Supporting Information

Synthesis and Conformational Studies of Peptides from New C-Linked Carbo-*β*-Amino Acids (*β*-Caas) with Anomeric Methylamino- and Difluorophenyl Moieties

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General Experimental: HOBT: (1-Hydroxy-1H benzotriazole), EDCI: (1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride) coupling reagents were used for peptide synthesis. All coupling reactions and Boc deprotection reactions were carried out under nitrogen atmosphere; TLC: Silica gel *60* F_{254} plates; detection with UV or dipping into the solution of ninhydrin followed by heating; Dichloromethane was distilled over CaH_2 and stored over 4Å molecular sieves, Et_3N was dried on KOH and distilled from ninhydrin, amino-acids and peptide coupling reagents were purchased from standard catalogues;

IR spectra were recorded in KBr pallets in the 400 – 4000 cm^{-1} range.

Melting points were checked using cover slips.

NMR spectra were recorded in $CDCl_3$ in 5-10 mM solution on 600 MHz (^1H: 600 MHz, ^{13}C: 150 MHz), 500 MHz (^1H: 500 MHz, ^{13}C: 125 MHz), 400 MHz (^1H: 400 Mz, ^{13}C: 100 MHz), and 300 MHz (^1H: 300 MHz, ^{13}C: 75 MHz) spectrometers. Chemical shifts (δ) are reported in ppm downfield with respect to TMS ($SiMe_4$) (= 0 ppm). The proton resonance assignments were carried out by using two-dimensional NMR experiments. Total correlation spectroscopy experiments (TOCSY) were run with mixing time of 0.08s and spin-lock field of 10 KHz (500 MHz) and while for the rotating frame Overhauser effect spectroscopy (ROESY) experiments mixing time of 0.2-0.3s and a spin lock field of about 2.5 KHz (500 MHz) used. ROESY experiments provided information on the spatial proximity of the protons. Information on the H-bonding was carried by solvent titration studies by sequentially adding the polar solvent DMSO-d_6 up to 300 μL to 600 μL $CDCl_3$ solution.

Molecular Dynamics (MD): Molecular dynamics simulations were carried out using Insight II(2005)/Discover program[1] on a Silicon Graphics Octane workstation, IRIX64 (6.5) Operating system, model Onyx3 Infinite Performance Fuel. Peptides were initially drawn using the Sketcher from the Builder module of Insight II. Initially sketching of a peptide is done in two dimensions (2D) which was followed by its conversion to three dimensional (3D) structure, which is a convenient alternative to build the peptide in 3D. All the hydrogen atoms are added automatically in the 3D conversion process. After the

completion of sketching the molecules, consistency of the chirality with that expected for at all the stereocenters was verified. After constructing the peptide model, the atom potential types and partial charges were set using the force field CVFF. We have used the default parameters throughout the simulations. Minimization's were first carried out with steepest decent method, followed by conjugate gradient method for a maximum of 3000 iterations each or RMS deviation of 0.001 kcal/mol, whichever was earlier. After minimization, those dihedral angles which had inputs from NMR data (coupling constants) were modified accordingly. Before these folded structures were subjected to undergo yet another round of minimization, the distance restraints derived from the volume integrals obtained from the ROESY spectra using a two-spin approximation and the reference distance of 1.8 Å for the geminal protons. The upper and lower bound of the distance constraints have been obtained by enhancing and reducing the derived distance by 10%. The distance constraints were applied as a square well potential with a force constant of 15 kcal mol^{-1} $Å^{-2}$. Using these restraint, energy minimization is carried out by using protocol mentioned above. This permits to remove initial strain in the structures.

The NMR restrained energy-minimized structures were then subjected to MD simulations. For MD runs, a temperature of 300K was used. The molecules were initially equilibrated for 20 ps and subsequently subjected to a 600 ps dynamics with a step size of 1 fs, sampling the trajectory at equal intervals of 6 ps. In the trajectory 100 samples were generated and minimized with above protocol. Out of these 20 selected lowest energy structures were aligned and compared with the experimental data. For peptide **10** backbone and heavy atom RMSDs are 0.90 Å and 1.25 Å respectively. The corresponding values for the peptides **11**, **12**, **15** and **16** were: 1.15 Å and 1.73Å; 1.20 Å and 1.82 Å; 0.83 Å and 1.40 Å; and 0.93 Å and 1.55 Å (See Supporting information II for **15** and **16**) respectively. For clarity all the protons have been removed and sugars are replaced with methyl groups after the MD calculations.

Reference:

1. Discover, Version 2.98, Biosym Molecular Simulations, SanDiego, CA, 1995

Circular Dichroism (CD) Spectra: The CD spectra were recorded at room temperature on a JASCO J-810 spectrometer using a rectangular fused quartz cell of 0.2 cm path length. CD cell was washed with an aqueous NaOH solution before the each new spectral

mesurement to remove any peptide adhering to the inner surface. Sample solutions (peptide concentration, 200 μM in methanol) were prepared 20 min before measurements. To improve the signal to noise(S/N) ratio all spectra were the averages of eight repeats obtained by collecting data from 260 to 190 nm at 0.2 nm intervals, with a response time of 1 sec for each point. Binomial method is used for smoothening the spectra. The plotted values are expressed in terms of [θ], the total molar ellipticity (deg cm^2 $dmol^{-1}$).

Evaluation of antibacterial activity (MIC):

Test organisms, *Bacillus subtilis* (MTCC 441), *Bacillus sphaericus* (MTCC 511), *Serratia marcescens* (MTCC 97), *Pseudomonas oleovorans* (MTCC 617), *Klebsiella aerogenes* (MTCC 39), *Chromobacterium violaceum* (MTCC 2656) were obtained from the Institute of Microbial Technology, Chandigarh, India. Cultures of test organisms were maintained on nutrient agar slants and were sub cultured prior to testing.

The minimum inhibitory concentration (MIC) was measured by broth dilution method (Villanova, 1982). A set of sterile test tubes with nutrient broth media were capped with cotton plugs (1-9). The test compound is dissolved in sterile water and concentration of 100μg/mL of the test compound is added to the first tube, which is serially diluted from 1 to 9. A fixed volume of 0.5 mL over night culture is added in all the test tubes and incubated at 37 ^{0}C for 24 h. After incubation period the tubes were measured for turbidity with spectrophotometer.

Reference:

Villanova, 1982. National committee for clinical laboratory standards (NCCLS), standard method for dilution antimicrobial susceptibility tests for bacteria, which grows aerobically, p.242.

High Performance Liquid Chromatography (HPLC):

Apparatus and chromatographic conditions

The HPLC system consisting of two LC-20AT pumps, an SPD-M20A diode array detector, a SIL-20AC auto sampler, a DGU-20A3 degasser and CBM-20A communications bus module (all from Shimadzu, Kyoto, Japan) was used. A reversed phase Waters C18 (Waters) column (25 cm×4.6mm i.d.; particle size 5 μm) was used for separation. The chromatographic and the integrated data were recorded using HP-Vectra (Hewlett Packard, Waldron, Germany) computer system using LC-Solution data acquiring software (Shimadzu, Kyoto, Japan).

The mobile phase was 0.02M ammonium acetate: acetonitrile. The analysis was carried out in a isocratic elution mode with 67% acetonitrile and 33% (0.02M) ammonium acetate using a flow rate of 1.0 ml/min. at room temperature. Before delivering into the system the solvent was filtered through 0.455 μm, PTFE filter and degassed under vacuum. The chromatograms were recorded at 254 nm.

Experimental Section:

***tert.*-Butyl *N*-((3a*R*,4*R*,6*R*,6a*S*)-6-[(1*R*)-1,2-dihydroxyethyl]-2,2-dimethylperhydro furo[3,4-*d*][1,3]dioxol-4-ylmethyl)carbamate (21):** A solution of **20** (2.35 g, 6.3 mmol) in methanol (10 mL) and water (2 mL) containing PTSA (catalytic) was stirred at room temperature for 8 h. Reaction mixture was neutralized with Et_3N, solvent evaporated and residue purified by column chromatography (Silica gel, 50% EtOAc in petroleum ether) to afford **21** (1.82 g, 87%) as a colorless syrup; $[\alpha]_D$ = +4.0 (*c* 2.5, $CHCl_3$); IR (neat): 3373, 2978, 2935, 1690, 1527, 1368, 1253, 1085, 893 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 4.86 (dd, 1H, *J* = 3.4, 5.9 Hz, C_3H), 4.84 (bs, 1H, m, NH), 4.54 (d, 1H, *J* = 5.9 Hz, C_2H), 4.05 (dd, 1H, *J* = 4.5, 10.2 Hz, C_1H), 3.97 (m, 1H, C_4H), 3.95 (m, 1H, C_5H), 3.79 (dd, 1H, *J* = 3.4, 11.8, Hz, C_6H), 3.75 (dd, 1H, *J* = 3.0, 11.8, Hz, $C_{6'}H$), 3.28 (m, 1H, CH_2a), 3.02 (m, 1H, CH_2b), 1.49 (s, 3H, Me), 1.44 (s, 9H, Boc), 1.34(s, 3H, Me); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.7, 112.8, 84.1, 82.6, 81.0, 78.5, 69.8, 63.6, 39.5, 28.3, 26.1, 24.8; HRMS (ESI): *m/z* calculated for $C_{15}H_{27}NO_7$ (M^++Na) 356.1685, found 356.1671.

Cbz-(*R*)-β-Caa(NHBoc)-OCH$_3$ (2): A mixture of **25** (0.83 g, 1.78 mmol) in methanol (3.0 mL) was treated with 10% Pd-C (0.1 g) as described for **26** to give *methyl (3R)-3-((3aS,4R,6R,6aR)-6-[(tert.-butoxycarbonyl)amino]methyl-2,2-dimethyl perhydrofuro[3,4-d][1,3]dioxol-4-yl)-3-aminopropanoate* (**27**) as a pale yellow liquid, which was used as such for the next reaction.

A solution of **27** (0.40 g, 1.06 mmol) and DIPEA (0.37 mL, 2.12 mmol) in CH_2Cl_2 (10 mL) at 0 °C was treated with Cbz-Cl (0.21 g, 1.23 mmol), as described for **1** to give **2** (0.49 g, 90%) as a syrup; $[\alpha]_D$ = +19.2 (*c* 0.5, $CHCl_3$); IR (Neat): 3358, 2982, 2289, 1744, 1540, 1447, 1376, 879, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.41-7.23 (m, 5H, Ar-H), 5.65 (d, 1H, *J* = 9.7 Hz, NH), 5.10 (m, 2H, $PhCH_2$), 4.73 (dd, 1H, *J* = 3.8, 6.0 Hz, C_3H), 4.70 (br.m, 1H, BocNH), 4.53 (d, 1H, *J* = 6.0 Hz, C_2H), 4.43 (m, 1H, $C_\beta H$), 4.07 (dd, 1H, *J* = 5.7, 9.2 Hz, C_1H), 4.04 (m, 1H, C_4H), 3.67 (s, 3H, COOMe), 3.28 (m, 1H, CH_2a), 3.00 (ddd, 1H, *J* = 4.1, 9.2, 13.9 Hz, 1H, CH_2b), 2.84 (dd, 1H, *J* = 7.1, 15.8 Hz, 1H, $C_\alpha H$), 2.69 (dd, 1H, *J* = 5.6, 15.8 Hz, 1H, $C_{\alpha'}H$), 1.49 (s, 3H, Me), 1.44 (s, 9H, Boc), 1.30 (s, 3H, Me); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.9, 155.8, 141.8, 136.5, 128.4, 128.2, 127.9, 127.8,

113.0, 83.0, 80.8, 80.7, 78.8, 66.5, 51.7, 47.8, 39.8, 36.1, 28.3, 26.1, 24.6; HRMS (ESI): *m/z* calculated for $C_{25}H_{36}N_2O_9$ (M^++H) 509.2499, found 509.2481.

Cbz-(*S*)-β-Caa(NHBoc)-OH (28): A solution of ester **1** (0.75 g, 1.47 mmol) in methanol (4 mL) was treated with aq. 4N NaOH solution (4 mL) at 0 ^oC to room temperature. After 2 h, methanol was removed and adjusted pH to 2-3 with aq. 1N HCl solution at 0 ^oC and extracted with EtOAc (2 x 10 mL). The organic layer was dried (Na_2SO_4) and concentrated to give **28** (0.62 g, 83%) as a white solid, m.p. 78-80 °C; $[\alpha]_D$ = +42.2 (*c* 0.25, $CHCl_3$); IR (KBr): 3364, 2980, 2934, 1712 1514, 1451, 1371, 1249, 1168, 1040 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.39-7.26 (m, 5H, Ar-H), 5.61 (d, 1H, *J* = 8.3 Hz, NH), 5.08 (m, 2H, $PhCH_2$), 4.88 (br.m, 1H, BocNH), 4.68 (m, 1H, C_3H), 4.53 (d, 1H, *J* = 5.9 Hz, C_2H), 4.35 (m, 1H, $C_\beta H$), 4.15-4.02 (m, 2H, C_4H, C_1H), 3.31 (m, 1H, CH_2a), 3.11 (m, 1H, CH_2b), 2.83 (m, 1H, $C_\alpha H$), 2.61 (m, 1H, $C_{\alpha'}H$), 1.47 (s, 3H, Me), 1.41 (s, 9H, Boc), 1.28 (s, 3H, Me); HRMS (ESI): *m/z* calculated for $C_{24}H_{34}N_2O_9$ (M^++Na) 517.2162, found 517.2163.

Cbz-(*R*)-β-Caa(NHBoc)-OH (29): A solution of **2** (0.50 g, 0.98 mmol) as described for **28** gave **29** (0.42 g, 86%) as a white solid; m.p. 78-80 °C; $[\alpha]_D$ = +56.73 (*c* 0.25, $CHCl_3$); IR(KBr): 3364, 2980, 2934, 1712, 1514, 1451, 1371, 1249, 1168, 1040; ^1H NMR (500 MHz, $CDCl_3$): δ 7.39-7.26 (m, 5H, Ar-H), 5.87 (d, 1H, *J* = 9.6 Hz, NH), 5.09 (m, 2H, $PhCH_2$), 4.97 (br.m, 1H, BocNH), 4.74 (m, 1H, C_3H), 4.53 (d, 1H, *J* = 5.9 Hz, C_2H), 4.45 (m, 1H, $C_\beta H$), 4.15-4.05 (m, 2H, C_4H, C_1H), 3.28 (m, 1H, CH_2a), 3.02 (ddd, 1H, *J* = 4.2, 8.9, 14.0 Hz, 1H, CH_2b), 2.84 (dd, 1H, *J* = 7.0, 15.9 Hz, 1H, $C_\alpha H$), 2.70 (dd, 1H, *J* = 6.3, 15.9 Hz, 1H, $C_{\alpha'}H$), 1.49 (s, 3H, Me), 1.43 (s, 9H, Boc), 1.30 (s, 3H, Me); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 175.1, 156.2, 156.1, 136.5, 128.4, 127.9, 127.7, 112.9, 83.1, 82.9, 80.9, 79.7, 78.5, 66.6, 47.8, 39.8, 36.2, 28.3 26.1, 24.5; HRMS (ESI): *m/z* calculated for $C_{24}H_{34}N_2O_9$ (M^++Na) 517.2162, found 517.2171.

(*S*)-Methyl-3-(benzylamino)-3-((3a*S*,4*S*,6*R*,6a*S*)-tetrahydro-4-methoxy-2,2-dimethyl furo[3,4-*d*][1,3]dioxol-6-yl)propanoate (31) and (*R*)-methyl-3-(benzylamino)-3-((3a*S*,4*S*, 6*R*,6a*S*)-tetrahydro-4-methoxy-2,2-dimethyl furo[3,4-*d*][1,3]dioxol-6-yl)propanoate (32): As described for the synthesis of **24**, a mixture of **30** (10.15 g, 39.3 mmol) and benzylamine (10 mL, 100 mmol) was stirred at room temperature for 12 h and purified the reaction mixture by column chromatography. First eluted was (Silica gel, 10%

EtOAc in petroleum ether) **32** (3.68 g, 25.6%) as a pale yellow syrup; $[\alpha]_D$ = +59.0 (*c* 0.25, $CHCl_3$); IR (Neat): 3356, 2988, 2938, 2838, 2833, 1736, 1438, 1375, 1194, 1097, 744 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.34 (m, 2H, ArH), 7.29 (m, 2H, ArH), 7.22 (m, 1H, ArH), 4.84 (s, 1H, C_1H), 4.78 (dd, 1H, *J* = 3.4, 5.9 Hz, C_3H), 4.54 (d, 1H, *J* = 5.9Hz, C_2H), 3.91 (dd, 1H, *J* = 3.4, 8.5 Hz, C_4H), 3.88 (s, 2H, $ArCH_2$), 3.67 (s, 3H, COOMe), 3.49 (m, 1H, $C_\beta H$), 3.29 (s, 3H, OMe), 2.76 (dd, 1H, *J* = 4.5, 15.4 Hz, $C_\alpha H$), 2.60 (dd, 1H, *J* = 7.0, 15.4 Hz, $C_{\alpha'}H$), 1.42 (s, 3H, Me), 1.31 (s, 3H, Me); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.7, 140.6, 128.2, 128.1, 126.8, 112.4, 106.7, 85.0, 81.2, 79.7, 54.3, 52.9, 51.4, 51.1, 36.1, 26.1, 24.9; HRMS (ESI): *m/z* calculated for $C_{19}H_{28}NO_6$ (M^++H) 366.1916, found 366.1913.

Second eluted was (Silica gel, 15% EtOAc in petroleum ether) **31** (5.51 g, 38%) as a pale yellow syrup; $[\alpha]_D$ = +48.0 (*c* 0.25, $CHCl_3$); IR (Neat): 3370, 2991, 2937, 2899, 1739, 1444, 1160, 1087, 1020, 738 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.34 (m, 2H, ArH), 7.31 (m, 2H, ArH), 7.23 (m, 1H, ArH), 4.89 (s, 1H, C_1H), 4.74 (dd, 1H, *J* = 3.7, 5.9 Hz, $C_\delta H$), 4.55 (d, 1H, *J* = 5.9 Hz, C_2H), 4.07 (dd, 1H, *J* = 3.7, 8.7 Hz, C_4H), 3.89 (qt, 2H, CH_2), 3.69 (s, 3H, COOMe), 3.46 (m, 1H, $C_\beta H$), 3.31 (s, 3H, OMe), 2.74 (dd, 1H, *J* = 5.2, 15.1 Hz, $C_\alpha H$), 2.58 (dd, 1H, *J* = 6.2, 15.1 Hz, $C_{\alpha'}H$), 1.42 (s, 3H, Me), 1.29 (s, 3H, Me); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.4, 140.3, 128.3, 126.8, 112.5, 106.8, 85.0, 81.4, 79.7, 54.6, 54.1, 51.6, 51.2, 35.7, 26.0, 24.8; HRMS (ESI): *m/z* calculated for $C_{19}H_{28}NO_6$ (M^++H) 366.1916, found 366.1918.

Boc-(*S*)-β-Caa-OCH_3 (5): A solution of **31** (1.10 g, 3.01 mmol) in methanol (5.0 mL) was treated with 10% Pd-C (0.10 g) for 12 h as described for **26** to give *methyl (3S)-3-[(3aS,4R,6S,6aS)-6-methoxy-2,2-dimethylperhydrofuro[3,4-d][1,3]dioxol-4-yl]-3-amino-propanoate* (**33**; 0.75 g, 90%) as a pale yellow liquid, which was used as such for the next reaction.

A solution of **33** (0.78 g, 2.82 mmol) and Et_3N (0.76 mL, 5.64 mmol) in THF (10 mL) at 0 °C was treated with $(Boc)_2O$ (0.68 mL, 2.82 mmol) and stirred at room temperature for 3 h. After completion of the reaction, solvent was evaporated and residue purified by column chromatography (Silica gel, 15% EtOAc in petroleum ether) to give **5** (0.97 g, 92%) as a syrup; $[\alpha]_D$ = +54.0 (*c* 0.25, $CHCl_3$); IR (Neat): 3380, 2975, 2943, 1710,

1505, 1335, 1165, 1102, 1010 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz,): δ 5.10 (br.s, 1H, NH), 4.90 (s, 1H, C_1H), 4.66 (dd, 1H, *J* = 3.8, 6.0 Hz, C_3H), 4.54 (d, 1H, *J* = 6.0 Hz, C_2H), 4.29 (m, 1H, $C_\beta H$), 4.14 (br.m, 1H, C_4H), 3.69 (s, 3H, COOMe), 3.30 (s, 3H, OMe), 2.80-2.68 (m, 2H, $C_\alpha H$, $C_{\alpha'}H$), 1.46 (s, 3H, Me), 1.44 (s, 9H, Boc), 1.29 (s, 3H, Me); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.0, 155.3, 112.7, 106.7, 85.1, 79.6, 79.2, 54.5, 51.7, 47.4, 36.5, 28.4, 25.9, 24.6; HRMS (ESI): *m/z* calculated for $C_{17}H_{29}NO_8$ (M^++Na) 398.1790, found 398.1800.

Boc-(*R*)-β-Caa-OCH$_3$ (6): A solution of **32** (0.80 g, 2.19 mmol) in methanol (3 mL) was treated with 10% Pd-C (cat.) as described for **26** gave *methyl (3R)-3-[(3aS,4R,6S,6aS)-6-methoxy-2,2-dimethylperhydrofuro[3,4-d][1,3] dioxol-4-yl]-3-ami- nopropanoate* (**34**; 0.58 g, 88%) as a yellow liquid, which was used as such for the next reaction.

As described for **5**, a solution of **34** (0.70 g, 2.5 mmol) and Et_3N (0.7 mL, 5.4 mmol) in THF (10 mL) was treated with Boc_2O (0.61 g, 2.5 mmol) to give **6** (0.84 g, 88%) as a syrup; $[\alpha]_D$ = +49.6 (*c* 0.25, $CHCl_3$); IR (Neat): 3335, 2960, 2925, 1723, 1702, 1509, 1306, 1230, 1150, 1075, 980, 847 cm^{-1}; ^1H NMR ($CDCl_3$, 500MHz,): δ 5.42 (d, 1H, *J* = 9.4 Hz, NH), 4.87 (s, 1H, C_1H), 4.72 (dd, 1H, *J* = 3.5, 5.8 Hz, C_3H), 4.53 (d, 1H, *J* = 5.8, C_2H), 4.34 (m, 1H, $C_\beta H$), 4.11 (m, 1H, C_4H), 3.69 (s, 3H, COOMe), 3.28 (s, 3H, OMe), 2.84 (dd, 1H, *J* = 5.4, 16.0 Hz, $C_\alpha H$), 2.68 (dd, 1H, *J* = 5.6, 16.0 Hz, $C_{\alpha'}H$), 1.48 (s, 3H, Me), 1.43 (s, 9H, Boc), 1.30 (s, 3H, Me); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.0, 155.3, 112.7, 106.8, 85.0, 79.7, 79.2, 78.7, 54.5, 51.6, 47.2, 36.3, 28.3, 25.9, 24.6; HRMS (ESI): *m/z* calculated for $C_{17}H_{29}NO_8$ (M^++Na) 398.1790, found 398.1783.

Boc-(*R*)-β-Caa-OH (35): As described for **28**, a solution of **6** (1.0 g, 2.6 mmol) gave **35** (0.87 g, 90%) as a semi solid; $[\alpha]_D$ = +51.2 (*c* 0.5, $CHCl_3$); IR (KBr): 3415, 2930, 2590, 1715, 1660, 1468, 1423, 1365, 1170, 1105, 844 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz,): δ 6.13 (br.s, 1H, NH), 5.47 (br.s, 1H, C_4H), 4.87 (s, 1H, C_1H), 4.73 (dd, 1H, *J* = 3.5, 5.9 Hz, C_3H), 4.54 (d, 1H, *J* = 5.9 Hz, C_2H), 4.33 (br.m, 1H, $C_\beta H$), 3.30 (s, 3H, OMe), 2.88 (m, 1H, $C_\alpha H$), 2.73 (m, 1H, $C_{\alpha'}H$), 1.48 (s, 3H, Me), 1.44 (s, 9H, Boc), 1.30 (s, 3H, Me); FABMS: *m/z* calculated for $C_{16}H_{27}NO_8$ 384 [26, $(M+Na)^+$],362 [28, $(M+H)^+$], 306 (50), 262 [100, $(M+H\text{-}Boc)^+$], 154 (12), 58 (68).

Cbz-(*S*)-β-Caa(NHBoc)-(*R*)-β-Caa-(*S*)-β-Caa-OH (38): As described for **28**, a solution of **7** (0.45 g, 0.45 mmol) gave **38** (0.40 g, 91%) as a white solid, which was used as such for further reaction.

Boc-(*S*)-β-Caa-OH (40): As described for **28**, a solution of **5** (0.60 g, 1.60 mmol) gave **40** (0.54 g, 94%) as a pale yellow syrup; $[\alpha]_D$ = +32.0 (*c* 0.25, $CHCl_3$); IR (Neat): 3331, 2992, 1739, 1713, 1591, 1392, 1367, 1272, 1213, 1190, 1083. 969 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 5.18 (br.s, 1H, NH), 4.91 (s, 1H, C_1H), 4.68 (dd, 1H, *J* = 3.7, 5.9 Hz, C_3H), 4.56 (d, 1H, *J* = 5.9 Hz, C_2H), 4.27 (br.m, 1H, $C_\beta H$), 4.15 (dd, 1H, *J* = 3.7, 7.3 Hz, C_4H), 3.32 (s, 3H, OMe), 2.80 (m, 2H, $C_\alpha H$, $C_{\alpha'}H$), 1.46 (s, 3H, Me), 1.45 (s, 9H, Boc), 1.29 (s, 3H, Me); FABMS: *m/z* calculated for $C_{16}H_{27}NO_8$ 384 [36, $(M+H-Na)^+$], 362 [32, $(M+H)^+$], 306 (44), 262 [100, $(M+H-Boc)^+$], 154 (28), 57 (58).

Boc-(*S*)-β-Caa-(*R*)-β-Caa-OCH_3 (41): A mixture of **40** (1.0 g, 2.27 mmol), HOBt (0.36 g, 2.7 mmol), EDCI (0.522 g, 2.7 mmol) in CH_2Cl_2 was stirred at 0 °C for 15 min and treated with **34** (1.01 g, 2.77 mmol) under nitrogen atmosphere for 8 h. Workup as described for **36** and purification by column chromatography (Silica gel, 48% EtOAc in petroleum ether) gave **41** (1.43 g, 84%) as a semi solid; $[\alpha]_D$ = +67.0 (*c* 0.25, $CHCl_3$); IR (KBr): 3389, 3296, 2938, 1748, 1703, 1655, 1507, 1374, 1317, 1277, 1178, 1099, 1027, 983, 885 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz); δ 6.61 (d, 1H, *J* = 8.7 Hz, NH-2), 5.49 (br.s, 1H, NH-1), 4.89 (s, 1H, C_1H-2), 4.86 (s, 1H, C_1H-1), 4.74 (dd, 1H, *J* = 3.4, 5.9 Hz, C_4H-2), 4.73 (dd, 1H, *J* = 3.5, 6.2 Hz, C_4H-1), 4.69 (m, 1H, $C_\beta H$-2), 4.54 (d, 1H, *J* = 5.9 Hz, C_2H-2), 4.53 (d, 1H, *J* = 6.2 Hz, C_2H-1), 4.18 (m, 1H, $C_\beta H$-1), 4.14 (dd, 1H, *J* = 3.3, 6.5 Hz, C_3H-2), 4.12 (br.m, 1H, C_3H-1), 3.69 (s, 3H, COOMe), 3.29 (s, 6H, OMe-1, OMe-2), 2.81 (dd, 1H, *J* = 7.1, 15.7 Hz, $C_\alpha H$-1), 2.67 (dd, 1H, *J* = 5.4, 15.7 Hz, $C_{\alpha'}H$-1), 2.59 (m, 2H, $C_\alpha H$, $C_{\alpha'}H$-2), 1.58 (s, 3H, Me), 1.51 (s, 3H, Me), 1.45 (s, 9H, Boc), 1.31 (s, 3H, Me), 1.28 (s, 3H, Me); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.7, 170.4, 155.6, 112.7, 112.5, 106.6, 106.5, 85.2, 84.9, 79.8, 79.7, 79.4, 77.9, 54.6, 54.4, 51.8, 48.1, 45.8, 38.1, 36.1, 28.4, 26.0, 25.9, 24.9, 24.2; FABMS: *m/z* calculated for $C_{28}H_{46}N_2O_{13}$ 619 [15, $(M+H)^+$], 519 [100, $(M+H-Boc)^+$], 286 (24), 276 (24), 147 (58), 155 (46); HRMS (ESI): *m/z* calculated for $C_{28}H_{46}N_2O_{13}$ (M^++Na) 641.2897, found 641.2882.

Cbz-(*R*)-β-Caa(NHBoc)-(*S*)-β-Caa-(*R*)-β-Caa-OCH$_3$ (10): A solution of **41** (0.78 g, 1.27 mmol) and TFA (0.8 mL) in CH_2Cl_2 was stirred at 0 ^oC to room temperature for 2 h. The solvent was evaporated under reduced pressure, resulting **42** was dried under high vaccum and used as such for further reaction.

A mixture of **29** (0.63 g, 1.27 mmol), HOBt (0.20 g, 1.53 mmol), EDCI (0.29 g, 1.53 mmol) in CH_2Cl_2 was stirred at 0 °C for 15 min and treated with **42** and DIPEA (0.4 mL, 2.54 mmol) under nitrogen atmosphere for 8 h. Workup as described for **36** and purification by column chromatography (Silica gel, 80% EtOAc in petroleum ether) gave **10** (0.84 g, 67%) as a white solid; m.p. 119-122 °C; $[\alpha]_D$ = +50.2 (*c* 0.25, $CHCl_3$); IR (KBr): 3351, 2987, 1717, 1666, 1525, 1449, 1377, 1028, 1100, 970 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.35-7.28 (m, 5H, Ar-H), 7.36 (d, 1H, *J* = 9.4 Hz, NH-3), 7.02 (d, 1H, *J* = 9.7 Hz, NH-2), 5.99 (d, 1H, *J* = 10.0 Hz, NH-1), 5.10 (d, 1H, *J* = 12.4 Hz, $PhCH_2A$), 5.07 (d, 1H, *J* = 12.4 Hz, $PhCH_2B$), 4.89 (dd, 1H, *J* = 4.0, 6.0 Hz, C_3H-2), 4.87 (s, 1H, C_1H-2), 4.86 (s, 1H, C_1H-3), 4.86 (br.s, 1H, NHBoc), 4.76 (dd, 1H, *J* = 3.7, 6.0 Hz, C_3H-1), 4.72 (m, 1H, $C_\beta H$-3), 4.70 (dd, 1H, *J* = 3.6, 6.0 Hz, C_3H-3), 4.54 (m, 1H, $C_\beta H$-1), 4.52 (d, 2H, *J* = 6.0 Hz, C_2H-1, C_2H-3), 4.51 (d, 1H, *J* = 6.0 Hz, C_2H-2), 4.51 (m, 1H, $C_\beta H$-2), 4.10 (dd, 1H, *J* = 5.3, 9.1 Hz, C_1H-1), 4.07 (dd, 1H, *J* = 4.0, 10.0 Hz, C_4H-2), 4.00 (dd, 1H, *J* = 3.6, 8.0 Hz, C_4H-3), 3.95 (dd, 1H, *J* = 3.7, 6.0 Hz, C_4H-1), 3.67 (s, 3H, COOMe), 3.28 (s, 3H, OMe), 3.28 (m, 1H, CH_2a), 3.27 (s, 3H, OMe), 3.01 (ddd, 1H, *J* = 4.2, 9.1, 13.9 Hz, CH_2b), 2.83 (dd, 1H, *J* = 4.5, 13.8 Hz, $C_\alpha H_{(pro\text{-}S)}$-3), 2.64 (dd, 1H, *J* = 4.8, 13.6 Hz, $C_\alpha H_{(pro\text{-}S)}$-1), 2.58 (dd, 1H, *J* = 9.2, 13.6 Hz, $C_\alpha H_{(pro\text{-}R)}$-1), 2.57 (dd, 1H, *J* = 9.4, 13.8 Hz, $C_\alpha H_{(pro\text{-}R)}$-3), 2.47 (dd, 1H, *J* = 4.2, 14.0 Hz, $C_\alpha H_{(pro\text{-}R)}$-2), 2.37 (dd, 1H, *J* = 4.7 Hz, 14.0, $C_\alpha H_{(pro\text{-}S)}$-2), 1.50 (s, 3H, Me), 1.48 (s, 3H, Me), 1.46 (s, 3H, Me), 1.43 (s, 9H, Boc), 1.28 (s, 6H, Me), 1.23 (s, 3H, Me); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.2, 169.9, 169.2, 156.7, 155.9, 136.6, 128.4, 127.8, 127.4, 113.0, 112.7, 112.5, 107.0, 106.7, 85.1, 84.9, 83.0, 82.9, 81.0, 79.6, 79.58, 79.5, 79.4, 79.3, 66.6, 54.6, 54.2, 52.0, 49.4, 46.3, 46.1, 40.1, 39.7, 38.0, 37.3, 28.3, 26.2, 26.1, 26.0, 24.9, 24.6; FABMS: *m/z* calculated for $C_{47}H_{70}N_4O_{19}$ 1017 [8, $(M+Na)^+$], 995 [32, $(M+H)^+$], 896 [18, $(M+H\text{-}Boc)^+$], 519 (40), 470 (41), 377 (48), 276 (100), 212 (47); HRMS (ESI): *m/z* calculated for $C_{47}H_{70}N_4O_{19}$ (M^++Na) 1017.4531, found 1017.4508.

Cbz-(*R*)-β-Caa(NHBoc)-(*S*)-β-Caa-(*R*)-β-Caa-(*S*)-β-Caa(NHBoc)-OCH_3 (11): A solution of **7** (0.40 g, 0.40 mmol) as described for **28**, gave **43** (0.35 g, 90%) as a white solid, which was used as such for further reaction.

A mixture of **43** (0.25 g, 0.25 mmol), HOBt (0.04 g, 0.30 mmol), EDCI (0.06 g, 0.30 mmol) and DIPEA (0.13 mL, 0.75 mmol) in CH_2Cl_2 was stirred at 0 °C for 15 min and treated with **26** (0.09 g, 0.25 mmol) under nitrogen atmosphere for 8 h. Workup as described for **36** and purification by column chromatography (Silica gel, 1.6% methanol in $CHCl_3$) gave **11** (0.18 g, 53%) as a white solid; m.p. 123-126 °C; $[\alpha]_D$ = +58.0 (*c* 0.25, $CHCl_3$); IR (KBr): 3340, 2982, 2938, 1716, 1658, 1522, 1371, 1272, 1209, 1150, 1050 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.35-7.27 (m, 5H, Ar-H), 7.62 (d, 1H, *J* = 9.4 Hz, NH-3), 7.53 (d, 1H, *J* = 8.9 Hz, NH-2), 7.16 (d, 1H, *J* = 8.7 Hz, NH-4), 6.15 (d, 1H, *J* = 9.9 Hz, NH-1), 5.38 (br.s, 1H, NHBoc-1), 5.30 (br.s, 1H, NHBoc-4), 5.10 (d, 1H, *J* = 12.4 Hz, $PhCH_2A$), 5.07 (d, 1H, *J* = 12.4 Hz, $PhCH_2B$), 4.88 (m, 1H, C_3H-2), 4.87 (s, 1H, C_1H-2), 4.86 (s, 1H, C_1H-3), 4,74 (dd, 1H, *J* = 3.6, 6.1 Hz, C_3H-1), 4.72 (dd, 1H, *J* = 3.6, 6.1 Hz, C_3H-3), 4.64 (m, 1H, $C_\beta H$-3), 4.62 (dd, 1H, *J* = 3.6, 6.0 Hz, C_3H-3), 4.54 (d, 1H, *J* = 6.0Hz, C_2H-4), 4.53 (d, 1H, *J* = 6.1 Hz, C_2H-3), 4.53 (m, 1H, $C_\beta H$-2), 4.52 (d, 2H, *J* = 6.0 Hz, C_2H-1, C_2H-2), 4.51 (m, 1H, $C_\beta H$-1), 4.45 (m, 1H, $C_\beta H$-4), 4.12 (dd, 1H, *J* = 4.9, 8.9 Hz, C_1H-4), 4.11 (dd, 1H, *J* = 4.3, 8.8 Hz, C_1H-1), 4.10 (dd, 1H, *J* = 3.4, 7.9 Hz, C_4H-2), 4.09 (dd, 1H, *J* = 3.6, 8.5 Hz, C_4H-4), 3.98 (dd, 1H, *J* = 3.6, 8.9 Hz, C_4H-3), 3.96 (dd, 1H, *J* = 3.6, 7.9 Hz, C_4H-1), 3.67 (s, 3H, COOMe), 3.30 (s, 3H, OMe), 3.30 (m, 1H, CH_2a-1), 3.29 (m, 1H, CH_2c-4), 3.27 (s, 3H, OMe), 2.97 (ddd, 2H, *J*= 4.3, 8.9, 14.1 Hz, CH_2b-1, CH_2d-4), 2.67 (dd, 1H, *J* = 5.5, 16.2 Hz, $C_\alpha H_{(pro\text{-}S)}$-4), 2.65 (dd, 1H, *J* = 5.9, 15.7 Hz, $C_\alpha H_{(pro\text{-}S)}$-3), 2.62 (dd, 1H, *J* = 4.4, 13.8 Hz, $C_\alpha H_{(pro\text{-}S)}$-1), 2.56 (dd, 1H, *J* = 9.2, 13.8 Hz, $C_\alpha H_{(pro\text{-}R)}$-1), 2.48 (dd, 1H, *J* = 9.3, 15.7 Hz, $C_\alpha H_{(pro\text{-}R)}$-3), 2.47 (m, 1H, $C_\alpha H_{(pro\text{-}R)}$-2), 2.44 (m, 1H, $C_\alpha H_{(pro\text{-}S)}$-2), 1.49 (s, 3H, Me), 1.48 (s, 3H, Me), 1.45 (s, 6H, Me), 1.43 (s, 9H, Boc), 1.29 (s, 6H, Me), 1.28 (s, 3H, Me); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 172.7, 170.7, 170.3, 170.0, 156.8, 156.1, 156.0, 136.7, 128.4, 127.8, 127.4, 113.0, 112.9, 112.6, 112.5, 107.0, 106.9, 85.1, 85.0, 83.5, 83.2, 83.1, 83.0, 81.1, 80.5, 79.7, 79.6, 79.5, 79.4, 79.2, 79.1, 66.5, 54.7, 54.3, 51.8, 49.8, 46.8, 46.4, 46.1, 40.3, 39.7, 39.6, 39.5, 38.4, 34.9, 28.4, 26.2(2), 26.1,

26.0, 25.0, 24.8, 24.7, 24.6; HRMS (ESI): m/*z* calculated for $C_{63}H_{96}N_6O_{25}$ (M^++Na) 1359.6322, found 1359.6298.

