Supporting information

Acetyl Group Migration across the Saccharide Units in Oligomannoside Model Compound

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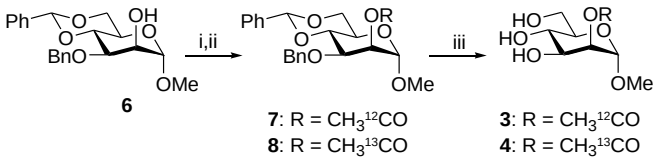
General information

For identification and characterization of the new compounds, a Bruker Avance-III spectrometer operating at 500.20 MHz (^{1}H) and 125.78 MHz (^{13}C) equipped with a Prodigy BBO CryoProbe was used. The characterization was performed using a standard set of 1D and 2D NMR spectroscopic techniques: ^{1}H, ^{13}C, 1D-TOCSY, DQF-COSY, Multiplicity edited HSQC (CH and CH_3 positive, CH_2 negative, both coupled and decoupled), and HMBC. The reported signals are referenced to an internal standard (TMS δ_H = 0.0 ppm, δ_C = 0.0 ppm) or residual solvent signal (MeOH δ_H = 3.3 ppm, δ_C = 49.0 ppm). Chemical shifts are reported with two decimals for ^{1}H and one decimal for ^{13}C; where this is not sufficient for distinguishing two signals an additional decimal is given. Coupling constants are reported in Hz with one decimal and mentioned only the first time they are encountered. Accurate coupling constants and shifts were extracted from the ^{1}H spectra using the NMR simulation software PERCH[1] or ChemAdder/SpinAdder.[2] HRMS was recorded on a Bruker daltonics micro-ToF with ESI in positive mode as ionization source. TLC analysis was performed on Merck silica gel 60 F254 plates and the spots were visualized with UV light and charring with H_2SO_4/MeOH (1:4) and heating. All reactions were monitored by TLC. Column chromatography was carried out using silica gel 60 (0.040 – 0.060 mm) as stationary phase and hexane:EtOAc or CH_2Cl_2:MeOH as eluents. All chemicals were purchased from Sigma-Aldrich and used as such. Dry dichloromethane was obtained by distillation from a suspension of CaH_2 under argon. Dry MeOH and DMF were purchased and used as such. Reactions with air or moisture sensitive reagents were carried out under argon atmosphere.

Synthesis of model compounds

Model monosaccharides

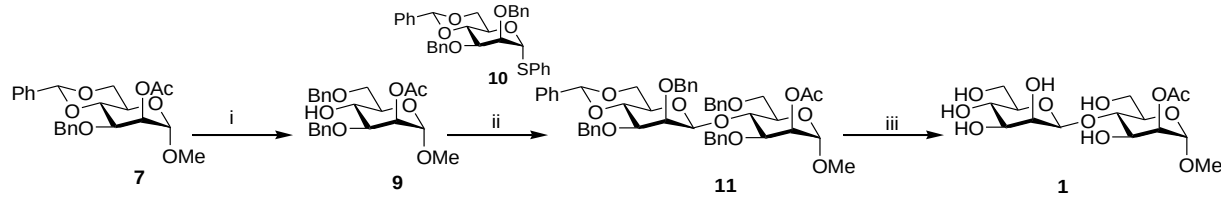
Synthesis of the monosaccharides followed conventional protection group procedures. The starting compound for the target monosaccharides was the well-known monosaccharide **6**. Subsequent acetylation with AcCl provided the precursor **7**, whereas acetylation using AcCl (1-^{13}C) gave compound **8** (Scheme S1). The final removal of benzyl and benzylidene groups was achieved by hydrogenolysis using H_2 over Pd/C in MeOH/AcOH.



Scheme S1. Synthesis of the monosaccharides **3** and **4**. (i) AcCl, pyridine, 0 °C → rt, 2 h, (85%); (ii) AcCl (1-^{13}C), pyridine, 0 °C → rt, 2 h, (59%); (iii) Pd/C, MeOH/AcOH, 4 h, (**3**: 95%; **4**: 96%).

Model disaccharide

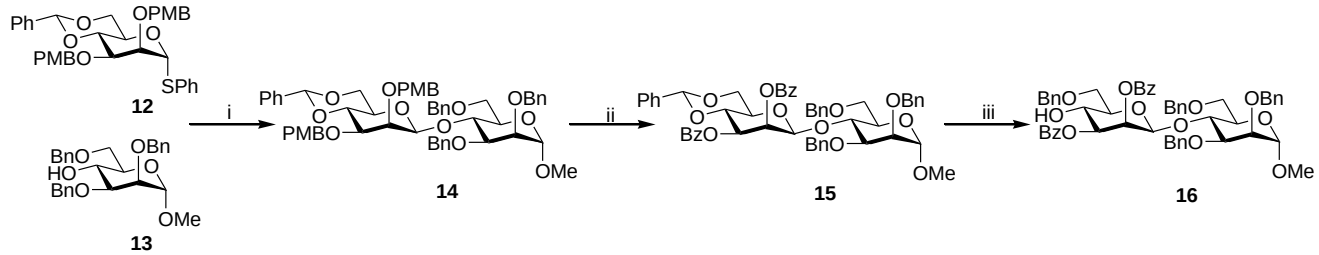
Preparation of the disaccharide **1** commenced from the well-known precursors **7** and **10** (Scheme S2). First, a selective opening of the benzylidene acetal was achieved by the method of DeNinno using TFA and $SiEt_3H$ to provide the building block **9** for the final target disaccharide.[3] Next, a Crich β-mannosylation[4,5] between the acceptor **9** and the donor **10**, utilizing the activation of a thioglycoside with Tf_2O/BSP, yielded the protected disaccharide **11**. The final step consisted of removal of the benzyl and benzylidene protecting groups by hydrogenolysis using H_2 over Pd/C in MeOH and AcOH in excellent yields.



Scheme S2. Synthesis of the target disaccharide. Reagents and conditions: (i) TFA, Et_3SiH, CH_2Cl_2, 2 h (50%); (ii) 1) **10**, BSP, TTBP, Tf_2O, CH_2Cl_2, –60 °C, 0.5 h, 2) –78 °C, **9**, 3 h (34%); (iii) Pd/C, MeOH/AcOH, 4 h (99%).

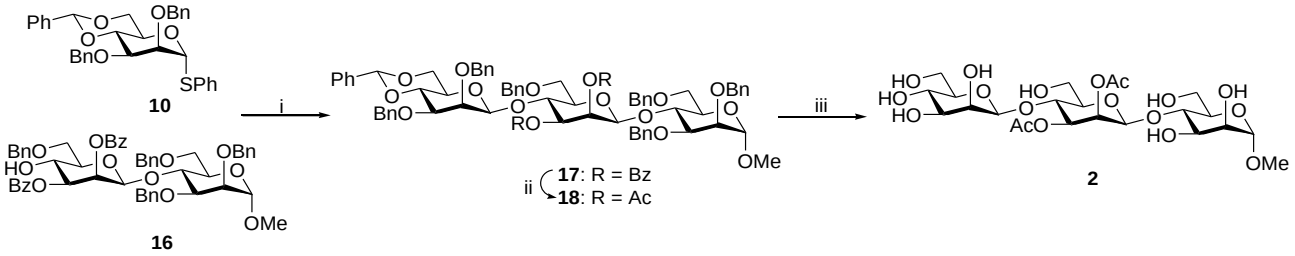
Model trisaccharide

For synthesis of the model trisaccharide, a β-mannosylation between the donor **12** and acceptor **13** was first performed to provide compound **14** (Scheme S3). A fair yield was obtained, considering the instability of the PMB-groups. Removal of the PMB protecting groups was initially carried out using a standard protocol based on DDQ in CH_2Cl_2:H_2O. In this reaction, the PMB group is removed by oxidation to an aldehyde which, however, may then react with the target product to form an acetal between the positions 2 and 3. Addition of methanol to form the corresponding dimethyl acetal proved to be an efficient way to circumvent this problem. By this method, the PMB-groups were cleaved from **14** and the product was benzoylated using standard procedures with BzCl in pyridine to obtain the disaccharide **15**. Due to the low yield of glycosylation reactions using the 2',3'-diacetylated analogue of **16**, benzoyl protecting groups were introduced as temporary protecting groups. The previously employed TFA/Et_3SiH method for selective ring-opening of the benzylidene group resulted in less than satisfactory yields for **16**. However, by use of an alternative procedure substituting TFA with $BF_3{\cdot}OEt_2$ in the presence of excess Et_3Si,[6] the disaccharide acceptor **16** was finally obtained in good yield (73%).



Scheme S3. Preparation of the disaccharide precursor for the trisaccharide. Reagents and conditions: (i) 1) **12**, BSP, TTBP, Tf_2O, CH_2Cl_2, –60 °C, 0.5 h, 2) –78 °C, **13**, 1 h (45%); (ii) 1) DDQ, CH_2Cl_2:MeOH:H_2O 92:4:4, 3 h (79%), 2) BzCl, pyridine, 1.5 h (81%); (iii) Et_3SiH, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 1 h (73%).

After the selective ring-opening, β-mannosylation of **16** with the donor **10** provided the protected trisaccharide **17** in fair yield (Scheme S4). Next, the benzoyl groups were exchanged for acetyl groups by deprotection under Zemplén conditions[7] followed by acetylation with Ac_2O in pyridine to yield the trisaccharide **18**. Finally, removal of the benzyl and benzylidene protecting groups by hydrogenolysis provided the model diacetylated trisaccharide **2**, used for the migration studies, in excellent yield over the last step of synthesis.



Scheme S4. The last three steps in the synthesis of the target trisaccharide. Reagents and conditions: (i) 1) **10**, BSP, TTBP, Tf_2O, CH_2Cl_2, –60 °C, 0.5 h, 2) **16**, –78 °C, 2.5 h (43%); (ii) 1) NaOMe, MeOH:THF 1:1, 25 h, 2) Ac_2O, pyridine, 48h (67%); (iii) Pd/C, MeOH, 18 h (92%).

Migration

^{1}H NMR chemical shifts of the monosaccharides in buffered D_2O/H_2O

Tabel S1. ^{1}H NMR chemical shifts of the monosaccharide migration products in buffered D_2O/H_2O at 25 °C and pD/H = 8.

	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	1-OMe	-OAc
3a,**4a**	n.d.[a]	5.00	3.88	3.62	3.58	3.82	3.70	3.33	2.08
3b,**4b**	n.d.[a]	4.00	4.91	3.78	3.63	3.82	3.70	3.34	2.08
3c,**4c**	n.d.[a]	3.86	3.87	4.94	3.70	3.87	3.73	3.35	2.07
3d,**4d**	n.d.[a]	3.86	3.68	3.62	3.72	4.35	4.20	3.31	2.06
5	n.d.[a]	3.84	3.67	3.55	3.53	3.81	3.67	3.32	-

[a]The signal was located under the water signal.

Migration in monosaccharides

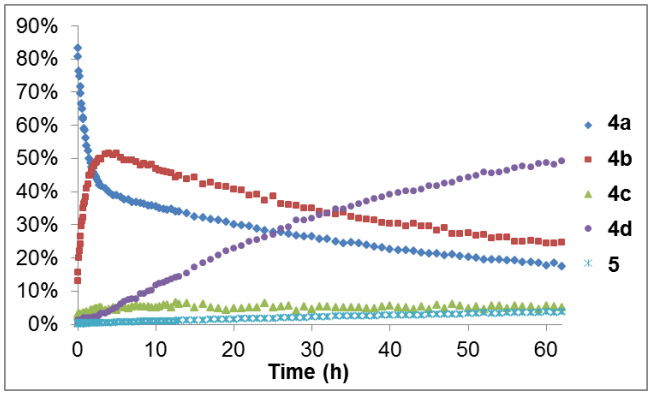


Figure S1. Migration of **4** in buffered D_2O at 25 °C and pD = 8.

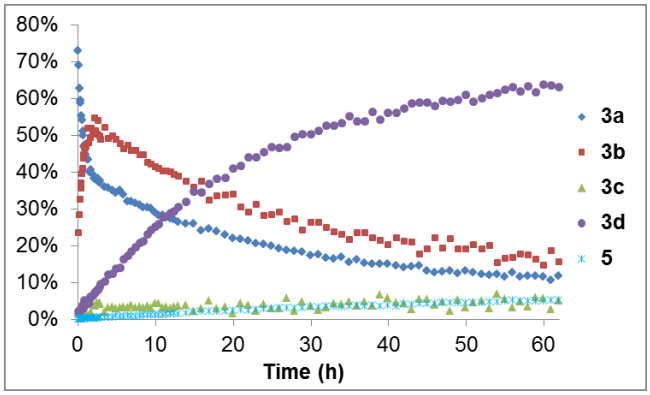


Figure S2. Migration of **3** in buffered H_2O at 25 °C and pH = 8.

Comparison of the different kinetic isotope effects

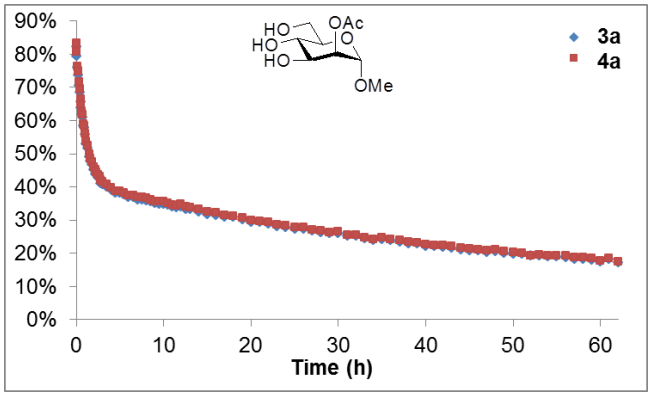


Figure S3. Comparison of the migration of **3** and **4** in buffered D_2O at 25 °C and pD = 8.

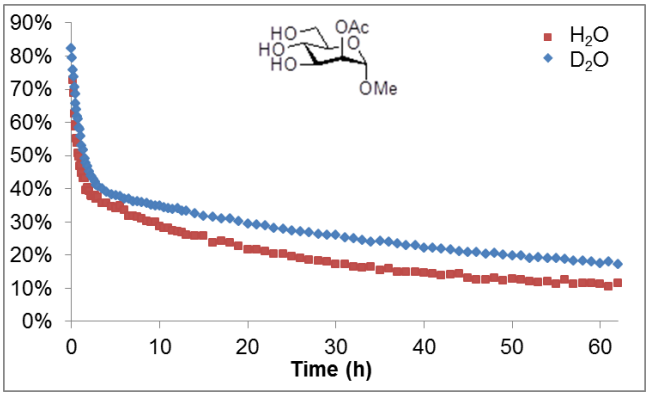


Figure S4. Comparison of the migration of **3** in buffered D_2O and buffered H_2O at 25 °C and pD/H = 8.

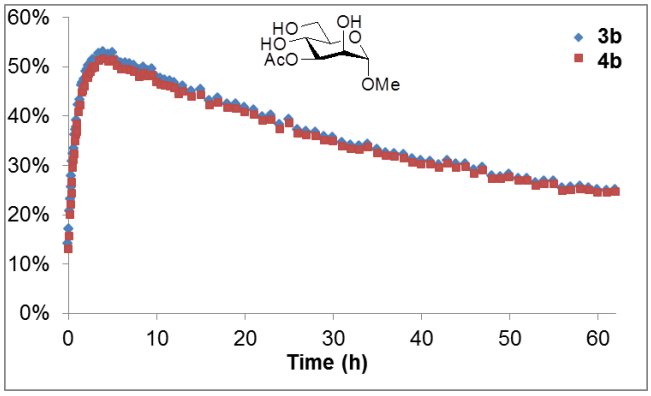


Figure S5. Comparison of the migration of **3** and **4** in buffered D_2O at 25 °C and pD = 8.

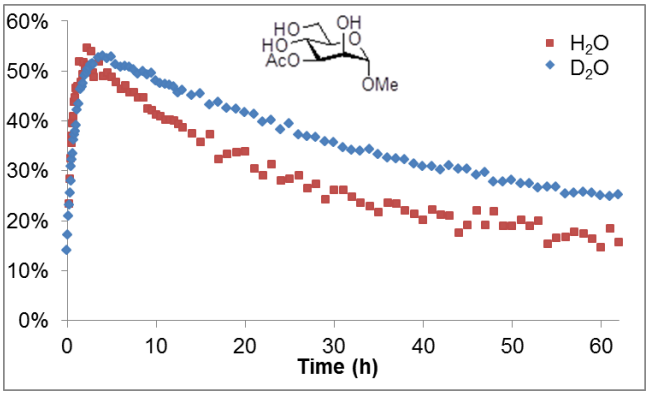


Figure S6. Comparison of the migration of **3** in buffered D_2O and buffered H_2O at 25 °C and pD/H = 8.

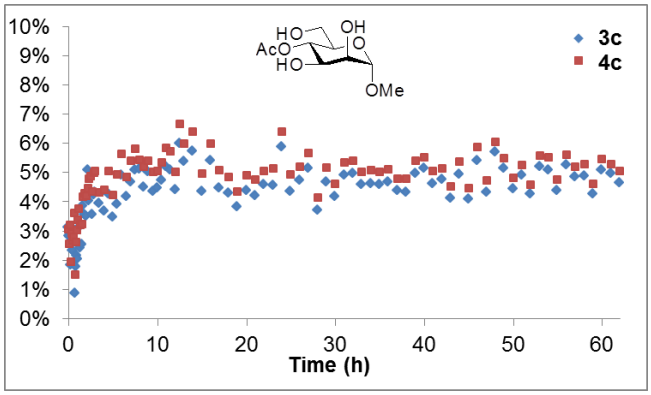


Figure S7. Comparison of the migration of **3** and **4** in buffered D_2O at 25 °C and pD = 8.

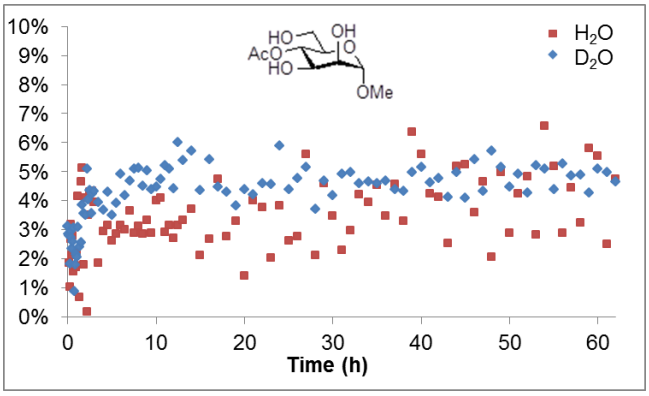


Figure S8. Comparison of the migration of **3** in buffered D_2O and buffered H_2O at 25 °C and pD/H = 8.

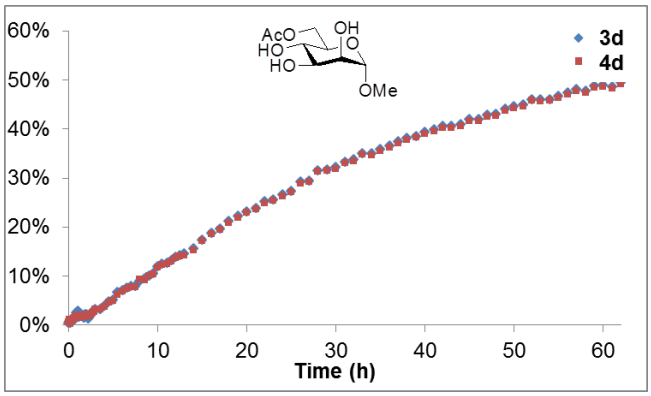


Figure S9. Comparison of the migration of **3** and **4** in buffered D_2O at 25 °C and pD = 8.

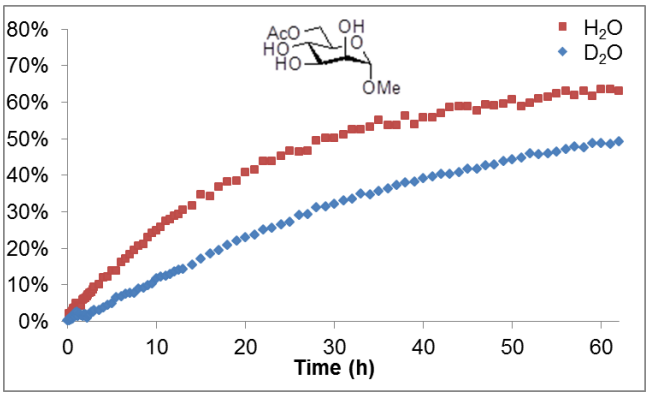


Figure S10. Comparison of the migration of **3** in buffered D_2O and buffered H_2O at 25 °C and pD/H = 8.

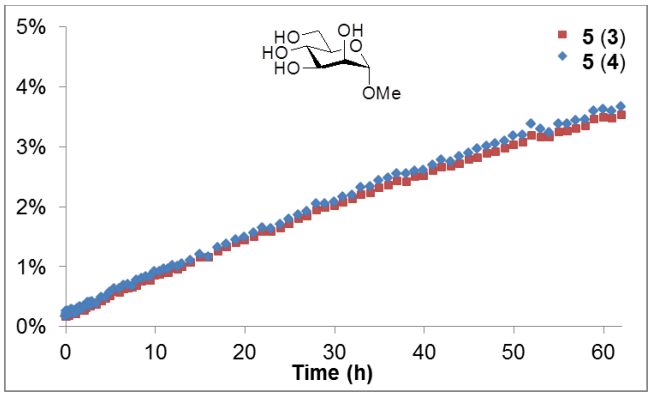


Figure S11. Comparison of the migration of **3** and **4** in buffered D_2O at 25 °C and pD = 8.

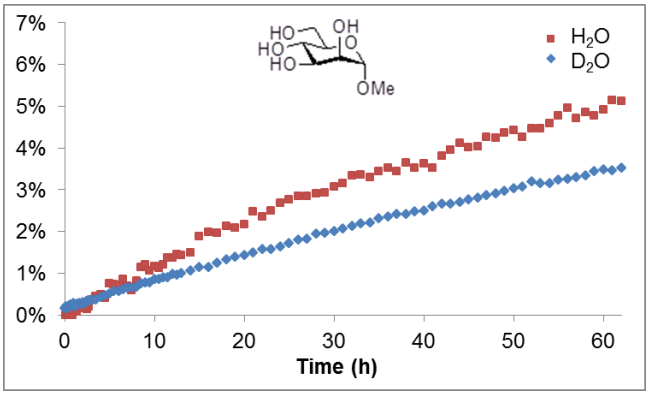


Figure S12. Comparison of the migration of **3** in buffered D_2O and buffered H_2O at 25 °C and pD/H = 8.

Kinetic modeling

Kinetic modeling of disaccharide 1

In Figure S13 and S14 is the kinetic modeling of the migration in **1** in buffered D_2O at 25 °C and pD = 8 shown. The kinetic model explains the experimental data with 99.94%.

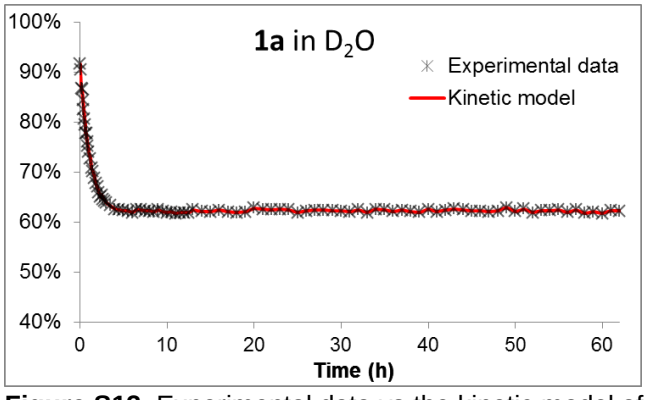


Figure S13. Experimental data vs the kinetic model of **1a**.

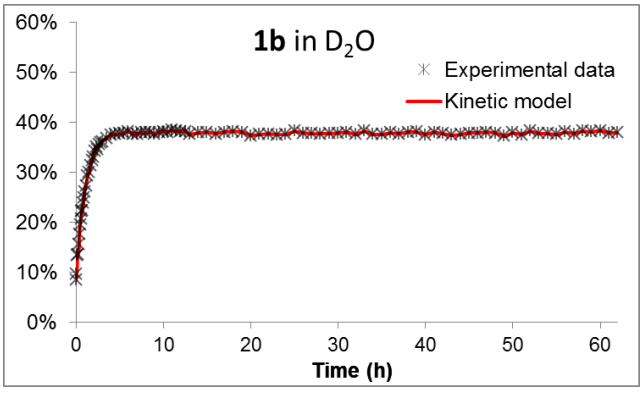


Figure S14. Experimental data vs the kinetic model of **1b**

Kinetic modeling of monosaccharide 3 in buffered D_2O

In Figure S15-S19 is the kinetic modeling of the migration in **3** in buffered D_2O at 25 °C and pD = 8 shown. The kinetic model explains the experimental data with 99.94%.

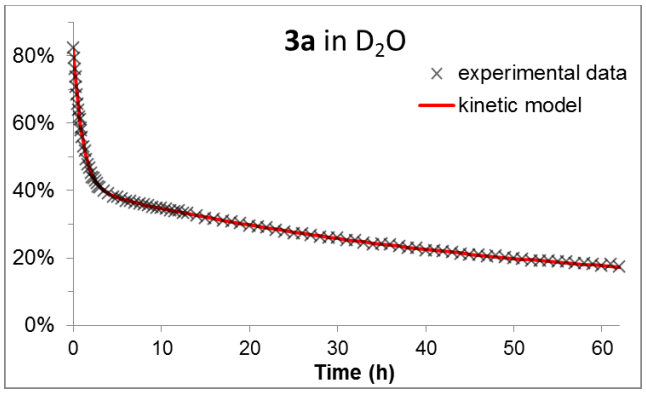


Figure S15. Experimental data vs the kinetic model of **3a** in buffered D_2O at 25 °C and pD = 8.

