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Deciphering minimal antigenic epitopes associated with *Burkholderia pseudomallei* and *Burkholderia mallei* lipopolysaccharide O-antigens

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Burkholderia pseudomallei (*Bp*) and *Burkholderia mallei* (*Bm*), the etiologic agents of melioidosis and glanders, respectively, cause severe disease in both humans and animals. Studies have highlighted the importance of *Bp* and *Bm* lipopolysaccharides (LPS) as vaccine candidates. Here we describe the synthesis of seven oligosaccharides as the minimal structures featuring all of the reported acetylation/methylation patterns associated with *Bp* and *Bm* LPS O-antigens (OAgs). Our approach is based on the conversion of an L-rhamnose into a 6-deoxy-L-talose residue at a late stage of the synthetic sequence. Using biochemical and biophysical methods, we demonstrate the binding of several *Bp* and *Bm* LPS-specific monoclonal antibodies with terminal OAg residues. Mice immunized with terminal disaccharide–CRM197 constructs produced high-titer antibody responses that crossreacted with *Bm*-like OAgs. Collectively, these studies serve as foundation for the development of novel therapeutics, diagnostics, and vaccine candidates to combat diseases caused by *Bp* and *Bm*.

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Burkholderia pseudomallei (*Bp*) is the causative agent of melioidosis, a multifaceted tropical disease leading to death in up to 50% of infected patients[1–3]. The genetically related *Burkholderia mallei* (*Bm*), the causative agent of glanders, primarily infects solipeds but can also lead to fatal infections in humans if left untreated[4]. These facultative intracellular, Gram-negative bacteria are both CDC Tier 1 select agents because of their high infectivity via inhalation, low infectious doses, and potential for misuse as biothreat agents, especially in the aerosolized form[5]. There are no clinically approved prophylactic vaccines currently available for either of these infections, thus the development of effective countermeasures is of outmost importance to combat disease caused by these bacterial pathogens[6–14].

Bp and *Bm* produce structurally similar lipopolysaccharides (LPS) anchored in their outer membranes. *Bp* and *Bm* LPS are potent activators of human Toll-like receptor 4[15, 16], stimulate human macrophage-like cells[15], are important virulence factors[17–19], and play a central role in host–pathogen interactions[20, 21]. Importantly, levels of anti-LPS antibodies are significantly higher in melioidosis patients who survive in comparison to those who succumb to disease[22]. Additionally, LPS-specific monoclonal antibodies (mAbs) have been shown to be passively protective in animal models of infection[23–28]. Several studies have highlighted the potential of *Bp* and *Bm* LPS as subunit vaccine candidates for melioidosis and glanders. Mice immunized with LPS from *Bp*, and from the non-pathogenic *Burkholderia thailandensis* (*Bt*), developed high-titer immunoglobulin G (IgG) responses and were partially protected against lethal challenges of *Bp*[29, 30]. In recent years, glycoconjugate vaccines composed of LPS (or detoxified LPS) covalently linked to carrier proteins and/or gold nanoparticles have been evaluated in mice and non-human primates with promising results according to their immunogenicity and protective efficacy[31–38].

Structurally, *Bp* and *Bm* LPS antigens comprise three distinct domains (e.g., lipid A[39], inner and outer core, and the O-antigen (OAg) repeat) (Fig. 1). The OAg structure consists of a linear heteropolymer featuring a disaccharide as the repeating unit in an equimolar ratio of (1→3)-linked 6-deoxy-α-L-talopyranose and β-D-glucopyranose[40–42]. Interspecies variations within the OAg lie in the different substitutions of the 6-deoxytalose residues, e.g., O-acetylation at both C4 and C2 and O-methylation at C2[43]. We have recently revisited the acetylation and methylation patterns of *Bp*, *Bm*, and *Bt* OAg and found that five intrachain (internal, **A**–**E**) as well as two terminal (non-reducing, **F** and **G**) disaccharides occur in variable proportions within the OAg (Fig. 1)[44, 45]. Although O-acetylation at the C4 position has been detected in significant amounts in *Bp*, *Bm* strains do not incorporate this modification. Moreover, as another atypical characteristic of these OAgs, the terminal residues at the non-reducing end are decorated with a methyl group at the C3 position. It has been shown that differences in colony morphology (mucoid vs non-mucoid strains of *Bp*) are associated with OAg substitution patterns, which influence interactions with LPS-specific mAbs[46]. We have hypothesized that these different OAg modifications could have profound impact for antibody recognition and immune responses[47], and therefore are crucial structural parameters to take into consideration for the development of LPS-based vaccines against *Bp* and *Bm*.

For the first time, we describe an efficient synthetic approach allowing access to seven oligosaccharides (**1**–**7**) featuring all of the reported intrachain (trisaccharides **1**–**5**) and terminal (disaccharides **6** and **7**) epitopes of *Bp* and *Bm* OAg. The synthetic routes and target compounds were devised in order to avoid potential acetyl migration on the all *cis*-triol 6-deoxytalose residue. Molecular interactions of the synthetic oligosaccharides with *Bp* and *Bm* LPS-specific mAbs were probed using enzyme-linked immunosorbent assay (ELISA) glycan arrays, surface plasmon resonance (SPR), and saturation transfer

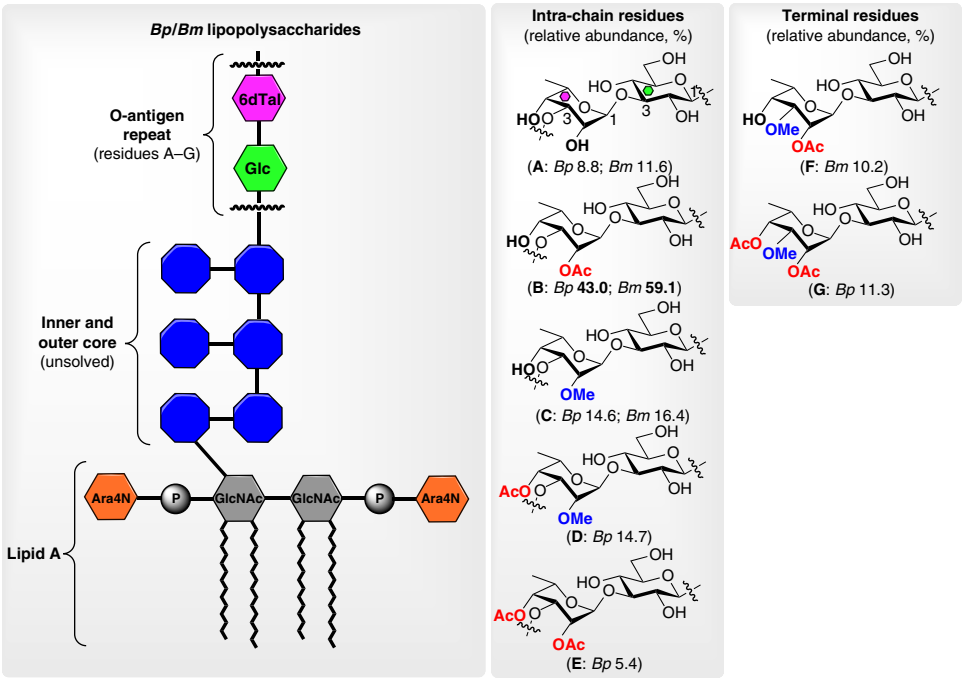


Fig. 1 Chemical structure of *B. pseudomallei* and *B. mallei* LPS antigens. Smooth LPS species consist of three major domains: the lipid A, the core, and the OAg repeat. The OAg is a linear heteropolymer featuring a disaccharide unit in an equimolar ratio of (1→3)-linked 6-deoxy-α-L-talopyranose and β-D-glucopyranose. Five internal (intrachain) and two terminal (non-reducing) disaccharide residues are present within the OAg. According to the species, they show different methylation and acetylation substitution patterns at the C2, C3, and C4 positions of the 6-deoxy-L-talose residue[45]

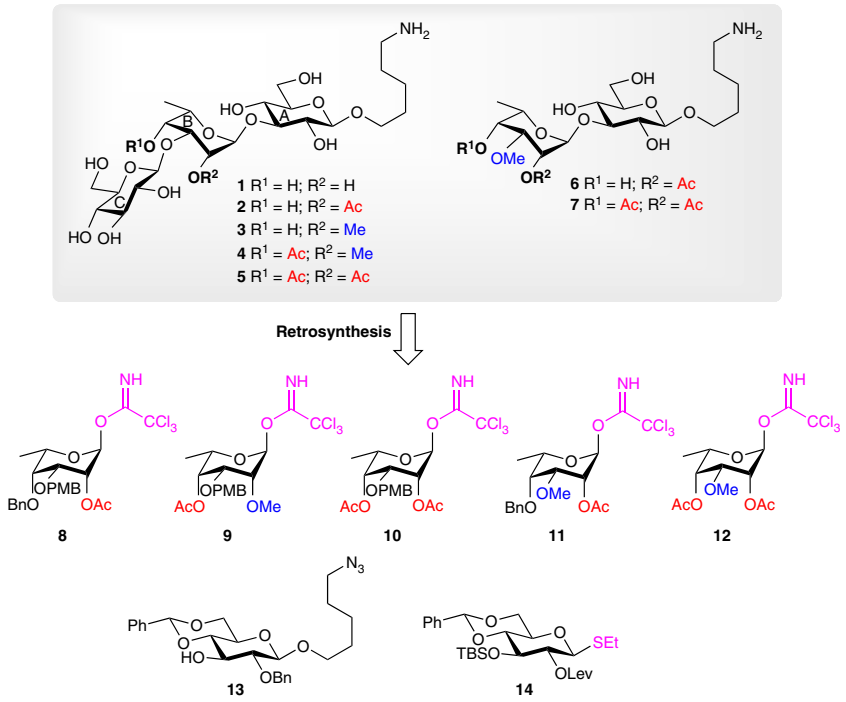


Fig. 2 Planned retrosynthetic analysis of the target oligosaccharides **1**–**7**. *Ac* acetyl, *Bn* benzyl, *Lev* levulinoyl, *Ph* phenyl, *PMB para*-methoxybenzyl, *SEt* thioethyl, *TBS tert*-butyldimethylsilyl

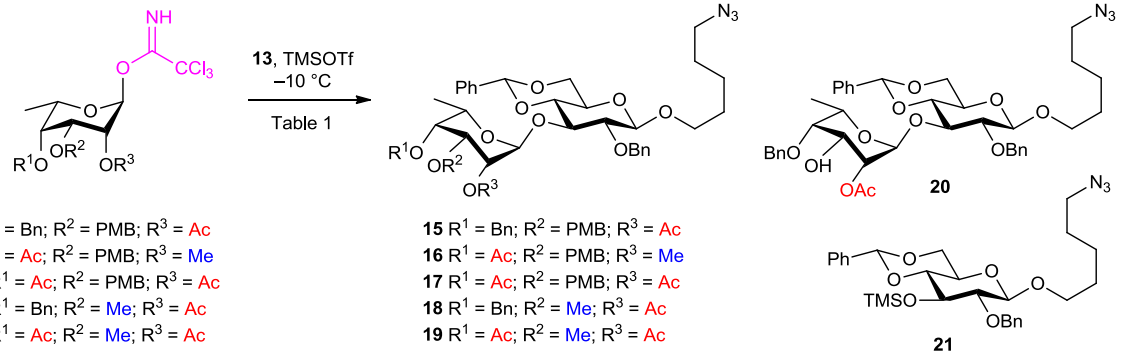
difference (STD)-nuclear magnetic resonance (NMR). We show that the mAbs strongly interact with the 6-deoxytalose residue of the 3-O-methylated terminal disaccharides. Based on these results, the two terminal disaccharides **6** and **7** were covalently linked to CRM197 carrier protein and evaluated in mice for their immunogenicity. High-titer antibody responses were raised against disaccharide **6** of the constructs, and these responses were crossreactive with *Bm*-like LPS. Collectively, these studies represent a novel platform for the development of glycoconjugate vaccines and diagnostics to combat melioidosis and glanders.

Results

Synthetic approach. The target compounds **1**–**7** were conceived as the shortest possible oligosaccharides mimicking the substitution epitopes of the 6-deoxytalose residue, without anticipated acetyl migration. We first planned to introduce the *O*-acetyl and *O*-methyl groups on the talose unit prior to its incorporation into the oligosaccharides. Thus, according to the retrosynthetic analysis depicted in Fig. 2, the target oligosaccharides would come from five suitably functionalized talose donors (**8**–**12**), which are activated at their anomeric position with a trichloroacetimidate (TCA) group[48]. The choice of the TCA group was motivated by the high-yielding coupling reported for structurally similar L-rhamnose donors in the context of the synthesis of bacterial glycans[49]. All of these donors (**8**–**12**) were synthesized using a C4 oxidation/reduction sequence from a common allylated rhamnose precursor followed by subsequent regioselective 3-O-methylation or 3-O-*para*-methoxybenzylation via optimization of the stannylene acetal chemistry[50] (Supplementary Figs. 1 and 2 and Supplementary Table 1). The *para*-methoxybenzyl (PMB) group would allow, once deprotected, the introduction of the terminal glucose moiety at the C3 position while the benzyl (Bn) group would act as a permanent blocker of the C4 position for donors **8** and **11**. The glucose residue at the reducing end, i.e., acceptor **13** (Supplementary Fig. 3), is functionalized with an aliphatic azidolinker chain, which would allow its transformation into a primary amine upon hydrogenolysis. This amine would serve as an anchor for subsequent biotinylation and covalent coupling with a carrier protein. Thioglycoside donor **14** (Supplementary Fig. 4) was conceived for the introduction of the terminal glucose unit. It bears a levulinoyl (Lev) group at C2, which would act as a neighboring participating group for the formation of the 1,2-*trans*-linkage in addition to being orthogonal to acetyl groups. The presence of a *tert*-butyldimethylsilyl (TBS) group at C4 would allow the synthesis of longer oligosaccharide chains upon deprotection. Furthermore, if the coupling proves unsuccessful with thioglycoside **14**, the latter would be readily convertible into other donors, such as anomeric fluorides and imidates.

Synthesis of protected disaccharides. Disaccharides **15**–**19** were prepared from TCA talose donors **8**–**12** and acceptor **13** under the catalytic promotion of trimethylsilyl trifluoromethanesulfonate (TMSOTf) at −10 °C. Optimization of the glycosylation reactions was first performed with donor **8** (entries 1–4, Table 1) by varying the solvent, reaction time, equivalents of TMSOTf, and the presence or absence of water-scavenging 4 Å molecular sieves (MS). When conducting the glycosylation in 1,2-dichloroethane (DCE) in the presence of MS (entry 1), desired disaccharide **15** was obtained in poor yield (30%) along with disaccharide **20** as the major compound resulting from the cleavage of the PMB under catalytic acid conditions, which was somewhat unexpected for this protecting group. Interestingly, reacting disaccharide **15** under TMSOTf-catalyzed conditions led to a complex mixture of degradation products while no disaccharide **20** was observed. Loss of the PMB during the course of the glycosylation reaction could thus be rationalized by the steric effect of the Bn group at C4 combined with the electron-donating properties of the PMB group at C3 (Supplementary Fig. 5). Indeed, the dioxalenium ion could be attacked by the C3 oxygen atom leading to PMB cleavage together with the formation of a 1,2,3-*O*-orthoacetyl species. Once activated by TMSOTf, this tricyclic orthoester could be converted into the thermodynamically favored alcohol **20** upon attack of acceptor **13**.

Table 1 Synthesis of protected disaccharides



8 R^1 = Bn; R^2 = PMB; R^3 = Ac
9 R^1 = Ac; R^2 = PMB; R^3 = Me
10 R^1 = Ac; R^2 = PMB; R^3 = Ac
11 R^1 = Bn; R^2 = Me; R^3 = Ac
12 R^1 = Ac; R^2 = Me; R^3 = Ac

15 R^1 = Bn; R^2 = PMB; R^3 = Ac
16 R^1 = Ac; R^2 = PMB; R^3 = Me
17 R^1 = Ac; R^2 = PMB; R^3 = Ac
18 R^1 = Bn; R^2 = Me; R^3 = Ac
19 R^1 = Ac; R^2 = Me; R^3 = Ac

Entry	Donor (equivalents)	Solvent[a]	4 Å MS[b]/time (h)	TMSOTf (equivalents)	Product yield (%)[c]	Ratio α/β[d]
1	**8** (1.3)	DCE	+/21	0.2	**15** (30)[e]	α only
2	**8** (2.0)	Et_2O	+/1	0.2	**15** (43)[f]	α only
3	**8** (1.5)	Et_2O	+/8	0.2	**15** (78)	α only
4	**8** (2.0)	Et_2O	−/0.2	0.02	**15** (95)	α only
5	**9** (2.0)	DCE	+/0.2	0.2	**16** (51)	α only
6	**9** (2.0)	Et_2O	−/0.2	0.01	**16** (90)	α only
7	**10** (2.0)	DCE	+/0.2	0.2	**17** (44)	α only
8	**10** (2.0)	Et_2O/DCE 5:1[g]	−/0.2	0.01	**17** (58)	α only
9	**11** (2.0)	Et_2O	−/0.2	0.01	**18** (81)	α only
10	**12** (2.0)	Et_2O	−/0.2	0.01	**19** (76)	α only

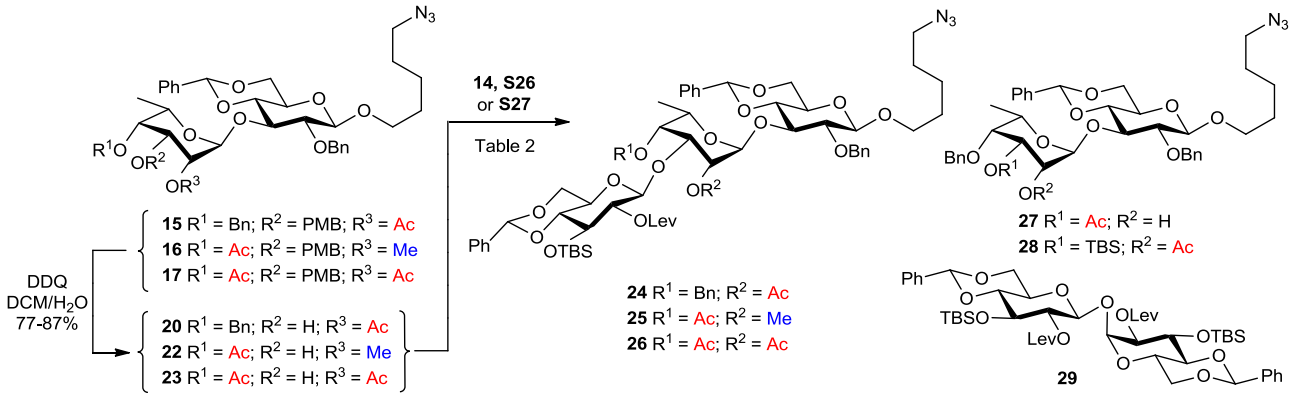
DCE 1,2-dichloroethane, *Et_2O* diethyl ether, *MS* molecular sieves, *TMSOTf* trimethylsilyltrifluoromethanesulfonate
[a]Anhydrous solvent over molecular sieves (~0.05 M)
[b]With (+) or without (−) freshly activated powdered molecular sieves
[c]Isolated yield
[d]Determined by ^{1}H NMR
[e]Disaccharide **20** was isolated as the major compound
[f]Silylated derivative **21** was isolated in 42% yield
[g]DCE was added to ensure the solubility of donor

Switching DCE for diethyl ether (Et_2O) as the solvent slightly increased the yield of disaccharide **15** (from 30% to 43%) while preventing the formation of disaccharide **20**; however, silylated glucose derivative **21** was isolated as a by-product. Increasing the reaction time from 1 h (entry 2) to 2 h (entry 3) enabled the conversion of silylated derivative **21** into disaccharide **15**, thereby enhancing the yield to 78%. We then discovered that performing the glycosylation without MS had a dramatic effect on the reaction kinetic and yield. Under these conditions (entry 4), reaction time was shortened to 20 min, only 0.02 equivalent of TMSOTf was needed, and the yield went up to 95% without PMB deprotection. The other disaccharides (**16**–**19**) were conveniently synthesized using these optimized conditions (entries 6, 8–10). Pleasingly, the glycosylation reactions were fully α-stereoselective for all disaccharides, even without participating group at C2, such as for 2-O-methylated donor **9**, and the anomeric configuration was ascertained by undecoupled ^{13}C NMR ($^1J_{C1,H1}$ = 174–176 Hz).

Synthesis of protected trisaccharides. With disaccharides **15**–**17** in hand, we then turn our attention to the synthesis of trisaccharides **24**–**26** (Table 2). Cleavage of the PMB group was performed under the action of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in dichloromethane (DCM) at room temperature affording disaccharides **20**, **22**, and **23** in very good yields (77–87%) and, importantly, without noticeable acetyl migration to the C3 position. Glycosylation of disaccharide **22** with thioglucoside **14** (entry 1) under the combined action of *N*-iodosuccinimide (NIS) and silver(I) trifluoromethanesulfonate (AgOTf)[51] at −10 °C in an Et_2O/DCE mixture led to trisaccharide **25** in 65% yield as the sole β-anomer. Applying these conditions to the synthesis of trisaccharide **26** also gave rewarding results (entry 2). However, we were surprised to find that glycosylation of disaccharide **20**, bearing a Bn group at C4, was not successful under these conditions (entry 3); instead degradation of donor was revealed by thin layer chromatography. We then tested several glycosylation conditions (the most relevant are shown in entries 4–10) using disaccharide **20** as an acceptor but without any success, as only traces of trisaccharide **24** were detected. When the reaction was performed in DCM at −78 °C using NIS/AgOTf as the promoter, dimerization of donor **14**, yielding diglucoside **29**, was observed (entry 5). Activation of thioglycoside **14** under the action of $CuBr_2$ in the presence of tetrabutylammonium bromide[52] was attempted in order to generate a more reactive bromide species[53]. However, this reaction mainly led to disaccharide **27** in which the acetyl group had migrated from the C2 to the C3 position (entry 6). Anomeric fluoride **S26** (entry 8) as well as *N*-phenyl-2,2,2-trifluoroacetimidate **S27** (entries 9 and 10) were also evaluated as donors but both failed to provide trisaccharide **24**.

We hypothesized that the steric hindrance and electronic effect of the Bn group at C4 can be invoked to explain these negative results. Therefore, 6-deoxytalose building block **S30** bearing a less hindered, electron-withdrawing Lev group at C4 together with a chloroacetyl (ClAc) group at C3 was prepared (Supplementary Fig. 6). Unfortunately, we were not able to selectively deprotect the ClAc group under a variety of conditions and therefore this route was abandoned. Regioselective glycosylation of diol **S29** bearing a Lev group at C4 was also investigated (Supplementary Fig. 7). Using thioglycoside **14** under the promotion of dimethyl(methylthio)sulfonium trifluoromethanesulfonate (DMTST)[54] in the presence of 2,6-di-*tert*-butyl-4-

Table 2 Synthesis of protected trisaccharides



Entry	Acceptor	Donor[a]	Promoter[b]	Solvent[c]	T (°C) (time (h))	Product	Yield (%)[d]
1	**22**	**14**	NIS, AgOTf	Et_2O/DCE	−10 (0.2)	**25**	65[e]
2	**23**	**14**	NIS, AgOTf	Et_2O/DCE	−10 (0.2)	**26**	50[e]
3	**20**	**14**	NIS, AgOTf	Et_2O/DCE	−10 (0.2)	**24**	ND[f]
4	**20**	**14**	NIS, AgOTf	DCE	−10 (1)	**24**	ND[f]
5	**20**	**14**	NIS, AgOTf	DCM	−78 (3)	**24**	ND[g]
6	**20**	**14**	$CuBr_2$, TBAB	DCM/DMF	22 (72)	**27**	90
7	**20**	**14**	DMTST, DTBMP	DCE	40 (48)	**24**	ND[h]
8	**20**	**S26** (F)	$SnCl_2$, AgOTf	Et_2O/DCM	−10 (0.3)	**24**	ND[f]
9	**20**	**S27** (PTFA)	TMSOTf	DCE	−10 (0.2)	**24**	ND[f]
10[i]	**20**	**S27** (PTFA)	TBSOTf	tol	75 (2)	**28**	60

AgOTf silver(I) trifluoromethanesulfonate, *DCM* dichloromethane, *DDQ* 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, *DMF* *N*,*N*-dimethylformamide, *DMTST* dimethyl(methylthio)sulfonium trifluoromethanesulfonate, *DTBMP* 2,6-di-*tert*-butyl-4-methylpyridine, *NIS* *N*-iodosuccinimide, *TBAB* tetrabutylammonium bromide, *TBSOTf* *tert*-butyldimethylsilyl trifluoromethanesulfonate, *tol* toluene
[a]Donor was used in excess (1.5 equivalents)
[b]The reaction was performed adding freshly activated powdered molecular sieves
[c]Anhydrous solvent over molecular sieves (~0.05 M)
[d]Isolated yield
[e]Only the β-anomer was detected by ^{1}H NMR
[f]Degradation of donor
[g]The dimer **29** was detected as the major compound
[h]No reaction
[i]Inverse procedure

methylpyridine led to the formation of disaccharide **S32**, having unfortunately the wrong regioselectivity.

In an attempt to enhance the regioselectivity of the glucosylation reaction at C3, 2-aminoethyl diphenylborinate catalyst was used following the conditions recently developed by Taylor and colleagues[55] (Supplementary Fig. 8). Thus triol **S3** was reacted with perbenzylated glucose chloride **S33** in the presence of Ag_2O in acetonitrile with a catalytic amount of 2-aminoethyl diphenylborinate. A mixture of regioisomeric disaccharides was formed in which desired disaccharide **S34** was isolated in 25% yield. The poor glycosylation yield coupled with anticipated difficulties for the subsequent selective monoacetylation at either C2 or C4 position led us to consider using diol **S5** instead. However, the presence of a Bn group at C4 reversed the regioselectivity of the glycosylation under Taylor conditions giving disaccharide **S35** in 58% yield following acetylation. At this point, it became obvious that the presence of protecting groups other than acetyl at the C4 position of the 6-deoxytalose residue hamper the glycosylation on the adjacent *cis* alcohol. Other synthetic avenues were thus investigated.

Second-generation synthesis of protected trisaccharides. On the basis of these previous results, we devised an alternative synthetic route in which an epimeric rhamnose moiety was glucosylated prior to its conversion into the talo-configuration. It was anticipated that the steric hindrance at the C4 position would be avoided in such a case. Therefore, as depicted in Fig. 3, alcohol **S1** was levulinoylated at C4 and the isopropylidene cleaved under acidic conditions to give diol **31** in 81% yield over two steps. Glucosylation using Taylor catalyst in the presence of 4 Å MS cleanly provided disaccharide **32** following acetylation (73% over two steps). The other regioisomer was not detected. Then the Lev group was removed using hydrazine acetate, the resulting alcohol oxidized with Dess–Martin periodinane in refluxing DCE[56], and the ketone reduced in the presence of $NaBH_4$ with full control of diastereoselectivity[57]. Attempts were made to protect the axial C4 position with a Lev group, yet, even under drastic conditions, only small amounts of the levulinoylated derivative were formed. We thus decided to go further leaving this hydroxyl free. Disaccharide **34** was transformed into the TCA derivative **35** in 65% over three steps involving: (1) isomerization of the allyl group using an iridium-based catalyst; (2) iodine-promoted hydrolysis; and (3) activation of the resulting hemiacetal into a TCA derivative. Then TCA **35** was coupled with glucose acceptor **13** in the presence of TMSOTf in an attempt to form a trisaccharide. However, acceptor **13** did not react while disaccharide **35** underwent rearrangement into tricyclic orthoester **36**, which was unexpectedly stable[58, 59]. The "all-*cis*" conformation of this intriguing compound was confirmed by single-crystal X-ray diffraction (CCDC 1520384, Supplementary Tables 2, 3, 4, and 5). It is likely that orthoester **36** would come from the intramolecular attack of the free C4 alcohol on the dioxalenium ion

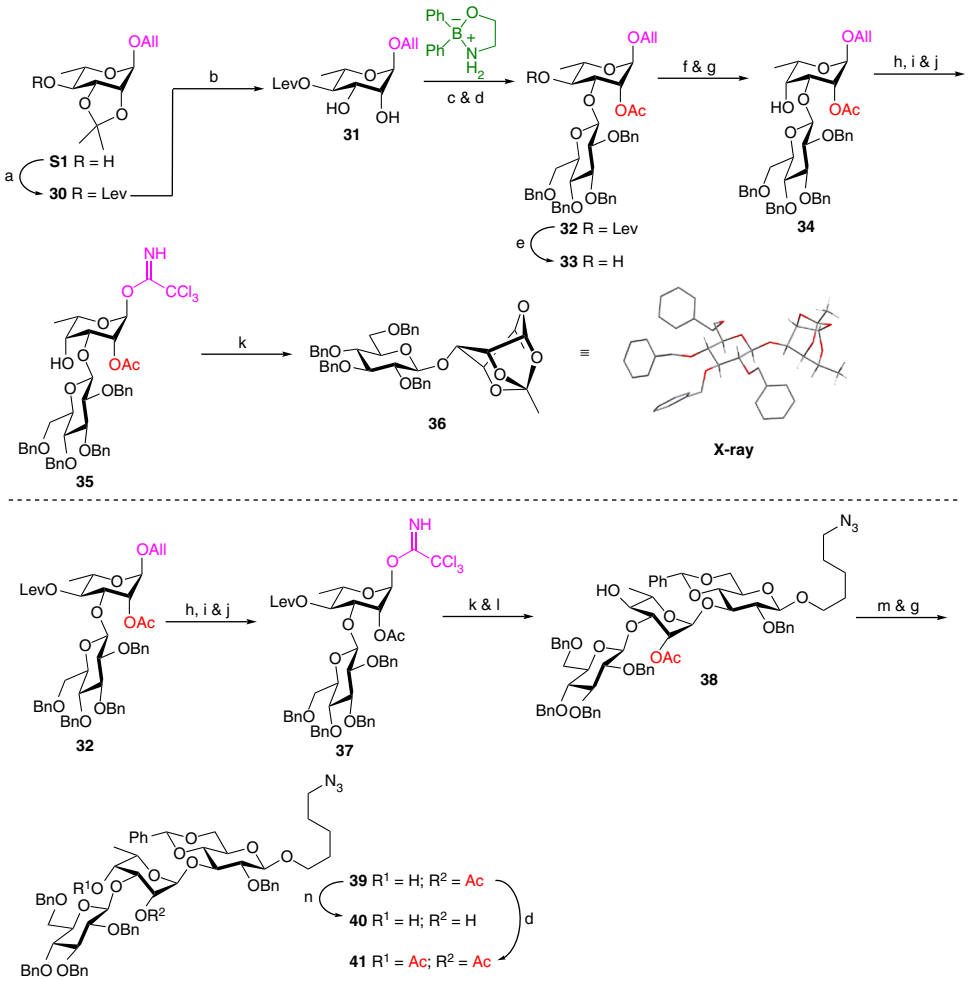


Fig. 3 Second-generation synthesis of protected trisaccharides. Reagents and conditions: a Lev_2O, py, DMAP, 50 °C, 2 h, 99%; b 80% aq. HOAc, 60 °C, 6 h, 82%; c chloride donor **S33**, 2-aminoethyl diphenylborinate (0.25 equivalent), Ag_2O, CH_3CN, 4 Å MS, 60 °C, overnight, 74%; d Ac_2O, py, DMAP, RT, 3–4 h, 98% (for **32**); 94% (for **41**); e H_2NNH_2.HOAc, DCM, MeOH, RT, overnight 82%; f Dess-Martin periodinane, DCE, 70 °C, 1 h; g $NaBH_4$, MeOH/DCM 5:1, −10 °C to RT, 71% (for **34**, over two steps); 85% (for **39**, over two steps); h $[Ir(COD)\{PMe(C_6H_5)_2\}_2]^+.PF_6^-$, H_2, THF, RT, 1 h; i I_2, THF, H_2O, RT, 2 h; j CCl_3CN, Cs_2CO_3, DCM, Me_2CO, RT, 2 h, 65% (for **35**, over three steps); 81% (for **37**, over three steps); k acceptor **13**, TMSOTf, 4 Å MS (only for **38**), Et_2O/DCE 5:1, −10 °C, 10 min, 41% (for **36**); l $H_2NNH_2.H_2O$, py, HOAc, 0 °C to RT, overnight, 77% (over two steps); m PDCP, DMSO, Et_3N, DCM, −10 °C to RT, 1 h; n NaOMe, MeOH/DCM 2:1, RT, overnight, 81%. *Ac_2O* acetic anhydride, *CCl_3CN* trichloroacetonitrile, *COD* cyclooctadienyl, *DMAP* 4-(dimethylamino)pyridine, *DMSO* dimethylsulfoxide, *Et_3N* triethylamine, *HOAc* acetic acid, *Lev_2O* levulinic anhydride, *PDCP* phenyl dichlorophosphate, *py* pyridine, *RT* room temperature, *THF* tetrahydrofuran

(Supplementary Fig. 9). Attempts to glucosylate compound **36** in the presence of TMSOTf in either DCE or Et_2O only led to orthoester degradation[60, 61].

In an ultimate synthetic sequence, conversion of the rhamno- into the talo-configuration was then attempted at the trisaccharide level (Fig. 3). Disaccharide **32** was converted into TCA derivative **37**, which was successfully coupled with acceptor **13** using the previously optimized conditions. The Lev group was cleaved under the action of hydrazine monohydrate to give trisaccharide **38** in 77% yield over two steps from TCA **37**. Oxidation of the free alcohol at C4 was performed using Dess–Martin periodinane, but degradation occurred and trisaccharide **39** was isolated in low yield following $NaBH_4$ reduction (31%, over two steps). By contrast, Pfitzner–Moffatt oxidation[62] of trisaccharide **38** using phenyl dichlorophosphate followed by subsequent reduction of the crude ketone cleanly provided target trisaccharide **39** in very good yield (85%, over two steps). The latter was deacetylated or acetylated under standard conditions to give trisaccharides **40** and **41**, respectively. A similar synthetic approach was successfully applied to the second-generation synthesis of terminal disaccharides **6** and **7** (Supplementary Fig. 10).

Deprotection of oligosaccharides. The last step in the synthesis of target oligosaccharides **1**–**7** was the global deprotection of trisaccharides **25**, **39**, **40**, and **41** as well as disaccharides **18** and **19** (Fig. 4). In order to provide trisaccharide **4** bearing an acetyl group at C4, a three-step synthetic sequence was performed starting from protected trisaccharide **25**, which consisted in delevulinoylation using hydrazine acetate, cleavage of the TBS group by treatment with triethylamine trihydrofluoride in refluxing tetrahydrofuran (THF), and hydrogenolysis with Pearlman catalyst through microfluidic conditions (H-Cube) in the presence of HCl (2 equivalents). Under these conditions, monoacetylated trisaccharide **4** was obtained in 72% yield over three steps. Zemplén deacylation of trisaccharide **25**, cleavage of the TBS group using tetrabutylammonium bromide in THF followed by microfluidic hydrogenolysis led to non-acetylated trisaccharide **3** in 69% yield over three steps. Finally, deprotection of oligosaccharides **39**, **40**, **41**, **18**, and **19** was best performed

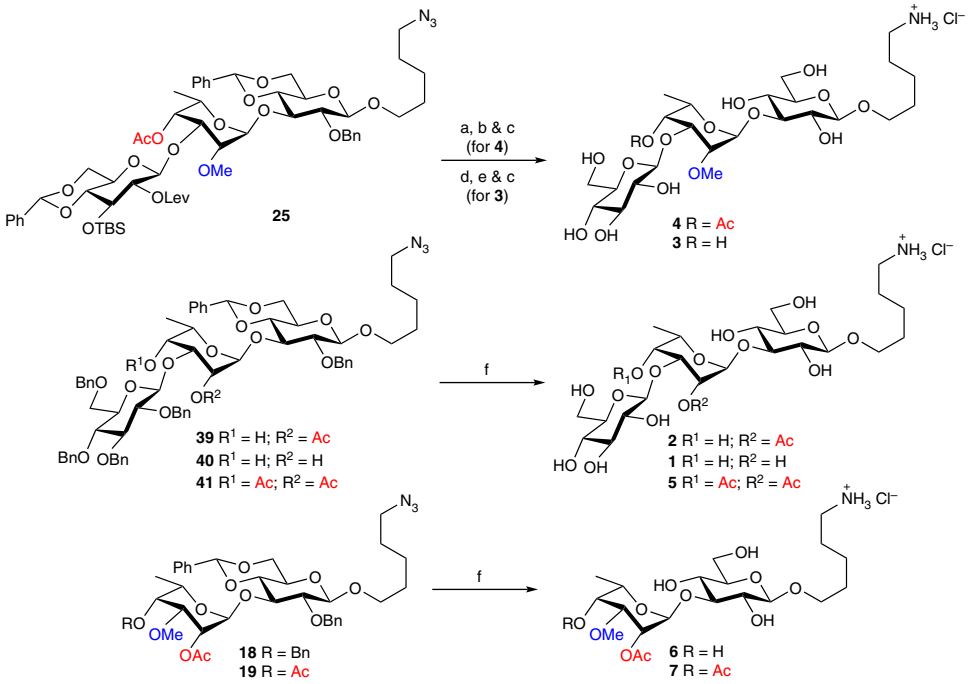


Fig. 4 Global deprotection allowing access to target oligosaccharides. Reagents and conditions: a H_2NNH_2.HOAc, MeOH/DCM 5:2, RT, overnight; b TREAT-HF, THF, reflux, 24 h, 92% (over two steps); c H-Cube, 20% $Pd(OH)_2$/C, HCl (2.0 equivalents), 10 bars, 40 °C, MeOH/DCE, 78% (for **4**); 78% (for **3**); d NaOMe, MeOH/DCM 2:1, RT, overnight; e TBAF, THF, 0 °C to RT, overnight, 89% (over two steps); f Pd black, H_2, HCl (1.0 equivalent), MeOH/DCE, quant. (for **1**, **2**, **5**, **6**, and **7**). *TBAF* tetrabutylammonium fluoride, *TREAT-HF* triethylaminetrihydrofluoride

through heterogeneous hydrogenolysis conditions using Pd black and 1.0 equivalent of HCl in a DCE/MeOH mixture affording target oligosaccharides **2**, **1**, **5**, **6**, and **7**, respectively, in quantitative yields. Importantly, using excess of HCl partially cleaved the acetyl group at C2, which was found to be more labile than the one at C4.

Reactivity of the oligosaccharides with LPS-specific mAbs. Several previous studies have identified mAbs that differentially recognize *Bp* or *Bm* LPS antigens[23, 26, 43, 47, 63]. Notably, mAb Pp-PS-W is specific for *Bp* OAg while mAbs 4C7, 3D11, and 9C1-2 are specific for *Bm* OAg[43, 47]. Although the OAgs expressed by *Bp* and *Bm* are structurally similar, *Bm* OAg lacks 4-*O*-acetyl substitutions on talose residues, a key difference that influences recognition of these antigens by mAbs[43, 47]. The structures of *Bp* (RR2808) and *Bm*-like (RR4744) OAgs and their corresponding mAb reactivity profiles are shown in Fig. 5a and Supplementary Fig. 167. To determine whether the oligosaccharides synthesized in this study were recognized by the various LPS-specific mAbs, ELISAs were conducted using all seven oligosaccharides along with LPS controls. Results demonstrated that mAbs 4C7, 3D11, and 9C1-2 reacted strongly with disaccharide **6**, which represents the capping residue associated with *Bm* OAg, and that mAb Pp-PS-W reacted strongly with disaccharide **7**, which represents the capping residue associated with *Bp* OAg (Fig. 5b). These findings are consistent with the LPS reactivity patterns observed and indicate that all of the mAbs tested appear to recognize the terminal residues of the either *Bp* or *Bm* OAgs. Additionally, these results confirm our previous work showing that mAb Pp-PS-W reacts only with →3)-β-D-glucopyranose-(1→3)-6-deoxy-α-L-talopyranose-(1→ polymers in which the 6-deoxytalose residues are coordinately acetylated at the *O*-2 and *O*-4 positions[43]. Importantly, as mAbs Pp-PS-W, 4C7, and 9C1-2 have been shown to be passively protective in animal models of melioidosis or glanders, our data support the use of disaccharides **6** and **7** as components of novel vaccine candidates.

Kinetic characterization of mAb 4C7/oligosaccharide interactions by SPR. SPR[64] was used for a real-time analysis of the binding affinities between mAb 4C7 and the synthetic oligosaccharides (Fig. 6 and Supplementary Figs. 168 and 169). mAb 4C7 was selected as a model IgG as it has recently been shown to provide significant protection of mice from a lethal challenge with *Bp* in the course of a passive immunization protocol[28]. Disaccharide **6**, which presented the highest recognition toward mAb 4C7 in the ELISA assay, was evaluated by SPR as well as disaccharide **7**, and trisaccharide **2**, which features the major intrachain epitope of *Bp*/*Bm* OAg. Therefore, oligosaccharides **2**, **6**, and **7** were biotinylated using NHS ester chemistry and the resulting constructs (**BIO-2**, **BIO-6**, and **BIO-7**, respectively, Fig. 6a) were immobilized on the surface of a streptavidin (SA)-coated sensor chip (Supplementary Figs. 11 and 170). Different concentrations of mAb 4C7 were injected for 180 s, followed by passive dissociation for 300 s. The changes in refractive index at the sensor chip surface, which reflect the magnitude of the interactions, were monitored and recorded in arbitrary response units. The kinetics of binding between mAb 4C7 and the biotinylated oligosaccharides were illustrated in the sensorgrams, which are plots of response units vs time. According to the sensorgrams, mAb 4C7 bound to immobilized **BIO-6** and **BIO-7**, but did not interact with immobilized **BIO-2** (Fig. 6b). The K_D values, which were calculated using a steady-state affinity model, demonstrated that mAb 4C7 had a higher affinity binding to **BIO-6** (22 nM) as compared with **BIO-7** (120 nM). In agreement with the results obtained by ELISA, the SPR-binding results indicate that mAb 4C7 tightly interacts with the terminal methylated talose residue found at the non-reducing end of *Bm*-like LPS OAg. Furthermore, the presence of an acetyl

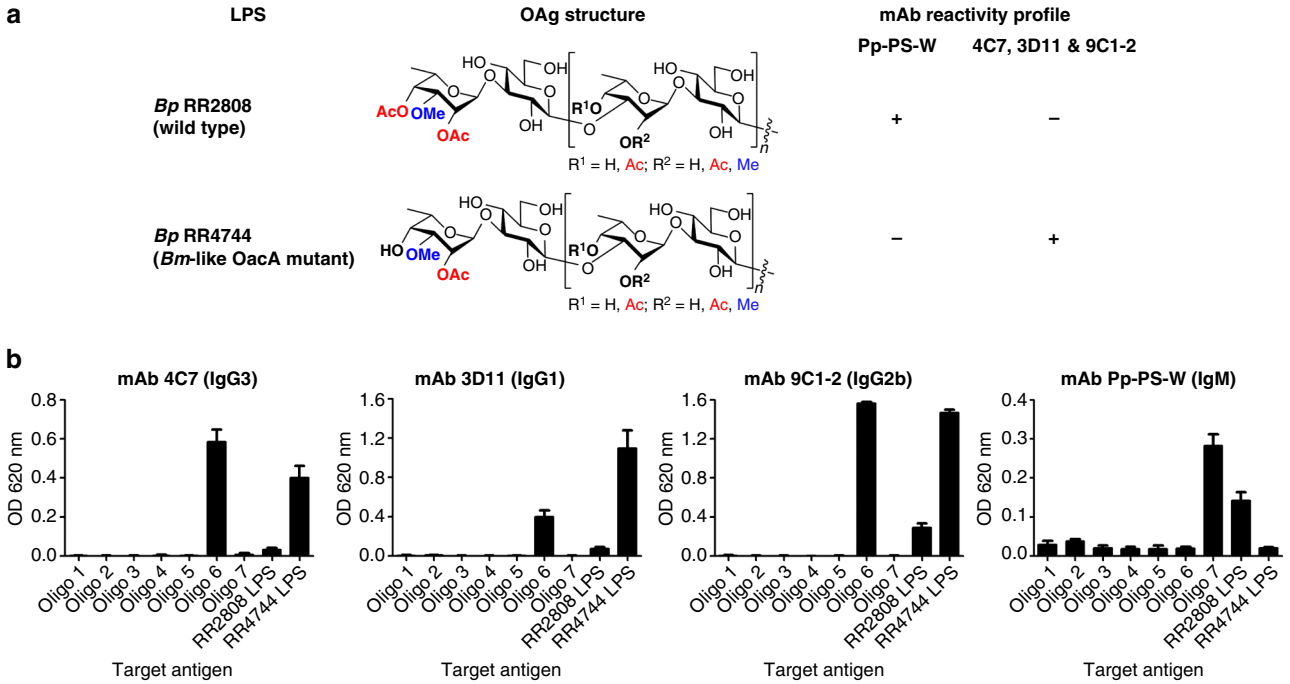


Fig. 5 Interactions of LPS-specific mAbs with synthetic oligosaccharides. **a** Reactivity profiles of mAbs Pp-PS-W, 4C7, 3D11, and 9C1-2 with LPS antigens purified from *Bp* strains RR2808 and RR4744 (see Supplementary Fig. 167). **b** Reactivity profiles of the mAbs with synthetic oligosaccharides **1**–**7**, RR2808, and RR4744 LPS as determined by ELISA. *Black bars* represent the mean±sd of assays conducted in triplicate

group at the C4 position of the talose unit significantly hampers the binding with mAb 4C7 by a five-fold order of magnitude.

Binding epitopes of mAb 4C7 with oligosaccharides by STD-NMR. In order to dissect, at a molecular level, the binding of mAb 4C7 to *Bp* and *Bm* OAg, we employed *ad hoc* NMR techniques aimed to identify and characterize the interactions of synthetic oligosaccharides to the monoclonal antibody[65]. STD-NMR spectroscopy is well suited to derive deep insights on the molecular features that govern antigen recognition from antibodies characterized by weak or medium affinity[66]. STD-NMR experiments were carried out with disaccharides **6** and **7** that differ in the acetylation pattern at the C4 position of the talose residue. The STD-NMR spectra performed on the mAb–disaccharide **7** mixture at 298 K did not show any signals (Supplementary Fig. 171) likely due to unfavorable binding kinetics. As the temperature strongly influences the kinetics and consequently the observed STD effects[67], we ran STD-NMR spectra at different temperatures (Supplementary Fig. 172 and Fig. 7b). Interestingly, at 283 K, some STD enhancements were observed for the mAb 4C7–disaccharide **7** complex (Fig. 7b). However, the characterization of the ligand epitope mapping of disaccharide **7** was hampered as only very low STD-NMR effects were observed. STD-NMR measurements gathered on disaccharide **6**, instead, allowed deducing a more accurate binding epitope, detecting the ligand region in closer contact to the antibody. A qualitative analysis of STD enhancements clearly evidenced the involvement of both glucose and talose moieties, which were both recognized by the mAb 4C7 (Fig. 7a). However, the strongest STD effects all belonged to the terminal talose unit, with the proton at position 2 experiencing the highest transfer of saturation (100% normalized STD effect). In addition, *O*-acetyl group (97%), H1 (96%), and H4 (88%) exhibited large STD enhancements indicating that they were important as well for antibody binding. Less pronounced STD signals were observed for protons of the glucose residue revealing that they participated to a minor extent in the interaction with mAb 4C7. In detail, proton H3 showed an STD effect close to 60%, whereas protons at positions 4, 5, and 6 displayed even lower STD intensities (<50%). Therefore, STD-NMR data suggest that the main contact surface area was positioned within the talose residue thus highlighting its role in the binding process, whereas the glucose moiety less contributed to the interaction with the antibody. In addition, considering the high contribution to the binding of hindered proton H4 in disaccharide **6**, this could explain why the presence of an acetyl group at this position, such as for disaccharide **7**, significantly weakens the binding with mAb 4C7 resulting in slight STD effects.

Immunization of mice with disaccharide- and OAg-based glycoconjugates. Extending upon the observation that disaccharides **6** and **7** reacted with *Bm* and *Bp* LPS-specific mAbs, respectively, we next wanted to determine whether these synthetic oligosaccharides were capable of stimulating immune responses in mice. Using NHS ester chemistry, disaccharides **6** and **7** were individually coupled to CRM197 resulting in the semi-synthetic oligosaccharide conjugates **SOC-6** and **SOC-7** (Supplementary Fig. 12). Following conjugation, the samples were examined by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). Results of these analyses demonstrated that, in both instances, the disaccharides had covalently linked to the protein carrier, as indicated by the shifts in molecular weights of the glycoconjugates relative to the molecular weight of the unconjugated CRM197 control (Supplementary Fig. 173). Additionally, western immunoblotting confirmed that the structural integrity/antigenicity of the disaccharide moieties remained intact following coupling to the protein carrier based upon their reactivity with mAbs 4C7, 3D11, and 9C1-2 or Pp-PS-W (Supplementary Fig. 173). Further analysis of the constructs by matrix assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) revealed that **SOC-6** and **SOC-7** consisted of about six and five disaccharides

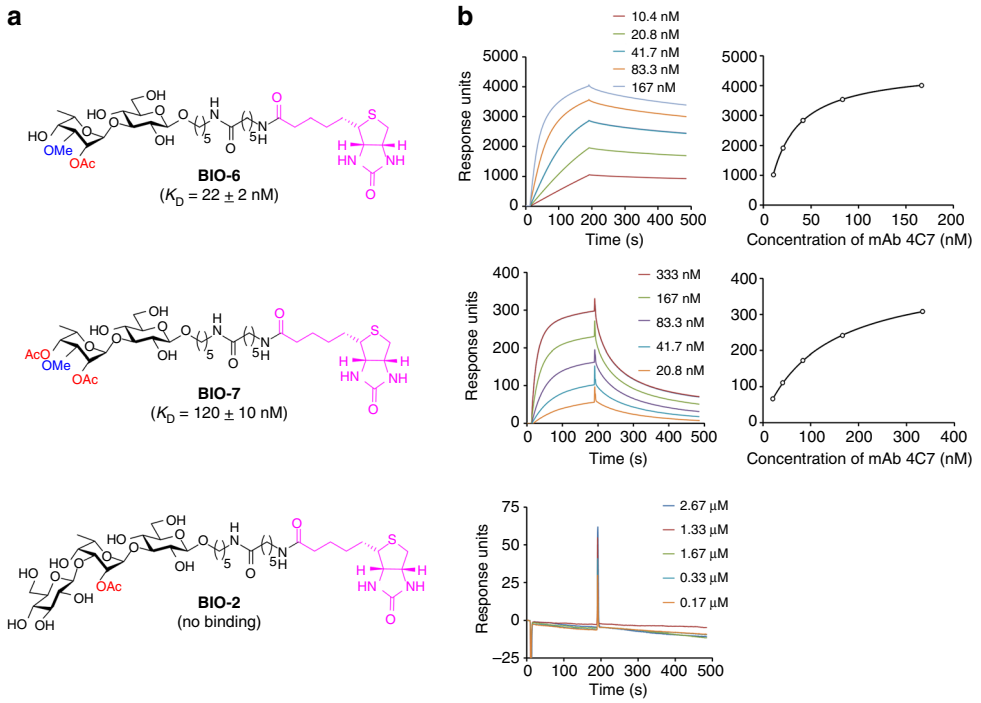


Fig. 6 K_D values of mAb 4C7 binding to biotinylated oligosaccharides inferred by SPR. **a** Chemical structures of the biotinylated oligosaccharides with their corresponding K_D values. The compounds were immobilized on the surface of a streptavidin-coated sensor chip. Samples (two-fold serial dilution of mAb 4C7) were injected over the sensor surface for 180 s (association), after which the mAb was allowed to passively dissociate for 300 s. K_D values were calculated with a steady-state affinity model (response units vs concentration plots). Indicated K_D values are the mean±sd of three runs. **b** Representative sensorgrams and steady-state affinity model fitting for each corresponding biotinylated oligosaccharides. See Supplementary Methods and Supplementary Figs. 11 and 168–170 for details

covalently linked to CRM197, respectively (Supplementary Fig. 174). The conjugates were ~95% protein (*w*/*w*) as measured by BCA assay.

To examine the immunogenic potential of the disaccharide-based glycoconjugates, groups of BALB/c mice were immunized with **SOC-6** or **SOC-7**. ELISAs were used to assess the reactivity of the immune serum samples with disaccharides and OAgs (Fig. 8a) while immunofluorescence microscopy was used to assess reactivity with whole cells (Supplementary Fig. 175). Results showed that **SOC-6** stimulated significantly higher antigen-specific IgG titers than did **SOC-7**. For disaccharide-specific responses, the end point titers elicited by **SOC-6** ranged from 1:400 to 1:64,000 while the end point titers achieved for **SOC-7** ranged from 1:200 to 1:800. Similar trends were observed for OAg-specific responses with **SOC-6** end point titers (vs RR4744 OAg) ranging from 1:400 to 1:64,000 and **SOC-7** end point titers (vs RR2808 OAg) ranging from 0 to 1:200. For control purposes, BALB/c mice were immunized with the OAg-based glycoconjugates OC-4744 and OC-2808. Consistent with the results shown in Fig. 8a, OC-4744-immunized mice demonstrated high-titer IgG responses against both disaccharide **6** and RR4744 OAg with end point titers ranging from 1:800 to 1:409,600 and from 1:128,000 to 1:512,000, respectively (Fig. 8b). In contrast, mice immunized with OC-2808 exhibited high-titer responses against RR2808 OAg (1:32,000–1:256,000) but failed to produce strong responses against disaccharide **7** (1:200–1:800). Similar results were also obtained when C57BL/6 mice were immunized with OC-2808 (Supplementary Fig. 176).

Human immune responses to *Bp* OAg. Based on our mouse studies, high-titer antibody responses that recognize the terminal disaccharide of *Bm* OAg could be produced by immunization with either **SOC-6** or OC-4744. In contrast, high-titer antibody responses that recognize the terminal epitope of *Bp* OAg could not be raised by immunization with either **SOC-7** or OC-2808. Potential reasons for this might be that the 4-*O*-acetyl group on the capping residue has a role in modulating immune responses against the *Bp* OAg or that mice have a hole in their B-cell repertoire against this motif. To investigate this, ELISAs were used to assess the reactivity of culture-confirmed Thai melioidosis patient and Thai healthy donor serum samples with RR2808 OAg and disaccharide **7**. As shown in Fig. 8c, immune serum samples exhibiting reactivity with *Bp* OAg also had the capacity to crossreact with disaccharide **7**. These results indicate that, unlike mice, humans have the ability to generate antibody responses against the terminal disaccharide of *Bp* OAg. Collectively, our findings suggest that the inability of mice to raise antibodies against the terminal epitope of *Bp* OAg may be a species-restricted phenomenon. Additional studies will be required to further investigate this observation as well as identify alternative animal models to help overcome this issue.

Discussion

In this study, we have been successful in synthesizing a unique series of oligosaccharides featuring all of the intrachain and terminal epitopes found within the LPS OAgs from *Bp* and *Bm*. The optimal approach involved the epimerization of the C4 position of a 3-O-methylated or 3-O-glucosylated L-rhamnose building block at a late stage of the synthetic route, generating terminal disaccharides **6** and **7**, and intrachain trisaccharides **1**–**5**, respectively. All of the glycosylation reactions were fully stereoselective, the coupling products were obtained in high yields, and, importantly, no acetyl migration was detected at any steps of the synthetic sequence. The knowledge learned from

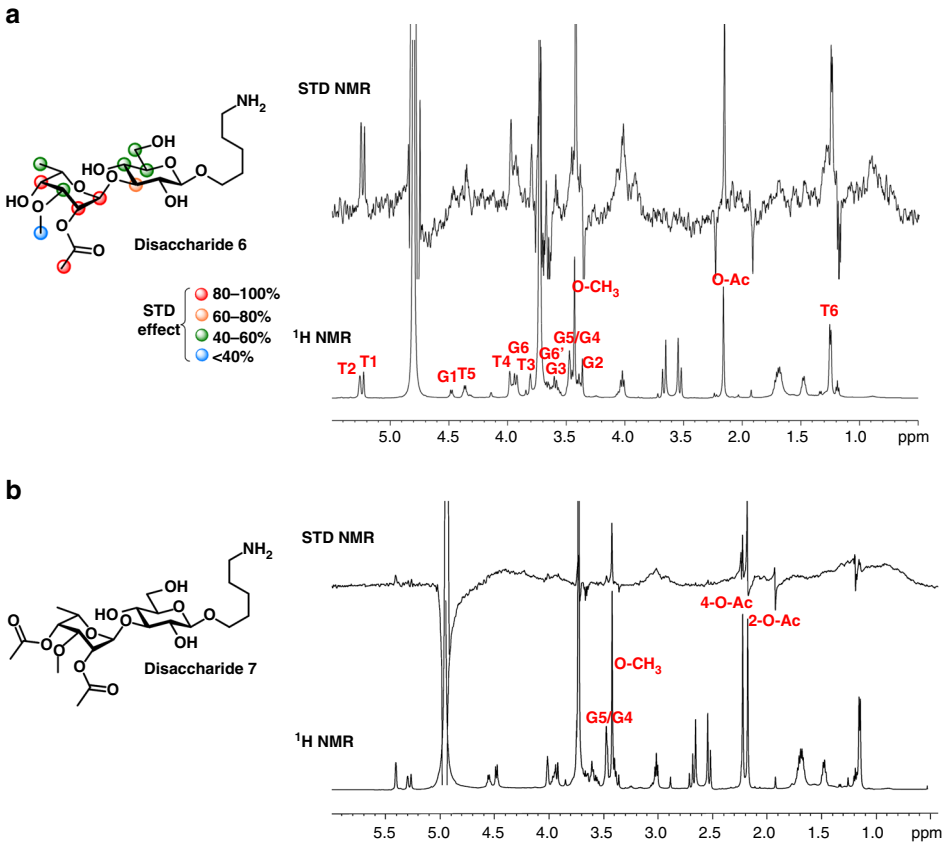


Fig. 7 Epitope mapping of disaccharides/mAb 4C7 interactions probed by STD-NMR. Chemical structures and epitope binding of disaccharides **6a** and **7b** to mAb 4C7 along with reference ^{1}H and STD NMR spectra at 298 and 283 K, respectively. *Color code* indicates the percentages of STD effects. Low and not quantifiable STD effects were detected for disaccharide **7**. Both STD 1D NMR spectra were run with a 1:100 mAb 4C7/disaccharide mixture. The irradiation frequency was set at 8 ppm and a saturation time of 2 s was used. The proton resonances belonging to talose and glucose residues were indicated with *letters*, **T** and **G**, respectively

this synthetic journey could be used as a base for the elaboration of longer oligosaccharide chains related to *Bp* and *Bm* OAg, which would feature, for instance, both intrachain and terminal epitopes.

The synthetic oligosaccharides were used to probe and characterize the minimal binding epitopes for a series of *Bp* and *Bm* LPS-specific mAbs, which have been shown to be passively protective in mouse models of melioidosis and glanders. To do so, biochemical and biophysical approaches, including ELISA assay, SPR, and STD-NMR, were employed to study the interactions of synthetic oligosaccharides **1**–**7** with various mAbs. The results of the ELISA assay strongly suggest that mAbs Pp-PS-W, 4C7, 3D11, and 9C1-2 are targeted to the terminal residues found at the non-reducing end of *Bp* and *Bm* OAgs. The interaction between mAb 4C7, which recognizes the *Bm*-like capping residue, and disaccharides **6** and **7** was further investigated by STD-NMR. These NMR analyses revealed that mAb 4C7 primarily binds to the 6-deoxy-L-talose residue of disaccharide **6**, especially with the *O*-acetyl group and protons at the C1, C2, and C4 positions which experienced the higher STD effects, and, to a lesser extent, with the glucose residue. In contrast, only weak STD effects were detected for disaccharide **7**, a result that could be explained by the presence of a supplemental acetyl group at the C4 position. SPR measurements with biotinylated disaccharides (**BIO-6** and **BIO-7**) in the presence of mAb 4C7 supported this behavior. Indeed, disaccharide **6** was shown to bind more strongly to mAb 4C7 than disaccharide **7**, with a K_D value in the low nanomolar range.

These results prompted us to evaluate the immunogenicity of disaccharides **6** and **7** in mice. To generate the semisynthetic glycoconjugates **SOC-6** and **SOC-7**, disaccharides **6** and **7** were covalently linked to CRM197. Mice immunized with **SOC-6** produced high-titer IgG responses that were raised against the disaccharide component of the constructs. Importantly, these responses were crossreactive with *Bm*-like OAgs. Optimization of the loading level as well as the multivalent display[68] of disaccharide epitopes could help improve the immunogenicity of the constructs. Moreover, the straightforward and high-yielding synthesis of disaccharide **6** represents an asset for the industrial and cost-effective production of such vaccines. Thus **SOC-6** stands as a promising vaccine candidate to be tested in animal models of glanders.

In summary, our results highlight the importance of *O*-acetyl and *O*-methyl modifications for recognition of OAgs by *Bp* and *Bm* LPS-specific mAbs. Furthermore, our findings support the use of synthetic chemistry for deciphering the immunogenic epitopes of non-stoichiometrically substituted surface polysaccharides in the context of antibacterial glycoconjugate vaccines. Collectively, it is anticipated that these studies will serve as foundation for the development of novel therapeutics, diagnostics, and vaccine candidates to combat diseases caused by *Bp* and *Bm*.

Methods

Chemical synthesis. The complete experimental details, compound characterization data, and X-ray crystallographic data can be found in

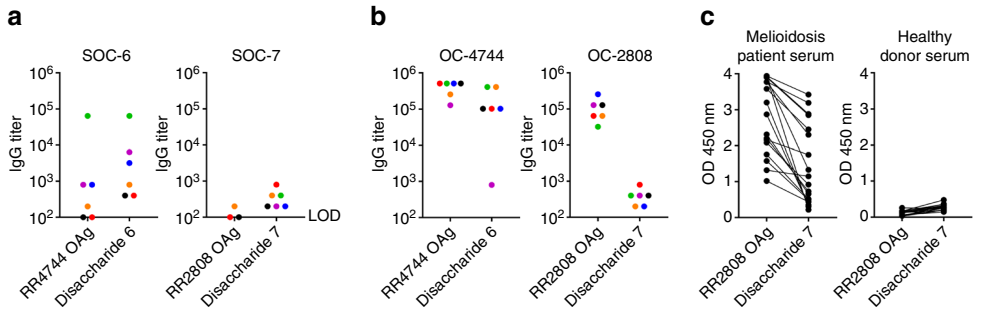


Fig. 8 Mouse and human immune responses to disaccharides and OAgs. BALB/c mice ($n = 6$ per group) were immunized with **a SOC-6** and **SOC-7**or **b** OC-4744 and OC-2808. ELISAs were used to quantitate immune serum IgG titers. *Colored dots* represent the mean end point titers for individual mice against the various target antigens. LOD, limit of detection. **c** Serum samples from culture-confirmed Thai melioidosis patients ($n = 18$) and Thai healthy donors ($n = 18$) were assayed for reactivity with the target antigens using single-dilution ELISAs. *Connecting lines* indicate identical serum samples

Supplementary Methods. For the NMR spectra of new compounds, see Supplementary Figs. 13–166.

mAb 4C7 production. mAb 4C7 was produced as previously described[63]. Briefly, BALB/c mice were intraperitoneally injected with 2×10^8 CFU of heat-inactivated *Bp* (strain 1026b) every 2 weeks for an 8-week period. The antibody titers to *Bp* were monitored using an indirect ELISA with the heat-inactivated strain 1026b in the solid phase. The last immunization was administered 3 days prior to splenectomy. Splenic cells were fused with myeloma cells to produce mAb-secreting hybridomas as previously described[69]. Western blotting analysis was performed to identify hybridoma clones that were producing mAbs reactive in the typical ladder-banding pattern of LPS[63]; as a result, the clone 4C7 was identified. To produce mAb 4C7, the hybridoma cell line was grown in Integra CL 1000 culture flasks (Integra Biosciences), and the mAb was purified by protein A affinity column chromatography.

ELISA assays. To assess the reactivity of LPS-specific mAbs (Pp-PS-W, 4C7, 3D11, and 9C1-2) with synthetic oligosaccharides **1**–**7** and *Burkholderia* OAgs, maleic anhydride 96-well plates (Pierce) were coated overnight at 4 °C with oligosaccharides **1**, **2**, **3**, **4**, **5**, **6** or **7** (5 µg/ml) or purified LPS (10 µg/ml) solubilized in carbonate buffer (pH 9.6). The LPS antigens used in this study were purified from *Bp* strains RR2808 (Δ*wcbB*; *Bp* LPS) and RR4744 (Δ*wcbB*Δ*oacA*; *Bm*-like LPS) as previously described[32, 45]. The coated plates were blocked at room temperature for 30 min with StartingBlock T20 (TBS) Blocking Buffer (SB; Pierce) and then incubated for 1 h at 37 °C with the various mAbs diluted 1/2000 in Tris-buffered saline + 0.05% Tween 20 (TBS-T)+10% SB. To facilitate detection, the plates were incubated for 1 h at 37 °C with 1/2000 dilutions of goat anti-mouse IgM or IgG-horse radish peroxidase (HRP) conjugates (Southern Biotech). The plates were then developed with TMB substrate (KPL) and read at 620 nm. The data were plotted and analyzed using GraphPad Prism 5 (GraphPad Software Inc.).

SPR experiments. SPR analysis of binding between mAb 4C7 and synthetic oligosaccharides was performed using a Biacore X-100 instrument (GE Healthcare). HBS-EP + buffer (10 mM HEPES, 150 mM NaCl, 3 mM EDTA, and 0.05% *v/v* Surfactant P20, pH 7.4, GE Healthcare) was used as a running buffer and diluent throughout the experiments. Biotinylated oligosaccharides **BIO-6**, **BIO-7**, and **BIO-2** (see Supplementary Methods) were separately immobilized on the surface of a SA-coated sensor chip (GE Healthcare); a second flow cell surface was left unmodified for reference subtraction. To generate sensorgrams, two-fold serial dilutions of mAb 4C7 were injected over the sensor chip surface with a flow rate of 30 µL/min for 180 s, followed by passive dissociation for 300 s. Between each cycle, the chip surface was regenerated with a 60 s pulse of 20 mM NaOH. Each analysis was performed in triplicate. Binding affinities (K_D) were calculated using the steady-state affinity model in the BIA evaluation software (version 2.0.1, GE Healthcare).

STD-NMR experiments. NMR experiments were performed with a Bruker 600 MHz DRX instrument equipped with a cryo probe at 283, 298, and 310 K. All the samples were dissolved in deuterated phosphate buffer (pH 7.4) and spectra were calibrated with internal sodium [D_4](trimethylsilyl)propionate (10 µm) at 0.0 ppm for ^{1}H NMR. The ligand resonances were assigned by using standard NMR experiments. Samples for STD-NMR contained an mAb/ligand molar ratio from 1:50 to 1:100 and the antibody concentration was 12 µM. STD-NMR experiments were carried out with 32k data points and zero filled to 64k data point prior processing. A total of 4000 scans were recorded. Selective on-resonance irradiation of antibody resonances was performed at 8 ppm; the off-resonance frequency was set at 100 ppm. The antibody saturation was achieved by using a pulse train of Gaussian shaped pulses of 50 ms duration and 1 ms interpulse delay with an irradiation power of 50 Hz. The saturation time was set at 2 s and a relaxation delay of 4 s was used. A T1ρ filter (50 db spin-lock pulse) and water suppression using excitation sculpting were applied. STD-NMR spectra of ligands in the absence of the antibody and spectra with antibody alone were acquired to obtain reference experiments. The STD effects were calculated by $(I_0-I_{sat})/I_0$, where (I_0-I_{sat}) is the intensity of the signal in the STD-NMR spectrum and I_0 is the peak intensity of the unsaturated reference spectrum (off-resonance). The STD signal with the highest intensity was set to 100%, and others were normalized to this. Data acquisition and processing were performed with TOPSPIN 3.2 software.

Preparation and characterization of glycoconjugates. Disaccharides **6** and **7** (200 µl of 15 mg/ml stocks in anhydrous dimethylsulfoxide (DMSO)) were added dropwise to disuccinimidylglutarate (DSG; 400 µl; 62.5 mg/ml stock in anhydrous DMSO) with trimethylamine (20 µl) and stirred for 2 h at room temperature. Phosphate-buffered saline (PBS; 800 µl, pH 7.2) was then added and the unreacted DSG was extracted twice with equal volumes of chloroform. The aqueous phase was recovered and reacted with CRM197 (2 mg, Reagent Proteins) solubilized in PBS (2 mL) at room temperature for 18–24 h. The reaction product was dialyzed extensively against dH_2O and concentrated using a 10 K MWCO Vivaspin Column (VIVAproducts). Conjugates were visualized by SDS-PAGE (4–12% Bolt gels; Life Technologies). Protein concentration was determined by BCA Assay (Pierce). The conjugates were further analysed by MALDI-TOF-MS. The results were acquired on a TOF/TOF 5800 System (AB SCIEX) using a linear positive mode. To improve ionization, the conjugated samples were dried and reconstituted with 50 mM ammonium bicarbonate buffer. The conjugates were mixed with 2,4,6-trihydroxyacetophenone, which was used as the matrix for the MALDI analysis. The resulting data were externally calibrated using bovine serum albumin. The disaccharide-based conjugates were named **SOC-6** and **SOC-7**, respectively. Glycoconjugates OC-4744 (RR4744 OAg+CRM197) and OC-2808 (RR2808 OAg +CRM197) were synthesized essentially as previously described[33]. The OAgs were purified from *Bp* RR2808 and RR4744 LPS as previously described[32, 45].

Immunogenicity evaluation. Groups of 6–8-week-old female BALB/c mice (Charles River) were immunized subcutaneously on days 0, 21, and 35 with 5 µg of the disaccharide-CRM197 glycoconjugates **SOC-6** and **SOC-7** or 10 µg of the OAg-CRM197 glycoconjugates OC-4744 and OC-2808 formulated in saline plus Alhydrogel 2% (500 µg/mouse; Brenntag) and PolyI:C (30 µg/mouse; InvivoGen). Terminal bleeds were conducted 14 days after the third immunization for the assessment of antibody responses. Six mice per group were chosen to qualitatively assess the immunogenicity of glycoconjugates. Therefore, no randomization, blinding, or statistical analysis was required for comparing the antibody levels. All procedures involving mice were performed according to protocols approved by the University of South Alabama Institutional Animal Care and Use Committee and were conducted in strict accordance with the recommendations in the Guide for the Care and Use of Laboratory Animals of the National Institutes of Health.

Antibody responses directed against disaccharides **6** and **7** as well as crossreactive responses against the *Burkholderia* OAgs were assessed by ELISA essentially as described above. To quantitate disaccharide-specific responses, maleic anhydride 96-well plates were coated with disaccharides **6** or **7** (5 µg/ml) solubilized in carbonate buffer. To quantitate OAg-specific responses, 96-well Maxisorp plates (Nunc) were coated with purified *Bp* RR2808 or RR4744 OAgs (1 µg/ml) solubilized in carbonate buffer. The OAgs were purified from *Bp* RR2808 and RR4744 LPS as previously described[32, 45]. The coated plates were blocked and then incubated for 1 h at 37 °C with the mouse serum samples serially diluted in TBS-T+10% SB. The plates were then incubated for 1 h at 37 °C with 1/2000 dilutions of anti-mouse IgG-HRP conjugate and developed as described above. The reciprocals of the highest dilutions exhibiting optical densities of two times background were used to determine the end point titers for the individual mice.

Human serum ELISAs. Serum samples from culture-confirmed Thai melioidosis patients ($n = 18$) and Thai healthy donors ($n = 18$) were assayed for reactivity with RR2808 OAg and disaccharide **7** essentially as previously described[70]. Plates were coated with RR2808 OAg or disaccharide **7** as described above. Serum samples were assayed at a fixed dilution of 1/2000. The study was approved by the Ethics Committee of Faculty of Tropical Medicine, Mahidol University (approval number MUTM 2014-079-02). Written informed consent was obtained from all subjects.

Data availability. The data that support the findings of this study are available from the corresponding authors (P.J.B. or C.G.) upon reasonable request. The X-ray crystallographic data of compound **36** (CCDC 1520384, Supplementary Tables 2, 3, 4, and 5) are available in the Supplementary Information file.

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Author contributions

M.T.K., M.M., A.N., and C.G. synthesized the oligosaccharides. M.T.K. and C.G. designed the synthetic experiments. Y.B. and J.M. performed the crystallographic study of compound **36**. T.N. and D.P.A. performed the SPR experiments. R.M., A.S., and A.M. performed the STD-NMR experiments. P.J.B. synthesized and characterized the glycoconjugates. P.J.B., T.L.S., and M.N.B. performed the immunogenicity study. K.S. and N.C. performed the human serum ELISAs. M.T.K., M.M., T.N., R.M., M.N.B., P.J.B., and C.G. wrote the manuscript. All authors read and approved the manuscript.

Additional information

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Competing interests: The authors declare no competing financial interests.

Reviewers' comments:

Reviewer #2 (Remarks to the Author):

The authors report the chemical synthesis of five trisaccharides and two disaccharides representing all of the reported inner and terminal fragments of the unique O-antigen polysaccharide of the lipopolysaccharides (LPS) of Burkholderia pseudomallei (Bp) and Burkholderia mallei (Bm). Bp and Bm are etiologic agents of melioidosis and glanders, respectively. These oligosaccharides bear an aminopentanyl aglycon therefore can be easily derivatized. The synthetic oligosaccharide derivatives are then subjected to binding studies with a series of Bp and Bm LPS-specific mAbs, which have previously been shown to be passively protective in mouse models of melioidosis and glanders. Biochemical and biophysical approaches, including ELISA assay, SPR, and STD-NMR are used and lead to conclusion that the mAbs target to the terminal disaccharide residues, especially the terminal 2-O-acetyl-3-O-methyl-6-deoxy-L-talose residue in disaccharide 6. Finally, the authors show that mice immunized with the terminal disaccharides covalently linked to CRM197 are able to produce high titer antibody responses that cross-reacted with Bm-like OAg antigens. These studies shall serve well as a starting point for the development of therapeutics, diagnostics, or vaccine candidates to combat diseases caused by Bp and Bm. The experiments are well done and data well presented. I recommend publication of this interdisciplinary work, with each part being performed by experts in the field, on Nat. Commun.
Minor points:
(1) In the synthesis part, the authors might comment on the unusual conditions used for the deprotection of the anomeric allyl group.
(2) In the binding studies, both disaccharides 6 and 7 show effective binding with mAb 4C7 in the ELISA and SPR assay (although the binding of 6 is indeed stronger), however, there is completely no binding of 7 in the STD-NMR experiments. The authors might comment on this. Additionally, the STD-NMR experiments show the strong involvement of the terminal talose residue in the binding with mAb, the authors might comment on if the appending 2-O-acetyl group also involves.
(3) Page 7, chloroacetyl group should not be abbreviated as AcCl (that is acetyl chloride) but ClAc.
(4) Page S13, Supplementary Fig. 12, the linker should be five carbon long instead of four carbon.

Reviewer #3 (Remarks to the Author):

This is an interesting study and expands on previous studies that demonstrated the protective efficacy of selected monoclonals. In this manuscript the authors go on to describe the recognised eptiopes. From a biological prospective it is interesting and would guide further research and worthy of publication and likely to impact future vaccine design.

The strategy to link the antigens to the CRM is standard.

The authors demonstrated that the antibody responses recognised the OAg antigens. I would have like to have seen antibody binding to the whole bacteria - more biological relevance not just the antigens.

Since B. pseudomallei is an intracellular pathogen I would have like to have seen some additional experiments and discussion on the cellular immune responses. Especially since the authors use PolyI:C adjuvant (with Alhydrogel) that would up-regulate innate immune responses through activation of TLR3 and subsequently up regulation of IL-12 and IFNs.

On the NMR and SPR data I make the following statements:

6 and 7 seem both to have high affinity according to SPR but only 6 binds in the NMR experiment. This doesn't match with the fact that the second OAc group of 7 might abolish binding. It's still

nanomolar.

I find it also intriguing that the only OAc-group of 6 at the talose moiety is completely subtracted and not interacting at all although the talose is strongest engaging residue. This could only happen if the OAc is completely solvent exposed.

The authors should run the STD of 7 at 283 K and 310 K to see if there is a temperature effect. It's plausible though that a second OAc group might abolish binding.

I don't understand how the authors determine 40% of the hydroxyl group at C3 of 6 ? (blue circle Figure 7). Did they not use D2O? This aspect doesn't make sense.

What are the T1/T2/.... in Figure 7? Needs to be labelled in the structure.

All in all the paper presents a range of interesting data, but to be accepted in the journal additional studies would need to be performed.

Reviewer #4 (Remarks to the Author):

In their manuscript entitled "Deciphering minimal antigenic epitopes associated with Burkholderia pseudomallei and Burkholderia mallei lipopolysaccharide O-antigens", Kenfack et al. describe a synthetic approach to access glycan epitopes of the Bp and Bm LPS O-antigens. This is a highly interesting and relevant study that highlights the utility of synthetic carbohydrate chemistry to identify immunogenic glycan epitopes as candidates for novel glycoconjugate vaccines. The authors' approach combines synthetic carbohydrate chemistry with a detailed characterization of the recognition of the minimal glycan epitopes by monoclonal antibodies (mAbs). Finally, they perform immunization studies in mice to determine the immunogenicity of the minimal glycan epitopes. The data on the molecular interaction of the synthetic oligosaccharides with LPS-specific mAbs as determined by glycan array are convincing. The performed SPR and STD-NMR measurements to determine KD values and binding epitopes, respectively, allow for an in-depth insight into the crucial role of the talose moiety in the glycan/mAb interaction. The manuscript is well written and of interest to a broad readership. While the strength of the manuscript is clearly the chemistry part and the biophysical characterization of the glycan/mAb interactions, its weakness is the murine immunization studies. In my opinion, the in vivo studies need to be extended and fine-tuned to render the manuscript acceptable for publication (see "Specific points"):

Specific points:
1.) Why was a steady-state affinity model applied to calculate the KD values from the SPR data (p.12) given that a mAb was used as analyte (i.e. a bivalent analyte)?

2.) The authors state that "future work [should] include optimizing the loading of oligosaccharides onto carrier proteins, varying the dose of the glycoconjugates delivered and determining the most effective adjuvant system" (p.15, ll. 462). In my opinion, however, the present data do not (yet) convincingly show strong immunogenicity of the selected glycan candidates (and the glycoconjugates used for immunization respectively). A prime-boost immunization protocol was employed (three immunizations in total) and a combination of the adjuvants Alum and PolyI:C was used. Still, the obtained IgG titers were fairly low given a limit of detection (LOD) of 100 (as shown in Figure 8C). While IgG responses were generally low for immunization with SOC-7, SOC-6 elicited higher antibody titers that, however, varied among mice (low titers in two out of six mice). I suggest trying alternative immunization protocols and adjuvants to obtain more reliable data on immunogenicity. In addition, the number of immunized mice could be increased to obtain more precise results for the endpoint titers.

3.) Along the same lines: The authors determined cross-reactivity of the antibodies induced by immunization with SOC-6 and SOC-7 with purified Bp O-antigens (Figure 8C). While strong cross-reactivity was observed upon immunization with SOC-6 in at least three out of six immunized mice, barely cross-reactive IgG responses were observed upon immunization with SOC-7. Still, even for SOC-6, there were generally marked reductions in IgG titers against the purified Bp O-antigens compared to the immobilized disaccharides (up to a half order of magnitude). What is the reason? For instance, have the authors determined antibody responses against the linker?

4.) Finally, it is well-known that LPS-specific monoclonal antibodies are protective in infection with Burkholderia and protection can be transferred by passive immunization (e.g. Trevino et al., Infect. Immun. 2006, 74, 1958; AuCoin et al., PLOS One 7, e35386, and other studies correctly cited by the authors). Since the potential of LPS-based subunit vaccines against Burkholderia has previously been shown, I consider a challenge study necessary in which the authors address the protective capacity of the glycoconjugates. Demonstrating the protective potential of CRM glycoconjugates would markedly strengthen the impact of the manuscript and would justify the authors' claim that "these studies serve as foundation for the development of novel therapeutics, diagnostics and vaccine candidates to combat diseases caused by Bp and Bm" as stated in the abstract (p.1).

RESPONSES TO REFEREES

Reviewer #2 (Remarks to the Author):

The authors report the chemical synthesis of five trisaccharides and two disaccharides representing all of the reported inner and terminal fragments of the unique O-antigen polysaccharide of the lipopolysaccharides (LPS) of Burkholderia pseudomallei (Bp) and Burkholderia mallei (Bm). Bp and Bm are etiologic agents of melioidosis and glanders, respectively. These oligosaccharides bear an aminopentanyl aglycon therefore can be easily derivatized. The synthetic oligosaccharide derivatives are then subjected to binding studies with a series of Bp and Bm LPS-specific mAbs, which have previously been shown to be passively protective in mouse models of melioidosis and glanders. Biochemical and biophysical approaches, including ELISA assay, SPR, and STD-NMR are used and lead to conclusion that the mAbs target to the terminal disaccharide residues, especially the terminal 2-O-acetyl-3-O-methyl-6-deoxy-L-talose residue in disaccharide 6. Finally, the authors show that mice immunized with the terminal disaccharides covalently linked to CRM197 are able to produce high titer antibody responses that cross-reacted with Bm-like OAg antigens. These studies shall serve well as a starting point for the development of therapeutics, diagnostics, or vaccine candidates to combat diseases caused by Bp and Bm. The experiments are well done and data well presented. I recommend publication of this interdisciplinary work, with each part being performed by experts in the field, on Nat. Commun.

Response: We thank the reviewer for his/her positive comments regarding our work.

Minor points:

(1) In the synthesis part, the authors might comment on the unusual conditions used for the deprotection of the anomeric allyl group.

Response: We agree with the reviewer that the conditions for the deprotection of the allyl group are somewhat unusual, *i.e.* using an iridium-based Crabtree-like catalyst for the anomerization of the allyl group followed by a iodine-promoted deprotection. However, these conditions have been previously successfully used by our group and others in many occasions (see Tamigney Kenfack, M. *et al. J. Org. Chem.* 2014, *79*, 4615-4634; Gauthier, C. *et al. Org. Biomol. Chem.* 2014, *12*, 4218-4232; Laroussarie, A. *et al. J. Org. Chem.* 2015, *80*, 10386-10396). As suggested, more details regarding the transformation of disaccharide **34** into TCA derivative **35** have been added in the revised manuscript (see Results: Second generation synthesis of protected trisaccharides).

(2) In the binding studies, both disaccharides 6 and 7 show effective binding with mAb 4C7 in the ELISA and SPR assay (although the binding of 6 is indeed stronger), however, there is completely no binding of 7 in the STD-NMR experiments. The authors might comment on this. Additionally, the STD-NMR experiments show the strong involvement of the terminal talose residue in the binding with mAb, the authors might comment on if the appending 2-O-acetyl group also involves.

Response: The absence of signals in the STD NMR spectrum of the disaccharide **7** could be due to unfavorable binding kinetics considering that the ligand off-rate is extremely important for the overall sensitivity of the experiment. Given that the temperature strongly influences the kinetics and consequently the observed STD effects, we decided to run a STD NMR spectrum decreasing the temperature to 283 K (see revised Figure 7). Interestingly, under these experimental conditions, some slight, although not quantifiable, STD enhancements were observed for the mAb 4C7 – disaccharide **7** complex, confirming that the temperature might have affected the $K_{off.}$.

In addition, as regards the contribution of the appending 2-*O*-acetyl group, we have further optimized the experimental conditions of STD NMR spectra in order to investigate the interaction between the disaccharide **6** and the monoclonal antibody. In the previous spectrum, the OAc-group of disaccharide **6** at the talose moiety was completely subtracted likely due to experimental conditions such as spin lock pulse applied to reduce the intensity of broad antibody resonances and/or antibody concentration. Thus, we acquired new STD spectra by using a lower concentration of the antibody (12 µM vs 33 µM) in deuterated phosphate buffer, a weaker spin lock (50 db vs 10 db) and a longer relaxation delay (4 sec). The resulting spectrum is reported in Figure 7 of the revised manuscript and shows a strong contribution of the acetyl group to the interaction, as expected.

(3) Page 7, chloroacetyl group should not be abbreviated as AcCl (that is acetyl chloride) but ClAc.

Response: This error has been corrected in the revised manuscript.

(4) Page S13, Supplementary Fig. 12, the linker should be five carbon long instead of four carbon.

Response: This error has been corrected in the revised supporting information file.

Reviewer #3 (Remarks to the Author):

This is an interesting study and expands on previous studies that demonstrated the protective efficacy of selected monoclonals. In this manuscript the authors go on to describe the recognised eptiopes. From a biological prospective it is interesting and would guide further research and worthy of publication and likely to impact future vaccine design.

Response: We thank the reviewer for his/her positive comments regarding our work.

The strategy to link the antigens to the CRM is standard.

The authors demonstrated that the antibody responses recognised the OAg antigens. I would have like to have seen antibody binding to the whole bacteria - more biological relevance not just the antigens.

Response: Additional experiments and text have been added to the revised manuscript to address this issue (see Results: Immunization of mice with disaccharide- and OAg-based glycoconjugates - second paragraph, Supplementary Figure 175 and Supplementary methods). Using ELISA and immunofluorescence staining/microscopy techniques, we were able to confirm that **SOC-6** immune serum reacts strongly with both purified *Bm*-like OAg and paraformaldehyde-fixed *Bm*, respectively. Due to the inability of BALB/c and C57BL/6 mice to produce antibody responses against the terminal epitope of *Bp* OAg or disaccharide **7** (see Results: Immunization of mice with disaccharide- and OAg-based glycoconjugates - second paragraph and revised Figure 8 and Supplementary Figure 176), similar studies were not conducted with **SOC-7** immune serum.

Since B. pseudomallei is an intracellular pathogen I would have like to have seen some additional experiments and discussion on the cellular immune responses. Especially since the authors use PolyI:C adjuvant (with Alhydrogel) that would up-regulate innate immune responses through activation of TLR3 and subsequently up regulation of IL-12 and IFNs.

Response: Other than raising T-cell responses against the CRM197 carrier protein (which are critical for enabling high titer IgG responses to be produced against the covalently-linked haptens - disaccharides **6** and **7**), immunization of mice with **SOC-6** or **SOC-7** would not be predicted to elicit any protective cellular responses. As the Reviewer is aware, the main objective of immunizing with glycoconjugates is to stimulate protective humoral responses. This being the case, we do eventually plan to assess the functional activity of our immune serum samples (via opsonophagocytosis/opsonophagocytic killing assays) but only once we are able to optimize the immunogenicity of **SOC-6** (e.g. obtain more reproducible responses against disaccharide **6**) and find a suitable animal model that enables us to produce antibody responses against the terminal epitope of *Bp* OAg or disaccharide **7** (see Results: Immunization of mice with disaccharide- and OAg-based glycoconjugates - second paragraph and revised Figure 8 and Supplementary Figure 176). As for the PolyI:C/Alhydrogel adjuvant system, it was not our intention to use it to promote protective cellular immune responses. Instead, we used this adjuvant system to formulate our glycoconjugates since, in our experience, it enables us to generate higher titer IgG responses against oligosaccharides/polysaccharides than using Alhydrogel alone (presumably due to the production of IL-12 and IFNs as noted by the Reviewer).

On the NMR and SPR data I make the following statements:

6 and 7 seem both to have high affinity according to SPR but only 6 binds in the NMR experiment. This doesn't match with the fact that the second OAc group of 7 might abolish binding. It's still nanomolar.

Response: The absence of signals in the STD NMR spectrum of the disaccharide **7** in the presence of the mAb 4C7 could be due to unfavourable binding kinetics since the ligand off-rate is extremely important for the overall sensitivity of the experiment. To confirm the above, a slight increase of some STD signals intensity was observed for disaccharide **7** in the presence of the mAb 4C7 when the temperature was decreased to 283 K (see revised Figure 7).

I find it also intriguing that the only OAc-group of 6 at the talose moiety is completely subtracted and not interacting at all although the talose is strongest engaging residue. This could only happen if the OAc is completely solvent exposed.

Response: The *O*-acetyl group of disaccharide **6** at the talose moiety was completely subtracted likely due to experimental conditions like spin lock pulse applied to reduce the intensity of broad antibody resonances and/or antibody concentration. Thus, we acquired new STD spectra by using a lower concentration of the antibody (12 μM vs 33 μM) in deuterated phosphate buffer, a weaker

spin lock (50 db vs 10 db) and a longer relaxation delay (4 sec). The resulting spectrum is reported in the Figure 7 of the revised manuscript and it shows a strong contribution of the acetyl group to the interaction, as expected.

The authors should run the STD of 7 at 283 K and 310 K to see if there is a temperature effect. It's plausible though that a second OAc group might abolish binding.

Response: We have run the STD spectra of disaccharide **7** in the presence of the mAb 4C7 at different temperatures, 283 K, 298 K and 310 K (see revised Figure 7 and Supplementary Figures 171 and 172). As also added to the main text of the revised manuscript, no STD signals were observed at 298 K and 310 K. However, when the temperature was set at 283 K, some slight STD enhancements were observed for the mAb 4C7 – disaccharide **7** complex, indicating a temperature effect.

I don't understand how the authors determine 40% of the hydroxyl group at C3 of 6 ? (blue circle Figure 7). Did they not use D2O? This aspect doesn't make sense.

Response: We determined the percentage of the STD effect belonging to the *O*-methyl group at C3 of the talose residue. It is not a hydroxyl group.

What are the T1/T2/.... in Figure 7? Needs to be labelled in the structure.

Response: The proton resonances belonging to talose and glucose residues were indicated with letters, **T** and **G**, respectively. We have modified the caption of the Figure 7, indicating what the letters stand for.

All in all the paper presents a range of interesting data, but to be accepted in the journal additional studies would need to be performed.

Reviewer #4 (Remarks to the Author):

In their manuscript entitled "Deciphering minimal antigenic epitopes associated with Burkholderia pseudomallei and Burkholderia mallei lipopolysaccharide O-antigens", Kenfack et al. describe a synthetic approach to access glycan epitopes of the Bp and Bm LPS O-antigens. This is a highly interesting and relevant study that highlights the utility of synthetic carbohydrate chemistry to identify immunogenic glycan epitopes as candidates for novel glycoconjugate vaccines. The authors' approach combines synthetic carbohydrate chemistry with a detailed characterization of the recognition of the minimal glycan epitopes by monoclonal antibodies (mAbs). Finally, they perform immunization studies in mice to determine the immunogenicity of the minimal glycan epitopes. The data on the molecular interaction of the synthetic oligosaccharides with LPS-specific mAbs as determined by glycan array are convincing. The performed SPR and STD-NMR measurements to determine KD values and binding epitopes, respectively, allow for an in-depth insight into the crucial role of the talose moiety in the glycan/mAb interaction. The manuscript is well written and of interest to a broad readership.

Response: We thank the reviewer for his/her positive comments regarding our work.

While the strength of the manuscript is clearly the chemistry part and the biophysical characterization of the glycan/mAb interactions, its weakness is the murine immunization studies. In my opinion, the in vivo studies need to be extended and fine-tuned to render the manuscript acceptable for publication (see "Specific points"):

Specific points:

1.) Why was a steady-state affinity model applied to calculate the KD values from the SPR data (p.12) given that a mAb was used as analyte (i.e. a bivalent analyte)?

Response: In the Biacore data analysis package, there are two ways to assess an experiment like ours. The first is the kinetic method, which results in an estimate of both the association rate constant (k_a) and the dissociation rate constant (k_d). These values can then be used to calculate the dissociation constant ($K_D = k_d/k_a$). The second method is the concentration method, in which a plot of RU_{max} *vs* mAb concentration is constructed and the subsequent analysis results in another estimate of the K_D. This value is sometimes referred to as the steady-state K_D or the apparent K_D. Initially, both kinetics and concentration methods were used to evaluate the binding affinity between mAb 4C7 and the synthesized oligosaccharides in this study. The results derived from both methods showed that mAb 4C7 binds to immobilized **BIO-6** with a higher affinity as compared to **BIO-7**. We agree with the reviewer that assessment of the binding affinity using the thermodynamic constants ($K_D = k_d/k_a$) is the traditional way to do this and results in somewhat higher estimates of

affinity. However, in this study we chose to report steady-state K_D because it is more reliable as suggested by the control statistic parameters (standard deviation and χ^2 values). In addition, in much of the literature, the steady-state K_D is used for purposes of comparison (e.g., analysis of a mAb binding to modified targets). Also, we feel though that the inclusion of the k_a and k_d values may be of interest to readers who want to compare rates of association/dissociation or calculate the K_D by the other method on their own. Again, thank you for your careful consideration of our study.

2.) The authors state that "future work [should] include optimizing the loading of oligosaccharides onto carrier proteins, varying the dose of the glycoconjugates delivered and determining the most effective adjuvant system" (p.15, ll. 462). In my opinion, however, the present data do not (yet) convincingly show strong immunogenicity of the selected glycan candidates (and the glycoconjugates used for immunization respectively). A prime-boost immunization protocol was employed (three immunizations in total) and a combination of the adjuvants Alum and PolyI:C was used. Still, the obtained IgG titers were fairly low given a limit of detection (LOD) of 100 (as shown in Figure 8C). While IgG responses were generally low for immunization with SOC-7, SOC-6 elicited higher antibody titers that, however, varied among mice (low titers in two out of six mice). I suggest trying alternative immunization protocols and adjuvants to obtain more reliable data on immunogenicity. In addition, the number of immunized mice could be increased to obtain more precise results for the endpoint titers.

Response: Additional experiments and text have been added to the revised manuscript to address these issues (see Results: Immunization of mice with disaccharide- and OAg-based glycoconjugates - second paragraph and revised Figure 8). In Figure 8b, we now show that when immunized with OC-4744 (RR4744 OAg-CRM197), high titer antibody responses in 5/6 mice can be produced against RR4744 OAg as well as disaccharide **6** (terminal epitope of the OAg). This being the case, it is unlikely that the adjuvant system or the number of mice that we used for our studies can account for the variable immunogenicity of **SOC-6**. Instead, as previously suggested, we think that optimizing the loading/presentation of disaccharide **6** on CRM197 will help to resolve this issue. As for the poor immunogenicity of **SOC-7**, immunization of BALB/c and C57BL/6 mice with OC-2808 (RR2808 OAg-CRM197) suggests that we will be unable to generate antibody responses against the terminal epitope of RR2808 OAg or disaccharide **7** in these animal models (see revised Figure 8 and Supplementary Figure 176). As previously suggested, this appears to be due to a hole in their B cell repertoire since humans have the ability to generate antibody responses against the terminal disaccharide of *Bp* OAg (see revised Figure 8).

3.) Along the same lines: The authors determined cross-reactivity of the antibodies induced by immunization with SOC-6 and SOC-7 with purified Bp O-antigens (Figure 8C). While strong cross-reactivity was observed upon immunization with SOC-6 in at least three out of six immunized mice,

barely cross-reactive IgG responses were observed upon immunization with SOC-7. Still, even for SOC-6, there were generally marked reductions in IgG titers against the purified Bp O-antigens compared to the immobilized disaccharides (up to a half order of magnitude). What is the reason? For instance, have the authors determined antibody responses against the linker?

Response: The observation that 5/6 of the **SOC**-6 serum samples did not exhibit equal levels of reactivity with disaccharide **6** and RR4744 OAg (which are two similar but non-identical target antigens) is not unexpected (see revised Figure 8a). While disaccharide **6** and the two terminal residues of RR4744 OAg are structurally identical to one another, in the context of an immune assay (e.g. ELISA), they are not displayed in the same manner (e.g. anchored by a small linker vs. a large polysaccharide chain) which may influence antibody binding to the target antigens resulting in differing levels of reactivity. This phenomenon is also observed with the mouse mAbs (Figure 5b), mouse immune serum (see revised Figure 8b and Supplementary Figure 176) and human immune serum (see revised Figure 8c) which further supports this explanation.

4.) Finally, it is well-known that LPS-specific monoclonal antibodies are protective in infection with Burkholderia and protection can be transferred by passive immunization (e.g. Trevino et al., Infect. Immun. 2006, 74, 1958; AuCoin et al., PLOS One 7, e35386, and other studies correctly cited by the authors). Since the potential of LPS-based subunit vaccines against Burkholderia has previously been shown, I consider a challenge study necessary in which the authors address the protective capacity of the glycoconjugates. Demonstrating the protective potential of CRM glycoconjugates would markedly strengthen the impact of the manuscript and would justify the authors' claim that "these studies serve as foundation for the development of novel therapeutics, diagnostics and vaccine candidates to combat diseases caused by Bp and Bm" as stated in the abstract (p.1).

Response: Immunization of BALB/c and C57BL/6 mice with OC-2808 (RR2808 OAg-CRM197) or **SOC-7** suggests that we will be unable to generate antibody responses against the terminal epitope of RR2808 OAg and disaccharide **7** in these animals (see Results: Immunization of mice with disaccharide- and OAg-based glycoconjugates - second paragraph and see revised Figure 8 and Supplementary Figure 176). Since these mouse strains are the most frequently used animal models of experimental melioidosis, we are unable to assess the protective capacity of **SOC**-7 until we identify an alternative animal model. As for **SOC-6**, it would be unethical (from an animal welfare/IACUC perspective) to conduct a challenge study prior to optimizing the immunogenicity of the construct. This being the case, and with all due respect to the Reviewer, we do not believe that the inability to conduct these experiments at the present time lessens the overall quality or impact of our study.

REVIEWERS' COMMENTS:

Reviewer #3 (Remarks to the Author):

The authors have responded to the majority of my comments and I believe that the manuscript is in much better shape. My view is that the paper is suitable for publication in the journal, subject to further editorial consideration.

Reviewer #4 (Remarks to the Author):

In their manuscript entitled "Deciphering minimal antigenic epitopes associated with Burkholderia pseudomallei and Burkholderia mallei lipopolysaccharide O-antigens", Kenfack et al. describe a synthetic approach to access glycan epitopes of the Bp and Bm LPS O-antigens. This is a highly interesting and relevant study that highlights the utility of synthetic carbohydrate chemistry to identify immunogenic glycan epitopes as candidates for novel glycoconjugate vaccines.

The manuscript has been considerably improved and the revised version addresses my main concerns. Although an in vivo challenge study has not been performed, I can accept the authors' explanation that immunogenicity of the construct has to be optimized first.

Reviewer #3 (Remarks to the Author):

The authors have responded to the majority of my comments and I believe that the manuscript is in much better shape. My view is that the paper is suitable for publication in the journal, subject to further editorial consideration.

We thank the reviewer for his/her positive comments regarding our work.

Reviewer #4 (Remarks to the Author):

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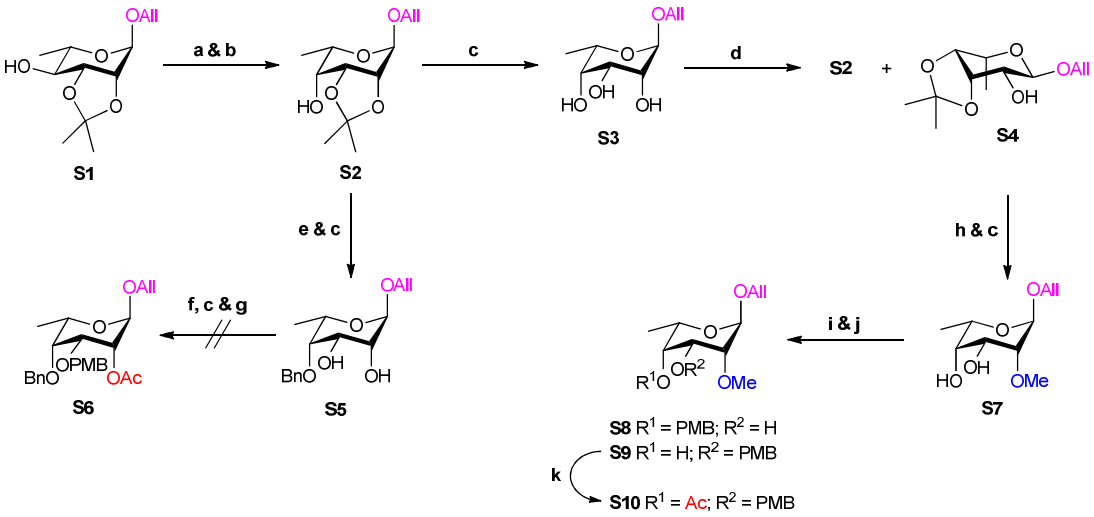
We thank the reviewer for his/her positive comments regarding our work.

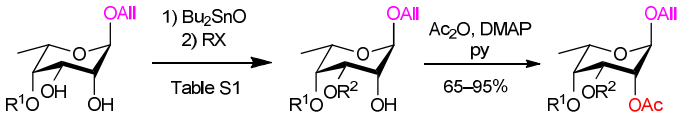
File Name: Supplementary Information
Description: Supplementary Figures, Supplementary Tables, Supplementary Methods and Supplementary References

File Name: Peer Review File
Description:



Supplementary Figure 1 | Synthesis of 6-deoxy-L-talose derivatives. Reagents and conditions: (**a**) PDCP, DMSO, Et_3N, DCM, –10 °C to RT, 40 min; or Dess-Martin periodinane, DCE, reflux, 1 h; (**b**) $NaBH_4$, DCM/MeOH, –10 to 0 °C, 1 h, 65–70% (over two steps); (**c**) 80% HOAc, 60 °C, 3 h, 96% (for **S3**); 99% (for **S5**, over two steps); 92% (for **S7**, over two steps); (**d**) 2,2-DMP, PTSA, Me_2CO, RT, 2 h, 83% (for **S4**); 14% (for **S2**); (**e**) BnBr, NaH, DMF, 0 °C to RT, 2 h; (**f**) $MeC(OMe)_3$, PTSA, CH_3CN; (**g**) PMBCl, Ag_2CO_3, tol, 60 °C; or PMBCl, Ag_2O, Me_2S, TBAI, CH_3CN; or PMBTCA, Et_2O, TfOH; (**h**) MeI, NaH, TBAI, DMF, 0 °C to RT, 5 h; (**i**) Bu_2SnO, tol, reflux, 3 h; (**j**) PMBCl, CsF, TBAI, tol, 50 °C, overnight, 13% (for **S8**, over two steps); 60% (for **S9**, over two steps); (**k**) Ac_2O, py, DMAP, RT, overnight, 84%. Ac, acetyl; Ac_2O, acetic anhydride; All, allyl; Bn, benzyl; BnBr, benzyl bromide; Bu_2SnO, dibutyltin oxide; DCE, 1,2-dichloroethane; DCM, dichloromethane; DMAP, 4-(dimethylamino)pyridine; DMF, *N*,*N*-dimethylformamide; 2,2-DMP, 2,2-dimethoxypropane; DMSO, dimethylsulfoxide; Et_2O, diethyl ether; HOAc, acetic acid; $MeC(OMe)_3$, trimethyl orthoacetate; PDCP, phenyl dichlorophosphate; PMB, *para*-methoxybenzyl; PMBCl, *para*-methoxybenzyl chloride; PMBTCA, *para*-methoxybenzyl trichloroacetimidate; PTSA, *para*-toluenesulfonic acid; py, pyridine; RT, room temperature; TBAI, tetrabutylammonium iodide; TfOH, trifluoromethanesulfonic acid; tol, toluene.

Supplementary Table 1 | Regioselective protection of diols via stannylene acetal.



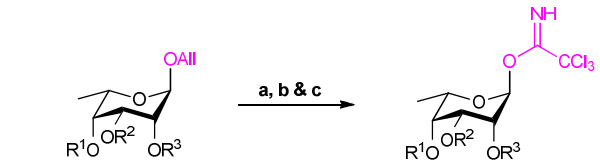
S3 R^1 = H
S5 R^1 = Bn

S11 R^1 = H; R^2 = PMB
S12 R^1 = H; R^2 = Me
S13 R^1 = Bn; R^2 = PMB
S14 R^1 = Bn; R^2 = Me

S15 R^1 = Ac; R^2 = PMB
S16 R^1 = Ac; R^2 = Me
S6 R^1 = Bn; R^2 = PMB
S17 R^1 = Bn; R^2 = Me

Entry	Compd	Reagents and conditions		Product	Yield[b] (%)
		Step 1)[a]	Step 2)[a]		
1	**S3**	tol	PMBCl, TBAI, tol	**S11**	43
2	**S3**	tol	PMBCl, CsF, tol	**S11**	trace
3	**S3**	tol	PMBCl, TBAI, CsF, tol	**S11**	31
4	**S3**	MeOH	PMBCl, TBAI, CsF, tol	**S11**	65
5	**S3**	MeOH	MeI, CsF, tol[c]	**S12**	28
6	**S3**	MeOH	MeI, CsF, DMF[c]	**S12**	38
7	**S5**	tol	MeI, CsF, tol	**S14**	85
8	**S5**	tol	PMBCl, TBAI, tol	**S13**	56[d]

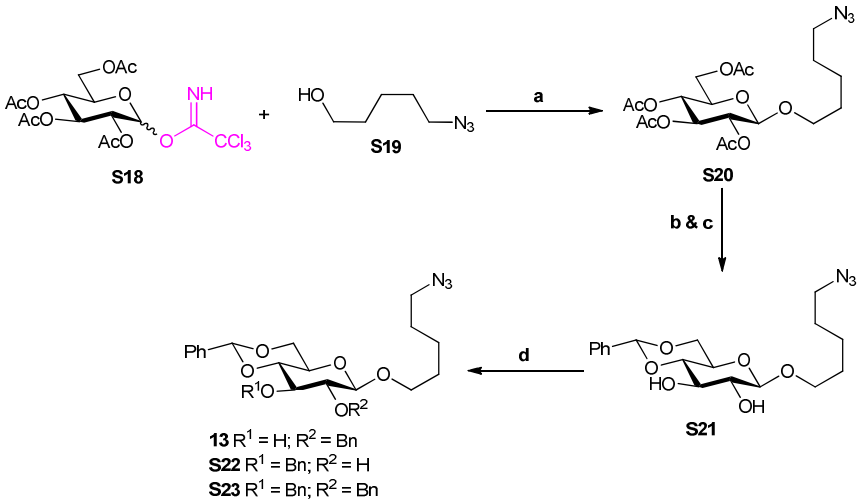
[a]The reaction was performed in refluxing toluene or MeOH.
[b]Isolated yield.
[c]The reaction was performed at 80 °C.
[d]The 2-*O*-PMB regioisomer was isolated as a minor compound (32% yield).



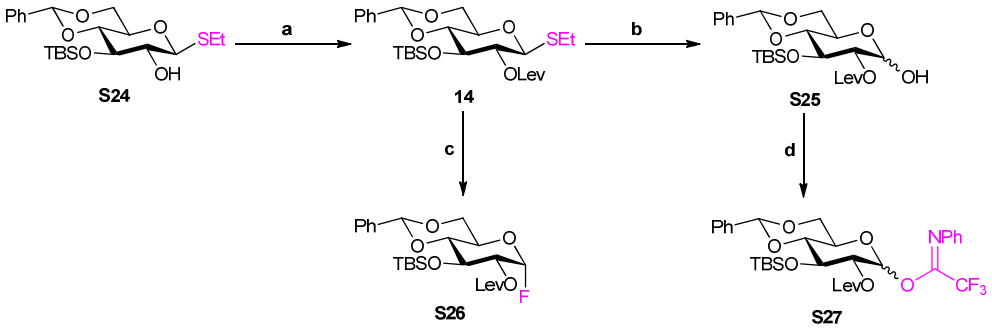
S6 R^1 = Bn; R^2 = PMB; R^3 = Ac
S10 R^1 = Ac; R^2 = PMB; R^3 = Me
S15 R^1 = Ac; R^2 = PMB; R^3 = Ac
S17 R^1 = Bn; R^2 = Me; R^3 = Ac
S16 R^1 = Ac; R^2 = Me; R^3 = Ac

8 R^1 = Bn; R^2 = PMB; R^3 = Ac
9 R^1 = Ac; R^2 = PMB; R^3 = Me
10 R^1 = Ac; R^2 = PMB; R^3 = Ac
11 R^1 = Bn; R^2 = Me; R^3 = Ac
12 R^1 = Ac; R^2 = Me; R^3 = Ac

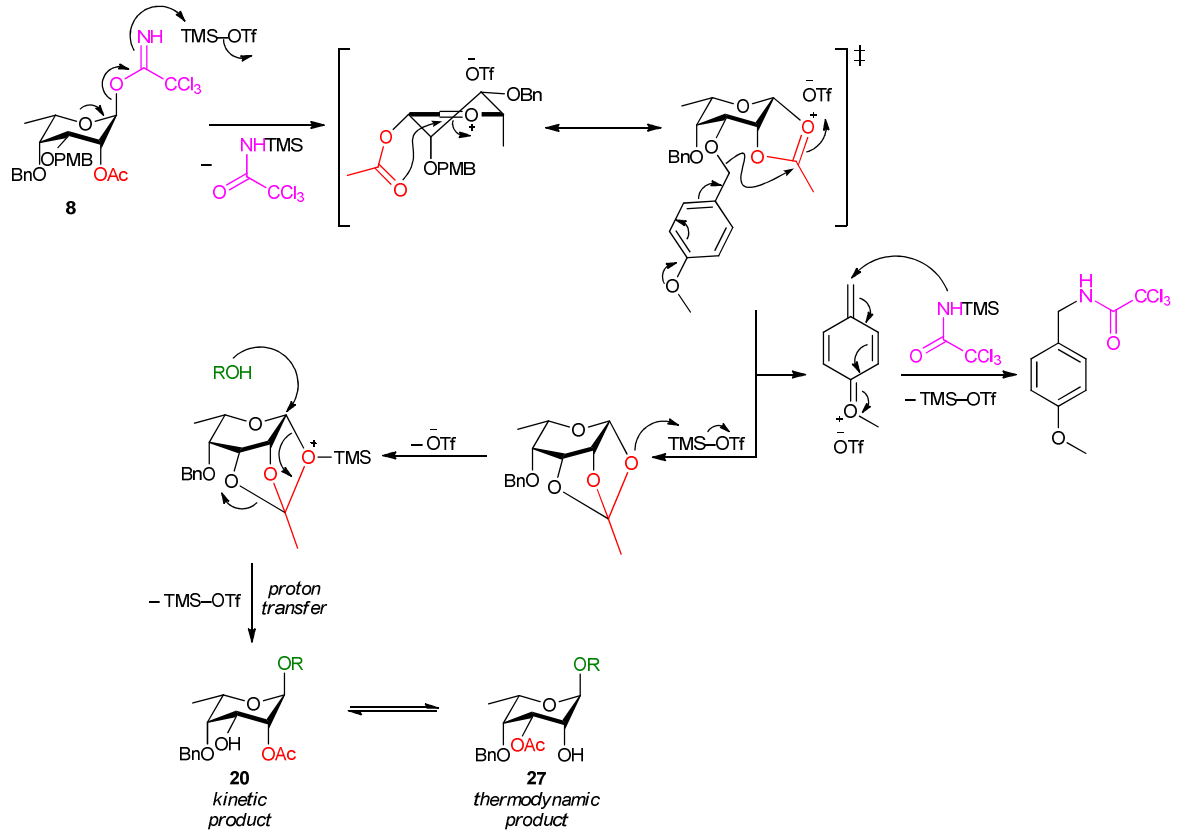
Supplementary Figure 2 | Synthesis of 6-deoxy-L-talopyranosyl trichloroacetimidate donors. Reagents and conditions: (**a**) $[Ir(COD)\{PMe(C_6H_5)_2\}_2]^+.PF_6^-$, H_2, THF, RT, 1 h; (**b**) I_2, THF, H_2O, RT, 2 h, 66–89% (over two steps); (**c**) CCl_3CN, Cs_2CO_3, DCM/Me_2CO or DBU, DCM/Me_2CO, RT, 2–4 h, 58–91% (over two steps). CCl_3CN, trichloroacetonitrile; COD, cyclooctadienyl; DBU, 1,8-diazabicyclo[5.4.0]undec-7-ene; THF, tetrahydrofuran.



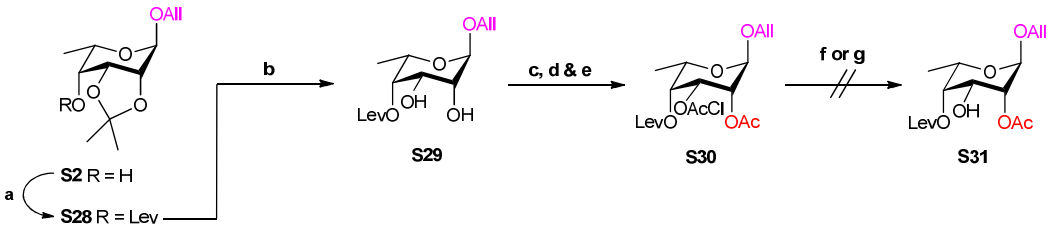
Supplementary Figure 3 | Synthesis of glucoside acceptor 13. Reagents and conditions: (**a**) TMSOTf, DCE, 4 Å MS, –10 °C to RT, overnight, 50%; (**b**) Et_3N, MeOH, RT, 48 h; (**c**) BDMA, CSA, CH_3CN, RT, 8 h, 78% (over two steps); (**d**) BnBr, TBAHS, 5% NaOH, DCM, reflux, 16 h, 55% (for **13**); 28% (for **S22**); 9% (for **S23**). BDMA, benzaldehyde dimethyl acetal; CSA, camphorsulfonic acid; Ph, phenyl; TBAHS, tetrabutylammonium hydrogenosulfonate; TMSOTf, trimethylsilyl trifluoromethanesulfonate.



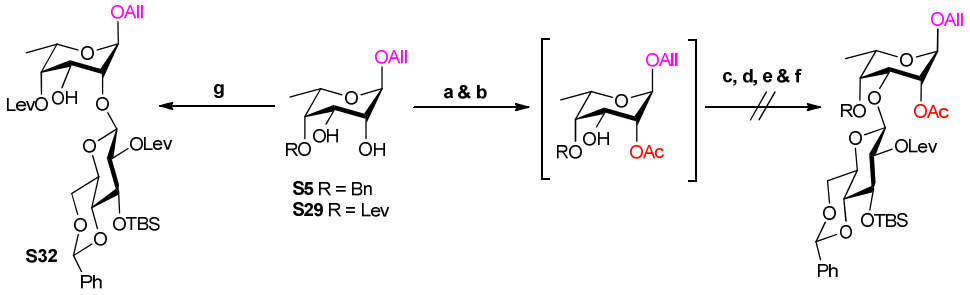
Supplementary Figure 4 | Synthesis of glucosydonors 14, S26, and S27. Reagents and conditions: (**a**) Lev_2O, py, DMAP, 50 °C, 6 h, 83%; (**b**) NBS, DCM, H_2O, 0 °C to RT, 2 h, 66%; (**c**) NBS, DAST, DCM, –10 °C to RT, 2 h, 73%; (**d**) PTFACl, K_2CO_3, Me_2CO, RT, 7 h, 58%. DAST, diethylaminosulfur trifluoride; Lev, levulinoyl; Lev_2O, levulinic anhydride; NBS, *N*-bromosuccinimide; PTFACl, *N*-phenyl-2,2,2-trifluoroacetimidoyl chloride; SEt, thioethyl; TBS, *tert*-butyldimethylsilyl.



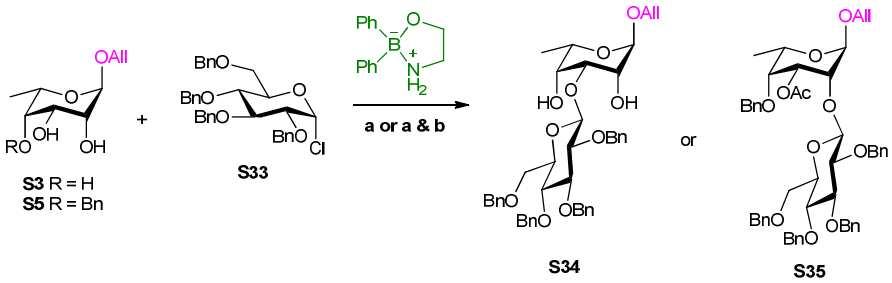
Supplementary Figure 5 | Proposed mechanism for the cleavage of PMB group during glycosylation. Formation of derivative **20** can be tentatively explained via a mechanism in which a transient tricylic orthoester intermediate is attacked by the alcohol acceptor on the α-side. The resulting kinetic product **20** can then be transformed into the more stable derivative **27** by migration of the acetyl group from the C2 to C3 position.



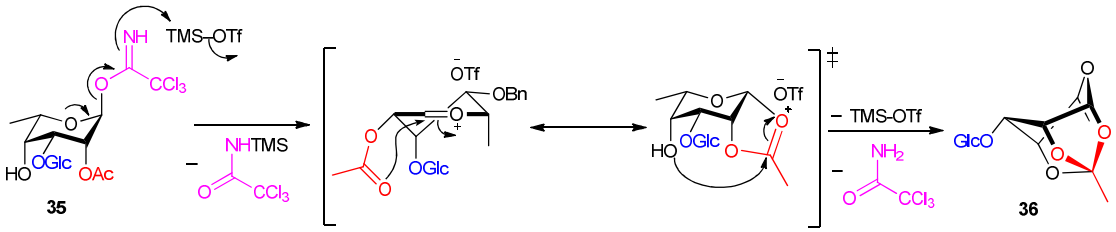
Supplementary Figure 6 | Attempts to synthesize taloside acceptor S31. Reagents and conditions: (**a**) Lev_2O, py, DMAP, 50 °C, 2 h, 95%; (**b**) 80% HOAc, 60 °C, 1 h; (**c**) $MeC(OMe)_3$, PTSA, CH_3CN, RT, 2 h; (**d**) 80% HOAc, 0 °C to RT, 2 h; (**e**) $(ClAc)_2O$, py, DMAP, RT, 10 min, 83% (over four steps from **S28**); (**f**) DABCO, 55 °C, EtOH/py 5:1; (**g**) TBAF, THF, RT. $(ClAc)_2O$, chloroacetic anhydride; DABCO, 1,4-diazabicyclo[2.2.2]octane; TBAF, tetrabutylammonium fluoride.



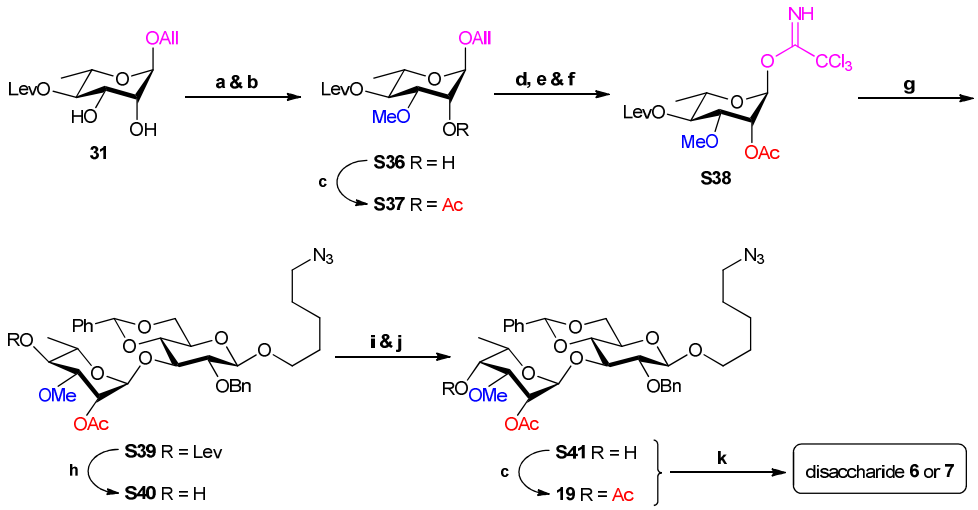
Supplementary Figure 7 | Attempts to synthesize (1→3)-linked disaccharides. Reagents and conditions: (**a**) $MeC(OMe)_3$, PTSA, CH_3CN, RT, 2 h; (**b**) 80% HOAc, 0 °C to RT, 2 h; (**c**) donor **14**, NIS, AgOTf, 4 Å MS, Et_2O, –10 °C; (**d**) donor **14**, DMTST, DTBMP, 4 Å MS, Et_2O, –10 to 40 °C; (**e**) donor **S26**, Cp_2ZrCl_2, AgOTf, 4 Å MS, Et_2O, –10 °C; (**f**) donor **S27**, TMSOTf, DCE, 4 Å MS, –10 °C; (**g**) donor **14**, DMTST, DTBMP, 4 Å MS, DCE, RT, 2 h, 43%. AgOTf, silver(I) trifluoromethanesulfonate; Cp_2ZrCl_2, bis(cyclopentadienyl)zirconium(IV) dichloride; DMTST, dimethyl(methylthio)sulfonium trifluoromethanesulfonate; DTBMP, 2,6-di-*tert*-butyl-4-methylpyridine; MS, molecular sieves; NIS, *N*-iodosuccinimide.



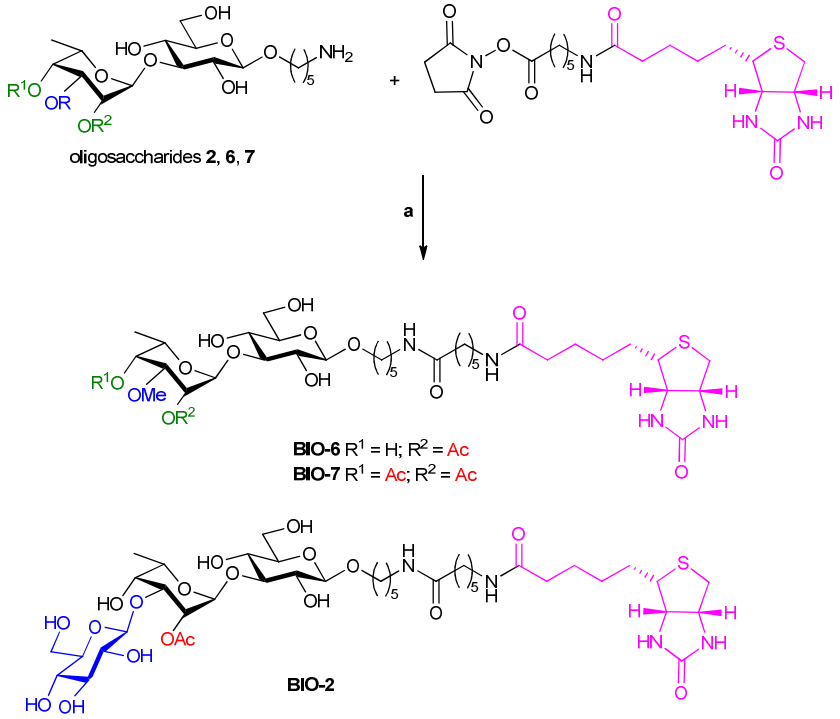
Supplementary Figure 8 | Glucosylation of diol S5 and triol S3 using Taylor catalyst. Reagents and conditions: (**a**) 2-aminoethyl diphenylborinate (0.25 equiv), Ag_2O, CH_3CN, 60 °C, 16–48 h, 25% (for **S34**); (**b**) Ac_2O, py, DMAP, RT, overnight, 58% (for **S35** over two steps).



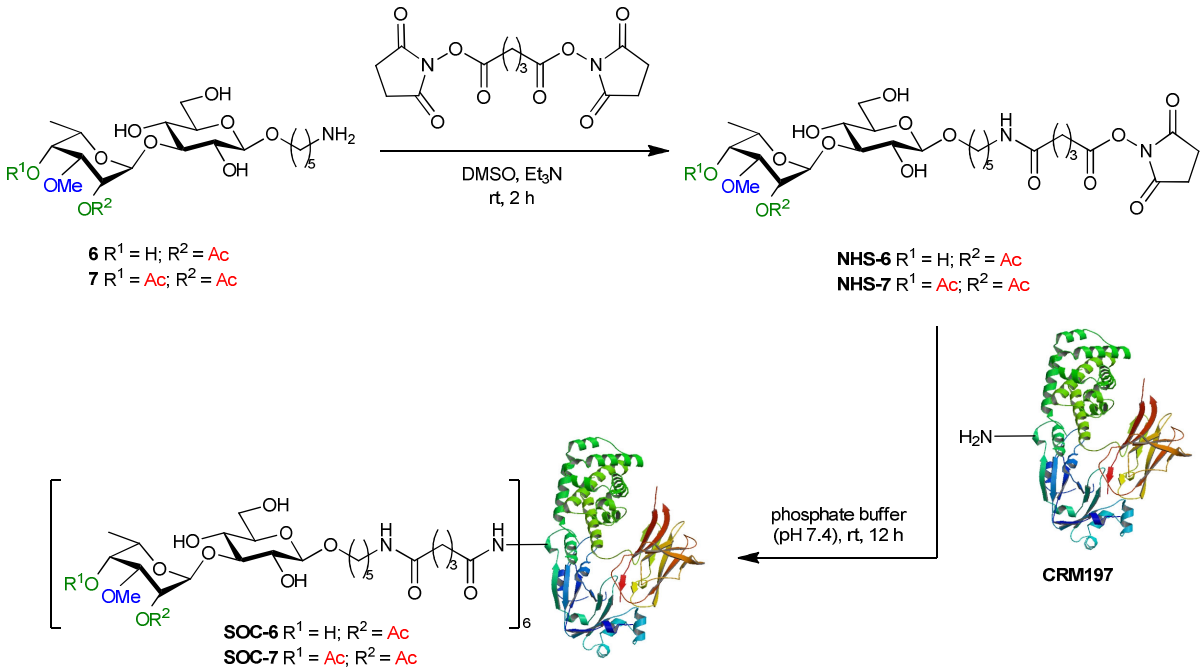
Supplementary Figure 9 | Proposed mechanism for the formation of tricyclic orthoester 36. Formation of derivative **36** can be tentatively explained by the attack of free alcohol C4 to the carbonyl group of the dioxalenium intermediate.



Supplementary Figure 10 | Second generation synthesis of target disaccharides 6 and 7. Reagents and conditions: (**a**) Bu_2SnO, tol, reflux, 5 h; (**b**) MeI, CsF, tol, 80 °C, overnight, 96% (over two steps); (**c**) Ac_2O, py, DMAP, RT, 16 h, 88% (for **S37**); 65% (for **19**); (**d**) $[Ir(COD)\{PMe(C_6H_5)_2\}_2]^+.PF_6^-$, H_2, THF; (**e**) I_2, THF, H_2O; (**f**) CCl_3CN, Cs_2CO_3, Me_2CO, 87% (over three steps); (**g**) acceptor **13**, TMSOTf (0.1 equiv), 4 Å MS, Et_2O/DCE 5:1, –10 °C to RT, 30 min, 92%; (**h**) $H_2NNH_2.H_2O$, py, HOAc, 0 °C to RT, overnight, 99%; (**i**) PDCP, DMSO, Et_3N, DCM, –10 °C to RT, 1 h; (**j**) $NaBH_4$, MeOH/DCM 3:1, –10 °C to RT, 1 h, 66% (over two steps); (**k**) Pd black, H_2, HCl (1.0 equiv), MeOH, DCM, 40 °C, quant. (for **6** and **7**).

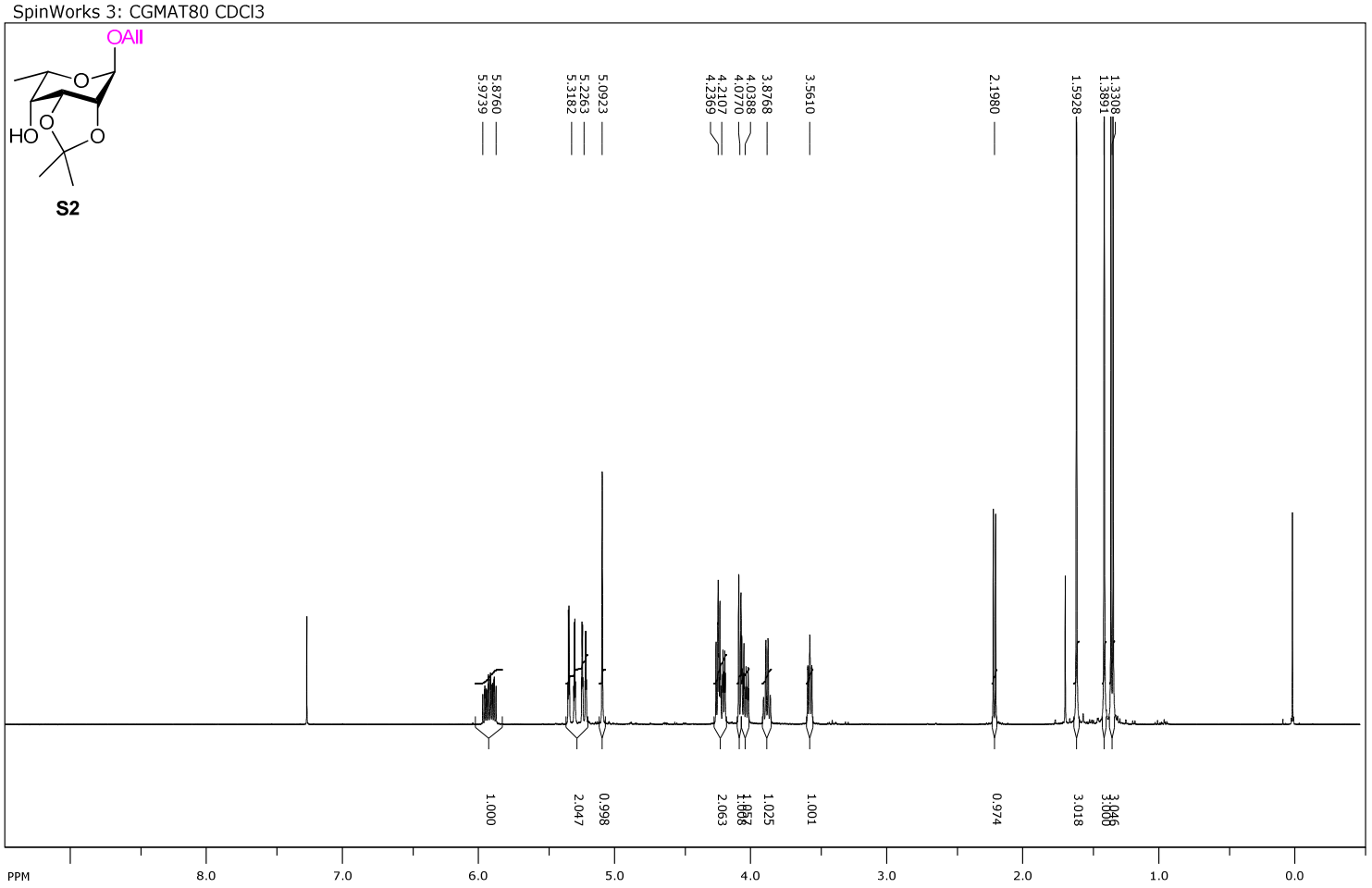


Supplementary Figure 11 | Synthesis of biotinylated oligosaccharides. Reagents and conditions: (**a**) Et_3N, DMF, H_2O, rt, 1 h, 69% (for **BIO-6**); 69% (for **BIO-7**); 55% (for **BIO-2**).



Supplementary Figure 12 | Synthesis of disaccharide:CRM197 conjugates SOC-6 and SOC-7. Disaccharide **6** or **7** was reacted with disuccinimidyl glutarate to generate derivative **NHS-6** or **NHS-7**, respectively, which upon reaction with CRM197 led to the formation of glycoconjugate vaccine **SOC-6** or **SOC-7**, respectively.

Supplementary Figure 13 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S2.



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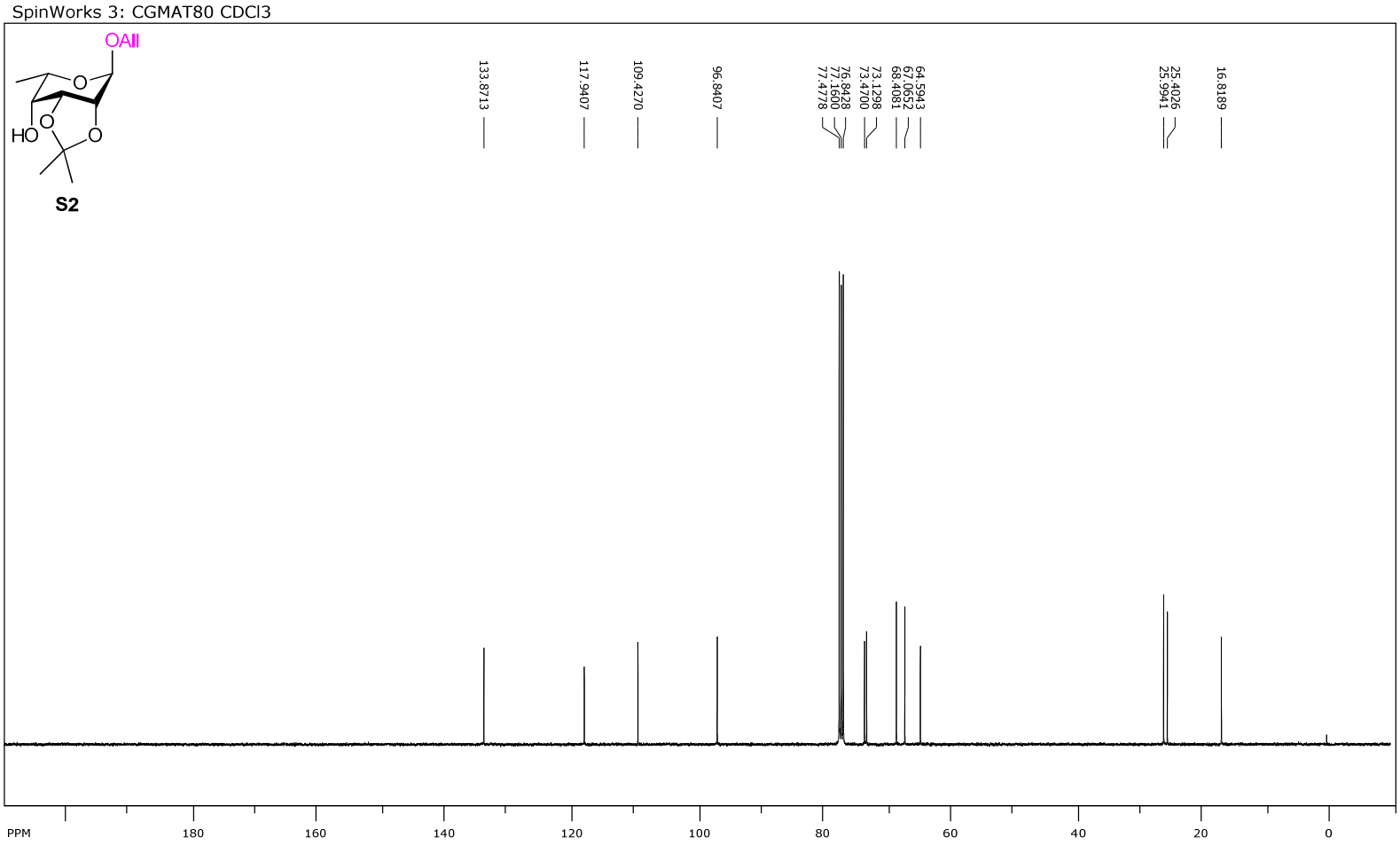
Supplementary Figure 14 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S2.



