Supporting Information

Synthesis and Immunomodulatory Activity of the Sulfated Tetrasaccharide Motif of Type B Ulvanobiuronic Acid 3-Sulfate

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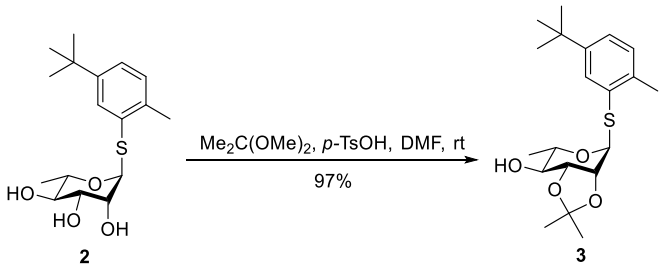
Contents

1. General Information. All reactions were performed with anhydrous solvents in oven-dried glassware with magnetic stirring under argon or nitrogen unless otherwise stated. The chemicals were used as supplied except where noted. Analytical thin layer chromatography (TLC) was conducted on precoated plates of silica gel (0.25-0.3 mm, Shanghai, China). The TLC plates were visualized by exposure to UV light or by staining with a sulfuric acid-ethanol solution. Silica gel column chromatography was performed on silica gel AR (100-200 mesh, Shanghai, China). Optical rotations (OR) were measured with a Rudolph Research Analytical Autopol I automatic polarimeter. NMR spectra were recorded with a Bruker Avance III 400, Bruker Avance III 500, or Bruker Avance III 600 spectrometer. The ^{1}H and ^{13}C NMR spectra were calibrated against the residual proton and carbon signals of the solvents as internal references ($CDCl_3$: δ_H = 7.26 ppm and δ_C = 77.2 ppm; CD_3OD: δ_H = 3.31 ppm and δ_C = 49.0 ppm; D_2O: δ_H = 4.79 ppm). Multiplicities are quoted as singlet (s), broad singlet (br s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplets (dt), triplet of doublets (td) or multiplet (m). All NMR chemical shifts (δ) were recorded in ppm and coupling constants (*J*) were reported in Hz. High-resolution mass spectra were recorded on ESI-TOF spectrometer.

2. Experimental details and characterization data of new compounds

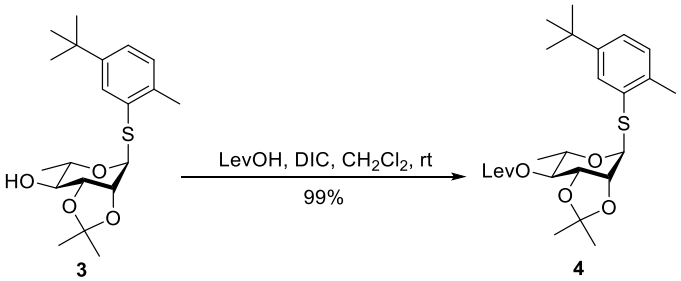
2.1. Synthesis of 2-methyl-5-*tert*-butylphenyl 2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside 3



To a solution of thioglycoside **2**[1] (4.3 g, 13.2 mmol) in DMF (43 mL) was added 2,2-dimethoxypropane (3.9 mL, 31.8 mmol) and *p*-toluenesulfonic acid monohydrate (609 mg, 3.2 mmol) at room temperature. After being stirred overnight, the reaction mixture was neutralized with triethylamine. The solution was diluted with CH_2Cl_2 and washed with brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc: 6/1→3/1) to give **3** (4.7 g, 97%) as a

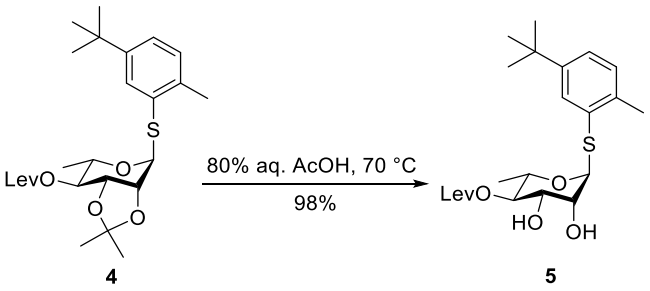
colorless syrup. $[\alpha]_D^{25}$ = –175.7 (*c* 0.39, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 2.0 Hz, 1 H), 7.22 (dd, *J* = 2.0, 8.0 Hz, 1 H), 7.14 (d, *J* = 8.0 Hz, 1 H), 5.74 (s, 1 H), 4.40 (d, *J* = 5.6 Hz, 1 H), 4.17–4.07 (m, 2 H), 3.50–3.45 (m, 1 H), 2.48 (d, *J* = 3.6 Hz, 1 H), 2.40 (s, 3 H), 1.55 (s, 3 H), 1.39 (s, 3 H), 1.30 (s, 9 H), 1.24 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 136.7, 132.2, 130.2, 129.8, 125.0, 109.9, 83.0, 78.6, 77.1, 75.5, 67.1, 34.6, 31.5, 28.4, 26.6, 20.3, 17.3; HRMS (ESI) *m/z* calcd for $C_{20}H_{30}O_4SNa$ $[M + Na]^+$ 389.1762, found 389.1760.

2.2. Synthesis of 2-methyl-5-*tert*-butylphenyl 2,3-*O*-isopropylidene-4-*O*-levulinoyl-1-thio-α-L-rhamnopyranoside 4



To a solution of compound **3** (4.7 g, 12.8 mmol) in anhydrous CH_2Cl_2 (40.0 mL) was added DMAP (1.7 g, 20.3 mmol), LevOH (2.1 mL, 20.3 mmol) and DIC (3.1 mL, 20.3 mmol) at 0 ℃. After being stirred at room temperature for 1 h, the reaction mixture was neutralized with saturated aqueous $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc: 9:1→6:1) to give **4** (5.9 g, 99%) as a colorless syrup. $[\alpha]_D^{25}$ = –135.2 (*c* 0.35, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.57 (d, *J* = 1.8 Hz, 1 H), 7.22 (dd, *J* = 1.8, 7.8 Hz, 1 H), 7.15 (d, *J* = 7.8 Hz, 1 H), 5.74 (s, 1H), 4.94 (dd, *J* = 7.8, 9.6 Hz, 1 H), 4.40 (d, *J* = 5.4 Hz, 1 H), 4.26 (dd, *J* = 4.8, 7.8 Hz, 1 H), 4.24–4.19 (m, 1 H), 2.91–2.85 (m, 1 H), 2.73–2.66 (m, 2 H), 2.61–2.56 (m, 1 H), 2.40 (s, 3 H), 2.19 (s, 3 H), 1.57 (s, 3 H), 1.37 (s, 3 H), 1.30 (s, 9 H), 1.14 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 206.6, 172.2, 149.9, 136.7, 132.0, 130.2, 129.9, 125.2, 110.2, 83.1, 77.0, 75.7, 75.2, 65.9, 38.1, 34.7, 31.5, 30.0, 28.2, 27.9, 26.8, 20.3, 17.0; HRMS (ESI) *m/z* calcd for $C_{25}H_{36}O_6SNa$ $[M + Na]^+$ 487.2130, found 487.2131.

