2291.

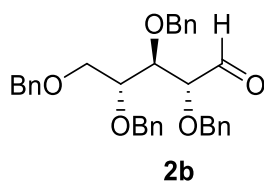
# <sup>1</sup>H NMR



# <sup>13</sup>C NMR



*2,3,4,5-Tetra-O-benzyl aldehydo D-ribose (2b).*

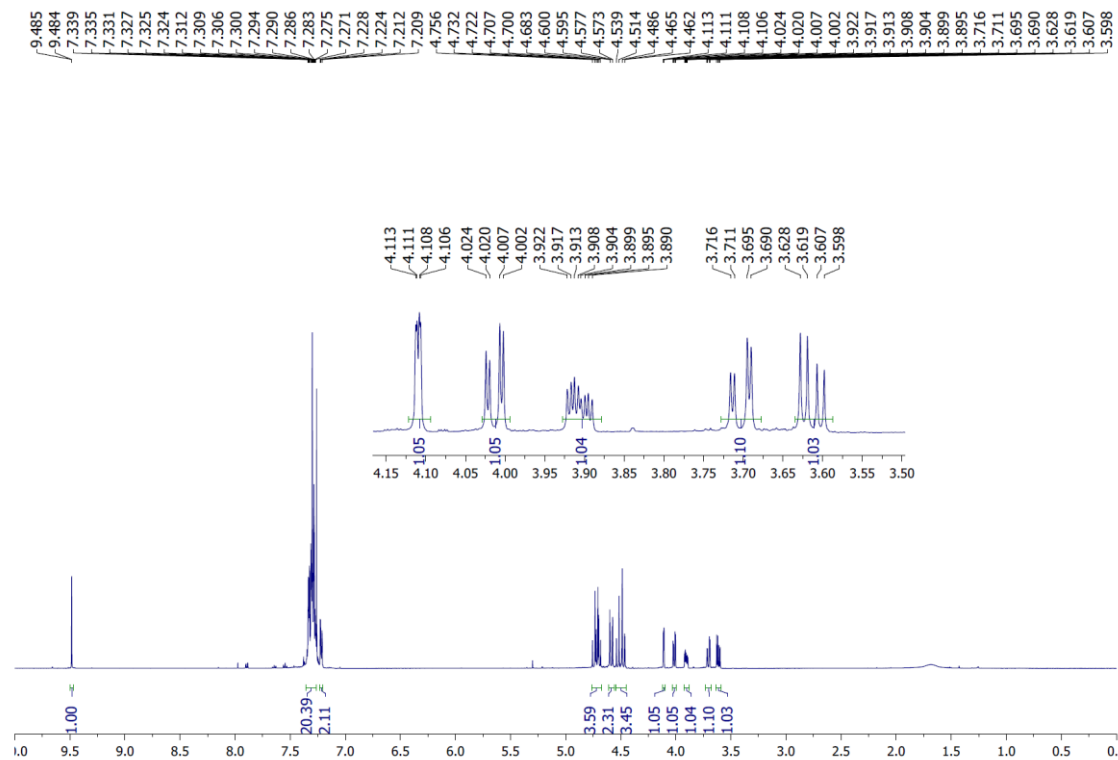


2,3,4,5-Tetra-O-benzyl diethyl dithioacetal D-ribose **1b** (1.7 g, 2.76 mmol) was dissolved in an acetone/water mixture (4/1, 28 ml). Sodium bicarbonate (510 mg, 6.07 mmol, 2.2 equiv.) and iodine (1.54 g, 6.07 mmol, 2.2 equiv.) were subsequently added at r.t. The mixture was stirred vigorously for 1h at room temperature. Then, saturated solution of sodium bicarbonate (8 ml) and saturated solution of sodium thiosulfate (8 ml) were added and acetone was removed under reduced pressure. The mixture was dissolved in Et<sub>2</sub>O, saturated solution of sodium thiosulfate (10 ml) was added and the solution was stirred for 15 min. (until formation of a clear solution). The aqueous phase was extracted with Et<sub>2</sub>O and the combined organic layer were washed with brine (2 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 95:5) gave compound **2b** (1.037 g, 74%) as a colorless oil.

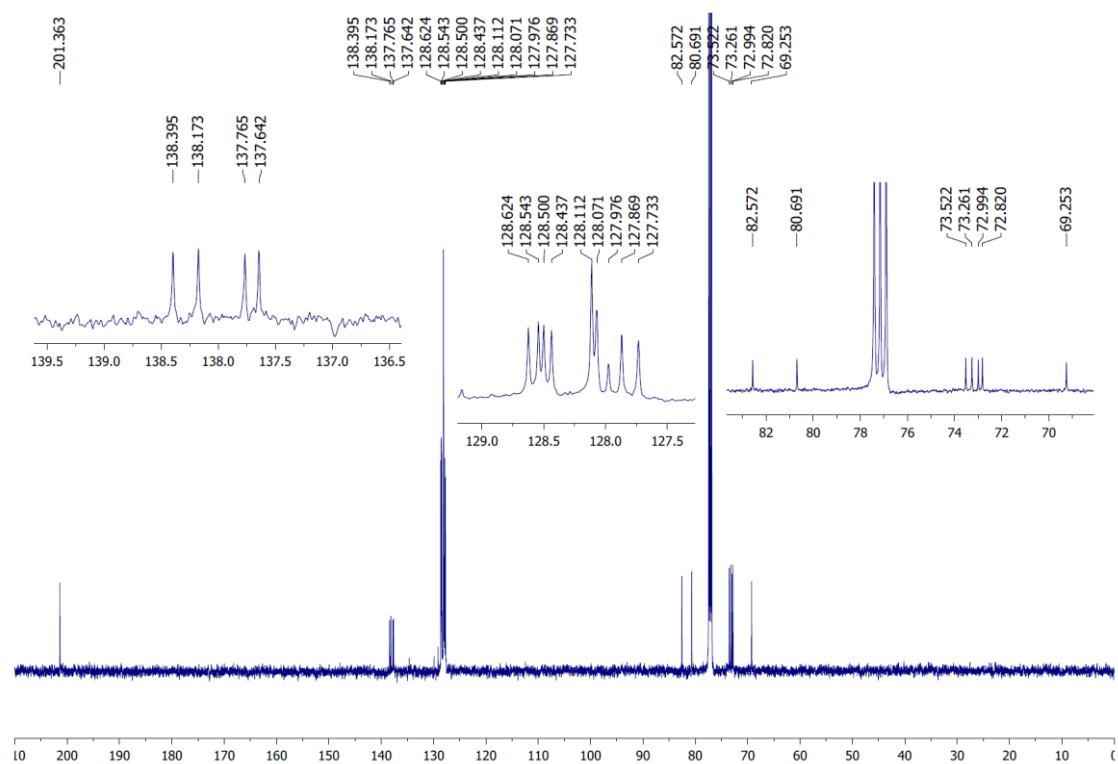
$[\alpha]_{20}^D$ : +20.4 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 9.48 (d, 1H,  $J_{1-2}$  = 0.9 Hz, H-1), 7.35-7.27 (m, 18H, H<sup>arom</sup>), 7.23-7.21 (m, 2H, H<sup>arom</sup>), 4.74 (AB, 1H,  $J_{A-B}$  = 12.1 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.71 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.69 (AB, 1H,  $J_{A-B}$  = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.60 (bs, 1H, CH<sub>2</sub><sup>Bn</sup>), 4.57 (bs, 1H, CH<sub>2</sub><sup>Bn</sup>), 4.52 (AB, 1H,  $J_{A-B}$  = 12.1 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.48 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.47 (AB, 1H,  $J_{A-B}$  = 12.1 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.11 (dd, 1H,  $J_{1-2}$  = 0.9 Hz,  $J_{2-3}$  = 2.2 Hz, H-2), 4.01 (dd, 1H,  $J_{2-3}$  = 2.2 Hz,  $J_{3-4}$  = 8.6 Hz, H-3), 3.92-3.88 (ddd, 1H,  $J_{3-4}$  = 8.6 Hz,  $J_{4-5a}$  = 2.5 Hz,  $J_{4-5b}$  = 4.4 Hz, H-4), 3.70 (ABX, 1H,  $J_{4-5a}$  = 2.5 Hz,  $J_{5a-5b}$  = 10.5 Hz, H-5a), 3.61 (ABX, 1H,  $J_{4-5b}$  = 4.4 Hz,  $J_{5a-5b}$  = 10.5 Hz, H-5b) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 201.3 (C-1), 138.4 (C<sub>q</sub><sup>arom</sup>), 138.2 (C<sub>q</sub><sup>arom</sup>), 137.8 (C<sub>q</sub><sup>arom</sup>), 137.6 (C<sub>q</sub><sup>arom</sup>), 128.6-127.7 (CH<sup>arom</sup>), 82.6 (C-2), 80.7 (C-3), 76.8 (C-4), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 73.3 (CH<sub>2</sub><sup>Bn</sup>), 73.0 (CH<sub>2</sub><sup>Bn</sup>), 72.8 (CH<sub>2</sub><sup>Bn</sup>), 69.3 (C-5) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for C<sub>33</sub>H<sub>34</sub>O<sub>5</sub>K [M+K]<sup>+</sup>: calc. 549.2038; found: 549.2039.



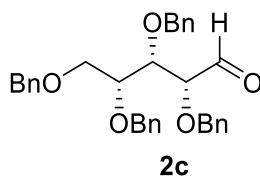
# <sup>1</sup>H NMR



# <sup>13</sup>C NMR



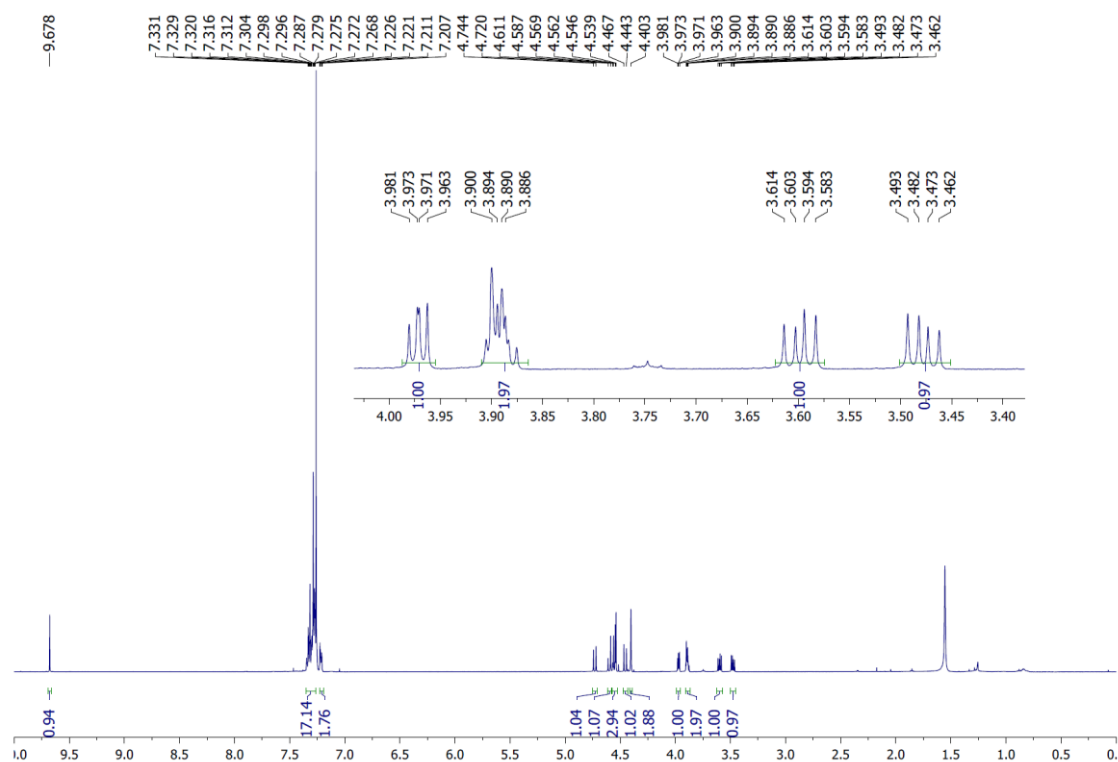
2,3,4,5-Tetra-O-benzyl aldehydo D-xylose (**2c**).



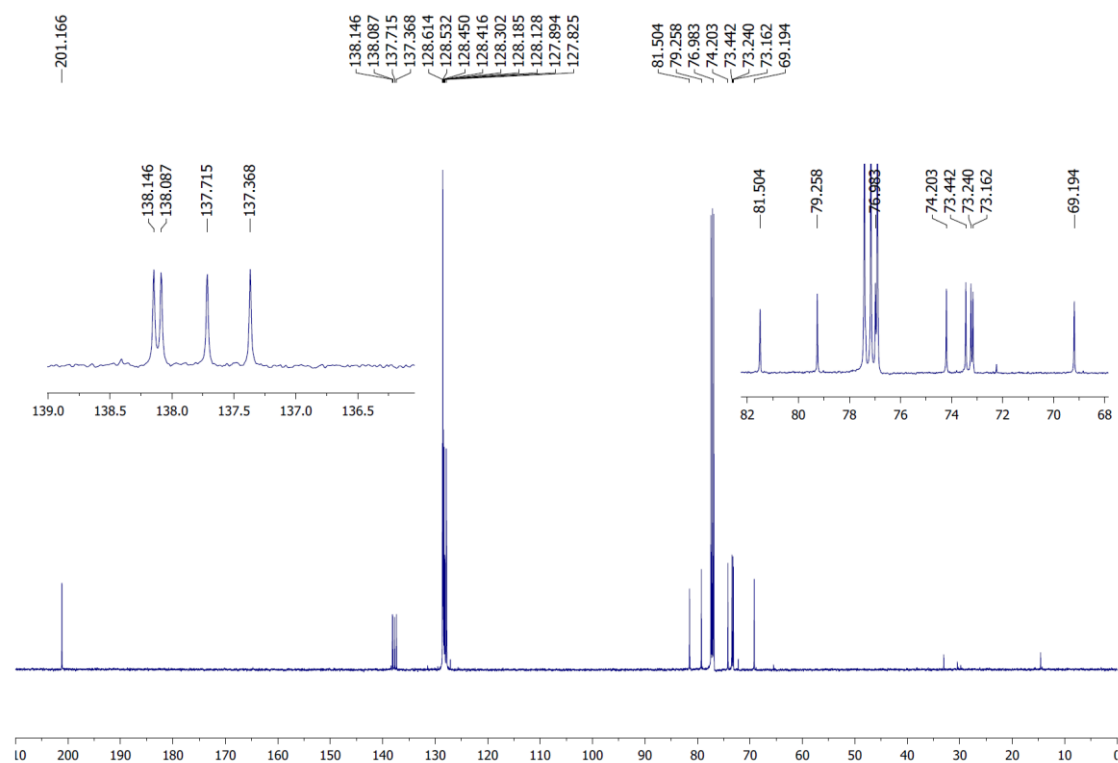
2,3,4,5-Tetra-O-benzyl diethyl dithioacetal D-xylose **1c** (530 mg, 0.856 mmol) was dissolved in an acetone/water mixture (4/1, 15 ml). Sodium bicarbonate (158 mg, 1.884 mmol, 2.2 equiv.) and iodine (478 mg, 1.884 mmol, 2.2 equiv.) were subsequently added at r.t. The mixture was stirred vigorously for 1h at room temperature. Then, saturated solution of sodium bicarbonate (8 ml) and saturated solution of sodium thiosulfate (8 ml) were added and acetone was removed under reduced pressure. The mixture was dissolved in Et<sub>2</sub>O, saturated solution of sodium thiosulfate (10 ml) was added and the solution was stirred for 15 min. (until formation of a clear solution). The aqueous phase was extracted with Et<sub>2</sub>O and the combined organic layer were washed with brine (2 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 95:5) gave compound **2b** (284 mg, 65%) as a colorless oil.

[ $\alpha$ ]<sub>D</sub><sup>20</sup>: +7.7 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 9.68 (s, 1H, H-1), 7.35-7.26 (m, 18H, H<sup>arom</sup>), 7.23-7.20 (m, 2H, H<sup>arom</sup>), 4.73 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.60 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.56 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.55 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.53 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.46 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.41 (AB, 1H,  $J_{A-B}$  = 12.6 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.39 (AB, 1H,  $J_{A-B}$  = 12.6 Hz, CH<sub>2</sub><sup>Bn</sup>), 3.97 (dd, 1H,  $J_{2-3}$  = 4.0 Hz,  $J_{3-4}$  = 4.6 Hz, H-3), 3.91-3.3.87 (m, 2H, H-2, H-4), 3.60 (ABX, 1H,  $J_{4-5a}$  = 5.7 Hz,  $J_{5a-5b}$  = 9.7 Hz, H-5a), 3.48 (ABX, 1H,  $J_{4-5b}$  = 5.2 Hz,  $J_{5a-5b}$  = 9.7 Hz, H-5b) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 201.2 (C-1), 138.2 (C<sub>q</sub><sup>arom</sup>), 138.1 (C<sub>q</sub><sup>arom</sup>), 137.7 (C<sub>q</sub><sup>arom</sup>), 137.4 (C<sub>q</sub><sup>arom</sup>), 128.7-127.8 (CH<sup>arom</sup>), 81.5 (C-2), 79.3 (C-3), 77.0 (C-4), 74.2 (CH<sub>2</sub><sup>Bn</sup>), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 73.2 (2 CH<sub>2</sub><sup>Bn</sup>), 69.2 (C-5) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for C<sub>33</sub>H<sub>34</sub>O<sub>5</sub>K [M+K]<sup>+</sup>: calc. 549.2038; found: 549.2040.

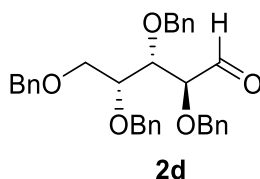
# <sup>1</sup>H NMR



# <sup>13</sup>C NMR



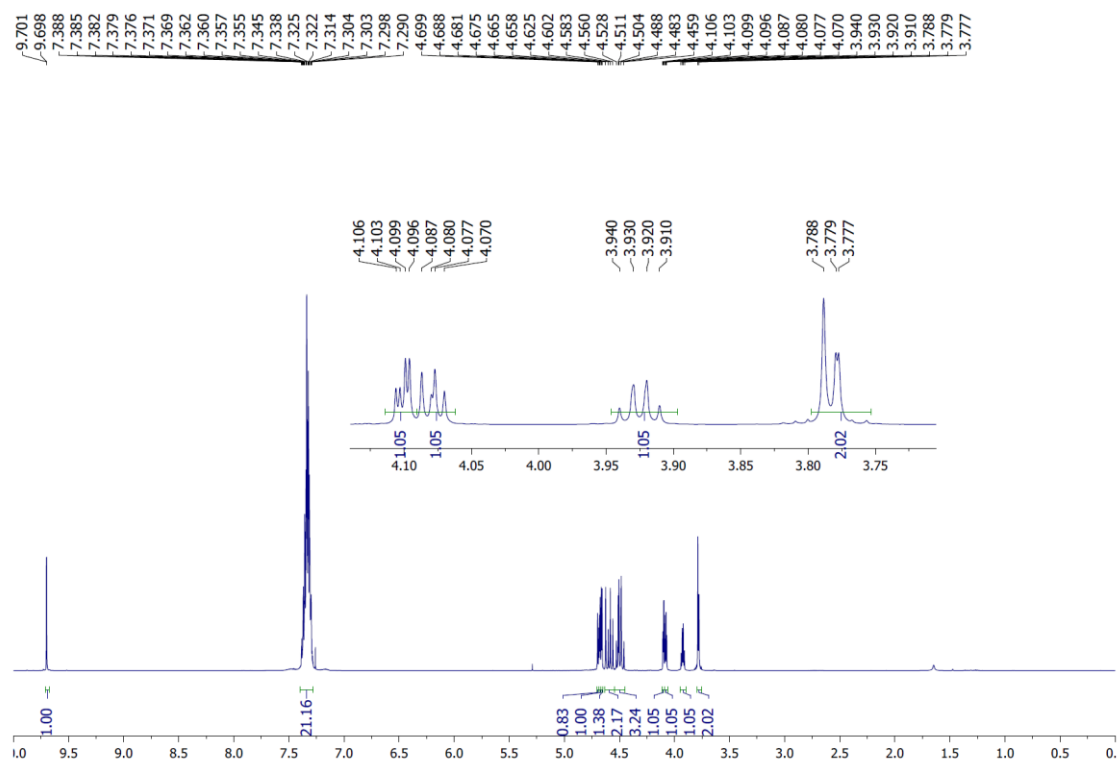
*2,3,4,5-Tetra-O-benzyl aldehydo D-lyxose (2d).*



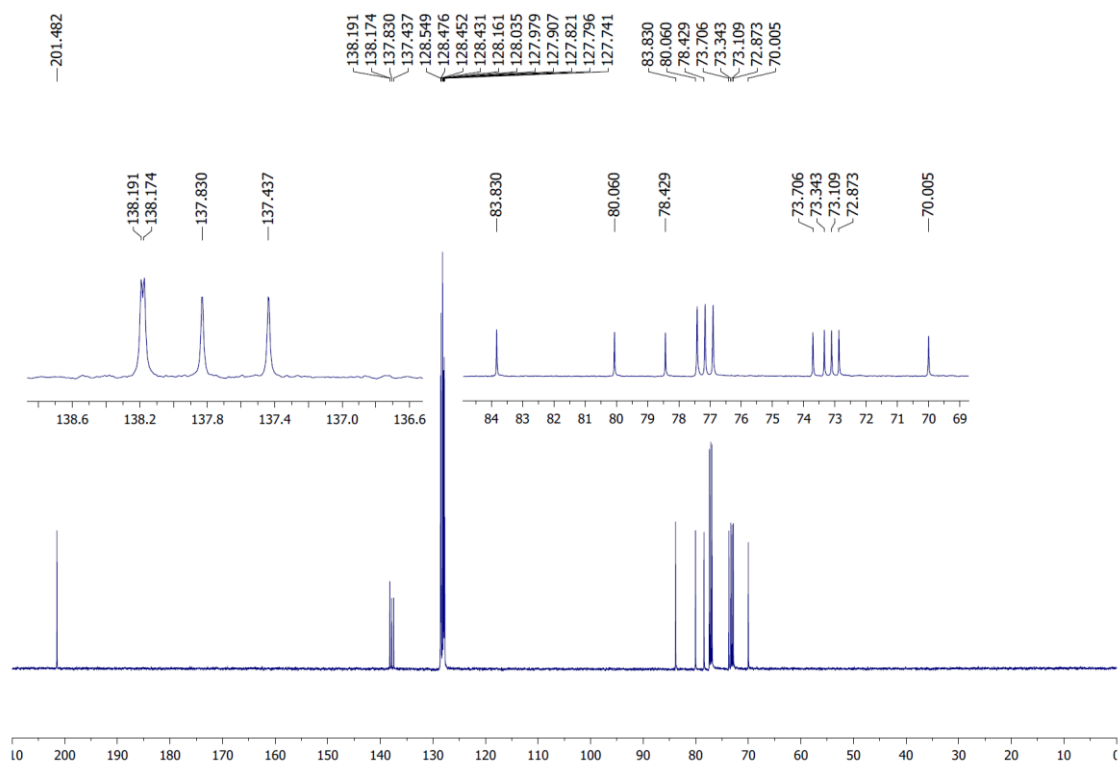
2,3,4,5-Tetra-O-benzyl diethyl dithioacetal D-lyxose **1d** (2.619 g, 4.25 mmol) was dissolved in an acetone/water mixture (4/1, 43 ml). Sodium bicarbonate (786 mg, 9.35 mmol, 2.2 equiv.) and iodine (2.37 g, 9.35 mmol, 2.2 equiv.) were subsequently added at r.t. The mixture was stirred vigorously for 2h30 at room temperature. Then, saturated solution of sodium bicarbonate (10 ml) and saturated solution of sodium thiosulfate (10 ml) were added and acetone was removed under reduced pressure. The mixture was dissolved in Et<sub>2</sub>O, saturated solution of sodium thiosulfate (10 ml) was added and the solution was stirred for 15 min. (until formation of a clear solution). The aqueous phase was extracted with Et<sub>2</sub>O and the combined organic layer were washed with brine (2 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. The crude was purified by flash chromatography on silica gel (Cy/EtOAc 92:8) to provide 2,3,4,5-tetra-O-benzyl-aldehydo-D-lyxose **2d** as a colorless oil (1.492 g, 69%).

[ $\alpha$ ]<sub>D</sub><sup>20</sup>: -15.0 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 9.70 (d,  $J_{1-2}$  = 1.5 Hz, 1H, H-1), 7.39-7.28 (m, 20H, H<sup>arom</sup>), 4.69 (AB, 1H,  $J_{A-B}$  = 11.8 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.68 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.67 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.61 (AB, 1H,  $J_{A-B}$  = 11.6 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.57 (AB, 1H,  $J_{A-B}$  = 11.8 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.52 (AB, 1H,  $J_{A-B}$  = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.50 (AB, 1H,  $J_{A-B}$  = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.47 (AB, 1H,  $J_{A-B}$  = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.10 (dd,  $J_{2-3}$  = 3.5,  $J_{1-2}$  = 1.5 Hz, 1H, H-2), 4.08 (dd,  $J_{3-4}$  = 4.9,  $J_{2-3}$  = 3.6 Hz, H-3), 3.92 (q, 1H,  $J_{3-4}$  = 5.0 Hz, H-4), 3.79 (s, 1H, H-5), 3.78 (d, 1H,  $J_{5a-5b}$  = 1.0 Hz, H-5) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 201.5 (C-1), 138.19 (C<sub>q</sub><sup>arom</sup>), 138.17 (C<sub>q</sub><sup>arom</sup>), 137.8 (C<sub>q</sub><sup>arom</sup>), 137.4 (C<sub>q</sub><sup>arom</sup>), 128.5 (CH<sup>arom</sup>), 128.55 (CH<sup>arom</sup>), 128.48 (CH<sup>arom</sup>), 128.45 (CH<sup>arom</sup>), 128.4 (CH<sup>arom</sup>), 128.2 (2 CH<sup>arom</sup>), 128.04 (CH<sup>arom</sup>), 127.97 (CH<sup>arom</sup>), 127.9 (CH<sup>arom</sup>), 127.82 (CH<sup>arom</sup>), 127.80 (CH<sup>arom</sup>), 127.7 (CH<sup>arom</sup>), 83.8 (C-2), 80.1 (C-3), 78.4 (C-4), 73.7 (CH<sub>2</sub><sup>Bn</sup>), 73.3 (CH<sub>2</sub><sup>Bn</sup>), 73.1 (CH<sub>2</sub><sup>Bn</sup>), 72.9 (CH<sub>2</sub><sup>Bn</sup>), 70.0 (C-5) ppm. HRMS (ESI+): m/z calculated for C<sub>33</sub>H<sub>34</sub>O<sub>5</sub>Na [M+Na]<sup>+</sup>: calc. 533.2298; found: 533.2297.

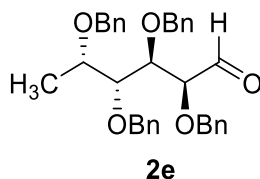
# <sup>1</sup>H NMR



# <sup>13</sup>C NMR



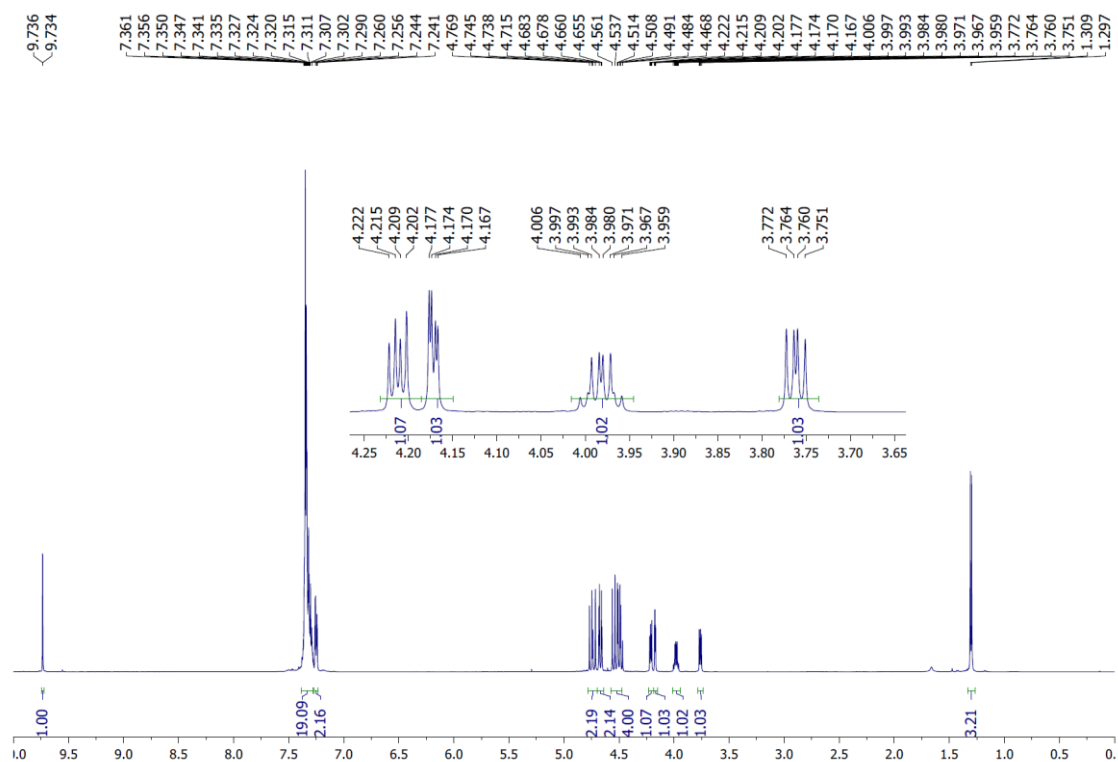
*2,3,4,5-Tetra-O-benzyl aldehydo L-fucose (2e).*



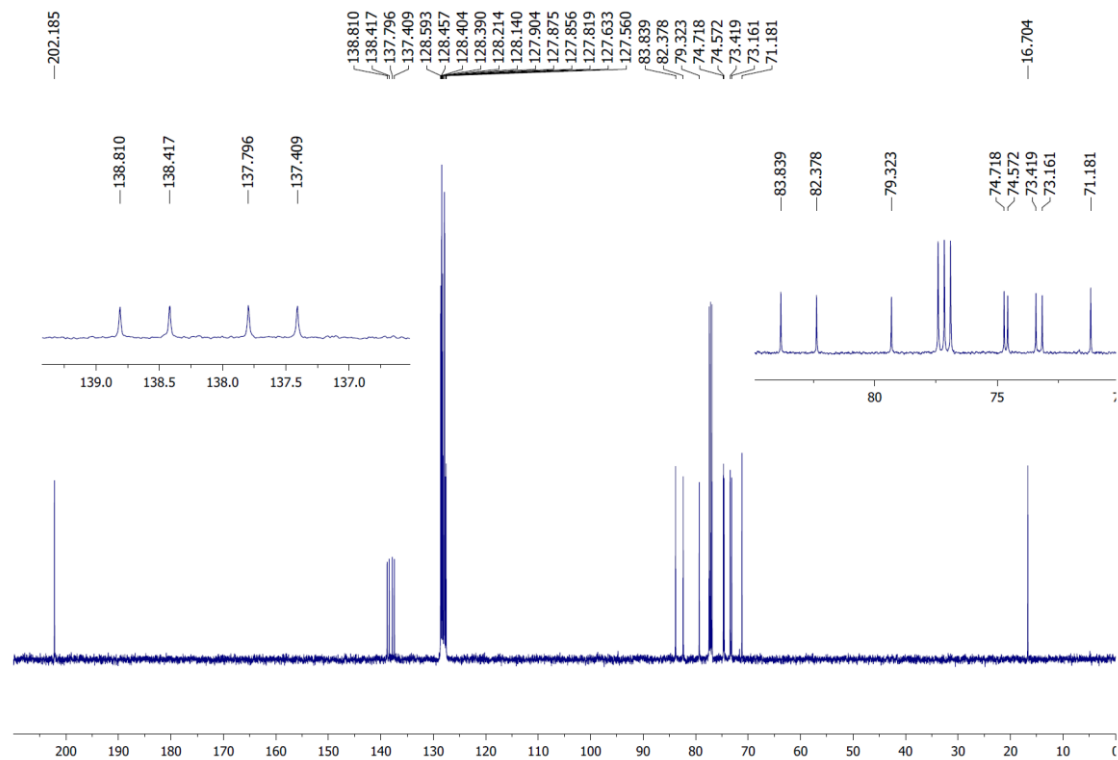
2,3,4,5-Tetra-O-benzyl diethyl dithioacetal L-fucose **1e** (1.755 g, 2.78 mmol) was dissolved in an acetone/water mixture (4/1, 28 ml). Sodium bicarbonate (514 mg, 5.56 mmol, 2.2 equiv.) and iodine (1.55 g, 5.56 mmol, 2.2 equiv.) were subsequently added at r.t. The mixture was stirred vigorously for 3h30 at room temperature. Then, saturated solution of sodium bicarbonate (10 ml) and saturated solution of sodium thiosulfate (10 ml) were added and acetone was removed under reduced pressure. The mixture was dissolved in Et<sub>2</sub>O, saturated solution of sodium thiosulfate (10 ml) was added and the solution was stirred for 15 min. (until formation of a clear solution). The aqueous phase was extracted with Et<sub>2</sub>O and the combined organic layer were washed with brine (2 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. The crude was purified by flash chromatography on silica gel (Cy/EtOAc 92:8) to provide 2,3,4,5-tetra-O-benzyl-aldehydo-L-fucose **2e** as a white solid (949 mg, 65%).

$[\alpha]_{20}^D$ : -12.1 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 9.74 (d,  $J_{1-2}$  = 1.4 Hz, 1H, H-1), 7.37-7.28 (m, 18H, H<sup>arom</sup>), 7.27-7.24 (m, 2H, H<sup>arom</sup>), 4.76 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.73 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.670 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.668 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.55 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.53 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.500 (AB, 1H,  $J_{A-B}$  = 11.6 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.497 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.21 (dd, 1H,  $J$  = 6.4,  $J_{2-3}$  = 3.6 Hz, H-3), 4.17 (dd, 1H,  $J_{2-3}$  = 3.6,  $J_{1-2}$  = 1.4 Hz, H-2), 3.98 (qd, 1H,  $J_{4-5}$  = 6.4,  $J_{5-6}$  = 4.4 Hz, H-5), 3.76 (dd, 1H,  $J_{3-4}$  = 6.4,  $J_{4-5}$  = 4.3 Hz, H-4), 1.30 (d, 3H,  $J_{5-6}$  = 6.4 Hz, H-6) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 202.2 (C-1), 138.8 (C<sub>q</sub><sup>arom</sup>), 138.4 (C<sub>q</sub><sup>arom</sup>), 137.8 (C<sub>q</sub><sup>arom</sup>), 137.4 (C<sub>q</sub><sup>arom</sup>), 128.6 (2 CH<sup>arom</sup>), 128.5 (2 CH<sup>arom</sup>), 128.40 (2 CH<sup>arom</sup>), 128.39 (2 CH<sup>arom</sup>), 128.2 (2 CH<sup>arom</sup>), 128.1 (CH<sup>arom</sup>), 127.90 (2 CH<sup>arom</sup>), 127.88 (CH<sup>arom</sup>), 127.86 (2 CH<sup>arom</sup>), 127.8 (2 CH<sup>arom</sup>), 127.63 (CH<sup>arom</sup>), 127.56 (CH<sup>arom</sup>), 83.8 (C-2), 82.4 (C-4), 79.3 (C-3), 74.7 (C-5), 74.6 (CH<sub>2</sub><sup>Bn</sup>), 73.4 (CH<sub>2</sub><sup>Bn</sup>), 73.2 (CH<sub>2</sub><sup>Bn</sup>), 71.2 (CH<sub>2</sub><sup>Bn</sup>), 16.7 (C-6) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for C<sub>34</sub>H<sub>36</sub>O<sub>5</sub>Na [M+Na]<sup>+</sup>: calc. 547.2455; found: 547.2454.

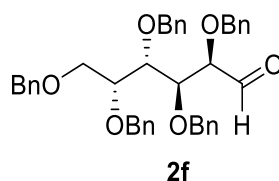
# <sup>1</sup>H NMR



# <sup>13</sup>C NMR



*2,3,4,5,6-Penta-O-benzyl aldehydo D-galactose (2f).*

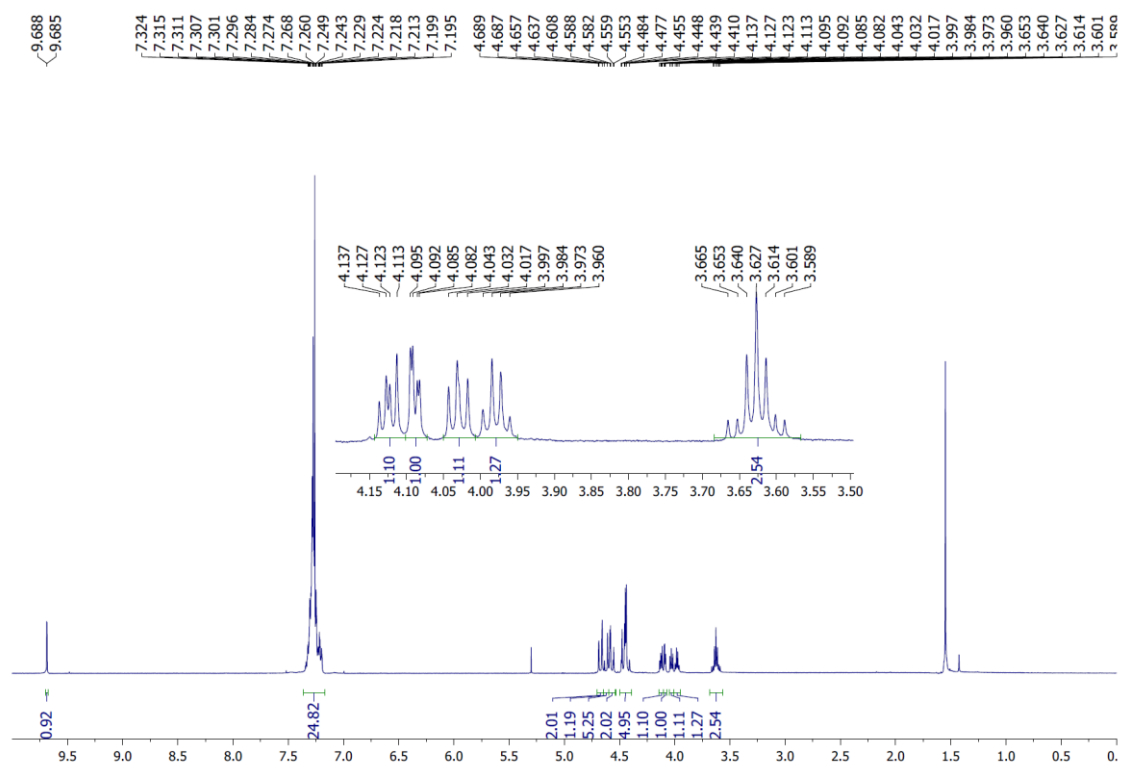


2,3,4,5,6-Penta-O-benzyl diethyl dithioacetal D-galactose **1f** (1.111 g, 1.507 mmol) was dissolved in an acetone/water mixture (4/1, 25 ml). Sodium bicarbonate (279 mg, 3.32 mmol, 2.2 equiv.) and iodine (843 mg, 3.32 mmol, 2.2 equiv.) were subsequently added at r.t. The mixture was stirred vigorously for 1h at room temperature. Then, saturated solution of sodium bicarbonate (10 ml) and saturated solution of sodium thiosulfate (10 ml) were added and acetone was removed under reduced pressure. The mixture was dissolved in Et<sub>2</sub>O, saturated solution of sodium thiosulfate (10 ml) was added and the solution was stirred for 15 min. (until formation of a clear solution). The aqueous phase was extracted with Et<sub>2</sub>O and the combined organic layer were washed with brine (2 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. The crude was purified by flash chromatography on silica gel (Cy/EtOAc 9:1) to provide 2,3,4,5,6-Penta-O-benzyl-aldehydo-D-galactose **2f** as a yellow oil (671 mg, 71%).

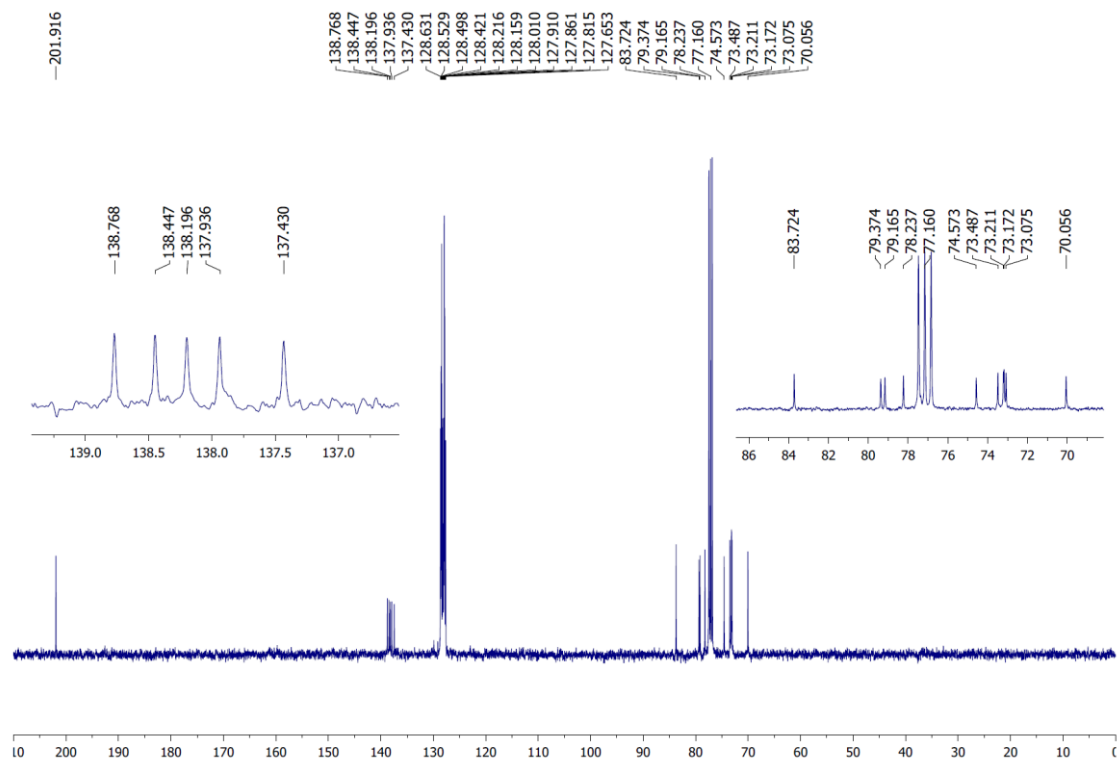
$[\alpha]_{\text{D}}^{20}$ : -0.3 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 9.69 (d, 1H,  $J_{1-2}$  = 1.2 Hz, H-1), 7.35-7.19 (m, 25H, H<sup>arom</sup>), 4.674 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.672 (AB, 1H,  $J_{\text{A-B}}$  = 11.8 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.62 (AB, 1H,  $J_{\text{A-B}}$  = 11.6 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.570 (AB, 1H,  $J_{\text{A-B}}$  = 11.6 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.568 (AB, 1H,  $J_{\text{A-B}}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.54 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.46 (AB, 2H,  $J_{\text{A-B}}$  = 11.8 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.42 (AB, 2H,  $J_{\text{A-B}}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.12 (dd, 1H,  $J_{3-4}$  = 5.7,  $J_{2-3}$  = 3.8 Hz, H-3), 4.09 (dd, 1H,  $J_{2-3}$  = 3.7,  $J_{1-2}$  = 1.2 Hz, H-2), 4.03 (dd, 1H,  $J_{3-4}$  = 5.7,  $J_{4-5}$  = 4.6 Hz, H-4), 3.98 (q, 1H,  $J_{4-5}$  = 4.9 Hz, H-5), 3.62 (dq, H,  $J_{6\text{a-}6\text{b}}$  = 10.0,  $J_{5-6}$  = 5.0 Hz, H-6) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 201.9 (C-1), 138.8 (C<sub>q</sub><sup>arom</sup>), 138.4 (C<sub>q</sub><sup>arom</sup>), 138.2 (C<sub>q</sub><sup>arom</sup>), 137.9 (C<sub>q</sub><sup>arom</sup>), 137.4 (C<sub>q</sub><sup>arom</sup>), 128.6-127.6 (CH<sup>arom</sup>), 83.7 (C-2), 79.4 (C-3), 79.2 (C-4), 78.2 (C-5), 74.6 (CH<sub>2</sub><sup>Bn</sup>), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 73.21 (CH<sub>2</sub><sup>Bn</sup>), 73.17 (CH<sub>2</sub><sup>Bn</sup>), 73.1 (CH<sub>2</sub><sup>Bn</sup>), 70.1 (C-6) ppm. HRMS (ESI<sup>+</sup>):  $m/z$  calculated for C<sub>40</sub>H<sub>42</sub>O<sub>6</sub>Na [M+Na]<sup>+</sup>: calc. 653.2874; found : 653.2875.



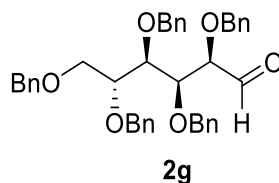
# <sup>1</sup>H NMR



# <sup>13</sup>C NMR



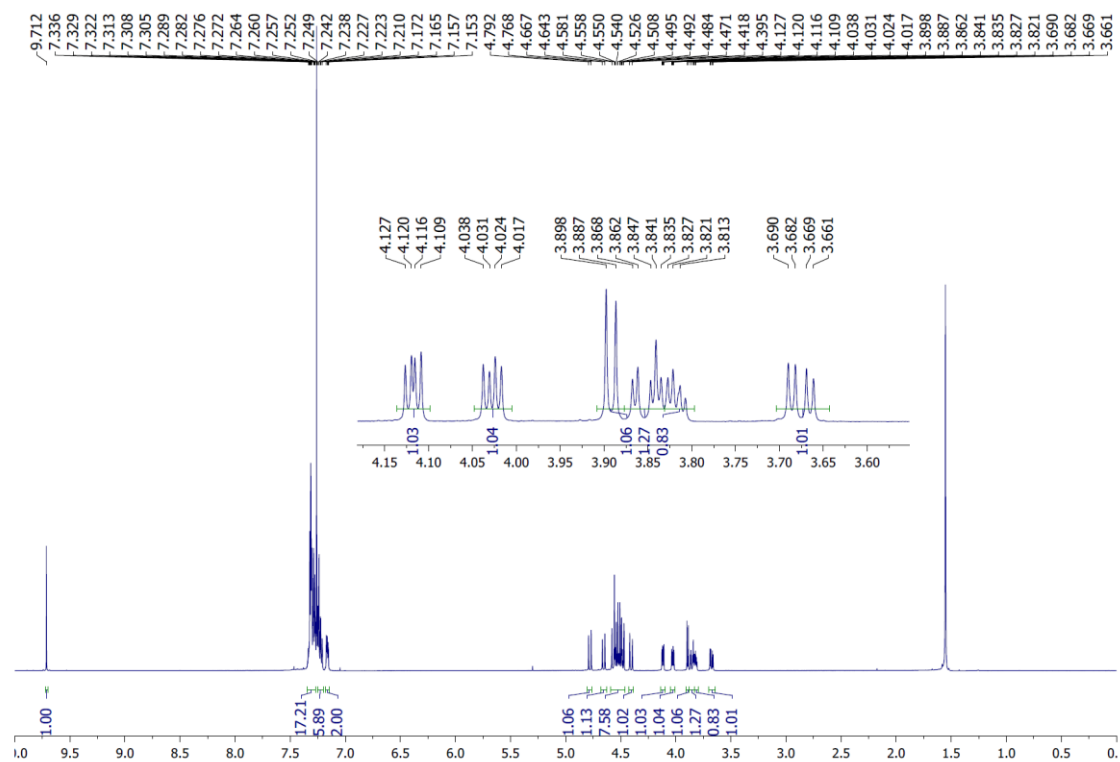
*2,3,4,5,6-Penta-O-benzyl aldehydo D-glucose (2g).*



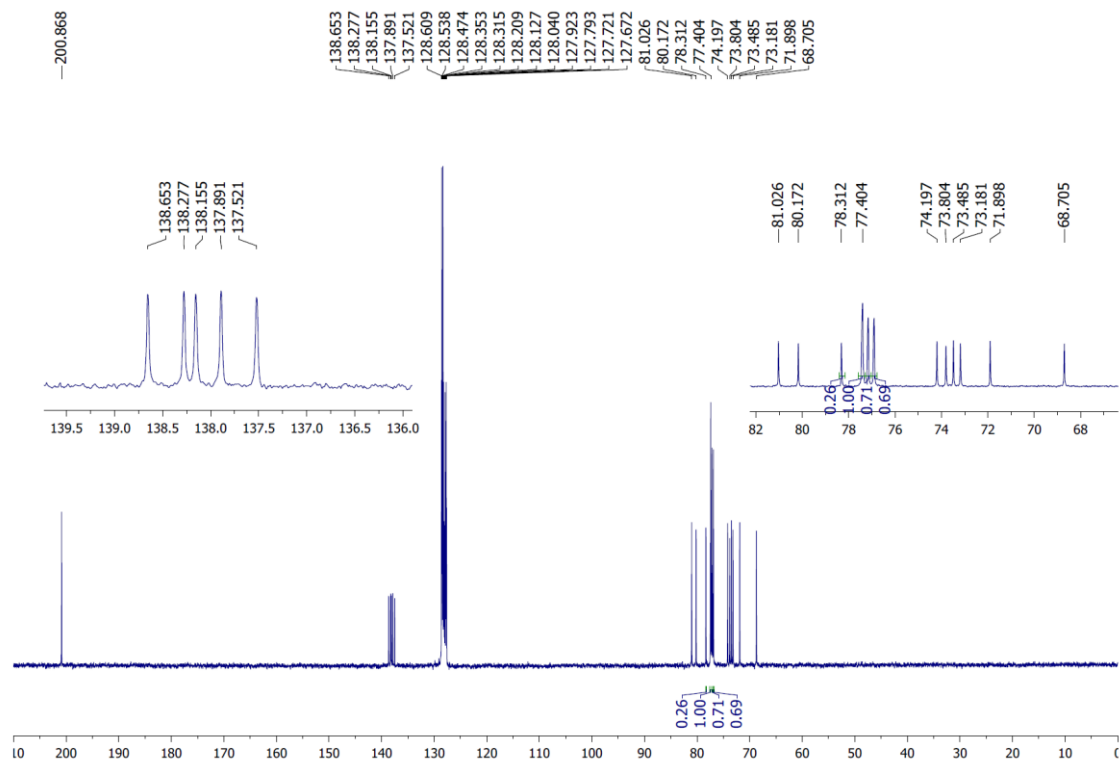
2,3,4,5,6-Penta-O-benzyl diethyl dithioacetal D-glucose **1g** (1.289 g, 1.749 mmol) was dissolved in an acetone/water mixture (4/1, 28 ml). Sodium bicarbonate (324 mg, 3.848 mmol, 2.2 equiv.) and iodine (977 mg, 3.848 mmol, 2.2 equiv.) were subsequently added at r.t. The mixture was stirred vigorously for 1h at room temperature. Then, saturated solution of sodium bicarbonate (10 ml) and saturated solution of sodium thiosulfate (10 ml) were added and acetone was removed under reduced pressure. The mixture was dissolved in Et<sub>2</sub>O, saturated solution of sodium thiosulfate (10 ml) was added and the solution was stirred for 15 min. (until formation of a clear solution). The aqueous phase was extracted with Et<sub>2</sub>O and the combined organic layer were washed with brine (2 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. The crude was purified by flash chromatography on silica gel (Cy/EtOAc 9:1) to provide 2,3,4,5,6-Penta-O-benzyl-aldehydo-D-glucose **2g** as a yellow oil (887 mg, 80%).

$[\alpha]_{20}^D$ : +2.8 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 9.71 (s, 1H, H-1), 7.34-7.20 (m, 23H, H<sup>arom</sup>), 7.18-7.15 (m, 2H, H<sup>arom</sup>), 4.78 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.65 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.59-4.46 (m, 7H, CH<sub>2</sub><sup>Bn</sup>), 4.41 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.12 (dd, 1H,  $J_{2-3}$  = 5.5,  $J_{3-4}$  = 3.5 Hz, H-3), 4.03 (dd, 1H,  $J_{4-5}$  = 6.8,  $J_{3-4}$  = 3.5 Hz, H-4), 3.89 (d, 1H,  $J_{2-3}$  = 5.5 Hz, H-2), 3.87-3.80 (m, 2H, H-6), 3.68 (dd, 1H,  $J_{5-6}$  = 10.4,  $J_{4-5}$  = 4.0 Hz, H-5) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 200.9 (C-1), 138.7 (C<sub>q</sub><sup>arom</sup>), 138.3 (C<sub>q</sub><sup>arom</sup>), 138.2 (C<sub>q</sub><sup>arom</sup>), 137.9 (C<sub>q</sub><sup>arom</sup>), 137.5 (C<sub>q</sub><sup>arom</sup>), 128.6-127.7 (CH<sup>arom</sup>), 81.0 (C-2), 80.2 (C-5), 78.3 (C-3), 77.4 (C-4), 74.2 (CH<sub>2</sub><sup>Bn</sup>), 73.8 (CH<sub>2</sub><sup>Bn</sup>), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 73.2 (CH<sub>2</sub><sup>Bn</sup>), 68.7 (C-6) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for C<sub>40</sub>H<sub>42</sub>O<sub>6</sub>Na [M+Na]<sup>+</sup>: calc. 653.2874; found: 653.2872.