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number of scans: 1024

freq. of 0 ppm: 100.612754 MHz
processed size: 32768 complex points
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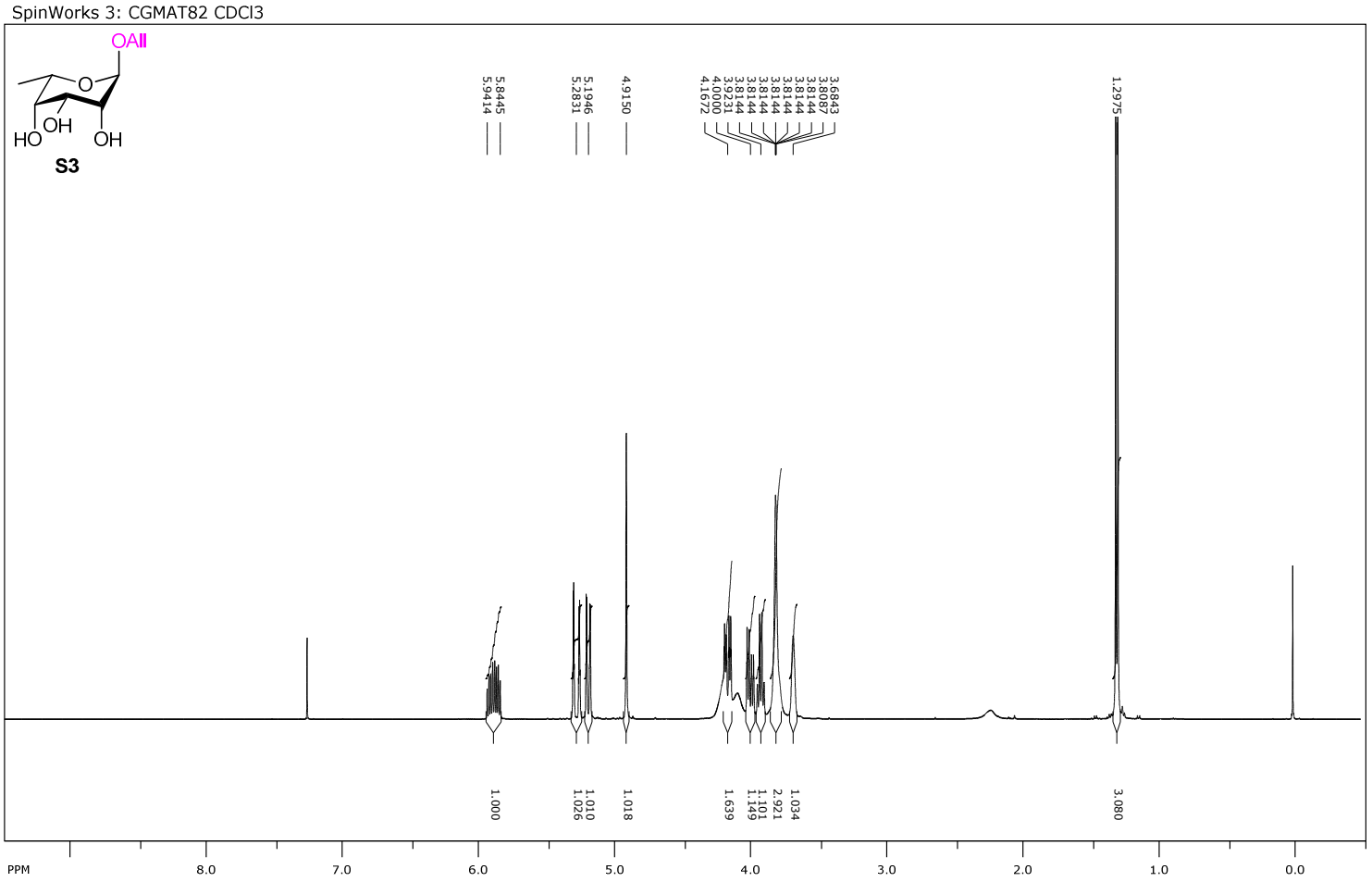
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 15 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S3.



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freq. of 0 ppm: 400.130006 MHz
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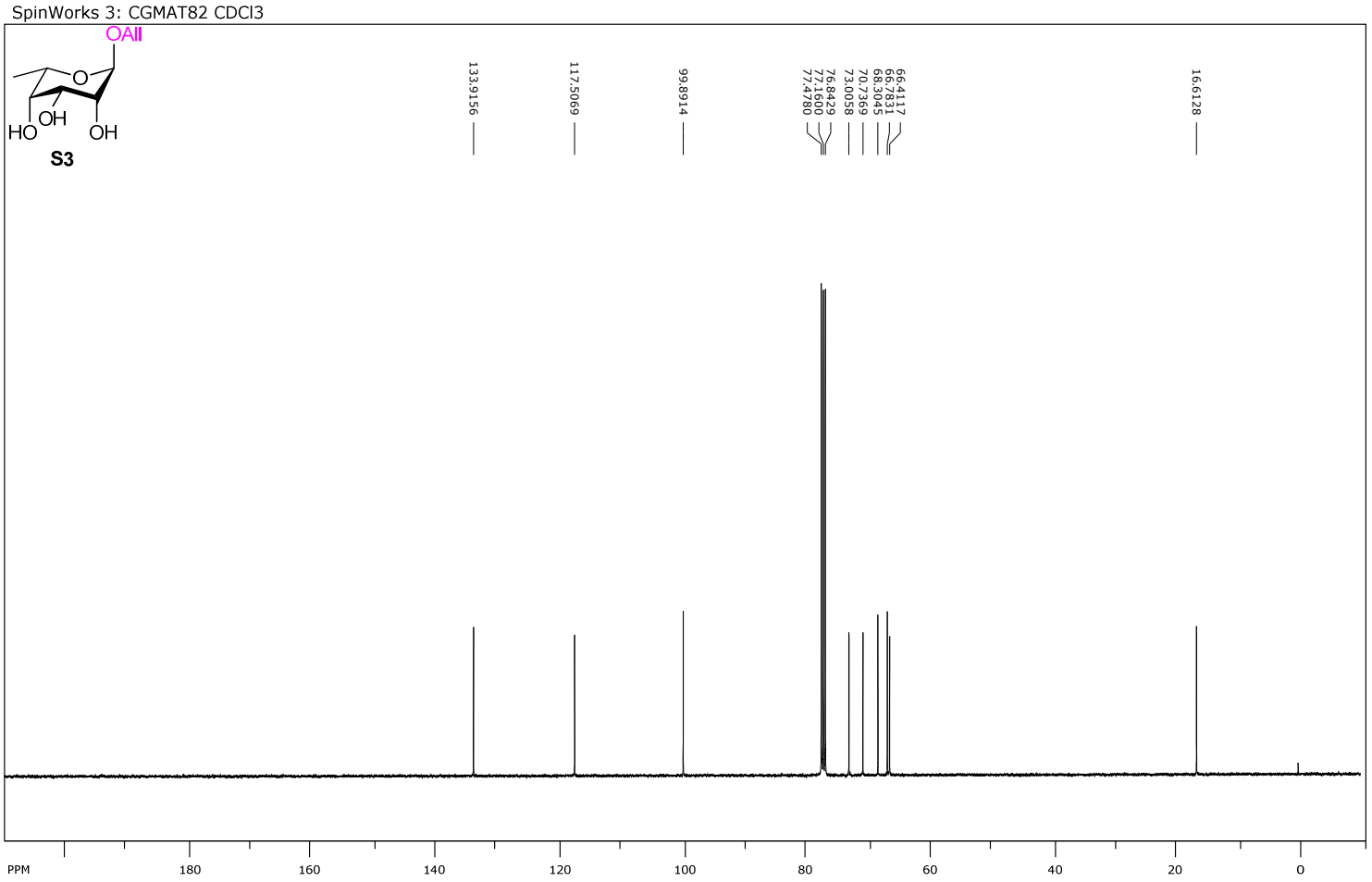
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 16 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S3.



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number of scans: 1024

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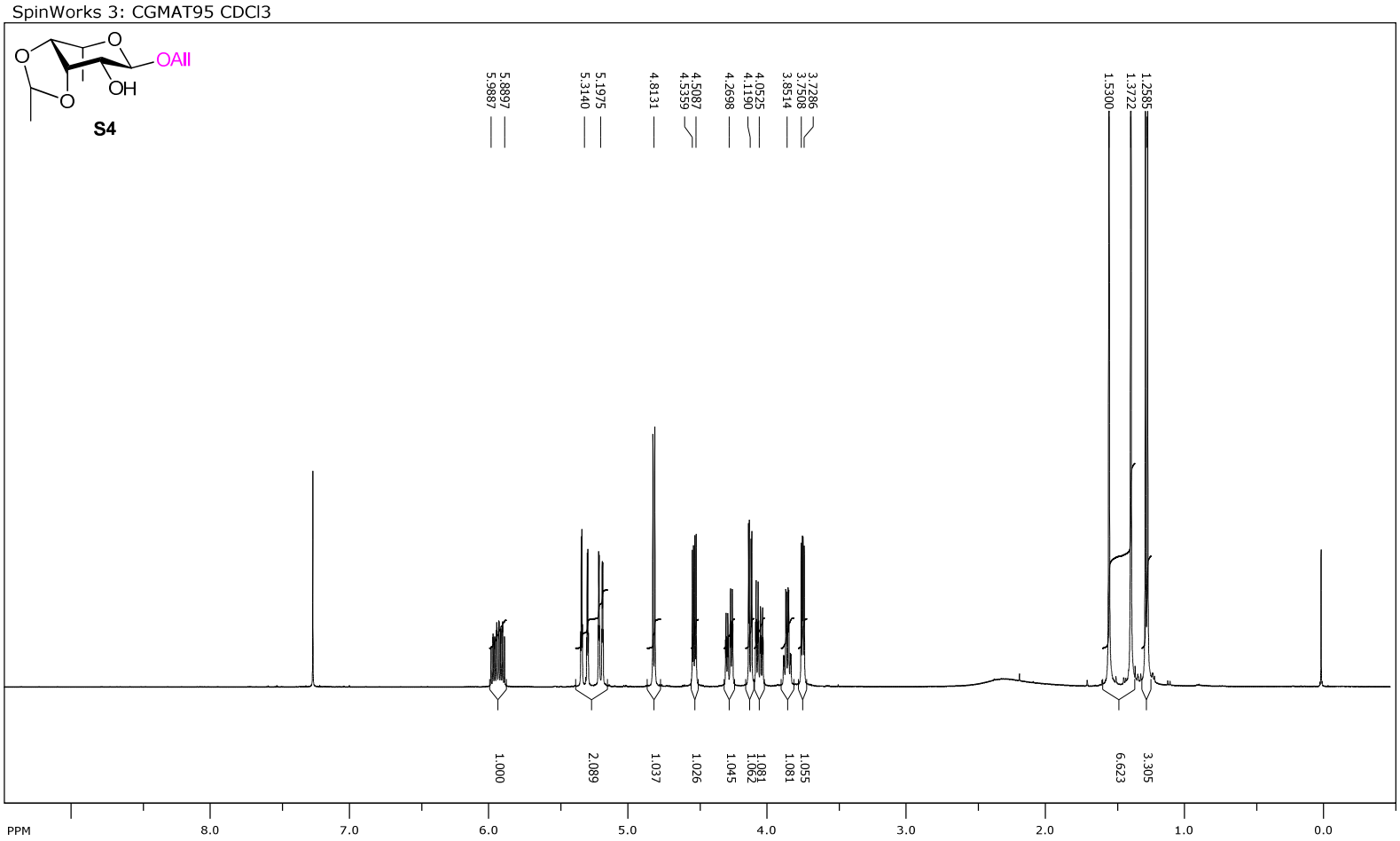
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 17 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S4.



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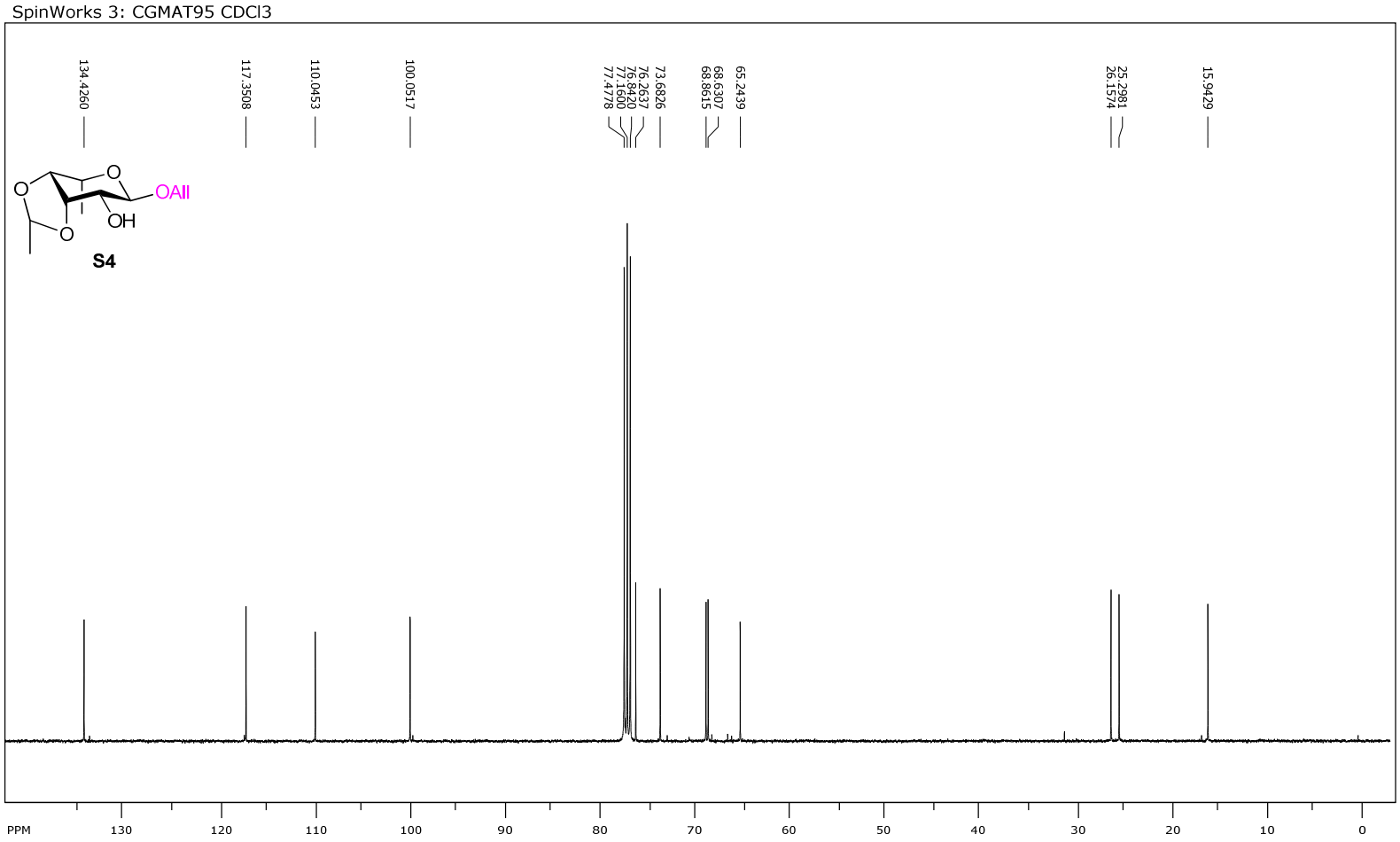
Supplementary Figure 18 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S4.



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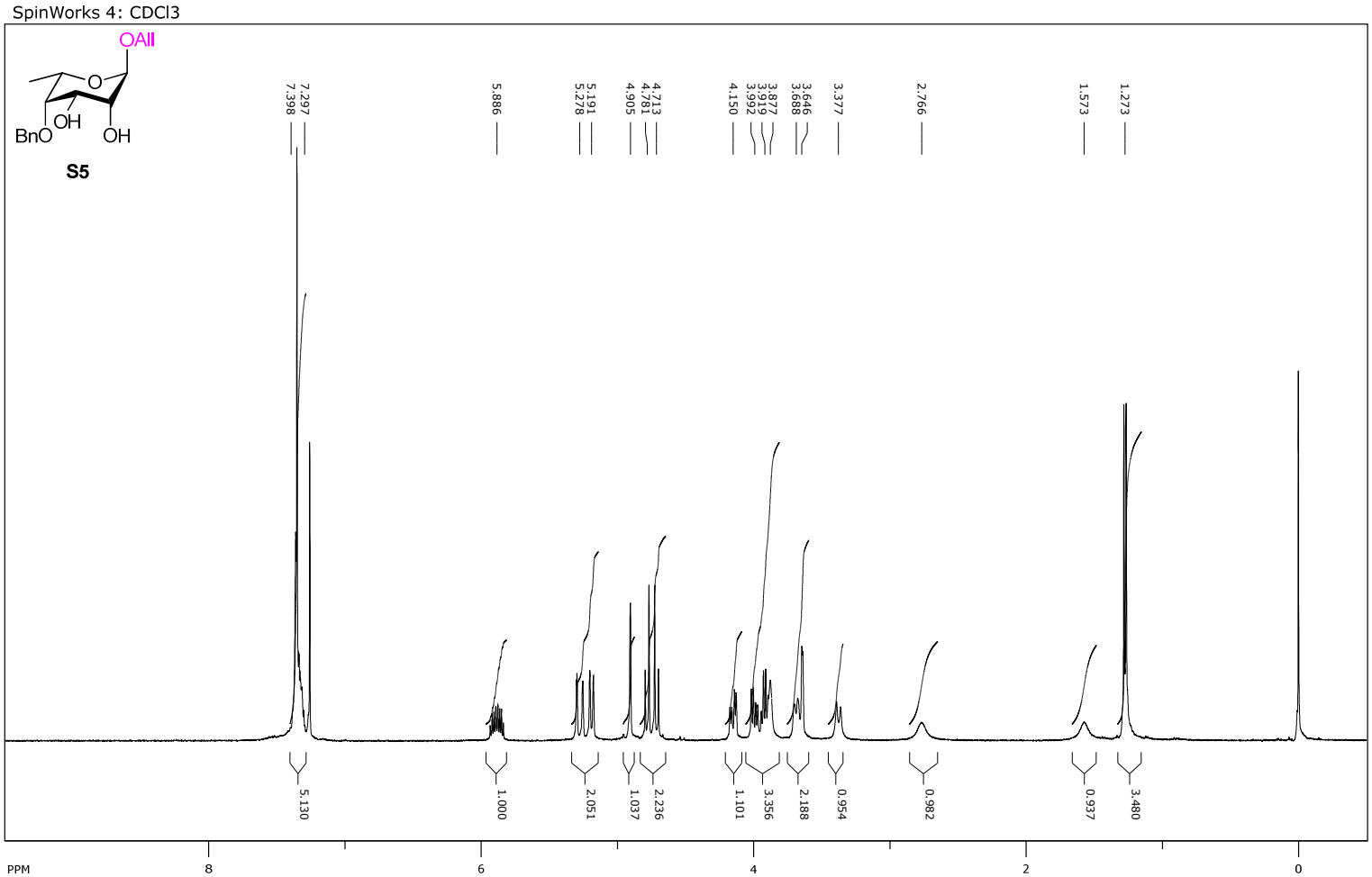
Supplementary Figure 19 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S5.



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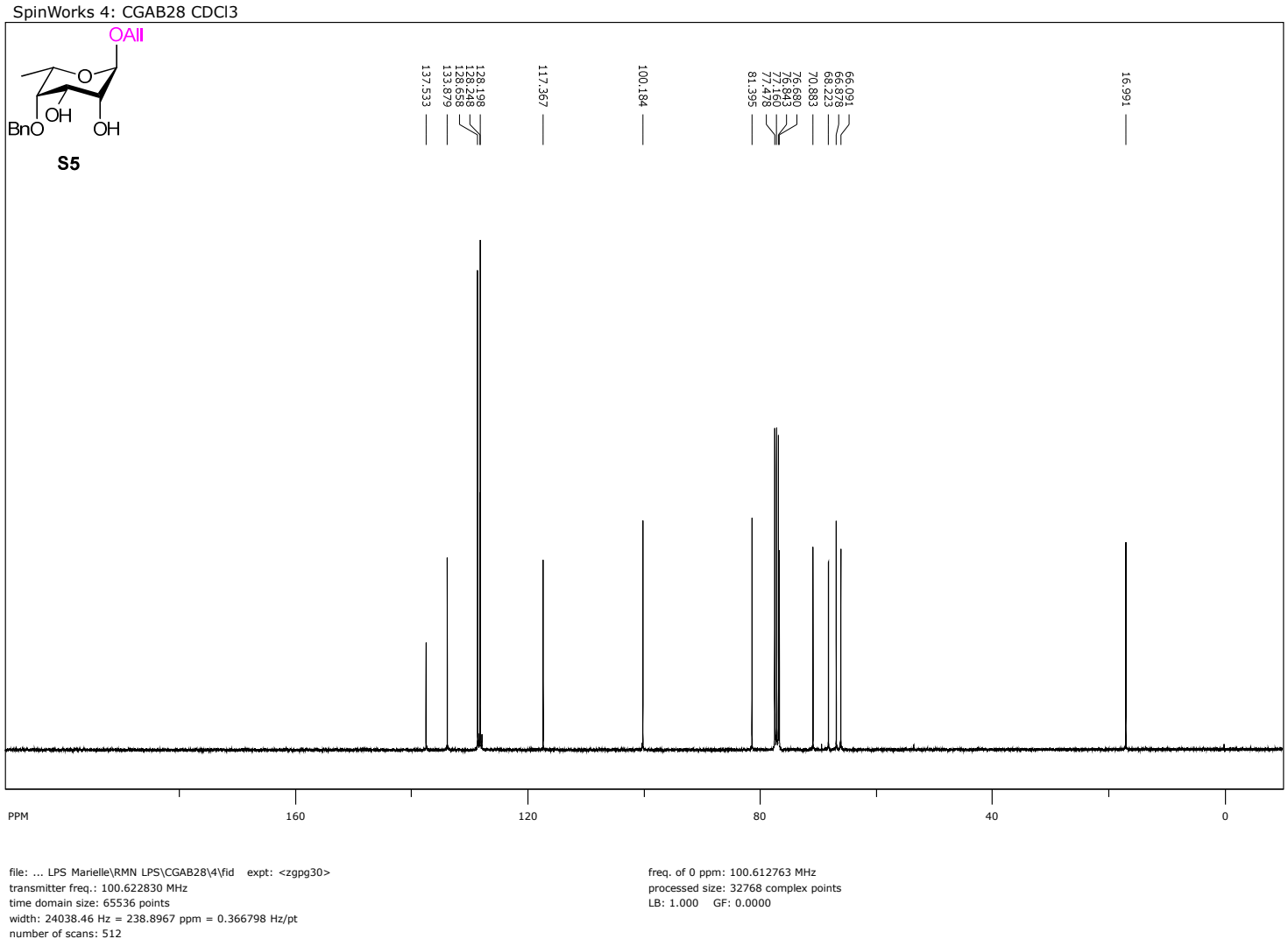
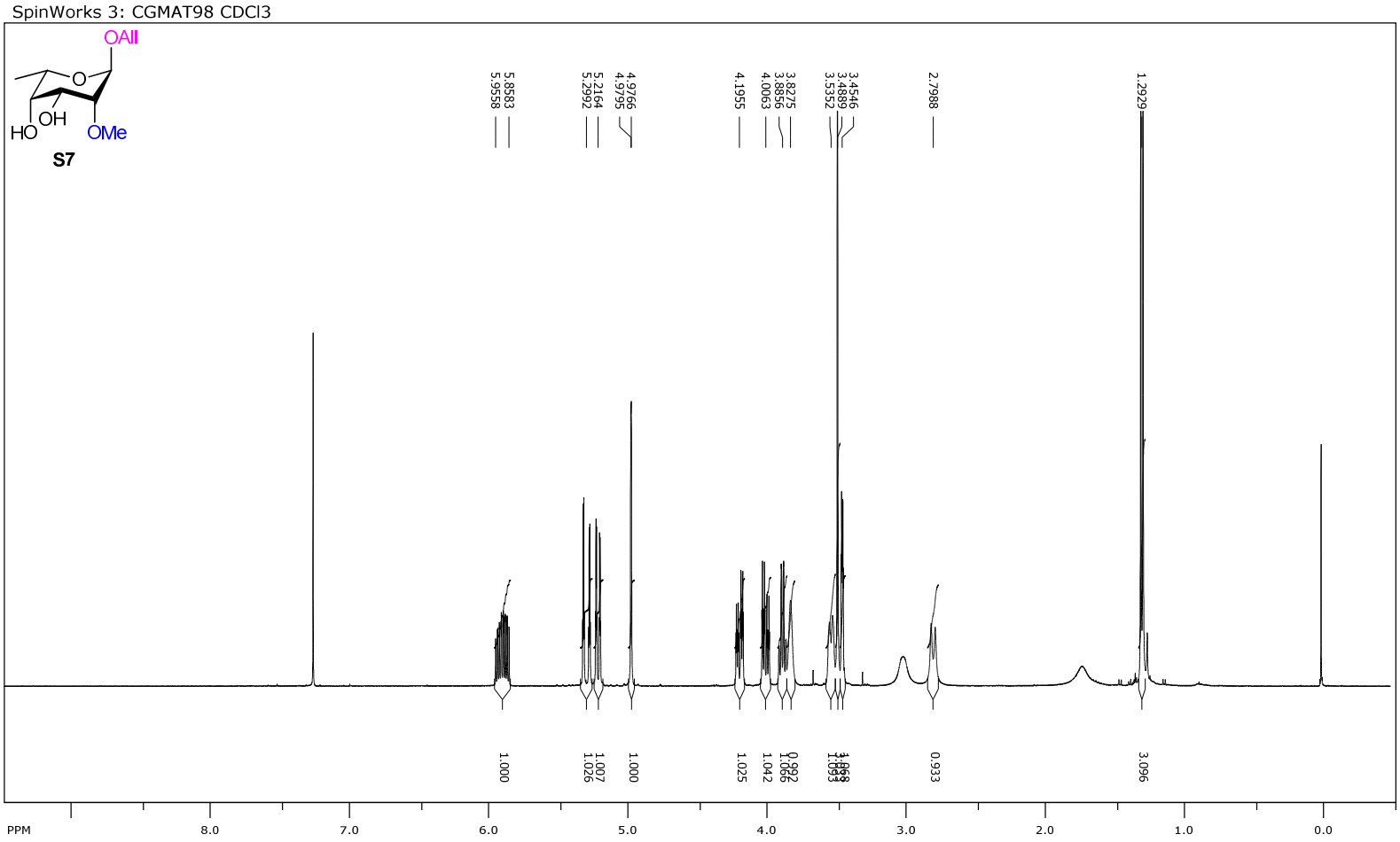
Supplementary Figure 20 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S5.



Supplementary Figure 21 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S7.



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processed size: 32768 complex points
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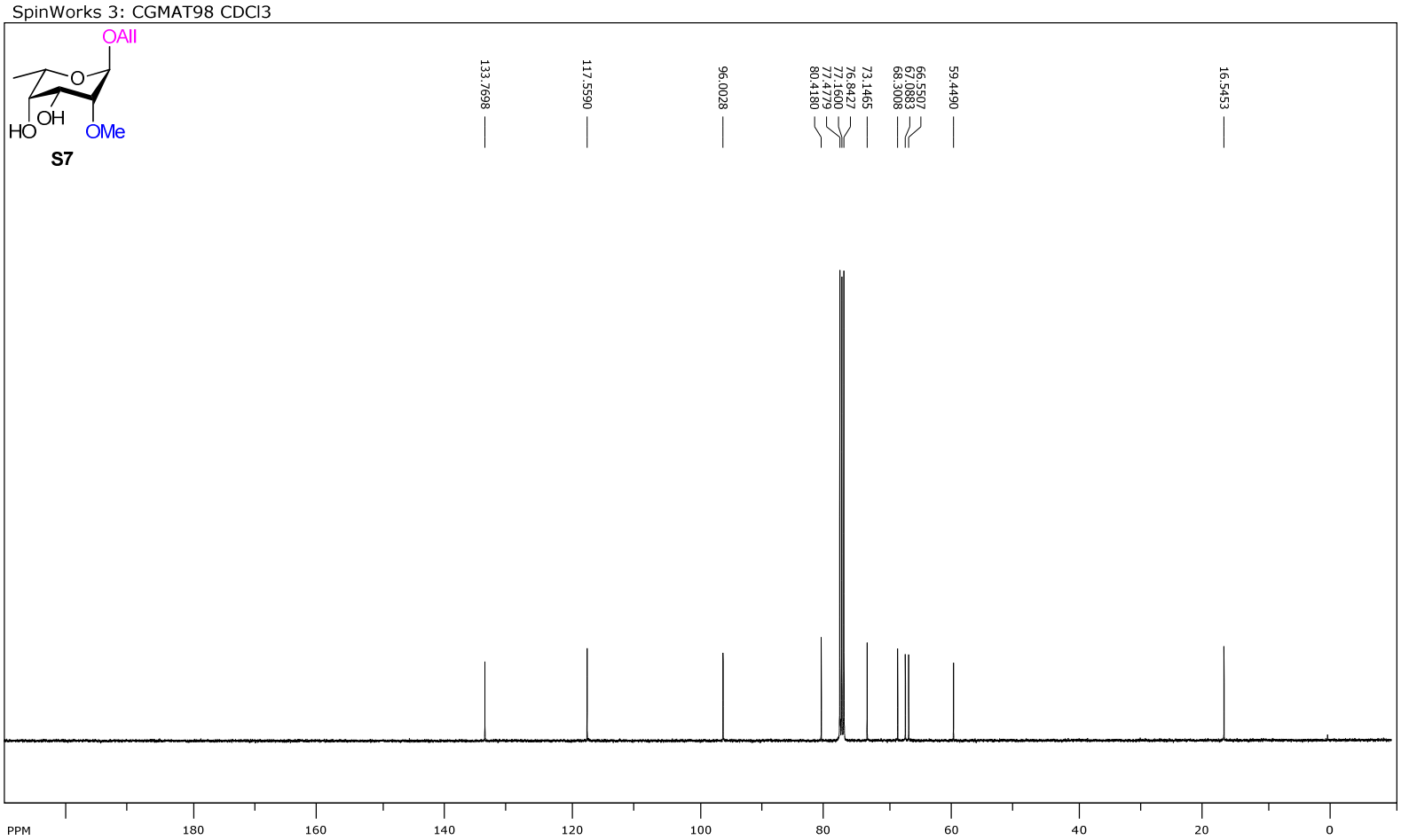
Supplementary Figure 22 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S7.



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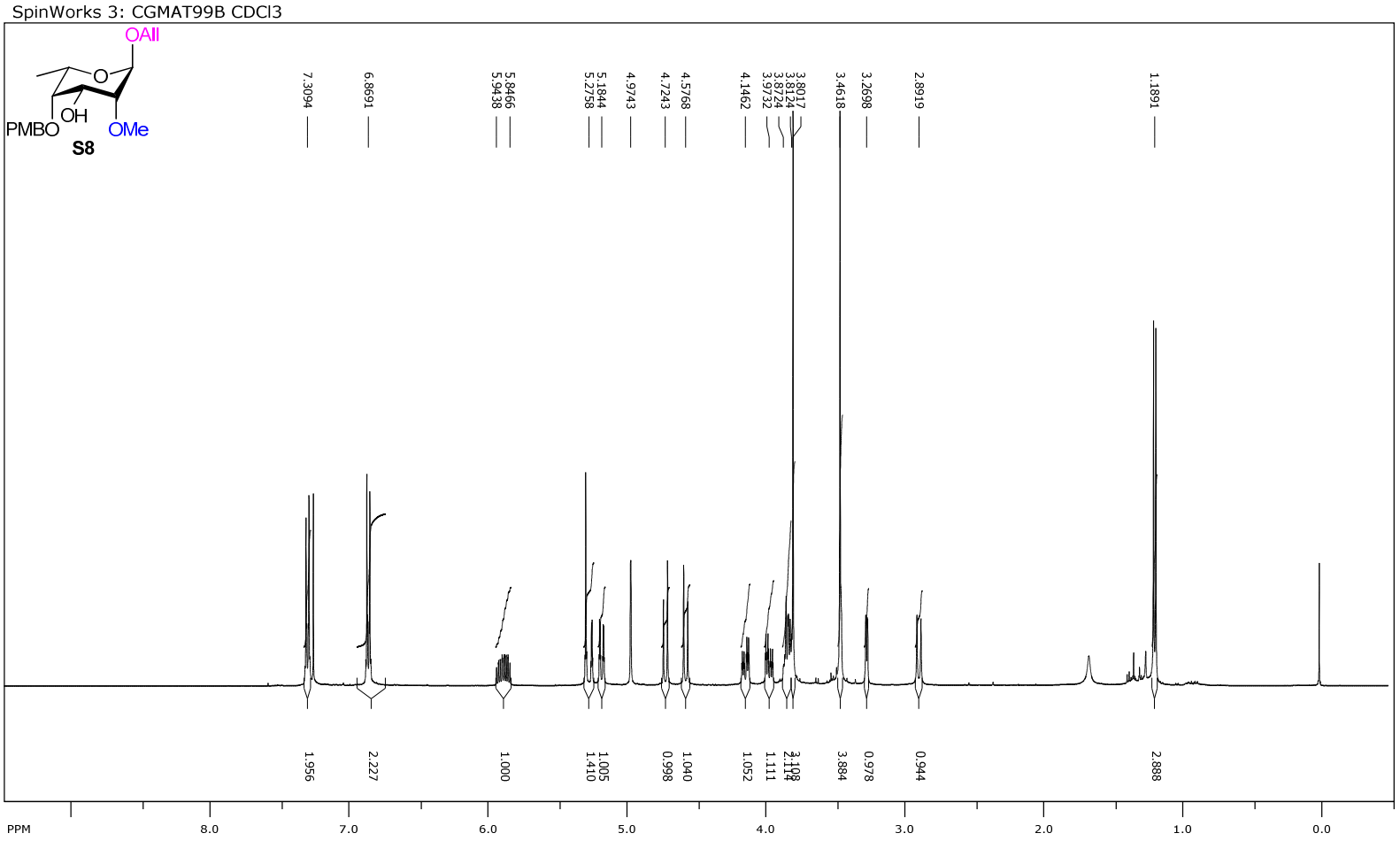
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 23 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S8.



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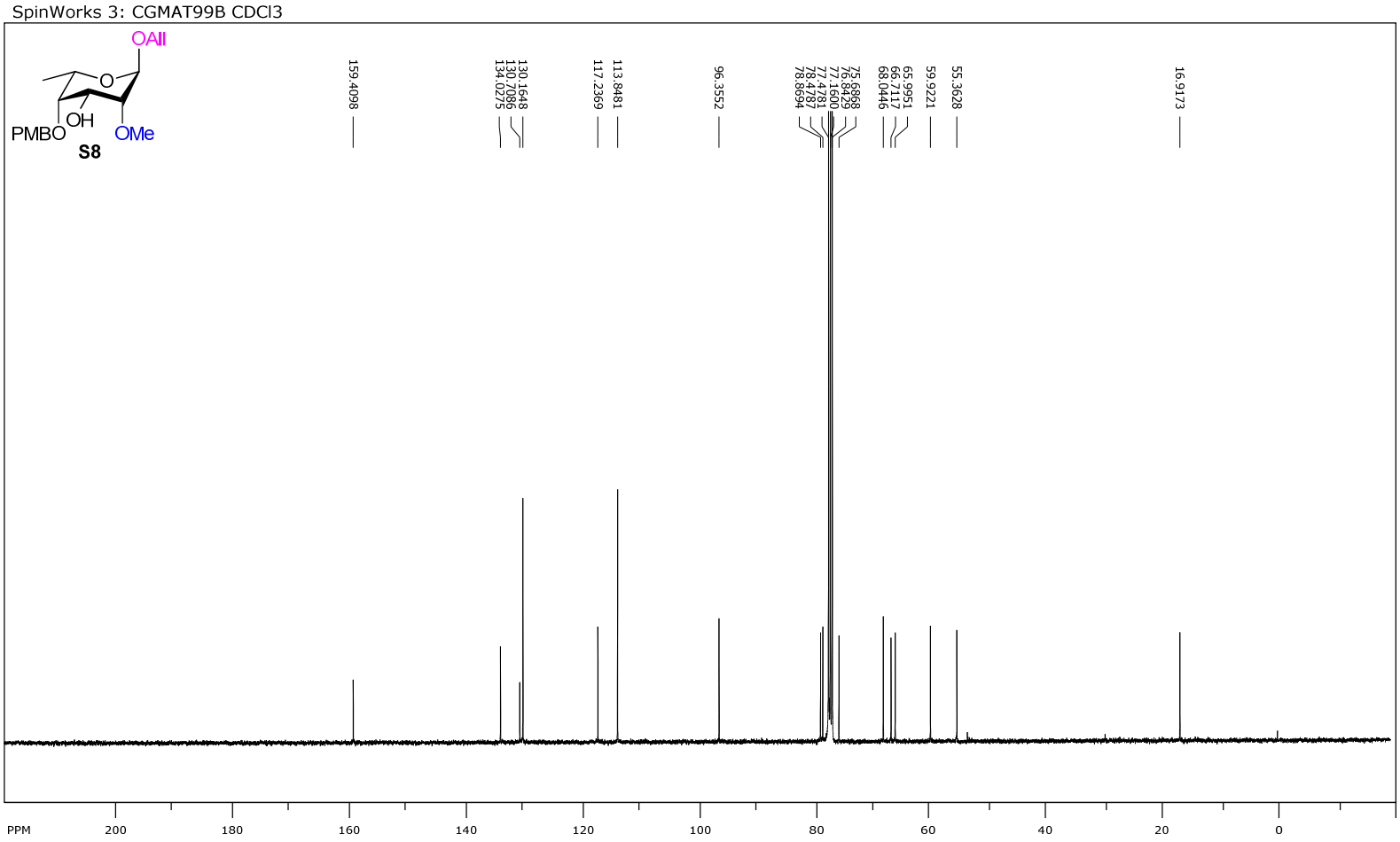
Supplementary Figure 24 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S8.



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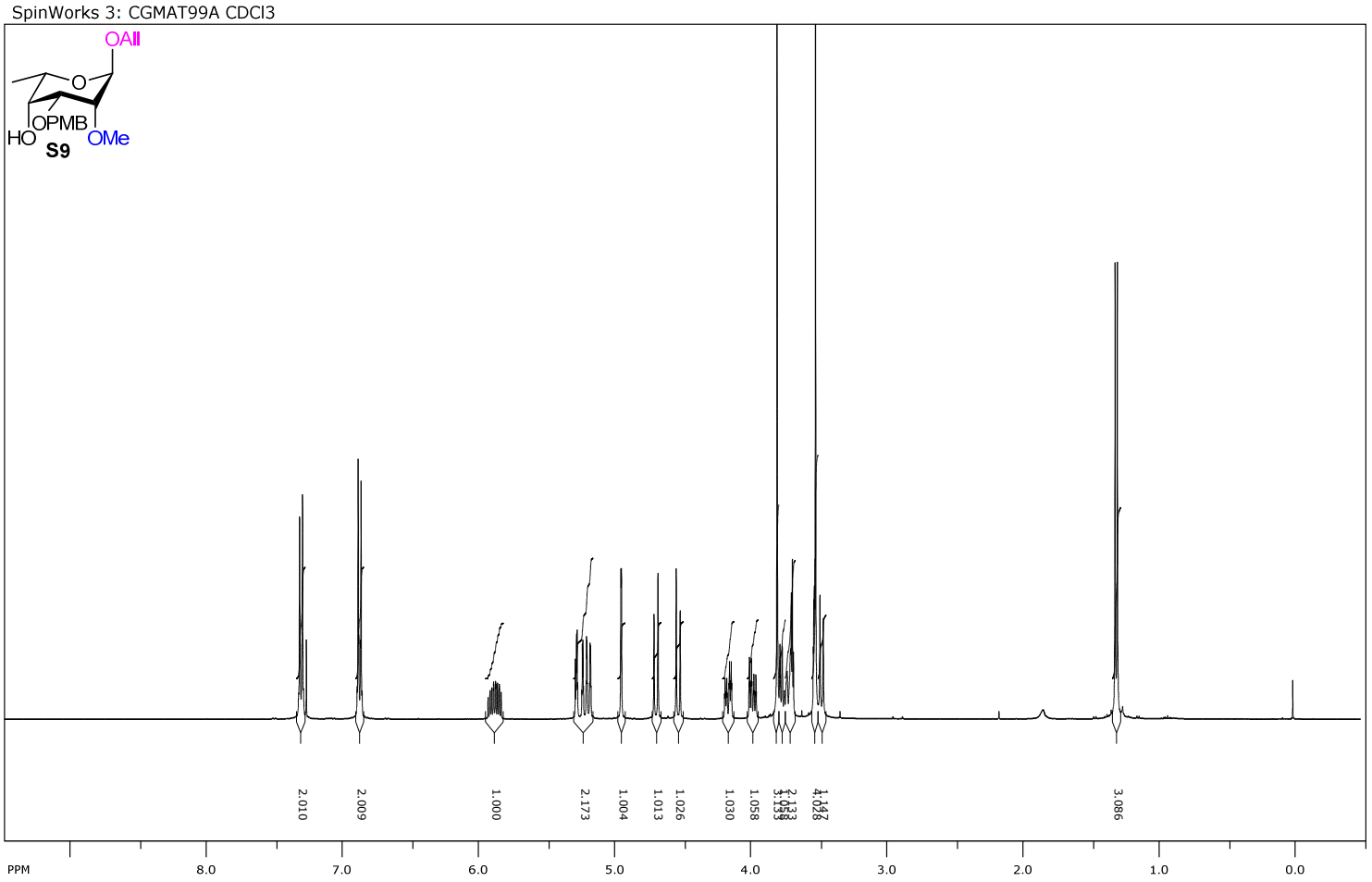
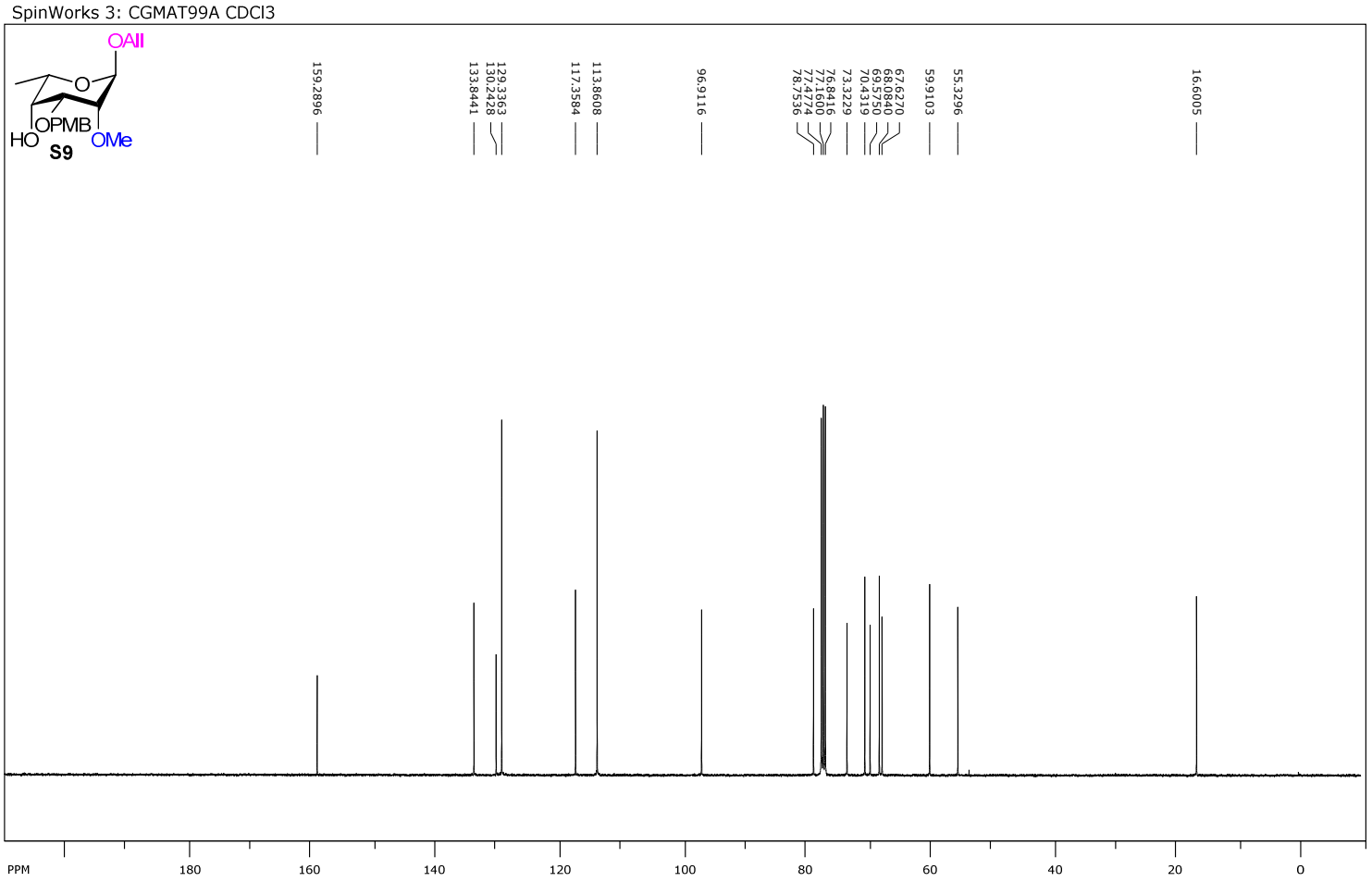
Supplementary Figure 25 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S9.



Supplementary Figure 26 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S9.



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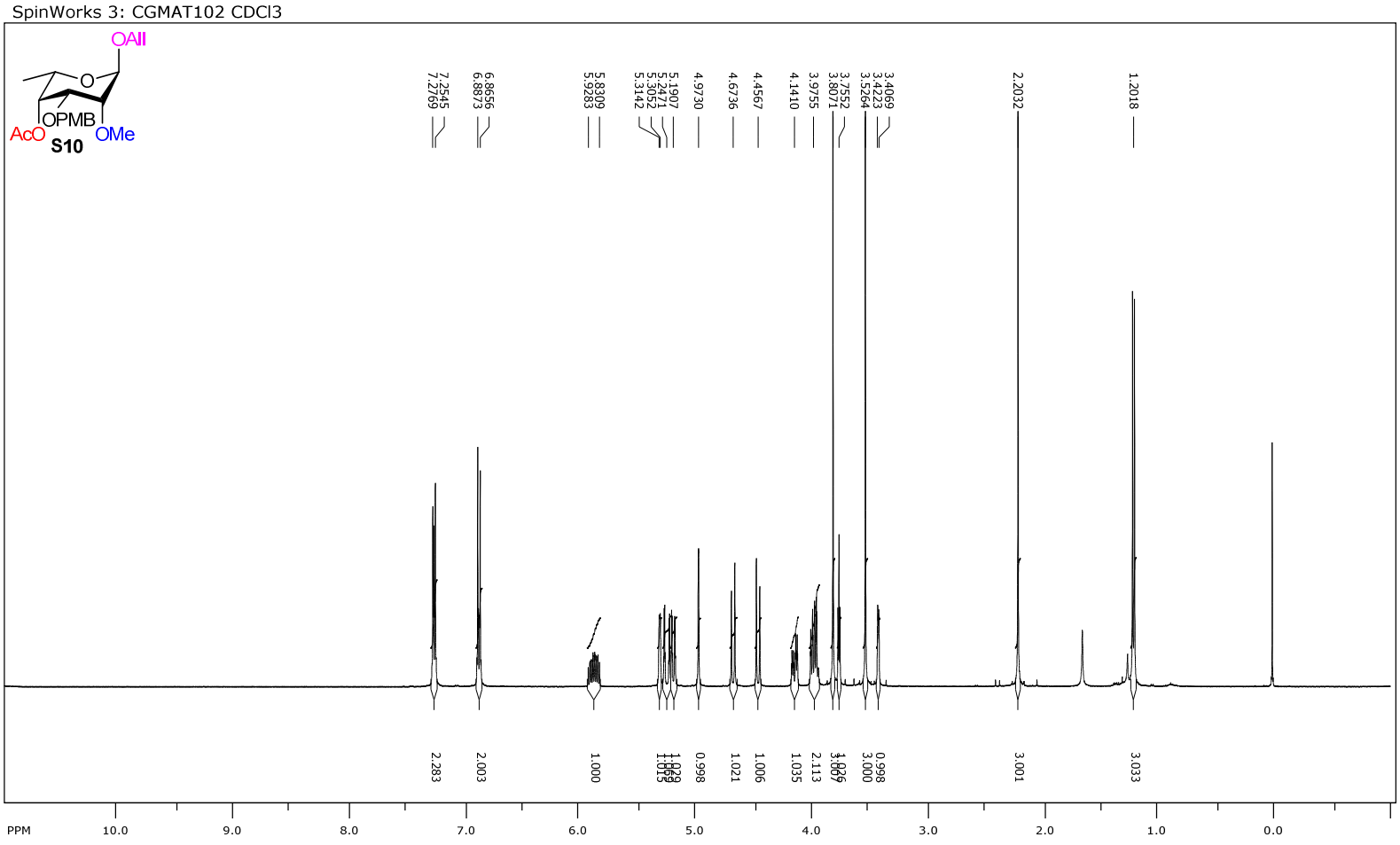
Supplementary Figure 27 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S10.



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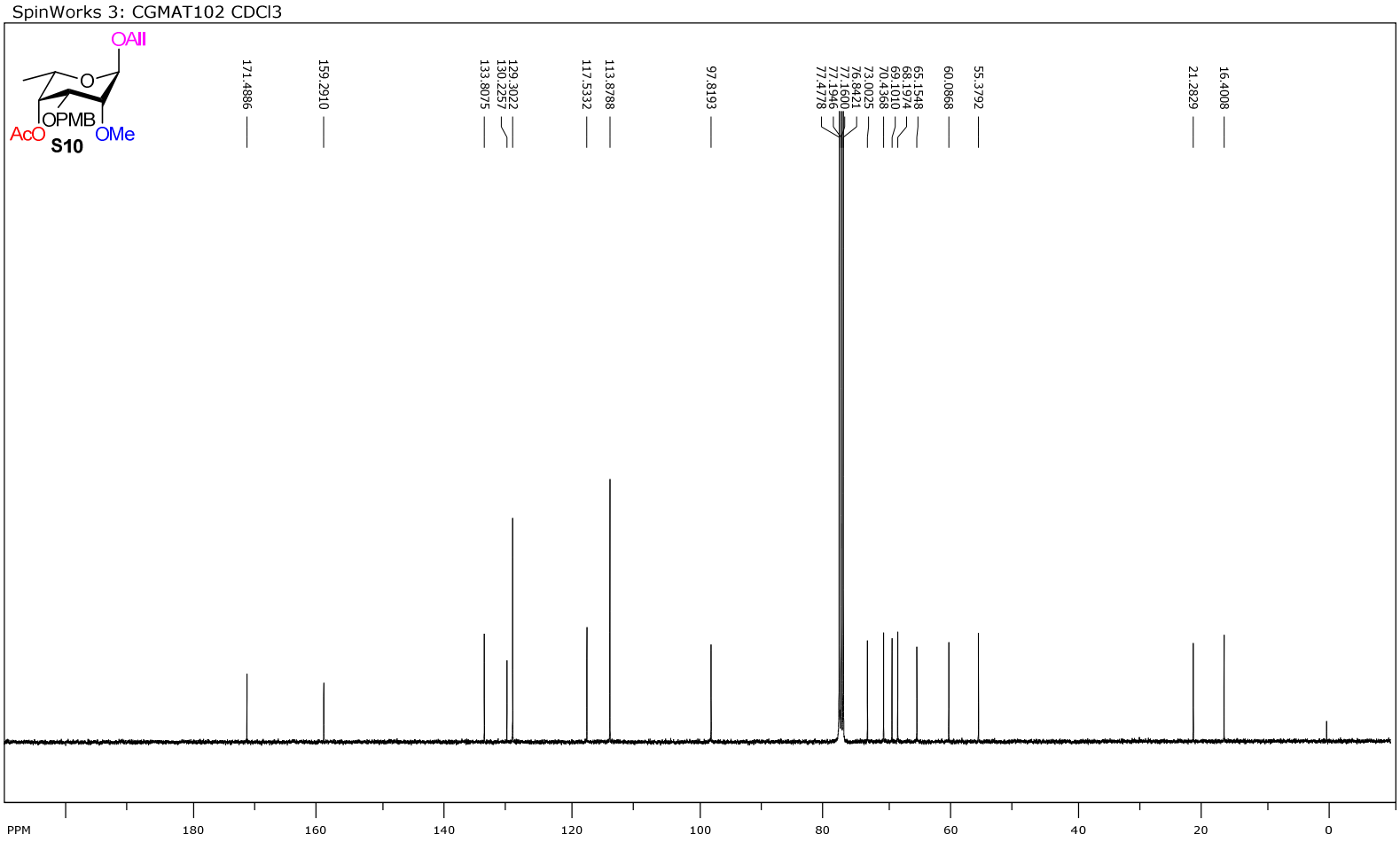
Supplementary Figure 28 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S10.



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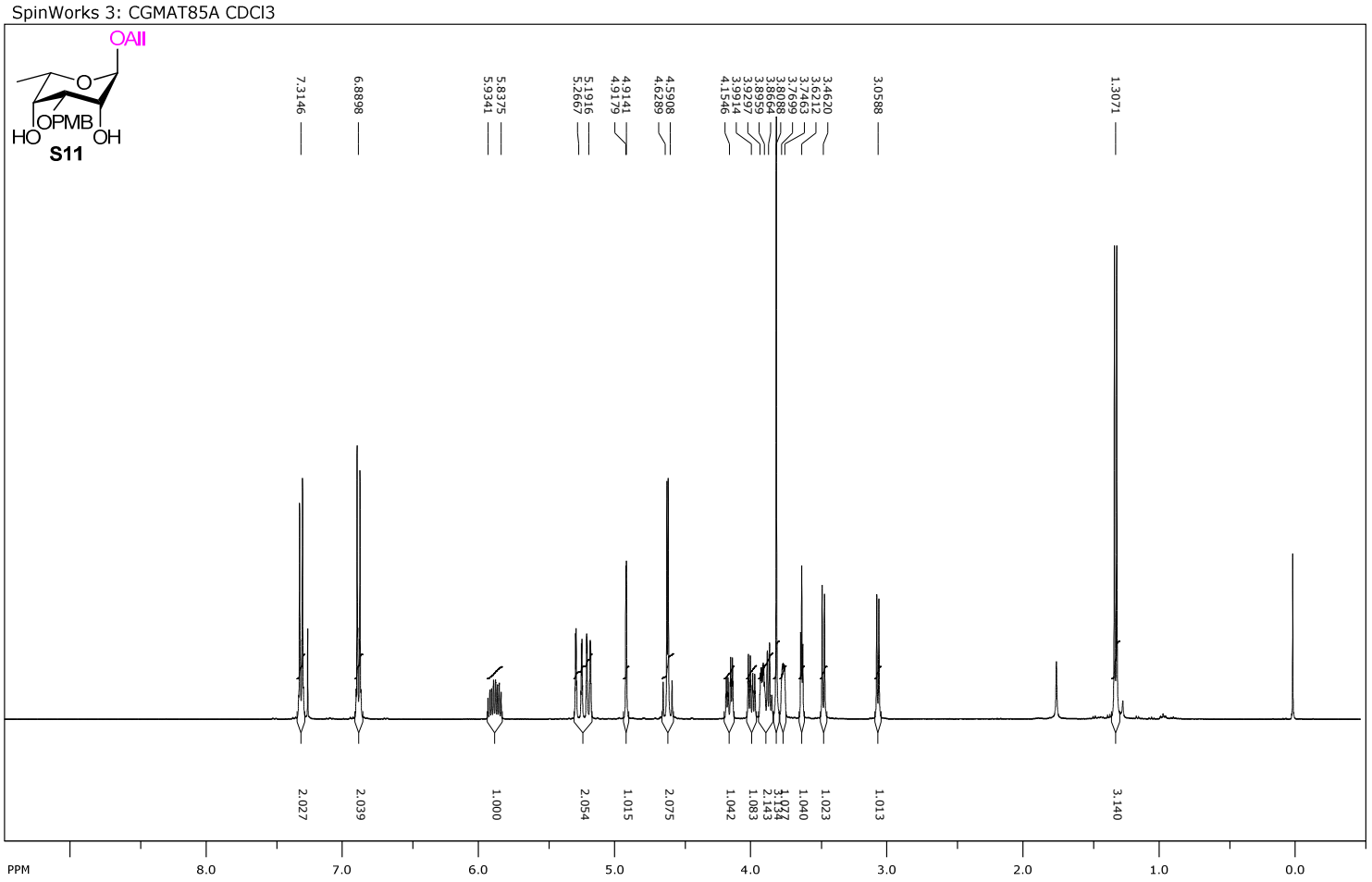
Supplementary Figure 29 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S11.



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processed size: 32768 complex points
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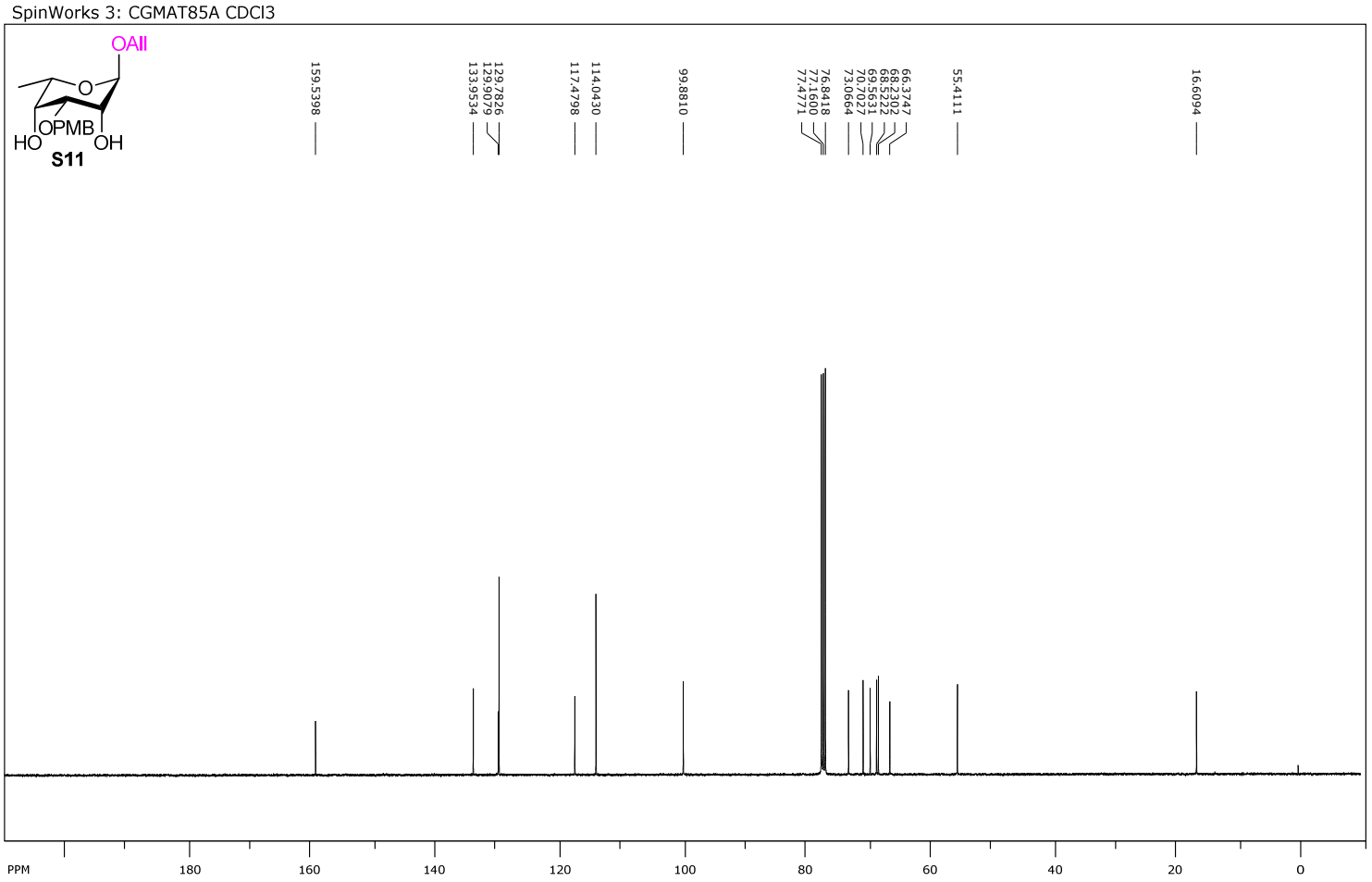
Supplementary Figure 30 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S11.



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number of scans: 1024

freq. of 0 ppm: 100.612757 MHz
processed size: 32768 complex points
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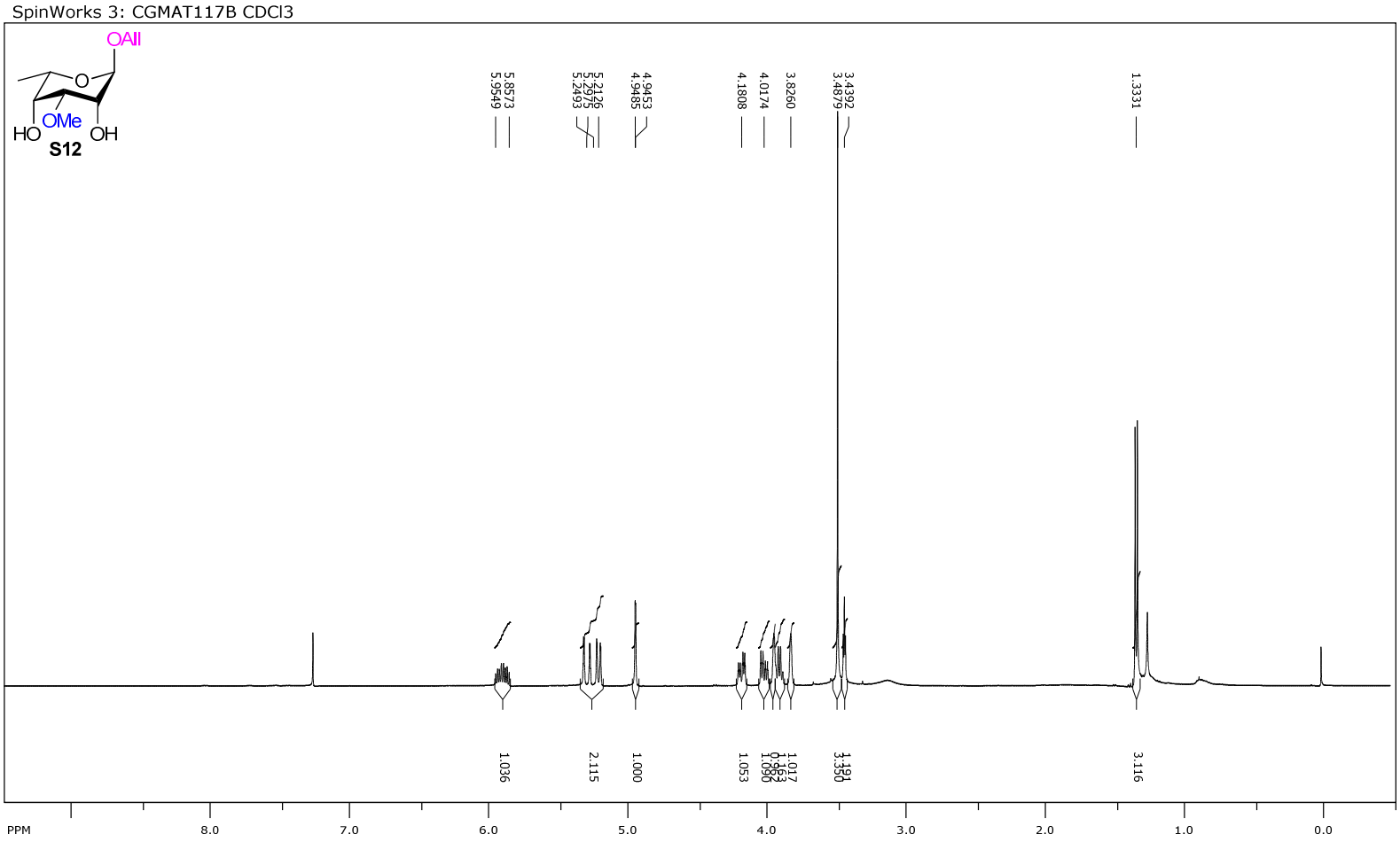
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 31 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S12.



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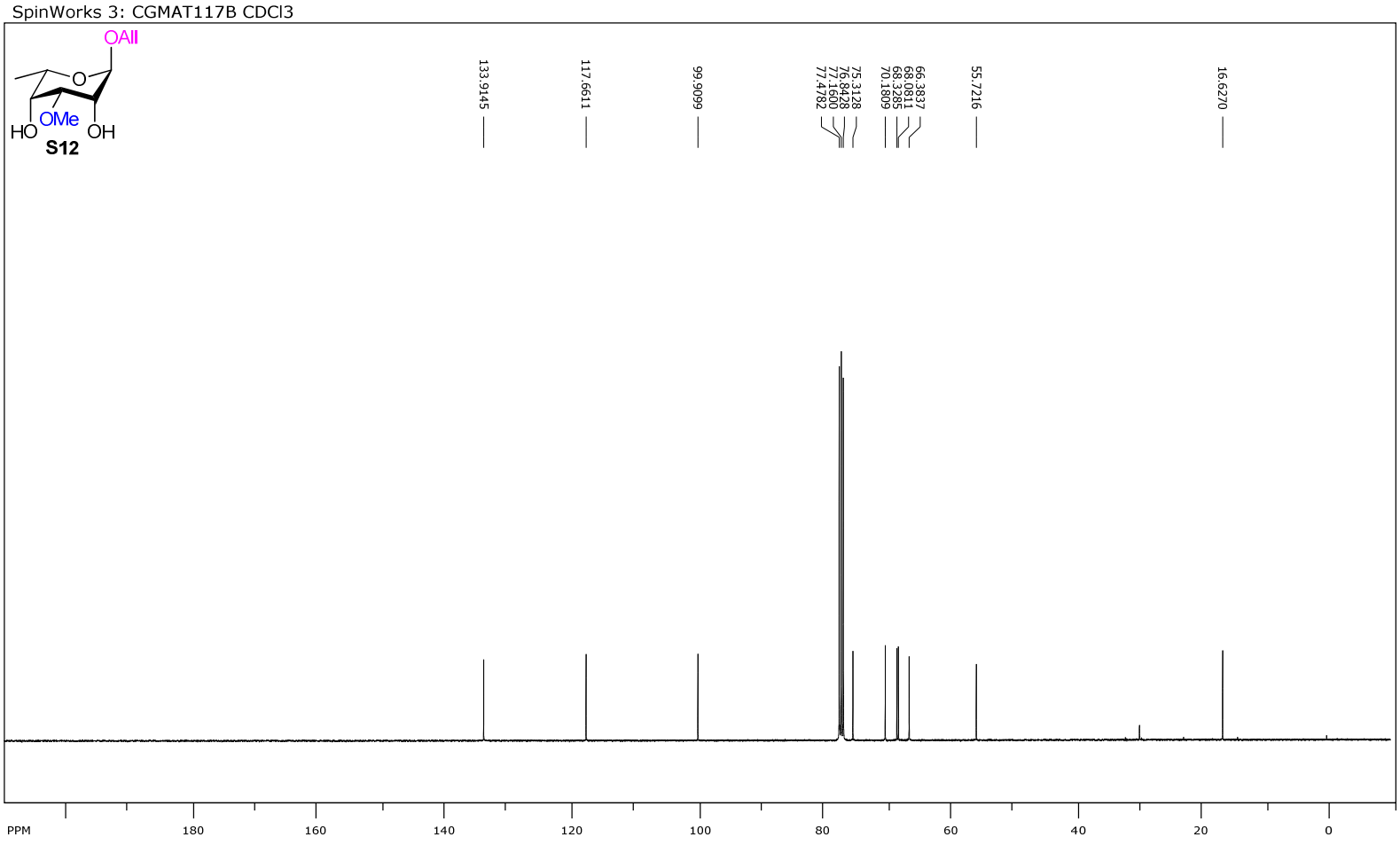
number of scans: 16

freq. of 0 ppm: 400.130005 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 32 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S12.



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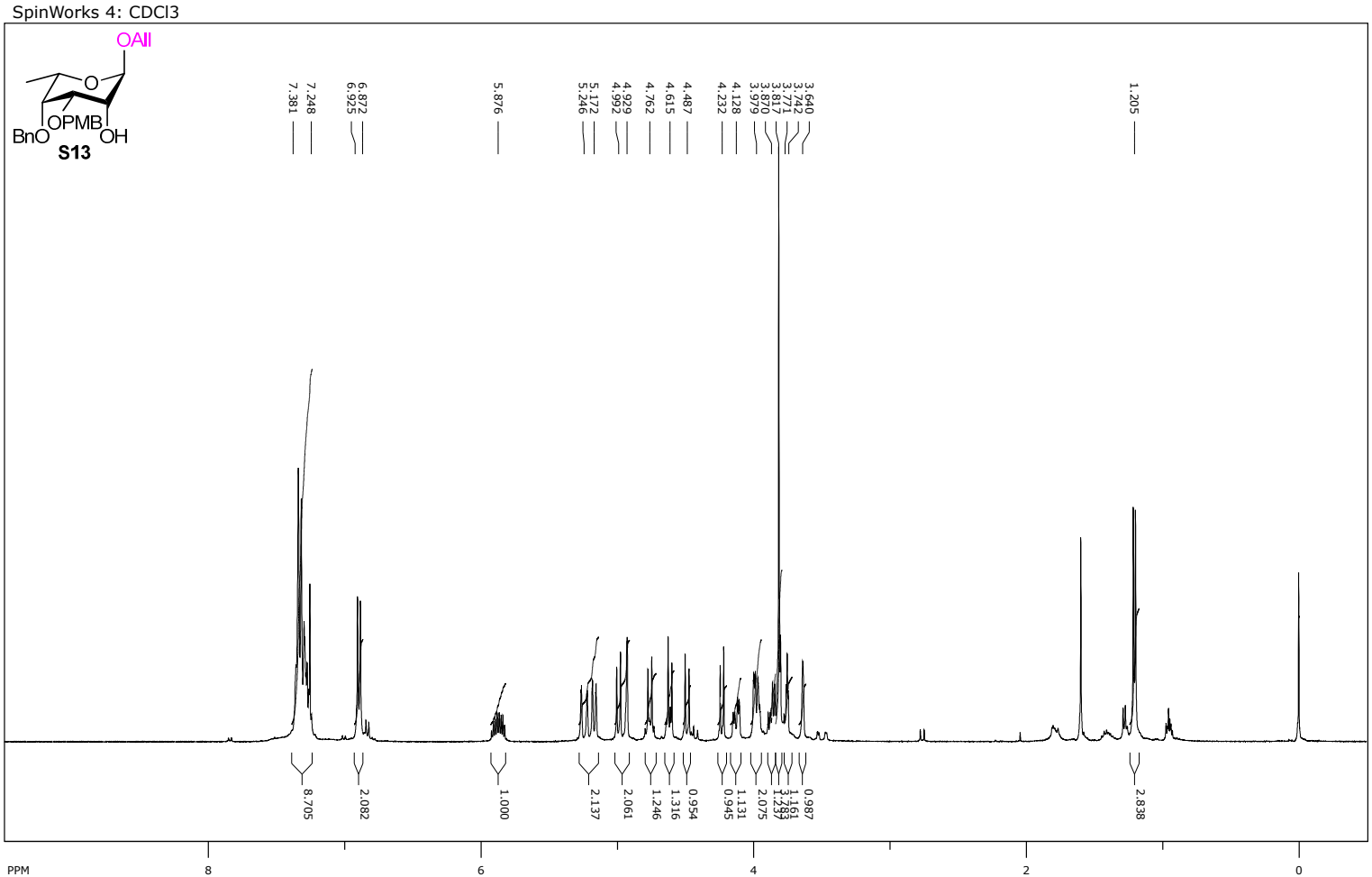
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 2048

freq. of 0 ppm: 100.612756 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 33 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S13.



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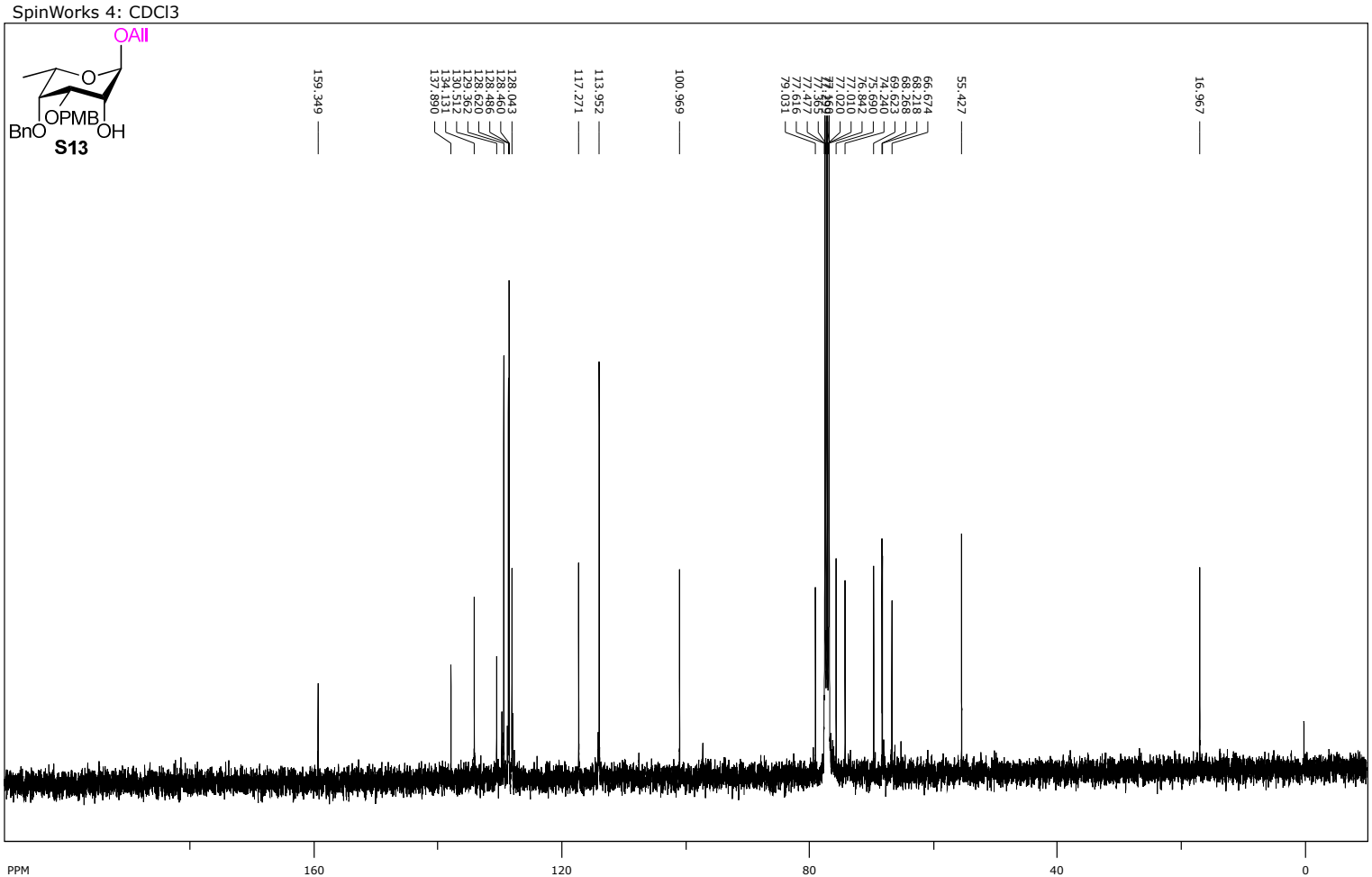
transmitter freq.: 400.132001 MHz
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 16

freq. of 0 ppm: 400.130011 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

Supplementary Figure 34 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S13.



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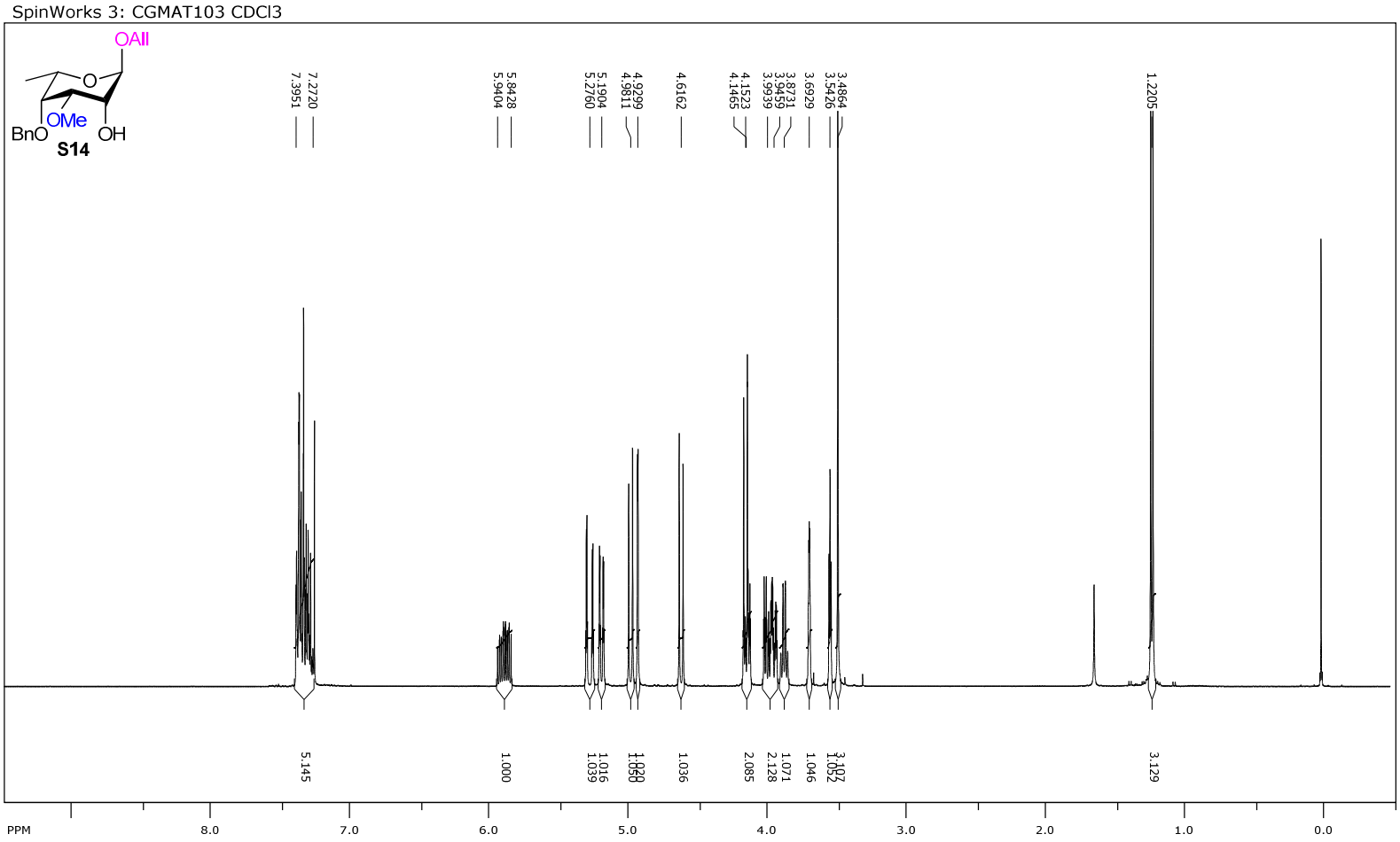
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 512

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

Supplementary Figure 35 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S14.



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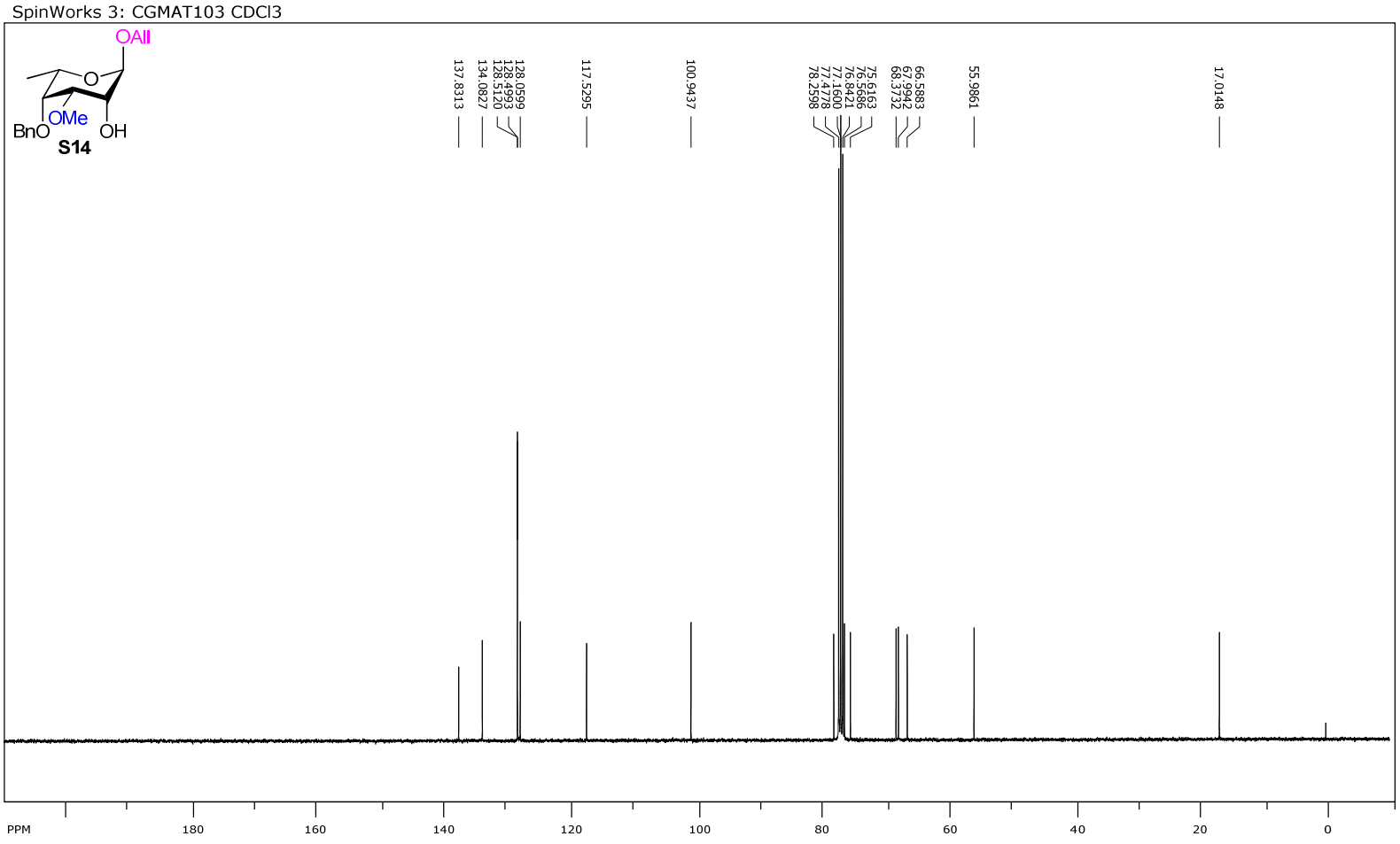
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 16

freq. of 0 ppm: 400.130008 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 36 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S14.



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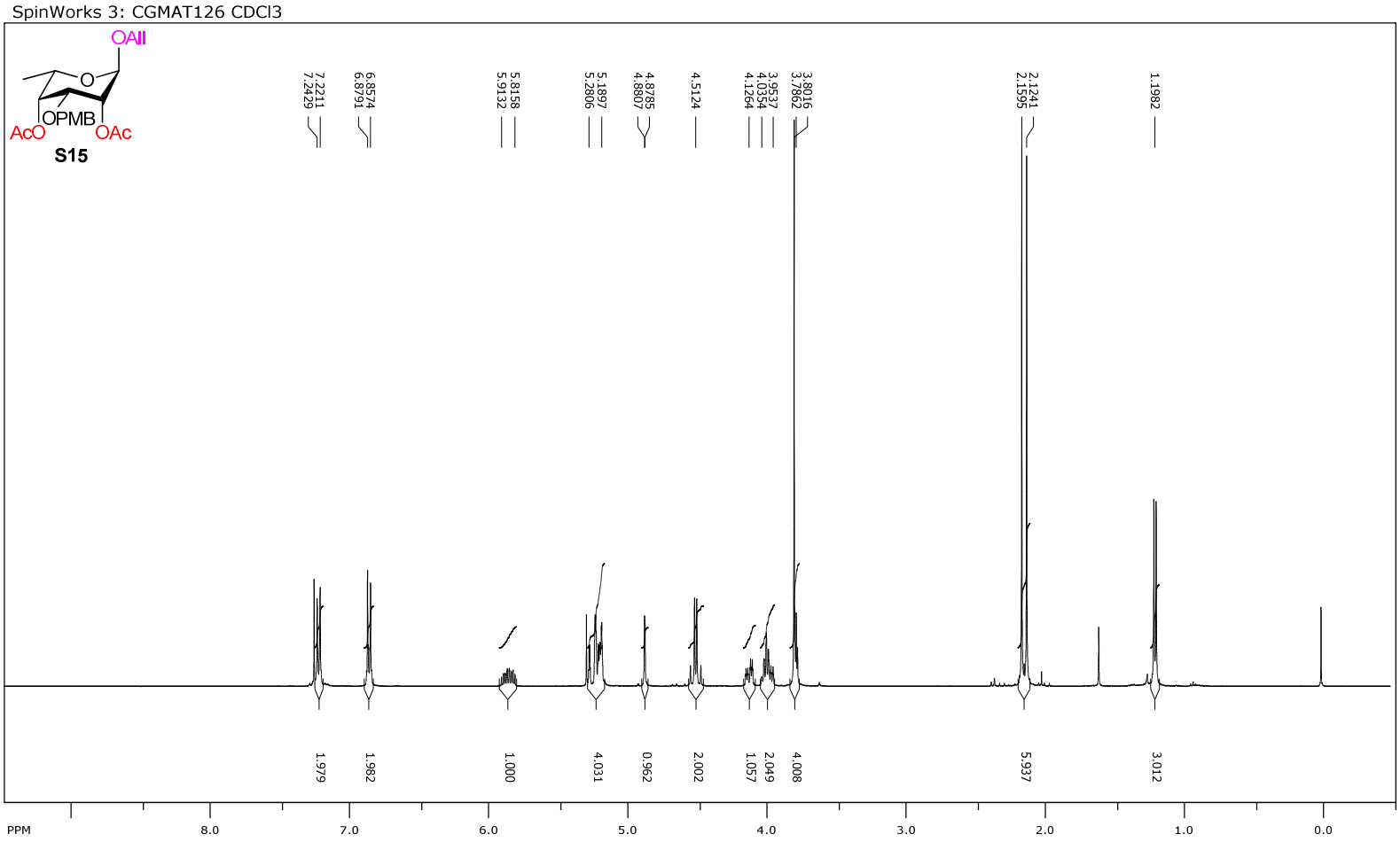
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612756 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 37 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S15.



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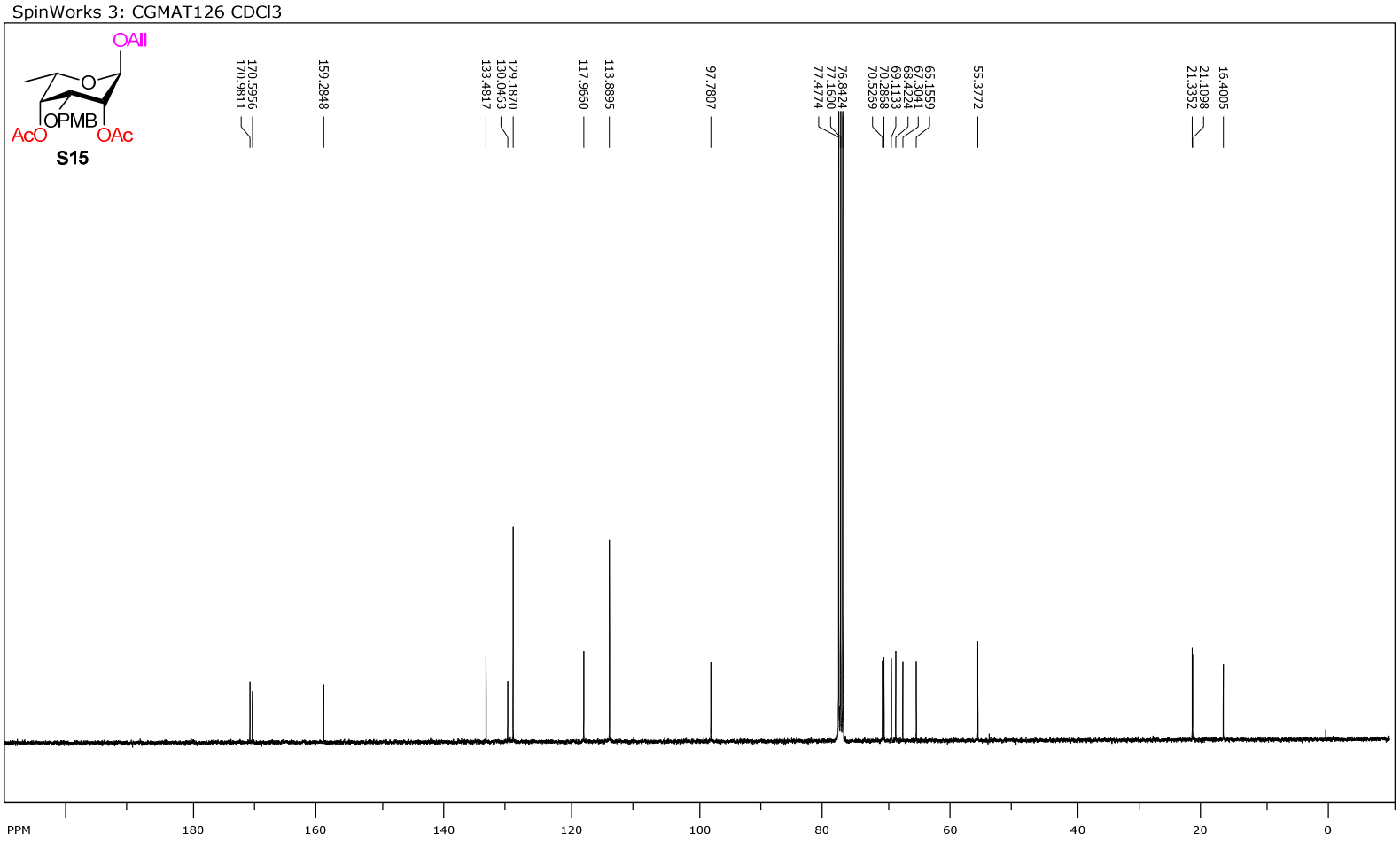
number of scans: 16

freq. of 0 ppm: 400.130008 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

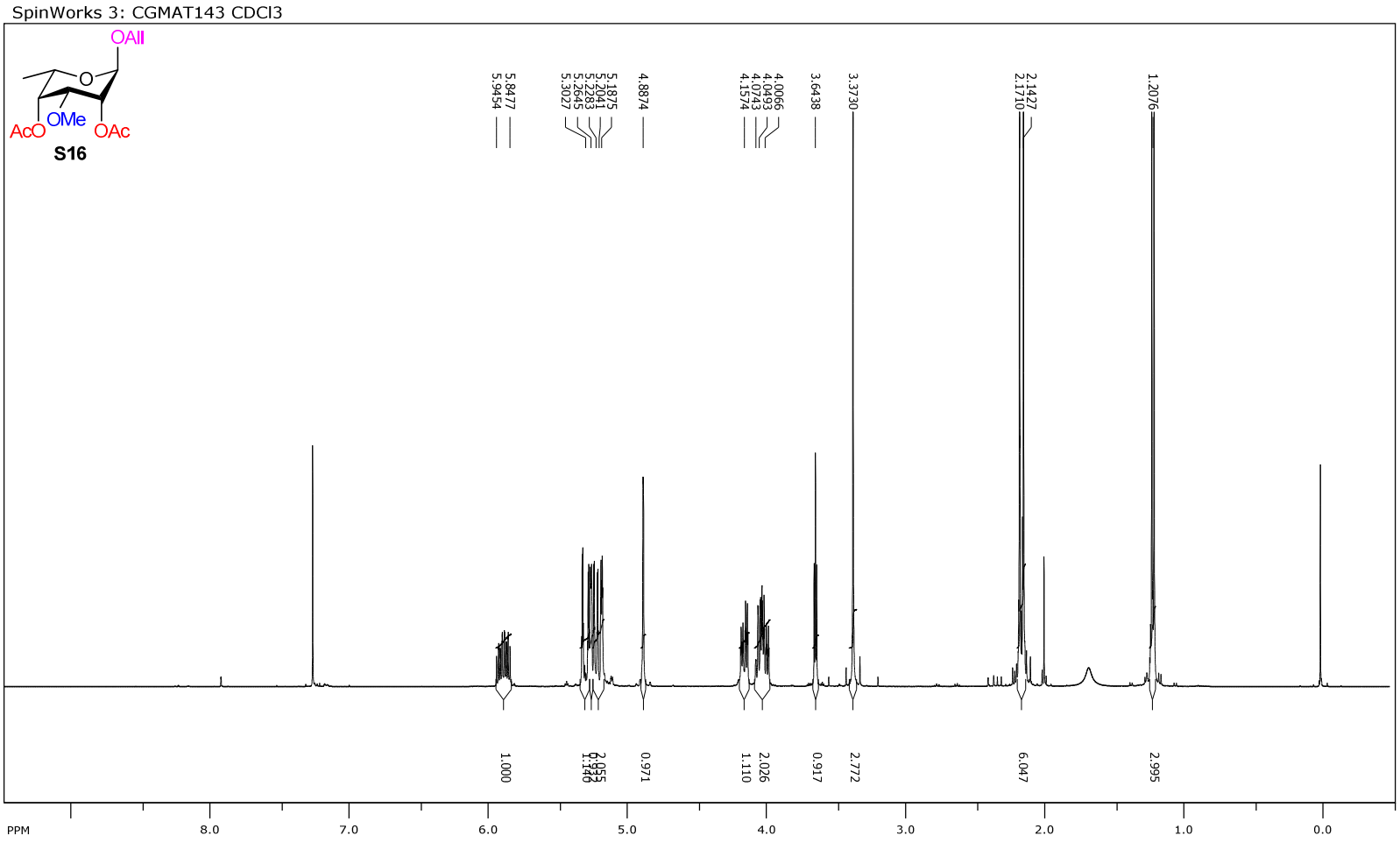
Supplementary Figure 38 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S15.



file: ...eau dossier\RMN LPS\CGMAT126\4\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612756 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

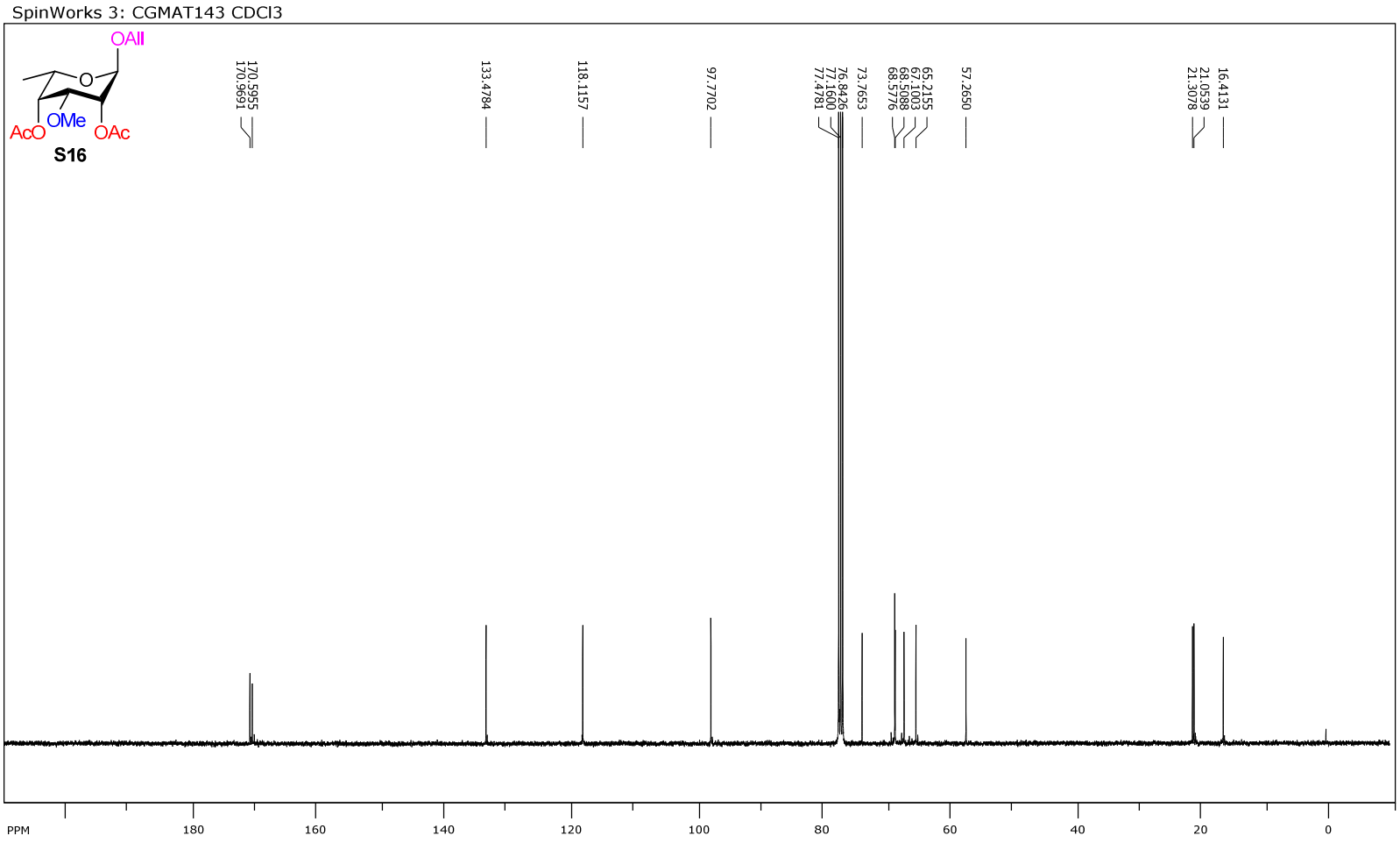
Supplementary Figure 39 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S16.



file: ...eau dossier\RMN LPS\CGMAT143\1\fid expt: <zg30>
transmitter freq.: 400.132001 MHz
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130005 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 40 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S16.



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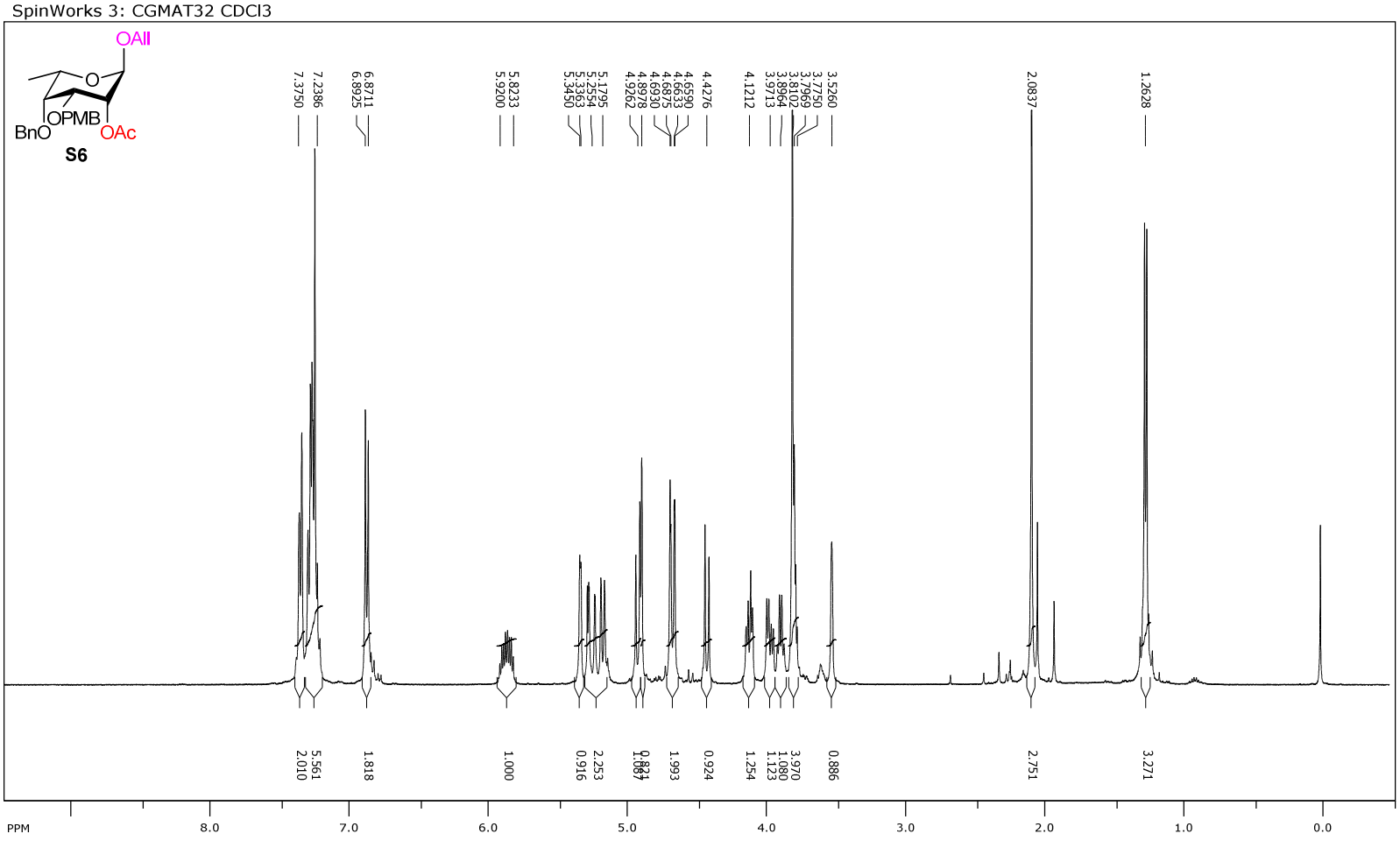
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 41 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S6.



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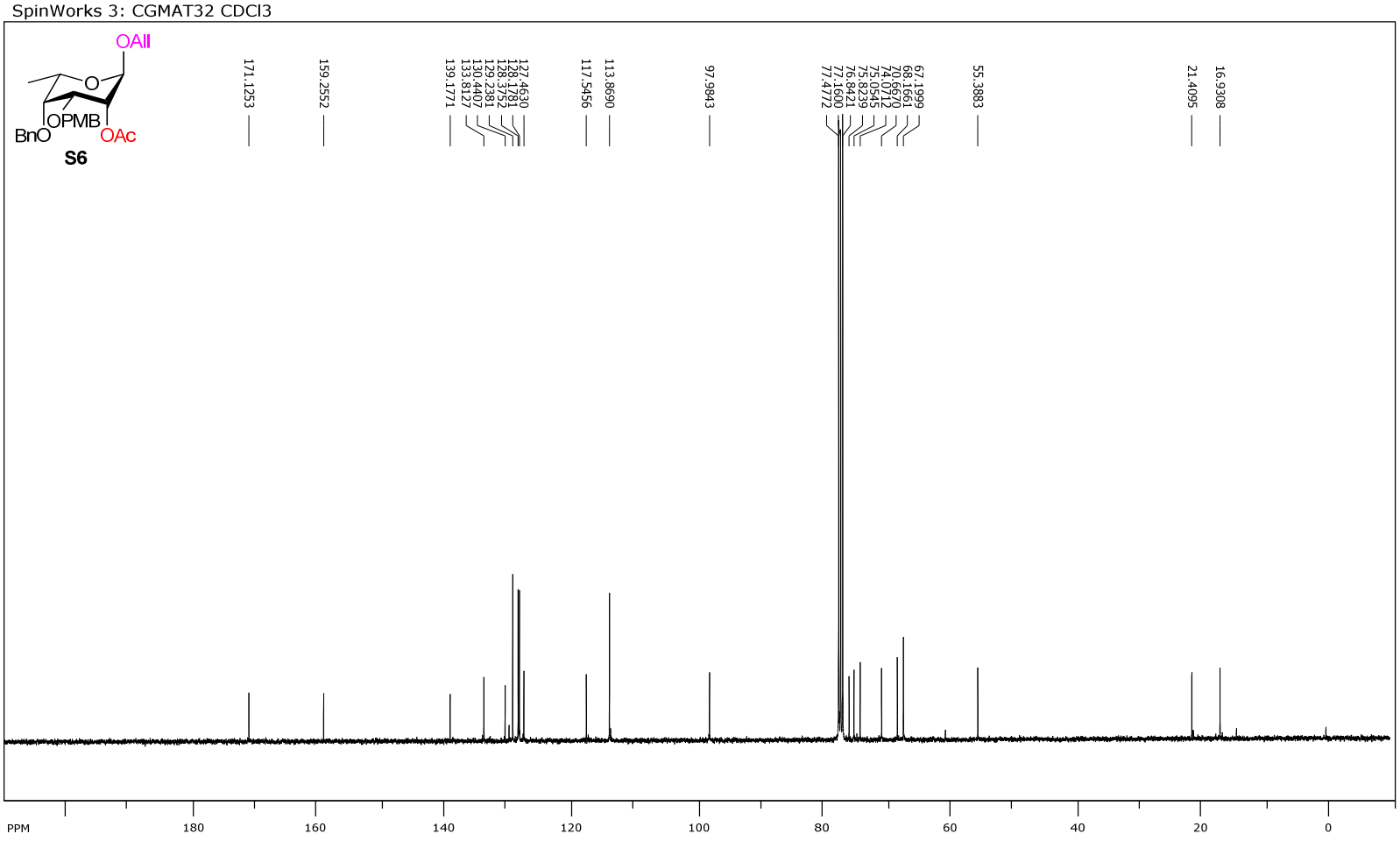
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 16

freq. of 0 ppm: 400.130011 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 42 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S6.



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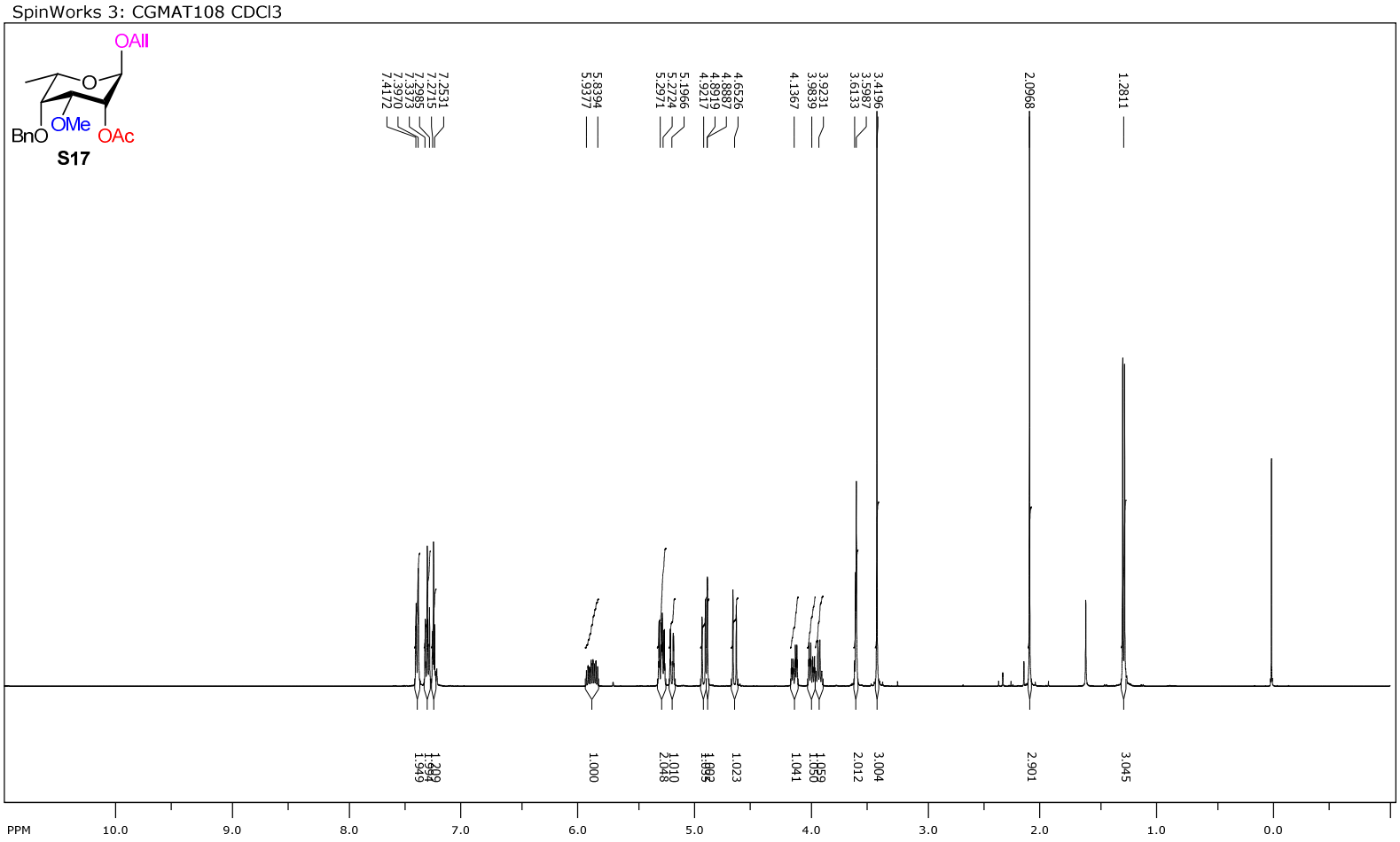
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 512

freq. of 0 ppm: 100.612758 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 43 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S17.



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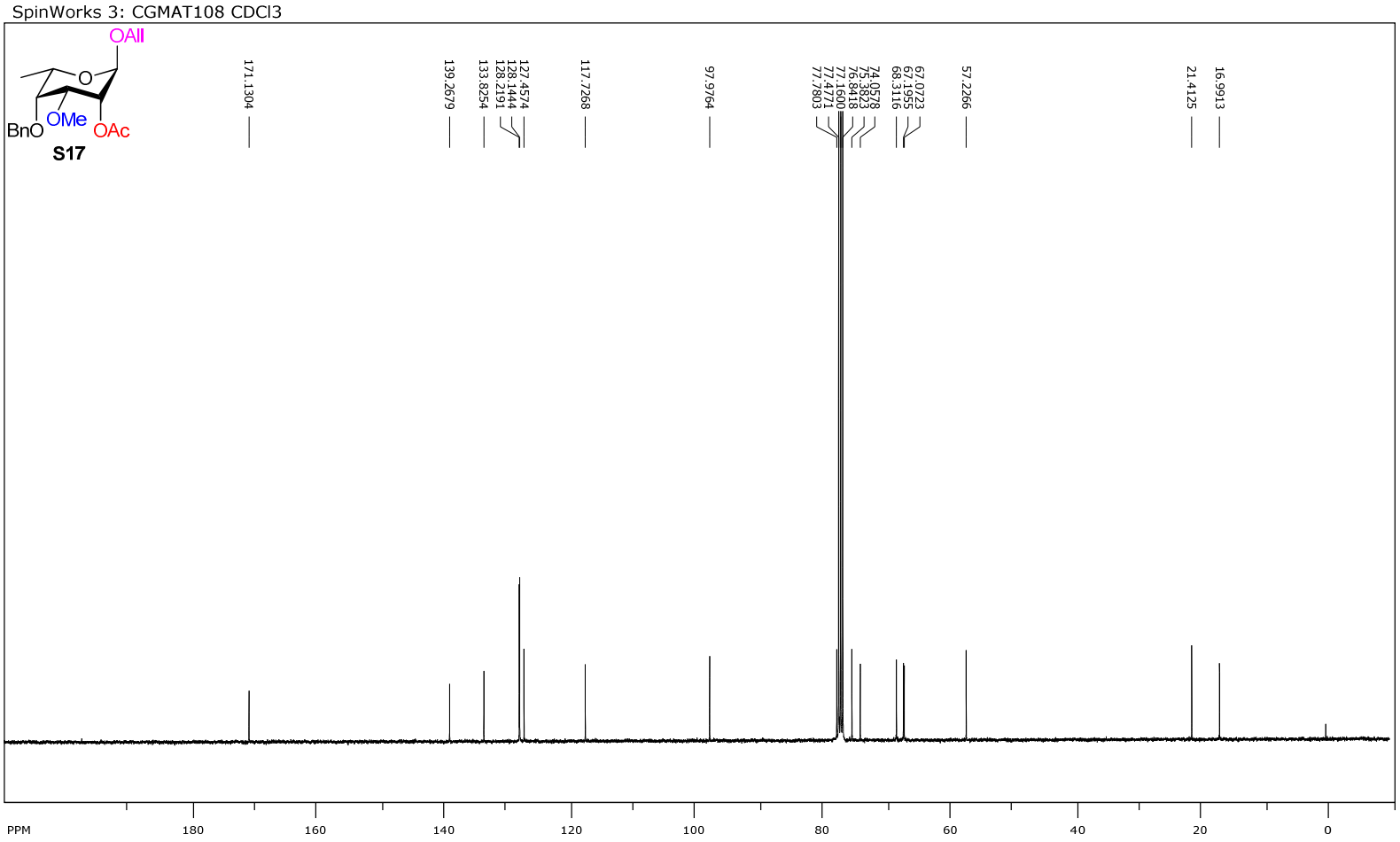
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 64

freq. of 0 ppm: 400.130009 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 192.308 ppm/cm: 0.48061

Supplementary Figure 44 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S17.



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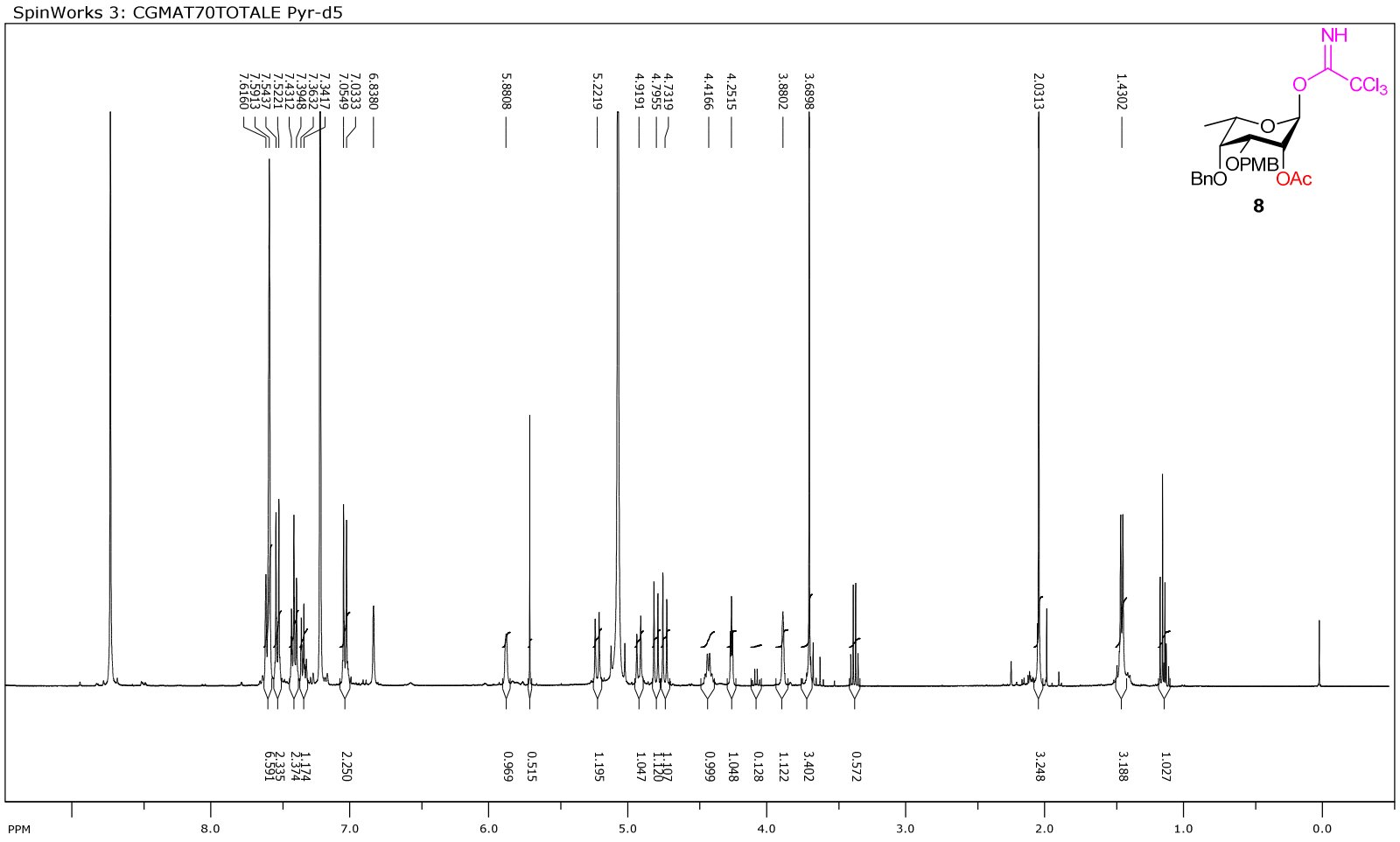
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612756 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 45 | ^{1}H NMR spectra (py-d_5, 400 MHz) of compound 8.



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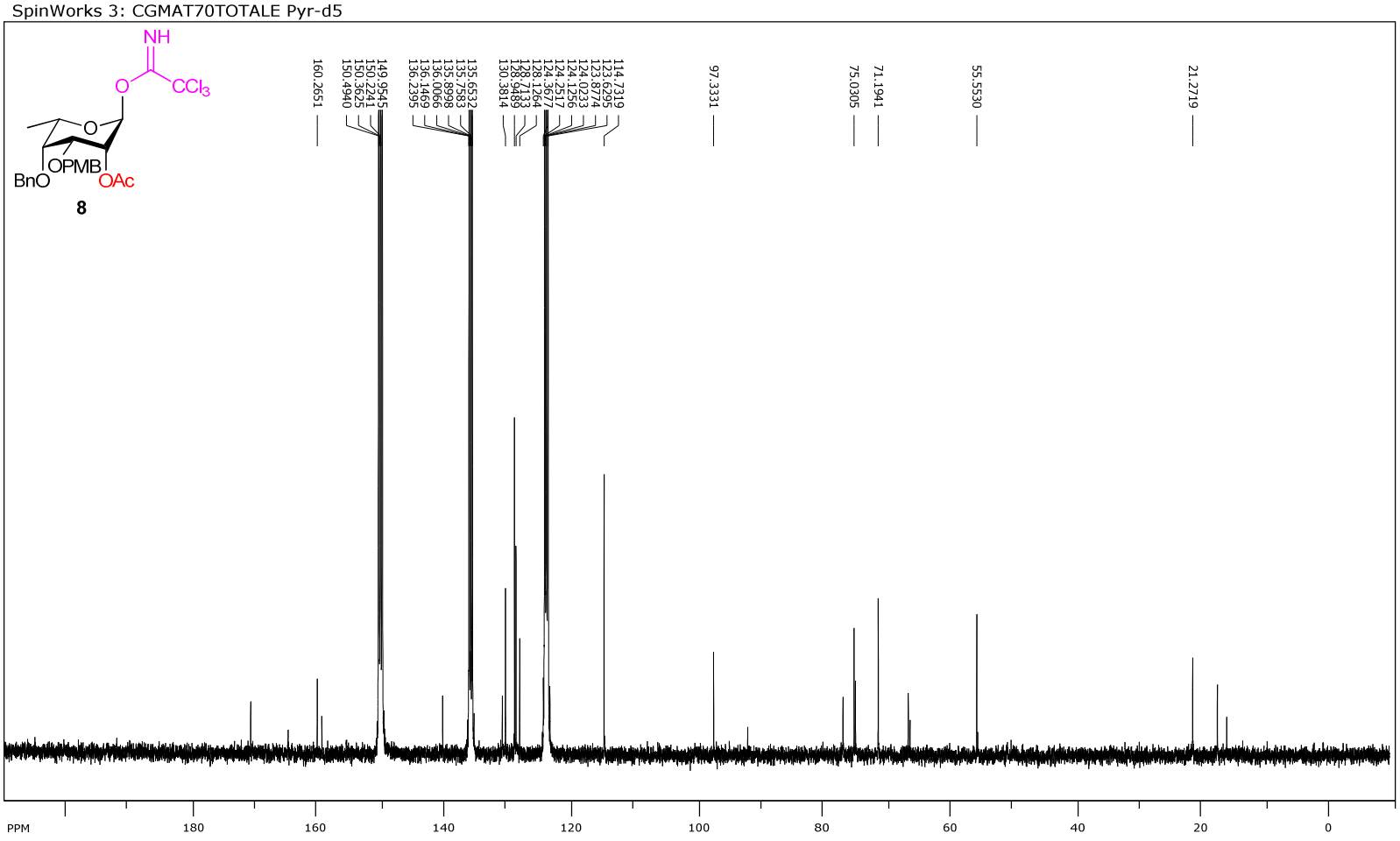
number of scans: 64

freq. of 0 ppm: 400.130588 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

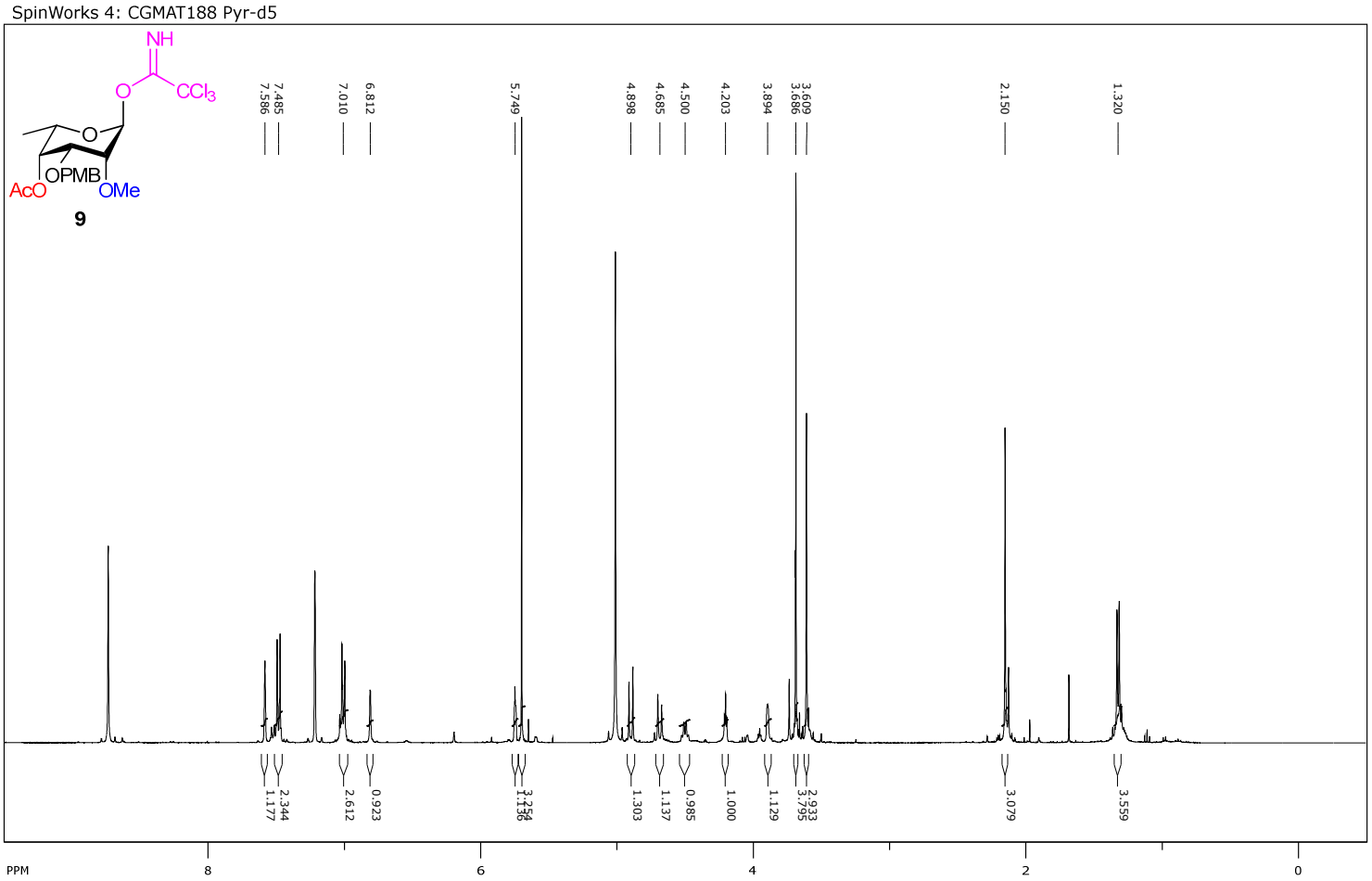
Supplementary Figure 46 | ^{13}C NMR spectra (py-d_5, 100 MHz) of compound 8.



file: ...ssier\RMN LPS\CGMAT70 TOTALE\3\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612860 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.393 ppm/cm: 8.79913

Supplementary Figure 47 | ^{1}H NMR spectra (py-d_5, 400 MHz) of compound 9.



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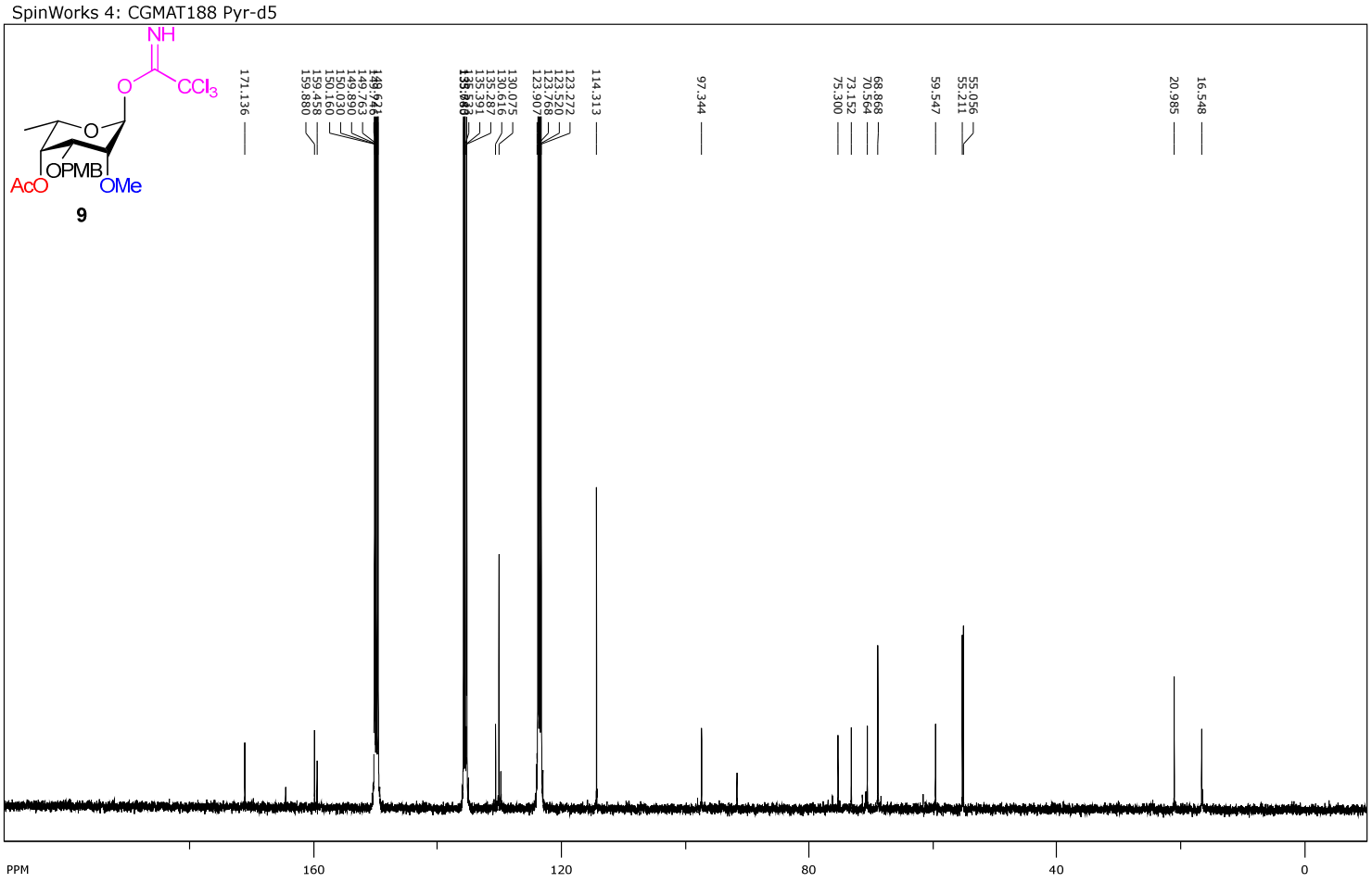
number of scans: 32

freq. of 0 ppm: 400.130591 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

Supplementary Figure 48 | ^{13}C NMR spectra (py-d_5, 100 MHz) of compound 9.



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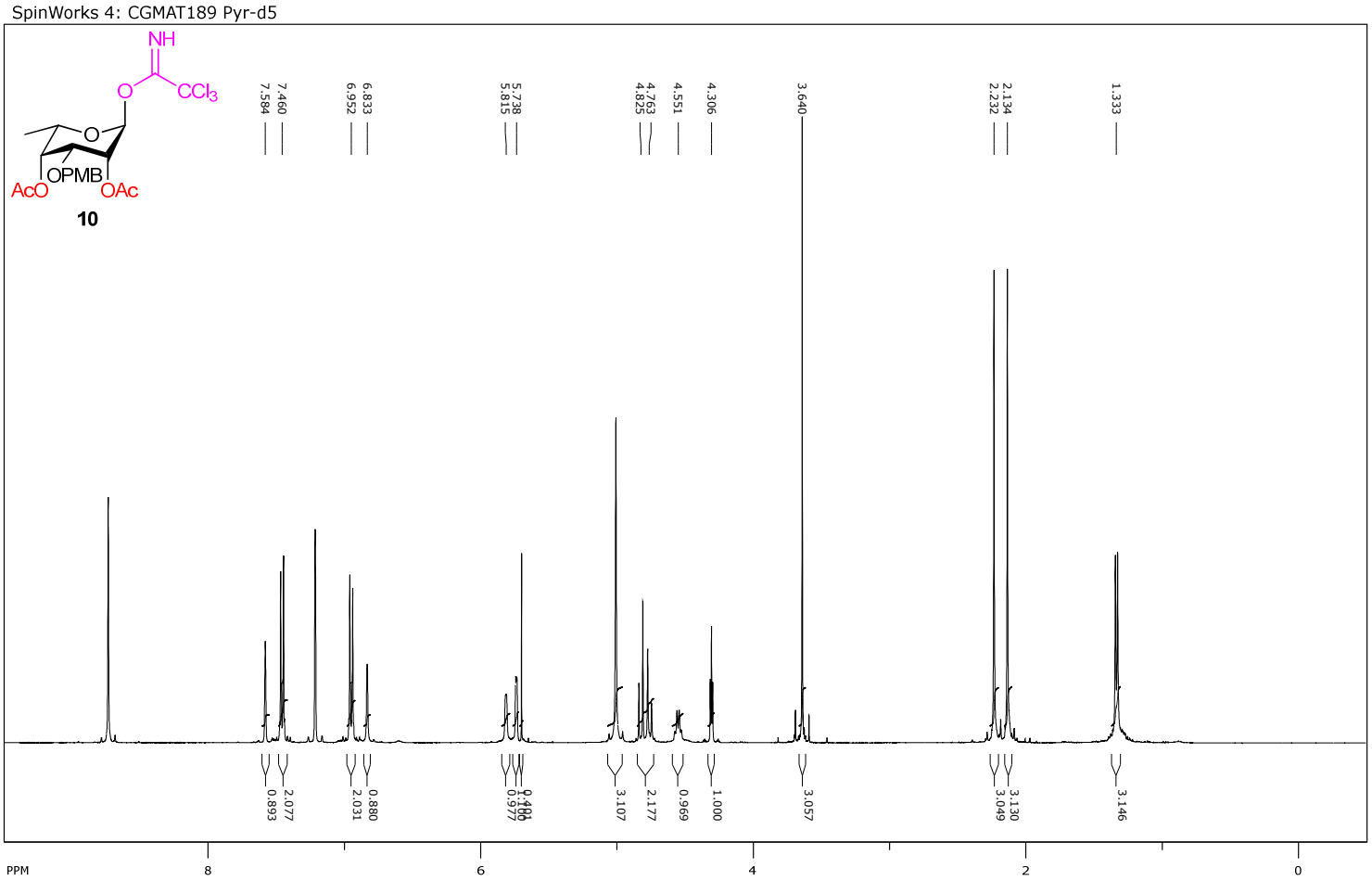
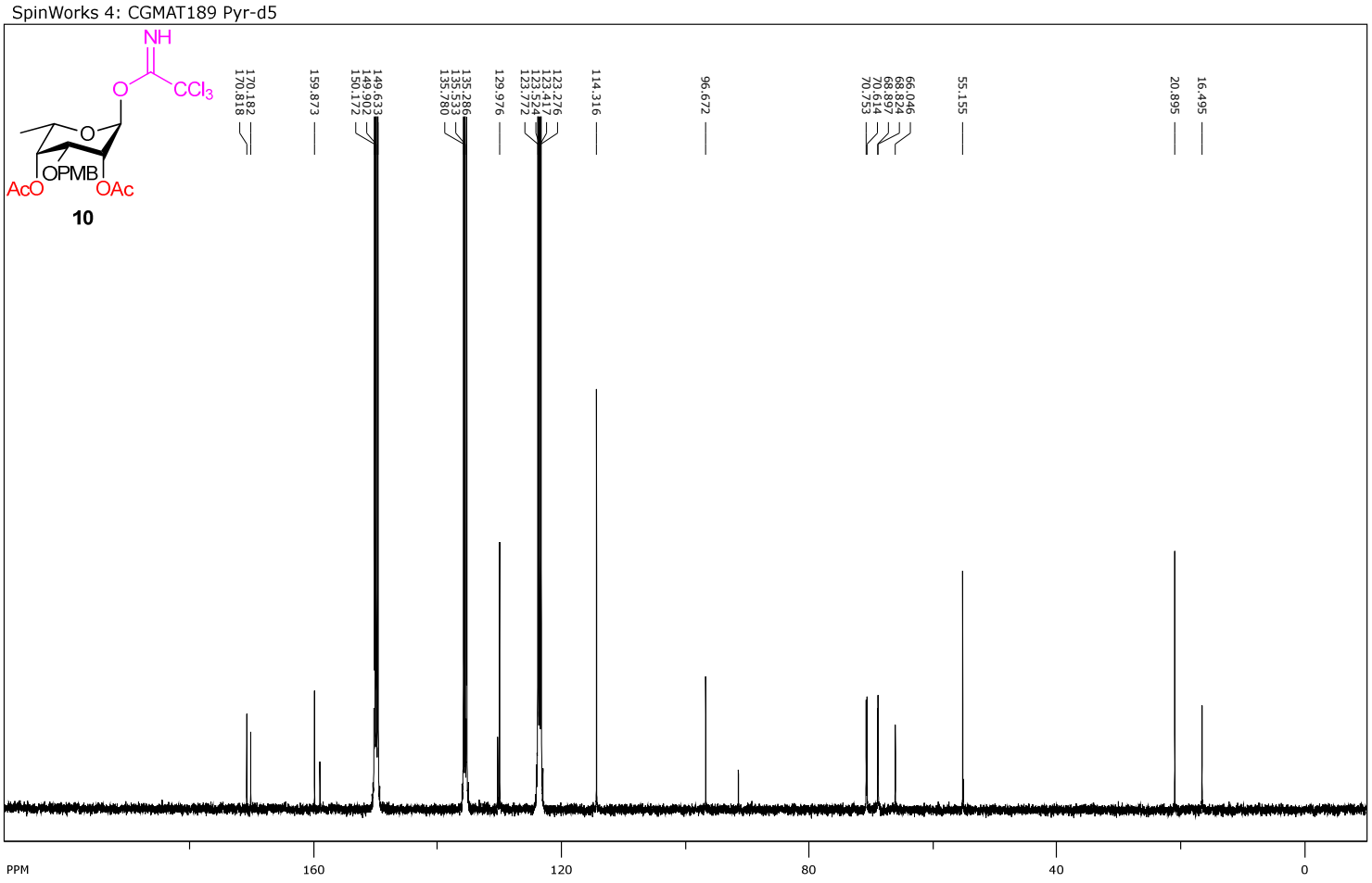
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612895 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

Supplementary Figure 49 | ^{1}H NMR spectra (py-d_5, 400 MHz) of compound 10.



