

Supporting Information

MOP and EE Protecting Groups in Synthesis of α - or β -Naphthyl-C-Glycosides from Glycals

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1. Optimization of the C-1 lithiation

Procedure for lithiation/deuteration experiments:

MOP or EE-protected D-glucal (50 mg, 0.14 mmol, 1 eq) was dissolved under Ar in anhydrous THF. This solution was cooled to -78 °C and then designated amount of *t*-BuLi (1.7 M in pentane) was added dropwise using a syringe pump. The reaction mixture was stirred at -78 °C for 5 min and then at 0 °C for 1 h. After 1 h, D₂O (0.249 mL, 13.79 mmol, 100 eq) was added dropwise at 0 °C and the mixture was stirred for 30 min at 0 °C and for 30 min at RT. The solution was diluted with EtOAc (30 mL) and washed with H₂O (50 mL). The organic layer was dried over MgSO₄ and concentrated *in vacuo*.

Deuterated material was subjected to ¹H NMR measurement in DMSO-*d*₆. The extent of deuteration at C1 was assumed from comparison of integral intensity of H1 with other signals in the molecule, as shown in Figures S2 and S3. Outline and results of the optimization are summarized in Figure S1.

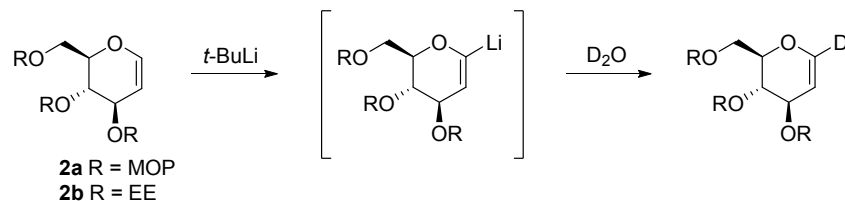
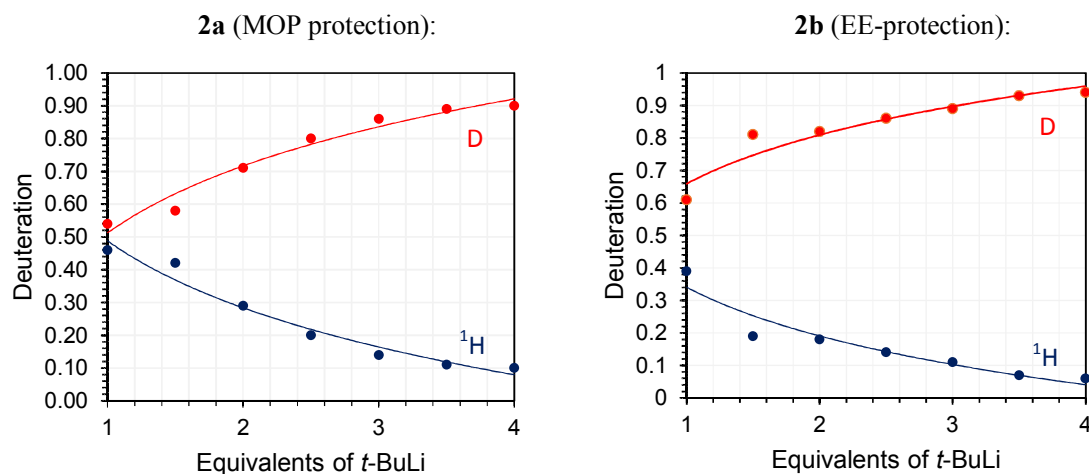


Figure S1. Optimization of the C-1 lithiation of protected glycals **2a** and **2b**.



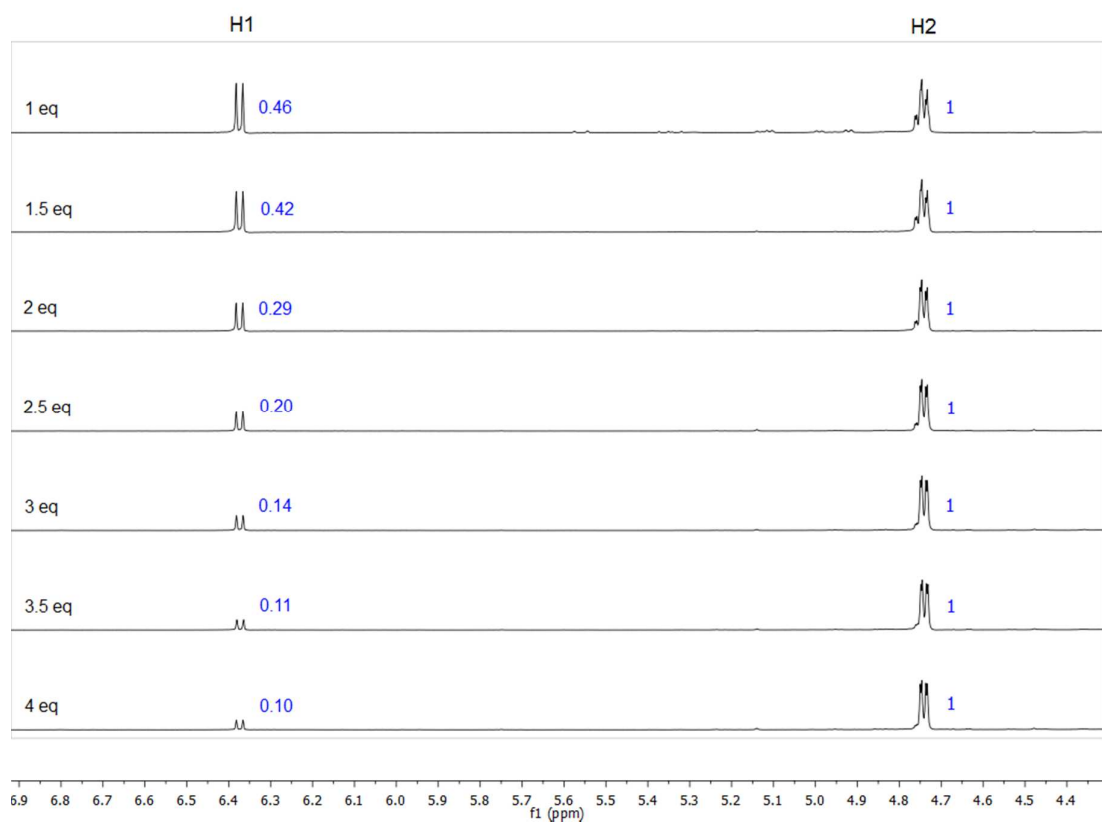


Figure S2. C-1 lithiation of **2a**

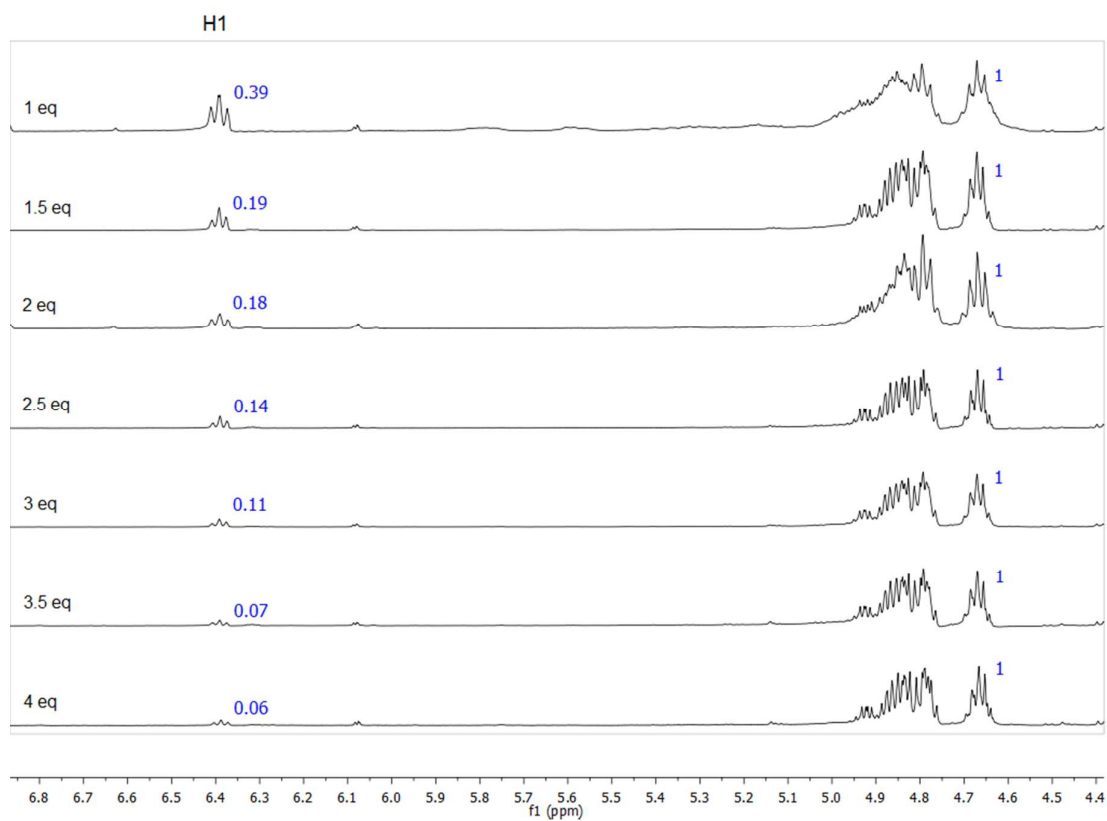
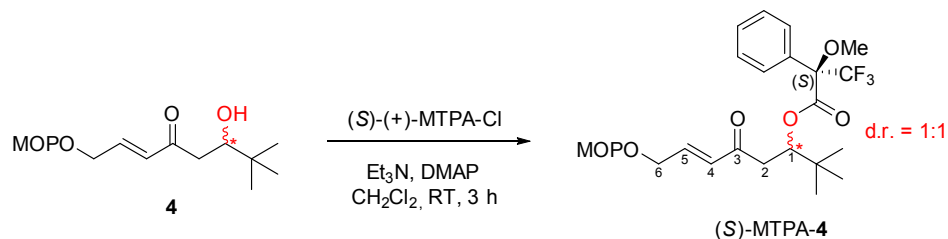


Figure S3. C-1 lithiation of **2b**.

2. Determination of enantiomeric composition of **4**



Et₃N (0.04 mL, 290 μ mol, 5 eq) and DMAP (709 μ g, 6 μ mol, 0.1 eq) were added to the solution of enone **4** (15 mg, 58 μ mol, 1 eq) in anhydrous CH₂Cl₂ (3 mL). After that, (S)-MTPA-Cl (0.02 mL, 116 μ mol, 2 eq) was added and the reaction mixture was stirred for 3 h at RT and then quenched by the addition of sat. aq. NH₄Cl (1 mL). The mixture was diluted with EtOAc (10 mL) and washed with H₂O (2 $\times$ 10 mL), dried over MgSO₄ and evaporated *in vacuo*.

Diastereomeric composition of the mixture was determined by NMR measurements of the crude (S)-MTPA-**4**. Diastereomeric ratio was estimated to be $\sim$ 1:1 based on characteristic ¹³C NMR signals (Figure S4).

