Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Unexpected furanose / pyranose equilibration of N-glycosyl sulfonamides, sulfamides and sulfamates

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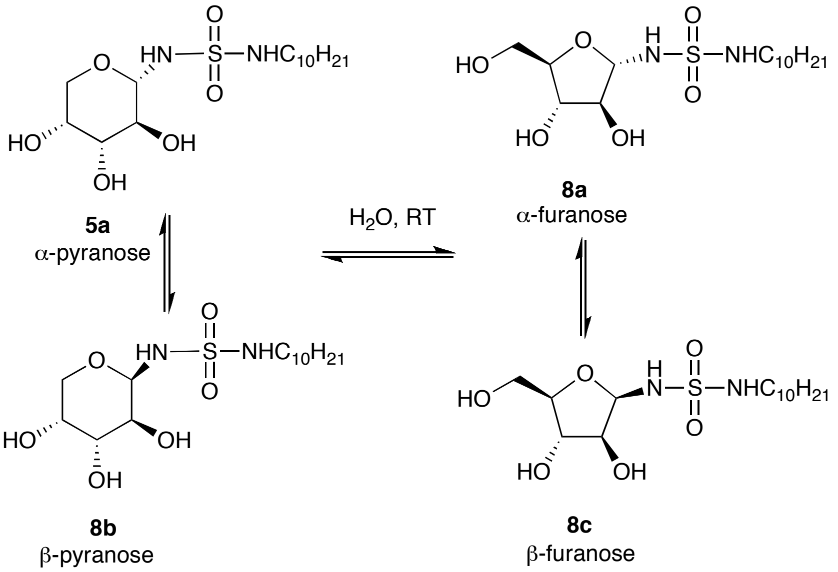
Equilibration Experiments



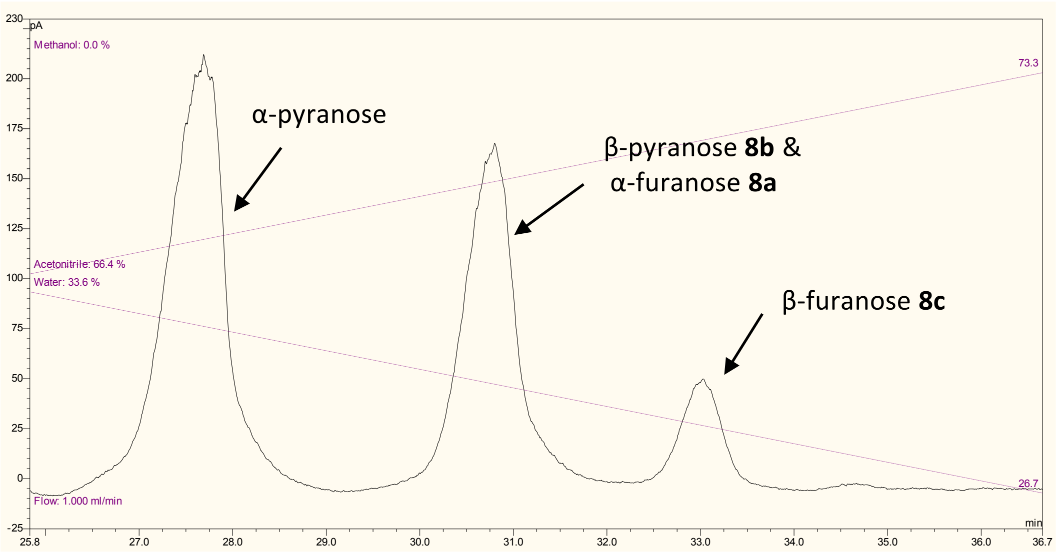


Fig. S1 RP-HPLC trace of *N*-(decyl)-*N'*-(α,β-D-arabinopyranosyl)sulfamide **5a/8b** and *N*-(decyl)-*N'*-(α,β-D-arabinofuranosyl)sulfamides **8a/8b** equilibrated in water.

Experimental Procedure

The debenzylated glycosyl sulfamide **5a** (10 mg, 0.03 mmol) was dissolved in methanol (1 mL), and purified by RP-HPLC (Luna C-18 column (Phenomenex); eluent: A (0.05 % TFA in H_2O) and B MeCN; gradient: the sample was run at 1 mL/min with a gradient of 50-85 % B; column oven: 15 °C; detection: CAD). Each of the three peaks **(Fig. S1)** were separated and immediately frozen. After freeze drying, the samples (1 mg, 0.003 mmol) were then dissolved in a mixture of H_2O and MeOH (4:1), and the equilibration of the three samples was analysed by RP-HPLC (Luna C-18 column (Phenomenex); eluent: A (0.05 % TFA in H_2O) and B MeCN; gradient: the sample was run at 1 mL/min with a gradient of 50-85 % B; column oven: 15 °C; detection: CAD) over a 48 hour time period. The results are shown in **Figures S2-4.**

*N-(*Decyl)-*N'*-(α-D-arabinofuranosyl)sulfamide 8a

δ_H (400 MHz, CD_3CN) 0.91 (3H, t, *J* 6.7 Hz, $C\underline{H}_3$), 1.25-1.40 (14H, m, $C\underline{H}_2$), 1.45-1.56 (2H, m, $NHCH_2C\underline{H}_2$), 2.93-3.00 (2H, t, $C\underline{H}_2NH$), 3.60-3.65 (2H, m, H-5, H-5'), 3.76 (1H, at, *J* 2.8 Hz, H-3), 3.89-3.95 (1H, m, H-2), 3.97-3.99 (1H, m, H-4), 4.95 (1H, dd, $J_{1,NH}$ 10.6 Hz, $J_{1,2}$ 2.7 Hz, H-1), 5.00 (1H, t, *J* 4.6 Hz, $N\underline{H}CH_2$), 5.98 (1H, d, $J_{1,NH}$ 11.2 Hz, NH-1).

*N-(*Decyl)-*N'*-(β-D-arabinopyranosyl)sulfamide 8b

δ_H (400 MHz, CD_3CN) 0.91 (3H, t, *J* 6.7 Hz, $C\underline{H}_3$), 1.25-1.40 (14H, m, $C\underline{H}_2$), 1.45-1.56 (2H, m, $NHCH_2C\underline{H}_2$), 2.93-3.00 (2H, t, $C\underline{H}_2NH$), 3.53 (1H, dd, $J_{5,5'}$ 11.0 Hz, $J_{4,5'}$ 9.0 Hz, H-5), 3.66 (1H, dd, $J_{5,5'}$ 11.6 Hz, $J_{4,5'}$ 4.3 Hz, H-5'), 3.70 (1H, dd, $J_{2,3}$ 5.5 Hz, $J_{1,2}$ 2.3 Hz H-2), 3.78-3.80 (1H, m, H-3), 3.86-3.89 (1H, m, H-4), 4.84 (1H, d, $J_{1,NH}$ 9.0 Hz, H-1), 5.06 (1H, t, *J* 4.6 Hz, $N\underline{H}CH_2$), 5.73 (1H, d, $J_{1,NH}$ 9.8 Hz, NH-1); δ_C (100 MHz, CD_3CN) 13.4 (q, CH_3), 22.4, 26.5, 28.9, 29.0, 29.3, 31.6 (6 x t, 8 x CH_2), 42.9 (t, $\underline{C}H_2NH$), 63.9 (t, C-5), 64.1 (d, C-4), 69.9 (d, C-2), 70.0 (d, C-3), 80.2 (d, C-1).

*N-(*Decyl)-*N'*-(β-D-arabinofuranosyl)sulfamide 8c

δ_H (400 MHz, CD_3CN) 0.91 (3H, t, *J* 6.7 Hz, $C\underline{H}_3$), 1.25-1.40 (14H, m, $C\underline{H}_2$), 1.45-1.56 (2H, m, $NHCH_2C\underline{H}_2$), 2.93-3.00 (2H, t, $C\underline{H}_2NH$), 3.60-3.65 (2H, m, H-5, H-5'), 3.68 (1H, at, *J* 2.8 Hz, H-3), 3.84 (1H, at, *J* 2.9 Hz, H-2), 4.02 (1H, aq, *J* 4,7 Hz, H-4), 5.13 (1H, d, $J_{1,2}$ 3.7 Hz, H-1), 5.00 (1H, t, *J* 4.6 Hz, $N\underline{H}CH_2$).

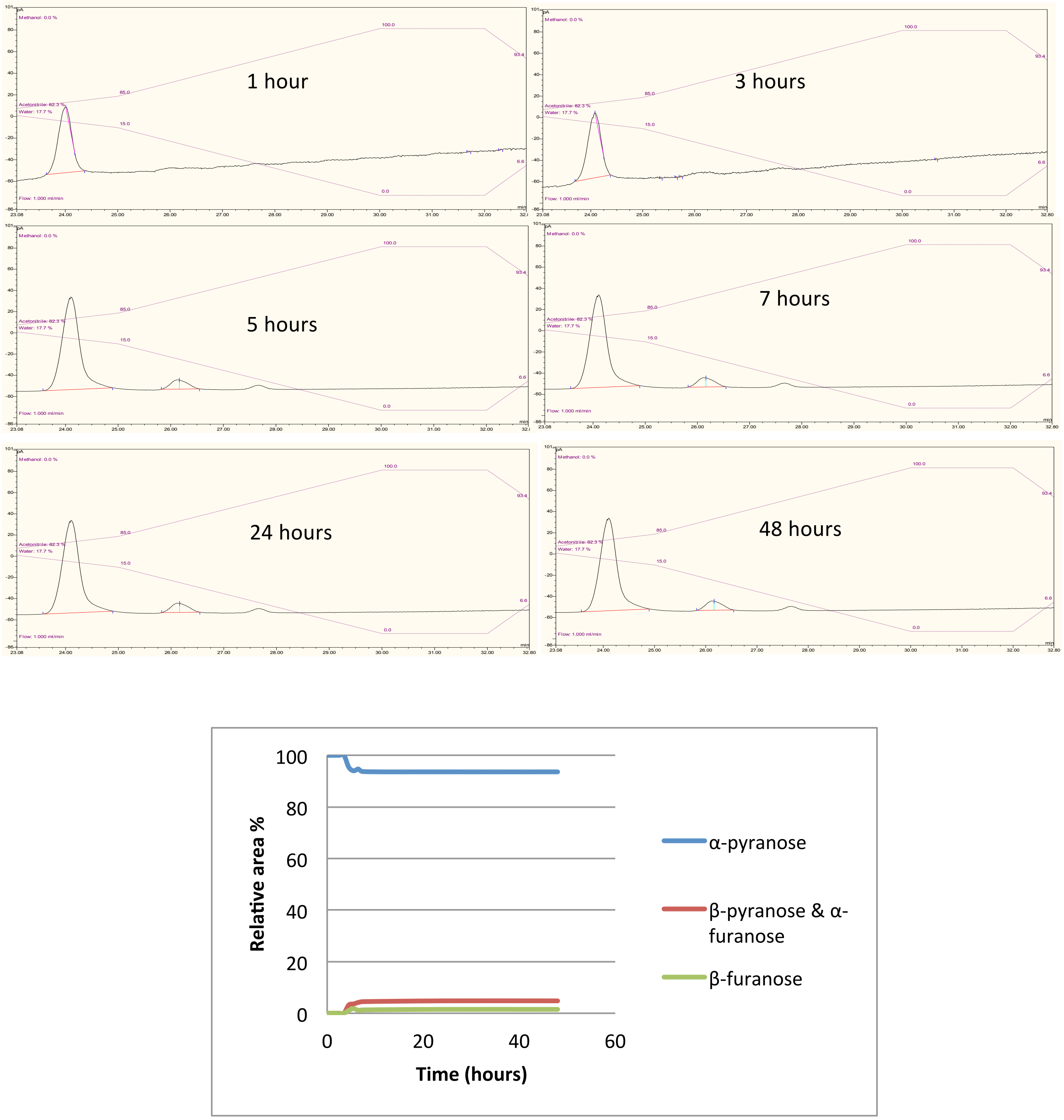


Fig. S2 RP-HPLC traces and time-dependence of equilibration of *N-(*decyl)-*N'*-(α-D-arabinopyranosyl)sulfamide **5a** in water.

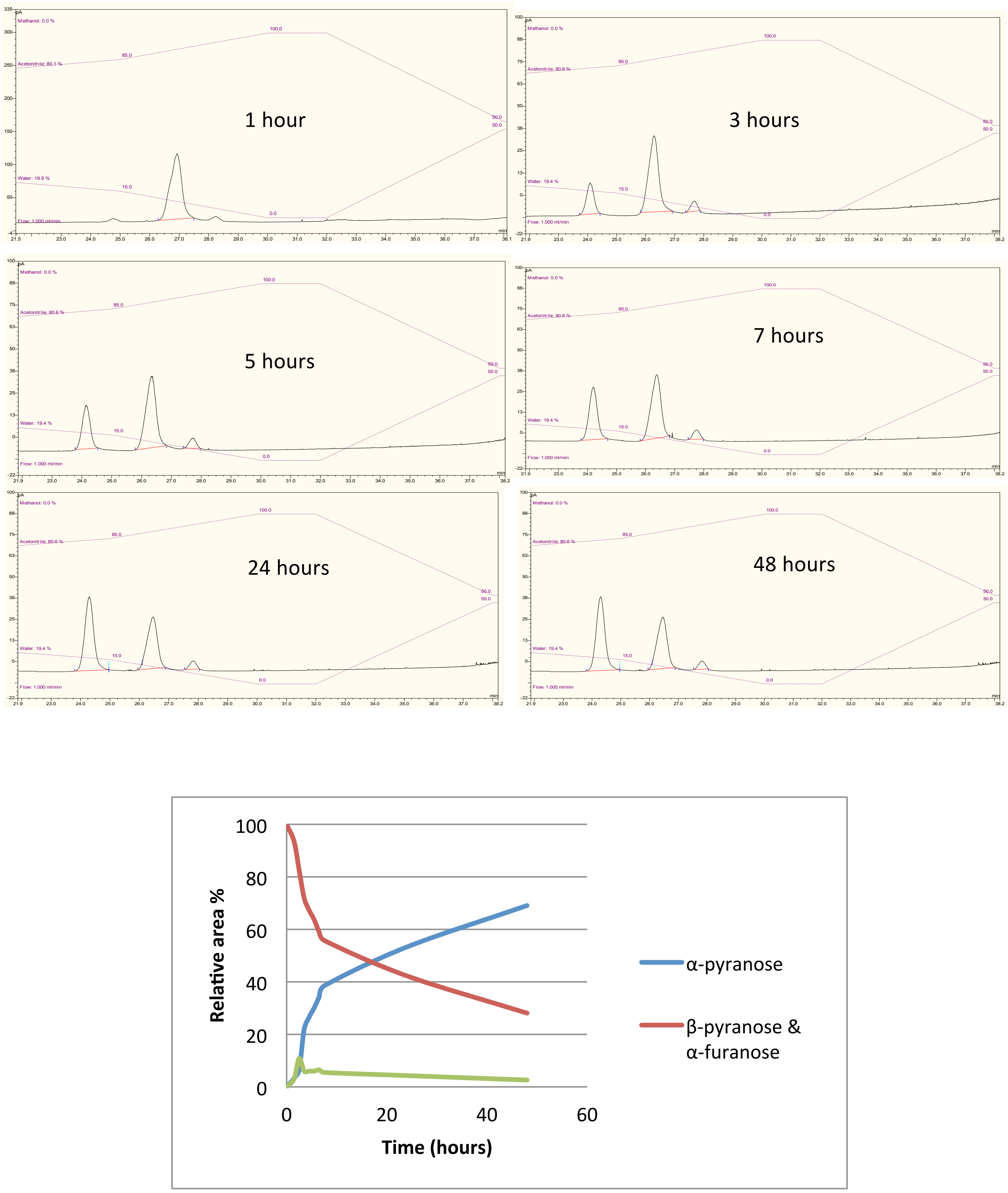


Fig. S3 RP-HPLC traces and time-dependence of equilibration of *N*-(decyl)-*N'*-(β-D-arabinopyranosyl)sulfamide **8b** and *N*-(decyl)-*N'*-(α-D-arabinofuranosyl)sulfamide **8a** in water.