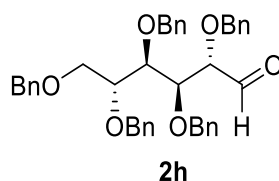
# <sup>1</sup>H NMR



# <sup>13</sup>C NMR



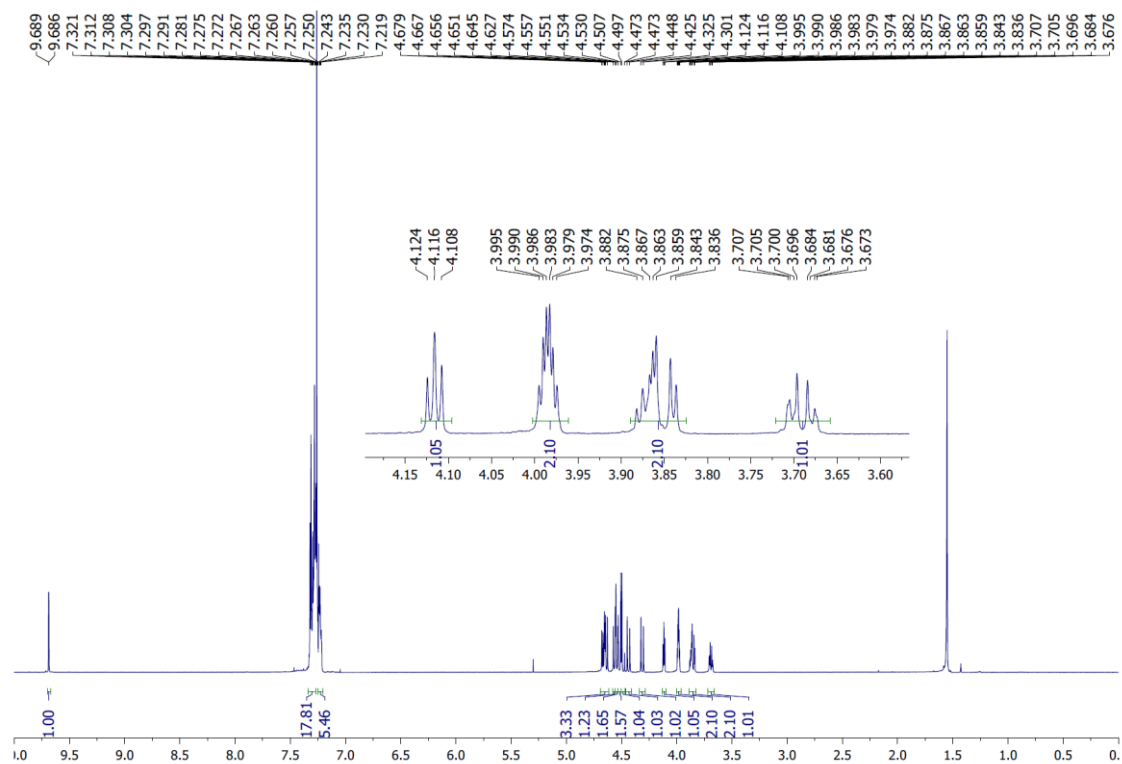
*2,3,4,5,6-Penta-O-benzyl aldehydo D-mannose (2h).*



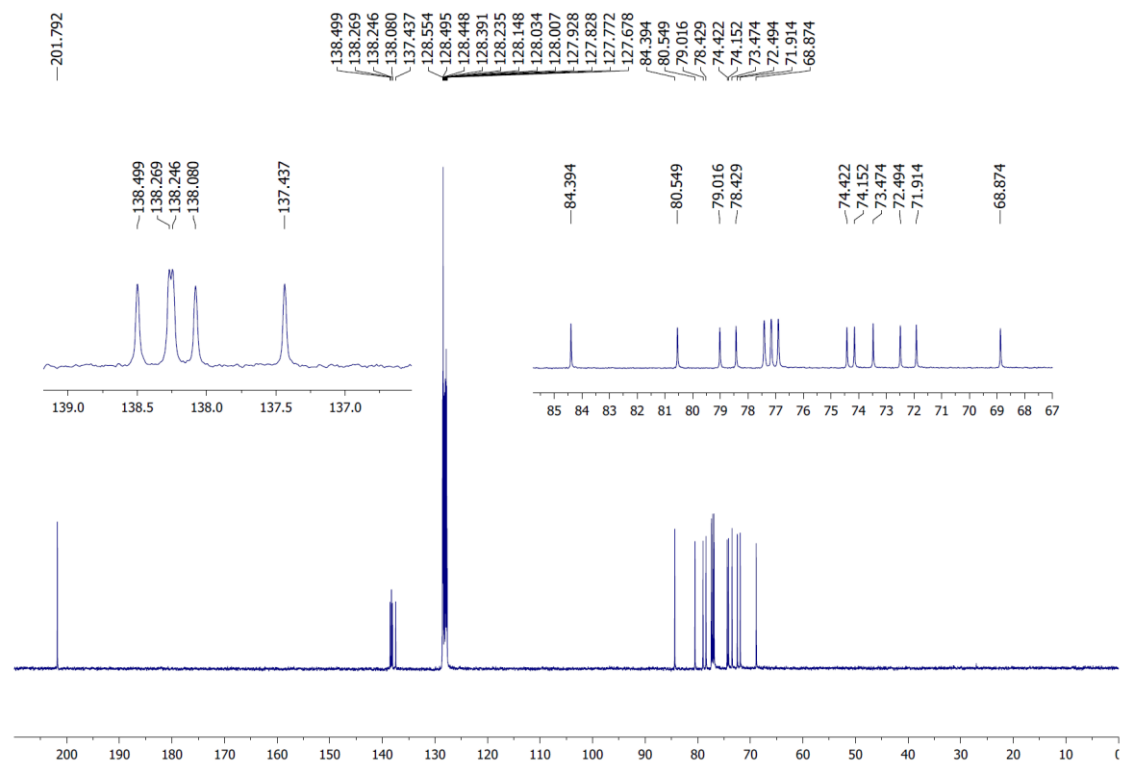
2,3,4,5,6-Penta-O-benzyl diethyl dithioacetal D-mannose **1h** (1.236 g, 1.677 mmol) was dissolved in an acetone/water mixture (4/1, 28 ml). Sodium bicarbonate (311 mg, 3.689 mmol, 2.2 equiv.) and iodine (939 mg, 3.689 mmol, 2.2 equiv.) were subsequently added at r.t. The mixture was stirred vigorously for 2h at room temperature. Then, saturated solution of sodium bicarbonate (10 ml) and saturated solution of sodium thiosulfate (10 ml) were added and acetone was removed under reduced pressure. The mixture was dissolved in Et<sub>2</sub>O, saturated solution of sodium thiosulfate (10 ml) was added and the solution was stirred for 15 min. (until formation of a clear solution). The aqueous phase was extracted with Et<sub>2</sub>O and the combined organic layer were washed with brine (2 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. The crude was purified by flash chromatography on silica gel (Cy/EtOAc 9:1) to provide 2,3,4,5,6-Penta-O-benzyl-aldehydo-D-mannose **2h** as a colorless oil (727 mg, 69%).

$[\alpha]_{20}^D$ : -4.6 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 9.69 (d, 1H,  $J$  = 1.8 Hz, H-1), 7.33-7.26 (m, 20H, H<sup>arom</sup>), 7.25-7.21 (m, 5H, H<sup>arom</sup>), 4.67 (AB, 1H,  $J_{A-B}$  = 5.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.65 (AB, 1H,  $J_{A-B}$  = 5.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.64 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.57 (AB, 1H,  $J_{A-B}$  = 8.2 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.54 (AB, 2H,  $J_{A-B}$  = 8.4 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.52 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.48 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.44 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.31 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.12 (t, 1H,  $J_{2-3}$  = 4.2 Hz, H-2), 3.98 (dq, 2H,  $J_{2-3}$  = 4.3,  $J_{3-4}$  = 2.4 Hz, H-3 and H-4), 3.89-3.83 (m, 2H, H-5 and H-6), 3.71-3.67 (m, 1H, H-6) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 201.8 (C-1), 138.5 (C<sub>q</sub><sup>arom</sup>), 138.3 (C<sub>q</sub><sup>arom</sup>), 138.2 (C<sub>q</sub><sup>arom</sup>), 138.1 (C<sub>q</sub><sup>arom</sup>), 137.4 (C<sub>q</sub><sup>arom</sup>), 128.5-127.7 (CH<sup>arom</sup>), 84.4 (C-3 or C-4), 80.5 (C-2), 79.0 (C-3 or C-4), 78.4 (C-5), 74.4 (CH<sub>2</sub><sup>Bn</sup>), 74.2 (CH<sub>2</sub><sup>Bn</sup>), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 72.5 (CH<sub>2</sub><sup>Bn</sup>), 71.9 (CH<sub>2</sub><sup>Bn</sup>), 68.9 (C-6) ppm. HRMS (ESI<sup>+</sup>):  $m/z$  calculated for C<sub>40</sub>H<sub>42</sub>O<sub>6</sub>Na [M+Na]<sup>+</sup>: calc. 653.2874; found: 653.2874.

# <sup>1</sup>H NMR



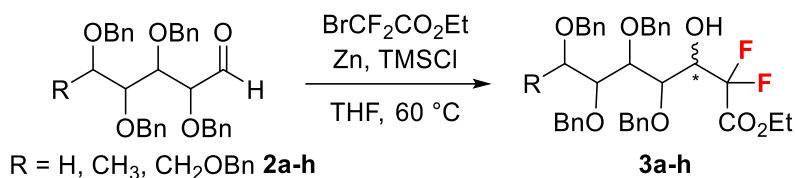
# <sup>13</sup>C NMR



## Reformatsky products

### General procedure Zinc activation

To a Buchner with two filter paper ( $\phi$  110 mm) was added zinc dust (100 g, 98+ %, < 10 microns). The solid was washed abundantly with HCl (10%, 500 ml) and triturated under the hood. Then, the solid was subsequently washed and triturated with H<sub>2</sub>O (500 ml), EtOH (500 ml) and Et<sub>2</sub>O (500 ml). The grey powder was dried and stored in the oven at 110°C.

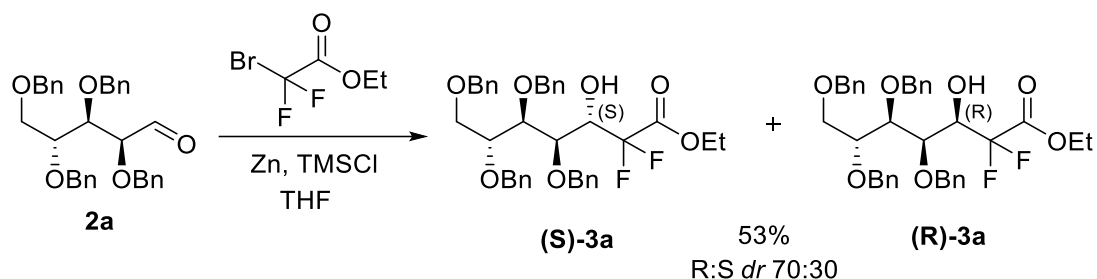


Sugar part	aldehyde	product, yield (%)	<i>dr</i> (%)
D-arabinose	<b>2a</b>	<b>3a</b> , 53	70:30
D-ribose	<b>2b</b>	<b>3b</b> , 47	75:25
D-xylose	<b>2c</b>	<b>3c</b> , 45	65:35 <sup>a</sup>
D-lyxose	<b>2d</b>	<b>3d</b> , 50	64:36 <sup>a</sup>
L-fucose	<b>2e</b>	<b>3e</b> , 43	43:57
D-galactose	<b>2f</b>	<b>3f</b> , 56	55:45
D-glucose	<b>2g</b>	<b>3g</b> , 60	69:31
D-mannose	<b>2h</b>	<b>3h</b> , 52	55:45

<sup>a</sup> Inseparable mixture by silica gel chromatography

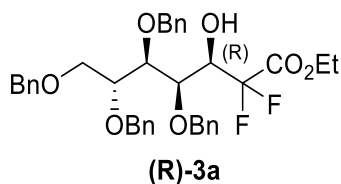
## D-Arabinose

Ethyl (1*R*/1*S*,2*R*,3*R*,4*R*)-2,3,4,5-tetra-*O*-benzyl-1',1'-difluoro-1-hydroxyheptanoate ((*R*/*S*)-**3a**).



To a dry two-necked round bottomed flask was added “activated zinc” powder (1.88 g, 28.77 mmol, 5.7 equiv.). The flask was heated up at 40°C and the zinc powder suspended in dry THF (15 ml) under argon atmosphere. Then, TMSCl (0.27 ml, 2.17 mmol, 0.4 equiv.) was added dropwise and the reaction was stirred at 60°C for 15 mins. Next, a solution of aldehyde **2a** (2.57 g, 5.04 mmol, 1.0 equiv.) and ethyl bromo-difluoroacetate (0.77 ml, 6.05 mmol, 1.2 equiv.) dissolved homogenously in dry THF (15 ml) under argon atmosphere was added dropwise at 60°C. The reaction was stirred vigorously for 1h at 60°C and then cooled at room temperature. Ice water (30 ml) and HCl (1M, 30 ml) were added and the mixture was diluted with EtOAc. The organic phase was washed with NaHCO<sub>3</sub>(sat) (2 times), brine, dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Crude NMR analysis showed the formation of two diastereoisomer (*R*)-**3a** and **3a**(*S*) in 70:30 *dr* ratio. Purification by silica gel chromatography (Cy/EtOAc 9:1) afforded pure diastereoisomer (*S*)-**3a** and an inseparable mixture of two diastereoisomers (*S*)-**3a** and (*R*)-**3a** in 89:11 *dr* ratio in 53% overall yield. Noteworthy, few milligrams (10 mg) of the diastereoisomer (*R*)-**3a** could be isolated and fully characterized.

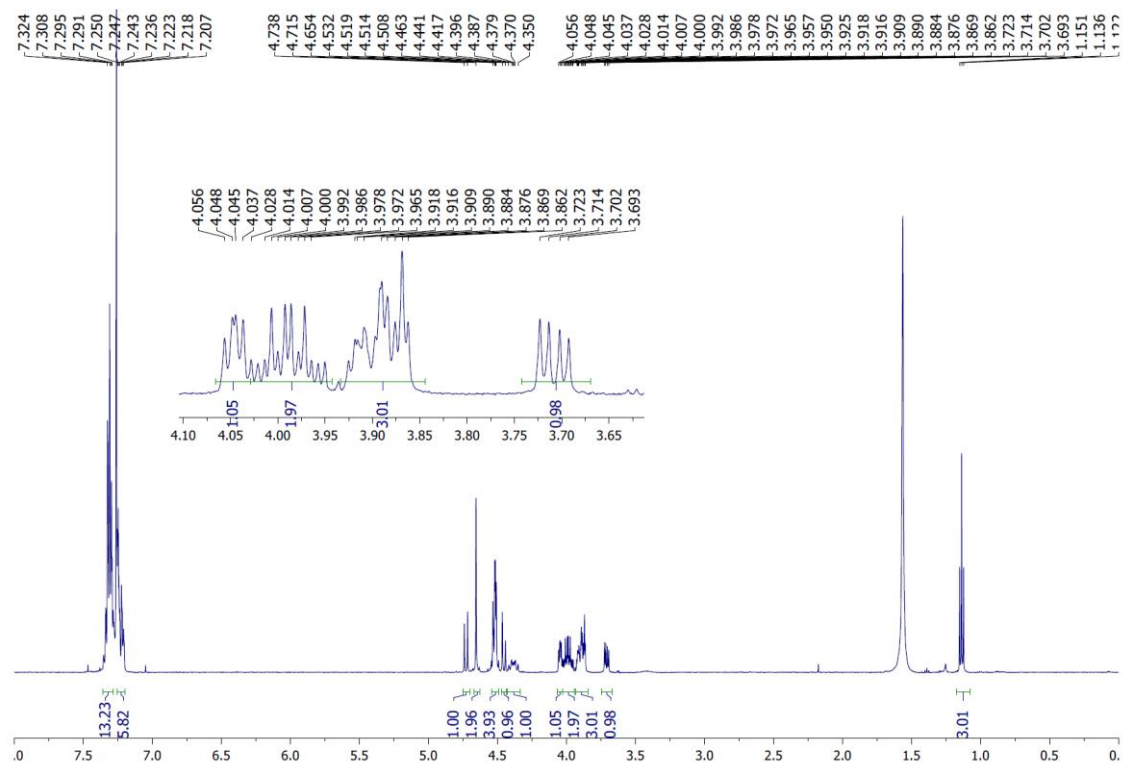
*Ethyl (1R,2R,3R,4R)-2,3,4,5-tetra-O-benzyl-1',1'-difluoro-1-hydroxyheptanoate ((R)-3a).*



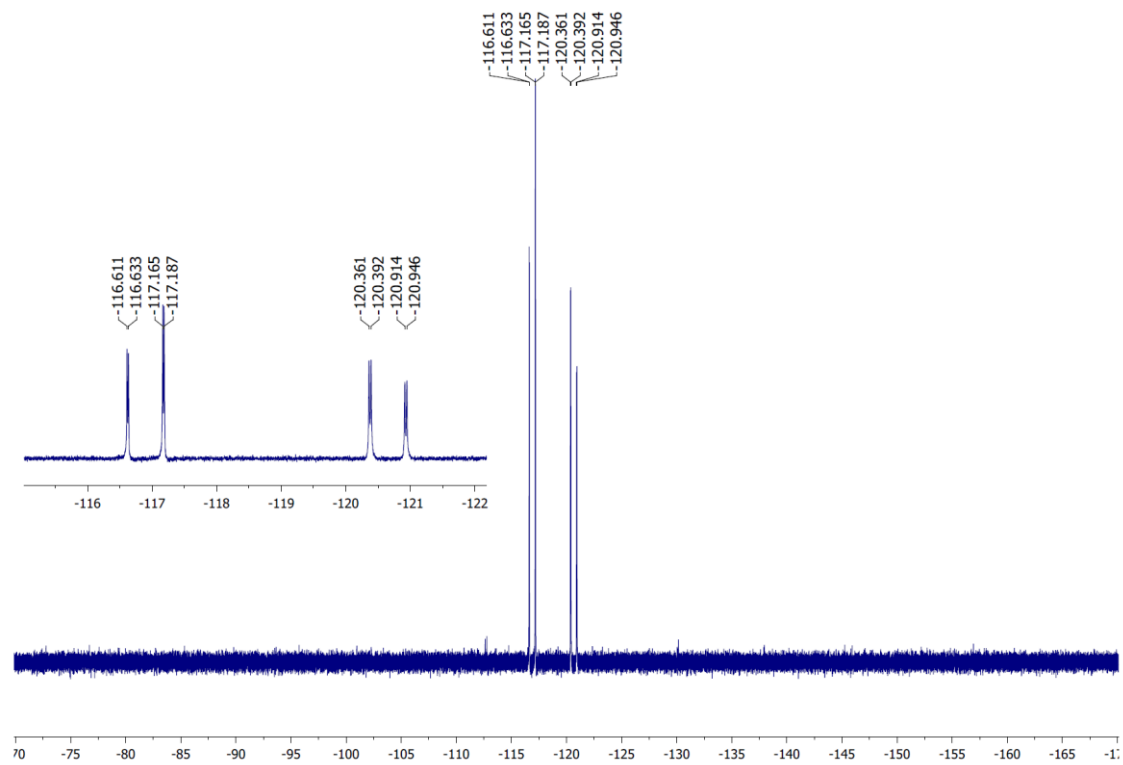
$[\alpha]_D^{20}$ : -3.1 (c 1.0,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.35-7.27 (m, 14H,  $\text{H}^{\text{arom}}$ ), 7.26-7.20 (m, 6H,  $\text{H}^{\text{arom}}$ ), 4.73 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.67 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.64 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.54-4.49 (m, 4H,  $\text{CH}_2^{\text{Bn}}$ ), 4.45 (AB, 1H,  $J_{\text{A-B}}$  = 10.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.38 (m, 1H, H-1), 4.05 (dd, 1H,  $J_{2-3}$  = 4.0 Hz,  $J_{3-4}$  = 5.7 Hz, H-3), 4.03-3.95 (m, 2H,  $\text{CH}_2\text{CH}_3$ ), 3.93-3.88 (m, 2H, H-4, H-5a), 3.87 (t, 1H,  $J_{2-3}$  = 3.4 Hz, H-2), 3.71 (ABX, 1H,  $J_{4-5b}$  = 4.6 Hz,  $J_{5a-5b}$  = 10.3 Hz, H-5b), 1.14 (t, 3H,  $J_{\text{CH}_2\text{CH}_3}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3$ ) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 163.3 (t,  $J_{\text{C-F}}$  = 31.4 Hz,  $\text{C}_q\text{O}_2\text{Et}$ ), 138.1 ( $\text{C}_q^{\text{arom}}$ ), 138.0 ( $\text{C}_q^{\text{arom}}$ ), 137.9 ( $\text{C}_q^{\text{arom}}$ ), 137.7 ( $\text{C}_q^{\text{arom}}$ ), 128.6-127.7 ( $\text{CH}^{\text{arom}}$ ), 114.8 (dd,  $J_{\text{C-F}}$  = 252.3 Hz,  $J_{\text{C-F}}$  = 255.9 Hz,  $\text{CF}_2$ ), 78.7 (C-4), 78.2 (C-3), 76.6 (C-2), 74.1 ( $\text{CH}_2^{\text{Bn}}$ ), 73.6 ( $\text{CH}_2^{\text{Bn}}$ ), 73.5 ( $\text{CH}_2^{\text{Bn}}$ ), 72.4 ( $\text{CH}_2^{\text{Bn}}$ ), 71.6 (t,  $J_{\text{C-F}}$  = 21.8 Hz, C-1), 69.2 (C-5), 62.8 ( $\text{CH}_2\text{CH}_3$ ), 13.9 ( $\text{CH}_2\text{CH}_3$ ) ppm.  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  = -116.9 (dd, 1F,  $J_{\text{H-Fa}}$  = 9.9 Hz,  $J_{\text{Fa-Fb}}$  = 260.9 Hz, Fa), -120.7 (dd, 1F,  $J_{\text{H-Fb}}$  = 15.3 Hz,  $J_{\text{Fa-Fb}}$  = 260.9 Hz, Fb) ppm. HRMS (ESI+): m/z calculated for  $\text{C}_{37}\text{H}_{40}\text{F}_2\text{NaO}_7$   $[\text{M}+\text{Na}]^+$ : calc. 657.2634; found: 657.2638.



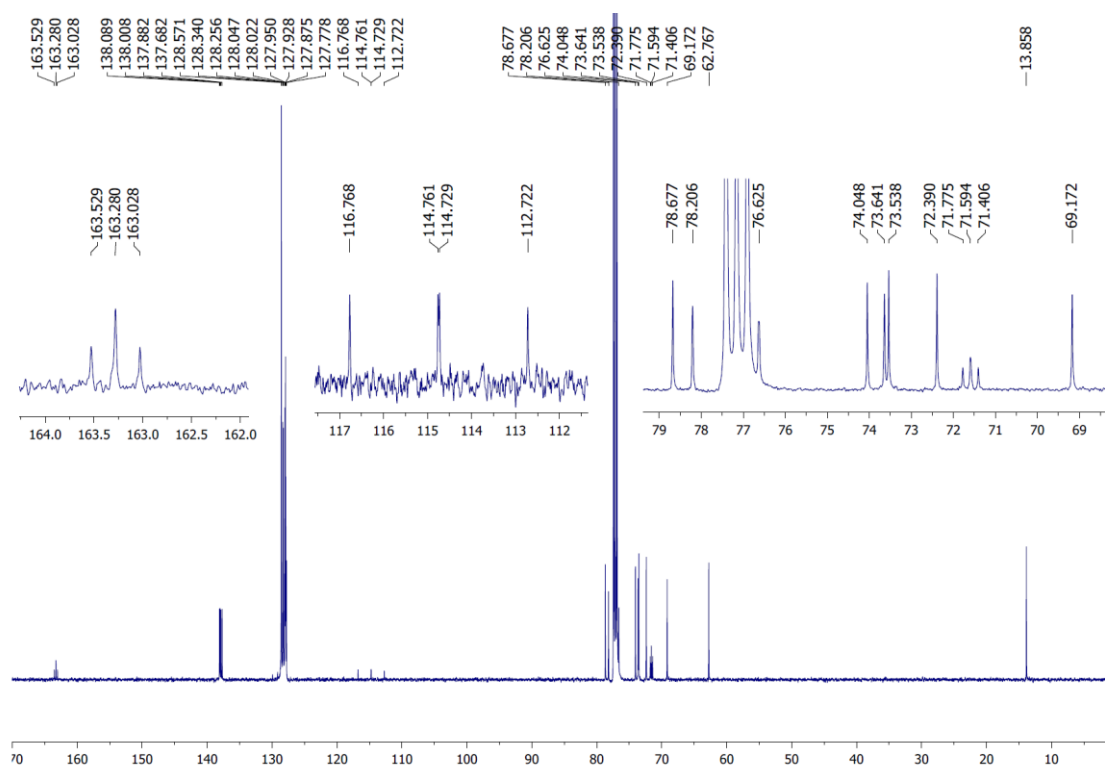
# <sup>1</sup>H NMR



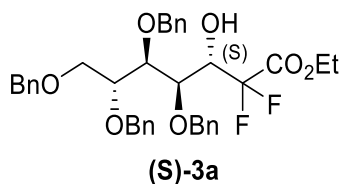
# <sup>19</sup>F NMR



# <sup>13</sup>C NMR

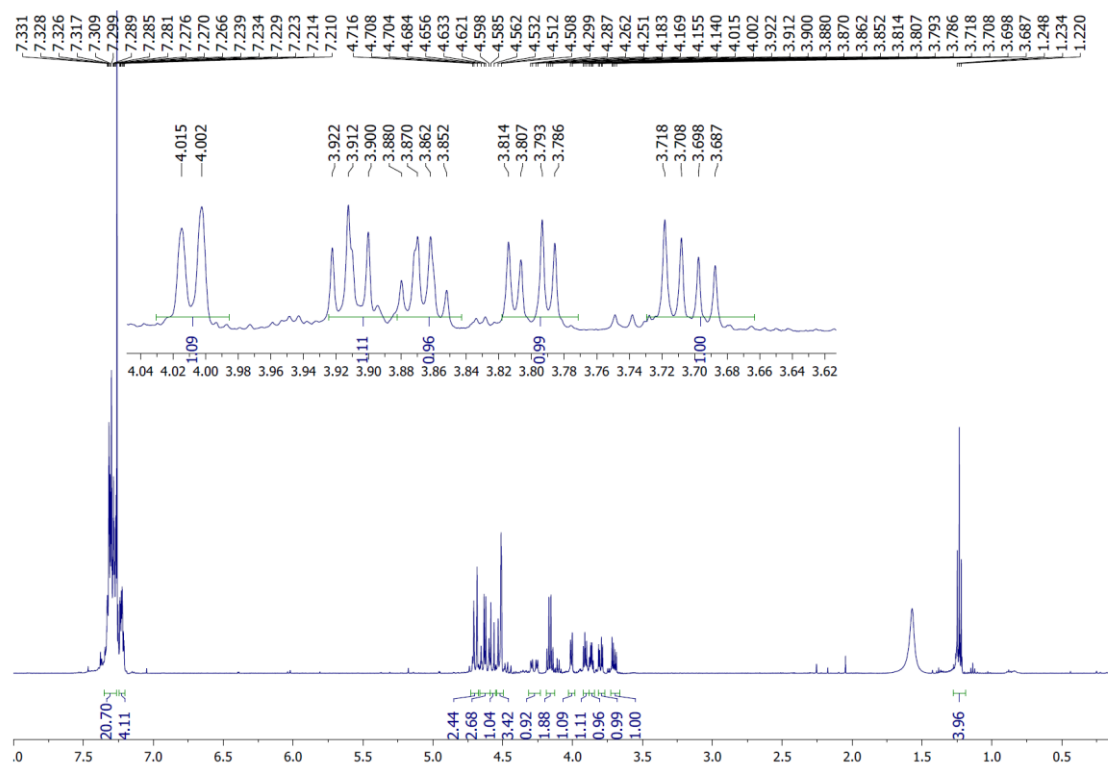


*Ethyl (1S,2R,3R,4R)-2,3,4,5-tetra-O-benzyl-1',1'-difluoro-1-hydroxyheptanoate ((S)-3a).*

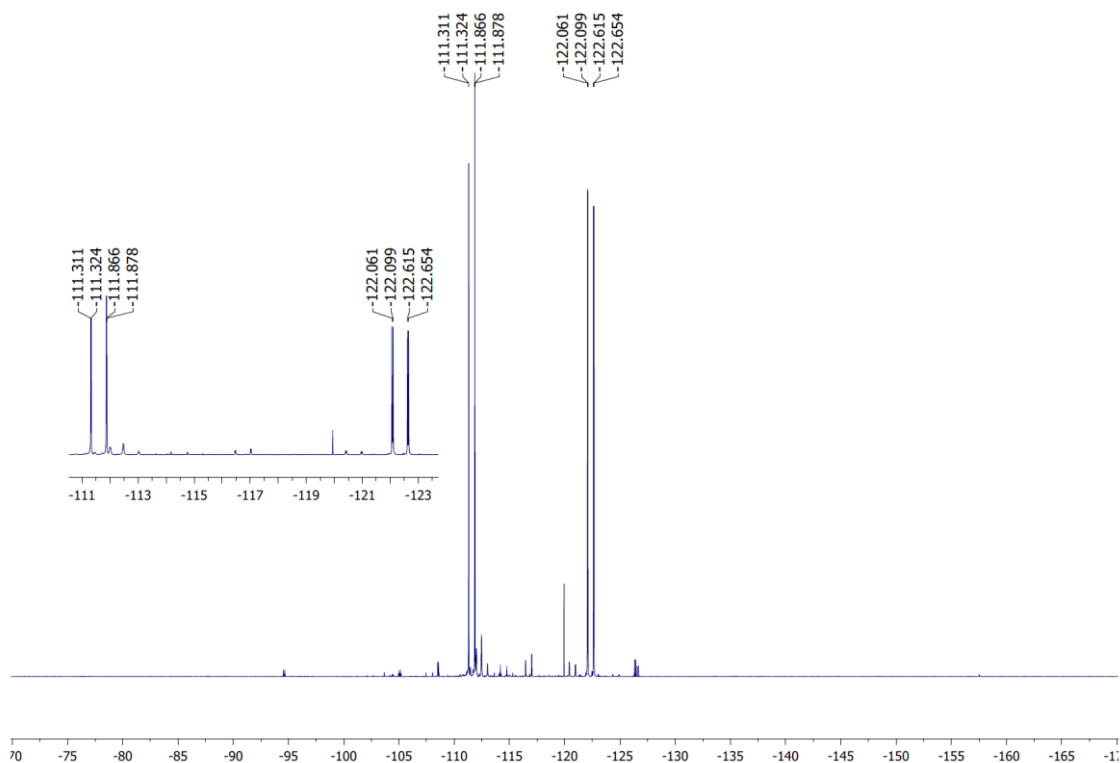


$[\alpha]_D^{20}$ : +2.1 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.33-7.26 (m, 16H, H<sup>arom</sup>), 7.25-7.21 (m, 4H, H<sup>arom</sup>), 4.70 (m, 2H, CH<sub>2</sub><sup>Bn</sup>), 4.64 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.61 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.57 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.53-4.48 (m, 3H, CH<sub>2</sub><sup>Bn</sup>), 4.28 (dd, 1H,  $J_{1-2} = J_{1-Fa} = 5.7$  Hz,  $J_{1-Fb} = 18.3$  Hz, H-1), 4.16 (q, 2H,  $J_{CH_2CH_3} = 7.5$  Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.01 (d, 1H,  $J_{1-2} = J_{2-3} = 5.7$  Hz, H-2), 3.91 (t, 1H,  $J_{2-3} = J_{3-4} = 5.7$  Hz, H-3), 3.87 (m, 1H, H-4), 3.80 (ABX, 1H,  $J_{4-5a} = 4.0$  Hz,  $J_{5a-5b} = 10.3$  Hz, H-5a), 3.70 (ABX, 1H,  $J_{4-5b} = 5.2$  Hz,  $J_{5a-5b} = 10.3$  Hz, H-5b), 1.23 (t, 3H,  $J_{CH_2CH_3} = 7.5$  Hz, CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.6 (dd,  $J_{C-F} = 30.2$  Hz,  $J_{C-F} = 33.8$  Hz, C<sub>q</sub>O<sub>2</sub>Et), 138.2 (2 C<sub>q</sub><sup>arom</sup>), 138.1 (C<sub>q</sub><sup>arom</sup>), 137.6 (C<sub>q</sub><sup>arom</sup>), 128.5-127.7 (CH<sup>arom</sup>), 114.5 (dd,  $J_{C-F} = 253.5$  Hz,  $J_{C-F} = 259.5$  Hz, CF<sub>2</sub>), 79.0 (C-4), 78.6 (C-3), 75.2 (C-2), 74.4 (CH<sub>2</sub><sup>Bn</sup>), 74.2 (CH<sub>2</sub><sup>Bn</sup>), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 72.5 (CH<sub>2</sub><sup>Bn</sup>), 70.4 (dd,  $J_{C-F} = 24.7$  Hz,  $J_{C-F} = 28.4$  Hz, C-1), 69.3 (C-5), 63.1 (CH<sub>2</sub>CH<sub>3</sub>), 14.0 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -111.6 (dd, 1F,  $J_{H1-Fa} = 5.7$  Hz,  $J_{Fa-Fb} = 260.9$  Hz, Fa), -122.4 (dd, 1F,  $J_{H-Fb} = 18.3$  Hz,  $J_{Fa-Fb} = 260.9$  Hz, Fb) ppm. HRMS (ESI<sup>+</sup>):  $m/z$  calculated for C<sub>37</sub>H<sub>40</sub>F<sub>2</sub>NaO<sub>7</sub> [M+Na]<sup>+</sup>: calc. 657.2634; found: 657.2640.

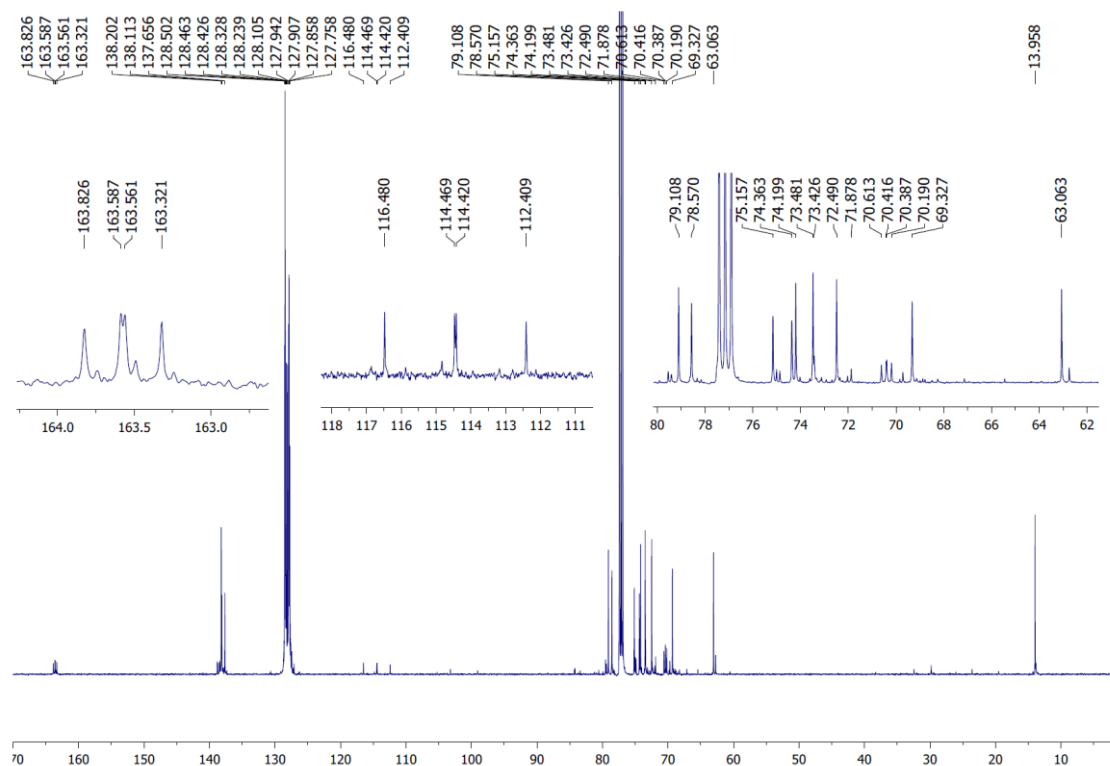
# <sup>1</sup>H NMR



# <sup>19</sup>F NMR

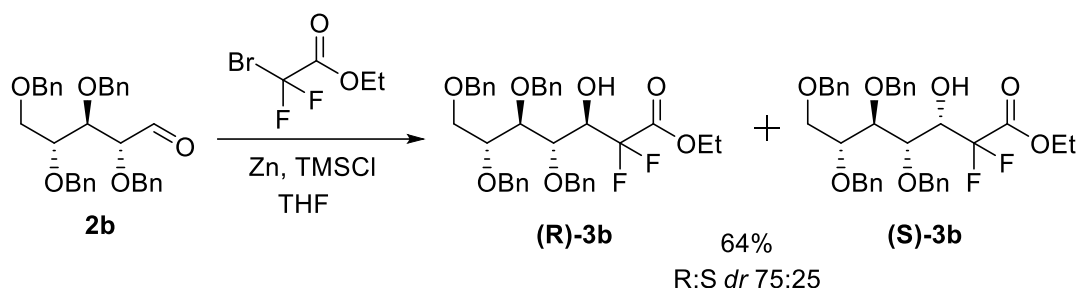


# <sup>13</sup>C NMR



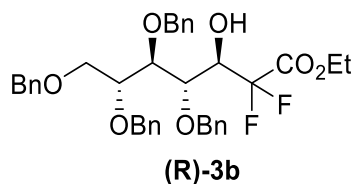
## D-Ribose

Ethyl (1*S*/1*R*,2*S*,3*R*,4*R*)-2,3,4,5-tetra-*O*-benzyl-1',1'-difluoro-1-hydroxyheptanoate ((*R*/*S*)-**3b**).



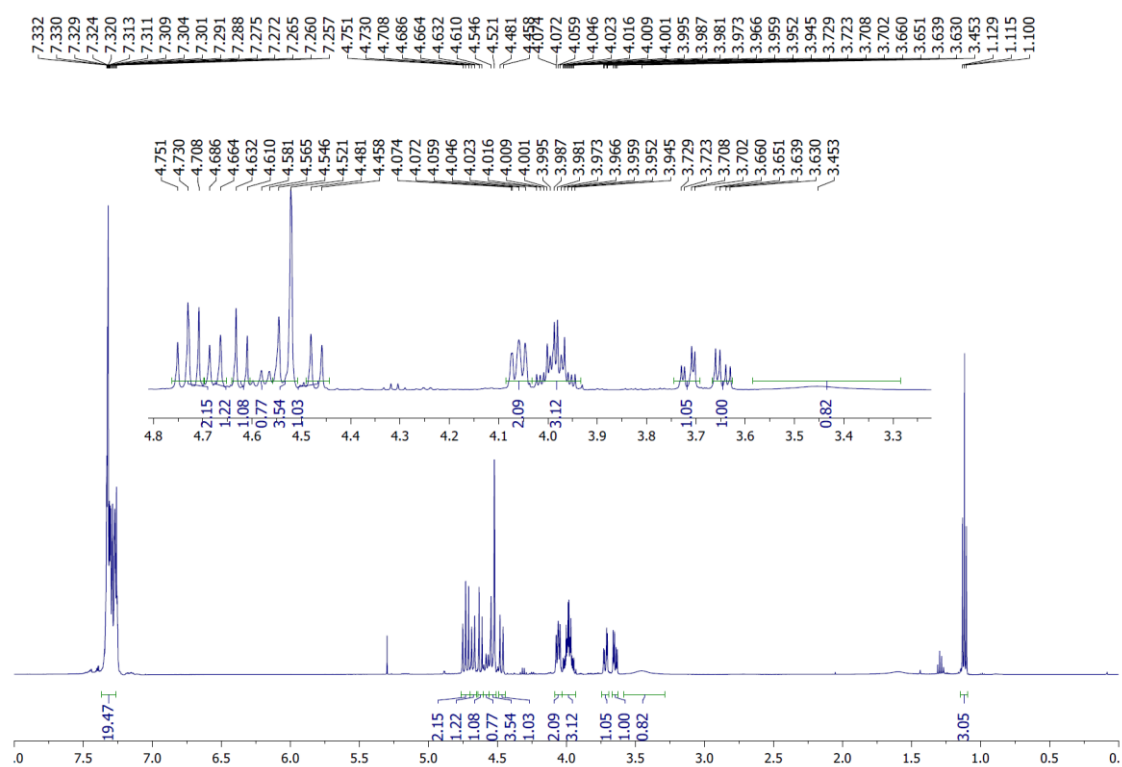
To a dry two-necked round bottomed flask was added “activated zinc” powder (753 mg, 11.52 mmol, 5.7 equiv.). The flask was heated up at 40°C and the zinc powder suspended in dry THF (15 ml) under argon atmosphere. Then, TMSCl (90 µl, 0.69 mmol, 0.4 equiv.) was added dropwise and the reaction was stirred at 60°C for 15 mins. Next, a solution of aldehyde **2b** (1.030 g, 2.02 mmol, 1.0 equiv.) and ethyl bromo-difluoroacetate (0.310 ml, 2.42 mmol, 1.2 equiv.) dissolved homogenously in dry THF (15 ml) under argon atmosphere was added dropwise at 60°C. The reaction was stirred vigorously for 2h at 60°C and then cooled at room temperature. Ice water (10 ml) and HCl (1M, 10 ml) were added and the mixture was diluted with EtOAc. The organic phase was washed with NaHCO<sub>3</sub>(sat) (2 times), brine, dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Crude NMR analysis showed the formation of two diastereoisomer (*R*)-**3b** and (*S*)-**3b** in 75:25 *dr* ratio. Purification by silica gel chromatography (Cy/EtOAc 9:1) afforded pure stereoisomer (*R*)-**3b** and (*S*)-**3b** in 64 % overall yield.

*Ethyl (1S/1R,2S,3R,4R)-2,3,4,5-tetra-O-benzyl-1',1'-difluoro-1-hydroxyheptanoate ((R)-3b).*

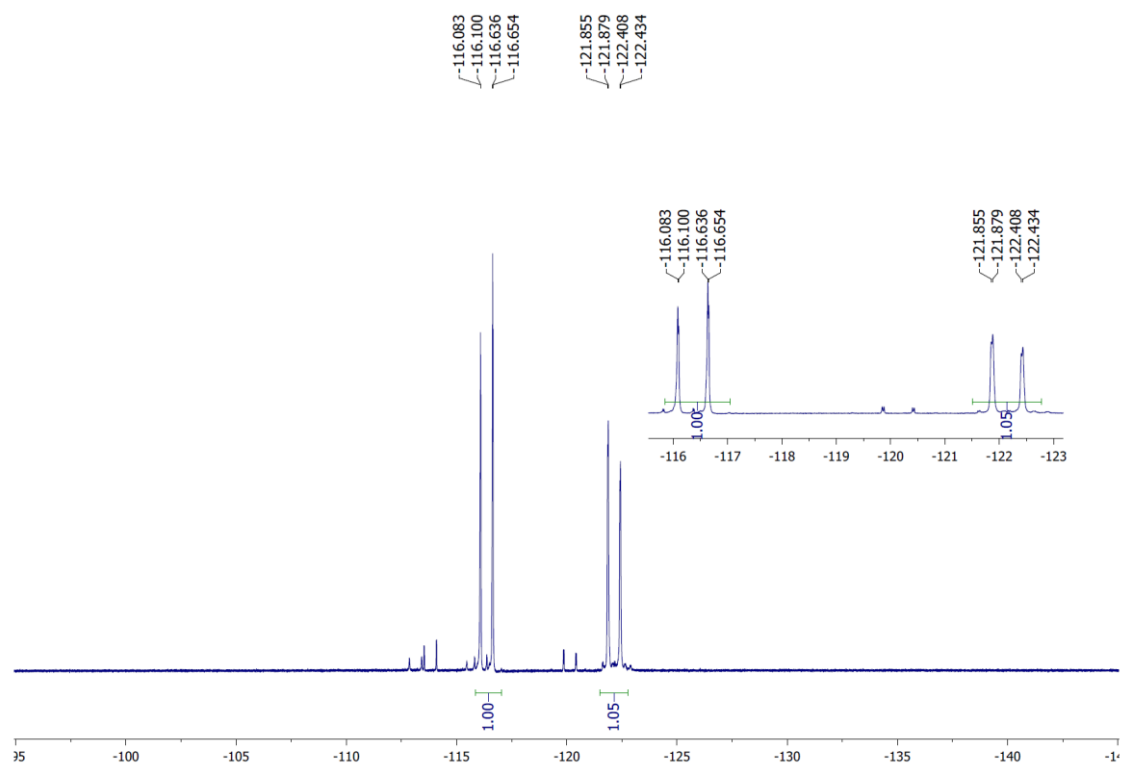


$[\alpha]_D^{20}$ : -5.3 (c 1.0,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.34-7.27 (m, 18H,  $\text{H}^{\text{arom}}$ ), 7.26-7.23 (m, 2H,  $\text{H}^{\text{arom}}$ ), 4.73 (AB, 1H,  $J_{\text{A-B}}$  = 10.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.71 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.67 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.61 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.59-4.49 (m, 4H, H-1,  $\text{CH}_2^{\text{Bn}}$ ), 4.46 (AB, 1H,  $J_{\text{A-B}}$  = 10.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.05 (t, 2H,  $J$  = 7.5 Hz, H-2, H-3), 4.02-3.94 (m, 3H, H-4,  $\text{CH}_2\text{CH}_3$ ), 3.71 (ABX, 1H,  $J_{4-5a}$  = 3.4 Hz,  $J_{5a-5b}$  = 10.3 Hz, H-5a), 3.64 (ABX, 1H,  $J_{4-5b}$  = 4.6 Hz,  $J_{5a-5b}$  = 10.3 Hz, H-5b), 3.44 (bs, 1H, OH), 1.11 (t, 3H,  $J_{\text{CH}_2\text{CH}_3}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3$ ) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 163.4 (t,  $J_{\text{C-F}}$  = 31.4 Hz,  $\text{C}_q\text{O}_2\text{Et}$ ), 138.3 ( $\text{C}_q^{\text{arom}}$ ), 138.1 ( $\text{C}_q^{\text{arom}}$ ), 137.8 (2  $\text{C}_q^{\text{arom}}$ ), 128.6-127.7 ( $\text{CH}^{\text{arom}}$ ), 114.8 (dd,  $J_{\text{C-F}}$  = 250.5 Hz,  $J_{\text{C-F}}$  = 256.5 Hz,  $\text{CF}_2$ ), 78.7 (C-4), 77.9 (C-2), 77.7 (C-3), 73.7 ( $\text{CH}_2^{\text{Bn}}$ ), 73.6 ( $\text{CH}_2^{\text{Bn}}$ ), 73.2 ( $\text{CH}_2^{\text{Bn}}$ ), 73.1 ( $\text{CH}_2^{\text{Bn}}$ ), 71.2 (t,  $J_{\text{C-F}}$  = 22.9 Hz, C-1), 69.3 (C-5), 62.6 ( $\text{CH}_2\text{CH}_3$ ), 13.8 ( $\text{CH}_2\text{CH}_3$ ) ppm.  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  = -116.5 (dd, 1F,  $J_{\text{H-Fa}}$  = 9.0 Hz,  $J_{\text{Fa-Fb}}$  = 260.9 Hz, Fa), -122.0 (dd, 1F,  $J_{\text{H-Fb}}$  = 15.9 Hz,  $J_{\text{Fa-Fb}}$  = 260.9 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for  $\text{C}_{37}\text{H}_{40}\text{F}_2\text{NaO}_7$   $[\text{M}+\text{Na}]^+$ : calc. 657.2634; found: 657.2625.

# <sup>1</sup>H NMR

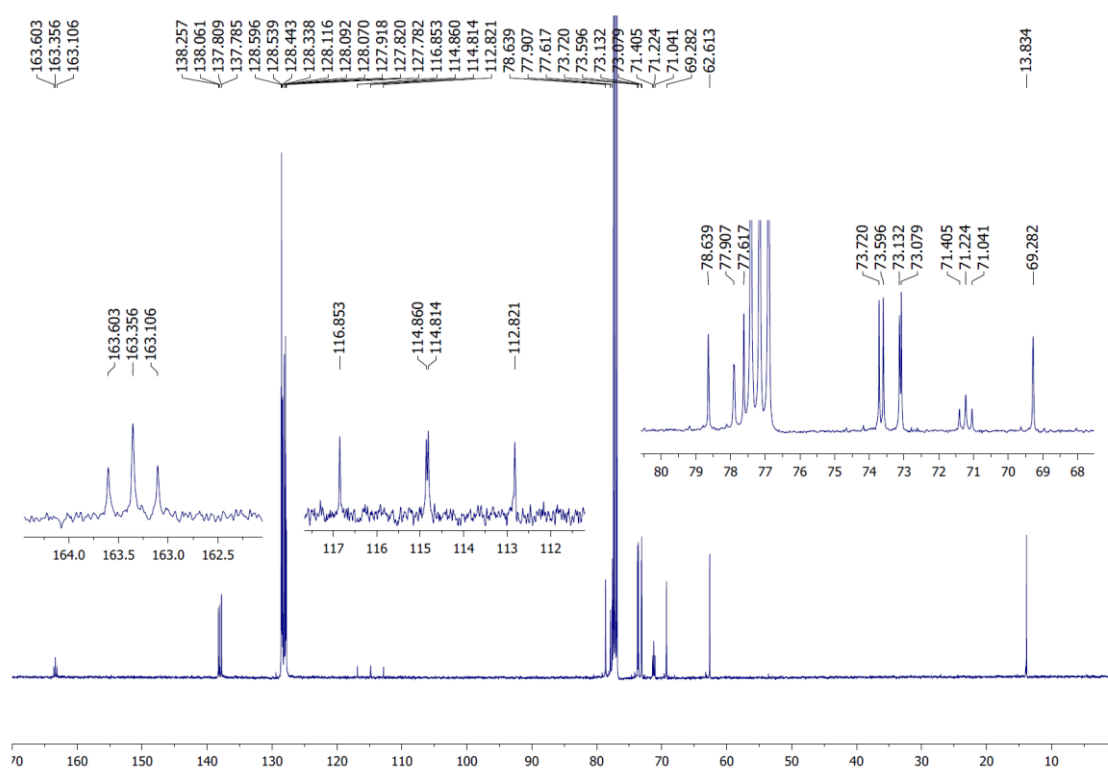


# <sup>19</sup>F NMR

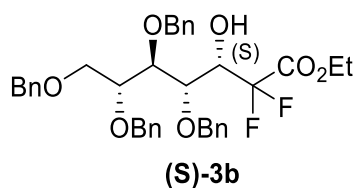




# <sup>13</sup>C NMR

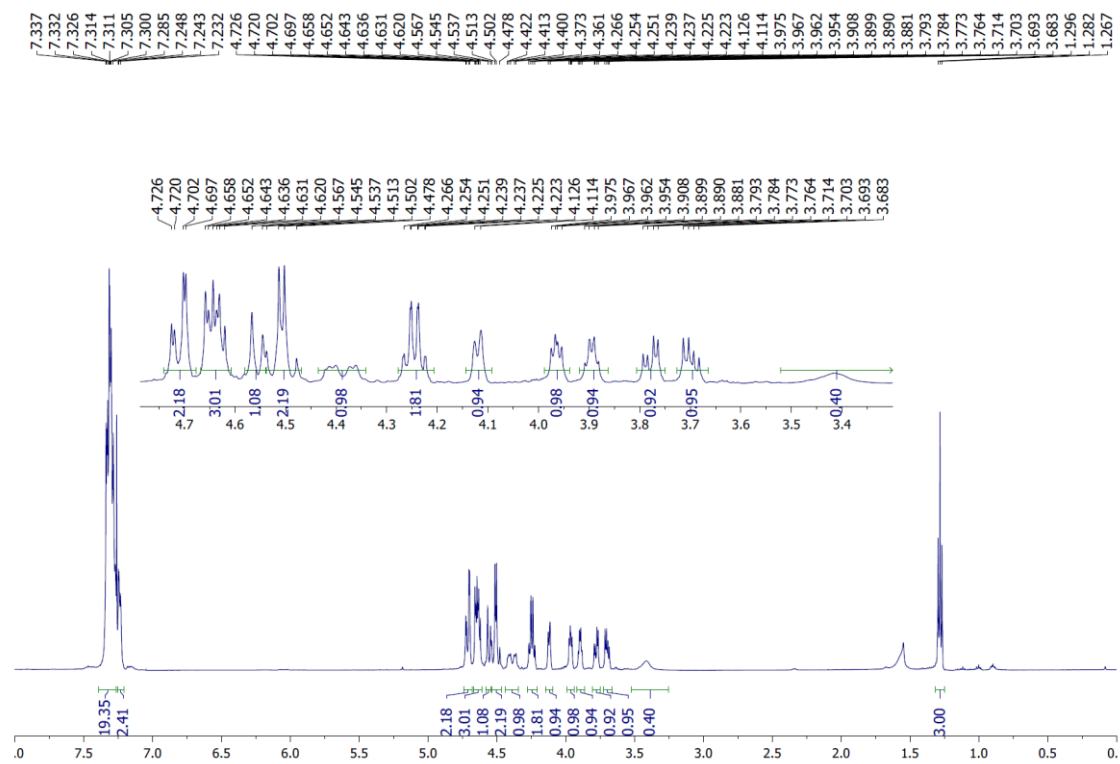


*Ethyl (1S/1R,2S,3R,4R)-2,3,4,5-tetra-O-benzyl-1',1'-difluoro-1-hydroxyheptanoate ((S)-3b).*

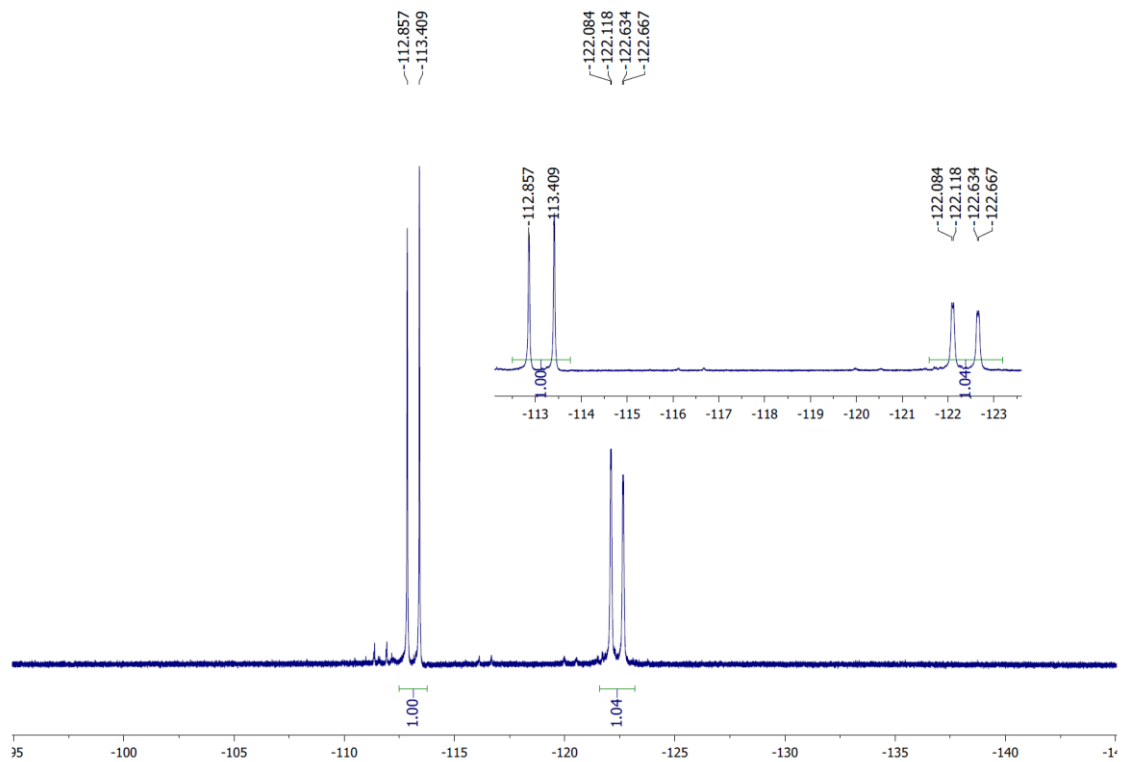


$[\alpha]_{20}^D$ : -2.7 (c 1.0,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.34-7.27 (m, 18H,  $\text{H}^{\text{arom}}$ ), 7.25-7.22 (m, 2H,  $\text{H}^{\text{arom}}$ ), 4.72 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.71 (AB, 1H,  $J_{\text{A-B}}$  = 10.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.66-4.62 (m, 3H,  $\text{CH}_2^{\text{Bn}}$ ), 4.55 (AB, 1H,  $J_{\text{A-B}}$  = 10.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.52 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.49 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.38 (dd, 1H,  $J_{1-2}$  = 6.3 Hz,  $J_{1-\text{Fb}}$  = 19.5 Hz, H-1), 4.24 (q, 2H,  $J_{\text{CH}_2\text{CH}_3}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3$ ), 4.12 (d, 1H,  $J_{1-2}$  = 6.3 Hz, H-2), 3.96 (m, 1H, H-3), 3.89 (q, 1H,  $J_{3-4} \sim J_{4-5a}$  = 3.4 Hz,  $J_{4-5b}$  = 5.2 Hz, H-4), 3.77 (ABX, 1H,  $J_{4-5a}$  = 3.4 Hz,  $J_{5a-5b}$  = 10.3 Hz, H-5a), 3.69 (ABX, 1H,  $J_{4-5b}$  = 5.2 Hz,  $J_{5a-5b}$  = 10.3 Hz, H-5b), 1.28 (t, 3H,  $J_{\text{CH}_2\text{CH}_3}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3$ ) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 163.6 (dd,  $J_{\text{C-F}}$  = 30.2 Hz,  $J_{\text{C-F}}$  = 33.8 Hz,  $\text{C}_q\text{O}_2\text{Et}$ ), 138.3 (2  $\text{C}_q^{\text{arom}}$ ), 138.0 ( $\text{C}_q^{\text{arom}}$ ), 137.4 ( $\text{C}_q^{\text{arom}}$ ), 128.6-127.7 ( $\text{CH}^{\text{arom}}$ ), 114.8 (dd,  $J_{\text{C-F}}$  = 254.1 Hz,  $J_{\text{C-F}}$  = 256.5 Hz,  $\text{CF}_2$ ), 79.2 (C-3), 78.1 (C-4), 74.7 (C-2), 74.2 ( $\text{CH}_2^{\text{Bn}}$ ), 73.6 ( $\text{CH}_2^{\text{Bn}}$ ), 73.5 ( $\text{CH}_2^{\text{Bn}}$ ), 72.6 ( $\text{CH}_2^{\text{Bn}}$ ), 69.6 (m, C-1, C-5), 63.1 ( $\text{CH}_2\text{CH}_3$ ), 14.0 ( $\text{CH}_2\text{CH}_3$ ) ppm.  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  = -113.1 (d, 1F,  $J_{\text{Fa-Fb}}$  = 260.5 Hz, Fa), -122.4 (dd, 1F,  $J_{\text{H1-Fb}}$  = 19.5 Hz,  $J_{\text{Fa-Fb}}$  = 260.5 Hz, Fb) ppm. HRMS (ESI+): m/z calculated for  $\text{C}_{37}\text{H}_{40}\text{F}_2\text{NaO}_7$   $[\text{M}+\text{Na}]^+$ : calc. 657.2634; found: 657.2630.