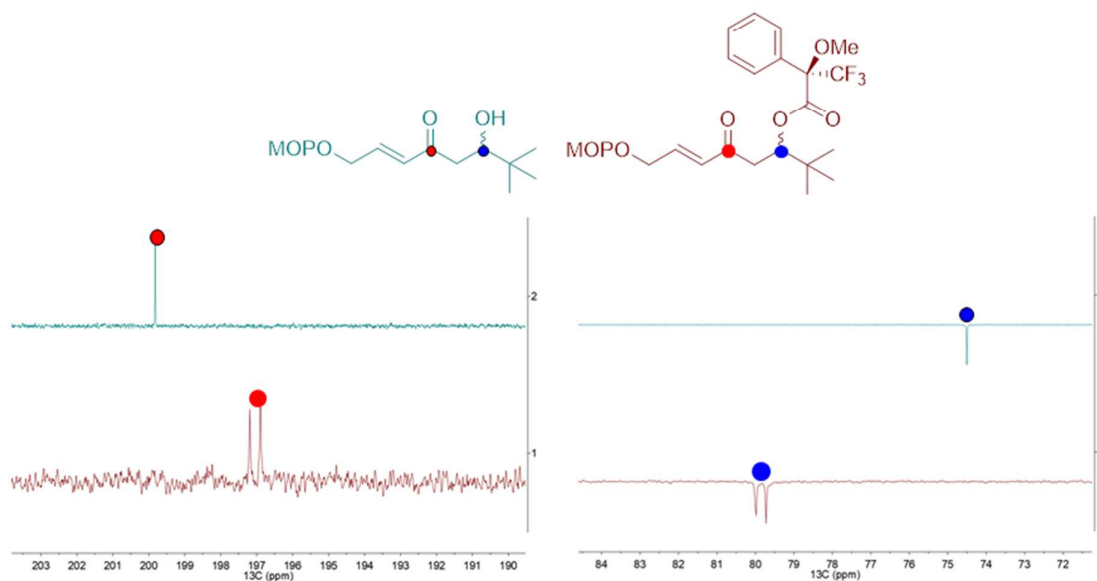
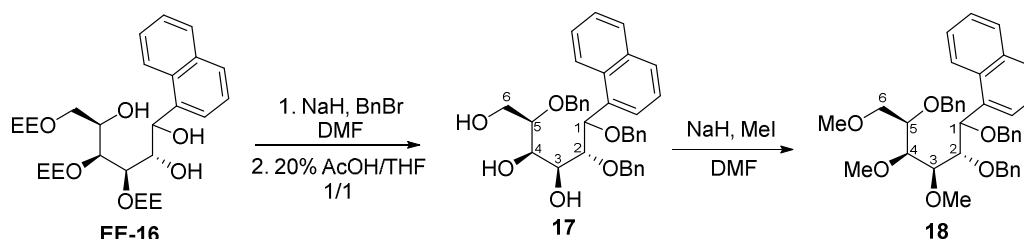


Figure S4. Characteristic ¹³C NMR signals used for estimation of diastereomeric ratio of (S)-MTPA-**4**.

3. Structural assignment of (2*S*,3*R*,4*S*,5*R*)-1-(naphthalen-1-yl)hexane-1,2,3,4,5,6-hexaol (16).

Structure of the intermediate (2*S*,3*R*,4*S*,5*R*)-1-(naphthalen-1-yl)hexane-(3,4,6-tri-*O*-(ethoxyethyl)-1,2,3,4,5,6-hexaol was confirmed by benzylation of the free hydroxyl groups and subsequent cleavage of the EE groups, which gave partially benzylated derivative **17**. The OH groups in positions 3, 4 and 6 were then methylated by the excess of MeI to give the product **18**. The positions of methyl and benzyl groups were then determined by analysis of HMBC spectra.

1-((2*S*,3*S*,4*S*,5*R*)-1,2,5-tris(benzyloxy)-3,4,6-trimethoxyhexyl)naphthalene (**18**).

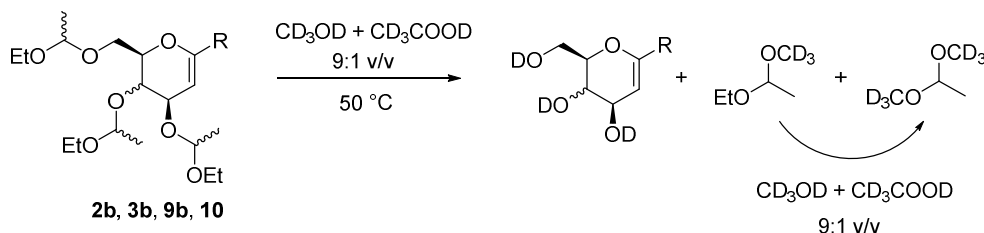


(2*R*,3*R*,4*S*,5*R*)-2,5,6-tris(benzyloxy)-6-(naphthalen-1-yl)hexane-1,3,4-triol (17**).** To a solution of derivative **EE-16** (50 mg, 95 μ mol, 1 eq) in anhydrous DMF (5 mL) at 0 °C was added NaH (22.87 mg, 572 μ mol, 60% in mineral oil, 6 eq). The reaction mixture was stirred for 30 min at RT and then BnBr (67.92 μ L, 572 μ mol, 6 eq) was slowly added dropwise at 0 °C. The resulting solution was stirred for 1 h at 0 °C and then overnight at RT. The reaction was quenched by careful addition of MeOH (10 mL) at 0 °C and evaporation *in vacuo*. The residue was taken up in EtOAc (50 mL) and washed with H₂O (3 $\times$ 50 mL), dried over MgSO₄ and evaporated *in vacuo*. The obtained material containing fully protected derivative was subjected to deprotection procedure **F** using 20% AcOH (5 mL) and THF (5 mL) and stirred overnight at RT. After evaporation, the residue was purified by column chromatography on silica gel (CHCl₃/MeOH 8/1 to 5/1), which yielded compound **17** (47 mg, 85 %) as a colorless oil: *R*_f = 0.36 (CHCl₃/MeOH 7/1); ¹H NMR (401.0 MHz, CDCl₃): 2.55, 3.27, 3.63 (3 $\times$ bs, 3 $\times$ 1H, OH-3,4,6); 3.66 (dd, 1H, *J*_{4,3} = 9.5, *J*_{4,5} = 2.3, H-4); 3.76–3.90 (m, 4H, H-5,6, CH_aH_bPh-2); 4.09 (d, 1H, *J*_{3,4} = 9.5, H-3); 4.21 (d, 1H, *J*_{2,1} = 7.2, H-2); 4.29 (d, 1H, *J*_{gem} = 10.9, CH_aH_bPh-2); 4.37, 4.59 (2 $\times$ d, 2 $\times$ 1H, *J*_{gem} = 11.6, CH₂Ph-1); 4.64, 4.72 (2 $\times$ d, 2 $\times$ 1H, *J*_{gem} = 11.2, CH₂Ph-5); 5.43 (d, 1H, *J*_{1,2} = 7.2, H-1); 6.76–6.83 (m, 2H, H-*o*-Bn-2); 7.11–7.25 (m, 3H, H-*m,p*-Bn-2); 7.26–7.37 (m, 10H, H-*o,m,p*-Bn-1,5); 7.41 (ddd, 1H, *J*_{7,8} = 8.4, *J*_{7,6} = 6.8, *J*_{7,5} = 1.4, H-7-naphth); 7.49 (ddd, 1H, *J*_{6,5} = 8.1, *J*_{6,7} = 6.8, *J*_{6,8} = 1.2, H-6-naphth); 7.53 (dd, 1H, *J*_{3,4} = 8.2, *J*_{3,2} = 7.1, H-3-naphth); 7.78 (dd, 1H, *J*_{2,3} = 7.1, *J*_{2,4} = 0.9, H-2-naphth); 7.83 – 7.94 (m, 3H, H-4,5,8-naphth); ¹³C NMR (100.8 MHz, CDCl₃): 63.1 (CH₂-6); 70.5 (CH-3); 71.2 (CH₂Ph-1); 72.5 (CH-4); 73.2 (CH₂Ph-5); 73.9 (CH₂Ph-2); 78.3 (CH-5); 78.7 (br, CH-1); 79.0 (CH-2); 123.6 (CH-8-naphth); 125.3 (CH-3-naphth); 125.7 (CH-2,6-naphth); 126.2 (CH-7-naphth); 127.8, 127.8, 127.9 (CH-*p*-Bn-1,2,5); 128.06, 128.09, 128.2 (CH-*m*-Bn-1,2,5); 128.4, 128.5 (CH-*o*-Bn-1,2,5); 128.7 (CH-4-naphth); 128.8 (CH-5-naphth); 131.9 (C-8a-naphth); 133.8 (C-4a-naphth); 134.6 (C-1-naphth); 137.5, 137.7, 138.0 (C-*i*-Bn-1,2,5); HRMS (ESI) *m/z* [M+Na]⁺ calcd for C₃₇H₃₈O₆Na 601.2561, found 601.2561.

1-((2*S*,3*S*,4*S*,5*R*)-1,2,5-tris(benzyloxy)-3,4,6-trimethoxyhexyl)naphthalene (18). To a solution of derivative **17** (47 mg, 81 μ mol, 1 eq) in anhydrous DMF (5 mL) at 0 °C was added NaH (19 mg, 487 μ mol, 60% in mineral oil, 6 eq). The reaction mixture was stirred for 30 min at RT and then MeI (30.34 μ L, 487 μ mol, 6 eq) was slowly added dropwise at 0 °C. The resulting solution was stirred for 1 h at 0 °C and then overnight at RT. The reaction was quenched by careful addition of MeOH (10 mL) at 0 °C and evaporation *in vacuo*. The residue was taken up in CH₂Cl₂ (30 mL) and washed with H₂O (3 $\times$ 30 mL), dried over MgSO₄ and evaporated *in vacuo*. The residue was purified by column chromatography on silica gel (Hexane/EtOAc 4/1), which yielded compound **18** (45 mg, 89%) as a colorless oil: R_f = 0.32 (Hexane/EtOAc 4/1); **HRMS** (ESI) m/z calculated for C₄₀H₄₄O₆Na [M+Na]⁺ 643.30301, found 643.30292. **¹H NMR** (401.0 MHz, CDCl₃): 3.13 (d, 1H, J_{gem} = 10.5, CH_aH_bPh-2); 3.37 (s, 3H, CH₃O-6); 3.39 (s, 3H, CH₃O-4); 3.42 (s, 3H, CH₃O-3); 3.62 – 3.70 (m, 2H, H-4,6b); 3.74 (dd, 1H, $J_{6a,6b}$ = 10.0, $J_{6a,5}$ = 6.4, H-6a); 3.88 (d, 1H, J_{gem} = 10.5, CH_aH_bPh-2); 3.96 (ddd, 1H, $J_{5,6}$ = 6.4, 5.1, $J_{5,4}$ = 2.5, H-5); 4.15 (bm, 1H, H-2); 4.22 (dd, 1H, $J_{3,4}$ = 8.6, $J_{3,2}$ = 1.4, H-3); 4.31, 4.44 (2 $\times$ d, 2 $\times$ 1H, J_{gem} = 11.4, CH₂Ph-1); 4.67, 4.86 (2 $\times$ d, 2 $\times$ 1H, J_{gem} = 11.9, CH₂Ph-5); 5.31 (bm, 1H, H-1); 6.50 – 6.60 (bm, 2H, H-*o*-Bn-2); 6.97 – 7.10 (m, 3H, H-*m,p*-Bn-2); 7.22 – 7.33, 7.33 – 7.42 (2 $\times$ m, 10H, H-*o,m,p*-Bn-1,5); 7.45 – 7.55 (m, 3H, H-3,6,7-naphth); 7.78 (bd, 1H, $J_{2,3}$ = 7.2, H-2-naphth); 7.86 – 7.93 (m, 2H, H-4,5-naphth); 8.51 (bm, 1H, H-8-naphth); **¹³C NMR** (100.8 MHz, CDCl₃): 58.95 (CH₃O-6); 59.47 (CH₃O-4); 60.47 (CH₃O-3); 69.93 (CH₂Ph-1); 72.35 (CH₂Ph-5); 73.84 (CH₂-6); 73.88 (CH₂Ph-2); 77.81 (CH-5); 78.98 (CH-3); 79.39 (CH-4); 124.71 (CH-8-naphth); 125.31 (CH-2,3-naphth); 125.67 (CH-6-naphth); 126.06 (CH-7-naphth); 127.10, 127.25, 127.42 (CH-*p*-Bn-1,2,5); 127.47, 127.75, 127.77 (CH-*m*-Bn-1,2,5); 128.09, 128.23, 128.25 (CH-*o*-Bn-1,2,5); 128.60 (CH-4-naphth); 128.75 (CH-5-naphth); 132.68 (C-8a-naphth); 133.89 (C-4a-naphth); 135.65 (C-1-naphth); 137.77, 138.18, 138.92 (C-*i*-Bn-1,2,5); **HRMS** (ESI) m/z [M+Na]⁺ calcd for C₄₀H₄₄O₆Na 643.3030, found 643.3029.

4. Characterization of EE-protected compounds by NMR

NMR spectra of EE-protected glycols are complicated by the presence of 8 sets of signals originating from all possible diastereoisomers due to asymmetric carbon of EE-group. As result, their ^1H and ^{13}C NMR are complex and not easily analyzable due to signal overlap. However, simple *in situ* deprotection using 1:9 (v/v) mixture of $\text{CD}_3\text{COOD}:\text{CD}_3\text{OD}$ at 50 °C for 45 – 120 minutes (Figure S5) significantly simplified the spectra and enabled structural characterization of EE-protected glycols by NMR. Simplification of ^1H and ^{13}C NMR spectra during *in situ* deprotection for EE-glycols **2b**, **3b**, **9b** and **10** is shown in Figures S6-S9.