Supplementary Figure 50 | ^{13}C NMR spectra (py-d_5, 100 MHz) of compound 10.



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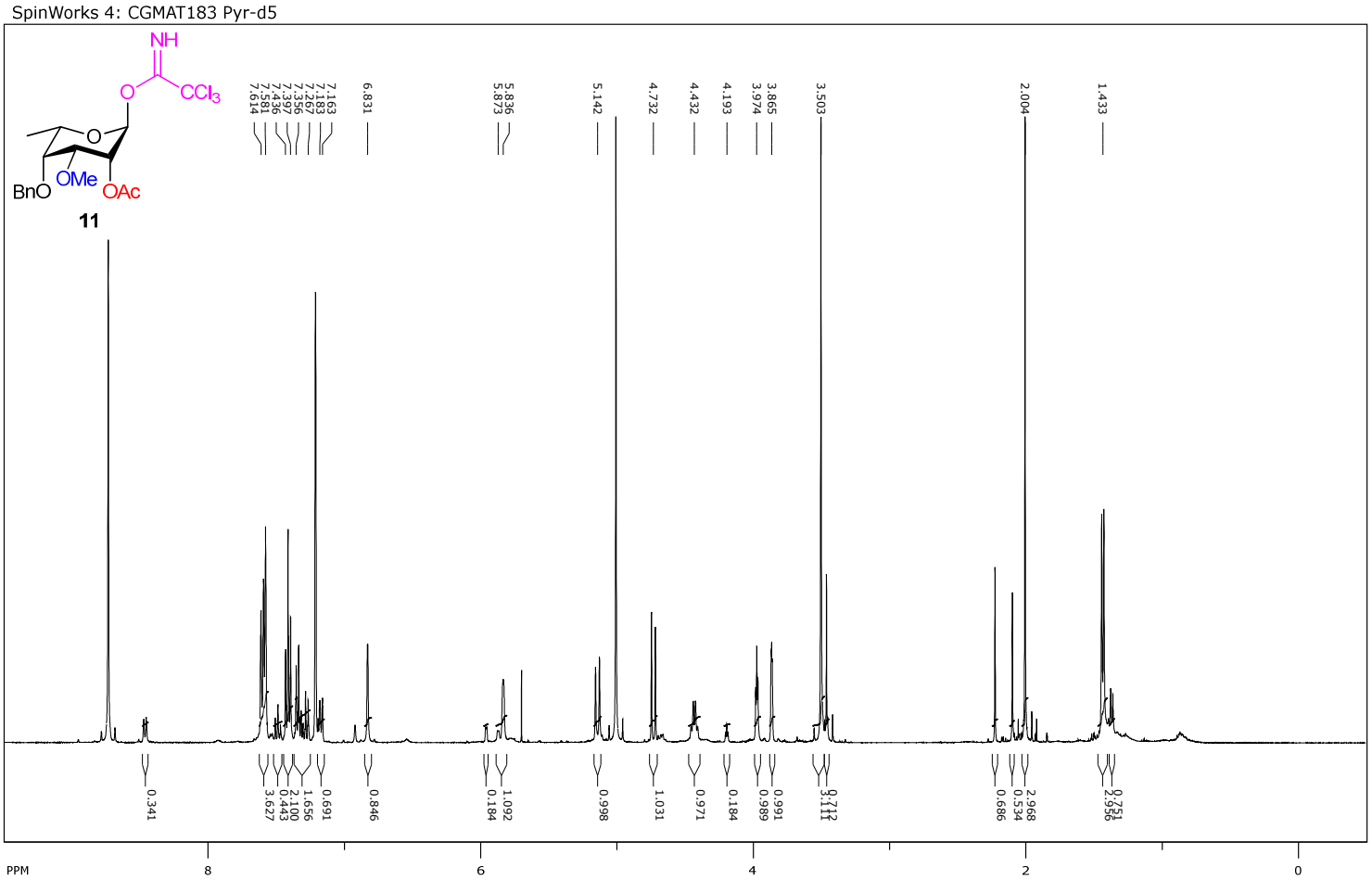
number of scans: 1024

freq. of 0 ppm: 100.612895 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

Supplementary Figure 51 | ^{1}H NMR spectra (py-d_5, 400 MHz) of compound 11.



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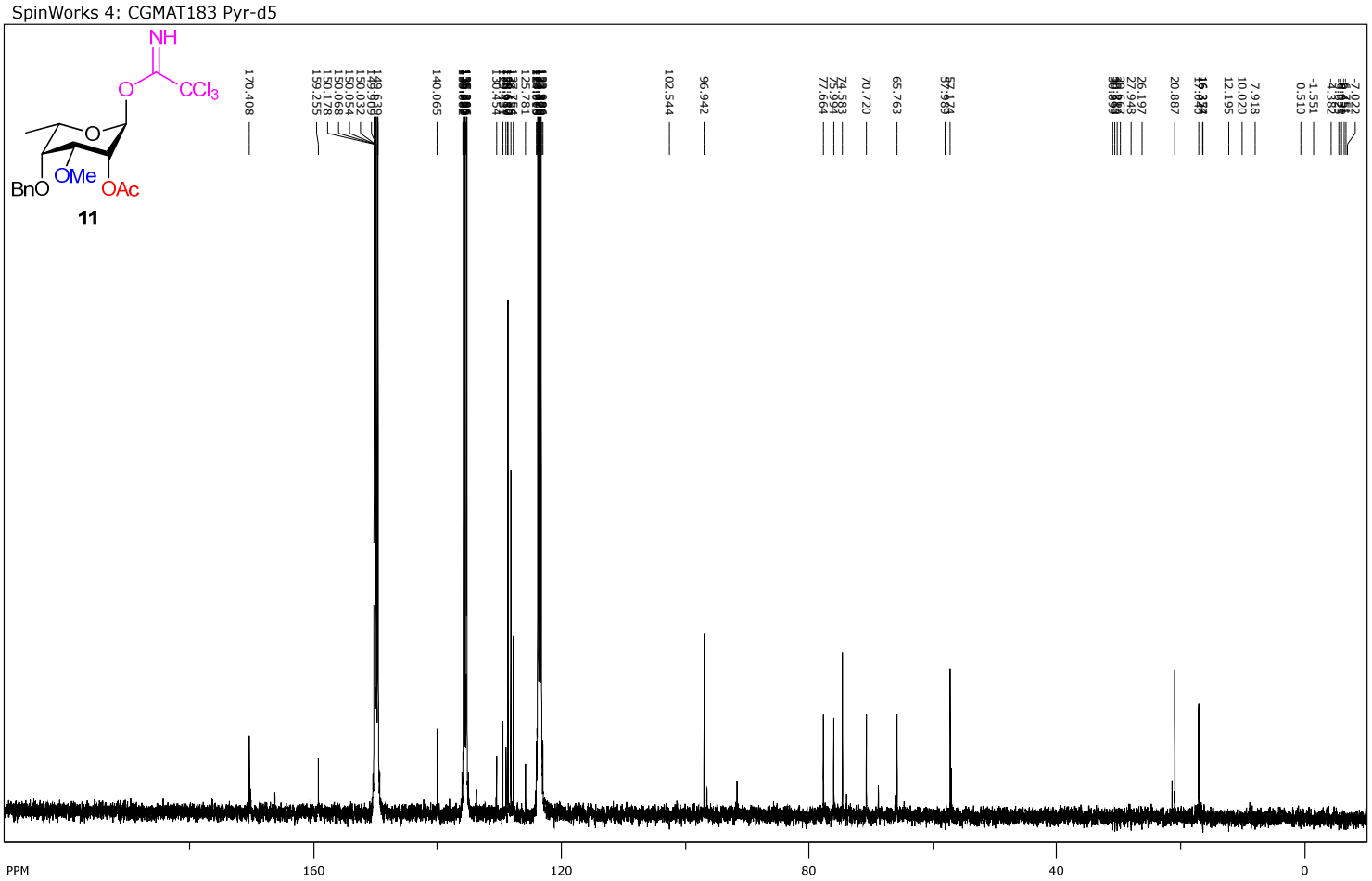
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130593 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

Supplementary Figure 52 | ^{13}C NMR spectra (py-d_5, 100 MHz) of compound 11.



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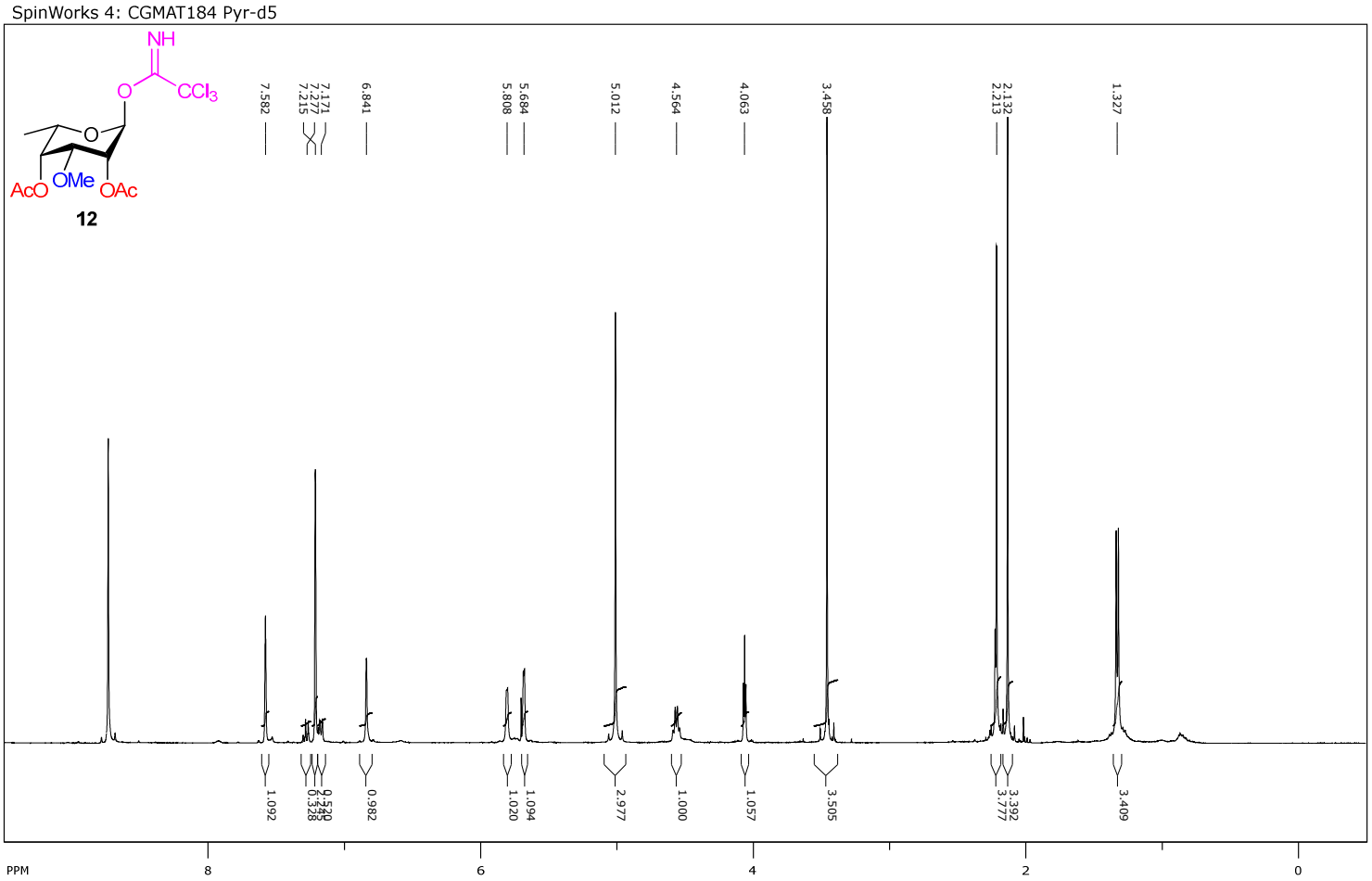
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612894 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

Supplementary Figure 53 | ^{1}H NMR spectra (py-d_5, 400 MHz) of compound 12.



file: ...eau dossier\RMN LPS\CGMAT184\1\fid expt: <zg30>
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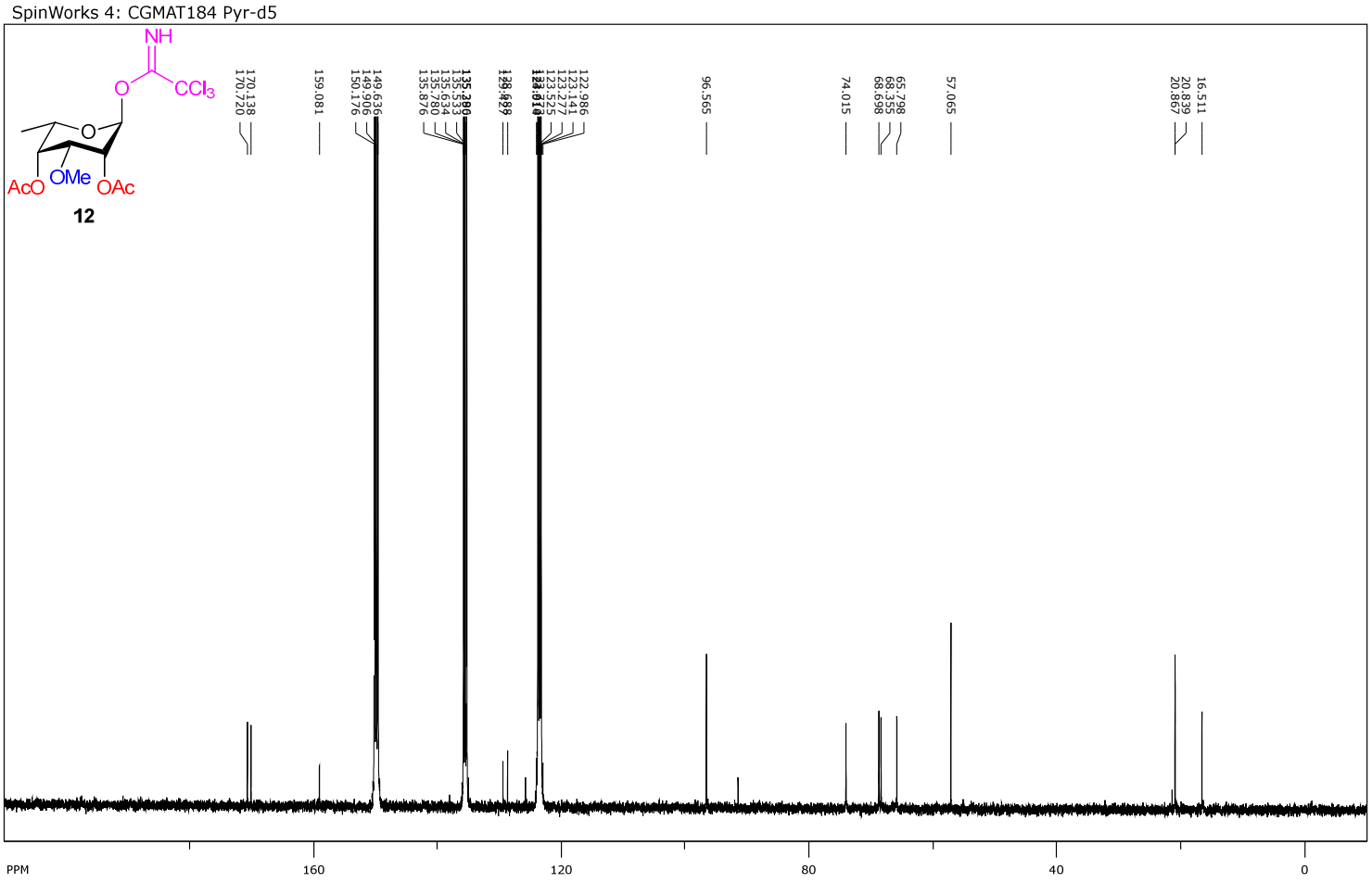
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130592 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

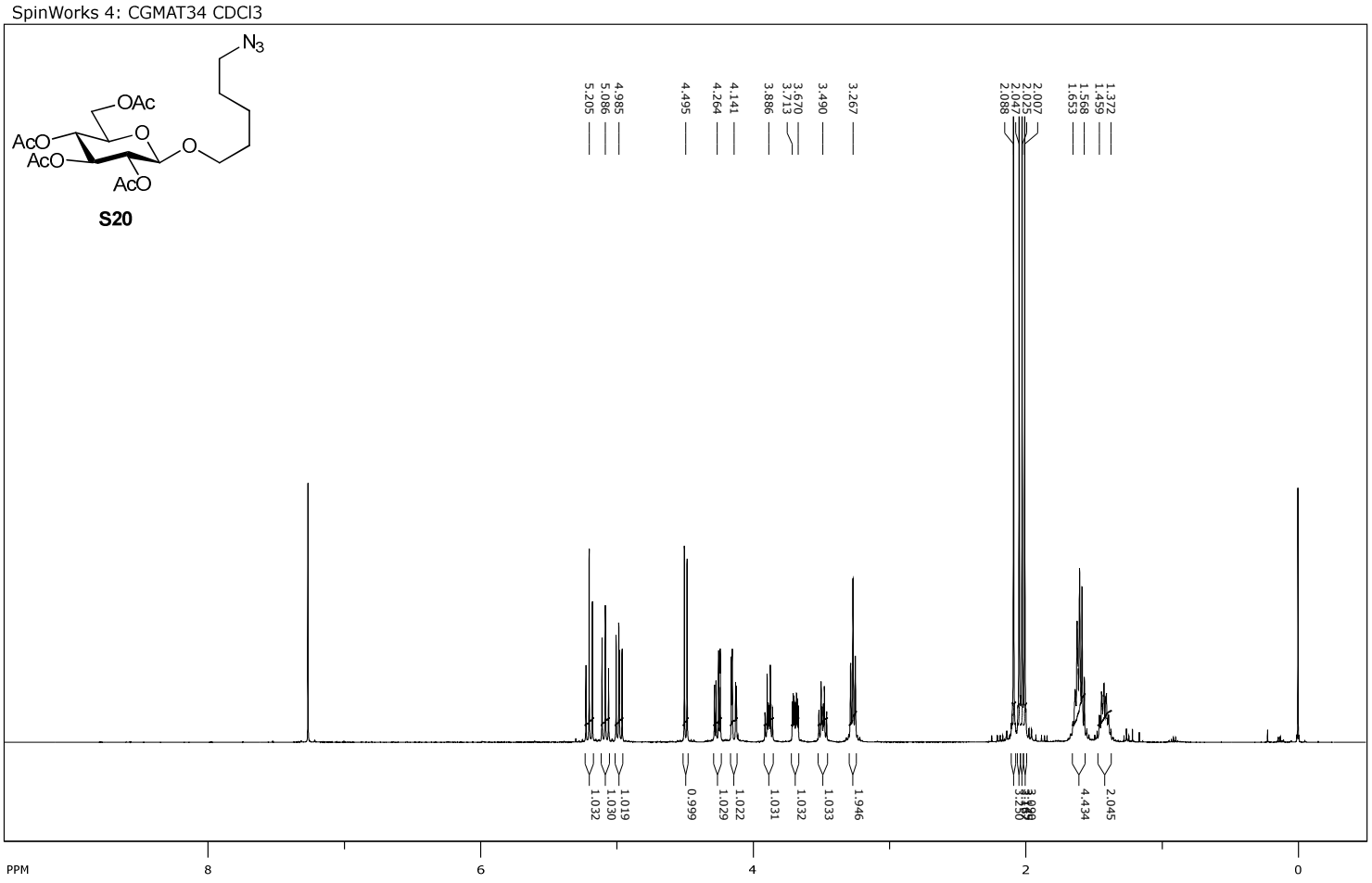
Supplementary Figure 54 | ^{13}C NMR spectra (py-d_5, 100 MHz) of compound 12.



file: ...eau dossier\RMN LPS\CGMAT184\3\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612895 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

Supplementary Figure 55 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S20.



file: ...veau dossier\RMN LPS\CGMAT34\1\fid expt: <zg30>
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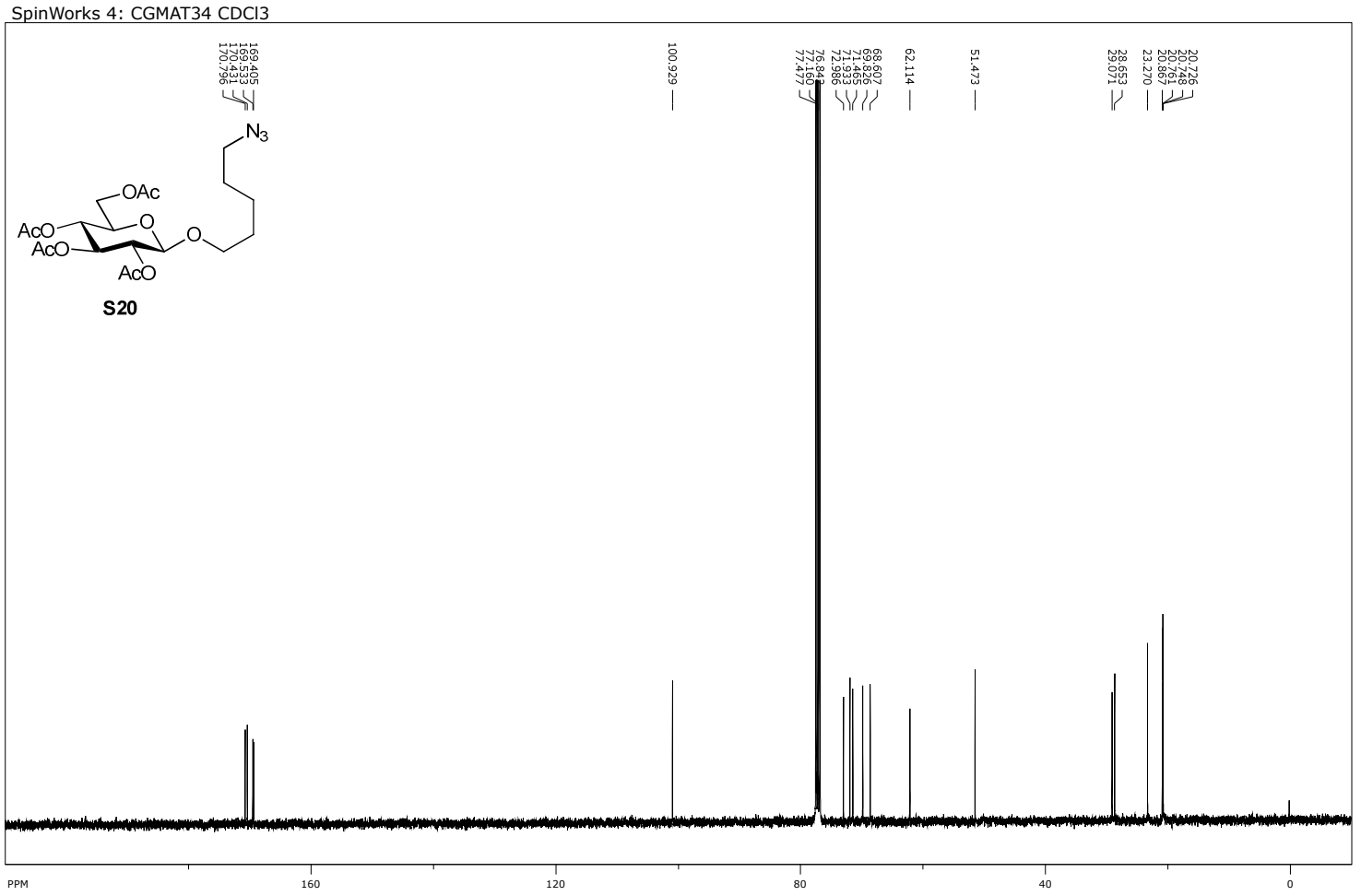
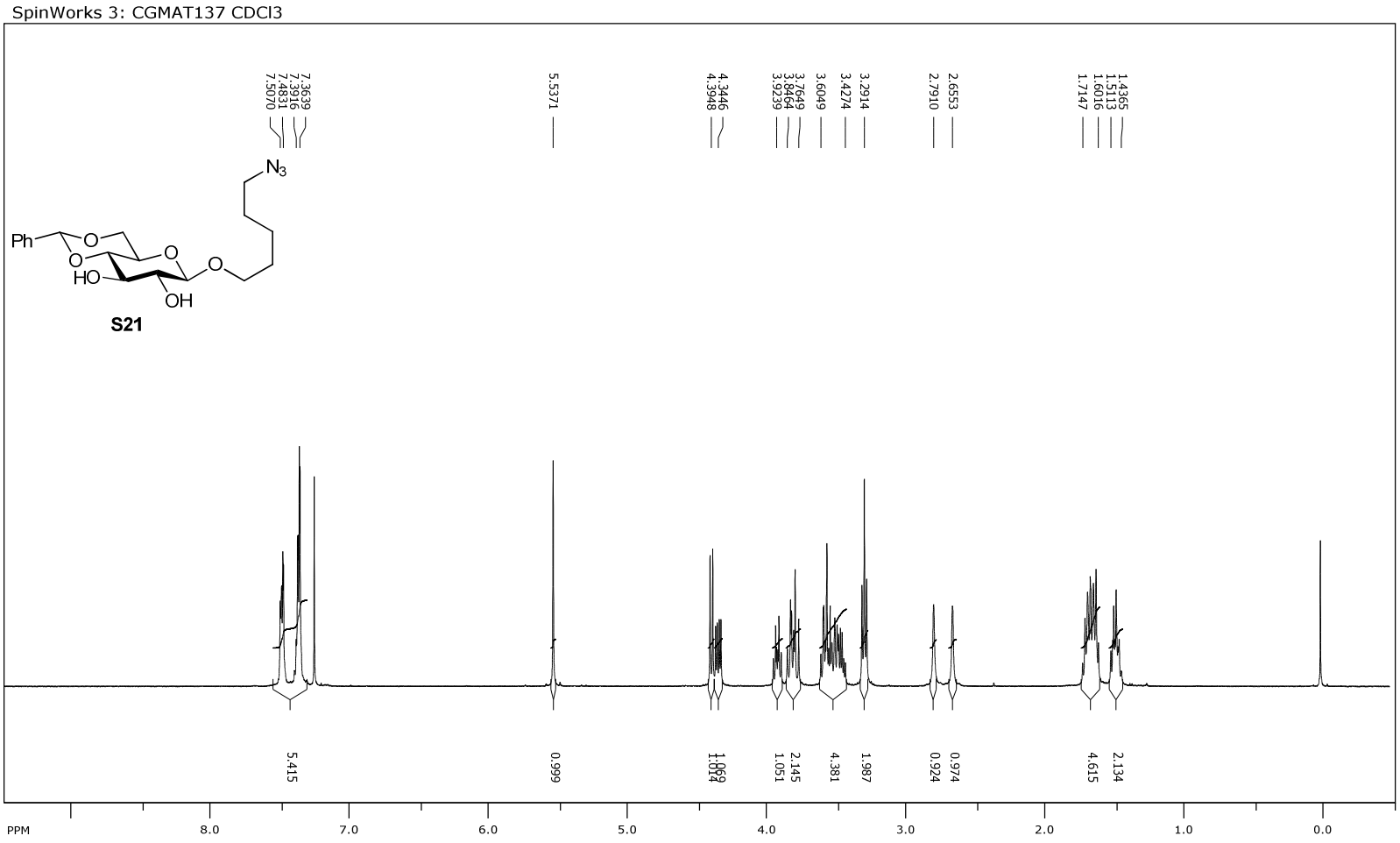
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 16

freq. of 0 ppm: 400.130006 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

Supplementary Figure 56 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S20.



Supplementary Figure 57 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S21.



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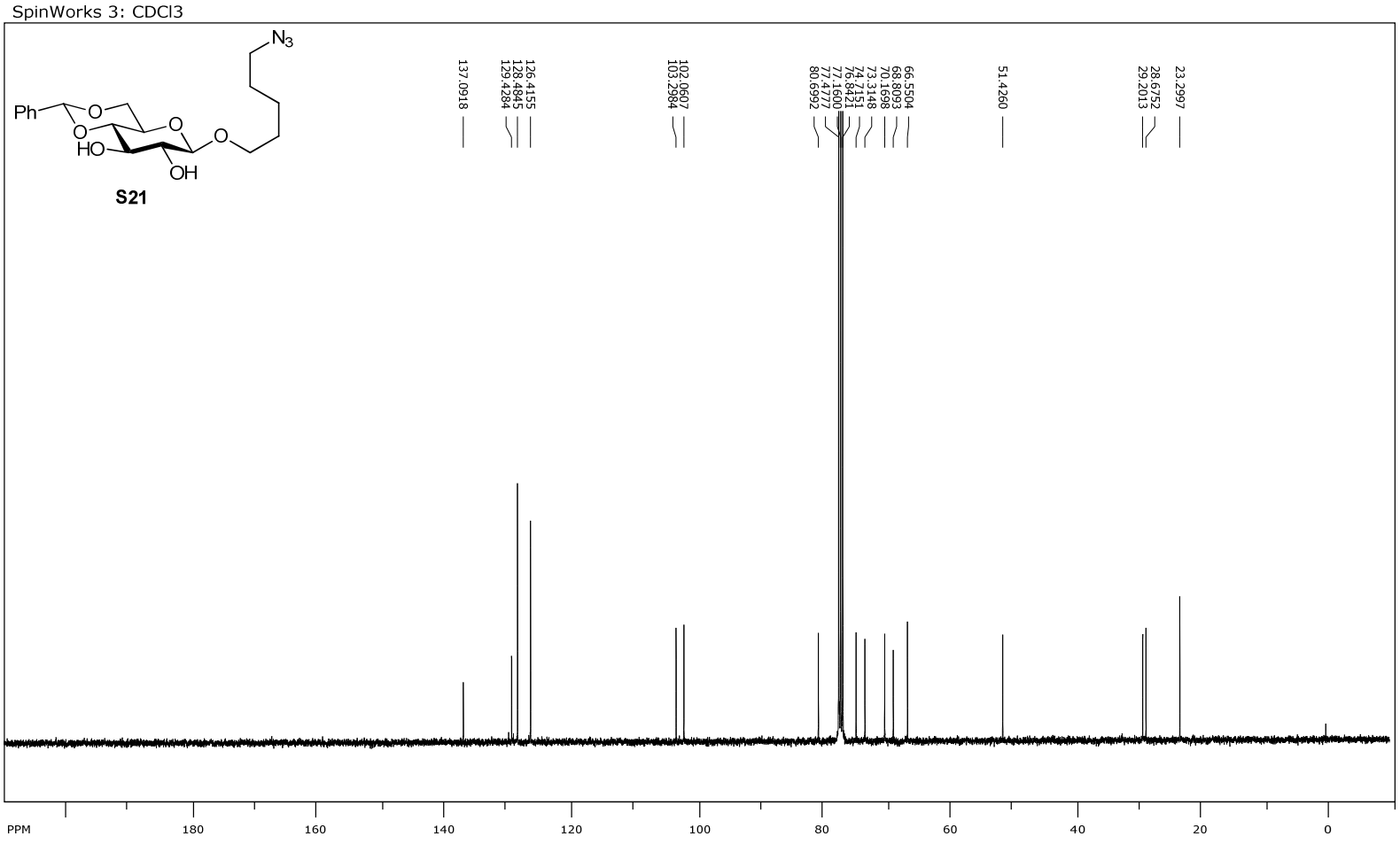
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 16

freq. of 0 ppm: 400.130009 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 58 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S21.



file: ...veau dossier\RMN LPS\CGMAT42\3\fid expt: <zgpg30>
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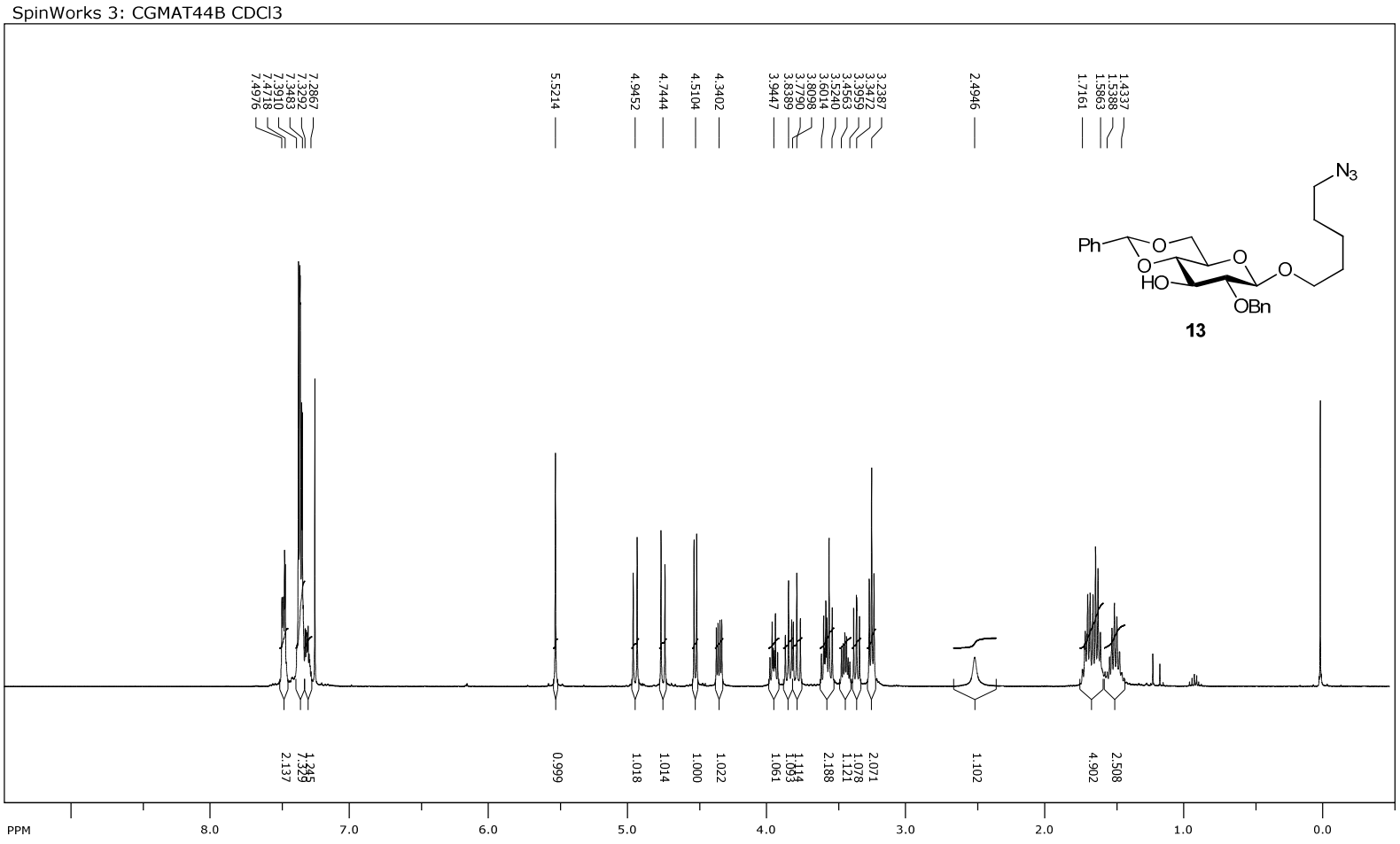
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 512

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 59 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 13.



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time domain size: 32768 points
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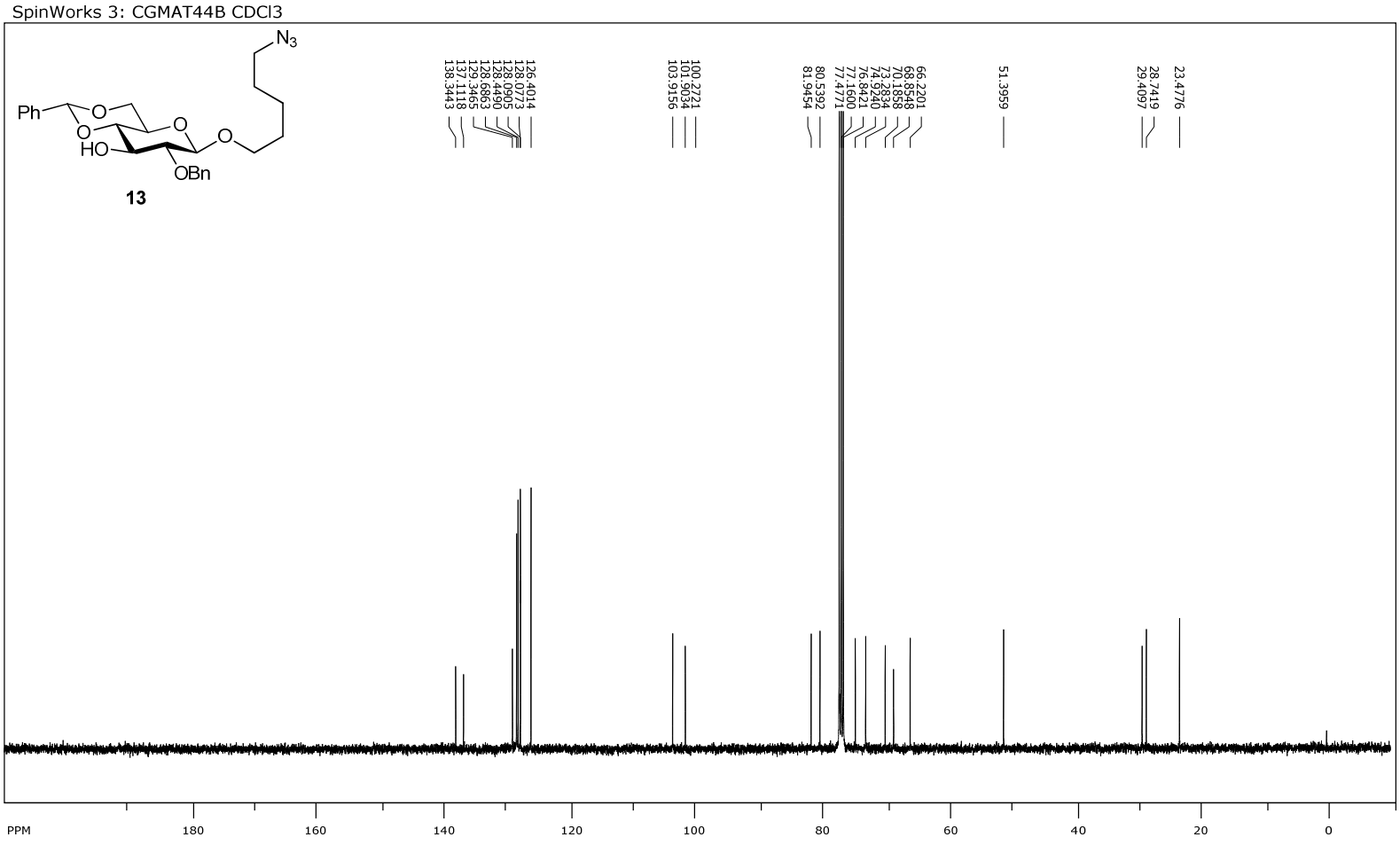
number of scans: 16

freq. of 0 ppm: 400.130011 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

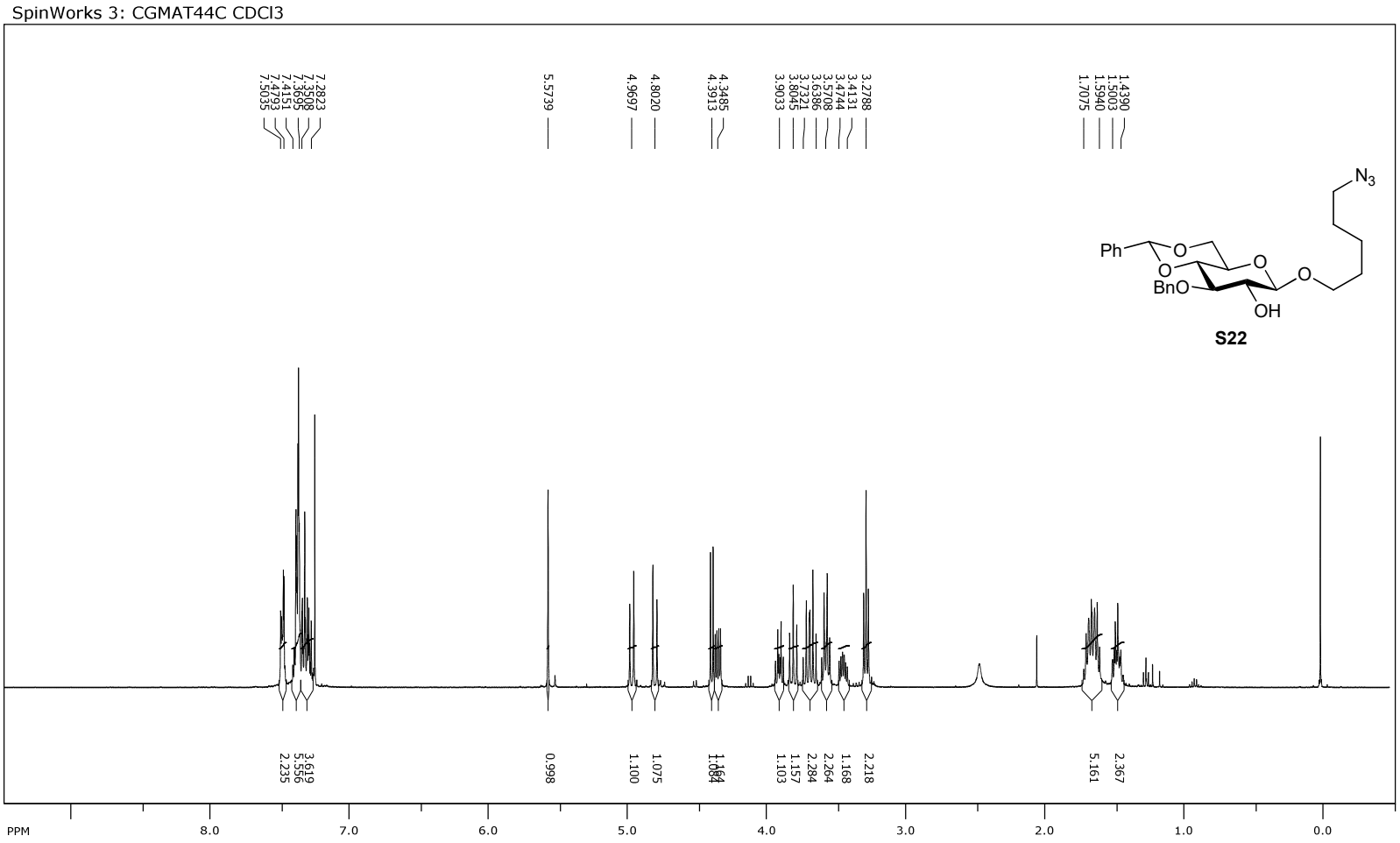
Supplementary Figure 60 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 13.



file: ...eau dossier\RMN LPS\CGMAT44B\4\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 512

freq. of 0 ppm: 100.612757 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 61 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S22.



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time domain size: 32768 points
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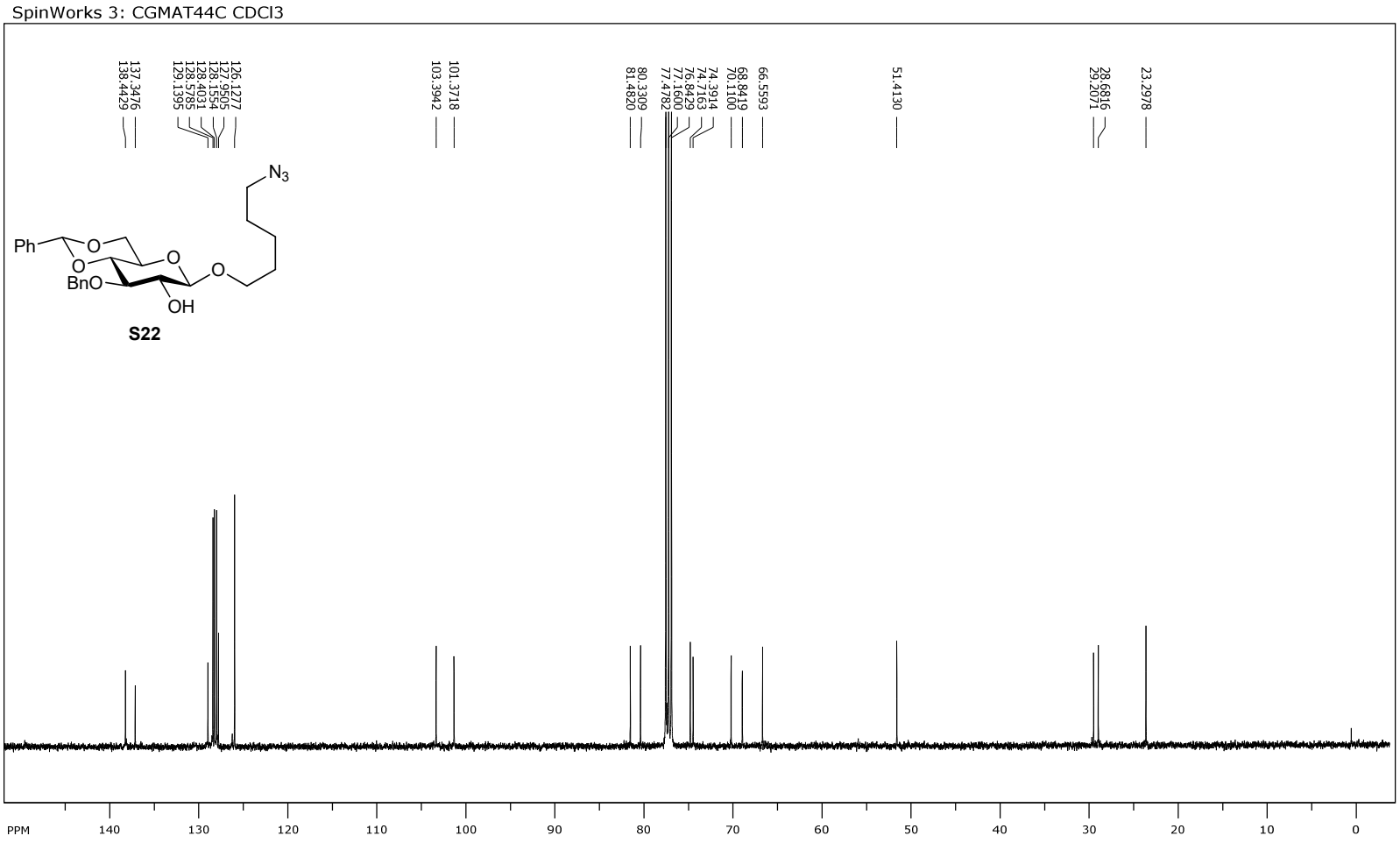
number of scans: 16

freq. of 0 ppm: 400.130011 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 62 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S22.



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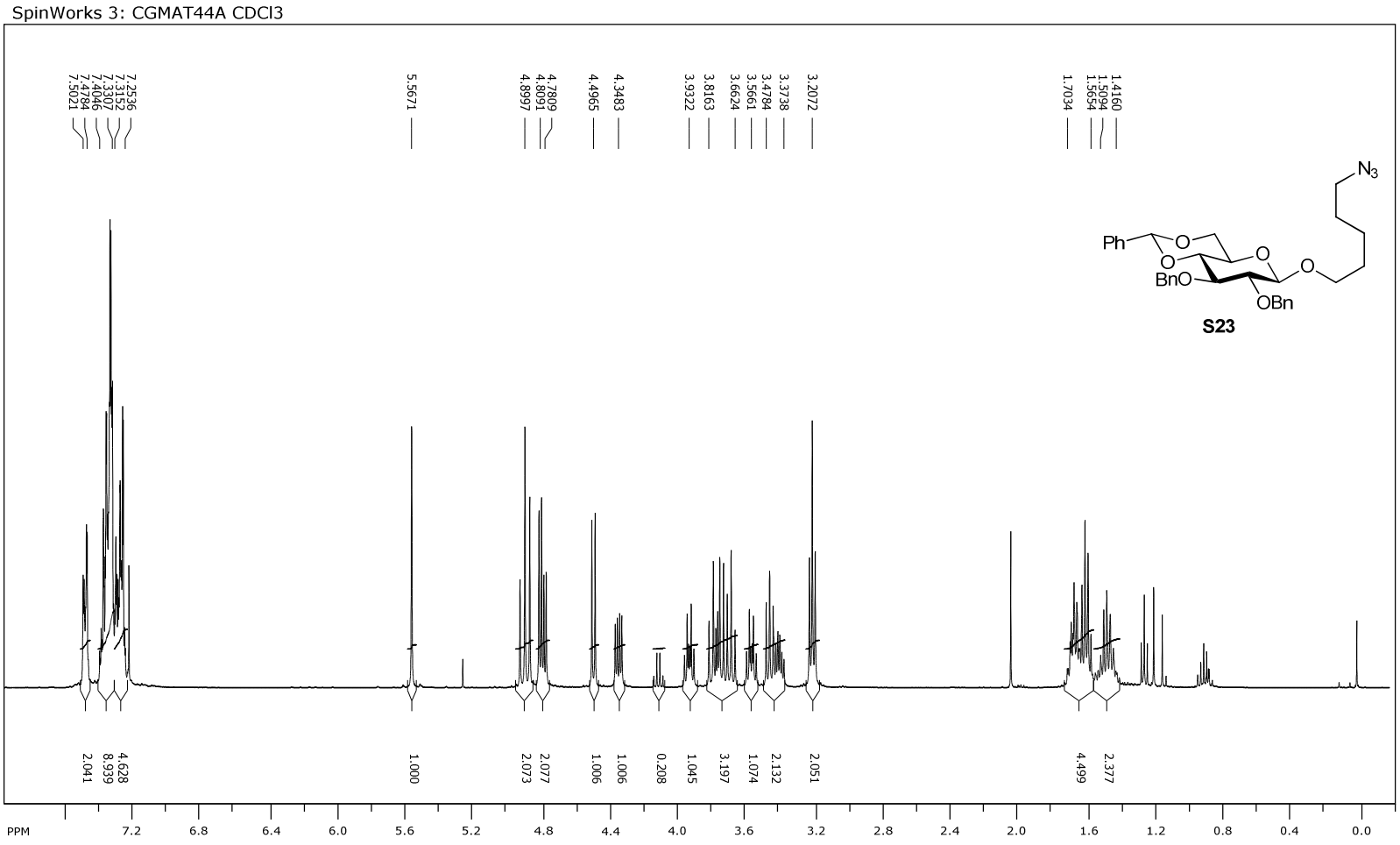
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 512

freq. of 0 ppm: 100.612757 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 629.194 ppm/cm: 6.25299

Supplementary Figure 63 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S23.



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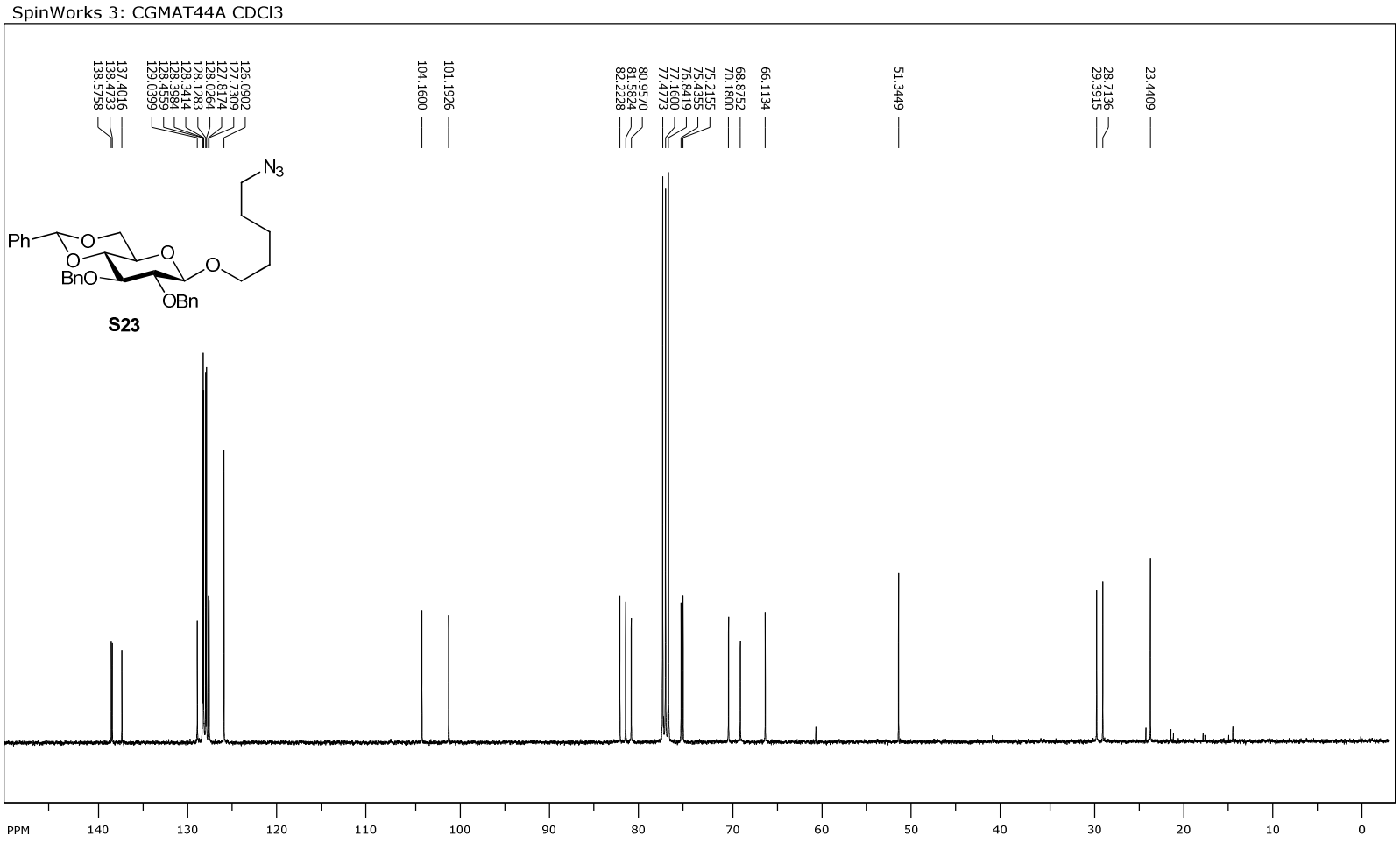
number of scans: 16

freq. of 0 ppm: 400.130021 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 130.630 ppm/cm: 0.32647

Supplementary Figure 64 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S23.



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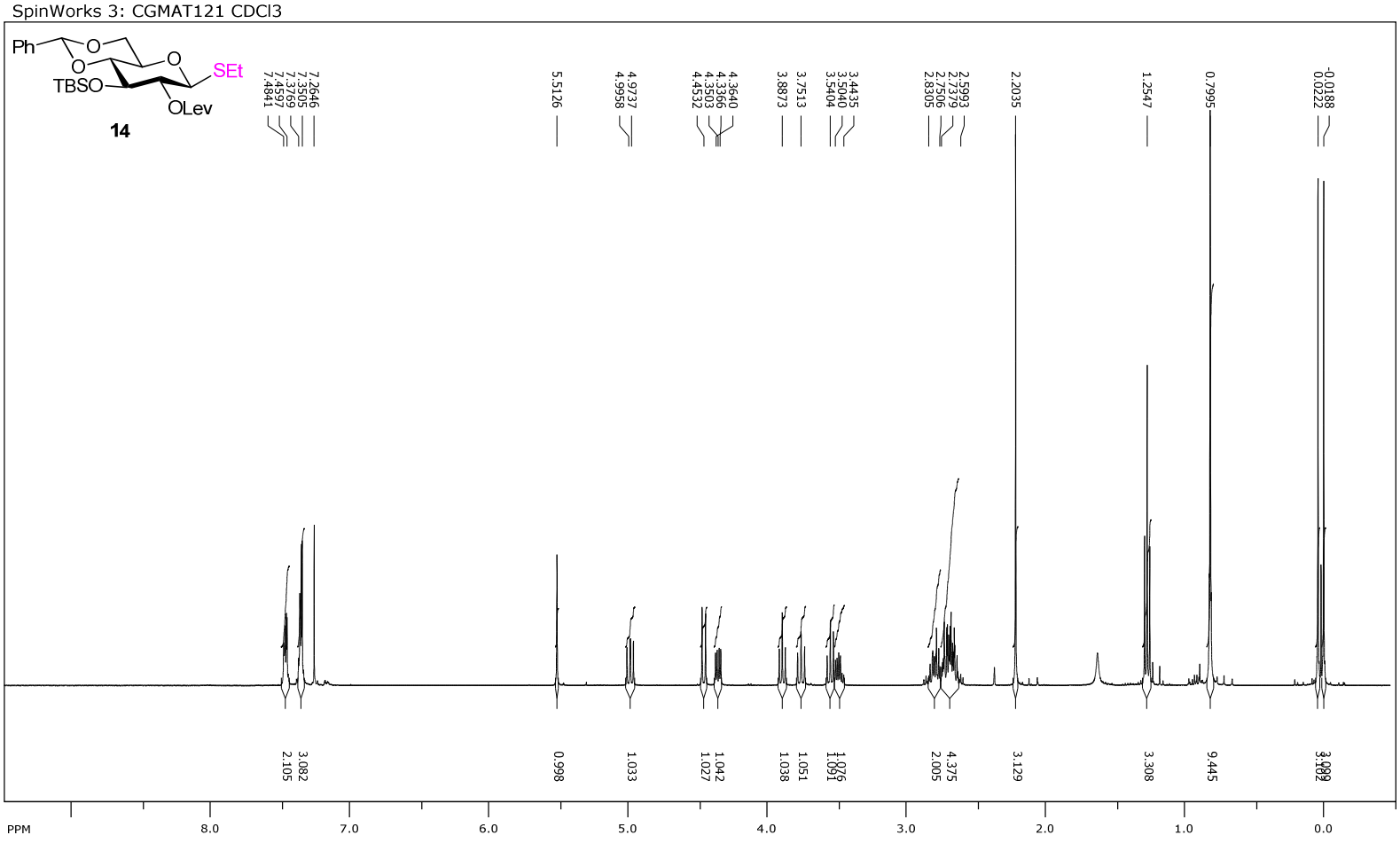
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 512

freq. of 0 ppm: 100.612763 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 617.891 ppm/cm: 6.14066

Supplementary Figure 65 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 14.



file: ...eau dossier\RMN LPS\CGMAT121\1\fid expt: <zg30>
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time domain size: 32768 points
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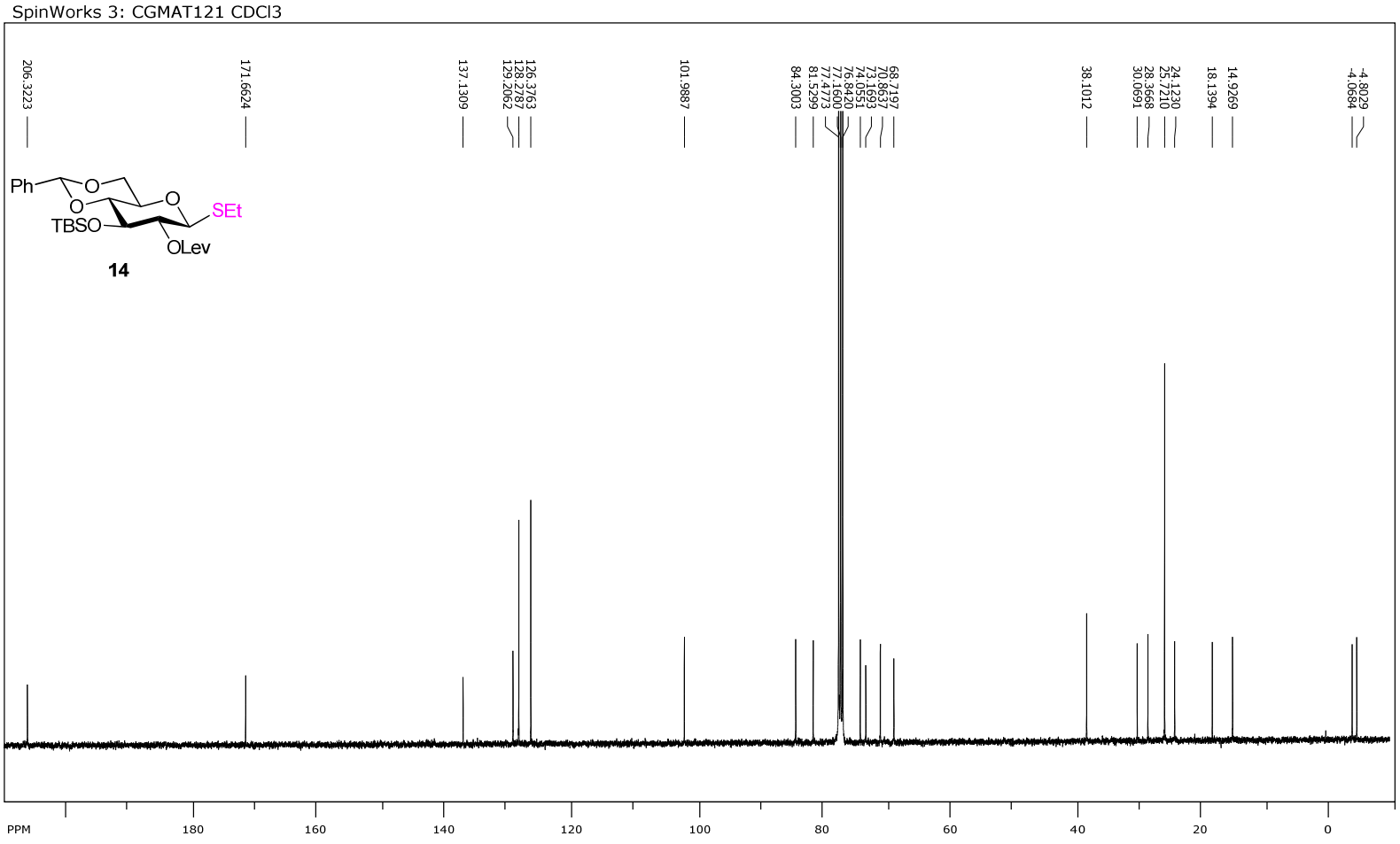
number of scans: 16

freq. of 0 ppm: 400.130008 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 66 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 14.



file: ...eau dossier\RMN LPS\CGMAT121\4\fid expt: <zgpg30>
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time domain size: 65536 points
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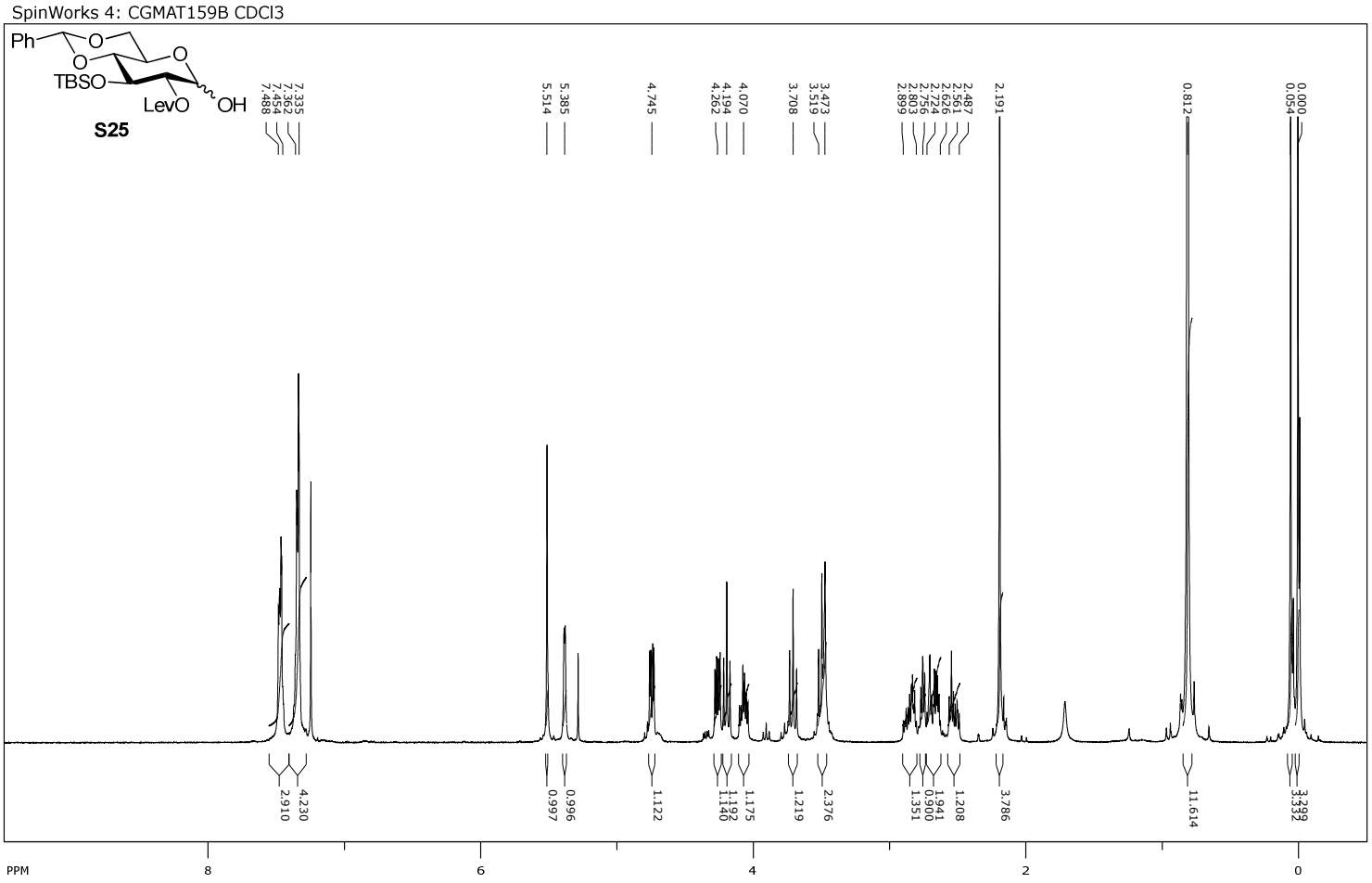
number of scans: 1024

freq. of 0 ppm: 100.612756 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 67 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S25.



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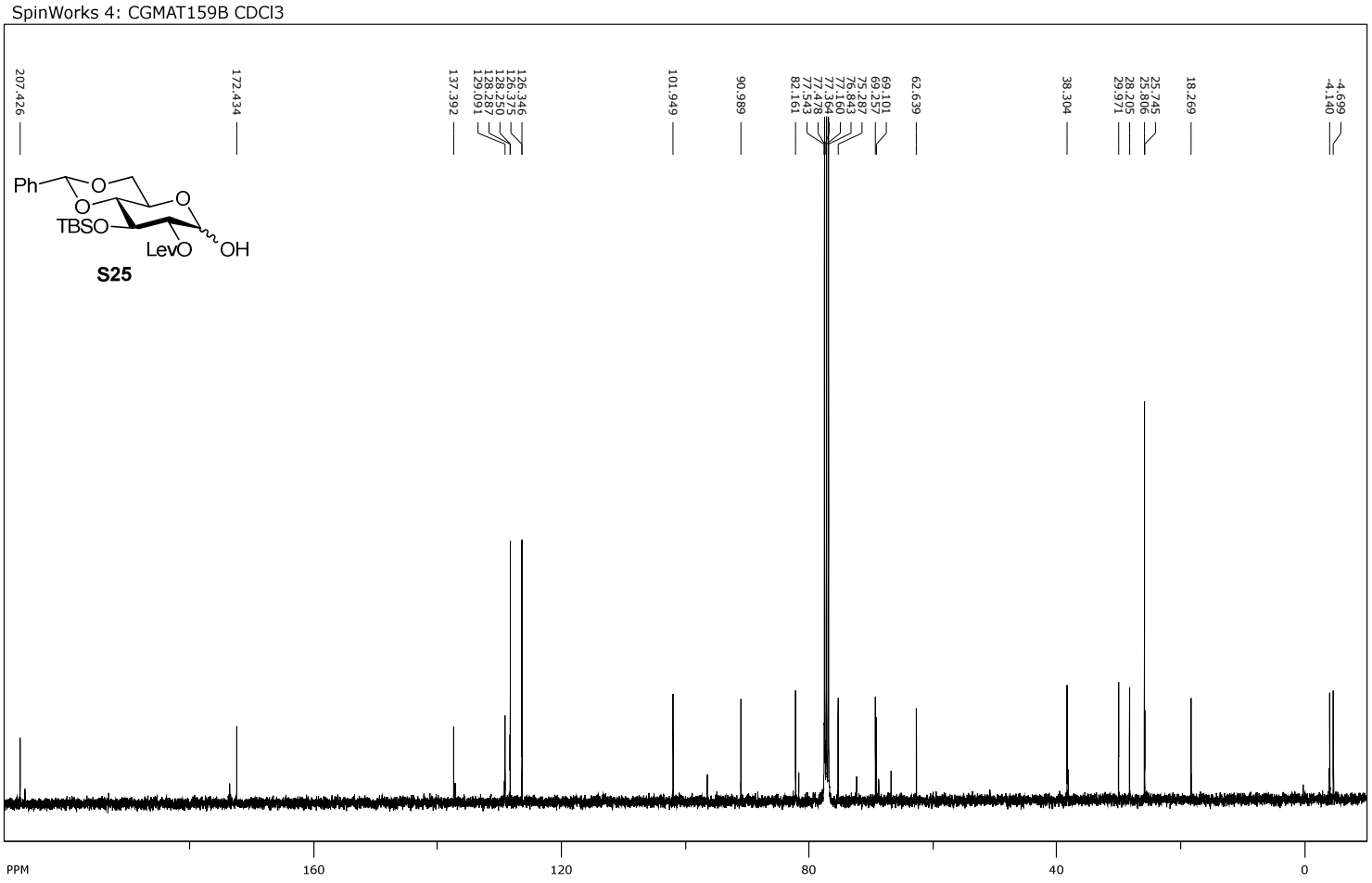
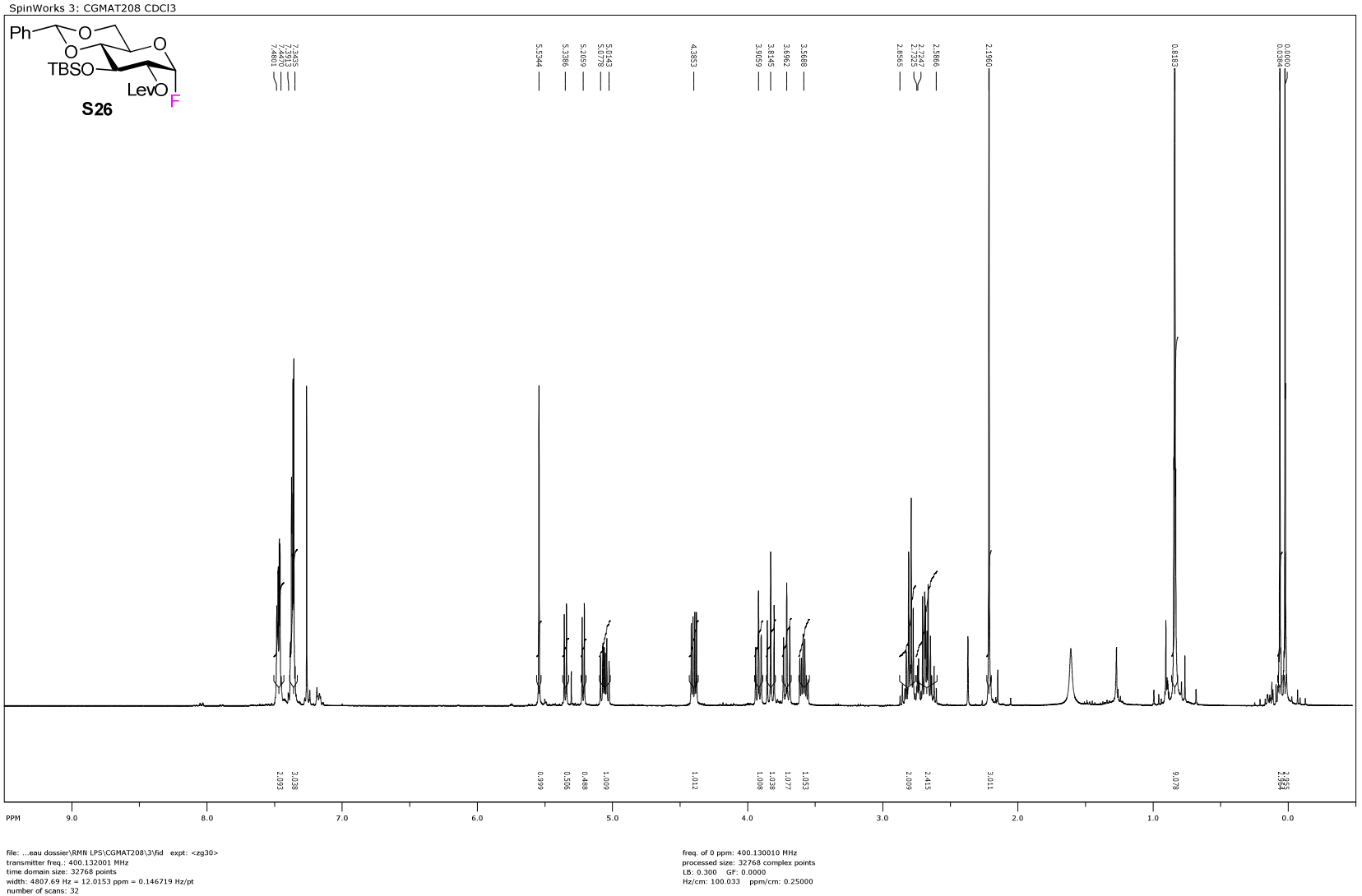
number of scans: 16

freq. of 0 ppm: 400.130014 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

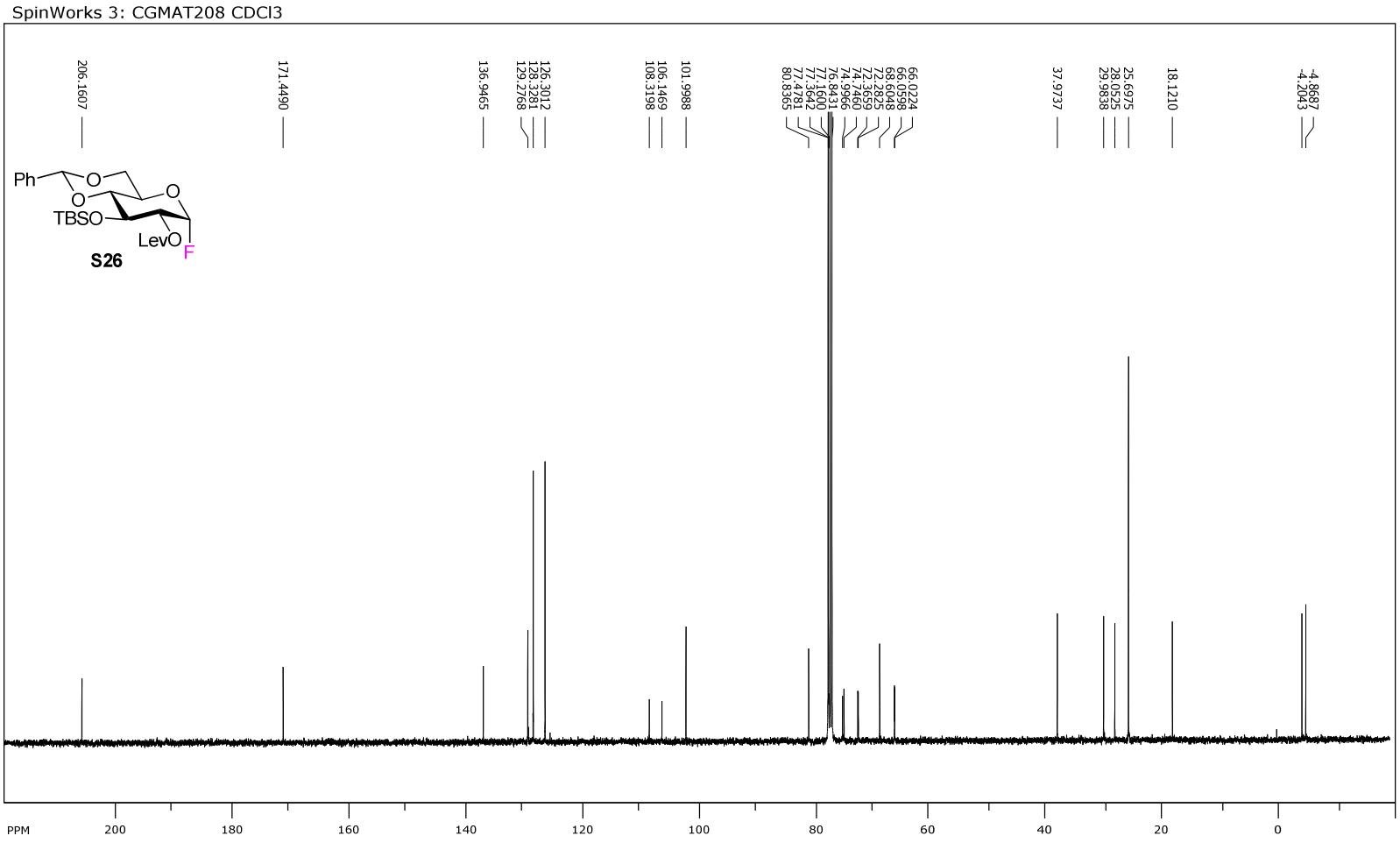
Supplementary Figure 68 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S25.



Supplementary Figure 69 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S26.



Supplementary Figure 70 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S26.



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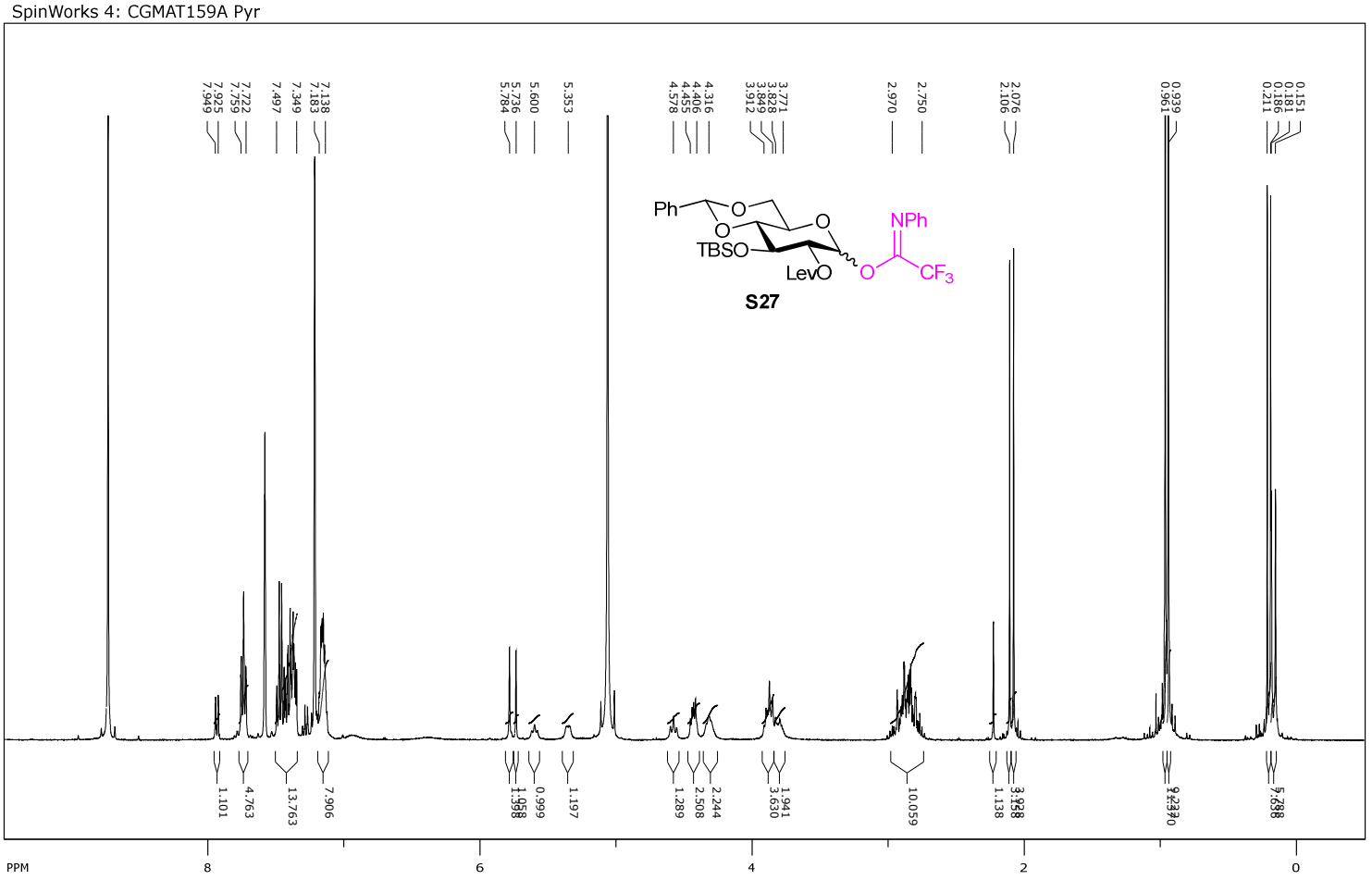
number of scans: 1024

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 961.538 ppm/cm: 9.55587

Supplementary Figure 71 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S27.



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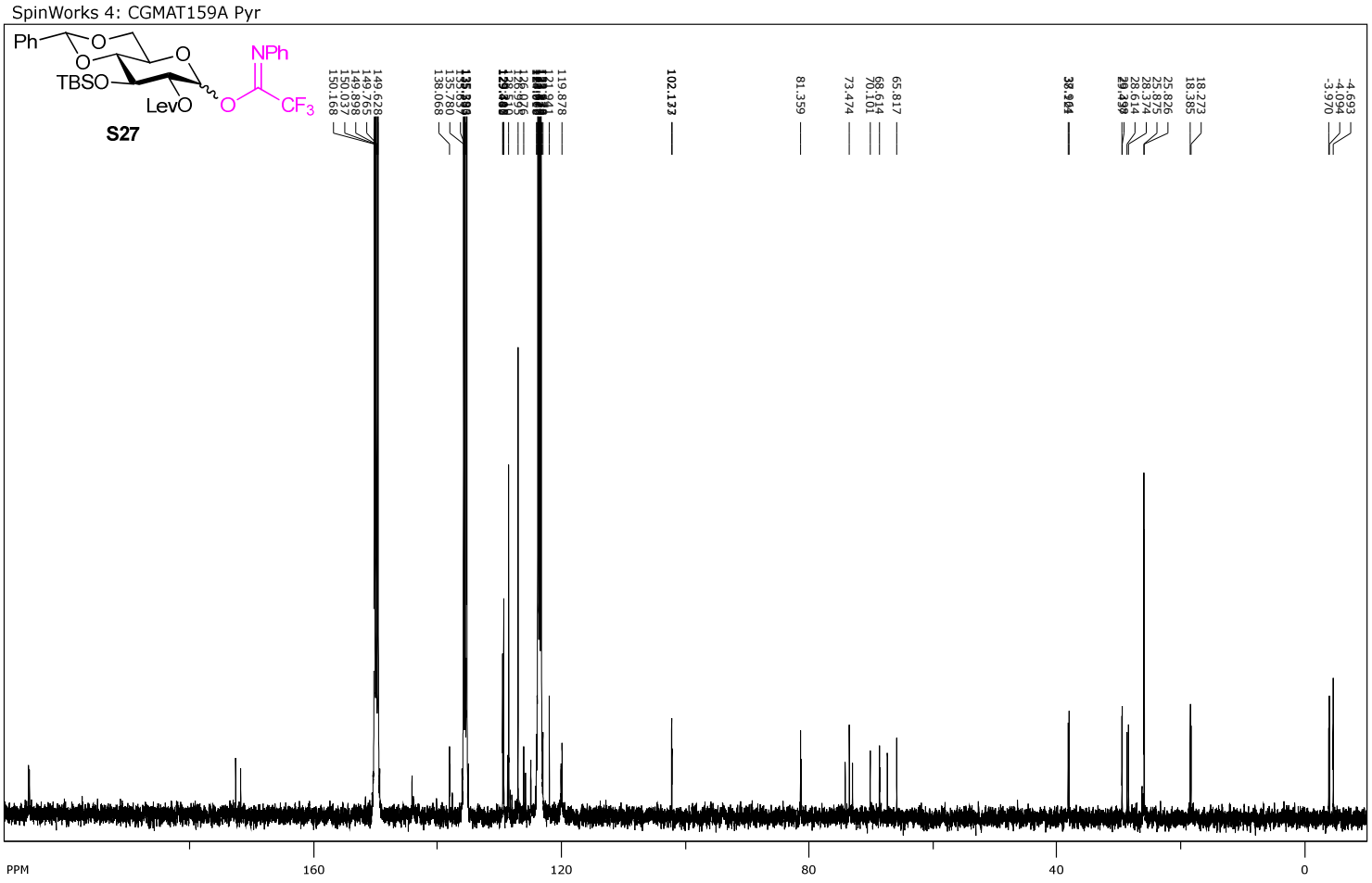
number of scans: 16

freq. of 0 ppm: 400.130593 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

Supplementary Figure 72 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S27.



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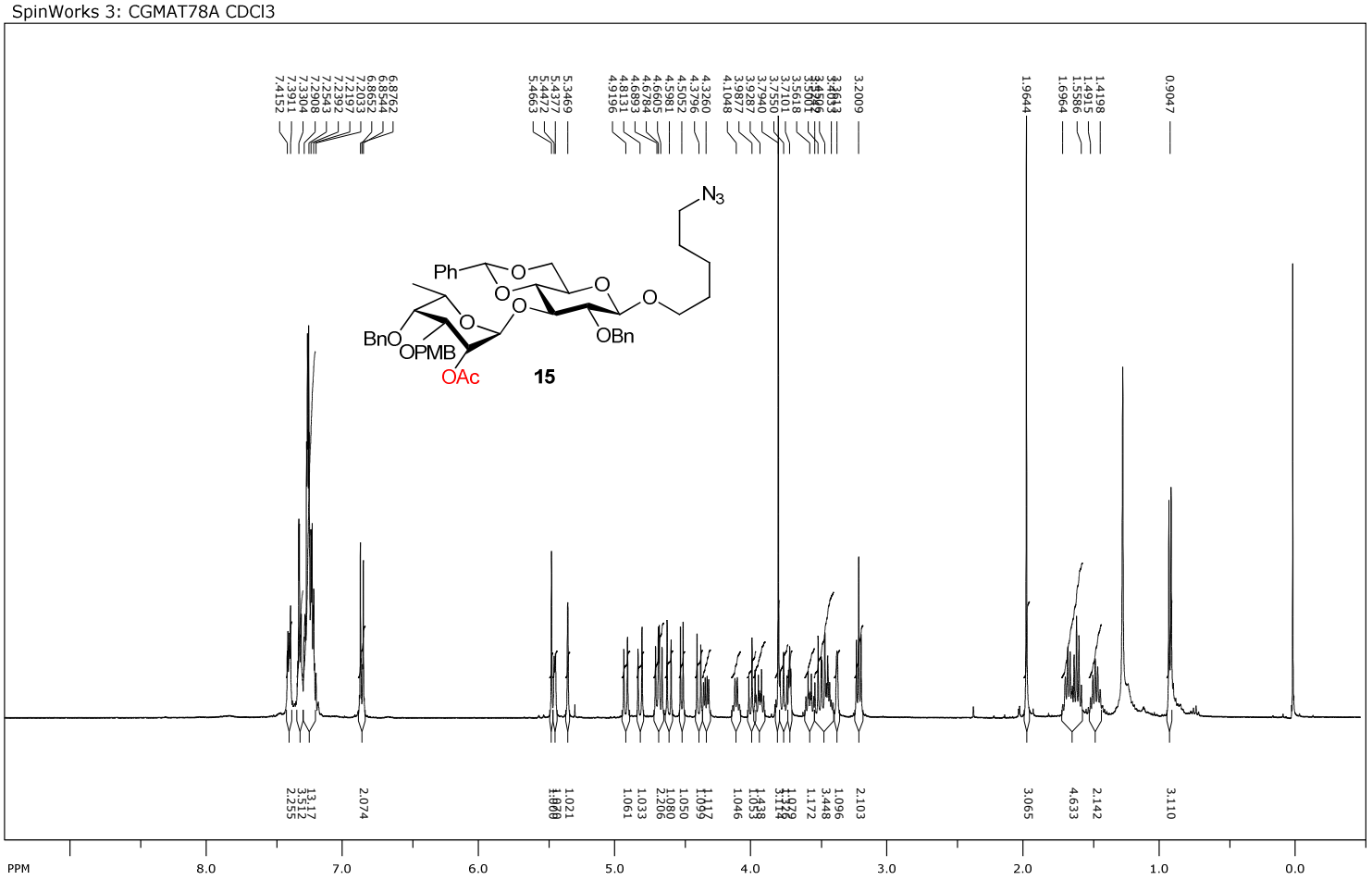
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612894 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

Supplementary Figure 73 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 15.



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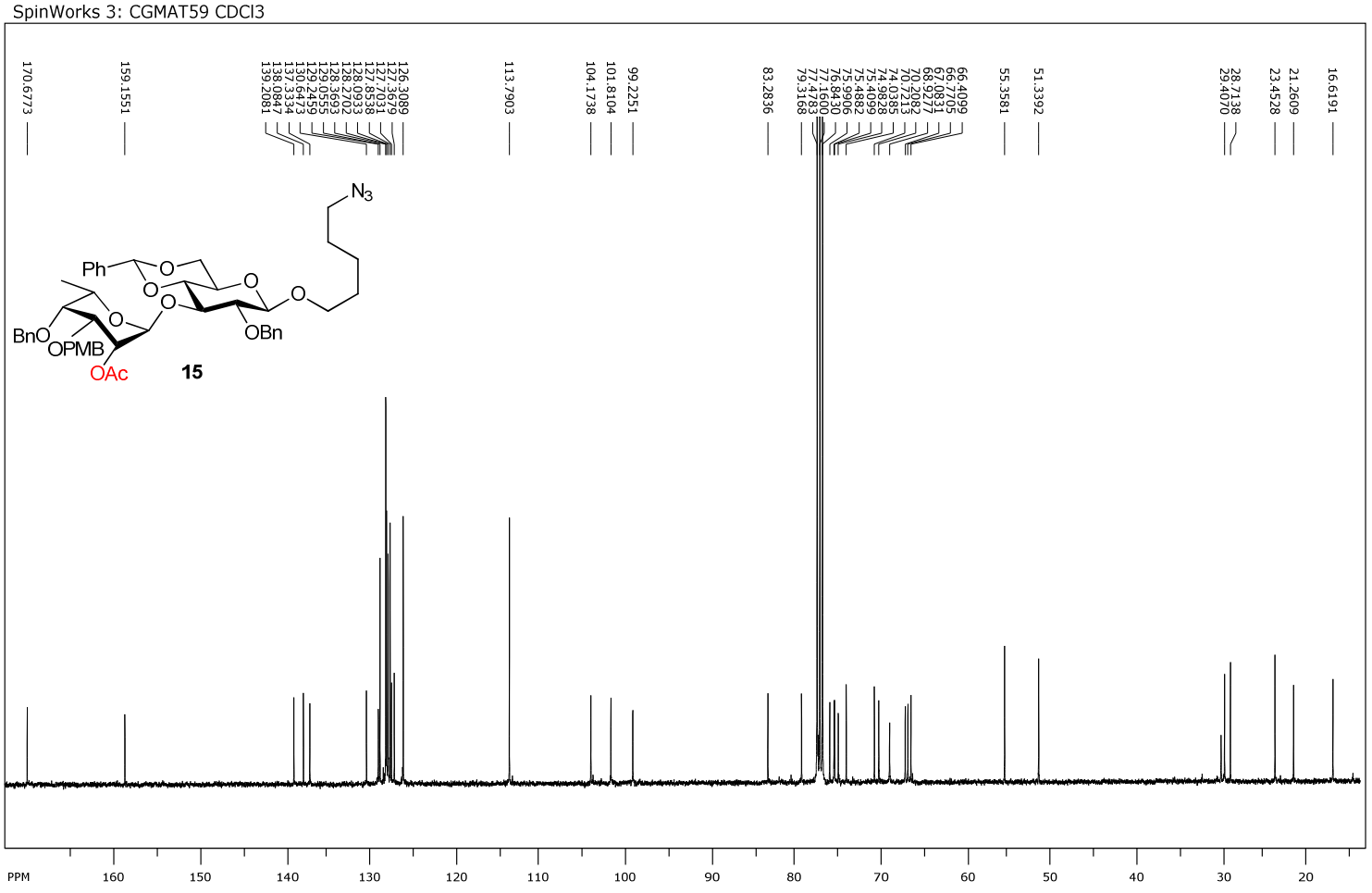
number of scans: 16

freq. of 0 ppm: 400.130012 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 74 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 15.



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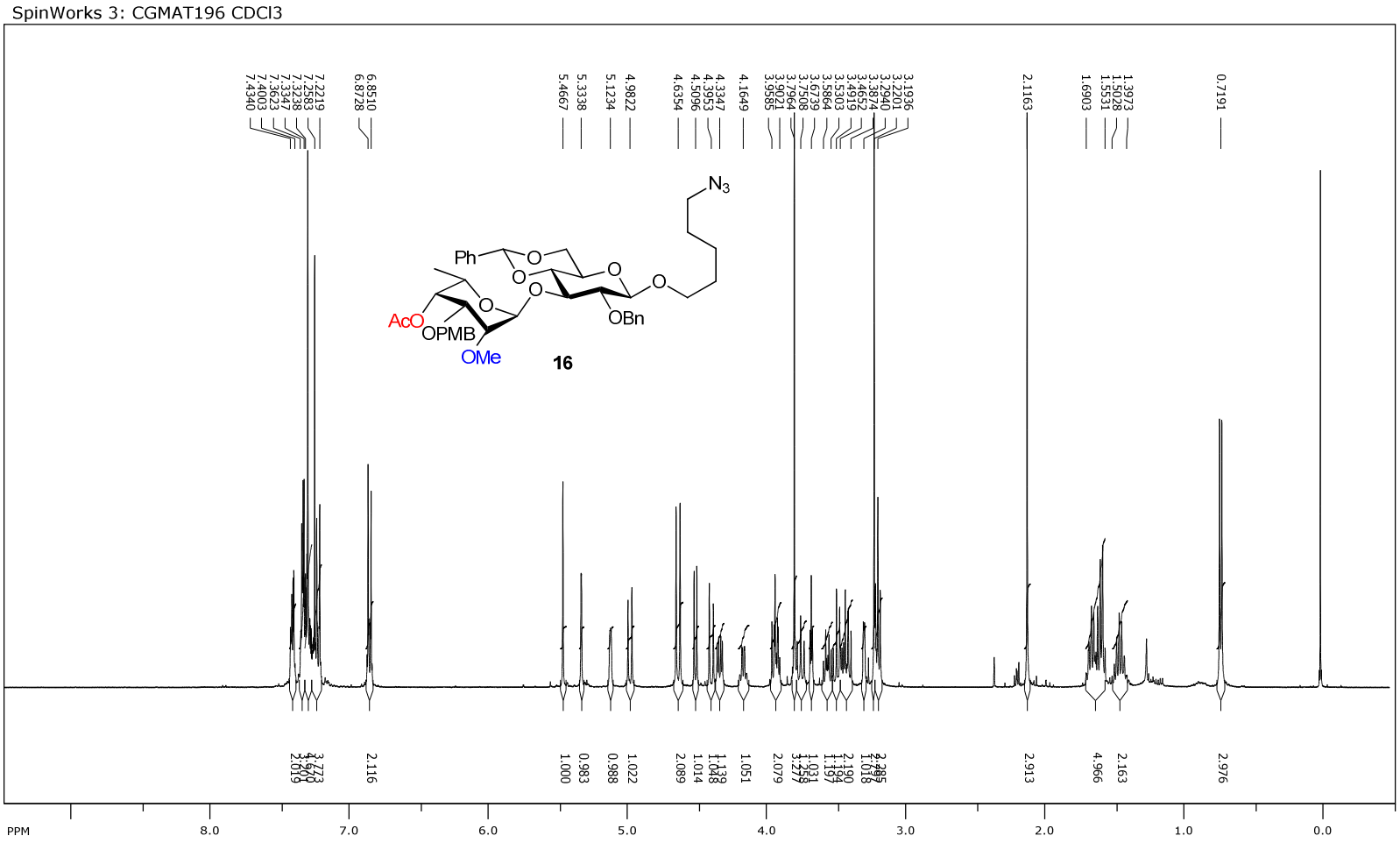
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612759 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 643.567 ppm/cm: 6.39584

Supplementary Figure 75 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 16.



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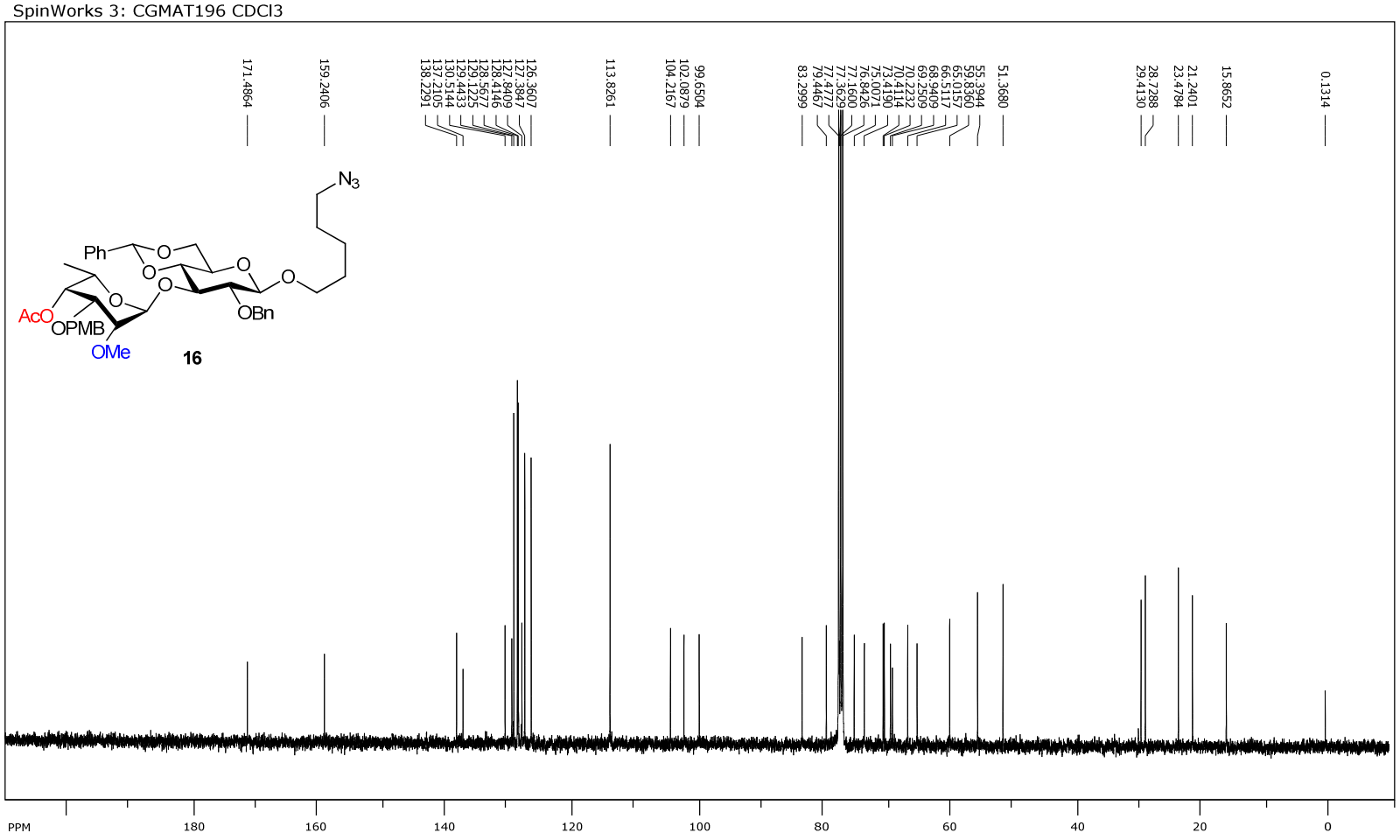
number of scans: 32

freq. of 0 ppm: 400.130010 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 76 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 16.



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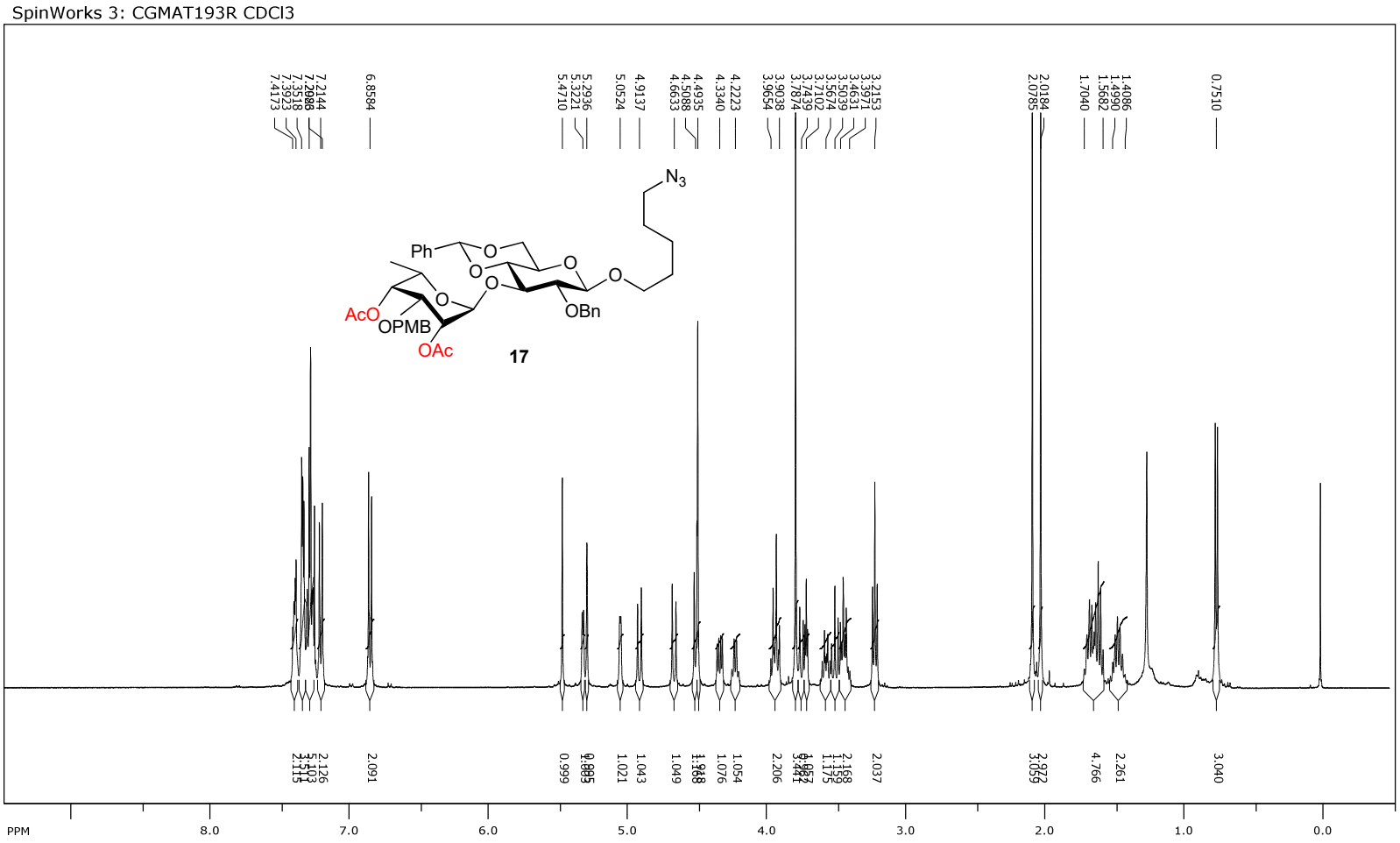
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 77 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 17.



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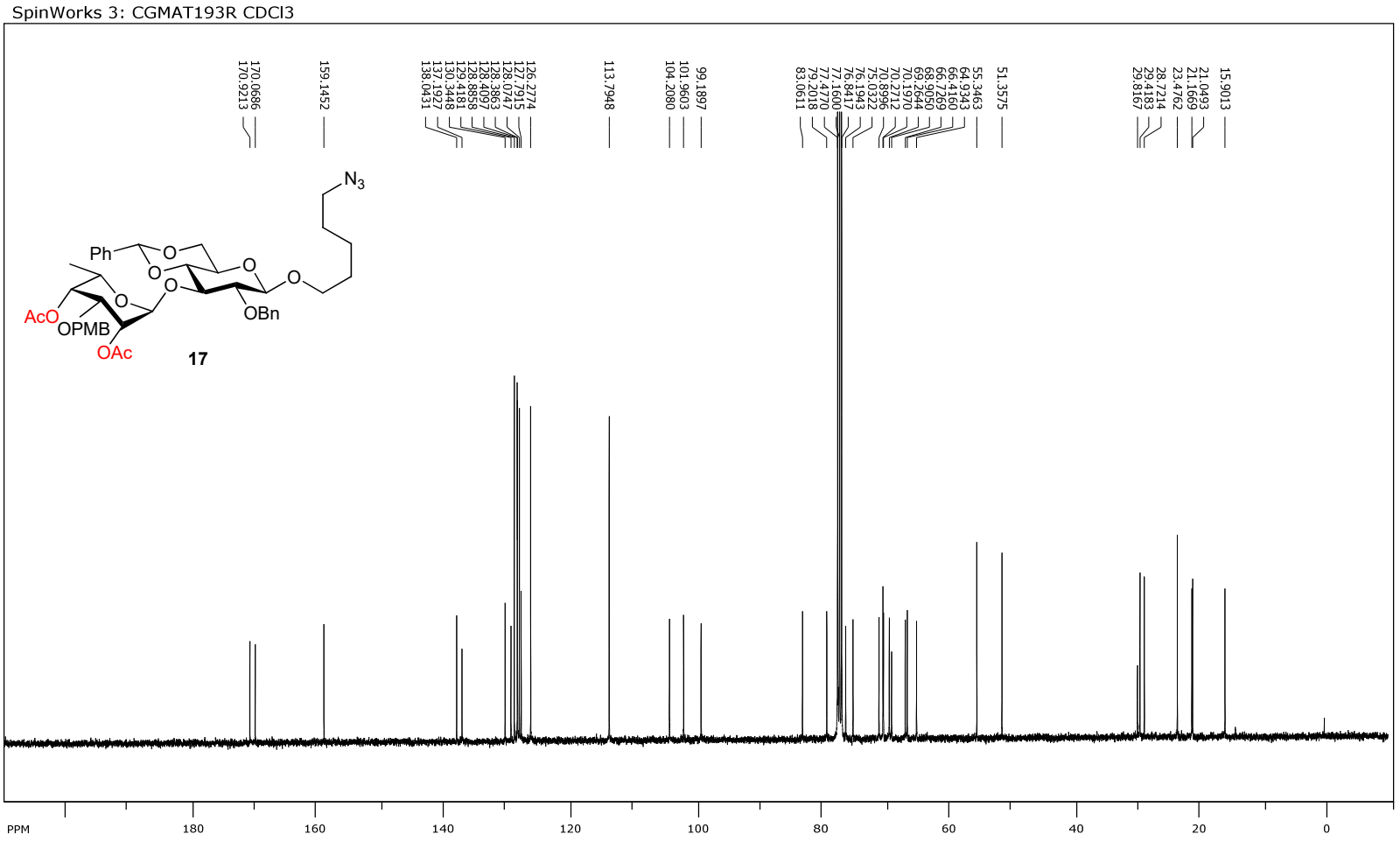
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 16

freq. of 0 ppm: 400.130009 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 78 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 17.



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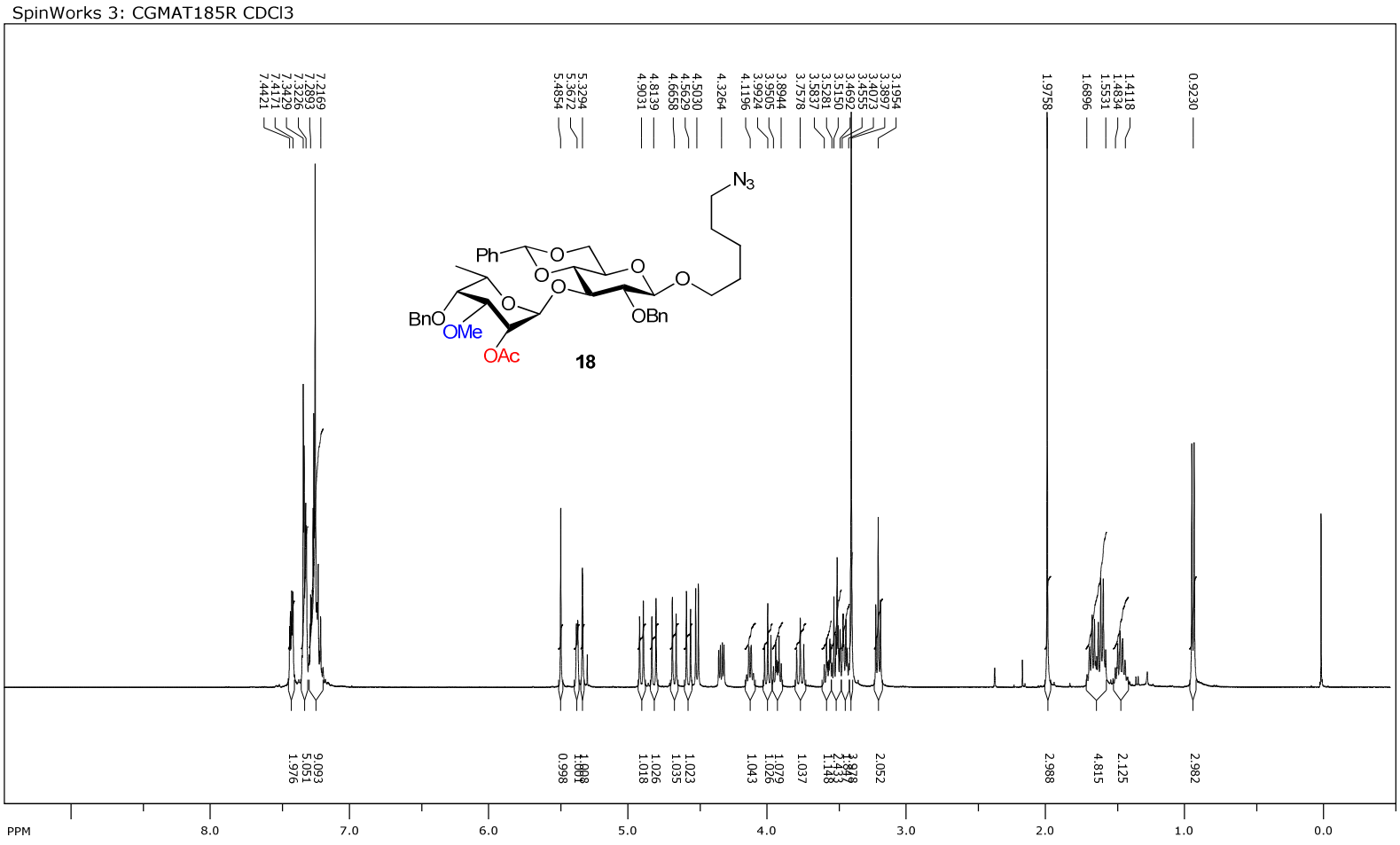
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612757 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 79 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 18.



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time domain size: 32768 points
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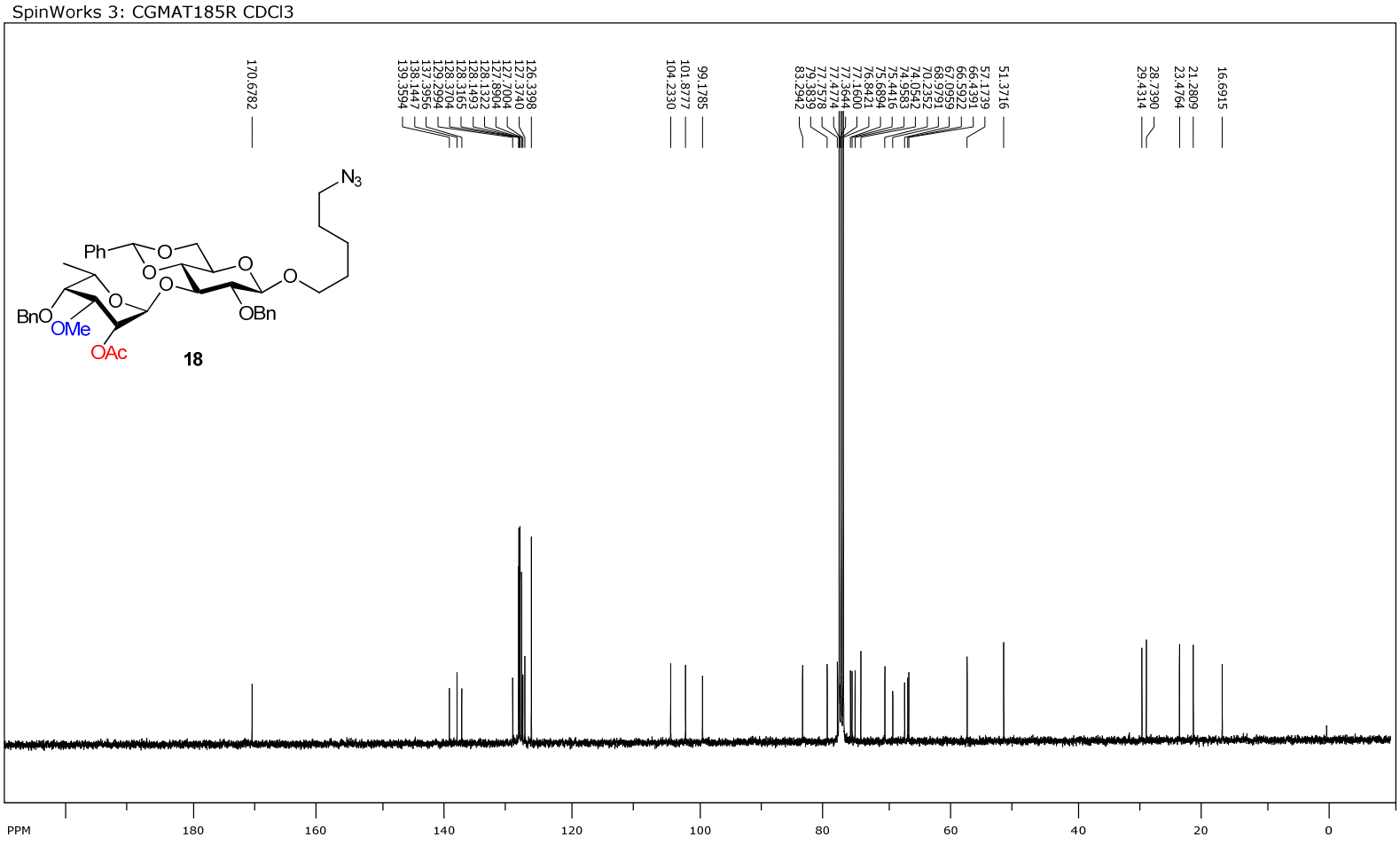
number of scans: 32

freq. of 0 ppm: 400.130010 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

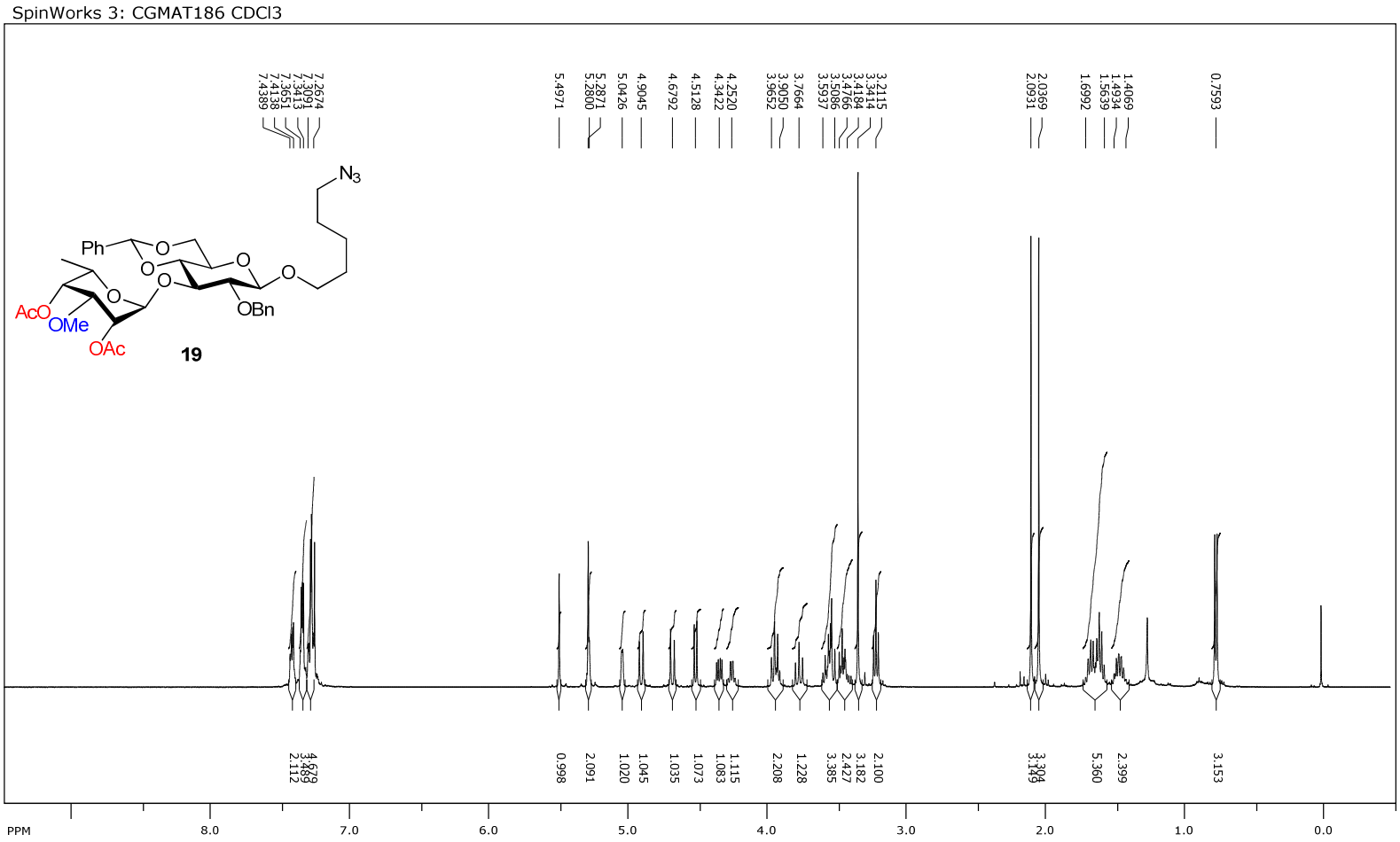
Supplementary Figure 80 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 18.



file: ...au dossier\RMN LPS\CGMAT185R\3\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

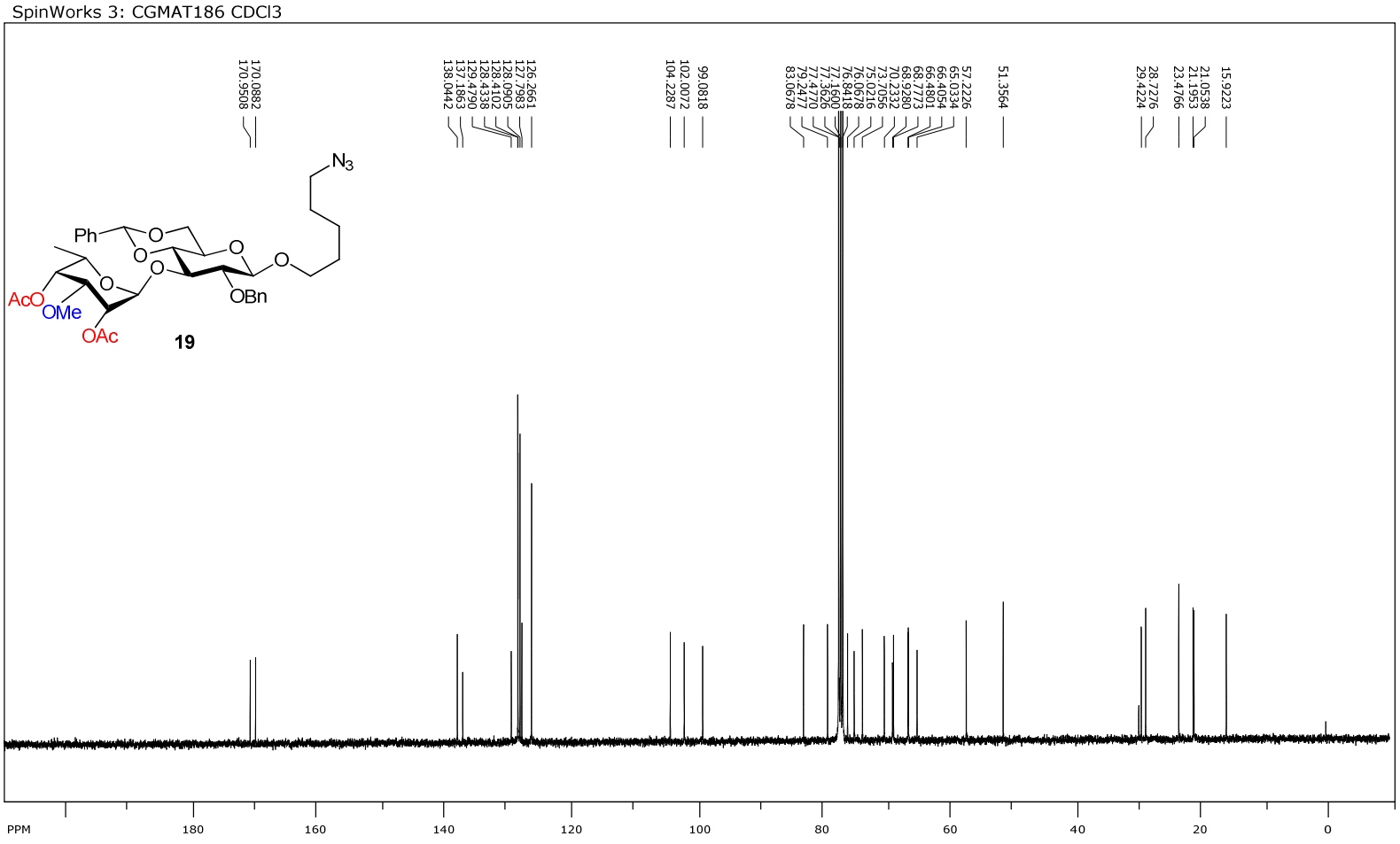
Supplementary Figure 81 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 19.



file: ...eau dossier\RMN LPS\CGMAT186\1\fid expt: <zg30>
transmitter freq.: 400.132001 MHz
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 16

freq. of 0 ppm: 400.130009 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

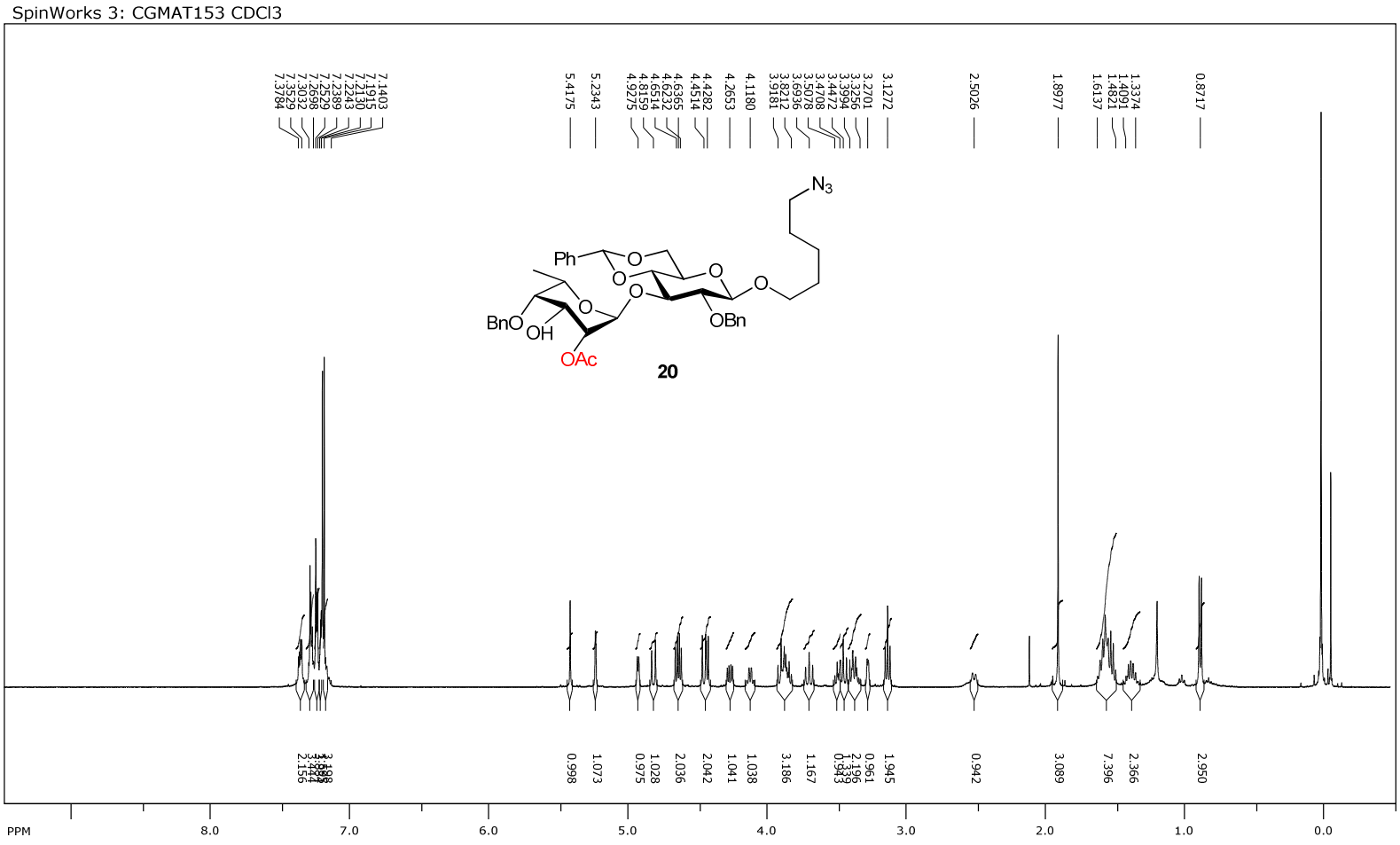
Supplementary Figure 82 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 19.



file: ...eau dossier\RMN LPS\CGMAT186\4\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612757 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 83 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 20.



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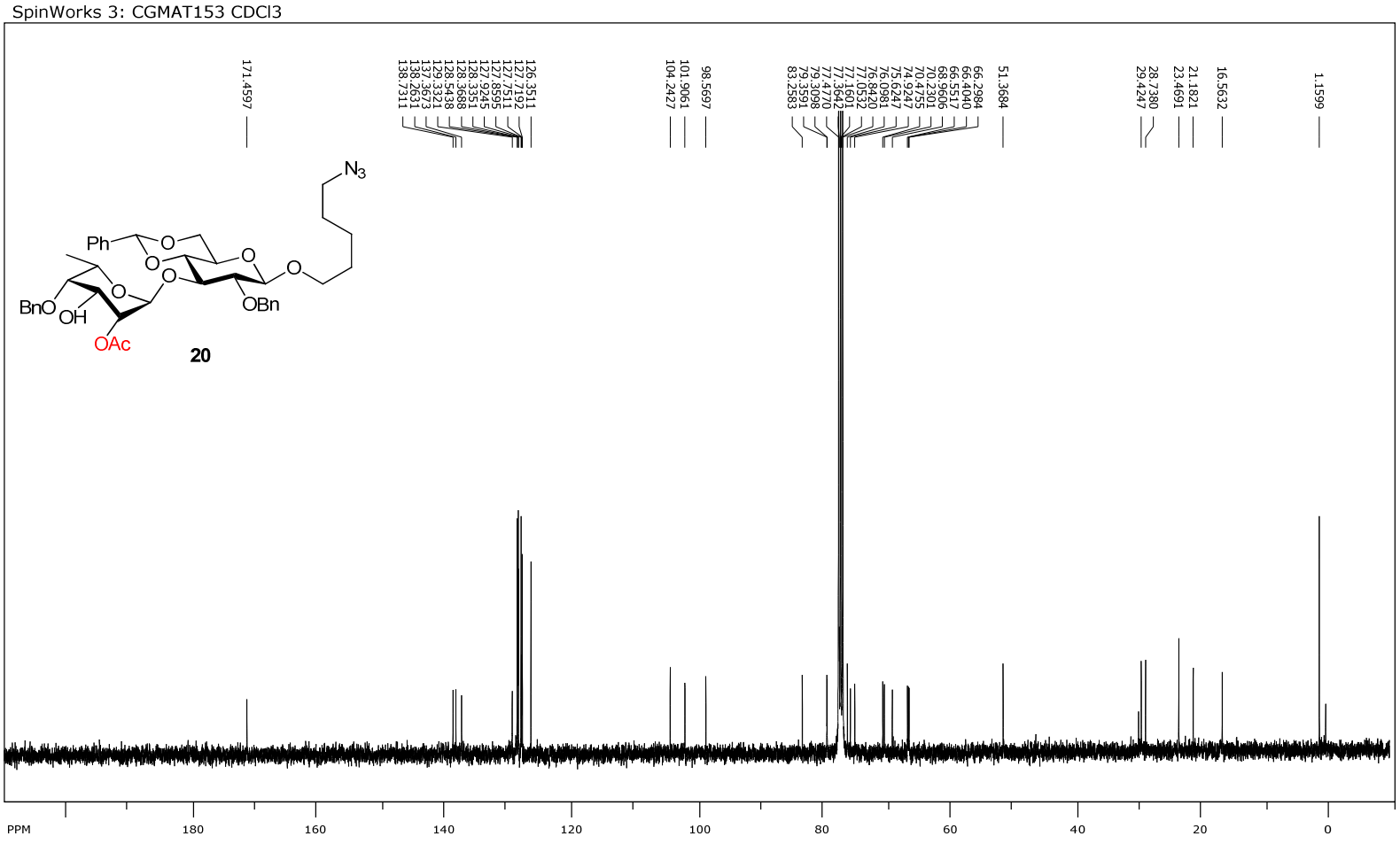
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130038 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 84 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 20.



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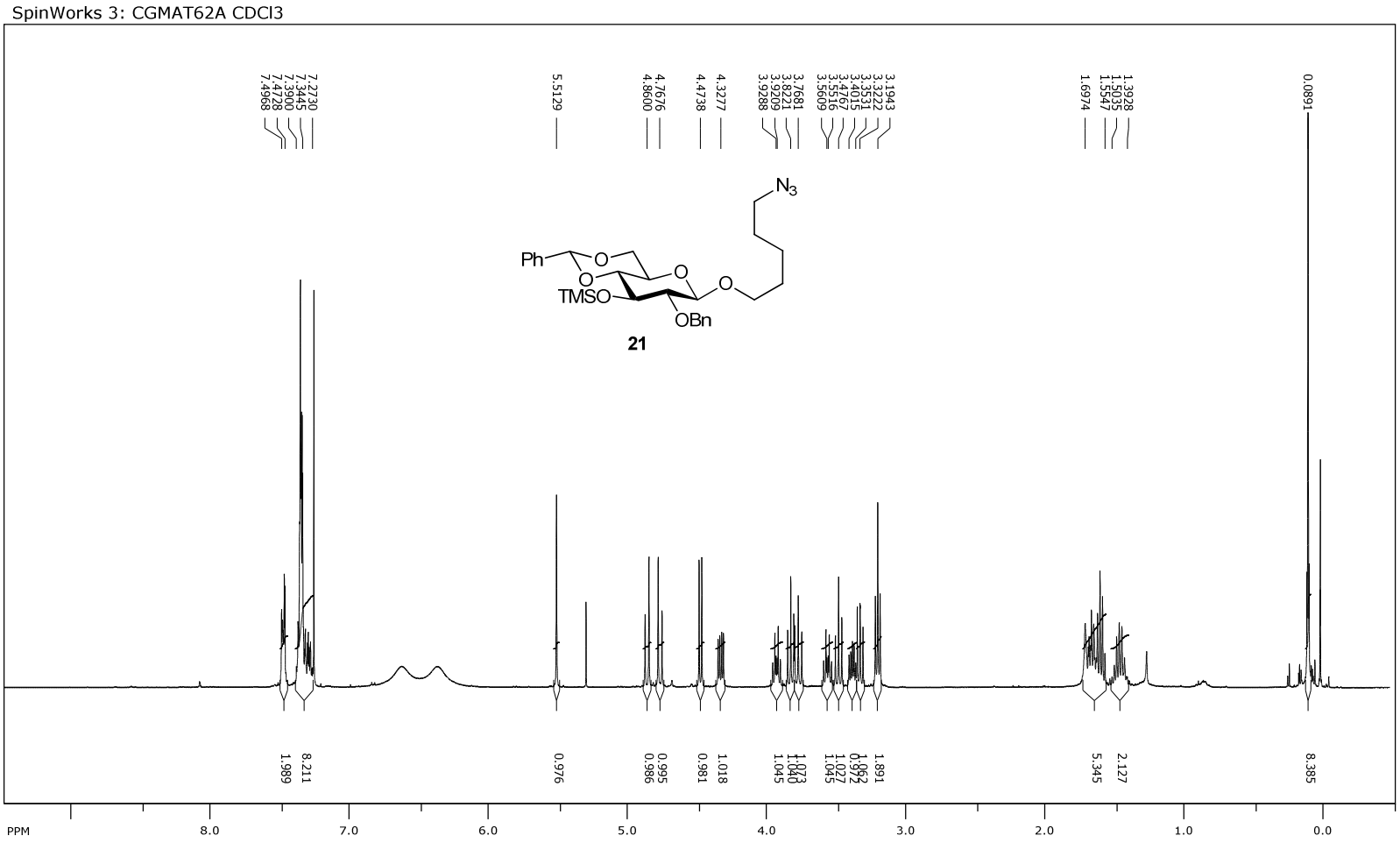
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 85 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 21.