Cbz-(*S*)-β-Caa(NHBoc)-(*R*)-β-Caa-(*S*)-β-Caa-(*R*)-β-Caa(NHBoc)-(*S*)-β-Caa-(*R)*-β-Caa-OCH$_3$ (9): Deprotection of **10** (0.17 g, 0.48 mmol) with 10% Pd-C in methanol (2.0 mL) was performed as described for **26**, to afford **44**, which was used as such which was used as such for further reaction.

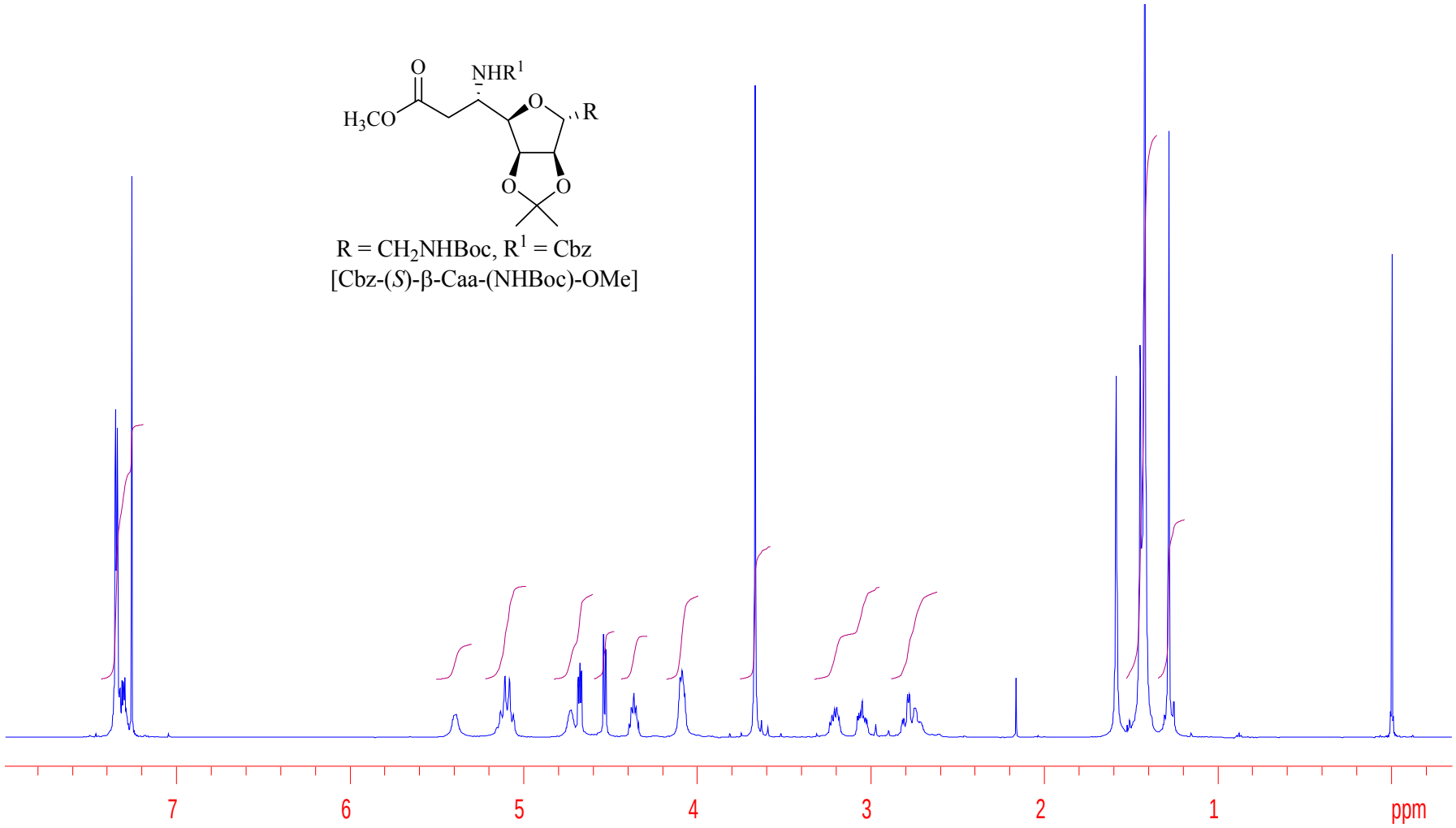
A mixture of **38** (0.20 g, 0.20 mmol), HOBt (0.03 g, 0.24 mmol), EDCI (0.03 g, 0.24 mmol) in CH_2Cl_2 was stirred at 0 °C for 15 min and treated with **44**, and DIPEA (0.05 mL, 0.030 mmol) under nitrogen atmosphere for 8 h. Workup as described for **36** and purification by column chromatography (Silica gel, 2.1% methanol in $CHCl_3$) to give **9** (0.20 g, 54%) as a white solid; m.p. 158-159 °C; $[\alpha]_D$ = +124.5 (c 0.25, $CHCl_3$); IR (KBr): 3292, 3089, 2986, 2940, 1719, 1653, 1529, 1378, 1268, 1167, 1101, 969, 872 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.39-7.27 (m, 5H, Ar-H), 9.07 (d, 1H, *J* = 9.1 Hz, NH-4), 8.72 (d, 1H, *J* = 9.7 Hz, NH-3), 8.55 (d, 1H, *J* = 9.3 Hz, NH-6), 7.70 (d, *J* = 9.2 Hz, 1H, NH-5), 7.25 (d, 1H, *J* = 9.7 Hz, NH-2), 7.07 (d, 1H, *J* = 8.5 Hz, NH-1), 5.21 (t, 1H, *J* = 6.2 Hz, BocNH-1), 5.17 (d, 1H, *J* = 12.5 Hz, $PhCH_2A$), 5.11 (d, 1H, *J* = 12.5 Hz, $PhCH_2B$), 5.09 (dd, 1H, *J* = 3.4, 5.9 Hz, C_3H-5), 4.90 (s, 1H, C_1H-2), 4.89 (s, 1H, C_1H-6), 4.89 (m, 1H, $C_\beta H$-2), 4.88 (s, 1H, C_1H-3), 4.87 (s, 1H, C_1H-5, C_1H-6), 4.85 (dd, 1H, *J* = 3.4, 5.9 Hz, C_3H-3), 4.81 (dd, 1H, *J* = 3.6 Hz, 5.9, C_3H-1), 4.74 (m, 1H, C_3H-6), 4.73 (dd, 1H, *J* = 3.0, 5.9 Hz, C_3H-2), 4.72 (dd, 1H, *J* = 3.3, 5.9 Hz, C_3H-4), 4.70 (m, 1H, $C_\beta H$-6), 4.69 (br.s, 1H, BocNH-2), 4.60 (m, 1H, $C_\beta H$-4), 4.56 (d, 1H, *J* = 5.9 Hz, C_2H-1), 4.55 (d, 1H, *J* = 5.9 Hz, C_2H-2, C_2H-6), 4.54 (d, 1H, *J* = 5.9 Hz, C_2H-4), 4.51 (d, 1H, *J* = 5.9 Hz, C_2H-5), 4.49 (d, 1H, *J* = 5.9 Hz, C_2H-3), 4.41 (m, 1H, $C_\beta H$-5), 4.38 (m, 1H, $C_\beta H$-3), 4.33 (m, 1H, $C_\beta H$-1), 4.19 (dd, 1H, *J* = 5.0, 9.7 Hz, C_1H-1), 4.10 (dd, 1H, *J* = 3.4, 10.4 Hz, C_4H-5), 4.06 (dd, 1H, *J* = 3.4, 10.2 Hz, C_4H-3), 4.03 (dd, 1H, *J*=3.6, 8.8 Hz, C_4H-1), 4.02 (m, 2H, C_4H-2, C_1H-4), 3.92 (dd, 1H, *J* = 3.4, 9.2 Hz, C_4H-6), 3.78 (dd, 1H, *J* = 3.4, 8.5 Hz, C_4H-4), 3.68 (s, 3H, COOMe), 3.36 (m, 1H, CH_2a), 3.34 (s, 3H, OMe), 3.33 (s, 3H, OMe), 3.31 (s, 3H, OMe), 3.30 (m, 1H, CH_2c), 3.26 (s, 3H, OMe), 3.00 (ddd, 1H, *J* = 2.9, 8.5 Hz, CH_2d), 2.96 (dd, 1H, *J* = 3.0, 12.1 Hz, $C_\alpha H_{(pro\text{-}S)}$-6), 2.94 (dd, 1H, *J* = 3.4, 12.5 Hz, $C_\alpha H_{(pro\text{-}S)}$-4), 2.88 (m, 1H, CH_2b), 2.73 (dd, 1H, *J* = 2.1, 12.2 Hz, $C_\alpha H_{(pro\text{-}S)}$-2), 2.60 (m, 2H, $C_\alpha H_{(pro\text{-}S)}$-1,

$C_\alpha H_{(pro\text{-}R)}$-1), 2.54 (dd, 1H, *J* = 2.8, 12.5 Hz, $C_\alpha H_{(pro\text{-}R)}$-3), 2.46 (dd, 1H, *J* = 3.3, 13.2 Hz, $C_\alpha H_{(pro\text{-}R)}$-5), 2.38 (t, 1H, *J* = 12.1 Hz, $C_\alpha H_{(pro\text{-}R)}$-6), 2.37 (dd, 1H, *J* = 5.2, 12.4 Hz, $C_\alpha H_{(pro\text{-}S)}$-3), 2.34 (t, 1H, *J* = 12.2 Hz, $C_\alpha H_{(pro\text{-}R)}$-2), 2.32 (dd, 1H, *J* = 4.9, 13.2 Hz, $C_\alpha H_{(pro\text{-}S)}$-5), 2.12 (t, 1H, *J* = 12.5 Hz, $C_\alpha H_{(pro\text{-}R)}$-4), 1.47 (s, 6H, Me), 1.43 (s, 9H, Boc), 1.42 (s, 6H, Me), 1.41 (s, 9H, Boc), 1.40 (s, 6H, Me), 1.28 (s, 6H, Me), 1.27 (s, 12H, Me); ^{13}C NMR ($CDCl_3$,150 MHz): δ 174.0, 171.3, 170.6, 170.1, 169.2, 156.0, 155.8, 155.7, 136.7, 128.4, 127.8, 127.6, 113.1, 112.7, 112.6(2), 112.4, 112.0, 108.2, 106.9, 106.7, 106.1, 85.0, 84.9, 84.8, 84.0, 83.3, 83.0, 82.9, 81.6, 81.5, 80.5, 80.4, 80.0, 79.9, 79.6(2), 79.3, 79.2, 79.1, 78.5, 78.0, 66.3, 55.3, 54.6, 54.1, 53.6, 52.4, 49.3, 48.7, 47.3, 46.6, 46.5, 46.0, 42.1, 40.3, 40.2, 40.0, 39.5, 39.4, 37.7, 37.4, 28.3, 26.7, 26.2, 26.0, 25.9, 25.8, 25.7, 25.1, 24.6(2), 24.5, 23.8; HRMS (ESI): m/*z* calculated for $C_{85}H_{130}N_8O_{35}$ (M^++Na) 1845.8536, found 1845.8606.

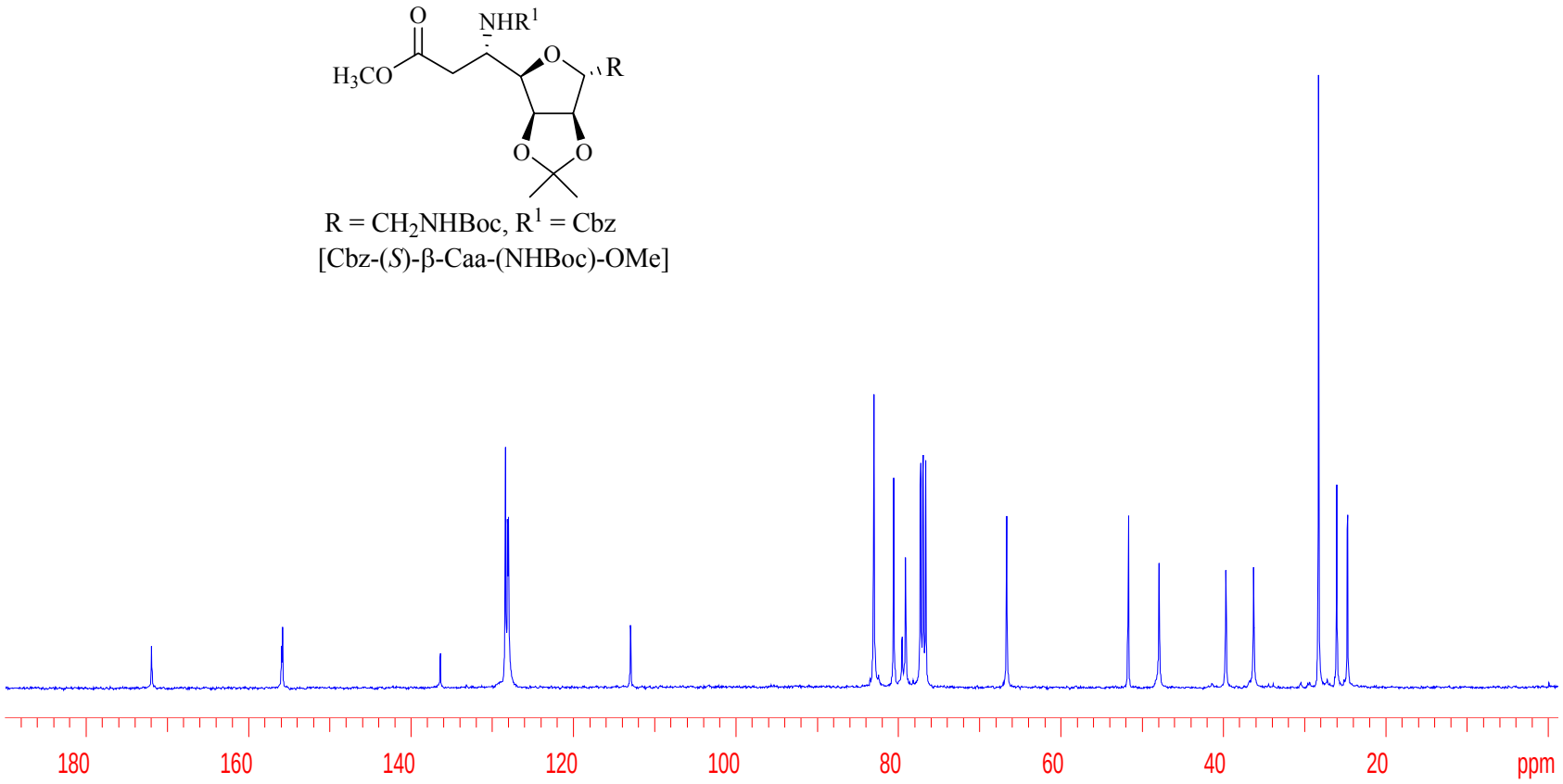
Cbz-(*R*)-β-Caa(NHBoc)-(*S*)-β-Caa-(*R*)-β-Caa-(*S*)-β-Caa(NHBoc)-(*R*)-β-Caa-(*S*)-β-Caa]-OCH$_3$ (12): Deprotection of **7** (0.21 g, 0.48 mmol) with 10% Pd-C in methanol (2.0 mL) was performed as described for **26**, furnished **39**, which was used as such for further reaction.

A mixture of **43** (0.20 g, 0.20 mmol), HOBt (0.03 g, 0.24 mmol), EDCI (0.03 g, 0.24 mmol) in CH_2Cl_2 was stirred at 0 °C for 15 min and treated with **39**, and DIPEA (0.05 mL, 0.30 mmol) under nitrogen atmosphere for 8 h. Workup as described for **36** and purification by column chromatography (Silica gel, 2.6% methanol in $CHCl_3$) to give **12** (0.2 g, 56%) as a white solid; m.p. 140-143 °C; $[\alpha]_D$ = +112.4 (*c* 0.5, $CHCl_3$); IR (KBr): 3307, 2986, 2940, 1716, 1658, 1525, 1450, 1378, 1266, 1207, 1166, 1100, 971, 870 cm^{-1}^{1}H NMR ($CDCl_3$+30 μL DMSO-d_6, 500 MHz); δ 8.47 (d, 1H, *J* = 8.0 Hz, NH-2), 8.38 (d, 1H, *J* = 9.5 Hz, NH-3), 8.27 (d, 1H, *J* = 8.6 Hz, NH-4), 8.25 (d, 1H, *J* = 8.8 Hz, NH-3), 7.05 (d, 1H, *J* = 8.8 Hz, NH-6), 6.41 (d, 1H, *J* = 9.8 Hz, NH-1), 5.20 (br.s, 1H, NHBoc-1), 5.30 (br.s, 1H, NHBoc-4), 5.13 (d, 1H, *J* = 12.8 Hz, $PhCH_2A$), 5.05 (d, 1H, *J* = 12.8 Hz, $PhCH_2B$), 5.02 (m, 1H, C_3H-4), 4.89 (m, 1H, C_1H-6), 4.87 (m, 1H, C_1H-5), 4.86 (s, 1H, C_1H-2), 4.86 (m, 1H, C_3H-2), 4.82 (s, 1H, C_1H-3), 4.76 (dd, 1H, *J* = 3.5, 5.9 Hz, C_3H-1), 4.75 (dd, 1H, *J* = 3.5, 5.9 Hz, C_3H-5), 4.63 (dd, 1H, *J* = 3.6, 5.9 Hz, C_3H-6), 4.57 (d, *J* = 5.9 Hz, 1H, C_2H-1), 4.56 (m, 1H, $C_\beta H$-3), 4.55 (m, 2H, $C_\beta H$-1, 5), 4.55 (d, 1H, *J* = 5.9 Hz,

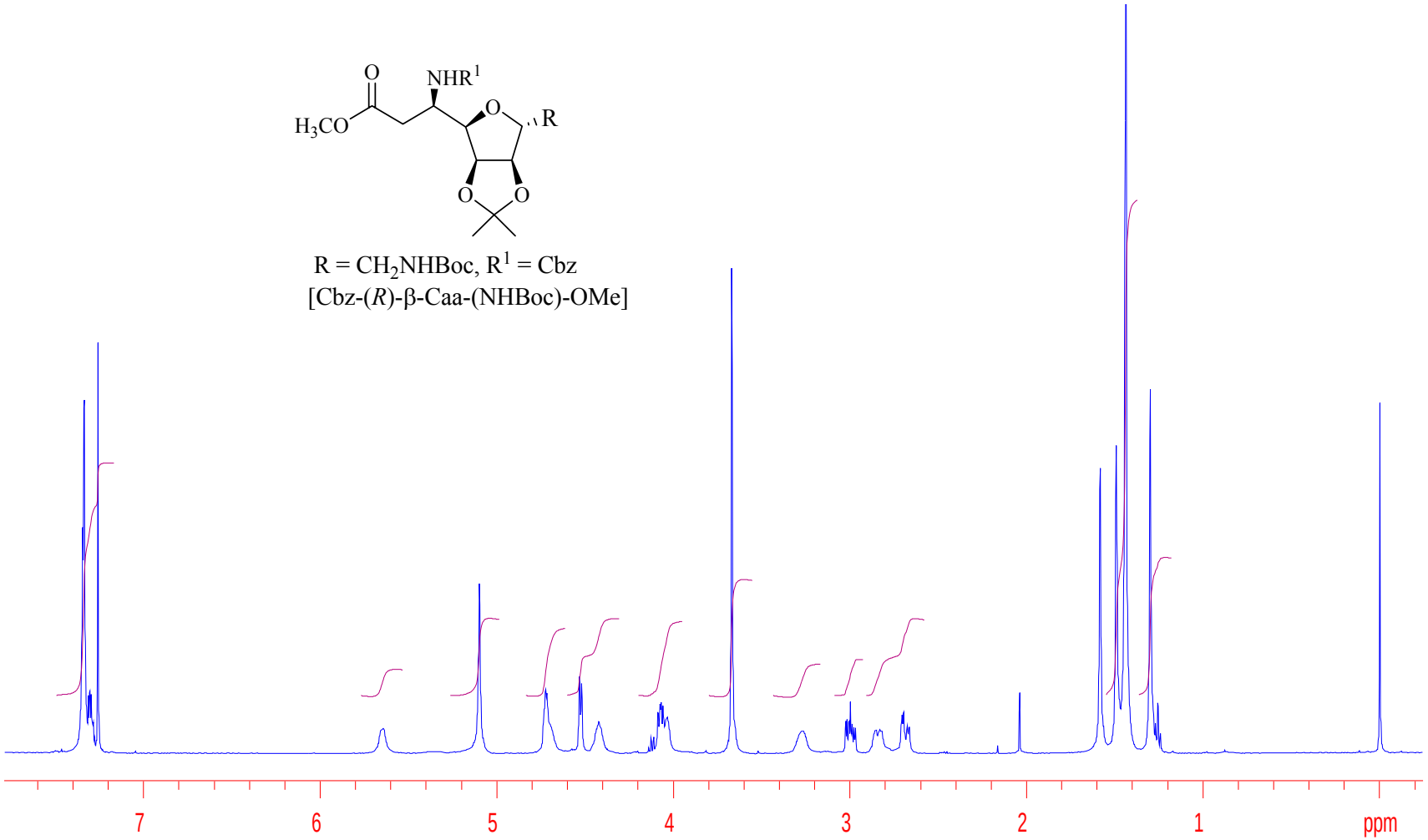
C_2H-4), 4.54 (d, 1H, *J* = 5.9 Hz, C_2H-6), 4.53 (d, 1H, *J* = 5.9 Hz, C_2H-5), 4.53 (m, 1H, C_βH-2), 4.51 (m, 1H, C_βH-6), 4.46 (d, 1H, *J* = 5.9Hz, C_2H-2), 4.44 (d, 1H, *J* = 5.9 Hz, C_2H-3), 4.39 (m, 1H, C_βH-2), 4.13 (m, 1H, C_4H-6), 4.11 (dd, 1H, *J* = 6.3, 8.6 Hz, C_1H-4), 4.11 (dd, 1H, *J* = 6.3, 8.6 Hz, C_1H-1), 4.04 (dd, 1H, *J* = 3.6, 9.8 Hz, C_4H-2), 4.02 (dd, 1H, *J* = 3.5, 9.4 Hz, C_4H-4), 3.95 (dd, 1H, *J* = 3.5, 8.9 Hz, C_4H-5), 3.94 (m, 1H, C_4H-3), 3.93 (m, 1H, C_4H-1), 3.71 (s, 3H, COOMe), 3.30 (s, 3H, OMe), 3.27 (s, 3H, OMe), 3.23-3.06 (m, 1H, CH_2a-1), 3.32-2.93 (m, 1H, CH_2c-4), 2.94 (dd, 1H, *J* = 5.6, 14.7 Hz, $C_\alpha H_{(pro\text{-}R)}$-6), 2.88 (dd, 1H, *J* = 4.1, 12.6 Hz, $C_\alpha H_{(pro\text{-}S)}$-2), 2.75 (dd, 1H, *J* = 4.0, 13..1 Hz, $C_\alpha H_{(pro\text{-}S)}$-1), 2.72 (dd, 1H, *J* = 2.1, 12.5 Hz, $C_\alpha H_{(pro\text{-}S)}$-5), 2.62 (dd, 1H, *J* = 5.4, 14.7 Hz, $C_\alpha H_{(pro\text{-}S)}$-6), 2.45 (m, 1H, $C_\alpha H_{(pro\text{-}R)}$-1), 2.44 (m, 1H, $C_\alpha H_{(pro\text{-}R)}$-2), 2.41 (dd, 1H, *J* = 3.5, 13.2 Hz, $C_\alpha H_{(pro\text{-}R)}$-4), 2.32 (dd, 1H, *J* = 5.0, 13.2 Hz, $C_\alpha H_{(pro\text{-}S)}$-4), 2.27 (s, 1H, $C_\alpha H_{(pro\text{-}S)}$-2), 2.26 (t, 1H, *J* = 12.5 Hz, $C_\alpha H_{(pro\text{-}R)}$-5), 2.20 (t, 1H, *J* = 12.6 Hz, $C_\alpha H_{(pro\text{-}R)}$-3), 1.50 (s, 3H, Me), 1.46 (s, 3H, Me), 1.45 (s, 6H, Me), 1.43 (s, 9H, Boc), 1.42 (s, 3H, Me), 1.29 (s, 6H, Me), 1.27 (s, 3H, Me), 1.26 (s, 6H, Me), 1.24 (s, 3H, Me); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 172.6, 171.0, 170.6, 170.5, 169.7, 169.6, 157.1, 155.9, 155.7, 136.8, 128.4, 127.7, 127.1, 113.1, 112.7, 112.5, 112.4, 112.2, 108.0, 107.4, 107.0, 106.0, 85.0, 84.9, 83.4, 83.3, 83.0, 81.1, 80.7, 80.3, 79.7, 79.6 (2), 79.5 (2), 79.4, 79.3, 79.1, 79.0, 66.6, 55.2, 54.7, 54.6, 53.6, 51.9, 50.3, 47.2, 46.9, 46.0, 45.8, 42.2, 41.5, 40.5, 39.9, 39.6, 38.5, 37.7, 35.3, 28.3, 26.4, 26.3, 26.2, 26.1, 26.0, 25.8, 25.0, 24.9, 24.7, 24.5, 24.4; HRMS (ESI): m/*z* calculated for $C_{85}H_{130}N_8O_{35}$ (M^++Na) 1845.8536, found 1845.8581.



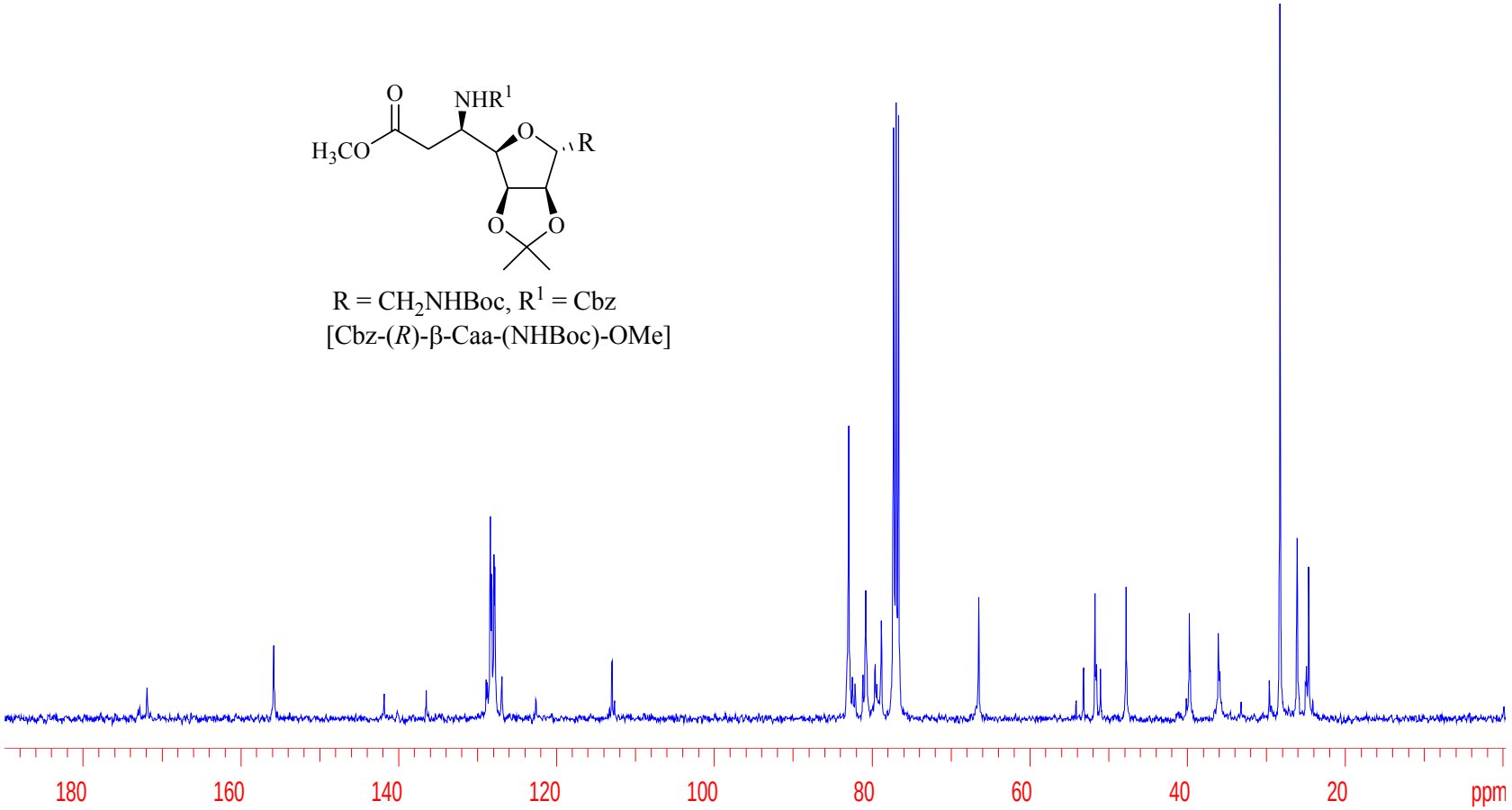
Supporting Fig 1: ^{1}H NMR Spectrum of 1 ($CDCl_3$, 303 K, 500 MHz)



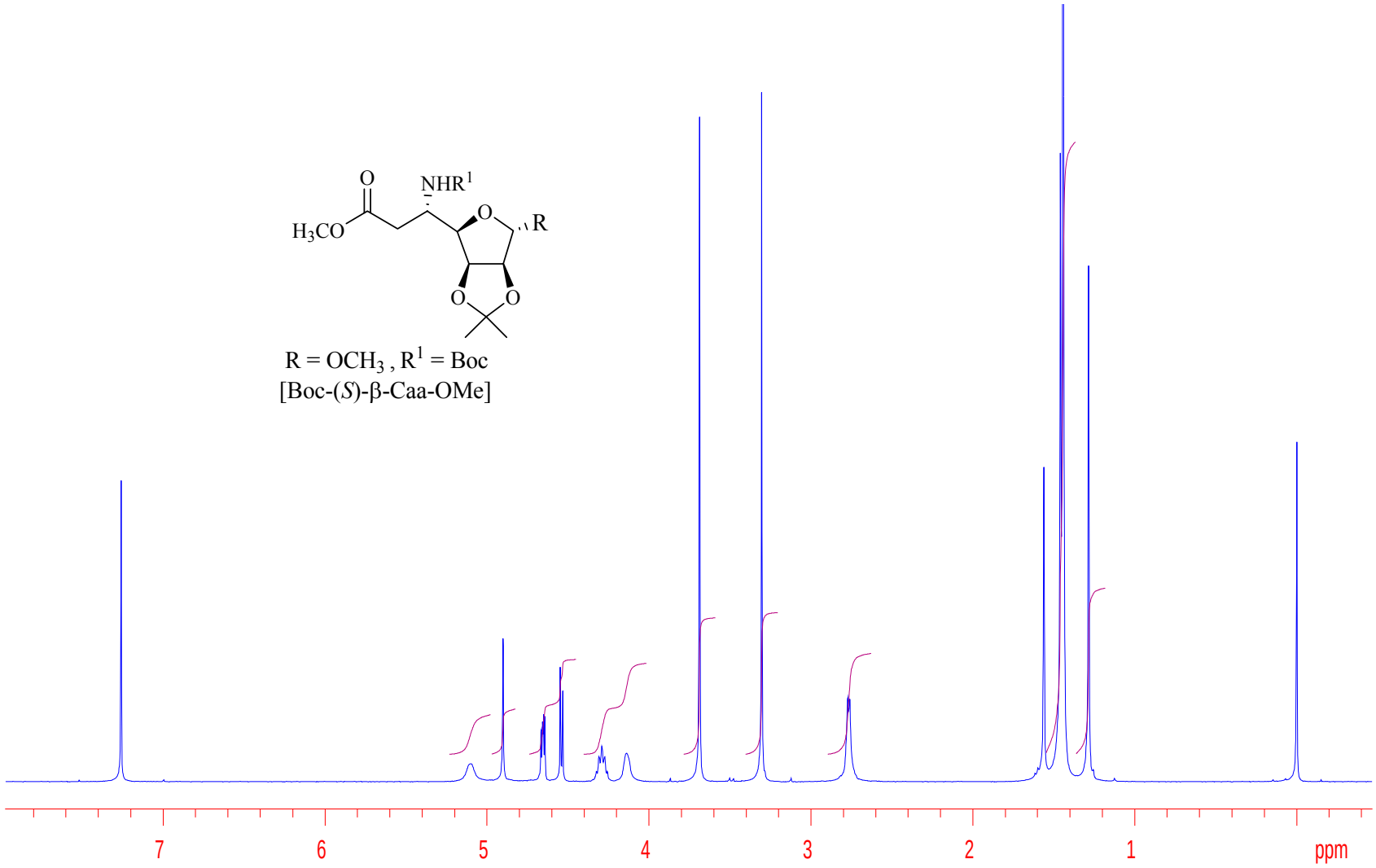
Supporting Fig 2: ^{13}C NMR Spectrum of 1 ($CDCl_3$, 303 K, 100 MHz)



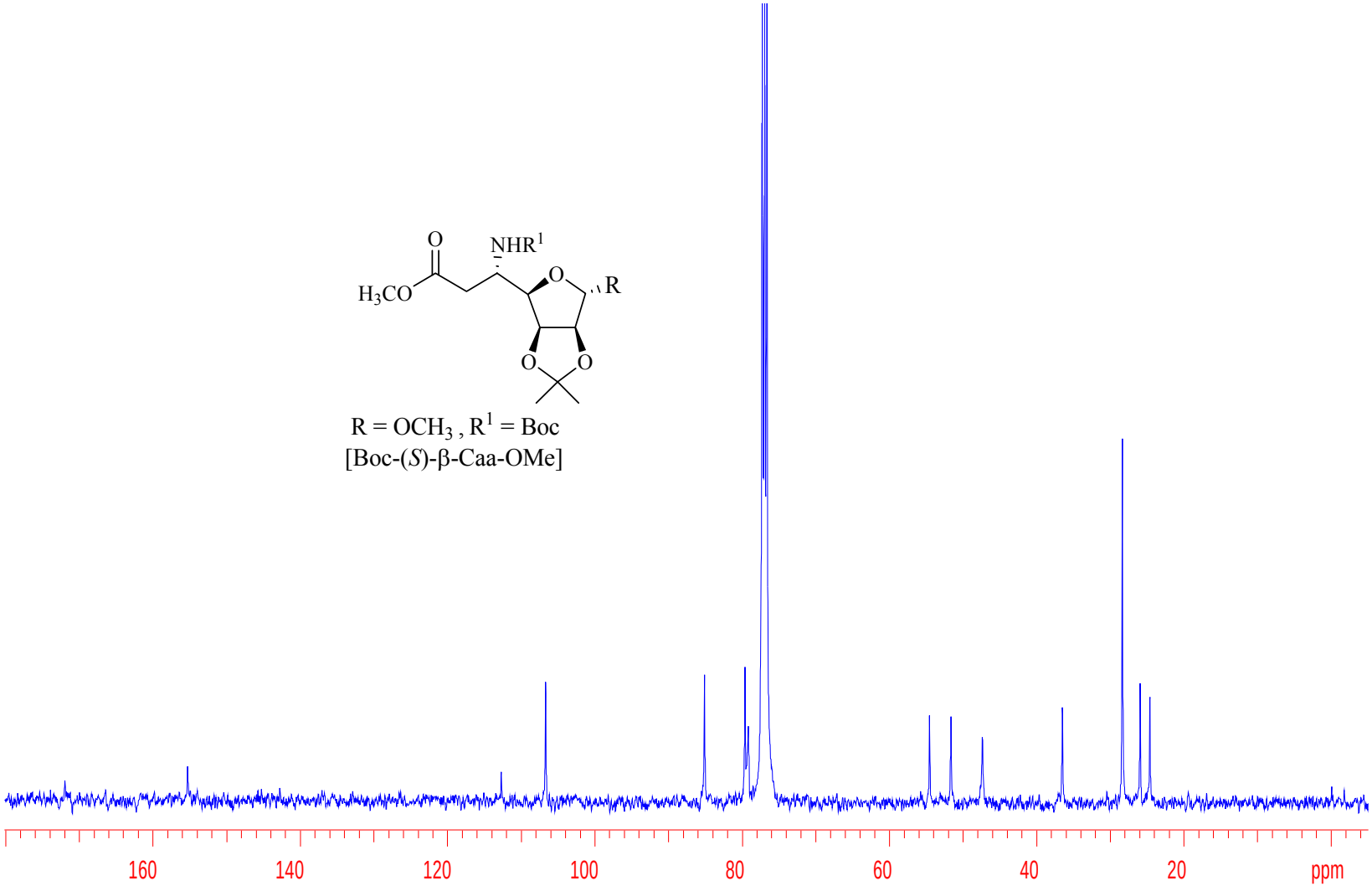
Supporting Fig 3: ^{1}H NMR Spectrum of 2 ($CDCl_3$, 303 K, 500 MHz)