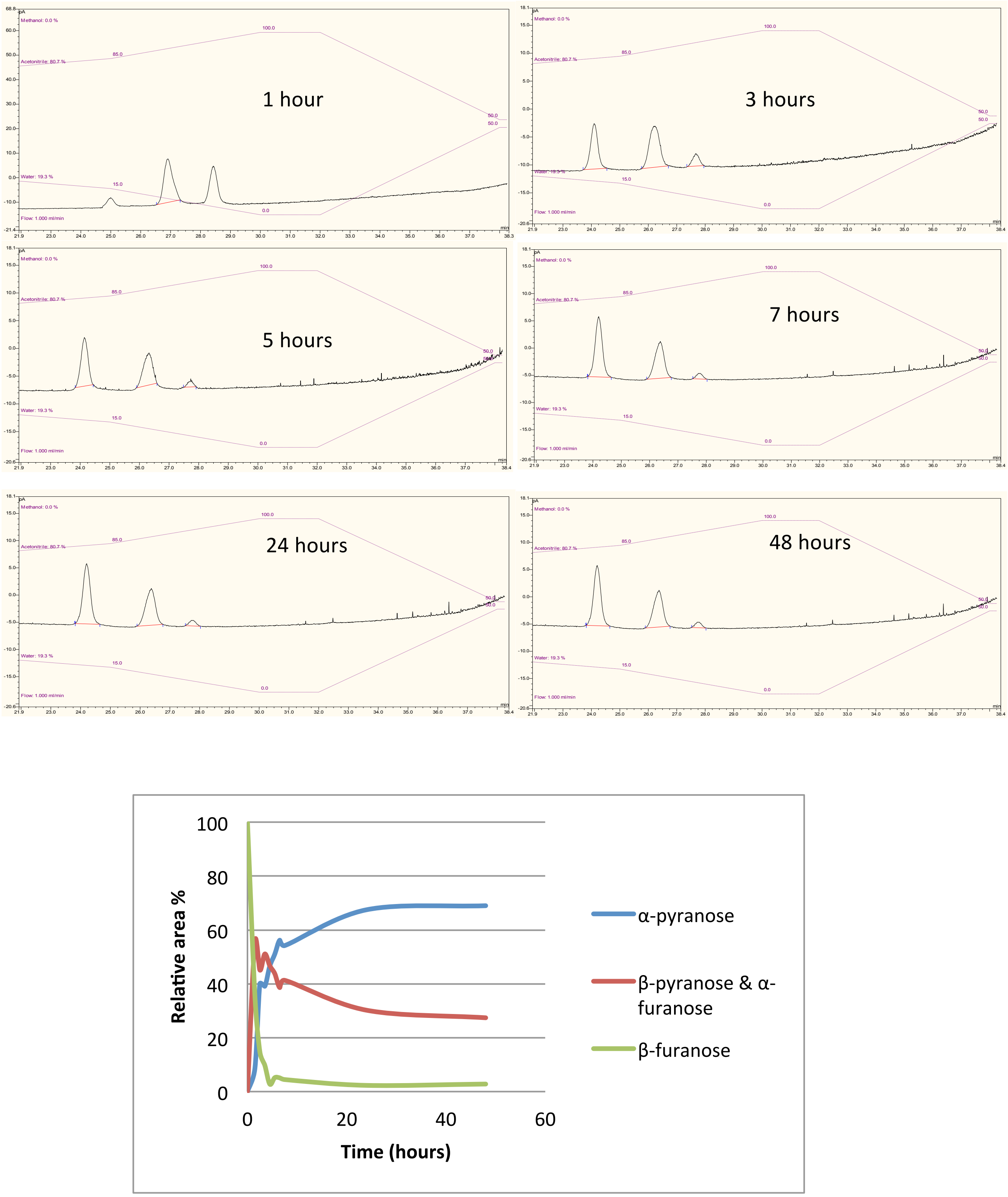


Fig. S4 RP-HPLC traces and time-dependence of equilibration of *N*-(decyl)-N'-(β-D-arabinofuranosyl)sulfamide **8c** in water.

Experimental procedure for attempted equilibration of 7.

The purified β-furanose trifluoromethanesulfonamide **7** (1 mg, 0.003 mmol) was dissolved in a mixture of H_2O and MeOH (4:1), and equilibration was analysed by RP-HPLC (Luna C-18 column (Phenomenex); eluent: A (0.05 % TFA in H_2O) and B MeCN; gradient: the sample was run at 1 mL/min with a gradient of 50-85 % B; column oven: 15 °C; detection: CAD) over a 48 hour time period. No mutarotation or equilibration to the pyranose form was observed. The results are shown in **Figure S5.**

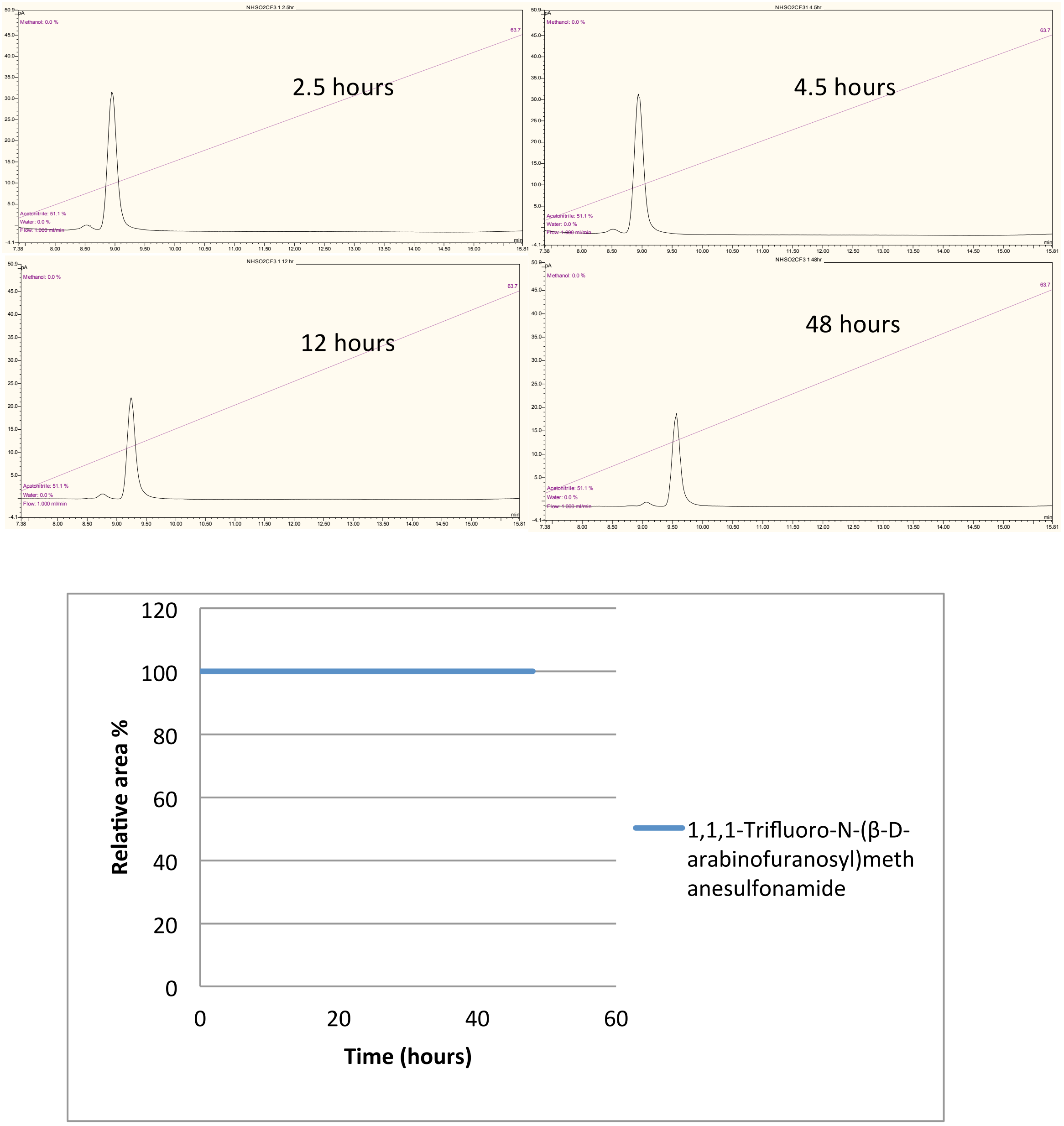
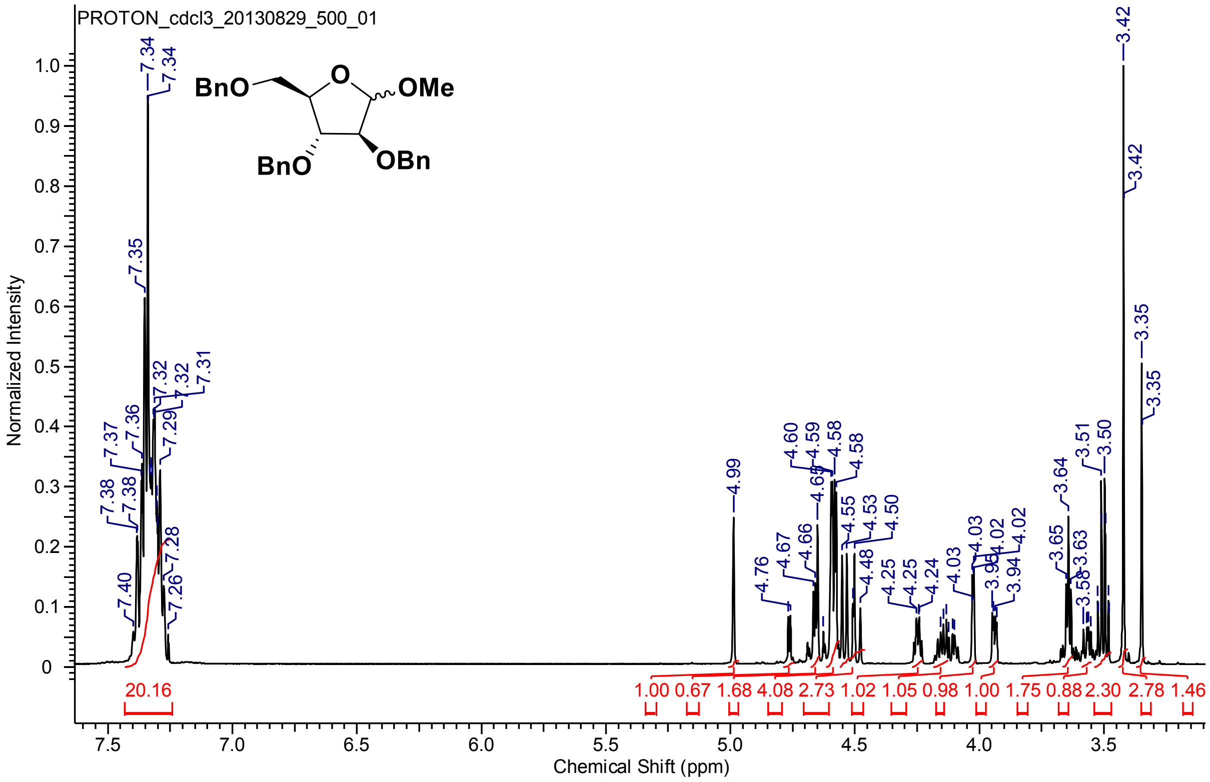
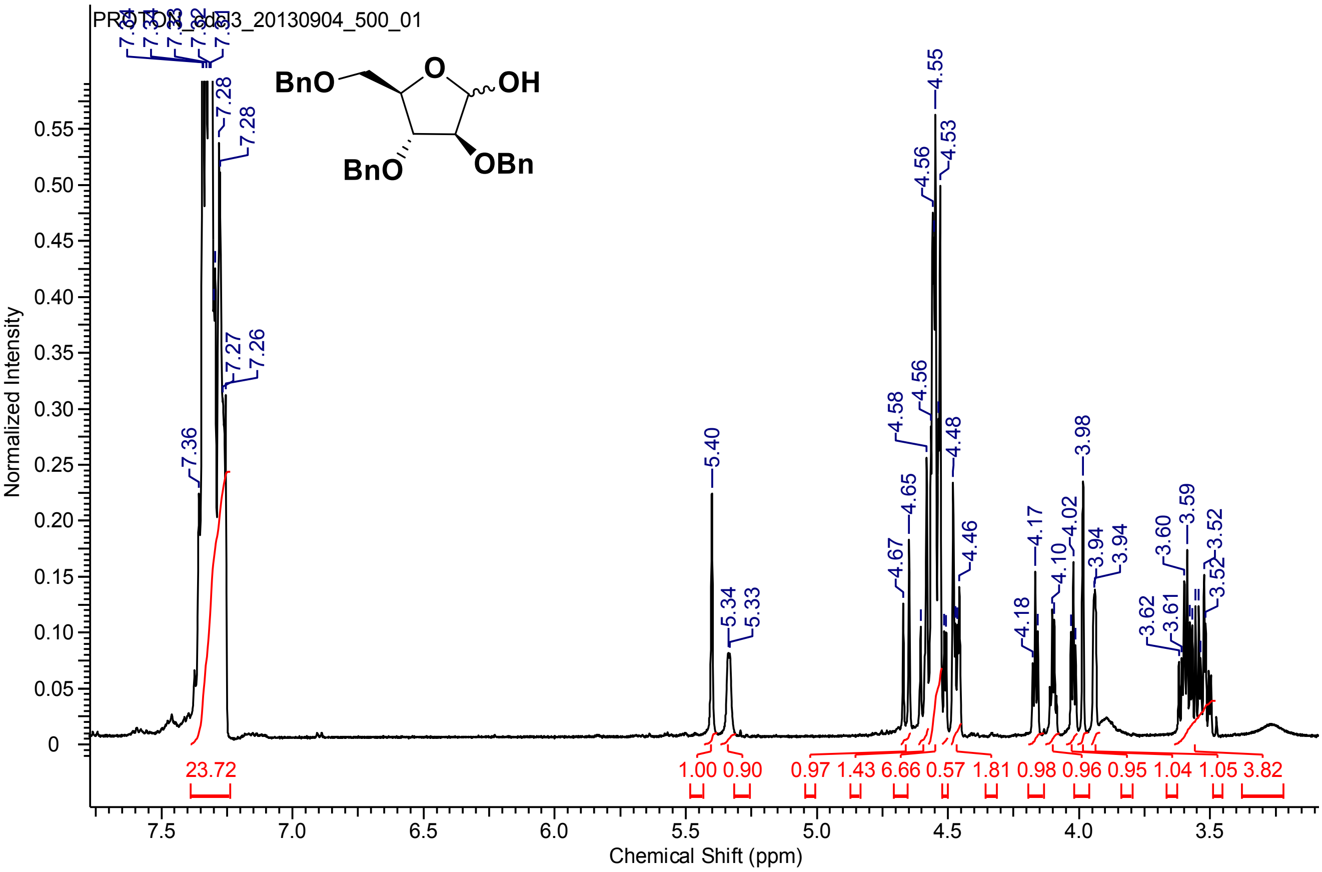


Fig. S5 RP-HPLC traces and time-dependence of equilibration of 1,1,1-trifluoro-*N*-(β-D-arabinofuranosyl)methanesulfonamide **7** in water.