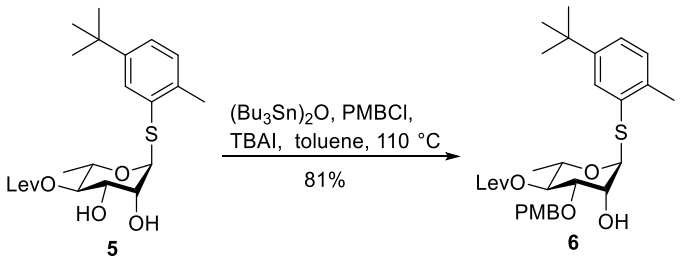
2.3. Synthesis of 2-methyl-5-*tert*-butylphenyl 4-*O*-levulinoyl-1-thio-α-L-rhamnopyranoside 5



4 5

To a solution of 80% aqueous acetic acid solution (69 mL) was added compound **4** (5.9 g, 12.7 mmol) at room temperature. After being stirred at 70 ℃ overnight, the reaction mixture was neutralized with saturated aqueous $NaHCO_3$. The solution was diluted with CH_2Cl_2 and washed with brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH: 50:1→40:1) to give **5** (5.3 g, 98%) as a white solid. $[\alpha]_D^{25}$ = –203.8 (*c* 0.44, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, *J* = 1.8 Hz, 1 H), 7.21 (dd, *J* = 1.8, 7.8 Hz, 1 H), 7.13 (d, *J* = 7.8 Hz, 1 H), 5.48 (d, *J* = 1.2 Hz, 1 H), 4.97 (t, *J* = 9.6 Hz, 1 H), 4.34–4.30 (m, 1 H), 4.27 (dd, *J* = 1.2, 3.0 Hz, 1 H), 4.02 (dd, *J* = 3.6, 9.6 Hz, 1 H), 3.47 (br s, 1 H), 2.95 (br s, 1 H), 2.89–2.80 (m, 2 H), 2.66–2.56 (m, 2 H), 2.38 (s, 3 H), 2.21 (s, 3 H), 1.30 (s, 9 H), 1.23 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.8, 173.6, 150.0, 136.4, 132.9, 130.1, 129.3, 124.9, 87.0, 75.9, 72.8, 70.8, 67.1, 38.5, 34.7, 31.5, 30.0, 28.4, 20.3, 17.5; HRMS (ESI) *m/z* calcd for $C_{22}H_{32}O_6SNa$ $[M + Na]^+$ 447.1817, found 447.1818.

2.4. Synthesis of 2-methyl-5-*tert*-butylphenyl 3-*O*-(4-methoxybenzyl)-4-*O*-levulinoyl-1-thio-α-L-rhamnopyranoside 6

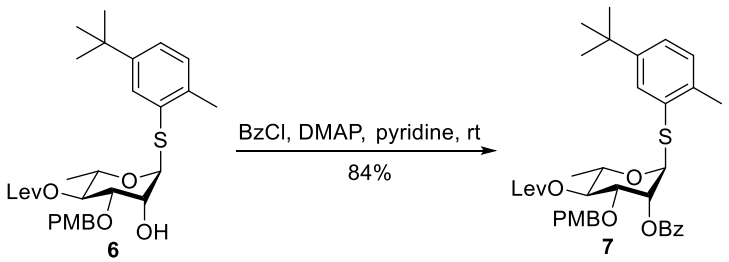


5 6

To a solution of diol **5** (482 mg, 1.14 mmol) in anhydrous toluene (22 mL) was added $(Bu_3Sn)_2O$ (698 μL, 1.37 mmol). The reaction mixture was stirred at 110 ℃ for 1 h, and then cooled to 60 ℃ before PMBCl (232 μL, 1.71 mmol) and TBAI (632 mg, 1.71 mmol) were added. The mixture was then stirred at 110 ℃ overnight and concentrated under reduced pressure. The resulting crude product was purified by silica gel column chromatography (petroleum ether/EtOAc: 8/1→4/1) to give **6** (504

mg, 81%) as a slightly yellow syrup. $[\alpha]_D^{25}$ = –149.6 (*c* 0.39, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 1.6 Hz, 1 H), 7.28 (d, *J* = 8.8 Hz, 2 H), 7.20 (dd, *J* = 2.0, 8.0 Hz, 1 H), 7.13 (d, *J* = 8.0 Hz, 1 H), 6.91 (d, *J* = 8.4 Hz, 2 H), 5.50 (d, *J* = 1.2 Hz, 1 H), 5.10 (t, *J* = 9.6 Hz, 1 H), 4.62 (d-like, *J* = 11.6 Hz, 1 H), 4.55 (d-like, *J* = 11.6 Hz, 1 H), 4.29–4.22 (m, 2 H), 3.82–3.79 (m, 4 H), 2.77–2.73 (m, 2 H), 2.58–2.50 (m, 2 H), 2.37 (s, 3 H), 2.20 (s, 3 H), 1.29 (s, 9 H), 1.19 (d, *J* = 6.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) 206.5, 172.2, 159.7, 150.0, 136.3, 132.8, 130.1, 129.8, 129.7, 129.4, 124.9, 114.2, 86.6, 73.1, 71.8, 70.4, 67.7, 55.5, 38.0, 34.7, 31.5, 30.0, 28.2, 20.3, 17.5; HRMS (ESI) *m/z* calcd for $C_{30}H_{40}O_7SNa$ $[M + Na]^+$ 567.2392, found 567.2393.

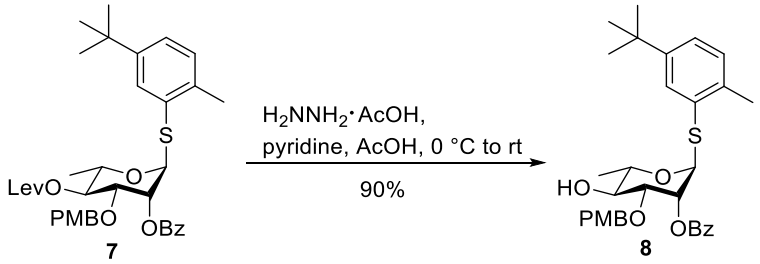
2.5. Synthesis of 2-methyl-5-*tert*-butylphenyl 2-*O*-benzoyl-3-*O*-(4-methoxybenzyl) -4-*O*-levulinoyl-1-thio-α-L-rhamnopyranoside 7



To a solution of **6** (1.0 g, 1.84 mmol) in anhydrous pyridine (3.5 mL) was added DMAP (61 mg, 0.5 mmol) and benzoyl chloride (627 μL, 5.4 mmol) at 0 ℃. The reaction mixture was allowed to warm to room temperature and stirred at room temperature for 5 h. The solution was diluted with water and extracted with ethyl acetate. The organic layer was washed with 1 M aqueous HCl, saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc: 10/1→8/1) to give **7** (1.0 g, 84%) as a slightly yellow syrup. $[\alpha]_D^{25}$ = –12.6 (*c* 0.78, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.2 Hz, 2 H), 7.58–7.55 (m, 2 H), 7.44 (t, *J* = 7.8 Hz, 2 H), 7.25–7.22 (m, 3 H), 7.15 (d, *J* = 7.8 Hz, 1 H), 6.86 (d, *J* = 8.4 Hz, 2 H), 5.81 (dd, *J* = 1.2, 3.0 Hz, 1 H), 5.47 (d, *J* = 1.8 Hz, 1 H), 5.22 (t, *J* = 9.6 Hz, 1 H), 4.64 (d-like, *J* = 12.0 Hz, 1 H), 4.46 (d-like, *J* = 12.0 Hz, 1 H), 4.39–2.59 (m, 2 H), 2.52–2.46 (m, 1 H), 2.43 (s, 3 H), 2.19 (s, 3 H), 1.30 (s, 9 H), 1.28 (d, *J* = 6.0 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 206.6, 172.2, 165.9, 159.5, 150.0, 137.0, 133.5, 132.4, 130.4, 130.3, 130.1, 129.9, 129.8, 129.7, 128.6, 125.5, 113.9, 86.0, 74.6, 73.2, 71.2, 71.0, 68.2, 55.4, 38.0, 34.6,

31.5, 30.0, 28.1, 20.5, 17.7; HRMS (ESI) *m/z* calcd for $C_{37}H_{44}O_8SNa$ $[M + Na]^+$ 671.2655, found 671.2654.