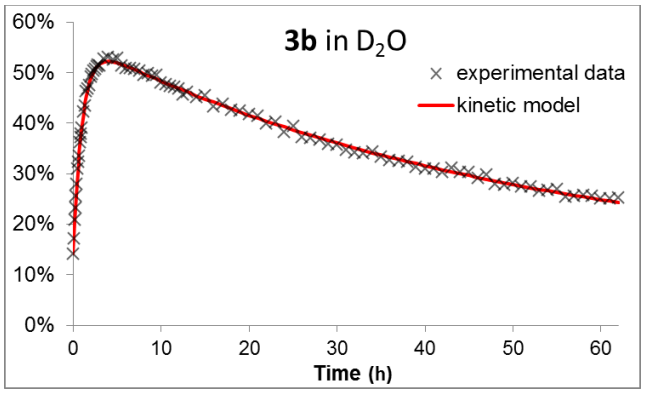


Figure S16. Experimental data vs the kinetic model of **3b** in buffered D_2O at 25 °C and pD = 8.

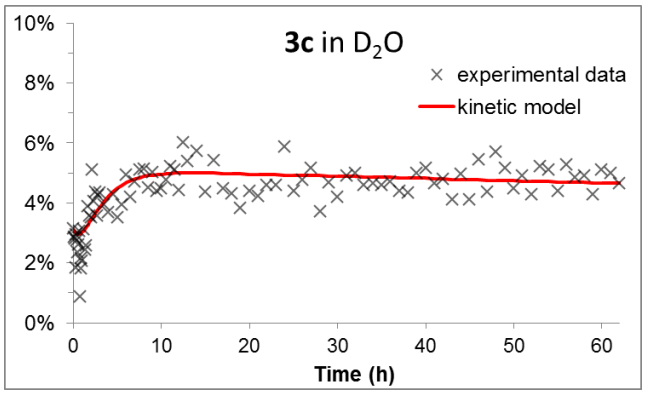


Figure S17. Experimental data vs the kinetic model of **3c** in buffered D_2O at 25 °C and pD = 8.

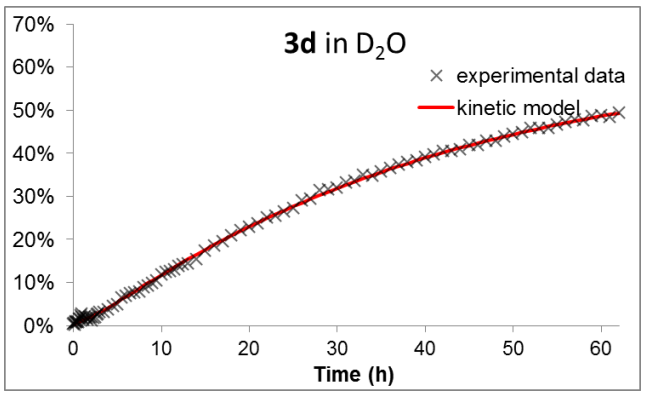


Figure S18. Experimental data vs the kinetic model of **3d** in buffered D_2O at 25 °C and pD = 8.

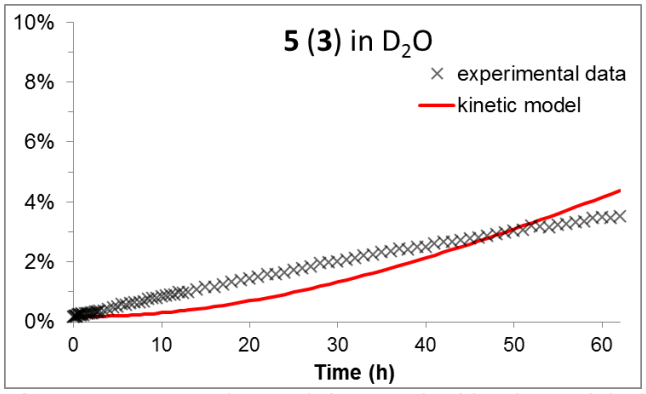


Figure S19. Experimental data vs the kinetic model of **5** from **3** in buffered D_2O at 25 °C and pD = 8.

Kinetic modeling of monosaccharide 4 in buffered D_2O

In Figure S20-S24 is the kinetic modeling of the migration in **4** in buffered D_2O at 25 °C and pD = 8 shown. The kinetic model explains the experimental data with 99.94%.

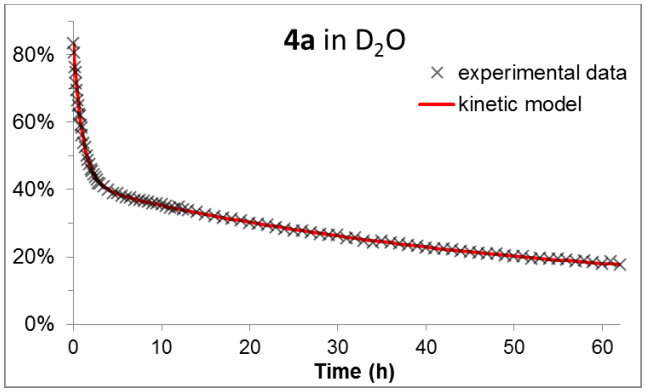


Figure S20. Experimental data vs the kinetic model of **4a** in buffered D_2O at 25 °C and pD = 8.

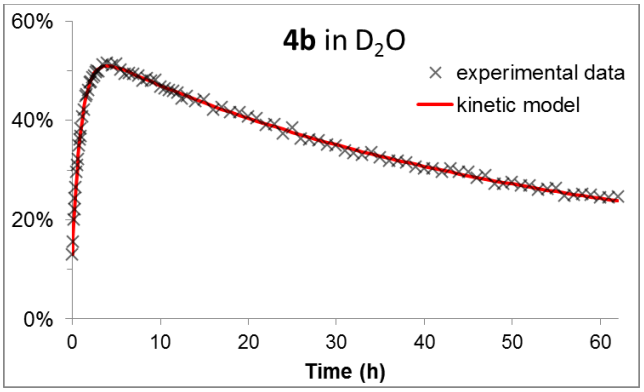


Figure S21. Experimental data vs the kinetic model of **4b** in buffered D_2O at 25 °C and pD = 8.

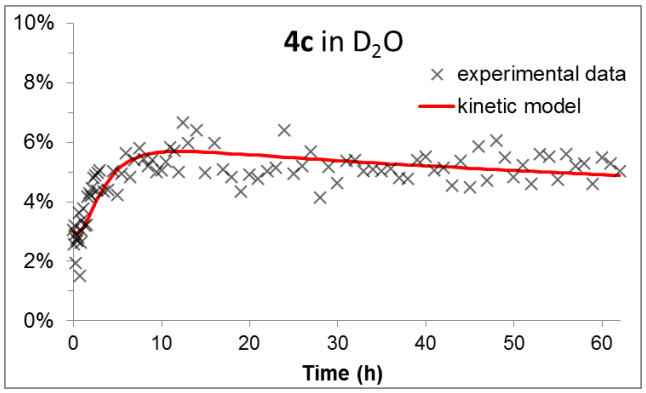


Figure S22. Experimental data vs the kinetic model of **4c** in buffered D_2O at 25 °C and pD = 8.

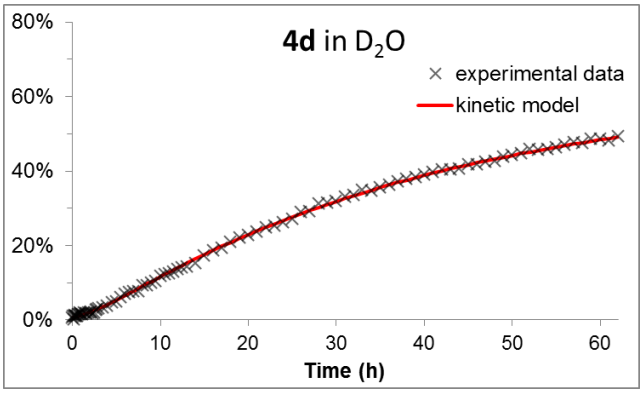


Figure S23. Experimental data vs the kinetic model of **4d** in buffered D_2O at 25 °C and pD = 8.

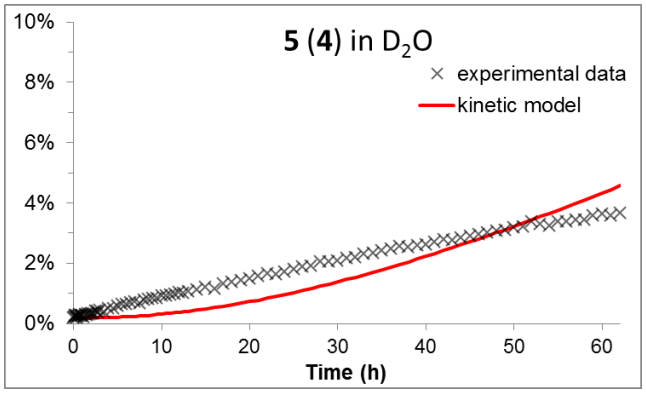


Figure S24. Experimental data vs the kinetic model of **5** from **4** in buffered D_2O at 25 °C and pD = 8.

Kinetic modeling of monosaccharide 3 in buffered H_2O

In Figure S25-S29 is the kinetic modeling of the migration in **3** in buffered H_2O at 25 °C and pD = 8 shown. The kinetic model explains the experimental data with 99.77%.

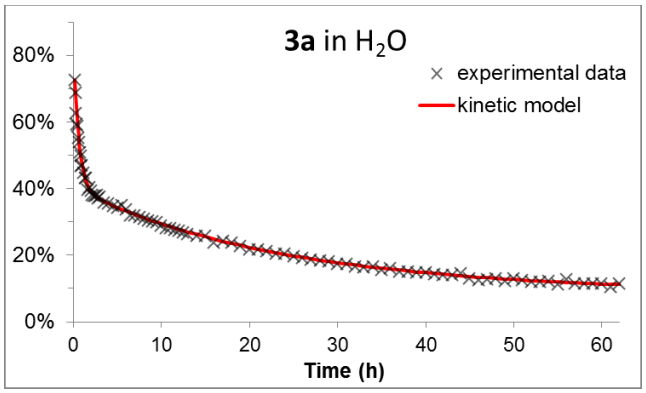


Figure S25. Experimental data vs the kinetic model of **3a** in buffered H_2O at 25 °C and pH= 8.

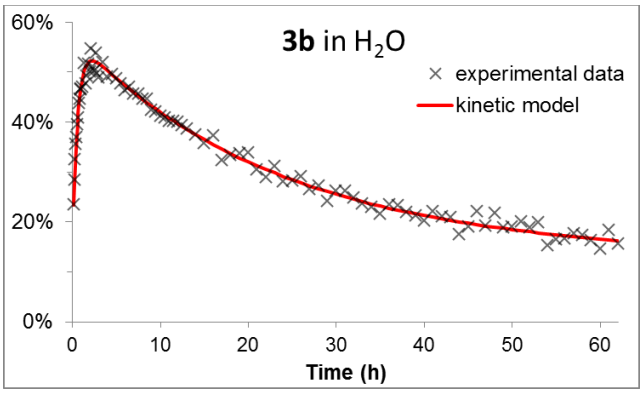


Figure S26. Experimental data vs the kinetic model of **3b** in buffered H_2O at 25 °C and pH= 8.

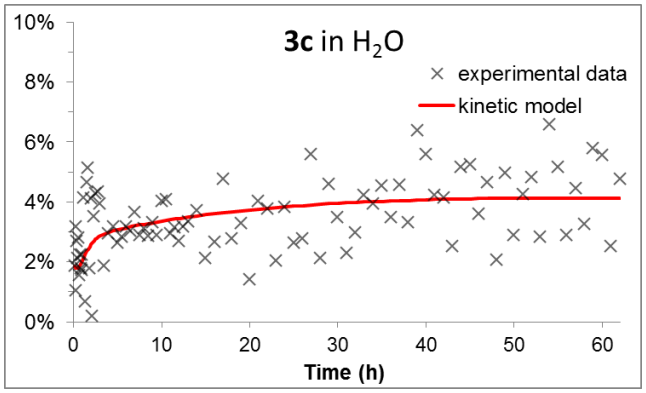


Figure S27. Experimental data vs the kinetic model of **3c** in buffered h$_2$O at 25 °C and pH = 8.

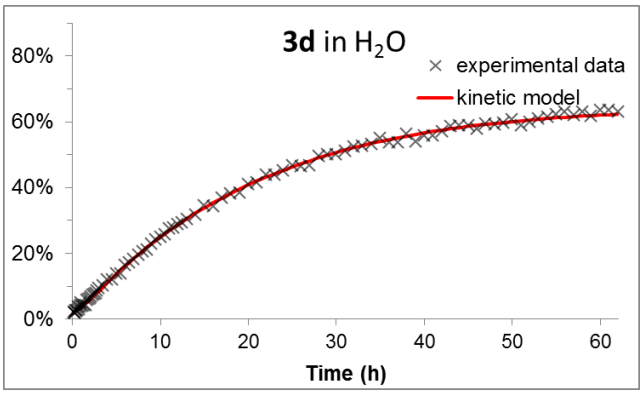


Figure S28. Experimental data vs the kinetic model of **3d** in buffered H_2O at 25 °C and pH = 8.

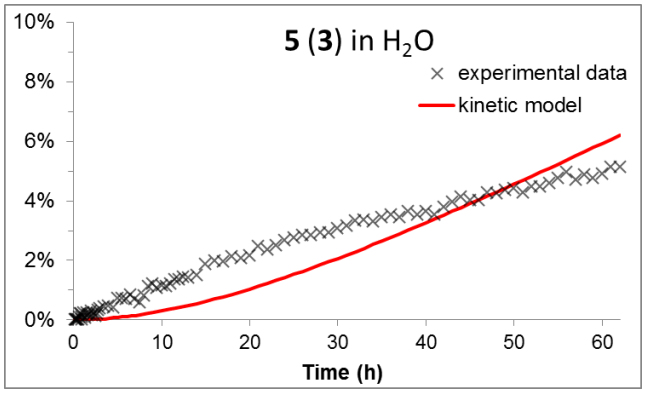


Figure S29. Experimental data vs the kinetic model of **5** from **3** in buffered H_2O at 25 °C and pH= 8.

Experimental procedures

Standard reaction procedure for β-mannosylation. To a solution of the donor (1 equivalent) in dry CH_2Cl_2 (1 ml/50 mg donor) at –60 °C (acetone + dry ice), 4 Å molecular sieves, BSP (1.2 equivalents), TTBP (1.5 equivalents) and Tf_2O (1.3 equivalents) were added. The reaction mixture was stirred for 0.5 h (until activation of the donor was complete). The reaction mixture was then cooled to –78 °C and the acceptor (0.7 or 0.9 equivalents), dissolved in CH_2Cl_2 (1 ml/70 mg acceptor), was added dropwise. The reaction was stirred at –78 °C for 1 – 3 h (until completion) and then quenched with Et_3N and stirred for 0.5 h. The reaction mixture was then warmed to room temperature and diluted with CH_2Cl_2. Next, the mixture was washed with saturated $NaHCO_3$ solution (80 ml/100 mg acceptor), water (80 ml/100 mg acceptor) and saturated NaCl solution (50 ml/100 mg acceptor). The organic phase was dried over Na_2SO_4 and the solvent evaporated. The product was purified using column chromatography.

Standard reaction procedures for hydrogenolysis of benzyl- and benzylidene protecting groups. General method A: To a solution of the substrate in dry MeOH (1.5 ml/10 mg substrate) Pd/C 10% w/w (2 weight equivalents) was added. The reaction mixture was stirred under 2 bar H_2-gas in an autoclave reactor for 17 – 20 h, followed by filtration and evaporation of the solvent. General method B: Alternatively, to a solution of the substrate in dry MeOH (1 ml/20 mg substrate) and AcOH (0.5 ml/20 mg substrate) Pd/C 10% w/w (2 weight equivalents) was added. The reaction mixture was stirred under 3 bar H_2-gas in an autoclave reactor for 4 h, after which the mixture was filtered and the solvent evaporated.

Methyl 2-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranoside (7). To a solution of **6** (900 mg, 1 equivalent) in pyridine (5 ml) at 0 °C was added AcCl (260 µl, 1.5 equivalents). After 1 h, the reaction mixture was warmed to room temperature and then after 1 h the reaction was quenched by the addition of MeOH followed by diluted with CH_2Cl_2 (100 ml) and washing with saturated $NaHCO_3$ solution (80 ml), 1 M HCl (80 ml) and saturated NaCl solution (50 ml). The organic phase was dried over Na_2SO_4, filtered and evaporated. The crude product was purified by column chromatography (hexane:EtOAc 4:1) to obtain **7** as a clear oil. Yield: 850 mg (85%), R_f = 0.25. ^{1}H NMR (500.20 MHz, $CDCl_3$, 25 °C): δ = 7.53 – 7.24 (m, 10 H, aromatic H), 5.64 (s, 1 H, 4,6-OC*H*Ph), 5.39 (dd, 1 H, $J_{H\text{-}1,H\text{-}2}$ = 1.6 Hz, $J_{H\text{-}2,H\text{-}3}$ = 3.5 Hz, H-2), 4.70 (d, 1 H, *J* = –12.2 Hz, 3-OC*H*$_2$Ph), 4.69 (d, 1 H, H-1), 4.65 (d, 1 H, 3-OC*H*$_2$Ph), 4.28 (dd, 1 H, $J_{H\text{-}5,H\text{-}6a}$ = 4.8 Hz, $J_{H\text{-}6a,H\text{-}6b}$ = – 10.3 Hz, H-6a), 4.06 (dd, 1 H, $J_{H\text{-}3,H\text{-}4}$ = 9.9 Hz, $J_{H\text{-}4,H\text{-}5}$ = 9.3 Hz, H-4), 4.00 (dd, 1 H, H-3), 3.86 (dd, 1 H, $J_{H\text{-}5,H\text{-}6b}$ = 10.4 Hz, H-6b), 3.83 (ddd, 1 H, H-5), 3.37 (s, 3 H, 1-OCH3), 2.17 (s, 3H, 2-OAc) ppm. ^{13}C NMR (125.78 MHz, $CDCl_3$, 25 °C): δ = 170.3 (2-O*C*OCH$_3$), 137.9, 137.4, 129.0, 128.4, 128.2, 127.70, 127.68, 126.1 (aromatic), 101.6 (4,6-O*C*HPh), 99.8 (C-1), 78.2 (C-4), 73.7 (C-3), 72.1 (3-O*C*H$_2$Ph), 69.6 (C-2), 68.8 (C-6), 63.7 (C-5), 55.1 (1-O*C*H3), 21.1 (2-OCO*C*H$_3$) ppm.

Methyl 2-*O*-acetyl-β-D-mannopyranoside (3). Prepared from **7** (20 mg, 0.05 mmol) by the general method B for hydrogenolysis of the benzyl and benzylidene protection groups. Yield: 11 mg (95%). ^{1}H NMR (500.20 MHz,

MeOD, 25 °C): δ = 4.97 (dd, 1 H, $J_{H-1,H-2}$ = 1.7 Hz, $J_{H-2,H-3}$ = 3.6 Hz, H-2), 4.64 (d, 1 H, H-1), 3.84 (dd, 1 H, $J_{H-5,H-6a}$ = 2.3 Hz, $J_{H-6a,H-6b}$ = – 11.9 Hz, H-6a), 3.83 (dd, 1 H, $J_{H-3,H-4}$ = 9.6 Hz, H-3), 3.70 (dd, 1 H, $J_{H-5,H-6b}$ = 6.0 Hz, H-6b), 3.60 (dd, 1 H, $J_{H-4,H-5}$ = 9.9 Hz, H-4), 3.51 (ddd, 1 H, H-5), 3.38 (s, 3 H, 1-OCH_3), 2.08 (s, 3 H, 2-OCOCH_3) ppm. ^{13}C NMR (125.78 MHz, MeOD, 25 °C): δ = 172.4 (2-O*C*OCH$_3$), 99.8 (C-1), 74.6 (C-5), 73.8 (C-2), 70.7 (C-3), 68.8 (C-4), 62.7 (C-6), 55.3 (1-O*C*H$_3$), 20.8 (2-OCO*C*H$_3$) ppm. HRMS: calculated for $C_9H_{16}O_7Na$, $[M + Na]^+$: 259.0788 and measured: 259.0839.

Methyl 2-*O*-acetyl-(1-^{13}C)-3-*O*-benzyl-4,6-*O*-benzylidene--β-D-mannopyranoside (8). To a solution of **6** (200 mg, 1 equivalent) in pyridine (1 ml) at 0 °C was added AcCl (1-^{13}C) (57 µl, 1.5 equivalents). After 1 h, the reaction mixture was warmed to room temperature. Next, after stirring for 1 h, the reaction was quenched by the addition of MeOH followed by dilution with CH_2Cl_2 (100 ml) and washing with saturated $NaHCO_3$ solution (80 ml), 1 M HCl (80 ml) and saturated NaCl solution (50 ml). The organic phase was dried over Na_2SO_4, filtered and evaporated. The crude product was purified by column chromatography (hexane:EtOAc 4:1) to provde **8** as a clear oil. Yield: 850 mg (59%), R_f = 0.28. ^{1}H NMR (500.20 MHz, $CDCl_3$, 25 °C): δ = 7.53 – 7.23 (m, 10 H, aromatic H), 5.63 (s, 1 H, 4,6-OC*H*Ph), 5.38 (ddd, 1 H, *J*H-2,H-1 = 1.6 Hz, *J*H-2,H-3 = 3.5 Hz, *J*H-2,2-O*C*CH3 = 4.0 Hz, H-2), 4.69 (d, 1 H, *J* = –12.2 Hz, 3-OC*H*2Ph), 4.68 (d, 1 H, H-1), 4.66 (d, 1 H, 3-OC*H*2Ph), 4.27 (dd, 1 H, *J*H-6a,H-5 = 4.8 Hz, *J*H-6a,H-6b = – 10.3 Hz, H-6a), 4.06 (dd, 1 H, *J*H-4,H-3 = 9.9 Hz, *J*H-4,H-5 = 9.3 Hz, H-4), 3.99 (dd, 1 H, H-3), 3.85 (dd, 1 H, *J*H-6b,H-5 = 10.4 Hz, H-6b), 3.83 (ddd, 1 H, H-5), 3.37 (s, 3 H, 1-OC*H*3), 2.16 (s, 3H, *J*2-OCOC*H$_3$*,2-O*C*CH$_3$ = 6.9 Hz, 2-O^{13}COC*H$_3$*) ppm. ^{13}C NMR (125.78 MHz, $CDCl_3$, 25 °C): δ = 170.2 (2-O*C*OCH$_3$), 138.0, 137.5, 128.0, 128.4, 128.2, 127.7, 127.6, 126.1 (aromatic), 101.6 (4,6-O*C*HPh), 99.8 (C-1), 78.3 (C-4), 73.8 (C-3), 72.1 (3-O*C*H2Ph), 69.7 (*J*C-2, 2-O*^{13}CO*CH$_3$ = 3 Hz, C-2), 68.8 (C-6), 63.7 (C-5), 55.1 (1-O*C*H3), 21.0 (*J*2-O^{13}C*OC*H$_3$, 2-O*^{13}CO*CH$_3$ = 60 Hz, 2-O^{13}CO*C*H$_3$) ppm.

Methyl 2-*O*-acetyl-(1-^{13}C)-β-D-mannopyranoside (4). Prepared from **8** (20 mg, 0.05 mmol) according to the general method A for hydrogenolysis of benzyl- and benzylidene protection groups. Yield: 11 mg (96%). ^{1}H NMR (500.20 MHz, MeOD, 25 °C): δ = 4.97 (dd, 1 H, $J_{H-1,H-2}$ = 1.7 Hz, $J_{H-2,H-3}$ = 3.5 Hz, *J* H-2, 2-O*^{13}*COCH$_3$= 3.7 Hz, H-2), 4.64 (d, 1 H, H-1), 3.84 (dd, 1 H, $J_{H-5,H-6a}$ = 2.3 Hz, $J_{H-6a,H-6b}$ = – 11.9 Hz, H-6a), 3.83 (dd, 1 H, $J_{H-3,H-4}$ = 9.6 Hz, H-3), 3.70 (dd, 1 H, $J_{H-5,H-6b}$ = 6.0 Hz, H-6b), 3.61 (dd, 1 H, $J_{H-4,H-5}$ = 9.9 Hz, H-4), 3.51 (ddd, 1 H, H-5), 3.38 (s, 3 H, 1-OCH_3), 2.08 (s, 3 H, *J*2-O^{13}COC*H$_3$*, 2-O*^{13}*COCH$_3$ = 6.9 Hz, 2-O^{13}COC*H$_3$*) ppm. ^{13}C NMR (125.78 MHz, MeOD, 25 °C): δ = 172.3 (2-O*C*OCH$_3$), 99.8 (C-1), 74.6 (C-5), 73.8 (*J*C-2, 2-O*^{13}CO*CH$_3$ = 3 Hz, C-2), 70.7 (C-3), 68.8 (C-4), 62.7 (C-6), 55.3 (1-O*C*H$_3$), 20.8 (*J*2-O^{13}C*OC*H$_3$, 2-O*^{13}CO*CH$_3$ = 60 Hz, 2-O^{13}CO*C*H$_3$) ppm.