EE-glycol	R	reaction time (mins)
2b	H	120
3b	H	75
9b	1-naphthyl	60
10	1-naphthyl	45

Figure S5. *In situ* deprotection of EE-glycols by $\text{CD}_3\text{COOD} + \text{CD}_3\text{OD}$ (1:9 (v/v)) in NMR tube at 50 °C.

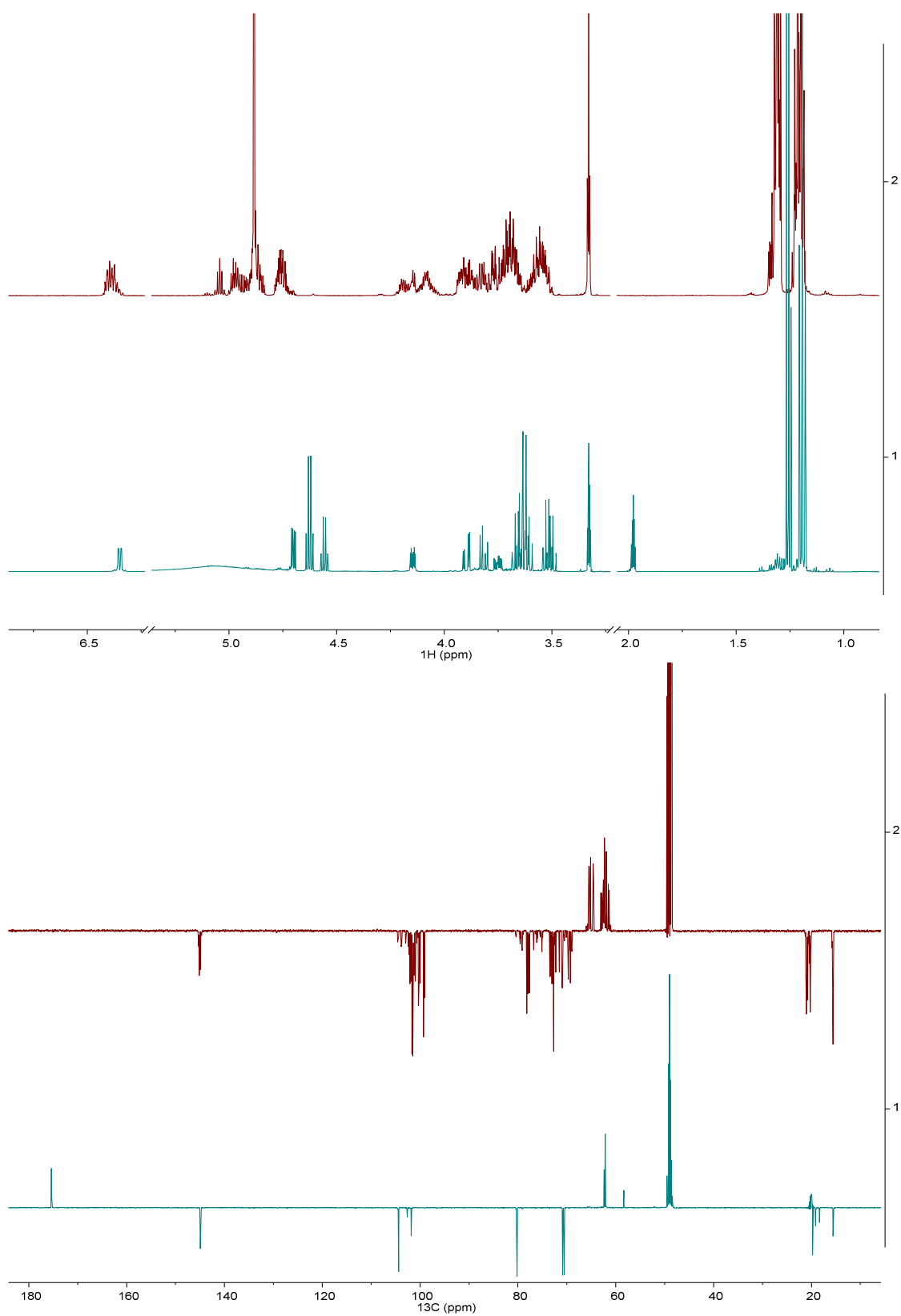


Figure S6. ^1H and ^{13}C NMR spectra of EE-glucal **2b** measured in CD_3OD (maroon) and corresponding NMR spectra after deprotection by CD_3COOD (teal).

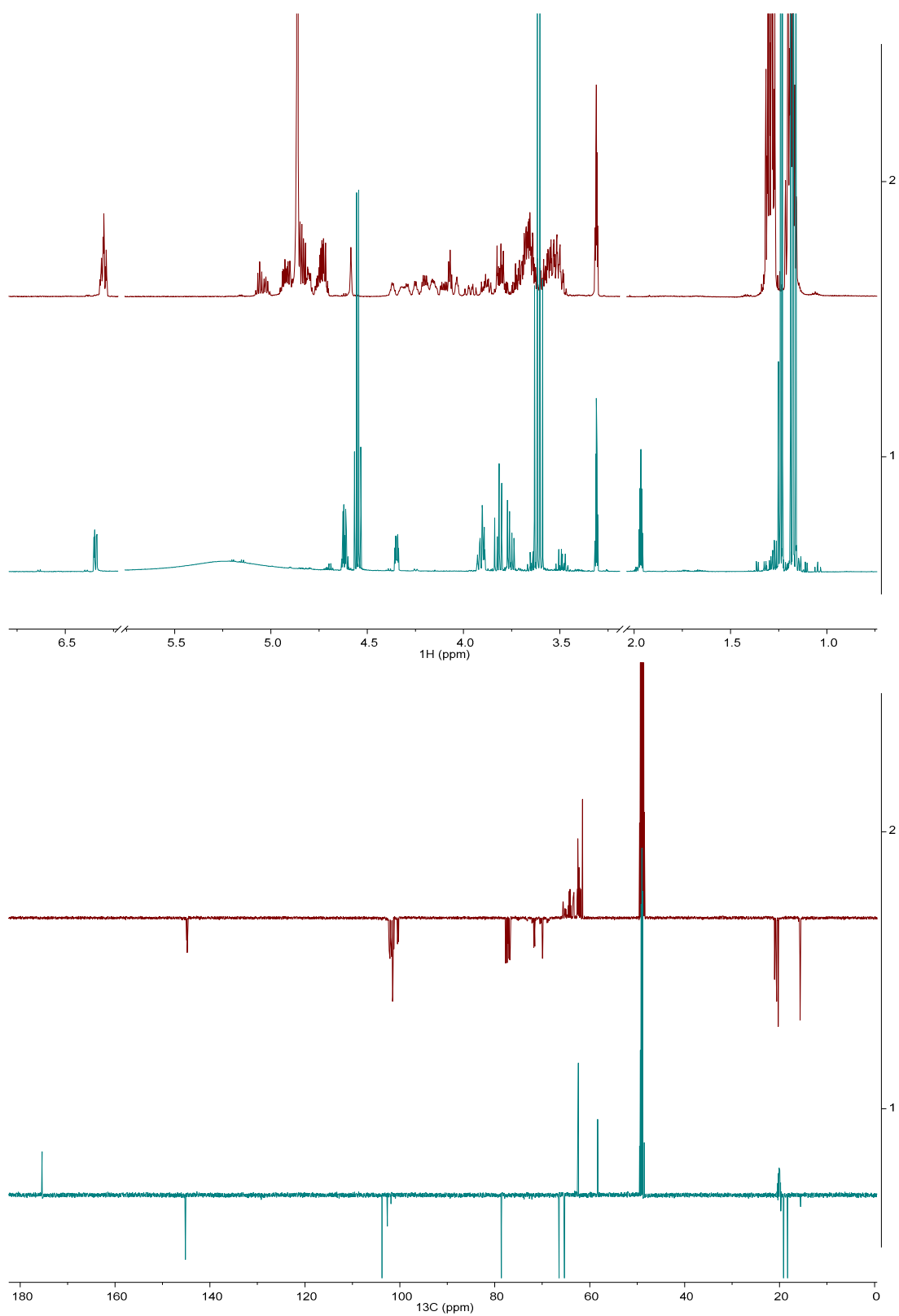


Figure S7. ^1H and ^{13}C NMR spectra of EE-galactal **3b** measured in CD_3OD (maroon) and corresponding NMR spectra after deprotection by CD_3COOD (teal).

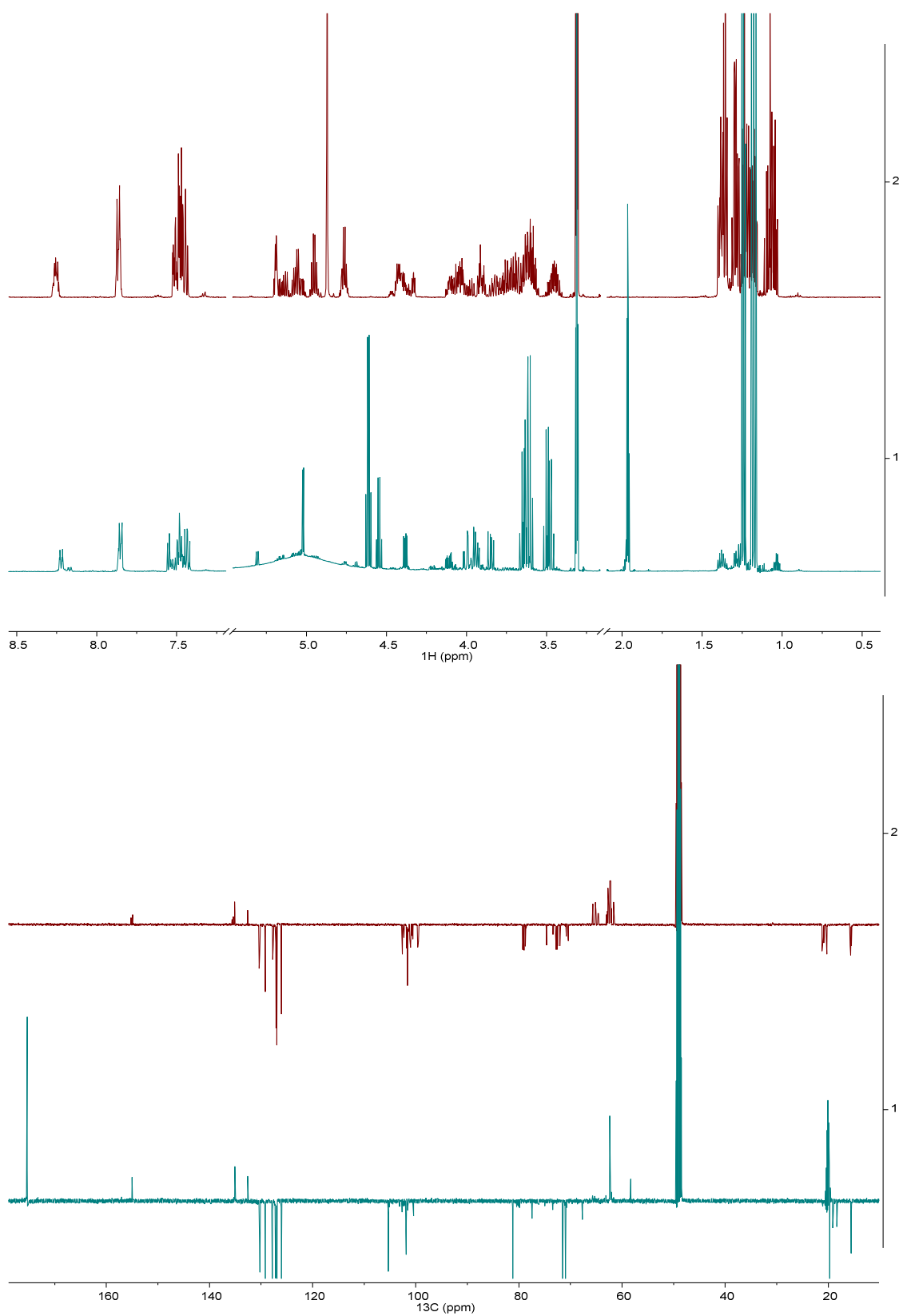


Figure S8. ^1H and ^{13}C NMR spectra of EE-protected 1-naphthylglucal **9b** measured in CD_3OD (maroon) and corresponding NMR spectra after deprotection by CD_3COOD (teal).