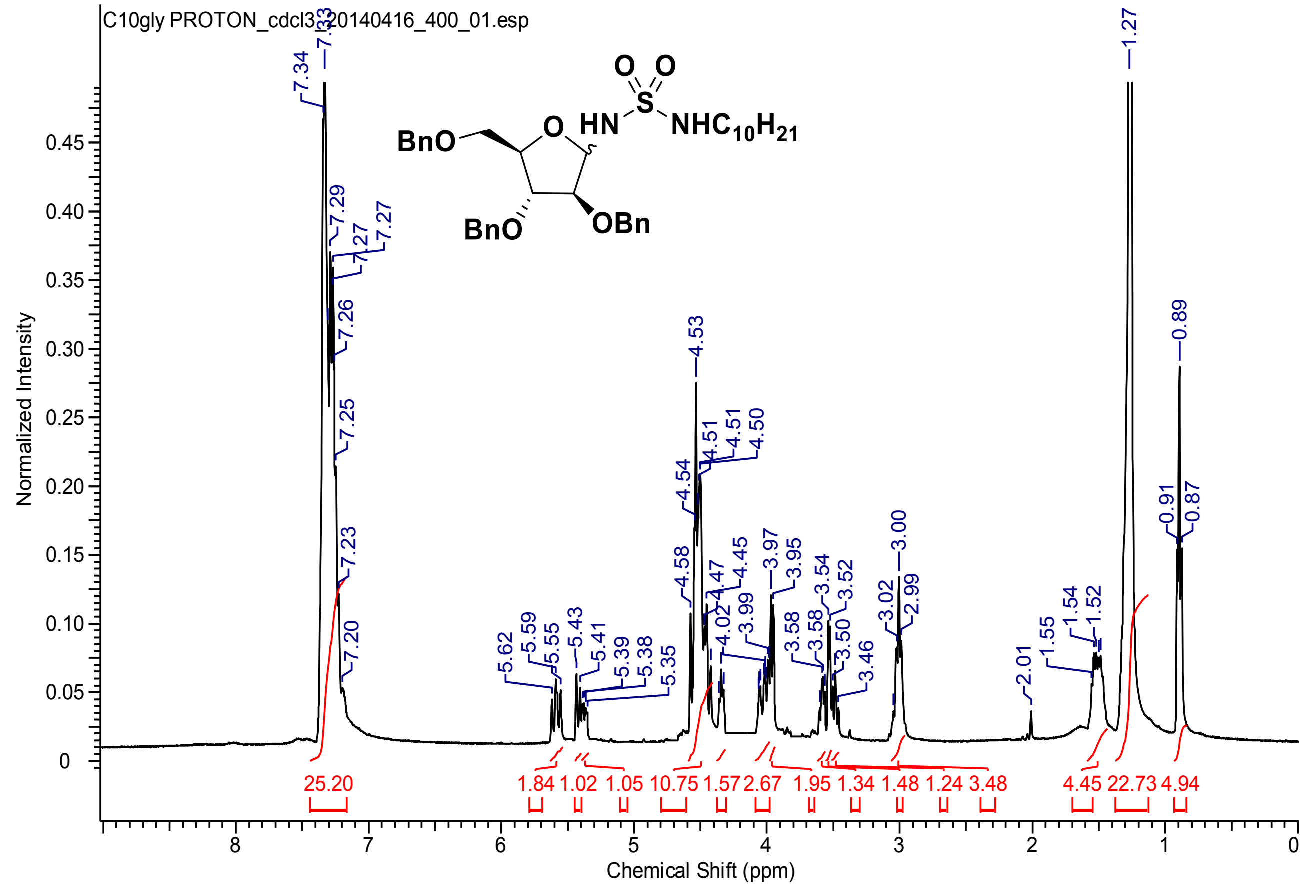
Methyl 2,3,5-tri-*O*-benzyl-α,β-D-arabinofuranoside