Methyl 2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (9). To a solution of **6** (85 mg, 0.2 mmol) in dry CH_2Cl_2 (4 ml) at 0 °C were added Et_3SiH (163 µl, 5 equivalents) and TFA (78 µl, 5 equivalents). After 2 h, the reaction was complete and the mixture was brought to room temperature. The reaction mixture was diluted with CH_2Cl_2 (20 ml) and washed with saturated $NaHCO_3$ solution (15 ml) and saturated NaCl solution (15 ml). The organic

phase was separated, dried over Na_2SO_4, filtered and the solvent was evaporated. The crude product was purified by column chromatography (hexane:EtOAc 1:1) to provide **9** as a colorless oil (43 mg, 50 %). ^{1}H NMR (500.20 MHz, $CDCl_3$, 25°C): δ = 7.48 – 7.20 (m, 10 H, aromatic H), 5.34 (dd, 1 H, $J_{H\text{-}2,H\text{-}1}$ = 1.8 Hz, $J_{H\text{-}2,H\text{-}3}$ = 3.2 Hz, H-2), 4.73 (d, 1 H, H-1), 4.70 (d, 1 H, *J* = –11.3 Hz, 6-OC*H*2Ph), 4.64 (d, 1 H, *J* = –12.1 Hz, 3-OC*H*2Ph), 4.58 (d, 1 H, 3-OC*H*2Ph), 4.45 (d, 1 H, *J* = –11.3 Hz, 6-OC*H*2Ph), 3.92 (ddd, 1 H, $J_{H\text{-}4,H\text{-}3}$ = 10.5 Hz, $J_{H\text{-}4,H\text{-}5}$ = 8.4 Hz, $J_{H\text{-}4,4\text{-}OH}$ = 1.7 Hz, H-4), 3.76 (dd, 1 H, $J_{H\text{-}6a,H\text{-}5}$ = 4.6 H z, $J_{H\text{-}6a,H\text{-}6b}$ = – 10.7 Hz, H-6a), 3.77 (dd, 1 H, $J_{H\text{-}6b,H\text{-}5}$ = 6.4 Hz, H-6b), 3.76 (dd, 1 H, H-3), 3.75 (ddd, 1 H, H-5), 3.37 (s, 3 H, 1-OC*H*3), 2.54 (d, 1H, 4-OH), 2.10 (s, 3H, 2-OCOC*H*$_3$) ppm. ^{13}C NMR (125.78 MHz, $CDCl_3$, 25 °C): δ = 170.4 (2-O*C*OCH_3), 138.2, 137.7, 128.6, 128.4, 128.1, 128.0, 127.6, 127.6 (aromatic), 99.0 (C-1), 77.6 (C-3), 73.6 (6-O*C*H2Ph), 71.6 (3-O*C*H2Ph), 71.2 (C-5), 69.8 (C-6), 67.9 (C-2), 67.2 (C-4), 55.1 (1-O*C*H_3), 21.0 (2-OCO*C*H_3) ppm. HRMS: Calculated for $C_{23}H_{28}O_7Na$ $[M + Na]^+$ 439.172, measured 439.194 (MALDI-TOF, positive mode).

Methyl *O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-α-D-mannopyranoside (11). Prepared from donor **10** (202 mg, 1 equivalent) and acceptor **9** (105 mg, 0.7 equivalent) according to the standard reaction procedure for β-mannosylation. The crude product was purified by column chromatography (hexane:EtOAc 3:1 and CH_2Cl_2:MeOH 80:1) to provide **11** as a clear oil. Yield: 69 mg (32%), R_f = 0.21 (CH_2Cl_2:MeOH 80:1).^{1}H NMR (500.20 MHz, $CDCl_3$, 25 °C): δ = 7.48 – 7.19 (m, 25 H, aromatic H), 5.53 (s, 1 H, 4',6'-OC*H*Ph), 5.28 (dd, 1 H, $J_{H\text{-}1,H\text{-}2}$ = 1.9 Hz, $J_{H\text{-}2,H\text{-}3}$ = 3.6 Hz, H-2), 4.78 (d, 1 H, *J* = –11.9 Hz, 2'-OCH_2Ph), 4.74 (d, 1 H, 2'-OCH_2Ph), 4.73 (d, 1 H, *J* = –12.4 Hz, 3'-OCH_2Ph), 4.71 (d, 1 H, H-1), 4.67 (d, 1 H, *J* = –12.1 Hz, 6-OCH_2Ph), 4.65 (d, 1 H, *J* = –11.6 Hz, 3-OCH_2Ph), 4.63 (d, 1 H, 3-OCH_2Ph), 4.58 (d, 1 H, 3'-OCH_2Ph), 4.50 (d, 1 H, $J_{H\text{-}1',H\text{-}'2}$ = 1.0 Hz, H-1'), 4.38 (d, 1 H, 6-OCH_2Ph), 4.11 (dd, 1 H, $J_{H\text{-}3,H\text{-}4}$ = 9.2 Hz, $J_{H\text{-}4,H\text{-}5}$ = 9.9 Hz, H-4), 4.09 (dd, 1 H, $J_{H\text{-}3',H\text{-}4'}$ = 10.0 Hz, $J_{H\text{-}4',H\text{-}5'}$ = 9.3 Hz, H-4'), 4.06 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'a}$ = 4.8 Hz, $J_{H\text{-}6'a,H\text{-}6'b}$ = –10.4 Hz, H-6'a), 3.92 (dd, 1 H, H-3), 3.70 (ddd, 1 H, $J_{H\text{-}5,H\text{-}6a}$ = 3.6 Hz, $J_{H\text{-}5,H\text{-}6b}$ = 2.1 Hz, H-5), 3.69 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'b}$ = 10.1 Hz, H-6'b), 3.67 (dd, 1 H, $J_{H\text{-}2',H\text{-}3'}$ = 3.1 Hz, H-2'), 3.61 (dd, 1 H, $J_{H\text{-}6a,H\text{-}6b}$ = –10.9 Hz, H-6a), 3.60 (dd, 1 H, H-6b), 3.40 (dd, 1 H, H-3'), 3.37 (s, 3 H, 1-OC*H*$_3$), 3.05 (ddd, 1 H, H-5'), 2.11 (s, 3 H, 2-OCOC*H*$_3$) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$, 25 °C): δ = 170.4 (2-O*C*OCH_3), 138.7 – 126.1 (aromatic C), 101.6 (C-1'), 101.4 (4'6'-O*C*HPh), 98.6 (C-1), 78.8 (C-4'), 78.4 (C-3'), 77.2 (C-2'), 75.6 (C-3), 75.2 (C-4), 74.9 (2'-O*C*H_2Ph), 73.5 (6-O*C*H_2Ph), 72.5 (3'-O*C*H_2Ph), 71.9 (3-O*C*H_2Ph), 70.7 (C-5), 69.1 (C-2), 68.8 (C-6), 68.6 (C-6'), 67.3 (C-5'), 55.1 (1-O*C*H_3), 21.1 (2-OCO*C*H_3) ppm. $^1J_{C\text{-}1,H\text{-}1}$ = 169 Hz (α), $^1J_{C\text{-}1',H\text{-}1'}$ = 157 Hz (β). HRMS: calculated for $C_{50}H_{54}O_{12}K$, $[M + K]^+$ 885.3247, measured 885.3271.

Methyl *O*-(β-D-mannopyranosyl)-(1→4)-2-*O*-acetyl-β-D-mannopyranoside (1). Prepared from **11** (23 mg, 0.03 mmol) according to the general method B for hydrogenolysis of benzyl and benzylidene protection groups. Yield: 11 mg (99%). ^{1}H NMR (500.20 MHz, MeOD, 25 °C): δ 5.05 (dd, 1 H, $J_{H\text{-}1,H\text{-}2}$ = 1.7 Hz, $J_{H\text{-}2,H\text{-}3}$ = 3.6 Hz, H-2), 4.66 (d, 1 H, $J_{H\text{-}1',H\text{-}'2}$ = 1.0 Hz, H-1'), 4.65 (d, 1 H, H-1), 3.99 (dd, 1 H, $J_{H\text{-}3,H\text{-}4}$ = 9.5 Hz, H-3), 3.95 (dd, 1 H, $J_{H\text{-}4,H\text{-}5}$ = 9.9 Hz, H-4), 3.91 (dd, 1 H, $J_{H\text{-}2',H\text{-}3'}$ = 3.2 Hz, H-2'), 3.89 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'a}$ = 2.3 Hz, $J_{H\text{-}6'a,H\text{-}6'b}$ = –12.0 Hz, H-6'a), 3.79 (dd, 1 H, $J_{H\text{-}5,H\text{-}6a}$ = 2.2 Hz, $J_{H\text{-}6a,H\text{-}6b}$ = –12.2 Hz, H-6a), 3.74 (dd, 1 H, $J_{H\text{-}5,H\text{-}6b}$ = 4.1 Hz, H-6b), 3.68 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'b}$ =

6.6 HzH-6'b), 3.58 (ddd, 1 H, H-5), 3.52 (dd, 1 H, $J_{H\text{-}3',H\text{-}4'}$ = 9.4 Hz, $J_{H\text{-}4',H\text{-}5'}$ = 9.8 Hz, H-4'), 3.46 (dd, 1 H, H-3'), 3.37 (s, 3 H, 1-OCH_3), 3.28 (ddd, 1 H, H-5'), 2.09 (s, 3 H, 2-OCOCH_3) ppm. ^{13}C NMR (125.8 MHz, MeOD, 25 °C): δ = 172.2 (2-OCOCH$_3$), 101.6 (C-1'), 99.8 (C-1), 78.6 (C-5'), 77.4 (C-4), 75.1 (C-3'), 73.2 (C-2), 73.0 (C-5), 72.5 (C-2'), 69.4 (C-3), 68.5 (C-4'), 62.8 (C-6'), 61.7 (C-6), 55.4 (1-OCH$_3$), 20.9 (2-OCOCH$_3$) ppm. HRMS: calculated for $C_{15}H_{26}O_{12}Na$, $[M + Na]^+$ 421.1316, measured 421.1320.

Methyl *O*-(4,6-*O*-benzylidene-2,3-di-*O*-*p*-methoxybenzyl-β-D-mannopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (14). Prepared from donor **12** (170 mg, 1 equivalent) and acceptor **13** (120 mg, 0.9 equivalent) according to the standard reaction procedure for β-mannosylation. The crude product was purified by column chromatography (hexane:EtOAc 3:1) to provide **14** as a clear oil. Yield: 110 mg (45%), R_f = 0.46. ^{1}H NMR (500.20 MHz, $CDCl_3$, 25 °C): δ = 7.47 – 6.78 (m, 28 H, aromatic H), 5.50 (s, 1 H, 4',6'-OCHPh), 4.83 (d, 1 H, J = –12.0 Hz, 3-OCH_2Ph), 4.74 (d, 1 H, $J_{H\text{-}1,H\text{-}2}$ = 2.4 Hz, H-1), 4.73, (d, 1 H, J = –12.3 Hz, 2-OCH_2Ph), 4.71 (d, 1 H, J = –11.6 Hz, 2'-OCH_2Ph), 4.69 (d, 1 H, 2'-OCH_2Ph), 4.67 (d, 1 H, 2-OCH_2Ph), 4.66 (d, 1 H, J = –12.0 Hz, 6-OCH_2Ph), 4.61 (d, 1 H, J = –11.9 Hz, 3'-OCH_2Ph), 4.57 (d, 1 H, 3-OCH_2Ph), 4.49 (d, 1 H, $J_{H\text{-}1',H\text{-}'2}$ = 0.9 Hz, H-1'), 4.48 (d, 1 H, 3'-OCH_2Ph), 4.43 (d, 1 H, 6-OCH_2Ph), 4.18 (dd, 1 H, $J_{H\text{-}3,H\text{-}4}$ = 8.4 Hz, $J_{H\text{-}4,H\text{-}5}$ = 9.4 Hz, H-4), 4.03 (dd, 1 H, $J_{H\text{-}3',H\text{-}4'}$ = 9.9 Hz, $J_{H\text{-}4',H\text{-}5'}$ = 9.3 Hz, H-4'), 4.02 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'a}$ = 4.8 Hz, $J_{H\text{-}6'a,H\text{-}6'b}$ = –10.4 Hz, H-6'a), 3.86 (dd, 1 H, $J_{H\text{-}2,H\text{-}3}$ = 3.2 Hz, H-3), 3.79 (s, 3 H, OCH$_2$Ph-*p*-OCH_3), 3.77 (s, 3 H, OCH$_2$Ph-*p*-OCH_3), 3.75 (dd, 1 H, H-2), 3.67 (ddd, 1 H, $J_{H\text{-}5,H\text{-}6}$ = 3.4 Hz, H-5), 3.67 (dd, 1 H, $J_{H\text{-}2',H\text{-}3'}$ = 3.0 Hz, H-2'), 3.62 (d, 2 H, H-6), 3.61 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'b}$ = 10.1 Hz, H-6'b), 3.38 (dd, 1 H, H-3'), 3.36 (s, 3 H, 1-OCH_3), 3.07 (ddd, 1 H, H-5') ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$, 25 °C): δ = 139.3 – 113.4 (aromaticC), 102.1 (C-1'), 101.3 (4'6'-OCHPh), 99.5 (C-1), 78.7 (C-4'), 78.1 (C-3, C-3'), 76.6 (C-2'), 76.3 (C-4), 75.8 (C-2), 74.5 (2'-OCH$_2$Ph-*p*-OCH$_3$), 73.5 (6-OCH$_2$Ph), 72.8 (2-OCH$_2$Ph), 72.6 (3-OCH$_2$Ph), 72.2 (3'-OCH$_2$Ph-*p*-OCH$_3$), 71.2 (C-5), 69.3 (C-6), 68.6 (C-6'), 67.3 (C-5'), 55.3 (OCH$_2$Ph-OCH$_3$), 55.2(OCH$_2$Ph-OCH$_3$), 54.9 (1-OCH$_3$) ppm. $^1J_{C\text{-}1,H\text{-}1}$ = 169 Hz (α), $^1J_{C\text{-}1',H\text{-}1'}$ = 156 Hz (β). HRMS: calculated for $C_{57}H_{62}O_{13}Na$, $[M + Na]^+$ 977.4083, measured 977.4048.

Methyl *O*-(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (15). To a solution of **14** (360 mg, 1 equivalent) in CH_2Cl_2:MeOH:H_2O 92:4:4 (11.4 ml) at 0 °C was added DDQ (260 mg, 3 equivalents) in CH_2Cl_2 (7.5 ml). After 3 h, the reaction mixture was diluted with CH_2Cl_2 (100 ml) and washed with saturated $NaHCO_3$ solution (2 × 80 ml), water (80 ml), and saturated NaCl solution (80 ml). The organic phase was dried over Na_2SO_4, filtered and the solvent was evaporated. The product was filtered through silica gel (hexane:EtOAc 3:1 → 1:1). The product (200 mg, 1 equivalent) was dissolved in pyridine (3 ml) and BzCl (115 µl, 3.5 equivalents) was added. After 1.5 h, the reaction mixture was diluted with CH_2Cl_2 (120 ml) and washed with saturated $NaHCO_3$ solution (2 × 80 ml), 1 M HCl (80 ml) and saturated NaCl solution (80 ml). The organic phase was dried over Na_2SO_4, filtered and evaporated. The crude product was purified by column chromatography (hexane:EtOAc 2:1) to provide **15** as a white foam. Yield: 210 mg (64%), R_f = 0.36. ^{1}H NMR (500.20 MHz, $CDCl_3$, 25 °C): δ = 8.06 – 7.24 (m, 30 H, aromatic H), 5.77 (dd, 1 H, $J_{H\text{-}1',H\text{-}2'}$ = 1.2 Hz, $J_{H\text{-}2',H\text{-}3'}$ = 3.4 Hz,

H-2'), 5.53 (s, 1 H, 4',6'-OC*H*Ph), 5.33 (dd, 1 H, $J_{H\text{-}3',H\text{-}4'}$ = 10.4 Hz, H-3'), 4.97 (d, 1 H, H-1'), 4.78 (d, 1 H, *J* = –11.8 Hz, 3-OCH_2Ph), 4.74 (d, 1 H, *J* = –12.4 Hz, 2-OCH_2Ph), 4.71 (d, 1 H, $J_{H\text{-}1,H\text{-}2}$ = 1.8 Hz, H-1), 4.69 (d, 1 H, *J* = –11.8 Hz, 6-OCH_2Ph), 4.68 (d, 1 H, 2-OCH_2Ph), 4.49 (d, 1 H, 6-OCH_2Ph), 4.46 (d, 1 H, 3-OCH_2Ph), 4.36 (dd, 1 H, $J_{H\text{-}3,H\text{-}4}$ = 9.2 Hz, $J_{H\text{-}4,H\text{-}5}$ = 9.7 Hz, H-4), 4.18 (dd, 1 H, $J_{H\text{-}5'a,H\text{-}6'a}$ = 4.8 Hz, $J_{H\text{-}6'a,H\text{-}6'b}$ = –10.5 Hz, H-6'a), 4.11 (dd, 1 H, $J_{H\text{-}3',H\text{-}4'}$ = 10.4 Hz, $J_{H\text{-}4',H\text{-}5'}$ = 9.5 Hz, H-4'), 3.78 (dd, 1 H, $J_{H\text{-}5,H\text{-}6a}$ = 4.1 Hz, $J_{H\text{-}6a,H\text{-}6b}$ = –11.0 Hz, H-6a), 3.76 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'b}$ = 10.0 Hz, H-6'b), 3.73 (dd, 1 H, $J_{H\text{-}2,H\text{-}3}$ = 3.3 Hz, H-3), 3.71 (dd, 1 H, H-2), 3.68 (dd, 1 H, $J_{H\text{-}5,H\text{-}6b}$ = 1.9 Hz, H-6b), 3.62 (ddd, 1 H, H-5), 3.30 (ddd, 1 H, H-5'), 3.27 (s, 3 H, 1-OCH_3) ppm. ^{13}C NMR (125.78 MHz, $CDCl_3$, 25 °C): δ = 165.5 (2-O*C*OPh), 165.4 (3-O*C*OPh), 139.2 – 126.2 (aromatic C), 101.8 (4'6'-O*C*HPh), 99.4 (C-1'), 99.2 (C-1), 78.4 (C-3), 76.4 (C-4), 75.6 (C-4'), 75.5 (C-2), 73.5 (6-O*C*H_2Ph), 72.8 (3-O*C*H_2Ph), 72.7 (2-O*C*H_2Ph), 70.9 (C-5), 70.8 (C-3'), 70.4 (C-2'), 70.0 (C-6), 68.7 (C-6'), 67.0 (C-5'), 54.8 (1-O*C*H_3) ppm. $^1J_{C\text{-}1,H\text{-}1}$ = 168 Hz (α), $^1J_{C\text{-}1',H\text{-}1'}$ = 156 Hz (β). HRMS: calculated for $C_{55}H_{54}O_{13}Na$, $[M + Na]^+$ 945.3457, measured 945.3526.

Methyl *O*-(2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-mannopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (16). To a solution of **15** (100 mg, 1 equivalent) in CH_2Cl_2 (2.5 ml) at 0 °C, Et_3SiH (215 µl, 12 equivalents) and $BF_3{\cdot}OEt_2$ (22 µl, 1.6 equivalents) were added and the reaction mixture was stirred for 6 h. The reaction mixture was then diluted with CH_2Cl_2 (80 ml) and washed with saturated $NaHCO_3$ solution (80 ml) and saturated NaCl solution (80 ml). The organic phase was dried over Na_2SO_4, filtered and evaporated. The crude product was purified by column chromatography (hexane:EtOAc 2:1) to provide **16** as a white foam. Yield: 75 mg (73%), R_f = 0.24. ^{1}H NMR (500.20 MHz, $CDCl_3$, 25 °C): δ = 8.03 – 7.23 (m, 30 H, aromatic H), 5.66 (dd, 1 H, $J_{H\text{-}1',H\text{-}2'}$ = 1.0 Hz, $J_{H\text{-}2',H\text{-}3'}$ = 3.3 Hz, H-2'), 5.10 (dd, 1 H, $J_{H\text{-}3',H\text{-}4'}$ = 9.8 Hz, H-3'), 4.92 (d, 1 H, H-1'), 4.78 (d, 1 H, *J* = –12.2 Hz, 3-OCH_2Ph), 4.71 (d, 1 H, *J* = –12.4 Hz, 2-OCH_2Ph), 4.70 (d, 1 H, $J_{H\text{-}1,H\text{-}2}$ = 1.9 Hz, H-1), 4.67 (d, 1 H, *J* = –11.8 Hz, 6-OCH_2Ph), 4.66 (d, 1 H, 2-OCH_2Ph), 4.55 (d, 1 H, *J* = –11.8 Hz, 6'-OCH_2Ph), 4.51 (d, 1 H, 6'-OCH_2Ph), 4.50 (d, 1 H, 6-OCH_2Ph), 4.45 (d, 1 H, 3-OCH_2Ph), 4.34 (dd, 1 H, $J_{H\text{-}3,H\text{-}4}$ = 9.2 Hz, $J_{H\text{-}4,H\text{-}5}$ = 9.8 Hz, H-4), 4.19 (dd, 1 H, $J_{H\text{-}4',H\text{-}5'}$ = 9.4 Hz, $J_{H\text{-}4',4\text{-}OH}$ = 2.8 Hz, H-4'), 3.77 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'a}$ = 4.3 Hz, $J_{H\text{-}6'a,H\text{-}6'b}$ = –11.0 Hz, H-6a), 3.76 (dd, 1 H, $J_{H\text{-}2,H\text{-}3}$ = 3.2 Hz, H-3), 3.74 (dd, 1 H, $J_{H\text{-}5,H\text{-}6'a}$ = 4.4 Hz, $J_{H\text{-}6'a,H\text{-}6'b}$ = –10.3 Hz, H-6'a), 3.69 (dd, 1 H, H-2), 3.68 (dd, 1 H, $J_{H\text{-}5'b,H\text{-}6'b}$ = 5.3 Hz, H-6'b), 3.68 (dd, 1 H, $J_{H\text{-}5,H\text{-}6b}$ = 2.0 Hz, H-6b), 3.64 (ddd, 1 H, H-5), 3.35 (ddd, 1 H, H-5'), 3.26 (s, 3 H, 1-OCH_3), 2.99 (d, 1 H, 4'-O*H*) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$, 25 °C): δ = 166.2 (3'-O*C*OPh), 165.6 (2'-O*C*OPh), 139.3 – 126.9 (aromatic C), 99.2 (C-1), 99.0 (C-1'), 78.5 (C-3), 75.4 (C-2), 75.4 (C-4), 74.5 (C-3'), 74.1 (C-5'), 73.9 (6'-O*C*H_2Ph), 73.4 (6-O*C*H_2Ph), 72.7 (2-O*C*H_2Ph), 72.6 (3-O*C*H_2Ph), 70.9 (C-5, C-6'), 70.0 (C-2'), 69.1 (C-6), 68.3 (C-4'), 54.7 (1-O*C*H_3) ppm. HRMS: calculated for $C_{55}H_{56}O_{13}K$, $[M + K]^+$ 963.3353, measured: 963.3365.

Methyl *O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)-(1→4)-*O*-(2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-mannopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (17). Prepared from donor **10** (76 mg, 1 equivalent) and acceptor **16** (110 mg, 0.9 equivalent) according to the standard reaction procedure for β-mannosylation. The crude product was purified by column chromatography (hexane:EtOAc 2:1) to provide **17** as a clear oil. Yield: 68 mg (43%), R_f = 0.30. ^{1}H NMR (500.20 MHz, $CDCl_3$, 25 °C): δ = 8.03 – 7.18 (m, 45 H, aromatic

H), 5.72 (dd, 1 H, $J_{H\text{-}1',H\text{-}2'}$ = 0.9 Hz, $J_{H\text{-}2',H\text{-}3'}$ = 3.3 Hz, H-2′), 5.33 (s, 1 H, 4′′,6′′-OC*H*Ph), 5.30 (dd, 1 H, $J_{H\text{-}3',H\text{-}4'}$ = 9.7 Hz, H-3′), 4.93 (d, 1 H, H-1′), 4.83 (d, 1 H, *J* = –12.4 Hz, 3-OCH_2Ph), 4.78 (d, 1 H, *J* = –12.0 Hz, 2′′-OCH_2Ph), 4.74 (d, 1 H, *J* = –12.4 Hz, 2-OCH_2Ph), 4.70 (d, 1 H, $J_{H\text{-}1,H\text{-}2}$ = 1.9 Hz, H-1), 4.68 (d, 1 H, 2-OCH_2Ph), 4.66 (d, 1 H, 2′′-OCH_2Ph), 4.66 (d, 1 H, *J* = –12.0 Hz, 6′-OCH_2Ph), 4.66 (d, 1 H, *J* = –11.8 Hz, 6-OCH_2Ph), 4.63 (d, 1 H, *J* = –12.4 Hz, 3′′-OCH_2Ph), 4.52 (d, 1 H, 6-OCH_2Ph), 4.48 (d, 1 H, 3′′-OCH_2Ph), 4.47 (d, 1 H, 3-OCH_2Ph), 4.41 (d, 1 H, $J_{H\text{-}1'',H\text{-}2''}$ = 0.9 Hz, H-1′′), 4.35 (dd, 1 H, $J_{H\text{-}3,H\text{-}4}$ = 9.2 Hz, $J_{H\text{-}4,H\text{-}5}$ = 9.8 Hz, H-4), 4.33 (dd, 1 H, $J_{H\text{-}4',H\text{-}5'}$ = 9.5 Hz, H-4′), 4.32 (d, 1 H, 6′-OCH_2Ph), 3.88 (dd, 1 H, $J_{H\text{-}3'',H\text{-}4''}$ = 9.8 Hz, $J_{H\text{-}4'',H\text{-}5''}$ = 9.3 Hz, H-4′′), 3.70 (dd, 1 H, $J_{H\text{-}2,H\text{-}3}$ = 3.2 Hz, H-2), 3.78 (dd, 1 H, $J_{H\text{-}5,H\text{-}6a}$ = 4.3 Hz, $J_{H\text{-}6a,H\text{-}6b}$ = –11.0 Hz, H-6a), 3.69 (dd, 1 H, $J_{H\text{-}5,H\text{-}6b}$ = 1.8 Hz, H-6b), 3.78 (dd, 1 H, H-3), 3.65 (ddd, 1 H, H-5), 3.64 (dd, 1 H, $J_{H\text{-}2'',H\text{-}3''}$ = 3.1 Hz, H-2′′), 3.51 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'a}$ = 1.9 Hz, $J_{H\text{-}6'a,H\text{-}6'b}$ = –11.5 Hz, H-6′a), 3.48 (dd, 1 H, $J_{H\text{-}5'',H\text{-}6''a}$ = 4.7 Hz, $J_{H\text{-}6''a,H\text{-}6''b}$ = –10.5 Hz, H-6′′a), 3.48 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'b}$ = 1.8 Hz, H-6′b), 3.33 (dd, 1 H, H-3′′), 3.26 (s, 3 H, 1-OCH_3), 3.25 (ddd, 1 H, H-5′), 3.17 (dd, 1 H, $J_{H\text{-}5'',H\text{-}6''b}$ = 10.0 Hz, H-6′′b), 2.91 (ddd, 1 H, H-5′′) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$, 25 °C): δ = 165.5 (2′-O*C*OPh), 165.0 (3′-O*C*OPh), 139.4 – 126.0 (aromatic C), 102.6 (C-1′′), 101.2 (4′′,6′′-O*C*HPh), 99.2 (C-1′), 99.1 (C-1), 78.6 (C-3), 78.4 (C-4′′), 78.1 (C-3′′), 76.5 (C-2′′), 75.6 (C-2), 75.4 (C-4), 75.1 (2′′-OCH$_2$Ph), 74.7 (C-5′), 74.1 (C-4′), 73.5 (6-OCH$_2$Ph), 73.4 (2-OCH$_2$Ph), 72.8 (6′-OCH$_2$Ph), 72.7 (3-OCH$_2$Ph), 72.4 (3′′-OCH$_2$Ph), 72.2 (C-3′), 70.9 (C-5), 70.5 (C-2′), 69.2 (C-6), 68.5 (C-6′), 68.1 (C-6′′), 67.3 (C-5′′), 54.7 (1-OCH$_3$) ppm. $^1J_{C\text{-}1,H\text{-}1}$ = 170 Hz (α), $^1J_{C\text{-}1',H\text{-}1'}$ = 161 Hz (β), $^1J_{C\text{-}1'',H\text{-}1''}$ = 158 Hz (β). HRMS: calculated for $C_{82}H_{82}O_{18}Na$, $[M + Na]^+$ 1377.5393 and measured 1377.5416.

