SUPPORTING INFORMATION - Potent metabolic sialylation inhibitors based on C-5 modified fluorinated sialic acids

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Supplementary Methods

Cell culture

B16-F10 mouse melanoma cells (ATCC, CRL-6475) were cultured in MEM medium (Gibco) containing 5 % FBS (GE Healthcare), 1 % MEM non-essential amino acids (Gibco), 0.15 % sodium bicarbonate (Gibco), 1 mM sodium pyruvate (Gibco), 1.5 % MEM vitamins (Gibco) and 1x antibiotic-antimycotic solution (Gibco). 9464D mouse neuroblastoma cells (kindly provided by Dr. Orentas, NIH, Bethesda) were cultured in DMEM Glutamax (Gibco) with 10 % FBS, 1 % non-essential amino acids, 50 µM 2-mercaptoethanol (Sigma-Aldrich) and 1x antibiotic-antimycotic solution. EL4 mouse T lymphocytes (ATCC, TIB-39) were cultured in IMDM medium (Gibco) containing 5 % FBS, 50 µM 2-mercaptoethanol and 1x antibiotic-antimycotic solution. Human THP-1 monocytic cells (ATCC, TIB-202) were cultured in RPMI 1640 medium (Gibco) supplemented with 10% FBS, 2 mM glutamine (Lonza) and 1x antibiotic-antimycotic solution. HEK293 human embryonic kidney cells (ATCC, CRL-1573) and HeLa human epithelial cells (ATCC, CRM-CCL-2) were cultured in DMEM Glutamax supplemented with 10 % FBS, 1 % non-essential amino acids and 1x antibiotic-antimycotic solution. The cell lines were initially grown and multiple aliquots were cryopreserved. The cells were used within 3 months after resuscitation and regularly tested for mycoplasma using a mycoplasma detection kit (Lonza). All cells were cultured in a humidified CO_2 incubator at 37°C. To determine the effective concentration of the sialic acid mimetics, the different cell lines were incubated for 3 days with increasing concentrations of the mimetics or equivalent concentrations of DMSO followed by lectin staining. Additionally, glycosylation of B16-F10 cells incubated for 3 days with 102.4 µM C-5-modified fluorinated sialic acids or DMSO control was assessed with different lectins. To determine the recovery speed of cell surface sialylation after inhibitor treatment, B16-F10 cells were treated for 3 days with 25.6 µM or 51.2 µM mimetics or DMSO control, washed, reseeded and analyzed daily by lectin staining for a period of 6 days.

Lectin staining and flow cytometry

Cells were harvested and stained with biotinylated lectins in 1x carbo-free blocking buffer (Vector Laboratories Inc.) containing 1 mM CaCl and 1 mM MgCl for 45-60 minutes at 4 °C. The lectins were obtained from Vector Laboratories Inc. and used at the following concentration; MALII (5 µg/ml), SNA-I (1 µg/ml), WGA (1 µg/ml), SJA (1 µg/ml), LCA (1 µg/ml), GSL-I (1 µg/ml), PHA-L (1 µg/ml), PSA (1 µg/ml), AAL (5 µg/ml) and PNA (5 µg/ml). Next cells were washed with PBA (1x PBS, 1 % BSA, and 0.02 % sodium azide) and stained with streptavidin-PE (eBioscience) for 20 minutes at 4 °C. Cells were washed, collected in PBA and analyzed using a CyAn flow cytometer (Beckman Coulter). Percentage lectin binding was calculated by normalizing the mean fluorescence intensity to control cells

MTT assay

B16-F10 cells were cultured for 3 days in the presence of 0-204.8 µM **1**, **2**, **4**-**12** or DMSO control and subjected to an MTT assay. Cells were washed and incubated in medium containing 0.5 mg/ml thiazolyl blue tetrazolium bromide (MTT, Sigma-Aldrich) for 30 minutes at 37 °C. Next, the cells were washed with 1x PBS and lysed in solubilizing solution (90 % isopropanol, 0.25 % SDS, 0.04 M HCL). Reduction of tetrazolium dye to purple formazan by the cells was quantified at 595 nm wavelength using a microplate absorbance reader (BioRad).

In silico *modeling*

Crystal structures of human ST6GalI (4JS2[1]), human ST8SiaIII (5BO9[2]) and murine CMAS (1QWJ[3]) were retrieved from the Protein Data Bank (PDB). Sialyltransferase crystal structures were superposed using the protein align function in MOE 2013.08[4] at default settings. In the CMAS structure, the binding pocket of domain D was used for modeling; water molecules were retained. The A-B dimer was neglected. The highest ranked alternative rotamer (suggested by MOE) for Ser120(D) was used to better accommodate the molecular environment and ligand interactions. Hydrogens were added using MOE's protonate 3D function at default settings and OH-groups were optimally oriented prior to energy minimizations. All energy minimizations were conducted using the AMBER12:EHT force field[5] in MOE, leaving the ligand atoms and all receptor and solvent atoms within 8Å free to move. Images were generated with UCSF Chimera 1.13[6].

CMP-sialic acid quantification

B16-F10 cells were incubated for 1, 2, 4, 8 or 24 hrs with 51.2 µM fluorinated sialic acid analogues or DMSO control. The cells were washed thoroughly with ammonium carbonate buffer (pH 7.4) and subsequently snap frozen in liquid nitrogen. For extraction, the wells were incubated two times for 3 minutes with cold extraction buffer (40% acetonitrile, 40% methanol, 20% water). The samples were centrifuged for 3 minutes at 13.000 rpm and vacuum dried. Next, the cell extracts were reconstituted in 10 mM triethylammonium acetate followed by analysis using reverse-phase ion pairing chromatography (Agilent Technologies 1290 Infinity) coupled to a triple quadrupole mass spectrometer operating in negative ion mode (Agilent Technologies 6490 Triple Quad LC/MS) by GlycoMScan B.V., Oss, The Netherlands (collaboration Dr. M. Van Scherpenzeel). For analysis of synthetic modified sugars, the MRM transitions were adapted based on fragmentation knowledge of the non-modified, endogenous compound.

Supporting figures and tables

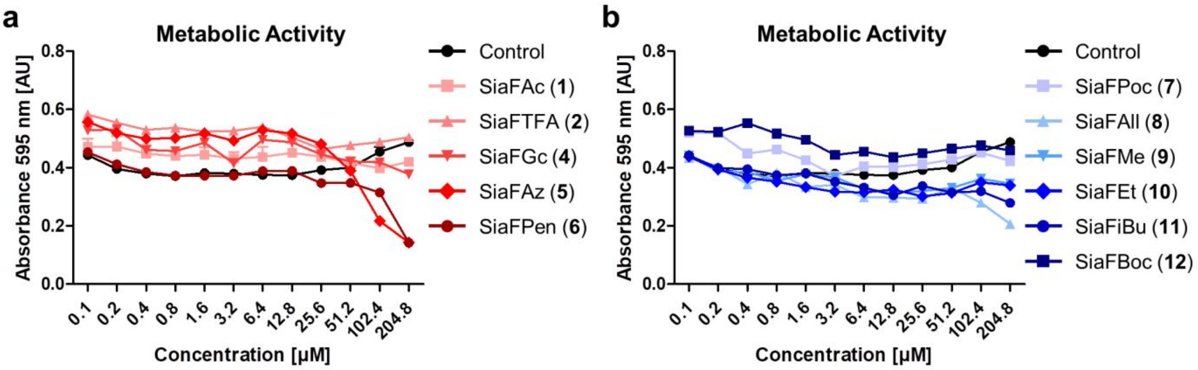


Figure S1: Effect of **1**, **2**, **4**-**12** on cell metabolic activity/viability. B16-F10 cells were cultured for three days with increasing concentrations of fluorine sialic acids or DMSO and subjected to an MTT assay. Representative graphs show absorbance at 595 nm for cells treated with amide (**a**) or carbamate (**b**) fluorine sialic acids.

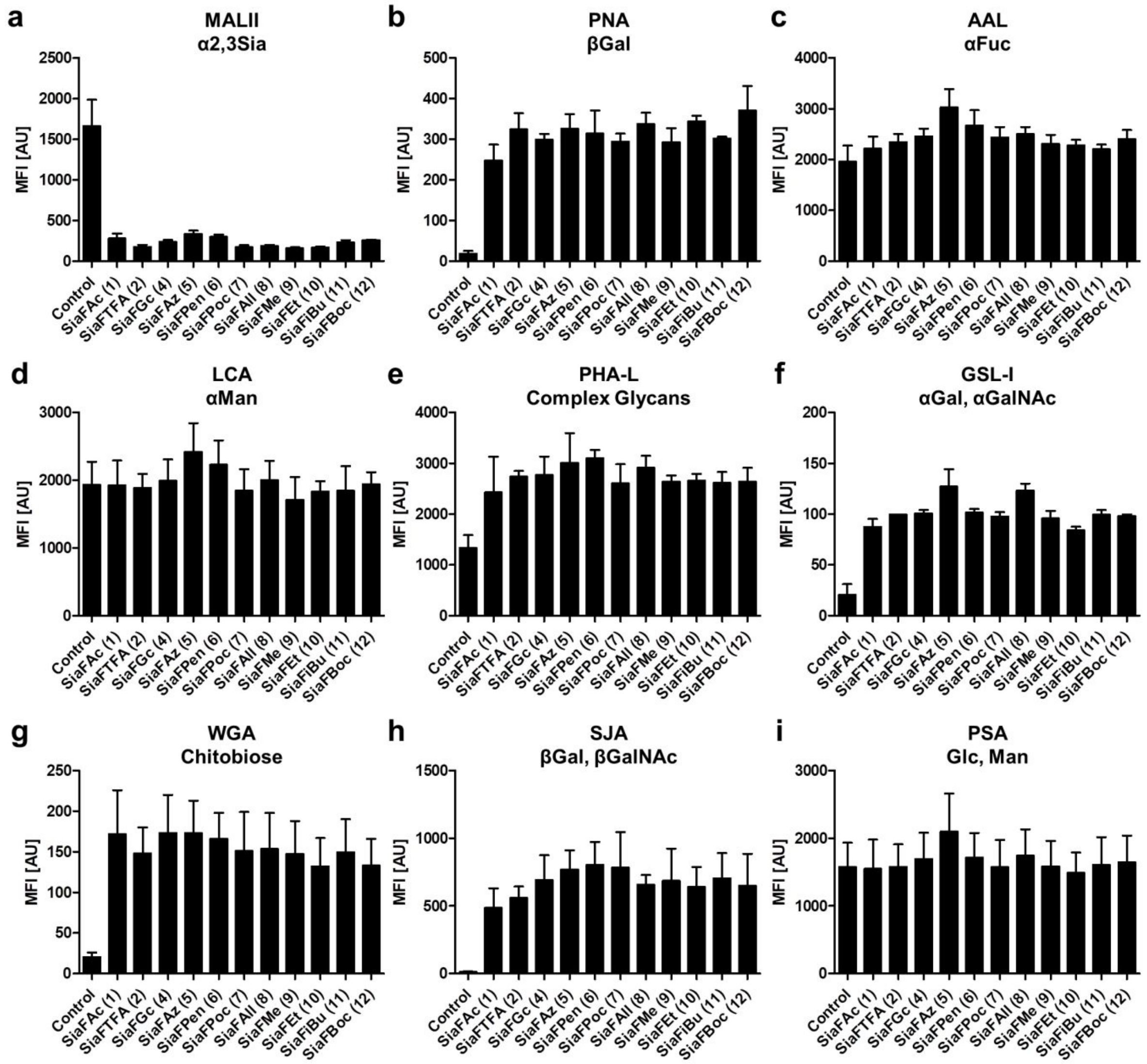


Figure S2: Effect of **1**, **2**, **4**-**12** on total cell surface glycosylation. B16-F10 cells treated for three days with 102.4 µM fluorine sialic acids or DMSO control were stained with a panel of biotinylated lectins and streptavidin-PE. Lectin binding was determined in two independent experiments by flow cytometry and is presented as mean fluorescence intensity (MFI) ± SEM. Bar diagrams show binding of MALII (**a**), PNA (**b**), AAL (**c**), LCA (**d**), PHA-L (**e**), GSL-I (**f**), WGA (**g**), SJA (**h**) and PSA (**i**).

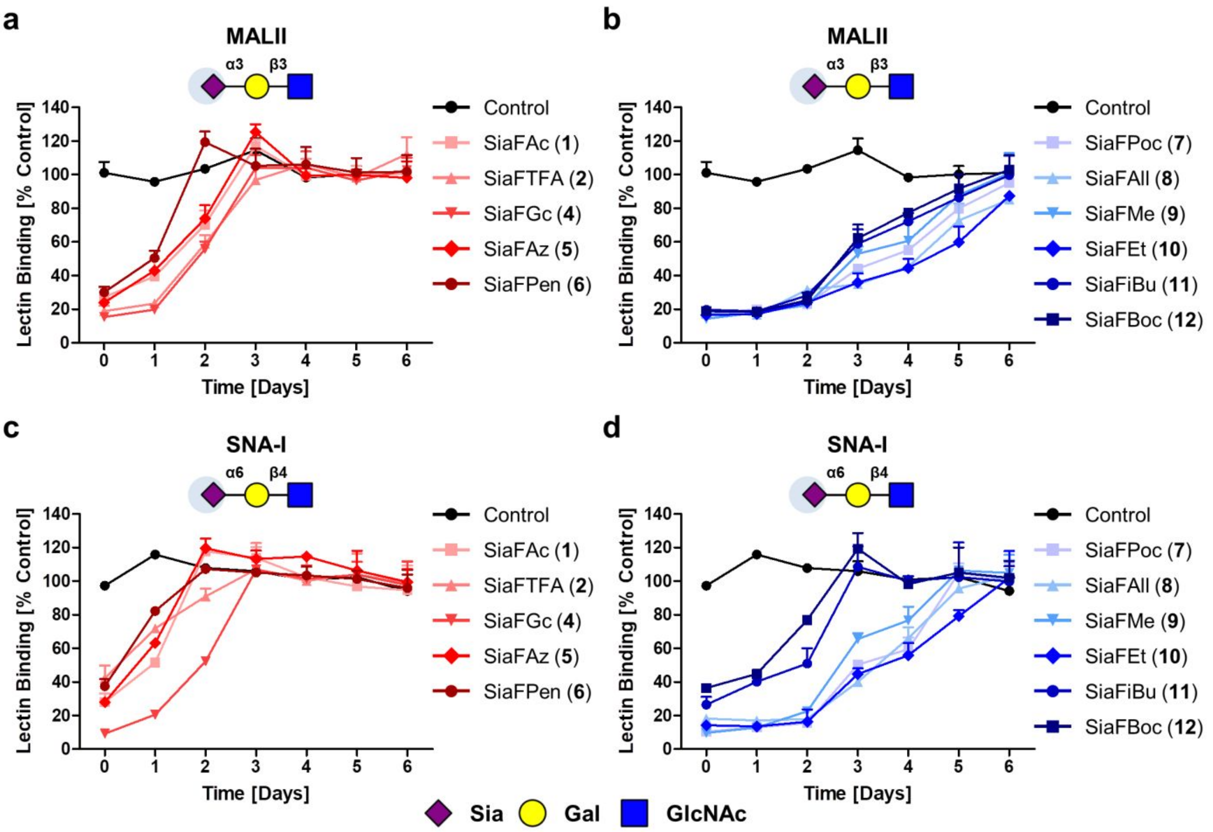


Figure S3: Recovery of sialylation after treatment with 25.6 µM fluorinated sialic acid mimetics. **a**-**d**) B16-F10 cells were treated with 25.6 µM fluorine sialic acids for three days, thoroughly washed and recovery of sialylation was followed in time by flow cytometry using MALII and SNA-I staining. Data of three independent experiments are presented as mean percentage lectin binding ± SEM normalized to control and show MALII and SNA-I binding after treatment with amide (**a**, **c**) and carbamate (**b**, **d**) fluorine sialic acids.

Group	SiaFR	B16-F10	rIP	THP-1	HEK293	HeLa	9464D	EL4
Amides	Ac (**1**)	32.80 ± 3.08		10.87 ± 2.47	36.69 ± 3.59	34.50 ± 2.18	> 102.4	> 102.4
	TFA (**2**)	33.33 ± 2.63	*1*	7.19 ± 3.60	41.36 ± 10.44	33.38 ± 4.38	> 102.4	> 102.4
	ClAc (**3**)	ND		ND	ND	ND	ND	ND
	Gc (**4**)	11.78 ± 2.27	*3*	5.94 ± 2.18	54.06 ± 15.34	12.50 ± 2.52	> 102.4	> 102.4
	Az (**5**)	32.82 ± 3.55	*1*	13.23 ± 3.02	47.21 ± 2.89	42.19 ± 8.42	> 102.4	> 102.4
	Pen (**6**)	52.49 ± 4.31	*1*	12.58 ± 3.51	44.71 ± 4.33	51.23 ± 6.06	> 102.4	> 102.4
Carbamates	Poc (**7**)	2.59 ± 0.07	*13*	0.44 ± 1.59	5.42 ± 1.40	1.37 ± 0.81	40.19 ± 6.56	51.65 ± 2.62
	All (**8**)	2.87 ± 0.80	*11*	0.38 ± 1.67	1.68 ± 3.20	2.04 ± 1.40	9.64 ± 3.93	50.9 ± 6.44
	Me (**9**)	7.54 ± 1.34	*4*	2.65 ± 1.60	4.77 ± 2.80	5.23 ± 1.88	29.60 ± 4.67	52.68 ± 5.45
	Et (**10**)	3.87 ± 1.14	*8*	0.37 ± 1.76	1.57 ± 4.23	1.67 ± 1.31	28.13 ± 5.51	50.58 ± 8.84
	iBu (**11**)	15.07 ± 3.70	*2*	0.62 ± 1.77	9.61 ± 4.83	4.32 ± 1.82	36.15 ± 6.40	51.07 ± 8.97
	Boc (**12**)	8.21 ± 0.67	*4*	1.72 ± 2.30	28.03 ± 2.57	20.55 ± 1.95	> 102.4	50.31 ± 3.99
	Cbz (**13**)	ND						
	PBn (**14**)	ND						
	nBu (**15**)	7.91 ± 1.95	*4*					
	Mox (**16**)	32.38 ± 1.38	*1*					
	Tro (**17**)	7.85 ± 2.07	*4*					
	FEt (**18**)	2.05 ± 1.29	*16*					

EC_{50} <5 µM
EC_{50} <20 µM
EC_{50} <50 µM

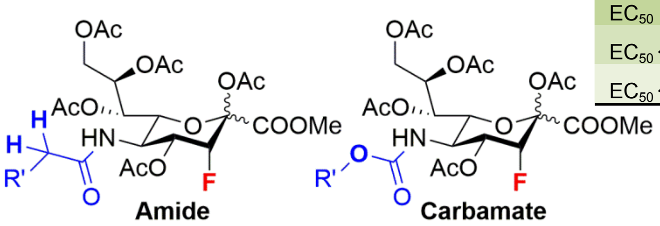


Table S1: EC_{50} values in µM for inhibition of α2,6-linked sialic acid. B16-F10 cells were treated with 0.1-205.8 µM, and THP-1, HEK293, HeLa, 9464D and EL4 cells with 0.1-102.4 µM amide or carbamate fluorinated sialic acids or DMSO vehicle control. After three days the cells were stained with biotinylated lectins that recognize α2,6-linked (SNA-I) sialic acids, and streptavidin-PE. Binding of the lectins was determined by flow cytometry, as mean percentage lectin binding ± SEM normalized to the control (n=3). The relative inhibitory potency (rIP) was calculated for the B16-F10 cell line by dividing the EC_{50} of SiaFAc (**1**) by the EC_{50} of the compound of interest.

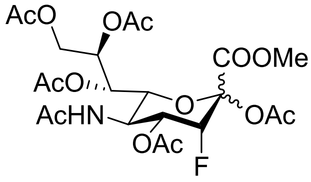
General synthetic procedures and abbreviations

General synthetic procedures^{1}H and ^{13}C NMR spectra were recorded on a Varian Iinova 400 MHz or Bruker Avance III 500 MHz spectrometer. Chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane (TMS) as the internal standard. NMR data is presented as follows: Chemical shift, multiplicity (s = singlet, bs = broad singlet, d = doublet, t = triplet, dd = doublet of doublet, dt = doublet of triplet, m = multiplet and/or multiple resonances), integration, coupling constant in Hertz (Hz). All NMR signals were assigned on the basis of ^{1}H, ^{13}C, ^{19}F NMR, COSY and HSQC experiments. Mass spectra were recorded on a JEOL JMS-T100CS AccuTOF mass spectrOCH$_3$ter. Automatic column chromatography was performed on Biotage Isolera Spektra One, using SNAP cartridges 10-50g filled with normal silica (Biotage, 30-100 μm, 60 Å) or water resistant iatro beads. Microwave reactions were perfOCH$_3$d on a Biotage Initiator 4.1.3. TLC analysis was conducted on TLC Silicagel, 60, F254, Merck, with detection by UV absorption (254 nm) where applicable, and by spraying with 20% sulfuric acid in methanol followed by charring at ~150 °C or by spraying with a solution of $(NH\text{-}4)_6Mo_7O_{24}\cdot H_2O$ (25 g l-1) in 10% sulfuric acid in methanol followed by charring at ~300°C. DCM, ACN and Tol were freshly distilled. All reactions were carried out under an argon atmosphere.

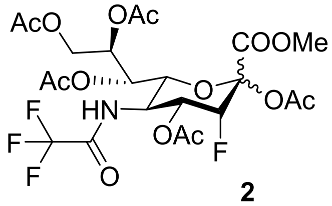
Commonly used abbreviations

Ac_2O	Acetic anhydride
Acet	Acetone
ACN	Acetonitrile
AcOH	Acetic acid
Alloc	Allyloxycarbonyl
Az	Azidoacetic acid
$BF_3 \cdot Et_2O$	Boron trifluoride etherate
BoC-2O	Di-*tert*-butyl dicarbonate
Br_2	Bromine
Cbz	Carboxybenzyl
CD_3OD	Deuterated methanol
$CDCl_3$	Deuterated chloroform
D_2O	Deuterium oxide
DCM	DichlorOCH$_3$thane
DMAP	Dimethylaminopyridine
DMF	*N*,*N*-Dimethylformamide
EtOAc	Ethyl acetate
Hept	Heptane
iBu	Iso-butyl
n-Bu	n-Butyl
Poc	Propargylcarboxycarbonyl
Pyr	Pyridine
ROSu	Hydroxysuccinimide ester
SAda	Adamantyl-thiol
STol	4-methylthiophenol
TBTA	Tris(benzyltriazolyl methyl)amine
tBu	Tert-butyl
TEA	Triethylamine
TFA	Trifluoroacetic acid
TFAA	Trifluoroacetic acid anhydride
TfOH	TrifluorOCH$_3$thanesulfonic acid
TMSOTf	Trimethylsilyl trifluorOCH$_3$thanesulfonate
Tol	Toluene
Troc	2,2,2 trichloroethoxycarbon

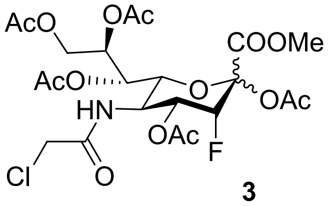
Synthetic experimental



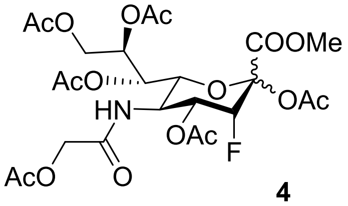
1 **Methyl 5-(acetamido)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (1)**. Synthesis was performed as described previously the data is identical to the data previously reported.[7] **TLC:** (Acet:DCM, 30:70 v/v) R_f = 0.40. **HRMS** *(m/z)*: [M+Na]+ calcd for C-2$_0$H$_{28}$FNO$_{13}$, 532.1443; found, 532.1442. The crude fluorinated alcohol was dissolved in Pyr (14.5 ml) and Ac$_2$O (7.3 ml), stirred for 16 hours at r.t. and was evaporated *in vacuo*. The resulting solid dissolved in EtOAc and sat. aq. NaHCO$_3$. The organic phase was separated and the solvent evaporated *in vacuo* and purified on silica flash-column chromatography (0 → 30% ACE in DCM) affording **1** (1.46 g, 2.54 mmol, 80% yield *two steps*) as a slightly yellow foam. **TLC:** (Acet:DCM, 30:70 v/v) R_f = 0.55. **^{1}H-NMR** (500 MHz, CD$_3$OD, major anOCH$_3$r) δ 5.58 (d, *J* = 8.9 Hz, 1H, NH), 5.46 (dd, J = 27.9, 10.7 Hz, 1H, H-4), 5.29 (dd, J = 5.0, 1.8 Hz, 1H, H-7), 5.05 (ddd, J = 6.7, 5.2, 2.5 Hz, 1H, H-8), 4.87 (dd, J = 49.1, 2.5 Hz, 1H, H-3), 4.51 (dd, J = 12.5, 2.5 Hz, 1H, H-9$_a$), 4.21 – 4.10 (m, 3H, H-9$_b$; H-5; H-6), 3.77 (s, 3H, OCH$_3$), 2.12 – 2.09 (m, 6H, 2xCH$_3$,OAc), 2.04 (s, 3H, CH$_3$,OAc), 1.98 (s, 3H, CH$_3$,OAc), 1.97 (s, 3H, CH$_3$,OAc), 1.85 (s, 3H, CH$_3$,NHAc).; **^{13}C-NMR** (126 MHz, CD$_3$OD) δ 170.58 (CO, Ac), 170.56 (CO, Ac), 170.50 (CO, Ac), 170.34 (CO, Ac), 167.11 (C-1), 95.16 (d, *J* = 28.8 Hz, C-2), 86.95 (d, *J* = 185.3 Hz, C-3), 71.91 (C-6), 71.37 (C-8), 68.40 (d, *J* = 17.2 Hz, C-4), 67.93 (C-7), 62.09 (C-9), 53.49 (OCH$_3$), 45.53 (C-5), 29.27 (CH$_3$,Ac), 20.88 (CH$_3$,Ac), 20.79 (CH$_3$,Ac) , 20.74 (CH$_3$,Ac), 20.65 (CH$_3$,Ac), 20.51 (CH$_3$,Ac); **HRMS** *(m/z)*: [M+Na]+ calcd for C$_{22}$H$_{30}$FNO$_{14}$, 574.1548**;** found, 574.1548.



2 **Methyl 5-(trifluoroacetamido)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (2)**. *TFA protected Sialic acid **2** was a common side product after TFA deprotection. Further investigation discovered that TFA, if not removed carefully, forms a mixed anhydride with chloroformates resulting in a quantitative coupling of TFA to the relatively unreactive amine. Later deprotection reactions were therefore done with TfOH which avoided this problem.* Boc inhibitor **12** (50 mg; 82 µmol) was dissolved in a 1:2 mixture of TFA and DCM (1.6 ml; 0.05 M). The mixture was stirred for 2 h at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09). The mixture was then concentrated *in vacuo*. The residue was dissolved in DCM (0.83 ml; 0.1 M) and additional TFA (188 µl, 2.5 mmol, 30 eq) and TEA (690 µl; 4.95 mmol; 60 eq.) were added. Isobutyl chloroformate (*also possible with other chloroformates*) (76 µl; 589 µmol; 20 eq.) was added and the reaction was stirred for 16 h. The mixture was diluted with DCM and washed successively with 0.1M HCl and sat. NaHCO$_3$. The organic layer was dried over MgSO$_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **2** (44 mg; 74 µmol; 90%) as a white solid. **TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.50 **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.02 (d, *J* = 9.1 Hz, 1H, NH), 5.61 (ddd, *J* = 27.4, 11.0, 2.5 Hz, 1H, H-4), 5.29 (dd, *J* = 5.3, 2.0 Hz, 1H, H-7), 5.13 (ddd, *J* = 6.1, 5.2, 2.4 Hz, 1H, H-8), 4.97 (dd, *J* = 48.9, 2.5 Hz, 1H, H-3), 4.57 (dd, *J* = 12.5, 2.5 Hz, 1H, H-9_a), 4.38 (ddd, *J* = 10.7, 2.0, 0.8 Hz, 1H, H-6), 4.26 – 4.17 (m, 2H, H-5; H-9_b), 3.85 (s, 3H, OCH_3), 2.19 (s, 3H, CH_3,OAc), 2.18 (s, 3H, CH_3,OAc), 2.11 (s, 3H, CH_3,OAc), 2.05 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.70 (CO, Ac), 170.78 (CO, Ac), 170.76 (CO, Ac), 170.51 (CO, Ac), 167.22 (C-1), 164.94 (CO, Ac), 157.68 (q, *J* = 37.8 Hz, CO, TFA), 115.50 (q, *J* = 288.4 Hz, CF_3), 95.16 (d, *J* = 29.0 Hz, C-2), 86.90 (d, *J* = 186.1 Hz, C-3), 71.27 (C-8), 71.00 (C-6), 68.00 (d, *J* = 16.9 Hz, C-4), 67.91 (C-7), 62.06 (C-9), 53.75 (OCH_3), 46.43 (d, *J* = 2.4 Hz, C-5), 20.99 (CH_3,OAc), 20.82 (CH_3,OAc), 20.80 (CH_3,OAc), 20.60 (CH_3,OAc), 20.56 (CH_3,OAc). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{22}H_{27}F_4NNaO_{14}$, 628.12654; found, 628.12591.