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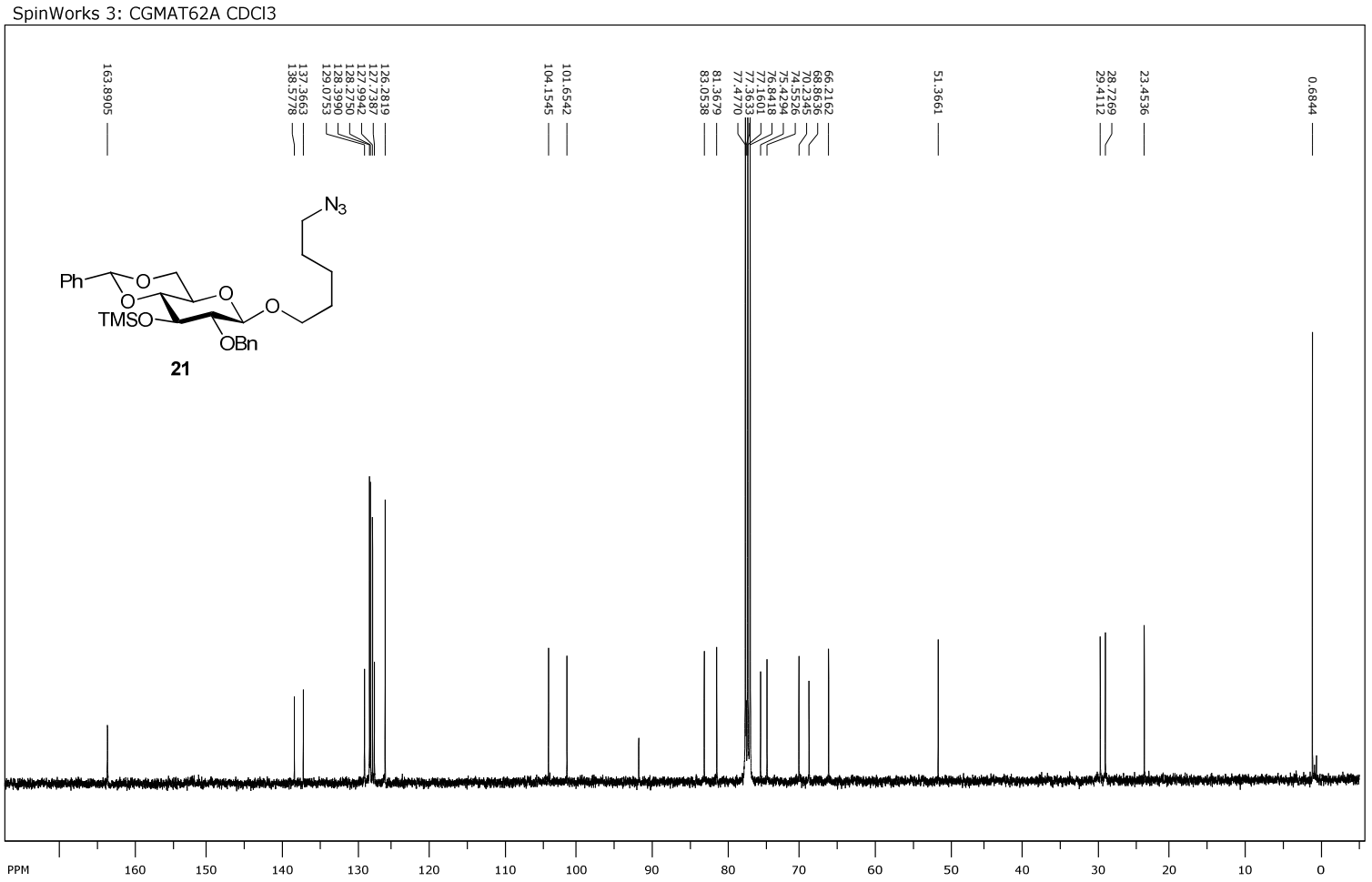
number of scans: 64

freq. of 0 ppm: 400.130008 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 86 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 21.



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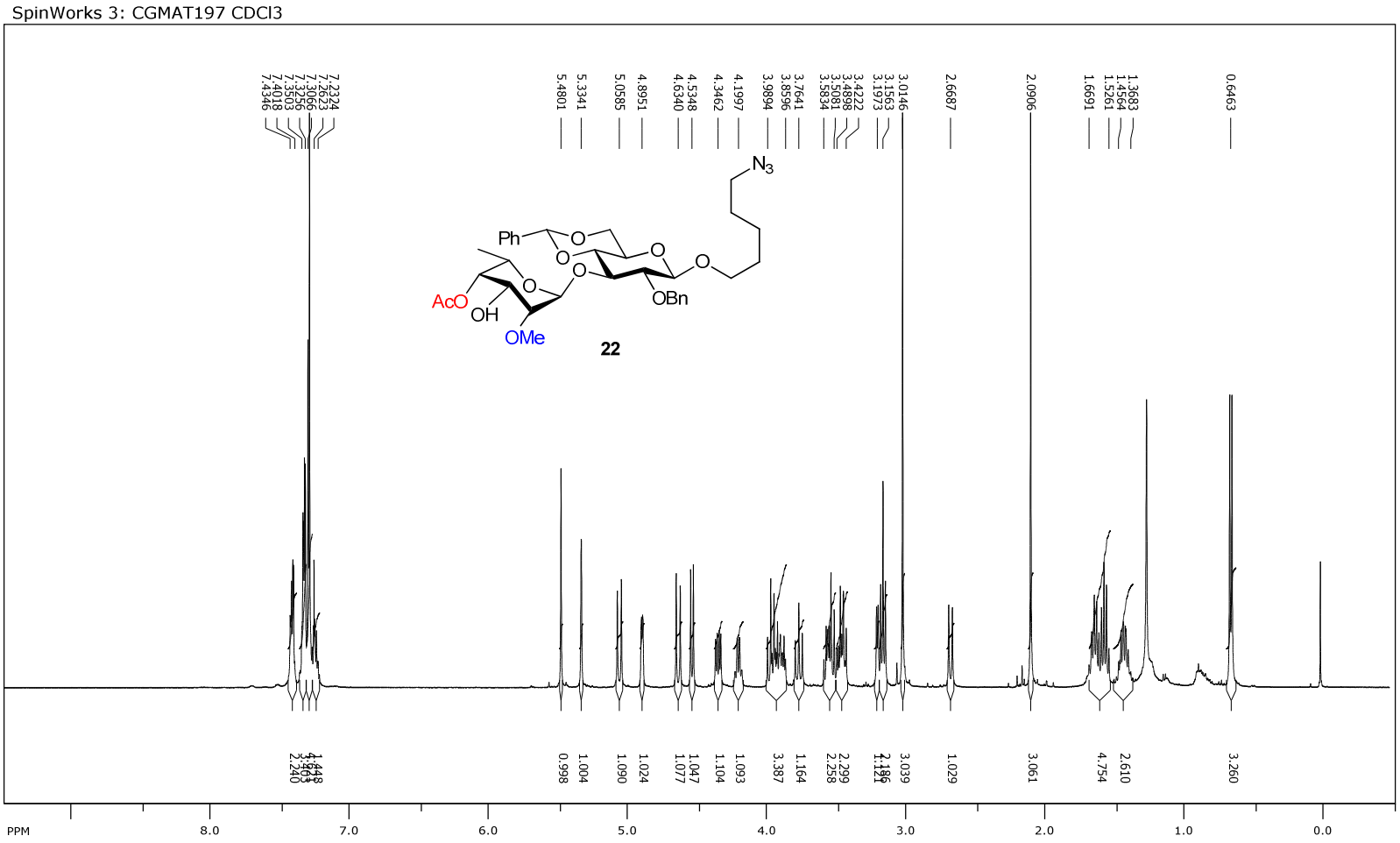
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612757 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 738.455 ppm/cm: 7.33884

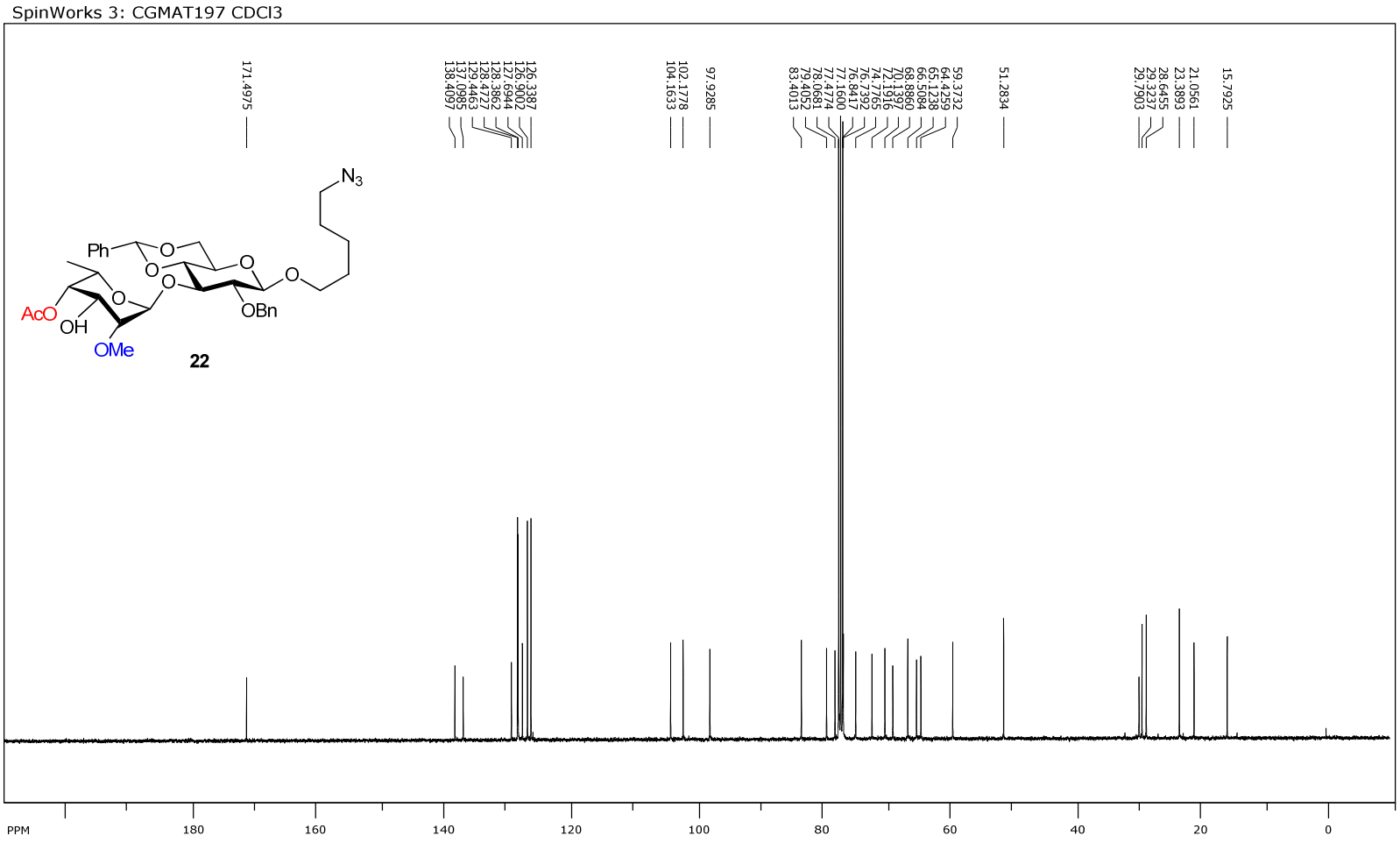
Supplementary Figure 87 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 22.



file: ...eau dossier\RMN LPS\CGMAT197\1\fid expt: <zg30>
transmitter freq.: 400.132001 MHz
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 16

freq. of 0 ppm: 400.130007 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 88 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 22.



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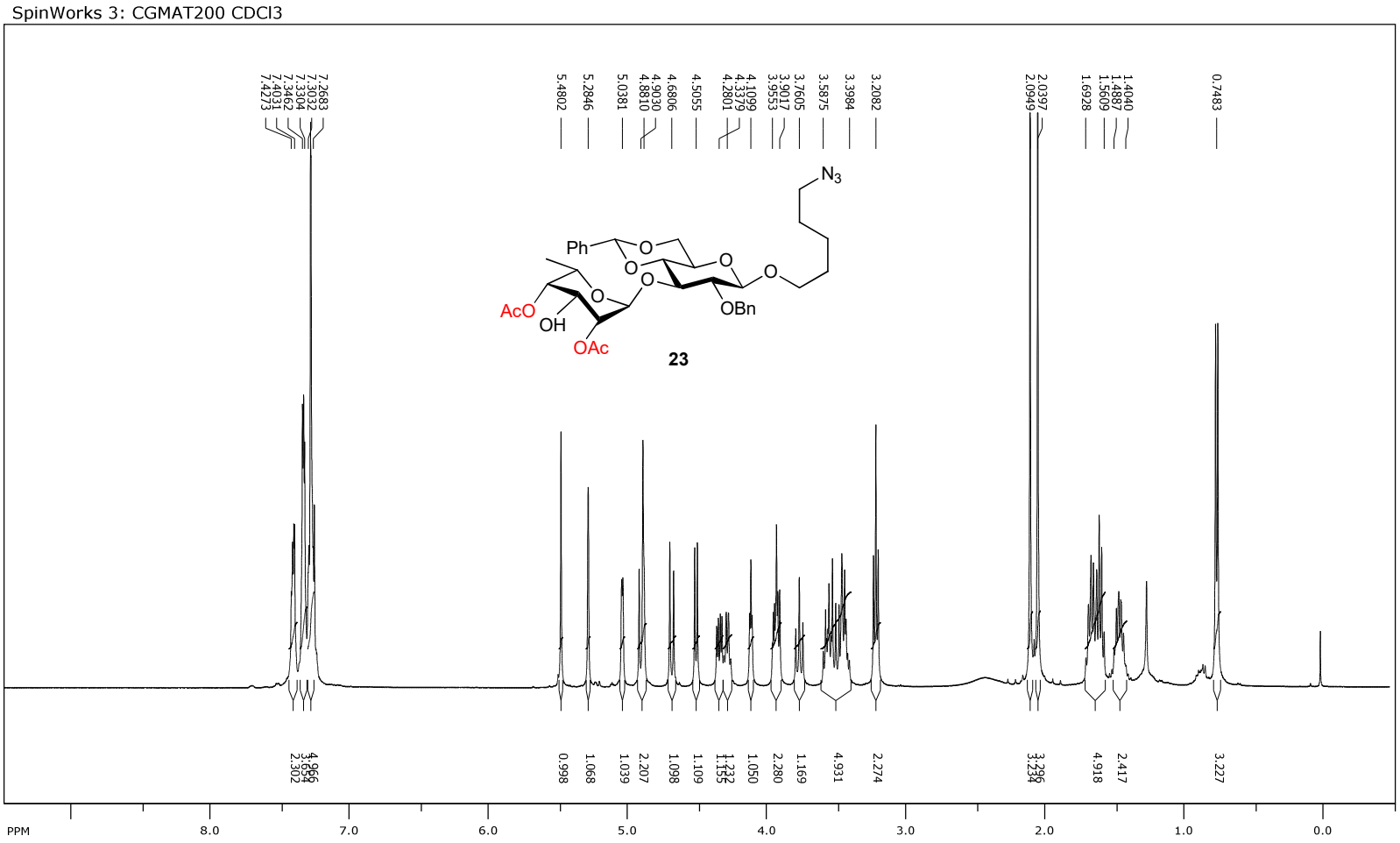
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612759 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 89 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 23.



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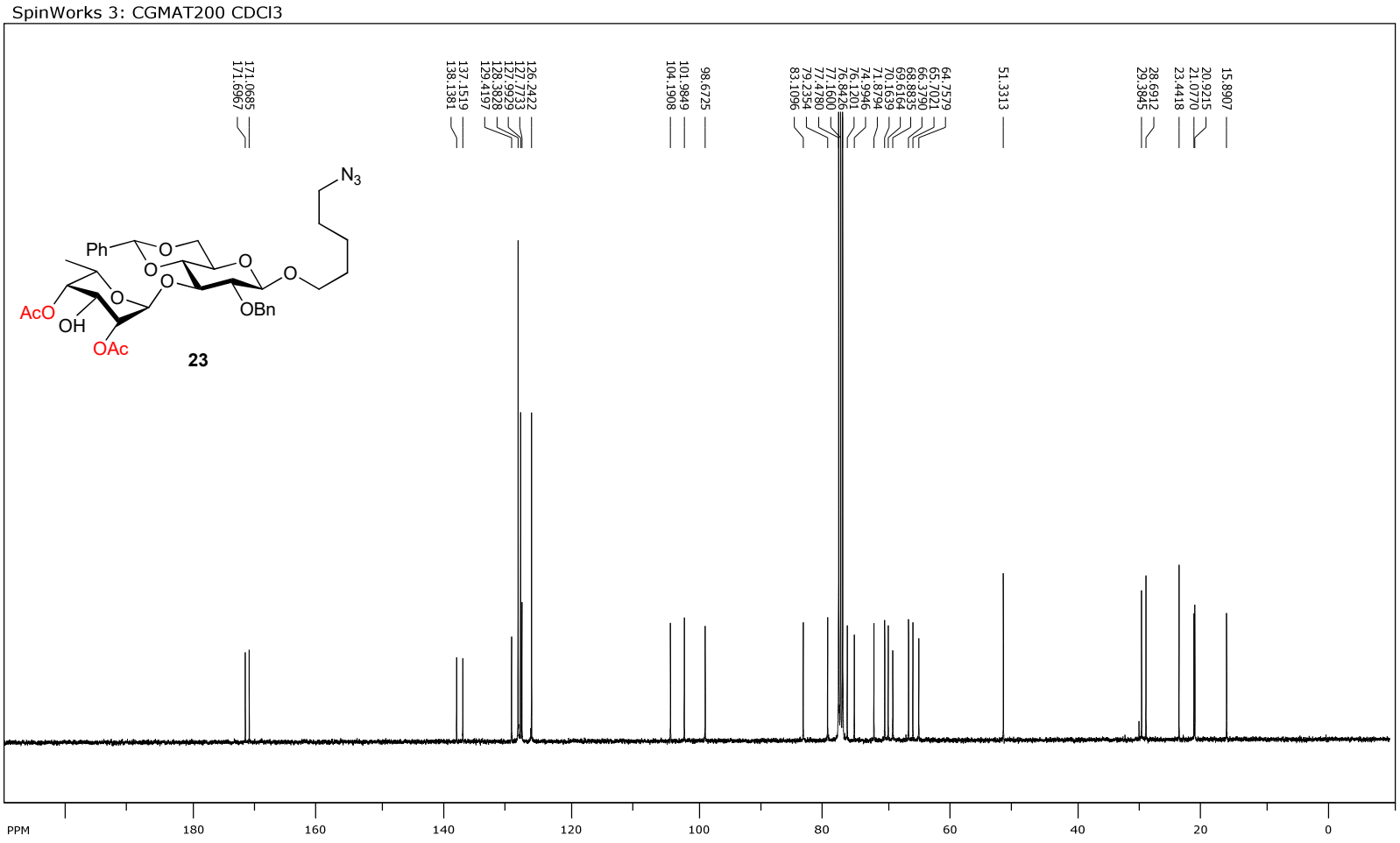
transmitter freq.: 400.132001 MHz
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130009 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 90 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 23.



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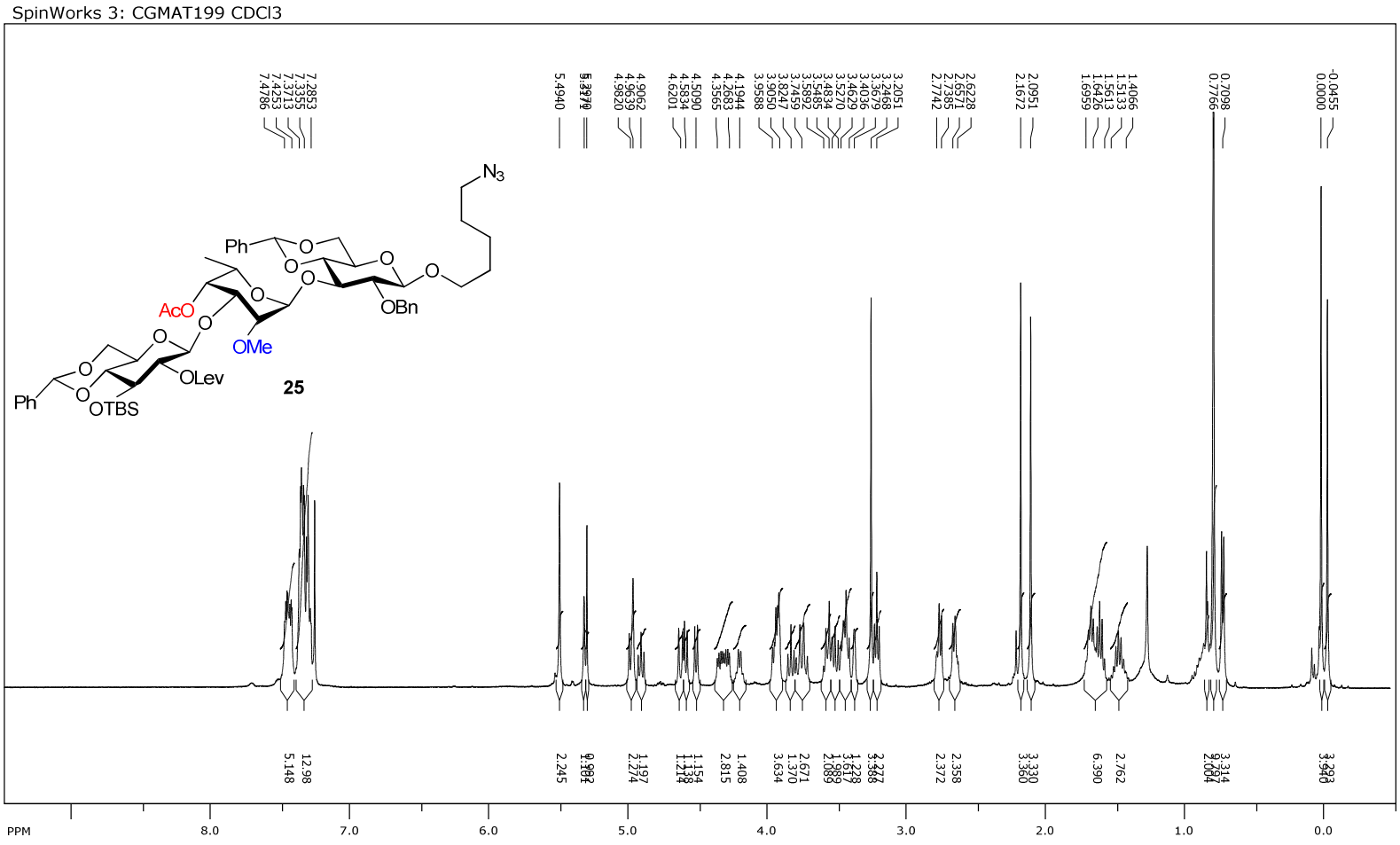
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612759 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

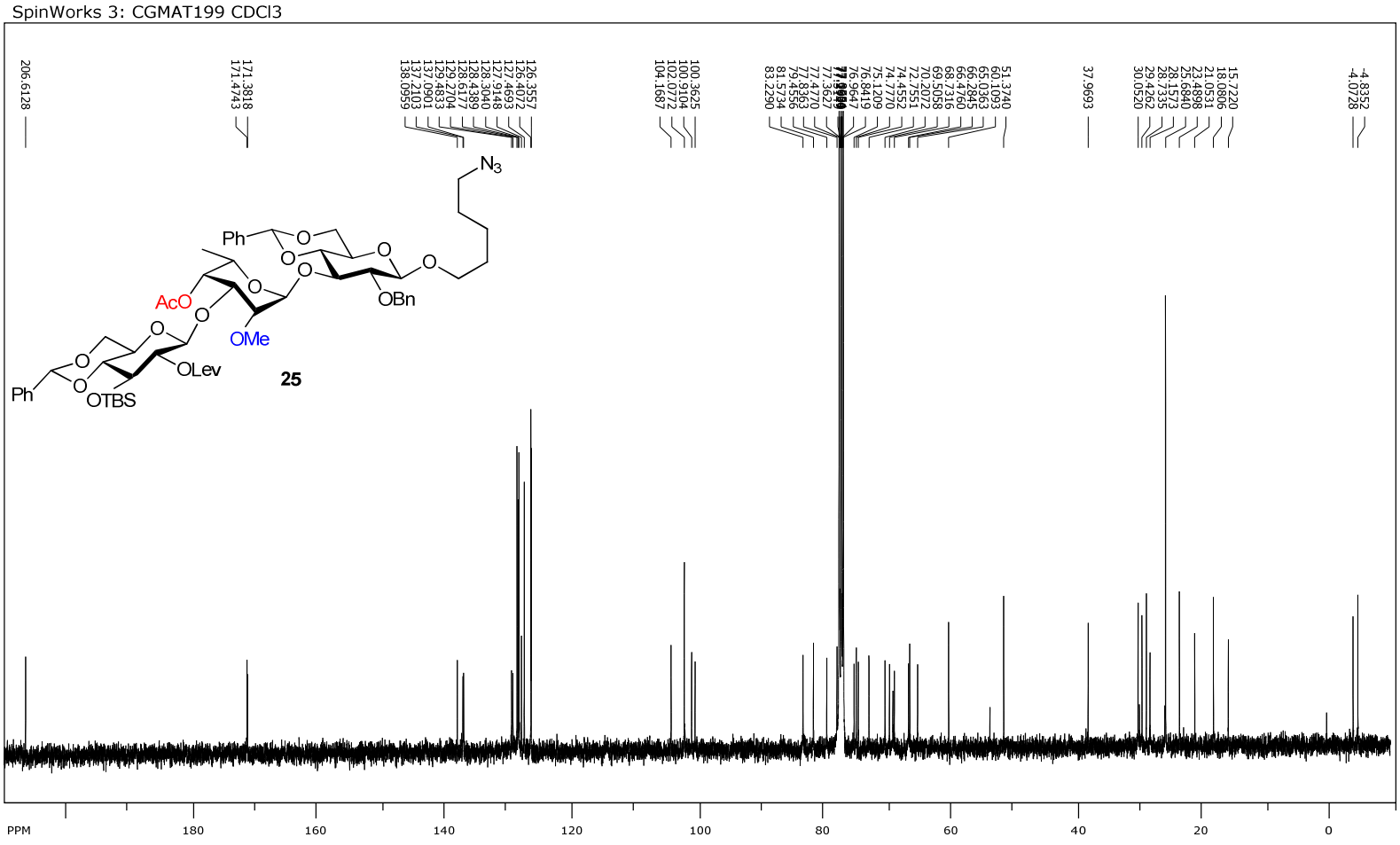
Supplementary Figure 91 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 25.



file: ...eau dossier\RMN LPS\CGMAT199\1\fid expt: <zg30>
transmitter freq.: 400.132001 MHz
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 16

freq. of 0 ppm: 400.130009 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

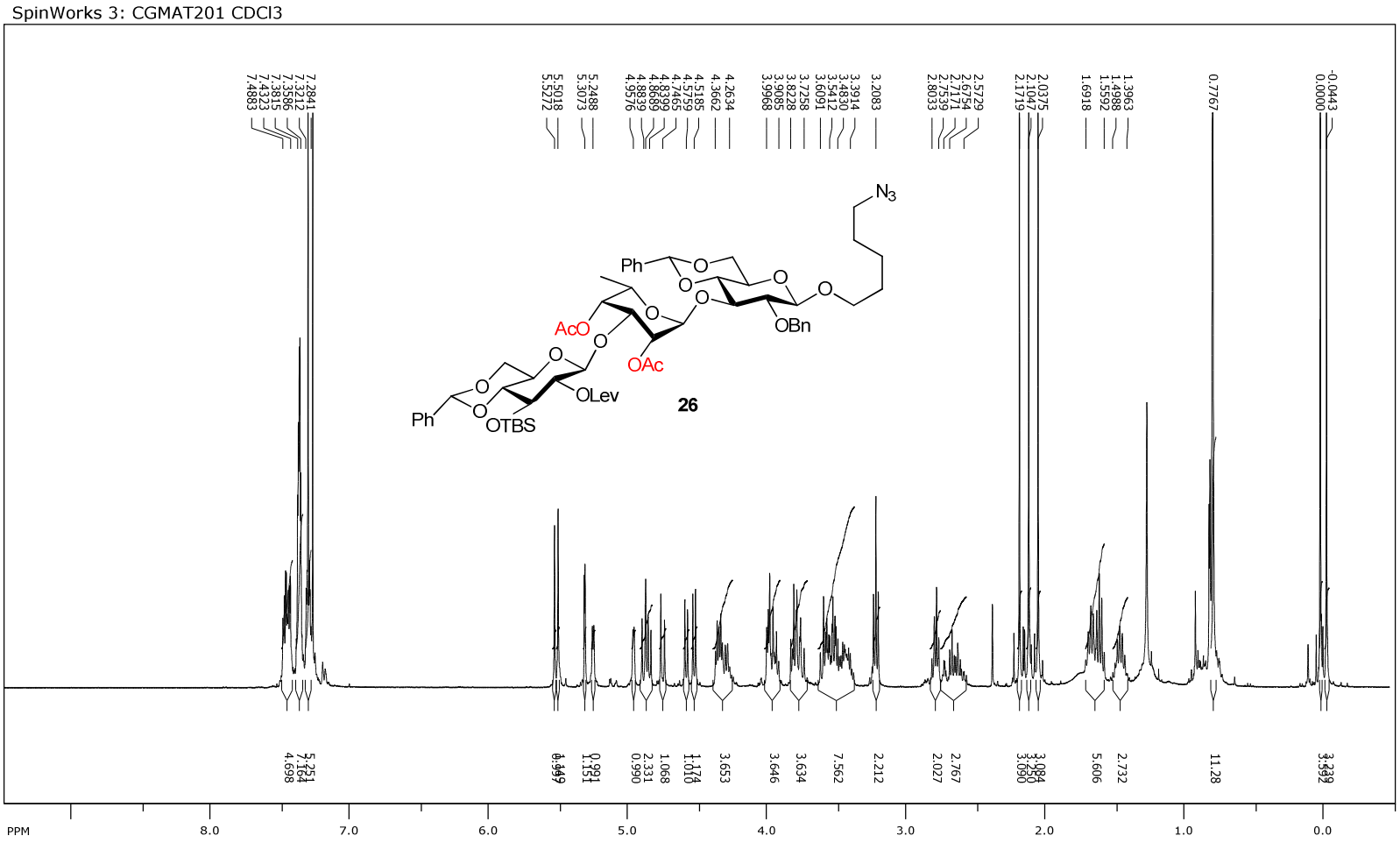
Supplementary Figure 92 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 25.



file: ...eau dossier\RMN LPS\CGMAT199\4\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

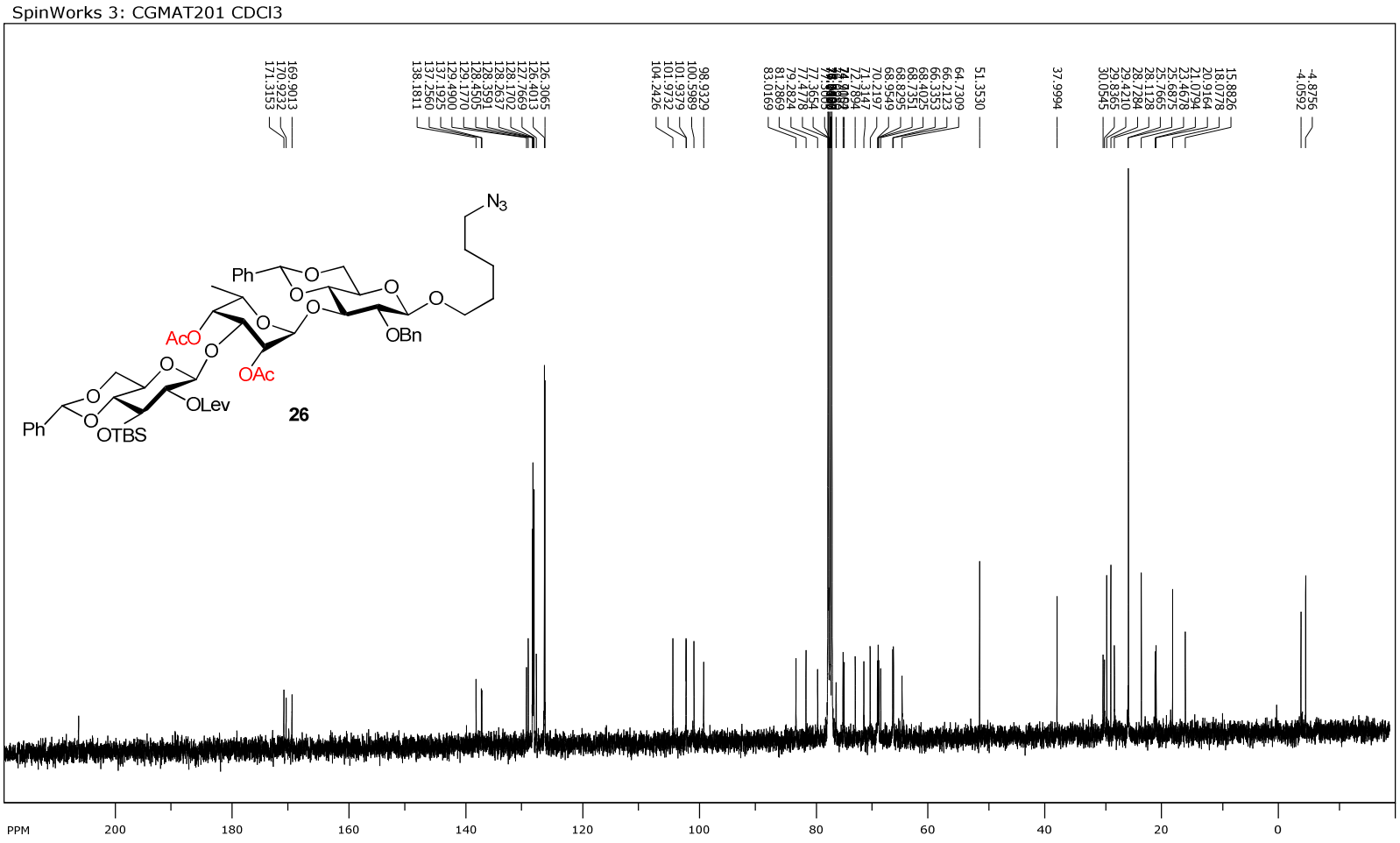
Supplementary Figure 93 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 26.



file: ...eau dossier\RMN LPS\CGMAT201\1\fid expt: <zg30>
transmitter freq.: 400.132001 MHz
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130006 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

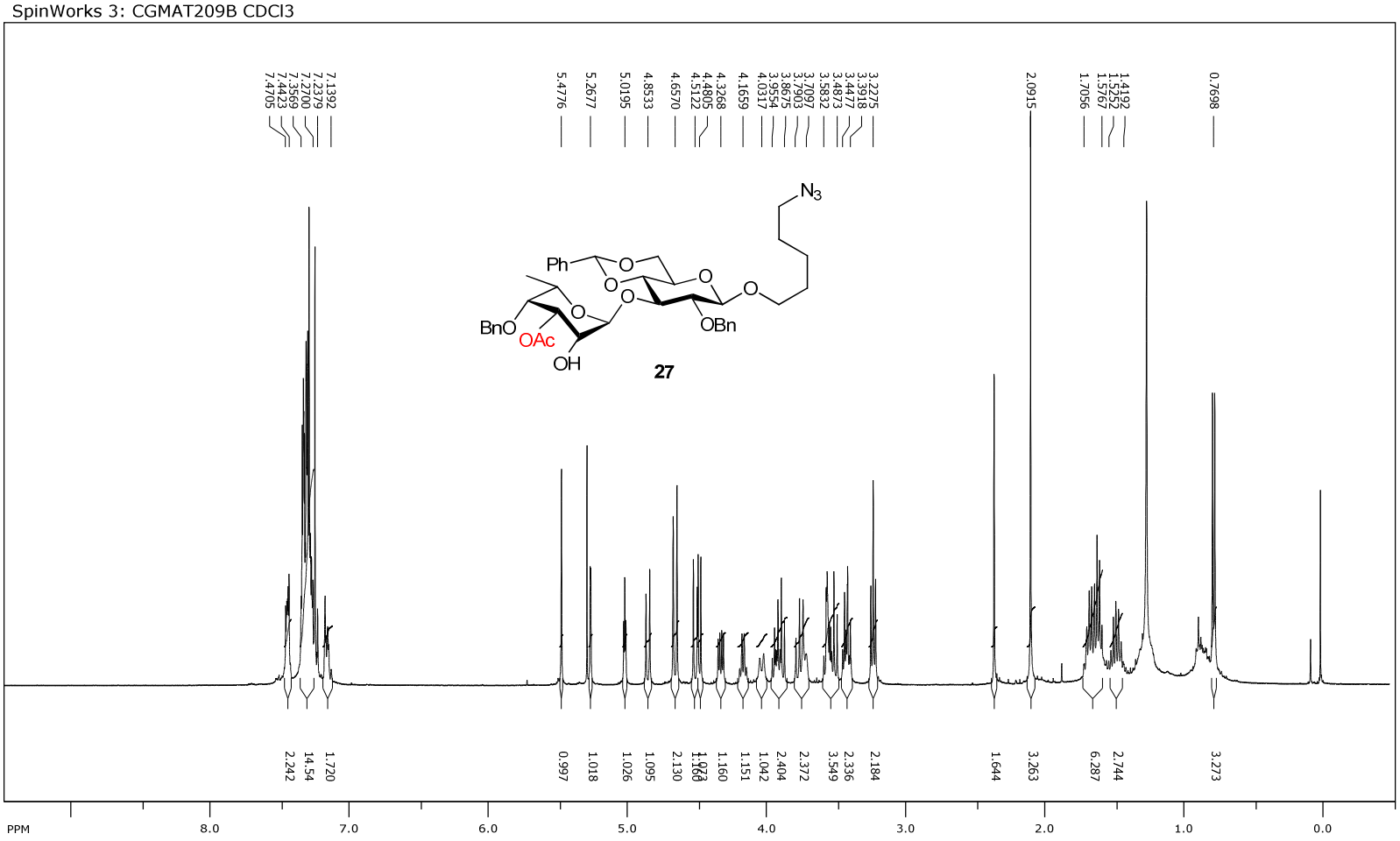
Supplementary Figure 94 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 26.



file: ...eau dossier\RMN LPS\CGMAT201\3\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612756 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 961.538 ppm/cm: 9.55587

Supplementary Figure 95 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 27.



file: ...au dossier\RMN LPS\CGMAT209B\1\fid expt: <zg30>
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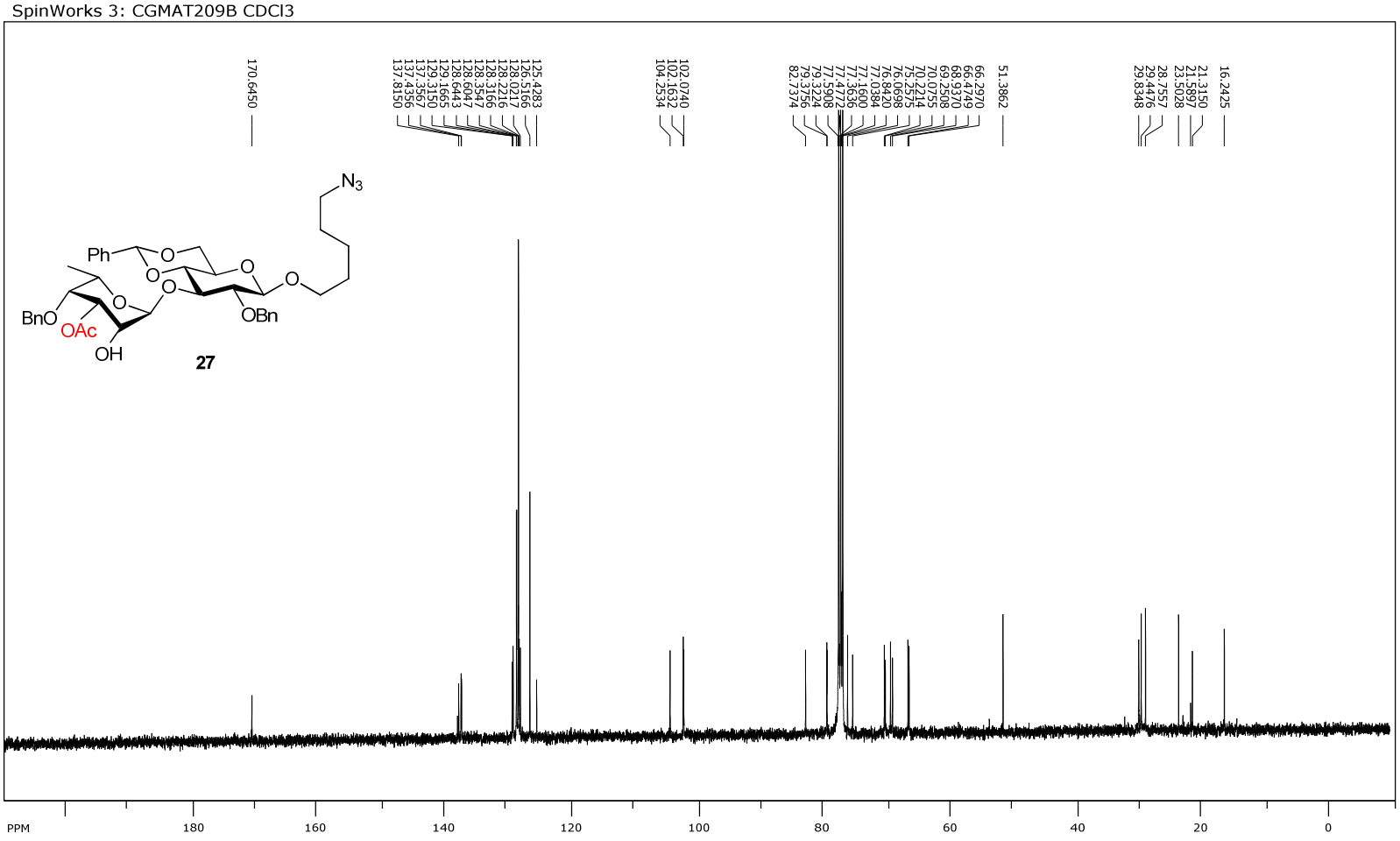
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130011 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

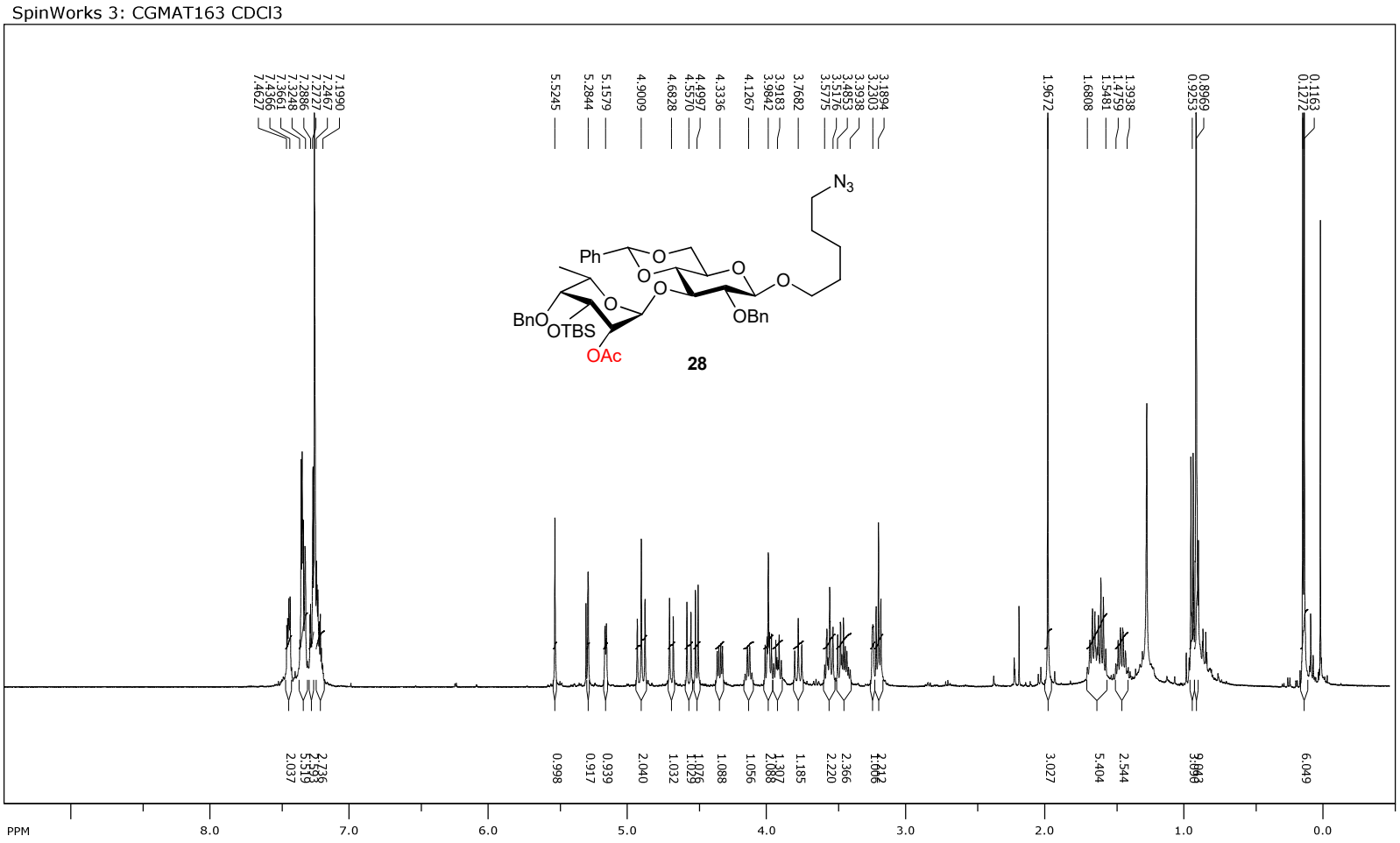
Supplementary Figure 96 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 27.



file: ...au dossier\RMN LPS\CGMAT209B\4\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612756 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

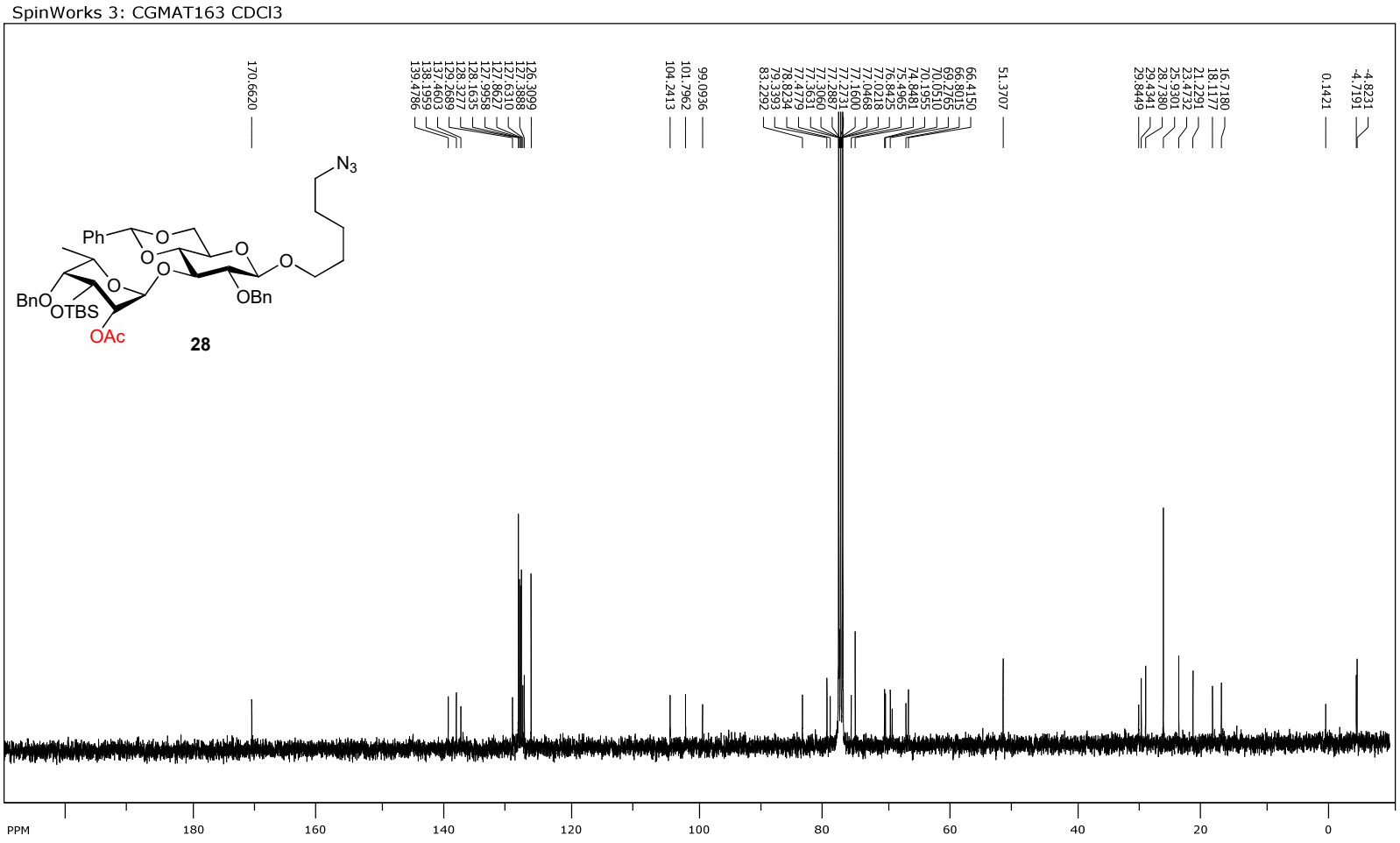
Supplementary Figure 97 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 28.



file: ...eau dossier\RMN LPS\CGMAT163\1\fid expt: <zg30>
transmitter freq.: 400.132001 MHz
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130010 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

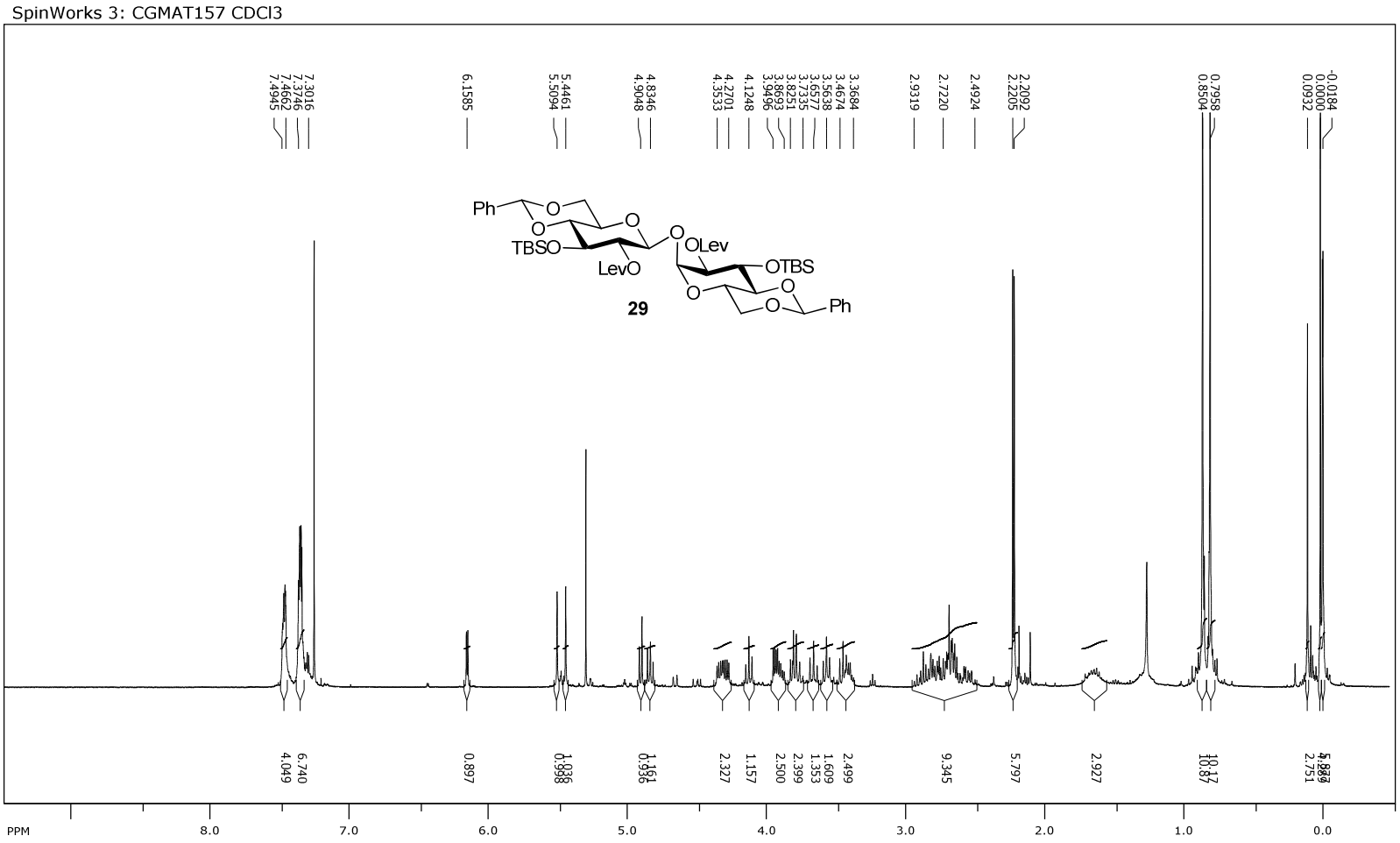
Supplementary Figure 98 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 28.



file: ...eau dossier\RMN LPS\CGMAT163\4\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 512

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

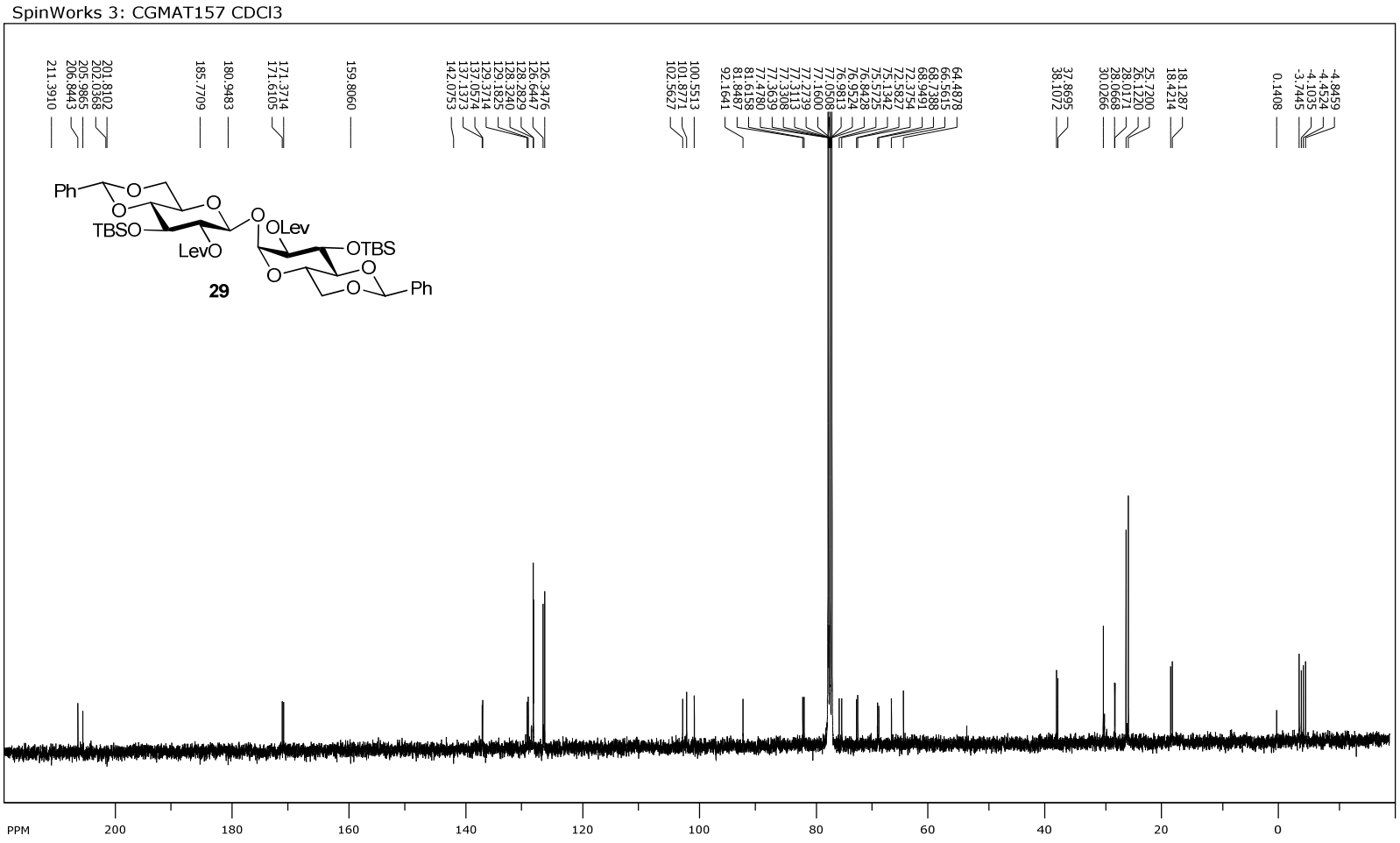
Supplementary Figure 99 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 29.



file: ...eau dossier\RMN LPS\CGMAT157\1\fid expt: <zg30>
transmitter freq.: 400.132001 MHz
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 64

freq. of 0 ppm: 400.130010 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

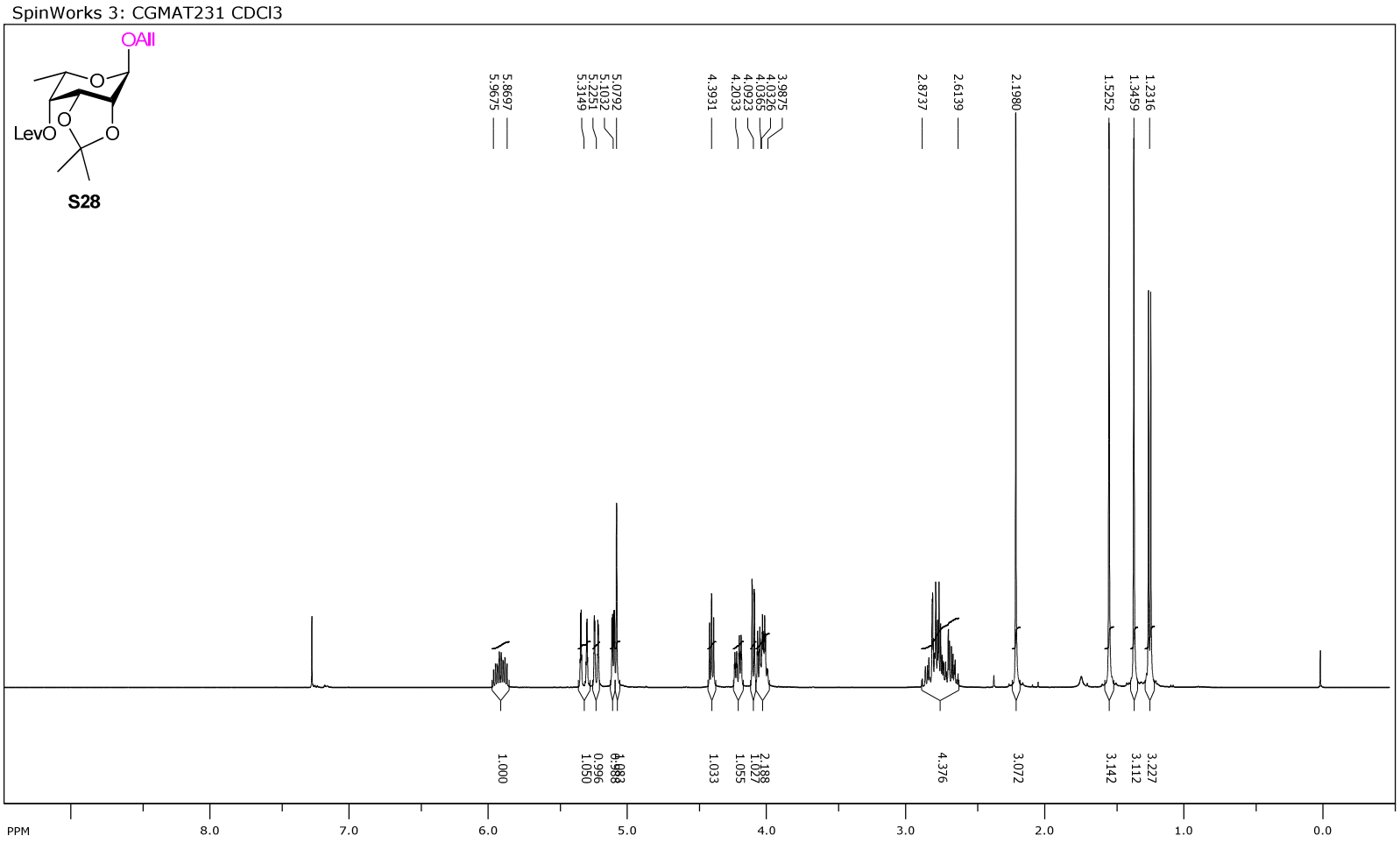
Supplementary Figure 100 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 29.



file: ...eau dossier\RMN LPS\CGMAT157\4\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 961.538 ppm/cm: 9.55587

Supplementary Figure 101 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S28.



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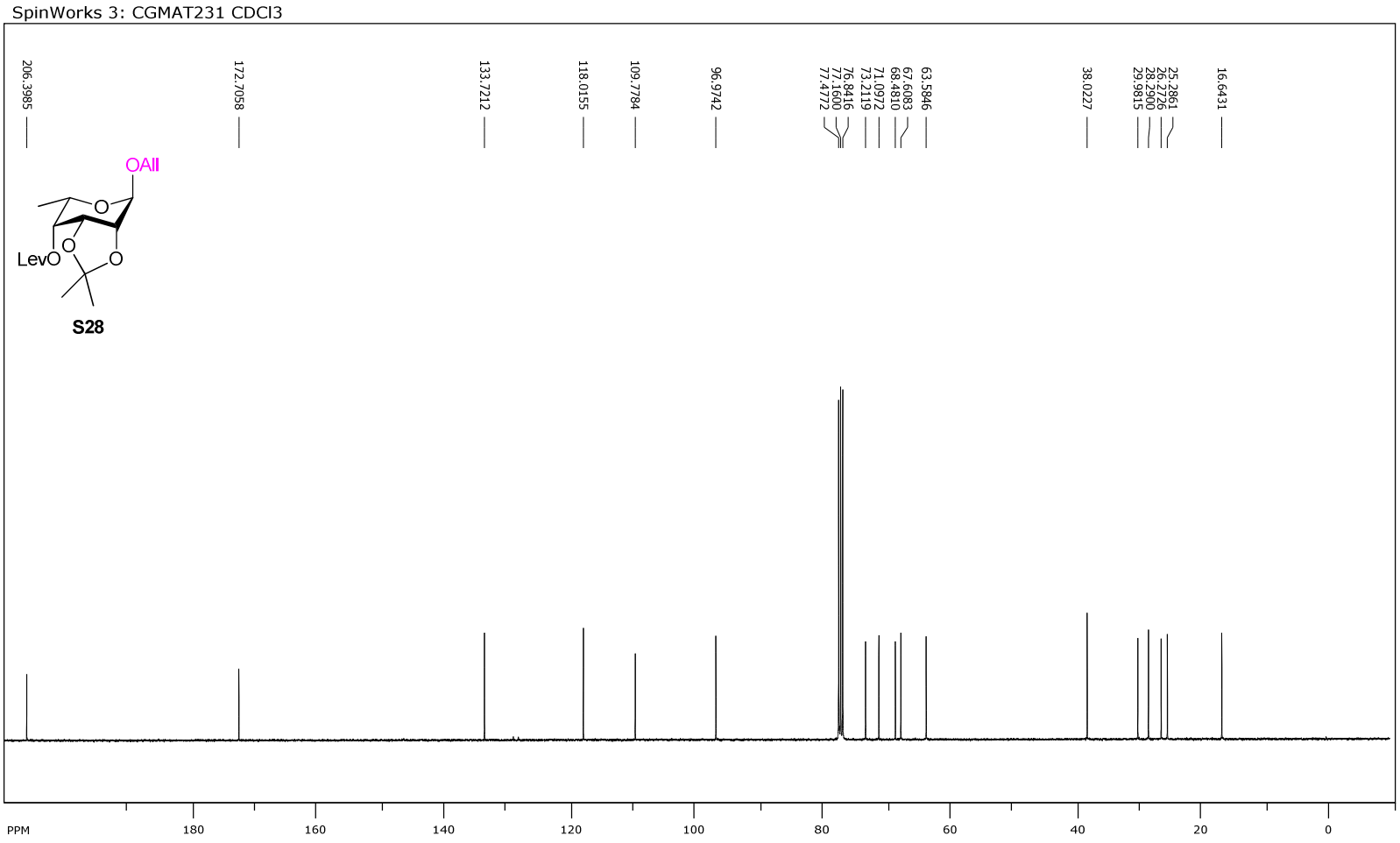
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 16

freq. of 0 ppm: 400.130002 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

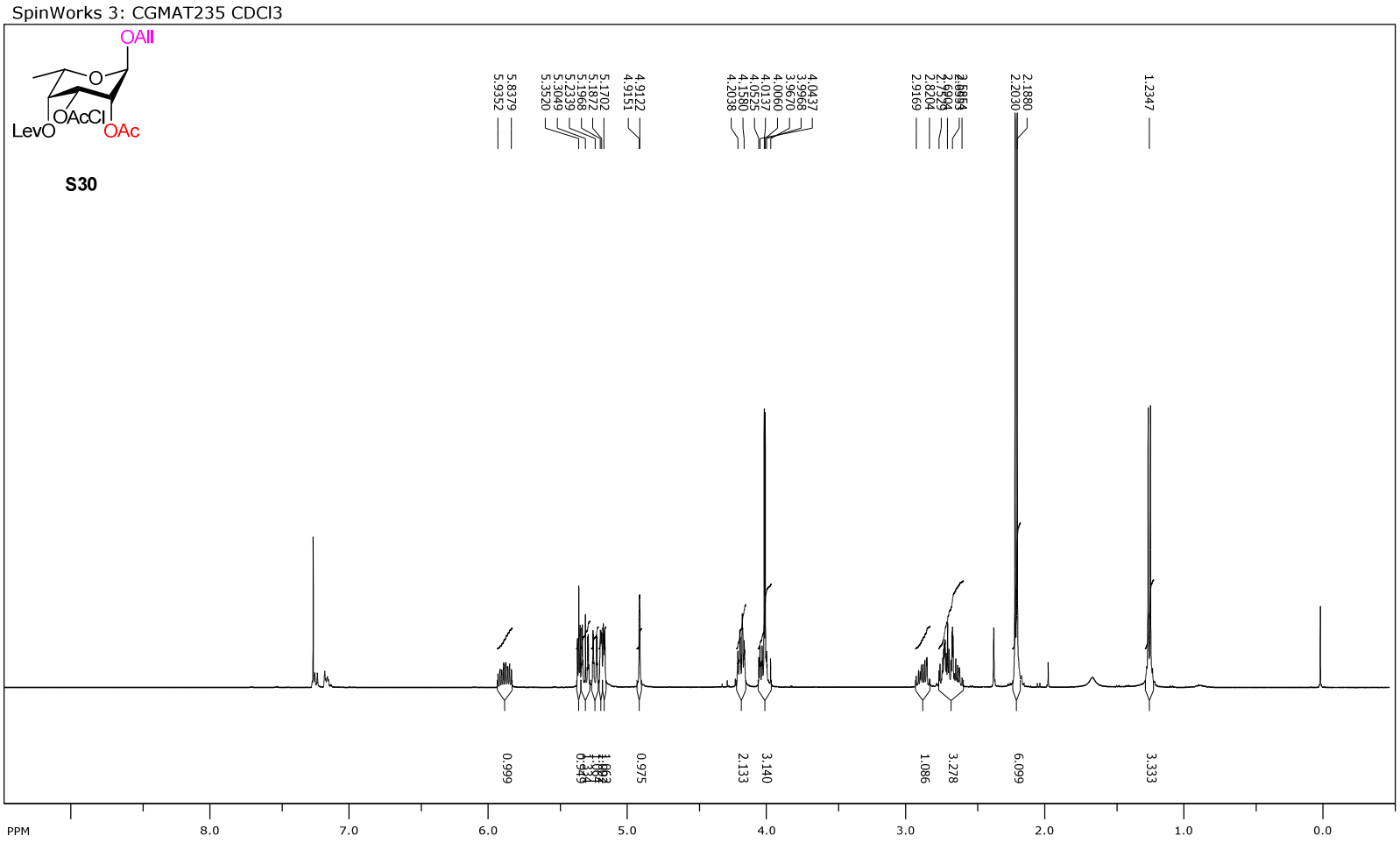
Supplementary Figure 102 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S28.



file: ...eau dossier\RMN LPS\CGMAT231\4\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612757 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 103 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S30.



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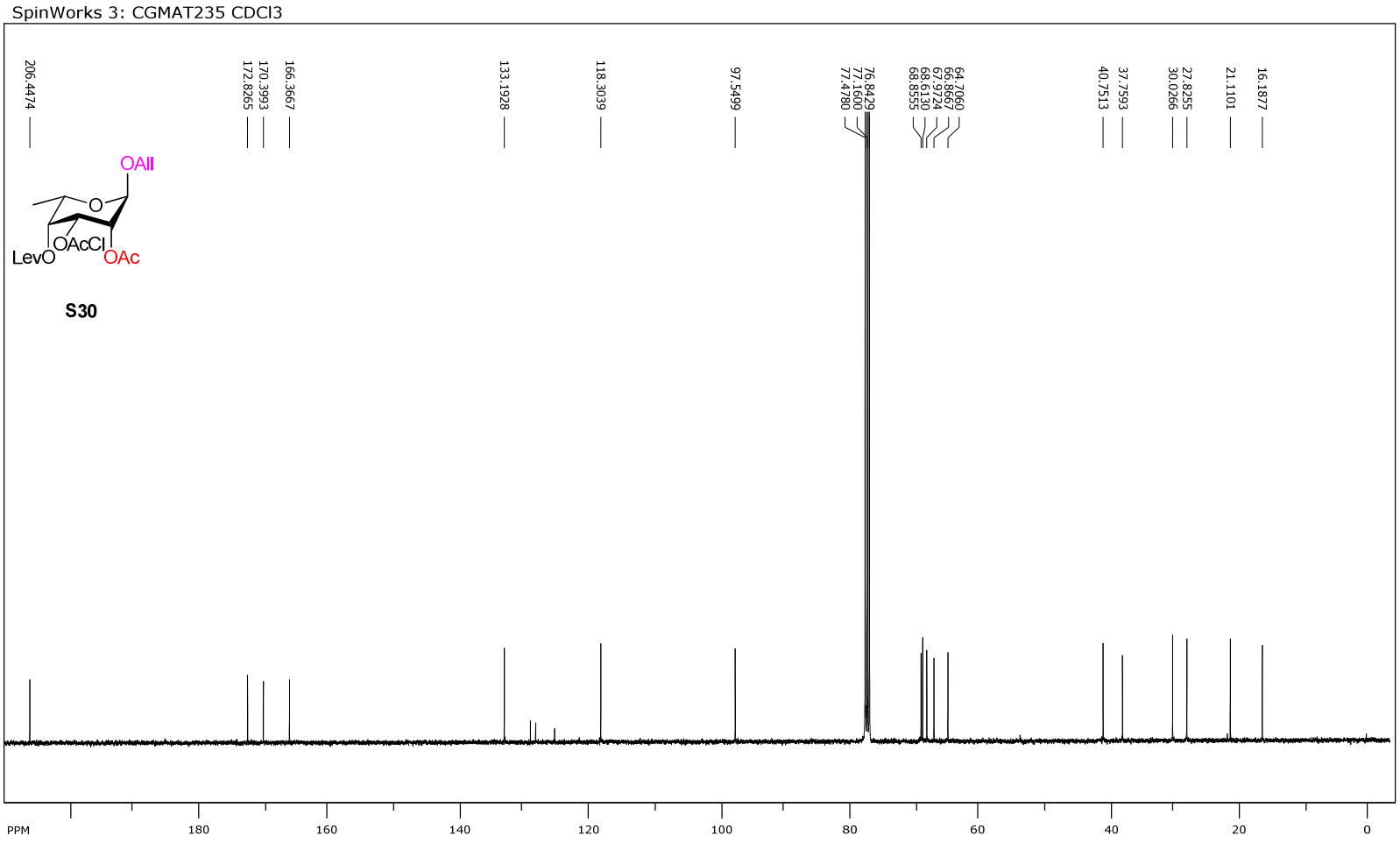
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130007 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

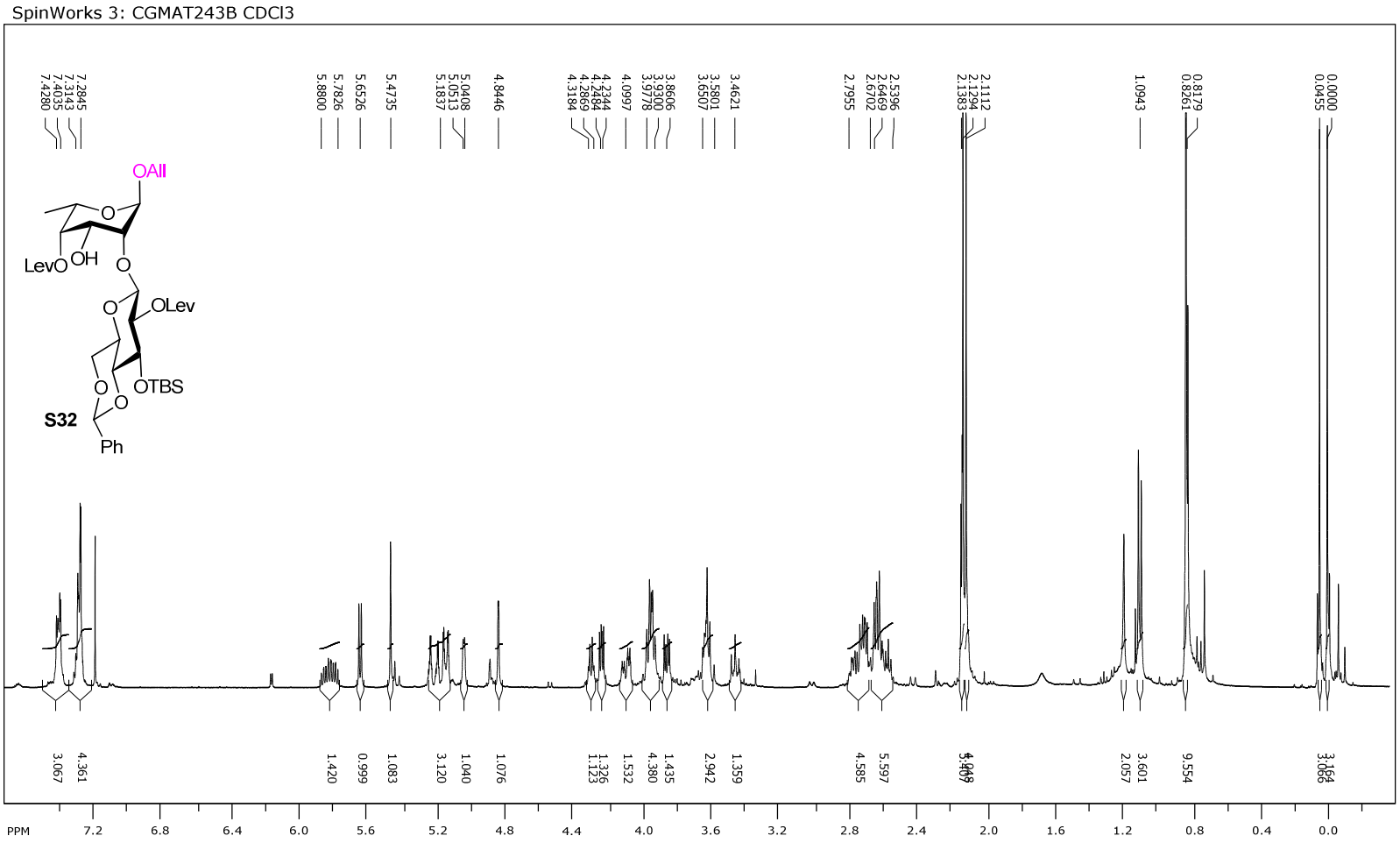
Supplementary Figure 104 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S30.



file: F:\CGMAT235\3\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 860.884 ppm/cm: 8.55555

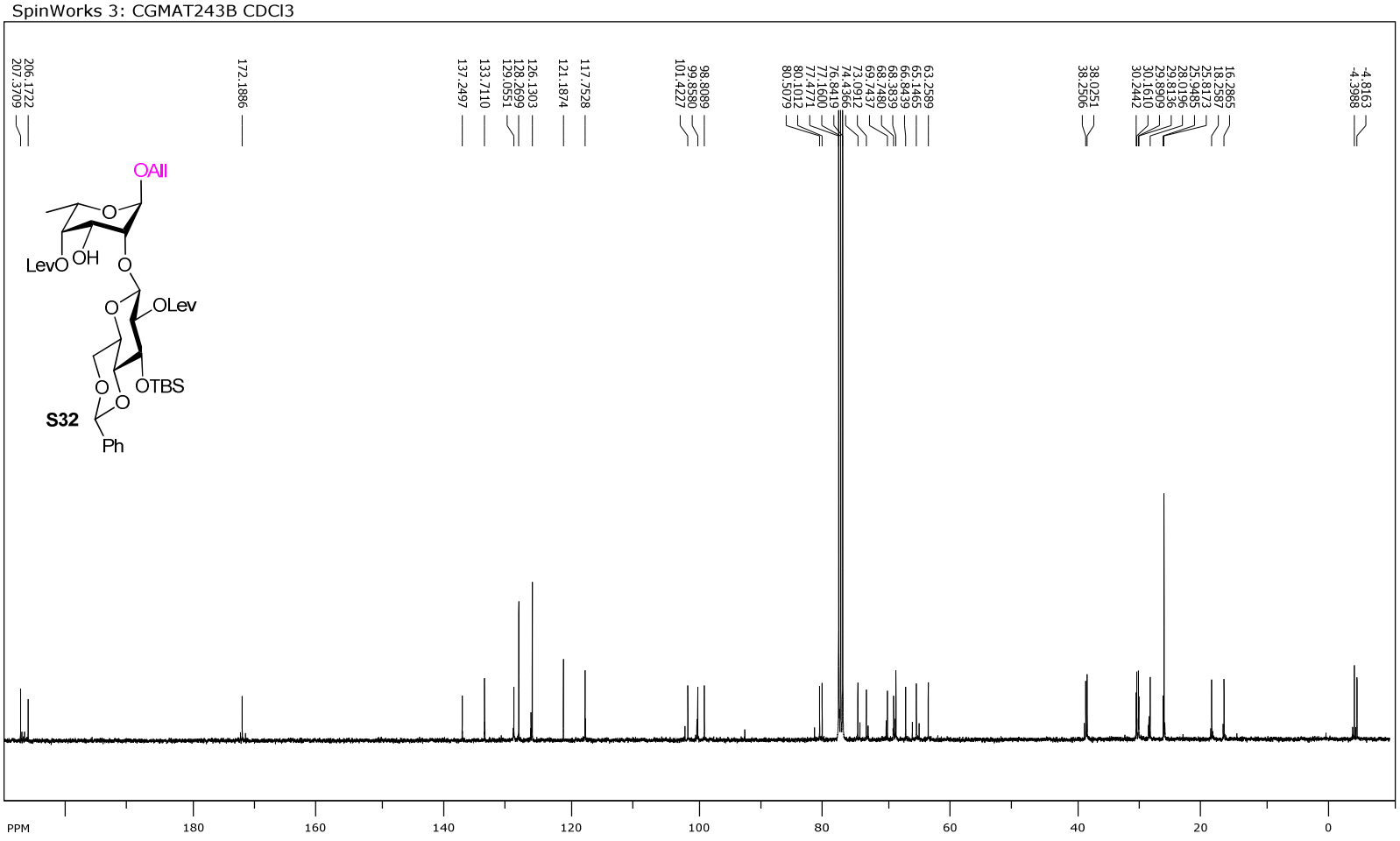
Supplementary Figure 105 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S32.



file: ...au dossier\RMN LPS\CGMAT243B\1\fid expt: <zg30>
transmitter freq.: 400.132001 MHz
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130033 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 129.624 ppm/cm: 0.32395

Supplementary Figure 106 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S32.



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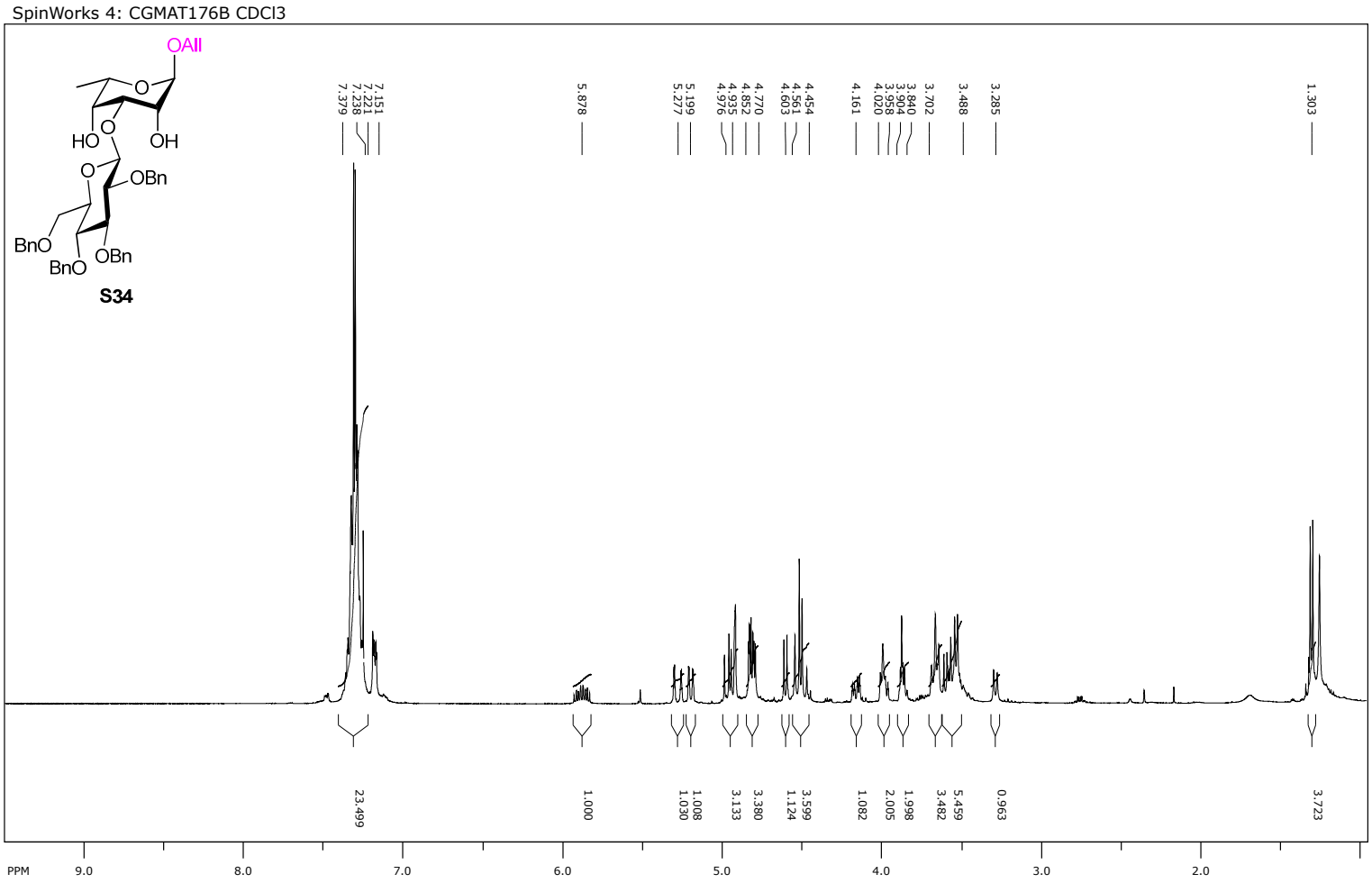
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612756 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

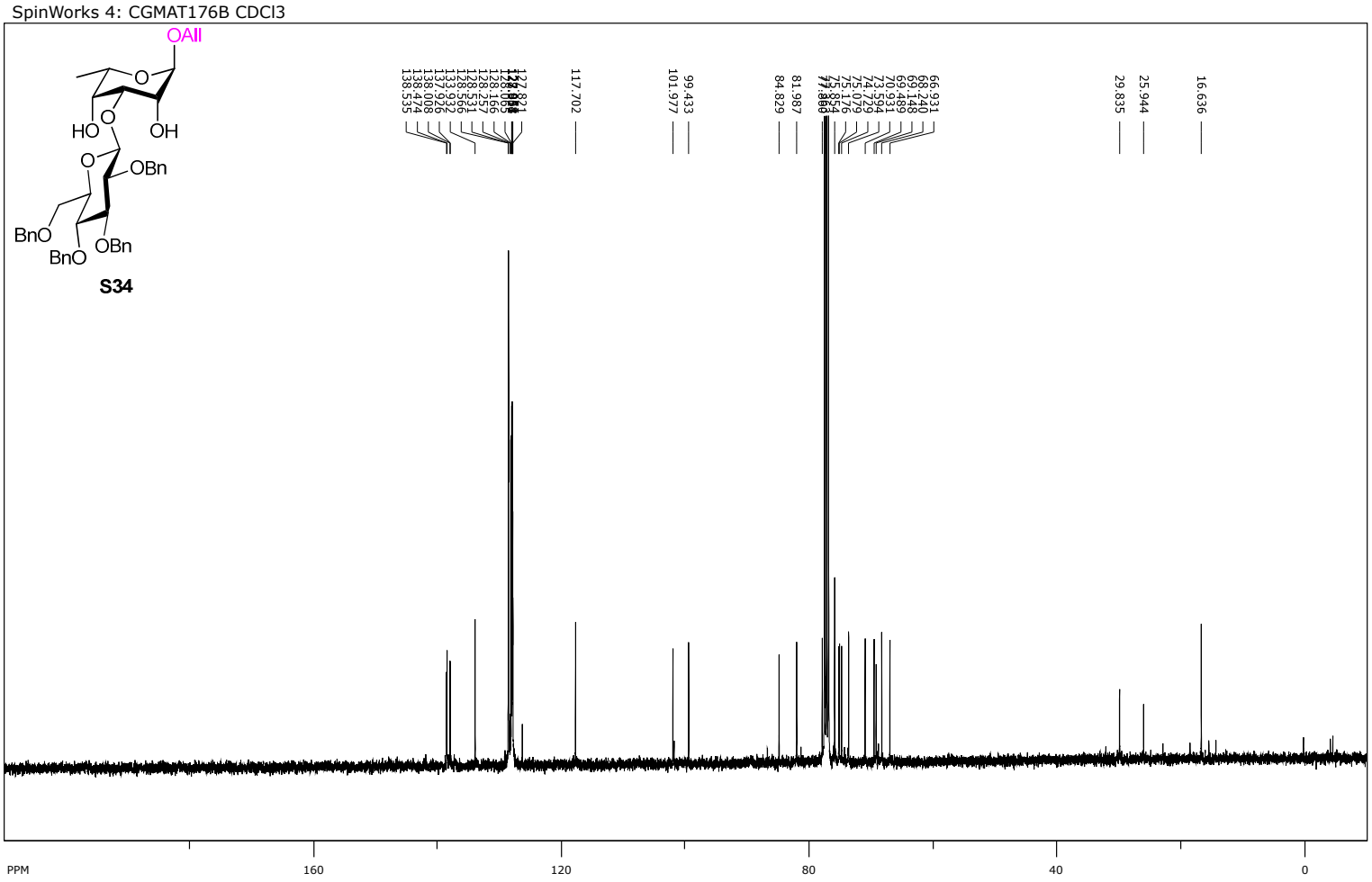
Supplementary Figure 107 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S34.



file: ...S Marielle\RMN LPS\CGMAT176B\1\fid expt: <zg30>
transmitter freq.: 400.132001 MHz
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130014 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

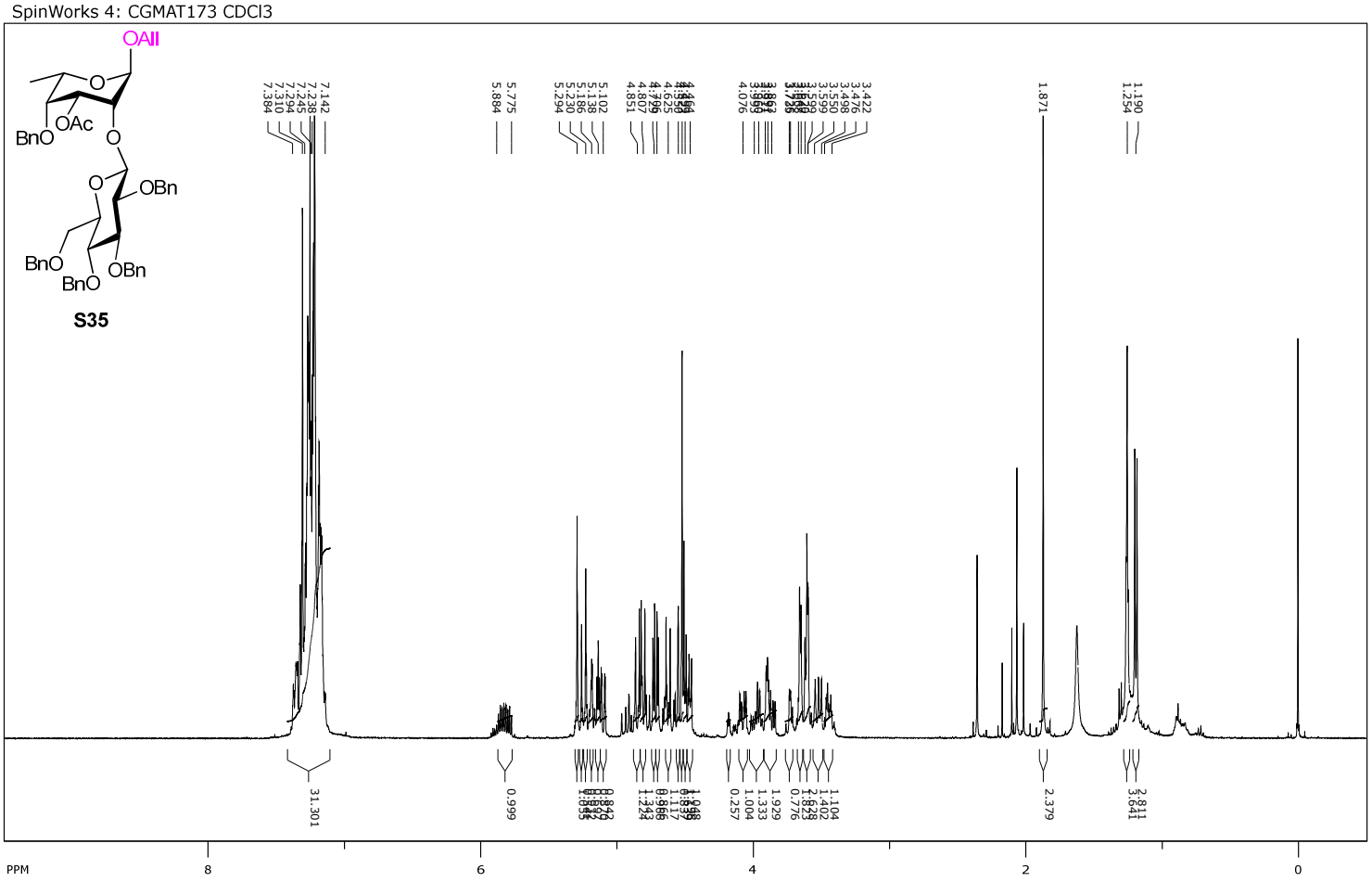
Supplementary Figure 108 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S34.



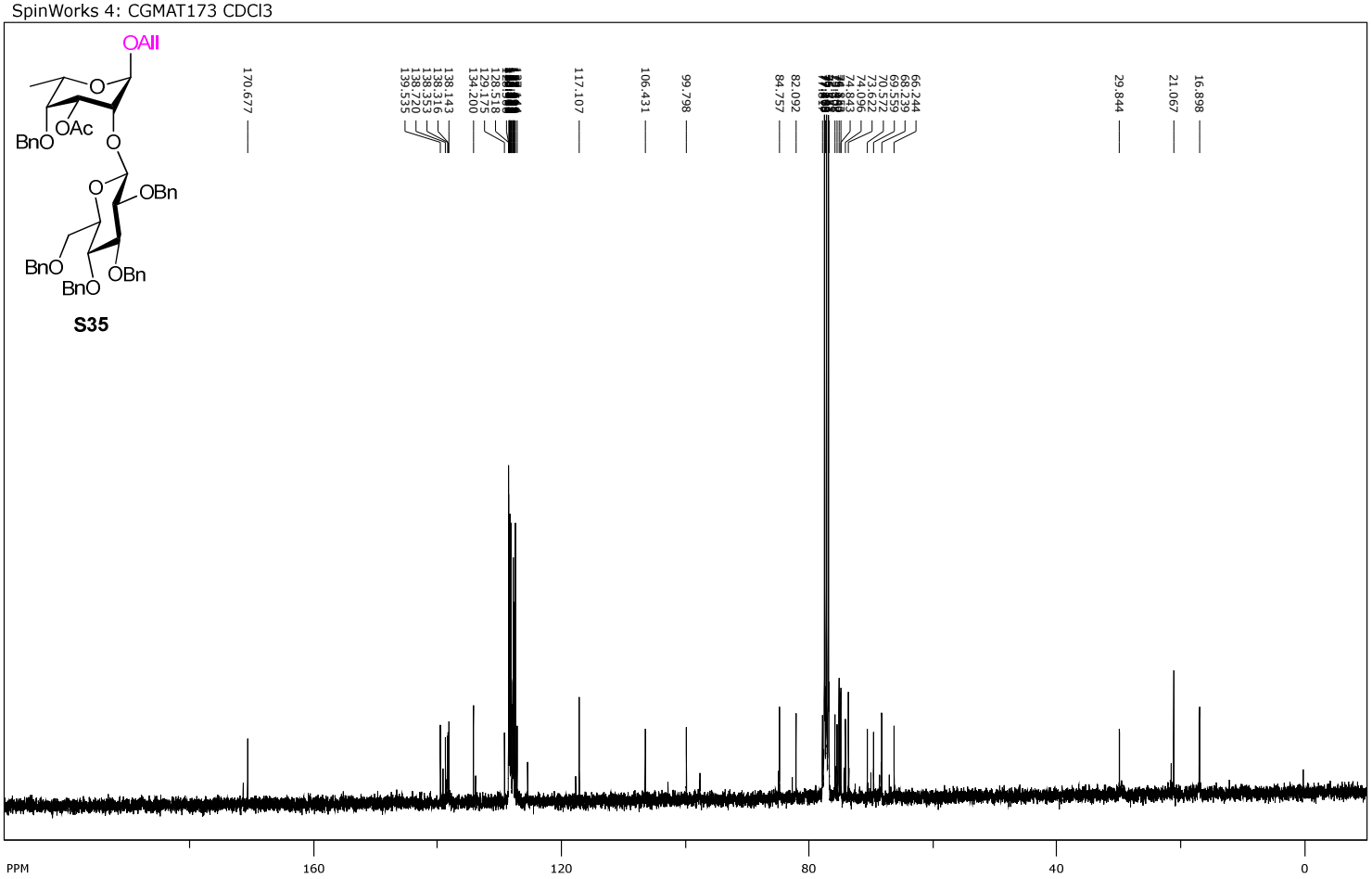
file: ...S Marielle\RMN LPS\CGMAT176B\3\fid expt: <zgpg30>
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612757 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

Supplementary Figure 109 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S35.



Supplementary Figure 110 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S35.



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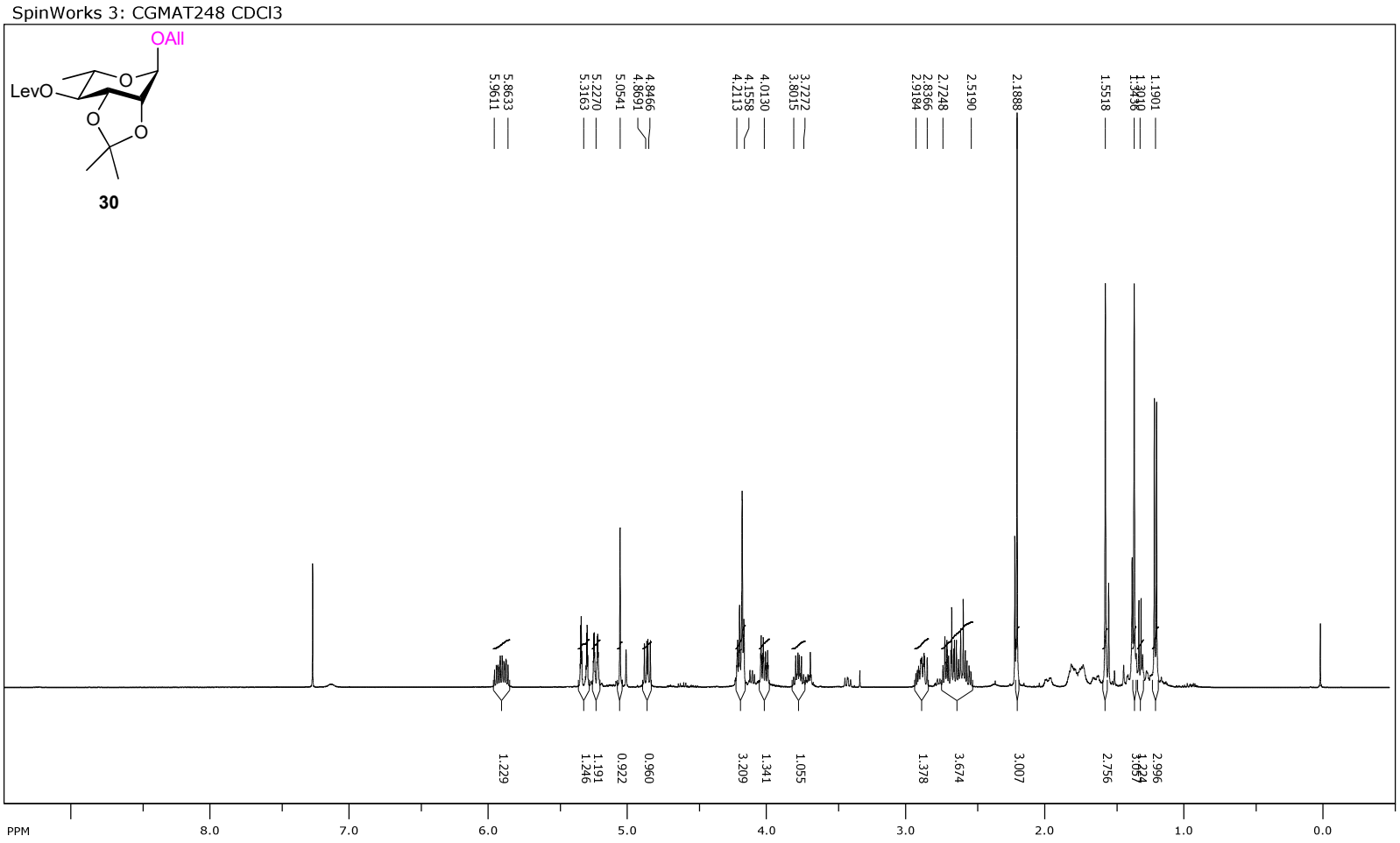
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612756 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

Supplementary Figure 111 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 30.



file: ...eau dossier\RMN LPS\CGMAT248\1\fid expt: <zg30>
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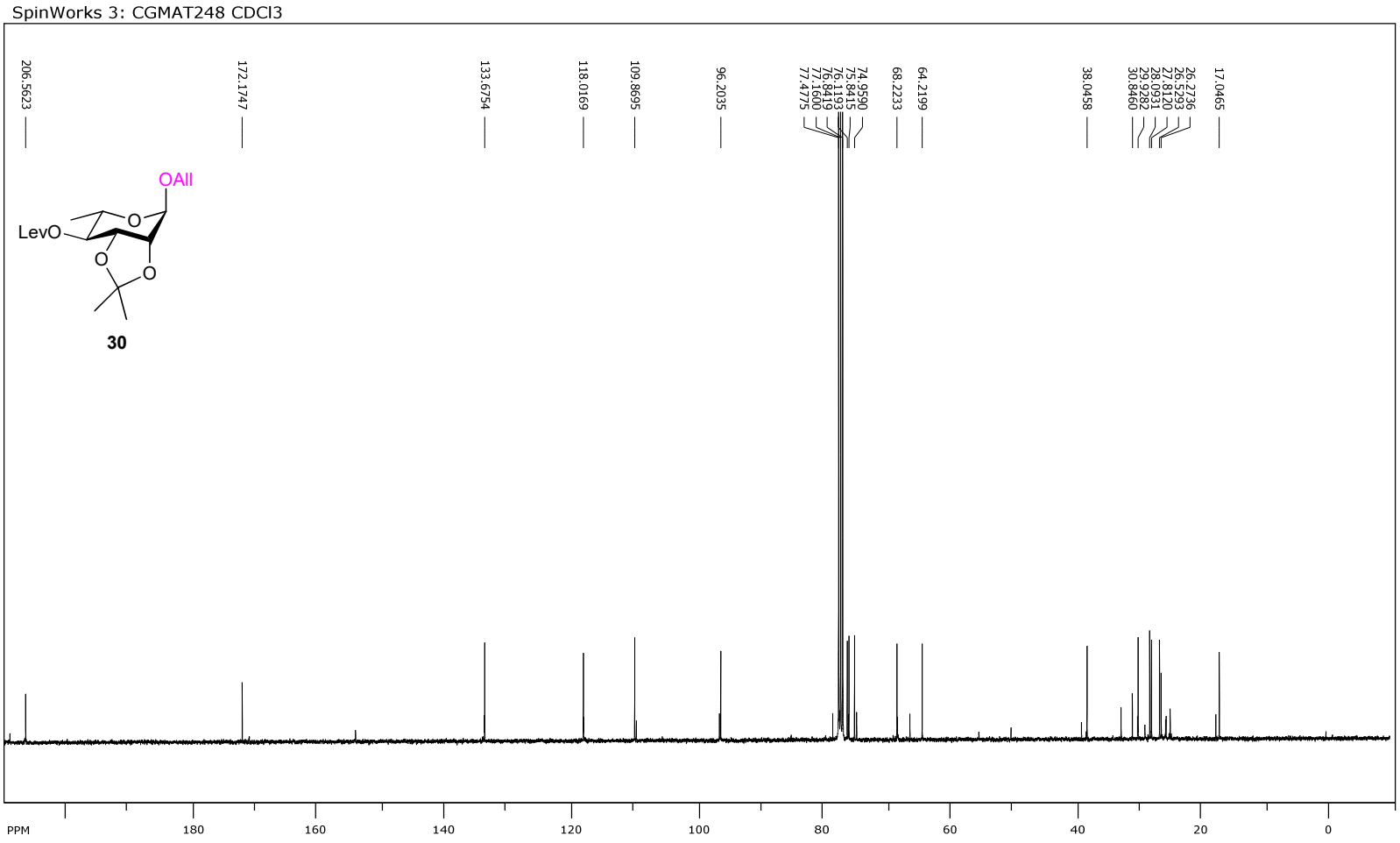
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130005 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 112 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 30.



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time domain size: 65536 points
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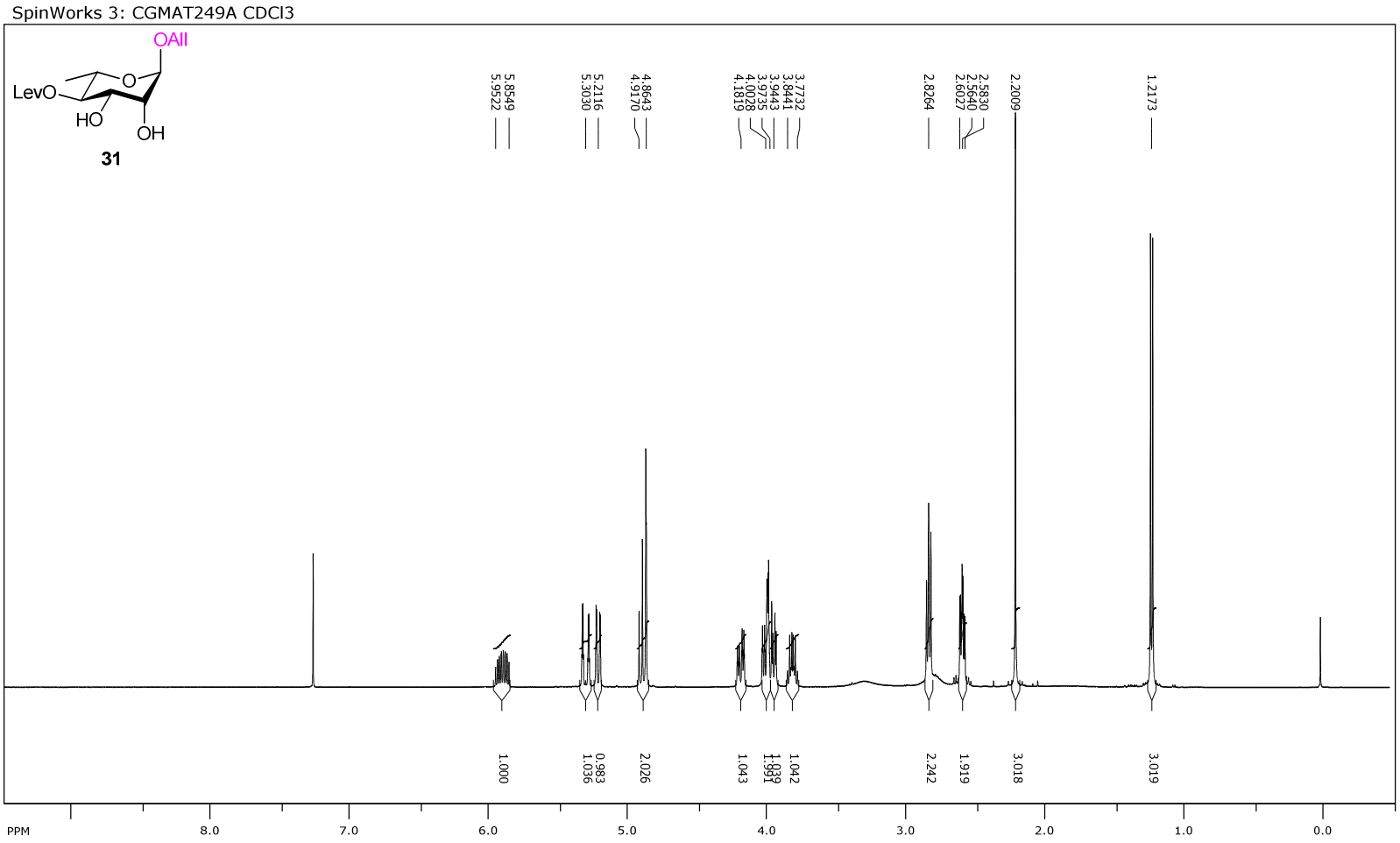
number of scans: 1024

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 113 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 31.



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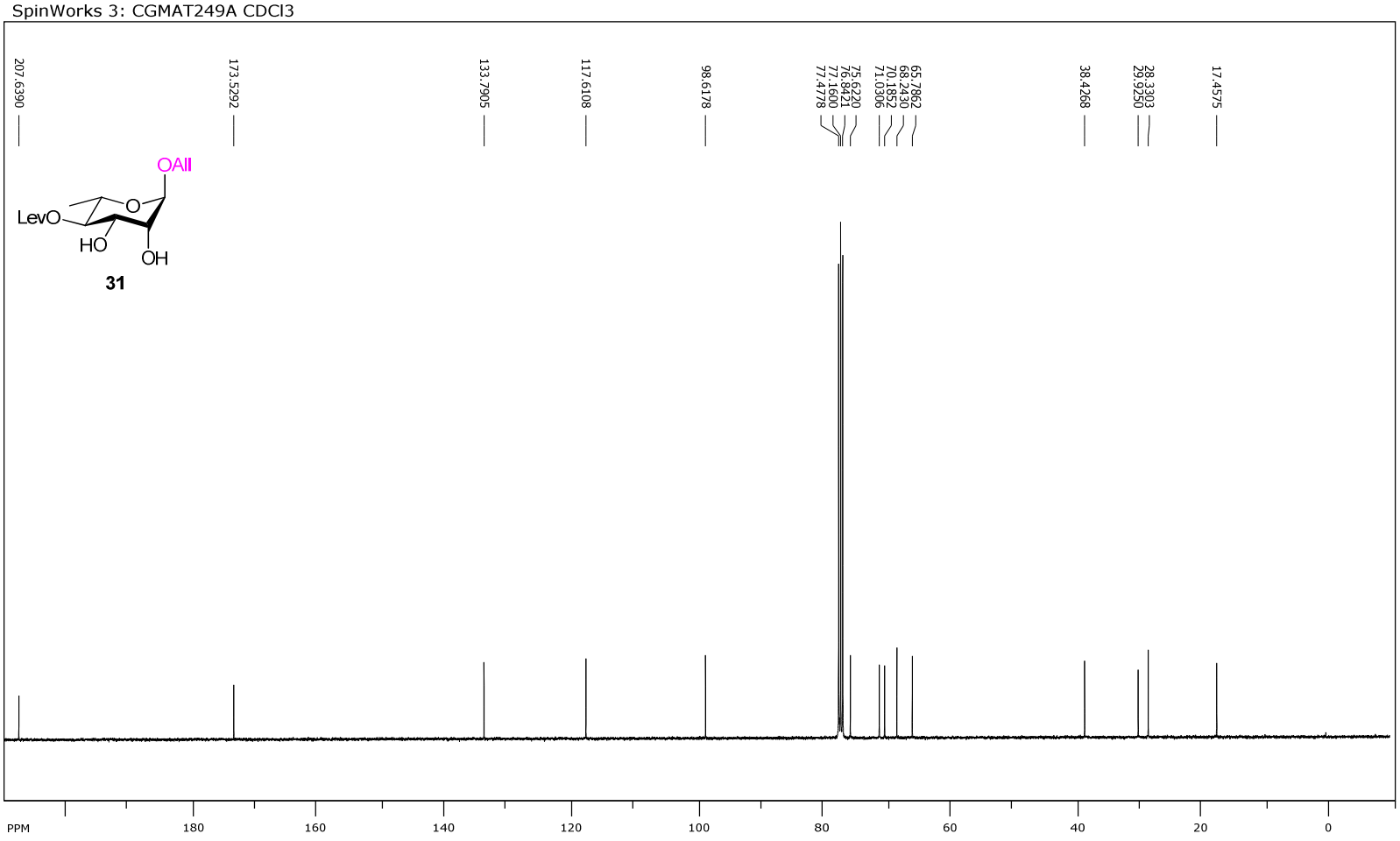
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130007 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 114 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 31.



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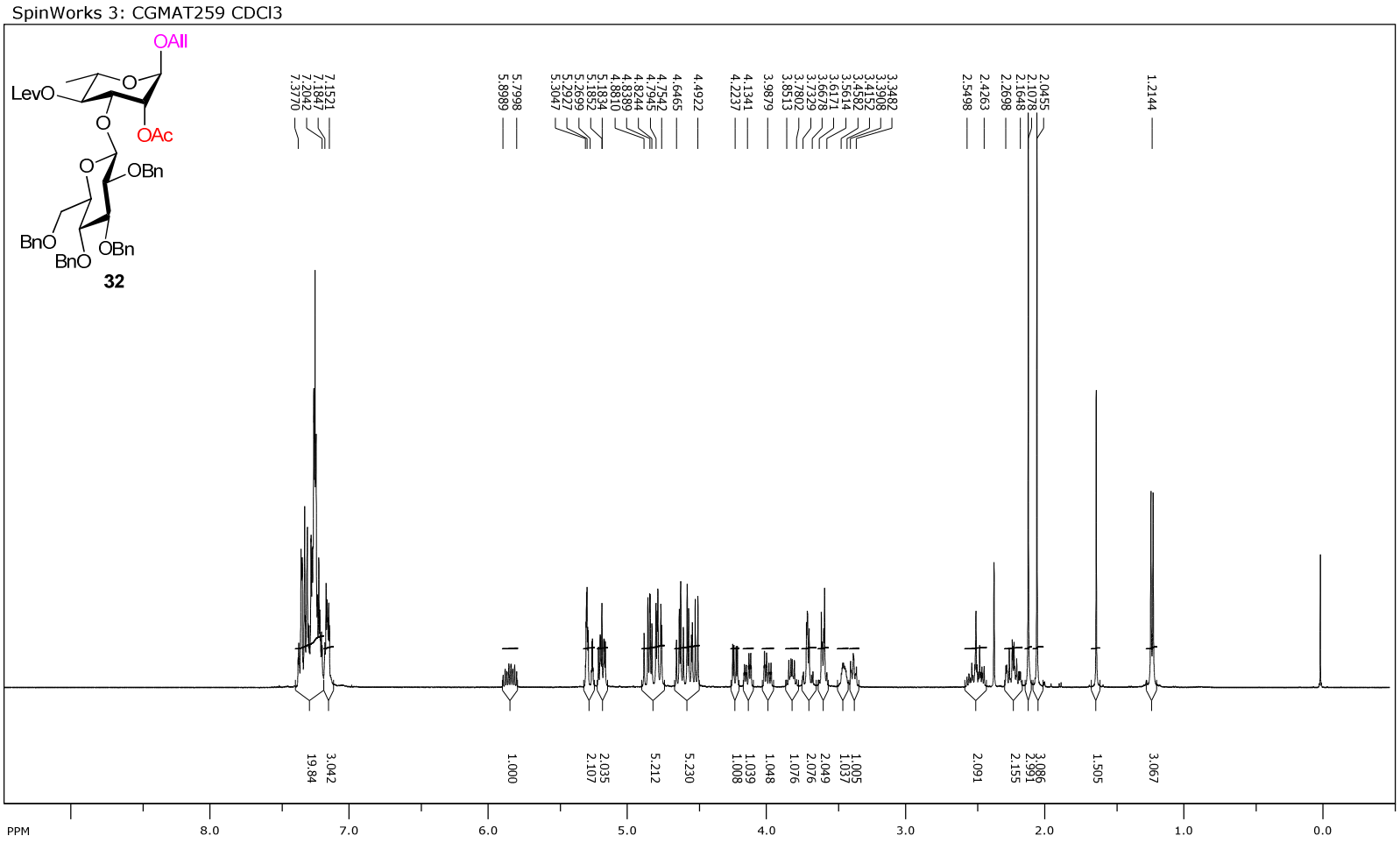
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 115 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 32.



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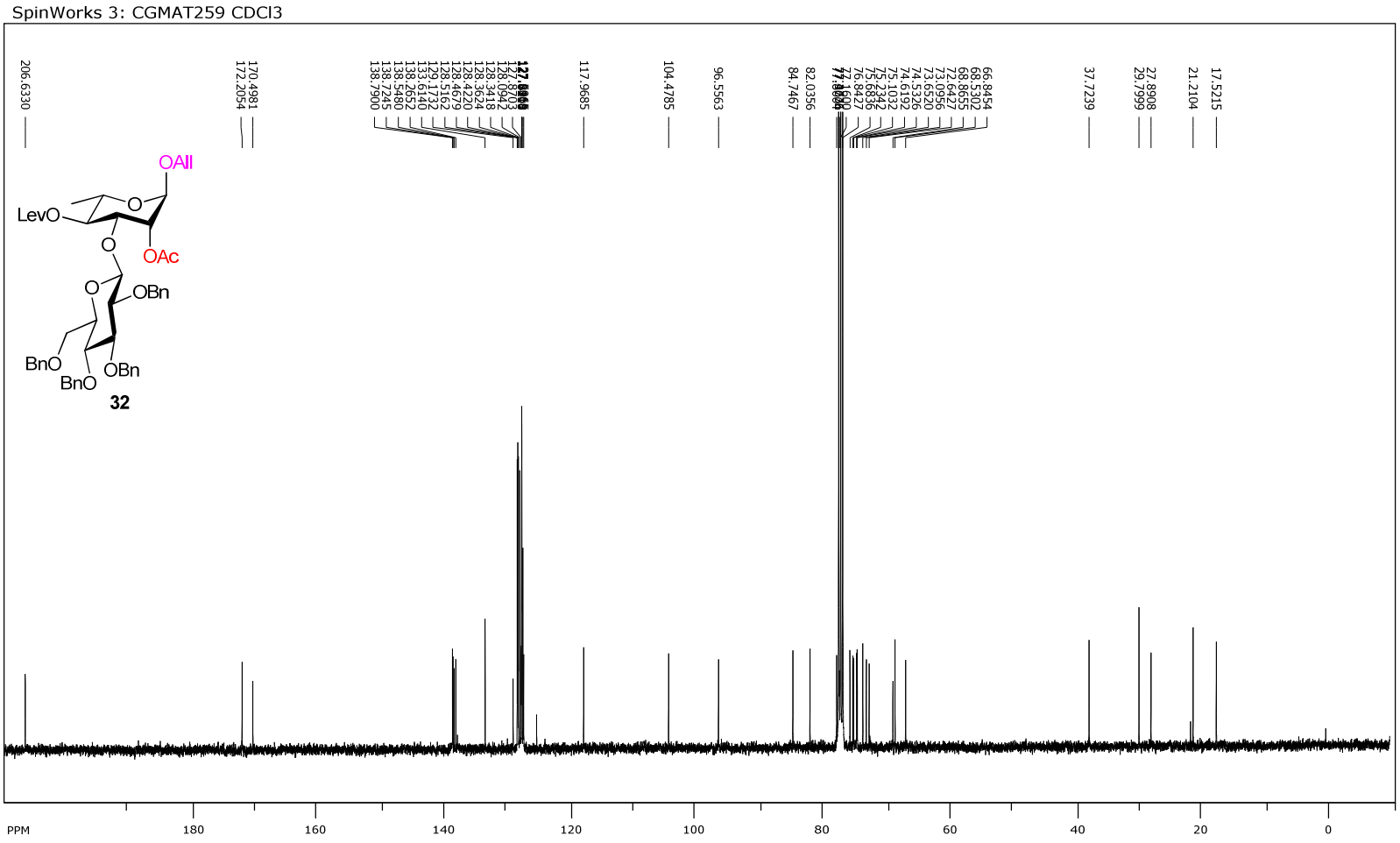
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 16

freq. of 0 ppm: 400.130011 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 116 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 32.



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time domain size: 65536 points
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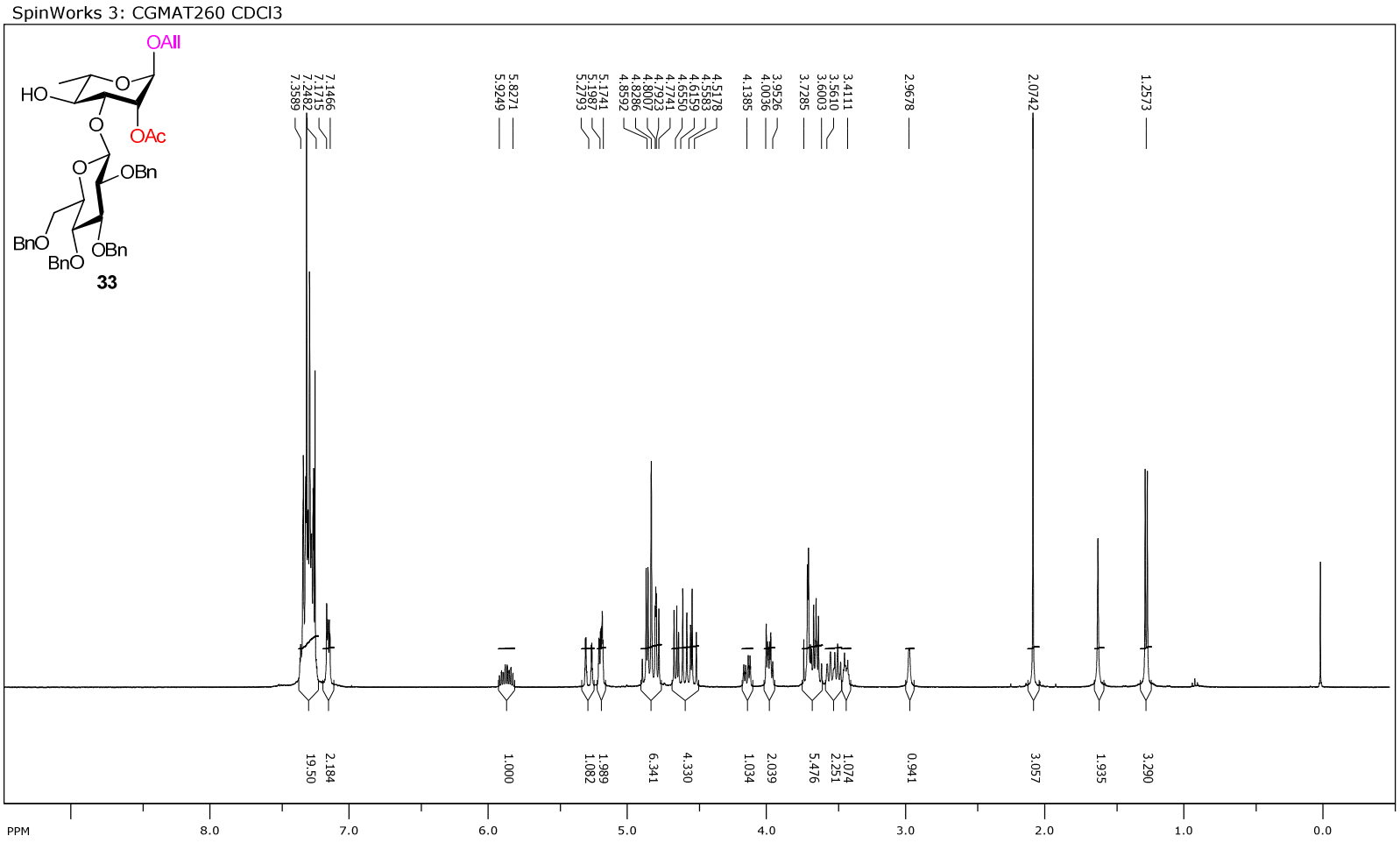
number of scans: 1024

freq. of 0 ppm: 100.612756 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 117 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 33.



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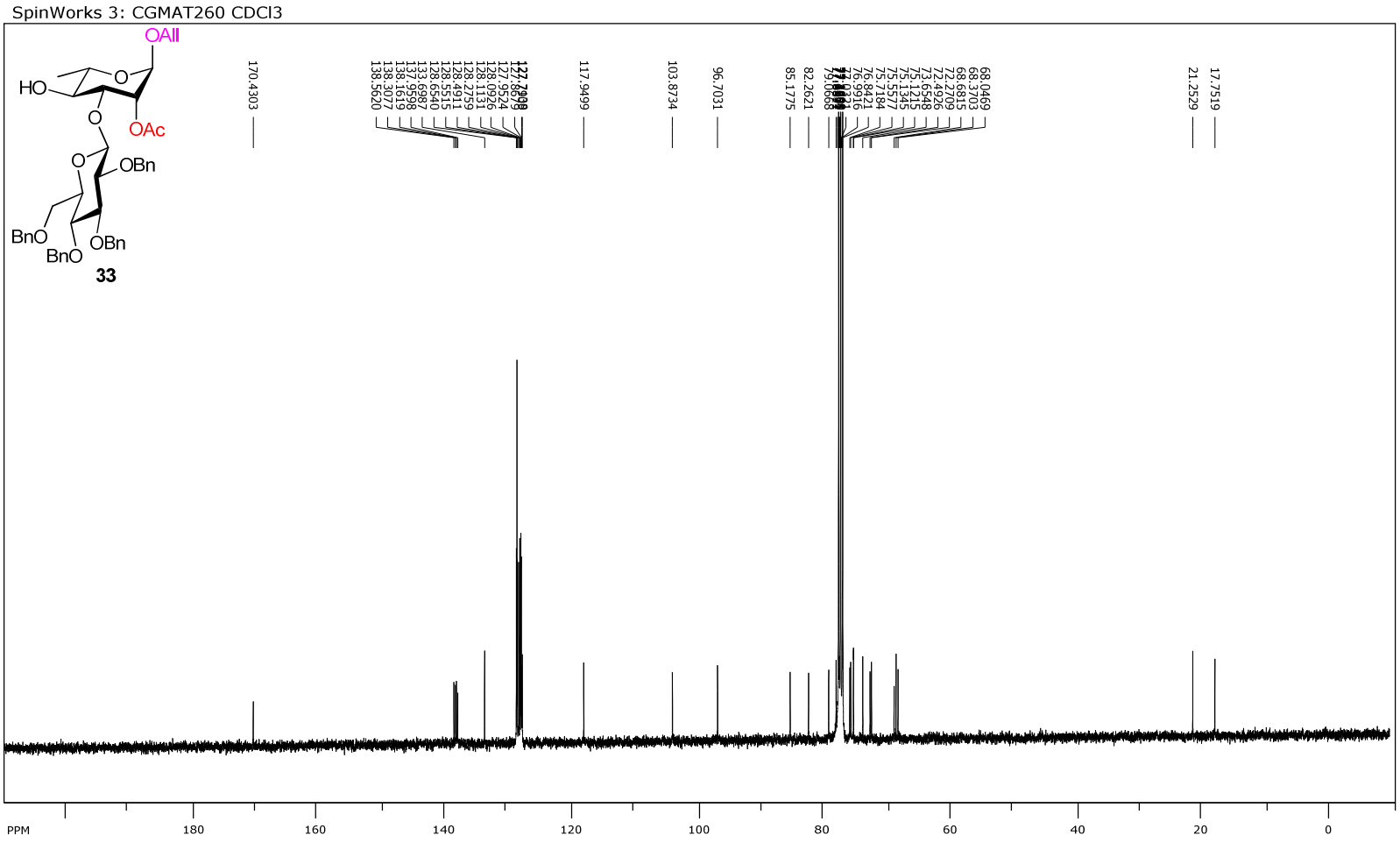
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 16

freq. of 0 ppm: 400.130011 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 118 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 33.



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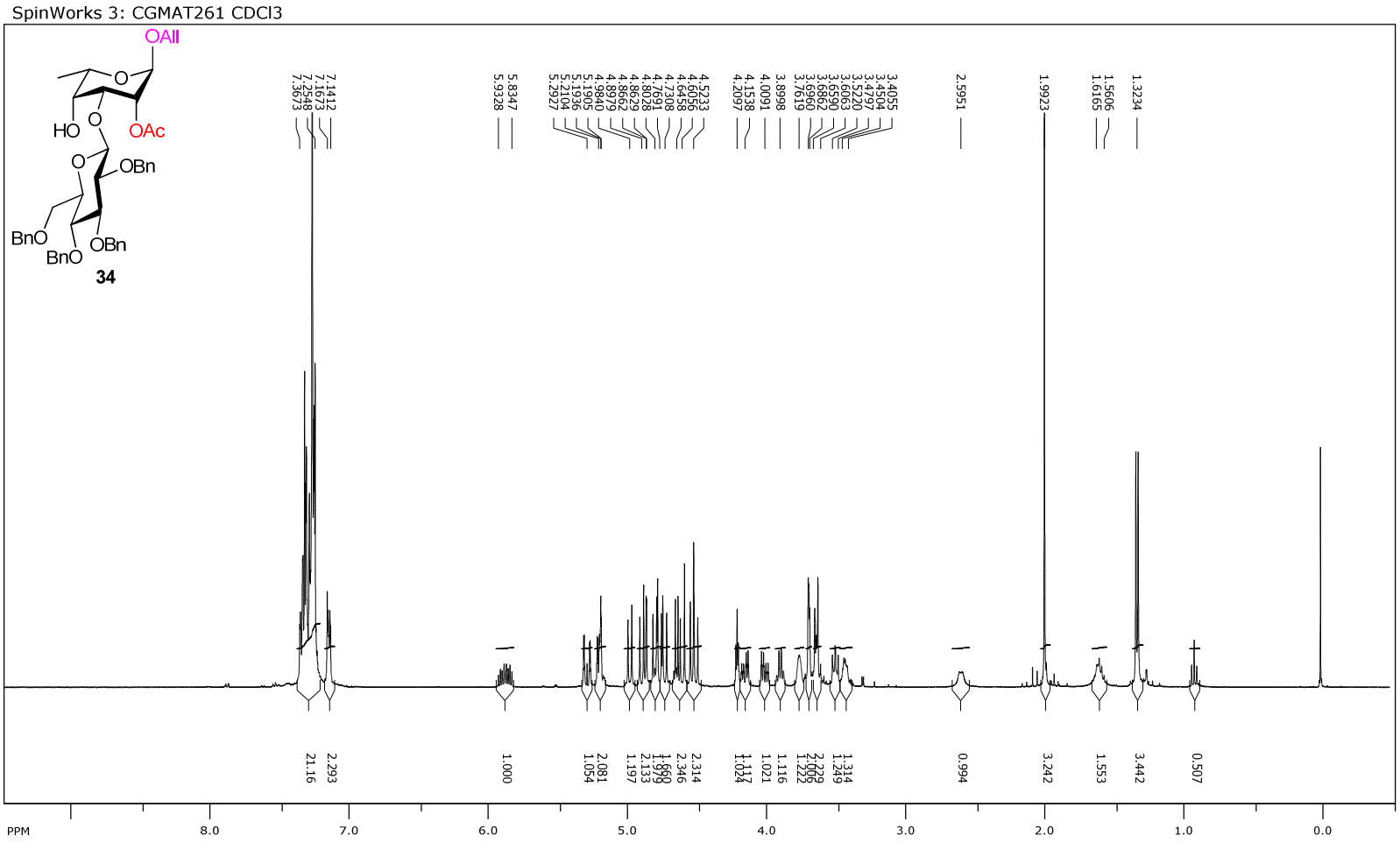
transmitter freq.: 100.622830 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 119 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 34.



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time domain size: 32768 points
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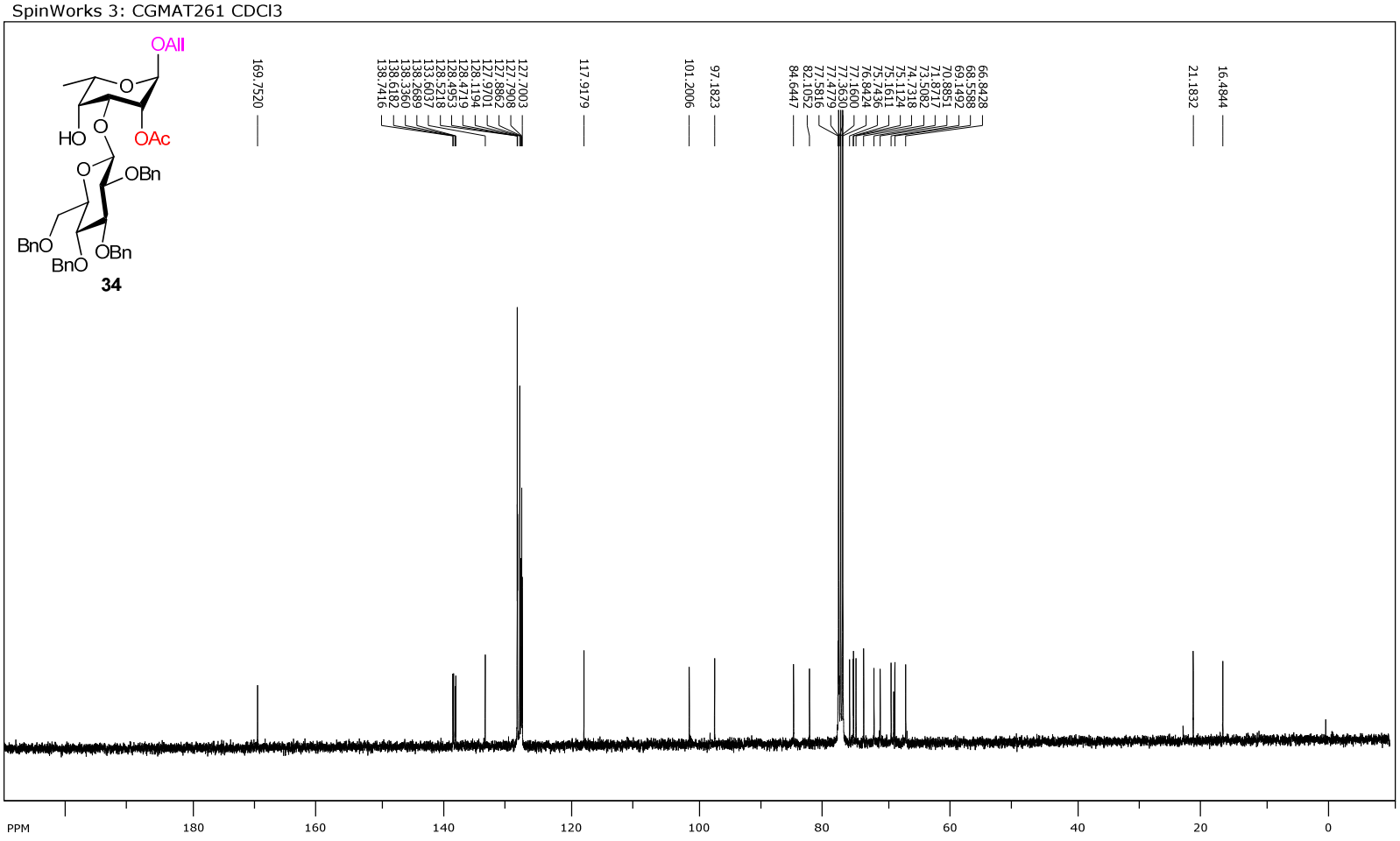
number of scans: 32

freq. of 0 ppm: 400.130012 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 120 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 34.



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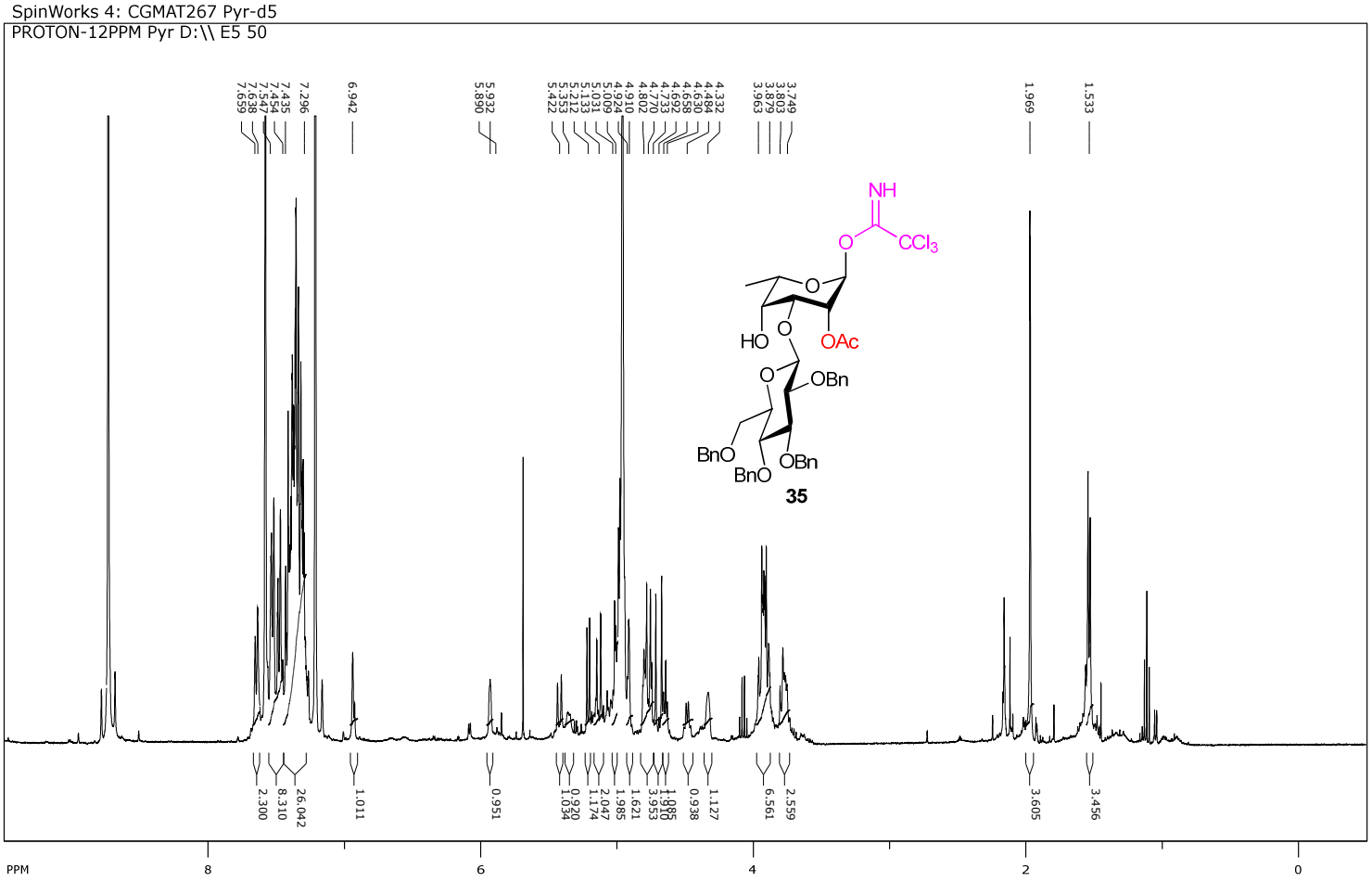
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 885.392 ppm/cm: 8.79912

Supplementary Figure 121 | ^{1}H NMR spectra (py-d_5, 400 MHz) of compound 35.