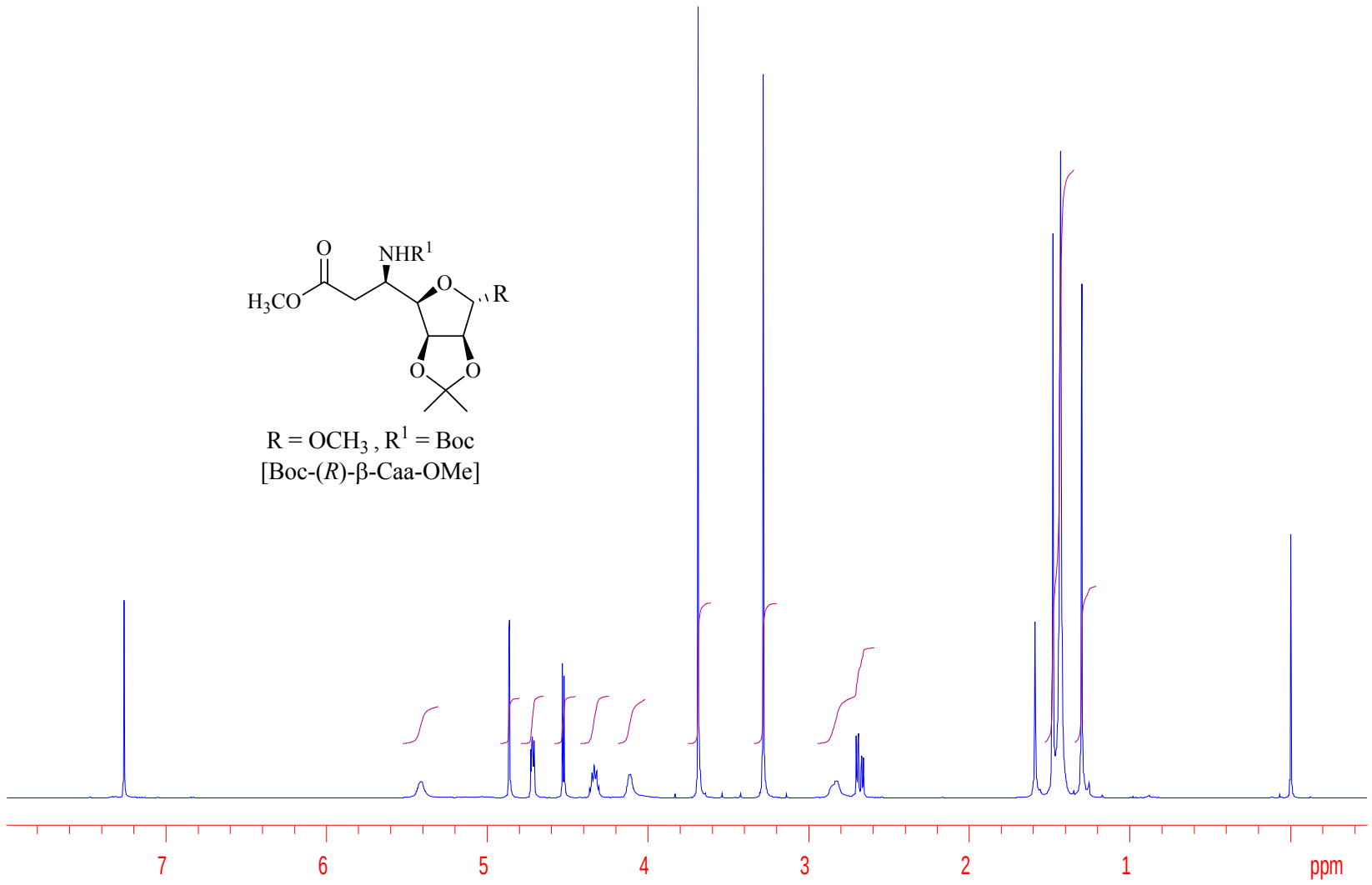
Supporting Fig 4: ^{13}C NMR Spectrum of 2 ($CDCl_3$, 303 K, 100 MHz)



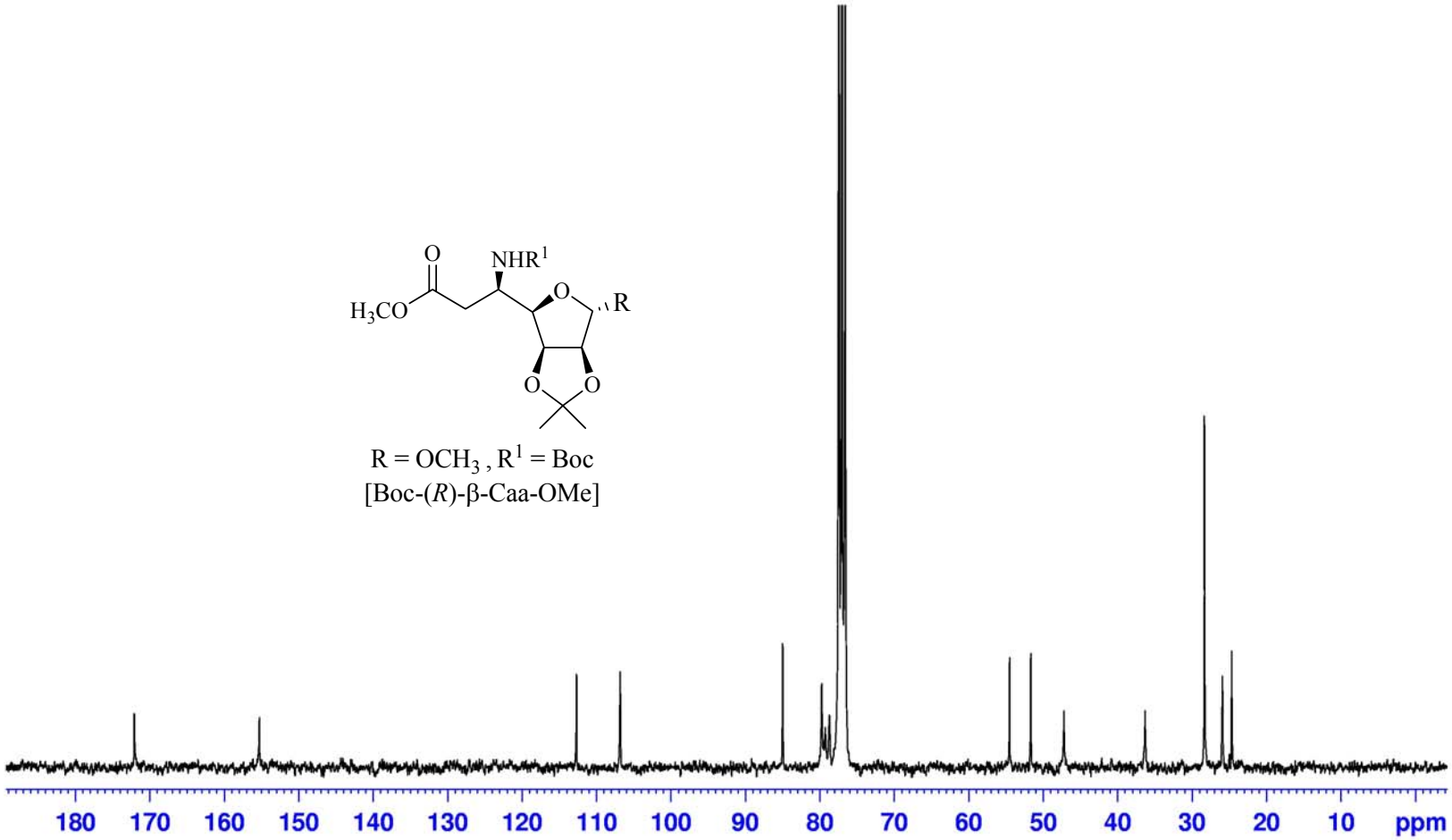
Supporting Fig 5: ^{1}H NMR Spectrum of 5 ($CDCl_3$, 303 K, 500 MHz)



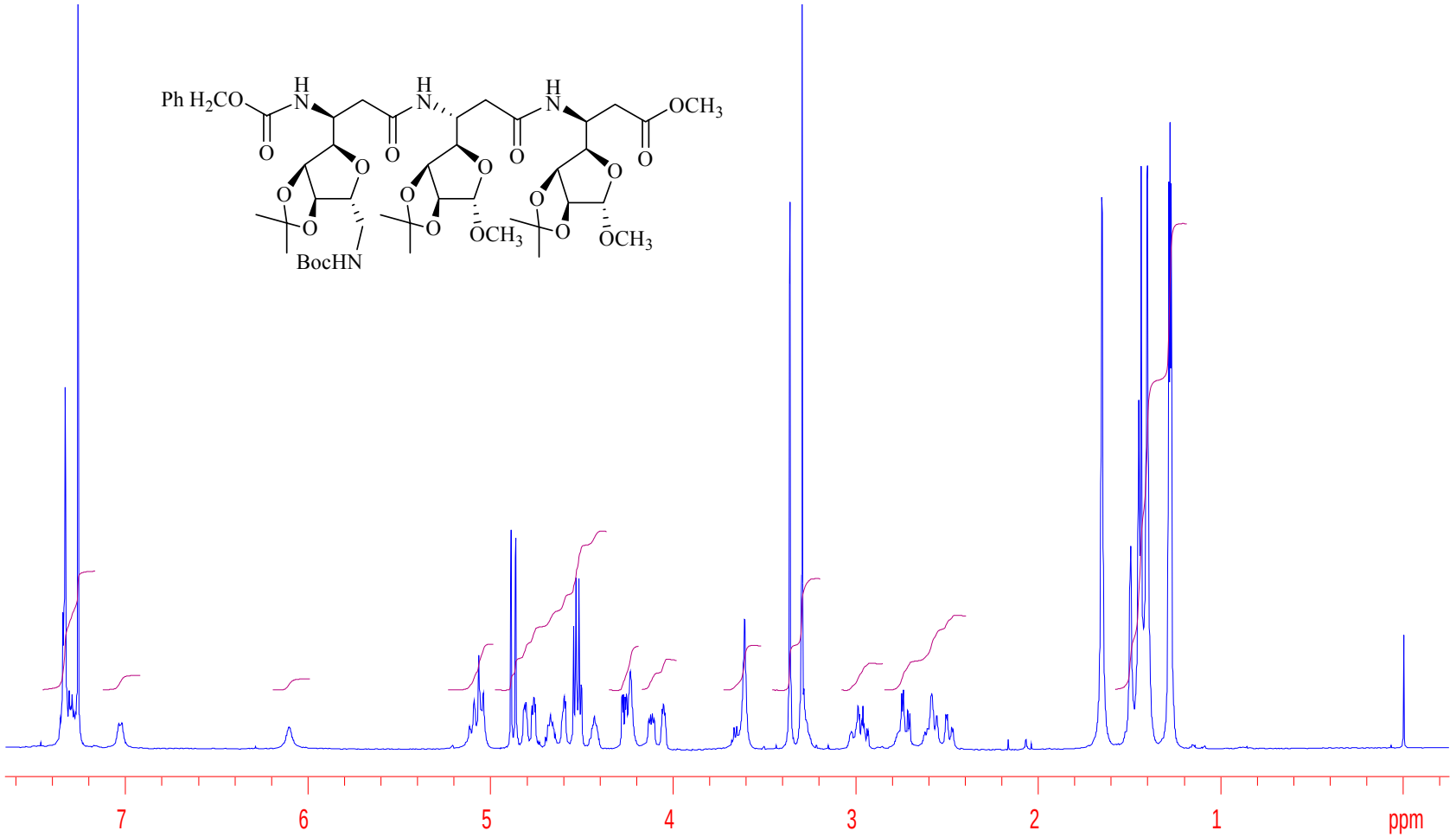
Supporting Fig 6: ^{13}C NMR Spectrum of 5 ($CDCl_3$, 303 K, 100 MHz)



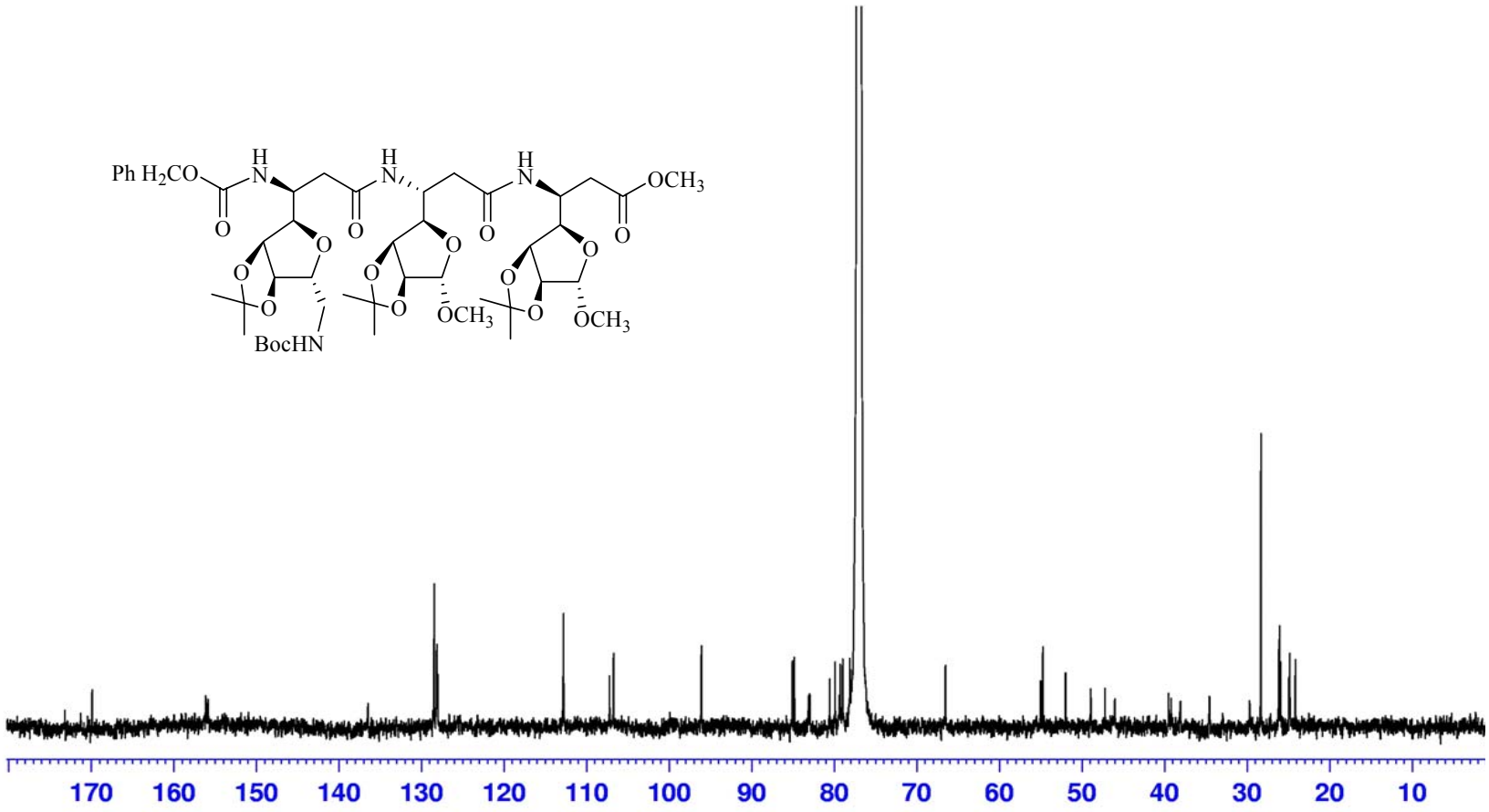
Supporting Fig 7: ^{1}H NMR Spectrum of 6 ($CDCl_3$, 303 K, 500 MHz)



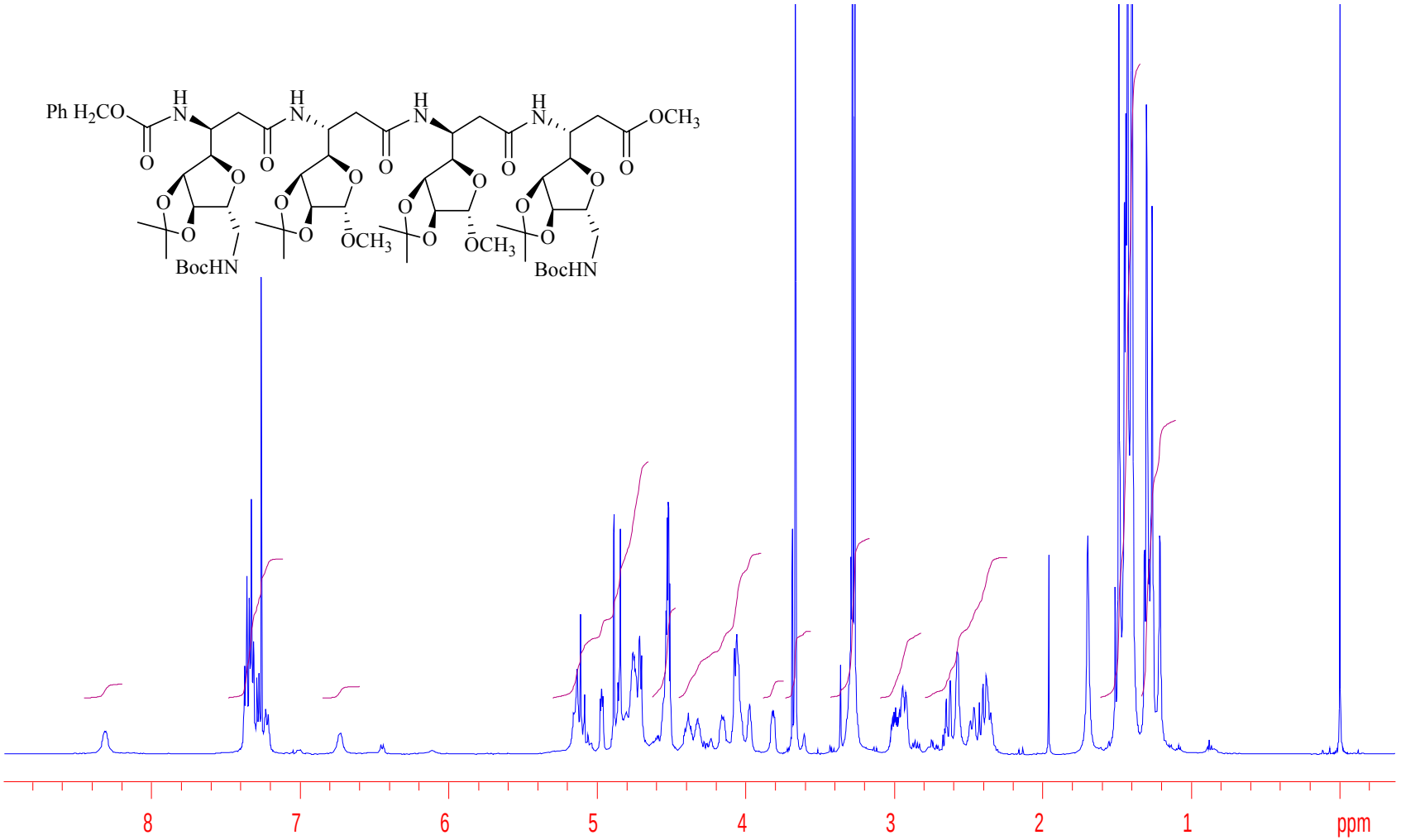
Supporting Fig 8: ^{13}C NMR Spectrum of 6 ($CDCl_3$, 294 K, 75 MHz)



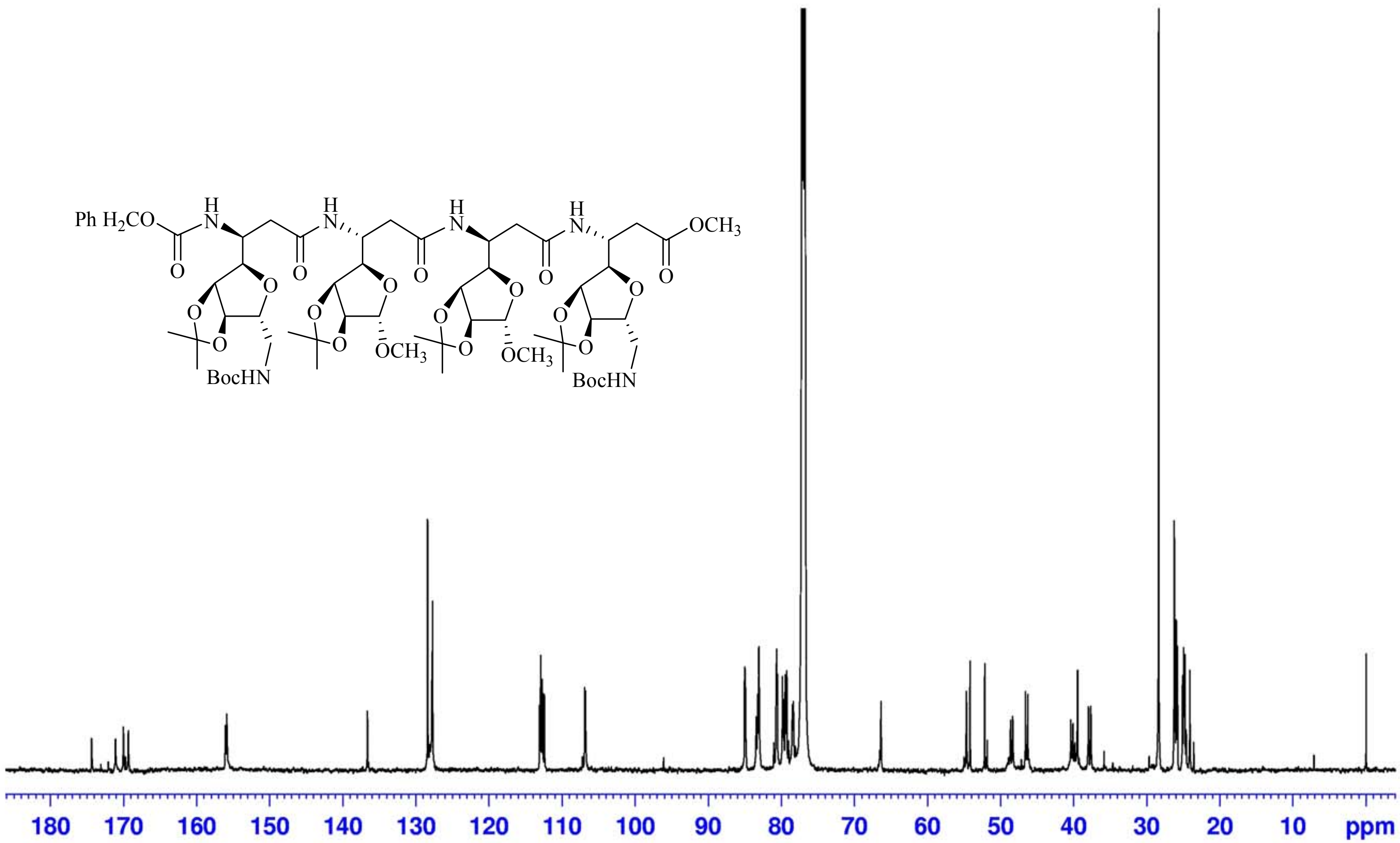
Supporting Fig 9: ^{1}H NMR Spectrum of 7 ($CDCl_3$, 303 K, 500 MHz)



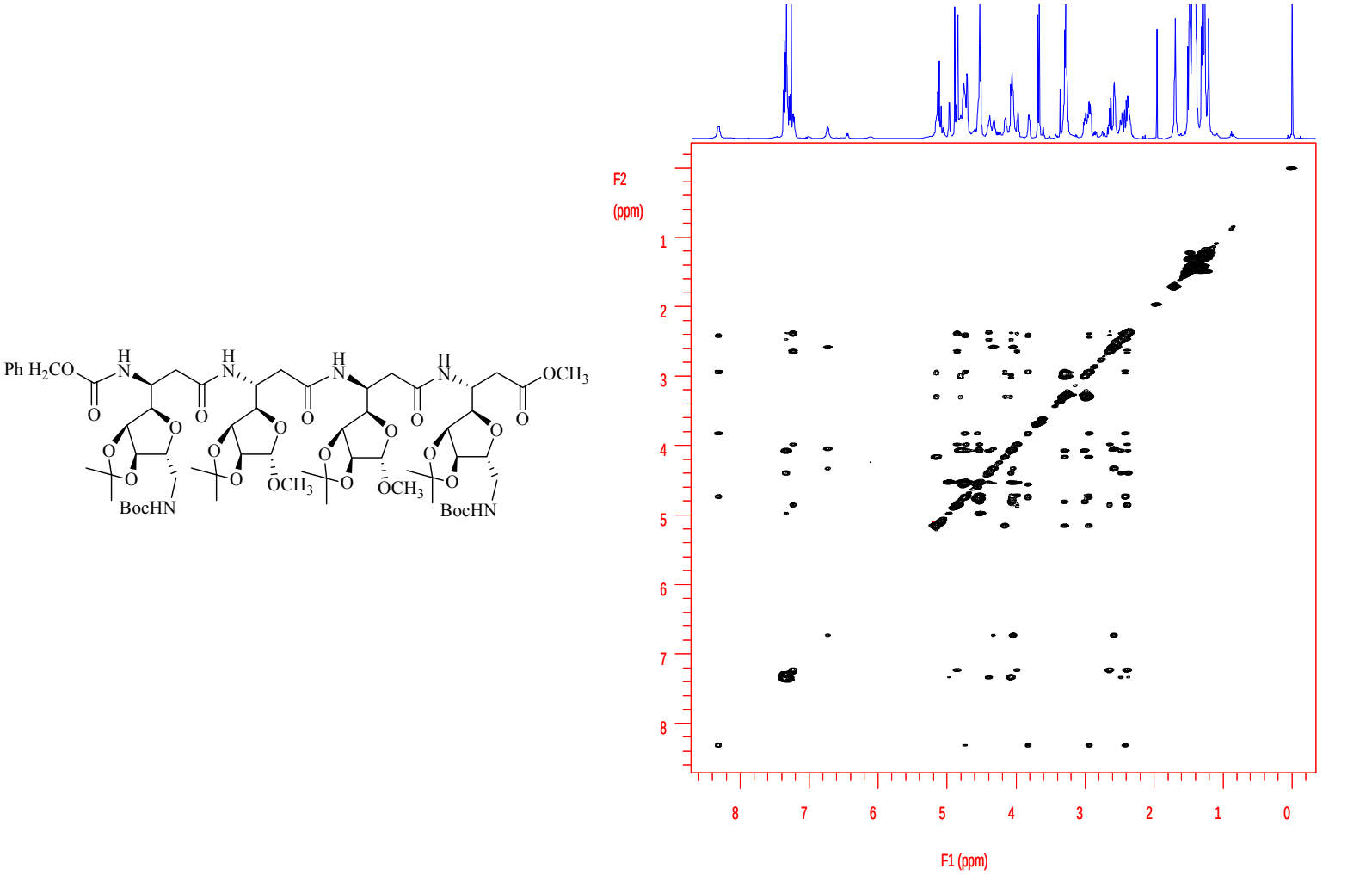
Supporting Fig 10: ^{13}C NMR Spectrum of 7 ($CDCl_3$, 303 K, 150 MHz)



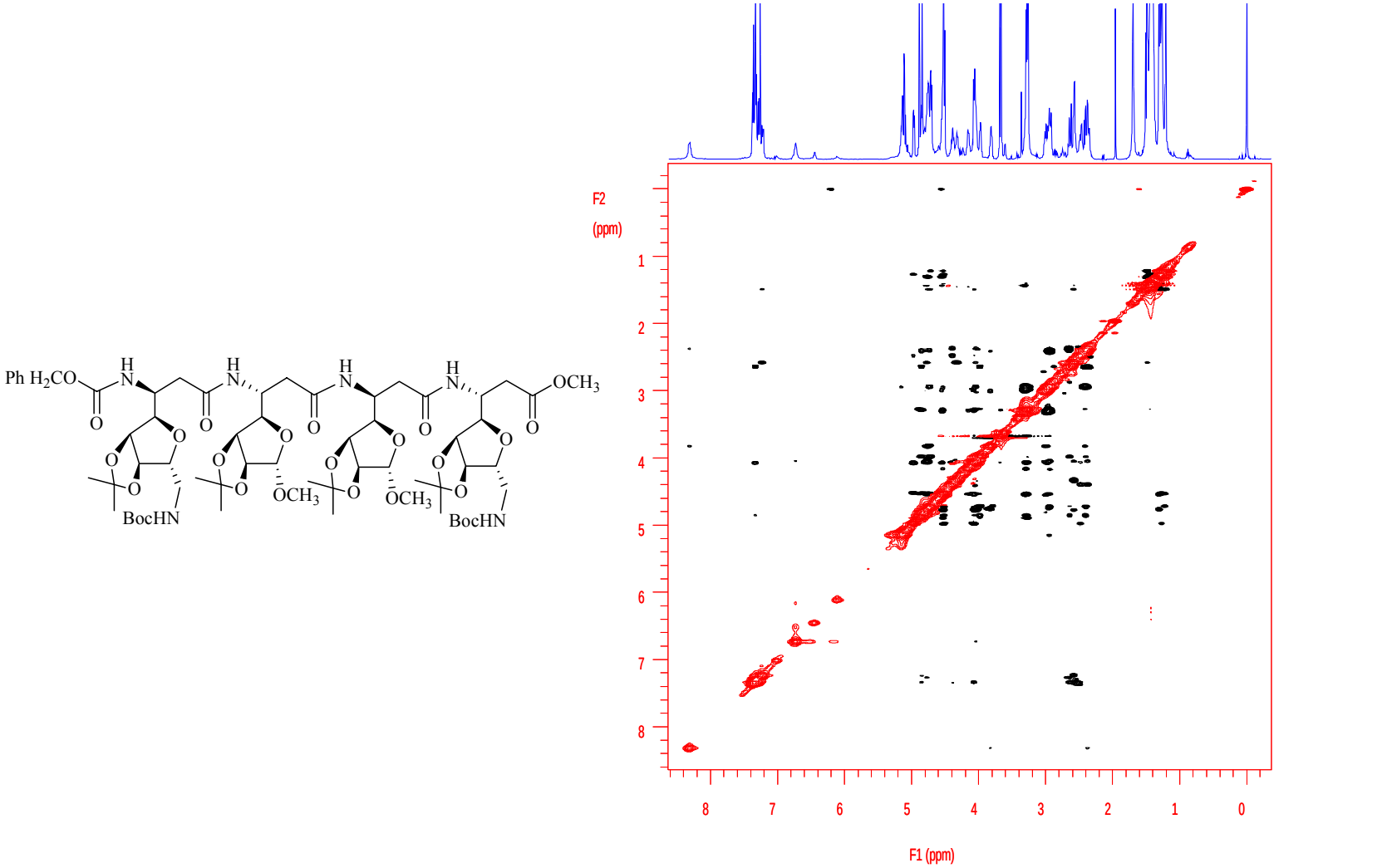
Supporting Fig 11: ^{1}H NMR Spectrum of 8 ($CDCl_3$, 303 K, 500 MHz)



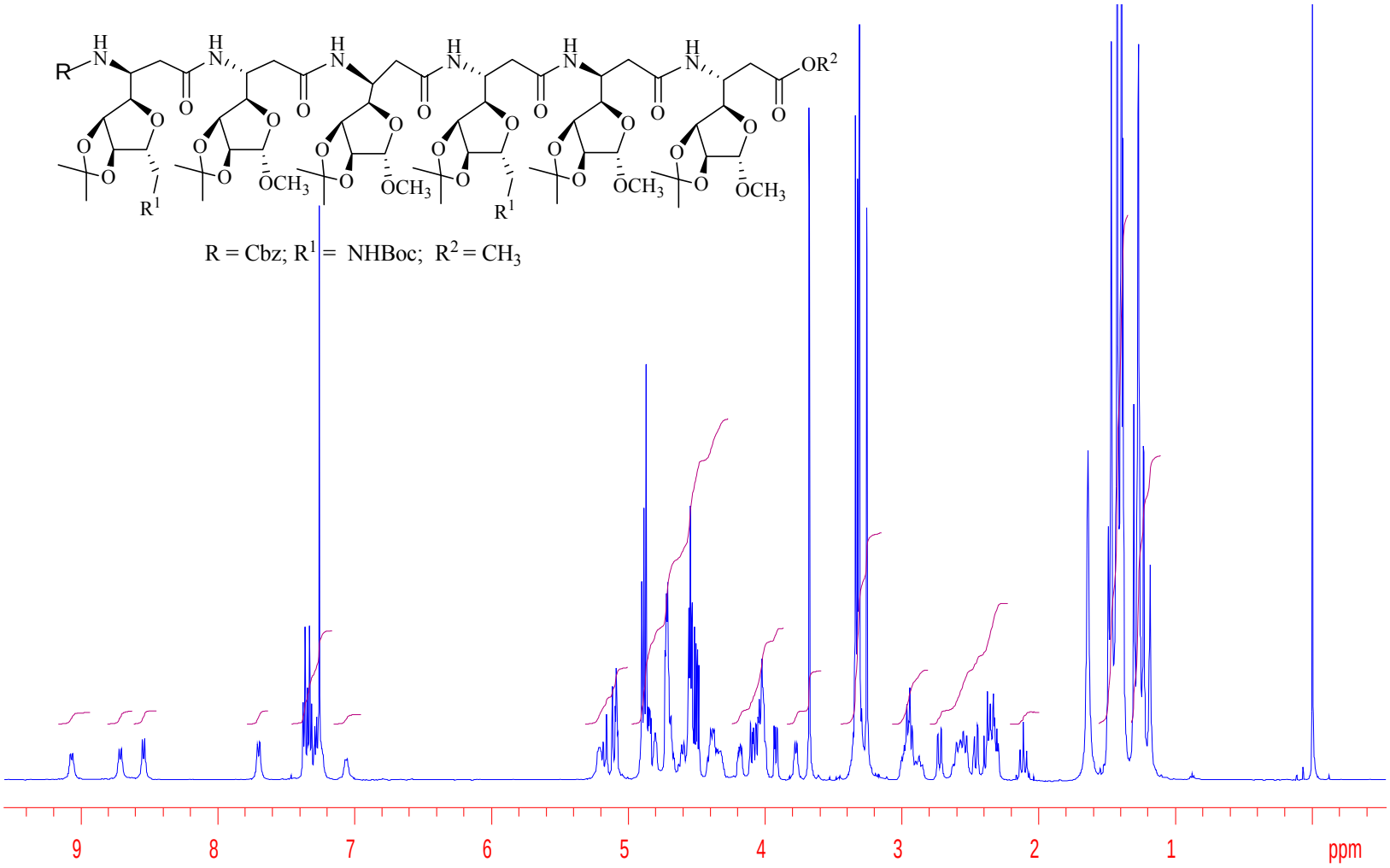
Supporting Fig 12: ^{13}C NMR Spectrum of 8 ($CDCl_3$, 303 K, 150 MHz)