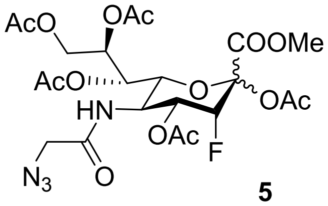


3 **Methyl 5-(chloroacetamido)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (3)**. Boc inhibitor **12** (200 mg; 329 µmol) was dissolved in a 1:1:2 mixture of DCM, H_2O and TFA (3.3 mL; 0.1 M). The mixture was stirred for 2 h at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09). The mixture was then diluted with H_2O and concentrated *in vacuo*. The residue was dissolved in DCM (3.3 mL; 0.1 M) and successively ClAcCl (39 µL; 492 µmol; 1.5 eq.) and TEA (273 µL; 1.97 mmol; 6 eq.) were added. After stirring at r.t. 16 h the mixture was concentrated *in vacuo*. The residue was dissolved in EtOAc and washed with sat. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **3** (116 mg; 198 µmol; 60 %) as a white solid. **TLC**: (EtOAc:Hept, 80:20 v/v) R_f = 0.48) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.63 (d, *J* = 8.6 Hz, 1H, NH), 5.58 (ddd, *J* = 27.5, 10.6, 2.5 Hz, 1H, H-4), 5.34 (dd, *J* = 5.2, 1.8 Hz, 1H, H-7), 5.12 (ddd, *J* = 6.4, 5.1, 2.4 Hz, 1H, H-8), 4.95 (dd, *J* = 49.0, 2.5 Hz, 1H, H-3), 4.59 (dd, *J* = 12.5, 2.5 Hz, 1H, H-9_a), 4.33 – 4.23 (m, 2H, H-6; H-5), 4.21 (dd, *J* = 12.5, 6.5 Hz, 1H, H-9_b), 4.02 – 3.93 (m, 2H, CH_2, ClAc), 3.85 (s, 3H, OCH_3), 2.19 (s, 3H, CH_3,OAc), 2.16 (s, 3H, CH_3,OAc), 2.12 (s, 3H, CH_3,OAc), 2.06 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.77 (CO, Ac), 170.66 (CO, Ac), 170.61 (CO, Ac), 170.47 (CO, Ac), 167.23 (C-1), 166.73 (CO, Ac), 165.08 (CO, ClAc), 95.28 (d, *J* = 29.0 Hz, C-2). 87.01 (d, *J* = 185.7 Hz, C-3), 71.79 (C-6), 71.50 (C-8), 68.14 (d, *J* = 17.2 Hz, C-4), 67.88 (C-7), 62.15 (C-9), 53.68 (OCH_3), 45.91 (d, *J* = 2.6 Hz, C-5), 42.56 (CH_2, ClAc), 21.03 (CH_3,Ac), 20.91 (CH_3,Ac), 20.86 (CH_3,Ac), 20.76 (CH_3,Ac), 20.66 (CH_3,Ac). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{22}H_{29}ClFNNaO_{14}$, 608.11583; found, 608.11438.

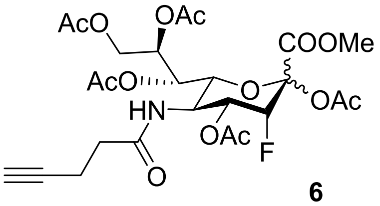


4 **Methyl 5-(acetoxyamido)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (4)**. Boc inhibitor **12** (40 mg; 66 µmol) was dissolved in a 1:1:2 mixture of DCM, H_2O and TFA (0.7 ml; 0.1 M). The mixture was stirred for 2 h

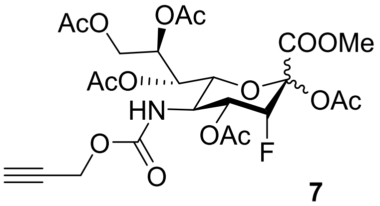
at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09). The mixture was then diluted with H_2O and concentrated *in vacuo*. The residue was dissolved in DCM (0.7 ml; 0.1 M) and successively acetoxyacetyl chloride (11 µl; 97 µmol; 1.5 eq.) and TEA (45 µl; 324 µmol; 5 eq.) were added. After stirring at r.t. 16 h the mixture was diluted with DCM and washed successively with 0.1M HCl and sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 60% EtOAc in Hept) afforded (17 mg; 28 µmol; 43%) as a white solid. **TLC**: (EtOAc:Hept, 80:20 v/v) R_f = 0.19. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.18 (d, *J* = 9.0 Hz, 1H, NH), 5.64 (ddd, *J* = 27.9, 11.0, 2.5 Hz, 1H, H-4), 5.28 (dd, *J* = 5.3, 2.0 Hz, 1H, H-7), 5.13 (ddd, *J* = 6.3, 5.2, 2.4 Hz, 1H, H-8), 4.95 (dd, *J* = 49.1, 2.5 Hz, 1H, H-3), 4.61 (d, *J* = 15.3 Hz, 1H, C***H***H Glc), 4.56 (dd, *J* = 12.5, 2.4 Hz, 1H, H-9_a), 4.32 (d, *J* = 15.3 Hz, 1H, CH***H*** Gc), 4.30 – 4.26 (m, 1H, H-6), 4.22 – 4.15 (m, 2H, H-9_b; H-5), 3.84 (s, 3H, OCH_3), 2.20 (s, 3H, CH_3,OAc), 2.19 (s, 3H, CH_3,OAc), 2.17 (s, 3H, CH_3,OAc), 2.11 (s, 3H, CH_3,OAc), 2.05 (s, 3H, CH_3,OAc), 2.05 (s, 3H, CH_3,OAc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.05 (CO, Ac), 170.88 (CO, Ac), 170.83 (CO, Ac), 170.53 (CO, Ac), 169.98 (CO, Ac), 168.03 (CO, Ac), 167.35 (CO, C-1), 165.23 (CO, NHGc), 95.38 (d, *J* = 29.0 Hz, C-2), 87.28 (d, *J* = 185.5 Hz, C-3), 71.91 (C-6), 71.41 (C-8), 68.27 (C-7), 67.98 (d, *J* = 17.1 Hz, C-4), 63.01 (CH_2, Gc), 62.20 (C-9), 53.76 (OCH_3), 45.88 (d, *J* = 2.6 Hz, C-5), 21.11 (CH_3,OAc), 21.07 (CH_3,OAc), 20.95 (CH_3,OAc), 20.85 (2xCH_3,OAc), 20.80 (CH_3,OAc). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{24}H_{32}FNNaO_{16}$, 632.16028; found, 632.15804.



5 **Methyl 5-(azidoacetamido)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (5)**. Boc inhibitor **12** (20 mg; 33 µmol) was dissolved in a 1:1:2 mixture of respectively DCM, H_2O and TFA (0.65 ml; 0.05 M). The mixture was stirred for 2 h at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09). The mixture was then diluted with water and concentrated *in vacuo*. The residue was dissolved in DCM (0.33 ml; 0.1 M) and successively AzOSu (42 mg; 167 µmol; 5 eq.), Pyr (27 µl; 334 µmol; 10 eq.) and DMAP (2 mg, 17 µmol; 0.5 eq.) were added. After stirring at r.t. for 23 h the mixture was diluted with DCM and washed successively with 0.1 M HCl and sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **5** (3.1 mg; 5.2 µmol; 16%). **TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.31 (d, *J* = 8.6 Hz, 1H, NH), 5.54 (ddd, *J* = 27.5, 10.6, 2.5 Hz, 1H, H-4), 5.34 (dd, *J* = 5.3, 1.8 Hz, 1H, H-7), 5.13 (td, *J* = 5.7, 2.4 Hz, 1H, H-8), 4.95 (dd, *J* = 49.0, 2.5 Hz, 1H, H-3), 4.55 (dd, *J* = 12.5, 2.4 Hz, 1H, H-9_a), 4.30 – 4.22 (m, 2H, H-5; H-6), 4.19 (dd, *J* = 12.6, 6.3 Hz, 1H, H-9_b), 3.94 – 3.83 (m, 5H, CH_2 NAz; OCH_3), 2.20 (s, 3H, CH_3,OAc), 2.16 (s, 3H, CH_3,OAc), 2.11 (s, 3H, CH_3,OAc), 2.05 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.94 (CO, Ac), 170.84 (CO, Ac), 170.66 (CO, Ac), 170.47 (CO, Ac), 167.52 (CO, Ac), 167.31 (C-1), 165.20 (CO, Az), 95.64 (d, *J* = 185.7 Hz, C-2), 87.16 (d, *J* = 185.7 Hz, C-3), 71.95 (C-6), 71.43 (C-8), 68.49 (d, *J* = 17.2 Hz, C-4), 68.02 (C-7), 62.16 (C-9), 53.82 (OCH_3), 52.89 (CH_2, Az), 49.50 (C-5), 21.13 (CH_3,OAc), 21.06 (CH_3,OAc), 21.00 (CH_3,OAc), 20.91 (CH_3,OAc), 20.81 (CH_3,OAc). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{22}H_{29}FN_4NaO_{14}$, 615.15620; found, 615.15758.

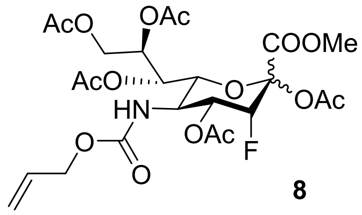


6 **Methyl 5-(4-pentynacetamido)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (6)**. Boc inhibitor **12** (50 mg; 82 µmol) was dissolved in a 1:1:2 mixture of respectively TFA, H_2O and DCM (1.6 ml; 0.05 M). The mixture was stirred for 2 h at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09). The mixture was then diluted with water and concentrated *in vacuo*. The residue was dissolved in DCM (0.83 ml; 0.1 M) and successively 4-Pentynoic acid-OSu (226 mg; 1.158 mmol; 14 eq.) and TEA (69 µl; 495 µmol; 6 eq.) were added. After stirring at r.t. 16 h the mixture was diluted with DCM and washed successively with 0.1M HCl and sat. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 55% EtOAc in Hept) afforded **6** (3.3 mg; 5.60 µmol; 7%) as a white solid. **TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.60 (ddd, *J* = 27.9, 11.0, 2.6 Hz, 1H, H-4), 5.54 (d, *J* = 9.0 Hz, 1H, NH), 5.37 (dd, *J* = 5.5, 2.0 Hz, 1H, H-7), 5.15 (ddd, *J* = 6.3, 5.4, 2.5 Hz, 1H, H-8), 4.95 (dd, *J* = 49.1, 2.5 Hz, 1H, H-3), 4.53 (dd, *J* = 12.5, 2.4 Hz, 1H, H-9_a), 4.30 – 4.26 (m, 1H, H-6), 4.21 (dd, *J* = 12.5, 6.3 Hz, 1H, H-9_b), 4.13 (q, *J* = 10.3 Hz, 1H, H-5), 3.84 (s, 3H, OCH_3), 2.56 – 2.44 (m, 2H, C***H₂***C≡CH), 2.40 – 2.27 (m, 2H, C***H₂***-CONH), 2.19 (s, 3H, CH_3,OAc), 2.16 (s, 3H, CH_3,OAc), 2.11 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc), 2.02 (t, *J* = 2.6 Hz, 1H, HC≡C). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.38 (CO, Ac), 170.85 (CO, Ac), 170.69 (CO, AC), 170.53 (CO, Ac), 170.31 (CO, Ac), 167.28 (C-1), 165.21 (CONH), 95.29 (d, *J* = 29.0 Hz, C-2), 87.12 (d, *J* = 185.1 Hz, C-3), 82.88 (HC≡***C***), 71.75 (C-6), 71.21 (C-8), 69.79 (H***C***≡C), 68.33 – 68.14 (m, C-4; C-7), 62.22 (C-9), 53.65 (OCH_3), 46.01 (C-5), 35.67 (***C***H_2CONH), 21.02 (CH_3,OAc), 20.98 (CH_3,OAc), 20.93 (CH_3,OAc), 20.92 (CH_3,OAc), 20.74 (CH_3,OAc), 14.80 (***C***H_2C≡CH). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{25}H_{32}FNNaO_{14}$, 612.17045; found, 612.16924.



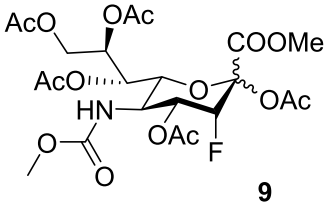
7 **Methyl 5-(propargylcarbamado)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (7).** Boc inhibitor **12** (50 mg; 82 µmol) was dissolved in a 1:1:2 mixture of respectively DCM, H_2O and TFA (1.6 ml; 0.05 M). The mixture was stirred for 2 h at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09). The mixture was then diluted with H_2O and concentrated *in vacuo*. The residue was dissolved in DCM (0.83 ml; 0.1 M) and successively PocOSu (98 mg; 497 µmol; 6 eq.) and TEA (35 µl; 248 µmol; 3 eq.) were added. After stirring at r.t. for 15 h the mixture was diluted with DCM and washed successively with 0.1 M HCl and sat. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 60% EtOAc in Hept) afforded **7** (20 mg; 83 µmol; 40%) as a white solid. **TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.36. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.53 (dd, *J* = 26.9, 10.8 Hz, 1H, H-4), 5.39 – 5.36 (m, 1H, H-7), 5.18 (td, *J* = 5.9, 2.5 Hz, 1H, H-8), 4.95 (dd, *J* = 49.1, 2.5 Hz, 1H, H-3), 4.87 (d, *J* = 9.5 Hz, 1H, NH), 4.73 (ddd, *J* = 15.5, 5.4, 2.5 Hz, 1H, C***H***H, Poc), 4.57 – 4.49 (m, 2H, C***H***H, Poc; H-9_a), 4.23 – 4.17

(m, 2H, H-9_b; H-6), 3.95 – 3.86 (m, 1H, H-5), 3.84 (s, 3H, OCH_3), 2.47 (t, *J* = 2.4 Hz, 1H, C≡CH, Poc), 2.18 (s, 3H, CH_3,OAc), 2.17 (s, 3H, CH_3,OAc), 2.13 (s, 3H, CH_3,OAc), 2.05 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.75 (CO, Ac), 170.69 (CO, Ac), 170.46 (CO, Ac), 170.24 (CO, Ac), 167.27 (C-1), 165.17 (CO, Ac), 154.75 (CO, Poc), 95.20 (d, *J* = 28.8 Hz, C-2), 87.18 (d, *J* = 185.1 Hz, C-3), 77.95 (***C***≡CH, Poc), 75.00 (C≡***C***H, Poc), 71.89 (C-6), 71.00 (C-8), 68.32 – 67.98 (m, C-4; C-7), 62.20 (C-9), 53.66 (OCH_3), 53.16 (CH_2, Poc), 47.37 (C-5), 21.00 (CH_3,OAc), 20.94 (CH_3,OAc), 20.92 (CH_3,OAc), 20.82 (CH_3,OAc), 20.72 (CH_3,OAc). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{24}H_{30}FNNaO_{15}$, 614.14972; found, 614.15007.



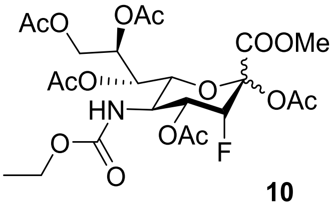
8

5-(alloxycarbamado)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (8). Boc inhibitor **12** (50 mg; 82 µmol) was dissolved in a 1:1:2 mixture of respectively TFA, H_2O and DCM (1.6 ml; 0.05 M). The mixture was stirred for 2 h at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09). The mixture was then diluted with water and concentrated *in vacuo*. The residue was dissolved in DCM (0.83 ml; 0.1 M) and Alloc-Cl (11 µl; 99 µmol; 1.2 eq.) and TEA (69 µl; 495 µmol; 6 eq.) were added. After stirring at r.t. for 1 hr additional Alloc-Cl (18 µl; 165 µmol; 2 eq.) was added. The reaction was stirred for 15 h after which the reaction was still not finished, so additional Alloc-Cl (90 µl; 844 µmol; 10.2 eq.) and TEA (35 µl; 252 µmol; 3 eq.) were added. After stirring at r.t. for 5.5 h the mixture was diluted with DCM and washed successively with 0.1M HCl and sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **8** (7.7 mg; 13 µmol; 16%) as a white solid. **TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.32. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.89 (tdd, *J* = 16.1, 8.3, 3.3 Hz, 1H, CHH=C***H***, Alloc), 5.54 (dd, *J* = 27.7, 10.9 Hz, 1H, H-4), 5.39 (dd, *J* = 5.5, 2.0 Hz, 1H, H-7), 5.28 (dd, *J* = 16.1, 2.4 Hz, 1H, C***H***H=CH, Alloc), 5.21 (d, *J* = 11.2 Hz, 1H, CH***H***=CH, Alloc), 5.18 (td, *J* = 6.0, 2.5 Hz, 1H, H-8), 4.95 (dd, *J* = 49.1, 2.5 Hz, 1H, H-3), 4.79 (d, *J* = 9.3 Hz, 1H, NH), 4.60 – 4.45 (m, 3H, H-9_a; OCH_2 Alloc), 4.24 – 4.17 (m, 2H, H-6; H-9_b), 3.94 – 3.87 (m, 1H, H-5), 3.84 (s, 3H, OCH_3), 2.18 (s, 3H, CH_3,OAc), 2.17 (s, 3H, CH_3,OAc), 2.11 (s, 3H, CH_3,OAc), 2.05 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.75 (CO, Ac), 170.66 (CO, Ac), 170.45 (CO, Ac), 170.27 (CO, Ac), 167.30 (C-1), 165.22 (CO, Ac), 155.41 (CO, Alloc), 132.65 (CH_2=***C***H, Alloc), 117.84 (***C***H_2=CH, Alloc), 95.21 (d, *J* = 28.8 Hz, C-2), 87.20 (d, *J* = 184.9 Hz, C-3), 71.98 (C-6), 71.07 (C-8), 68.17 – 67.92 (C-4; C-7), 66.09 (OCH_2, Alloc), 62.24 (C-9), 53.64 (OCH_3), 47.22 (C-5), 20.99 (CH_3,OAc), 20.93 (CH_3,OAc), 20.91 (CH_3,OAc), 20.80 (CH_3,OAc), 20.71 (CH_3,OAc). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{24}H_{32}FNNaO_{15}$, 616.16537; found, 616.16544.



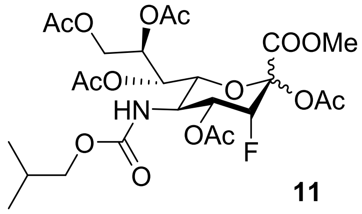
9

Methyl 5-(methylcarbamado)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (9). Boc inhibitor **12** (50 mg; 82 μmol) was dissolved in a 1:1:3 mixture of respectively TFA, water and DCM (1.6 ml; 0.05 M). The mixture was stirred for 2 h at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09). The mixture was then diluted with H_2O and concentrated *in vacuo*. The residue was dissolved in DCM (0.8 ml; 0.1 M) and Me-chloroformate (183 μl; 1.649 mmol; 20 eq.) and TEA (229 μl; 1.649 mmol; 20 eq.) were added. The reaction was stirred at r.t. 16 h after which the mixture was diluted with DCM and washed successively with 0.1M HCl and sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **9** (16 mg; 27 μmol; 33%). **TLC**: (EtOAc:Hept:MeOH, 45:45:10 v/v) R_f = 0.27. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.59 – 5.47 (m, 1H, H-4), 5.41 – 5.38 (m, 1H, H-7), 5.17 (ddd, *J* = 6.3, 5.3, 2.5 Hz, 1H, H-8), 4.95 (dd, *J* = 49.1, 2.6 Hz, 1H, H-3), 4.77 (d, *J* = 9.2 Hz, 1H, NH), 4.54 (dd, *J* = 12.5, 2.6 Hz, 1H, H-9_a), 4.25 – 4.17 (m, 2H, H-9_b; H-6), 3.88 – 3.85 (m, 1H, H-5), 3.84 (s, 3H, CH_3O-C-1), 3.64 (s, 3H, CH_3O-CONH), 2.18 (s, 3H, CH_3,OAc), 2.17 (s, 3H, CH_3,OAc), 2.12 (s, 3H, CH_3,OAc), 2.05 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.73 (2xCO, Ac), 170.45 (CO, Ac), 170.30 (CO, Ac), 167.30 (C-1), 165.21 (CO, Ac), 156.17 (NHCO), 95.20 (d, *J* = 28.7 Hz, C-2), 87.18 (d, *J* = 184.8 Hz, C-3), 72.04 (C-6), 71.20 (C-8), 68.42 – 68.16 (m, C-4; C-7), 62.26 (C-9), 53.62 (CH_3O-C-1), 52.76 (CH_3O-CONH), 47.26 (C-5), 20.99 (CH_3,OAc), 20.91 (CH_3,OAc), 20.90 (CH_3,OAc), 20.78 (CH_3,OAc), 20.68 (CH_3,OAc). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{22}H_{30}FNNaO_{15}$, 590.14972; found, 590.14874.



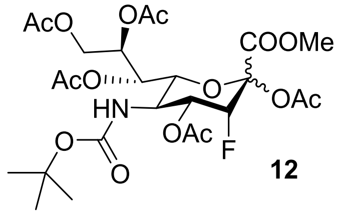
10

Methyl 5-(ethylcarbamado)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (10). Boc inhibitor **12** (50 mg; 82 μmol) was dissolved in a 1:1:3 mixture of respectively TFA, water and DCM (1.6 ml; 0.05 M). The mixture was stirred for 2 h at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09). The mixture was then diluted with water and concentrated *in vacuo*. The residue was dissolved in DCM (0.8 ml; 0.1 M) and Et-chloroformate (197 μl; 1.649 mmol; 20 eq.) and TEA (229 μl; 1.649 mmol; 20 eq.) were added. The reaction was stirred at r.t. 16 h after which the mixture was diluted with DCM and washed successively with 0.1M HCl and sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **10** (8 mg; 13 μmol; 16%). **TLC**: (EtOAc:Hept:MeOH, 45:45:10 v/v) R_f = 0.28. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.58 – 5.46 (m, 1H, H-4), 5.40 (dt, *J* = 5.0, 2.4 Hz, 1H, H-7), 5.18 (td, *J* = 5.8, 2.7 Hz, 1H, H-8), 4.95 (dd, *J* = 49.2, 2.5 Hz, 1H, H-3), 4.65 (d, *J* = 9.3 Hz, 1H, NH), 4.57 – 4.51 (m, 1H, H-9_a), 4.24 – 4.16 (m, 2H, H-9_b; H-6), 4.11 – 4.03 (m, 2H, CH_2, Et), 3.90 (d, *J* = 10.3 Hz, 1H, H-5), 3.84 (s, 3H, OCH_3), 2.18 (s, 3H, CH_3,OAc), 2.17 (s, 3H, CH_3,OAc), 2.12 (s, 3H, CH_3,OAc), 2.05 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc), 1.25 – 1.20 (m, 3H, CH_3,Et). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.73 (CO, Ac), 170.66 (CO, Ac), 170.42 (CO, Ac), 170.29 (CO, Ac), 167.27 (C-1), 165.42 (CO, Ac), 155.74 (CONH), 95.24 (d, *J* = 28.6 Hz, C-2), 87.23 (d, *J* = 184.8 Hz, C-3), 72.15 (C-6), 71.16 (C-8), 68.20 (C-4), 67.89 (C-7), 62.27 (C-9), 61.63 (CH_2, Et), 53.62 (OCH_3), 47.13 (C-5), 20.99 (CH_3,OAc), 20.93 (CH_3,OAc), 20.91 (CH_3,OAc), 20.78 (CH_3,OAc), 20.71 (CH_3,OAc), 14.62 (CH_3,Et). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{23}H_{32}FNNaO_{15}$, 604.16537; found, 604.16438.



11

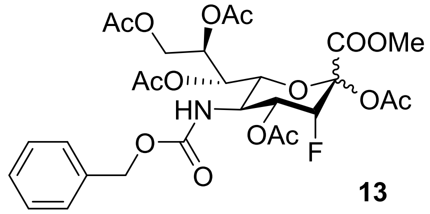
Methyl 5-(isobutylcarbamado)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (11). Boc inhibitor **12** (18 mg; 30 µmol) was dissolved in a 1:1:3 mixture of respectively TFA, H_2O and DCM (0.6 ml; 0.05 M). The mixture was stirred for 2 h at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09). The mixture was then diluted with H_2O and concentrated *in vacuo*. The mixture was redissolved in Tol and concentrated *in vacuo* three times. The residue was then dissolved in DCM (0.3 ml; 0.1 M) and ^{i}Bu chloroformate (76 µl; 589 µmol; 20 eq.) and TEA (82 µl; 589 µmol; 20 eq.) were added. The reaction was stirred at r.t. 16 h after which the mixture was diluted with DCM and washed successively with 0.1M HCl and sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **11** (6 mg; 9.8 µmol; 33%). **TLC**: (EtOAc:Hept:MeOH, 45:45:10 v/v) R_f = 0.40. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.64 – 5.49 (m, 1H, H-4), 5.42 – 5.37 (m, 1H, H-7), 5.18 (td, *J* = 6.0, 2.5 Hz, 1H, H-8), 4.95 (dd, *J* = 49.2, 2.5 Hz, 1H, H-3), 4.73 (d, *J* = 9.1 Hz, 1H, NH), 4.53 (dd, *J* = 12.5, 2.5 Hz, 1H, H-9_a), 4.25 – 4.17 (m, 2H, H-9_b; H-6), 3.92 – 3.75 (m, 6H, H-5; OCH_3; CH_2, ^{i}Bu), 2.18 (s, 3H, CH_3,OAc), 2.17 (s, 3H, CH_3,OAc), 2.11 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc), 1.95 – 1.84 (m, 1H, CH, ^{i}Bu), 0.90 (d, *J* = 6.8 Hz, 6H, 2xCH_3,^{i}Bu). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.72 (CO, Ac), 170.39 (CO, Ac), 170.21 (CO, Ac), 170.00 (CO, Ac), 167.28 (C-1), 165.24 (CO, Ac), 155.87 (CONH), 95.25 (d, *J* = 29.0 Hz, C-2), 87.24 (d, *J* = 184.8 Hz, C-3), 72.00 (C-6), 71.56 (CH_2, ^{i}Bu), 71.06 (C-8), 68.16 – 68.01 (m, C-7; C-4), 62.21 (C-9), 53.62 (OCH_3), 47.18 (C-5), 28.05 (CH_2, ^{i}Bu), 20.98 (CH_3,OAc), 20.92 (CH_3,OAc), 20.89 (CH_3,OAc), 20.75 (CH_3,OAc), 20.70 (CH_3,OAc), 19.02 (2xCH_3,^{i}Bu) **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{25}H_{36}FNNaO_{15}$, 632.19667; found, 632.19698.



12

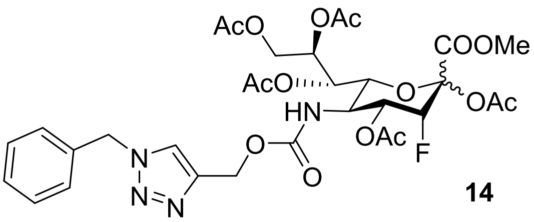
Methyl 5-(tert-butoxycarbamado)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (12). To a solution of **21** (789 mg; 1.39 mmol) in Pyr (12 ml; 148 mmol; 107 eq.), Ac_2O (6 ml; 63.6 mmol; 45.7 eq.) was slowly added. After stirring at r.t. for 24 h, the mixture was concentrated *in vacuo* using Tol for co-evaporation. The residue was dissolved in EtOAc and washed successively with HCl (0.1M) and sat. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **12** (717 mg; 1.176 mmol; 95%) as a white foam. **TLC**: (EtOAc:Hept, 50:50 v/v) R_f = 0.42 **^{1}H NMR** (500 MHz, $CDCl_3$)

δ 5.46 – 5.34 (m, 2H, H-7; H-4), 5.18 – 5.11 (m, 1H, H-8), 4.92 (dd, *J* = 49.1, 2.5 Hz, 1H, H-3), 4.60 – 4.54 (m, 1H, H-9$_a$), 4.48 (d, *J* = 9.5 Hz, 1H, NH), 4.19 (dd, *J* = 12.4, 6.6 Hz, 1H, H-9$_b$), 4.12 – 3.97 (m, 2H, H-6; H-5), 3.84 (s, 3H, OCH_3), 2.17 (s, 3H, CH_3,OAc), 2.16 (s, 3H, CH_3,OAc), 2.12 (s, 3H, CH_3,OAc), 2.05 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc), 1.40 (s, 9H, ^{t}Bu, Boc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.73 (CO, Ac), 170.48 (CO, Ac), 170.36 (CO, Ac), 170.25 (CO, Ac), 167.24 (CO, Ac), 165.28 (C-1), 154.88 (CO, Boc), 95.33 (d, *J* = 29.0 Hz, C-2), 87.21 (d, *J* = 185.1 Hz, C-3), 80.51 (***C***$(CH_3)_3$, Boc), 72.67 (C-6), 71.39 (C-8), 68.97 (d, *J* = 17.2 Hz, C-4), 68.09 (C-7), 62.32 (C-9), 53.60 (OCH_3), 46.32 (C-5), 28.27 (^{t}Bu, Boc), 21.00 (CH_3,OAc), 20.90 (CH_3,OAc), 20.86 (CH_3,OAc), 20.82 (CH_3,OAc), 20.74 (CH_3,OAc). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{25}H_{36}FNNaO_{15}$, 632.19667; found, 632.19540.