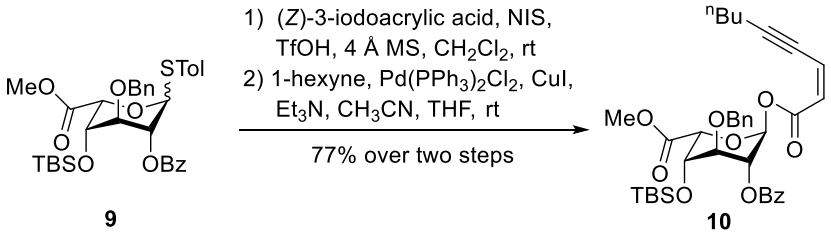
2.6. Synthesis of 2-methyl-5-*tert*-butylphenyl 2-*O*-benzoyl-3-*O*-(4-methoxybenzyl) -1-thio-α-L-rhamnoyranoside 8



7 8

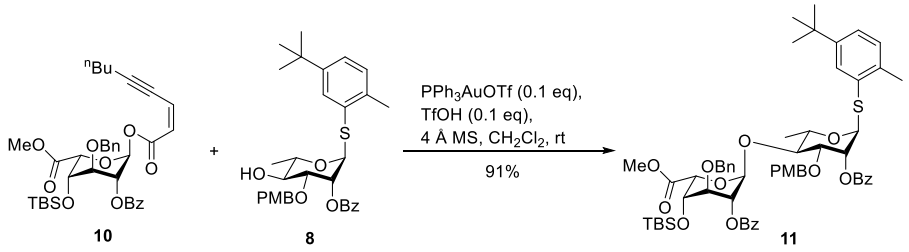
To a solution of compound **7** (1.7 g, 2.62 mmol) in pyridine/acetic acid (3/1, v/v, 22 mL) was added hydrazine acetate (1.2 g, 13.0 mmol) at 0 ℃. The reaction mixture was allowed to warm to room temperature and stirred for 4 h. Then acetone was added to quench the reaction. The aqueous phase was extracted with ethyl acetate. The organic layer was washed with 1 M aqueous HCl, saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc: 6/1→4/1) to give **8** (1.3 g, 90 %) as a white foam. $[\alpha]_D^{25}$ = –15.8 (*c* 0.94, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 1.2, 7.8 Hz, 2 H), 7.60–7.57 (m, 2 H), 7.46 (t, *J* = 7.8 Hz, 2 H), 7.26–7.23 (m, 3 H), 7.16 (d, *J* = 7.8 Hz, 1 H), 6.85 (d, *J* = 8.4 Hz, 2 H), 5.88 (dd, *J* = 1.8, 3.0 Hz, 1 H), 5.50 (d, *J* = 1.2 Hz, 1 H), 4.76 (d-like, *J* = 10.8 Hz, 1 H), 4.46 (d-like, *J* = 10.8 Hz, 1 H), 4.34–4.29 (m, 1 H), 3.87 (dd, *J* = 3.0, 9.6 Hz, 1 H), 3.79–3.76 (m, 4 H), 2.45 (s, 3 H), 1.40 (d, *J* = 6.0 Hz, 3 H), 1.32 (s, 9 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.9, 159.7, 149.9, 137.1, 133.5, 132.6, 130.5, 130.2, 130.1, 130.0, 129.9, 129.6, 128.6, 125.4, 114.2, 86.2, 78.0, 72.3, 71.2, 70.7, 69.6, 55.4, 34.6, 31.5, 20.5, 18.0; HRMS (ESI) *m/z* calcd for $C_{32}H_{38}O_6SNa$ $[M + Na]^+$ 573.2287, found 573.2288.

2.7. Synthesis of methyl ((*Z*)-ynenoyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl-α-L-idopyranoside)uronate 10



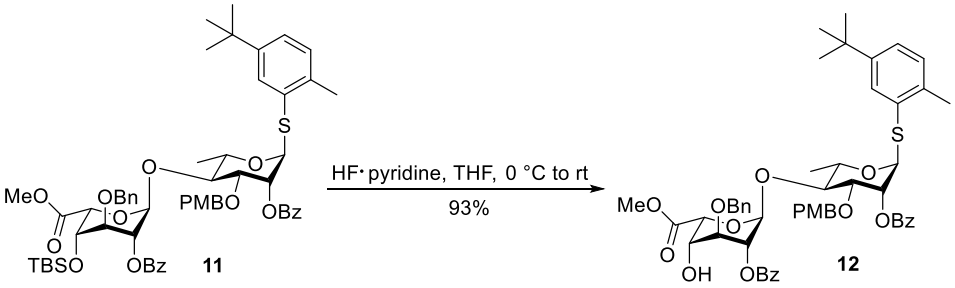
To a solution of thioglycoside **9**[2] (509 mg, 0.82 mmol) in anhydrous CH_2Cl_2 (20 mL) was added (*Z*)-3-iodoacrylic acid[3] (243 mg, 1.23 mmol) and 4 Å MS (800 mg). Then NIS (369 mg, 1.64 mmol) and TfOH (10.8 μL, 0.12 mmol) were added. After being stirred at room temperature for 1 h, the reaction mixture was neutralized with Et_3N and filtered through Celite. The filtrate was diluted with CH_2Cl_2, washed with saturated aqueous $Na_2S_2O_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc: 15/1→10/1) to give the corresponding glycosyl (*Z*)-3-iodoacrylate (515 mg, 90%) as an orange syrup. To a solution of the above glycosyl (*Z*)-3-iodoacrylate (515 mg, 0.74 mmol) in anhydrous CH_3CN/THF (2/1, v/v, 51 mL) was added $Pd(PPh_3)_2Cl_2$ (28 mg, 0.06 mmol) and CuI (141 mg, 0.74 mmol). After purged with argon for three times, Et_3N (205 μL, 1.48 mmol) and 1-hexyne (101 μL, 0.89 mmol) were added to the solution at room temperature and the solution was stirred overnight. The reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc: 15/1→10/1) to give **10** (410 mg, 85%) as an orange syrup. $[\alpha]_D^{25}$ = –36.1 (*c* 0.53, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 1.2, 8.4 Hz, 2 H), 7.57–7.54 (m, 1 H), 7.41 (t, *J* = 7.8 Hz, 2 H), 7.36 (d, *J* = 7.2 Hz, 2 H), 7.33–7.30 (m, 2 H), 7.28–7.26 (m, 1 H), 6.56 (s, 1 H), 6.21 (dt, *J* = 2.4, 11.4 Hz, 1 H), 6.00 (d, *J* = 11.4 Hz, 1 H), 5.17 (t, *J* = 2.4 Hz, 1 H), 4.90 (d, *J* = 2.4 Hz, 1 H), 4.84 (d-like, *J* = 12.0 Hz, 1 H), 4.71 (d-like, *J* = 12.0 Hz, 1 H), 4.12 (t, *J* = 3.0 Hz, 1 H), 3.86 (m, 1 H), 3.79 (s, 3 H), 2.42 (td, *J* = 2.4, 7.2 Hz, 1 H), 1.57–1.52 (m, 2 H), 1.45–1.39 (m, 2 H), 0.91 (t, *J* = 7.2 Hz, 3 H), 0.67 (s, 9 H), -0.10 (s, 3 H), -0.32 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 165.8, 162.5, 137.7, 133.5, 130.3, 129.5, 128.6, 128.4, 128.2, 128.1, 126.3, 126.1, 106.2, 92.4 ($^1J_{C1,H1}$ = 174.6 Hz), 78.0, 74.2, 72.5, 71.3, 68.9, 67.4, 52.3, 30.5, 25.6, 22.2, 20.0, 17.9, 13.8, -4.3, -5.6; HRMS (ESI) *m/z* calcd for $C_{36}H_{46}O_9SiNa$ [M + Na]$^+$ 673.2809, found 673.2808.