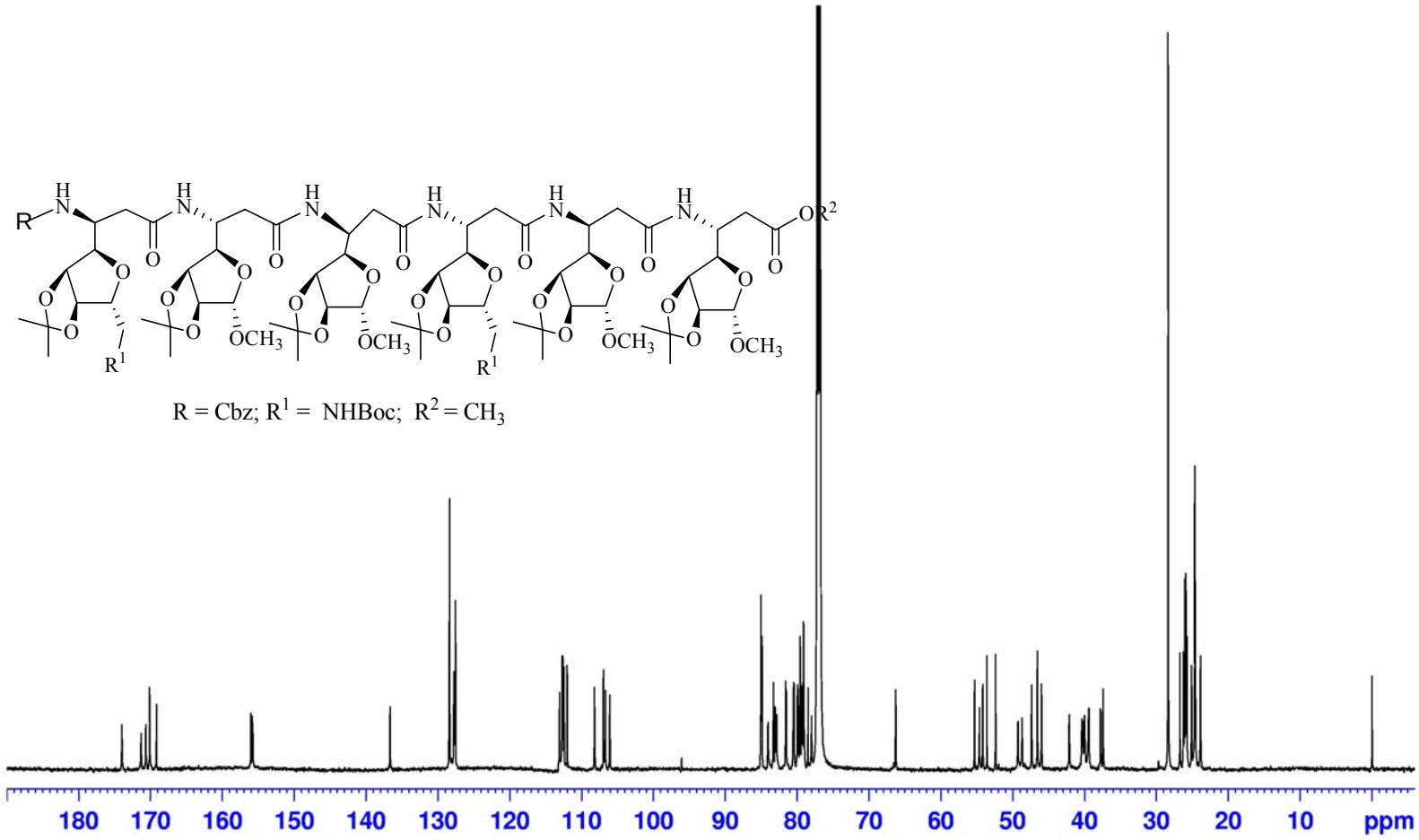
Supporting Fig 13: TOCSY Spectrum of 8 ($CDCl_3$, 303 K, 500 MHz)



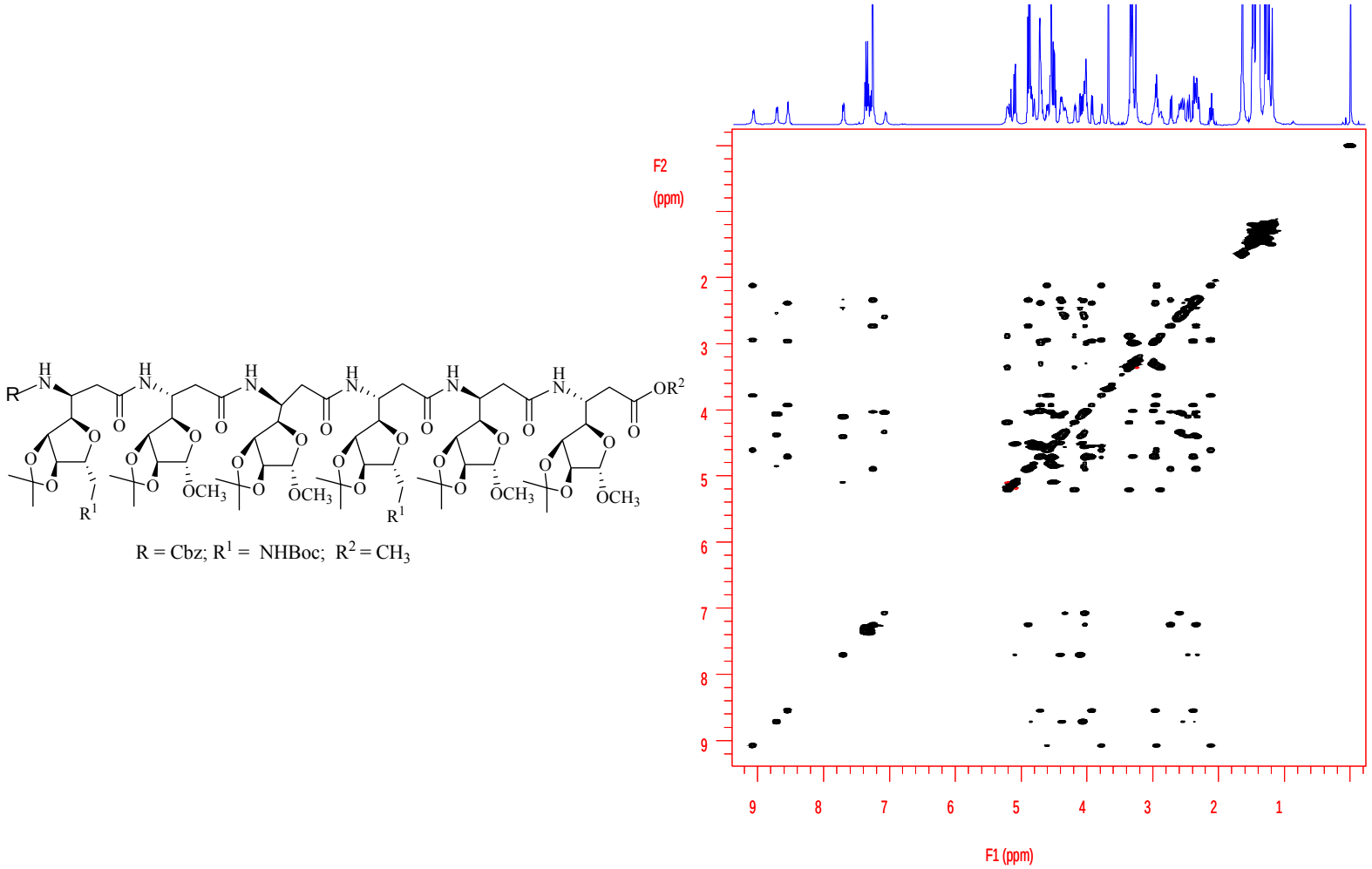
Supporting Fig 14: ROESY Spectrum of 8 ($CDCl_3$, 303 K, 500 MHz)



Supporting Fig 15: ^{1}H NMR Spectrum of 9 ($CDCl_3$, 303 K, 500 MHz)

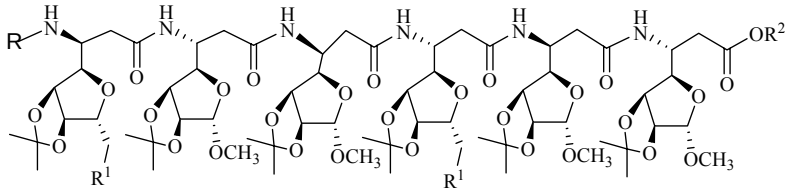


Supporting Fig 16: ^{13}C NMR Spectrum of 9 ($CDCl_3$, 303 K, 150 MHz)

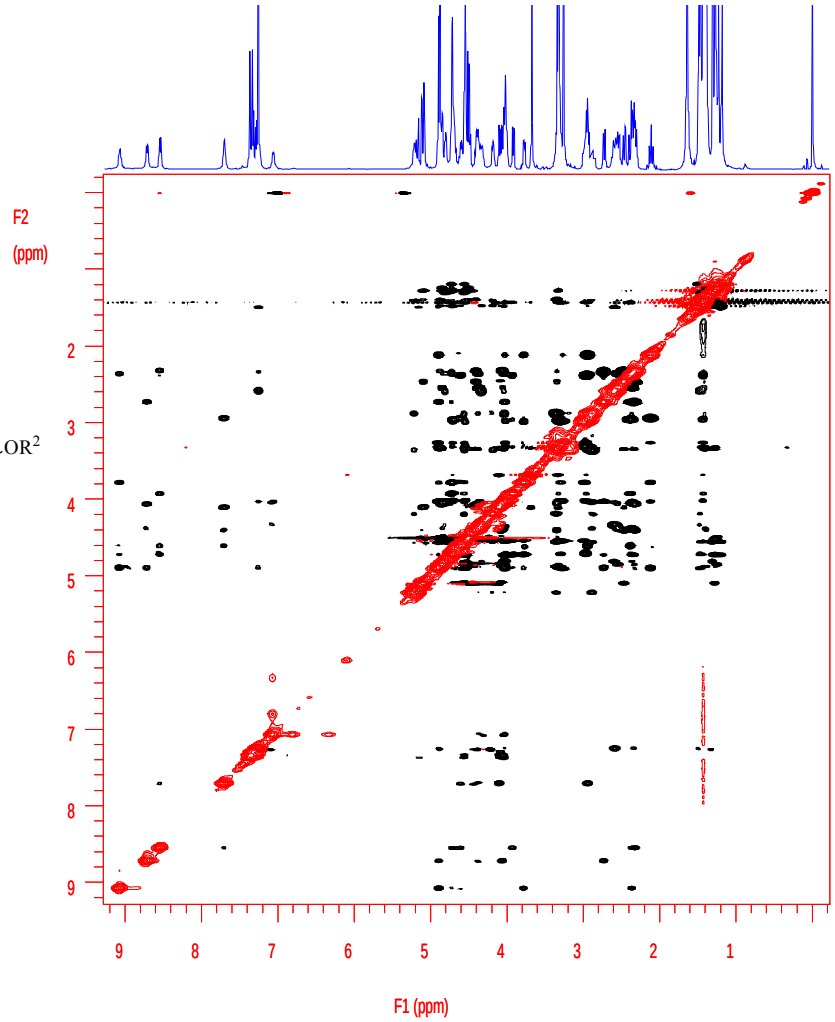


R = Cbz; R^1 = NHBoc; $R^2 = CH_3$

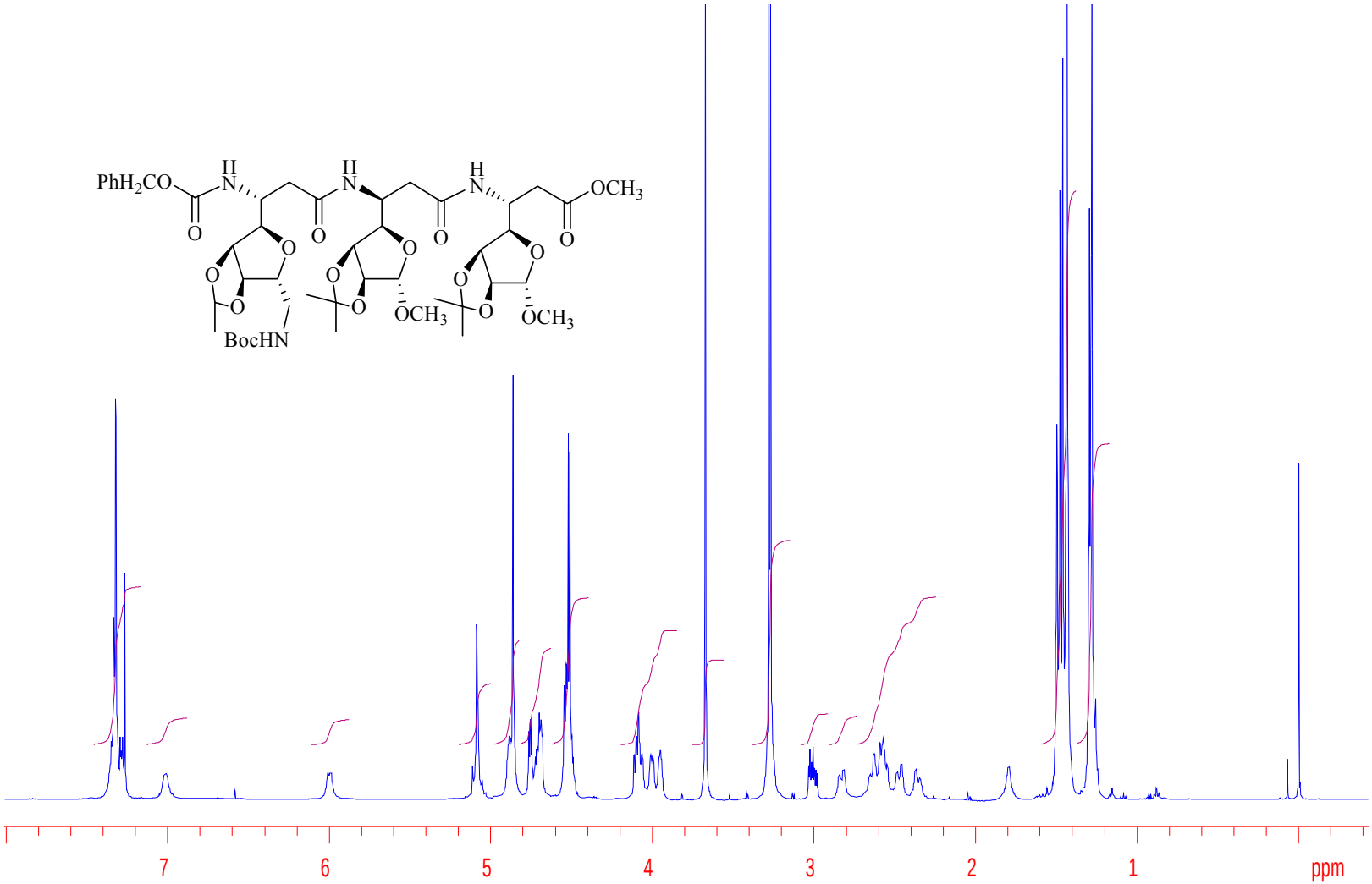
Supporting Fig 17: TOCSY Spectrum of 9 ($CDCl_3$, 303 K, 500 MHz)



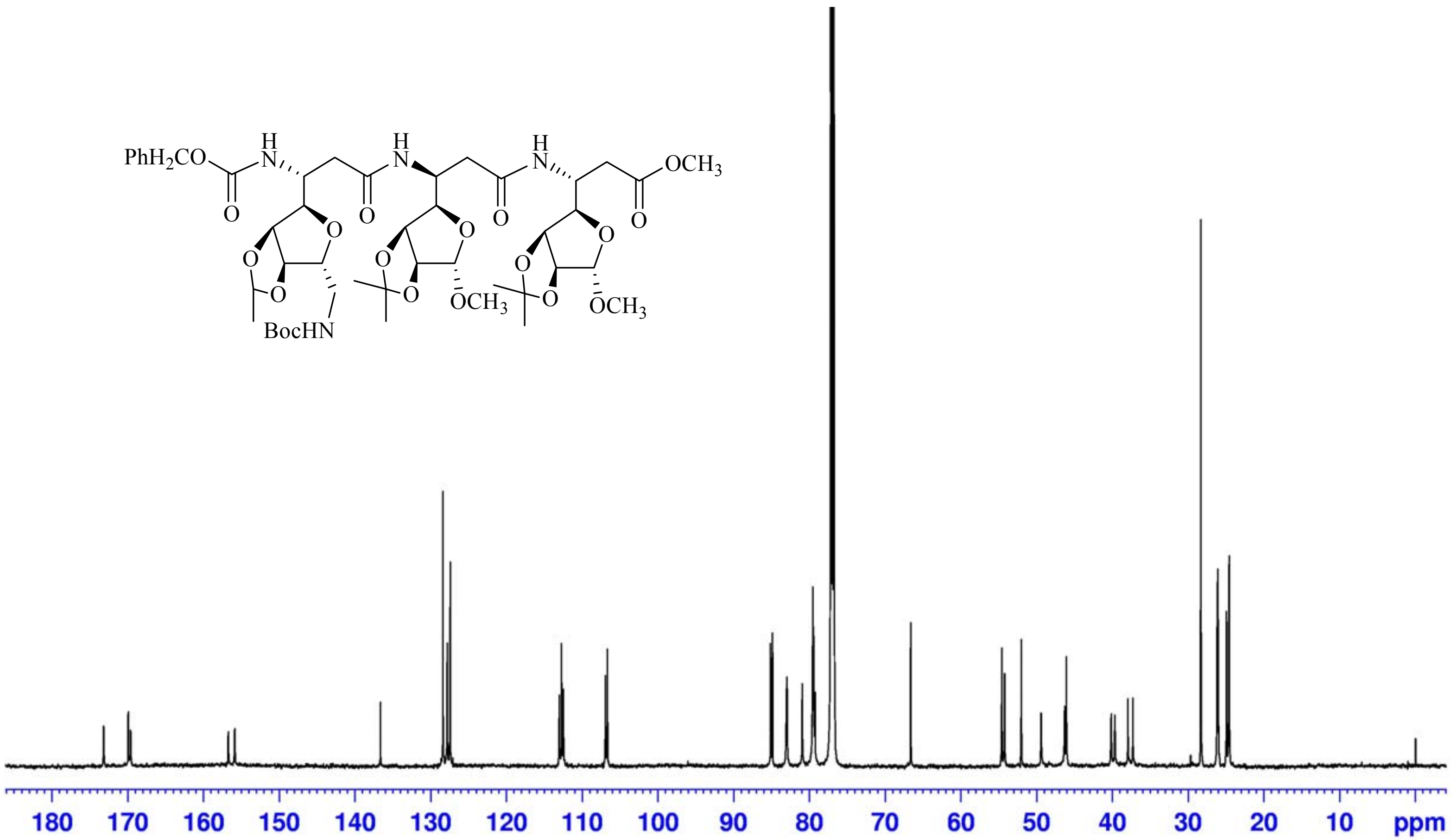
R = Cbz; R^1 = NHBoc; $R^2 = CH_3$



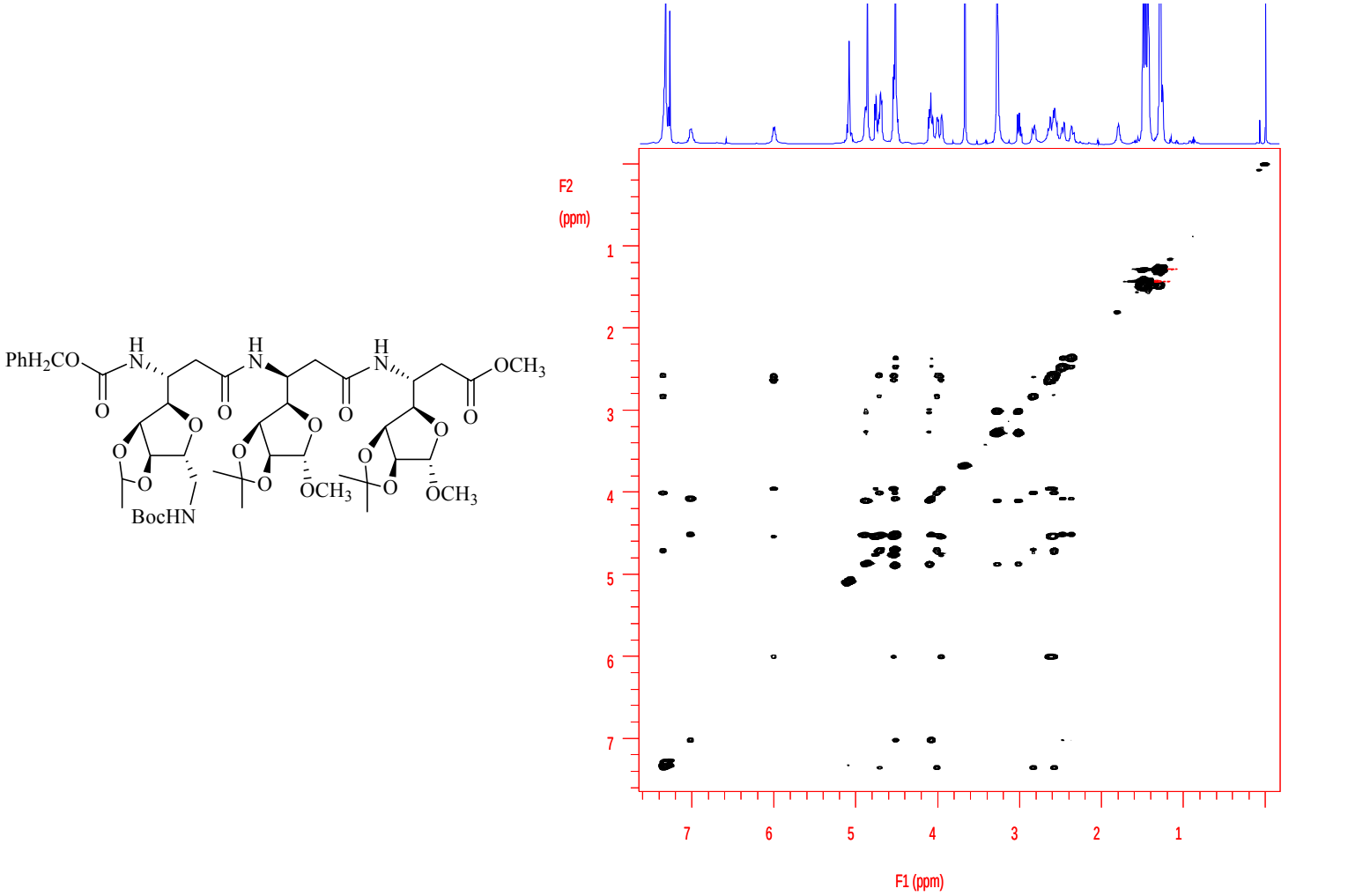
Supporting Fig 18: ROESY Spectrum of 9 ($CDCl_3$, 303 K, 500 MHz)



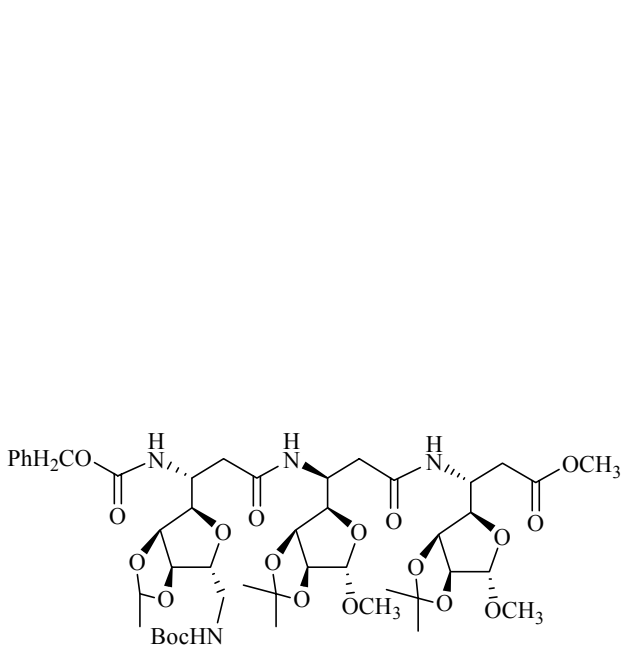
Supporting Fig 19: ^{1}H NMR Spectrum of 10 ($CDCl_3$, 303 K, 500 MHz)

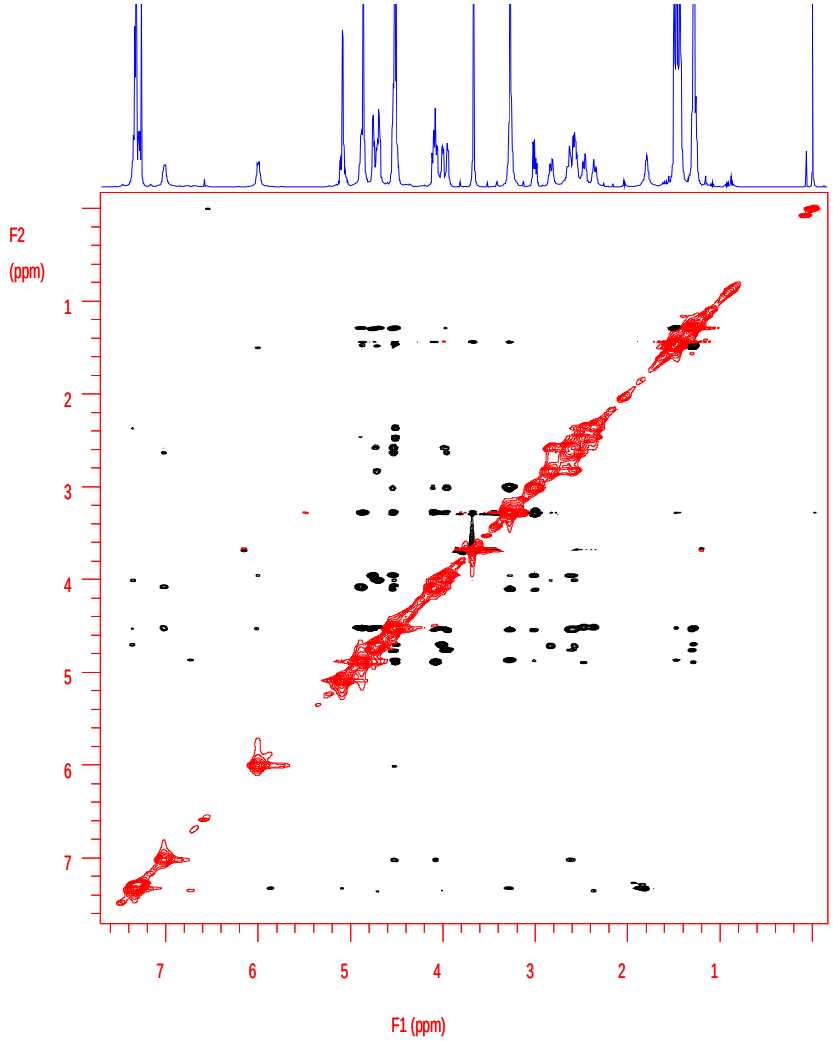


Supporting Fig 20: ^{13}C NMR Spectrum of 10 ($CDCl_3$, 303 K, 150 MHz)

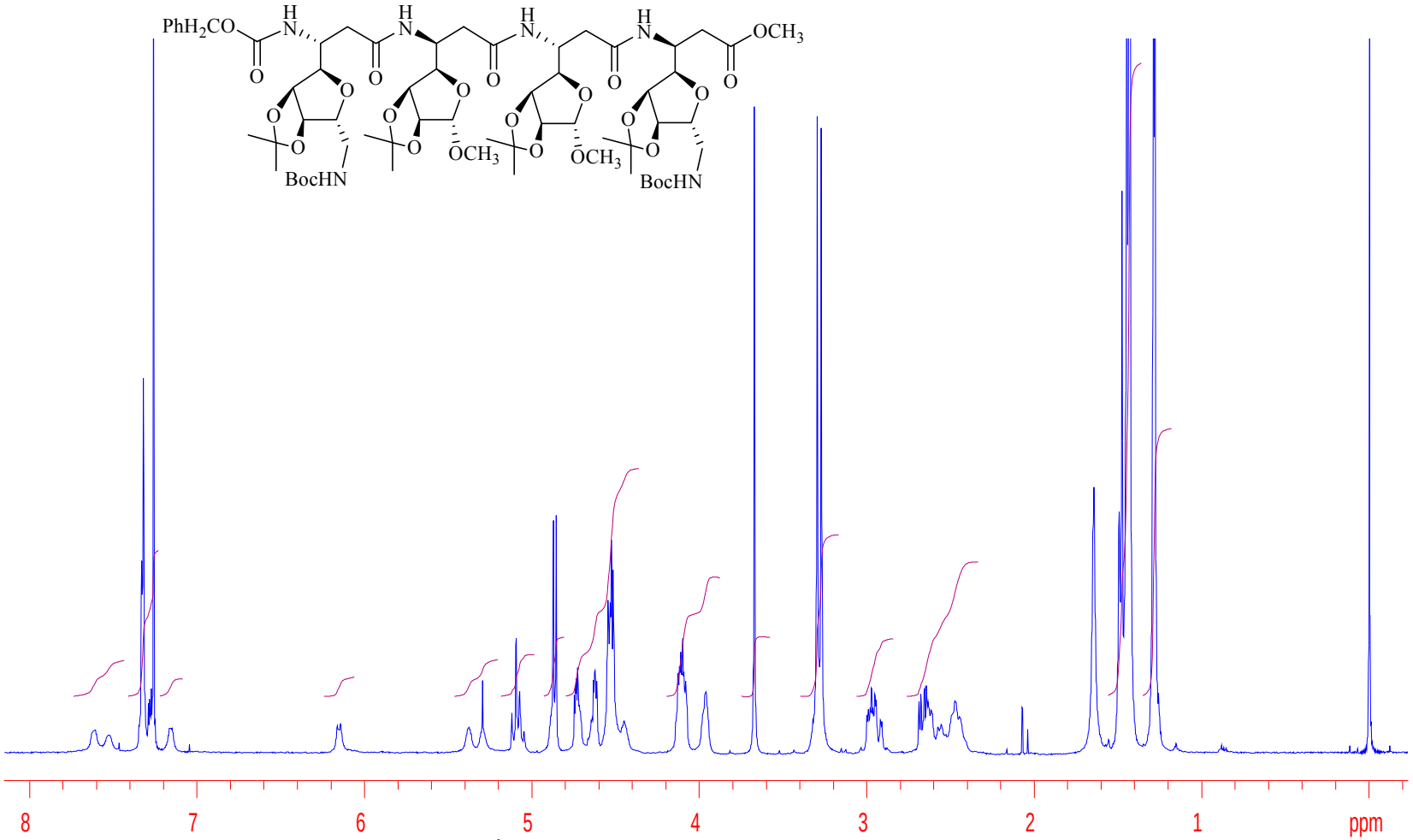


Supporting Fig 21: TOCSY Spectrum of 10 ($CDCl_3$, 303 K, 500 MHz)

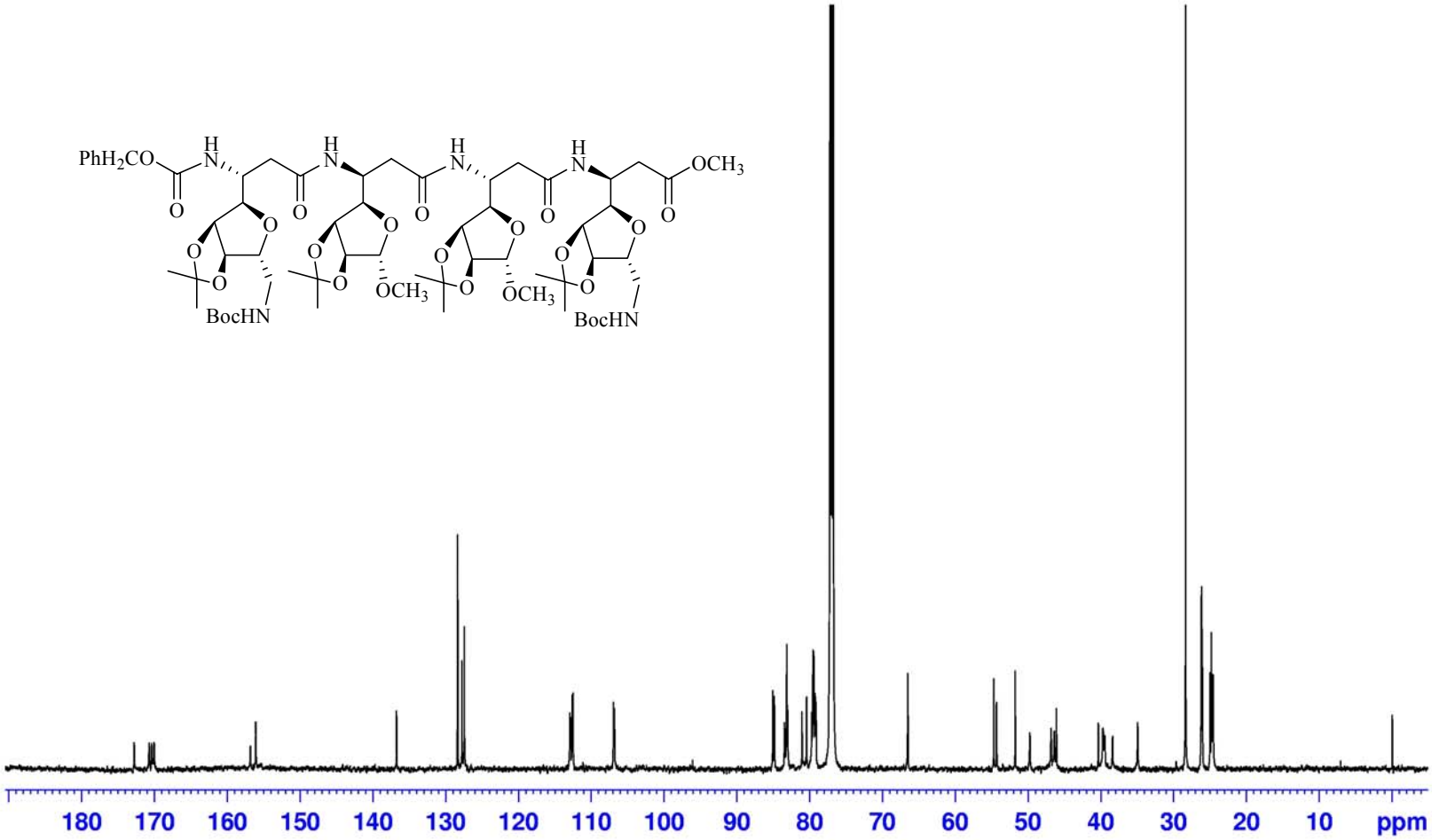




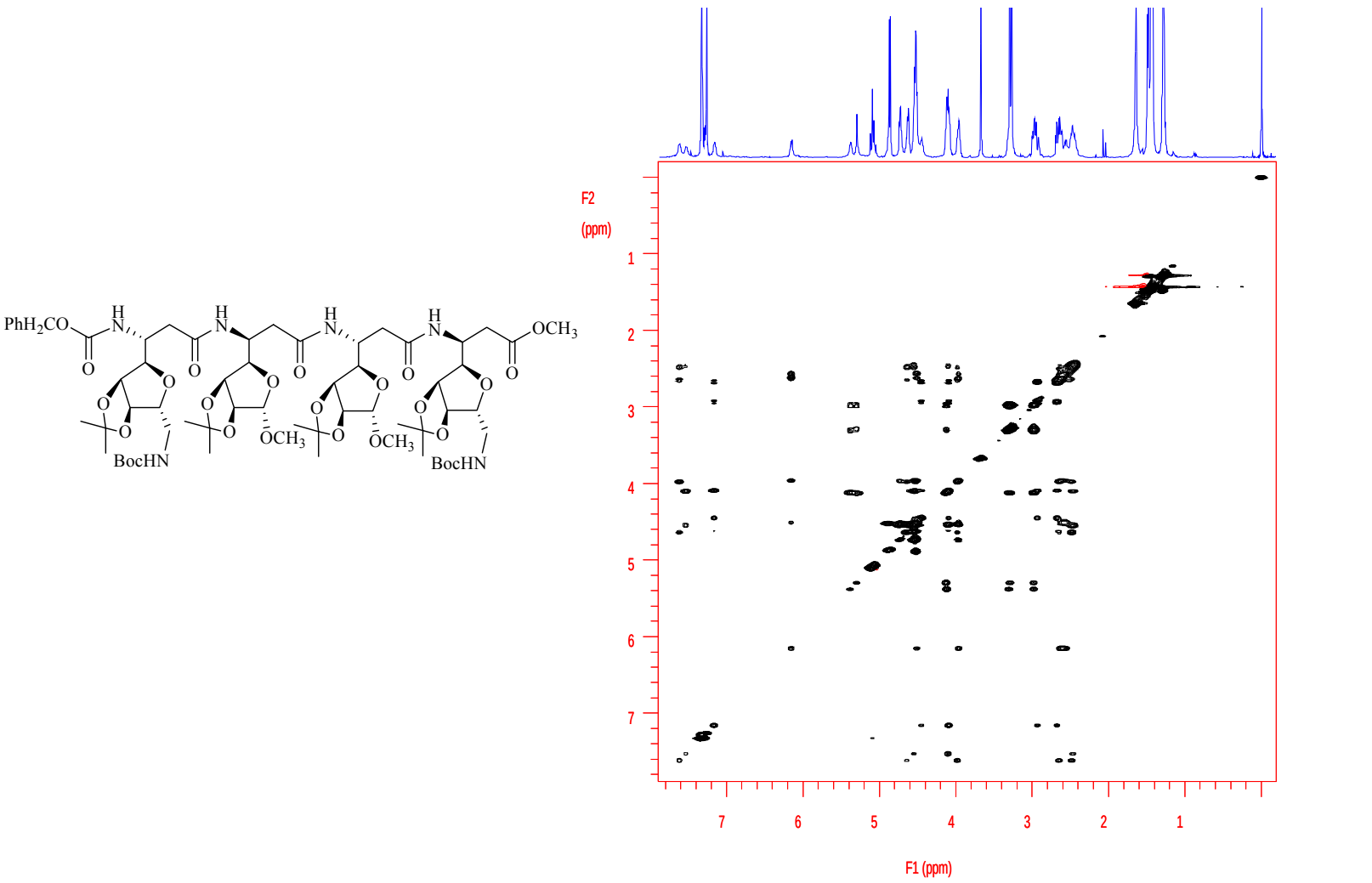
Supporting Fig 22: ROESY Spectrum of 10 ($CDCl_3$, 303 K, 500 MHz)