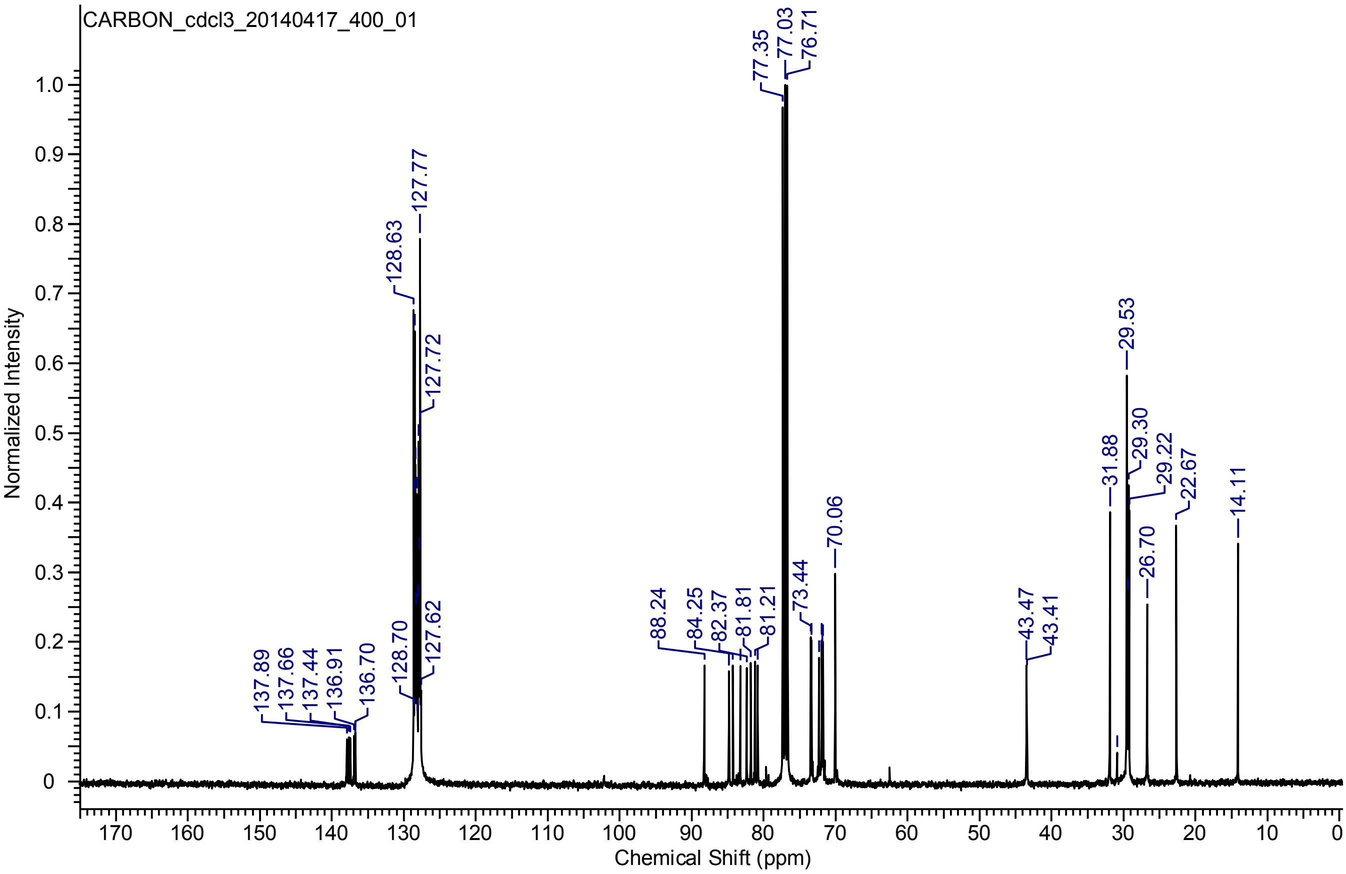


2,3,5-Tri-*O*-benzyl-α,β-D-arabinofuranose 3

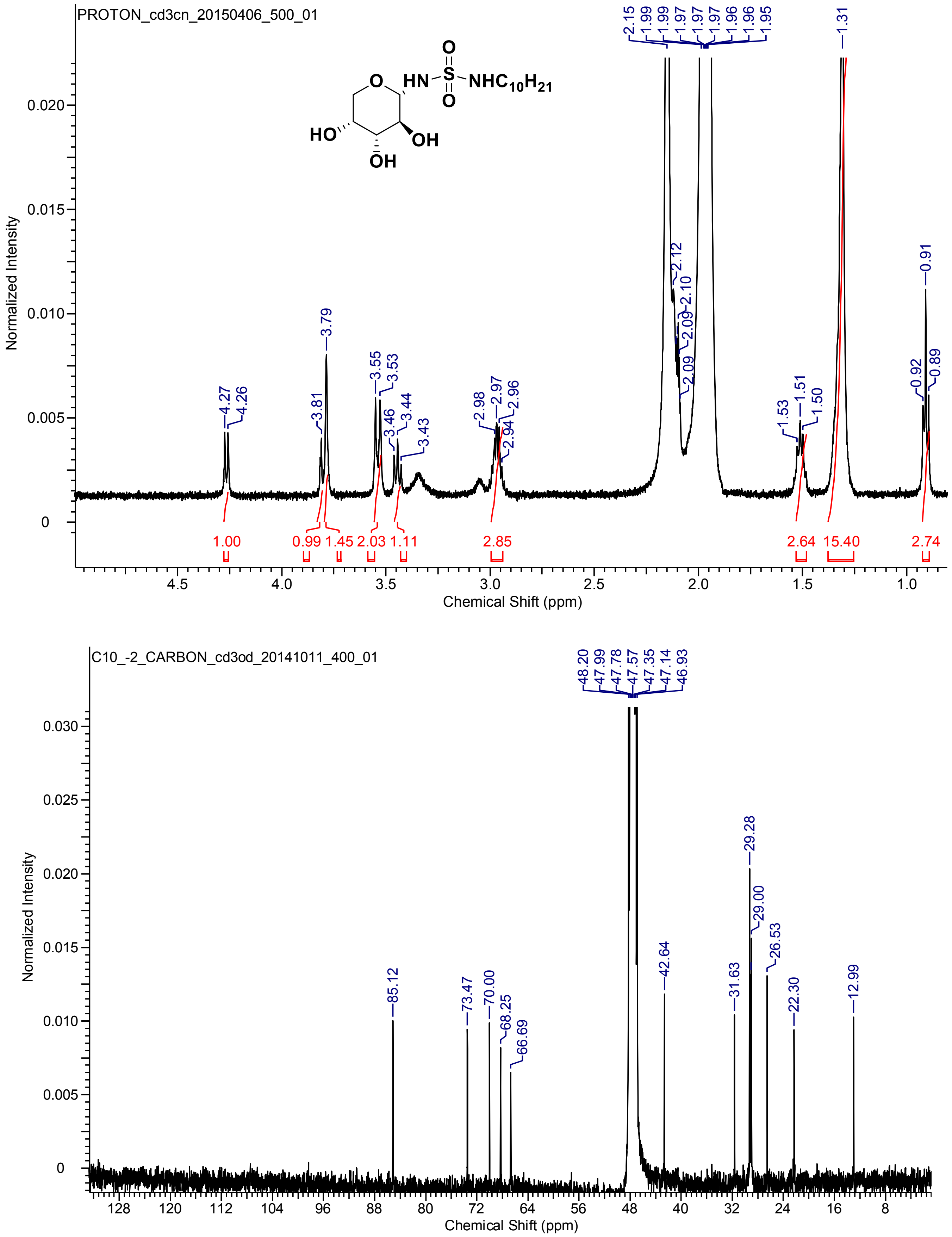


N-(Decyl)-*N*’-(2,3,5-tri-*O*-benzyl-α,β-D-arabinofuranosyl)sulfamide 4a

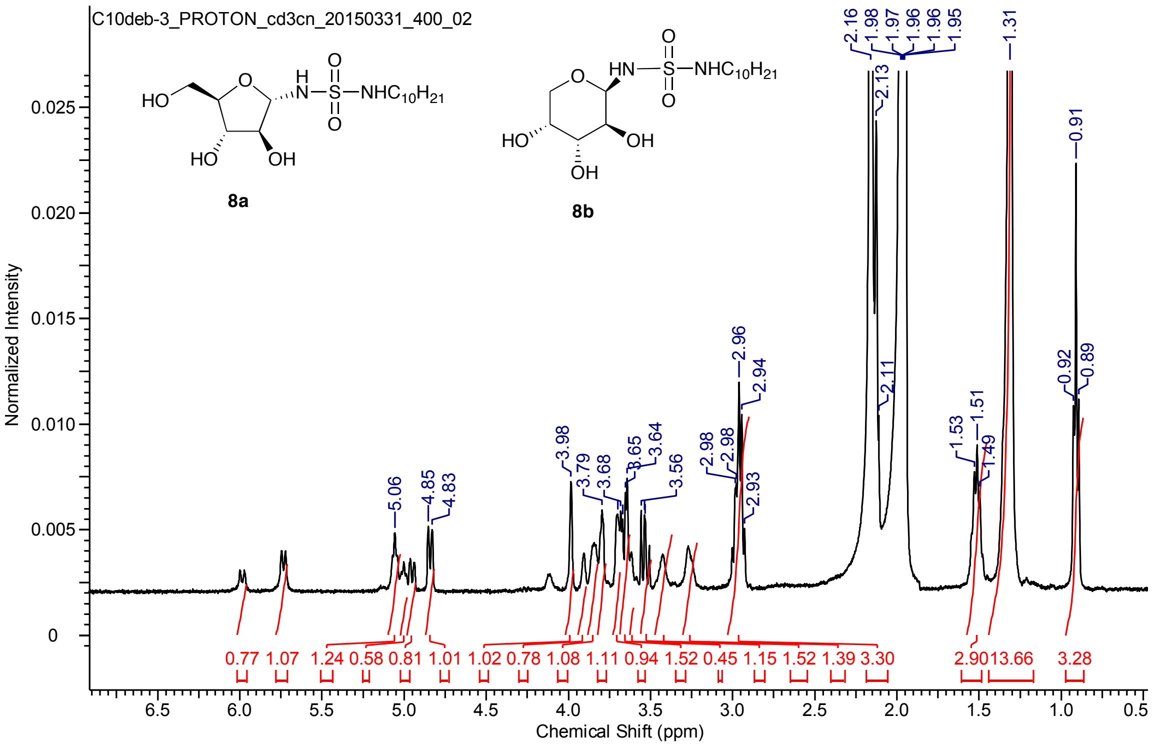


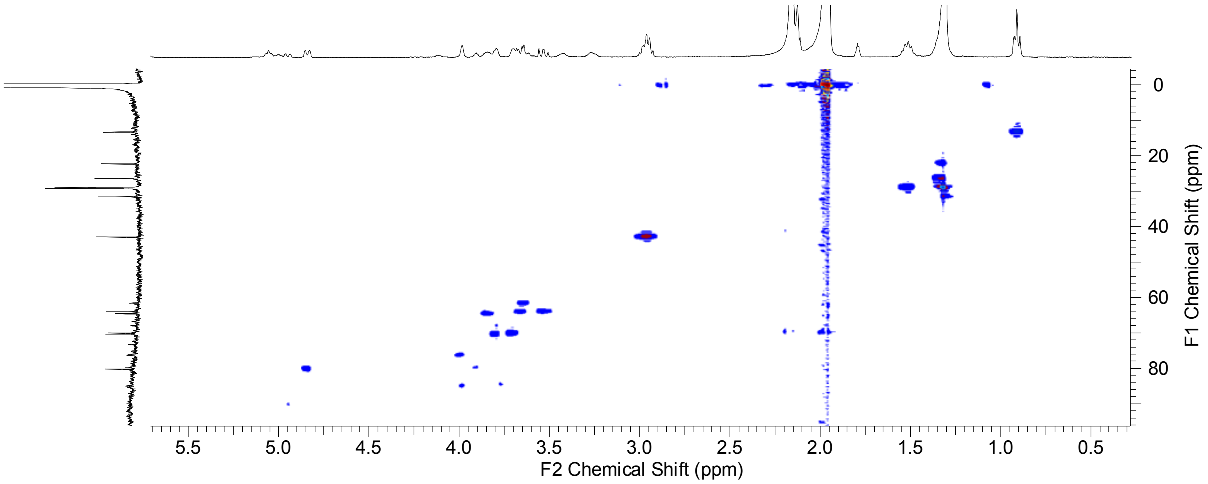


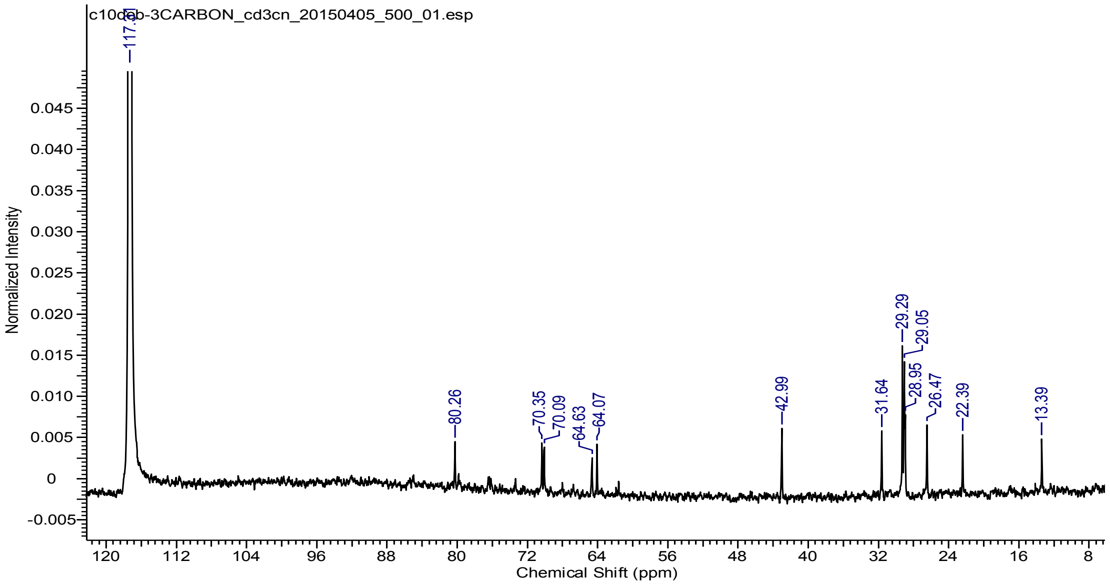
N-(Decyl)-*N’*-(α-D-arabinopyranosyl)sulfamide 5a



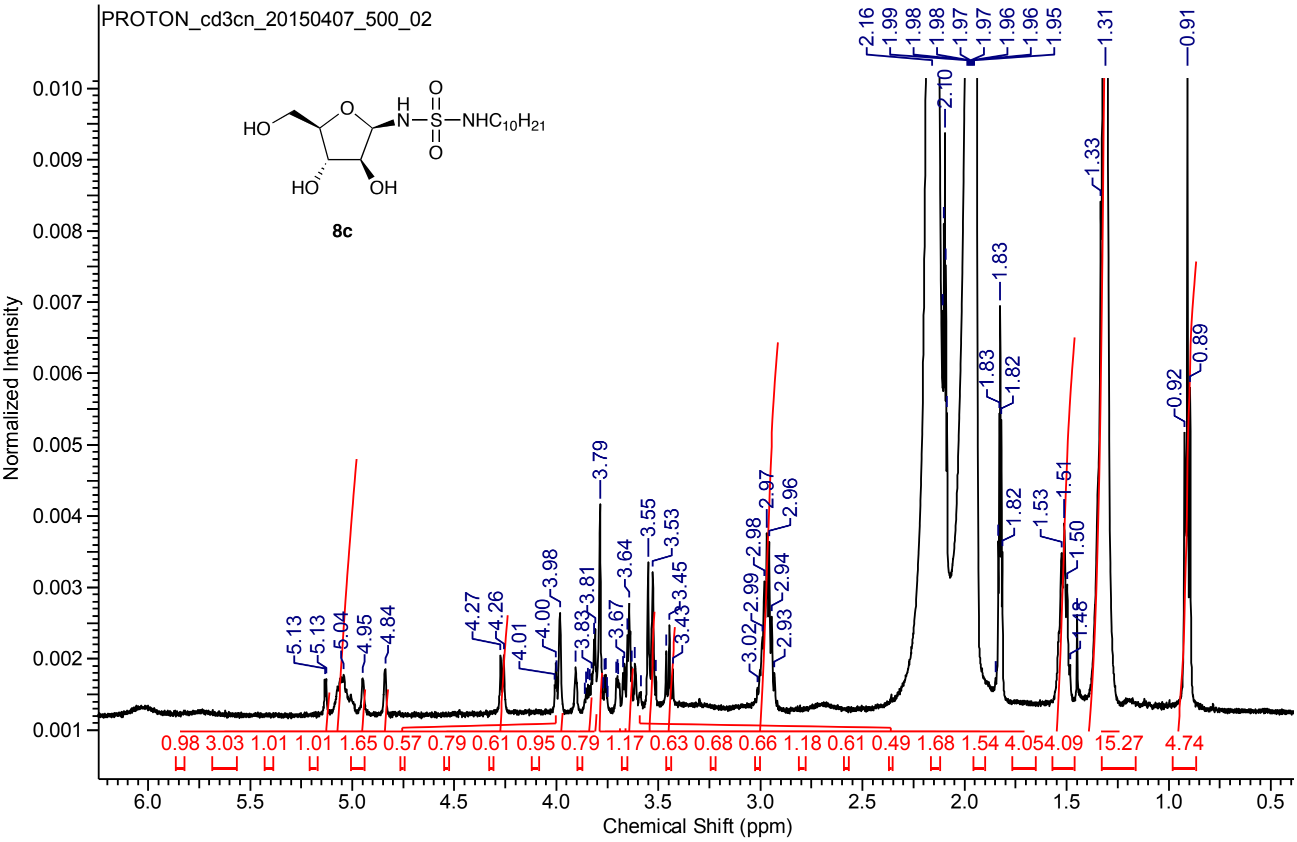
*N-(*Decyl)-*N’*-(β-D-arabinopyranosyl)sulfamide 8b and *N-(*decyl)-*N’*-(α-D-arabinofuranosyl)sulfamide 8a



