Electronic Supplementary Material (ESI) for ChemComm.

Supplementary Information

Chiral phosphoric acid-catalyzed desymmetrizative glycosylation of 2-deoxystreptamine and its application to aminoglycoside synthesis

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Table of contents

General Information

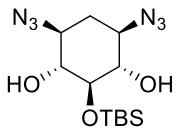
Methods and Reagents :

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. Toluene (PhMe), dichloromethane (DCM) and diethyl ether (Et_2O) were filtered through a column of activated alumina under nitrogen atmosphere (Innovative Technology PS-MD-5). All reactions were carried out under an atmosphere of nitrogen in flame- or oven-dried glassware with magnetic stirring. Reactions were cooled via external cooling baths: ice water (0 °C), Neslab Cryotrol CB-80 immersion cooler (0 to -60 °C) or Neslab Cryocool immersion cooler CC-100 II. Purification of the reactions mixtures was performed by flash chromatography using SiliCycleSiliaFlash P60 (230-400 mesh) silica gel.

Instrumentation :

All spectra were recorded on Varian vnmrs 700 (700 MHz), Varian vnmrs 500 (500 MHz), Varian MR400 (400 MHz), Varian Inova 500 (500 MHz) spectrometers and chemical shifts (δ) are reported in parts per million (ppm) and referenced to the ^1H signal of the internal tetramethylsilane according to IUPAC recommendations. Data are reported as (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sext = sextet, m = multiplet; coupling constant(s) in Hz; integration). High resolution mass spectra (HRMS) were recorded on MicromassAutoSpecUltima or VG (Micromass) 70-250-S Magnetic sector mass spectrometers in the University of Michigan mass spectrometry laboratory. Infrared (IR) spectra were recorded as thin films on NaCl plates on a Perkin Elmer Spectrum BX FT-IR spectrometer. Absorption peaks were reported in wavenumbers (cm^{-1}).

Preparation of 2-deoxystreptamine acceptor



1

(1R,2r,3S,4R,6S)-4,6-diazido-2-((tert-butyldimethylsilyl)oxy)-cyclohexane-1,3-diol (1). (1R,2R,3S,4R,6S)-4,6-diazidocyclohexane-1,2,3-triol [1] (770 mg, 3.60 mmol) was dissolved in 33 mL of dry THF under atmosphere of nitrogen, and cooled to 0 °C. To this solution 2,6-lutidine (1.51 mL, 13.1 mmol) and *tert*-butyldimehylsilyl trifluoromethanesulfonate (1.66 mL, 7.2 mmol) were added dropwise. The reaction mixture was warmed up to room temperature and quenched with methanol after 3 h. The resultant mixture was diluted with dichloromethane, washed with 1N HCl and NaHCO3(sat.) before being dried with magnesium sulfate and concentrated *in vacuo*. The residual oil was subjected to column chromatography (10 : 1 to 8 : 1 hexanes/ethyl acetate) resulting in white crystalline material **1** (964 mg, 81%). NMR spectra of **1** was in agreement with the NMR spectra of the same compound from the previous report.[2]

[1] Ding, Y.; Hofstadler, S. A.; Swayze, E. E.; Griffey, R. H. *Chemistry Letters*, **2003**, *32*, 908.

[2] Busscher, G. F.; Groothuys, S.; de Gelder, R.; Rutjes,F. P. J. T.; van Delft, F. L. *J. Org. Chem.* **2004**, *69*, 4477 (Please note that the values of reported in this reference ^{13}C NMR shifts are off by ~0.3-0.4 ppm, probably due to the different solvent reference value. In addition, the C5 peak at 77.3 ppm was not listed, probably, due to its overlap with the $CDCl_3$ peaks).

IR (thin film, cm^{-1}): 3489, 2926, 2170, 2103, 1472, 1357, 1249, 1137, 1071, 1029, 982, 874, 834, 778, 691. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.43 – 3.31 (5 H, m), 2.43 (2 OH, s), 2.22 – 2.16 (1 H, m), 1.44 – 1.32 (1 H, m), 0.92 (9 H, s), 0.16 (6 H, s). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 77.3, 76.7, 60.3, 32.1, 26.1, 18.4, -4.2.

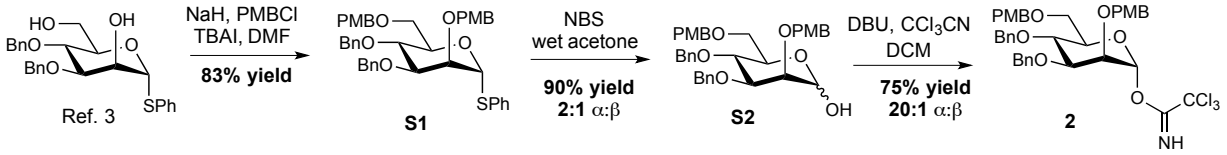
^{1}H NMR δ_H (400 MHz, C_6D_6) 2.97 (1 H, t, *J* 8.9), 2.75 (2 H, td, *J* 9.3, 3.4), 2.52 (2 H, ddd, *J* 12.4, 9.7, 4.5), 1.80 (2 H, d, *J* 3.3), 1.42 (1 H, dt, *J* 13.0, 4.6), 0.93 (9 H, s), 0.81 (1 H, q, *J* 12.6), 0.11 (6 H, s). **^{13}C NMR** δ_C (175 MHz, C_6D_6) 77.2, 76.8, 60.5, 31.8, 26.2, 18.5, -4.2.

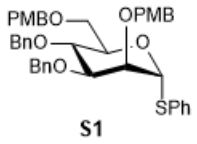
MP 110.6 °C (CAUTION).

Azide shock and heat stability of 1.

There are several tests available to evaluate the stability of organic azides. The impact sensitivity of energetic compounds is tested with the so-called fall hammer equipment. Samples are exposed to the impact of a falling weight from variable heights and measured sensitivity parameter is the height at which the samples explode or decompose. The drop test was performed on diazo-2-deoxystreptamine **1,** and it showed some mild shock sensitivity. Thus, 10 mg of **1** went off in 30 % of tests when 1 lbs weight was dropped from 145 cm height; however, it did not explode or decompose when the same weight was dropped from 125 cm height. While this test gave us only preliminary data, it became clear that diazo-2-deoxystreptamine **1** has to be treated with caution. Hence, this compound has always been stored in small, up to 200 mg, quantities. Diazo-2-deoxystreptamine **1** was not found to be heat sensitive based on the Differential Scanning Calorimetry (DSC) analysis, and its melting point is was determined to be 110.6 °C.

Preparation of mannose trichloroacetimidate donor



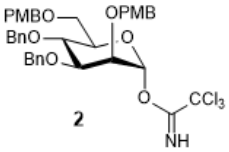


(2R,3R,4S,5S,6R)-3,4-bis(benzyloxy)-5-((4-methoxybenzyl)oxy)-2-(((4-methoxy benzyl)oxy)methyl)-6-(phenylthio)tetrahydro-2H-pyran (S1)

An oven dried and N_2 flushed 250 mL round bottom flask was charged with (2R,3S,4R,5R,6R)-4,5-bis(benzyloxy)-6-(hydroxymethyl)-2-(phenylthio)tetra-hydro-2H-pyran-3-ol[3] (1.74 g, 4.09 mmol) and anhydrous DMF (33 mL). This mixture was cooled to 0 °C and sodium hydride (60% w/w in mineral oil, 654 mg, 16.3 mmol) was added portionwise over 20 minute period. When the evolution of H_2 gas has stopped, *p*-methoxybenzyl chloride (PMBCl, 1.94 mL, 14.3 mmol) was added dropwise followed by tetra-n-butylammonium iodide (TBAI, 151 mg, 0.409 mmol). The reaction mixture was stirred at room temperature overnight, and then cooled to 0 °C and quenched by dropwise addition of methanol (3 mL) followed by addition of water (50 mL). Organic layer was extracted with diethyl ether, washed with water, and then dried with magnesium sulfate. The product was purified by column chromatography (5 : 1 to 3 : 1 hexanes/ethyl acetate) resulting in above compound (**S1**, 2.17 g, 83%) as colorless oil.

[3] Dudkin, V. Y.; Miller, J. S.; Dudkina, A. S.; Antczak, C.; Scheinberg, D. A.; Danishefsky, S. J. *JACS*, **2008**, *130*, 13598.

IR (thin film, cm^{-1}): 3061, 3001, 2930, 2865, 2059, 1884, 1756, 1612, 1585, 1248, 1097, 1034, 820, 698. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.46 – 7.41 (2 H, m), 7.34 (4 H, d, *J* = 4.3 Hz), 7.32 – 7.30 (1 H, m), 7.29 – 7.26 (5 H, m), 7.25 (5 H, dd, *J* = 6.7, 2.0 Hz), 7.18 (2 H, dd, *J* = 7.6, 1.8 Hz), 6.81 (4 H, dd, *J* = 8.4, 5.8 Hz), 5.58 (1 H, d, *J* = 1.7 Hz), 4.89 (1 H, d, *J* = 10.7 Hz), 4.67 (1 H, d, *J* = 12.0 Hz), 4.62 – 4.53 (4 H, m), 4.50 (1 H, d, *J* = 10.7 Hz), 4.41 (1 H, d, *J* = 11.6 Hz), 4.25 (1 H, ddd, *J* = 9.9, 5.0, 1.9 Hz), 4.04 (1 H, t, *J* = 9.5 Hz), 3.98 (1 H, dd, *J* = 3.2, 1.7 Hz), 3.85 – 3.80 (2 H, m), 3.79 (3 H, s), 3.77 (3 H, s), 3.70 (1 H, dd, *J* = 10.9, 1.9 Hz). **^{13}C NMR** (175 MHz, $CDCl_3$ δ_C (175 MHz, $CDCl_3$) 159.4, 159.2, 138.6, 138.4, 134.6, 131.7, 130.5, 130.0, 129.8, 129.6, 129.1, 128.5, 128.4, 128.1, 127.9, 127.8, 127.7, 127.5, 113.9, 113.8, 85.8, 80.2, 75.7, 75.3, 75.1, 73.0, 72.8, 72.1, 71.6, 68.8, 55.4, 55.4. **HRMS (ESI+)** (*m/z*): $[M+NH_4]^+$ calcd for $C_{42}H_{48}O_5NO_7S$ 710.3146, found 710.3122



(2R,3S,4S,5R,6R)-4,5-bis(benzyloxy)-3-((4-methoxybenzyl)oxy)-6-(((4methoxy benzyl)oxy)methyl) tetrahydro-2H-pyran-2-yl 2,2,2-trichloroacetimidate (2).

A 250 mL round bottom flask was charged with **S1** (2.17g, 3.119 mmol) and dissolved in a 9 : 1 mixture of acetone (18 mL) and water (2 mL). The reaction mixture was cooled down to 0 °C and N-bromosuccinimide (1.16 g, 6.55 mmol) was added. The completion of reaction was monitored by TLC and the mixture was quenched with solid $NaHCO_3$ upon reaction completion. Acetone was removed *in vacuo* and organics were extracted with ethyl acetate. The combined organic layer was washed with saturated sodium bicarbonate and brine, dried with magnesium sulfate, and concentrated *in vacuo*. The crude product **S2** was purified by flash column chromatography (3 : 1 to 1 : 1 hexanes/ ethyl acetate) resulting in 1.69 g (90 %) of colorless oil (α/β = 2 : 1).

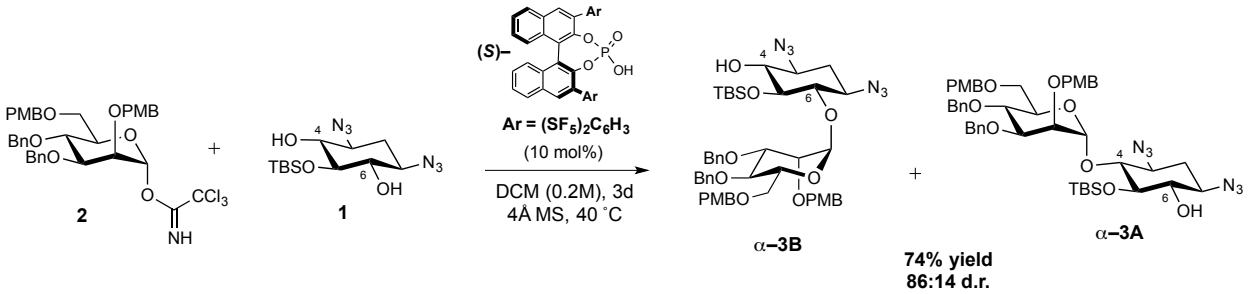
An oven dried and nitrogen flushed 250 mL round bottom flask was charged with the mannose derivative **S2** (1.69 g, 2.81 mmol) from the previous step and dry DCM (20 mL). The reaction mixture was cooled down to 0 °C and trichloroacetonitrile (0.847 mL, 8.40 mmol) was added, followed by 1,8-diaza bicyclo(5,4,0)undec-7ene (0.21 mL, 1.40 mmol). The resulting reaction mixture was warmed up to room temperature and stirred for 6 h. The crude product was purified by column chromatography (5 : 1 to 3 : 1 hexanes/ethyl acetate) resulting in pure product **2** as a pale-yellow oil (1.57 g, 75%, α/β = 20 : 1).

IR (thin film, cm^{-1}): 3473, 2928, 1723, 1612, 1514, 1454, 1363, 1249, 1108, 1035, 836, 698. **^{1}H NMR** δ_H (700 MHz, C_6D_6, α only) δ 8.47 (1 H, s), 7.30 (4 H, t, *J* = 7.8 Hz), 7.26 (2 H, d, *J* = 7.6 Hz), 7.22 (2 H, d, *J* = 8.4 Hz), 7.14 (3 H, dt, *J* = 7.5, 3.6 Hz), 7.10 – 7.04 (2 H, m), 6.77 – 6.72 (5 H, m), 5.00 (1 H, d, *J* = 11.0 Hz), 4.65 (1 H, d, *J* = 11.0 Hz), 4.61 – 4.49 (7 H, m), 4.39 (1 H, d, *J* = 11.5 Hz), 4.28 – 4.25 (1 H, m), 4.16 (1 H, dd, *J* = 9.6, 3.1 Hz), 4.03 (1 H, t, *J* = 2.6 Hz), 3.89 (1 H, dd, *J*= 11.3, 4.1 Hz), 3.73 (1 H, dd, *J* = 11.3, 1.7 Hz), 3.30 (3 H, s), 3.29 (3 H, s). **^{13}C NMR** δ_C (175 MHz, C_6D_6, α only) 160.7, 159.9, 159.7, 139.4, 139.0, 131.2, 130.7, 129.9, 129.7, 128.7, 128.6, 128.5, 128.3, 128.3, 127.8, 127.6, 114.1, 114.1, 97.0, 91.7 (CCl_3), 79.8, 76.1, 75.5, 74.9 (CH_2), 74.0, 73.4, 73.4 (CH_2), 72.8 (CH_2), 72.3 (CH_2), 68.9 (CH_2), 54.8, 54.8. **HRMS (ESI+) (*m/z*):** $[M+NH_4]^+$ calcd for $C_{38}H_{44}Cl_3N_2O_8$ 761.2158, found 761.2152.

Chiral Phosphoric Acid-Catalyzed Glycosylation Studies

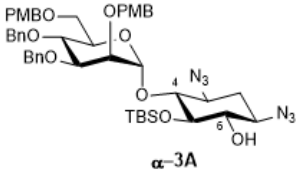
General Protocol for the Catalyst Screening Studies in Table 1:

A flame-dried 4 mL vial was charged with mannose trichloroacetimidate **2** (0.024 mmol), 2-deoxystreptamine **1** (0.012 mmol), 4 Å MS (~20 mg), and CPA catalyst (0.0024 mmol). The resulting mixture was refluxed in dry dichloromethane (0.1 mL) for 3 days, then quenched with triethylamine and analyzed by crude ^{1}H NMR.



(1R,2S,3S,4R,6S)-4,6-diazido-3-(((2S,3S,4S,5R,6R)-4,5-bis(benzyloxy)-3-((4-methoxybenzyl)oxy)-6-(((4-methoxybenzyl)oxy)methyl)tetrahydro-2H-pyran-2-yl)oxy)-2-((tert-butyldimethylsilyl)oxy)cyclohexan-1-ol (α–3A and α–3B).

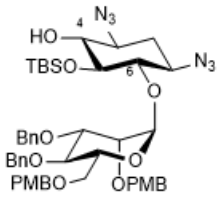
A flame-dried 4 mL vial was charged with the *D*-mannose trichloroacetimidate donor **2** (544 mg, 0.73 mmol), 2-deoxystreptamine acceptor **1** (150 mg, 0.457 mmol), flame dried 4 Å MS (150 mg), and (*S*)-SF_5-chiral phosphoric acid (CPA) catalyst[4] (45.9 mg, 0.0457 mmol). The resulting mixture was flushed with nitrogen, then dry DCM (2.4 mL) was added. The resulting mixture was refluxed for 3 days, then quenched with triethylamine. Crude ^{1}H NMR showed 88% conversion with 6:1 selectivity. The mixture was purified by column chromatography (9:1 hexanes/ethyl acetate). Purification resulted in some mixed fractions of glycal with glycosylated product and fractions of pure glycosylation products (5.7:1 mixture of **α-3B** : **α-3A**). The glycal free fractions containing pure mixture of glycosylation products **α-3B** and **α-3A** were combined and concentrated to provide a colorless oil (**α– 3A/B mix,** 307mg, 74% yield) The J^1(C-H) coupling constant for the anomeric C-H groups is consistent with the **α-3A** and **α-3B** configuration (169 and 173 Hz respectively).



α-3A (C4-glycosylated isomer): IR (thin film, cm^{-1}): 3478, 3031, 2933, 2857, 1612, 1514, 1248, 1095, 1037, 837. **^{1}H NMR** 700 MHz, C_6D_6) δ 7.44 (2 H, d, *J* = 8.5 Hz), 7.39 (2 H, d, *J* = 8.5 Hz), 7.30 (2 H, d, *J* = 7.5 Hz), 7.25 (2 H, d, *J* = 8.5 Hz), 7.21-7.17 (3 H, m), 7.14-7.05 (3 H, m), 6.82 (2 H, d, *J* = 8.5 Hz), 6.76 (2 H, d, *J* = 8.5 Hz), 5.70 (1 H, d, *J* = 1.6 Hz), 5.16 (1 H, d, *J* = 11.0 Hz), 5.01 (2 H, d, *J* = 11.7 Hz), 4.85 (1 H, d, *J* = 11.9 Hz), 4.79 (1 H, d, *J* = 11.0 Hz), 4.76 (1 H, d, *J* = 11.9 Hz), 4.67 (1 H, d, *J* = 11.4 Hz), 4.62 (1 H, d, *J* = 11.4 Hz), 4.55 (1 H, dd, *J* = 9.5, 5.0 Hz), 4.45 (1 H, d, *J* = 11.7 Hz), 4.34 (1 H, dd, *J* = 9.5, 2.4 Hz), 4.22 (1 H, t, *J* = 2.4 Hz), 3.96 (1 H, dd, *J* = 11.0, 4.8 Hz), 3.89 (1 H, dd, *J* = 11.0, 1.4 Hz), 3.50 (1 H, t, *J* = 9.5 Hz), 3.32 (3 H, s), 3.315 (3 H, s), 3.23 (1 H, t, *J* = 8.9 Hz), 2.68 (1 H, dd, *J* = 9.5, 4.0 Hz), 2.47 (1 H, ddd, *J* = 12.3, 9.7, 4.6 Hz), 1.81(1 H, d, *J* = 3.9 Hz), 1.49 (1 H, dt, *J* = 12.3, 4.6 Hz), 1.0 (9 H, s), 0.19 (3

[4] Lee, J.-W.; List, B. *J. Am. Chem. Soc.* **2012**, *134*, 18245.

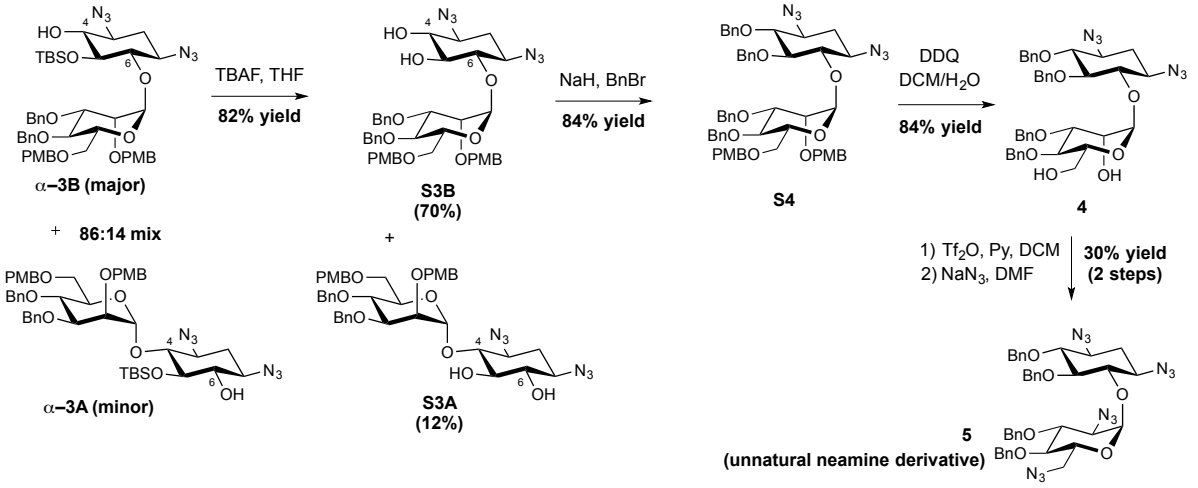
H, s), 0.18 (3 H, s). **^{13}C NMR** (175 MHz, C_6D_6, anomeric carbon signal): 99.8 ppm. **HRMS (ESI+) (*m/z*):** $[M+NH_4]^+$ calcd for $C_{48}H_{62}N_6O_{10}SiNH_4$ 928.4635, found 928.4635.

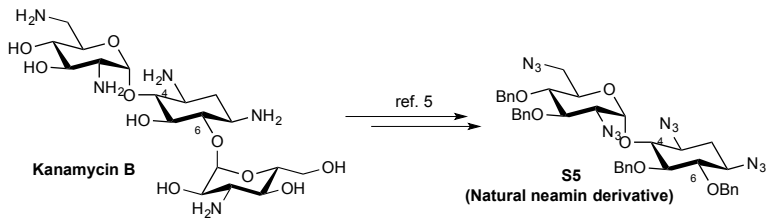


α–3B

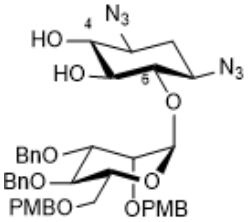
α-3B (C6-glycosylated isomer): IR (thin film, cm^{-1}):3478, 3031, 2933, 2857, 1612, 1514, 1248, 1095, 1037, 837. **^{1}H NMR** 700 MHz, C_6D_6) δ 7.40 (4 H, t, *J* = 8.0 Hz), 7.34 (2 H, d, *J* = 7.3 Hz), 7.30-7.25 (3 H, m), 7.25-7.18 (2 H, m), 7.12-7.07 (3 H, m), 6.82 (2 H, d, *J* = 8.3 Hz), 6.78 (2 H, d, *J* = 8.3 Hz), 5.64 (1 H, d, *J* = 1.7 Hz), 5.02 (1 H, d, *J* = 10.9 Hz), 4.85 (1 H, d, *J* = 12.5 Hz), 4.78 (1 H, d, *J* = 10.9 Hz), 4.75 (1 H, d, *J* = 5.5 Hz), 4.68 (1 H, d, *J* = 11.7 Hz), 4.61 (2 H, d, *J* = 10.9 Hz), 4.46-4.35 (4 H, m), 4.28 (1 H, m), 4.16 (1 H, *J* = 2.7 Hz, t), 3.92 (1 H, dd, *J* = 10.1, 4.7 Hz), 3.84 (1 H, d, *J* = 10.9 Hz), 3.33 (3 H, s), 3.31 (3 H, s), 3.18 (1 H, d, *J* = 8.4 Hz), 3.17 (1 H, d, *J* = 7.4 Hz), 2.79 (1 H, dt, *J* = 12.2, 9.5, 4.2 Hz), 2.69 (1 H, m), 2.49 (1 H, ddd, *J* = 12.5, 9.8, 4.8 Hz), 1.90 (1 H, d, *J* = 3.6 Hz), 1.45 (1 H, dt, *J* = 12.5, 4.5 Hz), 1.02 (9 H, s), 0.88 (1 H, q, *J* = 12.7 Hz), 0.33 (3 H, s), 0.21 (3 H, s). **^{13}C NMR** (175 MHz, C_6D_6) δ 159.8, 159.6, 139.6, 139.4, 131.4, 131.3, 129.7, 128.7, 128.5, 128.3, 128.1, 128.0, 128.0, 127.8, 114.1, 114.0, 99.0 (anomeric C), 81.6, 80.1, 77.8, 76.8, 76.6, 75.9, 75.1 (CH_2), 74.0 (CH_2), 73.3, 73.2 (CH_2), 72.5 (CH_2), 69.9 (CH_2), 60.7, 60.0, 54.8, 54.7, 32.2 (CH_2), 26.4, 18.6, -3.2. **HRMS (ESI+) (*m/z*):** $[M+NH_4]^+$ calcd for $C_{48}H_{62}N_6O_{10}SiNH_4$ 928.4635, found 928.4631.

Synthesis of Neamine and iso-Neamine Derivatives 5 and S5





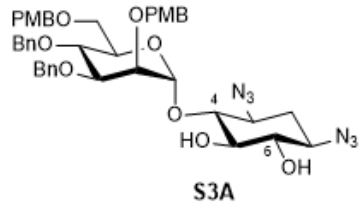
(1R,2S,3S,4R,6S)-4,6-diazido-3-(((2S,3S,4S,5R,6R)-4,5-bis(benzyloxy)-3-((4-methoxybenzyl)oxy)-6-(((4-methoxybenzyl)oxy)methyl)tetrahydro-2H-pyran-2-yl)oxy)cyclohexane-1,2-diol (S3B and S3A). The 86:14 mixture of disaccharide **α-3B : α-3A** (30.0 mg, 0.0329 mmol) was mixed with 25 mg of 4Å MS, flushed with nitrogen, and then dissolved in 1.5 mL dry THF. The reaction was cooled down to 0 °C, and tetra-n-butylammonium fluoride (TBAF, 1.0 M in THF, 0.066 ml, 0.066 mmol) was added. The reaction mixture was warmed up to room temperature and was stirred for overnight. Then the reaction mixture was quenched with saturated sodium bicarbonate and extracted with ethyl acetate. Organics were washed with brine/water (1:1) two times, then brine. Extracts were dried with magnesium sulfate, and concentrated *in vacuo*. The mixture was purified by column chromatography (3:1 to 2:1 hexanes/ethyl acetate) to afford compound **S3B** (18.3 mg, 70%) along with the C4-glycosylated isomer **S3A** (3.2 mg, 12%).



S3B

C6-glycosylated Diastereomer (S3B).

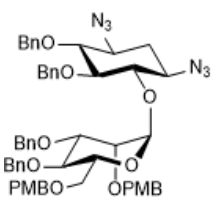
IR (thin film, cm^{-1}): 3469, 2654, 1702, 1613, 1586, 1369, 1256, 1109, 1033, 816, 689, 658. **^{1}H NMR** δ_H (500 MHz, C_6D_6) δ 7.45 – 7.39 (2 H, m), 7.34 (2 H, d, *J* = 8.6 Hz), 7.26 – 7.18 (6 H, m), 7.15 – 7.07 (4 H, m), 6.86 – 6.78 (4 H, m), 5.06 – 4.92 (3 H, m), 4.74 – 4.58 (4 H, m), 4.45 (1 H, d, *J* = 11.4 Hz), 4.27 – 4.20 (3 H, m), 4.15 (1 H, t, *J* = 2.5 Hz), 4.09 (1 H, dd, *J* = 9.1, 2.9 Hz), 4.01 (1 H, t, *J* = 9.5 Hz), 3.81 (1 H, dd, *J* = 9.6, 1.9 Hz), 3.53 (1 H, t, *J* = 9.1 Hz), 3.35 (3 H, s), 3.30 (3 H, s), 3.18 (1 H, t, *J* = 9.4 Hz), 3.06 (1 H, td, *J* = 8.8, 3.0 Hz), 2.96 – 2.83 (3 H, m), 2.56 (1 H, ddd, *J* = 12.7, 9.5, 4.7 Hz), 1.50 (1 H, dt, *J* = 13.2, 4.6 Hz), 0.93 – 0.85 (1 H, q, *J* = 12.4 Hz). **^{13}C NMR** δ_C (125 MHz, C_6D_6) 160.1, 160.1, 139.1, 139.1, 130.6, 130.1, 130.0, 129.9, 128.7, 128.6, 128.5, 128.3, 128.0, 127.9, 114.2, 114.2, 100.4, 88.1, 80.5, 76.4, 75.6, 75.2, 75.1, 75.1, 73.4, 73.3, 73.0, 72.0, 70.1, 59.6, 59.6, 54.9, 54.8, 32.3. **HRMS (ESI+) (*m/z*):** $[M+NH_4]^+$ calcd for $C_{42}H_{52}N_7O_{10}$ 814.3770, found 814.3767.



S3A

C4-glycosylated Diastereomer (S3A).

IR (thin film, cm^{-1}): 3428, 2926, 1720, 1612, 1586, 1514, 1454, 1364, 1250, 1104, 1033, 818, 699. **^{1}H NMR** δ_H (500 MHz, C_6D_6) δ 7.41 – 7.33 (4 H, m), 7.26 – 7.17 (7 H, m), 7.14 (1 H, s), 7.10 (2 H, dd, *J* = 7.2, 4.3 Hz), 6.79 (4 H, d, *J* = 8.6 Hz), 5.48 (1 H, d, *J* = 2.3 Hz), 4.95 (1 H, d, *J* = 11.5 Hz), 4.82 (1 H, d, *J* = 11.7 Hz), 4.70 (1 H, d, *J* = 11.7 Hz), 4.56 (2 H, s), 4.50 (2 H, dd, *J* = 10.3, 7.1 Hz), 4.40 (1 H, d, *J* = 11.1 Hz), 4.28 (1 H, d, *J* = 11.1 Hz), 4.19 – 4.12 (3 H, m), 3.88 (1 H, dd, *J* = 9.9, 2.0 Hz), 3.71 (1 H, dd, *J* = 10.0, 7.2 Hz), 3.42 (1 H, t, *J* = 9.9 Hz), 3.32 (3 H, s), 3.29 (3 H, s), 2.98 (1 H, t, *J* = 9.4 Hz), 2.69-2.59 (2 H, m), 1.53 – 1.49 (1 H, m), 1.55 (1 H, s), 0.91 (2 H, q, *J* = 12.4 Hz). **^{13}C NMR** δ_C (125 MHz, C_6D_6) 160.0, 160.0, 139.3, 139.2, 130.9, 130.2, 130.1, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 114.2, 114.2, 96.4, 80.9, 80.3, 76.6, 75.8, 75.7, 74.8, 74.8, 73.4, 73.2, 72.9, 72.4, 70.1, 59.9, 58.0, 54.8, 54.8, 32.4. **HRMS (ESI+) (*m/z*):** $[M+NH_4]^+$ calcd for $C_{42}H_{52}N_7O_{10}$ 814.3770, found 814.3769.

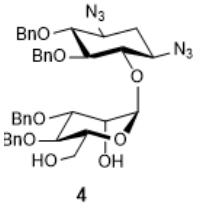


S4

(2R,3R,4R,5R,6R)-3-azido-6-(azidomethyl)-4,5-bis(benzyloxy)-2-(((1S,2S,3R, 4S,6R)-4,6-diazido-2,3-bis(benzyloxy)cyclohexyl)oxy)tetrahydro-2H-pyran (S4). The diol **S3B** (30.6 mg, 0.0384 mmol) isolated from the previous reaction was dissolved in dry

DMF (0.38 mL). To that, 60% sodium hydride in mineral oil (6.1 mg, 0.154 mmol) was added, and the reaction mixture was flushed with nitrogen. To the resultant mixture benzyl bromide (22.8 µL, 0.192 mmol) was added, and thus obtained solution was stirred at 40 °C overnight. The reaction mixture was then diluted with DCM, and aqueous ammonia chloride was added. Organics were extracted with DCM, and then washed with brine, dried with magnesium sulfate and concentrated *in vacuo*. Column chromatography (9:1 to 4:1 hexanes/ethyl acetate) resulted in 30.6 mg (84%) of **S4** as a colorless oil.