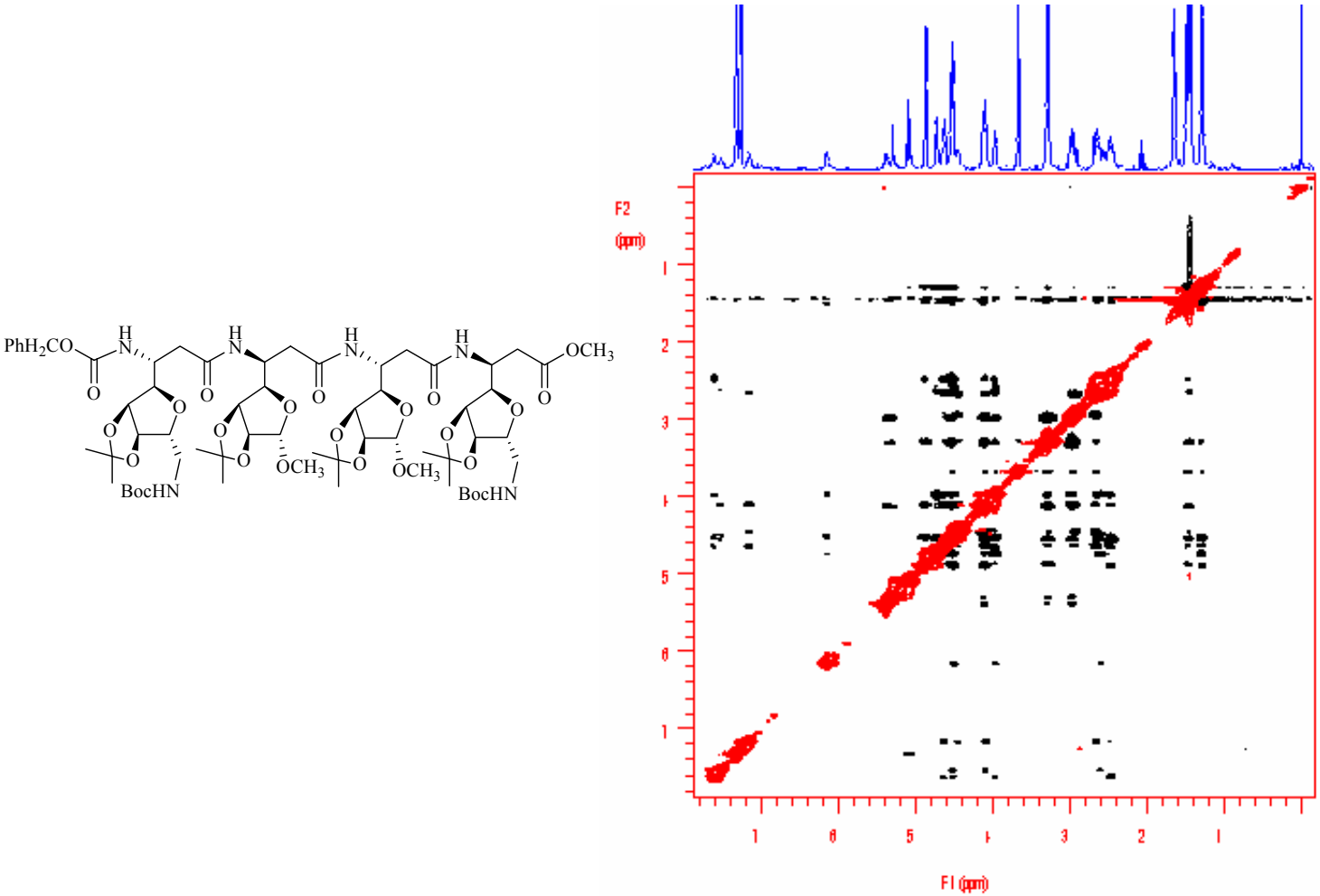
Supporting Fig 23: ^{1}H NMR Spectrum of 11 ($CDCl_3$, 303 K, 500 MHz)



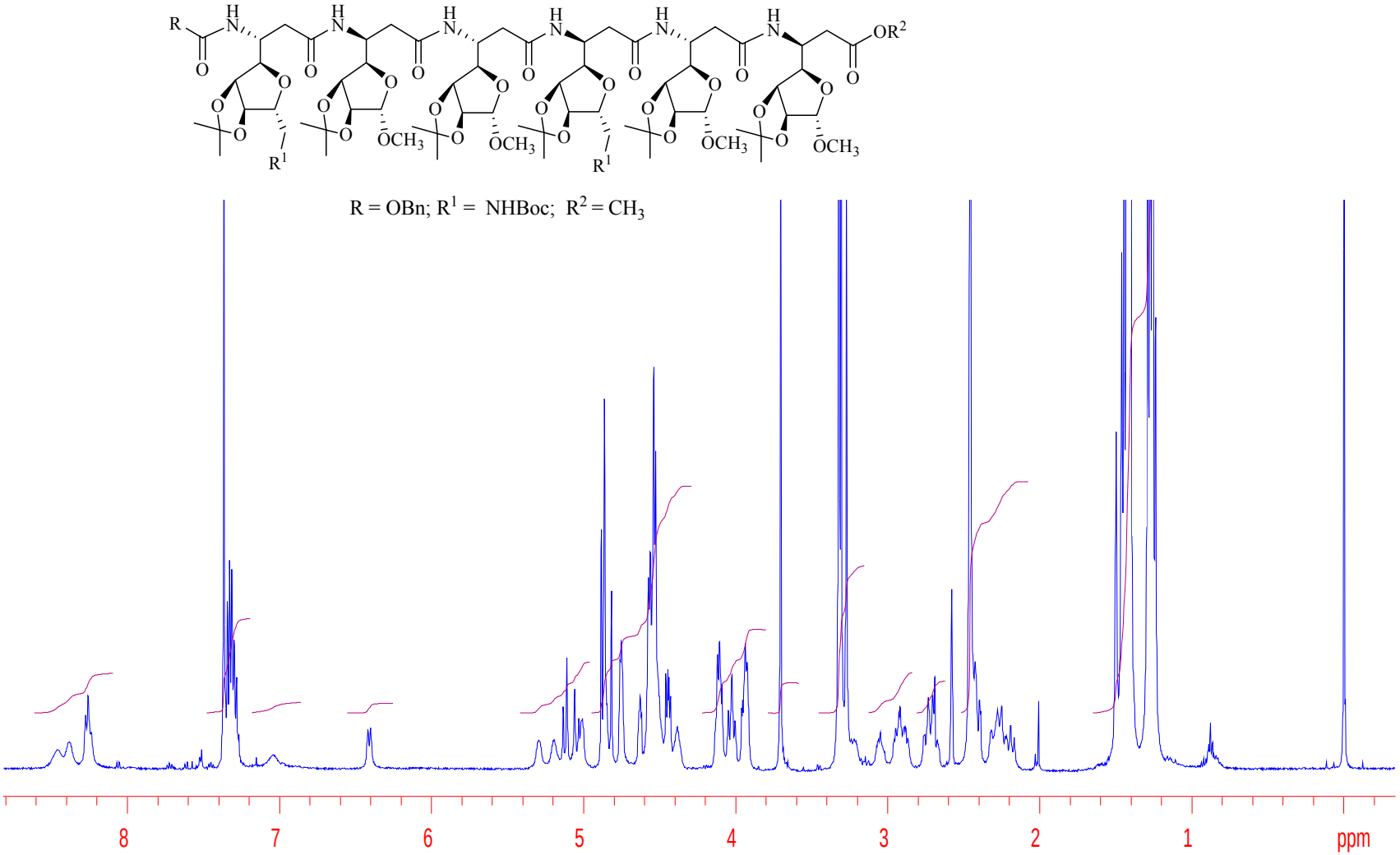
Supporting Fig 24: ^{13}C NMR Spectrum of 11 ($CDCl_3$, 303 K, 150 MHz)



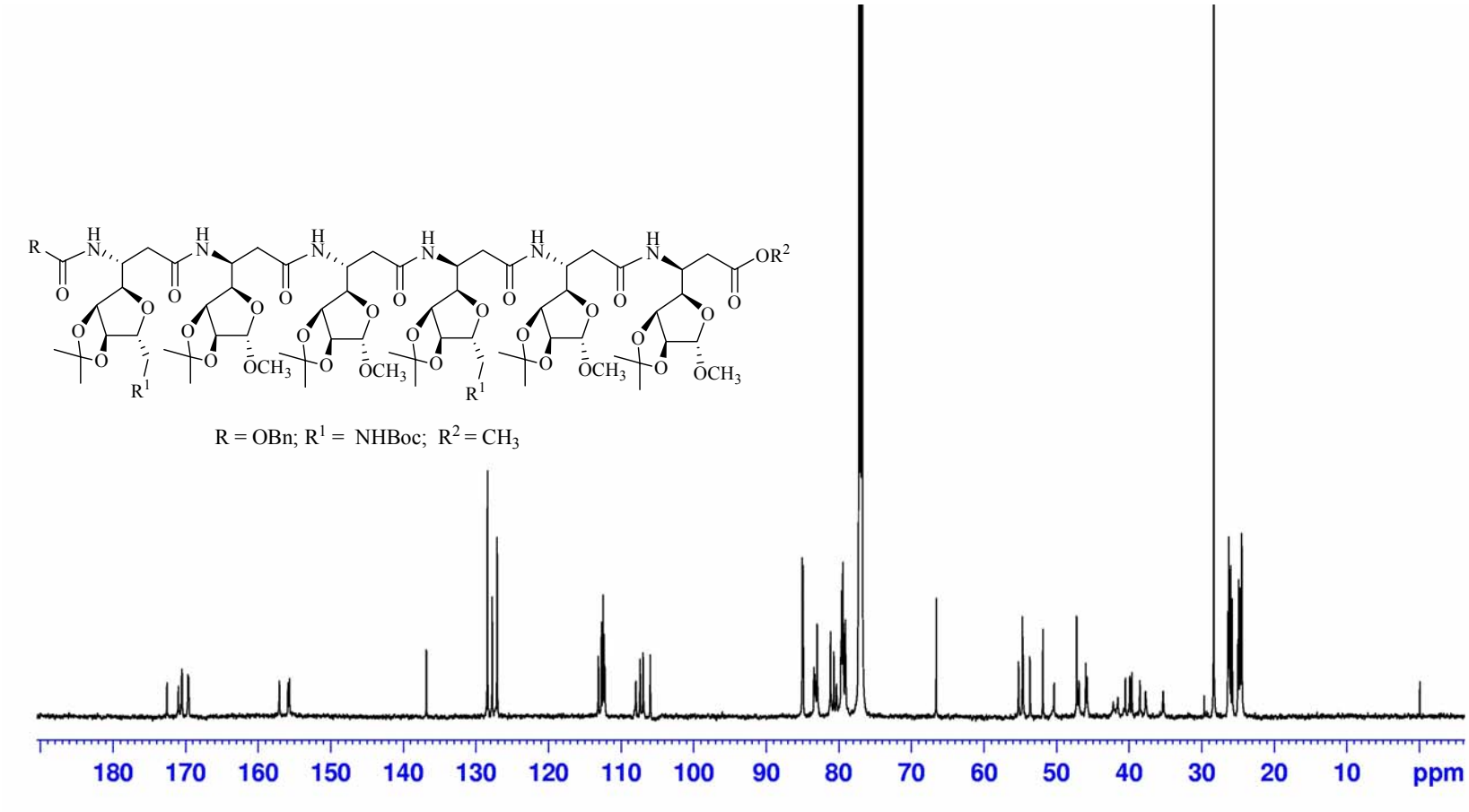
Supporting Fig 25: TOCSY Spectrum of 11 ($CDCl_3$, 303 K, 500 MHz)



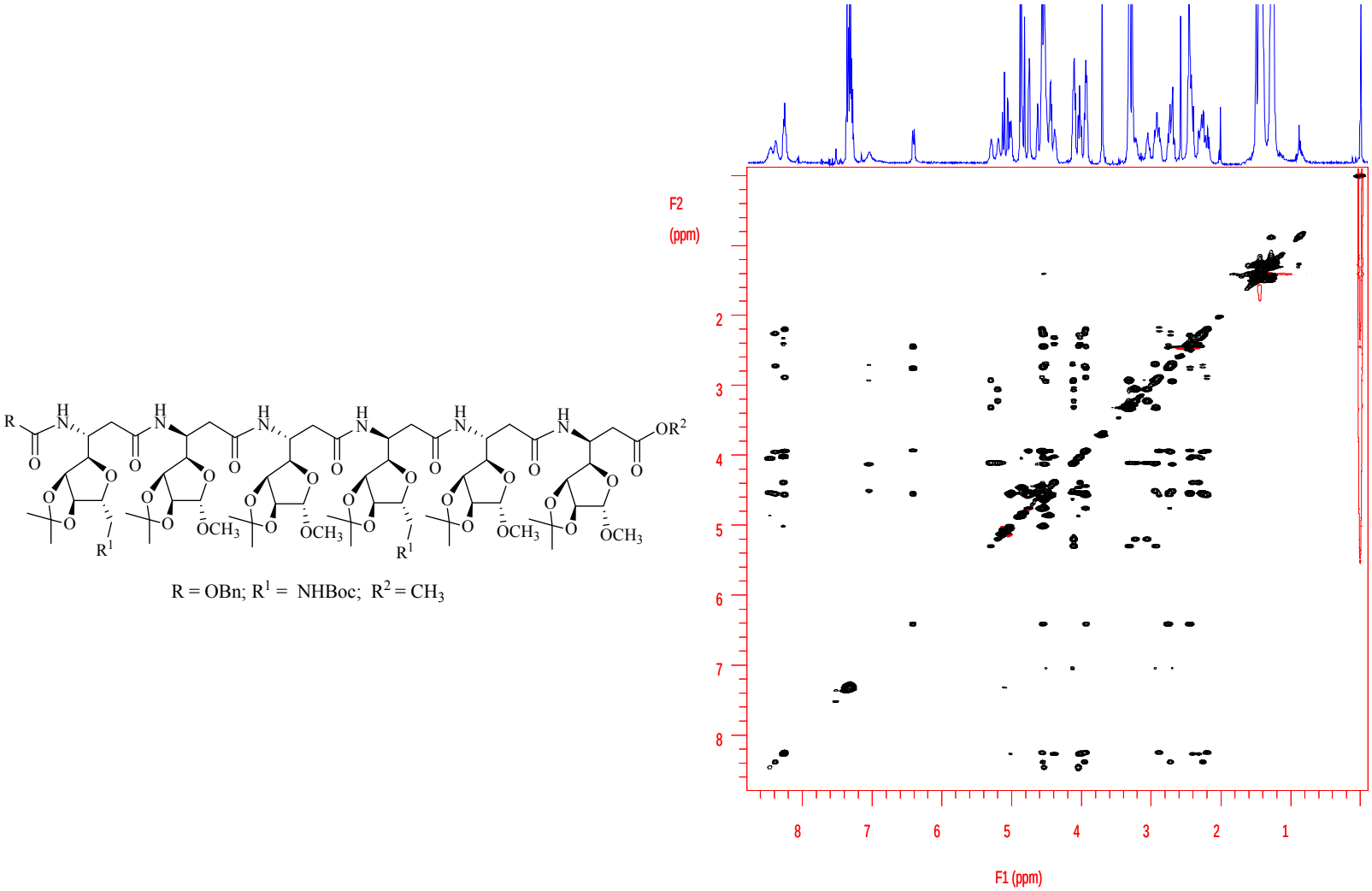
Supporting Fig 26: ROESY Spectrum of 11 ($CDCl_3$, 303 K, 500 MHz)



Supporting Fig 27: ^{1}H NMR Spectrum of 12 ($CDCl_3$+30 μL DMSO-d_6, 303 K, 500 MHz)

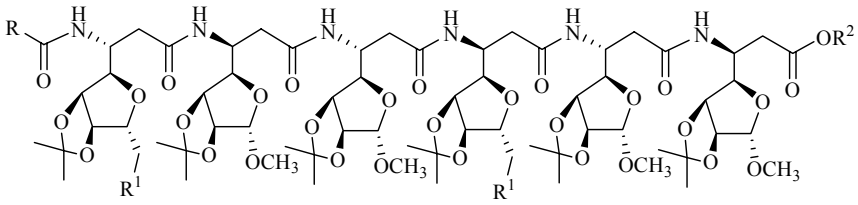


Supporting Fig 28: ^{13}C NMR Spectrum of 12 ($CDCl_3$, 303 K, 150 MHz)

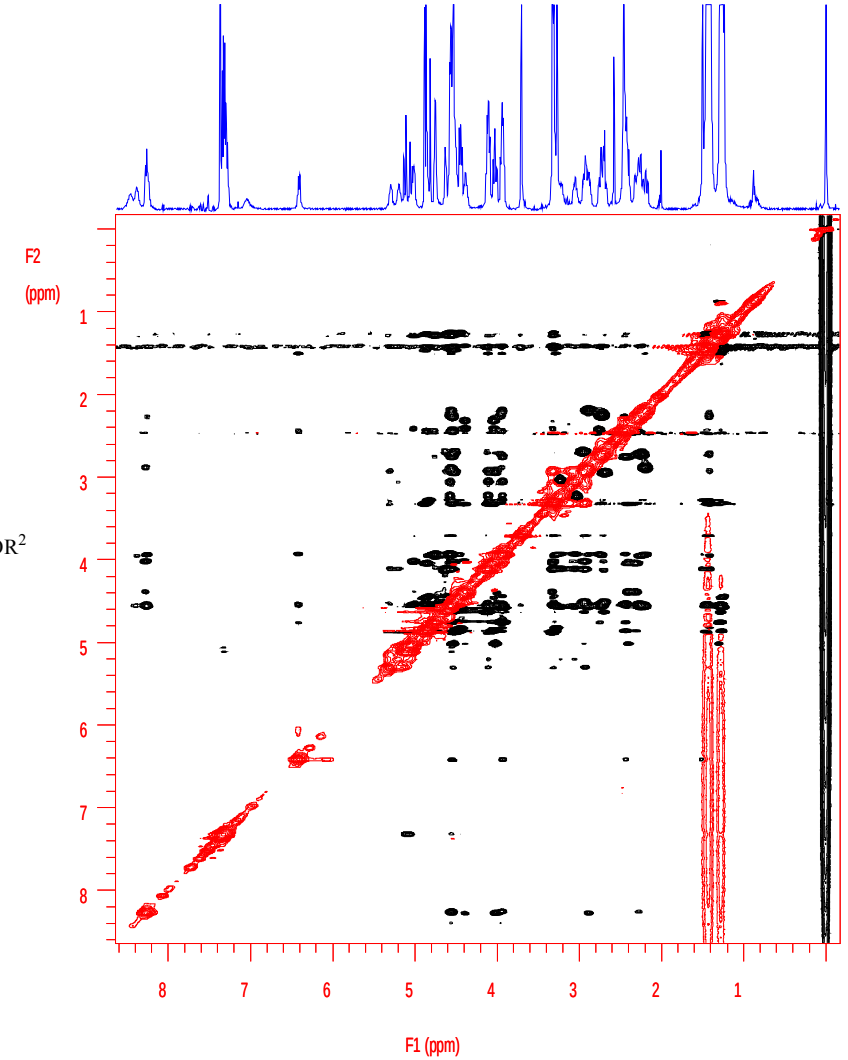


R = OBn; R^1 = NHBoc; $R^2 = CH_3$

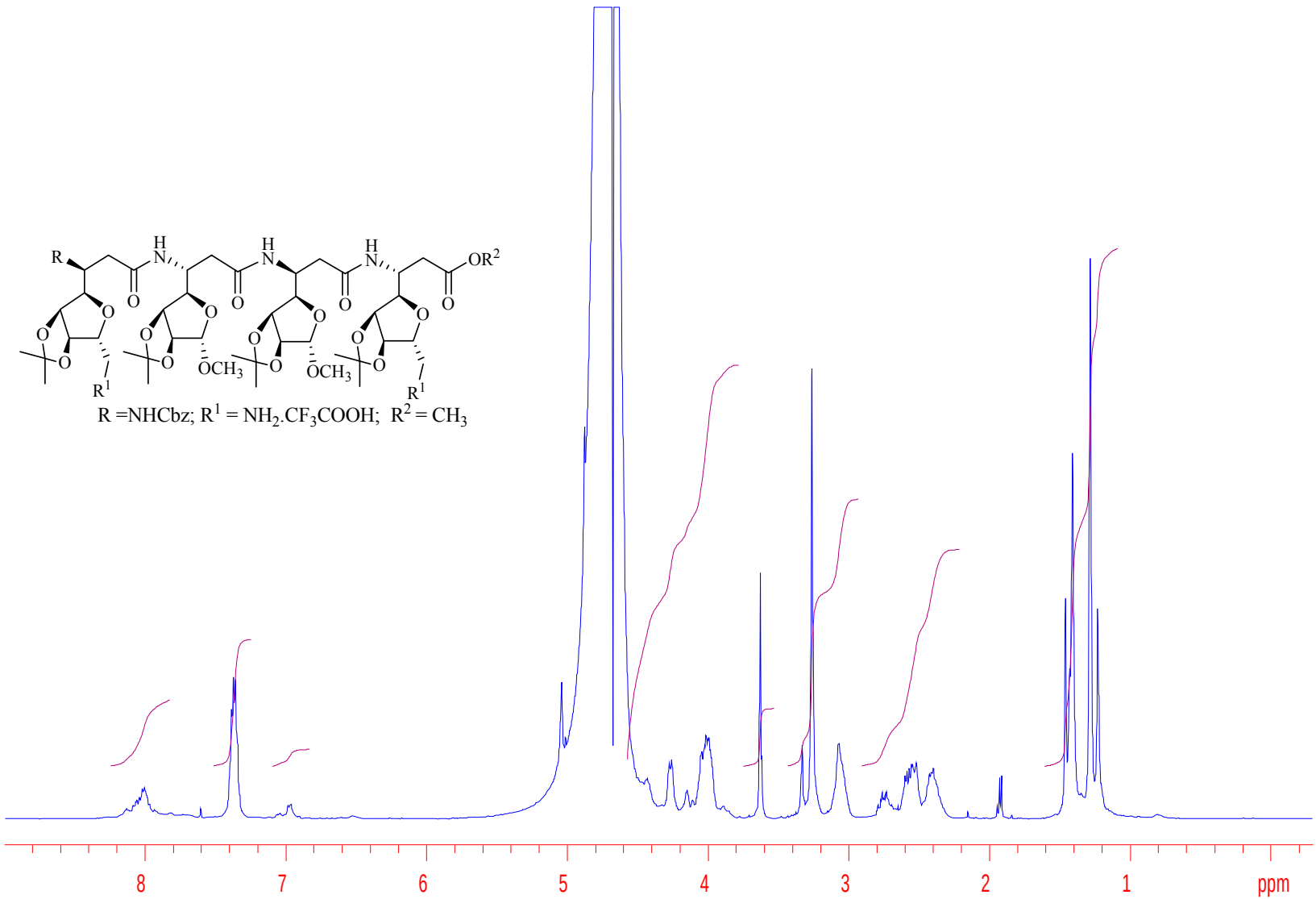
Supporting Fig 29: TOCSY Spectrum of 12 ($CDCl_3$+30 µL DMSO-d_6, 303 K, 500 MHz)



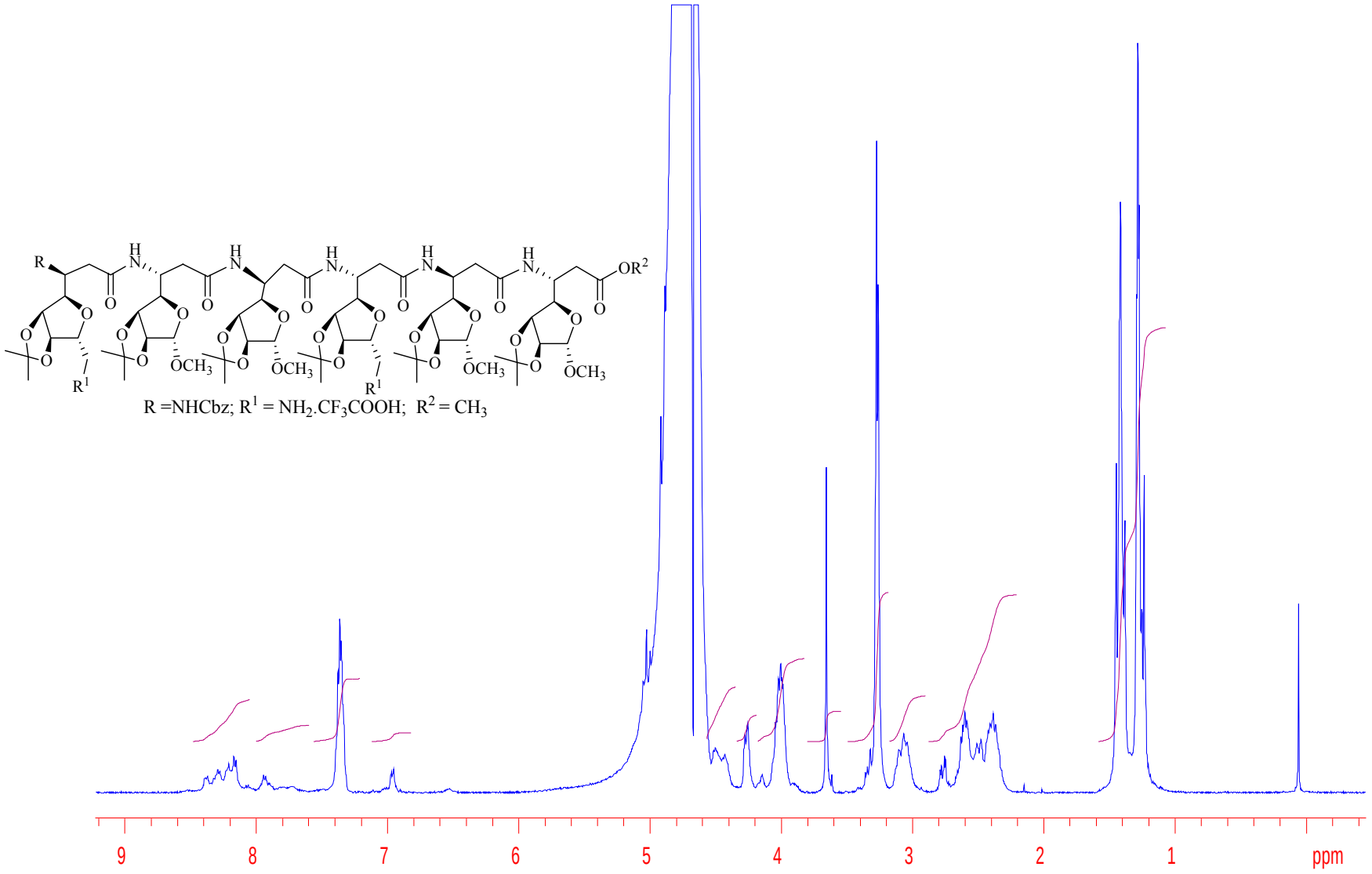
R = OBn; R^1 = NHBoc; $R^2 = CH_3$



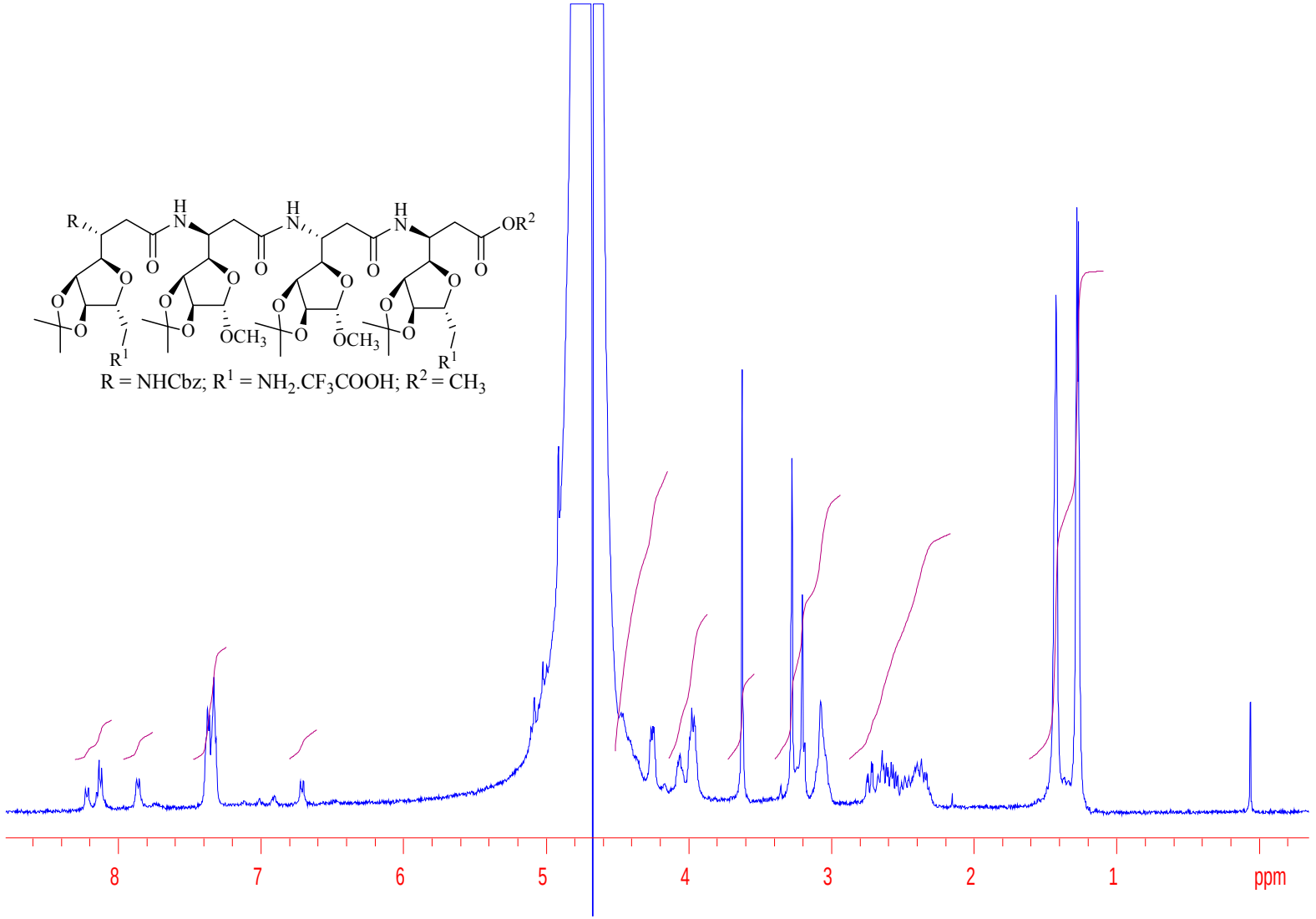
Supporting Fig 30: ROESY Spectrum of 12 ($CDCl_3$+30 µL DMSO-d_6, 303 K, 500 MHz)



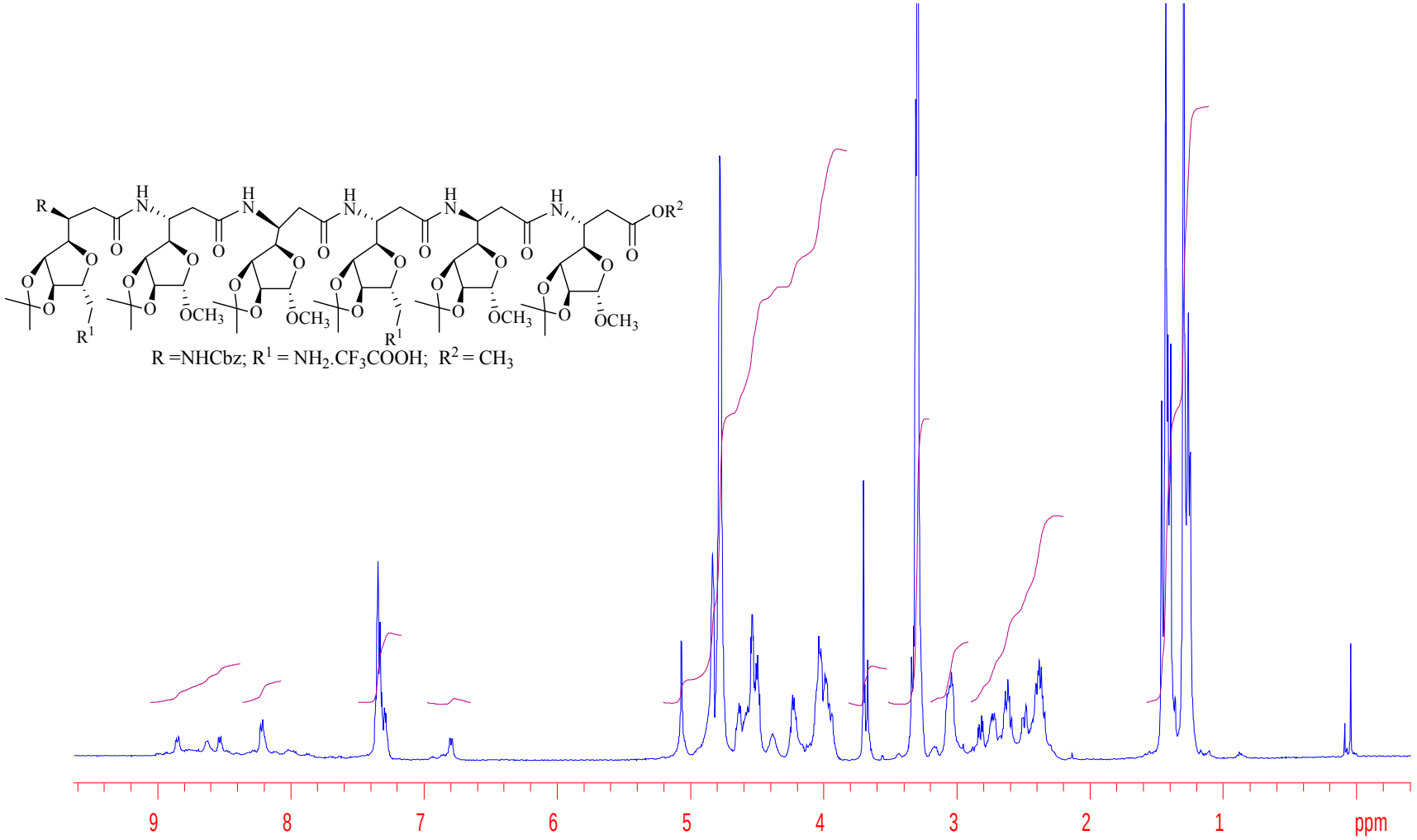
Supporting Fig 31: ^{1}H NMR Spectrum of 8b (90% H_2O+10% D_2O, 303 K, 500 MHz)



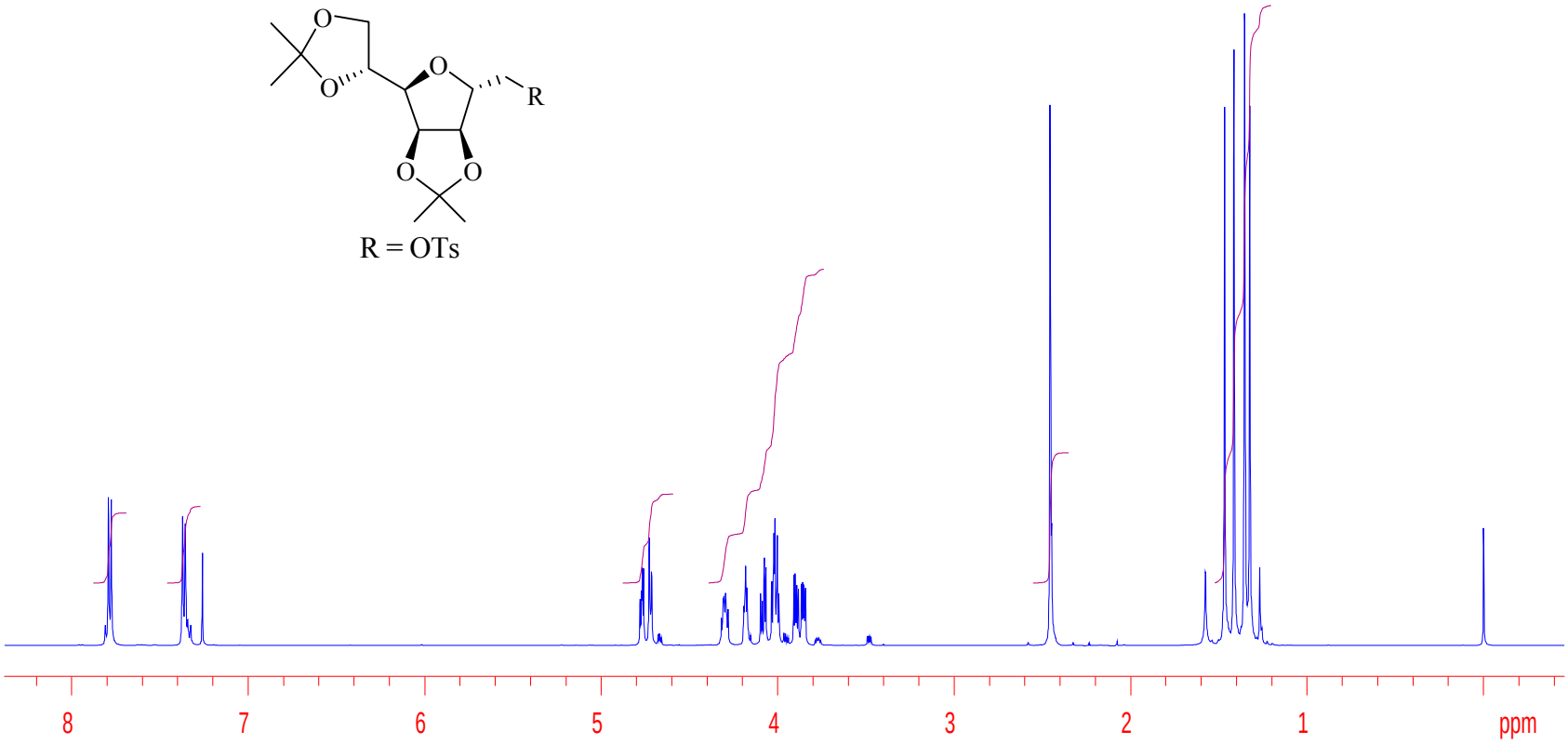
Supporting Fig 32: ^{1}H NMR Spectrum of 9b (90% H_2O+10% D_2O, 303 K, 500 MHz)