2.8. Synthesis of 2-methyl-5-*tert*-butylphenyl (methyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl-α-L-idopyranosyl uronate)-(1→4)-2-*O*-benzoyl-3-*O*-(4-methoxybenzyl)-1-thio-α-L-rhamnoyranoside 11



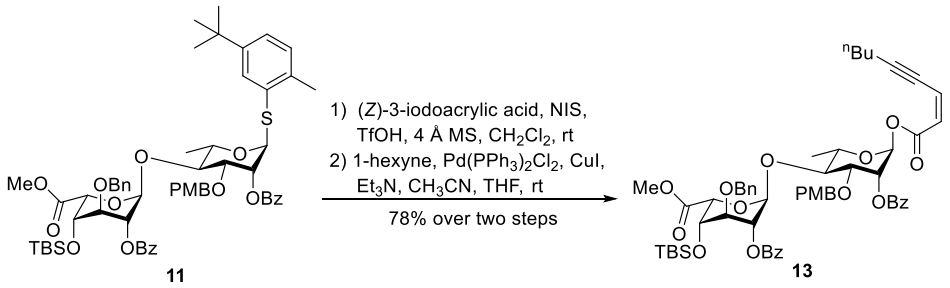
A solution of donor **10** (405 mg, 0.62 mmol), acceptor **8** (225.6 mg, 0.41 mmol) and freshly activated 4 Å MS (650 mg) in anhydrous CH_2Cl_2 (15.0 mL) was stirred at room temperature for 0.5 h under argon. A freshly prepared solution of PPh_3AuOTf in CH_2Cl_2 (0.82 mL, 0.05 M) and TfOH (3.6 μL, 0.041 mmol) were added successively and the solution was stirred overnight. The mixture was quenched with Et_3N and filtered through Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (toluene/EtOAc: 30/1→20/1) to give **11** (389.6 mg, 91%) as a slightly yellow foam. $[\alpha]_D^{25}$ = –41.0 (*c* 0.89, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.06 (m, 2 H), 7.98 (m, 2 H), 7.59–7.57 (m, 2 H), 7.52 (t, *J* = 7.2 Hz, 1 H), 7.48–7.44 (m, 4 H), 7.39 (t, *J* = 7.8 Hz, 2 H), 7.35 (t, *J* = 7.8 Hz, 2 H), 7.30 (t, *J* = 7.2 Hz, 1 H), 7.22 (dd, *J* = 1.8, 7.8 Hz, 1 H), 7.16 (d, *J* = 7.8 Hz, 1 H), 7.03 (d, *J* = 8.4 Hz, 2 H), 6.44 (d, *J* = 8.4 Hz, 2 H), 5.83 (t, *J* = 1.8 Hz, 1 H), 5.70 (s, 1 H), 5.47 (d, *J* = 1.2 Hz, 1 H), 5.14 (s, 1 H), 4.93 (d, *J* = 11.4 Hz, 1 H), 4.90 (d, *J* = 1.8 Hz, 1 H), 4.74 (d, *J* = 11.4 Hz, 1 H), 4.59 (d, *J* = 10.8 Hz, 1 H), 4.39–4.34 (m, 2 H), 4.10 (br s, 1 H), 4.02–3.97 (m, 2 H), 3.77 (m, 4 H), 3.46 (s, 3 H), 2.46 (s, 3 H), 1.38 (d, *J* = 6.6 Hz, 3 H), 1.30 (s, 9 H), 0.62 (s, 9 H), -0.11 (s, 3 H), -0.36 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.2, 166.0, 165.8, 159.1, 150.0, 138.2, 137.0, 133.4, 133.3, 132.8, 130.4, 130.3, 130.2, 130.1, 129.8, 129.6, 129.3, 128.6, 128.5, 128.3, 128.2, 128.0, 125.3, 113.8, 100.5, 86.1, 79.1, 78.0, 74.3, 72.1, 70.8, 70.7, 69.2, 68.9, 68.5, 68.1, 55.0, 52.2, 34.6, 31.5, 25.6, 20.6, 18.5, 17.9, -4.2, -5.7; HRMS (ESI) *m/z* calcd for $C_{59}H_{72}O_{13}SSiNa$ $[M + Na]^+$ 1071.4361, found 1071.4363.

2.9. Synthesis of 2-methyl-5-*tert*-butylphenyl (methyl 2-*O*-benzoyl-3-*O*-benzyl-α-L-idopyranosyl uronate)-(1→4)-2-*O*-benzoyl-3-*O*-(4-methoxybenzyl)-1-thio-α-L-rhamnoyranoside 12



To a solution of **11** (87.6 mg, 0.084 mmol) in anhydrous THF (1.2 mL) was added slowly 70% HF pyridine (324 μL, 2.52 mmol) at 0 ℃. The reaction was gradually warmed to room temperature and stirred for 2 d. The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc: 4/1→2/1) to afford **12** (73.1 mg, 93%) as a white foam. $[\alpha]_D^{25}$ = –34.4 (*c* 0.66, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (m, 2 H), 7.92 (dd, *J* = 0.6, 7.8 Hz, 2 H), 7.59–7.56 (m, 3 H), 7.46 (t, *J* = 7.8 Hz, 2 H), 7.43–7.39 (m, 6 H), 7.33–7.30 (m, 1 H), 7.24 (dd, *J* = 1.8, 7.8 Hz, 1 H), 7.17 (d, *J* = 7.8 Hz, 1 H), 7.08 (d, *J* = 8.4 Hz, 2 H), 6.50 (d, *J* = 9.0 Hz, 2 H), 5.87 (dd, *J* = 1.8, 3.0 Hz, 1 H), 5.65 (s, 1 H), 5.47 (d, *J* = 1.2 Hz, 1 H), 5.28 (m, 1 H), 5.00 (d, *J* = 1.2 Hz, 1 H), 4.84 (d-like, *J* = 11.4 Hz, 1 H), 4.70 (d-like, *J* = 11.4 Hz, 1 H), 4.63 (d-like, *J* = 10.8 Hz, 1 H), 4.39–4.34 (m, 2 H), 4.09 (d, *J* = 12.0 Hz, 1 H), 4.03 (dd, *J* = 3.0, 9.0 Hz, 1 H), 3.97 (t, *J* = 9.6 Hz, 1 H), 3.89 (t, *J* = 2.4 Hz, 1 H), 3.79 (s, 3 H), 3.46 (s, 3 H), 2.70 (d, *J* = 12.0 Hz, 1 H), 2.46 (s, 3 H), 1.37 (d, *J* = 6.0 Hz, 3 H), 1.31 (s, 9 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.1, 165.9, 164.9, 159.2, 150.0, 137.9, 137.1, 133.7, 133.5, 132.6, 130.5, 130.3, 130.1, 129.9, 129.8, 129.7, 129.2, 129.1, 128.7, 128.6, 128.1, 125.5, 113.8, 100.3, 86.2, 78.9, 78.0, 74.1, 72.2, 70.7, 70.6, 68.7, 68.4, 68.2, 67.5, 55.0, 52.6, 34.6, 31.5, 20.6, 18.5; HRMS (ESI) *m/z* calcd for $C_{53}H_{58}O_{13}SNa$ $[M + Na]^+$ 957.3496, found 957.3495.