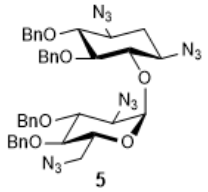
^{1}H NMR (400 MHz, C_6D_6) δ 7.44 (2 H, d, *J* = 6.7 Hz), 7.41 – 7.32 (7 H, m), 7.25 – 7.18 (8 H, m), 7.14 – 7.04 (7 H, m), 6.81 (2 H, d, *J* = 8.5 Hz), 6.75 (2 H, d, *J* = 8.5 Hz), 5.68 (1 H, s), 5.01 (1 H, d, *J* = 11.2 Hz), 4.84 (2 H, d, *J* = 5.4 Hz), 4.80 (2 H, d, *J* = 3.5 Hz), 4.73 (2 H, q, *J* = 10.8 Hz), 4.66 (2 H, s), 4.61 (2 H, dd, *J* = 11.4, 8.3 Hz), 4.47 (1 H, d, *J* = 9.2 Hz), 4.38 (1 H, d, *J* = 11.6 Hz), 4.30 (1 H, dd, *J* = 8.2, 4.8 Hz), 4.15 (2 H, d, *J* = 8.5 Hz), 3.66 (1 H, s), 3.39 (1 H, t, *J* = 9.6 Hz), 3.33 (3 H, s), 3.30 (3 H, s), 3.04 (1 H, t, *J* = 9.3 Hz), 2.95 (1 H, t, *J* = 9.4 Hz), 2.71-2.60 (2 H, m), 1.44 (1 H, dt, *J* = 13.1, 4.6 Hz), 0.92 (1 H, t, *J* = 7.1 Hz).



4

(2S,3S,4R,5R,6R)-4,5-bis(benzyloxy)-2-(((1S,2S,3R,4S,6R)-4,6-diazido-2,3-bis(benzyloxy)cyclohexyl)oxy)-6-(hydroxymethyl)tetrahydro-2H-pyran-3-ol (4). The benzylated product **S4** from above (45.8 mg, 0.0469 mmol) was mixed together with DDQ (21.3 mg, 0.0937 mmol), then 0.32 mL of DCM was added along with 1 drop of water. The mixture was stirred at room temperature for 1.5 hours. Then the reaction was quenched with saturated sodium bicarbonate, and extracted with DCM. Organics were washed with saturated sodium bicarbonate, brine, dried with magnesium sulfate and concentrated *in vacuo*. Column chromatography (4:1 to 3:2 hexanes/ethyl acetate resulted in 23.1 mg (67%) of **4** as a colorless oil.

^{1}H NMR (400 MHz, Benzene-d_6) δ 7.37 – 7.31 (4 H, m), 7.26 – 7.21 (4 H, m), 7.18 (3 H, d, *J* = 7.3 Hz), 7.14 – 7.02 (9 H, m), 5.65 (1 H, d, *J* = 1.7 Hz), 4.90-4.82 (2 H, m), 4.75 – 4.62 (4 H, m), 4.53 (2 H, s), 4.29 (1 H, t, *J* = 2.4 Hz), 4.15 – 4.04 (2 H, m), 3.97 (1 H, dd, *J* = 8.5, 3.2 Hz), 3.73 (1 H, dd, *J* = 12.2, 2.1 Hz), 3.61 (1 H, d, *J* = 12.1 Hz), 3.28 (1 H, t, *J* = 9.5 Hz), 3.01-2.90 (2 H, m), 2.71-2.59 (3 H, m), 1.44 (1 H, dt, *J* = 13.1, 4.5 Hz), 0.85 (1 H, q, *J* = 12.7 Hz).



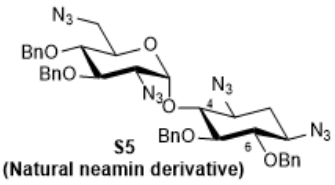
5
(unnatural neamine derivative)

(2R,3R,4R,5R,6R)-3-azido-6-(azidomethyl)-4,5-bis(benzyloxy)-2-(((1S,2S,3R,4S,6R)-4,6-diazido-2,3-bis(benzyloxy)cyclohexyl)oxy)tetrahydro-2H-pyran (5).

Diol **4** (23.1 mg, 0.0314 mmol) was dissolved in 0.17 mL of dry DCM, and cooled down to -15 °C under nitrogen. To this mixture pyridine (12.6 µL, 0.157 mmol) and trifluoromethanesulfonic anhydride (21.1 µL, 0.125 mmol) were added. The resulting solution was stirred at the same temperature for 10 minutes before being diluted with DCM and water. Organics were extracted with DCM, and the extracts were washed with saturated sodium bicarbonate and water and then dried with magnesium sulfate, filtered and concentrated *in vacuo*.

The resulting crude triflate from above was dissolved in dry DMF under nitrogen. To that solution sodium azide (7.8 mg, 0.120 mmol) was added, the mixture was stirred at 40 °C for 4 hours, and then was diluted with DCM and water. The organics were extracted with DCM, then washed with brine/water (1:1) and brine, dried over magnesium sulfate and concentrated *in vacuo*. The product was purified by column chromatography (4:1 hexanes/ethyl acetate). This procedure resulted in 3.0 mg (30 %, 2 steps) of the desired product **5**.

IR (thin film, cm^{-1}): 2924, 2103, 1722, 1454, 1361, 1260, 1124, 739, 697. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.39 – 7.31 (7 H, m), 7.28 (7 H, d, *J* = 9.6 Hz), 7.24 – 7.10 (6 H, m), 5.56 (1 H, d, *J* = 3.8 Hz), 5.02 (1 H, d, *J* = 11.0 Hz), 4.90 – 4.86 (3 H, m), 4.84 (1 H, d, *J* = 10.5 Hz), 4.79 (1 H, d, *J* = 11.1 Hz), 4.68 (1 H, d, *J* = 11.1 Hz), 4.47 (1 H, d, *J* = 11.1 Hz), 4.01 – 3.97 (1 H, m), 3.87 (1 H, t, *J* = 9.6 Hz), 3.61 – 3.56 (1 H, m), 3.54 – 3.51 (1 H, m), 3.50 – 3.48 (2 H, m)), 3.46 – 3.43 (2 H, m), 3.40 (1 H, dd, *J* = 10.3, 3.7 Hz), 3.04 (1 H, dd, *J* = 13.6, 2.4 Hz), 2.68 (1 H, dd, *J* = 13.5, 3.5 Hz), 2.31 (1 H, dt, *J* = 13.4, 4.5 Hz), 1.51 – 1.47 (1 H, m). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 138.1, 137.8, 137.6, 137.3, 128.6, 128.5, 128.5, 128.4, 128.2, 128.2, 128.1, 127.9, 127.9, 127.8, 127.7, 127.4, 97.6, 84.8, 81.9, 80.1, 78.6, 76.2, 76.0 (CH_2), 75.6 (CH_2), 75.1 (CH_2), 70.5, 63.6, 61.6, 60.5, 50.4 (CH_2), 32.9 (CH_2), 29.9 (CH_2). **HRMS (ESI+) (*m/z*)**: $[M+Na]^+$ calcd for $C_{40}H_{42}N_{12}O_6Na$ 809.3242, found 809.3232.



S5
(Natural neamin derivative)

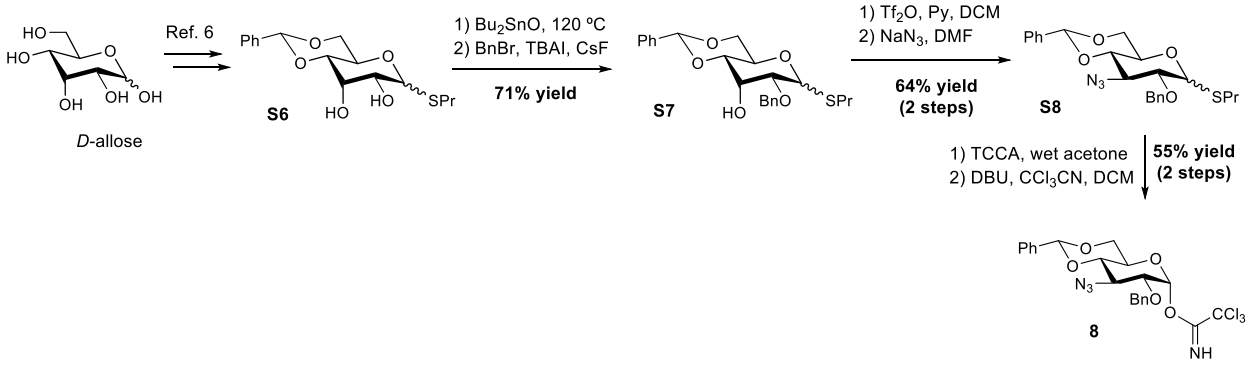
(2R,3R,4R,5R,6R)-3-azido-6-(azidomethyl)-4,5-bis(benzyloxy)-2-(((1R,2R, 3S,4R,6S)-4,6-diazido-2,3-bis(benzyloxy)cyclohexyl)oxy)tetrahydro-2H-pyran (S5).

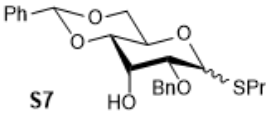
Protected neamine **S5** was prepared from kanamycin B following the literature prep[5,] and its 1H NMR data were consistent with the previously published data for the same compound.[6] The spectra of **S5** and **5** were compared to each other in the spectra section below and were found to be distinctly different.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.26 (20 H, m), 5.58 (1 H, d, *J* = 3.9 Hz), 5.03 (1 H, d, *J* = 10.8 Hz,), 4.94 (1 H, d, *J* = 10.9 Hz), 4.90 – 4.86 (4 H, m), 4.83 (2 H, m) 4.88 (3 H, d, *J* = 8.8 Hz), 4.83 (2 H, d, *J* = 10.5 Hz), 4.62 (1 H, d, *J* = 11.2 Hz), 4.28 (1 H, ddd, *J* = 10.0, 4.3, 2.4 Hz), 4.01 (1 H, dd, *J* = 10.3, 8.9 Hz), 3.66 – 3.57 (2 H, m), 3.56 – 3.47 (3 H, m), 3.47 – 3.37 (3 H, m), 3.32 (1 H, dd, *J* = 10.4, 3.9 Hz), 2.38 – 2.29 (1 H, m), 1.50 (1 H, d, *J* = 12.7 Hz). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 138.1, 137.8, 137.8, 137.4, 128.7, 128.6, 128.6, 128.6, 128.3, 128.2, 128.2, 128.1, 128.1, 127.9, 127.8, 127.0, 97.7, 84.8, 84.5, 80.2, 78.8, 77.7, 76.1, 75.7, 75.4, 75.2, 71.1, 63.4, 60.4, 59.4, 51.1, 32.4.

Preparation of trichloroacetimidate 8

[5] van den Broek, S. A. M. W.; Gruijters, B. W. T.; Rutjes, F. P. J. T.; van Delft F. L.; Blaauw, R. H. *J. Org. Chem.* **2007**, *72*, 3577.
[6] Pang, L.-J.; Wang, D.; Zhou, J.; Zhang, L.-H.; Ye, X.-S. *Org. Biomol. Chem.* **2009**, *7*, 4252.

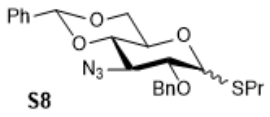




(2R,4aR,7R,8R,8aS)-7-(benzyloxy)-2-phenyl-6-(propylthio)hexahydropyrano [3,2-d][1,3]dioxin-8-ol (S7).

Diol **S6**[7] (1.38 g, 4.21 mmol) was mixed with dibutyltin(IV) oxide (1.07 g, 4.30 mmol), and then dissolved in dry toluene (70 mL) under atmosphere of nitrogen. The reaction mixture was stirred at 120 °C for 3 h, cooled down to room temperature, and then tetra-n-butylammonium iodide (1.65 g, 4.46 mmol), cesium fluoride (653 mg, 4.30 mmol), and benzyl bromide (0.51 mL, 4.42 mmol) were added sequentially. The reaction mixture was stirred at 120 °C for 3 h again and cooled down to room temperature. The resulting mixture was diluted with ethyl acetate and saturated sodium bicarbonate and extracted with ethyl acetate (x 3). Organics were washed with brine/water (1:1) mixture (x 2), and then with brine (x 2). The combined extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The mixture was purified by flash column chromatography (3:1 to 1:1 hexanes/ethyl acetate) to afford compound **S7** (1.20 g, 71%) as a mixture of anomers (β:α = 4.8:1).

β-S7: IR (thin film, cm^{-1}): 3489, 2923, 1972, 1709, 1496, 1454, 1378, 1217, 1072, 998, 909. **^{1}H NMR** δ_H (Only major β-isomer is reported, 700 MHz, $CDCl_3$) 7.48 (2 H, dd, *J* = 7.6, 2.1 Hz), 7.41 (2 H, d, *J* = 7.1 Hz), 7.37 – 7.34 (5 H, m), 7.33 – 7.31 (1 H, m), 5.51 (1 H, s), 4.88 (1 H, d, *J* = 9.7 Hz), 4.80 (1 H, d, *J* = 11.8 Hz), 4.71 (1 H, d, *J* = 11.8 Hz), 4.37 (1 H, dd, *J* = 10.4, 5.2 Hz), 4.34 (1 H, d, *J* = 2.8 Hz), 4.03 (1 H, td, *J* = 9.9, 5.2 Hz), 3.70 (1 H, t, *J* = 10.4 Hz), 3.52 (1 H, dd, *J* = 9.5, 2.5 Hz), 3.38 (1 H, dd, *J* = 9.8, 2.8 Hz), 2.74 (1 H, ddd, *J* = 12.6, 8.1, 6.4 Hz), 2.67 (1 H, dt, *J* = 12.6, 7.3 Hz), 2.47 (OH, s), 1.71 – 1.66 (2 H, m), 1.02 (3 H, t, *J* = 7.4 Hz). **^{13}C NMR** δ_C (Only major isomer reported, 175 MHz, $CDCl_3$) 137.3, 137.2, 129.3, 128.7, 128.4, 128.4, 128.4, 126.4, 102.1, 82.3, 78.7, 72.8 (CH_2), 69.3 (CH_2), 67.2, 65.6, 58.3, 33.2 (CH_2), 23.4 (CH_2), 13.7. **(ESI+) (*m/z*):** $[M+Na]^+$ calcd for $C_{23}H_{28}O_5SNa$ 439.1555, found 439.1543.



(2R,4aR,7R,8S,8aS)-8-azido-7-(benzyloxy)-2-phenyl-6-(propylthio)hexahydro pyrano[3,2-d][1,3]dioxine (S8).

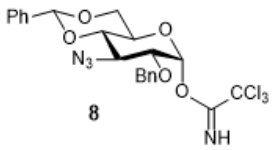
To a solution of thioglycoside **S2** (1.20 g, 2.87 mmol) in DCM (45 mL) at 0 °C, pyridine (1.16 mL, 14.4 mmol) and then triflic anhydride (0.966 mL, 5.74 mmol) were added dropwise.

[7] Wang, Y.; Li, Q.; Cheng, S.; Wu, Y.; Guo, D.; Fan, Q.-H.; Wang, X.; Zhang, L.-H.; Ye, X.-S. *Org. Lett.* **2005**, *7*, 5577.

The resulting mixture was stirred at 0°C for 30 minute before being quenched with iced water. The organic layer was separated and aqueous layer was extracted with DCM (x 3). The combined organic layer was washed with water (x 3), dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to afford crude triflate (1.58 g, 2.87 mmol).

To the solution of triflate from above (1.58 g, 2.87 mmol) in N,N-dimethylformamide (35 mL) sodium azide (1.87 g, 28.7 mmol) was added in one portion. The reaction mixture was allowed to stir at room temperature for 3 h. The mixture was diluted with brine and extracted with ethyl acetate (x 3). The combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The resulting crude residue was purified by flash column chromatography (hexanes : ethyl acetate = 4:1 to 2:1) to obtain the title compound **S8** (815 mg, 64% yield over 2 steps)

β-S8: IR (thin film, cm^{-1}): 3042, 2867, 2106, 1908, 1497, 1453, 1375, 1261, 1214, 1083, 1027, 966. **^{1}H NMR** δ_H (Only major β-isomer is reported, 500 MHz, $CDCl_3$) 7.52 – 7.43 (4 H, m), 7.40 – 7.30 (6 H, m), 5.56 (1 H, s), 4.94 (1 H, d, *J* = 10.0 Hz), 4.80 (1 H, d, *J* = 10.0 Hz), 4.55 (1 H, d, *J* = 9.6 Hz), 4.36 (1 H, dd, *J* = 10.6, 4.7 Hz), 3.75 (2 H, td, *J* = 9.7, 3.2 Hz), 3.54 – 3.44 (2 H, m), 3.31 (1 H, t, *J* = 9.3 Hz), 2.80 – 2.65 (2 H, m), 1.75 – 1.63 (2 H, m), 1.02 (3 H, t, *J* = 7.3 Hz). **^{13}C NMR** δ_C (Only major β-isomer is reported, 125 MHz, $CDCl_3$) 137.4, 136.9, 129.3, 128.8, 128.6, 128.5, 128.3, 126.2, 101.6, 86.5, 80.5, 79.4, 76.0, 71.1, 68.8, 66.9, 33.5, 23.4, 13.6. **HRMS (ESI+) (*m/z*):** $[M+NH4]^+$ calcd for $C_{23}H_{31}N_4O_4S$+ 459.2061, found 459.2056.



8

(2R,4aR,6R,7R,8S,8aS)-8-azido-7-(benzyloxy)-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-6-yl 2,2,2-trichloroacetimidate (8).

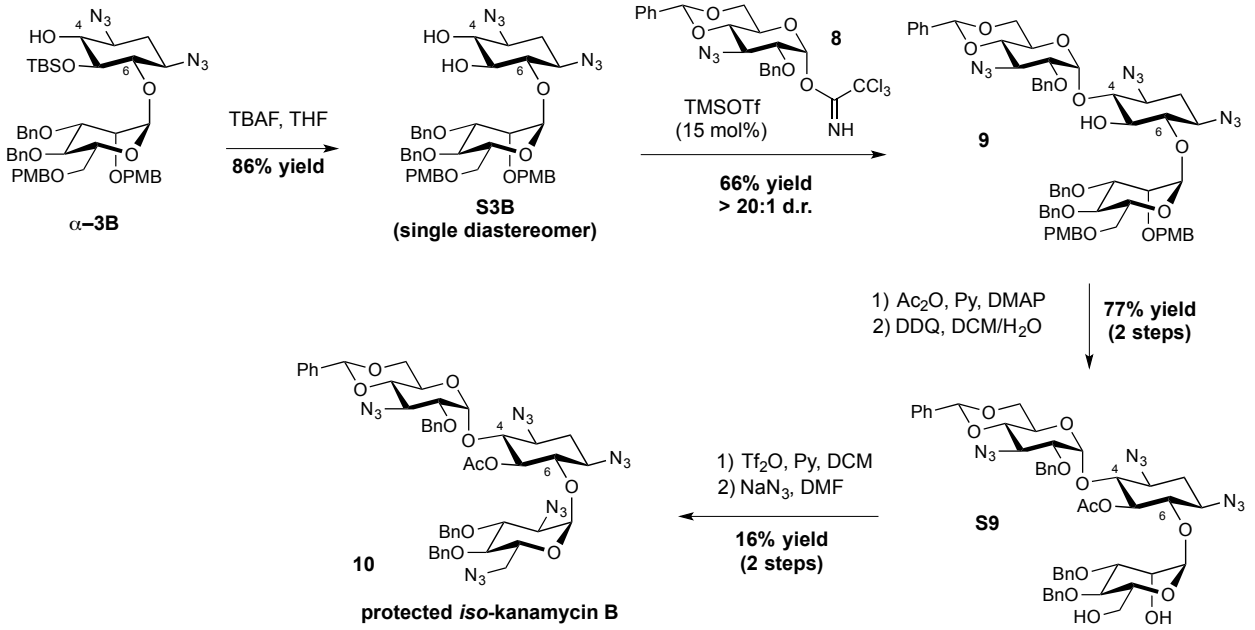
Thioglycoside **S8** (784 mg, 1.77 mmol) was dissolved in 25% (v/v) solution of water in acetone and cooled to 0 ºC. To this solution trichloroisocyanuric acid (825 mg, 3.55 mmol) was added. The resultant mixture was allowed to warm up to room temperature while being monitored by TLC. Upon its full conversion to hemiacetal, the mixture was concentrated *in vacuo* and diluted with methylene chloride. The resultant mixture was washed with the saturated solution of sodium bicarbonate, water, dried over magnesium sulfate, filtered and concentrated *in vacuo*. The residual oil was purified by flash column chromatography (3:1 hexanes/ethyl acetate) to provide the corresponding product (400 mg, 59%) as a colorless oil.

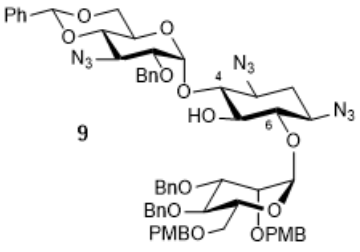
The product from above (355 mg, 0.928 mmol) was dissolved in DCM (17 mL) under the atmosphere of N_2. The reaction mixture was cooled down to 0 ^{o}C, and trichloroacetonitrile (0.28 mL, 2.783 mmol) and 1,8-Diazabicyclo(5.4.0)undec-7-ene (0.069 mL, 0.464 mmol) were sequentially added. The reaction mixture was allowed to warm up to room temperature and then diluted with toluene and the solvent was evaporated *in vacuo*. The residue was purified by flash column chromatography (5:1 to 3:1 hexanes/ethyl acetate) to afford the α-anomer of the title compound **8** (1.20 g, 91%).

IR (thin film, cm^{-1}): 3329, 2923, 2867, 2108, 1908,1672, 1454, 1370, 1278, 1088, 986, 905. **^{1}H NMR** δ_H (500 MHz, $CDCl_3$) 8.65 (NH, s), 7.50 (2 H, dd, *J* = 7.6, 1.9 Hz), 7.41 – 7.28 (8 H, m), 6.40 (1 H, d, *J* = 3.6 Hz), 5.57 (1 H, s), 4.73 (2 H, s), 4.33 (1 H, dd, *J* = 10.5, 4.9 Hz), 4.12 (1 H, t, *J* = 10.0 Hz), 4.04 (1 H, td, *J* = 9.9, 4.9 Hz), 3.71 (1 H, t, *J* = 10.3 Hz), 3.61 (1 H, dd, *J* = 9.8, 3.6 Hz), 3.54 (1 H, t, *J* = 9.9 Hz). **^{13}C NMR** δ_C (125 MHz, $CDCl_3$) 161.4, 137.1, 136.7, 129.3, 128.7, 128.5, 128.3, 128.1, 126.1, 101.8, 93.6, 91.0, 79.5, 77.4,

73.3 (CH_2), 68.8 (CH_2), 65.3, 61.7. **$[\alpha]_D^{25}$** = -8.1 (c = 1.3, CH_2Cl_2). **HRMS (ESI+)** (*m*/*z*): $[M - O\text{-}C(=NH)CCl_3]^+$ calcd for $C_{20}H_{20}N_3O_4$ 366.145 found 366.145

Preparation of *iso*-kanamycin B derivative 10



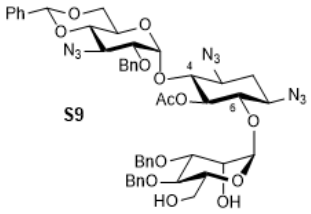


(1*S*,2*R*,3*S*,5*R*,6*S*)-3,5-diazido-2-(((2*R*,4a*R*,6*S*,7*R*,8*S*,8a*S*)-8-azido-7-(benzyloxy)-2-phenylhexahydro pyrano[3,2-*d*][1,3]dioxin-6-yl)oxy)-6-(((2*R*,3*R*,4*R*,5*S*,6*S*)-4,5-bis(benzyloxy)-3-((4-methoxybenzyl)oxy) -6-(((4-methoxybenzyl)oxy)methyl)tetrahydro-2*H*-pyran-2-yl)oxy)cyclohexan-1-ol (9).

The disaccharide acceptor **S3B** (119 mg 0.150 mmol) and donor **8** (119 mg, 0.224 mmol) were azeotropped with toluene (x 3), and further dried under high vacuum for 3 h. To the flask containing the resultant residue under the atmosphere of N_2, dried 4 Å molecular sieves and dried DCM (0.6 mL) and Et_2O (0.6 mL) were added. The reaction mixture was cooled down to -78 °C, and TMSOTf (4 µL, 0.022 mmol) was injected. The resultant mixture was stirred at -78 °C for 1 h, and then quenched by triethyl amine at -78 °C and warmed up. The reaction mixture was diluted with DCM and the mixture was concentrated *in vacuo*. The residue was purified by flash column chromatography (5:1 to 2:1 hexanes/ethyl acetate) to afford trisaccharide **9** as a single α–anomer (115 mg, 66 %).

IR (thin film, cm^{-1}): 3498, 2922, 2855, 2339, 2102, 1512, 1456, 1254, 1092, 972. **^{1}H NMR** δ_H (700 MHz, C_6D_6) 7.71 (2 H, d), 7.52 (2 H, d), 7.41 (2 H, d), 7.38 (2 H, d, *J* = 8.5 Hz), 7.30 (2 H, d), 7.28 – 7.17 (9 H, m), 7.13 – 7.04 (5 H, m), 6.84 – 6.80 (4 H, m), 5.66 (1 H, d, *J* = 3.8 Hz), 5.36 (1 H, s), 5.15 (1 H, d, *J* = 1.9 Hz), 5.08 (1 H, d, *J* = 11.1 Hz), 4.77 (1 H, d, *J* = 11.8 Hz), 4.72 (1 H, d, *J* = 11.8 Hz), 4.68 (1 H, d, *J* = 11.9 Hz), 4.63 (1 H, d, *J* = 11.9 Hz), 4.56 (2 H, m), 4.50 – 4.46 (2 H, m), 4.44 – 4.36 (5 H, m), 4.26 – 4.21 (3 H, m), 4.13 (1 H, dd, *J* = 9.3, 3.0 Hz), 3.87 (1 H, dd, *J* = 10.3, 1.8 Hz), 3.73 (1 H, dd, *J* = 10.2, 7.0 Hz), 3.56 (1 H, t, *J* = 10.2 Hz), 3.38 (3 H, s), 3.34 (1 H, t, *J* = 1.9 Hz), 3.33 – 3.32 (1 H, m), 3.31 (3 H, s), 3.29 (1 H, dd, *J* = 8.9,

2.1 Hz), 3.22 (1 H, dd, *J* = 10.0, 8.7 Hz), 2.91 (1 H, t, *J* = 9.3 Hz), 2.54 (1 H, ddd, *J* = 12.6, 9.9, 4.5 Hz), 2.47 (1 H, ddd, *J* = 12.6, 9.8, 4.4 Hz), 1.39 (1 H, dt, *J* = 12.8, 4.4 Hz), 0.80 (1 H, q = 12.7 Hz). **^{13}C NMR** δ_C (125 MHz, C_6D_6) 160.1, 159.8, 139.3, 139.1, 139.0, 138.2, 138.0, 130.7, 130.6, 130.1, 129.8, 129.1, 128.9, 128.7, 128.6, 128.5, 128.4, 128.4, 128.2, 128.0, 127.8, 126.7, 114.2, 114.1, 102.0, 101.2, 97.7, 86.3, 80.6, 80.3, 80.2, 78.5, 75.7, 75.6, 75.4 (CH_2), 74.8, 73.6 (CH_2), 73.6, 73.2 (CH_2), 72.8 (CH_2), 72.0 (CH_2), 70.2 (CH_2), 69.4 (CH_2), 63.8, 62.7, 60.0, 59.1, 54.9, 54.8, 31.7 (CH_2). **HRMS (ESI+)** (*m*/*z*): $[M+NH_4]^+$ calcd for $C_{62}H_{71}N_{10}O_{14}$ 1179.5146 found 1179.5141



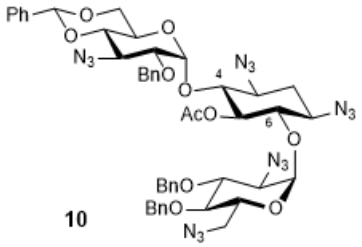
S9

(1*R*,2*R*,3*S*,5*R*,6*S*)-3,5-diazido-2-(((2*R*,4a*R*,6*S*,7*R*,8*S*,8a*S*)-8-azido-7-(benzyl oxy)-2-phenylhexahydro pyrano[3,2-*d*][1,3]dioxin-6-yl)oxy)-6-(((2*R*,3*R*, 4*S*,5*S*,6*S*)-4,5-bis(benzyloxy)-3-hydroxy-6-(hydroxyl methyl)tetrahydro-2*H*-pyran-2-yl)oxy)cyclohexyl acetate (S9).

Trisaccharide **9** (130 mg, 0.141 mmol) was combined with DMAP (1.5 mg, 0.012 mmol), acetic anhydride (85 μL, 0.902 mmol) and pyridine (5 mL) at 0 ºC. The resultant solution was warmed up to room temperature and left stirring overnight. The resultant mixture was concentrated *in vacuo*, redissolved in methylene chloride and washed with 1M hydrochloric acid (x 2) saturated sodium bicarbonate (x 2), water (x 2) and brine (x 2). The organic phase was dried with sodium sulfate, filtered and concentrated *in vacuo* to provide colorless oil (120 mg, 88%) that was used in the next step without further purification.

To the solution of acetylated product from above, (80.0 mg, 0.0665 mmol) in DCM (1.5 mL) and water (0.2 mL) pre-cooled to 0 ^{o}C, DDQ, (45.3 mg, 0.200 mmol) was added, and the resultant mixture was stirred at room temperature overnight. The reaction mixture was diluted with DCM and organic layer was separated and washed with saturated sodium bicarbonate and water until the wash became colorless. The combined organic layer was dried over sodium sulfate, concentrated *in vacuo*, and the reaction mixture was purified by the flash coloumn chromatography (5:1 to 2:1 hexanes / ethyl acetate) to afford diol **S9** (55mg, 86 %)

IR (thin film, cm^{-1}): 3496, 2925, 2104, 1752, 1453, 1372, 1223, 1085, 988. **^{1}H NMR** δ_H (700 MHz, CD_3OD) 7.48 – 7.44 (4 H, m), 7.38 – 7.34 (7 H, m), 7.31 – 7.23 (9 H, m), 5.58 (1 H, s), 5.26 (1 H, s), 5.13 (1 H, d, *J* = 3.2 Hz), 5.07 (1 H, t, *J* = 9.4 Hz), 4.85 (1 H, d, *J* = 11.1 Hz), 4.72 – 4.67 (3 H, m), 4.61 (1 H, d, *J* = 11.0 Hz), 4.55 (1 H, d, *J* = 11.7 Hz), 4.27 (1 H, dd, *J* = 10.3, 4.9 Hz), 4.09 (1 H, m), 4.05 (1 H, td, *J* = 9.9, 4.8 Hz), 3.84 (1 H, t, *J* = 9.7 Hz), 3.81 – 3.65 (11 H, m), 3.51 – 3.45 (3 H, m), 2.37 – 2.33 (1 H, m), 1.80 (3 H, s), 1.55 (1 H, q, *J* = 12.5 Hz). **^{13}C NMR** δ_C (175 MHz, CD_3OD) 172.7, 140.1, 139.7, 139.0, 138.8, 130.0, 129.9, 129.5, 129.3, 129.2, 129.2, 129.1, 129.1, 128.8, 128.6, 128.5, 127.4, 102.9, 102.0, 99.9, 82.7, 80.8, 80.7, 80.7, 78.8, 76.0, 74.8, 74.8, 74.7, 74.3, 72.5, 69.9, 69.1, 65.3, 63.4, 62.7, 62.2, 61.8, 33.5, 22.0. **HRMS (ESI+) (*m*/*z*):** $[M+Na]^+$ calcd for $C_{48}H_{53}N_9O_{13}Na$ 986.3661, found 986.3657.



10

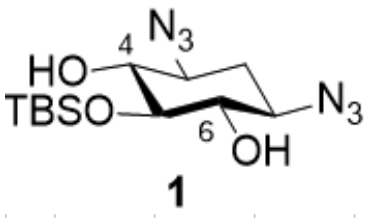
protected *iso*-kanamycin B

(1*R*,2*S*,3*R*,5*S*,6*R*)-3,5-diazido-2-(((2*S*,3*S*,4*S*,5*S*,6*S*)-3-azido-6-(azido methyl)-4,5-bis(benzyloxy)tetrahydro-2*H*-pyran-2-yl)oxy)-6-(((2*R*, 4*R*,6*S*,7*R*,8*S*,8a*S*)-8-azido-7-(benzyloxy)-2-phenylhexahydropyrano [3,2-*d*][1,3]dioxin-6-yl)oxy)cyclohexyl acetate (10).

To a solution of diol **S9** (12.2 mg, 0.0126 mmol) in DCM (0.3 mL) at -78 ^{o}C, 2,6-lutidine (14 µL, 0.126 mmol) and triflic anhydride (8 µL, 0.0504 mmol) were added sequentially. The reaction mixture was stirred at -78 ^{o}C for 1 h and then quenched with water / THF solution before being warmed up to room temperature. The resulting mixture was extracted with DCM (x 3), and the combined organic layer was washed with water (x 3), dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to obtain *bis*-triflate (14.5 mg, 0.0118 mmol).