Methyl *O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)-(1→4)-*O*-(2,3-di-*O*-acetyl-6-*O*-benzyl-β-D-mannopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (18). To a solution of **17** (61 mg, 1 equivalent) in MeOH (1.5 ml) and THF (1.5 ml) was 5.4 M NaOMe in MeOH (50 µg, 6 equivalents) added. The reaction mixture was stirred for 25 h and then neutralized with DOWEX 50WX8 H^+ form. The mixture was filtered and the solvent evaporated. The product was dissolved in pyridine (1 ml) and Ac_2O (51 µl, 12 equivalents) was added. After 46 h, the reaction mixture was diluted with CH_2Cl_2 (50 ml) and washed with saturated $NaHCO_3$ solution (40 ml), 1 M HCl (40 ml) and saturated NaCl solution (40 ml). The organic phase was dried over Na_2SO_4, filtered and evaporated. The crude product was purified by column chromatography (hexane:EtOAc 2:1) to provide **18** as a clear oil. Yield: 37 mg (67%), R_f = 0.16. ^{1}H NMR (500.20 MHz, $CDCl_3$, 25 °C): δ = 7.48 – 7.16 (m, 35 H, aromatic H), 5.56 (s, 1 H, 4′′,6′′-OC*H*Ph), 5.34 (dd, 1 H, $J_{H\text{-}1',H\text{-}2'}$ = 1.0 Hz, $J_{H\text{-}2',H\text{-}3'}$ = 3.4 Hz, H-2′), 4.95 (dd, 1 H, $J_{H\text{-}3',H\text{-}4'}$ = 9.7 Hz, H-3′), 4.81 (d, 1 H, *J* = –12.2 Hz, 3-OCH_2Ph), 4.76 (d, 1 H, H-1′), 4.73 (d, 1 H, $J_{H\text{-}1,H\text{-}2}$ = 1.9 Hz, H-1), 4.72 (d, 1 H, *J* = –12.1 Hz, 2′′-OCH_2Ph), 4.69 (d, 1 H, *J* = –12.4 Hz, 2-OCH_2Ph), 4.68 (d, 2 H, *J* = –11.9 Hz, 6-OCH_2Ph), 4.67 (d, 2 H, *J* = –12.4 Hz, 3′′-OCH_2Ph), 4.66 (d, 1 H, 2-OCH_2Ph), 4.62 (d, 1 H, 2′′-OCH_2Ph), 4.56 (d, 1 H, 3-OCH_2Ph), 4.55 (d, 1 H, 6-OCH_2Ph), 4.53 (d, 1 H, 3′′-OCH_2Ph), 4.50 (d, 1 H, *J* = –12.1 Hz, 6′-OCH_2Ph), 4.36 (d, 1 H, $J_{H\text{-}1'',H\text{-}2''}$ = 0.8 Hz, H-1′′), 4.26 (dd, 1 H, $J_{H\text{-}3,H\text{-}4}$ = 9.1 Hz, $J_{H\text{-}4,H\text{-}5}$ = 9.7 Hz, H-4), 4.22 (d, 1 H, 6′-OCH_2Ph), 4.22 (dd, 1 H, $J_{H\text{-}5'',H\text{-}6''a}$ = 4.7 Hz, $J_{H\text{-}6''a,H\text{-}6''b}$ = –10.4 Hz, H-6′′a), 4.08 (dd, 1 H, $J_{H\text{-}3'',H\text{-}4''}$ = 10.1 Hz, $J_{H\text{-}4'',H\text{-}5''}$ = 9.5 Hz, H-4′′), 3.96 (dd, 1 H, $J_{H\text{-}4',H\text{-}5'}$ = 9.7 Hz, H-4′), 3.84 (dd, 1 H, $J_{H\text{-}2,H\text{-}3}$ = 3.2 Hz, H-3), 3.81 (dd, 1 H, $J_{H\text{-}5'',H\text{-}6''b}$ = 10.0 Hz, H-

6''b), 3.73 (dd, 1 H, H-2), 3.72 (dd, 1 H, $J_{H\text{-}5,H\text{-}6a}$ = 4.6 Hz, $J_{H\text{-}6a,H\text{-}6b}$ = –10.9 Hz, H-6a), 3.68 (dd, 1 H, $J_{H\text{-}5,H\text{-}6b}$ = 1.8 Hz, H-6b), 3.69 (ddd, 1 H, H-5), 3.59 (dd, 1 H, $J_{H\text{-}2'',H\text{-}3''}$ = 3.1 Hz, H-2''), 3.39 (dd, 1 H, H-3''), 3.31 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'a}$ = 3.0 Hz, $J_{H\text{-}6'a,H\text{-}6'b}$ = –10.0 Hz, H-6'a), 3.31 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'b}$ = 2.3 Hz, H-6'b), 3.31 (s, 3 H, 1-OCH_3), 3.16 (ddd, 1 H, H-5''), 3.10 (ddd, 1 H, H-5'), 2.09 (s, 3 H, 2'-OCOCH_3), 1.98 (s, 3 H, 3'-OCOCH_3) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$, 25 °C): δ = 170.3 (2'-OCOCH$_3$), 169.4 (3'-OCOCH$_3$), 139.3 – 126.0 (aromatic C), 102.4 (C-1''), 101.4 (4'',6''-OCHPh), 99.1 (C-1), 99.0 (C-1'), 78.8 (C-3), 78.6 (C-4''), 78.1 (C-3''), 76.6 (C-2''), 75.5 (C-4), 75.1 (C-2), 74.9 (C-5'), 74.8 (2''-OCH$_2$Ph), 74.0 (C-4'), 73.5 (6'-OCH$_2$Ph), 73.4 (6-OCH$_2$Ph), 72.7 (2-OCH$_2$Ph), 72.4 (3''-OCH$_2$Ph), 72.3 (3-OCH$_2$Ph), 71.6 (C-3'), 70.8 (C-5), 69.7 (C-2'), 69.1 (C-6), 68.6 (C-6''), 68.4 (C-6'), 67.4 (C-5''), 54.8 (1-OCH$_3$), 21.0 (2'-OCOCH$_3$), 20.4 (3'-OCOCH$_3$) ppm. HRMS: calculated for $C_{78}H_{78}O_{18}Na$, $[M + Na]^+$ 1253.5080 and measured 1253.5109.

Methyl *O*-(β-D-mannopyranosyl)-(1→4)-*O*-(2,3-di-*O*-acetyl-β-D-mannopyranosyl)-(1→4)-α-D-mannopyranoside (2): Prepared from **18** (12 mg, 0.01 mmol) according to the general method A for hydrogenolysis of benzyl and benzylidene protecting groups. Yield: 5 mg (92%). ^{1}H NMR (500.20 MHz, MeOD, 25 °C): δ = 5.46 (dd, 1 H, $J_{H\text{-}1',H\text{-}2'}$ = 1.1 Hz, $J_{H\text{-}2',H\text{-}3'}$ = 3.6 Hz, H-2'), 5.19 (dd, 1 H, $J_{H\text{-}3',H\text{-}4'}$ = 9.8 Hz, H-3'), 4.90 (d, 1 H, H-1'), 4.63 (d, 1 H, $J_{H\text{-}1,H\text{-}2}$ = 1.7 Hz, H-1), 4.63 (d, 1 H, $J_{H\text{-}1'',H\text{-}2''}$ = 0.9 Hz, H-1''), 4.05 (dd, 1 H, $J_{H\text{-}4',H\text{-}5'}$ = 9.7 Hz, H-4'), 3.94 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'a}$ = 2.0 Hz, $J_{H\text{-}6'a,H\text{-}6'b}$ = –12.2 Hz, H-6'a), 3.88 (dd, 1 H, $J_{H\text{-}3,H\text{-}4}$ = 9.3 Hz, $J_{H\text{-}4,H\text{-}5}$ = 9.9 Hz, H-4), 3.85 (dd, 1 H, $J_{H\text{-}5'',H\text{-}6''a}$ = 2.4 Hz, $J_{H\text{-}6''a,H\text{-}6''b}$ = –11.6 Hz, H-6''a), 3.84 (dd, 1 H, $J_{H\text{-}2,H\text{-}3}$ = 3.5 Hz, H-2), 3.84 (dd, 1 H, $J_{H\text{-}2'',H\text{-}3''}$ = 3.2 Hz, H-2''), 3.77 (dd, 1 H, $J_{H\text{-}5',H\text{-}6'a}$ = 4.8 Hz, $J_{H\text{-}6'a,H\text{-}6'b}$ = –12.2 Hz, H-6'b), 3.75 (dd, 1 H, H-3), 3.75 (dd, 1 H, $J_{H\text{-}5,H\text{-}6a}$ = 2.0 Hz, $J_{H\text{-}6a,H\text{-}6b}$ = –12.2 Hz, H-6a), 3.73 (dd, 1 H, $J_{H\text{-}5''b,H\text{-}6''}$ = 5.3 Hz, H-6''b), 3.70 (dd, 1 H, $J_{H\text{-}5,H\text{-}6b}$ = 4.3 Hz, H-6b), 3.59 (ddd, 1 H, H-5'), 3.58 (dd, 1 H, $J_{H\text{-}3'',H\text{-}4''}$ = 9.5 Hz, $J_{H\text{-}4'',H\text{-}5''}$ = 9.7 Hz, H-4''), 3.47 (ddd, 1 H, H-5), 3.44 (dd, 1 H, H-3''), 3.35 (s, 3 H, 1-OCH_3), 3.21 (ddd, 1 H, H-5''), 2.11 (s, 3 H, 3'-OCOCH_3), 2.05 (s, 3 H, 2'-OCOCH_3) ppm. ^{13}C NMR (125.8 MHz, MeOD, 25 °C): δ = 172.07 (3'-OCOCH$_3$), 172.05 (2'-OCOCH$_3$), 102.5 (C-1), 101.7 (C-1''), 100.2 (C-1'), 79.2 (C-4), 78.2 (C-5''), 77.3 (C-5'), 75.1 (C-3''), 74.3 (C-4'), 72.6 (C-2''), 72.54 (C-5), 72.52 (C-3'), 71.6 (C-2), 71.1 (C-3), 70.9 (C-2'), 68.2 (C-4''), 62.8 (C-6''), 61.94 (C-6), 61.86 (C-6'), 55.3 (1-OCH$_3$), 21.0 (2'-OCOCH$_3$), 20.7 (3'-OCOCH$_3$) ppm. HRMS: calculated for $C_{23}H_{38}O_{18}Na$, $[M + Na]^+$ 625.1950 and measured 625.1910.

Modeling of molecular structures

The atomic coordinates are in standard XYZ format (Ångström units). The title line describes the level of theory used for optimization.

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1a: TPSSh/def2-TZVPP/COSMO, ε=78

C	2.31022	1.84066	2.45545
C	1.81572	3.25418	2.37987
O	2.63736	1.25740	3.46669
H	1.90011	3.72923	3.35327

H	0.77164	3.25204	2.05922
H	2.38560	3.80896	1.63397
H	-0.42454	-0.77280	1.43388
C	-4.13671	-0.24363	-0.05756
C	-3.86430	-0.70141	-1.49296
C	-2.52480	-1.42173	-1.61407
C	-1.44553	-0.53947	-1.00067
O	-1.78540	-0.20972	0.34451
C	-2.96749	0.59773	0.43948
H	-4.23895	-1.12232	0.59011
O	-5.31745	0.55131	-0.01059
H	-3.84693	0.18261	-2.13442
O	-4.93671	-1.51207	-1.96697
H	-2.28875	-1.58853	-2.67000
O	-2.65539	-2.65956	-0.92507
H	-1.34255	0.39162	-1.57436
H	-2.84592	1.48409	-0.19554
C	-3.07139	1.01459	1.89302
H	-6.00266	0.05474	-0.48045
H	-4.81506	-2.39198	-1.57988
H	-1.82098	-3.13938	-1.00690
H	-3.19163	0.12348	2.51900
H	-3.93701	1.66006	2.02932
O	-1.92710	1.76686	2.30111
H	-1.14833	1.20728	2.16958
O	-0.24444	-1.23964	-0.95696
C	0.88593	-0.43158	-0.57294
C	1.40376	-0.88527	0.78547
C	2.67272	-0.11286	1.12048
C	3.69201	-0.23609	-0.00596
O	3.13600	0.15042	-1.25134
C	1.97004	-0.59779	-1.63630
H	0.58106	0.61506	-0.52378
H	1.66837	-1.94639	0.71769
O	0.46153	-0.68231	1.83094
H	3.09993	-0.45113	2.06149
O	2.34474	1.28756	1.22358
O	4.13038	-1.56617	-0.00542
H	2.22172	-1.65869	-1.73667
C	1.55772	-0.05526	-2.99114
H	0.68865	-0.60143	-3.35475
H	2.38359	-0.20311	-3.69381
O	1.18324	1.32019	-2.93081
C	5.21764	-1.79471	-0.91068
H	4.52524	0.45491	0.14633

H	1.93713	1.80562	-2.56936
H	6.05211	-1.12787	-0.67437
H	4.90266	-1.63280	-1.94330
H	5.51863	-2.83045	-0.77366

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1b: TPSSh/def2-TZVPP/COSMO, ε=78

C	-3.88931	1.13744	-3.39248
C	-3.38949	1.98951	-4.51880
O	-4.71199	1.47417	-2.56560
H	-3.85383	1.64549	-5.44648
H	-2.31061	1.88566	-4.62851
H	-3.66140	3.02693	-4.34434
H	-2.03159	-3.14831	-3.00767
C	-9.57001	-0.87035	-2.22072
C	-8.80904	0.36786	-2.69398
C	-7.63772	-0.00317	-3.59378
C	-6.79727	-1.06012	-2.88449
O	-7.59641	-2.18154	-2.53851
C	-8.59676	-1.84866	-1.57119
H	-10.03836	-1.35966	-3.08292
O	-10.55762	-0.50091	-1.26127
H	-8.42288	0.88628	-1.81313
O	-9.69350	1.28610	-3.33452
H	-7.01747	0.87903	-3.77534
O	-8.18735	-0.49202	-4.81341
H	-6.36699	-0.62791	-1.97178
H	-8.12185	-1.37269	-0.70202
C	-9.23922	-3.15469	-1.14276
H	-11.04495	0.24359	-1.64213
H	-9.84934	0.94575	-4.22817
H	-7.45619	-0.71739	-5.40300
H	-9.63400	-3.66288	-2.03023
H	-10.06877	-2.93710	-0.47061
O	-8.33692	-3.99335	-0.43211
H	-7.66107	-4.33863	-1.04909
O	-5.80332	-1.49475	-3.76537
C	-4.63307	-2.09204	-3.18307
C	-3.77455	-1.05964	-2.46202
C	-2.56177	-1.71312	-1.80443
C	-3.06219	-2.80444	-0.86228
O	-3.76605	-3.77325	-1.64006
C	-4.97058	-3.24835	-2.23129
H	-4.08208	-2.47574	-4.04328
H	-4.34978	-0.54629	-1.69376

O	-3.31551	-0.08530	-3.42156
H	-1.99663	-0.96399	-1.25143
O	-1.66740	-2.28841	-2.74970
O	-3.85748	-2.21171	0.11865
H	-5.62091	-2.88493	-1.43510
C	-5.64956	-4.40374	-2.93617
H	-4.90861	-4.97997	-3.49666
H	-6.40277	-4.02084	-3.61779
O	-6.34558	-5.25003	-2.01246
C	-4.28556	-3.13074	1.13241
H	-2.22842	-3.35865	-0.42367
H	-5.69401	-5.67671	-1.44067
H	-3.42195	-3.63368	1.57564
H	-4.96830	-3.87540	0.71777
H	-4.80058	-2.53861	1.88437

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2a: TPSSh/def2-SVP(D)/COSMO, ε=78

C	-5.09889	0.44922	1.86612
C	-5.78513	-0.26067	0.69813
C	-4.81934	-1.23965	0.02664
C	-3.49049	-0.54395	-0.28377
O	-2.96092	0.08073	0.87394
C	-3.79808	1.10600	1.40322
H	-4.83994	-0.30471	2.63366
O	-5.95047	1.44955	2.40946
H	-6.10119	0.50183	-0.03123
O	-6.95273	-0.92637	1.14197
H	-5.25901	-1.61693	-0.90867
O	-4.60755	-2.31051	0.94684
H	-3.63920	0.22221	-1.07102
H	-4.02121	1.85953	0.62217
C	-3.03152	1.77932	2.53980
H	-6.77491	1.00725	2.67874
H	-6.63291	-1.75276	1.55263
H	-4.57759	-3.14199	0.44725
H	-2.06190	2.13306	2.15561
H	-2.82682	1.02064	3.32132
O	-3.73425	2.89660	3.04572
H	-4.66028	2.60281	3.16462
O	-2.60702	-1.53915	-0.68868
O	2.60268	0.20082	-0.47435
O	1.05129	-0.49601	-2.59337
C	-1.98237	1.46713	-3.17265
C	-2.51092	1.40819	-4.57486

O	-1.87712	2.46010	-2.48418
H	-3.13045	0.51285	-4.71903
H	-1.65207	1.34083	-5.26171
H	-3.07948	2.31873	-4.79611
C	-1.22819	-1.21190	-0.86889
C	-0.96973	0.16921	-1.45470
C	0.53697	0.40803	-1.60463
C	1.24308	0.11206	-0.28929
O	0.94375	-1.23357	0.12267
C	-0.44071	-1.37467	0.44428
H	-0.85518	-1.96927	-1.57374
H	-1.38321	0.95675	-0.80942
O	-1.60081	0.23694	-2.74218
H	0.72709	1.44134	-1.91842
H	-0.73171	-0.58974	1.16117
C	-0.67664	-2.73056	1.11270
H	0.19248	-2.93359	1.75725
H	-0.71668	-3.52680	0.34384
O	-1.81877	-2.73041	1.94209
H	-2.59670	-2.45315	1.41829
H	0.91298	0.83168	0.48564
O	4.79114	-1.64351	2.75241
C	1.27164	-0.02889	-3.83673
C	1.79074	-1.11636	-4.73227
O	1.07137	1.12695	-4.16197
H	1.06801	-1.94503	-4.76027
H	2.73138	-1.51137	-4.32120
H	1.95584	-0.72577	-5.74199
C	3.38022	0.04298	0.72707
C	4.29415	-1.14871	0.45711
C	5.38020	-1.26752	1.52159
C	6.07230	0.08193	1.70298
O	5.16193	1.10362	2.01406
C	4.10444	1.34649	1.06731
H	2.71526	-0.21854	1.56607
H	4.76641	-1.00172	-0.52962
O	3.54180	-2.35987	0.48634
H	6.13840	-2.00544	1.19794
O	6.78148	0.32928	0.51446
H	4.52234	1.76839	0.13475
C	3.17028	2.36313	1.77166
H	4.09433	-2.27691	2.49090
H	3.82755	3.25292	1.97718
H	3.01202	1.89938	2.78631
O	2.01157	2.65191	1.11310

C	7.59381	1.49496	0.56886
H	6.75877	0.04772	2.56859
H	8.34297	1.41472	1.37746
H	6.98562	2.39879	0.73716
H	8.10767	1.57366	-0.39797
H	2.61036	-2.13625	0.27215

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2TS: TPSSh/def2-SVP(D)/COSMO, ε=78

C	-5.34137	0.88740	1.47961
C	-5.93486	0.27386	0.21027
C	-5.02921	-0.83948	-0.31165
C	-3.59227	-0.32924	-0.44374
O	-3.14767	0.20594	0.79359
C	-3.89766	1.33397	1.24173
H	-5.33510	0.11666	2.27301
O	-6.09984	2.01928	1.88718
H	-6.01527	1.06596	-0.55113
O	-7.24617	-0.20010	0.45627
H	-5.38832	-1.18834	-1.29341
O	-5.08556	-1.88579	0.65187
H	-3.52645	0.46073	-1.21737
H	-3.88157	2.12988	0.47205
C	-3.22195	1.84818	2.51183
H	-7.01404	1.71520	2.02739
H	-7.13457	-1.05422	0.91454
H	-4.76042	-2.69892	0.23163
H	-2.16412	2.06021	2.29246
H	-3.25226	1.04119	3.27113
O	-3.82093	3.04338	2.97032
H	-4.78827	2.90263	2.91550
O	-2.80679	-1.43746	-0.74560
O	2.54609	-0.67805	-0.13206
O	1.38512	-0.37430	-2.36018
C	-1.86256	1.14101	-3.21884
C	-2.29152	0.98744	-4.64969
O	-2.02052	2.13028	-2.53175
H	-2.95775	0.11646	-4.74156
H	-1.41253	0.80097	-5.28449
H	-2.80839	1.89567	-4.97934
C	-1.37834	-1.31251	-0.74866
C	-0.87103	-0.02472	-1.38720
C	0.66274	0.17439	-1.28153
C	1.22127	-0.37617	0.04593
O	0.61662	-1.59487	0.48342

C	-0.78761	-1.43334	0.66571
H	-1.03517	-2.18491	-1.32399
H	-1.33458	0.82724	-0.87016
O	-1.29217	0.00485	-2.75771
H	0.84478	1.25783	-1.29521
H	-0.98044	-0.51518	1.24594
C	-1.32453	-2.61450	1.47740
H	-0.53160	-2.90522	2.18368
H	-1.51076	-3.47801	0.81014
O	-2.45969	-2.28292	2.25016
H	-3.12029	-1.85557	1.67292
H	1.07517	0.38228	0.83919
O	4.19462	0.37867	3.56621
C	2.13655	0.56435	-3.12559
C	2.67773	-0.16277	-4.33528
O	1.77942	1.74877	-3.11464
H	1.85375	-0.68383	-4.84551
H	3.43238	-0.89763	-4.03321
H	3.13148	0.56024	-5.02437
C	3.47327	-0.12713	0.77610
C	3.92574	-1.18395	1.76590
C	4.90708	-0.51757	2.73145
C	5.97772	0.27492	1.96179
O	5.45388	1.13708	0.96581
C	4.64430	0.43914	-0.00185
H	3.00771	0.70194	1.33608
H	4.42587	-2.00306	1.21916
O	2.82935	-1.67224	2.53122
H	5.43056	-1.28632	3.32913
O	6.84861	-0.68495	1.42185
H	5.24037	-0.37592	-0.44478
C	4.18894	1.33394	-1.17549
H	3.34182	-0.06946	3.73000
H	4.99648	2.09156	-1.32049
H	3.28562	1.91591	-0.86904
O	3.95641	0.57076	-2.30212
C	8.01196	-0.13225	0.81940
H	6.50915	0.94558	2.65992
H	8.60910	0.42537	1.56324
H	7.74849	0.54609	-0.00816
H	8.60167	-0.97325	0.43246
H	2.09213	-1.85199	1.91012

78

2b: TPSSh/def2-SVP(D)/COSMO, ε=78

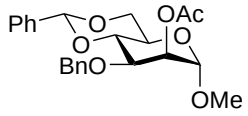
C	15.02120	8.65682	3.09196
C	14.74704	9.50264	1.84832
C	15.32027	8.82139	0.60620
C	16.78053	8.41921	0.83784
O	16.91040	7.65582	2.02827
C	16.51413	8.34640	3.20810
H	14.48391	7.69506	2.98983
O	14.60108	9.34576	4.26330
H	15.22893	10.48378	1.98510
O	13.35716	9.73411	1.70415
H	15.26363	9.50518	-0.25532
O	14.52083	7.66191	0.37928
H	17.42129	9.31935	0.91208
H	17.08007	9.29353	3.30997
C	16.84075	7.43809	4.39189
H	13.65494	9.54624	4.15094
H	13.00515	8.91667	1.30214
H	14.53172	7.46902	-0.57204
H	17.91081	7.18123	4.35835
H	16.26556	6.49770	4.27527
O	16.58307	8.07721	5.62643
H	15.70744	8.50476	5.53283
O	17.13545	7.61131	-0.23448
O	21.91784	4.98976	0.56880
O	21.27611	7.03225	-1.23183
C	20.21373	10.14019	0.13010
C	20.23780	11.32742	-0.79440
O	20.72413	10.09979	1.23376
H	19.28518	11.42370	-1.33259
H	21.03339	11.17292	-1.54113
H	20.45728	12.23771	-0.22372
C	18.43939	7.00594	-0.24599
C	19.56699	7.85514	0.29976
C	20.92416	7.11203	0.06554
C	20.77627	5.74619	0.77201
O	19.66296	4.99702	0.22618
C	18.41786	5.65184	0.48493
H	18.64182	6.80922	-1.30886
H	19.42180	8.07213	1.36950
O	19.55931	9.10468	-0.42168
H	21.66490	7.65801	0.70227
H	18.30487	5.81019	1.57130
C	17.27763	4.74444	0.01450
H	17.55142	3.70473	0.25284
H	17.17807	4.81688	-1.08650