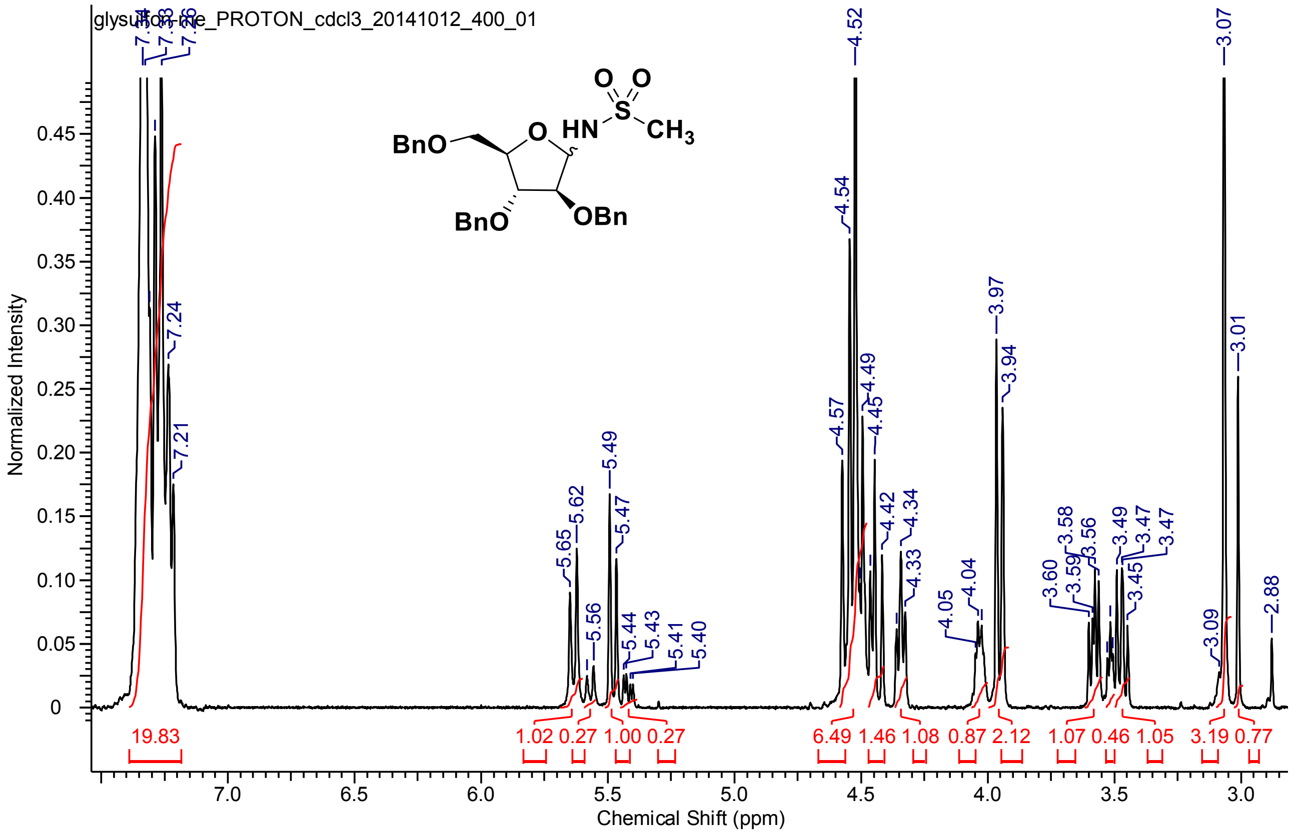


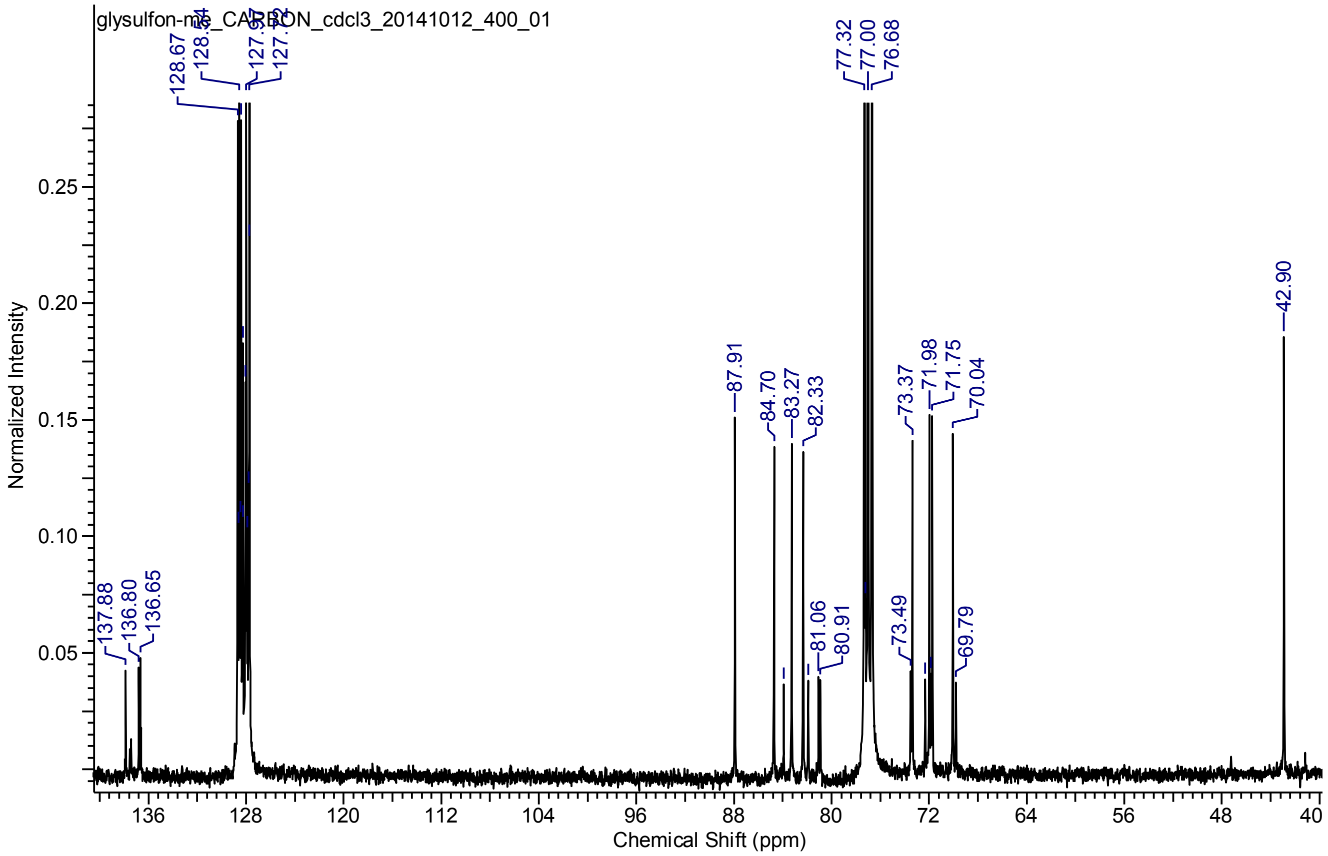


N- *(*Decyl)-*N’*-(β-D-arabinofuranosyl)sulfamide 8c

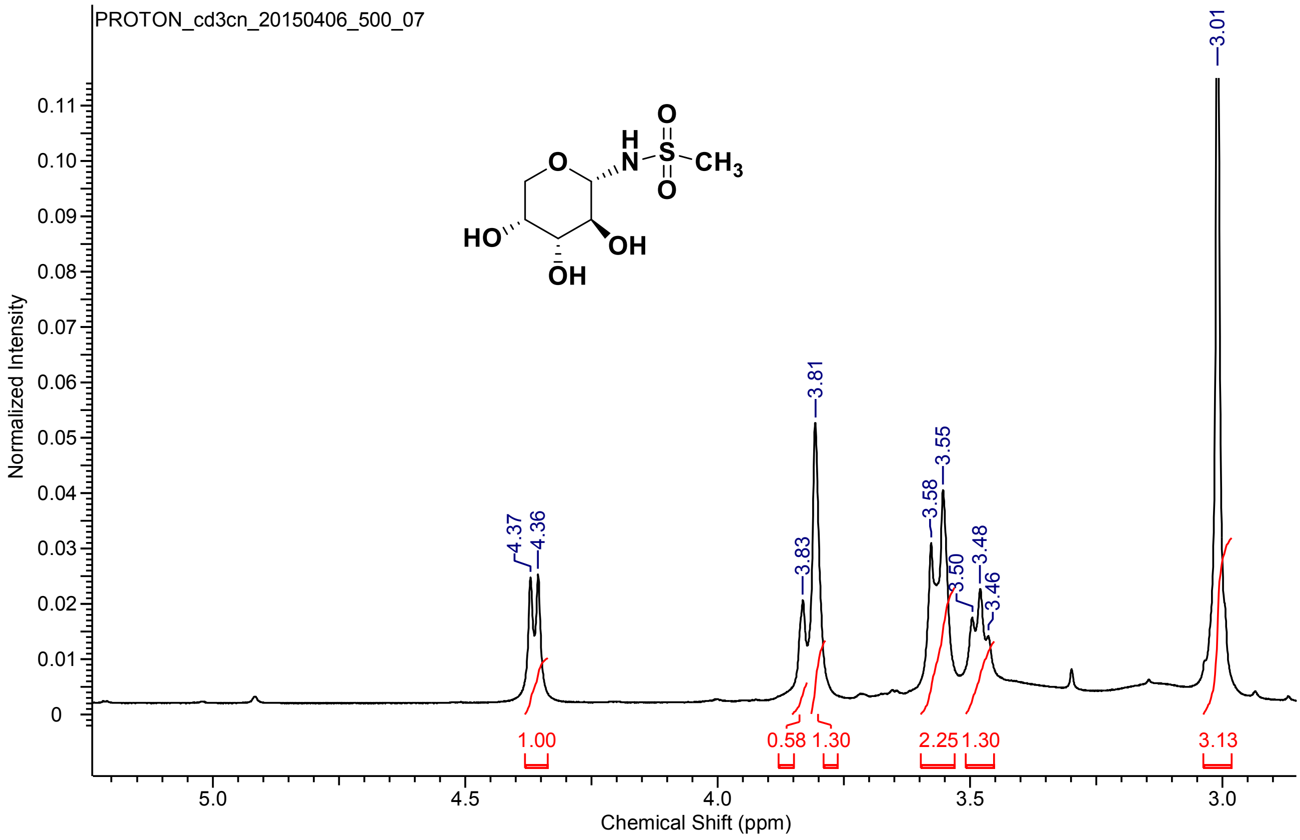


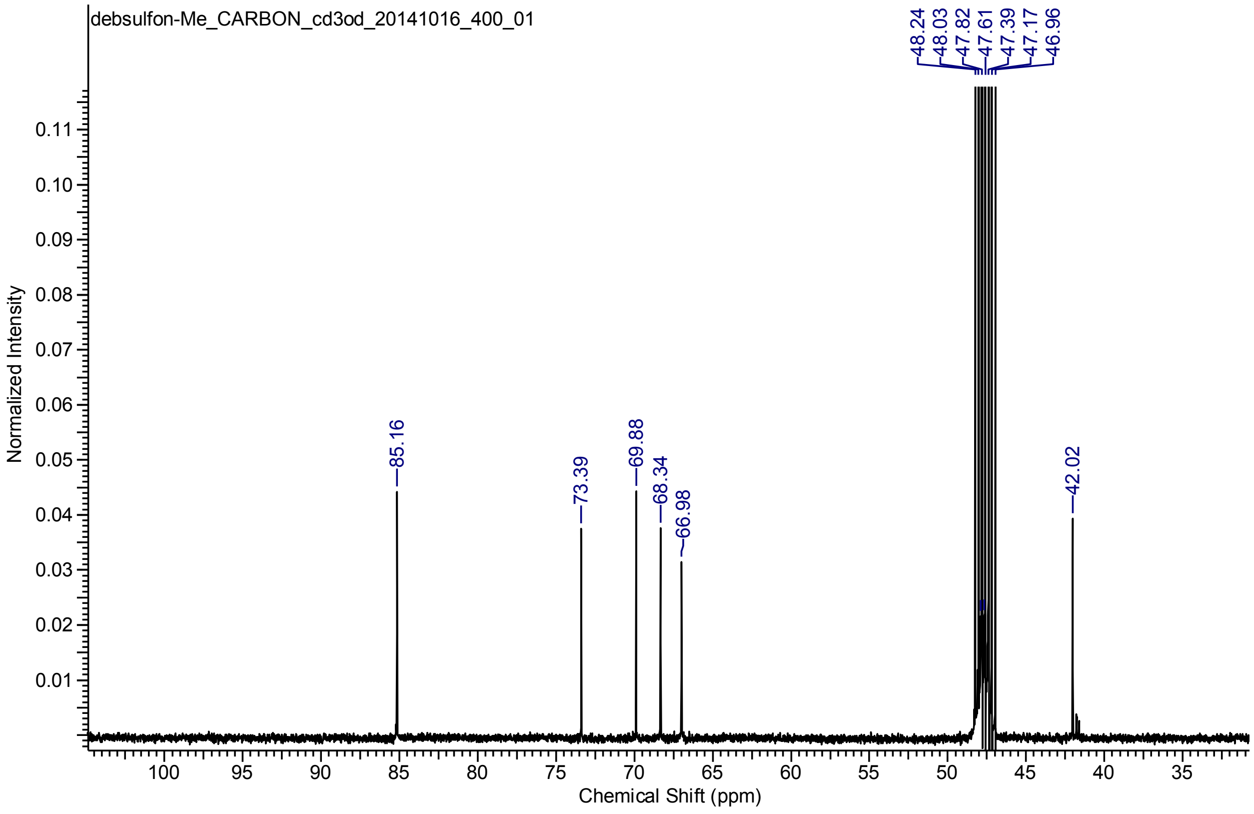
N-(2,3,5-Tri-*O*-benzyl-α,β-D-arabinofuranosyl)methanesulfonamide 4b



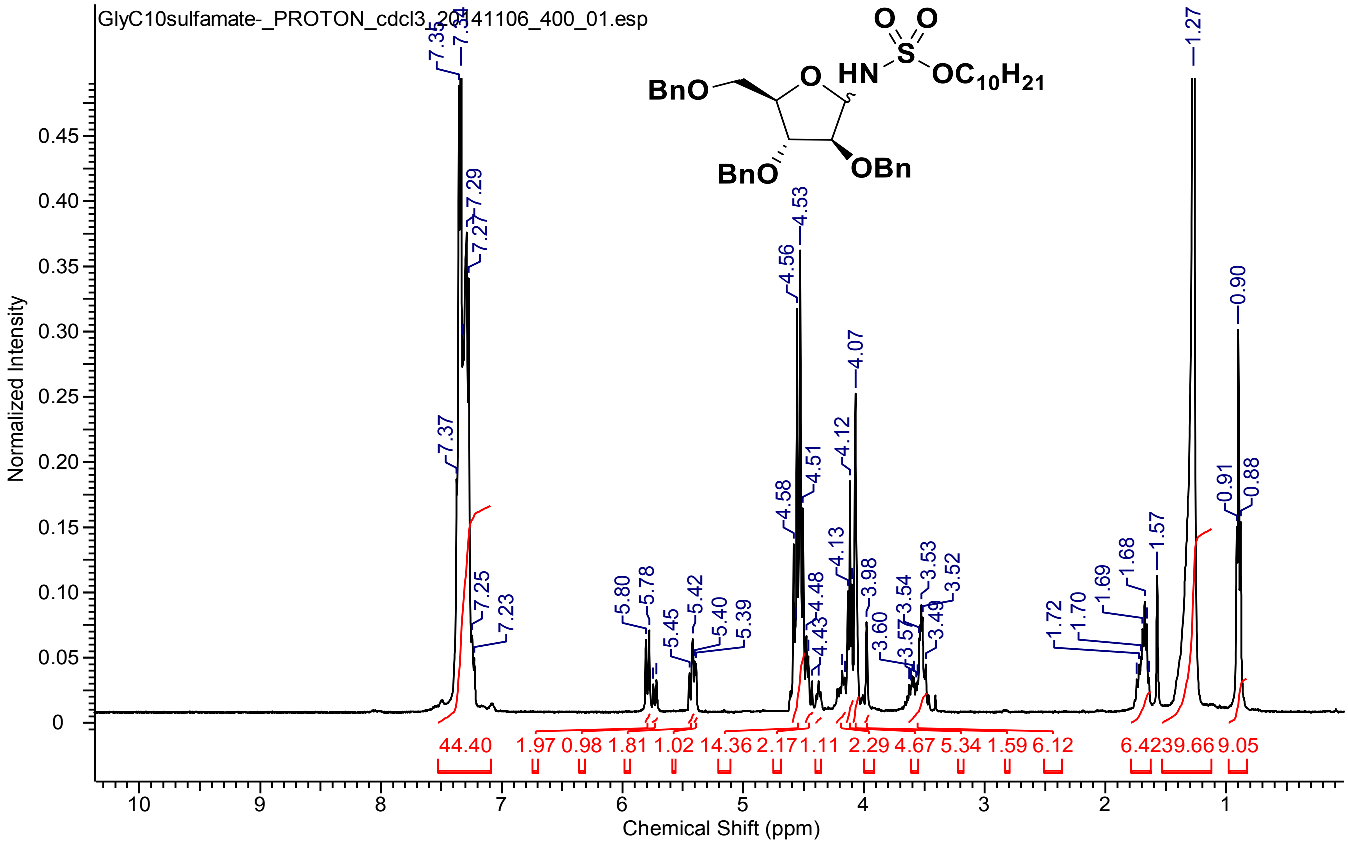


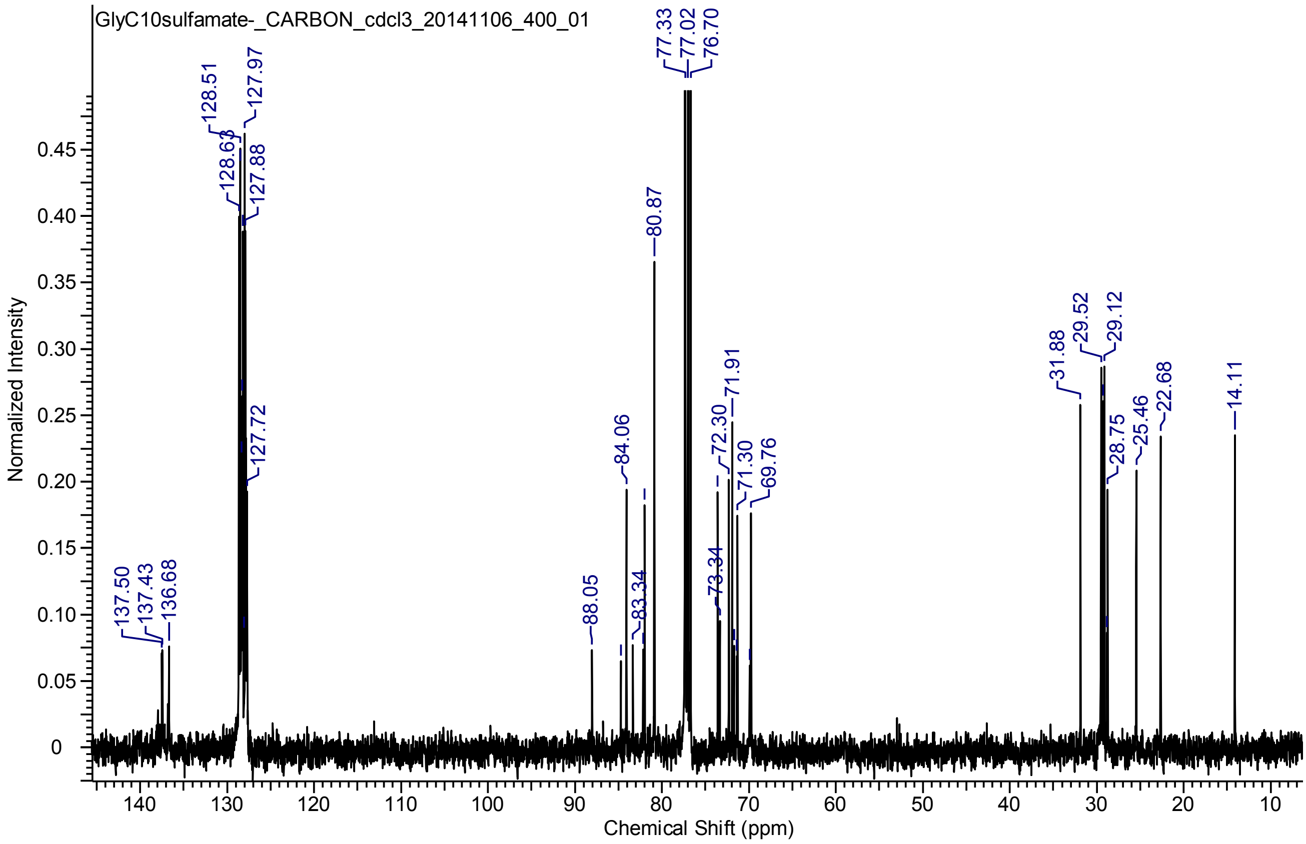
N-(α-D-Arabinopyranosyl)methanesulfonamide 5b