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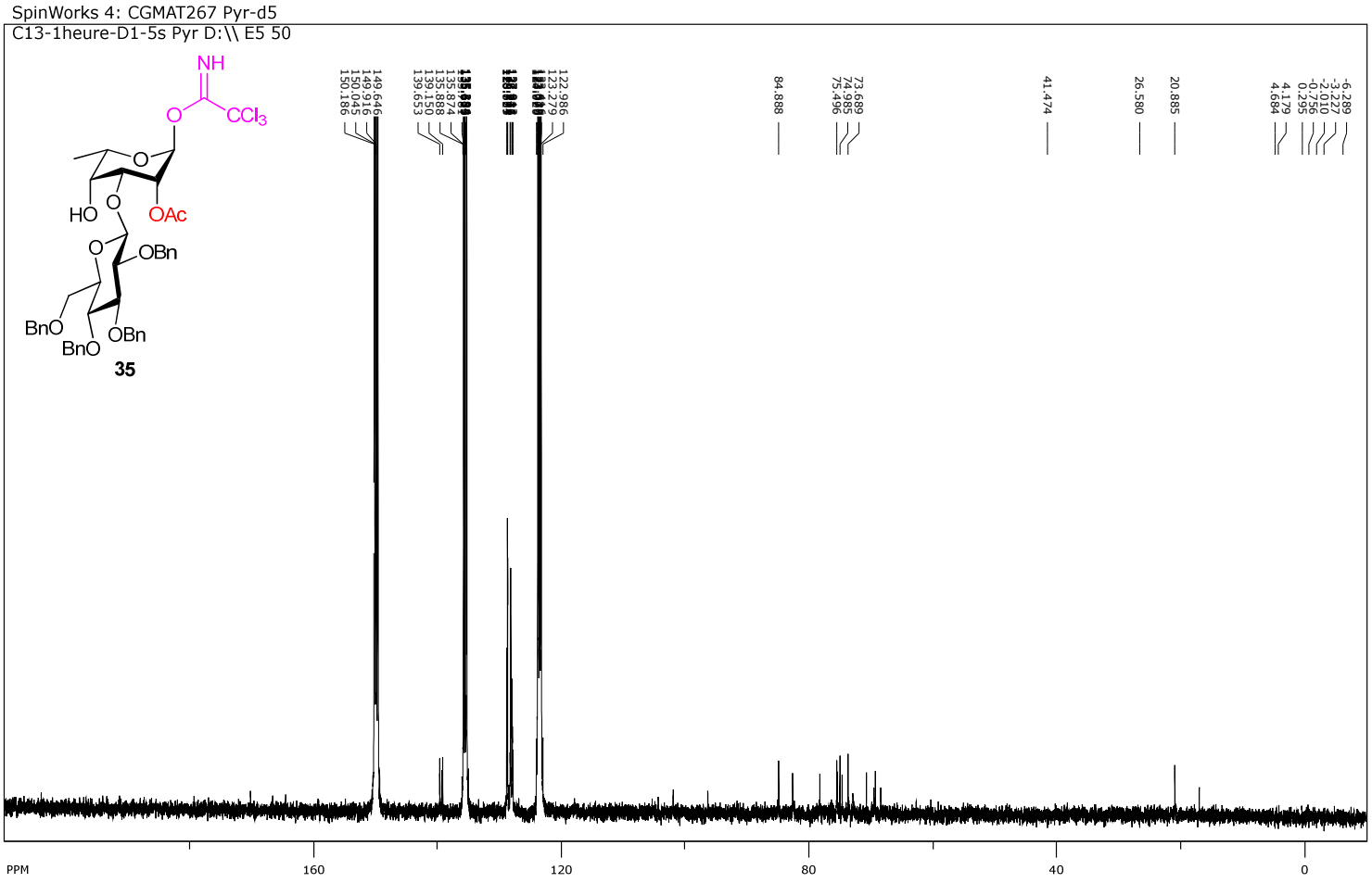
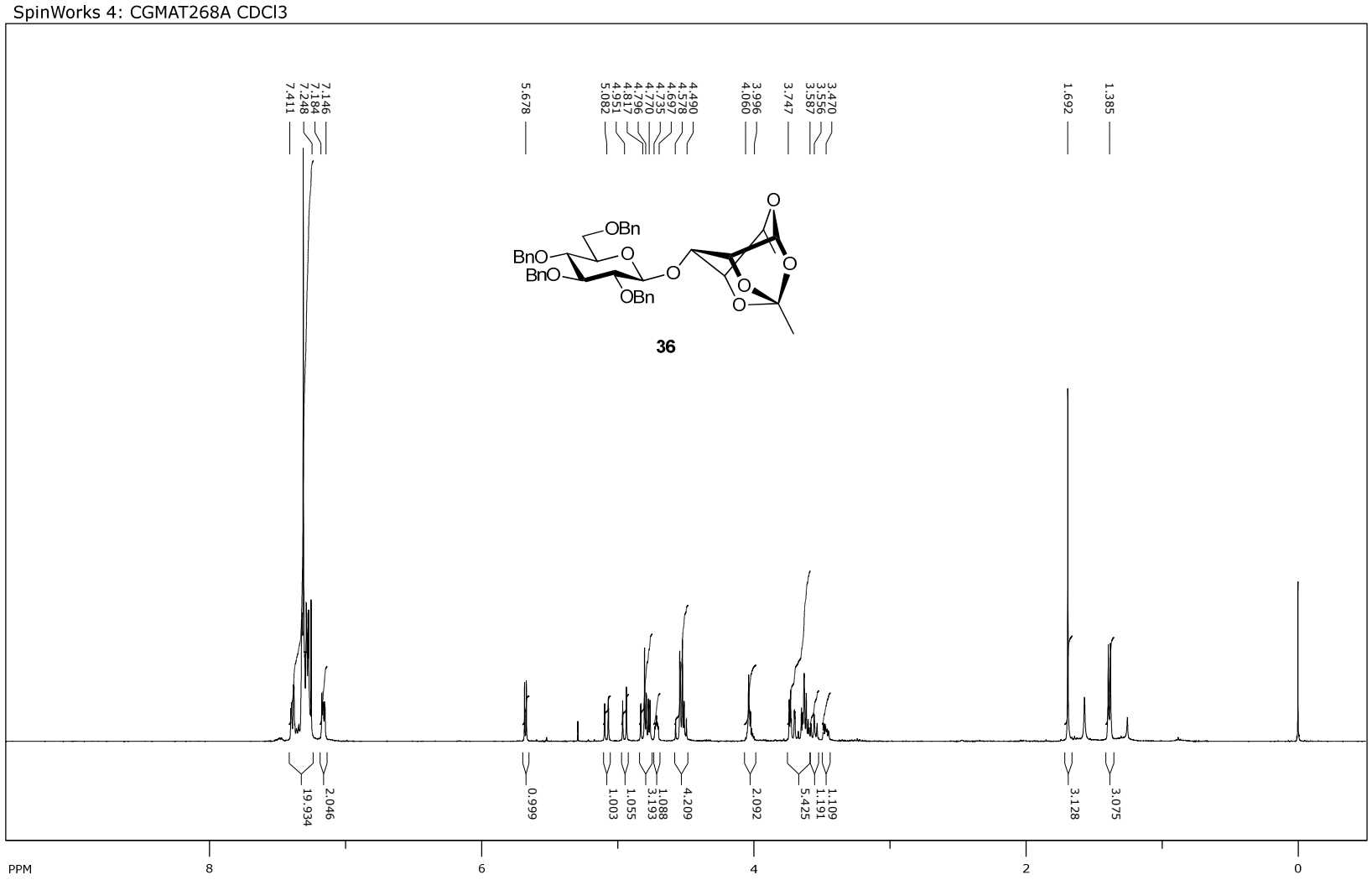
number of scans: 32

freq. of 0 ppm: 400.130592 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

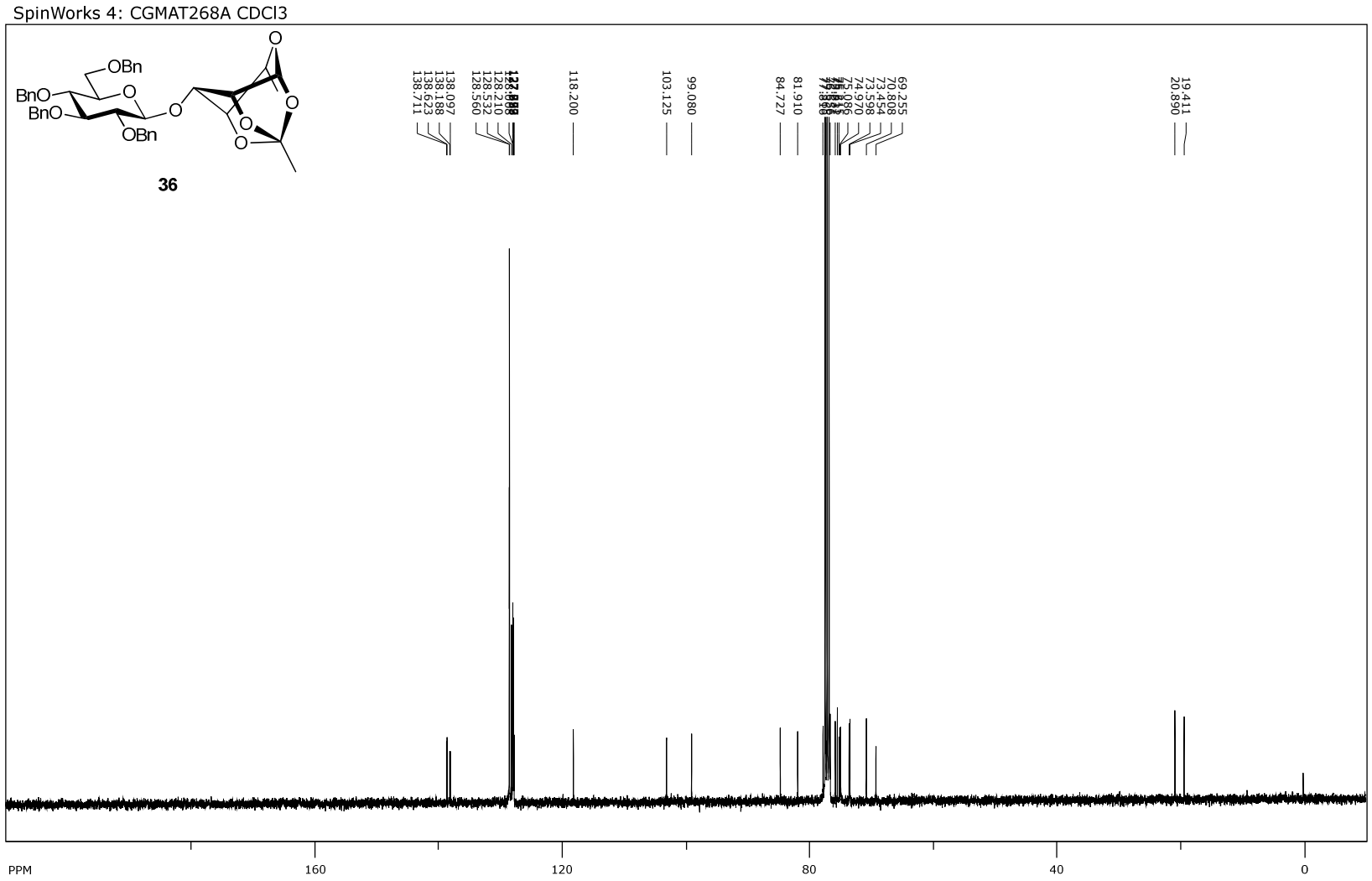
Supplementary Figure 122 | ^{13}C NMR spectra (py-d_5, 100 MHz) of compound 35.



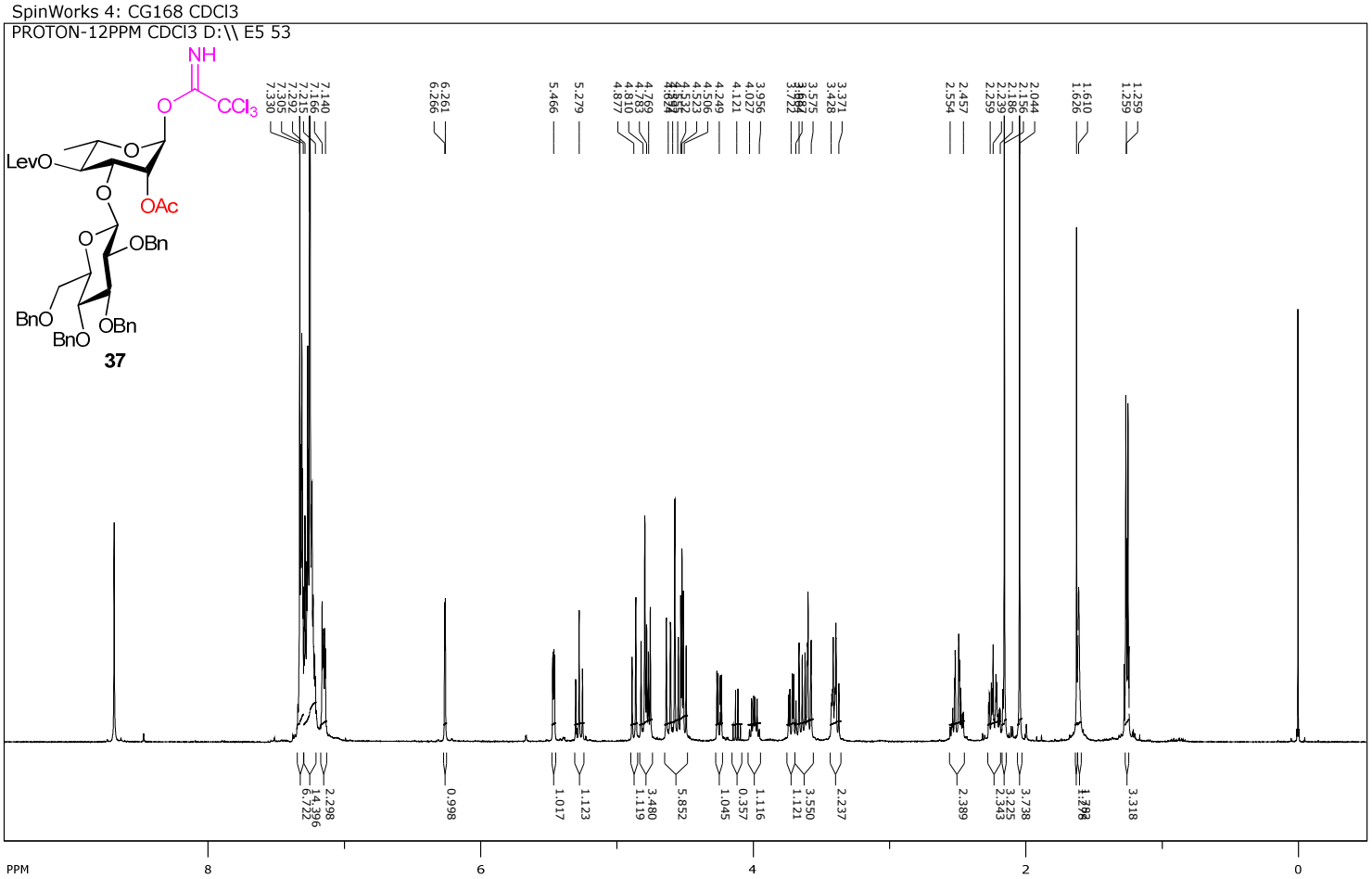
Supplementary Figure 123 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 36.



Supplementary Figure 124 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 36.



Supplementary Figure 125 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 37.



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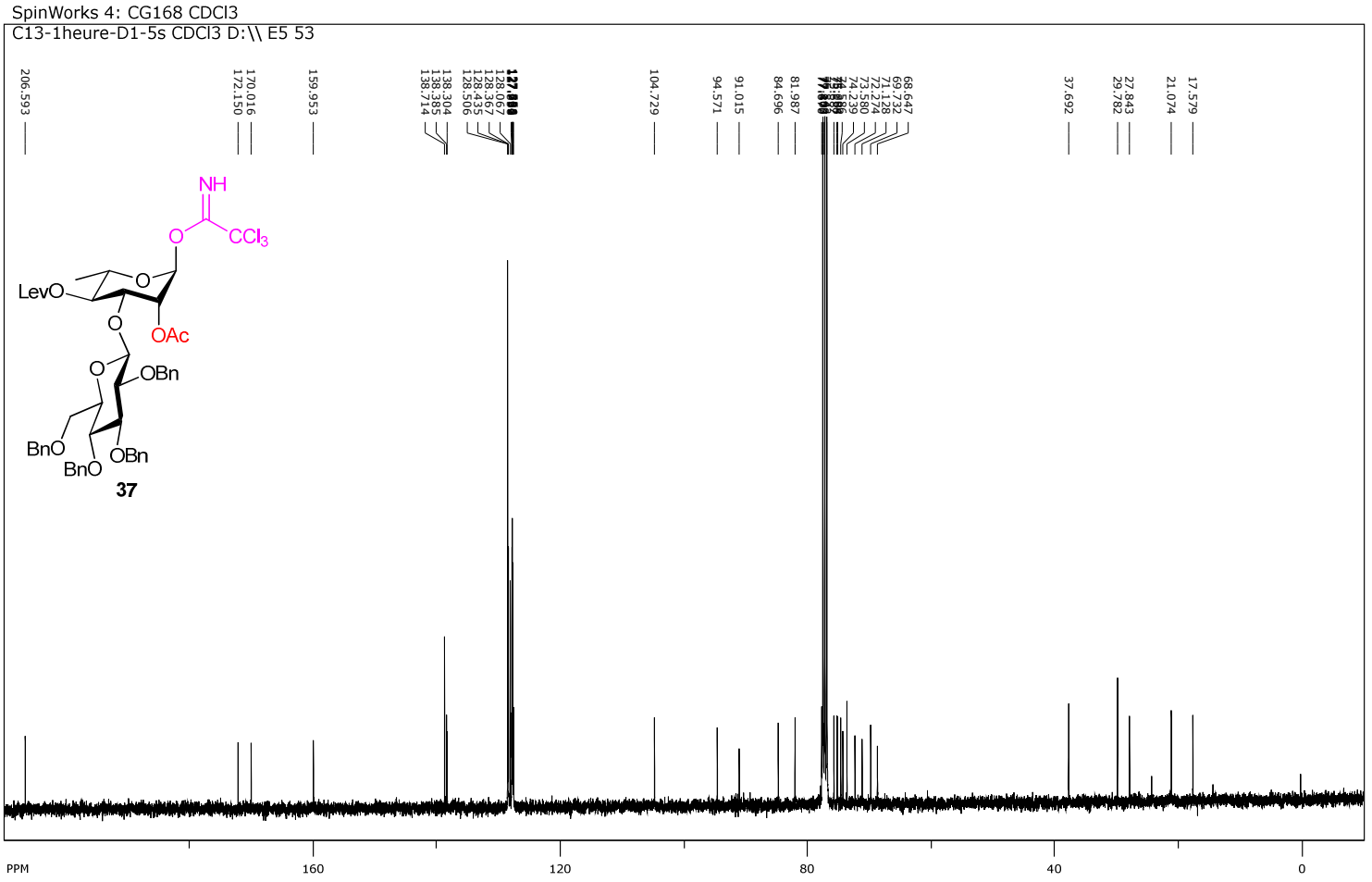
number of scans: 32

freq. of 0 ppm: 400.130010 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

Supplementary Figure 126 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 37.



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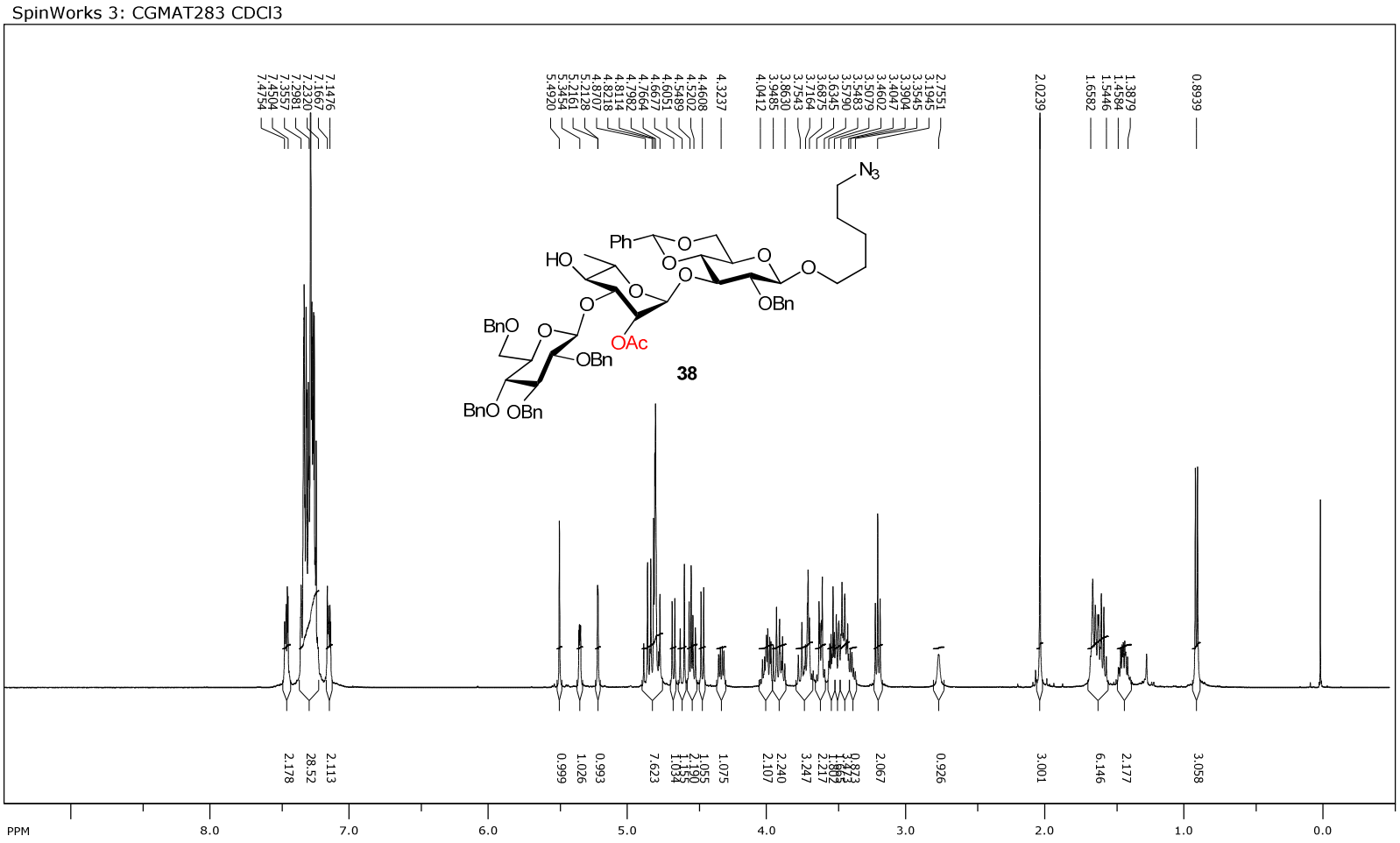
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612755 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

Supplementary Figure 127 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 38.



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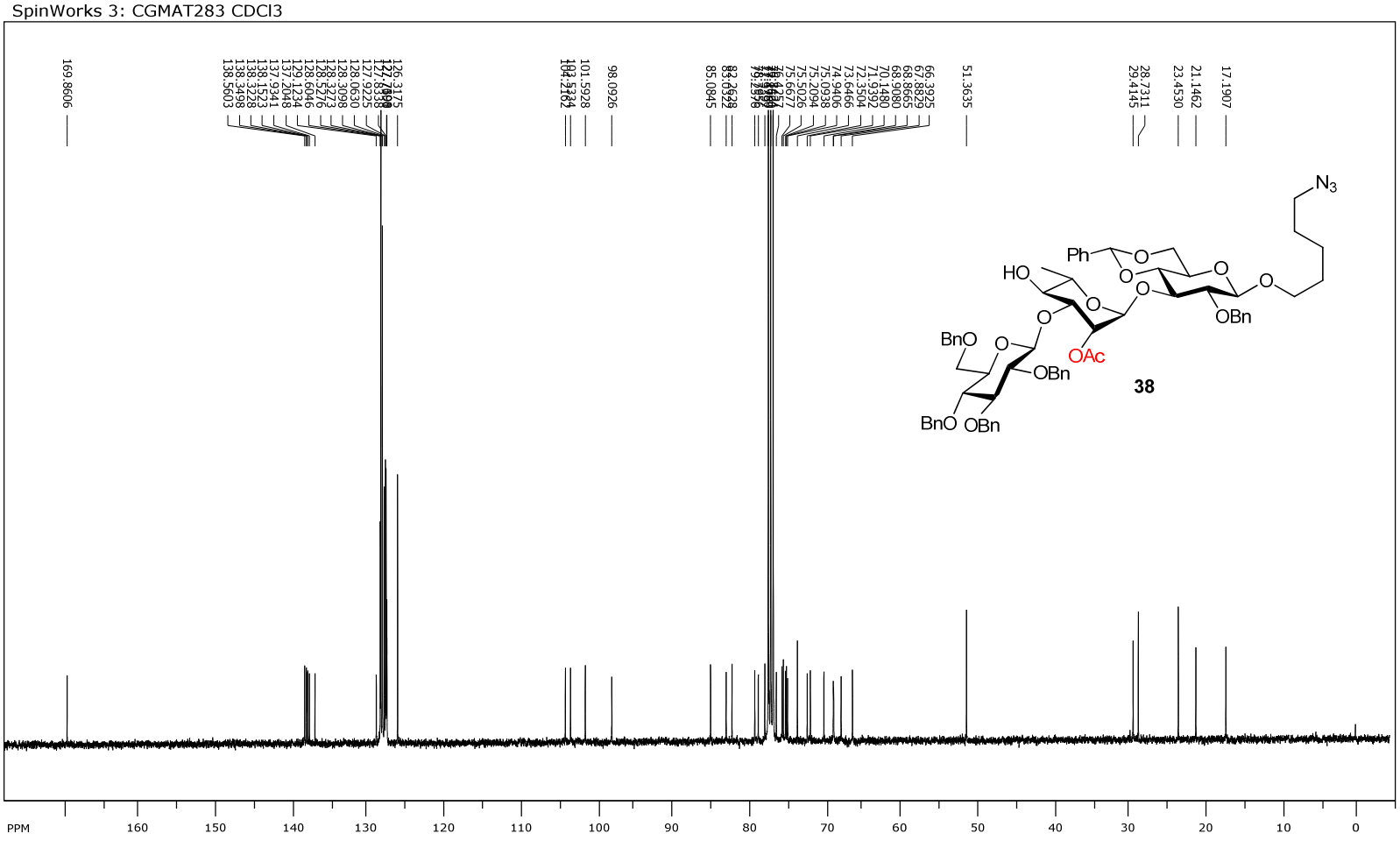
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130016 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 160.052 ppm/cm: 0.40000

Supplementary Figure 128 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 38.



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time domain size: 65536 points
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number of scans: 1024

freq. of 0 ppm: 100.612757 MHz
processed size: 32768 complex points
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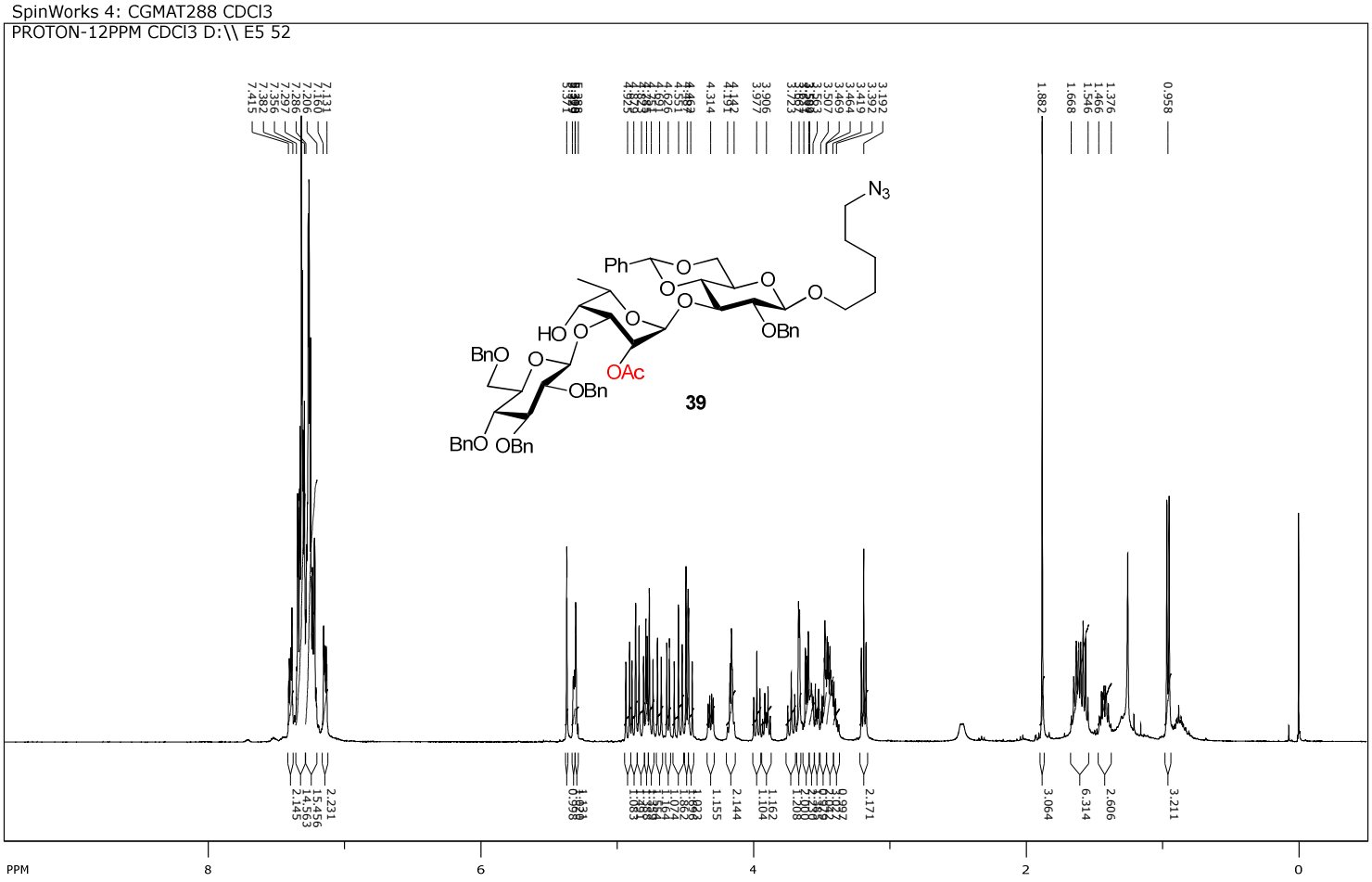
Hz/cm: 734.687 ppm/cm: 7.30140

Supplementary Figure 129 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 39.



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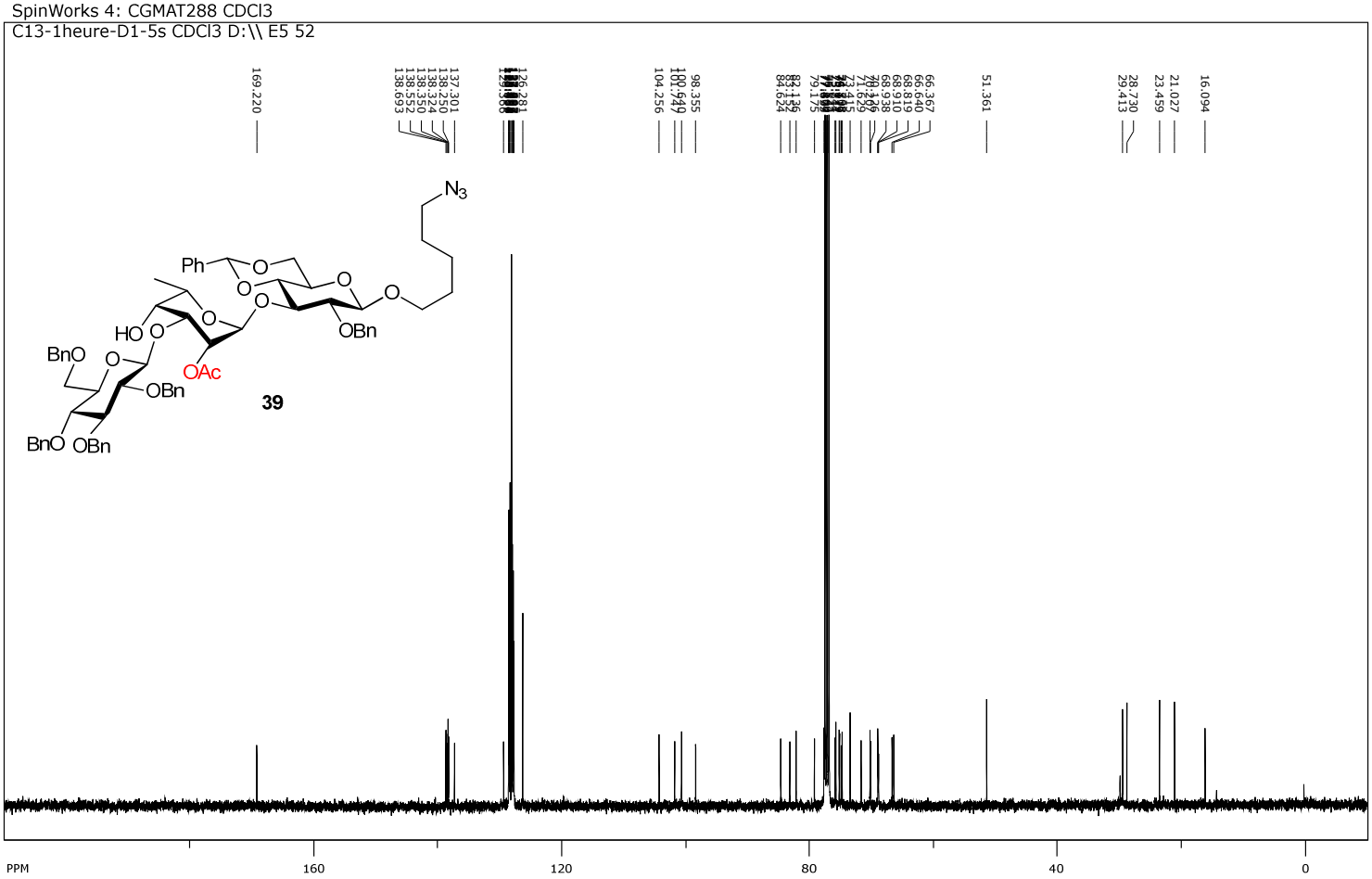
number of scans: 32

freq. of 0 ppm: 400.130014 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

Supplementary Figure 130 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 39.



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time domain size: 65536 points
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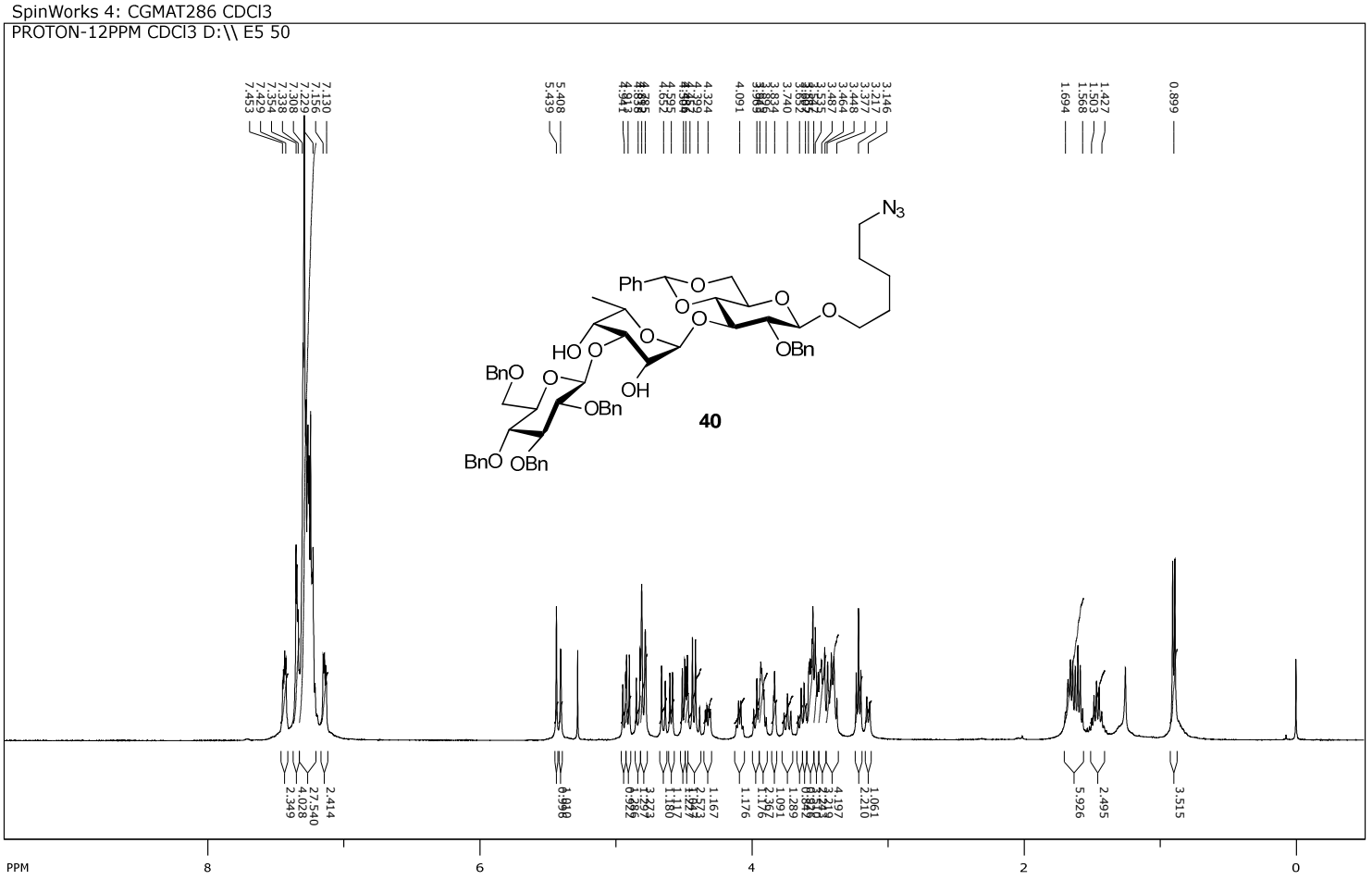
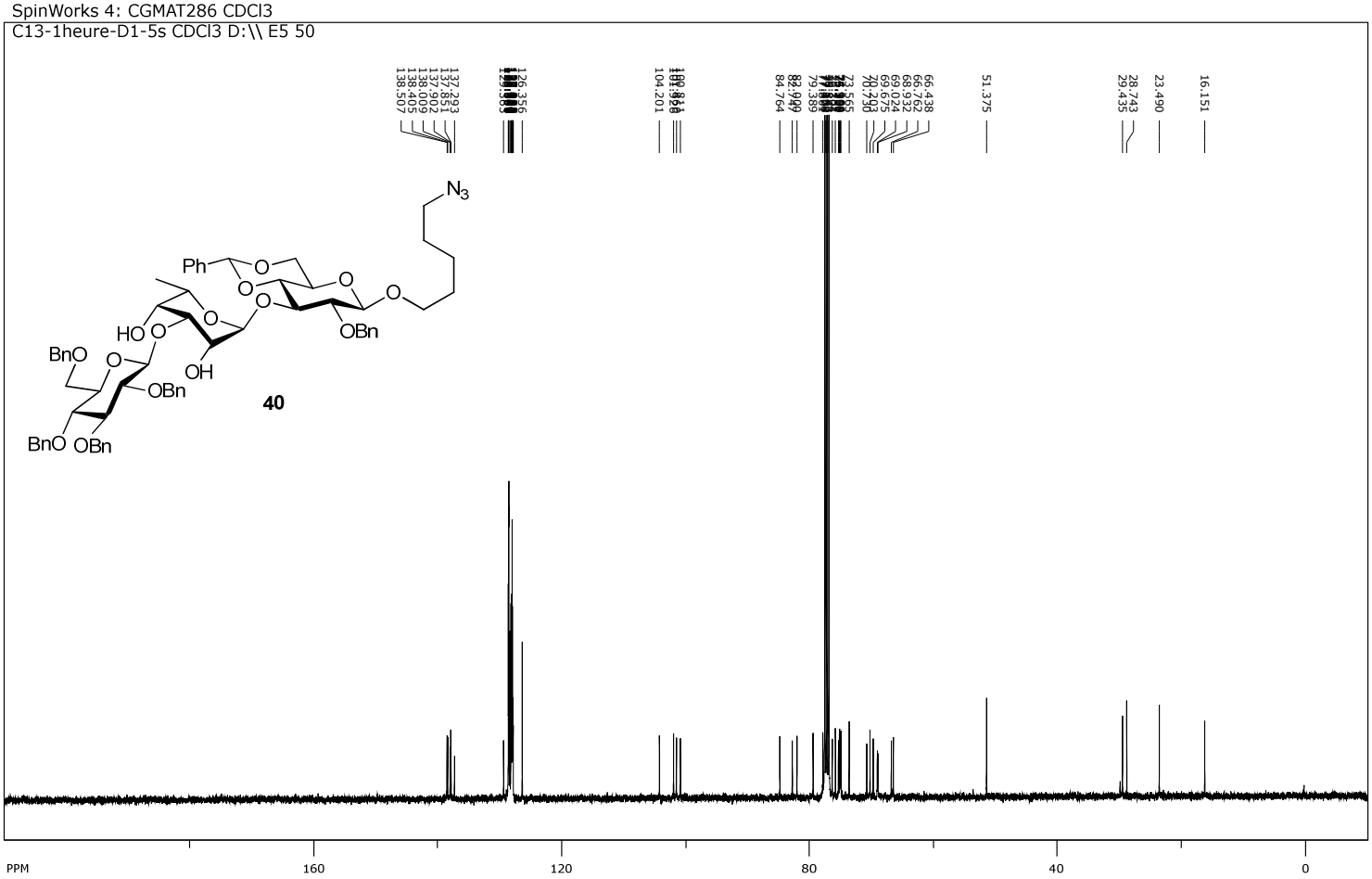
number of scans: 1024

freq. of 0 ppm: 100.612756 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

Supplementary Figure 131 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 40.



Supplementary Figure 132 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 40.



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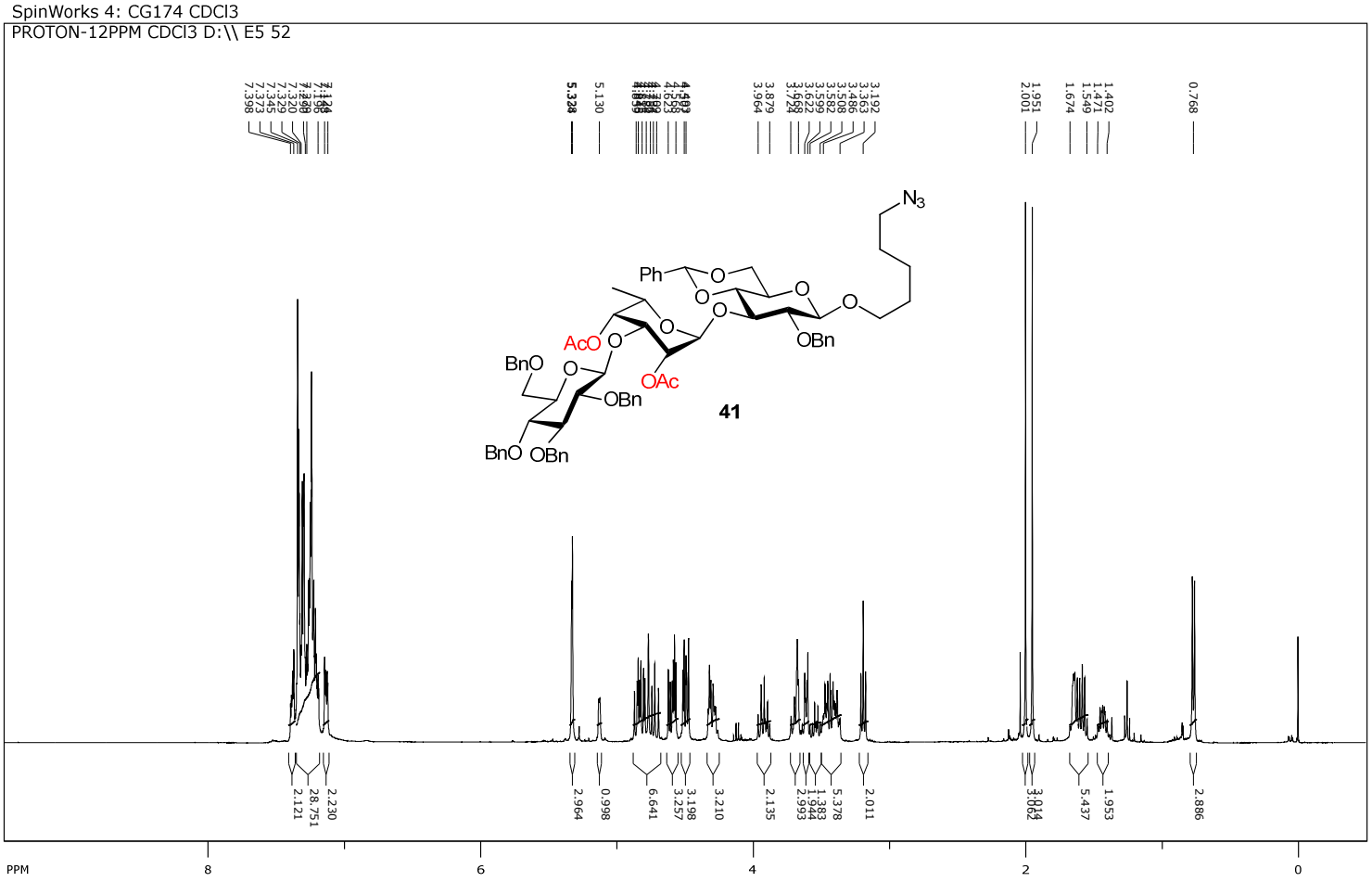
number of scans: 1024

freq. of 0 ppm: 100.612758 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

Supplementary Figure 133 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound 41.



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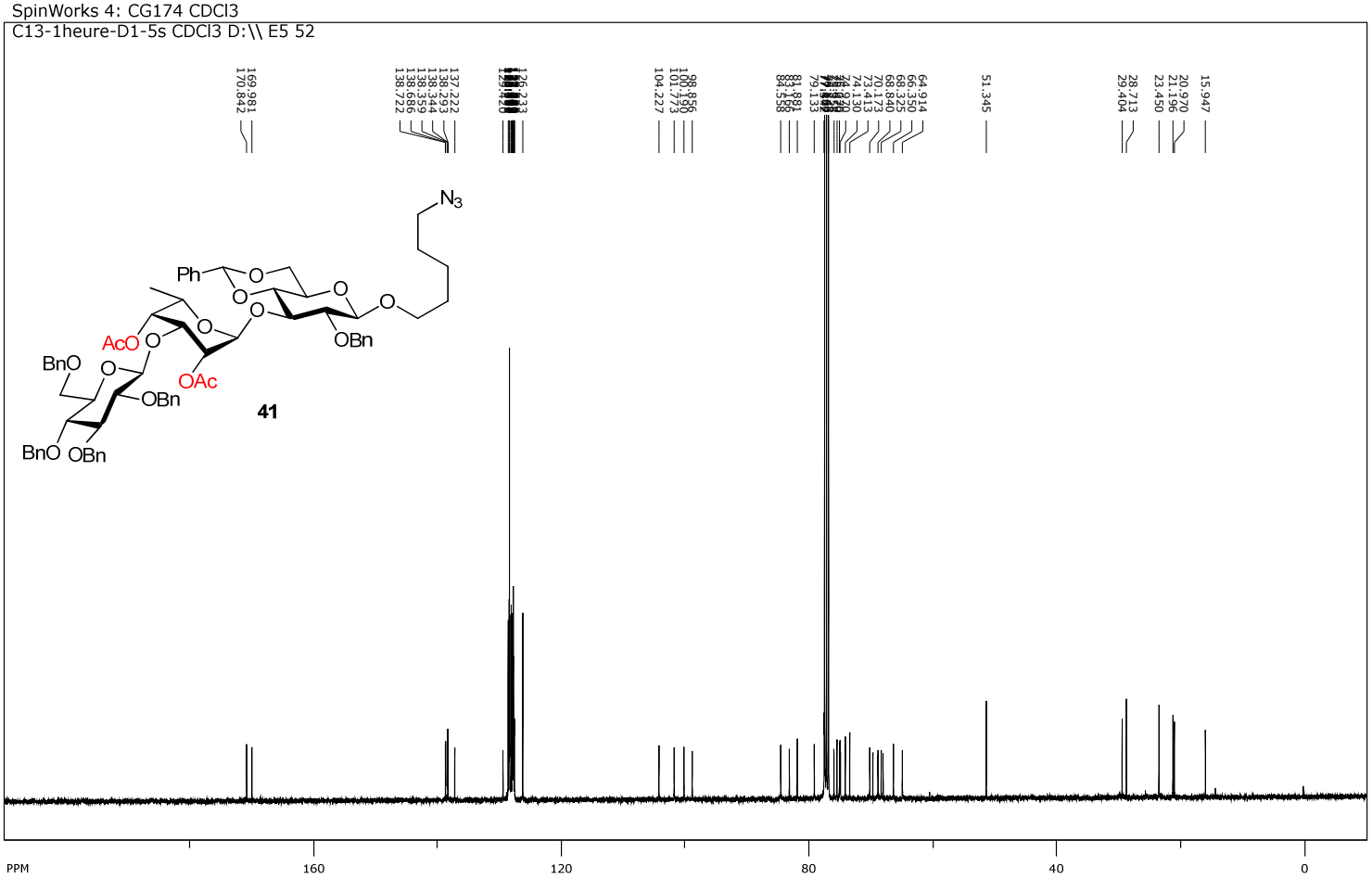
time domain size: 32768 points
width: 4807.69 Hz = 12.0153 ppm = 0.146719 Hz/pt
number of scans: 32

freq. of 0 ppm: 400.130016 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

Supplementary Figure 134 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound 41.



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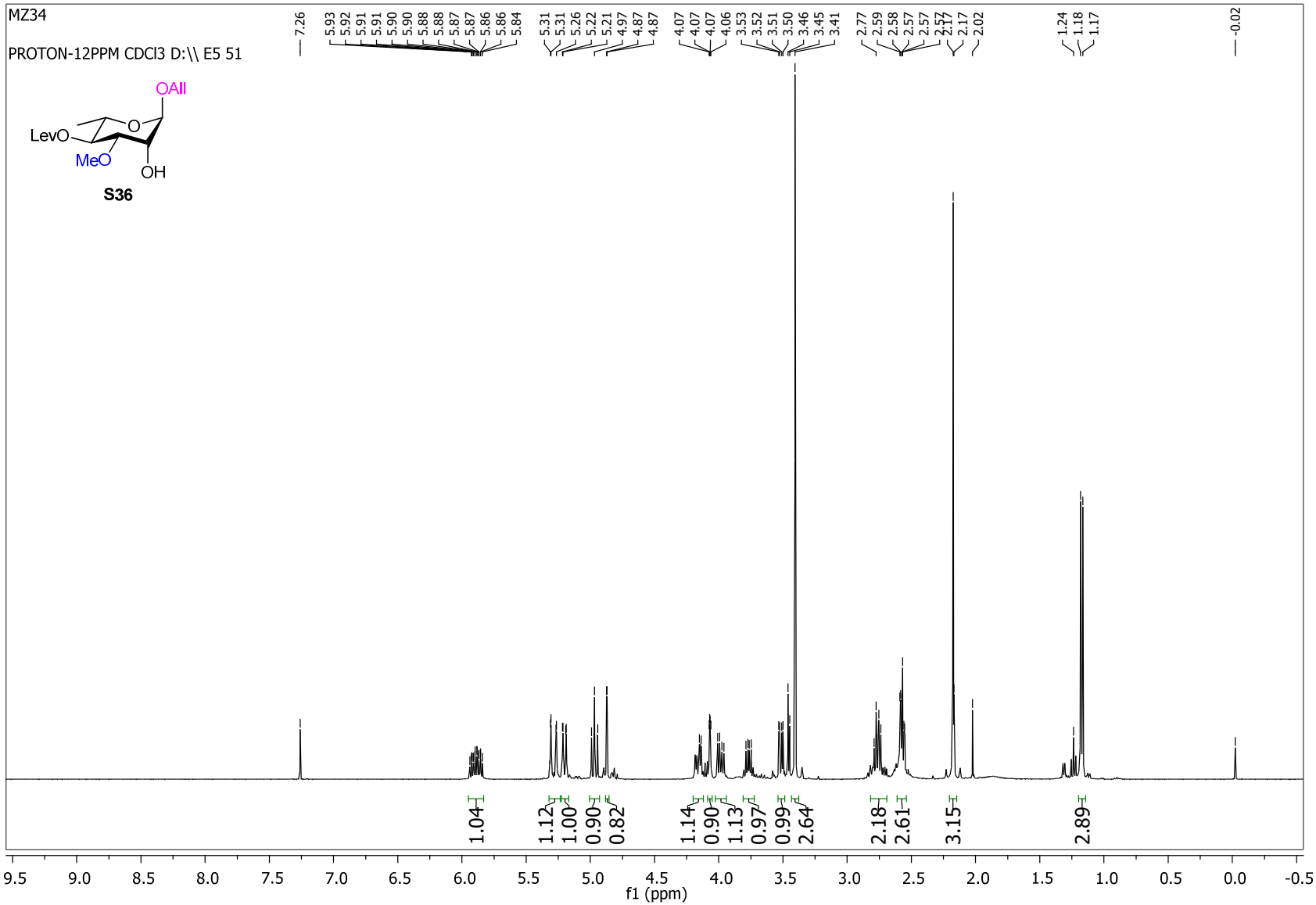
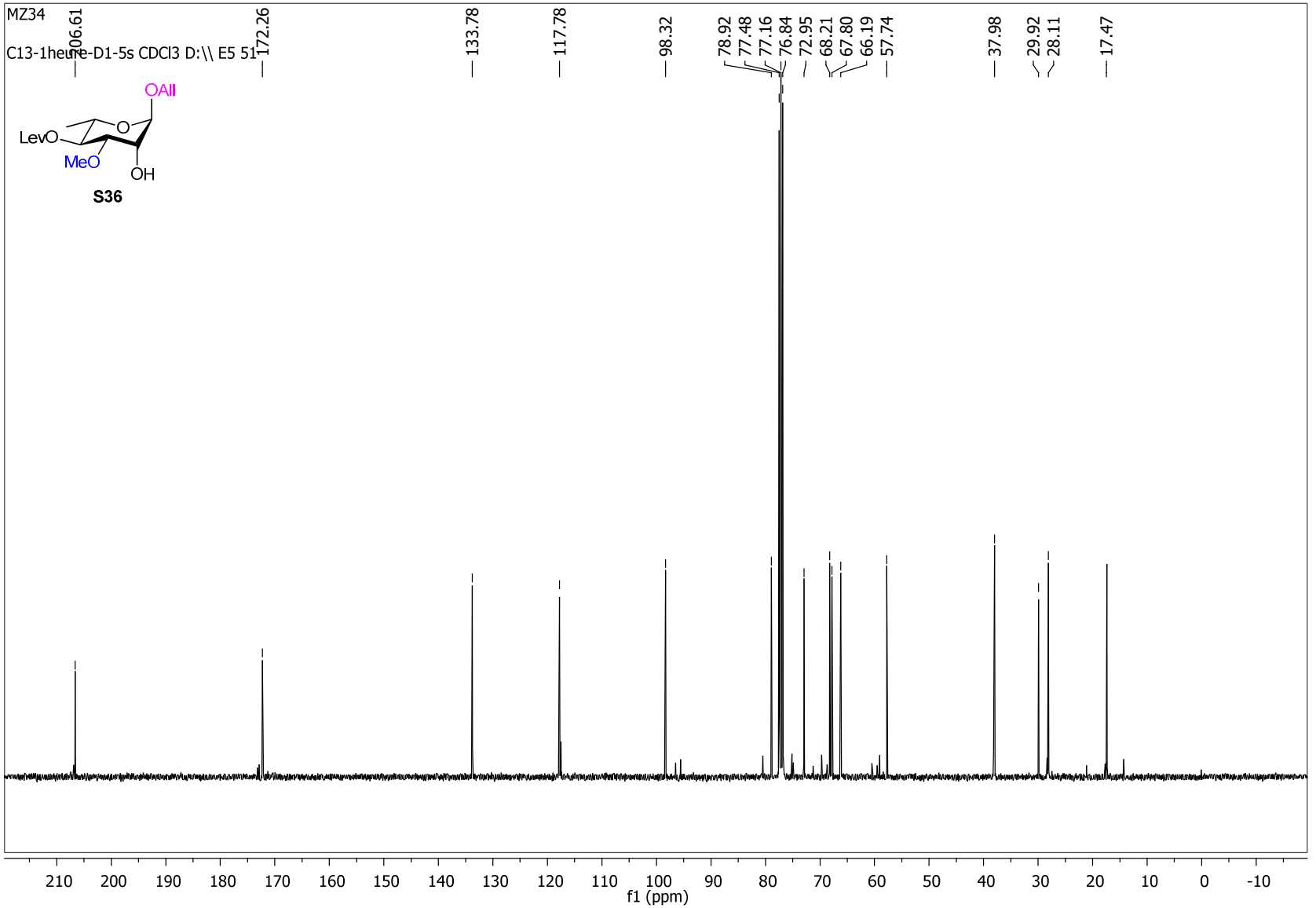
time domain size: 65536 points
width: 24038.46 Hz = 238.8967 ppm = 0.366798 Hz/pt
number of scans: 1024

freq. of 0 ppm: 100.612759 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

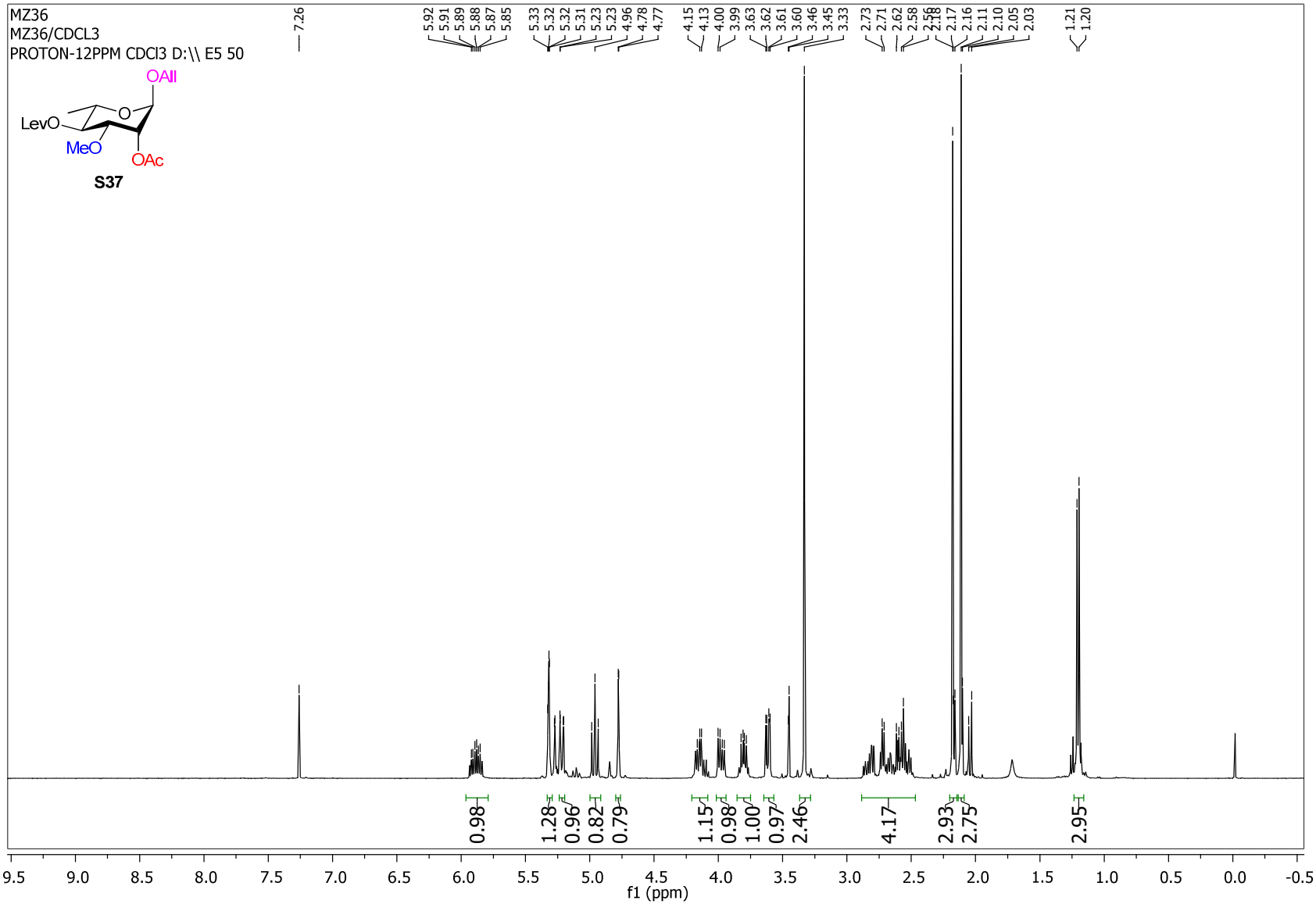
Supplementary Figure 135 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S36.



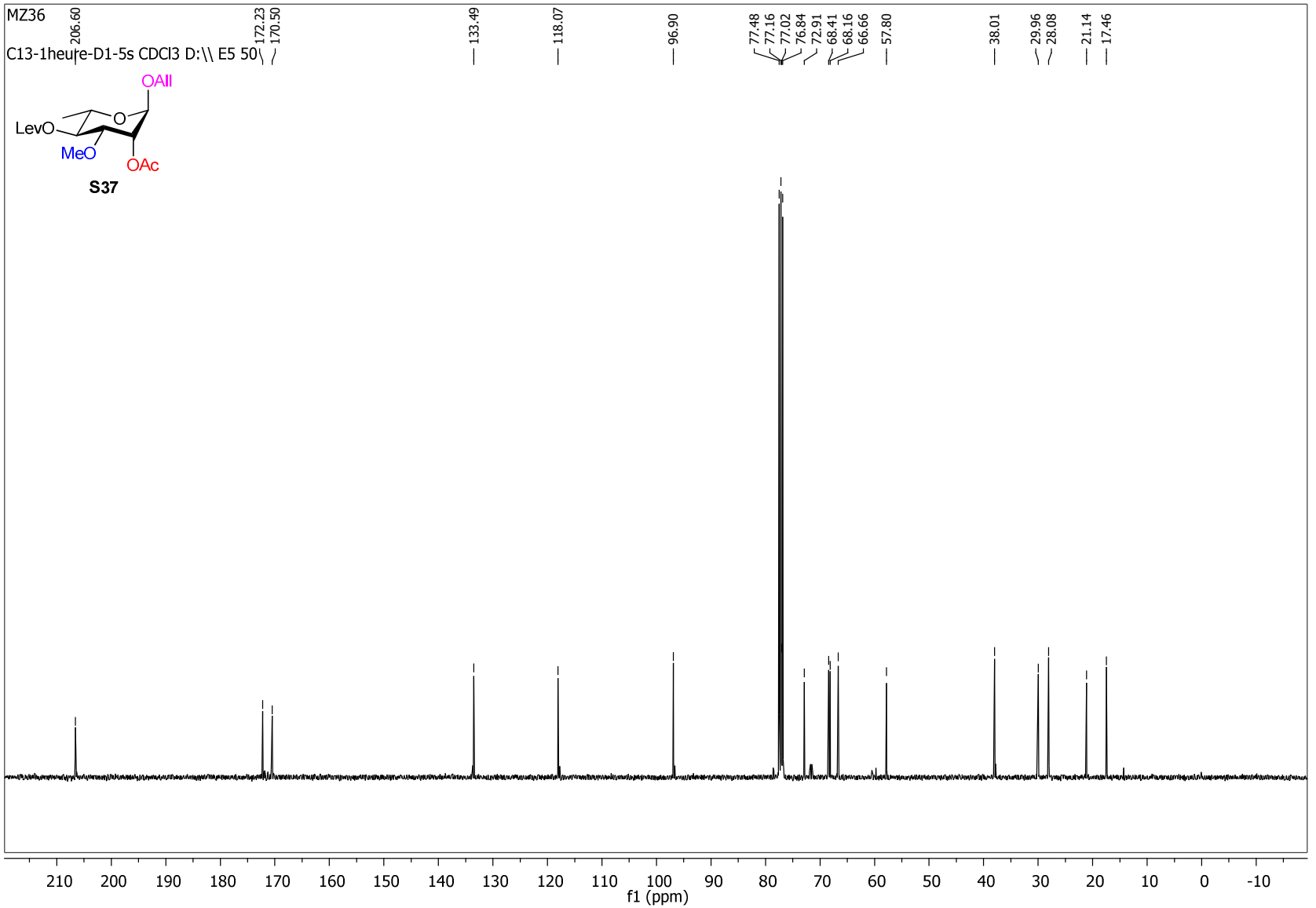
Supplementary Figure 136 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S36.



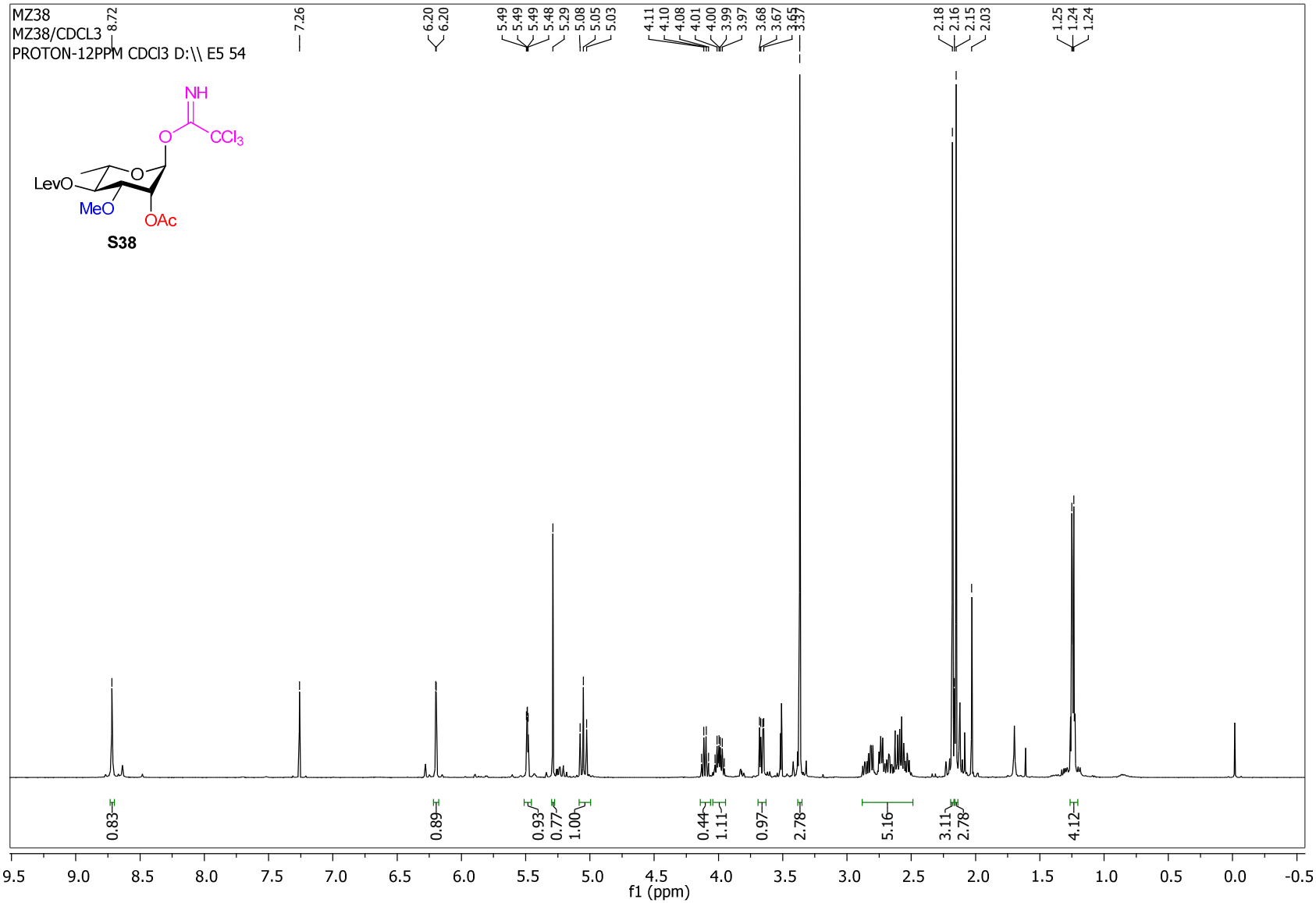
Supplementary Figure 137 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S37.



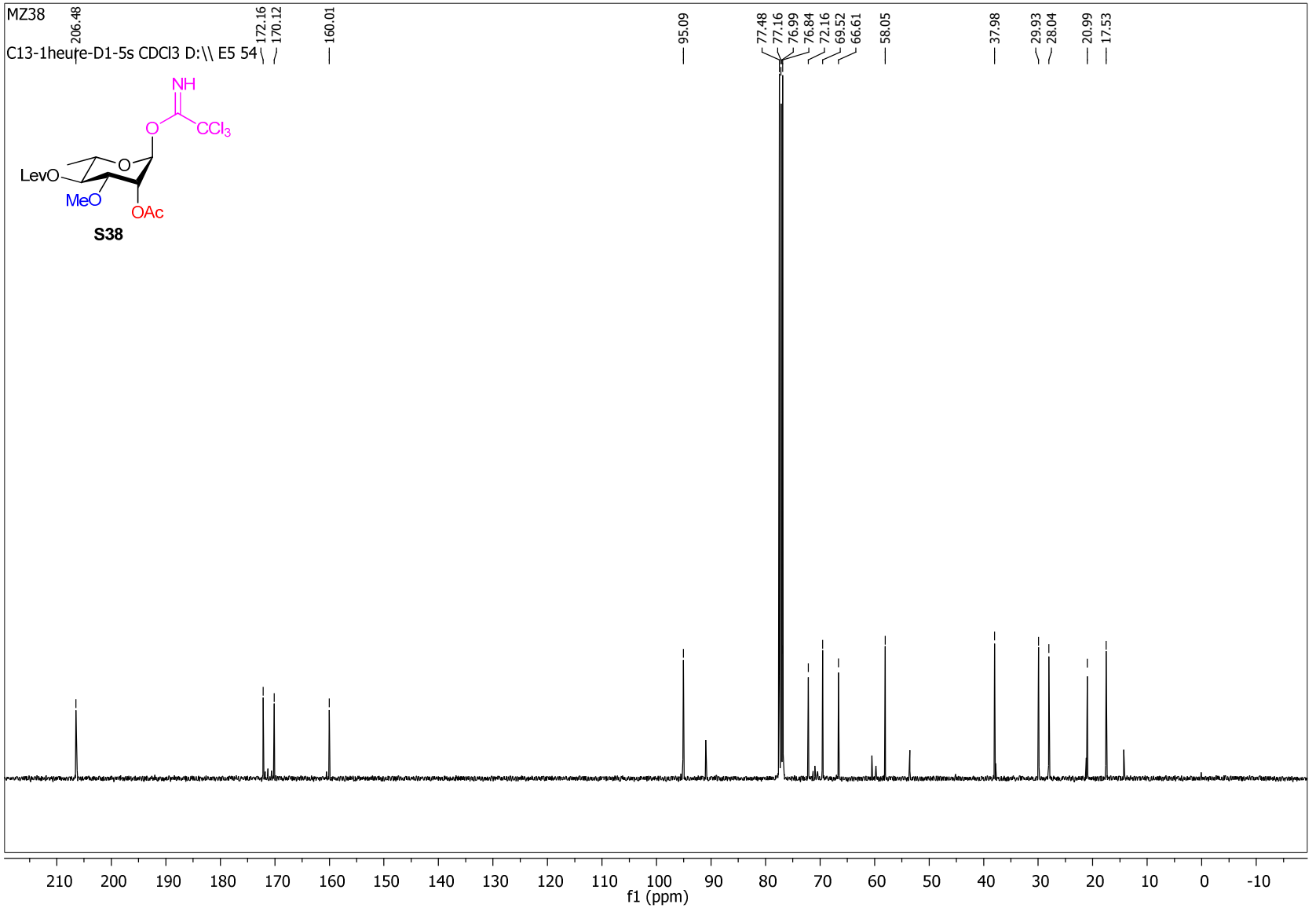
Supplementary Figure 138 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S37.



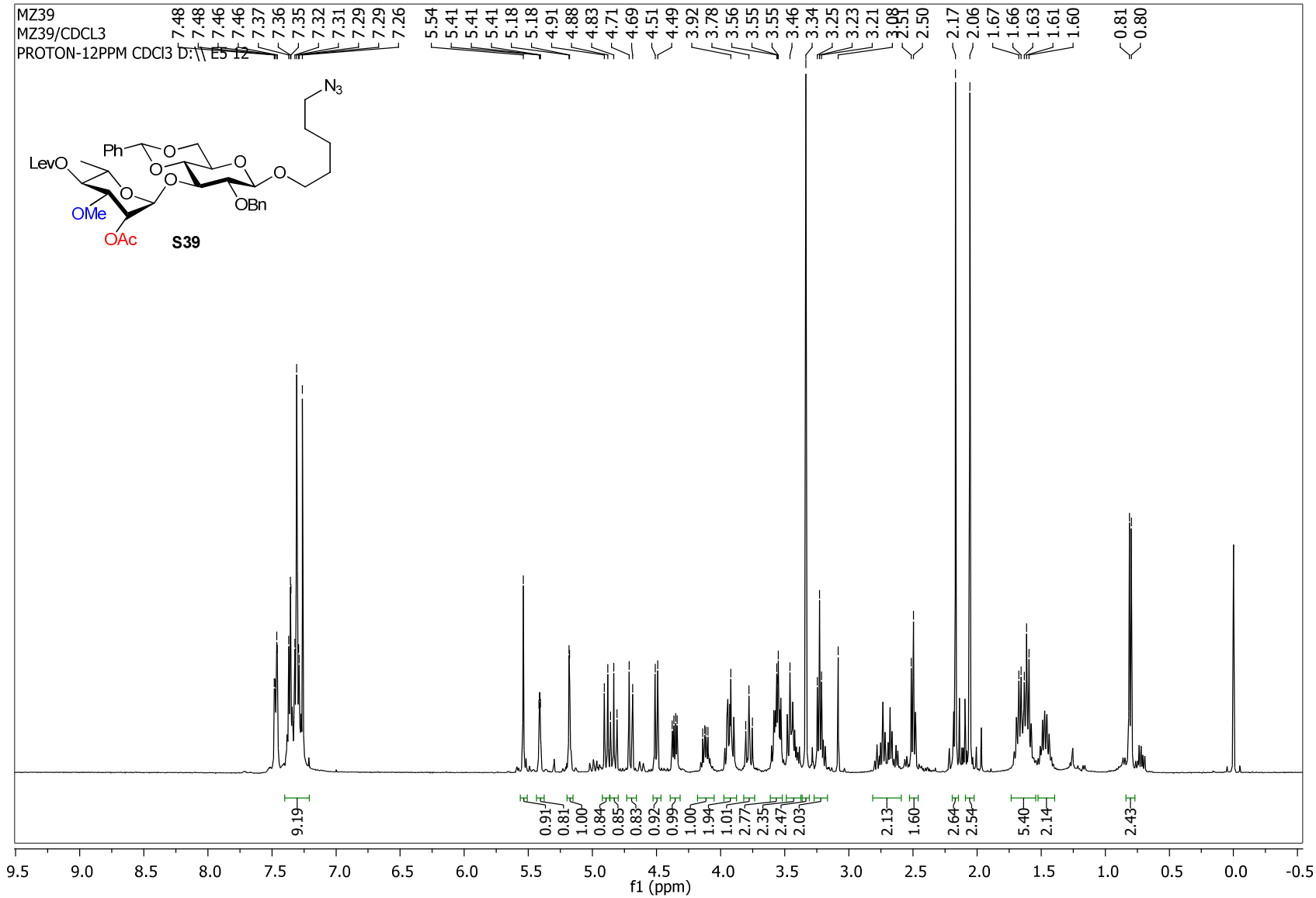
Supplementary Figure 139 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S38.



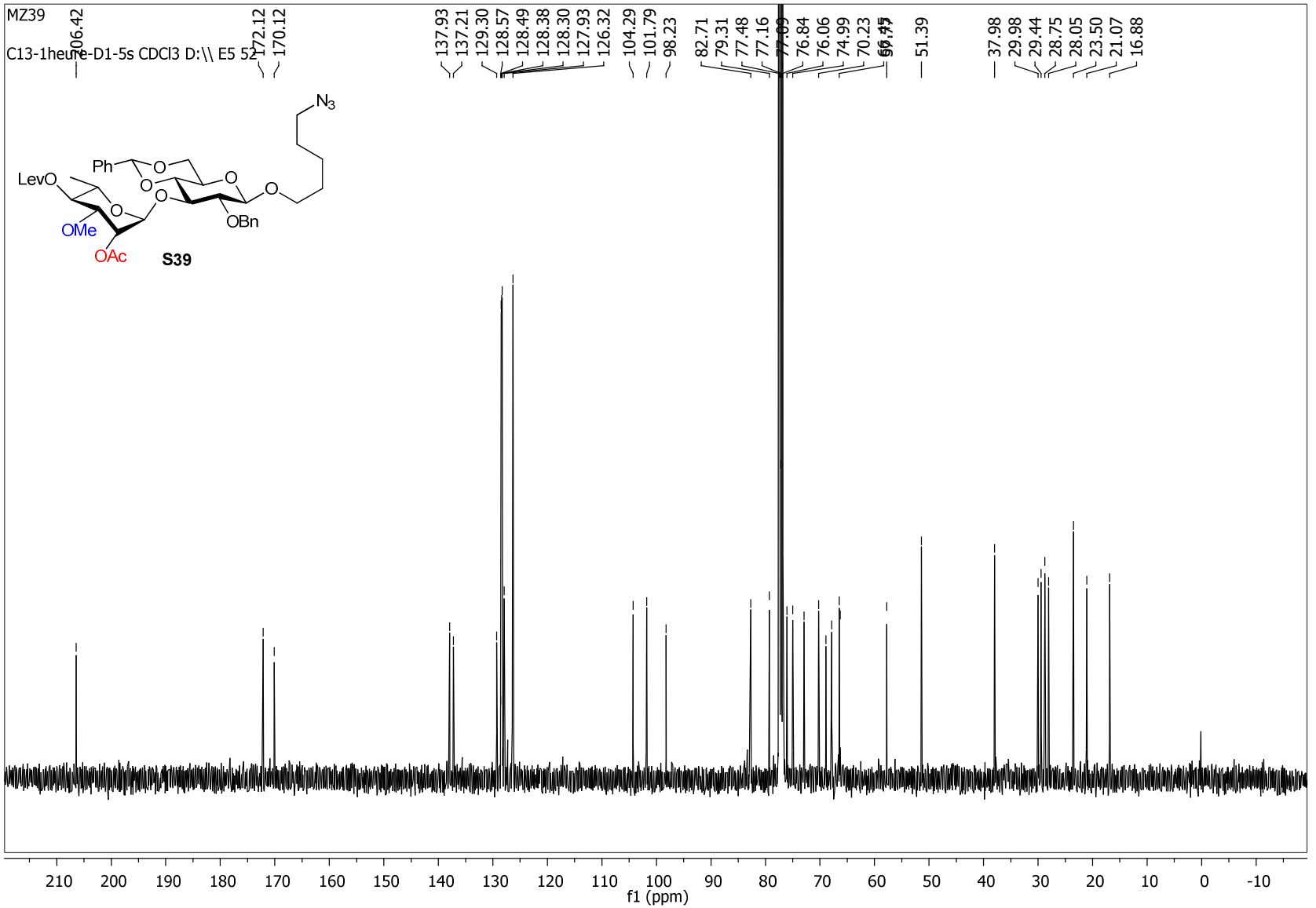
Supplementary Figure 140 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S38.



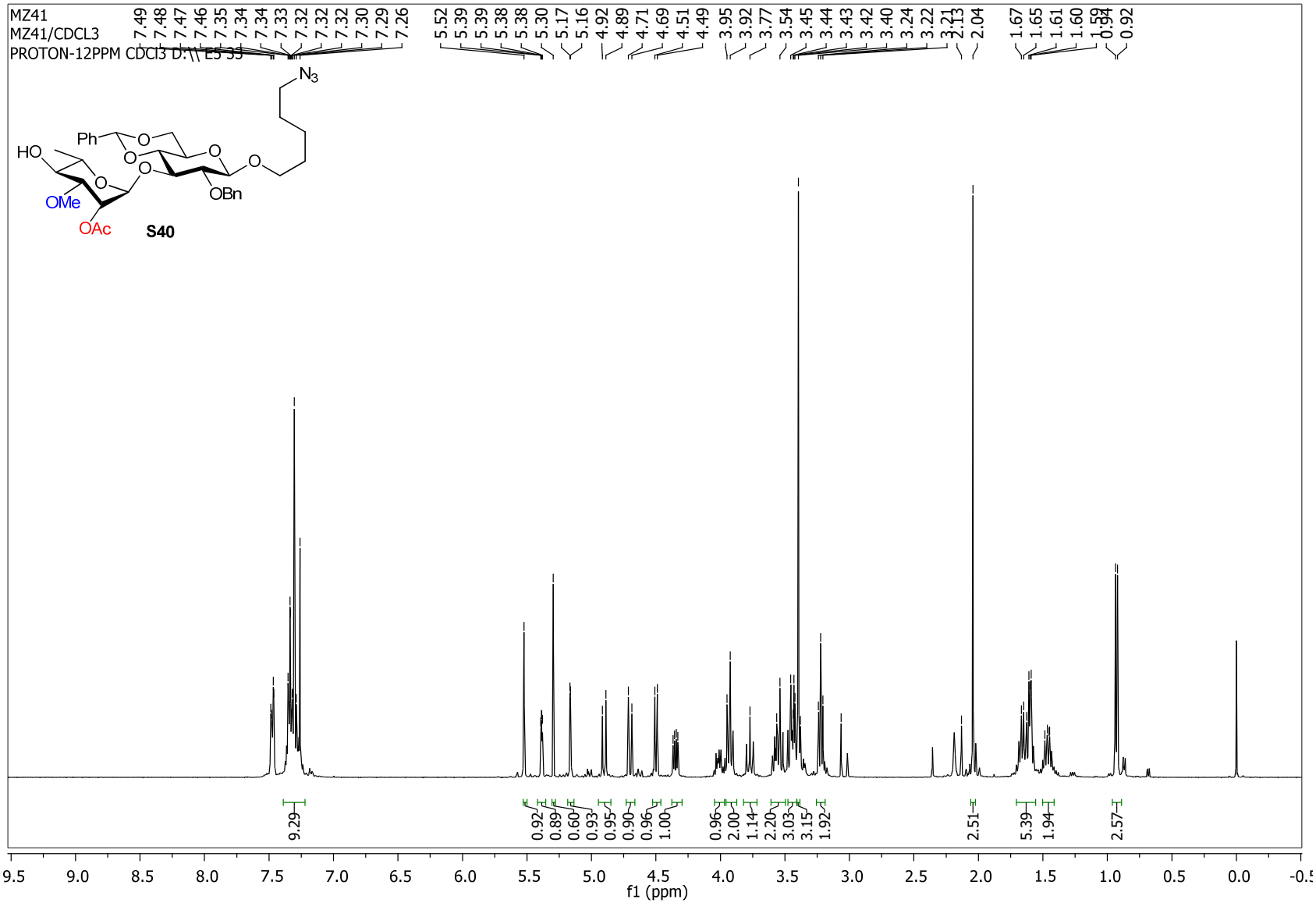
Supplementary Figure 141 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S39.



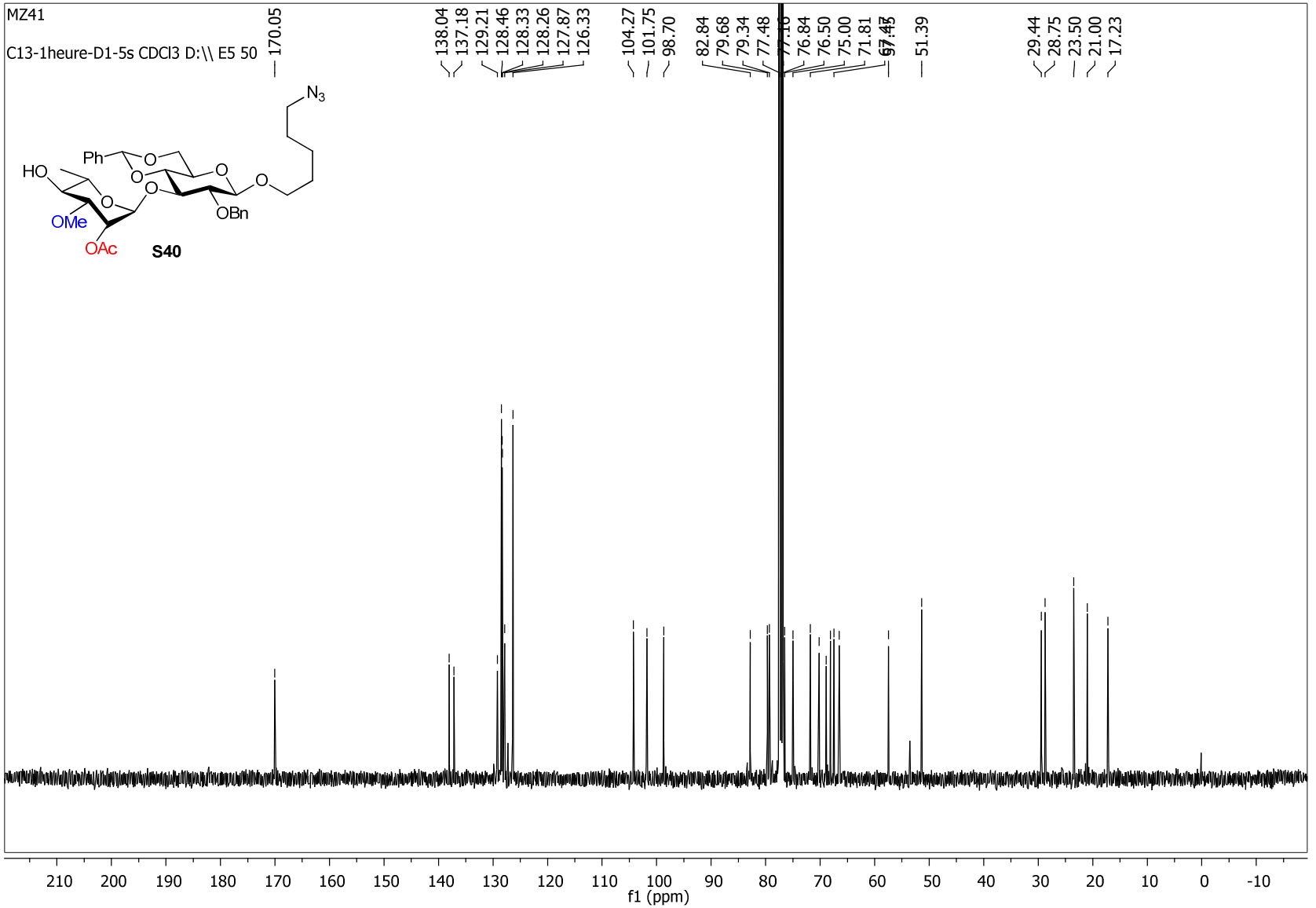
Supplementary Figure 142 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S39.



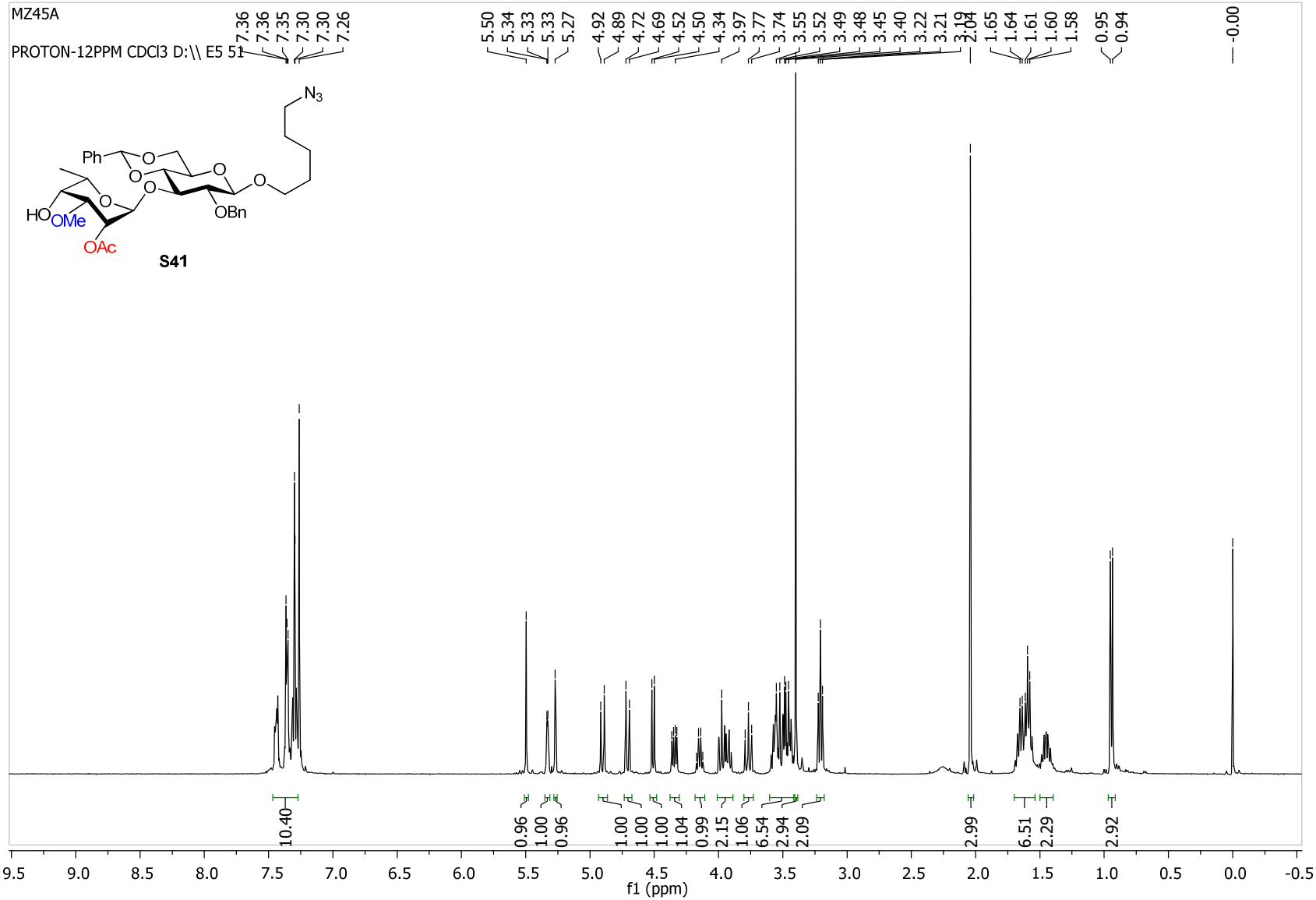
Supplementary Figure 143 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S40.



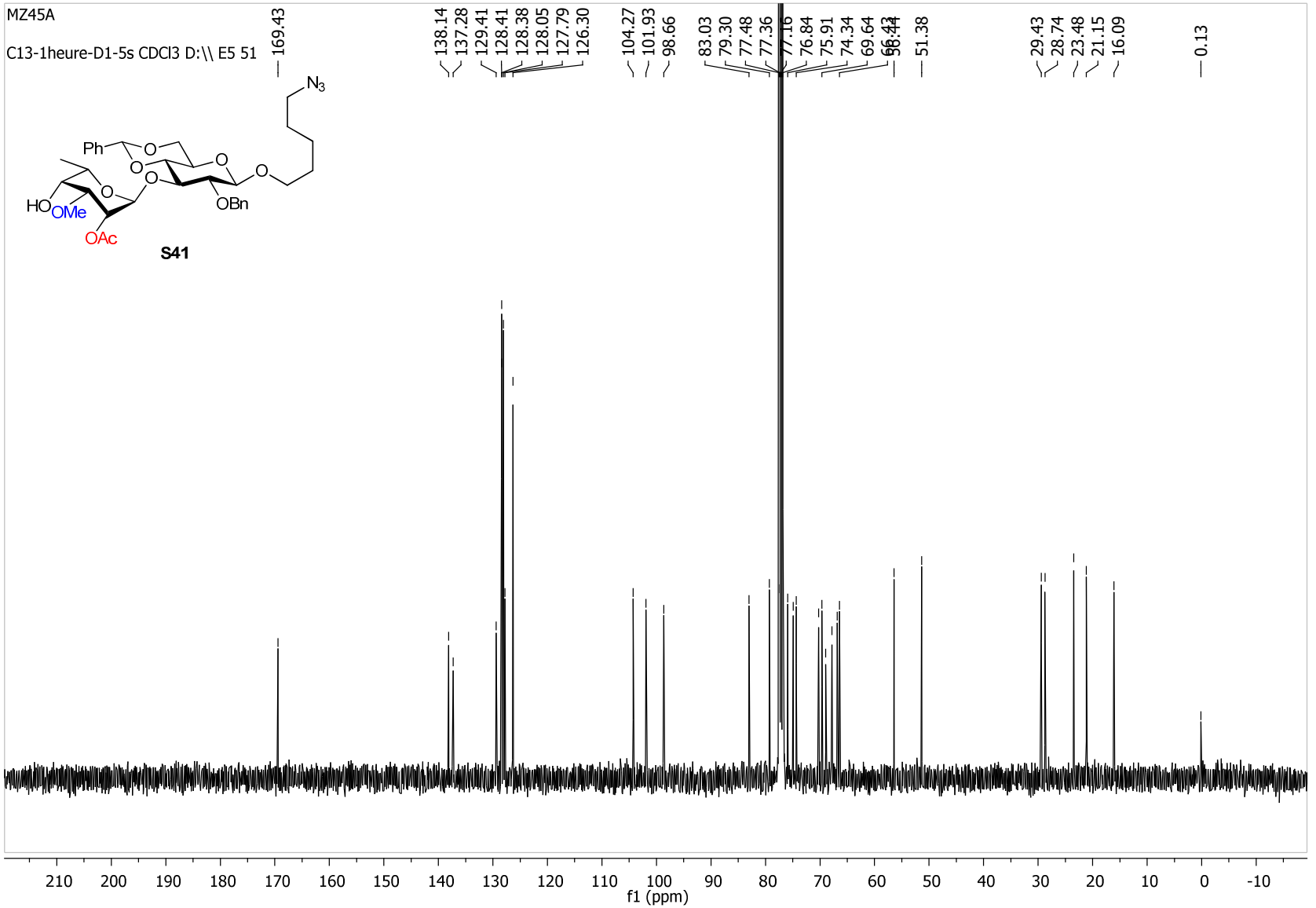
Supplementary Figure 144 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S40.



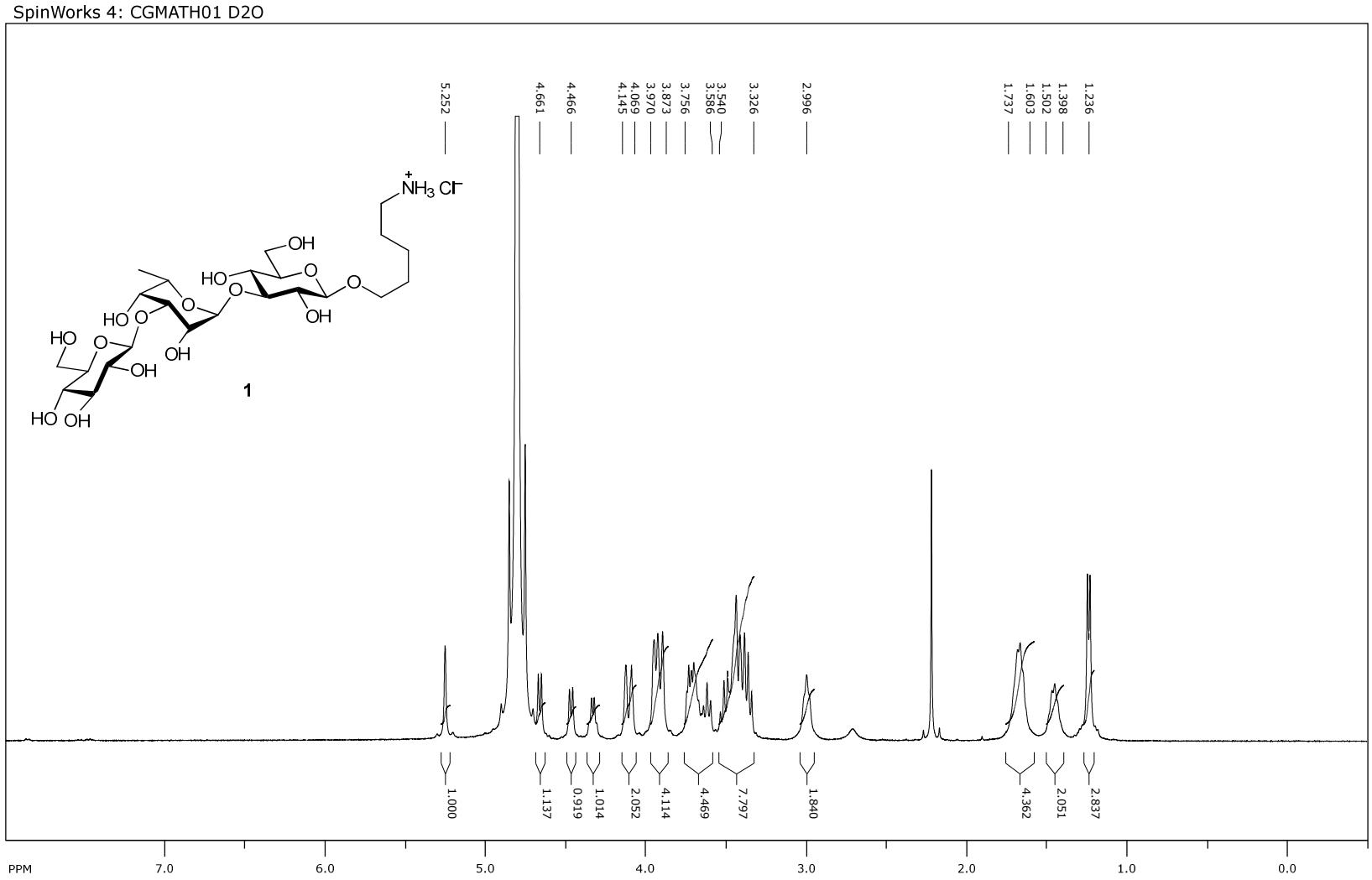
Supplementary Figure 145 | ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of compound S41.



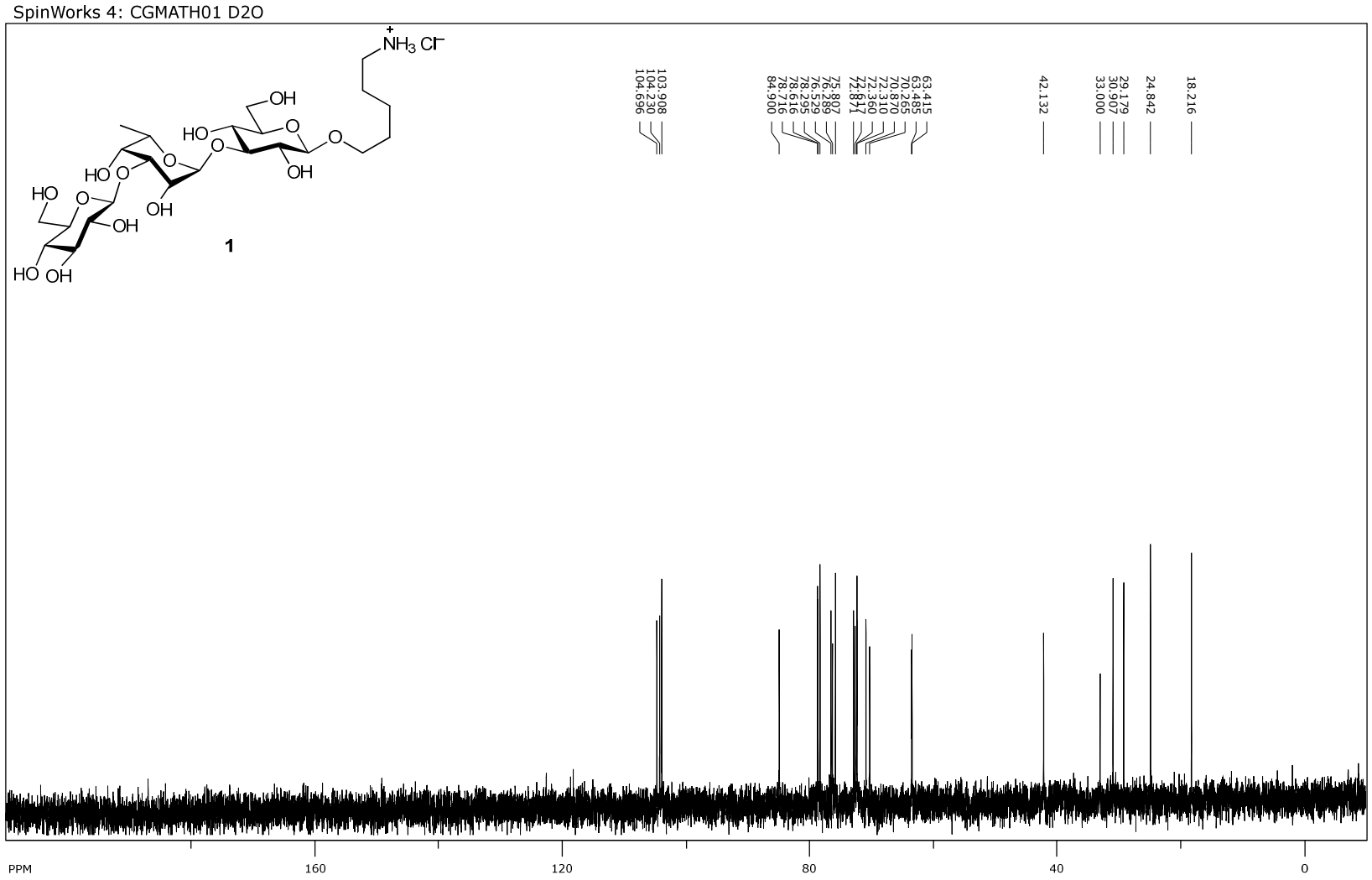
Supplementary Figure 146 | ^{13}C NMR spectra ($CDCl_3$, 100 MHz) of compound S41.



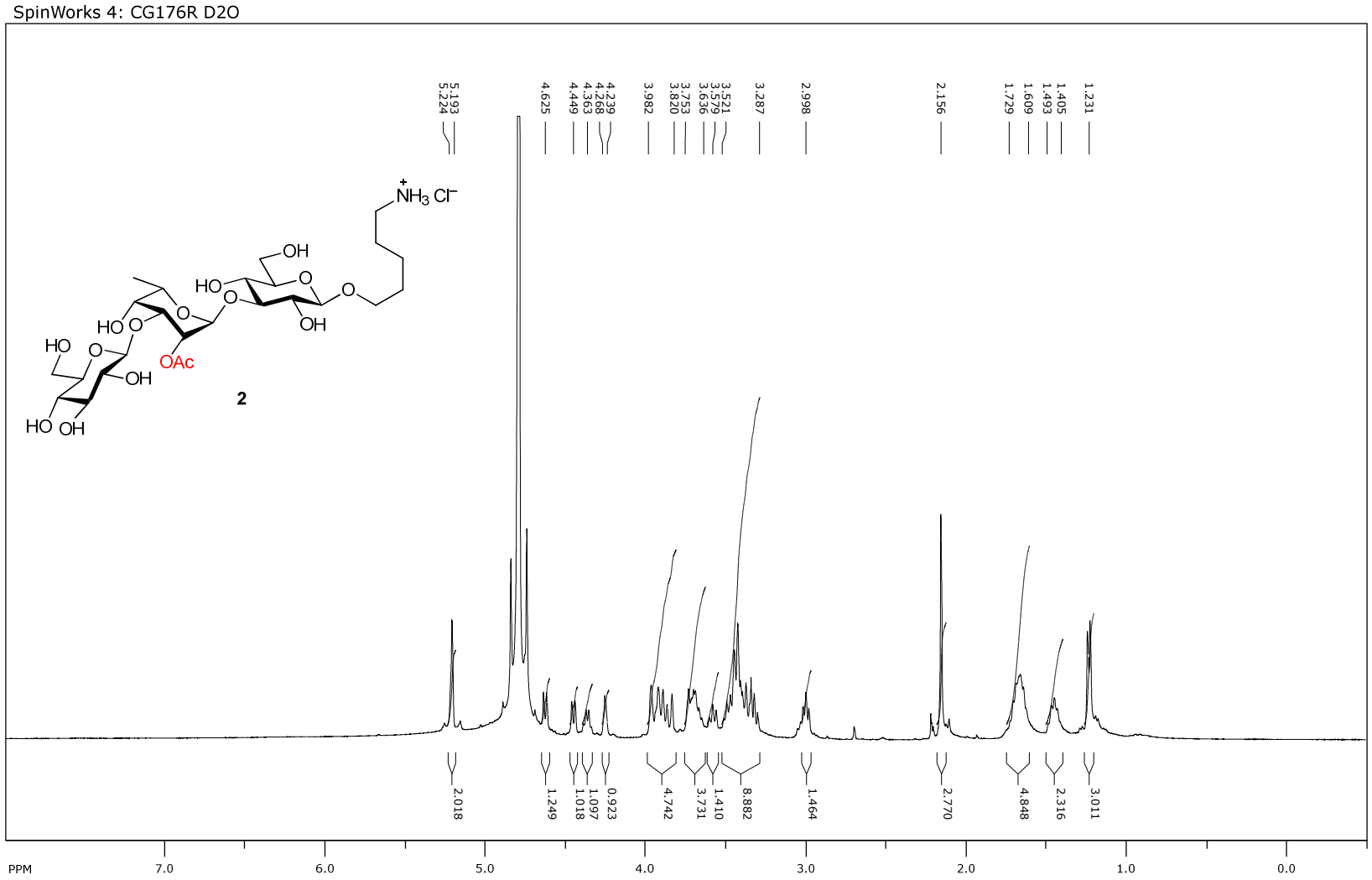
Supplementary Figure 147 | ^{1}H NMR spectra (D_2O + acetone, 400 MHz) of compound 1.



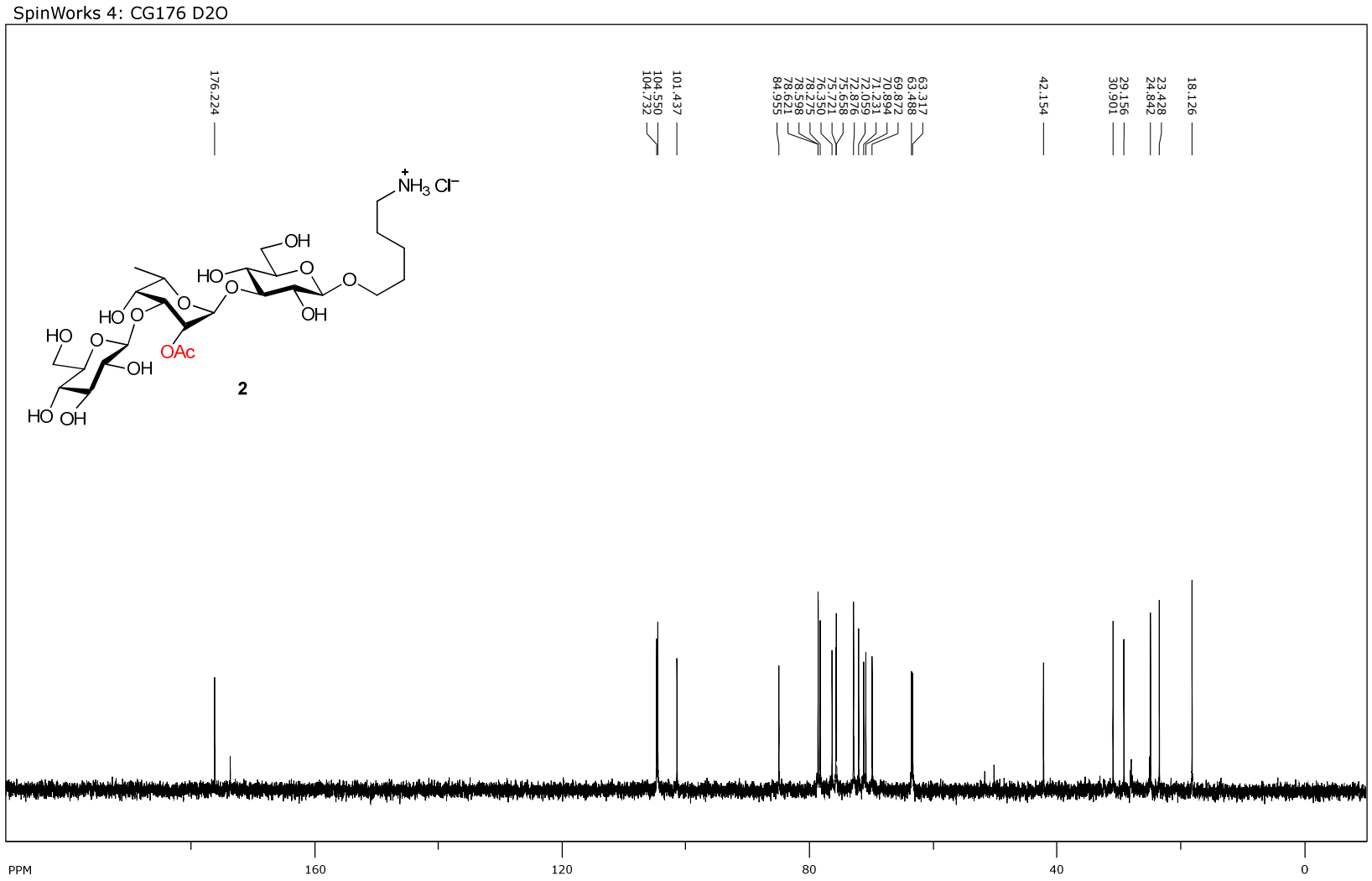
Supplementary Figure 148 | ^{13}C NMR spectra (D_2O + acetone, 100 MHz) of compound 1.



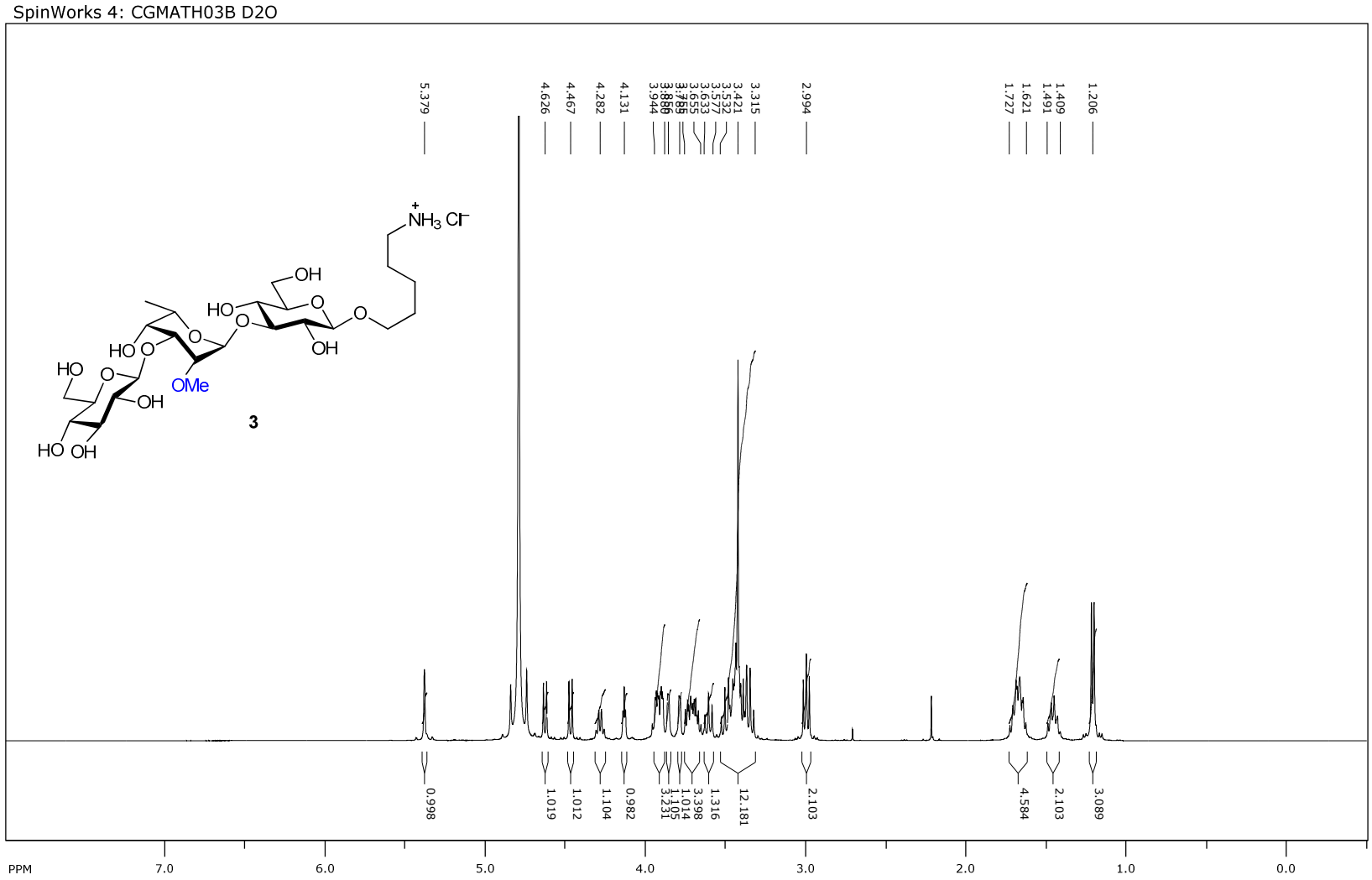
Supplementary Figure 149 | ^{1}H NMR spectra (D_2O + acetone, 400 MHz) of compound 2.



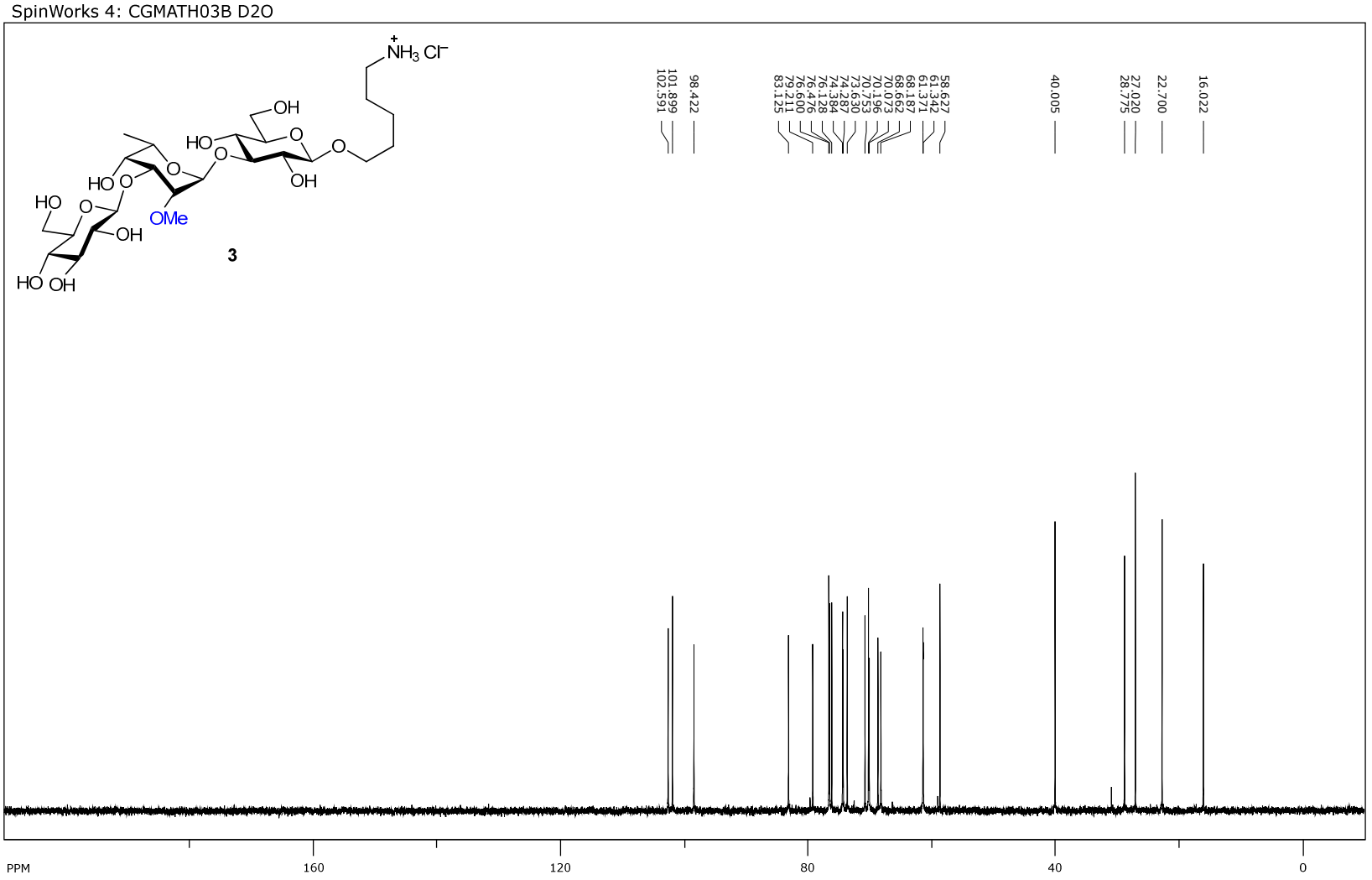
Supplementary Figure 150 | ^{13}C NMR spectra (D_2O + acetone, 100 MHz) of compound 2.



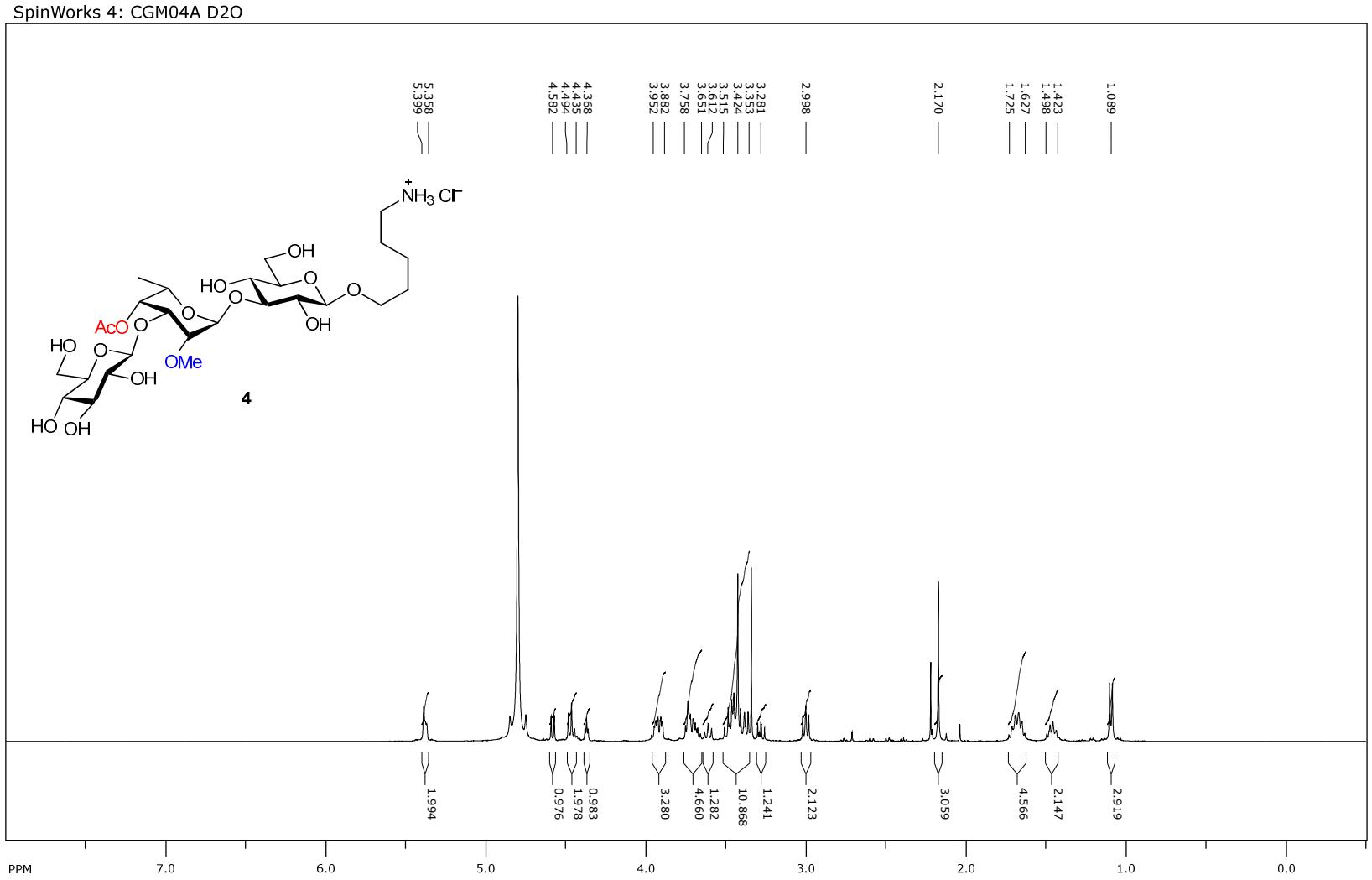
Supplementary Figure 151 | ^{1}H NMR spectra (D_2O + acetone, 400 MHz) of compound 3.



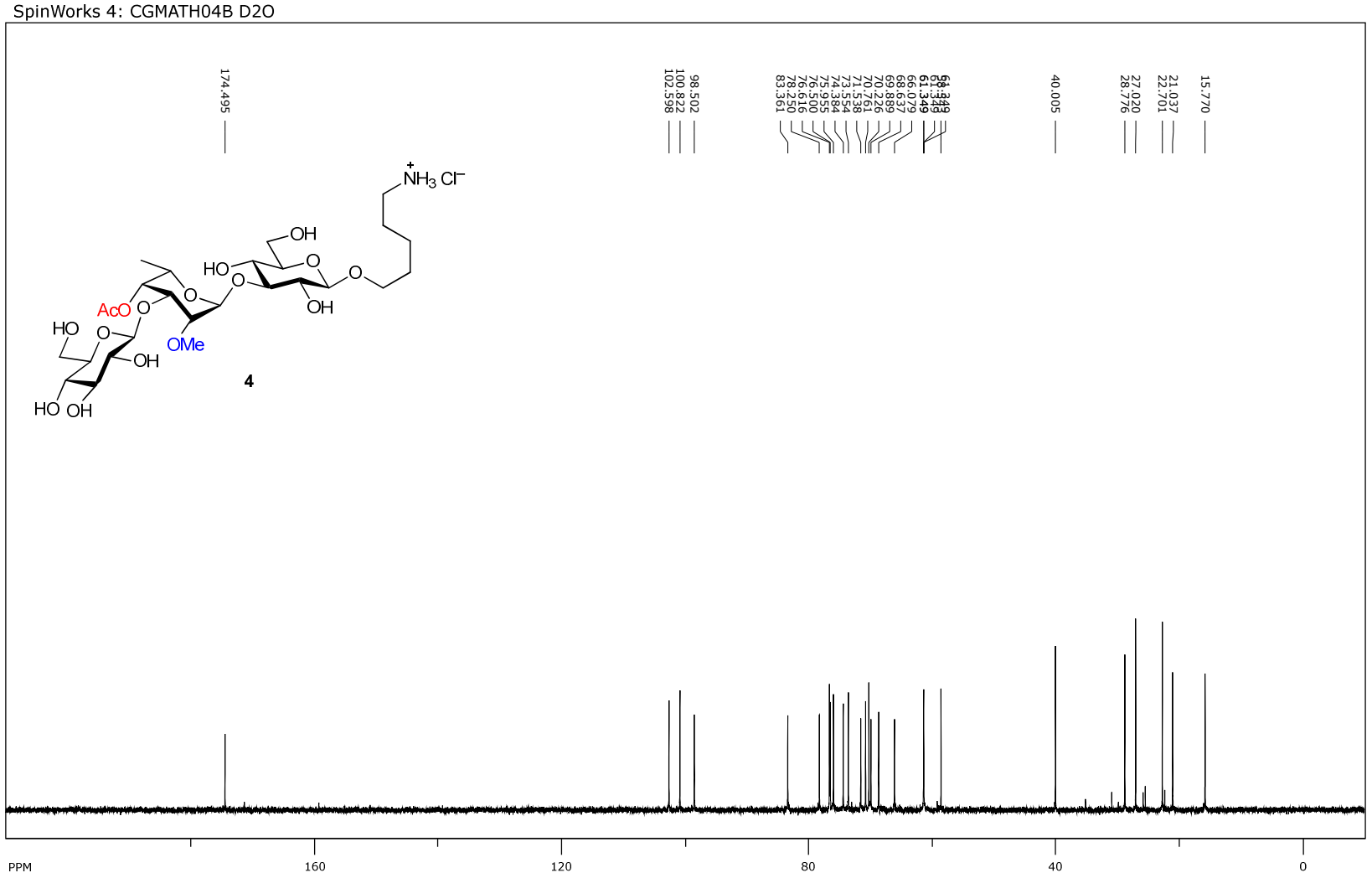
Supplementary Figure 152 | ^{13}C NMR spectra (D_2O + acetone, 100 MHz) of compound 3.



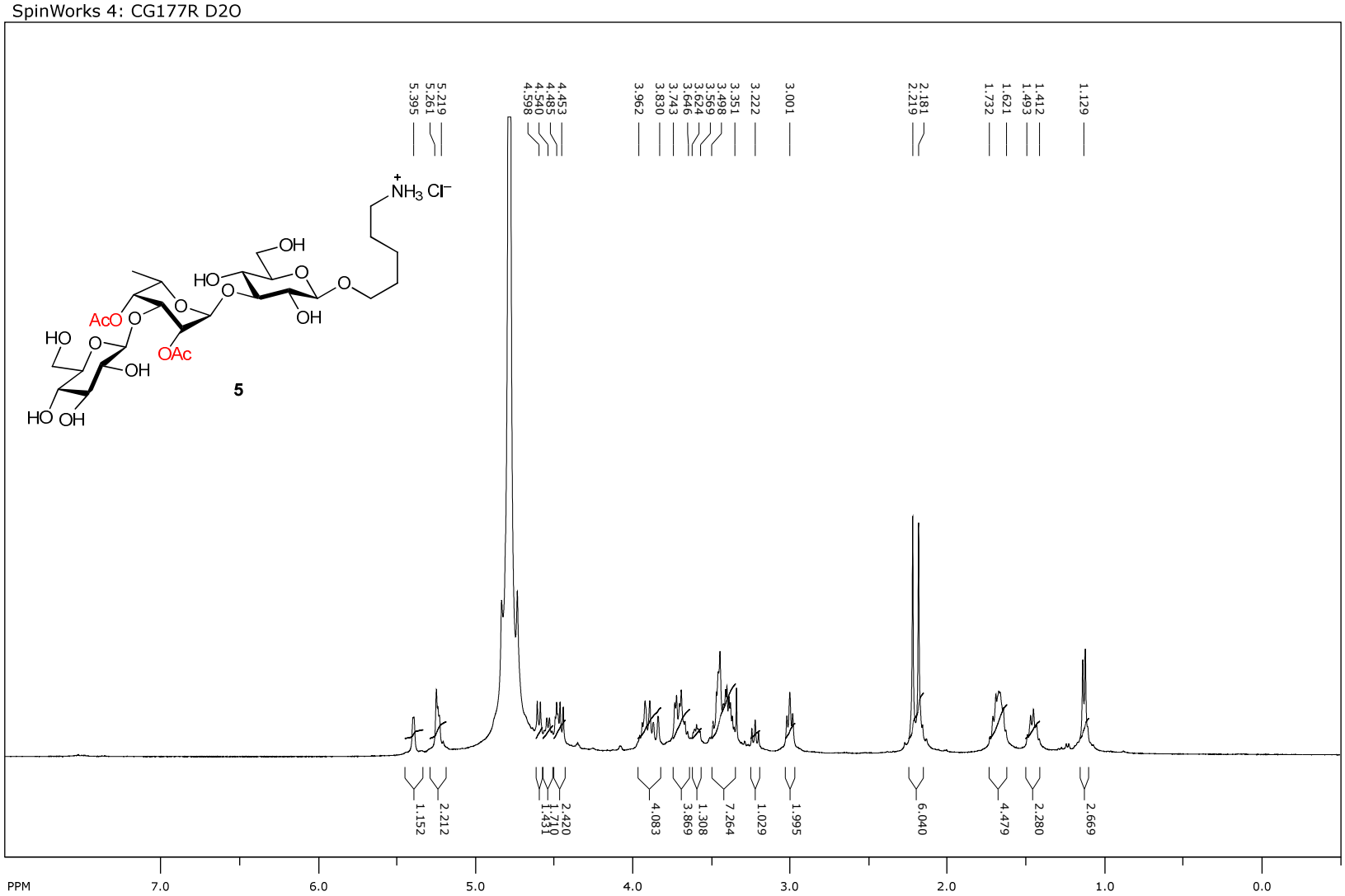
Supplementary Figure 153 | ^{1}H NMR spectra (D_2O + acetone, 400 MHz) of compound 4.



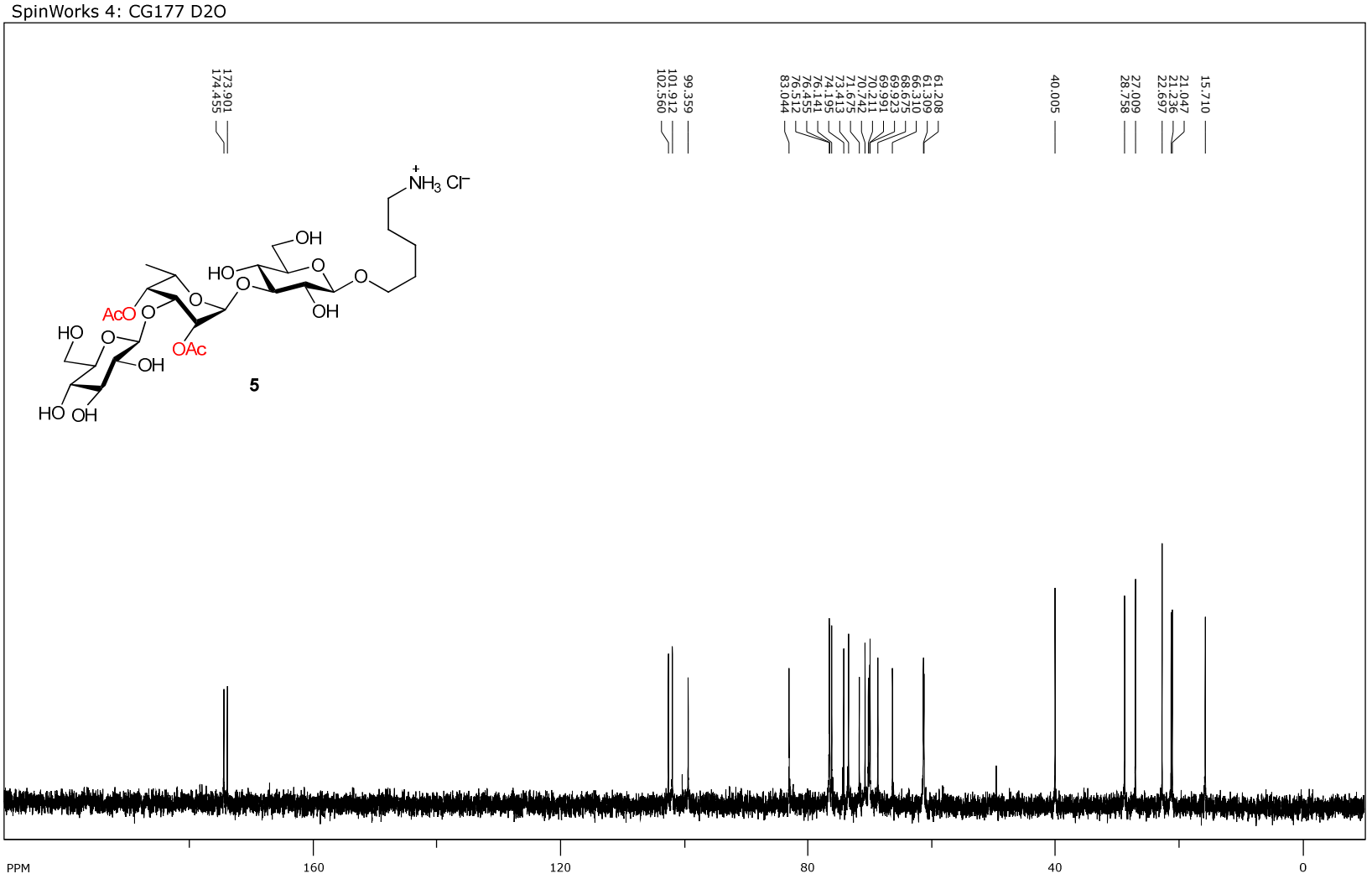
Supplementary Figure 154 | ^{13}C NMR spectra (D_2O + acetone, 100 MHz) of compound 4.