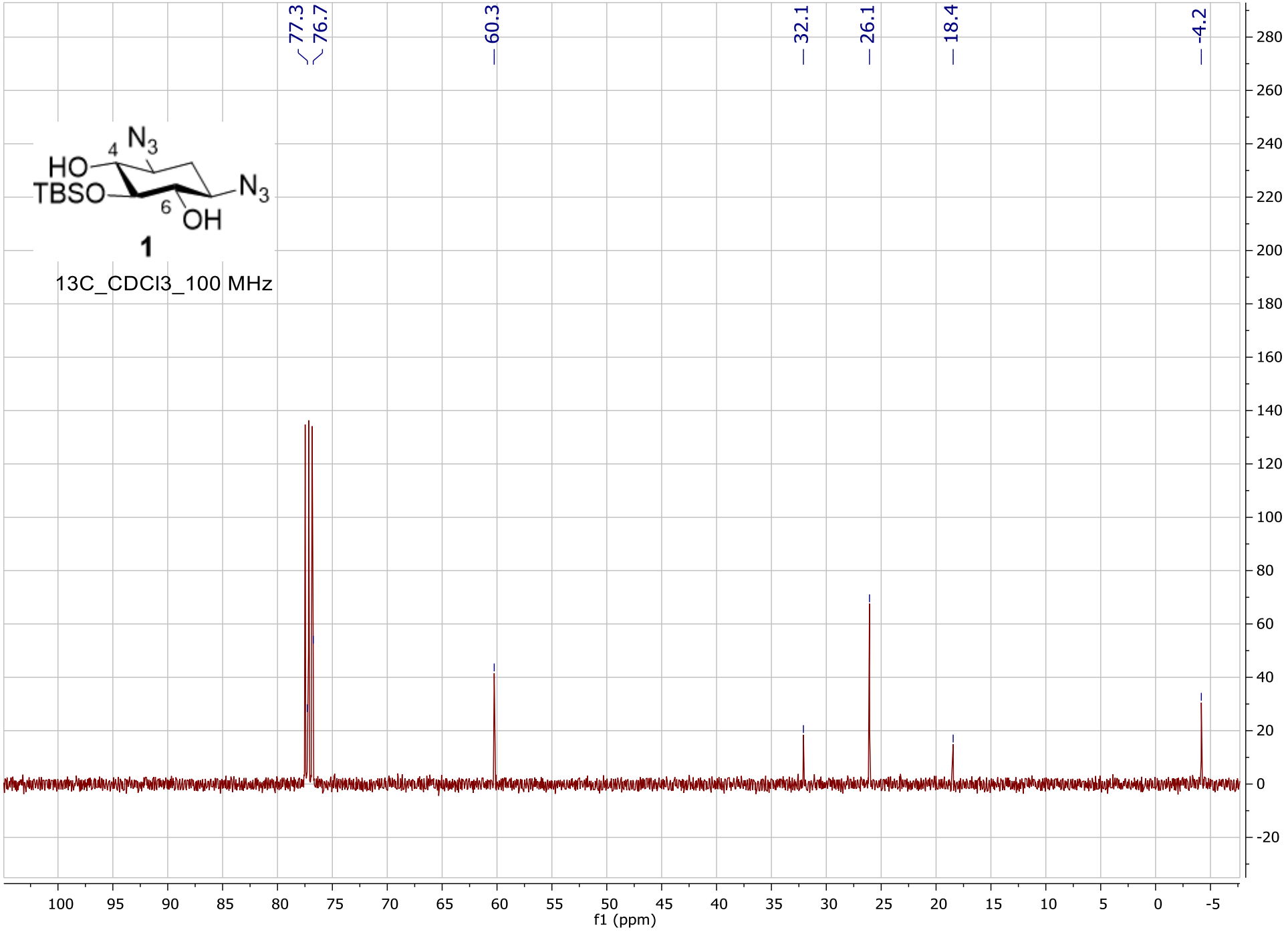
To the solution of crude triflate from above (14.5 mg, 0.0118 mmol) in dimethyl sulfoxide (2 mL), sodium azide (15 mg, 0.236 mmol) was added in one portion. The reaction mixture was allowed to stir at 90 ^{o}C overnight. Then the reaction mixture was cooled, diluted with brine, and the organic layer was extracted with DCM (x 3) and dried over sodium sulfate, filtered and concentrated *in vacuo*. The resulting crude oil was purified by flash column chromatography (7:1 to 3:1 hexanes / ethyl acetate) to afford the protected *iso*-kanamycin **10** (3.6 mg, 16% yield, 2 steps).

IR (thin film, cm^{-1}): 2920, 2845, 2101, 1755, 1457, 1201, 1116. **^{1}H NMR** δ_H (700 MHz, C_6D_6) 7.70 – 7.65 (2 H, m), 7.38 (2 H, d, *J* = 7.6 Hz), 7.33 (2 H, d, *J* = 7.5 Hz), 7.27 (3 H, s), 7.21 (5 H, s), 7.13 – 7.07 (4 H, m), 7.05 (2 H, s), 5.34 (1 H, s), 4.99 (1 H, d, *J* = 3.4 Hz), 4.95 (1 H, t, *J* = 9.5 Hz), 4.92 (1 H, d, *J* = 10.9 Hz), 4.86 (1 H, d, *J* = 3.2 Hz), 4.78 (2 H, d, *J* = 11.3 Hz), 4.52 – 4.50 (1 H, m), 4.50 – 4.46 (2 H, m), 4.35 (1 H, d, *J* = 11.8 Hz), 4.25 – 4.17 (2 H, m), 4.03 (1 H, t, *J* = 9.6 Hz), 3.97 (1 H, dt, *J* = 9.8, 3.4 Hz), 3.53 (1 H, t, *J* = 10.4 Hz), 3.47 (1 H, t, *J* = 9.4 Hz), 3.39 (1 H, dd, *J* = 13.5, 2.5 Hz), 3.23 – 3.19 (2 H, m), 3.16 (1 H, t, *J* = 9.7 Hz), 3.09 – 3.04 (2 H, m), 2.87 (2 H, qd, *J* = 9.6, 5.5 Hz), 2.39 (1 H, ddd, *J* = 12.3, 9.4, 4.7 Hz), 1.97 (3 H, s), 1.41 (1 H, dt, *J* = 13.0, 4.5 Hz), 0.84 (1 H, q, *J* = 12.7 Hz). **^{13}C NMR** δ_C (175 MHz, C_6D_6) 169.9, 138.5, 138.4, 137.8, 137.8, 129.2, 128.9, 128.7, 128.7, 128.7, 128.7, 128.4, 128.4, 128.3, 128.3, 127.8, 126.7, 102.1, 99.2, 98.5, 82.3, 80.2, 79.8, 78.6, 75.6 (CH_2), 75.2 (CH_2), 74.0 (CH_2), 72.1, 69.3 (CH_2), 64.6, 64.3, 62.3, 61.4, 60.4, 60.1, 51.0, 30.2, 21.6.**HRMS (ESI+) (*m/z*):** $[M+Na]^+$ calcd for $C_{48}H_{51}N_{15}O_{11}Na$ 1036.3790, found 1036.3785.



1

1H_CDCl3_400 MHz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76.7
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32.1
26.1
18.4
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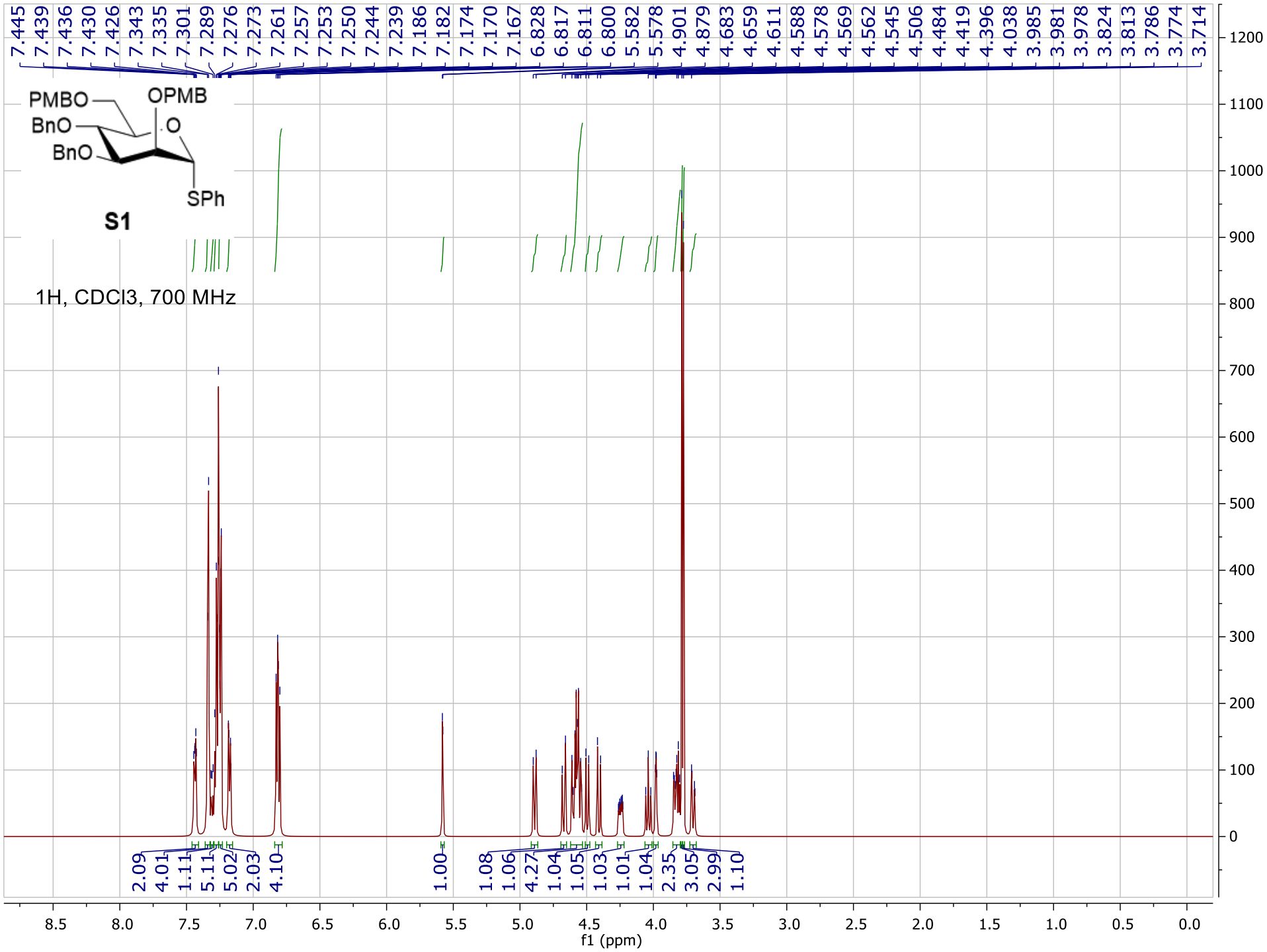
HO
TBSO
N_3
N_3
4
6
OH
1
13C_CDCl3_100 MHz
f1 (ppm)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OPMB
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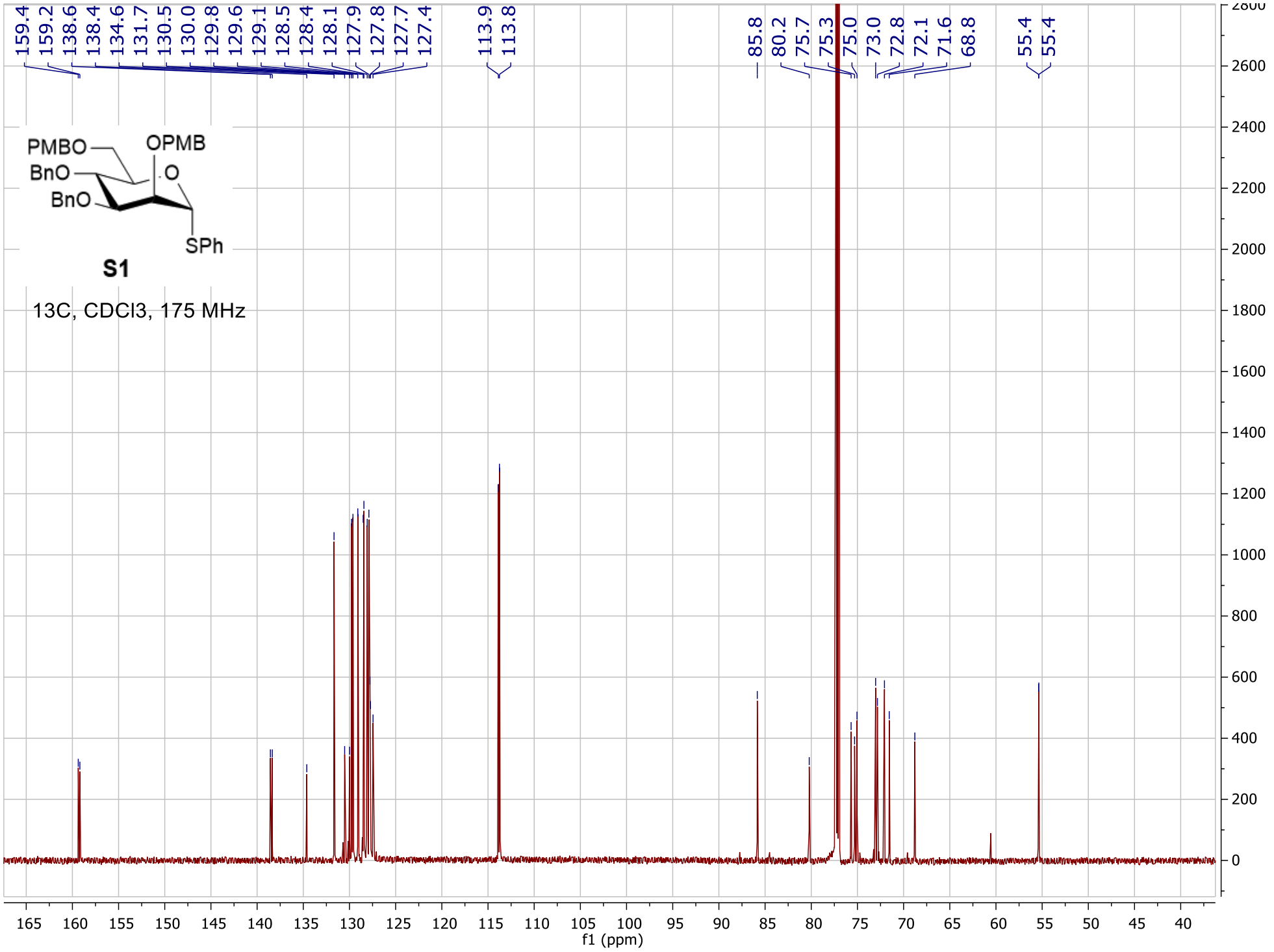
O
BnO
SPh
S1
1H, CDCl3, 700 MHz
f1 (ppm)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128.1
127.9
127.8
127.7
127.4
113.9
113.8
85.8
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75.3
75.0
73.0
72.8
72.1
71.6
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SPh
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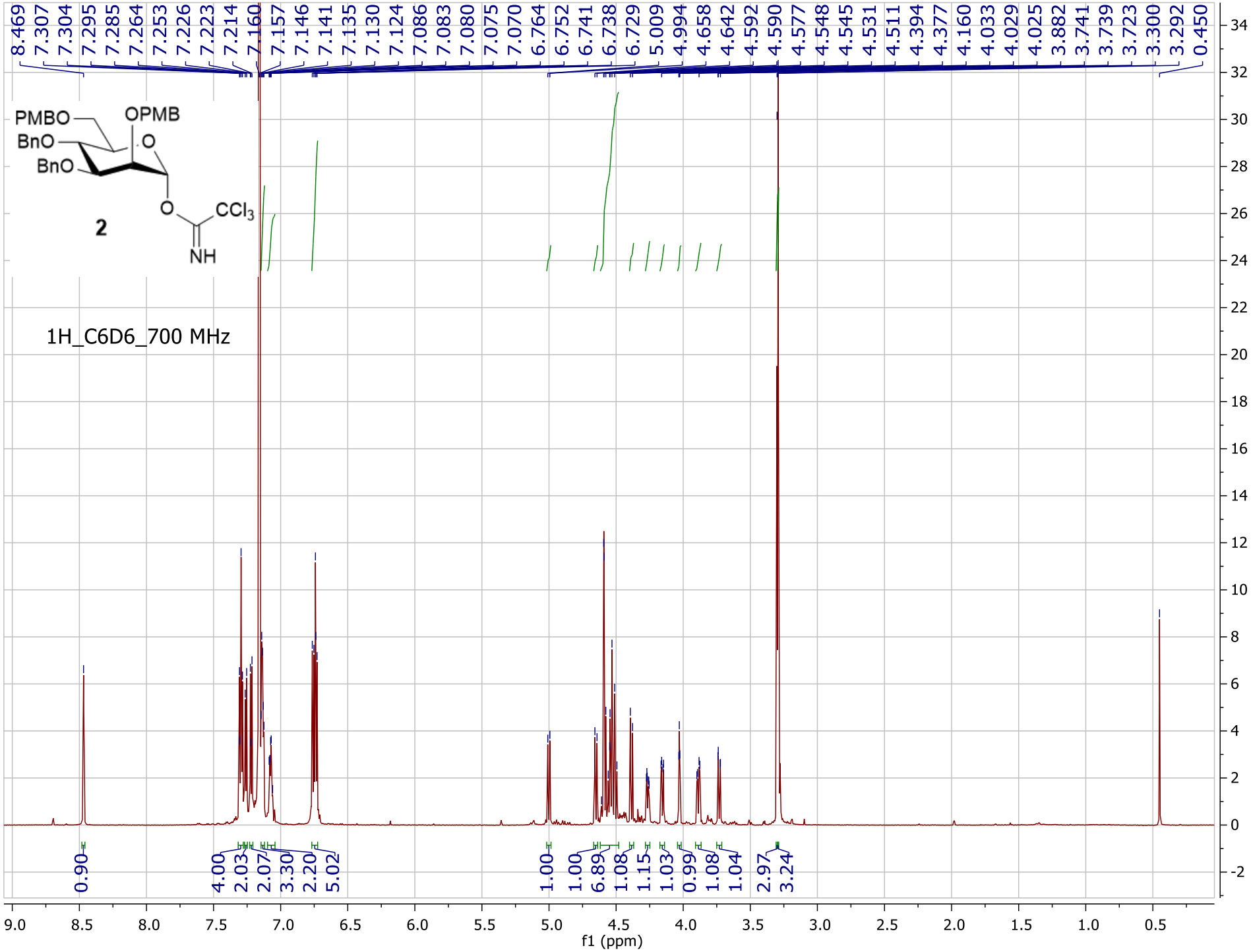
13C, CDCl3, 175 MHz
f1 (ppm)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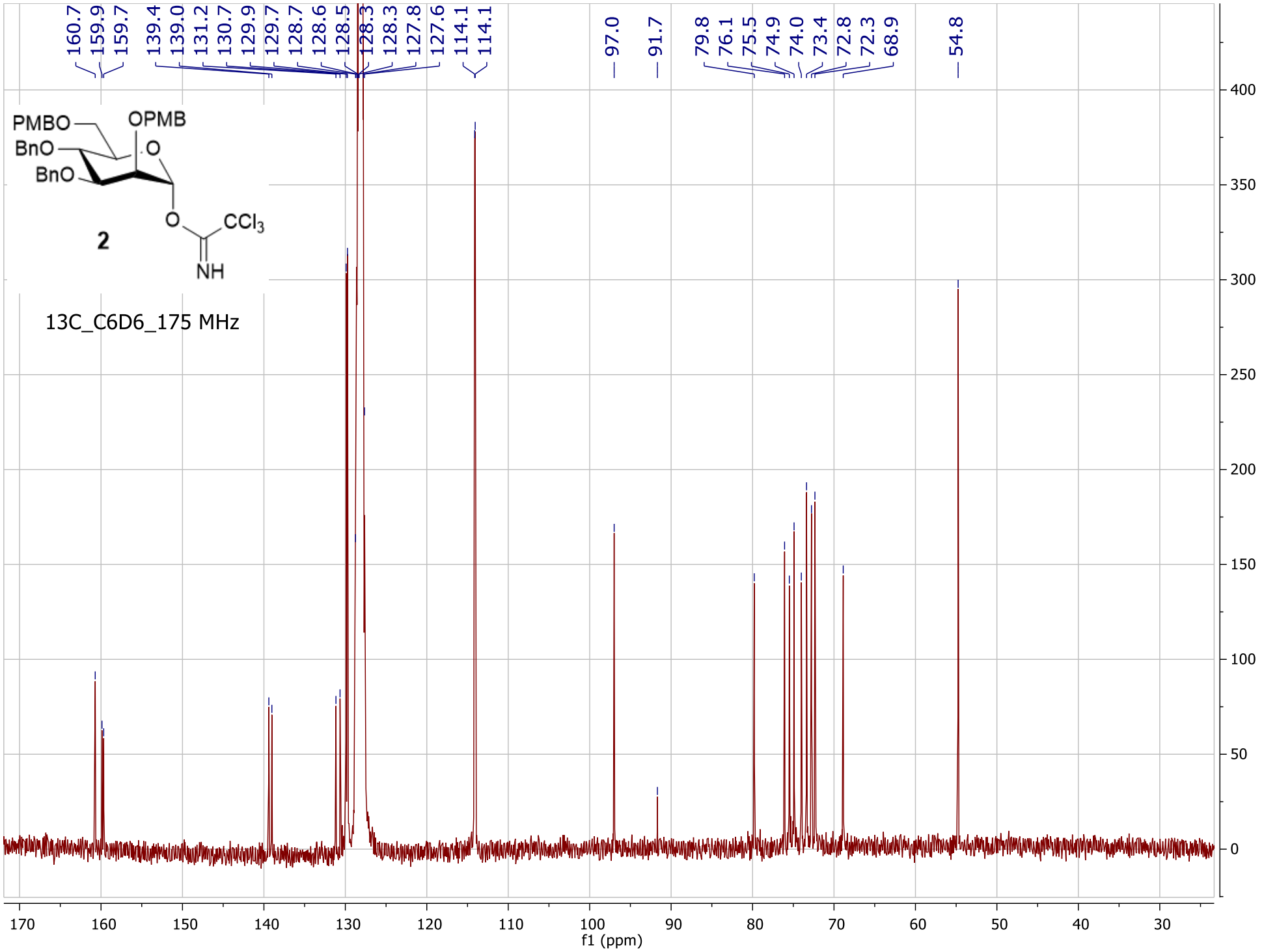
PMBO
OPMB
BnO
O
BnO
O
CCl3
NH
2
1H_C6D6_700 MHz
0.90 4.00 2.03 2.07 3.30 2.20 5.02 1.00 1.00 6.89 1.08 1.15 1.03 0.99 1.08 1.04 2.97 3.24
f1 (ppm)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128.3
128.3
127.8
127.6
114.1
114.1
97.0
91.7
79.8
76.1
75.5
74.9
74.0
73.4
72.8
72.3
68.9
54.8
PMBO
OPMB
BnO
O
BnO
O
CCl3
NH
2
13C_C6D6_175 MHz
400
350
300
250
200
150
100
50
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)