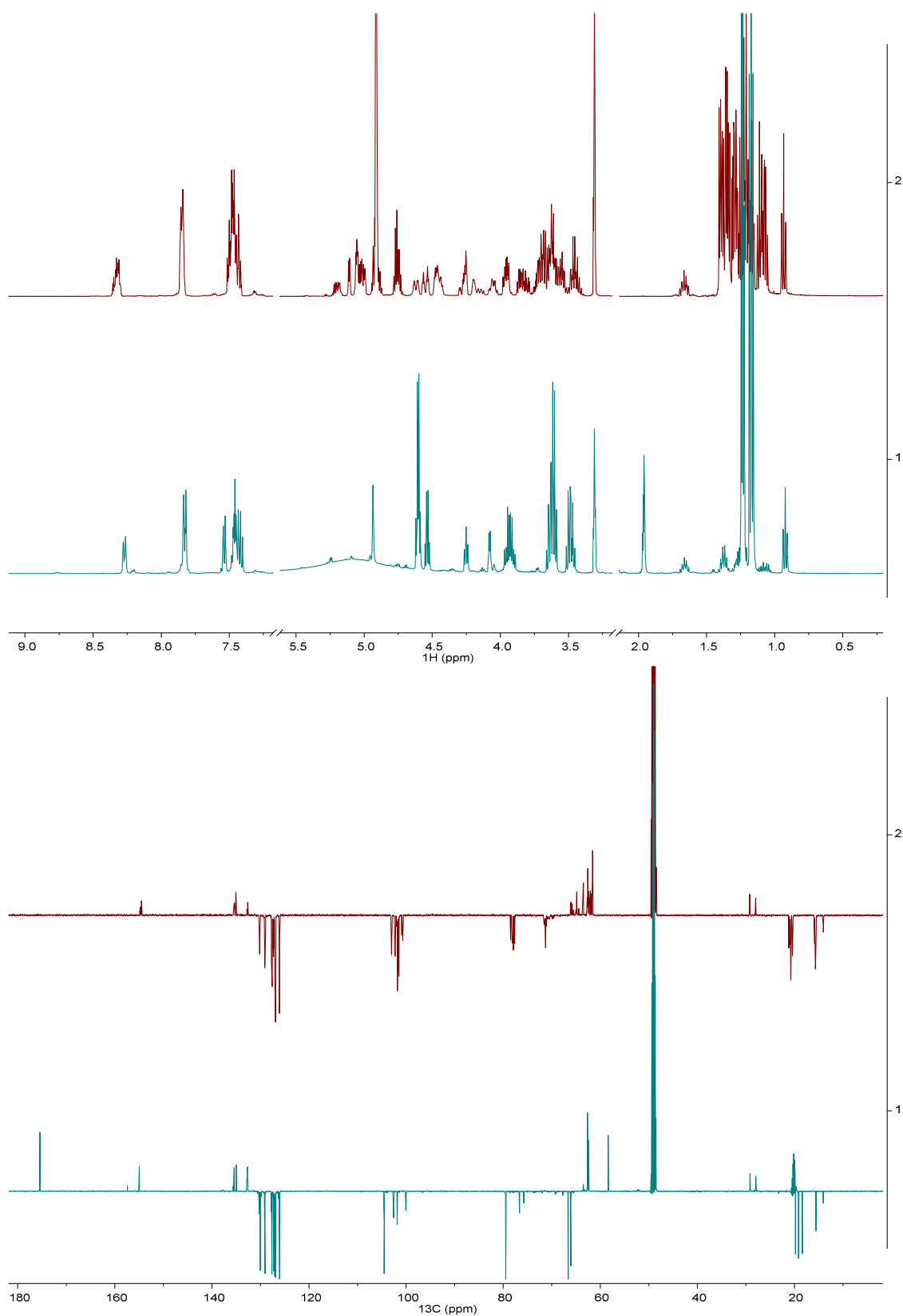
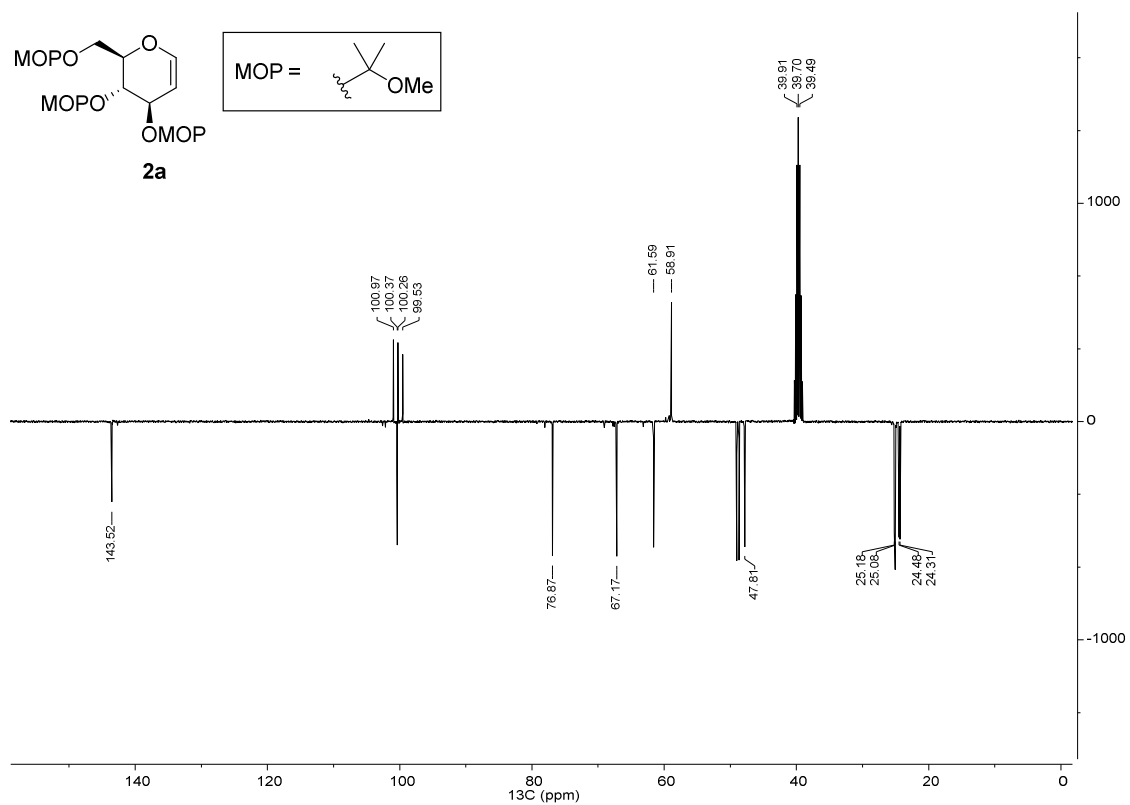
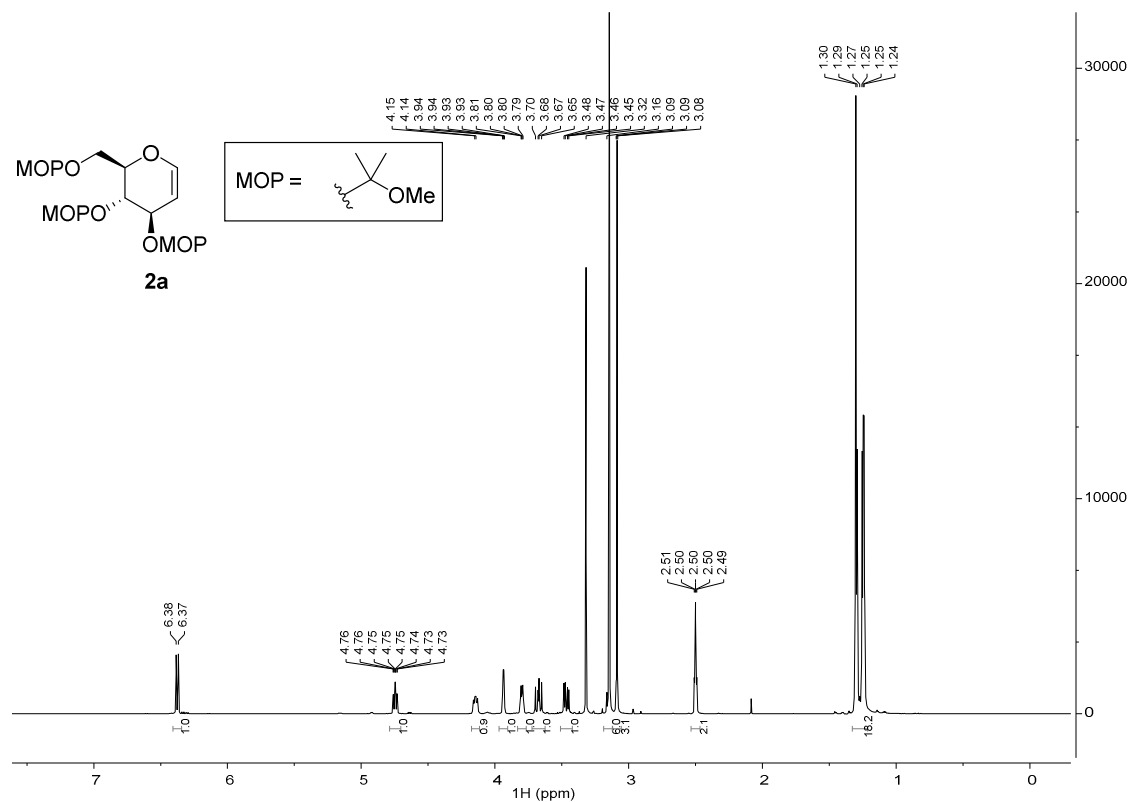


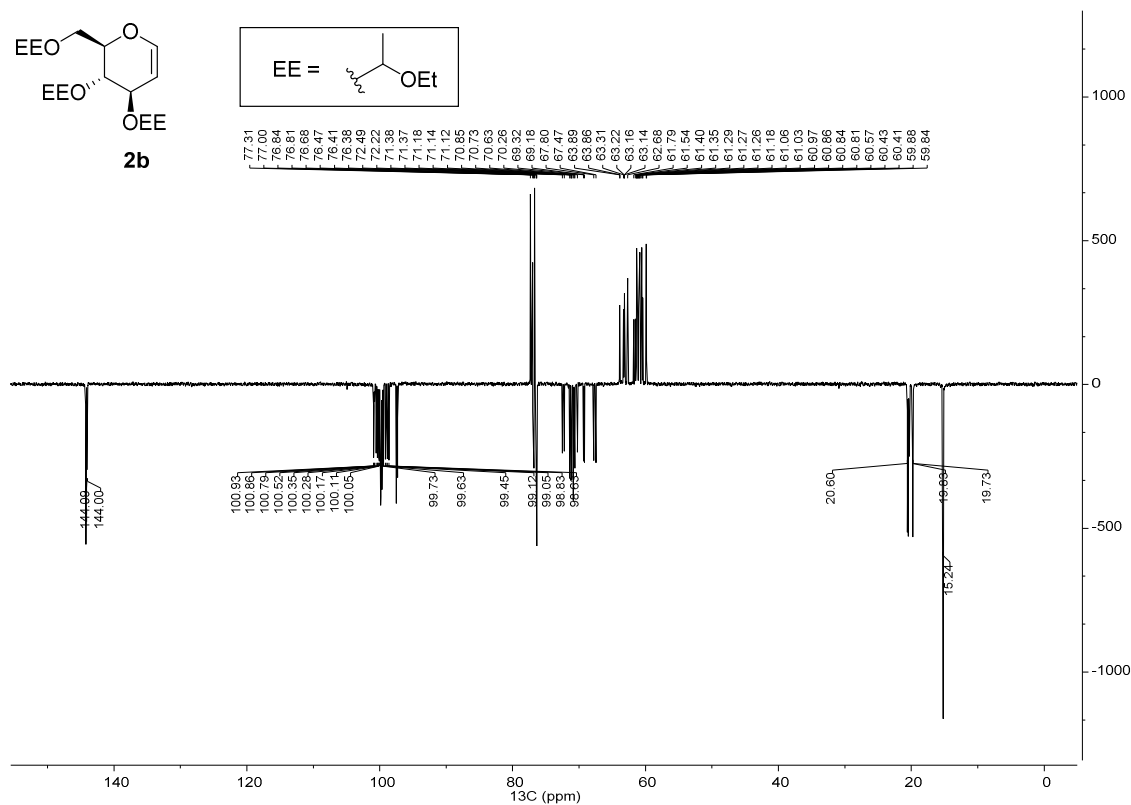
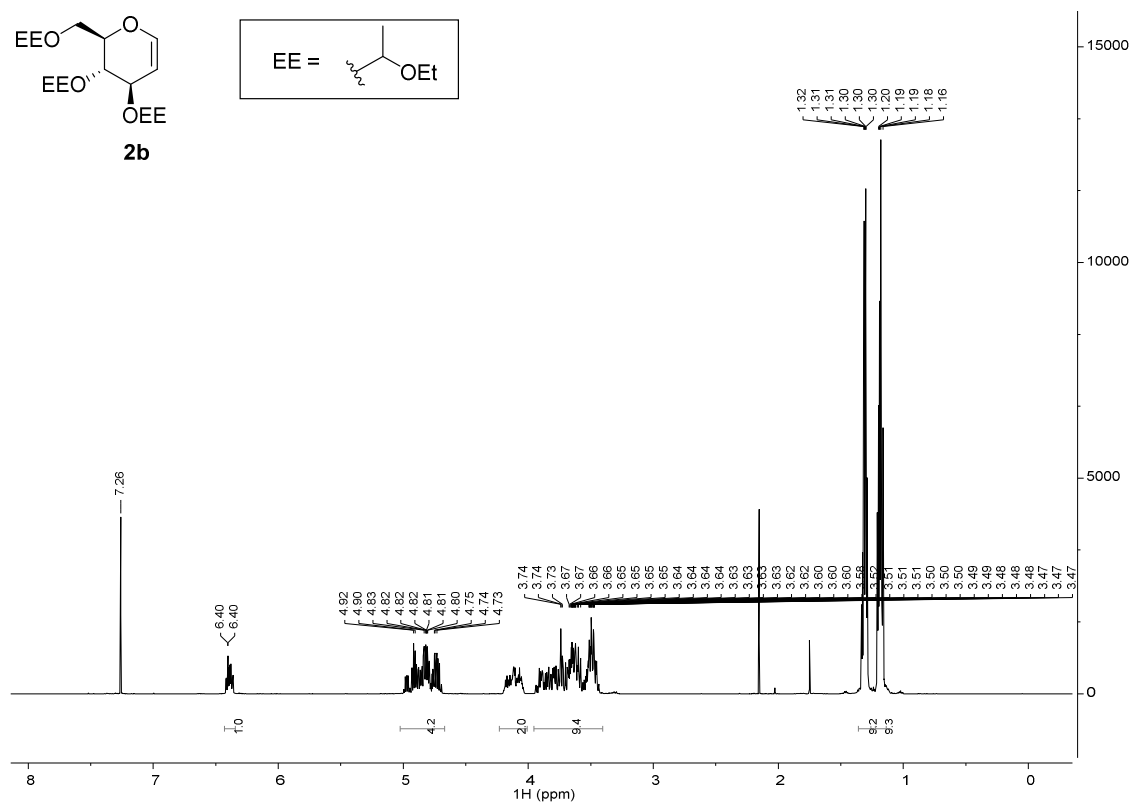
Figure S9. ^1H and ^{13}C NMR spectra of EE-protected 1-naphthylgalactal **10** measured in CD_3OD (maroon) and corresponding NMR spectra after deprotection by CD_3COOD (teal).

