Development of αGlcN(1↔1)αMan-based Lipid A Mimetics as Novel Class of Potent Toll-like Receptor 4 (TLR4) Agonists

Florian Adanitsch, Simon Ittig, Johannes Stöckl, Alja Oblak, Mira Haegman, Roman Jerala, Rudi Beyaert, Paul Kosma, and Alla Zamyatina*

e-mail: alla.zamyatina@boku.ac.at

Supporting Information

Content

Supplementary SI-Table 1

Glycosylation of lactol 8 with 2-*O*-levulinoyl-protected mannosyl donors

A coupling of the TCA donor **18** and lactol acceptor **8** using trimethylsilyl trifluoromethanesulfonate (TMSOTf) as promoter resulted in the formation of orthoester **23** as the major product (23%), along with hydrolyzed donor **16** and unreacted acceptor **8** (Scheme 4A, SI-Table 1: Entry 1). By lowering the reaction temperature and using higher amounts of promoter, the formation of the orthoester could be suppressed, although the target α,α–disaccharide **22** was obtained in only 8% yield (SI-Table 1: Entry 2) together with concurrently formed donor self-coupling product **24** (Scheme 4A). With the less reactive NPTFA donor **19** the formation of the orthoester was not observed, however the desired product **22** was isolated only in trace amounts (SI-Table 1: Entry 3).

The failure of the imidate-mediated couplings was initially linked to the diminished reactivity of the axial 1-OH group in acceptor **8** due to the H-bonding with the carbamate NH group. Therefore, an inverse glycosylation procedure[1] was employed where TMSOTf was exchanged to boron trifluoroetherate (BF_3•Et_2O) as promoter to avoid 1-*O*-silylation of the relatively unreactive acceptor **8** (SI-Table 1: Entry 4). Again, a preponderant formation of the orthoester **23** was observed. Since orthoesters can be rearranged to glycosides,[2] *in situ* activation of **23** with additional amount of promoter was attempted (SI-Table 1: Entry 4, 5) which did not result in the formation of the desired α,α-product **22**. Varying temperature, amount of the donor/promoter (TMSOTf) and the solvent did not improve the glycosylation outcome (SI-Table 1: Entry 5). With thioglycoside donor **14** only a trace amount of the disaccharide **22** was obtained (SI-Table 1: Entry 6).

SI-Table 1. Glycosylation outcome of the couplings between acceptor 8 and donors 18, 19 and 14 (according to Scheme 4A).

	Donor (eq)	Promotor (eq)	Solvent	T / °C	Product / Yield
1	**18** (1)	TMSOTf (0.05)	CH_2Cl_2	0	**23** / 23%
2	**18** (1)	TMSOTf (0.2)	CH_2Cl_2	-15	**22** / 8%
3	**19** (1.5)	TMSOTf (0.05÷1.5)	CH_2Cl_2	-15÷0÷25	**22** / traces
4	**19** (1.5)	BF_3•Et_2O (0.05)	CH_2Cl_2	0	**23** / *in situ* activation BF_3•Et_2O (0.05 eq.)
5	**19** (1.5)	TMSOTf (0.01)	CH_3CN-CH_2Cl_2, 10:1	0	**23** / *in situ* activation TMSOTf (0.01 eq.)
6	**14** (1.2)	TfOH/NIS (0.1/1.0)	CH_2Cl_2	0	**22** / traces

^{1}H- and ^{13}C- NMR-data for orthogonally protected GlcN(1↔1)Man disaccharides

Supplementary SI-Table 2

SI-Table 2: ^{1}H- and ^{13}C-NMR shifts and the corresponding coupling constants ($^1J_{C1,H1}$ and $^3J_{H1,H2}$) of the anomeric protons/carbons of GlcN(1↔1)Man disaccharides.

Compound	GlcN(1←				→)Man				
	C-1	$^1J_{C,H}$	H-1	$^3J_{1,2}$	C-1′	$^1J_{C,H}$	H-1	$^3J_{1,2}$	H-5
	ppm	Hz	ppm	Hz	ppm	Hz	ppm	Hz	ppm
22 (αα)	92.77	175	5.14	3.7	93.44	172	5.02	1.1	3.68
28 (αα)	91.95	178	5.23	3.6	92.58	174	5.11	-	3.77
35 (αα)	92.96	173	5.15	3.8	93.72	170	5.09	1.6	3.63
36 (αα)	93.07	172	5.20	3.5	93.70	173	5.12	-	3.70
37 (αα)	93.92	175	5.13	3.1	94.87	178	5.11	1.3	3.68
38 (αβ) [a]	97.83	173	5.15	3.6	101.35	157	4.62	-	3.28
39 (αβ)	98.20	177	5.08	3.5	101.37	155	4.61	-	3.29
40 (αβ)	97.79	175	4.94	3.2	99.86	156	4.60	-	3.26
41 (βα)	100.12	n.d.	4.74	-	100.12	n.d.	4.96	-	4.03
44 (βα)	100.20	159	4.72	8.4	99.81	172	4.94	1.3	4.04
43 (βα)	101.68	160	4.78	8.3	100.70	171	5.0	-	4.10

[a] The first anomeric prefix (e.g. αβ) designate the configuration at the GlcN moiety as depicted in the formula αGlcN(1↔1)βMan.

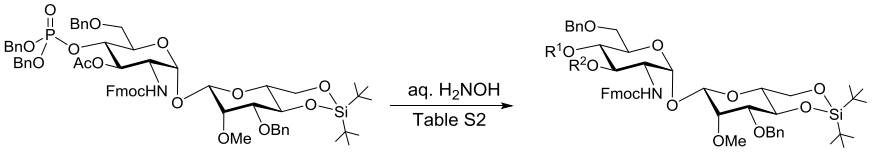
3-*O*-Deacetylation in the presence of the adjacent 2-*N*-Fmoc group.

To establish the conditions for the removal of 3-*O*-acetate protecting group in the α,α-disaccharide **36** the trial experiments with αGlcN(1↔1)βMan disaccharide **39** which possesses the same protecting group pattern as **36** but has a β−configuration at C-1 of Man were performed first. Our attempts were directed either to simultaneous removal of 3-*O*-Ac and 2-*N*-Fmoc groups or, alternatively, to the regioselective cleavage of the 3-*O*-acetae in the presence of the adjacent 2*N*-Fmoc protection.

First, a simultaneous removal of both 3-*O*-Ac and 2*N*-Fmoc protecting groups was attempted. If successful, the regioselective *N*-acylation of the free amino group would precede the DIC/DMAP-mediated *O*-acylation. Treatment of **39** with MeONa/MeOH or aq. Et_3N in methanol resulted in the cleavage of Fmoc group to furnish a free amine as a single product (positive ninhydrin-staining of the intermediate on TLC and appearance of a UV-positive apolar spot which was rationalized as released dibenzofulvene) whereas the acetate group persisted. Longer reaction times resulted in the removal of 3-*O*-acetate though the 4-*O*-phosphate group was cleaved. Although a successful acetate removal under Zemplén conditions in the presence of a phosphotriester group has been reported,[3] the loss of the 4-*O*-dibenzylphosphate group in **39** under basic conditions could be expected.

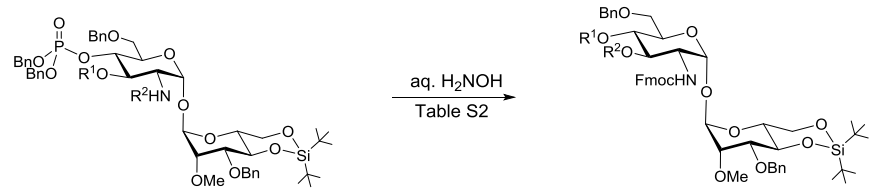
At the same time, the procedures for the exclusive cleavage of 3-*O*-acetate were investigated. A successful application of 4 Å molecular sieves in methanol for the cleavage of acetates in the presence of *N*-Fmoc group has been reported.[4] Upon application of these conditions for the deprotection of **39** no reaction was observed. By using 3 Å molecular sieves in methanol-CH_2Cl_2[5] the acetate cleavage in **39** was extremely sluggish and was accompanied by decomposition. To check the feasibility of both methods in our hands, we submitted the peracetylated monosaccharide **11** to deacetylation with 3 Å or 4 Å molecular sieves in methanol. According to HPLC-MS both reactions cleanly afforded deacetylated thiomannoside **12**, demonstrating the practicability of these deprotection approaches, which, however, were not applicable to the 3-*O*-deacetylation of the (1↔1) disaccharide **39.** Application of *p*-toluenesulfonic acid[6] for the cleavage of 3-*O*-Ac group did not bring any improvements.

Supplementary SI-Scheme 1.



39

S1 R^1 = P(O)OBn$_2$, R^2 = H
S2 R^1 = H, R^2 = P(O)OBn$_2$
S3 R^1 = P(O)(OBn)OH, R^2 = H



36

46 R^1 = P(O)OBn$_2$, R^2 = H
47 R^1 = H, R^2 = P(O)OBn$_2$
48 R^1 = P(O)(OBn)OH, R^2 = H

Next, the possibility of using the powerful α-nucleophile hydroxylamine,[7,8] which has been reported to serve as an effective acyl group acceptor[9] capable of cleaving amides[10] and esters[11] was exploited (SI-Scheme 1). Upon treatment of **39** with 50% aq. hydroxylamine in a biphasic mixture with THF the 3-*O*-deacetylated compound **S1** was isolated as the major product (55%) whereas the *N*-Fmoc group was retained. The reaction was accompanied by migration of the phosphate group from C-4 to the liberated OH group at C-3 to furnish compound **S2**. A partial loss of a benzyl protecting group at phosphorus leading to the phosphodiester **S3** was also observed. (SI-Table 3: Entry 1).

Supplementary SI-Table 3

SI-Table 3: Conditions for 3-*O*-deacetylation of **36** and **39** with aq. hydroxylamine.

	Com-pound	H_2NOH equiv.	Solvent	T °C	Time h	Product (Yield [%])			
1	**39**	725	THF	0	84	**S1** (55)	**S2** (7)	**S3** (5)	**39** (7)
2	**39**	160	$CHCl_3$-MeOH, 6:1	25	48	**S1** (31)	n.d.	n.d	n.d
3	**39**	160	Pyr-AcOH, 2:1	25	72	decomposition			
4	**39**	8	DMF	0	22	decomposition			
5	**36**	**725**	**THF**	**0**	**48**	**46** (53)	**47** (2)	**48** (9)	**36** (15)
6	**36**	80	CH_3CN	25	24	**46** (33)	**47** (9)	**48** (29)	**36** (18)

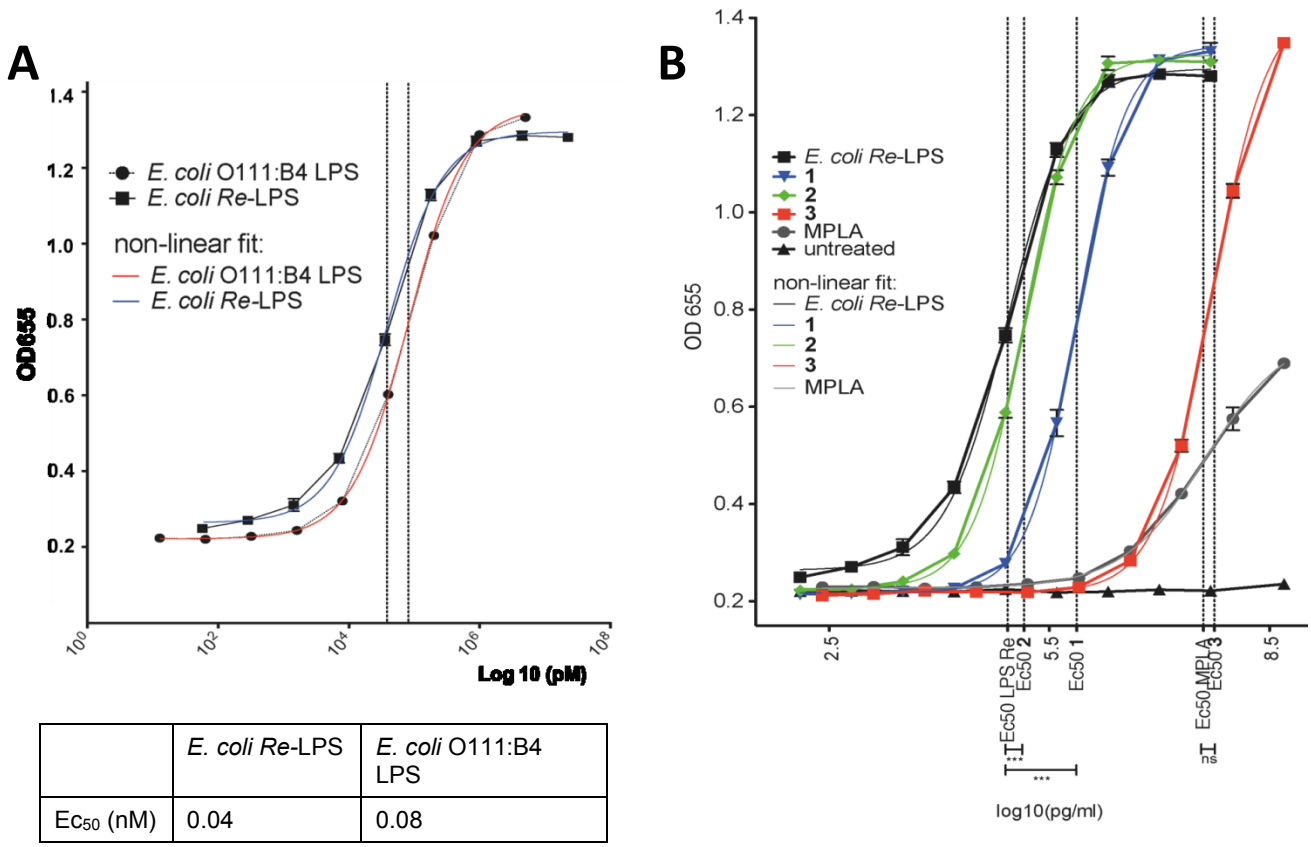
A mechanism for the partial debenzylation of phosphotriesters upon treatment with NH_2OH was proposed by Nome.[12,13] Accordingly, a nucleophilic attack of the OH group of hydroxylamine at the phosphorus atom results in the exchange of a benzyl ether for an hydroxyamino group. The amino group at the phosphate reacts further with another molecule of hydroxylamine and water to form monobenzylated phosphate diester and diimide, which disproportionates to N_2 and hydrazine.

Further optimization of reaction conditions by varying the amount of nucleophile (NH_2OH), reaction temperature and solvents did not result in any improvement (SI-Table 3: Entries 2-4). Thus, the conditions of Entry 1 in SI-Table 2 were applied to the deprotection of the key αGlcN(1↔1)αMan disaccharide **36** resulting in a successful isolation of the 3-*O*-deacetylated compound **46** as the main product (SI-Table 3: Entry 5). Minor amounts of concomitantly formed 3-*O*-phosphate **47** and partially debenzylated phosphodiester **48** were isolated as well. Upon application of acetonitrile as solvent the yield of the target compound **46** declined, whereas the proportion of debenzylated **48** increased (SI-Table 3: Entry 6).

Thus, the most high-yielding and reproducible conditions for the cleavage of 3-*O*-acetate in **36** entailed the stirring a 23 mM solution of **36** in THF with an equal volume of aq. hydroxylamine at 0 °C for 48 h. The reaction was stopped prior to completion, and the remaining starting material **36** was isolated and subjected to another reaction cycle. Accordingly, compound **46** was obtained in a 53% yield together with 2% of **47**, 9% of **48** and 15% of recovered **36** over three reaction cycles.

The same deprotection protocol was applied to the 3-*O*-deacetylation of the 2-*N*-Troc protected αGlcN(1↔1)αMan disaccharide **35**. The isolation of the target product was however much more tidies and complicated by the presence of the co-migrating by-products, so that this route was not pursued.

Supplementary SI-Figure 1



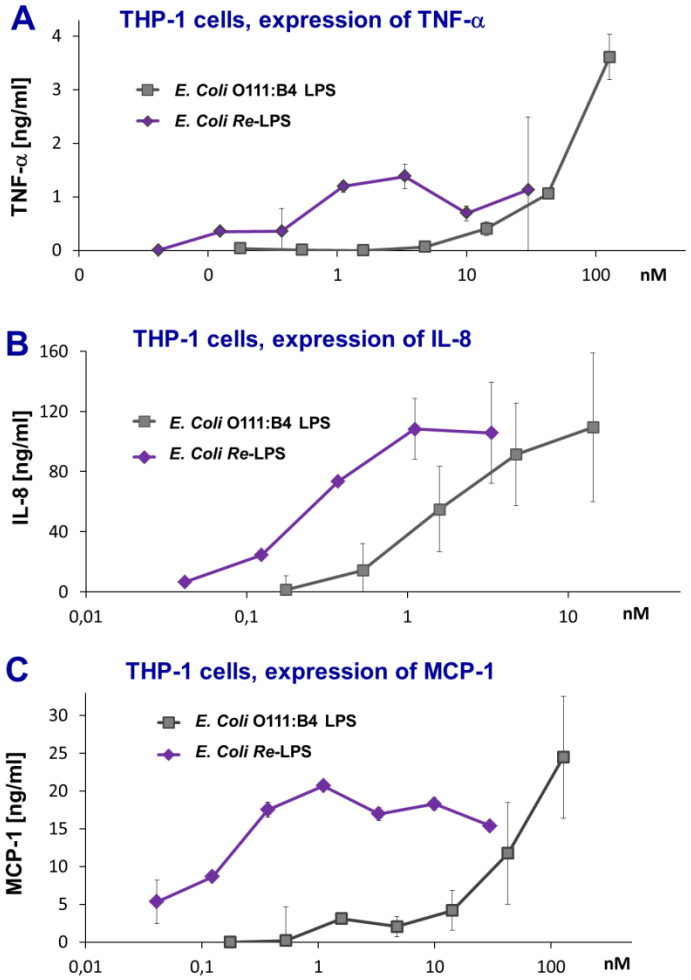
	E. coli Re-LPS	*E. coli* O111:B4 LPS
Ec_{50} (nM)	0.04	0.08

SI-Figure 1. (A) Dose-dependent activation of TLR4 signaling in hTLR4/hMD-2/hCD14 transfected HEK293 cells (HEK-Blue) by *E. coli* Re-LPS compared to *E. coli* O111:B4 LPS. [nM] concentrations were calculated from [ng/ml] concentrations based on the following molecular weights (MW): $MW_{E.\ coli\ Re\text{-}LPS}$ 2339 Da, $MW_{E.\ coli\ O111:B4\ LPS}$ 10000 Da. **(B)** Dose-dependent activation of TLR4 signaling in hTLR4/hMD-2/hCD14 transfected HEK293 cells (HEK-Blue) by Lipid A mimetics **1- 3** compared to *E. coli Re*-LPS and *S. minnesota* MPLA. Non-linear curve fit (variable slope) was calculated using GraphPad Prism and is shown for the mean curves. Dotted lines indicate corresponding Ec_{50} values. Statistical analysis was performed on non-linear curve fits on individual datasets using an un-paired two-tailed t-test (*** indicates a p value < 0.001, ns indicates non-significant change). Top, bottom, hill slope and Ec_{50} values of non-linear curve fit on individual datasets are shown.

	***E. coli Re*-LPS**			**1**			**2**			**3**			**SM-MPLA**		
	n1	n2	n3	n1	n2	n3	n1	n2	n3	n1	n2	n3	n1	n2	n3
Bottom	0.262	0.276	0.253	0.212	0.225	0.215	0.216	0.232	0.236	0.217	0.221	0.216	0.217	0.236	0.229
Top	1.277	1.304	1.308	1.369	1.312	1.348	1.330	1.319	1.320	1.425	1.426	1.453	0.8932	0.7332	0.7252
HillSlope	1.115	1.082	0.8908	1.282	1.341	1.257	1.193	1.250	1.246	1.120	1.170	1.145	0.6005	0.8738	0.8395
Ec50 (ng/ml)	0.089	0.0868	0.082	0.894	0.623	0.745	0.154	0.144	0.132	51.5	47.62	57.65	111	35.04	29.9

Supplementary SI-Figure 2

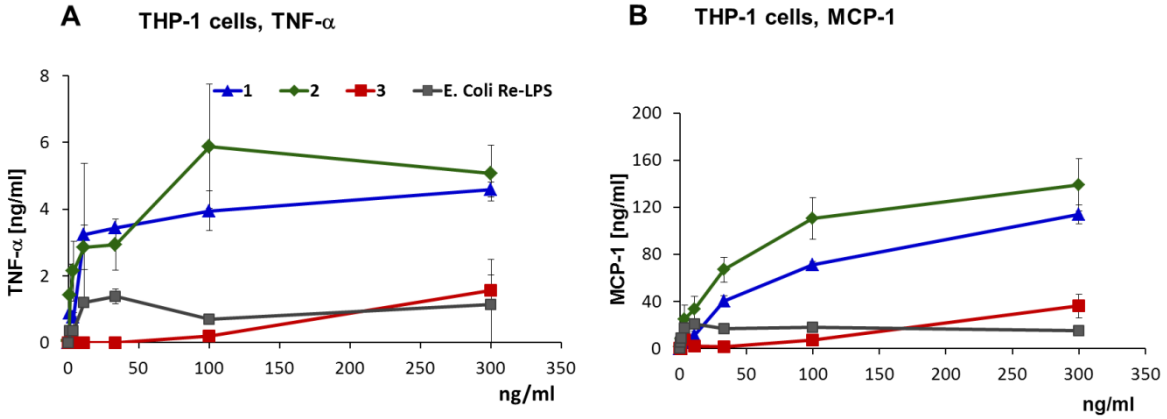
E. coli wild type O111:B4 LPS is a large heterogeneous molecule with molecular weight (MW) comprising 10-15 kDa. Since we were particularly interested in the molecular recognition mechanisms implicated in the binding of LPS by the MD-2·TLR4 complex wherein the Lipid A/Re-LPS (MW 1.8/2.2 kDa, respectively) portion of LPS is mostly involved, we have analyzed the dose-dependent THP-1 cells activation by synthetic α,α-GM-LAM **1-3** (at the concentrations 0.1 – 300 ng/ml) compared to *E. coli Re*-LPS which is more appropriate in this instance. Since the divergences in the expression of different cytokines by *E. coli* LPS vs. *Re*-LPS are only scarcely reported in the literature, we have performed dose-dependent activation experiments comparing expression of TNF-α, IL-8 and MCP-1 by *E. coli* O111:B4 LPS and *E. coli Re*-LPS at the concentrations 0.4 – 100 nM. Wild-type LPS (MW 10 kDa) induced the release of somewhat lower levels of pro-inflammatory cytokines at the nanomolar concentration range (0.4 – 10 nM), whereas at the concentrations above 10 nM (50 nM for MCP-1) the levels of cytokines production did not differ significantly. This might be explained by a different aggregation state of *Re*-LPS and wild type LPS, and, therefore, the alterations in the transfer of a single LPS molecule to TLR4·MD-2 complex by LBP and CD-14. Higher MW (> 10 kDa) of the LPS molecule applied for the calculations of the concentrations in [nM] would result in the shift of the activation profile induced by wild-type LPS. Calculation of EC_{50} values were hardly possible, since the maximum TLR4 saturation levels were not achieved at the concentrations tested.



SI-Figure 2. Dose-dependent expression of pro-inflammatory cytokines TNF-α, IL-8 and MCP-1 in human macrophage cell line THP-1 by *E. coli Re*-LPS compared to *E. coli* wild-type O111:B4 LPS. (**A**) Comparative expression of TNF-a; (**B**) comparative expression of IL-8; (**C**) comparative expression of MCP-1

Supplementary SI-Figure 3

Dose-dependent responses (THP-1 cells: α,α-GM-LAM **1-3** and *Re*-LPS) at the concentration range 0.4 – 100 ng/ml which are presented in the **Figure 5**, were extended to the higher concentration range (up to 300 ng/ml).

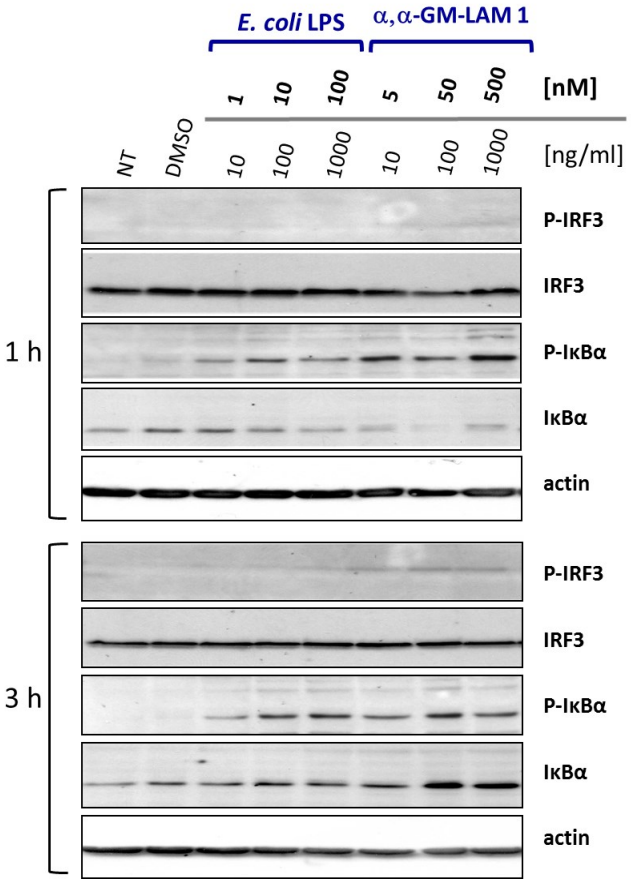


SI-Figure 3. Dose-dependent expression of cytokines induced by α,α-GM-LAM **1-3** in macrophage cell line THP-1 compared to *E. coli Re*-LPS at the concentration range 0.4 – 300 ng/ml. (**A**) Production of TNF-α; (**B**) Induction of the expression of MCP-1.

Supplementary SI-Figure 4

Lipid A mimetic **1** was examined for the activation of NF-κB (Nuclear factor kappaB) and IRF3 (Interferon regulatory factor 3). IRF3 activation (revealed by IRF-3 phosphorylation) was not noticeable after 1h stimulation, though was detectable after 3h stimulation with **1**, but not with LPS. At 1h stimulation the α,α-GM-LAM **1** was comparable with LPS in the activation NF-κB, whereas at 3h simulation compound **1** (at a concentration higher than 50 nM) was more potent activator of NF-κB than LPS as revealed by stronger phosphorylation of IκBa (P-IκBa levels) as well as the higher levels of IκBa (reflecting the NF-κB dependent re-synthesis of IκB following its degradation after 3h).

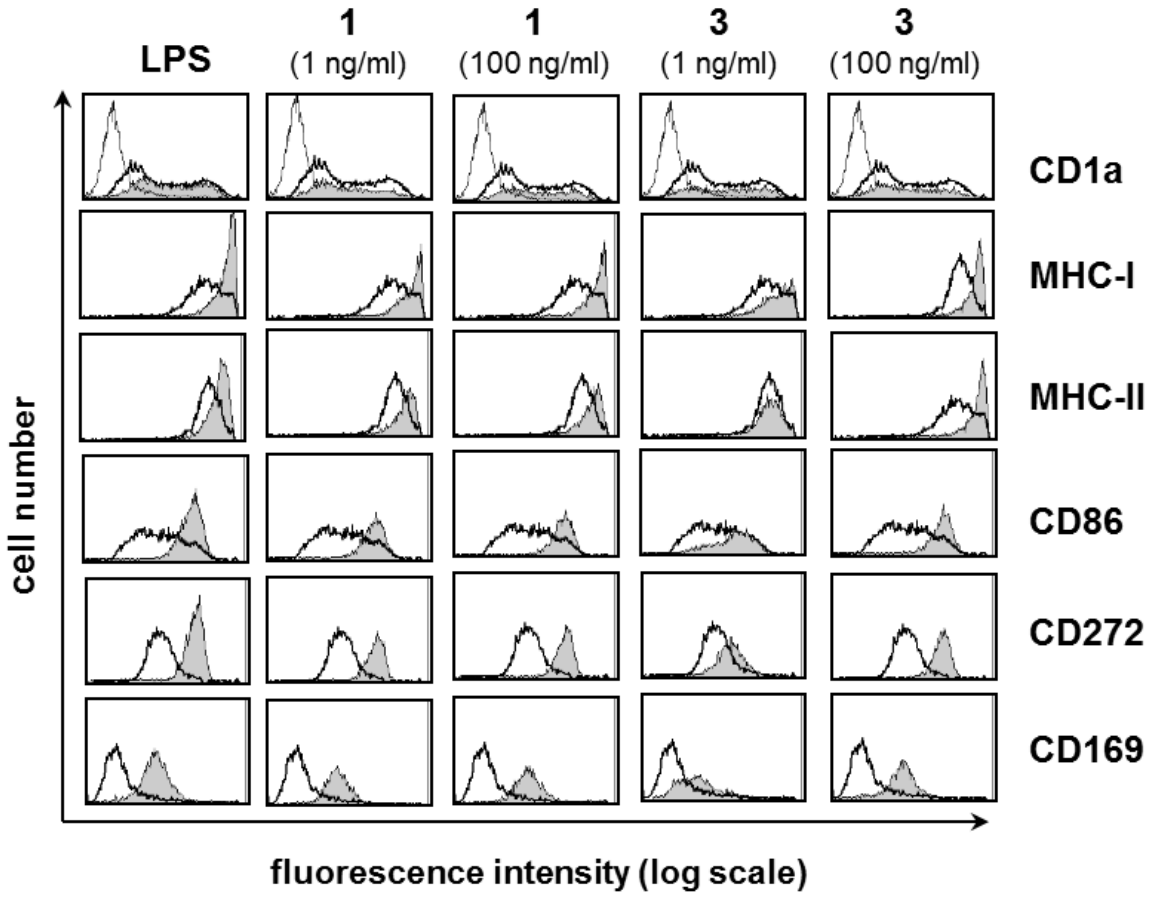
Thus, IRF3 activation and NF-κB activation (revealed by IκBα phosphorylation, IκBα degradation and its NF-κB dependent resynthesis) were more strongly induced by compound **1** compared to LPS after 3h stimulation.



SI-Figure 4. NF-κB and IRF-3 activation by LPS and α,α-GM-LAM **1** in macrophage-like cell line THP-1. THP-1 cells were treated for 1 h (upper panel) or for 3 h (lower panel) with **1** or with *E. coli* O111:B4 LPS at the concentrations 10, 100 and 1000 ng/ml. Non treated cells (NT) or cells treated with DMSO were used as controls. Cell extracts were separated by SDS polyacrylamide gel electrophoresis. Phosphorylated or total IRF-3 and IκBα was detected by western blotting as indicated. Actin detection was used as a control for equal loading in each line.

Supplementary SI-Figure 5

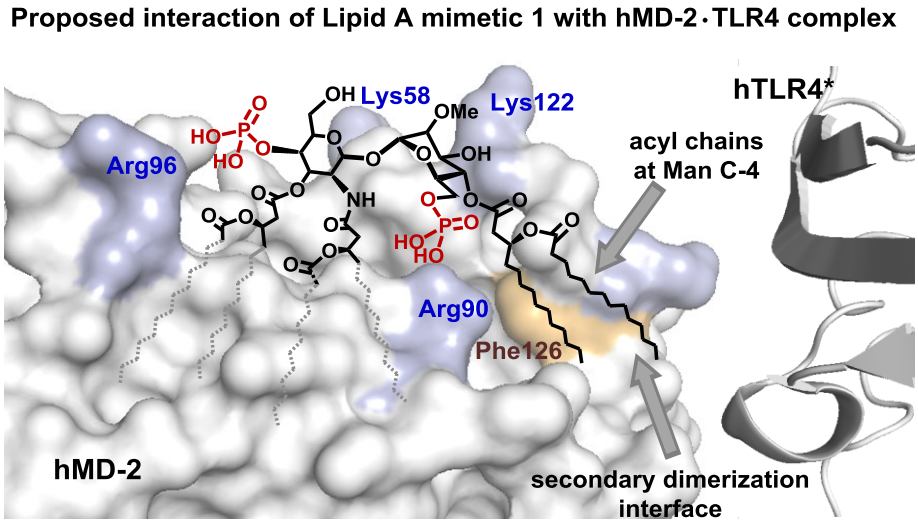
Stimulation of DCs with **1** (1 mg/ml) was as potent as by LPS in inducing DCs maturation, up-regulation of the co-stimulatory molecules CD86 as well as the antigen presenting structures MHC class I and MHC class II, which are necessary for the induction of an adaptive immune response (SI-Figure 5). Similar to LPS, α,α-GM-LAM **1** induced up-regulation of the inhibitory B7-H1 (CD272) and Sialoadhesin (CD169), which is known to be indirectly up-regulated in DCs due to release of type-I interferons. Thus, our data demonstrate that α,α-GM-LAM **1** is a potent stimulator not only of the NF-κB- but also of the IRF-pathway. Stimulation of DCs with the monophosphoryl α,α-GM-LAM **3** resulted in a less pronounced activation marker profile.



SI-Figure 5. Bisphosphoryl α,α-GM-LAM **1** and monophosphoryl α,α-GM-LAM **3** induce the expression of maturation markers in human DCs. Human peripheral blood monocytes were cultured for 6 days in GM-CSF and IL-4 to receive immature monocyte-derived DCs (*open histograms, bold line*), and were stimulated in parallel for the last 24hs of culture with **1, 3** or LPS (10 ng/ml) (gray histograms). The cells were then harvested and the surface expression level of the indicated markers was measured by flow cytometry. The thin line in the CD1a histograms represents VIAP staining (isotype control). Results are representative of three (for compound **1**) and two (for compound **3**) independent experiments.

Supplementary SI-Figure 6

The relative contribution of hydrophobic (acyl chains of Lipid A) and electrostatic (phosphate groups of Lipid A) interactions at the dimerization interface of two TLR4·MD-2·LPS complexes as well as the impact of the molecular shape of MD-2–bound Lipid A on the initiation of TLR4-mediated immune response remains largely unknown. Assuming that the two acyl lipid chains at Man C-4 of α,α-GM-LAM **1** are not included into the hydrophobic cluster formed by the four long-chain acyl residues attached to the GlcN moiety, the four lipid tails linked to GlcN unit should by fully inserted into the hydrophobic binding pocket of hMD-2 whereas the two acyl chains at Man C-4 are presumed to be exposed on the surface of the protein (SI-Figure 6). Thus, α,α-GM-LAM **1-3** should be able bridging two TLR4·MD-2 complexes by exposure of two lipid chains at Man C-4 on the surface of MD-2 thereby forming an effective hydrophobic homodimerization interface. The phosphate group at Man C-6 in α,α-GM-LAMs **1** and **2** could be either involved in the interaction with the second TLR4*·MD-2*-ligand complex or, alternatively, support the binding of the ligand by MD-2 *via* establishing ionic interaction with Arg90 at the rim of the binding groove of the co-receptor protein. According to our experimental data, the presence of the phosphate group at Man C-6 in α,α-GM-LAM **1** and **2** significantly enhances the TLR-4 stimulating activity compared to the monophosphate **3**. This might indicate both a stronger binding of the diphosphates **1** and **2** to hMD-2 due to the formation of salt bridges with positively charged Lys and Arg at the rim of the binding groove of hMD-2 and an involvement of the phosphate group at Man C-6 in the dimerization interface of two TLR4·MD-2·α,α-GM-LAM complexes.



SI-Figure 6. Proposed orientation of Lipid A mimetic **1** within the binding pocket of hMD-2 (hMD-2 from PDB code: 3FXI). Acyl chains at Man C-4 which are exposed on the surface of hMD-2 should stabilize the inward positioning of Phe126 and support hydrophobic interactions at the dimerization interface with the second TLR4*·MD-2*–α,α-GM-LAM **1** complex. Image was generated with PyMol and ChemDraw.

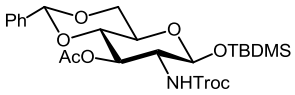
Experimental Procedures: Biological assays

Detection of IRF-3 and IκBα phosphorylation by western blotting.

THP1 monocytic cells were seeded at (2.75 x 106) cells/well in a 6-well plate in 2 ml culture medium and differentiated into macrophages by treatment with 200 nM TPA for 24 h. Next, the cells were washed twice with complete RPMI-1640 medium to remove the cells that did not adhere, refreshed with 2 ml medium and left for 1 h to recover. Cells were stimulated with 10 ng/ml, 100 ng/ml or 1000 ng/ml *E. coli* O111:B4 LPS or α,α-GM-LAM **1** which was added in 200µl complete RPMI-1640 medium (total volume 2.2 ml/well). The cells were stimulated for 1 h and 3 h at 37°C after which cells were washed with PBS and lysed in E1A buffer (50 mM Hepes pH 7.6, 250 mM NaCl, 5 mM EDTA and 0.5% NP-40) supplemented with protease inhibitors (2.1 mM leupeptine, 0.15 mM aprotinine, and 1 mM pefabloc) and phosphatase inhibitors (200 mM sodium orthovanadate, 10 mM sodium fluoride and 5 mg/ml β-glycerophosphate). Cell extracts were centrifuged at 14000 r.p.m. for 15 min in an Eppendorf centrifuge and 60 µg of the soluble fraction was separated by SDS polyacrylamide gel electrophoresis, followed by western blotting. Phosphorylated and total IRF-3 or IκBα was detected by incubating the blots with the corresponding antibodies, followed by secondary antibodies conjugated with HRP and detection by chemiluminescence. The following antibodies were used: anti-phosphoSer396-IRF3 (4D4G) and anti-phosphoSer32/36-IκBα (5A5) (Cell Signaling Technology), anti-IκBα (C-21; Sc-371) and anti-IRF3 (FL-425; Sc-9082 (Santa Cruz), anti-actin (MP Biomedicals). A secondary mouse or rabbit antibody conjugated with HRP was obtained from Amersham , secondary goat antibody conjugated with HRP was obtained from Santa Cruz.

Experimental Procedures: Synthesis

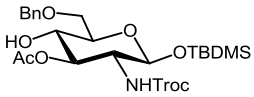
Synthesis of 5



***tert*-Butyldimethylsilyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (5).**

To a stirred solution of **4**[14] (4.50 g, 8.08 mmol) and DMAP (10 mg, 82 µmol) in pyridine (70 mL) was added acetic acid anhydride (3.00 mL, 31.9 mmol) at rt. The mixture was stirred for 3 h, then diluted with EtOAc (200 mL) and washed with aq. HCl (2 M, 500 mL), sat. aq. $NaHCO_3$ (250 mL), water (250 mL) and brine (250 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated to afford crude **5** (4.71 g, 7.86 mmol, 97%) as white solid. For analysis 540 mg of crude **5** was purified by MPLC (toluene → toluene - EtOAc, 20 : 1) to give 400 mg of **5** as white amorphous solid. R_f = 0.43 (toluene - EtOAc, 10 : 1); $[\alpha]_D^{20}$ = -35 (*c* 0.8, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.46-7.43 (m, 2H, Ph), 7.40-7.35 (m, 3H, Ph), 5.51 (s, 1H, C*H*Ph), 5.27 (t, 1H, $^3J_{3,2}$ = $^3J_{3,4}$ = 9.9 Hz, H-3), 5.08 (d, 1H, $^3J_{NH,2}$ = 9.5 Hz, N*H*), 4.81 (AB, 1H, ^2J = 12.5 Hz, CH_2, Troc), 4.80 (d, 1H, $^3J_{1,2}$ = 7.6 Hz, H-1), 4.61 (AB, 1H, ^2J = 11.8 Hz, CH_2, Troc), 4.32 (dd, 1H, $^3J_{6a,5}$ = 5.0 Hz, $^2J_{6a,6b}$ = 10.5 Hz, H-6a), 3.82 (t, 1H, $^3J_{6b,5}$ = $^2J_{6b,6a}$ = 10.3 Hz, H-6b), 3.76-3.68 (m, 1H, H-2), 3.72 (t, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = 9.4 Hz, H-4), 3.52 (ddd, 1H, $^3J_{5,4}$ = $^3J_{5,6b}$ = 9.7 Hz, $^3J_{5,6a}$ = 4.9 Hz, H-5), 2.07 (s, 3H, CH_3, Ac), 0.89 (s, 9H, 3×CH_3, TBDMS), 0.13 (s, 3H, CH_3, TBDMS), 0.11 (s, 3H, CH_3, TBDMS); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.94 (*C*O, Ac), 154.21 (*C*O, Troc), 136.93 (*C*q, CHPh), 129.12, 128.23, 126.17 (5×*C*H, CHPh), 101.47 (*C*HPh), 97.13 (C-1), 78.77 (C-4), 74.63 (*C*H_2, Troc), 71.17 (C-3), 68.60 (C-6), 66.60 (C-5), 58.89 (C-2), 25.49 (3×*C*H_3, TBDMS), 20.82 (*C*H_3, Ac),17.85 (*C*q, TBDMS), -4.21, -5.33 (2×*C*H_3, TBDMS); HRMS (ESI): *m/z* calcd for $C_{24}H_{34}Cl_3NO_8Si$-H$^-$: 596.1047 [M-H]$^-$; found 596.1042.

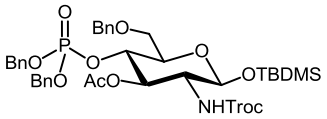
Synthesis of 6



***tert*-Butyldimethylsilyl 3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (6).**

A mixture of **5** (3.50 g, 5.84 mmol) and activated powdered 4 Å molecular sieves in dry CH_2Cl_2 (70 mL) was stirred at r.t. for 1.5 h under atmosphere of Ar. The mixture was then cooled to -78 °C and triethylsilane (1.70 mL, 10.7 mmol) and triflic acid (1.70 mL, 12.0 mmol) were added successively. After stirring for 2 h, the reaction was quenched by successive addition of MeOH (3 mL) and Et_3N (3 mL). The mixture was warmed to r.t., diluted with EtOAc (250 mL) and filtered over a pad of Celite. The filtrate was washed with aq. HCl (2 M, 100 mL), sat. aq. $NaHCO_3$ (200 mL), water (200 mL) and brine (200 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by MPLC (toluene - EtOAc, 5 : 1) to afford compound **6** (2.40 g, 3.99 mmol, 68%) as white amorphous solid. R_f = 0.35 (toluene – EtOAc, 2 : 1); $[\alpha]_D^{20}$ = -26 (*c* 0.9, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.37-7.27 (m, 5H, CH_2Ph), 5.02 (dd, 1H, ^3J = 10.9 Hz, ^3J = 9.1 Hz, H-3), 5.05-5.00 (m, 1H, N*H*), 4.77 (AB, 1H, ^2J = 11.6 Hz, CH_2, Troc), 4.70 (d, 1H, $^3J_{1,2}$ = 7.9 Hz, H-1), 4.61 (AB, 1H, CH_2, Troc), 4.61 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph), 4.57 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 3.82-3.73 (m, 3H, H-4, H-6a, H-6b), 3.64-3.57 (m, 1H, H-2), 3.57-3.51 (m, 1H, H-5), 2.10 (s, 3H, CH_3, Ac), 0.88 (s, 9H, 3xCH_3, TBDMS), 0.12 (s, 3H, CH_3, TBDMS), 0.09 (s, 3H, CH_3, TBDMS); ^{13}C-NMR (101 MHz, $CDCl_3$): δ 171.82 (*C*O, Ac), 154.18 (*C*O, Troc), 137.56 (*C*q, CH_2Ph), 128.48, 127.88, 127.66 (5×*C*H, CH_2Ph), 96.46 (C-1), 95.38 (*C*Cl_3, Troc), 74.88 (C-3), 74.57 (*C*H_2, Troc), 73.95 (C-5), 73.80 (*C*H_2Ph), 71.14 (C-4), 70.55 (C-6), 57.89 (C-2), 25.53 (3×*C*H_3, TBDMS), 20.91 (*C*H_3, Ac), 17.88 (*C*q, TBDMS), -4.17, -5.31 (2×*C*H_3, TBDMS); HRMS (ESI): *m/z* calcd for $C_{24}H_{36}Cl_3NO_8Si$-H$^-$: 598.1203 [M-H]$^-$; found 598.1202.

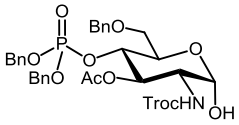
Synthesis of 7



***tert*-Butyldimethylsilyl 3-*O*-acetyl-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (7).**

To a solution of **6** (2.40 g, 3.99 mmol) in dry CH_2Cl_2 (40 mL) were added dibenzyl *N,N*-diisopropylphosphoramidite (2.00 mL, 5.36 mmol, 90%) and a solution of 1*H*-tetrazole in CH_3CN (17.7 mL, 5.99 mmol, 0.45 M in CH_3CN) at r.t. under atmosphere of Ar. After 30 min the mixture was cooled to -78 °C and *m*CPBA (2 g, 8.11 mmol, 70% in 40 ml CH_2Cl_2) was added. After stirring for 1 h, the reaction was quenched by addition of Et_3N (1.3 ml) and it was warmed to rt. The mixture was diluted with EtOAc (300 ml) and washed with sat. aq. $NaHCO_3$ (300 ml) and brine (300 ml). The organic layer was dried over $MgSO_4$, filtered and concentrated. The residue was purified by MPLC (toluene - EtOAc, 4 : 1) to afford **7** (3.10 g, 3.60 mmol, 90%) as white amorphous solid. R_f = 0.29 (toluene : EtOAc = 5 : 1); $[\alpha]_D^{20}$ = -1 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.36-7.22 (m, 15H, CH_2Ph), 5.26 (dd, 1H, ^3J = 10.8 Hz, ^3J = 9.1 Hz, H-3), 5.02-4.98 (m, 1H, 2-N*H*), 4.98-4.88 (m, 4H, OP(O)(OCH_2Ph)$_2$)), 4.76 (d, 1H, $^3J_{1,2}$ = 7.8 Hz, H-1), 4.74 (AB, 1H, ^2J = 11.7 Hz, CH_2, Troc), 4.62 (AB, 1H, ^2J = 11.7 Hz, CH_2, Troc), 4.52 (AB, 1H, ^2J = 12.2 Hz, CH_2Ph), 4.51-4.47 (m, 1H, H-4), 4.47 (AB, 1H, ^2J = 12.3 Hz, CH_2Ph), 3.79-3.75 (m, 1H, H-6a), 3.65-3.55 (m, 3H, H-2, H-5, H-6b), 1.89 (s, 3H, CH_3, Ac), 0.87 (s, 9H, 3×CH_3, TBDMS), 0.13 (s, 3H, CH_3, TBDMS), 0.09 (s, 3H, CH_3, TBDMS); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 171.08 (*C*O, Ac), 153.98 (*C*O, Troc), 138.11 (C_q, CH_2Ph), 135.56 (C_q, $^3J_{C,P}$ = 7 Hz, OP(O)(OCH_2Ph)$_2$)), 135.46 (C_q, $^3J_{C,P}$ = 8 Hz, OP(O)(OCH_2Ph)$_2$), 128.61, 128.59, 128.28, 128.00, 127.95, 127.49, 127.47 (15×*C*H, CH_2Ph), 96.17 (C-1), 74.56 (*C*H_2, Troc), 74.33 (C-4 or C-5, $J_{C,P}$ = 5.8 Hz), 74.05 (C-4 or C-5, $J_{C,P}$ = 6.1 Hz), 73.39 (*C*H_2Ph), 72.39 (C-3), 69.64, 69.61, 69.58, 69.56 (2×*C*H_2, OP(O)(O*C*H_2Ph)$_2$), 68.66 (C-6), 58.28 (C-2), 25.53 (3×*C*H_3, TBDMS), 20.68 (*C*H_3, Ac), 17.87 (*C*q, TBDMS), -4.16, -5.30 (2×*C*H_3, TBDMS); ^{31}P-NMR (162 MHz, $CDCl_3$): δ -2.16; HRMS (ESI): *m/z* calcd for $C_{38}H_{49}Cl_3NO_{11}PSi$-H$^-$: 858.1805 [M-H]$^-$: found 858.1807.

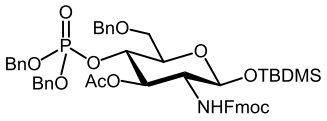
Synthesis of 8



3-*O*-Acetyl-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(2,2,2-trichloroethoxy-carbonylamino)-D-glucopyranose (8).

To a solution of **7** (1.50 g, 1.74 mmol) in dry THF (20 ml) in a PTFE-vial was a solution of HF•Py in Pyridine (2.5 ml, 70% HF) was added at 0 °C under atmosphere of Ar. After 10 min the mixture was warmed to rt and stirred for 12 h. The solution was diluted with EtOAc (200 ml) and washed with sat. aq. $NaHCO_3$ (2×30 ml), water (30 ml) and brine (30 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by MPLC (CH_2Cl_2 – MeOH, 50 : 1 → 25 : 1) to afford **8** (1.19 g, 1.59 mmol, 91%, α : β = 9 : 1) as white amorphous solid. R_f = 0.37 (hexane – EtOAc, 1 : 1); $[\alpha]_D^{20}$ = +20 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$ + 1% MeOD): δ 7.35-7.24 (m, 15H, CH_2Ph), 5.38 (dd, 1H, $^3J_{3,2}$ = 10.7 Hz, $^3J_{3,4}$ = 9.1 Hz, H-3), 5.21 (d, 1H, $^3J_{1,2}$ = 3.5 Hz, H-1), 4.98-4.83 (m, 4H, 2×CH_2, OP(O)(OCH_2Ph)$_2$), 4.78 (AB, 1H, ^2J = 12.0 Hz, CH_2, Troc), 4.62 (AB, 1H, ^2J = 12.0 Hz, CH_2, Troc), 4.51 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph), 4.43 (AB, 1H, ^2J = 11.7 Hz, CH_2Ph), 4.42-4.36 (m, 1H, H-4), 4.18 (ddd, 1H, $^3J_{5,4}$ = 10.0 Hz, $^3J_{5,6a}$ = 1.8 Hz, $^3J_{5,6b}$ = 6.5 Hz, H-5), 3.94 (dd, 1H, $^3J_{2,1}$ = 3.6 Hz, $^3J_{2,3}$ = 10.7 Hz, H-2), 3.77 (dd, 1H, $^3J_{6a,5}$ = 1.9 Hz, $^2J_{6a,6b}$ = 10.6 Hz, H-6a), 3.61 (dd, 1H, $^3J_{6b,5}$ = 6.5 Hz, $^2J_{6b,6a}$ = 10.6 Hz, H-6b), 1.85 (s, 3H, CH_3, Ac); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 171.18 (*C*O, Ac), 154.14 (*C*O, Troc), 137.50 (C_q, CH_2Ph), 135.38 (2×C_q, OP(O)(OCH_2Ph)$_2$), 128.73, 128.68, 128.66, 128.60, 128.39, 128.04, 127.99, 127.90, 127.84 (15×*C*H, CH_2Ph), 95.33 (*C*Cl_3, Troc), 91.47 (C-1), 74.51 (*C*H_2, Troc), 73.95 (C-4, $^2J_{C4,P}$ = 6.2 Hz), 73.47 (*C*H_2, *C*H_2Ph), 70.96 (C-3, $^3J_{C3,P}$ = 6.2 Hz), 69.65 (*C*H_2, $^2J_{C,P}$ = 5.9 Hz, OP(O)(O*C*H_2Ph)$_2$), 69.56 (*C*H_2, $^2J_{C,P}$ = 5.9 Hz, OP(O)(O*C*H_2Ph)$_2$), 69.31 (C-5, $^3J_{C5,P}$ = 5.8 Hz), 68.57 (C-6), 54.15 (C-2), 20.69 (*C*H_3, Ac); ^{31}P-NMR (162 MHz, $CDCl_3$): δ -2.21; HRMS (ESI): *m/z* calcd for $C_{32}H_{35}Cl_3NO_{11}P$+H$^+$: 746.1089 [M+H$^+$]; found 746.1086.

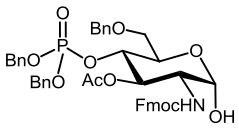
Synthesis of 9



tert-Butyldimethylsilyl 3-*O*-acetyl-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(9-fluorenylmethoxycarbonylamino)-β-D-glucopyranoside (9).

To a solution of **8** (645 mg, 749 µmol) in dry CH_2Cl_2 (40 ml), Zn dust (2.4 g) and acetic acid (18 ml) were added at 0 °C under atmosphere of Ar. The mixture was sonicated for 1.5 h, while the temperature of the reaction mixture was kept in the range of 5 °C – 20 °C. The mixture was diluted with CH_2Cl_2 (200 ml), filtered over a pad of Celite, the filtrate was washed with sat. aq. $NaHCO_3$ (2×200 ml) and brine (100 ml). The organic phase was dried over Na_2SO_4, filtered and concentrated to afford the intermediate amine (513 mg) as a pale yellow syrup. The crude amine was dissolved in dry CH_2Cl_2 (6 ml) and diisopropylethylamine (150 µL, 908µmol) and a solution of 9-fluorenylmethyl chloroformate (255 mg, 986 µmol) in dry CH_2Cl_2 (1 ml) were added at 0 °C. The mixture was stirred for 2 h. at r. t., diluted with CH_2Cl_2 (80 ml) and washed with brine (100 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by MPLC (toluene – EtOAc, 5 : 1) to afford **9** (608 mg, 670 µmol, 89%, over 2 steps) as amorphous solid. R_f = 0.47 (toluene - EtOAc, 5 : 3); $[\alpha]_D^{20}$ = -2 (*c* 1.1, $CHCl_3$); ^{1}H-NMR (300 MHz, DMSO-d6): δ 7.90-7.87 (m, 2H, arom.), 7.66-7.64 (m, 2H, arom.), 7.46-7.22 (m, 19H, arom.), 5.19 (t, 1H, $^3J_{2,3}$ = $^3J_{3,4}$ = 9.8 Hz, H-3), 4.98-4.92 (m, 4H, OP(O)(OCH_2Ph)$_2$), 4.80 (d, 1H, $^3J_{1,2}$ = 7.9 Hz, H-1), 4.47-4.28 (m, 4H, H-6, CH_2Ph, CH_2, Fmoc,), 4.20-4.13 (m, 2H, CH_2, C*H*, Fmoc), 3.71-3.65 (m, 2H, H-5, H-6a), 3.56 (dd, 1H, *J* = 5.8 Hz, *J* = 11.6 Hz, H-6b), 3.44-3.34 (m, 2H, H-2, N*H*), 1.80 (s, 3H, CH_3, Ac), 0.78 (s, 9H, 3×CH_3, TBDMS), 0.06 (s, 3H, CH_3, TBDMS), 0.03 (s, 3H, CH_3, TBDMS); ^{13}C-NMR (75 MHz, DMSO-d6): δ 169.76 (*C*O, Ac), 155.88 (*C*O, Fmoc), 143.80, 143.75, 140.73, 140.71 (4×*C*q, Fmoc), 138.28 (*C*q, CH_2Ph), 135.88 (*C*q, $^3J_{C,P}$ = 7.0 Hz, OP(O)(OCH_2Ph)$_2$), 135.79 (*C*q, $^3J_{C,P}$ = 7.2 Hz, OP(O)(OCH_2Ph)$_2$), 128.51, 128.17, 127.93, 127.86, 127.65, 127.37, 127.23, 127.07, 125.21, 125.10, 120.15 (23×*C*H, arom.), 95.56 (C-1), 73.95, 73.17 (C-4, C-5, $J_{C,P}$ = 5.8 Hz, $J_{C,P}$ = 6.0 Hz,), 72.80 (C-3), 72.26 (*C*H$_2$Ph), 68.90, 68.83 (2×*C*H$_2$, OP(O)(OCH_2Ph)$_2$), 68.38 (C-6), 65.60 (*C*H$_2$, Fmoc), 57.30 (C-2), 46.56 (*C*H, Fmoc), 25.44 (3×*C*H$_3$, TBDMS), 20.67 (*C*q, TBDMS), 17.55 (*C*H$_3$, Ac), -4.34, -5.30 (2×*C*H$_3$, TBDMS); ^{31}P-NMR (122 MHz, DMSO-d6) δ -1.96; HRMS (ESI): *m/z* calcd for $C_{50}H_{58}NO_{11}PSi$+COOH$^-$: 952.3499 [M+COOH$^-$]; found 952.3501.

Synthesis of 10

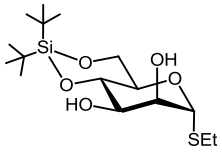


3-*O*-Acetyl-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(9-fluorenylmethoxycarbonyl-amino)-D-glucopyranose (10).

To a solution of **9** (539 mg, 594 µmol) in dry THF (6 ml) in a PTFE-vial a solution of HF•Py (400 µL, 70% HF) was added at 0 °C under atmosphere of Ar. After 10 min the mixture was warmed to r. t. and stirred for 15 h. The solution was diluted with CH_2Cl_2 (200 ml), washed with sat. aq. $NaHCO_3$ (100 ml) and brine (100 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by MPLC (toluene - EtOAc, 1 : 1) to afford **10** (448 mg, 564 µmol, 94%, α/β = 9 : 1) as amorphous solid. R_f = 0.33 and 0.21 (toluene – EtOAc, 1 : 1); $[\alpha]_D^{20}$ = +23 (*c* 1.4, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$, α-anomer): δ 7.74-7.72 (m, 2H, arom.), 7.56-7.51 (m, 2H, arom.), 7-39-7.20 (m, 19H, arom.), 5.38 (dd, 1H, ^3J = 10.7 Hz, ^3J = 9.2 Hz, H-3), 5.22 (t, 1H, $^3J_{1,2}$ = $^3J_{1,OH}$ = 3.3 Hz, H-1), 5.17 (d, 1H, $^3J_{NH,2}$ = 9.8 Hz, N*H*), 4.93-4.84 (m, 4H, OP(O)(OCH_2Ph)$_2$), 4.54-4.35 (m, 5H, 1-O*H*, H-4, CH_2Ph, CH_2 Fmoc), 4.23-4-13 (m, 3H, H-5, CH_2, C*H* Fmoc) 3.95 (td, 1H, $^3J_{1,2}$ = 2.6 Hz, $^3J_{2,3}$ = $^3J_{2,NH}$ = 10.3 Hz, H-2), 3.73-3.69 (m, 1H, H-6a), 3.60 (dd, 1H, *J* = 10.7 Hz, *J* = 5.9 Hz, H-6b), 1.83 (s, 3H, CH_3, Ac); ^{13}C-NMR (75 MHz, $CDCl_3$, α-anomer): δ 171.29 (*C*O, Ac), 155.83 (*C*O, Fmoc), 143.73, 141.65, 141.23, 141.18 (4×*C*q, Fmoc), 137.54 (*C*q, CH_2Ph), 135.46 (*C*q, $^3J_{C,P}$ = 7.0 Hz, OP(O)(OCH_2Ph)$_2$) 135.36 (*C*q, $^3J_{C,P}$ = 7.1 Hz, OP(O)(OCH_2Ph)$_2$), 128.66, 128.58, 128.54, 128.32, 127.98, 127.93, 127.83, 127.73, 127.66, 127.04, 125.02, 119.93, (23×*C*H, arom.), 91.54 (C-1), 74.12 (C-4, $^2J_{C4,P}$ = 6.3 Hz), 73.40 (*C*H$_2$Ph), 71.15 (C-3), 69.59 (OP(O)(O*C*H$_2$Ph)$_2$, $^2J_{C,P}$ = 5.8 Hz), 69.51

(OP(O)(OCH_2Ph)$_2$, $^2J_{C,P}$ = 6.1 Hz), 69.23 (C-5, $^3J_{C5,P}$ = 6.1 Hz), 68.60 (C-6), 67.06 (CH_2, Fmoc), 54.06 (C-2), 47.00 (*C*H, Fmoc), 20.71 (C*H*$_3$, Ac); ^{31}P-NMR (122 MHz, $CDCl_3$): δ -2.30; HRMS (ESI): *m/z* calcd for $C_{44}H_{44}NO_{11}P$+Na^+: 816.2544 [M+Na^+]; found 816.2543.

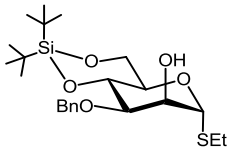
Synthesis of 12



Ethyl 4,6-*O*-di-*tert*-butylsilylene-1-thio-α-D-mannopyranoside (12).