PMBO
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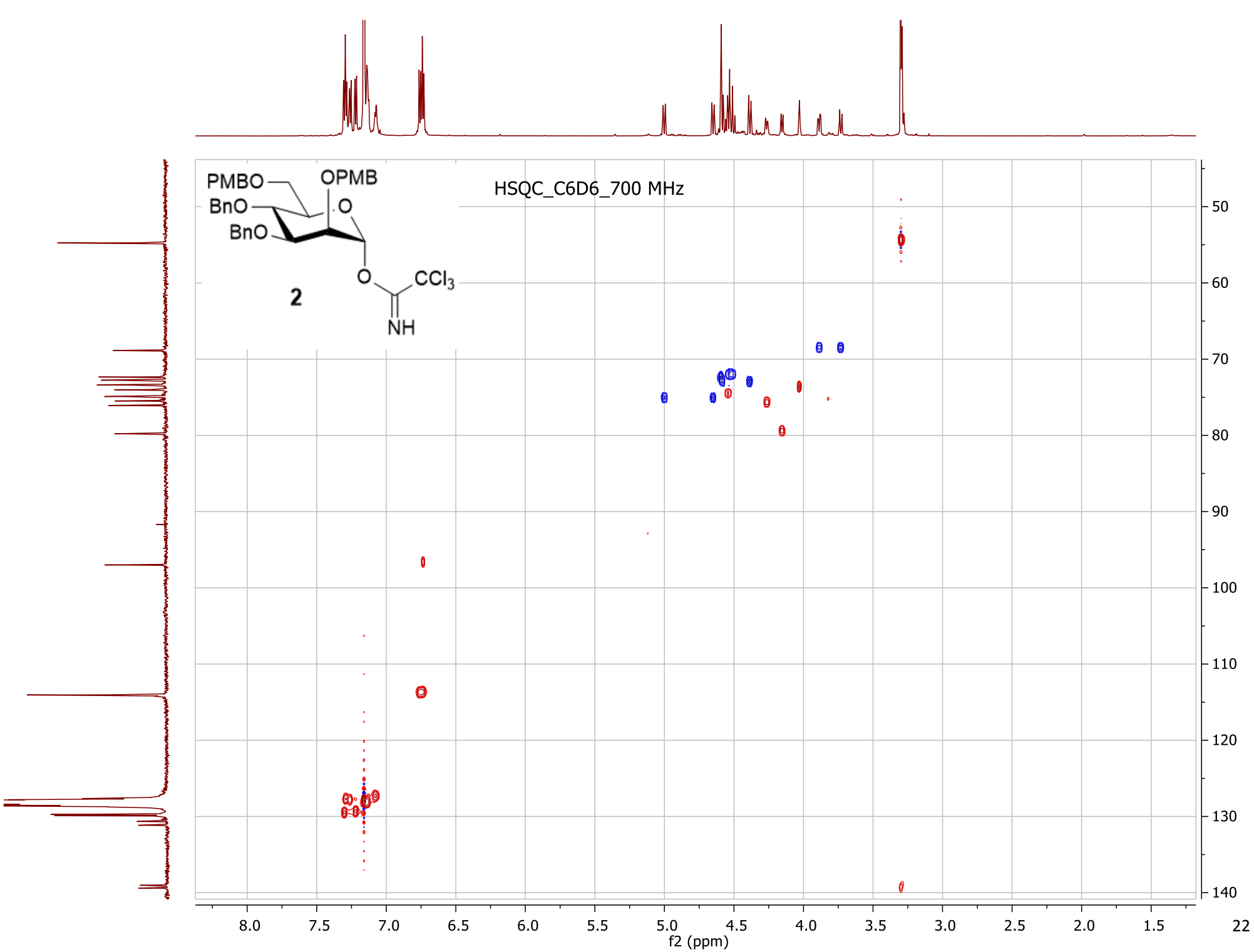
f2 (ppm)
f1 (ppm)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100
110
120
130
140
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7.0
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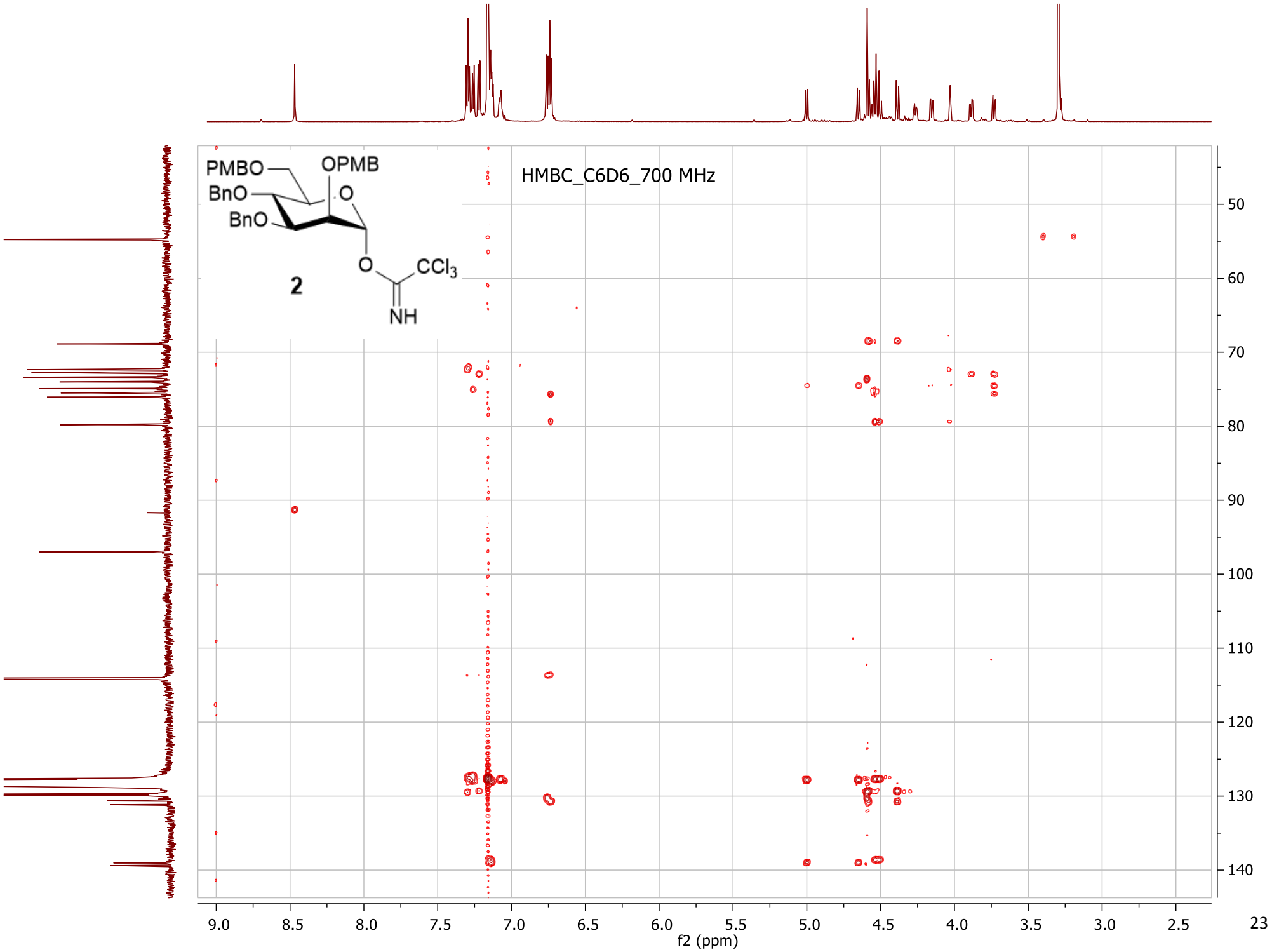
3.5
3.0
2.5
2.0
1.5
f2 (ppm)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60
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90
100
110
120
130
140
9.0
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8.0
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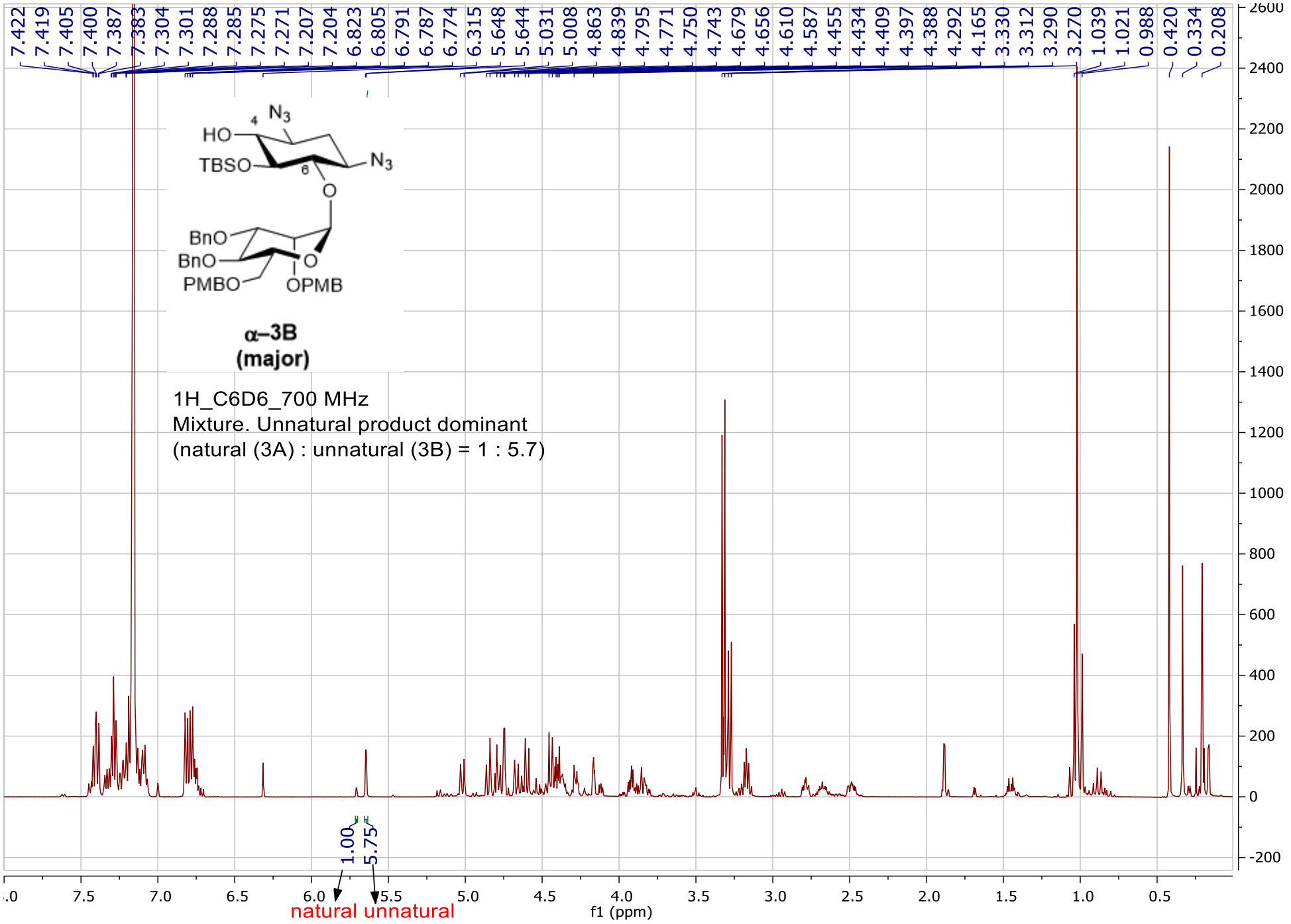
5.0
4.5
4.0
3.5
3.0
2.5
f2 (ppm)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4.388
4.292
4.165
3.330
3.312
3.290
3.270
1.039
1.021
0.988
0.420
0.334
0.208
HO
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N3
TBSO
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N3
O
BnO
BnO
O
PMBO
OPMB
α–3B
(major)
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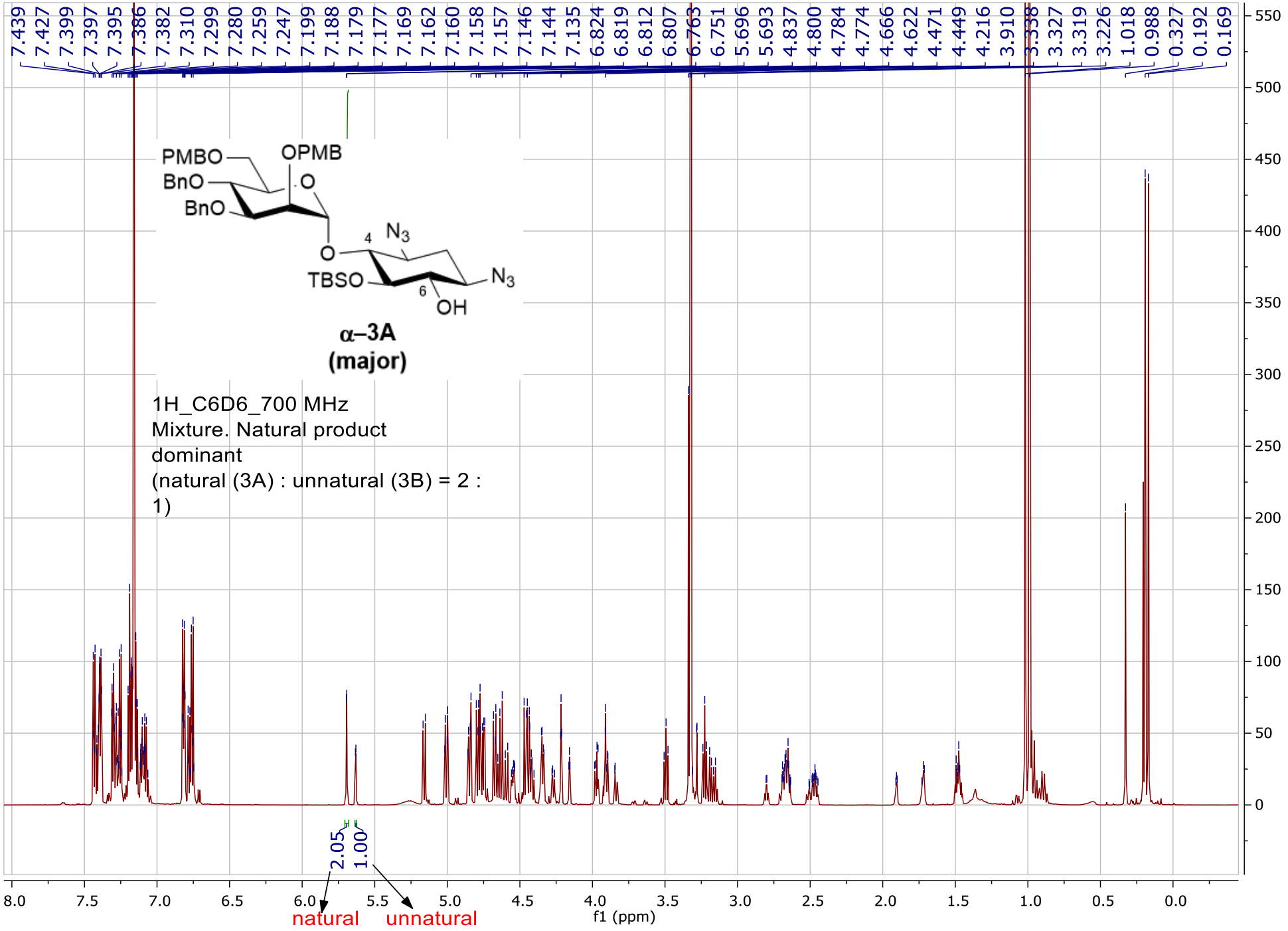
Mixture. Unnatural product dominant
(natural (3A) : unnatural (3B) = 1 : 5.7)
1.00
5.75
natural unnatural
f1 (ppm)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4
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TBSO
6
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α–3A
(major)
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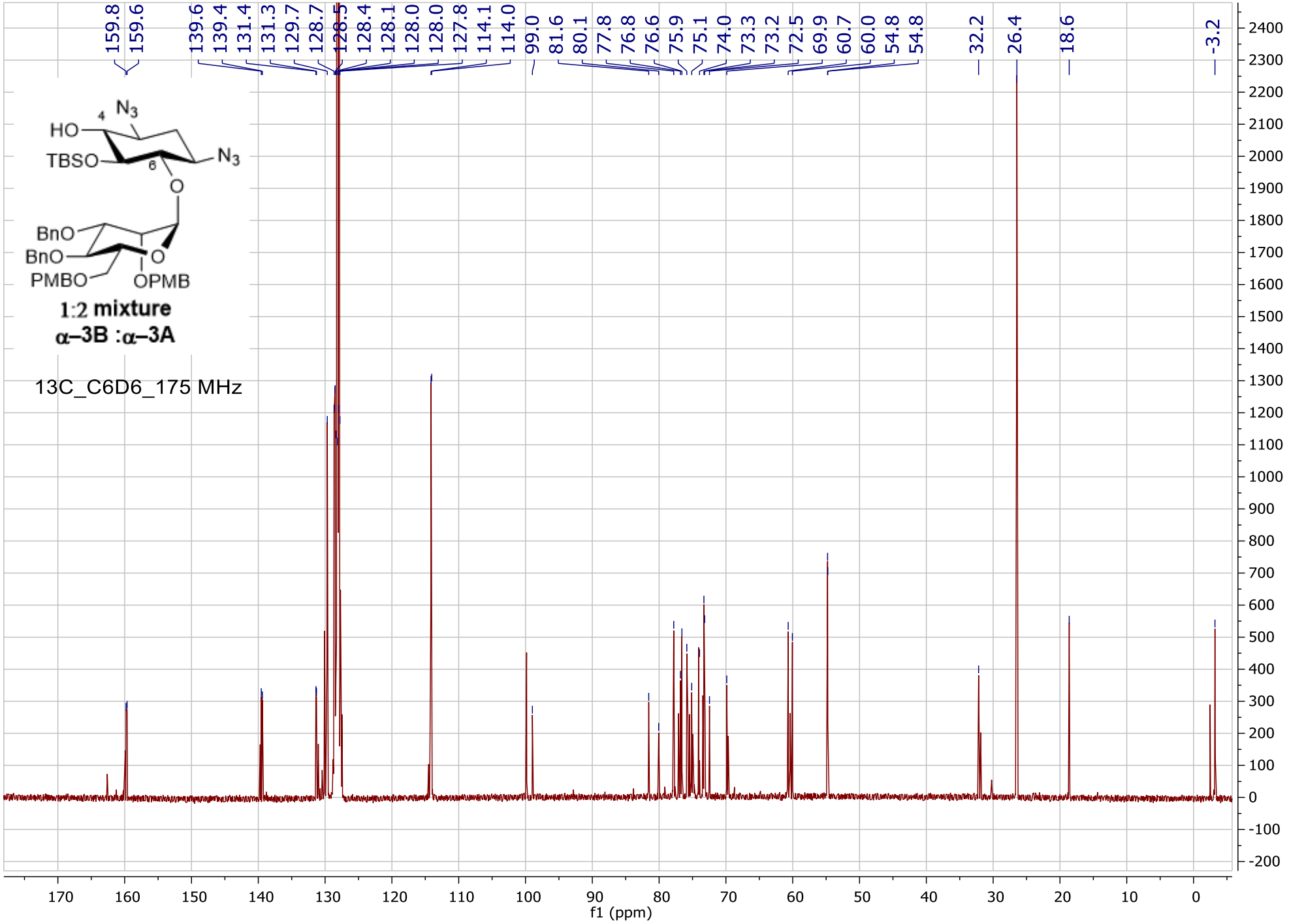
Mixture. Natural product dominant
(natural (3A) : unnatural (3B) = 2 : 1)
2.05
1.00
natural
unnatural
f1 (ppm)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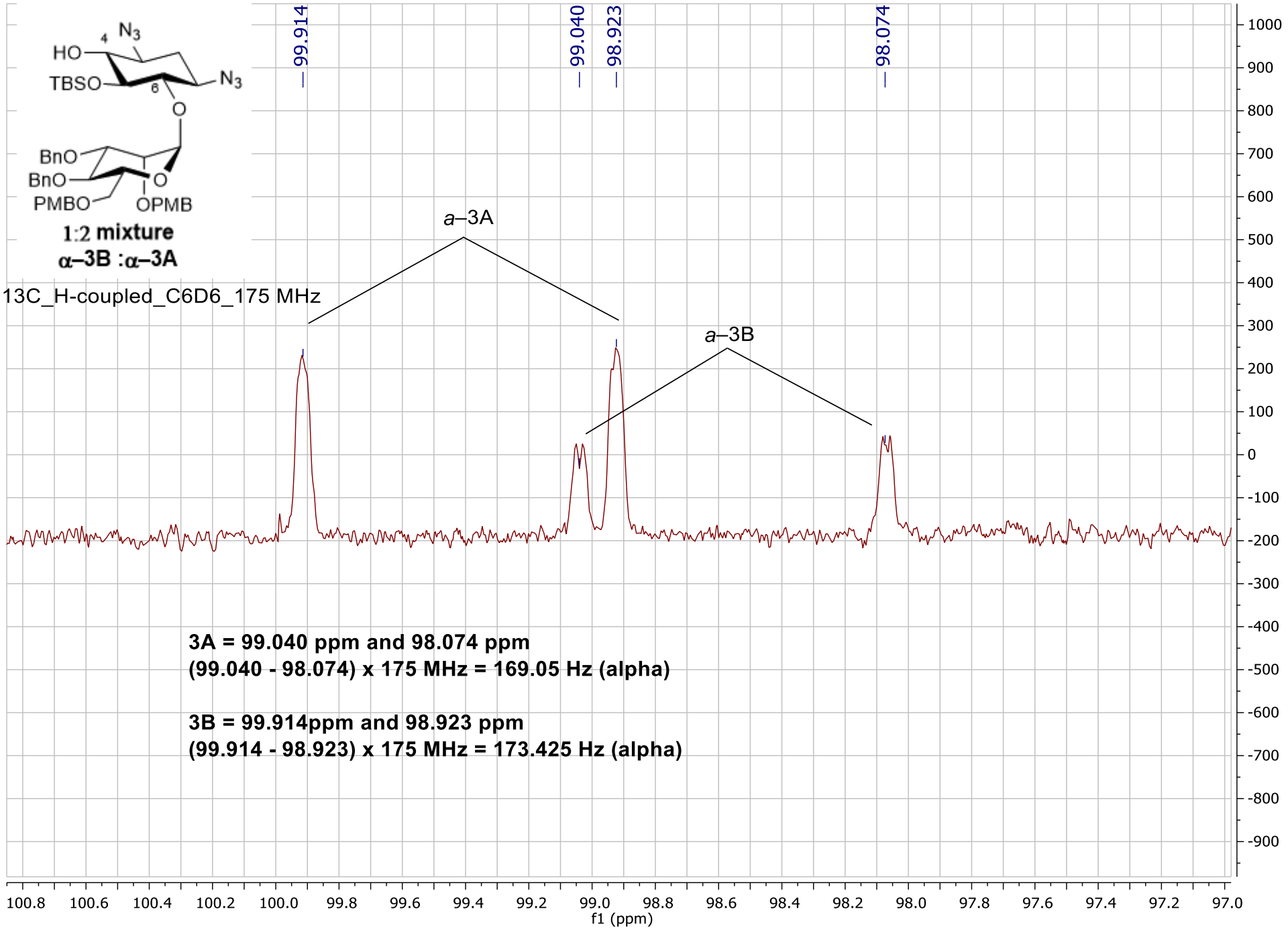
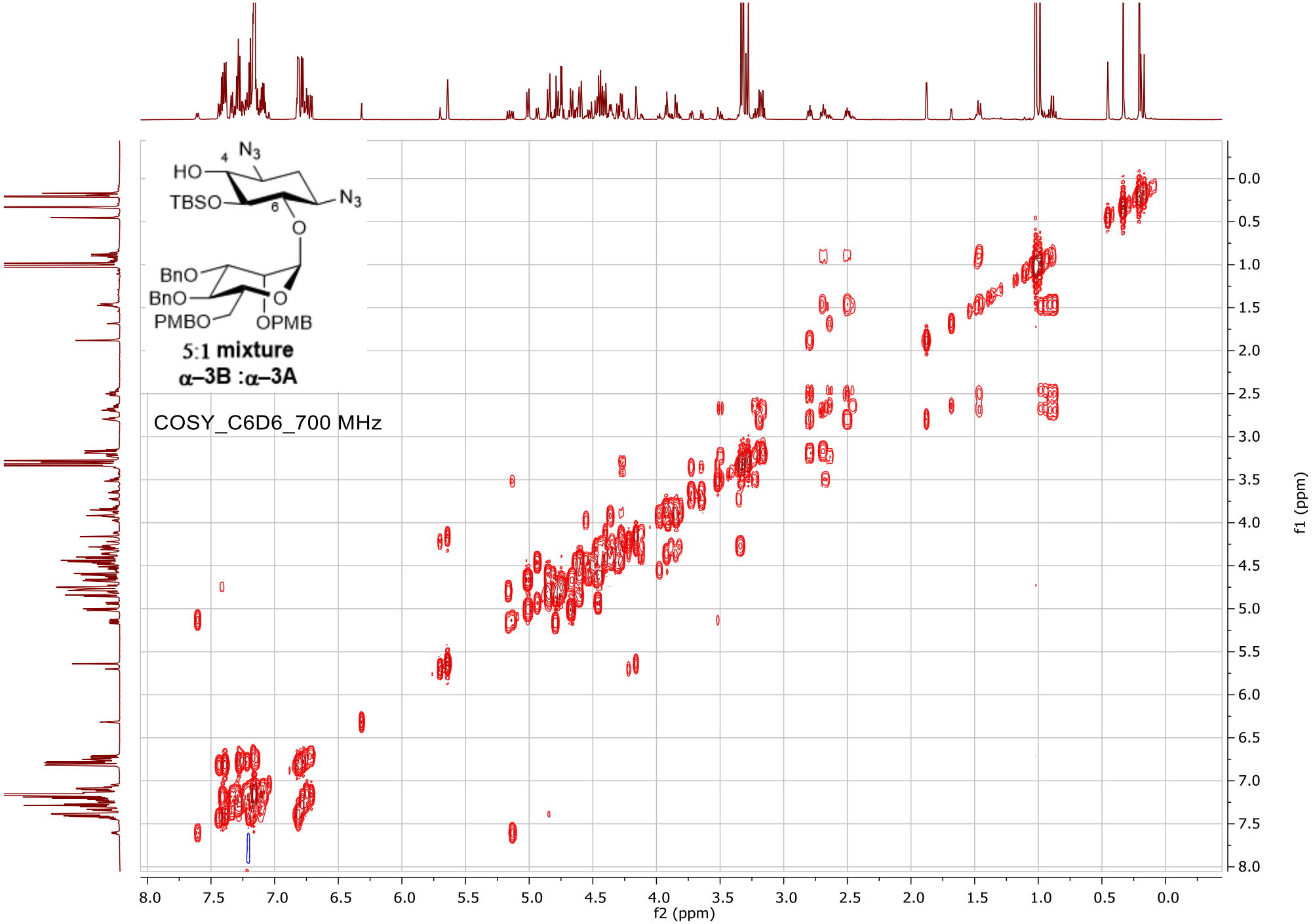
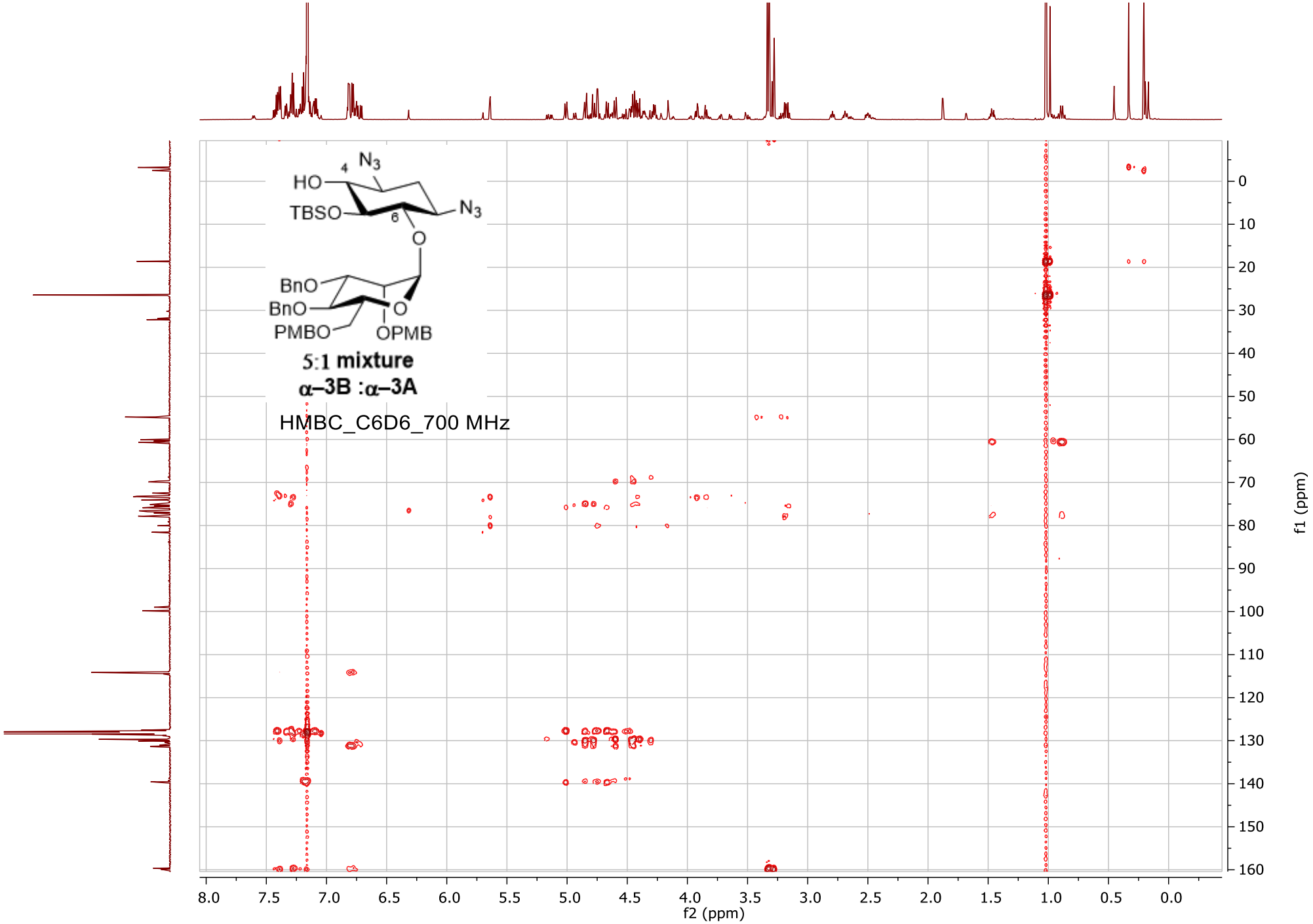
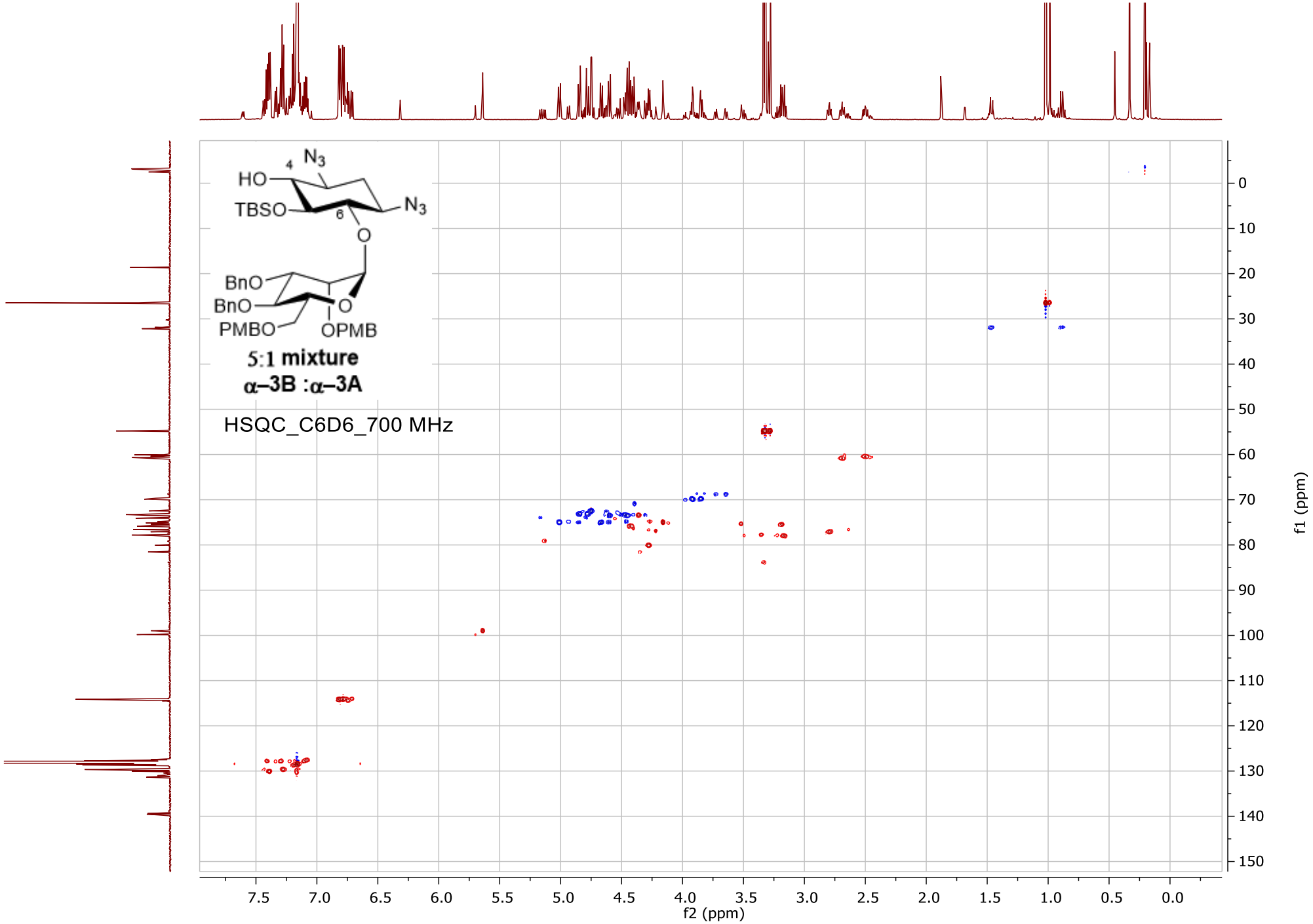
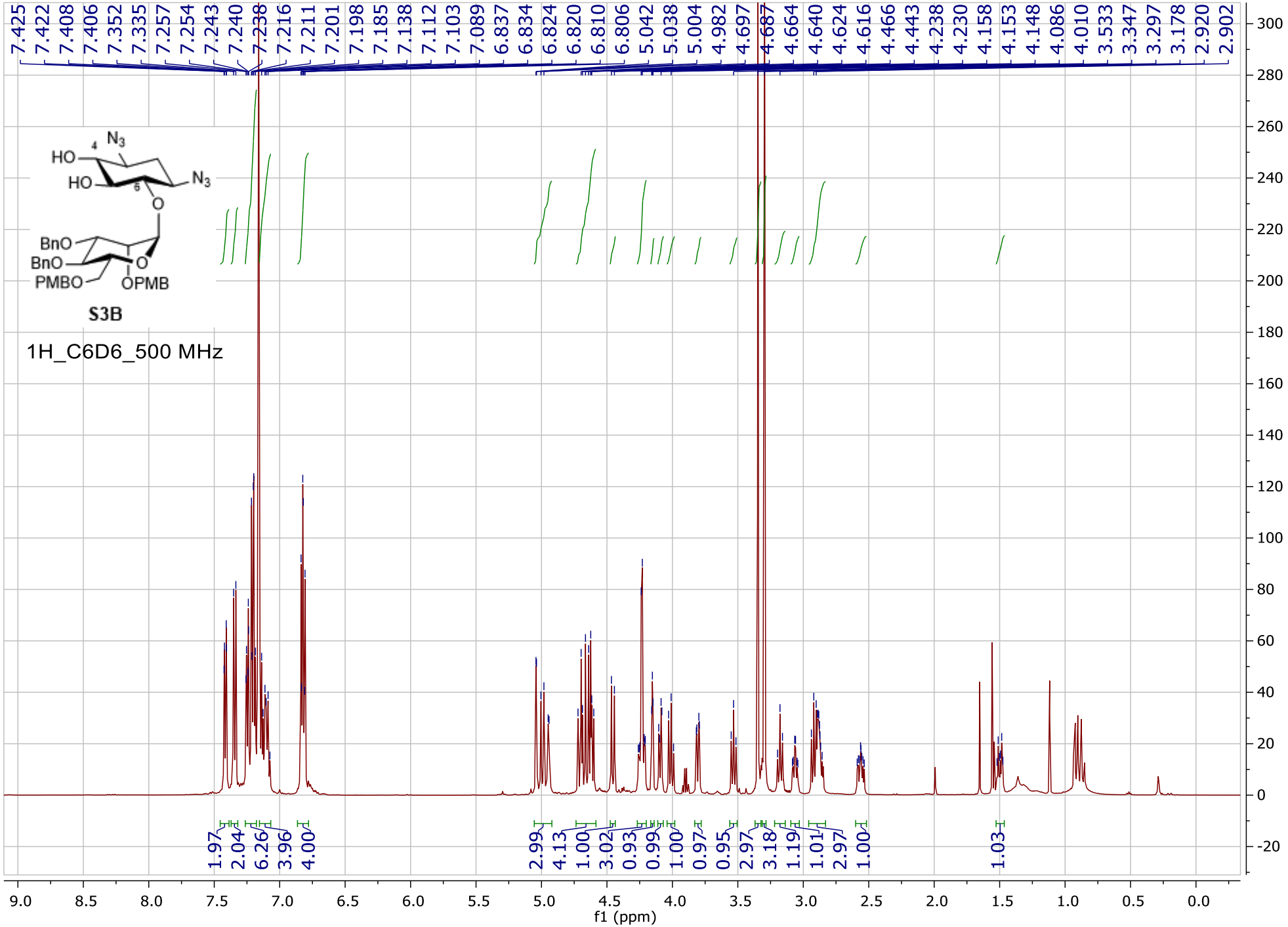
128.0
128.0
127.8
114.1
114.0
99.0
81.6
80.1
77.8
76.8
76.6
75.9
75.1
74.0
73.3
73.2
72.5
69.9
60.7
60.0
54.8
54.8
32.2
26.4
18.6
-3.2
HO
4
N3
TBSO
6
N3
O
BnO
BnO
PMBO
O
OPMB
1:2 mixture
α–3B :α–3A
13C_C6D6_175 MHz
f1 (ppm)

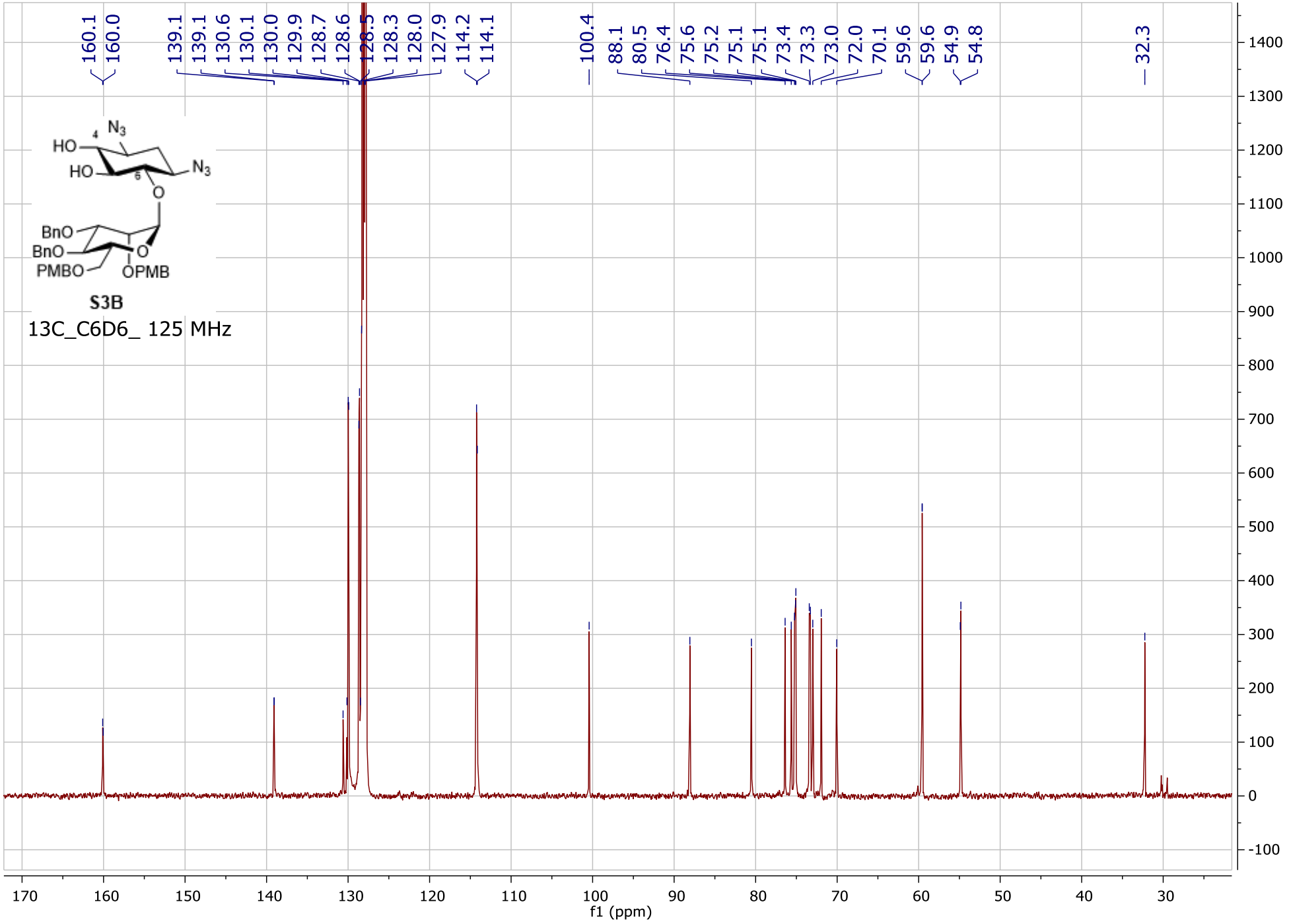

99.914
99.040
98.923
98.074
HO
TBSO
N3
N3
BnO
BnO
PMBO
OPMB
1:2 mixture
α–3B :α–3A
13C_H-coupled_C6D6_175 MHz
a–3A
a–3B
3A = 99.040 ppm and 98.074 ppm
(99.040 - 98.074) x 175 MHz = 169.05 Hz (alpha)
3B = 99.914ppm and 98.923 ppm
(99.914 - 98.923) x 175 MHz = 173.425 Hz (alpha)
f1 (ppm)