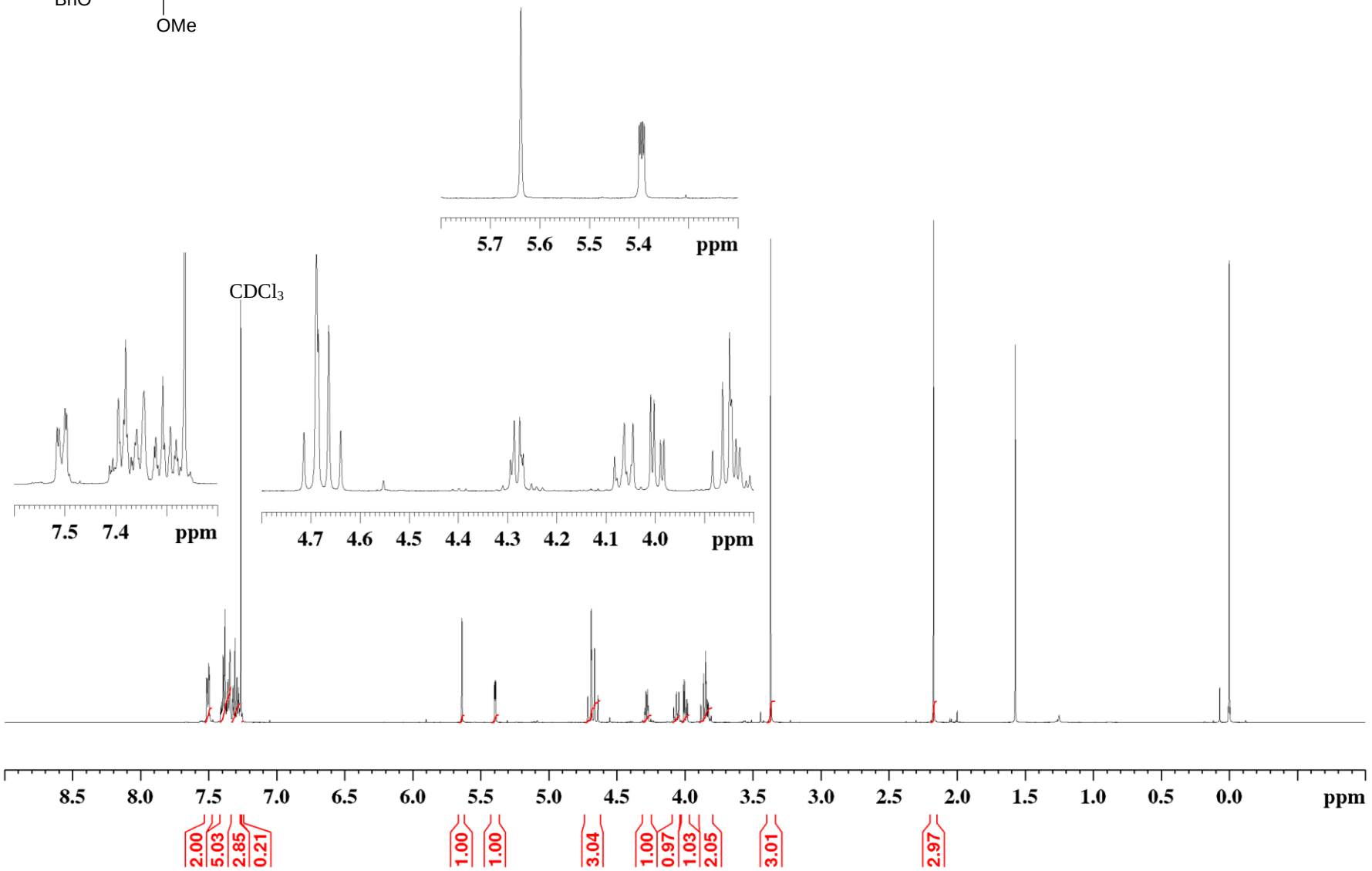
O	16.05883	5.00690	0.67833
H	15.85847	5.95912	0.59759
H	20.58441	5.87537	1.85752
O	21.60143	1.69778	3.31670
C	24.65988	6.59072	0.37140
C	24.15481	7.79893	-0.34640
O	25.46727	5.78651	-0.06915
H	23.97654	8.62870	0.35071
H	23.17377	7.52669	-0.81092
H	24.86649	8.09236	-1.12750
C	22.23620	4.00650	1.55259
C	21.72931	2.62884	1.10890
C	22.23525	1.54244	2.06003
C	23.74302	1.65384	2.26832
O	24.11975	2.96201	2.65561
C	23.75823	3.98048	1.71709
H	21.76545	4.26724	2.51644
H	22.11529	2.43619	0.09107
O	20.31473	2.55242	1.15260
H	22.02080	0.54924	1.62327
O	24.35283	1.25990	1.07196
H	24.21447	3.77000	0.73717
C	24.38145	5.24255	2.31508
H	20.68893	1.96339	3.08813
H	25.46933	5.09840	2.37578
H	23.97602	5.41490	3.31961
O	24.08942	6.44215	1.58349
C	25.77149	1.16505	1.15155
H	24.06319	1.01673	3.11103
H	26.07153	0.44991	1.93799
H	26.22580	2.14569	1.36806
H	26.12207	0.80625	0.17562
H	19.95612	3.38681	0.75867

NMR spectra

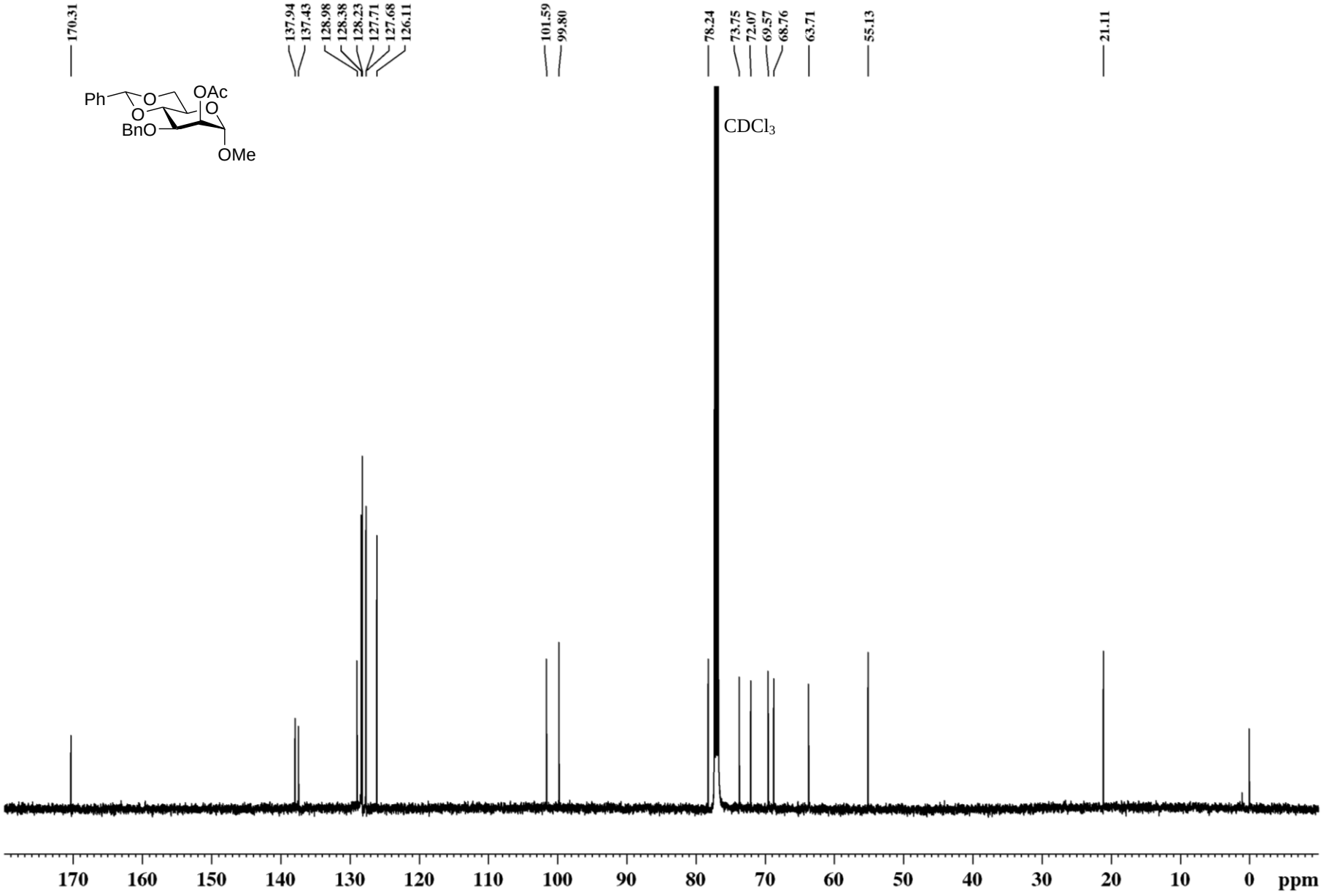
Methyl 2-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranoside (7)

^{1}H NMR (500.20 MHz, $CDCl_3$, 25°C):



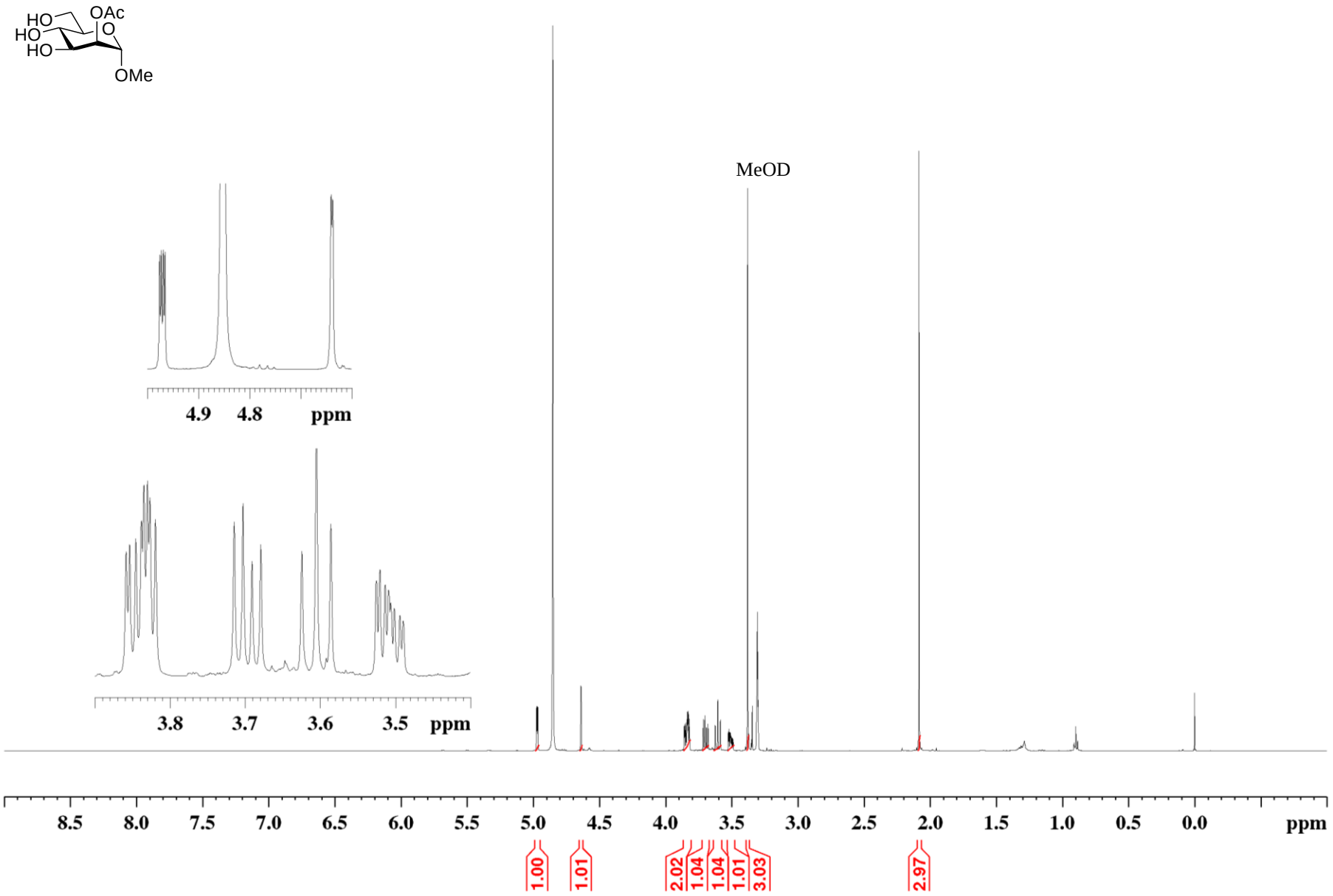


^{13}C NMR (125.8 MHz, $CDCl_3$, 25°C):

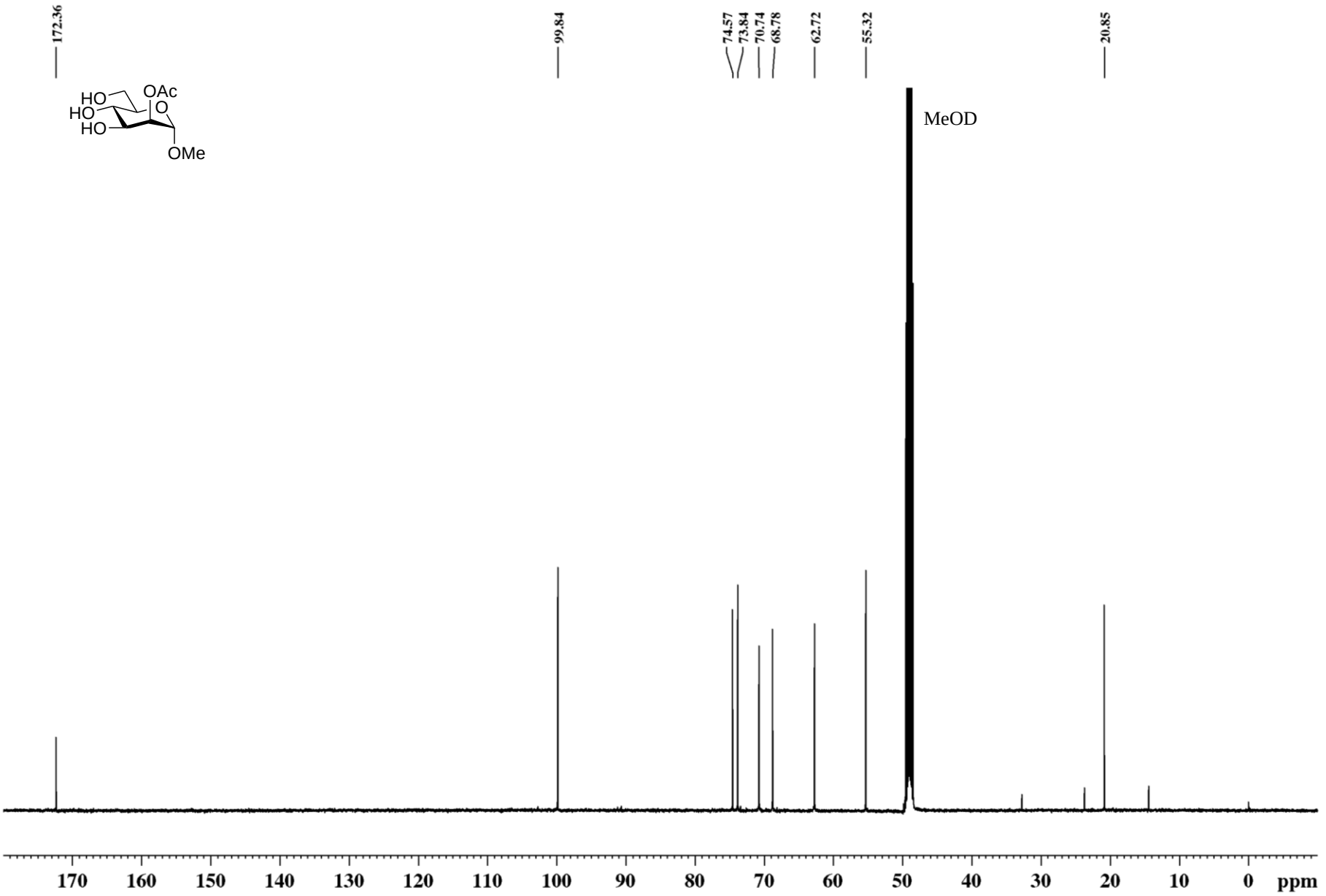


Methyl 2-*O*-acetyl-β-D-mannopyranoside (3):

^{1}H NMR (500.20 MHz, MeOD, 25°C):

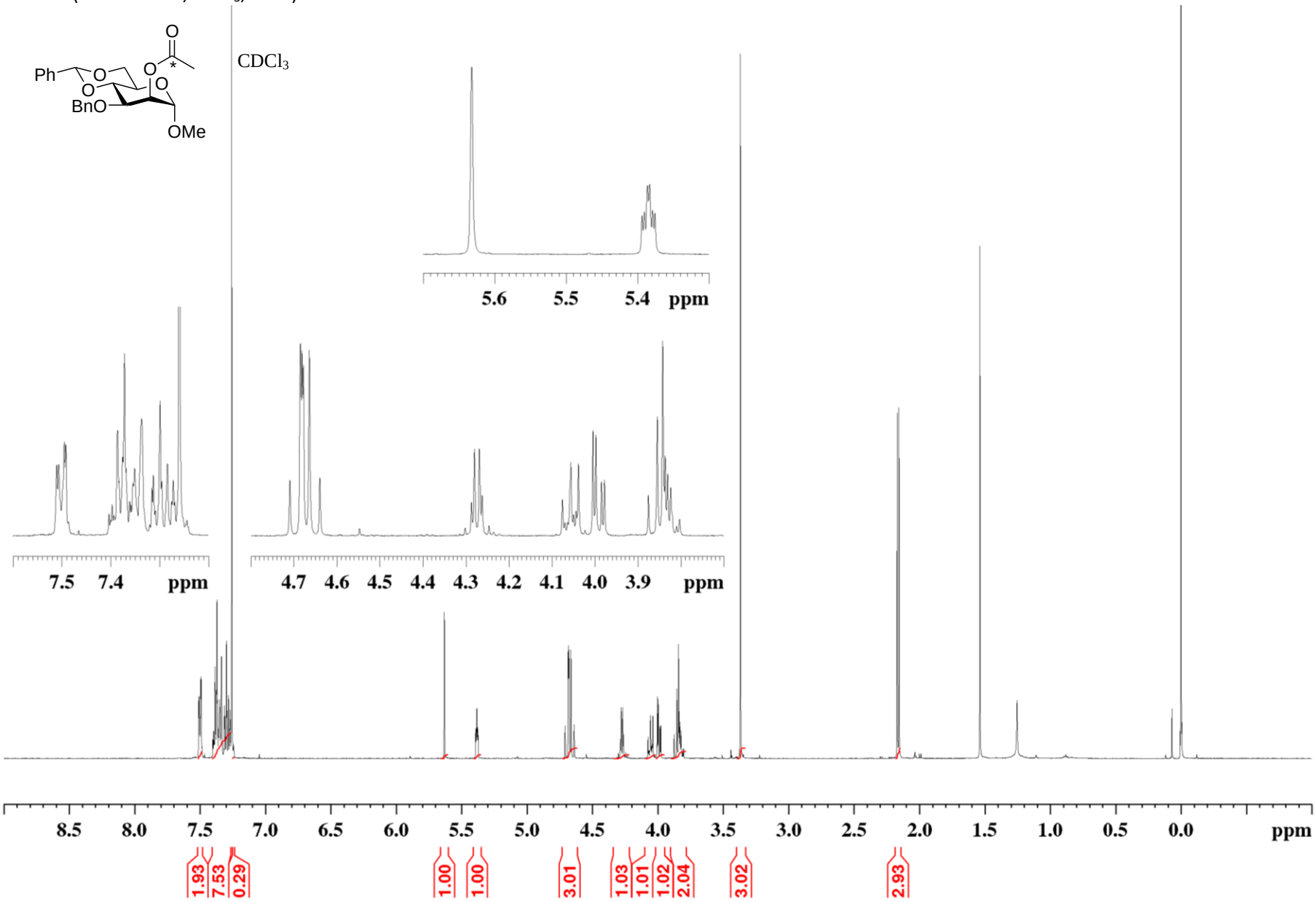


^{13}C NMR (125.8 MHz, MeOD, 25°C):

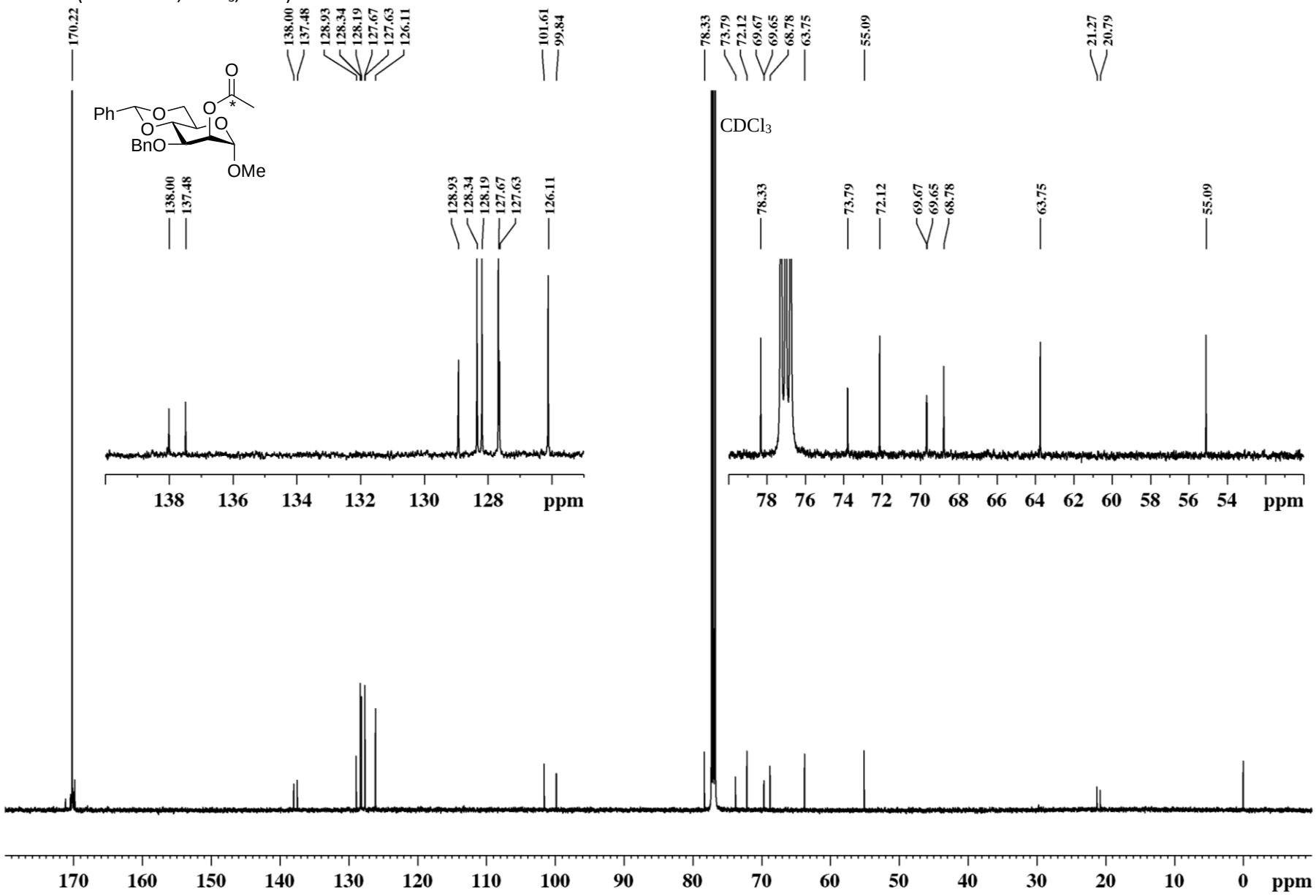


Methyl 2-*O*-acetyl-(1-^{13}C)-3-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranoside (8):

^{1}H NMR (500.20 MHz, $CDCl_3$, 25°C):