To a solution of **11**[15,16] (19.5 g, 49.7 mmol, α : β = 6 : 1) in MeOH (260 ml) a solution of NaOMe in MeOH (0.25 M, 4.7 ml) was added at r. t. After stirring for 2 h the pH of the solution was adjusted to 7 by addition of Dowex 50 (H^+) cation-exchange resin. The resin was removed by filtration and the filtrate was concentrated to afford crude tetraol[2] (10.9 g) as a syrup. A solution of the tetraol (10.9 g) and pyridine (12 ml, 148.4 mmol) in dry DMF (120 ml) was cooled to -35 °C and (tBu)$_2$Si(OTf)$_2$ (17 ml, 52.47 mmol) was added dropwise over a period of 15 min under atmosphere of Ar. The mixture was stirred at -35 °C for 60 min and then the reaction was quenched by addition of MeOH (3 ml). The mixture was warmed to r. t., diluted with EtOAc (300 ml) and washed with sat. aq. $NaHCO_3$ (3×150 ml) and brine (150 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was co-evaporated with toluene (2×100 ml) and the crude product was purified by crystallization from Et_2O (3.5 ml×g^{-1}) to afford **12** (16.2 g, 44.4 mmol, 89% over 2 steps, α/β = 5 : 1) as white solid. R_f = 0.47 (toluene - EtOAc, 1 : 1); m.p. = 145 °C (Et_2O); $[\alpha]_D^{20}$ = +168.2 (*c* 1.1, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$, α-anomer): δ 5.30 (d, 1H, $^3J_{1,2}$ = 1.1 Hz, H-1), 4.18-3.94 (m, 5H, H-2, H-4, H-5, H-6a, H-6b), 3.81 (dd, 1H, J = 3.4 Hz, J = 8.8 Hz, H-3), 2.76-2.52 (m, 2H, CH_2, SEt), 1.29 (t, 3H, J = 7.4 Hz, CH_3, SEt), 1.06 (s, 9H, 3×CH_3, DTBS), 1.01 (s, 9H, 3×CH_3, DTBS). ^{13}C-NMR (75 MHz, $CDCl_3$, α-anomer): δ 84.02 (C-1), 74.98 (C-2 or C-4), 72.28 (C-3), 71.96 (C-2 or C-4), 66.96 (C-5), 66.20 (C-6), 27.44, 27.01 (6×*C*H$_3$, DTBS), 25.17 (*C*H$_2$, SEt), 22.63, 20.00 (2×C_q, DTBS), 14.88 (*C*H$_3$, SEt); HRMS (ESI): *m/z* calcd for $C_{16}H_{32}O_5SSi$+NH_4^+: 382.2078 [M+NH_4^+]; found 382.2083.

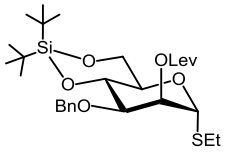
Synthesis of 13



Ethyl 3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-1-thio-α-D-mannopyranoside (13).

A solution of **12** (2.07 g, 5.68 mmol) and Bu_2SnO (1.65 g, 6.63 mmol) in dry toluene (100 ml) was refluxed in a Dean-Stark apparatus for 3.5 h. The mixture was cooled to r. t. and tetrabutylammonium iodide (2.31 g, 6.25 mmol), dry DMF (5 ml) and BnBr (0.75 ml, 6.3 mmol) were added. The mixture was refluxed for 3.5 h, cooled to r. t., diluted with EtOAc (200 ml) and washed with 1 M aq. HCl (3×300 ml) and $NaHCO_3$ (300 ml). The organic layer was filtered over a pad of Celite, the filtrate was washed with 5% aq. $Na_2S_2O_3$ (200 ml), water (200 ml) and brine (200 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel chromatography (toluene – EtOAc, 10 : 1) to afford **13** (2.40 g, 5.28 mmol, 93%) as a pale yellow syrup. R_f = 0.57 (toluene – EtOAc, 3 : 1); $[\alpha]_D^{20}$ = +118 (*c* 1.4, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.41-7.28 (m, 5H, CH_2Ph), 5.30 (s, 1H, H-1), 4.93 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.78 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.29 (t, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = 9.1 Hz, H-4), 4.14 (td, 1H, $^3J_{5,6}$ = $^3J_{5,4}$ = 9.8 Hz, $^3J_{5,6}$ = 4.7 Hz, H-5), 4.10-3.96 (m, 3H, H-2, H6a, H6b), 3.63 (dd, 1H, $^3J_{3,4}$ = 3.4 Hz, $^3J_{3,4}$ = 8.9 Hz, H-3), 2.78 (d, 1H, J = 1.7 Hz, 2-O*H*), 2.70-2.50 (m, 2H, CH_2, SEt), 1.28 (t, 3H, J = 7.4 Hz, *C*H$_3$, SEt), 1.08 (s, 9H, 3×CH_3, DTBS), 1.03 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 138.24 (C_q, CH_2Ph), 128.42, 127.81, 127.71 (5×*C*H, CH_2Ph), 83.82 (C-1), 78.58 (C-3), 75.34 (C-4), 73.37 (*C*H$_2$, 3-OBn), 71.58 (C-2), 67.41 (C-5), 66.49 (C-6), 27.44, 27.07 (6×*C*H$_3$, DTBS), 24.99 (*C*H$_2$, SEt), 22.62, 20.02 (2×C_q, DTBS), 14.88 (*C*H$_3$, SEt); HRMS (ESI): *m/z* calcd for $C_{23}H_{38}O_5SSi$+Na^+: 477.2101 [M+Na^+]; found 477.2101.

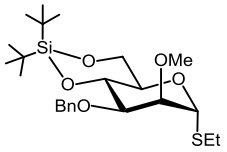
Synthesis of 14



Ethyl 3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-levulinoyl-1-thio-α-D-mannopyranoside (14).

To a stirred solution of compound **13** (604 mg, 1.33 mmol), levulinic acid (270 µl, 2.66 mmol) and DMAP (10 mg, 82 µmol) in dry CH_2Cl_2 (10 ml), was added *N,N'*-diisopropylcarbodiimide (416 µL, 2.66 mmol) at 0 °C under atmosphere of Ar. After 15 min the reaction was warmed to r. t. and stirred for 4 h. The solids were removed by filtration over a pad of Celite, the filtrate was concentrated, the residue was purified by silica gel chromatography (hexane – EtOAc, 2 : 1) to afford **14** (666 mg, 1.20 mmol, 90%) as a syrup. R_f = 0.39 (hexane – EtOAc, 2 : 1); $[\alpha]_D^{20}$ = +53 (*c* 1.1, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.32-7.16 (m, 5H, CH_2Ph), 5.28 (dd, 1H, $^3J_{2,1}$ = 1.4 Hz, $^3J_{2,3}$ = 3.5 Hz, H-2), 5.10 (d, 1H, $^3J_{1,2}$ = 1.4 Hz, H-1), 4.64 (s, 2H, CH_2Ph), 4.12 (t, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = 8.9 Hz, H-4), 4.06 (dd, 1H $^3J_{6a,5}$ = 4.4 Hz, $^2J_{6a,6b}$ = 9.7 Hz, H-6a), 4.02-3.93 (m, 1H, H-5), 3.90 (t, 1H, $^3J_{6b,5}$ = $^2J_{6b,6a}$ = 9.7 Hz, H-6b), 3.59 (dd, 1H, $^3J_{3,2}$ = 3.5 Hz, $^3J_{3,4}$ = 8.9 Hz, H-3), 2.79-2.44 (m, 6H, 3×CH_2, SEt, Lev), 2.09 (s, 3H, CH_3, Lev), 1.20 (t, 3H, ^3J = 7.4 Hz, CH_3, SEt), 1.02 (s, 9H, 3×CH_3, DTBS), 0.94 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 206.36 (*C*O, Lev), 171.98 (*C*O, Lev), 138.39 (C_q, CH_2Ph), 128.25, 127.42, 127.40 (5×*C*H, CH_2Ph), 83.07 (C-1), 76.60 (C-3), 74.96 (C-4), 72.33 (*C*H_2, *C*H_2Ph), 72.00 (C-2), 68.03 (C-5), 66.48 (C-6), 38.03 (*C*H_2, Lev), 29.77 (*C*H_3, Lev), 28.12 (*C*H_2, Lev), 27.40, 27.04 (6×*C*H_3, DTBS), 25.58 (*C*H_2, SEt), 22.67, 19.98 (2×C_q, DTBS), 14.92 (*C*H_3, SEt); HRMS (ESI): *m/z* calcd for $C_{28}H_{44}O_7SSi+Na^+$: 575.2469 [M+Na^+]; found 575.2470.

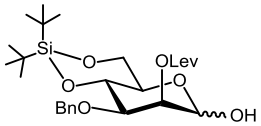
Synthesis of 15



Ethyl 3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-1-thio-α-D-mannopyranoside (15).

A slurry of **13** (1.30 g, 2.86 mmol) and NaH (210 mg, 8.75 mmol, 60% in mineral oil) in dry DMF (50 ml) was stirred at -40 °C for 1.5 h under atmosphere of Ar. Then CH_3I (300 µL, 4.82 mmol) was added, the mixture was warmed to r. t. and stirred for 2.5 h. Methanol (10 ml) was added and the mixture was stirred for 10 min, diluted with $CHCl_3$ (100 ml) and washed with aq. HCl (1 M, 300 ml), sat. aq. $NaHCO_3$ (200 ml), aq. $Na_2S_2O_3$ (5%, 100 ml) and brine (100 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel chromatography (toluene – EtOAc, 30 : 1) to afford **15** (1.13 g, 2.41 mmol, 84%, α/β = 30 : 1) as a pale yellow syrup. R_f = 0.61 (hexane – EtOAc, 3 : 1); $[\alpha]_D^{20}$ = +101 (*c* 0.9, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$, α-anomer): δ 7.41-7.25 (m, 5H, CH_2Ph), 5.30 (d, 1H, $^3J_{1,2}$ = 1.3 Hz, H-1), 4.92 (AB, 1H, ^2J = 12.3 Hz, CH_2Ph), 4.76 (AB, 1H, ^2J = 12.4 Hz, CH_2Ph) ,4.31 (t, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = 9.1 Hz, H-4), 4.13-3.95 (m, 3H, H-5, H-6a, H-6b), 3.63 (dd, 1H, $^3J_{3,2}$ = 3.3 Hz, $^3J_{3,4}$ = 9.2 Hz, H-3), 3.59 (dd, 1H, $^3J_{2,1}$ = 1.4 Hz, $^3J_{2,3}$ = 3.3 Hz, H-2), 3.50 (s, 3H, CH_3, Me), 2.70-2.52 (m, 2H, CH_2, SEt), 1.28 (t, 3H, ^3J = 7.4 Hz, CH_3, SEt), 1.08 (s, 9H, 3×CH_3, DTBS), 1.03 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (75 MHz, $CDCl_3$, α-anomer): δ 138.89 (*C*q, CH_2Ph), 128.28, 127.55, 127.45 (5×*C*H, CH_2Ph), 82.48 (C-1), 81.34 (C-2), 78.75 (C-3), 75.43 (C-4), 73.48 (*C*H_2Ph), 68.14 (C-5), 66.51 (C-6), 59.18 (*C*H_3, Me), 27.45, 27.13 (6×*C*H_3, DTBS), 25.44 (*C*H_2, SEt), 22.60, 20.01 (2×*C*q, DTBS), 15.00 (*C*H_3, SEt); HRMS (ESI): *m/z* calcd for $C_{24}H_{40}O_5SSi+H^+$: 469.2438 [M+H^+]; found 469.2431.

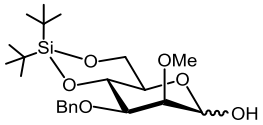
Synthesis of 16



3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-levulinoyl-D-mannopyranose (16).

Compound **14** (600 mg, 1.09 mmol) was dissolved in acetone - water (8 ml, 24 : 1) and added to a stirred solution of NBS (846 mg, 4.75 mmol) in the same solvent mixture (8 ml) at 0 °C. The mixture was stirred for 15 min and then the reaction was quenched by addition of aq. 5% $Na_2S_2O_3$ (5 ml). The mixture was warmed to r. t., diluted with EtOAc (50 ml) and washed with water (50 ml) and brine (50 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel chromatography (hexane – EtOAc, 2 : 1) to afford **16** (427 mg, 0.84 mmol, 77%, α/β = 6 : 1) as a syrup. R_f = 0.44 (hexane – EtOAc, 1 : 1); $[\alpha]_D^{20}$ = -19 (*c* 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, α-anomer): δ 7.40-7.23 (m, 5H, CH_2Ph), 5.30 (dd, 1H, $^3J_{2,1}$ = 1.6 Hz, $^3J_{2,3}$ = 3.5 Hz, H-2), 5.11 (dd, 1H, $^3J_{1,2}$ = 1.4 Hz, $^3J_{1,OH}$ = 3.8 Hz, H-1), 4.74 (s, 2H, C*H*$_2$Ph), 4.22-3.90 (m, 4H, H-4, H-5, H-6a, H-6b), 3.80 (dd, 1H, $^3J_{3,2}$ = 3.5 Hz, $^3J_{3,4}$ = 9.4 Hz, H-3), 3.13 (d, 1H, $^3J_{OH,1}$ = 4.0 Hz, 1-OH), 2.91-2.54 (m, 2×C*H*$_2$, Lev), 2.15 (s, C*H*$_3$, Lev), 1.10 (s, 3×C*H*$_3$, DTBS), 1.00 (s, 3×C*H*$_3$, DTBS); ^{13}C NMR (75 MHz, $CDCl_3$, α-anomer): δ 206.59 (*C*O, Lev), 171.13 (*C*O, Lev), 138.61(*C*q, CH_2Ph), 128.24, 127.40, 127.35 (5×*C*H, CH_2Ph), 92.93 (C-1), 75.69 (C-3), 74.80 (C-4), 72.31 (*C*H$_2$Ph), 70.49 (C-2), 67.53 (C-5), 66.33 (C-6), 38.05 (C*H*$_2$, Lev), 29.76 (*C*H$_3$, Lev), 28.11 (*C*H$_2$, Lev), 27.43, 27.05 (6×*C*H$_3$, DTBS), 22.71, 19.92 (2×*C*q, DTBS); HRMS (ESI): *m/z* calcd for $C_{26}H_{40}NaO_8Si+Na^+$: 531.2385 [M+Na$^+$]; found 531.2387.

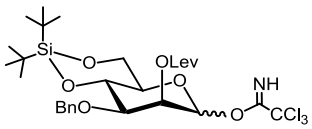
Synthesis of 17



3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-D-mannopyranose (17).

Compound **15** (1.04 g, 2.22 mmol) was dissolved in acetone - water (100 ml, 24 : 1) and added to a stirred solution of NBS (2.01 g, 11.3 mmol) in the same solvent mixture (100 ml) at 0 °C. The mixture was stirred for 15 min and then the reaction was quenched by addition of aq. $Na_2S_2O_3$ (5%, 50 ml). The mixture was warmed to r. t., diluted with EtOAc (300 ml) and washed with water (100 ml) and brine (100 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel chromatography (hexane – EtOAc, 2 : 1) to afford **17** (840 mg, 1.98 mmol, 89%, α/β = 4 : 1) as a syrup. R_f = 0.19 (hexane – EtOAc, 3 : 1); $[\alpha]_D^{20}$ = +25 (*c* 1.2, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$, α-anomer): δ 7.43-7.24 (m, 5H, CH_2Ph), 5.22 (dd, 1H, $^3J_{1,2}$ = 1.7 Hz, $^3J_{1,OH}$ = 3.5 Hz, H-1), 4.92 (AB, 1H, ^2J= 12.4 Hz, C*H*$_2$Ph), 4.76 (AB, 1H, ^2J= 12.4 Hz, C*H*$_2$Ph), 4.30 (t, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = 9.3 Hz, H-4), 4.09-3.87 (m, 3H, H-5, H-6a, H-6b), 3.76 (dd, 1H, $^3J_{3,2}$ = 3.2 Hz, $^3J_{3,4}$ = 9.5 Hz, H-3), 3.56 (dd, 1H, $^3J_{2,1}$ = 1.7 Hz, $^3J_{2,3}$ = 3.2 Hz, H-2), 3.53 (s, 3H, C*H*$_3$, Me), 2.57 (d, 1H, $^3J_{OH,1}$ = 3.5 Hz, 1-O*H*), 1.08 (s, 9H, 3×C*H*$_3$, DTBS), 1.02 (s, 9H, 3×C*H*$_3$, DTBS); ^{13}C-NMR (75 MHz, $CDCl_3$,α-anomer): δ 139.14 (*C*q, CH_2Ph), 128.27, 127.46, 127.39 (5×*C*H, CH_2Ph), 93.16 (C-1), 79.81 (C-2), 78.07 (C-3), 75.32 (C-4), 73.60 (*C*H$_2$Ph), 68.00 (C-5), 66.72 (C-6), 60.01 (*C*H$_3$, Me), 27.47, 27.13 (6×*C*H$_3$, DTBS), 22.64, 19.95 (2×*C*q, DTBS); HRMS (ESI): *m/z* calcd for $C_{22}H_{36}O_6Si+Na^+$: 447.2173 [M+Na$^+$]; found 447.2174.

Synthesis of 18

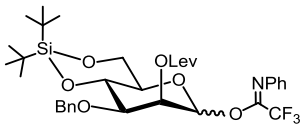


3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-levulinoyl-α-D-mannopyranose trichloroacetimidate (18).

To a solution of **16** (90 mg, 177 µmol) in dry CH_2Cl_2 (2 ml) trichloroacetonitrile (75 µL, 752 µmol) and a solution of DBU (2 µL, 15 µmol) in CH_2Cl_2 (0.5 ml) were added successively at 0 °C. The mixture was stirred for 1h., then warmed to r. t., diluted with EtOAc (10 ml) and washed with sat. aq. $NaHCO_3$ (10 ml) and brine (10 ml). The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by silica gel chromatography (hexane – EtOAc, 3 : 1 supplemented by 1% Et_3N) to afford **18** (104 mg, 159 µmol, 90%) as a syrup. R_f = 0.60 and 0.68 (hexane – EtOAc, 1 : 1 + 1% Et_3N); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.68 (s, 1H, N*H*), 7.39-7.24 (m, 5H, CH_2Ph), 6.13 (d, 1H, $^3J_{1,2}$= 1.9 Hz, H-1), 5.38 (dd, 1H, $^3J_{2,1}$ = 1.9 Hz, $^3J_{2,3}$ = 3.5 Hz, H-2), 4.77 (s, 2H, -C*H*$_2$Ph), 4.25

(t, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = 9.2 Hz, H-4), 4.15-4.11 (m, 1H, H-6a), 3.99-3.98 (m, 2H, H-5, H-6b), 3.82 (dd, 1H, $^3J_{3,2}$ = 3.5 Hz, $^3J_{3,4}$ = 9.5 Hz, H-3), 2.87-2.67 (m, 4H, 2×CH_2, Lev), 2.17 (s, 3H, CH_3, Lev), 1.11 (s, 9H, 3×CH_3, DTBS), 0.97 (s, 9H, 3×CH_3, DTBS). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 206.03 (*C*O, Lev), 171.81 (*C*O, Lev), 159.62 (O*C*(NH)CCl_3), 138.10 (C_q CH_2Ph), 128.29, 127.77, 127.58 (5×*C*H, CH_2Ph), 94.97 (C-1), 90.66 (OC(NH)*C*Cl_3), 75.25 (C-3), 74.23 (C-4), 72.70 (*C*H_2Ph), 69.90 (C-5), 68.76 (C-2), 66.35 (C-6), 37.97 (*C*H_2, Lev), 29.73 (*C*H_3, Lev), 28.01 (*C*H_2, Lev), 27.35, 26.92 (6×*C*H_3, DTBS), 22.63, 19.96 (2×C_q, DTBS).

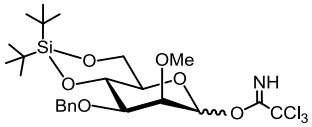
Synthesis of 19



3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-levulinoyl-D-mannopyranose *N*-phenyltrifluoroacetimidate (19).

To a vigorously stirred suspension of **16** (129 mg, 254 µmol) and K_2CO_3 (75 mg, 543 µmol) in acetone (5 ml) 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (100 µL, 630 µmol) was added. The mixture was stirred for 1 h., diluted with acetone (10 ml), the solids were removed by filtration over a pad of Celite and the filtrate was concentrated. The residue was purified by silica gel chromatography (hexane – EtOAc, 3 : 1 supplemented by 1% Et_3N) to afford **19** (172 mg, 253 µmol, 99%, α : β ~ 6 : 1) as a syrup. R_f = 0.71 and 0.67 (hexane – EtOAc, 1 : 1); ^{1}H-NMR (300 MHz, $CDCl_3$, α-anomer): δ 7.44-7.23 (m, 6H, CH_2Ph), 7.18-7.08 (m, 2H, CH_2Ph), 6.83-6.80 (m, 2H, CH_2Ph), 6.07 (br. s, 1H, H-1), 5.40 (dd, 1H, $^3J_{2,1}$ = 1.7 Hz, $^3J_{2,3}$ = 3.5 Hz, H-2), 4.80 (AB, 1H, ^2J = 12.3 Hz, CH_2Ph), 4.74 (AB, 1H, ^2J = 12.3 Hz, CH_2Ph), 4.23 (t, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = 9.4 Hz, H-4), 4.13 (dd, 1H, $^3J_{6a,5}$ = 4.7 Hz, $^2J_{6a,6b}$ = 9.8 Hz, H-6a), 3.96 (t, 1H, $^3J_{6b,5}$ = $^2J_{6b,6a}$ = 10.1 Hz, H-6b), 3.88-3.84 (m, 1H, H-5), 3.78 (dd, 1H, $^3J_{3,4}$ = 9.4 Hz, $^3J_{3,2}$ = 3.6 Hz, H-3), 2.81-2.64 (m, 4H, 2×CH_2, Lev), 2.24 (s, 3H, CH_3, Lev), 1.10 (s, 9H, 3×CH_3, DTBS), 1.00 (s, 9H, 3×CH_3, DTBS). ^{13}C-NMR (75 MHz, $CDCl_3$, α-anomer): δ 205.98 (*C*O, Lev), 171.74 (*C*O, Lev), 143.01 (O*C*(NH)CF_3), 138.20 (*C*q, *C*H_2Ph), 128.77, 128.29, 127.57, 124.59, 119.38 (10×*C*H CH_2Ph), 95.60 (*C*F_3), 94.14 (C-1), 75.73 (C-3), 74.13 (C-4), 72.89 (*C*H_2Ph), 69.75 (C-5), 68.72 (C-2), 66.31 (C-6), 37.97 (*C*H_2, Lev), 29.69 (*C*H_3, Lev), 27.98 (*C*H_2, Lev), 27.34, 26.91 (6×*C*H_3, DTBS), 22.67, 19.88 (2×*C*q, DTBS).

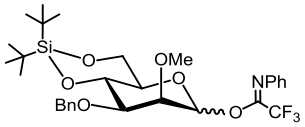
Synthesis of 20



3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-D-mannopyranose trichloroacetimidate (20).

To a solution of **17** (113 mg, 266 µmol) in dry CH_2Cl_2 (3 ml) trichloroacetonitril (140 µL, 1.40 µmol) and a solution of DBU (3.4 µL, 23 µmol)in CH_2Cl_2 (0.5 ml) were added successively at 0 °C. The mixture was stirred for 1.5 h, then warmed to r. t., diluted with EtOAc (30 ml) and washed with sat. aq. $NaHCO_3$ (30 ml) and brine (30 ml). The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (hexane – EtOAc, 4 : 1 supplemented by 1% Et_3N) to afford **20** (143 mg, 251 µmol, 94%, α/β = 7 : 1) as a pale yellow syrup. R_f = 0.61 and 0.50 and (hexane - EtOAc, 3 : 1); ^{1}H-NMR (300 MHz, $CDCl_3$, α-anomer): δ 8.59 (s, 1H, N*H*), 7.42-7.24 (m, 5H, CH_2Ph), 6.21 (d, 1H, $^3J_{1,2}$ = 1.8 Hz, H-1), 4.97 (AB, 1H, ^2J = 12.3 Hz, CH_2Ph), 4.80 (AB, 1H, ^2J = 12.3 Hz, CH_2Ph), 4.37 (t, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = 9.3 Hz, H-4), 4.13-4.07 (m, 1H, H-6a), 4.00-3.86 (m, 2H, H-5, H-6b), 3.77 (dd, 1H, $^3J_{3,2}$ = 3.3 Hz, $^3J_{3,4}$ = 9.5 Hz, H-3), 3.58 (dd, 1H, $^3J_{2,1}$ = 1.8 Hz, $^3J_{2,3}$ = 3.4 Hz, H-2), 3.57 (s, 3H, CH_3, Me), 1.08 (s, 9H, 3×CH_3, DTBS), 0.99 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (75 MHz, $CDCl_3$, α-anomer): δ 160.16 (O*C*(NH)CCl_3), 138.64 (*C*q, CH_2Ph), 128.34, 127.92, 127.61 (5×*C*H, CH_2Ph), 95.27 (C-1), 78.15 (C-2), 77.09 (C-3), 74.65 (C-4), 73.73 (*C*H_2Ph), 70.33 (C-5), 66.38 (C-6), 59.84 (*C*H_3, Me), 27.39, 27.01 (6×*C*H_3, DTBS), 22.57, 19.99 (2×*C*q, DTBS).

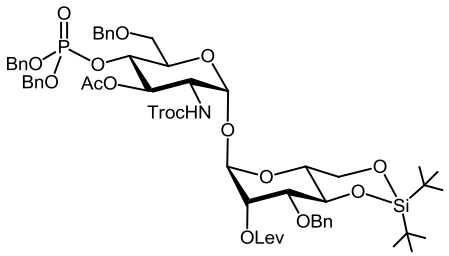
Synthesis of 21



3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-D-mannopyranose *N*-phenyl trifluoroacetimidate (21).

To a vigorously stirred suspension of **17** (840 mg, 1.98 μmol) and K_2CO_3 (550 mg, 3.96 μmol) in acetone (70 ml) 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (750 μL, 4.97 μmol) was added at r. t. and the mixture was stirred for 3 h. The solids were removed by filtration over a pad of Celite and the filtrate was concentrated. The residue was purified by silica gel chromatography (hexane – EtOAc, 20 : 1 + 1% Et_3N → 9 : 1 supplemented by 1% Et_3N) to afford **21** (1.1 g, 1.85 mmol, 93%, α/β ~ 10 :1) as a slightly yellow syrup. R_f = 0.61 and 0.56 (hexane – EtOAc, 4 : 1); ^{1}H-NMR (300 MHz, $CDCl_3$, α-anomer): δ 7.43-7.26 (m, 7H, CH_2Ph), 7.14-7.09 (m, 1H, CH_2Ph), 6.83-6.80 (m, 1H, CH_2Ph), 6.10 (br. s, 1H, H-1), 5.00 (AB, 1H, ^2J = 12.2 Hz, CH_2Ph), 7.78 (AB, 1H, ^2J = 12.2 Hz, CH_2Ph), 4.34 (t, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = 9.5 Hz, H-4), 4.11 (dd, 1H, $^3J_{6a,5}$ = 4.8 Hz, $^2J_{6a,6b}$ = 9.8 Hz, H-6a), 3.96 (t, 1H, $^3J_{6b,5}$ = $^2J_{6b,6a}$ = 10.1 Hz, H-6b), 3.82 (td, 1H, $^3J_{5,4}$ = $^3J_{5,6b}$ = 9.9 Hz, $^3J_{5,6a}$ = 4.8 Hz, H-5), 3.71 (dd, 1H, $^3J_{3,2}$ = 3.29 Hz, $^3J_{3,4}$ = 9.6 Hz, H-3), 3.57 (br. s, 1H, H-2), 3.47 (s, 3H, CH_3, Me), 1.08 (s, 9H, 3×CH_3, DTBS), 1.02 (s, 9H, 3×CH_3, DTBS). ^{13}C-NMR (75 MHz, $CDCl_3$, α-anomer): δ 143.30 (O*C*(NH)CF_3), 138.68 (*C*q, CH_2Ph), 128.86, 128.34, 127.75, 127.63, 124.63, 119.45 (10×*C*H, arom.), 78.14 (C-2), 77.62 (C-3), 74.43 (C-4), 74.01 (*C*H_2Ph), 70.25 (C-5), 66.29 (C-6), 59.84 (*C*H_3, Me), 27.40, 26.99 (6×*C*H_3, DTBS), 22.60, 19.91 (2×*C*q, DTBS).

Synthesis of 22

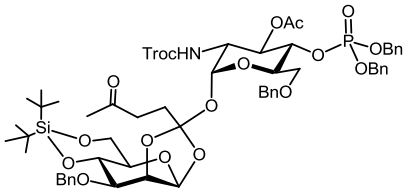


3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-levulinoyl-α-D-mannopyranosyl-(1↔1)-3-*O*-acetyl-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (22).

A solution of glycosyl donor **18** (60 mg, 92 μmol) and glycosyl acceptor **8** (68 mg, 91 μmol) in dry CH_2Cl_2 (1 ml) was stirred with activated powdered molecular sieves 4 Å for 1.5 h. at r. t. under atmosphere of Ar . The mixture was cooled to -15 °C and a solution of TMSOTf (3.3 μL, 18 μmol) in dry CH_2Cl_2 (165 μL of a stock solution prepared from 10 μL TMSOTf in 500 μL CH_2Cl_2) was added. The mixture was stirred for 40 min and warmed to 0 °C. The reaction was quenched by addition of sat. aq. $NaHCO_3$ (500 μL), diluted with EtOAc (20 ml), the solids were removed by filtration over a pad of Celite and the filtrate was washed with water (10 ml) and brine (10 ml). The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by HPLC(three successive columns: toluene - EtOAc, 8 : 1 → 3 : 1; toluene – EtOAc, 10 : 1 → 3 : 1, column B and toluene – acetone, 8 : 1) to afford compound **22** (9.4 mg, 7.6 μmol, 8%) as a syrup. R_f = 0.17 (toluene – EtOAc, 3 : 1); $[\alpha]_D^{20}$ = +39.0 (*c* 0.5, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.38-7.21 (m, 20H, CH_2Ph), 5.25 (t, 1H, $^3J_{3,4}$ = $^3J_{3,4}$ = 9.7 Hz, H-3), 5.16 (dd, 1H, $^3J_{2',1'}$ = 1.4 Hz, $^3J_{2',3'}$ = 3.6 Hz, H-2′), 5.14 (d, 1H, $^3J_{1,2}$ = 3.7 Hz, H-1), 5.10 (d, 1H, $^3J_{NH,2}$ = 9.7 Hz, N*H*), 5.07 (AB, 1H, ^2J = 12.2 Hz, CH_2Ph or Troc), 5.02 (d, 1H, $^3J_{1',2'}$ =1.1 Hz, H-1′), 4.98-4.90 (m, 4H, OP(O)(OCH_2Ph)$_2$), 4.86 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph or Troc), 4.77 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph or Troc), 4.67 (ddd, 1H, $^3J_{4,5}$ = $^3J_{4,3}$ = $^3J_{4,P}$ = 9.2 Hz, H-4), 4.50 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph or Troc) 4.46 (AB, 1H, ^2J = 12.1Hz, CH_2, CH_2Ph or Troc), 4.34 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph or Troc), 4.20 (t, 1H, $^3J_{4',3'}$ = $^3J_{4',5'}$ = 9.5 Hz, H-4′), 4.11-4.07 (m, 1H, H-2), 4.02 (dd, 1H, $^3J_{6a',5'}$ = 5.0 Hz, $^2J_{6a',6b'}$ = 10.3 Hz, H-6a′), 3.92 (t, 1H, $^3J_{6b',5'}$ = $^2J_{6b',6a'}$ = 10.3 Hz, H-6b′), 3.82 (dt, 1H, *J* = 10.0 Hz, *J* = 2.8 Hz, H-5), 3.77 (dd, 1H, $^3J_{3',2'}$ = 3.6 Hz, $^3J_{3',4'}$ = 9.5 Hz, H-3′), 3.70-3.65 (m, 3H, H-5′, H-6a, H-6b), 2.71-2.61

(m, 4H, 2×CH_2, Lev), 2.10 (s, 3H, CH_3, Lev), 1.90 (s, 3H, CH_3, Ac), 1.10 (s, 9H, 3×CH_3, DTBS), 0.98 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 206.02 (*C*O, Lev), 172.00, 171.51 (2×*C*O, Ac, Lev), 154.19 (*C*O, Troc), 138.27, 138.01 (2×*C*q, CH_2Ph), 135.50, 135.43 (2×*C*q, $OP(O)(OCH_2Ph)_2$), 129.03, 128.66, 128.61, 128.54, 128.36, 128.29, 128.21, 127.99, 127.85, 127.44, 127.56, 127.52 (20×*C*H, CH_2Ph), 95.30 (*C*Cl_3, Troc), 93.44 (C-1′, $^1J_{C,H}$ = 172 Hz), 92.77 (C-1, $^1J_{C,H}$ = 175 Hz), 75.77 (C-3′), 74.45 (C-4′), 73.41, 73.29, (2×*C*H_2, Troc, *C*H_2Ph), 73.09 (C-4, $^2J_{C4,P}$ = 5.7 Hz), 71.09 (C-3), 70.44 (C-5, $^3J_{C5,P}$ = 6.9 Hz), 70.30 (C-2′), 69.67, 69.64, 69.60 (2×*C*H_2, $OP(O)(OCH_2Ph)_2$), 68.79 (C-5′), 67.60 (C-6), 66.28 (C-6′), 53.74 (C-2), 38.00 (*C*H_2, Lev), 29.67 (*C*H_3, Lev), 28.09 (*C*H_2, Lev), 27.44, 27.07 (6×*C*H_3, DTBS), 22.69 (*C*q, DTBS), 20.70 (*C*H_3, Ac), 19.84 (*C*q, DTBS); ^{31}P-NMR (243 MHz, $CDCl_3$): δ -2.26; HRMS (ESI): *m/z* calcd for $C_{58}H_{73}Cl_3NO_{18}PSi+H^+$: 1236.3473 $[M+H]^+$; found 1236.3461.

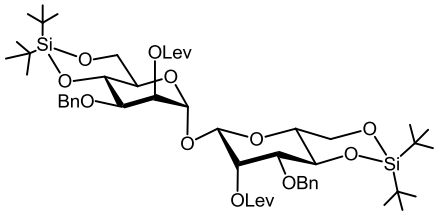
Synthesis of 23



Orthoester (23).

A solution of glycosyl donor **18** (23 mg, 35 µmol) and glycosyl acceptor **8** (27 mg, 36 µmol) in dry CH_2Cl_2 (1 ml) was stirred with activated powdered 4 Å molecular sieves for 1 h. at r. t. under atmosphere of Ar. The mixture was cooled to 0 °C and a solution of TMSOTf (0.3 µL, 2 µmol) in dry CH_2Cl_2 (30 µL of a stock solution prepared from 10 µL TMSOTf in 1 ml CH_2Cl_2) was added. The mixture was stirred for 45 min and then the reaction was quenched by addition of sat. aq. $NaHCO_3$ (500 µL) and diluted with EtOAc (20 ml). The solids were removed by filtration over a pad of Celite, the filtrate was washed with water (10 ml) and brine (10 ml). The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by HPLC (two successive columns: toluene - EtOAc, 4 : 1 and toluene – EtOAc,10 : 1 → 4 : 1, column B) to afford compound **23** (11 mg, 8.9 µmol, 25%) as a syrup. R_f = 0.43 (toluene – EtOAc, 3 : 1); $[\alpha]_D^{20}$ = +13 (*c* 0.4, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.44-7.28 (m, 15H, CH_2Ph), 7.19-7.13 (m, 3H, CH_2Ph), 7.06-7.04 (m, 2H, CH_2Ph), 5.44 (d, 1H, $^3J_{NH,2}$ = 9.9 Hz, N*H*), 5.37 (d, 1H, $^3J_{1,2}$ = 3.7 Hz, H-1), 5.22 (dd, 1H, ^3J = 9.0 Hz, ^3J = 10.8 Hz, H-3), 5.00-4.93 (m, 4H, $OP(O)(OCH_2Ph)_2$), 4.88 (AB, 1H, ^2J = 12.8 Hz, CH_2Ph or Troc), 4.83 (AB, 1H, ^2J = 12.9 Hz, CH_2Ph or Troc), 4.80 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph or Troc), 4.64 (d, 1H, $^3J_{1',2'}$ = 2.2 Hz, H-1′), 4.64 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph or Troc), 4.60 (dd, 1H, $^3J_{2',1'}$ = 2.3 Hz, $^3J_{2',3'}$ = 4.1 Hz, H-2′), 4.34 (ddd, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = $^3J_{4,P}$ = 9.4 Hz, H-4), 4.27 (AB, 1H, ^2J = 10.4 Hz, CH_2Ph or Troc), 4.20 (AB, 1H, ^2J = 10.5 Hz, CH_2Ph or Troc), 4.19-4.16 (m, 1H, H-5), 4.05-3.98 (m, 2H, H-2, H-6a′), 4.04 (t, 1H, $^3J_{4',5'}$ = $^3J_{4',3'}$ = 9.3 Hz, H-4′), 3.78-3.74 (m, 2H, H-6a, H-6b′), 3.51 (dd, 1H, *J* = 7.7 Hz, *J* = 10.4 Hz, H-6b), 3.20 (dd, 1H, $^3J_{3',2'}$ = 4.1 Hz, $^3J_{3',4'}$ = 9.2 Hz, H-3′), 2.79-2.70 (m, 2H, H-5′, CH_2, Lev), 2.52-2.47 (m, 1H, CH_2, Lev), 2.40 (dt, 1H, *J* = 7.2 Hz, *J* = 14.3 Hz, CH_2, Lev), 2.17 (s, 3H, CH_3, Lev), 2.02-1.98 (m, 1H, CH_2, Lev), 1.85 (s, 3H, CH_3, Ac), 1.08 (s, 9H, 3×CH_3, DTBS), 1.02 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 208.04 (*C*O, Lev), 170.98 (*C*O, Lev), 154.39 (*C*O, Troc), 138.32, 137.86 (2×*C*q, CH_2Ph), 135.54, 135.36 (2×*C*q, $OP(O)(OCH_2Ph)_2$), 128.77, 128.72, 128.65, 128.56, 128.40, 128.34, 128.15, 128.02, 127.90, 127.89, 127.76 (20×*C*H, CH_2Ph), 123.87 (*C*q, orthoester), 97.16 (C-1′), 95.42 (*C*Cl_3, Troc), 90.96 (C-1), 79.09 (C-2′), 76.60 (C-3′), 74.54 (*C*H_2, *C*H_2Ph or Troc), 74.26 (C-4, $^2J_{C4,P}$ = 5.9 Hz), 74.14 (C-4′), 73.60, 72.91 (2×*C*H_2, *C*H_2Ph or Troc), 71.00 (C-3), 69.89 (C-5, $^3J_{C5,P}$ = 5.3 Hz), 69.78, 69.74, 69.71, 69.67, 69.63 (C-6, $OP(O)(OCH_2Ph)_2$), 68.78 (C-5′), 66.19 (C-6′), 53.81 (C-2), 37.97, 32.99 (2×*C*H_2, Lev), 30.20 (*C*H_3, Lev), 27.46, 27.03 (6×*C*H_3, DTBS), 22.74 (*C*q, DTBS), 20.65 (*C*H_3, Ac), 19.89 (*C*q, DTBS); ^{31}P-NMR (243 MHz, $CDCl_3$): δ -1.92; HRMS (ESI): *m/z* calcd for $C_{58}H_{73}Cl_3NO_{18}PSi+NH_4^+$: 1253.3738 $[M+NH_4^+]$; found 1253.3734.

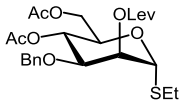
Synthesis of 24



3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-levulinoyl-β-D-mannopyranosyl-(1↔1)-3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-levulinoyl-α-D-mannopyranoside (24).

24 was isolated as by-product from glycosylation reactions between donors **18** or **19** and acceptor **8**. R_f = 0.43 (toluene – EtOAc, 3 : 1); $[\alpha]_D^{20}$ = -21 (*c* 0.5, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.38-7.22 (m, 10H, CH_2Ph), 5.44 (dd, 1H, $^3J_{2',1'}$ = 0.9 Hz, $^3J_{2',3'}$ = 3.3 Hz, H-2′), 5.20 (dd, 1H, $^3J_{2,1}$ = 1.6 Hz, $^3J_{2,3}$ = 3.5 Hz, H-2), 4.90 (d, 1H, $^3J_{1,2}$ = 1.3 Hz, H-1), 4.76-4.67 (m, 4H, 2×CH_2Ph), 4.67 (s, 1H, H-1′), 4.14-4.07 (m, 3H, H-4, H-4′, H-6a′), 4.01 (dd, 1H, $^3J_{6a,5}$ =4.7 Hz, $^2J_{6a,6b}$ =9.5 Hz, H-6a), 3.97-3.92 (m, 2H, H-5, H-6b′), 3.87 (t, 1H, $^3J_{6b,5}$ = $^2J_{6b,6a}$ = 9.8 Hz, H-6b), 3.74 (dd, 1H, $^3J_{3,2}$ = 3.6 Hz, $^3J_{3,4}$ = 9.4 Hz, H-3), 3.41 (dd, 1H, $^3J_{3',2'}$ = 3.4 Hz, $^3J_{3',4'}$ = 9.3 Hz, H-3′), 3.31 (dt, 1H, *J* = 5.0 Hz, *J* = 9.8 Hz, H-5′), 2.79-2.59 (s, 8H, 4×CH_2, Lev), 2.14 (s, 3H, CH_3, Lev), 2.11 (s, 3H, CH_3, Lev), 1.09, 1.08, 0.99, 0.98 (4×s, 36H, 12×CH_3, DTBS); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 206.30, 205.76 (2×*C*O), 171.90, 171.86 (2×*C*O), 138.85, 138.16 (2×*C*q, CH_2Ph), 128.36, 128.19, 127.55, 127.44, 127.33, 127.28 (10×*C*H, CH_2Ph), 98.11 (C-1), 97.78 (C-1′), 77.52 (C-3′), 76.11 (C-3), 74.37, 73.96 (C-4, C-4′), 72.42, 71.67 (2×*C*H_2Ph), 71.54 (C-5′), 69.74 (C-2′), 68.99 (C-2), 68.23 (C-5), 66.43, 66.25 (C-6, C-6′), 38.07, 38.04 (2×*C*H_2, Lev), 29.74 (2×CH_3, Lev), 28.11, 28.06 (2×CH_2, Lev), 27.43, 27.38, 27.06, 27.03 (12×*C*H_3, DTBS), 22.69, 22.64, 20.01, 19.92 (4×*C*q, DTBS); HRMS (ESI): *m/z* calcd for $C_{52}H_{78}O_{15}Si_2$+Na^+: 1021.4771 [M+Na^+]; found 1021.4771.

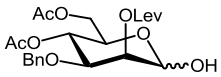
Synthesis of 25



Ethyl 4,6-di-*O*-acetyl-3-*O*-benzyl-2-*O*-levulinoyl-1-thio-α-D-mannopyranoside (25).

A solution of **14** (89 mg, 161 μmol) in dry THF (2 ml) was stirred with solution of HF•Py (200 μL, 70%) in a PTFE-vial at r. t. for 45 min. under atmosphere of Ar. The mixture was diluted with EtOAc (20 ml) and washed with sat. aq. $NaHCO_3$ (2×20 ml) and brine (20 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated to afford the intermediate 4,6-diol (R_f = 0.31, EtOAc). The diol (74 mg) was dissolved in pyridine (1.5 ml) and acetic acid anhydride (111 μL, 1.18 mmol) and DMAP (catalytic amount) were successively added at 0 °C. The mixture was stirred at at r. t. for 2 h, diluted with EtOAc (20 ml) and washed with aq. HCl (2 M, 10 ml), sat. aq. $NaHCO_3$ (20 ml) and brine (20 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel chromatography (hexane – EtOAc, 2 : 1) to afford **25** (68 mg, 137 μmol, 85%, 2 steps) as a syrup. R_f = 0.56 (toluene – EtOAc, 1 : 2); $[\alpha]_D^{20}$ = +2 (*c* 0.7, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.36-7.23 (m, 5H, CH_2Ph), 5.42 (dd, 1H, $^3J_{2,1}$ = 1.7 Hz, $^3J_{2,3}$ = 3.3 Hz, H-2), 5.30 (d, 1H, $^3J_{1,2}$ = 1.6 Hz, H-1), 5.21 (t, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = 9.6 Hz, H-4), 4.60 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph), 4.38 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph), 4.29-4.22 (m, 2H, H-5, H-6a), 4.08 (dd, 1H, *J* = 5.0 Hz, *J* = 14.7 Hz, H-6b), 3.77 (dd, 1H, $^3J_{3,2}$ = 3.3 Hz, $^3J_{3,4}$ = 9.7 Hz, H-3), 2.79-2.53 (m, 6H, 3×CH_2, Lev, SEt), 2.17 (s, 3H, CH_3, Lev), 2.08 (s, 3H, CH_3, Ac), 2.01 (s, 3H, CH_3, Ac), 1.29 (t, 3H, ^3J = 7.4 Hz, CH_3, SEt); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 206.22 (C*O*, Lev), 171.83, 170.64, 169.66 (3×*C*O, Lev, Ac), 137.44 (*C*q, CH_2Ph), 128.38, 127.86 (5×*C*H, CH_2Ph), 82.46 (C-1), 74.91 (C-3), 71.32 (*C*H_2Ph), 70.03 (C-2), 69.07 (C-5), 67.59 (C-4), 62.70 (C-6), 38.00 (CH_2, Lev), 29.74 (*C*H_3, Lev), 28.18 (*C*H_2, Lev), 25.61 (*C*H_2, SEt), 20.80, 20.73 (2×*C*H_3, Ac), 14.84 (*C*H_3, SEt); HRMS (ESI): *m/z* calcd for $C_{24}H_{32}O_9S$+Na^+: 519.1659 [M+Na^+]; found 519.1654.

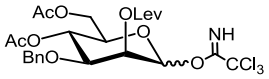
Synthesis of 26



4,6-di-*O*-Acetyl-3-*O*-benzyl-2-*O*-levulinoyl-D-mannopyranose (26).

Compound **25** (62 mg, 125 µmol) was dissolved in acetone - water (2 ml, 24 : 1) and added to a solution of NBS (111 mg, 941 µmol) in the same solvent mixture (2 ml) at 0 °C. The mixture was stirred for 10 min and then the reaction was quenched by addition of aq. 5% $Na_2S_2O_3$ (2 ml). The mixture was warmed to r. t., diluted with EtOAc (10 ml) and washed with sat. aq. $NaHCO_3$ (20 ml), water (20 ml) and brine (20 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel chromatography (hexane – EtOAc, 1 : 1) to afford **26** (50 mg, 111 µmol, 89%, α/β = 7 : 1) as a syrup. R_f = 0.44 (toluene – EtOAc, 1 : 5); $[\alpha]_D^{20}$ = 1 (*c* 1.4, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$, α-anomer): δ 7.36-7.23 (m, 5H, CH_2Ph), 5.37 (dd, 1H, $^3J_{2,1}$ = 1.9 Hz, $^3J_{2,3}$ = 3.3 Hz, H-2), 5.25 (d, 1H, $^3J_{1,2}$ = 1.9 Hz, H-1), 5.21 (t, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = 9.7 Hz, H-4), 4.63 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph), 4.41 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph), 4.21 (dd, 1H, *J* = 5.8 Hz, *J* = 12.5 Hz, H-6a), 4.15-4.07 (m, 2H, H-5, H-6b), 3.93 (dd, 1H, $^3J_{3,2}$ = 3.4 Hz, $^3J_{3,4}$ = 9.7 Hz, H-3), 2.90-2.58 (m, 4H, 2×CH_2, Lev), 2.16 (s, 3H, CH_3, Lev), 2.09 (s, 3H, CH_3, Ac), 2.01 (s, 3H, CH_3, Ac); ^{13}C-NMR (75 MHz, $CDCl_3$, α-anomer): δ 206.47 (*C*O, Lev), 171.97, 170.81, 169.72 (3×*C*O, Lev, Ac), 137.71 (*C*q, CH_2Ph), 128.33, 127.75, 127.72 (5×*C*H, CH_2Ph), 92.42 (C-1), 74.00 (C-3), 71.28 (*C*H_2Ph), 68.74, 68.67 (C-2, C-5), 67.42 (C-4), 62.86 (C-6), 38.02 (CH_2, Lev), 29.72 (*C*H_3, Lev), 28.16 (*C*H_2, Lev), 20.82, 20.79 (2×*C*H_3, Ac); HRMS (ESI): *m/z* calcd for $C_{22}H_{28}O_{10}$+$COOH^-$: 497.1664 [M+$COOH^-$]; found 497.1670.

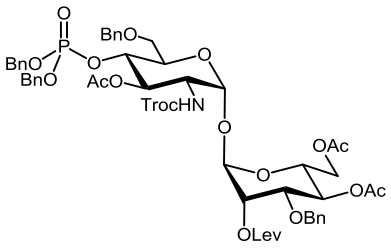
Synthesis of 27



4,6-di-*O*-Acetyl-3-*O*-benzyl-2-*O*-levulinoyl-D-mannopyranose trichloroacetimidate (27).

To a solution of **26** (36 mg, 80 µmol) in dry CH_2Cl_2 (1ml) trichloroacetonitrile (70 µL, 718 µmol) and DBU (2 µL, 14 µmol) were added successively at 0 °C. The mixture was stirred for 3.5 h at 0 °C, then warmed to r. t., diluted with EtOAc (10 ml) and washed with sat. aq. $NaHCO_3$ (10 ml) and brine (10 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel chromatography (hexane – EtOAc, 2 : 1 supplemented by 1% Et_3N) to afford **27** (32 mg, 54 µmol, 67%, α/β = 32 : 1) as a yellow syrup. R_f = 0.53 (hexane – EtOAc, 1 : 1 + 1% Et_3N); ^{1}H-NMR (600 MHz, $CDCl_3$, α-anomer): δ 8.75 (s, 1H, N*H*), 7.34-7.24 (m, 5H, CH_2Ph), 6.28 (d, 1H, $^3J_{1,2}$ = 1.7 Hz, H-1), 5.48 (dd, 1H, $^3J_{2,1}$ = 2.1 Hz, $^3J_{2,3}$ = 3.1 Hz, H-2), 5.30 (t, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = 10.1 Hz, H-4), 4.64 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph), 4.44 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph), 4.21 (dd, 1H, $^3J_{6a,5}$ = 5.3 Hz, $^2J_{6a,6b}$ = 12.4 Hz, H-6a), 4.13 (dd, 1H, $^3J_{6b,5}$ = 2.3 Hz, $^2J_{6b,6a}$ = 12.4 Hz, H-6b), 4.04 (ddd, 1H, $^3J_{5,4}$ = 10.2 Hz, $^3J_{5,6a}$ = 5.2 Hz, $^3J_{5,6b}$ = 2.2 Hz, H-5), 3.92 (dd, 1H, $^3J_{3,2}$ = 3.3 Hz, $^3J_{3,4}$ = 9.8 Hz, H-3), 2.82-2.69 (m, 4H, 2×CH_2, Lev), 2.18 (s, 3H, CH_3, Lev), 2.06 (s, 3H, CH_3, Ac), 2.04 (s, 3H, CH_3, Ac); ^{13}C-NMR (75 MHz, $CDCl_3$, α-anomer): δ 206.01 (*C*O, Lev), 171.64, 170.58, 169.53 (3×*C*O, Lev, Ac), 159.53 (O*C*(NH)CCl_3), 137.11 (*C*q, CH_2Ph), 128.40, 128.06, 128.00 (5×*C*H, CH_2Ph), 94.76 (C-1), 90.58 (*C*Cl_3), 73.64 (C-3), 71.48 (*C*H_2, CH_2Ph), 71.30 (C-5), 66.89 (C-2), 66.58 (C-4), 62.26 (C-6), 37.93 (CH_2, Lev), 29.69 (*C*H_3, Lev), 28.03 (*C*H_2, Lev), 20.75, 20.67 (2×*C*H_3, Ac).

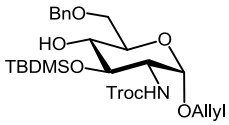
Synthesis of 28



4,6-di-*O*-Acetyl-3-*O*-benzyl-2-*O*-levulinoyl-α-D-mannopyranosyl-(1↔1)-3-*O*-acetyl-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (28).

A solution of glycosyl donor **27** (32 mg, 54 μmol) and glycosyl acceptor **8** (33 mg, 44 μmol) in dry CH_2Cl_2 (1 ml) was stirred with activated powdered 4 Å molecular sieves was stirred for 1.5 h. at r. t. under atmosphere of Ar. The mixture was cooled to 0 °C and a solution of TMSOTf (0.5 μL, 3 μmol) in dry CH_2Cl_2 (50 μL of a stock solution prepared from 10 μL TMSOTf in 1 ml CH_2Cl_2) was added. The mixture was stirred at 0 °C for 3 h. and then the reaction was quenched by addition of Et_3N (10 μL). The mixture was warmed to r. t., diluted with EtOAc (10 ml), filtered over a pad of Celite and the filtrate was concentrated. The residue was purified by HPLC (two successive columns: CH_2Cl_2 – MeOH, 50 : 1 and hexane – EtOAc, 2 : 1→ 1 : 2→ 1 : 1, column B) to afford **28** (5 mg, 4 μmol, 8%) as a syrup. R_f = 0.59 (hexane - EtOAc, 1 : 2); $[\alpha]_D^{20}$ = +33 (*c* 0.4, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.37-7.23 (m, 20H, CH_2Ph), 5.29 (t, 1H, $^3J_{3,2}$ = $^3J_{3,4}$ = 10.0 Hz, H-3), 5.23 (d, 1H, $^3J_{1,2}$ = 3.6 Hz, H-1), 5.22 (br s, 1H, H-2′), 5.18 (d, 1H, $^3J_{NH,2}$ = 8.8 Hz, N*H*), 5.15 (t, 1H, $^3J_{4',3'}$ = $^3J_{4',5'}$ = 10.0 Hz, H-4′), 5.11 (br s, 1H, H-1′), 5.00-4.92 (m, 4H, OP(O)(OCH_2Ph)$_2$), 4.71-4.65 (m, 4H, H-4, CH_2Ph or Troc), 4.54-4.46 (m, 3H, CH_2Ph or Troc), 4.14 (dd, 1H, *J* = 6.5 Hz, *J* = 12.2 Hz, H-6a′), 4.06-4.02 (m, 2H, H-2, H-6b′), 3.89 (dd, 1H, *J* = 3.1 Hz, *J* = 9.6 Hz, H-3′), 3.82 (br d, 1H, *J* = 9.6 Hz, H-5), 3.78-3.75 (m, 1H, H-5′), 3.71 (m, 2H, H-6a, H-6b), 2.73-2.63 (m, 4H, 2×CH_2, Lev), 2.12 (s, 3H, CH_3, Lev), 2.05 (s, 3H, CH_3, Ac), 2.02 (s, 3H, CH_3, Ac), 1.96 (s, 3H, CH_3, Ac); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 206.00 (*C*O, Lev), 171.87, 171.84, 170.55, 169.63 (4×*C*O, Lev, Ac), 153.93 (*C*O, Troc), 137.90, 137.31 (2×*C*q, CH_2Ph), 135.47 (2×*C*q, OP(O)(OCH_2Ph)$_2$), 128.71, 128.64, 128.50, 128.34, 128.06, 127.99, 127.63, 127.59 (20×*C*H, CH_2Ph), 95.21 (*C*Cl_3, Troc), 92.58 (C-1′, $^1J_{C',H'}$ = 174 Hz), 91.95 (C-1, $^1J_{C,H}$ = 178 Hz), 74.74 (*C*H_2, *C*H_2Ph or Troc), 74.12 (C-3′), 73.50 (*C*H_2, *C*H_2Ph or Troc), 73.04 (C-4, $^2J_{C4,P}$ = 6.2 Hz), 72.01 (*C*H_2, *C*H_2Ph or Troc), 70.71 (C-3), 70.51 (C-5, $^3J_{C5,P}$ = 5.9 Hz), 69.87 (C-5′), 69.71, 69.69, 69,68, 69.66 (2×*C*H_2, OP(O)(O*C*H_2Ph)$_2$), 68.36 (C-2′), 67.54 (C-6), 67.16 (C-4′), 62.47 (C-6′), 53.81 (C-2), 37.93 (*C*H_2, Lev), 29.67 (*C*H_3, Lev), 28.09 (*C*H_2, Lev), 20.81, 20.79, 20.70 (3×*C*H_3, Ac); ^{31}P-NMR (243 MHz, $CDCl_3$): δ -2.26; HRMS (ESI): *m/z* calcd for $C_{54}H_{61}Cl_3NO_{20}P$+Na^+: 1202.2482 [M+Na^+]; found 1202.2477.

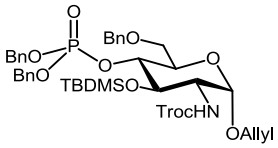
Synthesis of 30



Allyl 6-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (30).

A solution of **29**[17] (6.5 g, 10.9 mmol), trifluoroacetic anhydride (4.5 ml, 32.4 mmol), triethylsilane (8.8 ml, 54.5 mmol) and trifluoroacetic acid (4.0 ml, 54.0 mmol) in dry CH_2Cl_2 (50 ml) was stirred at 0 °C for 3 h. under atmosphere of Ar, then sat. aq. $NaHCO_3$ (50 ml) was added and the mixture was warmed to r. t. The mixture was diluted with EtOAc (200 ml) and washed with sat. aq. $NaHCO_3$ (200 ml), water (100 ml) and brine (100 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel chromatography (toluene – EtOAc, 20 : 1) to afford **30** (5.9 g, 9.9 mmol, 90%) as a syrup. R_f = 0.23 (toluene–EtOAc, 20 : 1); $[\alpha]_D^{20}$ = +61 (*c* 1.2, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.38-7.28 (m, 5H, CH_2Ph), 5.90 (dddd, 1H, ^3J = 5.3 Hz, ^3J = 6.5 Hz, $^3J_{cis}$ = 10.5 Hz, $^3J_{trans}$ = 17.1 Hz, C*H*, Allyl), 5.28 (dq, 1H, ^4J = 1.6 Hz, $^3J_{trans}$ = 17.2 Hz, CH_2, Allyl), 5.21 (dq, 1H, ^4J = 1.3 Hz, $^3J_{cis}$ = 10.4 Hz, CH_2, Allyl), 5.05 (d, 1H, $^3J_{NH,2}$ = 10.0 Hz, N*H*), 4.86 (d, 1H, $^3J_{1,2}$ = 3.6 Hz, H-1), 4.78 (AB, ^2J = 11.9 Hz, CH_2, Troc), 4.64 (AB, ^2J = 12.1 Hz, CH_2Ph), 4.60 (AB, ^2J = 11.9 Hz, CH_2, Troc), 4.56 (AB, ^2J = 12.1 Hz, CH_2Ph), 4.17 (ddt, 1H, ^4J = 1.5 Hz, ^3J = 5.3, ^2J = 12.9 Hz, CH_2, Allyl), 4.00 (ddt, 1H, ^4J = 1.3 Hz, ^3J = 6.4 Hz, ^2J = 12.9 Hz, CH_2, Allyl), 3.85 (td, 1H, $^3J_{2,1}$ = 3.6 Hz, $^3J_{2,3}$ = $^3J_{2,NH}$ = 10.1 Hz, H-2), 3.77-3.66 (m, 4H, H-3, H-5, H-6a, H-6b), 3.58 (td, 1H, $^3J_{4,OH}$ = 3.1 Hz, $^3J_{4,5}$ = $^3J_{4,3}$ = 8.6 Hz, H-4), 2.36 (d, 1H, $^3J_{OH,4}$ = 3.0 Hz, 4-O*H*), 0.88 (s, 9H, 3×CH_3, TBDMS), 0.12 (s, 3H, CH_3, TBDMS), 0.09 (s, 3H, CH_3, TBDMS); ^{13}C-NMR (101 MHz, $CDCl_3$): δ 154.12 (*C*O, Troc), 137.87 (*C*q, CH_2Ph), 133.57 (*C*H, Allyl), 128.45, 127.79, 127.71 (5×*C*H, CH_2Ph), 117.96 (*C*H_2, Allyl), 96.96 (C-1), 74.96 (*C*H_2, Troc), 73.69 (C-3), 73.65 (*C*H_2Ph), 72.85 (C-4), 70.20 (C-5), 69.96 (C-6), 68.31 (*C*H_2, Allyl), 55.60 (C-2), 25.76 (3×*C*H_3, TBDMS), 18.12 (*C*q, TBDMS), -4.09, -4.62 (2×*C*H_3, TBDMS); HRMS (ESI): *m/z* calcd for $C_{25}H_{38}Cl_3NO_7Si$+Na^+: 620.1375 [M+Na^+]; found 620.1376.