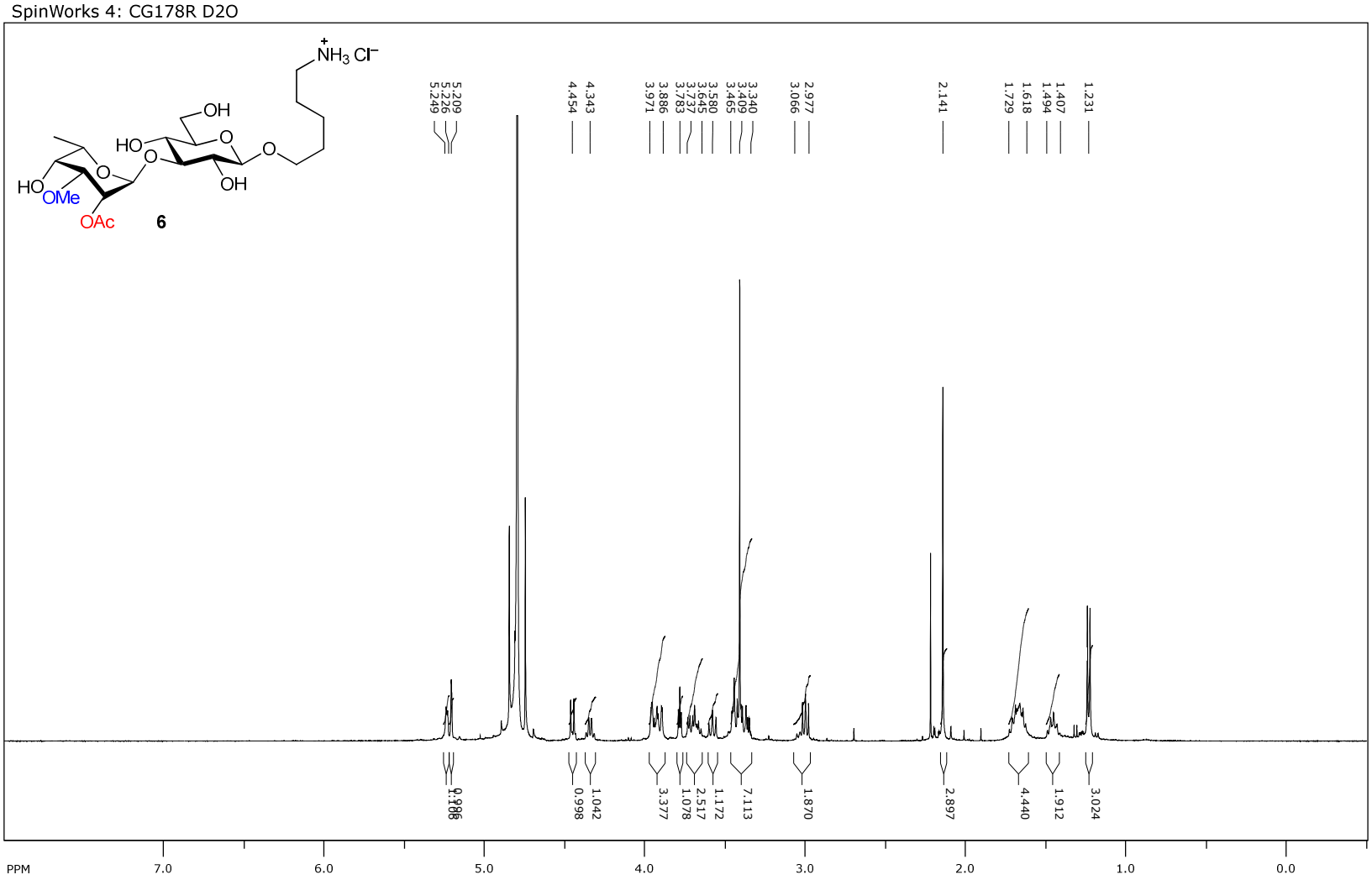
Supplementary Figure 155 | ^{1}H NMR spectra (D_2O + acetone, 400 MHz) of compound 5.



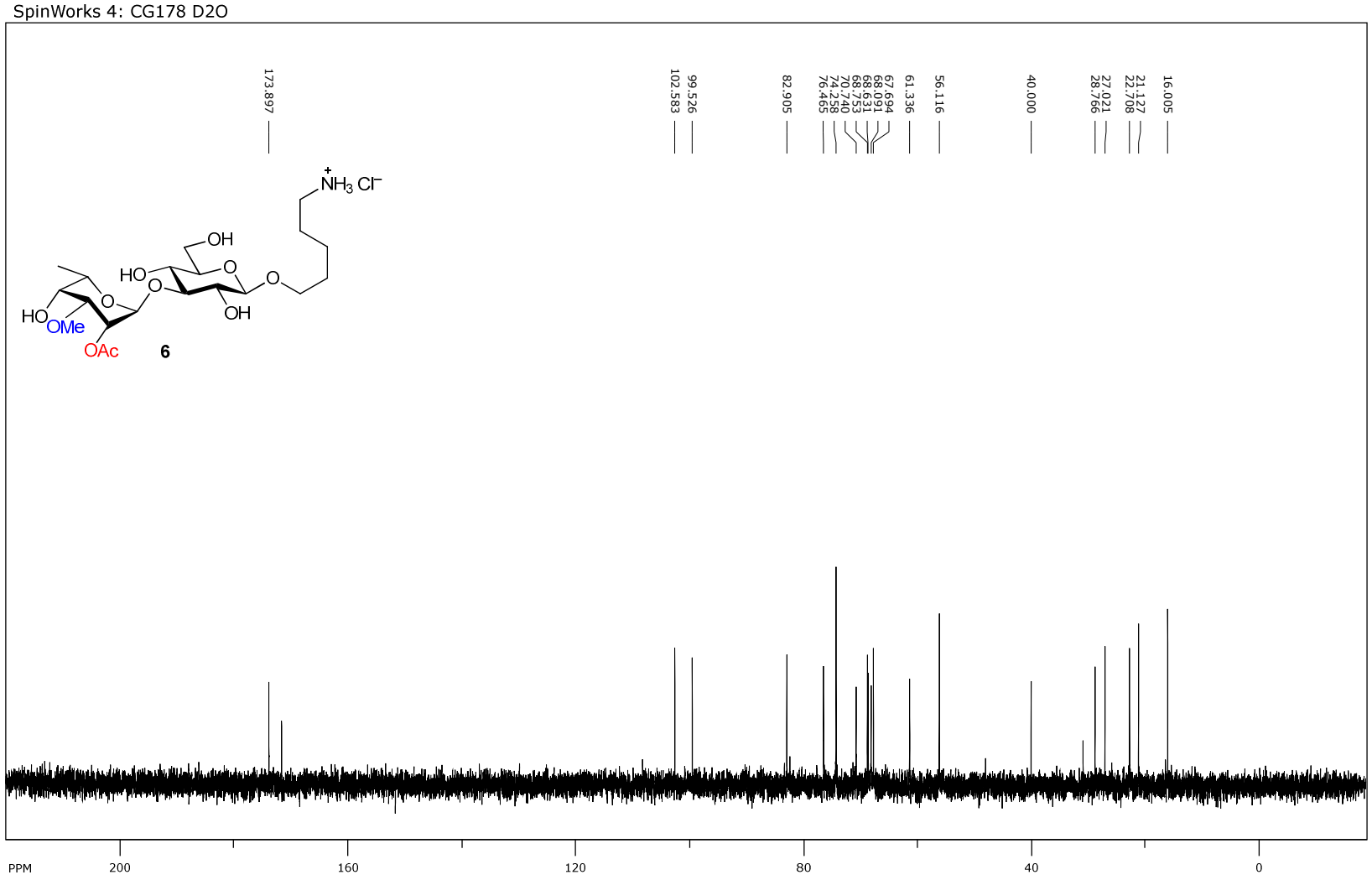
Supplementary Figure 156 | ^{13}C NMR spectra (D_2O + acetone, 100 MHz) of compound 5.



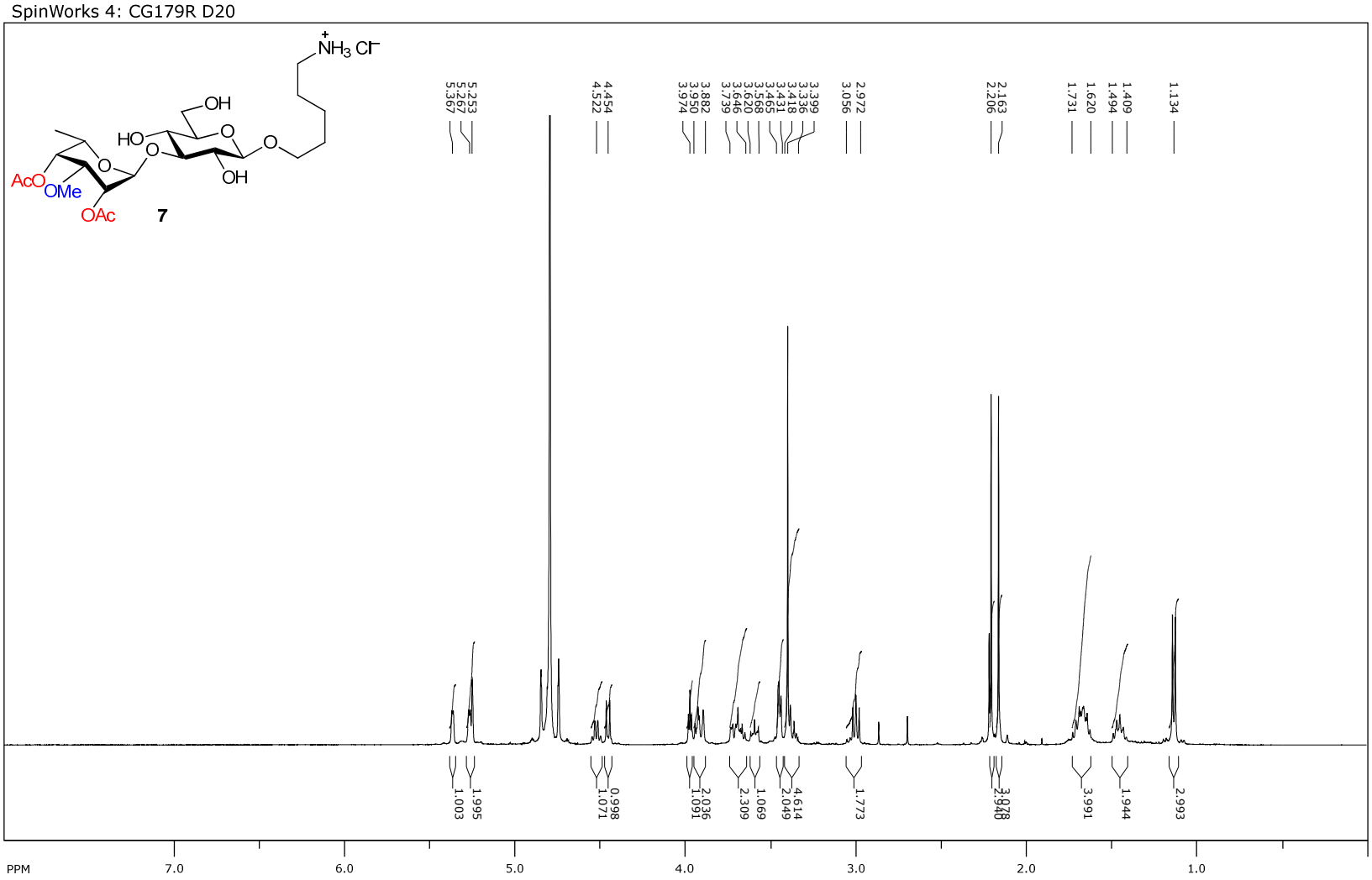
Supplementary Figure 157 | ^{1}H NMR spectra (D_2O + acetone, 400 MHz) of compound 6.



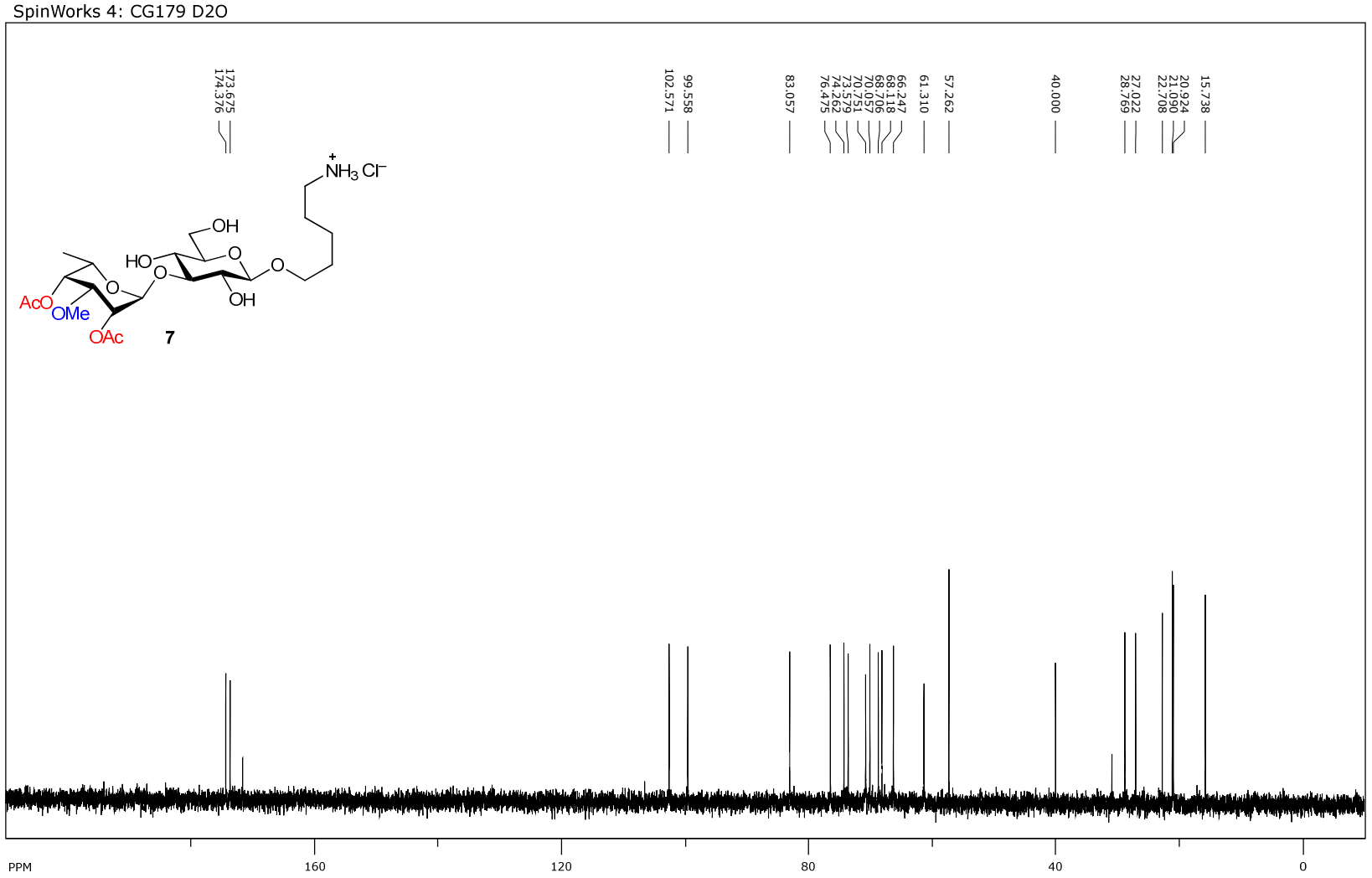
Supplementary Figure 158 | ^{13}C NMR spectra (D_2O + acetone, 100 MHz) of compound 6.



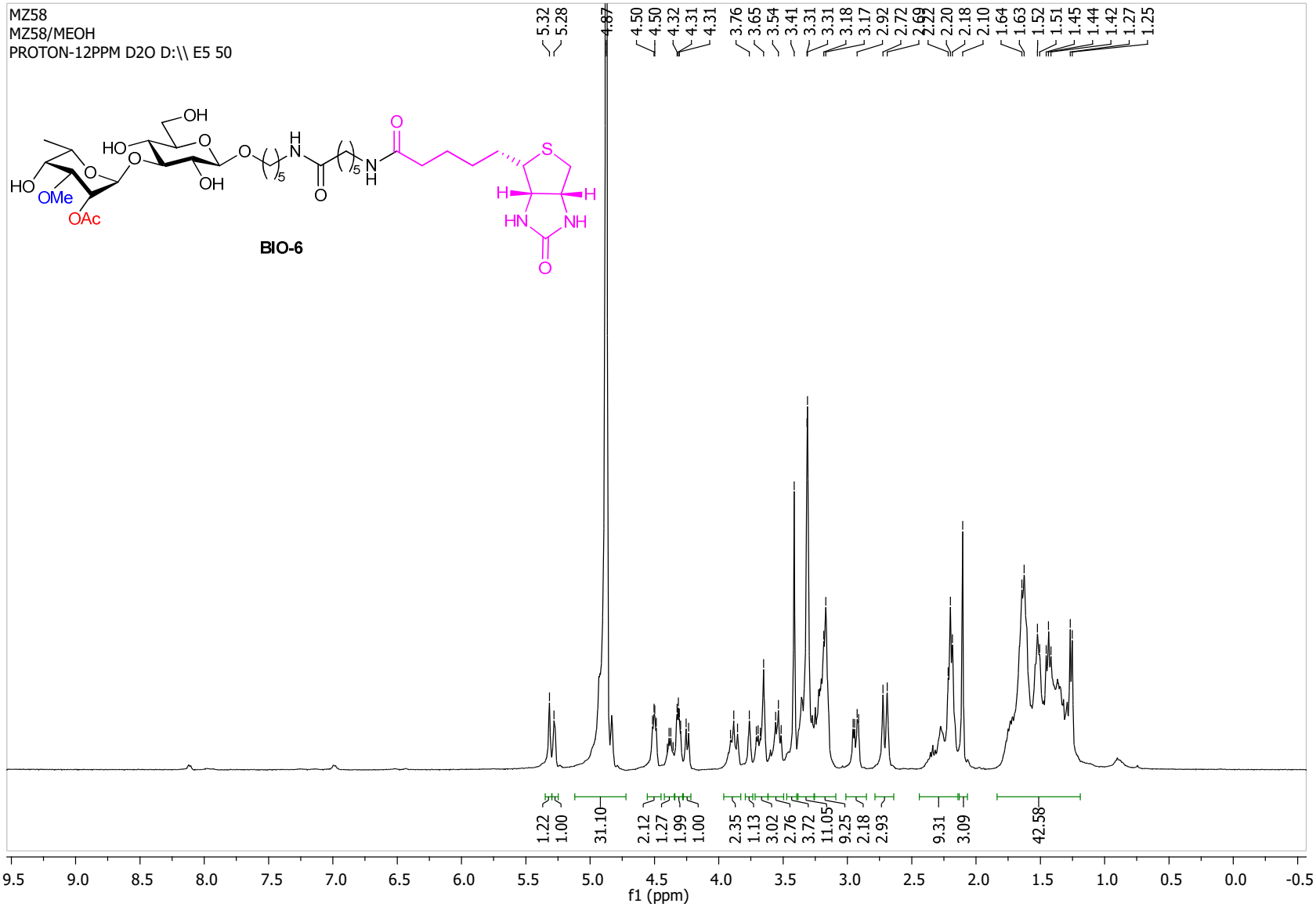
Supplementary Figure 159 | ^{1}H NMR spectra (D_2O + acetone, 400 MHz) of compound 7.



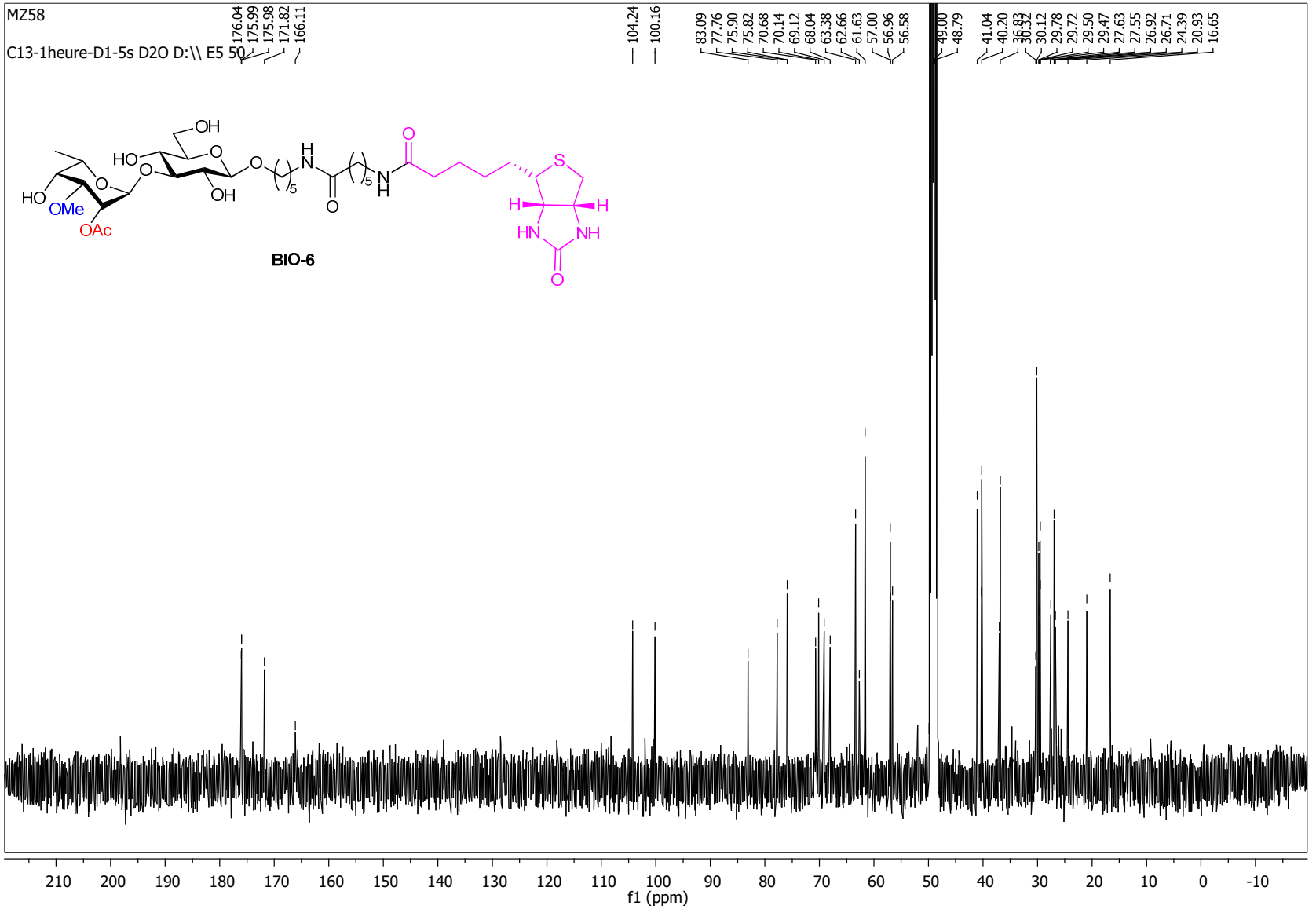
Supplementary Figure 160 | ^{13}C NMR spectra (D_2O + acetone, 100 MHz) of compound 7.



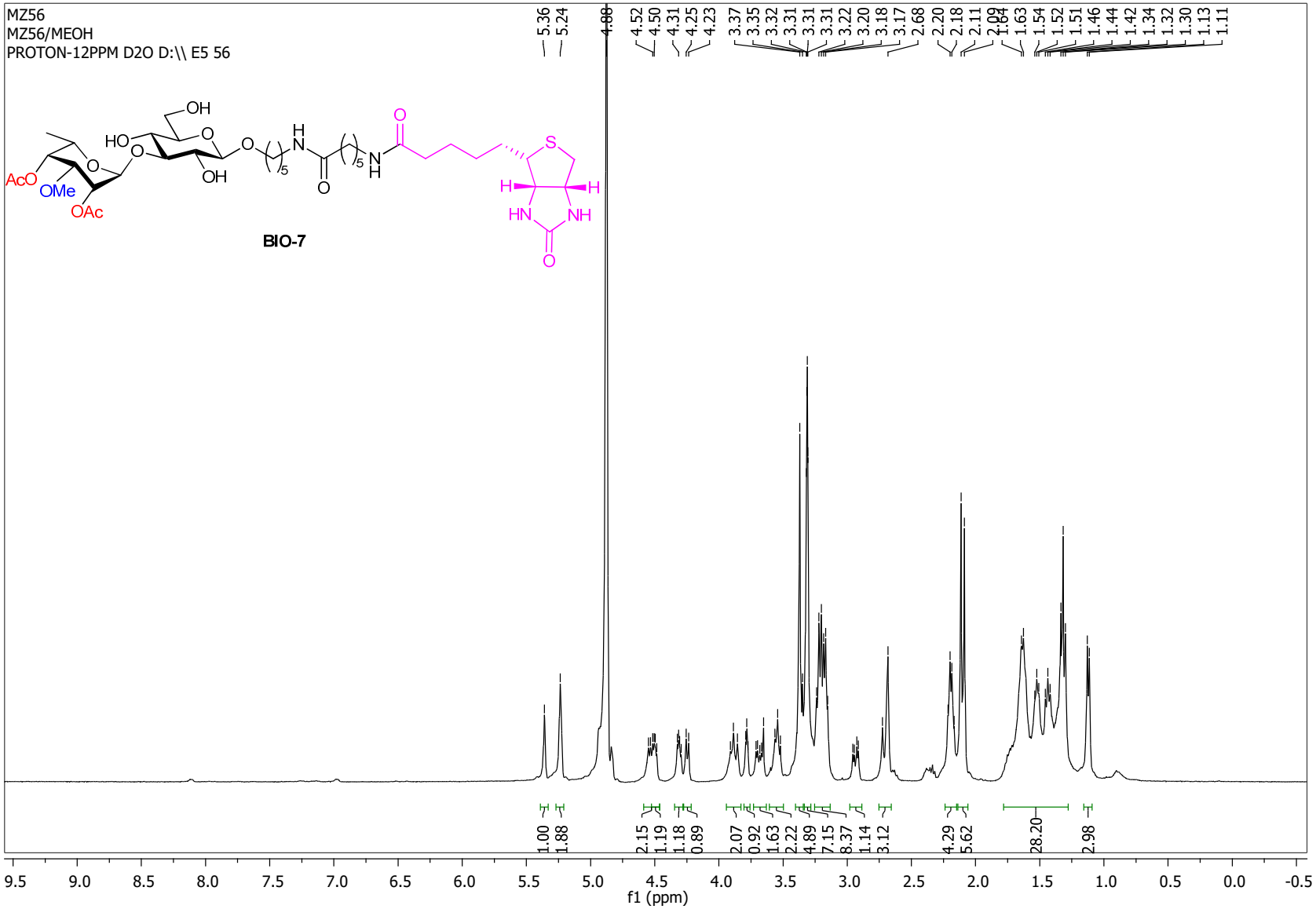
Supplementary Figure 161 | ^{1}H NMR spectra (MeOD, 400 MHz) of compound BIO-6.



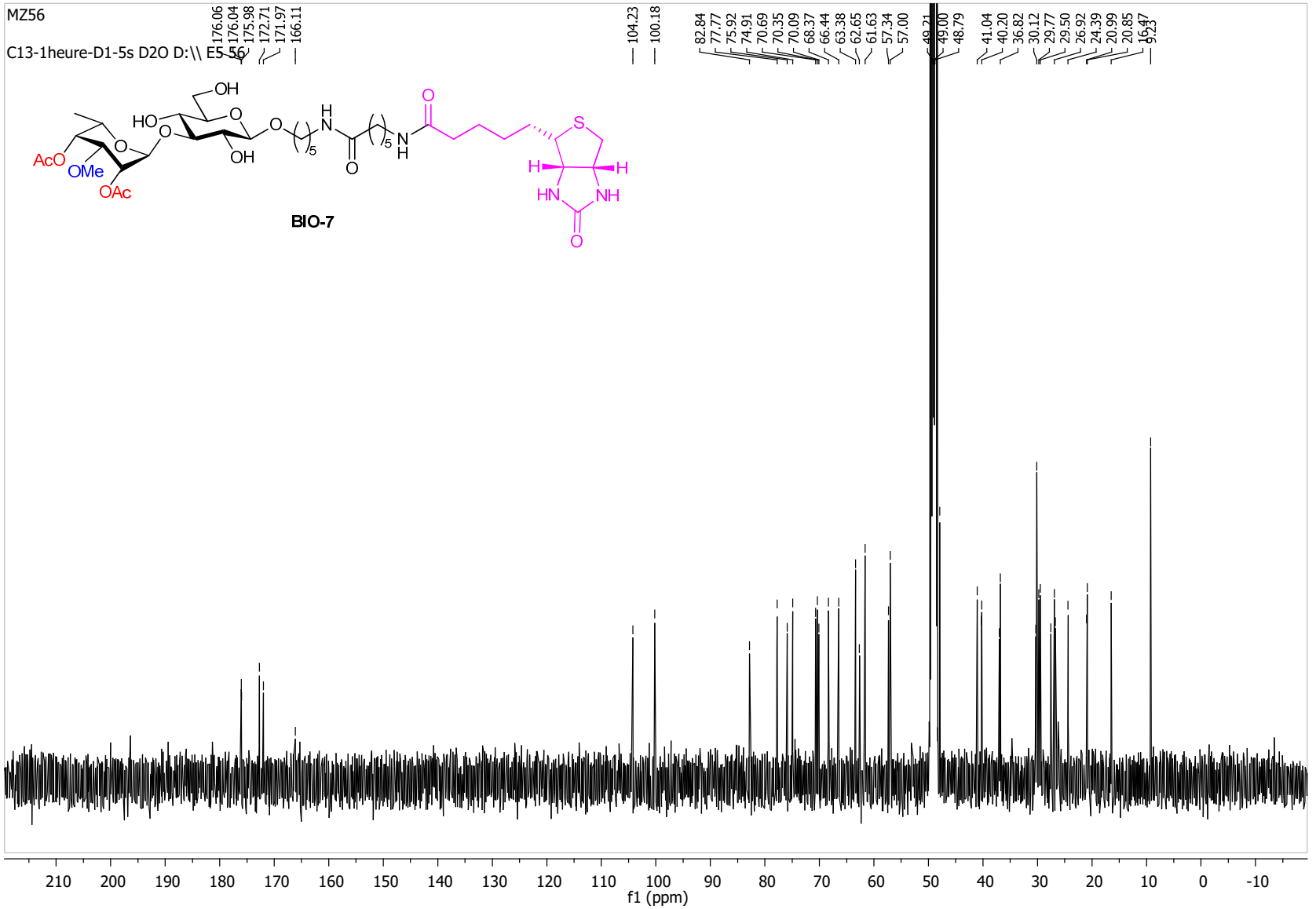
Supplementary Figure 162 | ^{13}C NMR spectra (MeOD, 100 MHz) of compound BIO-6.



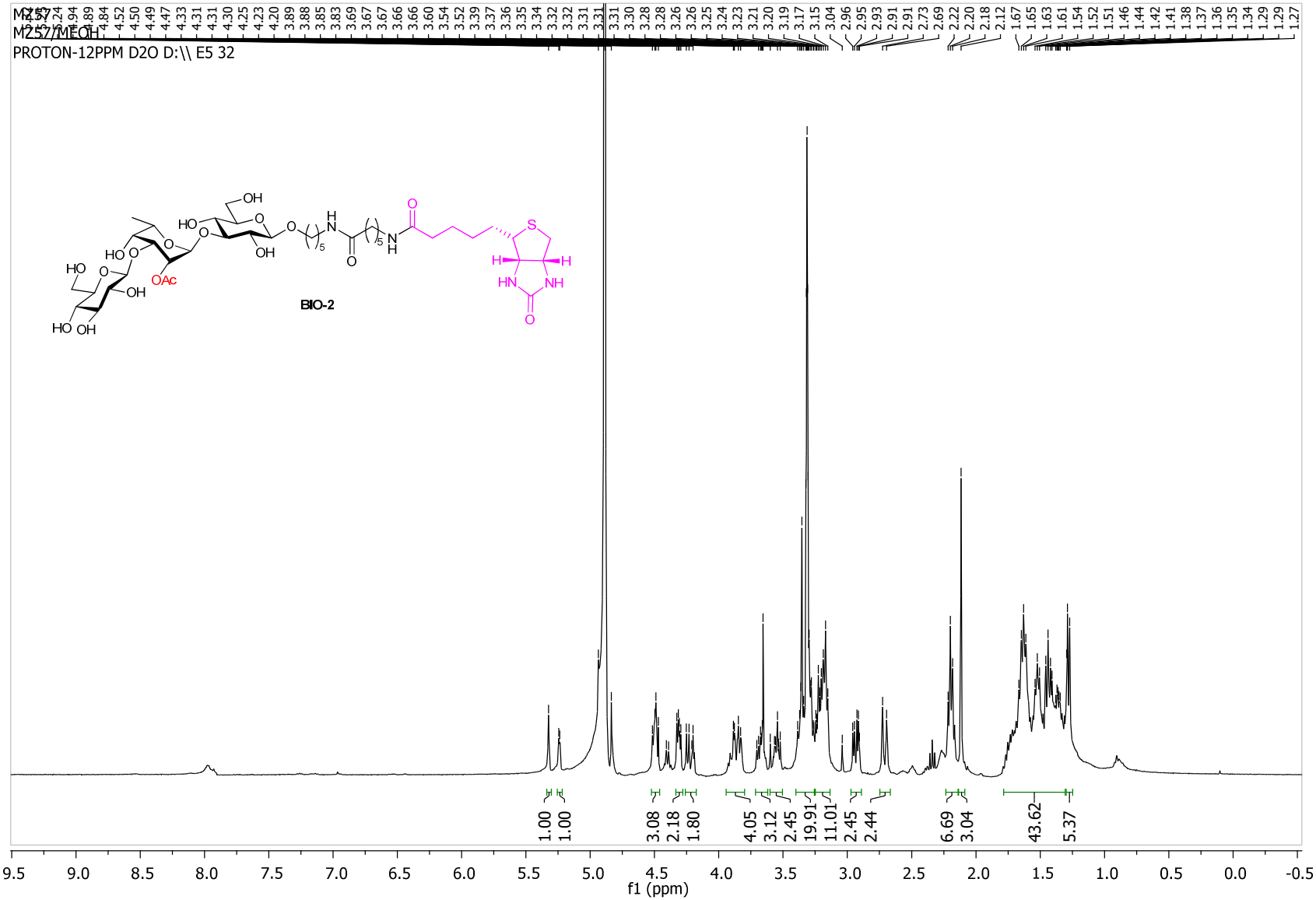
Supplementary Figure 163 | ^{1}H NMR spectra (MeOD, 400 MHz) of compound BIO-7.



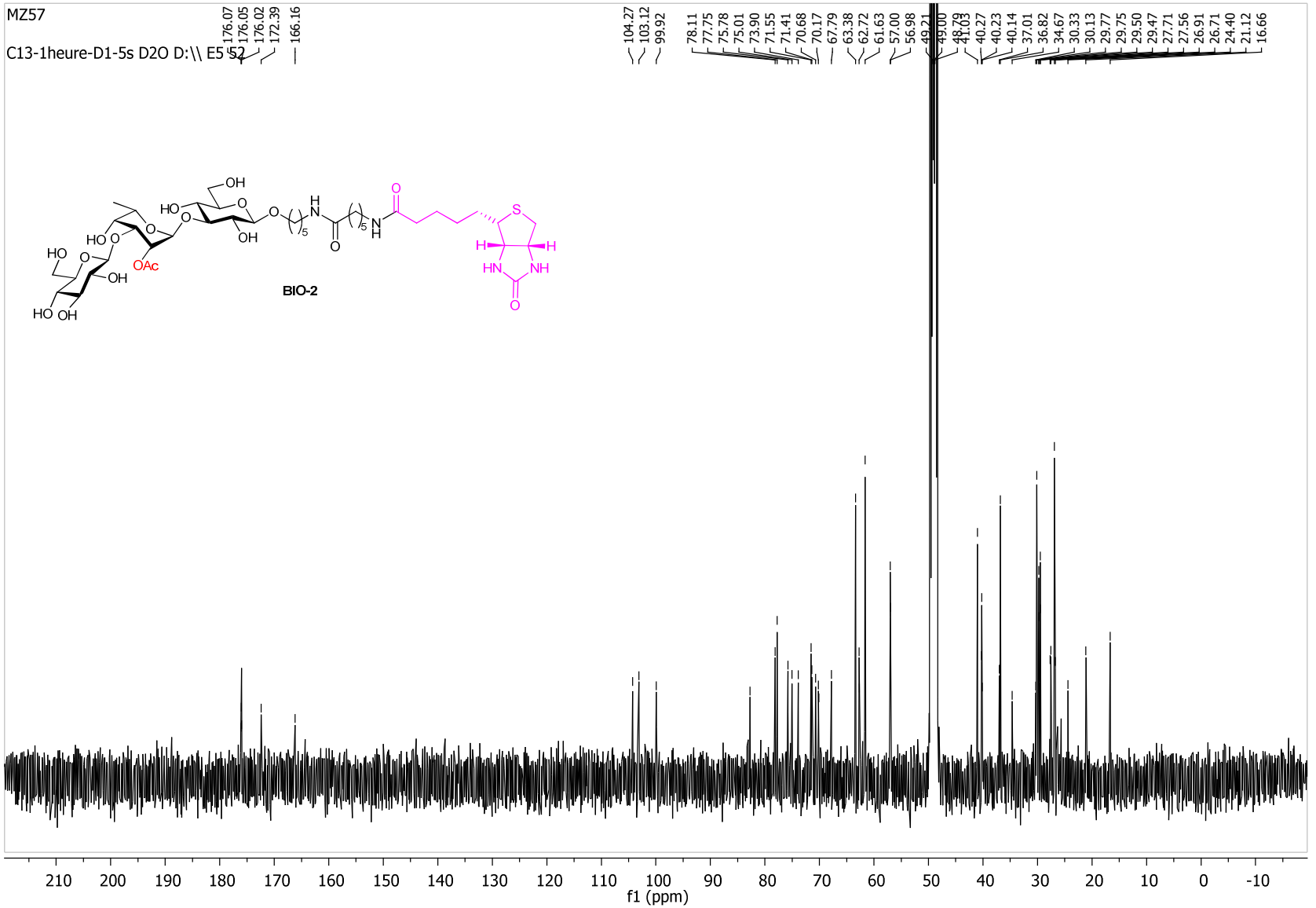
Supplementary Figure 164 | ^{13}C NMR spectra (MeOD, 100 MHz) of compound BIO-7.

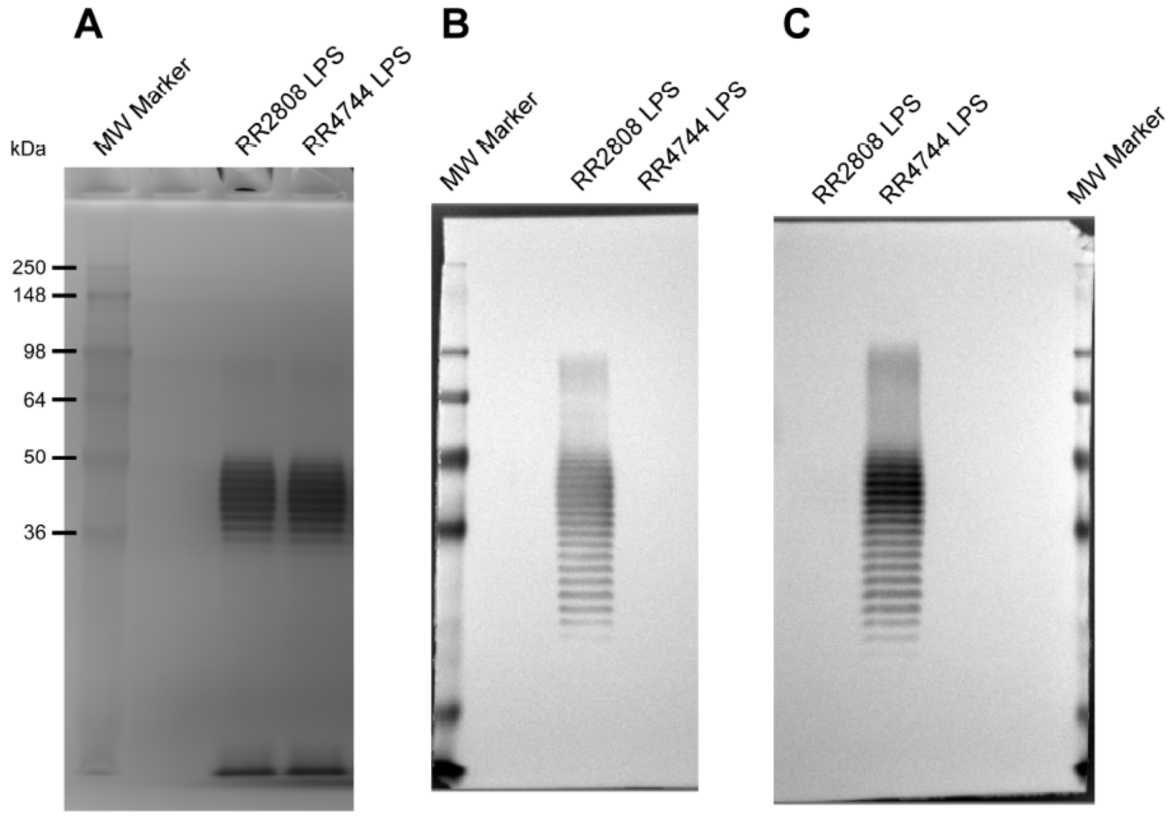


Supplementary Figure 165 | ^{1}H NMR spectra (MeOD, 400 MHz) of compound BIO-2.

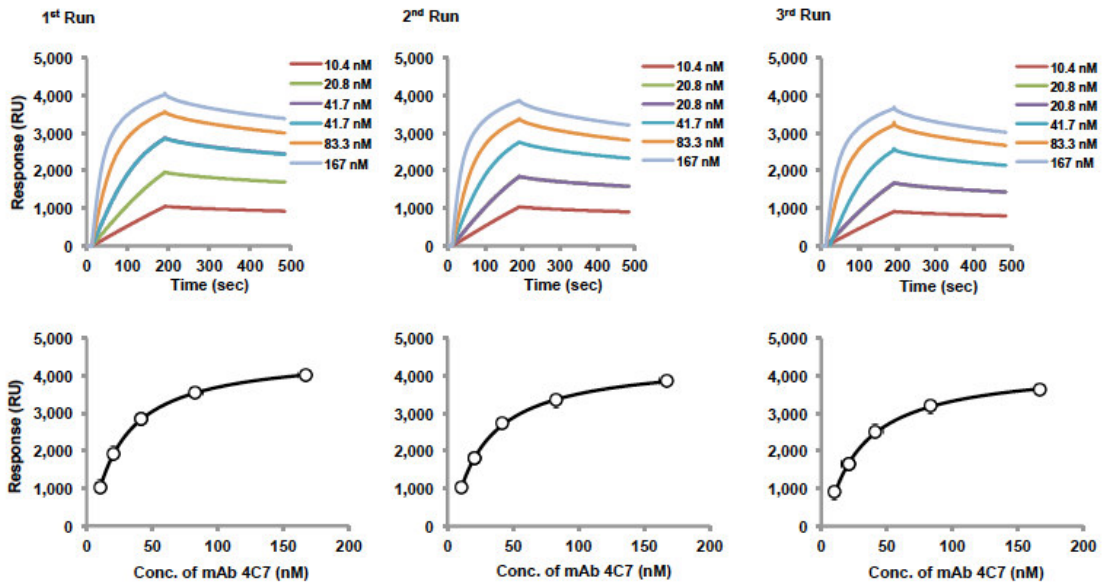


Supplementary Figure 166 | ^{13}C NMR spectra (MeOD, 100 MHz) of compound BIO-2.



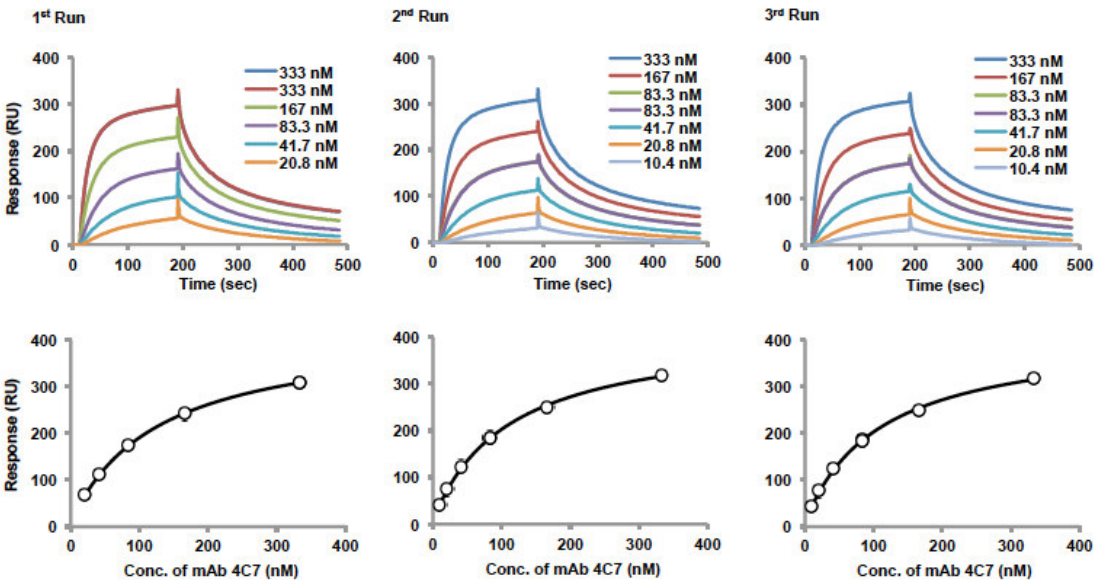


Supplementary Figure 167 | Analysis of LPS antigens purified from wild type and mutant strains of *B. pseudomallei*. LPS antigens (2 μg/lane) were separated on 12% Tris-Glycine gels and visualized by (A) silver staining. For Western immunoblotting, LPS antigens were electrophoretically transferred to nitrocellulose membranes and probed with (B) mAb Pp-PS-W or (C) mAb 3D11. Wild type LPS was purified from *B. pseudomallei* RR2808 while OacA mutant LPS was purified from *B. pseudomallei* Bp RR4744. Data not shown: Similar to mAb 3D11, mAbs 4C7 and 9C1-2 only reacted with RR4744 LPS. Likewise, *B. mallei* LPS only reacted with mAbs 3D11, 4C7 and 9C1-2. Based on these results, Bp RR4744 OPS and *B. mallei* OPS antigens appeared to share a common epitope (see Figure 2).



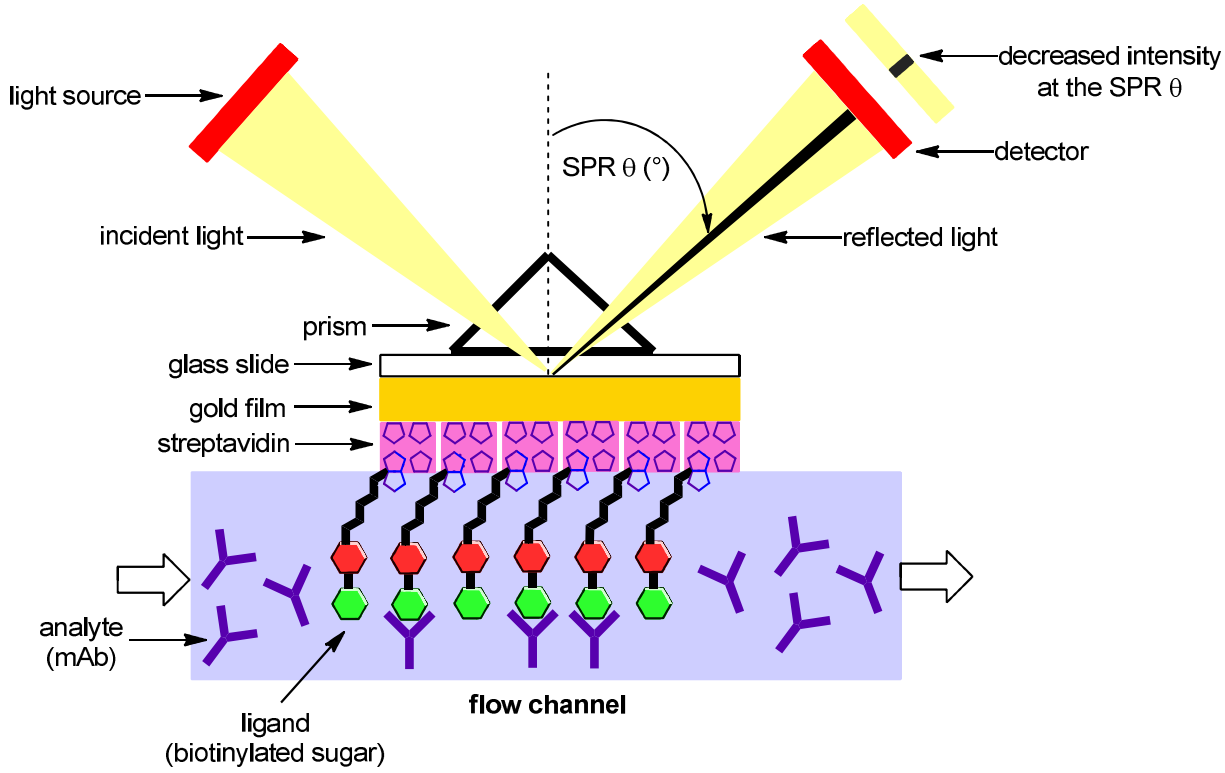
K_D (nM)	20.1	22.2	24.0
R_{max} (RU)	5421	5038	4859
χ^2 (RU^2)	113	1370	924

Supplementary Figure 168 │ Epitope mapping of disaccharide 6:mAb 4C7 interaction by STD-NMR (sensorgrams and steady-state affinity model fitting). SPR analysis was performed between mAb 4C7 and biotinylated oligosaccharide **BIO-6**. Binding affinities (K_D) were calculated using a steady-state affinity model.

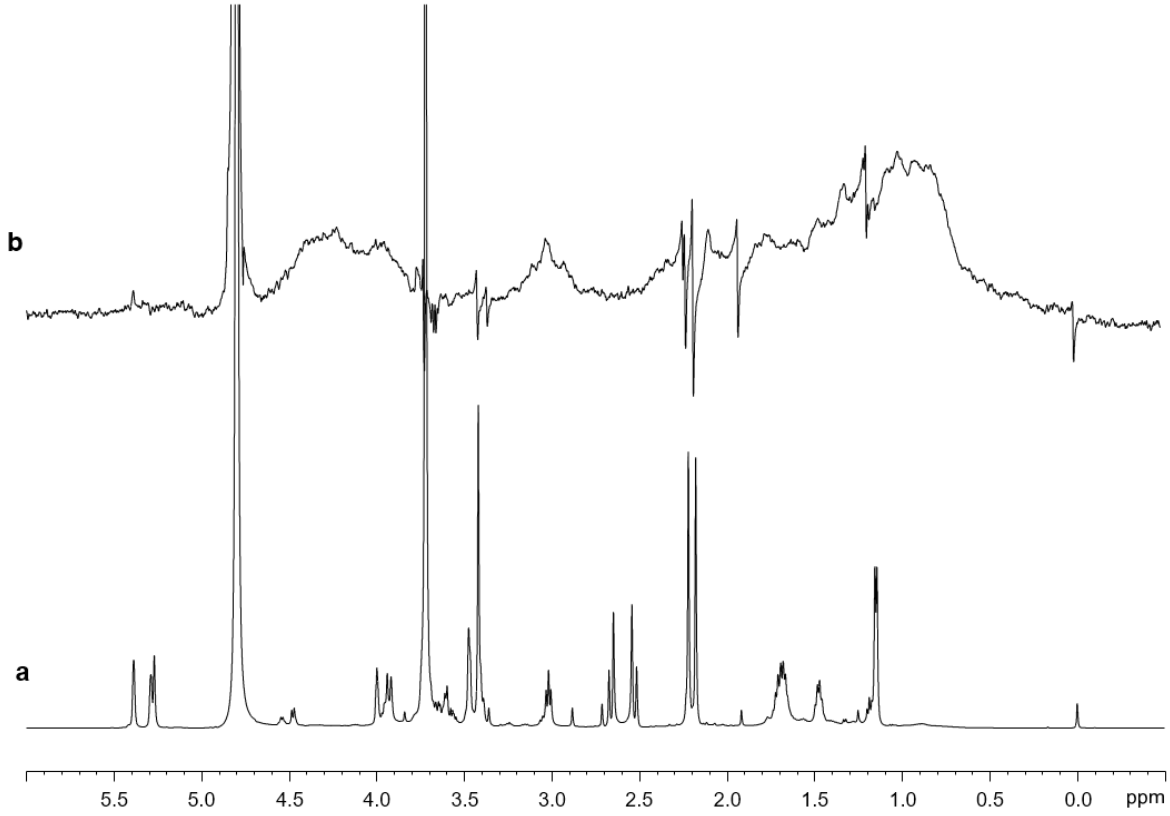


K_D (nM)	**128**	**110**	**110**
R_{max} (RU)	413	410	405
χ^2 (RU^2)	1.57	9.85	15.1

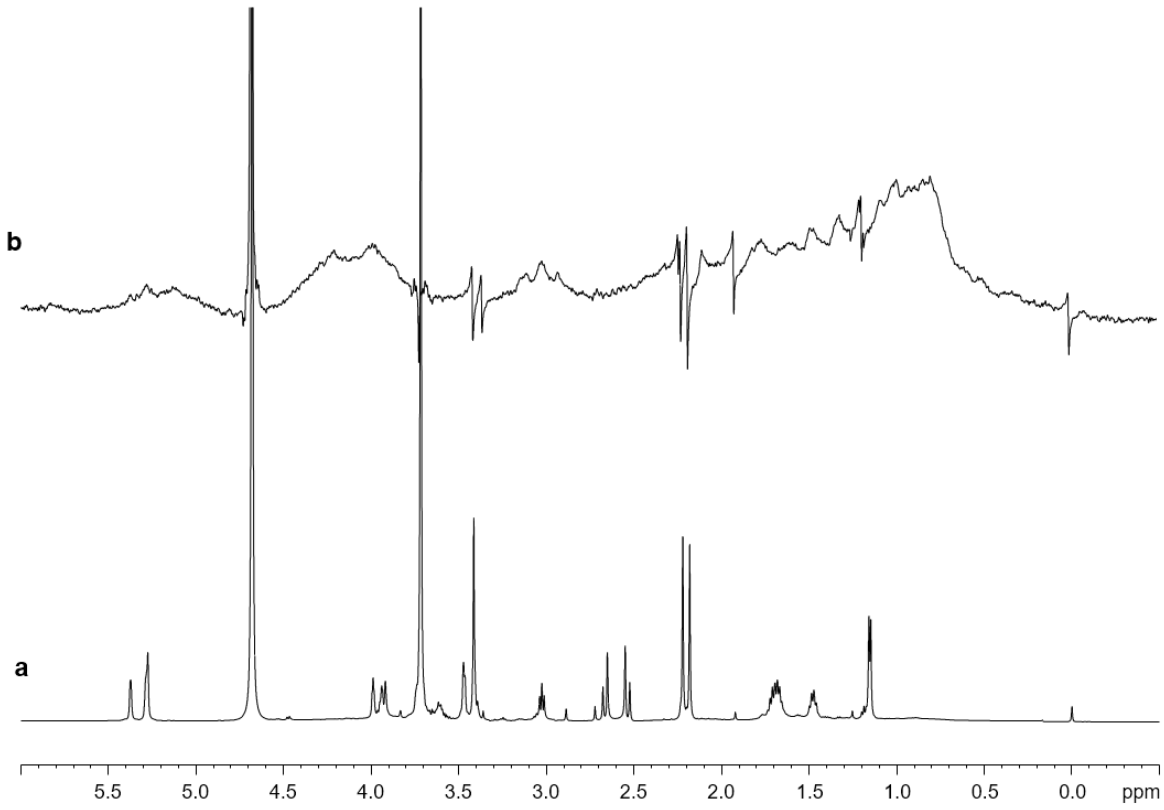
Supplementary Figure 169 ｜ Epitope mapping of disaccharide 7:mAb 4C7 interaction by STD-NMR (sensorgrams and steady-state affinity model fitting). SPR analysis was performed between mAb 4C7 and biotinylated oligosaccharide **BIO-7**. Binding affinities (K_D) were calculated using a steady-state affinity model.



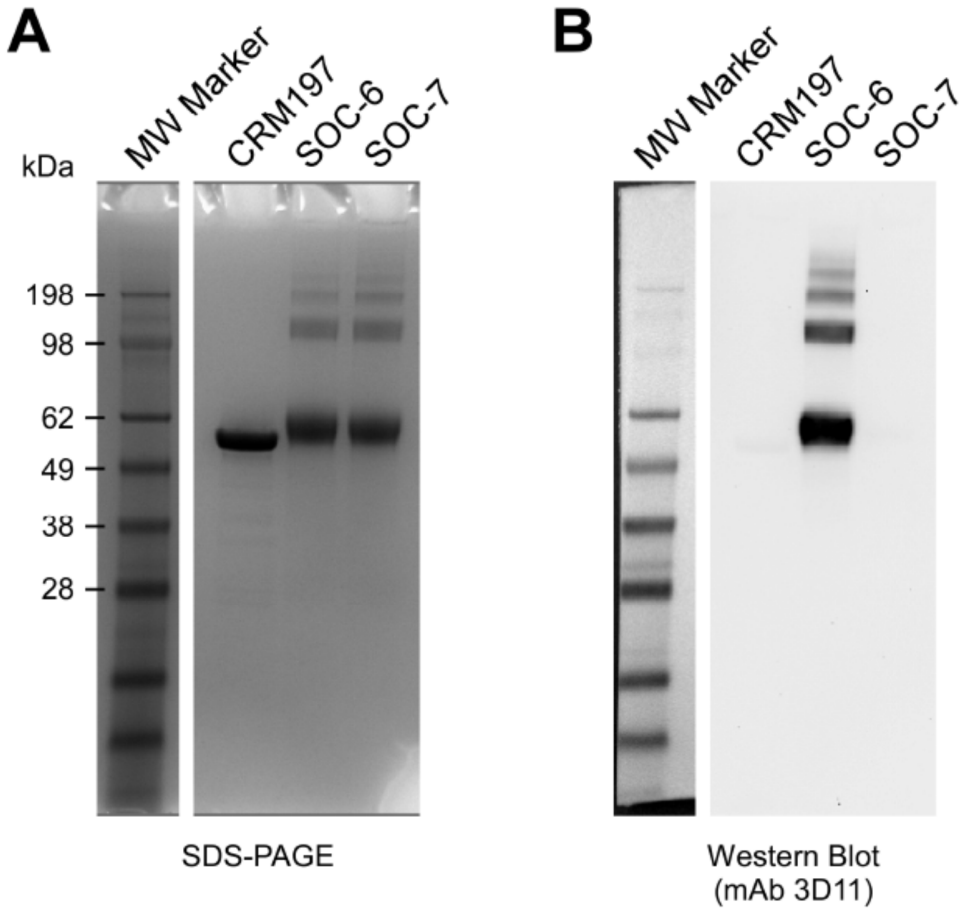
Supplementary Figure 170 | Schematic illustration of the SPR experiments. Streptavidin-coated sensor chips were used in order to measure the K_D values of the biotinylated oligosaccharides:mAb 4C7 interactions.



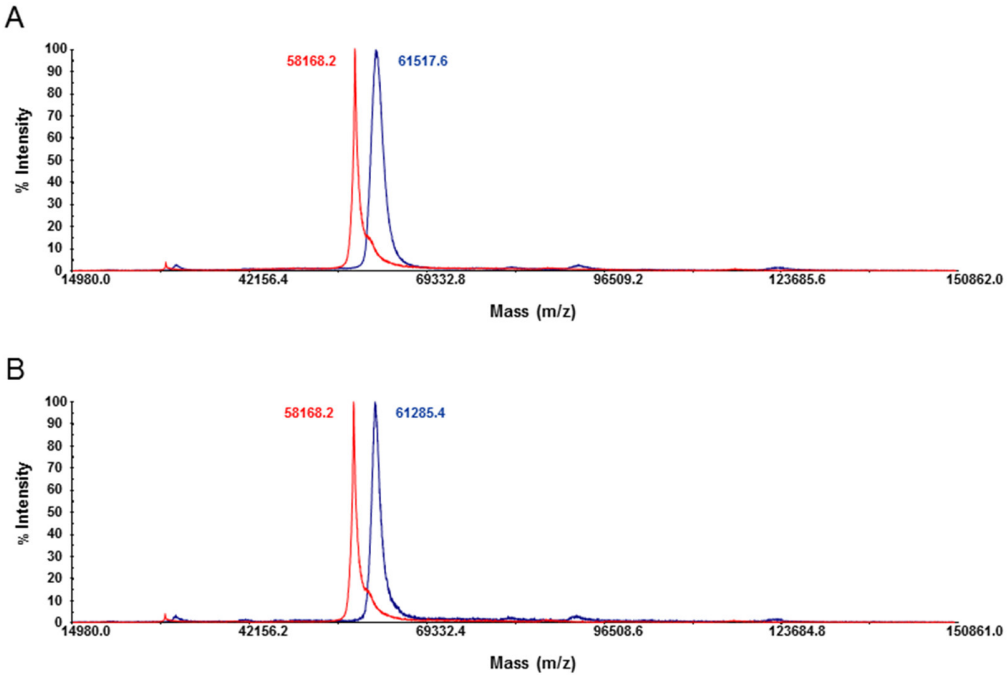
Supplementary Figure 171 | STD-NMR spectrum of disaccharide 7 and mAb 4C7 mixture. (**a**) Reference ^{1}H NMR spectrum of disaccharide **7** at 298 K. (**b**) STD 1D NMR spectrum of a 1:100 mAb 4C7/disaccharide mixture. The irradiation frequency was set at 8 ppm and a saturation time of 2 seconds was used.



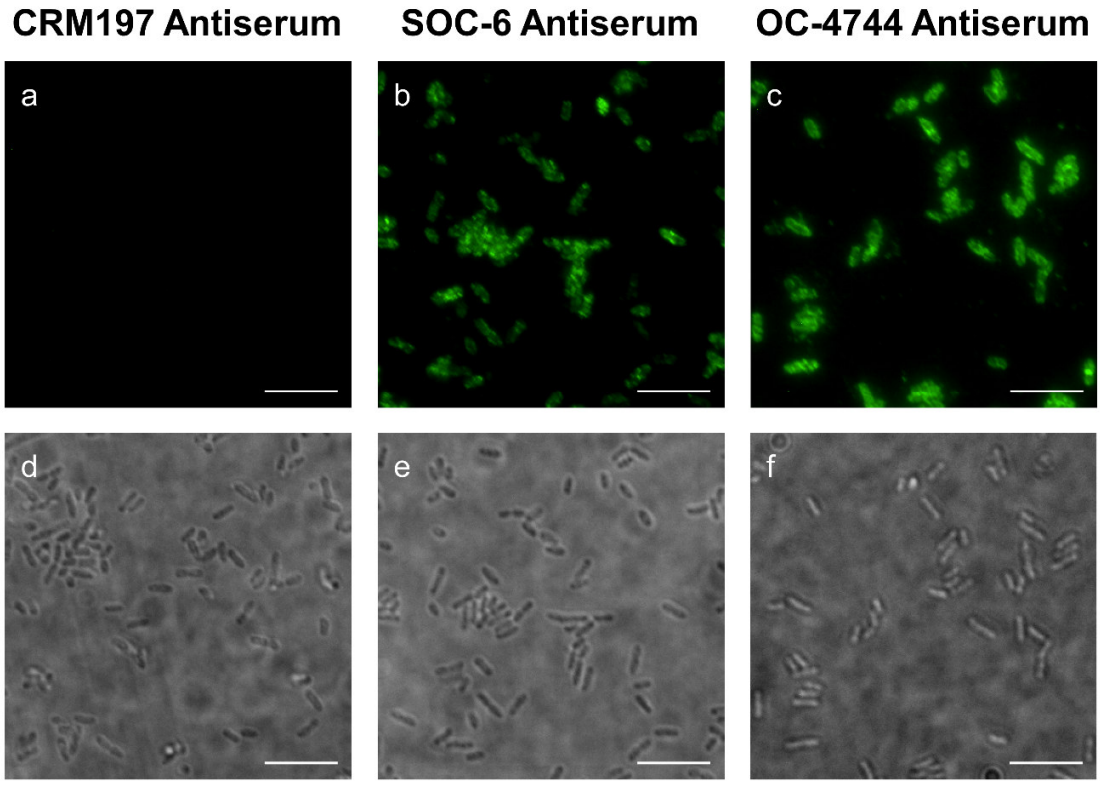
Supplementary Figure 172 | STD-NMR spectrum of disaccharide 7 and mAb 4C7 mixture. (**a**) Reference ^{1}H NMR spectrum of disaccharide **7** at 310 K. (**b**) STD 1D NMR spectrum of a 1:100 mAb 4C7/disaccharide mixture. The irradiation frequency was set at 8 ppm and a saturation time of 2 seconds was used.



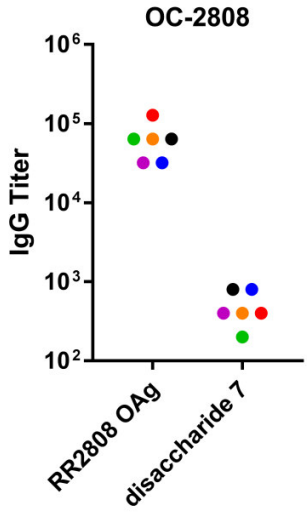
Supplementary Figure 173 │ SDS-PAGE and Western immunoblot analysis of synthetic oligosaccharide conjugates. (A) The carrier protein and conjugates (3 μg protein per lane) were separated on a 4-12% Bis-Tris Bolt gel and stained with CBB R-250; (B) The carrier protein and conjugates (1.5 μg protein per lane) were separated on 4-12% Bis-Tris Bolt gels and electrophoretically transferred to nitrocellulose. SOC-6 was detected by chemiluminescence using a 1/2000 dilution of mAb 3D11 and a 1/5000 dilution of an anti-mouse IgG-HRP conjugate. Results similar to mAb 3D11 were observed using mAbs 4C7 and 9C1-2 (data not shown). In contrast, SOC-7 was detected by chemiluminescence using a 1/400 dilution of mAb Pp-PS-W and a 1/5000 dilution of an anti-mouse IgM-HRP conjugate (data not shown).



Supplementary Figure 174 | MALDI-TOF-MS spectra of SOC-6 and SOC-7. (**a**) SOC-6 (blue line) and (**b**) SOC-7 (blue line) as well as unconjugated CRM197 (red line) were dried and reconstituted in 50 mM ammonium bicarbonate buffer (20 µL). The samples were deposited on a MALDI plate using premix method with 2,4,6-trihydroxyacetophenone (THAP) as the matrix. The MALDI analysis results were acquired on a TOF/TOFTM 5800 system (AB sCIEX) using linear positive ion mode. The data were externally calibrated using BSA. The analysis suggested that the mass of CRM197, SOC-6, and SOC-7 were 58.2 kDa, 61.5 kDa and 61.3 kDa, respectively. The mass differences indicated that SOC-6 and SOC-7 consisted of about 6 and 5 disaccharides covalently linked to CRM197, respectively.



Supplementary Figure 175 | Reactivity of CRM197, SOC-6 and OC-4744 antiserum with *B. mallei*. Paraformaldehyde-fixed *B. mallei* were labeled with CRM197 antiserum (a and d), **SOC-6** antiserum (b and e), or OC-4744 antiserum (c and f) and anti-mouse IgG-Alexa488 conjugate as described in the Supplementary Methods. Panels a-c show immunofluorescence images and panels d-f show bright field images. Scale bars are 5 µm.



Supplementary Figure 176 | Immune responses to OC-2808. C57BL/6 mice (n = 6 per group) were immunized with OC-2808. ELISAs were used to quantitate immune serum IgG titers. Colored dots represent the mean endpoint titers for individual mice against the various target antigens.

Supplementary Methods

General methods

All starting materials and reagents were purchased from commercial sources, and used as received without further purification. Air and water sensitive reactions were performed in heat gun-dried glassware under Ar atmosphere. Moisture sensitive reagents were introduced via a dry syringe. Anhydrous solvents were supplied over molecular sieves, and used as received. Petroleum ether (PE) refers to the 40-60 °C boiling fraction. Powdered 4 Å molecular sieves were activated before use by heating with a heat gun for ~5 min under high vacuum. Reactions were monitored by thin-layer chromatography (TLC) with silica gel 60 F_{254} 0.25 mm pre-coated aluminium foil plates. Compounds were visualized by using UV_{254} and/or orcinol (1 mg·mL^{-1}) in 10% aq H_2SO_4 solution and/or Hanessian's stain [2.5 g $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$, 1.0 g $Ce(NH_4)_4(SO_4)_4\cdot 2H_2O$, 90 mL H_2O, 10 mL H_2SO_4] with heating. Normal-phase flash column chromatography was performed on silica gel 60 Å (15-40 μm). Reversed-phase flash column chromatography was performed on C_{18} silica gel (fully capped, 25-40 μm). NMR spectra were recorded at 297 K in the indicated solvent ($CDCl_3$, py-d_5, D_2O or MeOD) with a 400 MHz instrument, employing standard softwares given by the manufacturer. ^{1}H and ^{13}C NMR spectra were referenced to tetramethylsilane (TMS, $\delta_H = \delta_C = 0.00$ ppm) as internal reference for spectra in $CDCl_3$, py-d_5, and MeOD or to internal acetone (δ_H = 2.218 ppm; δ_C = 33.0 ppm) for spectra in D_2O. Assignments were based on ^{1}H, ^{13}C, DEPT-135, COSY, HSQC, undecoupled HSQC and HMBC experiments. Interchangeable assignments are marked with an asterisk. High-resolution mass spectra (HRMS) were recorded on an ESI-Q-TOF mass spectrometer.

General procedures

Synthesis of trichloroacetimidate donors. 1,5-Cyclooctadiene-bis(methyldiphenylphosphine)-iridium(I) hexafluorophosphate (0.02–0.1 equiv) was dissolved in anhydrous THF (5 mL·mmol^{-1}) and the red solution was degassed under Ar. Hydrogen was bubbled through the solution for 5 min, and then the yellow solution was once again degassed under Ar. A solution of allyl taloside (1.0 equiv) in anhydrous THF (5.0 mL·mmol^{-1}) was added. The mixture was stirred for 2 h at rt under Ar. Then, a solution of iodine (2.0–2.5 equiv) in THF/H_2O (6.0 mL·mmol^{-1}, 4:1 *v/v*) was added to the mixture, which was stirred for another 1 h at rt. The excess of iodine was quenched by adding a freshly prepared 10% $Na_2S_2O_3$(aq) solution and stirred until the color turned bright yellow (~5 min). The aqueous phase was extracted with EtOAc (3 ×). The combined organic layers were washed with a saturated $NaHCO_3$(aq) solution and brine. The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography to give the corresponding hemiacetal as an α/β mixture. To a cooled (0 °C) solution of the hemiacetal (1.0 equiv) in DCM/acetone (14 mL·mmol^{-1}, 8:3 *v/v*) were added DBU (0.3 equiv) or Cs_2CO_3 (0.2 equiv) followed by CCl_3CN (5.0–6.0 equiv). The mixture was stirred for 1 h at rt, then the suspension was filtered over Celite and rinsed with DCM. The solvents were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography to give the trichloroacemidate donor, the α-anomer being the major compound.

Synthesis of protected disaccharides. Acceptor **13** (1.0 equiv) and donor **8**-**12** (2.0 equiv) were dried for 2 h under high vacuum and then dissolved in anhydrous Et_2O (20 mL·mmol^{-1}). The solution was cooled to –10 °C and TMSOTf (0.01–0.2 equiv) was added keeping rigorous anhydrous conditions. The mixture was stirred at –10 °C for 10 min under Ar, and then quenched with a few drops of Et_3N. The suspension was filtered over Celite, rinsed with DCM and the filtrate was concentrated under reduced pressure. The residue was purified by combi-flash chromatography to give the target disaccharide as a pure α-anomer.

Deprotection of PMB group. To a solution of disaccharide **15**–**17** (1.0 equiv) in DCM/H_2O (22 mL·mmol^{-1}, 10:1 *v/v*) was added DDQ (2.0 equiv) and the deep-green mixture was stirred for 2 h at rt. The reaction was quenched by adding a saturated $NaHCO_3$(aq) solution, stirred until the color turned bright yellow (~10 min), and diluted with EtOAc. The organic phase was washed with a saturated $NaHCO_3$(aq) solution and brine. The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography to give the corresponding alcohol.

Hydrogenolysis using the H-Cube system. The oligosaccharide (1.0 equiv) was dissolved in DCE (10 mL·mmol^{-1}), then MeOH (250 mL·mmol^{-1}) followed by concentrated HCl (2.0 equiv) were added. The solution was passed without delay through a 20% $Pd(OH)_2$/C cartridge (CatCart30) using a H-Cube continuous flow system in control mode (10 bars). The temperature was set at 40 °C, and the flow rate was fixed at 1.0 mL·mmol^{-1}. After one run, the cartridge was rinsed with MeOH and the solutions were concentrated under reduced pressure keeping the bath temperature below 40 °C. The residue was subjected to C_{18} reversed-phase flash chromatography (H_2O/MeOH 10:0 to 6:4) followed by freeze-drying to give the target oligosaccharide in the form of a hydrochloride salt.

Hydrogenolysis under heterogeneous conditions. The oligosaccharide (1.0 equiv) was dissolved in anhydrous DCE (10 mL·mmol^{-1}), then anhydrous MeOH (250 mL·mmol^{-1}) followed by concentrated HCl (1.0 equiv) were added. The solution was degassed with Ar and Pd black (1 mg·mg^{-1} of compound) was added. The suspension was stirred under an atmosphere of H_2 at 40 °C for 16 h. The mixture was filtered over Celite to remove the catalyst, and the cake was rinsed with MeOH. The solutions were concentrated under reduced pressure keeping the bath temperature below 40 °C. The soluble part of the residue was dissolved in D_2O, filtered over Celite using a pipette, rinsed with D_2O and the solutions were concentrated under reduced pressure to give the target oligosaccharide in the form of a hydrochloride salt.

Biotinylation of oligosaccharides. A solution of the free oligosaccharide (1.0 equiv) and 6-biotinylamidohexanoic acid *N*-hydroxysuccinimidoyl ester (2.0 equiv) in DMF (22.5 mL·mmol^{-1}), Et_3N (2.5 mL·mmol^{-1}), and H_2O (25.0 mL·mmol^{-1}) was stirred for 1 h at rt. The solvents were concentrated under reduced pressure. The resulting residue was dissolved in EtOH and the soluble fraction was purified by silica gel flash chromatography (DCM/MeOH) to give the biotinylated oligosaccharide.

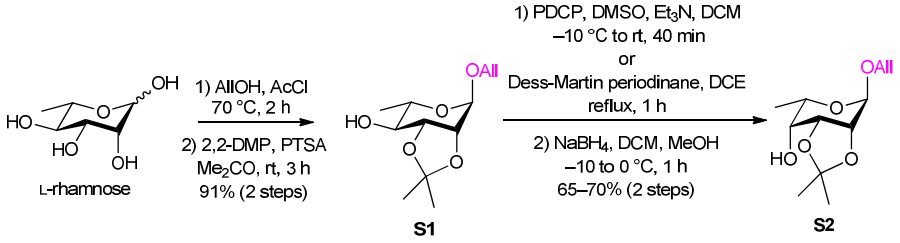
SDS-PAGE and Western immunoblotting. Glycoconjugate samples were solubilized in 1X SDS-PAGE sample buffer and heated to 100 °C for 5 min prior to electrophoresis on 4-12% Bis-Tris Bolt gels (Life Technologies). Proteins were visualized via staining with Coomassie Blue R-250. For Western immunoblot analyses, the glycoconjugate samples and CRM197 were separated on the same 4-12% gels and electrophoretically transferred to nitrocellulose membranes. The membranes were blocked with 3% skim milk in high salt Tris-buffered saline (HS-TBS; 20 mM Tris, 500 mM NaCl, pH 7.5) for 60 min at room temperature and then incubated overnight at 4 °C with 1/400 - 1/2000 dilutions of a *B. pseudomallei* (Pp-PS-W) or *B. mallei* OPS-specific mAbs (4C7, 3D11 and 9C1-2). To facilitate detection, the membranes were incubated for 1 h at room temperature with 1/5000 dilutions of an anti-mouse IgG horse radish peroxidase conjugate (SouthernBiotech). The blots were then visualized using Pierce ECL Western Blotting Substrate (Pierce).

Immunofluorescence staining and microscopy. *B. mallei* ATCC 23344 was cultured at 37 °C with aeration (200 rpm) in LB Lennox broth (Fisher Scientific) supplemented with 4% glycerol. Mid log phase bacteria were pelleted by centrifugation, fixed with 2.5% paraformaldehyde for 15 min then washed extensively with PBS and then blocked with PBS containing 10% normal goat serum (PBS-G; Invitrogen) for 20 min. Bacteria were stained with CRM197, OC-4744 or SOC-6 mouse antiserum (from mice represented by green dots in Fig 8a and 8b) diluted 1/500 in PBS-G for 30 min, washed three times with PBS and then incubated with Alexa Fluor 488 goat anti-mouse IgG (Invitrogen) diluted 1/1000 in PBS-G for 30 min. Stained bacteria were then washed three times with PBS, rinsed two times with water and mounted onto glass slides with ProLong Gold (Invitrogen) medium. Fluorescence and bright field microscopy was performed using a Nikon Eclipse 90i imaging system using a CFI Plan APO VC 100X/1.4 oil objective (Nikon Instruments Inc.). Images were acquired using NIS-Elements Advanced Research software (Nikon Instruments Inc.). All manipulations of *B. mallei* were conducted in CDC-approved and -registered biosafety level 3 facility at the University of South Alabama in accordance with standard select agent operating practices in compliance with the rules and regulations of the U.S. Federal Select Agent Program.

Immunogenicity evaluation. Groups of 6–8 week old female C57BL/6 mice (Charles River) were immunized subcutaneously on days 0, 21 and 35 with 10 μg of the OAg-CRM197 glycoconjugate OC-2808 formulated in saline plus Alhydrogel 2% (500 μg/mouse; Brenntag) and PolyI:C (PIC; 30 μg/mouse; InvivoGen). Terminal bleeds were conducted 14 days after the third immunization for the assessment of antibody responses. All procedures involving mice were performed according to protocols approved by the University of South Alabama Institutional Animal Care and Use Committee and were conducted in strict accordance with the recommendations in the Guide for the Care and Use of Laboratory Animals of the National Institutes of Health.

Synthetic methods and characterization data

Allyl 6-Deoxy-2,3-*O*-isopropylidene-*α*-L-talopyranoside (**S2**).



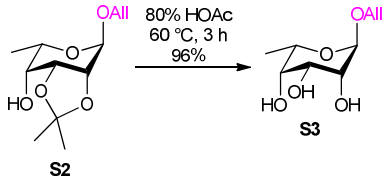
To a cooled (0 °C) solution of allylic alcohol (128 mL) was added dropwise acetyl chloride (9.9 mL, 138.8 mmol, 2.5 equiv). After 1 h, L-rhamnose (10 g, 55.5 mmol, 1.0 equiv) was added to the former solution and the reaction mixture was stirred at 70 °C. After 2 h, the reaction mixture was allowed to slowly warm up to rt and then solid $NaHCO_3$ was added. The mixture was filtered over Celite, rinsed with MeOH and the filtrate was concentrated under reduced pressure. The crude triol was dissolved in anhydrous acetone (61 mL) and 2,2-dimethoxypropane (21 mL, 166.5 mmol, 3.0 equiv) followed by a catalytic amount of PTSA (1.5 mg, 8.4 mmol, 0.15 equiv) were added. The reaction mixture was stirred for 3 h at rt under N_2 and diluted with DCM (150 mL). The organic phase was washed with water (3 × 50 mL). The solvents of the dried ($MgSO_4$) solution were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 6:4 to 5:5) to give alcohol **S1**[1] (9.4 g, 91%, two steps) as a yellow oil: R_f 0.5 (DCM/MeOH 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.95–5.85 (m, 1H, H-2$_{All}$), 5.31 (ddd, J = 17.2, 3.8, 1.7 Hz, 1H, H-3a$_{All}$), 5.22 (ddd, J = 10.3, 3.3, 1.4 Hz, 1H, H-3b$_{All}$), 5.01 (s, 1H, H-1), 4.19 (ddt, J = 12.5, 5.1, 1.9 Hz, 1H, H-1a$_{All}$), 4.17 (d, J = 5.6 Hz, 1H, H-2), 4.10 (t, J = 6.9 Hz, 1H, H-3), 4.01 (ddt, J = 12.6, 6.2, 2.0 Hz, 1H, H-1b$_{All}$), 3.73–3.66 (m, 1H, H-5), 3.40 (ddd, J = 9.3, 5.9, 4.6, 2.0 Hz, 1H, H-4), 2.50 (d, J = 4.6 Hz, 1H, O*H*), 1.53 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.30 (d, J = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 133.6 (C-2$_{All}$), 117.9 (C-3$_{All}$), 109.5 ($C(CH_3)_2$), 96.2 (C-1), 78.3 (C-3), 75.8 (C-2), 74.5 (C-4), 68.0 (C-1$_{All}$), 65.9 (C-5), 27.9, 26.1 (2 x CH_3), 17.5 (CH_{3Tal}).

Route A (Dess-Martin periodinane procedure): Alcohol **S1** (500 mg, 2.1 mmol, 1.0 equiv) was dissolved in anhydrous DCE (31 mL) at rt under Ar. Dess-Martin periodinane (1.9 g, 4.5 mmol, 2.2 equiv) was added and the mixture was refluxed for 1 h. The reaction mixture was cooled down to rt, diluted with DCM (30 mL) and washed with a 10% $Na_2S_2O_3$(aq) solution (20 mL). The organic phase was washed with brine (50 mL) and dried ($MgSO_4$). The solvents were concentrated under reduced pressure. The ketone was dissolved in MeOH/DCM (38 mL, 4:1 *v/v*), the solution was cooled to –10 °C, and $NaBH_4$ (250 mg, 6.5 mmol, 3.2 equiv) was slowly added. The mixture was stirred from –10 to 0 °C under Ar for 1 h. The reaction mixture was quenched by adding a 10% HOAc(aq) solution (2 mL) and then concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 90:10 to 85:15) to give alcohol **S2** (310 mg, 65%, two steps) as a colorless oil: R_f 0.4 (tol/EtOAc 8:2).

Route B (Pfitzner-Moffatt procedure): To a solution of DMSO (4.4 mL, 61.4 mmol, 5.0 equiv) in anhydrous DCM (123 mL) at –10 °C under Ar were added sequentially with stirring PDCP (5.5 mL, 36.8 mmol, 3.0 equiv) and Et_3N (8.6 mL, 61.4 mmol, 5.0 equiv). Then a solution of alcohol

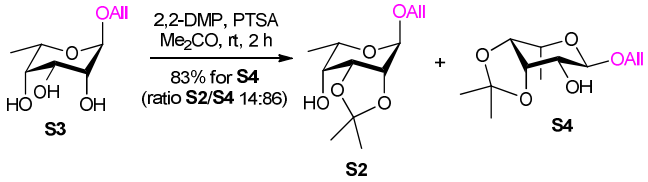
S1 (3.0 g, 12.3 mmol, 1.0 equiv) in DCM (61 mL) was added dropwise during 1 h. The reaction mixture was stirred at –10 °C for 10 min, then allowed to slowly warm up to rt. After 30 min, water (100 mL) was added. The organic phase was separated and the aqueous phase was extracted with DCM (3 × 40 mL). The combined organic phases were washed with brine. The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. To a cooled (–10 °C) solution of the ketone in MeOH (123 mL) was slowly added $NaBH_4$ (558 mg, 22.1 mmol, 1.8 equiv). The mixture was stirred from –10 to 0 °C under Ar for 1 h. Then, the reaction mixture was diluted with DCM (200 mL) and the organic layer was washed with water (120 mL). The aqueous layer was back extracted with DCM (3 × 50 mL). The combined organic phases were washed with brine, dried ($MgSO_4$) and then concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 8:2) to give alcohol **S2** (2.1 g, 70%, two steps) as a colorless oil: R_f 0.2 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = –46 (*c* 1.3, $CHCl_3$/THF 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97–5.87 (m, 1H, H-2$_{All}$), 5.31 (ddd, *J* = 17.2, 3.5, 1.6 Hz, 1H, H-3a$_{All}$), 5.22 (ddd, *J* = 10.3, 3.2, 1.6 Hz, 1H, H-3b$_{All}$), 5.09 (s, 1H, H-1), 4.25-4.18 (m, 2H, H-3, H-1a$_{All}$), 4.07 (td, *J* = 6.4, 0.6 Hz, 1H, H-2), 4.03 (ddt, *J* = 12.8, 6.3, 1.3 Hz, 1H, H-1b$_{All}$), 3.87 (dd, *J* = 13.9, 6.5 Hz, 1H, H-5), 3.56 (t, *J* = 5.8 Hz, 1H, H-4), 2.19 (d, *J* = 6.7 Hz, 1H, O*H*), 1.59 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.33 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.8 (C-2$_{All}$), 117.9 (C-3$_{All}$), 109.4 (*C*$(CH_3)_2$), 96.8 (C-1), 73.5 (C-2), 73.1 (C-3), 68.4 (C-1$_{All}$), 67.1 (C-4), 64.6 (C-5), 25.9, 25.4 (2 × *C*H_3), 16.8 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{12}H_{21}O_5$ 245.1384; found 245.1381; *m/z* $[M + Na]^+$ calcd for $C_{12}H_{20}NaO_5$ 267.1203; found 267.1206; *m/z* $[M + K]^+$ calcd for $C_{12}H_{20}KO_5$ 283.0942; found 283.0939.

Allyl 6-Deoxy-*α*-L-talopyranoside (**S3**).



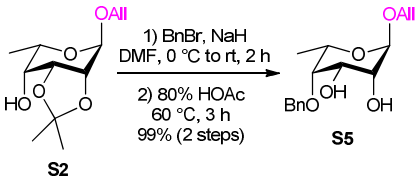
Alcohol **S2** (4.3 g, 17.5 mmol, 1.0 equiv) was dissolved in a 80% HOAc(aq) solution (220 mL). The reaction mixture was stirred at 60 °C for 3 h. Then, the mixture was concentrated under reduced pressure and co-evaporated with toluene (3 ×). Purification by silica gel flash chromatography (DCM/MeOH 98:2 to 85:15) gave triol **S3** (3.4 g, 96%) as a yellow oil: R_f 0.2 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = –97 (*c* 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94–5.84 (m, 1H, H-2_{All}), 5.28 (ddd, *J* = 17.2, 3.8, 2.4 Hz, 1H, H-$3a_{All}$), 5.19 (ddd, *J* = 10.4, 3.4, 2.1 Hz, 1H, H-$3b_{All}$), 4.91 (s, 1H, H-1), 4.16 (ddt, *J* = 13.0, 5.2, 1.5 Hz, 1H, H-$1a_{All}$), 4.00 (ddt, *J* = 12.9, 6.0, 1.3 Hz, 1H, H-$1b_{All}$), 3.92 (dd, *J* = 14.0, 6.5 Hz, 1H, H-5), 3.81–3.80 (m, 2H, H-2, H-3), 3.68 (s, 1H, H-4), 1.29 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.9 (C-2_{All}), 117.5 (C-3_{All}), 99.9 (C-1), 73.0 (C-4), 70.7 (C-2), 68.3 (C-1_{All}), 66.8 (C-3), 66.4 (C-5), 16.6 (CH_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_9H_{16}NaO_5$ 227.0890; found 227.0887.

Allyl 6-Deoxy-3,4-*O*-isopropylidene-*α*-L-talopyranoside (**S4**).



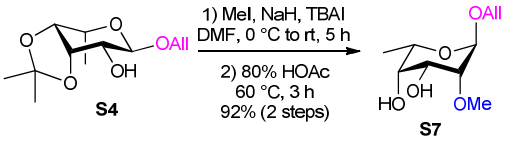
Triol **S3** (1.2 g, 6.1 mmol, 1.0 equiv) was dissolved in anhydrous acetone (7 mL). 2.2-DMP (2.2 mL, 18.4 mmol, 3.0 equiv) and PTSA (58 mg, 310 μmol, 0.05 equiv) were added sequentially. The mixture was stirred for 2 h at rt under Ar, then diluted with DCM (20 mL). The organic phase was washed with a saturated $NaHCO_3$(aq) solution (10 mL) and water (10 mL). The solvents of the dried ($MgSO_4$) solution were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 7:3) to give alcohol **S4** (1.2 g, 83%) as a yellow oil: R_f 0.4 (PE/EtOAc 6:4); $[\alpha]_D^{20}$ = –43 (*c* 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98–5.88 (m, 1H, H-2$_{All}$), 5.31 (ddd, *J* = 17.2, 3.7, 1.6 Hz, 1H, H-3a$_{All}$), 5.19 (ddd, *J* = 10.4, 3.4, 0.9 Hz, 1H, H-3b$_{All}$), 4.81 (d, $J_{1,2}$ = 5.4 Hz, 1H, H-1), 4.52 (dd, *J* = 7.4, 3.4 Hz, 1H, H-3), 4.27 (ddt, *J* = 12.9, 5.3, 1.8 Hz, 1H, H-1a$_{All}$), 4.12 (dd, *J* = 7.4, 2.0 Hz, 1H, H-4), 4.05 (ddt, *J* = 12.8, 6.0, 1.7 Hz, 1H, H-1b$_{All}$), 3.85 (ddd, *J* = 13.8, 6.5, 2.0 Hz, 1H, H-5), 3.73 (dd, *J* = 5.5, 3.4 Hz, 1H, H-2), 1.53 (s, 3H, C*H*$_3$), 1.37 (s, 3H, C*H*$_3$), 1.25 (d, *J* = 6.5 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.4 (C-2$_{All}$), 117.3 (C-3$_{All}$), 110.0 (*C*(CH$_3$)$_2$), 100.0 (C-1), 76.2 (C-4), 73.7 (C-3), 68.8 (C-2), 68.6 (C-1$_{All}$), 65.2 (C-5), 26.1, 25.3 (2 × *C*H$_3$), 15.9 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{12}H_{20}NaO_5$ 267.1203; found 267.1209; *m/z* [M + K]$^+$ calcd for $C_{12}H_{20}KO_5$ 283.0942; found 283.0941.

Allyl 4-*O*-Benzyl-6-deoxy-*α*-L-talopyranoside (**S5**).



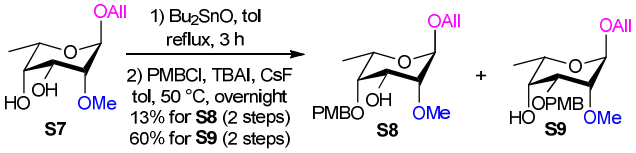
To a cooled (0 °C) solution of alcohol **S2** (6.0 g, 24.6 mmol, 1.0 equiv) in anhydrous DMF (100 mL), was slowly added NaH (60% oil dispersion, 1.5 g, 37.0 mmol, 1.5 equiv) under Ar and the reaction mixture was stirred for 1 h from 0 °C to rt. Then, the mixture was cooled again to 0 °C, BnBr (4.4 mL, 37 mmol, 1.5 equiv) was added dropwise and the reaction mixture was gradually warmed to rt. After being stirred for 2 h under Ar, the reaction was quenched with MeOH (5 mL) and diluted with EtOAc (250 mL). The organic layer was washed with water (2 × 50 mL), a 10% HCl(aq) solution (50 mL) and a saturated $NaHCO_3$(aq) solution (50 mL). Aqueous phases were back extracted with EtOAc (3 × 50 mL). Then, combined organic phases were washed with brine (100 mL) and the solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was dried under high vacuum overnight, then dissolved in a 80% HOAc(aq) solution (308 mL). The reaction mixture was stirred at 60 °C for 3 h. Then, the mixture was concentrated under reduced pressure and co-evaporated with toluene (3 ×). Purification by silica gel flash chromatography (PE/EtOAc 9:1 to 6:4) gave diol **S5** (7.2 g, 99%, two steps) as a lite yellow foam: R_f 0.4 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = –88 (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.28 (m, 5H, C*H*-Ar), 5.93–5.83 (m, 1H, H-2_{All}), 5.27 (ddd, *J* = 17.3, 3.6, 1.6 Hz, 1H, H-$3a_{All}$), 5.18 (ddd, *J* = 10.4, 3.4, 1.4 Hz, 1H, H-$3b_{All}$), 4.90 (s, 1H, H-1), 4.78 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.71 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.15 (ddt, *J* = 13.0, 5.1, 2.8 Hz, 1H, H-$1a_{All}$), 3.99 (ddt, *J* = 13.2, 6.0, 2.9 Hz, 1H, H-$1b_{All}$), 3.92 (dd, *J* = 13.8, 6.6 Hz, 1H, H-5), 3.87 (br s, 1H, H-4), 3.68 (d, *J* = 10.1 Hz, 1H, H-2), 3.64 (br s, 1H, H-3), 3.37 (d, *J* = 11.9 Hz, 1H, O*H*), 2.76 (s, 1H, O*H*), 1.27 (d, *J* = 6.6 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3 (C-Ar), 133.8 (C-2_{All}), 128.6, 128.2, 128.0 (3 × *C*H-Ar), 117.3 (C-3_{All}), 100.1 (C-1), 81.4 (C-3), 76.7 (CH_2Ph), 70.8 (C-2), 68.2 (C-1_{All}), 66.8 (C-4), 66.0 (C-5), 16.9 (CH_{3Tal}); HRMS (ESI-TOF) *m/z* [M + H]$^+$ calcd for $C_{16}H_{23}O_5$ 295.1540; found 295.1542; *m/z* [M + NH_4]$^+$ calcd for $C_{16}H_{26}NO_5$ 312.1805; found 312.1804; *m/z* [M + Na]$^+$ calcd for $C_{16}H_{22}NaO_5$ 317.1359; found 317.1359.

Allyl 6-Deoxy-2-*O*-methyl-*α*-L-talopyranoside (**S7**).



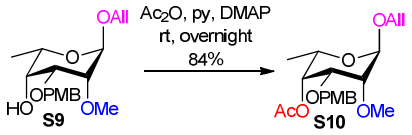
NaH (60% oil dispersion, 94 mg, 2.3 mmol, 2.5 equiv) was added dropwise to a cooled (0 °C) solution of alcohol **S4** (230 mg, 940 μmol, 1.0 equiv) in anhydrous DMF (5 mL). The mixture was stirred for 15 min at this temperature, then MeI (293 μL, 4.7 mmol, 5.0 equiv) and TBAI (35 mg, 94 μmol, 0.1 equiv) were added. The mixture was allowed to warm to rt and stirred for 5 h under Ar. The reaction mixture was diluted with EtOAc (20 mL), then poured into ice-cold brine (10 mL). The organic layer was washed again with brine (2 × 10 mL), dried over $MgSO_4$, concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was dissolved in a 80% HOAc(aq) solution (11 mL). The reaction mixture was stirred at 60 °C for 3 h. Then, the mixture was concentrated under reduced pressure and co-evaporated with toluene (3 ×). Purification by silica gel flash chromatography (PE/EtOAc 8:2 to 7:3) gave diol **S7** (188 mg, 92%, two steps) as a yellow oil: R_f 0.2 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = –42 (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95–5.85 (m, 1H, H-2_{All}), 5.29 (ddd, *J* = 17.2, 3.7, 1.6 Hz, 1H, H-$3a_{All}$), 5.21 (ddd, *J* = 10.4, 3.3, 1.3 Hz, 1H, H-$3b_{All}$), 4.97 (d, $J_{1,2}$ = 1.2 Hz, 1H, H-1), 4.19 (ddt, *J* = 13.0, 5.1, 1.8 Hz, 1H, H-$1a_{All}$), 4.00 (ddt, *J* = 13.0, 6.0, 1.6 Hz, 1H, H-$1b_{All}$), 3.88 (ddd, *J* = 13.8, 6.5, 0.8 Hz, 1H, H-5), 3.82 (br s, 1H, H-3), 3.53 (d, *J* = 9.4 Hz, 1H, H-4), 3.49 (s, 3H, CH_{3Me}), 3.45 (dt, *J* = 3.5, 1.6 Hz, 1H, H-2), 3.02 (s, 1H, O*H*), 2.79 (d, *J* = 11.7 Hz, 1H, O*H*), 1.29 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.7 (C-2_{All}), 117.5 (C-3_{All}), 96 (C-1), 80.4 (C-2), 73.1 (C-4), 68.3 (C-1_{All}), 67.1 (C-5), 66.5 (C-3), 59.4 (*C*H_{3Me}), 16.5 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{10}H_{18}NaO_5$ 241.1046; found 241.1050.

Allyl 6-Deoxy-4-*O*-*para*-methoxybenzyl-2-*O*-methyl-*α*-L-talopyranoside (S8) and Allyl 6-Deoxy-3-*O*-*para*-methoxybenzyl-2-*O*-methyl-*α*-L-talopyranoside (S9).



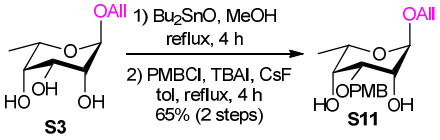
In a vessel equipped with a Dean-Stark apparatus, a suspension of Bu_2SnO (204 mg, 819 μmol, 1.05 equiv) and diol **S7** (170 mg, 780 μmol, 1.0 equiv) was refluxed in toluene (8 mL) for 5 h. The temperature was cooled to 50 °C, then TBAI (303 mg, 819 μmol, 1.05 equiv), CsF (121 mg, 796 μmol, 1.02 equiv) and PMBCl (116 μL, 858 μmol, 1.1 equiv) were successively added and the reaction was refluxed overnight. The reaction mixture was then concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 7:3) to give alcohol **S9** (196 mg, 60%) as a yellow amorphous solid along with its regioisomer **S8** (36 mg, 13%) as a yellow oil. Analytical data for **S9**: R_f 0.3 (PE/EtOAc 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.29 (m, 2H, C*H*-Ar), 6.89–6.86 (m, 2H, C*H*-Ar), 5.93–5.83 (m, 1H, H-2$_{All}$), 5.26 (ddd, J = 17.2, 3.8, 1.6 Hz, 1H, H-3a$_{All}$), 5.19 (ddd, J = 10.4, 3.4, 1.4 Hz, 1H, H-3b$_{All}$), 4.95 (d, $J_{1,2}$ = 1.5 Hz, 1H, H-1), 4.69 (d, J = 11.7 Hz, 1H, C*H*H$_{PMB}$), 4.53 (d, J = 11.7 Hz, 1H, CH*H*$_{PMB}$), 4.16 (ddt, J = 13.1, 5.0, 1.8 Hz, 1H, H-1a$_{All}$), 3.98 (ddt, J = 12.9, 6.0, 1.7 Hz, 1H, H-1b$_{All}$), 3.80 (s, 3H, C*H*$_{3PMB}$), 3.77 (dd, J = 13.0, 6.3 Hz, 1H, H-5), 3.74–3.70 (m, 1H, H-4), 3.69 (t, J = 3.3 Hz, 1H, H-3), 3.53 (dd, $J_{2,3}$ = 3.2 Hz, $J_{1,2}$ = 1.6 Hz, 1H, H-2), 3.53 (s, 3H, C*H*$_{3Me}$), 3.47 (d, J = 9.9 Hz, 1H, O*H*), 2.89 (d, J = 11.6 Hz, 1H, O*H*), 1.30 (d, J = 6.5 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2 (C-Ar), 133.8 (C-2$_{All}$), 130.2 (C-Ar), 129.3 (*C*H-Ar), 117.3 (C-3$_{All}$), 113.8 (*C*H-Ar), 96.9 (C-1), 78.7 (C-2), 73.3 (C-3), 70.4 (C-4), 69.6 (*C*H$_{2PMB}$), 68.1 (C-1$_{All}$), 67.6 (C-5), 59.9 (*C*H$_{3Me}$), 55.3 (*C*H$_{3PMB}$), 16.6 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{18}H_{26}NaO_6$ 361.1622; found 361.1626. Analytical data for **S8**: R_f 0.2 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = –50 (*c* 4.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.29 (m, 2H, C*H*-Ar), 6.88–6.85 (m, 2H, C*H*-Ar), 5.94–5.84 (m, 1H, H-2$_{All}$), 5.27 (ddd, J = 17.2, 3.8, 1.6 Hz, 1H, H-3a$_{All}$), 5.18 (ddd, J = 10.3, 3.3, 1.3 Hz, 1H, H-3b$_{All}$), 4.97 (d, $J_{1,2}$ = 1.1 Hz, 1H, H-1), 4.72 (d, J = 11.8 Hz, 1H, C*H*H$_{PMB}$), 4.57 (d, J = 11.8 Hz, 1H, CH*H*$_{PMB}$), 4.14 (ddt, J = 13.1, 5.1, 1.8 Hz, 1H, H-1a$_{All}$), 3.97 (ddt, J = 12.9, 6.0, 1.7 Hz, 1H, H-1b$_{All}$), 3.87–3.81 (m, 2H, H-5, H-3), 3.80 (s, 3H, C*H*$_{3PMB}$), 3.46 (s, 3H, C*H*$_{3Me}$), 3.45 (d, J = 1.7 Hz, 1H, H-4), 3.27 (dd, J = 4.5, 6.3 Hz, 1H, H-2), 2.89 (d, J = 11.6 Hz, 1H, O*H*), 1.19 (d, J = 6.5 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4 (C-Ar), 134.0 (C-2$_{All}$), 130.7 (C-Ar), 130.1 (*C*H-Ar), 117.2 (C-3$_{All}$), 113.8 (*C*H-Ar), 96.3 (C-1), 78.8 (C-2), 78.4 (C-4), 75.7 (*C*H$_{2PMB}$), 68.0 (C-1$_{All}$), 66.7 (C-5), 65.9 (C-3), 59.9 (*C*H$_{3Me}$), 55.3 (*C*H$_{3PMB}$), 16.9 (*C*H$_{3Tal}$).

Allyl 4-*O*-Acetyl-6-deoxy-3-*O*-*para*-methoxybenzyl-2-*O*-methyl-*α*-L-talopyranoside (S10).



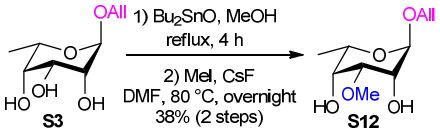
Alcohol **S9** (751 mg, 2.2 mmol, 1.0 equiv) was dissolved in anhydrous py (3 mL). Ac_2O (6 mL) and DMAP (27 mg, 222 μmol, 0.1 equiv) were added. The reaction mixture was stirred overnight at rt under Ar. The mixture was then concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 7:3) to give derivative **S10** (714 mg, 84%) as a yellow amorphous solid: R_f 0.2 (tol/EtOAc 7:3); $[\alpha]_D^{20}$ = –107 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.25 (m, 2H, C*H*-Ar), 6.88–6.86 (m, 2H, C*H*-Ar), 5.93–5.83 (m, 1H, H-2$_{All}$), 5.31 (t, *J* = 2.1 Hz, 1H, H-4), 5.25 (ddd, *J* = 17.2, 3.8, 1.6 Hz, 1H, H-3a$_{All}$), 5.19 (ddd, *J* = 10.4, 3.3, 1.3 Hz, 1H, H-3b$_{All}$), 4.97 (d, $J_{1,2}$ = 1.2 Hz, 1H, H-1), 4.67 (d, *J* = 11.8 Hz, 1H, C*H*H$_{PMB}$), 4.56 (d, *J* = 11.8 Hz, 1H, CH*H*$_{PMB}$), 4.14 (ddt, *J* = 13.0, 5.1, 1.8 Hz, 1H, H-1a$_{All}$), 3.99–3.93 (m, 2H, H-1b$_{All}$, H-5), 3.80 (s, 3H, C*H*$_{3PMB}$), 3.75 (t, *J* = 3.8 Hz, 1H, H-3), 3.53 (s, 3H, C*H*$_{3Me}$), 3.41 (dt, *J* = 3.6, 1.5 Hz, 1H, H-2), 2.20 (s, 3H, C*H*$_{3Ac}$), 1.20 (d, *J* = 6.5 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, (*C*O), 159.3 (C-Ar), 133.8 (C-2$_{All}$), 130.2 (C-Ar), 129.3 (*C*H-Ar), 117.5 (C-3$_{All}$), 113.8 (*C*H-Ar), 97.8 (C-1), 77.2 (C-2), 73.0 (C-3), 70.4 (*C*H$_{2PMB}$), 69.1 (C-4), 68.2 (C-1$_{All}$), 65.1 (C-5), 60.1 (*C*H$_{3Me}$), 55.3 (*C*H$_{3PMB}$), 21.3, (*C*H$_{3Ac}$), 16.4 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{20}H_{28}NaO_7$ 403.1727; found 403.1738; *m/z* [M + K]$^+$ calcd for $C_{20}H_{28}KO_7$ 419.1467; found 419.1462; *m/z* [2M + Na]$^+$ calcd for $C_{40}H_{56}NaO_{14}$ 783.3562; found 783.3566.

Allyl 6-Deoxy-3-*O*-*para*-methoxybenzyl-α-L-talopyranoside (**S11**).



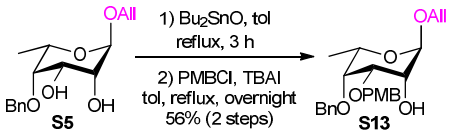
A suspension of Bu_2SnO (1.0 g, 4.0 mmol, 1.1 equiv) and triol **S3** (750 mg, 3.7 mmol, 1.0 equiv) was refluxed in MeOH (37 mL) for 4 h using a Dean-Stark apparatus. Then, the solvents were concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was dissolved in toluene (19 mL). CsF (569 mg, 3.7 mmol, 1.02 equiv), TBAI (587 mg, 3.7 mmol, 1.05 equiv) and PMBCl (523 μL, 3.9 mmol, 1.05 equiv) were successively added and the reaction was refluxed for an additional 4 h. The mixture was then concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (DCM/MeOH 97:3) to give diol **S11** (769 mg, 65%) as a yellow oil, which solidified upon standing at rt: R_f 0.6 (DCM/MeOH 95:5); $[\alpha]_D^{20}$ = –72 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.29 (m, 2H, C*H*-Ar), 6.90–6.87 (m, 2H, C*H*-Ar), 5.93–5.83 (m, 1H, H-2$_{All}$), 5.26 (ddd, *J* = 17.2, 3.7, 1.9 Hz, 1H, H-3a$_{All}$), 5.19 (ddd, *J* = 10.4, 3.5, 1.9 Hz, 1H, H-3b$_{All}$), 4.91 (d, $J_{1,2}$ = 1.5 Hz, 1H, H-1), 4.62 (d, *J* = 11.2 Hz, 1H, C*H*H$_{PMB}$), 4.58 (d, *J* = 11.2 Hz, 1H, CH*H*$_{PMB}$), 4.15 (ddt, *J* = 12.9, 5.2, 1.5 Hz, 1H, H-1a$_{All}$), 3.99 (ddt, *J* = 13.0, 6.0, 1.3 Hz, 1H, H-1b$_{All}$), 3.93–3.89 (m, 1H, H-2), 3.86 (dd, *J* = 13.9, 6.7 Hz, 1H, H-5), 3.80 (s, 3H, C*H*$_{3PMB}$), 3.76–3.74 (m, 1H, H-4), 3.62 (t, *J* = 3.3 Hz, 1H, H-3), 3.46 (d, *J* = 7.2 Hz, 1H, O*H*), 3.05 (d, *J* = 6.2 Hz, 1H, O*H*), 1.30 (d, *J* = 6.6 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5 (C-Ar), 133.9 (C-2$_{All}$), 129.9 (C-Ar), 129.8 (*C*H-Ar), 117.5 (C-3$_{All}$), 114.0 (*C*H-Ar), 99.9 (C-1), 73.0 (C-3), 70.7 (C-4), 69.6 (*C*H$_{2PMB}$), 68.5 (C-2), 68.2 (C-1$_{All}$), 66.4 (C-5), 55.4 (*C*H$_{3PMB}$), 16.6 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{17}H_{24}NaO_6$ 347.1465; found 347.1472; *m/z* $[M + K]^+$ calcd for $C_{17}H_{24}KO_6$ 363.1204; found 363.1202; *m/z* $[2M + Na]^+$ calcd for $C_{34}H_{48}NaO_{12}$ 671.3038; found 671.3044.

Allyl 6-Deoxy-3-*O*-methyl-*α*-L-talopyranoside (**S12**).



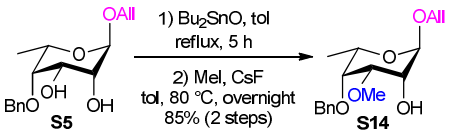
To a solution of triol **S3** (750 mg, 3.7 mmol, 1.0 equiv) in MeOH (37 mL) was added Bu_2SnO (1.0 g, 4.0 mmol, 1.1 equiv) and the mixture was refluxed for 4 h. Then, the solvents were concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was dissolved in DMF (19 mL). CsF (569 mg, 3.7 mmol, 1.02 equiv) and MeI (23 mL, 367 mmol, 100 equiv) were sequentially added. After stirring overnight at 80 °C, the mixture was concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was purified by silica gel flash chromatography (DCM/MeOH 98:2 to 97:3) to give diol **S12** (303 mg, 38%) as a yellow oil: R_f 0.2 (DCM/MeOH 97:3); $[\alpha]_D^{20}$ = –87 (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95–5.85 (m, 1H, H-2$_{All}$), 5.29 (ddd, *J* = 17.2, 3.7, 1.6 Hz, 1H, H-3a$_{All}$), 5.20 (ddd, *J* = 10.4, 3.4, 1.3 Hz, 1H, H-3b$_{All}$), 4.94 (d, $J_{1,2}$ = 0.9 Hz, 1H, H-1), 4.17 (ddt, *J* = 12.9, 5.3, 1.5 Hz, 1H, H-1a$_{All}$), 4.01 (ddt, *J* = 12.9, 6.1, 1.3 Hz, 1H, H-1b$_{All}$), 3.94–3.87 (m, 2H, H-2, H-5), 3.82 (br s, 1H, H-4), 3.53 (d, *J* = 6.0 Hz, 1H, O*H*), 3.47 (s, 3H, CH_{3Me}), 3.43 (t, *J* = 3.3 Hz, 1H, H-3), 1.32 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.9 (C-2$_{All}$), 117.7 (C-3$_{All}$), 99.9 (C-1), 75.3 (C-3), 70.2 (C-4), 68.3 (C-1$_{All}$), 68.1 (C-2), 66.4 (C-5), 55.7 (*C*H$_{3Me}$), 16.6 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{10}H_{18}NaO_5$ 241.1046; found 241.1054; *m/z* [2M + Na]$^+$ calcd for $C_{20}H_{36}NaO_{10}$ 459.2201; found 459.2201.

Allyl 4-*O*-Benzyl-6-deoxy-3-*O*-*para*-methoxybenzyl-*α*-L-talopyranoside (S13).



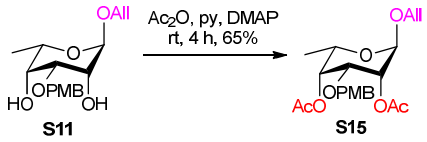
To a solution of diol **S5** (500 mg, 1.7 mmol, 1.0 equiv) in toluene (20 mL) was added Bu_2SnO (444 mg, 1.8 mmol, 1.05 equiv) and the mixture was refluxed using a Dean-Stark apparatus for 3 h. The temperature was cooled to 30 °C, then TBAI (659 mg, 1.8 mmol, 1.05 equiv) and PMBCl (253 μL, 1.9 mmol, 1.1 equiv) were successively added. After refluxing overnight, the mixture was concentrated under reduced pressure. Purification by silica gel flash chromatography (PE/EtOAc 9:1 to 8:2) gave alcohol **S13** (398 mg, 56%) as a yellow oil: R_f 0.4 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = –38 (*c* 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.24 (m, 7H, C*H*-Ar), 6.92–6.87 (m, 2H, C*H*-Ar), 5.92–5.82 (m, 1H, H-2$_{All}$), 5.24 (ddd, *J* = 17.2, 3.7, 1.5 Hz, 1H, H-3a$_{All}$), 5.17 (ddd, *J* = 10.4, 3.5, 1.3 Hz, 1H, H-3b$_{All}$), 4.99 (d, *J* = 11.1 Hz, 1H, CH*H* Ph), 4.92 (d, $J_{1,2}$ = 0.8 Hz, 1H, H-1), 4.76 (d, *J* = 11.4 Hz, 1H, C*H*H$_{PMB}$), 4.61 (d, *J* = 11.1 Hz, 1H, CH*H*Ph), 4.49 (d, *J* = 11.4 Hz, 1H, C*H*H$_{PMB}$), 4.23 (d, *J* = 10.3 Hz, 1H, O*H*), 4.13 (ddt, *J* = 12.9, 5.1, 1.6 Hz, 1H, H-1a$_{All}$), 4.01–3.95 (m, 2H, H-1b$_{All}$, H-2), 3.85 (dd, *J* = 13.1, 6.5 Hz, 1H, H-5), 3.82 (s, 3H, C*H*$_{3PMB}$), 3.75 (t, *J* = 3.3 Hz, 1H, H-3), 3.64 (t, *J* = 1.5 Hz, 1H, H-4), 1.20 (d, *J* = 6.5 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 137.7 (2 × C-Ar), 133.9 (C-2$_{All}$), 130.4 (C-Ar), 129.2–127.9 (*C*H-Ar), 117.1 (C-3$_{All}$), 113.8 (*C*H-Ar), 100.8 (C-1), 78.9 (C-4), 75.5 (*C*H$_2$Ph), 74.1 (C-3), 69.5 (*C*H$_{2PMB}$), 68.1 (C-1$_{All}$), 68.0 (C-2), 66.5 (C-5), 55.3 (*C*H$_{3PMB}$), 16.8 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{24}H_{31}O_6$ 415.2115; found 415.2109; *m/z* $[M + NH_4]^+$ calcd for $C_{24}H_{34}NO_6$ 432.2380; found 432.2379; *m/z* $[M + Na]^+$ calcd for $C_{24}H_{30}NaO_6$ 437.1934; found 437.1931.

Allyl 4-*O*-Benzyl-6-deoxy-3-*O*-methyl-*α*-L-talopyranoside (**S14**).



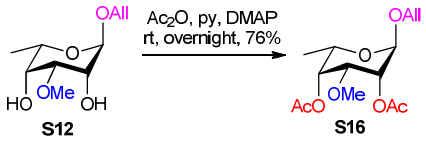
To a solution of diol **S5** (500 mg, 1.7 mmol, 1.0 equiv) in toluene (7 mL) was added Bu_2SnO (465 mg, 1.9 mmol, 1.1 equiv) and the mixture was refluxed using a Dean-Stark apparatus for 5 h. The temperature was cooled to 30 °C, then CsF (263 mg, 1.7 mmol, 1.02 equiv) and MeI (11 mL, 170 mmol, 100 equiv) were successively added. After stirring overnight at 80 °C, the mixture was concentrated under reduced pressure. Purification by silica gel flash chromatography (PE/EtOAc 9:1 to 8:2) gave alcohol **S14** (446 mg, 85%) as a yellow oil: R_f 0.4 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = –52 (*c* 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.27 (m, 5H, C*H*-Ar), 5.94–5.84 (m, 1H, H-2_{All}), 5.28 (ddd, *J* = 17.2, 3.7, 1.6 Hz, 1H, H-$3a_{All}$), 5.19 (ddd, *J* = 10.4, 3.2, 1.3 Hz, 1H, H-$3b_{All}$), 4.98 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.93 (d, $J_{1,2}$ = 1.7 Hz, 1H, H-1), 4.61 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.15–4.11 (m, 2H, OH, H-$1a_{All}$), 4.01 (ddt, *J* = 13.0, 6.1, 1.3 Hz, 1H, H-$1b_{All}$), 3.96–3.92 (m, 1H, H-2), 3.87 (dd, *J* = 13.8, 6.5 Hz, 1H, H-5), 3.69–3.68 (m, 1H, H-4), 3.54 (t, *J* = 3.2 Hz, 1H, H-3), 3.48 (s, 3H, CH_{3Me}), 1.22 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8 (C-Ar), 134.0 (C-2_{All}), 128.5-128.1 (*C*H-Ar), 117.5 (C-3_{All}), 100.9 (C-1), 78.2 (C-4), 76.6 (C-3), 75.6 (*C*H_2Ph), 68.3 (C-1_{All}), 67.9 (C-2), 66.6 (C-5), 55.9 (*C*H_{3Me}), 17.0 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{17}H_{24}NaO_5$ 331.1516; found 331.1519; *m/z* $[2M + Na]^+$ calcd for $C_{34}H_{48}NaO_{10}$ 639.3140; found 639.3138.

Allyl 2,4-*O*-Di-acetyl-6-deoxy-3-*O*-*para*-methoxybenzyl-*α*-L-talopyranoside (S15).



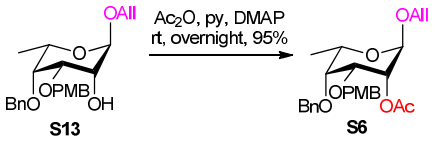
Diol **S11** (766 mg, 2.4 mmol, 1.0 equiv) was dissolved in anhydrous py (12 mL). Ac_2O (12 mL) and DMAP (29 mg, 240 μmol, 0.1 equiv) were added. The reaction mixture was stirred for 4 h at rt under Ar. Then, the mixture was concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was purified by silica gel flash chromatography (DCM/MeOH 1:0) to give derivative **S15** (632 mg, 65%) as a white amorphous solid: R_f 0.8 (DCM/MeOH 96:4); $[\alpha]_D^{20}$ = –64 (*c* 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.22 (m, 2H, C*H*-Ar), 6.87–6.85 (m, 2H, C*H*-Ar), 5.91–5.81 (m, 1H, H-2$_{All}$), 5.28–2.18 (m, 4H, H-3a$_{All}$, H-3b$_{All}$, H-4, H-2), 5.22-5.18 (m, 2H, H-2, H-3b$_{All}$), 4.88 (d, $J_{1,2}$ = 0.9 Hz, 1H, H-1), 4.53 (d, *J* = 11.8 Hz, 1H, C*H*H$_{PMB}$), 4.49 (d, *J* = 11.8 Hz, 1H, CH*H*$_{PMB}$), 4.12 (ddt, *J* = 13.1, 5.2, 1.9 Hz, 1H, H-1a$_{All}$), 4.03 (dd, *J* = 6.6, 1.2 Hz, 1H, H-5), 3.97 (ddt, *J* = 12.7, 6.1, 1.8 Hz, 1H, H-1b$_{All}$), 3.80 (s, 3H, C*H*$_{3PMB}$), 3.78 (t, *J* = 3.9 Hz, 1H, H-3), 2.16 (s, 3H, C*H*$_{3Ac}$), 2.12 (s, 3H, C*H*$_{3Ac}$), 1.19 (d, *J* = 6.5 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.6 (2 × CO), 159.3 (C-Ar), 133.5 (C-2$_{All}$), 130.0 (C-Ar), 129.2 (*C*H-Ar), 117.9 (C-3$_{All}$), 113.8 (*C*H-Ar), 97.8 (C-1), 70.5 (C-3), 70.3 (*C*H$_{2PMB}$), 69.1 (C-4), 68.4 (C-1$_{All}$), 67.3 (C-2), 65.1 (C-5), 55.4 (*C*H$_{3PMB}$), 21.3, 21.1(2 × *C*H$_{3Ac}$), 16.4 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{21}H_{28}NaO_8$ 431.1676; found 431.1690; *m/z* [2M + Na]$^+$ calcd for $C_{42}H_{56}NaO_{16}$ 839.3461; found 839.3468.

Allyl 2,4-*O*-Di-acetyl-6-deoxy-3-*O*-methyl-α-L-talopyranoside (S16).



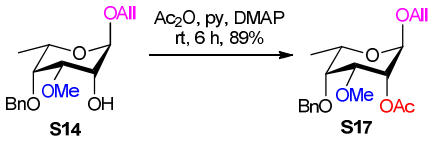
Diol **S12** (319 mg, 1.5 mmol, 1.0 equiv) was dissolved in anhydrous py (7 mL). Ac_2O (7 mL) and DMAP (18 mg, 150 μmol, 0.1 equiv) were added. The reaction mixture was stirred overnight at rt under Ar. Then, the mixture was concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was purified by silica gel flash chromatography (PE/EtOAc 85:15 to 75:15) to give derivative **S16** (338 mg, 76%) as a yellow oil: R_f 0.8 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = –69 (*c* 1.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94–5.84 (m, 1H, H-2$_{All}$), 5.30 (ddd, *J* = 17.1, 3.5, 1.6 Hz, 1H, H-3a$_{All}$), 5.26 (d, *J* = 3.6 Hz, 1H, H-4), 5.23 (ddd, *J* = 10.4, 3.2, 1.3 Hz, 1H, H-3b$_{All}$), 5.18 (dt, *J* = 3.8, 1.5 Hz, 1H, H-2), 4.88 (d, $J_{1,2}$ = 1.1 Hz, 1H, H-1), 4.15 (ddt, *J* = 12.7, 5.3, 1.7 Hz, 1H, H-1a$_{All}$), 4.05 (ddd, *J* = 12.5, 6.6, 1.2 Hz, 1H, H-5), 4.00 (ddt, *J* = 12.4, 6.2, 1.6 Hz, 1H, H-1b$_{All}$), 3.64 (t, *J* = 3.9 Hz, 1H, H-3), 3.37 (s, 3H, C*H*$_{3Me}$), 2.17 (s, 3H, C*H*$_{3Ac}$), 2.14 (s, 3H, C*H*$_{3Ac}$), 1.20 (d, *J* = 6.5 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.6 (2 × *C*O), 133.4 (C-2$_{All}$), 118.1 (C-3$_{All}$), 97.8 (C-1), 73.7 (C-3), 68.6 (C-1$_{All}$), 68.5 (C-4), 67.1 (C-2), 65.2 (C-5), 57.3 (*C*H$_{3Me}$), 21.3, 21.1 (2 × *C*H$_{3Ac}$), 16.4 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{14}H_{22}NaO_7$ 325.1258; found 325.1261.

Allyl 2-*O*-Acetyl-4-*O*-benzyl-6-deoxy-3-*O*-*para*-methoxybenzyl-*α*-L-talopyranoside (**S6**).



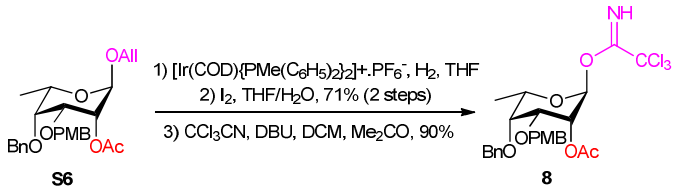
Alcohol **S13** (381 mg, 920 μmol, 1.0 equiv) was dissolved in anhydrous py (3 mL). Ac_2O (3 mL) and DMAP (11 mg, 90 μmol, 0.1 equiv) were added. The reaction mixture was stirred at rt overnight under Ar. Then, solvents were concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 8:2) to give derivative **S6** (397 mg, 95%) as a colorless oil: R_f 0.5 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = –15 (*c* 0.92, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.23 (m, 7H, C*H*-Ar), 6.89–6.87 (m, 2H, C*H*-Ar), 5.92–5.82 (m, 1H, H-2$_{All}$), 5.34 (d, *J* = 3.5 Hz, 1H, H-2), 5.25 (ddd, *J* = 17.2, 3.8, 1.7 Hz, 1H, H-3a$_{All}$), 5.17 (ddd, *J* = 10.3, 3.4, 1.4 Hz, 1H, H-3b$_{All}$), 4.92 (d, *J* = 11.6 Hz, 1H, CH*H*Ph), 4.89 (s, 1H, H-1), 4.68 (d, *J* = 11.6 Hz, 1H, C*H*HPh), 4.67 (d, *J* = 11.5 Hz, 1H, CH*H*$_{PMB}$), 4.42 (d, *J* = 11.5 Hz, 1H, CH*H*$_{PMB}$), 4.12 (dd, *J* = 13.0, 6.4 Hz, 1H, H-1a$_{All}$), 3.97 (dd, *J* = 13.0, 6.0 Hz, 1H, H-1b$_{All}$), 3.89 (dd, *J* = 14.2, 6.5 Hz, 1H, H-5), 3.81 (s, 3H, C*H*$_{3PMB}$), 3.78 (t, *J* = 4.1 Hz, 1H, H-3), 3.52 (s, 1H, H-4), 2.08 (s, 3H, C*H*$_{3Ac}$), 1.26 (d, *J* = 6.5 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1 (*C*O), 159.2, 139.1 (2 × C-Ar), 133.8 (C-2$_{All}$), 130.4 (C-Ar), 129.2–127.4 (*C*H-Ar), 117.5 (C-3$_{All}$), 113.8 (*C*H-Ar), 97.9 (C-1), 75.8 (C-4), 75.0 (C-3), 74.1 (*C*H$_2$Ph), 70.7 (*C*H$_{2PMB}$), 68.2 (C-1$_{All}$), 67.2 (C-2, C-5), 55.4 (*C*H$_{3PMB}$), 21.4 (*C*H$_{3Ac}$), 16.9 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + H]$^+$ calcd for $C_{26}H_{33}O_7$ 457.2221; found 457.2218; *m/z* [M + NH_4]$^+$ calcd for $C_{26}H_{36}NO_7$ 474.2486; found 474.2487; *m/z* [M + Na]$^+$ calcd for $C_{26}H_{32}NaO_7$ 479.2040; found 479.2041.

Allyl 2-*O*-Acetyl-4-*O*-benzyl-6-deoxy-3-*O*-methyl-*α*-L-talopyranoside (**S17**).



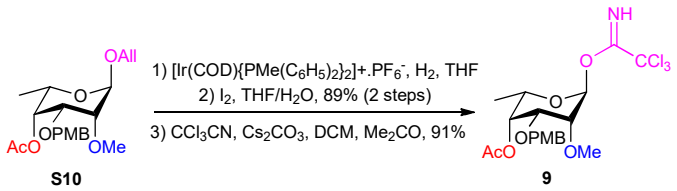
Alcohol **S14** (430 mg, 1.4 mmol, 1.0 equiv) was dissolved in anhydrous py (4 mL). Ac_2O (4 mL) and DMAP (17 mg, 139 μmol, 0.1 equiv) were added. The reaction mixture was stirred for 6 h at rt under Ar. Then, solvents were concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1) to give derivative **S17** (432 mg, 89%) as a yellow oil: R_f 0.5 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = –20 (*c* 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.25 (m, 5H, C*H*-Ar), 5.93–5.83 (m, 1H, H-2$_{All}$), 5.29-5.27 (m, 1H, H-2), 5.28 (ddd, *J* = 17.2, 3.8, 1.5 Hz, 1H, H-3a$_{All}$), 5.19 (ddd, *J* = 10.4, 3.3, 1.2 Hz, 1H, H-3b$_{All}$), 4.92 (d, *J* = 11.8 Hz, 1H, CH*H* Ph), 4.88 (d, $J_{1,2}$ = 1.3 Hz, 1H, H-1), 4.65 (d, *J* = 11.8 Hz, 1H, CH*H* Ph), 4.14 (ddt, *J* = 12.8, 5.2, 1.7 Hz, 1H, H-1a$_{All}$), 3.98 (ddt, *J* = 13.1, 6.1, 1.7 Hz, 1H, H-1b$_{All}$), 3.92 (dd, *J* = 14.1, 6.3 Hz, 1H, H-5), 3.61–3.59 (m, 2H, H-3, H-4), 3.41 (s, 3H, C*H*$_{3Me}$), 2.09 (s, 3H, C*H*$_{3Ac}$), 1.28 (d, *J* = 6.5 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, (*C*O), 139.3 (C-Ar), 133.8 (C-2$_{All}$), 128.2, 128.1, 127.4 (3 × *C*H-Ar), 117.7 (C-3$_{All}$), 97.9 (C-1), 77.8 (C-3), 75.4 (C-4), 74.0 (*C*H_2Ph), 68.3 (C-1$_{All}$), 67.2 (C-5), 67.1 (C-2), 57.2 (*C*H_{3Me}), 21.3 (*C*H_{3Ac}), 16.9 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{19}H_{26}NaO_6$ 373.1622; found 373.1624; *m/z* $[M + K]^+$ calcd for $C_{19}H_{26}KO_6$ 389.1361; found 389.1360.

2-*O*-Acetyl-4-*O*-benzyl-6-deoxy-3-*O*-*para*-methoxybenzyl-*α*-L-talopyranosyl 2,2,2-Trichloroacetimidate (8).



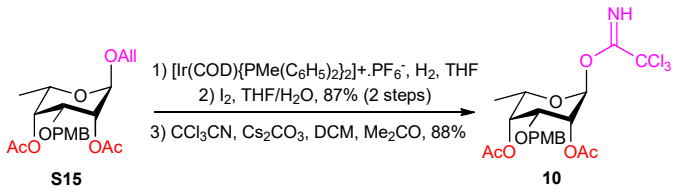
Allyl taloside **S6** (397 mg, 870 μmol, 1.0 equiv) was reacted according to the general procedure for the synthesis of trichloroacetimidate donors (first part). Purification by silica gel flash chromatography (PE/EtOAc 9:1 to 7:3) gave a hemiacetal (258 mg, 71%, ratio α/β ~ 3:1) as a yellow oil: R_f 0.4 (PE/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.25 (m, 8H, C*H*-Ar), 6.90–6.87 (m, 2H, C*H*-Ar), 5.32–5.31 (m, 1H, H-2), 5.29 (s, 1H, H-1), 4.91 (d, J = 11.8 Hz, 1H, C*H*HPh), 4.69 (d, J = 11.8 Hz, 1H, CH*H*Ph), 4.67 (d, J = 11.5 Hz, 1H, C*H*H$_{PMB}$), 4.45 (d, J = 11.5 Hz, 1H, C*H*H$_{PMB}$), 4.14 (ddd, J = 13.7, 6.5, 1.3 Hz, 1H, H-5), 3.84 (t, J = 3.5 Hz, 1H, H-3), 3.81 (s, 3H, C*H*$_{3PMB}$), 3.54 (t, J = 1.6 Hz, 1H, H-4), 2.76 (s, 1H, O*H*), 2.10 (s, 3H, C*H*$_{3Ac}$), 1.27 (d, J = 6.6 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1 (*C*O), 159.3, 139.0, 130.4 (3 × C-Ar), 129.3, 128.4, 128.2, 127.6 (4 × *C*H-Ar), 113.9 (C-Ar), 93.6 (C-1), 75.8 (C-4), 74.5 (C-3), 73.9 (*C*H$_2$Ph), 70.8 (*C*H$_{2PMB}$), 67.6 (C-2), 67.5 (C-5), 55.4 (*C*H$_{3PMB}$), 21.4 (*C*H$_{3Ac}$), 16.9 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + NH_4]$^+$ calcd for $C_{23}H_{32}NO_7$ 434.2173; found 434.2169; *m/z* [M + Na]$^+$ calcd for $C_{23}H_{28}NaO_7$ 439.1727; found 439.1725. The hemiacetal (50 mg, 120 μmol, 1.0 equiv) was reacted in the presence of DBU (4 μL, 40 μmol, 0.3 equiv) and CCl_3CN (60 μL, 600 μmol, 5.0 equiv). Purification by silica gel flash chromatography (PE/EtOAc 85:15 to 8:2 + 1% Et_3N) gave imidate **8** (61 mg, 90%) as a colorless oil: R_f 0.5 (PE/EtOAc 6:4); $[\alpha]_D^{20}$ = +3.4 (*c* 0.80, $CHCl_3$); ^{1}H NMR (400 MHz, py-d_5) δ 7.54–7.48 (m, 7H, C*H*-Ar), 7.05–7.03 (m, 2H, C*H*-Ar), 6.83 (s, 1H, H-1), 5.88 (t, J = 1.8 Hz, 1H, H-2), 5.22 (d, J = 11.3 Hz, 1H, C*H*HPh), 4.91 (d, J = 11.3 Hz, 1H, C*H*HPh), 4.79 (d, J = 11.4 Hz, 1H, C*H*H$_{PMB}$), 4.73 (d, J = 11.4 Hz, 1H, C*H*H$_{PMB}$), 4.41 (dd, J = 14.3, 6.3 Hz, 1H, H-5), 4.25 (t, J = 3.6 Hz, 1H, H-3), 3.88 (t, J = 1.5 Hz, 1H, H-4), 3.69 (s, 3H, C*H*$_{3PMB}$), 2.03 (s, 3H, C*H*$_{3Ac}$), 1.43 (d, J = 6.5 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, py-d_5) δ 171.8 (CO), 160.2, 159.9 (2 × C-Ar), 130.4 (*C*H-Ar), 128.9, 128.7, 128.1 (3 × *C*H-Ar), 114.7 (*C*H-Ar), 97.3 (C-1), 76.8 (C-4), 75.0 (*C*H$_2$Ph), 74.8 (C-3), 71.2 (CH$_{2PMB}$, C-5), 66.4 (C-2), 55.5 (*C*H$_{3PMB}$), 21.3 (*C*H$_{3Ac}$), 17.3 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + NH_4]$^+$ calcd for $C_{25}H_{32}Cl_3N_2O_7$ 577.1269; found 577.1264; *m/z* [M + Na]$^+$ calcd for $C_{25}H_{28}Cl_3NNaO_7$ 582.0823; found 582.0822.

4-*O*-Acetyl-6-deoxy-3-*O*-*para*-methoxybenzyl-2-*O*-methyl-*α*-L-talopyranosyl 2,2,2-Trichloroacmetimidate (9).