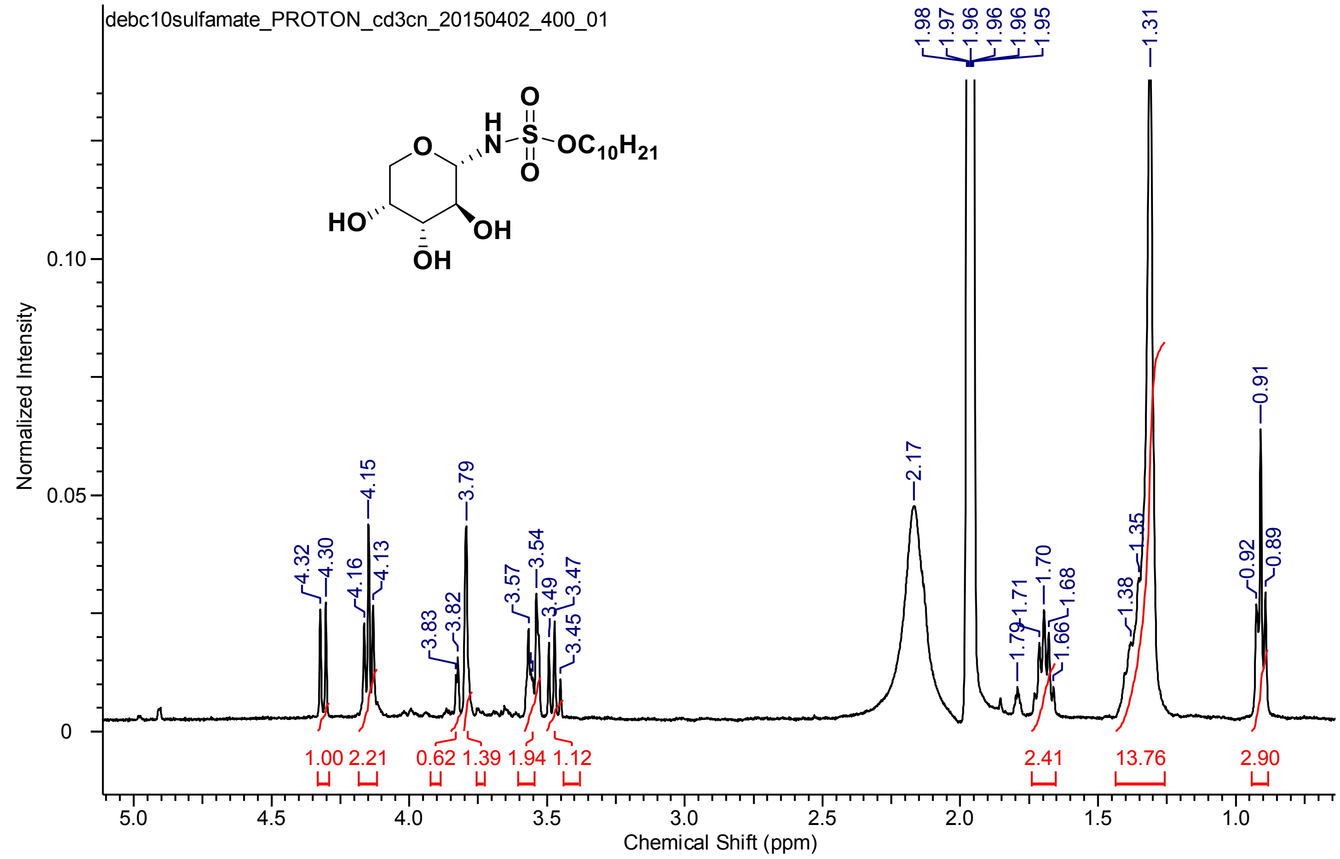


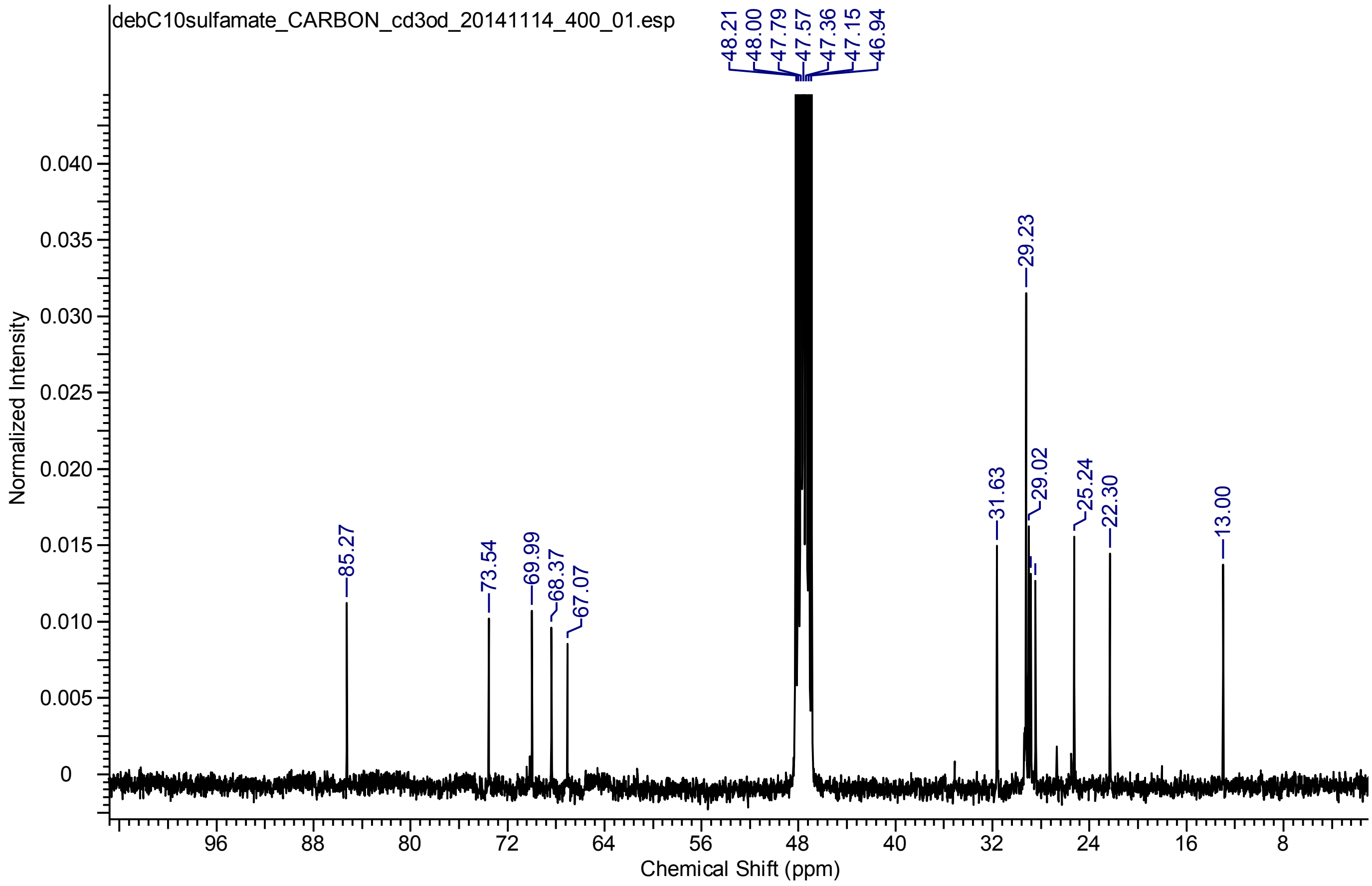
Decyl-*N*-(2,3,5-tri-*O*-benzyl-α,β-D-arabinofuranosyl)sulfamate 4c



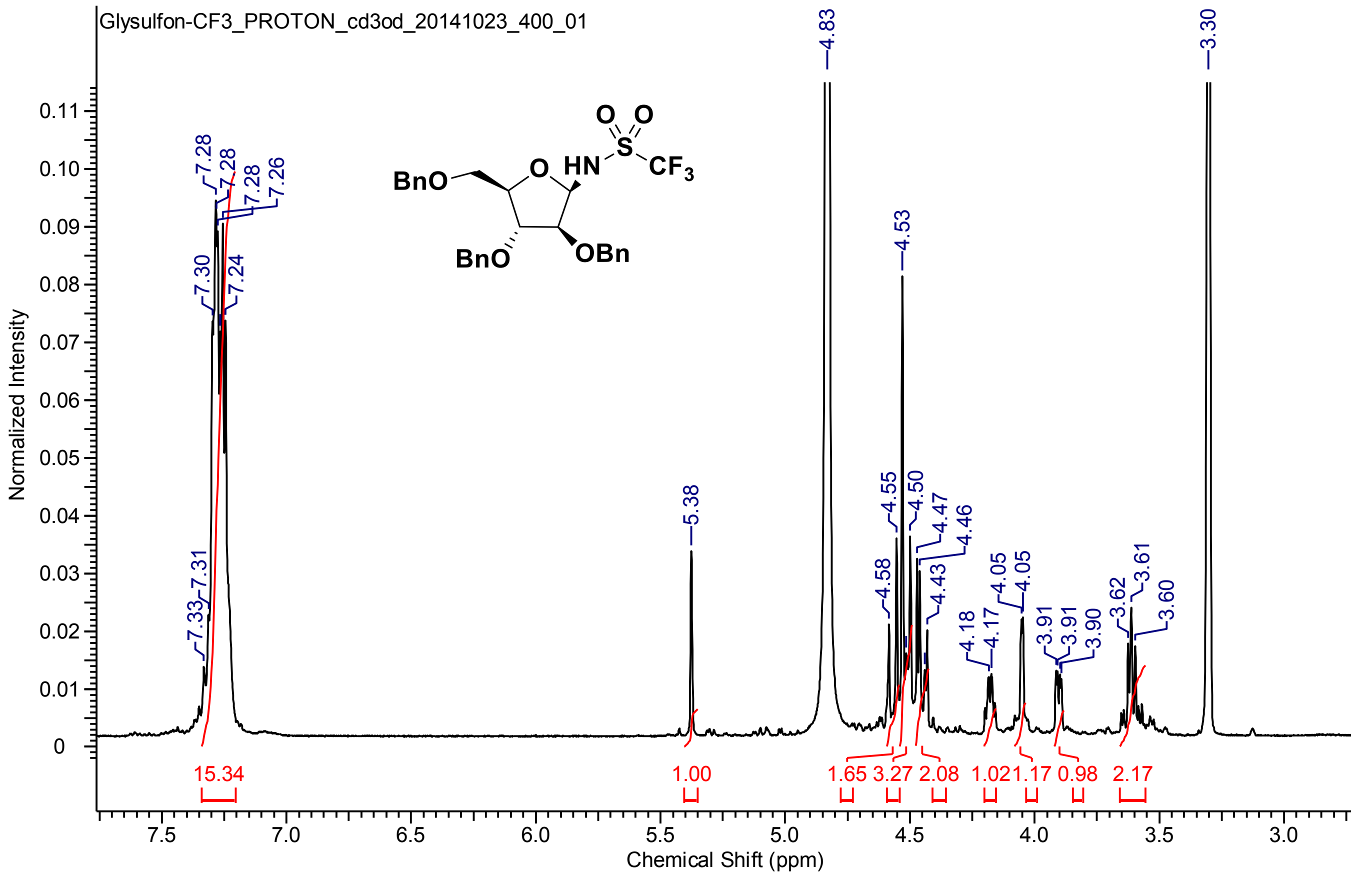


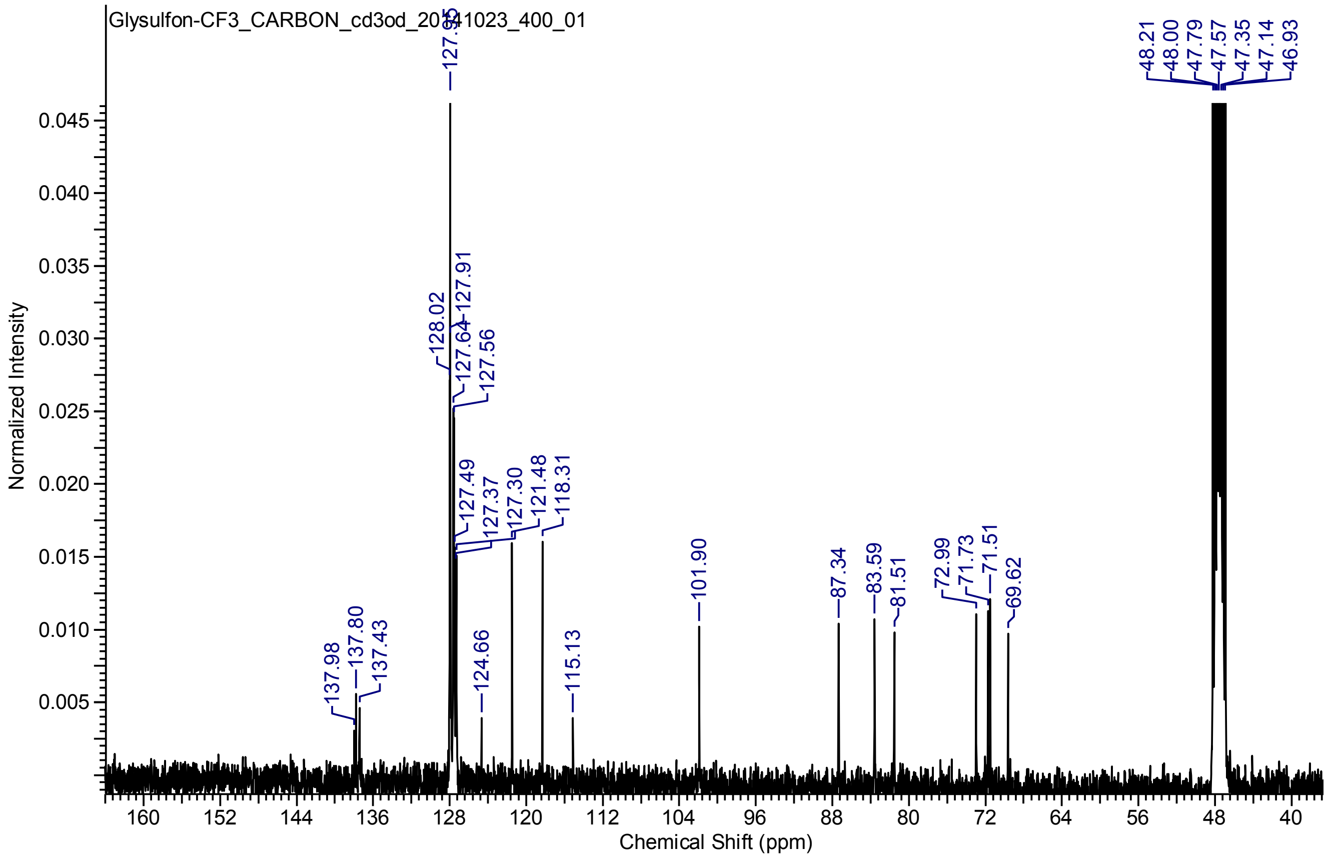
Decyl-*N*-(α-D-arabinopyranosyl)sulfamate 5c