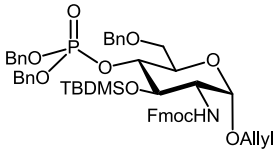
Synthesis of 31



Allyl 6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (31).

To a stirred solution of **30** (5.92 g, 9.88 mmol) and dibenzyl *N,N*-diisopropylphosphoramidite (6.30 ml, 16.9 mmol, 90%) in dry CH_2Cl_2 (50 ml) a solution of 1*H*-tetrazole (43.80 ml, 19.7 mmol, 0.45 M in CH_3CN) was added at r. t. under atmosphere of Ar. After 2 h the mixture was cooled to -78 °C and a solution of *m*CPBA (3.60 g, 14.5 mmol, 70%) in CH_2Cl_2 (50 ml) was added. The reaction mixture was stirred for 1 h. to -78 °C, then quenched by addition of Et_3N (3.20 ml) and warmed to r. t. The mixture was diluted with EtOAc (200 ml) and washed with aq. citric acid (0.25 M, 100 ml), sat. aq. $NaHCO_3$ (100 ml), water (100 ml) and brine (100 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by MPLC (toluene – EtOAc, 10 : 1 → 7 : 1) to afford **31** (7.77 g, 9.04 mmol, 91%) as a syrup. R_f = 0.45 (hexane – EtOAc, 2 : 1); $[\alpha]_D^{20}$ = +46.0 (*c* 1.1, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.34-7.23 (m, 15H, CH_2Ph), 5.91 (dddd, 1H, ^3J = 5.1 Hz, ^3J = 6.3 Hz, $^3J_{cis}$ = 10.7 Hz, $^3J_{trans}$ = 16.9 Hz, C*H*, Allyl), 5.29 (dq, 1H, ^4J = 1.5 Hz, $^3J_{trans}$ = 17.2 Hz, CH_2, Allyl), 5.23 (dq, 1H, ^4J = 1.3 Hz, $^3J_{cis}$ = 10.5 Hz, CH_2, Allyl), 5.03 (d, 1H, $^3J_{NH,2}$ = 9.7 Hz, N*H*), 4.98-4.87 (m, 5H, H-1, OP(O)(OCH_2Ph)$_2$), 4.80 (AB, 1H, ^2J = 11.9 Hz, CH_2 Troc or CH_2Ph), 4.59 (m, 2H, CH_2 Troc or CH_2Ph), 4.49 (AB, ^2J = 12.0 Hz, CH_2 Troc or CH_2Ph), 4.32 (dt, *J* = 9.6 Hz, *J* = 7.9 Hz, H-4), 4.20 (ddt, 1H, ^4J = 1.4 Hz, ^3J = 5.2 Hz, ^2J = 12.9 Hz, CH_2, Allyl), 4.03 (ddt, 1H, ^4J = 1.2 Hz, ^3J = 6.3 Hz, ^2J = 13.1 Hz, CH_2, Allyl), 3.93-3.85 (m, 4H, H-2, H-3, H-5, H-6a), 3.82 (dd, 1H, *J* = 2.3 Hz, *J* = 10.7 Hz, H-6b), 0.85 (s, 9H, 3×CH_3, TBDMS), 0.13 (s, 3H, CH_3, TBDMS), 0.10 (s, 3H, CH_3, TBDMS); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 153.99 (*C*O, Troc), 138.42 (*C*q, CH_2Ph), 135.78, 135.72 (2×*C*q, OP(O)(OCH_2Ph)$_2$), 133.46 (*C*H, Allyl), 128.50, 128.46, 128.23, 128.16, 128.02, 127.54, 127.44, 127.37 (15×*C*H, CH_2Ph), 118.03 (*C*H_2, Allyl), 96.13 (C-1), 95.18 (*C*Cl_3, Troc), 76.93 (C-4, $^2J_{C4,P}$ = 6.6 Hz), 75.02, 73.00 (*C*H_2Ph, *C*H_2 Troc), 71.62 (C-3, $^3J_{C3,P}$ = 4.7 Hz), 70.65 (C-5), 69.80 (OP(O)(O*C*H_2Ph)$_2$, $^2J_{C,P}$ = 5.2 Hz), 69.34 (OP(O)(O*C*H_2Ph)$_2$, $^2J_{C,P}$ = 4.7 Hz), 68.60 (C-6), 68.37 (*C*H_2, Allyl), 55.79 (C-2), 25.83 (3×*C*H_3, TBDMS), 17.82 (*C*q, TBDMS), -4.07 (2×*C*H_3, TBDMS); ^{31}P-NMR (243 MHz, $CDCl_3$): δ -1.87; HRMS (ESI): *m/z* calcd for $C_{39}H_{51}Cl_3NO_{10}PSi+Na^+$: 880.1978 [M+$Na^+$]; found 880.1975.

Synthesis of 32

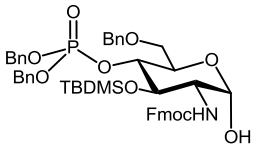


Allyl 6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-2-(9-fluorenylmethoxycarbonylamino)-α-D-glucopyranoside (32).

To a solution of **31** (5.05 g, 5.88 mmol) in dry CH_2Cl_2 (100 ml), Zn dust (16.0 g, 10 μm) and dry acetic acid (50 ml) were added at 0 °C under atmosphere of Ar. The mixture was stirred for 3.5 h at 0 °C, then diluted with CH_2Cl_2 (200 ml), filtered over a pad of Celite and the filtrate was washed with sat. aq. $NaHCO_3$ (2×200 ml) and water (200 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated to afford crude amine (3.34 g) as a syrup. R_f = 0.21 (hexane – EtOAc, 1 : 1). The crude amine (2.93 g, 4.28 mmol) was dissolved in dry DMF (15 ml) and diisopropylethylamine (1.12 ml, 6.41 mmol) and 9-fluorenylmethyl chloroformate (1.66 g, 6.42 mmol) were added at 0 °C under atmosphere of Ar. The mixture was stirred for 2 h. at r. t., diluted with EtOAc (200 ml) and washed with water (4×100 ml) and brine (200 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel chromatography (hexane – EtOAc, 5 : 1 → 4 : 1 → 3 : 1) to afford **32** (3.41 g, 3.76 mmol, 87%) as a syrup. R_f = 0.23 (hexane - EtOAc, 3 : 1); $[\alpha]_D^{20}$ = +42 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.76 (d, 2H, *J* = 7.5 Hz, arom.), 7.61-7.58 (m, 2H, arom.), 7.41-7.21 (m, 19H, arom.), 5.90 (^3J = 5.3 Hz, ^3J = 6.4 Hz, $^3J_{cis}$ = 10.5 Hz, $^3J_{trans}$ = 17.1 Hz, C*H*, Allyl), 5.27 (dq, ^4J = 1.6 Hz, $^3J_{trans}$ = 17.2 Hz,

CH_2, Allyl), 5.21 (dq, ^4J = 1.3 Hz, $^3J_{cis}$ = 10.4 Hz, CH_2, Allyl), 4.97-4.78 (m, 5H, H-1, OP(O)(OCH_2Ph)$_2$), 4.58 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.50-4.46 (m, 1H, CH_2, Fmoc), 4.47 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.33-4.26 (m, 2H, H-4, CH_2, Fmoc), 4.21-4.16 (m, 2H, CH_2 Allyl, CH, Fmoc), 4.03-3.96 (m, 1H, CH_2, Allyl), 3.92-3.79 (m, 5H, H-2, H-3, H-5, H-6a, H-6b), 0.80 (s, 9H, 3×CH_3, TBDMS), 0.09 (s, 3H, CH_3, TBDMS), 0.01 (s, 3H, CH_3, TBDMS); ^{13}C-NMR (101 MHz, $CDCl_3$): δ 155.73 (*C*O, Fmoc), 143.87, 141.31 (4×*C*q, Fmoc), 138.44 (*C*q, CH_2Ph), 135.80, 135.75 (2×*C*q, OP(O)(OCH_2Ph)$_2$), 133.61 (*C*H, Allyl), 128.48, 128.21, 128.14, 128.00, 127.68, 127.43, 127.34, 127.02, 126.95, 125.14, 124.92, 119.96, 119.93 (23×*C*H, arom.), 117.81 (*C*H_2, Allyl), 96.53 (C-1), 77.09 (C-4, $^2J_{C4,P}$ = 6.6 Hz), 72.98 (*C*H_2Ph), 71.80 (C-5, $^3J_{C5,P}$ = 4.7 Hz), 70.51 (C-3), 69.77 (OP(O)(O*C*H_2Ph)$_2$, ^2J = 5.5 Hz), 69.30 (OP(O)(O*C*H_2Ph)$_2$, ^2J = 4.8 Hz), 68.69, 68.35 (C-6, CH_2 Allyl), 66.95 (*C*H_2, Fmoc), 55.50 (C-2), 47.17 (C*H*, Fmoc), 25.78 (3×*C*H_3, TBDMS), 17.84 (*C*q, TBDMS), -4.05, -4.11 (2×*C*H_3, TBDMS); ^{31}P-NMR (162 MHz, $CDCl_3$): δ -1.89; HRMS (ESI): *m/z* calcd for $C_{51}H_{60}NO_{10}PSi+Na^+$: 928.3616 [M+$Na^+$]; found 928.3622.

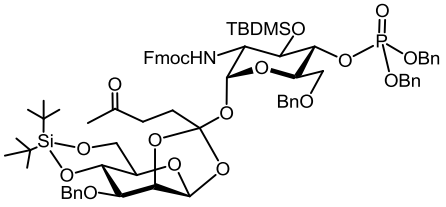
Synthesis of 33



6-*O*-Benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-2-(9-fluorenylmethoxycarbonylamino)-α-D-glucopyranose (33).

A degassed solution of H_2-activated (1,5-Cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate (191 mg, 226 µmol) in dry THF (30 ml) was added to a degassed solution of **32** (2.05 g, 2.26 mmol) in dry THF (100 ml) under atmosphere of Ar. The mixture was stirred for 4 h. at r. t., cooled to 0°C and a solution of I_2 (1.07 g, 4.21 mmol) in THF - H_2O (1 : 1, 16 ml) was added. The mixture was stirred for 3 h. at 0 °C, diluted with CH_2Cl_2 (200 ml) and washed with aq. 5% $Na_2S_2O_3$ (100 ml). The aqueous phase was extracted with CH_2Cl_2 (2×100 ml) and the combined organic phases were washed with sat. aq. $NaHCO_3$ (100 ml) and water (100 ml), dried over $MgSO_4$, filtered and concentrated. The residue was purified by silica gel chromatography (toluene – EtOAc, 3 : 1 → 1 : 1) to afford **33** (1.70 g, 1.96 mmol, 86%) as a syrup. R_f = 0.23 (hexane - EtOAc, 1 : 1); $[\alpha]_D^{20}$ = +22.0 (*c* 1.1, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.75 (d, 2H, *J* = 7.6 Hz, arom.), 7.58 (t, 2H, *J* = 6.6 Hz, arom.), 7.38 (t, 2H, *J* = 7.4 Hz, arom.), 7.32-7.20 (m, 17H, arom.), 5.15 (t, 1H, $^3J_{1,2}$ = $^3J_{1,OH}$ = 3.6 Hz, H-1), 4.95-4.83 (m, 5H, N*H*, OP(O)(OCH_2Ph)$_2$), 4.55- 4.43 (m, 3H, CH_2Ph, CH_2 Fmoc), 4.32 (dd, 1H, *J* = 6.8 Hz, *J* = 10.6 Hz, CH_2, Fmoc), 4.20-4.09 (m, 3H, H-4, H-5, C*H* Fmoc), 3.91 (dd, 1H, *J* = 7.2 Hz, *J* = 8.9 Hz, H-3), 3.84-3.78 (m, 2H, H-2, H-6a), 3.73 (dd, 1H, *J* = 6.1 Hz, *J* = 10.4 Hz, H-6b), 3.38 (d, 1H, $^3J_{OH,1}$ = 3.9 Hz, 1-O*H*), 0.80 (s, 9H, 3×CH_3, TBDMS), 0.06 (s, 3H, CH_3, TBDMS), -0.01 (s, 3H, CH_3, TBDMS); ^{13}C-NMR (101 MHz, $CDCl_3$): δ 155.96 (*C*O, Fmoc), 143.88, 143.81, 141.32 (4×*C*q, Fmoc), 138.03 (*C*q, CH_2Ph), 135.69, 135.63 (2×*C*q, OP(O)(OCH_2Ph)$_2$), 128.53, 128.31, 128.15, 128.03, 127.78, 127.68, 127.60, 127.07, 127.00, 125.12, 124.92, 119.95 (23×C*H*, arom.), 91.04 (C-1), 77.32-76.68 (C-4), 73.17 (*C*H_2Ph), 71.27, 70.98 (C-3, C-4), 69.76 (OP(O)(O*C*H_2Ph)$_2$, ^2J = 5.4 Hz), 69.39 (OP(O)(O*C*H_2Ph)$_2$, ^2J = 5.1 Hz), 68.80 (C-6), 66.92 (*C*H_2, Fmoc), 55.39 (C-2), 47.16 (*C*H, Fmoc), 25.75 (3×*C*H_3, TBDMS), 17.82 (*C*q, TBDMS), -4.25, -4.35 (2×*C*H_3, TBDMS); ^{31}P-NMR (243 MHz, $CDCl_3$): δ -1.76; HRMS (ESI): *m/z* calcd for $C_{48}H_{56}NO_{10}PSi+Na^+$: 888.3303 [M+$Na^+$]; found 888.3295.

Synthesis of 34

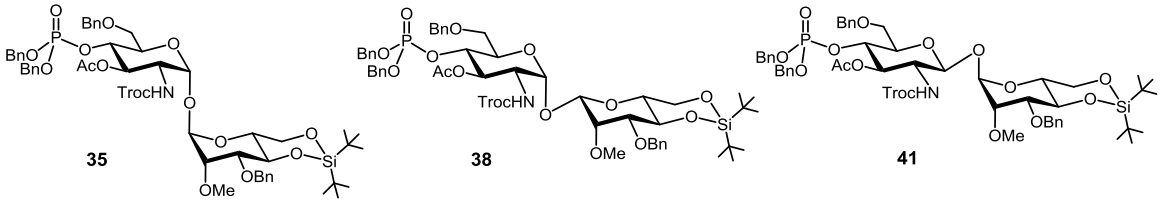


Orthoester (34).

A solution of glycosyl donor **18** (60 mg, 92 µmol) and glycosyl acceptor **33** (110 mg, 127 µmol) in dry CH_2Cl_2 (1 ml) was stirred with activated powdered 4 Å molecular sieves for 1.5 h. at r. t. under atmosphere of Ar. The

mixture was cooled to 0 °C and a solution of TMSOTf (0.83 µL, 4.6 µmol) in dry CH_2Cl_2 (42 µL of a stock solution prepared from 10µL TMSOTf in 500 µL CH_2Cl_2) was added. The mixture was stirred at 0 °C for 40 min and then the reaction was quenched by addition of Et_3N (10 µL). The mixture was warmed to r. t., diluted with EtOAc (20 ml), filtered over a pad of Celite and the filtrate was washed with water (10 ml) and brine (10 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by HPLC (two successive columns: toluene – EtOAc, 7 : 1 → 1 : 1 and hexane : EtOAc, 7 : 1 → 3 : 1, column B) to afford **34** (51 mg, 38 µmol, 40%) as a colorless syrup. R_f = 0.17 (hexane – EtOAc, 3 : 1); $[\alpha]_D^{20}$ = +18 (*c* 1.0, DCM); ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.74-7.66 (m, 4H, arom.), 7.44-7.27 (m, 19H, arom.), 7.16-7.09 (m, 3H, arom.), 6.99-6.98 (m, 2H, arom.) 5.33 (d, 1H, $^3J_{1,2}$ = 3.7 Hz, H-1), 5.24 (d, 1H, $^3J_{NH,2}$ = 10.3 Hz, N*H*), 5.04-4.83 (m, 6H, 3×CH_2, CH_2Ph, OP(O)(OCH_2Ph)$_2$), 4.62 (dd, 1H,$^3J_{2',1'}$ = 2.2 Hz, $^3J_{2',3'}$ = 3.9 Hz, H-2′), 4.50 (d, 1H, $^3J_{1',2'}$ = 2.0 Hz, H-1′), 4.42 (dd, 1H, ^3J = 6.9 Hz, ^2J = 10.4 Hz, CH_2, Fmoc), 4.29 (dd, 1H, ^3J = 7.4 Hz, ^2J = 10.4 Hz, CH_2, Fmoc), 4.23 (AB, 1H, ^2J = 10.3 Hz, CH_2Ph), 4.20 (t, ^3J = 7.2 Hz, C*H*, Fmoc), 4.17 (AB, 1H, ^2J = 10.3 Hz, CH_2Ph), 4.13-4.07 (m, 2H, H-4, H-5), 4.03 (t, 1H, $^3J_{4',3'}$ = $^3J_{4',5'}$ = 9.3 Hz, H-4′), 3.98 (dd, 1H, $^3J_{6a',5'}$ = 5.1 Hz, $^2J_{6a',6b'}$ = 10.4 Hz, H-6a′), 3.95-3.93 (m, 1H, H-6a), 3.90 (td, 1H, $^3J_{2,1}$ = 3.6 Hz, $^3J_{2,3}$ = $^3J_{2,NH}$ = 10.2 Hz, H-2), 3.77-3.72 (m, 2H, H-3, H-6b′), 3.53 (dd, 1H, $^3J_{6b,5}$ = 7.7 Hz, $^2J_{6b,6a}$ = 10.1 Hz, H-6b), 3.15 (dd, 1H, $^3J_{3',2'}$ = 4.1 Hz, $^3J_{3',4'}$ = 9.2 Hz, H-3′), 2.75 (ddd, 1H, *J* = 5.6 Hz, *J* =8.0 Hz, *J* = 18.1 Hz, CH_2, Lev), 2.65 (td, 1H, $^3J_{5',6a'}$ = 5.1 Hz, $^3J_{5',4'}$ = $^3J_{5',6b'}$ = 9.8 Hz, H-5′), 2.52 (dt, 1H, *J* = 6.2 Hz, *J* = 18.1 Hz, CH_2, Lev), 2.43 (ddd, 1H, *J* = 5.7 Hz, *J* = 8.2 Hz, *J* = 14.0 Hz, CH_2, Lev), 2.11 (s, 3H, CH_3, Lev), 2.01-1.93 (m, 1H, CH_2, Lev), 1.08 (s, 9H, 3×CH_3, DTBS), 1.03 (s, 9H, 3×CH_3, DTBS), 0.82 (s, 9H, 3×CH_3, TBDMS), 0.11 (s, 3H, CH_3, TBDMS), 0.07 (s, 3H, CH_3, TBDMS); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 207.86 (*C*O, Lev), 171.06 (*C*O, Lev), 155.95 (*C*O, Fmoc), 144.11, 143.90, 141.26, 141.22 (4x*C*q, Fmoc), 138.34, 138.18 (2x*C*q, CH_2Ph), 135.76, 135.72, 135.67 (2×*C*q, OP(O)(OCH_2Ph)$_2$), 128.59, 128.56, 128.52, 128.45, 128.27, 128.25, 128.01, 127.83, 127.72, 127.58, 127.52, 127.07, 126.98, 125.49, 125.20 (26x*C*H, arom.), 123.61 (*C*q orthoester), 119.81, 119.76 (2x*C*H, Fmoc), 97.09 (C-1′, $^1J_{C,H}$ = 180 Hz), 91.62 (C-1, $^1J_{C,H}$ = 172 Hz), 78.94 (C-2′), 77.82 (C-4, $^2J_{C4,P}$ = 6.6 Hz), 76.23 (C-3′), 74.12 (C-4′), 73.41, 72.62 (2×CH_2, *C*H_2Ph), 71.65 (C-3, $^3J_{C3,P}$ = 4.7 Hz), 70.32 (C-6), 70.24 (C-5), 69.82 ((OP(O)(O*C*H_2Ph)$_2$, $^2J_{C,P}$ = 5.3 Hz), 69.33 ((OP(O)(O*C*H_2Ph)$_2$, $^2J_{C,P}$ = 5.2 Hz), 68.63 (C-5′), 67.11 (*C*H_2, Fmoc), 66.24 (C-6′), 55.43 (C-2), 47.14 (*C*H, Fmoc), 37.95, 33.01 (2×*C*H_2, Lev), 30.15 (*C*H_3, Lev), 27.45, 27.01, 25.80 (9×*C*H_3, DTBS, TBDMS), 22.72, 19.86, 17.84 (3×*C*q, DTBS, TBDMS), -4.03, -4.10 (2×Si*C*H_3, TBDMS); ^{31}P-NMR (243 MHz, $CDCl_3$): δ -1.62; HRMS (ESI): *m/z* calcd for $C_{74}H_{94}NO_{17}PSi_2$+NH_4^+: 1373.6136 [M+NH_4^+]; found 1373.6057.

Synthesis of 35, 38 and 41



3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-α-D-mannopyranosyl-(1↔1)-3-*O*-acetyl-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (35),

3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-β-D-mannopyranosyl-(1↔1)-3-*O*-acetyl-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (38) and

3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-α-D-mannopyranosyl-(1↔1)-3-*O*-acetyl-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (41).

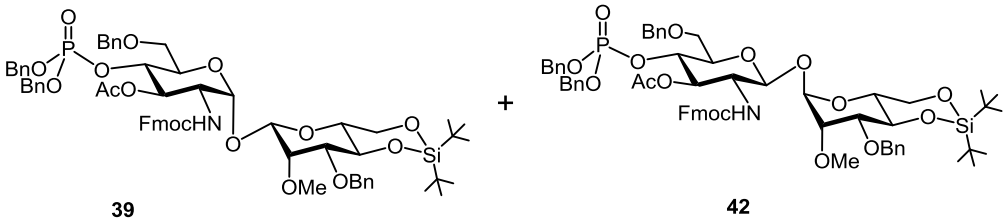
A solution of glycosyl donor **21** (72 mg, 121 µmol) and glycosyl acceptor **8** (78 mg, 104 µmol) in dry CH_2Cl_2 (2 ml) was stirred with powdered activated 4 Å molecular sieves for 2 h. at r. t. under atmosphere of Ar. The mixture was cooled to 0 °C and a solution of TMSOTf (1.1 µL, 6 µmol) in dry CH_2Cl_2 (55 µL of a stock solution prepared from 10µL TMSOTf in 500 µL CH_2Cl_2) was added. The mixture was stirred at 0 °C for 10 min and then the reaction was quenched by addition of Et_3N (10 µL). The mixture was warmed to r. t., diluted with toluene (10 ml), filtered over a pad of Celite and the filtrate was concentrated. The residue was purified by HPLC (two successive columns: toluene - EtOAc, 4 : 1 → 0:1 and hexane – EtOAc, 3 : 1 → 2 : 1, column A) to afford **35** (62 mg, 54 µmol, 51%), **38** (9 mg, 7.8 µmol, 7 %) and **41** (4 mg, 3.5 µmol, 3%) as syrups. **35:** R_f = 0.25 (hexane – EtOAc, 2 : 1); $[\alpha]_D^{20}$ = +64 (*c* 1.0,

$CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.44-7.42 (m, 2H, CH_2Ph), 7.37-7.33 (m, 9H, CH_2Ph), 7.30-7.22 (m, 9H, CH_2Ph), 5.20 (dd, 1H, $^3J_{3,4}$ = 9.1 Hz, $^3J_{3,2}$ = 10.9 Hz, H-3), 5.15 (d, 1H, $^3J_{1,2}$ = 3.8 Hz, H-1), 5.09 (d, 1H, $^3J_{1',2'}$ = 1.6 Hz, H-1′), 5.07 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph or Troc), 5.02 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph or Troc), 5.02-4.92 (m, 5H, N*H*, OP(O)(OCH_2Ph)$_2$), 4.80 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph or Troc), 4.50 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph or Troc), 4.49 (q, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = $^3J_{4,P}$ = 9.2 Hz, H-4), 4.42 (AB, 1H ^2J = 11.8 Hz, CH_2Ph or Troc), 4.37 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph or Troc), 4.31 (t, 1H, $^3J_{4',3'}$ = $^3J_{4',5'}$ = 9.5 Hz, H-4′), 4.08 (ddd, 1H, $^3J_{2,1}$ = 3.8 Hz, $^3J_{2,3}$ = 10.9 Hz, $^3J_{2,NH}$ = 9.5 Hz, H-2), 4.00 (dd, 1H, $^3J_{6a',5'}$ = 4.9 Hz, $^2J_{6a',6b'}$ = 10.2 Hz, H-6a′), 3.93 (t, 1H, $^3J_{6b',5'}$ = $^2J_{6b',6a'}$ = 10.4 Hz, H-6b′), 3.76-3.74 (m, 1H, H-5), 3.75 (dd, 1H, $^3J_{6a,5}$ = 1.8 Hz, $^2J_{6a,6b}$ = 11.3 Hz, H-6a), 3.68 (dd, 1H, $^3J_{3',2'}$ = 3.3 Hz, $^3J_{3',4'}$ = 9.5 Hz, H-3′), 3.65-3.62 (m, 1H, H-5′), 3.61 (dd, 1H, $^3J_{6b,5}$ = 6.2 Hz, $^2J_{6b,6a}$ = 11.2 Hz, H-6b), 3.38 (s, 3H, CH_3, Me), 3.37 (dd, 1H, $^3J_{2',1'}$ = 1.7 Hz, $^3J_{2',3'}$ = 3.2 Hz, H-2′), 1.89 (s, 3H, CH_3, Ac), 1.07 (s, 9H, 3×CH_3, DTBS), 1.01 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (151 MHz, $CDCl_3$): 171.33 (*C*O, Ac), 154.17 (*C*O, Troc), 138.72, 137.75 (2×*C*q, CH_2Ph), 135.46 (*C*q, $^3J_{C,P}$ = 7.3 Hz, OP(O)(OCH_2Ph)$_2$), 135.37 (*C*q, $^3J_{C,P}$ = 6.9 Hz, OP(O)(OCH_2Ph)$_2$), 128.77, 128.76, 128.66, 128.39, 128.35, 128.05, 128.03, 127.99, 127.77, 127.71, 127.64 (20×*C*H, CH_2Ph), 93.72 (C-1′, $^1J_{C',H'}$ = 170 Hz), 92.96 (C-1, $^1J_{C,H}$ = 173 Hz), 79.62 (C-2′), 77.76 (C-3′), 74.73 (C-4′), 74.49, 74.13, 73.57 (3×*C*H$_2$, CH_2Ph, Troc), 73.46 (C-4, $^2J_{C4,P}$ = 5.8 Hz), 71.12 (C-3), 70.65 (C-5, $^3J_{C5,P}$ = 5.7 Hz), 69.76. 6974, 69.72, 69.71 (2×*C*H$_2$, OP(O)(O*C*H$_2$Ph)$_2$), 69.30 (C-5′), 68.25 (C-6), 66.33 (C-6′), 59.69 (*C*H$_3$, Me), 53.76 (C-2), 27.45, 27.09 (6×*C*H$_3$, DTBS), 22.60 (*C*q, DTBS), 20.67 (CH_3, Ac), 19.86 (*C*q, DTBS); ^{31}P-NMR (242MHz, $CDCl_3$): δ -1.95; HRMS (ESI): *m/z* calcd for $C_{54}H_{69}NO_{16}PSi+H^+$: 1152.3262 [M+H$^+$]; found 1152.3281.

(38): R_f = 0.20 (hexane – EtOAc, 2 : 1); $[\alpha]_D^{20}$ = +23 (*c* 0.8, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.40-7.22 (m, 20H, CH_2Ph), 5.39 (dd, 1H, $^3J_{3,4}$ = 9.5 Hz, $^3J_{3,2}$ =10.7 Hz, H-4), 5.30 (d, 1H, $^3J_{NH,2}$ = 9.1 Hz, N*H*), 5.15 (d, 1H, $^3J_{1,2}$ = 3.6 Hz, H-1), 4.94-4.81 (m, 6H, OP(O)(OCH_2Ph)$_2$, CH_2Ph or Troc), 4.78 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph or Troc), 4.67 (ddd, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = $^2J_{H,P}$ = 9.2 Hz, H-4), 4.63 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph or Troc), 4.62 (s, 1H, H-1′), 4.50 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph or Troc), 4.44 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph or Troc), 4.28 (t, 1H, $^3J_{4',3'}$ = $^3J_{4',5'}$ = 9.4 Hz, H-4′), 4.22-4.19 (m, 1H, H-5), 4.06 (dd, 1H, $^3J_{6a',5'}$ = 5.0 Hz, $^2J_{6a',6b'}$ = 10.2 Hz, H-6a′), 3.98 (t, 1H, $^3J_{6b',5'}$ = $^2J_{6b',6a'}$ =10.1 Hz, H-6b′), 3.98-3.94 (m, 1H, H-2), 3.69 (s, 3H, CH_3, Me), 3.68-3.63 (m, 2H, H-6a, H-6b), 3.58 (d, 1H, $^3J_{2',3'}$ = 2.8 Hz, H-2′), 3.35 (dd, 1H, $^3J_{3',2'}$ = 2.9 Hz, $^3J_{3',4'}$ = 9.2 Hz, H-3′), 3.28 (dt, 1H, $^3J_{5',6a'}$ = 4.9 Hz, $^3J_{5',6b'}$ = $^3J_{5',4'}$ = 9.7 Hz, H-5′), 1.88 (s, 3H, CH_3, Ac), 1.08 (s, 9H, 3×CH_3, DTBS), 0.99 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 171.62 (*C*O, Ac), 154.06 (*C*O, Troc), 138.59, 137.87 (2×*C*q, CH_2Ph), 135.56 (*C*q, $^3J_{C,P}$ = 7.5 Hz, OP(O)(OCH_2Ph)$_2$), 135.47 (*C*q, $^3J_{C,P}$ = 7.7 Hz, OP(O)(OCH_2Ph)$_2$), 128.57, 128.45, 128.32, 127.98, 127.92, 127.68, 127.61, 127.57 (20×*C*H, CH_2Ph), 101.35 (C-1′, $^1J_{C,H}$ = 157 Hz), 97.83 (C-1, $^1J_{C,H}$ = 173 Hz), 95.45 (*C*Cl$_3$, Troc), 79.89 (C-3′), 79.70 (C-2′), 74.76 (C-4′), 74.47, 73.41 (2×*C*H$_2$, CH_2Ph or Troc), 73.12 (C-4, $^2J_{C4,P}$ = 6.0 Hz), 73.00 (*C*H$_2$, CH_2Ph or Troc), 71.79 (C-5′), 71.01 (C-3), 70.40 (C-5, $^3J_{C5,P}$ = 5.7 Hz), 69.61 (*C*H$_2$, $^2J_{C,P}$ = 5.8 Hz, OP(O)(OCH_2Ph)$_2$), 69.46 (*C*H$_2$, $^2J_{C,P}$ = 5.3 Hz, OP(O)(OCH_2Ph)$_2$), 67.62 (C-6), 66.17 (C-6′), 62.34 (*C*H$_3$, Me), 54.41 (C-2), 27.44, 27.07 (6×*C*H$_3$, DTBS), 22.61 (*C*q, DTBS), 20.69 (*C*H$_3$, Ac), 19.92 (*C*q, DTBS); ^{31}P-NMR (243 MHz, $CDCl_3$): δ -2.51; HRMS (ESI): *m/z* calcd for $C_{54}H_{69}NO_{16}PSi+H^+$: 1152.3262 [M+H$^+$]; found 1152.3268;

(41): R_f = 0.15 (hexane – EtOAc, 2 : 1); $[\alpha]_D^{20}$ = +9 (*c* 0.4, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.40-7.21 (m, 20H, CH_2Ph), 5.31 (t, 1H, $^3J_{2,3}$ = $^3J_{3,4}$ = 10.2 Hz, H-3), 5.08 (d, 1H, $^3J_{2,NH}$ = 9.5 Hz, N*H*), 4.96-4.95 (s, 1H, H-1′), 4.95 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph or Troc), 4.92-4.83 (m, 4H, OP(O)(OCH_2Ph)$_2$), 4.75-4.73 (m, 2H, H-1, AB, CH_2Ph or Troc), 4.74 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph or Troc), 4.69 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph or Troc), 4.55 (ddd, 1H, $^3J_{3,4}$ = $^3J_{4,5}$ = $^3J_{4,P}$ = 9.2 Hz, H-4), 4.52 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph or Troc), 4.43 (AB, 1H, ^2J = 11.8 Hz, CH_2, CH_2Ph or Troc), 4.27 (t, 1H, $^3J_{3',4'}$ = $^3J_{4',5'}$ = 9.5 Hz, H-4′), 4.07 (dd, 1H, $^3J_{5',6a'}$ = 4.8 Hz, $^2J_{6a',6b'}$ = 9.2 Hz, 1H), 4.05-4.01 (m, 1H, H-5′), 3.88 (t, 1H, $^3J_{5',6b'}$ = $^2J_{6a',6b'}$ = 9.6 Hz, H-6b′), 3.74-3.72 (m, 1H, H-6a), 3.70 (dd, 1H, $^3J_{2',3'}$ = 2.8 Hz, $^3J_{3',4'}$ = 9.4 Hz, H-3′), 3.67-3.58 (m, 3H, H-2, H-5, H-6b), 3.48-3.47 (m, 1H, H-2′), 3.47 (s, 3H, CH_3, OMe), 1.89 (s, 3H, CH_3, Ac), 1.06 (s, 9H, 3×CH_3, DTBS), 0.99 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (151 MHz, CDCl3): δ 171.08 (*C*O, Ac), 153.90 (*C*O, Troc), 139.17, 137.85 (2×*C*q, CH_2Ph), 128.65, 128.58, 128.31, 128.27, 127.98, 127.78, 127.63, 127.41, 127.36 (20×*C*H, CH_2Ph) 100.12 (C-1, C-1′), 79.16 (C-2′), 78.82 (C-3′), 75.07 (C-4′), 74.57 (C-5, $^3J_{C5,P}$ = 6.3 Hz), 74.39, 73.86, 73.67 (3×*C*H$_2$, CH_2Ph and Troc), 73.47 (*C*-4, $^2J_{C4,P}$ = 5.9 Hz), 72.19 (C-3), 69.64, 69.60, 69.58, 69.54 (OP(O)(O*C*H$_2$Ph)$_2$), 68.65 (C-6), 68.53 (C-5′), 66.26 (C-6′), 60.15 (*C*H$_3$, Me), 56.49 (C-2), 27.43, 27.14 (6×*C*H$_3$, DTBS), 22.59 (*C*q, DTBS), 20.67 (*C*H$_3$, Ac), 19.98 (*C*q, DTBS); ^{31}P-NMR (243 MHz, $CDCl_3$): δ = -2.20; HRMS (ESI): *m/z* calcd for $C_{54}H_{69}NO_{16}PSi+H^+$ 1152.3262 [M+H]; found 1152.3239.

Synthesis of 39 and 42



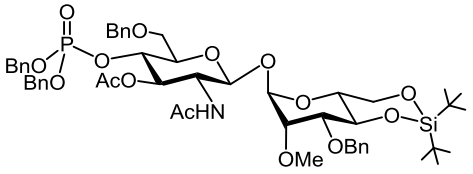
39 **42**

3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-β-D-mannopyranosyl-(1↔1)-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(9-fluorenylmethoxycarbonylamino)-α-D-glucopyranoside (39) and 3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-α-D-mannopyranosyl-(1↔1)-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(9-fluorenylmethoxycarbonyl-amino)-β-D-glucopyranoside (42)

(β,α- and α,β- by-products in the synthesis of **36**)
(39): R_f = 0.25 (hexane - EtOAc, 1:1); $[\alpha]_D^{20}$ = +35 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ: 7.75-7.71 (m, 2H, arom), 7.54-7.51 (m, 2H, arom), 7.40-7.20 (m, 24H, 24×C*H*, arom), 5.37 (t, 1H, $^3J_{3,2}$ = $^3J_{3,4}$ = 10.1 Hz, H-3), 5.08 (d, 1H, $^3J_{1,2}$ = 3.5 Hz, H-1), 5.05 (d, 1H, $^3J_{NH,2}$ = 9.1 Hz, N*H*), 4.95 (AB, 1H, ^2J=12.5 Hz, CH_2Ph), 4.93-4.83 (m, 4H, OP(O)(OCH_2Ph)$_2$), 4.82 (AB, 1H, ^2J = 12.5 Hz, CH_2Ph), 4.65 (ddd, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = $^3J_{H,P}$ = 9.2 Hz, H-4), 4.61 (s, 1H, H-1′), 4.51 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.43 (dd, 1H, ^3J = 6.7 Hz, ^2J = 10.7 Hz, CH_2, Fmoc), 4.44 (AB, 1H, ^2J = 11.1 Hz, CH_2Ph), 4.31 (dd, 1H, ^3J = 7.4 Hz, ^2J = 10.6 Hz, CH_2, Fmoc), 4.29 (t, 1H, $^3J_{4',3'}$ = $^3J_{4',5'}$ = 9.3 Hz, H-4′), 4.22-4.19 (m, 1H, H-5), 4.16 (t, 1H, ^3J = 7.0 Hz, C*H*, Fmoc), 4.06 (dd, 1H, $^3J_{6a',5'}$ = 5.0 Hz, $^2J_{6a',6b'}$ = 10.2 Hz, H-6a′), 3.98 (t, 1H, $^3J_{6b',5'}$ = $^2J_{6b',6a'}$ = 10.2 Hz, H-6b′), 3.98-3.94 (m, 1H, H-2), 3.68-3.65 (m, 4H, H-6a, H-6b, CH_3, Me), 3.56 (d, 1H, $^3J_{2',3'}$ = 2.8 Hz, H-2′), 3.37 (dd, 1H, $^3J_{3',2'}$ = 2.9 Hz, $^3J_{3',4'}$ = 9.2 Hz, H-3′), 3.29 (dt, 1H, $^3J_{5',6a'}$ = 5.0 Hz, $^3J_{5',4'}$ = $^3J_{5',6b'}$ = 9.8 Hz, H-5′), 1.86 (s, 3H, CH_3, Ac), 1.08 (s, 9H, 3×CH_3, DTBS), 1.00 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (151 MHz, $CDCl_3$): δ: 171.63 (*C*O, Ac), 155.65 (*C*O, Fmoc), 143.78, 143.47, 141.36, 141.25 (4×*C*q, Fmoc), 138.66, 137.89 (2×*C*q, CH_2Ph), 135.59 (*C*q, $^3J_{C,P}$=7.0 Hz, OP(O)(OCH_2Ph)$_2$), 135.49 (*C*q, $^3J_{C,P}$=7.4 Hz, OP(O)(OCH_2Ph)$_2$), 128.55, 128.42, 128.30, 127.96, 127.91, 127.79, 127.74, 127.68, 127.65, 127.57, 127.07, 127.03, 124.99, 124.93, 120.05, 119.99 (28×*C*H, arom), 101.37 (C-1′, $^1J_{C,H}$ = 155 Hz), 98.20 (C-1, $^1J_{C,H}$ = 177 Hz), 80.13 (C-3′), 79.87 (C-2′), 74.77 (C-4′), 73.40 (*C*H$_2$Ph), 73.25 (C-4, $^2J_{C4,P}$ = 6.3 Hz), 73.17 (*C*H$_2$Ph), 71.79 (C-5′), 71.13 (C-3), 70.36 (C-5, $^3J_{C5,P}$ = 6.2 Hz), 69.57 (OP(O)(O*C*H$_2$Ph)$_2$, $^2J_{C,P}$ = 5.6 Hz), 69.42 (OP(O)(O*C*H$_2$Ph)$_2$, $^2J_{C,P}$ = 5.4 Hz), 67.70 (C-6), 67.02 (*C*H$_2$, Fmoc), 66.16 (C-6′), 62.34 (*C*H$_3$, Me), 54.12 (C-2), 47.11 (*C*H, Fmoc), 27.44, 27.07 (6×*C*H$_3$, DTBS), 22.60 (*C*q, DTBS), 20.72 (*C*H$_3$, Ac), 19.92 (*C*q, DTBS); ^{31}P-NMR (243 MHz, $CDCl_3$): δ –2.53; HRMS (ESI): *m/z* calcd for $C_{66}H_{78}NO_{16}PSi+H^+$: 1200.4900 [M+H$^+$]; found 1200.4912.

Compound **42** was deprotected at C-2 and acetylated to provide compound **44** suitable for characterization by NMR.

Synthesis of 44

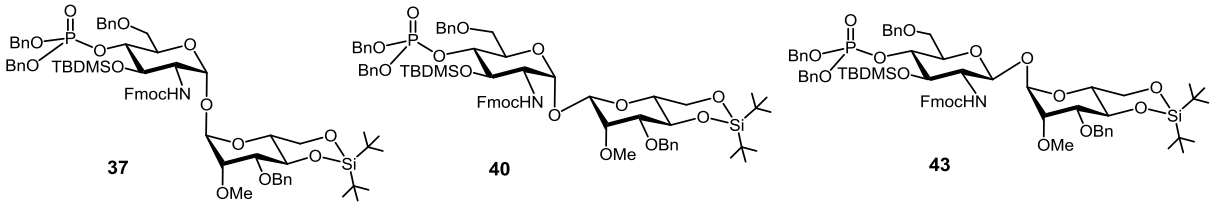


3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-α-D-mannopyranosyl-(1↔1)-2-acetamido-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-α-D-gluco-pyranoside (44).

To a stirred solution of **42** (20 mg, 17 µmol) in dry CH_2Cl_2 (1 ml) a solution of DBU (0.7 µl, 5 µmol) in dry CH_2Cl_2 (70 µl of a stock solution prepared from 10 µl DBU in 1 ml CH_2Cl_2) was added. The mixture was stirred for 1 h and successively added dropwise to a solution of acetic acid anhydride (20 µL, 212 µmol) in pyridine (300 µl) at 0 °C. The stirring was continued for 20 min, the mixture was diluted with EtOAc (10 ml), washed with aq. citric acid (0.25 M, 10 ml), sat. aq. $NaHCO_3$ (10 ml) and brine (10 ml). The organic phase was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel chromatography (toluene-EtOAc, 1:1→1:2) to afford **44** (13 mg, 13 µmol, 76%). R_f = 0.19 (toluene–EtOAc, 1:1); $[\alpha]_D^{20}$ = +11 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.40-

7.39 (m, 2H, CH_2Ph), 7.34-7.20 (m, 18H, CH_2Ph), 5.50 (d, 1H, $^3J_{NH,2}$ = 8.8 Hz, N*H*), 5.24 (dd, 1H, ^3J = 9.0 Hz, ^3J = 10.7 Hz, H-3), 4.95 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph), 4.94 (d, 1H, $^3J_{1',2'}$ = 1.3 Hz, H-1′), 4.92-4.84 (m, 4H, OP(O)(OCH_2Ph)$_2$), 4.73 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.72 (d, 1H, $^3J_{1,2}$ = 8.4 Hz, H-1), 4.54-4.49 (m, 1H, H-4), 4.52 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.44 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.26 (t, 1H, $^3J_{4',3'}$ = $^3J_{4',5'}$ = 9.5 Hz, H-4′), 4.08-4.00 (m, 2H, H-5′, H-6a′), 3.92-3.86 (H-2, H-6b′), 3.74-3.71 (m, 2H, H-3′, H-6a), 3.66-3.60 (m, 2H, H-5, H-6b), 3.49 (dd, 1H, $^3J_{2',1'}$ = 1.6 Hz, $^3J_{2',3'}$ = 3.1 Hz, H-2′), 3.47 (s, 3H, CH_3, Me), 1.92 (s, 3H, CH_3, Ac), 1.89 (s, 3H, CH_3, Ac), 1.06 (s, 9H, DTBS), 0.98 (s, 9H, DTBS); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 171.43, 169.98 (2x*C*O, Ac), 139.24, 137.92 (2×*C*q, CH_2Ph), 135.52 (*C*q, $^3J_{C,P}$ = 7.1 Hz, OP(O)(OCH_2Ph)$_2$), 135.46 (*C*q, $^3J_{C,P}$ = 6.8 Hz, OP(O)(OCH_2Ph)$_2$), 128.62, 128.59, 128.57, 128.30, 128.23, 127.96, 127.94, 127.75, 127.59, 127.46, 127.31 (20x*C*H, CH_2Ph), 100.20 (C-1, $^1J_{C,H}$ = 159 Hz), 99.81 (C-1′, $^1J_{C,H}$ = 172 Hz), 79.29 (C-2′), 78.92 (C-3′), 75.08 (C-4′), 74.66 (C-4 or C-5, $J_{C,P}$ = 6.4 Hz), 73.91, 73.68 (2×*C*H_2Ph), 73.57 (C-4 or C-5, $J_{C,P}$ = 6.4 Hz), 72.96 (C-3), 69.60 (*C*H_2, $^2J_{C,P}$ = 5.2 Hz, OP(O)(O*C*H_2Ph)$_2$), 69.57 (*C*H_2, $^2J_{C,P}$ = 5.0 Hz, OP(O)(O*C*H_2Ph)$_2$), 68.81 (C-6), 68.53 (C-5′), 66.32 (C-6′), 60.06 (*C*H_3, Me), 54.89 (C-2), 27.44, 27.15 (6×*C*H_3, DTBS), 23.27 (*C*H_3, Ac), 22.58 (*C*q, DTBS), 20.67 (*C*H_3, Ac), 19.98 (*C*q, DTBS); ^{31}P-NMR (243 MHz, $CDCl_3$): δ -2.39; HRMS (ESI): *m/z* calcd for $C_{53}H_{70}NO_{15}PSi+H^+$: 1020.4325 [M+H$^+$]; found 1020.4323.

Synthesis of 37, 40 and 43



3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-α-D-mannopyranosyl-(1↔1)-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-3-*O*-di-*tert*-butyldimethylsilyl-2-deoxy-2-(9-fluorenylmethoxy-carbonylamino)-α-D-glucopyranoside (37),

3-*O*-benzyl-4,6-di-*O*-di-*tert*-butylsilylene-2-*O*-methyl-β-D-mannopyranosyl-(1↔1)-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-2-(9-fluorenylmethoxy-carbonylamino)-α-D-glucopyranoside (40) and

3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-α-D-mannopyranosyl-(1↔1)-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-2-(9-fluorenylmethoxy-carbonylamino)-β-D-glucopyranoside (43).

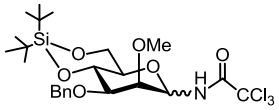
A solution of glycosyl donor **21** (57 mg, 96 μmol) and glycosyl acceptor **33** (86 mg, 99 μmol) in dry CH_2Cl_2 (1.5 ml) was stirred with powdered activated 4 Å molecular sieves for 2 h. at r. t. under atmosphere of Ar. The mixture was cooled to 0 °C and a solution of TMSOTf (1 μL, 6 μmol) in dry CH_2Cl_2 (50 μL of a stock solution prepared from 10μL TMSOTf in 500 μL CH_2Cl_2) was added. The mixture was stirred at 0 °C for 10 min and then the reaction was quenched by addition of Et_3N (10 μL). The mixture was warmed to r. t., diluted with toluene (10 ml), filtered over a pad of Celite and the filtrate was concentrated. The residue was purified by HPLC (two successive columns: toluene - EtOAc, 4 : 1 → 0 : 1 and hexane – EtOAc, 3 : 1 → 2 : 1, column A) to afford **37** (63 mg, 50 μmol, 52%), **40** (24 mg, 19 μmol, 19%) and **43** (16 mg, 13 μmol, 13%) as syrups. **37:** R_f = 0.40 (toluene – EtOAc, 3 : 1); $[\alpha]_D^{20}$ = +52 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.76-7.75 (m, 2H, arom.), 7.59-7.56 (m, 2H, arom.), 7.40-7.22 (m, 24H, arom.), 5.13 (d, 1H, $^3J_{1,2}$ = 3.1 Hz, H-1), 5.11 (d, 1H, $^3J_{1',2'}$ = 1.3 Hz, H-1′), 4.98-4.88 (m, 5H, OP(O)(OCH_2Ph)$_2$, CH_2Ph), 4.78 (AB, 1H, ^2J = 12.6 Hz, CH_2Ph), 4.67 (d, 1H, $^3J_{NH,2}$ = 9.4 Hz, N*H*), 4.53 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph), 4.44 (AB, 1H, ^2J = 11.7 Hz, CH_2Ph), 4.33-4.30 (m, 3H, H-4′, CH_2, Fmoc), 4.20-4.16 (m, 2H, H-4, C*H*, Fmoc), 4.02 (dd, 1H, $^3J_{6a',5'}$ = 5.0 Hz, $^2J_{6a',6b'}$ = 10.1 Hz, H-6a′), 3.96 (t, 1H, $^3J_{6b',5'}$ = $^2J_{6b',6a'}$ = 10.3 Hz, H-6b′), 3.88 (td, 1H, $^3J_{2,1}$ = 3.2 Hz, $^3J_{2,NH}$ = $^3J_{2,3}$ = 9.4 Hz, H-2), 3.83-3.79 (m, 2H, H-5, H-6a), 3.75-3.71 (m, 2H, H-3, H-6b), 3.68 (td, $^3J_{5',6a'}$ = 4.9 Hz, $^3J_{5',4'}$ = $^3J_{5',6b'}$ = 9.9 Hz, H-5′), 3.59 (dd, 1H, $^3J_{3',2'}$ = 3.2 Hz, $^3J_{3',4'}$ = 9.5 Hz, H-3′), 3.41 (dd, 1H, $^3J_{2',1'}$ = 1.7 Hz, $^3J_{2',3'}$ = 3.0 Hz, H-2′), 3.38 (s, 3H, CH_3, Me), 1.06 (s, 9H, 3×CH_3, DTBS), 0.96 (s, 9H, 3×CH_3, DTBS), 0.81 (s, 9H, 3×CH_3, TBDMS), 0.13 (s, 3H, CH_3, TBDMS), 0.03 (s, 3H, CH_3, TBDMS); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 155.79 (*C*O, Fmoc), 143.84, 143.77, 141.22 (4×*C*q, Fmoc), 138.71, 138.08 (2×*C*q,

C*H*$_2$Ph), 135.66, 135.61 (2×*C*q, OP(O)(OCH$_2$Ph)$_2$), 128.65, 128.62, 128.59, 128.35, 128.31, 128.22, 128.07, 128.05, 127.74, 127.72, 127.66, 127.61, 127.09, 127.02, 125.26, 125.10, 119.98 (28x*C*H, arom.), 94.87 (C-1′, $^1J_{C,H}$ = 178 Hz), 93.92 (C-1, $^1J_{C,H}$ = 175 Hz), 79.62 (C-2′), 77.03 (C-3′), 76.05 (C-4, $^2J_{C4,P}$ = 6.4 Hz), 74.84 (C-4′), 73.31, 73.25 (2×C*H*$_2$Ph), 72.45 (C-5), 71.11 (C-3, $^3J_{C3,P}$ = 4.6 Hz), 69.91 (*C*H$_2$, $^2J_{C,P}$ = 5.3 Hz, OP(O)(O*C*H$_2$Ph)$_2$), 69.48 (*C*H$_2$, $^2J_{C,P}$ = 4.8 Hz, OP(O)(O*C*H$_2$Ph)$_2$), 69.26 (C-5′), 68.56 (C-6), 67.81 (*C*H$_2$, Fmoc), 66.38 (C-6′), 59.57 (*C*H$_3$, Me), 54.93 (C-2), 47.07 (*C*H, Fmoc), 27.42, 27.08, 25.67 (9×*C*H$_3$, DTBS, TBDMS), 22.58, 19.84, 17.78 (3×*C*q, DTBS, TBDMS), -4.07, -4.33 (2×*C*H$_3$, TBDMS); ^{31}P-NMR (243 MHz, CDCl$_3$): δ -1.40ppm; HRMS (ESI) *m/z*: calcd for $C_{70}H_{90}NO_{15}PSi_2$+Na$^+$: 1294.5479 [M+Na$^+$]; found 1294.5444;

(40): R_f = 0.48 (toluene – EtOAc, 3 : 1); $[\alpha]_D^{20}$ = +35 (*c* 1.0, CHCl$_3$); ^{1}H-NMR (600 MHz, CDCl$_3$): δ 7.73-7.71 (m, 2H, arom.), 7.54-7.53 (m, 2H, arom.), 7.40-7.18 (m, 24H, arom.), 4.94 (d, 1H, $^3J_{1,2}$ = 3.2 Hz, H-1), 4.94 (AB, 1H, ^2J = 12.4 Hz, C*H*$_2$Ph), 4.91-4.82 (m, 4H, OP(O)(OC*H*$_2$Ph)$_2$), 4.80 (AB, 1H, ^2J = 12.7 Hz, C*H*$_2$Ph), 4.62-4.60 (m, 1H, N*H*), 4.60 (s, 1H, H-1′), 4.56 (AB, 1H, ^2J = 12.2 Hz, C*H*$_2$Ph), 4.52 (dd, 1H, ^3J = 6.0 Hz, ^2J = 10.7 Hz, C*H*$_2$, Fmoc), 4.44 (dd, 1H, ^3J = 5.8 Hz, ^2J = 10.6 Hz, C*H*$_2$, Fmoc), 4.40 (AB, 1H, ^2J = 12.0 Hz, C*H*$_2$Ph), 4.32 (ddd, 1H, $^3J_{4,5}$ = $^3J_{4,3}$ = $^3J_{4,P}$ = 9.0 Hz, H-4), 4.26 (t, 1H, $^3J_{4',5'}$ = $^3J_{4',3'}$ = 9.3 Hz, H-4′), 4.15 (t, 1H, ^3J = 5.8 Hz, C*H*, Fmoc), 4.09-4.06 (m, 1H, H-5), 4.05 (dd, 1H, $^3J_{6a',5'}$ = 5.1 Hz, $^2J_{6a',6b'}$ = 10.3 Hz, H-6a′), 3.97 (t, 1H, $^3J_{6b',5'}$ = $^2J_{6b'6a'}$ = 10.1 Hz, H-6b′), 3.87-3.80 (m, 3H, H-2, H-3, H-6a), 3.72-3.69 (m, 1H, H-6b), 3.46 (d, 1H, *J* = 2.3 Hz, H-2′), 3.44 (s, 3H, C*H*$_3$, Me), 3.35 (dd, 1H, $^3J_{3',2'}$ = 2.9 Hz, $^3J_{3',4'}$ = 9.3 Hz, H-3′), 3.26 (td, 1H, $^3J_{5',6a'}$ = 4.8 Hz, $^3J_{5',6b'}$ = $^3J_{5',4'}$ = 9.9 Hz, H-5′), 1.07 (s, 9H, 3×C*H*$_3$, DTBS), 0.98 (s, 9H, 3×C*H*$_3$, DTBS), 0.77 (s, 9H, 3×C*H*$_3$, TBDMS), 0.03 (s, 3H, C*H*$_3$, TBDMS), -0.14 (s, 3H, C*H*$_3$, TBDMS); ^{13}C-NMR (151 MHz, CDCl$_3$): δ 155.49 (*C*O, Fmoc), 143.82, 143.67, 141.47, 141.37 (4×*C*q, Fmoc), 138.64, 138.32 (2×*C*q, *C*H$_2$Ph), 135.78, 135.74 (2×*C*q, OP(O)(OCH$_2$Ph)$_2$), 128.46, 128.44, 128.41, 128.21, 128.07, 127.94, 127.72, 127.69, 127.57, 127.50, 127.38, 127.06, 126.90, 124.72, 124.63, 119.99, 119.93 (28×*C*H, arom.), 99.86 (C-1′, $^1J_{C,H}$ = 156 Hz), 97.79 (C-1, $^1J_{C,H}$ = 175 Hz), 80.35 (C-3′), 79.53 (C-2′), 76.57 (C-4, $^2J_{C4,P}$ = 7.5 Hz), 74.77 (C-4′), 73.31, 72.84 (2×*C*H$_2$Ph), 71.78 (C-5′), 71.46 (C-3, $^3J_{C3,P}$ = 4.5 Hz, 1C), 70.88 (C-5), 69.73 (OP(O)(O*C*H$_2$Ph)$_2$, $^2J_{C,P}$ = 5.4 Hz), 69.25 (OP(O)(O*C*H$_2$Ph)$_2$, $^2J_{C,P}$ = 4.5 Hz), 68.26 (C-6), 66.53 (*C*H$_2$, Fmoc), 66.08 (C-6′), 62.12 (*C*H$_3$, Me), 55.35 (C-2), 47.15 (*C*H, Fmoc), 27.43, 27.06, 25.73 (9×*C*H$_3$, DTBS, TBDMS), 22.58, 19.90, 17.77 (3×*C*q, DTBS, TBDMS), -4.10, -4.26 (2×*C*H$_3$, TBDMS); ^{31}P-NMR (243MHz, CDCl$_3$): δ -1.97; HRMS (ESI): *m/z* calcd for $C_{70}H_{90}NO_{15}PSi_2$+Na$^+$: 1294.5479 [M+Na$^+$]; found 1294.5459;

(43): R_f = 0.22 (toluene : EtOAc, 3 : 1); $[\alpha]_D^{20}$ = +15 (*c* 1.2, CHCl$_3$); ^{1}H-NMR (600 MHz, acetone-d6): δ 7.86 (d, 2H, *J* = 7.6 Hz, arom.), 7.69 (t, 2H, *J* = 6.0 Hz, arom.), 7.42-7.19 (m, 24H, arom.), 6.55 (d, 1H, $^3J_{NH,2}$ = 9.7 Hz, N*H*), 5.04-4.96 (m, 5H, H-1′, OP(O)(OC*H*$_2$Ph)$_2$), 4.85 (AB, 1H, ^2J = 12.2 Hz, C*H*$_2$Ph), 4.78 (d, 1H, $^3J_{1,2}$ = 8.3 Hz, H-1), 4.67 (AB, 1H, ^2J = 12.1 Hz, C*H*$_2$Ph), 4.58 (AB, 1H, ^2J = 11.9 Hz, C*H*$_2$Ph), 4.48-4.46 (m, 2H, C*H*$_2$, Fmoc, C*H*$_2$Ph), 4.36-4.28 (m, 2H, H-4, C*H*$_2$, Fmoc), 4.23 (t, 1H, *J* = 6.8 Hz, C*H*, Fmoc), 4.20 (t, 1H, $^3J_{4',3'}$ = $^3J_{4',5'}$ = 9.4 Hz, H-4′), 4.12-4.08 (m, 2H, H-5′, H-6a′), 4.00 (t, 1H, $^3J_{3,4}$ = $^3J_{3,2}$ = 9.0 Hz, H-3), 3.92-3.90 (m, 1H, H-6a), 3.82 (dd, 1H, *J* = 5.2 Hz, *J* = 11.0 Hz, H-6b), 3.79-3.75 (m, 1H, H-6b′), 3.73-3.68 (m, 2H, H-3′, H-5), 3.60-3.55 (m, 1H, H-2), 3.50 (br. s, 1H, H-2′), 3.23 (s, 3H, C*H*$_3$, Me), 1.06 (s, 9H, 3×C*H*$_3$, DTBS), 1.00 (s, 9H, 3×C*H*$_3$, DTBS), 0.84 (s, 9H, 3×C*H*$_3$, TBDMS), 0.12 (s, 3H, C*H*$_3$, TBDMS), 0.05 (s, 3H, C*H*$_3$, TBDMS); ^{13}C-NMR (151 MHz, acetone-d6): δ 157.06 (*C*O, Fmoc), 145.22, 144.96, 142.20, 140.43, 139.76, 137.34, 137.29 (6×*C*q, arom.), 129.35, 129.31, 129.23, 129.19, 129.01, 128.98, 128.95, 128.60, 128.48, 128.14, 127.99, 125.99, 125.92, 120.90 (28×*C*H, arom.), 101.68 (C-1, $^1J_{C,H}$ = 160 Hz), 100.70 (C-1′, $^1J_{C,H}$ = 171 Hz), 79.98, 79.82 (C-2′, C-3′), 78.22 (C-4, $^2J_{C4,P}$ = 6.5 Hz), 76.09 (C-4′), 75.47 (C-5), 74.96 (C-3, $^3J_{C3,P}$ = 4.4 Hz), 73.91, 73.76 (2×*C*H$_2$Ph), 70.51 (C-6), 70.18 (OP(O)(O*C*H$_2$Ph)$_2$, ^2J = 5.4 Hz), 69.95 (OP(O)(O*C*H$_2$Ph)$_2$, ^2J = 4.7 Hz), 69.10 (C-5′), 67.35, 67.21 (C-6′, *C*H$_2$ Fmoc), 59.85 (*C*H$_3$, Me), 59.41 (C-2), 48.10 (*C*H Fmoc), 27.86, 27.65, 26.53 (9×*C*H$_3$, DTBS, TBDMS), 23.19, 20.61, 18.64 (3×*C*q, DTBS, TBDMS), -3.56, -3.78 (2×*C*H$_3$, TBDMS); ^{31}P-NMR (243 MHz, acetone-d6) δ -1.84; HRMS (ESI): *m/z* calcd for $C_{70}H_{90}NO_{15}PSi_2$+Na$^+$: 1294.5479 [M+Na$^+$]; found 1294.5460.