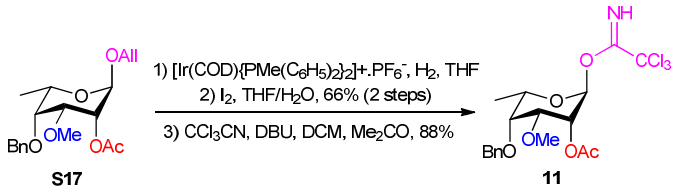
Allyl taloside **S10** (829 mg, 2.2 mmol, 1.0 equiv) was reacted according to the general procedure for the synthesis of trichloroacetimidate donors (first part). Purification by silica gel flash chromatography (PE/EtOAc 85:15 to 5:5) gave a hemiacetal (658 mg, 89%, ratio α/β ~ 3:1) as a yellow amorphous solid: R_f 0.6 (DCM/MeOH 95:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.24 (m, 4H, C*H*-Ar), 6.90–6.87 (m, 4H, C*H*-Ar), 5.35 (dd, J = 3.4, 1.4 Hz, 1H, H-1α), 5.31 (t, J = 1.7 Hz, 1H, H-4α), 5.29–5.27 (m, 1H, H-4β), 4.70 (d, J = 11.5 Hz, 1H, C*H*HPh), 4.68 (d, J = 11.8 Hz, 1H, C*H*HPh), 4.58 (d, J = 12.6 Hz, 1H, H-1β), 4.46 (d, J = 11.8 Hz, 1H, C*H*HPh), 4.42 (d, J = 11.5 Hz, 1H, C*H*HPh), 4.22 (ddd, J = 13.6, 6.5, 1.5 Hz, 1H, H-5α), 4.09 (d, J = 12.6 Hz, 1H, O*H*), 3.81 (s, 3H, CH_{3PMB}), 3.80 (s, 3H, CH_{3PMB}), 3.79 (t, J = 3.8 Hz, 1H, H-3α), 3.66 (s, 3H, CH_{3Me}), 3.61 (ddd, J = 13.8, 6.5, 1.5 Hz, 1H, H-5β), 3.54 (s, 3H, CH_{3Me}), 3.50 (s, 1H, H-3β), 3.49 (d, J = 0.6 Hz, 1H, H-2β), 3.43–3.41 (m, 1H, H-2α), 2.94 (d, J = 3.4 Hz, 1H, O*H*), 2.21, 2.20 (2 × s, 6H, 2 × CH_{3Ac}), 1.26 (d, J = 6.5 Hz, 3H, CH_{3Tal}), 1.20 (d, J = 6.6 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 171.3 (2 × *C*O), 159.3, 159.1 (2 × C-Ar), 130.1, 129.8 (2 × C-Ar), 129.4, 129.3 (2 × *C*H-Ar), 114.0, 113.9 (2 × *C*H-Ar), 94.1 (C-1β), 93.4 (C-1α), 77.9 (C-2β), 77.3 (C-2α), 77.0 (C-3β), 72.4 (C-3α), 70.7 (*C*H_{2PMB}), 70.4 (*C*H_{2PMB}), 69.9 (C-5β), 69.1 (C-4α), 67.6 (C-4β), 65.2 (C-5α), 61.6, 60.1 (2 × *C*H_{3Me}), 55.4, 55.3 (2 × *C*H_{3PMB}), 21.3, 21.2 (2 × *C*H_{3Ac}), 16.5, 16.4 (2 × *C*H_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{17}H_{24}NaO_7$ 363.1414; found 363.1427. The hemiacetal (644 mg, 1.9 mmol, 1.0 equiv) was reacted in the presence of Cs_2CO_3 (123 mg, 380 μmol, 0.2 equiv) and CCl_3CN (950 μL, 9.5 mmol, 5.0 equiv). Purification by silica gel flash chromatography (PE/EtOAc 1:0 to 5:5 + 1% Et_3N) gave imidate **9** (834 mg, 91%) as a yellow oil: R_f 0.6 (PE/EtOAc 5:5 + 1% Et_3N); $[\alpha]_D^{20}$ = –46 (*c* 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, py-d_5) δ 7.58–7.48 (m, 2H, C*H*-Ar), 7.02–6.99 (m, 2H, C*H*-Ar), 6.81 (s, 1H, H-1), 5.74 (br s, 1H, H-4), 4.89 (d, J = 11.4 Hz, 1H, C*H*H$_{PMB}$), 4.68 (d, J = 11.4 Hz, 1H, C*H*H$_{PMB}$), 4.50 (dd, J = 14.0, 6.3 Hz, 1H, H-5), 4.20 (t, J = 3.8 Hz, 1H, H-3), 3.89 (t, J = 1.9 Hz, 1H, H-2), 3.68 (s, 3H, CH_{3PMB}), 3.61 (s, 3H, CH_{3Me}), 2.15 (s, 3H, CH_{3Ac}), 1.32 (d, J = 6.6 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, py-d_5) δ 171.1 (*C*O), 159.9 (C-Ar), 159.4 (C$_{imine}$), 130.1, 114.3 (2 × *C*H-Ar), 97.3 (C-1), 75.3 (C-2), 73.1 (C-3), 70.5 (*C*H_{2PMB}), 68.9 (C-4, C-5), 59.5 (*C*H_{3Me}), 55.2 (*C*H_{3PMB}), 21.0 (*C*H_{3Ac}), 16.6 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{19}H_{24}Cl_3NNaO_7$ 506.0511; found 506.0511.

2,4-Di-*O*-acetyl-6-deoxy-3-*O*-*para*-methoxybenzyl-*α*-L-talopyranosyl 2,2,2-Trichloroacetimidate (10).



Allyl taloside **S15** (602 mg, 1.5 mmol, 1.0 equiv) was reacted according to the general procedure for the synthesis of trichloroacetimidate donors (first part). Purification by silica gel flash chromatography (DCM/MeOH 98:2 to 96:4) gave a hemiacetal (471 mg, 87%, ratio α/β ~ 3:1) as a white amorphous solid: R_f 0.5 (DCM/MeOH 95:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.22 (m, 4H, C*H*-Ar), 6.88–6.85 (m, 2H, C*H*-Ar), 5.32–5.31 (m, 1H, H-2), 5.26 (d, J = 2.4 Hz, 1H, H-1), 5.23 (d, J = 2.9 Hz, 1H, H-4), 5.17 (dt, J = 3.7, 1.4 Hz, 1H, H-2), 4.55 (d, J = 11.8 Hz, 1H, C*H*H$_{PMB}$), 4.49 (d, J = 11.8 Hz, 1H, C*H*H$_{PMB}$), 4.25 (ddd, J = 14.1, 6.6, 1.1 Hz, 1H, H-5), 3.83 (t, J = 3.9 Hz, 1H, H-3), 3.80 (s, 3H, C*H*$_{3PMB}$), 3.15 (d, J = 3.8 Hz, 1H, O*H*), 2.16, 2.13 (2 × s, 6H, 2 × C*H*$_{3Ac}$), 1.19 (d, J = 6.6 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 170.7 (2 × *C*O), 159.3, 129.9 (2 × C-Ar), 129.2 (*C*H-Ar), 113.9 (C-Ar), 93.4 (C-1), 70.3 (*C*H$_{2PMB}$), 69.3 (C-3), 69.1 (C-4), 67.6 (C-2), 65.2 (C-5), 55.4 (*C*H$_{3PMB}$), 21.3, 21.1 (2 × *C*H$_{3Ac}$), 16.5 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{18}H_{24}NaO_8$ 391.1363; found 391.1376; *m/z* [2M + Na]$^+$ calcd for $C_{36}H_{48}NaO_{16}$ 759.2835; found 759.2841. The hemiacetal (455 mg, 1.2 mmol, 1.0 equiv) was reacted in the presence of Cs_2CO_3 (80 mg, 250 μmol, 0.2 equiv) and CCl_3CN (620 μL, 6.2 mmol, 5.0 equiv). Purification by silica gel flash chromatography (PE/EtOAc 1:0 to 7:3 + 1% Et_3N) gave imidate **10** (558 mg, 88%) as a yellow amorphous solid: R_f 0.5 (PE/EtOAc 7:3 + 1% Et_3N); $[\alpha]_D^{20}$ = –32 (*c* 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, py-d_5) δ 7.58–7.46 (m, 2H, C*H*-Ar), 6.96–6.94 (m, 2H, C*H*-Ar), 6.83 (s, 1H, H-1), 5.81 (br s, 1H, H-2), 5.74 (t, J = 1.7 Hz, 1H, H-4), 4.82 (d, J = 11.6 Hz, 1H, C*H*H$_{PMB}$), 4.76 (d, J = 11.6 Hz, 1H, C*H*H$_{PMB}$), 4.55 (dd, J = 14.2, 6.5 Hz, 1H, H-5), 4.31 (t, J = 4.0 Hz, 1H, H-3), 3.64 (s, 3H, C*H*$_{3PMB}$), 2.23, 2.13 (2 × s, 6H, 2 × C*H*$_{3Ac}$), 1.33 (d, J = 6.6 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, py-d_5) δ 170.8, 170.2 (2 × CO), 159.9 (C-Ar), 159.4 (C$_{imine}$), 129.9, 114.3 (2 × *C*H-Ar), 96.7 (C-1), 70.7 (C-3), 70.6 (*C*H$_{2PMB}$), 68.9 (C-4), 68.8 (C-5), 66.0 (C-2), 55.1 (*C*H$_{3PMB}$), 20.9 (2 × *C*H$_{3Ac}$), 16.5 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{20}H_{24}Cl_3NNaO_8$ 534.0460; found 534.0467.

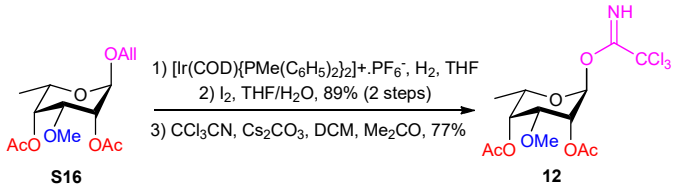
2-*O*-Acetyl-4-*O*-benzyl-6-deoxy-3-*O*-methyl-*α*-L-talopyranosyl 2,2,2-Trichloroacetimidate (11).



S17 11

Allyl taloside **29** (413 mg, 1.2 mmol, 1.0 equiv) was reacted according to the general procedure for the synthesis of trichloroacetimidate donors (first part). Purification by silica gel flash chromatography (PE/EtOAc 85:5 to 8:2 + 1% Et_3N) gave a hemiacetal (242 mg, 66%, ratio α/β ~ 4:1) as a yellow oil: R_f 0.5 (PE/EtOAc 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.27 (m, 5H, C*H*-Ar), 5.29 (br s, 1H, H-1), 5.26 (dd, J = 3.6, 1.2 Hz, 1H, H-2), 4.90 (d, J = 11.8 Hz, 1H, C*H*HPh), 4.65 (d, J = 11.8 Hz, 1H, C*H*HPh), 4.17 (ddd, J = 13.8, 6.5, 1.4 Hz, 1H, H-5), 3.65 (t, J = 3.4 Hz, 1H, H-3), 3.62 (t, J = 1.6 Hz, 1H, H-4), 3.43 (s, 3H, CH_{3Me}), 2.91 (d, J = 3.7 Hz, 1H, O*H*), 2.11 (s, 3H, CH_{3Ac}), 1.29 (d, J = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2 (*C*O), 139.1 (C-Ar), 128.3, 128.2, 127.5 (3 × *C*H-Ar), 93.4 (C-1), 77.4 (C-3), 75.3 (C-4), 73.9 (*C*H_2Ph), 67.5 (C-2), 67.4 (C-5), 57.4 (*C*H_{3Me}), 21.4 (*C*H_{3Ac}), 17.0 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{16}H_{22}NaO_6$ 333.1309; found 333.1316; *m/z* [2M + Na]$^+$ calcd for $C_{32}H_{44}NaO_{12}$ 643.2725; found 643.2744. The hemiacetal (228 mg, 730 μmol, 1.0 equiv) was reacted in the presence of Cs_2CO_3 (48 mg, 150 μmol, 0.2 equiv) and CCl_3CN (370 μL, 3.7 mmol, 5.0 equiv). Purification by silica gel flash chromatography (PE/EtOAc 1:0 to 4:6 + 1% Et_3N) gave imidate **11** (558 mg, 88%) as a yellow oil: R_f 0.7 (PE/EtOAc 7:3 + 1% Et_3N); $[\alpha]_D^{20}$ = –6.4 (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, py-d_5) δ 7.61–7.16 (m, 5H, C*H*-Ar), 6.83 (s, 1H, H-1), 5.84 (t, J = 1.9 Hz, 1H, H-2), 5.14 (d, J = 11.4 Hz, 1H, C*H*HPh), 4.73 (d, J = 11.4 Hz, 1H, CH*H*Ph), 4.43 (dd, J = 14.0, 6.6 Hz, 1H, H-5), 3.97 (t, J = 3.7 Hz, 1H, H-3), 3.87–3.85 (m, 1H, H-4), 3.50 (s, 3H, CH_{3Me}), 2.00 (s, 3H, CH_{3Ac}), 1.43 (d, J = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, py-d_5) δ 170.4 (*C*O), 159.2 (C-Ar), 128.9, 128.6, 127.8 (3 × *C*H-Ar), 96.9 (C-1), 77.7 (C-3), 76.0 (C-4), 74.6 (*C*H_2Ph), 70.7 (C-5), 65.7 (C-2), 57.2 (*C*H_{3Me}), 20.9 (*C*H_{3Ac}), 17.0 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{18}H_{22}Cl_3NNaO_6$ 476.0405; found 476.0417.

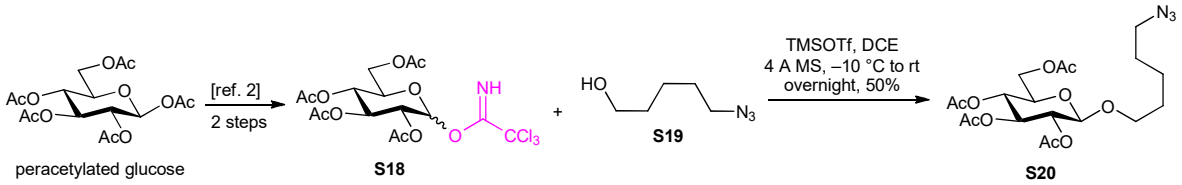
2,4-Di-*O*-acetyl-6-deoxy-3-*O*-methyl-*α*-L-talopyranosyl 2,2,2-Trichloroacetimidate (12).



S16 12

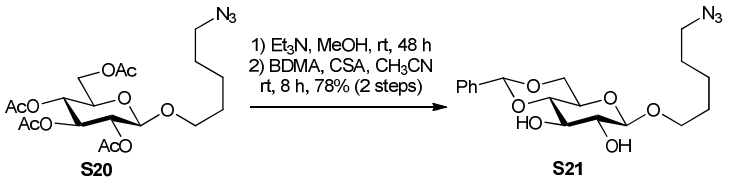
Allyl taloside **S16** (320 mg, 1.1 mmol, 1.0 equiv) was reacted according to the general procedure for the synthesis of trichloroacetimidate donors (first part). Purification by silica gel flash chromatography (PE/EtOAc 85:5 to 6:4 + 1% Et_3N) gave a hemiacetal (248 mg, 89%, ratio α/β ~ 3:1) as a yellow oil: R_f 0.2 (PE/EtOAc 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.28–5.27 (m, 2H, H-1, H-2), 5.18 (td, J = 3.8, 1.5 Hz, 1H, H-4), 4.30 (ddd, J = 13.7, 6.6, 1.2 Hz, 1H, H-5), 3.70 (t, J = 3.8 Hz, 1H, H-3), 3.38 (s, 3H, CH_{3Me}), 2.17, 2.15 (2 × s, 6H, 2 × CH_{3Ac}), 1.20 (d, J = 6.6 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 170.8 (2 × *C*O), 93.2 (C-1), 73.3 (C-3), 68.5 (C-4), 67.4 (C-2), 65.2 (C-5), 57.3 (*C*H_{3Me}), 21.3, 21.1 (2 × *C*H_{3Ac}), 16.5 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{11}H_{18}NaO_7$ 285.0945; found 285.0950. The hemiacetal (234 mg, 890 μmol, 1.0 equiv) was reacted in the presence of Cs_2CO_3 (58 mg, 180 μmol, 0.2 equiv) and CCl_3CN (450 μL, 4.5 mmol, 5.0 equiv). Purification by silica gel flash chromatography (PE/EtOAc 1:0 to 4:6 + 1% Et_3N) gave imidate **12** (281 mg, 77%) as a yellow oil: R_f 0.5 (PE/EtOAc 8:2 + 1% Et_3N); $[\alpha]_D^{20}$ = –18 (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, py-d_5) δ 6.84 (s, 1H, H-1), 5.80 (d, J = 3.4 Hz, 1H, H-2), 5.68 (t, J = 1.7 Hz, 1H, H-4), 4.56 (dd, J = 14.5, 6.3 Hz, 1H, H-5), 4.06 (t, J = 3.9 Hz, 1H, H-3), 3.46 (s, 3H, CH_{3Me}), 2.21, 2.13 (2 × s, 6H, 2 × CH_{3Ac}), 1.32 (d, J = 6.6 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, py-d_5) δ 170.7, 170.1 (2 × CO), 159.1 (C_{imine}), 96.6 (C-1), 74.0 (C-3), 68.7 (C-5), 68.4 (C-4), 65.8 (C-2), 57.1 (*C*H_{3Me}), 20.9, 20.8 (2 × *C*H_{3Ac}), 16.5 (*C*H_{3Tal}).

(5-Azido-1-pentyl) 2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranoside (S20).



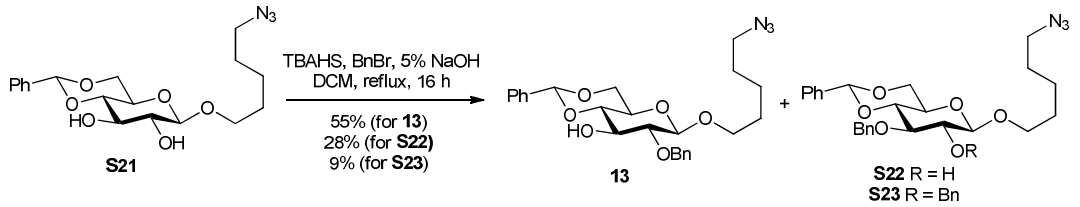
To a solution of glycosyl donor **S18**[2] (562 mg, 1.1 mmol, 1.0 equiv) and 5-azido-1-pentanol **S19**[3] (221 mg, 1.7 mmol, 1.5 equiv) in anhydrous DCE (11 mL) was added freshly activated 4 Å powdered molecular sieves (2.0 g). The mixture was stirred for 1 h at rt under Ar. Then, the reaction mixture was cooled to −10 °C and TMSOTf (60 μL, 303 μmol, 0.3 equiv) was added dropwise. The mixture was stirred from –10 °C to rt for 24 h under Ar. The reaction was quenched with Et_3N (100 μL), filtered over Celite and rinsed with DCM. The filtrate was concentrated under reduced pressure and purified by silica gel flash chromatography (PE/EtOAc 9:1 to 7:3) to give glucoside **S20** (260 mg, 50%) as a colorless oil, which solidified upon standing at 4 °C: R_f 0.5 (PE/EtOAc 6:4); $[\alpha]_D^{20}$ = –12 (*c* 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.20 (t, *J* = 9.7 Hz, 1H, H-3), 5.08 (t, *J* = 9.9 Hz, 1H, H-4), 4.98 (dd, *J* = 9.4, 8.0 Hz, 1H, H-2), 4.49 (d, *J* = 8.1 Hz, 1H, H-1), 4.26 (dd, *J* = 12.4 Hz, 4.7 Hz, 1H, H-6a), 4.14 (dd, *J* = 12.4 Hz, 2.6 Hz, 1H, H-6b), 3.88 (td, *J* = 9.6, 6.6, 6.1, 1H, H-1a$_{linker}$), 3.69 (ddd, *J* = 9.9, 4.8, 2.6 Hz, 1H, H-5), 3.49 (dt, *J* = 9.6, 7.1, 1H, H-1b$_{linker}$), 3.27 (t, *J* = 7.1 Hz, 2H, H-5$_{linker}$), 2.09, 2.05, 2.02, 2.01 (4 × s, 12H, 4 × C*H*$_{3Ac}$), 1.65–1.56 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.46–1.37 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.4, 169.5, 169.4 (4 × *C*O), 100.9 (C-1), 72.9 (C-3), 71.9 (C-5), 71.4 (C-2), 69.8 (C-1$_{linker}$), 68.6 (C-4), 62.1 (C-6), 51.5 (C-5$_{linker}$), 29.1 (C-2$_{linker}$), 28.6 (C-4$_{linker}$), 23.3 (C-3$_{linker}$), 20.9, 20.8, 20.7, 20.6 (4 × *C*H$_{3Ac}$); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{19}H_{30}N_3O_{10}$ 460.1925; found 460.1926; *m/z* $[M + NH_4]^+$ calcd for $C_{19}H_{33}N_4O_{10}$ 477.2191; found 477.2192; *m/z* $[M + Na]^+$ calcd for $C_{19}H_{29}N_3NaO_{10}$ 482.1745; found 482.1746.

(5-Azido-1-pentyl) 4,6-*O*-Benzylidene-*β*-D-glucopyranoside (S21).



Glucoside **S20** (1.2 g, 2.6 mmol, 1.0 equiv) was dissolved in anhydrous MeOH (20 mL). Et_3N (2.1 mL, 15 mmol, 6.0 equiv) was added and the reaction mixture was stirred 48 h at rt under Ar. Then, the mixture was concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was dissolved in anhydrous CH_3CN (10 mL) and BDMA (0.8 mL, 5.2 mmol, 2.0 equiv) followed by CSA (60 mg, 260 μmol, 0.1 equiv) were added. The mixture was stirred for 8 h at rt under Ar. Then, the reaction mixture was quenched with Et_3N (100 μL), concentrated under reduced pressure and purified by silica gel flash chromatography (PE/EtOAc 85:15 to 5:5) to give diol **S21** (776 mg, 78%, two steps) as a white amorphous solid: R_f 0.4 (DCM/MeOH 95:5); $[\alpha]_D^{20}$ = –25 (*c* 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.48 (m, 2H, C*H*-Ar), 7.39–7.36 (m, 3H, C*H*-Ar), 5.53 (s, 1H, H-7), 4.39 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 4.34 (dd, J = 10.7, 4.9 Hz, 1H, H-6a), 3.92 (td, J = 8.9, 6.6 Hz, 1H, H-1a $_{linker}$), 3.84–3.76 (m, 2H, H-3, H-6b), 3.60–3.42 (m, 4H, H-1b$_{linker}$, H-4, H-2, H-5), 3.29 (t, J = 7.2 Hz, 2H, H-5$_{linker}$), 2.79 (s, 1H, O*H*), 2.65 (s, 1H, O*H*), 1.71–1.60 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.51–1.43 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1 (C-Ar), 129.4, 128.5, 126.4 (3 × *C*H-Ar), 103.3 (C-1), 102.0 (C-7), 80.7 (C-4), 74.7 (C-2), 73.3 (C-3), 70.1 (C-1$_{linker}$), 68.8 (C-6), 66.5 (C-5), 51.4 (C-5$_{linker}$), 29.2 (C-2$_{linker}$), 28.6 (C-4$_{linker}$), 23.3 (C-3$_{linker}$); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{18}H_{26}N_3O_6$ 380.1816; found 380.1820; *m/z* $[M + NH_4]^+$ calcd for $C_{18}H_{29}N_4O_6$ 397.2082; found 397.2078; *m/z* $[M + Na]^+$ calcd for $C_{18}H_{25}N_3NaO_6$ 402.1635; found 402.1638.

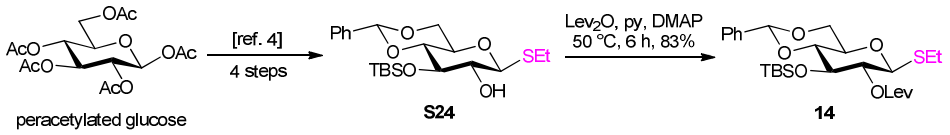
(5-Azido-1-pentyl) 2-*O*-Benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (13).



Diol **S21** (475 mg, 1.2 mmol, 1.0 equiv) was dissolved in DCM (14 mL), then a 5% NaOH(aq) solution (4 mL) was added followed by Bu_4NHSO_4 (85 mg, 250 μmol, 0.2 equiv) and benzyl bromide (261 μL, 2.2 mmol, 1.8 equiv). The emulsion was refluxed for 16 h under Ar. The reaction mixture was poured into a separatory funnel and the aqueous phase was extracted with DCM (3 × 30 mL). The organic layer was dried ($MgSO_4$) and the solvents were concentrated under reduced pressure. Purification by silica gel flash chromatography (PE/EtOAc 9:1 to 7:3) gave alcohol **13** (320 mg, 55%) as a white amorphous powder along with its regioisomer **S22** (160 mg, 28%) as a white foam, and fully benzylated **S23** (62 mg, 9%) as a colorless oil. Analytical data for **13**: R_f 0.4 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = –14 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.47 (m, 2H, C*H*-Ar), 7.39–7.28 (m, 8H, C*H*-Ar), 5.52 (s, 1H, H-7), 4.94 (d, *J* = 11.5 Hz, 1H, C*H*HPh), 4.74 (d, *J* = 11.5 Hz, 1H, CH*H*Ph), 4.51 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 4.34 (dd, *J* = 10.6, 4.9 Hz, 1H, H-6a), 3.94 (td, *J* = 8.9, 6.5 Hz, 1H, H-1a$_{linker}$), 3.83 (t, *J* = 9.5 Hz, 1H, H-3), 3.77 (t, *J* = 10.7 Hz, 1H, H-6b), 3.57 (dt, *J* = 9.6, 7.1 Hz, 1H, H-1b$_{linker}$), 3.54 (t, *J* = 9.6 Hz, 1H, H-4), 3.45–3.39 (m, 1H, H-5), 3.34 (dd, *J* = 9.3, 7.8 Hz, 1H, H-2), 3.24 (t, *J* = 7.3 Hz, 2H, H-5$_{linker}$), 2.49 (s, 1H, O*H*), 1.72–1.58 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.54–1.43 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 137.1 (2 × C-Ar), 129.3–126.4 (6 × *C*H-Ar), 103.9 (C-1), 101.9 (C-7), 81.9 (C-2), 80.5 (C-4), 74.9 (*C*H$_2$Ph), 73.3 (C-3), 70.1 (C-1$_{linker}$), 68.8 (C-6), 66.2 (C-5), 51.4 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.5 (C-3$_{linker}$); HRMS (ESI-TOF) *m/z* [M + H]$^+$ calcd for $C_{25}H_{32}N_3O_6$ 470.2285; found 470.2286; *m/z* [M + NH_4]$^+$ calcd for $C_{25}H_{35}N_4O_6$ 487.2551; found 487.2551; *m/z* [M + Na]$^+$ calcd for $C_{25}H_{31}N_3NaO_6$ 492.2105; found 492.2102. Analytical data for **S22**: $[\alpha]_D^{20}$ = –26 (*c* 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.48 (m, 2H, C*H*-Ar), 7.41–7.28 (m, 8H, C*H*-Ar), 5.57 (s, 1H, H-7), 4.96 (d, *J* = 11.7 Hz, 1H, C*H*HPh), 4.80 (d, *J* = 11.7 Hz, 1H, CH*H*Ph), 4.39 (d, $J_{1,2}$ = 7.6 Hz, 1H, H-1), 4.34 (dd, *J* = 10.6, 4.9 Hz, 1H, H-6a), 3.90 (dt, *J* = 9.6, 6.7 Hz, 1H, H-1a$_{linker}$), 3.80 (t, *J* = 10.6 Hz, 1H, H-6b), 3.71 (t, *J* = 9.4 Hz, 1H, H-4), 3.66 (t, *J* = 9.2 Hz, 1H, H-3), 3.57 (dt, *J* = 9.2, 7.4 Hz, 1H, H-1b$_{linker}$), 3.47–3.41 (m, 1H, H-5), 3.28 (t, *J* = 7.1 Hz, 2H, H-5$_{linker}$), 2.46 (s, 1H, O*H*), 1.70–1.59 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.50–1.43 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 137.3 (2 × C-Ar), 129.1–126.1 (6 × *C*H-Ar), 103.4 (C-1), 101.4 (C-7), 81.5 (C-4), 80.3 (C-3), 74.7 (*C*H$_2$Ph), 74.4 (C-2), 70.1 (C-1$_{linker}$), 68.8 (C-6), 66.5 (C-5), 51.4 (C-5$_{linker}$), 29.2 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.3 (C-3$_{linker}$); HRMS (ESI-TOF) *m/z* [M + H]$^+$ calcd for $C_{25}H_{32}N_3O_6$ 470.2285; found 470.2286; *m/z* [M + NH_4]$^+$ calcd for $C_{25}H_{35}N_4O_6$ 487.2551; found 487.2551; *m/z* [M + Na]$^+$ calcd for $C_{25}H_{31}N_3NaO_6$ 492.2105; found 492.2102. Analytical data for **S23**: $[\alpha]_D^{20}$ = –27 (*c* 5.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.25 (m, 15H, C*H*-Ar), 5.56 (s, 1H, H-7), 4.91 (d, *J* = 11.7 Hz, 1H, C*H*HPh), 4.88 (d, *J* = 11.7 Hz, 1H, CH*H*Ph), 4.80 (d, *J* = 5.9 Hz, 1H, C*H*HPh), 4.78 (d, *J* = 5.9 Hz, 1H, CH*H*Ph), 4.49 (d, $J_{1,2}$ = 7.7 Hz, 1H, H-1), 4.34 (dd, *J* = 10.4, 5.1 Hz, 1H, H-6a), 3.93 (dt, *J* = 9.7, 6.8 Hz, 1H, H-1a$_{linker}$), 3.78 (t, *J* = 10.8 Hz, 1H, H-6b), 3.75 (t, *J* = 9.4 Hz, 1H, H-3), 3.68 (t, *J* = 9.5 Hz, 1H, H-4), 3.56 (dt, *J* = 9.7, 7.1 Hz, 1H, H-1b$_{linker}$), 3.45 (t, *J* = 8.6 Hz, 1H, H-2), 3.43–3.37 (m, 1H, H-5), 3.21 (t, *J* = 7.3 Hz, 2H, H-5$_{linker}$), 1.70–1.56 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.50–1.41 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 138.4, 137.3 (3 × C-

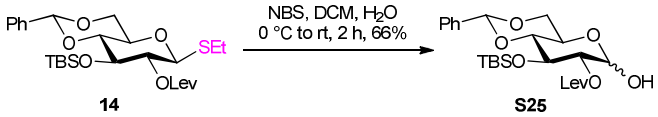
Ar), 129.0–126.1 (9 × *C*H-Ar), 104.1 (C-1), 101.2 (C-7), 82.2 (C-2), 81.6 (C-4), 80.9 (C-3), 75.4, 75.2 (2 × *C*H_2Ph), 70.2 (C-1_{linker}), 68.8 (C-6), 66.1 (C-5), 51.3 (C-5_{linker}), 29.4 (C-2_{linker}), 28.7 (C-4_{linker}), 23.4 (C-3_{linker}); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{32}H_{38}N_3O_6$ 560.2755; found 560.2751; *m/z* $[M + NH_4]^+$ calcd for $C_{32}H_{41}N_4O_6$ 577.3020; found 577.3019; *m/z* $[M + Na]^+$ calcd for $C_{32}H_{37}N_3NaO_6$ 582.2574; found 582.2565.

Ethyl 4,6-*O*-Benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-*O*-levulinoyl-1-thio-*β*-D-glucopyranoside (14).



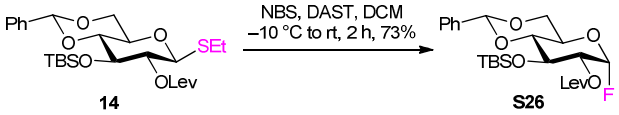
To a solution of alcohol **S24**[4] (1.8 g, 4.3 mmol, 1.0 equiv) in anhydrous py (28 mL) was added DMAP (1.3 g, 10.8 mmol, 2.5 equiv). A solution of levulinic anhydride[5] (8.3 g, 38.8 mmol, 9.0 equiv) in anhydrous py (38 mL) was added dropwise over 30 min to the former mixture. The reaction mixture was then heated to 50 °C and stirred under Ar for 6 h. The solvents were concentrated under reduced pressure and the residue was purified by silica gel flash chromatography (PE/EtOAc 95:5 to 85:15) to give **14** (1.9 g, 83%) as a yellow oil: R_f 0.3 (tol/EtOAc 95:5); $[\alpha]_D^{20}$ = –48 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.45 (m, 2H, C*H*-Ar), 7.37–7.35 (m, 3H, C*H*-Ar), 5.51 (s, 1H, H-7), 2.76 (dd, *J* = 10.3, 8.6 Hz, 1H, H-2), 4.45 (d, $J_{1,2}$ = 10.1 Hz, 1H, H-1), 4.32 (dd, *J* = 10.5, 4.8 Hz, 1H, H-6a), 3.88 (t, *J* = 9.0 Hz, 1H, H-3), 3.75 (t, *J* = 10.5 Hz, 1H, H-6b), 3.54 (t, *J* = 9.4 Hz, 1H, H-4), 3.50–3.44 (m, 1H, H-5), 2.83–275 (m, 2H, CH_{2SEt}), 2.73–2.59 (m, 4H, 2 × CH_{2Lev}), 2.20 (s, 3H, CH_{3Lev}), 1.25 (t, *J* = 7.4 Hz, 3H, CH_{3SEt}), 0.80 (s, 9H, C(CH_3)$_3$), 0.02, –0.02 (2 × s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.3 (CO), 171.7 (CO), 137.1 (C-Ar), 129.2, 128.3, 126.3 (3 × *C*H-Ar), 101.9 (C-7), 84.3 (C-1), 81.5 (C-4), 74.0 (C-3), 73.2 (C-2), 70.8 (C-5), 68.7 (C-6), 38.1 (*C*H_{2SEt}), 30.1 (*C*H_{3Lev}), 28,4 (*C*H_{2Lev}), 25.7 (C(*C*H_3)$_3$), 24.1 (*C*H_{2Lev}), 18.1 (*C*(CH$_3$)$_3$), 14.9 (*C*H_{3SEt}), –4.06, –4.80 (2 × *C*H_3); HRMS (ESI-TOF *m/z* [M + Na]$^+$ calcd for $C_{26}H_{40}NaO_7SSi$ 547.2156; found 547.2162; *m/z* [2M + Na]$^+$ calcd for $C_{52}H_{80}NaO_{14}S_2Si_2$ 1071.4420; found 1071.4425.

4,6-*O*-Benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-*O*-levulinoyl-*α*,*β*-D-glucopyranose (S25).



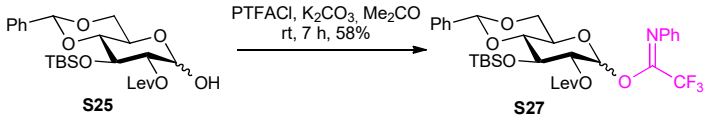
To a cooled (0 °C) solution of thioglucoside **14** (1.0 g, 1.9 mmol, 1.0 equiv) dissolved in DCM/water (22 mL, 10:1 *v/v*) was added NBS (498 mg, 2.7 mmol, 1.4 equiv). The reaction mixture was stirred from 0 °C to rt for 2 h. The mixture was then diluted with DCM (20 mL) and washed with a saturated $NaHCO_3$(aq) solution (10 mL). The aqueous phase was extracted with DCM (3 × 10 mL). The combined organic layers were washed with brine (20 mL). Solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure and the residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 7:3) to give hemiacetal **S25** (630 mg, 66%, ratio *α*/*β* ~ 5:1) as a yellow oil: R_f 0.3 (tol/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.45 (m, 2H, C*H*-Ar), 7.36–7.33 (m, 3H, C*H*-Ar), 5.51 (s, 1H, H-7), 5.38 (d, J = 3.2 Hz, 1H, H-2), 4.74 (dd, J = 9.5, 3.6 Hz, 1H, H-3), 4.26 (dd, J = 10.3, 4.9 Hz, 1H, H-6a), 4.19 (t, J = 9.7 Hz, 1H, H-4), 4.07 (td, J = 10.4, 4.9 Hz, 1H, H-5), 3.71 (t, J = 10.8 Hz, 1H, H-6b), 3.47 (d, $J_{1,2}$ = 9.0 Hz, 1H, H-1), 2.89–272 (m, 2H, CH_{2Lev}), 2.62–2.48 (m, 2H, CH_{2Lev}), 2.19 (s, 3H, CH_{3Lev}), 0.81 (s, 9H, C(CH_3)$_3$), 0.05, 0.00 (2 × s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.4 (*C*O), 172.4 (*C*O), 137.4 (C-Ar), 129.1, 128.3, 126.3 (3 × *C*H-Ar), 101.9 (C-7), 90.9 (C-2), 82.1 (C-1), 75.3 (C-3), 69.3 (C-4), 69.1 (C-6), 62.6 (C-5), 38.3 (*C*H$_{2Lev}$), 29.9 (*C*H$_{3Lev}$), 28.2 (*C*H$_{2Lev}$), 25.8 (C(*C*H$_3$)$_3$), 18.3 (*C*(CH$_3$)$_3$), –4.14, –4.69 (2 × *C*H$_3$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{24}H_{36}NaO_8Si$ 503.2072; found 503.2082.

4,6-*O*-Benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-*O*-levulinoyl-*α*-D-glucopyranosyl Fluoride (S26).



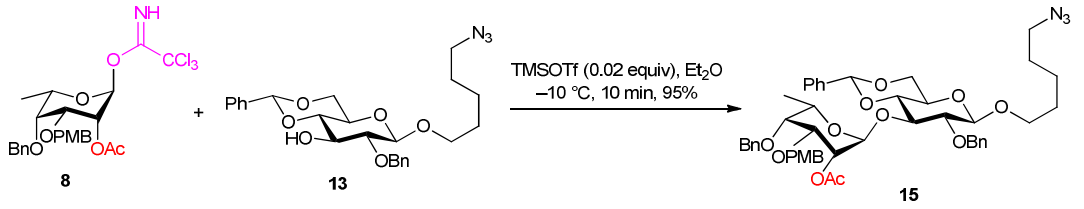
To a cooled (–10 °C) solution of thioglucoside **14** (100 mg, 191 μmol, 1.0 equiv) in anhydrous DCM (2 mL) was added DAST (76 μL, 572 μmol, 3.0 equiv). The reaction mixture was stirred for 8 min, then NBS (47 mg, 267 μmol, 1.4 equiv) was added. The mixture was stirred for 2 h from –10 °C to rt under Ar. The solution was diluted with DCM (20 mL). The organic phase was washed with a saturated $NaHCO_3$(aq) solution (2 × 10 mL) and brine (10 mL). Solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure and the residue was purified by silica gel flash chromatography (PE/EtOAc 85:15) to give fluoride **S26** (68 mg, 73%) as a yellow oil: R_f 0.2 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –41 (*c* 0.63, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.44 (m, 2H, C*H*-Ar), 7.39–7.34 (m, 3H, C*H*-Ar), 5.53 (s, 1H, H-7), 5.34 (dd, $J_{1,F}$ = 53.1, $J_{1,2}$ = 6.5 Hz, 1H, H-1), 5.08–5.01 (m, 1H, H-2), 4.38 (dd, J = 10.5, 4.8 Hz, 1H, H-6a), 3.90 (t, J = 8.6 Hz, 1H, H-3), 3.81 (t, J = 10.5 Hz, 1H, H-6b), 3.70 (t, J = 9.7 Hz, 1H, H-4), 3.56 (td, J = 10.1, 4.9 Hz, 1H, H-5), 2.83–273 (m, 2H, CH_{2Lev}), 2.72–2.58 (m, 2H, CH_{2Lev}), 2.19 (s, 3H, CH_{3Lev}), 0.81 (s, 9H, C(CH_3)$_3$), 0.04, 0.00 (2 × s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.2 (*C*O), 171.4 (*C*O), 136.9 (C-Ar), 129.3, 128.3, 126.3 (3 × *C*H-Ar), 108.3–106.1 (C-1), 101.9 (C-7), 80.8 (C-4), 74.9–74.7 (C-2), 72.3–72.2 (C-3), 68.6 (C-6), 66.1–66.0 (C-5), 37.9 (*C*H$_{2Lev}$), 29.9 (*C*H$_{3Lev}$), 28.0 (*C*H$_{2Lev}$), 25.7 (C(*C*H$_3$)$_3$), 18.1 (*C*(CH$_3$)$_3$), –4.20, –4.86 (2 × *C*H$_3$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{24}H_{35}FNaO_7Si$ 505.2028; found 505.2046.

4,6-*O*-Benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-*O*-levulinoyl-*α,β*-D-glucopyranosyl *N*-Phenyl-2,2,2-trifluoroacetimidate (S27).



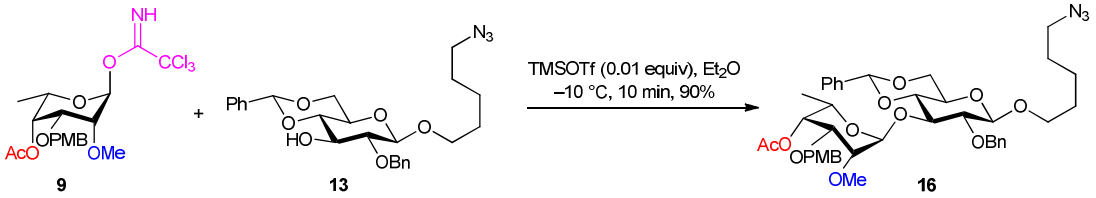
To a solution of hemiacetal **S25** (630 mg, 1.3 mmol, 1.0 equiv) in acetone (26 mL) were added K_2CO_3 (272 mg, 1.9 mmol, 1.5 equiv) followed by 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (PTFACl, 419 μL, 2.6 mmol, 2.0 equiv). The mixture was stirred for 7 h at rt under Ar, then the suspension was filtered over Celite and rinsed with DCM. The solvents were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 + 1% Et_3N) to give imidate **S27** (499 mg, 58%, ratio $\alpha/\beta \sim$ 1:1) as a yellow amorphous solid: R_f 0.6 (PE/EtOAc 7:3); ^{1}H NMR (400 MHz, py-d_5) δ 7.50–7.34 (m, 6H, C*H*-Ar), 7.18–7.13 (m, 4H, C*H*-Ar), 5.78 (s, 1H, H-7), 5.60 (t, J = 9.2 Hz, 1H, H-2), 5.32 (d, J = 7.5 Hz, 1H, H-3), 4.58 (t, J = 9.9 Hz, 1H, H-4), 4.45–4.41 (m, 1H, H-6a), 4.32 (t, J = 9.5 Hz, 1H, H-5), 3.91–3.85 (m, 2H, H-1, H-6b), 2.97–2.75 (m, 4H, 2 × CH_{2Lev}), 2.10 (s, 3H, CH_{3Lev}), 0.96 (s, 9H, C(CH_3)$_3$), 0.21, 0.18 (2 × s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, py-d_5) δ 207.4 (*C*O), 172.4 (*C*O), 138.0, 137.4 (2 × C-Ar), 129.1–121.9 (6 × *C*H-Ar), 102.1 (C-7), 81.3 (C-1), 74.1 (C-2), 73.5 (C-3), 70.1 (C-4), 68.6 (C-6), 65.8 (C-5), 38.1 (*C*H$_{2Lev}$), 29.4 (*C*H$_{3Lev}$), 28.6 (*C*H$_{2Lev}$), 25.9 (C(*C*H$_3$)$_3$), 18.4 (*C*(CH$_3$)$_3$), –4.09, –4.69 (2 × *C*H$_3$).

(5-Azido-1-pentyl) 2-*O*-Acetyl-4-*O*-benzyl-6-deoxy-3-*O*-*para*-methoxybenzyl-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (15).



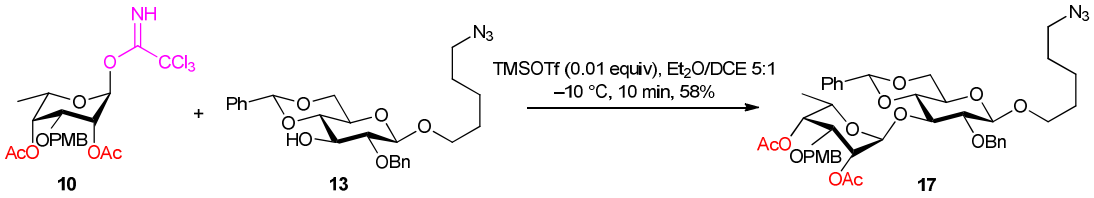
According to the general procedure for the synthesis of protected disaccharides, acceptor **13** (400 mg, 850 μmol, 1.0 equiv) and donor **8** (956 mg, 1.7 mmol, 2.0 equiv) were reacted in the presence of TMSOTf (6 μL, 34 μmol, 0.02 equiv). Purification by combi-flash chromatography (tol/Et_2O 98:2 to 94:6) gave disaccharide **15** (698 mg, 95%) as a white amorphous solid. R_f 0.8 (tol/Et_2O 7:3); $[\alpha]_D^{20}$ = –20 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.20 (m, 17H, C*H*-Ar), 6.86–6.87 (m, 2H, C*H*-Ar), 5.46 (s, 1H, H-7), 5.44 (d, *J* = 3.7 Hz, 1H, H-2B), 5.34 (s, 1H, H-1B), 4.92 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.81 (d, *J* = 11.8 Hz, 1H, CH*H*Ph), 4.69 (d, *J* = 11.2 Hz, 1H, C*H*HPh), 4.66 (d, *J* = 10.9 Hz, 1H, CH*H*Ph), 4.59 (d, *J* = 11.8 Hz, 1H, C*H*HPh), 4.50 (d, $J_{1A,2A}$ = 7.6 Hz, 1H, H-1A), 4.38 (d, *J* = 11.2 Hz, 1H, CH*H*Ph), 4.32 (dd, *J* = 10.8, 4.8 Hz, 1H, H-6aA), 4.10 (dd, *J* = 13.6, 6.3 Hz, 1H, H-5B), 3.98 (t, *J* = 9.4 Hz, 1H, H-3A), 3.92 (dt, *J* = 9.6, 6.4 Hz, 1H, H-1a$_{linker}$), 3.79 (s, 3H, CH_{3PMB}), 3.75 (t, *J* = 10.5 Hz, 1H, H-6bA), 3.70 (t, *J* = 3.7 Hz, 1H, H-3B), 3.56 (dt, *J* = 9.6, 6.9 Hz, 1H, H-1b$_{linker}$), 3.50 (t, *J* = 9.6 Hz, 1H, H-4A), 3.45 (t, *J* = 9.0 Hz, 1H, H-2A), 3.45–3.39 (m, 1H, H-5A), 3.36 (t, *J* = 1.4 Hz, 1H, H-4B), 3.19 (t, *J* = 7.3 Hz, 2H, H-5$_{linker}$), 1.96 (s, 3H, CH_{3Ac}), 1.69–1.55 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.49–1.42 (m, 2H, H-3$_{linker}$), 0.91 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7 (*C*O), 159.1 (C-Ar), 139.2, 138.1, 137.3, 130.6 (4 × C-Ar), 129.4–126.3 (10 × *C*H-Ar), 113.8 (*C*H-Ar), 104.1 (C-1A), 101.8 (C-7), 99.2 (C-1B), 83.3 (C-2A), 79.3 (C-4A), 75.9 (C-4B), 75.5 (C-3A), 75.4 (C-3B), 74.9, 74.0, 70.7 (3 × *C*H_2Ph), 70.2 (C-1$_{linker}$), 68.9 (C-6), 67.1 (C-5B), 66.8 (C-2B), 66.4 (C-5A), 55.4 (*C*H_{3PMB}), 51.3 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.4 (C-3$_{linker}$), 21.3 (*C*H_{3Ac}), 16.6 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{48}H_{57}N_3NaO_{12}$ 890.3834; found 890.3849.

(5-Azido-1-pentyl) 4-*O*-Acetyl-6-deoxy-3-*O*-*para*-methoxybenzyl-2-*O*-methyl-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (16).



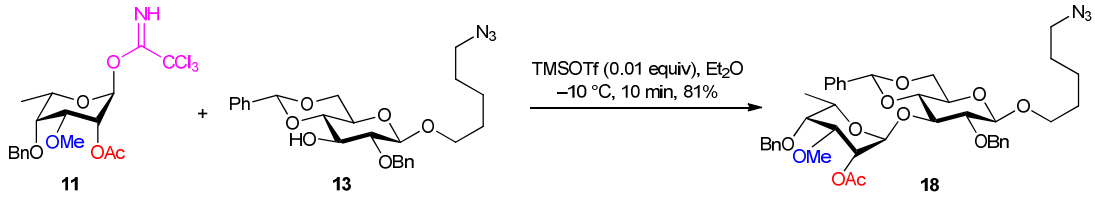
According to the general procedure for the synthesis of protected disaccharides, acceptor **13** (405 mg, 862 μmol, 1.0 equiv) and donor **9** (956 mg, 1.7 mmol, 2.0 equiv) were reacted in the presence of TMSOTf (2 μL, 9 μmol, 0.01 equiv). Purification by combi-flash chromatography (PE/EtOAc 73:27) gave disaccharide **16** (615 mg, 90%) as a white amorphous solid. R_f 0.6 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –72 (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.22 (m, 12H, C*H*-Ar), 6.87–6.85 (m, 2H, C*H*-Ar), 5.46 (s, 1H, H-7), 5.33 (d , J = 1.1 Hz, 1H, H-1B), 5.12 (t, J = 2.0 Hz, 1H, H-4B), 4.98 (d, J = 11.6 Hz, 1H, C*H*HPh), 4.63 (d, J = 11.5 Hz, 2H, CH_{2PMB}), 4.51 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.39 (d, J = 11.6 Hz, 1H, CH*H*Ph), 4.59 (d, J = 11.8 Hz, 1H, C*H*HPh), 4.33 (dd, J = 10.6, 4.7 Hz, 1H, H-6aA), 4.16 (ddd, J = 13.7, 6.5, 1.4 Hz, 1H, H-5B), 3.95–3.90 (m, 2H, H-3A, H-1a$_{linker}$), 3.79 (s, 3H, CH_{3PMB}), 3.75 (t, J = 10.6 Hz, 1H, H-6bA), 3.67 (t, J = 3.7 Hz, 1H, H-3B), 3.56 (dt, J = 9.5, 7.0 Hz, 1H, H-1b$_{linker}$), 3.49 (t, J = 9.4 Hz, 1H, H-4A), 3.46–3.38 (m, 2H, H-2A, H-5A), 3.29 (dt, J = 3.6, 1.5 Hz, 1H, H-2B), 3.22 (s, 3H, CH_{3Me}), 3.19 (t, J = 7.3 Hz, 2H, H-5$_{linker}$), 2.11 (s, 3H, CH_{3Ac}), 1.69–1.55 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.50–1.39 (m, 2H, H-3$_{linker}$), 0.79 (d, J = 6.4 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5 (*C*O), 159.2 (C-Ar), 138.2, 137.2, 130.5 (3 × C-Ar), 129.4–126.3 (7 × *C*H-Ar), 113.8 (*C*H-Ar), 104.2 (C-1A), 102.1 (C-7), 99.6 (C-1B), 83.3 (C-2A), 79.4 (C-4A), 77.1 (C-2B), 76.8 (C-3A), 75.0 (CH_2Ph), 73.4 (C-3B), 70.4 (CH_2Ph), 70.2 (C-1$_{linker}$), 69.2 (C-4B), 68.9 (C-6), 66.5 (C-5A), 65.0 (C-5B), 59.8 (CH_{3Me}), 55.4 (CH_{3PMB}), 51.4 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.5 (C-3$_{linker}$), 21.2 (CH_{3Ac}), 15.8 (CH_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{42}H_{53}N_3NaO_{12}$ 814.3521; found 814.3515.

(5-Azido-1-pentyl) 2,4-Di-*O*-acetyl-6-deoxy-3-*O*-*para*-methoxybenzyl-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (17).



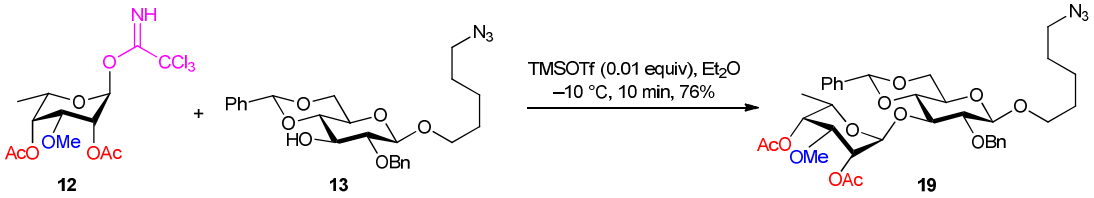
According to the general procedure for the synthesis of protected disaccharides, acceptor **13** (221 mg, 470 μmol, 1.0 equiv) and donor **10** (482 mg, 940 μmol, 2.0 equiv) were reacted in the presence of TMSOTf (1 μL, 5 μmol, 0.01 equiv). Purification by combi-flash chromatography (PE/EtOAc 75:25) gave disaccharide **17** (227 mg, 58%) as a white amorphous solid. R_f 0.5 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –53 (*c* 3.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.21 (m, 12H, C*H*-Ar), 6.86–6.84 (m, 2H, C*H*-Ar), 5.47 (s, 1H, H-7), 5.32 (d, J = 4.0 Hz, 1H, H-2B), 5.29 (s, 1H, H-1B), 5.05 (d, J = 3.2 Hz, 1H, H-4B), 4.91 (d, J = 10.7 Hz, 1H, C*H*HPh), 4.66 (d, J = 10.7 Hz, 1H, CH*H*Ph), 4.50 (d, $J_{1A,2A}$ = 8.0 Hz, 1H, H-1A), 4.49 (s, 2H, CH_{2PMB}), 4.33 (dd, J = 10.6, 4.8 Hz, 1H, H-6aA), 4.22 (dd, J = 14.1, 6.5 Hz, 1H, H-5B), 3.96–3.90 (m, 2H, H-3A, H-1a$_{linker}$), 3.79 (s, 3H, CH_{3PMB}), 3.74 (t, J = 10.0 Hz, 1H, H-6bA), 3.71 (t, J = 3.6 Hz, 1H, H-3B), 3.56 (dt, J = 9.5, 6.7 Hz, 1H, H-1b$_{linker}$), 3.50 (t, J = 9.7 Hz, 1H, H-4A), 3.46–3.39 (m, 2H, H-2A, H-5A), 3.21 (t, J = 7.3 Hz, 2H, H-5$_{linker}$), 2.07, 2.02 (2 × s, 6H, 2 × CH_{3Ac}), 1.70–1.56 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.49–1.41 (m, 2H, H-3$_{linker}$), 0.75 (d, J = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.1 (2 × *C*O), 159.1 (C-Ar), 138.0, 137.2, 130.3 (3 × C-Ar), 129.4–126.3 (7 × *C*H-Ar), 113.8 (*C*H-Ar), 104.2 (C-1A), 101.9 (C-7), 99.2 (C-1B), 83.1 (C-2A), 79.2 (C-4A), 76.2 (C-3A), 75.0 (CH_2Ph), 70.9 (C-3B), 70.3 (CH_{2PMB}), 70.2 (C-1$_{linker}$), 69.3 (C-4B), 68.9 (C-6), 66.7 (C-2B), 66.4 (C-5A), 64.9 (C-5B), 55.3 (CH_{3PMB}), 51.3 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.5 (C-3$_{linker}$), 21.2, 21.0 (2 × CH_{3Ac}), 15.9 (CH_{3Tal}). HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{43}H_{53}N_3NaO_{13}$ 842.3471; found 842.3473; *m/z* [2M + Na]$^+$ calcd for $C_{86}H_{106}N_6NaO_{26}$ 1661.7049; found 10661.7047.

(5-Azido-1-pentyl) 2-*O*-Acetyl-4-*O*-benzyl-6-deoxy-3-*O*-methyl-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (18).



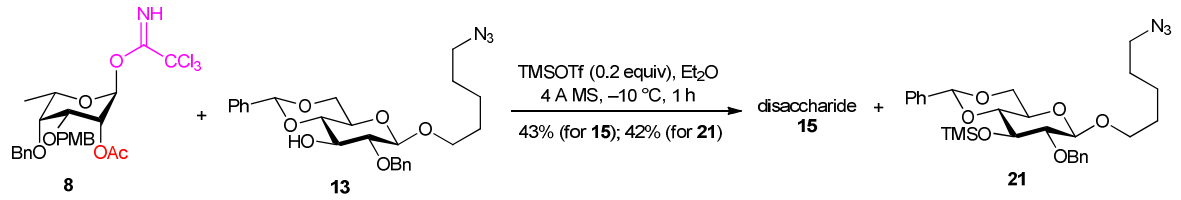
According to the general procedure for the synthesis of protected disaccharides, acceptor **13** (128 mg, 273 μmol, 1.0 equiv) and donor **11** (248 mg, 546 μmol, 2.0 equiv) were reacted in the presence of TMSOTf (0.5 μL, 3 μmol, 0.01 equiv). Purification by combi-flash chromatography (PE/EtOAc 85:15) gave disaccharide **47** (169 mg, 81%) as a white amorphous solid: R_f 0.6 (tol/EtOAc 85:15); $[\alpha]_D^{20}$ = –38 (*c* 0.13, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.21 (m, 15H, C*H*-Ar), 5.48 (s, 1H, H-7), 5.37 (dt, *J* = 3.8, 1.4 Hz, 1H, H-2B), 5.33 (s, 1H, H-1B), 4.90 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.81 (d, *J* = 11.8 Hz, 1H, CH*H*Ph), 4.66 (d, *J* = 10.8 Hz, 1H, CH*H*Ph), 4.56 (d, *J* = 11.8 Hz, 1H, CH*H*Ph), 4.50 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.32 (dd, *J* = 10.6, 4.9 Hz, 1H, H-6aA), 4.12 (dd, *J* = 13.6, 6.5 Hz, 1H, H-5B), 3.99 (t, *J* = 9.5 Hz, 1H, H-3A), 3.92 (dt, *J* = 9.6, 6.5 Hz, 1H, H-1a$_{linker}$), 3.75 (t, *J* = 10.6 Hz, 1H, H-6bA), 3.57 (dt, *J* = 9.6, 6.8 Hz, 1H, H-1b$_{linker}$), 3.51 (t, *J* = 9.2 Hz, 1H, H-4A), 3.49 (t, *J* = 3.9 Hz, 1H, H-3B), 3.47–3.41 (m, 3H, H-2A, H-4A, H-5A), 3.39 (s, 3H, CH_{3Me}), 3.19 (t, *J* = 7.3 Hz, 2H, H-5$_{linker}$), 1.97 (s, 3H, CH_{3Ac}), 1.68–1.55 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.48–1.41 (m, 2H, H-3$_{linker}$), 0.92 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7 (*C*O), 139.3, 138.1, 137.4 (3 × C-Ar), 129.3–126.3 (9 × *C*H-Ar), 104.2 (C-1A), 101.8 (C-7), 99.2 (C-1B), 83.3 (C-2A), 79.4 (C-4A), 77.7 (C-3B), 75.7 (C-4B), 75.4 (C-3A), 74.9 (*C*H_2Ph), 74.0 (*C*H_2Ph), 70.2 (C-1$_{linker}$), 68.9 (C-6), 67.1 (C-5B), 66.6 (C-2B), 66.4 (C-5A), 57.1 (*C*H_{3Me}), 51.3 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.5 (C-3$_{linker}$), 21.3 (*C*H_{3Ac}), 16.7 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{41}H_{51}N_3NaO_{11}$ 784.3416; found 784.3435; *m/z* [2M + Na]$^+$ calcd for $C_{82}H_{102}N_6NaO_{22}$ 1545.6939; found 1545.6987.

(5-Azido-1-pentyl) 2,4-Di-*O*-acetyl-6-deoxy-3-*O*-methyl-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (19).



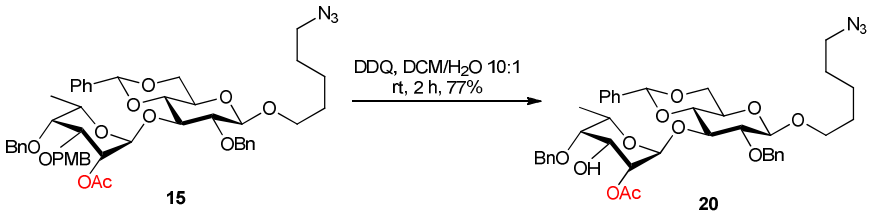
According to the general procedure for the synthesis of protected disaccharides, acceptor **13** (153 mg, 326 μmol, 1.0 equiv) and donor **12** (265 mg, 651 μmol, 2.0 equiv) were reacted in the presence of TMSOTf (0.6 μL, 3 μmol, 0.01 equiv). Purification by silica gel flash chromatography (tol/EtOAc 9:1 to 8:2) gave disaccharide **19** (176 mg, 76%) as a white amorphous solid: R_f 0.4 (tol/EtOAc 7:3); $[\alpha]_D^{20}$ = –62 (*c* 0.13, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.26 (m, 10H, C*H*-Ar), 5.49 (s, 1H, H-7), 5.29 (s, 1H, H-1B), 5.28 (br s, 1H, H-2B), 5.04 (d, J = 3.0 Hz, 1H, H-4B), 4.90 (d, J = 10.7 Hz, 1H, C*H*HPh), 4.68 (d, J = 10.7 Hz, 1H, CH*H*Ph), 4.51 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.34 (dd, J = 10.5, 4.9 Hz, 1H, H-6aA), 4.25 (ddd, J = 13.8, 6.5, 1.1 Hz, 1H, H-5B), 3.96–3.90 (m, 2H, H-3A , H-1a$_{linker}$), 3.77 (t, J = 10.6 Hz, 1H, H-6bA), 3.59–3.42 (m, 5H, H-2A, H-3B, H-4A, H-5A, H-1b$_{linker}$), 3.34 (s, 3H, CH_{3Me}), 3.21 (t, J = 7.3 Hz, 2H, H-5$_{linker}$), 2.09, 2.03 (2 × s, 6H, 2 × CH_{3Ac}), 1.69–1.56 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.49–1.40 (m, 2H, H-3$_{linker}$), 0.76 (d, J = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.1 (2 × *C*O), 138.0, 137.2 (2 × C-Ar), 129.5–126.3 (6 × *C*H-Ar), 104.2 (C-1A), 102.0 (C-7), 99.1 (C-1B), 83.1 (C-2A), 79.2 (C-4A), 76.1 (C-3A), 75.0 (*C*H$_2$Ph), 73.7 (C-3B), 70.2 (C-1$_{linker}$), 68.9 (C-6), 68.8 (C-4B), 66.5 (C-5A), 66.4 (C-2B), 65 (C-5B), 57.2 (*C*H$_{3Me}$), 51.3 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.5 (C-3$_{linker}$), 21.2, 21.0 (2 × *C*H$_{3Ac}$), 15.6 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{36}H_{47}N_3NaO_{12}$ 736.3052; found 736.3061; *m/z* [2M + Na]$^+$ calcd for $C_{72}H_{94}N_6NaO_{24}$ 1449.6212; found 1449.6246.

(5-Azido-1-pentyl) 2-*O*-Benzyl-4,6-*O*-benzylidene-3-*O*-trimethylsilyl-*β*-D-glucopyranoside (21).



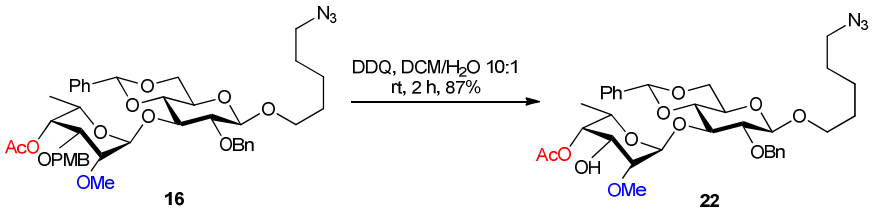
According to the general procedure for the synthesis of protected disaccharides, this derivative was obtained when the reaction was performed for only 1 h in anhydrous Et_2O with 4 Å molecular sieves. Purification by silica gel combi-flash chromatography (tol/Et_2O) gave silylated derivative **21** (42%) as a white amorphous powder along with disaccharide **15** (43%). Analytical data for **21**: $[\alpha]_D^{20}$ = –10 (*c* 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.27 (m, 10H, C*H*-Ar), 5.51 (s, 1H, H-7), 4.86 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.76 (d, *J* = 11.1 Hz, 1H, CH*H*Ph), 4.47 (d, $J_{1,2}$ = 9.8 Hz, 1H, H-1), 4.33 (dd, *J* = 10.4, 4.9 Hz, 1H, H-6aA), 3.92 (dt, *J* = 9.5, 6.6 Hz, 1H, H-1a$_{linker}$), 3.82 (t, *J* = 9.2 Hz, 1H, H-3), 3.77 (t, *J* = 10.4 Hz, 1H, H-6bA), 3.55 (dt, *J* = 9.6, 7.0 Hz, 1H, H-1b$_{linker}$), 3.48 (t, *J* = 9.6 Hz, 1H, H-4), 3.37 (dd, *J* = 9.7, 5.0 Hz, 1H, H-5), 3.32 (dd, *J* = 8.5, 8.0 Hz, 1H, H-2), 3.21 (t, *J* = 7.1 Hz, 2H, H-5$_{linker}$), 1.69–1.55 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.50–1.39 (m, 2H, H-3$_{linker}$), 0.09 (s, 9H, 3 × C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 137.4 (2 × C-Ar), 129.1–126.3 (6 × *C*H-Ar), 104.1 (C-1), 101.6 (C-7), 83.1 (C-2), 81.4 (C-4), 75.4 (*C*H$_2$Ph), 74.5 (C-3), 70.2 (C-1$_{linker}$), 68.9 (C-6), 66.2 (C-5), 51.4 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.4 (C-3$_{linker}$), 0.68 ((*C*H$_3$)$_3$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{28}H_{39}N_3NaO_6Si$ 564.2500; found 564.2503.

(5-Azido-1-pentyl) 2-*O*-Acetyl-4-*O*-benzyl-6-deoxy-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (20).



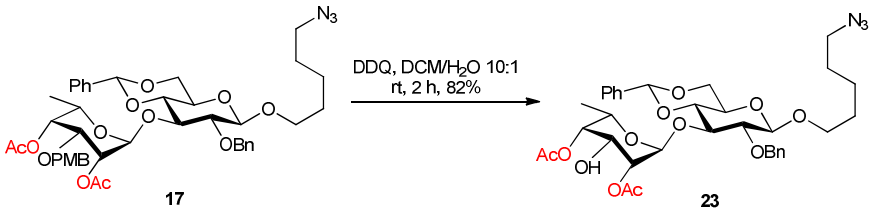
According to the general procedure for the deprotection of PMB group, disaccharide **15** (344 mg, 400 μmol, 1.0 equiv) was reacted in the presence of DDQ (180 mg, 790 μmol, 2.0 equiv). Purification by silica gel flash chromatography (PE/EtOAc 85:15 to 5:5) gave alcohol **20** (255 mg, 77%) as a white amorphous powder: R_f 0.4 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –70 (*c* 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.16 (m, 15H, C*H*-Ar), 5.42 (s, 1H, H-7), 5.24 (s, 1H, H-1B), 4.92 (d, *J* = 4.2 Hz, 1H, H-2B), 4.82 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.64 (d, *J* = 11.6 Hz, 1H, CH*H*Ph), 4.63 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.45 (d, *J* = 11.6 Hz, 1H, CH*H*Ph), 4.42 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.26 (dd, *J* = 10.4, 5.0 Hz, 1H, H-6aA), 4.12 (dd, *J* = 14.2, 6.6 Hz, 1H, H-5B), 3.92–3.82 (m, 3H, H-3A, H-3B, H-1a$_{linker}$), 3.69 (t, *J* = 10.5 Hz, 1H, H-6bA), 3.51–3.33 (m, 4H, H-1b$_{linker}$, H-4A, H-2A, H-5A), 3.27 (d, *J* = 3.5 Hz, 1H, H-4B), 3.13 (t, *J* = 7.1 Hz, 2H, H-5$_{linker}$), 2.50 (d, *J* = 9.2 Hz, 1H, O*H*), 1.89 (s, 3H, CH_{3Ac}), 1.61–1.48 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.42–1.30 (m, 2H, H-3$_{linker}$), 0.87 (d, *J* = 6.6 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4 (*C*O), 138.7, 138.3, 137.4 (3 × C-Ar), 129.3–126.3 (9 × *C*H-Ar), 104.2 (C-1A), 101.9 (C-7), 98.6 (C-1B), 83.2 (C-2A), 79.4 (C-4B), 79.3 (C-4A), 76.1 (*C*H_2Ph), 75.6 (C-3A), 74.9 (*C*H_2Ph), 70.4 (C-2B), 70.2 (C-1$_{linker}$), 68.9 (C-6), 66.5 (C-3B), 66.4 (C-5A), 66.3 (C-5B), 51.4 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.5 (C-3$_{linker}$), 21.2 (*C*H_{3Ac}), 16.6 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{40}H_{49}N_3NaO_{11}$ 770.3259; found 770.3270.

(5-Azido-1-pentyl) 4-*O*-Acetyl-6-deoxy-2-*O*-methyl-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (22).



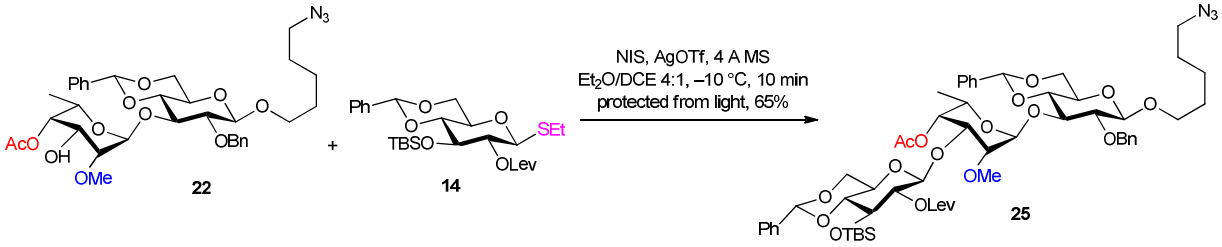
According to the general procedure for the deprotection of PMB group, disaccharide **16** (50 mg, 60 μmol, 1.0 equiv) was reacted in the presence of DDQ (28 mg, 120 μmol, 2.0 equiv). Purification by silica gel flash chromatography (PE/EtOAc 8:2 to 5:5) gave alcohol **22** (35 mg, 87%) as a white amorphous powder: R_f 0.3 (tol/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.23 (m, 10H, C*H*-Ar), 5.48 (s, 1H, H-7), 5.33 (s, 1H, H-1B), 5.06 (d, J = 11.6 Hz, 1H, C*H*HPh), 4.89 (d, J = 4.1 Hz, 1H, H-4B), 4.63 (d, J = 11.6 Hz, 1H, CH*H*Ph), 4.53 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.35 (dd, J = 10.3, 4.8 Hz, 1H, H-6aA), 4.20 (dd, J = 14.0, 6.4 Hz, 1H, H-5B), 3.96 (t, J = 9.8 Hz, 1H, H-3A), 3.95–3.86 (m, 2H, H-1a$_{linker}$, H-3B), 3.76 (t, J = 10.7 Hz, 1H, H-6bA), 3.58–3.42 (m, 4H, H-1b$_{linker}$, H-2A, H-4A, H-5A), 3.20 (d, J = 4.3 Hz, 1H, H-2B), 3.16 (t, J = 7.2 Hz, 2H, H-5$_{linker}$), 3.01 (s, 3H, C*H*$_{3Me}$), 2.67 (d, J = 10.6 Hz, 1H, O*H*), 2.09 (s, 3H, C*H*$_{3Ac}$), 1.67–1.52 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.45–1.37 (m, 2H, H-3$_{linker}$), 0.64 (d, J = 6.6 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5 (*C*O), 138.4, 137.1 (2 × C-Ar), 129.4–126.3 (6 × *C*H-Ar), 104.1 (C-1A), 102.1 (C-7), 97.9 (C-1B), 83.4 (C-2A), 79.4 (C-4A), 78.0 (C-2B), 76.7 (C-3A), 74.7 (*C*H$_2$Ph), 72.2 (C-4B), 70.1 (C-1$_{linker}$), 68.9 (C-6), 66.5 (C-5A), 65.1 (C-3B), 64.4 (C-5B), 59.4 (*C*H$_{3Me}$), 51.3 (C-5$_{linker}$), 29.3 (C-2$_{linker}$), 28.6 (C-4$_{linker}$), 23.4 (C-3$_{linker}$), 21.0 (*C*H$_{3Ac}$), 15.8 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{34}H_{45}N_3NaO_{11}$ 694.2946; found 694.2952; *m/z* [2M + Na]$^+$ calcd for $C_{68}H_{90}N_6NaO_{22}$ 1365.6000; found 1365.6012.

(5-Azido-1-pentyl) 2,4-Di-*O*-acetyl-6-deoxy-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (23).



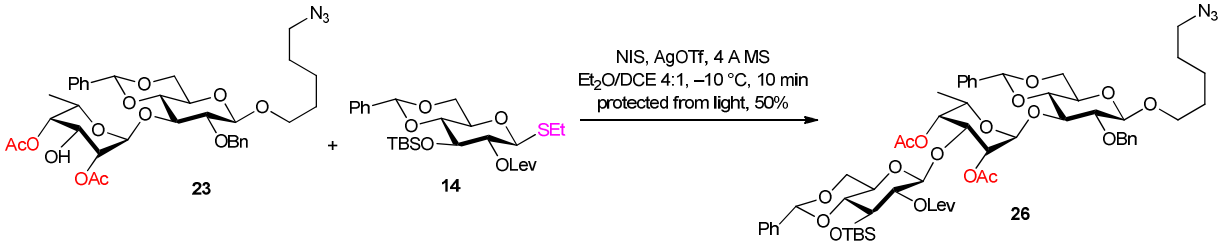
According to the general procedure for the deprotection of PMB group, disaccharide **17** (50 mg, 60 μmol, 1.0 equiv) was reacted in the presence of DDQ (27 mg, 120 μmol, 2.0 equiv). Purification by silica gel flash chromatography (PE/EtOAc 7:3 to 6:4) gave alcohol **23** (35 mg, 82%) as a white amorphous powder: R_f 0.2 (PE/EtOAc 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.27 (m, 10H, C*H*-Ar), 5.48 (s, 1H, H-7), 5.28 (s, 1H, H-1B), 5.04 (d, J = 3.5 Hz, 1H, H-2B), 4.90 (d, J = 10.9 Hz, 1H, C*H*HPh), 4.88 (s, 1H, H-4B), 4.68 (d, J = 10.9 Hz, 1H, CH*H*Ph), 4.50 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.34 (dd, J = 10.6, 4.8 Hz, 1H, H-6aA), 4.28 (dd, J = 14.7, 6.6 Hz, 1H, H-5B), 4.11 (t, J = 4.3 Hz, 1H, H-3B), 3.95–3.90 (m, 2H, H-1a$_{linker}$, H-3A), 3.76 (t, J = 10.8 Hz, 1H, H-6bA), 3.58–3.40 (m, 4H, H-1b$_{linker}$, H-2A, H-4A, H-5A), 3.20 (t, J = 7.3 Hz, 2H, H-5$_{linker}$), 2.09, 2.04 (2 × s, 6H, 2 × CH_{3Ac}), 1.69–1.56 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.48–1.40 (m, 2H, H-3$_{linker}$), 0.75 (d, J = 6.6 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 171.1 (2 × *C*O), 138.1, 137.1 (2 × C-Ar), 129.4–126.2 (6 × *C*H-Ar), 104.2 (C-1A), 101.9 (C-7), 98.7 (C-1B), 83.1 (C-2A), 79.2 (C-4A), 76.1 (C-3A), 74.9 (*C*H$_2$Ph), 71.8 (C-4B), 70.2 (C-1$_{linker}$), 69.6 (C-2B), 68.9 (C-6), 66.4 (C-5A), 65.7 (C-3B), 64.7 (C-5B), 51.3 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.4 (C-3$_{linker}$), 21.1, 20.9 (2 × *C*H$_{3Ac}$), 15.9 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{35}H_{45}N_3NaO_{12}$ 722.2895; found 722.2886; *m/z* [2M + Na]$^+$ calcd for $C_{70}H_{90}N_6NaO_{24}$ 1421.5899; found 1421.5888.

(5-Azido-1-pentyl) 4,6-*O*-Benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-*O*-levulinoyl-*β*-D-glucopyranosyl-(1→3)-4-*O*-acetyl-6-deoxy-2-*O*-methyl-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (25).



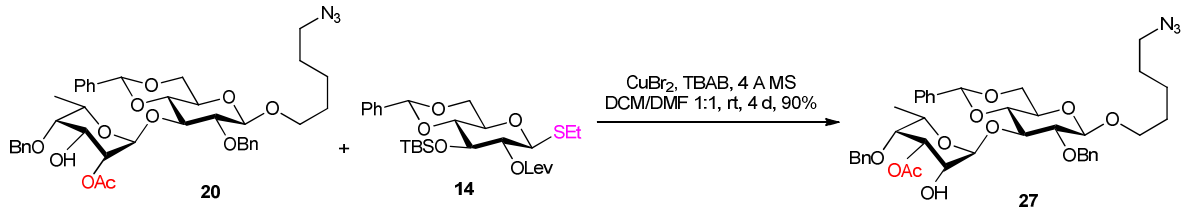
To a solution of donor **14** (457 mg, 871 μmol, 1.5 equiv) and acceptor **22 (**390 mg, 581 μmol, 1.0 equiv) in anhydrous Et_2O/DCE (17 mL, 4:1 *v/v*) was added freshly activated 4 Å molecular sieves (1.5 g). The mixture was stirred at rt for 1 h under Ar. Then, the suspension was cooled to –10 °C, AgOTf (149 mg, 581 μmol, 1.0 equiv) and NIS (261 mg, 1.2 mmol, 2.0 equiv) were added and the flask was protected from light. The reaction mixture was stirred for 10 min at –10 °C under Ar and then quenched with a few drops of Et_3N. The suspension was filtered over Celite, rinsed with DCM and the filtrate was concentrated under reduced pressure. The residue was purified by combi-flash chromatography (PE/EtOAc 71:29) to give trisaccharide **25** (432 mg, 65%) as a yellow amorphous solid: R_f 0.3 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –57 (*c* 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.28 (m, 15H, C*H*-Ar), 5.49 (s, 2H, H-7A, H-7C), 5.32 (s, 1H, H-1B), 4.98 (d, *J* = 11.4 Hz, 1H, C*H*HPh), 4.96 (s, 1H, H-4B), 4.90 (t, *J* = 9.0 Hz, 1H, H-2C), 4.62 (d, *J* = 11.4 Hz, 1H, CH*H*Ph), 4.58 (d, $J_{1C,2C}$ = 7.8 Hz, 1H, H-1C), 4.51 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.31 (ddd, *J* = 19.6, 10.4, 4.9 Hz, 2H, H-6aA, H-6aC), 4.19 (dd, *J* = 15.8, 5.8 Hz, 1H, H-5B), 3.95–3.90 (m, 3H, H-1a$_{linker}$, H-3A, H-3B), 3.82 (t, *J* = 9.3 Hz, 1H, H-3C), 3.78–3.70 (m, 2H, H-6bA, H-6bC), 3.58–3.53 (m, 2H, H-1b$_{linker}$, H-4A), 3.50 (t, *J* = 8.9 Hz, 1H, H-4C), 3.46–3.40 (m, 3H, H-2A, H-5A, H-5C), 3.37 (br s, 1H, H-2B), 3.24 (s, 3H, CH_{3Me}), 3.20 (t, *J* = 7.3 Hz, 2H, H-5$_{linker}$), 2.77–2.74 (m, 2H, CH_{2Lev}), 2.66–2.62 (m, 2H, CH_{2Lev}), 2.16 (s, 3H, CH_{3Lev}), 2.09 (s, 3H, CH_{3Ac}), 1.69–1.56 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.51–1.40 (m, 2H, H-3$_{linker}$), 0.78 (s, 9H, C(CH_3)$_3$), 0.71 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}), 0.00, –0.04 (2 × s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6 (*C*O), 171.5, 171.4 (2 × *C*O), 138.1, 137.2, 137.1 (3 × C-Ar), 129.4–126.3 (9 × *C*H-Ar), 104.1 (C-1A), 102.1 (C-7A, C-7C), 100.9 (C-1C), 100.4 (C-1B), 83.2 (C-2A), 81.6 (C-4C), 79.4 (C-4A), 77.8 (C-2B), 77.0 (C-3A), 75.1 (*C*H$_2$Ph), 74.7 (C-2C), 74.4 (C-3B), 72.7 (C-3C), 70.2 (C-1$_{linker}$), 69.5 (C-4B), 68.9 (C-6A), 68.7 (C-6C), 66.5 (C-5A), 66.3 (C-5C), 65.0 (C-5B), 60.1 (*C*H$_{3Me}$), 51.4 (C-5$_{linker}$), 37.9 (*C*H$_{2Lev}$), 30.1 (*C*H$_{3Lev}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 28.1 (*C*H$_{2Lev}$), 25.7 (C(*C*H$_3$)$_3$), 23.5 (C-3$_{linker}$), 21.1 (*C*H$_{3Ac}$), 18.1 (*C*(CH$_3$)$_3$), 15.7 (*C*H$_{3Tal}$), –4.07, –4.83 (2 × *C*H$_3$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{58}H_{79}N_3NaO_{18}Si$ 1156.5020; found 1156.5040.

(5-Azido-1-pentyl) 4,6-*O*-Benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-*O*-levulinoyl-*β*-D-glucopyranosyl-(1→3)-2,4-di-*O*-acetyl-6-deoxy-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (26).



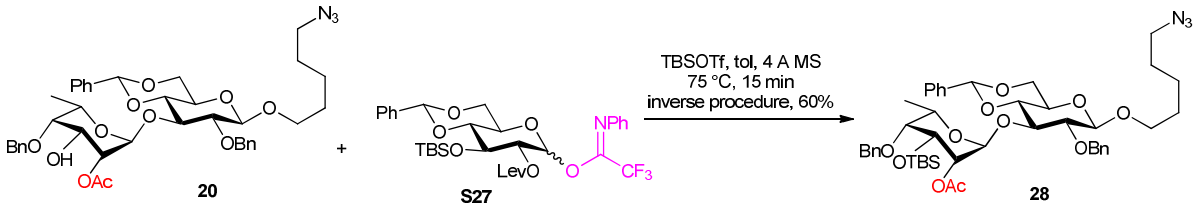
To a solution of donor **14** (105 mg, 200 μmol, 1.5 equiv) and acceptor **23 (**93 mg, 133 μmol, 1.0 equiv) in anhydrous Et_2O/DCE (4 mL, 4:1 *v/v*) was added freshly activated 4 Å molecular sieves (374 mg). The mixture was stirred at rt for 1 h under Ar. Then, the suspension was cooled to –10 °C, AgOTf (34 mg, 133 μmol, 1.0 equiv) and NIS (60 mg, 267 μmol, 2.0 equiv) were added and the flask was protected from light. The reaction mixture was stirred for 10 min at –10 °C under Ar and then quenched with a few drops of Et_3N. The suspension was filtered over Celite, rinsed with DCM and the filtrate was concentrated under reduced pressure. The residue was purified by combi-flash chromatography (PE/EtOAc 8:2) to give trisaccharide **26** (77 mg, 50%) as a colorless solid: R_f 0.5 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –65 (*c* 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.28 (m, 15H, C*H*-Ar), 5.53 (s, 1H, H-7A), 5.50 (s, 1H, H-7C), 5.31 (s, 1H, H-1B), 5.24 (d, *J* = 3.9 Hz, 1H, H-2B), 4.96 (d, *J* = 3.3 Hz, 1H, H-4B), 4.88 (d, *J* = 10.6 Hz, 1H, C*H*HPh), 4.85 (dd, *J* = 7.9, 7.7 Hz, 1H, H-2C), 4.74 (d, *J* = 10.6 Hz, 1H, CH*H*Ph), 4.57 (d, $J_{1C,2C}$ = 7.8 Hz, 1H, H-1C), 4.52 (d, $J_{1A,2A}$ = 7.7 Hz, 1H, H-1A), 4.34 (dt, *J* = 10.3, 4.9 Hz, 2H, H-6aA, H-6aC), 4.19 (dd, *J* = 13.9, 6.2 Hz, 1H, H-5B), 3.99–3.90 (m, 3H, H-1a$_{linker}$, H-3A, H-3B), 3.82–3.72 (m, 3H, H-6bA, H-6bC, H-3C), 3.61–3.37 (m, 6H, H-1b$_{linker}$, H-4A, H-4C, H-2A, H-5A, H-5C), 3.21 (t, *J* = 7.2 Hz, 2H, H-5$_{linker}$), 2.80–2.71 (m, 2H, CH_{2Lev}), 2.67–2.57 (m, 2H, CH_{2Lev}), 2.17 (s, 3H, CH_{3Lev}), 2.10 (s, 3H, CH_{3Ac}), 2.04 (s, 3H, CH_{3Ac}), 1.69–1.56 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.50–1.40 (m, 2H, H-3$_{linker}$), 0.80 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}), 0.77 (s, 9H, C(CH_3)$_3$), 0.00, –0.04 (2 × s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6 (*C*O), 171.3 (*C*O), 170.9, 169.9 (2 × *C*O), 138.2, 137.2, 137.1 (3 × C-Ar), 129.4–126.3 (9 × *C*H-Ar), 104.2 (C-1A), 102.0 (C-7A), 101.9 (C-7C), 100.6 (C-1C), 98.9 (C-1B), 83.0 (C-2A), 81.3 (C-4C), 79.3 (C-4A), 76.1 (C-3A), 74.9 (*C*H$_2$Ph), 74.7 (C-2C), 72.8 (C-3C), 71.3 (C-3B), 70.2 (C-1$_{linker}$), 68.9 (C-6), 68.8 (C-4B), 68.7 (C-6C), 68.4 (C-2B), 66.3 (C-5A), 66.2 (C-5C), 64.7 (C-5B), 51.3 (C-5$_{linker}$), 37.9 (*C*H$_{2Lev}$), 30.0 (*C*H$_{3Lev}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 28.1 (*C*H$_{2Lev}$), 25.7 (C(*C*H$_3$)$_3$), 23.4 (C-3$_{linker}$), 21.1, 20.9 (2 × *C*H$_{3Ac}$), 18.1 (*C*(CH$_3$)$_3$), 15.9 (*C*H$_{3Tal}$), –4.06, –4.87 (2 × *C*H$_3$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{59}H_{79}N_3NaO_{19}Si$ 1184.4969; found 1184.4986.

(5-Azido-1-pentyl) 3-*O*-Acetyl-4-*O*-benzyl-6-deoxy-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (27).



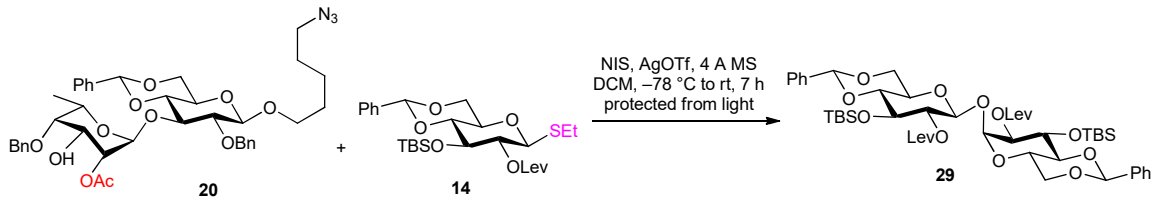
The acceptor **20** (15 mg, 20 μmol, 1.0 equiv) and the donor **14** (21 mg, 40 μmol, 2.0 equiv) were dissolved in anhydrous DCM/DMF (800 μL, 1:1 *v/v*). Freshly activated powdered molecular sieves (4 Å, 60 mg) were added and the mixture was stirred for 1 h at rt under Ar. Then, Bu_4NBr (14 mg, 42 μmol, 2.1 equiv) followed by $CuBr_2$ (9 mg, 40 μmol, 2.0 equiv) were added and the mixture was stirred for 4 d at rt under Ar. The solution was filtered over Celite, rinsed and diluted with DCM (20 mL). The organic phase was washed with a saturated $NaHCO_3$(aq) solution (3 × 10 mL). The aqueous phase was back extracted with DCM (10 mL). The combined organic phases were washed with brine (15 mL) and the solvents of the dried ($MgSO_4$) solution were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 85:15 to 8:2) to give alcohol **27** (14 mg, 90%) as a yellow oil: R_f 0.5 (tol/EtOAc 85:15); $[\alpha]_D^{20}$ = –58 (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.13 (m, 15H, C*H*-Ar), 5.48 (s, 1H, H-7), 5.23 (d, *J* = 1.6 Hz, 1H, H-1B), 5.02 (t, *J* = 3.4 Hz, 1H, H-3B), 4.85 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.66 (d, *J* = 10.8 Hz, 2H, CH_2Ph), 4.51 (d, *J* = 10.8 Hz, 1H, CH*H*Ph), 4.48 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.32 (dd, *J* = 10.4, 5.0 Hz, 1H, H-6aA), 4.16 (dd, *J* = 13.8, 6.4 Hz, 1H, H-5B), 4.03 (d, *J* = 11.2 Hz, 1H, O*H*), 3.92 (dt, *J* = 9.8, 6.3 Hz, 1H, H-1a$_{linker}$), 3.89 (t, *J* = 9.5 Hz, 1H, H-3A), 3.76 (t, *J* = 10.4 Hz, 1H, H-6bA), 3.71 (br s, 1H, H-2B), 3.58–3.53 (m, 2H, H-4B, H-1b$_{linker}$), 3.51 (t, *J* = 9.8 Hz, 1H, H-4A), 3.45–3.39 (m, 2H, H-5A, H-2A), 3.22 (t, *J* = 7.3 Hz, 2H, H-5$_{linker}$), 2.09 (s, 3H, CH_{3Ac}), 1.70–1.58 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.52–1.42 (m, 2H, H-3$_{linker}$), 0.77 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6 (*C*O), 137.8, 137.4, 137.3 (3 × C-Ar), 129.3–125.4 (9 × *C*H-Ar), 104.2 (C-1A), 102.2 (C-1B), 102.1 (C-7), 82.7 (C-2A), 79.4 (C-4A), 79.3 (C-4B), 77.6 (C-3A), 76.1, 75.2 (2 × *C*H_2Ph), 70.2 (C-1$_{linker}$), 70.1 (C-3B), 69.2 (C-2B), 68.9 (C-6), 66.5 (C-5A), 66.3 (C-5B), 51.4 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.5 (C-3$_{linker}$), 21.3 (*C*H_{3Ac}), 16.2 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{40}H_{49}N_3NaO_{11}$ 770.3259; found 770.3266; *m/z* $[2M + Na]^+$ calcd for $C_{80}H_{98}N_6NaO_{22}$ 1517.6626; found 1517.6666.

(5-Azido-1-pentyl) 2-*O*-Acetyl-4-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-6-deoxy-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (28).



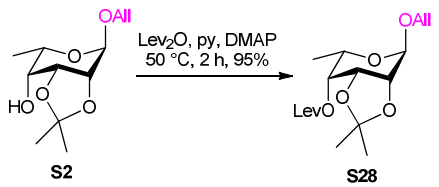
To a solution of acceptor **20** (15 mg, 20 μmol, 1.0 equiv) in anhydrous toluene (1 mL) was added freshly activated powdered molecular sieves (4 Å, 171 mg) and the mixture was stirred for 40 min at rt under Ar. TBSOTf (2 μL, 9 μmol, 0.3 equiv) was injected keeping rigorous anhydrous conditions and the mixture was heated at 75 °C for 15 min. A solution of donor **S27** (20 mg, 30 μmol, 1.5 equiv) in anhydrous toluene (1 mL) was added dropwise at the same temperature over 10 min to the former mixture. After stirring for 1 h at 75 °C, the reaction mixture was allowed to slowly warm up to rt and then quenched with few drops of Et_3N. The suspension was filtered over Celite, rinsed with DCM and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (tol/EtOAc 95:5) to give silylated derivative **28** (10 mg, 60%) as a yellow oil: R_f 0.5 (tol/EtOAc 85:15); $[\alpha]_D^{20}$ = –32 (*c* 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.20 (m, 15H, C*H*-Ar), 5.52 (s, 1H, H-7), 5.28 (s, 1H, H-1B), 5.16 (d, *J* = 4.1 Hz, 1H, H-2B), 4.92 (d, *J* = 11.6 Hz, 1H, C*H*HPh), 4.88 (d, *J* = 10.7 Hz, 1H, CH*H*Ph), 4.68 (d, *J* = 10.7 Hz, 1H, C*H*HPh), 4.56 (d, *J* = 11.6 Hz, 1H, CH*H*Ph), 4.50 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.33 (dd, *J* = 10.7, 4.8 Hz, 1H, H-6aA), 4.13 (dd, *J* = 13.9, 6.4 Hz, 1H, H-5B), 4.00–3.96 (m, 2H, H-3A, H-3B), 3.91 (dt, *J* = 9.6, 6.4 Hz, 1H, H-1a$_{linker}$), 3.77 (t, *J* = 10.7 Hz, 1H, H-6bA), 3.58–3.52 (m, 2H, H-1b$_{linker}$, H-4A), 3.48–3.39 (m, 2H, H-2A, H-5A), 3.23 (t, *J* = 1.6 Hz, 1H, H-4B), 3.19 (t, *J* = 7.2 Hz, 2H, H-5$_{linker}$), 1.96 (s, 3H, CH_{3Ac}), 1.68–1.54 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.47–1.40 (m, 2H, H-3$_{linker}$), 0.92 (d, *J* = 6.4 Hz, 3H, CH_{3Tal}), 0.89 (s, 9H, C(CH_3)$_3$), 0.12, 0.11 (2 × s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7 (*C*O), 139.5, 138.2, 137.5 (3 × C-Ar), 129.3–126.3 (9 × *C*H-Ar), 104.2 (C-1A), 101.8 (C-7), 99.1 (C-1B), 83.2 (C-2A), 79.3 (C-4A), 78.8 (C-4B), 75.5 (C-3B), 74.8 (2 × *C*H$_2$Ph), 70.2 (C-1$_{linker}$), 70.0 (C-2B), 69.2 (C-3A), 68.9 (C-6), 66.8 (C-5B), 66.4 (C-5A), 51.4 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 25.9 (C(*C*H$_3$)$_3$), 23.5 (C-3$_{linker}$), 21.2 (*C*H$_{3Ac}$), 18.1 (*C*(CH$_3$)$_3$), 16.7 (*C*H$_{3Tal}$), –4.71, –4.82 (2 × *C*H$_3$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{46}H_{63}N_3NaO_{11}Si$ 884.4124; found 884.4151.

4,6-*O*-Benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-*O*-levulinoyl-*β*-D-glucopyranosyl-(1↔1)-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-*O*-levulinoyl-*α*-D-glucopyranoside (29).



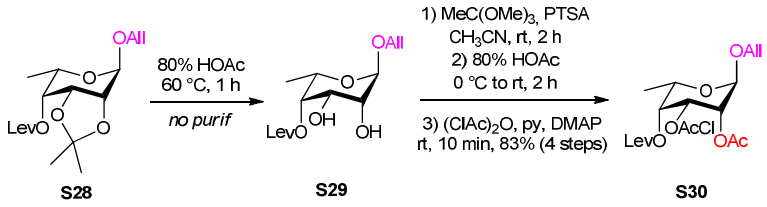
To a solution of donor **14** (28 mg, 53 μmol, 2.0 equiv) and acceptor **20 (**20 mg, 27 μmol, 1.0 equiv) in anhydrous DCM (500 μL) was added freshly activated 4 Å molecular sieves (80 mg). The mixture was stirred at rt for 30 min under Ar. Then, the suspension was cooled to –78 °C and AgOTf (7 mg, 27 μmol, 1.0 equiv) followed by NIS (12 mg, 53 μmol, 2.0 equiv) were added. The flask was protected from light and the reaction mixture was stirred from –78 °C to rt for 7 h under Ar and then quenched with a few drops of Et_3N. The suspension was filtered over Celite, rinsed with DCM and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (tol/EtOAc 9:1) to give dimer **29** (major compound, variable yields) as a colorless oil: R_f 0.7 (tol/EtOAc 85:15); $[\alpha]_D^{20}$ = –47 (*c* 0.77, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.46 (m, 4H, C*H*-Ar), 7.37–7.30 (m, 6H, C*H*-Ar), 6.15 (d, *J* = 4.0 Hz, 1H, H-1A), 5.51 (s, 1H, H-7A), 5.45 (s, 1H, H-7B), 4.90 (d, *J* = 7.7 Hz, 1H, H-1B), 4.83 (t, *J* = 8.5 Hz, 1H, H-2B), 4.33 (dd, *J* = 10.7, 4.9 Hz, 1H, H-6aA), 4.28 (dd, *J* = 10.4, 4.8 Hz, 1H, H-6aB), 4.12 (t, *J* = 9.2 Hz, 1H, H-3A), 3.93 (dd, *J* = 8.4, 3.9 Hz, 1H, H-2A), 3.88 (dd, *J* = 9.8, 4.7 Hz, 1H, H-5A), 3.80 (t, *J* = 9.0 Hz, 1H, H-3B), 3.78 (t, *J* = 10.1 Hz, 1H, H-6bB), 3.66 (t, *J* = 10.7 Hz, 1H, H-6bA), 3.56 (t, *J* = 9.4 Hz, 1H, H-4B), 3.47 (t, *J* = 9.7 Hz, 1H, H-4A), 3.37 (dd, *J* = 9.7, 4.7 Hz, 1H, H-5), 2.93–2.49 (m, 8H, 4 × CH_{2Lev}), 2.22, 2.21 (2 × s, 6H, 2 × CH_{3Lev}), 0.85, 0.79 (2 × s, 18H, 2 × C(CH_3)$_3$), –0.01, –0.00 (2 × s, 12H, 4 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.8, 205.9 (2 × *C*O), 171.6, 171.4 (2 × *C*O), 137.1, 137.0 (2 × C-Ar), 129.4–126.3 (6 × *C*H-Ar), 102.6 (C-7B), 101.9 (C-7A), 100.5 (C-1B), 92.2 (C-1A), 81.8 (C-4A), 81.6 (C-4B), 75.6 (C-2A), 75.1 (C-2B), 72.6 (C-3B), 72.3 (C-3A), 68.9 (C-6B), 68.7 (C-6A), 66.5 (C-5B), 64.5 (C-5A), 38.1, 37.8 (2 × *C*H$_{2Lev}$), 30.0 (2 × *C*H$_{3Lev}$), 28.1, 28.0 (2 × *C*H$_{2Lev}$), 26.1, 25.7 (2 × C(*C*H$_3$)$_3$), 18.4, 18.1 (2 × *C*(CH$_3$)$_3$), –3.74, –4.10, –4.45, –4.84 (4 × *C*H$_3$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{48}H_{70}NaO_{15}Si_2$ 965.4145; found 965.4165.

Allyl 6-Deoxy-2,3-*O*-isopropylidene-4-*O*-levulinoyl-*α*-L-talopyranoside (**S28**).



Alcohol **S2** (3.5 g, 14.9 mmol, 1.0 equiv) was dissolved in anhydrous py (95 mL) and DMAP (4.4 g, 35.9 mmol, 2.5 equiv) was added. A solution of levulinic anhydride[5] (24.6 g, 115 mmol, 8.0 equiv) in anhydrous py (127 mL) was added dropwise over 50 min to the former mixture. The reaction mixture was then heated to 50 °C and stirred under Ar for an additional 2 h. The solvents were concentrated under reduced pressure and the residue was purified by silica gel flash chromatography (PE/EtOAc, 8:2 to 7:3) to give derivative **S28** (4.7 g, 95%) as a yellow oil: R_f 0.5 (PE/EtOAc, 6:4); $[\alpha]_D^{20}$ = –11 (*c* 2.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96–5.86 (m, 1H, H-2_{All}), 5.31 (ddd, *J* = 17.2, 3.5, 1.5 Hz, 1H, H-$3a_{All}$), 5.22 (ddd, *J* = 10.3, 3.3, 1.2 Hz, 1H, H-$3b_{All}$), 5.10 (dd, *J* = 5.5, 2.2 Hz, 1H, H-4), 5.08 (s, 1H, H-1), 4.39 (t, *J* = 6.4 Hz, 1H, H-3), 4.20 (ddt , *J* = 12.8, 5.3, 1.4 Hz, 1H, H-1aAll), 4.09 (dd, *J* = 6.5, 09 Hz, 1H, H-2), 4.03–3.98 (m, 2H, H-$1b_{All}$, H-5), 2.87–2.61 (m, 4H, 2 × CH_{2Lev}), 2.19 (s, 3H, CH_{3Lev}), 1.52, 1.34 (2 × s, 6H, 2 × CH_3), 1.23 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.4 (*C*O), 172.7 (*C*O), 133.7 (C-2_{All}), 118.0 (C-3_{All}), 109.8 (*C*$(CH_3)_2$), 96.9 (C-1), 73.2 (C-2), 71.1 (C-3), 68.5 (C-1_{All}), 67.6 (C-4), 63.6 (C-5), 38.0 (*C*H_{2Lev}), 30.0 (*C*H_{3Lev}), 28.3 (*C*H_{2Lev}), 26.3, 25.8 (2 × *C*H_3), 16.6 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{17}H_{26}NaO_7$ 365.1571; found 365.1580.

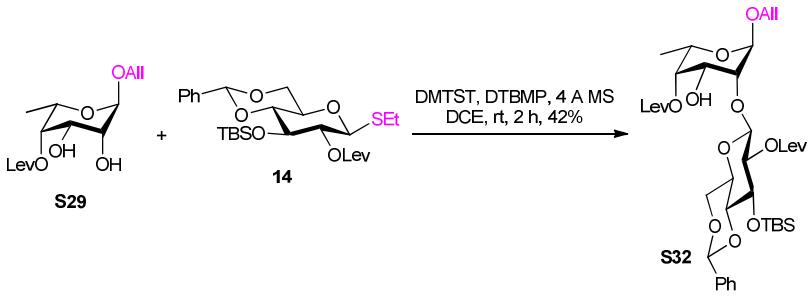
Allyl 2-*O*-Acetyl-3-*O*-chloroacetyl-6-deoxy-4-*O*-levulinoyl-*α*-L-talopyranoside (**S30**).



S28 **S29** **S30**

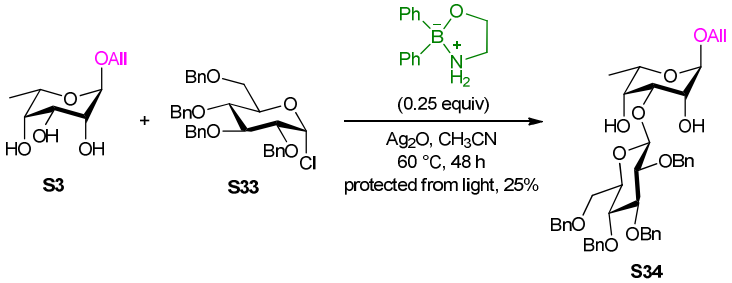
Compound **S28** (4.6 g, 13.6 mmol, 1.0 equiv) was dissolved in a 80% HOAc(aq) solution (170 mL). The reaction mixture was stirred at 60 °C for 1 h. Then, the mixture was concentrated under reduced pressure and co-evaporated with toluene (3 ×). Crude diol **S29** was obtained as a yellow amorphous solid [R_f 0.3 (DCM/MeOH 98:2)], which was used directly for the next step without purification in order to avoid migration of the levulinoyl group. Diol **S29** (250 mg, 730 μmol, 1.0 equiv) was dissolved in anhydrous acetonitrile (3 mL). Trimethyl orthoactetate (186 μL, 1.5 mmol, 2.0 equiv) and PTSA (7 mg, 37 μmol, 0.05 equiv) were added sequentially. The reaction mixture was stirred for 2 h at rt under Ar. The suspension was then cooled to 0 °C and a 80% HOAc(aq) solution (3 mL) was added. The mixture was stirred at 0 °C for 10 min, then allowed to slowly warm up to rt. After 2 h, cooled water (20 mL) was added and the mixture was diluted with DCM (30 mL). The aqueous layer was extracted with DCM (2 × 10 mL). The combined organic phases were washed with brine (30 mL). The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was dissolved in anhydrous py (6 mL), then chloroacetyl anhydride (437 mg, 2.5 mmol, 3.5 equiv) and DMAP (9 mg, 73 μmol, 0.1 equiv) were added. The reaction mixture was stirred at rt for 10 min under Ar. Then, the suspension was diluted with EtOAc (30 mL) and the organic phase was washed with a saturated NH_4Cl(aq) solution (3 × 15 mL) and brine (20 mL). The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 8:2 to 6:4) to give derivative **S30** (254 mg, 83%, four steps) as a yellow oil: R_f 0.3 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –57 (*c* 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93–5.83 (m, 1H, H-2$_{All}$), 5.35 (t, J = 4.0 Hz, 1H, H-3), 5.30 (ddd, J = 17.2, 3.6, 1.6 Hz, 1H, H-3a$_{All}$), 5.23 (ddd, J = 10.4, 3.1, 2.0 Hz, 1H, H-3b$_{All}$), 5.19 (d, J = 3.7 Hz, 1H, H-4), 5.17 (dt, J = 3.9, 1.5 Hz, 1H, H-2), 4.91 (d, $J_{1,2}$ = 1.1 Hz, 1H, H-1), 4.20–4.13 (m, 2H, H-1aAll, H-5), 4.02 (ddt, J = 13.3, 6.1, 1.6 Hz, 1H, H-1b$_{All}$), 4.01 (d, J = 2.9 Hz, 2H, CH_{2Cl}), 2.91–2.82 (m, 1H, CHH$_{Lev}$), 2.75–2.58 (m, 3H, CH_{2Lev}), 2.20 (CH_{3Lev}), 2.19 (s, 3H, CH_{3Ac}), 1.23 (d, J = 6.4 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.4 (*C*O), 172.8, 170.4, 166.4 (3 × *C*O), 133.2 (C-2$_{All}$), 118.3 (C-3$_{All}$), 97.5 (C-1), 68.8 (C-4), 68.6 (C-1$_{All}$), 67.9 (C-3), 66.8 (C-2), 64.7 (C-5), 40.7 (*C*H$_{2Cl}$), 37.7 (*C*H$_{2Lev}$), 30.0 (*C*H$_{3Lev}$), 27.8 (*C*H$_{2Lev}$), 21.1 (*C*H$_{3Ac}$), 16.2 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{18}H_{25}ClNaO_9$ 443.1079; found 443.1097.

Allyl 4,6-*O*-Benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-*O*-levulinoyl-*β*-D-glucopyranosyl-(1→2)-6-deoxy-4-*O*-levulinoyl-*α*-L-talopyranoside (**S32**).



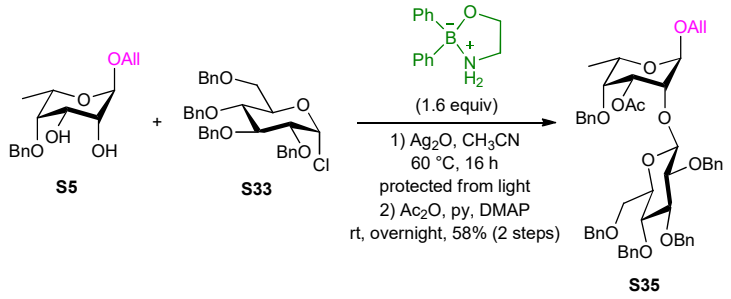
To a solution of donor **14** (56 mg, 108 μmol, 1.3 equiv), acceptor **S29** (25 mg, 83 μmol, 1.0 equiv) and DTBMP (51 mg, 248 μmol, 3.0 equiv) in anhydrous DCE (1.5 mL) was added freshly activated 4 Å powdered molecular sieves (100 mg). The mixture was stirred for 30 min at rt under Ar. Then, Me_2S_2 (22 μL, 248 μmol, 3.0 equiv) and MeOTf (28 μL, 248 μmol, 3.0 equiv) were added. The solution was stirred for an additional 2 h at rt. Then, the reaction mixture was quenched with few drops of Et_3N, filtered over Celite and rinsed with DCM. The filtrate was concentrated under reduced pressure and purified by silica gel flash chromatography (PE/EtOAc 7:3 to 4:6) to give disaccharide **S32** (26 mg, 42%, major regioisomer) as a yellow oil: R_f 0.5 (tol/EtOAc 5:5); $[\alpha]_D^{20}$ = –5.6 (*c* 2.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.40 (m, 2H, C*H*-Ar), 7.31–7.28 (m, 3H, C*H*-Ar), 5.88–5.78 (m, 1H, H-2$_{All}$), 5.64 (d, $J_{1C,2C}$ = 5.7 Hz, 1H, H-1C), 5.47 (s, 1H, H-7), 5.22 (ddd, *J* = 17.2, 3.7, 1.8 Hz, 1H, H-3a$_{All}$), 5.15 (ddd, *J* = 10.4, 3.3, 1.2 Hz, 1H, H-3b$_{All}$), 5.04 (d, *J* = 3.5 Hz, 1H, H-4B), 4.84 (d, $J_{1A,2A}$ = 1.4 Hz, 1H, H-1B), 4.30 (dd, *J* = 10.6, 3.8 Hz, 1H, H-6aC), 4.24 (dd, *J* = 5.6, 3.9 Hz, 1H, H-2C), 4.10 (ddt, *J* = 13.0, 5.1, 1.4 Hz, 1H, H-1a$_{All}$), 3.97–3.93 (m, 3H, H-1b$_{All}$, H-3B, H-5B), 3.86 (dd, *J* = 8.8, 3.8 Hz, 1H, H-3C), 3.65–3.58 (m, 3H, H-2B, H-5C, H-6bC), 3.46 (t, *J* = 9.3 Hz, 1H, H-4C), 2.79–2.67 (m, 4H, 2 × C*H*$_{2Lev}$), 2.64–2.54 (m, 4H, 2 × C*H*$_{2Lev}$), 2.13 (s, 3H, C*H*$_{3Lev}$), 2.11 (s, 3H, C*H*$_{3Lev}$), 1.09 (d, *J* = 6.6 Hz, 3H, C*H*$_{3Tal}$), 0.82 (s, 9H, C(C*H*$_3$)$_3$), 0.45, 0.00 (2 × s, 6H, 2 × C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.4, 206.2 (2 × *C*O), 172.2, 172.1 (2 × *C*O), 137.2 (C-Ar), 133.7 (C-2$_{All}$), 129.8, 128.3, 126.1 (3 × *C*H-Ar), 117.7 (C-3$_{All}$), 101.4 (C-7), 99.8 (C-1B), 98.8 (C-1C), 80.5 (C-2C), 80.1 (C-4C), 74.4 (C-3C), 73.1 (C-4B), 69.7 (C-2B), 68.7 (C-6C), 68.4 (C-1$_{All}$), 66.8 (C-3B), 65.1 (C-5B), 63.3 (C-5C), 38.2, 38.0 (2 × *C*H$_{2Lev}$), 30.2, 30.1 (2 × *C*H$_{3Lev}$), 28.0 (2 × *C*H$_{2Lev}$), 25.8 (C(*C*H$_3$)$_3$), 18.2 (*C*(CH$_3$)$_3$), 16.3 (*C*H$_{3Tal}$), –4.40, –4.82 (2 × *C*H$_3$); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{38}H_{56}NaO_{14}Si$ 787.3332; found 787.3347.

Allyl 2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→3)-6-deoxy-*α*-L-talopyranoside (**S34**).



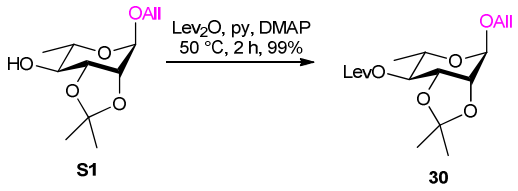
To a solution of donor **S33**[6] (75 mg, 134 μmol, 1.0 equiv) and acceptor **S3** (30 mg, 147 μmol, 1.1 equiv) in anhydrous acetonitrile (1.5 mL) were added silver(I) oxide (62 mg, 267 μmol, 2.0 equiv) and 2-aminoethyl diphenylborinate (8 mg, 33 μmol, 0.25 equiv). The flask was purged with a stream of Ar for 5 min, then protected from light. The reaction mixture was stirred at 60 °C under Ar for 48 h. The solution was then quenched with a few drops of MeOH, diluted with DCM and filtered through a plug of Celite. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (tol/EtOAc 95:5 to 85:15) to give disaccharide **S34** (25 mg, 25%, major regioisomer) as a yellow amorphous solid: R_f 0.5 (tol/EtOAc 7:3); $[\alpha]_D^{20}$ = –14 (*c* 2.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.25 (m, 18H, C*H*-Ar), 7.19–7.15 (m, 2H, C*H*-Ar), 5.92–5.82 (m, 1H, H-2$_{All}$), 5.27 (ddd, *J* = 17.2, 3.8, 1.5 Hz, 1H, H-3a$_{All}$), 5.19 (ddd, *J* = 10.4, 3.4, 1.2 Hz, 1H, H-3b$_{All}$), 4.97 (d, *J* = 11.3 Hz, 1H, C*H*HPh), 4.92 (d, $J_{1B,2B}$ = 1.6 Hz, 1H, H-1B), 4.91 (d, *J* = 10.8 Hz, 1H, CH*H*Ph), 4.82 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.81 (d, *J* = 11.3 Hz, 1H, CH*H*Ph), 4.80 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.60 (d, $J_{1B,2B}$ = 7.7 Hz, 1H, H-1C), 4.53 (d, *J* = 11.8 Hz, 1H, CH*H*Ph), 4.52 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.48 (d, *J* = 11.8 Hz, 1H, CH*H*Ph), 4.16 (ddt, *J* = 13.0, 5.2, 1.4 Hz, 1H, H-1a$_{All}$), 4.01–3.95 (m, 2H, H-1b$_{All}$, H-2B), 3.89–3.83 (m, 2H, H-3B, H-5B), 3.69–3.63 (m, 3H, H-4B, H-4C, H-6aC), 3.61–3.49 (m, 5H, H-2C, H-3C, H-5C, H-6bC, O*H*), 3.29 (d, *J* = 8.8 Hz, 1H, O*H*), 1.30 (d, *J* = 6.6 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 138.3, 137.9, 137.8 (4 × C-Ar), 133.8 (C-2$_{All}$), 128.4–127.5 (12 × *C*H-Ar), 117.6 (C-3$_{All}$), 101.8 (C-1C), 99.3 (C-1B), 84.7 (C-4B), 81.9 (C-2C), 77.7 (C-3C), 75.7 (C-3B), 75.8 (*C*H$_2$Ph), 75.1 (*C*H$_2$Ph), 74.9 (*C*H$_2$Ph), 74.6 (C-5B), 73.5 (*C*H$_2$Ph), 70.8 (C-4C), 69.4 (C-2B), 69.0 (C-6C), 68.6 (C-1$_{All}$), 66.8 (C-5B), 16.5 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{43}H_{57}NaO_{10}$ 749.3296; found 749.3303; *m/z* [2M + Na]$^+$ calcd for $C_{86}H_{100}NaO_{20}$ 1475.6700; found 1475.6737.

Allyl 2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→2)-3-*O*-acetyl-4-*O*-benzyl-6-deoxy-*α*-L-talopyranoside (**S35**).



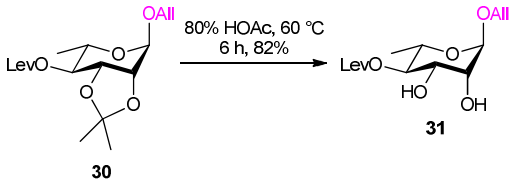
To a solution of donor **S33**[6] (52 mg, 93 μmol, 1.0 equiv) and acceptor **S5** (30 mg, 102 μmol, 1.1 equiv) in anhydrous acetonitrile (3 mL) were added silver(I) oxide (42 mg, 186 μmol, 2.0 equiv) and 2-aminoethyl diphenylborinate (34 mg, 149 μmol, 1.6 equiv). The round bottom flask was purged with a stream of Ar for 5 min, then protected from light and the reaction mixture was stirred at 60 °C under Ar. After 16 h, the reaction was quenched with a few drops of MeOH, diluted with DCM and filtered through a plug of Celite. The filtrate was concentrated under reduced pressure. The residue was dissolved in anhydrous py (0.4 mL), then Ac_2O (0.4 mL) and DMAP (1.1 mg, 9 μmol, 0.1 equiv) were added. The suspension was stirred at rt overnight under Ar. Then, the mixture was concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was purified by silica gel flash chromatography (tol/EtOAc 98:2 to 96:4) to give disaccharide **S35** (45 mg, 58%, two steps) as a yellow oil: R_f 0.5 (tol/EtOAc 9:1); $[\alpha]_D^{20}$ = –1.3 (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.14 (m, 25H, C*H*-Ar), 5.88–5.78 (m, 1H, H-2_{All}), 5.29 (s, 1H, H-1B), 5.24 (d, *J* = 12.2 Hz, 1H, C*H*HPh), 5.23–5.18 (m, 1H, H-$3a_{All}$), 5.13 (t, *J* = 4.0 Hz, 1H, H-3B), 5.10 (ddd, *J* = 10.4, 3.3, 1.2 Hz, 1H, H-$3b_{All}$), 4.85 (d, *J* = 10.2 Hz, 1H, CH*H*Ph), 4.81 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.72 (d, *J* = 12.1 Hz, 1H, CH*H*Ph), 4.71 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.62 (d, *J* = 12.1 Hz, 1H, CH*H*Ph), 4.55–4.49 (m, 4H, 2 × CH_2Ph), 4.46 (d, $J_{1C,2C}$ = 7.5 Hz, 1H, H-1C), 4.07 (ddt, *J* = 12.7, 5.2, 1.5 Hz, 1H, H-$1a_{All}$), 3.96 (dd, *J* = 13.7, 6.8 Hz, 1H, H-5B), 3.91–3.89 (m, 1H, H-2B), 3.86 (ddt, *J* = 13.0, 5.9, 1.7 Hz, 1H, H-$1b_{All}$), 3.67–3.65 (m, 2H, H-6aC, H-6bC), 3.62–3.59 (m, 3H, H-2C, H-3C, H-4B), 3.52 (dd, *J* = 9.5, 7.7 Hz, 1H, H-4C), 3.47–3.39 (m, 1H, H-5C), 1.87 (s, 3H, CH_{3Ac}), 1.19 (d, *J* = 6.6 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7 (*C*O), 139.5, 138.7, 138.3, 138.2, 138.1 (5 × C-Ar), 134.2 (C-2_{All}), 129.2–127.5 (15 × *C*H-Ar), 117.1 (C-3_{All}), 106.4 (C-1C), 99.8 (C-1B), 84.7 (C-3C), 82.1 (C-4B), 77.8 (C-4C), 76.7 (C-2B), 75.8 (*C*H_2Ph), 75.4 (C-2C), 75.1 (*C*H_2Ph), 74.9 (*C*H_2Ph), 74.8 (C-5C), 74.1 (*C*H_2Ph), 73.6 (*C*H_2Ph), 70.6 (C-3B), 69.5 (C-6C), 68.2 (C-1_{All}), 66.2 (C-5B), 21.1 (*C*H_{3Ac}), 16.9 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{52}H_{58}N_3NaO_{11}$ 881.3871; found 881.3885.

Allyl 2,3-*O*-Isopropylidene-4-*O*-levulinoyl-*α*-L-rhamnopyranoside (**30**).



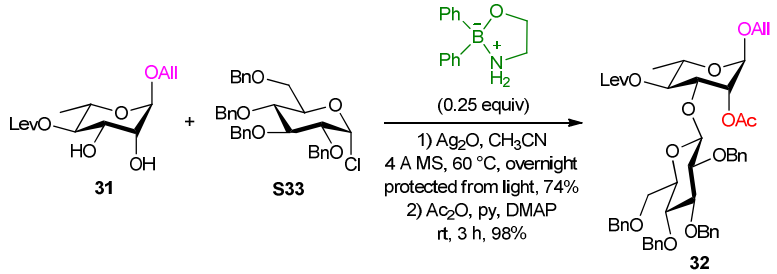
Alcohol **S1** (9.8 g, 40 mmol, 1.0 equiv) was dissolved in anhydrous py (240 mL) and DMAP (9.8 g, 80 mmol, 2.0 equiv) was added. A solution of levulinic anhydride[5] (25.7 g, 120 mmol, 3.0 equiv) in anhydrous py (200 mL) was added dropwise over 1 h to the former mixture. The reaction mixture was then heated to 50 °C and stirred under Ar for an additional 2 h. The solvents were concentrated under reduced pressure and the residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 75:25) to give derivative **30** (13.6 g, 99%) as a yellow oil: R_f 0.5 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –10 (*c* 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96–5.86 (m, 1H, H-2$_{All}$), 5.32 (ddd, *J* = 17.2, 3.5, 1.6 Hz, 1H, H-3a$_{All}$), 5.23 (ddd, *J* = 10.4, 3.0, 1.2 Hz, 1H, H-3b$_{All}$), 5.05 (s, 1H, H-1), 4.85 (dd, *J* = 10.3, 7.1 Hz, 1H, H-4), 4.21–4.15 (m, 3H, H-1a$_{All}$, H-2, H-3), 4.01 (ddt, *J* = 12.8, 6.2, 1.3 Hz, 1H, H-1b$_{All}$), 3.80–3.72 (m, 1H, H-5), 2.91–2.84 (m, 1H, C*H*$_{2Lev}$), 2.72–2.52 (m, 3H, C*H*$_{2Lev}$), 2.19 (s, 3H, C*H*$_{3Lev}$), 1.55 (s, 3H, C*H*$_3$), 1.34 (s, 3H, C*H*$_3$), 1.19 (d, *J* = 6.3 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.5 (*C*O), 172.2 (*C*O), 133.7 (C-2$_{All}$), 118.0 (C-3$_{All}$), 109.9 (*C*(CH$_3$)$_2$), 96.2 (C-1), 76.1 (C-2), 75.8 (C-3), 74.9 (C-4), 68.2 (C-1$_{All}$), 64.2 (C-5), 38.0 (*C*H$_{2Lev}$), 29.9 (*C*H$_{3Lev}$), 28.1 (*C*H$_{2Lev}$), 27.8, 26.5 (2 × *C*H$_3$), 17.0 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{17}H_{26}NaO_7$ 365.1571; found 365.1585.

Allyl 4-*O*-Levulinoyl-*α*-L-rhamnopyranoside (70).



Compound **30** (13.6 g, 39.8 mmol, 1.0 equiv) was dissolved in a 80% HOAc(aq) solution (500 mL). The reaction mixture was stirred at 60 °C for 6 h. Then, the mixture was concentrated under reduced pressure and co-evaporated with toluene (3 ×). Purification by silica gel flash chromatography (DCM/MeOH 98:2 to 96:4) gave diol **31** (9.9 g, 82%) as a white amorphous solid: R_f 0.3 (DCM/MeOH 95:5); $[\alpha]_D^{20}$ = –71 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95–5.85 (m, 1H, H-2$_{All}$), 5.30 (ddd, *J* = 17.2, 3.7, 1.5 Hz, 1H, H-3a$_{All}$), 5.21 (ddd, *J* = 10.4, 3.4, 1.3 Hz, 1H, H-3b$_{All}$), 4.91 (t, *J* = 9.7 Hz, 1H, H-4), 4.86 (s, 1H, H-1), 4.18 (ddt, *J* = 12.9, 5.1, 1.4 Hz, 1H, H-1a$_{All}$), 4.03–3.97 (m, 2H, H-1b$_{All}$, H-2), 3.94 (dd, *J* = 9.4, 3.5 Hz, 1H, H-3), 3.84–3.77 (m, 1H, H-5), 2.82 (t, *J* = 6.7 Hz, 1H, C*H*H$_{Lev}$), 2.60–2.56 (m, 3H, C*H*$_{2Lev}$), 2.20 (s, 3H, C*H*$_{3Lev}$), 1.21 (d, *J* = 6.2 Hz, 3H, C*H*$_{3Tal}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.6 (*C*O), 173.5 (*C*O), 133.8 (C-2$_{All}$), 117.6 (C-3$_{All}$), 98.6 (C-1), 75.6 (C-4), 71.0 (C-2), 70.2 (C-3), 68.2 (C-1$_{All}$), 65.8 (C-5), 38.4 (*C*H$_{2Lev}$), 29.9 (*C*H$_{3Lev}$), 28.3 (*C*H$_{2Lev}$), 17.4 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{14}H_{22}NaO_7$ 325.1258; found 325.1258; *m/z* [2M + Na]$^+$ calcd for $C_{28}H_{44}NaO_{14}$ 627.2623; found 627.2654.

Allyl 2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-levulinoyl-*α*-L-rhamnopyranoside (32).

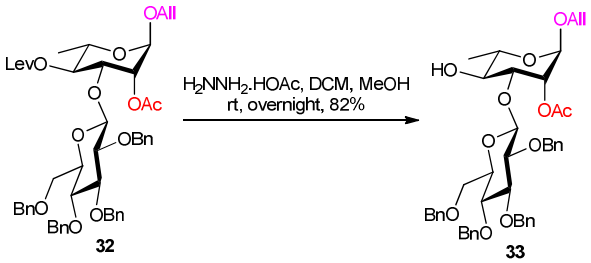


To a solution of donor **S33** (13.4 mg, 2.4 mmol, 1.5 equiv) and acceptor **31** (482 mg, 1.6 mmol, 1.0 equiv) in anhydrous acetonitrile (32 mL) was added freshly activated 4 Å powdered molecular sieves (2.0 g) and the suspension was stirred for 1 h at rt under Ar. Then, silver(I) oxide (738 mg, 3.2 mmol, 2.0 equiv) and 2-aminoethyl diphenylborinate (89.6 mg, 398 μmol, 0.25 equiv) were added and the round bottom flask was protected from light. The reaction mixture was stirred overnight at 60 °C under Ar, quenched with a few drops of MeOH, diluted with DCM (10 mL) and filtered through a plug of Celite. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 8:2 to 6:4) to give allyl 2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→3)-4-*O*-levulinoyl-*α*-L-rhamnopyranoside (978 mg, 74%) as a white amorphous solid: R_f 0.3 (tol/EtOAc 9:1); $[\alpha]_D^{20}$ = –13 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.16 (m, 20H, C*H*-Ar), 5.93–5.83 (m, 1H, H-2$_{All}$), 5.29 (ddd, *J* = 17.2, 3.6, 1.6 Hz, 1H, H-3a$_{All}$), 5.21 (ddd, *J* = 10.4, 3.3, 1.2 Hz, 1H, H-3b$_{All}$), 5.18 (t, *J* = 9.9 Hz, 1H, H-4B), 4.86 (d, $J_{1B,2B}$ = 1.5 Hz, 1H, H-1B), 4.85 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.84 (d, *J* = 11.5 Hz, 1H, CH*H*Ph), 4.80 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.75 (d, *J* = 10.9 Hz, 1H, CH*H*Ph), 4.63 (d, *J* = 11.5 Hz, 1H, C*H*HPh), 4.54 (d, $J_{1C,2C}$ = 7.7 Hz, 1H, H-1C), 4.52 (d, *J* = 10.9 Hz, 1H, CH*H*Ph), 4.49 (s, 2H, CH_2Ph), 4.16–4.13 (m, 2H, H-1a$_{All}$, H-2B), 4.05 (dd, *J* = 9.6, 3.4 Hz, 1H, H-3B), 3.97 (ddt, *J* = 12.9, 6.2, 1.2 Hz, 1H, H-1b$_{All}$), 3.85–3.78 (m, 1H, H-5B), 3.68 (dd, *J* = 10.4, 1.7 Hz, 1H, H-6aC), 3.62 (t, *J* = 9.1 Hz, 1H, H-3C), 3.57 (dd, *J* = 10.9, 5.2 Hz, 1H, H-6bC), 3.53 (t, *J* = 9.4 Hz, 1H, H-4C), 3.51–3.43 (m, 2H, H-2C, H-5C), 2.57–2.49 (m, 1H, CH_{2Lev}), 2.44–2.36 (m, 1H, CH_{2Lev}), 2.28–2.20 (m, 1H, CH_{2Lev}), 2.13–2.06 (m, 1H, CH_{2Lev}), 2.04 (s, 3H, CH_{3Lev}), 1.32 (d, *J* = 6.3 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.5 (*C*O), 172.1 (*C*O), 138.5, 138.3, 138.1, 138.0 (4 × C-Ar), 133.8 (C-2$_{All}$), 128.6–127.7 (12 × *C*H-Ar), 117.9 (C-3$_{All}$), 103.6 (C-1C), 98.5 (C-1B), 84.7 (C-3C), 81.8 (C-2C), 78.9 (C-3B), 77.7 (C-4C), 75.8 (*C*H_2Ph), 75.1 (*C*H_2Ph), 74.7 (C-5C), 74.5 (*C*H_2Ph), 73.7 (*C*H_2Ph), 72.7 (C-4B), 70.1 (C-2B), 69.0 (C-6C), 68.2 (C-1$_{All}$), 66.5 (C-5B), 37.7 (*C*H_{2Lev}), 29.8 (*C*H_{3Lev}), 27.8 (*C*H_{2Lev}), 17.5 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{48}H_{56}NaO_{12}$ 847.3664; found 847.3661.

The latter compound (2.9 g, 3.6 mmol, 1.0 equiv) was dissolved in anhydrous py (15 mL), then Ac_2O (15 mL) and DMAP (44 mg, 360 μmol, 0.1 equiv) were added. The reaction mixture was stirred at rt for 3 h under Ar. The mixture was then concentrated under reduced pressure and the residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 75:25) to give disaccharide **32** (3.0 g, 98%) as a colorless oil: R_f 0.5 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = +6.6 (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.15 (m, 20H, C*H*-Ar), 5.89–5.79 (m, 1H, H-2$_{All}$), 5.29–5.24 (m, 2H, H-2B, H-3a$_{All}$), 5.18 (t, *J* = 9.9 Hz, 1H, H-4B), 5.17 (ddd, *J* = 10.4, 3.1, 1.3 Hz, 1H, H-3b$_{All}$), 4.86 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.84 (d, $J_{1B,2B}$ = 1.6 Hz, 1H, H-1B), 4.81 (d, *J* = 11.6 Hz,

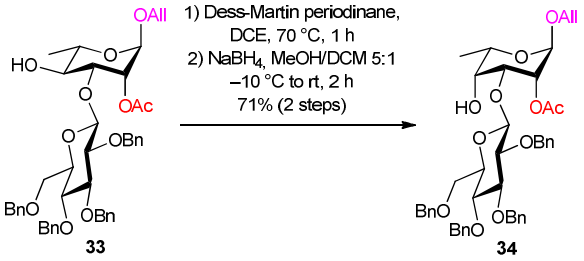
1H, CH*H*Ph), 4.77 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.76 (d, *J* = 10.9 Hz, 1H, CH*H*Ph), 4.63 (d, *J* = 12.2 Hz, 1H, C*H*HPh), 4.61 (d, *J* = 11.6 Hz, 1H, CH*H*Ph), 4.55 (d, *J* = 12.2 Hz, 1H, C*H*HPh), 4.54 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.50 (d, $J_{1C,2C}$ = 7.7 Hz, 1H, H-1C), 4.22 (dd, *J* = 9.9, 3.5 Hz, 1H, H-3B), 4.13 (ddt, *J* = 12.9, 5.3, 1.4 Hz, 1H, H-1a$_{All}$), 3.98 (ddt, *J* = 12.9, 6.1, 1.3 Hz, 1H, H-1b$_{All}$), 3.85–3.78 (m, 1H, H-5B), 3.73–3.66 (m, 2H, H-6aC, H-6bC), 3.61–3.56 (m, 2H, H-3C, H-4C), 3.46–3.42 (m, 1H, H-5C), 3.37 (td, *J* = 7.6, 2.4 Hz, 1H, H-2C), 2.55–2.42 (m, 2H, CH_{2Lev}), 2.27–2.17 (m, 2H, CH_{2Lev}), 2.10 (s, 3H, CH_{3Ac}), 2.04 (s, 3H, CH_{3Lev}), 1.21 (d, *J* = 6.3 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6 (*C*O), 172.2, 170.5 (2 × *C*O), 138.8, 138.7, 138.6, 138.3 (4 × C-Ar), 133.6 (C-2$_{All}$), 128.5–127.5 (12 × *C*H-Ar), 117.9 (C-3$_{All}$), 104.5 (C-1C), 96.6 (C-1B), 84.7 (C-4C), 82.0 (C-2C), 77.8 (C-3C), 75.7 (*C*H_2Ph), 75.3 (C-5C), 75.1 (*C*H_2Ph), 74.6 (C-3B), 74.5 (*C*H_2Ph), 73.7 (*C*H_2Ph), 73.1 (C-4B), 72.7 (C-2B), 68.9 (C-6C), 68.5 (C-1$_{All}$), 66.8 (C-5B), 37.7 (*C*H_{2Lev}), 29.7 (*C*H_{3Lev}), 27.9 (*C*H_{2Lev}), 21.2 (*C*H_{3Ac}), 17.5 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{50}H_{58}NaO_{13}$ 889.3770; found 889.3750.

Allyl 2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→3)-2-*O*-acetyl-*α*-L-rhamnopyranoside (33).



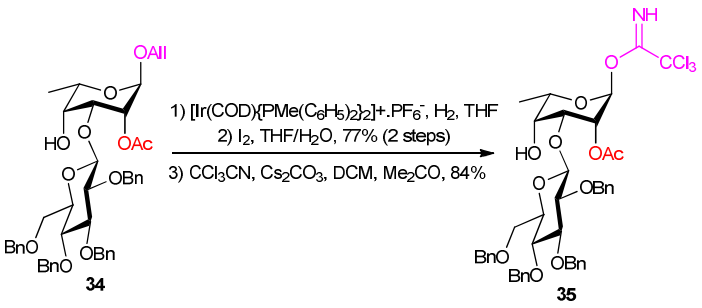
To a solution of disaccharide **32** (983 mg, 1.1 mmol, 1.0 equiv) in anhydrous DCM (5 mL) were added MeOH (11 mL) and hydrazine acetate (209 mg, 2.3 mmol, 2.0 equiv). After stirring at rt overnight, the reaction mixture was concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 75:25) to give alcohol **33** (715 mg, 82%) as a yellow oil: R_f 0.5 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –72 (*c* 0.90, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.15 (m, 20H, C*H*-Ar), 5.92–5.82 (m, 1H, H-2$_{All}$), 5.28 (ddd, *J* = 17.2, 3.8, 1.6 Hz, 1H, H-3a$_{All}$), 5.19–5.17 (m, 2H, H-2B, H-3b$_{All}$), 4.88 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.84 (d, *J* = 10.5 Hz, 1H, CH*H*Ph), 4.81 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.79 (d, $J_{1B,2B}$ = 1.8 Hz, 1H, H-1B), 4.78 (d, *J* = 10.5 Hz, 1H, CH*H*Ph), 4.65 (d, $J_{1C,2C}$ = 7.8 Hz, 1H, H-1C), 4.61 (d, *J* = 12.1 Hz, 1H, C*H*HPh), 4.59 (d, *J* = 11.8 Hz, 1H, CH*H*Ph), 4.58 (d, *J* = 11.8 Hz, 1H, C*H*HPh), 4.52 (d, *J* = 12.1 Hz, 1H, CH*H*Ph), 4.13 (ddt, *J* = 12.9, 5.3, 1.6 Hz, 1H, H-1a$_{All}$), 4.00–3.95 (m, 2H, H-1b$_{All}$, H-3B), 3.73–3.60 (m, 5H, H-3C, H-4C, H-5B, H-6aC, H-6bC), 3.53 (t, *J* = 9.6 Hz, 1H, H-4B), 3.48 (t, *J* = 8.5 Hz, 1H, H-2C), 3.42 (dt, *J* = 9.3, 3.2 Hz, 1H, H-5C), 2.97 (d, *J* = 2.4 Hz, 1H, O*H*), 2.07 (s, 3H, CH_{3Ac}), 1.25 (d, *J* = 6.3 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4 (*C*O), 138.5, 138.3, 138.2, 137.9 (4 × C-Ar), 133.6 (C-2$_{All}$), 128.6–127.7 (12 × *C*H-Ar), 117.9 (C-3$_{All}$), 103.9 (C-1C), 96.7 (C-1B), 85.2 (C-3C), 82.3 (C-2C), 79.1 (C-3B), 77.9 (C-4C), 75.7 (*C*H$_2$Ph), 75.6 (*C*H$_2$Ph), 75.2 (*C*H$_2$Ph), 75.1 (C-5C), 73.6 (*C*H$_2$Ph), 72.5 (C-4B), 72.3 (C-2B), 68.7 (C-6C), 68.4 (C-1$_{All}$), 68.0 (C-5B), 21.2 (*C*H$_{3Ac}$), 17.7 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{45}H_{52}NaO_{11}$ 791.3402; found 791.3399.

Allyl 2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→3)-2-*O*-acetyl-6-deoxy-*α*-L-talopyranoside (34).