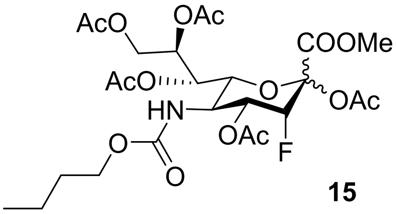


13

Methyl 5-(benzylcarbamado)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (13). Boc inhibitor **12** (50 mg; 82 µmol) was dissolved in a 1:1:2 mixture of respectively TFA, H_2O and DCM (1.6 mL; 0.05 M). The mixture was stirred for 2 h at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09). The mixture was then diluted with H_2O and concentrated *in vacuo*. The residue was dissolved in DCM (0.83 mL; 0.1 M) and Cbz-Cl (14 µl; 99 µmol; 1.2 eq.) and TEA (69 µl; 495 µmol; 6 eq.) were added. After stirring at r.t. for 1 hr additional Cbz-Cl (24 µl; 165 µmol; 2 eq.) was added. The reaction was stirred for 15 h after which the reaction was still not finished, so additional Cbz-Cl (125 µl; 874 µmol; 10.5 eq.) and TEA (35 µl; 252 µmol; 3 eq.) were added. After stirring at r.t. for 5.5 h the mixture was diluted with DCM and washed successively with 0.1M HCl and sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **13** (3.3 mg; 5.1 µmol; 6%) as a white solid. **TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.43. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 5H, 5xCH, Cbz), 5.52 (dd, *J* = 27.7, 11.0 Hz, 1H, H-4), 5.41 (dd, *J* = 5.8, 2.0 Hz, 1H, H-7), 5.18 (td, *J* = 5.9, 2.6 Hz, 1H, H-8), 5.15 (d, *J* = 12.4 Hz, 1H, C***H***H, Cbz), 5.02 – 4.88 (m, 2H, CH***H***, Cbz; H-3), 4.78 (d, *J* = 9.5 Hz, 1H, NH), 4.56 – 4.49 (m, 1H, H-9$_a$), 4.24 – 4.17 (m, 2H, H-9$_b$; H-6), 3.91 (q, *J* = 10.5 Hz, 1H, H-5), 3.83 (s, 3H, OCH_3), 2.16 (s, 3H, CH_3,OAc), 2.17 (s, 3H, CH_3,OAc), 2.03 (s, 3H, CH_3,OAc), 2.02 (s, 3H, CH_3,OAc), 1.97 (s, 3H, CH_3,OAc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.74 (CO, Ac), 170.64 (CO, Ac), 170.43 (CO, Ac), 170.20 (CO, Ac), 167.26 (C-1), 165.21 (CO, Ac), 155.54 (CO, Cbz), 136.39 (C, Cbz), 128.68 (2xCH, *ortho* Cbz), 128.36 (CH, *para* Cbz), 128.15 (2xCH, *meta* Cbz), 95.22 (d, *J* = 29.0 Hz, C-2), 87.21 (d, *J* = 184.9 Hz, C-3), 71.99 (C-6), 70.98 (C-8), 68.11 – 67.91 (m, C-4; C-7), 67.18 (CH_2, Cbz), 62.21 (C-9), 53.64 (OCH_3), 47.27 (C-5), 20.97 (CH_3,OAc), 20.94 (CH_3,OAc), 20.92 (CH_3,OAc), 20.72 (CH_3,OAc), 20.62 (CH_3,OAc). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{28}H_{34}FNNaO_{15}$, 666.18102; found, 666.18010.

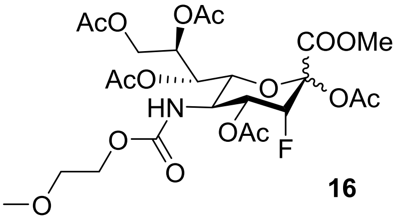


14 **Methyl 5-[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methylcarbamado]-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (14)**. To a mixture of **7** (10 mg; 17 µmol) in a 1:9 mixture of H_2O and ${}^tBuOH$ (0.19 ml; 0.09 M), Bn-N_3 (4.5 mg; 34 µmol; 2 eq.) was added. A premixture of TBTA (29 mg), DMF (750 µL) and CuI (5.1 mg) was agitated until a homogenous solution was obtained. The TBTA mixture (95 µl) was added to the H_2O/${}^tBuOH$ mixture and 10 mg of copper flakes were added. The reaction was stirred at r.t. 16 h, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 80% EtOAc in Hept) afforded **14** (5.7 mg; 17 µmol; 46%) as a white solid. **TLC**: (EtOAc:Hept, 80:20 v/v) R_f = 0.37. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.64 (s, 1H, CH, triazole), 7.37 (d, *J* = 2.2 Hz, 2H, 2xCH, *ortho* Bn), 7.32 – 7.29 (m, 2H, 2xCH, *meta* Bn), 6.91 (dd, *J* = 10.3, 6.8 Hz, 1H, CH, *para* Bn), 5.58 – 5.41 (m, 2H, CH_2, Bn), 5.34 – 5.28 (m, 1H, H-7), 5.23 – 5.05 (m, 2H, CH_2, Poc), 5.00 (d, *J* = 8.9 Hz, 1H, NH), 4.93 (dd, *J* = 49.1, 2.5 Hz, 1H, H-3), 4.50 (dd, *J* = 12.6, 2.6 Hz, 1H, H-9_a), 4.20 – 4.14 (m, 2H, H-9_b; H-6), 3.92 (q, *J* = 10.4 Hz, 1H, H-5), 3.83 (s, 3H, OCH_3), 2.16 (s, 3H, CH_3,OAc), 2.14 (s, 3H, CH_3,OAc), 2.02 (s, 3H, CH_3,OAc), 2.02 (s, 3H, CH_3,OAc), 1.97 (s, 3H, CH_3,OAc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.88 (CO, Ac), 170.72 (CO, Ac), 170.52 (CO, Ac), 170.34 (CO, Ac), 167.39 (C-1), 165.27 (CO, Ac), 155.63 (CO, Poc), 134.64 (C, Bn), 129.38 (2xCH, *meta* Bn), 129.09 (CH, *para* Bn), 128.44 (2xCH, *ortho* Bn), 125.00 (CH, triazole), 95.25 (d, *J* = 28.9 Hz, C-2), 87.21 (d, *J* = 185.0 Hz, C-3), 72.15 (C-6), 71.15 (C-8), 68.47 (d, *J* = 17.0 Hz, C-4), 68.30 (C-7), 62.30 (C-9), 58.65 (CH_2, Poc), 54.52 (CH_2, Bn), 53.74 (OCH_3), 47.22 (C-5), 21.07 (CH_3,OAc), 21.05 (CH_3,OAc), 21.01 (CH_3,OAc), 20.78 (CH_3,OAc), 20.74 (CH_3,OAc). **HR-ESI-TOF/MS** (*m/z*): $[M+Na]^+$ calcd. for $C_{31}H_{37}FN_4NaO_{15}$, 747.21371; found, 747.21371.

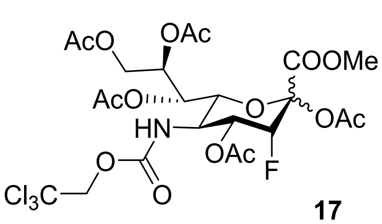


15 **Methyl 5-(butylcarbamado)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (15)**. Boc inhibitor **12** (25 mg; 41 µmol) was dissolved in DCM (1 ml; 0.041 M) and TfOH (14 µl; 164 µm; 4 eq.)) was added and stirred for 5 min at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09) then n-Bu chloroformate (27 µl; 205 µm; 5 eq.) and TEA (57 µl; 410 µm; 10 eq.) were added. The reaction was left stirring for 16 h at r.t., diluted with an excess of DCM washed successively with 0.1M HCl and sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **15** (8 mg; 41 µmol; 32%) as a white solid. **TLC**: (EtOAc) R_f = 0.90. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.54 (dd, *J* = 27.9, 11.3 Hz, 1H, H-4), 5.39 (d, *J* = 5.9 Hz, 1H, H-7), 5.18 (td, *J* = 6.0, 2.5 Hz, 1H, H-8), 4.95 (dd, *J* = 49.2, 2.5 Hz, 1H, H-3), 4.73 – 4.66 (m, 1H, NH), 4.53 (dd, *J* = 12.4, 2.6 Hz, 1H, H-9_a), 4.24 – 4.17 (m, 2H, H-9_b; H-6), 4.08 – 3.96 (m, 2H, (CO)CH_2, n-Bu), 3.93 – 3.84 (m, 1H, H-5), 3.84 (s, 3H, OCH_3), 2.18 (s, 3H, CH_3,OAc), 2.17 (s, 3H, CH_3,OAc), 2.11 (s, 3H, CH_3, OAc), 2.05 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc), 1.61 – 1.54 (m, 2H, $CH_2C\boldsymbol{H_2}CH_2$, n- Bu), 1.39 – 1.32 (m, 2H, $C\boldsymbol{H_2}CH_3$, n-Bu), 0.93

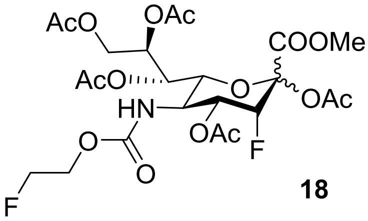
(t, *J* = 7.4 Hz, 3H, $CH_2C\boldsymbol{H}_3$, n-Bu). **^{13}C NMR** (126 MHz, Chloroform-*d*) δ 170.59 (CO, Ac), 170.45 (CO, Ac), 170.25 (CO, Ac), 170.09 (CO, Ac), 167.14 (C-1), 165.10 (CO, Ac), 155.70 (CONH), 95.09 (d, *J* = 28.8 Hz, C-2), 87.08 (d, *J* = 184.7 Hz, C-3),71.92 (C-6), 70.96 (C-8), 69.30 (d, *J* = 13.5 Hz, C-4), 68.00 (C-7), 65.31 ($C(O)\boldsymbol{C}H_2$, n-Bu), 62.09 (C-9), 53.48 (OCH_3), 46.99 (C-5), 30.85 ($CH_2\boldsymbol{C}H_2CH_2$, n-Bu), 20.84 ($CH_3$,OAc), 20.78 ($CH_3$,OAc), 20.75 ($CH_3$,OAc), 20.62 ($CH_3$,OAc), 20.56 ($CH_3$,OAc), 18.93 ($\boldsymbol{C}H_2CH_3$, n-Bu), 13.68 ($CH_2\boldsymbol{C}H_3$, n-Bu). **^{19}F NMR** (470 MHz, $CDCl_3$) δ -209.10 (dd, *J* = 49.1, 27.9 Hz). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{25}H_{36}FN_4NaO_{15}$, 632.19667; found, 632.19640.



16 **Methyl 5-(2-methoxy-ethylcarbamado)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (16)**. Boc inhibitor **12** (40 mg; 66 µmol) was dissolved in DCM (1 ml; 0.066 M) and TfOH (23 µl; 262 µm; 4 eq.)) was added and stirred for 5 min at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09) then 2-methoxyethyl chloroformate (38 µl; 328 µm; 5 eq.) and TEA (91 µl; 656 µm; 10 eq.) were added. The reaction was left stirring for 16 h at r.t., diluted with an excess of DCM washed successively with 0.1M HCl and sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **16** (36 mg; 66 µmol; 90%) as a white solid. **TLC**: (EtOAc) R_f = 0.80.**^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.51 (ddd, *J* = 27.9, 11.1, 3.1 Hz, 1H, H-4), 5.39 (dd, *J* = 5.7, 1.9 Hz, 1H, H-7), 5.21 – 5.14 (m, 1H, H-8), 4.95 (dd, *J* = 49.1, 2.5 Hz, 1H, H3), 4.86 (d, *J* = 9.1 Hz, 1H, NH), 4.52 (dd, *J* = 12.5, 2.6 Hz, 1H, H-9a), 4.23 – 4.15 (m, 4H, H-9b, H-6, $CH_2C\boldsymbol{H_2}C(O)$), 3.92 – 3.86 (m, 1H, H-5), 3.83 (s, 3H, $COOCH_3$), 3.55 (ddd, *J* = 6.6, 5.2, 2.7 Hz, 2H, $CH_3OC\boldsymbol{H_2}CH_2$), 3.37 (s, 3H, OCH_3), 2.17 (s, 3H, CH_3, OAc), 2.15 (s, 3H, CH_3, OAc), 2.11 (s, 3H, CH_3, OAc), 2.04 (s, 3H, CH_3, OAc), 2.03 (s, 3H, CH_3, OAc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.61 (CO), 170.44 (CO), 170.26 (CO), 170.04 (CO), 167.17 (CO), 165.07 (CO), 155.43 (CONH), 95.05 (d, *J* = 28.9 Hz, C-2), 87.01 (d, *J* = 184.8 Hz, C-3), 71.82 (C-6), 70.66 (C-8), 70.61 $CH_2\boldsymbol{C}H_2C(O)$, 68.16 (d, *J* = 17.1 Hz, C-4), 67.98 (C-7), 64.46 ($CH_3O\boldsymbol{C}H_2CH_{2)}$, 62.06 (C-9), 58.87 ($OCH_3$), 53.47 ($COO\boldsymbol{C}H_3$), 46.99 (C-5), 20.83 ($CH_3$, OAc), 20.78 ($CH_3$, OAc), 20.76 ($CH_3$, OAc), 20.63 ($CH_3$, OAc), 20.56 ($CH_3$, OAc). **^{19}F NMR** (470 MHz, $CDCl_3$) δ -209.21 (dd, *J* = 49.2, 27.9 Hz). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{24}H_{34}FNNaO_{16}$, 634.17593; found, 634.17656.

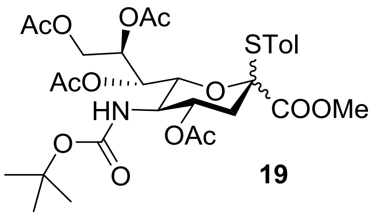


17 **Methyl 5-(2,2,2-trichloroethylcarbamado)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (17)**. Boc inhibitor **12** (27 mg; 44 µmol) was dissolved in DCM (1 ml; 0.044 M) and TfOH (16 µl; 262 µm; 4 eq.)) was added and stirred for 5 min at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09) TrocCl (31 µl; 221 µm; 5 eq.) and TEA (62 µl; 443 µm; 10 eq.) were added. The reaction was left stirring for 16 h at r.t., diluted with an excess of DCM washed successively with 0.1M HCl and sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **17** (5.2 mg; 66 µmol; 17%) as a white solid. **TLC**: (EtOAc) R_f = 0.85. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.67 (ddd, *J* = 27.9, 11.1, 2.5 Hz, 1H, H-4), 5.37 (dd, *J* = 6.3, 1.7 Hz, 1H, H-7), 5.26 – 5.16 (m, 2H, NH, H-8), 4.97 (dd, *J* = 49.1, 2.5 Hz, 1H, H3), 4.91 (d, 1H, C*H*H Troc), 4.53 (d, *J* = 12.1 Hz, 1H, CH*H* Troc), 4.49 (dd, *J* = 12.6, 2.5 Hz, 1H, H-9a), 4.29 (d, *J* = 10.4 Hz, 1H, H-6), 4.23 (dd, *J* = 12.6, 5.6 Hz, 1H, H-9b), 3.84 (s, 3H, OCH_3), 3.83 – 3.78 (m, 1H, H-5), 2.18 – 2.17 (m, 6H, 2xCH_3, OAc), 2.17 (s, 3H, CH_3, OAc), 2.04 (s, 3H, CH_3, OAc), 2.04 (s, 3H, CH_3, OAc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.75 (CO), 170.56 (CO), 170.12 (CO), 169.87(CO), 167.04 (CO), 164.93 (CO), 153.75 (CONH), 95.05 (d, *J* = 28.9 Hz, C-2), 86.97 (d, *J* = 184.9 Hz, C-3), 95.11 (CCl_3 Troc), 74.33 (CH_2 Troc), 70.99 (C-6), 70.50 (C-8), 67.85 (C-7), 67.62 (d, *J* = 17.5 Hz, C-4), 61.84 (C-9), 53.50 (OCH_3), 47.43 (C-5), 30.93 (CH_3, OAc), 20.79 (CH_3, OAc), 20.73 (CH_3, OAc), 20.65 (CH_3, OAc), 20.52 (CH_3, OAc). **^{19}F NMR** (470 MHz, $CDCl_3$) δ -209.54 (dd, *J* = 49.1, 27.7 Hz). **HR-ESI-TOF/MS** (*m/z*): $[M+Na]^+$ calcd. for $C_{23}H_{29}Cl_3FNNaO_{15}$, 706.04845; found, 706.04999.



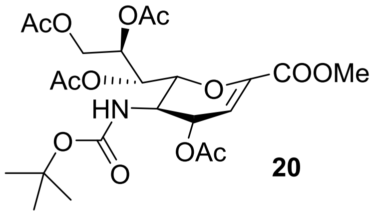
18

Methyl 5-(2-fluoroethylcarbamado)-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (18). Boc inhibitor **12** (27 mg; 44 µmol) was dissolved in DCM (1 ml; 0.044 M) and TfOH (16 µl; 262 µm; 4 eq.)) was added and stirred for 5 min at r.t. (**TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.09) 2-fluoroethyl chloroformate (21 µl; 221 µm; 5 eq.) and TEA (62 µl; 443 µm; 10 eq.) were added. The reaction was left stirring for 16 h at r.t., diluted with an excess of DCM washed successively with 0.1M HCl and sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **18** (16 mg; 66 µmol; 60%) as a white solid. **TLC**: (EtOAc) R_f = 0.85. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.51 (ddd, *J* = 27.9, 11.0, 2.5 Hz, 1H, H-4), 5.40 (dd, *J* = 5.4, 2.0 Hz, 1H, H-7), 5.17 (td, *J* = 5.9, 2.5 Hz, 1H, H-8), 4.95 (dd, *J* = 49.1, 2.5 Hz, 1H, H3), 4.94 (d, *J* = 9.4 Hz, 1H, NH), 4.67 – 4.46 (m, 3H, FC***H₂***CH₂, H-9a), 4.41 – 4.24 (m, 2H FCH₂C***H₂***), 4.25 – 4.16 (m, 2H, H-9b, H-6), 4.00 – 3.89 (m, 1H, H-5), 3.84 (s, 3H, OCH_3), 2.18 (s, 3H, CH_3, OAc), 2.16 (s, 3H, CH_3, OAc), 2.12 (s, 3H, CH_3, OAc), 2.05 (s, 3H, CH_3, OAc), 2.04 (s, 3H, CH_3, OAc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.63 (CO), 170.48 (CO), 170.37 (CO), 170.12 (CO), 167.13 (CO), 165.04 (CO), 155.24 (CONH), 95.07 (d, *J* = 28.7 Hz, C-2), 87.03 (d, *J* = 185.2 Hz, C-3), 81.60 (d, *J* = 170.2 Hz, F***C***H₂CH₂), 71.91 (C-6), 71.00 (C-8), 68.21 (d, *J* = 17.3 Hz, C-4), 67.96 (C-7) 64.29 (d, *J* = 19.9 Hz, FCH₂***C***H₂), 62.02 (C-9), 53.50 (OCH_3), 47.05 (C-5), 20.83 (CH_3, OAc), 20.77 (CH_3, OAc), 20.75 (CH_3, OAc), 20.57 (CH_3, OAc), 20.54 (CH_3, OAc). **^{19}F NMR** (470 MHz, $CDCl_3$) δ -209.07 (dd, *J* = 49.1, 27.9 Hz). **HR-ESI-TOF/MS** (*m/z*): $[M+Na]^+$ calcd. for $C_{23}H_{31}F_2NNaO_{15}$, 622.15594; found, 622.15531.



19

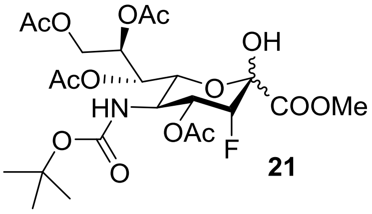
Methyl 5-(tert-butoxycarbamado)-4,7,8,9-penta-O-acetyl-2,3,5-dideoxy-2-para-methylthiophenol-D-glycero-β-galacto-non-2-ulopyranosonate (19). As described previously[8], thiocresol protected *N*Boc methyl ester sialic acid (8.39 g; 17.2 mmol) was dissolved in pyr (62 ml; 764 mmol; 44.4 eq.). Ac_2O (36 ml; 382 mmol; 22.2 eq.) was slowly added. After stirring at r.t. for 7 h, the mixture was concentrated *in vacuo* using Tol for co-evaporation. The residue was dissolved in EtOAc and washed successively with HCl (0.1 M) and sat. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$ and filtered and concentrated *in vacuo.* Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **19** (10.26 g; 15.6 mmol; 91%) as a white foam. **TLC**: (EtOAc:Hept, 50:50 v/v) R_f = 0.47 **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.32 (d, J = 7.7 Hz, 2H, 2xCH, *meta* STol), 7.14 (d, J = 7.7 Hz, 2H, 2xCH, *ortho* STol), 5.55 (t, J = 2.6 Hz, 1H, H-7), 5.33 (td, J = 11.1, 4.8 Hz, 1H, H-4), 5.01 (dt, J = 8.5, 2.5 Hz, 1H, H-8), 4.55 (dd, J = 10.5, 2.6 Hz, 1H, H-6), 4.51 (dd, J = 12.2, 2.3 Hz, 1H, H-9$_a$), 4.45 (d, J = 10.7 Hz, 1H, NH), 4.04 (dd, J = 12.2, 8.5 Hz, 1H, H-9$_b$), 3.79 (q, J = 10.6 Hz, 1H, H-5), 3.61 (s, 3H, OCH_3), 2.67 (dd, J = 13.8, 4.8 Hz, 1H, H-3$_{eq}$), 2.34 (s, 3H, CH_3,STol), 2.10 (s, 3H, CH_3,OAc), 2.08 (s, 3H, CH_3,OAc), 2.04 (s, 4H, H-3$_{ax}$; CH_3,OAc), 1.97 (s, 3H, CH_3,OAc), 1.40 (s, 9H, ^{t}Bu, Boc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.98 (CO, OAc), 170.61 (CO, OAc), 170.43 (CO, OAc), 169.93 (CO, OAc), 168.48 (C-1), 155.35 (CO, Boc), 140.22 (***C***-CH_3,STol) 136.38 (2xCH, *meta* STol), 129.99 (2xCH *ortho* STol), 125.41 (C-S, STol), 88.87 (C-2), 80.29 (***C***$(CH_3)_3$, Boc), 73.34 (C-6), 72.90 (C-8), 69.51 (C-4), 69.12 (C-7), 62.92 (C-9), 52.68 (OCH_3), 50.96 (C-5), 37.59 (C-3), 28.28 (^{t}Bu, Boc), 21.44 (CH_3,STol), 21.21 (CH_3,OAc), 20.94 (CH_3,OAc), 20.83 (CH_3,OAc), 20.82 (CH_3,OAc). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{30}H_{41}NNaO_{13}S$, 678.21963; found, 678.21799.



20

methyl 5-(tert-butoxycarbamado]-4,7,8,9-tetra-O-acetyl-2,6-anhydro-3,5-dideoxy-D-glycero-D-galacto-non-2-enonate (20). To a solution of **19** (2.757 g; 4.22 mmol) in DCM (42.2 ml; 0.1 M), slowly Br_2 (0.239 ml; 4.64 mmol; 1.1 eq.) was added. After 2.5 h stirring at r.t., the reaction was diluted with DCM and washed with 10% $Na_2S_2O_3$. The milky organic layer was dried over $MgSO_4$, filtered and the clear filtrate was extracted once more with 10% $Na_2S_2O_3$ aq. before drying over $MgSO_4$, filtering. The filtrate was concentrated *in vacuo*, redissolved in DCM (42.0 ml; 0.1 M) and TEA (1.699 g; 16.79 mmol; 4 eq.) was added. The reaction was stirred 16 h at r.t. and concentrated *in vacuo*. The residue was dissolved in EtOAc and washed successively with HCl (0.1 M) and sat. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and again concentrated *in vacuo*. Silicagel flash column chromatography (0% → 45% EtOAc in Hept) afforded **20** (1.734 g; 3.26 mmol; 78% *two steps*) as a white solid. **TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.62 **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.99 (d, J = 3.1 Hz, 1H, H-3), 5.55 (t, J = 4.3 Hz, 1H, H-7), 5.47 (dd, J = 7.5, 3.1 Hz, 1H, H-4), 5.37 (ddd, J = 6.8, 4.9, 3.4 Hz, 1H, H-8), 4.65 (d, J = 9.9 Hz, 1H, NH), 4.60 (dd, J = 12.3, 3.4 Hz, 1H, H-9$_a$), 4.33 (dd, J = 9.0, 3.8 Hz, 1H, H-6), 4.19 (dd, J = 12.2, 6.8 Hz, 1H, H-9$_b$), 4.09 (q, J = 8.9 Hz, 1H, H-5), 3.80 (s, 3H,

OCH_3), 2.13 (s, 3H, CH_3,OAc), 2.08 (s, 3H, CH_3,OAc), 2.06 (s, 3H, CH_3,OAc), 1.41 (s, 9H, ^{t}Bu, Boc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.73 (CO, Ac), 170.68 (CO, Ac), 170.05 (CO, Ac), 169.91 (CO, Ac), 161.78 (C-1), 154.98 (CO, Boc), 145.15 (C-2), 108.11 (C-3), 80.57 (***C***$(CH_3)_3$, Boc), 76.94 (C-6), 70.58 (C-8), 68.60 (C-4), 67.92 (C-7), 62.10 (C-9), 52.66 (OCH_3), 48.01 (C-5), 28.27 (^{t}Bu, Boc), 20.96 (CH_3,OAc), 20.91 (CH_3,OAc), 20.85 (CH_3,OAc), 20.80 (CH_3,OAc). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{23}H_{33}NNaO_{13}$, 554.18496; found, 554.18611.



21

Methyl 5-(tert-butoxycarbamado)-4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-fluoro-D-glycero-β-galacto-non-2-ulopyranosonate (21). To a solution of **20** (1.724 g; 3.24 mmol) in a 1:3 mixture of H_2O and DMF (32 ml; 0.1 M), Selectfluor (3.45 g; 9.73 mmol; 3 eq.) was added. The reaction was stirred at 60 ˚C for 3 h. The mixture was quenched with sat. aq. $NaHCO_3$ and concentrated *in vacuo*- even though conversion was incomplete. The residue was dissolved in EtOAc and washed successively with HCl (0.1M) and sat. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Silicagel flash column chromatography (0% → 50% EtOAc in Hept) afforded **21** (789 mg; 1.39 mmol; 72% based on recovery of starting material) as a white foam. **TLC**: (EtOAc:Hept, 60:40 v/v) R_f = 0.47 **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.52 (s, 1H, OH), 5.47 (dd, J = 4.4, 2.3 Hz, 1H, H-7), 5.37 – 5.23 (m, 2H, H-8; H-4), 4.94 (d, J = 10.3 Hz, 1H, NH), 4.92 (dd, J = 49.8, 2.1 Hz, 1H, H-3), 4.81 (dd, J = 12.3, 2.5 Hz, 1H, H-9_a), 4.26 (dd, J = 10.6, 2.3 Hz, 1H, H-6), 4.18 – 4.08 (m, 2H, H-5; H-9_b), 3.85 (s, 3H, OCH_3), 2.16 (s, 3H, CH_3,OAc), 2.09 (s, 3H, CH_3,OAc), 2.09 (s, 3H, CH_3,OAc), 2.04 (s, 3H, CH_3,OAc), 1.40 (s, 9H, ^{t}Bu, Boc). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.68 (CO, Ac), 171.48 (CO, Ac), 170.60 (CO, Ac), 170.19 (CO, Ac), 167.70 (C-1), 155.22 (CO, Boc), 94.45 (d, J = 25.5 Hz, C-2), 87.06 (d, J = 185.1 Hz, C-3), 80.09 (***C***$(CH_3)_3$, Boc), 71.91 (C-8), 71.46 (C-6), 69.96 (d, J = 17.3 Hz, C-4), 68.63 (C-7), 63.01 (C-9), 53.50 (OCH_3), 46.36 (C-5), 28.31 (^{t}Bu, Boc), 21.13 (CH_3,OAc), 20.99 (CH_3,OAc), 20.85 (CH_3,OAc), 20.78 (CH_3,OAc). **HR-ESI-TOF/MS** (*m*/*z*): $[M+Na]^+$ calcd. for $C_{23}H_{34}FNNaO_{14}$, 590.18610; found, 590.18498.