Synthesis of 45

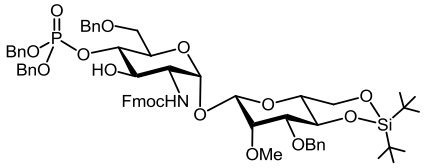


Trichloroacetyl 1-amino-3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-1-deoxy-2-*O*-methyl-D-mannopyranoside (45).

Glycosyl amide **45** was isolated from glycosylation reactions of acceptors **8** and **33** with donor **20**. R_f = 0.40 and 0.13 (hexane – EtOAc, 5 : 1); $[\alpha]_D^{20}$ = +30 (*c* 0.3, CHCl$_3$); ^{1}H-NMR (300 MHz, CDCl$_3$, β-anomer): δ 7.55 (d, 1H, $^3J_{NH,1}$ = 9.3 Hz, N*H*), 7.41-7.27 (m, 5H, arom.), 5.19 (dd, 1H, $^3J_{1,2}$ = 1.5 Hz, $^3J_{NH,1}$ = 9.3 Hz, H-1), 4.99 (AB, 1H, ^2J =

12.3 Hz, CH_2Ph), 4.80 (AB, 1H, ^2J = 12.3 Hz, CH_2Ph), 4.26 (t, 1H, $^3J_{4,5}$ = $^3J_{4,3}$ = 9.4 Hz, H-4), 4.18 (dd, 1H, $^3J_{6a,5}$ = 5.0 Hz, $^2J_{6a,6b}$ = 10.2 Hz, H.6b), 3.93 (t, 1H, $^3J_{6b,5}$ = $^2J_{6b,6a}$ = 10.2 Hz, H-6b), 3.71 (s, 3H, CH_3, Me), 3.60 (dd, 1H, $^3J_{2,1}$ = 1.5 Hz, $^3J_{2,3}$ = 3.1 Hz, H-2), 3.53 (dd, 1H, $^3J_{3,2}$ = 3.0 Hz, $^3J_{3,4}$ = 9.3 Hz, H-3), 3.44 (dt, $^3J_{5,6a}$ = 4.9 Hz, $^3J_{5,4}$ = $^3J_{5,6b}$ = 9.8 Hz, H-3), 1.09 (s, 9H, 3×CH_3, DTBS), 1.02 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (75 MHz, $CDCl_3$, β-anomer): δ 161.20 (*C*O), 138.51 (*C*q, CH_2Ph), 128.47, 127.75, 127.54 (5×*C*H, CH_2Ph), 81.45 (C-3), 79.42, 78.99 (not assigned C-1, C-2), 74.76 (C-4), 73.83 (*C*H_2Ph), 73.00 (C-5), 66.10 (C-6), 62.23 (*C*H_3, Me), 27.42, 27.07 (6×*C*H_3, DTBS), 22.64, 19.96 (2×*C*q, DTBS); HRMS (ESI): m/z calcd for $C_{24}H_{35}NO_6Si$-H: 566.1305 [M-H]$^-$; found 566.1305.

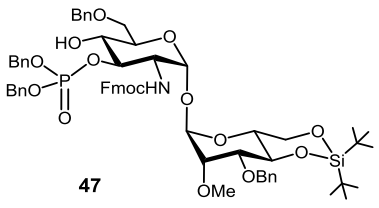
Synthesis of S1



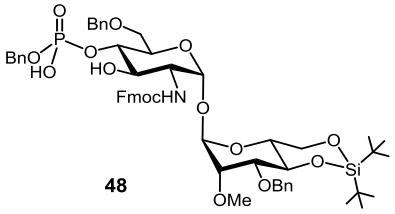
3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-β-D-mannopyranosyl-(1↔1)-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(9-fluorenylmethoxycarbonylamino)-α-D-glucopyranoside (S1).

A bi-phasic mixture of **39** (20 mg, 17 µmol), THF (420 µL) and aq. hydroxylamine (50%, 420 µL) was vigorously stirred at 0 °C for 3 days. The mixture was diluted with EtOAc (10 ml) and washed with aq. citric acid (0.25 M, 15 ml), aq. sat $NaHCO_3$ (15 ml) and brine (15 ml). The organic ayer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by MPLC (hexane - EtOAc, 3 : 1 → 1 : 1) to afford compound **S1** (11 mg, 9.5 µmol, 55%) as a syrup. R_f = 0.18 (hexane – EtOAc, 1 : 1); $[\alpha]_D^{20}$ = +55 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.74 (t, 2H, *J* = 7.5 Hz, arom.), 7.57 (t, 2H, *J* = 6.7 Hz, arom.), 7.40 -7.15 (m, 24H, arom.), 5.21 (d, 1H, $3J_{1,2}$ = 2.8 Hz, H-1), 5.05 (d, 1H, $3J_{NH,2}$ = 7.1 Hz, N*H*), 5.00-4.90 (m, 5H, CH_2Ph, OP(O)(OCH_2Ph)$_2$), 4.79 (AB, 1H, 2*J* = 12.5 Hz, CH_2Ph), 4.60 (s, 1H, H-1′), 4.48-4.44 (m, 3H, CH_2Ph, CH_2 Fmoc), 4.42-4.37 (m, 2H, H-4, CH_2 Fmoc), 4.25 (t, 1H, $3J_{4',5'}$ = $3J_{4',3'}$ = 9.4 Hz, H-4′), 4.21 (t, 1H, *J* = 6.5 Hz, C*H*, Fmoc), 4.10 (br. d, *J* = 9.5 Hz, H-5), 4.04 (dd, 1H, $3J_{6a',5'}$ = 5.0 Hz, $2J_{6a',6b'}$ = 10.1 Hz, H-6a′), 4.01-3.97 (m, 1H, H-3), 3.96 (t, 1H, $3J_{6b',6a'}$ = $2J_{6b',6a'}$ = 10.2 Hz, H-6b′), 3.84-3.80 (m, 1H, H-2), 3.65-3.53 (m, 5H, H-6a, H-6b, CH_3 Me), 3.52 (d, 1H, $3J_{2',3'}$ = 2.4 Hz, H-2′), 3.35 (dd, 1H, $3J_{3',2'}$ = 2.9 Hz, $3J_{3',4'}$ = 9.2 Hz, H-3′), 3.27 (td, 1H, $3J_{5',4'}$ = $3J_{5',6b'}$ = 9.8 Hz, $3J_{5',6a'}$ = 4.9 Hz, H-5′), 1.07 (s, 9H, 3×CH_3, DTBS), 0.99 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 156.22 (*C*O, Fmoc), 143.95, 143.62, 141.38, 141.30 (4×*C*q, Fmoc), 138.64, 137.82 (2×*C*q, *C*H_2Ph), 135.30 (*C*q, $3J_{C,P}$ = 7.2 Hz, OP(O)(OCH_2Ph)$_2$), 135.25 (*C*q, $3J_{C,P}$ = 8.0 Hz, OP(O)(OCH_2Ph)$_2$), 128.73, 128.65, 128.63, 128.59, 128.40, 128.31, 128.13, 127.87, 127.73, 127.64, 127.60, 127.55, 127.52, 127.03, 125.02, 124.93, 120.00 (28×*C*H, arom.), 101.34 (C-1′), 98.11 (C-1), 80.18 (C-3′), 79.80 (C-2′), 77.05 (C-4), 74.74 (C-4′), 73.45, 73.14 (2×*C*H_2Ph), 71.73 (C-5′), 70.97 (C-3), 70.30 (*C*H_2, $^3J_{C,P}$ = 5.1 Hz, OP(O)(O*C*H_2Ph)$_2$), 69.92 (*C*H_2, $^3J_{C,P}$ = 5.5 Hz, OP(O)(O*C*H_2Ph)$_2$), 69.74 (C-5, $3J_{C5,P}$ = 9.9 Hz), 67.70 (C-6), 66.90 (*C*H_2, Fmoc), 66.16 (C-6′), 62.20 (*C*H_3, Me), 55.12 (C-2), 47.16 (*C*H, Fmoc), 27.43, 27.07 (6×*C*H_3, DTBS), 22.58, 19.91 (2×*C*q, DTBS); ^{31}P-NMR (243 MHz, $CDCl_3$): δ 0.35; HRMS (ESI): *m/z* calcd for $C_{64}H_{76}NO_{15}PSi$+H^+: 1158.4795 [M+H]$^+$; found 1158.4796.

Synthesis of 47 and 48



47



48

3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-α-D-mannopyranosyl-(1↔1)-6-*O*-benzyl-3-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(9-fluorenylmethoxycarbonylamino)-α-D-glucopyranoside (47) and

3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-2-*O*-methyl-α-D-mannopyranosyl-(1↔1)-6-*O*-benzyl-4-*O*-(benzyloxyphosphoryl)-2-deoxy-2-(9-fluorenylmethoxycarbonylamino)-α-D-glucopyranoside (48).

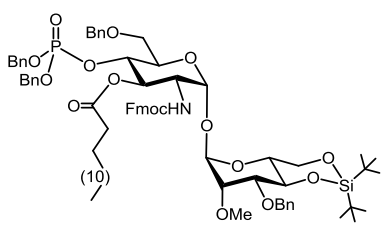
47: Phosphate-migration by-product from reaction of **36** with hydroxylamine, R_f = 0.66 (toluene – EtOAc, 1 : 1); $[\alpha]_D^{20}$ = +55 (*c* 0.9, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.73-7.71 (m, 2H, arom.), 7.59-7.54 (m, 2H, arom.), 7.44-7.13 (m, 24H, arom.), 5.43 (d, 1H, $^3J_{NH,2}$ = 8.5 Hz, N*H*), 5.24 (d, 1H, $^3J_{1,2}$ = 3.2 Hz, H-1), 5.11 (s, 1H, H-1′), 5.09-4.95 (m, 5H, CH_2Ph, OP(O)(OCH_2Ph)$_2$), 4.80 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.59 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph), 4.56 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.39 (ddd, 1H, $^3J_{3,2}$ = $^3J_{3,4}$ = $^3J_{H,P}$ = 8.6 Hz, H-3), 4.33 (t, 1H, $^3J_{4',3'}$ = $^3J_{4',5'}$ = 9.5 Hz, H-4′), 4.30-4.27 (m, 1H, CH_2, Fmoc), 4.19-4.16 (m, 1H, C*H*, Fmoc), 4.13-4.11 (m, 1H, CH_2, Fmoc), 4.07 (dd, 1H, $^3J_{6a',5'}$ = 4.8 Hz, $^2J_{6a',6b'}$ = 10.2 Hz, H-6a′), 3.97 (t, 1H, $^3J_{6b',5'}$ = $^2J_{6b',6a'}$ = 10.4 Hz, H-6b′), 3.80-3.69 (m, 6H, H-3′, H-4, H-5, H-5′, H-6a, H-6b), 3.43 (s, 1H, H-2′), 3.41 (s, 3H, CH_3, Me), 1.06 (s, 9H, 3×CH_3, DTBS), 0.95 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 156.14 (*C*O, Fmoc), 143.86, 143.57, 141.21, 141.18 (4×*C*q, Fmoc), 138.93, 137.76 (2×*C*q, CH_2Ph), 135.26 (*C*q, $^3J_{C,P}$ = 7.5 Hz, OP(O)(OCH_2Ph)$_2$), 135.13 (*C*q, $^3J_{C,P}$ = 7.5 Hz, OP(O)(OCH_2Ph)$_2$), 128.69, 128.64, 128.60, 128.56, 128.42, 128.37, 127.96, 127.80, 127.75, 127.72, 127.67, 127.61, 127.15, 125.40 , 125.17, 119.92, 119.88 (28×*C*H, arom.), 93.73 (C-1′), 93.53 (C-1), 79.82 (C-3), 79.62 (C-2′), 78.31 (C-3′), 74.82 (C-4′), 73.94, 73.74 (2×*C*H$_2$Ph), 71.17 (C-4 or C-5 or C-5′), 70.44 (C-4 or C-5 or C-5′), 70.09 (*C*H$_2$, $^2J_{C,P}$ = 5.8 Hz, OP(O)(O*C*H$_2$Ph)$_2$), 69.90 (*C*H$_2$, $^2J_{C,P}$ = 5.0 Hz, OP(O)(O*C*H$_2$Ph)$_2$), 69.42 (C-6), 69.13 (C-4 or C-5 or C-5′), 67.81 (*C*H$_2$, Fmoc), 66.43 (C-6′), 59.78 (*C*H$_3$, Me), 53.76 (C-2, $^3J_{C2,P}$ = 4.0 Hz), 46.93 (*C*H, Fmoc), 27.46, 27.08 (6×*C*H$_3$, DTBS), 22.60, 19.82 (2×*C*q, DTBS); ^{31}P-NMR (243 MHz, $CDCl_3$): δ 0.41; HRMS (ESI): *m/z* calcd for $C_{64}H_{76}NO_{15}PSi+H^+$: 1158.4795 [M+H$^+$]; found 1158.4794;

48: Debenzylation by-product from reaction of **36** with hydroxylamine, R_f = 0.20 (EtOAc – MeOH, 5:1); $[\alpha]_D^{20}$ = +36 (*c* 0.9, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$: MeOD = 3 : 1): δ 7.76-7.75 (m, 2H, arom.), 7.62-7.58 (m, 2H, arom.), 7.42-7.19 (m, 18H, arom.), 5.19 (br. s, 1H, H-1), 5.14 (s, 1H, H-1′), 4.99-4.89 (m, 2H, OP(O)(OCH_2Ph)OH), 4.97 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.80 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph), 4.53 (dd, 1H, ^3J = 7.7 Hz, ^2J = 10.2 Hz, CH_2, Fmoc), 4.42 (AB, 1H, ^2J = 11.6 Hz, CH_2Ph), 4.33 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.30 (t, 1H, $^3J_{4',5'}$ = $^3J_{4',3'}$ = 9.5 Hz, H-4′), 4.23 (t, 1H, *J* = 7.3 Hz, C*H*, Fmoc), 4.18-4.11 (m, 1H, CH_2, Fmoc), 4.10-4.03 (m, 1H, H-4), 4.07 (dd, 1H, $^3J_{6a',5'}$ = 4.7 Hz, $^2J_{6a'+,6b'}$ = 10.0 Hz, H-6b′), 3.95 (t, 1H, $^3J_{6b',5'}$ = $^2J_{6b',6a'}$ = 10.3 Hz, H-6b′), 3.88-3.82 (m, 1H, H-2), 3.81-3.69 (m, 5H, H-3, H-3′, H-5, H-5′, H-6a), 3.59-3.53 (m, 1H, H-6b), 3.46 (s, 1H, H-2′), 3.33 (s, 3H, CH_3, Me), 1.07 (s, 9H, 3×CH_3, DTBS), 0.96 (s, 9H, 3×CH_3, DTBS); ^{13}C-NMR (151 MHz, $CDCl_3$: MeOD = 3 : 1): δ 156.80 (*C*O, Fmoc), 143.53, 143.38, 140.96, 140.94 (4×*C*q, Fmoc), 138.40, 137.49 (2×*C*q, CH_2Ph), 137.12 (*C*q, OP(O)(OCH_2Ph)OH), 128.09, 128.07, 127.98, 127.64, 127.47, 127.40, 127.38, 127.31, 127.03, 126.81, 126.76, 124.85, 124.83, 119.68 (18×*C*H, arom.), 92.95, 92.89 (not assigned C-1, C-1′), 79.17 (C-2′), 77.62 (C-3′), 74.67 (C-4), 74.35 (C-4′), 73.21 (2×*C*H$_2$Ph), 70.90 (not assigned C-5 or C-5′ or C-3), 68.86 (C-6), 68.64 (not assigned C-5 or C-5′ or C-3), 67.63 (OP(O)(O*C*H$_2$Ph)OH), 67.15 (*C*H$_2$, Fmoc), 66.19 (C-6′), 58.95 (*C*H$_3$, Me), 54.40 (C-2), 46.78 (*C*H, Fmoc), 27.06, 26.68 (6×*C*H$_3$, DTBS), 22.27, 19.47 (2×*C*q, DTBS); ^{31}P-NMR (243 MHz, $CDCl_3$: MeOD = 3 : 1): δ -1.87; HRMS (ESI) *m/z* calcd for $C_{57}H_{70}NO_{15}PSi$-H: 1066.4180 [M-H]$^-$; found 1066.4170.

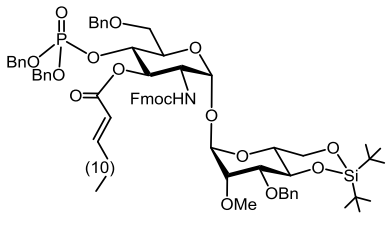
Synthesis of 49-51

(*R*)-3-(alkanoyloxy)alkanoic acids **49-51** were prepared according to the reported procedures.[18,19]

Synthesis of 53 and 54



53



54

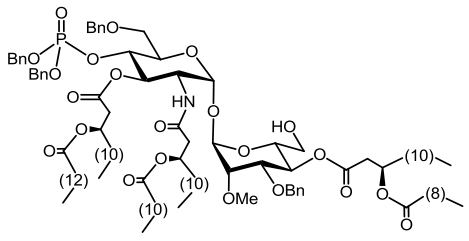
3-*O*-Benzyl-4,6-*O*-di-*tert*-butylsilylene-*O*-methyl-α-D-mannopyranosyl-(1↔1)-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(9-fluorenylmethoxycarbonylamino)-3-*O*-tetradecanoyl-α-D-glucopyranoside (53) and

3-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-*O*-methyl-α-D-mannopyranosyl-(1↔1)-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-(9-fluorenylmethoxycarbonylamino)-3-*O*-tetradec-2-enoyl-α-D-glucopyranoside (54).

53: a by-product formed upon acylation of **46** with **49** (to afford **52** as the major product): R_f = 0.28 (hexane – EtOAc, 2 : 1); $[\alpha]_D^{20}$ = +53 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.75 (d, 2H, *J* = 7.5 Hz, arom.), 7.57-7.22 (m, 26H, arom.), 5.26 (t, 1H, $^3J_{3,4} = {}^3J_{3,2}$ = 9.9 Hz, H-3), 5.20 (d, 1H, $^3J_{1,2}$ = 3.5 Hz, H-1), 5.12 (s, 1H, H-1′), 5.04 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.98-4.92 (m, 4H, OP(O)(OCH_2Ph)$_2$), 4.82 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.52 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph), 4.51 (ddd, 1H, $^3J_{4,5} = {}^3J_{4,3} = {}^3J_{4,P}$ = 9.4 Hz, H-4), 4.43-4.40 (m, 1H, CH_2, Fmoc), 4.43 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.32 (t, 1H, $^3J_{4',3'} = 3J_{4',5'}$ = 9.5 Hz, H-4′), 4.18 (t, 1H, *J* = 7.5 Hz, C*H*, Fmoc), 4.12-4.07 (m, 2H, H-2, CH_2, Fmoc), 4.05 (dd, 1H, $^3J_{6a',5'}$ = 4.7 Hz, $^2J_{6a',6b'}$ = 10.2 Hz, H-6a′), 3.96 (t, 1H, $^3J_{6b',5'} = {}^2J_{6b',6a'}$ =10.3 Hz, H-6b′), 3.80-3.70 (m, 4H, H-5, H-5′, H-3′, H-6a), 3.64 (dd, 1H, *J* = 5.9 Hz, *J* = 11.0 Hz, H-6b), 3.42 (br. s, 1H, H-2′), 3.39 (s, 3H, CH_3, Me), 2.15 (t, 2H, *J* = 7.8 Hz, α^{Myr}-CH_2), 1.45-0.95 (m, 11×CH_2, 6×CH_3, DTBS), 0.88 (t, 3H, *J* = 7.1 Hz, ω^{Myr}-CH_3); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 174.47 (*C*O), 155.71 (*C*O, Fmoc), 143.74, 143.54, 141.21 (4×*C*q, Fmoc), 138.81, 137.83 (2×*C*q, *C*H_2Ph), 135.50 (OP(O)(OCH$_2$Ph)$_2$, $3J_{C,P}$ = 6.9 Hz), 135.43 (OP(O)(OCH$_2$Ph)$_2$, $3J_{C,P}$ = 7.3 Hz), 128.71, 128.64, 128.38, 128.34, 127.98, 127.95, 127.92, 127.80, 127.76, 127.68, 127.64, 127.12, 125.28, 125.13, 119.97 (28×*C*H, arom.), 93.80 (C-1′), 93.23 (C-1), 79.64 (C-2′), 78.03 (C-3′), 74.81 (C-4′), 74.10 (*C*H_2Ph), 73.58 (C-4), 73.55 (*C*H_2Ph), 71.06 (C-3), 70.67 (C-5, $3J_{C5,P}$ = 5.6 Hz), 69.70, 69.67, 69.64 (OP(O)(O*C*H$_2$Ph)$_2$), 69.23 (C-5′), 68.36 (C-6), 67.94 (*C*H_2, Fmoc), 66.39 (C-6′), 59.70 (*C*H_3, Me), 53.76 (C-2), 46.93 (*C*H, Fmoc), 34.18 (α-CH_2), 31.92, 29.67, 29.62, 29.58, 29.40, 29.35, 29.20, 29.13 (9×*C*H$_2$), 27.44, 27.05 (6×*C*H$_3$, DTBS), 24.72, 22.68, 22.59, 19.81 (2×*C*H$_2$, 2×*C*q, DTBS), 14.11 (ω-*C*H$_3$); ^{31}P-NMR (243 MHz, $CDCl_3$): δ -2.04; HRMS (ESI): m/z calcd for $C_{78}H_{102}NO_{16}PSi+H^+$ $[M+H]^+$ 1368.6778, found 1368.6771.

54: a by-product formed upon acylation of **46** with **49** (to afford **52** as the major product): R_f = 0.25 (hexane – EtOAc, 2 : 1); $[\alpha]_D^{20}$ = +51 (*c* 0.3, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.74-7.23 (m, 28H, arom.), 6.95 (td, 1H, *J* = 6.9 Hz, *J* = 15.5 Hz, β-CH), 5.70 (d, 1H, *J* = 15.7 Hz, α-C*H*), 5.36 (dd, 1H, $^3J_{3,4}$ = 9.7 Hz, $^3J_{3,2}$ = 10.6 Hz, H-3), 5.23 (d, 1H, $^3J_{1,2}$ = 3.7 Hz, H-1), 5.13 (s, 1H, H-1′), 5.04 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 5.00 (d, 1H, $^3J_{NH,2}$ = 9.3 Hz, N*H*), 4.96-4.87 (m, 4H, OP(O)(OCH_2Ph)$_2$), 4.83 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.63 (q, 1H, $^3J_{4,5} = {}^3J_{4,3} = {}^3J_{4,P}$ = 9.3 Hz, H-4), 4.54-4.51 (m, 1H, CH_2, Fmoc), 4.52 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph), 4.43 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph), 4.32 (t, 1H, $^3J_{4',5'} = {}^3J_{4',3'}$ = 9.6 Hz, H-4′), 4.17-4.11 (m, 2H, H-2, CH_2, Fmoc), 4.04 (dd, 1H, $^3J_{6a',5'}$ = 4.7 Hz, $^2J_{6a',6b'}$ = 9.9 Hz, H-6a′), 3.95 (t, 1H, $^3J_{6b',6a'} = {}^2J_{6b',5'}$ = 10.0 Hz, 1H), 3.92 (dd, 1H, *J* = 7.7 Hz, *J* = 10.3 Hz, CH_2, Fmoc), 3.85-3.81 (m, 1H, H-5), 3.79-3.78 (m, 1H, H-6a), 3.75-3.70 (H-3′, H-5′), 3.67 (dd, 1H, *J* = 5.8 Hz, *J* = 10.9 Hz, H-6b), 3.43 (br. s, 1H, H-2′), 3.40 (s, 3H, CH_3, Me), 1.87-1.82 (m, 2H, γ-CH_2), 1.35-0.94 (m, 36H, 9×CH$_2$, 6×CH_3, DTBS), 0.88 (t, 3H, *J* = 7.1 Hz, ω-CH$_3$); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 166.98 (*C*O), 155.78 (*C*O, Fmoc), 152.31 (β-*C*H), 143.87, 143.57, 141.22, 141.14 (4×*C*q, Fmoc), 138.82, 137.87 (2×*C*q, CH_2Ph), 135.57, 135.51 (2×*C*q, OP(O)(OCH$_2$Ph)$_2$), 128.60, 128.57, 128.55, 128.39, 128.34, 127.97, 127.87, 127.77, 127.70, 127.66, 127.15, 127.06, 125.34, 125.24 (27×*C*H, arom.), 119.89, 119.77 (α-*C*H, *C*H, arom.), 93.67 (C-1′), 93.10 (C-1), 79.62 (C-2′), 78.04 (C-3′), 74.84 (C-4′), 74.12, 73.55 (2×*C*H$_2$Ph), 73.51 (C-4, $2J_{C4,P}$ = 5.3 Hz), 71.37 (C-3), 70.77 (C-5, $3J_{C5,P}$ = 4.7 Hz), 69.53, 69.49, 69.15 (OP(O)(O*C*H$_2$Ph)$_2$), 68.38 (C-6), 67.84 (*C*H$_2$, Fmoc), 66.39 (C-6′), 59.72 (*C*H$_3$, Me), 53.97 (C-2), 47.01 (*C*H, Fmoc), 32.31 (γ-*C*H$_2$), 31.92, 29.70, 29.63, 29.58, 29.43, 29.34, 29.27, 29.20, 27.64 (9×*C*H$_2$), 27.44, 27.05 (6×*C*H$_3$, DTBS), 22.69, 22.59, 19.81 (*C*H$_2$, 2×*C*q, DTBS), 14.12 (ω-*C*H$_3$); ^{31}P-NMR (243 MHz, $CDCl_3$): δ -2.07; HRMS (ESI) m/z calcd for $C_{78}H_{100}NO_{16}PSi+H^+$: 1366.6622 $[M+H^+]$; found 1366.6616.

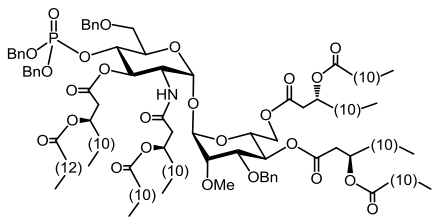
Synthesis of 58



3-*O*-Benzyl-4-*O*-[(*R*)-3-(decanoyloxy)tetradecanoyl]-2-*O*-methyl-α-D-mannopyranosyl-(1↔1)-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-[(*R*)-3-dodecanoyloxy)tetradecanoylamino]-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecanyol]-α-D-glucopyranoside (58).

To a stirred solution of **56** (30 mg, 18 µmol) and DMAP (0.2 mg, 1.6 µmol) in dry CH_2Cl_2 (400 µl) a solution of **51** (8 mg, 20 µmol) in CH_2Cl_2 (83 µl of a stock solution prepared from 29 mg of **51** in 300 µl CH_2Cl_2) was added under atmosphere of Ar. The mixture was cooled to 0 °C and DIC (6 mg, 48 µmol) from a 50 mg·ml^{-1} stock solution in toluene was added dropwise over a period of 2 h. Then an additional amount of **51** (2 mg, 5.0 µmol) and DIC (0.4 mg, 0.3 µmol) from the indicated stock solutions was added dropwise over a period of 1 h. The mixture was diluted with EtOAc (20 ml) and washed with aq. HCl (2 M, 20 ml), sat. aq. $NaHCO_3$ (20 ml) and brine (20 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by HPLC (two successive columns: toluene – EtOAc, 3 : 1 → 1 : 1 and hexane – EtOAc, 2 : 1 → 1 : 1, column B) to afford **58** (24 mg, 12 µmol, 65%) as a syrup. Fractions containing by-product **60** were purified HPLC (hexane – EtOAc, 4 : 1 → 3 : 1, column B) to afford 4,6-di-*O*-acylated compound **60** (5.7 mg, 2.4 µmol, 13%). Compound **58:** R_f = 0.40 (toluene – EtOAc, 1 : 1); $[\alpha]_D^{20}$ = +36 (1.0, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.38-7.22 (m, 20H, CH_2Ph), 6.34 (d, 1H, $^3J_{NH,2}$ = 8.0 Hz, N*H*), 5.24-5.15 (m, 5H, H-1, H-3, H-4′, 2×β^{Myr}-C*H*), 5.12 (d, 1H, $^3J_{1',2'}$ = 2.0 Hz, H-1′), 5.07-5.03 (m, 1H, β^{Myr}-C*H*), 4.97 (d, 2H, *J* = 8.1 Hz, OP(O)(OCH_2Ph)$_2$), 4.95 (d, 2H, *J* = 8.2 Hz, OP(O)(OCH_2Ph)$_2$), 4.69 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.64 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph), 4.48 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph), 4.43 (ddd, 1H, $^3J_{4,3}$ = $^3J_{4,5}$ = $^3J_{H,P}$ = 9.3 Hz, H-4), 4.40 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph), 4.24 (ddd, 1H, $^3J_{2,1}$ = 3.5 Hz, $^3J_{2,NH}$ = 7.9, $^3J_{2,3}$ = 11.2 Hz, H-2), 3.93 (dd, 1H, $^3J_{3',2'}$ = 3.1 Hz, $^3J_{3',4'}$ = 9.4 Hz, H-3′), 3.75-3.72 (m, 2H, H-5, H-6a), 3.61-3.54 (m, 4H, H-5′, H-6b, H-6a′, H-6b′), 3.30-3.29 (m, 1H, H-2′), 3.29 (s, 3H, CH_3, Me), 2.60 (dd, 1H, *J* = 7.6 Hz, *J* = 15.5 Hz, α^{Myr}-CH_2), 2.54-2.47 (m, 3H, α^{Myr}-CH_2), 2.44 (dd, *J* = 7.1 Hz, *J* = 15.1 Hz, α^{Myr}-CH_2), 2.37 (dd, 1H, *J* = 5.5 Hz, *J* = 15.1 Hz, α^{Myr}-CH_2), 2.32-2.26 (m, 2H, α-CH_2), 2.24-2.19 (m, 4H, 2×α-CH_2), 1.62-1.46 (m, 12H, 3×γ^{Myr}-CH_2, β^{Myr}-CH_2, β^{Lau}-CH_2, β^{Cap}-CH_2), 1.32 -1.20 (m, 102H, 51×CH_2), 0.89-0.86 (m, 18H, 4xω^{Myr}-CH_3, ω^{Lau}-CH_3, β^{Cap}-CH_3); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 173.63, 173.38, 173.08, 171.42, 169.91, 169.87 (6×*C*O), 138.00, 137.87 (2×*C*q, CH_2Ph), 135.54, 135.50 (2×*C*q, OP(O)(OCH_2Ph)$_2$), 128.71, 128.64, 128.52, 128.31, 128.11, 128.10, 128.03, 127.92, 127.64, 127.59 (20×C*H*, CH_2Ph), 94.02 (C-1′), 93.50 (C-1), 77.80 (C-2′), 75.89 (C-3′), 73.66 (C-4, $^2J_{C4,P}$ = 5.8 Hz), 73.48 (*C*H$_2$Ph), 72.73 (C-5′), 72.51 (*C*H$_2$Ph), 71.08 (C-3), 70.83 (β^{Myr}-*C*H), 70.67 (C-5, $^3J_{C5,P}$ = 5.3 Hz), 69.94 (β^{Myr}-*C*H), 69.87 (β^{Myr}-*C*H), 69.76, 69.72 (OP(O)(O*C*H$_2$Ph)$_2$), 68.35 (C-6), 68.33 (C-4′), 61.69 (C-6′), 59.09 (*C*H$_3$, Me), 51.80 (C-2), 41.37, 39.15, 39.00 (3×α^{Myr}-*C*H$_2$), 34.59, 34.52, 34.43, 34.26, 34.03 (3×γ^{Myr}-*C*H$_2$, α^{Myr}-C*H*$_2$, α^{Lau}-C*H*$_2$, α^{Cap}-C*H*$_2$), 31.92, 31.86, 29.71, 29.68, 29.66, 29.61, 29.58, 29.56, 29.54, 29.50, 29.47, 29.41, 29.38, 29.36, 29.30, 29.28, 29.19, 29.18, 25.35, 25.16, 25.09, 24.99, 22.68, 22.66 (54×*C*H$_2$), 14.09 (4×ω^{Myr}-*C*H$_3$, ω^{Lau}-C*H*$_3$, ω^{Cap}-C*H*$_3$); ^{31}P-NMR (243 MHz, $CDCl_3$): δ -1.70; HRMS (ESI): m/z calcd for $C_{119}H_{194}NO_{22}P+Na^+$: 2043.3722 [M+Na$^+$]; found 2043.3762.

Synthesis of 59

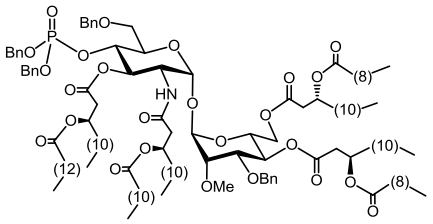


3-*O*-Benzyl-4,6-di-*O*-[(*R*)-3-(dodecanoyloxy)tetradecanoyl]-2-*O*-methyl-α-D-mannopyranosyl-(1↔1)-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-[(*R*)-3-(dodecanoyloxy)-tetradecanoylamino]-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecanyol]-α-D-glucopyranoside (59)

by-product from reaction of **56** with fatty acid **50** (to furnish **57** as major product), R_f = 0.44 (toluene – EtOAc, 4 : 1); $[\alpha]_D^{20}$ = +32 (*c* 0.7, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.38-7.22 (m, 20H, CH_2Ph), 6.38 (d, 1H, $^3J_{NH,2}$ = 7.7 Hz, N*H*), 5.27 (t, 1H, $^3J_{4',5'}$ = $^3J_{4',3'}$ = 9.8 Hz, H-4′), 5.23-5.14 (m, 5H, H-1, H-3, 3×β^{Myr}-C*H*), 5.12 (d, 1H, $^3J_{1',2'}$ = 1.6 Hz, H-1′), 5.08-5.04 (m, 1H, β^{Myr}-C*H*), 4.98-4.94 (m, 4H, OP(O)(OCH_2Ph)$_2$), 4.68 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.64 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.47 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.45-4.41 (m, 1H, H-4), 4.40 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph), 4.25 (ddd, 1H, $^3J_{2,1}$ = 3.5 Hz, $^3J_{2,3}$ = 11.2 Hz, $^3J_{2,NH}$ = 7.9 Hz, H-2), 4.16 (dd, 1H, *J* = 5.5 Hz, *J* = 12.2 Hz, H-6a′), 3.99-3.97 (m, 2H, H-3′, H-6b′), 3.79-3.70 (m, 3H, H-5, H-5′, H-6a), 3.58 (dd, 1H, *J* = 5.6 Hz, *J* = 10.7 Hz, H-6b), 3.28 (s, 3H, CH_3, Me), 3.27 (br. s, 1H, H-2′), 2.61-2.18 (m, 16H, 5×α^{Myr}-CH_2, 3×α^{Lau}-

CH_2), 1.63-1.49 (m, 16H, β^{Myr}-CH_2, 3×β^{Lau}-CH_2, 4×γ^{Myr}-CH_2), 1.31-1.22 (m, 140H, 70×CH_2), 0.89-0.87 (m, 24H, 5×ω^{Myr}-CH_3, 3×ω^{Lau}-CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.78, 173.32, 173.00, 172.91, 171.41, 170.27, 169.68, 168.99 (8×*C*O), 138.02, 137.88 (2×*C*q, CH_2Ph), 135.56, 135.51 (2×*C*q, OP(O)(OCH_2Ph)$_2$), 128.70, 128.63, 128.53, 128.31, 128.11, 128.08, 128.02, 127.89, 127.63, 127.57 (20×*C*H, CH_2Ph), 92.86 (C-1′), 92.46 (C-1), 77.50 (C-2′), 76.14 (C-3′), 73.68 (C-4), 73.47, 72.52 (2×CH_2, CH_2Ph), 71.11 (C-3), 70.61 (C-5, $^3J_{C5,P}$ = 5.6 Hz), 70.56 (β^{Myr}-*C*H), 70.15, 70.09, 69.87, 69.80 (C-5′, 3×β^{Myr}-*C*H), 69.74 (OP(O)(O*C*H$_2$Ph)$_2$, $^2J_{C,P}$ = 5.2 Hz,), 69.72 (OP(O)(O*C*H$_2$Ph)$_2$, $^2J_{C,P}$ = 5.4 Hz), 68.35 (C-6), 67.47 (C-4′), 62.45 (C-6′), 59.11 (*C*H$_3$, Me), 51.65 (C-2), 41.57, 38.97, 38.87, 38.77 (4×α^{Myr}-*C*H$_2$), 34.79, 34.53, 34.47, 34.43, 34.42, 34.26, 33.99, 33.94 (α^{Myr}-*C*H$_2$, 3×α^{Lau}-*C*H$_2$, 4xγ^{Myr}-*C*H$_2$), 31.94, 31.93, 29.78, 29.76, 29.74, 29.67, 29.66, 29.58, 29.57, 29.54, 29.47, 29.42, 29.40, 29.38, 29.37, 29.32, 29.22, 29.20, 25.39, 25.18, 25.15, 25.11, 25.10, 25.02, 22.69 (74×*C*H$_2$), 14.10 (5×ω^{Myr}-*C*H$_3$, 3×ω^{Lau}-*C*H$_3$); ^{31}P NMR (243 MHz, $CDCl_3$): δ -1.71; HRMS (ESI): m/z calcd for $C_{147}H_{246}NO_{25}P+Na^+$: 2479.7639 [M+$Na^+$]; found 2479.7628;

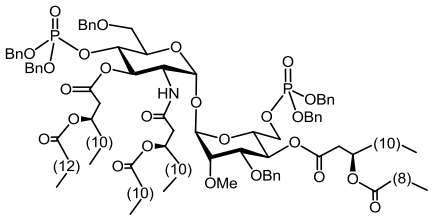
Synthesis of 60



3-*O*-Benzyl-4,6-di-*O*-[(*R*)-3-(decanoyloxy)tetradecanoyl]-2-*O*-methyl-α-D-mannopyranosyl-(1↔1)-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phosphoryl]-2-deoxy-2-[(*R*)-3-(dodecanoyloxy)-tetradecanoylamino]-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecanyol]-α-D-glucopyranoside (60)

by-product from reaction of **56** with fatty acid **51** (to furnish **58** as major product), R_f = 0.60 (toluene – EtOAc, 3 : 1); $[\alpha]_D^{20}$ = +36 (*c* 0.5, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.39-7.21 (m, 20H, CH_2Ph), 6.44 (d, 1H, $^3J_{NH,2}$ = 8.2 Hz, N*H*), 5.27 (t, 1H, *J* = 9.8 Hz, H-4′), 5.23-5.14 (m, 5H, H-1, H-3, 3×β^{Myr}-C*H*), 5.12 (d, 1H, $^3J_{1',2'}$ = 1.9 Hz, H-1′), 5.08-5.04 (m, 1H, β-^{Myr}C*H*), 4.97 (d, 2H, *J* = 8.2 Hz, OP(O)(OCH_2Ph)$_2$), 4.94 (d, 2H, *J* = 8.2 Hz, OP(O)(OCH_2Ph)$_2$), 4.68 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph), 4.64 (AB, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.47 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.45-4.41 (m, 1H, H-4), 4.40 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.27-4.23 (m, 1H, H-2), 4.16 (dd, 1H, *J* = 5.5 Hz, *J* = 12.2 Hz, H-6a′), 4.00-3.96 (m, 2H, H-3′, H-6b′), 3.79-3.76 (m, 1H, H-5′), 3.75-3.70 (m, 2H, H-5, H-6a), 3.58 (dd, 1H, *J* = 5.6 Hz, *J* = 10.7 Hz, H-6b), 3.28 (s, 3H, CH_3, Me), 3.26-3.25 (m, 1H, H-2), 2.61-2.36 (m, 8H, 4×α^{Myr}-CH_2), 2.36-2.17 (m, 8H, α^{Myr}-CH_2, α^{Lau}-CH_2, 2×α^{Cap}-CH_2), 1.63-1.46 (m, 16H, 4×γ^{Myr}-CH_2, β^{Myr}-CH_2, β^{Lau}-CH_2, 2×β^{Cap}-CH_2), 1.33-1.20 (m, 132H, 66×CH_2), 0.89-0.86 (m, 24H, 5xω^{Myr}-*C*H$_3$, ω^{Lau}-CH_3, 2×ω^{Cap}-CH_3); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 173.77, 173.33, 173.01, 172.94, 171.41, 170.28, 169.70, 168.99 (8×*C*O), 138.02, 137.88 (2×*C*q, CH_2Ph), 135.55, 135.51 (2×*C*q, OP(O)(OCH_2Ph)$_2$), 128.70, 128.63, 128.53, 128.31, 128.12, 128.09, 128.02, 127.90, 127.63, 127.57 (20×*C*H, CH_2Ph), 92.87 (C-1′), 92.49 (C-1), 77.50 (C-2′), 76.11 (C-3′), 73.68 (c-4, $^2J_{C4,P}$ = 5.5 Hz), 73.47, 72.51 (2×*C*H$_2$Ph), 71.10 (C-3, $^3J_{C3,P}$ = 2.0 Hz), 70.64, 70.60, 70.58 (C-5, β^{Myr}-*C*H), 70.15, 70.08, 69.89, 69.81 (C-5′, 3×β^{Myr}-*C*H), 69.76, 69.74, 69.73 (OP(O)(O*C*H$_2$Ph)$_2$), 68.35 (C-6), 67.47 (C-4′), 62.44 (C-6′), 59.11 (*C*H$_3$, Me), 51.63 (C-2), 41.55, 38.99, 38.88, 38.77 (4×α^{Myr}-*C*H$_2$), 34.78, 34.54, 34.47, 34.43, 34.42, 34.26, 34.00, 33.94 (4×γ^{Myr}-*C*H$_2$, α^{Myr}-*C*H$_2$, α^{Lau}-*C*H$_2$, 2× α^{Cap}-*C*H$_2$), 31.93, 31.88, 29.78, 29.76, 29.74, 29.71, 29.69, 29.67, 29.66, 29.64, 29.57, 29.54, 29.53, 29.51, 29.47, 29.42, 29.40, 29.37, 29.35, 29.32, 29.31, 29.20, 29.19, 25.39, 25.17, 25.15, 25.11, 25.09, 25.01, 22.69 (70×*C*H$_2$), 14.09 (5×ω^{Myr}-*C*H$_3$, ω^{Lau}-C*H*$_3$, 2×ω^{Cap}-C*H*$_3$); ^{31}P-NMR (243 MHz, $CDCl_3$): δ -1.71; HRMS (ESI): m/z calcd for $C_{143}H_{238}NO_{25}P+Na^+$: 2423.7013[M+$Na^+$]; found 2423.6967;

Synthesis of 62



3-*O*-Benzyl-6-*O*-[bis(benzyloxy)phosphoryl]-4-*O*-[(*R*)-3-(decanoyloxy)tetradecanoyl]-2-*O*-methyl-α-mannopyranosyl-(1↔1)-6-*O*-benzyl-4-*O*-[bis(benzyloxy)phophoryl]-2-deoxy-2-[(*R*)-3-(dodecanoyloxy)tetradecanoylamino]-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecanoyl]-α-D-glucopyranoside (62).

To a stirred solution of **58** (18 mg, 8.9 μmol) and dibenzyl *N,N*-diisopropylphosphoramidite (10 μL, 27 μmol, 90%) in dry CH_2Cl_2 (400 μL) a solution of 1*H*-tetrazole (100 μL, 45 μmol, 0.45 M in CH_3CN) was added under atmosphere of Ar. The mixture was stirred for 1 h, cooled to -78 ° and a solution of *m*CPBA (10 mg, 41 μmol, 70%) in CH_2Cl_2 (150 μL of a stock solution prepared from 20 mg in 300 μL CH_2Cl_2) was added. After stirring for 1 h, the reaction was quenched by addition of Et_3N (15 μL), the mixture was warmed to r. t., diluted with EtOAc (20 ml) and washed with aq. citric acid (0.25 M, 20 ml), sat. aq. $NaHCO_3$ (20 ml) and brine (20 ml). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by HPLC (two successive columns: toluene – EtOAc, 10 : 1 → 5 : 1 and hexane : EtOAc, 2 : 1 → 1 : 1, column B) to afford **62** (18 mg, 7.9 μmol, 88%) as a syrup. R_f = 0.53 (toluene – EtOAc, 1 : 1), $[\alpha]_D^{20}$ = +32 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.38-7.20 (m, 30H, CH_2Ph), 6.46 (d, 1H, $^3J_{NH,2}$ = 8.5 Hz, N*H*), 5.30 (t, 1H, $^3J_{4',3'} = {}^3J_{4',5'}$ = 9.7 Hz, H-4′), 5.23-5.16 (m, 3H, H-3, 2×β^{Myr}-C*H*), 5.15 (d, 1H, $^3J_{1',2'}$ = 3.7 Hz, H-1), 5.10-5.06 (m, 1H, β^{Myr}-C*H*), 5.10 (d, 1H, $^3J_{1',2'}$ = 1.9 Hz, H-1′), 5.03-4.93 (m, 8H, OP(O)(OCH_2Ph)$_2$), 4.68 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph), 4.63 (AB, 1H, ^2J = 12.1 Hz, CH_2Ph), 4.45 (AB, 1H, ^2J = 11.8 Hz, CH_2Ph), 4.43-4.39 (m, 1H, H-4), 4.38 (AB, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.28 (ddd, 1H, $^3J_{2,1}$ = 3.5 Hz, $^3J_{2,NH}$ = 8.3 Hz, $^3J_{2,3}$ = 11.1 Hz, H-2), 4.09-4.03 (m, 2H, H-6a′, H-6b′), 4.01 (dd, 1H, $^3J_{3',2'}$ = 3.0 Hz, $^3J_{3',4'}$ = 9.5 Hz, H-3′), 3.89-3.86 (m, 1H, H-5′), 3.76-3.69 (m, 2H, H-5, H-6a), 3.56 (dd, 1H, *J* = 5.9 Hz, *J* = 10.7 Hz, H-6b), 3.28 (t, 1H, *J* = 2.5 Hz, H-2′), 3.23 (s, 3H, CH_3, Me), 2.58-2.44 (m, 5H, α^{Myr}-CH_2), 2.40 (dd, 1H, *J* = 4.7 Hz, *J* = 15.6 Hz, α^{Myr}-CH_2), 2.34-2.25 (m, 2H, α-CH_2), 2.20-2.16 (m, 4H, 2×α-CH_2), 1.61-1.49 (m, 12H, 3×γ^{Myr}-CH_2, β^{Myr}-CH_2, β^{Lau}-CH_2, β^{Cap}-CH_2), 1.32-1.20 (m, 102H, 51×CH_2), 0.89-0.86 (m, 18H, 4×ω^{Myr}-CH_3, ω^{Lau}-CH_3, ω^{Cap}-CH_3); ^{13}C-NMR (151 MHz, $CDCl_3$): δ 173.89, 173.23, 172.92, 171.19, 169.75, 169.07 (6×*C*O), 137.98, 137.85 (2×*C*q, CH_2Ph), 135.98, 135.94, 135.56, 135.51 (4×*C*q, OP(O)(OCH_2Ph)$_2$), 128.68, 128.62, 128.53, 128.45, 128.43, 128.29, 128.28, 128.27, 128.13, 128.01, 127.94, 127.91, 127.86, 127.63, 127.59 (30×*C*H, CH_2Ph), 93.35 (C-1′), 93.16 (C-1), 77.54 (C-2′), 75.95 (C-3′), 73.67 (C-4, $^2J_{C,P}$ = 5.9 Hz), 73.48, 72.45 (2×*C*H_2Ph), 71.24 (C-3), 70.93 (C-5′, $^3J_{C,P}$ = 7.3 Hz), 70.63 (C-5, ^3J = 5.4 Hz), 70.58, 69.79, 69.74 (3×β^{Myr}-*C*H), 69.76, 69.72, 69.68 (OP(O)(O*C*H_2Ph)$_2$), 69.28, 69.26 (OP(O)(O*C*H_2Ph)$_2$), 68.46 (C-6), 67.50 (C-4′), 66.09 (C-6′, ^2J = 5.0 Hz), 58.99 (*C*H_3, Me), 51.43 (C-2), 41.53, 38.92, 38.75 (3×α^{Myr}-*C*H_2), 34.75, 34.52, 34.42, 43.39, 34.19, 33.98 (3×γ^{Myr}-*C*H_2, α^{Myr}-CH_2, α^{Lau}-CH_2, α^{Cap}-CH_2), 31.94, 31.92, 31.87, 29.76, 29.74, 29.72, 29.70, 29.69, 29.67, 29.64, 29.62, 29.60, 29.55, 29.54, 29.50, 29.47, 29.46, 29.40, 29.38, 29.36, 29.34, 29.32, 29.30, 29.28, 29.19, 29.17, 25.35, 25.17, 25.14, 25.11, 25.00, 22.68 (54×*C*H_2), 14.09 (4×ω^{Myr}-*C*H_3, ω^{Lau}-CH_3, ω^{Cap}-CH_3); ^{31}P-NMR (243 MHz, $CDCl_3$): δ -1.61, -1.69; HRMS (ESI): m/z calcd for $C_{133}H_{207}NO_{25}P+Na^+$: 2303.4325 [M+$Na^+$]; found 2303.4282.

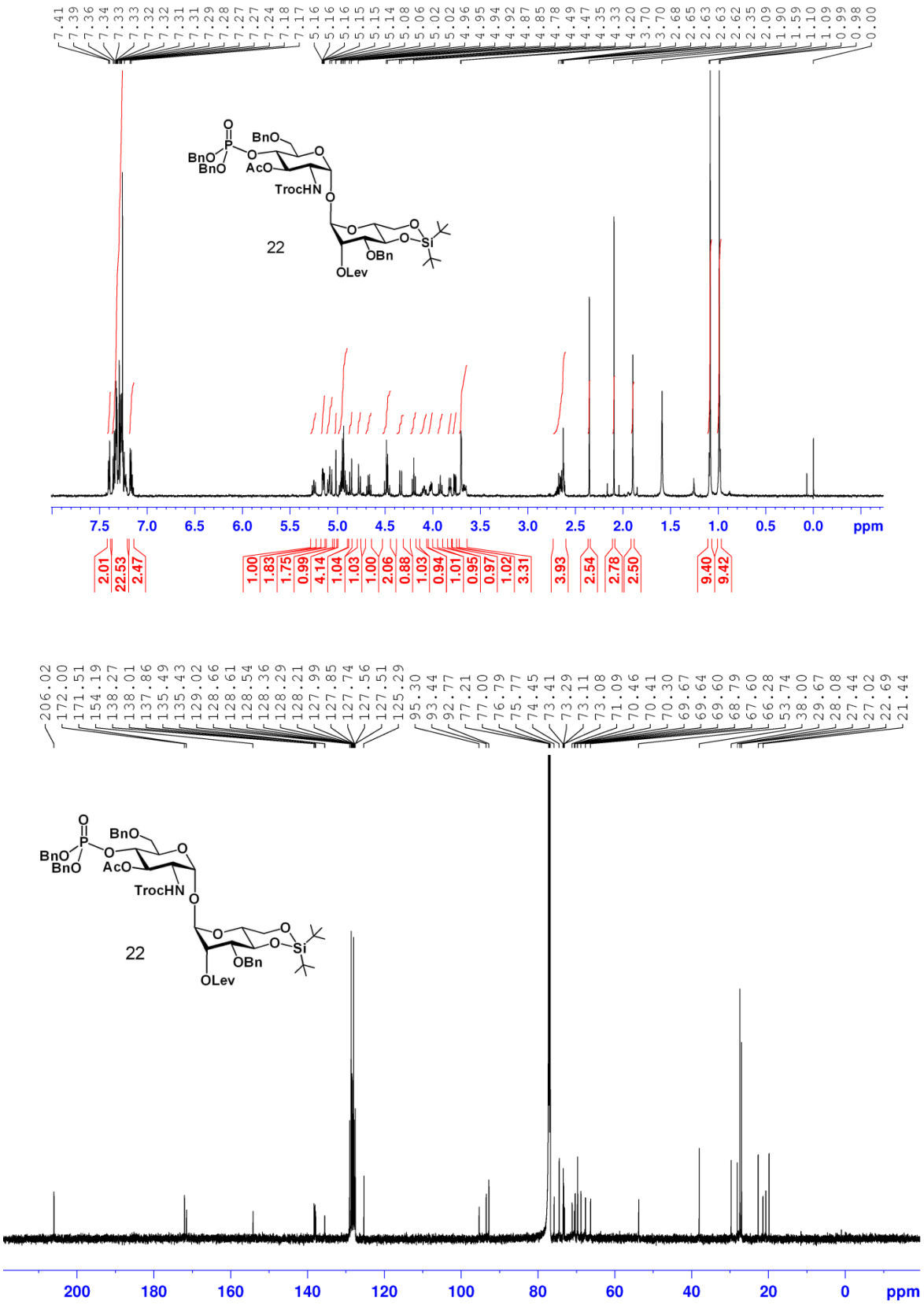
References

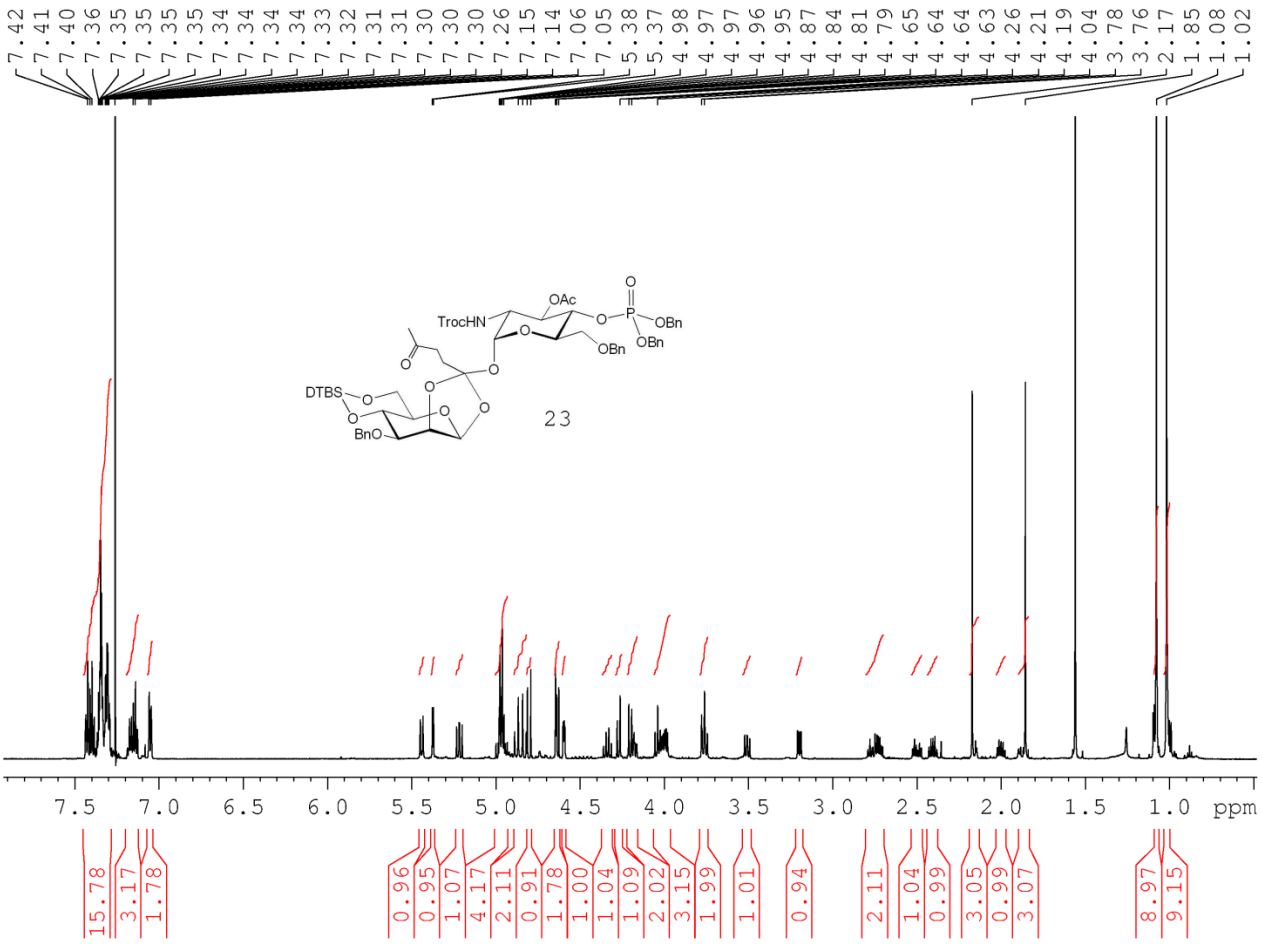
(1) Schmidt, R. R.; Toepfer, A. Glycosylation with highly reactive glycosyl donors: efficiency of the inverse procedure. *Tetrahedron Lett.* **1991,** *28*, 3353-3356.

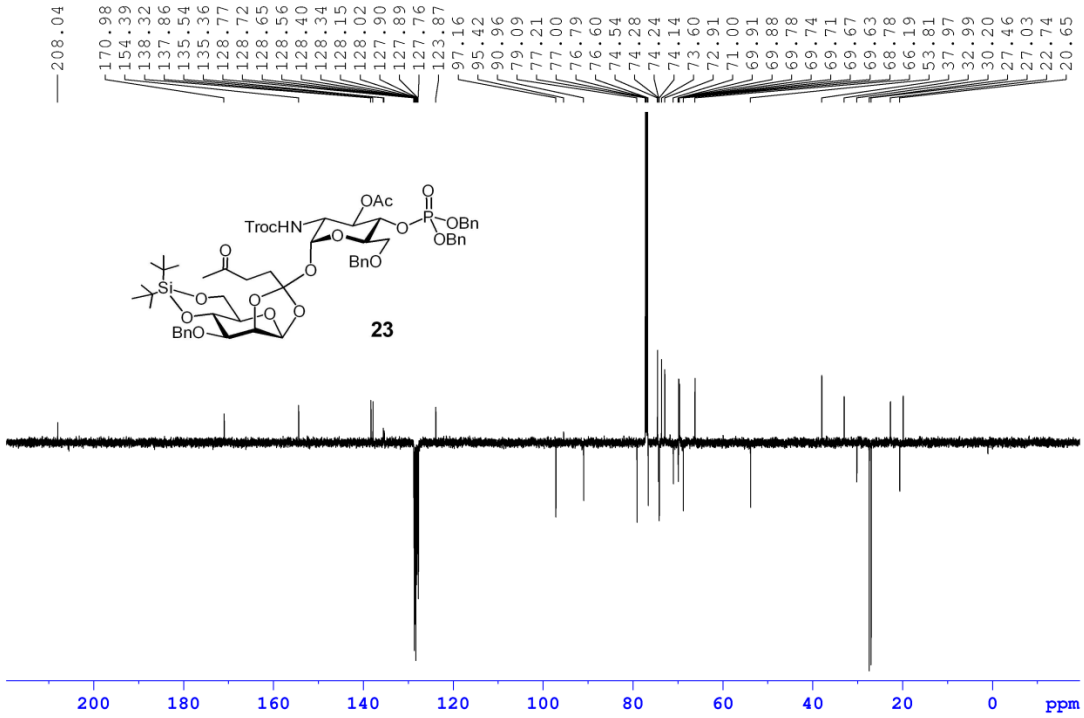
(2) Kong, F. Recent studies on reaction pathways and applications of sugar orthoesters in synthesis of oligosaccharides. *Carbohydr. Res.* **2007,** *3-4*, 345-373.