5. ^1H NMR and ^{13}C Spectra

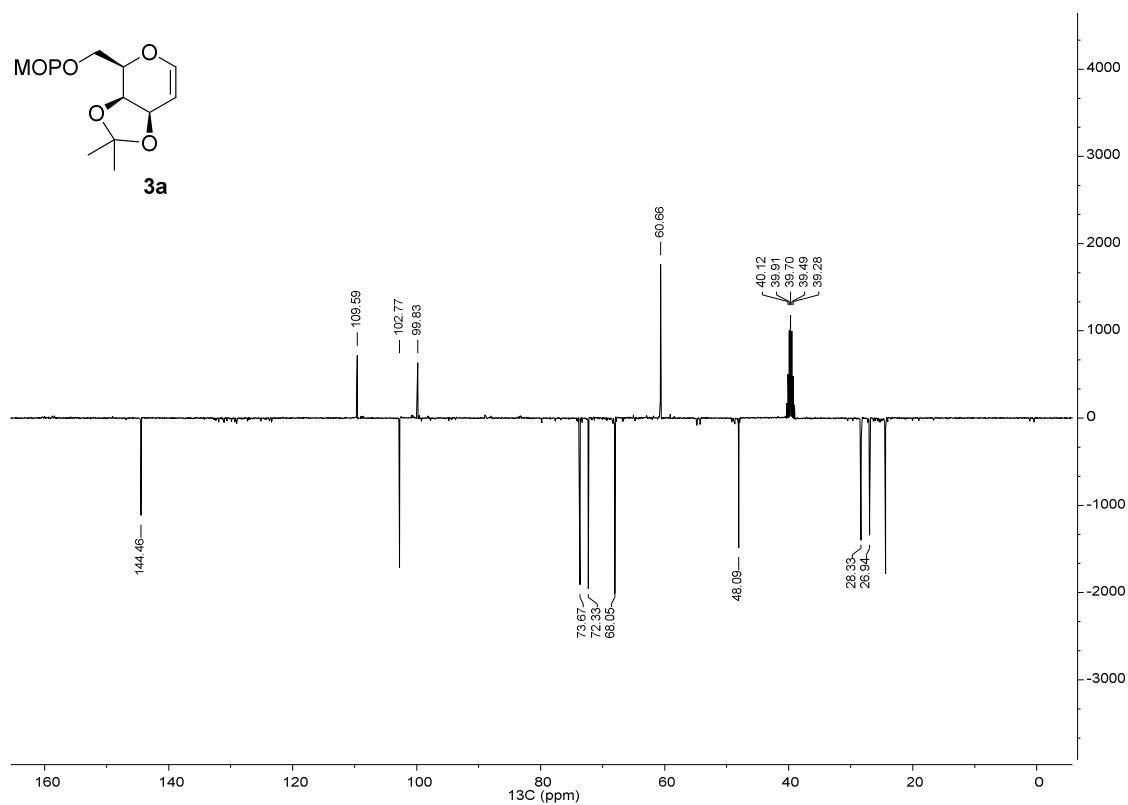
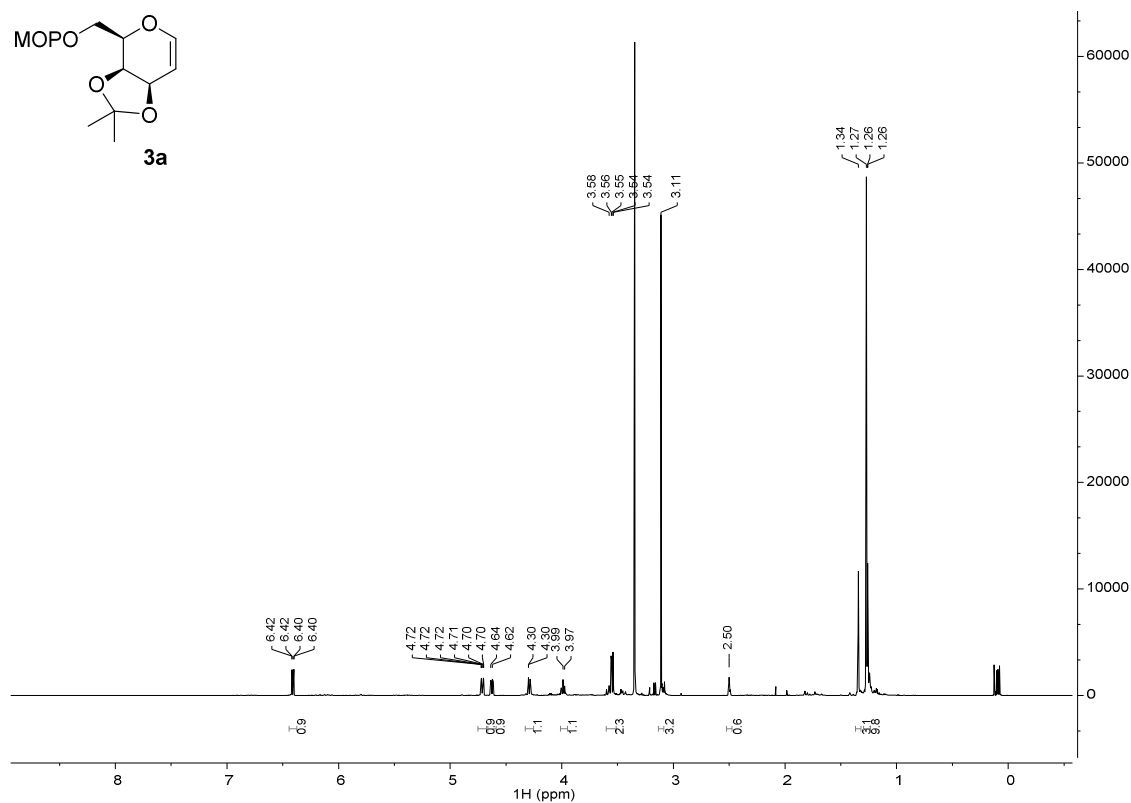
Spectra S1. ^1H and ^{13}C NMR of compound **2a**.



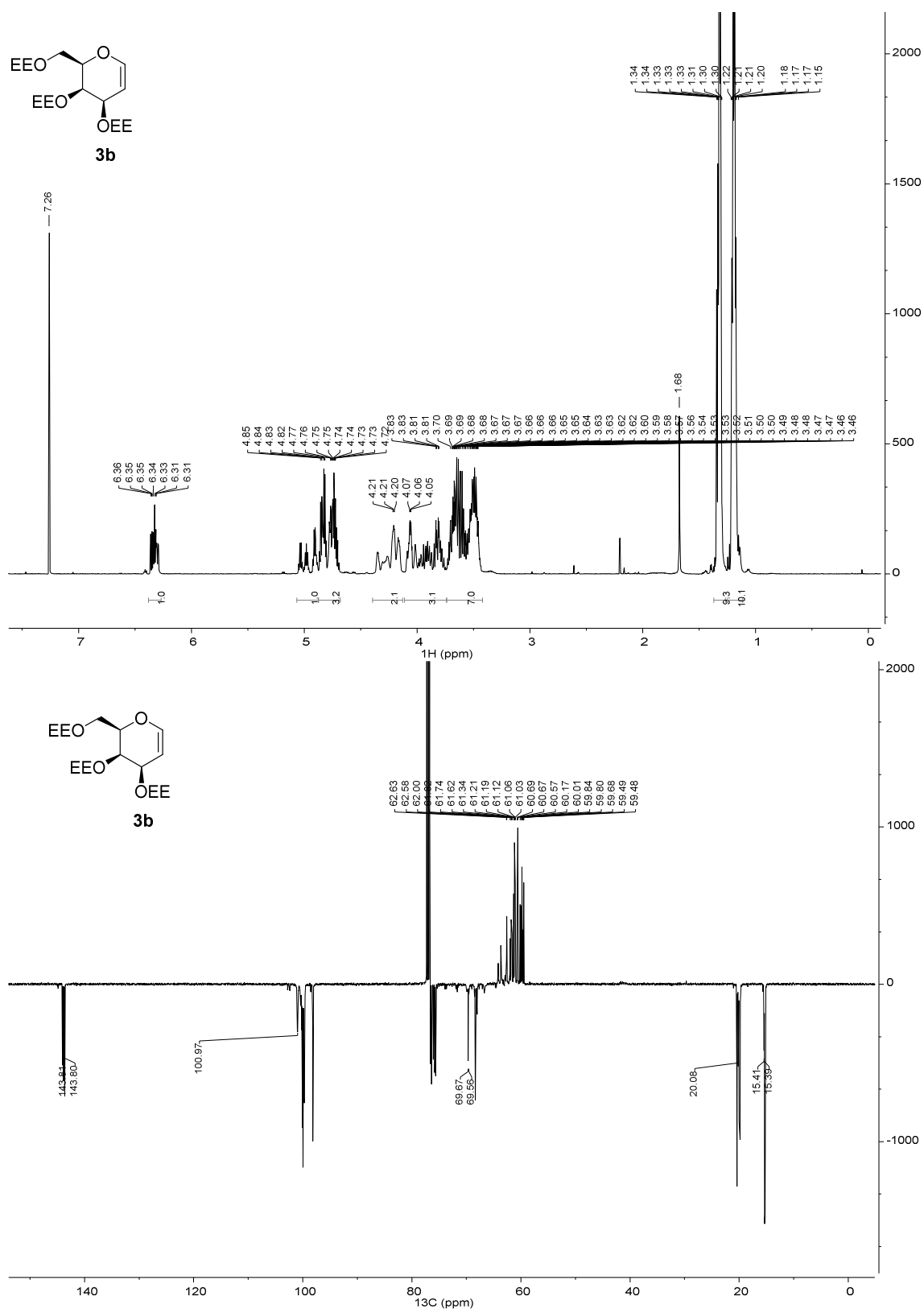
Spectra S2. ^1H and ^{13}C NMR of compound **2b**.