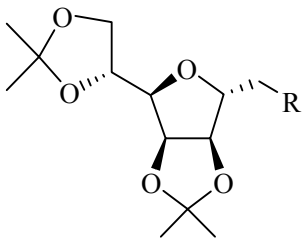
Supporting Fig 33: ^{1}H NMR Spectrum of 11a (90% H_2O+10% D_2O, 303 K, 500 MHz)



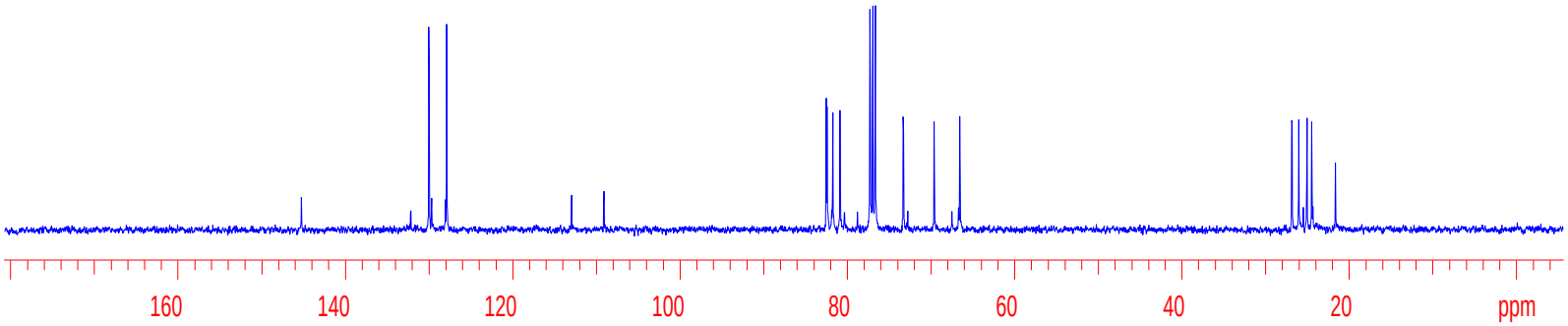
Supporting Fig 34: ^{1}H NMR Spectrum of 9b (CD_3OH, 303 K, 500 MHz)



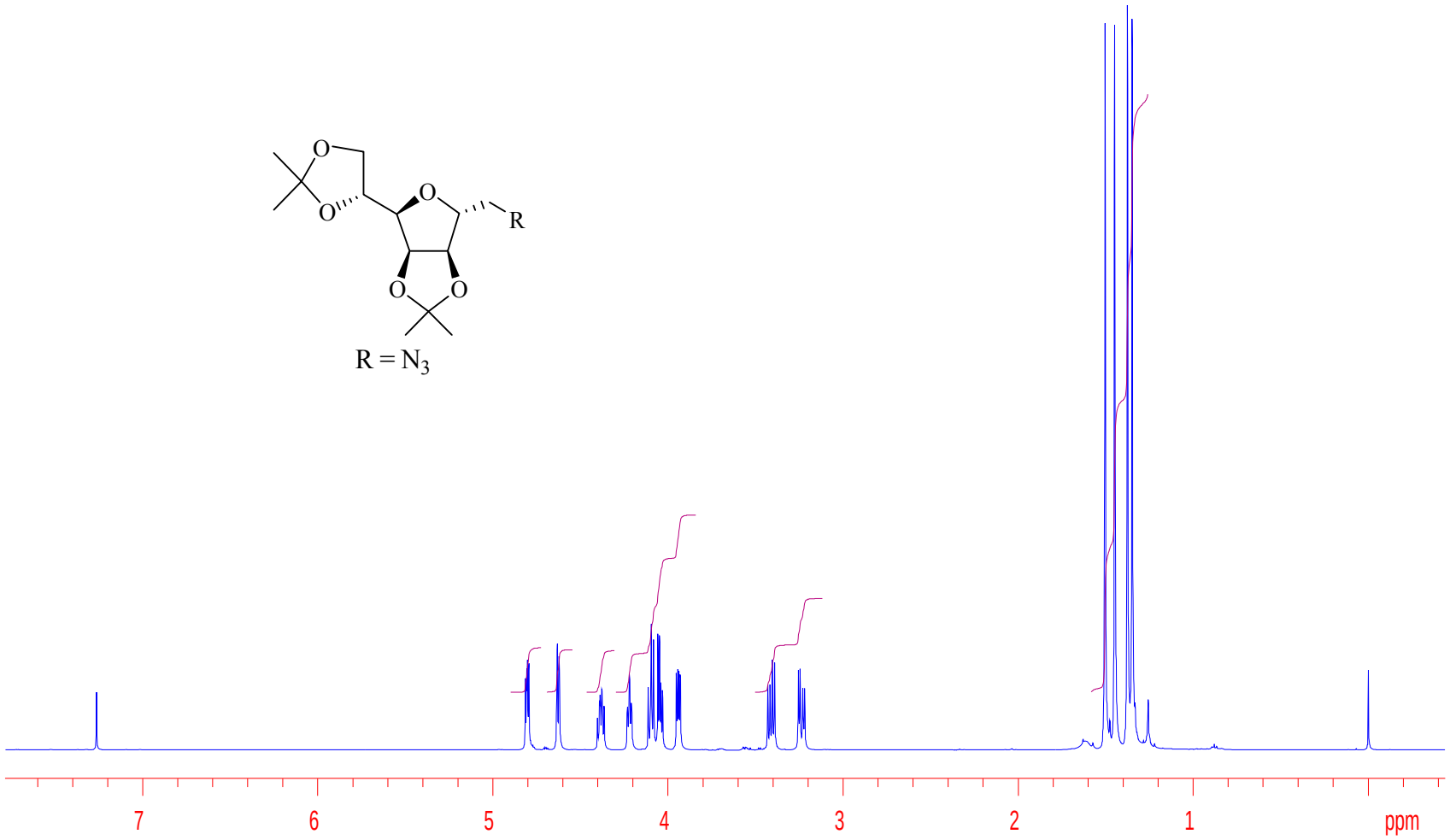
Supporting Fig 35: ^{1}H NMR Spectrum of 18 ($CDCl_3$, 303 K, 500 MHz)



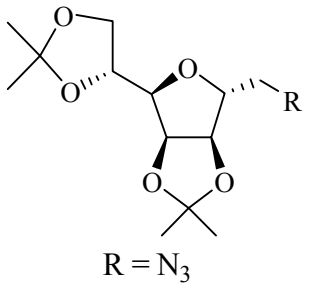
R = OTs

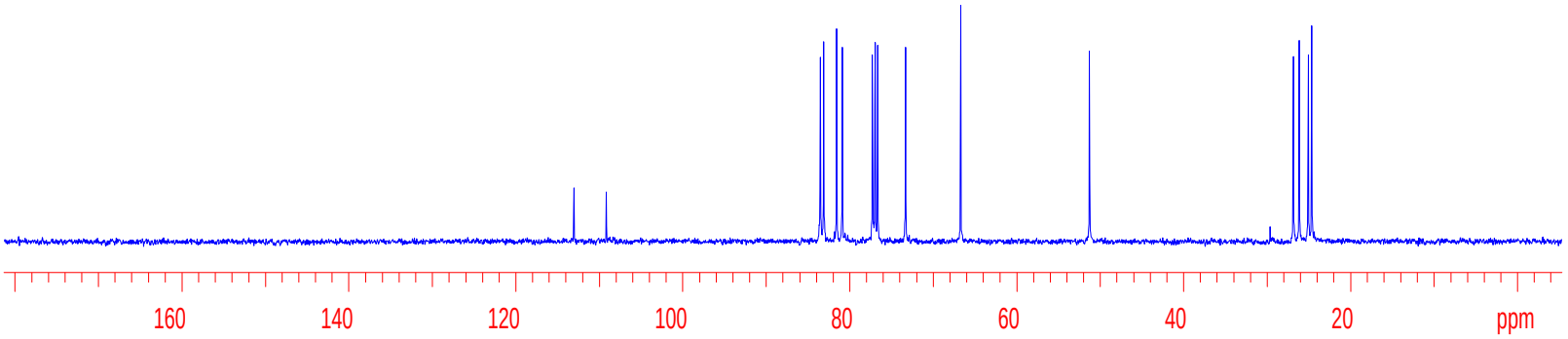


Supporting Fig 36: ^{13}C NMR Spectrum of 18 ($CDCl_3$, 303 K, 100 MHz)

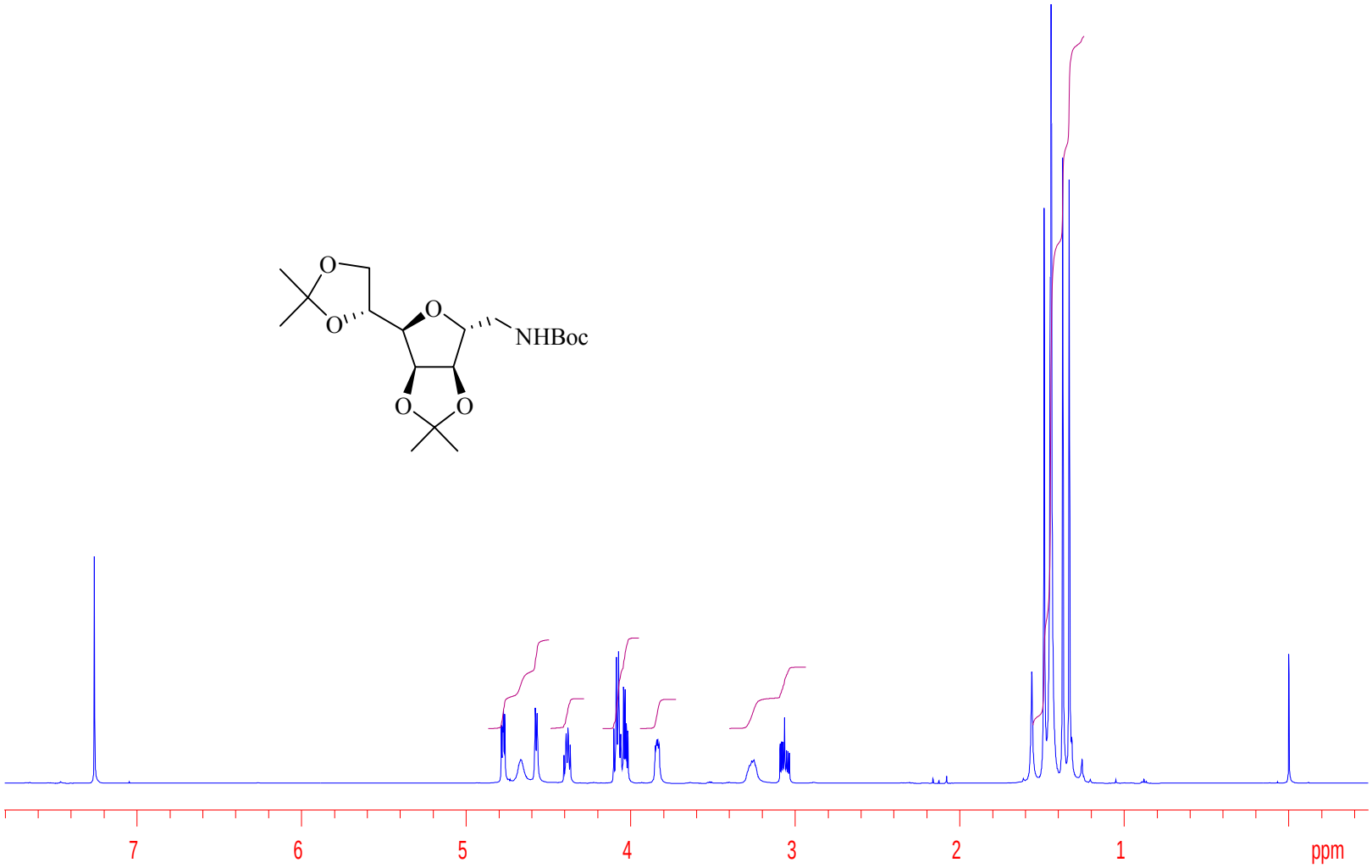


Supporting Fig 37: ^{1}H NMR Spectrum of 19 ($CDCl_3$, 303 K, 500 MHz)

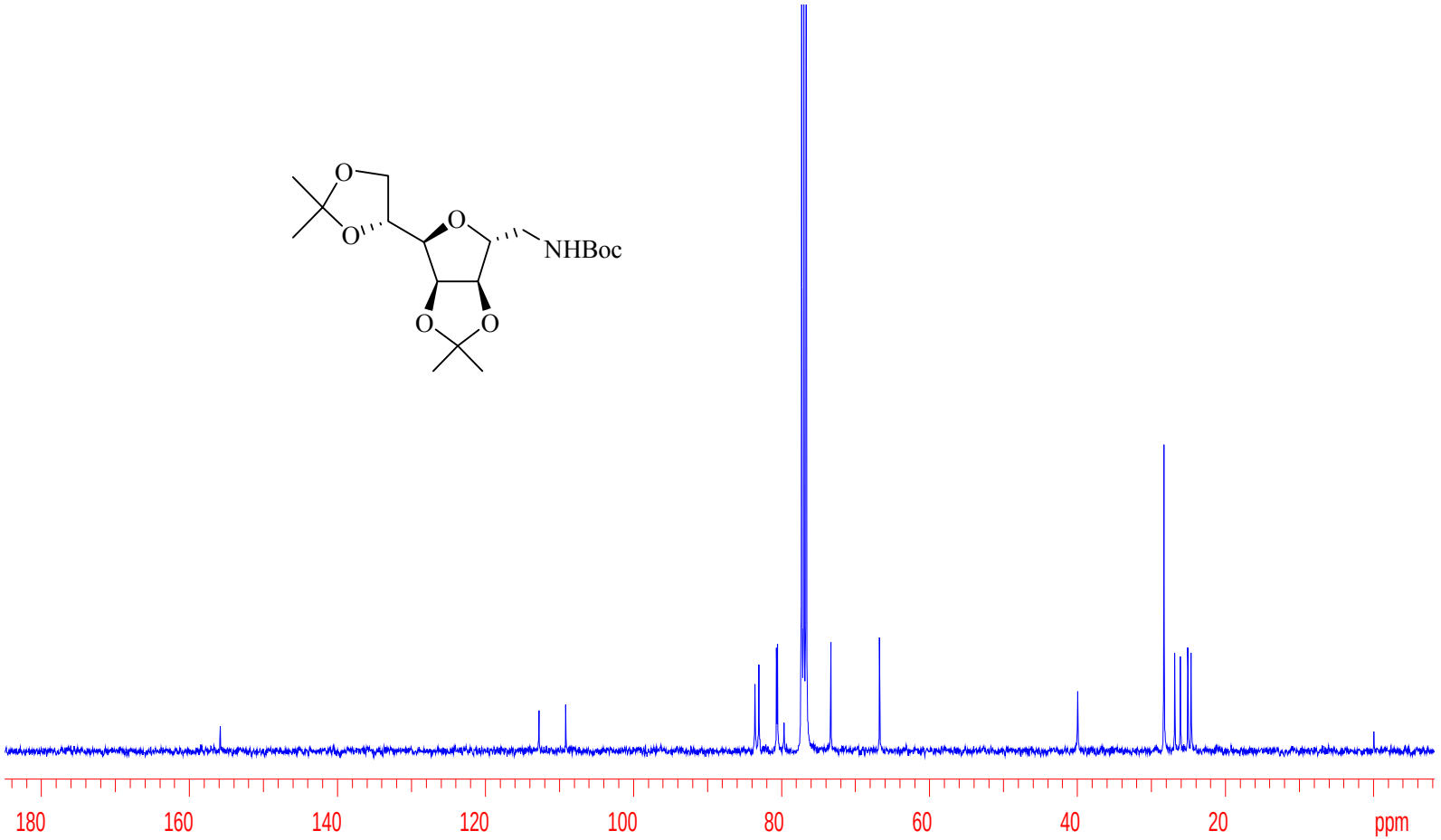




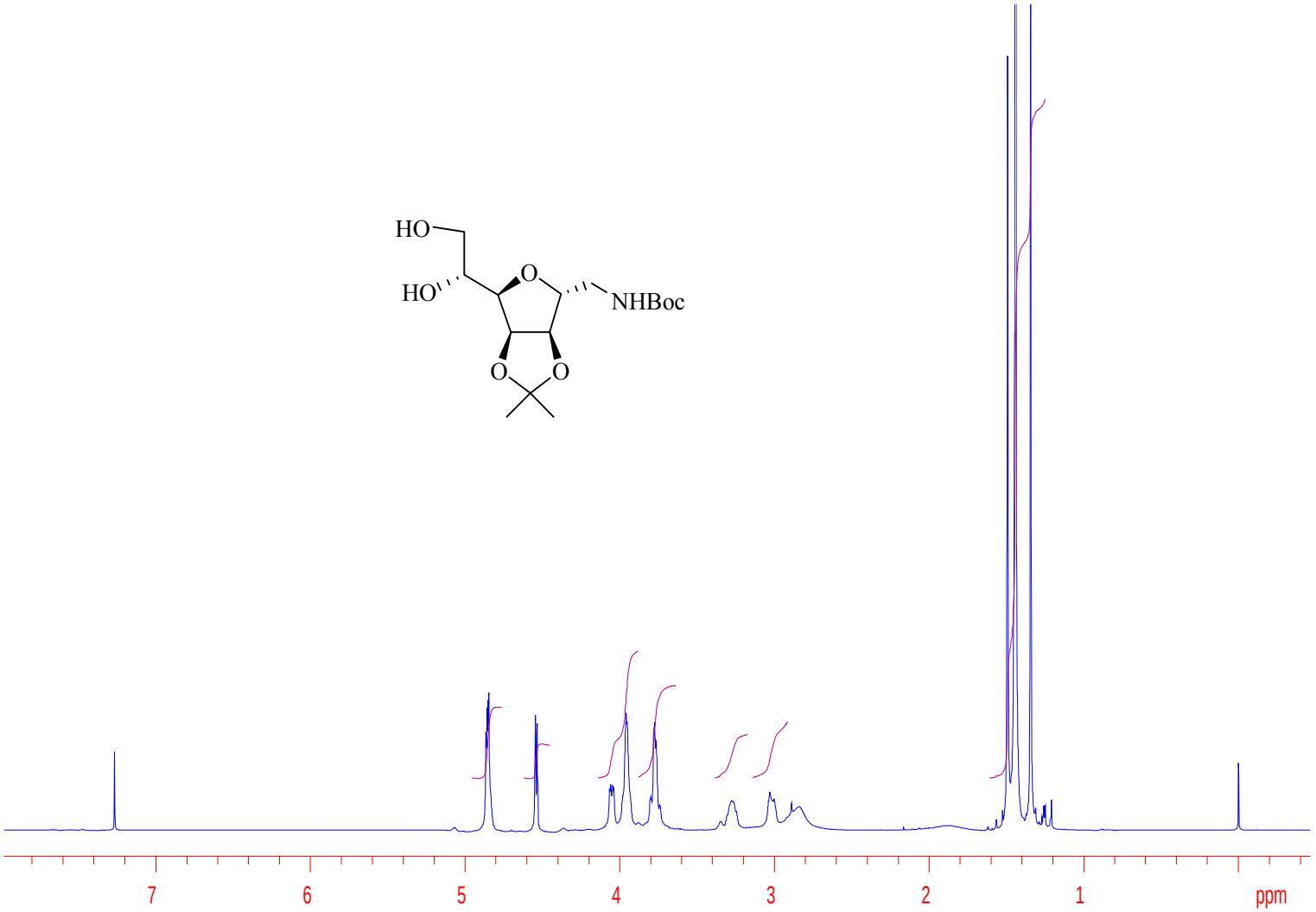
Supporting Fig 38: ^{13}C NMR Spectrum of 19 ($CDCl_3$, 303 K, 100 MHz)



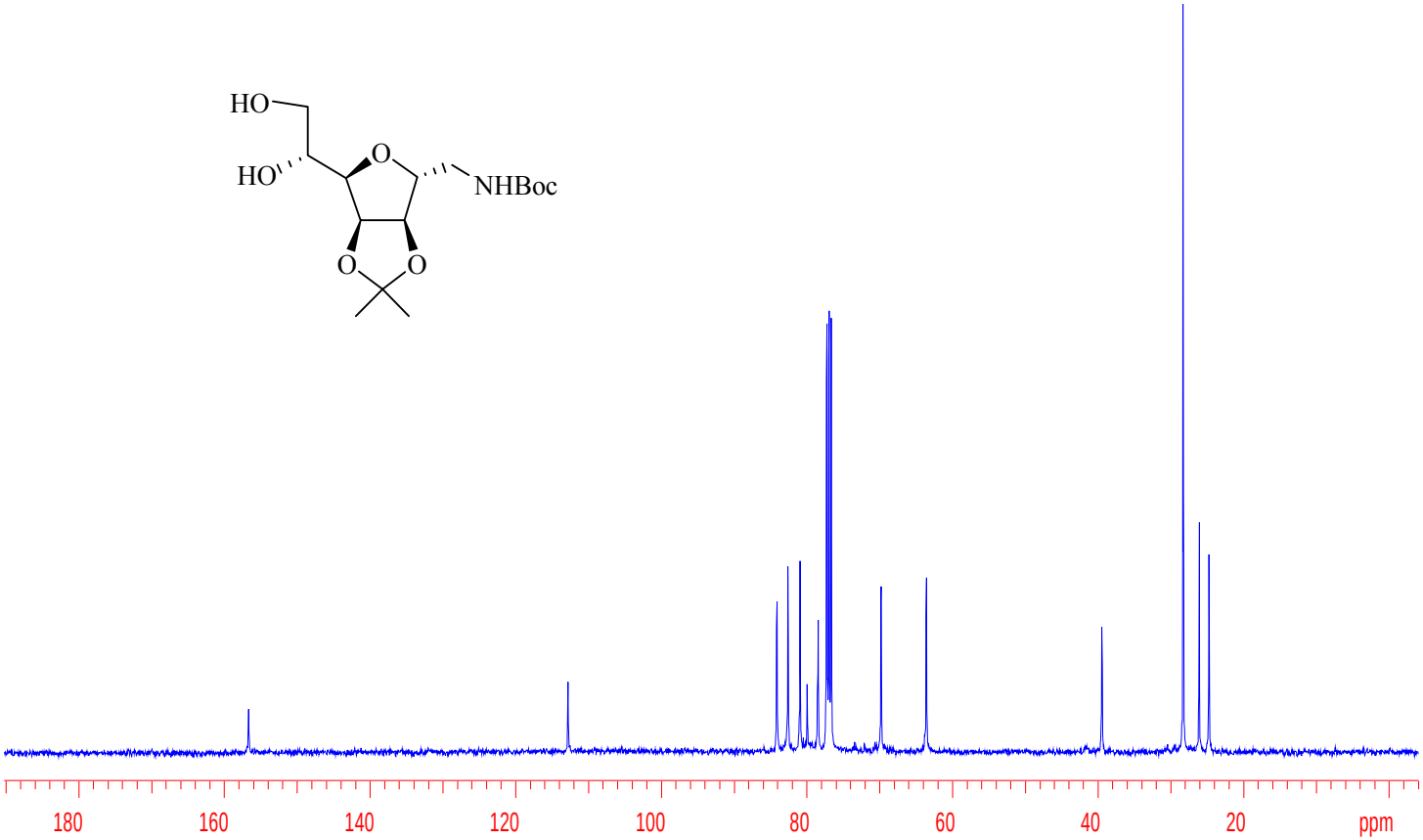
Supporting Fig 39: ^{1}H NMR Spectrum of 20 ($CDCl_3$, 303 K, 500 MHz)



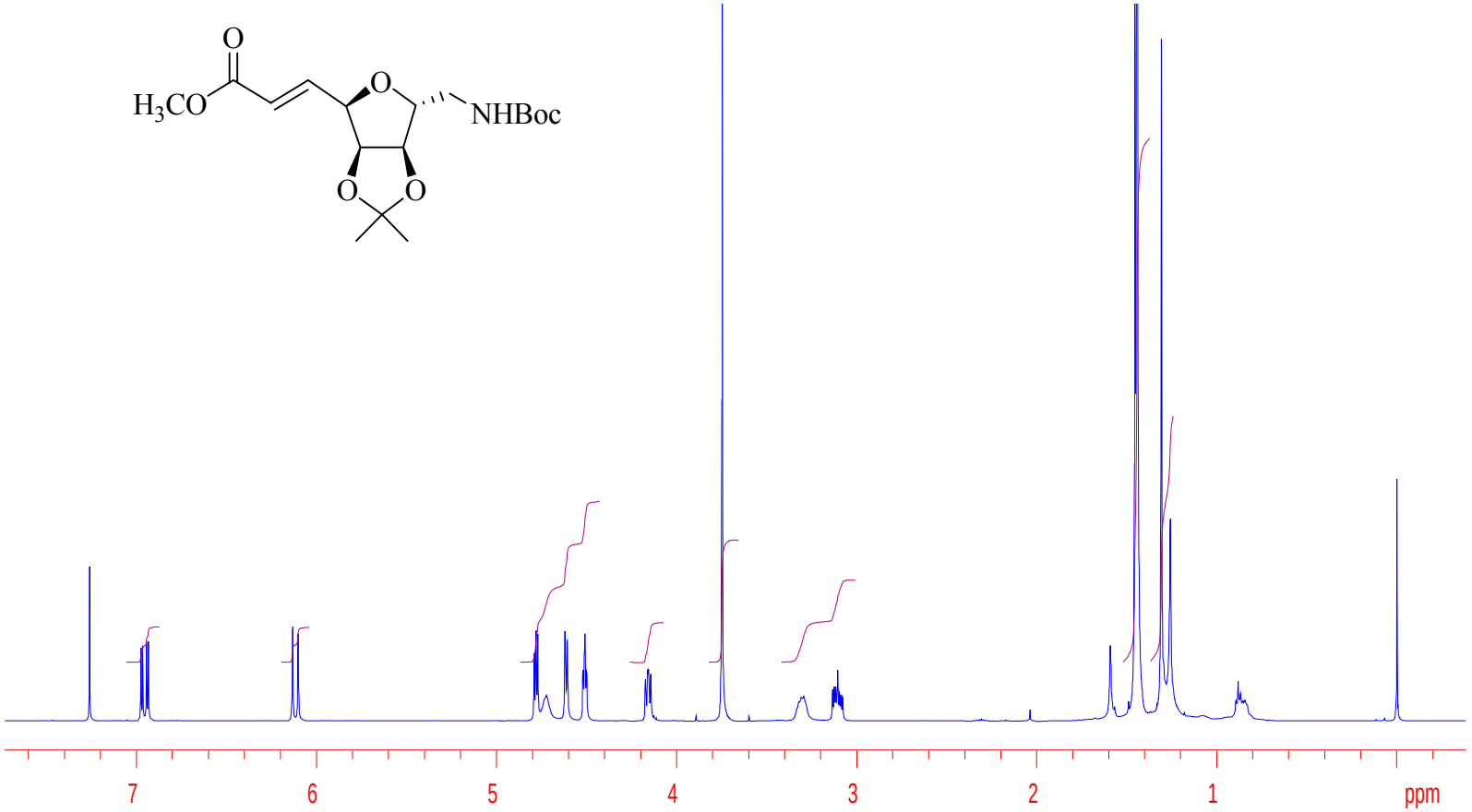
Supporting Fig 40: ^{13}C NMR Spectrum of 20 ($CDCl_3$, 303 K, 100 MHz)



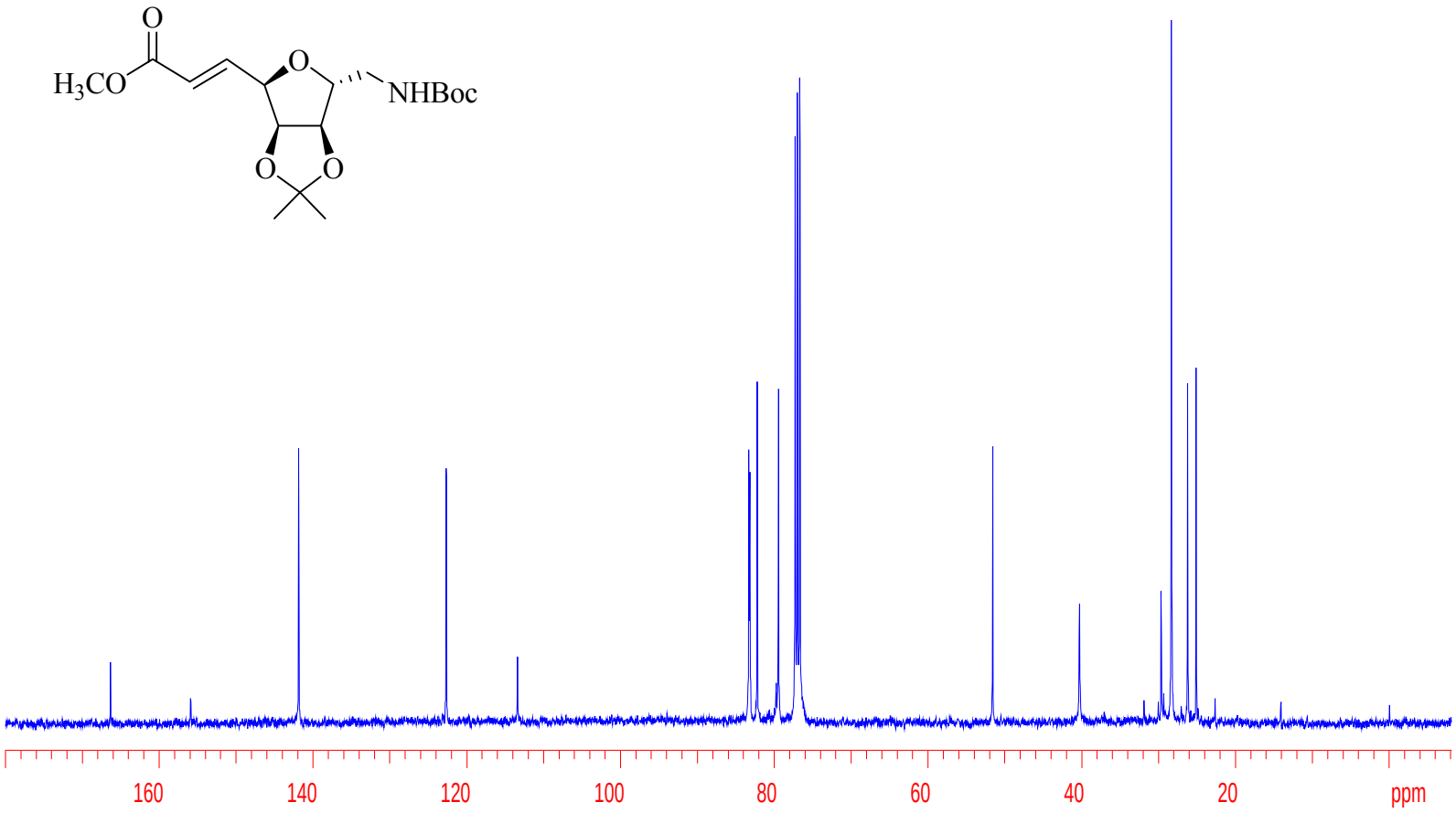
Supporting Fig 41: ^{1}H NMR Spectrum of 21 ($CDCl_3$, 303 K, 500 MHz)



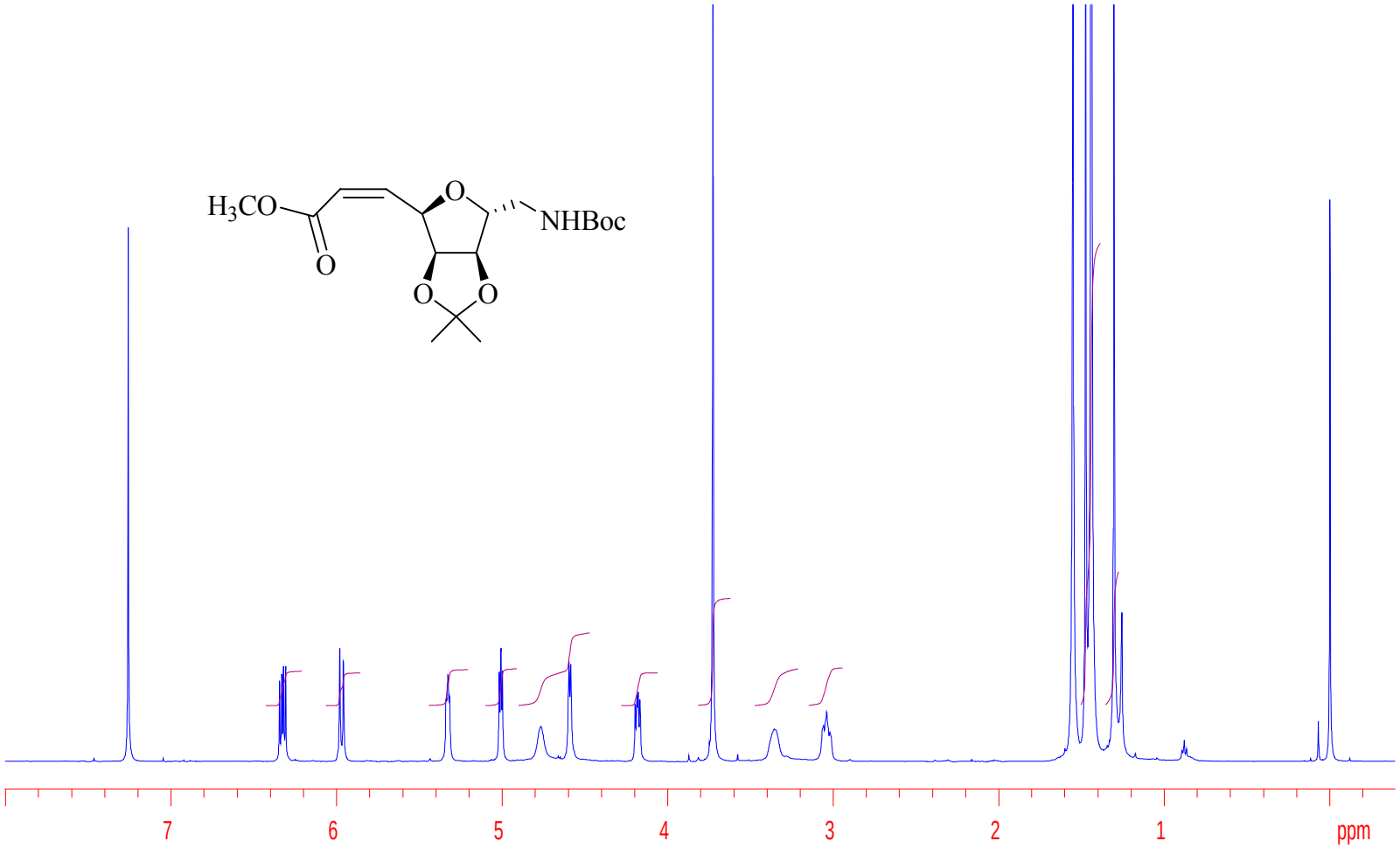
Supporting Fig 42: ^{13}C NMR Spectrum of 21 ($CDCl_3$, 303 K, 100 MHz)