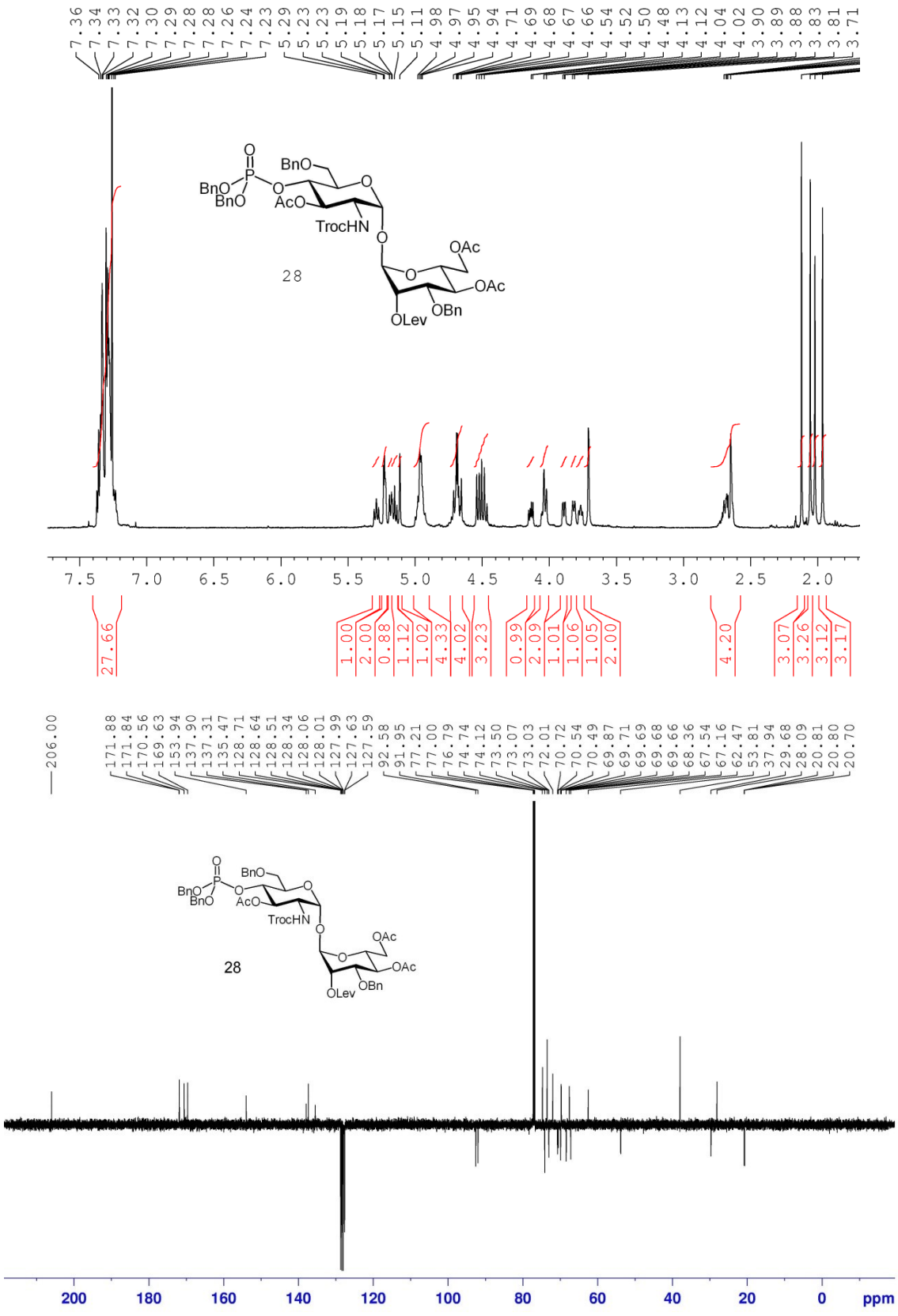
(3) John, F.; Hendrickson, T. L. Synthesis of truncated analogues for studying the process of glycosyl phosphatidylinositol modification. *Org. Lett.* **2010,** *9*, 2080-2083.
(4) Ravindranathan Kartha, K. P.; Mukhopadhyay, B.; Field, R. A. Practical de-*O*-acylation reactions promoted by molecular sieves. *Carbohydr. Res.* **2004,** *3*, 729-732.
(5) Mizuno, M.; Kobayashi, K.; Nakajima, H.; Koya, M.; Inazu, T. Unexpected reaction using methanol dried over molecular sieves. *Synth. Commun.* **2002,** *11*, 1665-1670.
(6) Gonzalez, A. G.; Brouard, I.; Leon, F.; Padron, J. I.; Bermejo, J. A facile chemoselective deacetylation in the presence of benzoyl and *p*-bromobenzoyl groups using *p*-toluenesulfonic acid. *Tetrahedron Lett.* **2001,** *18*, 3187-3188.
(7) Jencks, W. P.; Carriuolo, J. Reactivity of nucleophilic reagents toward esters. *J. Am. Chem. Soc.* **1960,** *7*, 1778-1786.
(8) Edwards, J. O.; Pearson, R. G. The factors determining nucleophilic reactivities. *J. Am. Chem. Soc.* **1962,** *1*, 16-24.
(9) Simanenko, S.; Popov, A.; Prokop'eva, T.; Karpichev, E.; Savelova, V.; Suprun, I.; Bunton, C. Inorganic anionic oxygen-containing α-nucleophiles-effective acyl group acceptors: hydroxylamine ranks first among the α-nucleophile series. *Russ. J. Org. Chem.* **2002,** *9*, 1286-1298.
(10) Jencks, W. P.; Gilchrist, M. The reaction of hydroxylamine with amides. Kinetic evidence for the existence of a tetrahedral addition intermediate. *J. Am. Chem. Soc.* **1964,** *24*, 5616-5620.
(11) Mazera, D. J.; Gesser, J. C.; Pliego, J. R. On the mechanism of the reaction between aryl acetates and hydroxylamine. *ARKIVOC* **2007,** *15*, 199-214.
(12) Kirby, A. J.; Souza, B. S.; Medeiros, M.; Priebe, J. P.; Manfredi, A. M.; Nome, F. Hydroxylamine as an oxygen nucleophile. Chemical evidence from its reaction with a phosphate triester. *Chem. Commun.* **2008,** *37*, 4428-4429.
(13) Medeiros, M.; Wanderlind, E. H.; Mora, J. R.; Moreira, R.; Kirby, A. J.; Nome, F. Major mechanistic differences between the reactions of hydroxylamine with phosphate di- and tri-esters. *Org. Biomol. Chem.* **2013,** *37*, 6272-6284.
(14) Kunz, H.; Zimmer, J. Glycoside synthesis *via* electrophile-induced activation of *N*-allyl carbamates. *Tetrahedron Lett.* **1993,** *18*, 2907-2910.
(15) Wang, C.; Sanders, B.; Baker, D. C. Synthesis of a glycodendrimer incorporating multiple mannosides on a glucoside core. *Can. J. Chem.* **2011,** *8*, 959-963.
(16) Saibal, K. D.; Roy, N. An improved method for the preparation of some ethyl 1-thioglycosides. *Carbohydr. Res.* **1996,** *1-4*, 275-277.
(17) Artner, D.; Oblak, A.; Ittig, S.; Garate, J. A.; Horvat, S.; Arrieumerlou, C.; Hofinger, A.; Oostenbrink, C.; Jerala, R.; Kosma, P.; Zamyatina, A. Conformationally constrained Lipid A mimetics for exploration of structural basis of TLR4/MD-2 activation by lipopolysaccharide. *ACS Chem. Biol.* **2013,** *11*, 2423-2432.
(18) Keegan, D. S.; Hagen, S. R.; Johnson, D. A. Efficient asymmetric synthesis of (*R*)-3-hydroxy- and alkanoyloxytetradecanoic acids and method for the determination of enantiomeric purity. *Tetrahedron: Asymmetry* **1996,** *12*, 3559-3564.
(19) Bazin, H. G.; Bess, L. S.; Livesay, M. T.; Ryter, K. T.; Johnson, C. L.; Arnold, J. S.; Johnson, D. A. New synthesis of glycolipid immunostimulants RC-529 and CRX-524. *Tetrahedron Lett.* **2006,** *13*, 2087-2092.

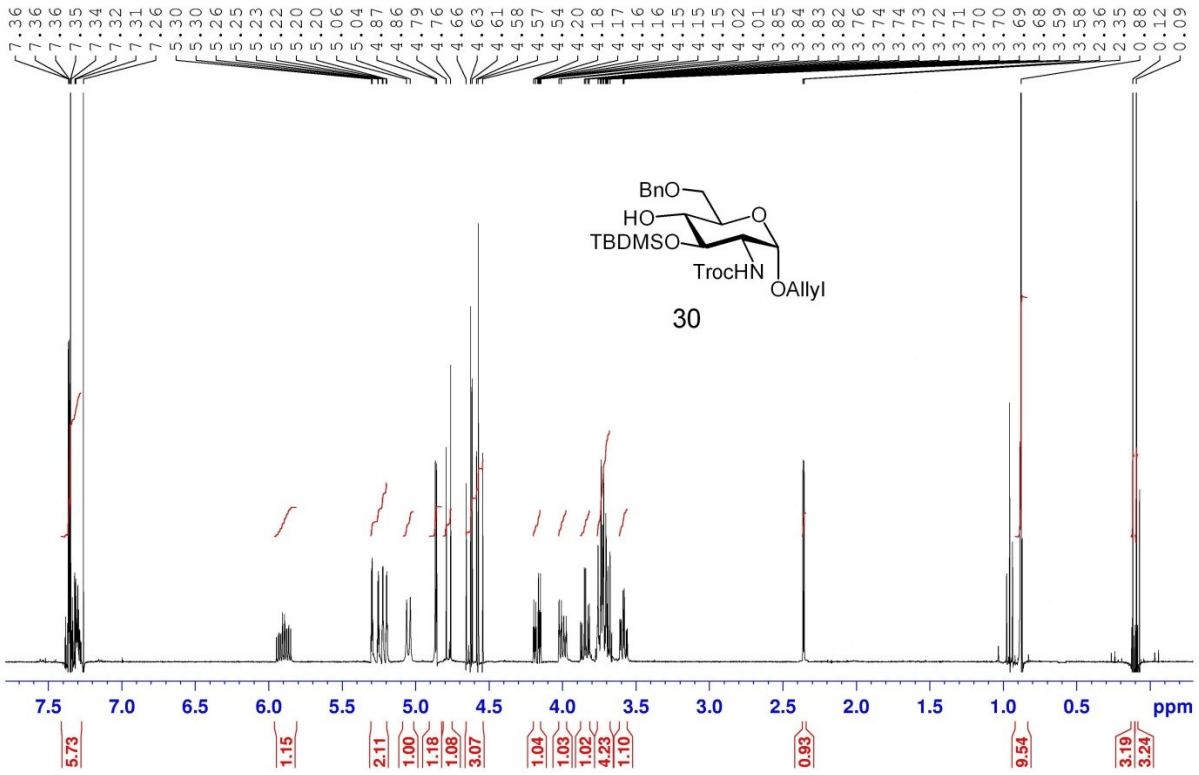
NMR and MALDI-TOF spectra

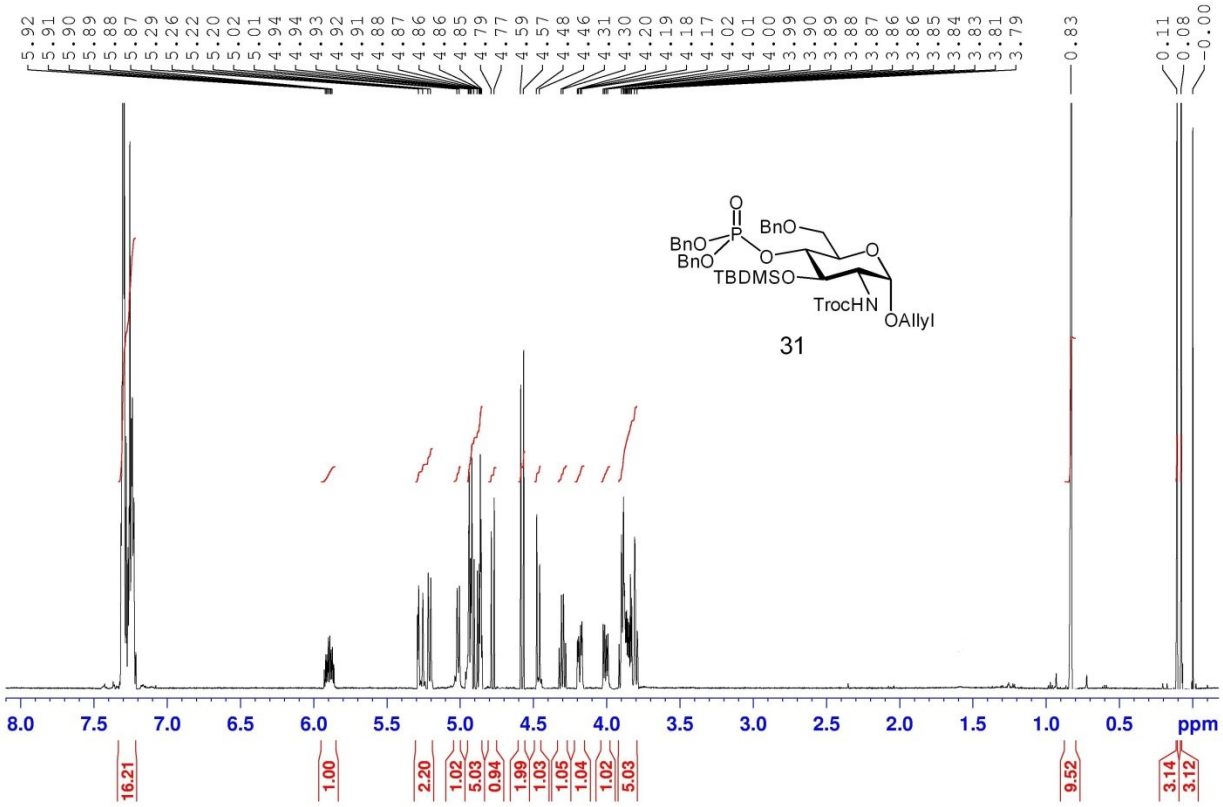

22
22

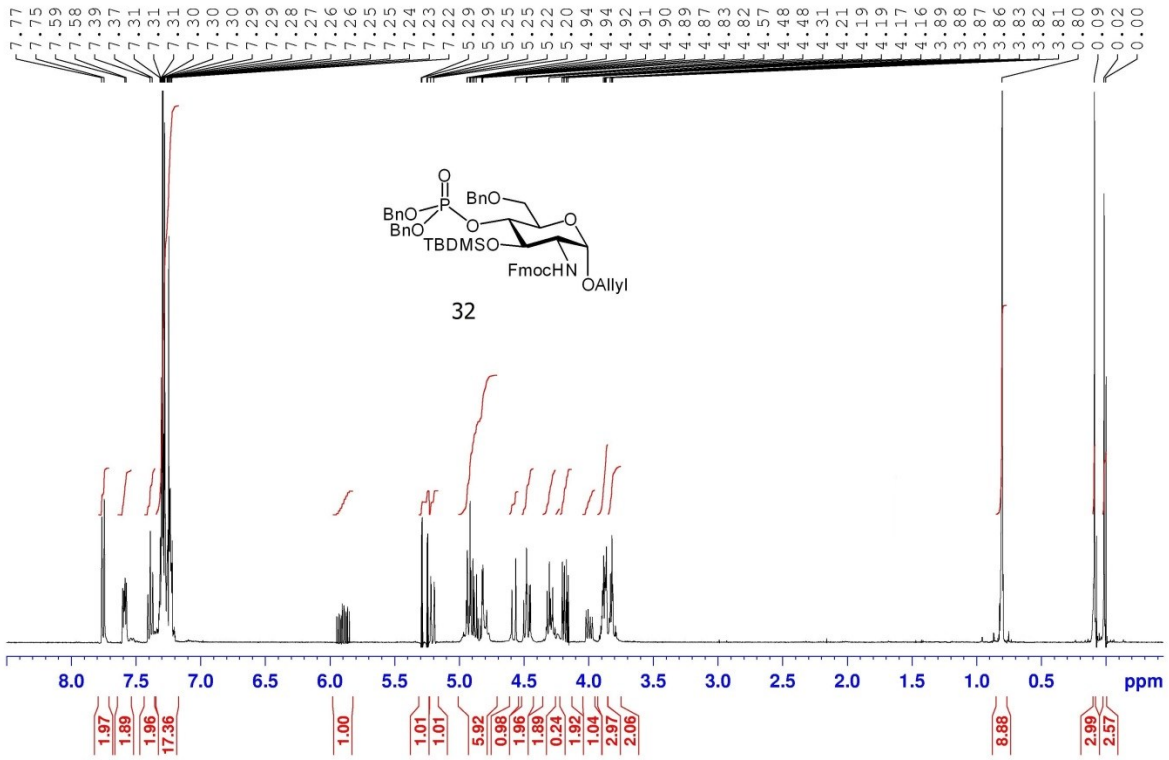

7.42 7.41 7.40 7.36 7.35 7.35 7.35 7.35 7.34 7.34 7.34 7.34 7.33 7.32 7.31 7.31 7.30 7.30 7.30 7.26 7.15 7.14 7.06 7.05 5.38 5.37 4.98 4.97 4.96 4.95 4.87 4.84 4.81 4.79 4.65 4.64 4.64 4.63 4.26 4.21 4.19 4.04 3.78 3.76 2.17 1.85 1.08 1.02
TrocHN
OAc
OBn
OBn
OBn
DTBS
BnO
23
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
15.78 3.17 1.78 0.96 0.95 1.07 4.17 2.11 0.91 1.78 1.00 1.04 1.09 2.02 3.15 1.99 1.01 0.94 2.11 1.04 0.99 3.05 0.99 3.07 8.97 9.15

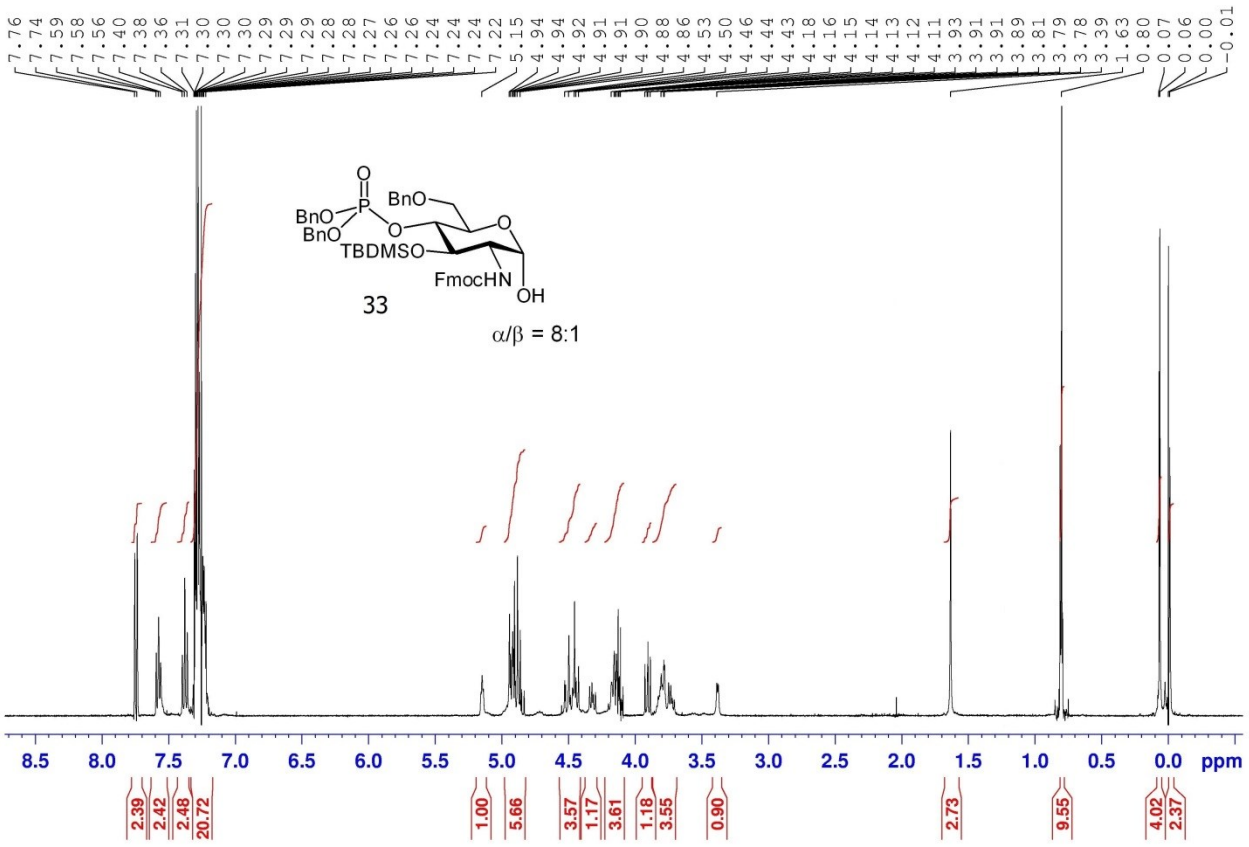

208.04 170.98 154.39 138.32 137.86 135.54 135.36 128.77 128.72 128.65 128.56 128.40 128.34 128.15 128.02 127.90 127.89 127.76 123.87 97.16 95.42 90.96 79.09 77.21 77.00 76.79 76.60 74.54 74.28 74.24 74.14 73.60 72.91 71.00 69.91 69.88 69.78 69.74 69.71 69.67 69.63 68.78 66.19 53.81 37.97 32.99 30.20 27.46 27.03 22.74 20.65
TrocHN
OAc
OBn
OBn
BnO
Si
BnO
23
200 180 160 140 120 100 80 60 40 20 0 ppm

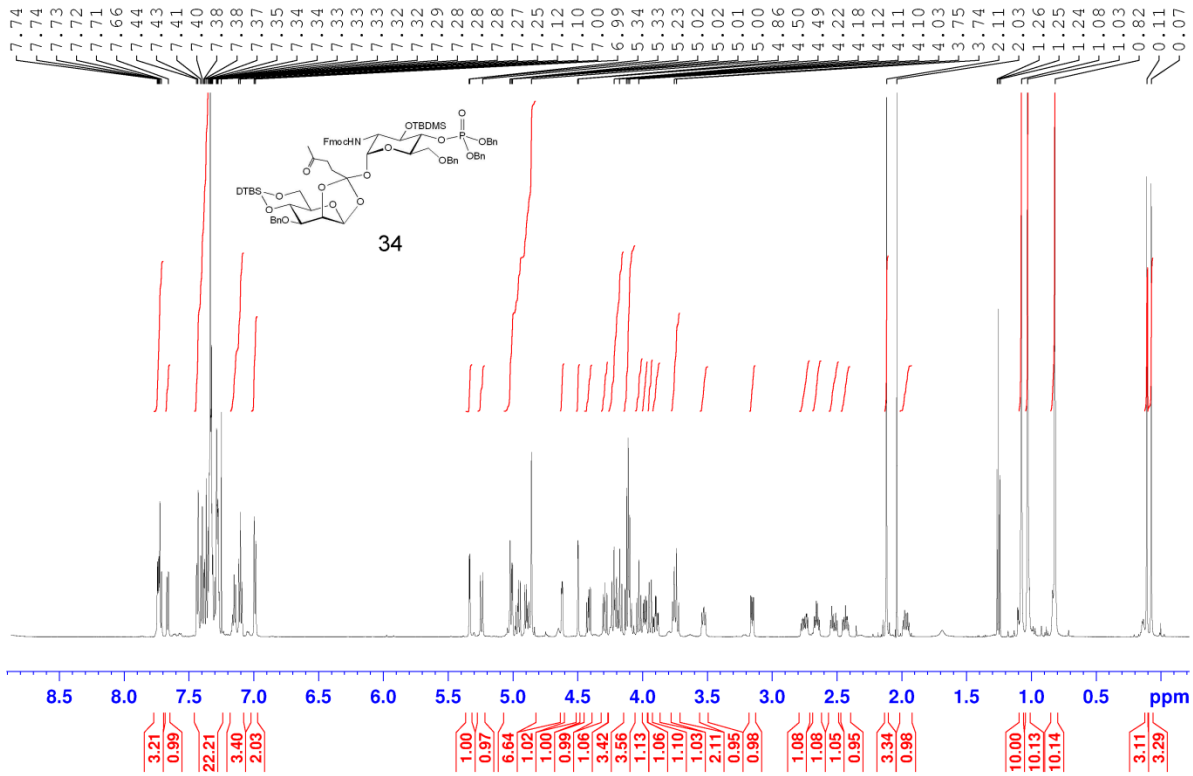

7.36 7.34 7.33 7.32 7.30 7.29 7.28 7.28 7.26 7.24 7.23
5.29 5.23 5.23 5.19 5.18 5.17 5.15 5.11 4.98 4.97 4.95 4.94 4.71 4.69 4.68 4.67 4.66 4.54 4.52 4.50 4.48 4.13 4.12 4.04 4.02 3.90 3.89 3.88 3.83 3.81 3.71
BnO
BnO
BnO
AcO
TrocHN
OAc
OAc
OBn
OLev
28
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0
27.66
1.00 2.00 0.88 1.12 1.02 4.33 4.02 3.23
0.99 2.09 1.01 1.06 1.05 2.00
4.20
3.07 3.26 3.12 3.17
206.00
171.88 171.84 170.56 169.63 153.94 137.90 137.31 135.47 128.71 128.64 128.51 128.34 128.06 128.01 127.99 127.63 127.59
92.58 91.95 77.21 77.00 76.79 74.74 74.12 73.50 73.07 73.03 72.01 70.72 70.54 70.49 69.87 69.71 69.69 69.68 69.66 68.36 67.54 67.16 62.47 53.81 37.94 29.68 28.09 20.81 20.80 20.70
200 180 160 140 120 100 80 60 40 20 0 ppm

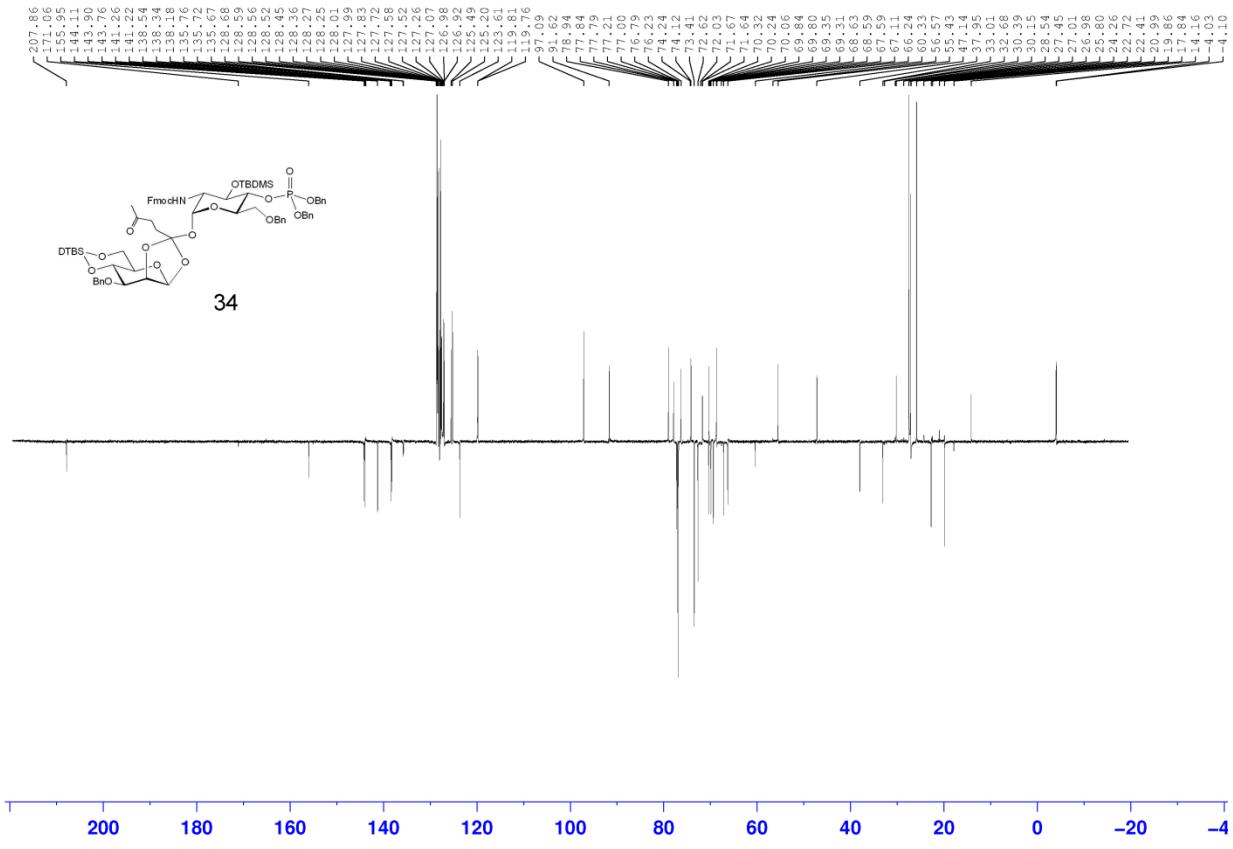

BnO
HO
TBDMSO
TrocHN
OAllyl
30

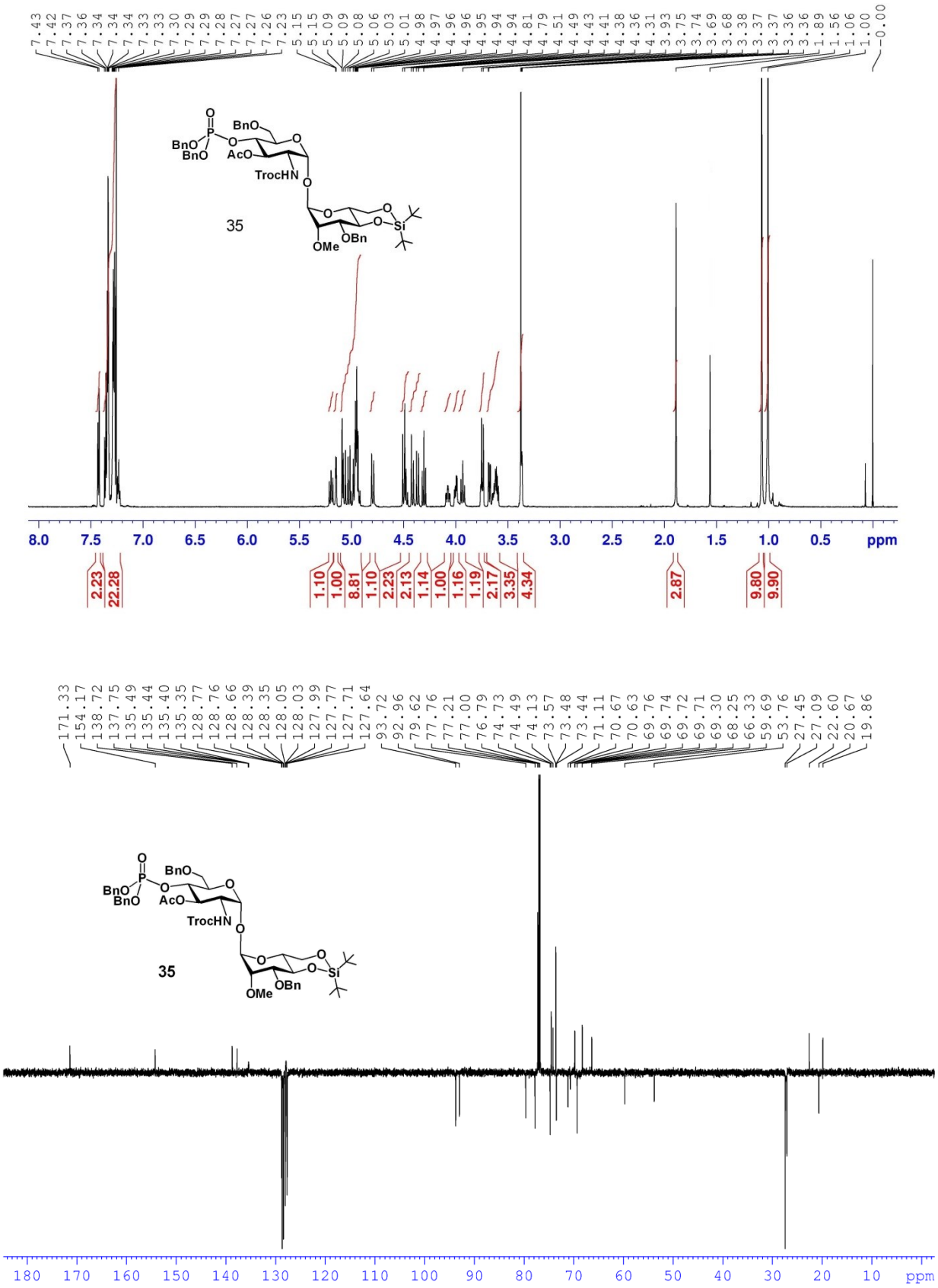

BnO
BnO
BnO
TBDMSO
TrocHN
OAllyl
31

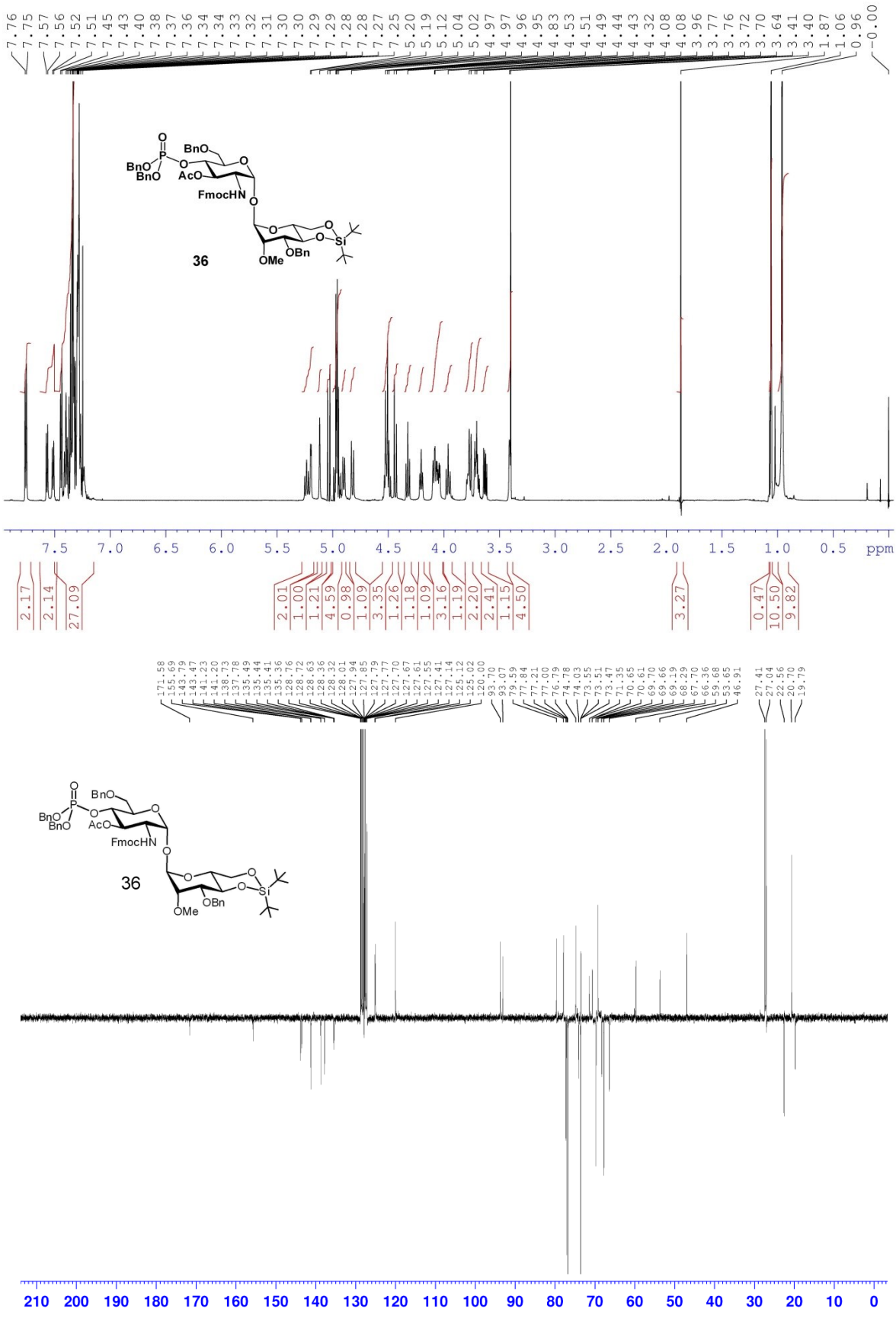

BnO
BnO
BnO
TBDMSO
FmocHN
OAllyl
32
ppm

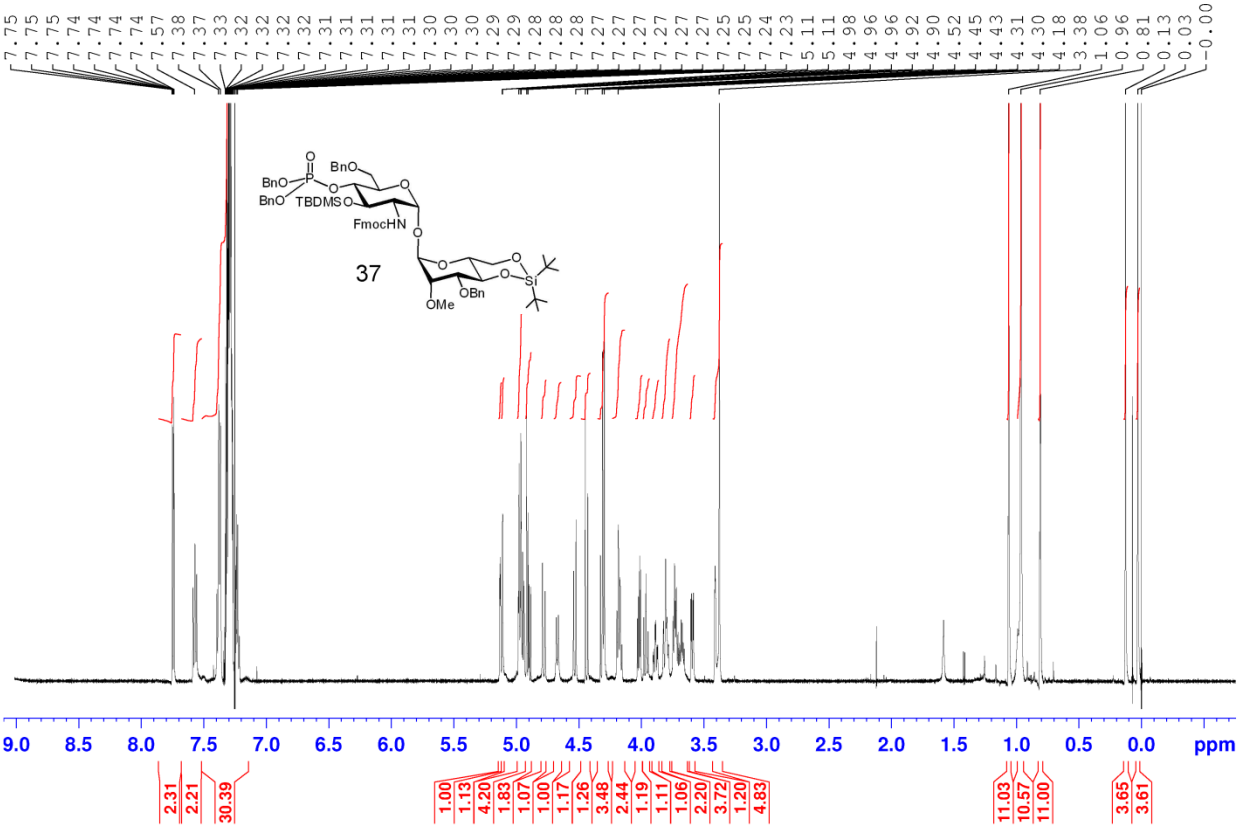

BnO
BnO
BnO
TBDMSO
FmocHN
OH
33
α/β = 8:1
ppm

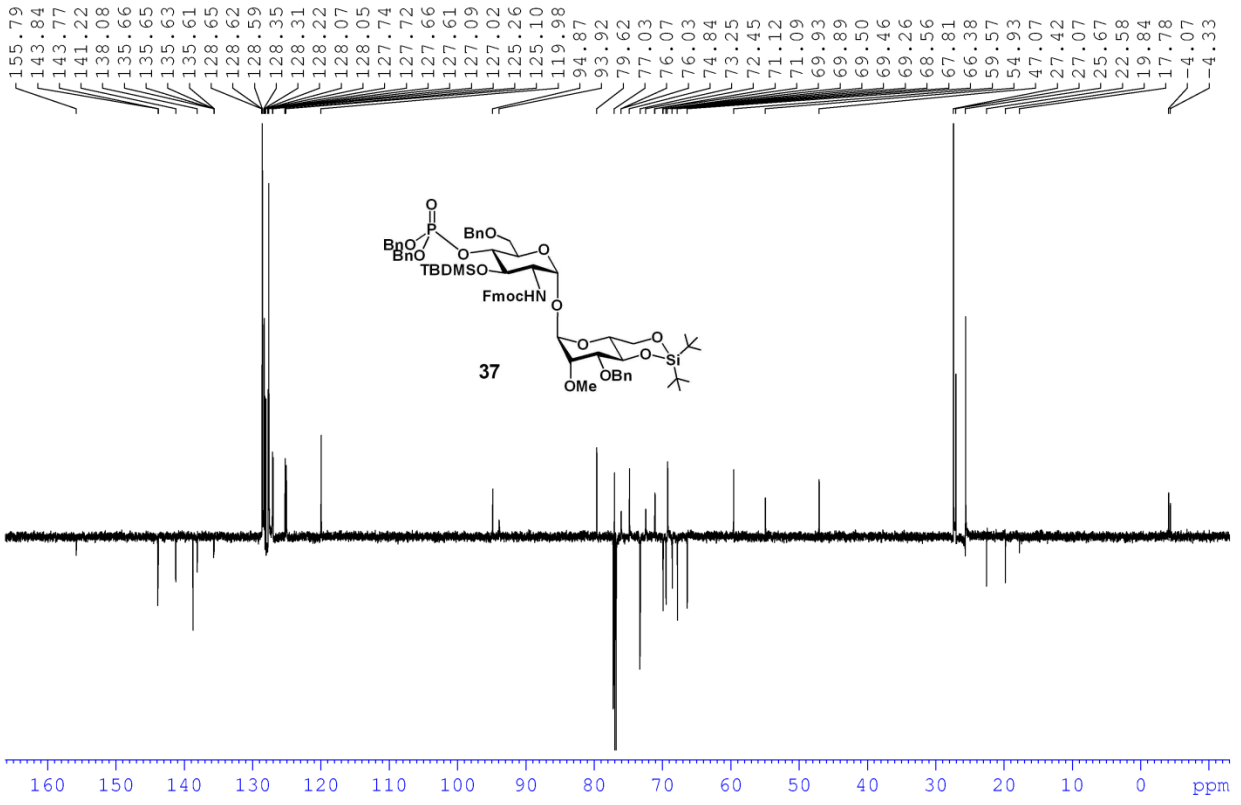

34

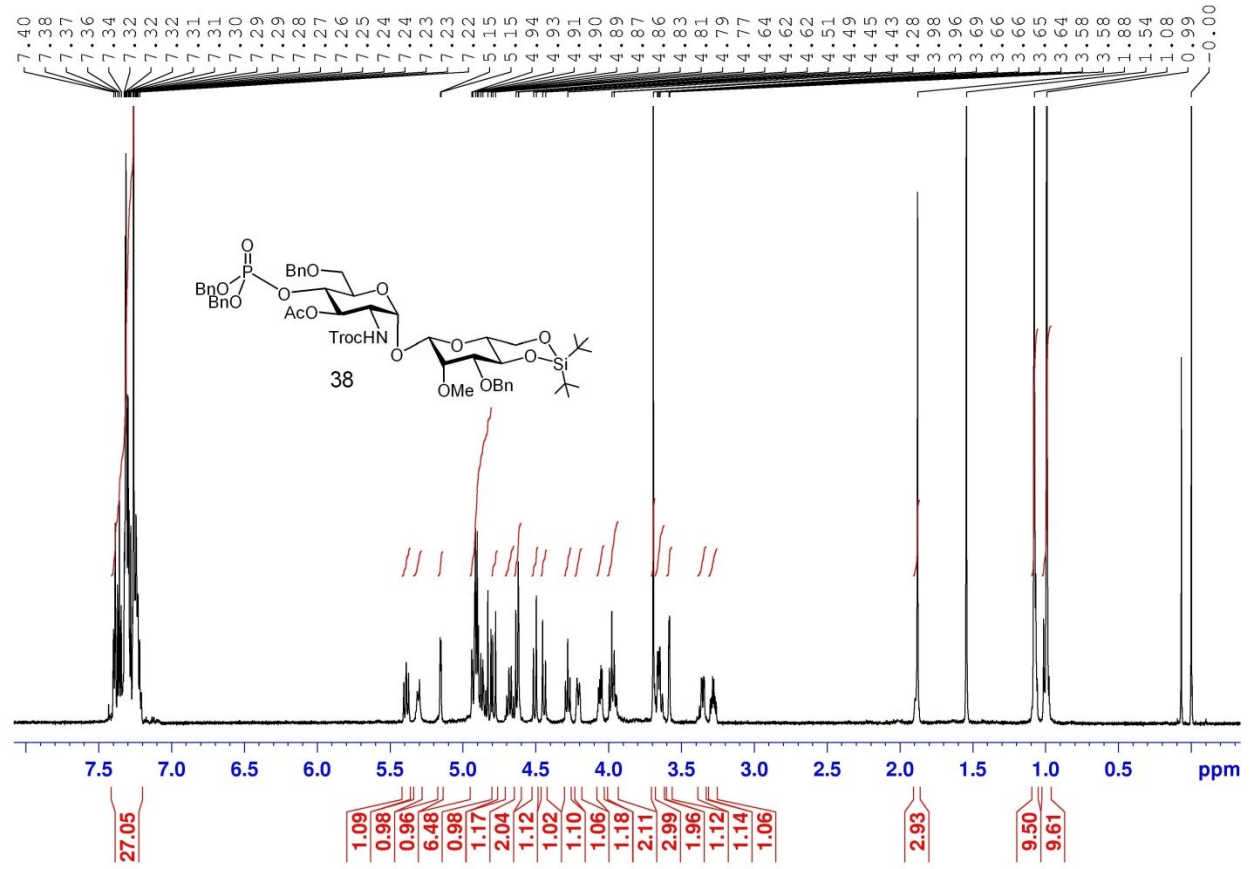

34

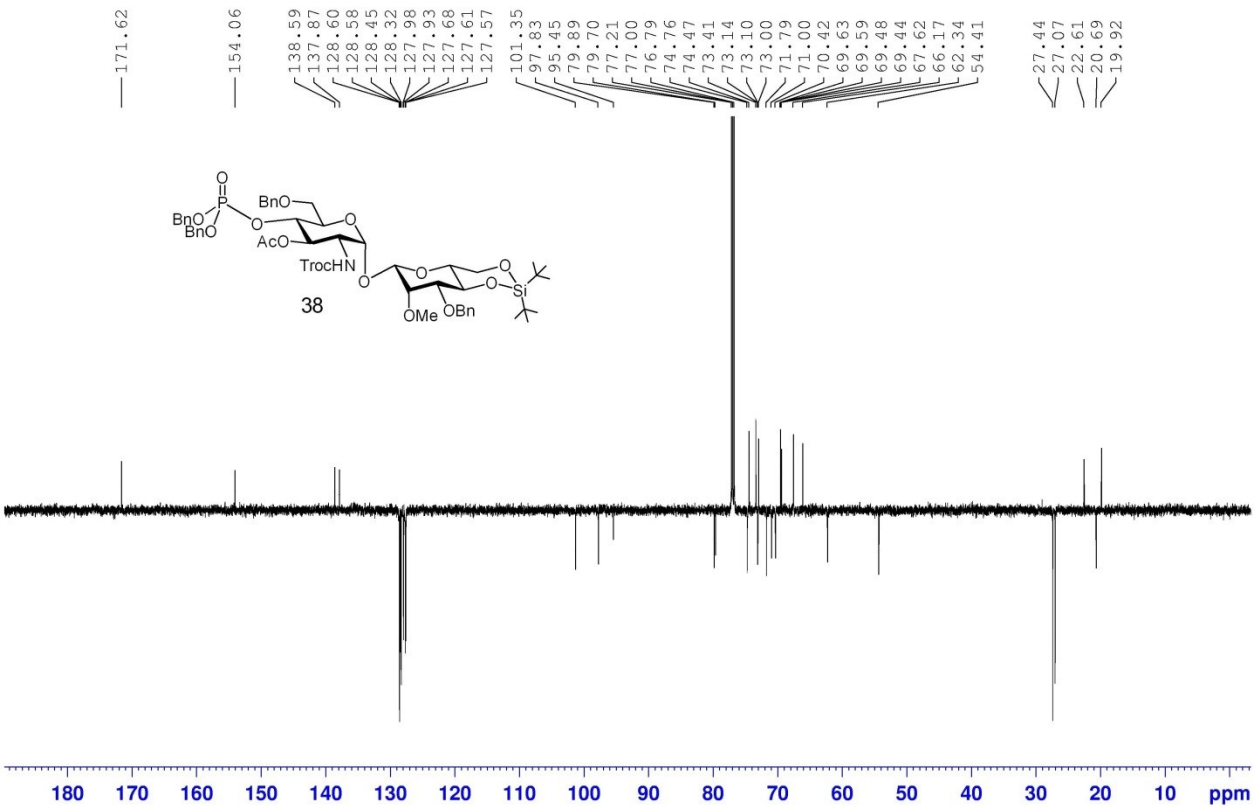

35
35

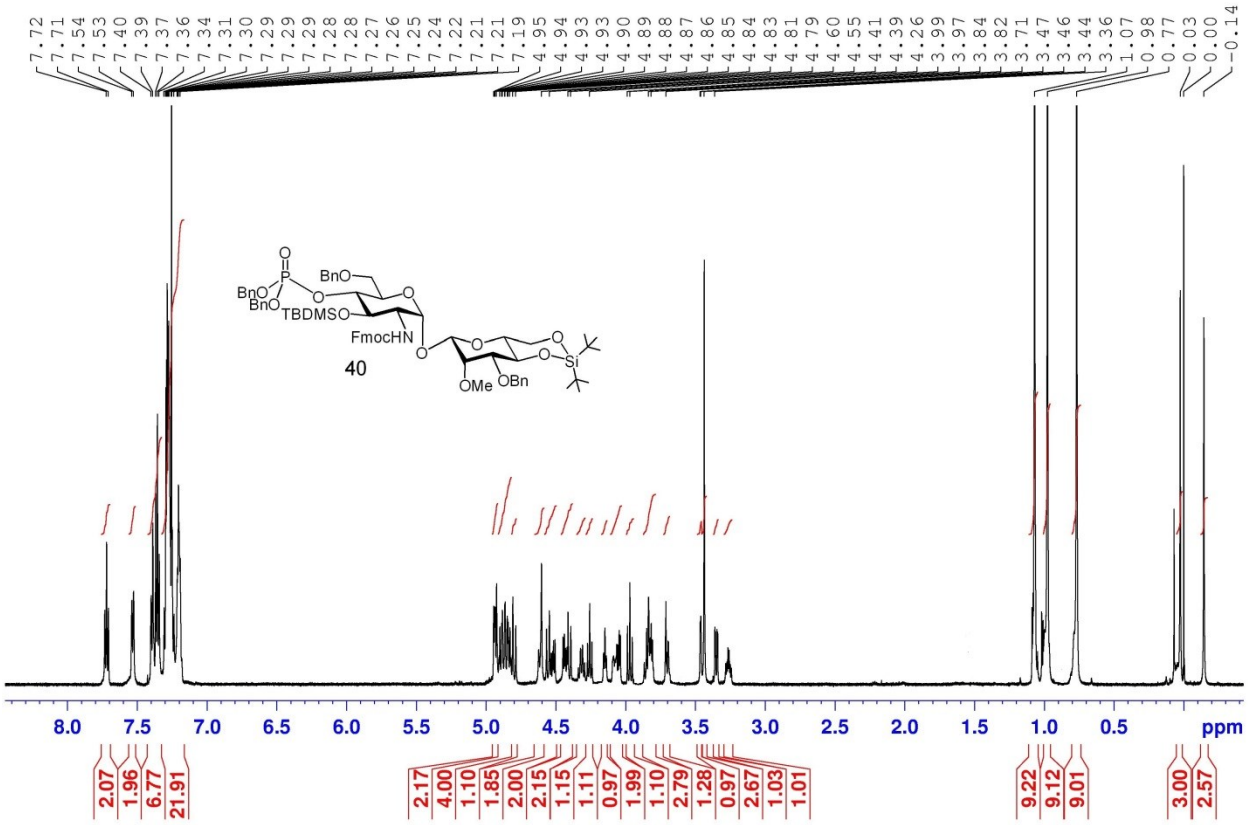

36
36

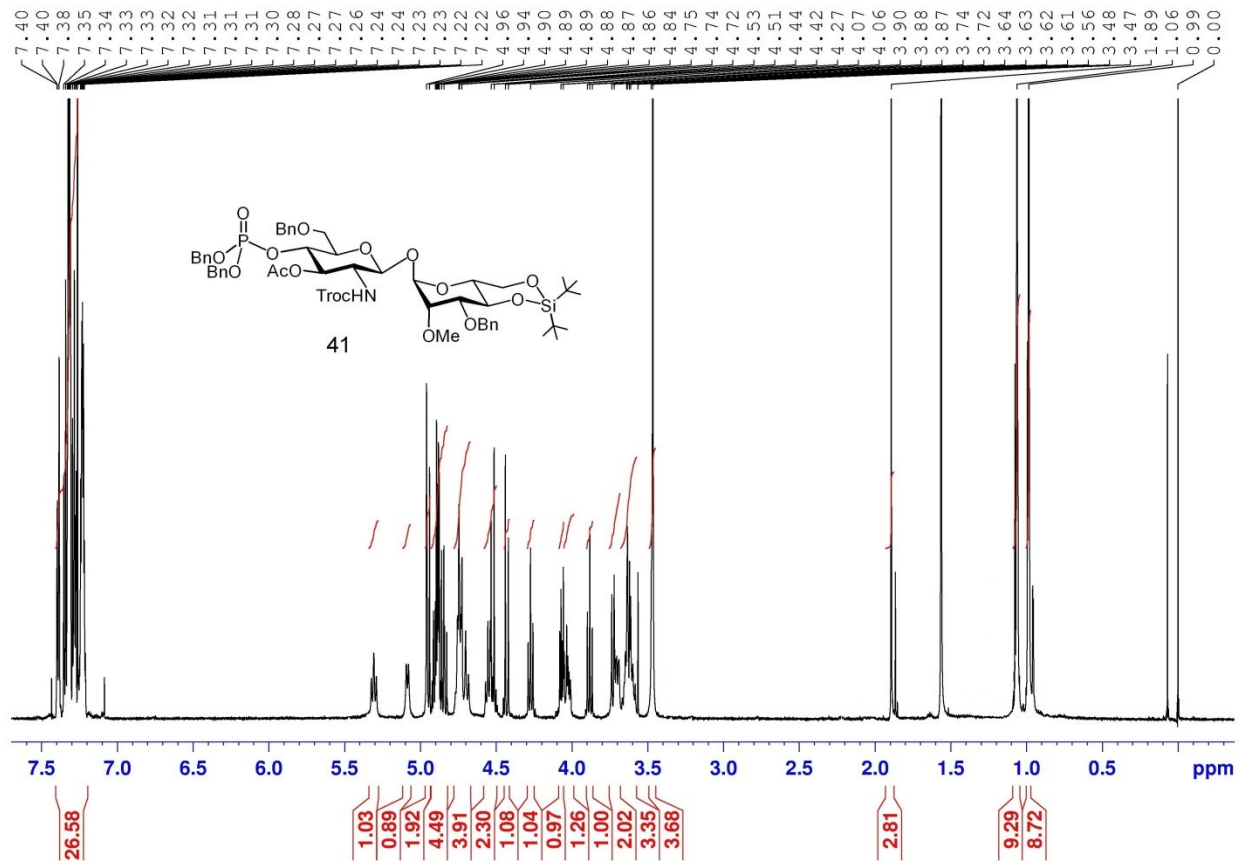

7.75 7.75 7.75 7.74 7.74 7.74 7.74 7.57 7.38 7.37 7.33 7.32 7.32 7.32 7.31 7.31 7.31 7.31 7.30 7.30 7.30 7.29 7.29 7.28 7.28 7.27 7.27 7.27 7.27 7.27 7.25 7.25 7.24 7.23 5.11 5.11 4.98 4.96 4.96 4.92 4.90 4.52 4.45 4.43 4.31 4.30 4.18 3.38 1.06 0.96 0.81 0.13 0.03 -0.00
BnO
BnO
BnO
TBDMSO
FmocHN
37
OMe
OBn
Si
9.0 8.5 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 0.0 ppm
2.31 2.21 30.39 1.00 1.13 4.20 1.83 1.07 1.00 1.17 1.26 3.48 2.44 1.19 1.11 1.06 2.20 3.72 1.20 4.83 11.03 10.57 11.00 3.65 3.61

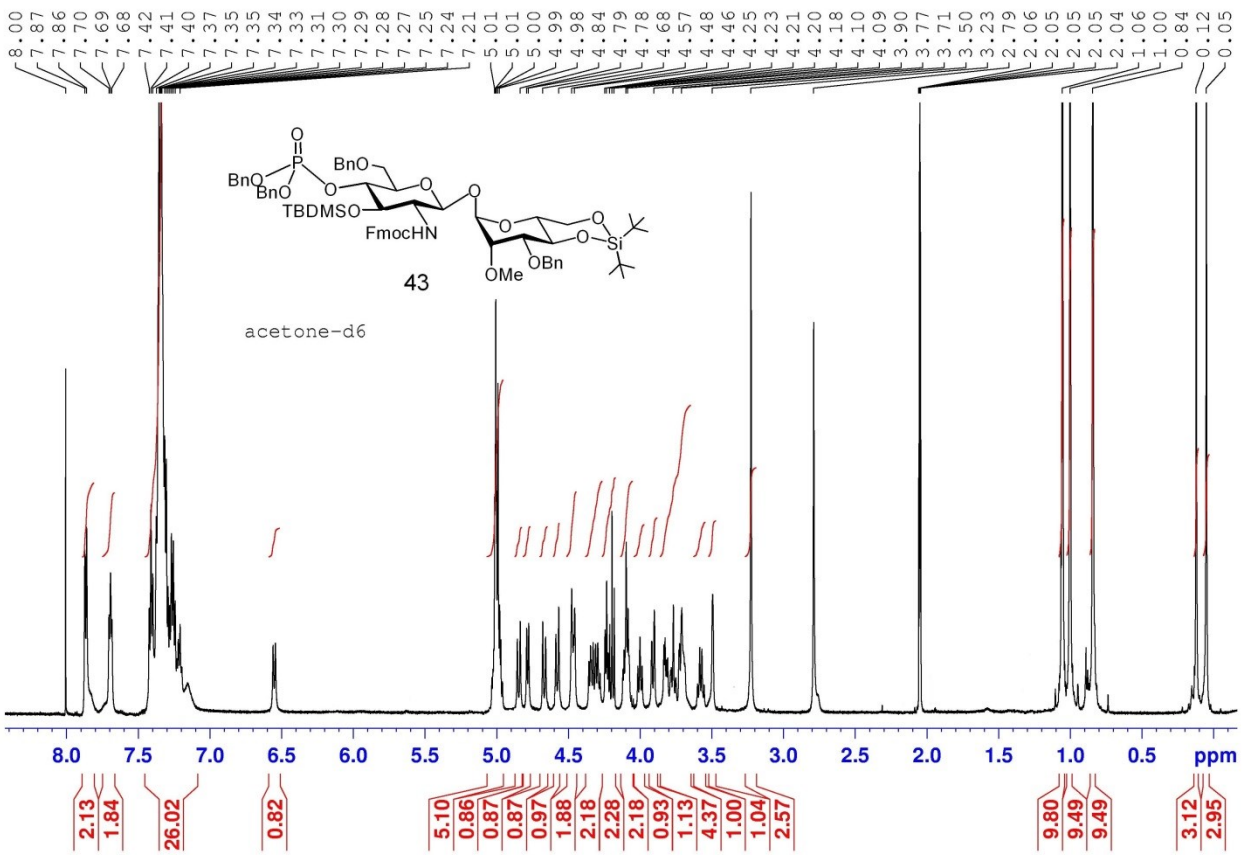

155.79 143.84 143.77 141.22 138.08 135.66 135.65 135.63 135.61 128.65 128.62 128.59 128.35 128.31 128.22 128.07 128.05 127.74 127.72 127.66 127.61 127.09 127.02 125.26 125.10 119.98 94.87 93.92 79.62 77.03 76.07 76.03 74.84 73.25 72.45 71.12 71.09 69.93 69.89 69.50 69.46 69.26 68.56 67.81 66.38 59.57 54.93 47.07 27.42 27.07 25.67 22.58 19.84 17.78 -4.07 -4.33
BnO
BnO
BnO
TBDMSO
FmocHN
37
OMe
OBn
Si
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