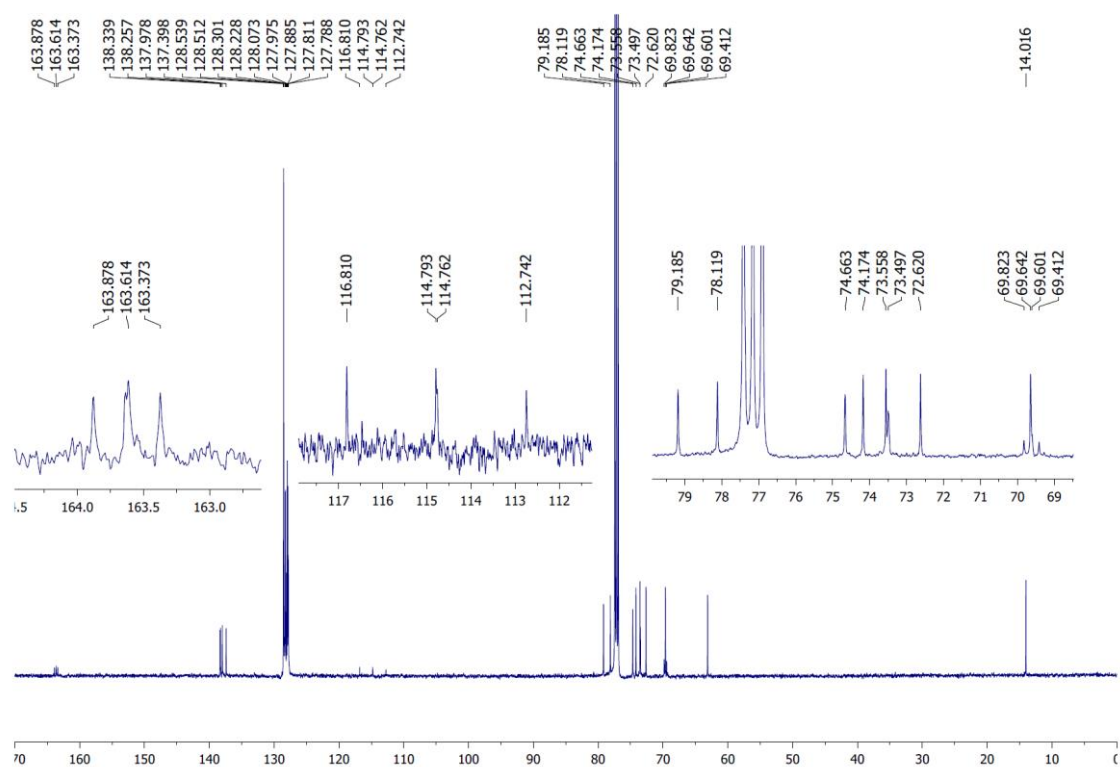
# <sup>1</sup>H NMR



# <sup>19</sup>F NMR

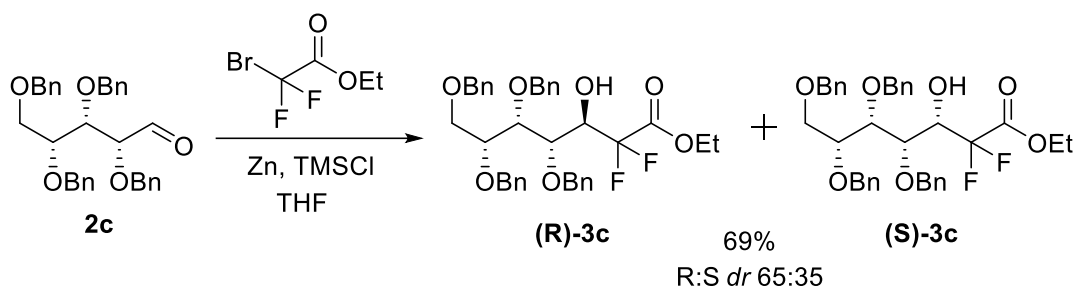


# <sup>13</sup>C NMR



## D-Xylose

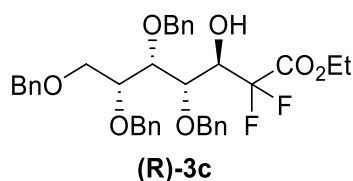
Ethyl (1*S*/1*R*,2*S*,3*S*,4*R*)-2,3,4,5-tetra-*O*-benzyl-1',1'-difluoro-1-hydroxyheptanoate ((*R*/*S*)-**3c**).



To a dry two-necked round bottomed flask was added “activated zinc” powder (298 mg, 4.55 mmol, 5.7 equiv.). The flask was heated up at 40°C and the zinc powder suspended in dry THF (5 ml) under argon atmosphere. Then, TMSCl (44  $\mu$ l, 0.34 mmol, 0.4 equiv.) was added dropwise and the reaction was stirred at 60°C for 15 mins. Next, a solution of aldehyde **2c** (407 mg, 0.80 mmol, 1.0 equiv.) and ethyl bromo-difluoroacetate (0.122 ml, 0.96 mmol, 1.2 equiv.) dissolved homogenously in dry THF (5 ml) under argon atmosphere was added dropwise at 60°C. The reaction was stirred vigorously for 1.5h at 60°C and then cooled at room temperature. Ice water (10 ml) and HCl (1M, 10 ml) were added and the mixture was diluted with EtOAc. The organic phase was washed with NaHCO<sub>3</sub>(sat) (2 times), brine, dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by silica gel chromatography (Cy/EtOAc 8:2) gave an inseparable mixture of two diastereoisomers (*R*)-**3c** and (*S*)-**3c** in 65:35 *dr* ratio (326 mg, 69%).

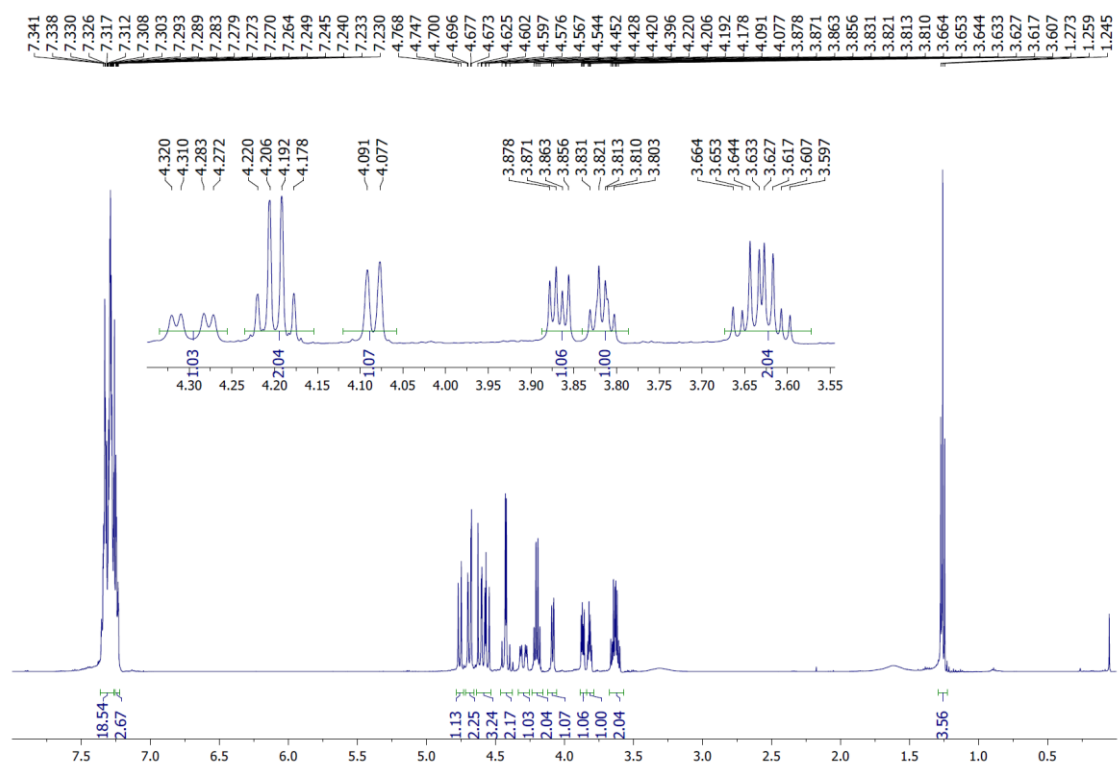
Noteworthy, few milligrams (15 mg) of the major diastereoisomer (*R*)-**3c** could be isolated and fully characterized.

*Ethyl (1S/1R,2S,3S,4R)-2,3,4,5-tetra-O-benzyl-1',1''-difluoro-1-hydroxyheptanoate ((R)-3c).*

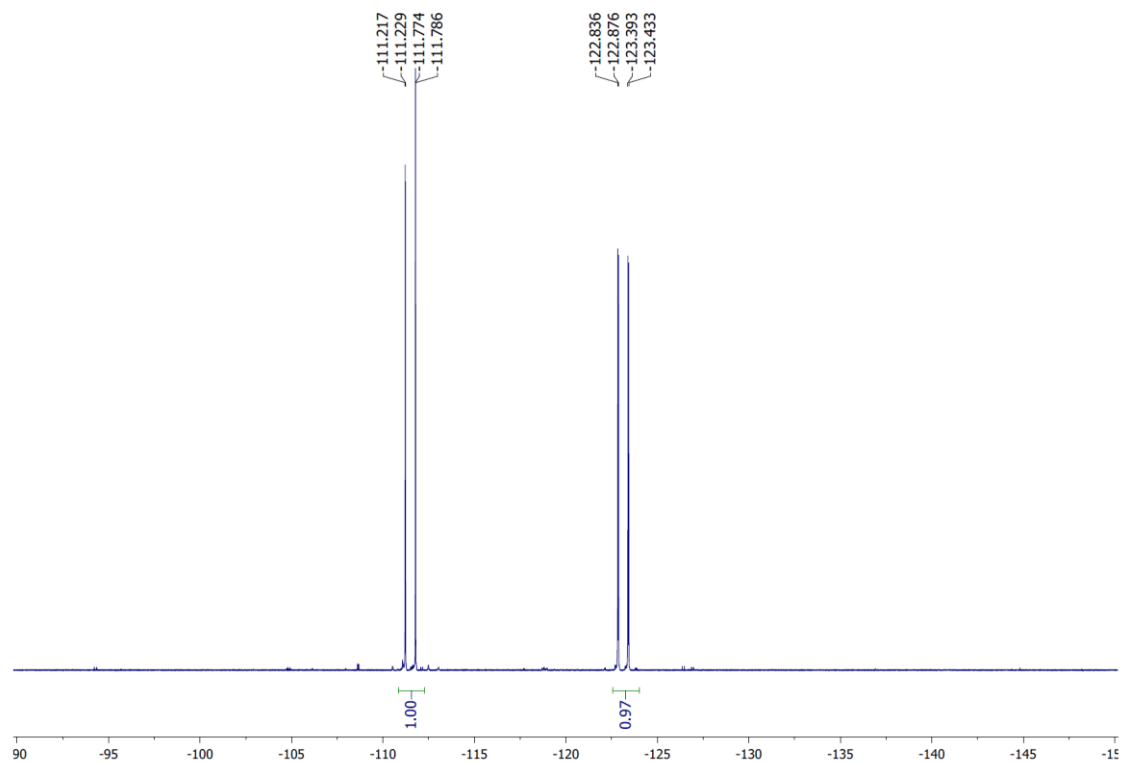


$[\alpha]_{20}^D$ : -2.1 (c 1.0,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.36-7.22 (m, 20H,  $\text{H}^{\text{arom}}$ ), 4.76 (AB, 1H,  $J_{\text{A-B}}$  = 10.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.68 (AB, 2H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.61 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.59 (AB, 1H,  $J_{\text{A-B}}$  = 10.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.56 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.44 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.41 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.30 (dd, 1H,  $J_{\text{H1-Fa}}$  = 5.7 Hz,  $J_{\text{H1-Fb}}$  = 18.9 Hz, H-1), 4.20 (q, 2H,  $J_{\text{CH}_2\text{CH}_3}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3$ ), 4.08 (d, 1H,  $J_{2-3}$  = 7.4 Hz, H-2), 3.87 (dd, 1H,  $J_{2-3}$  = 7.4 Hz,  $J_{3-4}$  = 4.0 Hz, H-3), 3.82 (td, 1H,  $J_{3-4}$  = 4.0 Hz,  $J_{4-5a}$  =  $J_{4-5b}$  = 5.2 Hz, H-4), 3.65 (ABX, 1H,  $J_{4-5a}$  = 5.2 Hz,  $J_{5a-5b}$  = 9.7 Hz, H-5a), 3.61 (ABX, 1H,  $J_{4-5b}$  = 5.2 Hz,  $J_{5a-5b}$  = 9.7 Hz, H-5b), 1.26 (t, 3H,  $J_{\text{CH}_2\text{CH}_3}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3$ ) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 163.6 (dd,  $J_{\text{C-F}}$  = 29.9 Hz,  $J_{\text{C-F}}$  = 32.8 Hz,  $\text{C}_q\text{O}_2\text{Et}$ ), 138.2 (2  $\text{C}_q^{\text{arom}}$ ), 138.1 ( $\text{C}_q^{\text{arom}}$ ), 137.7 ( $\text{C}_q^{\text{arom}}$ ), 128.6-127.7 ( $\text{CH}^{\text{arom}}$ ), 114.5 (dd,  $J_{\text{C-F}}$  = 253.4 Hz,  $J_{\text{C-F}}$  = 258.2 Hz,  $\text{CF}_2$ ), 78.5 (C-3), 77.3 (C-4), 74.8 (2  $\text{CH}_2^{\text{Bn}}$ ), 74.5 (C-2), 73.4 ( $\text{CH}_2^{\text{Bn}}$ ), 73.1 ( $\text{CH}_2^{\text{Bn}}$ ), 69.9 (dd,  $J_{\text{C-F}}$  = 24.5 Hz,  $J_{\text{C-F}}$  = 28.5 Hz, C-1), 69.6 (C-5), 63.1 ( $\text{CH}_2\text{CH}_3$ ), 14.0 ( $\text{CH}_2\text{CH}_3$ ) ppm.  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  = -111.5 (dd, 1F,  $J_{\text{H1-Fa}}$  = 5.7 Hz,  $J_{\text{Fa-Fb}}$  = 261.7 Hz, Fa), -123.1 (dd, 1F,  $J_{\text{H1-Fb}}$  = 18.9 Hz,  $J_{\text{Fa-Fb}}$  = 261.7 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for  $\text{C}_{37}\text{H}_{40}\text{F}_2\text{NaO}_7$   $[\text{M}+\text{Na}]^+$ : calc. 657.2634; found: 657.2626.

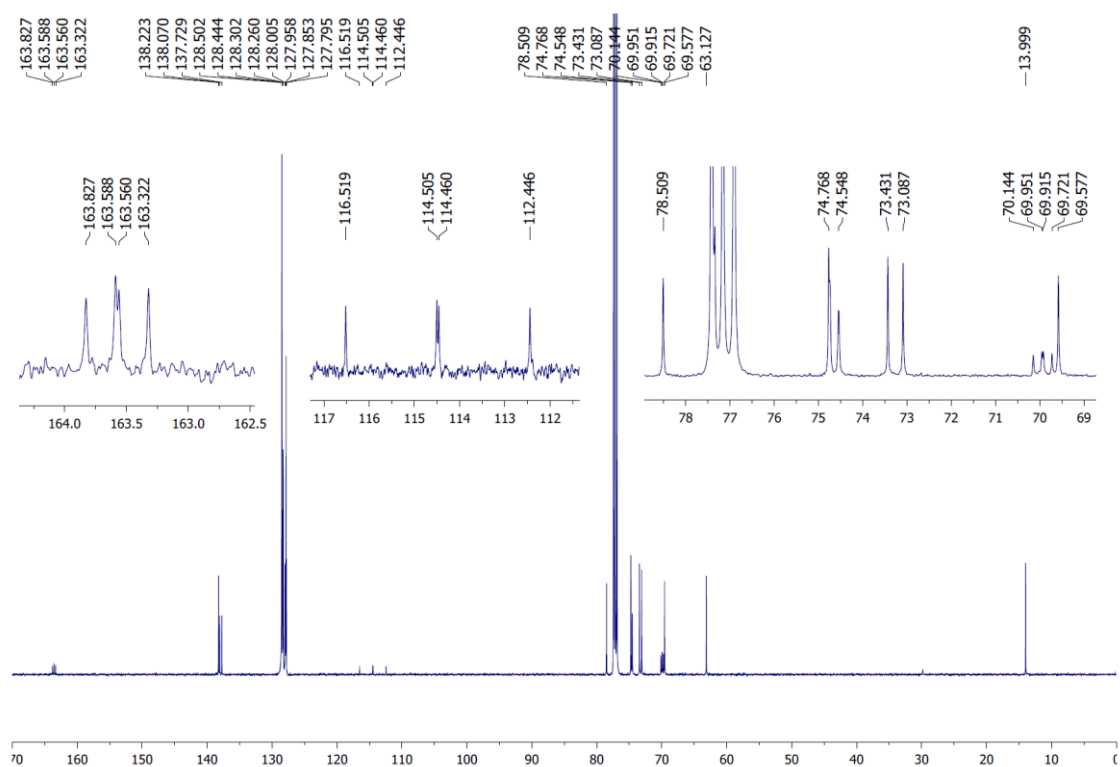
# <sup>1</sup>H NMR



# <sup>19</sup>F NMR

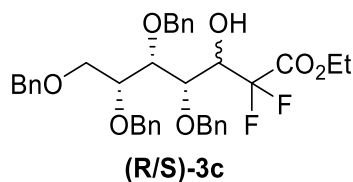


# <sup>13</sup>C NMR



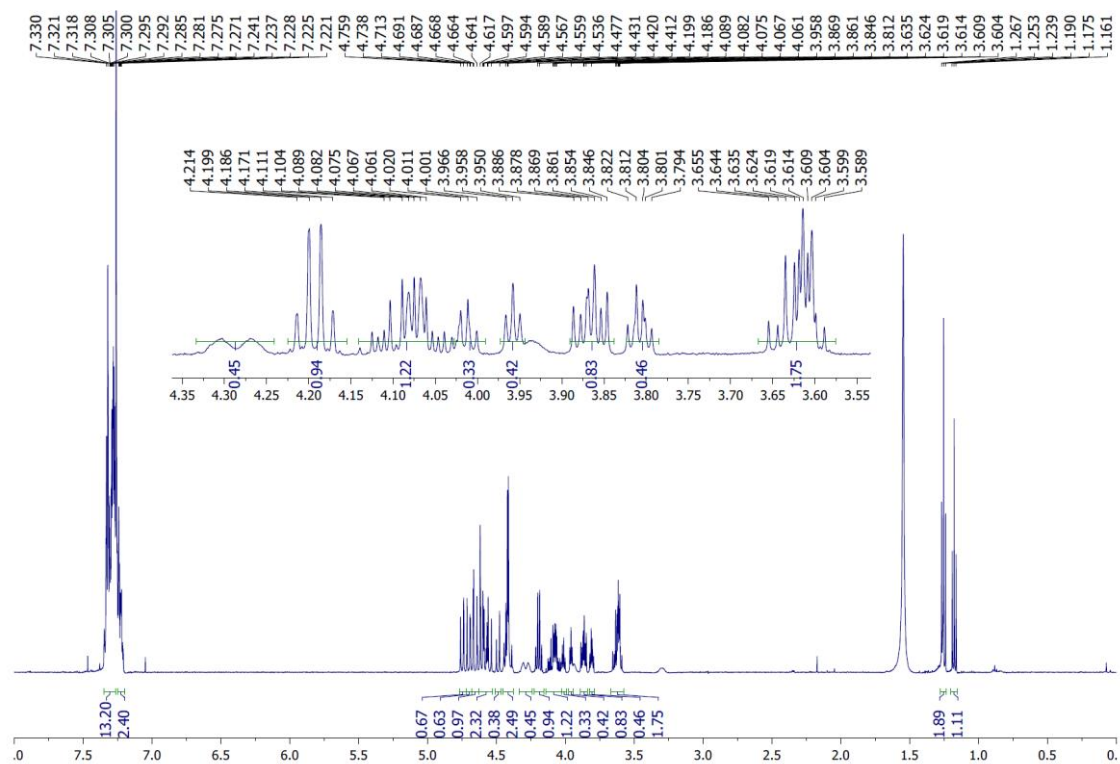


*Ethyl (1S/1R,2S,3S,4R)-2,3,4,5-tetra-O-benzyl-1',1'-difluoro-1-hydroxyheptanoate ((R/S)-3c).*

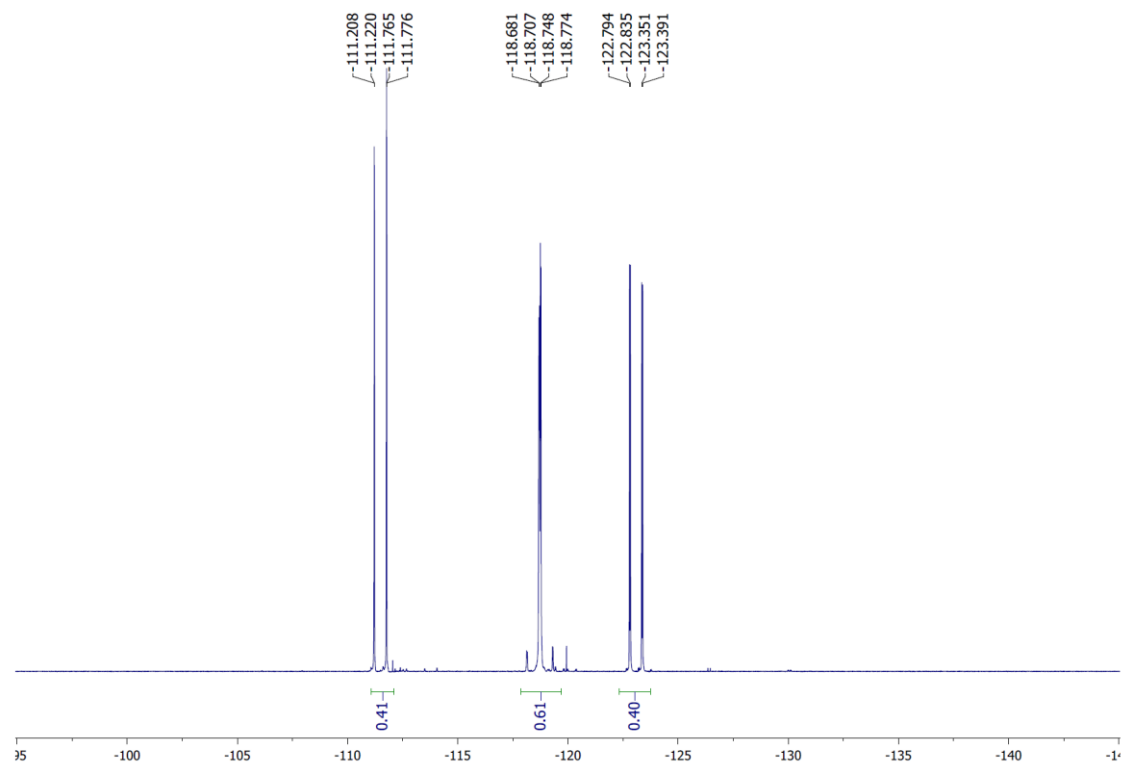


$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.35-7.27 (m, 32H, 16  $\text{H}_\text{A}^\text{arom}$ , 16  $\text{H}_\text{B}^\text{arom}$ ), 7.25-7.17 (m, 8H, 4  $\text{H}_\text{A}^\text{arom}$ , 4  $\text{H}_\text{B}^\text{arom}$ ), 4.75 (AB, 1H,  $J_{\text{A-B}}$  = 10.9 Hz,  $\text{CH}_2\text{A}^\text{Bn}$ ), 4.73 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2\text{B}^\text{Bn}$ ), 4.68 (AB, 2H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2\text{A}^\text{Bn}$ ), 4.65-4.53 (m, 6H, 3  $\text{CH}_2\text{A}^\text{Bn}$ , 3  $\text{CH}_2\text{B}^\text{Bn}$ ), 4.49 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2\text{B}^\text{Bn}$ ), 4.44-4.38 (m, 6H, H-1B, 2  $\text{CH}_2\text{A}^\text{Bn}$ , 3  $\text{CH}_2\text{B}^\text{Bn}$ ), 4.29 (m, 1H, H-1A), 4.19 (q, 2H,  $J_{\text{CH}_2\text{CH}_3\text{A}}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3\text{A}$ ), 4.13-4.04 (m, 3H, H-2A,  $\text{CH}_2\text{CH}_3\text{B}$ ), 4.01 (t, 1H,  $J$  = 4.0 Hz, H-4B), 3.96 (t, 1H,  $J$  = 4.6 Hz, H-3B), 3.93 (bs, 1H, OHB), 3.88 (d, 1H,  $J_{2-3}$  = 4.6 Hz, H-2B), 3.86 (dd, 1H,  $J_{2-3}$  = 7.4 Hz,  $J_{3-4}$  = 4.0 Hz, H-3A), 3.81 (td, 1H,  $J_{3-4}$  = 4.0 Hz,  $J_{4-5\text{a}}$  =  $J_{4-5\text{b}}$  = 5.2 Hz, H-4A), 3.66-3.59 (m, 4 H, H-5aA, H-5bA, H-5aB, H-5bB), 1.25 (t, 3H,  $J_{\text{CH}_2\text{CH}_3\text{A}}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3\text{A}$ ), 1.18 (t, 3H,  $J_{\text{CH}_2\text{CH}_3\text{B}}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3\text{B}$ ) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 163.6 (dd,  $J_{\text{C-F}}$  = 30.2 Hz,  $J_{\text{C-F}}$  = 33.8 Hz,  $\text{C}_\text{q}\text{O}_2\text{EtA}$ ), 163.3 (t,  $J_{\text{C-F}}$  = 31.4 Hz,  $\text{C}_\text{q}\text{O}_2\text{EtB}$ ), 138.2 (2  $\text{C}_\text{q}\text{A}^\text{arom}$ ,  $\text{C}_\text{q}\text{B}^\text{arom}$ ), 138.1 ( $\text{C}_\text{q}\text{A}^\text{arom}$ ), 137.9 ( $\text{C}_\text{q}\text{B}^\text{arom}$ ), 137.7 ( $\text{C}_\text{q}\text{A}^\text{arom}$ ), 137.4 (2  $\text{C}_\text{q}\text{B}^\text{arom}$ ), 128.7-127.7 ( $\text{C}_\text{q}\text{A}^\text{arom}$ ,  $\text{C}_\text{q}\text{B}^\text{arom}$ ), 114.8 (t,  $J_{\text{C-F}}$  = 255.5 Hz,  $\text{CF}_2\text{B}$ ), 114.5 (dd,  $J_{\text{C-F}}$  = 252.8 Hz,  $J_{\text{C-F}}$  = 258.9 Hz,  $\text{CF}_2\text{A}$ ), 78.5 (C-3A), 78.2 (C-3B), 77.4 (C-4A), 77.3 (C-4B), 74.7 (2  $\text{CH}_2\text{A}^\text{Bn}$ ), 74.5 (C-2A), 74.4 (C-2B), 74.0 ( $\text{CH}_2\text{B}^\text{Bn}$ ), 73.4 ( $\text{CH}_2\text{A}^\text{Bn}$ ,  $\text{CH}_2\text{B}^\text{Bn}$ ), 73.2 ( $\text{CH}_2\text{B}^\text{Bn}$ ), 73.2 ( $\text{CH}_2\text{B}^\text{Bn}$ ), 73.1 ( $\text{CH}_2\text{A}^\text{Bn}$ ), 71.7 (t,  $J_{\text{C-F}}$  = 23.5 Hz, C-1B), 69.9 (dd,  $J_{\text{C-F}}$  = 24.5 Hz,  $J_{\text{C-F}}$  = 28.5 Hz, C-1A), 69.6 (C-5A), 69.5 (C-5B), 63.1 ( $\text{CH}_2\text{CH}_3\text{A}$ ), 62.8 ( $\text{CH}_2\text{CH}_3\text{B}$ ), 14.0 ( $\text{CH}_2\text{CH}_3\text{A}$ ), 13.9 ( $\text{CH}_2\text{CH}_3\text{B}$ ) ppm.  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  = -111.5 (dd, 1F,  $J_{\text{H1-Fa}}$  = 5.7 Hz,  $J_{\text{Fa-Fb}}$  = 261.7 Hz, FaA), -118.4 (dd, 1F,  $J$  = 12.0 Hz,  $J_{\text{Fa-Fb}}$  = 259.7 Hz, FaB), -119.0 (dd, 1F,  $J$  = 12.3 Hz,  $J_{\text{Fa-Fb}}$  = 259.7 Hz, FbB), -123.1 (dd, 1F,  $J_{\text{H1-Fb}}$  = 18.9 Hz,  $J_{\text{Fa-Fb}}$  = 261.7 Hz, FbA) ppm. HRMS (ESI<sup>+</sup>):  $m/z$  calculated for  $\text{C}_{37}\text{H}_{40}\text{F}_2\text{NaO}_7$  [ $\text{M}+\text{Na}$ ]<sup>+</sup>: calc. 657.2634; found: 657.2628.

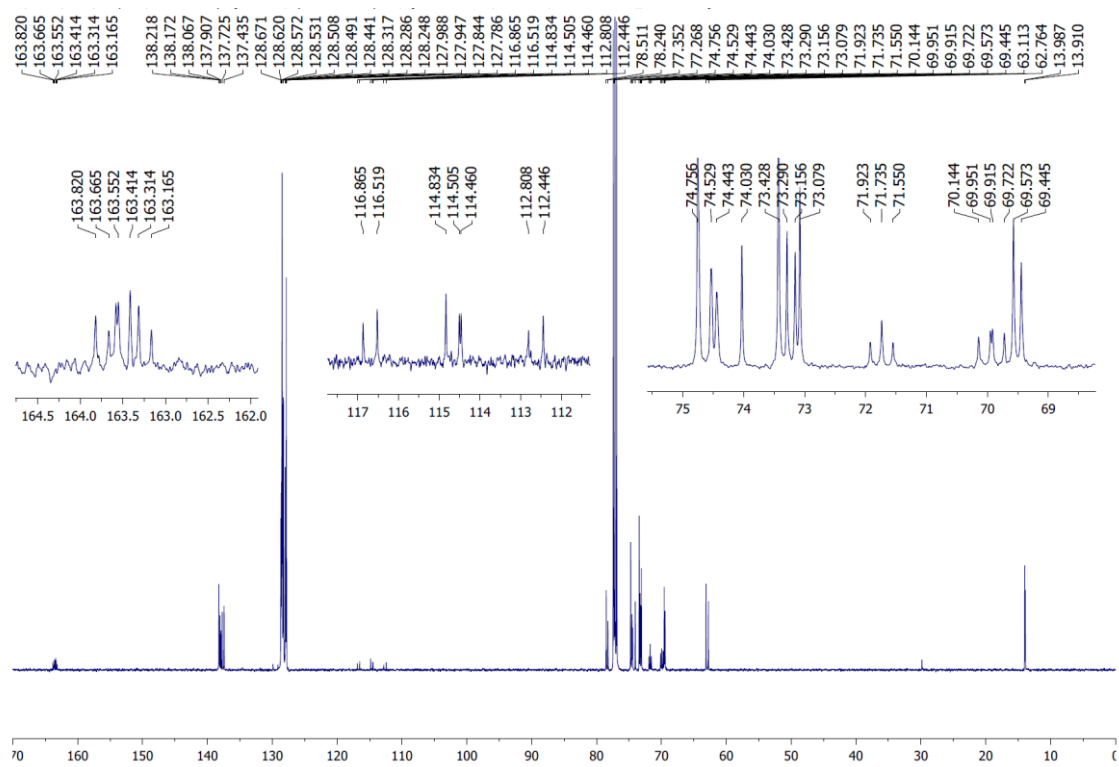
### <sup>1</sup>H NMR



**$^{19}\text{F}$  NMR**

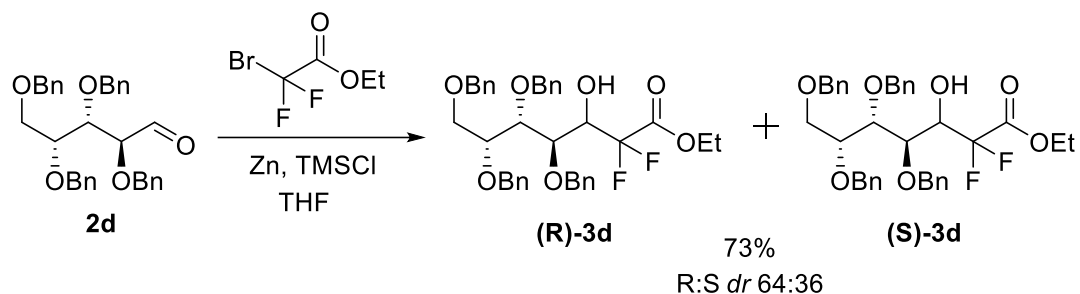


### <sup>13</sup>C NMR



## D-Lyxose

Ethyl 2,3,4,5-tetra-*O*-benzyl-1',1'-difluoro-1-hydroxyheptanoate ((*R/S*)-**3d**).

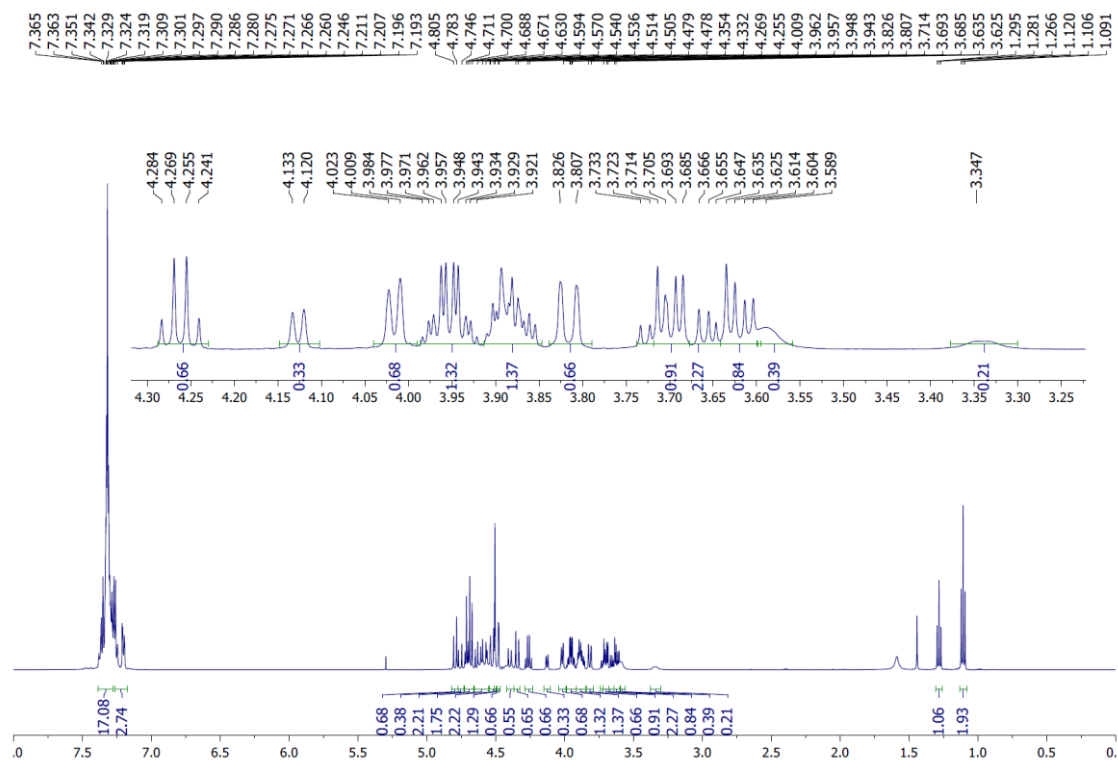


To a dry two-necked round bottomed flask was added “activated zinc” powder (1.472 g, 16.44 mmol, 5.7 equiv.). The flask was heated up at 40°C and the zinc powder suspended in dry THF (20 ml) under argon atmosphere. Then, TMSCl (120  $\mu$ l, 0.98 mmol, 0.4 equiv.) was added dropwise and the reaction was stirred at 60°C for 15 mins. Next, a solution of aldehyde **2c** (1.472 g, 2.88 mmol, 1.0 equiv.) and ethyl bromo-difluoroacetate (0.44 ml, 3.46 mmol, 1.2 equiv.) dissolved homogenously in dry THF (20 ml) under argon atmosphere was added dropwise at 60°C. The reaction was stirred vigorously for 1.5h at 60°C and then cooled at room temperature. Ice water (20 ml) and HCl (1M, 20 ml) were added and the mixture was diluted with EtOAc. The organic phase was washed with NaHCO<sub>3</sub>(sat) (2 times), brine, dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by silica gel chromatography (Cy/EtOAc 92:8) gave an inseparable mixture of two diastereoisomers (*R*)-**3d** and (*S*)-**3d** in 64:36 *dr* ratio (1.337 g, 73%).

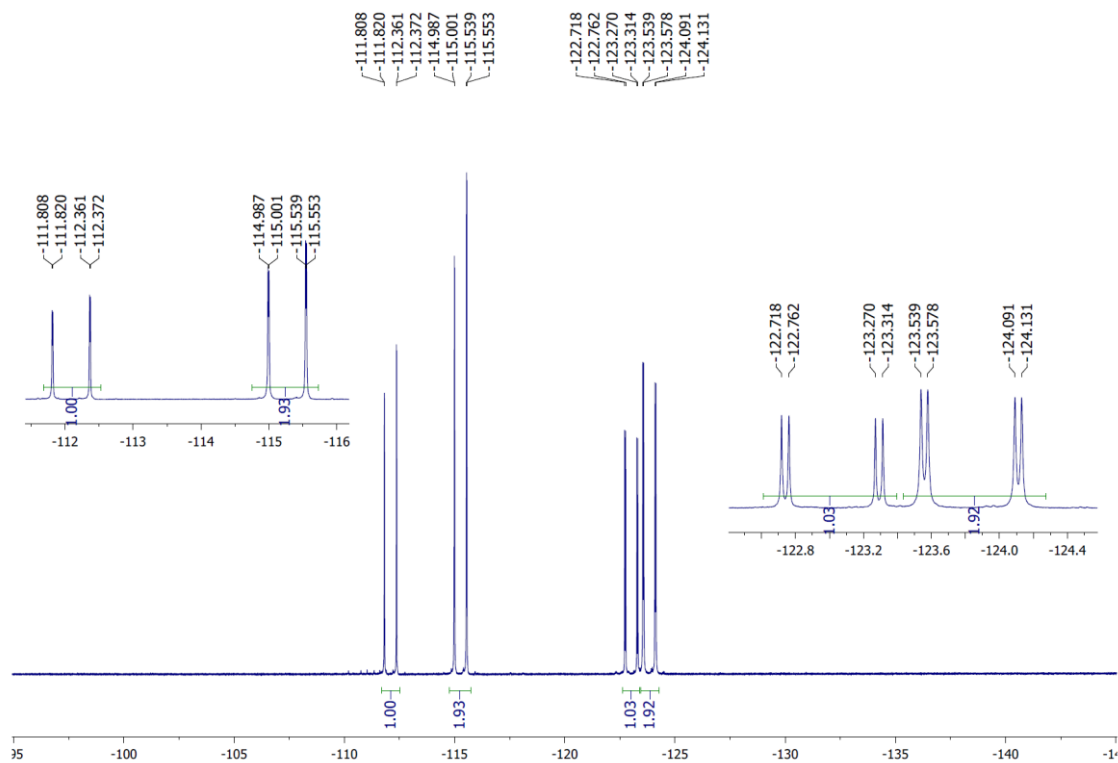
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.38-7.24 (m, 17H, H<sup>arom</sup>), 7.22-7.19 (m, 3H, H<sup>arom</sup>), 4.79 (AB, 1H,  $J_{A-B}$  = 11.3 Hz, CH<sub>2</sub>R<sup>Bn</sup>), 4.76 (AB, 1H,  $J_{A-B}$  = 11.9 Hz, CH<sub>2</sub>S<sup>Bn</sup>), 4.71 (AB, 1H,  $J_{A-B}$  = 11.3 Hz, CH<sub>2</sub>S<sup>Bn</sup>), 4.70 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub>R<sup>Bn</sup>), 4.66 (AB, 1H,  $J_{A-B}$  = 11.6 Hz, CH<sub>2</sub>R<sup>Bn</sup>), 4.66 (AB, 1H,  $J_{A-B}$  = 11.3 Hz, CH<sub>2</sub>S<sup>Bn</sup>), 4.62 (AB, 1H,  $J_{A-B}$  = 11.3 Hz, CH<sub>2</sub>S<sup>Bn</sup>), 4.58 (AB, 1H,  $J_{A-B}$  = 11.9 Hz, CH<sub>2</sub>S<sup>Bn</sup>), 4.55 (AB, 1H,  $J_{A-B}$  = 11.0 Hz, CH<sub>2</sub>S<sup>Bn</sup>), 4.53 (AB, 1H,  $J_{A-B}$  = 11.1 Hz, CH<sub>2</sub>R<sup>Bn</sup>), 4.51 (s, 2H, CH<sub>2</sub>R<sup>Bn</sup>), 4.48 (s, 2H, CH<sub>2</sub>S<sup>Bn</sup>), 4.40 (AB, 1H,  $J_{A-B}$  = 10.8 Hz, CH<sub>2</sub>S<sup>Bn</sup>), 4.34 (AB, 1H,  $J_{A-B}$  = 11.0 Hz, CH<sub>2</sub>R<sup>Bn</sup>), 4.26 (q, 2H,  $J_{CH_2CH_3}$  = 7.1 Hz, CH<sub>2</sub>CH<sub>3</sub>S), 4.13 (d, 1H,  $J_{1-2}$  = 6.5 Hz, H-1S), 4.02 (d, 1H,  $J_{1-2}$  = 6.6 Hz, H-1R), 3.95 (qd, 2H,  $J_{CH_2CH_3}$  = 7.2, 2.8 Hz, CH<sub>2</sub>CH<sub>3</sub>R), 3.91-3.85 (m, 5H, H-2R, H-2S, H-3R, H-3S, H-4R), 3.82 (d, 1H,  $J_{3-4} = J_{4-5} = 9.3$  Hz, H-4R), 3.72 (dd, 1H,  $J_{4-5} = 9.3$ ,  $J_{5a-5b} = 4.9$  Hz, H-5S), 3.70 (dd, 1H,  $J_{4-5} = 10.3$ ,  $J_{5a-5b} = 4.3$  Hz, H-5R), 3.65 (dd, 1H,  $J = 5.8, 9.8$  Hz, H-5S), 3.62 (dd, 1H,  $J = 10.6, 4.9$  Hz, H-5R), 3.59 (bs, 1H, OHR), 3.34 (bs, 1H, OHS), 1.28 (t, 3H,  $J_{CH_2CH_3} = 7.1$  Hz, CH<sub>2</sub>CH<sub>3</sub>S), 1.11 (t, 3H,  $J_{CH_2CH_3} = 7.2$  Hz, CH<sub>2</sub>CH<sub>3</sub>R) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.6 (t,  $J_{C-F} = 30.4$  Hz, C<sub>q</sub>O<sub>2</sub>EtR), 163.3 (t,  $J_{C-F} = 30.3$  Hz, C<sub>q</sub>O<sub>2</sub>EtS), 138.43 (C<sub>q</sub><sup>arom</sup>), 138.41 (C<sub>q</sub><sup>arom</sup>), 138.0 (C<sub>q</sub><sup>arom</sup>), 137.9 (C<sub>q</sub><sup>arom</sup>), 137.55 (C<sub>q</sub><sup>arom</sup>), 137.49 (C<sub>q</sub><sup>arom</sup>), 137.3 (C<sub>q</sub><sup>arom</sup>), 128.6-127.8 (CH<sup>arom</sup>), 114.9 (dd,  $J_{C-F} = 256.7$  Hz,  $J_{C-F} = 249.3$  Hz, CF<sub>2</sub>R), 114.7 (dd,  $J_{C-F} = 258.3$  Hz,  $J_{C-F} = 253.8$  Hz, CF<sub>2</sub>S), 80.8 (C-1R), 79.4 (C-2R, 2S, 3R, 3S or 4S), 78.9 (C-2R, 2S, 3R, 3S or 4S), 78.49 (C-2R, 2S, 3R, 3S or 4S), 78.46 (C-4R), 77.4 (C-2R, 2S, 3R, 3S or 4S), 74.94, 74.91, 74.5 (C-1S), 73.7 (CH<sub>2</sub><sup>Bn</sup>), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 73.4 (CH<sub>2</sub><sup>Bn</sup>), 72.8 (CH<sub>2</sub><sup>Bn</sup>), 72.4

(CH<sub>2</sub><sup>Bn</sup>), 70.2 (t, J = 22.3 Hz, CF<sub>2</sub>R), 69.7 (C-5R), 69.6 (C-5S), 69.4 (t, J = 25.9 Hz, CF<sub>2</sub>R), 63.1 (CH<sub>2</sub>CH<sub>3</sub>S), 62.5 (CH<sub>2</sub>CH<sub>3</sub>R), 14.0 (CH<sub>2</sub>CH<sub>3</sub>S), 13.8 (CH<sub>2</sub>CH<sub>3</sub>R) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>) δ = -112.1 (dd, 1F, J<sub>H1-Fa</sub> = 5.5 Hz, J<sub>Fa-Fb</sub> = 259.9 Hz, FaS), -115.3 (dd, 1F, J<sub>H1-Fa</sub> = 6.6 Hz, J<sub>Fa-Fb</sub> = 260.1 Hz, FaR), -123.0 (dd, 1F, J<sub>H-Fb</sub> = 20.4 Hz, J<sub>Fa-Fb</sub> = 259.9 Hz, FbS), -123.8 (dd, 1F, J<sub>H-Fb</sub> = 18.7 Hz, J<sub>Fa-Fb</sub> = 260.1 Hz, FbR) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for C<sub>37</sub>H<sub>41</sub>F<sub>2</sub>O<sub>7</sub> [M+H]<sup>+</sup>: calc. 635.2815; found: 635.2817.

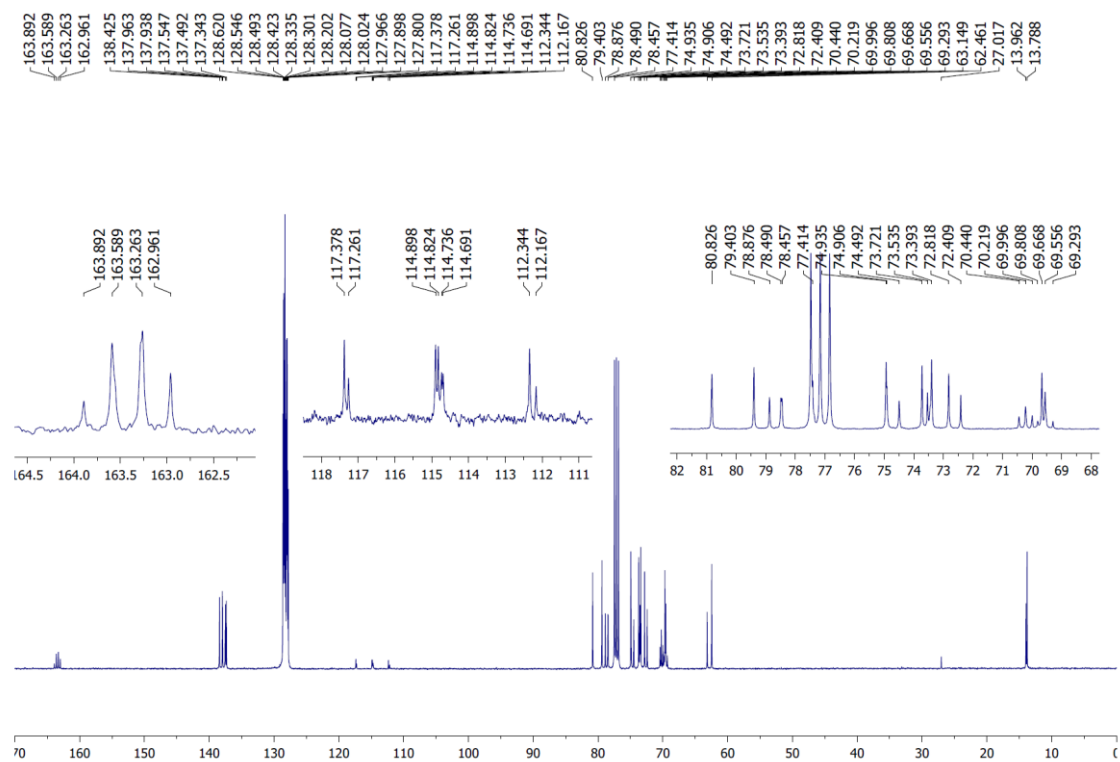
# <sup>1</sup>H NMR



# <sup>19</sup>F NMR

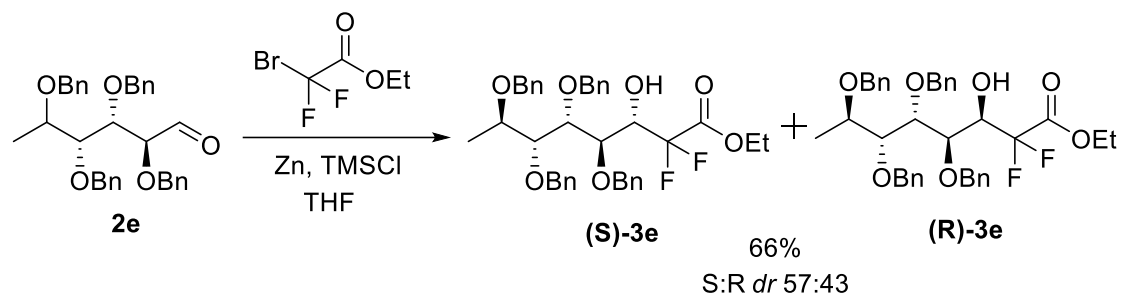


# <sup>13</sup>C NMR



## L-Fucose

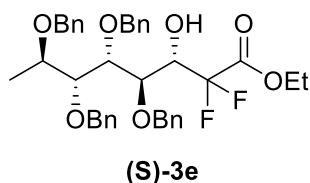
Ethyl 2,3,4,5-tetra-*O*-benzyl-1',1'-difluoro-1-hydroxyoctanoate ((*S/R*)-**3e**).



To a dry two-necked round bottomed flask was added “activated zinc” powder (660 mg, 10.1 mmol, 5.7 equiv.). The flask was heated up at 40°C and the zinc powder suspended in dry THF (13 ml) under argon atmosphere. Then, TMSCl (80  $\mu$ l, 0.60 mmol, 0.4 equiv.) was added dropwise and the reaction was stirred at 60°C for 15 mins. Next, a solution of aldehyde **2e** (929 mg, 1.77 mmol, 1.0 equiv.) and ethyl bromo-difluoroacetate (0.27 ml, 2.12 mmol, 1.2 equiv.) dissolved homogenously in dry THF (13 ml) under argon atmosphere was added dropwise at 60°C. The reaction was stirred vigorously for 2h at 60°C and then cooled at room temperature. Ice water (20 ml) and HCl (1M, 20 ml) were added and the mixture was diluted with EtOAc. The organic phase was washed with NaHCO<sub>3</sub>(sat) (2 times), brine, dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Crude NMR analysis showed the formation of two diastereoisomer (*S*)-**3e** and (*R*)-**3e** in 57:43 *dr* ratio. Purification by silica gel chromatography (Cy/EtOAc 93:7) afforded pure stereoisomer (*S*)-**3e** and (*R*)-**3e** in 66 % overall yield.

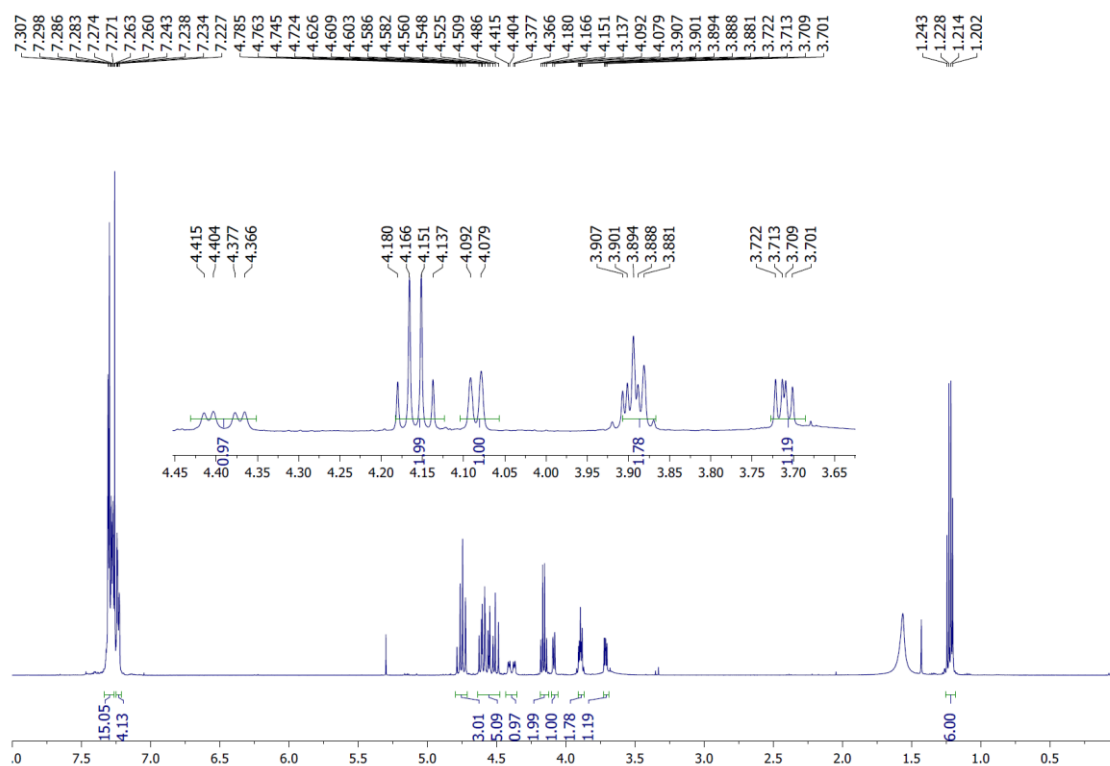


*Ethyl 4,5,6,7-tetrakis(benzyloxy)-2,2-difluoro-3-hydroxyoctanoate ((S)-3e).*

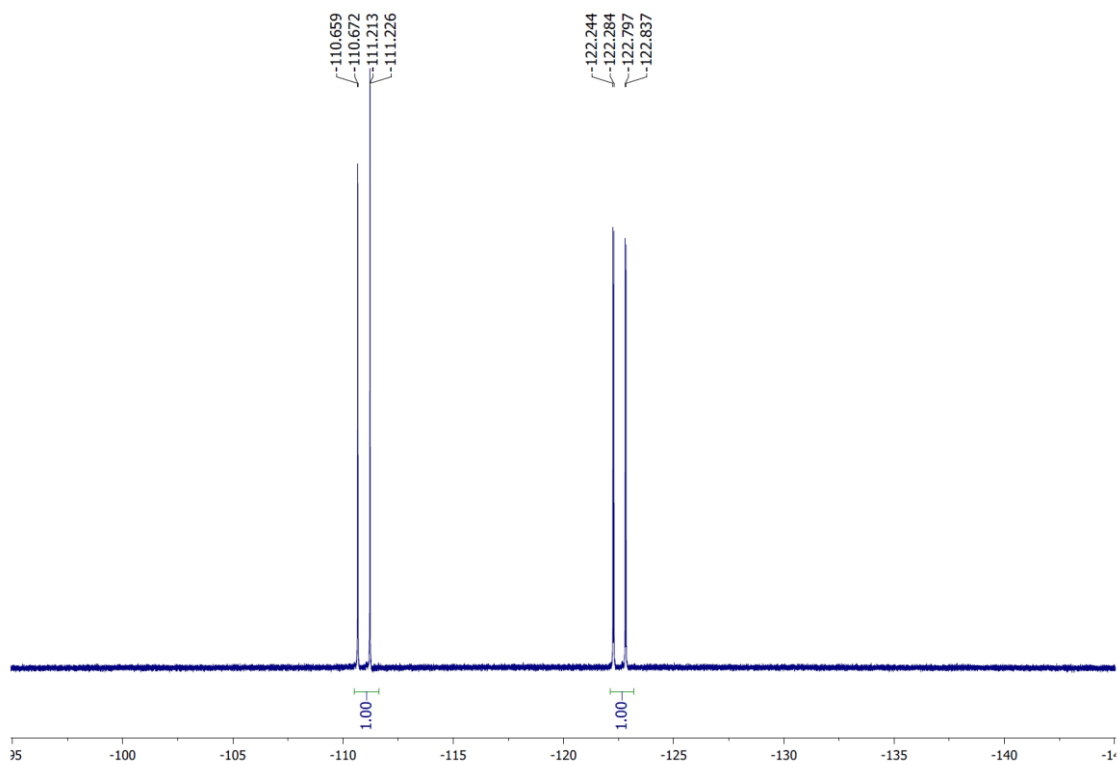


$[\alpha]_{20}^D$ : -0.2 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.33-7.27 (m, 16H, H<sup>arom</sup>), 7.25-7.12 (m, 4H, H<sup>arom</sup>), 4.78 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.74 (AB, 2H,  $J_{A-B}$  = 10.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.62 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.60 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.57 (AB, 1H,  $J_{A-B}$  = 10.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.53 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.50 (AB, 1H,  $J_{A-B}$  = 10.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.40 (dd, 1H,  $J_{1-Fa}$  = 5.7 Hz,  $J_{1-Fb}$  = 18.9 Hz, H-1), 4.16 (q, 2H,  $J_{CH_2CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.09 (d, 1H,  $J_{3-4}$  = 6.3 Hz, H-3), 3.92-3.87 (m, 2H, H-2, H-5), 3.71 (dd, 1H,  $J_{4-5}$  = 4.0 Hz,  $J_{3-4}$  = 6.3 Hz, H-4), 1.23 (t, 3H,  $J_{CH_2CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>), 1.21 (d, 3H,  $J_{5-CH_3}$  = 6.3 Hz, CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.6 (dd,  $J_{C-F}$  = 30.2 Hz,  $J_{C-F}$  = 32.6 Hz, C<sub>q</sub>O<sub>2</sub>Et), 138.8 (C<sub>q</sub><sup>arom</sup>), 138.2 (C<sub>q</sub><sup>arom</sup>), 138.1 (C<sub>q</sub><sup>arom</sup>), 137.7 (C<sub>q</sub><sup>arom</sup>), 128.5- 127.5 (CH<sup>arom</sup>), 114.6 (dd,  $J_{C-F}$  = 252.3 Hz,  $J_{C-F}$  = 259.5 Hz, CF<sub>2</sub>), 84.3 (C-4), 78.7 (C-2), 75.7 (C-5), 75.5 (C-3), 74.8 (CH<sub>2</sub><sup>Bn</sup>), 74.4 (CH<sub>2</sub><sup>Bn</sup>), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 71.8 (CH<sub>2</sub><sup>Bn</sup>), 70.0 (dd,  $J_{C-F}$  = 24.1 Hz,  $J_{C-F}$  = 27.8 Hz, C-1), 63.0 (CH<sub>2</sub>CH<sub>3</sub>), 17.0 (CH<sub>3</sub>), 13.9 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -111.0 (dd, 1F,  $J_{H1-Fa}$  = 5.7 Hz,  $J_{Fa-Fb}$  = 260.5 Hz, Fa), -122.6 (dd, 1F,  $J_{H1-Fb}$  = 18.9 Hz,  $J_{Fa-Fb}$  = 260.5 Hz, Fb) ppm. HRMS (ESI+): m/z calculated for C<sub>38</sub>H<sub>43</sub>F<sub>2</sub>O<sub>7</sub> [M+H]<sup>+</sup>: calc. 649.2971; found: 649.2971.