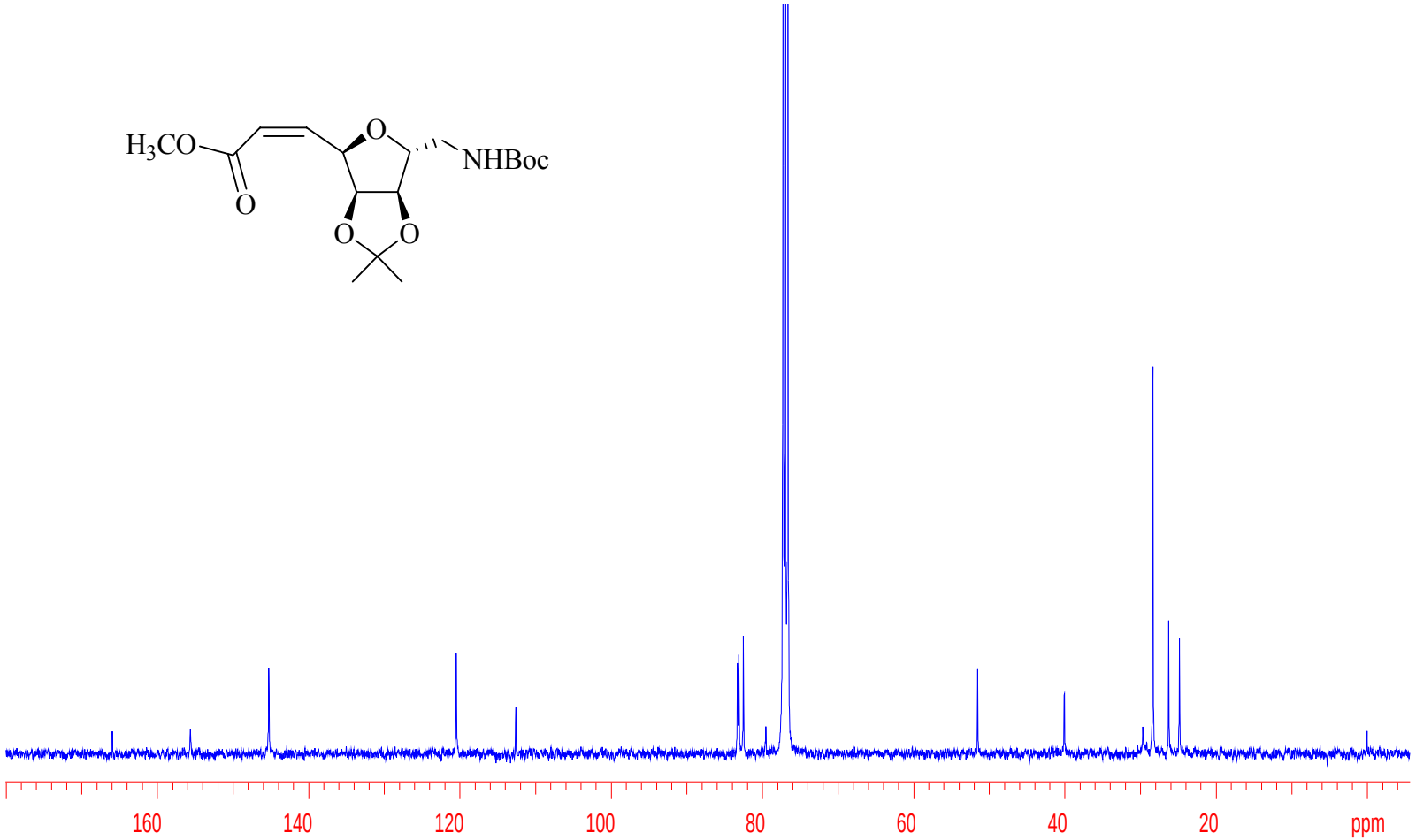
Supporting Fig 43: ^{1}H NMR Spectrum of 23 (*trans*) ($CDCl_3$, 303 K, 500 MHz)



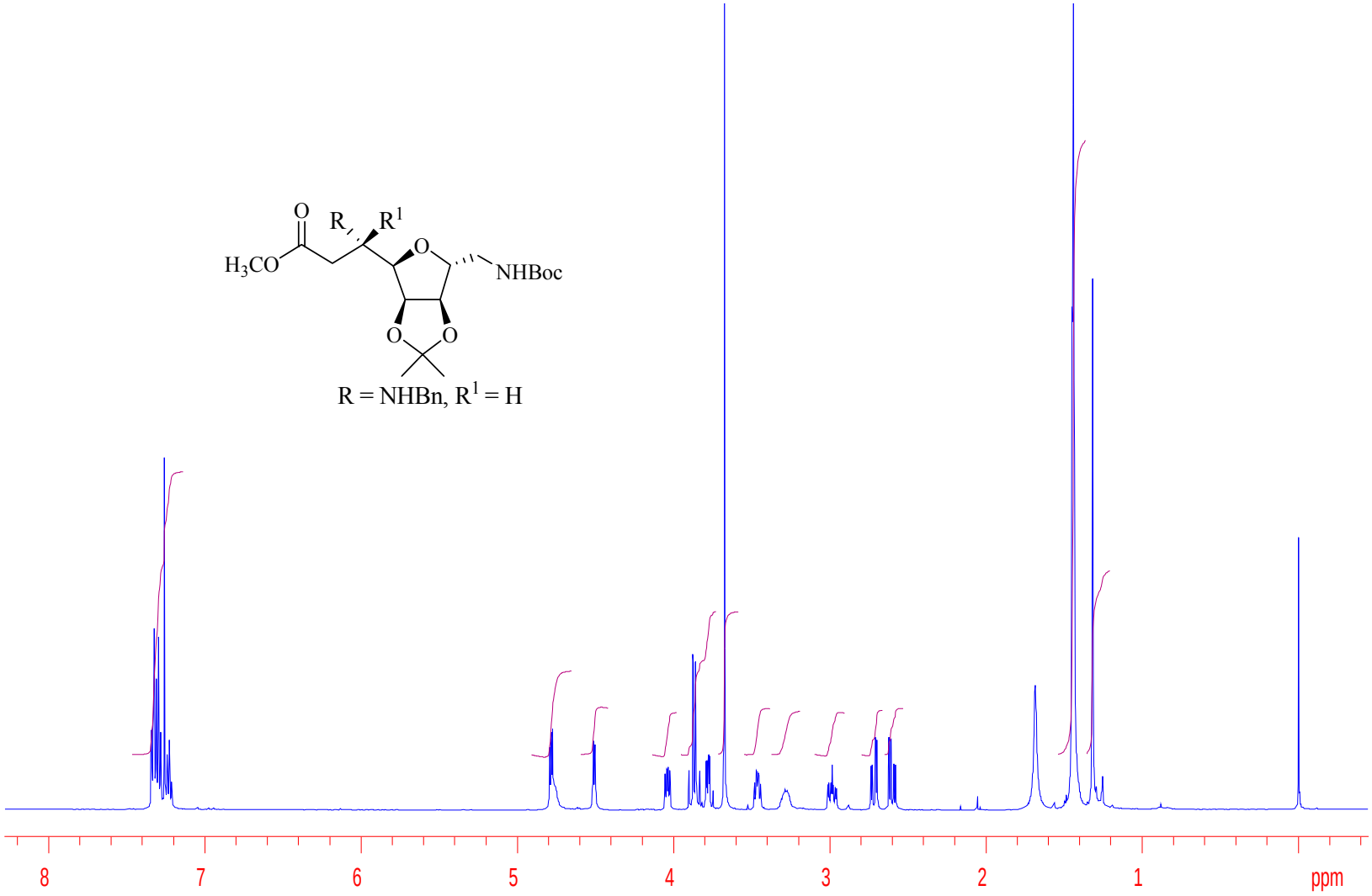
Supporting Fig 44: ^{13}C NMR Spectrum of 23 (*trans*) ($CDCl_3$, 303 K, 100 MHz)



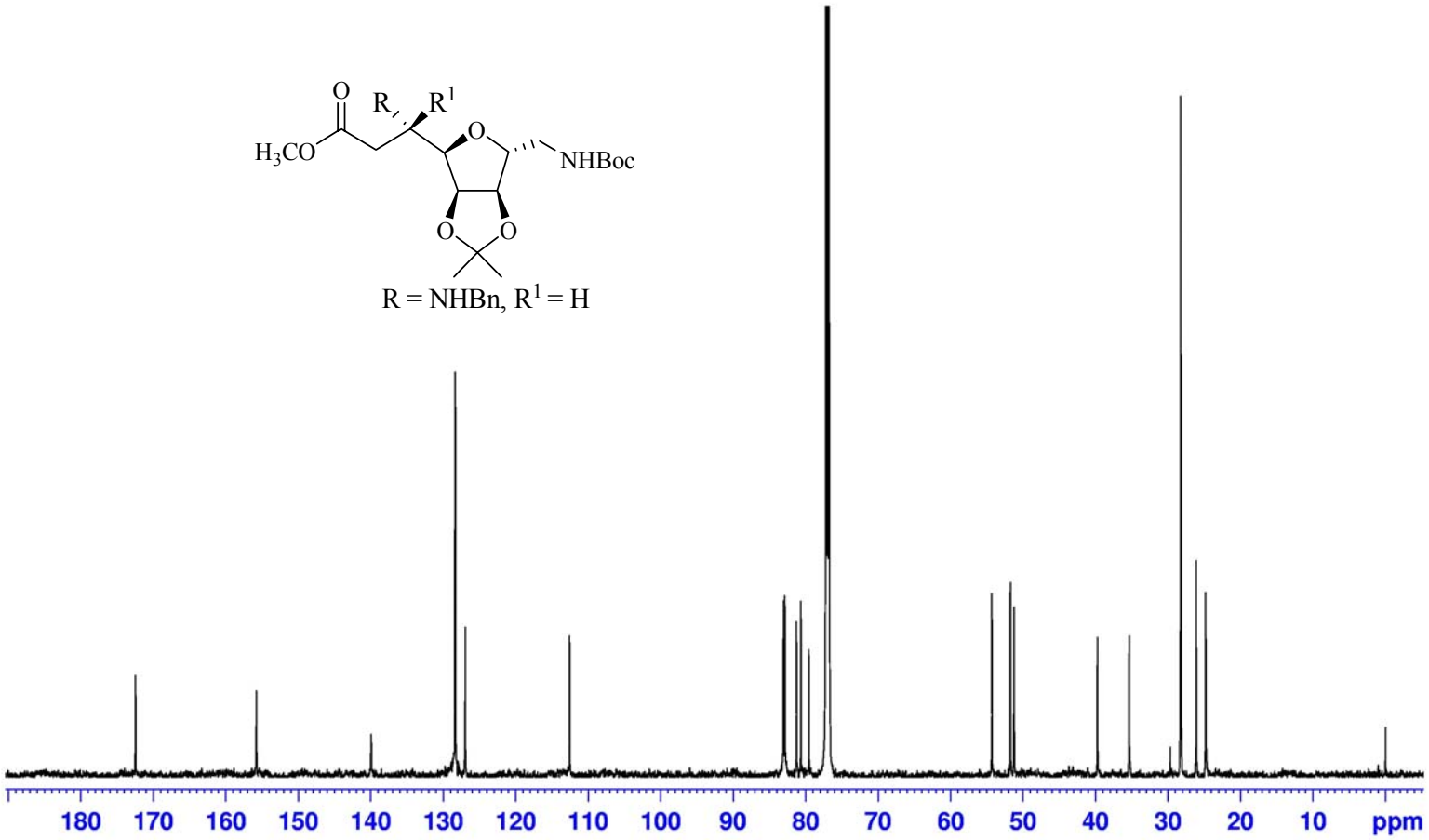
Supporting Fig 45: ^{1}H NMR Spectrum of 23 (*cis*) ($CDCl_3$, 303 K, 500 MHz)



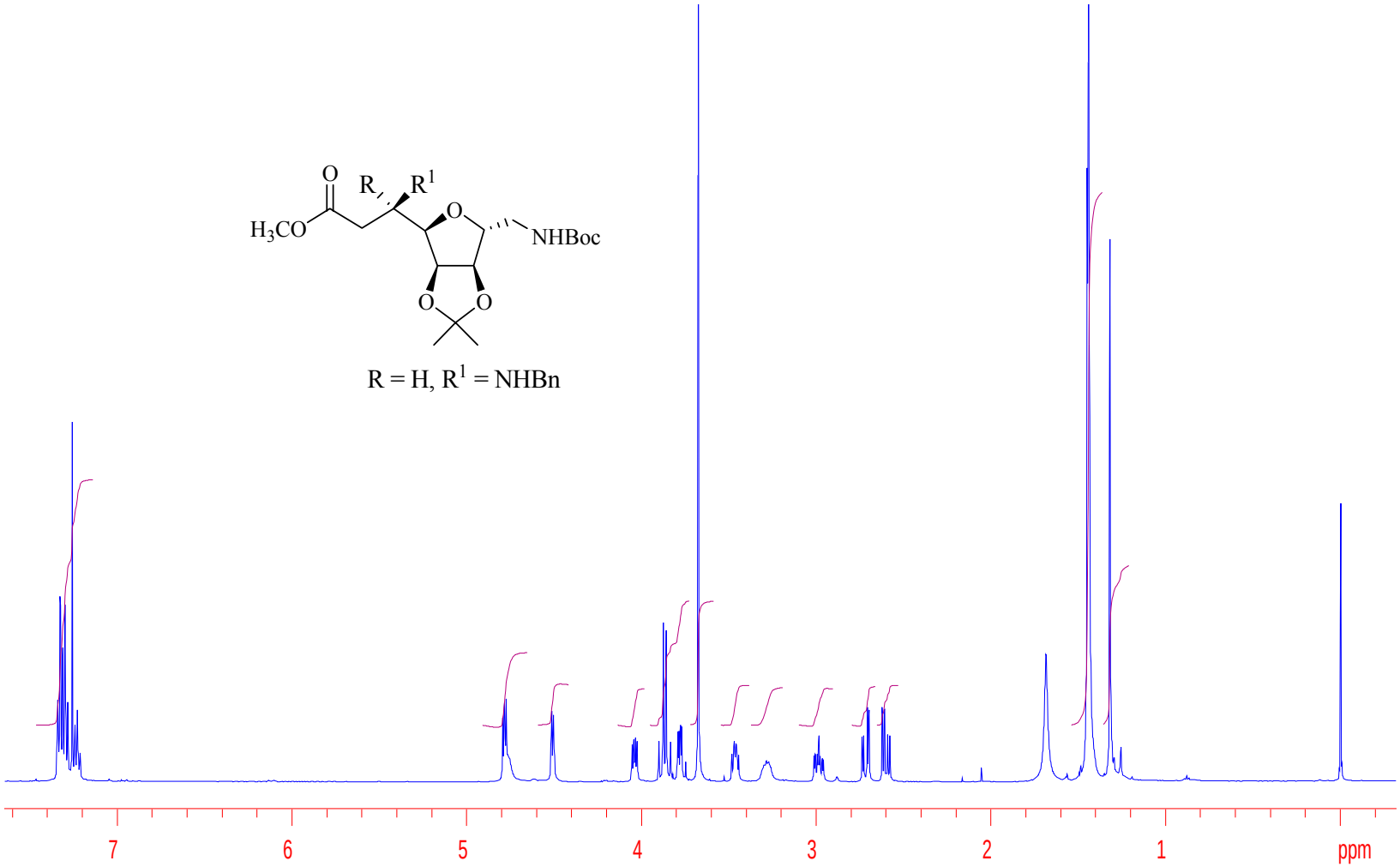
Supporting Fig 46: ^{13}C NMR Spectrum of 23 (*cis*) ($CDCl_3$, 303 K, 100 MHz)



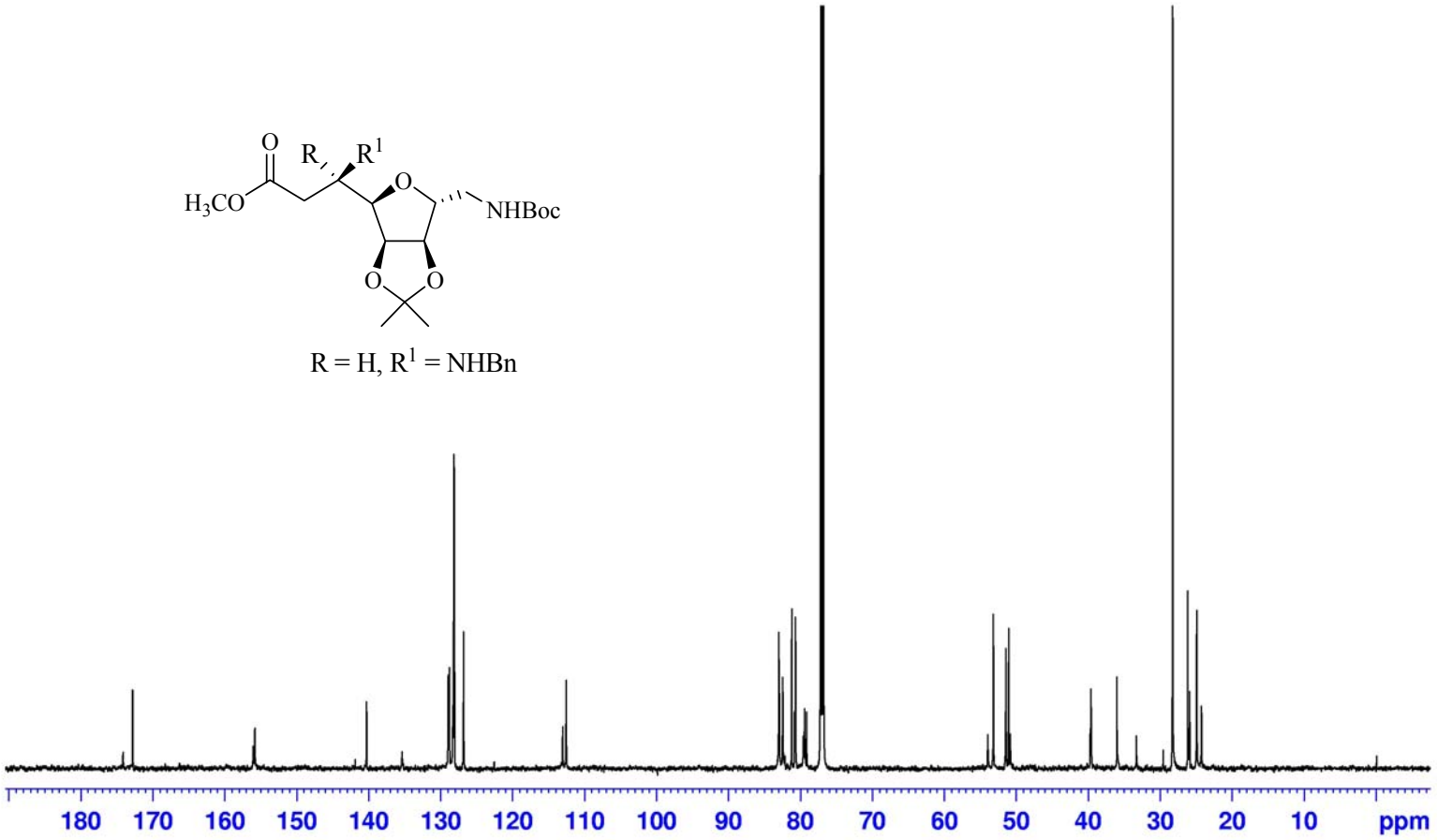
Supporting Fig 47: ^{1}H NMR Spectrum of 24 ($CDCl_3$, 303 K, 500 MHz)



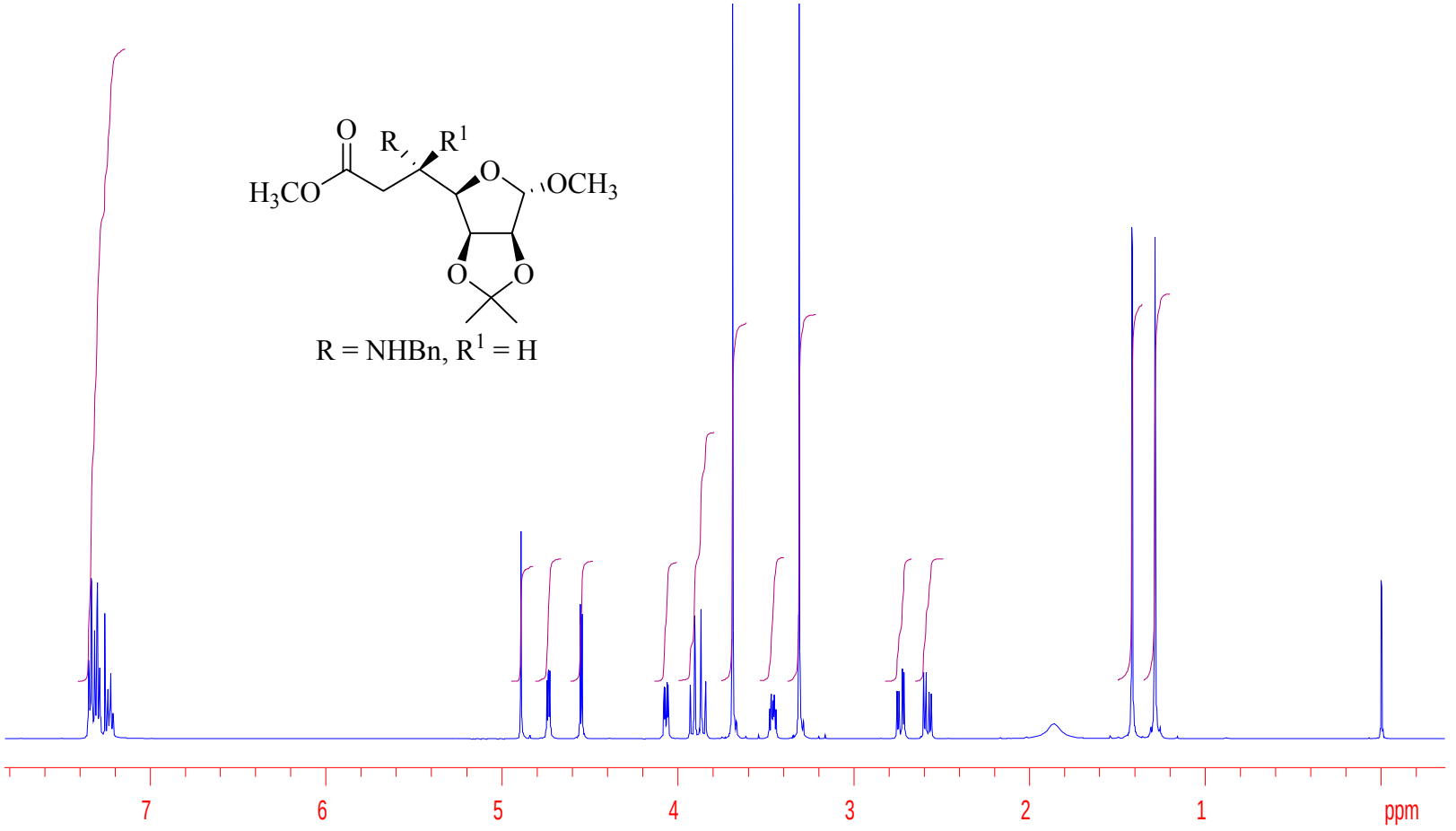
Supporting Fig 48: ^{13}C Spectrum of 24 ($CDCl_3$, 303 K, 150 MHz)



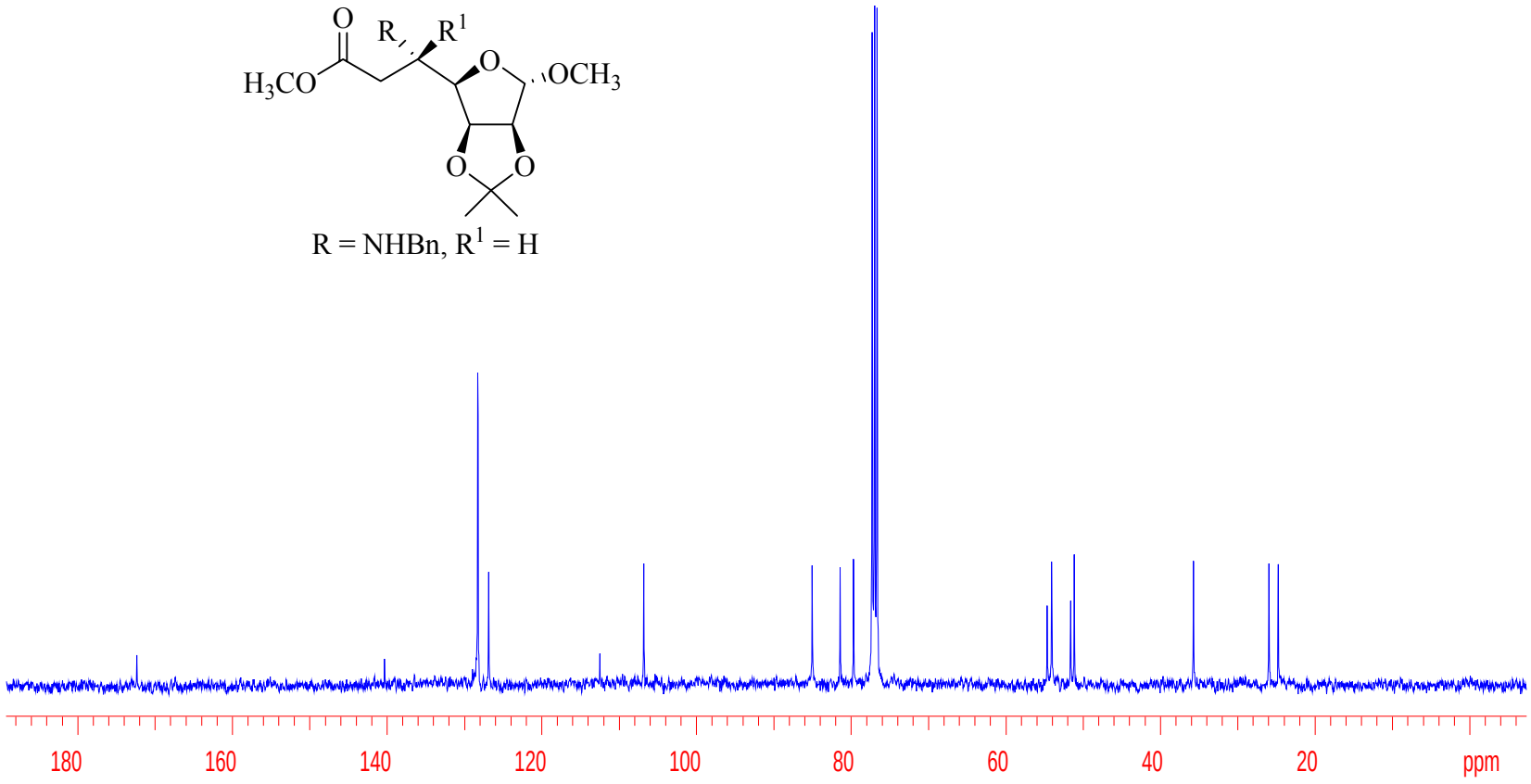
Supporting Fig 49: ^{1}H NMR Spectrum of 25 ($CDCl_3$, 303 K, 500 MHz)



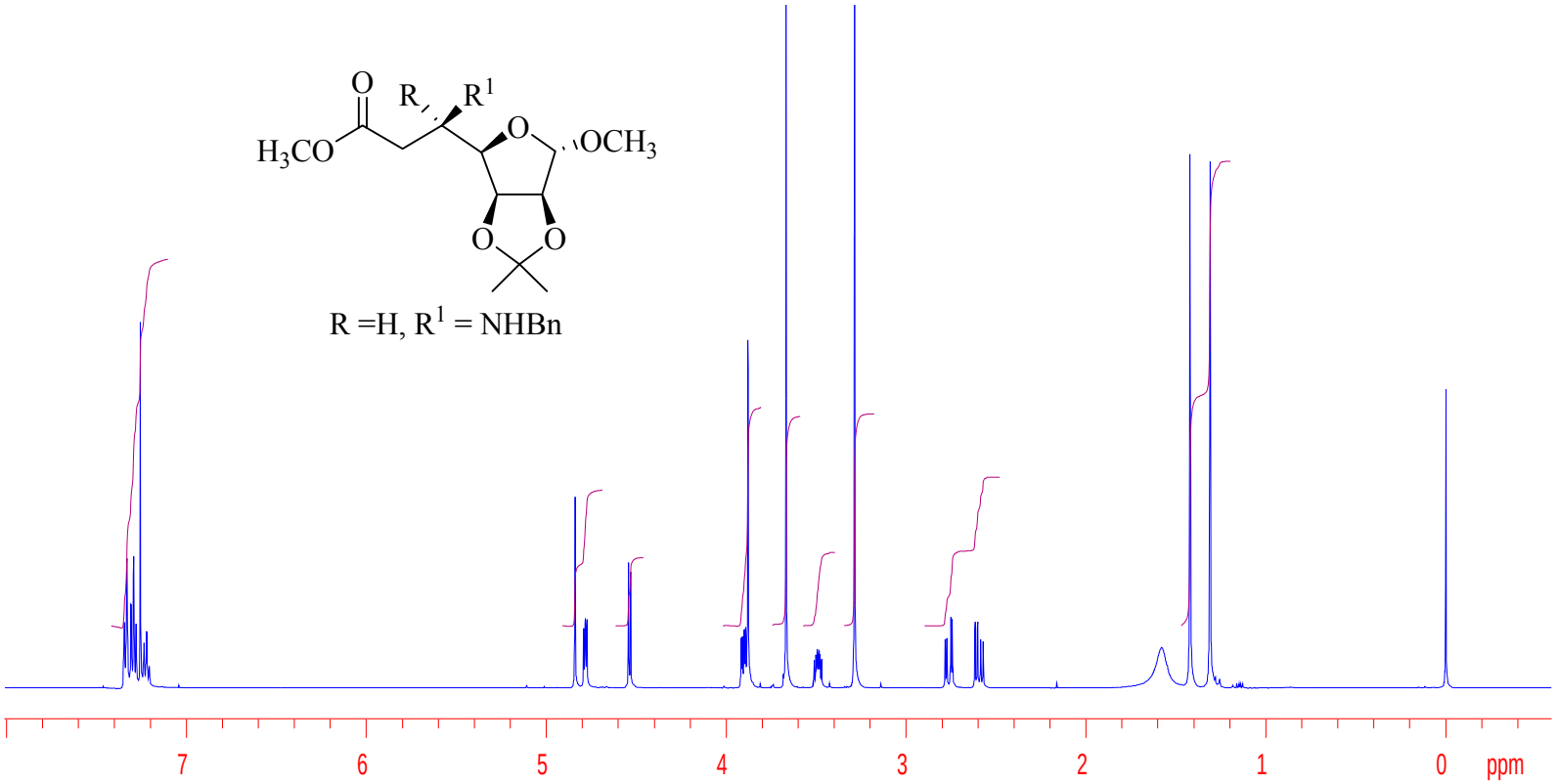
Supporting Fig 50: ^{13}C Spectrum of 25 ($CDCl_3$, 303 K, 150 MHz)



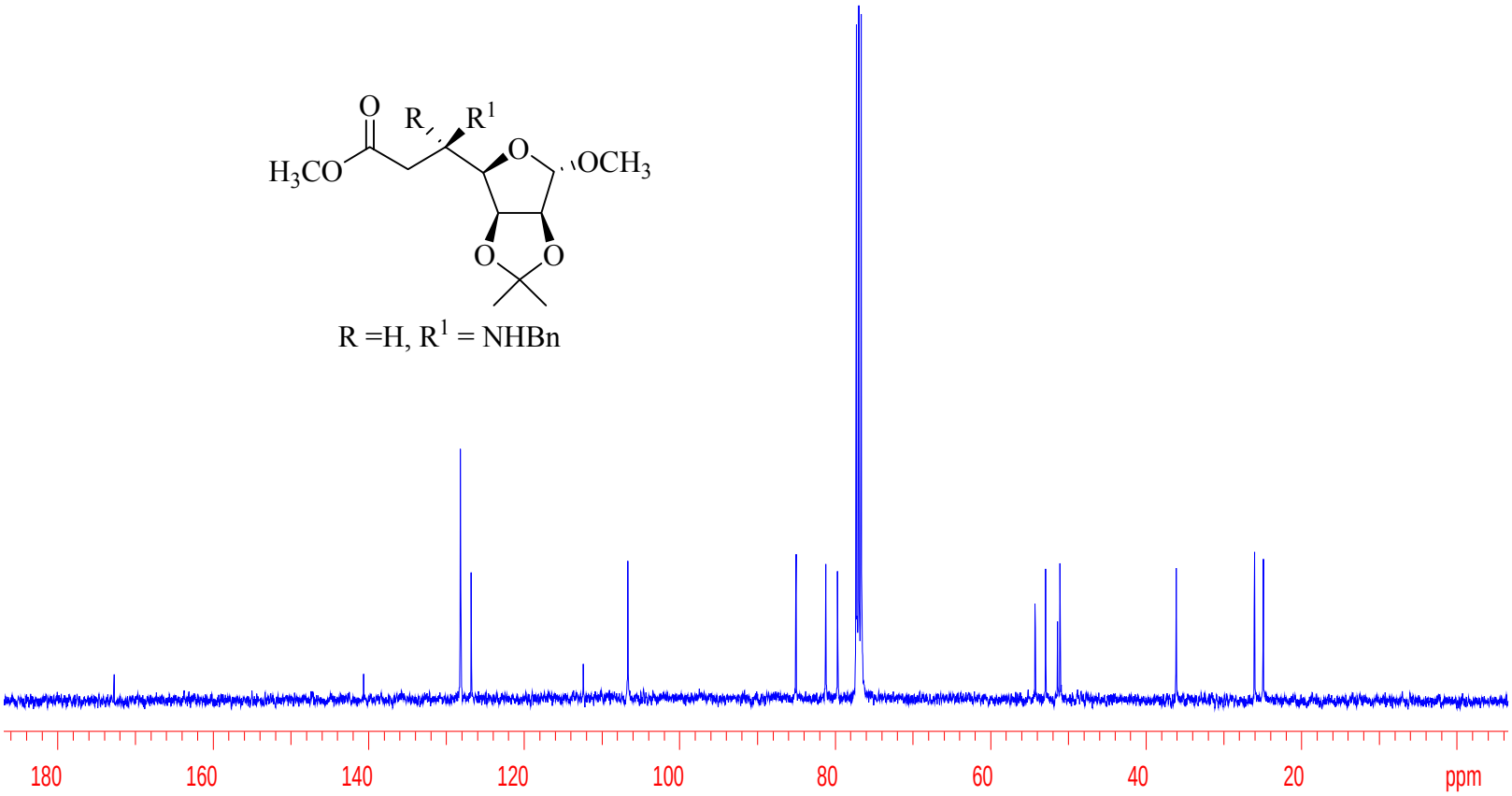
Supporting Fig 51: ^{1}H NMR Spectrum of 31 ($CDCl_3$, 303 K, 500 MHz)



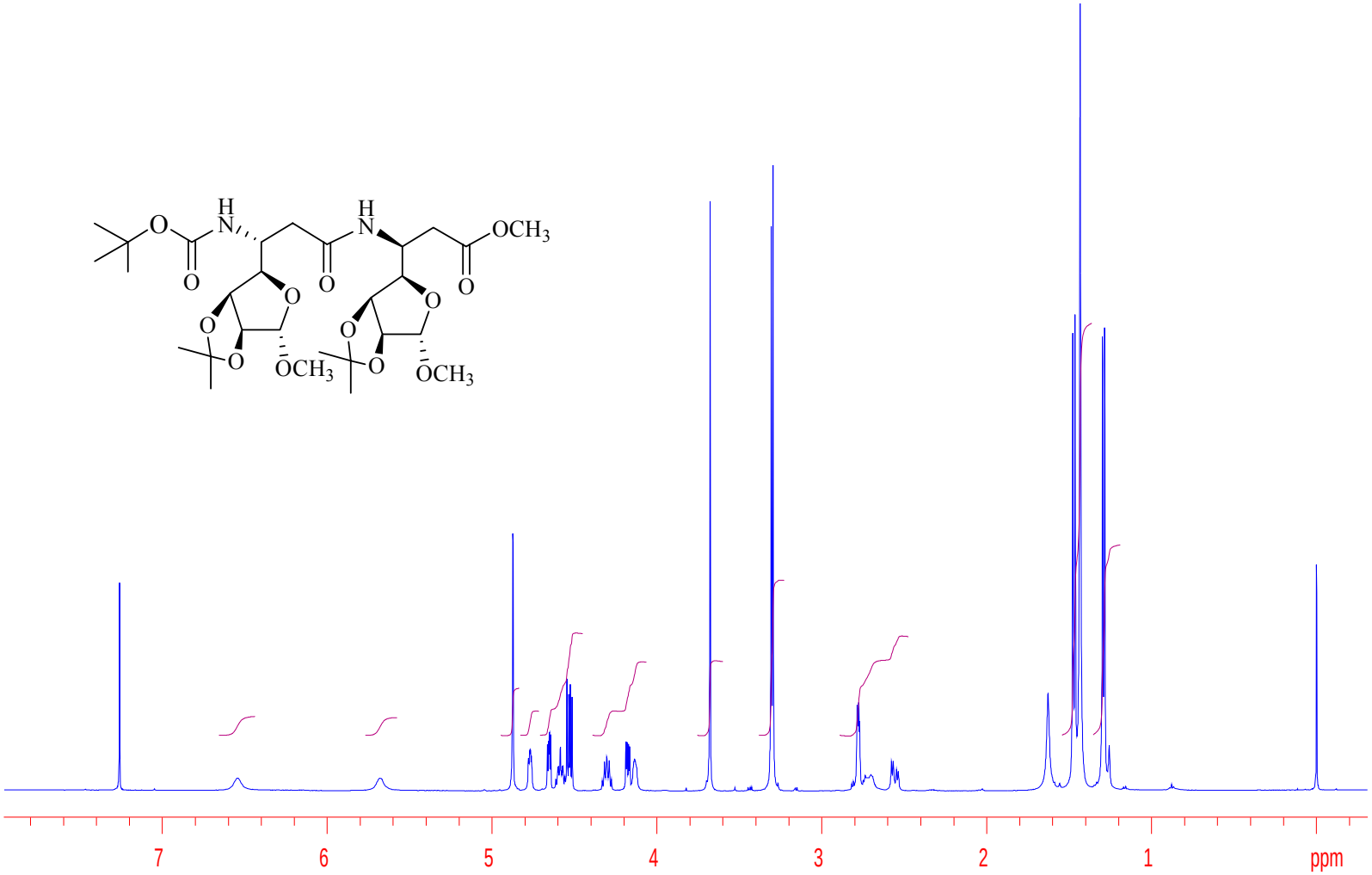
Supporting Fig 52: ^{13}C Spectrum of 31 ($CDCl_3$, 303 K, 100 MHz)