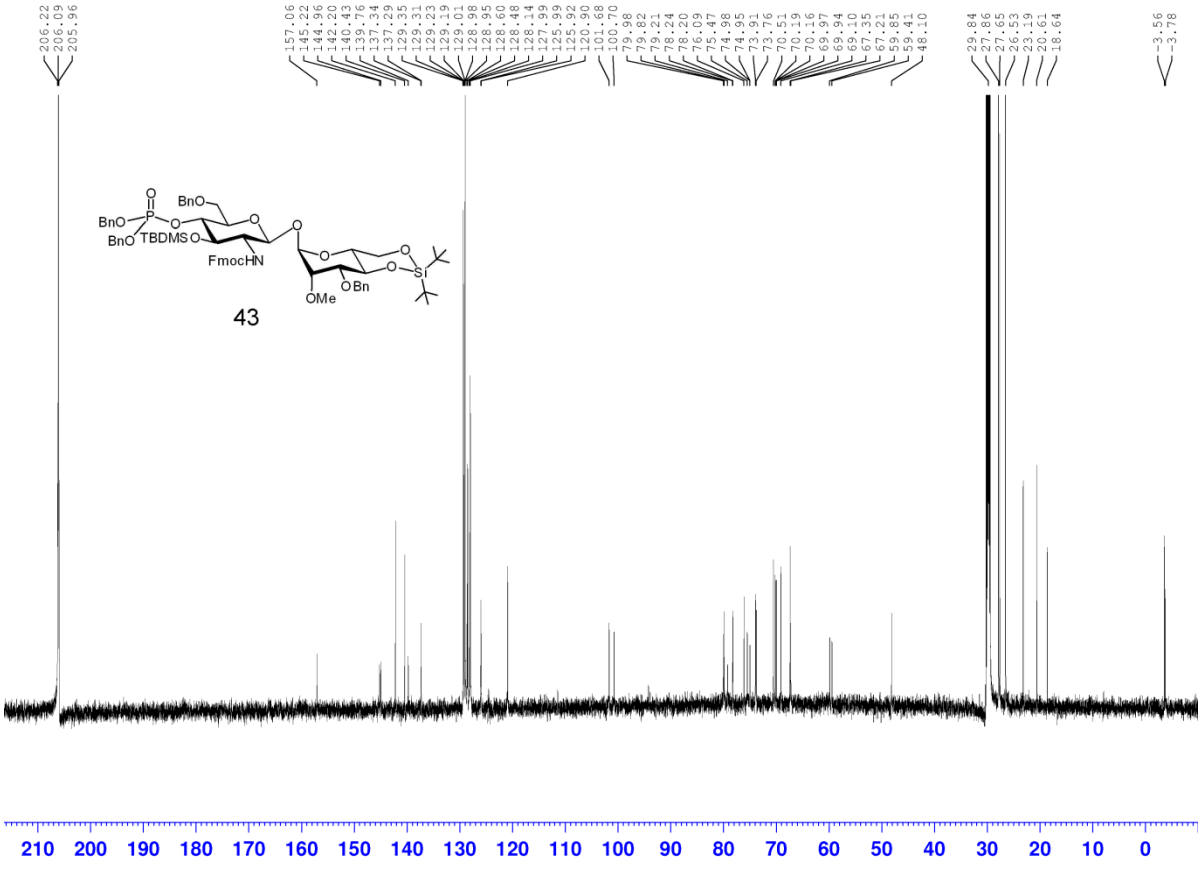

38
ppm

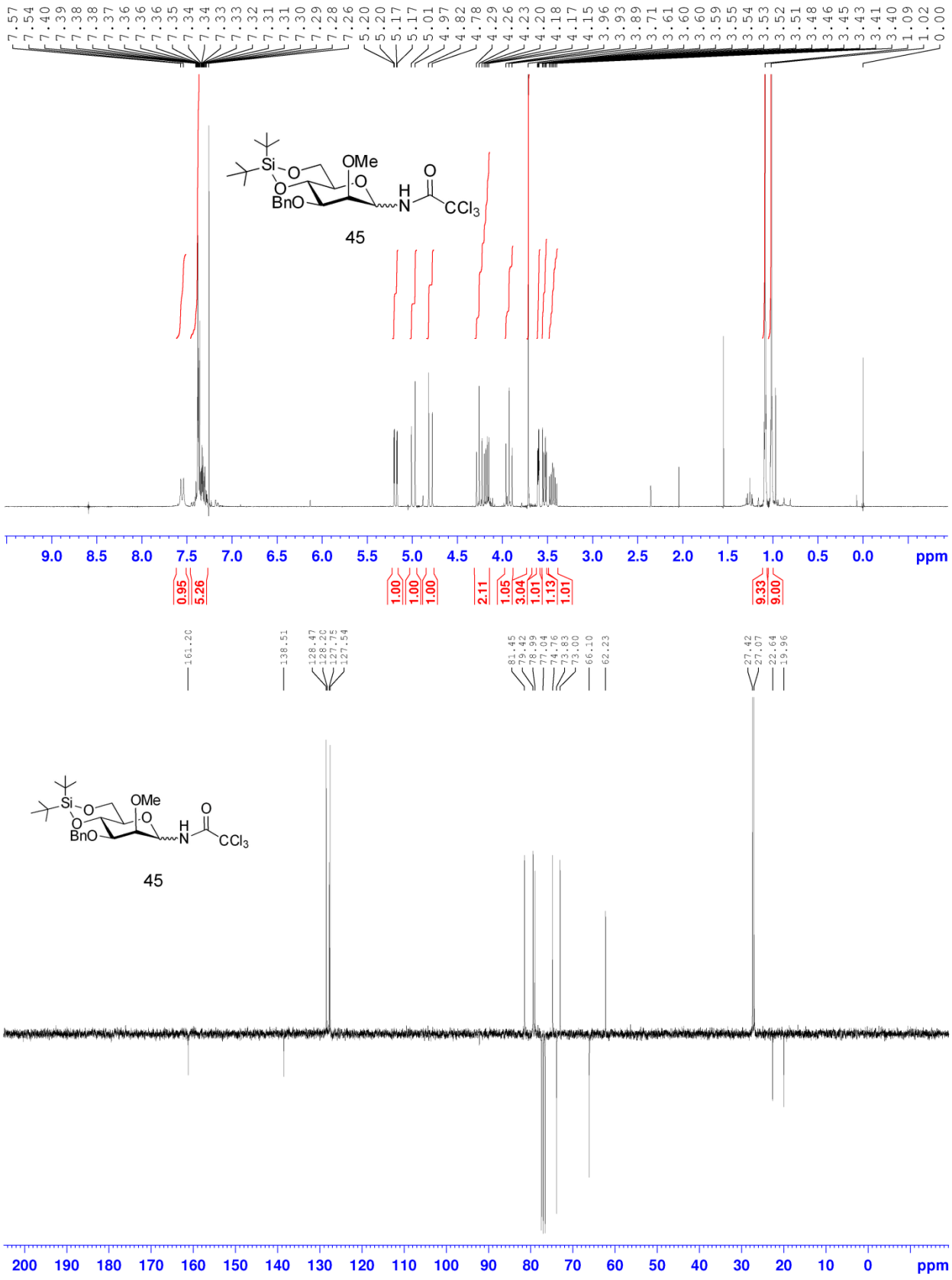

38
ppm

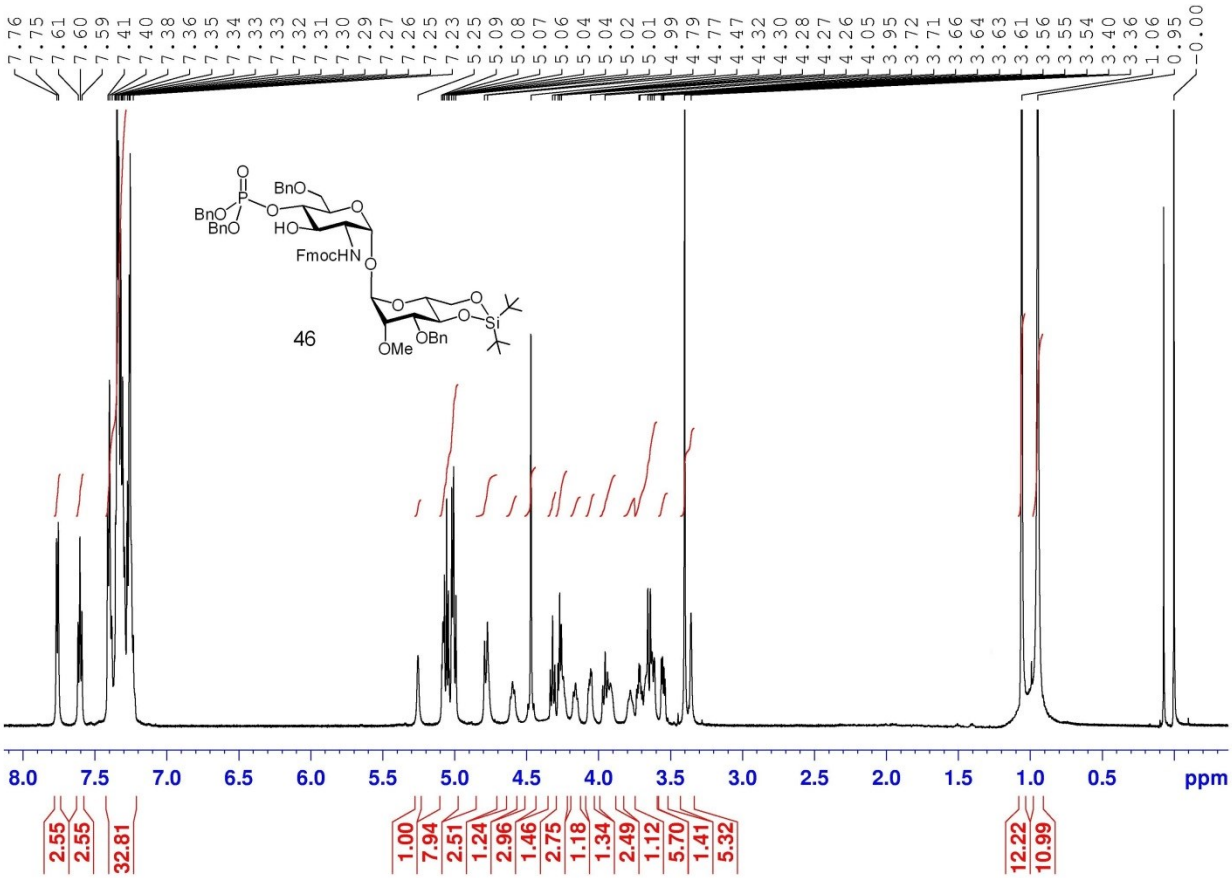

40
BnO
BnO
BnO
TBDMSO
FmocHN
OMe
OBn
Si
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.07 1.96 6.77 21.91 2.17 4.00 1.10 1.85 2.00 2.15 1.15 1.11 0.97 1.99 1.10 2.79 1.28 0.97 2.67 1.03 1.01 9.22 9.12 9.01 3.00 2.57

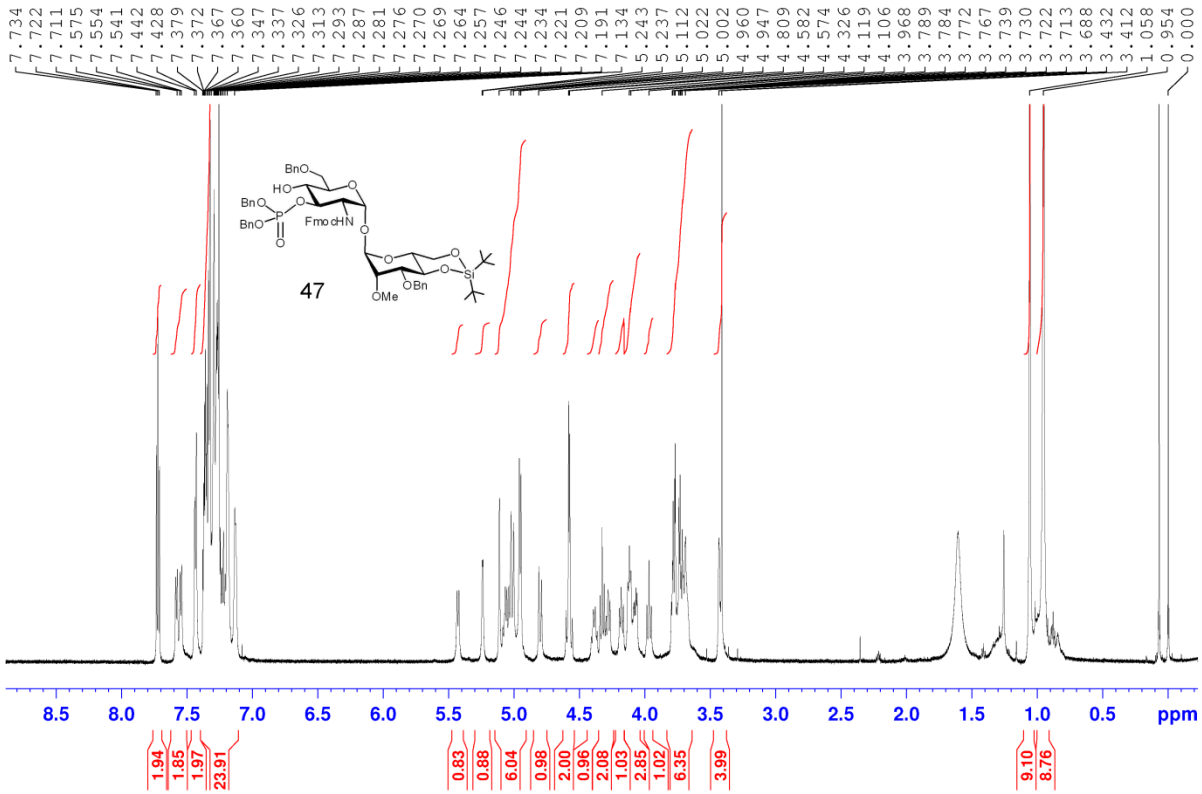

41
BnO
BnO
BnO
AcO
TrocHN
OMe
OBn
Si
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
26.58 1.03 0.89 1.92 4.49 3.91 2.30 1.08 1.04 0.97 1.26 1.00 2.02 3.35 3.68 2.81 9.29 8.72

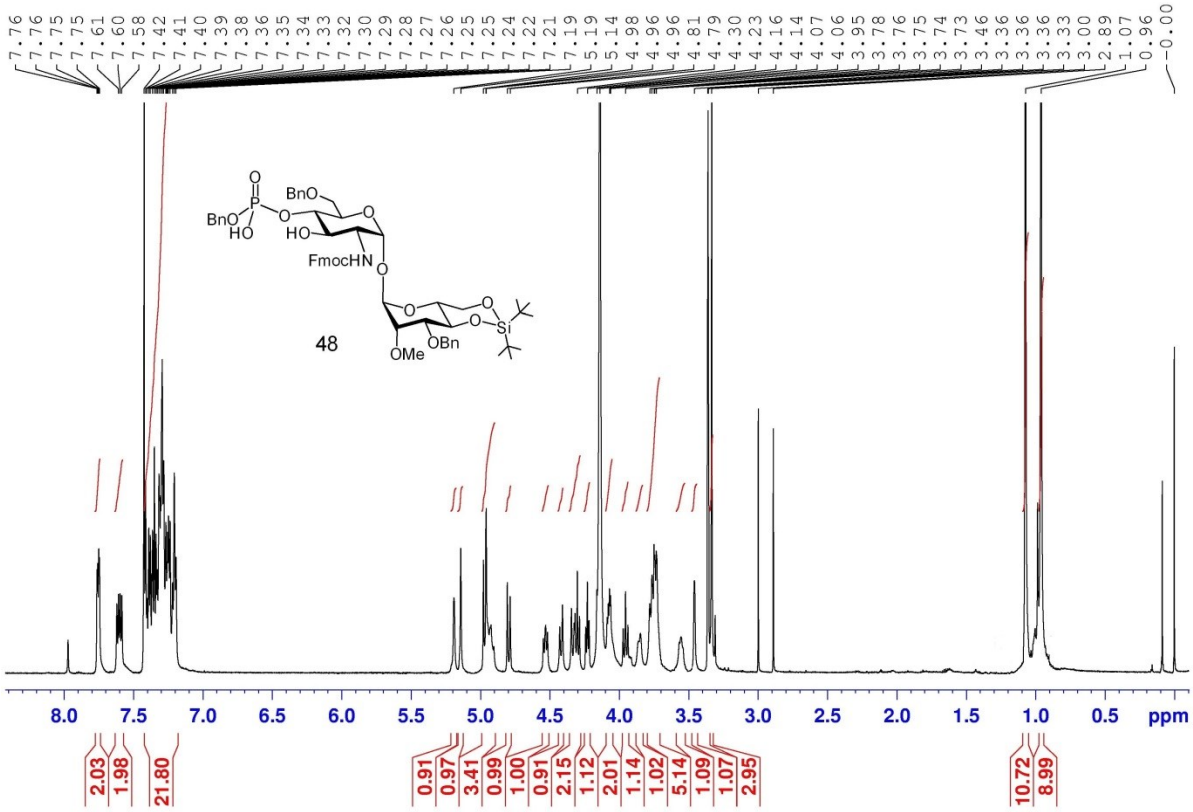

8.00 7.87 7.86 7.70 7.69 7.68 7.42 7.41 7.40 7.37 7.35 7.34 7.33 7.31 7.30 7.29 7.28 7.27 7.25 7.24 7.21 5.01 5.01 5.00 4.99 4.98 4.84 4.79 4.78 4.68 4.57 4.48 4.46 4.25 4.23 4.21 4.20 4.18 4.10 4.09 3.90 3.77 3.71 3.50 3.23 2.79 2.06 2.05 2.05 2.05 2.04 1.06 1.00 0.84 0.12 0.05
BnO
BnO
BnO
TBDMSO
FmocHN
OMe
OBn
43
acetone-d6
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 ppm
2.13 1.84 26.02 0.82 5.10 0.86 0.87 0.87 0.97 1.88 2.18 2.28 2.18 0.93 1.13 4.37 1.00 1.04 2.57 9.80 9.49 9.49 3.12 2.95

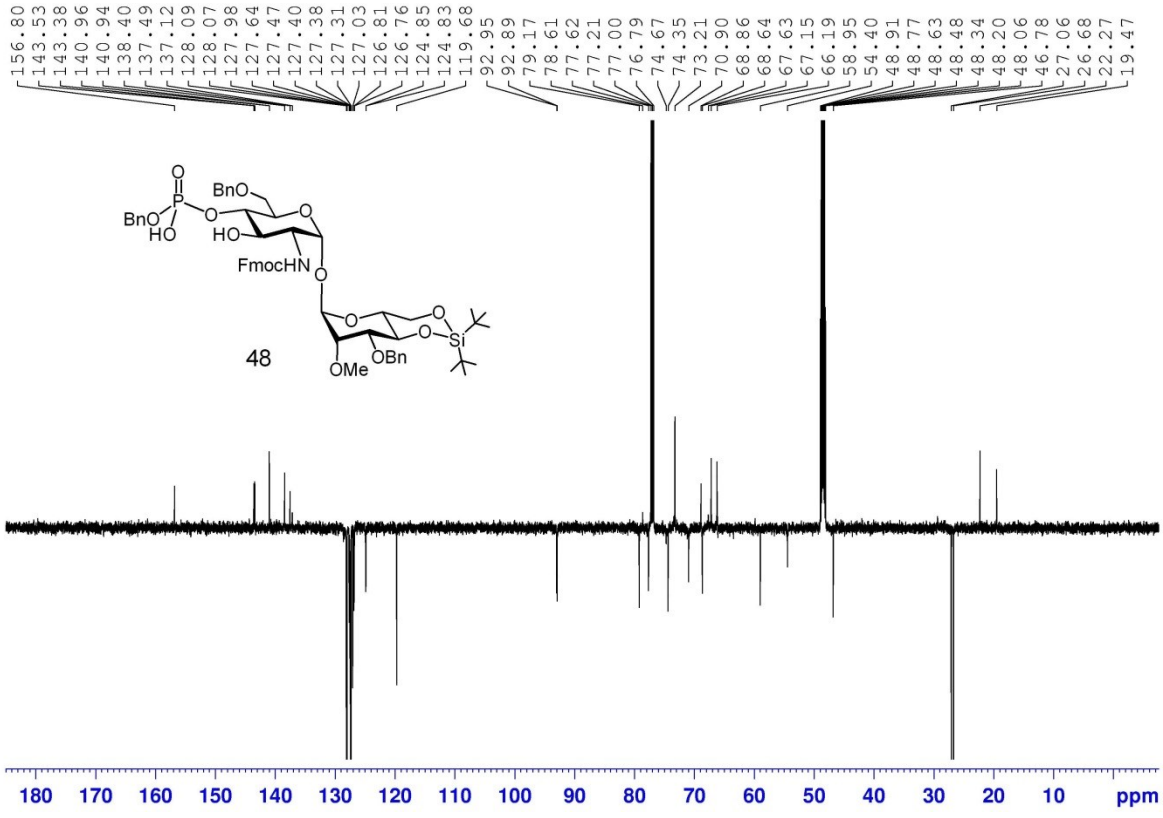

206.22 206.09 205.96
157.06 145.22 144.96 142.20 140.43 139.76 137.34 137.29 129.35 129.31 129.23 129.19 129.01 128.98 128.95 128.60 128.48 128.14 127.99 125.99 125.92 120.90 101.68 100.70 79.98 79.82 79.21 78.24 78.20 76.09 75.47 74.98 74.95 73.91 73.76 70.51 70.19 70.16 69.97 69.94 69.10 67.35 67.21 59.85 59.41 48.10
29.84 27.86 27.65 26.53 23.19 20.61 18.64
-3.56 -3.78
BnO
BnO
BnO
TBDMSO
FmocHN
OMe
OBn
43
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

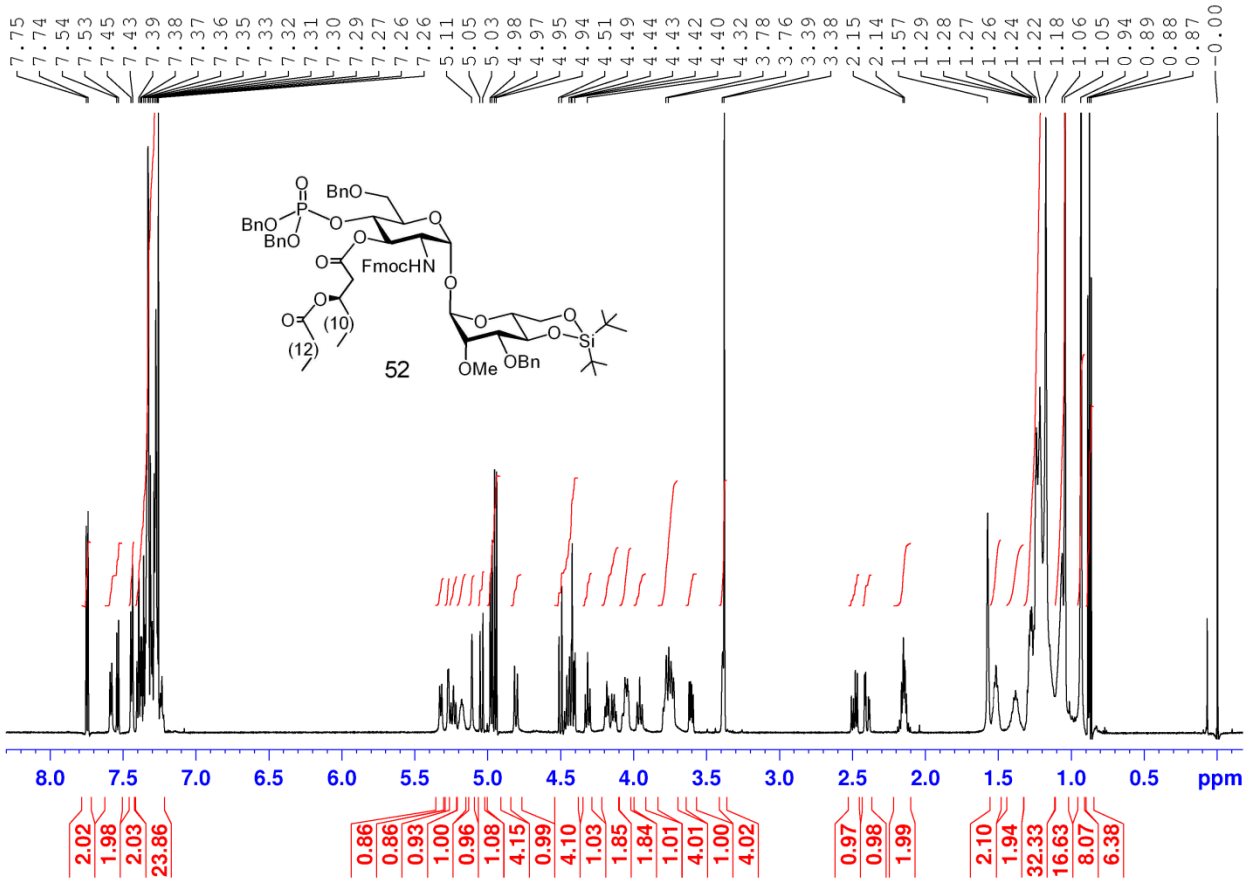

45
45
ppm
ppm

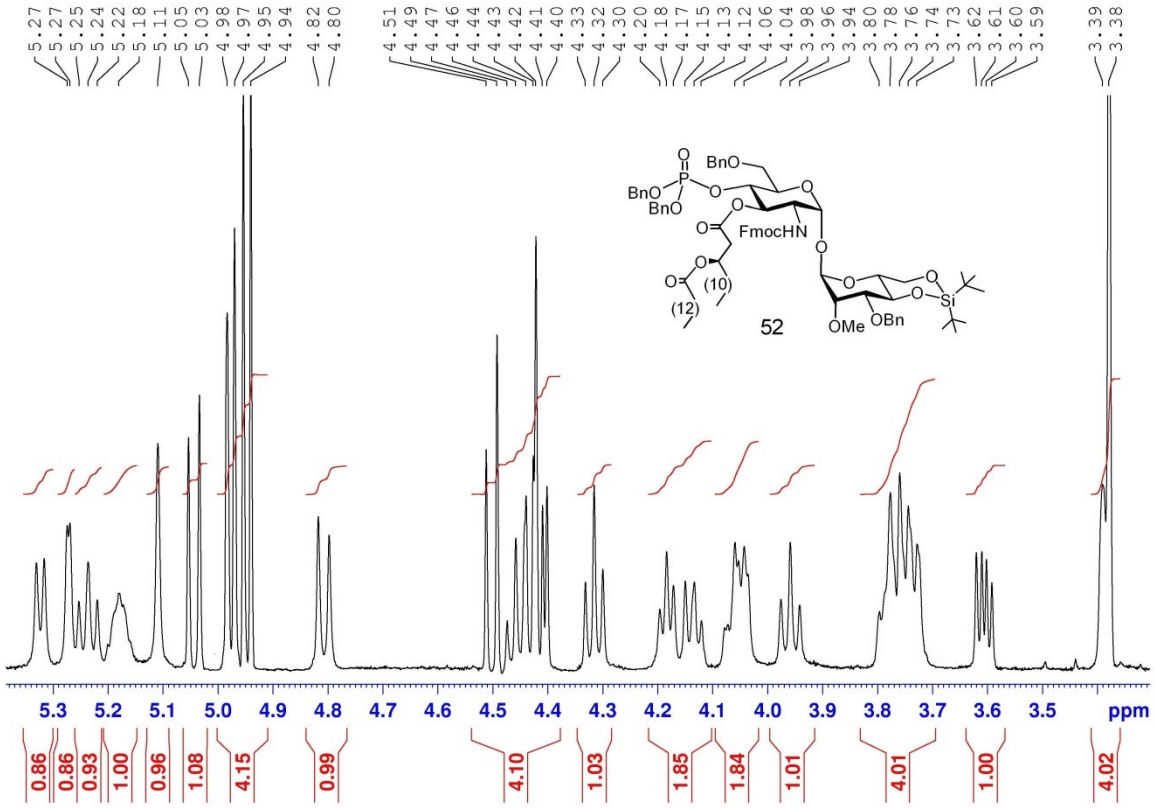

46
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

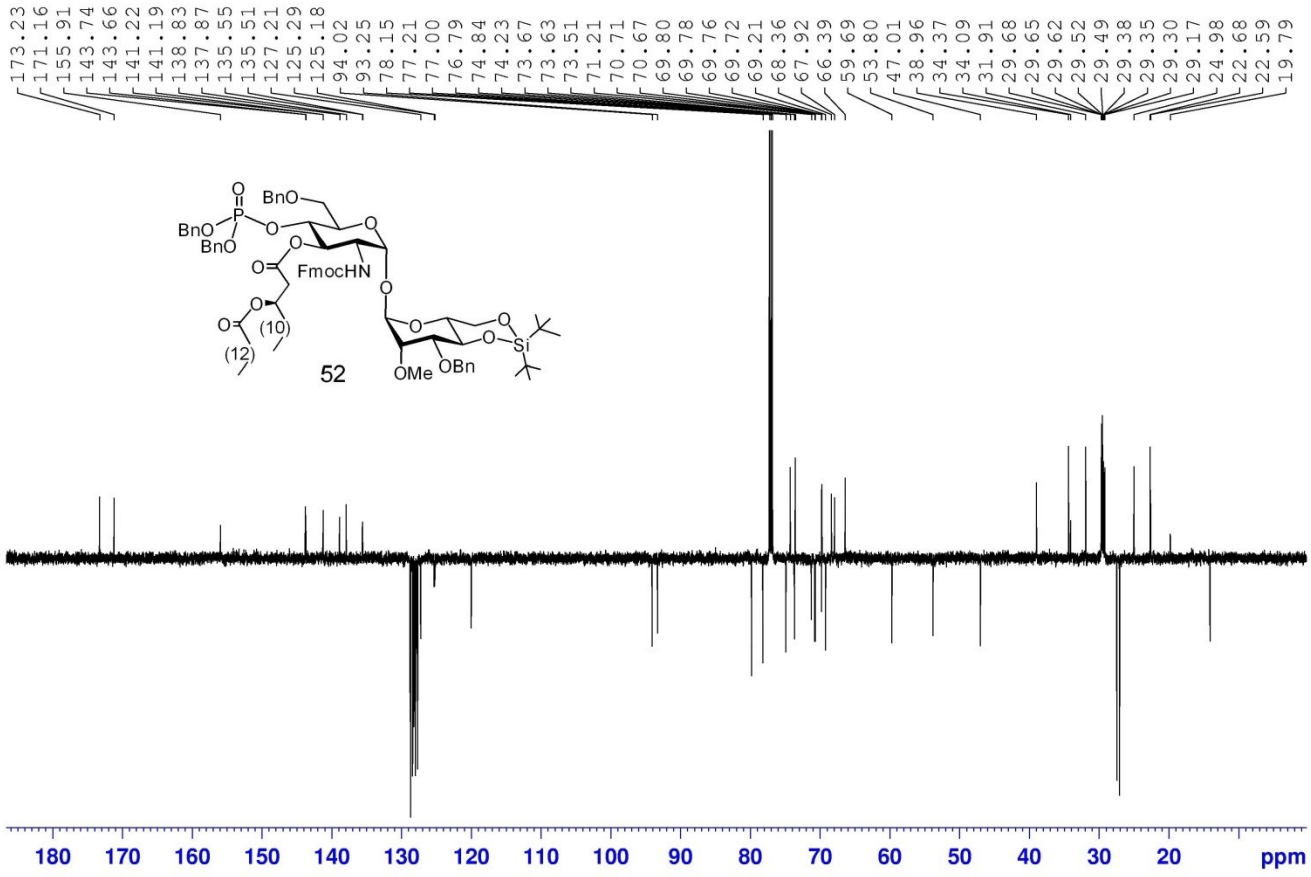

47
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

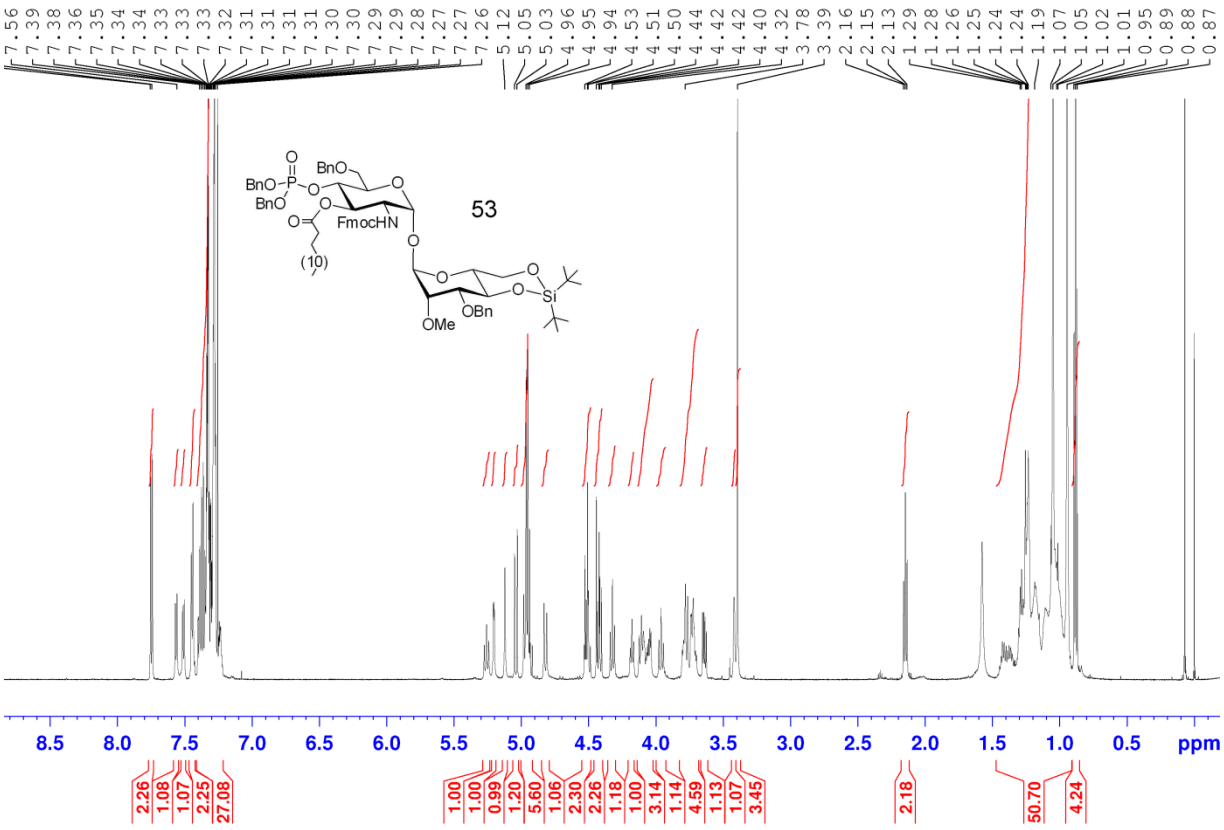

48
ppm

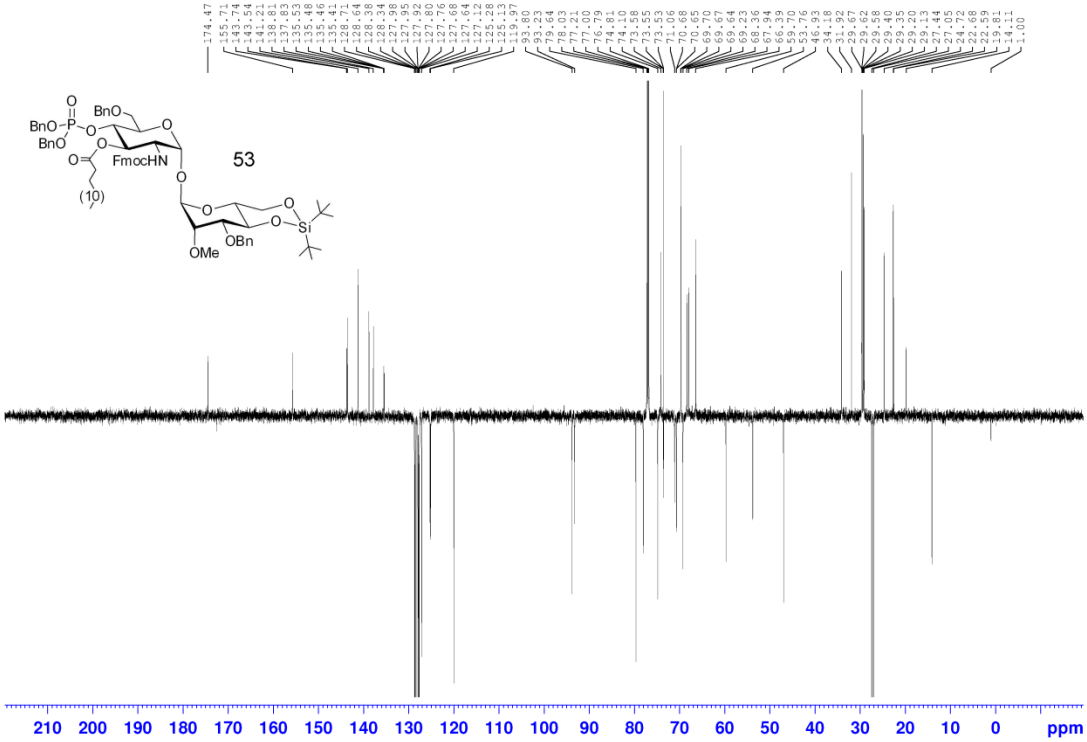

48
ppm

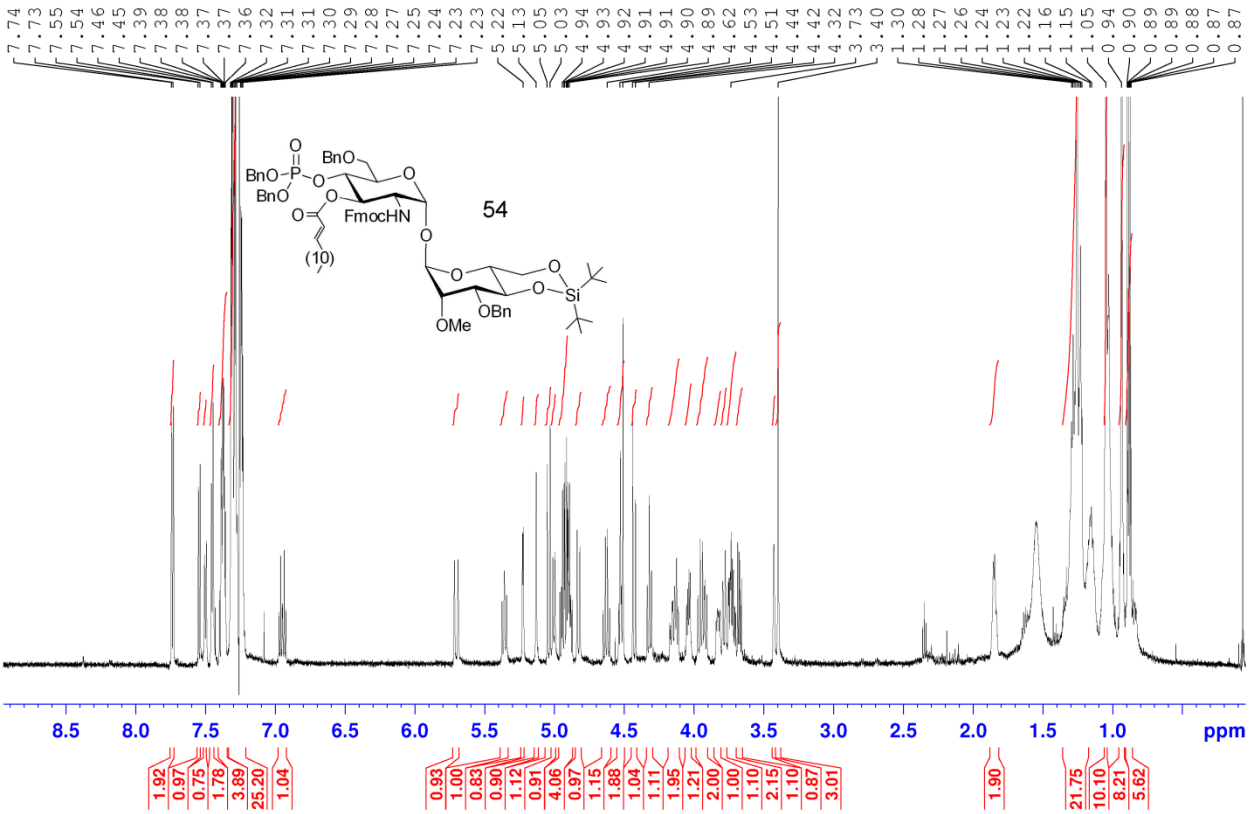

7.75 7.74 7.54 7.53 7.45 7.43 7.39 7.38 7.37 7.36 7.35 7.33 7.32 7.31 7.30 7.29 7.27 7.26 7.26
5.11 5.05 5.03 4.98 4.97 4.95 4.94 4.51 4.49 4.44 4.43 4.42 4.40 4.32 3.78 3.76 3.39 3.38
2.15 2.14 1.57 1.29 1.28 1.27 1.26 1.24 1.22 1.18 1.06 1.05 0.94 0.89 0.88 0.87 0.00
BnO
BnO
BnO
FmocHN
(10)
(12)
52
OMe
OBn
Si
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 ppm
2.02 1.98 2.03 23.86 0.86 0.86 0.93 1.00 0.96 1.08 4.15 0.99 4.10 1.03 1.85 1.84 1.01 4.01 1.00 4.02 0.97 0.98 1.99 2.10 1.94 32.33 16.63 8.07 6.38

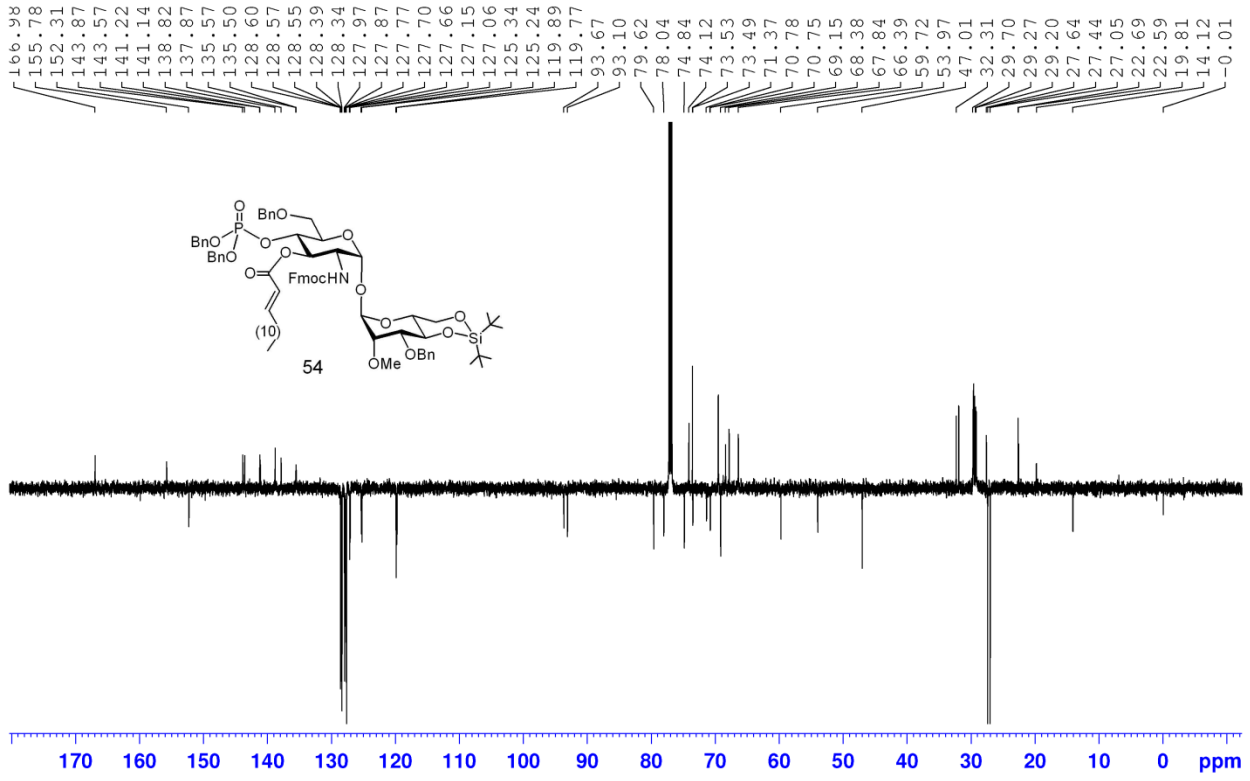

5.27 5.27 5.25 5.24 5.22 5.18 5.11 5.05 5.03 4.98 4.97 4.95 4.94 4.82 4.80
4.51 4.49 4.47 4.46 4.44 4.43 4.42 4.41 4.40 4.33 4.32 4.30 4.20 4.18 4.17 4.15 4.13 4.12 4.06 4.04 3.98 3.96 3.94 3.80 3.78 3.76 3.74 3.73 3.62 3.61 3.60 3.59
3.39 3.38
BnO
BnO
BnO
FmocHN
(10)
(12)
52
OMe
OBn
Si
5.3 5.2 5.1 5.0 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 ppm
0.86 0.86 0.93 1.00 0.96 1.08 4.15 0.99 4.10 1.03 1.85 1.84 1.01 4.01 1.00 4.02

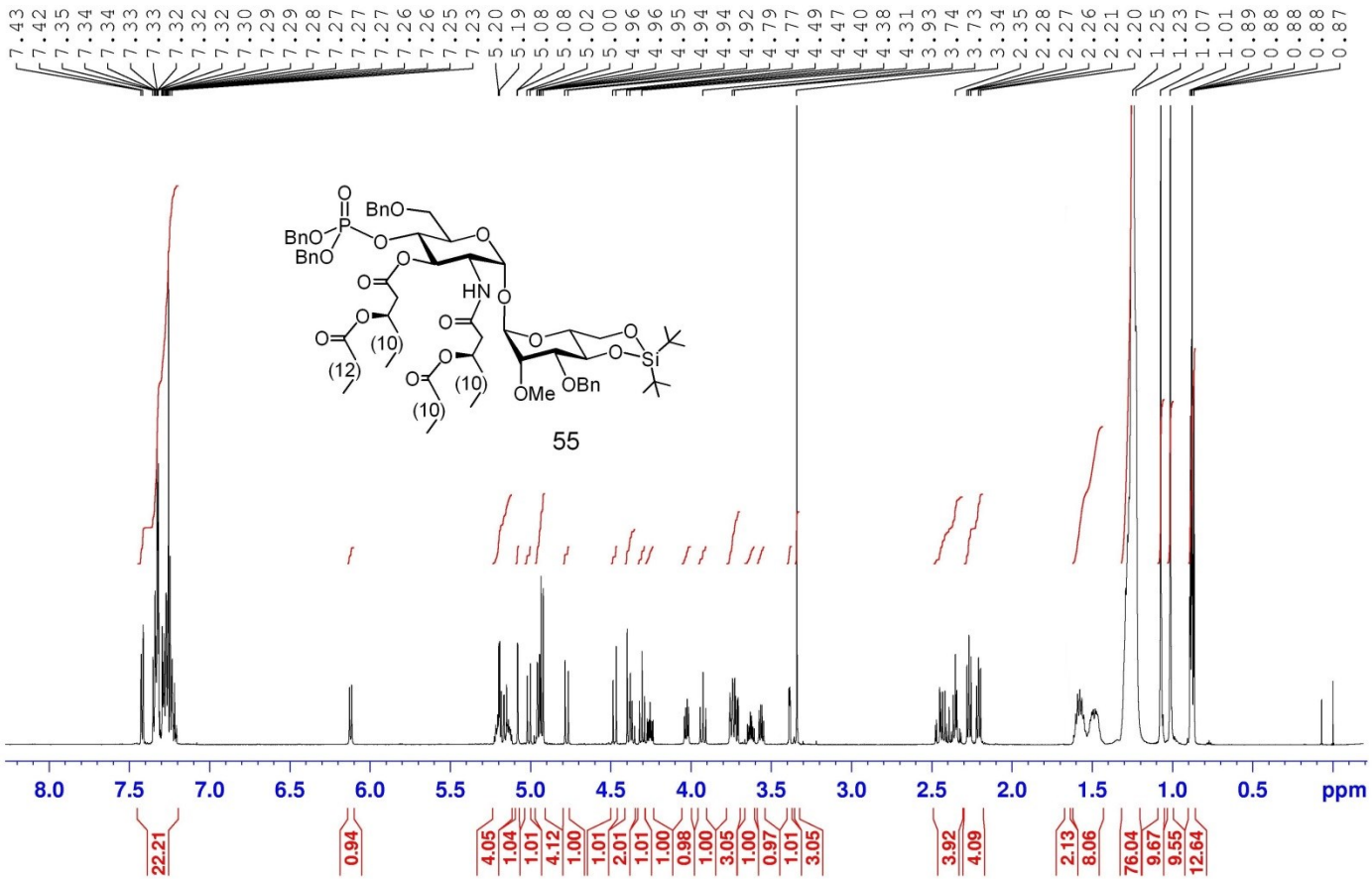

173.23
171.16
155.91
143.74
143.66
141.22
141.19
138.83
137.87
135.55
135.51
127.21
125.29
125.18
94.02
93.25
78.15
77.21
77.00
76.79
74.84
74.23
73.67
73.63
73.51
71.21
70.71
70.67
69.80
69.78
69.76
69.72
69.21
68.36
67.92
66.39
59.69
53.80
47.01
38.96
34.37
34.09
31.91
29.68
29.65
29.62
29.52
29.49
29.38
29.35
29.30
29.17
24.98
22.68
22.59
19.79
BnO
BnO
BnO
FmocHN
(10)
(12)
52
OMe
OBn
Si
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