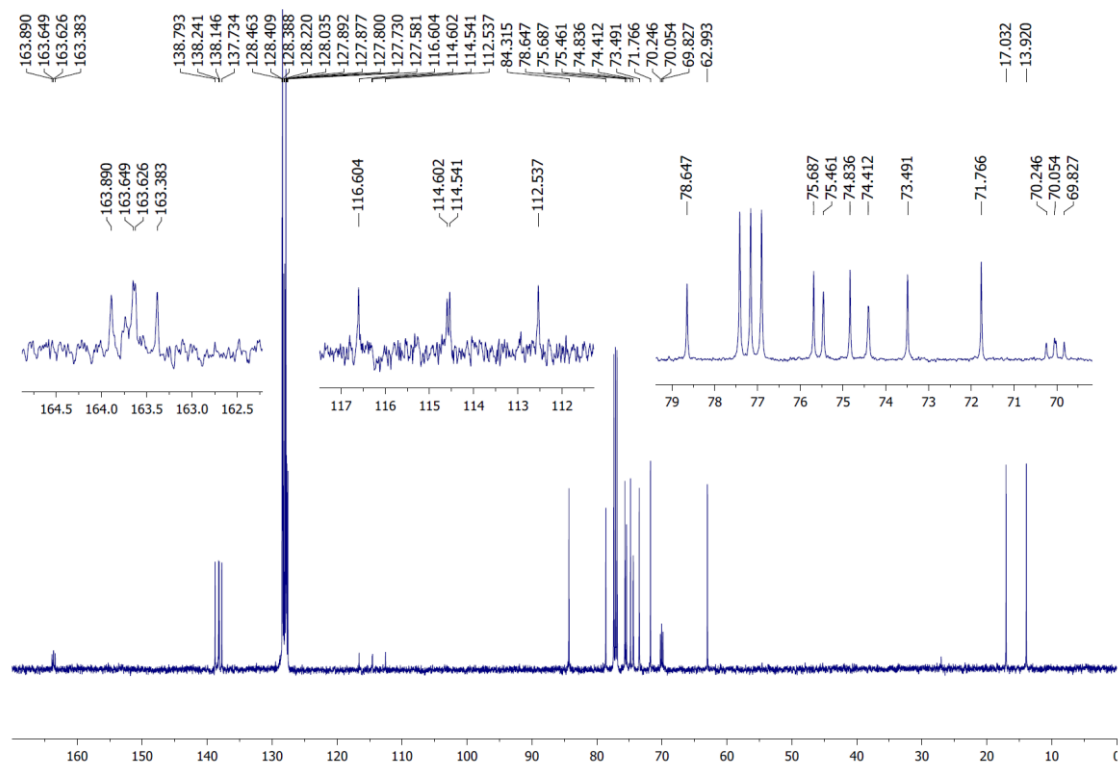
# <sup>1</sup>H NMR



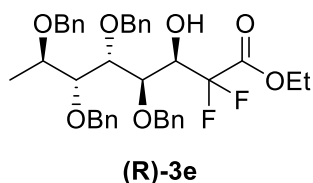
# <sup>19</sup>F NMR



# <sup>13</sup>C NMR

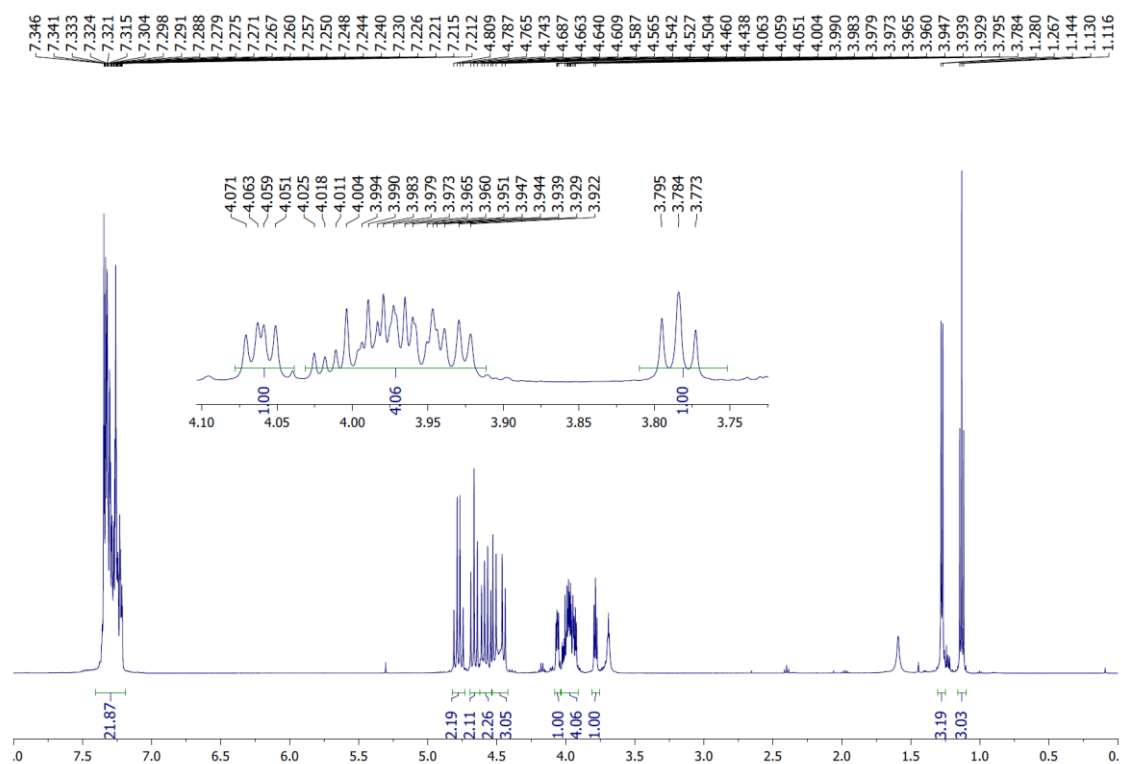


*Ethyl 4,5,6,7-tetrakis(benzyloxy)-2,2-difluoro-3-hydroxyoctanoate ((R)-3e).*

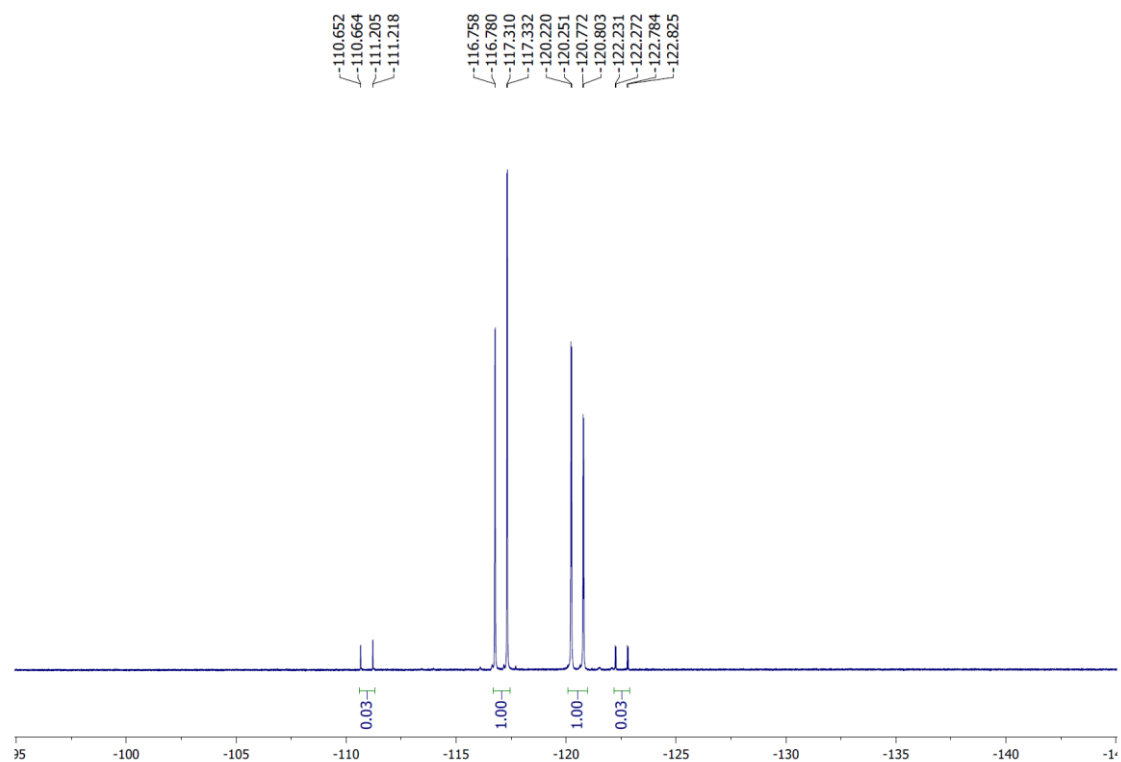


$[\alpha]_{20}^D$ : +26.3 (c 1.0,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.36-7.20 (m, 20H,  $\text{H}^{\text{arom}}$ ), 4.79 (AB, 1H,  $J_{\text{A-B}} = 10.9$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.75 (AB, 1H,  $J_{\text{A-B}} = 10.9$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.67 (AB, 1H,  $J_{\text{A-B}} = 10.9$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.65 (AB, 1H,  $J_{\text{A-B}} = 11.5$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.59 (AB, 1H,  $J_{\text{A-B}} = 10.9$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.55 (AB, 1H,  $J_{\text{A-B}} = 10.9$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.51 (AB, 1H,  $J_{\text{A-B}} = 11.5$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.51-4.44 (m, 1H, H-1), 4.44 (AB, 1H,  $J_{\text{A-B}} = 10.9$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.05 (dd, 1H,  $J_{\text{H1-Fa}} = 4.0$  Hz,  $J_{\text{H3-4}} = 6.3$  Hz, H-3), 4.02-3.91 (m, 4H, H-2, H-5,  $\text{CH}_2\text{CH}_3$ ), 3.78 (t, 1H,  $J_{\text{H3-4}} = 6.3$  Hz, H-4), 3.69 (bs, 1H, OH), 1.27 (d, 3H,  $J_{\text{H5-CH}_3} = 6.3$  Hz,  $\text{CH}_3$ ), 1.12 (t, 3H,  $J_{\text{CH}_2\text{CH}_3} = 7.5$  Hz,  $\text{CH}_2\text{CH}_3$ ) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 163.4 (t,  $J_{\text{C-F}} = 31.4$  Hz,  $\text{C}_q\text{O}_2\text{Et}$ ), 138.7 ( $\text{C}_q^{\text{arom}}$ ), 138.0 ( $\text{C}_q^{\text{arom}}$ ), 137.9 ( $\text{C}_q^{\text{arom}}$ ), 137.6 ( $\text{C}_q^{\text{arom}}$ ), 128.6- 127.6 ( $\text{CH}^{\text{arom}}$ ), 114.8 (dd,  $J_{\text{C-F}} = 252.8$  Hz,  $J_{\text{C-F}} = 255.4$  Hz,  $\text{CF}_2$ ), 83.0 (C-4), 77.7 (C-3), 76.7 (C-2), 75.2 (C-5), 74.8 ( $\text{CH}_2^{\text{Bn}}$ ), 73.4 (2  $\text{CH}_2^{\text{Bn}}$ ), 72.0 (t,  $J_{\text{C-F}} = 23.9$  Hz, C-1), 71.4 ( $\text{CH}_2^{\text{Bn}}$ ), 62.7 ( $\text{CH}_2\text{CH}_3$ ), 17.0 ( $\text{CH}_3$ ), 13.9 ( $\text{CH}_2\text{CH}_3$ ) ppm.  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  = -117.1 (dd, 1F,  $J_{\text{H1-Fa}} = 9.9$  Hz,  $J_{\text{Fa-Fb}} = 260.0$  Hz, Fa), -120.5 (dd, 1F,  $J_{\text{H1-Fb}} = 14.8$  Hz,  $J_{\text{Fa-Fb}} = 260.0$  Hz, Fb) ppm. HRMS (ESI+): m/z calculated for  $\text{C}_{38}\text{H}_{43}\text{F}_2\text{O}_7$   $[\text{M}+\text{H}]^+$ : calc. 649.2971; found: 649.2964.

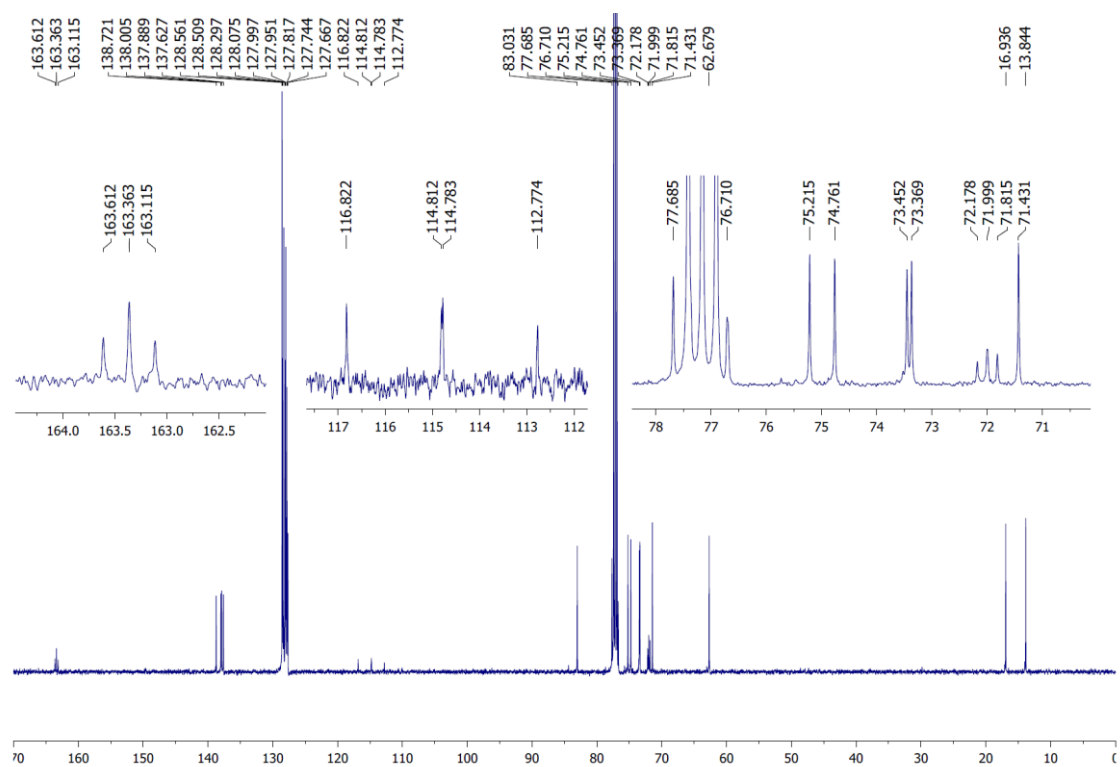
# <sup>1</sup>H NMR



# <sup>19</sup>F NMR

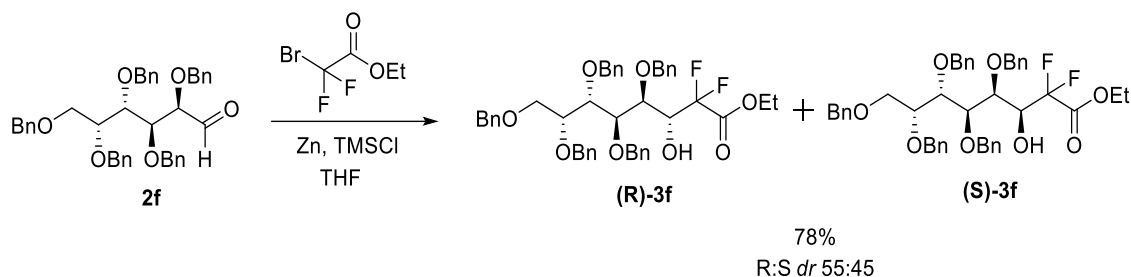


# $^{13}\text{C}$ NMR



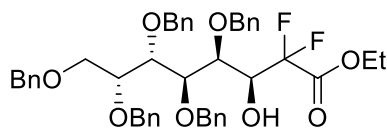
## D-Galactose

Ethyl (3*R*,4*S*,5*R*,6*S*,7*R*)-4,5,6,7,8-pentakis(benzyloxy)-2,2-difluoro-3-hydroxyoctanoate ((*R/S*)-**3f**).



To a dry two-necked round bottomed flask was added “activated zinc” powder (309 mg, 4.73 mmol, 5.7 equiv.). The flask was heated up at 40°C and the zinc powder suspended in dry THF (6 ml) under argon atmosphere. Then, TMSCl (35  $\mu$ l, 0.28 mmol, 0.4 equiv.) was added dropwise and the reaction was stirred at 60°C for 15 mins. Next, a solution of aldehyde **2f** (522 mg, 0.828 mmol, 1.0 equiv.) and ethyl bromo-difluoroacetate (0.13 ml, 1.01 mmol, 1.2 equiv.) dissolved homogenously in dry THF (6 ml) under argon atmosphere was added dropwise at 60°C. The reaction was stirred vigorously for 1.5h at 60°C and then cooled at room temperature. Ice water (5 ml) and HCl (1M, 10 ml) were added and the mixture was diluted with EtOAc. The organic phase was washed with NaHCO<sub>3</sub>(sat) (2 times), brine, dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Crude NMR analysis showed the formation of two diastereoisomer (*R*)-**3f** and (*S*)-**3f** in 55:45 *dr* ratio. Purification by silica gel chromatography (Cy/Et<sub>2</sub>O 85:15) afforded pure diastereoisomers (*R*)-**3f** and (*S*)-**3f** in 78% overall yield.

*Ethyl (3R,4S,5R,6S,7R)-4,5,6,7,8-pentakis(benzyloxy)-2,2-difluoro-3-hydroxyoctanoate ((S)-3f).*

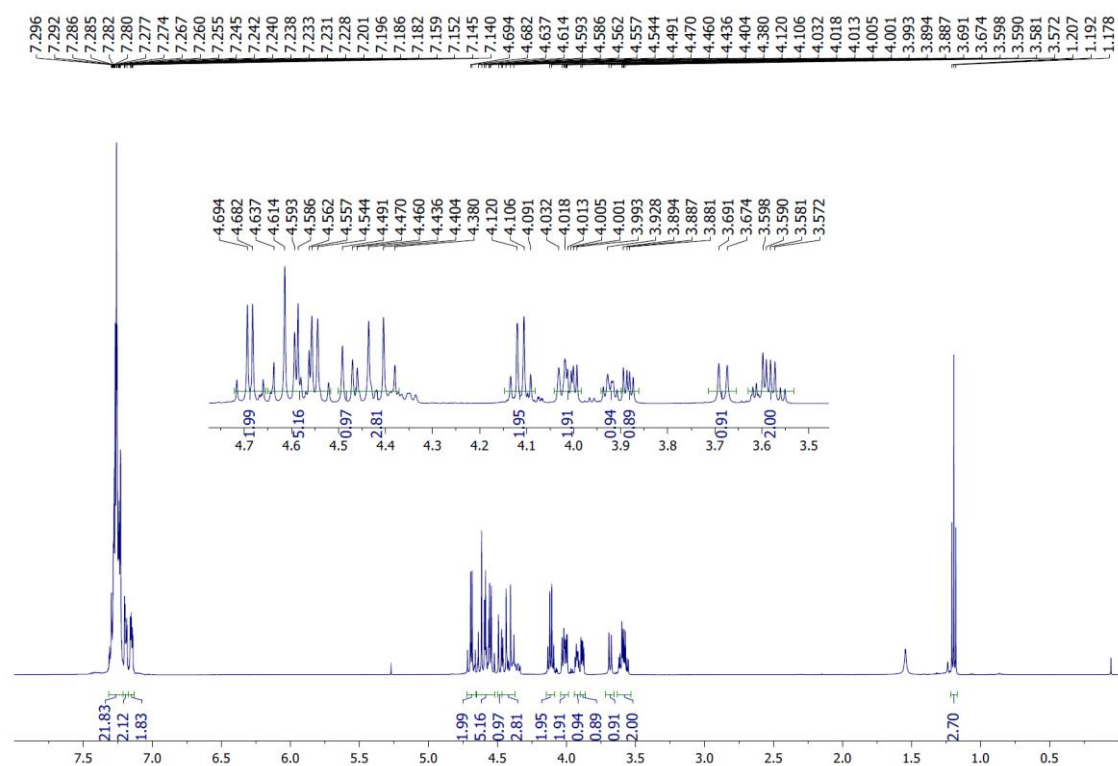


**(S)-3f**

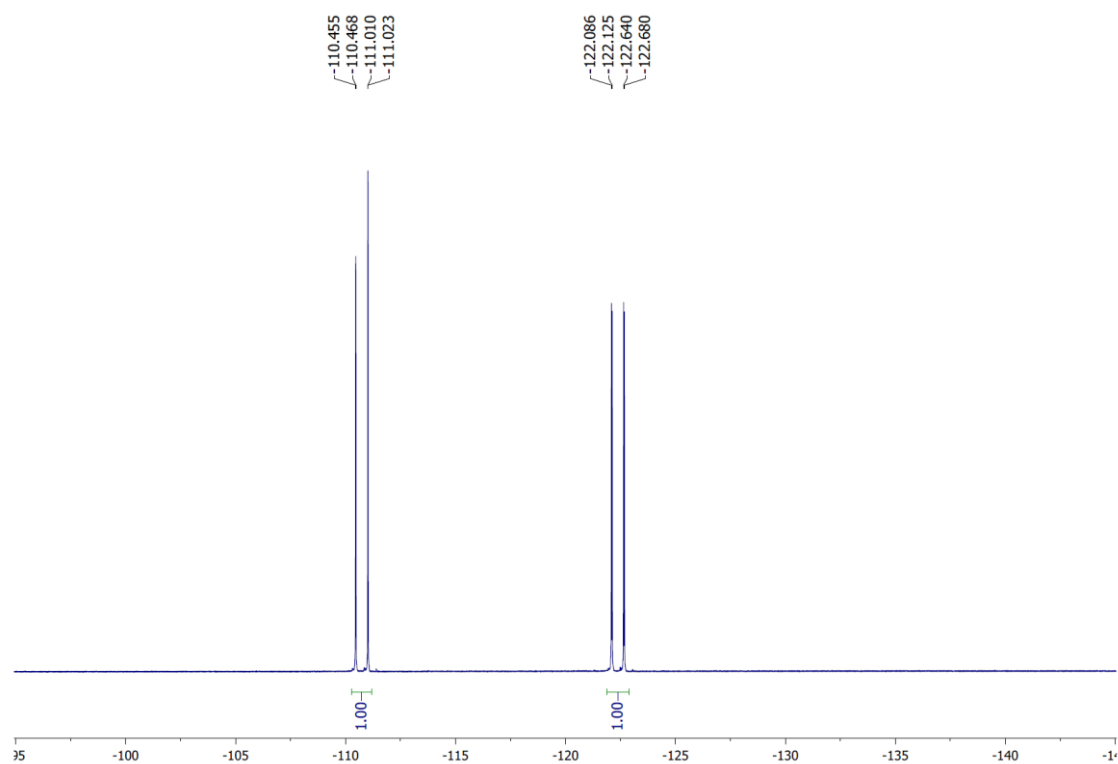
$[\alpha]_{20}^D$ : -1.0 (c 1.0,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.34-7.25 (m, 21H,  $\text{H}^{\text{arom}}$ ), 7.23-7.21 (m, 2H,  $\text{H}^{\text{arom}}$ ), 7.19-7.17 (m, 2H,  $\text{H}^{\text{arom}}$ ), 4.73 (AB, 1H,  $J_{\text{A-B}}$  = 10.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.70 (AB, 1H,  $J_{\text{A-B}}$  = 10.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.65 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.64-4.58 (m, 3H,  $\text{CH}_2^{\text{Bn}}$ ), 4.56 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.51 (AB, 1H,  $J_{\text{A-B}}$  = 10.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.48 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.45-4.36 (m, 1H, H-1), 4.42 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.14 (q, 2H,  $J_{\text{CH}_2\text{CH}_3}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3$ ), 4.05 (d, 1H,  $J_{2-3}$  = 6.3 Hz, H-2), 4.03 (dd, 1H,  $J_{2-3}$  = 6.3 Hz,  $J_{3-4}$  = 4.0 Hz, H-3), 3.97-3.93 (m, 1H, H-5), 3.91 (dd, 1H,  $J_{3-4}$  = 4.0 Hz,  $J_{4-5}$  = 6.9 Hz, H-4), 3.71 (d, 1H,  $J_{1-\text{OH}}$  = 8.6 Hz, OH), 3.63 (ABX, 1H,  $J_{5-6a}$  = 4.0 Hz,  $J_{6a-6b}$  = 10.3 Hz, H-6a), 3.59 (ABX, 1H,  $J_{5-6a}$  = 4.6 Hz,  $J_{6a-6b}$  = 10.3 Hz, H-6b), 1.22 (t, 3H,  $J_{\text{CH}_2\text{CH}_3}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3$ ) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 163.7 (dd,  $J_{\text{C-F}}$  = 28.9 Hz,  $J_{\text{C-F}}$  = 31.7 Hz,  $\text{C}_q\text{O}_2\text{Et}$ ), 138.7 ( $\text{C}_q^{\text{arom}}$ ), 138.3 ( $\text{C}_q^{\text{arom}}$ ), 138.2 (2  $\text{C}_q^{\text{arom}}$ ), 137.8 ( $\text{C}_q^{\text{arom}}$ ), 128.6-127.6 ( $\text{CH}^{\text{arom}}$ ), 114.6 (dd,  $J_{\text{C-F}}$  = 252.5 Hz,  $J_{\text{C-F}}$  = 254.9 Hz,  $\text{CF}_2$ ), 80.6 (C-3), 77.9 (C-4, C-5), 75.7 (C-2), 74.8 ( $\text{CH}_2^{\text{Bn}}$ ), 74.4 ( $\text{CH}_2^{\text{Bn}}$ ), 73.6 ( $\text{CH}_2^{\text{Bn}}$ ), 73.5 ( $\text{CH}_2^{\text{Bn}}$ ), 73.3 ( $\text{CH}_2^{\text{Bn}}$ ), 70.2 (C-6), 70.1 (dd,  $J_{\text{C-F}}$  = 13.3 Hz,  $J_{\text{C-F}}$  = 39.8 Hz, C-1), 63.0 ( $\text{CH}_2\text{CH}_3$ ), 14.0 ( $\text{CH}_2\text{CH}_3$ ) ppm.  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  = -110.8 (dd, 1F,  $J_{\text{H1-Fa}}$  = 6.3 Hz,  $J_{\text{Fa-Fb}}$  = 261.4 Hz, Fa), -122.4 (dd, 1F,  $J_{\text{H1-Fb}}$  = 18.4 Hz,  $J_{\text{Fa-Fb}}$  = 261.4 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for  $\text{C}_{45}\text{H}_{49}\text{F}_2\text{O}_8$   $[\text{M}+\text{H}]^+$ : calc. 755.3390; found: 755.3383.



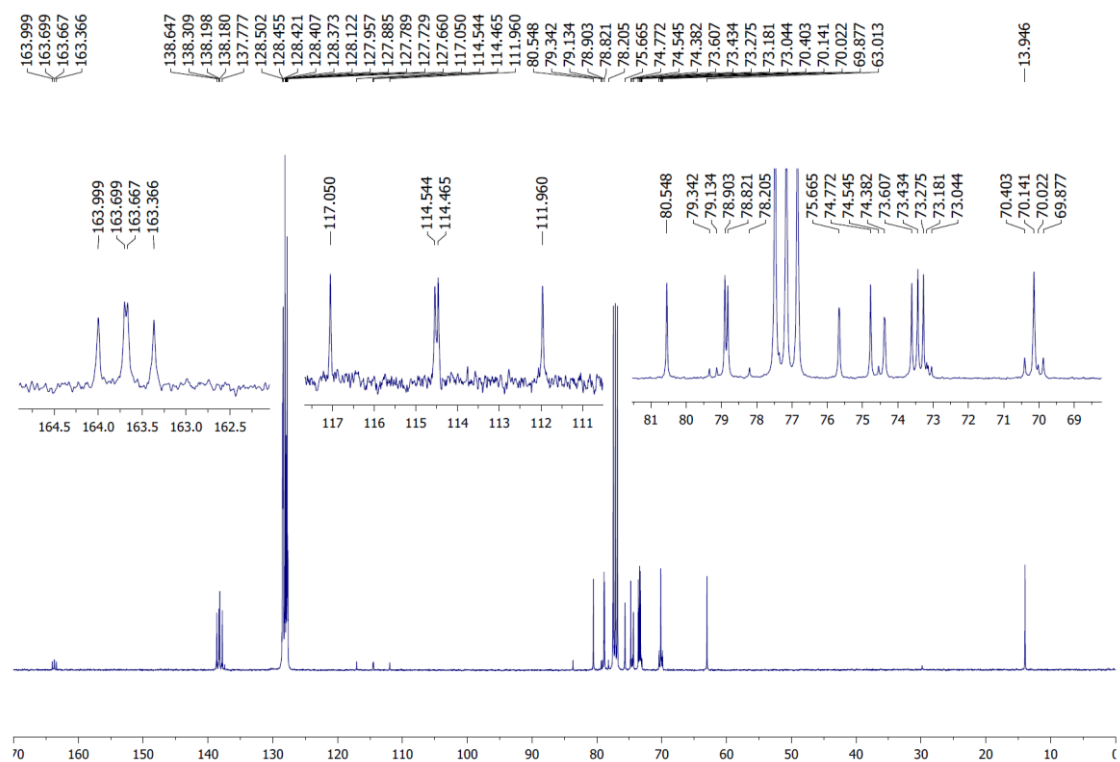
# <sup>1</sup>H NMR



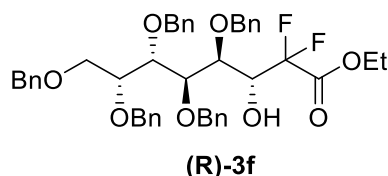
# <sup>19</sup>F NMR



# <sup>13</sup>C NMR

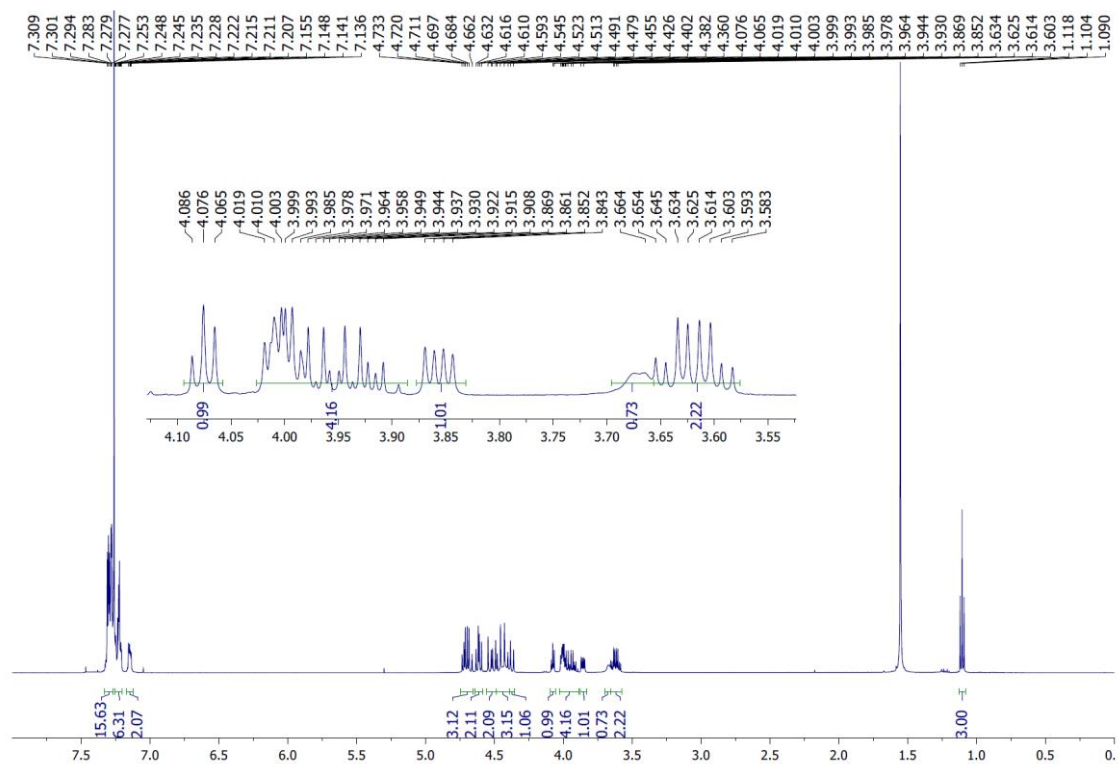


*Ethyl 4,5,6,7,8-pentakis(benzyloxy)-2,2-difluoro-3-hydroxyoctanoate ((R)-3f).*

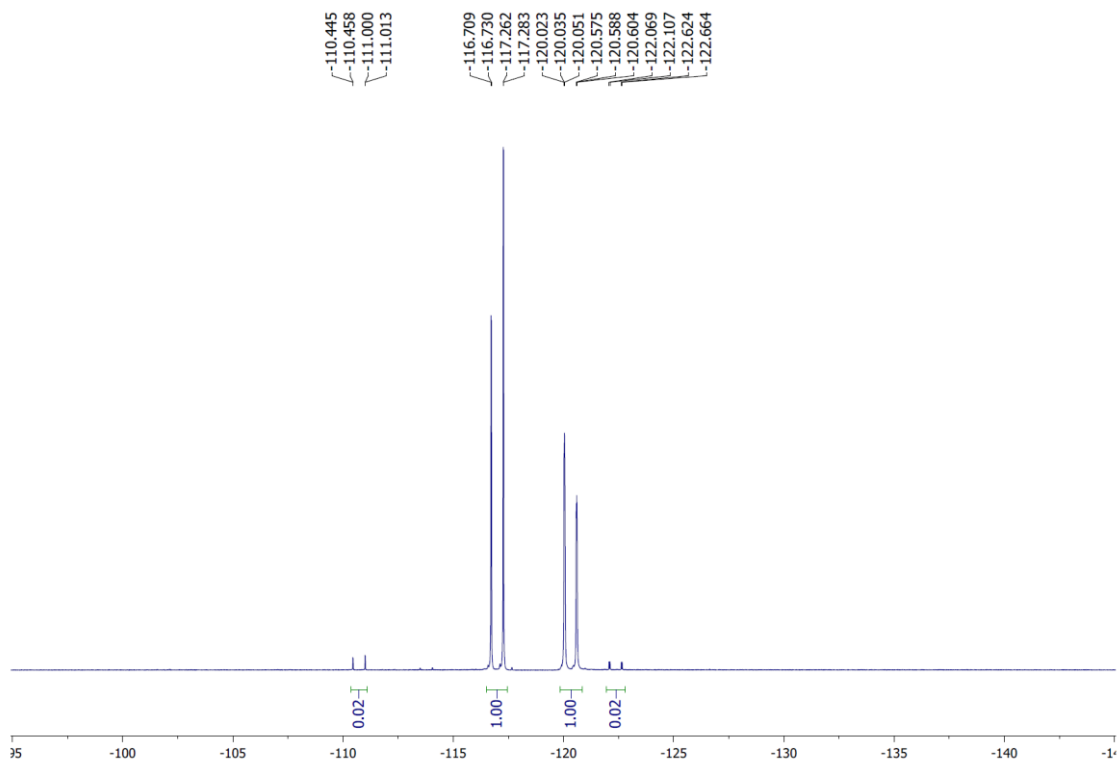


$[\alpha]_{20}^D$ : +1.1 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.32-7.27 (m, 17H, H<sup>arom</sup>), 7.24-7.21 (m, 6H, H<sup>arom</sup>), 7.16-7.13 (m, 2H, H<sup>arom</sup>), 4.72 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.71 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.67 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.62 (AB, 1H,  $J_{A-B}$  = 10.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.60 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.53 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.50 (AB, 1H,  $J_{A-B}$  = 10.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.47 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.46-4.37 (m, 1H, H-1), 4.41 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.37 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.08 (t, 1H,  $J$  = 5.2 Hz, H-4), 4.02-3.98 (m, 2H, H-3, H-5), 3.98-3.89 (m, 2H, CH<sub>2</sub>CH<sub>3</sub>), 3.86 (dd, 1H,  $J$  = 4.6 Hz,  $J$  = 8.6 Hz, H-2), 3.67 (m, 1H, OH), 3.64 (ABX, 1H,  $J_{5-6a}$  = 4.6 Hz,  $J_{6a-6b}$  = 10.3 Hz, H-6a), 3.60 (ABX, 1H,  $J_{5-6b}$  = 5.2 Hz,  $J_{6a-6b}$  = 10.3 Hz, H-6b), 1.10 (t, 3H,  $J_{CH_2-CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.3 (t,  $J_{C-F}$  = 31.4 Hz, C<sub>q</sub>O<sub>2</sub>Et), 138.5 (C<sub>q</sub><sup>arom</sup>), 138.1 (C<sub>q</sub><sup>arom</sup>), 138.0 (C<sub>q</sub><sup>arom</sup>), 137.9 (C<sub>q</sub><sup>arom</sup>), 137.6 (C<sub>q</sub><sup>arom</sup>), 128.6- 127.7 (CH<sup>arom</sup>), 114.8 (dd,  $J_{C-F}$  = 252.8 Hz,  $J_{C-F}$  = 256.5 Hz, CF<sub>2</sub>), 79.5 (C-4), 78.3 (C-3 or C-5), 78.2 (C-3 or C-5), 76.8 (C-2), 74.7 (CH<sub>2</sub><sup>Bn</sup>), 73.6 (CH<sub>2</sub><sup>Bn</sup>), 73.5 (2 CH<sub>2</sub><sup>Bn</sup>), 73.1 (CH<sub>2</sub><sup>Bn</sup>), 72.0 (t,  $J_{C-F}$  = 22.9 Hz, C-1), 70.0 (C-6), 62.7 (CH<sub>2</sub>CH<sub>3</sub>), 13.8 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -117.0 (dd, 1F,  $J_{H-Fa}$  = 9.9 Hz,  $J_{Fa-Fb}$  = 260.0 Hz, Fa), -120.3 (dd, 1F,  $J_{H-Fb}$  = 6.6 Hz,  $J_{H-Fb}$  = 13.5 Hz,  $J_{Fa-Fb}$  = 260.0 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for C<sub>45</sub>H<sub>49</sub>F<sub>2</sub>O<sub>8</sub> [M+H]<sup>+</sup>: calc. 755.3390; found: 755.3380.

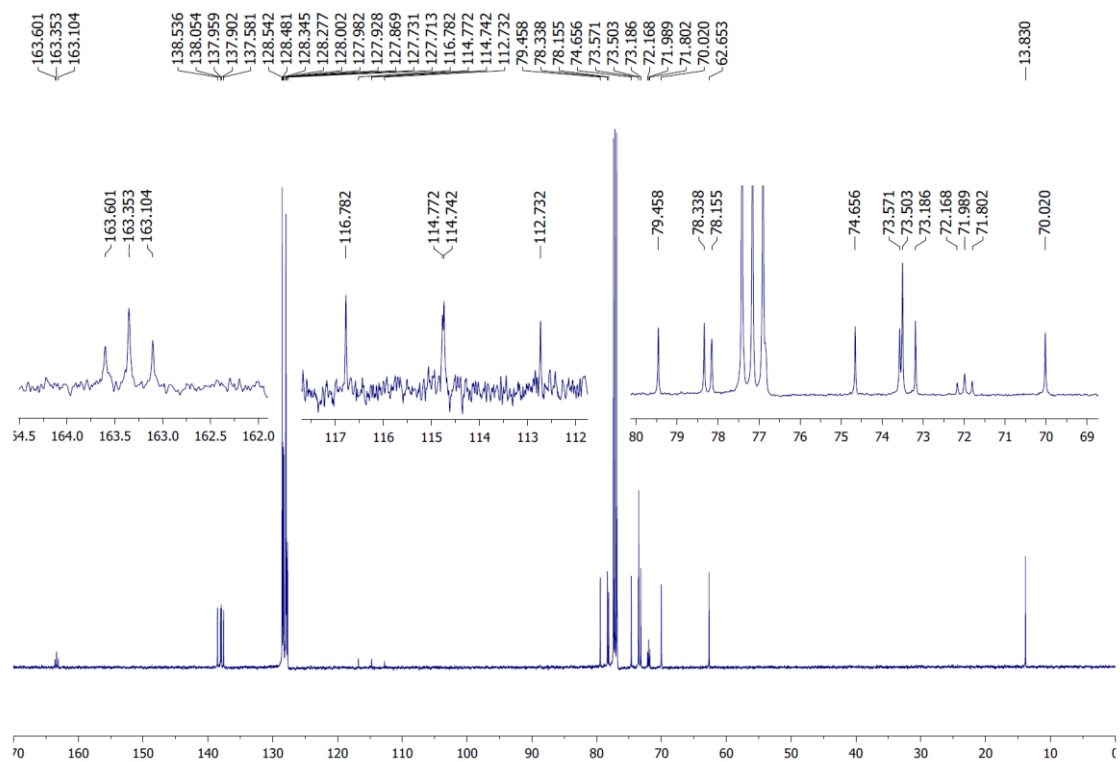
# <sup>1</sup>H NMR



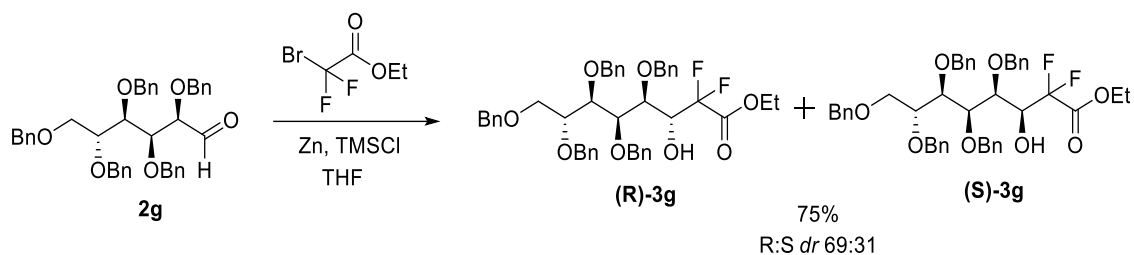
# <sup>19</sup>F NMR



# <sup>13</sup>C NMR

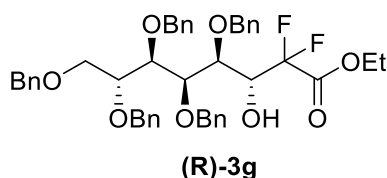


*Ethyl 4,5,6,7,8-pentakis(benzyloxy)-2,2-difluoro-3-hydroxyoctanoate ((R/S)-3g).*



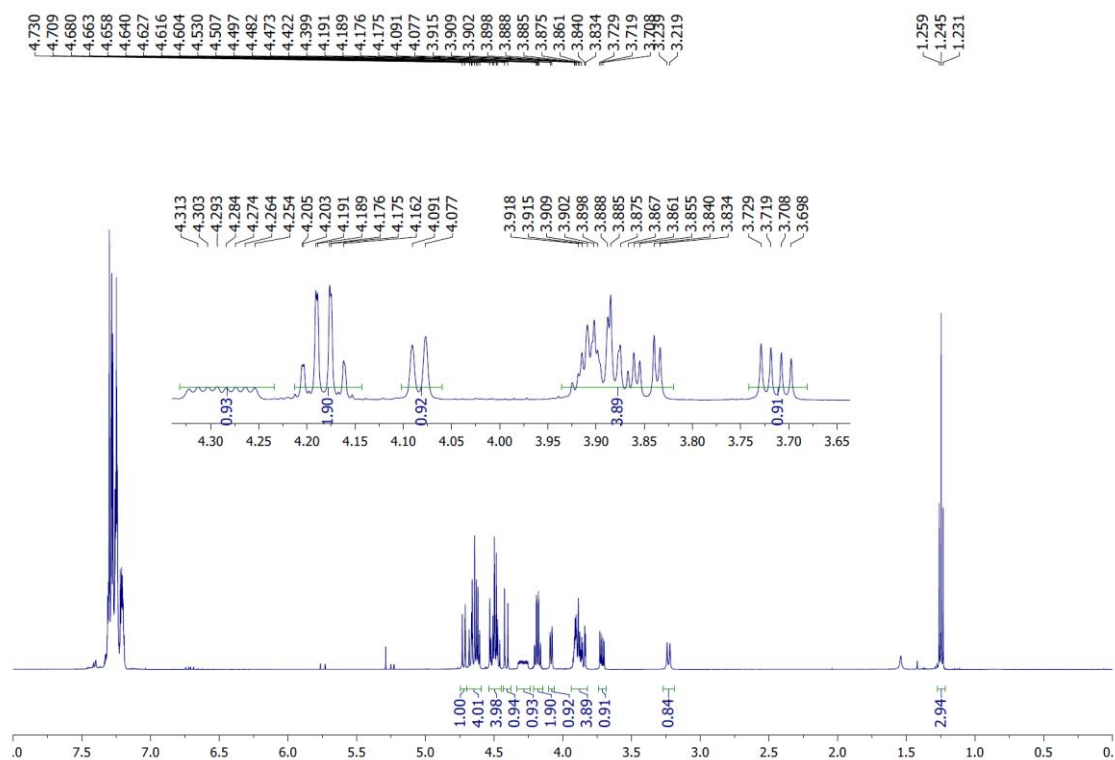
To a dry two-necked round bottomed flask was added “activated zinc” powder (398 mg, 6.09 mmol, 5.7 equiv.). The flask was heated up at 40°C and the zinc powder suspended in dry THF (8 ml) under argon atmosphere. Then, TMSCl (50 µl, 0.36 mmol, 0.4 equiv.) was added dropwise and the reaction was stirred at 60°C for 15 mins. Next, a solution of aldehyde **2g** (672 g, 1.065 mmol, 1.0 equiv.) and ethyl bromo-difluoroacetate (0.17 ml, 1.28 mmol, 1.2 equiv.) dissolved homogenously in dry THF (8 ml) under argon atmosphere was added dropwise at 60°C. The reaction was stirred vigorously for 1.5h at 60°C and then cooled at room temperature. Ice water (5 ml) and HCl (1M, 10 ml) were added and the mixture was diluted with EtOAc. The organic phase was washed with NaHCO<sub>3</sub>(sat) (2 times), brine, dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Crude NMR analysis showed the formation of two diastereoisomer **(R)-3g** and **(S)-3g** in 69:31 *dr* ratio. Purification by silica gel chromatography (Cy/EtOAc 92:8) afforded pure diastereoisomers **(R)-3g** and **(S)-3g** in 75% overall yield.

*Ethyl 4,5,6,7,8-pentakis(benzyloxy)-2,2-difluoro-3-hydroxyoctanoate ((R)-3g).*

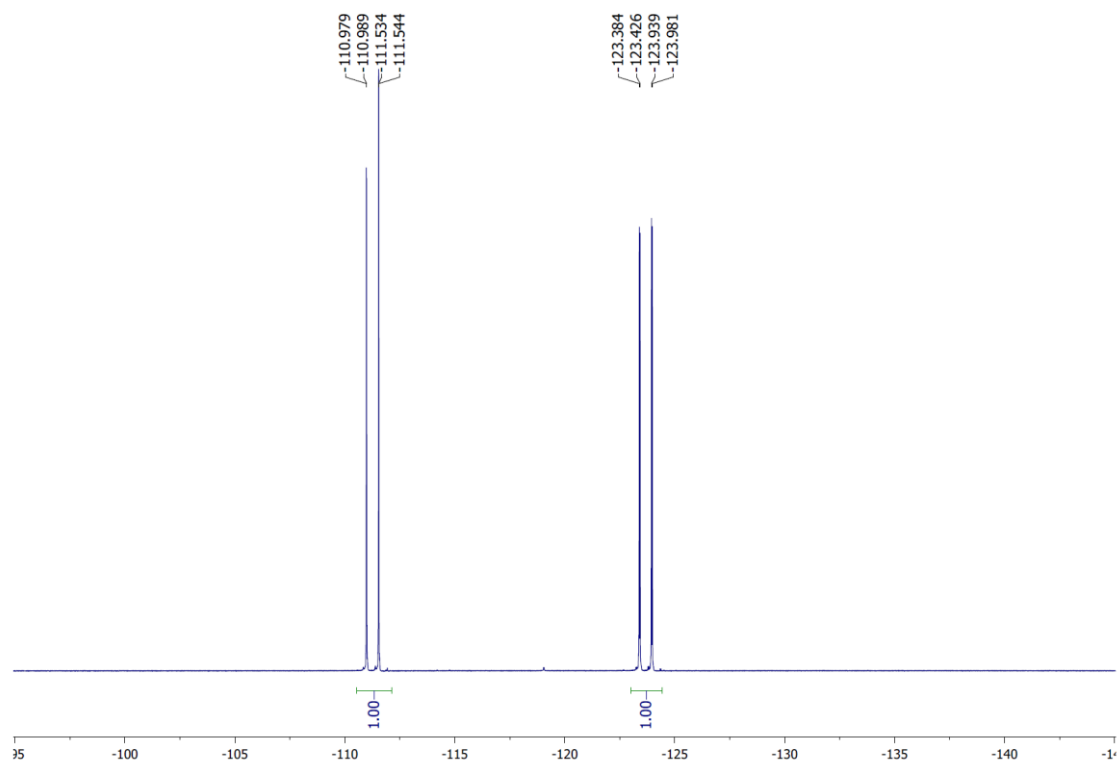


$[\alpha]_{20}^D$ : +5.0 (c 1.0,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.33-7.24 (m, 21H,  $\text{H}^{\text{arom}}$ ), 7.23-7.20 (m, 4H,  $\text{H}^{\text{arom}}$ ), 4.73 (AB, 1H,  $J_{\text{A-B}}$  = 10.3 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.68 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.66 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.64 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.63 (AB, 1H,  $J_{\text{A-B}}$  = 10.3 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.53 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.52 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.50 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.48 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.42 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.30 (ddd, 1H,  $J_{1-\text{Fa}}$  = 4.6 Hz,  $J_{1-\text{OH}}$  = 9.7 Hz,  $J_{1-\text{Fb}}$  = 19.5 Hz, H-1), 4.20 (q, 2H,  $J_{\text{CH}_2-\text{CH}_3}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3$ ), 4.10 (d, 1H,  $J$  = 6.9 Hz, H-3), 3.94-3.88 (m, 3H, H-2, H-4, H-5), 3.86 (ABX, 1H,  $J_{5-6a}$  = 3.4 Hz,  $J_{6a-6b}$  = 10.3 Hz, H-6a), 3.72 (ABX, 1H,  $J_{5-6b}$  = 5.2 Hz,  $J_{6a-6b}$  = 10.3 Hz, H-6b), 3.24 (d, 1H,  $J_{1-\text{OH}}$  = 9.7 Hz, OH), 1.26 (t, 3H,  $J_{\text{CH}_2-\text{CH}_3}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3$ ) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 163.5 (dd,  $J_{\text{C-F}}$  = 29.0 Hz,  $J_{\text{C-F}}$  = 33.8 Hz,  $\text{C}_q\text{O}_2\text{Et}$ ), 138.7 ( $\text{C}_q^{\text{arom}}$ ), 138.4 ( $\text{C}_q^{\text{arom}}$ ), 138.3 ( $\text{C}_q^{\text{arom}}$ ), 138.2 ( $\text{C}_q^{\text{arom}}$ ), 137.5 ( $\text{C}_q^{\text{arom}}$ ), 128.5- 127.6 ( $\text{CH}^{\text{arom}}$ ), 114.6 (dd,  $J_{\text{C-F}}$  = 252.9 Hz,  $J_{\text{C-F}}$  = 258.9 Hz,  $\text{CF}_2$ ), 78.7 (C-2, C-4), 78.3 (C-5), 74.7 ( $\text{CH}_2^{\text{Bn}}$ ), 74.6 (C-3), 74.5 ( $\text{CH}_2^{\text{Bn}}$ ), 74.1 ( $\text{CH}_2^{\text{Bn}}$ ), 73.5 ( $\text{CH}_2^{\text{Bn}}$ ), 71.9 ( $\text{CH}_2^{\text{Bn}}$ ), 69.8 (dd,  $J_{\text{C-F}}$  = 24.1 Hz,  $J_{\text{C-F}}$  = 29.0 Hz, C-1), 69.7 (C-6), 63.2 ( $\text{CH}_2\text{CH}_3$ ), 14.0 ( $\text{CH}_2\text{CH}_3$ ) ppm.  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  = -111.3 (dd, 1F,  $J_{\text{H1-Fa}}$  = 4.6 Hz,  $J_{\text{Fa-Fb}}$  = 261.4 Hz, Fa), -123.7 (dd, 1F,  $J_{\text{H1-Fb}}$  = 19.5 Hz,  $J_{\text{Fa-Fb}}$  = 261.4 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for  $\text{C}_{45}\text{H}_{49}\text{F}_2\text{O}_8$   $[\text{M}+\text{H}]^+$ : calc. 755.3390; found: 755.3376.