References and Notes

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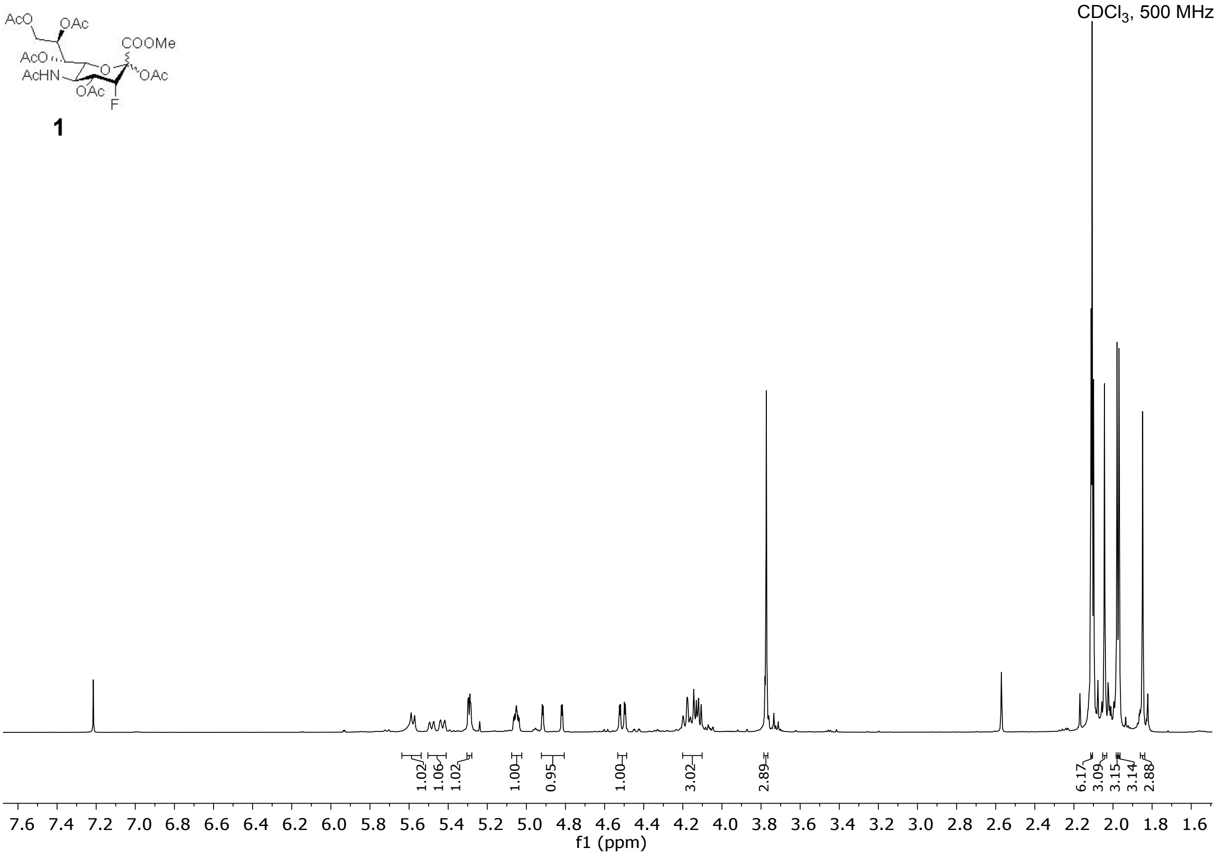
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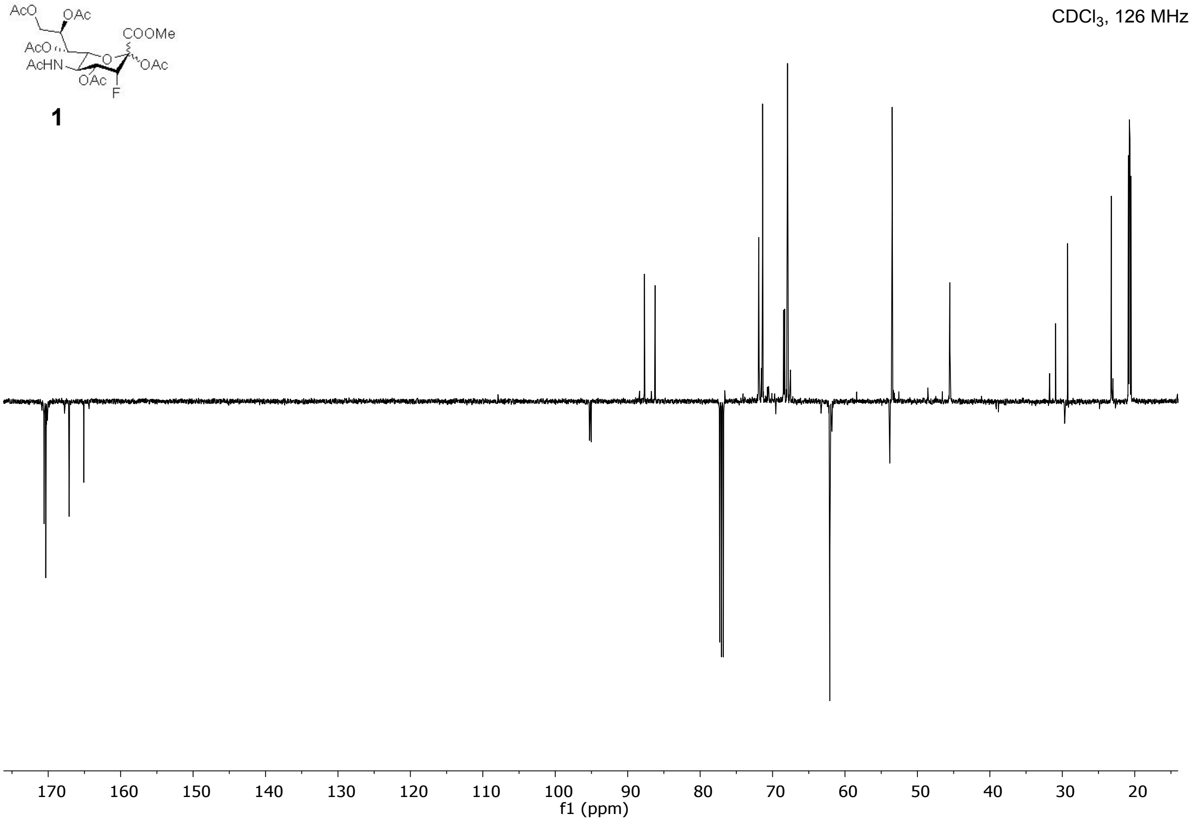
1.02
1.00
0.95
1.00
3.02
2.89
6.17
3.09
3.15
3.14
2.88
7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6
f1 (ppm)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COOMe
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OAc
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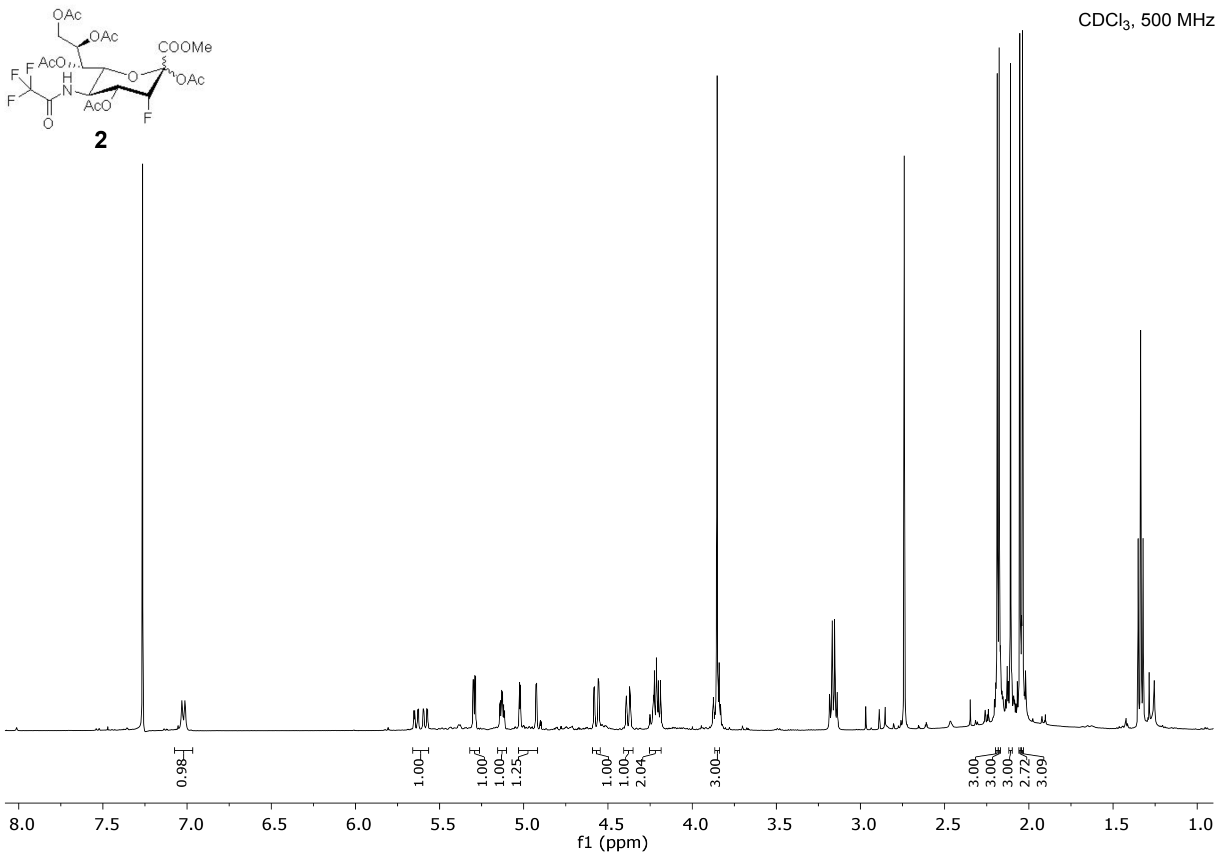
f1 (ppm)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1.00
1.00
1.00
1.25
1.00
1.00
2.04
3.00
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3.00
3.00
2.72
3.09
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7.5
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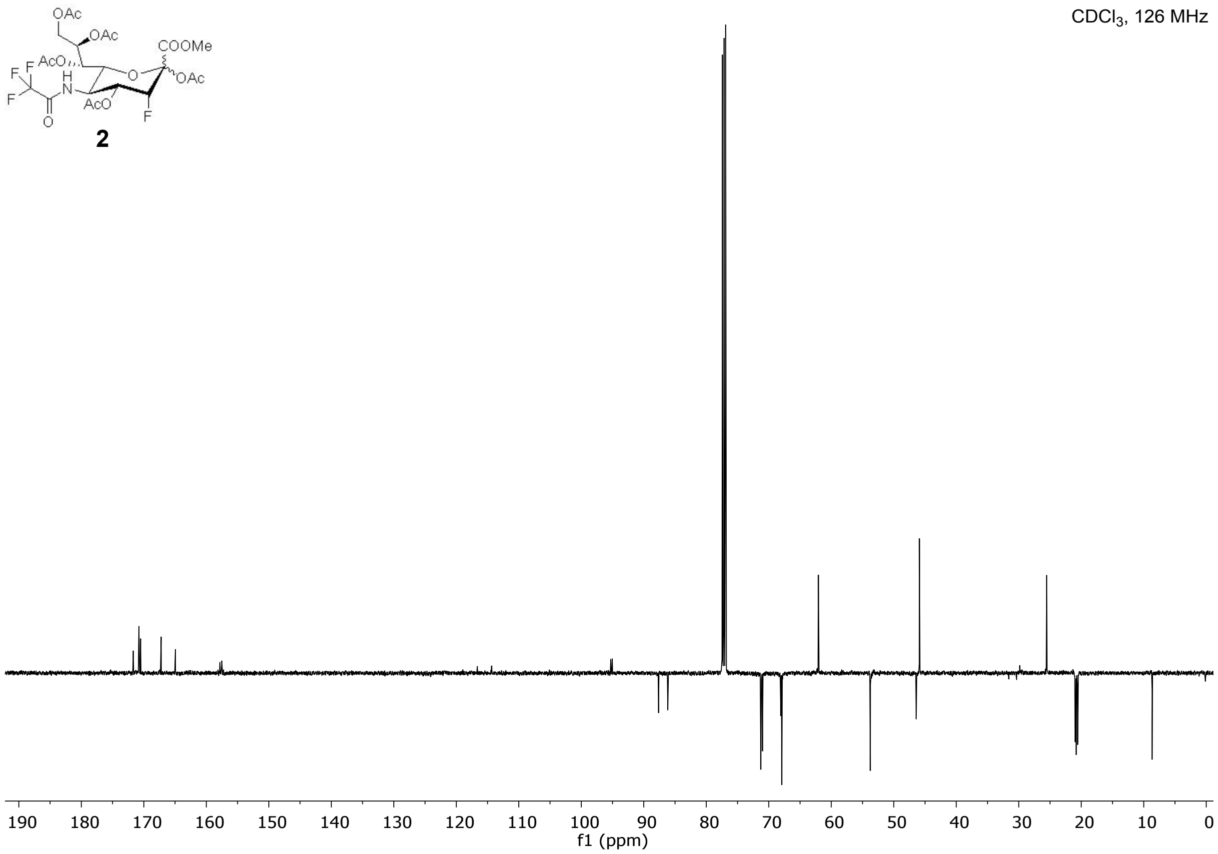
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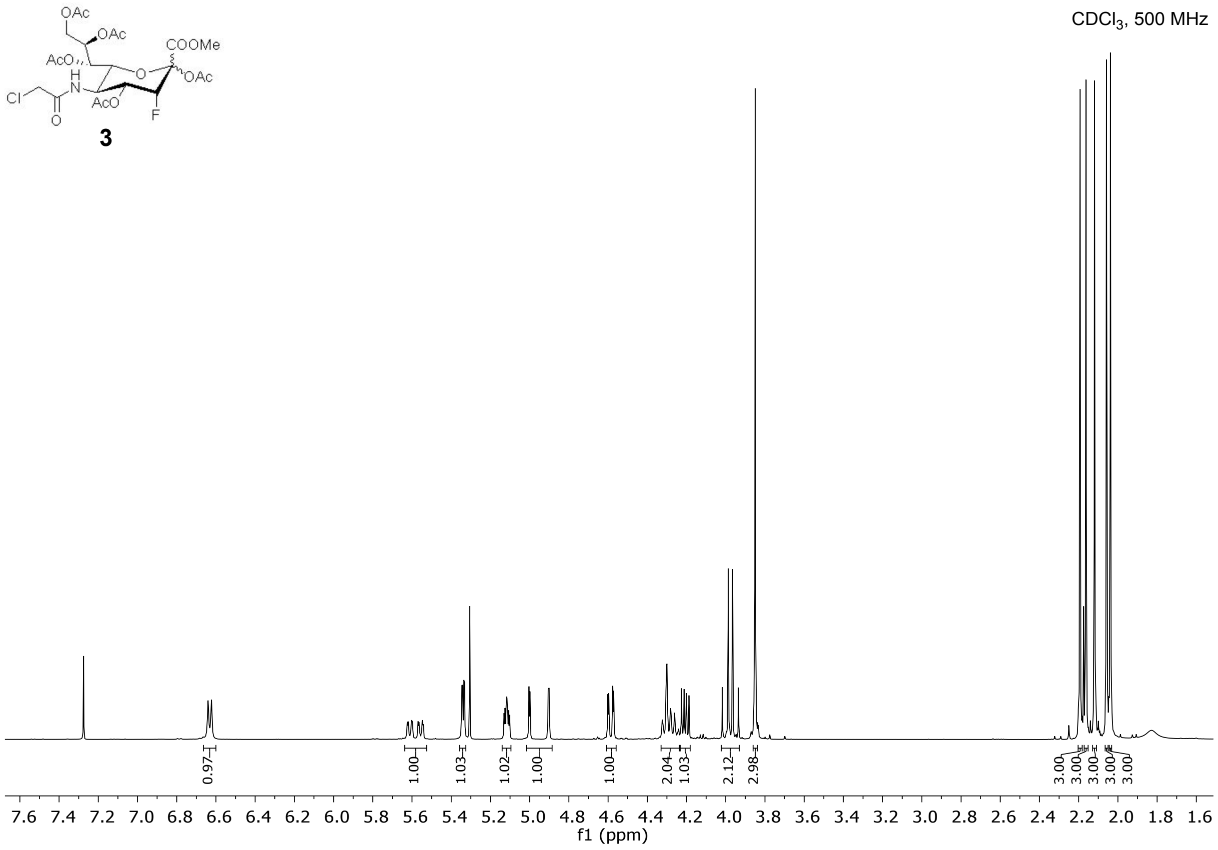
f1 (ppm)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1.02
1.00
1.00
2.04
1.03
2.12
2.98
3.00
3.00
3.00
3.00
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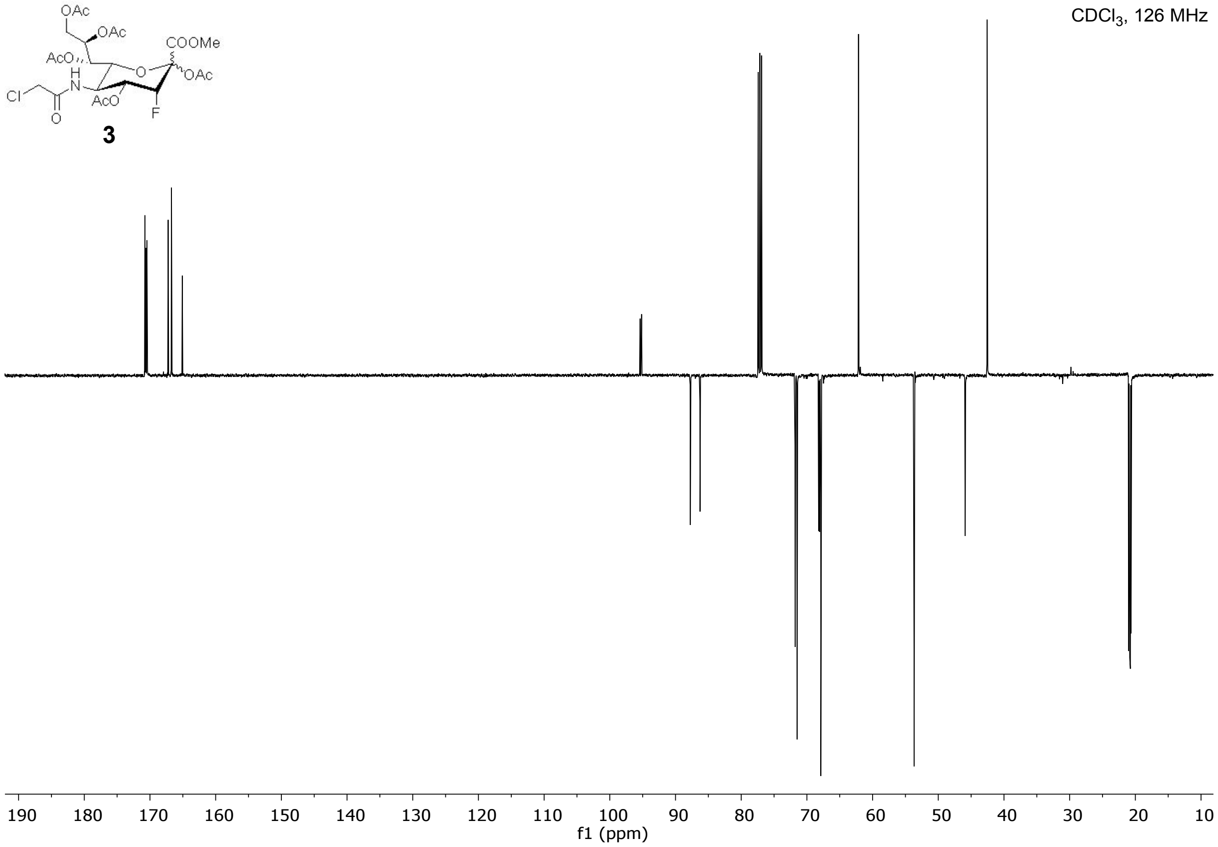
f1 (ppm)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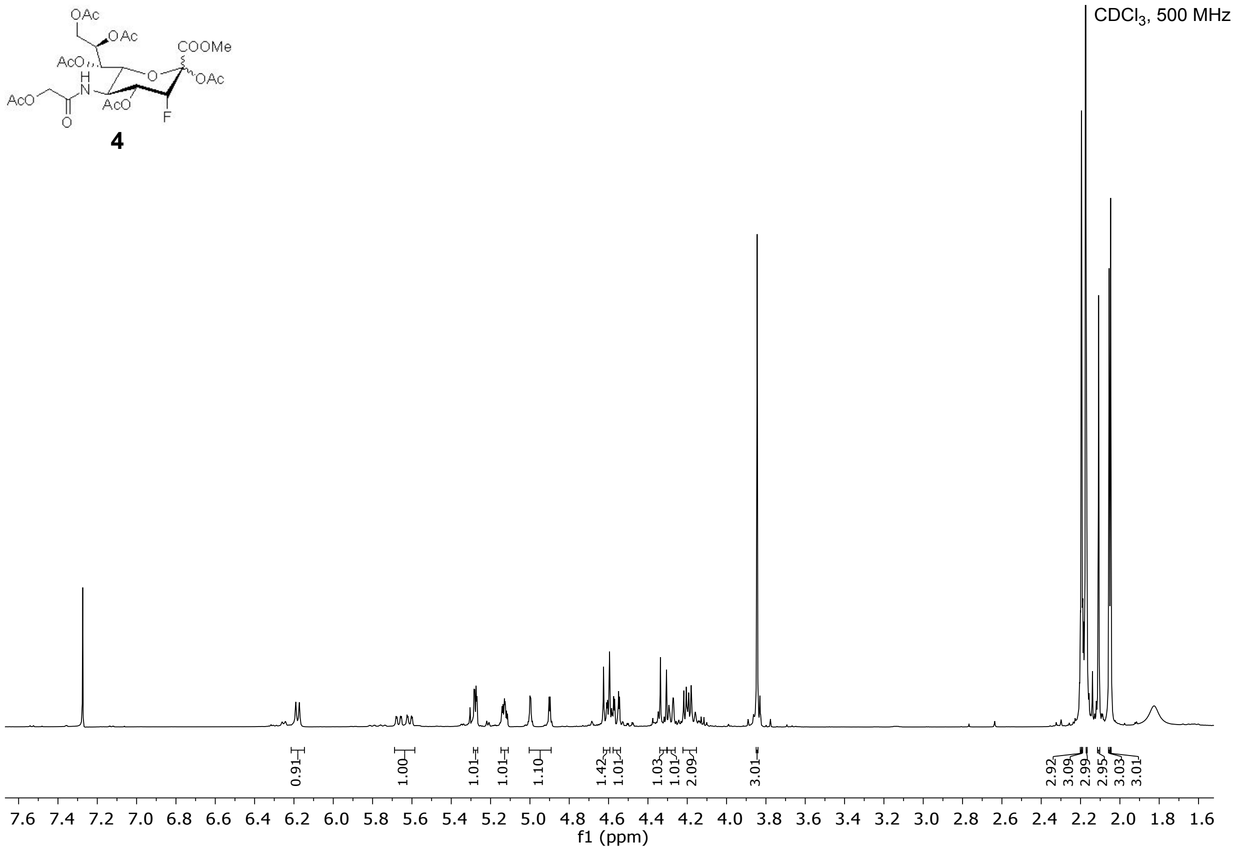
f1 (ppm)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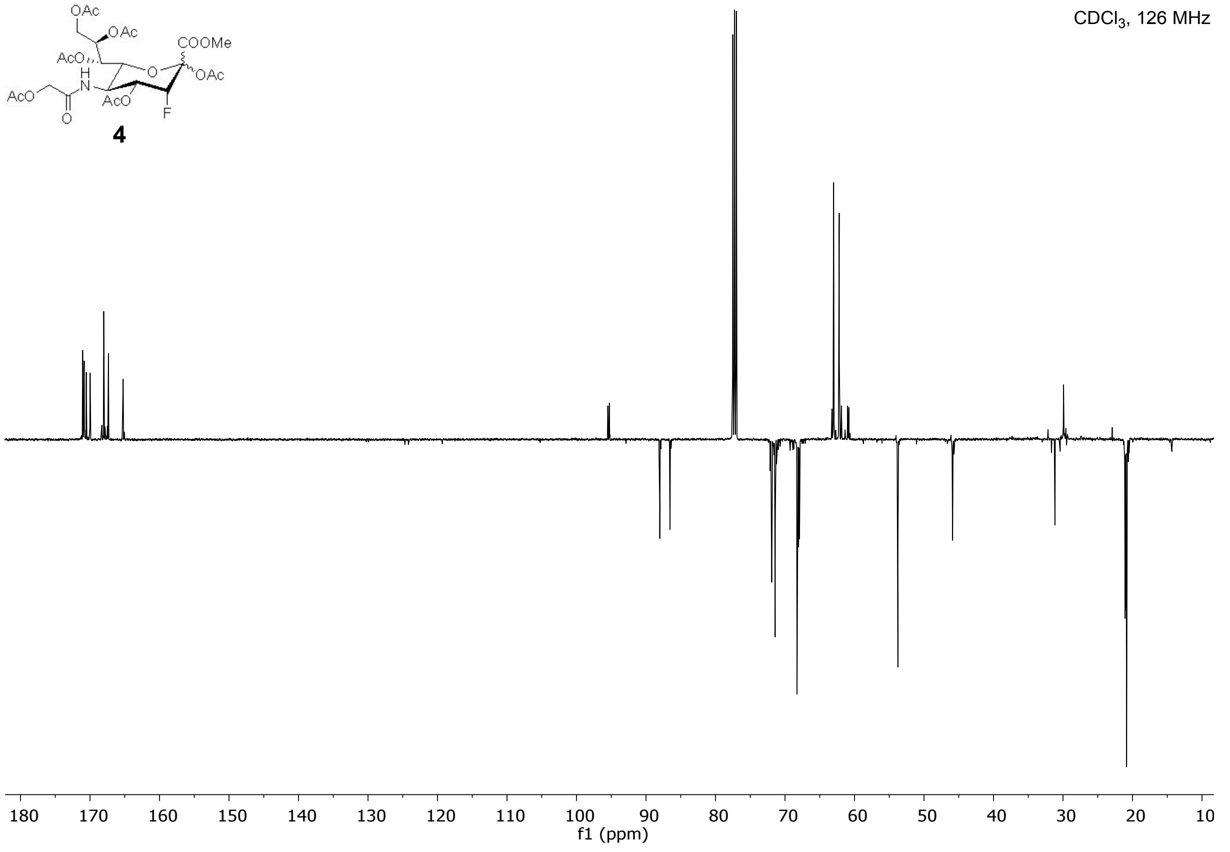
f1 (ppm)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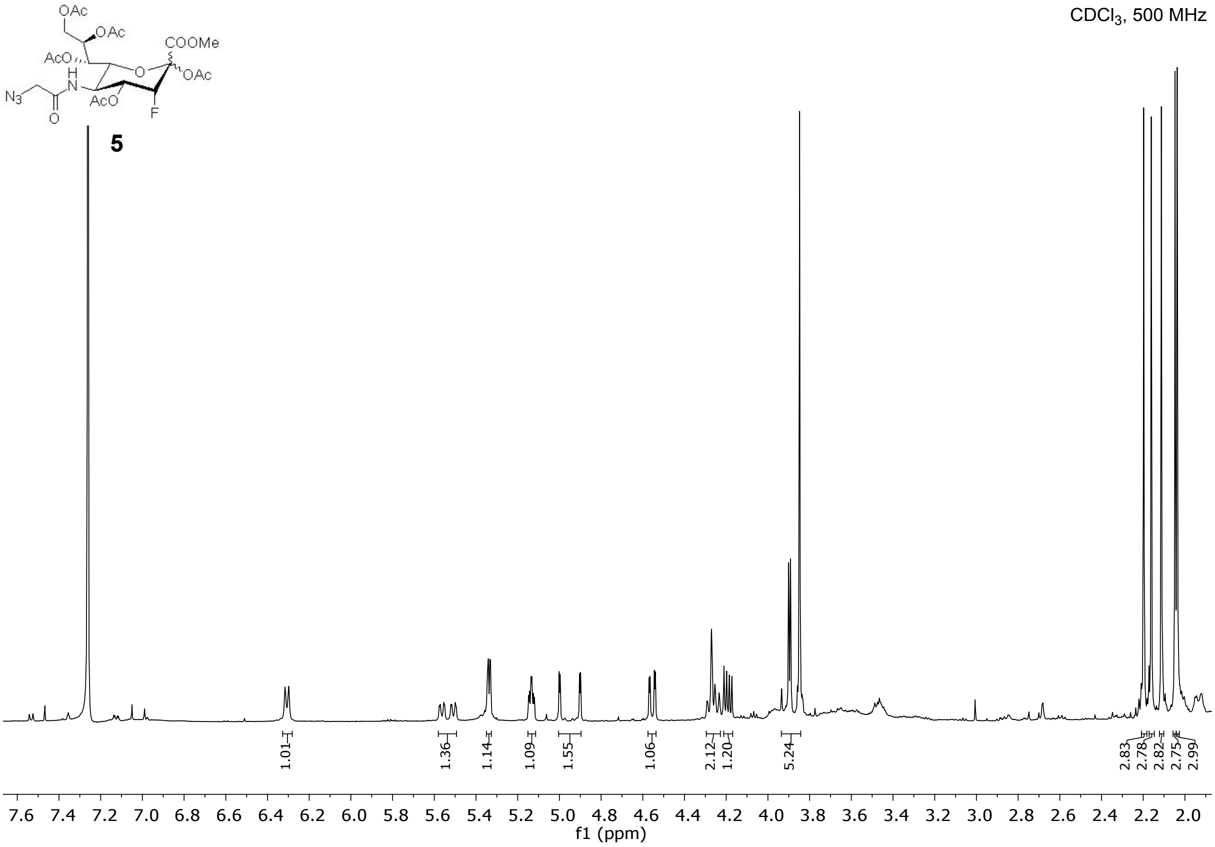
f1 (ppm)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1.09
1.55
1.06
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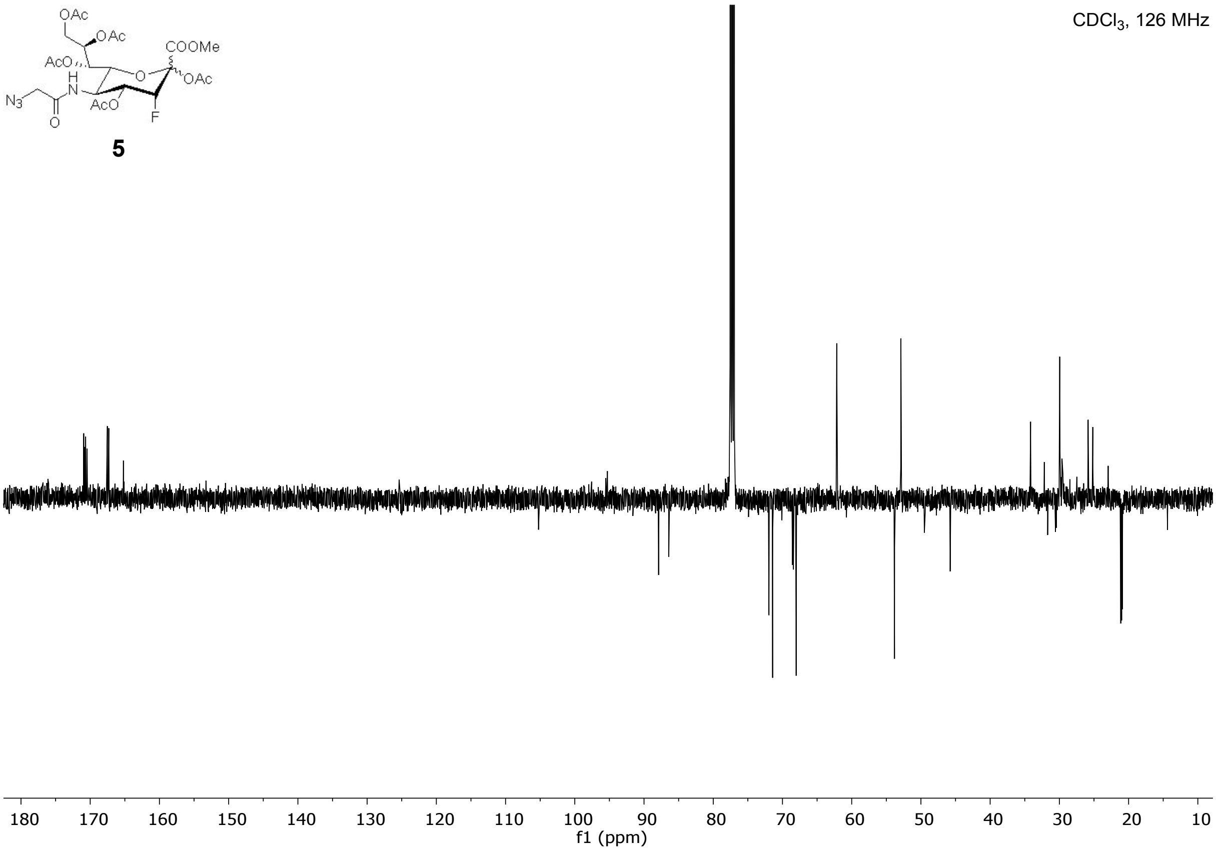
1.20
5.24
2.83
2.78
2.82
2.75
2.99
7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0
f1 (ppm)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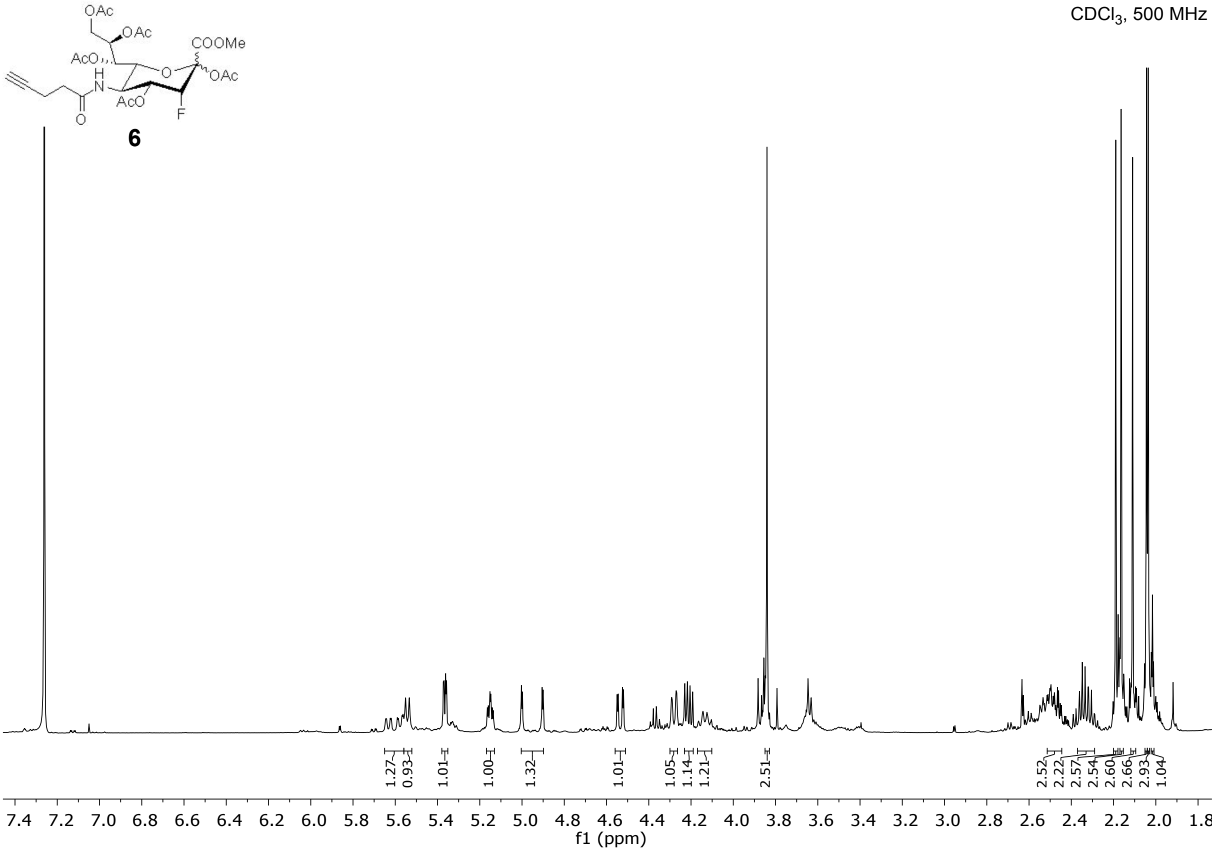
f1 (ppm)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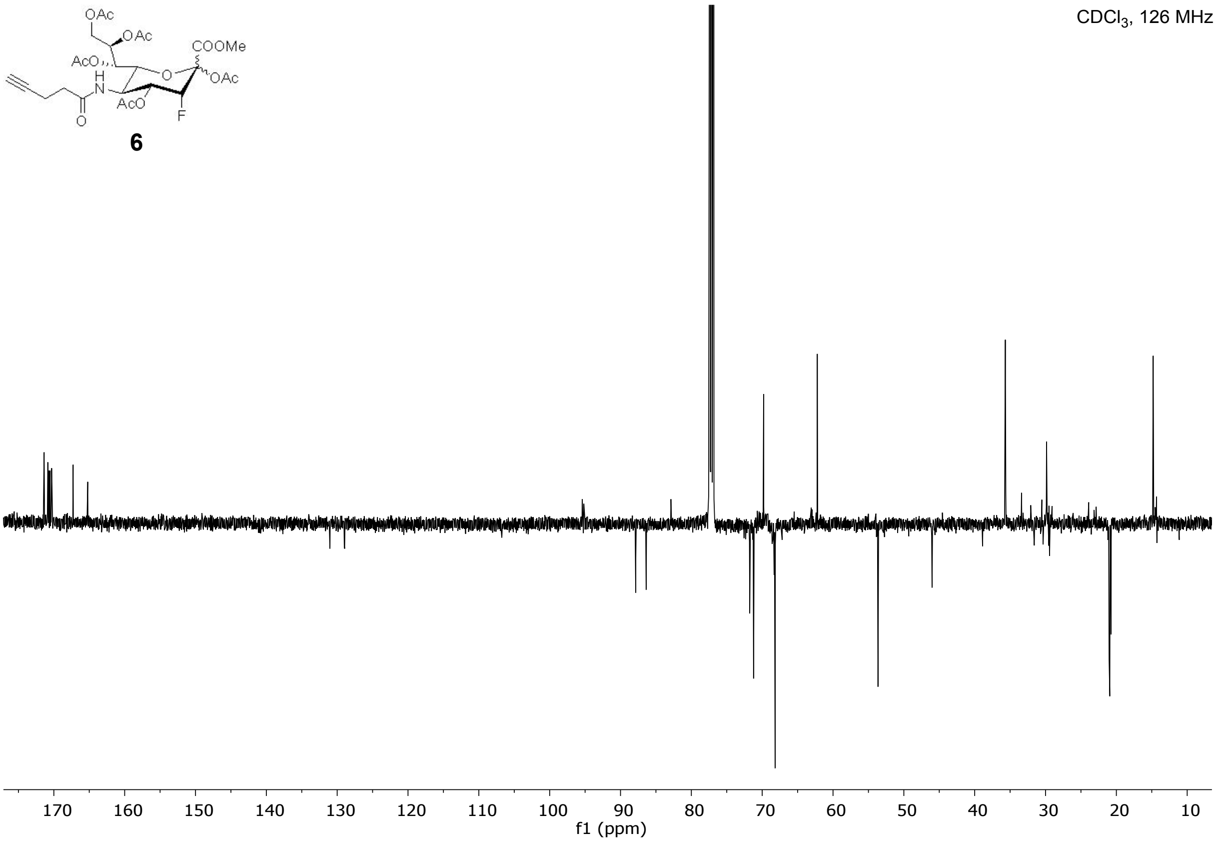
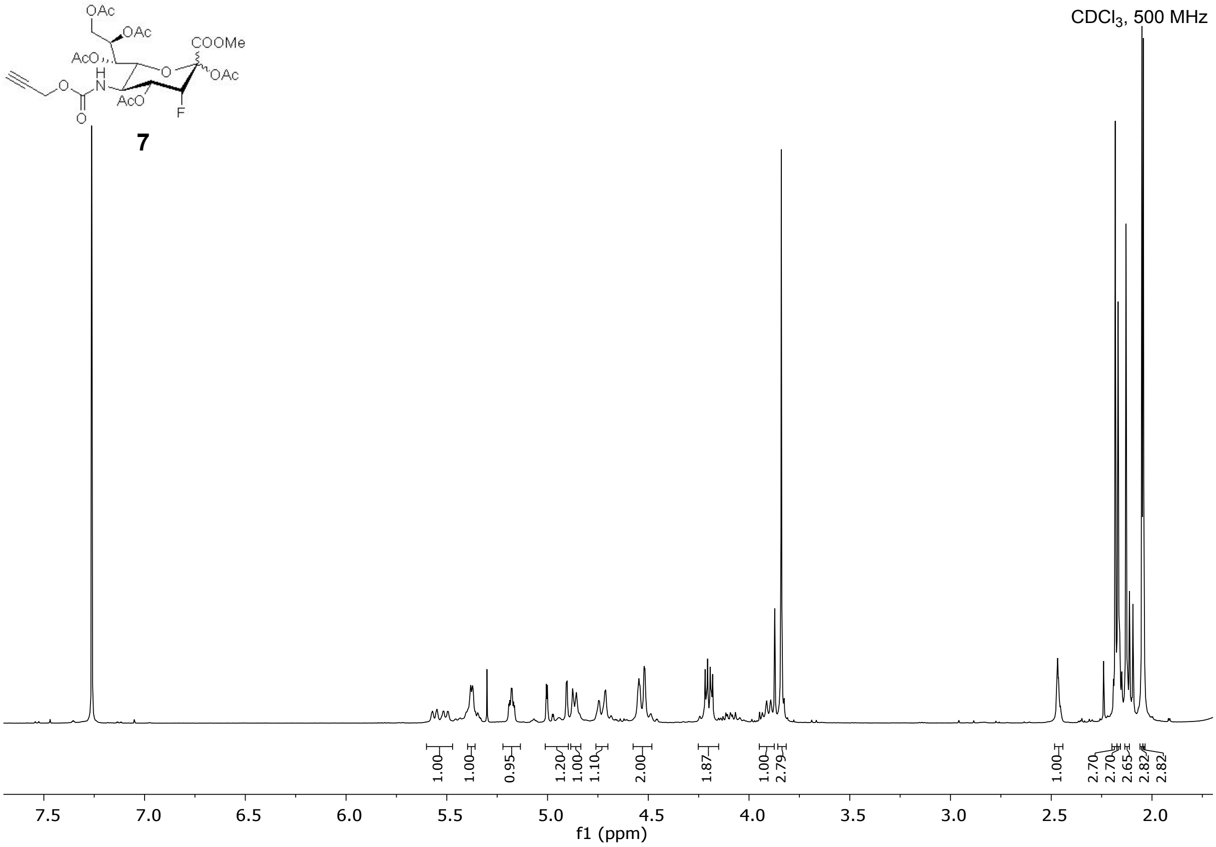
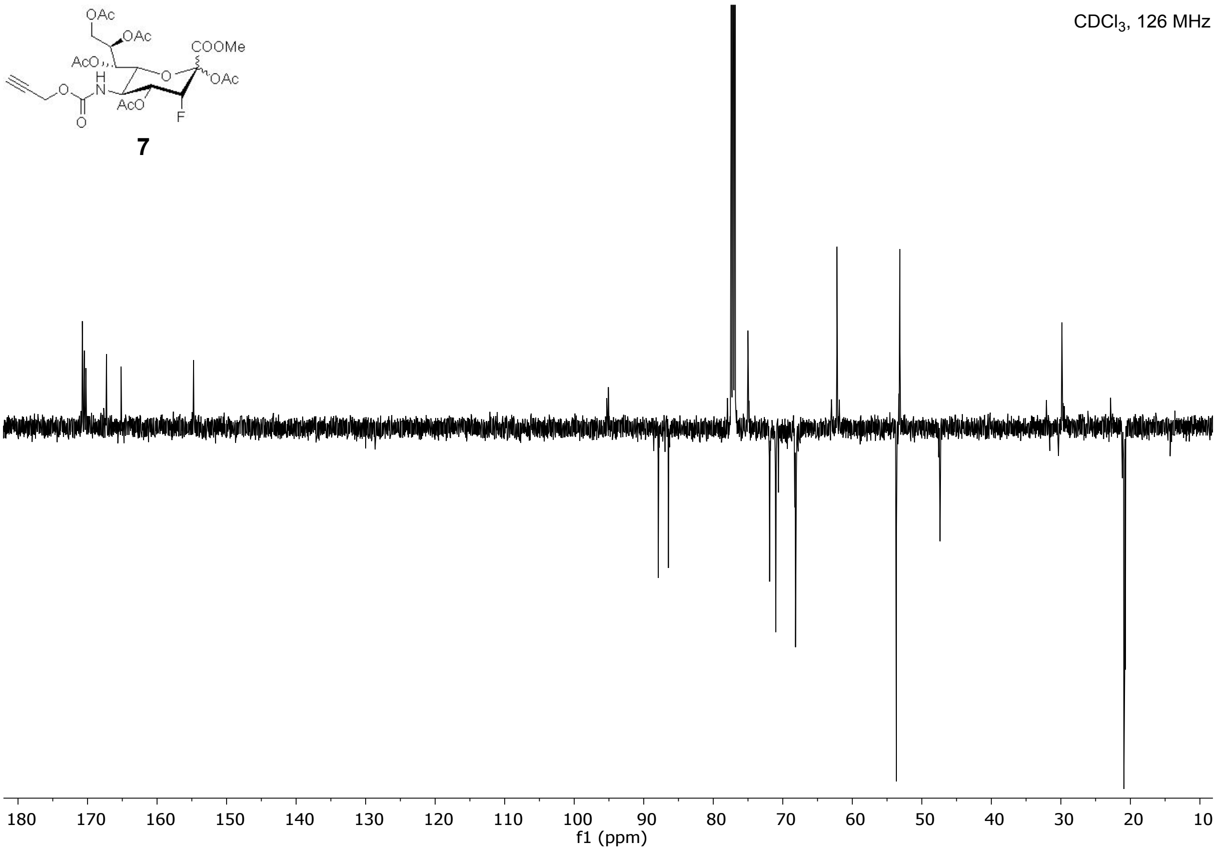
2.54
2.60
2.66
2.93
1.04
7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8
f1 (ppm)