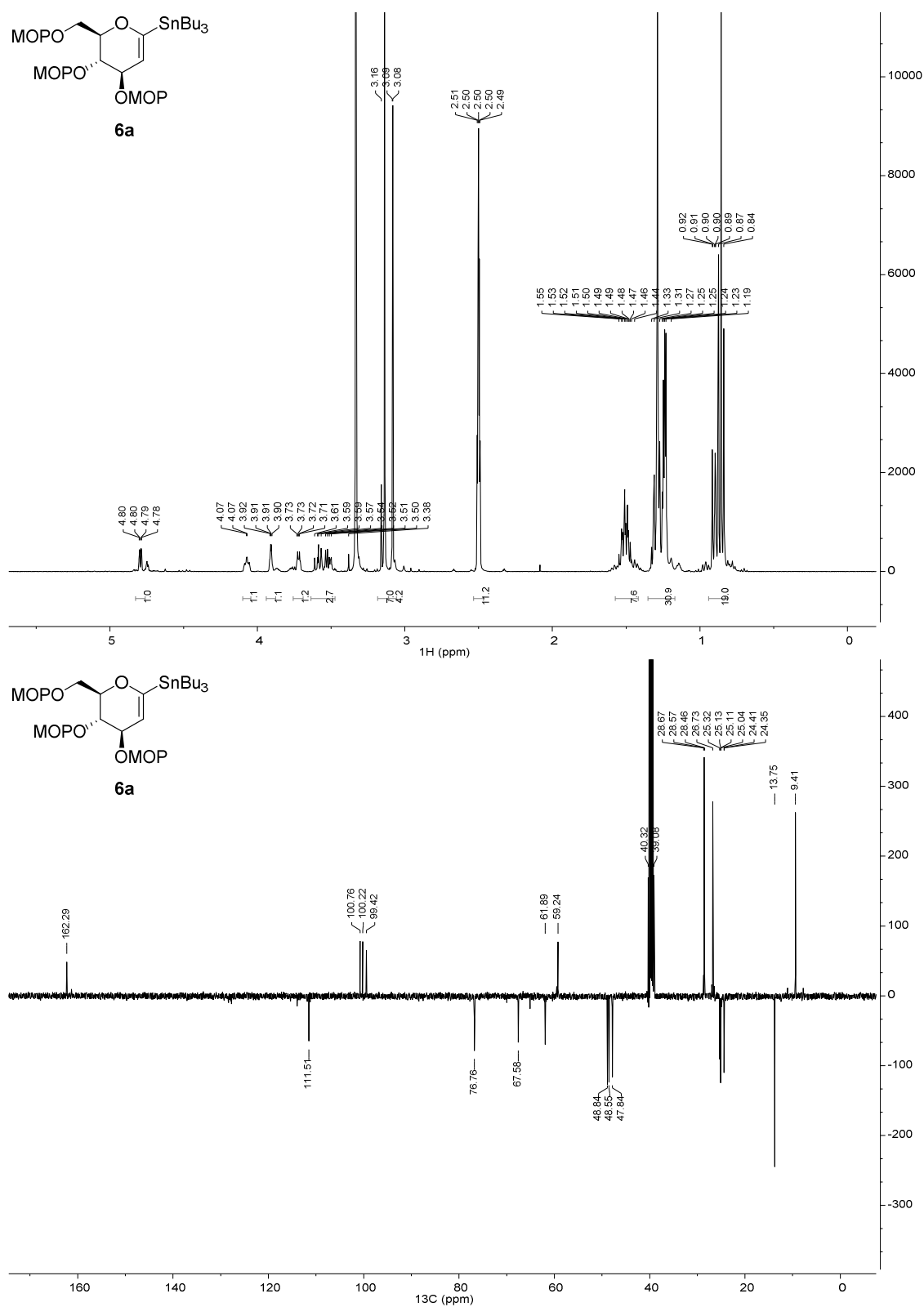
Spectra S3. ^1H and ^{13}C NMR of compound **3a**.



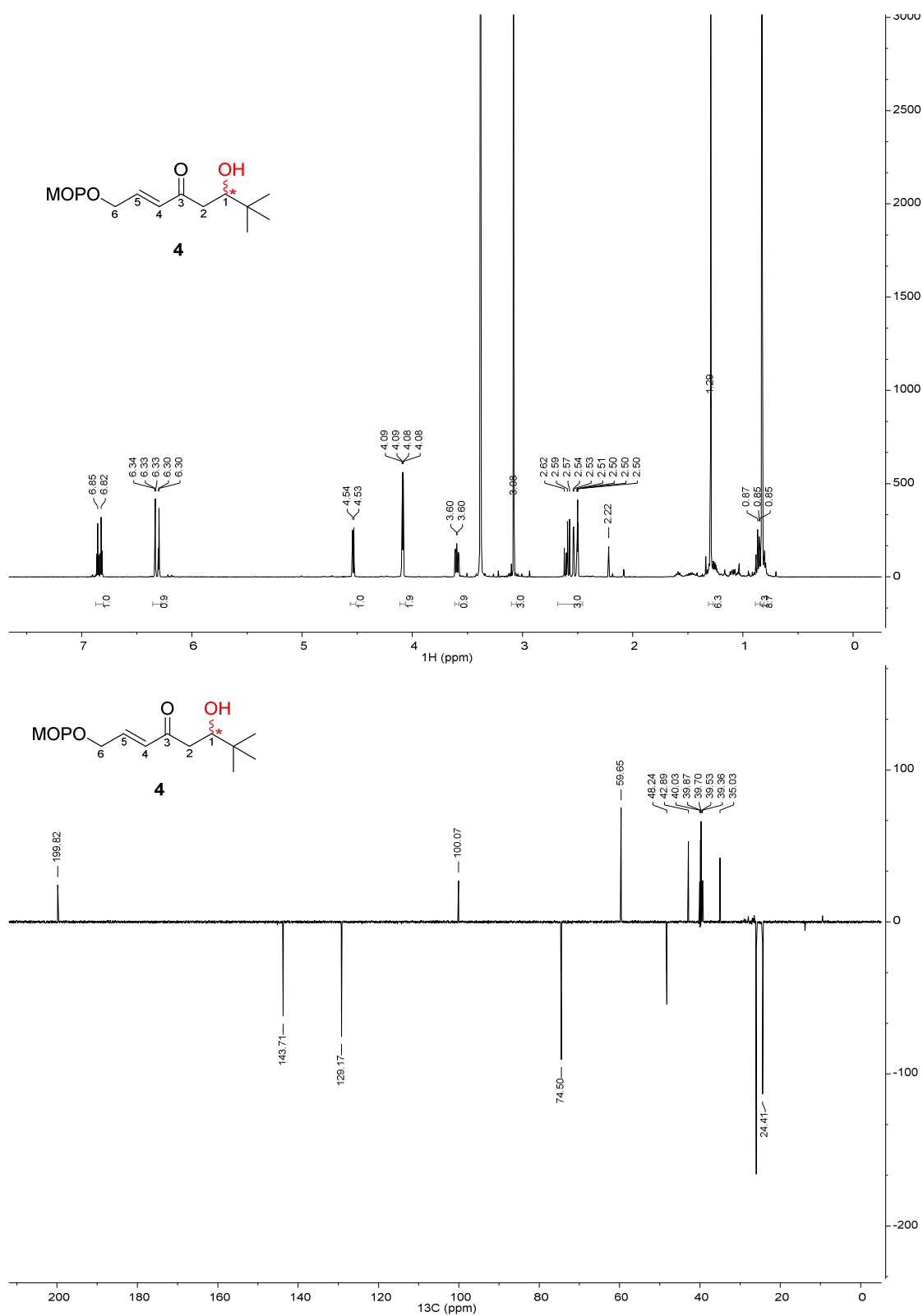
Spectra S4. ^1H and ^{13}C NMR of compound **3b**.



Spectra S5. ^1H and ^{13}C NMR of compound **6a**.



Spectra S6. ^1H and ^{13}C NMR of compound 4.



Chemical structure of **6b** is shown above the spectrum. The spectrum displays peaks corresponding to the structure, with chemical shifts (ppm) labeled above the peaks and integration values below the baseline.

Chemical shifts (ppm) labeled above the peaks:

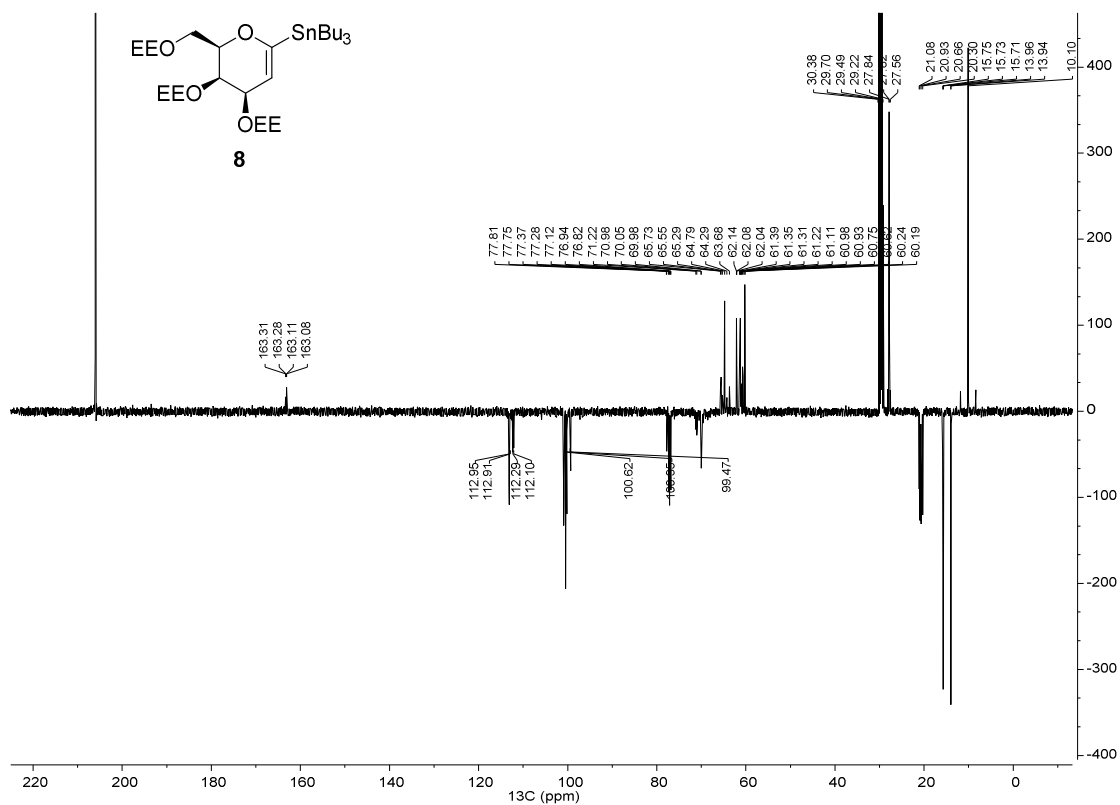
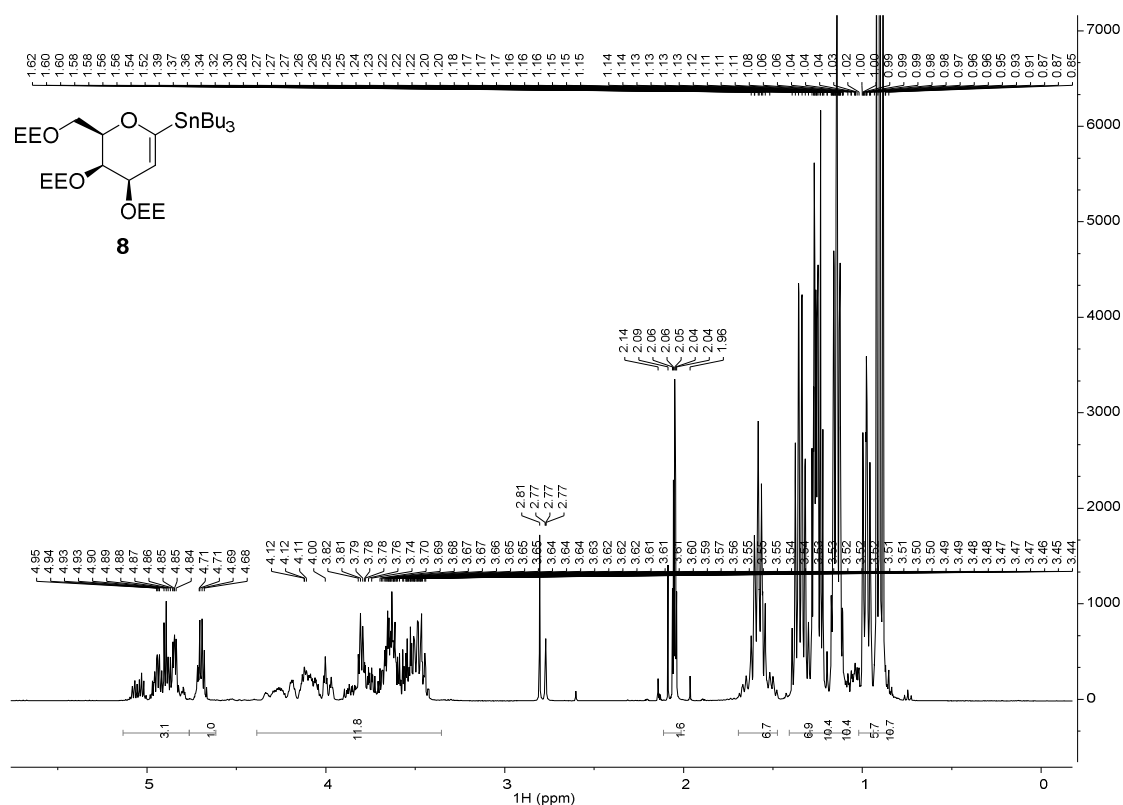
- 7.26
- 4.92, 4.86, 4.85, 4.84, 4.83, 4.82, 4.80, 4.79, 4.75, 4.74, 4.73
- 3.81, 3.80, 3.79, 3.78, 3.75, 3.72, 3.70, 3.69, 3.68, 3.68, 3.67, 3.67, 3.66, 3.65, 3.65, 3.64, 3.64, 3.63, 3.63, 3.61, 3.61, 3.59, 3.54, 3.54, 3.52, 3.52, 3.51, 3.51, 3.50, 3.50, 3.49, 3.48, 3.48, 3.47, 3.45
- 2.16
- 1.52, 1.50, 1.48, 1.46, 1.45, 1.31, 1.28, 1.28, 1.27, 1.27, 1.22, 1.21, 1.21, 1.19, 1.18, 1.18, 1.17, 0.95, 0.94, 0.94, 0.92, 0.91, 0.90