# <sup>1</sup>H NMR

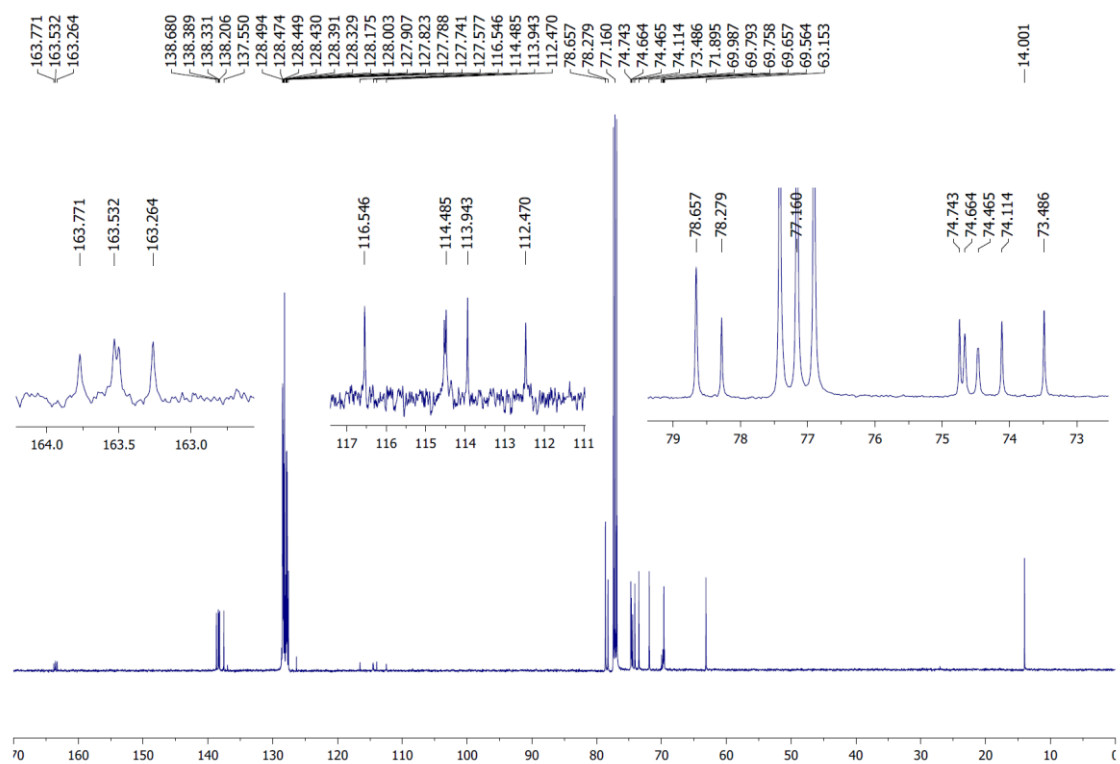


# <sup>19</sup>F NMR

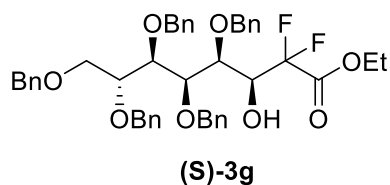




# <sup>13</sup>C NMR

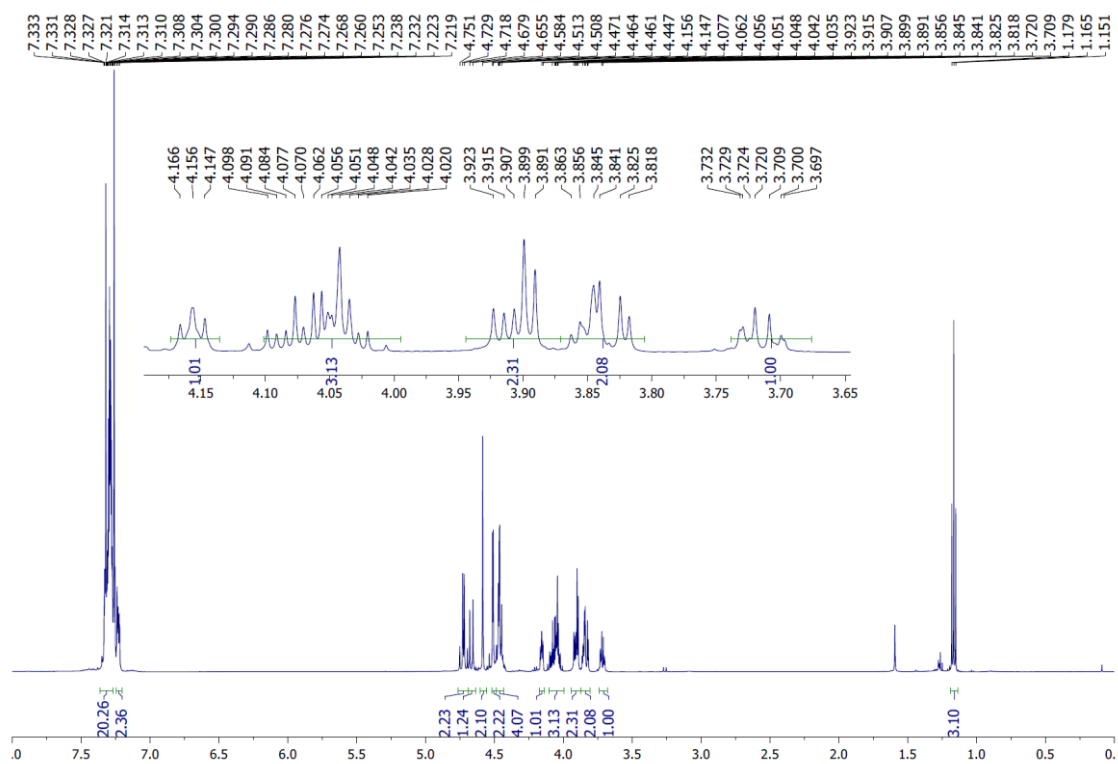


*Ethyl 4,5,6,7,8-pentakis(benzyloxy)-2,2-difluoro-3-hydroxyoctanoate ((S)-3g).*

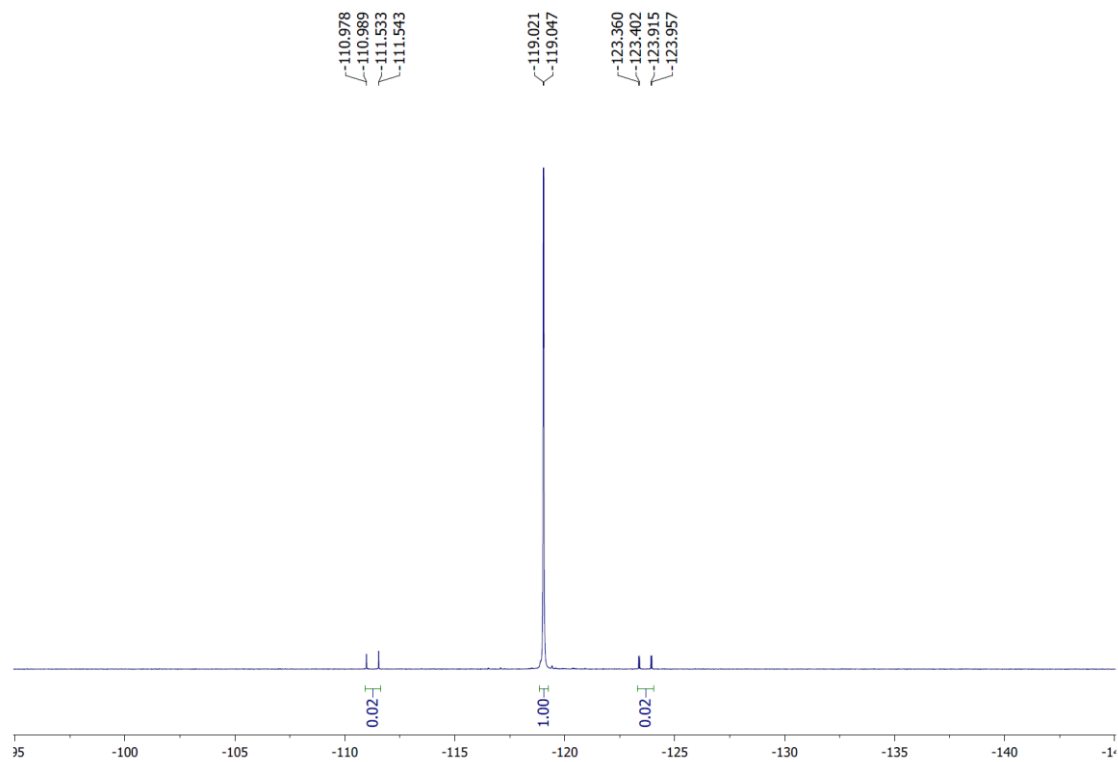


$[\alpha]_{20}^D$ : -0.2 (c 0.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.34-7.27 (m, 23H, H<sup>arom</sup>), 7.24-7.22 (m, 2H, H<sup>arom</sup>), 4.74 (AB, 1H,  $J_{A-B}$  = 10.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.71 (AB, 1H,  $J_{A-B}$  = 10.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.67 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.58 (s, 2H, CH<sub>2</sub><sup>Bn</sup>), 4.53 (AB, 1H,  $J_{A-B}$  = 12.6 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.50 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.48-4.44 (m, 4H, 3 CH<sub>2</sub><sup>Bn</sup>, H-1), 4.16 (t, 1H,  $J_{3-4}$  =  $J_{4-5}$  = 4.6 Hz, H-4), 4.10-4.02 (m, 3H, H-3, CH<sub>2</sub>CH<sub>3</sub>), 3.91 (dd, 1H,  $J$  = 4.0 Hz,  $J$  = 8.0 Hz, H-2), 3.89 (d, 1H,  $J_{1-OH}$  = 4.0 Hz, OH), 3.86-3.81 (m, 2H, H-5, H-6a), 3.71 (ABX, 1H,  $J_{5-6b}$  = 4.6 Hz,  $J_{6a-6b}$  = 10.3 Hz, H-6b), 1.17 (t, 3H,  $J_{CH_2-CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.3 (t,  $J_{C-F}$  = 31.4 Hz, C<sub>q</sub>O<sub>2</sub>Et), 138.5 (C<sub>q</sub><sup>arom</sup>), 138.3 (C<sub>q</sub><sup>arom</sup>), 138.1 (C<sub>q</sub><sup>arom</sup>), 137.5 (C<sub>q</sub><sup>arom</sup>), 137.4 (C<sub>q</sub><sup>arom</sup>), 128.6- 127.7 (CH<sup>arom</sup>), 114.8 (t,  $J_{C-F}$  = 255.2 Hz, CF<sub>2</sub>), 79.1 (C-5), 78.7 (C-3), 77.9 (C-4), 74.4 (C-2), 74.3 (CH<sub>2</sub><sup>Bn</sup>), 74.2 (CH<sub>2</sub><sup>Bn</sup>), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 73.1 (CH<sub>2</sub><sup>Bn</sup>), 72.1 (CH<sub>2</sub><sup>Bn</sup>), 71.8 (t,  $J_{C-F}$  = 22.9 Hz, C-1), 69.2 (C-6), 62.8 (CH<sub>2</sub>CH<sub>3</sub>), 13.9 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -119.0 (s, 1F, Fa), -119.1 (s, 1F, Fb) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for C<sub>45</sub>H<sub>49</sub>F<sub>2</sub>O<sub>8</sub> [M+H]<sup>+</sup>: calc. 755.3390; found: 755.3381.

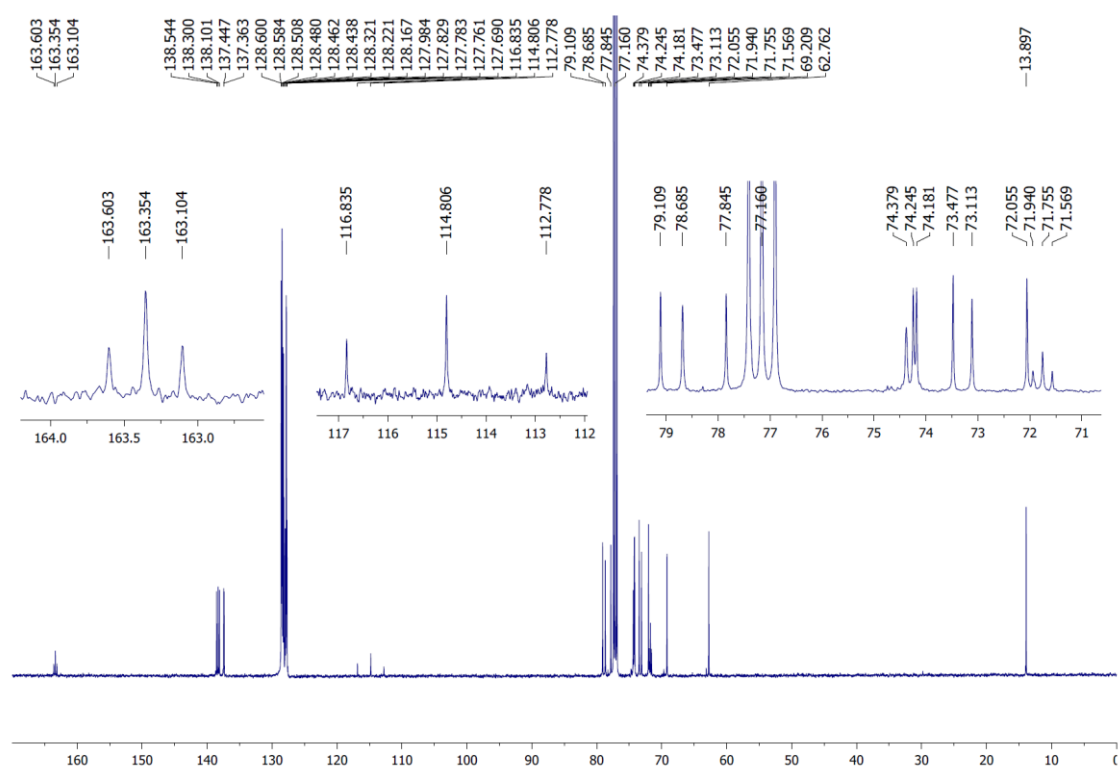
# <sup>1</sup>H NMR



# <sup>19</sup>F NMR

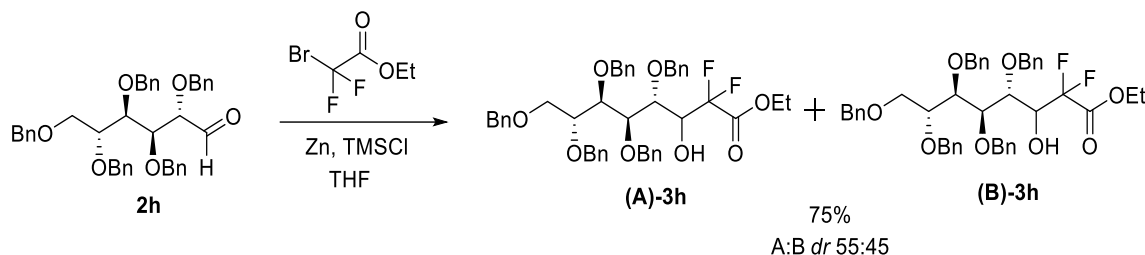


# <sup>13</sup>C NMR



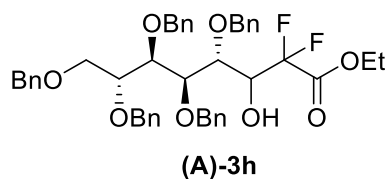
## D-Mannose

Ethyl 4,5,6,7,8-pentakis(benzyloxy)-2,2-difluoro-3-hydroxyoctanoate ((A/B)-**3h**).



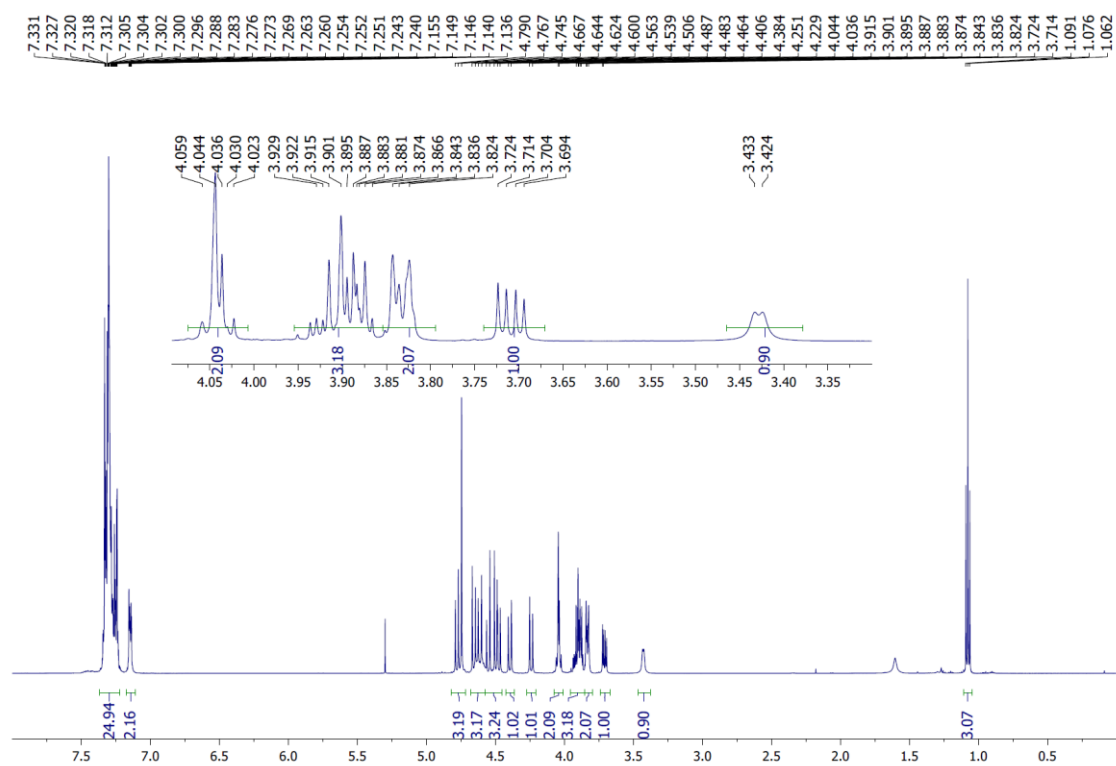
To a dry two-necked round bottomed flask was added “activated zinc” powder (293 mg, 4.46 mmol, 5.7 equiv.). The flask was heated up at 40°C and the zinc powder suspended in dry THF (6 ml) under argon atmosphere. Then, TMSCl (40 µl, 0.266 mmol, 0.4 equiv.) was added dropwise and the reaction was stirred at 60°C for 15 mins. Next, a solution of aldehyde **2h** (493 g, 0.782 mmol, 1.0 equiv.) and ethyl bromo-difluoroacetate (0.12 ml, 0.938 mmol, 1.2 equiv.) dissolved homogenously in dry THF (6 ml) under argon atmosphere was added dropwise at 60°C. The reaction was stirred vigorously for 1.5h at 60°C and then cooled at room temperature. Ice water (5 ml) and HCl (1M, 10 ml) were added and the mixture was diluted with EtOAc. The organic phase was washed with NaHCO<sub>3</sub>(sat) (2 times), brine, dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Crude NMR analysis showed the formation of two diastereoisomer **(A)-3h** and **(B)-3h** in 55:45 *dr* ratio. Purification by silica gel chromatography (Cy/EtOAc 92:8) afforded pure diastereoisomers **(A)-3h** and **(B)-3h** in 75% overall yield.

*Ethyl 4,5,6,7,8-pentakis(benzyloxy)-2,2-difluoro-3-hydroxyoctanoate ((A)-3h).*

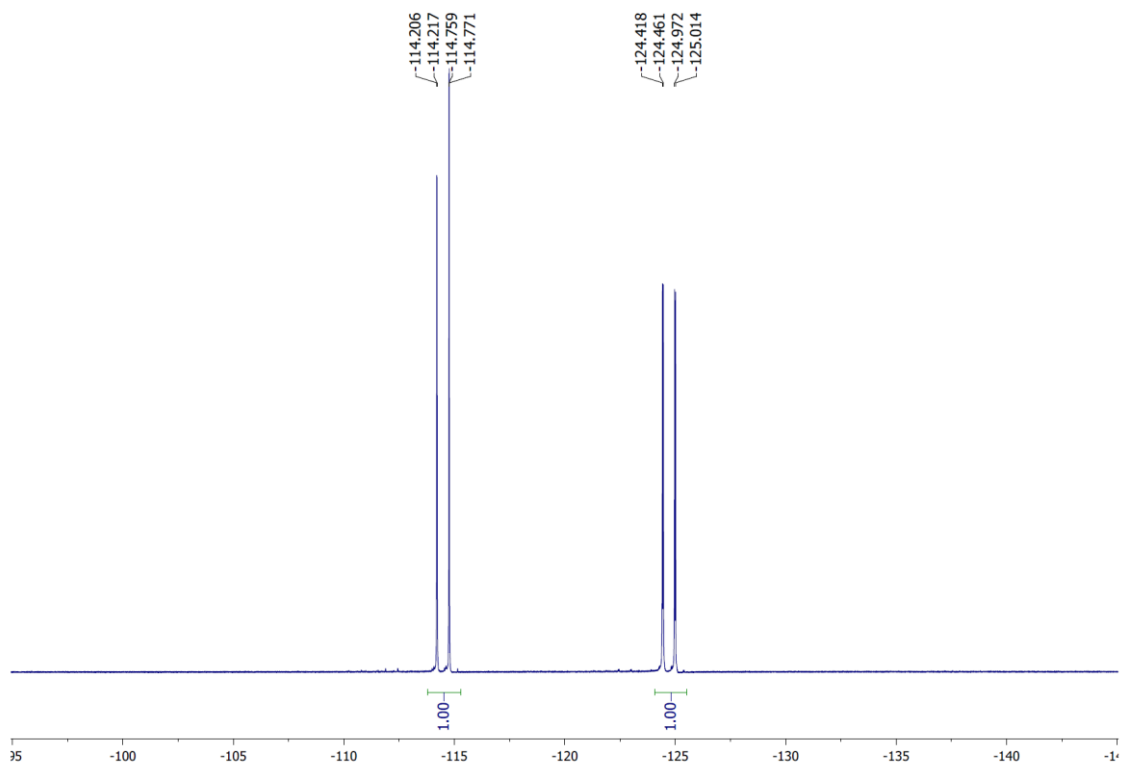


$[\alpha]_{20}^D$ : +2.4 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.35-7.26 (m, 20H, H<sup>arom</sup>), 7.26-7.23 (m, 3H, H<sup>arom</sup>), 7.16-7.13 (m, 2H, H<sup>arom</sup>), 4.78 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.74 (s, 2H, CH<sub>2</sub><sup>Bn</sup>), 4.66-4.57 (m, 1H, H-1), 4.66 (AB, 1H,  $J_{A-B}$  = 10.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.61 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.55 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.49 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.48 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.39 (AB, 1H,  $J_{A-B}$  = 10.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.24 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.06-4.02 (m, 2H, H-3, H-4), 3.94-3.86 (m, 3H, H-6a, CH<sub>2</sub>CH<sub>3</sub>), 3.85-3.81 (m, 2H, H-2, H-5), 3.71 (ABX, 1H,  $J_{5-6b}$  = 4.6 Hz,  $J_{6a-6b}$  = 10.3 Hz, H-6b), 3.43 (d, 1H,  $J_{1-OH}$  = 4.6 Hz, OH), 1.08 (t, 3H,  $J_{CH_2-CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.2 (dd,  $J_{C-F}$  = 30.2 Hz,  $J_{C-F}$  = 32.6 Hz, C<sub>q</sub>O<sub>2</sub>Et), 138.5 (C<sub>q</sub><sup>arom</sup>), 138.3 (C<sub>q</sub><sup>arom</sup>), 138.2 (C<sub>q</sub><sup>arom</sup>), 138.1 (C<sub>q</sub><sup>arom</sup>), 137.4 (C<sub>q</sub><sup>arom</sup>), 128.6- 127.7 (CH<sup>arom</sup>), 114.9 (dd,  $J_{C-F}$  = 247.8 Hz,  $J_{C-F}$  = 258.4 Hz, CF<sub>2</sub>), 81.0 (C-3 or C-4), 80.0 (C-3 or C-4), 79.0 (C-5), 78.9 (d,  $J_{C-F}$  = 3.6 Hz, C-2), 75.2 (CH<sub>2</sub><sup>Bn</sup>), 74.8 (CH<sub>2</sub><sup>Bn</sup>), 73.6 (CH<sub>2</sub><sup>Bn</sup>), 72.6 (CH<sub>2</sub><sup>Bn</sup>), 72.1 (CH<sub>2</sub><sup>Bn</sup>), 70.2 (t,  $J_{C-F}$  = 22.2 Hz, C-1), 69.1 (C-6), 62.5 (CH<sub>2</sub>CH<sub>3</sub>), 13.8 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -114.5 (dd, 1F,  $J_{H-Fa}$  = 5.4 Hz,  $J_{Fa-Fb}$  = 260.5 Hz, Fa), -124.7 (dd, 1F,  $J_{H-Fb}$  = 19.8 Hz,  $J_{Fa-Fb}$  = 260.5 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for C<sub>45</sub>H<sub>49</sub>F<sub>2</sub>O<sub>8</sub> [M+H]<sup>+</sup>: calc. 755.3390; found: 755.3385.

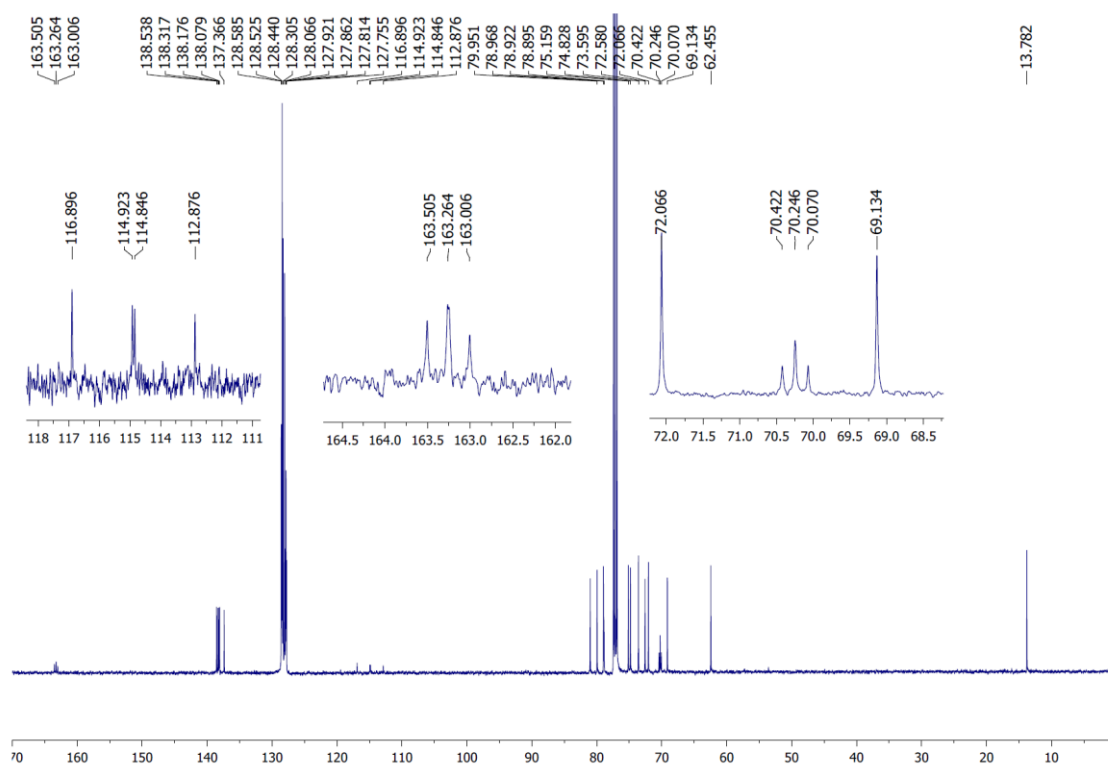
# <sup>1</sup>H NMR



# <sup>19</sup>F NMR

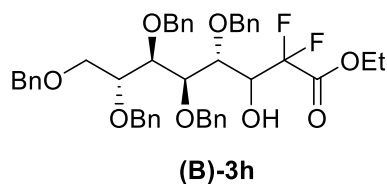


# <sup>13</sup>C NMR



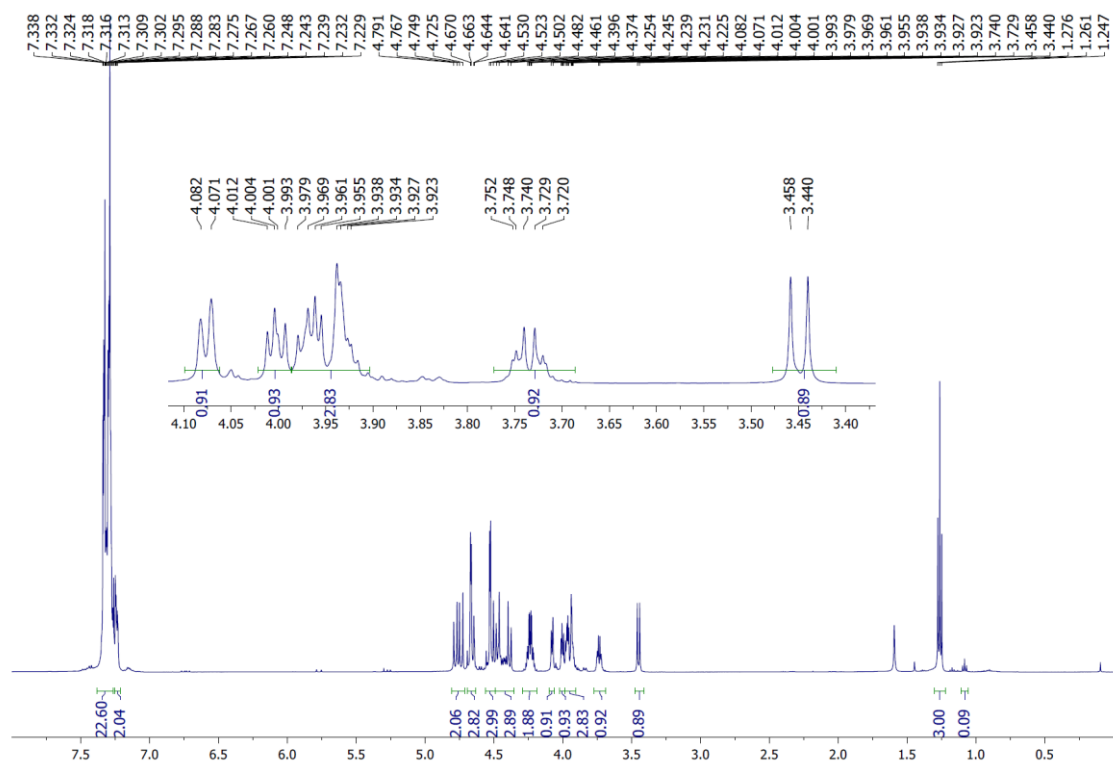


*Ethyl 4,5,6,7,8-pentakis(benzyloxy)-2,2-difluoro-3-hydroxyoctanoate ((B)-3h).*

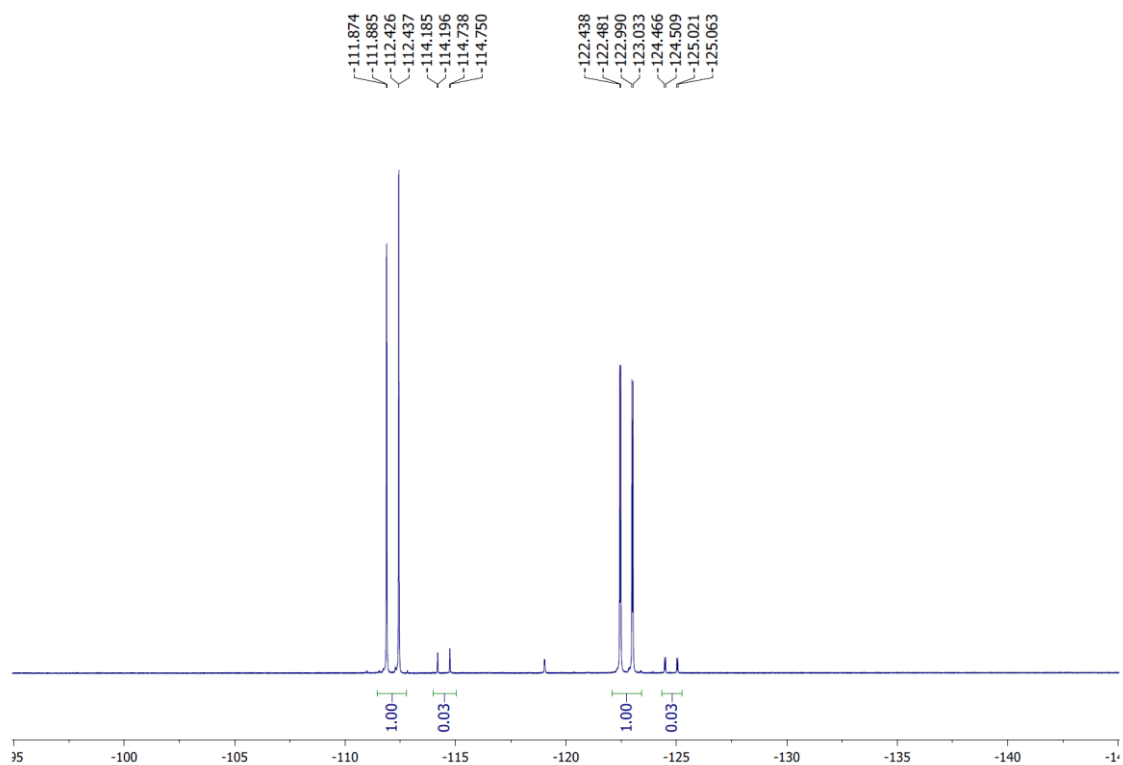


$[\alpha]_{20}^D$ : +1.9 (c 1.0,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.32-7.26 (m, 20H,  $\text{H}^{\text{arom}}$ ), 7.26-7.20 (m, 5H,  $\text{H}^{\text{arom}}$ ), 4.75 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.71 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.67-4.61 (m, 3H,  $\text{CH}_2^{\text{Bn}}$ ), 4.51 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.50-4.47 (m, 2H,  $\text{CH}_2^{\text{Bn}}$ ), 4.44 (AB, 1H,  $J_{\text{A-B}}$  = 10.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.43-4.37 (m, 1H, H-1), 4.36 (AB, 1H,  $J_{\text{A-B}}$  = 10.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.21 (qd, 2H,  $J$  = 2.9 Hz,  $J_{\text{CH}_2\text{-CH}_3}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3$ ), 4.05 (d, 1H,  $J$  = 5.7 Hz, H-2), 3.97 (dd, 1H,  $J$  = 4.0 Hz,  $J$  = 5.7 Hz, H-3), 3.95-3.88 (m, 3H, H-4, H-5, H-6a), 3.71 (ABX, 1H,  $J_{5\text{-}6b}$  = 4.0 Hz,  $J_{6a\text{-}6b}$  = 9.7 Hz, H-6b), 3.42 (d, 1H,  $J_{1\text{-OH}}$  = 9.2 Hz, OH), 1.23 (t, 3H,  $J_{\text{CH}_2\text{-CH}_3}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3$ ) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 163.5 (dd,  $J_{\text{C-F}}$  = 30.2 Hz,  $J_{\text{C-F}}$  = 33.8 Hz,  $\text{C}_q\text{O}_2\text{Et}$ ), 138.5 (2  $\text{C}_q^{\text{arom}}$ ), 138.2 ( $\text{C}_q^{\text{arom}}$ ), 138.1 ( $\text{C}_q^{\text{arom}}$ ), 137.5 ( $\text{C}_q^{\text{arom}}$ ), 128.6-127.7 ( $\text{CH}^{\text{arom}}$ ), 114.6 (dd,  $J_{\text{C-F}}$  = 254.2 Hz,  $J_{\text{C-F}}$  = 257.8 Hz,  $\text{CF}_2$ ), 79.6 (C-3), 78.7 (C-4 or C-5), 78.4 (C-4 or C-5), 75.1 (C-2), 75.0 ( $\text{CH}_2^{\text{Bn}}$ ), 73.6 ( $\text{CH}_2^{\text{Bn}}$ ), 73.2 (2  $\text{CH}_2^{\text{Bn}}$ ), 72.1 ( $\text{CH}_2^{\text{Bn}}$ ), 69.7 (dd,  $J_{\text{C-F}}$  = 24.1 Hz,  $J_{\text{C-F}}$  = 29.0 Hz, C-1), 69.6 (C-6), 63.1 ( $\text{CH}_2\text{CH}_3$ ), 14.0 ( $\text{CH}_2\text{CH}_3$ ) ppm.  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  = -112.2 (dd, 1F,  $J_{\text{H-Fa}}$  = 5.4 Hz,  $J_{\text{Fa-Fb}}$  = 260.0 Hz, Fa), -127.7 (dd, 1F,  $J_{\text{H-Fb}}$  = 20.2 Hz,  $J_{\text{Fa-Fb}}$  = 260.0 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for  $\text{C}_{45}\text{H}_{49}\text{F}_2\text{O}_8$   $[\text{M}+\text{H}]^+$ : calc. 755.3390; found: 755.3379.

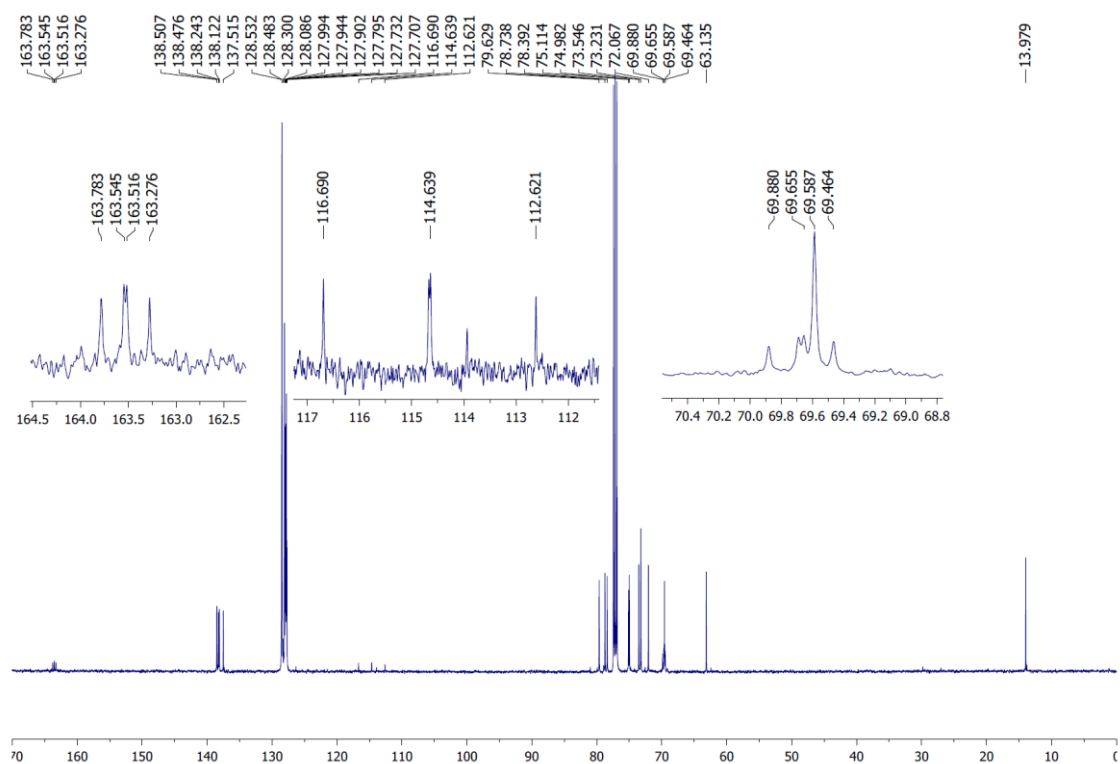
# <sup>1</sup>H NMR



# <sup>19</sup>F NMR



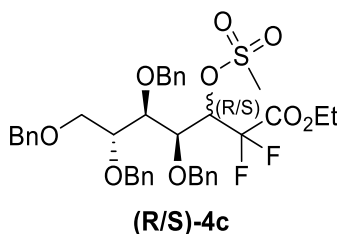
# <sup>13</sup>C NMR



## DBCE

### D-Arabinose

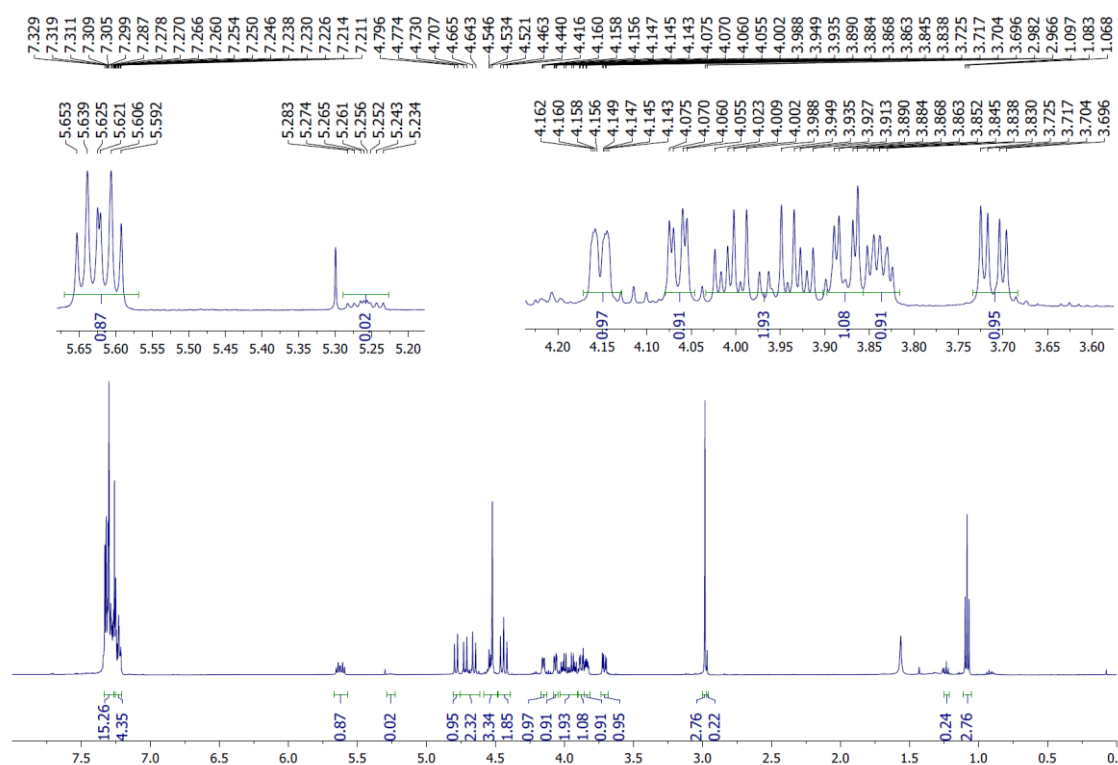
2,3,4,5-tetra-*O*-benzyl-1',1'-difluoro-1-hydroxy-2-((methylsulfonyl)oxy)heptanoate ((*R/S*)-**4c**).



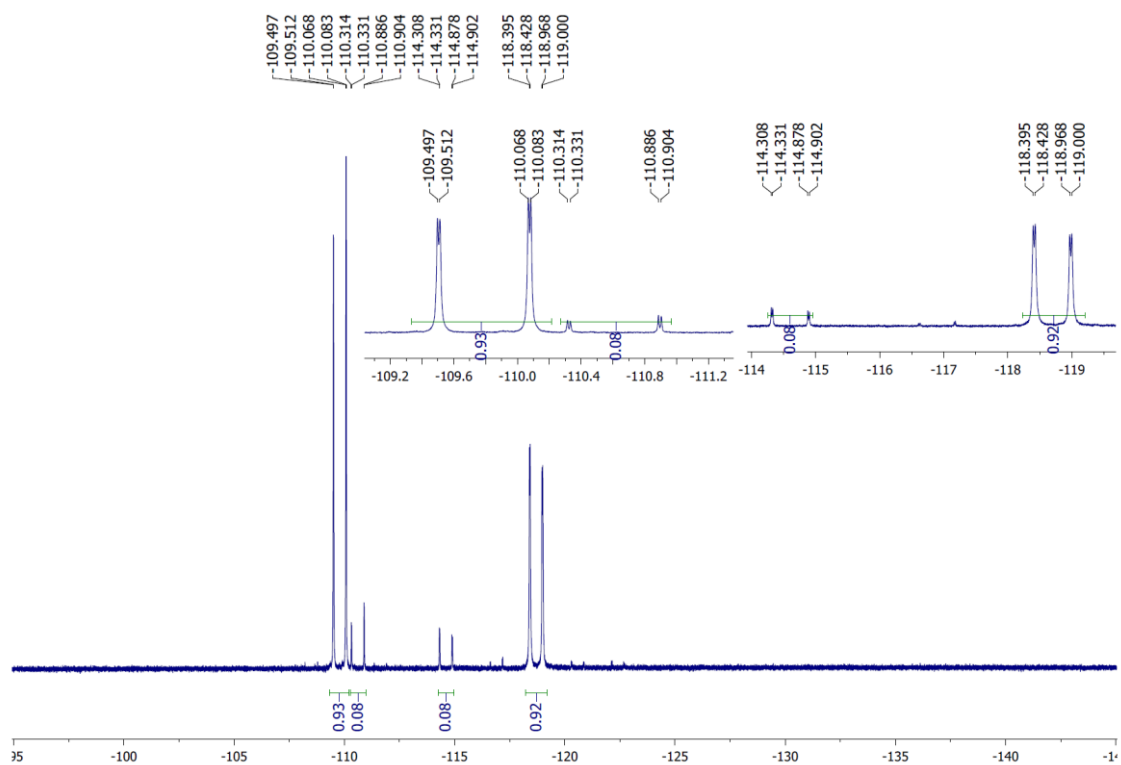
To a solution of alcohol (*R/S*)-**3a** (66 mg, 0.105 mmol, 93:7 S/R ratio) in dry DCM (2 ml) under argon atmosphere was added Et<sub>3</sub>N (23  $\mu$ L, 0.165 mmol, 1.5 equiv.) and MsCl (13  $\mu$ L, 0.165 mmol, 1.5 equiv.). The reaction was stirred for 17h at r.t. before adding EtOAc (10 mL) and an aqueous sat. sol. of NH<sub>4</sub>Cl (10 mL). The aqueous phase was extracted with EtOAc (3 times) and the combined organic phases were washed with brine, dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 9:1) gave the mesylated product (*R/S*)-**4c** as a colorless oil (53 mg, 0.0744 mmol, 71%, 93:7 *dr* ratio).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.34-7.26 (m, 16H, H<sup>arom</sup>), 7.25-7.20 (m, 4H, H<sup>arom</sup>), 5.62 (dt, 1H,  $J_{1-F}$  = 16.2,  $J_{1-2}$  = 7.0 Hz, H-1), 5.62\* (ddd, 1H,  $J_{1-Fa}$  = 11.0,  $J_{1-Fb}$  = 8.8,  $J_{1-2}$  = 4.5 Hz, H-1), 4.78 (AB, 1H,  $J_{A-B}$  = 11.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.72 (AB, 1H,  $J_{A-B}$  = 11.7 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.65 (AB, 1H,  $J_{A-B}$  = 11.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.56-4.51 (m, 1H, CH<sub>2</sub><sup>Bn</sup>), 4.52 (s, 2H, CH<sub>2</sub><sup>Bn</sup>), 4.45 (AB, 1H,  $J_{A-B}$  = 11.3 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.43 (AB, 1H,  $J_{A-B}$  = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.15 (ddd, 1H,  $J_{1-2}$  = 6.6,  $J_{2-3}$  = 2.1, 1.0 Hz, H-2), 4.06 (dd, 1H,  $J_{3-4}$  = 7.5,  $J_{4-5}$  = 2.3 Hz, H-4), 4.04-3.90 (m, 2H, CH<sub>2</sub>CH<sub>3</sub>), 3.88 (dd, 1H,  $J_{5a-5b}$  = 10.6,  $J_{4-5}$  = 2.8 Hz, H-5), 3.84 (dt, 1H,  $J_{3-4}$  = 7.1,  $J_{2-3}$  = 3.3 Hz, H-3), 3.71 (dd, 1H,  $J_{5a-5b}$  = 10.5,  $J_{4-5}$  = 3.9 Hz, H-5), 2.98 (s, 3H, SO<sub>2</sub>CH<sub>3</sub>), 2.97\* (s, 3H, SO<sub>2</sub>CH<sub>3</sub>), 1.23\* (t, 3H,  $J_{CH_2CH_3}$  = 7.2 Hz, CH<sub>2</sub>CH<sub>3</sub>), 1.08 (t, 3H,  $J_{CH_2CH_3}$  = 7.2 Hz, CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 161.4 (dd, JC-F = 29.8 Hz, JC-F = 32.0 Hz, C<sub>q</sub>O<sub>2</sub>Et), 138.4 (C<sub>q</sub><sup>arom</sup>), 138.3 (C<sub>q</sub><sup>arom</sup>), 138.1 (C<sub>q</sub><sup>arom</sup>), 137.3 (C<sub>q</sub><sup>arom</sup>), 128.5- 127.7 (CH<sup>arom</sup>), 112.8 (dd,  $J_{C-F}$  = 253.2 Hz,  $J_{C-F}$  = 257.4 Hz, CF<sub>2</sub>), 77.8 (C-3), 77.4 (dd,  $J_{C-F}$  = 22.6 Hz,  $J_{C-F}$  = 25.0 Hz, C-1), 76.8 (C-4), 76.0 (C-2), 74.1 (CH<sub>2</sub><sup>Bn</sup>), 73.9 (CH<sub>2</sub><sup>Bn</sup>), 73.6\* (CH<sub>2</sub><sup>Bn</sup>), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 72.0\* (CH<sub>2</sub><sup>Bn</sup>), 71.5 (CH<sub>2</sub><sup>Bn</sup>), 68.7\* (C-5), 68.3 (C-5), 63.7\* (CH<sub>2</sub>CH<sub>3</sub>), 63.5 (CH<sub>2</sub>CH<sub>3</sub>), 39.3 (SO<sub>2</sub>CH<sub>3</sub>), 13.9\* (CH<sub>2</sub>CH<sub>3</sub>), 13.7 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -109.8 (dd, 1F,  $J_{H1-Fa}$  = 7.1 Hz,  $J_{Fa-Fb}$  = 268.7 Hz, Fa), -110.6\* (dd, 1F,  $J_{H1-Fa}$  = 8.3 Hz,  $J_{Fa-Fb}$  = 269.3 Hz, Fa), -114.6\* (dd, 1F,  $J_{H-Fb}$  = 11.0 Hz,  $J_{Fa-Fb}$  = 268.6 Hz, Fb), -118.7 (dd, 1F,  $J_{H-Fb}$  = 15.4 Hz,  $J_{Fa-Fb}$  = 269.3 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): *m/z* calculated for C<sub>38</sub>H<sub>43</sub>F<sub>2</sub>O<sub>9</sub>S [M+H]<sup>+</sup>: calc. 713.2590; found: 713.2584.

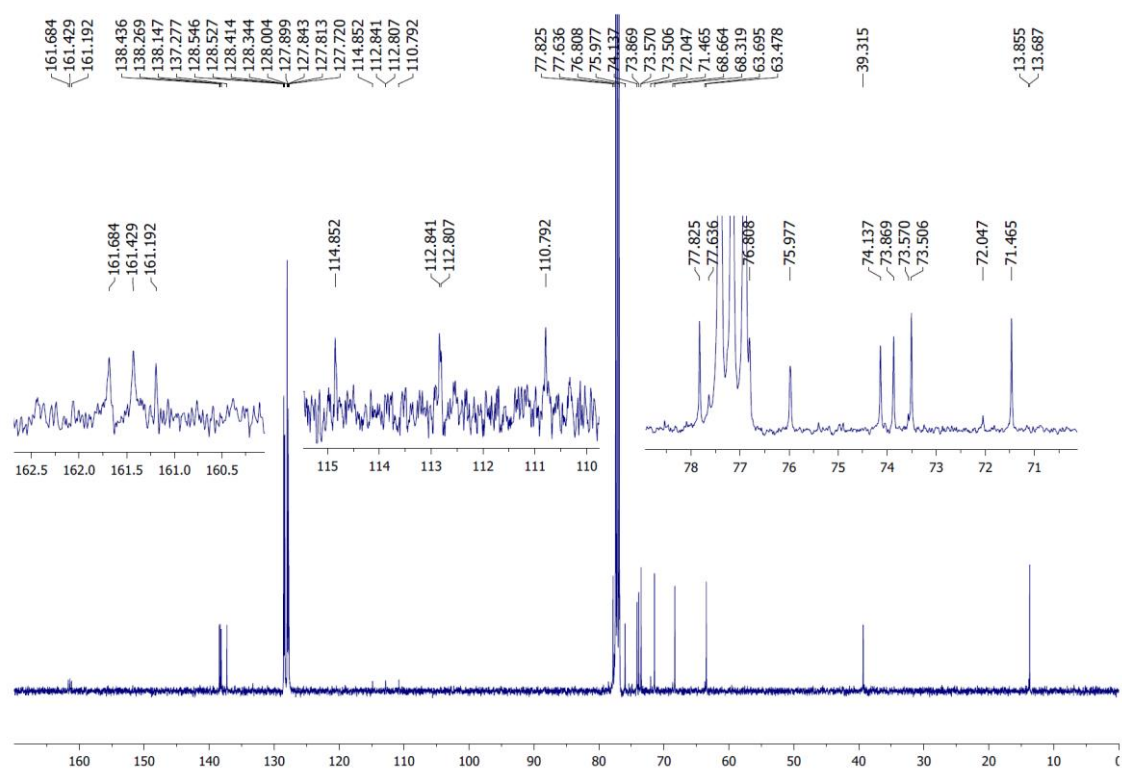
### <sup>1</sup>H NMR



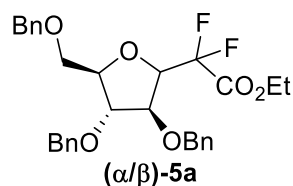
**$^{19}\text{F}$  NMR**



# $^{13}\text{C}$ NMR



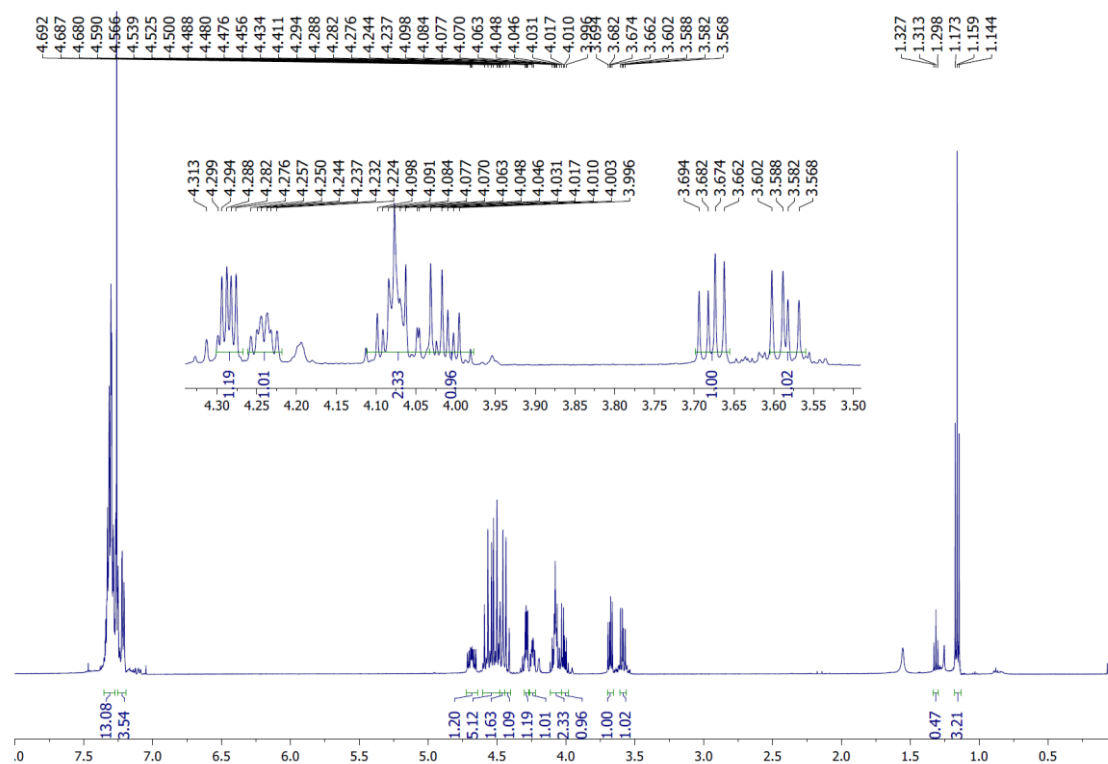
2,3,5-tri-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate- $\alpha$ -D-arabinofuranose ( $\alpha/\beta$ )-**5a**).