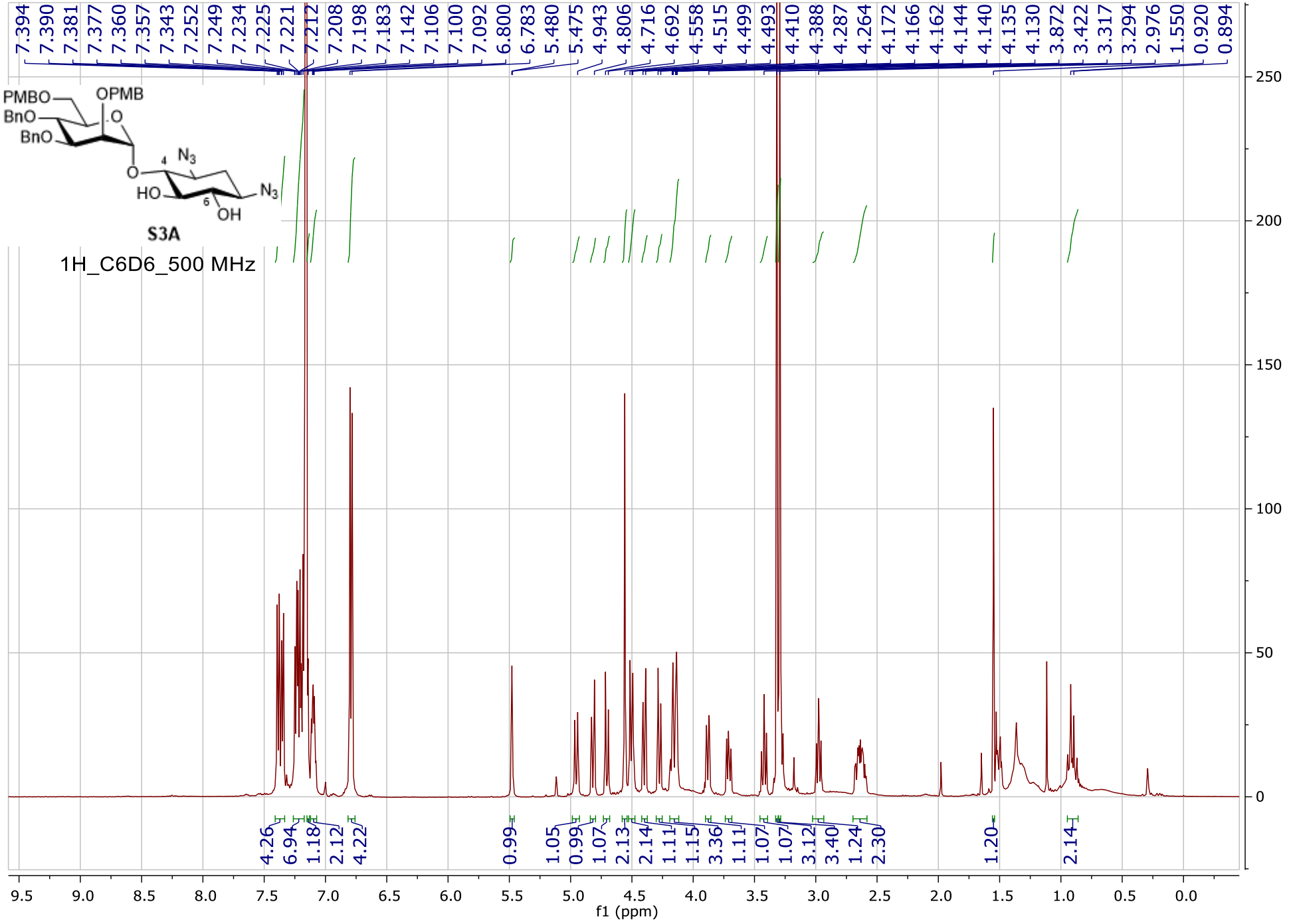

HO
4
N3
TBSO
6
N3
O
BnO
BnO
O
PMBO
OPMB
5:1 mixture
α–3B :α–3A
COSY_C6D6_700 MHz
f2 (ppm)
f1 (ppm)

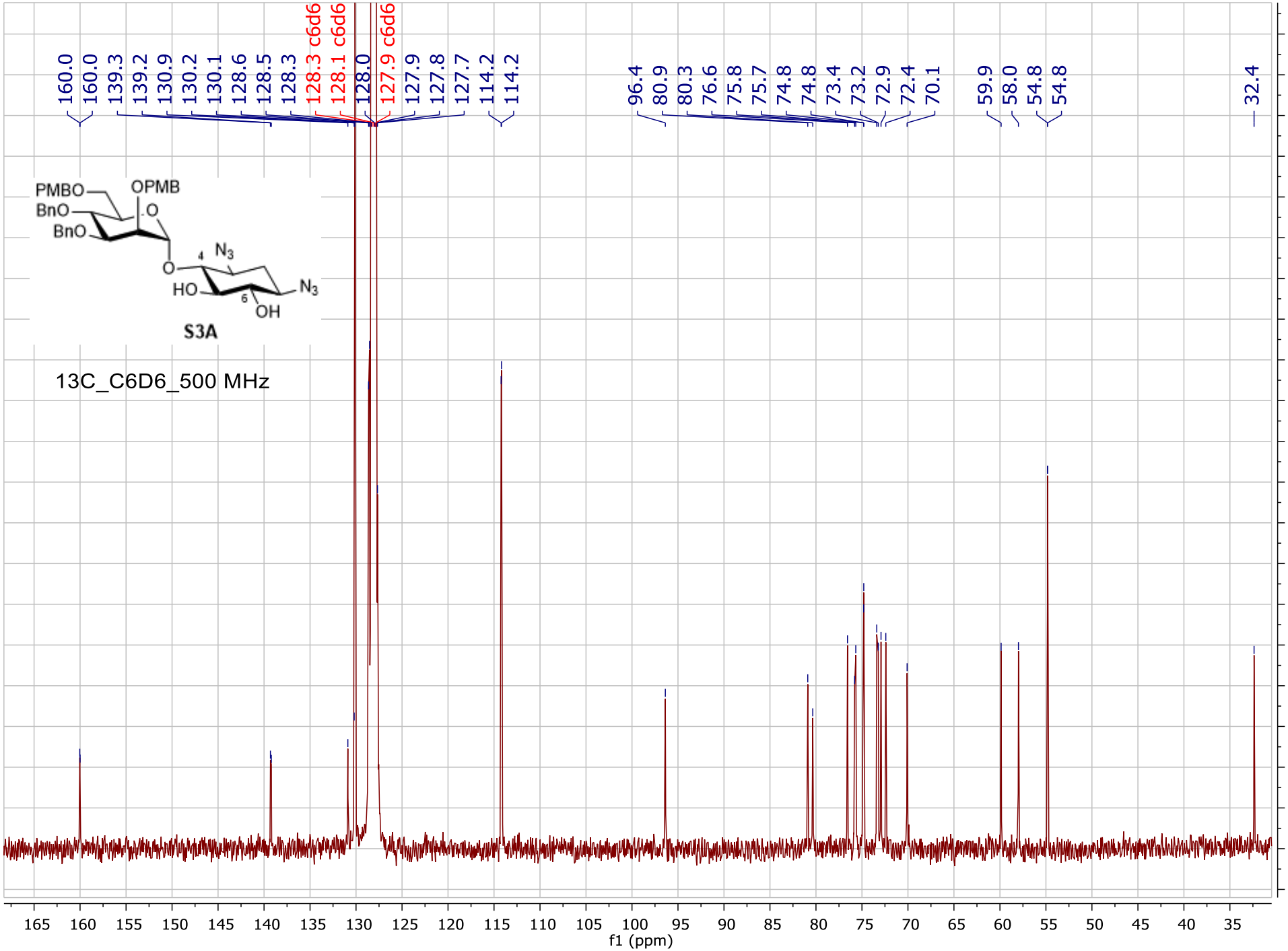

HO
TBSO
N3
N3
BnO
BnO
PMBO
OPMB
5:1 mixture
α–3B :α–3A
HMBC_C6D6_700 MHz
f2 (ppm)
f1 (ppm)

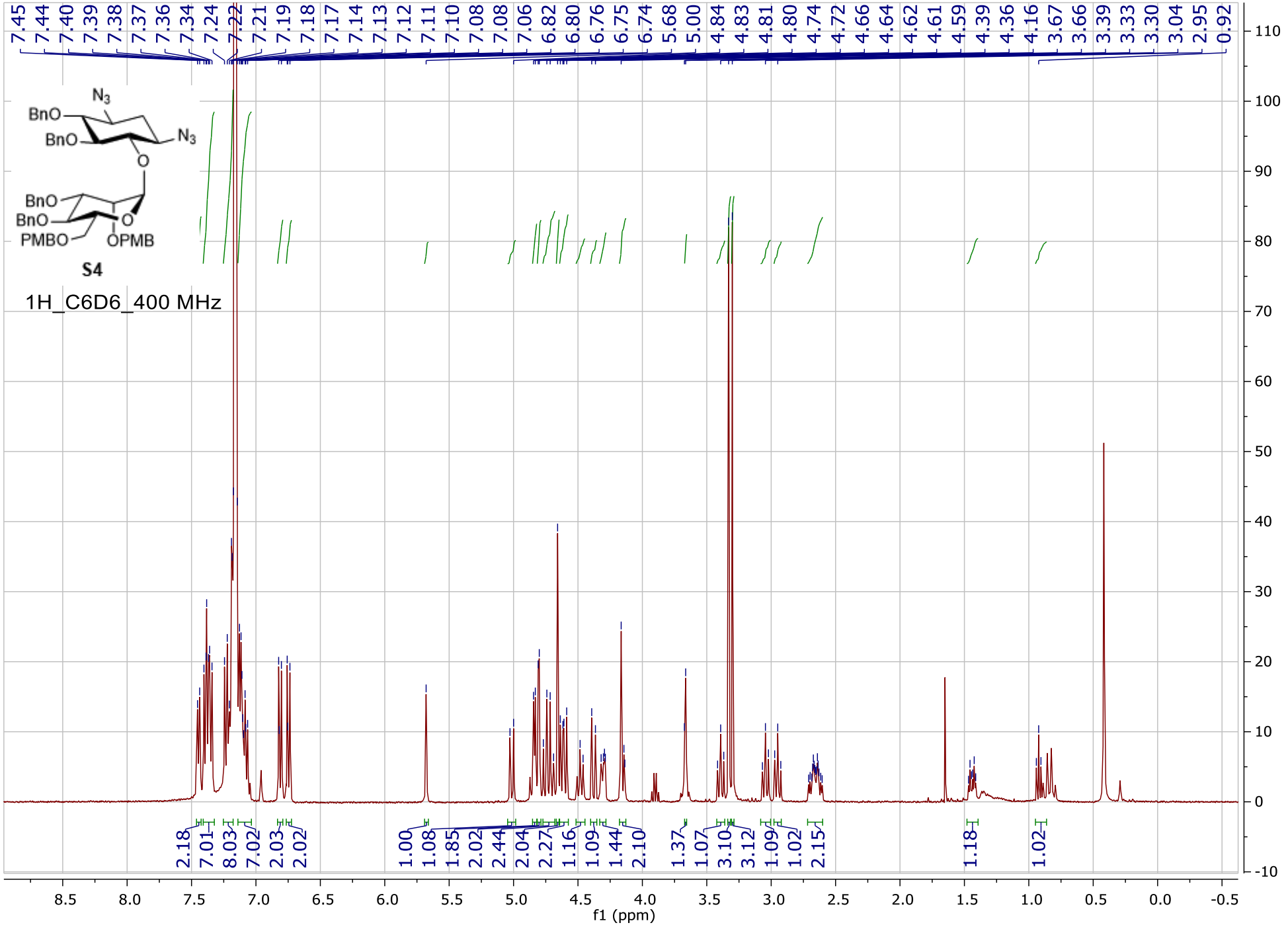

HO
TBSO
N3
N3
4
6
O
BnO
BnO
O
PMBO
OPMB
5:1 mixture
α–3B :α–3A
HSQC_C6D6_700 MHz
f2 (ppm)
f1 (ppm)

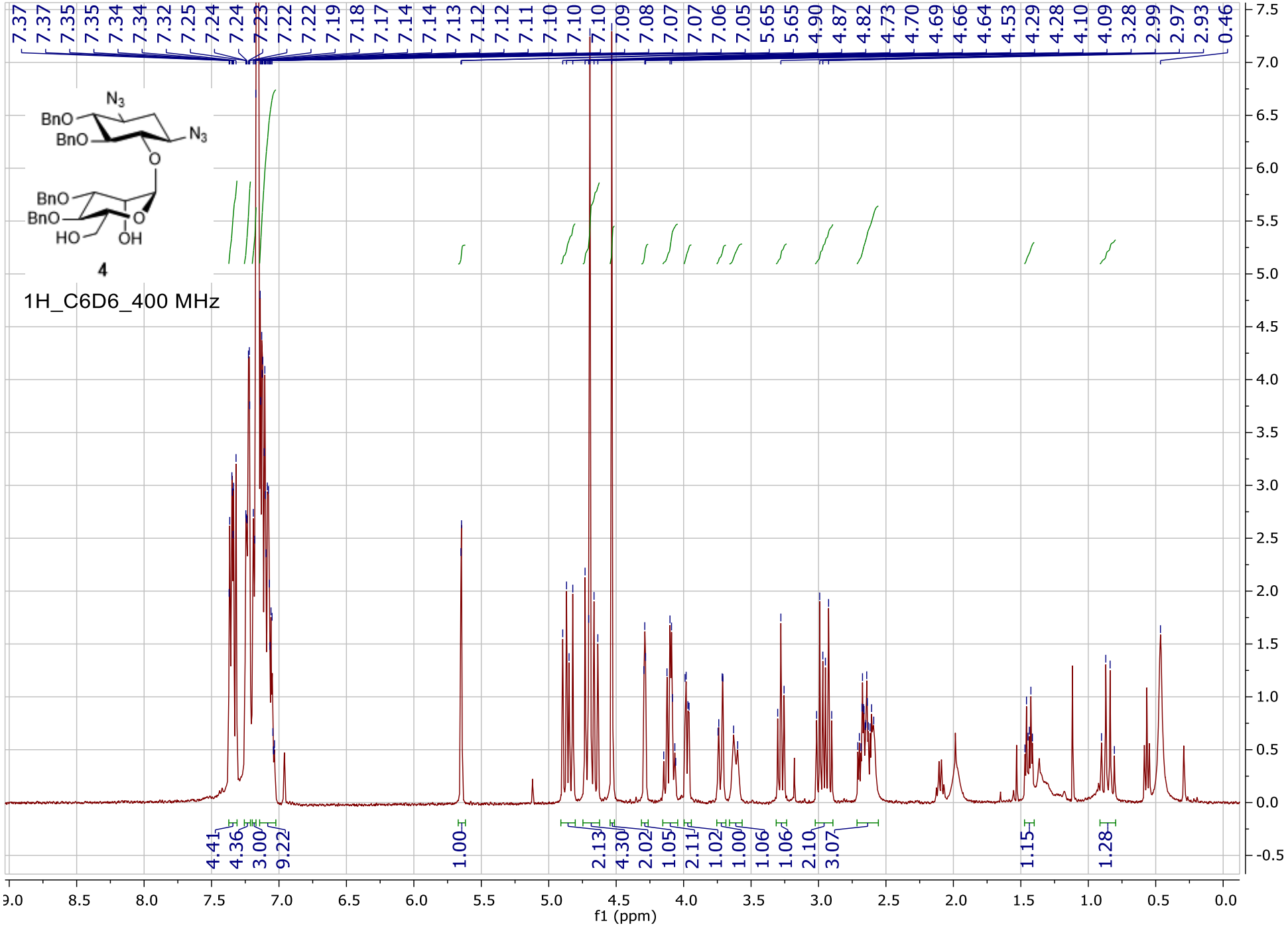

7.425 7.422 7.408 7.406 7.352 7.335 7.257 7.254 7.243 7.240 7.238 7.216 7.211 7.201 7.198 7.185 7.138 7.112 7.103 7.089 6.837 6.834 6.824 6.820 6.810 6.806 5.042 5.038 5.004 4.982 4.697 4.687 4.664 4.640 4.624 4.616 4.466 4.443 4.238 4.230 4.158 4.153 4.148 4.086 4.010 3.533 3.347 3.297 3.178 2.920 2.902
HO
4
N3
HO
6
N3
O
BnO
BnO
O
PMBO
OPMB
S3B
1H_C6D6_500 MHz
1.97 2.04 6.26 3.96 4.00 2.99 4.13 1.00 3.02 0.93 0.99 1.00 0.97 0.95 2.97 3.18 1.19 1.01 2.97 1.00 1.03
f1 (ppm)

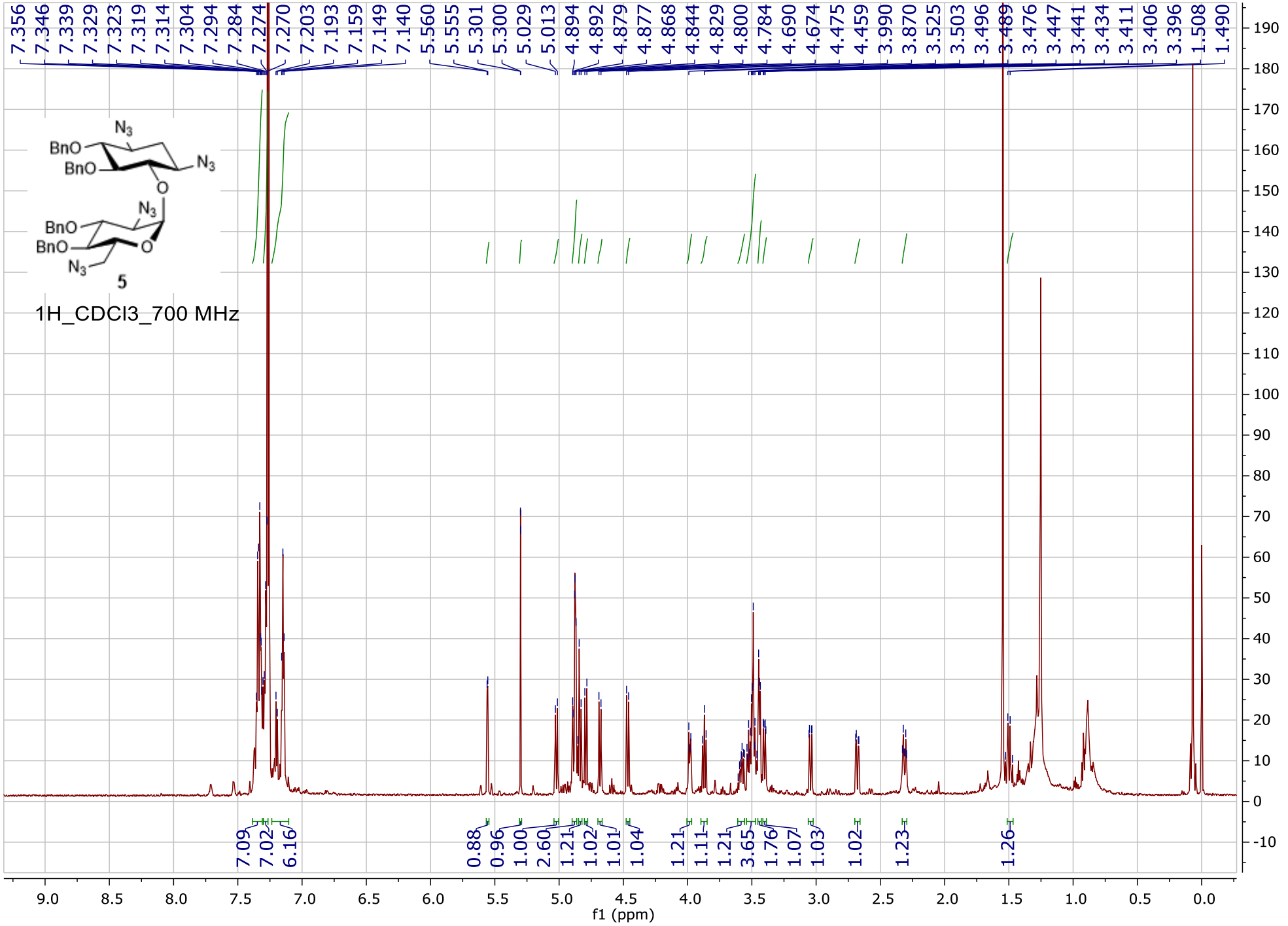

160.1
160.0
139.1
139.1
130.6
130.1
130.0
129.9
128.7
128.6
128.5
128.3
128.0
127.9
114.2
114.1
100.4
88.1
80.5
76.4
75.6
75.2
75.1
75.1
73.4
73.3
73.0
72.0
70.1
59.6
59.6
54.9
54.8
32.3
HO
HO
N3
N3
O
BnO
BnO
PMBO
O
OPMB
S3B
13C_C6D6_ 125 MHz
f1 (ppm)

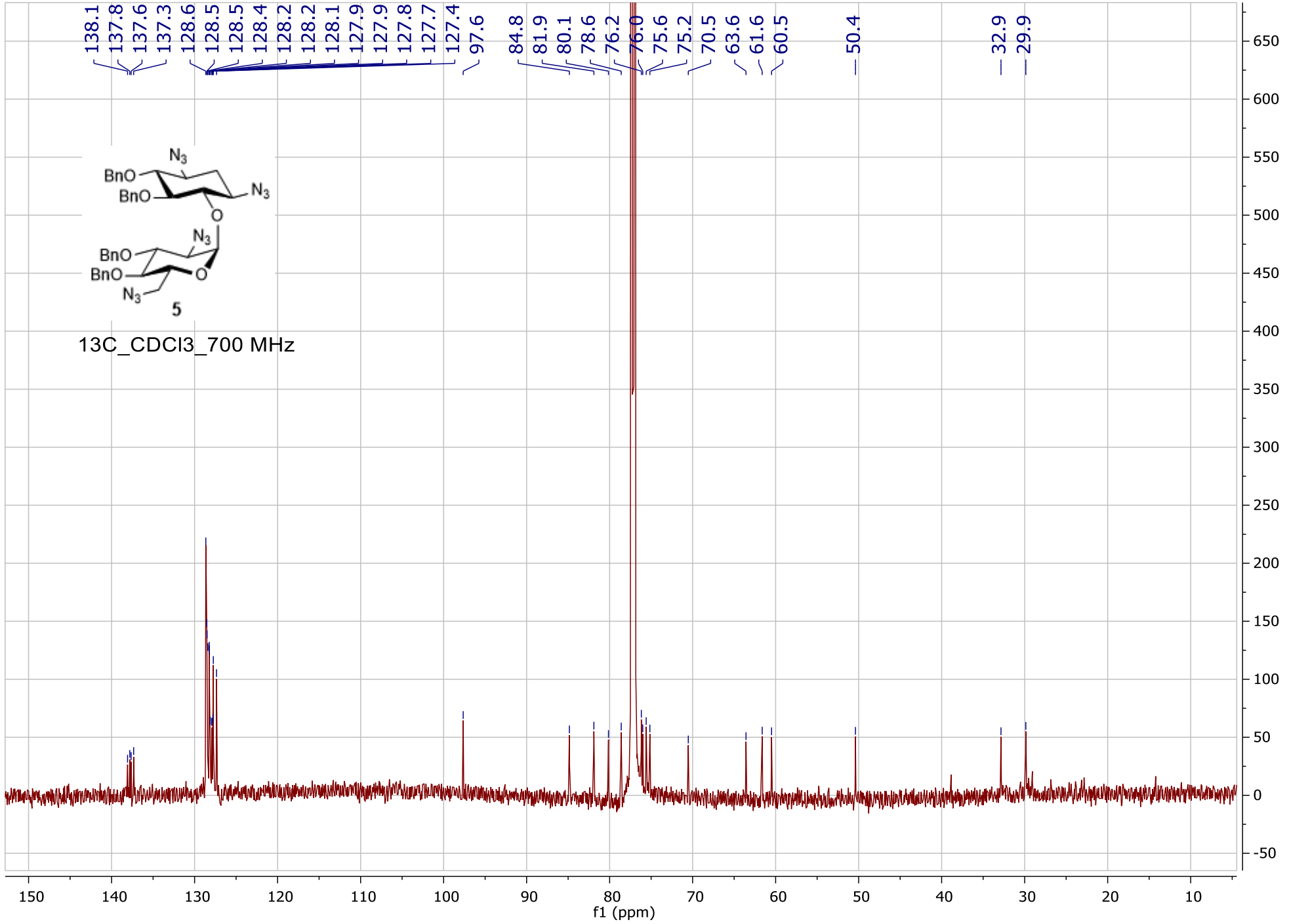

7.394
7.390
7.381
7.377
7.360
7.357
7.343
7.252
7.249
7.234
7.225
7.221
7.212
7.208
7.198
7.183
7.142
7.106
7.100
7.092
6.800
6.783
5.480
5.475
4.943
4.806
4.716
4.692
4.558
4.515
4.499
4.493
4.410
4.388
4.287
4.264
4.172
4.166
4.162
4.144
4.140
4.135
4.130
3.872
3.422
3.317
3.294
2.976
1.550
0.920
0.894
PMBO
OPMB
BnO
O
BnO
O
4
N3
HO
6
OH
N3
S3A
1H_C6D6_500 MHz
4.26
6.94
1.18
2.12
4.22
0.99
1.05
0.99
1.07
2.13
2.14
1.11
1.15
3.36
1.11
1.07
1.07
3.12
3.40
1.24
2.30
1.20
2.14
250
200
150
100
50
0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

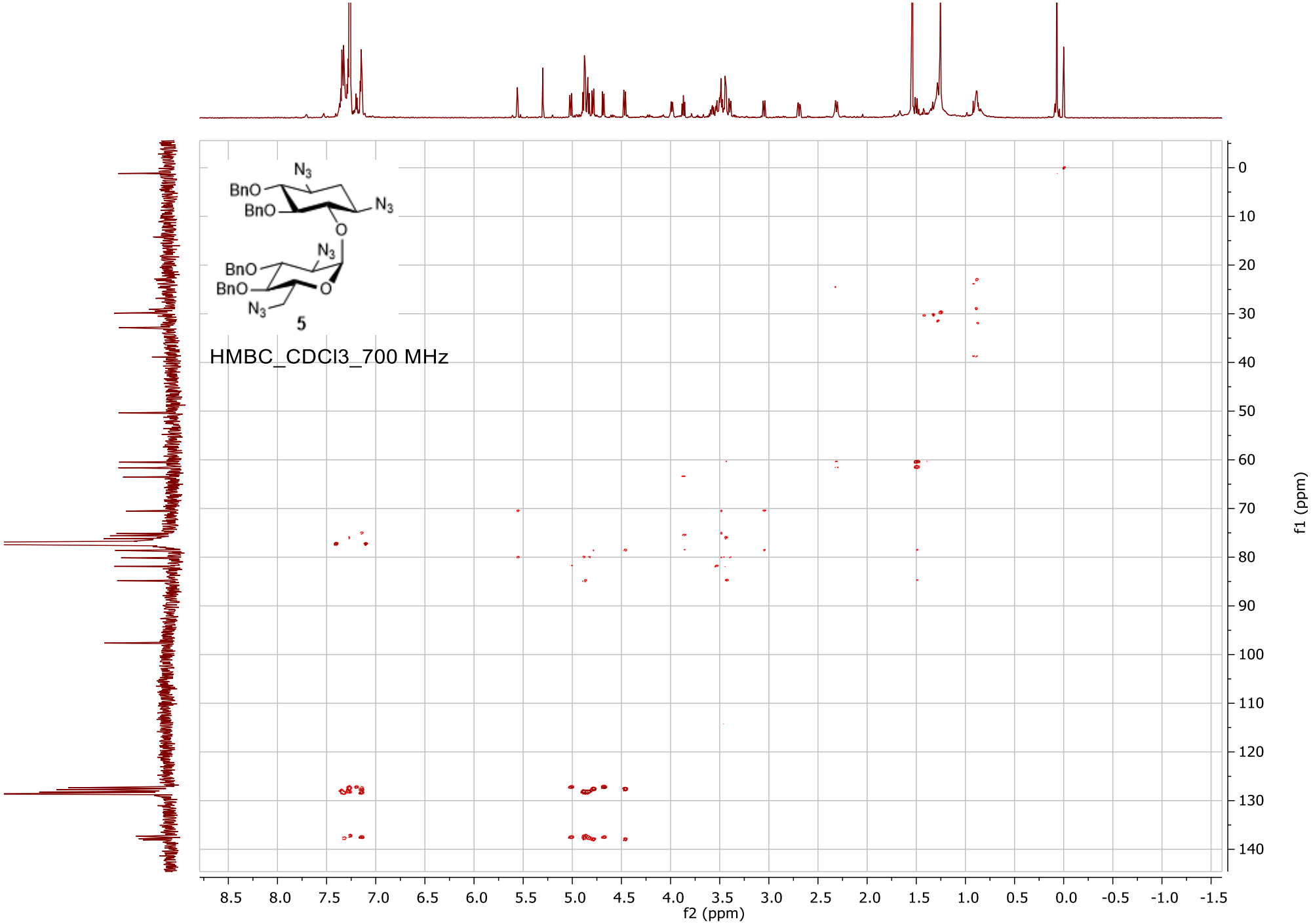

160.0
160.0
139.3
139.2
130.9
130.2
130.1
128.6
128.5
128.3
128.3 c6d6
128.1 c6d6
128.0
127.9 c6d6
127.9
127.8
127.7
114.2
114.2
96.4
80.9
80.3
76.6
75.8
75.7
74.8
74.8
73.4
73.2
72.9
72.4
70.1
59.9
58.0
54.8
54.8
32.4
PMBO
OPMB
BnO
O
BnO
4
N3
O
HO
6
N3
OH
S3A
13C_C6D6_500 MHz
f1 (ppm)

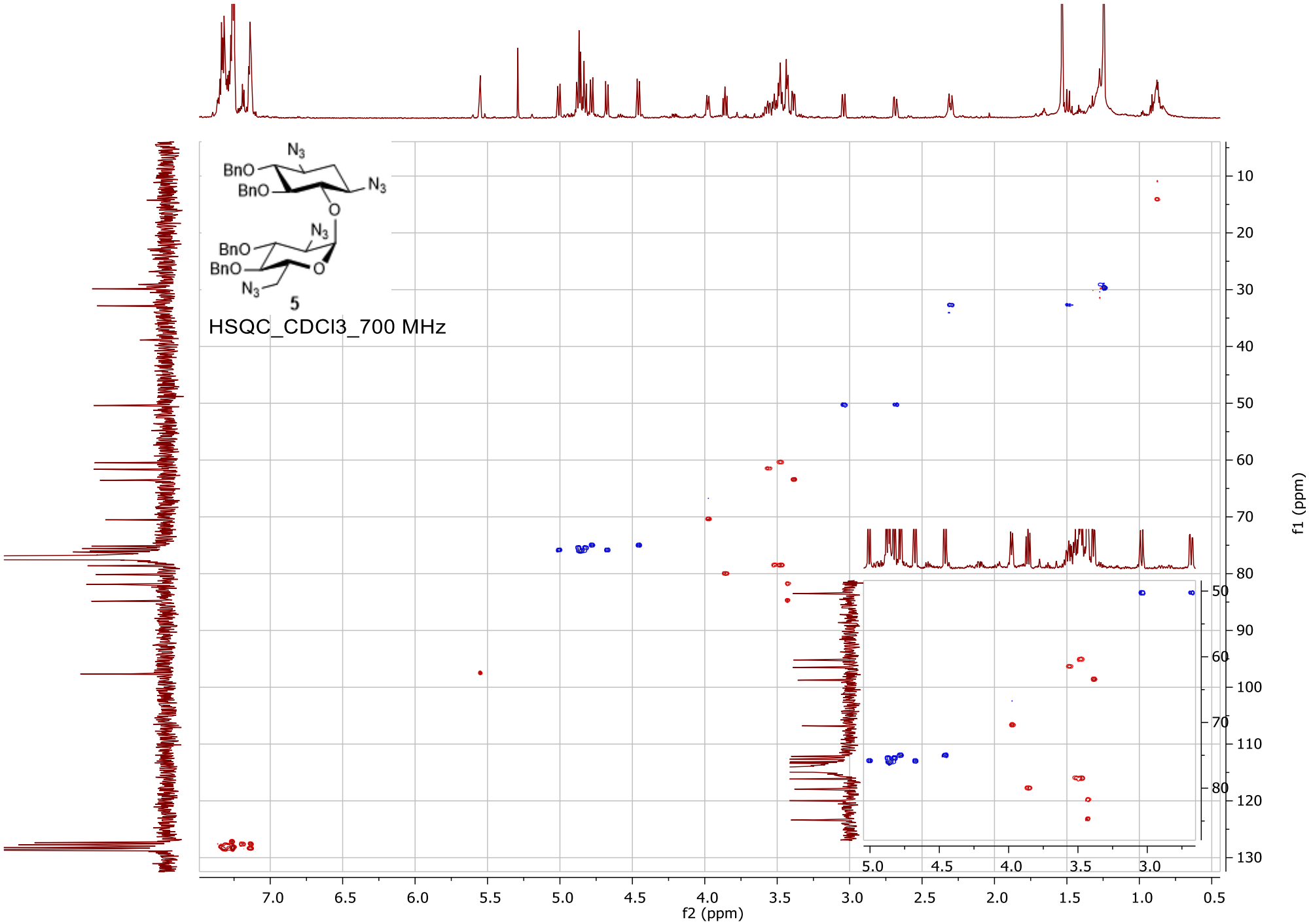

7.45 7.44 7.40 7.39 7.38 7.37 7.36 7.34 7.24 7.22 7.21 7.19 7.18 7.17 7.14 7.13 7.12 7.11 7.10 7.08 7.08 7.06 6.82 6.80 6.76 6.75 6.74 5.68 5.00 4.84 4.83 4.81 4.80 4.74 4.72 4.66 4.64 4.62 4.61 4.59 4.39 4.36 4.16 3.67 3.66 3.39 3.33 3.30 3.04 2.95 0.92
N3
BnO
BnO
N3
O
BnO
BnO
O
PMBO
OPMB
S4
1H_C6D6_400 MHz
2.18 7.01 8.03 7.02 2.03 2.02 1.00 1.08 1.85 2.02 2.44 2.04 2.27 1.16 1.09 1.44 2.10 1.37 1.07 3.10 3.12 1.09 1.02 2.15 1.18 1.02
f1 (ppm)