Integration values labeled below the baseline:

- 4.1
- 10.4
- 6.5
- 25.2
- 16.1



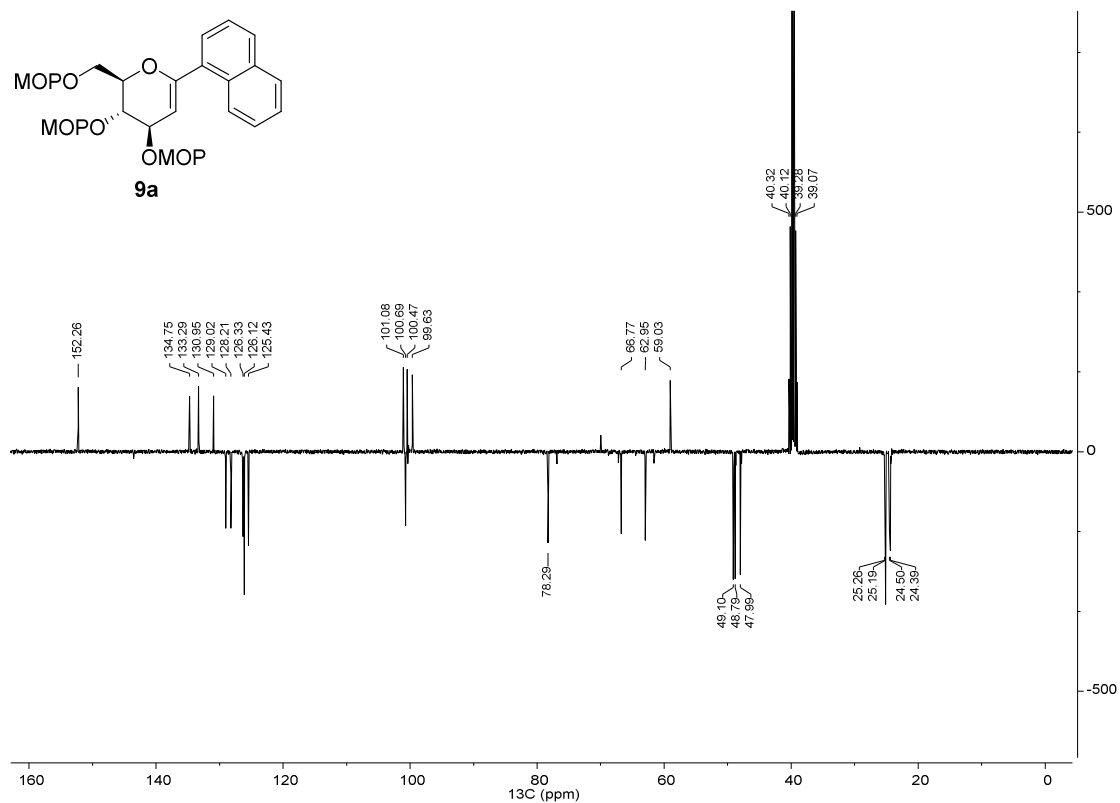
Spectra S8. ^1H and ^{13}C NMR of compound **8**.



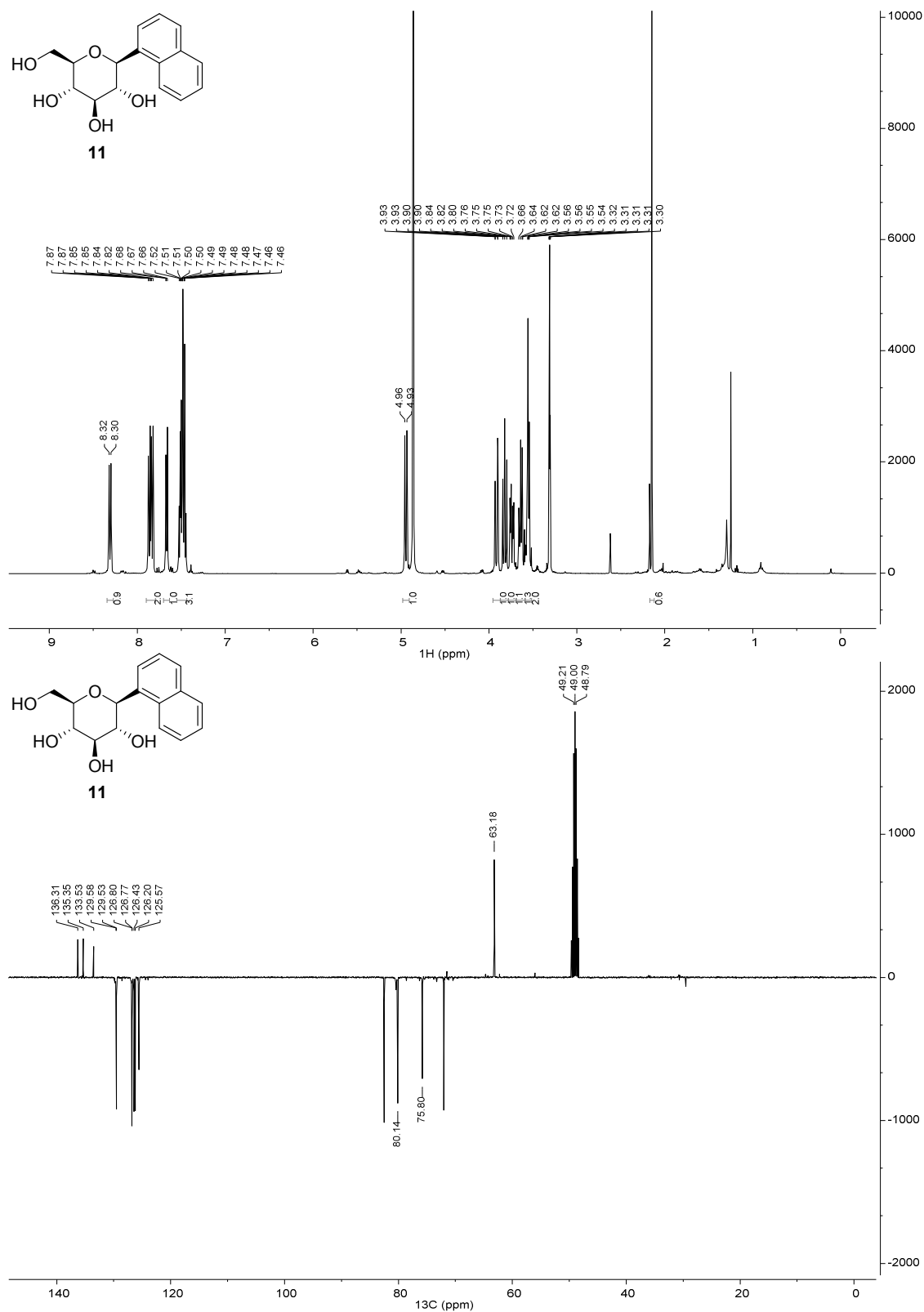
Chemical structure of 9a: COc1cc(OC)c(cc1-c1ccc2ccccc2c1)COP(=O)(OC)OC

¹H NMR spectrum (CDCl₃):

- Chemical shifts (ppm):** 8.36, 8.35, 8.34, 8.34, 7.94, 7.93, 7.93, 7.92, 7.92, 7.92, 7.92, 7.91, 7.91, 7.91, 5.07, 5.07, 5.05, 4.45, 4.44, 4.44, 4.09, 4.08, 3.97, 3.97, 3.64, 3.62, 3.61, 3.23, 3.23, 3.20, 3.05, 2.50, 2.50, 2.50, 1.42, 1.35, 1.32, 1.31, 1.31, 1.30, 1.26, 1.26.
- Integration values:** 1.0, 2.0, 4.1, 1.0, 0.9, 1.0, 1.1, 1.0, 0.9, 3.0, 4.2, 1.0, 1.0.



Spectra S10. ^1H and ^{13}C NMR of compound **11**.



The figure displays the chemical structure of compound **12** and its corresponding ¹H and ¹³C NMR spectra.

Chemical Structure of 12: A naphthalene ring is attached to a 2,3,4-trihydroxy-6-(hydroxymethyl)tetrahydropyran ring. The naphthalene ring is at position 1, and the tetrahydropyran ring is at position 2. The tetrahydropyran ring has hydroxyl groups at positions 2, 3, and 4, and a hydroxymethyl group at position 6.

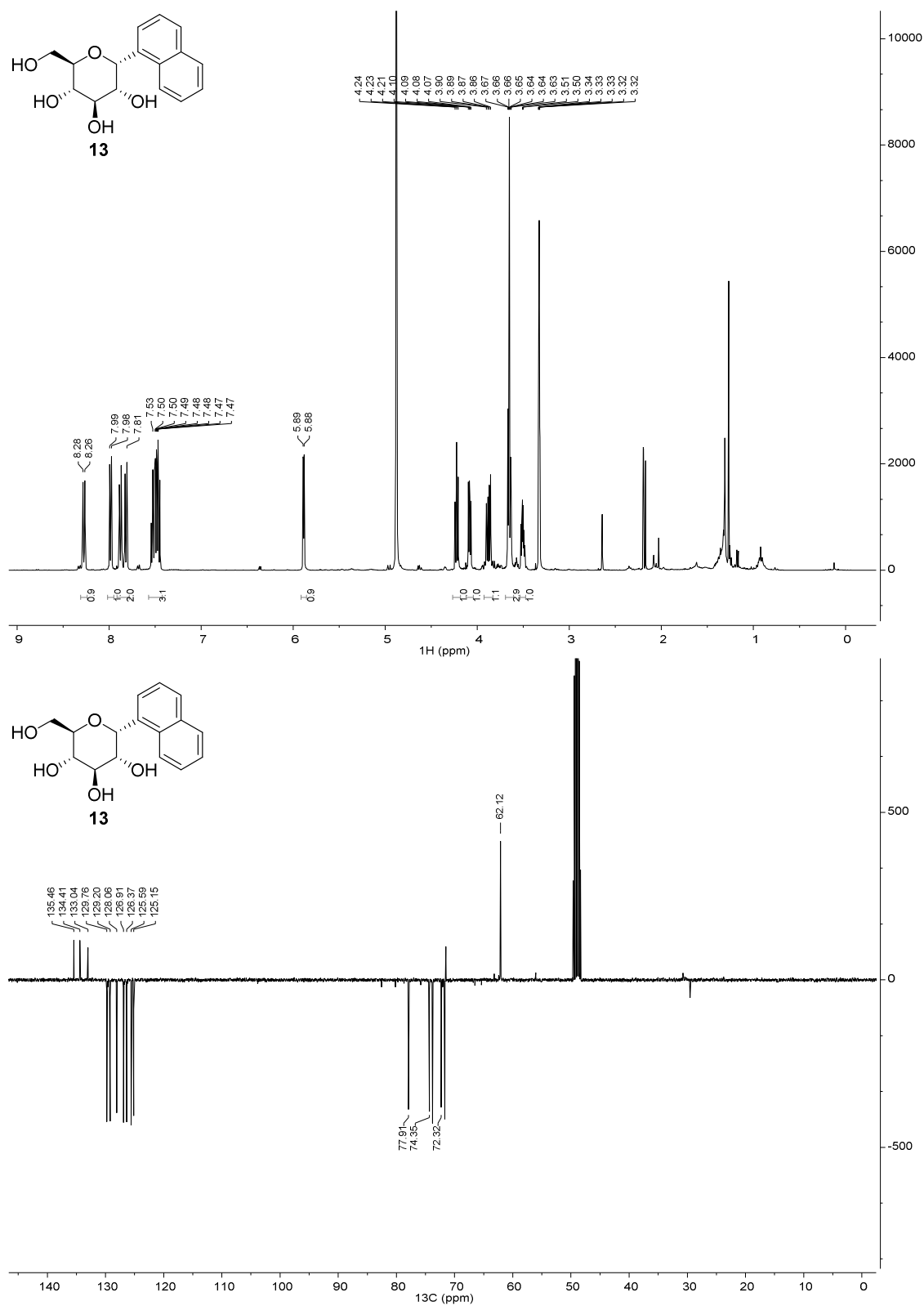
¹H NMR Spectrum (Top): The spectrum shows peaks in the aromatic region (7.41–7.86 ppm), a sugar region (3.62–4.38 ppm), and a solvent peak (2.1 ppm). Integration values are provided below the peaks.