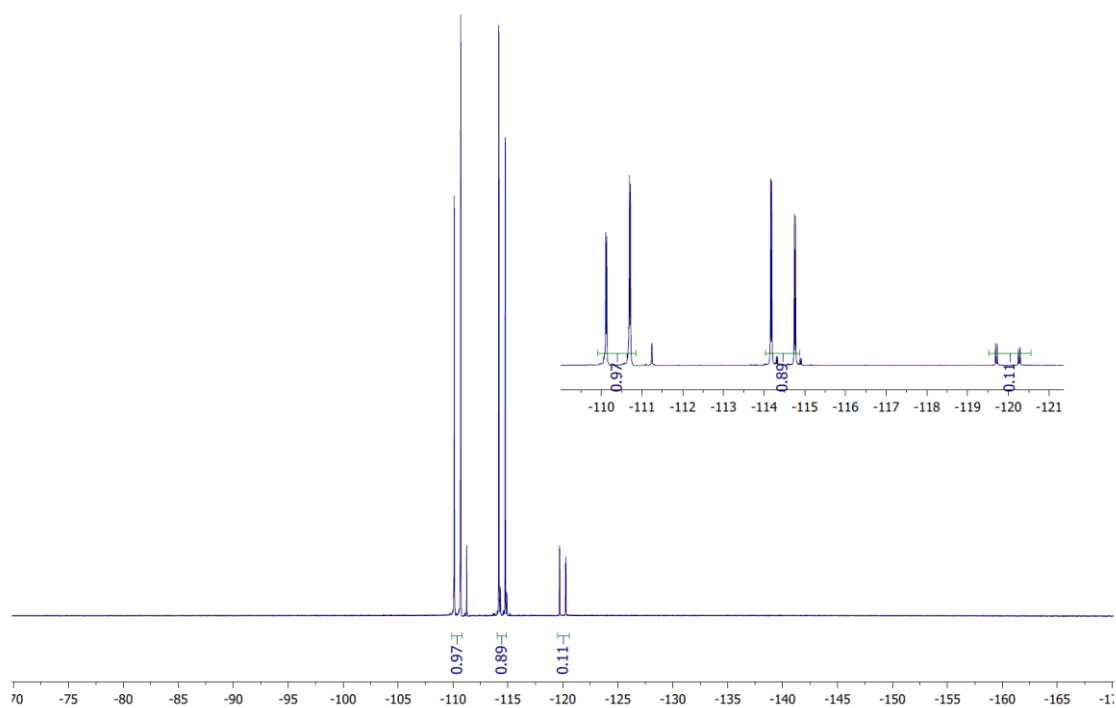
To a solution of alcohols (*R/S*)-**3a** (67 mg, 0.12 mmol, 89:11 *R*:*S* ratio) in dry DCM (1.5 ml) under argon atmosphere was added DAST (28  $\mu$ l, 0.24 mmol, 2.0 equiv.) dropwise at  $-78^{\circ}\text{C}$ . The reaction was allowed to warm from  $-78^{\circ}\text{C}$  to r.t for 2.5h and stirred for 24h at r.t. Then, the crude was diluted with dichloromethane. The organic phase was washed with  $\text{H}_2\text{O}$  (3 times) and brine (3 times), dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 9:1) gave the cyclized products ( $\alpha$ )-**5a** and ( $\beta$ )-**5a** as a colorless oil (44 mg, 74%, 89:11  $\alpha$ : $\beta$  ratio).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.35-7.26 (m, 13H,  $\text{H}^{\text{arom}}$ ), 7.26-7.20 (m, 2H,  $\text{H}^{\text{arom}}$ ), 4.68 (ddd, 1H,  $J_{1-2} = 5.7$  Hz,  $J_{1-\text{Fa}} = 10.8$  Hz,  $J_{1-\text{Fb}} = 13.8$  Hz, H-1), 4.58 (AB, 1H,  $J_{\text{A-B}} = 12.6$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.55 (AB, 1H,  $J_{\text{A-B}} = 12.0$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.51 (AB, 1H,  $J_{\text{A-B}} = 12.6$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.49 (AB, 1H,  $J_{\text{A-B}} = 12.0$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.47 (AB, 1H,  $J_{\text{A-B}} = 12.0$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.43 (AB, 1H,  $J_{\text{A-B}} = 12.0$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.28 (dd, 1H,  $J_{1-2} = 5.7$  Hz,  $J_{2-3} = 3.4$  Hz, H-2), 4.24 (td, 1H,  $J_{3-4} = 4.0$  Hz,  $J_{4-5a} = J_{4-5b} = 6.3$  Hz, H-4), 4.12-3.99 (m, 3H, H-3,  $\text{CH}_2\text{CH}_3$ ), 3.68 (ABX, 1H,  $J_{4-5a} = 6.3$  Hz,  $J_{5a-5b} = 10.3$  Hz, H-5a), 3.59 (ABX, 1H,  $J_{4-5b} = 6.3$  Hz,  $J_{5a-5b} = 10.3$  Hz, H-5b), 1.16 (t, 3H,  $J_{\text{CH}_2-\text{CH}_3} = 7.5$  Hz,  $\text{CH}_2\text{CH}_3$ ).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 163.0 (t,  $J_{\text{C-F}} = 30.7$  Hz,  $\text{C}_q\text{O}_2\text{Et}$ ), 138.2 ( $\text{C}_q^{\text{arom}}$ ), 137.6 ( $\text{C}_q^{\text{arom}}$ ), 137.0 ( $\text{C}_q^{\text{arom}}$ ), 128.7-126.7 ( $\text{CH}^{\text{arom}}$ ), 113.1 (dd,  $J_{\text{C-F}} = 249.9$  Hz,  $J_{\text{C-F}} = 258.3$  Hz,  $\text{CF}_2$ ), 82.8 (C-2, C-3, C-4), 79.1 (dd,  $J_{\text{C-F}} = 23.5$  Hz,  $J_{\text{C-F}} = 26.6$  Hz, C-1), 73.5 ( $\text{CH}_2^{\text{Bn}}$ ), 72.8 ( $\text{CH}_2^{\text{Bn}}$ ), 72.0 ( $\text{CH}_2^{\text{Bn}}$ ), 70.1 (C-5), 62.7 ( $\text{CH}_2\text{CH}_3$ ), 13.9 ( $\text{CH}_2\text{CH}_3$ ).  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  = -110.4 (dd, 1F,  $J_{\text{H1-Fa}} = 10.8$  Hz,  $J_{\text{Fa-Fb}} = 274.4$  Hz, Fa), -114.5 (dd, 1F,  $J_{\text{H1-Fb}} = 13.8$  Hz,  $J_{\text{Fa-Fb}} = 274.4$  Hz, Fb). HRMS (ESI $^{+}$ ):  $m/z$  calculated for  $\text{C}_{30}\text{H}_{32}\text{F}_2\text{NaO}_6$  [ $\text{M}+\text{Na}$ ] $^{+}$ : calc. 549.2059; found: 549.2063. nOe: Correlation between H-1 and H-4 observed.

# <sup>1</sup>H NMR

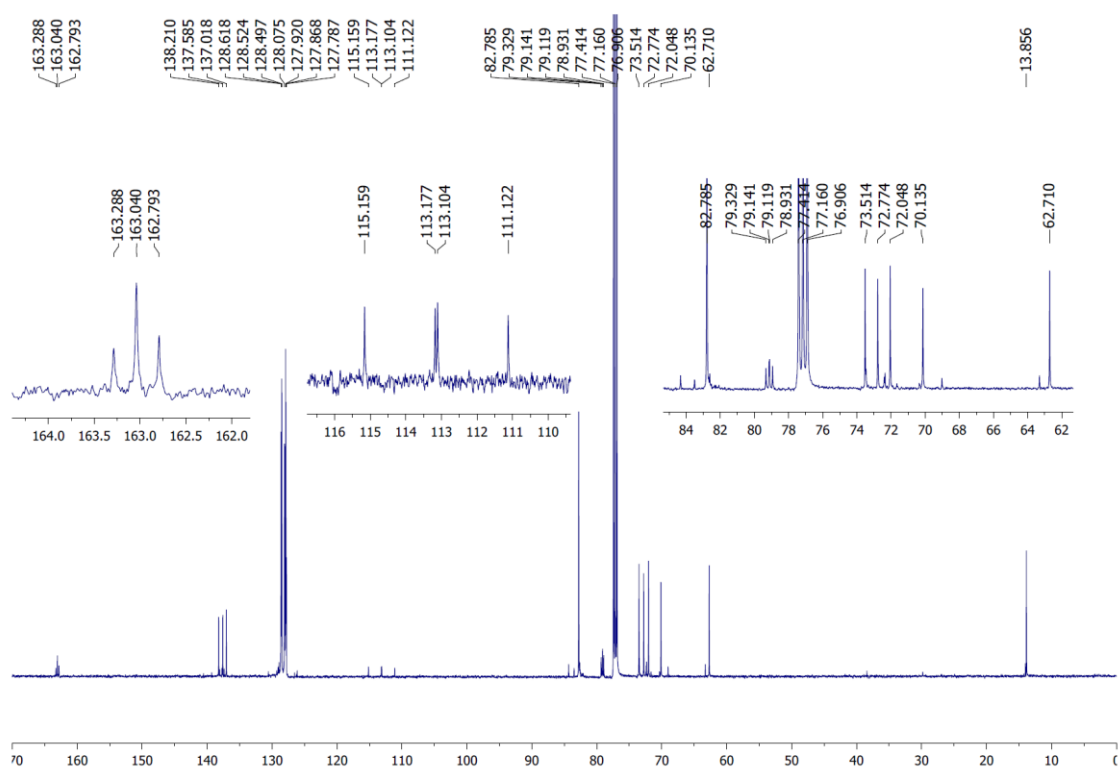


# <sup>19</sup>F NMR

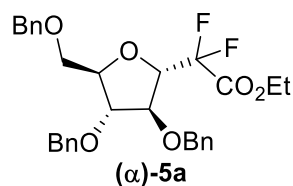




# <sup>13</sup>C NMR



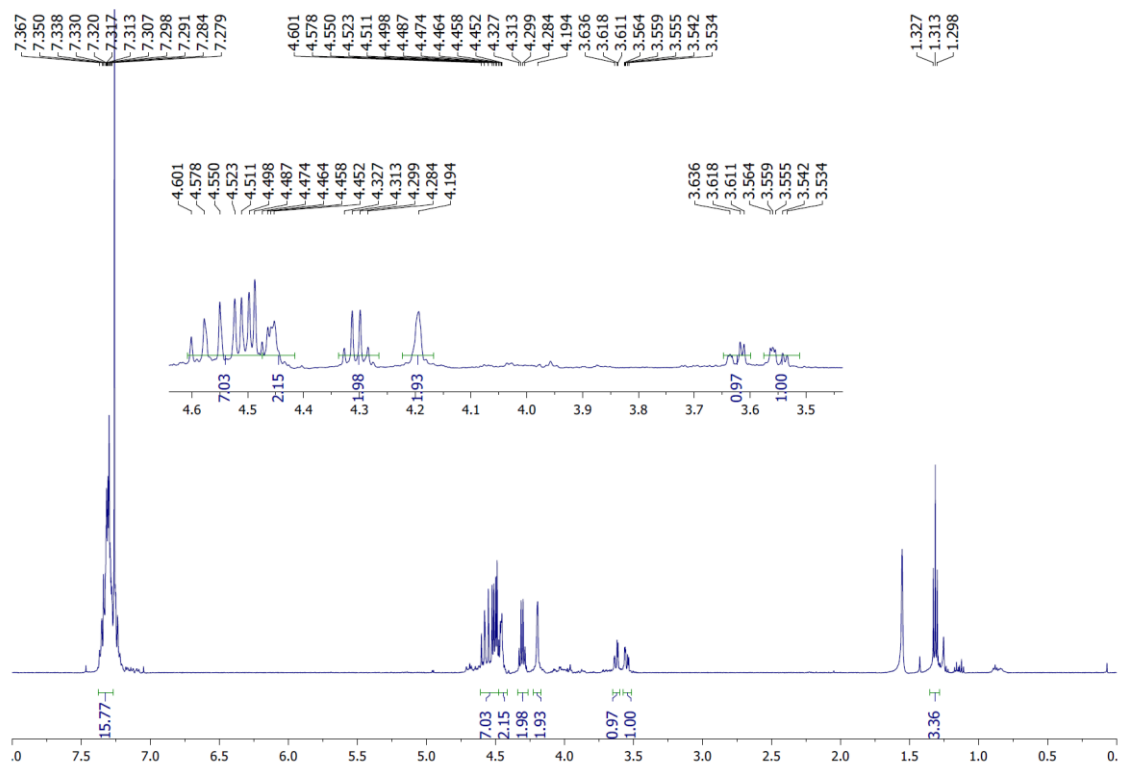
2,3,5-tri-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate- $\alpha$ -D-arabinofuranose (( $\alpha$ )-**5a**).



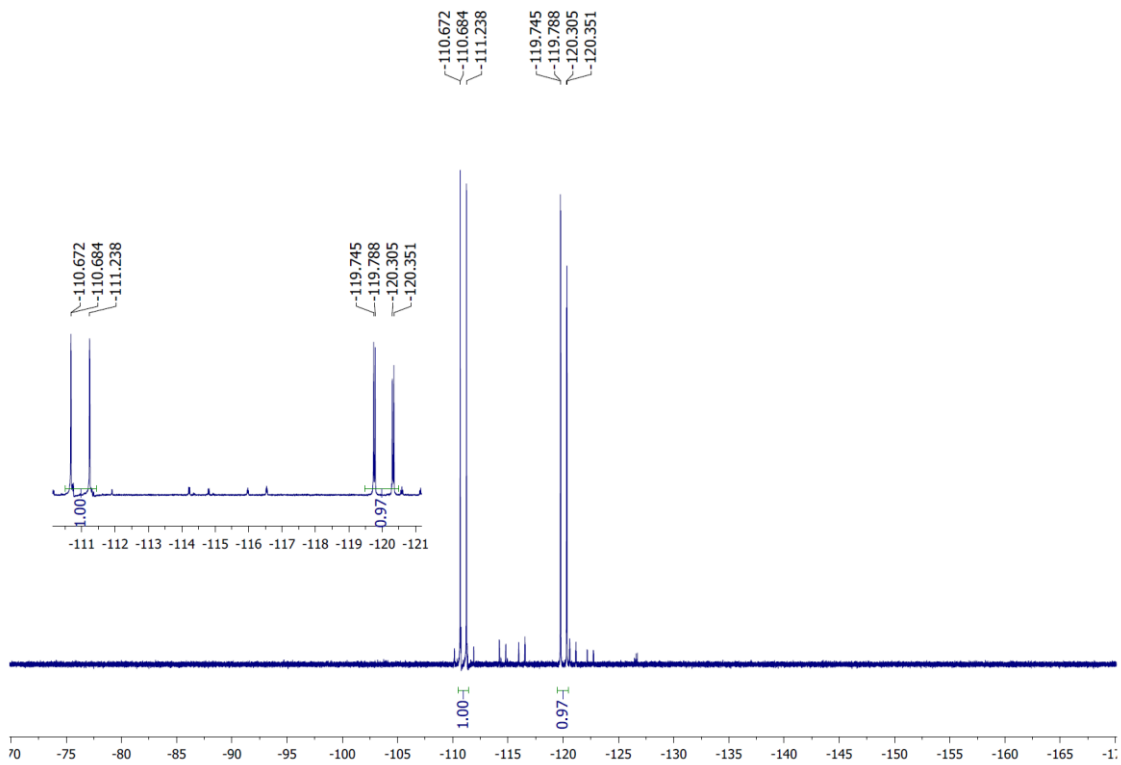
To a solution of alcohol (*R*)-**3a** (63 mg, 0.11 mmol) in dry DCM (1.5 ml) under argon atmosphere was added DAST (26  $\mu$ l, 0.22 mmol, 2.0 equiv.) dropwise at  $-78^{\circ}\text{C}$ . The reaction was allowed to warm from  $-78^{\circ}\text{C}$  to r.t for 2.5h and stirred for 24h at r.t. Then, the crude was diluted with dichloromethane. The organic phase was washed with  $\text{H}_2\text{O}$  (3 times) and brine (3 times), dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 9:1) gave the cyclized product ( $\alpha$ )-**5a** as a colorless oil (35 mg, 62%).

$[\alpha]_{20}^{\text{D}}$ : -0.3 (c 1.0,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.37-7.23 (m, 15H,  $\text{H}^{\text{arom}}$ ), 4.59 (AB, 1H,  $J_{\text{A-B}}$  = 11.7 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.56 (AB, 1H,  $J_{\text{A-B}}$  = 12.2 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.54 (AB, 1H,  $J_{\text{A-B}}$  = 12.2 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.51 (AB, 1H,  $J_{\text{A-B}}$  = 11.8 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.50 (AB, 1H,  $J_{\text{A-B}}$  = 11.8 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.48 (AB, 1H,  $J_{\text{A-B}}$  = 11.7 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.50-4.44 (m, 2H, H-1, H-2), 4.31 (q, 2H,  $J_{\text{CH}_2\text{-CH}_3}$  = 7.1 Hz,  $\text{CH}_2\text{CH}_3$ ), 4.21-4.18 (m, 2H, H-3, H-4), 3.63 (ABX, 1H,  $J_{4-5a}$  = 3.8 Hz,  $J_{5a-5b}$  = 10.8 Hz, H-5a), 3.55 (ABX, 1H,  $J_{4-5b}$  = 4.2 Hz,  $J_{5a-5b}$  = 10.8 Hz, H-5b), 1.31 (t, 3H,  $J_{\text{CH}_2\text{-CH}_3}$  = 7.1 Hz,  $\text{CH}_2\text{CH}_3$ ).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 163.0 (dd,  $J_{\text{C-F}}$  = 30.2 Hz,  $J_{\text{C-F}}$  = 32.6 Hz,  $\text{C}_q\text{O}_2\text{Et}$ ), 138.1 ( $\text{C}_q^{\text{arom}}$ ), 137.7 ( $\text{C}_q^{\text{arom}}$ ), 137.4 ( $\text{C}_q^{\text{arom}}$ ), 128.7-127.7 ( $\text{CH}^{\text{arom}}$ ), 113.8 (dd,  $J_{\text{C-F}}$  = 252.3 Hz,  $J_{\text{C-F}}$  = 259.6 Hz,  $\text{CF}_2$ ), 84.3 (C-2), 83.5 (C-4), 82.6 (C-3), 82.3 (dd,  $J_{\text{C-F}}$  = 24.1 Hz,  $J_{\text{C-F}}$  = 31.4 Hz, C-1), 73.5 ( $\text{CH}_2^{\text{Bn}}$ ), 72.4 (2  $\text{CH}_2^{\text{Bn}}$ ), 69.0 (C-5), 63.3 ( $\text{CH}_2\text{CH}_3$ ), 14.0 ( $\text{CH}_2\text{CH}_3$ ).  $^{19}\text{F}$  NMR (471MHz,  $\text{CDCl}_3$ )  $\delta$  = -111.0 (dd, 1F,  $J_{\text{H-Fa}}$  = 5.4 Hz,  $J_{\text{Fa-Fb}}$  = 264.5 Hz, Fa), -120.0 (dd, 1F,  $J_{\text{H-Fb}}$  = 20.7 Hz,  $J_{\text{Fa-Fb}}$  = 264.5 Hz, Fb). HRMS (ESI+):  $m/z$  calculated for  $\text{C}_{30}\text{H}_{32}\text{F}_2\text{NaO}_6$   $[\text{M}+\text{Na}]^+$ : calc. 549.2059; found: 549.2059. nOe: Correlation between H-1 and H-3 observed.

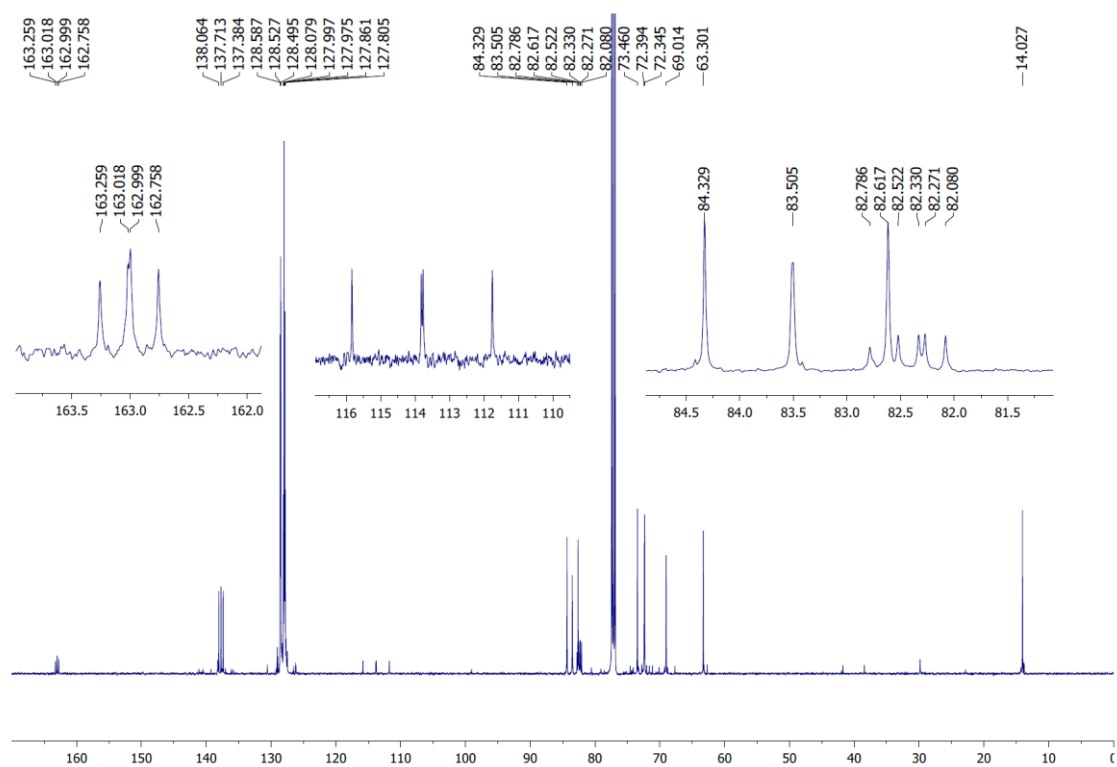
# <sup>1</sup>H NMR



# <sup>19</sup>F NMR

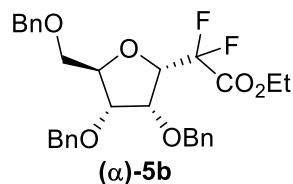


# <sup>13</sup>C NMR



## D-Ribose

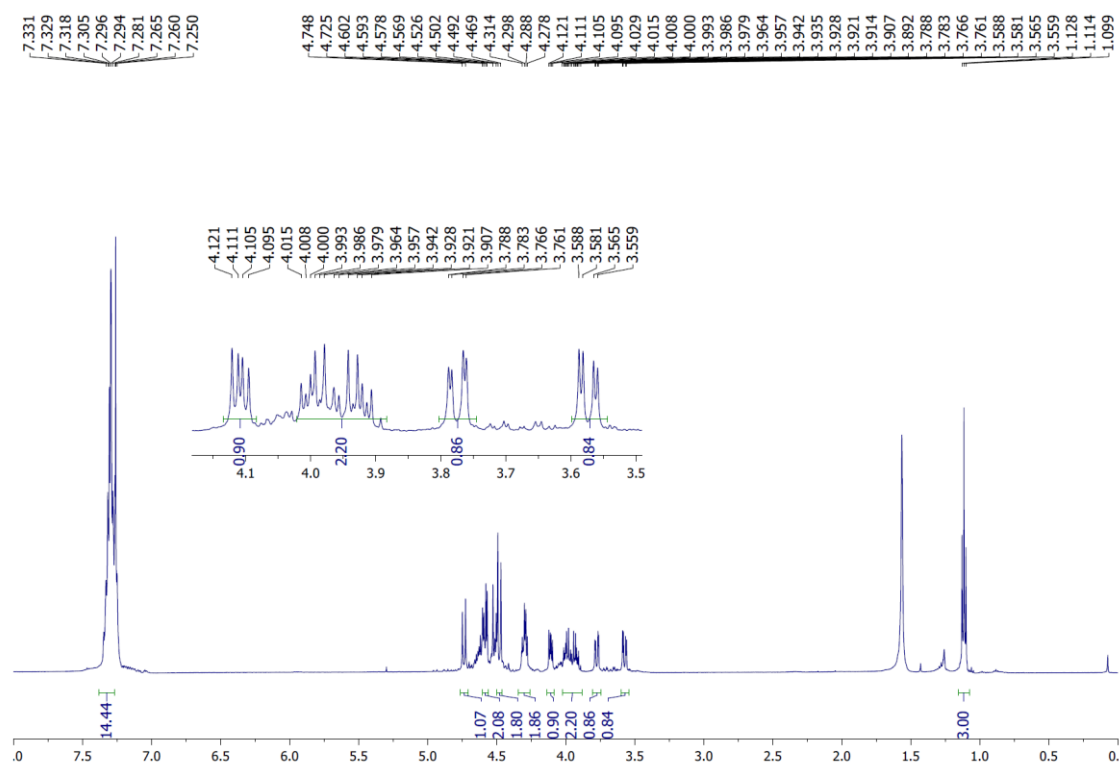
2,3,5-tri-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate-*D*-ribofuranose (( $\alpha$ )-**5b**).



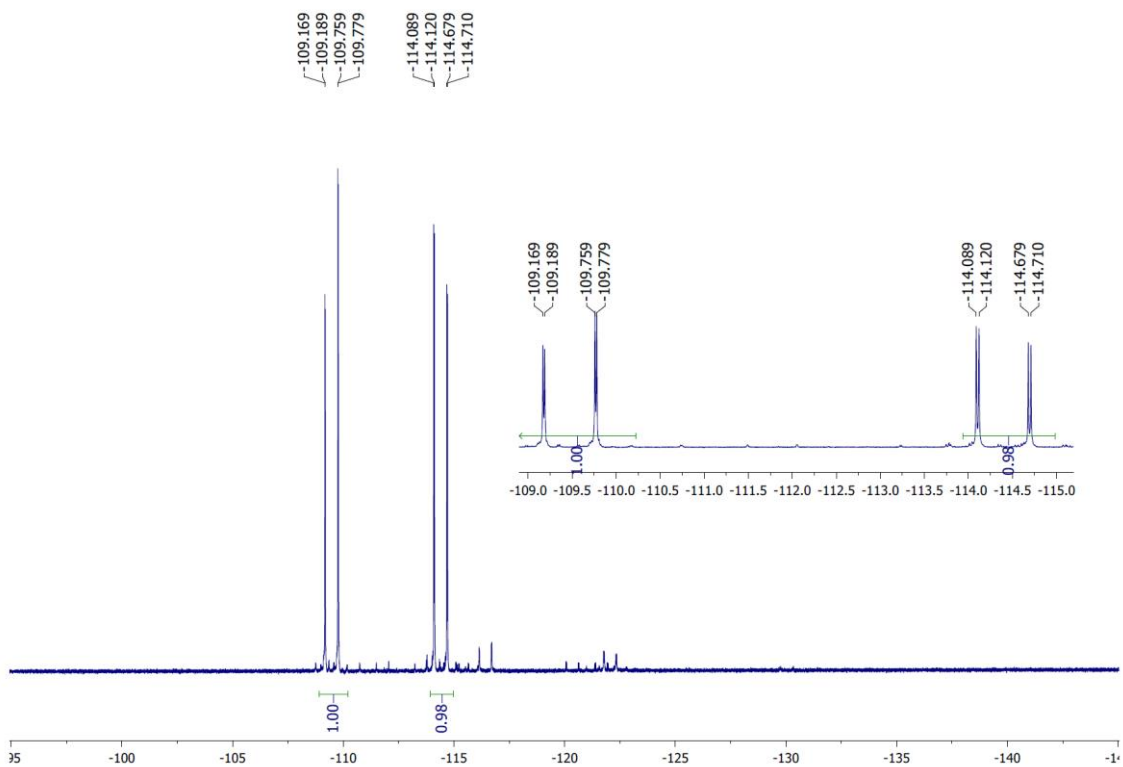
To a solution of alcohol (*R*)-**3b** (75 mg, 0.118 mmol) in dry DCM (2 ml) under argon atmosphere was added DAST (62  $\mu$ l, 0.473 mmol, 4.0 equiv.) dropwise at 0°C. The reaction was allowed to warm from 0°C to r.t and stirred for 22h. DAST (62  $\mu$ l, 0.473 mmol, 4.0 equiv.) was added sequentially at 0°C and the reaction was allowed to warm from 0°C to r.t and stirred for 23h. Then, the crude was diluted with dichloromethane. The organic phase was washed with H<sub>2</sub>O (2 times) and brine (1 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 9:1) gave the cyclized product ( $\alpha$ )-**5b** as a colorless oil (4 mg, 6%).

[ $\alpha$ ]<sub>D</sub><sup>20</sup>: +10.6 (c 0.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.35-7.23 (m, 15H, H<sup>arom</sup>), 4.74 (d, 1H, *J*<sub>A-B</sub> = 11.1 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.67-4.59 (m, 1H, H-1), 4.59 (dd, 2H, *J*<sub>A-B</sub> = 11.9, 4.5 Hz, H-1, CH<sub>2</sub><sup>Bn</sup>), 4.51 (d, 1H, *J*<sub>A-B</sub> = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.48 (d, 2H, *J*<sub>A-B</sub> = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.33-4.27 (m, 2H, H-4 and H-3), 4.11 (dd, 1H, *J*<sub>1-2</sub> or *J*<sub>2-3</sub> = 8.1 Hz, *J*<sub>1-2</sub> or *J*<sub>2-3</sub> = 4.8 Hz, H-2), 4.03-3.89 (m, 2H, CH<sub>2</sub>CH<sub>3</sub>), 3.77 (d, 1H, *J*<sub>5a-5b</sub> = 11.2 Hz, *J*<sub>4-5a</sub> = 2.4 Hz, H-5a), 3.57 (dd, 1H, *J*<sub>5a-5b</sub> = 11.2, *J*<sub>4-5b</sub> = 3.1 Hz, H-5b), 1.11 (t, 3H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.2 Hz, CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.1 (t, *J*<sub>C-F</sub> = 30.9 Hz, CqO<sub>2</sub>Et), 138.1 (Cq arom), 137.7 (Cq arom), 137.5 (Cq arom), 128.5-127.8 (CH<sup>arom</sup>), 113.2 (dd, *J*<sub>C-F</sub> = 247.4 Hz, *J*<sub>C-F</sub> = 259.3 Hz, CF<sub>2</sub>), 80.7 (C-3), 79.7 (dd, *J*<sub>C-F</sub> = 22.8 Hz, *J*<sub>C-F</sub> = 29.0 Hz, C-1), 78.5 (C-4), 77.5 (C-2), 74.0 (CH<sub>2</sub><sup>Bn</sup>), 73.6 (CH<sub>2</sub><sup>Bn</sup>), 73.1 (CH<sub>2</sub><sup>Bn</sup>), 68.6 (C-5), 62.5 (CH<sub>2</sub>CH<sub>3</sub>), 13.7 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -109.5 (dd, 1F, *J*<sub>H-Fa</sub> = 9.5 Hz, *J*<sub>Fa-Fb</sub> = 277.9 Hz, Fa), -114.4 (dd, 1F, *J*<sub>H-Fb</sub> = 14.6 Hz, *J*<sub>Fa-Fb</sub> = 277.9 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): *m/z* calculated for C<sub>30</sub>H<sub>33</sub>F<sub>2</sub>O<sub>6</sub> [M+H]<sup>+</sup>: calc. 527.2240; found: 527.2241. nOe: Correlations were inconclusive.

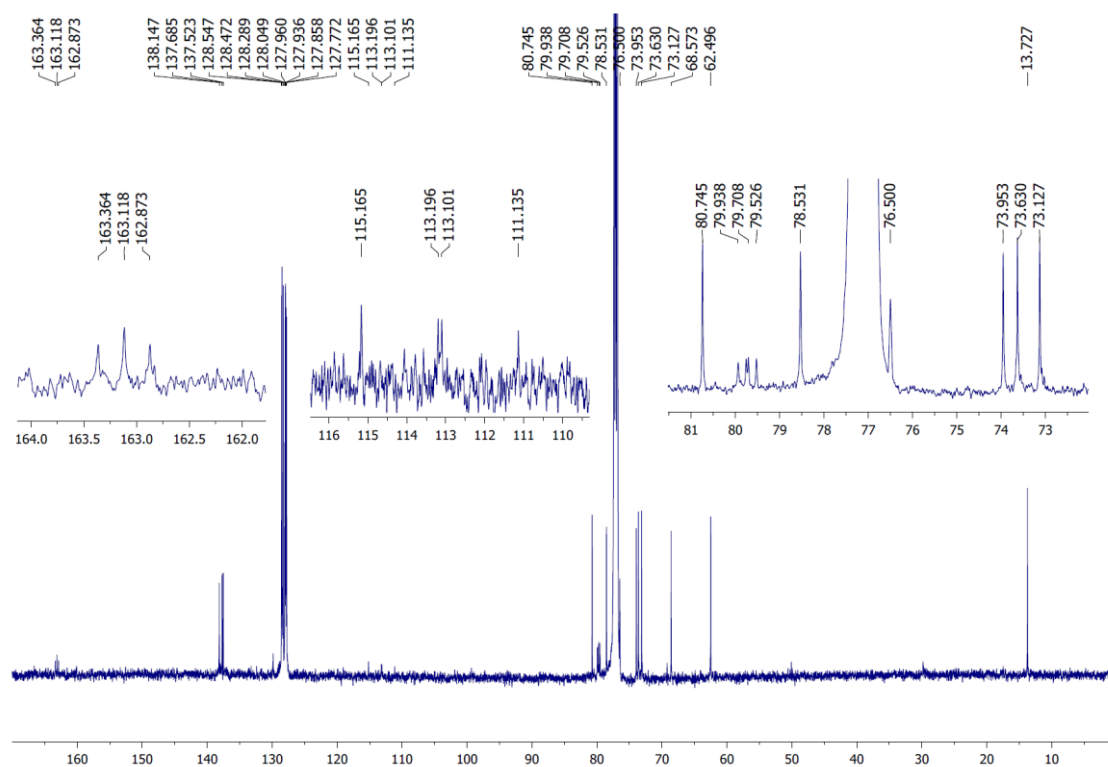
# <sup>1</sup>H NMR



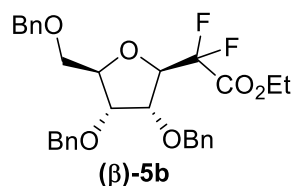
# <sup>19</sup>F NMR



# <sup>13</sup>C NMR



2,3,5-tri-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate-*D*-ribofuranose (( $\beta$ )-**5b**).

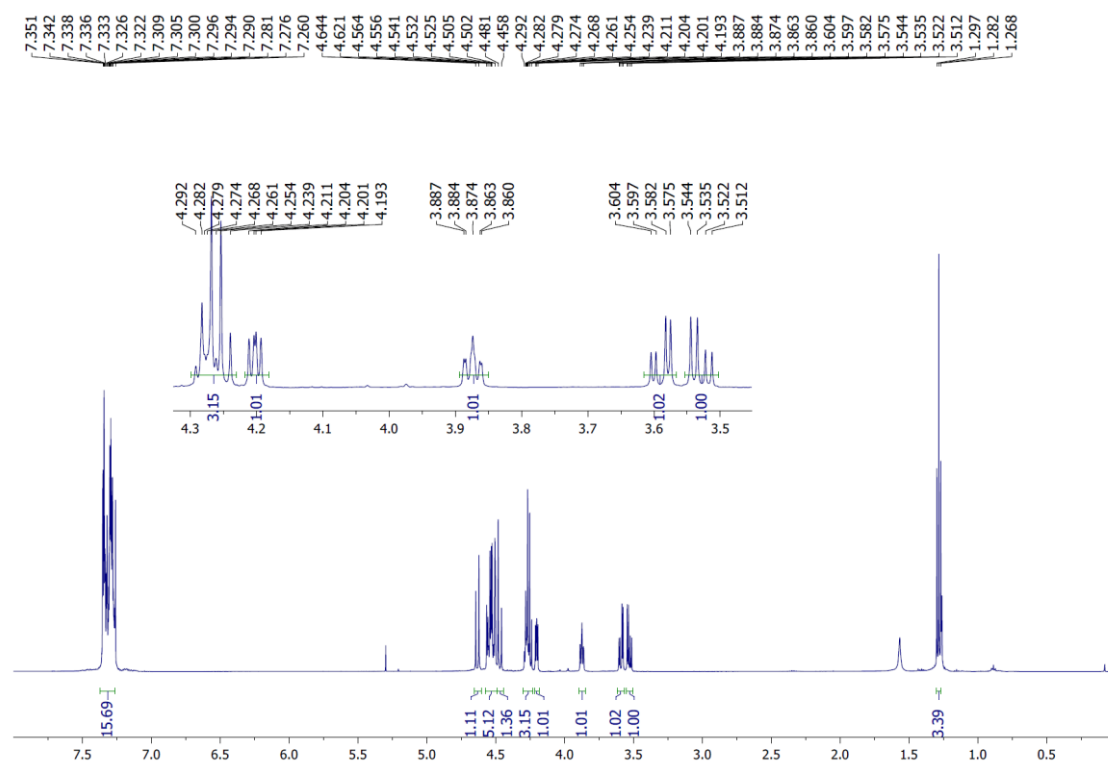


To a solution of alcohol (*S*)-**3b** (33 mg, 0.05 mmol) in dry DCM (1.5 ml) under argon atmosphere was added DAST (27  $\mu$ l, 0.20 mmol, 4.0 equiv.) dropwise at 0°C. The reaction was allowed to warm from 0°C to r.t and stirred for 19h. Then, the crude was diluted with dichloromethane. The organic phase was washed with H<sub>2</sub>O (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 9:1) gave the cyclized product ( $\beta$ )-**5b** as a yellowish oil (17 mg, 62%).

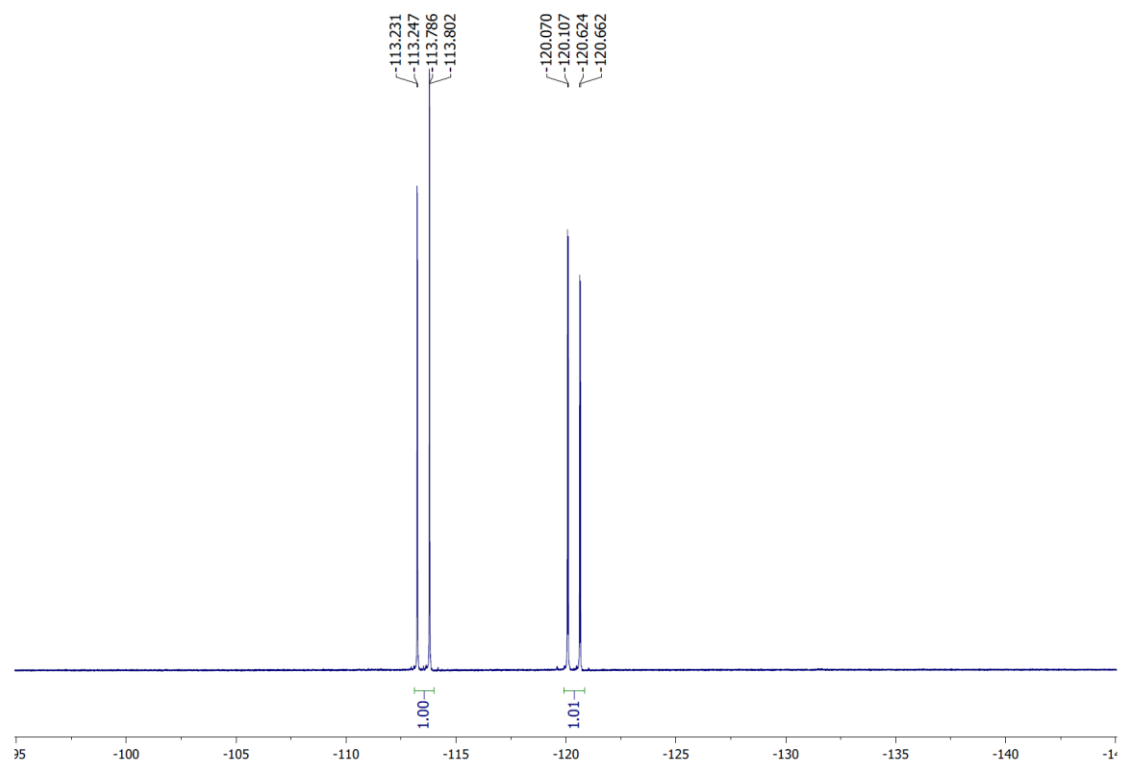
$[\alpha]_D^{20}$ : +32.4 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.36-7.26 (m, 15H, H<sup>arom</sup>), 4.63 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.57-4.49 (m, 5H, H-1, 2x CH<sub>2</sub><sup>Bn</sup>), 4.47 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.29-4.25 (m, 1H, H-4), 4.26 (q, 2H,  $J_{CH_2-CH_3}$  = 7.1 Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.20 (dd, 1H,  $J_{1-2}$  = 3.4 Hz,  $J_{2-3}$  = 5.2 Hz, H-2), 3.87 (td, 1H,  $J_{3-4}$  = 1.2 Hz,  $J_{2-3}$  = 5.2 Hz, H-3), 3.59 (ABX, 1H,  $J_{4-5a}$  = 4.0 Hz,  $J_{5a-5b}$  = 10.9 Hz, H-5a), 3.53 (ABX, 1H,  $J_{4-5b}$  = 4.6 Hz,  $J_{5a-5b}$  = 10.9 Hz, H-5b), 1.28 (t, 3H,  $J_{CH_2-CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 162.8 (dd,  $J_{C-F}$  = 30.2 Hz,  $J_{C-F}$  = 32.6 Hz, CqO<sub>2</sub>Et), 138.3 (C<sub>q</sub><sup>arom</sup>), 137.6 (C<sub>q</sub><sup>arom</sup>), 137.3 (C<sub>q</sub><sup>arom</sup>), 128.6-127.7 (CH<sup>arom</sup>), 113.3 (dd,  $J_{C-F}$  = 251.6 Hz,  $J_{C-F}$  = 256.5 Hz, CF<sub>2</sub>), 81.9 (dd,  $J_{C-F}$  = 25.4 Hz,  $J_{C-F}$  = 31.4 Hz, C-1), 81.7 (C-4), 77.8 (C-3), 75.9 (C-2), 73.6 (CH<sub>2</sub><sup>Bn</sup>), 72.4 (CH<sub>2</sub><sup>Bn</sup>), 72.2 (CH<sub>2</sub><sup>Bn</sup>), 69.7 (C-5), 62.3 (CH<sub>2</sub>CH<sub>3</sub>), 14.0 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -113.5 (dd, 1F,  $J_{H-Fa}$  = 7.7 Hz,  $J_{Fa-Fb}$  = 261.4 Hz, Fa), -120.4 (dd, 1F,  $J_{H-Fb}$  = 18.0 Hz,  $J_{Fa-Fb}$  = 261.4 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for C<sub>30</sub>H<sub>32</sub>F<sub>2</sub>NaO<sub>6</sub> [M+Na]<sup>+</sup>: calc. 549.2059; found: 549.2057. nOe: No correlation between H-1 and H-2 or H-3 observed.



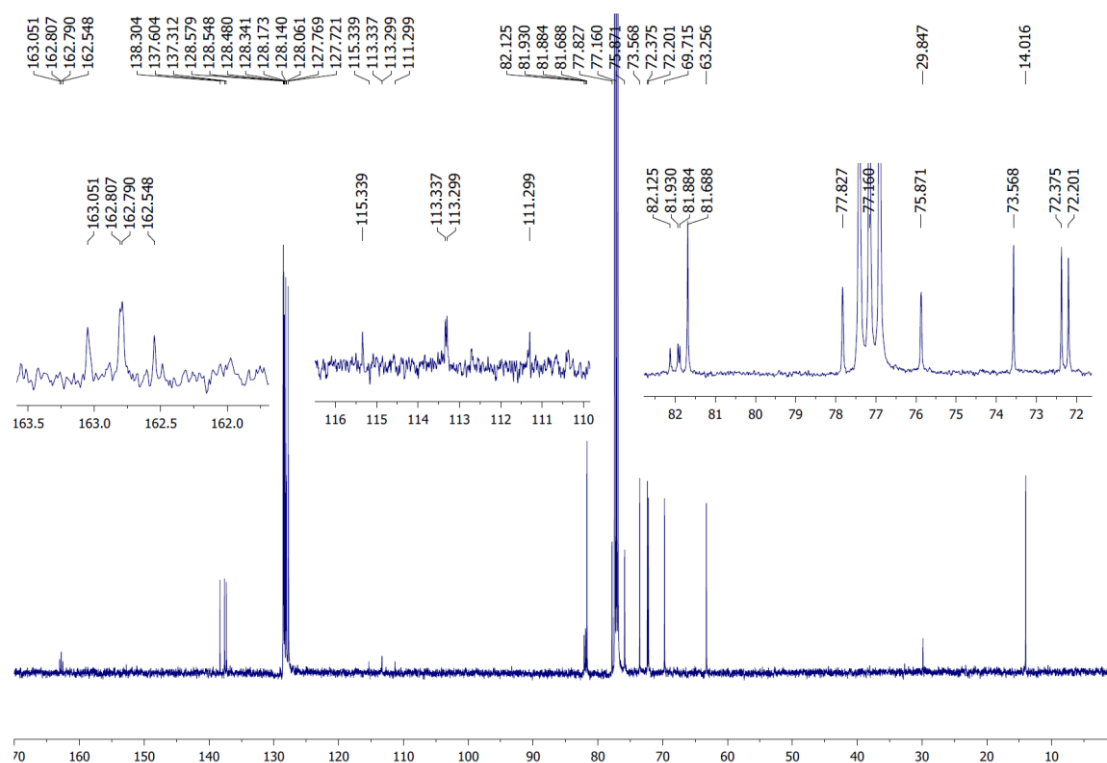
# $^1\text{H}$ NMR



# $^{19}\text{F}$ NMR

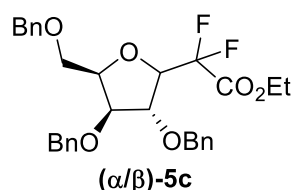


# <sup>13</sup>C NMR



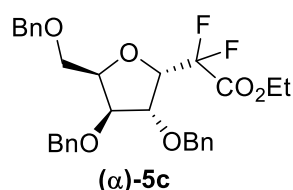
## D-Xylose

2,3,5-tri-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate- $\alpha,\beta$ -D-xylofuranose (( $\alpha/\beta$ )-**5c**).



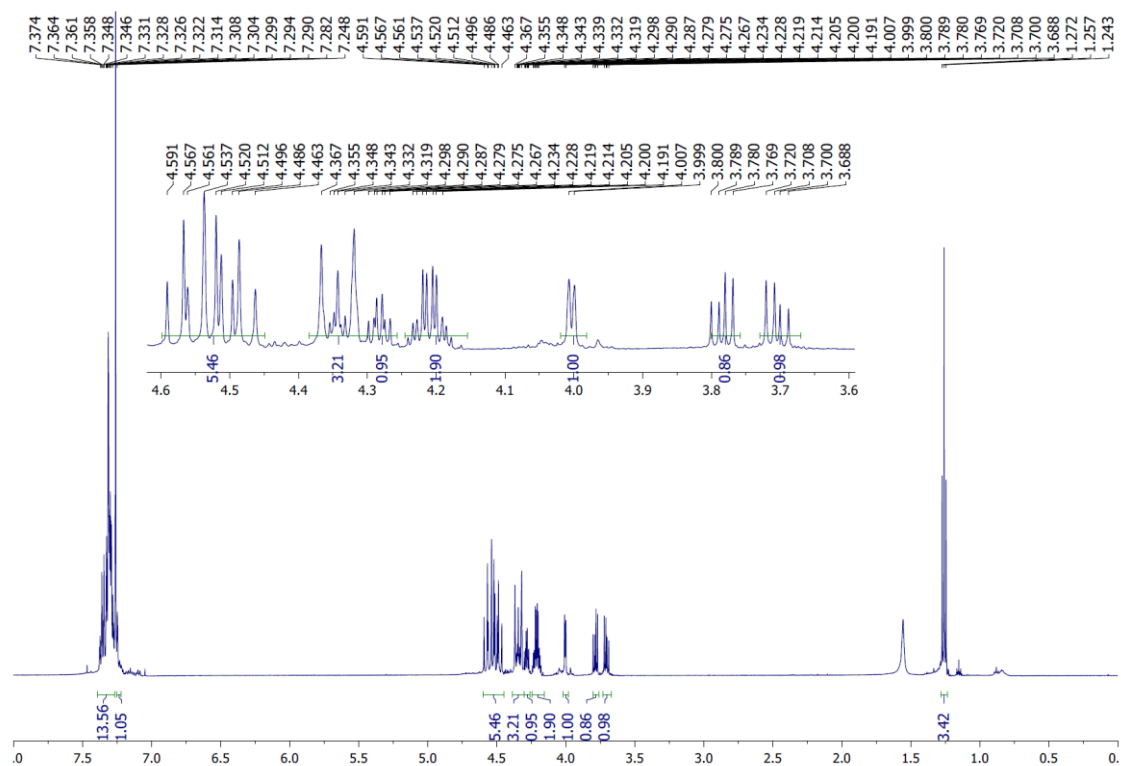
To a solution of alcohols (*R/S*)-**3c** (84 mg, 0.14 mmol) in dry DCM (1.7 ml) under argon atmosphere was added DAST (35  $\mu$ l, 0.28 mmol, 2.0 equiv.) dropwise at  $-78^{\circ}\text{C}$ . The reaction was allowed to warm from  $0^{\circ}\text{C}$  to r.t over 5h. TLC showed that starting material was still present. Thus, DAST (35  $\mu$ l, 0.28 mmol, 2.0 equiv.) was added at  $0^{\circ}\text{C}$  and the reaction was stirred for 16h at r.t. The crude was then diluted with dichloromethane and the organic phase was washed with  $\text{H}_2\text{O}$  (3 times) and brine (3 times), dried over  $\text{MgSO}_4$  and concentrated under reduced pressure.  $^1\text{H}$  and  $^{19}\text{F}$  crude NMR showed that the cyclized products ( $\alpha/\beta$ )-**5c** were formed in 65:35 *dr* ratio. Purification by chromatography on silica gel (Cy/EtOAc 9:1) afforded pure compound ( $\alpha$ )-**5c** (15 mg) and a mixture of ( $\alpha/\beta$ )-**5c** in 54:46 *dr* ratio (47 mg) in 83% overall yield.

2,3,5-tri-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate- $\alpha,\beta$ -D-xylofuranose (( $\alpha$ )-**5c**).

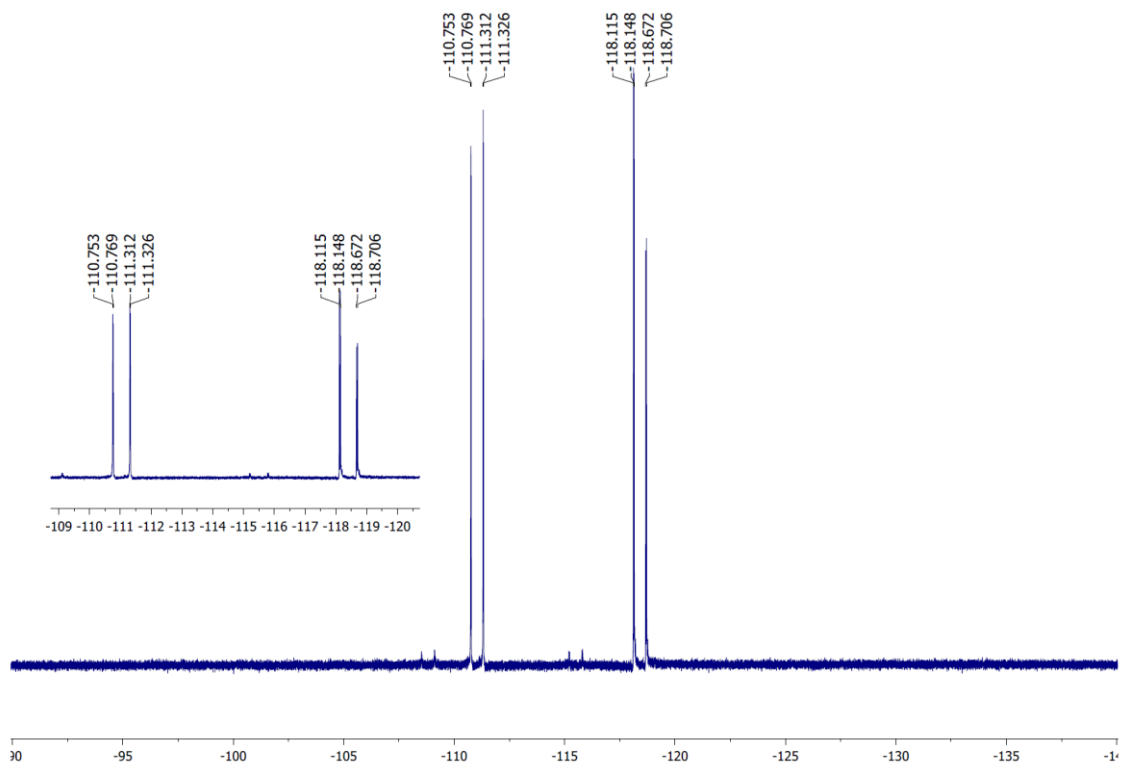


$[\alpha]_{\text{D}}^{20}$ : -23.1 (c 1.0,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.38-7.26 (m, 13H,  $\text{H}^{\text{arom}}$ ), 7.26-7.24 (m, 2H,  $\text{H}^{\text{arom}}$ ), 4.58 (AB, 1H,  $J_{\text{A-B}} = 11.5$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.55 (AB, 1H,  $J_{\text{A-B}} = 12.0$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.53 (AB, 1H,  $J_{\text{A-B}} = 12.0$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.51 (AB, 1H,  $J_{\text{A-B}} = 11.5$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.48 (AB, 1H,  $J_{\text{A-B}} = 11.5$  Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.37- 4.31 (m, 3H, H-1, H-2,  $\text{CH}_2^{\text{Bn}}$ ), 4.28 (td, 1H,  $J_{3-4} = 4.0$  Hz,  $J_{4-5a} = J_{4-5b} = 5.7$  Hz, H-4), 4.21 (qd, 2H,  $J = 2.9$  Hz,  $J_{\text{CH}_2-\text{CH}_3} = 7.5$  Hz,  $\text{CH}_2\text{CH}_3$ ), 4.00 (d, 1H,  $J_{2-3} \sim J_{3-4} = 4.0$  Hz, H-3), 3.79 (ABX, 1H,  $J_{4-5a} = 5.7$  Hz,  $J_{5a-5b} = 10.3$  Hz, H-5a), 3.70 (ABX, 1H,  $J_{4-5b} = 5.7$  Hz,  $J_{5a-5b} = 10.3$  Hz, H-5b), 1.26 (t, 3H,  $J_{\text{CH}_2-\text{CH}_3} = 7.5$  Hz,  $\text{CH}_2\text{CH}_3$ ) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 162.9 (dd,  $J_{\text{C-F}} = 30.3$  Hz,  $J_{\text{C-F}} = 32.3$  Hz,  $\text{CqO}_2\text{Et}$ ), 138.2 ( $\text{C}_q^{\text{arom}}$ ), 137.6 ( $\text{C}_q^{\text{arom}}$ ), 137.3 ( $\text{C}_q^{\text{arom}}$ ), 128.7-127.8 ( $\text{CH}^{\text{arom}}$ ), 113.1 (dd,  $J_{\text{C-F}} = 251.4$  Hz,  $J_{\text{C-F}} = 256.2$  Hz,  $\text{CF}_2$ ), 84.0 (dd,  $J_{\text{C-F}} = 27.5$  Hz,  $J_{\text{C-F}} = 30.3$  Hz, C-1), 82.2 (C-3), 81.7 (C-2, C-4), 73.6 ( $\text{CH}_2^{\text{Bn}}$ ), 72.1 ( $\text{CH}_2^{\text{Bn}}$ ), 71.6 ( $\text{CH}_2^{\text{Bn}}$ ), 67.8 (C-5), 63.2 ( $\text{CH}_2\text{CH}_3$ ), 14.0 ( $\text{CH}_2\text{CH}_3$ ) ppm.  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  = -111.0 (dd, 1F,  $J_{\text{H-Fa}} = 7.2$  Hz,  $J_{\text{Fa-Fb}} = 262.3$  Hz, Fa), -118.4 (dd, 1F,  $J_{\text{H-Fb}} = 15.7$  Hz,  $J_{\text{Fa-Fb}} = 262.3$  Hz, Fb) ppm. HRMS (ESI $^{+}$ ): *m/z* calculated for  $\text{C}_{30}\text{H}_{32}\text{F}_2\text{NaO}_6$  [ $\text{M}+\text{Na}$ ] $^{+}$ : calc. 549.2059; found: 549.2056. nOe: Correlations were inconclusive.