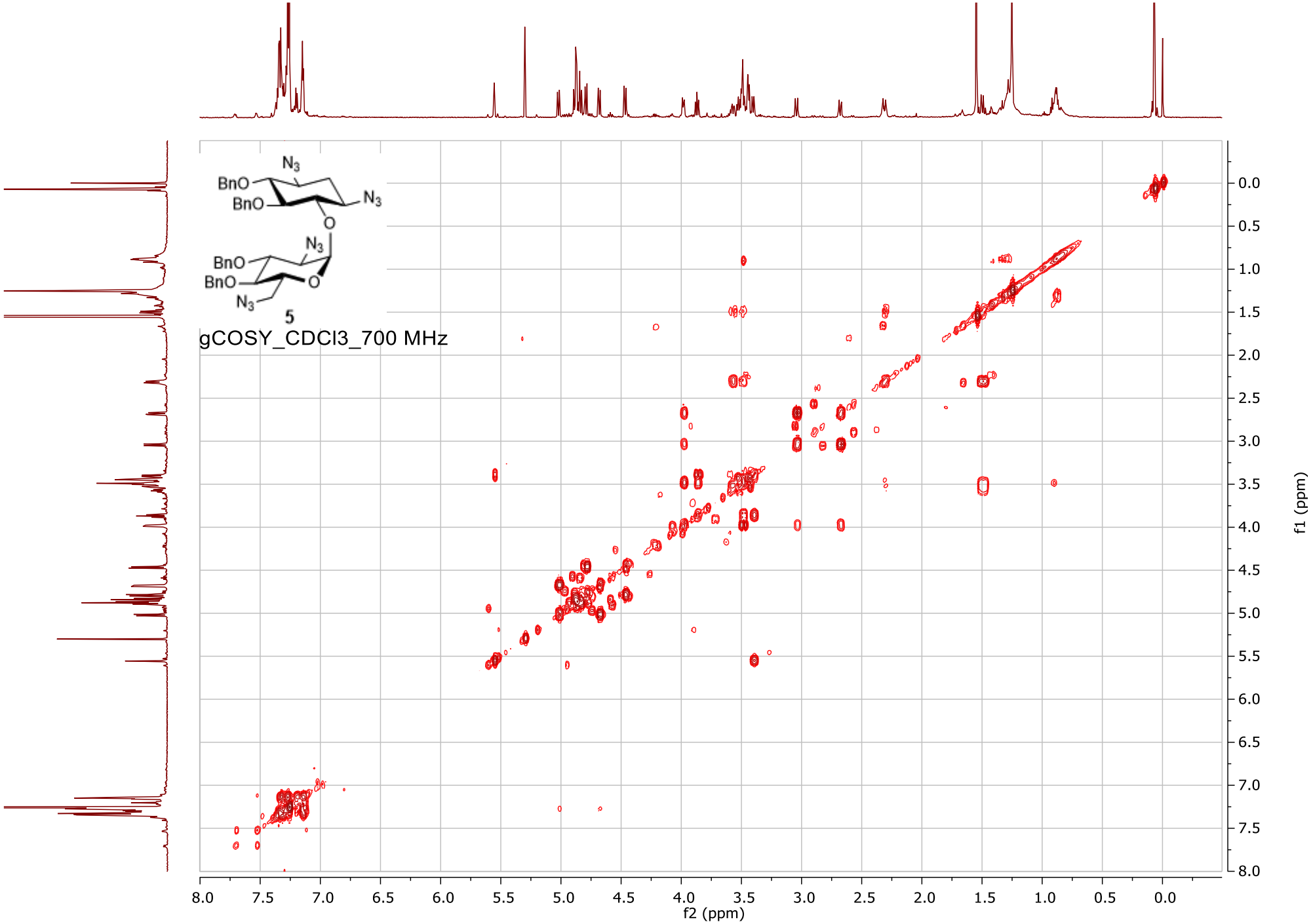

7.37 7.37 7.35 7.35 7.34 7.34 7.32 7.25 7.24 7.24 7.23 7.22 7.22 7.19 7.18 7.17 7.14 7.14 7.13 7.12 7.12 7.11 7.10 7.10 7.10 7.09 7.08 7.07 7.07 7.06 7.05 5.65 5.65 4.90 4.87 4.82 4.73 4.70 4.69 4.66 4.64 4.53 4.29 4.28 4.10 4.09 3.28 2.99 2.97 2.93 0.46
BnO
BnO
N3
N3
O
BnO
BnO
O
HO
OH
4
1H_C6D6_400 MHz
4.41 4.36 3.00 9.22 1.00 2.13 4.30 2.02 1.05 2.11 1.02 1.00 1.06 1.06 2.10 3.07 1.15 1.28
f1 (ppm)

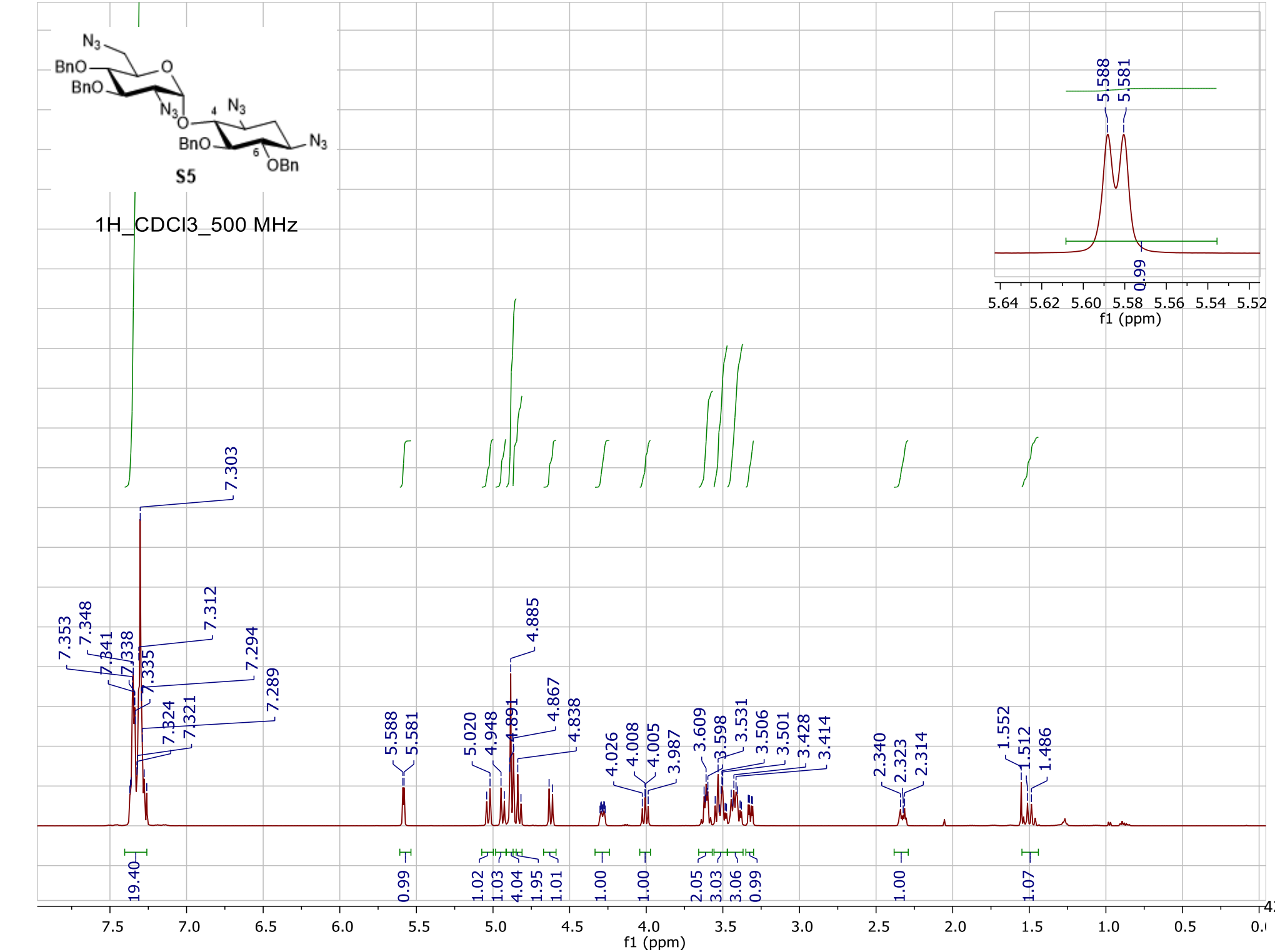

7.356 7.346 7.339 7.329 7.323 7.319 7.314 7.304 7.294 7.284 7.274 7.270 7.203 7.193 7.159 7.149 7.140 5.560 5.555 5.301 5.300 5.029 5.013 4.894 4.892 4.879 4.877 4.868 4.844 4.829 4.800 4.784 4.690 4.674 4.475 4.459 3.990 3.870 3.525 3.503 3.496 3.489 3.476 3.447 3.441 3.434 3.411 3.406 3.396 1.508 1.490
N3
BnO
BnO
N3
O
N3
BnO
BnO
O
N3
5
1H_CDCl3_700 MHz
7.09 7.02 6.16 0.88 0.96 1.00 2.60 1.21 1.02 1.01 1.04 1.21 1.11 1.21 3.65 1.76 1.07 1.03 1.02 1.23 1.26
f1 (ppm)

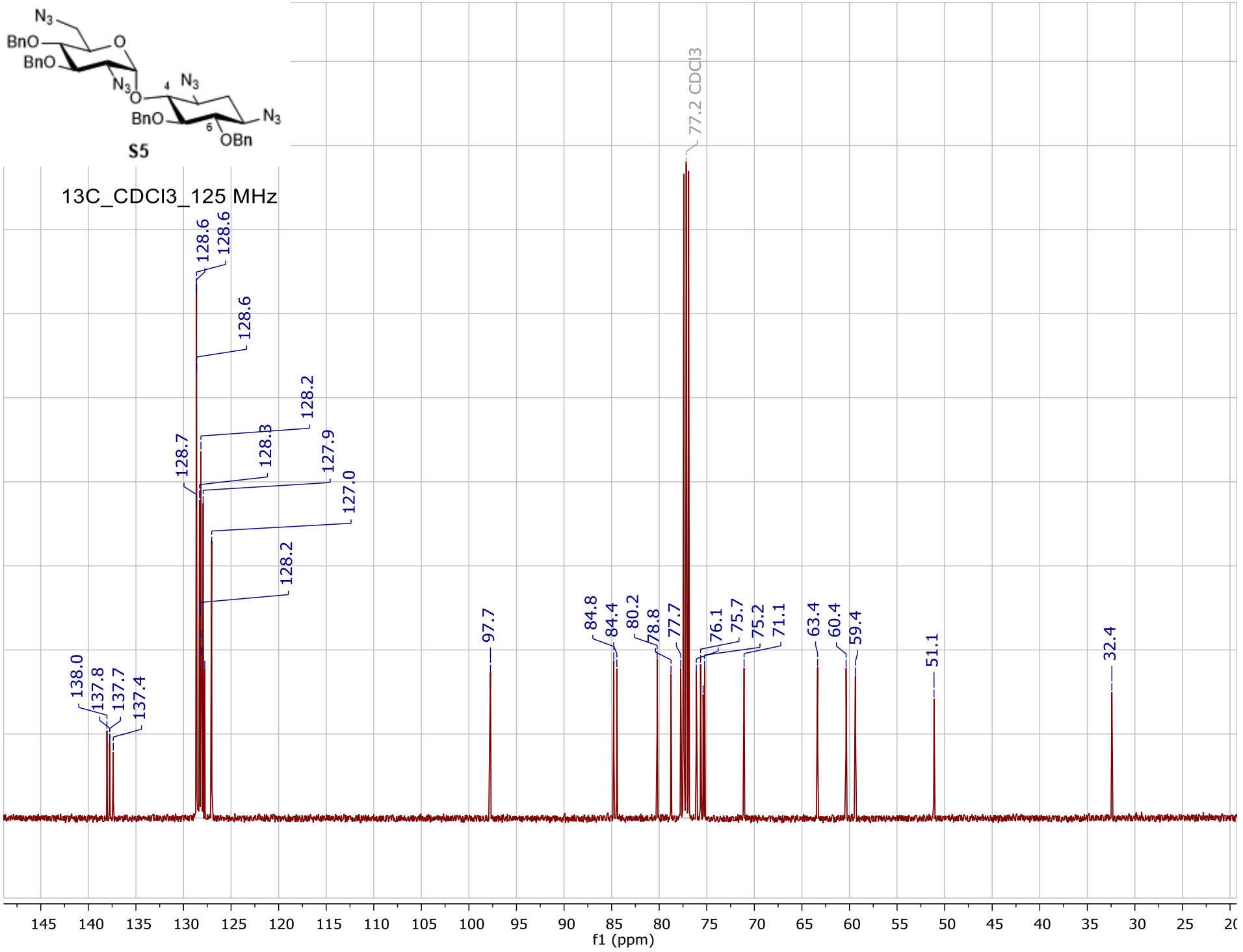

138.1
137.8
137.6
137.3
128.6
128.5
128.5
128.4
128.2
128.2
128.1
127.9
127.9
127.8
127.7
127.4
97.6
84.8
81.9
80.1
78.6
76.2
76.0
75.6
75.2
70.5
63.6
61.6
60.5
50.4
32.9
29.9
N3
BnO
BnO
N3
O
N3
BnO
BnO
O
N3
5
13C_CDCl3_700 MHz
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

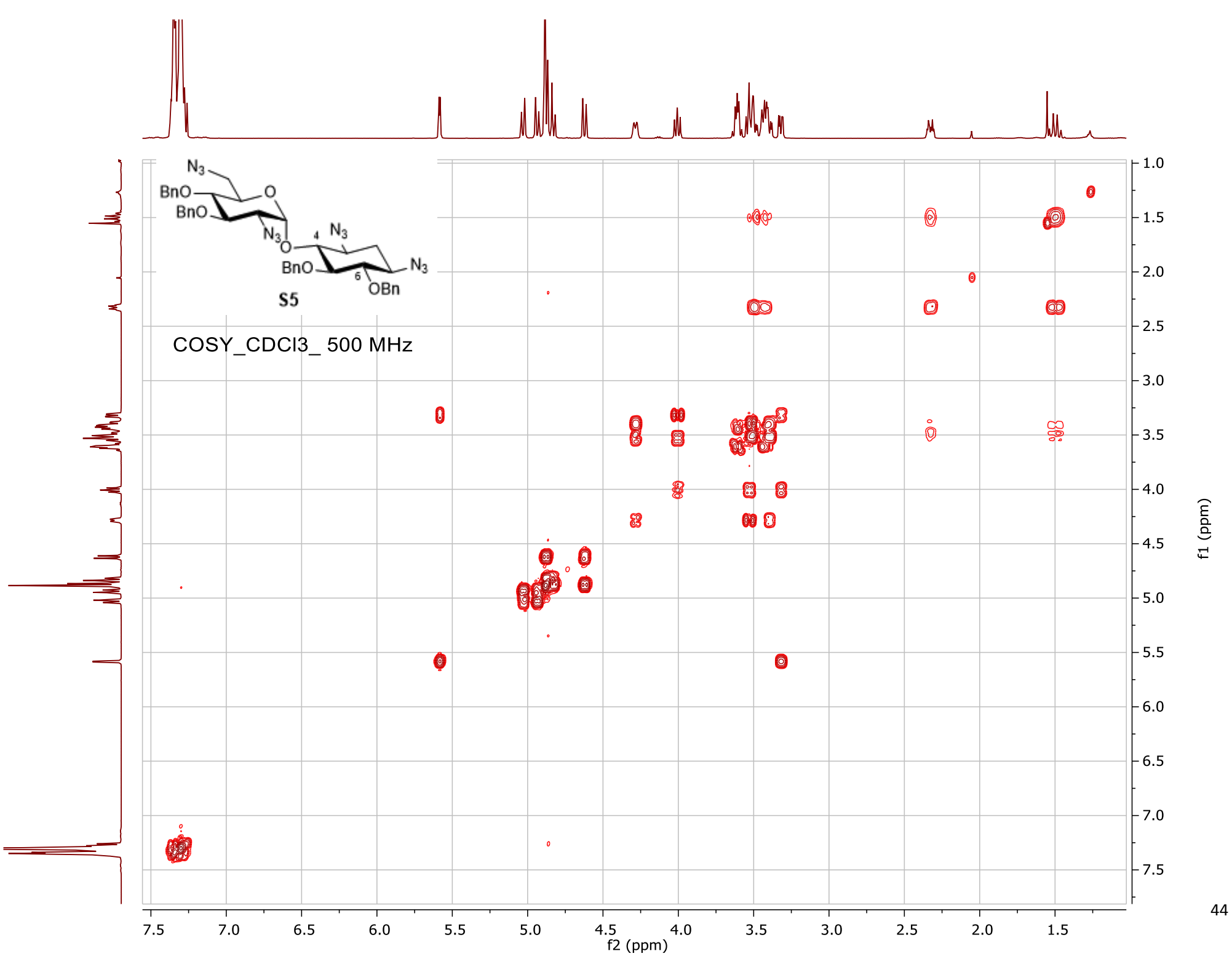

N3
BnO
BnO
N3
O
N3
BnO
BnO
O
N3
5
HMBC_CDCl3_700 MHz
f2 (ppm)
f1 (ppm)

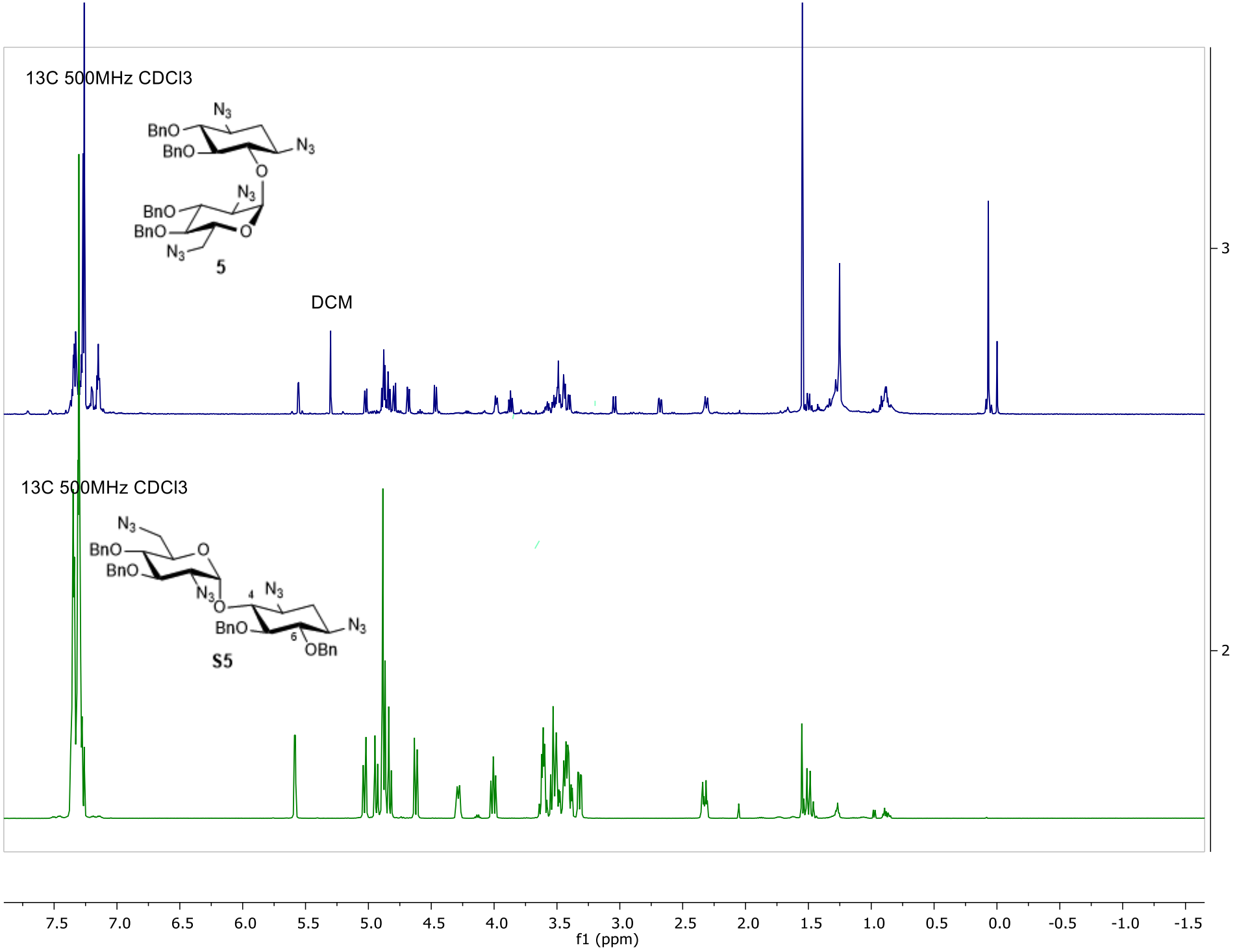

N3
BnO
BnO
N3
O
N3
BnO
BnO
O
N3
5
HSQC_CDCl3_700 MHz
f2 (ppm)
f1 (ppm)

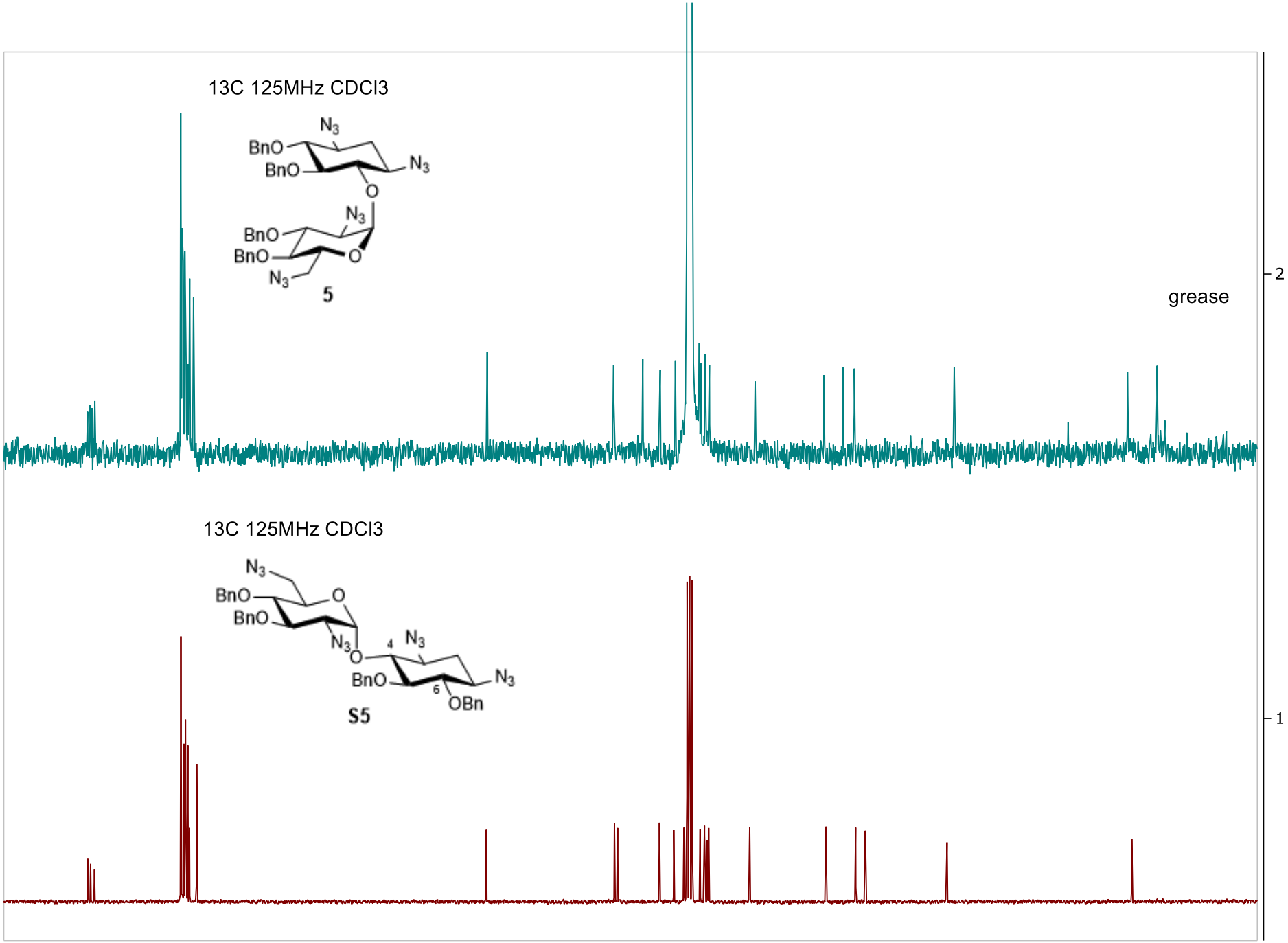

N3
BnO
BnO
N3
O
N3
BnO
BnO
O
N3
5
gCOSY_CDCl3_700 MHz
f2 (ppm)
f1 (ppm)

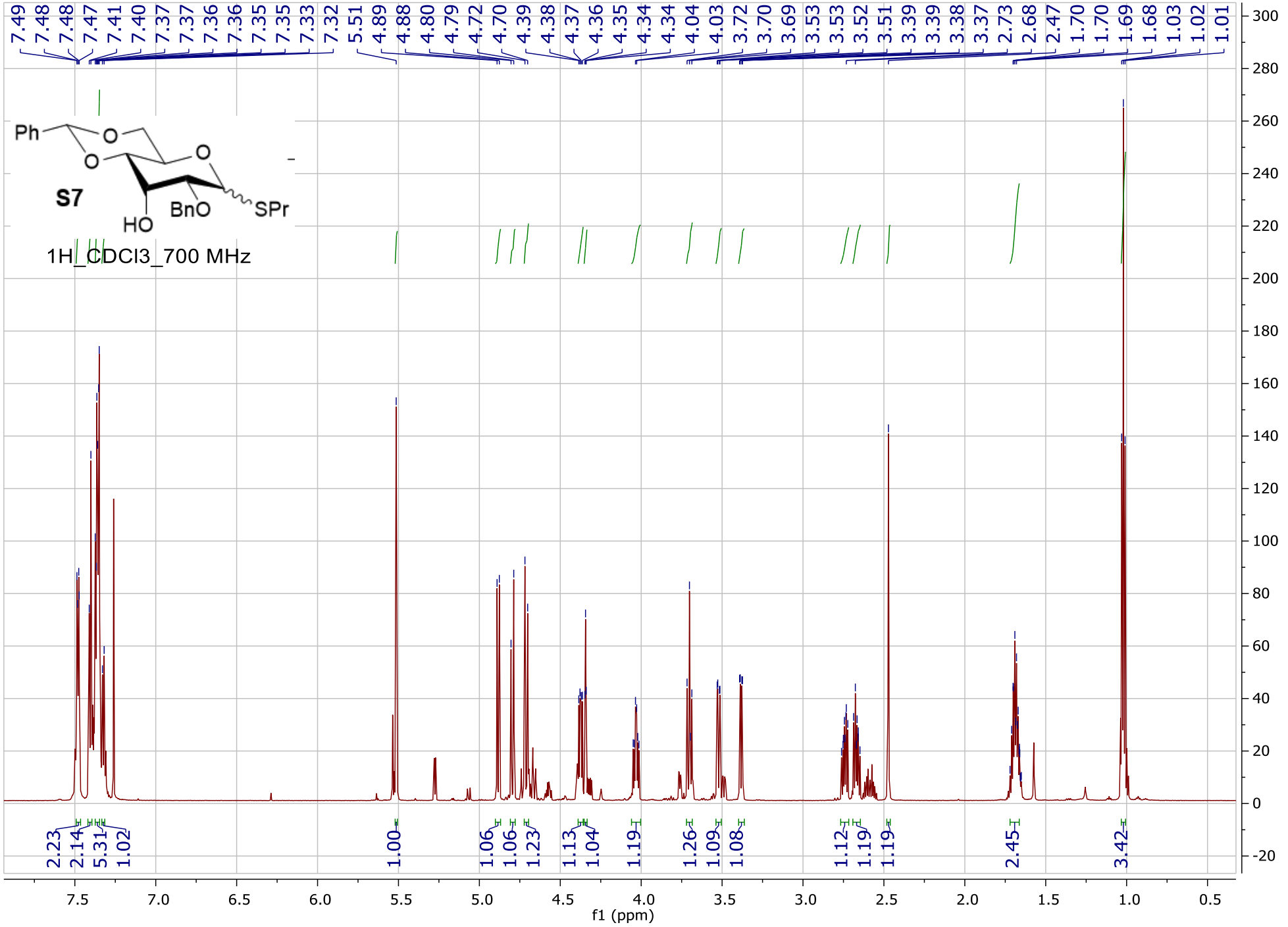

S5
1H_CDCl3_500 MHz
7.303
7.353
7.348
7.341
7.338
7.335
7.312
7.294
7.289
7.324
7.321
5.588
5.581
5.020
4.948
4.891
4.885
4.867
4.838
4.026
4.008
4.005
3.987
3.609
3.598
3.531
3.506
3.501
3.428
3.414
2.340
2.323
2.314
1.552
1.512
1.486
19.40
0.99
1.02
1.03
4.04
1.95
1.01
1.00
1.00
2.05
3.03
3.06
0.99
1.00
1.07
f1 (ppm)
5.588
5.581
0.99
5.64 5.62 5.60 5.58 5.56 5.54 5.52
f1 (ppm)

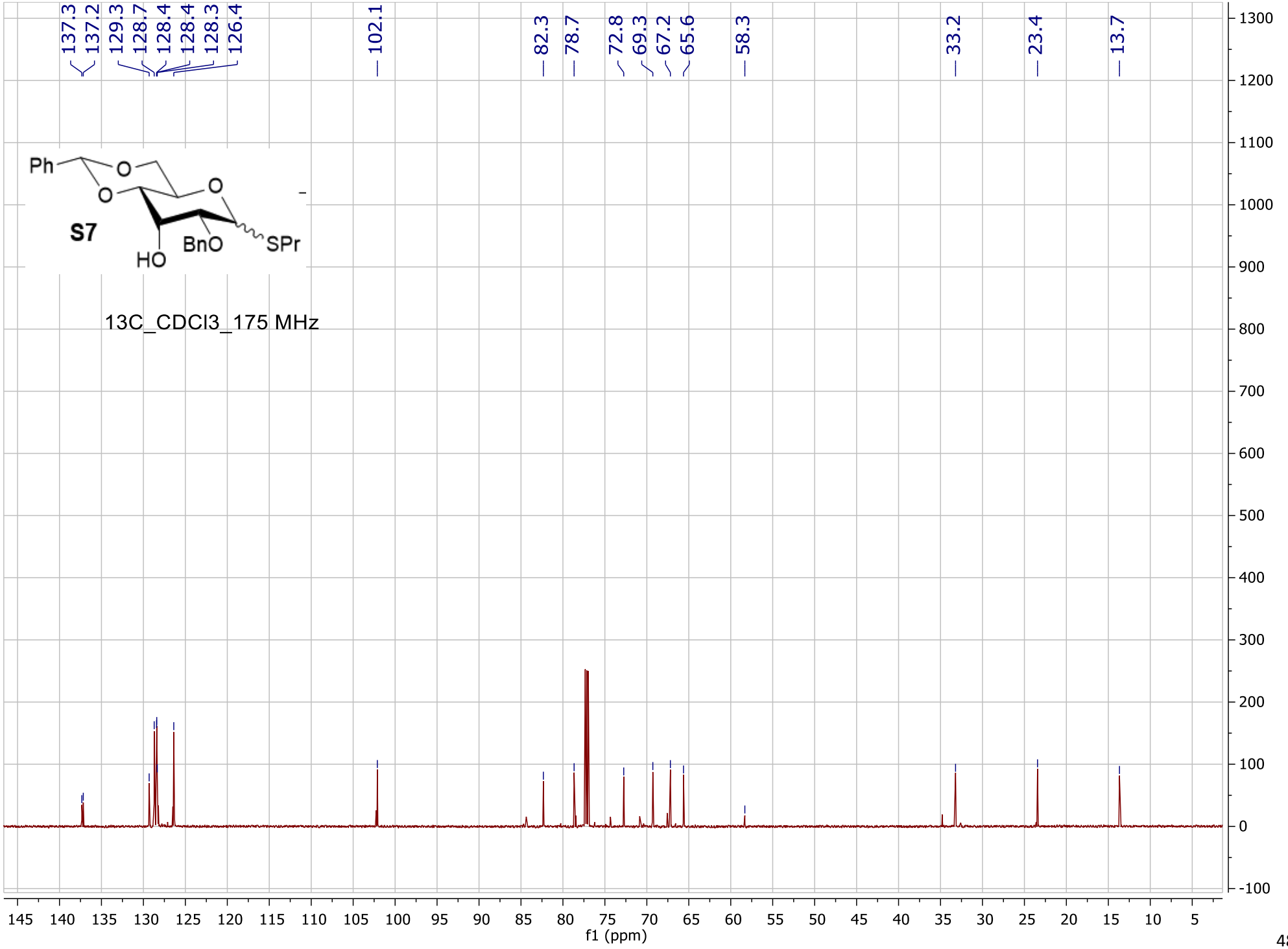

S5
13C_CDCl3_125 MHz
77.2 CDCl3
128.6
128.6
128.6
128.2
128.3
128.7
127.9
127.0
128.2
138.0
137.8
137.7
137.4
97.7
84.8
84.4
80.2
78.8
77.7
76.1
75.7
75.2
71.1
63.4
60.4
59.4
51.1
32.4
f1 (ppm)