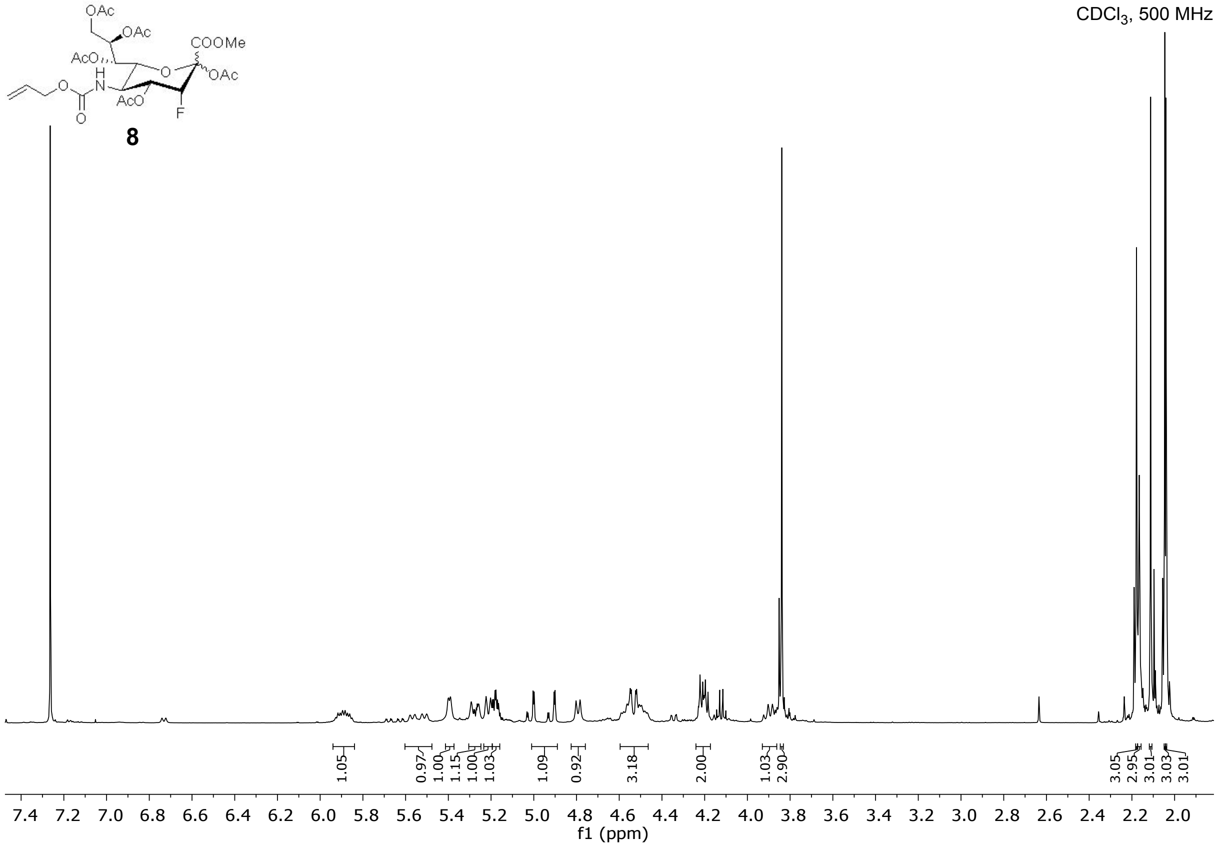

OAc
OAc
COOMe
AcO
H
O
OAc
N
AcO
F
O
6
CDCl$_3$, 126 MHz
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

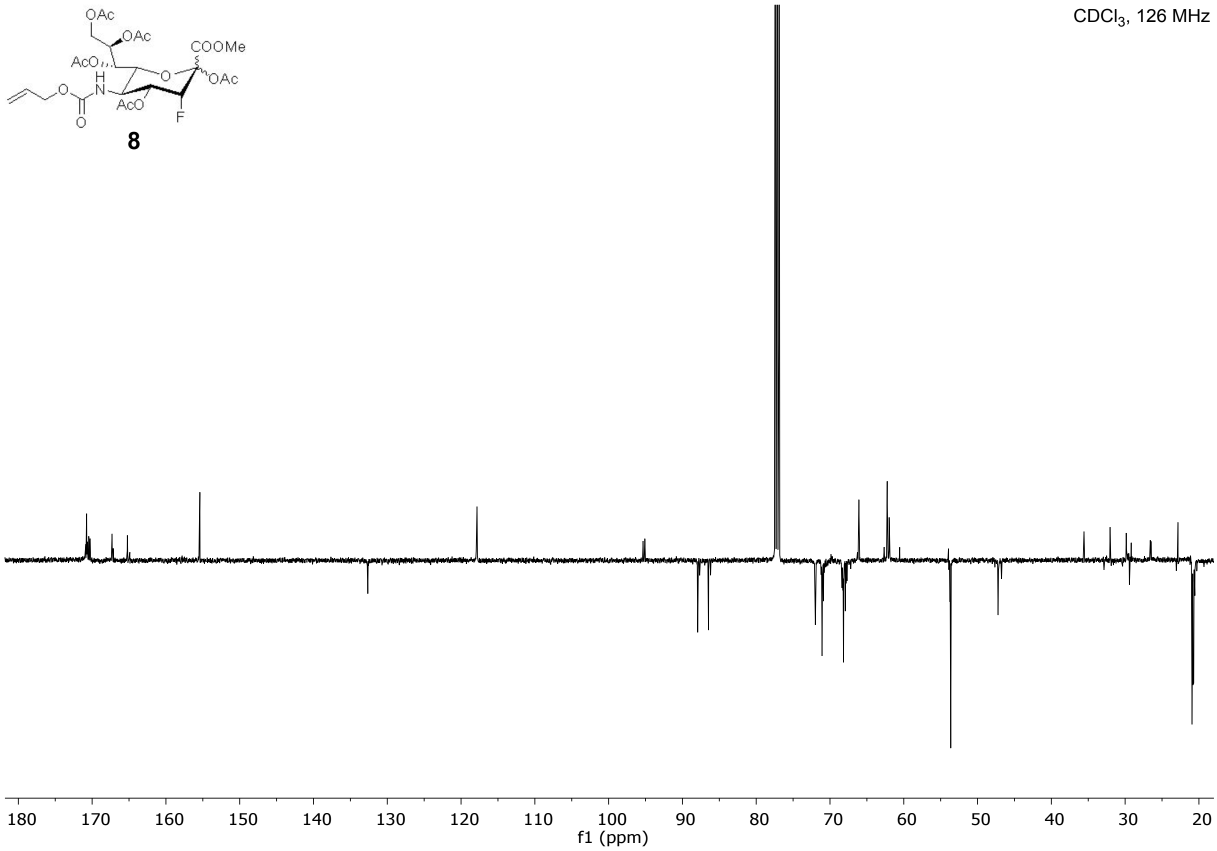


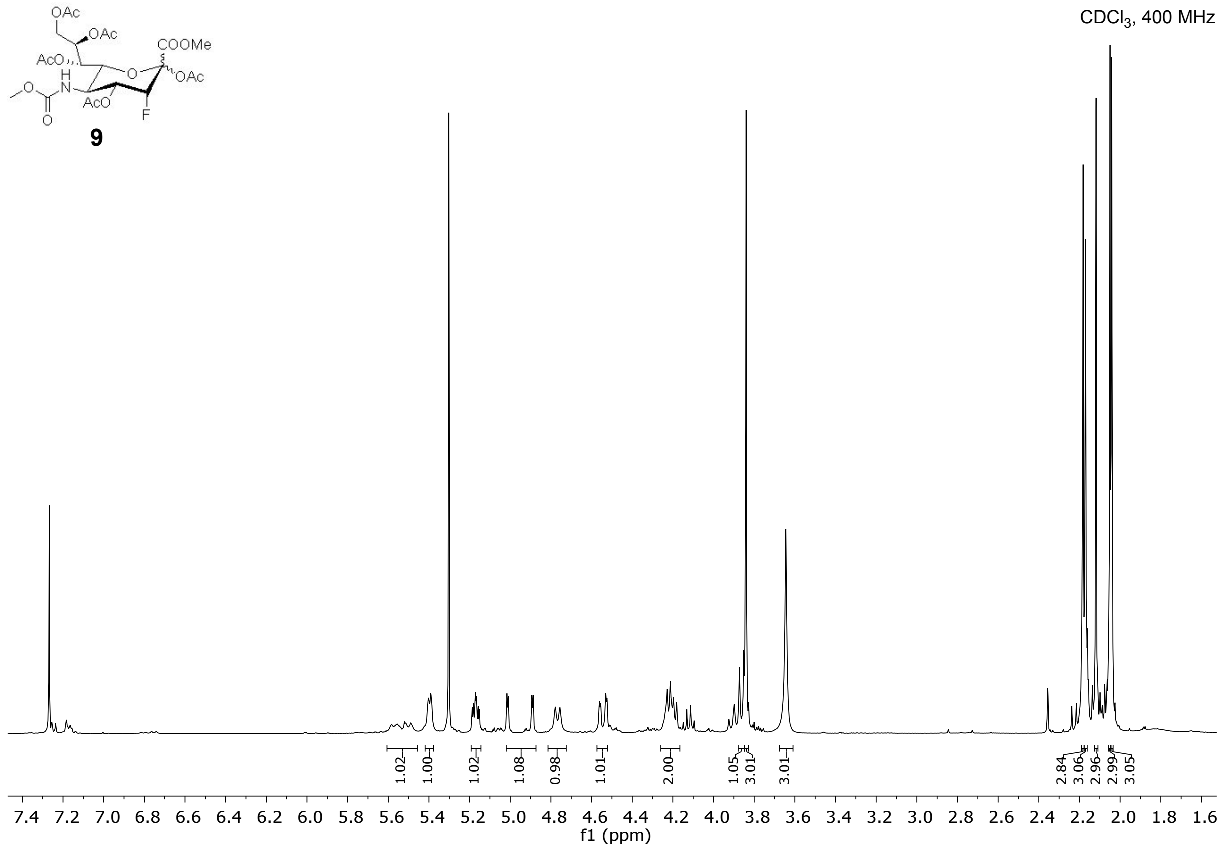
OAc
OAc
COOMe
AcO
H
N
O
OAc
O
O
AcO
F
7
CDCl3, 500 MHz
1.00
1.00
0.95
1.20
1.00
1.10
2.00
1.87
1.00
2.79
1.00
2.70
2.70
2.65
2.82
2.82
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)



OAc
OAc
COOMe
AcO
H
N
O
OAc
O
O
AcO
F
7
CDCl3, 126 MHz
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