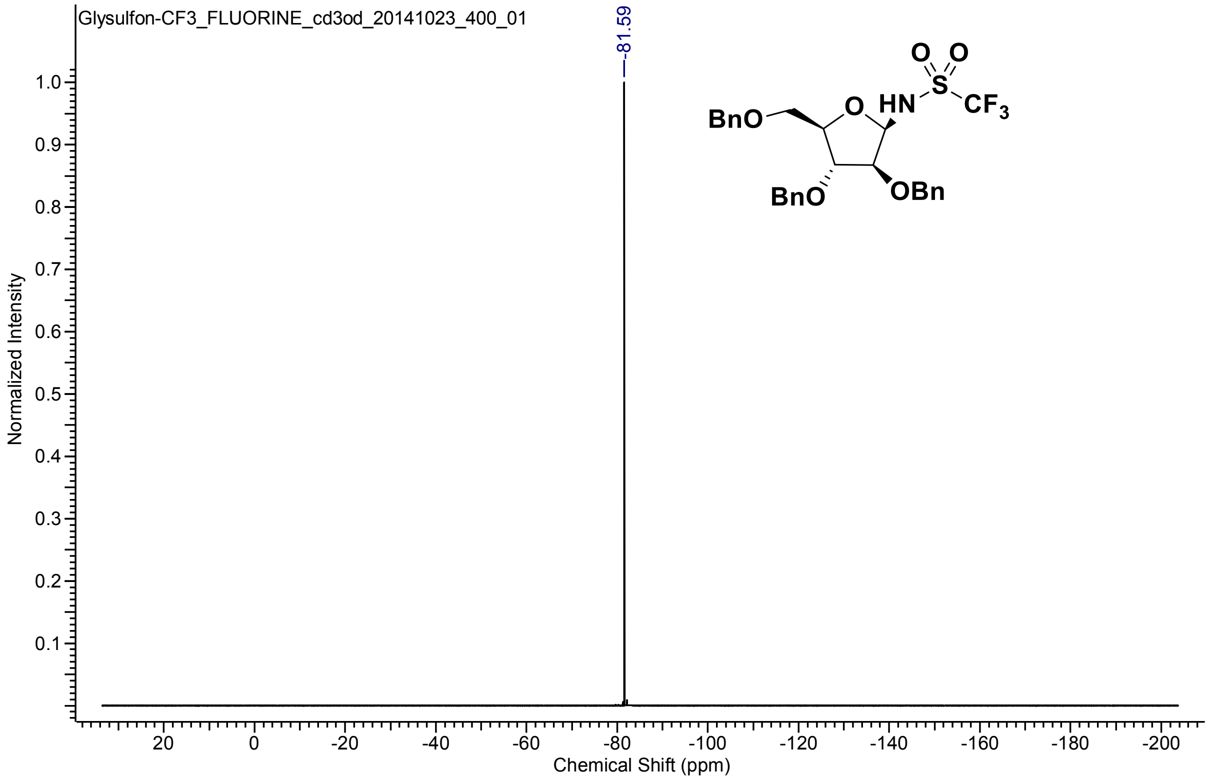


1,1,1-Trifluoro- *N*-(2,3,5-tri-*O*-benzyl-β-D-arabinofuranosyl)methanesulfonamide 6

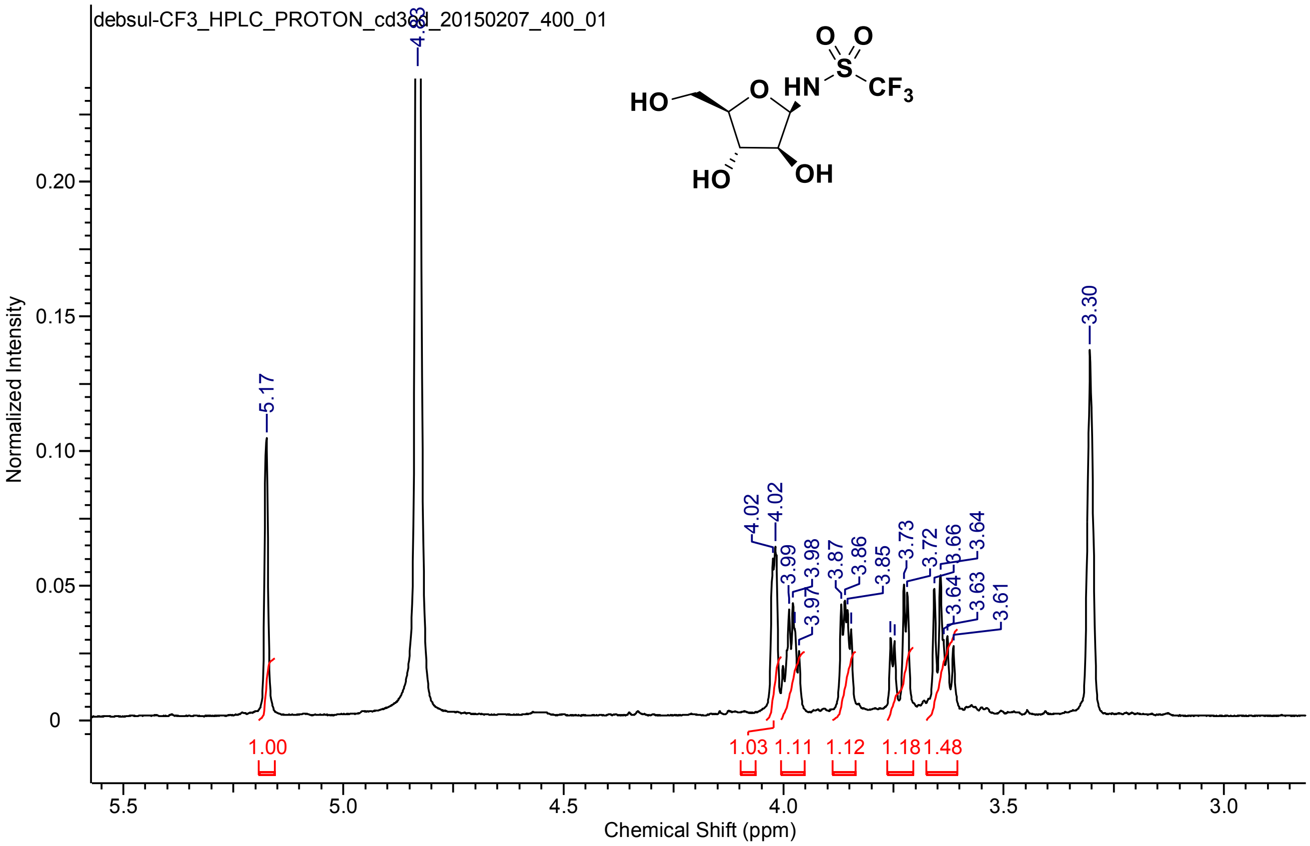




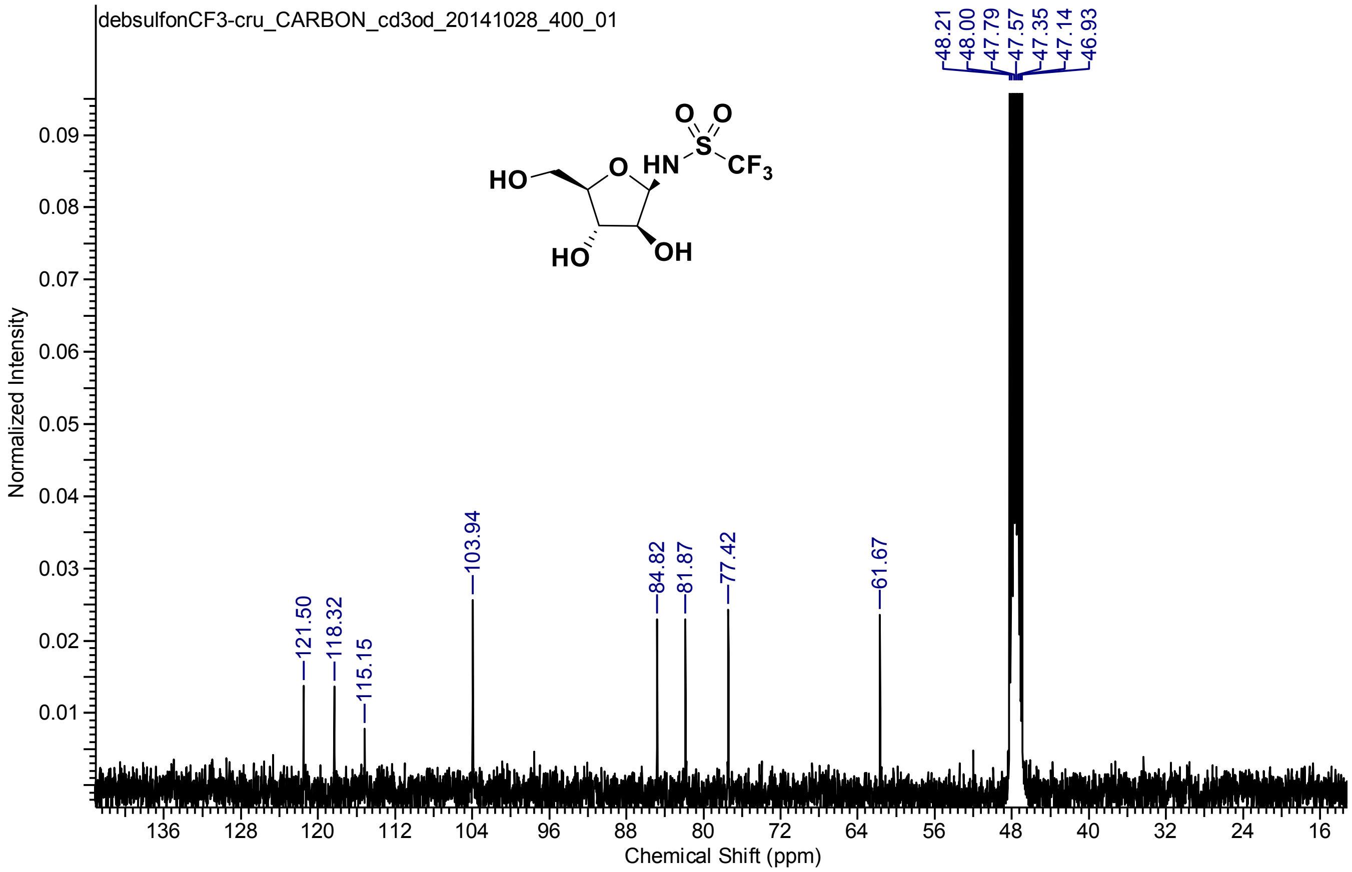
1,1,1-Trifluoro-*N*-(2,3,5-tri-*O*-benzyl-β-D-arabinofuranosyl)methanesulfonamide 6