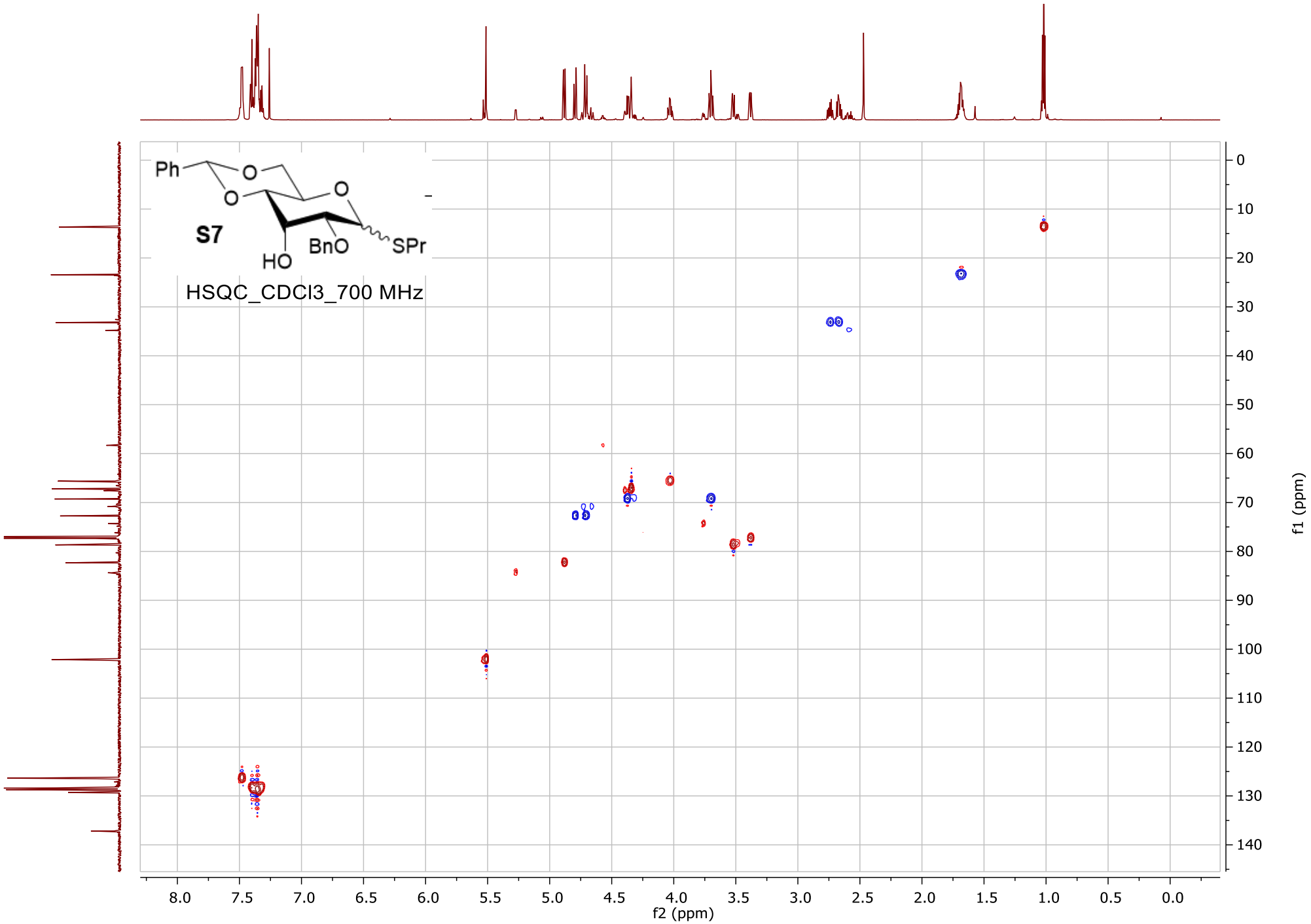

S5
COSY_CDCl3_ 500 MHz
f2 (ppm)
f1 (ppm)

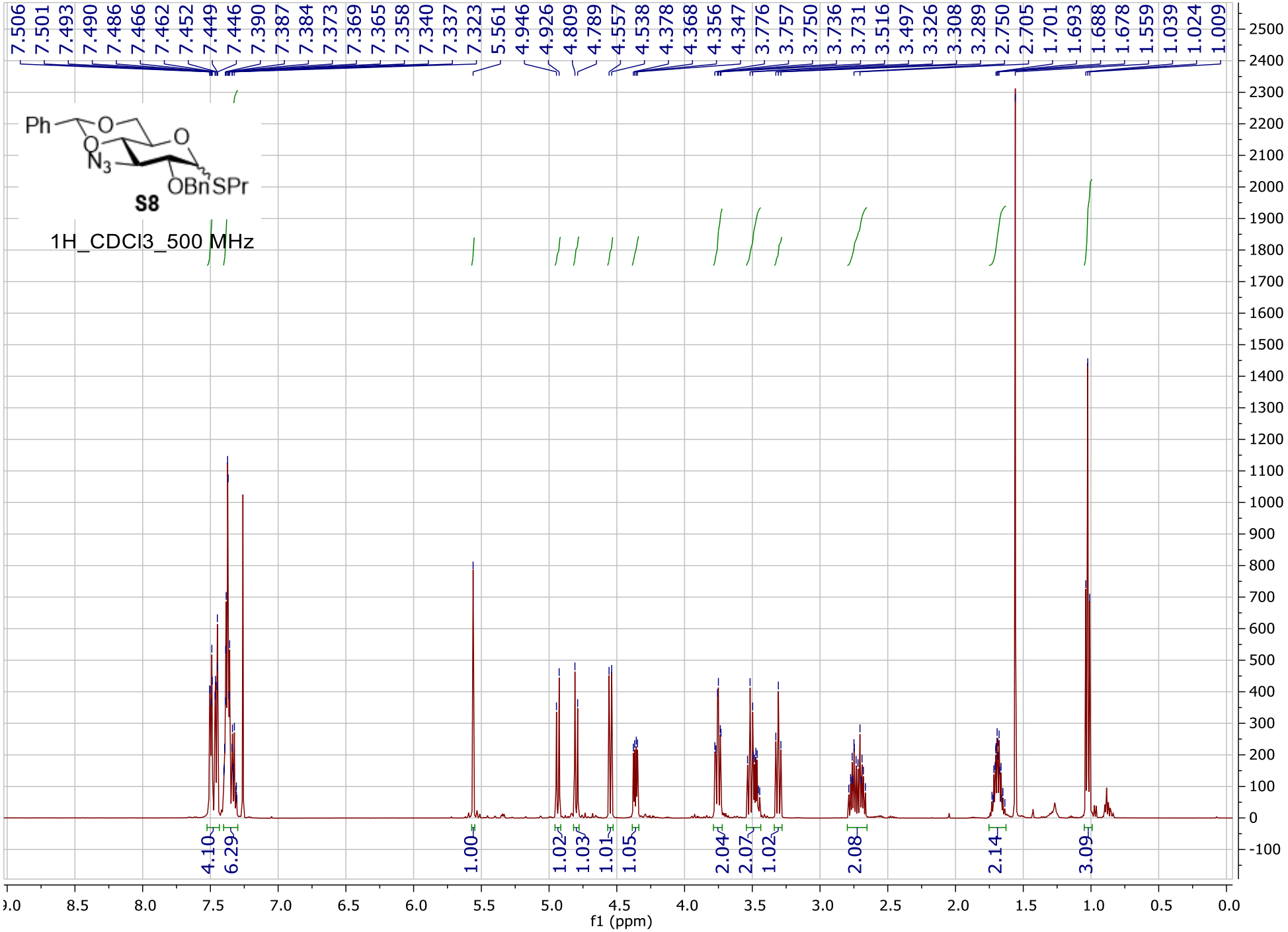

13C 500MHz CDCl3
BnO
BnO
N3
N3
O
BnO
BnO
N3
N3
O
5
DCM
3
13C 500MHz CDCl3
N3
BnO
BnO
O
N3
O
4
N3
BnO
6
N3
OBn
S5
2
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
f1 (ppm)

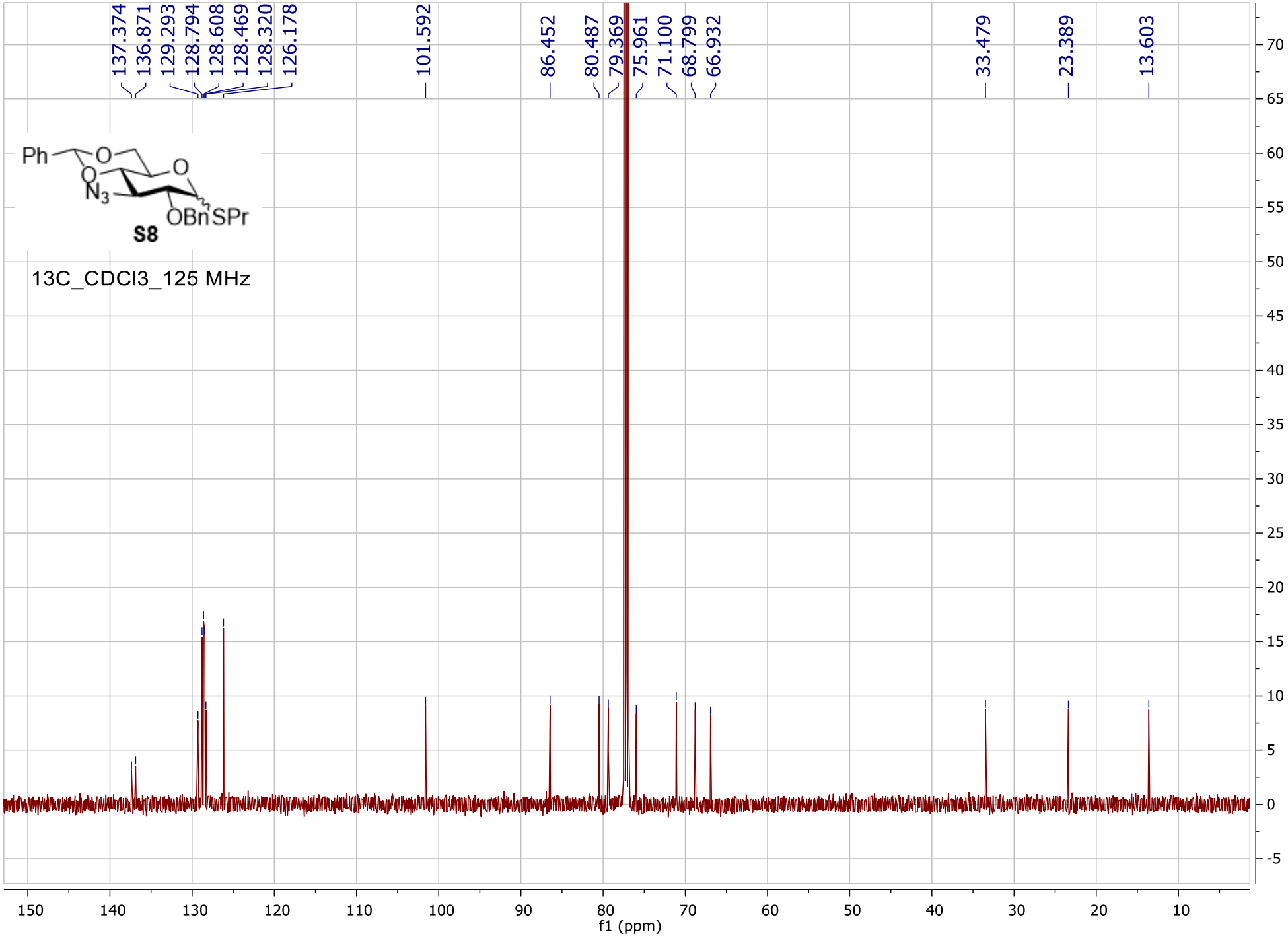

13C 125MHz CDCl3
BnO
BnO
N3
N3
O
BnO
BnO
N3
N3
O
5
grease
2
13C 125MHz CDCl3
N3
BnO
BnO
O
N3
O
4
N3
BnO
6
OBn
N3
S5
1
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)

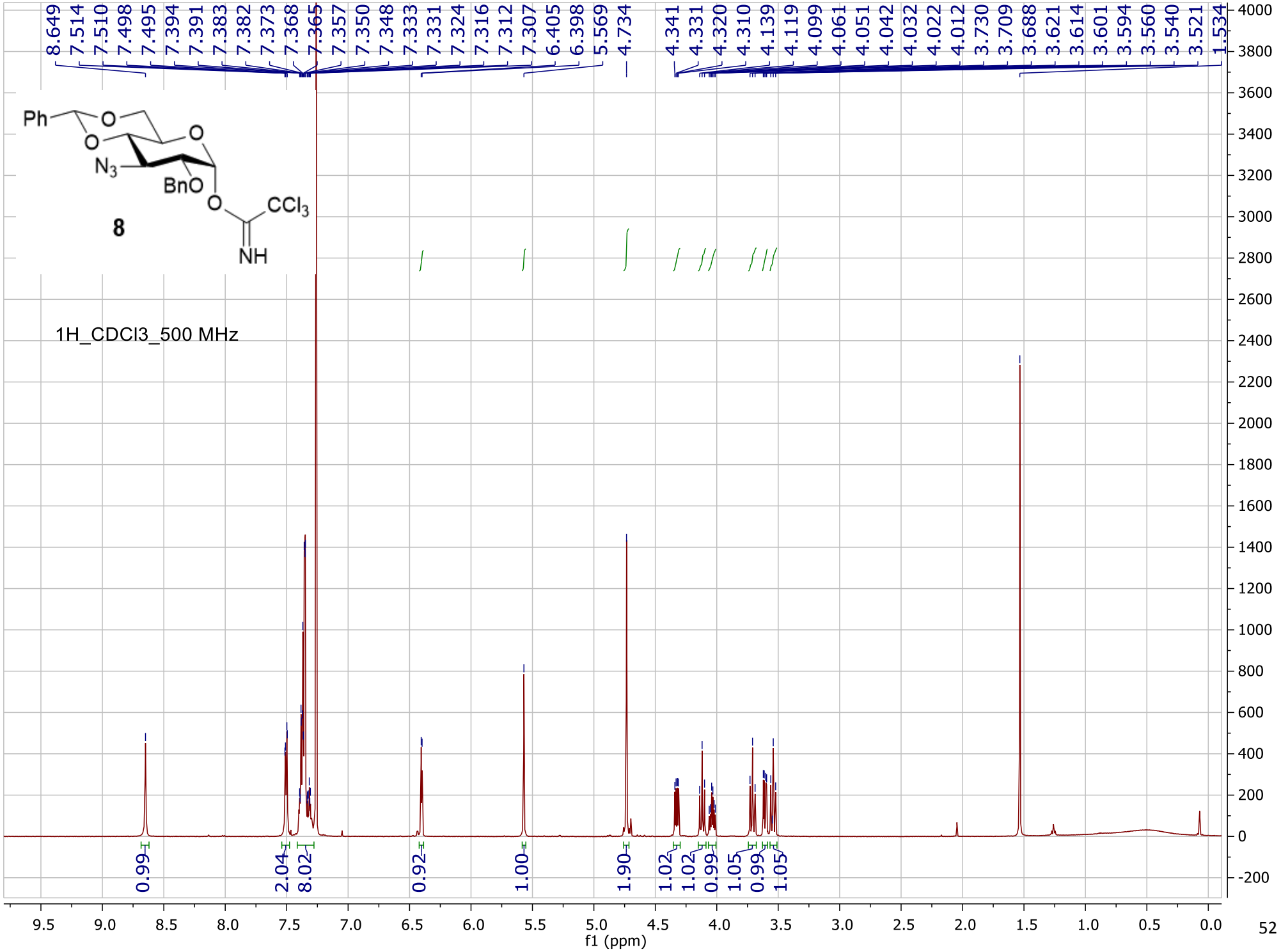

7.49 7.48 7.48 7.47 7.41 7.40 7.37 7.37 7.36 7.36 7.35 7.35 7.33 7.32 5.51 4.89 4.88 4.80 4.79 4.72 4.70 4.39 4.38 4.37 4.36 4.35 4.34 4.34 4.04 4.03 3.72 3.70 3.69 3.53 3.53 3.52 3.51 3.39 3.39 3.38 3.37 2.73 2.68 2.47 1.70 1.70 1.69 1.68 1.03 1.02 1.01
Ph
O
O
O
S7
BnO
SPr
HO
1H_CDCl3_700 MHz
2.23 2.14 5.31 1.02 1.00 1.06 1.06 1.23 1.13 1.04 1.19 1.26 1.09 1.08 1.12 1.19 1.19 2.45 3.42
f1 (ppm)

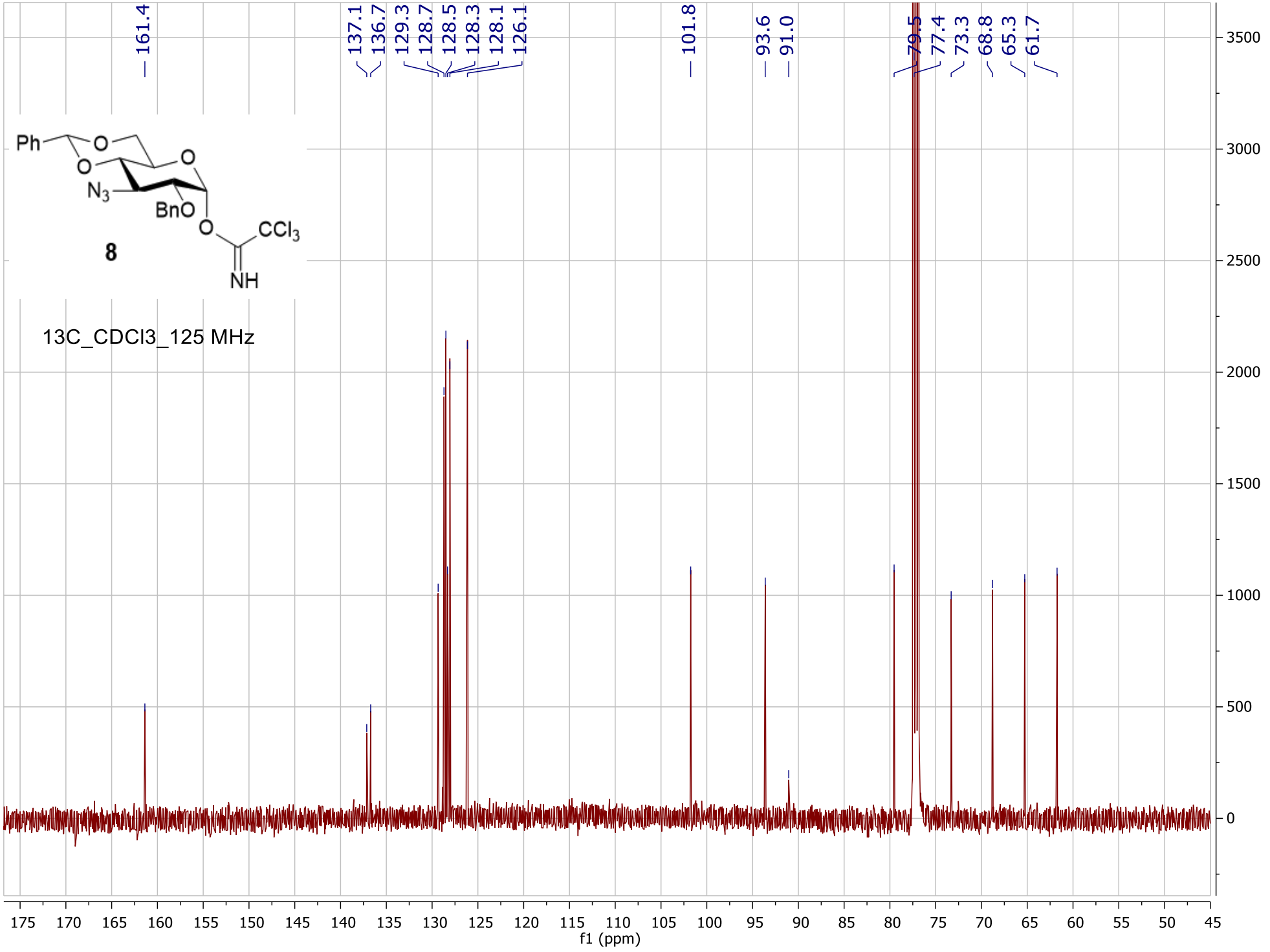

137.3
137.2
129.3
128.7
128.4
128.4
128.3
126.4
102.1
82.3
78.7
72.8
69.3
67.2
65.6
58.3
33.2
23.4
13.7
Ph
O
O
O
S7
HO
BnO
SPr
13C_CDCl3_175 MHz
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5
f1 (ppm)


Ph
O
O
O
S7
HO
BnO
SPr
HSQC_CDCl3_700 MHz
f2 (ppm)
f1 (ppm)

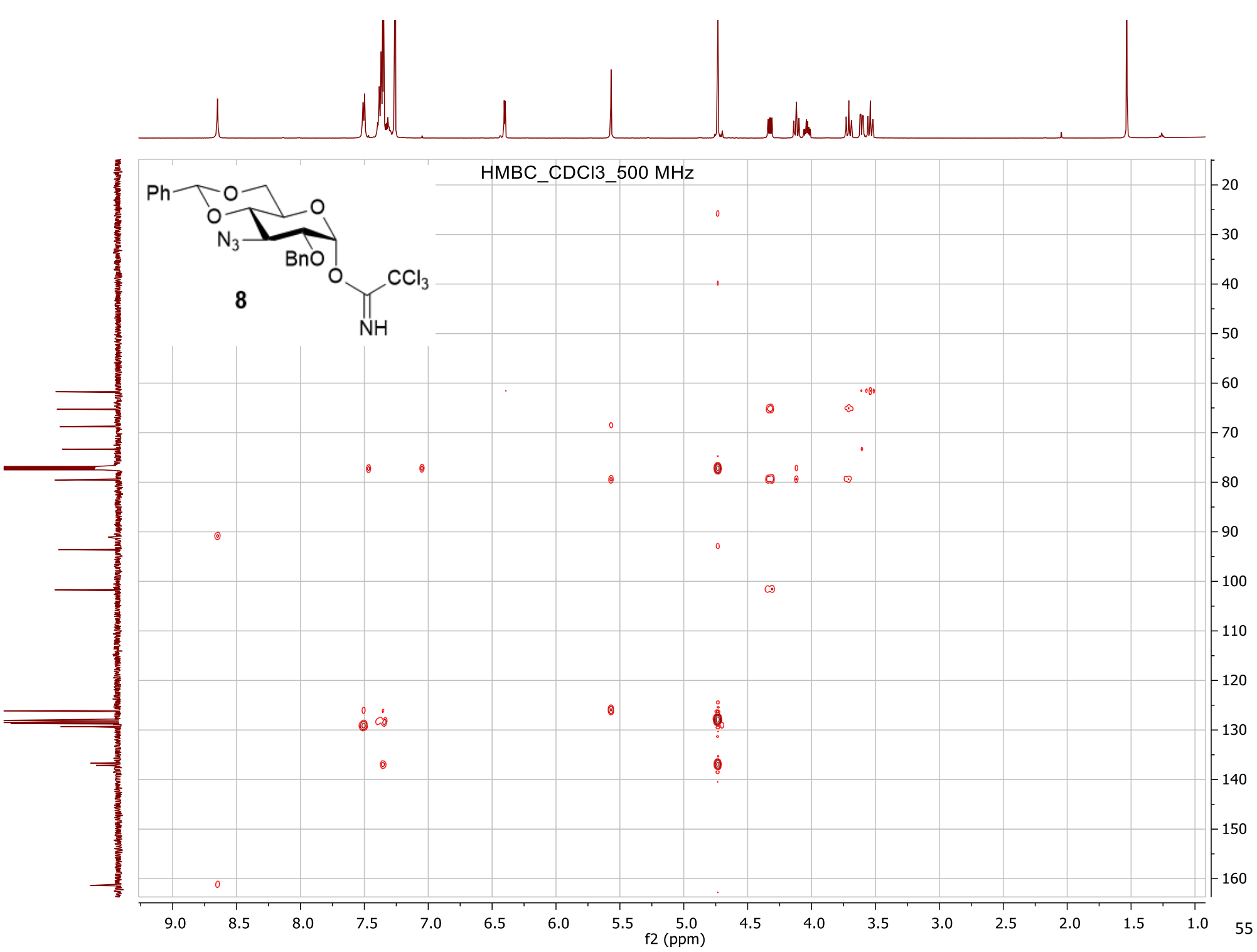

7.506
7.501
7.493
7.490
7.486
7.466
7.462
7.452
7.449
7.446
7.390
7.387
7.384
7.373
7.369
7.365
7.358
7.340
7.337
7.323
5.561
4.946
4.926
4.809
4.789
4.557
4.538
4.378
4.368
4.356
4.347
3.776
3.757
3.750
3.736
3.731
3.516
3.497
3.326
3.308
3.289
2.750
2.705
1.701
1.693
1.688
1.678
1.559
1.039
1.024
1.009
Ph
O
O
O
N3
OBn
SPr
S8
1H_CDCl3_500 MHz
4.10
6.29
1.00
1.02
1.03
1.01
1.05
2.04
2.07
1.02
2.08
2.14
3.09
f1 (ppm)

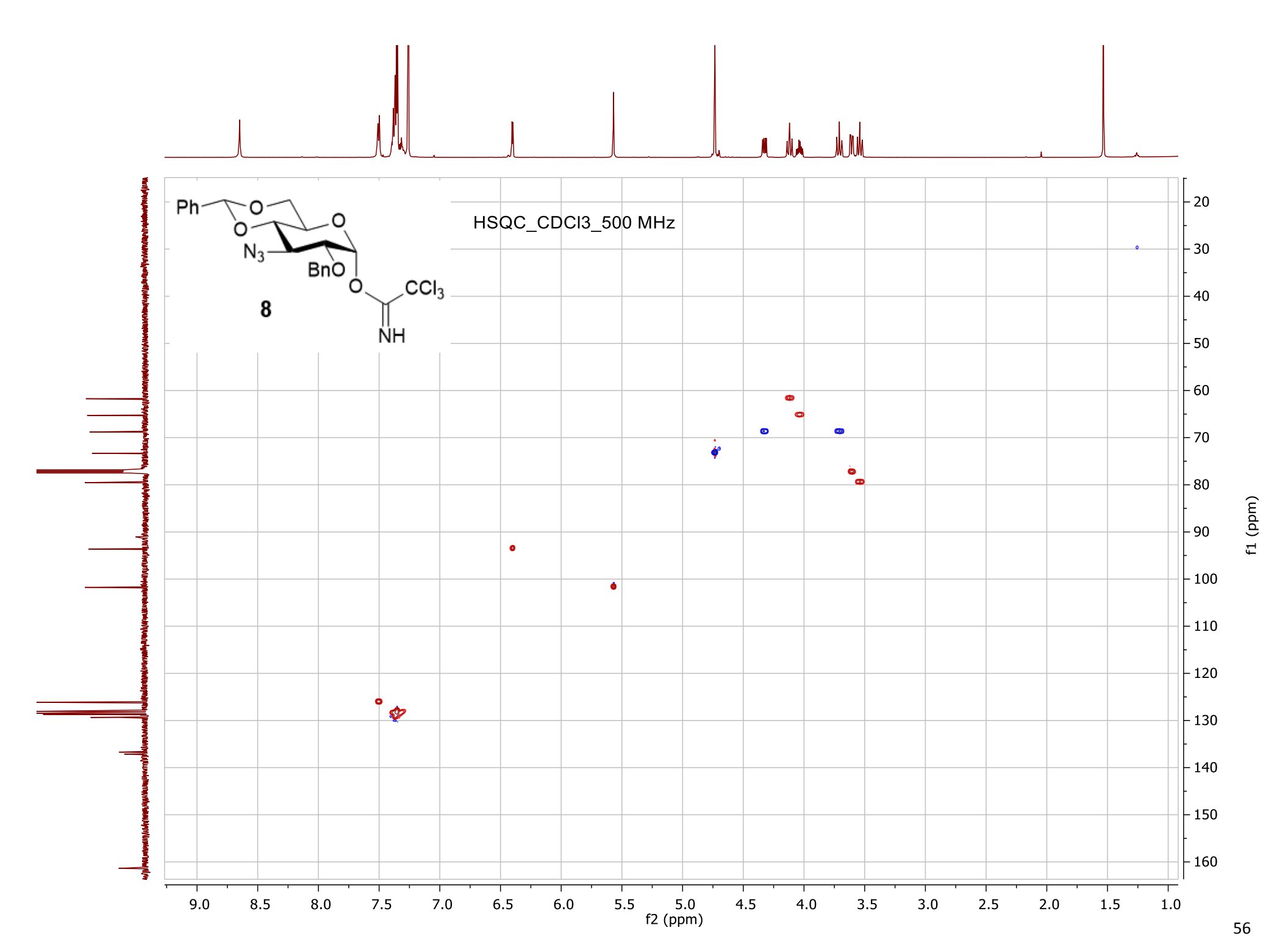

137.374
136.871
129.293
128.794
128.608
128.469
128.320
126.178
101.592
86.452
80.487
79.369
75.961
71.100
68.799
66.932
33.479
23.389
13.603
Ph
O
O
O
N3
OBn
SPr
S8
13C_CDCl3_125 MHz
f1 (ppm)

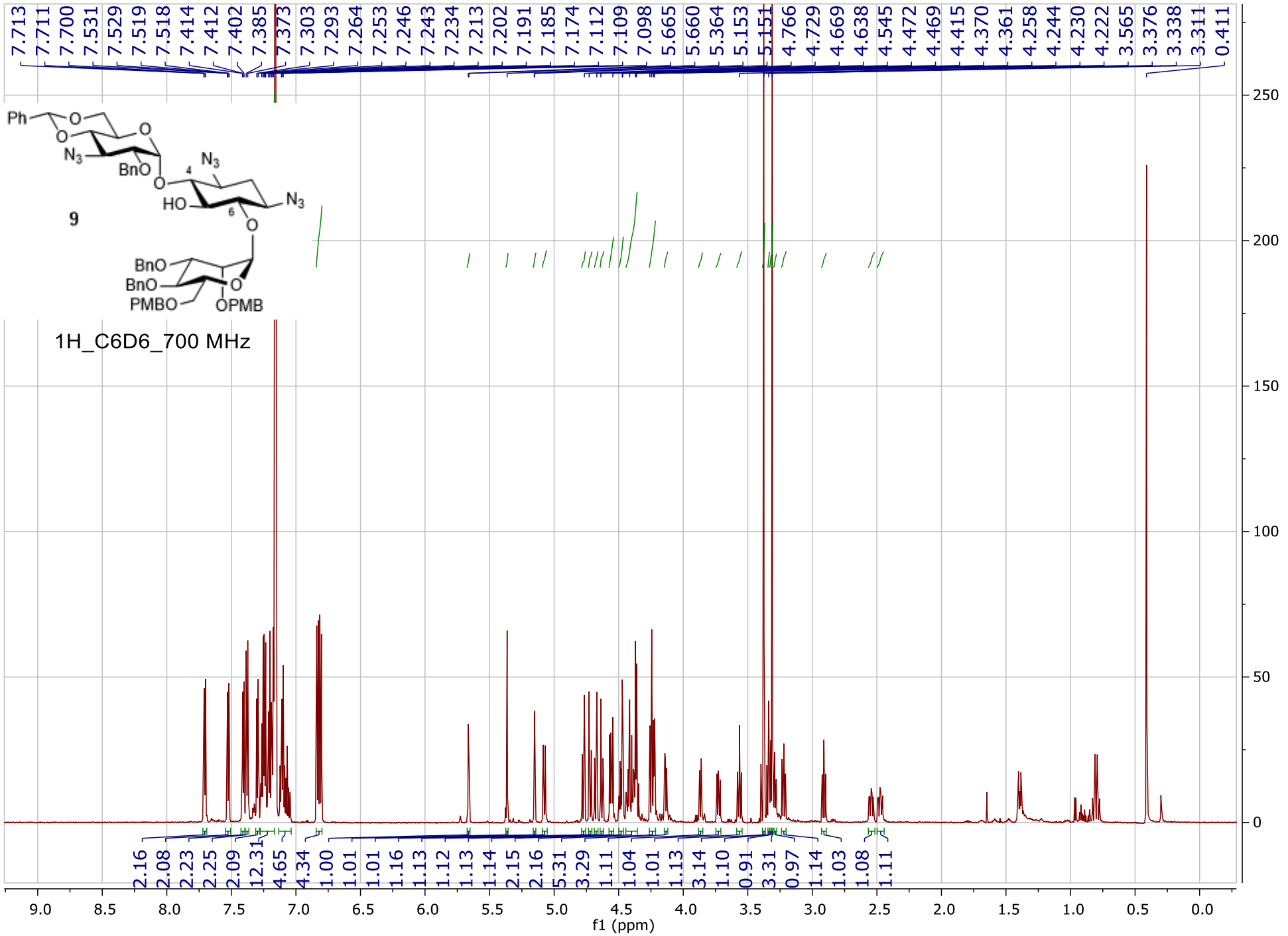

8.649
7.514
7.510
7.498
7.495
7.394
7.391
7.383
7.382
7.373
7.368
7.365
7.357
7.350
7.348
7.333
7.331
7.324
7.316
7.312
7.307
6.405
6.398
5.569
4.734
4.341
4.331
4.320
4.310
4.139
4.119
4.099
4.061
4.051
4.042
4.032
4.022
4.012
3.730
3.709
3.688
3.621
3.614
3.601
3.594
3.560
3.540
3.521
1.534
Ph
O
O
O
N3
BnO
O
CCl3
NH
8
1H_CDCl3_500 MHz
0.99
2.04
8.02
0.92
1.00
1.90
1.02
1.02
0.99
1.05
0.99
1.05
f1 (ppm)