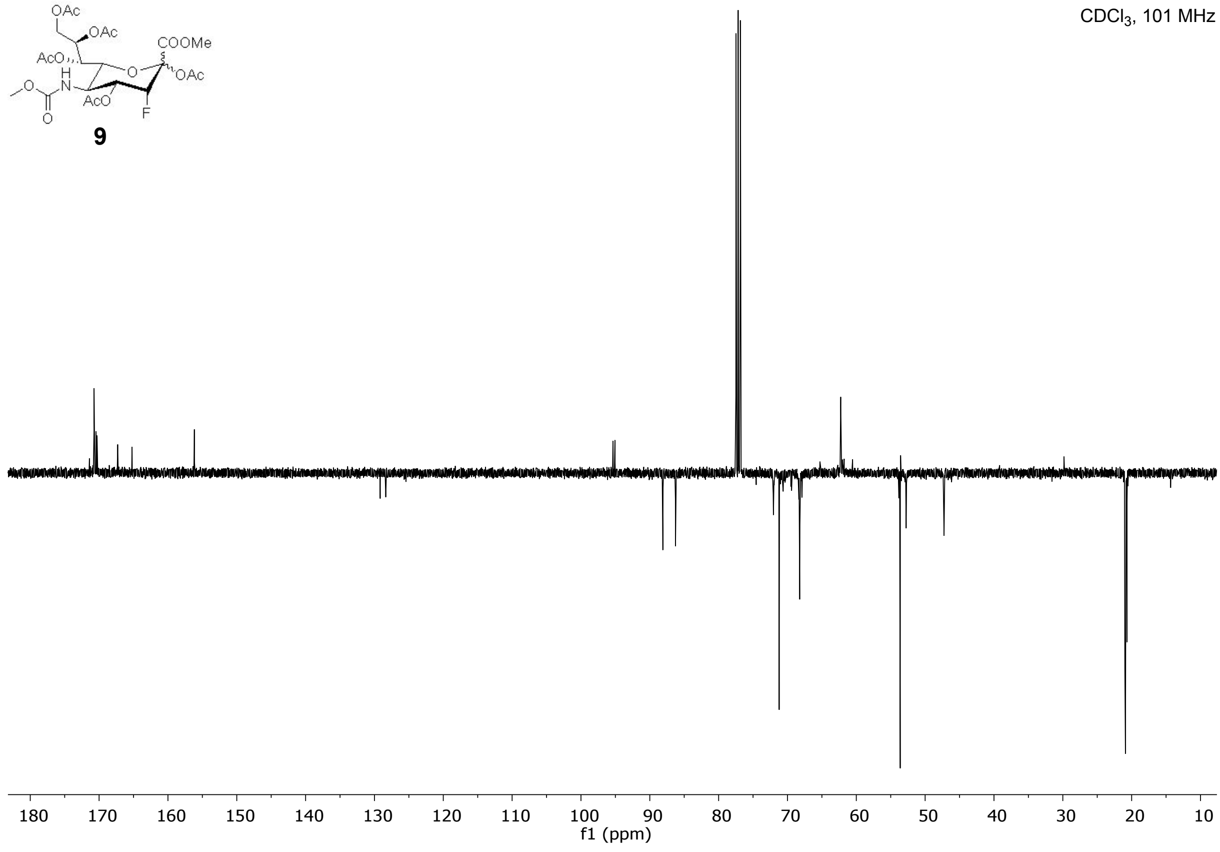

8
CDCl3, 500 MHz
1.05
0.97
1.00
1.15
1.00
1.03
1.09
0.92
3.18
2.00
1.03
2.90
3.05
2.95
3.01
3.03
3.01
7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0
f1 (ppm)


8
CDCl3, 126 MHz
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)



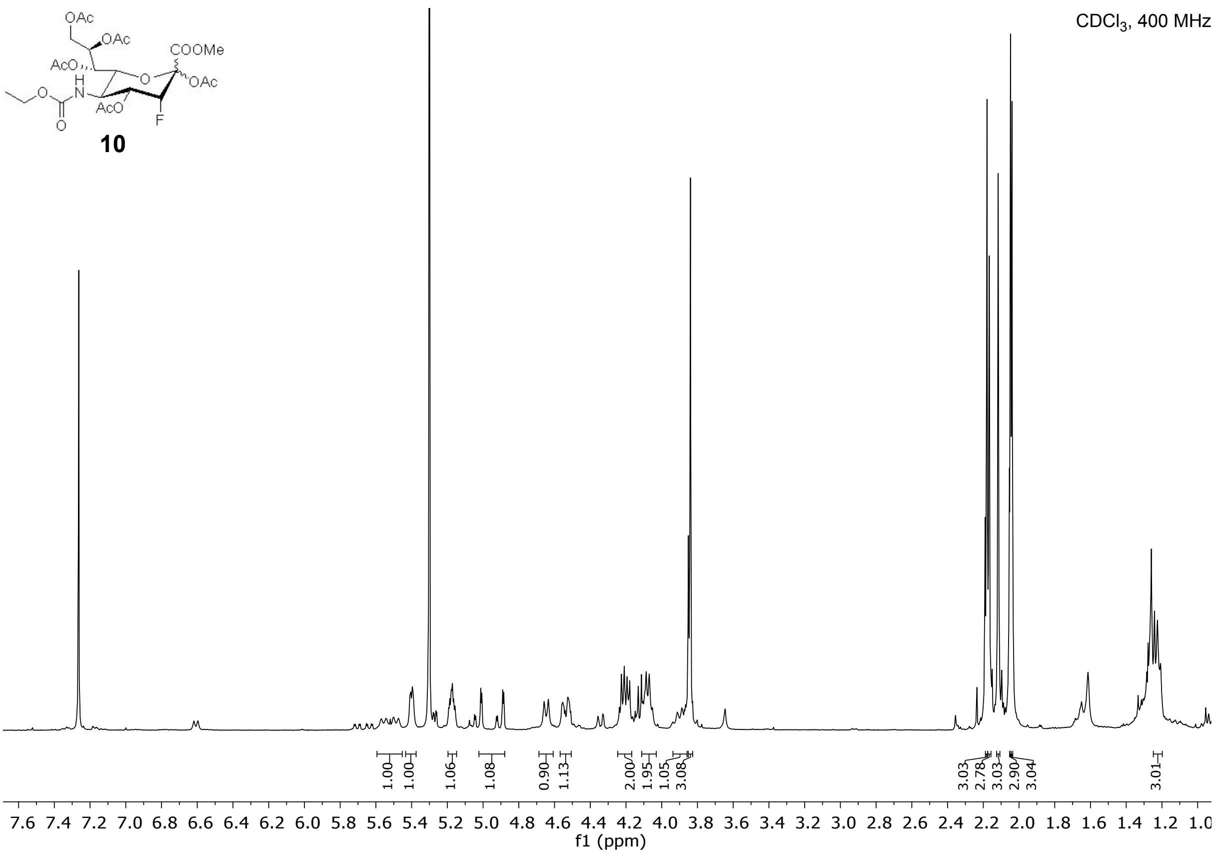
9

CDCl$_3$, 400 MHz
1.02
1.00
1.02
1.08
0.98
1.01
2.00
1.05
3.01
3.01
2.84
3.06
2.96
2.99
3.05
7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6
f1 (ppm)

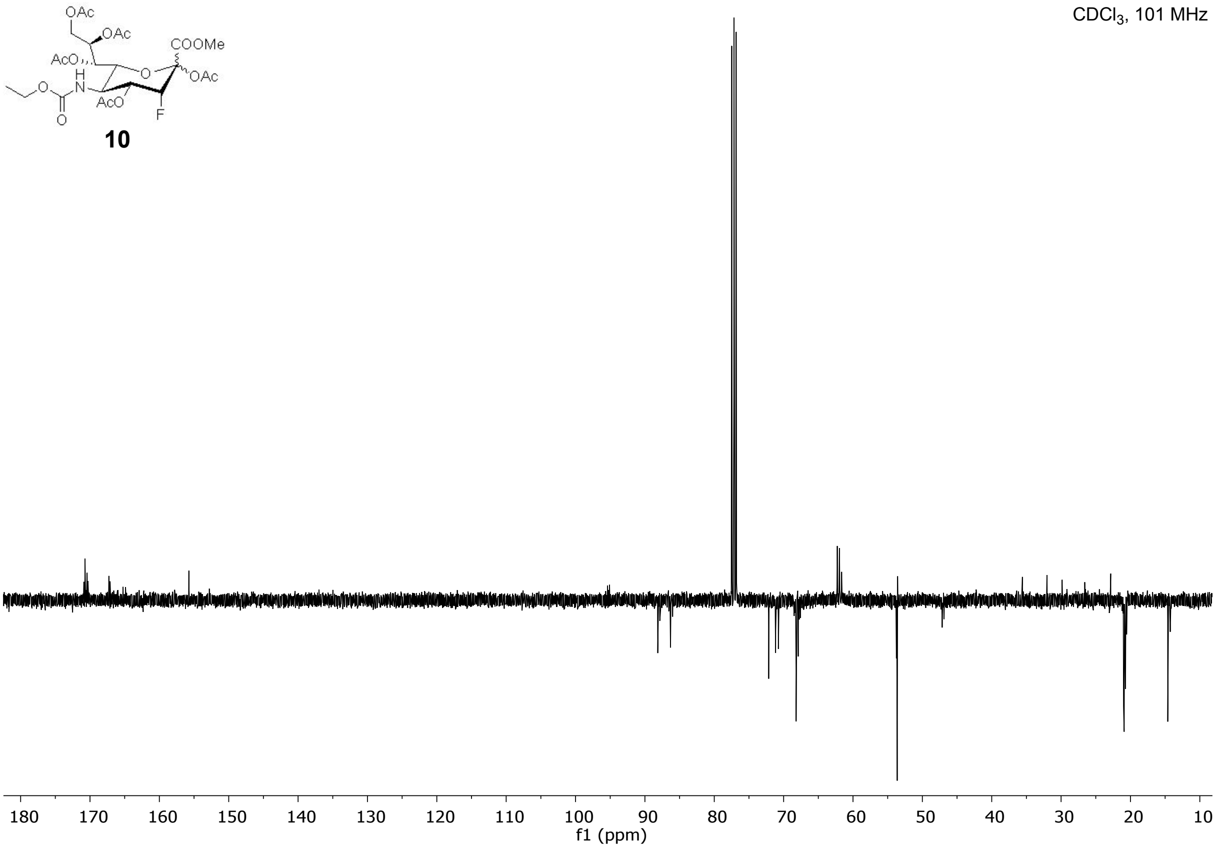


9

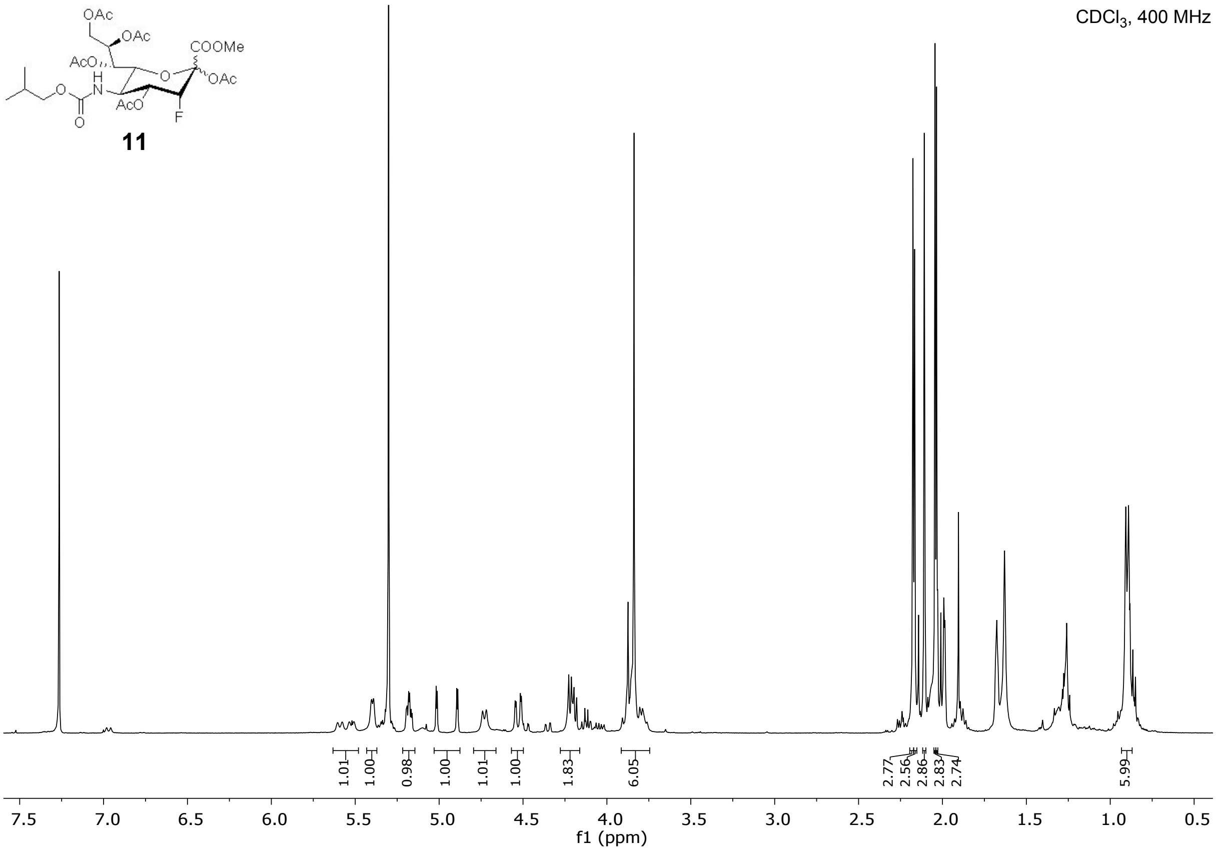
CDCl$_3$, 101 MHz
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


10

OAc
OAc
COOMe
AcO
H
N
O
OAc
AcO
F
O
O
CDCl$_3$, 400 MHz
1.00
1.00
1.06
1.08
0.90
1.13
2.00
1.95
1.05
3.08
3.03
2.78
3.03
2.90
3.04
3.01
7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0
f1 (ppm)

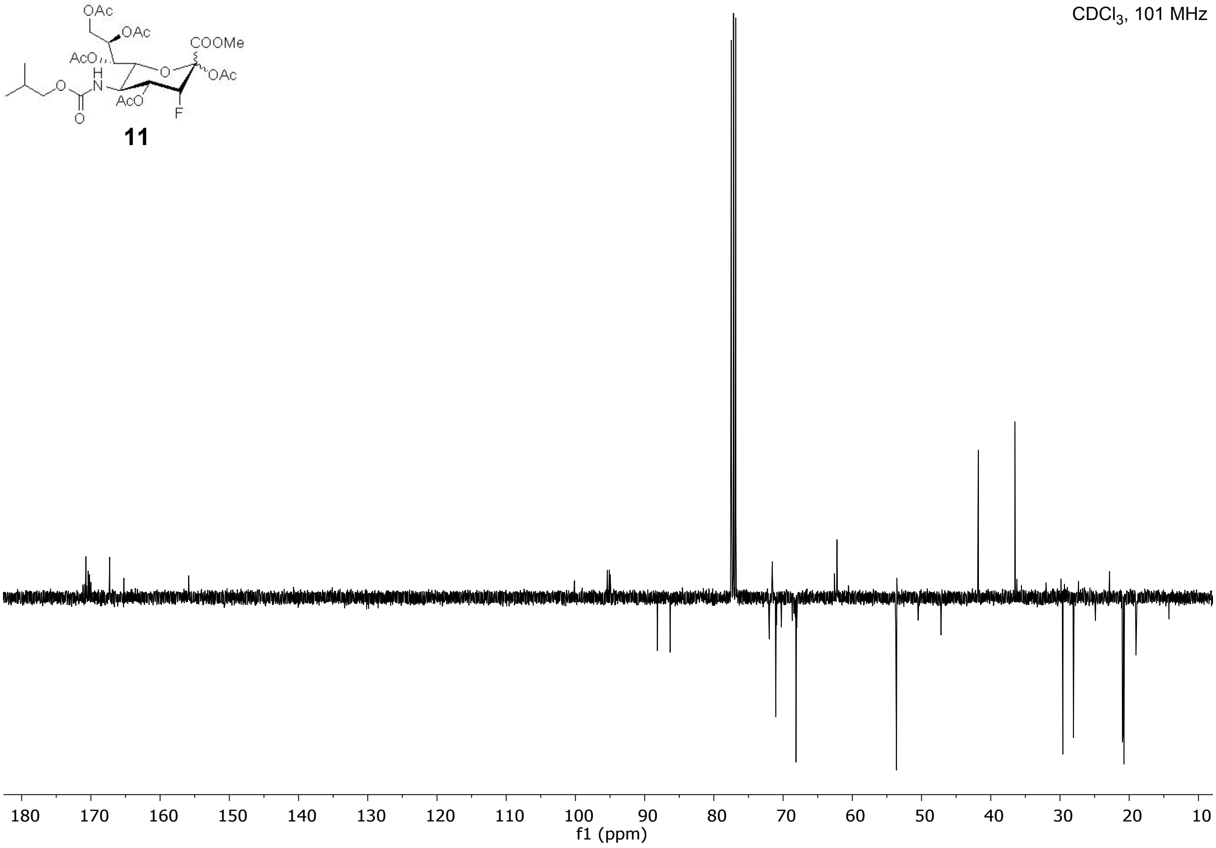

10

OAc
OAc
COOMe
AcO
H
N
O
OAc
AcO
F
O
O
CDCl$_3$, 101 MHz
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



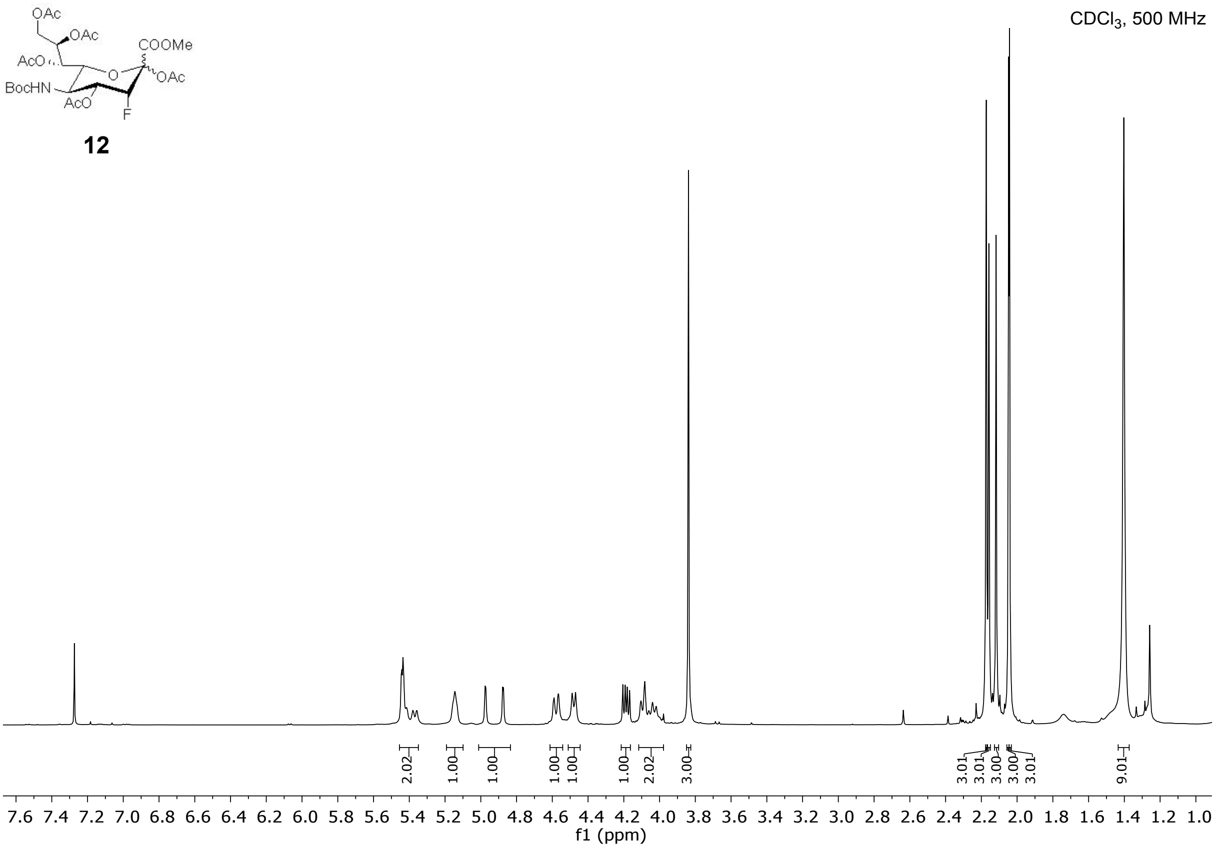
11

CDCl$_3$, 400 MHz



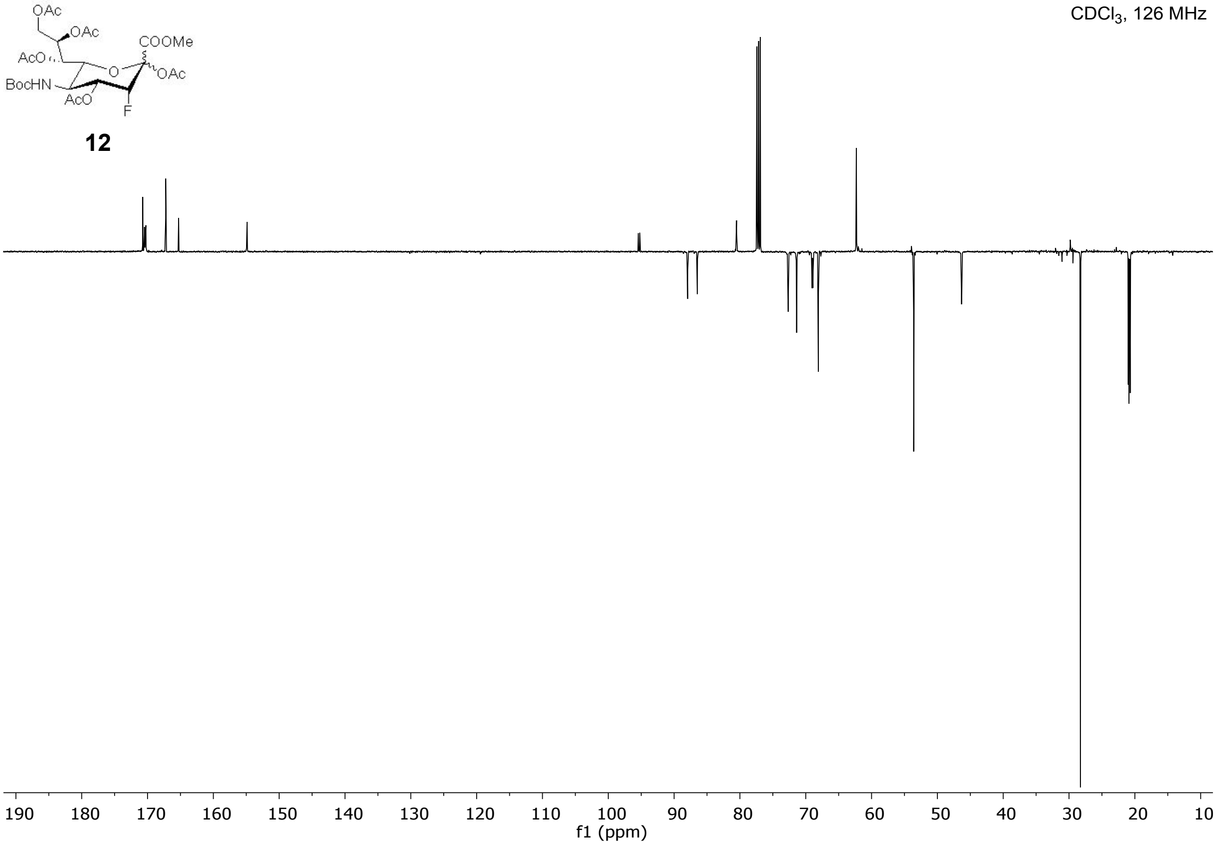
11

CDCl$_3$, 101 MHz



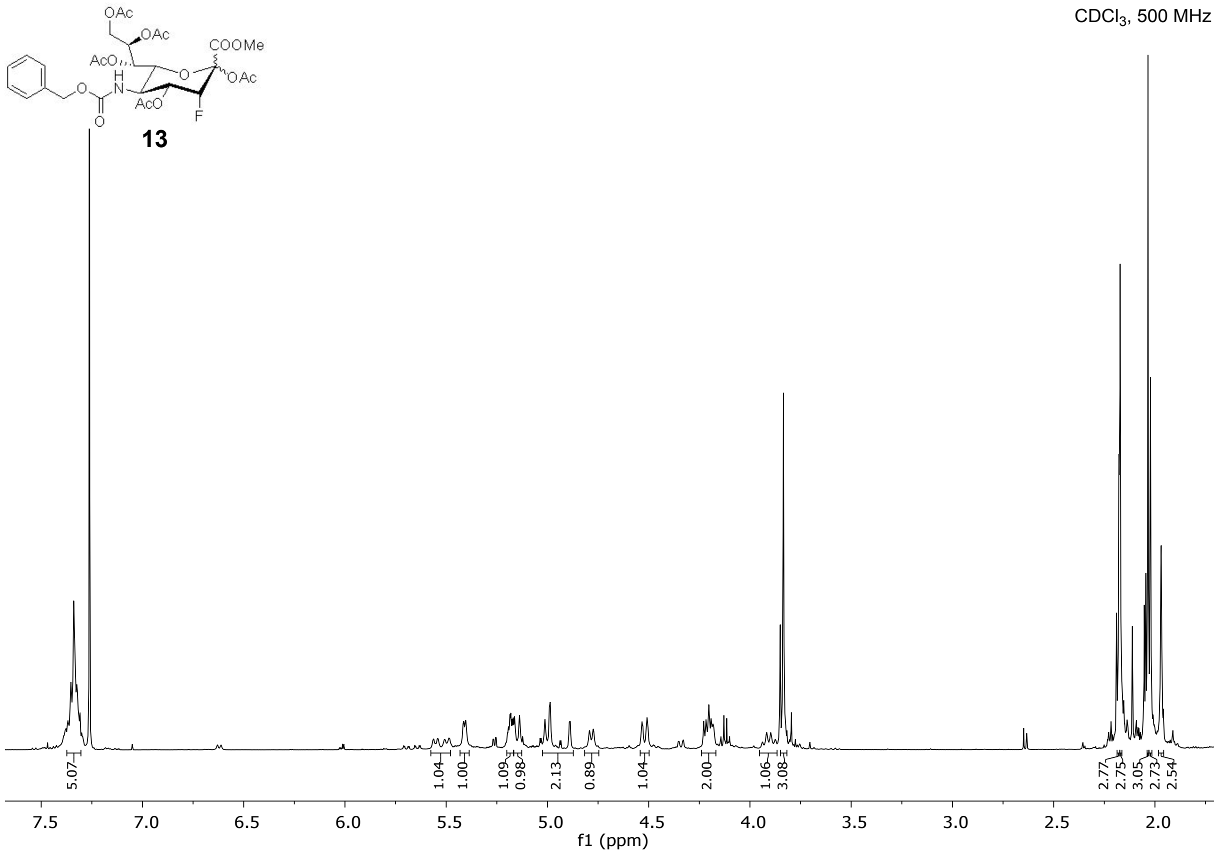
12

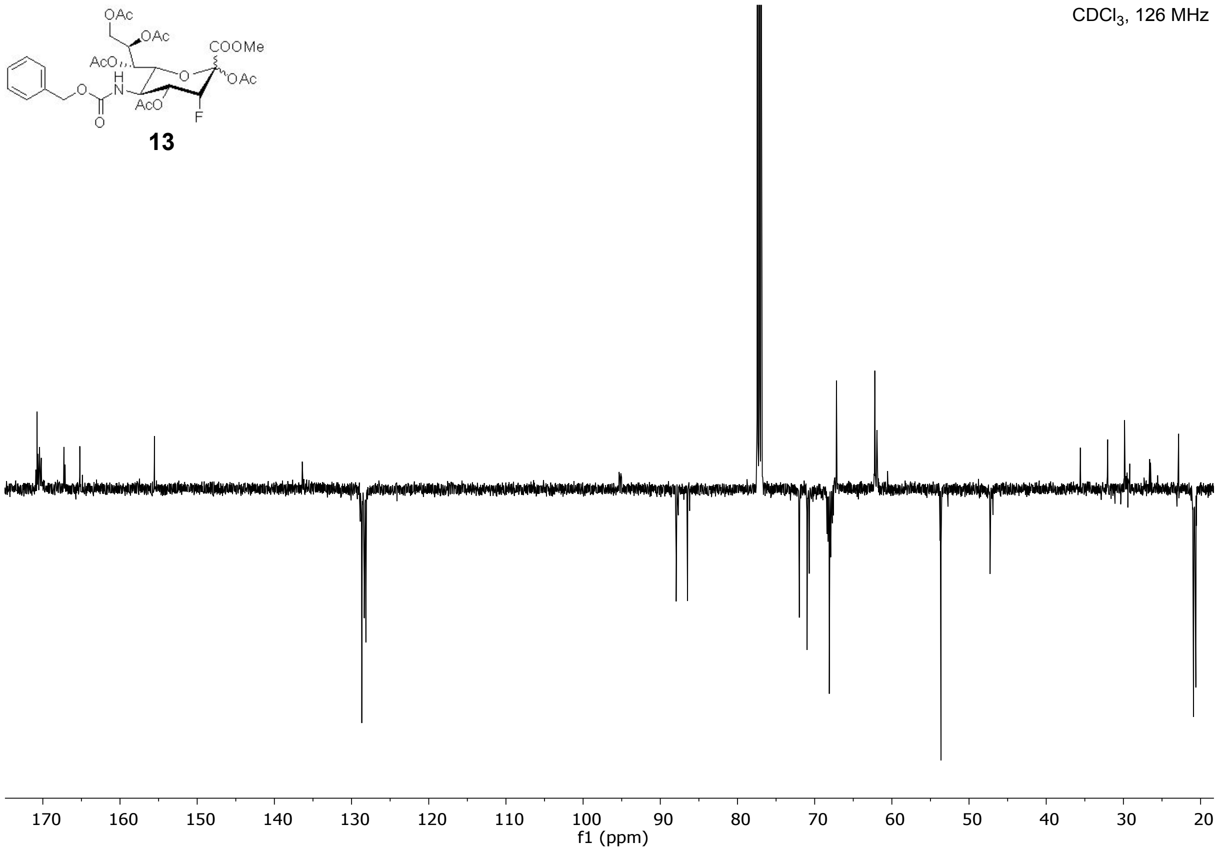
OAc
OAc
AcO
COOMe
OAc
BocHN
AcO
O
F
CDCl$_3$, 500 MHz
2.02
1.00
1.00
1.00
1.00
1.00
2.02
3.00
3.01
3.01
3.00
3.00
3.01
9.01
7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0
f1 (ppm)