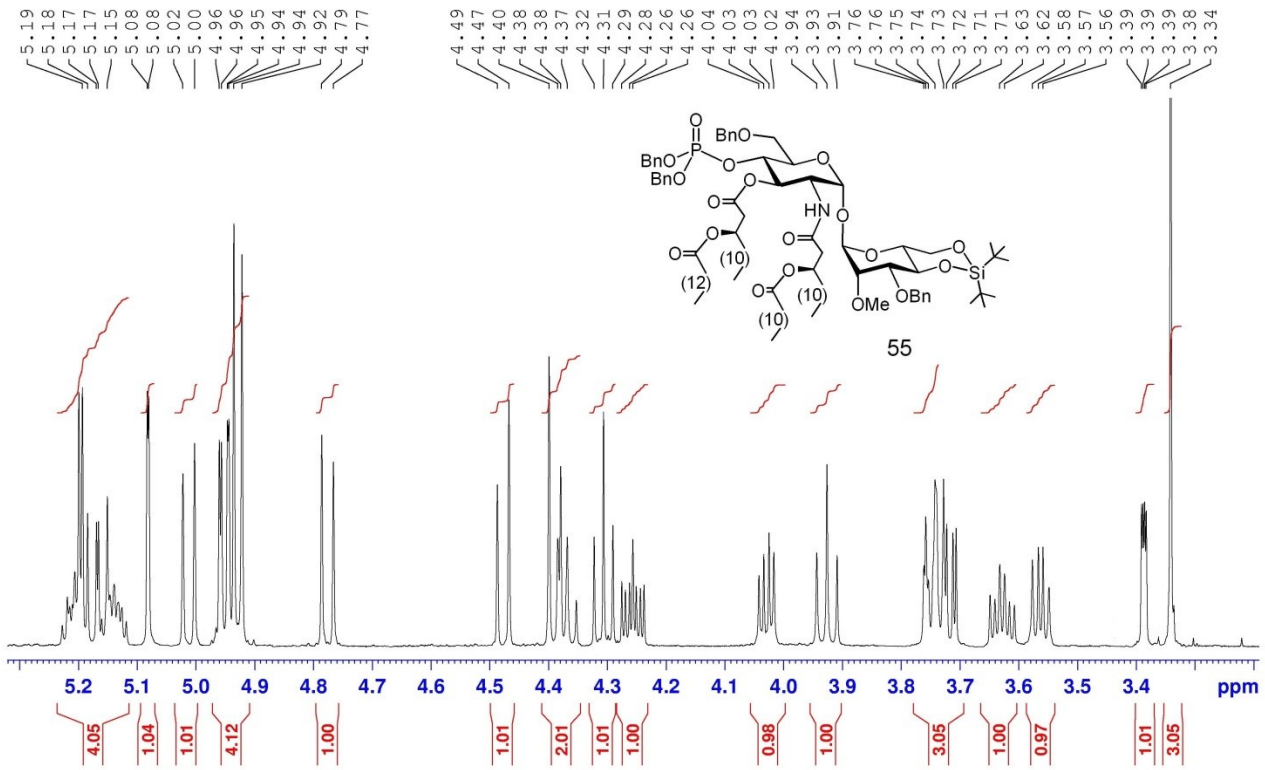

53
FmocHN
(10)
BnO
OBn
OMe
Si
ppm

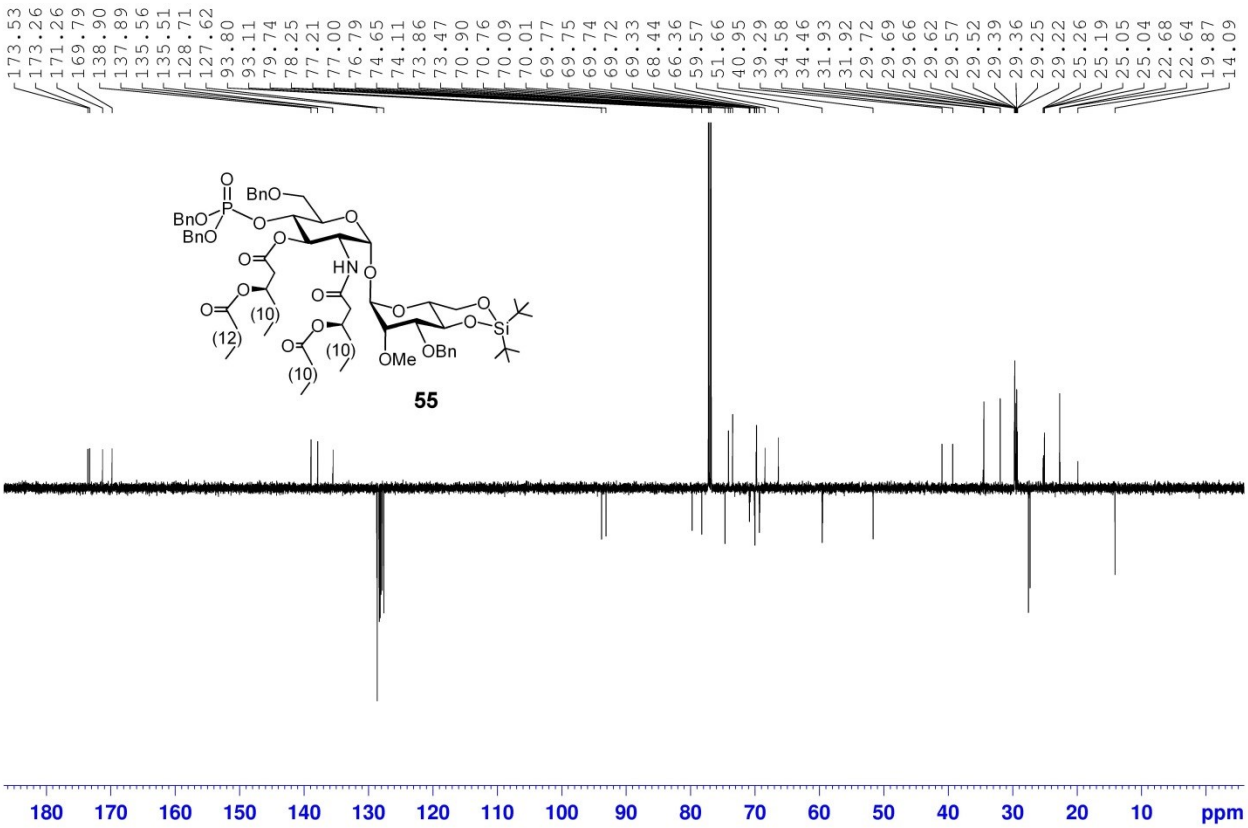

53
FmocHN
(10)
BnO
OBn
OMe
Si
ppm

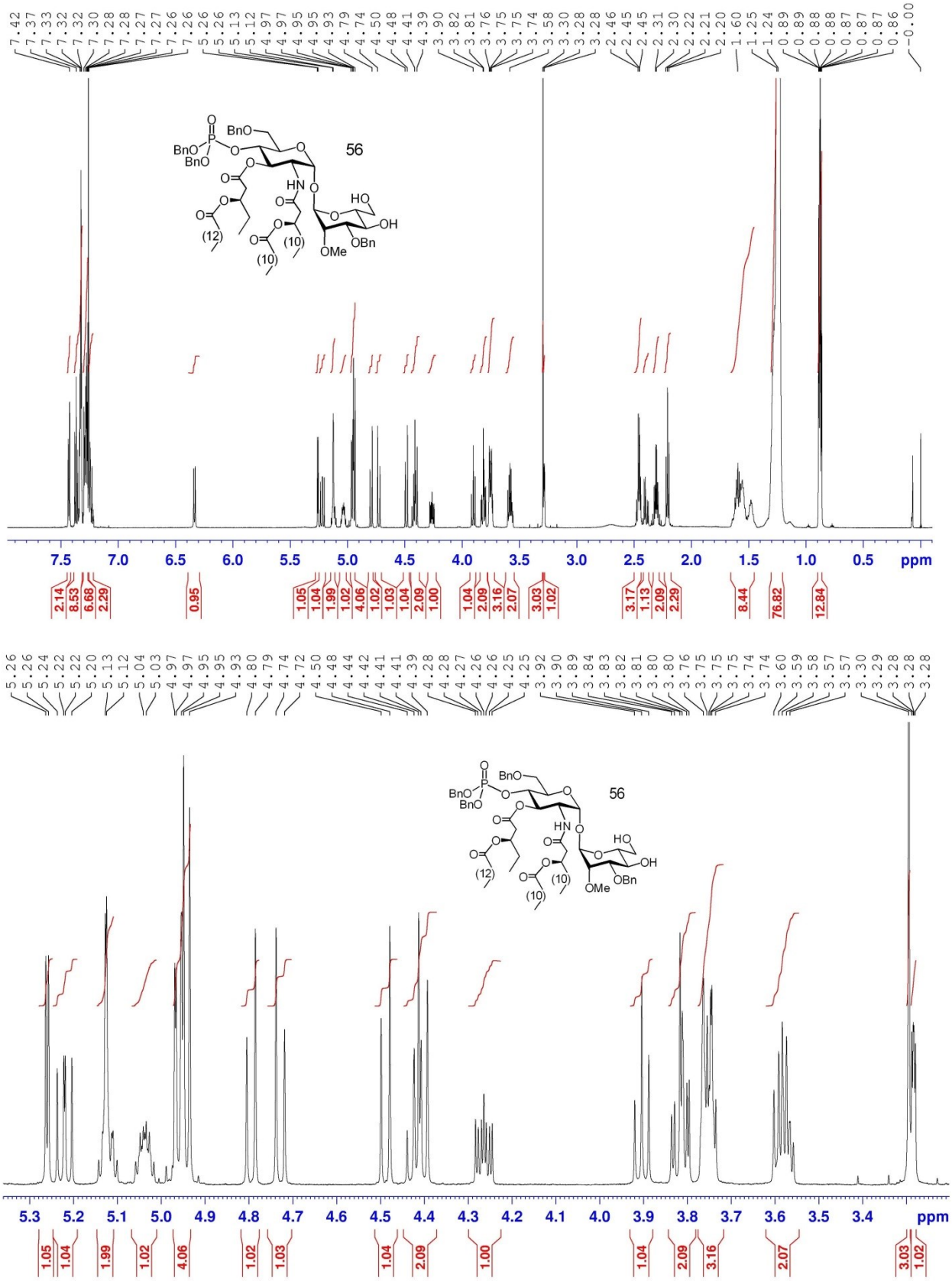

54
FmocHN
BnO
OBn
OMe
ppm

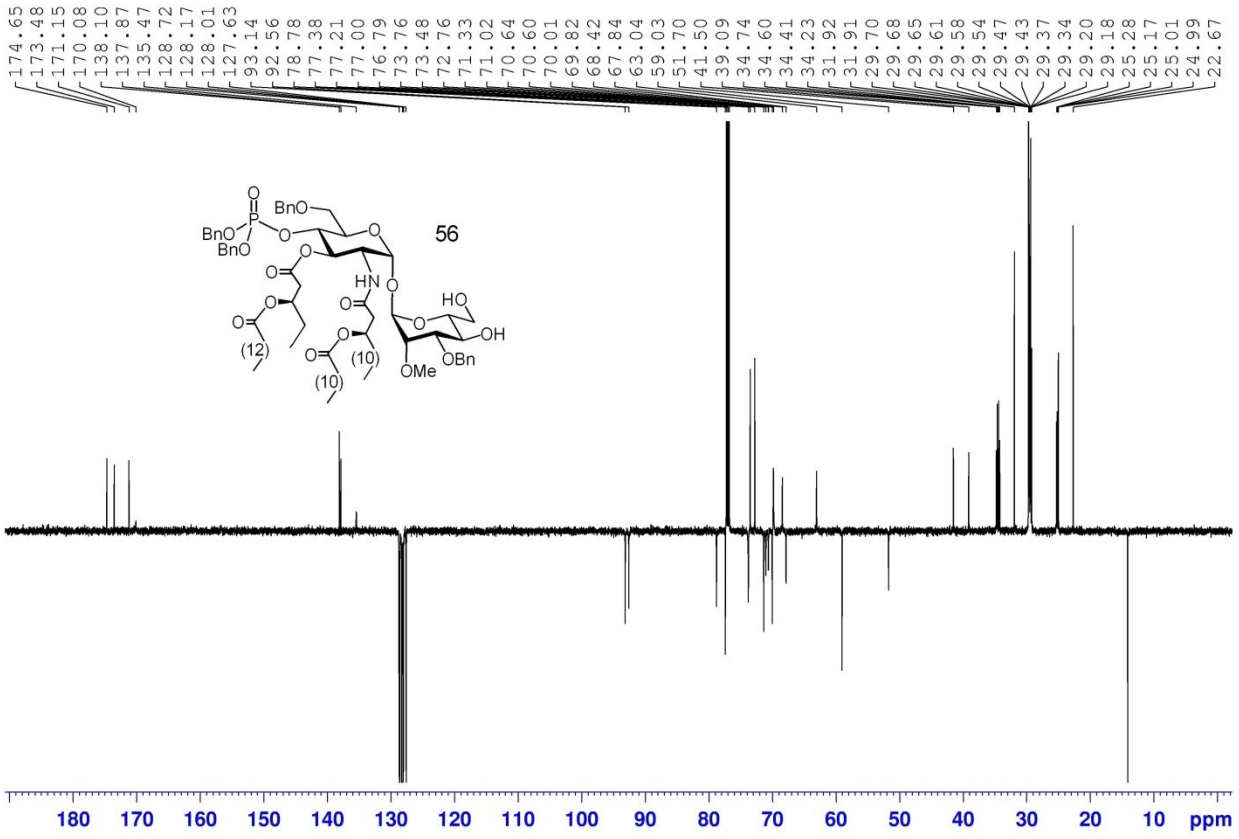

54
FmocHN
BnO
OBn
OMe
ppm

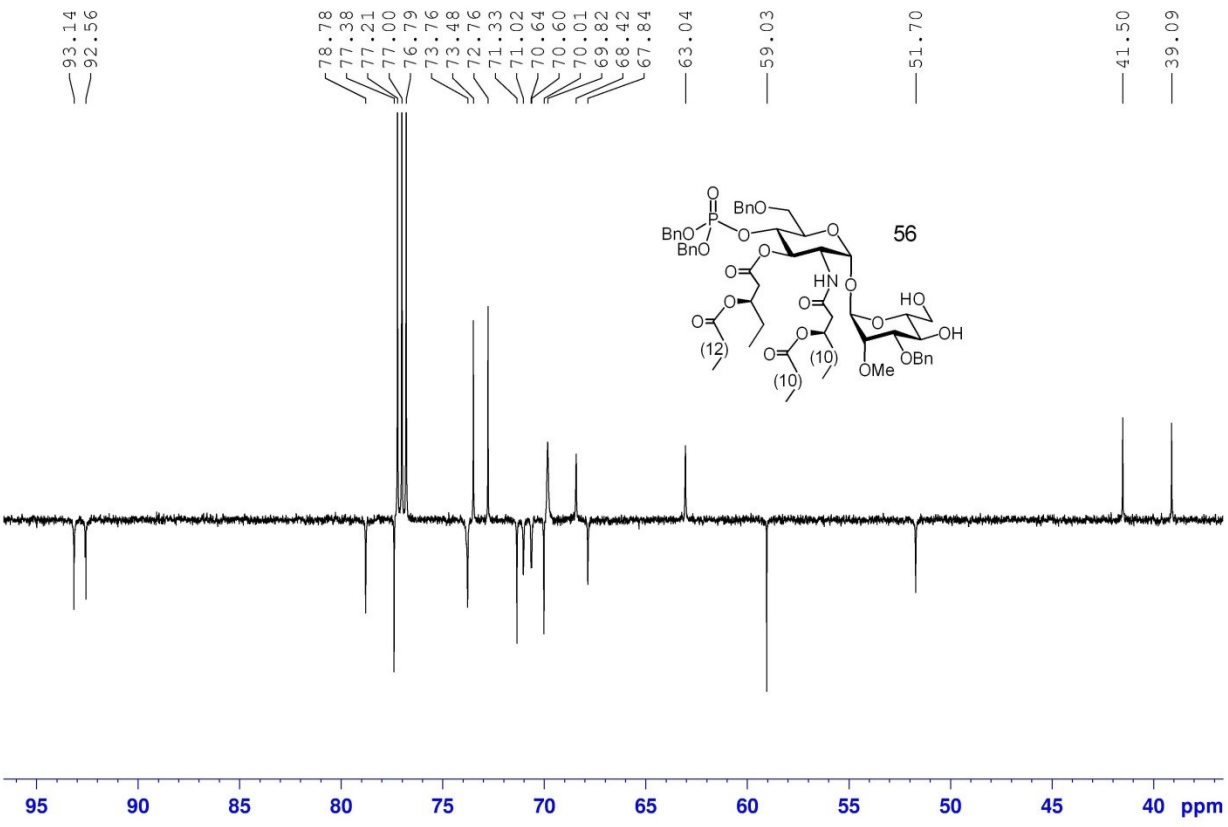

7.43 7.42 7.35 7.34 7.34 7.33 7.33 7.32 7.32 7.32 7.30 7.29 7.29 7.28 7.27 7.27 7.27 7.26 7.26 7.25 7.23 5.20 5.19 5.08 5.08 5.02 5.00 4.96 4.96 4.95 4.94 4.94 4.92 4.79 4.77 4.49 4.47 4.40 4.38 4.31 3.93 3.74 3.73 3.34 2.35 2.28 2.27 2.26 2.21 2.20 1.25 1.23 1.07 1.01 0.89 0.88 0.88 0.88 0.87
BnO
BnO
BnO
HN
(10)
(12)
(10)
(10)
OMe
OBn
Si
55
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 ppm
22.21 0.94 4.05 1.04 1.01 4.12 1.00 1.01 2.01 1.01 1.00 0.98 1.00 3.05 1.00 0.97 1.01 3.05 3.92 4.09 2.13 8.06 76.04 9.67 9.55 12.64

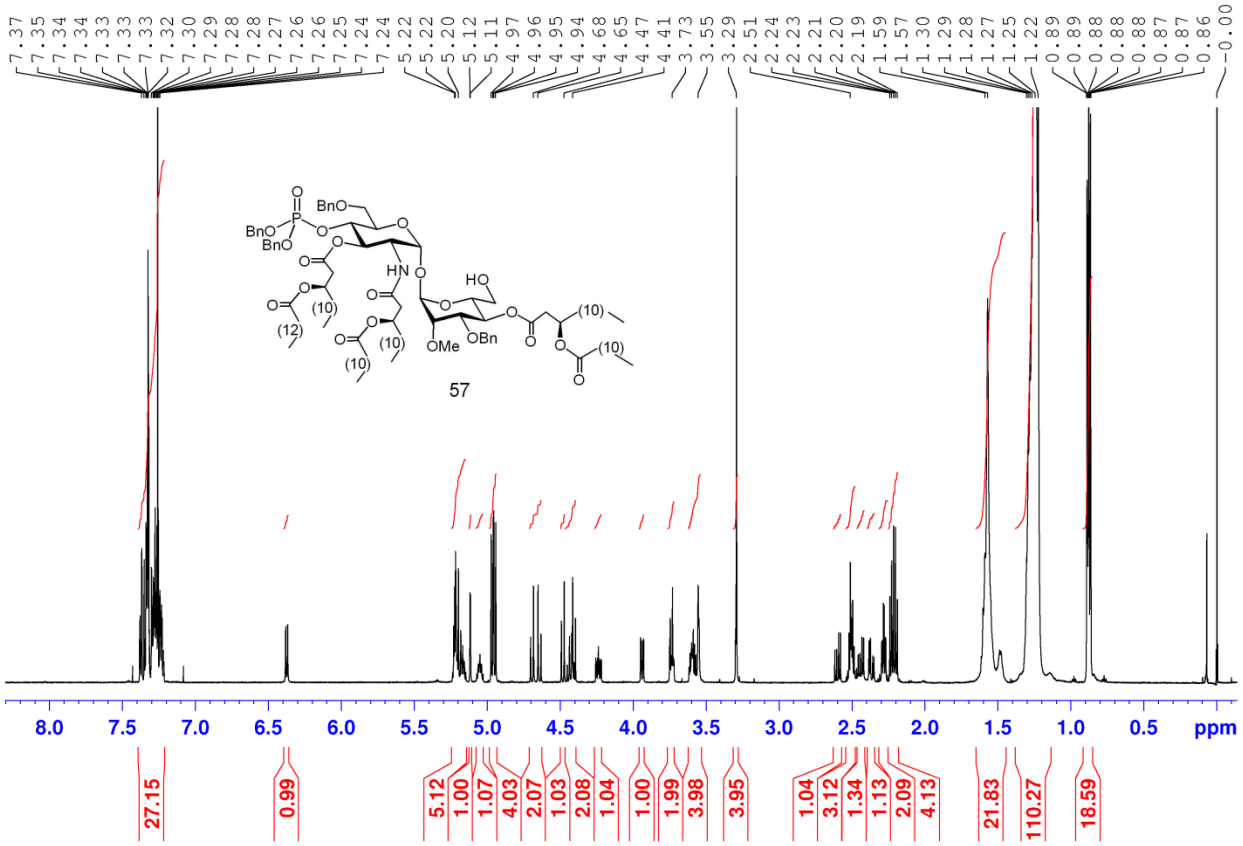

5.19 5.18 5.17 5.17 5.15 5.08 5.08 5.02 5.00 4.96 4.96 4.95 4.94 4.94 4.92 4.79 4.77
4.49 4.47 4.40 4.38 4.38 4.37 4.32 4.31 4.29 4.28 4.26 4.26 4.04 4.03 4.03 4.02 3.94 3.93 3.91 3.76 3.76 3.75 3.74 3.73 3.72 3.71 3.71 3.63 3.62 3.58 3.57 3.56 3.39 3.39 3.39 3.38 3.34
BnO
BnO
BnO
HN
(10)
(12)
(10)
(10)
OMe
OBn
Si
55
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 ppm
4.05 1.04 1.01 4.12 1.00 1.01 2.01 1.01 1.00 0.98 1.00 3.05 1.00 0.97 1.01 3.05

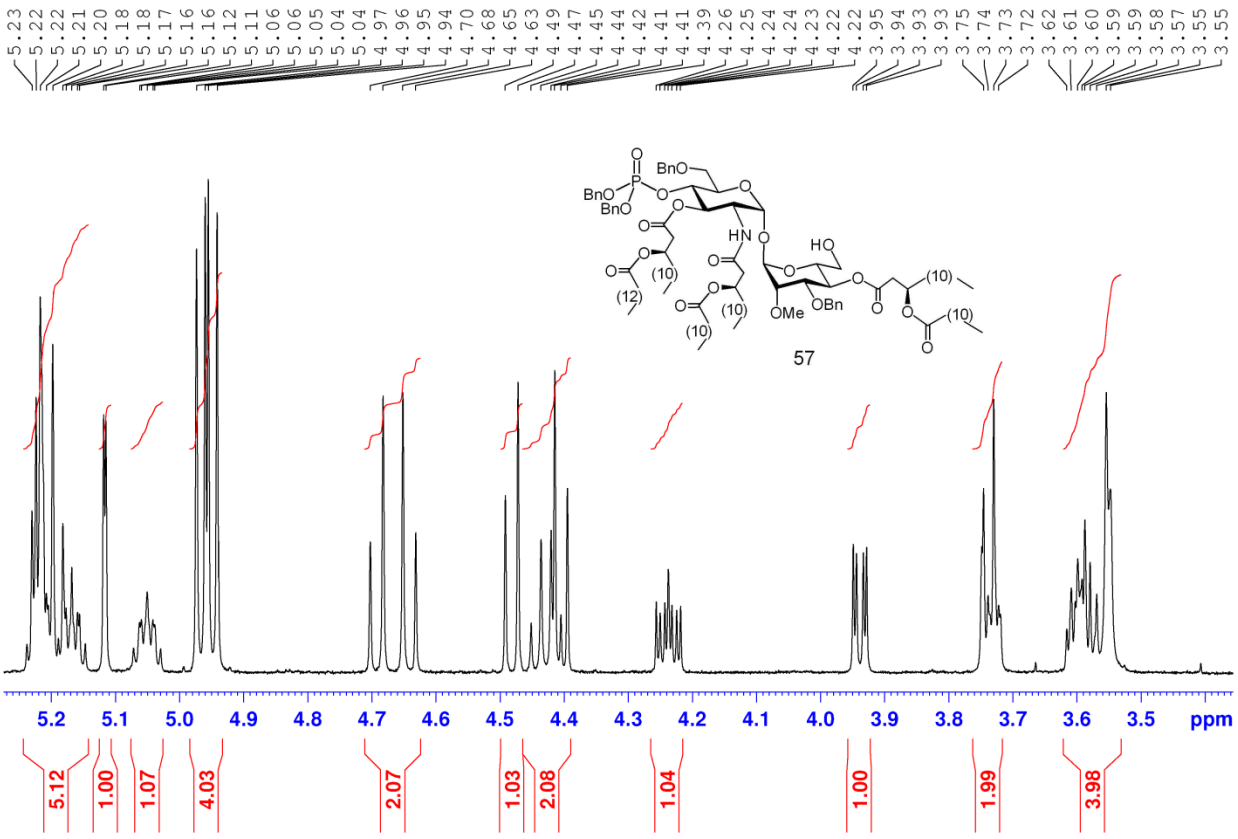

173.53 173.26 171.26 169.79 138.90 137.89 135.56 135.51 128.71 127.62 93.80 93.11 79.74 78.25 77.21 77.00 76.79 74.65 74.11 73.86 73.47 70.90 70.76 70.09 70.01 69.77 69.75 69.74 69.72 69.33 68.44 66.36 59.57 51.66 40.95 39.29 34.58 34.46 31.93 31.92 29.72 29.69 29.66 29.62 29.57 29.52 29.39 29.36 29.25 29.22 25.26 25.19 25.05 25.04 22.68 22.64 19.87 14.09
BnO
BnO
BnO
HN
(10)
(12)
(10)
(10)
OMe
OBn
Si
55
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

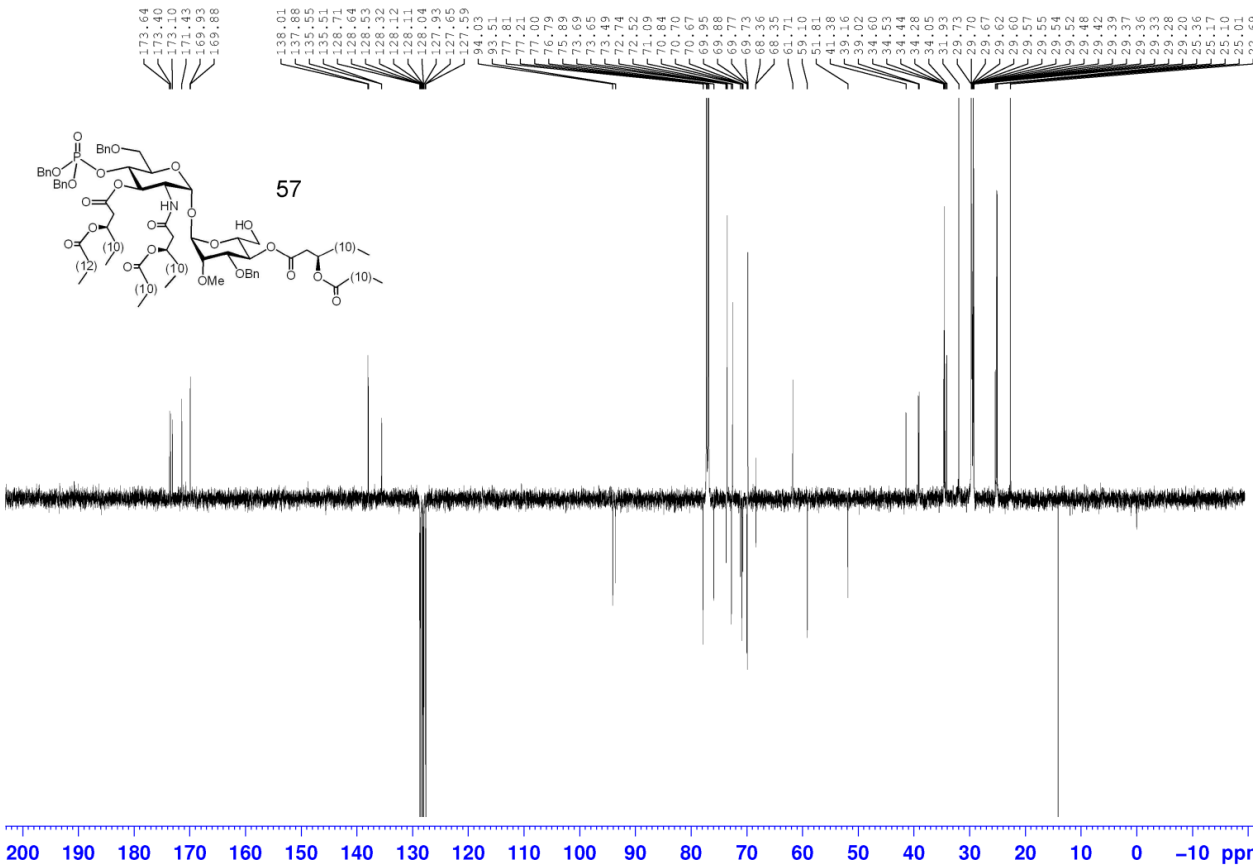

56
56

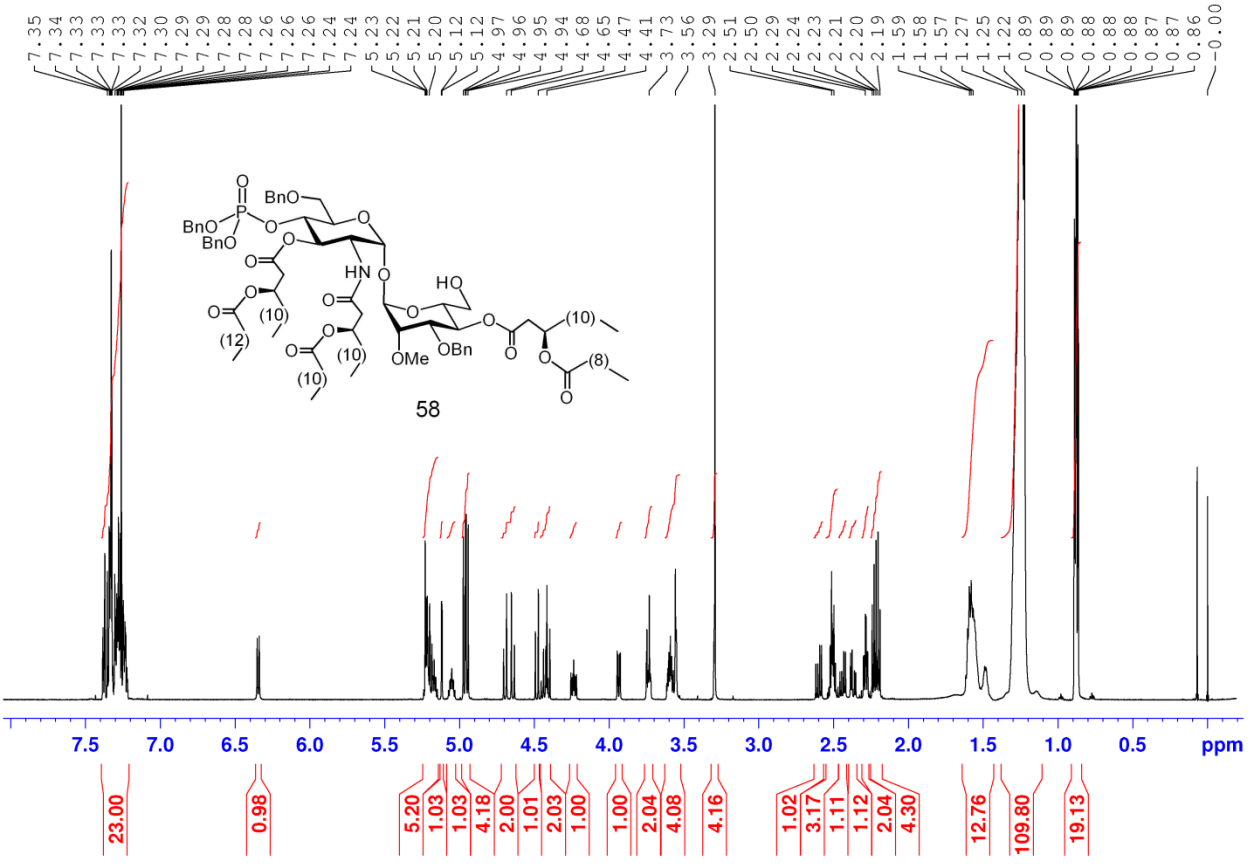

174.65
173.48
171.15
170.08
138.10
137.87
135.47
128.72
128.17
128.01
127.63
93.14
92.56
78.78
77.38
77.21
77.00
76.79
73.76
73.48
72.76
71.33
71.02
70.64
70.60
70.01
69.82
68.42
67.84
63.04
59.03
51.70
41.50
39.09
34.74
34.60
34.41
34.23
31.92
31.91
29.70
29.68
29.65
29.61
29.58
29.54
29.47
29.43
29.37
29.34
29.20
29.18
25.28
25.17
25.01
24.99
22.67
56
BnO
BnO
BnO
HN
HO
OH
OBn
OMe
(12)
(10)
(10)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

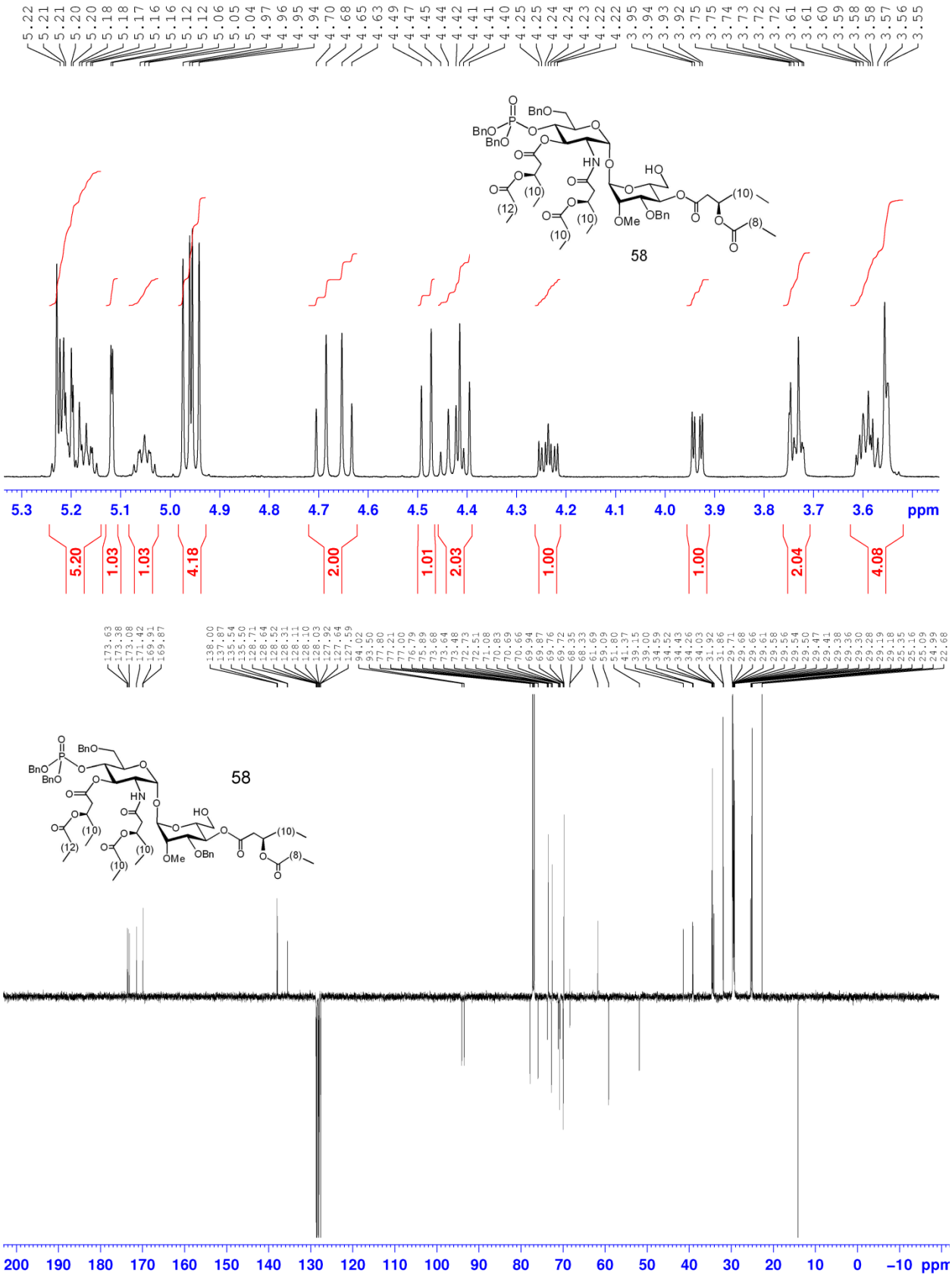

93.14
92.56
78.78
77.38
77.21
77.00
76.79
73.76
73.48
72.76
71.33
71.02
70.64
70.60
70.01
69.82
68.42
67.84
63.04
59.03
51.70
41.50
39.09
56
BnO
BnO
BnO
HN
HO
OH
OBn
OMe
(12)
(10)
(10)
95 90 85 80 75 70 65 60 55 50 45 40 ppm

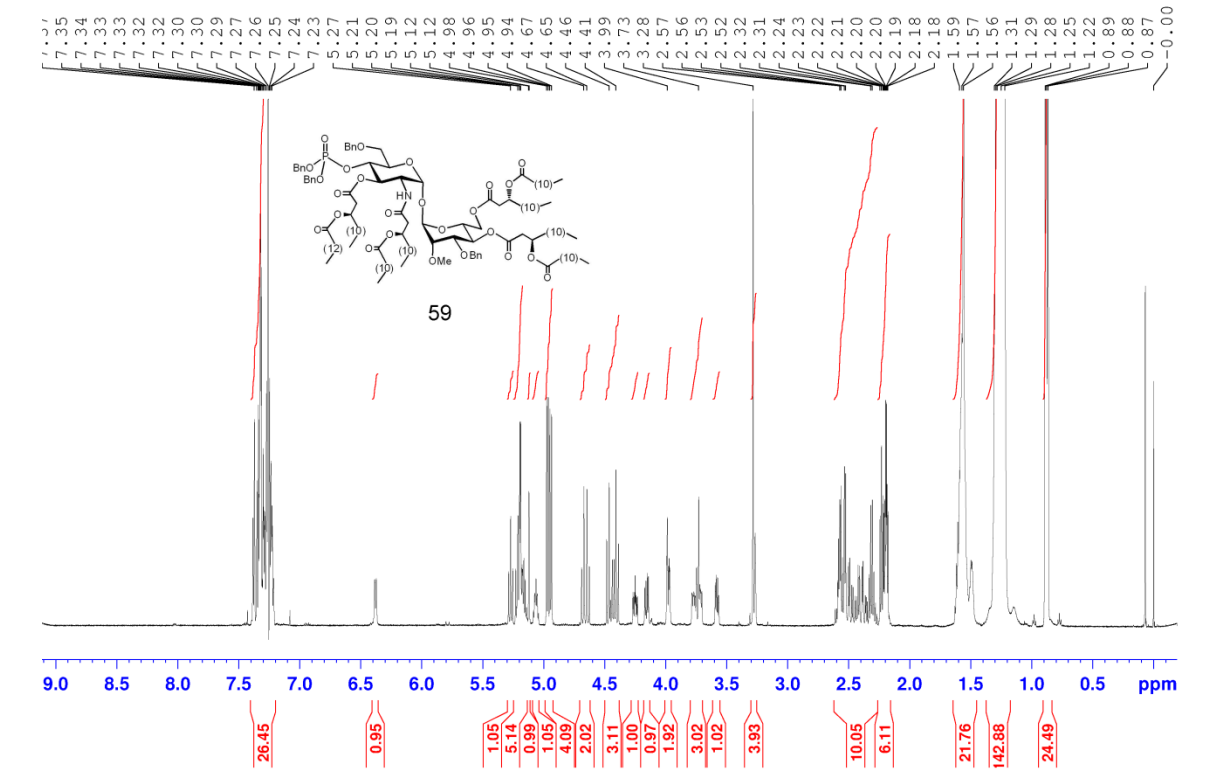

7.37 7.35 7.34 7.34 7.33 7.33 7.33 7.32 7.30 7.29 7.28 7.28 7.27 7.26 7.26 7.25 7.24 7.24 5.22 5.22 5.20 5.12 5.11 4.97 4.96 4.95 4.94 4.68 4.65 4.47 4.41 3.73 3.55 3.29 2.51 2.24 2.23 2.21 2.20 2.19 1.59 1.57 1.30 1.29 1.28 1.27 1.25 1.22 0.89 0.89 0.88 0.88 0.88 0.87 0.87 0.86 -0.00
BnO
BnO
BnO
HN
HO
OMe
OBn
(10)
(12)
57
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 ppm
27.15 0.99 5.12 1.00 1.07 4.03 2.07 1.03 2.08 1.04 1.00 1.99 3.98 3.95 1.04 3.12 1.34 1.13 2.09 4.13 21.83 110.27 18.59

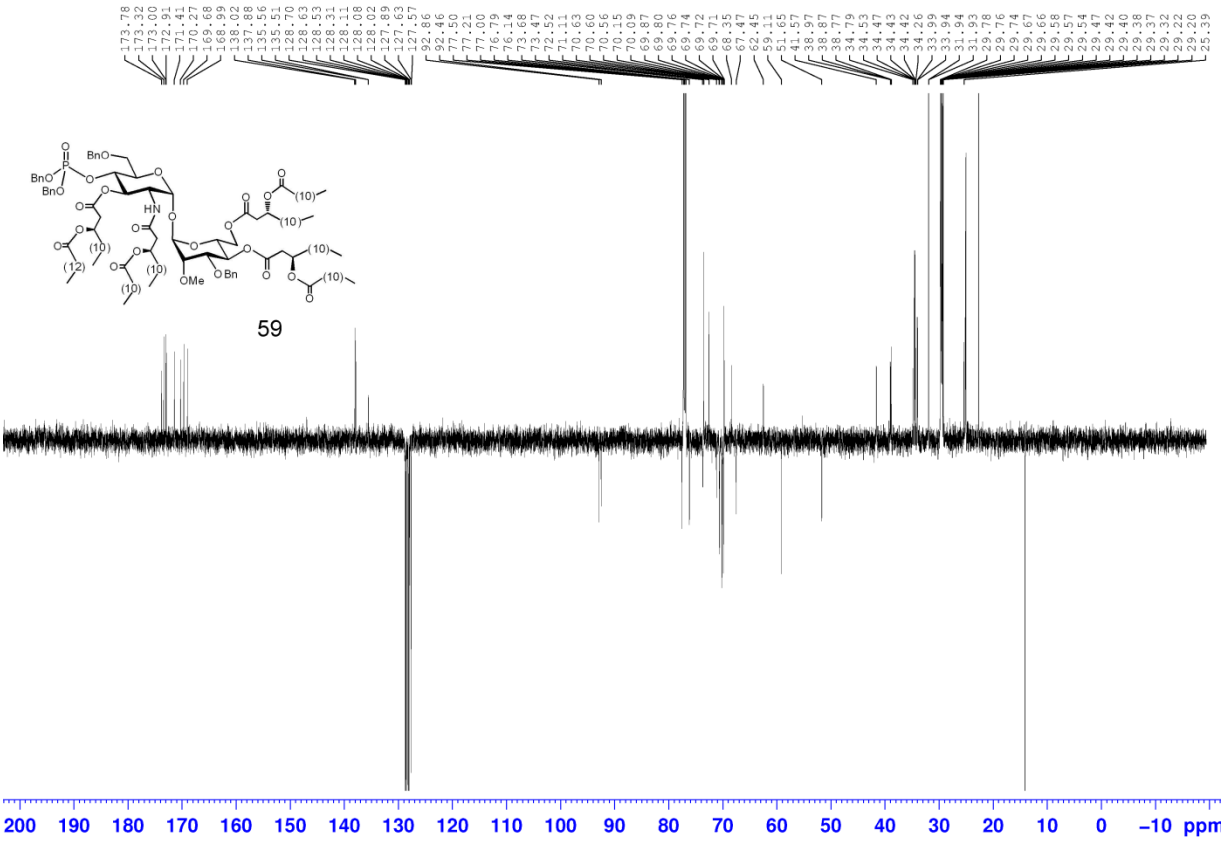

5.23 5.22 5.22 5.21 5.20 5.18 5.17 5.16 5.16 5.12 5.11 5.06 5.06 5.05 5.04 5.04 4.97 4.96 4.95 4.94 4.70 4.68 4.65 4.63 4.49 4.47 4.45 4.44 4.42 4.41 4.41 4.39 4.26 4.25 4.24 4.24 4.23 4.22 4.22 3.95 3.94 3.93 3.93 3.75 3.74 3.73 3.72 3.62 3.61 3.60 3.59 3.59 3.58 3.57 3.55 3.55
BnO
BnO
BnO
HN
HO
OMe
OBn
(10)
(12)
57
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 ppm
5.12 1.00 1.07 4.03 2.07 1.03 2.08 1.04 1.00 1.99 3.98

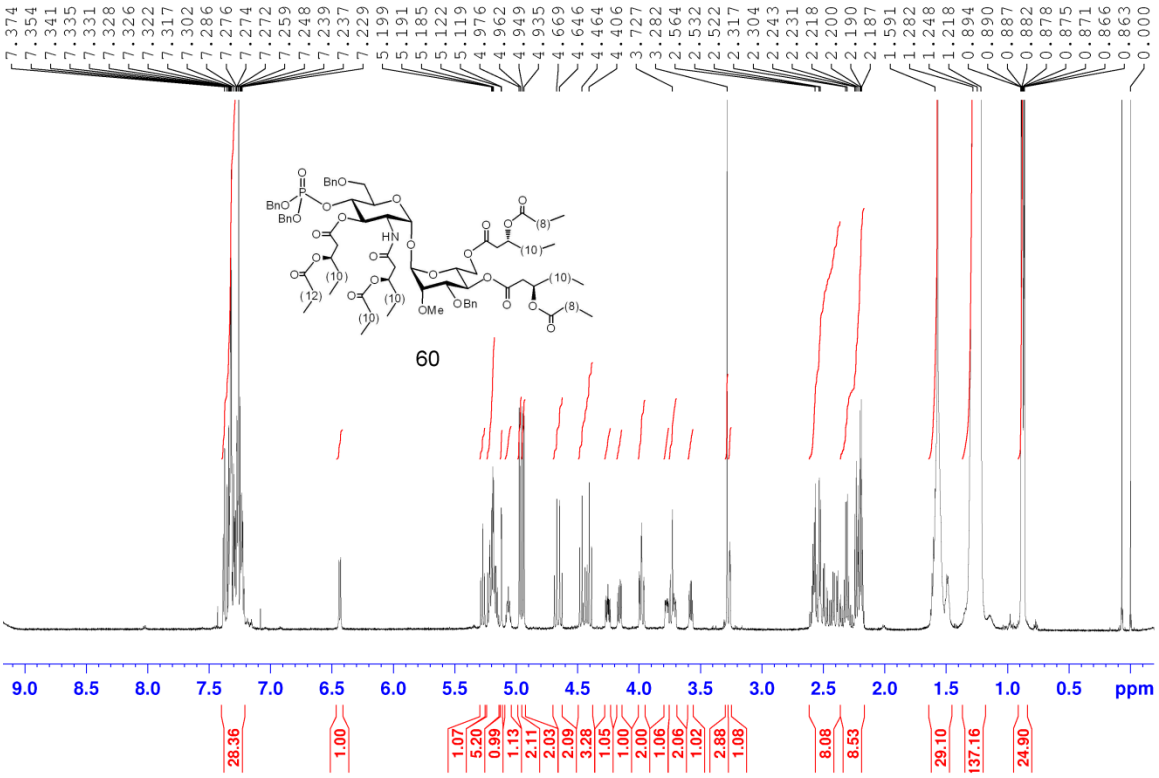

57
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 ppm

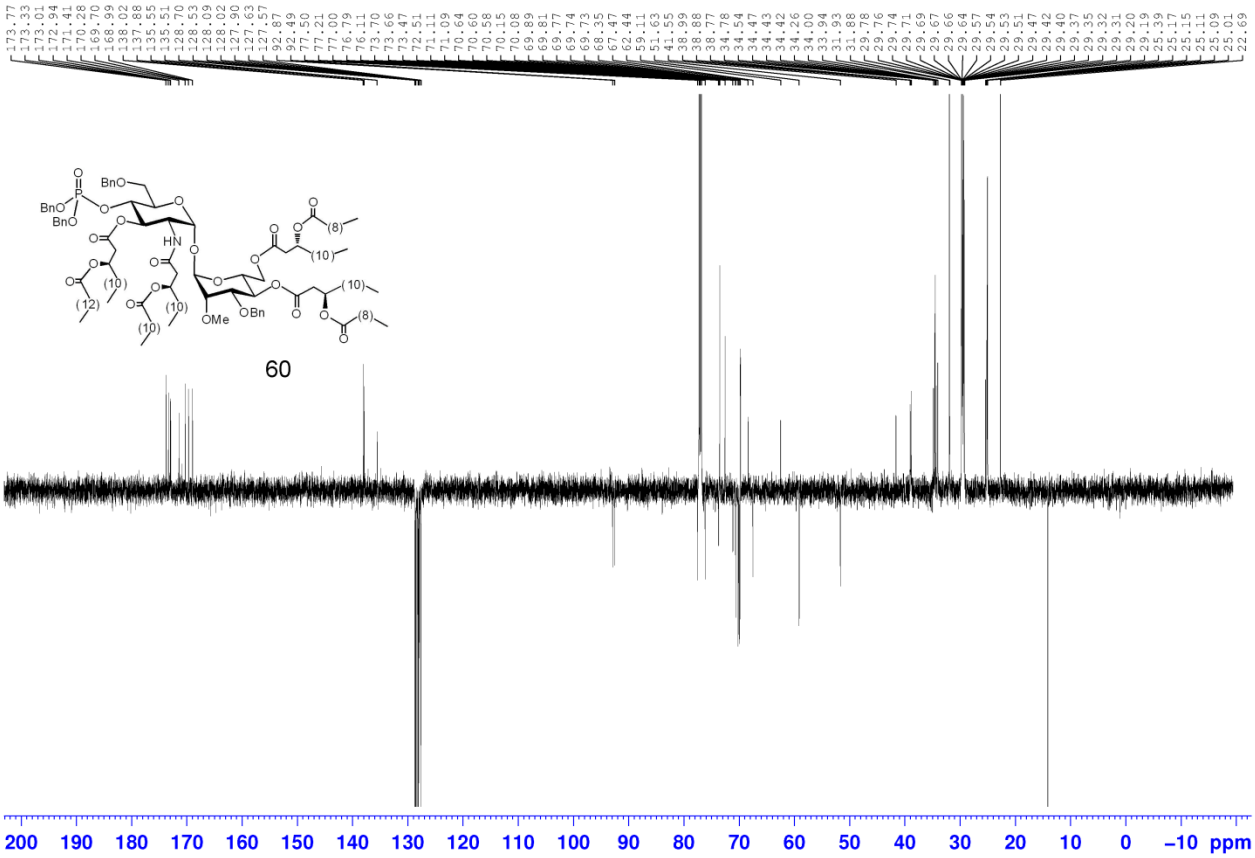

58
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
23.00 0.98 5.20 1.03 1.03 4.18 2.00 1.01 2.03 1.00 1.00 2.04 4.08 4.16 1.02 3.17 1.11 1.12 2.04 4.30 12.76 109.80 19.13

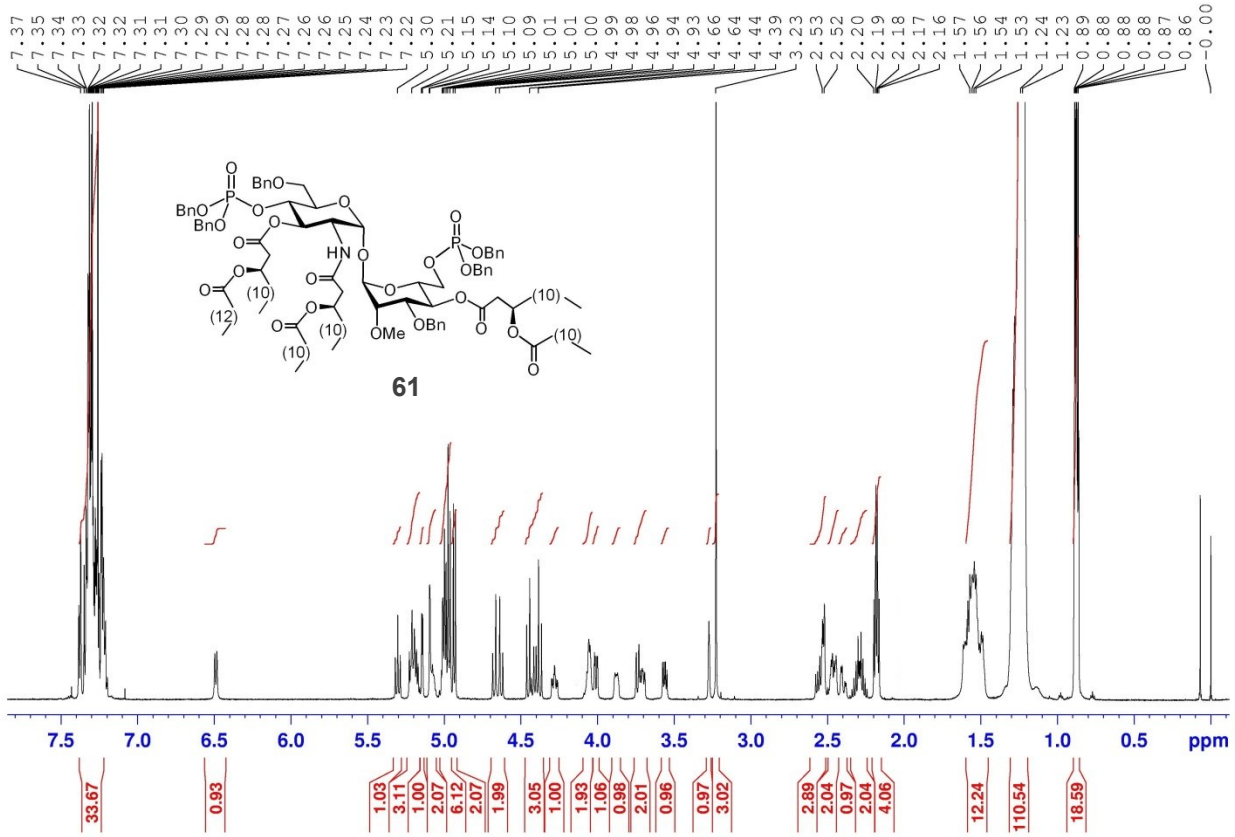

5.22 5.21 5.21 5.20 5.20 5.18 5.18 5.17 5.16 5.16 5.12 5.12 5.06 5.05 5.04 4.97 4.96 4.95 4.94 4.70 4.68 4.65 4.63 4.49 4.47 4.45 4.44 4.42 4.41 4.41 4.40 4.25 4.25 4.24 4.24 4.23 4.22 4.22 3.95 3.94 3.93 3.92 3.75 3.75 3.74 3.73 3.72 3.72 3.61 3.61 3.60 3.59 3.58 3.58 3.57 3.56 3.55
BnO
BnO
BnO
HN
HO
OMe
OBn
(12)
(10)
(8)
58
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 ppm
5.20 1.03 1.03 4.18 2.00 1.01 2.03 1.00 1.00 2.04 4.08
173.63 173.38 173.08 171.42 169.91 169.87
138.00 137.87 135.54 135.50 128.71 128.64 128.52 128.31 128.11 128.10 128.03 127.92 127.64 127.59 94.02 93.50 77.80 77.21 77.00 76.79 75.89 73.68 73.64 73.48 72.73 72.51 71.08 70.83 70.69 70.66 69.94 69.87 69.76 69.72 68.35 68.33 61.69 59.09 51.80 41.37 39.15 39.00 34.59 34.52 34.43 34.26 34.03 31.92 31.86 29.71 29.68 29.66 29.61 29.58 29.56 29.54 29.50 29.47 29.41 29.38 29.36 29.30 29.28 29.19 29.18 25.35 25.16 25.09 24.99 22.68
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 ppm

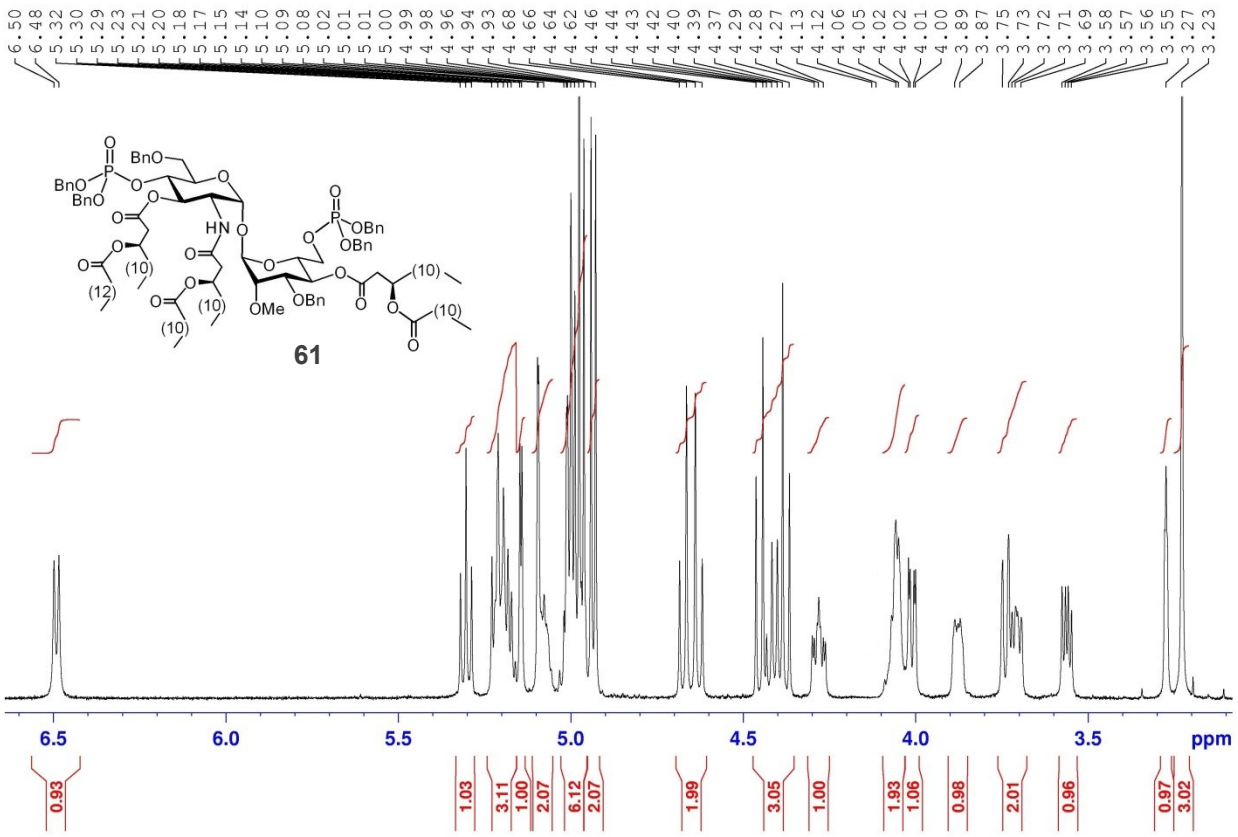

59
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
26.45 0.95 1.05 5.14 0.99 1.05 4.09 2.02 3.11 1.00 0.97 1.92 3.02 1.02 3.93 10.05 6.11 21.76 142.88 24.49

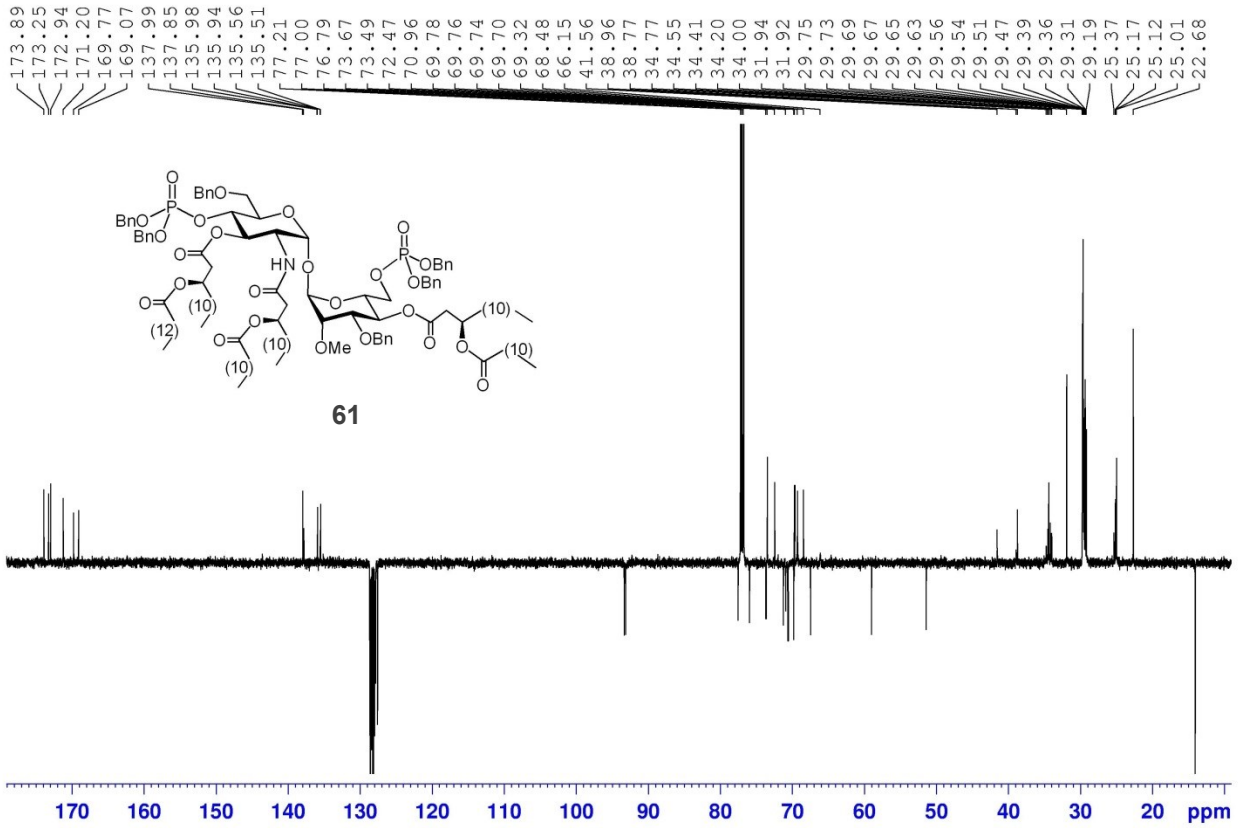

59
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 ppm


60

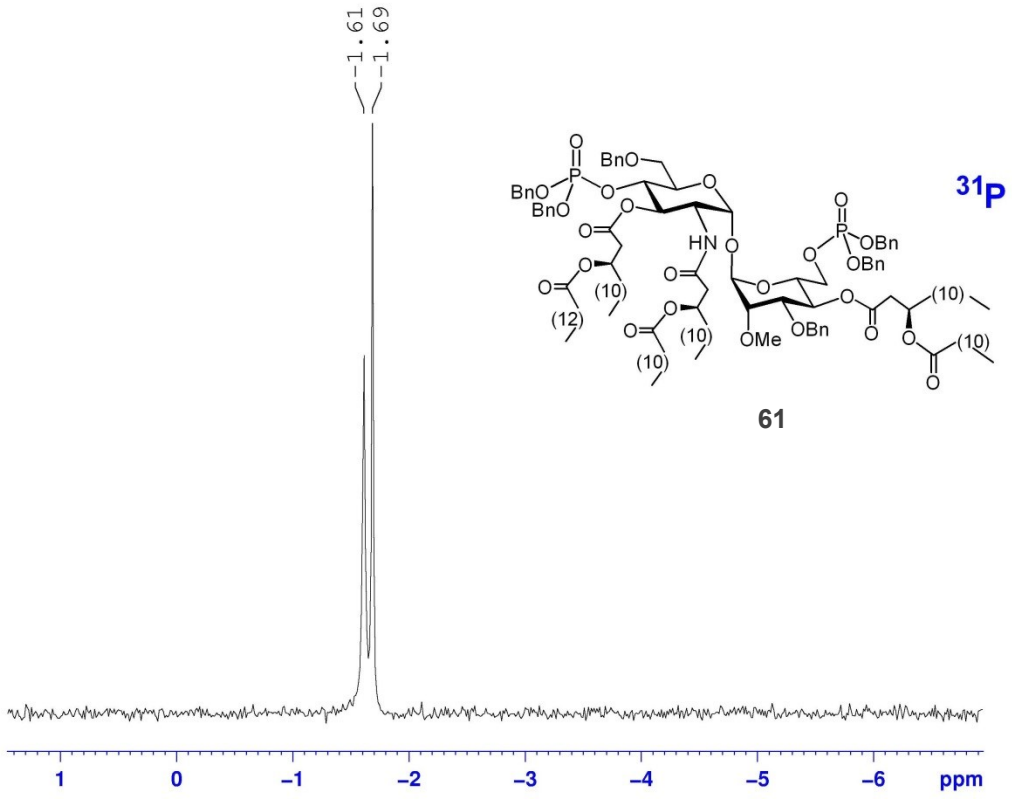

60


61

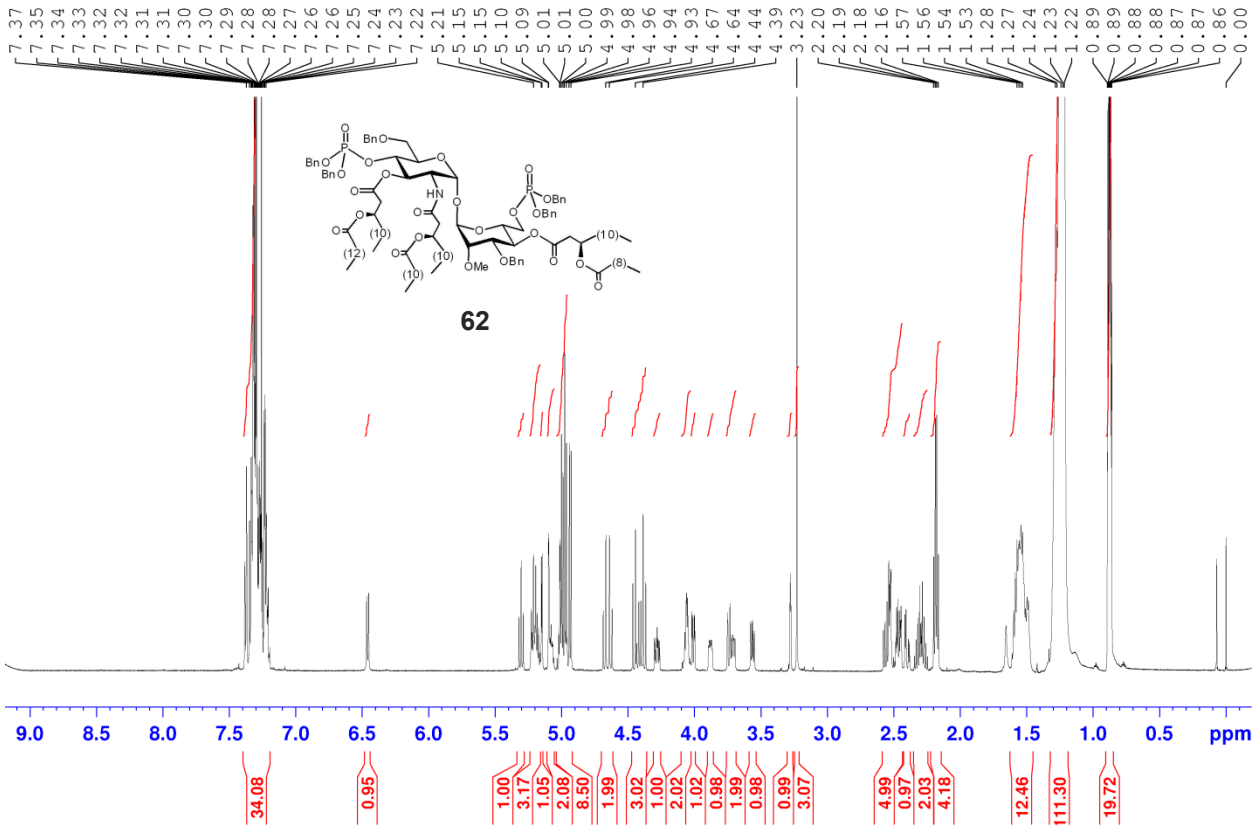

61

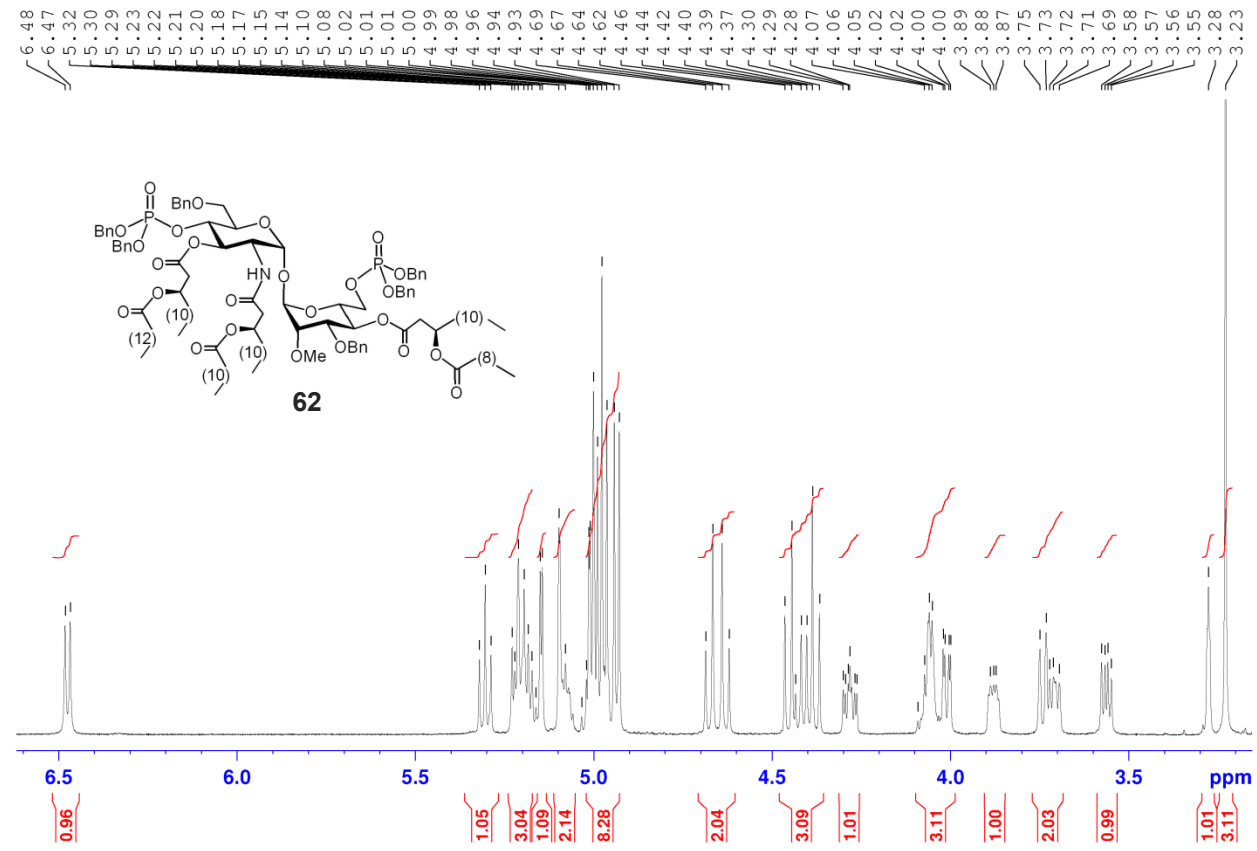

173.89
173.25
172.94
171.20
169.77
169.07
137.99
137.85
135.98
135.94
135.56
135.51
77.21
77.00
76.79
73.67
73.49
72.47
70.96
69.78
69.76
69.74
69.70
69.32
68.48
66.15
41.56
38.96
38.77
34.77
34.55
34.41
34.20
34.00
31.94
31.92
29.75
29.73
29.69
29.67
29.65
29.63
29.56
29.54
29.51
29.47
29.39
29.36
29.31
29.19
25.37
25.17
25.12
25.01
22.68
BnO
BnO
BnO
HN
OBn
OBn
OMe
OBn
(10)
(12)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