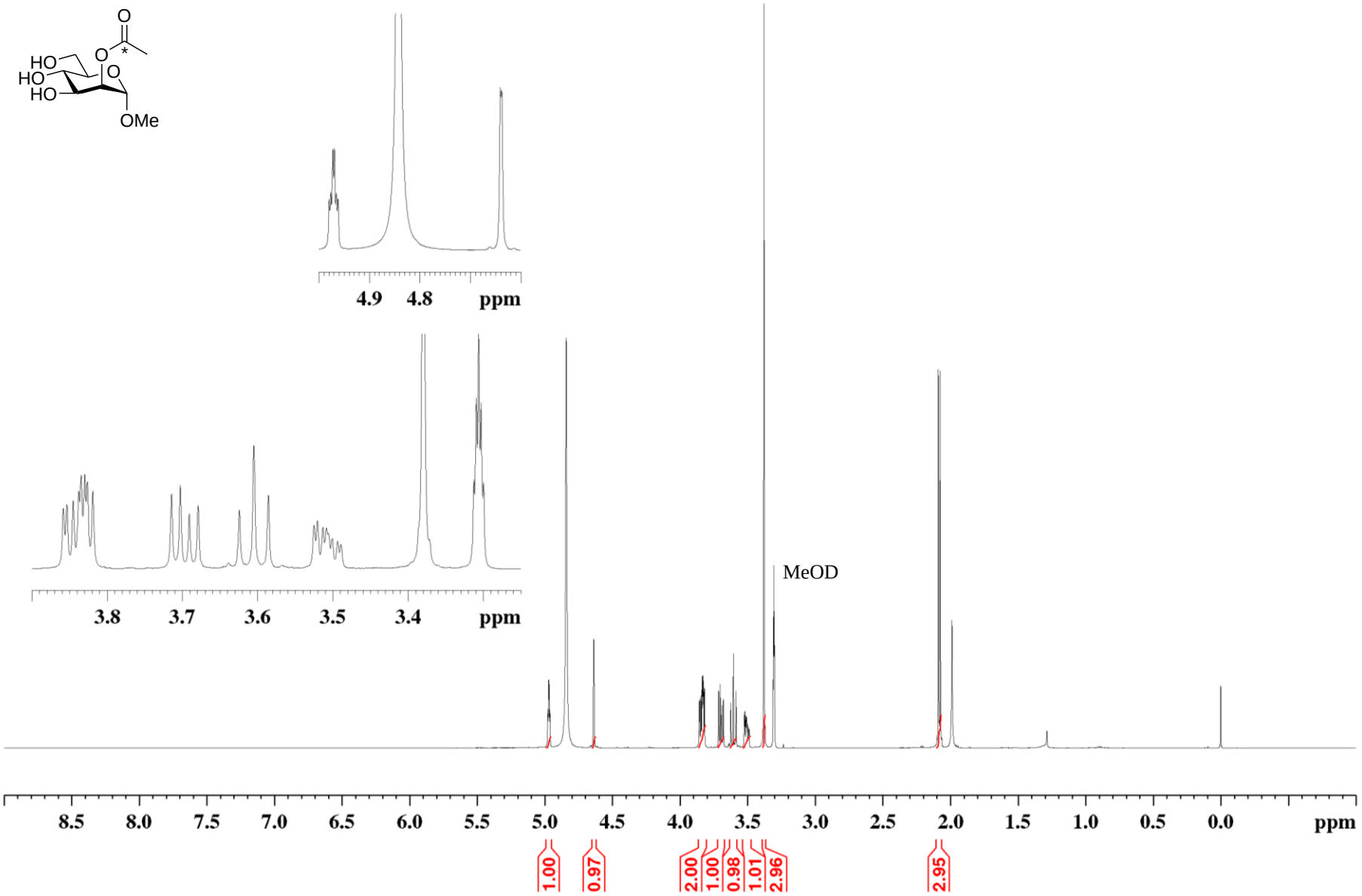


^{13}C NMR (125.8 MHz, $CDCl_3$, 25°C):

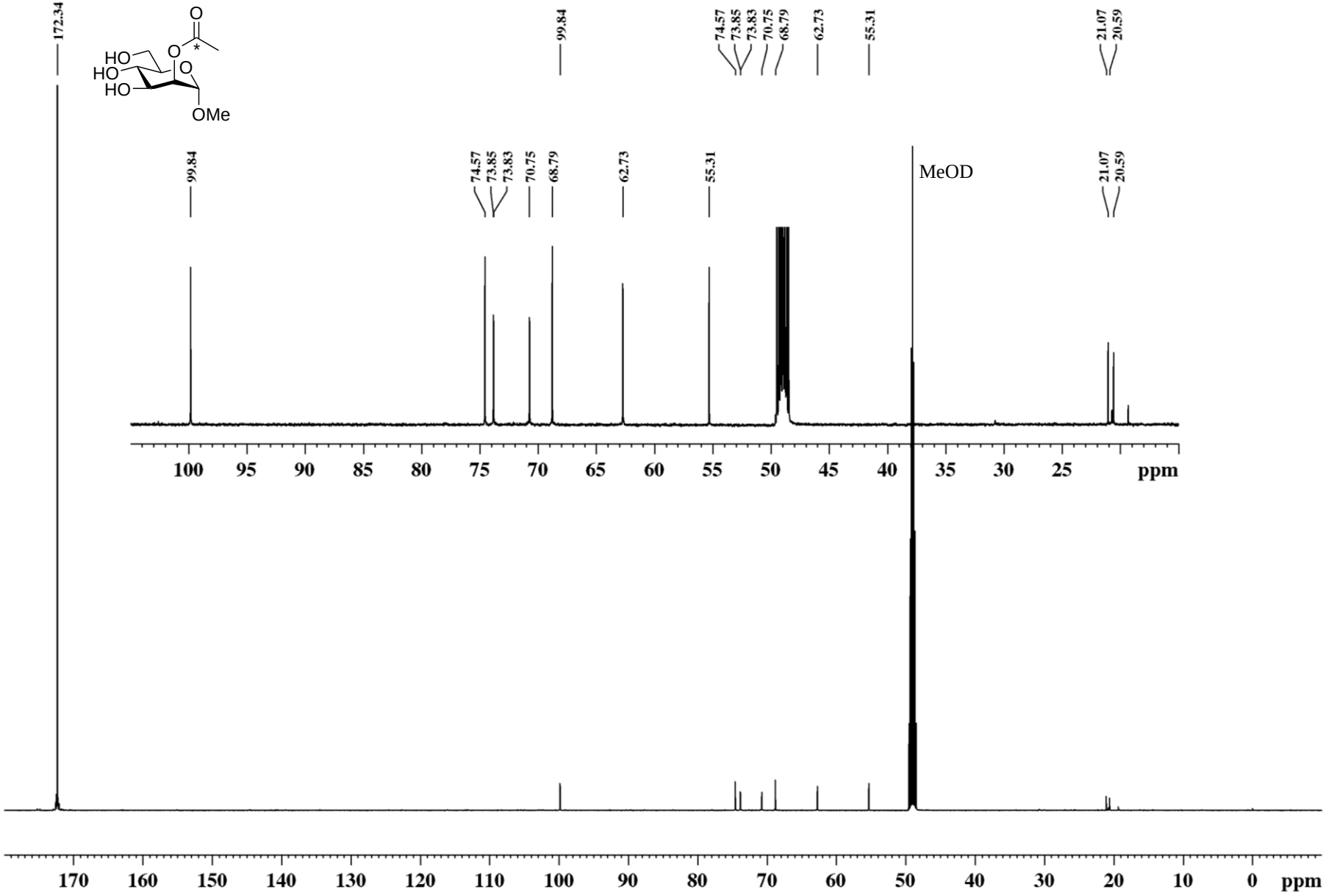


Methyl 2-*O*-acetyl-(1-^{13}C)-β-D-mannopyranoside (4):

^{1}H NMR (500.20 MHz, $CDCl_3$, 25°C):

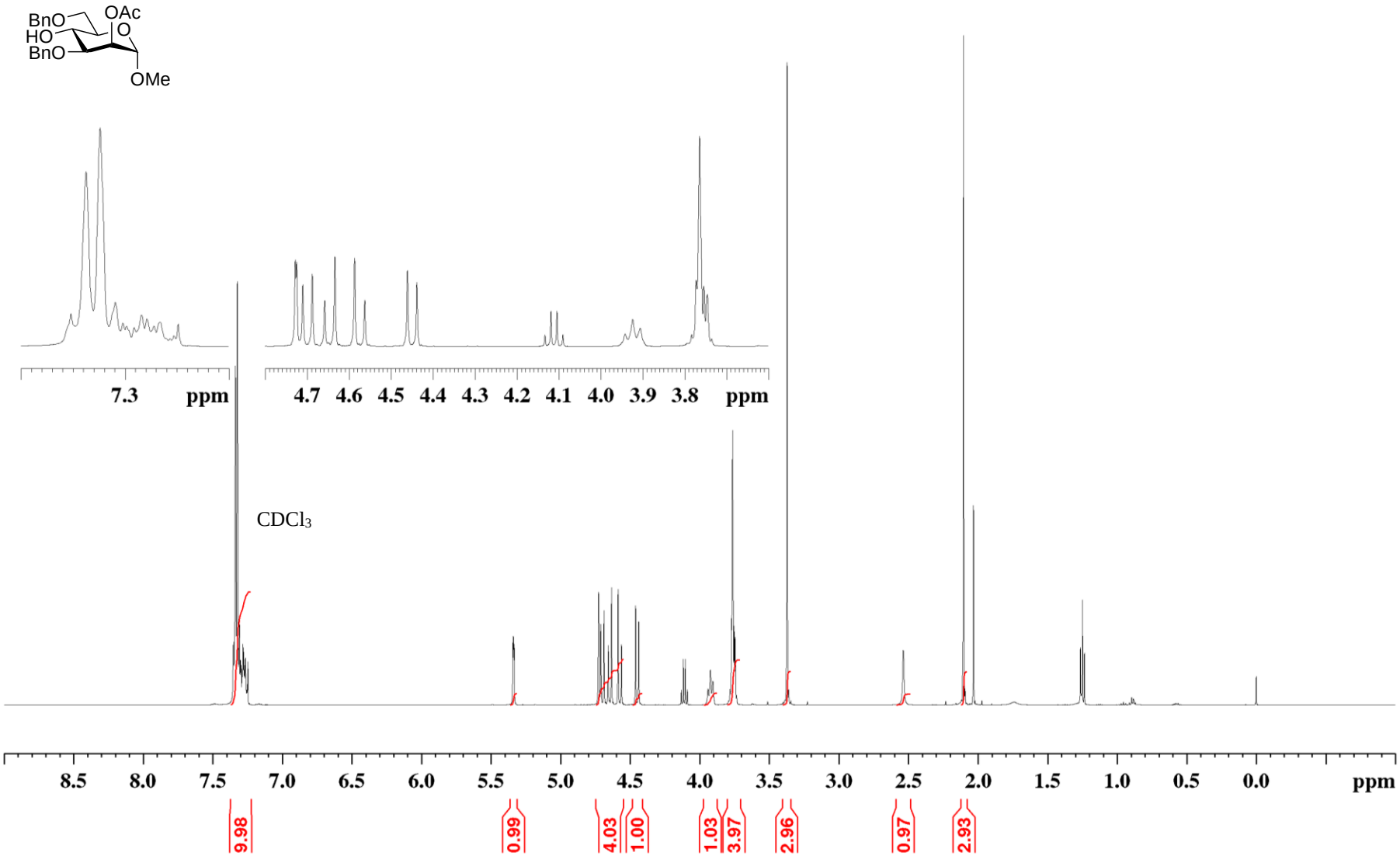


^{13}C NMR (125.8 MHz, $CDCl_3$, 25°C):

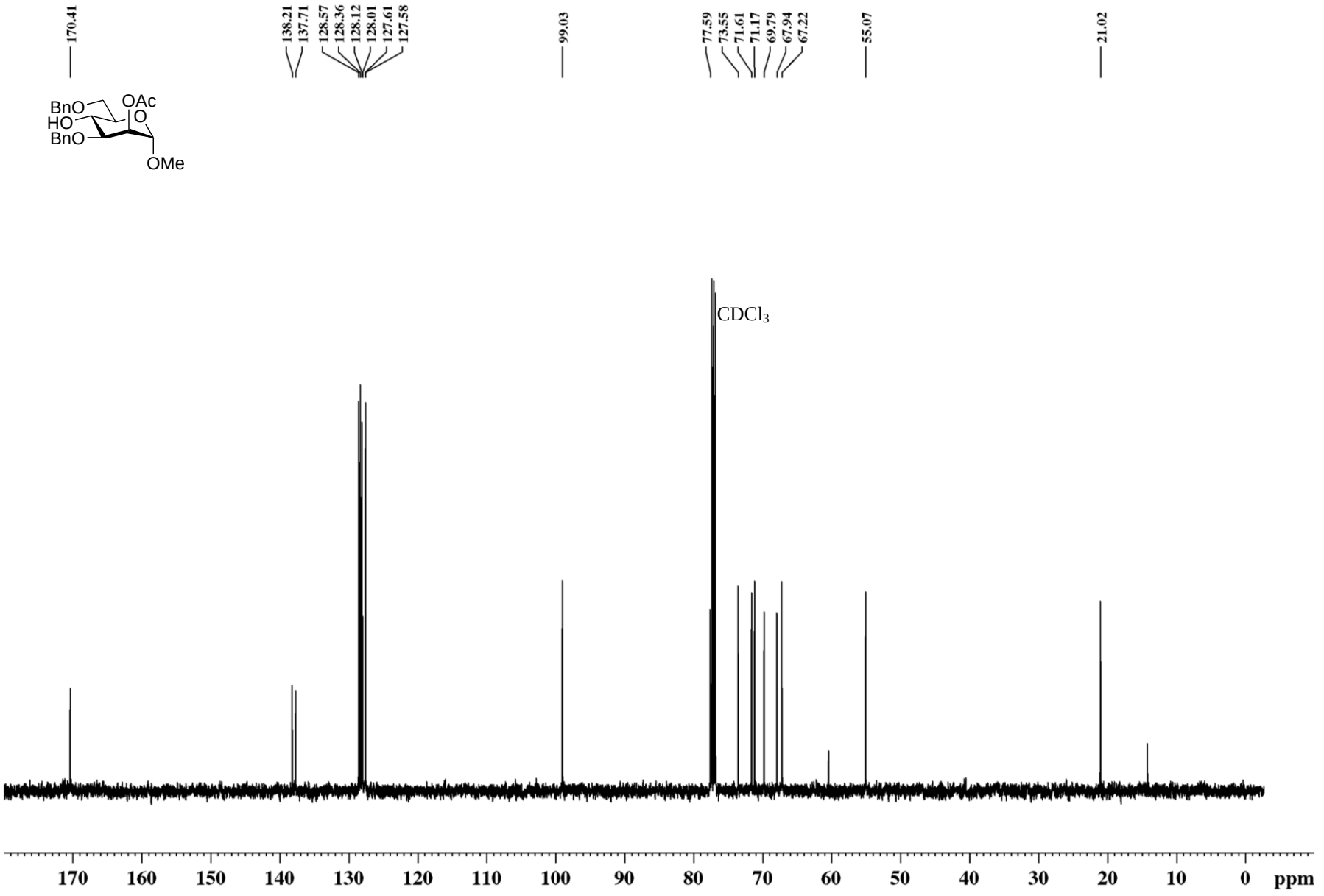


Methyl 2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranoside (9):

^{1}H NMR (500.20 MHz, $CDCl_3$, 25°C):

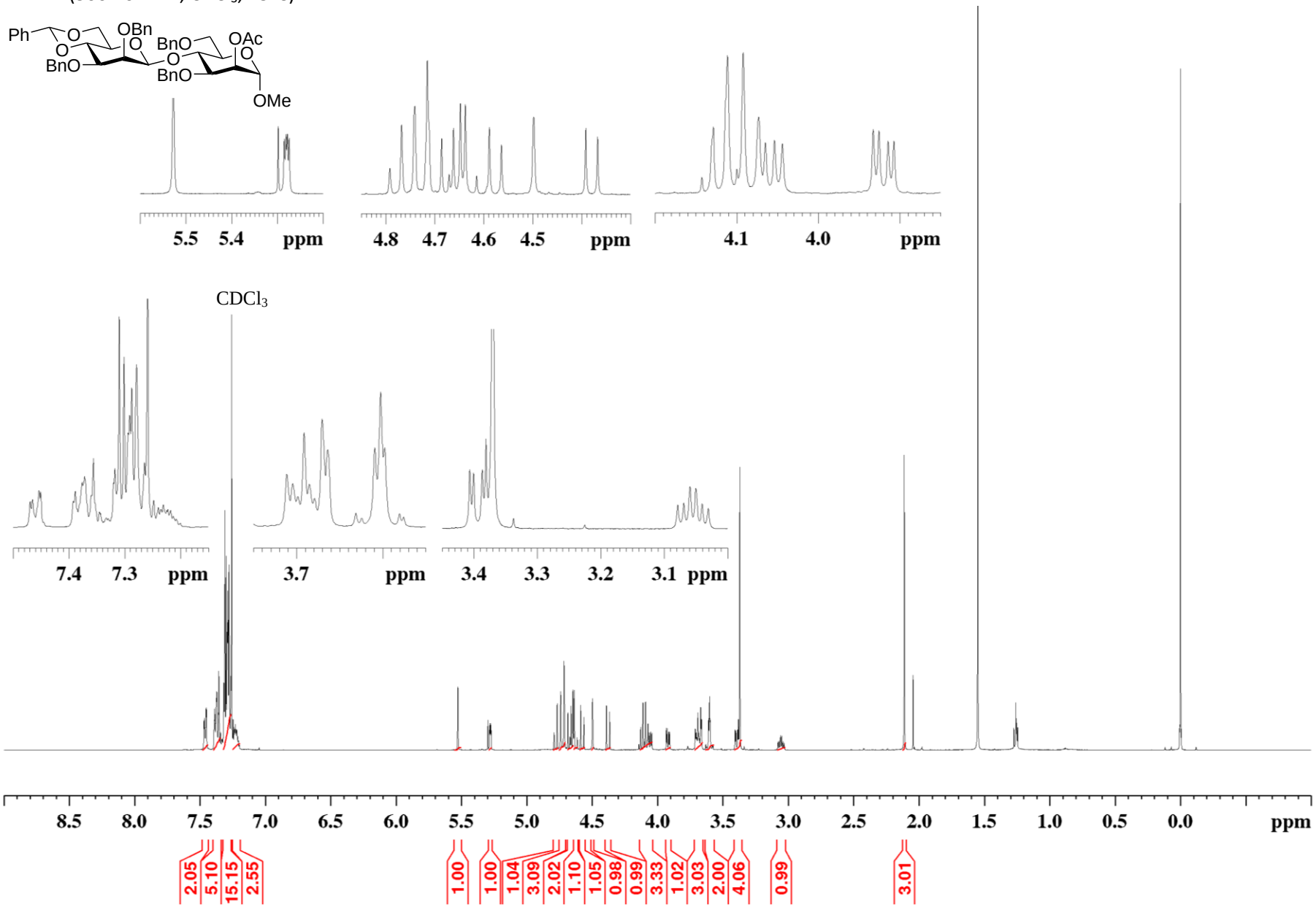


^{13}C NMR (125.8 MHz, $CDCl_3$, 25°C):

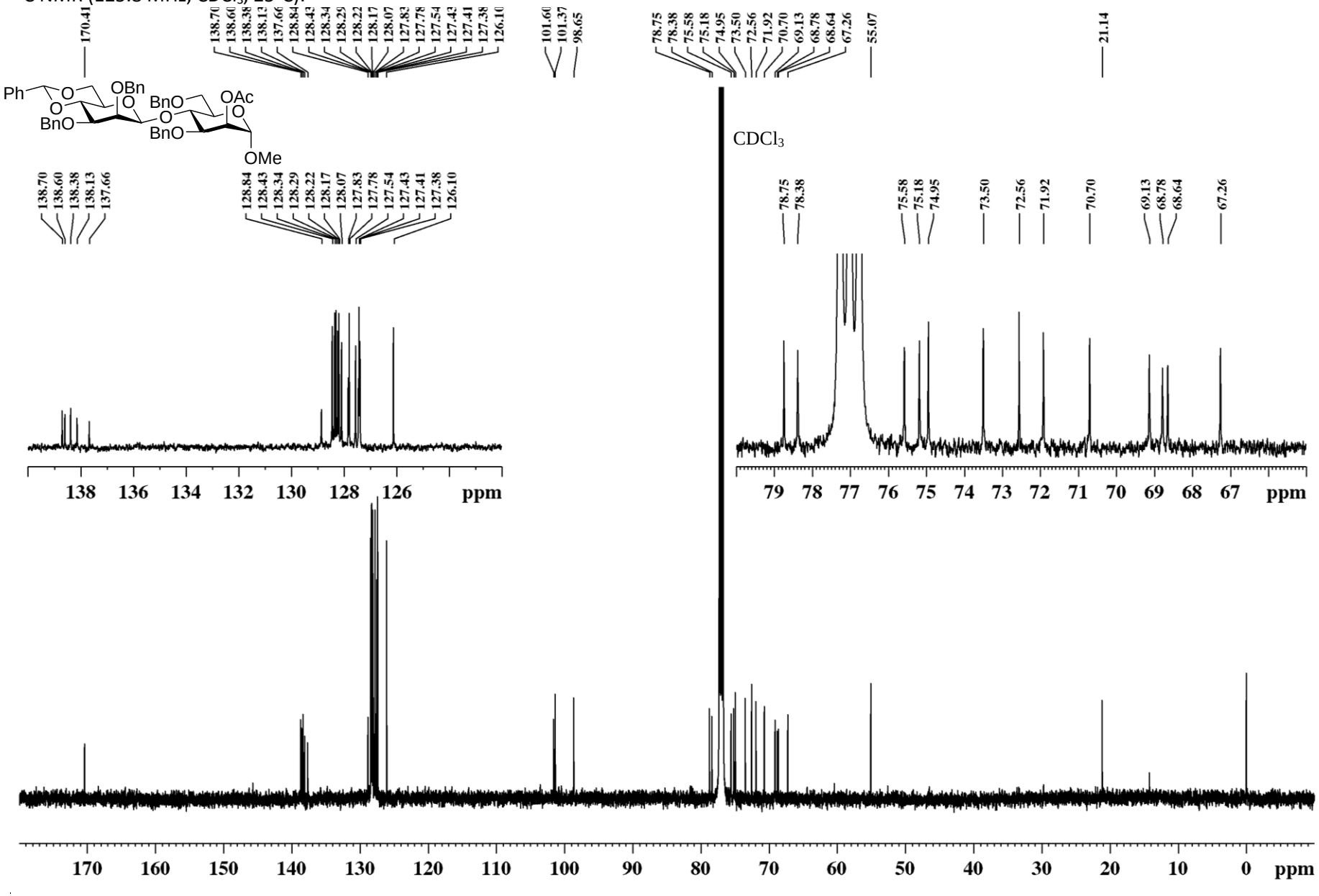


Methyl *O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)-(1→4)-2-*O*-acetyl-3,6-di-*O*-benzyl-α-D-mannopyranoside (11):

^{1}H NMR (500.20 MHz, $CDCl_3$, 25°C):

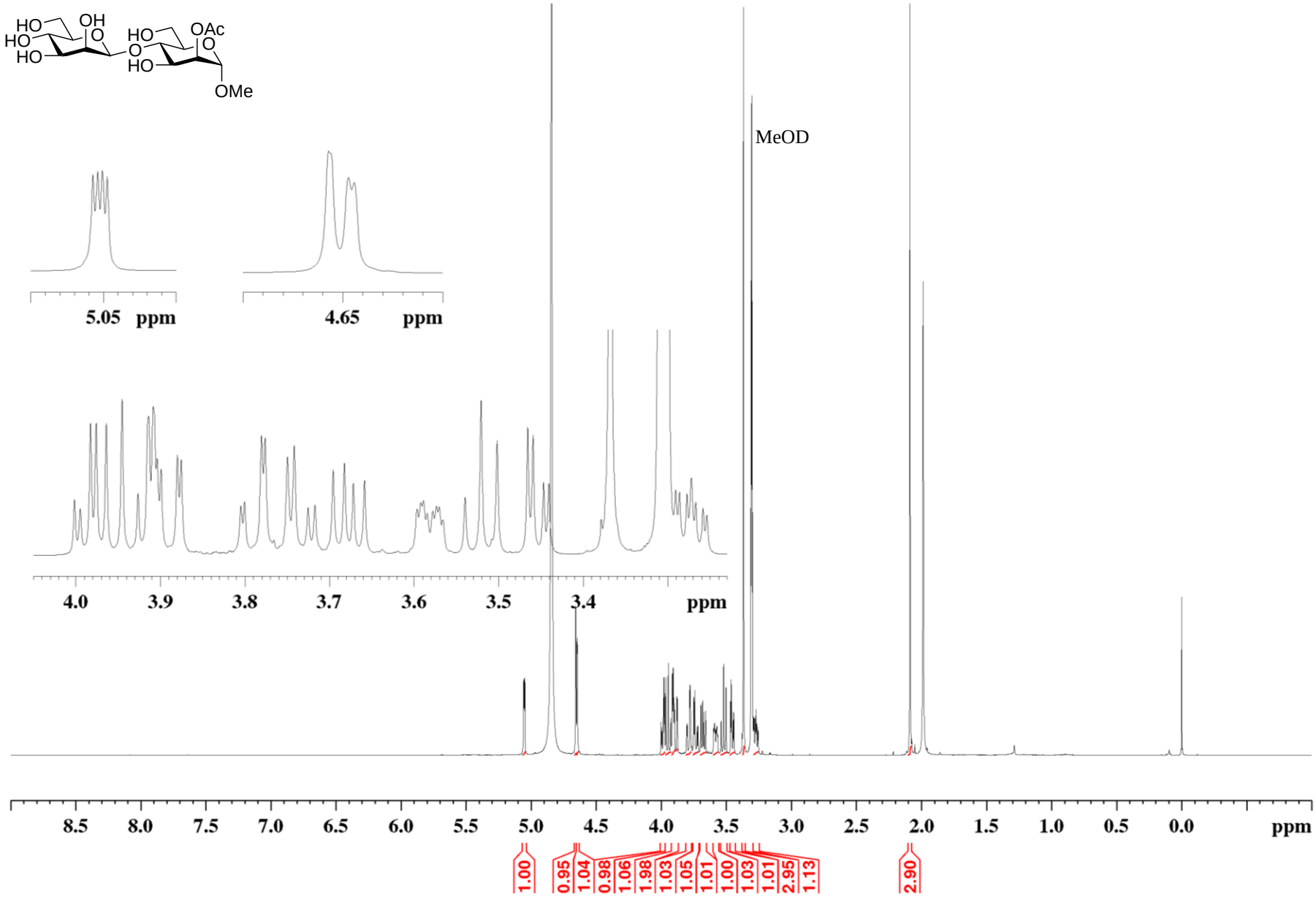


^{13}C NMR (125.8 MHz, $CDCl_3$, 25°C):