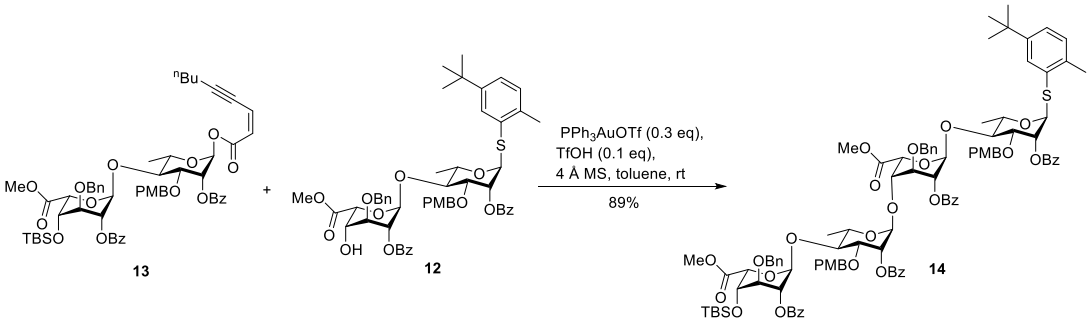
2.10. Synthesis of methyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl-α-L-idopyranosyl uronate-(1→4)-2-*O*-benzoyl-3-*O*-(4-methoxybenzyl)-α-L-rhamnopyranosyl (*Z*)-ynenoate 13



To a solution of **11** (244 mg, 0.23 mmol) in anhydrous CH_2Cl_2 (5.5 mL) was added (*Z*)-3-iodoacrylic acid (69.3 mg, 0.35 mmol) and 4 Å MS (350 mg). Then NIS (103.5 mg, 0.46 mmol) and TfOH (3.0 μL, 0.035 mmol) were added. After being stirred at room temperature for 5 h, the reaction mixture was neutralized with Et_3N and filtered through Celite. The filtrate was diluted with CH_2Cl_2, washed with saturated aqueous $Na_2S_2O_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc: 15/1→10/1) to give the corresponding glycosyl (*Z*)-3-iodoacrylate (204.8 mg, 84%) as a yellow syrup. To a solution of the above glycosyl (*Z*)-3-iodoacrylate (204.8 mg, 0.19 mmol) in anhydrous CH_3CN/THF (2/1, v/v, 12.9 mL) were added $Pd(PPh_3)_2Cl_2$ (7.0 mg, 0.01 mmol) and CuI (36.1 mg, 0.19 mmol). After purged with argon for three times, Et_3N (53 μL, 0.38 mmol) and 1-hexyne (43 μL, 0.38 mmol) were added to the solution at room temperature and the solution was stirred overnight. The reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc: 15/1→8/1) to give **13** (179.4 mg, 93%) as an orange syrup. $[\alpha]_D^{25}$ = –24.9 (*c* 0.71, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (m, 2 H), 7.94 (m, 2 H), 7.59 (t, *J* = 7.8 Hz, 1 H), 7.51 (t, *J* = 7.8 Hz, 1 H), 7.47 (t, *J* = 7.8 Hz, 2 H), 7.39 (d, *J* = 7.2 Hz, 2 H), 7.35–7.32 (m, 4 H), 7.28 (t, *J* = 7.2 Hz, 1 H), 6.99 (d, *J* = 8.4 Hz, 2 H), 6.41 (d, *J* = 9.0 Hz, 2 H), 6.30 (dt, *J* = 2.4, 11.4 Hz, 1 H), 6.27 (d, *J* = 1.8 Hz, 1 H), 6.06 (d, *J* = 11.4 Hz, 1 H), 5.72 (s, 1 H), 5.60 (m, 1 H), 5.08 (s, 1 H), 4.85 (d-like, *J* = 12.0 Hz, 1 H), 4.83 (d, *J* = 2.4 Hz, 1 H), 4.71 (d-like, *J* = 12.0 Hz, 1 H), 4.59 (d-like, *J* = 10.8 Hz, 1 H), 4.30 (d-like, *J* = 10.8 Hz, 1 H), 4.06 (t-like, *J* = 1.8 Hz, 1 H), 4.04 (dd, *J* = 3.0, 9.0 Hz, 1 H), 4.00–3.94 (m, 2 H), 3.76 (s, 3 H), 3.72 (t, *J* = 2.4 Hz, 1 H), 3.47 (s, 3 H), 2.45–2.41 (m, 2 H), 1.57–1.52 (m, 2 H), 1.47–1.41 (m, 2 H), 1.37 (d, *J* = 5.4 Hz, 3 H), 0.91 (t, *J* = 7.8 Hz, 3 H), 0.61 (s, 9 H), -0.15 (s, 3 H), -0.40 (s, 3 H);

^{13}C NMR (150 MHz, $CDCl_3$) δ 170.1, 165.8, 165.7, 162.4, 159.0, 138.0, 133.5, 133.3, 130.2, 129.7, 129.6, 129.4, 128.6, 128.5, 128.3, 128.2, 128.1, 126.2, 126.1, 113.7, 106.3, 100.2 ($^1J_{C1,H1}$ = 175.2 Hz), 91.5 ($^1J_{C1,H1}$ = 175.2 Hz), 78.2, 77.6, 74.5, 72.2, 70.8, 69.7, 69.4, 68.7, 67.8, 55.0, 52.2, 30.5, 25.6, 22.2, 20.1, 18.6, 17.8, 13.8, -4.3, -5.8; HRMS (ESI) *m/z* calcd for $C_{57}H_{68}O_{15}SiNa$ $[M + Na]^+$ 1043.4225, found 1043.4224.

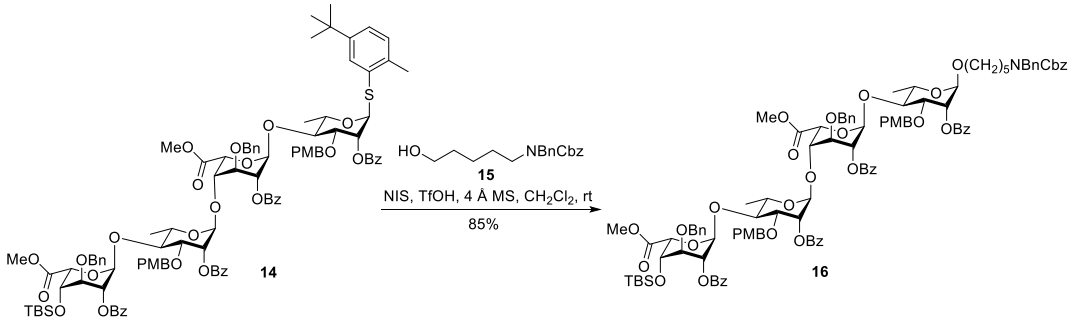
2.11. Synthesis of 2-methyl-5-*tert*-butylphenyl (methyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl-α-L-idopyranosyl uronate)-(1→4)-2-*O*-benzoyl-3-*O*-(4-methoxybenzyl)-α-L-rhamnopyranosyl-(1→4)-(methyl 2-*O*-benzoyl-3-*O*-benzyl-α-L-idopyranosyl uronate)-(1→4)-2-*O*-benzoyl-3-*O*-(4-methoxybenzyl)-1-thio-α-L-rhamnopyranoside 14