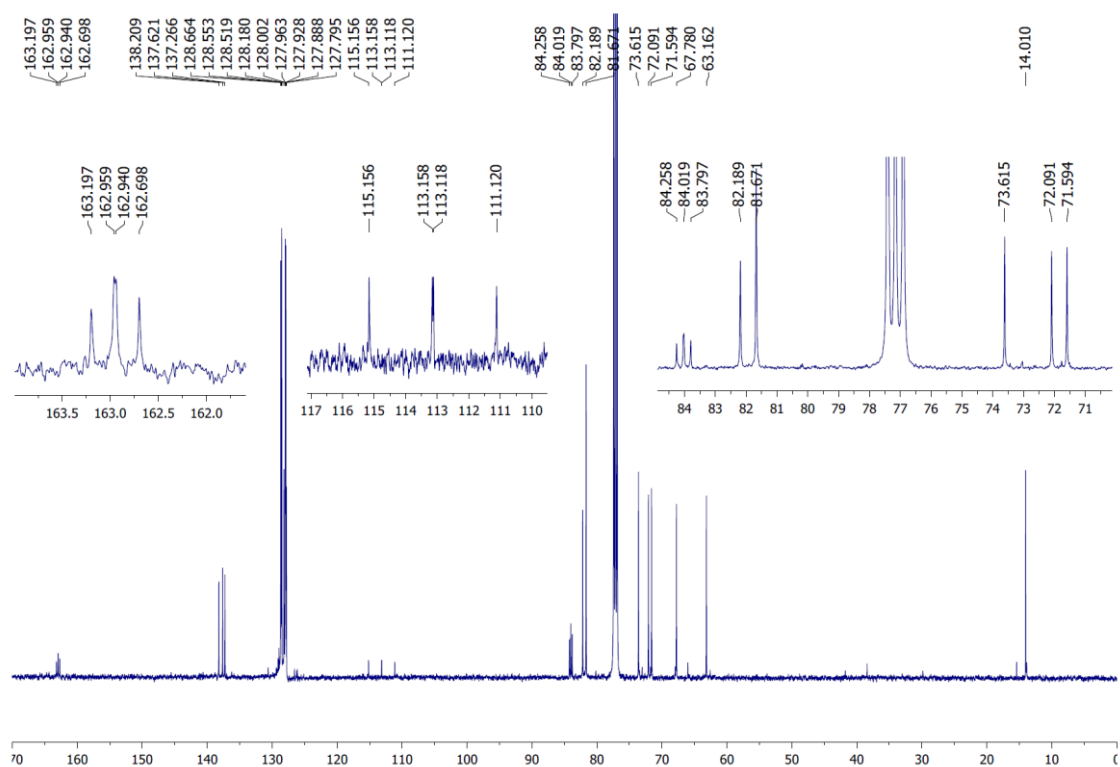
### <sup>1</sup>H NMR



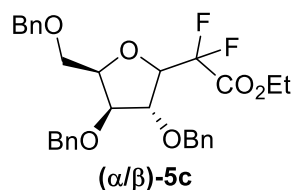
## <sup>19</sup>F NMR



# <sup>13</sup>C NMR



2,3,5-tri-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate- $\alpha,\beta$ -D-xylofuranose (( $\alpha/\beta$ )-**5c**).



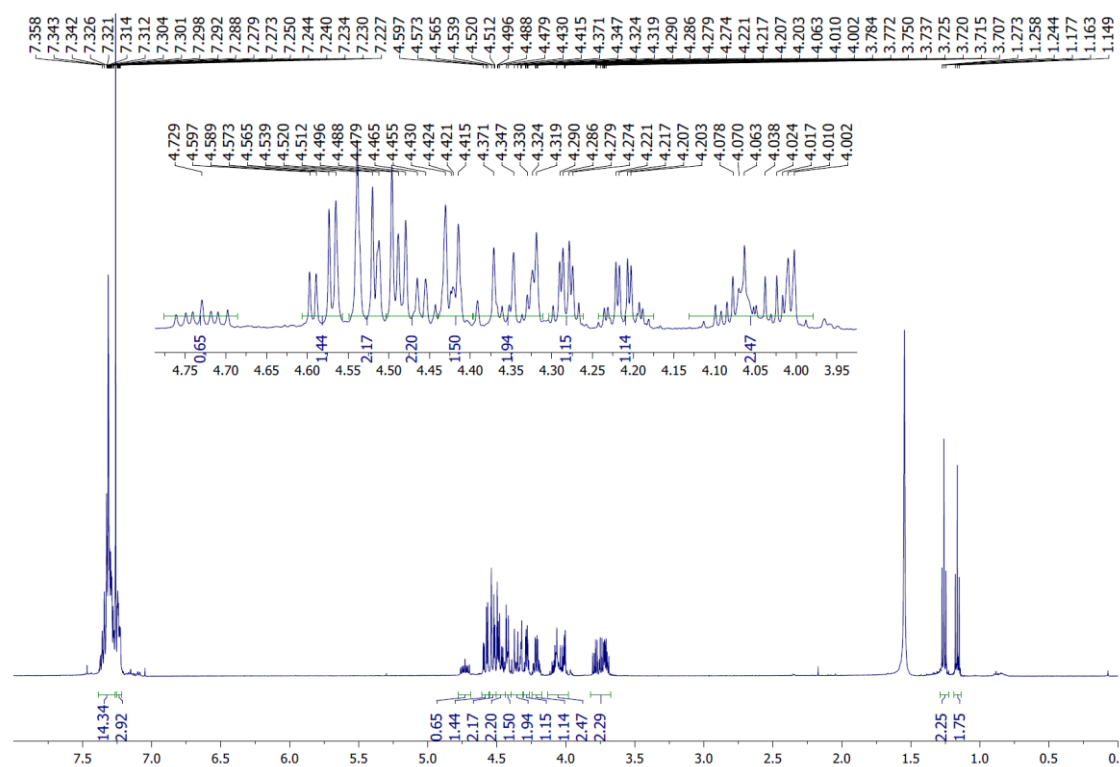
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.38-7.26 (m, 26H, 13  $\text{H}\alpha^{\text{arom}}$ , 13  $\text{H}\beta^{\text{arom}}$ ), 7.26-7.22 (m, 4H, 2  $\text{H}\alpha^{\text{arom}}$ , 2  $\text{H}\beta^{\text{arom}}$ ), 4.73 (ddd, 1H,  $J_{1-2}$  = 5.7 Hz,  $J_{1-\text{Fa}}$  = 9.7 Hz,  $J_{1-\text{Fb}}$  = 15.5 Hz, H-1 $\beta$ ), 4.59 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2\beta^{\text{Bn}}$ ), 4.58 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2\alpha^{\text{Bn}}$ ), 4.55-4.52 (m, 4H, 2  $\text{CH}_2\alpha^{\text{Bn}}$ , 2  $\text{CH}_2\beta^{\text{Bn}}$ ), 4.51 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2\alpha^{\text{Bn}}$ ), 4.50 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2\beta^{\text{Bn}}$ ), 4.47 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2\alpha^{\text{Bn}}$ ), 4.44 (AB, 1H,  $J_{\text{A-B}}$  = 12.0 Hz,  $\text{CH}_2\beta^{\text{Bn}}$ ), 4.40 (AB, 1H,  $J_{\text{A-B}}$  = 11.5 Hz,  $\text{CH}_2\beta^{\text{Bn}}$ ), 4.38-4.31 (m, 3H, H-1 $\alpha$ , H-2 $\alpha$ ,  $\text{CH}_2\alpha^{\text{Bn}}$ ), 4.30-4.27 (m, 2H, H-4 $\alpha$ , H-2 $\beta$ ), 4.21 (qd, 2H,  $J$  = 2.3 Hz,  $J_{\text{CH}_2-\text{CH}_3}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3\alpha$ ), 4.10-4.00 (m, 5H, H-3 $\alpha$ , H-3 $\beta$ , H-4 $\beta$ ,  $\text{CH}_2\text{CH}_3\beta$ ), 3.79 (ABX, 1H,  $J_{4-5a}$  = 5.7 Hz,  $J_{5a-5b}$  = 10.3 Hz, H-5a $\alpha$ ), 3.77-3.69 (m, 3H, H-5b $\alpha$ , H-5a $\beta$ , H-5b $\beta$ ), 1.26 (t, 3H,  $J_{\text{CH}_2-\text{CH}_3\alpha}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3\alpha$ ), 1.16 (t, 3H,  $J_{\text{CH}_2-\text{CH}_3\beta}$  = 7.5 Hz,  $\text{CH}_2\text{CH}_3\beta$ ) ppm.

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 163.2 (t,  $J_{\text{C-F}}$  = 31.3 Hz,  $\text{CqO}_2\text{Et}\beta$ ), 162.9 (dd,  $J_{\text{C-F}}$  = 30.8 Hz,  $J_{\text{C-F}}$  = 32.8 Hz,  $\text{CqO}_2\text{Et}\alpha$ ), 138.2 ( $\text{C}_q\alpha^{\text{arom}}$ ,  $\text{C}_q\beta^{\text{arom}}$ ), 137.7 ( $\text{C}_q\beta^{\text{arom}}$ ), 137.6 ( $\text{C}_q\alpha^{\text{arom}}$ ), 137.3 ( $\text{C}_q\alpha^{\text{arom}}$ ), 137.0 ( $\text{C}_q\beta^{\text{arom}}$ ), 128.7-127.7 ( $\text{CH}\alpha^{\text{arom}}$ ,  $\text{CH}\beta^{\text{arom}}$ ), 113.5 (dd,  $J_{\text{C-F}}$  = 248.1 Hz,  $J_{\text{C-F}}$  = 259.6 Hz,  $\text{CF}_2\beta$ ), 113.1 (dd,  $J_{\text{C-F}}$  = 251.4 Hz,  $J_{\text{C-F}}$  = 256.2 Hz,  $\text{CF}_2\alpha$ ), 84.0 (dd,  $J_{\text{C-F}}$  = 27.9 Hz,  $J_{\text{C-F}}$  = 29.9 Hz, C-1 $\alpha$ ), 82.2 (C-3 $\alpha$ ), 82.0 (d,  $J_{\text{C-F}}$  = 2.9 Hz, C-2 $\beta$ ), 81.7 (C-2 $\alpha$ , C-4 $\alpha$ ), 81.3 (C-3 $\beta$ ), 80.2 (C-4 $\beta$ ), 79.2 (dd,  $J_{\text{C-F}}$  = 22.2 Hz,  $J_{\text{C-F}}$  = 27.0 Hz, C-1 $\beta$ ), 73.7 ( $\text{CH}_2\beta^{\text{Bn}}$ ), 73.6 ( $\text{CH}_2\alpha^{\text{Bn}}$ ), 73.1 ( $\text{CH}_2\beta^{\text{Bn}}$ ), 72.7 ( $\text{CH}_2\beta^{\text{Bn}}$ ), 72.1 ( $\text{CH}_2\alpha^{\text{Bn}}$ ), 71.6 ( $\text{CH}_2\alpha^{\text{Bn}}$ ), 67.8 (C-5 $\alpha$ , C-5 $\beta$ ), 63.2 ( $\text{CH}_2\text{CH}_3\alpha$ ), 62.6 ( $\text{CH}_2\text{CH}_3\beta$ ), 14.0 ( $\text{CH}_2\text{CH}_3\alpha$ ), 13.9 ( $\text{CH}_2\text{CH}_3\beta$ ) ppm.

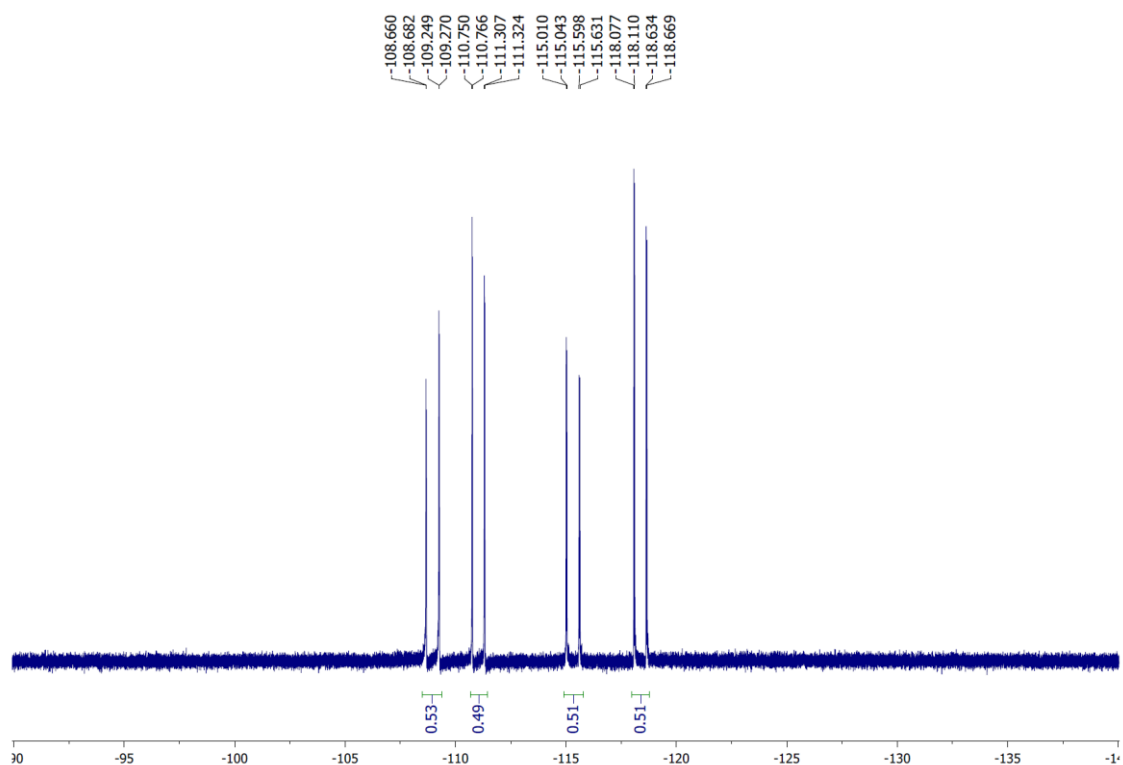
$^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  = -109.0 (dd, 1F,  $J_{\text{H-Fa}}$  = 9.7 Hz,  $J_{\text{Fa-Fb}}$  = 277.1 Hz, Fa $\beta$ ), -111.0 (dd, 1F,  $J_{\text{H-Fa}}$  = 7.7 Hz,  $J_{\text{Fa-Fb}}$  = 262.3 Hz, Fa $\alpha$ ), -115.3 (dd, 1F,  $J_{\text{H-Fb}}$  = 15.3 Hz,  $J_{\text{Fa-Fb}}$  = 277.1 Hz, Fb $\beta$ ), -118.4 (dd, 1F,  $J_{\text{H-Fb}}$  = 15.3 Hz,  $J_{\text{Fa-Fb}}$  = 262.3 Hz, Fb $\alpha$ ) ppm.

HRMS (ESI $^+$ ):  $m/z$  calculated for  $\text{C}_{30}\text{H}_{32}\text{F}_2\text{NaO}_6$  [ $\text{M}+\text{Na}$ ] $^+$ : calc. 549.2059; found: 549.2054. nOe ( $\beta$  anomer): Correlation between H-1 and H-2 observed. No correlation between H-1 and H-3 or H-4 observed.

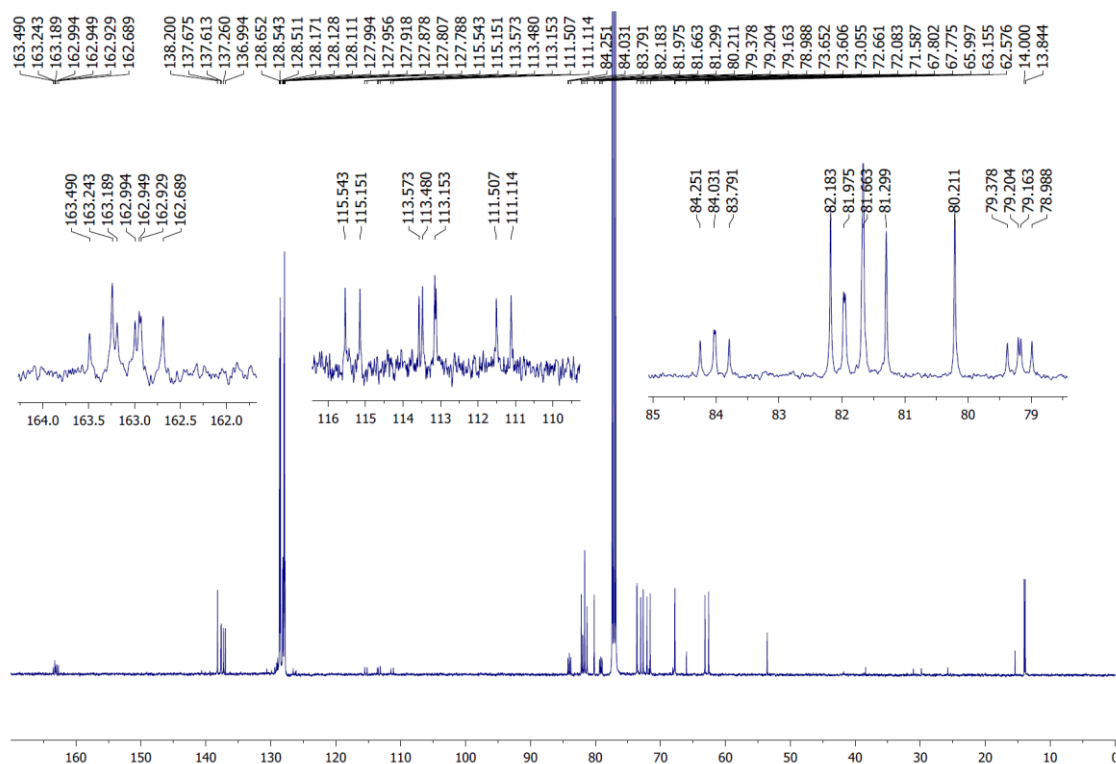
# <sup>1</sup>H NMR



# <sup>19</sup>F NMR



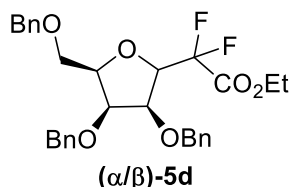
# <sup>13</sup>C NMR





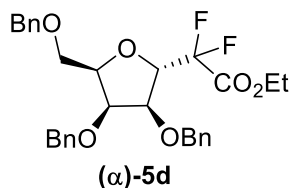
## D-Lyxose

2,3,5-tri-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate- $\alpha,\beta$ -D-lyxofuranose (( $\alpha/\beta$ )-**5d**).



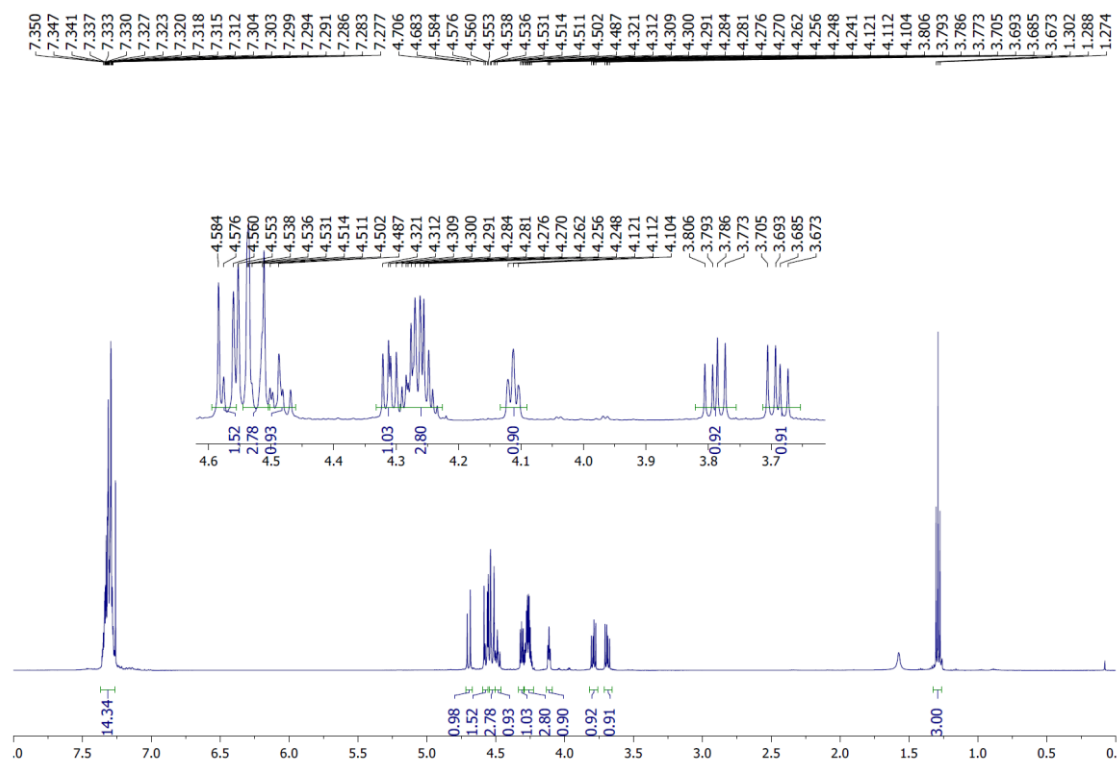
To a solution of alcohols (*R/S*)-**3d** (111 mg, 0.175 mmol, 64:36 *dr* ratio) in dry DCM (3 ml) under argon atmosphere was added DAST (92  $\mu$ l, 0.7 mmol, 4.0 equiv.) dropwise at 0°C. The reaction was allowed to warm from 0°C to r.t. and the reaction was stirred for 18h at r.t. The crude was then diluted with CH<sub>2</sub>Cl<sub>2</sub> and the organic phase was washed with H<sub>2</sub>O (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. <sup>1</sup>H and <sup>19</sup>F crude NMR showed that the cyclized products ( $\alpha/\beta$ )-**5d** were formed in 51:49 *dr* ratio with an overall conversion of 72%. Purification by chromatography on silica gel (Cy/EtOAc 95:5 to 9:1) afforded pure compound ( $\alpha$ )-**5d** (16 mg) and ( $\beta$ )-**5d** (22 mg) in 41% overall yield.

2,3,5-tri-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate- $\alpha,\beta$ -D-lyxofuranose (( $\alpha$ )-**5d**).

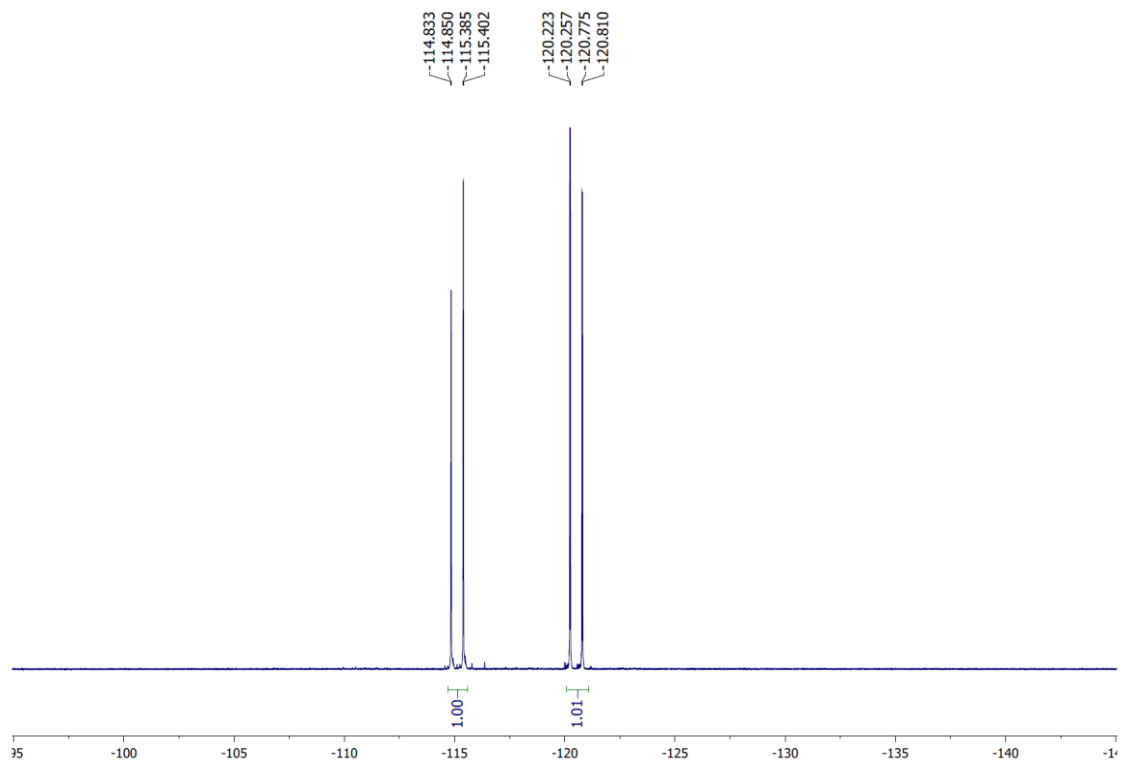


[ $\alpha$ ]<sub>D</sub><sup>20</sup>: +0.5 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.36-7.26 (m, 15H, H<sup>arom</sup>), 4.69 (AB, 1H, *J*<sub>A-B</sub> = 11.6 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.57 (AB, 1H, *J*<sub>A-B</sub> = 11.9 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.56 (AB, 1H, *J*<sub>A-B</sub> = 11.6 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.54-4.51 (m, 3H, CH<sub>2</sub><sup>Bn</sup>), 4.50-4.47 (m, 1H, H-1), 4.31 (dd, 1H, *J*<sub>1-2</sub> = 6.2 Hz, *J*<sub>2-3</sub> = 4.6 Hz, H-2), 4.28-4.25 (m, 1H, H-4), 4.27 (ddq, 2H, *J* = 10.1 Hz, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.1 Hz, *J* = 3.2 Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.11 (t, 1H, *J*<sub>2-3</sub> = *J*<sub>3-4</sub> = 4.2 Hz, H-3), 3.79 (dd, 1H, *J*<sub>5a-5b</sub> = 10.0 Hz, *J*<sub>4-5</sub> = 6.3 Hz, H-5), 3.69 (dd, 1H, *J* = *J*<sub>5a-5b</sub> = 10.0, *J*<sub>4-5</sub> = 6.3 Hz, H-5), 1.29 (t, 3H, *J*<sub>CH<sub>2</sub>CH<sub>3</sub></sub> = 7.2 Hz, CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.0 (t, *J*<sub>C-F</sub> = 31.6 Hz, C<sub>q</sub>O<sub>2</sub>Et), 138.1 (C<sub>q</sub><sup>arom</sup>), 138.0 (C<sub>q</sub><sup>arom</sup>), 137.3 (C<sub>q</sub><sup>arom</sup>), 128.6-127.8 (CH<sup>arom</sup>), 114.0 (dd, *J*<sub>C-F</sub> = 252.6 Hz, *J*<sub>C-F</sub> = 256.7 Hz, CF<sub>2</sub>), 80.7 (C-4), 80.0 (dd, *J*<sub>C-F</sub> = 23.7 Hz, *J*<sub>C-F</sub> = 29.4 Hz, C-1), 78.66 (d, *J*<sub>C-F</sub> = 2.7 Hz, C-2), 77.3 (C-3), 73.64 (CH<sub>2</sub><sup>Bn</sup>), 73.56 (CH<sub>2</sub><sup>Bn</sup>), 72.9 (CH<sub>2</sub><sup>Bn</sup>), 68.1 (C-5), 63.2 (CH<sub>2</sub>CH<sub>3</sub>), 14.0 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -115.1 (dd, 1F, *J*<sub>H-Fa</sub> = 8.1 Hz, *J*<sub>Fa-Fb</sub> = 259.9 Hz, Fa), -120.5 (dd, 1F, *J*<sub>H-Fb</sub> = 16.4 Hz, *J*<sub>Fa-Fb</sub> = 259.9 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): *m/z* calculated for C<sub>30</sub>H<sub>33</sub>F<sub>2</sub>O<sub>6</sub> [M+H]<sup>+</sup>: calc. 527.2240; found: 527.2235. nOe: Correlations were inconclusive.

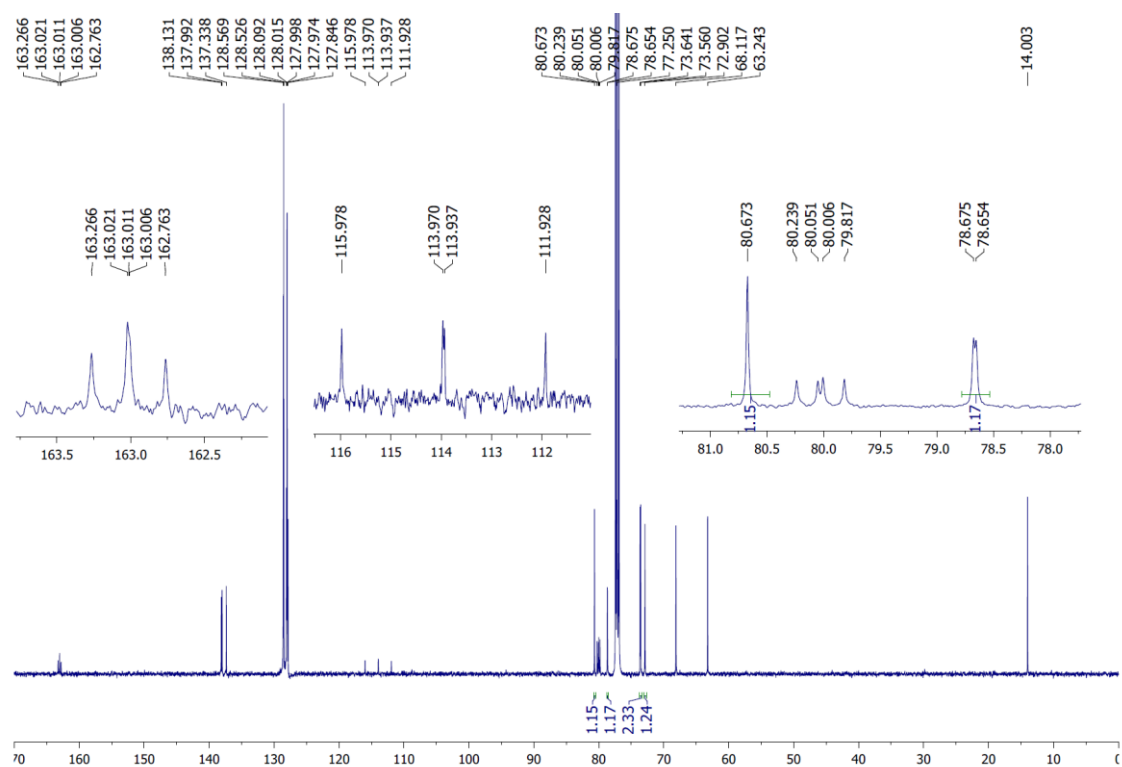
# <sup>1</sup>H NMR



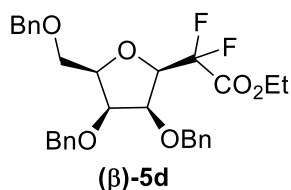
# <sup>19</sup>F NMR



# <sup>13</sup>C NMR

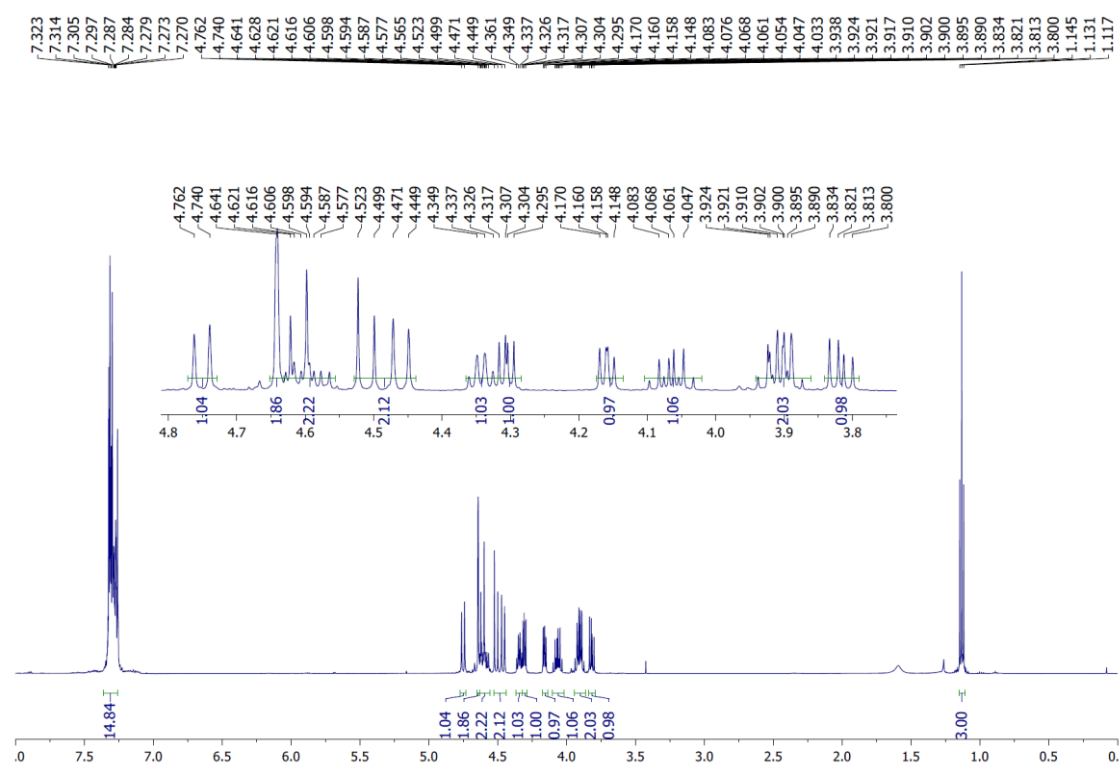


2,3,5-tri-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate- $\alpha,\beta$ -D-lyxofuranose (( $\beta$ )-**5d**).

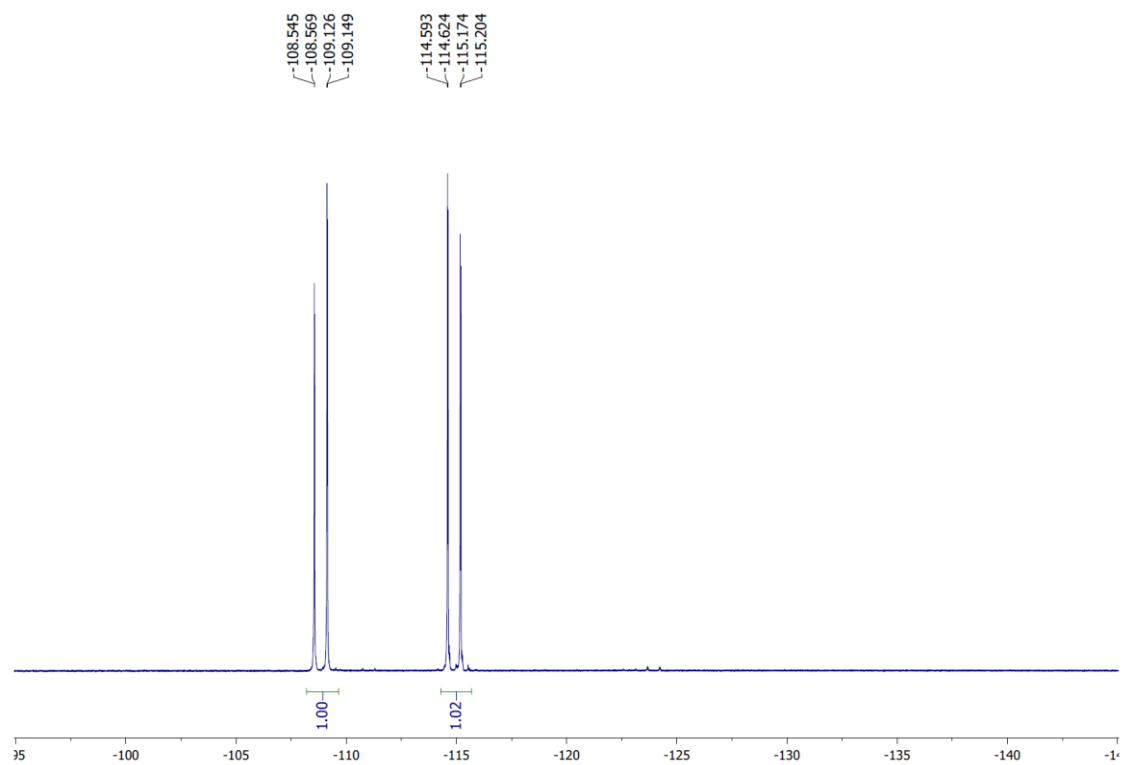


$[\alpha]_{\text{D}}^{20}$ : -0.2 (c 1.0,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.34-7.25 (m, 15H,  $\text{H}^{\text{arom}}$ ), 4.75 (AB, 1H,  $J_{\text{A-B}}$  = 11.4 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.64 (brs, 2H,  $\text{CH}_2^{\text{Bn}}$ ), 4.61 (AB, 1H,  $J_{\text{A-B}}$  = 11.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.63-4.56 (m, 1H, H-1), 4.51 (AB, 1H,  $J_{\text{A-B}}$  = 11.9 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.46 (AB, 1H,  $J_{\text{A-B}}$  = 11.3 Hz,  $\text{CH}_2^{\text{Bn}}$ ), 4.34 (q, 1H,  $J_{3-4} = J_{4-5}$  = 6.0 Hz, H-4), 4.31 (dd, 1H,  $J_{1-2}$  = 6.2 Hz,  $J_{2-3}$  = 4.6 Hz, H-2), 4.16 (dd, 1H,  $J_{3-4}$  = 5.9 Hz,  $J_{2-3}$  = 4.7 Hz, H-3), 4.06 (dq, 1H,  $J_{\text{CH}_2\text{CH}_3}$  = 10.8 Hz,  $J_{\text{CH}_2\text{CH}_3}$  = 7.2 Hz,  $\text{CH}_2\text{CH}_3$ ), 3.94-3.87 (m, 2H,  $\text{CH}_2\text{CH}_3$  and H-5), 3.82 (dd, 1H,  $J_{5a-5b}$  = 10.5 Hz,  $J_{4-5}$  = 6.5 Hz, H-5), 1.13 (t, 3H,  $J_{\text{CH}_2\text{CH}_3}$  = 7.2 Hz,  $\text{CH}_2\text{CH}_3$ ) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  = 163.3 (t,  $J_{\text{C-F}}$  = 30.9 Hz,  $\text{C}_q\text{O}_2\text{Et}$ ), 138.4 ( $\text{C}_q^{\text{arom}}$ ), 137.9 ( $\text{C}_q^{\text{arom}}$ ), 137.5 ( $\text{C}_q^{\text{arom}}$ ), 128.5-127.6 ( $\text{CH}^{\text{arom}}$ ), 112.9 (dd,  $J_{\text{C-F}}$  = 247.5 Hz,  $J_{\text{C-F}}$  = 261.7 Hz,  $\text{CF}_2$ ), 79.7 (C-4), 78.44 (dd,  $J_{\text{C-F}}$  = 23.1 Hz,  $J_{\text{C-F}}$  = 26.3 Hz, C-1), 78.36 (C-3), 78.3 (d,  $J_{\text{C-F}}$  = 3.5 Hz, C-2), 73.9 ( $\text{CH}_2^{\text{Bn}}$ ), 73.6 ( $\text{CH}_2^{\text{Bn}}$ ), 73.4 ( $\text{CH}_2^{\text{Bn}}$ ), 69.4 (C-5), 62.6 ( $\text{CH}_2\text{CH}_3$ ), 13.8 ( $\text{CH}_2\text{CH}_3$ ) ppm.  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  = -108.9 (dd, 1F,  $J_{\text{H-Fa}}$  = 11.2 Hz,  $J_{\text{Fa-Fb}}$  = 273.1 Hz, Fa), -114.9 (dd, 1F,  $J_{\text{H-Fb}}$  = 14.4 Hz,  $J_{\text{Fa-Fb}}$  = 273.2 Hz, Fb) ppm. HRMS (ESI+): m/z calculated for  $\text{C}_{30}\text{H}_{33}\text{F}_2\text{O}_6$   $[\text{M}+\text{H}]^+$ : calc. 527.2240; found: 527.2237. nOe: Correlation between H-1 and H-3 observed.

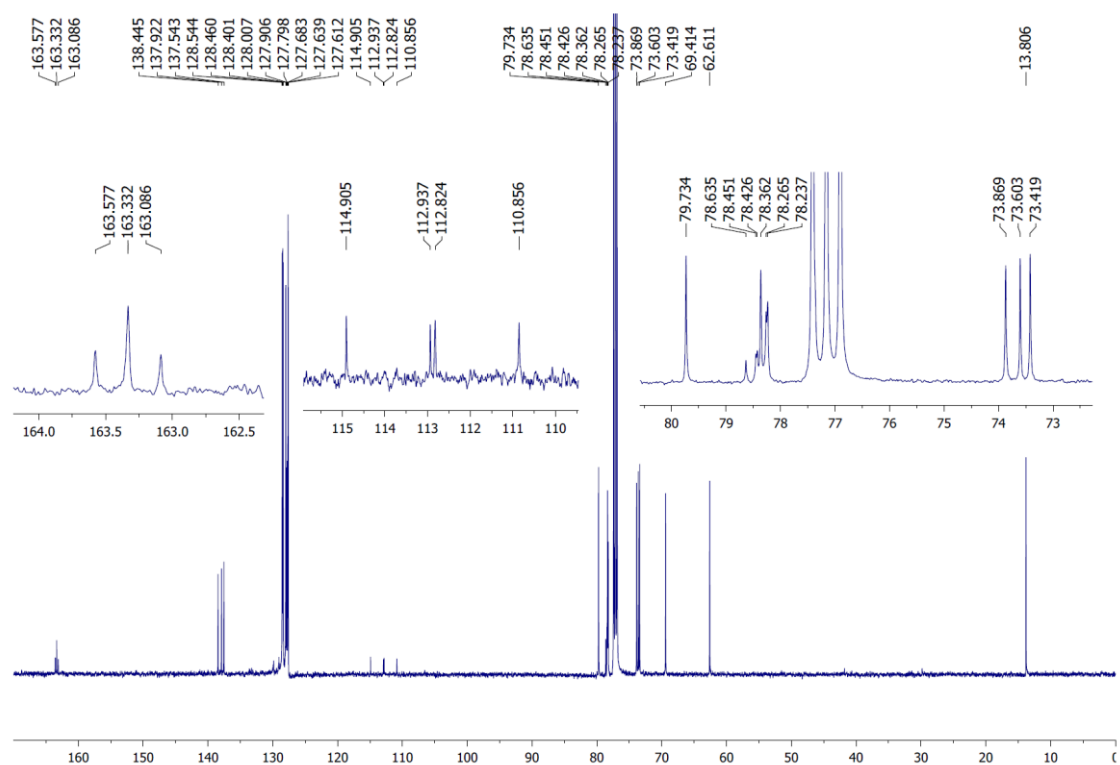
### <sup>1</sup>H NMR



## <sup>19</sup>F NMR

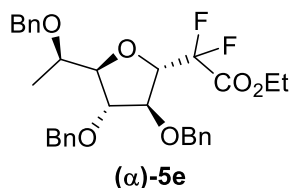


# <sup>13</sup>C NMR



## L-Fucose

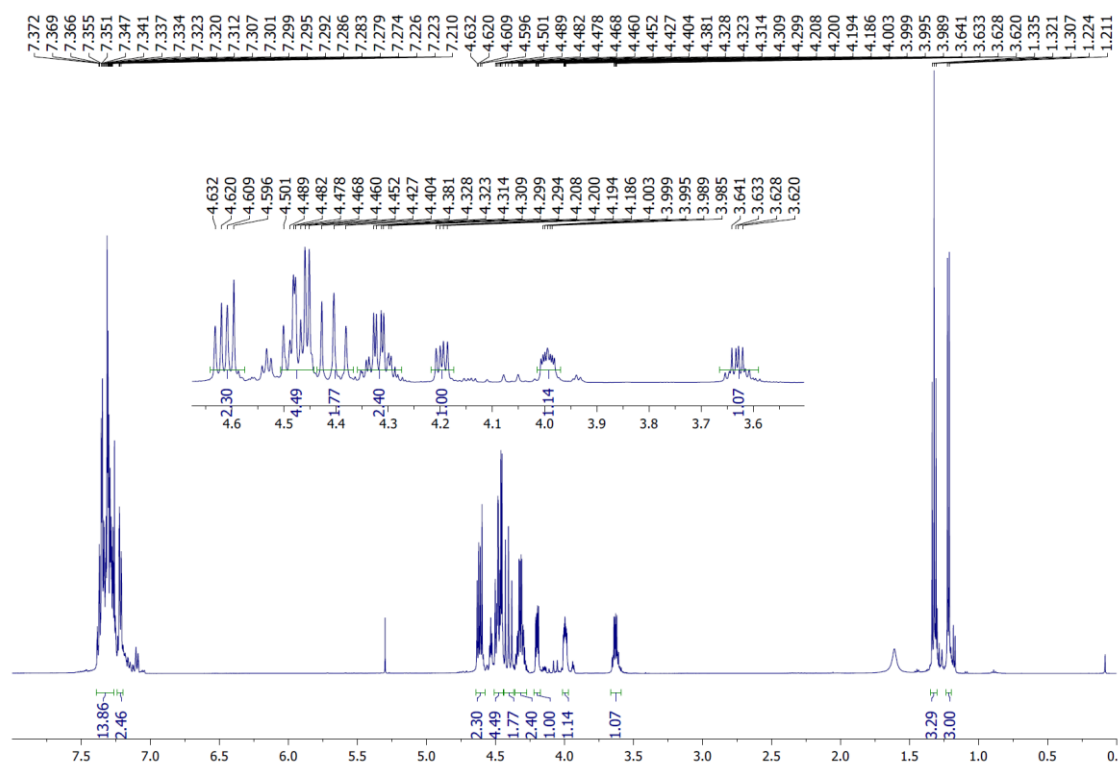
5-methyl-2,3,5-tri-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate- $\alpha,\beta$ -D-fucofuranose (( $\alpha$ )-**5e**).



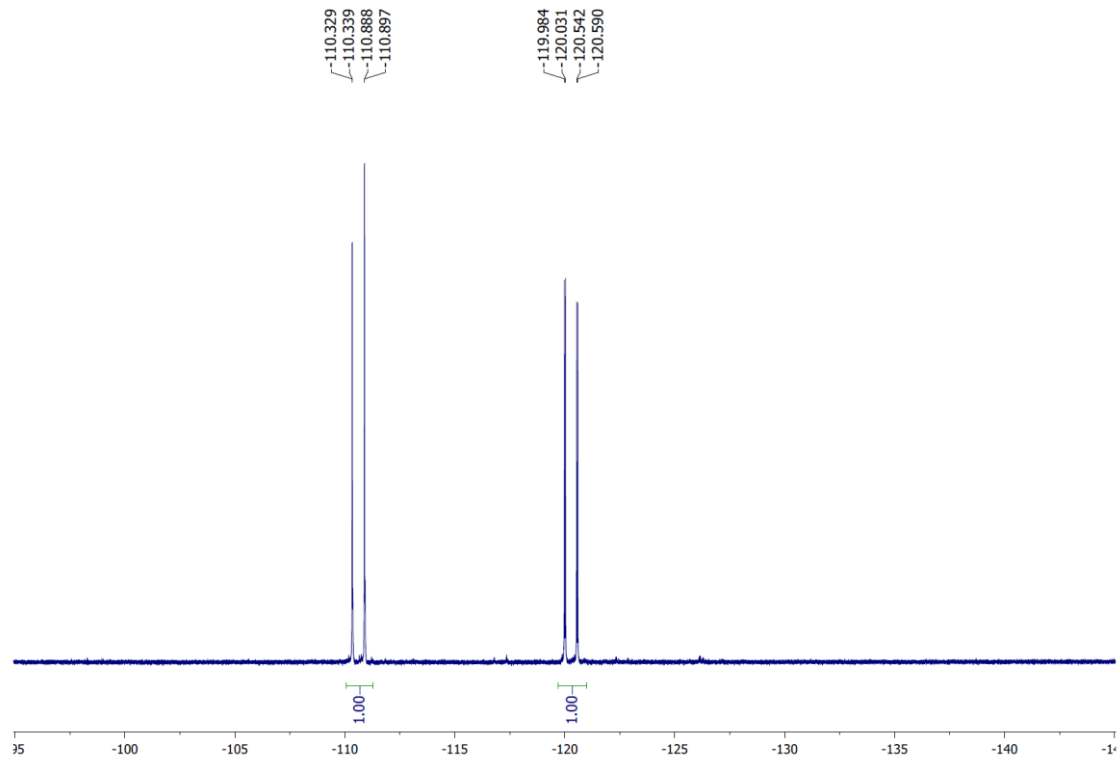
To a solution of alcohol (*R*)-**3e** (58.2 mg, 0.09 mmol) in dry DCM (2 ml) under argon atmosphere was added DAST (48  $\mu$ l, 0.36 mmol, 4.0 equiv.) dropwise at 0°C. The reaction was allowed to warm from 0°C to r.t. and the reaction was stirred for 18h at r.t. The crude was then diluted with CH<sub>2</sub>Cl<sub>2</sub> and the organic phase was washed with H<sub>2</sub>O (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 95:5) afforded pure compound ( $\alpha$ )-**5e** (26 mg, 0.048 mmol, 53%) as a colorless oil.

$[\alpha]_{20}^D$ : +2.9 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.37-7.27 (m, 13H, H<sup>arom</sup>), 7.22-7.20 (m, 2H, H<sup>arom</sup>), 4.61 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.60 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.54-4.41 (m, 5H, H-1, H-2, CH<sub>2</sub><sup>Bn</sup>), 4.39 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.31 (qd, 2H,  $J$  = 2.3 Hz,  $J_{CH_2-CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.19 (dd, 1H,  $J$  = 4.0 Hz,  $J_{3-4}$  = 6.9 Hz, H-3), 3.99 (ddd, 1H,  $J$  = 2.3 Hz,  $J_{4-5}$  = 4.0 Hz,  $J_{3-4}$  = 6.9 Hz, H-4), 3.62 (qd, 1H,  $J_{4-5}$  = 4.0 Hz,  $J_{5-CH_3}$  = 6.3 Hz, H-5), 1.32 (t, 3H,  $J_{CH_2-CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>), 1.21 (d, 3H,  $J_{5-CH_3}$  = 6.3 Hz, CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.1 (dd,  $J_{C-F}$  = 30.8 Hz,  $J_{C-F}$  = 33.2 Hz, C<sub>q</sub>O<sub>2</sub>Et), 138.5 (C<sub>q</sub><sup>arom</sup>), 137.8 (C<sub>q</sub><sup>arom</sup>), 137.5 (C<sub>q</sub><sup>arom</sup>), 128.6-127.7 (CH<sup>arom</sup>), 114.0 (dd,  $J_{C-F}$  = 252.8 Hz,  $J_{C-F}$  = 260.2 Hz, CF<sub>2</sub>), 86.0 (C-4), 84.4 (C-3), 83.8 (C-2), 82.1 (dd,  $J_{C-F}$  = 24.1 Hz,  $J_{C-F}$  = 32.6 Hz, C-1), 73.1 (C-5), 72.3 (2 CH<sub>2</sub><sup>Bn</sup>), 71.3 (CH<sub>2</sub><sup>Bn</sup>), 63.2 (CH<sub>2</sub>CH<sub>3</sub>), 15.9 (CH<sub>3</sub>), 14.1 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -110.6 (dd, 1F,  $J_{H-Fa}$  = 4.5 Hz,  $J_{Fa-Fb}$  = 262.9 Hz, Fa), -120.3 (dd, 1F,  $J_{H-Fb}$  = 22.3 Hz,  $J_{Fa-Fb}$  = 262.9 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>):  $m/z$  calculated for C<sub>31</sub>H<sub>35</sub>F<sub>2</sub>O<sub>6</sub> [M+H]<sup>+</sup>: calc. 541.2396; found: 541.2395. nOe: Correlations were inconclusive.

# <sup>1</sup>H NMR

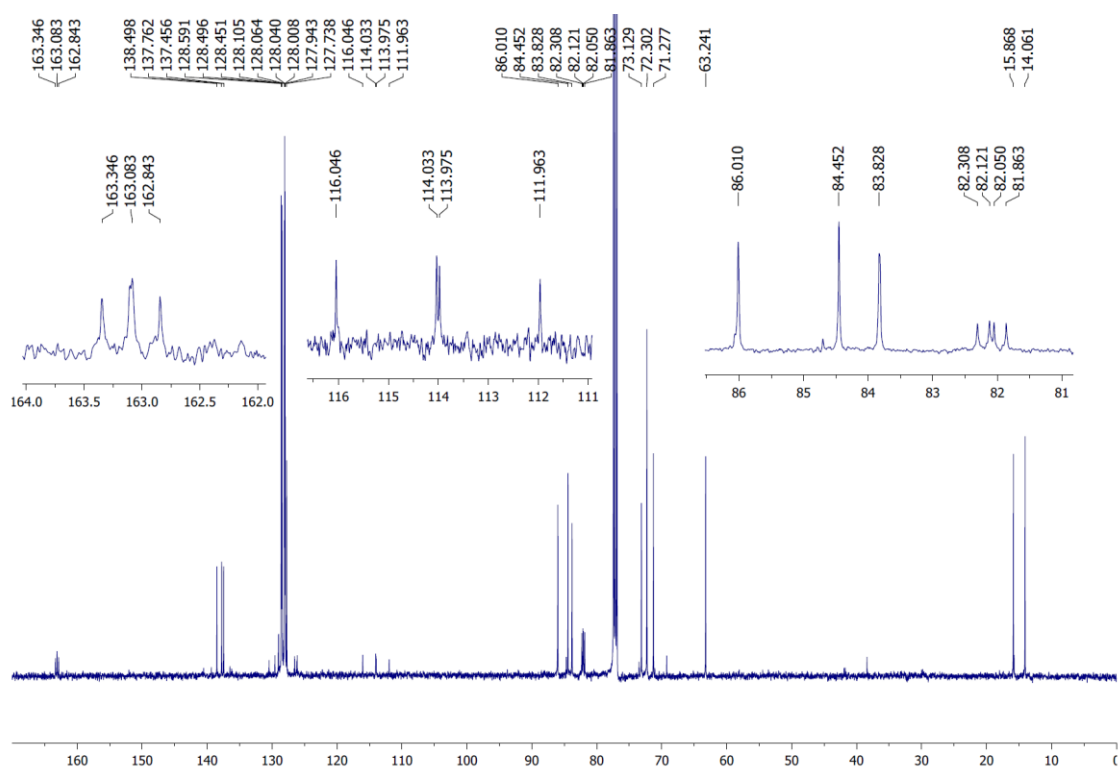


# <sup>19</sup>F NMR



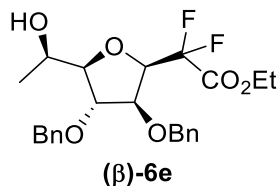


# <sup>13</sup>C NMR



5-methyl-2,3-tri-*O*-benzyl-5-hydroxy-1-deoxy-1,1-difluoroethyl  
fucofuranose (( $\beta$ )-**6e**).