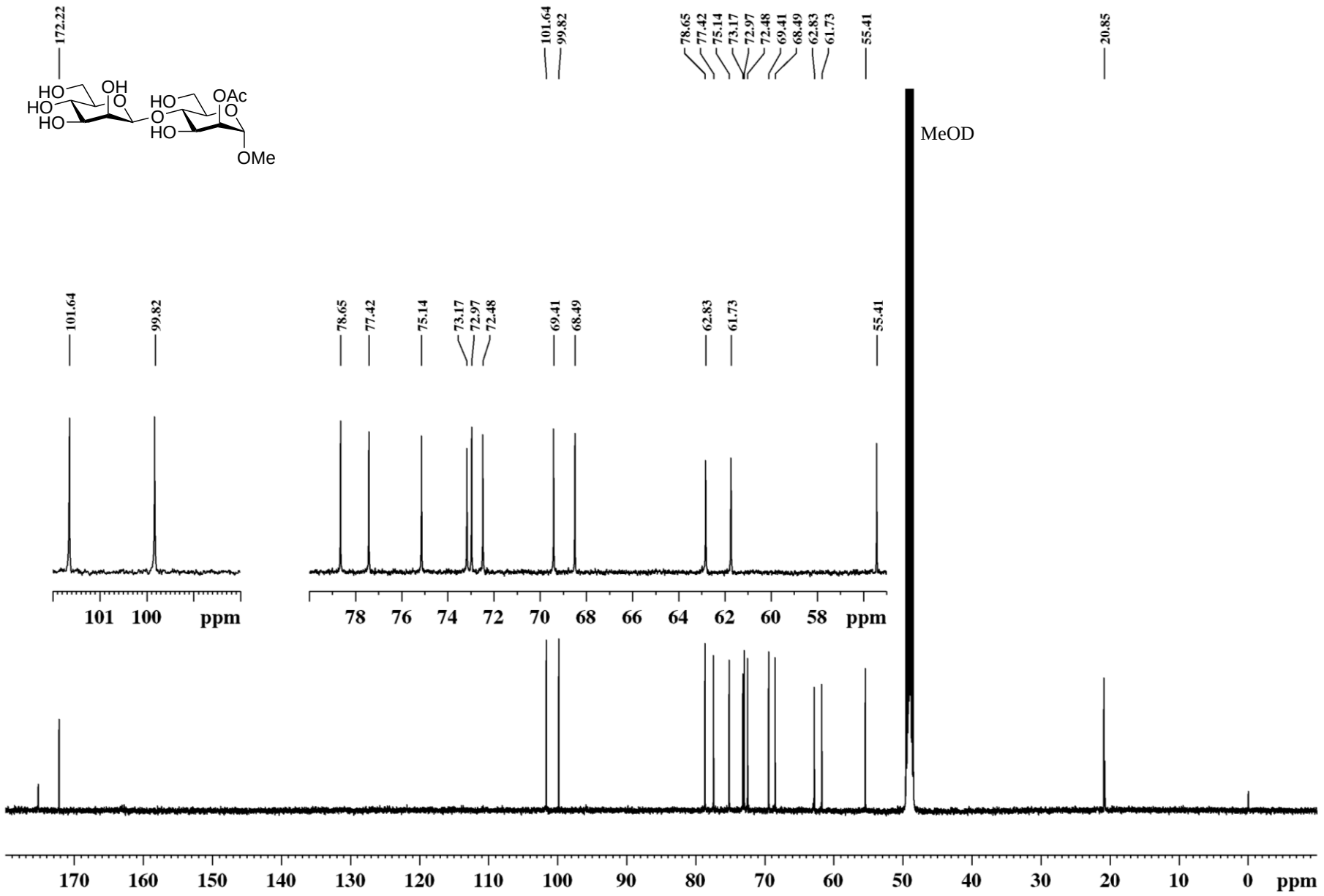


Metyl *O*-(β-D-mannopyranosyl)-(1→4)-2-*O*-acetyl-β-D-mannopyranoside (1):

^{1}H NMR (500.20 MHz, $CDCl_3$, 25°C):

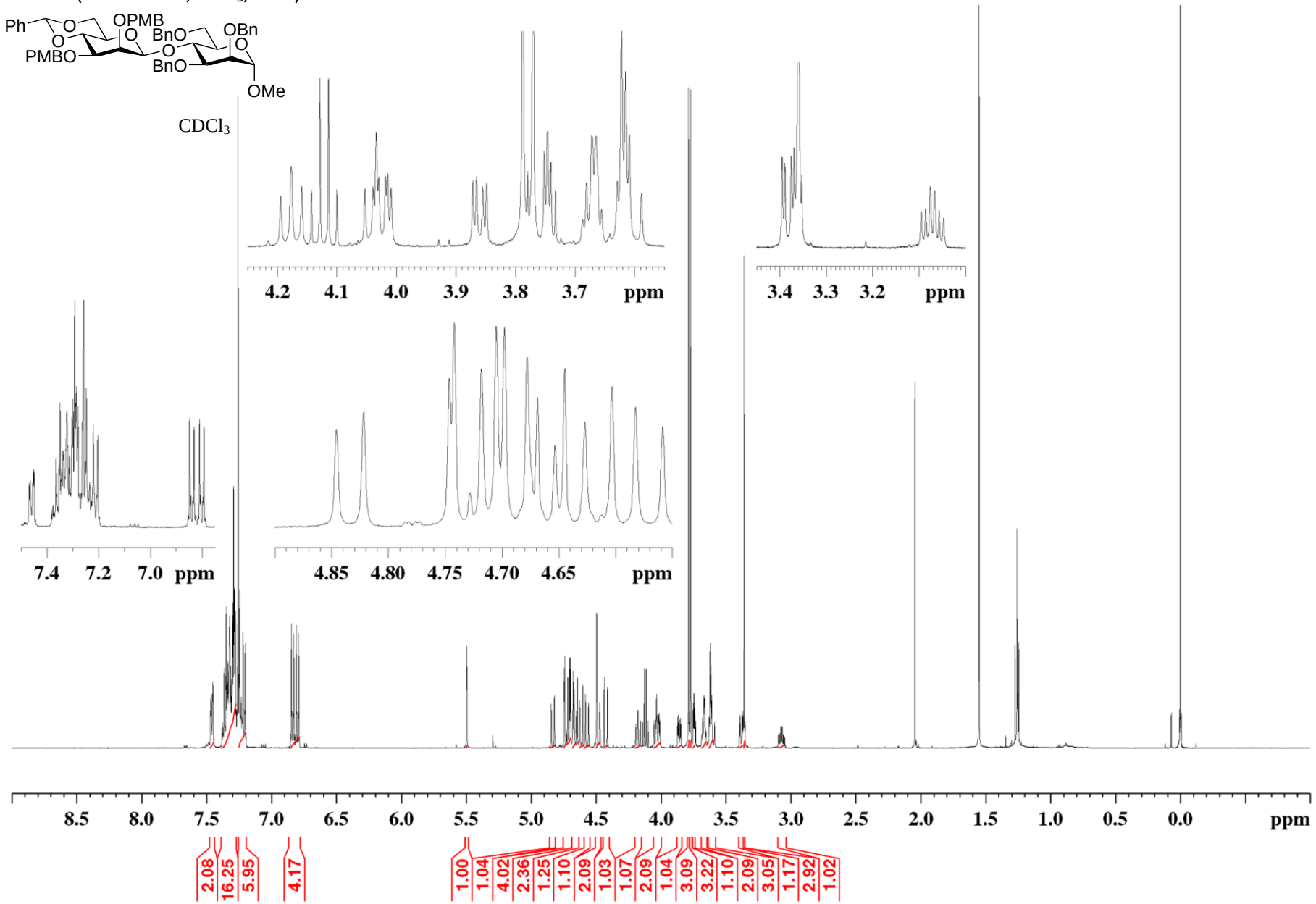


^{13}C NMR (125.8 MHz, $CDCl_3$, 25°C):

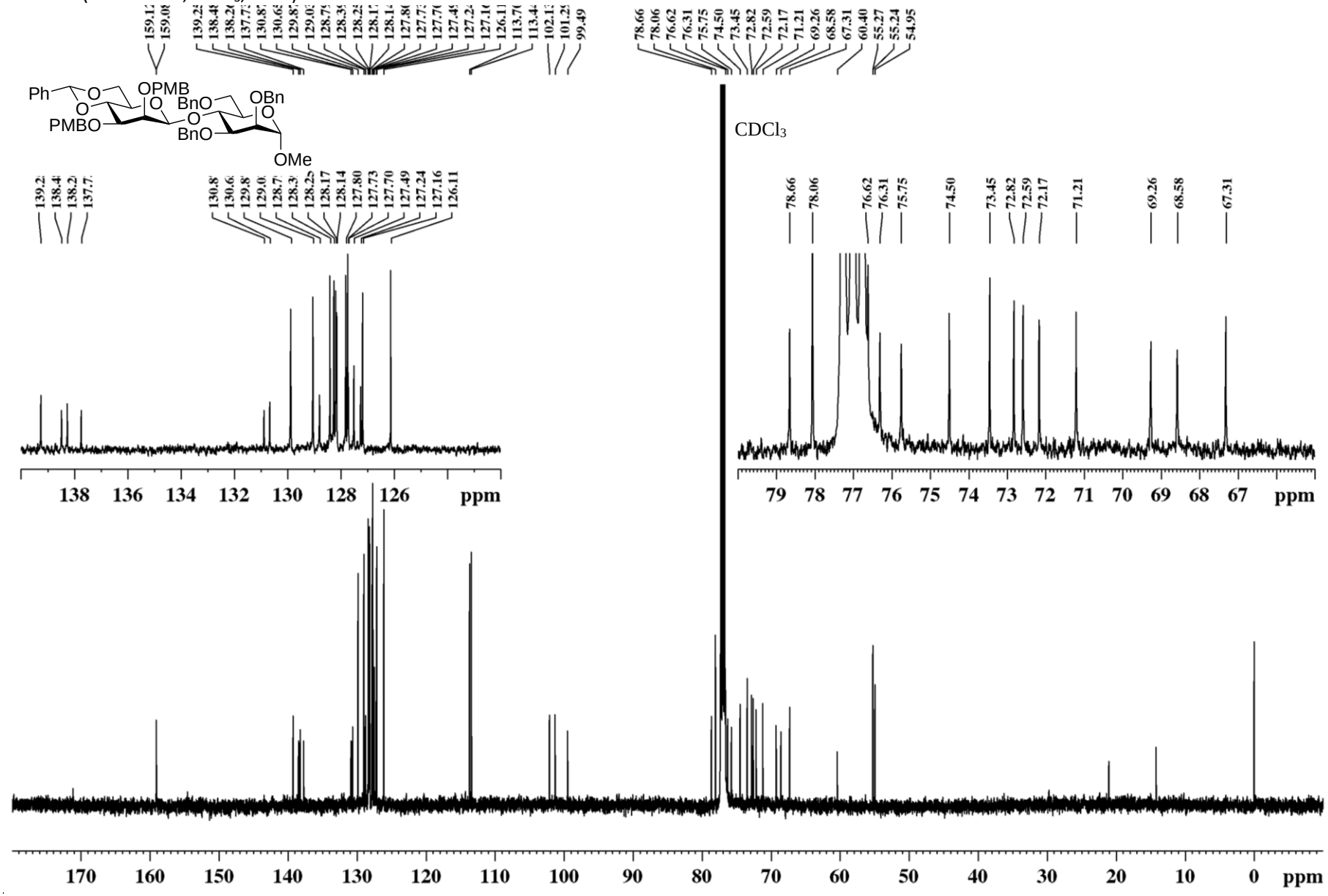


Methyl *O*-(4,6-*O*-benzylidene-2,3-di-*O*-*p*-methoxybenzyl-β-D-mannopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (14):

^{1}H NMR (500.20 MHz, $CDCl_3$, 25°C):

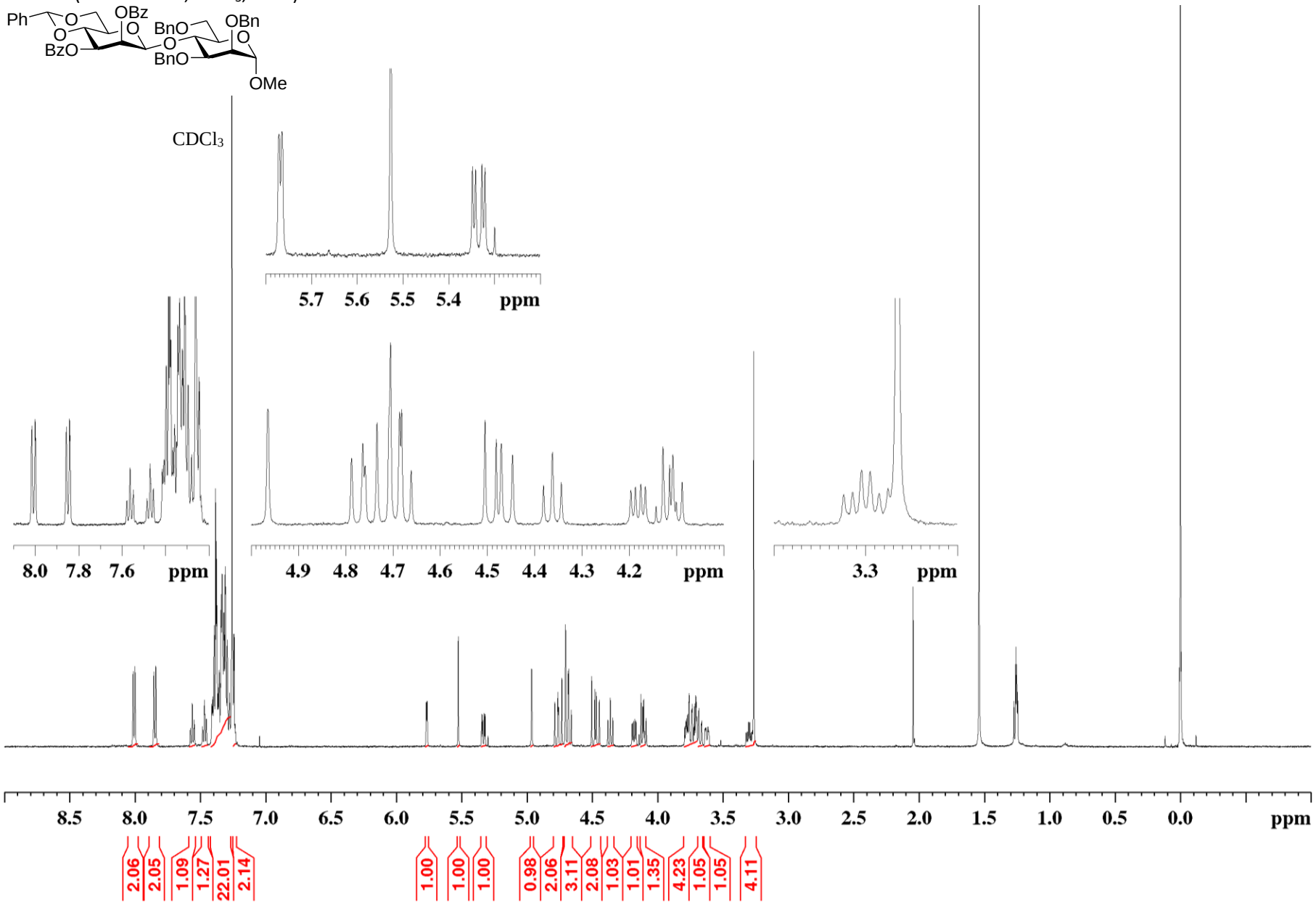


^{13}C NMR (125.8 MHz, $CDCl_3$, 25°C):

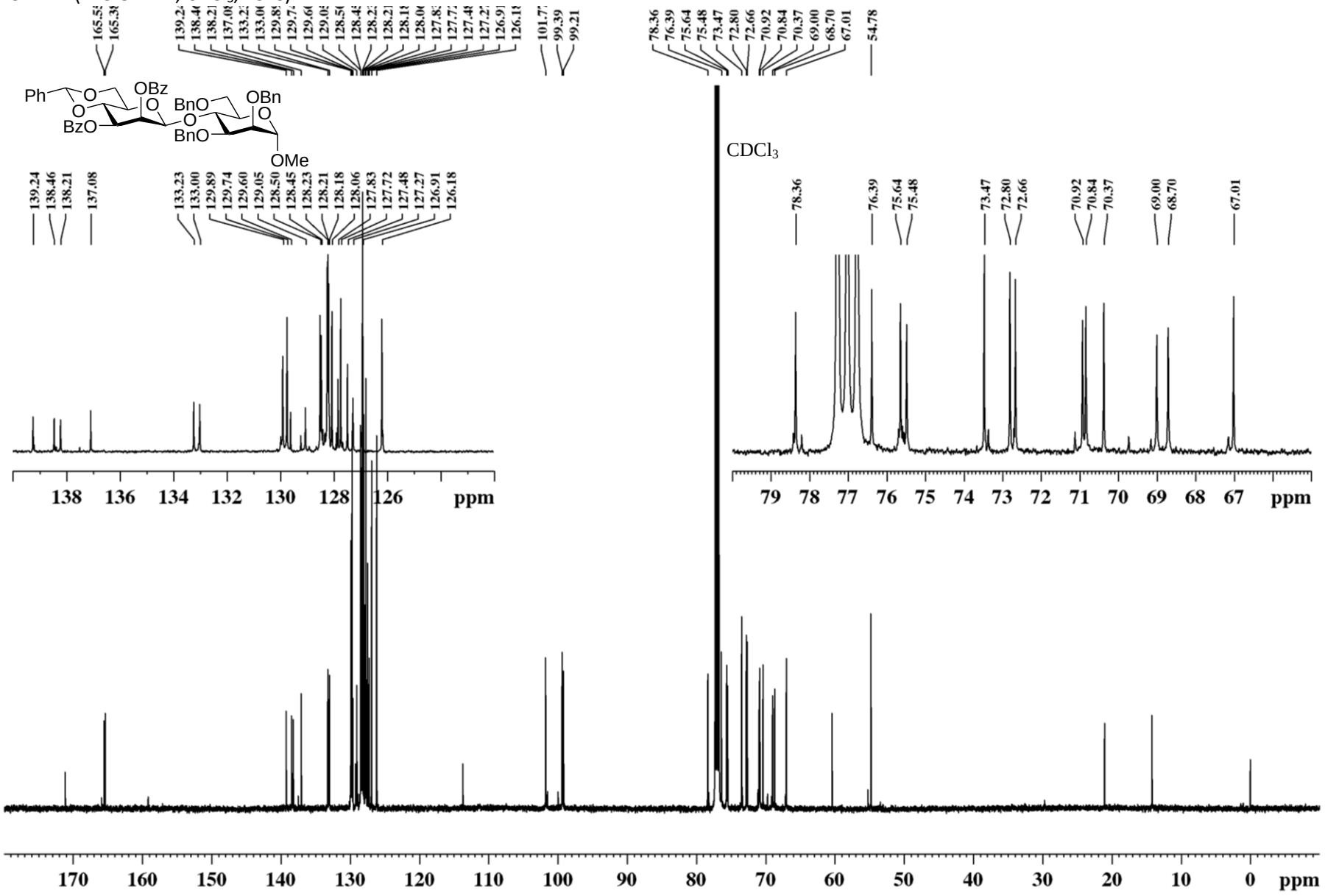


Methyl *O*-(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (15):

^{1}H NMR (500.20 MHz, $CDCl_3$, 25°C):

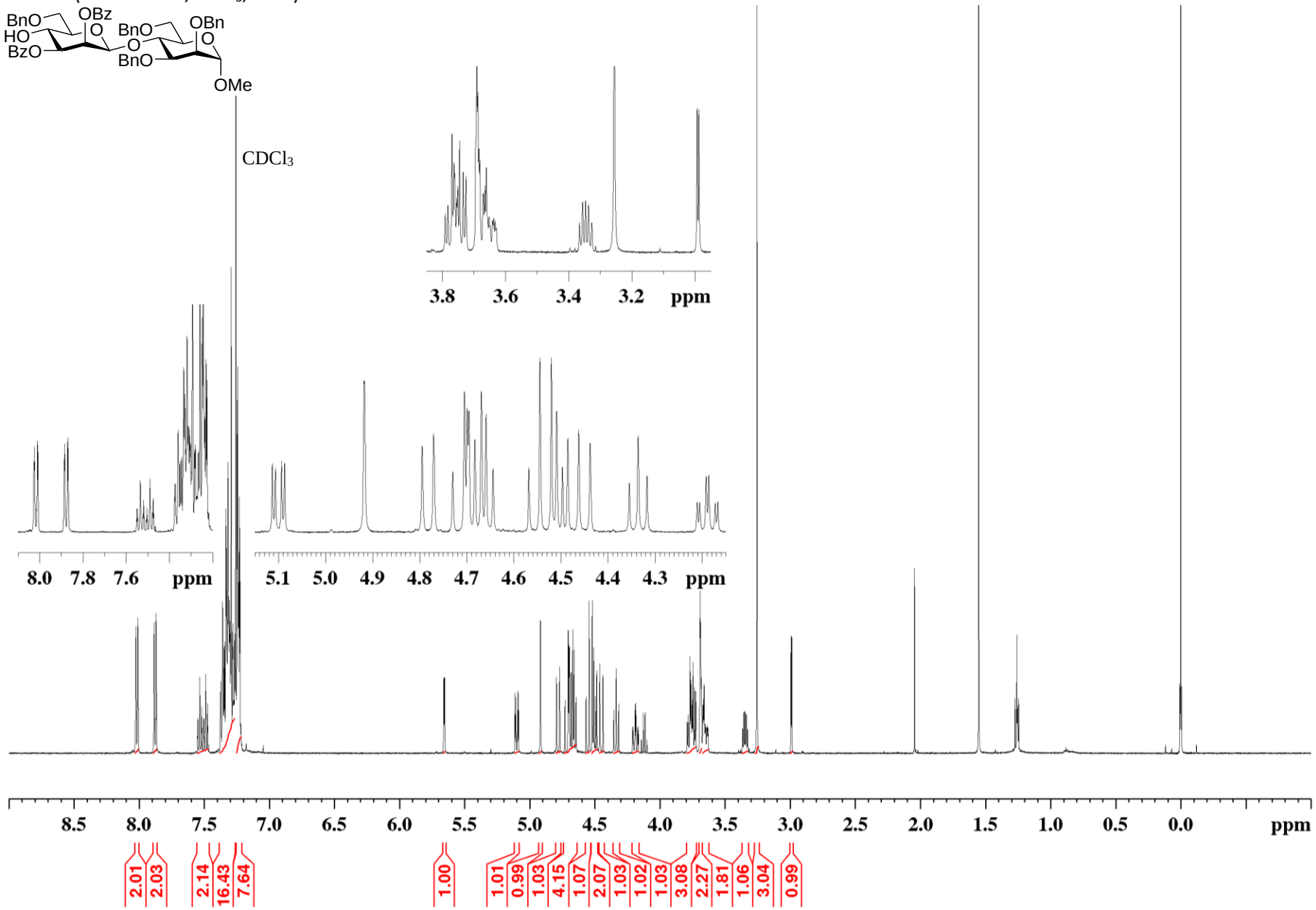


^{13}C NMR (125.8 MHz, $CDCl_3$, 25°C):

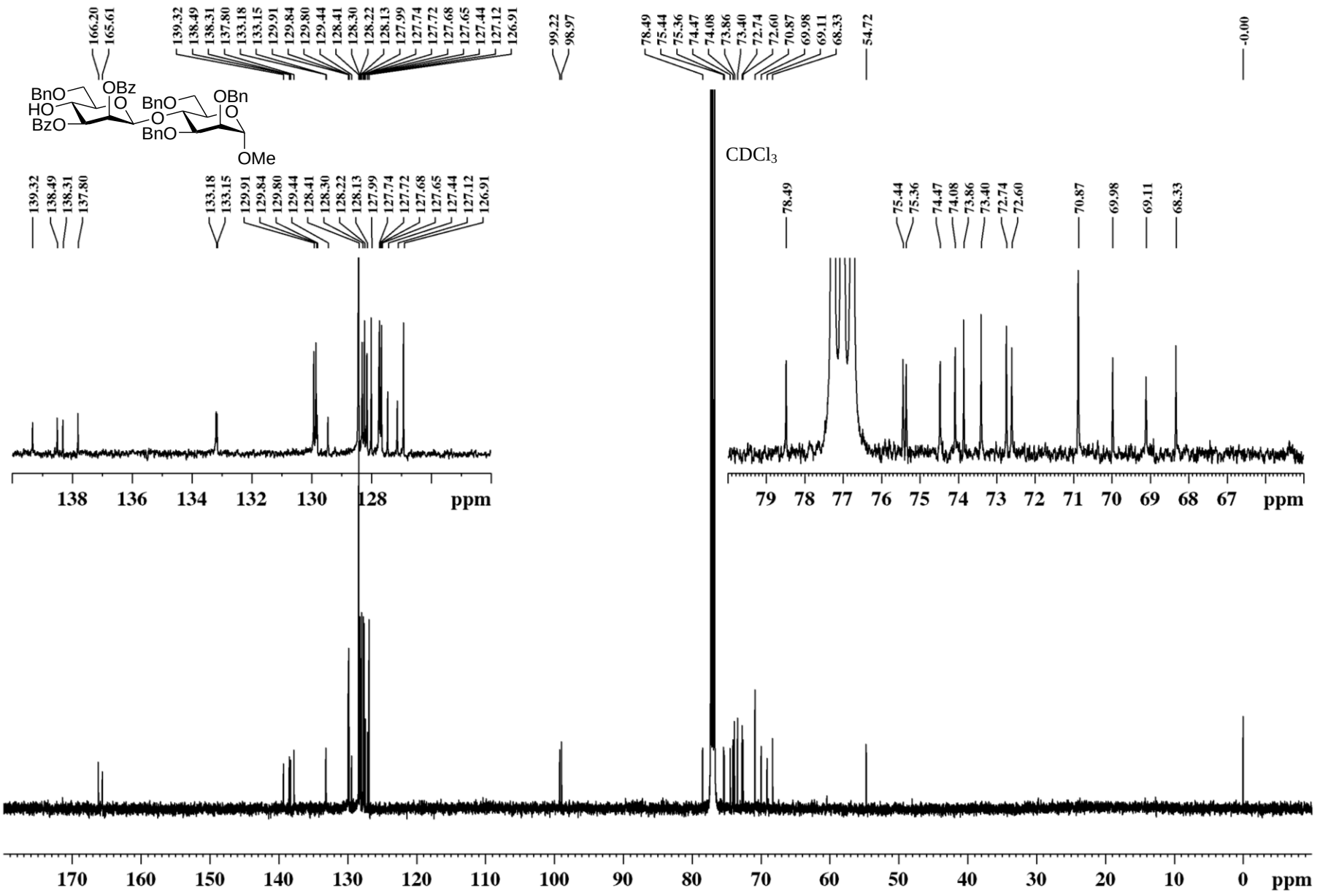


Methyl *O*-(2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-mannopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (16):