A solution of donor **13** (605.5 mg, 0.59 mmol), acceptor **12** (334.8 mg, 0.36 mmol) and freshly activated 4 Å MS (1.2 g) in anhydrous toluene (14 mL) was stirred at room temperature for 0.5 h under argon. A freshly prepared solution of PPh_3AuOTf in CH_2Cl_2 (2.2 mL, 0.05 M) and a solution of TfOH in CH_2Cl_2 (25.6 μL, 1.40 M) were added successively and the solution was stirred overnight. The mixture was quenched with Et_3N and filtered through Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (toluene/EtOAc: 30/1→20/1) to give **14** (578.1 mg, 89%) as a slightly yellow foam. $[\alpha]_D^{25}$ = –49.7 (*c* 0.56, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (m, 2 H), 8.01 (m, 2 H), 7.96 (m, 2 H), 7.93 (m, 2 H), 7.58–7.55 (m, 4 H), 7.51 (t, *J* = 7.2 Hz, 1 H), 7.47–7.32 (m, 16 H), 7.30–7.27 (m, 2 H), 7.23 (dd, *J* = 1.8, 7.8 Hz, 1 H), 7.16 (d, *J* = 7.8 Hz, 1 H), 7.03 (d, *J* = 8.4 Hz, 2 H), 6.88 (d, *J* = 8.4 Hz, 2 H), 6.43 (d, *J* = 8.4 Hz, 2 H), 6.34 (d, *J* = 8.4 Hz, 2 H), 5.85 (dd, *J* = 1.8, 2.4 Hz, 1 H), 5.76 (s, 1 H), 5.54 (s, 1 H), 5.47 (d, *J* = 1.2 Hz, 1 H), 5.33 (dd, *J* = 1.8, 3.0 Hz, 1 H), 5.23 (s, 1 H), 4.99 (d, *J* = 2.4 Hz, 1 H), 4.89 (d-like, *J* = 12.0 Hz, 1 H), 4.86 (d-like, *J* = 9.6 Hz,

2 H), 4.76 (t, *J* = 12.6 Hz, 2 H), 4.63–4.59 (m, 3 H), 4.39–4.31 (m, 3 H), 4.18 (br s, 1 H), 4.05–3.98 (m, 5 H), 3.87 (s, 3 H), 3.76 (t, *J* = 9.6 Hz, 1 H), 3.75 (s, 3 H), 3.68 (dd, *J* = 3.6, 9.6 Hz, 1 H), 3.64 (br s, 1 H), 3.60–3.55 (m, 1 H), 3.45 (s, 3 H), 3.42 (s, 3 H), 2.46 (s, 3 H), 1.37 (d, *J* = 6.6 Hz, 3 H), 1.30 (s, 9 H), 0.89 (d, *J* = 6.0 Hz, 3 H), 0.58 (s, 9 H), -0.18 (s, 3 H), -0.44 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.1, 169.8, 166.0, 165.8, 165.7, 165.5, 159.1, 158.9, 150.0, 137.9, 137.0, 133.8, 133.5, 133.3, 133.2, 132.7, 130.4, 130.3, 130.2, 130.1, 129.8, 129.7, 129.6, 129.5, 129.3, 129.1, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 125.4, 113.8, 113.6, 100.2, 99.8, 86.1, 78.5, 78.2, 78.1, 76.9, 75.2, 74.3, 73.8, 72.5, 72.1, 70.8, 70.7, 69.2, 68.9, 68.7, 68.6, 68.4, 68.3, 67.7, 67.6, 55.1, 55.0, 52.8, 52.2, 34.6, 31.5, 31.4, 25.6, 20.6, 18.6, 18.0, 17.8, -4.3, -5.8; HRMS (ESI) *m/z* calcd for $C_{101}H_{114}O_{26}SSiNa$ $[M + Na]^+$ 1825.6986, found 1825.6962.

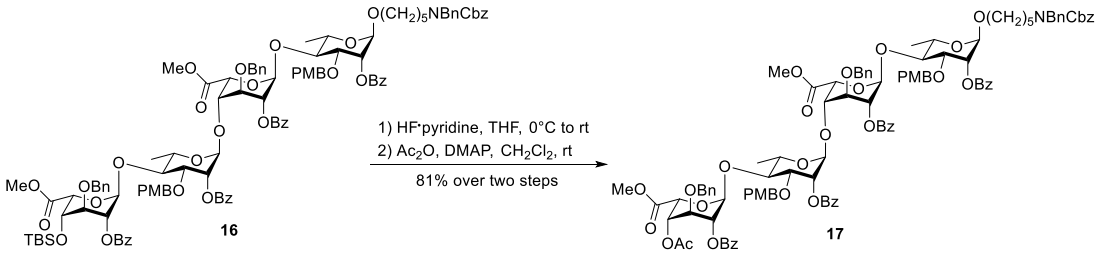
2.12. Synthesis of methyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl-α-L-idopyranosyl uronate-(1→4)-2-*O*-benzoyl-3-*O*-(4-methoxybenzyl)-α-L-rhamno pyranosyl-(1→4)-(methyl 2-*O*-benzoyl-3-*O*-benzyl-α-L-idopyranosyl uronate)-(1→4)-(*N*-benzyl-benzyloxycarbonyl-5-aminopentyl 2-*O*-benzoyl-3-*O*-(4-methoxy benzyl)-α-L-rhamnopyranoside) 16



A solution of **14** (578.1 mg, 0.32 mmol), linker **15**[4] (209.4 mg, 0.64 mmol), and freshly activated 4 Å MS (900.0 mg) in anhydrous CH_2Cl_2 (9.0 mL) was stirred at room temperature for 0.5 h under argon. Then NIS (144 mg, 0.64 mmol) and TfOH (4.2 μL, 0.048 mmol) were added. After being stirred at room temperature for 4 h, the reaction mixture was neutralized with Et_3N and filtered through Celite. The filtrate was diluted with CH_2Cl_2, washed with saturated aqueous $Na_2S_2O_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc: 6/1→3/1) to give **16** (531.4 mg, 85%) as a slightly yellow foam. $[\alpha]_D^{25}$ = –17.4 (*c* 0.49, $CHCl_3$); ^{1}H

NMR (600 MHz, $CDCl_3$) δ 8.05 (m, 2 H), 8.00 (m, 2 H), 7.93–7.91 (m, 4 H), 7.58–7.54 (m, 3 H), 7.52–7.50 (m, 1 H), 7.47–7.43 (m, 4 H), 7.38–7.18 (m, 24 H), 6.96 (d, *J* = 8.4 Hz, 2 H), 6.87 (d, *J* = 9.0 Hz, 2 H), 6.36 (d, *J* = 9.0 Hz, 2 H), 6.33 (d, *J* = 9.0 Hz, 2 H), 5.76 (s, 1 H), 5.54 (br s, 2 H), 5.32 (dd, *J* = 1.8, 3.0 Hz, 1 H), 5.19 (t, *J* = 10.2 Hz, 3 H), 4.96 (d, *J* = 2.4 Hz, 1 H), 4.85–4.81 (m, 4 H), 4.75 (d-like, *J* = 11.4 Hz, 1 H), 4.72 (d-like, *J* = 12.0 Hz, 1 H), 4.62–4.60 (m, 2 H), 4.57–4.51 (m, 3 H), 4.32 (d, *J* = 10.2 Hz, 1 H), 4.28 (d, *J* = 10.2 Hz, 1 H), 4.16 (br s, 1 H), 4.00–3.96 (m, 4 H), 3.91 (t, *J* = 9.6 Hz, 1 H), 3.87 (s, 3 H), 3.80–3.74 (m, 5 H), 3.68–3.53 (m, 4 H), 3.43 (s, 3 H), 3.41 (s, 3 H), 3.39–3.23 (m, 3 H), 1.61–1.55 (m, 4 H), 1.34 (d, *J* = 6.6 Hz, 3 H), 1.28–1.26 (m, 2 H), 0.86 (d, *J* = 6.6 Hz, 3 H), 0.58 (s, 9 H), -0.18 (s, 3 H), -0.45 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.1, 169.8, 166.1, 165.8, 165.7, 165.5, 158.9, 158.8, 138.1, 137.9, 137.8, 133.7, 133.4, 133.3, 133.2, 130.3, 130.1, 129.9, 129.8, 129.7, 129.6, 129.4, 129.3, 129.1, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.5, 127.4, 113.6, 100.1, 100.0, 99.8, 97.8, 78.1, 78.0, 75.1, 74.3, 73.9, 73.8, 72.5, 72.1, 70.8, 70.7, 69.2, 69.0, 68.9, 68.7, 68.6, 68.3, 68.0, 67.9, 67.8, 67.4, 67.0, 55.0, 54.9, 52.8, 52.1, 50.8, 50.5, 47.3, 46.3, 29.3, 28.1, 27.7, 25.6, 23.5, 18.6, 18.0, 17.8, -4.3, -5.8; HRMS (ESI) *m/z* calcd for $C_{110}H_{123}O_{29}NSiNa$ $[M + Na]^+$ 1973.7881, found 1973.7882.