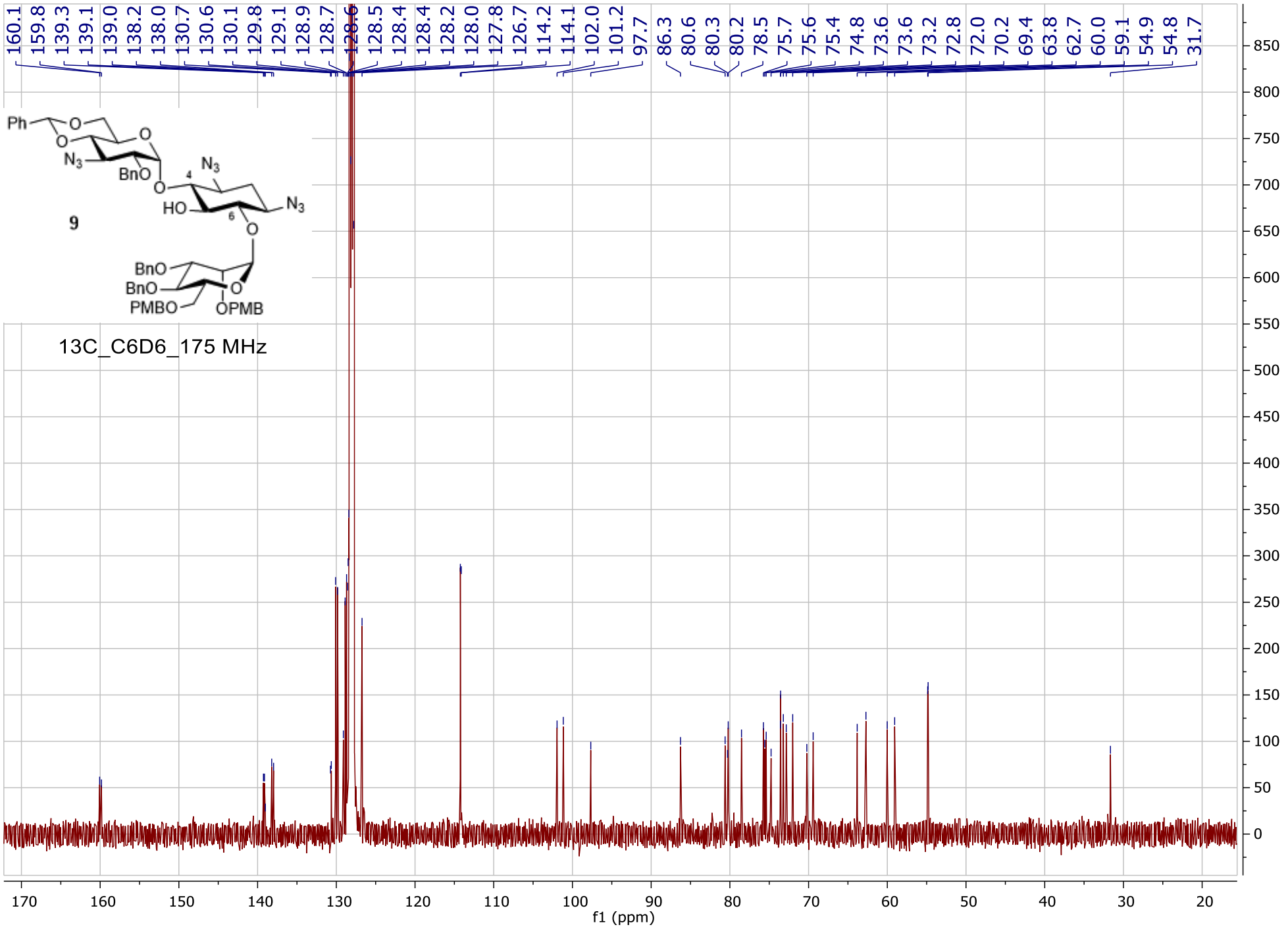

161.4
137.1
136.7
129.3
128.7
128.5
128.3
128.1
126.1
101.8
93.6
91.0
79.5
77.4
73.3
68.8
65.3
61.7
Ph
O
O
O
N3
BnO
O
CCl3
NH
8
13C_CDCl3_125 MHz
3500
3000
2500
2000
1500
1000
500
0
175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45
f1 (ppm)

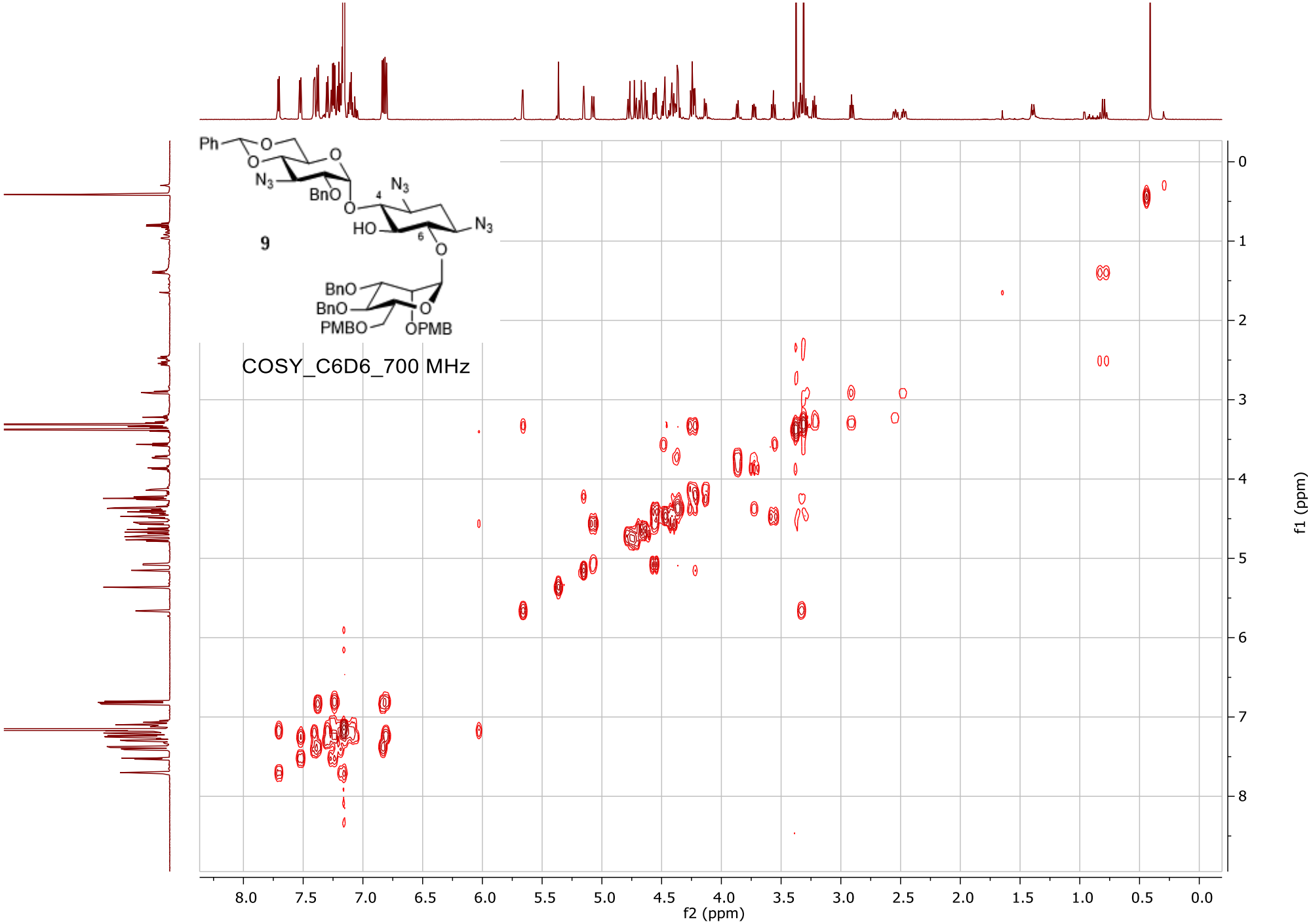

COSY_CDCl3_500 MHz
Ph
O
O
O
N3
BnO
O
CCl3
NH
8
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)
0
1
2
3
4
5
6
7
8
9

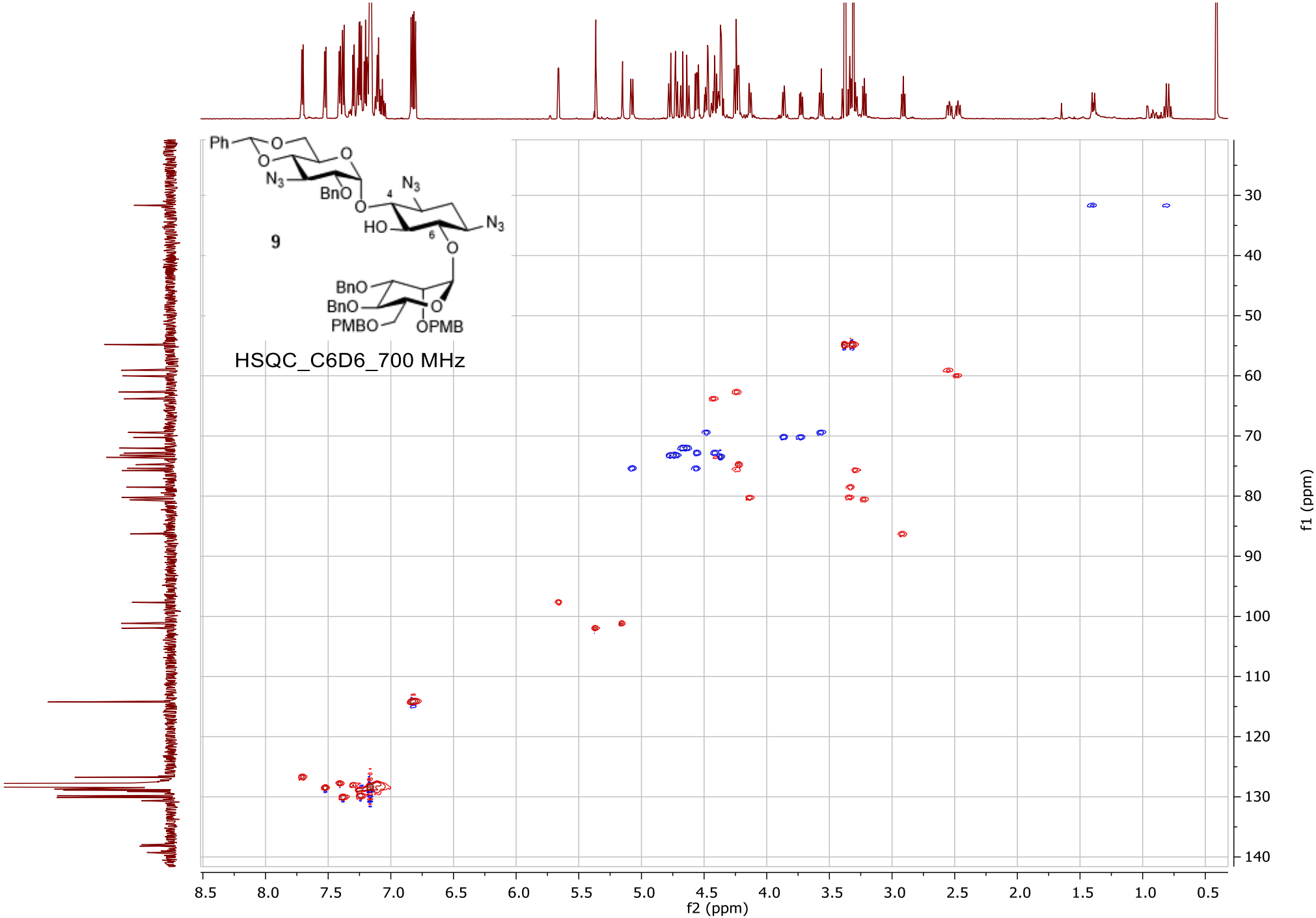

HMBC_CDCl3_500 MHz
Ph
O
O
O
N3
BnO
O
CCl3
NH
8
f2 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160

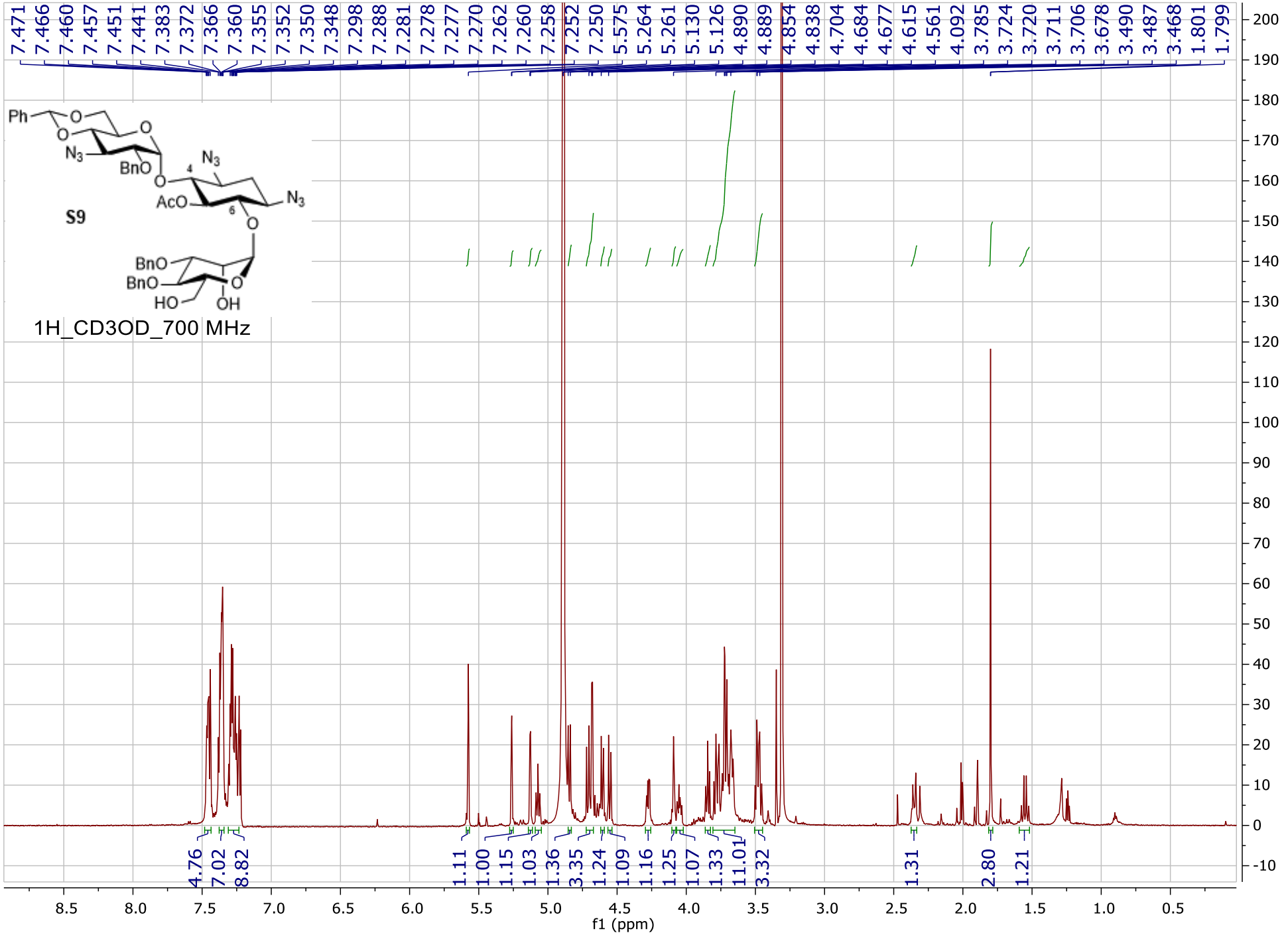

HSQC_CDCl3_500 MHz
Ph
O
O
O
N3
BnO
O
CCl3
NH
8
f2 (ppm)
f1 (ppm)

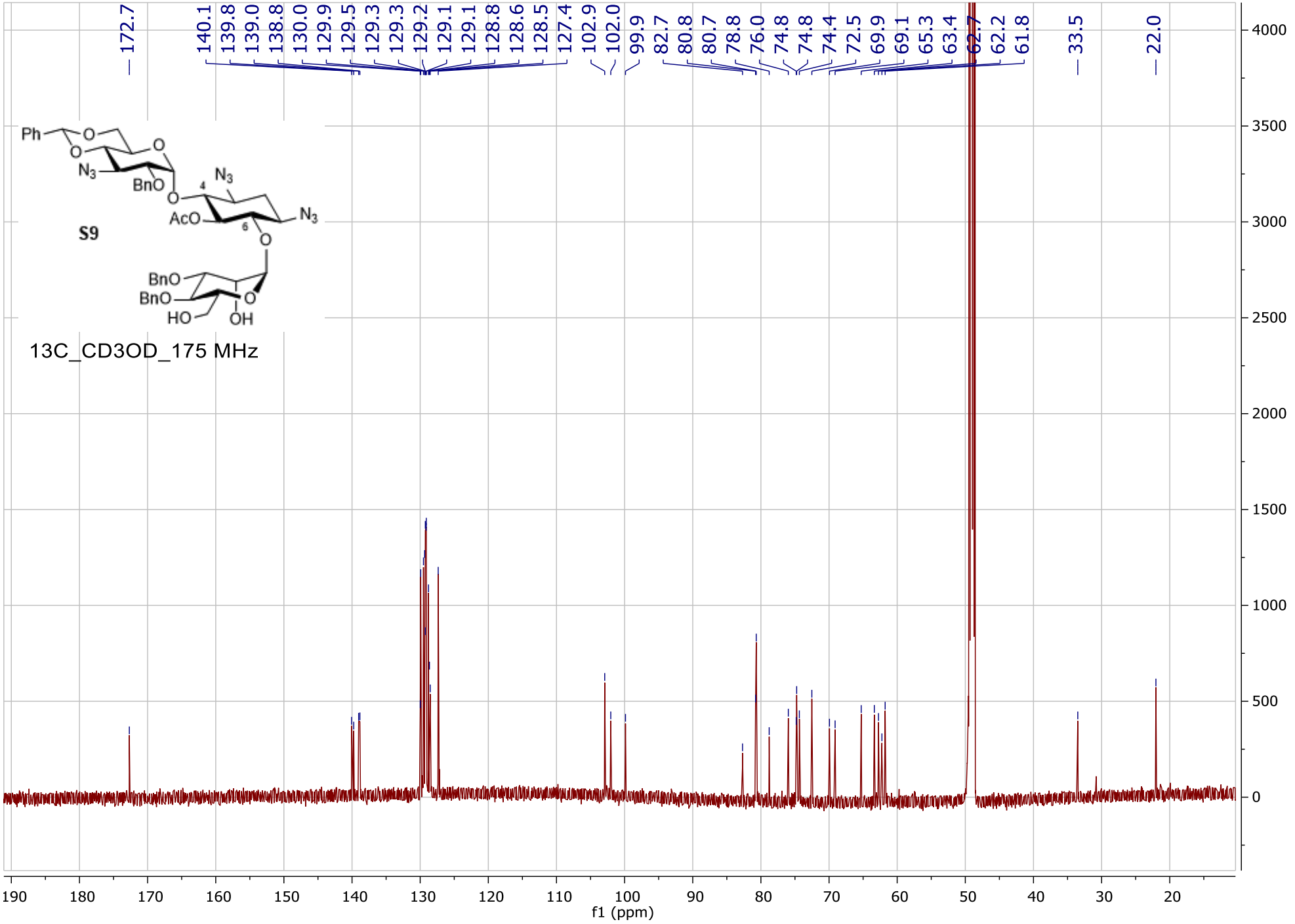

7.713 7.711 7.700 7.531 7.529 7.519 7.518 7.414 7.412 7.402 7.385 7.373 7.303 7.293 7.264 7.253 7.246 7.243 7.234 7.213 7.202 7.191 7.185 7.174 7.112 7.109 7.098 5.665 5.660 5.364 5.153 5.151 4.766 4.729 4.669 4.638 4.545 4.472 4.469 4.415 4.370 4.361 4.258 4.244 4.230 4.222 3.565 3.376 3.338 3.311 0.411
Ph
O
O
O
N3
BnO
4
N3
O
HO
6
N3
O
9
BnO
BnO
O
PMBO
OPMB
1H_C6D6_700 MHz
250
200
150
100
50
0
2.16 2.08 2.23 2.25 2.09 12.31 4.65 4.34 1.00 1.01 1.01 1.16 1.13 1.12 1.13 1.14 2.15 2.16 5.31 3.29 1.11 1.04 1.01 1.13 3.14 1.10 0.91 3.31 0.97 1.14 1.03 1.08 1.11
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

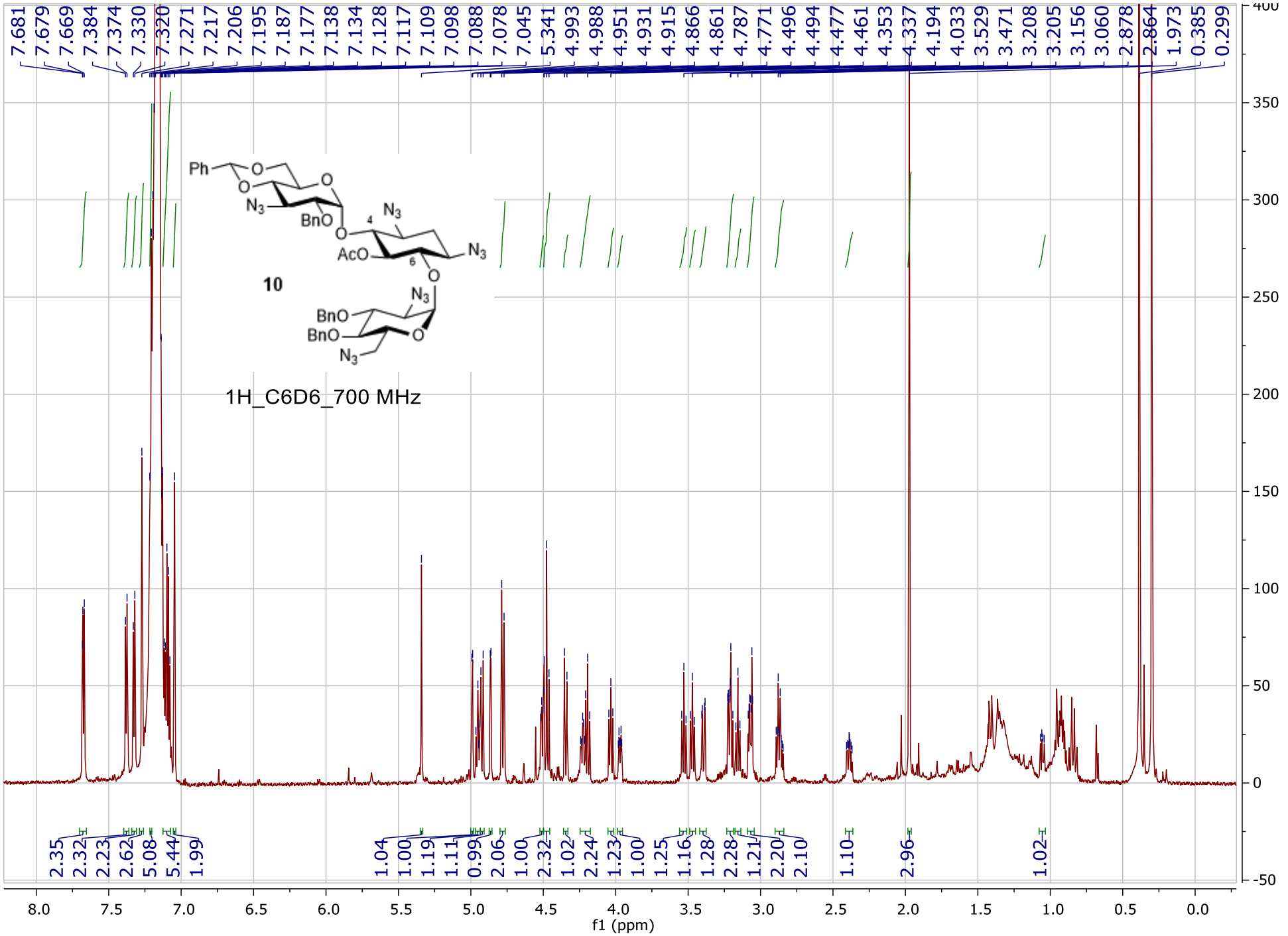

160.1
159.8
139.3
139.1
139.0
138.2
138.0
130.7
130.6
130.1
129.8
129.1
128.9
128.7
128.5
128.4
128.4
128.2
128.0
127.8
126.7
114.2
114.1
102.0
101.2
97.7
86.3
80.6
80.3
80.2
78.5
75.7
75.6
75.4
74.8
73.6
73.6
73.2
72.8
72.0
70.2
69.4
63.8
62.7
60.0
59.1
54.9
54.8
31.7
Ph
O
O
O
N3
BnO
4
N3
O
HO
6
N3
O
BnO
BnO
O
PMBO
OPMB
9
13C_C6D6_175 MHz
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

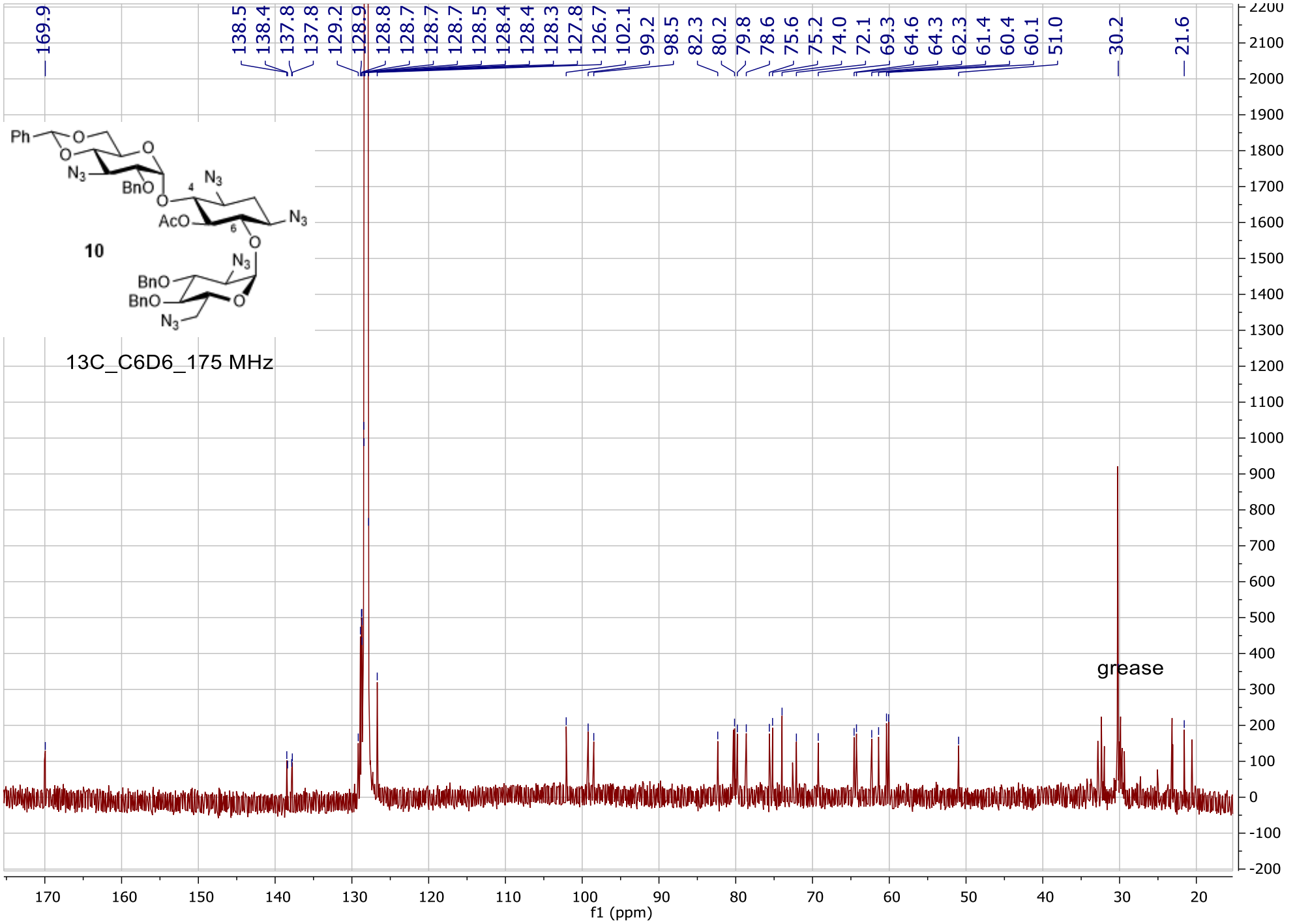

Ph
O
O
O
N3
BnO
O
4
N3
HO
6
N3
O
9
BnO
BnO
O
PMBO
OPMB
COSY_C6D6_700 MHz
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)
0
1
2
3
4
5
6
7
8
f1 (ppm)

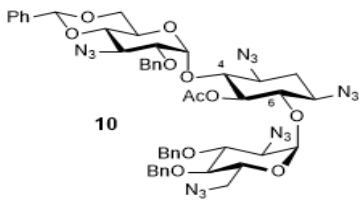

Ph
O
O
O
N3
BnO
O
4
N3
HO
6
N3
O
9
BnO
BnO
O
PMBO
OPMB
HSQC_C6D6_700 MHz
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)


7.471 7.466 7.460 7.457 7.451 7.441 7.383 7.372 7.366 7.360 7.355 7.352 7.350 7.348 7.298 7.288 7.281 7.278 7.277 7.270 7.262 7.260 7.258 7.252 7.250 5.575 5.264 5.261 5.130 5.126 4.890 4.889 4.854 4.838 4.704 4.684 4.677 4.615 4.561 4.092 3.785 3.724 3.720 3.711 3.706 3.678 3.490 3.487 3.468 1.801 1.799
Ph
BnO
N3
AcO
S9
BnO
HO
OH
1H_CD3OD_700 MHz
4.76 7.02 8.82 1.11 1.00 1.15 1.03 1.36 3.35 1.24 1.09 1.16 1.25 1.07 1.33 11.01 3.32 1.31 2.80 1.21
f1 (ppm)


172.7
140.1
139.8
139.0
138.8
130.0
129.9
129.5
129.3
129.3
129.2
129.1
129.1
128.8
128.6
128.5
127.4
102.9
102.0
99.9
82.7
80.8
80.7
78.8
76.0
74.8
74.8
74.4
72.5
69.9
69.1
65.3
63.4
62.7
62.2
61.8
33.5
22.0
Ph
O
O
O
N3
BnO
O
4
N3
AcO
6
N3
O
BnO
BnO
O
HO
OH
S9
13C_CD3OD_175 MHz
4000
3500
3000
2500
2000
1500
1000
500
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


7.681 7.679 7.669 7.384 7.374 7.330 7.320 7.271 7.217 7.206 7.195 7.187 7.177 7.138 7.134 7.128 7.117 7.109 7.098 7.088 7.078 7.045 5.341 4.993 4.988 4.951 4.931 4.915 4.866 4.861 4.787 4.771 4.496 4.494 4.477 4.461 4.353 4.337 4.194 4.033 3.529 3.471 3.208 3.205 3.156 3.060 2.878 2.864 1.973 0.385 0.299
Ph
O
O
O
N3
BnO
4
N3
O
AcO
6
N3
O
10
N3
BnO
BnO
O
N3
1H_C6D6_700 MHz
2.35 2.32 2.23 2.62 5.08 5.44 1.99
1.04 1.00 1.19 1.11 0.99 2.06 1.00 2.32 1.02 2.24 1.23 1.00 1.25 1.16 1.28 2.28 1.21 2.20 2.10 1.10 2.96 1.02
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
400 350 300 250 200 150 100 50 0 -50


169.9
138.5
138.4
137.8
137.8
129.2
128.9
128.8
128.7
128.7
128.7
128.5
128.4
128.4
128.3
127.8
126.7
102.1
99.2
98.5
82.3
80.2
79.8
78.6
75.6
75.2
74.0
72.1
69.3
64.6
64.3
62.3
61.4
60.4
60.1
51.0
30.2
21.6
Ph
O
O
O
N3
BnO
4
N3
O
AcO
6
N3
O
N3
BnO
BnO
O
N3
10
13C_C6D6_175 MHz
grease
f1 (ppm)



HSQC_C6D6_700_MHz