1,1,1-Trifluoro-*N*-(β-D-arabinofuranosyl)methanesulfonamide 7



1,1,1-Trifluoro-*N*-(β-D-arabinofuranosyl)methanesulfonamide 7



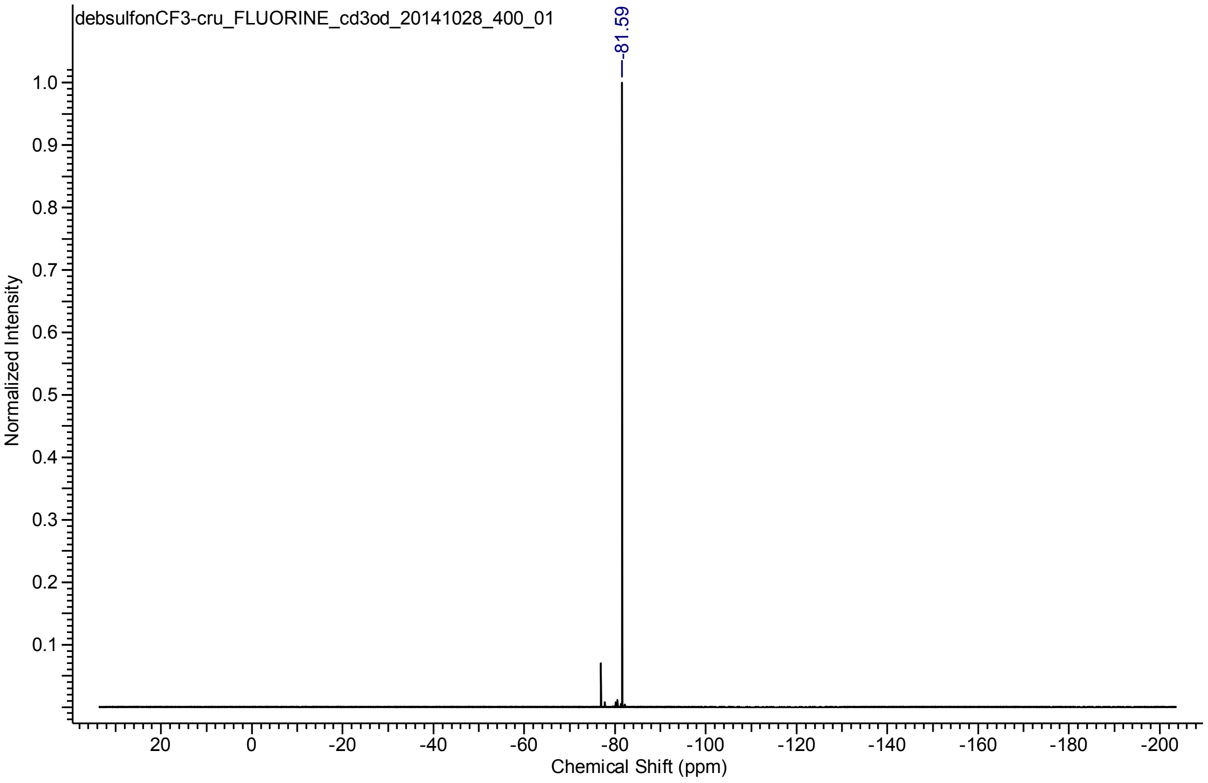


Table S1 Crystal data and structure refinement **3**, **5a** and **5b**

Identification code	KJK3a (**5b**)	PP6-1 (**5a**)	KJA2R-M (**3**)
Empirical formula	$C_6H_{13}NO_6S$	$C_{30}H_{66}N_4O_{13}S_2$	$C_{26}H_{28}O_5$
Formula weight	227.23	754.98	420.48
Temperature/K	120.01(10)	100(2)	100(2)
Crystal system	orthorhombic	triclinic	monoclinic
Space group	$P2_12_12_1$	P1	$P2_1$
a/Å	5.14008(6)	5.0940(10)	4.7090(9)
b/Å	9.60877(9)	12.212(2)	38.306(8)
c/Å	18.4697(2)	30.472(6)	11.942(2)
α/°	90	96.75(3)	90
β/°	90	94.01(3)	90.36(3)
γ/°	90	92.39(3)	90
Volume/Å^3	912.217(16)	1875.5(6)	2154.1(7)
Z	4	4	4
ρ_{calc}g/cm^3	1.655	1.337	1.297
μ/mm^{-1}	0.361	0.208	0.089
F(000)	480.0	820.0	896.0
Crystal size/mm^3	0.6961 × 0.0831 × 0.0614	0.16 × 0.01 × 0.01	0.505 × 0.022 × 0.02
Radiation	MoKα (λ = 0.71073)	synchrotron (λ = 0.7108)	synchrotron (λ = 0.7108)
2Θ range for data collection/°	6.118 to 72.634	2.7 to 50.504	2.126 to 53.1
Index ranges	$-8 \le h \le 8$, $-16 \le k \le 16$, $-30 \le l \le 30$	$-6 \le h \le 6$, $-14 \le k \le 14$, $-36 \le l \le 36$	$-5 \le h \le 5$, $-48 \le k \le 48$, $-15 \le l \le 15$
Reflections collected	60915	23752	10557
Independent reflections	4421 [R_{int} = 0.0545, R_{sigma} = 0.0197]	11954 [R_{int} = 0.1353, R_{sigma} = 0.1850]	8786 [R_{int} = 0.0889, R_{sigma} = 0.0504]
Data/restraints/parameters	4421/4/140	11954/157/911	8786/60/610
Goodness-of-fit on F^2	1.172	1.101	1.127
Final R indexes [I>=2σ (I)]	R_1 = 0.0266, wR_2 = 0.0799	R_1 = 0.1302, wR_2 = 0.3223	R_1 = 0.0840, wR_2 = 0.2101
Final R indexes [all data]	R_1 = 0.0293, wR_2 = 0.0819	R_1 = 0.1916, wR_2 = 0.3623	R_1 = 0.1008, wR_2 = 0.2231
Largest diff. peak/hole / e Å^{-3}	0.53/-0.42	1.47/-0.56	0.50/-0.53
Flack parameter	-0.028(18)	0.22(12)	0.1(6)

Experimental

Single crystals of $C_6H_{13}NO_6S$ [**5b**] were produced by slow evaporation of an ethyl acetate solution. A suitable crystal was selected and mounted in perfluoronated oil in a nylon loop on a SuperNova, Dual, Cu at zero, Atlas diffractometer. The crystal was kept at 120.01(10) K during data collection. Using Olex2[1], the structure was solved with the ShelXT[2] structure solution program using Direct Methods and refined with the ShelXL[3] refinement package using Least Squares minimisation.

O-H and N-H hydrogen atoms were located in the residual electron density map and inserted with fixed bond lengths for O-H (0.86 Å) and N-H (0.9 Å) hydrogens. C-H hydrogens were inserted in geometric positions as riding atoms. All hydrogen atoms were assigned thermal parameters dependant on the riding atom.

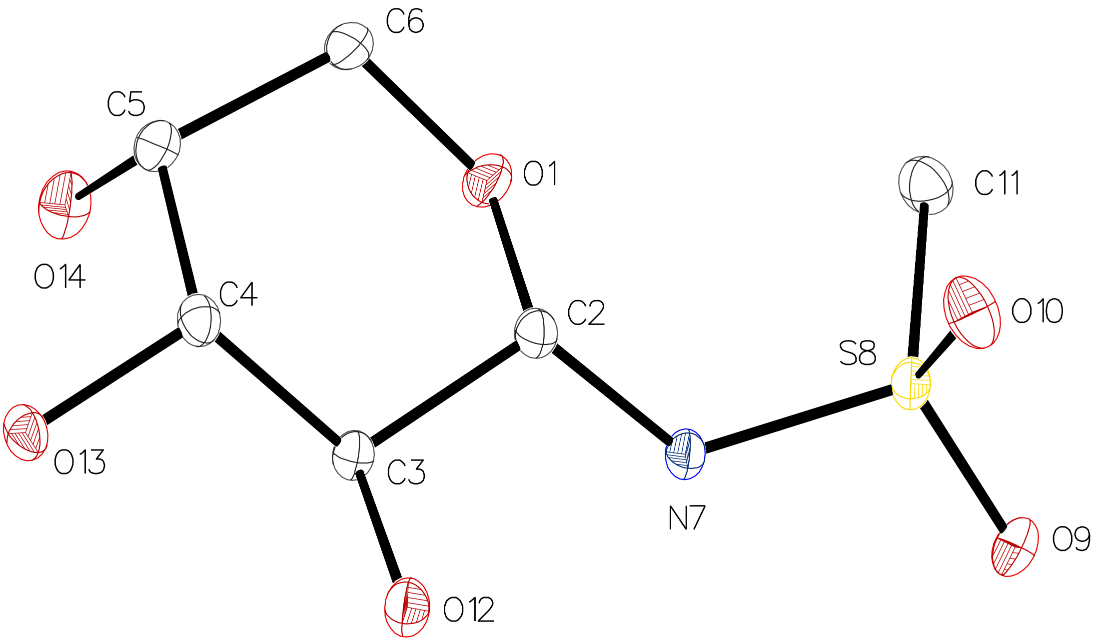


Fig S6. Complete asymmetric unit of structure **5b**. Hydrogens have been omitted for clarity

Single crystals of $C_{30}H_{66}N_4O_{13}S_2$ [**5a**] were produced by slow evaporation of an ethyl acetate solution. A suitable crystal was selected and mounted in perfluoronated oil in a nylon loop at the Mx1 beamline at the Australian synchrotron ($\lambda = 0.7108$ Å). The crystal was kept at 100 (2) K during data collection. BluIce[4] was used for the data collection and XDS[5] was used to process the data. Using Olex2[1], the structure was solved with the ShelXT[2] structure solution program using Direct Methods and refined with the ShelXL[3] refinement package using Least Squares minimisation.

A solution to the structure was found in $P2_1$ by forcing two of the unit cell angles to be 90; the reason for this attempt was the observed similarity of the pairs of molecules in the unit cell and the lack of data along the short axis, which could lead to a high level of inaccuracy in the unit cell parameters. A solution was found, but exhibited strong correlations in the thermal ellipsoids of the decyl chains (one chain becoming NPD, the other stretching to cover a wide area). The P1 solution was selected as the superior solution. Strong RIGU restraints were still required for two of the decyl chains. Water hydrogens were located in the electron density map and fixed at 0.86 Å and antibumping constraint of 1.2 Å. Other oxygen hydrogens were found in the electron density map but were refined as rotation OH groups (idealised tetrahedron, at 0.86 Å). The nitrogen hydrogens could not be found and were inserted in geometric positions, in an arrangement most similar to the other structures included in this paper, as amide hydrogens. C-H hydrogens were inserted in geometric positions as riding atoms. All hydrogen atoms were assigned thermal parameters dependant on the riding atom.

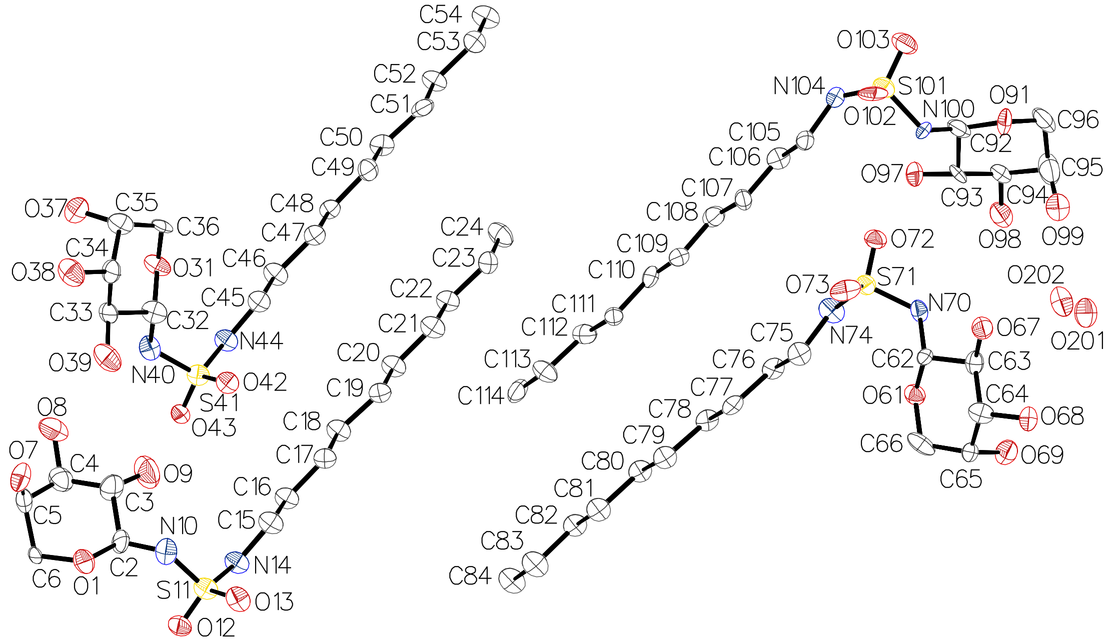


Fig S7. Complete asymmetric unit of structure **5a**. Hydrogens have been omitted for clarity

Single crystals of $C_{26}H_{28}O_5$ [**3**] were produced by slow evaporation of an ethyl acetate solution. A suitable crystal was selected and mounted in perfluoronated oil in a nylon loop at the Mx1 beamline at the Australian synchrotron (λ = 0.7108 Å). The crystal was kept at 100 (2) K during data collection. BluIce[4] was used for the data collection and XDS[5] was used to process the data. Using Olex2[1], the structure was solved with the ShelXT[2] structure solution program using Direct Methods and refined with the ShelXL[3] refinement package using Least Squares minimisation.

Two near identical molecules are found in the asymmetric unit, with one molecule having a significant disorder in one of the phenyl rings, breaking the potential orthorhombic symmetry. O-H hydrogen atoms were located in the residual electron density map and inserted with fixed bond lengths (0.86 Å). C-H hydrogens were inserted in geometric positions as riding atoms. All hydrogen atoms were assigned thermal parameters dependant on the riding atom.

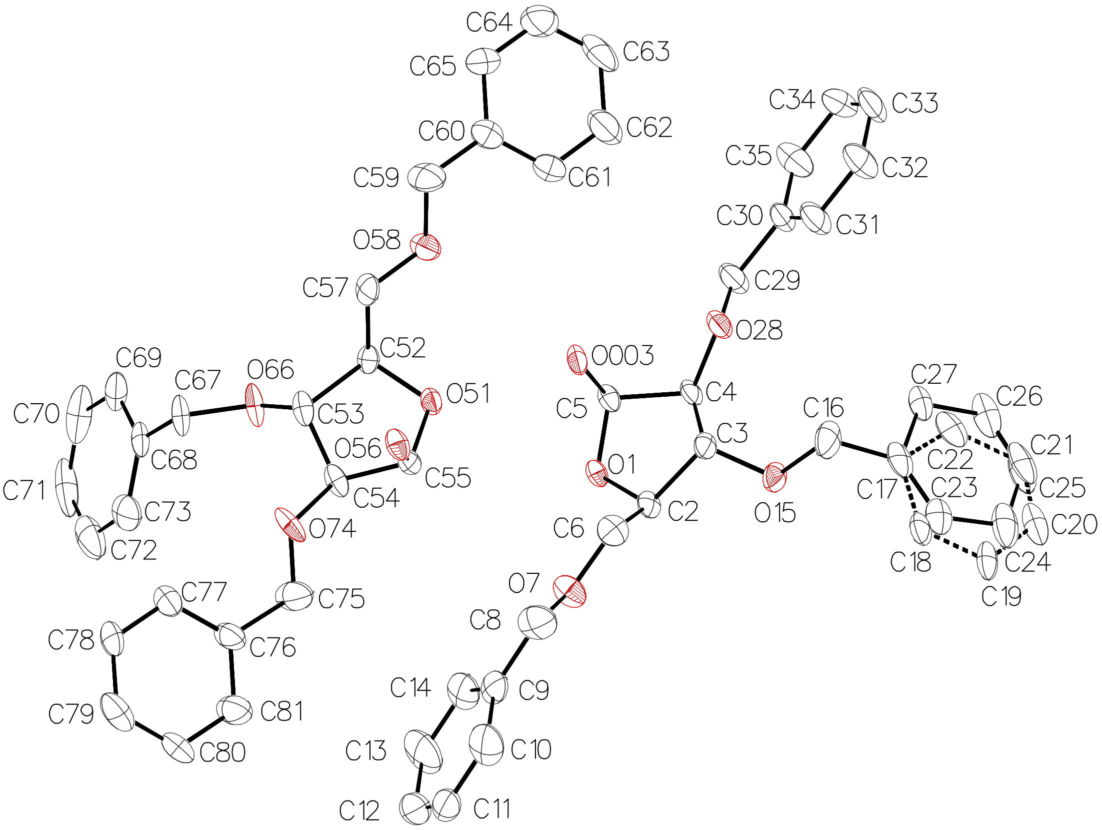


Fig S8. Complete asymmetric unit of **3**. Hydrogens have been omitted for clarity

References

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. **2009***, J. Appl. Cryst.* 42, 339-341
2. Sheldrick, G.M. **2015** *Acta Cryst*. A71, 3-8
3. Sheldrick, G.M. **2015** *Acta Cryst*. C71, 3-8
4. T.M. McPhillips, S.E. McPhillips, H.J. Chiu, A.E. Cohen, A.M. Deacon, P.J. Ellis, E. Garman, A. Gonzalez, N.K. Sauter, R.P. Phizackerley, S.M. Soltis and P. Kuhn, *J. Synchrotron Radiat.*, **2002**, 9, 401.
5. W. Kabsch*, J. Appl. Cryst.*, **1993**, 26, 795.