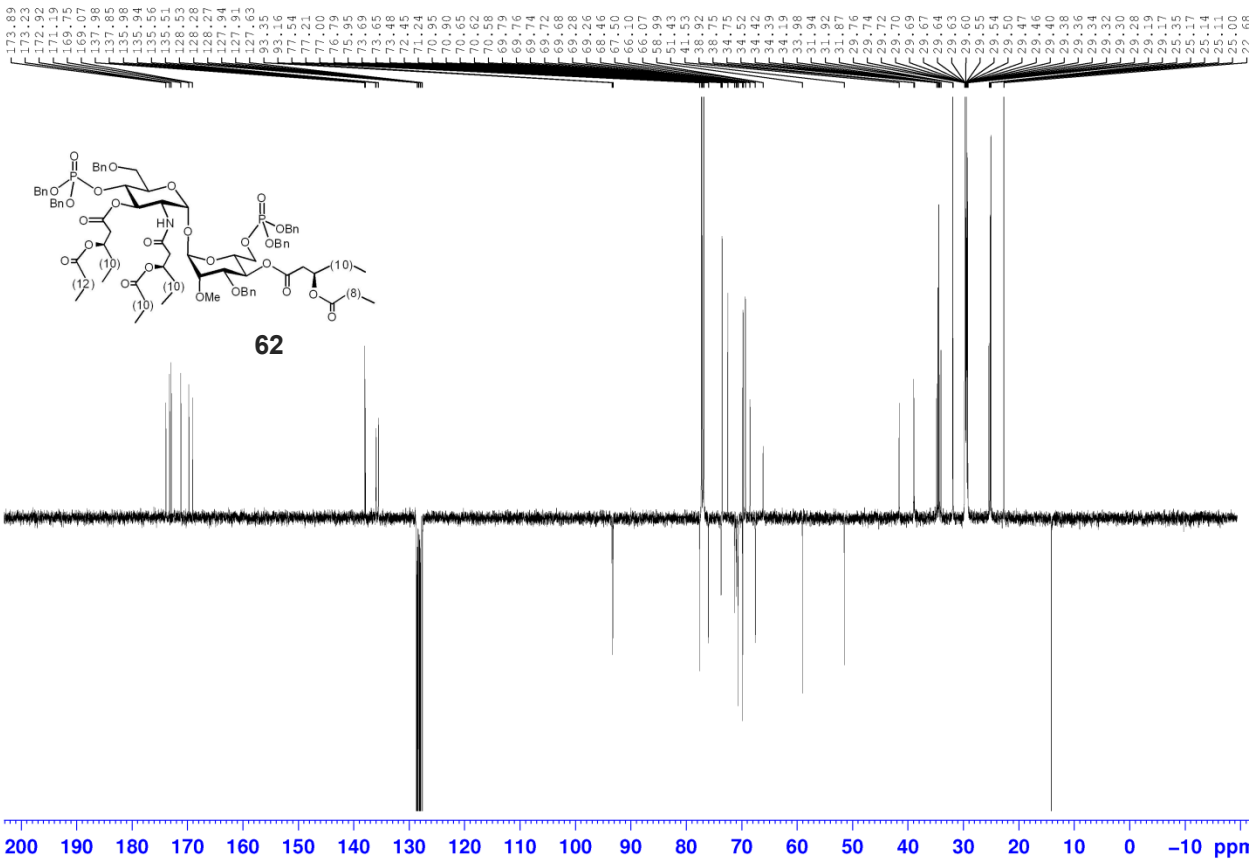
61

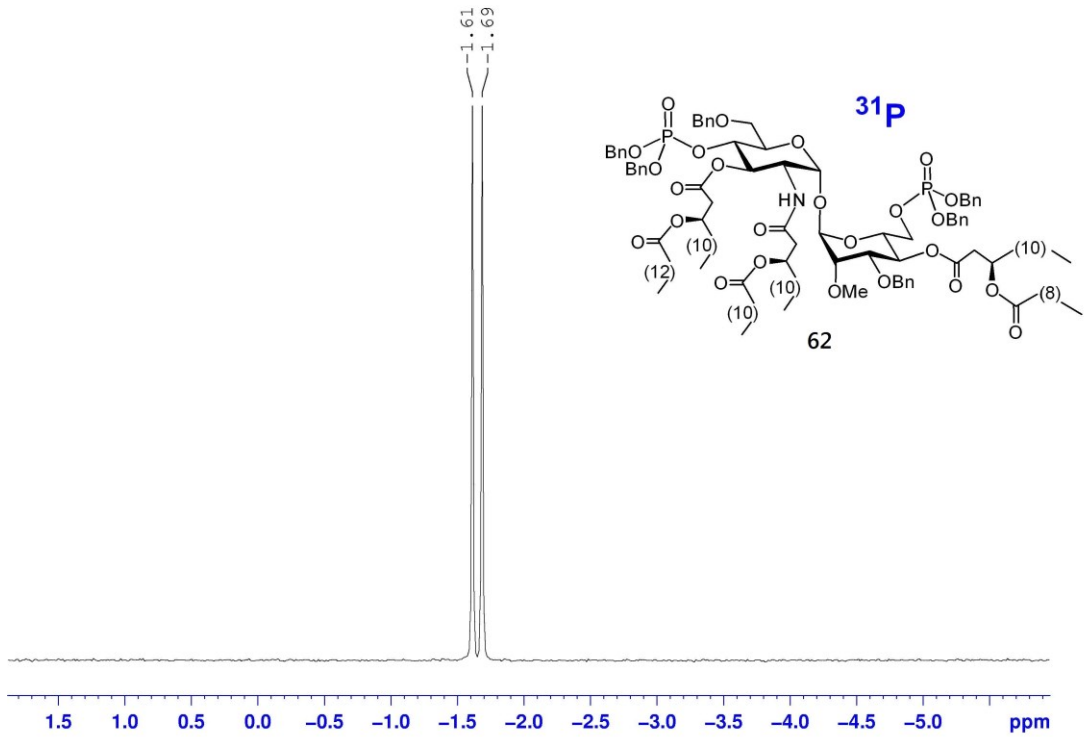

-1.61
-1.69
BnO
BnO
BnO
HN
OBn
OBn
OMe
OBn
(10)
(12)
31P
1
0
–1
–2
–3
–4
–5
–6
ppm

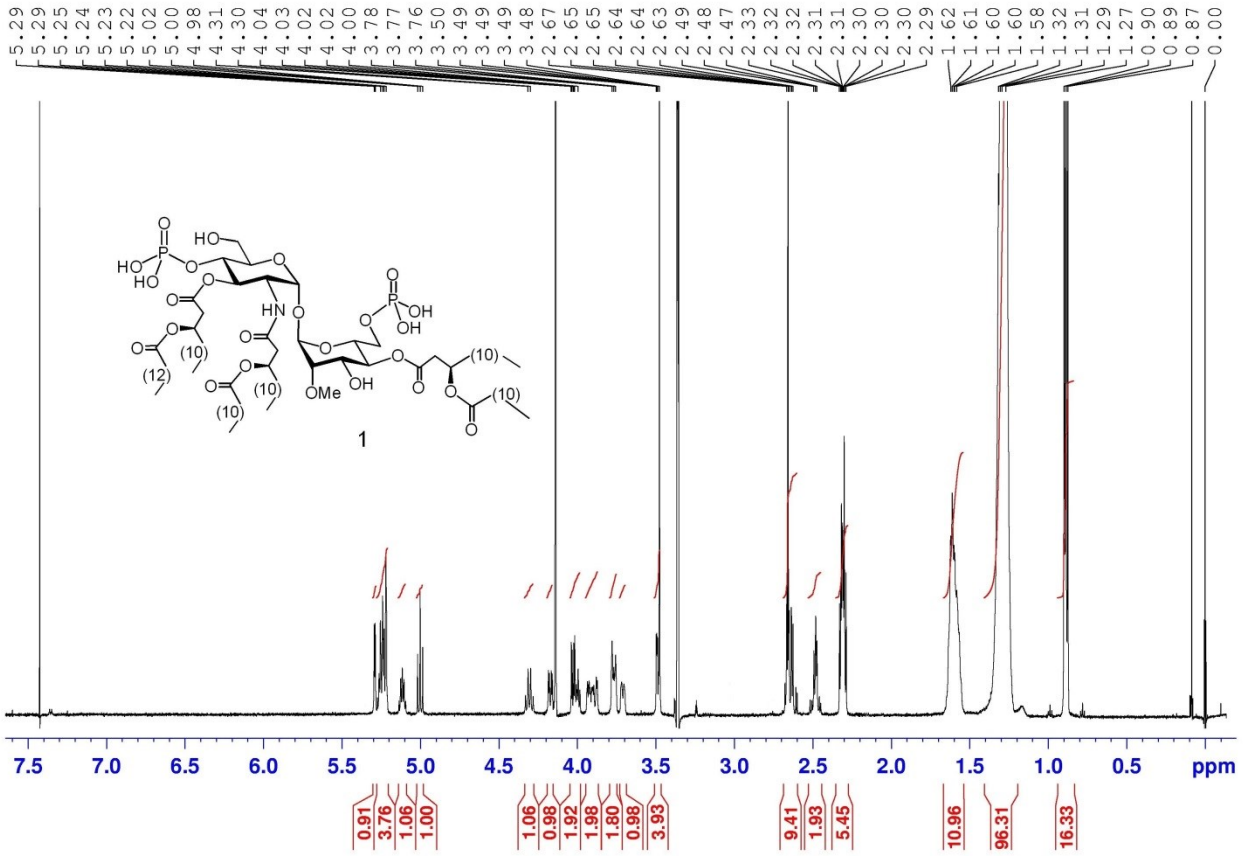
61

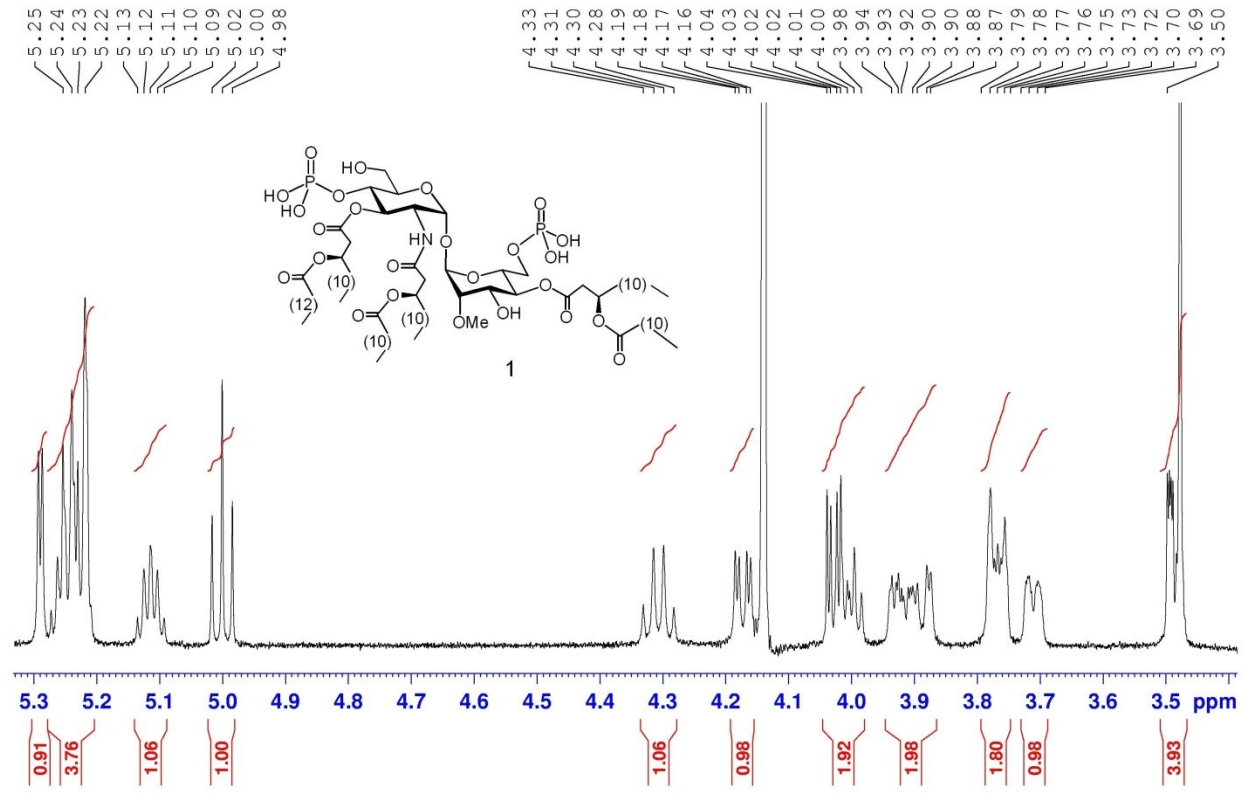

62


62

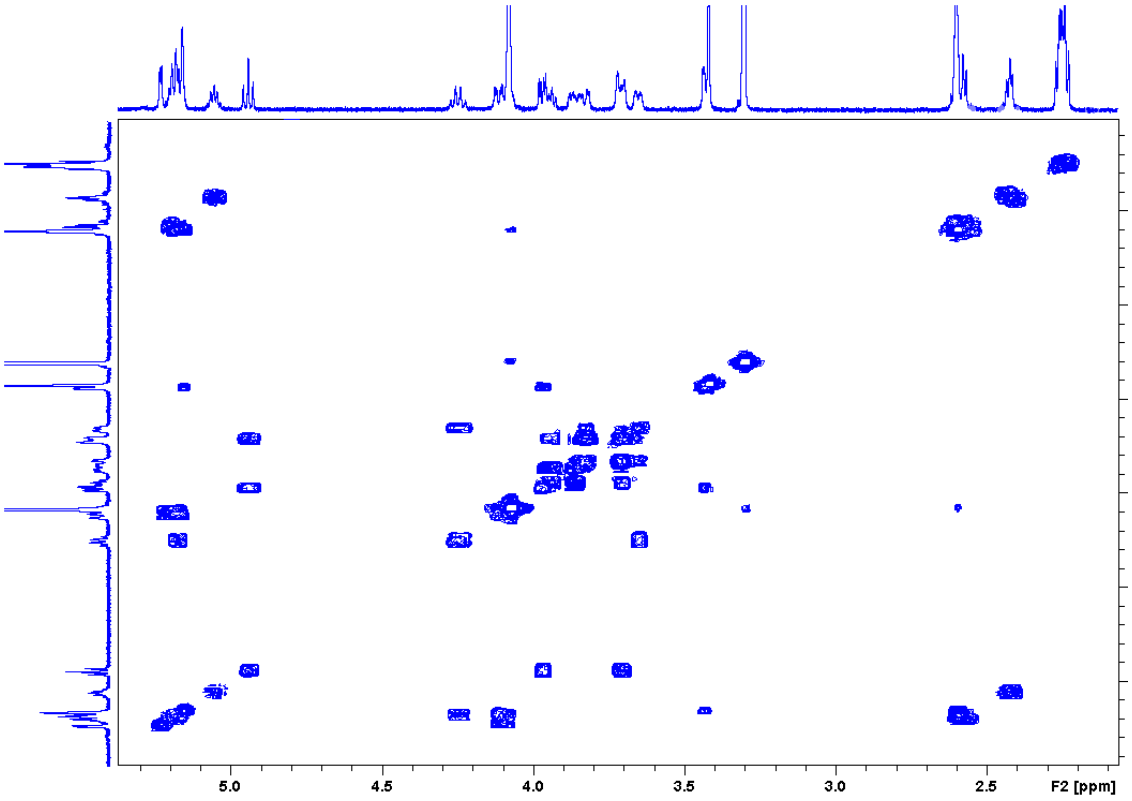

62
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 –10 ppm


31P
62
1.5 1.0 0.5 0.0 –0.5 –1.0 –1.5 –2.0 –2.5 –3.0 –3.5 –4.0 –4.5 –5.0 ppm

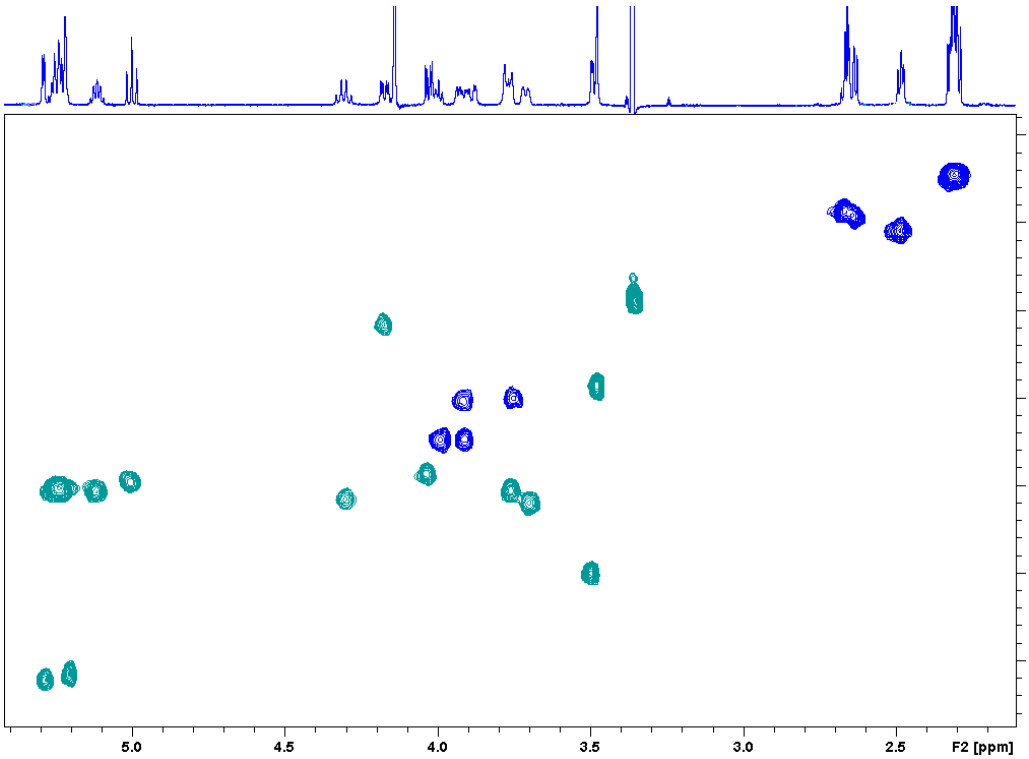

5.29 5.29 5.25 5.24 5.23 5.22 5.02 5.00 4.98 4.31 4.30 4.04 4.03 4.02 4.02 4.00 3.78 3.77 3.76 3.50 3.49 3.49 3.48 2.67 2.65 2.65 2.64 2.64 2.63 2.49 2.48 2.47 2.33 2.32 2.31 2.31 2.30 2.30 2.29 1.62 1.61 1.60 1.60 1.58 1.32 1.31 1.29 1.27 0.90 0.89 0.87 0.00
HO HO HO HN OMe OH (10) (12)
1
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.91 3.76 1.06 1.00 1.06 0.98 1.92 1.98 1.80 0.98 3.93 9.41 1.93 5.45 10.96 96.31 16.33


5.25 5.24 5.23 5.22 5.13 5.12 5.11 5.10 5.09 5.02 5.00 4.98
4.33 4.31 4.30 4.28 4.19 4.18 4.17 4.16 4.04 4.03 4.02 4.02 4.01 4.00 3.98 3.94 3.93 3.92 3.90 3.88 3.87 3.79 3.78 3.77 3.76 3.75 3.73 3.72 3.70 3.69 3.50
HO HO HO HN OMe OH (10) (12)
1
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 ppm
0.91 3.76 1.06 1.00 1.06 0.98 1.92 1.98 1.80 0.98 3.93

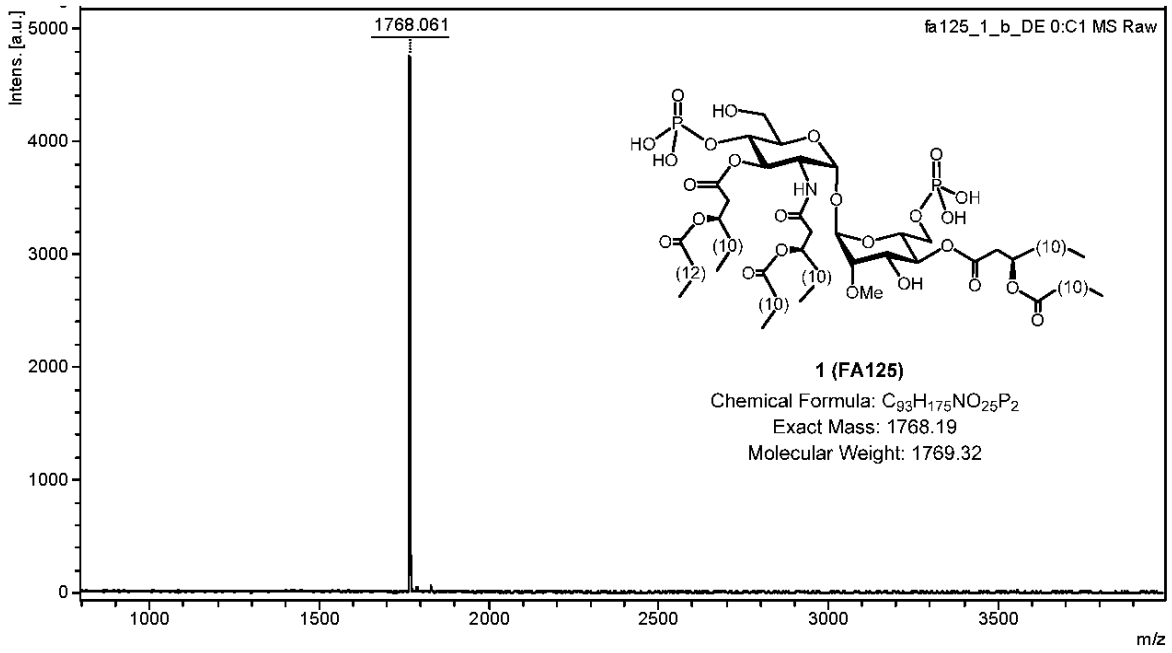
α,α-GM-LAM **1**, COSY, 600 MHz, $CDCl_3$-CD_3OD, 3:1

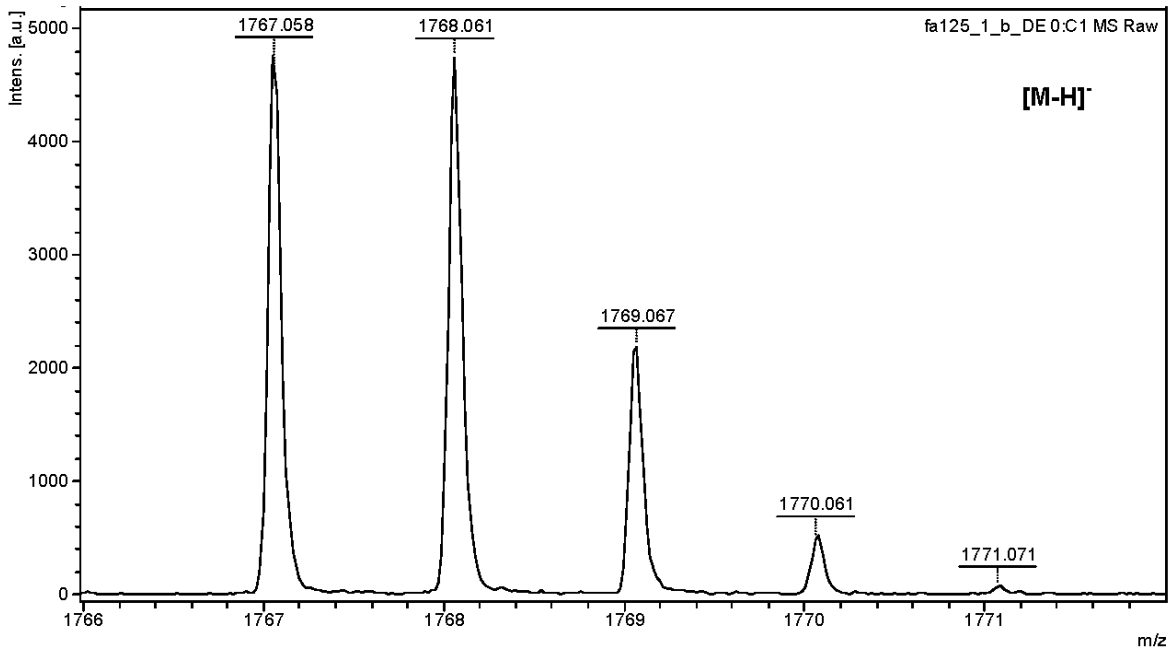


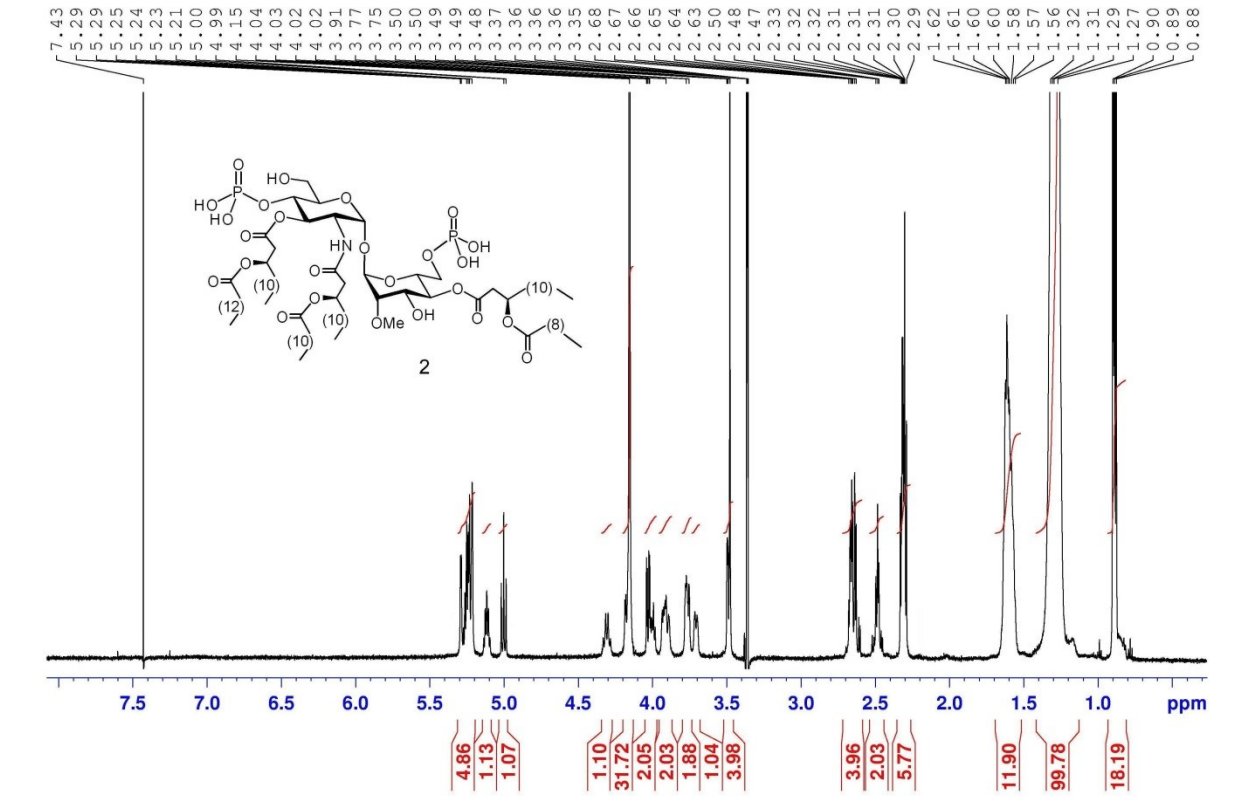
α,α-GM-LAM **1**, HSQC, $CDCl_3$-CD_3OD, 3:1

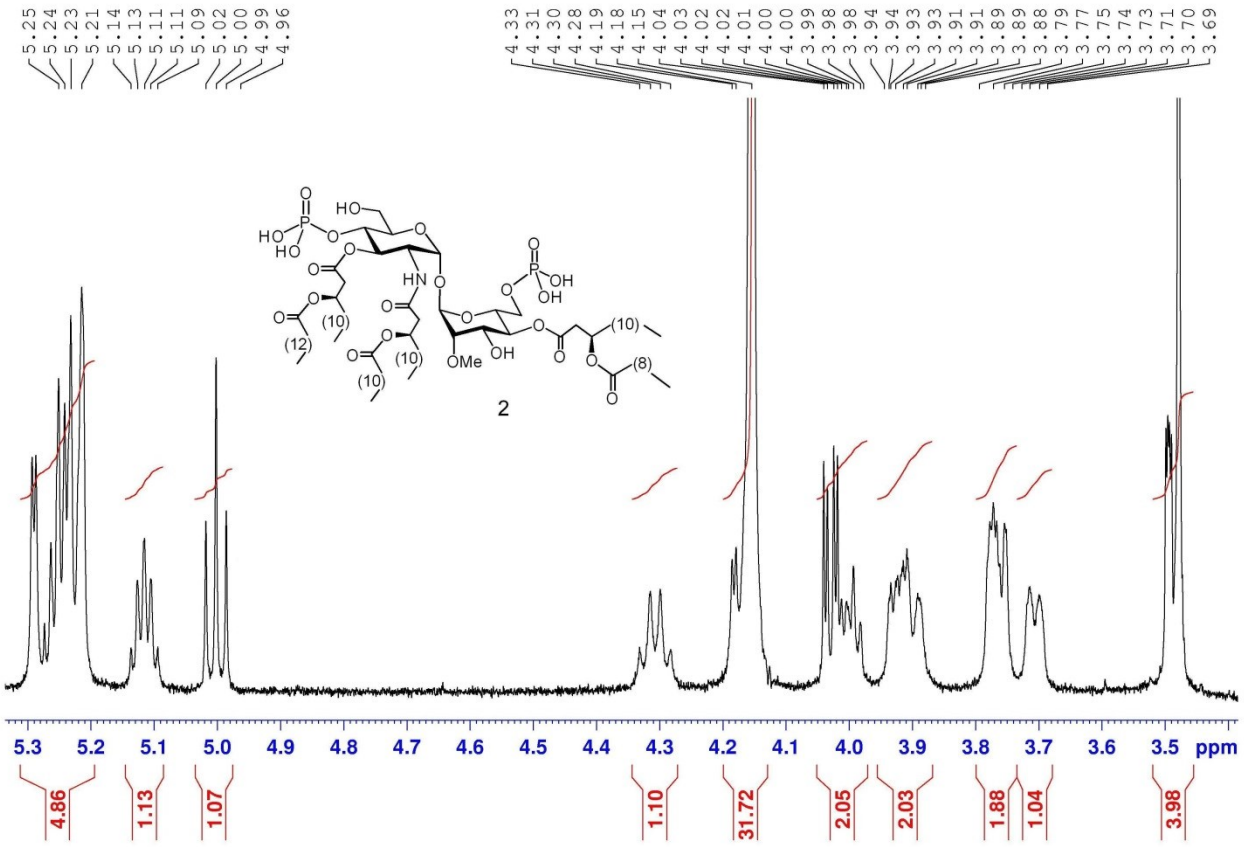


MALDI-TOF (neg. mode) spectrum of **1**

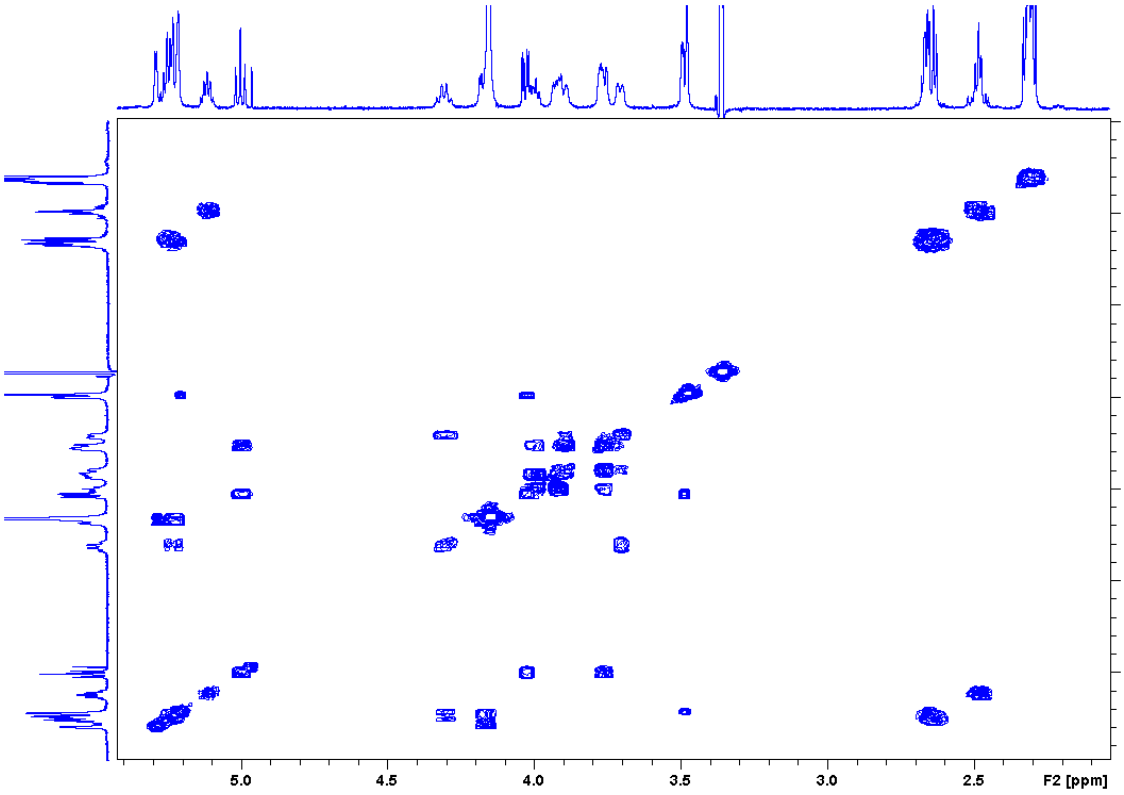




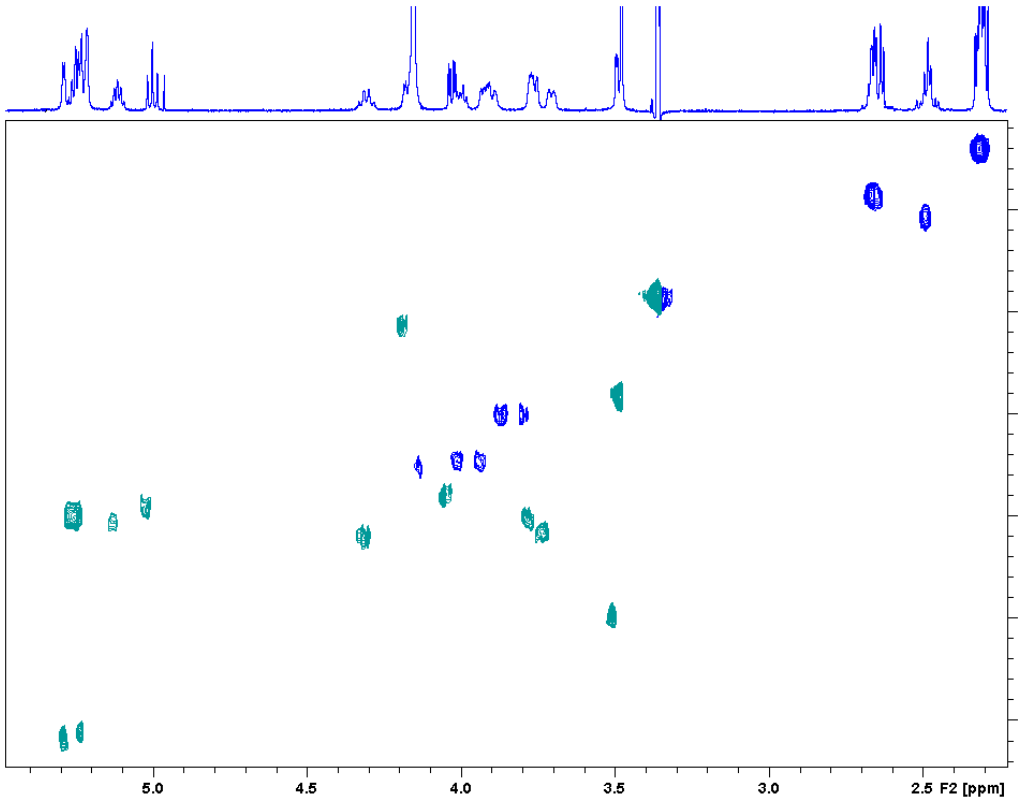

7.43 5.29 5.29 5.25 5.24 5.23 5.21 5.00 4.99 4.15 4.04 4.03 4.02 4.02 3.91 3.77 3.75 3.50 3.50 3.49 3.48 3.37 3.36 3.36 3.35 2.68 2.67 2.66 2.65 2.64 2.63 2.50 2.48 2.47 2.33 2.32 2.31 2.31 2.30 2.29 1.62 1.61 1.60 1.60 1.58 1.57 1.56 1.32 1.31 1.29 1.27 0.90 0.89 0.88
2
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
4.86 1.13 1.07 1.10 31.72 2.05 2.03 1.88 1.04 3.98 3.96 2.03 5.77 11.90 99.78 18.19


5.25 5.24 5.23 5.21 5.14 5.13 5.11 5.11 5.09 5.02 5.00 4.99 4.96 4.33 4.31 4.30 4.28 4.19 4.18 4.15 4.04 4.03 4.02 4.02 4.01 4.00 4.00 3.99 3.98 3.98 3.94 3.94 3.93 3.93 3.91 3.89 3.89 3.88 3.79 3.77 3.75 3.74 3.73 3.71 3.70 3.69
2
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 ppm
4.86 1.13 1.07 1.10 31.72 2.05 2.03 1.88 1.04 3.98

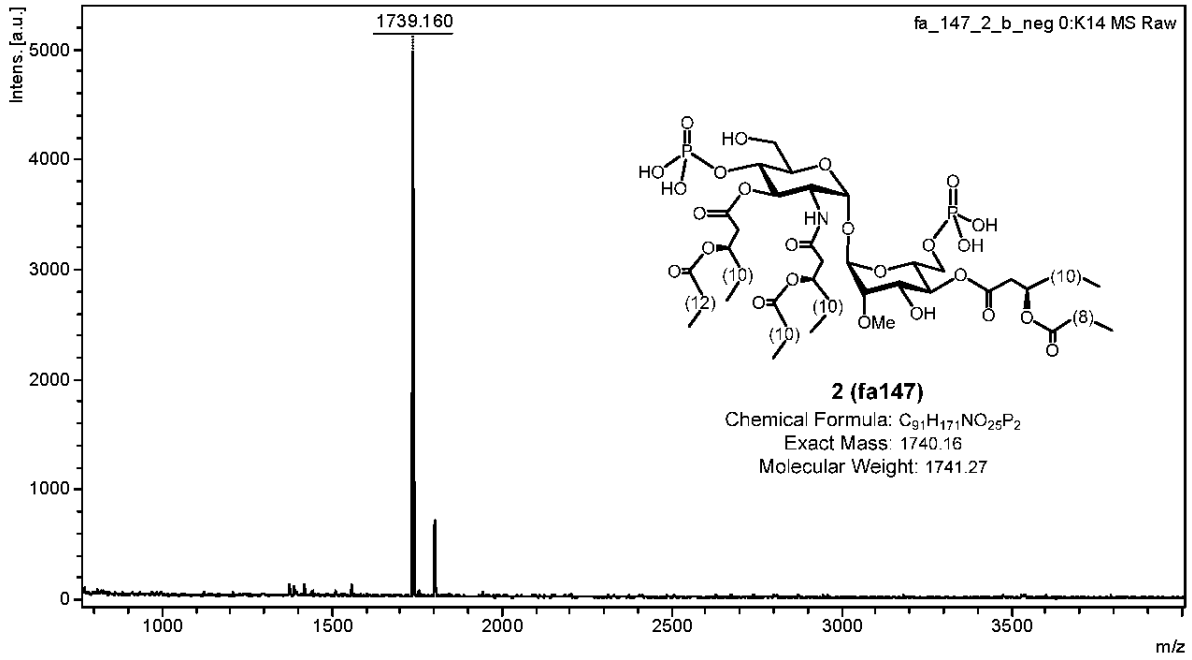
α,α-GM-LAM **2**, COSY, 600 MHz, $CDCl_3$-CD_3OD, 3:1

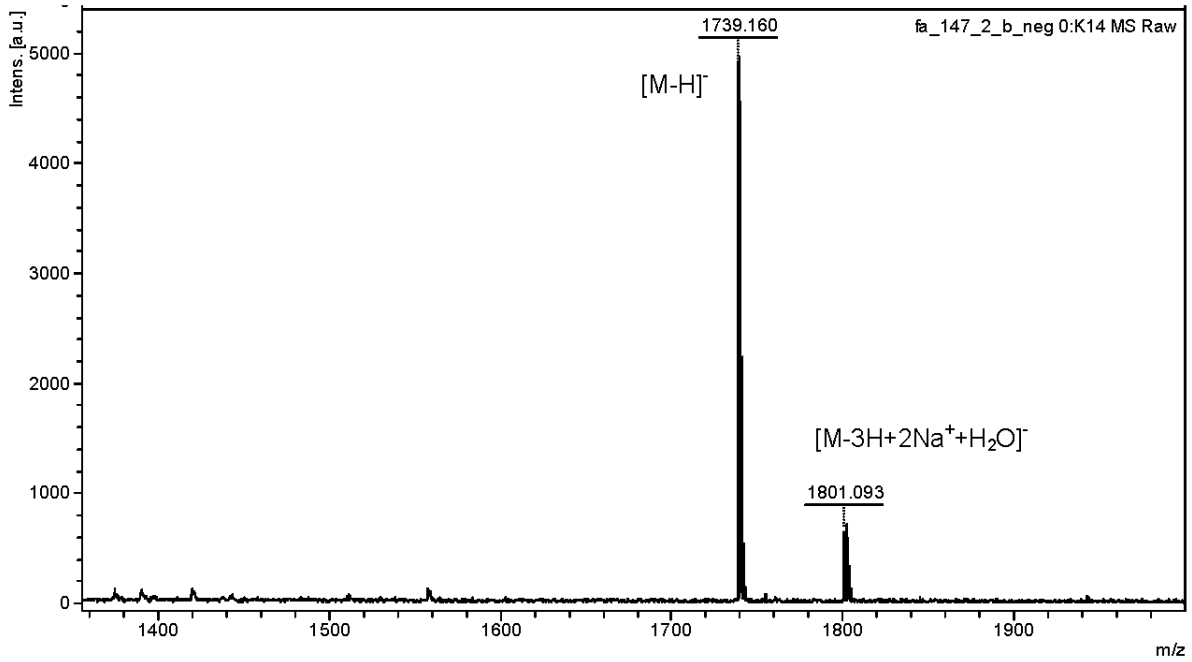


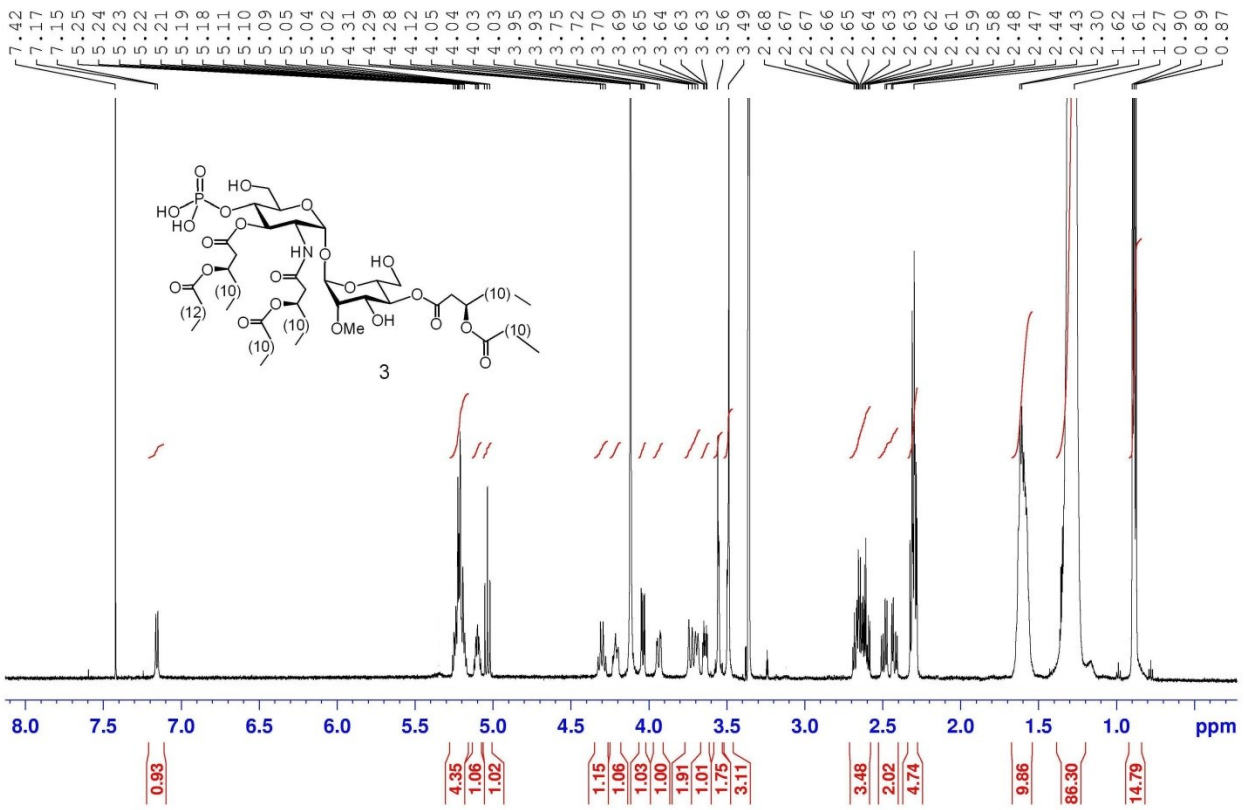
α,α-GM-LAM **2**, HSQC, $CDCl_3$-CD_3OD, 3:1

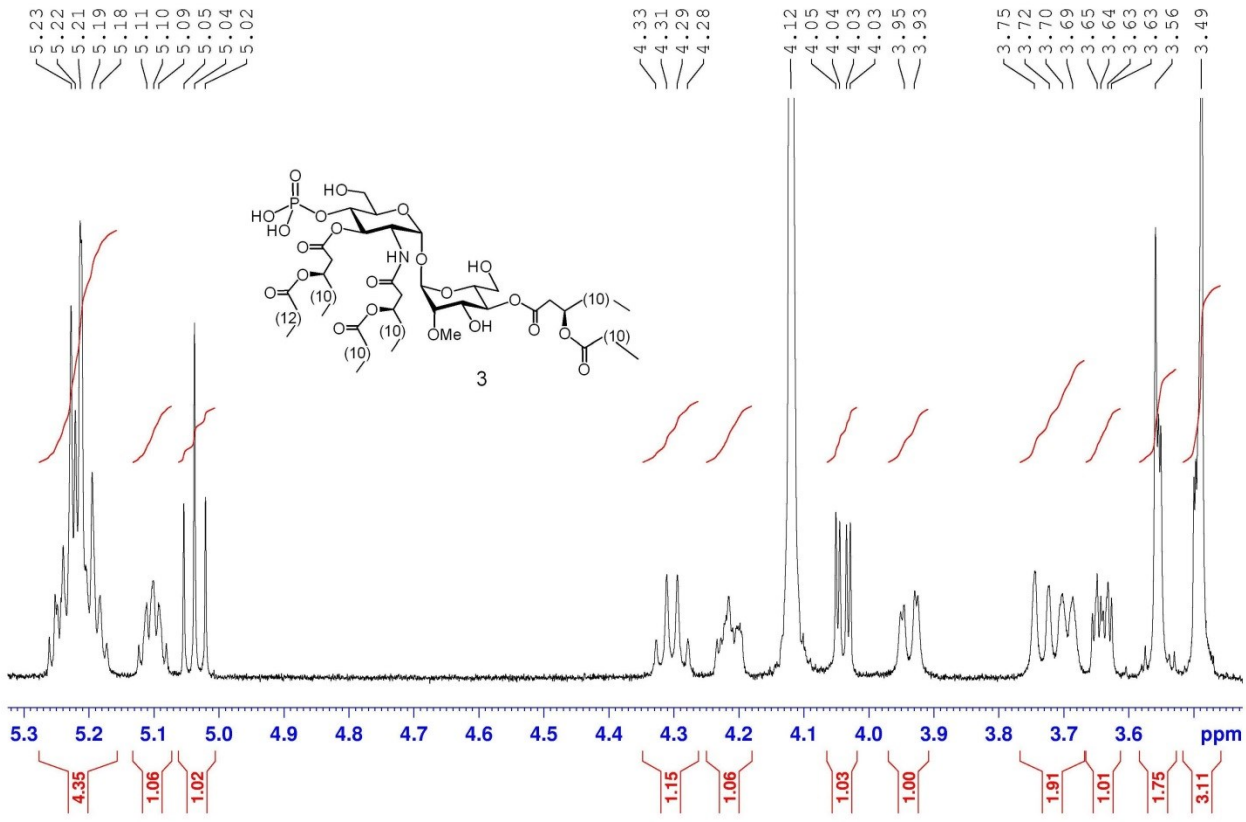


MALDI-TOF (neg. mode) of **2**

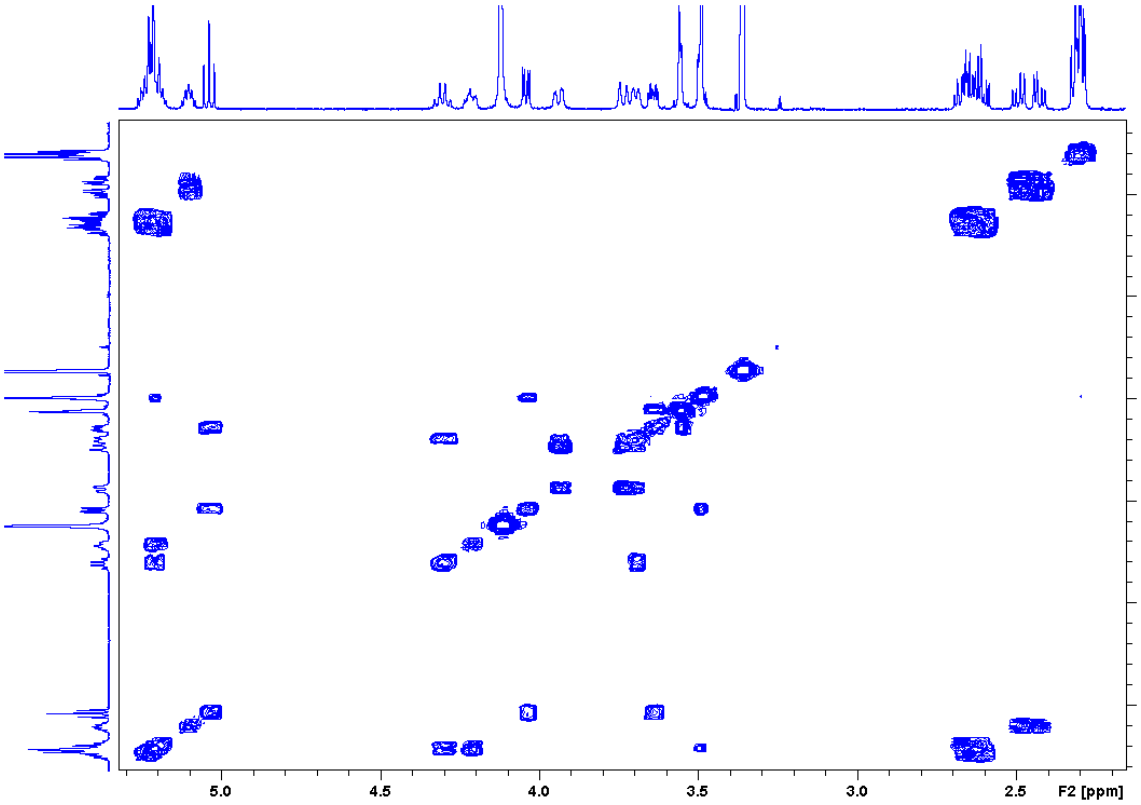




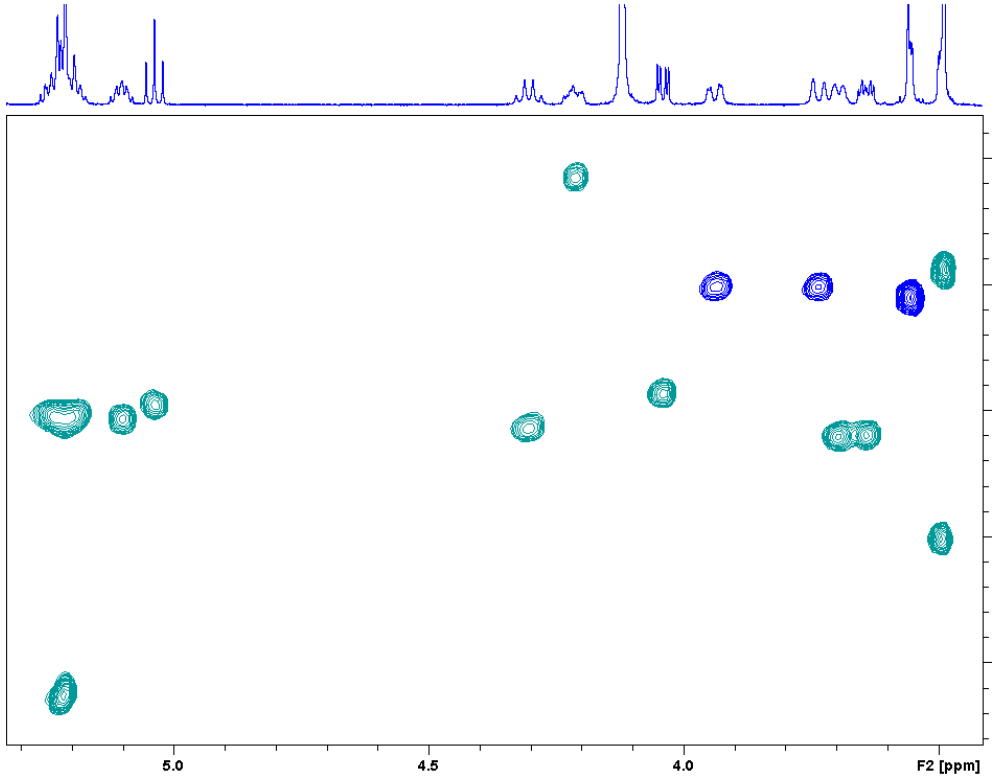

7.42 7.17 7.15 5.25 5.24 5.23 5.22 5.21 5.19 5.18 5.11 5.10 5.09 5.05 5.04 5.02 4.31 4.29 4.28 4.12 4.05 4.04 4.03 4.03 3.95 3.93 3.75 3.72 3.70 3.69 3.65 3.64 3.63 3.63 3.56 3.49 2.68 2.67 2.67 2.66 2.65 2.64 2.63 2.63 2.62 2.61 2.59 2.58 2.48 2.47 2.44 2.43 2.30 1.62 1.61 1.27 0.90 0.89 0.87
3
8.0 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 ppm
0.93 4.35 1.06 1.02 1.15 1.06 1.03 1.00 1.91 1.01 1.75 3.11 3.48 2.02 4.74 9.66 86.30 14.79


5.23 5.22 5.21 5.19 5.18 5.11 5.10 5.09 5.05 5.04 5.02 4.33 4.31 4.29 4.28 4.12 4.05 4.04 4.03 4.03 3.95 3.93 3.75 3.72 3.70 3.69 3.65 3.64 3.63 3.63 3.56 3.49
3
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 ppm
4.35 1.06 1.02 1.15 1.06 1.03 1.00 1.91 1.01 1.75 3.11

α,α-GM-LAM **3**, COSY, 600 MHz, $CDCl_3$-CD_3OD, 3:1



α,α-GM-LAM **3**, HSQC, $CDCl_3$-CD_3OD, 3:1



ESI-TOF (neg. mode) spectrum of **3**