^{1}H NMR (500.20 MHz, $CDCl_3$, 25°C):

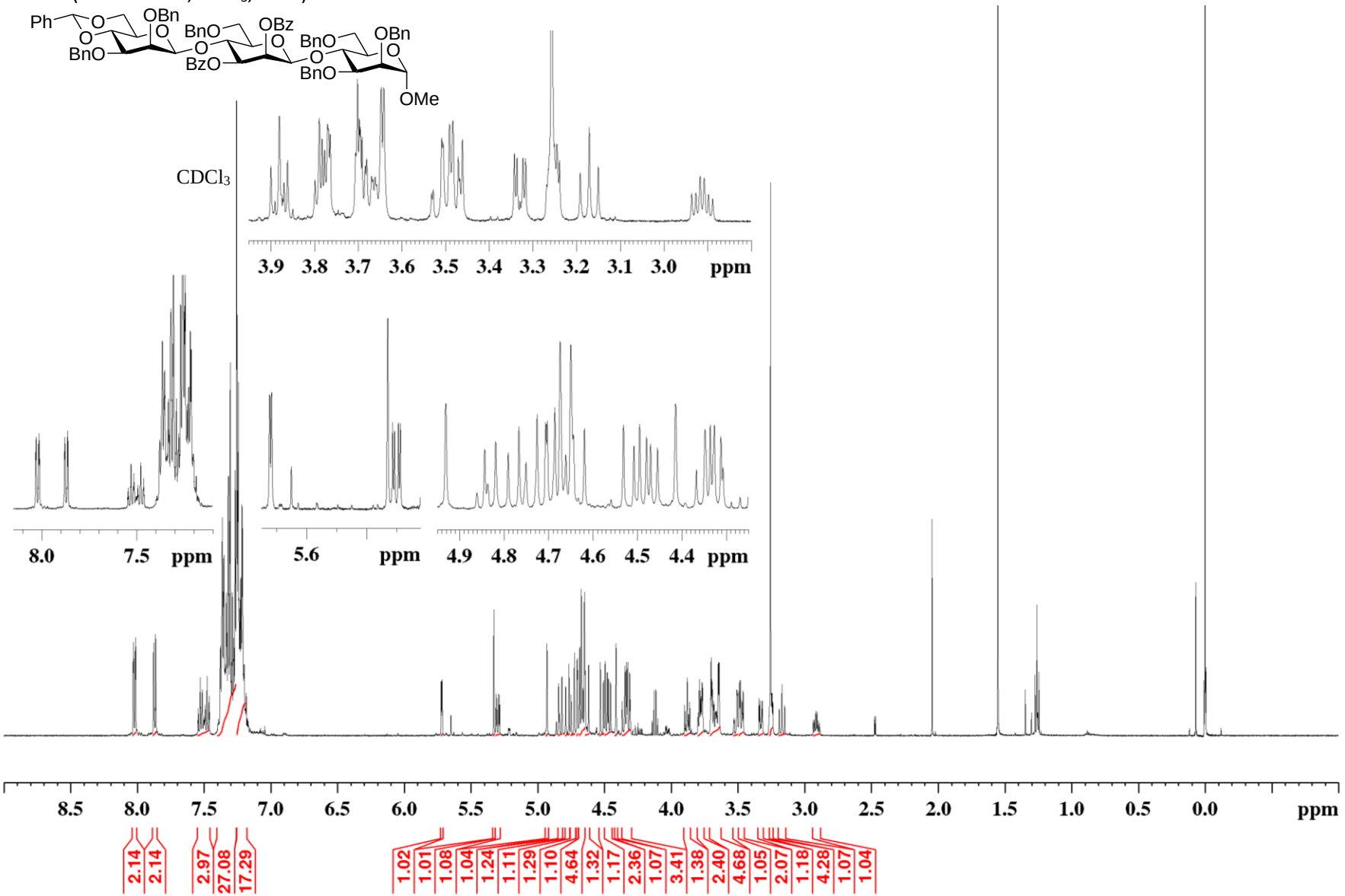


^{13}C NMR (125.8 MHz, $CDCl_3$, 25°C):

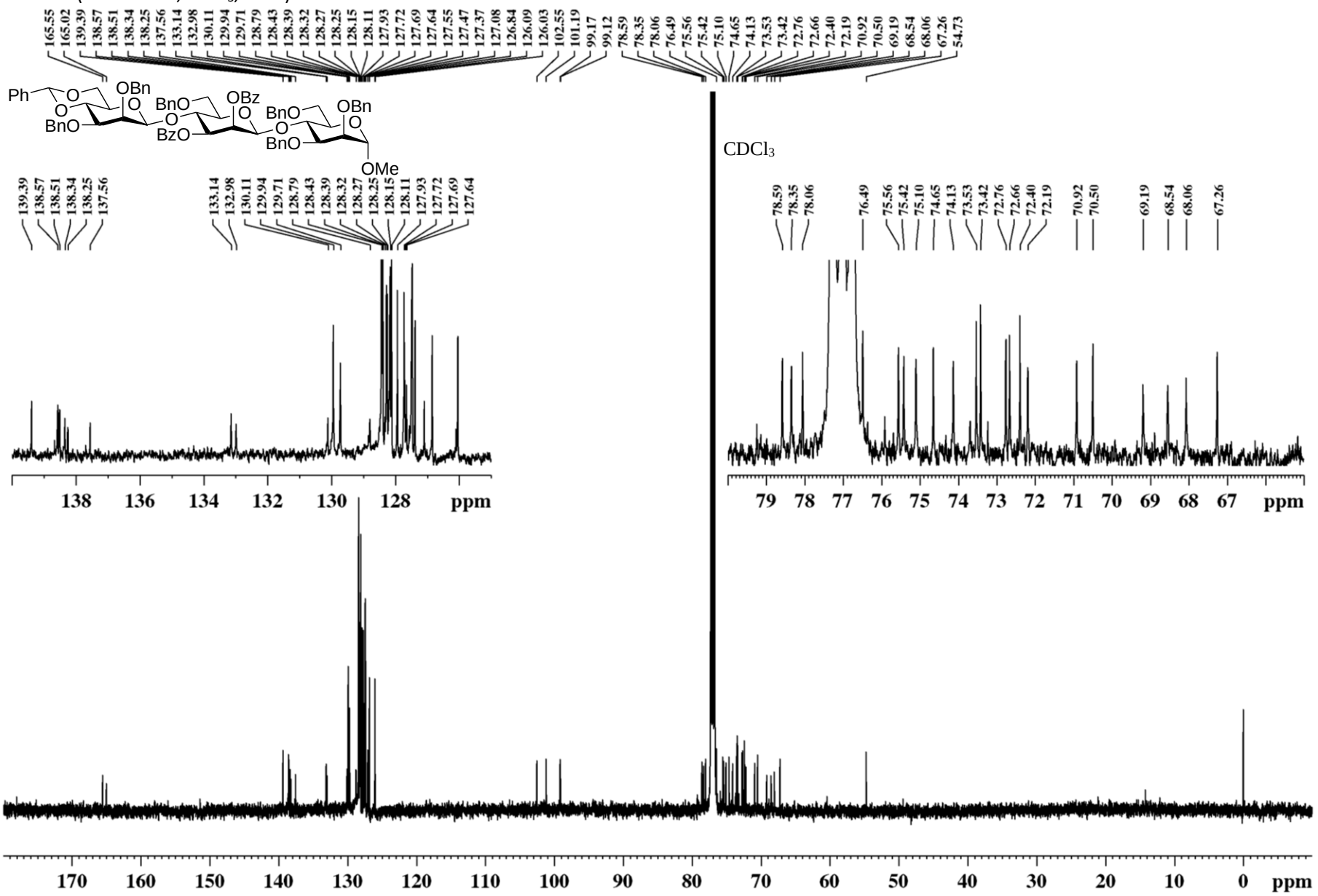


Methyl *O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)-(1→4)-*O*-(2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-mannopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (17):

^{1}H NMR (500.20 MHz, $CDCl_3$, 25°C):

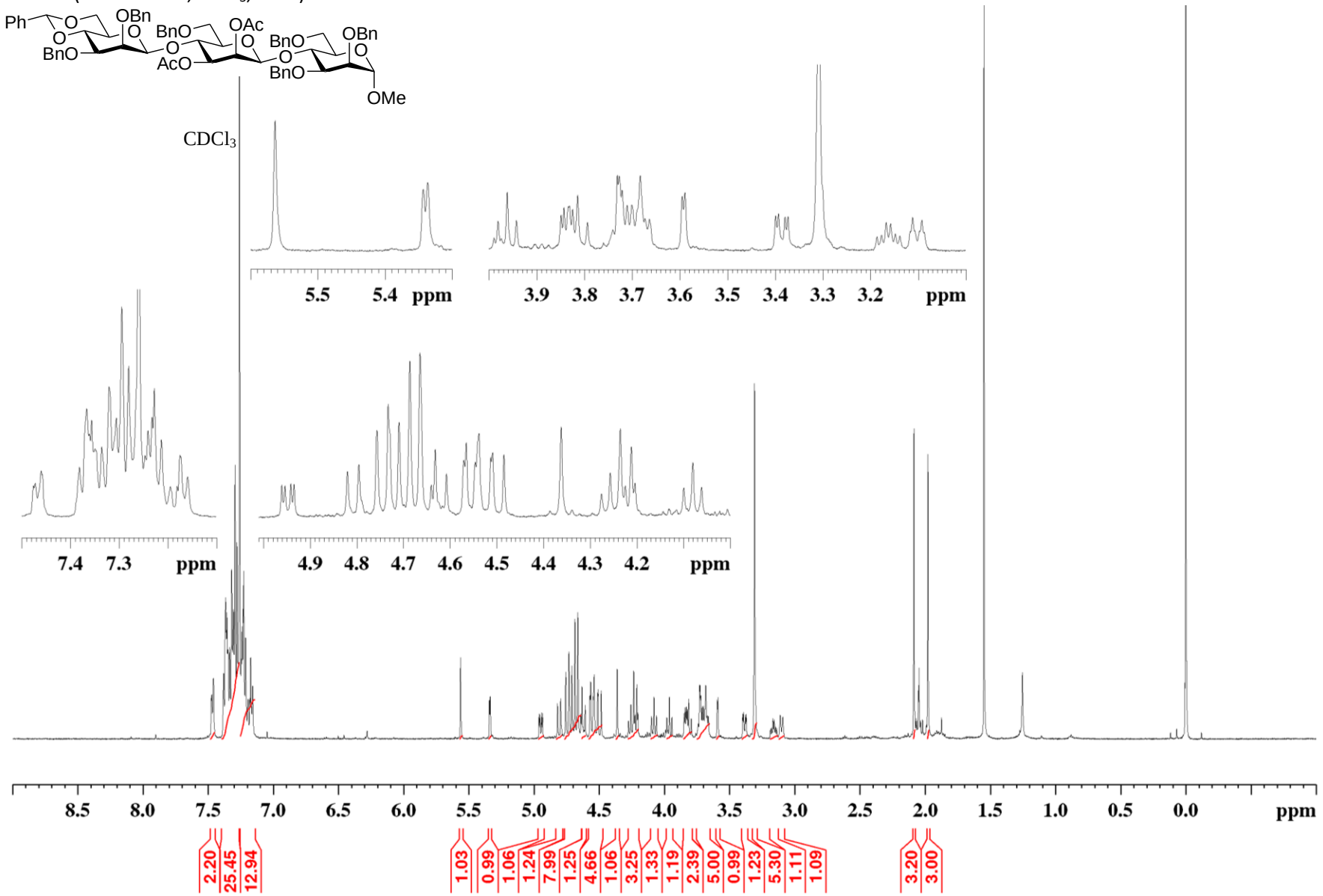


^{13}C NMR (125.8 MHz, $CDCl_3$, 25°C):

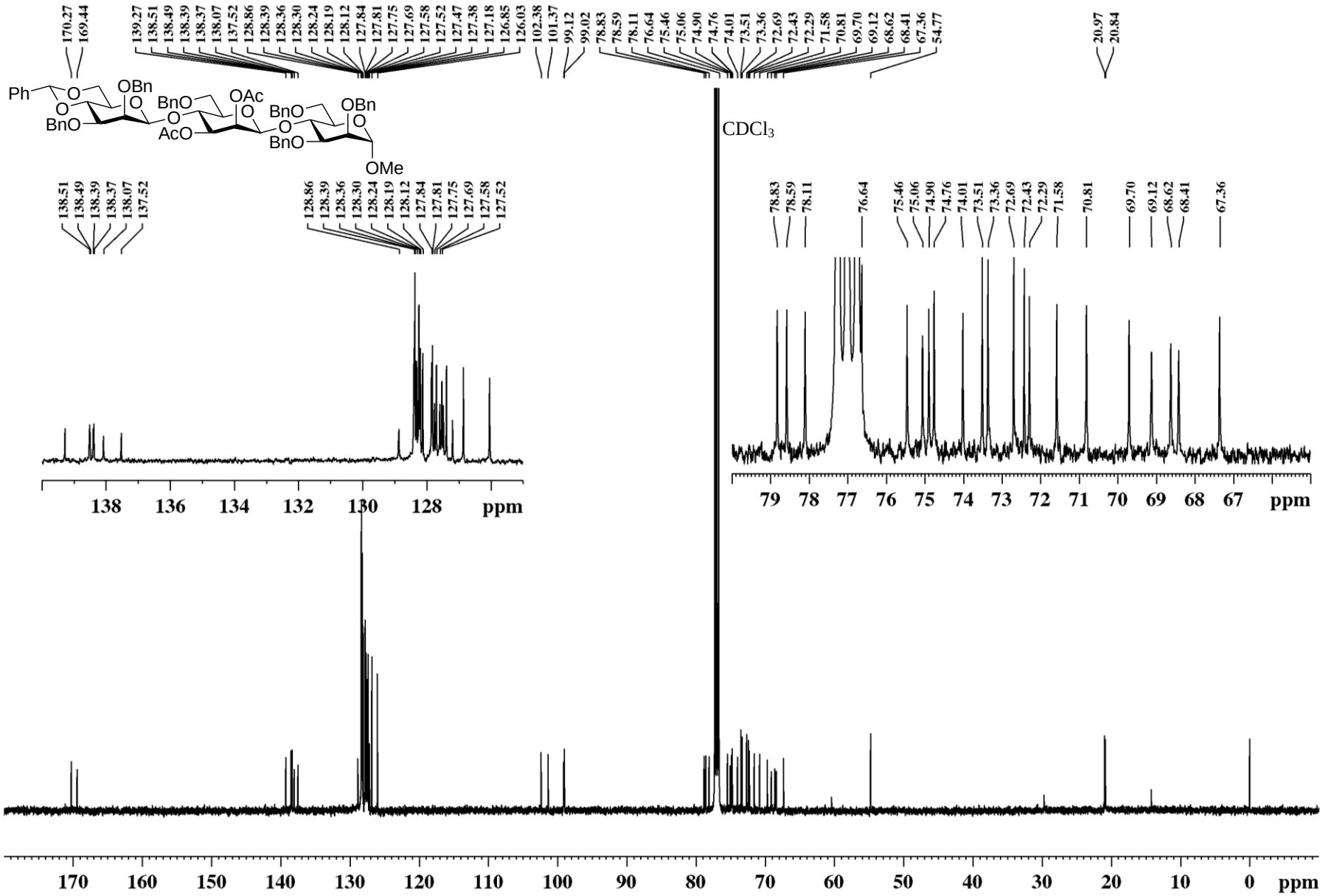


Methyl *O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)-(1→4)-*O*-(2,3-di-*O*-acetyl-6-*O*-benzyl-β-D-mannopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (18):

^{1}H NMR (500.20 MHz, $CDCl_3$, 25°C):

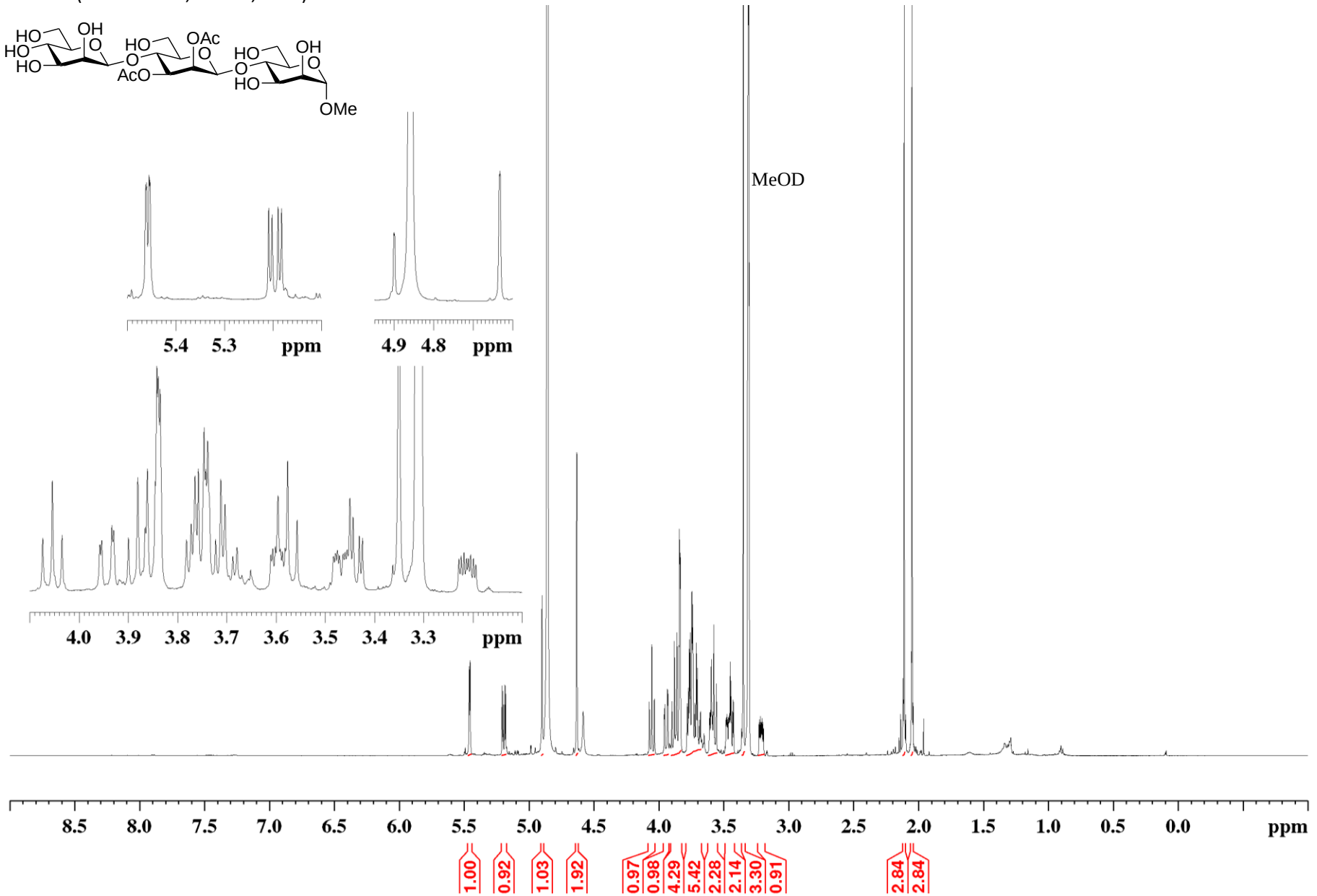


^{13}C NMR (125.8 MHz, $CDCl_3$, 25°C):

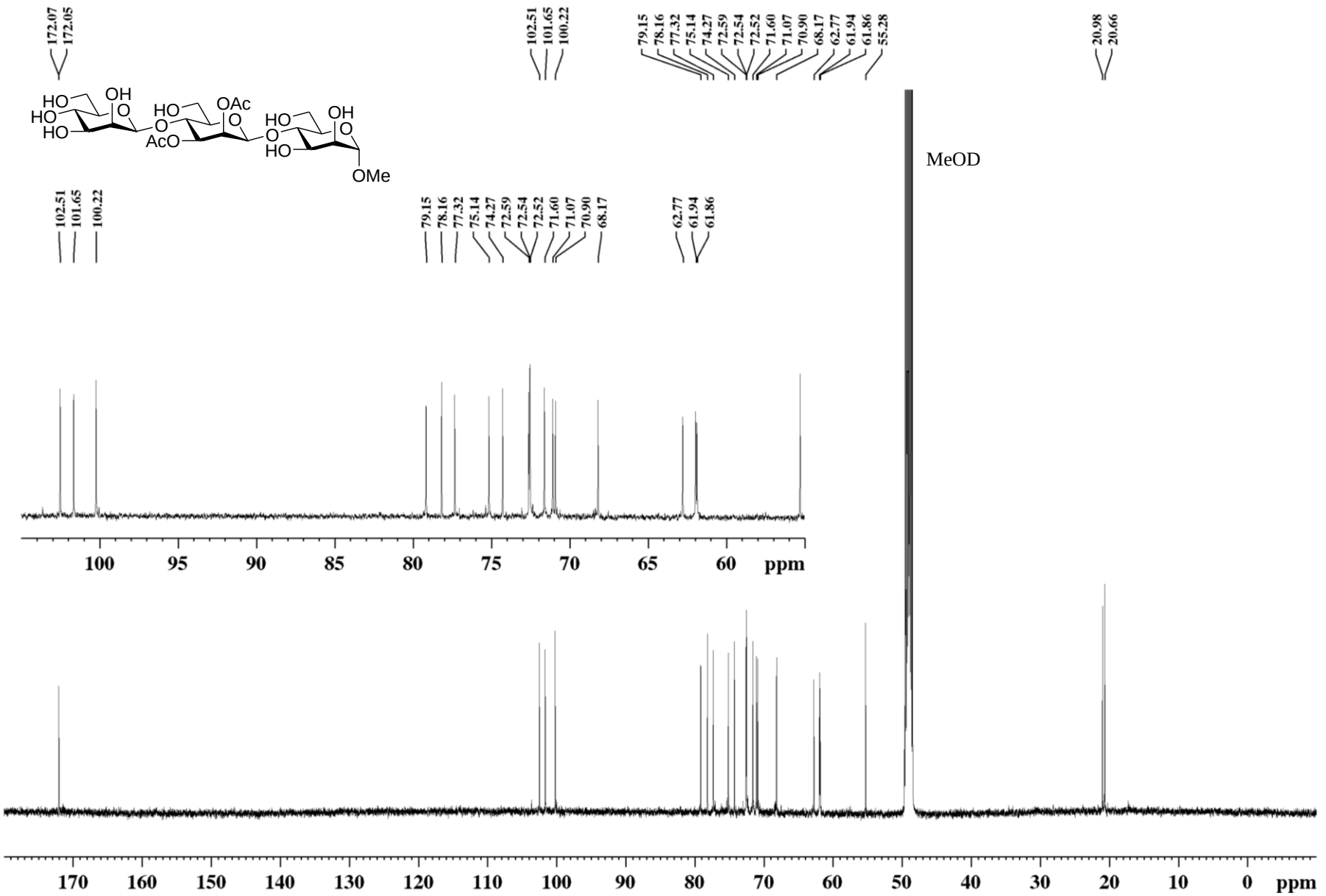


Metyl *O*-(β-D-mannopyranosyl)-(1→4)-*O*-(2,3-di-*O*-acetyl-β-D-mannopyranosyl)-(1→4)-α-D-mannopyranoside (2):

^{1}H NMR (500.20 MHz, MeOD, 25°C):



^{13}C NMR (125.8 MHz, MeOD, 25°C):



References

(1) PERCH solutions. PERCH. Kuopio 2014.

(2) ChemAdder/SpinAdder. Spin Discoveries Ltd (http://www.chemadder.com).

(3) DeNinno, M. P.; Etienne, J. B.; Duplantier, K. C. A Method for the Selective Reduction of Carbohydrate 4,6-*O*-Benzylidene Acetals. *Tetrahedron Lett.* **1995**, *36*, 669–672.

(4) Crich, D.; Smith, M. 1-Benzenesulfinyl Piperidine/Trifluoromethanesulfonic Anhydride: A Potent Combination of Shelf-Stable Reagents for the Low-Temperature Conversion of Thioglycosides to Glycosyl Triflates and for the Formation of Diverse Glycosidic Linkages. *J. Am. Chem. Soc.* **2001**, *123*, 9015–9020.

(5) Crich, D.; Chandrasekera, N. S. Mechanism of 4,6-*O*-Benzylidene-Directed β-Mannosylation as Determined by α-Deuterium Kinetic Isotope Effects. *Angew. Chemie - Int. Ed.* **2004**, *43*, 5386–5389.

(6) Debenham, S. D.; Toone, E. J. Regioselective Reduction of 4,6-*O*-Benzylidenes Using Triethylsilane and $BF_3{\cdot}Et_2O$. *Tetrahedron: Asymmetry* **2000**, *11*, 385–387.

(7) Zemplén, G.; Kunz, A. Studien Über Amygdalin, IV: Synthese Des Natürlichen l-Amygdalins. *Ber. Dtsch. Chem. Ges.* **1924**, *57*, 1357–1359.