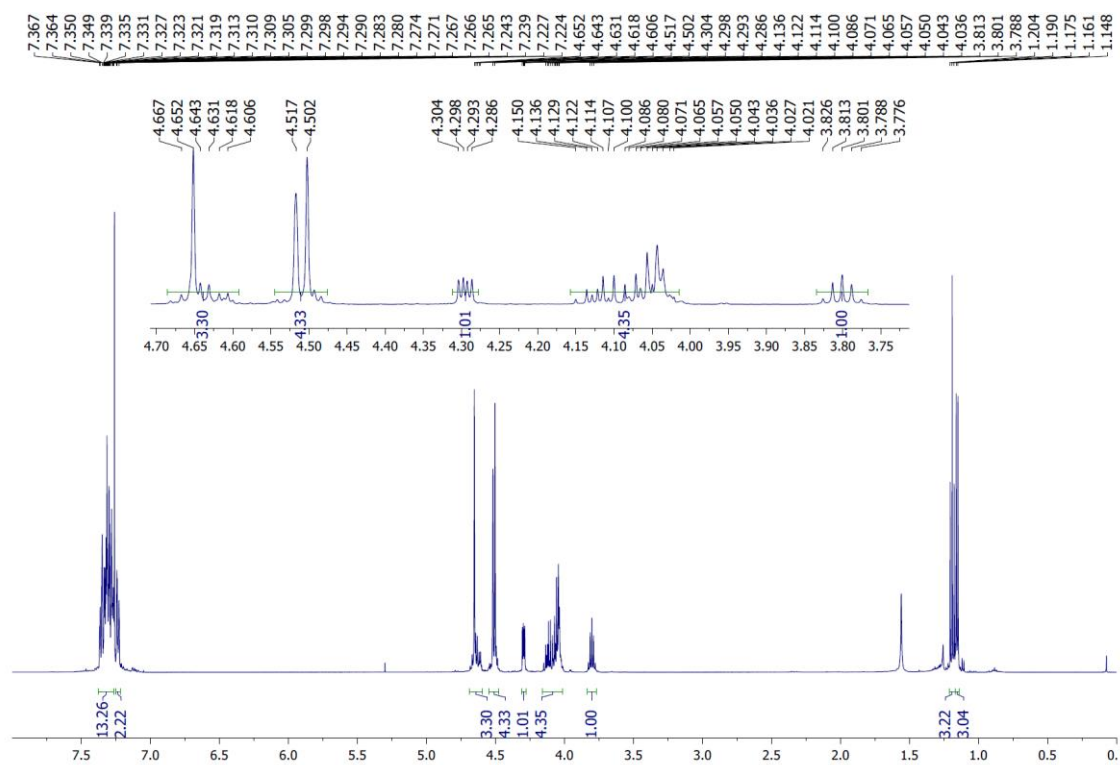
acetate- $\alpha,\beta$ -D-



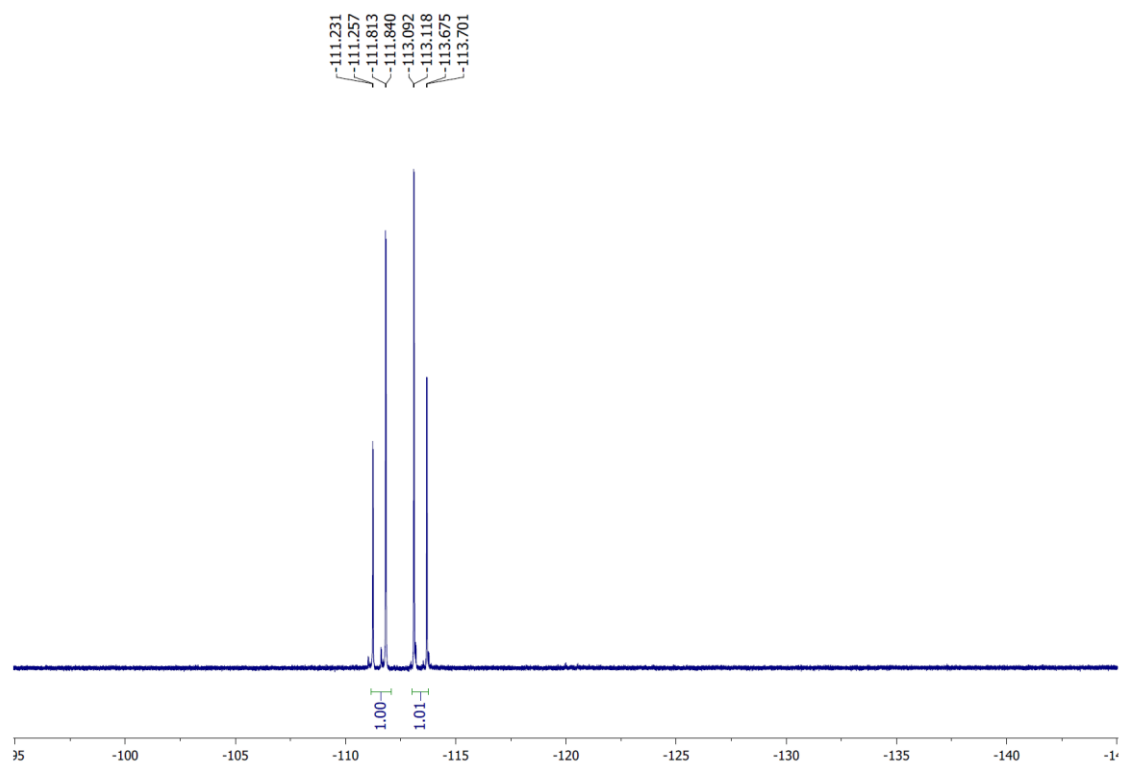
To a solution of alcohol (*S*)-**3e** (52.6 mg, 0.081 mmol) in dry DCM (2 ml) under argon atmosphere was added DAST (43  $\mu$ l, 0.32 mmol, 4.0 equiv.) dropwise at 0°C. The reaction was allowed to warm from 0°C to r.t. and the reaction was stirred for 18h at r.t. The crude was then diluted with CH<sub>2</sub>Cl<sub>2</sub> and the organic phase was washed with H<sub>2</sub>O (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 95:5) afforded pure compound ( $\beta$ )-**5e** (11 mg, 0.0203 mmol, 25%) as a colorless oil and a side product ( $\beta$ )-**6e** (13 mg, 0.029 mmol, 36%) identified as similar to ( $\beta$ )-**5e** with a free alcohol in C-5.

$[\alpha]_{20}^D$ : -4.5 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.38-7.27 (m, 10H, H<sup>arom</sup>), 4.64 (td, 1H,  $J_{1-2}$  = 5.2 Hz,  $J_{1-Fa}$  =  $J_{1-Fb}$  = 10.9 Hz, H-1), 4.53 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.50-4.47 (m, 3H, CH<sub>2</sub><sup>Bn</sup>), 4.26 (dd, 1H,  $J_{2-3}$  = 2.3 Hz,  $J_{1-2}$  = 5.2 Hz, H-2), 4.06 (qd, 2H,  $J$  = 2.9 Hz,  $J_{CH_2-CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>), 3.98 (m, 1H, H-3), 3.88-3.81 (m, 2H, H-4, H-5), 1.19 (t, 3H,  $J_{CH_2-CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>), 1.16 (d, 3H,  $J_{5-CH_3}$  = 6.3 Hz, CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.1 (t,  $J_{C-F}$  = 30.7 Hz, C<sub>q</sub>O<sub>2</sub>Et), 137.3 (C<sub>q</sub><sup>arom</sup>), 136.7 (C<sub>q</sub><sup>arom</sup>), 128.8-127.8 (CH<sup>arom</sup>), 113.0 (t,  $J_{C-F}$  = 253.5 Hz, CF<sub>2</sub>), 88.5 (C-4), 82.7 (C-2), 82.3 (C-3), 79.8 (t,  $J_{C-F}$  = 27.1 Hz, C-1), 73.0 (CH<sub>2</sub><sup>Bn</sup>), 72.2 (CH<sub>2</sub><sup>Bn</sup>), 67.2 (C-5), 62.9 (CH<sub>2</sub>CH<sub>3</sub>), 19.2 (CH<sub>3</sub>), 13.9 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -111.1 (dd, 1F,  $J_{H1-Fa}$  = 10.9 Hz,  $J_{Fa-Fb}$  = 278.0 Hz, Fa), -111.8 (dd, 1F,  $J_{H1-Fb}$  = 10.9 Hz,  $J_{Fa-Fb}$  = 278.0 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): *m/z* calculated for C<sub>24</sub>H<sub>29</sub>F<sub>2</sub>O<sub>6</sub> [M+H]<sup>+</sup>: calc. 451.1927; found: 451.1926. nOe: Correlation between H-1 and H-4 observed.

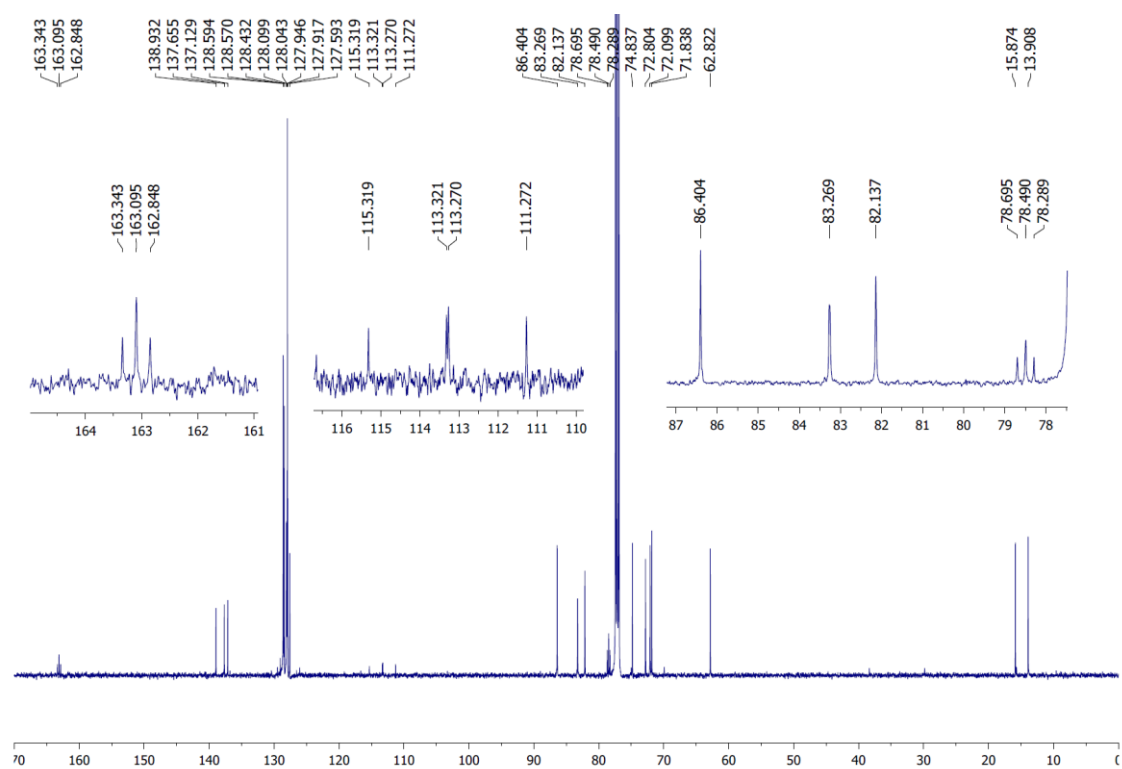
# <sup>1</sup>H NMR



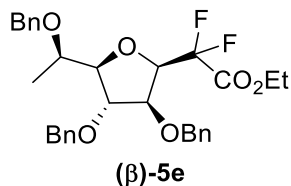
# <sup>19</sup>F NMR



# <sup>13</sup>C NMR



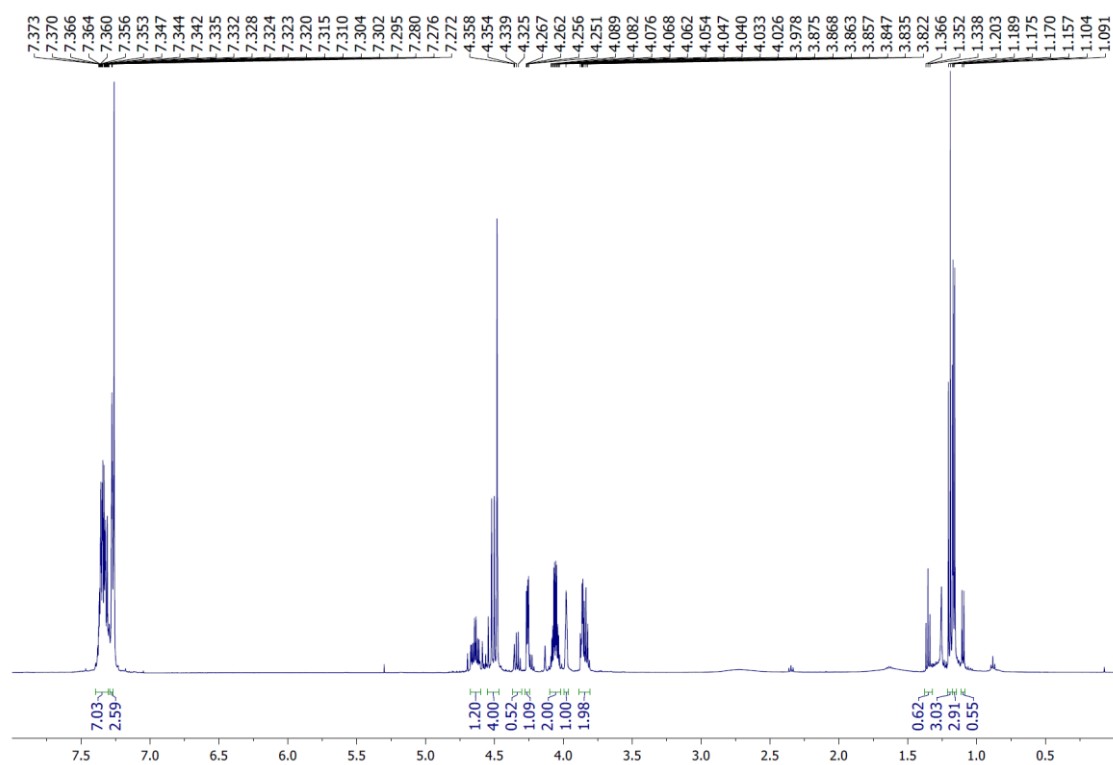
5-methyl-2,3,5-tri-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate- $\alpha,\beta$ -D-fucofuranose (( $\beta$ )-**5e**).



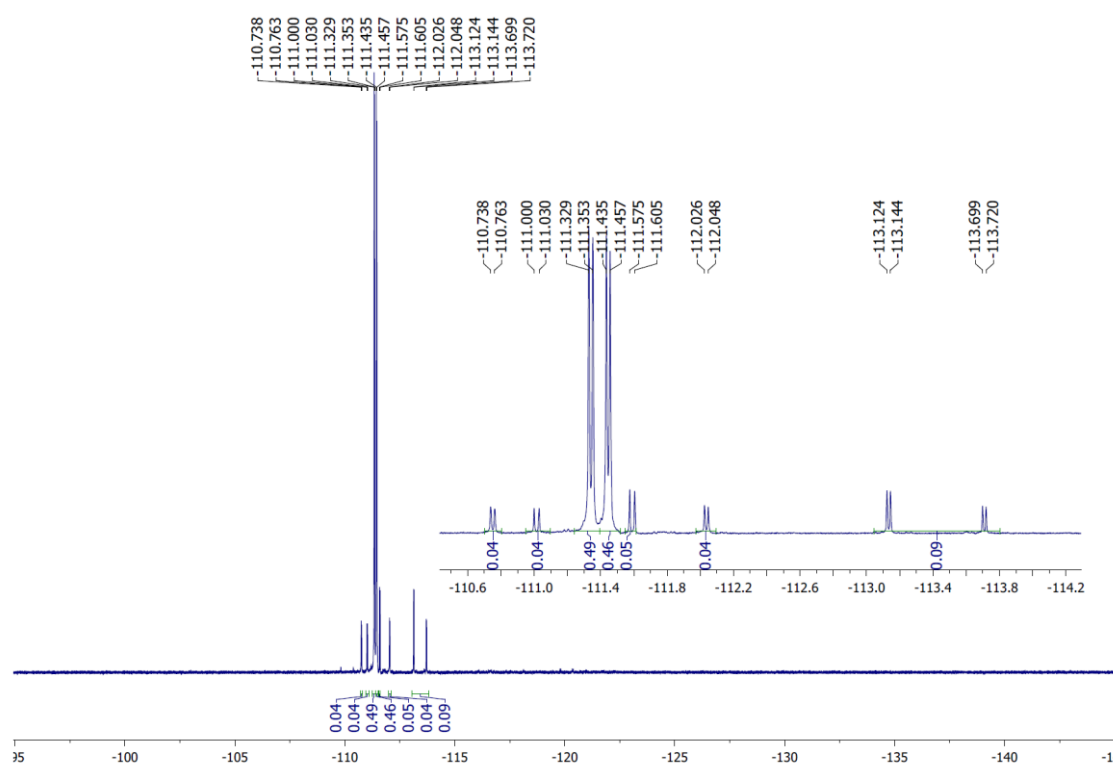
To a solution of alcohol (*S*)-**3e** (52.6 mg, 0.081 mmol) in dry DCM (2 ml) under argon atmosphere was added DAST (43  $\mu$ l, 0.32 mmol, 4.0 equiv.) dropwise at 0°C. The reaction was allowed to warm from 0°C to r.t. and the reaction was stirred for 18h at r.t. The crude was then diluted with CH<sub>2</sub>Cl<sub>2</sub> and the organic phase was washed with H<sub>2</sub>O (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 95:5) afforded pure compound ( $\beta$ )-**5e** (11 mg, 0.0203 mmol, 25%) as a colorless oil and a side product ( $\beta$ )-**6e** (13 mg, 0.029 mmol, 36%) identified as similar to ( $\beta$ )-**5e** with a free alcohol in C-5.

$[\alpha]_{20}^D$ : -7.2 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.37-7.27 (m, 13H, H<sup>arom</sup>), 7.24-7.22 (m, 2H, H<sup>arom</sup>), 4.68-4.60 (td, 1H,  $J_{1-2}$  = 5.7 Hz,  $J_{1-Fa}$  =  $J_{1-Fb}$  = 12.6 Hz, H-1), 4.65 (bs, 2H, CH<sub>2</sub><sup>Bn</sup>), 4.54-4.48 (m, 4H, CH<sub>2</sub><sup>Bn</sup>), 4.30 (dd, 1H,  $J_{2-3}$  = 3.4 Hz,  $J_{1-2}$  = 5.7 Hz, H-2), 4.15-4.02 (m, 4H, H-3, H-4, CH<sub>2</sub>CH<sub>3</sub>), 3.80 (quin, 1H,  $J$  = 6.3 Hz, H-5), 1.19 (t, 3H,  $J_{CH_2-CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>), 1.15 (d, 3H,  $J_{5-CH_3}$  = 6.3 Hz, CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.1 (t,  $J_{C-F}$  = 30.8 Hz, C<sub>q</sub>O<sub>2</sub>Et), 138.9 (C<sub>q</sub><sup>arom</sup>), 137.7 (C<sub>q</sub><sup>arom</sup>), 137.1 (C<sub>q</sub><sup>arom</sup>), 128.6-127.6 (CH<sup>arom</sup>), 113.3 (dd,  $J_{C-F}$  = 251.1 Hz,  $J_{C-F}$  = 258.3 Hz, CF<sub>2</sub>), 86.4 (C-4), 83.3 (C-2), 82.1 (C-3), 78.5 (t,  $J_{C-F}$  = 25.4 Hz, C-1), 74.8 (C-5), 72.8 (CH<sub>2</sub><sup>Bn</sup>), 72.1 (CH<sub>2</sub><sup>Bn</sup>), 71.8 (CH<sub>2</sub><sup>Bn</sup>), 62.8 (CH<sub>2</sub>CH<sub>3</sub>), 15.9 (CH<sub>3</sub>), 13.9 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -111.6 (dd, 1F,  $J_{H1-Fa}$  = 12.6 Hz,  $J_{Fa-Fb}$  = 274.0 Hz, Fa), -113.4 (dd, 1F,  $J_{H1-Fb}$  = 12.6 Hz,  $J_{Fa-Fb}$  = 274.0 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for C<sub>31</sub>H<sub>35</sub>F<sub>2</sub>O<sub>6</sub> [M+H]<sup>+</sup>: calc. 541.2396; found: 541.2396. nOe: Correlations were inconclusive.

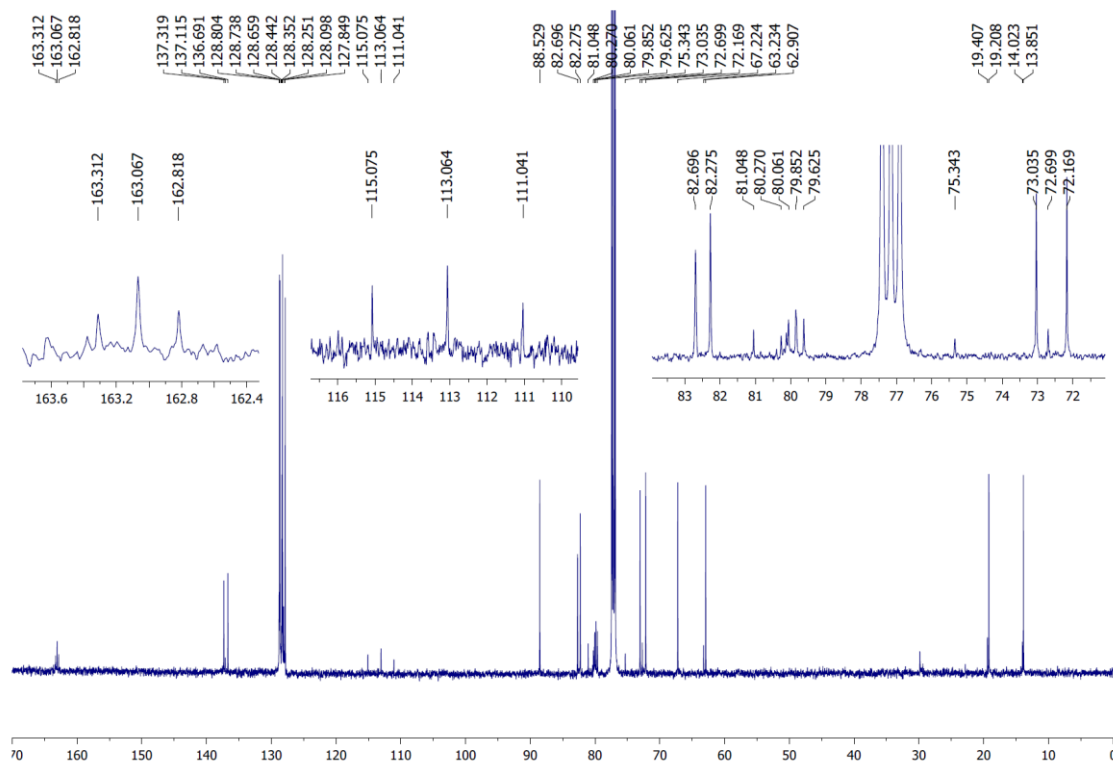
# <sup>1</sup>H NMR



# <sup>19</sup>F NMR

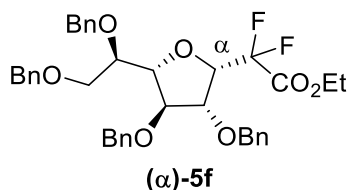


# <sup>13</sup>C NMR



## D-Galactose

2,3,5,6-tetra-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate- $\alpha,\beta$ -D-galactofuranose (( $\alpha$ )-**5f**).

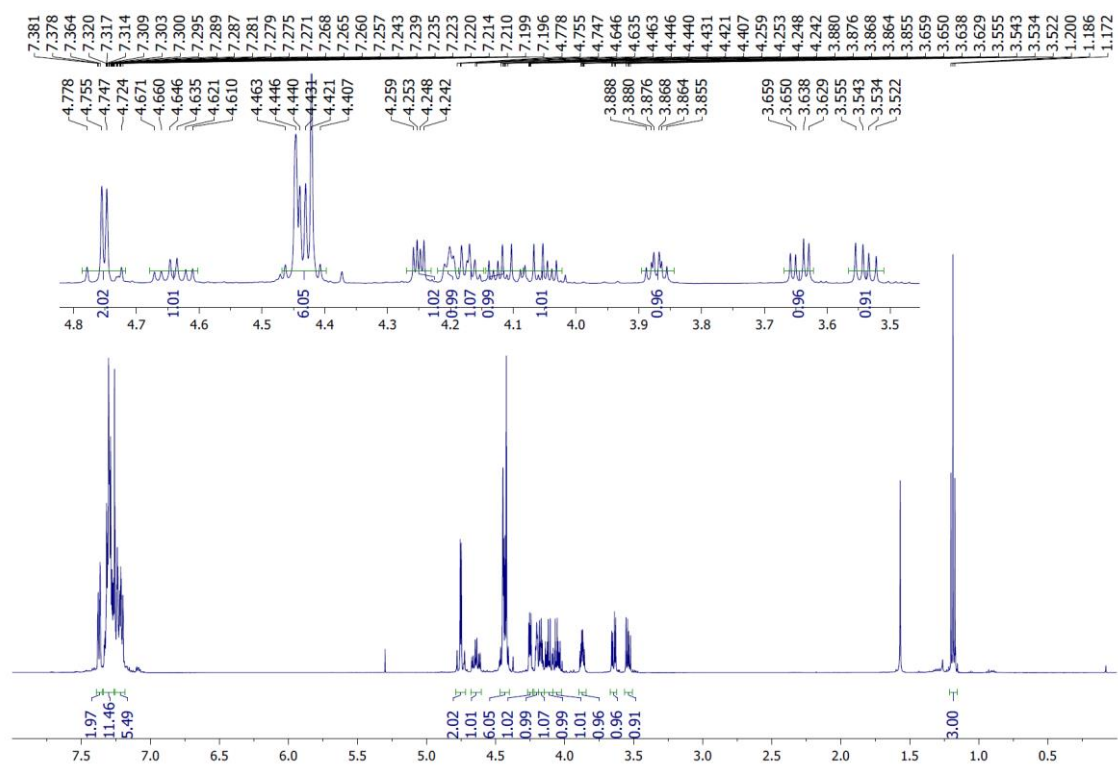


To a solution of alcohol (*R*)-**3f** (38 mg, 0.0503 mmol) in dry DCM (1.5 ml) under argon atmosphere was added DAST (26  $\mu$ l, 0.20 mmol, 4.0 equiv.) dropwise at 0°C. The reaction was allowed to warm from 0°C to r.t. and the reaction was stirred for 18h at r.t. The crude was then diluted with CH<sub>2</sub>Cl<sub>2</sub> and the organic phase was washed with H<sub>2</sub>O (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 95:5) afforded pure compound ( $\alpha$ )-**5f** (19 mg, 0.0294 mmol, 58%) as a colorless oil.

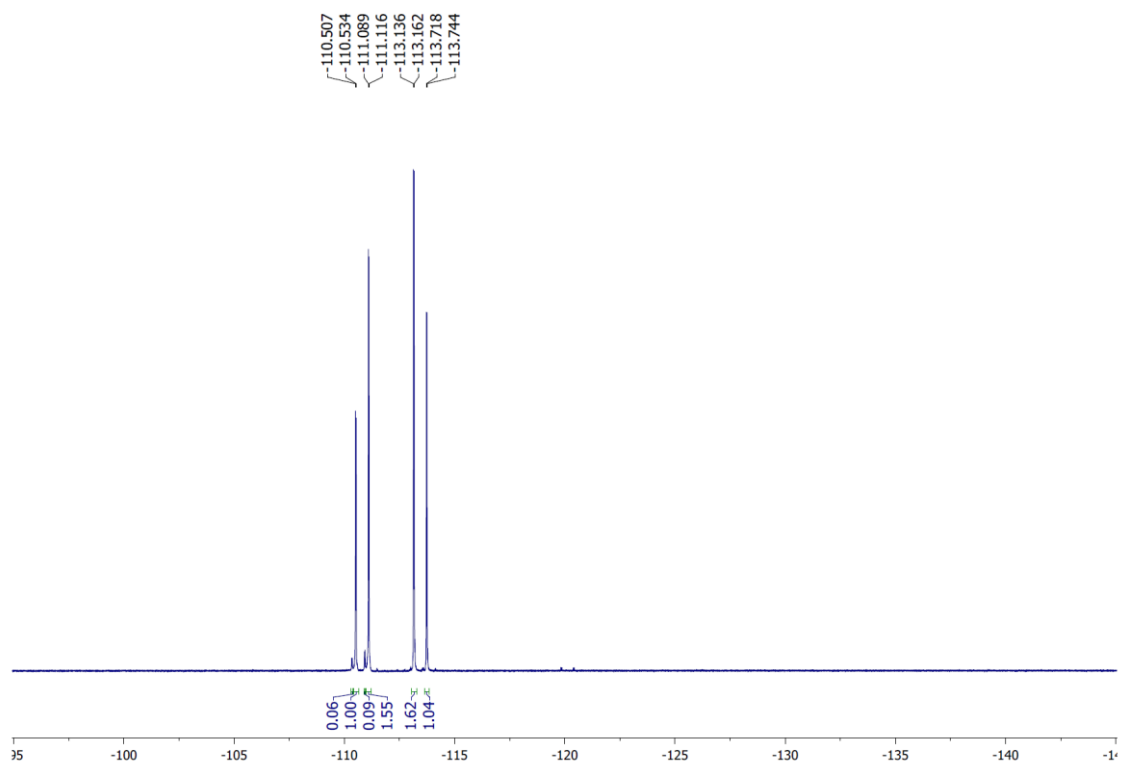
$[\alpha]_{20}^D$ : +2.9 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.38-7.36 (m, 2H, H<sup>arom</sup>), 7.33-7.26 (m, 12H, H<sup>arom</sup>), 7.26-7.19 (m, 6H, H<sup>arom</sup>), 4.77 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.74 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.64 (td, 1H,  $J_{1-2}$  = 5.2 Hz,  $J_{1-Fa}$  =  $J_{1-Fb}$  = 12.6 Hz, H-1), 4.46-4.41 (m, 6H, CH<sub>2</sub><sup>Bn</sup>), 4.25 (dd, 1H,  $J_{1-2}$  = 5.2 Hz,  $J_{2-3}$  = 3.4 Hz, H-2), 4.20 (m, 1H, H-3), 4.17 (dd, 1H,  $J_{3-4}$  = 4.0 Hz,  $J_{4-5}$  = 5.7 Hz, H-2), 4.15-4.01 (m, 2H, CH<sub>2</sub>CH<sub>3</sub>), 3.87 (td, 1H,  $J_{5-6a}$  = 4.0 Hz,  $J_{4-5}$  =  $J_{5-6b}$  = 5.7 Hz, H-5), 3.64 (ABX, 1H,  $J_{5-6a}$  = 4.0 Hz,  $J_{6a-6b}$  = 10.3 Hz, H-6a), 3.54 (ABX, 1H,  $J_{5-6b}$  = 5.7 Hz,  $J_{6a-6b}$  = 10.3 Hz, H-6b), 1.19 (t, 3H,  $J_{CH_2-CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.1 (t,  $J_{C-F}$  = 31.4 Hz, C<sub>q</sub>O<sub>2</sub>Et), 138.9 (C<sub>q</sub><sup>arom</sup>), 138.4 (C<sub>q</sub><sup>arom</sup>), 137.8 (C<sub>q</sub><sup>arom</sup>), 137.2 (C<sub>q</sub><sup>arom</sup>), 128.6-127.6 (CH<sup>arom</sup>), 113.2 (dd,  $J_{C-F}$  = 251.1 Hz,  $J_{C-F}$  = 258.3 Hz, CF<sub>2</sub>), 85.0 (C-4), 83.0 (C-2), 81.6 (C-3), 78.8 (t,  $J_{C-F}$  = 25.4 Hz, C-1), 77.9 (C-5), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 73.4 (CH<sub>2</sub><sup>Bn</sup>), 72.6 (CH<sub>2</sub><sup>Bn</sup>), 72.0 (CH<sub>2</sub><sup>Bn</sup>), 70.7 (C-6), 62.8 (CH<sub>2</sub>CH<sub>3</sub>), 13.9 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -110.8 (dd, 1F,  $J_{H1-Fa}$  = 12.6 Hz,  $J_{Fa-Fb}$  = 274.0 Hz, Fa), -113.5 (dd, 1F,  $J_{H1-Fb}$  = 12.6 Hz,  $J_{Fa-Fb}$  = 274.0 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for C<sub>38</sub>H<sub>41</sub>F<sub>2</sub>O<sub>7</sub> [M+H]<sup>+</sup>: calc. 647.2815; found: 647.2814. nOe: Correlation H-1 - H-2 and H-1 - H-4 observed.



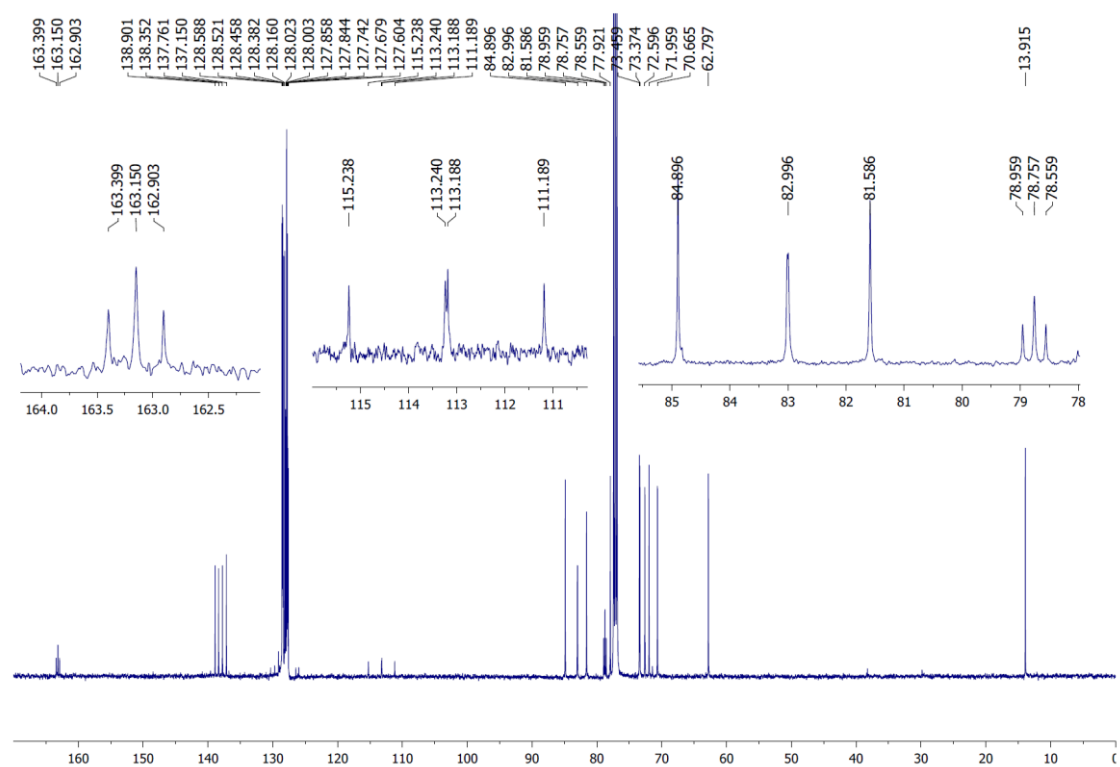
# <sup>1</sup>H NMR



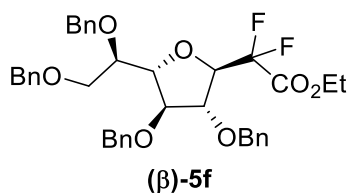
# <sup>19</sup>F NMR



# <sup>13</sup>C NMR



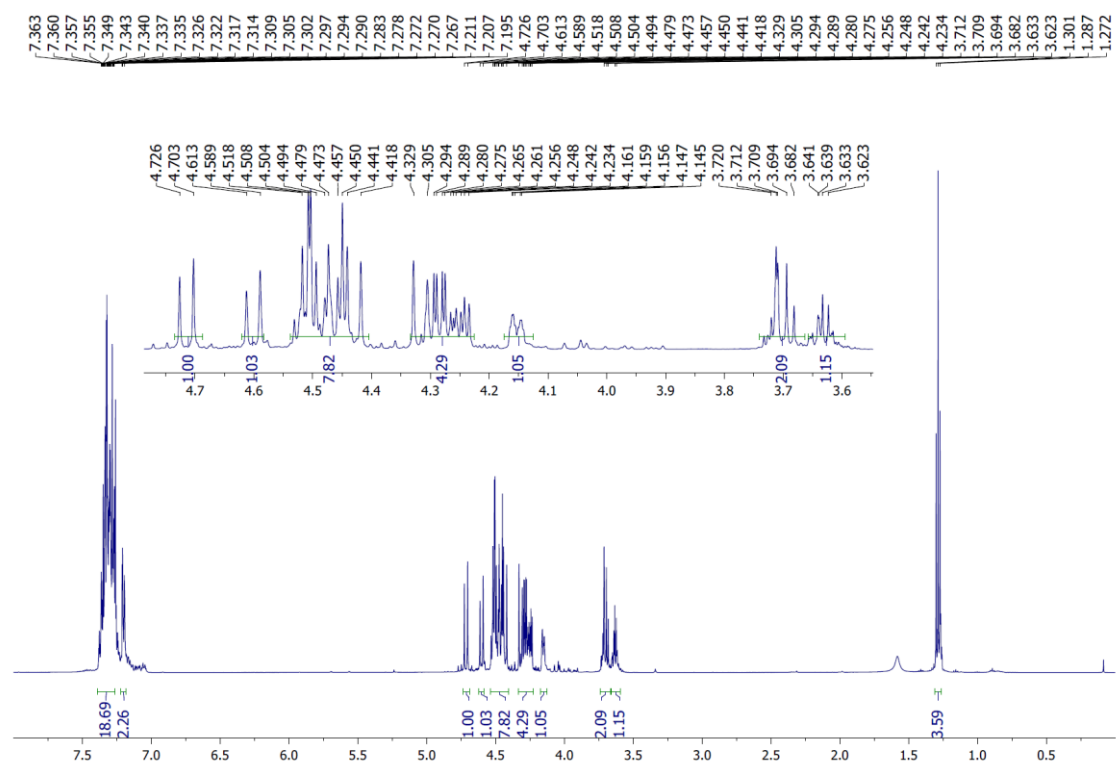
2,3,5,6-tetra-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate- $\alpha,\beta$ -D-galactofuranose (( $\beta$ )-**5f**).



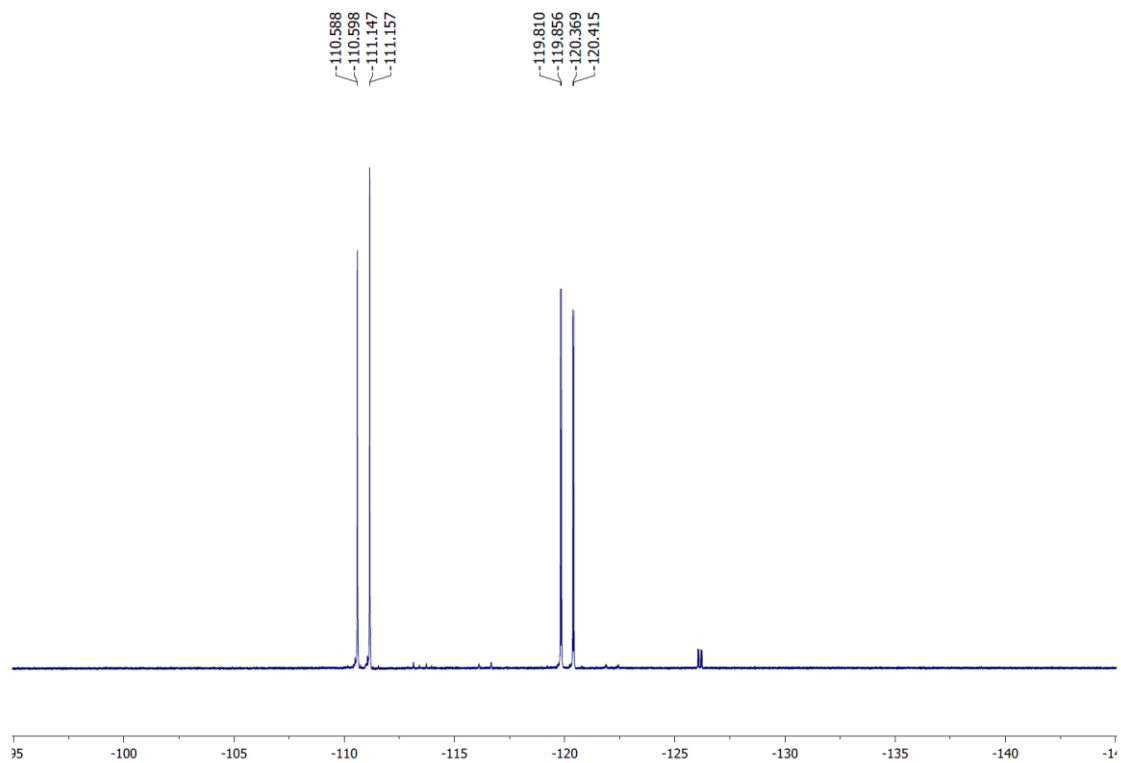
To a solution of alcohol (*S*)-**3f** (86 mg, 0.1139 mmol) in dry DCM (2 ml) under argon atmosphere was added DAST (60  $\mu$ l, 0.456 mmol, 4.0 equiv.) dropwise at 0°C. The reaction was allowed to warm from 0°C to r.t. and the reaction was stirred for 18h at r.t. The crude was then diluted with CH<sub>2</sub>Cl<sub>2</sub> and the organic phase was washed with H<sub>2</sub>O (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 95:5) afforded pure compound ( $\beta$ )-**5f** (40 mg, 0.062 mmol, 54%) as a colorless oil.

$[\alpha]_{20}^D$ : -13.3 (c 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.38-7.26 (m, 18H, H<sup>arom</sup>), 7.21-7.18 (m, 2H, H<sup>arom</sup>), 4.71 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.60 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.52-4.44 (m, 6H, CH<sub>2</sub><sup>Bn</sup>, H-1, H-2), 4.43 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.31 (AB, 1H,  $J_{A-B}$  = 12.0 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.30-4.25 (m, 2H, CH<sub>2</sub>CH<sub>3</sub>), 4.25-4.22 (dd, 1H,  $J$  = 4.0 Hz,  $J$  = 6.9 Hz, H-3), 4.15 (m, 1H, H-4), 3.72-3.68 (m, 2H, H-5, H-6a), 3.64-3.61 (m, 1H, H-6b), 1.28 (t, 3H,  $J_{CH_2-CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.0 (dd,  $J_{C-F}$  = 30.8 Hz,  $J_{C-F}$  = 32.0 Hz, C<sub>q</sub>O<sub>2</sub>Et), 138.3 (2 C<sub>q</sub><sup>arom</sup>), 137.8 (C<sub>q</sub><sup>arom</sup>), 137.5 (C<sub>q</sub><sup>arom</sup>), 128.6-127.7 (CH<sup>arom</sup>), 113.9 (dd,  $J_{C-F}$  = 252.9 Hz,  $J_{C-F}$  = 260.2 Hz, CF<sub>2</sub>), 84.1 (C-3), 83.8 (C-2), 83.2 (C-4), 82.2 (dd,  $J_{C-F}$  = 23.5 Hz,  $J_{C-F}$  = 32.0 Hz, C-1), 76.4 (C-5), 73.7 (CH<sub>2</sub><sup>Bn</sup>), 73.3 (CH<sub>2</sub><sup>Bn</sup>), 72.3 (2 CH<sub>2</sub><sup>Bn</sup>), 70.8 (C-6), 63.2 (CH<sub>2</sub>CH<sub>3</sub>), 14.0 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -110.9 (dd, 1F,  $J_{H-Fa}$  = 4.5 Hz,  $J_{Fa-Fb}$  = 263.1 Hz, Fa), -120.1 (dd, 1F,  $J_{H-Fb}$  = 22.0 Hz,  $J_{Fa-Fb}$  = 263.1 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>):  $m/z$  calculated for C<sub>38</sub>H<sub>40</sub>F<sub>2</sub>O<sub>7</sub>Na [M+Na]<sup>+</sup>: calc. 669.2634; found: 669.2623. nOe: Correlations were inconclusive.

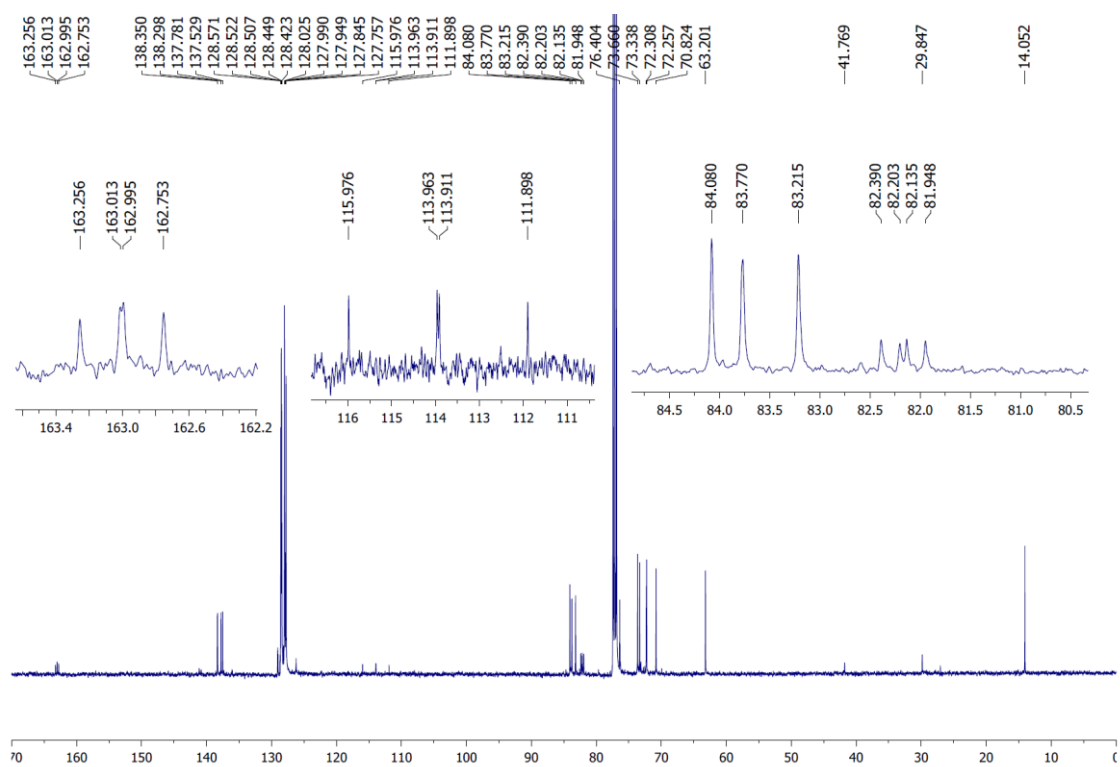
# <sup>1</sup>H NMR



# <sup>19</sup>F NMR

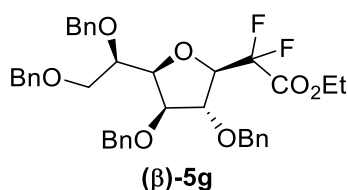


# <sup>13</sup>C NMR



## D-Glucose

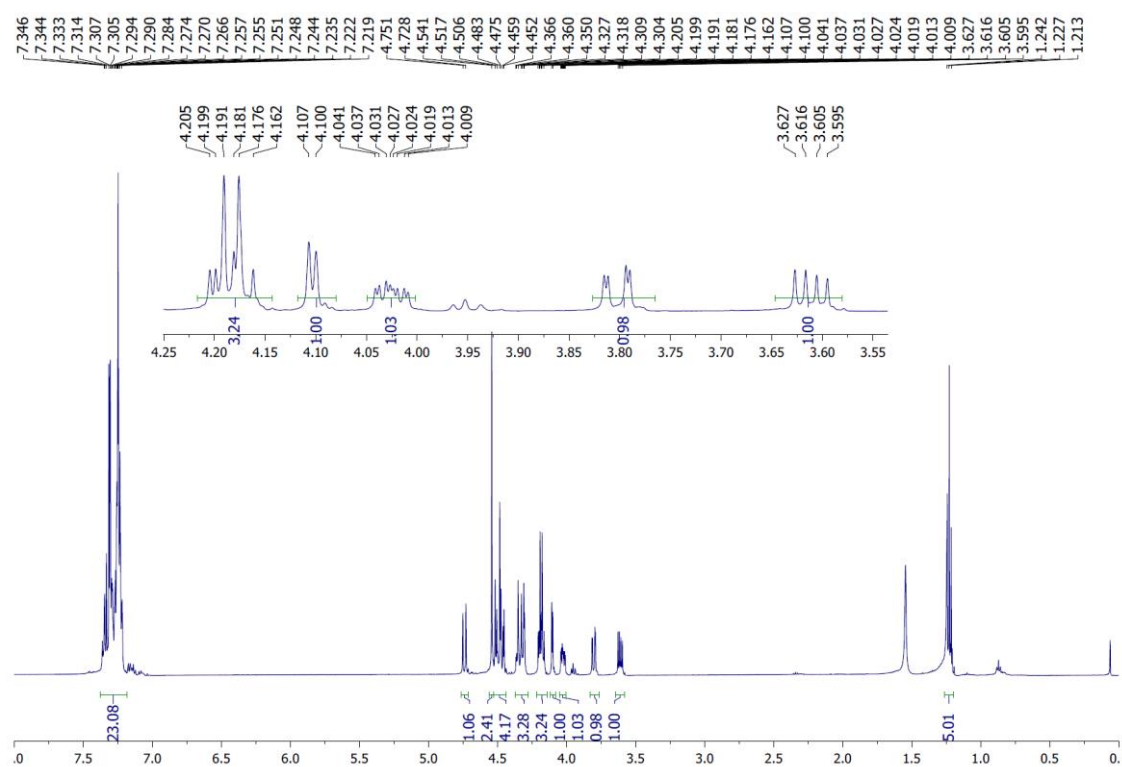
2,3,5,6-tetra-*O*-benzyl-1-deoxy-1,1-difluoroethyl acetate- $\alpha,\beta$ -D-glucofuranose (( $\beta$ )-**5g**).



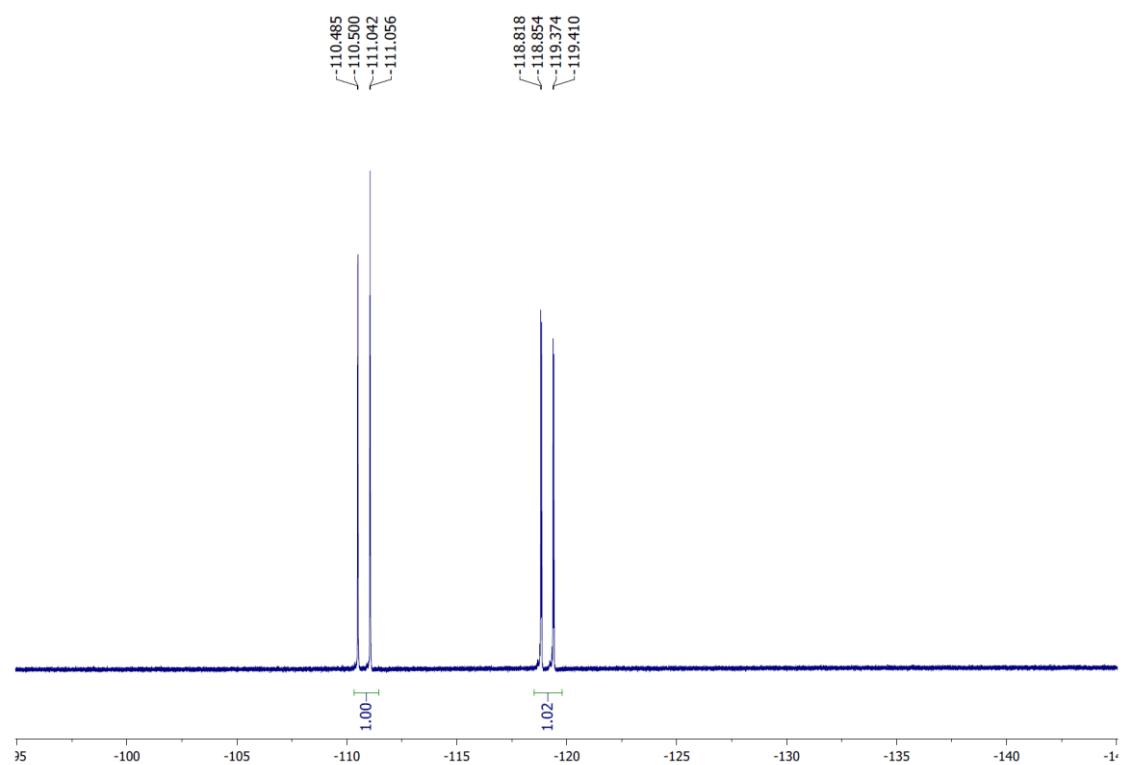
To a solution of alcohol (*S*)-**3g** (60.5 mg, 0.0801 mmol) in dry DCM (1.5 ml) under argon atmosphere was added DAST (42  $\mu$ l, 0.32 mmol, 4.0 equiv.) dropwise at 0°C. The reaction was allowed to warm from 0°C to r.t. and the reaction was stirred for 18h at r.t. The crude was then diluted with CH<sub>2</sub>Cl<sub>2</sub> and the organic phase was washed with H<sub>2</sub>O (3 times) and brine (3 times), dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Purification by chromatography on silica gel (Cy/EtOAc 96:4) afforded pure compound ( $\beta$ )-**5g** (45 mg, 0.0696 mmol, 87%) as a colorless oil.

$[\alpha]_{20}^D$ : -10.9 (c 0.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.37-7.23 (m, 20H, H<sup>arom</sup>), 4.75 (AB, 1H,  $J_{A-B}$  = 11.5 Hz, CH<sub>2</sub><sup>Bn</sup>), 4.56-4.53 (m, 3H, CH<sub>2</sub><sup>Bn</sup>), 4.52-4.46 (m, 3H, CH<sub>2</sub><sup>Bn</sup>), 4.38-4.31 (m, 3H, H-1, H-3, CH<sub>2</sub><sup>Bn</sup>), 4.20 (q, 2H,  $J_{CH_2-CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.22-4.17 (m, 1H, H-4), 4.12 (d, 1H,  $J$  = 3.4 Hz, H-2), 4.00 (ddd, 1H,  $J_{5-6a}$  = 1.7 Hz,  $J_{5-6b}$  = 5.2 Hz,  $J_{4-5}$  = 8.6 Hz, H-5), 3.81 (ABX, 1H,  $J_{5-6a}$  = 1.7 Hz,  $J_{6a-6b}$  = 10.9 Hz, H-6a), 3.62 (ABX, 1H,  $J_{5-6b}$  = 5.2 Hz,  $J_{6a-6b}$  = 10.9 Hz, H-6b), 1.24 (t, 3H,  $J_{CH_2-CH_3}$  = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  = 163.0 (dd,  $J_{C-F}$  = 30.2 Hz,  $J_{C-F}$  = 32.6 Hz, C<sub>q</sub>O<sub>2</sub>Et), 138.9 (C<sub>q</sub><sup>arom</sup>), 138.7 (C<sub>q</sub><sup>arom</sup>), 137.6 (C<sub>q</sub><sup>arom</sup>), 137.3 (C<sub>q</sub><sup>arom</sup>), 128.7-127.5 (CH<sup>arom</sup>), 113.1 (dd,  $J_{C-F}$  = 249.9 Hz,  $J_{C-F}$  = 257.1 Hz, CF<sub>2</sub>), 84.5 (dd,  $J_{C-F}$  = 27.0 Hz,  $J_{C-F}$  = 31.7 Hz, C-1), 82.1 (C-2), 81.4 (C-4), 81.3 (C-3), 75.6 (C-5), 73.5 (CH<sub>2</sub><sup>Bn</sup>), 72.7 (CH<sub>2</sub><sup>Bn</sup>), 72.0 (CH<sub>2</sub><sup>Bn</sup>), 71.6 (CH<sub>2</sub><sup>Bn</sup>), 70.6 (C-6), 63.0 (CH<sub>2</sub>CH<sub>3</sub>), 14.1 (CH<sub>2</sub>CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  = -110.8 (dd, 1F,  $J_{H-Fa}$  = 7.2 Hz,  $J_{Fa-Fb}$  = 262.0 Hz, Fa), -119.1 (dd, 1F,  $J_{H-Fb}$  = 17.1 Hz,  $J_{Fa-Fb}$  = 262.0 Hz, Fb) ppm. HRMS (ESI<sup>+</sup>): m/z calculated for C<sub>38</sub>H<sub>41</sub>F<sub>2</sub>O<sub>7</sub> [M+H]<sup>+</sup>: calc. 647.2815; found: 647.2809. nOe: Correlation between H-1 and H-3 observed.

# <sup>1</sup>H NMR



# <sup>19</sup>F NMR



# <sup>13</sup>C NMR