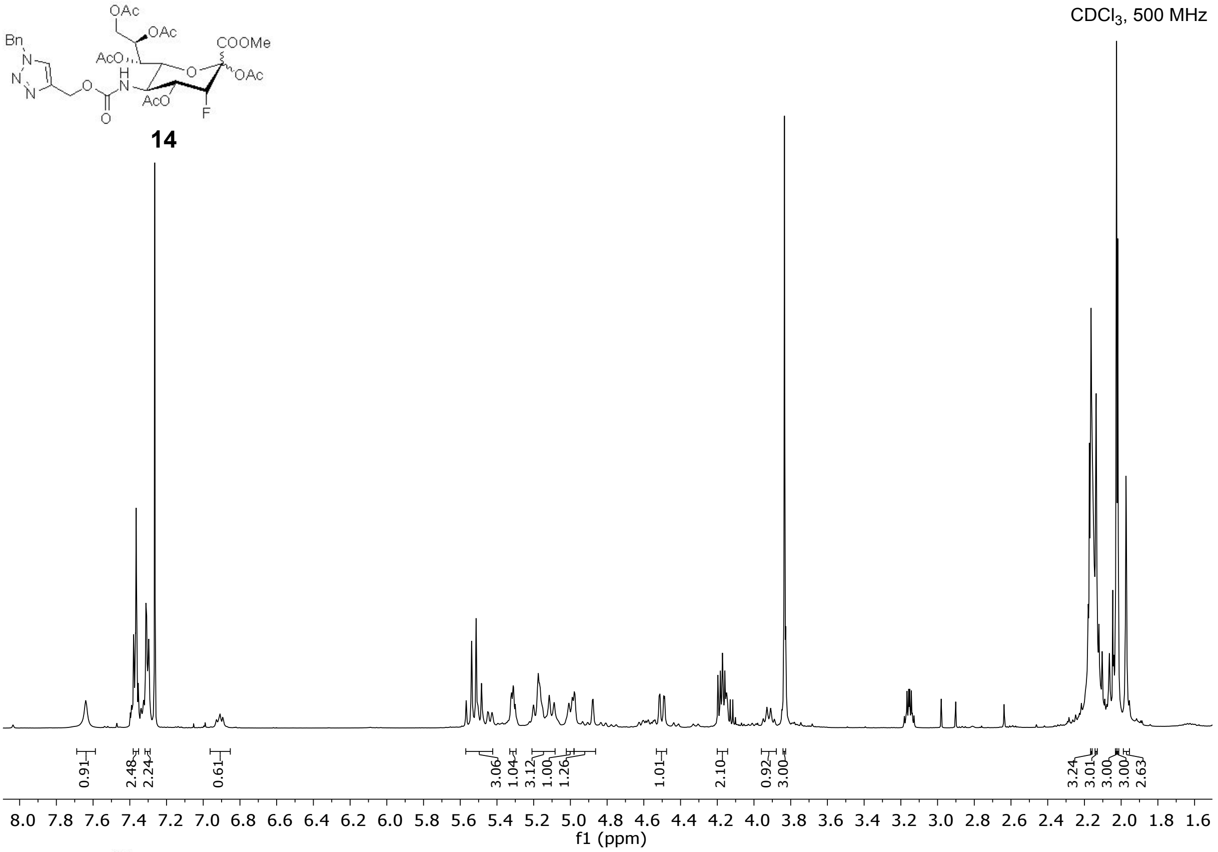


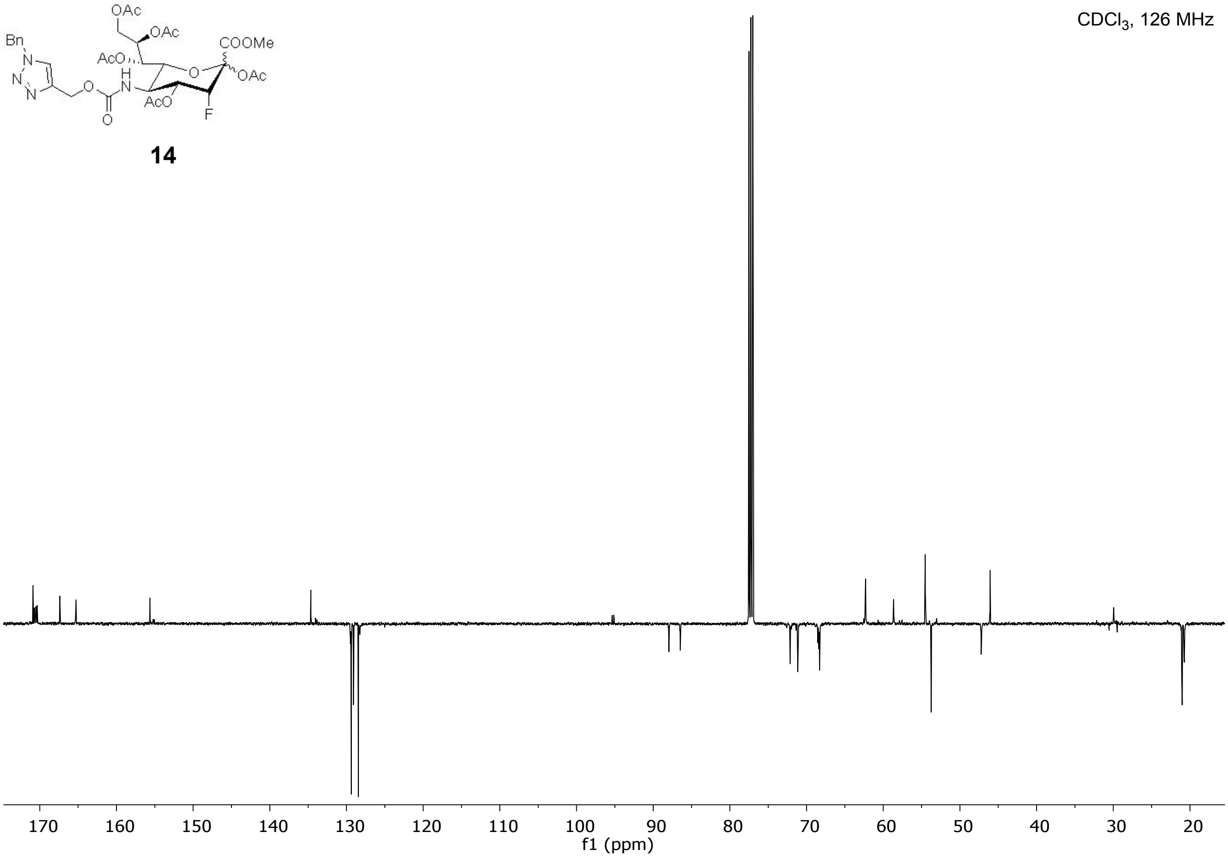
12

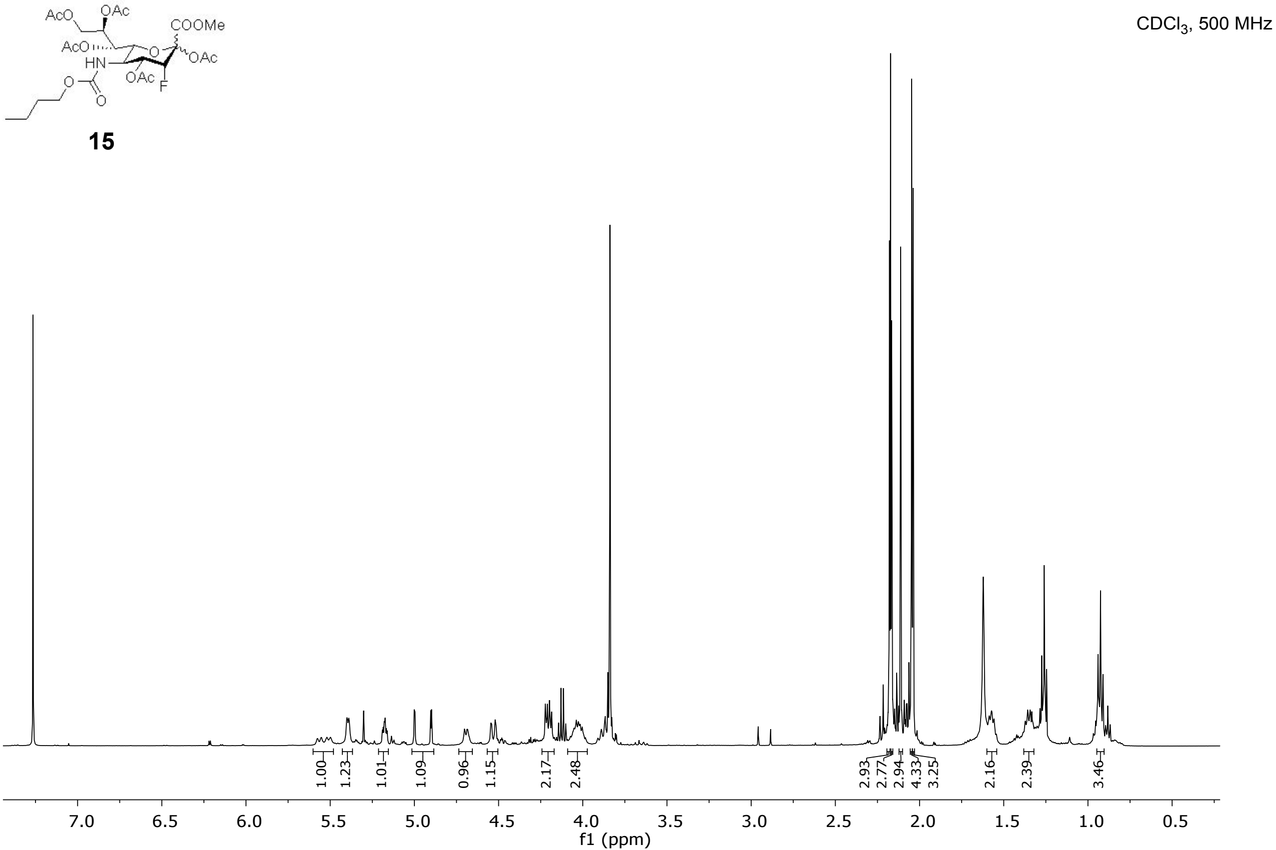
OAc
OAc
AcO
COOMe
OAc
BocHN
AcO
O
F
CDCl$_3$, 126 MHz
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

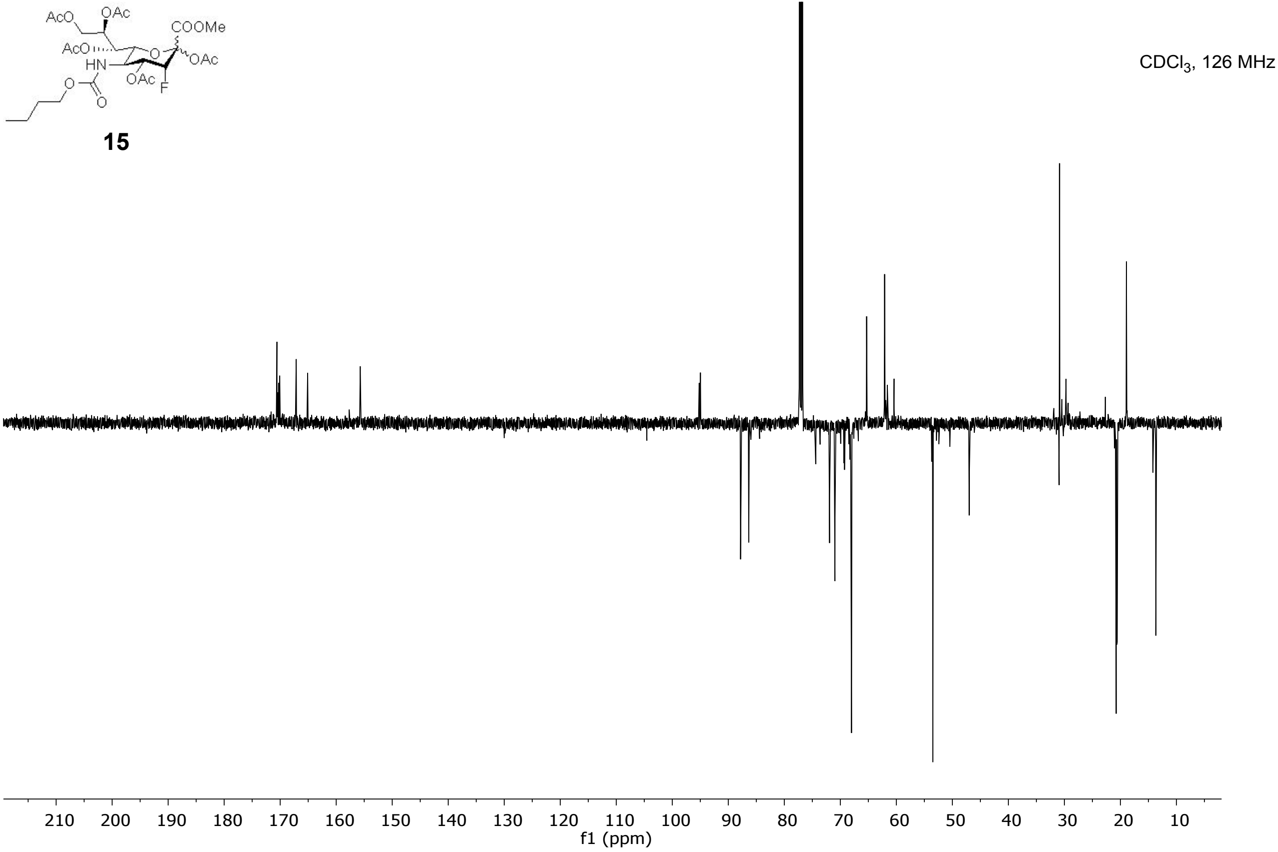

OAc
OAc
COOMe
AcO
H
N
O
OAc
O
AcO
F
O
13
CDCl$_3$, 500 MHz
5.07
1.04
1.00
1.09
0.98
2.13
0.89
1.04
2.00
1.06
3.08
2.77
2.75
3.05
2.73
2.54
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)

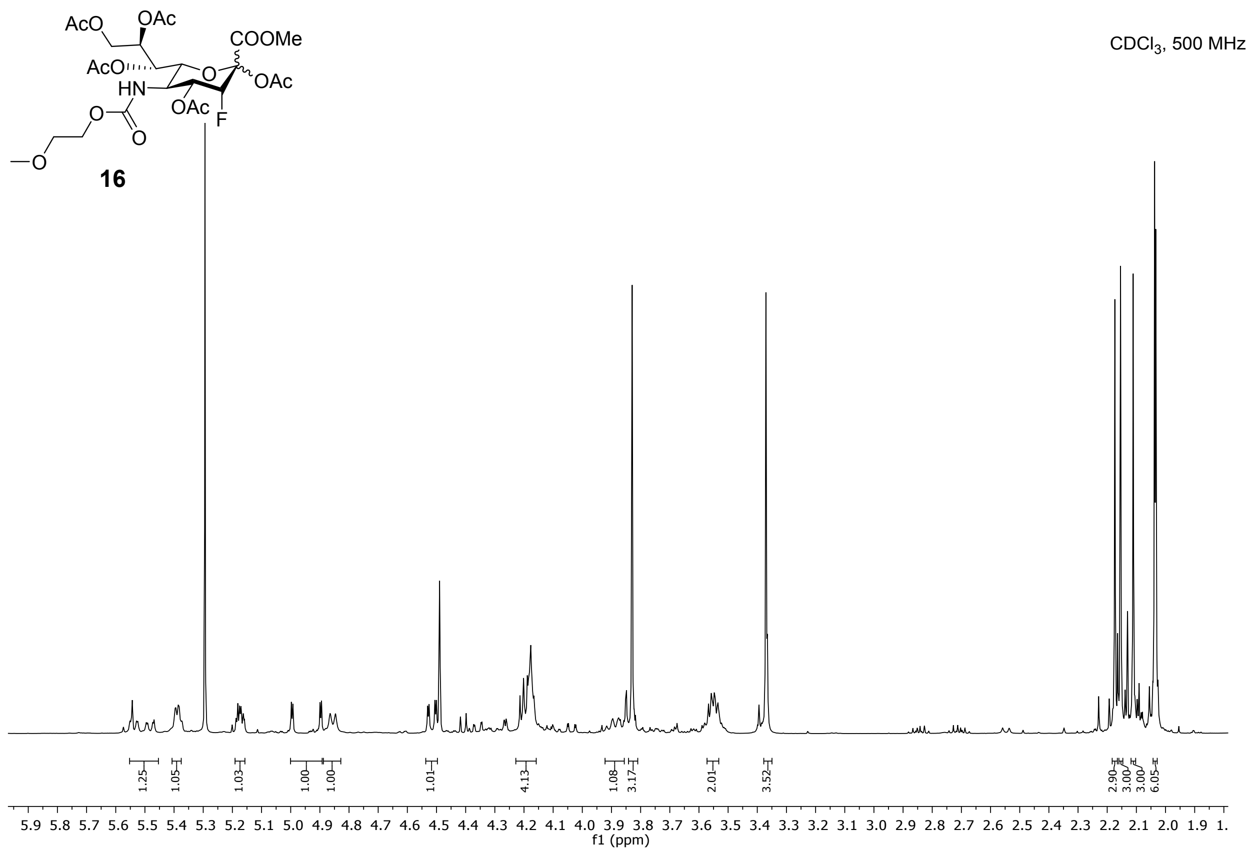

OAc
OAc
COOMe
AcO
H
N
O
OAc
O
AcO
F
O
13
CDCl$_3$, 126 MHz
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

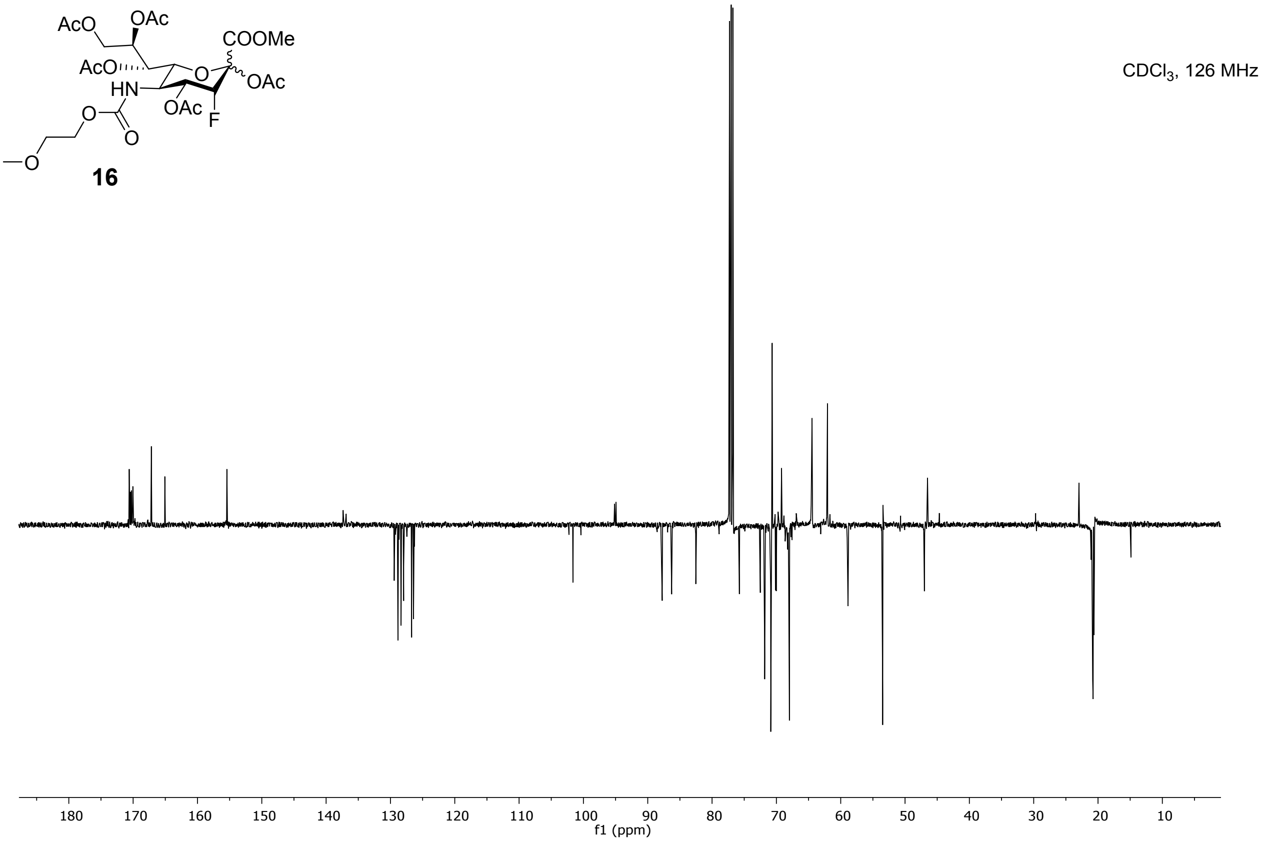

Bn
OAc
OAc
COOMe
AcO
H
N
O
OAc
AcO
F
O
14
CDCl$_3$, 500 MHz
0.91
2.48
2.24
0.61
3.06
1.04
3.12
1.00
1.26
1.01
2.10
0.92
3.00
3.24
3.01
3.00
3.00
2.63
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6
f1 (ppm)

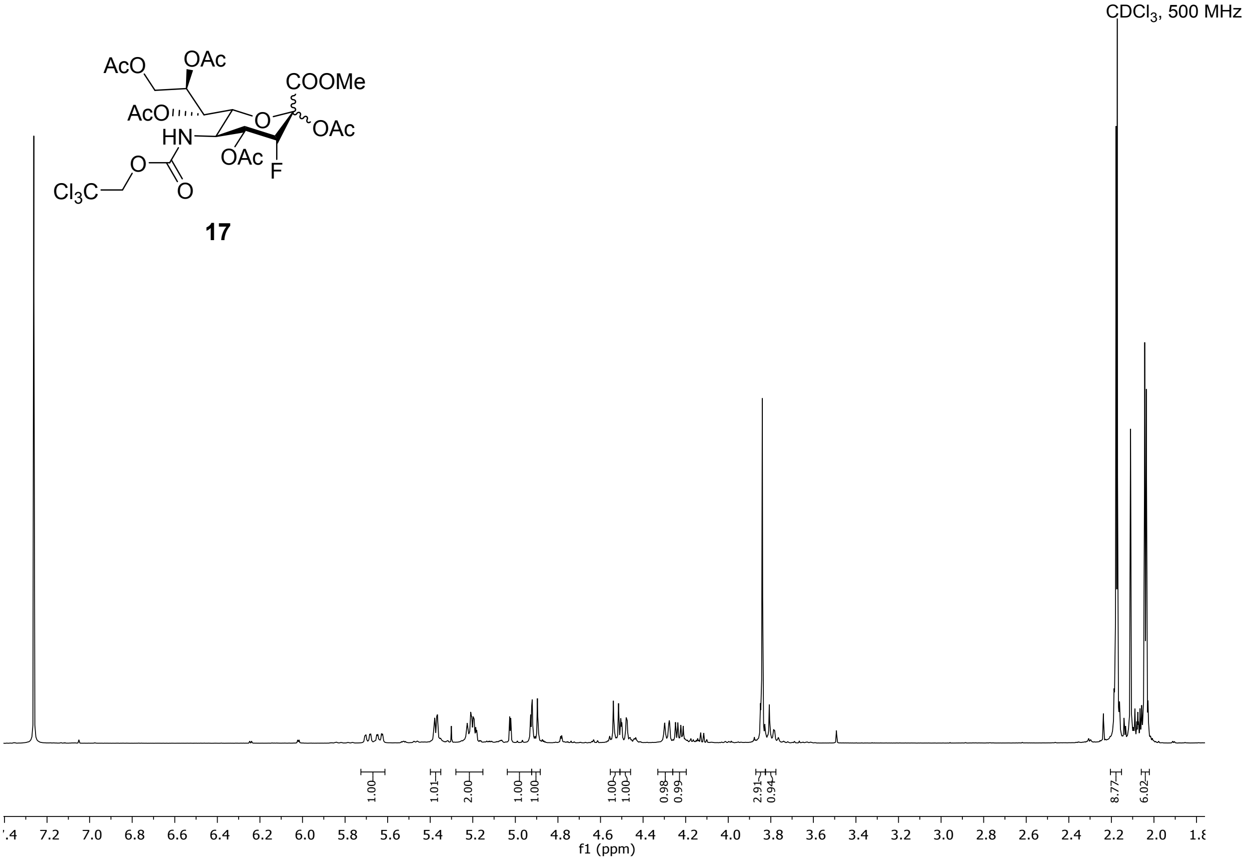

Bn
OAc
OAc
COOMe
AcO
H
N
O
OAc
AcO
F
O
14
CDCl$_3$, 126 MHz
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)

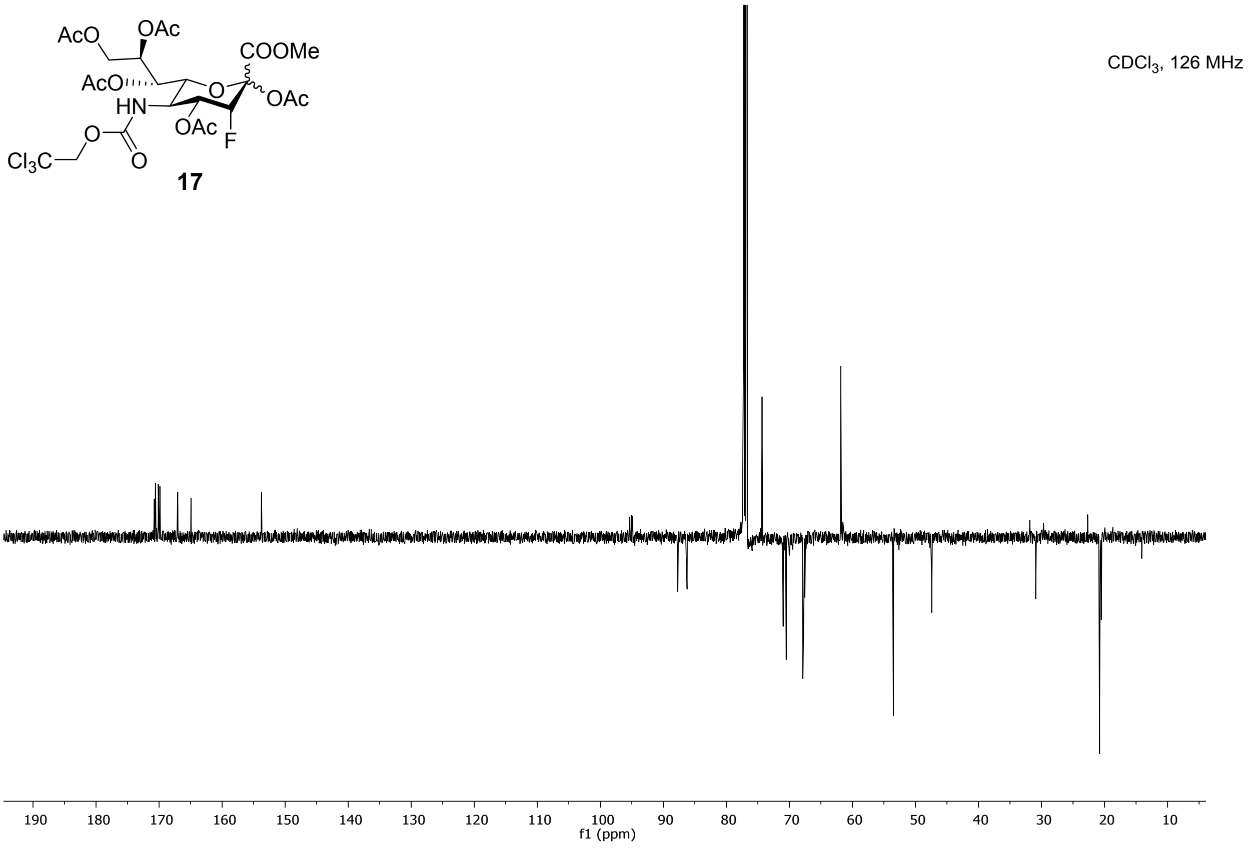

AcO
OAc
COOMe
AcO
HN
O
OAc
OAc
F
O
O
15
CDCl$_3$, 500 MHz
1.00
1.23
1.01
1.09
0.96
1.15
2.17
2.48
2.93
2.77
2.94
4.33
3.25
2.16
2.39
3.46
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