Chemical Shift (ppm)	Integration
8.24, 8.24, 8.24, 8.22, 8.22	1.0
7.86, 7.86, 7.86, 7.85, 7.84, 7.84, 7.84	1.9
7.56, 7.56, 7.56, 7.55, 7.54, 7.50, 7.49, 7.48, 7.48, 7.46, 7.43, 7.41	2.9
5.02, 5.01	1.0
4.38, 4.38, 4.36, 4.36, 4.13, 4.11, 4.10, 4.10, 4.09, 4.08, 4.02, 4.02, 3.99, 3.99, 3.95, 3.94, 3.92, 3.91, 3.86, 3.84, 3.83, 3.82	1.0, 1.0, 1.0, 1.0, 2.2
2.1	1.0

¹³C NMR Spectrum (Bottom): The spectrum shows peaks in the aromatic region (126.03–135.08 ppm), a sugar region (62.32 ppm), and a solvent peak (71.53, 70.98 ppm).

Chemical Shift (ppm)
154.98
135.08, 135.04, 132.62, 130.20, 129.16, 127.79, 127.16, 126.60, 126.03
105.39
81.28
71.53, 70.98
62.32

Spectra S12. ^1H and ^{13}C NMR of compound **13**.



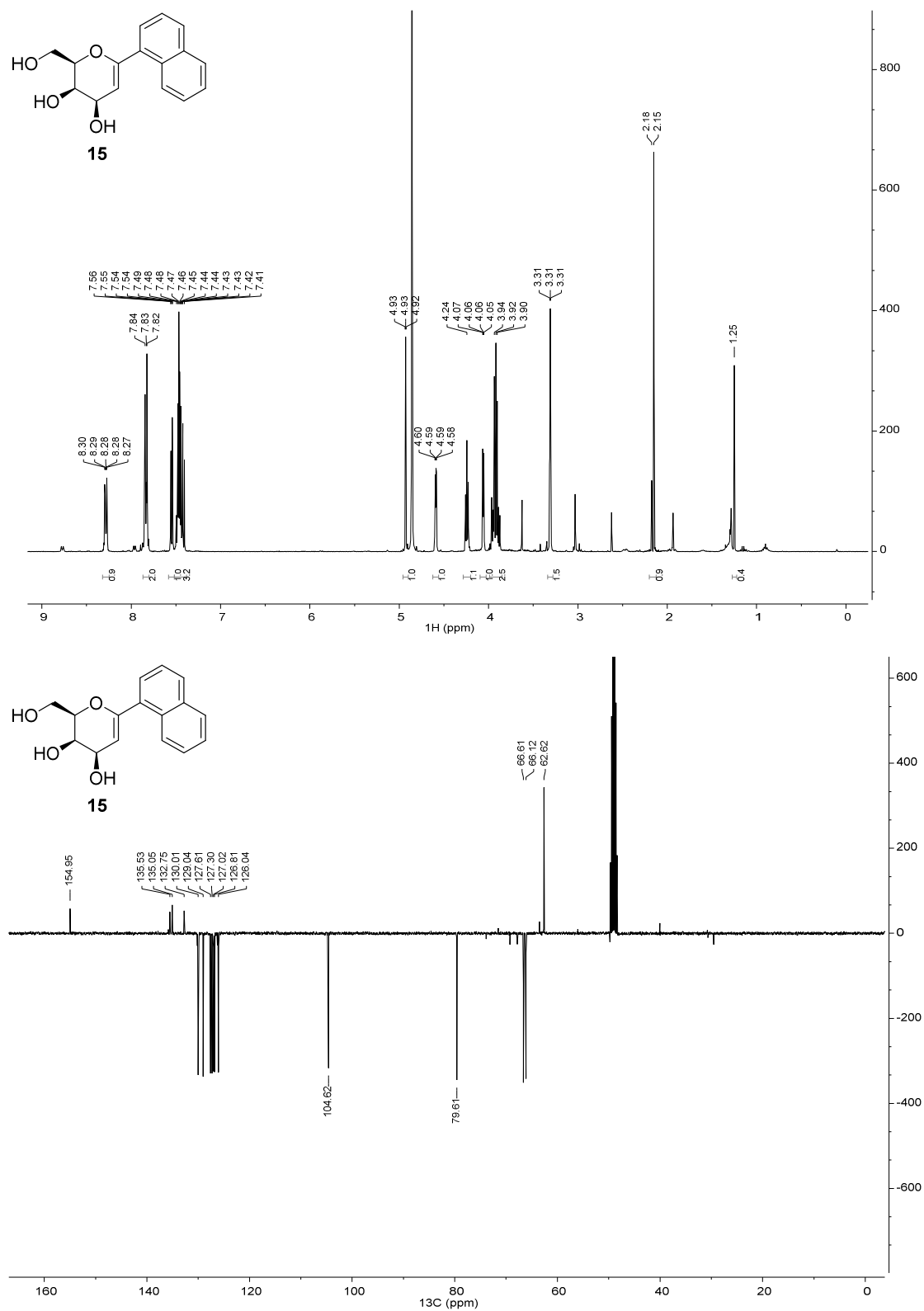
The figure displays the chemical structure of compound **14** and its corresponding ¹H and ¹³C NMR spectra.

Chemical Structure of 14: A bicyclic molecule consisting of a naphthalene ring system fused to a six-membered ring containing an oxygen atom (a tetrahydropyran derivative). The structure is substituted with a hydroxyl group (OH) and a hydroxymethyl group (CH₂OH).

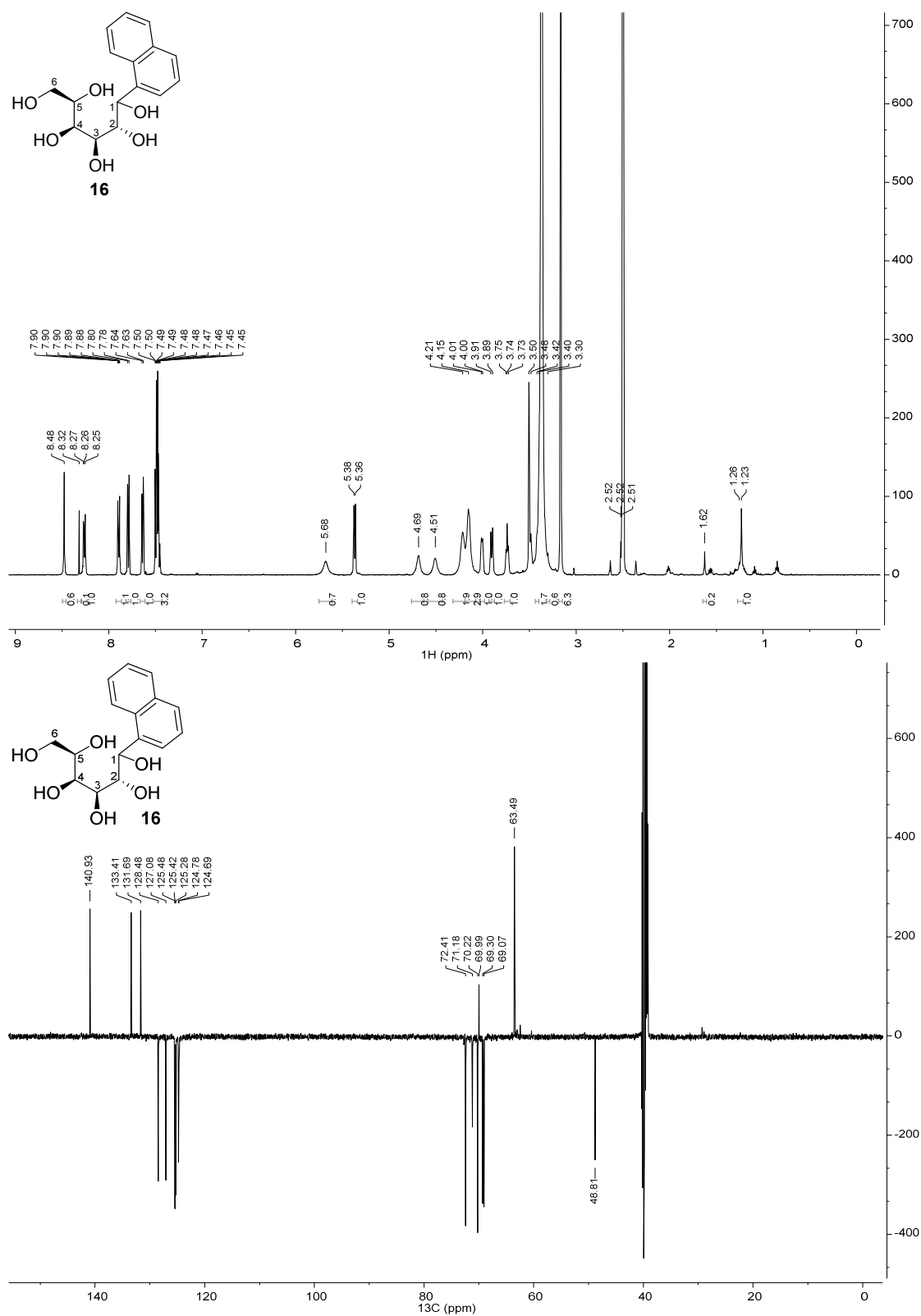
¹H NMR Spectrum (Top): The spectrum shows chemical shifts in ppm (0 to 9) and integration values (0.9, 2.0, 1.4, 3.0, 1.0, 1.0, 1.0, 4.1). Key peaks are labeled with their chemical shifts: 8.47, 8.45, 7.87, 7.86, 7.85, 7.84, 7.84, 7.84, 7.84, 7.82, 7.82, 7.81, 7.81, 7.69, 7.68, 7.67, 7.67, 7.49, 7.49, 7.49, 7.47, 7.47, 7.46, 7.46, 7.45, 7.45, 3.82, 3.81, 3.79, 3.78, 3.78, 3.77, 3.77, 3.76, 3.76, 3.74, 3.73, 3.72, 3.71, 3.63, 3.63, 3.31, 3.31, 3.31, 3.30, 2.37, 1.25, and 0.93.

¹³C NMR Spectrum (Bottom): The spectrum shows chemical shifts in ppm (0 to 140) and integration values (82.01, 72.59). Key peaks are labeled with their chemical shifts: 136.41, 135.45, 133.49, 129.82, 129.46, 127.39, 126.71, 126.40, 126.11, 126.06, 63.09, 49.21, 49.00, and 48.79.

Spectra S14. ^1H and ^{13}C NMR of compound **15**.



Spectra S15. ^1H and ^{13}C NMR of compound **16**.



[illegible]

Spectra S17. ^1H and ^{13}C NMR of compound **18**.