2.13. Synthesis of methyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-acetyl-α-L-idopyranosyl uronate-(1→4)-2-*O*-benzoyl-3-*O*-(4-methoxybenzyl)-α-L-rhamnopyranosyl-(1→4)-(methyl 2-*O*-benzoyl-3-*O*-benzyl-α-L-idopyranosyl uronate)-(1→4)-(*N*-benzyloxycarbonyl-5-aminopentyl 2-*O*-benzoyl-3-*O*-(4-methoxybenzyl)-α-L-rhamnopyranoside) 17



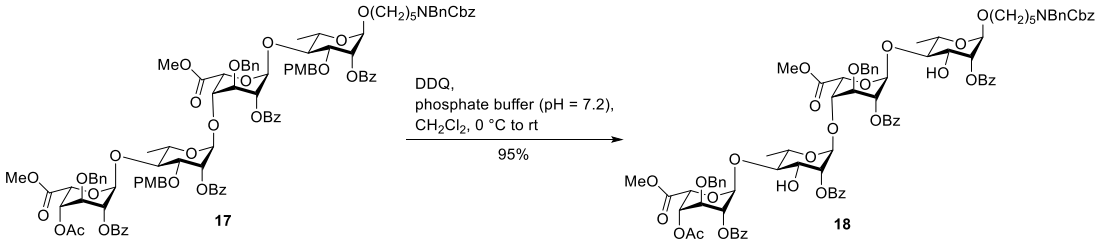
To a solution of **16** (531.4 mg, 0.27 mmol) in anhydrous THF (29 mL) was added slowly 70% HF·pyridine (7.9 mL) at 0 ℃. The reaction was then gradually warmed to room temperature and stirred for 2 d. The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The

residue was purified by silica gel column chromatography (petroleum ether/EtOAc: 4/1→2/1) to afford the corresponding alcohol **S1** (418 mg, 84%) as a white foam. $[\alpha]_D^{25}$ = –16.3 (*c* 0.28, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (m, 2 H), 7.98 (m, 2 H), 7.90 (m, 2 H), 7.87 (m, 2 H), 7.60–7.54 (m, 4 H), 7.47–7.19 (m, 28 H), 6.96 (d, *J* = 8.4 Hz, 2 H), 6.89 (d, *J* = 8.4 Hz, 2 H), 6.37 (d, *J* = 8.4 Hz, 2 H), 6.35 (d, *J* = 8.4 Hz, 2 H), 5.76 (s, 1 H), 5.54 (br s, 1 H), 5.52 (s, 1 H), 5.38 (dd, *J* = 1.8, 3.0 Hz, 1 H), 5.20–5.17 (m, 3 H), 4.98 (m, 2 H), 4.87–4.82 (m, 3 H), 4.73 (d-like, *J* = 12.0 Hz, 1 H), 4.69 (d, *J* = 1.2 Hz, 1 H), 4.62 (d-like, *J* = 11.4 Hz, 1 H), 4.56 (d, *J* = 10.2 Hz, 1 H), 4.54–4.52 (m, 3 H), 4.35 (d, *J* = 10.2 Hz, 1 H), 4.28 (d, *J* = 10.2 Hz, 1 H), 4.17 (br s, 1 H), 4.00–3.95 (m, 4 H), 3.92 (t, *J* = 9.6 Hz, 1 H), 3.89 (s, 3 H), 3.80 (m, 1 H), 3.77 (s, 3 H), 3.76–3.54 (m, 5 H), 3.43 (s, 3 H), 3.41 (s, 3 H), 3.36–3.23 (m, 3 H), 2.58 (d, *J* = 11.4 Hz, 1 H), 1.62–1.54 (m, 4 H), 1.34 (d, *J* = 6.0 Hz, 3 H), 1.29 (m, 2 H), 0.87 (d, *J* = 6.0 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.9, 169.8, 166.1, 165.7, 165.4, 164.8, 159.0, 158.9, 138.1, 137.9, 137.5, 133.7, 133.6, 133.4, 130.3, 130.1, 130.0, 129.9, 129.8, 129.7, 129.5, 129.4, 129.3, 129.2, 128.8, 128.7, 128.6, 128.5, 128.2, 128.1, 128.0, 127.9, 127.5, 127.4, 113.7, 113.6, 100.1, 100.0, 99.5, 97.8, 78.3, 78.1, 78.0, 76.1, 75.0, 74.0, 73.8, 73.7, 72.4, 72.2, 70.8, 70.7, 69.0, 68.8, 68.3, 68.2, 68.0, 67.9, 67.7, 67.6, 67.4, 67.3, 67.0, 55.0, 52.9, 52.5, 50.8, 50.5, 47.3, 46.3, 29.4, 28.1, 27.7, 23.6, 18.6, 18.0; HRMS (ESI) *m/z* calcd for $C_{104}H_{109}O_{29}NNa$ $[M + Na]^+$ 1859.7017, found 1859.7021.

To a solution of the above alcohol **S1** (418 mg, 0.23 mmol) and DMAP (56.2 mg, 0.46 mmol) in anhydrous CH_2Cl_2 (25.0 mL) was added Ac_2O (217 μL) under argon. The reaction was then stirred at room temperature for 5 h. The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc: 4/1→2/1) to afford **17** (416.2 mg, 96%) as a white foam. $[\alpha]_D^{25}$ = –9.1 (*c* 0.58, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.06 (m, 2 H), 7.99–7.97 (m, 4 H), 7.90 (d-like, *J* = 7.2 Hz, 2 H), 7.60–7.53 (m, 4 H), 7.47–7.18 (m, 28 H), 6.97 (d, *J* = 8.4 Hz, 2 H), 6.88 (d, *J* = 8.4 Hz, 2 H), 6.36–6.34 (m, 4 H), 5.76 (s, 1 H), 5.56 (br s, 2 H), 5.35 (dd, *J* = 1.8, 3.0 Hz, 1 H), 5.21–5.16 (m, 4 H), 4.97 (d, *J* = 1.8 Hz, 1 H), 4.94 (s, 1 H), 4.86–4.82 (m, 3 H), 4.75–4.73 (m, 2 H), 4.67 (d-like, *J* = 11.4 Hz, 1 H), 4.62 (d-like, *J* = 11.4 Hz, 1 H), 4.57 (d-like, *J* = 10.2 Hz, 1 H), 4.53–4.51 (m, 2 H), 4.33 (d, *J* = 10.2 Hz, 1 H), 4.28 (d, *J* = 10.2 Hz, 1 H), 4.17 (br s, 1 H), 4.00 (m, 1 H), 3.97–3.91 (m, 3 H), 3.89 (s,

3 H), 3.79 (m, 2 H), 3.76–3.73 (m, 4 H), 3.68–3.51 (m, 3 H), 3.42 (s, 3 H), 3.39 (s, 3 H), 3.35–3.23 (m, 3 H), 1.78 (s, 3 H), 1.63–1.56 (m, 4 H), 1.35 (d, *J* = 6.0 Hz, 3 H), 1.29 (m, 2 H), 0.86 (d, *J* = 6.0 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.0, 169.8, 169.0, 166.1, 165.7, 165.5, 164.9, 159.0, 158.9, 138.1, 137.9, 137.4, 137.0, 133.7, 133.6, 133.4, 133.3, 130.3, 130.1, 130.0, 129.9, 129.8, 129.6, 129.5, 129.4, 129.3, 128.7, 128.6, 128.5, 128.4, 128.2, 128.0, 127.9, 127.5, 127.4, 127.3, 113.7, 113.6, 100.2 ($^1J_{C1,H1}$ = 171.6 Hz), 100.0 ($^1J_{C1,H1}$ = 174.0 Hz), 99.3 ($^1J_{C1,H1}$ = 175.2 Hz), 97.8 ($^1J_{C1,H1}$ = 172.2 Hz), 78.2, 78.1, 78.0, 76.0, 75.0, 73.5, 72.4, 72.3, 72.0, 70.8, 70.7, 69.0, 68.9, 68.1, 67.9, 67.7, 67.4, 67.3, 67.1, 67.0, 66.2, 55.0, 52.9, 52.6, 50.8, 50.5, 47.3, 46.3, 29.3, 28.1, 27.7, 23.5, 20.7, 18.6, 17.9; HRMS (ESI) *m/z* calcd for $C_{106}H_{111}O_{30}NNa$ $[M + Na]^+$ 1901.7122, found 1901.7124.