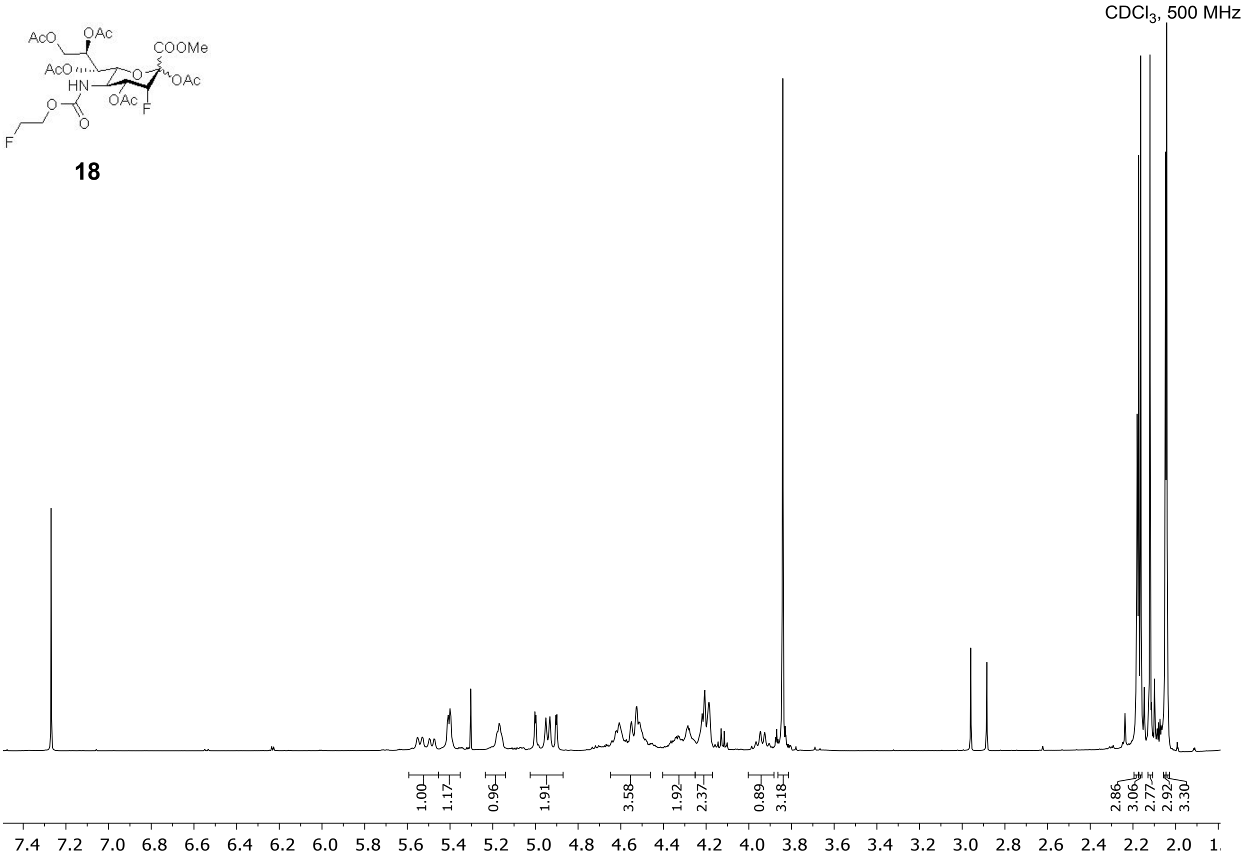

AcO
OAc
COOMe
AcO
HN
O
OAc
OAc
F
O
O
15
CDCl$_3$, 126 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


AcO
OAc
COOMe
AcO
HN
O
OAc
OAc
F
O
O
O
16
CDCl₃, 500 MHz
1.25
1.05
1.03
1.00
1.00
1.01
4.13
1.08
3.17
2.01
3.52
2.90
3.00
3.00
6.05
5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.
f1 (ppm)

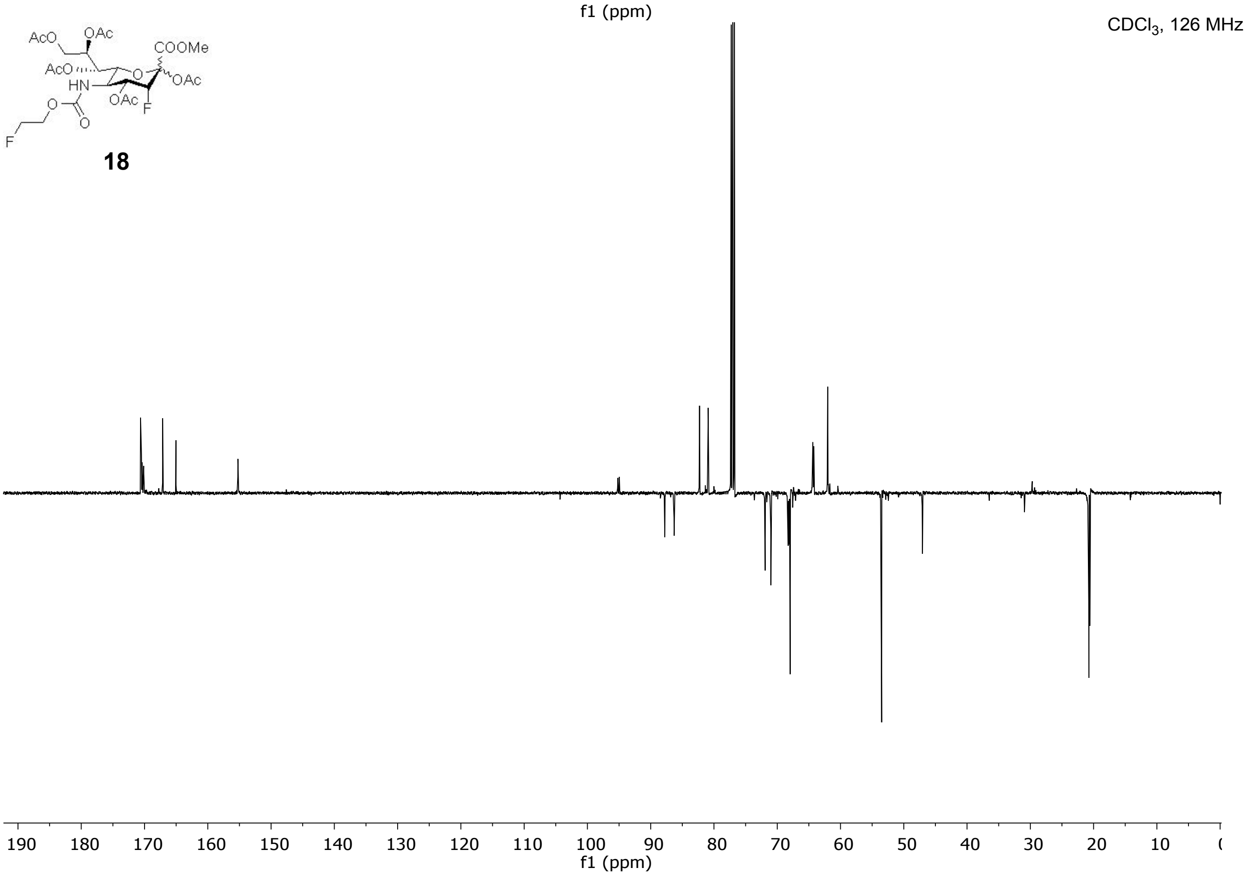

AcO
OAc
COOMe
AcO
HN
O
OAc
OAc
F
O
O
O
16
CDCl₃, 126 MHz
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


CDCl$_3$, 500 MHz
AcO
OAc
COOMe
AcO
O
OAc
HN
OAc
F
O
Cl$_3$C
O
17
1.00
1.01
2.00
1.00
1.00
1.00
1.00
0.98
0.99
2.91
0.94
8.77
6.02
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
f1 (ppm)

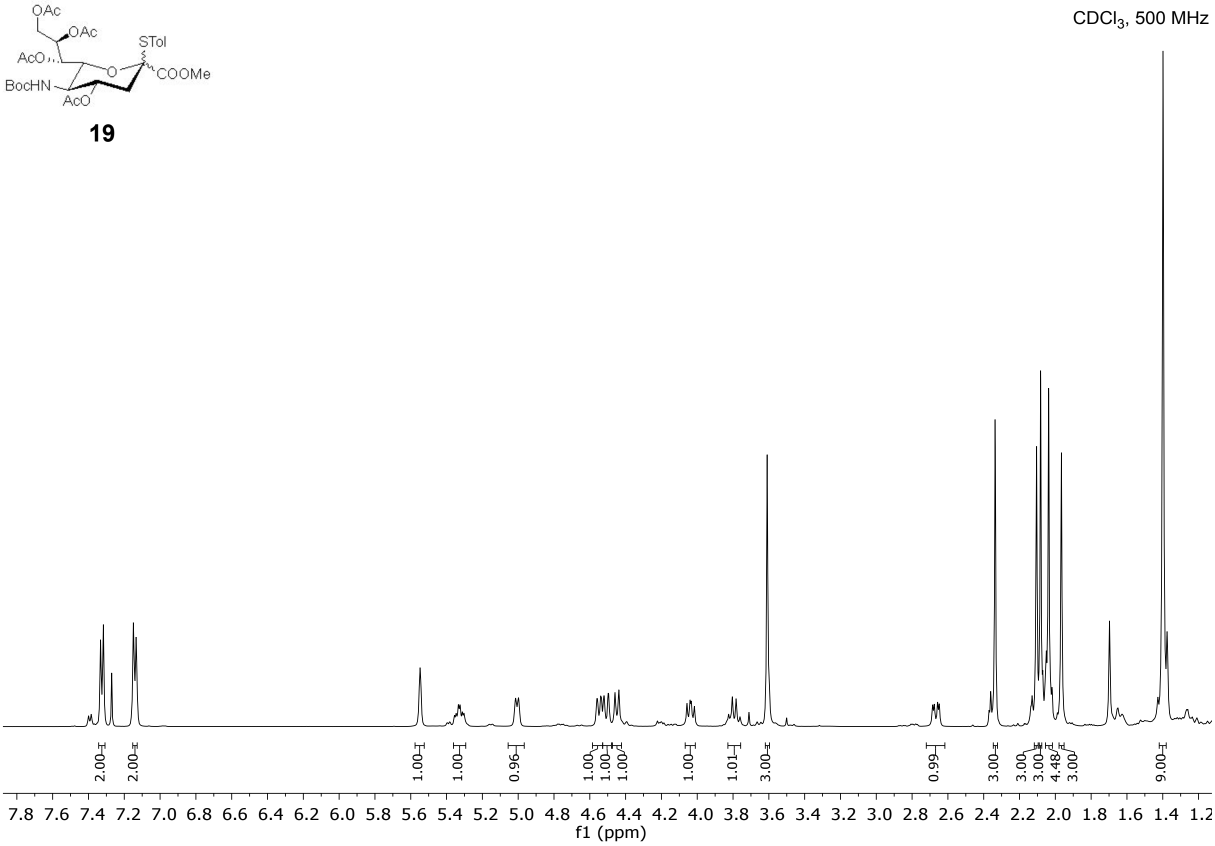

AcO
OAc
COOMe
AcO
O
OAc
HN
OAc
F
O
Cl$_3$C
O
17
CDCl$_3$, 126 MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

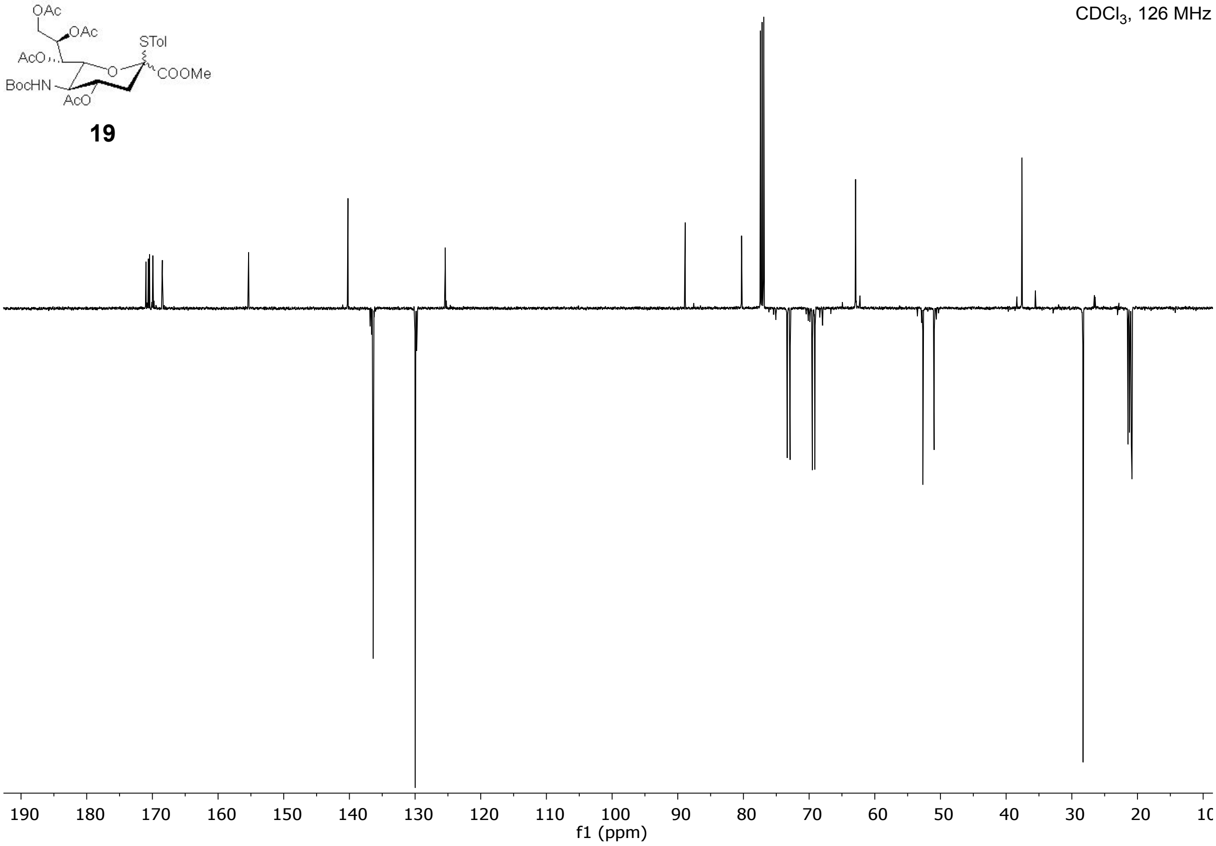

CDCl$_3$, 500 MHz
AcO
OAc
COOMe
AcO
HN
O
OAc
OAc
F
O
O
F
1.00
1.17
0.96
1.91
3.58
1.92
2.37
0.89
3.18
2.86
3.06
2.77
2.92
3.30
7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0
f1 (ppm)

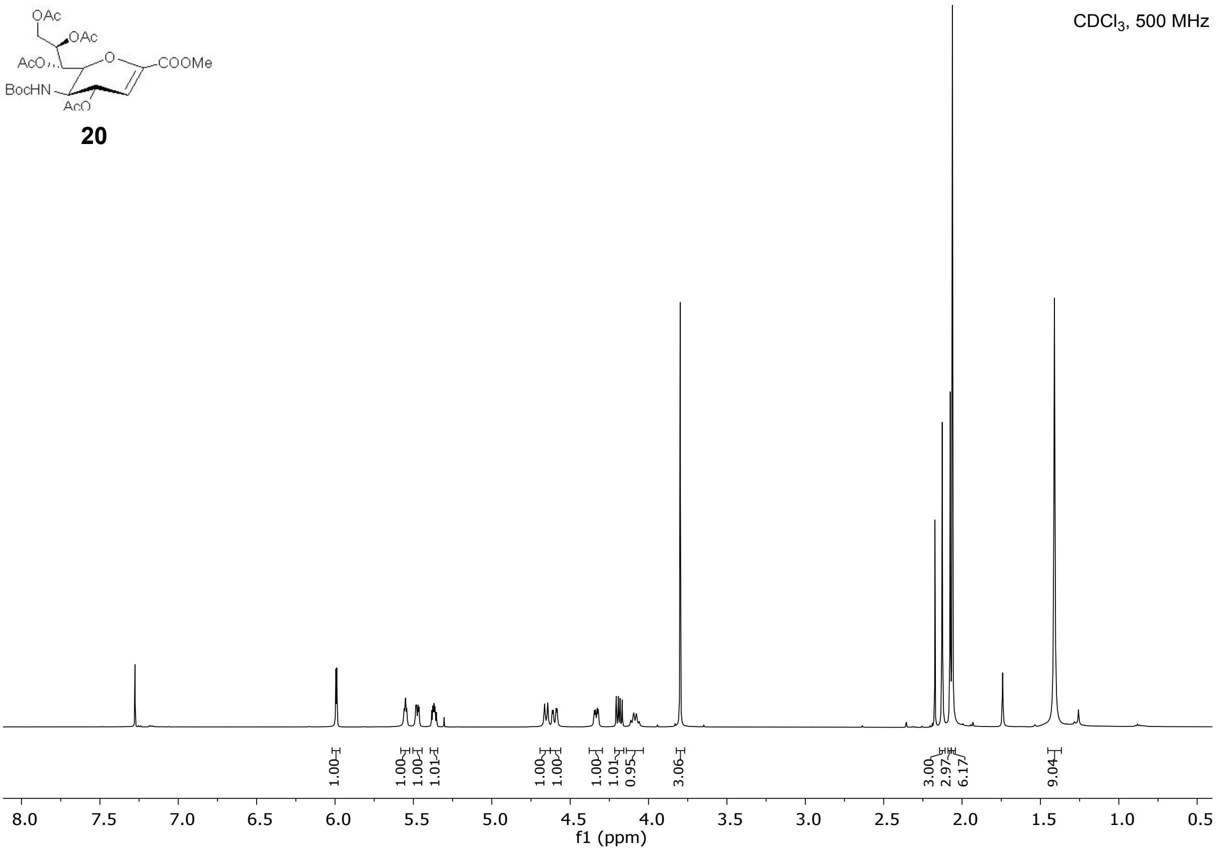
18

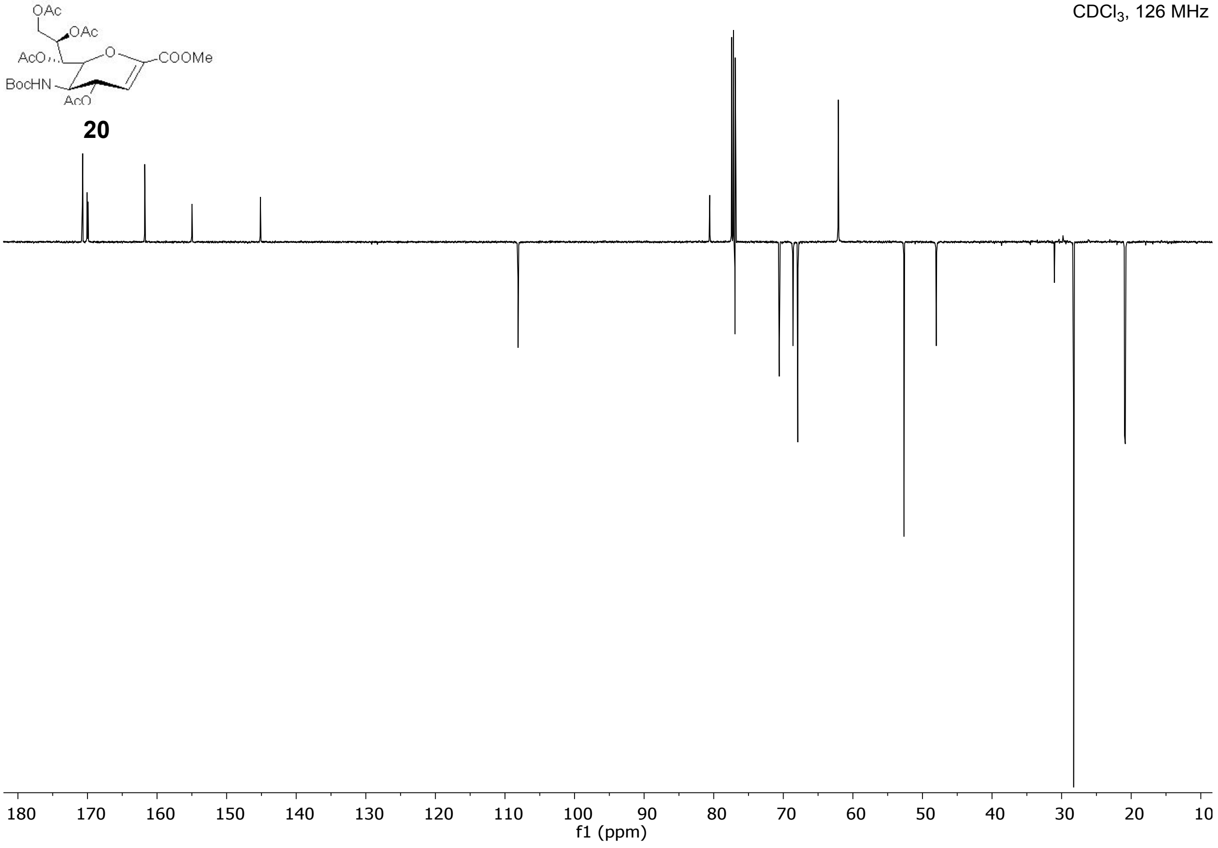

CDCl$_3$, 126 MHz
AcO
OAc
COOMe
AcO
HN
O
OAc
OAc
F
O
O
F
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

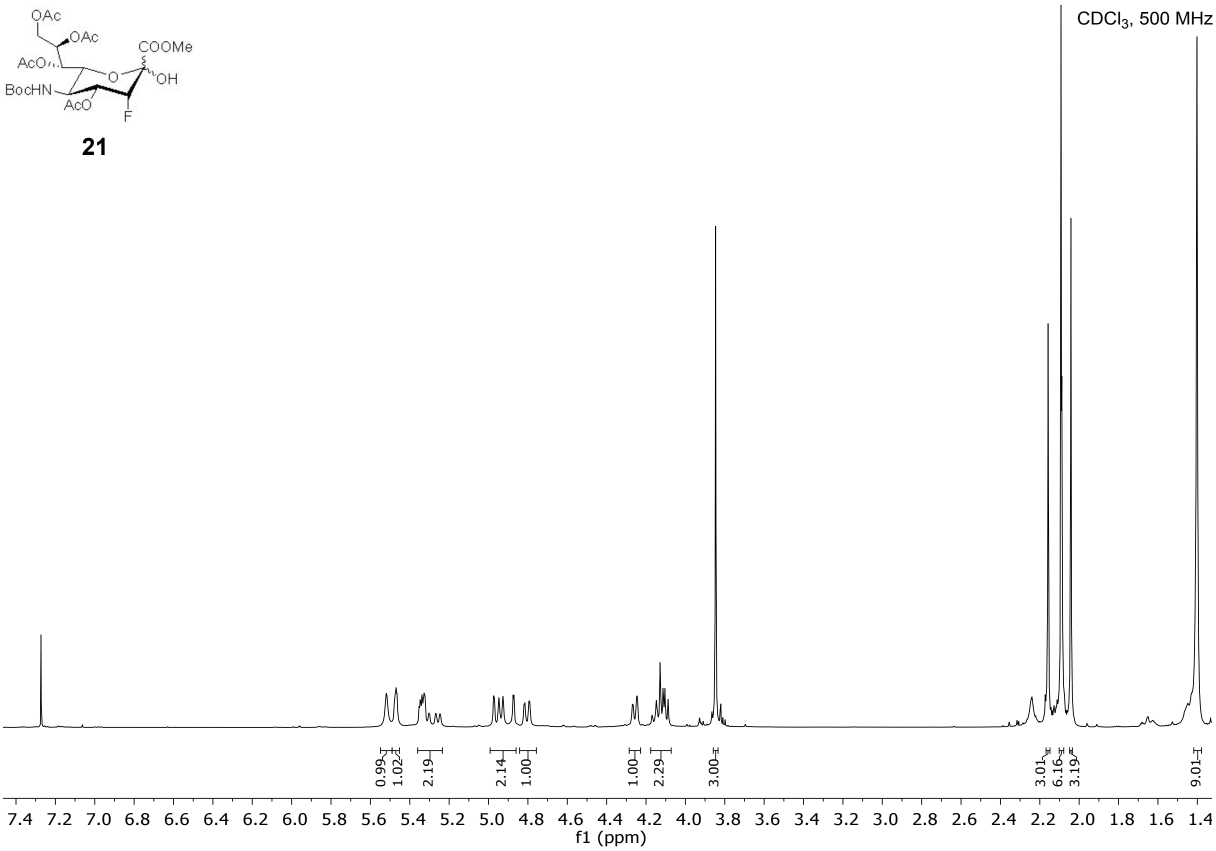
18

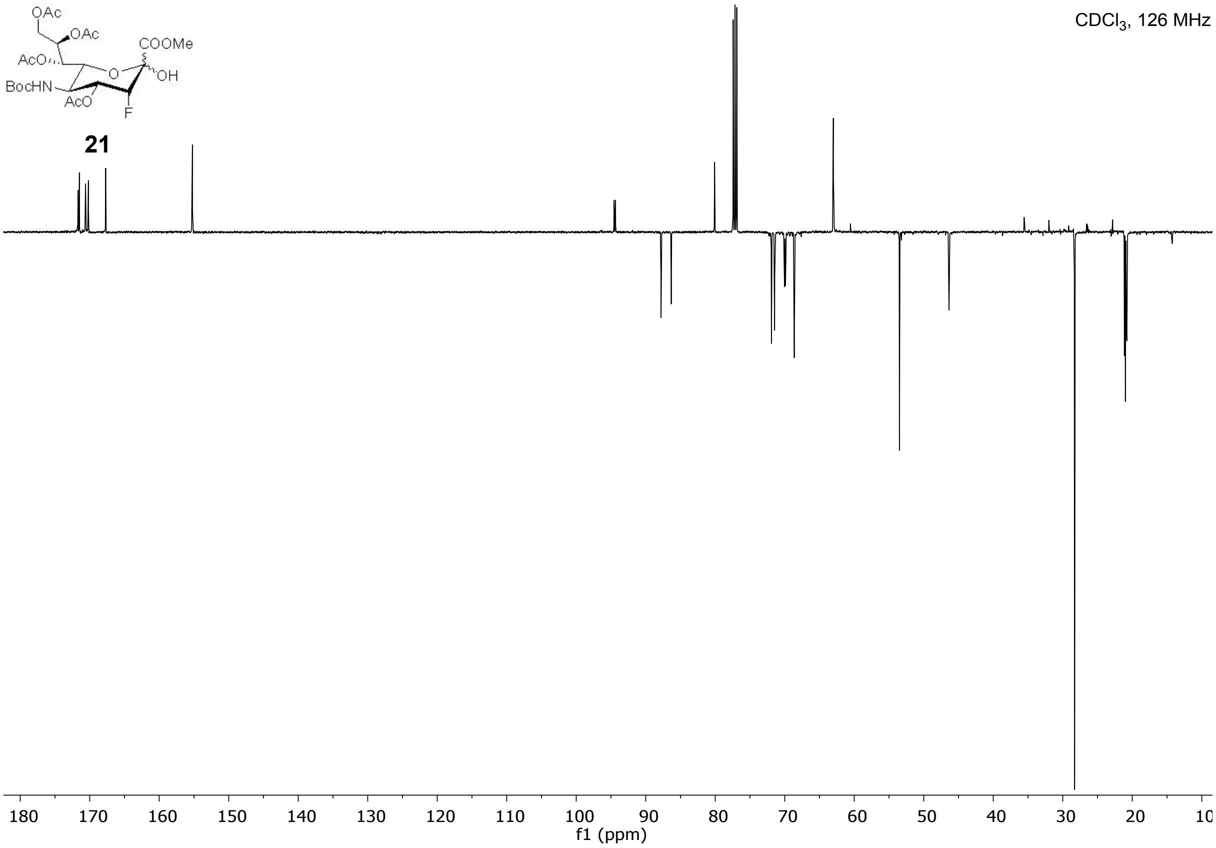

OAc
OAc
STol
AcO
O
COOMe
BocHN
AcO
19
CDCl$_3$, 500 MHz
2.00
2.00
1.00
1.00
0.96
1.00
1.00
1.00
1.00
1.01
3.00
0.99
3.00
3.00
3.00
4.48
3.00
9.00
7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
f1 (ppm)


OAc
OAc
STol
AcO
O
COOMe
BocHN
AcO
19
CDCl$_3$, 126 MHz
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


OAc
OAc
AcO
O
COOMe
BocHN
AcO
20
CDCl$_3$, 500 MHz
1.00
1.00
1.00
1.01
1.00
1.00
1.00
1.01
0.95
3.06
3.00
2.97
6.17
9.04
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


OAc
OAc
AcO
O
COOMe
BocHN
AcO
20
CDCl$_3$, 126 MHz
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


OAc
OAc
AcO
COOMe
O
OH
BocHN
AcO
F
21
CDCl$_3$, 500 MHz
0.99
1.02
2.19
2.14
1.00
1.00
2.29
3.00
3.01
6.16
3.19
9.01
7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
f1 (ppm)


OAc
OAc
AcO
COOMe
O
OH
BocHN
AcO
F
21
CDCl$_3$, 126 MHz
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)