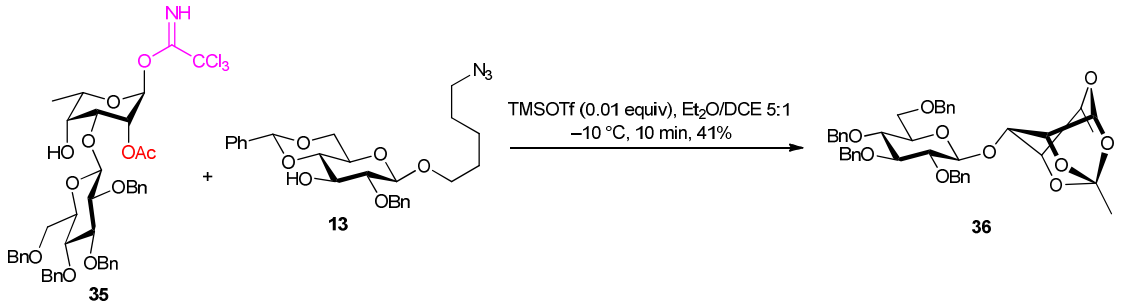
Dess-Martin periodinane (857 mg, 2.0 mmol, 2.2 equiv) was added to a solution of alcohol **33** (706 mg, 918 μmol, 1.0 equiv) in anhydrous DCE (18 mL) and the combined mixture was heated at 70 °C under Ar for 1 h. The mixture was cooled to rt, then diluted with DCM (25 mL) and quenched with a 10% $Na_2S_2O_3$(aq) solution (25 mL). The organic phase was washed with brine (30 mL) and dried ($MgSO_4$). The solvents were concentrated under reduced pressure to give a ketone. To a cooled (–10 °C) solution of the ketone in MeOH/DCM (22 mL, 5:1 *v/v*), $NaBH_4$ (69 mg, 1.8 mmol, 2.0 equiv) was slowly added and the mixture was stirred from –10 °C to rt under Ar for 2 h. The reaction mixture was treated with a 10% HOAc(aq) solution (2 mL) and then concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 85:15 to 8:2) to give alcohol **34** (504 mg, 71%, two steps) as a colorless oil: R_f 0.4 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –64 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.14 (m, 20H, C*H*-Ar), 5.93–5.83 (m, 1H, H-2$_{All}$), 5.29 (ddd, *J* = 17.2, 3.6, 1.6 Hz, 1H, H-3a$_{All}$), 5.21–5.19 (m, 2H, H-2B, H-3b$_{All}$), 4.98 (d, *J* = 11.0 Hz, 1H, C*H*HPh), 4.89 (d, *J* = 11.0 Hz, 1H, CH*H*Ph), 4.86 (d, $J_{1B,2B}$ = 1.4 Hz, 1H, H-1B), 4.80 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.77 (d, *J* = 11.0 Hz, 1H, CH*H*Ph), 4.73 (d, *J* = 11.0 Hz, 1H, C*H*HPh), 4.64 (d, $J_{1C,2C}$ = 7.6 Hz, 1H, H-1C), 4.60 (d, *J* = 12.1 Hz, 1H, CH*H*Ph), 4.53 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.51 (d, *J* = 12.1 Hz, 1H, CH*H*Ph), 4.21 (t, *J* = 3.8 Hz, 1H, H-3B), 4.15 (ddt, *J* = 12.9, 5.3, 1.4 Hz, 1H, H-1a$_{All}$), 4.01 (ddt, *J* = 12.9, 6.0, 1.6 Hz, 1H, H-1b$_{All}$), 3.89 (dd, *J* = 13.3, 6.6 Hz, 1H, H-5B), 3.76 (br s, 1H, H-4B), 3.69–3.68 (m, 2H, H-6aC, H-6bC), 3.66–3.60 (m, 2H, H-3C, H-4C), 3.45–3.40 (m, 1H, H-5C), 1.99 (s, 3H, CH_{3Ac}), 1.32 (d, *J* = 6.6 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7 (*C*O), 138.7, 138.6, 138.3, 138.2 (4 × C-Ar), 133.6 (C-2$_{All}$), 128.5–127.7 (12 × *C*H-Ar), 117.9 (C-3$_{All}$), 101.2 (C-1C), 97.2 (C-1B), 84.6 (C-3C), 82.1 (C-2C), 77.6 (C-4C), 75.7 (*C*H_2Ph), 75.2 (*C*H_2Ph), 75.1 (C-5C), 74.7 (*C*H_2Ph), 73.5 (*C*H_2Ph), 71.9 (C-3B), 70.9 (C-2B), 69.1 (C-4B), 68.7 (C-6C), 68.6 (C-1$_{All}$), 66.8 (C-5B), 21.2 (*C*H_{3Ac}), 16.5 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{45}H_{52}NaO_{11}$ 791.3402; found 791.3418.

2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→3)-2-*O*-acetyl-6-deoxy-*α*-L-talopyranosyl 2,2,2-Trichloroacetimidate (**35**).



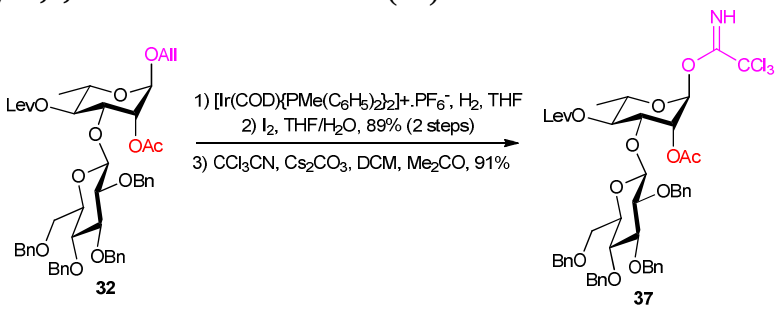
Allyl taloside **34** (458 mg, 600 μmol, 1.0 equiv) was reacted according to the general procedure for the synthesis of trichloroacetimidate donors (first part). Purification by silica gel flash chromatography (PE/EtOAc 9:1 to 5:5) gave a hemiacetal (292 mg, 77%, ratio α/β ~ 3:1) as a yellow amorphous solid: R_f 0.2 (tol/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.14 (m, 20H, C*H*-Ar), 5.24–5.19 (m, 2H, H-1B, H-2B), 4.98 (d, J = 11.1 Hz, 1H, C*H*HPh), 4.90 (d, J = 11.1 Hz, 1H, CH*H*Ph), 4.80 (d, J = 10.8 Hz, 1H, C*H*HPh), 4.77 (d, J = 11.7 Hz, 1H, CH*H*Ph), 4.74 (d, J = 11.7 Hz, 1H, C*H*HPh), 4.65 (d, $J_{1C,2C}$ = 7.7 Hz, 1H, H-1C), 4.60 (d, J = 12.1 Hz, 1H, CH*H*Ph), 4.52 (d, J = 10.8 Hz, 1H, C*H*HPh), 4.50 (d, J = 12.1 Hz, 1H, CH*H*Ph), 4.26 (t, J = 3.7 Hz, 1H, H-3B), 4.16–4.11 (m, 1H, H-5B), 3.78–3.75 (m, 1H, H-4B), 3.70–3.67 (m, 2H, H-6aC, H-6bC), 3.65–3.3.62 (m, 2H, H-3C, H-4C), 3.52 (dd, J = 7.5, 1.8 Hz, 1H, H-2C), 3.45–3.41 (m, 1H, H-5C), 2.92 (d, J = 3.8 Hz, 1H, O*H*), 2.59 (d, J = 9.1 Hz, 1H, O*H*), 2.00 (s, 3H, CH_{3Ac}), 1.32 (d, J = 6.6 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8 (*C*O), 138.7, 138.6, 138.3, 138.2 (4 × C-Ar), 128.1–127.5 (12 × *C*H-Ar), 101.3 (C-1C), 92.7 (C-1B), 84.6 (C-3C), 82.1 (C-2C), 77.6 (C-4C), 75.7 (*C*H_2Ph), 75.2 (*C*H_2Ph), 75.0 (C-5C), 74.7 (*C*H_2Ph), 73.5 (*C*H_2Ph), 71.5 (C-3B), 71.2 (C-2B), 69.2 (C-4B), 68.8 (C-6C), 66.9 (C-5B), 21.2 (*C*H_{3Ac}), 16.6 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{42}H_{48}NaO_{11}$ 751.3089; found 751.3100; *m/z* [2M + Na]$^+$ calcd for $C_{84}H_{96}NaO_{22}$ 1479.6285; found 1479.6306. Then, the hemiacetal (282 mg, 390 μmol, 1.0 equiv) was reacted in the presence of Cs_2CO_3 (25 mg, 80 μmol, 0.2 equiv) and CCl_3CN (190 μL, 1.9 mmol, 5.0 equiv). Purification by silica gel flash chromatography (PE/EtOAc 8:2 to 6:4 + 1% Et_3N) gave imidate **35** (285 mg, 84%) as a yellow oil: R_f 0.4 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = +32 (*c* 0.82, $CHCl_3$); ^{1}H NMR (400 MHz, py-d_5) δ 7.65–7.29 (m, 20H, C*H*-Ar), 6.94 (s, 1H, H-1B), 5.93 (br s, 1H, H-2B), 5.42 (d, J = 11.1 Hz, 1H, C*H*HPh), 5.21 (d, $J_{1C,2C}$ = 7.7 Hz, 1H, H-1C), 5.13 (d, J = 11.1 Hz, 1H, CH*H*Ph), 5.00 (d, J = 10.9 Hz, 1H, C*H*HPh), 4.97–4.91 (m, 2H, 2 × CH_2Ph), 4.80 (t, J = 4.3 Hz, 1H, H-3B), 4.76 (d, J = 11.1 Hz, 1H, CH*H*Ph), 4.73 (d, J = 12.1 Hz, 1H, C*H*HPh), 4.65 (d, J = 12.1 Hz, 1H, CH*H*Ph), 4.48 (dd, J = 14.2, 6.3 Hz, 1H, H-5B), 3.33 (br s, 1H, H-4B), 3.96–3.88 (m, 4H, H-3C, H-4C, H-6aC, H-6bC), 3.80–3.75 (m, 2H, H-2C, H-5C), 1.96 (s, 3H, CH_{3Ac}), 1.53 (d, J = 6.6 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, py-d_5) δ 169.7 (*C*O), 139.6, 139.1, 138.3, 138.2 (4 × C-Ar), 128.5–127.7 (12 × *C*H-Ar), 101.9 (C-1C), 96.3 (C-1B), 84.8 (C-4C), 82.6 (C-2C), 78.2 (C-3C), 75.6 (*C*H_2Ph), 75.5 (C-5C), 74.9 (*C*H_2Ph), 74.6 (*C*H_2Ph), 73.7 (*C*H_2Ph), 72.9 (C-3B), 70.7 (C-5B), 69.5 (C-6C), 69.2 (C-2B), 68.4 (C-4B), 20.9 (*C*H_{3Ac}), 16.9 (*C*H_{3Tal}).

2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→3)-6-deoxy-1,2,4-*O*-orthoacetyl-*β*-L-talopyranose (36).



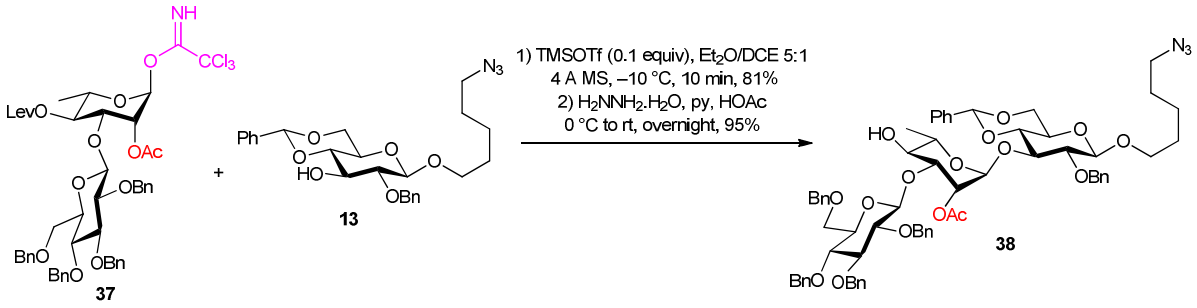
A mixture of acceptor **13** (223 mg, 476 μmol, 1.5 equiv) and donor **35** (277 mg, 317 μmol, 1.0 equiv) in anhydrous Et_2O/DCE (8 mL, 5:1 *v/v*) was cooled to –10 °C and TMSOTf (0.6 μL, 3 μmol, 0.01 equiv) was added keeping rigorous anhydrous conditions. The mixture was stirred for 10 min at –10 °C under Ar and then quenched with a few drops of Et_3N. The suspension was filtered over Celite, rinsed with DCM and the filtrate was concentrated under reduced pressure. The residue was purified by combi-flash chromatography (PE/acetone 92:8) to give tricyclic orthoester **36** (92 mg, 41%) as a white amorphous powder, which was recrystallized in EtOAc: R_f 0.6 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = +17 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.25 (m, 18H, C*H*-Ar), 7.18–7.15 (m, 2H, C*H*-Ar), 5.68 (d, $J_{1,2}$ = 5.1 Hz, 1H, H-1B), 5.08 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.95 (d, *J* = 11.0 Hz, 1H, C*H*HPh), 4.82 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.79 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.78 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.74–4.70 (m, 1H, H-2B), 4.58–4.49 (m, 4H, H-1C, CH_2Ph, C*H*HPh), 4.06–4.00 (m, 2H, H-4B, H-5B), 3.75–3.69 (m, 2H, H-6aC, H-3B), 3.67–3.59 (m, 3H, H-2C, H-3C, H-6bC), 3.56 (t, $J_{3,4} \approx J_{4,5} \approx$ 9.6 Hz, 1H, H-4C), 3.47 (ddd, $J_{4,5}$ = 9.6 Hz, $J_{5,6a}$ = 5.4 Hz, $J_{5,6b}$ = 1.8 Hz, 1H, H-5C), 1.69 (s, 3H, C$H_{3orthoester}$), 1.39 (d, $J_{5,6}$ = 6.4 Hz, 3H, H-6B); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 138.6, 138.2, 138.1 (4 × C-Ar), 128.6–127.8 (*C*H-Ar), 118.2 ($C_{orthoester}$), 103.1 (C-1C), 99.1 (C-1B), 84.7 (C-2C), 81.9 (C-3C), 77.8 (C-4C), 76.7 (C-5B), 75.8 (*C*H_2Ph), 75.5 (C-2B), 75.2 (*C*H_2Ph), 75.1 (C-5C), 75.0 (*C*H_2Ph), 73.6 (*C*H_2Ph), 73.5 (C-4B), 70.8 (C-3B), 69.3 (C-6C), 20.9 (*C*$H_{3orthoester}$), 19.4 (C-6B); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{42}H_{46}NaO_{10}$ 733.2983; found 733.2995.

2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-levulinoyl-*α*-L-rhamnopyranosyl 2,2,2-Trichloroacetimidate (37).



Taloside **32** (1.0 g, 1.2 mmol, 1.0 equiv) was reacted according to the general procedure for the synthesis of trichloroacetimidate donors (first part). Purification by silica gel flash chromatography (PE/EtOAc 85:15 to 65:35) gave a hemiacetal (881 mg, 89%, ratio α/β ~ 10:1) as a white foam: R_f 0.2 (tol/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.15 (m, 20H, C*H*-Ar), 5.30 (dd, J = 3.5, 1.8 Hz, 1H, H-2B), 5.19 (d, $J_{1B,2B}$ = 1.7 Hz, 1H, H-1B), 5.18 (t, J = 10.0 Hz, 1H, H-4B), 4.87 (d, J = 10.9 Hz, 1H, C*H*HPh), 4.81 (d, J = 11.7 Hz, 1H, CH*H*Ph), 4.77 (d, J = 10.9 Hz, 1H, C*H*HPh), 4.76 (d, J = 10.9 Hz, 1H, CH*H*Ph), 4.62 (d, J = 12.1 Hz, 1H, C*H*HPh), 4.61 (d, J = 11.7 Hz, 1H, CH*H*Ph), 4.55 (d, J = 12.1 Hz, 1H, C*H*HPh), 4.54 (d, J = 10.9 Hz, 1H, CH*H*Ph), 4.51 (d, $J_{1C,2C}$ = 7.8 Hz, 1H, H-1C), 4.27 (dd, J = 10.0, 3.4 Hz, 1H, H-3B), 4.07–4.00 (m, 1H, H-5B), 3.73 (dd, J = 10.9, 1.9 Hz, 1H, H-6aC), 3.66 (dd, J = 10.6, 4.7 Hz, 1H, H-6bC), 3.60 (t, J = 9.0 Hz, 1H, H-3C), 3.56 (t, J = 8.8 Hz, 1H, H-4C), 3.48–3.43 (m, 1H, H-5C), 3.37 (dd, J = 8.4, 7.9 Hz, 1H, H-2C), 3.01 (d, J = 3.9 Hz, 1H, O*H*), 2.53–2.43 (m, 2H, CH_{2Lev}), 2.26–2.23 (m, 2H, CH_{2Lev}), 2.19 (s, 3H, CH_{3Ac}), 2.04 (s, 3H, CH_{3Lev}), 1.20 (d, J = 6.3 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.7 (*C*O), 172.2, 170.5 (2 × *C*O), 138.8, 138.7, 138.5, 138.2 (4 × C-Ar), 128.5–127.5 (12 × *C*H-Ar), 104.6 (C-1C), 92.1 (C-1B), 84.7 (C-3C), 81.9 (C-2C), 77.9 (C-4C), 75.7 (*C*H_2Ph), 75.1 (*C*H_2Ph), 75.0 (C-5C), 74.5 (*C*H_2Ph), 74.2 (C-3B), 73.6 (*C*H_2Ph), 73.1 (C-2B, C-4B), 69.1 (C-6C), 66.8 (C-5B), 37.7 (*C*H_{2Lev}), 29.8 (*C*H_{3Lev}), 27.9 (*C*H_{2Lev}), 21.2 (*C*H_{3Ac}), 17.6 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{47}H_{54}NaO_{13}$ 849.3457; found 849.3489. Then, the hemiacetal (861 mg, 1.0 mmol, 1.0 equiv) was reacted in the presence of Cs_2CO_3 (68 mg, 210 μmol, 0.2 equiv) and CCl_3CN (630 μL, 6.5 mmol, 6.0 equiv). Purification by silica gel flash chromatography (PE/EtOAc 8:2 to 6:4 + 1% Et_3N) gave imidate **37** (921 mg, 91%) as a white foam: R_f 0.4 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = +44 (*c* 0.82, $CHCl_3$/THF 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.14 (m, 20H, C*H*-Ar), 6.26 (d, $J_{1B,2B}$ = 1.9 Hz, 1H, H-1B), 5.46 (dd, J = 3.5, 1.9 Hz, 1H, H-2B), 5.28 (t, J = 10.2 Hz, 1H, H-4B), 4.88 (d, J = 11.0 Hz, 1H, C*H*HPh), 4.81 (d, J = 11.0 Hz, 1H, CH*H*Ph), 4.78 (d, J = 10.8 Hz, 1H, C*H*HPh), 4.77 (d, J = 10.8 Hz, 1H, CH*H*Ph), 4.62 (d, J = 12.3 Hz, 1H, C*H*HPh), 4.59 (d, J = 11.9 Hz, 1H, CH*H*Ph), 4.56 (d, J = 11.9 Hz, 1H, C*H*HPh), 4.52 (d, $J_{1C,2C}$ = 7.8 Hz, 1H, H-1C), 4.51 (d, J = 12.3 Hz, 1H, C*H*HPh), 4.25 (dd, J = 10.1, 3.5 Hz, 1H, H-3B), 4.03–3.95 (m, 1H, H-5B), 3.72 (dd, J = 11.0, 3.9 Hz, 1H, H-6aC), 3.66 (t, J = 9.4 Hz, 1H, H-3C), 3.62–3.57 (m, 2H, H-4C, H-6bC), 3.43–3.37 (m, 2H, H-2C, H-5C), 2.55–2.46 (m, 2H, CH_{2Lev}), 2.26–2.18 (m, 2H, CH_{2Lev}), 2.16 (s, 3H, CH_{3Ac}), 2.04 (s, 3H, CH_{3Lev}), 1.25 (d, J = 6.3 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6 (*C*O), 172.1, 170.0 (2 × *C*O), 159.9 (C-Ar), 138.7, 138.4, 138.3 (3 × C-Ar), 128.5–127.5 (12 × *C*H-Ar), 104.7 (C-1C), 94.6 (C-1B), 84.7 (C-4C), 81.9 (C-2C), 77.7 (C-3C), 75.7 (*C*H_2Ph), 75.2 (C-5C), 75.1 (*C*H_2Ph), 74.6 (*C*H_2Ph), 74.2 (C-3B), 73.6 (*C*H_2Ph), 72.3 (C-4B), 71.1 (C-2B), 69.7 (C-5B), 68.6 (C-6C), 37.7 (*C*H_{2Lev}), 29.8 (*C*H_{3Lev}), 27.8 (*C*H_{2Lev}), 21.1 (*C*H_{3Ac}), 17.6 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{49}H_{54}Cl_3NNaO_{13}$ 992.2553; found 992.2552.

(5-Azido-1-pentyl) 2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→3)-2-*O*-acetyl-*α*-L-rhamnopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (38).

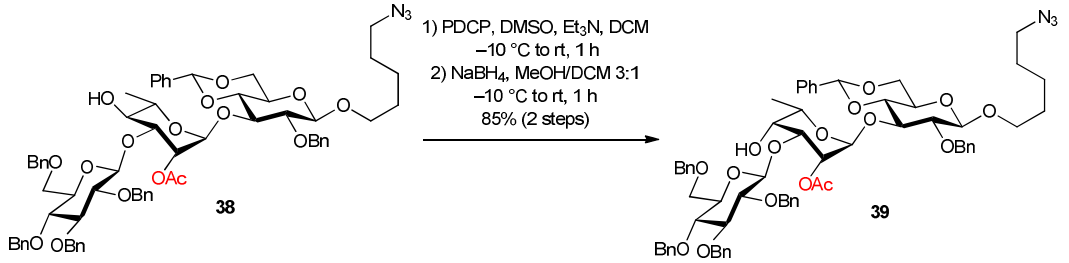


Acceptor **13** (350 mg, 745 μmol, 1.0 equiv) and donor **37** (869 mg, 895 μmol, 1.2 equiv) were dried for 4 h under high vacuum and then dissolved in anhydrous Et_2O/DCE (18 mL, 5:1 *v/v*). Freshly activated 4 Å powdered molecular sieves (1.4 g) were added and the suspension was stirred for 40 min at rt under Ar. Then, the reaction mixture was cooled to −10 °C and TMSOTf (14 μL, 75 μmol, 0.1 equiv) was injected. The mixture was stirred at –10 °C for 10 min under Ar. The reaction was then quenched with Et_3N (100 μL), filtered over Celite and rinsed with DCM. The filtrate was concentrated under reduced pressure and purified by combi-flash chromatography (PE/EtOAc 7:3) to give (5-azido-1-pentyl) 2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-levulinoyl-*α*-L-rhamnopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (768 mg, 81%) as a white foam: R_f 0.6 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –17 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.15 (m, 30H, C*H*-Ar), 5.48 (s, 1H, H-7A), 5.43 (dd, *J* = 3.6, 1.5 Hz, 1H, H-2B), 5.24 (d, *J* = 1.3 Hz, 1H, H-1B), 5.08 (t, *J* = 10.2 Hz, 1H, H-4B), 4.85 (d, *J* = 11.0 Hz, 1H, C*H*HPh), 4.78 (d, *J* = 11.7 Hz, 1H, CH*H*Ph), 4.77 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.76 (d, *J* = 10.8 Hz, 1H, CH*H*Ph), 4.75 (d, *J* = 11.0 Hz, 1H, C*H*HPh), 4.73 (d, *J* = 10.8 Hz, 1H, CH*H*Ph), 4.63 (d, *J* = 12.1 Hz, 1H, C*H*HPh), 4.57 (d, *J* = 12.1 Hz, 1H, CH*H*Ph), 4.56 (d, *J* = 11.7 Hz, 1H, C*H*HPh), 4.53 (d, *J* = 10.9 Hz, 1H, CH*H*Ph), 4.49 (d, $J_{1C,2C}$ = 7.6 Hz, 1H, H-1C), 4.45 (d, $J_{1A,2A}$ = 7.7 Hz, 1H, H-1A), 4.32 (dd, *J* = 10.5, 4.8 Hz, 1H, H-6aA), 4.18 (dd, *J* = 10.0, 3.6 Hz, 1H, H-3B), 4.15–4.09 (m, 1H, H-5B), 3.92 (t, *J* = 9.5 Hz, 1H, H-3A), 3.90–3.86 (m, 1H, H-1a$_{linker}$), 3.77–3.68 (m, 3H, H-6bA, H-6aC, H-6bC), 3.59–3.49 (m, 3H, H-1b$_{linker}$, H-3C, H-4A), 3.44 (t, *J* = 9.5 Hz, 1H, H-4C), 3.40–3.32 (m, 4H, H-2A, H-2C, H-5A, H-5C), 3.20 (t, *J* = 7.2 Hz, 2H, H-5$_{linker}$), 2.50–2.33 (m, 2H, CH_{2Lev}), 2.25–2.16 (m, 2H, CH_{2Lev}), 2.04 (s, 3H, CH_{3Ac}), 2.02 (s, 3H, CH_{3Lev}), 1.66–1.55 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.46–1.37 (m, 2H, H-3$_{linker}$), 0.82 (d, *J* = 6.3 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6 (*C*O), 171.9, 169.7 (2 × *C*O), 138.7, 138.6, 138.4, 138.2, 138.1, 137.1 (6 × C-Ar), 129.2–126.2 (18 × *C*H-Ar), 104.1 (C-1A), 103.9 (C-1C), 101.6 (C-7A), 97.7 (C-1B), 84.6 (C-3C), 82.9 (C-2A), 82.1 (C-2C), 79.0 (C-4C*), 77.8 (C-4A*), 75.9 (C-3A), 75.5 (*C*H_2Ph), 75.3 (C-5C), 74.9 (*C*H_2Ph), 74.8 (*C*H_2Ph), 74.4 (*C*H_2Ph), 74.2 (C-3B), 73.7 (*C*H_2Ph), 73.1 (C-4B), 71.9 (C-2B), 70.0 (C-1$_{linker}$), 69.2 (C-6A*), 68.8 (C-6C*), 66.3 (C-5A*), 66.2 (C-5B*), 51.3 (C-5$_{linker}$), 37.5 (*C*H_{2Lev}), 29.7 (*C*H_{3Lev}), 29.3 (C-2$_{linker}$), 28.6 (C-4$_{linker}$), 27.7 (*C*H_{2Lev}), 23.3 (C-3$_{linker}$), 20.9 (*C*H_{3Ac}), 16.8 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{72}H_{83}N_3NaO_{18}$ 1300.5564; found 1300.5586.

Acetic acid (2.6 mL) and hydrazine monohydrate (151 μL, 3.1 mmol, 5.0 equiv) were slowly added to a stirred solution of the latter compound (796 mg, 620 μmol, 1.0 equiv) in anhydrous py (4 mL) at 0 °C under Ar. Then, the reaction mixture was stirred from 0 °C to rt overnight. After this time,

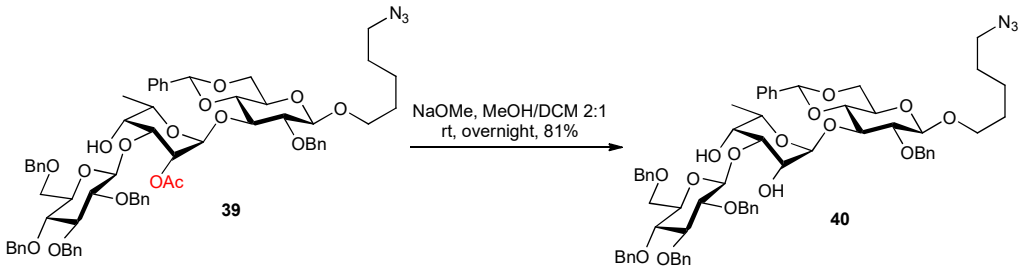
solvents were concentrated and co-evaporated with toluene (3 ×). The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 8:2) to give alcohol **38** (696 mg, 95%) as a colorless oil: R_f 0.6 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –20 (*c* 0.79, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.15 (m, 30H, C*H*-Ar), 5.49 (s, 1H, H-7A), 5.34 (dd, *J* = 3.7, 1.5 Hz, 1H, H-2B), 5.21 (d, *J* = 1.4 Hz, 1H, H-1B), 4.87 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.83–4.76 (m, 6H, 3 × CH_2Ph), 4.67 (d, $J_{1C,2C}$ = 7.8 Hz, 1H, H-1C), 4.60 (d, *J* = 12.1 Hz, 1H, CH*H*Ph), 4.54 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.52 (d, *J* = 12.1 Hz, 1H, CH*H*Ph), 4.46 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.32 (dd, *J* = 10.4, 4.9 Hz, 1H, H-6aA), 4.04–4.00 (m, 1H, H-5B), 3.98 (dd, *J* = 9.6, 3.5 Hz, 1H, H-3B), 3.92 (t, *J* = 9.5 Hz, 1H, H-3A), 3.90–3.86 (m, 1H, H-1a$_{linker}$), 3.74 (t, *J* = 10.7 Hz, 1H, H-6bA), 3.70–3.67 (m, 2H, H-6aC, H-6bC), 3.63–3.57 (m, 2H, H-3C, H-4C), 3.54 (dd, *J* = 6.9, 2.9 Hz, 1H, H-4A), 3.51–3.40 (m, 5H, H-1b$_{linker}$, H-2A, H-2C, H-4B, H-5C), 3.37 (dd, *J* = 9.8, 4.8 Hz, 1H, H-5A), 3.19 (t, *J* = 7.3 Hz, 2H, H-5$_{linker}$), 2.75 (s, 1H, O*H*), 2.02 (s, 3H, CH_{3Ac}), 1.66–1.55 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.46–1.39 (m, 2H, H-3$_{linker}$), 0.89 (d, *J* = 6.2 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9 (*C*O), 138.6, 138.4, 138.3, 138.2, 137.9, 137.2 (6 × C-Ar), 129.1–126.3 (18 × *C*H-Ar), 104.2 (C-1A), 103.5 (C-1C), 101.6 (C-7A), 98.1 (C-1B), 85.1 (C-3C), 83.0 (C-2A), 82.2 (C-2C), 79.2 (C-4A), 78.8 (C-3B), 77.9 (C-4C), 76.4 (C-3A), 75.7 (*C*H_2Ph), 75.5 (*C*H_2Ph), 75.2 (C-5C), 75.1 (*C*H_2Ph), 74.9 (*C*H_2Ph), 73.6 (*C*H_2Ph), 72.3 (C-4B), 71.9 (C-2B), 70.1 (C-1$_{linker}$), 68.9 (C-6A*), 68.8 (C-6C*), 67.9 (C-5B), 66.4 (C-5A), 51.4 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.4 (C-3$_{linker}$), 21.1 (*C*H_{3Ac}), 17.2 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{67}H_{77}N_3NaO_{16}$ 1202.5196; found 1202.5220.

(5-Azido-1-pentyl) 2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→3)-2-*O*-acetyl-6-deoxy-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (39).



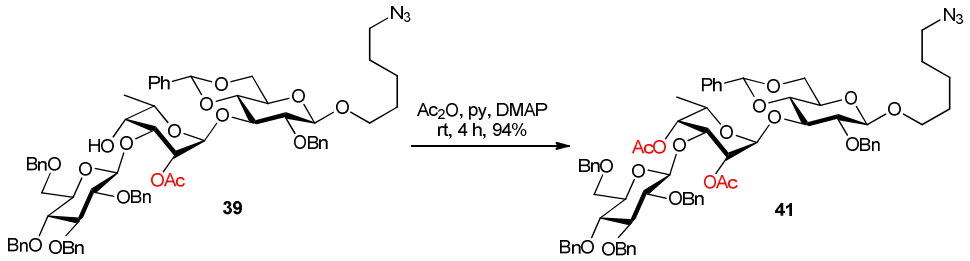
To a solution of DMSO (20 μL, 216 μmol, 10 equiv) in anhydrous DCM (0.4 mL) at –10 °C under Ar were sequentially added PDCP (20 μL, 130 μmol, 6.0 equiv) and Et_3N (40 μL, 216 μmol, 10 equiv). Then, a solution of trisaccharide **38** (26 mg, 22 μmol, 1.0 equiv) in DCM (0.1 mL) was added dropwise. The reaction mixture was stirred at –10 °C for 10 min, then allowed to slowly warm up to rt. After 1 h, DCM (6 mL) was added. The organic phase was washed with water (3 × 3 mL). The aqueous layer was back extracted with DCM (6 mL). The combined organic phases were washed with brine (5 mL). Then, the solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure to give a ketone. To a cooled (–10 °C) solution of the ketone in MeOH/DCM (0.4 mL, 3:1 *v/v*), $NaBH_4$ (3.2 mg, 86 μmol, 4.0 equiv) was slowly added. The mixture was stirred from –10 °C to rt under Ar for 1 h. Then, the reaction mixture was diluted with DCM (6 mL) and the organic phase was washed with water (3 × 4 mL). The aqueous layer was extracted with DCM (2 × 3 mL). The combined organic phases were washed with brine, dried ($MgSO_4$) and then concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 8:2 to 75:25) to give alcohol **39** (22 mg, 85%, two steps) as a colorless solid: R_f 0.5 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –45 (*c* 0.34, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.13 (m, 30H, C*H*-Ar), 5.37 (s, 1H, H-7A), 5.32 (dd, *J* = 3.7, 1.2 Hz, 1H, H-2B), 5.30 (d, *J* = 1.2 Hz, 1H, H-1B), 4.92 (d, *J* = 11.0 Hz, 1H, C*H*HPh), 4.88 (d, *J* = 11.0 Hz, 1H, CH*H*Ph), 4.85 (d, *J* = 10.2 Hz, 1H, C*H*HPh), 4.79 (d, *J* = 10.8 Hz, 1H, CH*H*Ph), 4.77 (d, *J* = 10.2 Hz, 1H, C*H*HPh), 4.75 (d, *J* = 10.8 Hz, 1H, CH*H*Ph), 4.69 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.63 (d, $J_{1C,2C}$ = 7.6 Hz, 1H, H-1C), 4.56 (d, *J* = 12.2 Hz, 1H, CH*H*Ph), 4.54 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.49 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.46 (d, *J* = 12.2 Hz, 1H, CH*H*Ph), 4.31 (dd, *J* = 10.5, 4.8 Hz, 1H, H-6aA), 4.19–4.14 (m, 2H, H-3B, H-5B), 3.97 (t, *J* = 9.4 Hz, 1H, H-3A), 3.91 (dt, *J* = 9.5, 6.8 Hz, 1H, H-1a$_{linker}$), 3.72 (t, *J* = 10.4 Hz, 1H, H-6bA), 3.67 (d, *J* = 2.9 Hz, 2H, H-6aC, H-6bC), 3.63–3.57 (m, 3H, H-3C, H-4B, H-4C), 3.53 (dt, *J* = 9.5, 6.9 Hz, 1H, H-1b$_{linker}$), 3.49–3.42 (m, 4H, H-2A, H-2C, H-4A, H-5C), 3.37 (dd, *J* = 9.6, 4.7 Hz, 1H, H-5A), 3.19 (t, *J* = 7.3 Hz, 2H, H-5$_{linker}$), 1.88 (s, 3H, CH_{3Ac}), 1.67–1.54 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.47–1.37 (m, 2H, H-3$_{linker}$), 0.96 (d, *J* = 6.4 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2 (*C*O), 138.7, 138.6, 138.4, 138.3, 138.2, 137.3 (6 × C-Ar), 129.1–126.3 (18 × *C*H-Ar), 104.2 (C-1A), 101.7 (C-7A), 100.6 (C-1C), 98.3 (C-1B), 84.6 (C-3C), 83.1 (C-2A), 82.1 (C-2C), 79.2 (C-4A), 77.6 (C-4C), 75.8 (C-3A), 75.7 (*C*H$_2$Ph), 75.2 (C-5C), 75.1 (*C*H$_2$Ph), 74.8 (*C*H$_2$Ph), 74.7 (*C*H$_2$Ph), 73.4 (*C*H$_2$Ph), 71.6 (C-3B), 70.2 (C-1$_{linker}$), 70.1 (C-2B), 68.9 (C-4B, C-6A*), 68.8 (C-6C*), 66.6 (C-5B), 66.4 (C-5A), 51.4 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.4 (C-3$_{linker}$), 21.0 (*C*H$_{3Ac}$), 16.1 (*C*H$_{3Tal}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{67}H_{77}N_3NaO_{16}$ 1202.5196; found 1202.5225.

(5-Azido-1-pentyl) 2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→3)-6-deoxy-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (40).



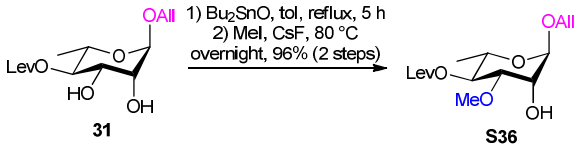
To a solution of compound **39** (29 mg, 25 μmol, 1.0 equiv) in anhydrous MeOH/DCM (0.8 mL, 2:1 *v/v*) was added NaOMe (25% in MeOH, 2.4 μL, 10 μmol, 0.4 equiv). The reaction mixture was stirred overnight at rt under Ar. Dowex H^+ was added until neutralization, then the solution was filtered off and the solvents were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 85:15 to 7:3) to give diol **40** (23 mg, 81%) as a colorless solid: R_f 0.6 (tol/EtOAc 8:2); $[\alpha]_D^{20}$ = –34 (*c* 0.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.13 (m, 30H, C*H*-Ar), 5.43 (s, 1H, H-7A), 5.30 (br s, 1H, H-1B), 4.93 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.91 (d, *J* = 10.9 Hz, 1H, CH*H*Ph), 4.85–4.78 (m, 4H, 2 × CH_2Ph), 4.65 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.59 (d, $J_{1C,2C}$ = 7.7 Hz, 1H, H-1C), 4.49 (d, *J* = 10.8 Hz, 1H, CH*H*Ph), 4.48 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.45 (d, *J* = 12.2 Hz, 1H, C*H*HPh), 4.40 (d, *J* = 12.2 Hz, 1H, CH*H*Ph), 4.32 (dd, *J* = 10.7, 4.6 Hz, 1H, H-6aA), 4.09 (dd, *J* = 13.9, 6.2 Hz, H-5B), 3.96 (t, *J* = 9.4 Hz, 1H, H-3A), 3.94–3.89 (m, 2H, H-2B, H-1a$_{linker}$), 3.83 (t, *J* = 3.6 Hz, 1H, H-3B), 3.74 (t, *J* = 10.4 Hz, 1H, H-6bA), 3.64 (t, *J* = 9.3 Hz, 1H, H-3C), 3.60–3.37 (m, 10H, H-1b$_{linker}$, H-2A, H-2C, H-4A, H-4B, H-4C, H-5A, H-5C, H-6aC, H-6bC), 3.22 (t, *J* = 7.3 Hz, 2H, H-5$_{linker}$), 3.14 (d, *J* = 8.5 Hz, O*H*), 1.69–1.57 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.50–1.43 (m, 2H, H-3$_{linker}$), 0.89 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 138.4, 138.0, 137.9, 137.8, 137.3 (6 × C-Ar), 129.1–126.3 (18 × *C*H-Ar), 104.2 (C-1A), 101.9 (C-7A), 101.4 (C-1C), 100.8 (C-1B), 84.7 (C-3C), 82.7 (C-2A), 81.9 (C-2C), 79.4 (C-4A), 77.8 (C-4C), 76.3 (C-3A), 75.8 (*C*H_2Ph), 75.3 (C-3B), 75.2 (*C*H_2Ph), 75.1 (*C*H_2Ph), 75.0 (*C*H_2Ph), 74.9 (C-5C), 73.6 (*C*H_2Ph), 70.7 (C-4B), 70.2 (C-1$_{linker}$), 69.7 (C-2B), 69.0 (C-6A*), 68.9 (C-6C*), 66.7 (C-5B), 66.4 (C-5A), 51.4 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.4 (C-3$_{linker}$), 16.1 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{65}H_{75}N_3NaO_{15}$ 1160.5090; found 1160.5083.

(5-Azido-1-pentyl) 2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1→3)-2,4-di-*O*-acetyl-6-deoxy-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (41).



Ac_2O (0.4 mL) and DMAP (500 μg, 4.2 μmol, 0.1 equiv) were added to a solution of alcohol **39** (50 mg, 40 μmol, 1.0 equiv) in anhydrous py (0.4 mL). The reaction mixture was stirred at rt for 4 h under Ar. The solution was then concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 7:3) to give diacetylated trisaccharide **41** (49 mg, 94%) as a colorless oil: $[\alpha]_D^{20}$ = –46 (*c* 0.34, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.12 (m, 30H, C*H*-Ar), 5.34–5.32 (m, 3H, H-1B, H-2B, H-7A), 5.13 (d, *J* = 3.1 Hz, 1H, H-4B), 4.86 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.83 (d, *J* = 10.9 Hz, 1H, CH*H*Ph), 4.82 (d, *J* = 11.6 Hz, 1H, C*H*HPh), 4.78 (d, *J* = 10.7 Hz, 1H, CH*H*Ph), 4.75 (d, *J* = 10.7 Hz, 1H, C*H*HPh), 4.71 (d, *J* = 10.9 Hz, 1H, CH*H*Ph), 4.61 (d, *J* = 11.6 Hz, 1H, C*H*HPh), 4.59 (d, *J* = 12.4 Hz, 1H, CH*H*Ph), 4.57 (d, $J_{1C,2C}$ = 7.4 Hz, 1H, H-1C), 4.50 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.49 (d, *J* = 12.4 Hz, 1H, CH*H*Ph), 4.48 (d, $J_{1A,2A}$ = 7.4 Hz, 1H, H-1A), 4.33–4.26 (m, 3H, H-3B, H-5B, H-6aA), 3.94 (t, *J* = 9.3 Hz, 1H, H-3A), 3.90 (dt, *J* = 9.5, 6.9 Hz, 1H, H-1a$_{linker}$), 3.72– 3.65 (m, 3H, H-6bA, H-6aC, H-6bC), 3.64–3.58 (m, 2H, H-3C, H-4C), 3.54 (dt, *J* = 9.5, 6.9 Hz, 1H, H-1b$_{linker}$), 3.49–3.36 (m, 5H, H-2A, H-2C, H-4A, H-5A, H-5C), 3.19 (t, *J* = 7.4 Hz, 2H, H-5$_{linker}$), 2.00 (s, 3H, CH_{3Ac}), 1.95 (s, 3H, CH_{3Ac}), 1.67–1.55 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.47–1.40 (m, 2H, H-3$_{linker}$), 0.77 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 169.2 (2 × *C*O), 138.7, 138.6, 138.4, 138.3, 138.2, 137.2 (6 × C-Ar), 129.4–126.2 (18 × *C*H-Ar), 104.2 (C-1A), 101.8 (C-7A), 100.2 (C-1C), 98.8 (C-1B), 84.5 (C-3C), 83.2 (C-2A), 81.8 (C-2C), 79.1 (C-5C), 77.5 (C-4C), 75.9 (C-3A), 75.5 (*C*H_2Ph), 75.1 (C-4A), 75.0 (*C*H_2Ph), 74.9 (*C*H_2Ph), 74.1 (*C*H_2Ph), 73.4 (*C*H_2Ph), 70.2 (C-1$_{linker}$), 69.7 (C-3B), 68.9 (C-6A*), 68.8 (C-6C*), 68.3 (C-2B), 68.0 (C-4B), 66.3 (C-5A), 64.9 (C-5B), 51.3 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.4 (C-3$_{linker}$), 21.2, 21.0 (2 × *C*H_{3Ac}), 15.9 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{69}H_{79}N_3NaO_{17}$ 1244.5302; found 1244.5309.

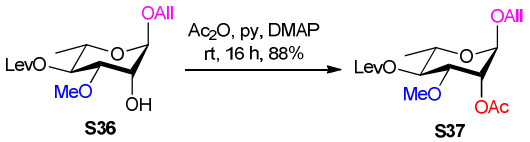
Allyl 4-*O*-Levulinoyl-3-*O*-methyl-*α*-L-rhamnopyranoside (**S36**).



31 **S36**

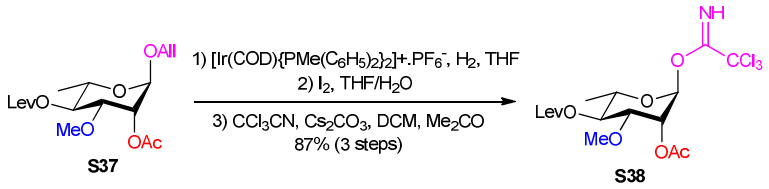
To a solution of diol **31** (500 mg, 1.7 mmol, 1.0 equiv) in toluene (7 mL) was added Bu_2SnO (465 mg, 1.9 mmol, 1.1 equiv) and the mixture was refluxed using a Dean-Stark apparatus for 5 h. The temperature was cooled to 30 °C, then CsF (263 mg, 1.7 mmol, 1.02 equiv) and MeI (5.2 mL, 85 mmol, 50 equiv) were successively added. After stirring overnight at 80 °C, the mixture was concentrated under reduced pressure. Purification by silica gel flash chromatography (PE/EtOAc 8:2 to 5:5) gave alcohol **S36** (503 mg, 96%) as a yellow oil: $[\alpha]_D^{20} = -48$ (*c*, 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89 (dddd, *J* = 16.6, 10.4, 6.1, 5.3 Hz, 1H, H-2_{All}), 5.29 (ddd, *J* = 17.2, 3.1, 1.6 Hz, 1H, H-$3a_{All}$), 5.20 (ddd, *J* = 11.6, 2.6, 1.2 Hz, 1H, H-$3b_{All}$), 4.97 (t, *J* = 9.7 Hz, 1H, H-4), 4.87 (d, *J* = 1.5 Hz, 1H, H-1), 4.15 (ddt, *J* = 12.9, 5.2, 1.4 Hz, 1H, H-$1a_{All}$), 4.07 (dd, *J* = 3.3, 1.7 Hz, 1H, H-2), 3.98 (ddt, *J* = 12.9, 6.2, 1.3 Hz, 1H, H-$1b_{All}$), 3.77 (dq, *J* = 10.1, 6.3 Hz, 1H, H-5), 3.52 (dd, *J* = 9.6, 3.4 Hz, 1H, H-3), 3.41 (s, 3H, -OCH_3), 2.85–2.54 (m, 4H, $(CH_2)_{2Lev}$), 2.17 (s, 3H, CH_{3Lev}), 1.17 (d, 3H, *J* = 6.3 Hz, CH_{3Rha}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6 (*C*O), 172.3 (*C*O), 133.8 (C-2_{All}), 117.8 (C-3_{All}), 98.3 (C-1), 78.9 (C-3), 73.0 (C-4), 68.2 (C-1_{All}), 67.8 (C-2), 66.2 (C-5), 57.7 (-OCH_3), 38.0 (CH_{2Lev}), 29.9 (CH_{3Lev}), 28.1 (CH_{2Lev}), 17.5 (CH_{3Rha}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{15}H_{24}NaO_7$ 339.1414; found 339.1407.

Allyl 2-*O*-Acetyl-4-*O*-levulinoyl-3-*O*-methyl-*α*-L-rhamnopyranoside (**S37**).



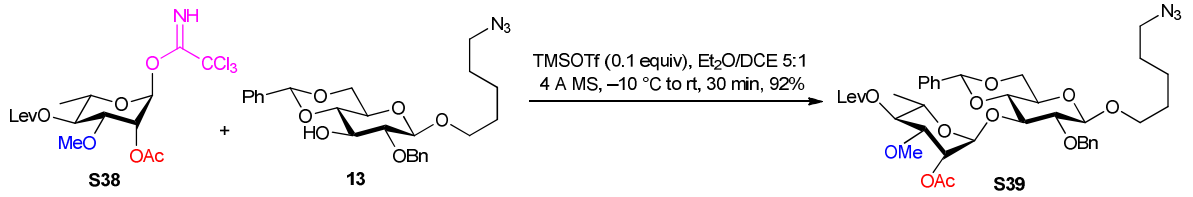
Alcohol **S36** (473 mg, 1.5 mmol, 1.0 equiv) was dissolved in anhydrous py (10 mL). Ac_2O (10 mL) and DMAP (2 mg, 15 µmol, 0.01 equiv) were added. The reaction mixture was stirred for 16 h at rt under Ar. Then, solvents were concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was purified by silica gel flash chromatography (PE/EtOAc 8:2 to 65:35) to give derivative **S37** (520 mg, 88%) as a colorless oil: $[\alpha]_D^{20} = -39$ (*c*, 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ5.89 (ddd, *J* = 22.3, 10.9, 5.9 Hz, 1H, H-2_{All}) 5.32 (m, 2H, H-2, H-$3a_{All}$), 5.22 (dd, *J* = 10.4, 1.3 Hz, 1H, H-$3b_{All}$), 4.96 (t, *J* = 9.8 Hz, 1H, H-4), 4.78 (d, *J* = 1.6 Hz, 1H, H-1), 4.16 (ddt, *J* = 12.8, 5.2, 1.3 Hz, 1H, H-$1a_{All}$), 3.98 (ddt, *J* = 12.8, 6.2, 1.1 Hz, 1H, H-$1b_{All}$), 3.80 (dq, *J* = 9.8, 6.3 Hz, 1H, H-5), 3.61 (dd, *J* = 9.9, 3.4 Hz, 1H, H-3), 3.33 (s, 3H, -OCH_3), 2.88 – 2.48 (m, 4H, (CH_2)$_{2Lev}$), 2.18 (s, 3H, CH_{3Lev}), 2.11 (s, 3H, CH_{3Ac}), 1.20 (d, 3H, *J* = 6.3 Hz, CH_{3Rha}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6 (*C*O_{Lev}), 172.2 (*C*O_{Lev}), 170.5 (*C*O_{Ac}), 133.5 (C-2_{All}), 118.1 (C-3_{All}), 96.9 (C-1), 77.0 (C-3), 72.9 (C-4), 68.4 (C-1_{All}), 68.2 (C-2), 66.7 (C-5), 57.8 (-O*C*H_3), 38.0 (*C*H_{2Lev}), 30.0 (*C*H_{3Lev}), 28.1 (*C*H_{2Lev}), 21.1 (*C*H_{3Ac}), 17.5 (*C*H_{3Rha}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{17}H_{26}NaO_8$ 381.1520; found 381.1514.

2-*O*-Acetyl-4-*O*-levulinoyl-3-*O*-methyl-*α*-L-rhamnopyranosyl 2,2,2-Trichloroacetimidate (S38).



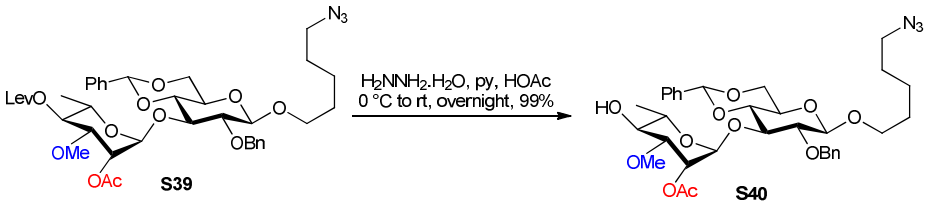
Derivative **S37** (500 mg, 1.4 mmol, 1.0 equiv) was reacted according to the general procedure for the synthesis of trichloroacetimidate donors. Purification by silica gel flash chromatography (PE/EtOAc 7:3 to 4:6 + 1% Et_3N) gave trichloroacetimidate donor **S38** (560 mg, 87%, over three steps) as a yellow oil: $[\alpha]_D^{20}$ = –28 (*c*, 2.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H, N*H*), 6.20 (d, *J* = 1.9 Hz, 1H, H-1), 5.49 (dd, *J* = 3.3, 2.0, 1H, H-2), 5.06 (t, *J* = 9.9 Hz, 1H, H-4), 3.99 (dq, *J* = 10.0, 6.3 Hz, 1H, H-5), 3.66 (dd, *J* = 9.9, 3.4 Hz, 1H, H-3), 3.37 (s, 3H, CH_{3Me}), 2.90 – 2.48 (m, 4H, (CH_2)$_{2Lev}$), 2.18 (s, 3H, CH_{3Lev}), 2.15 (s, 3H, CH_{3Ac}), 1.24 (d, 3H, *J* = 6.4 Hz, CH_{3Rha}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.5 (*C*O$_{Lev}$), 172.2 (*C*O$_{Lev}$), 170.1 (*C*O$_{Ac}$), 160.0 (C$_{imine}$), 95.1(C-1), 91.0 (*C*Cl$_3$), 77.0 (C-3), 72.2 (C-4), 69.5 (C-5), 66.6 (C-2), 58.1 (*C*H$_{3Me}$), 38.0 (*C*H$_{2Lev}$), 29.9 (*C*H$_{3Lev}$), 28.0 (*C*H$_{2Lev}$), 21.0 (*C*H$_{3Ac}$), 17.5 (*C*H$_{3Rha}$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{16}H_{22}Cl_3NNaO_8$ 484.0303; found 484.0288.

(5-Azido-1-pentyl) 2-*O*-Acetyl-4-*O*-levulinoyl-3-*O*-methyl-*α*-L-rhamnopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (S39).



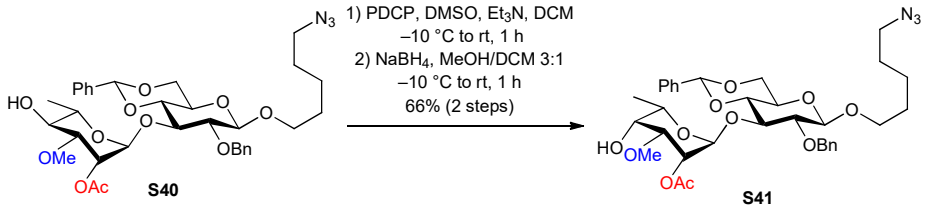
Acceptor **13** (222 mg, 473 μmol, 1.0 equiv) and donor **S38** (263 mg, 567 μmol, 1.2 equiv) were dried for 4 h under high vacuum and then dissolved in anhydrous Et_2O/DCE (11 mL, 5:1 *v/v*). Freshly activated 4 Å powdered molecular sieves (890 mg) were added and the suspension was stirred for 40 min at rt under Ar. Then, the reaction mixture was cooled to −10 °C and TMSOTf (8.6 μL, 47 μmol, 0.1 equiv) was injected. The mixture was stirred at –10 °C for 10 min under Ar and after that time 20 min at rt. The reaction was then quenched with Et_3N (63 μL), filtered over Celite and rinsed with DCM. The filtrate was concentrated under reduced pressure and purified by flash chromatography (PE/EtOAc 8:2 to 65:35) to give disaccharide **S39** (336 mg, 92%) as a white amorphous solid: $[\alpha]_D^{20}$ = –41 (*c*, 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ7.50-7.20 (m, 10H, C*H*-Ar), 5.54 (s, 1H, H-7), 5.41 (dd, *J* = 3.3, 1.7 Hz, 1H, H-2B), 5.18 (d, *J* = 1.3 Hz, 1H, H-1B), 4.89 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.83 (t, *J* = 9.9 Hz, 1H, H-4B), 4.70 (d, *J* = 10.8 Hz, 1H, CH*H*Ph), 4.50 (d, *J* = 7.8 Hz, 1H, H-1), 4.36 (dd, *J* = 10.5, 4.9 Hz, 1H, H-6aA), 4.12 (dq, *J* = 12.6, 6.3 Hz, 1H, H-5B), 3.98 – 3.88 (m, 2H, H-3, H-1a$_{linker}$), 3.78 (t, *J* = 10.2 Hz, 1H, H-6bA), 3.61 – 3.52 (m, 3H, H-4, H-3B, H-1b$_{linker}$), 3.49 – 3.38 (m, 2H, H-2, H-5), 3.34 (s, 3H, CH_{3Me}), 3.23 (t, *J* = 6.8 Hz, 2H, H-5$_{linker}$), 2.81 – 2.60 (m, 2H, CH_2-3$_{Lev}$), 2.50 (t, *J* = 6.7 Hz, 2H, CH_2-2$_{Lev}$), 2.17 (s, 3H, CH_{3Lev}), 2.06 (s, 3H, CH_{3Ac}), 1.72 – 1.57 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.52- 1.41 (m, 2H, H-3$_{linker}$), 0.80 (d, *J* = 6.2 Hz, 3H, CH_3-6B); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.4 (*C*O$_{Lev}$), 172.1 (*C*O$_{Lev}$), 170.1 (*C*O$_{Ac}$), 137.9, 137.2 (2 × C-Ar), 129.3 – 126.3 (6 × C-Ar), 104.3 (C-1), 101.8 (C-7), 98.2 (C-1B), 82.7 (C-2), 79.3 (C-4), 77.1 (C-3B), 76.1 (C-3), 75.0 (*C*H$_2$Ph), 72.9 (C-4B), 70.2 (C-1$_{linker}$), 68.9 (C-6), 67.9 (C-2B), 66.5 (C-5), 66.3 (C-5B), 57.8 (*C*H$_{3Me}$), 51.4 (C-5$_{Linker}$), 38.0 (C-3$_{Lev}$), 30.0 (*C*H$_{3Lev}$), 29.4 (C-2$_{linker}$), 28.8 (C-4$_{linker}$), 28.1 (C-2$_{Lev}$), 23.5 (C-3$_{linker}$), 21.1 (*C*H$_{3Ac}$), 16.9 (C-6B); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{39}H_{51}N_3NaO_{13}$ 792.3314; found 792.3296.

(5-Azido-1-pentyl) 2-*O*-Acetyl-3-*O*-methyl-*α*-L-rhamnopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (S40).



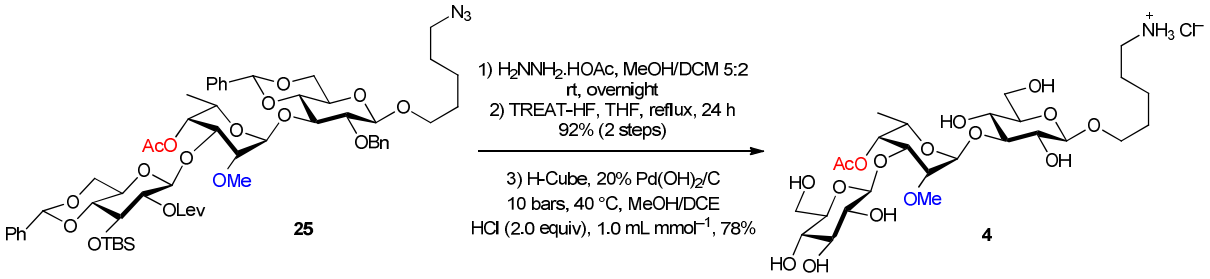
Acetic acid (2.1 mL) and hydrazine monohydrate (124 μL, 2.6 mmol, 5.0 equiv) were slowly added to a stirred solution of disaccharide **S39** (394 mg, 511 μmol, 1.0 equiv) in anhydrous Py (3.3 mL) at 0 °C under Ar. Then, the reaction mixture was stirred from 0 °C to rt overnight. After this time, solvents were concentrated and co-evaporated with toluene (3 ×). The residue was purified by silica gel flash chromatography (PE/EtOAc 85:15 to 8:2) to give alcohol **S40** (340 mg, 99%) as a white amorphous solid: $[\alpha]_D^{20} = -36$ (*c*, 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ7.50 – 7.23 (m, 10H, C*H*-Ar), 5.52 (s, 1H, H-7), 5.39 (dd, *J* = 3.0, 1.7 Hz, 1H, H-2B), 5.16 (d, *J* = 1.4 Hz, 1H, H-1B), 4.90 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.70 (d, *J* = 10.8 Hz, 1H, CH*H*Ph), 4.50 (d, *J* = 7.8 Hz, 1H, H-1), 4.35 (dd, *J* = 10.5, 4.9 Hz, 1H, H-6aA), 4.02 (dq, *J* = 9.0, 6.2 Hz, 1H, H-5B), 3.97 – 3.89 (m, 2H, H-3, H-1a$_{linker}$), 3.77 (t, *J* = 10.2 Hz, 1H, H-6bA), 3.61 – 3.51 (m, 2H, H-4, H-1b$_{linker}$), 3.48 – 3.36 (m, 4H, H-2, H-3B, H-4B, H-5), 3.40 (s, 3H, CH_{3Me}), 3.22 (t, *J* = 6.8 Hz, 2H, H-5$_{linker}$), 2.04 (s, 3H, CH_{3Ac}), 1.72 – 1.56 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.52- 1.38 (m, 2H, H-3$_{linker}$), 0.93 (d, *J* = 6.2 Hz, 3H, CH_3-6B); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1 (CO_{Ac}), 138.0, 137.2 (2 × C-Ar), 129.2 – 126.3 (6 × C-Ar), 104.3 (C-1), 101.8 (C-7), 98.7 (C-1B), 82.8 (C-2), 79.7 (C-3B), 79.3 (C-4), 76.5 (C-3), 75.0 (CH_2Ph), 71.8 (C-4B), 70.2 (C-1$_{Linker}$), 68.9 (C-6), 68.1 (C-5B), 67.5 (C-2B), 66.5 (C-5), 57.5 (CH_{3Me}), 51.4 (C-5$_{Linker}$), 29.4 (C-2$_{Linker}$), 28.8 (C-4$_{Linker}$), 23.5 (C-3$_{Linker}$), 21.0 (CH_{3Ac}), 17.2 (C-6B); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{34}H_{45}N_3NaO_{11}$ 694.2946; found 694.2934.

(5-Azido-1-pentyl) 2-*O*-Acetyl-6-deoxy-3-*O*-methyl-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (S41).



To a solution of DMSO (172 μL, 5 equiv) in anhydrous DCM (7 mL) at –10 °C under Ar were sequentially added phenyl dichlorophosphate (PDCP, 216 μL, 1.45 mmol, 3 equiv) and Et_3N (337 μL, 5 equiv). Then, a solution of disaccharide **S40** (324 mg, 483 μmol, 1.0 equiv) in DCM (4 mL) was added dropwise. The reaction mixture was stirred at –10 °C for 10 min, then allowed to slowly warm up to rt. After 1 h, DCM (20 mL) was added. The organic phase was washed with water (3 × 20 mL). The aqueous layer was back extracted with DCM (20 mL). The combined organic phases were washed with brine (20 mL). Then, the solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure to give a ketone. To a cooled (–10 °C) solution of the ketone in MeOH/DCM (10 mL, 3:1 *v/v*), $NaBH_4$ (55 mg, 1.4 mmol, 3.0 equiv) was slowly added. The mixture was stirred from –10 °C to rt under Ar for 1 h. Then, the reaction mixture was diluted with DCM (10 mL) and the organic phase was washed with water (3 × 10 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The combined organic phases were washed with brine, dried ($MgSO_4$) and then concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 8:2) to give alcohol **S41** (213 mg, 66%, two steps) as a white solid: $[\alpha]_D^{20}$ = –57 (*c*, 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.27 (m, 10H, C*H*-Ar), 5.50 (s, 1H, H-7), 5.33 (m, 1H, H-2B), 5.27 (s, 1H, H-1B), 4.90 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.71 (d, *J* = 10.9 Hz, 1H, CH*H*Ph), 4.51 (d, *J* = 7.8 Hz, 1H, H-1), 4.34 (dd, *J* = 10.5, 4.8 Hz, 1H, H-6aA), 4.15 (q, *J* = 6.3 Hz, 1H, H-5B), 3.97 (t, *J* = 9.1, 1H, H-3), 3.93 (dt, *J* = 9.5, 6.4 Hz, 1H, H-1a$_{linker}$), 3.77 (t, *J* = 10.2 Hz, 1H, H-6bA), 3.60 – 3.42 (m, 6H, H-1b$_{linker}$, H-2, H-3B, H-4, H-4B, H-5), 3.40 (s, 3H, C*H*$_{3Me}$), 3.21 (t, *J* = 6.9 Hz, 2H, H-5$_{linker}$), 2.04 (s, 3H, C*H*$_{3Ac}$), 1.70 – 1.55 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.50- 1.40 (m, 2H, H-3$_{linker}$), 0.94 (d, *J* = 6.6 Hz, 3H, C*H*$_3$-6B); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.43 (*C*O$_{Ac}$), 138.1, 137.3 (2 × C-Ar), 129.4 – 126.3 (6 × C-Ar), 104.3 (C-1), 101.7(C-7), 98.7 (C-1B), 83.0 (C-2), 79.37 (C-4), 75.9 (C-3), 74.9 (*C*H$_2$Ph), 74.3 (C-3B), 70.3 (C-1$_{Linker}$), 69.6 (C-4B), 69.0 (C-6), 67.8 (C-5B), 66.9 (C-2B), 66.4 (C-5), 56.4 (*C*H$_{3Me}$), 51.4 (C-5$_{Linker}$), 29.4 (C-2$_{Linker}$), 28.7 (C-4$_{Linker}$), 23.5 (C-3$_{Linker}$), 21.2 (*C*H$_{3Ac}$), 16.1 (C-6B); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{34}H_{45}N_3NaO_{11}$ 694.2946; found 694.2945.

(5-Amino-1-pentyl) *β*-D-Glucopyranosyl-(1→3)-4-*O*-acetyl-6-deoxy-2-*O*-methyl-*α*-L-talopyranosyl-(1→3)-*β*-D-glucopyranoside Hydrochloride (4).



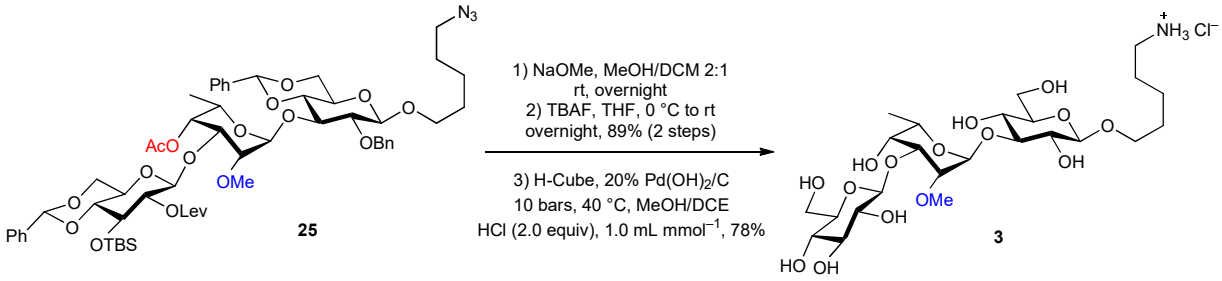
To a solution of trisaccharide **25** (983 mg, 1.1 mmol, 1.0 equiv) in anhydrous MeOH/DCM (0.3 mL, 5:2 *v/v*) was added hydrazine acetate (209 mg, 2.3 mmol, 2.0 equiv). After being stirred overnight at rt under Ar, the reaction mixture was concentrated under reduced pressure and co-evaporated with toluene (3 ×) to give an alcohol. For analytical data, a small sample was purified by silica gel flash chromatography (DCM/MeOH 98:2): $[\alpha]_D^{20}$ = –52 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.50–7.27 (m, 15H, C*H*-Ar), 5.51 (s, 1H, H-7A*), 5.49 (s, 1H, H-7C*), 5.35 (s, 1H, H-1B), 4.99 (d, *J* = 11.2 Hz, 1H, C*H*HPh), 4.93 (br s, 1H, H-4B), 4.66 (d, *J* = 11.2 Hz, 1H, CH*H*Ph), 4.52 (d, $J_{1A,2A}$ = 7.7 Hz, 1H, H-1A), 4.42 (d, $J_{1C,2C}$ = 7.6 Hz, 1H, H-1C), 4.33 (td, *J* = 11.0, 4.9 Hz, 2H, H-6aA, H-6aC), 4.22 (dd, *J* = 13.9, 6.4 Hz, 1H, H-5B), 3.92–3.88 (m, 1H, H-1a$_{linker}$), 3.91 (t, *J* = 9.7 Hz, 1H, H-3A), 3.86 (t, *J* = 4.1 Hz, 1H, H-3B), 3.79–3.71 (m, 3H, H-3C, H-6bA, H-6bC), 3.55–3.51 (m, 1H, H-1b$_{linker}$), 3.52 (t, *J* = 9.8 Hz, 1H, H-4A), 3.44–3.34 (m, 4H, H-2A, H-4C, H-5A, H-5C), 3.35–3.31 (m, 2H, H-2B, H-2C), 3.21 (s, 3H, CH_{3Me}), 3.20 (t, *J* = 7.0 Hz, 2H, H-5$_{linker}$), 1.69–1.56 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.50–1.42 (m, 2H, H-3$_{linker}$), 0.86 (s, 9H, C(CH_3)$_3$), 0.70 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}), 0.10, 0.04 (2 × s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 173.0 (*C*O), 138.2, 137.4, 137.2 (3 × C-Ar), 129.5–126.3 (9 × *C*H-Ar), 105.7 (C-1C), 104.2 (C-1A), 102.2 (C-7A*), 101.7 (C-7C*), 99.7 (C-1B), 83.1 (C-2A), 81.5 (C-4C), 79.4 (C-4A), 78.1 (C-2B), 76.9 (C-3B), 76.8 (C-3A), 75.4 (C-2C), 74.9 (*C*H$_2$Ph), 74.2 (C-3C), 71.1 (C-4B), 70.2 (C-1$_{linker}$), 68.9 (C-6A), 68.8 (C-6C), 66.6 (C-5A), 66.5 (C-5C), 64.7 (C-5B), 60.0 (*C*H$_{3Me}$), 51.4 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 25.9 (C(*C*H$_3$)$_3$), 23.5 (C-3$_{linker}$), 21.1 (*C*H$_{3Ac}$), 18.5 (*C*(CH$_3$)$_3$), 15.7 (*C*H$_{3Tal}$), –4.41, –4.44 (2 × *C*H$_3$); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{53}H_{73}N_3NaO_{16}Si$ 1058.4652; found 1058.4690.

To a solution of the latter alcohol in anhydrous THF (5 mL) was added TREAT-HF (372 *μ*L, 2.3 mmol, 15 equiv). The mixture was refluxed for 24 h under Ar, then additional TREAT-HF (124 *μ*L, 760 *μ*mol, 5.0 equiv) was added and the reaction was refluxed for another 24 h under Ar. The solution was cooled to rt and diluted with EtOAc (10 mL). The organic phase was washed with a saturated $NaHCO_3$(aq) solution (2 × 5 mL) and brine (10 mL). The solvents of the dried ($MgSO_4$) solution were concentrated under reduced pressure and the residue was purified by silica gel flash chromatography (PE/EtOAc 3:7 to 1:9) to give (5-azido-1-pentyl) 4,6-*O*-benzylidene-*β*-D-glucopyranosyl-(1→3)-4-*O*-acetyl-6-deoxy-2-*O*-methyl-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (128 mg, 92%, two steps) as a white amorphous solid: R_f 0.4 (DCM/MeOH 98:2); $[\alpha]_D^{20}$ = –67 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.51–7.27 (m, 15H, C*H*-Ar), 5.54 (s, 1H, H-7A*), 5.49 (s, 1H, H-7C*), 5.35 (s, 1H, H-1B), 5.00 (d, *J* = 11.4 Hz, 1H, C*H*HPh), 4.92 (br s, 1H, H-4B), 4.65 (d, *J* = 11.4 Hz, 1H, CH*H*Ph), 4.53 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.47 (d, $J_{1C,2C}$ = 7.5 Hz, 1H, H-1C), 4.35 (dd, *J* = 10.5, 4.8 Hz, 2H, H-6aA, H-6aC),

4.24 (dd, J = 13.9, 6.5 Hz, 1H, H-5B), 3.96 (t, J = 9.7 Hz, 1H, H-3A), 3.95–3.91 (m, 2H, H-1a$_{linker}$, H-3B), 3.82 (t, J = 9.6 Hz, 1H, H-3C), 3.77 (td, J = 10.8, 6.2 Hz, 2H, H-6bA, H-6bC), 3.59–3.52 (m, 3H, H-1b$_{linker}$, H-4A, H-4C), 3.50–3.44 (m, 3H, H-2A, H-5A, H-5C), 3.40 (dd, J = 9.1, 7.8 Hz, 1H, H-2C), 3.32 (d, J = 3.5 Hz, 1H, H-2B), 3.20 (t, J = 7.8 Hz, 2H, H-5$_{linker}$), 3.19 (s, 3H, CH_{3Me}), 2.12 (s, 3H, CH_{3Ac}), 1.69–1.56 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.50–1.40 (m, 2H, H-3$_{linker}$), 0.72 (d, J = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3 (*C*O), 138.2, 137.2, 137.1 (3 × C-Ar), 129.5–126.4 (9 × *C*H-Ar), 105.3 (C-1C), 104.2 (C-1A), 102.2 (C-7A*), 102.0 (C-7C*), 99.5 (C-1B), 83.1 (C-2A), 80.4 (C-4C), 79.4 (C-4A), 78.1 (C-2B), 77.4 (C-3B), 76.9 (C-3A), 74.9 (*C*H_2Ph), 74.6 (C-2C), 73.1 (C-3C), 71.1 (C-4B), 70.2 (C-1$_{linker}$), 68.9 (C-6A), 68.8 (C-6C), 66.6 (C-5A), 66.5 (C-5C), 64.5 (C-5B), 59.9 (*C*H_{3Me}), 51.3 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.5 (C-3$_{linker}$), 21.4 (*C*H_{3Ac}), 15.7 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{47}H_{60}N_3O_{16}$ 922.3968; found 922.3986; *m/z* $[M + Na]^+$ calcd for $C_{47}H_{59}N_3NaO_{16}$ 944.3788; found 944.3807; *m/z* $[2M + Na]^+$ calcd for $C_{94}H_{118}N_6NaO_{32}$ 1865.7683; found 1865.7707.

The latter compound (42.4 mg, 46.0 μmol) was reacted according to the general procedure for hydrogenolysis using the H-Cube system giving target trisaccharide **4** (24 mg, 78%) as a white amorphous powder: $[\alpha]_D^{20}$ = –56 (*c* 0.11, H_2O); ^{1}H NMR (400 MHz, D_2O) δ 5.40–5.36 (m, 2H, H-1B, H-4B), 4.58 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1A), 4.49–4.44 (m, 1H, H-5B), 4.47 (d, $J_{1,2}$ = 8.2 Hz, 1H, H-1C), 4.37 (t, $J_{2,3} \approx J_{3,4} \approx$ 3.8 Hz, 1H, H-3B), 3.95–3.88 (m, 3H, H-6aA, H-1a$_{linker}$, H-6aC), 3.76–3.65 (m, 4H, H-6bA, H-1b$_{linker}$, H-6bC, H-2B), 3.61 (t, $J_{2,3} \approx J_{3,4} \approx$ 8.8 Hz, 1H, H-3A), 3.52–3.35 (m, 6H, H-3C, H-5A, H-5C, H-4A, H-4C, H-2A), 3.42 (s, 3H, OCH_3), 3.28 (dd, $J_{2,3}$ = 9.1 Hz, $J_{1,2}$ = 7.9 Hz, 1H, H-2C), 3.00 (t, J = 7.5 Hz, 2H, H-5ab$_{linker}$), 2.17 (s, 3H, COCH_3), 1.73–1.63 (m, 4H, H-4ab$_{linker}$, H-2ab$_{linker}$), 1.50–1.42 (m, 2H, H-3ab$_{linker}$), 1.09 (d, $J_{5,6}$ = 6.6 Hz, 3H, H-6B); ^{13}C NMR (100 MHz, D_2O) δ 174.5 (*C*OCH_3), 102.6 (C-1A), 100.8 (C-1C), 95.5 (C-1B), 83.4 (C-3A), 78.3 (C-2B), 76.6, 76.5 (C-5A, C-5C), 74.4 (C-2C), 73.6 (C-2A), 71.5 (C-3B), 70.8 (C-6C), 70.2, 69.9 (C-4B, C-4A*), 68.6 (C-4C*), 66.1 (C-5B), 61.3 (C-6A, C-1$_{linker}$), 58.5 (O*C*H_3), 40.0 (C-5$_{linker}$), 28.8 (C-2$_{linker}$), 27.0 (C-4$_{linker}$), 22.7 (C-3$_{linker}$), 21.0 (CO*C*H_3), 15.8 (C-6B); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{26}H_{48}NO_{16}$ 630.2973; found 630.3018.

(5-Amino-1-pentyl) *β*-D-Glucopyranosyl-(1→3)-6-deoxy-2-*O*-methyl-*α*-L-talopyranosyl-(1→3)-*β*-D-glucopyranoside Hydrochloride (3).

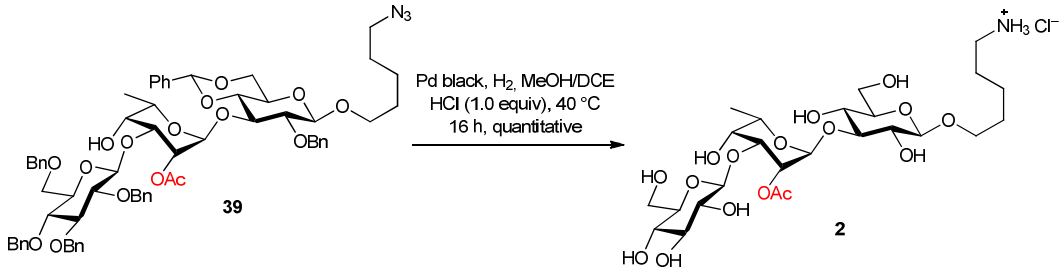


NaOMe (25% in MeOH, 40 μL, 168 μmol, 1.1 equiv) was added to a solution of trisaccharide **25** (173 mg, 153 μmol, 1.0 equiv) in anhydrous MeOH/DCM (5 mL, 2:1 *v/v*). The reaction mixture was stirred overnight at rt under Ar. Dowex H^+ resin was added to neutralize the reaction, then the suspension was filtered off and the solvents were concentrated under reduced pressure and co-evaporated with toluene (3 ×). The residue was dissolved in THF (8 mL). The solution was cooled to 0 °C and TBAF (1.5 mL, 1.0 M solution in THF, 1.5 mmol, 10 equiv) was added. After being stirred under Ar from 0 °C to rt overnight, the mixture was concentrated under reduced pressure. Purification by silica gel flash chromatography (DCM/MeOH 99:1 to 98:2) gave (5-azido-1-pentyl) 4,6-*O*-benzylidene-*β*-D-glucopyranosyl-(1→3)-6-deoxy-2-*O*-methyl-*α*-L-talopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (120 mg, 89%, two steps) as a white foam: R_f 0.5 (DCM/MeOH 95:5); $[\alpha]_D^{20}$ = –58 (*c* 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.32 (m, 15H, C*H*-Ar), 5.54 (s, 1H, H-7A*), 5.49 (s, 1H, H-7C*), 5.27 (d, *J* = 1.5 Hz, 1H, H-1B), 5.05 (d, *J* = 11.5 Hz, 1H, C*H*HPh), 4.58 (d, *J* = 11.5 Hz, 1H, CH*H*Ph), 4.52 (d, $J_{1A,2A}$ = 7.8 Hz, 1H, H-1A), 4.51 (d, $J_{1C,2C}$ = 7.6 Hz, 1H, H-1C), 4.34 (td, *J* = 10.3, 5.2, 4.8 Hz, 2H, H-6aA, H-6aC), 4.05 (dd, *J* = 13.7, 6.4 Hz, 1H, H-5B), 3.97–3.90 (m, 3H, H-1a$_{linker}$, H-3A, H-3B), 3.84–3.74 (m, 3H, H-3C, H-6bA, H-6bC), 3.61–3.45 (m, 8H, H-1b$_{linker}$, H-2B, H-2C, H-4A, H-4B, H-4C, H-5A, H-5C), 3.42 (dd, *J* = 9.2, 7.8 Hz, 1H, H-2A), 3.19 (t, *J* = 7.2 Hz, 2H, H-5$_{linker}$), 3.10 (s, 3H, CH_{3Me}), 1.69–1.56 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.48–1.40 (m, 2H, H-3$_{linker}$), 0.87 (d, *J* = 6.5 Hz, 3H, CH_{3Tal}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 137.2, 137.1 (3 × C-Ar), 129.5–126.4 (9 × *C*H-Ar), 104.2 (C-1A), 102.1 (C-7A*), 102.0 (C-7C*), 101.6 (C-1C), 98.4 (C-1B), 83.5 (C-2A), 80.4 (C-4C), 79.4 (C-4A), 79.3 (C-2B), 77.2 (C-3A), 75.1 (*C*H_2Ph), 74.9 (C-2C), 74.2 (C-3B), 73.3 (C-3C), 70.7 (C-4B), 70.2 (C-1$_{linker}$), 68.9 (C-6A), 68.8 (C-6C), 66.9 (C-5A), 66.8 (C-5C), 66.5 (C-5B), 59.5 (*C*H_{3Me}), 51.4 (C-5$_{linker}$), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.5 (C-3$_{linker}$), 16.0 (*C*H_{3Tal}); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{45}H_{57}N_3NaO_{15}$ 902.3682; found 902.3659.

The latter compound (62.8 mg, 71.4 μmol) was reacted according to the general procedure for hydrogenolysis using the H-Cube system giving target trisaccharide **3** (35 mg, 78%) as a white amorphous powder: $[\alpha]_D^{20}$ = –53 (*c* 0.18, H_2O); ^{1}H NMR (400 MHz, D_2O) δ 5.38 (s, 1H, H-1B), 4.63 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1C), 4.47 (d, $J_{1,2}$ = 8.1 Hz, 1H, H-1A), 4.28 (q, $J_{5,6}$ = 6.5 Hz, 1H, H-5B), 4.13 (t, $J_{2,3} \approx J_{3,4} \approx$ 3.3 Hz, 1H, H-3B), 3.94–3.88 (m, 3H, H-6aC, H-6aA, H-1a$_{linker}$), 3.86 (br s, 1H, H-4$_B$), 3.79 (br s, 1H, H-2$_B$), 3.76–3.66 (m, 3H, H-6bA, H-1b$_{linker}$, H-6bC), 3.61 (t, $J_{2,3} \approx J_{3,4} \approx$ 8.9 Hz, 1H, H-3A), 3.53–3.32 (m, 7H, H-3C, H-5A, H-5C, H-4A, H-4C, H-2A, H-2C), 3.42 (s, 3H, OCH_3), 2.99 (t, *J* = 7.5 Hz, 2H, H-5ab$_{linker}$), 1.73–1.62 (m, 4H, H-4ab$_{linker}$, H-2ab$_{linker}$), 1.49–1.41 (m, 2H, H-3ab$_{linker}$), 1.21 (d, $J_{5,6}$ = 6.5 Hz, 3H, H-6B); ^{13}C NMR (100 MHz, D_2O) δ 102.6 (C-

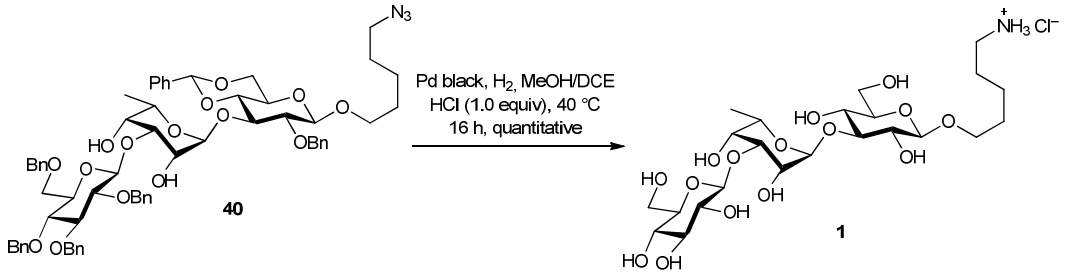
1A), 101.9 (C-1C), 98.4 (C-1B), 83.1 (C-3A), 79.2 (C-2B), 76.6, 76.5 (C-5A, C-5C), 76.1 (C-3C), 74.4, 74.3, 73.6 (C-2A, C-2B, C-2C), 70.6 (C-6C), 70.2, 70.1 (C-4B, C-4A*), 68.7 (C-4C*), 68.2 (C-5B), 61.4, 61.3 (C-6A, C-1_{linker}), 58.6 (O*C*H_3), 40.0 (C-5_{linker}), 28.8 (C-2_{linker}), 27.0 (C-4_{linker}), 22.7 (C-3_{linker}), 16.0 (C-6B); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{24}H_{46}NO_{15}$ 588.2867; found 588.2849.

(5-Amino-1-pentyl) *β*-D-Glucopyranosyl-(1→3)-2-*O*-acetyl-6-deoxy-*α*-L-talopyranosyl-(1→3)-*β*-D-glucopyranoside Hydrochloride (2).



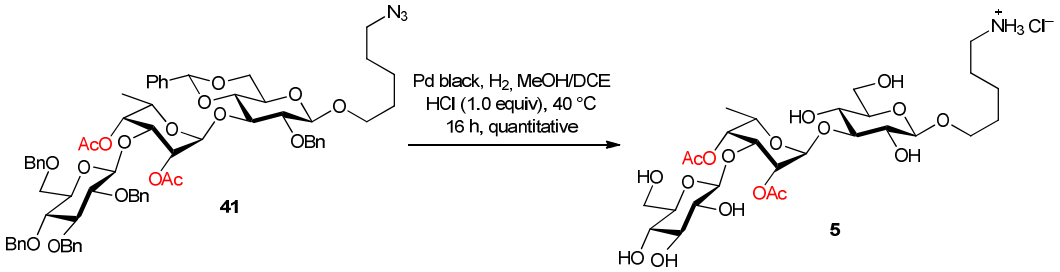
Protected trisaccharide **39** (50 mg, 42 μmol, 1.0 equiv) was reacted according to the general procedure for hydrogenolysis under heterogeneous conditions to give target trisaccharide **2** (28 mg, quant.) as a white foam: $[\alpha]_D^{20}$ = –37 (*c* 0.27, H_2O); ^{1}H NMR (400 MHz, D_2O) δ 5.22–5.19 (m, 2H, H-1B, H-2B), 4.63 (d, $J_{1,2}$ = 7.9 Hz, 1H, H-1C), 4.45 (d, $J_{1,2}$ = 8.1 Hz, 1H, H-1A), 4.36 (q, $J_{5,6}$ = 6.6 Hz, 1H, H-5B), 4.27–4.24 (m, 1H, H-3B), 3.98–3.82 (m, 4H, H-4B, H-6aC, H-6aA, H-1a$_{linker}$), 3.75–3.64 (m, 3H, H-6bA, H-1b$_{linker}$, H-6bC), 3.58 (t, $J_{2,3} \approx J_{3,4} \approx$ 8.4 Hz, 1H, H-3A), 3.52–3.29 (m, 7H, H-3C, H-5A, H-5C, H-4A, H-4C, H-2A, H-2C), 3.06–2.97 (m, 2H, H-5ab$_{linker}$), 2.16 (s, 3H, COC*H*$_3$), 1.73–1.61 (m, 4H, H-4ab$_{linker}$, H-2ab$_{linker}$), 1.49–1.41 (m, 2H, H-3ab$_{linker}$), 1.23 (d, $J_{5,6}$ = 6.4 Hz, 3H, H-6B); ^{13}C NMR (100 MHz, D_2O) δ 176.2 (*C*OCH$_3$), 104.7 (C-1A), 104.6 (C-1C), 101.4 (C-1B), 85.0 (C-3A), 78.62, 78.60 (C-5A, C-5C), 78.3 (C-3C), 76.4 (C-2C), 75.72, 75.66 (C-2A, C-3B), 72.9 (C-2B, C-6C), 72.1 (C-4A*), 71.2 (C-4B), 70.9 (C-4C*), 69.9 (C-5B), 63.5, 63.3 (C-6A, C-1$_{linker}$), 42.2 (C-5$_{linker}$), 30.9 (C-2$_{linker}$), 29.2 (C-4$_{linker}$), 24.8 (C-3$_{linker}$), 23.4 (COC*H*$_3$), 18.1 (C-6B); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{25}H_{46}NO_{16}$ 616.2817; found 616.2775.

(5-Amino-1-pentyl) β-D-Glucopyranosyl-(1→3)-6-deoxy-α-L-talopyranosyl-(1→3)-β-D-glucopyranoside Hydrochloride (1).



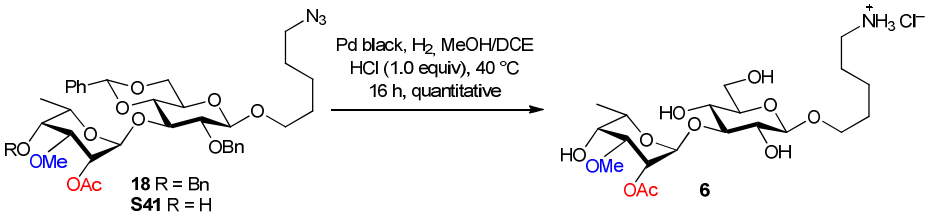
Trisaccharide **40** (20.2 mg, 17.7 μmol, 1.0 equiv) was reacted according to the general procedure for hydrogenolysis under heterogeneous conditions to give target trisaccharide **1** (10.8 mg, quant.) as a white amorphous powder: $[\alpha]_D^{20}$ = –42 (*c* 0.48, H_2O); ^{1}H NMR (400 MHz, D_2O) δ 5.25 (br s, 1H, H-1B), 4.66 (d, $J_{1,2}$ = 7.7 Hz, 1H, H-1C), 4.47 (d, $J_{1,2}$ = 8.0 Hz, 1H, H-1A), 4.33 (dt, $J_{4,5}$ = 12.9 Hz, $J_{5,6a} \approx J_{5,6b} \approx$ 6.4 Hz, 1H, H-5B), 4.15–4.07 (m, 2H, H-2B, H-3B), 3.97–3.87 (m, 4H, H-4B, H-6aA, H-6aC, H-1a$_{linker}$), 3.76–3.59 (m, 4H, H-1b$_{linker}$, H-6bA, H-6bC, H-3A), 3.54–3.33 (m, 7H, H-3C, H-5A, H-5C, H-4A, H-4C, H-2A, H-2C), 3.00 (t, *J* = 6.9 Hz, 2H, H-5ab$_{linker}$), 1.73–1.60 (m, 4H, H-4ab$_{linker}$, H-2ab$_{linker}$), 1.50–1.40 (m, 2H, H-3ab$_{linker}$), 1.24 (d, $J_{5,6}$ = 6.4 Hz, 3H, H-6B); ^{13}C NMR (100 MHz, D_2O) δ 104.7 (C-1A), 104.2 (C-1B), 103.9 (C-1C), 84.9 (C-3A), 78.7 (C-5C), 78.6 (C-5A), 78.3 (C-3C), 76.5 (C-2C), 76.3 (C-3B), 75.8 (C-2A), 72.9 (C-6C), 72.6 (C-4B), 72.4 (C-2B), 72.3 (C-4C), 70.9 (C-4A), 70.3 (C-5B), 63.5, 63.4 (C-6A, C-1$_{linker}$), 42.1 (C-5$_{linker}$), 30.9 (C-2$_{linker}$), 29.2 (C-4$_{linker}$), 24.8 (C-3$_{linker}$), 18.2 (C-6B); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{23}H_{44}NO_{15}$ 574.2711; found 574.2762.

(5-Amino-1-pentyl) *β*-D-Glucopyranosyl-(1→3)-2,4-di-*O*-acetyl-6-deoxy-*α*-L-talopyranosyl-(1→3)-*β*-D-glucopyranoside Hydrochloride (5).



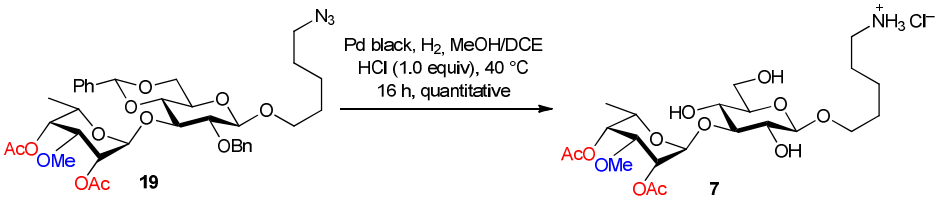
Trisaccharide **41** (45.0 mg, 36.8 μmol) was reacted according to the general procedure for hydrogenolysis under heterogeneous conditions giving deprotected trisaccharide **5** (26 mg, quant.) as a white foam: $[\alpha]_D^{20}$ = –40 (*c* 0.17, H_2O); ^{1}H NMR (400 MHz, D_2O) δ 5.40 (br s, 1H, H-4B), 5.26–5.22 (m, 2H, H-1B, H-2B), 4.60 (d, $J_{1,2}$ = 7.9 Hz, 1H, H-1C), 4.54 (q, $J_{5,6}$ = 6.5 Hz, 1H, H-5B), 4.49 (t, $J_{2,3} \approx J_{3,4} \approx$ 3.5 Hz, 1H, H-3B), 4.45 (d, $J_{1,2}$ = 8.1 Hz, 1H, H-1A), 3.96–3.83 (m, 3H, H-6aC, H-6aA, H-1a$_{linker}$), 3.74–3.65 (m, 3H, H-6bA, H-1b$_{linker}$, H-6bC), 3.62–3.60 (m, 1H, H-3A), 3.50–3.35 (m, 6H, H-3C, H-5A, H-5C, H-4A, H-4C, H-2A), 3.22 (t, $J_{1,2} \approx J_{2,3} \approx$ 8.3 Hz, 1H, H-2C), 3.00 (t, *J* = 7.4 Hz, 2H, H-5ab$_{linker}$), 2.22 (s, 3H, COC*H*$_3$), 2.18 (s, 3H, COC*H*$_3$), 1.73–1.62 (m, 4H, H-4ab$_{linker}$, H-2ab$_{linker}$), 1.46–1.41 (m, 2H, H-3ab$_{linker}$), 1.13 (d, $J_{5,6}$ = 6.5 Hz, 3H, H-6B); ^{13}C NMR (100 MHz, D_2O) δ 174.5, 173.9 (2 × *C*OCH$_3$), 102.6 (C-1A), 101.9 (C-1C), 99.4 (C-1B), 83.0 (C-3A), 76.51, 76.46 (C-5A, C-5C), 76.1 (C-3C), 74.2 (C-2A), 73.4 (C-2C), 71.7 (C-3B), 70.7 (C-6C), 70.2 (C-4B), 70.0, 69.9 (C-2B, C-4A*), 68.7 (C-4C*), 66.3 (C-5B), 61.3, 61.2 (C-6B, C-1$_{linker}$), 40.0 (C-5$_{linker}$), 28.8 (C-2$_{linker}$), 27.0 (C-4$_{linker}$), 22.7 (C-3$_{linker}$), 21.2, 21.0 (2 × CO*C*H$_3$), 15.7 (C-6B); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{27}H_{48}NO_{17}$ 658.2922; found 658.2925.

(5-Amino-1-pentyl) 2-*O*-Acetyl-6-deoxy-3-*O*-methyl-α-L-talopyranosyl-(1→3)-β-D-glucopyranoside Hydrochloride (6).



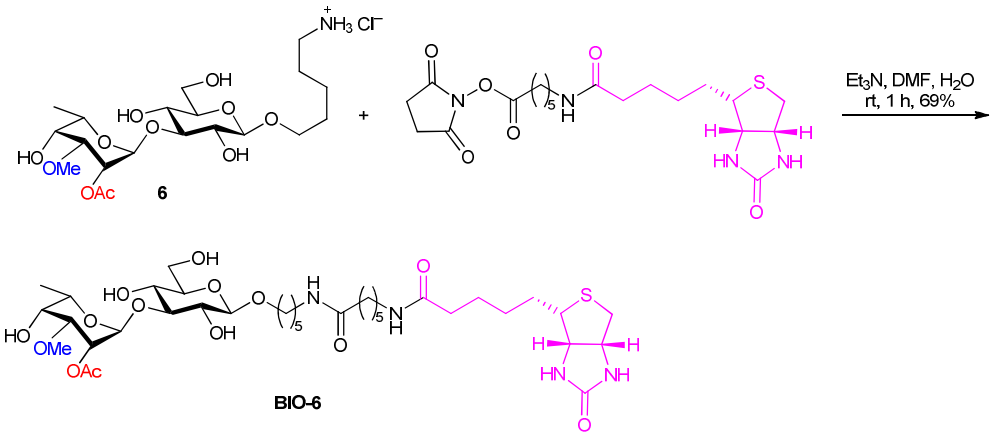
Disaccharide **18** (15.4 mg, 20.2 μmol) or disaccharide **S41** (50 mg, 74 μmol) was reacted according to the representative procedure for hydrogenolysis under heterogeneous conditions giving target disaccharide **6** (10.2 mg or 38 mg, quant.) as a white amorphous powder: $[\alpha]_D^{20}$ = –16 (*c* 0.12, H_2O); ^{1}H NMR (400 MHz, D_2O) δ 5.25–5.23 (m, 1H, H-2B), 5.21 (s, 1H, H-1B), 4.45 (d, $J_{1,2}$ = 8.1 Hz, 1H, H-1A), 4.34 (q, $J_{5,6}$ = 6.5 Hz, 1H, H-5B), 3.97–3.89 (m, 3H, H-4B, H-6aA, H-1a$_{linker}$), 3.78 (t, $J_{2,3} \approx J_{3,4} \approx$ 3.6 Hz, 1H, H-3B), 3.74–3.65 (m, 2H, H-1b$_{linker}$, H-6bA), 3.58 (t, $J_{2,3} \approx J_{3,4} \approx$ 8.9 Hz, 1H, H-3A), 3.47–3.34 (m, 3H, H-5A, H-4A, H-2A), 3.41 (s, 3H, OC*H*$_3$), 3.07–2.98 (m, 2H, H-5ab$_{linker}$), 2.14 (s, 3H, COC*H*$_3$), 1.73–1.62 (m, 4H, H-4ab$_{linker}$, H-2ab$_{linker}$), 1.49–1.41 (m, 2H, H-3ab$_{linker}$), 1.23 (d, $J_{5,6}$ = 6.6 Hz, 3H, H-6B); ^{13}C NMR (100 MHz, D_2O) δ 173.9 (*C*OCH$_3$), 102.6 (C-1A), 99.5 (C-1B), 82.9 (C-3A), 76.5 (C-5A); 74.3 (C-3B, C-2A), 70.7 (C-6A), 68.8 (C-4A), 68.6 (C-2B), 68.1 (C-4B), 67.7 (C-5B), 61.3 (C-1$_{linker}$), 56.1 (O*C*H$_3$), 40.0 (C-5$_{linker}$), 28.8 (C-2$_{linker}$), 27.0 (C-4$_{linker}$), 22.7 (C-3$_{linker}$), 21.1 (CO*C*H$_3$), 16.0 (C-6B); HRMS (ESI-TOF) *m/z* [M + H]$^+$ calcd for $C_{20}H_{38}NO_{11}$ 468.2445; found 468.2449.

(5-Amino-1-pentyl) 2,4-Di-*O*-acetyl-6-deoxy-3-*O*-methyl-α-L-talopyranosyl-(1→3)-β-D-glucopyranoside Hydrochloride (7).



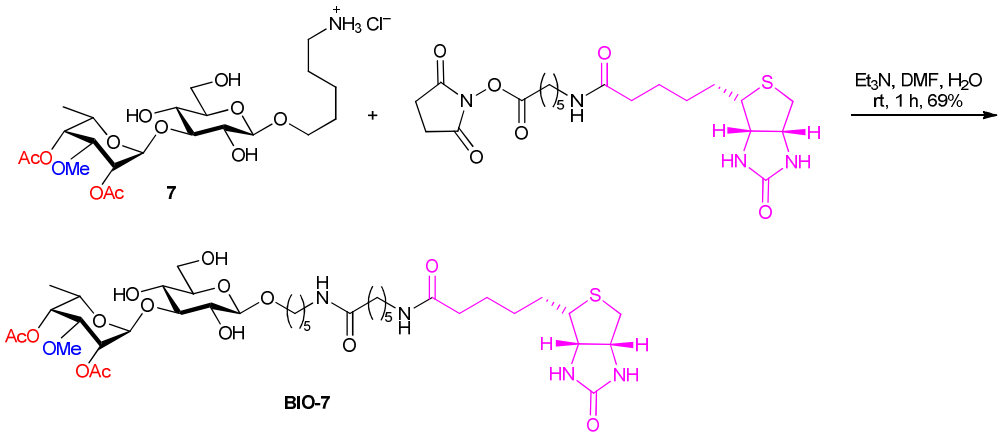
Disaccharide **19** (99 mg, 14 μmol) was reacted according to the representative procedure for hydrogenolysis under heterogeneous conditions giving target disaccharide **7** (76 mg, quant.) as a white amorphous powder: $[\alpha]_D^{20}$ = –24 (*c* 0.08, H_2O); ^{1}H NMR (400 MHz, D_2O) δ 5.37 (br d, $J_{3,4}$ = 3.2 Hz, 1H, H-4B), 5.27 (br d, $J_{2,3}$ = 3.8 Hz, 1H, H-2B), 5.25 (s, 1H, H-1B), 4.52 (q, $J_{5,6}$ = 6.6 Hz, 1H, H-5B), 4.45 (d, $J_{1,2}$ = 8.1 Hz, 1H, H-1A), 3.97 (t, $J_{2,3} \approx J_{3,4} \approx$ 3.6 Hz, 1H, H-3B), 3.95–3.88 (m, 2H, H-6aA, H-1a$_{linker}$), 3.74–3.65 (m, 2H, H-1b$_{linker}$, H-6bA), 3.62–3.57 (m, 1H, H-3A), 3.47–3.34 (m, 3H, H-5A, H-4A, H-2A), 3.40 (s, 3H, OC*H*$_3$), 3.06–2.97 (m, 2H, H-5ab$_{linker}$), 2.21 (s, 3H, COC*H*$_3$), 2.16 (s, 3H, COC*H*$_3$), 1.73–1.62 (m, 4H, H-4ab$_{linker}$, H-2ab$_{linker}$), 1.49–1.41 (m, 2H, H-3ab$_{linker}$), 1.13 (d, $J_{5,6}$ = 6.6 Hz, 3H, H-6B); ^{13}C NMR (100 MHz, D_2O) δ 174.4, 173.7 (2 × *C*OCH$_3$), 102.6 (C-1A), 99.6 (C-1B), 83.1 (C-3A), 76.5 (C-5A), 74.3 (C-2A), 73.6 (C-3B), 70.8 (C-6A), 70.1 (C-4B), 68.7 (C-4A), 68.1 (C-2B), 66.2 (C-5B), 61.3 (C-1$_{linker}$), 57.3 (O*C*H$_3$), 40.0 (C-5$_{linker}$), 28.8 (C-2$_{linker}$), 27.0 (C-4$_{linker}$), 22.7 (C-3$_{linker}$), 21.1, 20.9 (2 × CO*C*H$_3$), 15.7 (C-6B); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{22}H_{40}NO_{12}$ 510.2551; found 510.2541.

Biotinylated Disaccharide 6 (BIO-6).



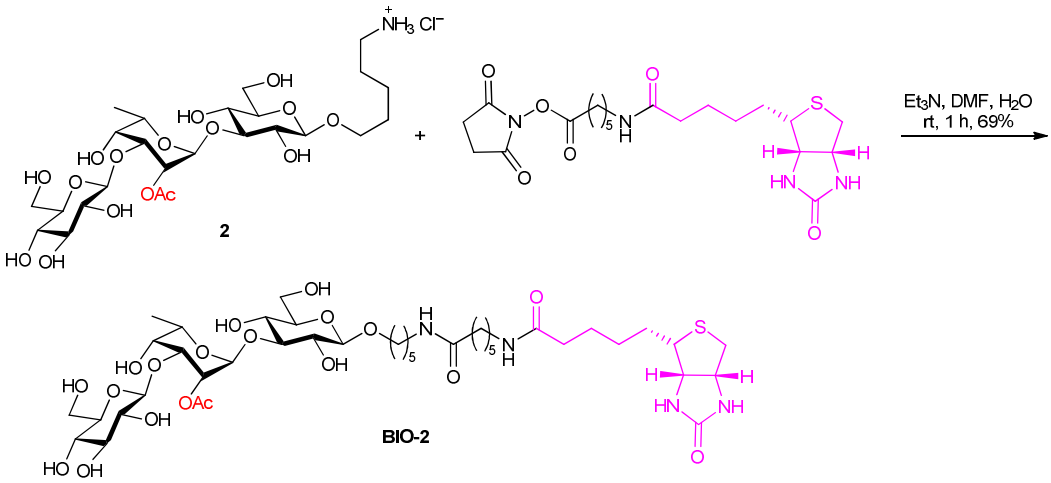
Disaccharide **6** (10 mg, 20 μmol, 1.0 equiv) was reacted according to the general procedure for the synthesis of biotinylated oligosaccharides to give derivative **BIO-6** (11 mg, 69%) as a white amorphous powder: $[\alpha]_D^{20}$ = 12 (*c*, 1.0, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ5.32 (s, 1H, H-1B), 5.28 (s, 1H, H-2B), 4.50 (dd, *J* = 7.1, 4.7 Hz, 1H, H-8$_{biotin}$), 4.42-4.35 (m, 1H, H-5B), 4.34-4.28 (m, 1H, H-7$_{biotin}$), 4.28-4.22 (m, 1H, H-1A), 3.96-3.83 (m, 2H, H-6aA, H-1$_{linker}$), 3.76 (s, 1H, H-4B), 3.73-3.62 (m, 2H, H-3B, H-1$_{linker}$), 3.60-3.50 (m, 2H, H-3A, H-6bA), 3.41 (s, 3H, C*H*$_{3Me}$), 3.38-3.27 (m, 2H, H-2A, H-5H), 3.26-3.27 (m, 5H, H-5$_{linker}$, H-6$_{biotin}$, H-1'$_{biotin}$), 2.93 (dd, *J* = 12.7, 4.7 Hz, 1H, H-9a$_{biotin}$), 2.71 (d, *J* = 13.0 Hz, 1H, H-9b$_{biotin}$), 2.24-2.14 (m, 4H, H-2$_{biotin}$, H-5'$_{biotin}$), 2.10 (s, 3H, C*H*$_{3Ac}$), 1.80-1.28 (m, 18H, H-2$_{linker}$, H-3$_{linker}$, H-4$_{linker}$, H-3$_{biotin}$, H-4$_{biotin}$, H-5$_{biotin}$, H-2'$_{biotin}$, H-3'$_{biotin}$, H-4'$_{biotin}$), 1.26 (d, *J* = 6.5 Hz, 3H, C*H*$_3$-6B); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0-171.8 (3 × *C*O), 166.1 (C-10$_{biotin}$), 104.2 (C-1A), 100.2 (C-1B), 83.1 (C-3A), 77.8 (C-5A), 75.9, 75.8 (C-2A, C-3B), 70.7 (C-6A), 70.1 (C-4A), 70.1 (C-4B), 69.1 (C-2B), 68.0 (C-5B), 63.4 (C-7$_{biotin}$), 62.7 (C-1$_{linker}$), 61.6 (C-8$_{biotin}$), 57.0 (C-6$_{biotin}$), 56.6 (*C*H$_{3Me}$), 41.04 (C-9$_{biotin}$), 40.3, 40.2 (C-1'$_{biotin}$, C-5$_{linker}$), 37.0, 36.8 (C-2$_{biotin}$, C-5'$_{biotin}$), 30.3-24.4 (9 × CH$_2$), 20.9 (*C*H$_{3Ac}$), 16.7 (C-6B); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{36}H_{62}N_4NaO_{14}S$ 829.3875; found 829.3881.

Biotinylated Disaccharide 7 (BIO-7).



Disaccharide **7** (10 mg, 18 μmol, 1.0 equiv) was reacted according to the general procedure for the synthesis of biotinylated oligosaccharides to give derivative **BIO-7** (11 mg, 69%) as a white amorphous powder: $[\alpha]_D^{20}$ = -8 (*c*, 0.9, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36 (s, 1H, H-1B), 5.24 (m, 2H, H-2B and H-4B), 4.52 (m, 2H, H-5B, H-8_{biotin}), 4.31 (dd, *J* = 7.6, 4.3 Hz, 1H, H-7_{biotin}), 4.24 (m, 1H, H-1A), 3.89 (m, 2H, H-6aA, H-$1a_{linker}$), 3.78 (t, *J* = 3.4 Hz, 1H, H-3B), 3.68 (m, 1H, H-$1b_{linker}$), 3.54 (m, 2H, H-6aA and H-3A), 3.37 (s, 3H, CH_{3Me}), 3.36 – 3.29 (m, 3H, H-2A, H-4A, H-5A), 3.26 – 3.12 (m, 5H, H-5_{linker}, H-1'$_{biotin}$, H-6_{biotin}), 2.93 (dd, *J* = 12.7, 4.8, 1H, H-$9a_{biotin}$), 2.71 (d, *J* = 13.2 Hz, 1H, H-$9b_{biotin}$), 2.19 (m, 4H, H-2_{biotin}, H-5'$_{biotin}$), 2.11, 2.09 (2 × s, 6H, 2 × CH_{3Ac}), 1.79 – 1.26 (m, 18H, 9 × CH_2), 1.12 (d, *J* = 6.4 Hz, 3H, CH_3-6B); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0 - 172.0 (4 × *C*O), 166.1 (C-10_{biotin}), 104.2 (C-1A), 100.2 (C-1B), 82.8 (C-3A), 77.8 (C-5A), 75.9 (C-2A), 74.9 (C-3B), 70.7 (C-6A), 70.4 (C-4B), 70.1 (C-4A), 68.4 (C-2B), 66.4 (C-5B), 63.4 (C-7_{biotin}), 62.7 (C-1_{linker}), 61.6 (C-8_{biotin}), 57.3 (*C*H_{3Me}), 57.0 (C-6_{biotin}), 47.9 (C-1_{Et3N}), 41.1 (C-9_{biotin}), 40.3, 40.2 (C-5_{linker}, C-1'$_{biotin}$), 30.3 – 24.4 (9 × *C*H_2), 21.0, 20.9 (2 × *C*H_{3Ac}), 16.5 (C-6B), 9.2 (C-2_{Et3N}); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{38}H_{64}N_4NaO_{15}S$ 871.3981; found 871.3992.

Biotinylated Trisaccharide 2 (BIO-2).



Trisaccharide **2** (10 mg, 15 μmol, 1.0 equiv) was reacted according to the general procedure for the synthesis of biotinylated oligosaccharides to give derivative **BIO-2** (8 mg, 55%) as a white amorphous powder: $[\alpha]_D^{20}$ = 11 (*c*, 0.7, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.32 (s, 1H, H-1B), 5.24 (d, *J* = 3.7 Hz, H-2B), 4.52 – 4.46 (m, 2H, H-1C, H-8$_{biotin}$), 4.43-4.37 (m, 1H, H-5B), 4.34-4.28 (m, 1H, H-7$_{biotin}$), 4.24 (d, *J* = 7.9 Hz, 1H, H-1A), 4.20 (t, *J* = 3.6 Hz, 1H, H-3B), 3.93-3.81 (m, 4H, H-6aA, H-4B, H-6aC, H-1a$_{linker}$), 3.72-3.62 (m, 2H, H-6bC, H-1b$_{linker}$), 3.58-3.51 (m, 2H, H-3A, H-6bA), 3.40-3.14 (m, 12H, H-2A, H-4A, H-5A, H-2C, H-3C, H-4C, H-5C, H-5$_{linker}$, H-6$_{biotin}$, H-1'$_{biotin}$), 2.94 (dd, *J* = 12.8, 4.9 Hz, 1H, H-9a$_{biotin}$), 2.71 (d, *J* = 12.8 Hz, 1H, H-9b$_{biotin}$), 2.25-2.14 (m, 4H, H-2$_{biotin}$, H-5'$_{biotin}$), 2.12 (s, 3H, C*H*$_{3Ac}$), 1.80-1.31 (m, 18H, H-2$_{linker}$, H-3$_{linker}$, H-4$_{linker}$, H-3$_{biotin}$, H-4$_{biotin}$, H-5$_{biotin}$, H-2'$_{biotin}$, H-3'$_{biotin}$, H-4'$_{biotin}$), 1.28 (d, *J* = 6.6 Hz, 3H, C*H*$_3$-6B); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1-172.4 (3 × *C*O), 166.2 (C-10$_{biotin}$), 104.3 (C-1A), 103.1 (C-1C), 99.9 (C-1B), 82.8 (C-3A), 78.1-77.8 (C-5A, C-3C, C-5C), 75.8, 75.0 (C-2A, C-2C), 73.9 (C-3B), 71.6 (C-2B), 71.4 (C-4A), 70.7 (C-6A), 70.2, 70.1 (C-4B, C-4C), 67.8 (C-5B), 63.4 (C-7$_{biotin}$), 62.7, 62.7 (C-6C, C-1$_{linker}$), 61.6 (C-8$_{biotin}$), 57.0 (C-6$_{biotin}$), 41.0 (C-9$_{biotin}$), 40.3, 40.2 (C-5$_{linker}$, C-1'$_{biotin}$), 36.8 (C-2 $_{biotin}$, C-5'$_{biotin}$), 30.3-24.4 (9 × *C*H$_2$), 21.1 (*C*H$_{3Ac}$), 16.7 (C-6B); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{41}H_{70}N_4NaO_{19}S$ 977.4247; found 977.4261.

Crystal data and structure refinement of compound 36

Identification code	bl7_a	
Empirical formula	C_{42} H_{46} O_{10}	
Formula weight	710.79	
Temperature	200(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 13.068(2) Å	α= 90°.
	b = 8.6099(13) Å	β= 102.761(7)°.
	c = 16.359(2) Å	γ = 90°.
Volume	1795.1(5) $Å^3$	
Z	2	
Density (calculated)	1.315 Mg/m^3	
Absorption coefficient	0.093 mm^{-1}	
F(000)	756	
Crystal size	0.300 x 0.080 x 0.040 mm^3	
Theta range for data collection	2.255 to 30.062°.	
Index ranges	-18<=h<=18, -12<=k<=12, -23<=l<=22	
Reflections collected	122253	
Independent reflections	10457 [R(int) = 0.0505]	
Completeness to theta = 25.242°	99.4 %	
Absorption correction	Semi-empirical from equivalents	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	10457 / 1 / 471	
Goodness-of-fit on F^2	1.147	
Final R indices [I>2sigma(I)]	R1 = 0.0465, wR2 = 0.1322	
R indices (all data)	R1 = 0.0637, wR2 = 0.1548	
Absolute structure parameter	0.06(13)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.777 and -0.912 e.$Å^{-3}$	

Supplementary Table 2 | Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	4627(2)	4249(3)	5691(1)	22(1)
C(2)	4984(2)	4696(3)	4897(1)	22(1)
C(3)	4194(2)	4168(2)	4118(1)	21(1)
C(4)	3102(2)	4762(3)	4148(1)	24(1)
O(5)	2833(1)	4293(2)	4914(1)	26(1)
C(6)	3527(2)	4892(3)	5637(1)	23(1)
O(7)	3172(2)	4378(2)	6332(1)	30(1)
C(8)	2541(2)	5447(3)	6667(1)	25(1)
C(9)	1460(2)	4781(4)	6651(2)	33(1)
C(10)	936(2)	5755(4)	7253(2)	37(1)
O(11)	1372(2)	7231(3)	7435(1)	37(1)
C(12)	2484(2)	7234(3)	7812(2)	30(1)
C(13)	3002(2)	5755(3)	7591(1)	24(1)
O(14)	1611(2)	3300(2)	7062(1)	36(1)
C(15)	1866(2)	3731(3)	7911(2)	32(1)
O(16)	2872(1)	4427(2)	8106(1)	27(1)
O(17)	1083(2)	4824(3)	7986(1)	38(1)
C(18)	2691(3)	7591(4)	8740(2)	41(1)
C(19)	1850(3)	2376(4)	8479(2)	47(1)
O(20)	5343(1)	4887(2)	6396(1)	27(1)
C(21)	5594(3)	3825(3)	7082(2)	43(1)
C(22)	6424(2)	4515(3)	7773(2)	37(1)
C(23)	6273(3)	4452(4)	8584(2)	47(1)
C(24)	7035(4)	5024(5)	9246(2)	56(1)
C(25)	7939(3)	5651(5)	9111(2)	58(1)
C(26)	8091(3)	5740(6)	8298(3)	62(1)
C(27)	7334(3)	5164(5)	7635(2)	50(1)
O(28)	5989(1)	4054(2)	4892(1)	26(1)
C(29)	6770(2)	5238(4)	4935(3)	51(1)
C(30)	7783(2)	4512(3)	4842(2)	31(1)

C(31)	8281(3)	3381(4)	5367(2)	46(1)
C(32)	9199(3)	2750(5)	5275(3)	66(1)
C(33)	9648(3)	3225(6)	4671(3)	66(1)
C(34)	9194(3)	4381(6)	4109(3)	70(2)
C(35)	8226(3)	5051(4)	4196(2)	45(1)
O(36)	4435(1)	4826(2)	3381(1)	27(1)
C(37)	5079(3)	3876(4)	2982(2)	42(1)
C(38)	4941(2)	4423(3)	2089(1)	28(1)
C(39)	5534(2)	5654(4)	1899(2)	36(1)
C(40)	5416(3)	6172(5)	1089(3)	58(1)
C(41)	4715(4)	5446(7)	450(2)	73(2)
C(42)	4129(3)	4235(8)	628(2)	73(2)
C(43)	4234(3)	3699(5)	1458(2)	49(1)
C(44)	2259(2)	4127(4)	3441(2)	34(1)
O(45)	1346(2)	5070(3)	3291(1)	47(1)
C(46)	1313(3)	6161(5)	2651(2)	55(1)
C(47)	1041(2)	5446(4)	1782(2)	37(1)
C(48)	1578(3)	5886(6)	1181(4)	70(1)
C(49)	1282(5)	5223(7)	364(3)	84(2)
C(50)	480(4)	4178(7)	186(2)	70(1)
C(51)	-28(3)	3773(6)	780(2)	59(1)
C(52)	252(2)	4378(4)	1578(2)	41(1)

Supplementary Table 3 │ Bond lengths [Å] and angles [°].

C(1)-O(20)	1.425(3)
C(1)-C(2)	1.522(3)
C(1)-C(6)	1.525(3)
C(1)-H(1)	1.0000
C(2)-O(28)	1.427(3)
C(2)-C(3)	1.522(3)
C(2)-H(2)	1.0000
C(3)-O(36)	1.428(2)
C(3)-C(4)	1.527(3)
C(3)-H(3)	1.0000
C(4)-O(5)	1.433(2)
C(4)-C(44)	1.512(3)
C(4)-H(4)	1.0000
O(5)-C(6)	1.419(3)
C(6)-O(7)	1.391(3)
C(6)-H(6)	1.0000
O(7)-C(8)	1.424(3)
C(8)-C(9)	1.520(3)
C(8)-C(13)	1.522(3)
C(8)-H(8)	1.0000
C(9)-O(14)	1.434(4)
C(9)-C(10)	1.562(4)
C(9)-H(9)	1.0000
C(10)-O(11)	1.398(4)
C(10)-O(17)	1.420(4)
C(10)-H(10)	1.0000
O(11)-C(12)	1.447(4)
C(12)-C(18)	1.512(4)
C(12)-C(13)	1.523(3)
C(12)-H(12)	1.0000
C(13)-O(16)	1.453(3)
C(13)-H(13)	1.0000
O(14)-C(15)	1.404(3)
C(15)-O(17)	1.415(3)

C(15)-O(16)	1.416(3)
C(15)-C(19)	1.495(4)
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
O(20)-C(21)	1.429(3)
C(21)-C(22)	1.505(4)
C(21)-H(21A)	0.9900
C(21)-H(21B)	0.9900
C(22)-C(27)	1.376(5)
C(22)-C(23)	1.385(4)
C(23)-C(24)	1.389(5)
C(23)-H(23)	0.9500
C(24)-C(25)	1.360(6)
C(24)-H(24)	0.9500
C(25)-C(26)	1.389(7)
C(25)-H(25)	0.9500
C(26)-C(27)	1.388(5)
C(26)-H(26)	0.9500
C(27)-H(27)	0.9500
O(28)-C(29)	1.433(3)
C(29)-C(30)	1.502(4)
C(29)-H(29A)	0.9900
C(29)-H(29B)	0.9900
C(30)-C(31)	1.364(4)
C(30)-C(35)	1.392(4)
C(31)-C(32)	1.355(6)
C(31)-H(31)	0.9500
C(32)-C(33)	1.321(7)
C(32)-H(32)	0.9500
C(33)-C(34)	1.396(8)
C(33)-H(33)	0.9500
C(34)-C(35)	1.426(6)

C(34)-H(34)	0.9500
C(35)-H(35)	0.9500
O(36)-C(37)	1.431(3)
C(37)-C(38)	1.508(3)
C(37)-H(37A)	0.9900
C(37)-H(37B)	0.9900
C(38)-C(43)	1.373(4)
C(38)-C(39)	1.388(4)
C(39)-C(40)	1.374(4)
C(39)-H(39)	0.9500
C(40)-C(41)	1.378(8)
C(40)-H(40)	0.9500
C(41)-C(42)	1.363(9)
C(41)-H(41)	0.9500
C(42)-C(43)	1.411(6)
C(42)-H(42)	0.9500
C(43)-H(43)	0.9500
C(44)-O(45)	1.419(3)
C(44)-H(44A)	0.9900
C(44)-H(44B)	0.9900
O(45)-C(46)	1.400(5)
C(46)-C(47)	1.517(5)
C(46)-H(46A)	0.9900
C(46)-H(46B)	0.9900
C(47)-C(52)	1.368(4)
C(47)-C(48)	1.381(5)
C(48)-C(49)	1.425(9)
C(48)-H(48)	0.9500
C(49)-C(50)	1.363(9)
C(49)-H(49)	0.9500
C(50)-C(51)	1.339(7)
C(50)-H(50)	0.9500
C(51)-C(52)	1.377(5)
C(51)-H(51)	0.9500
C(52)-H(52)	0.9500

O(20)-C(1)-C(2)	108.85(17)
O(20)-C(1)-C(6)	110.41(17)
C(2)-C(1)-C(6)	108.80(17)
O(20)-C(1)-H(1)	109.6
C(2)-C(1)-H(1)	109.6
C(6)-C(1)-H(1)	109.6
O(28)-C(2)-C(3)	109.55(17)
O(28)-C(2)-C(1)	111.30(18)
C(3)-C(2)-C(1)	111.09(17)
O(28)-C(2)-H(2)	108.3
C(3)-C(2)-H(2)	108.3
C(1)-C(2)-H(2)	108.3
O(36)-C(3)-C(2)	110.71(17)
O(36)-C(3)-C(4)	106.00(17)
C(2)-C(3)-C(4)	109.86(16)
O(36)-C(3)-H(3)	110.1
C(2)-C(3)-H(3)	110.1
C(4)-C(3)-H(3)	110.1
O(5)-C(4)-C(44)	106.78(19)
O(5)-C(4)-C(3)	110.22(17)
C(44)-C(4)-C(3)	112.54(18)
O(5)-C(4)-H(4)	109.1
C(44)-C(4)-H(4)	109.1
C(3)-C(4)-H(4)	109.1
C(6)-O(5)-C(4)	113.06(17)
O(7)-C(6)-O(5)	107.38(18)
O(7)-C(6)-C(1)	108.56(18)
O(5)-C(6)-C(1)	109.72(17)
O(7)-C(6)-H(6)	110.4
O(5)-C(6)-H(6)	110.4
C(1)-C(6)-H(6)	110.4
C(6)-O(7)-C(8)	115.81(18)
O(7)-C(8)-C(9)	111.4(2)
O(7)-C(8)-C(13)	111.06(19)
C(9)-C(8)-C(13)	104.20(18)
O(7)-C(8)-H(8)	110.0

C(9)-C(8)-H(8)	110.0
C(13)-C(8)-H(8)	110.0
O(14)-C(9)-C(8)	107.2(2)
O(14)-C(9)-C(10)	102.5(2)
C(8)-C(9)-C(10)	108.8(2)
O(14)-C(9)-H(9)	112.6
C(8)-C(9)-H(9)	112.6
C(10)-C(9)-H(9)	112.6
O(11)-C(10)-O(17)	111.2(2)
O(11)-C(10)-C(9)	114.0(2)
O(17)-C(10)-C(9)	103.5(2)
O(11)-C(10)-H(10)	109.3
O(17)-C(10)-H(10)	109.3
C(9)-C(10)-H(10)	109.3
C(10)-O(11)-C(12)	114.6(2)
O(11)-C(12)-C(18)	111.7(2)
O(11)-C(12)-C(13)	110.8(2)
C(18)-C(12)-C(13)	114.7(2)
O(11)-C(12)-H(12)	106.4
C(18)-C(12)-H(12)	106.4
C(13)-C(12)-H(12)	106.4
O(16)-C(13)-C(8)	111.54(19)
O(16)-C(13)-C(12)	113.90(18)
C(8)-C(13)-C(12)	106.43(19)
O(16)-C(13)-H(13)	108.3
C(8)-C(13)-H(13)	108.3
C(12)-C(13)-H(13)	108.3
C(15)-O(14)-C(9)	101.9(2)
O(14)-C(15)-O(17)	104.1(2)
O(14)-C(15)-O(16)	109.93(19)
O(17)-C(15)-O(16)	110.6(2)
O(14)-C(15)-C(19)	112.1(3)
O(17)-C(15)-C(19)	110.8(2)
O(16)-C(15)-C(19)	109.2(2)
C(15)-O(16)-C(13)	115.10(18)
C(15)-O(17)-C(10)	105.47(19)

C(12)-C(18)-H(18A)	109.5
C(12)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(12)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(15)-C(19)-H(19A)	109.5
C(15)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(15)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
C(1)-O(20)-C(21)	112.67(19)
O(20)-C(21)-C(22)	109.9(2)
O(20)-C(21)-H(21A)	109.7
C(22)-C(21)-H(21A)	109.7
O(20)-C(21)-H(21B)	109.7
C(22)-C(21)-H(21B)	109.7
H(21A)-C(21)-H(21B)	108.2
C(27)-C(22)-C(23)	118.9(3)
C(27)-C(22)-C(21)	122.9(3)
C(23)-C(22)-C(21)	118.2(3)
C(22)-C(23)-C(24)	120.3(3)
C(22)-C(23)-H(23)	119.9
C(24)-C(23)-H(23)	119.9
C(25)-C(24)-C(23)	120.8(3)
C(25)-C(24)-H(24)	119.6
C(23)-C(24)-H(24)	119.6
C(24)-C(25)-C(26)	119.4(3)
C(24)-C(25)-H(25)	120.3
C(26)-C(25)-H(25)	120.3
C(27)-C(26)-C(25)	120.0(4)
C(27)-C(26)-H(26)	120.0
C(25)-C(26)-H(26)	120.0
C(22)-C(27)-C(26)	120.6(3)
C(22)-C(27)-H(27)	119.7

C(26)-C(27)-H(27)	119.7
C(2)-O(28)-C(29)	111.74(19)
O(28)-C(29)-C(30)	109.5(2)
O(28)-C(29)-H(29A)	109.8
C(30)-C(29)-H(29A)	109.8
O(28)-C(29)-H(29B)	109.8
C(30)-C(29)-H(29B)	109.8
H(29A)-C(29)-H(29B)	108.2
C(31)-C(30)-C(35)	119.7(3)
C(31)-C(30)-C(29)	122.8(3)
C(35)-C(30)-C(29)	117.5(3)
C(32)-C(31)-C(30)	121.8(4)
C(32)-C(31)-H(31)	119.1
C(30)-C(31)-H(31)	119.1
C(33)-C(32)-C(31)	120.6(4)
C(33)-C(32)-H(32)	119.7
C(31)-C(32)-H(32)	119.7
C(32)-C(33)-C(34)	121.3(3)
C(32)-C(33)-H(33)	119.3
C(34)-C(33)-H(33)	119.3
C(33)-C(34)-C(35)	118.6(3)
C(33)-C(34)-H(34)	120.7
C(35)-C(34)-H(34)	120.7
C(30)-C(35)-C(34)	117.9(3)
C(30)-C(35)-H(35)	121.0
C(34)-C(35)-H(35)	121.0
C(3)-O(36)-C(37)	114.84(18)
O(36)-C(37)-C(38)	107.9(2)
O(36)-C(37)-H(37A)	110.1
C(38)-C(37)-H(37A)	110.1
O(36)-C(37)-H(37B)	110.1
C(38)-C(37)-H(37B)	110.1
H(37A)-C(37)-H(37B)	108.4
C(43)-C(38)-C(39)	119.6(3)
C(43)-C(38)-C(37)	120.2(3)
C(39)-C(38)-C(37)	120.2(3)

C(40)-C(39)-C(38)	121.0(3)
C(40)-C(39)-H(39)	119.5
C(38)-C(39)-H(39)	119.5
C(39)-C(40)-C(41)	119.9(4)
C(39)-C(40)-H(40)	120.1
C(41)-C(40)-H(40)	120.1
C(42)-C(41)-C(40)	119.7(3)
C(42)-C(41)-H(41)	120.1
C(40)-C(41)-H(41)	120.1
C(41)-C(42)-C(43)	121.1(4)
C(41)-C(42)-H(42)	119.5
C(43)-C(42)-H(42)	119.5
C(38)-C(43)-C(42)	118.7(4)
C(38)-C(43)-H(43)	120.6
C(42)-C(43)-H(43)	120.6
O(45)-C(44)-C(4)	111.6(2)
O(45)-C(44)-H(44A)	109.3
C(4)-C(44)-H(44A)	109.3
O(45)-C(44)-H(44B)	109.3
C(4)-C(44)-H(44B)	109.3
H(44A)-C(44)-H(44B)	108.0
C(46)-O(45)-C(44)	113.5(3)
O(45)-C(46)-C(47)	113.0(3)
O(45)-C(46)-H(46A)	109.0
C(47)-C(46)-H(46A)	109.0
O(45)-C(46)-H(46B)	109.0
C(47)-C(46)-H(46B)	109.0
H(46A)-C(46)-H(46B)	107.8
C(52)-C(47)-C(48)	118.9(3)
C(52)-C(47)-C(46)	120.6(3)
C(48)-C(47)-C(46)	120.4(4)
C(47)-C(48)-C(49)	118.9(4)
C(47)-C(48)-H(48)	120.6
C(49)-C(48)-H(48)	120.6
C(50)-C(49)-C(48)	120.1(4)
C(50)-C(49)-H(49)	120.0

C(48)-C(49)-H(49)	120.0
C(51)-C(50)-C(49)	119.8(4)
C(51)-C(50)-H(50)	120.1
C(49)-C(50)-H(50)	120.1
C(50)-C(51)-C(52)	121.3(4)
C(50)-C(51)-H(51)	119.3
C(52)-C(51)-H(51)	119.3
C(47)-C(52)-C(51)	120.9(3)
C(47)-C(52)-H(52)	119.5
C(51)-C(52)-H(52)	119.5

Symmetry transformations used to generate equivalent atoms.

Supplementary Table 4 | Anisotropic displacement parameters ($Å^2$ x 10^3). The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	26(1)	19(1)	20(1)	-4(1)	5(1)	-2(1)
C(2)	22(1)	20(1)	25(1)	-1(1)	8(1)	-2(1)
C(3)	24(1)	22(1)	19(1)	1(1)	9(1)	0(1)
C(4)	25(1)	29(1)	20(1)	-1(1)	8(1)	2(1)
O(5)	23(1)	34(1)	21(1)	-3(1)	8(1)	-2(1)
C(6)	27(1)	24(1)	19(1)	-2(1)	9(1)	0(1)
O(7)	42(1)	28(1)	25(1)	2(1)	20(1)	7(1)
C(8)	30(1)	29(1)	20(1)	-1(1)	11(1)	3(1)
C(9)	27(1)	44(1)	28(1)	-5(1)	3(1)	0(1)
C(10)	24(1)	51(2)	37(1)	1(1)	10(1)	4(1)
O(11)	37(1)	38(1)	40(1)	2(1)	15(1)	13(1)
C(12)	39(1)	28(1)	27(1)	-2(1)	15(1)	1(1)
C(13)	26(1)	26(1)	22(1)	-1(1)	9(1)	-2(1)
O(14)	37(1)	36(1)	35(1)	-10(1)	10(1)	-12(1)
C(15)	32(1)	32(1)	34(1)	-3(1)	14(1)	-4(1)
O(16)	30(1)	27(1)	24(1)	2(1)	7(1)	-2(1)
O(17)	34(1)	45(1)	40(1)	2(1)	21(1)	1(1)
C(18)	60(2)	36(1)	30(1)	-9(1)	18(1)	-4(1)
C(19)	57(2)	38(2)	55(2)	8(1)	28(2)	-7(1)
O(20)	35(1)	20(1)	22(1)	-2(1)	0(1)	-4(1)
C(21)	56(2)	28(1)	36(1)	6(1)	-10(1)	-6(1)
C(22)	44(1)	25(1)	33(1)	3(1)	-7(1)	1(1)
C(23)	55(2)	41(2)	40(1)	8(1)	1(1)	-4(1)
C(24)	82(3)	50(2)	28(1)	7(1)	-5(1)	0(2)
C(25)	60(2)	49(2)	50(2)	-2(2)	-23(2)	2(2)
C(26)	44(2)	63(2)	75(3)	-8(2)	4(2)	-11(2)
C(27)	54(2)	53(2)	42(2)	-2(1)	8(1)	-8(2)
O(28)	20(1)	26(1)	35(1)	-1(1)	8(1)	0(1)
C(29)	31(1)	29(1)	98(3)	-9(2)	24(2)	-4(1)
C(30)	23(1)	28(1)	44(1)	-4(1)	9(1)	-4(1)
C(31)	46(2)	42(2)	49(2)	12(1)	5(1)	-3(1)

C(32)	43(2)	53(2)	91(3)	-3(2)	-7(2)	13(2)
C(33)	29(1)	71(3)	95(3)	-41(3)	7(2)	6(2)
C(34)	69(2)	98(3)	59(2)	-44(2)	44(2)	-59(3)
C(35)	50(2)	41(2)	39(1)	3(1)	2(1)	-18(1)
O(36)	36(1)	25(1)	23(1)	4(1)	16(1)	6(1)
C(37)	59(2)	45(2)	31(1)	12(1)	29(1)	25(1)
C(38)	34(1)	30(1)	25(1)	-1(1)	15(1)	5(1)
C(39)	37(1)	36(1)	38(1)	2(1)	14(1)	1(1)
C(40)	63(2)	63(2)	60(2)	33(2)	38(2)	23(2)
C(41)	74(3)	119(4)	32(2)	27(2)	25(2)	55(3)
C(42)	55(2)	119(4)	37(2)	-30(2)	-5(2)	21(3)
C(43)	43(2)	56(2)	52(2)	-22(2)	16(1)	-9(1)
C(44)	28(1)	45(2)	25(1)	-9(1)	3(1)	1(1)
O(45)	26(1)	80(2)	33(1)	-8(1)	4(1)	12(1)
C(46)	48(2)	49(2)	57(2)	-8(2)	-13(2)	6(2)
C(47)	31(1)	40(1)	39(1)	9(1)	5(1)	6(1)
C(48)	53(2)	66(3)	97(3)	32(2)	28(2)	-3(2)
C(49)	99(4)	106(4)	66(3)	45(3)	57(3)	44(3)
C(50)	70(2)	102(4)	34(2)	-2(2)	6(2)	43(3)
C(51)	43(2)	74(3)	54(2)	-18(2)	0(1)	10(2)
C(52)	35(1)	49(2)	39(1)	1(1)	8(1)	0(1)

Supplementary Table 5 | Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3).

	x	y	z	U(eq)
H(1)	4616	3093	5742	26
H(2)	5040	5853	4880	26
H(3)	4190	3009	4080	25
H(4)	3098	5922	4116	29
H(6)	3536	6052	5620	28
H(8)	2475	6443	6346	30
H(9)	1013	4714	6071	40
H(10)	168	5859	7004	44
H(12)	2795	8109	7547	36
H(13)	3770	5959	7663	29
H(18A)	2307	8530	8829	61
H(18B)	3445	7757	8955	61
H(18C)	2457	6717	9036	61
H(19A)	2021	2728	9063	71
H(19B)	2368	1606	8392	71
H(19C)	1150	1905	8354	71
H(21A)	5851	2837	6891	52
H(21B)	4957	3599	7295	52
H(23)	5647	4016	8688	56
H(24)	6924	4976	9800	68
H(25)	8461	6025	9568	70
H(26)	8713	6195	8196	74
H(27)	7445	5218	7081	60
H(29A)	6875	5784	5480	61
H(29B)	6535	6007	4483	61
H(31)	7975	3025	5808	56
H(32)	9522	1959	5649	79
H(33)	10293	2772	4619	80
H(34)	9523	4715	3676	85
H(35)	7893	5841	3825	54

H(37A)	4868	2773	2994	50
H(37B)	5824	3968	3279	50
H(39)	6028	6146	2335	44
H(40)	5817	7029	969	70
H(41)	4641	5788	-112	88
H(42)	3642	3743	187	87
H(43)	3824	2853	1577	59
H(44A)	2534	4070	2924	40
H(44B)	2074	3061	3583	40
H(46A)	2004	6679	2732	66
H(46B)	785	6965	2692	66
H(48)	2134	6617	1309	84
H(49)	1645	5509	-56	101
H(50)	281	3738	-359	84
H(51)	-592	3055	650	70
H(52)	-109	4049	1992	49

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