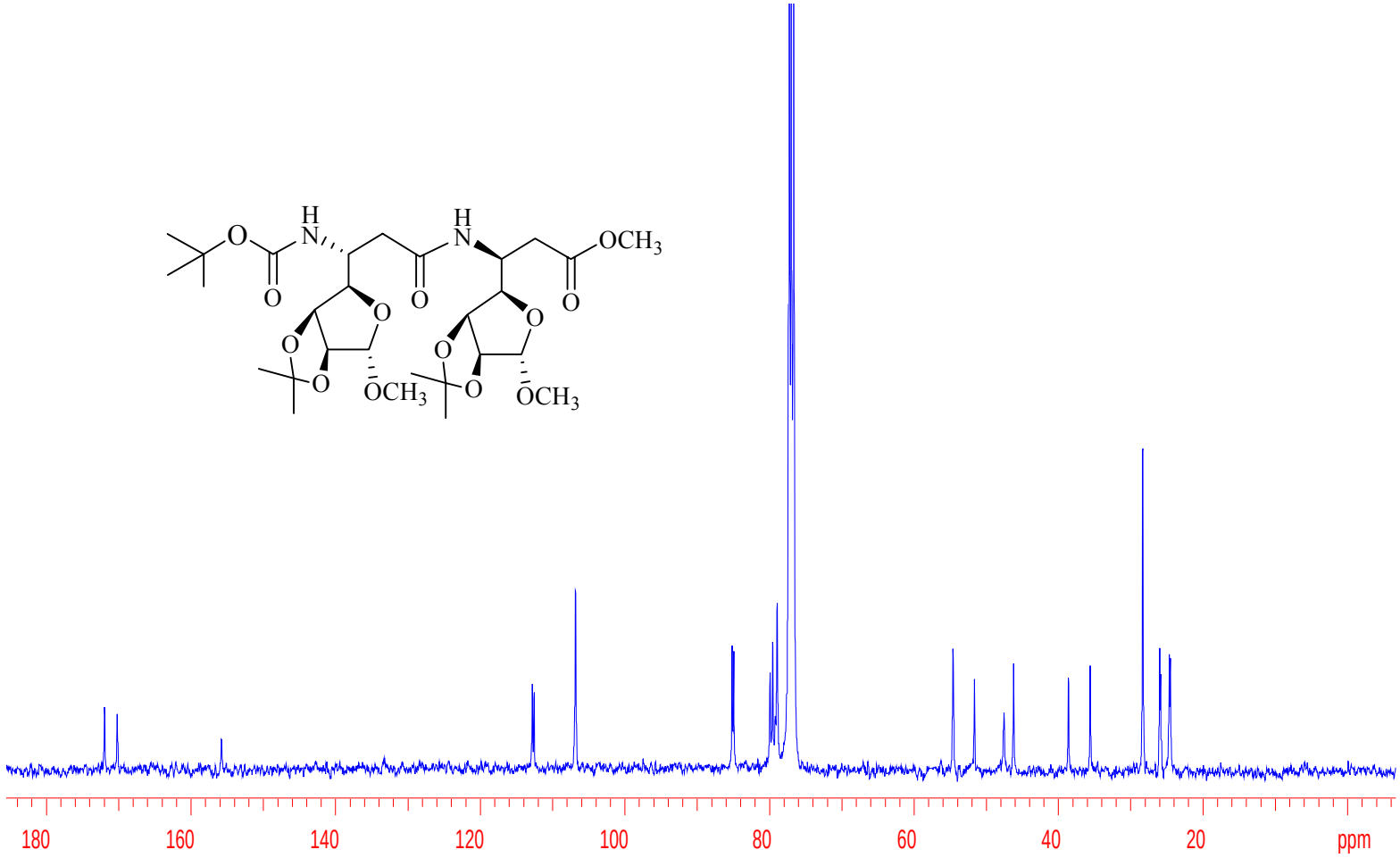
Supporting Fig 53: ^{1}H NMR Spectrum of 32 ($CDCl_3$, 303 K, 500 MHz)



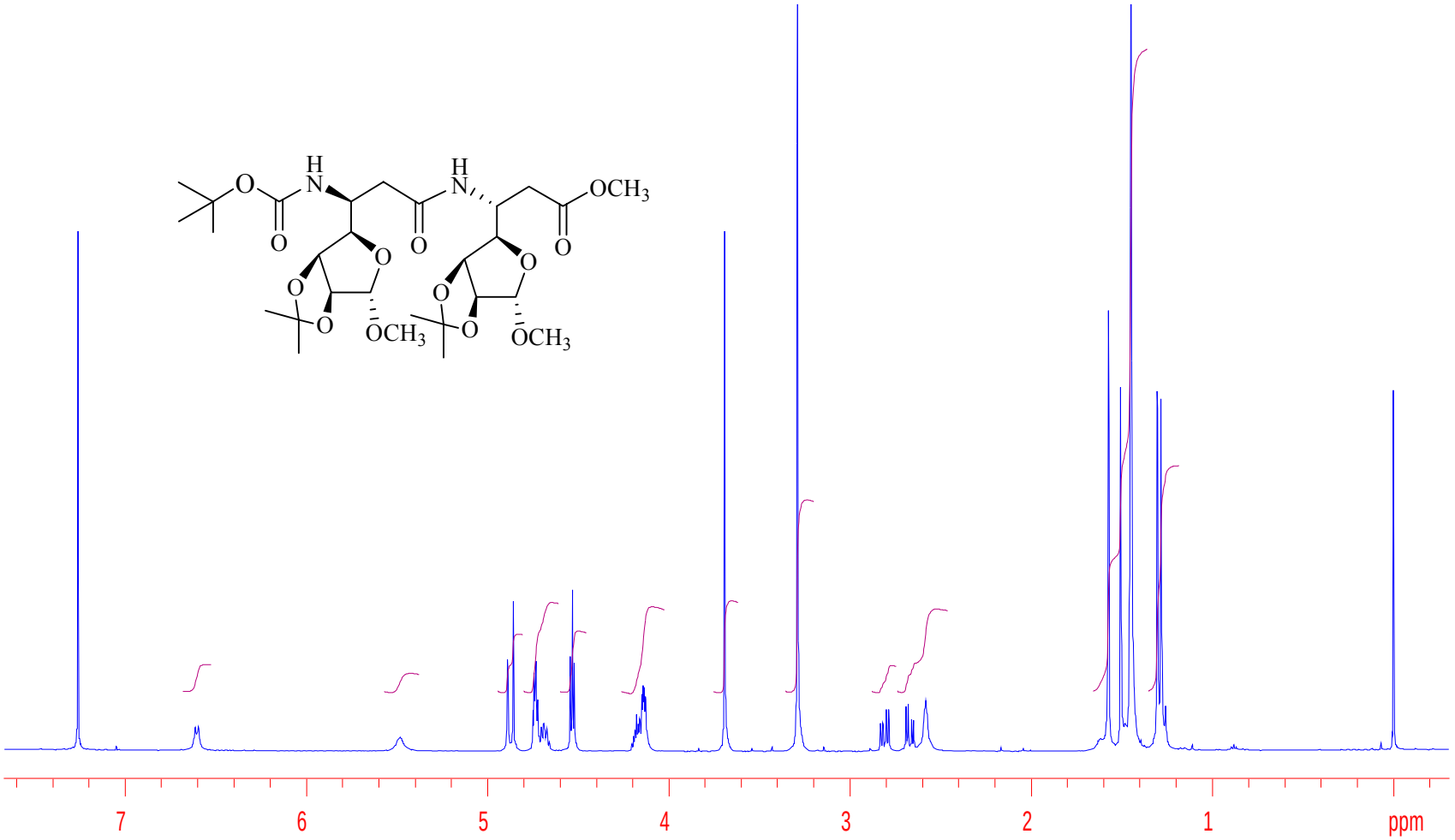
Supporting Fig 54: ^{13}C Spectrum of 32 ($CDCl_3$, 303 K, 100 MHz)



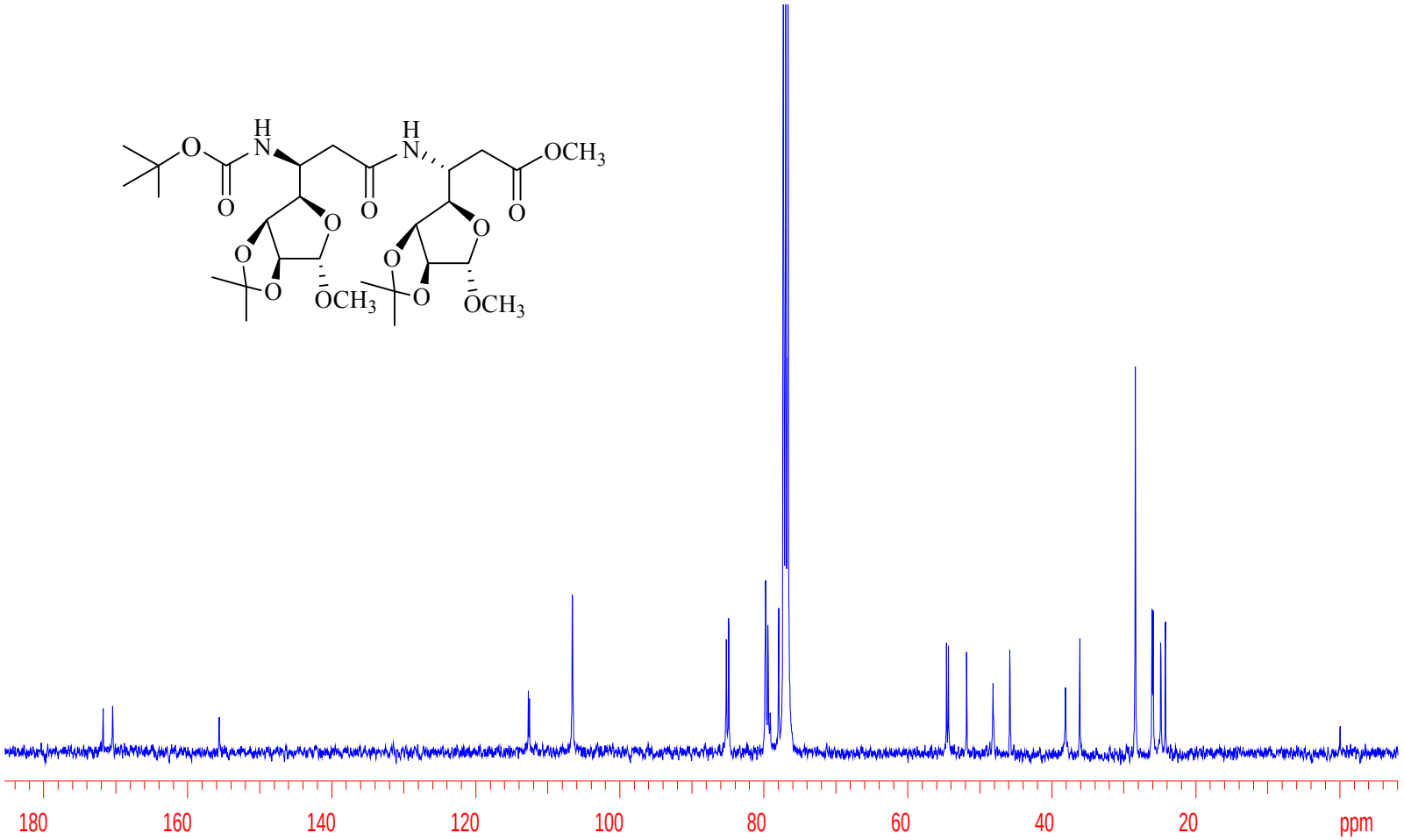
Supporting Fig 55: ^{1}H NMR Spectrum of 36 ($CDCl_3$, 303 K, 400 MHz)



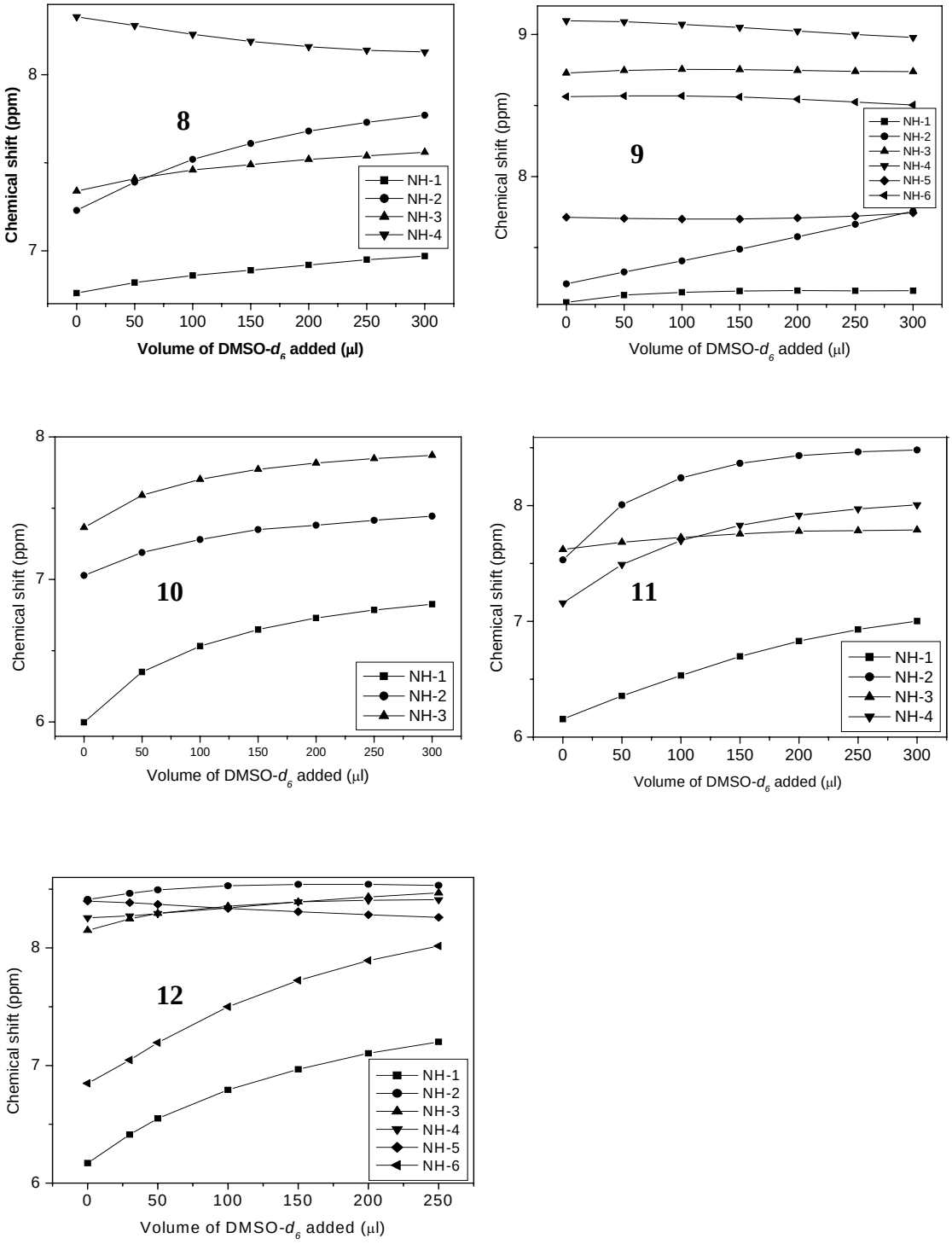
Supporting Fig 56: ^{13}C Spectrum of 36 ($CDCl_3$, 303 K, 100 MHz)



Supporting Fig 57: ^{1}H NMR Spectrum of 41 ($CDCl_3$, 303 K, 500 MHz)

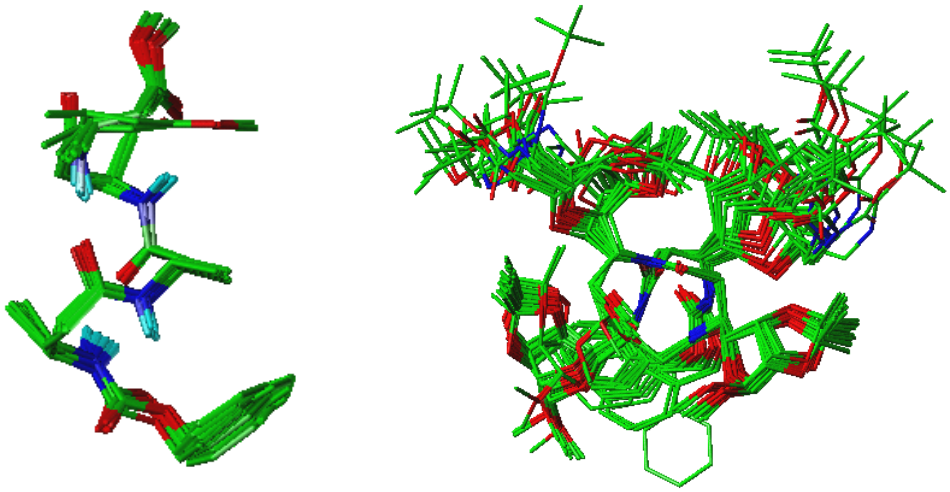


Supporting Fig 58: ^{13}C Spectrum of 41 ($CDCl_3$, 303 K, 100 MHz)



Supporting Fig 59: Solvent titration plots for 8-12

Supporting Fig 60: Superimposed 20 minimum energy structures for 8
(A) side view and (B) top view with sugars



(A) **(B)**

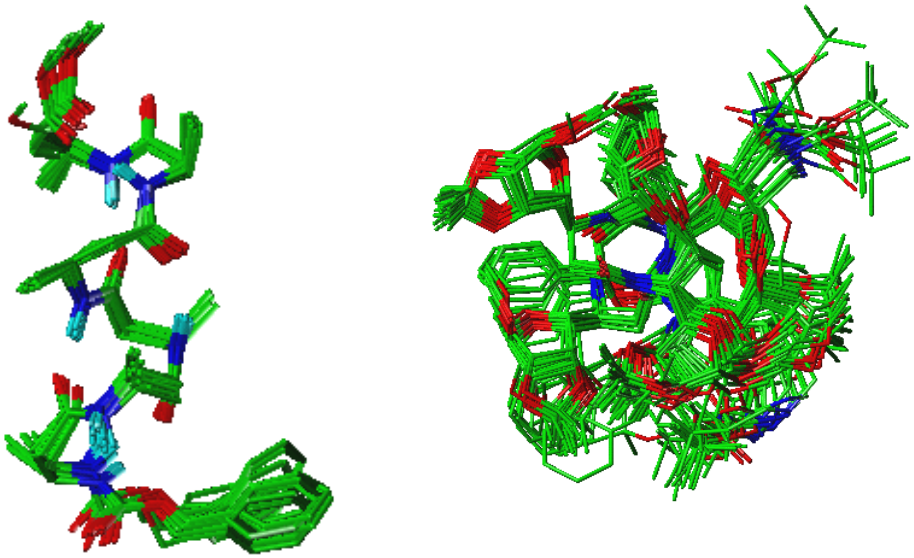
Supporting Table 1: Distance constraints used in MD calculations for 8, derived from ROESY experiment in $CDCl_3$ (500 MHz, 303K)

Residue	Atom	Residue	Atom	Lower bound	Upper bound
1	NH	1	C_4H	2.33	2.85
1	NH	1	$C_\alpha H$	2.06	2.52
1	NH	2	NH	2.80	3.43
1	$C_\alpha H$	1	C_4H	2.23	2.72
1	$C_\alpha H$	2	NH	2.00	2.45
2	NH	2	C_4H	2.51	3.07
2	NH	2	$C_\alpha H_{(Pro\text{-}R)}$	2.55	3.12

2	$C_\beta H$	3	NH	2.35	2.88
2	$C_\beta H$	4	NH	2.52	3.08
2	$C_\beta H$	4	$C_\alpha H_{(Pro\text{-}R)}$	2.13	2.65
2	$C_\alpha H_{(Pro\text{-}S)}$	2	C_4H	2.00	2.45
2	$C_\alpha H_{(Pro\text{-}S)}$	3	NH	2.25	2.75
3	NH	1(Boc)	NH	2.74	3.35
3	NH	3	C_4H	2.07	2.53
3	NH	3	$C_\alpha H_{(Pro\text{-}S)}$	2.52	3.08
3	NH	4	NH	3.20	3.91
3	$C_\alpha H_{(Pro\text{-}R)}$	3	C_4H	2.46	3.01
3	$C_\alpha H_{\mathbf{(Pro\text{-}R)}}$	4	NH	2.50	3.05
4	NH	4	C_4H	2.35	2.88
4	NH	4	$C_\alpha H_{(Pro\text{-}R)}$	2.49	3.04
4	$C_\alpha H_{(Pro\text{-}R)}$	4	C_4H	2.15	2.63

Supporting Fig 61: Superimposed 20 minimum energy structures for 9

(A) side view and (B) top view with sugars



(A) **(B)**

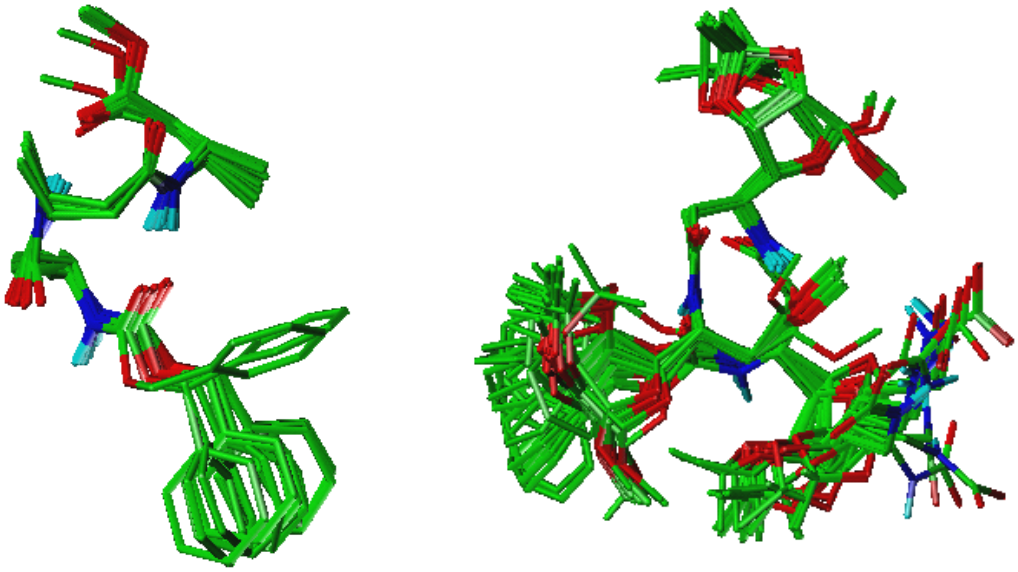
Supporting Table 2: Distance constraints used in MD calculations for 9, derived from ROESY experiment in $CDCl_3$ (500 MHz, 303K)

Residue	Atom	Residue	Atom	Lower bound	Upper bound
1	NH	1	C_4H	2.54	3.10
1	NH	1	$C_\alpha H$	3.51	4.29
1	$C_\alpha H$	1	C_4H	2.77	3.38
1	$C_\alpha H$	2	NH	2.33	2.85
1	C_4H	Boc-1	NH	2,82	3.44
2	NH	2	C_4H	2.88	3.52

2	NH	2	$C_{\alpha}H_{(Pro\text{-}R)}$	2.71	3.31
2	$C_{\beta}H$	3	NH	2.57	3.14
2	$C_{\beta}H$	4	NH	2.37	2.90
2	$C_{\beta}H$	4	$C_{\alpha}H_{(Pro\text{-}R)}$	2.19	2.68
2	$C_{\alpha}H_{(Pro\text{-}S)}$	2	C_4H	2.16	2.64
2	$C_{\alpha}H_{(Pro\text{-}S)}$	3	NH	2.49	3.04
3	NH	3	C_4H	2.37	2.90
3	NH	4	NH	3.47	4.24
3	$C_{\beta}H$	Boc-1	NH	2.59	3.16
3	$C_{\alpha}H_{(Pro\text{-}S)}$	3	C_4H	2.07	2.53
3	$C_{\alpha}H_{\mathbf{(Pro\text{-}S)}}$	4	NH	2.66	3.25
4	NH	4	C_4H	2.52	3.08
4	NH	4	$C_{\alpha}H_{(Pro\text{-}R)}$	3.77	4.61
4	$C_{\beta}H$	5	NH	2.65	3.24
4	$C_{\beta}H$	6	NH	2.62	3.20
4	$C_{\beta}H$	6	$C_{\alpha}H_{(Pro\text{-}R)}$	2.25	2.75
4	$C_{\alpha}H_{(Pro\text{-}S)}$	4	C_4H	2.26	2.77
4	$C_{\alpha}H_{(Pro\text{-}S)}$	5	NH	2.26	2.77
5	NH	5	C_4H	2.23	2.73
5	NH	5	$C_{\alpha}H_{(Pro\text{-}S)}$	3.48	4.25
5	NH	6	NH	2.95	3.61

5	$C_\alpha H_{(\textbf{\textit{Pro-S}})}$	5	C_4H	2.58	3.15
5	$C_\alpha H_{(\textbf{\textit{Pro-S}})}$	6	NH	2.51	3.07
5	$C_\alpha H_{(\textbf{\textit{Pro-R}})}$	5	C_4H	2.92	3.57
6	NH	6	C_4H	2.51	3.07
6	NH	6	$C_\alpha H_{(\textit{Pro-R})}$	3.14	3.88
6	$C_\alpha H_{(\textit{Pro-R})}$	6	C_4H	2.29	2.80

Supporting Fig 62: Superimposed 20 minimum energy structures for 10 (A) side view and (B) top view with sugars



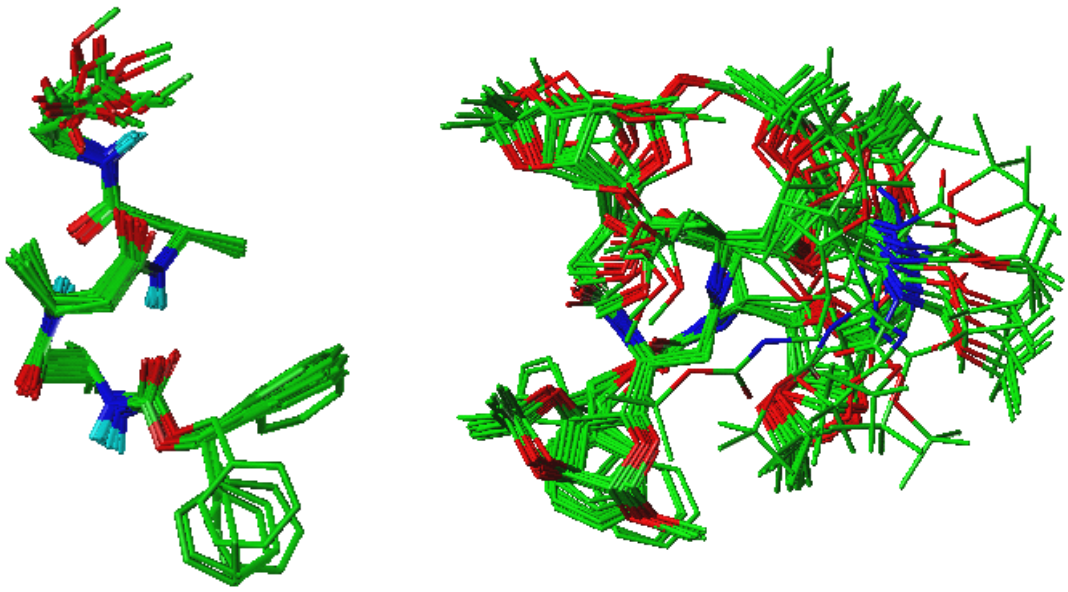
(A) **(B)**

Supporting Table 3: Distance constraints used in MD calculations for 10, derived from ROESY experiment in $CDCl_3$ (500 MHz, 288K)

Residue	Atom	Residue	Atom	Lower bound	Upper bound
1	NH	1	C_4H	2.42	2.96
1	NH	1	$C_\alpha H_{(Pro\text{-}R)}$	2.80	3.43
1	NH	Boc	NH	2.98	3.64
1	$C_\beta H$	2	NH	2.35	2.88
1	$C_\beta H$	3	NH	2.65	3.24
1	$C_\beta H$	3	$C_\alpha H_{(Pro\text{-}R)}$	2.11	2.58
1	$C_\alpha H_{\mathbf{(Pro\text{-}S)}}$	1	C_4H	2.26	2.76
1	$C_\alpha H_{(Pro\text{-}S)}$	2	NH	2.53	3.09
1	$C_\alpha H_{\mathbf{(Pro\text{-}R)}}$	1	C_4H	2.23	2.72
1	C_4H	Boc	NH	2.70	3.30
2	NH	2	C_4H	2.22	2.71
2	NH	3	NH	2.70	3.30
2	$C_\alpha H_{(Pro\text{-}S)}$	2	C_4H	2.78	3.40
2	$C_\alpha H_{(Pro\text{-}S)}$	3	NH	2.49	3.04
2	$C_\alpha H_{(Pro\text{-}R)}$	2	C_4H	2.60	3.18
2	$C_\alpha H_{(Pro\text{-}R)}$	3	NH	2.80	3.43
3	NH	3	C_4H	2.40	2.93
3	NH	3	$C_\alpha H_{(Pro\text{-}R)}$	2.99	3.66

3	$C_{\alpha}H_{(Pro\text{-}S)}$	3	C_4H	2.44	2.98
3	$C_{\alpha}H_{(Pro\text{-}R)}$	3	C_4H	2.30	2.81

Supporting Fig 63: Superimposed 20 minimum energy structures for 11
(A) side view and (B) top view with sugars



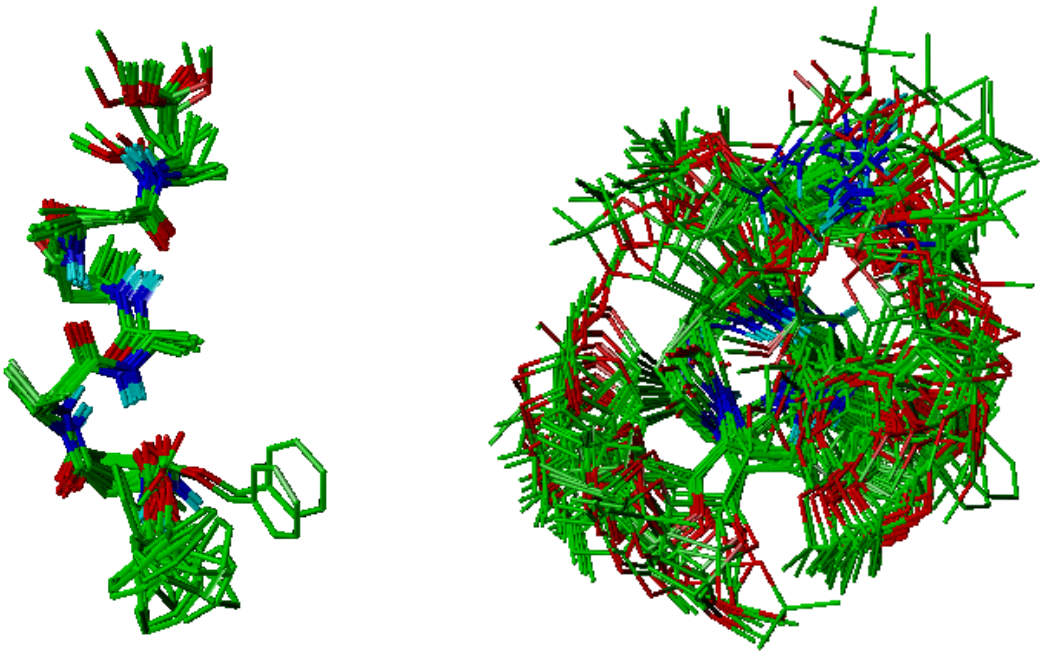
(A) **(B)**

Supporting Table 4: Distance constraints used in MD calculations for 11, derived from ROESY experiment in $CDCl_3$ (500 MHz, 288K)

Residue	Atom	Residue	Atom	Lower bound	Upper bound
1	NH	1	C_4H	2.38	2.91
1	NH	1	$C_\alpha H_{(Pro\text{-}R)}$	2.72	3.33
1	$C_\beta H$	2	NH	2.53	3.09
1	$C_\beta H$	3	NH	2.56	3.13
1	$C_\beta H$	3	$C_\alpha H_{(Pro\text{-}R)}$	2.20	2.69
1	$C_\alpha H_{(Pro\text{-}S)}$	1	C_4H	2.09	2.56
1	$C_\alpha H_{(Pro\text{-}S)}$	2	NH	2.70	3.30
2	NH	2	C_4H	2.41	2.94
2	NH	2	$C_\alpha H_{(Pro\text{-}R)}$	3.16	3.86
2	$C_\alpha H_{(Pro\text{-}R)}$	2	C_4H	2.43	2.97
3	NH	3	C_4H	2.37	2.90
3	NH	3	$C_\alpha H_{(Pro\text{-}R)}$	2.35	2.88
3	$C_\beta H$	4	NH	2.21	2.70
3	$C_\alpha H_{(Pro\text{-}S)}$	4	NH	2.44	2.98
3	$C_\alpha H_{(Pro\text{-}R)}$	3	C_4H	2.31	2.82
4	NH	4	C_4H	2.15	2.63
4	NH	4	$C_\alpha H_{(Pro\text{-}S)}$	2.44	2.98

4	$C_\alpha H_{(Pro\text{-}R)}$	4	C_4H	2.10	2.57

Supporting Fig 64: Superimposed 20 minimum energy structures for 12
(A) side view and (B) top view with sugars



(A) **(B)**

Supporting Table 5: Distance constraints used in MD calculations for 12, derived from ROESY experiment in $CDCl_3$ (500 MHz, 303K)

Residue	Atom	Residue	Atom	Lower bound	Upper bound
1	NH	1	C_4H	2.27	2.77
1	NH	1	$C_\alpha H_{(Pro\text{-}R)}$	2.56	3.13

1	$C_{\beta}H$	2	NH	2.60	3.20
1	$C_{\beta}H$	3	NH	2.35	2.89
1	$C_{\beta}H$	3	$C_{\alpha}H_{(Pro\text{-}R)}$	2.20	2.69
1	$C_{\alpha}H_{(Pro\text{-}S)}$	1	C_4H	2.32	2.84
1	$C_{\alpha}H_{(Pro\text{-}S)}$	2	NH	2.43	2.97
1	C_4H	Boc-1	NH	2.82	3.44
2	NH	2	C_4H	2.86	3.50
2	NH	2	$C_{\alpha}H_{(Pro\text{-}S)}$	2.71	3.31
2	$C_{\alpha}H_{(Pro\text{-}R)}$	3	NH	2.63	3.22
3	NH	3	C_4H	2.20	2.69
3	NH	3	$C_{\alpha}H_{(Pro\text{-}R)}$	2.63	3.22
3	$C_{\beta}H$	4	NH	2.70	3.30
3	$C_{\beta}H$	5	NH	2.40	2.98
3	$C_{\beta}H$	5	$C_{\alpha}H_{(Pro\text{-}R)}$	2.10	2.56
3	$C_{\alpha}H_{(Pro\text{-}R)}$	3	C_4H	1.99	2.43
3	$C_{\alpha}H_{(Pro\text{-}S)}$	3	C_4H	2.43	2.97
4	NH	4	C_4H	2.40	2.98
4	NH	4	$C_{\alpha}H_{(Pro\text{-}S)}$	2.99	3.66
4	$C_{\alpha}H_{(Pro\text{-}R)}$	4	C_4H	2.10	2.57
4	$C_{\alpha}H_{(Pro\text{-}R)}$	5	NH	2.43	2.97
5	NH	5	C_4H	2.43	2.97

5	NH	5	$C_{\alpha}H_{(Pro\text{-}R)}$	2.71	3.31
5	$C_{\beta}H$	6	NH	2.60	3.20
5	$C_{\alpha}H_{(Pro\text{-}R)}$	5	C_4H	2.24	2.74
5	$C_{\alpha}H_{(Pro\text{-}S)}$	6	NH	2.44	2.98
6	NH	6	C_4H	2.42	2.96
6	NH	6	$C_{\alpha}H_{(Pro\text{-}S)}$	2.56	3.13
6	$C_{\alpha}H_{(Pro\text{-}S)}$	6	C_4H	2.40	2.88