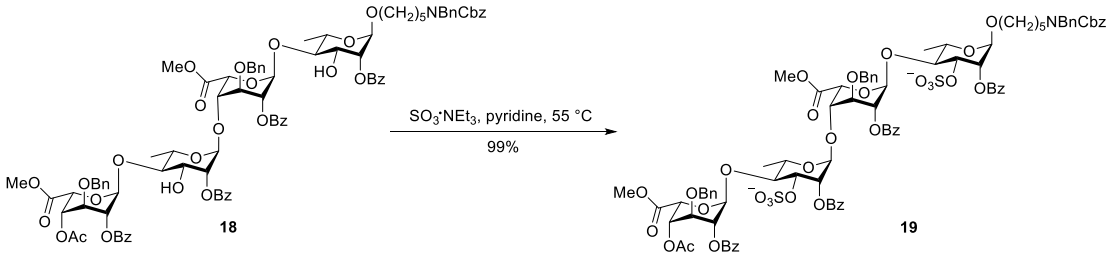
2.14. Synthesis of methyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-acetyl-α-L-idopyranosyl uronate-(1→4)-2-*O*-benzoyl-α-L-rhamnopyranosyl-(1→4)-(methyl 2-*O*-benzoyl-3-*O*-benzyl-α-L-idopyranosyl uronate)-(1→4)-(*N*-benzyl-benzyloxycarbonyl-5-aminopentyl 2-*O*-benzoyl-α-L-rhamnopyranoside) 18



To a solution of **17** (197.1 mg, 0.11 mmol) in dichloromethane and pH 7.2 phosphate buffer (10/1, v/v, 6.2 mL) was added DDQ (119.2 mg, 0.53 mmol) at 0 ℃. After stirring at 0 ℃ for 1 h, the reaction was gradually warmed to room temperature and stirred for 4 h. The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc: 4/1→2/1) to afford **18** (170.4 mg, 95%) as a white foam. $[\alpha]_D^{25}$ = –20.2 (*c* 0.77, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11–8.08 (m, 4 H), 8.02–8.00 (m, 4 H), 7.60–7.56 (m, 3 H), 7.51 (t, *J* = 7.2 Hz, 1 H), 7.48–7.45 (m, 4 H), 7.42 (t, *J* = 7.8 Hz, 2 H), 7.36–7.17 (m, 22 H), 5.67 (d, *J* = 2.4 Hz, 1 H), 5.41 (s, 1 H), 5.28–5.24 (m, 3 H), 5.19 (dd, *J* = 1.2, 3.0 Hz, 2 H), 5.16 (s, 1 H), 5.07 (s, 1 H), 4.97 (d, *J* = 2.4 Hz, 1 H), 4.93 (s, 1 H), 4.82 (d-like, *J* = 11.4 Hz, 2 H), 4.74 (d-like, *J* = 12.0 Hz, 1 H), 4.71 (d, *J* = 1.8 Hz, 1 H), 4.64 (s, 2 H), 4.50 (d-like, *J*

= 11.4 Hz, 2 H), 4.20 (t-like, *J* = 3.0 Hz, 2 H), 4.07–4.04 (m, 1 H), 3.96 (s, 3 H), 3.90 (t, *J* = 3.0 Hz, 1 H), 3.88–3.86 (m, 2 H), 3.80 (s, 3 H), 3.75 (t, *J* = 9.6 Hz, 2 H), 3.67–3.58 (m, 2 H), 3.39–3.20 (m, 3 H), 2.99 (d, *J* = 5.4 Hz, 1 H), 2.80 (d-like, *J* = 9.0 Hz, 1 H), 2.00 (s, 3 H), 1.58–1.51 (m, 4 H), 1.34 (d, *J* = 6.0 Hz, 3 H), 1.26 (m, 2 H), 0.93 (d, *J* = 6.0 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.0, 169.8, 168.8, 166.5, 166.0, 165.8, 165.4, 138.1, 137.3, 137.0, 136.9, 136.7, 133.8, 133.7, 133.5, 130.2, 130.1, 130.0, 129.8, 129.7, 129.4, 129.3, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.5, 127.4, 99.9, 99.3, 99.0, 97.4, 80.1, 78.6, 75.1, 74.9, 74.8, 73.8, 73.2, 73.0, 72.8, 72.7, 70.5, 69.9, 69.2, 69.1, 69.0, 68.1, 67.9, 67.8, 67.5, 67.4, 67.3, 67.0, 66.8, 53.0, 52.7, 50.7, 50.4, 47.3, 46.3, 29.3, 28.1, 27.7, 23.5, 20.8, 18.2, 17.4; HRMS (ESI) *m/z* calcd for $C_{90}H_{95}O_{28}NNa$ $[M + Na]^+$ 1660.5938, found 1660.5930.

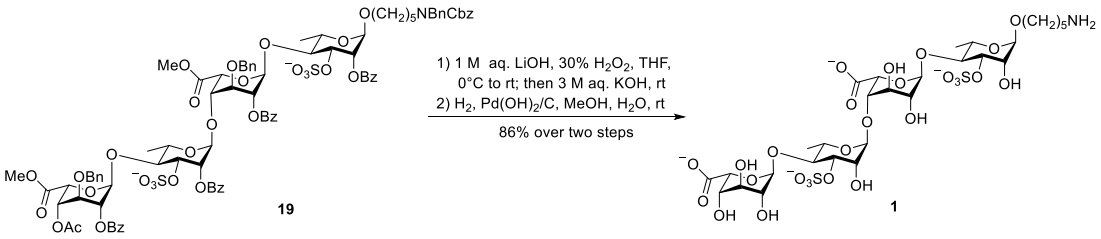
2.15. Synthesis of methyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-acetyl-α-L-idopyranosyl uronate-(1→4)-2-*O*-benzoyl-3-*O*-sulfo-α-L-rhamnopyranosyl-(1→4)-(methyl 2-*O*-benzoyl-3-*O*-benzyl-α-L-idopyranosyl uronate)-(1→4)-(*N*-benzyl-benzyloxycarbonyl-5-aminopentyl 2-*O*-benzoyl-3-*O*-sulfo-α-L-rhamnopyranoside) 19



To a solution of **18** (56 mg, 0.034 mmol) in anhydrous pyridine (3.4 mL) was added SO_3·NEt_3 (370 mg, 2.04 mmol). The reaction mixture was stirred at 55 ℃ for 6 h. The reaction mixture was then quenched with methanol (124 mL, 3.06 mmol), adjusted to pH 7~8 by Et_3N, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH: 50/1→30/1, + 1% Et_3N). The fractions containing product were concentrated *in vacuo*, and the residue was immediately passed through a column of Dowex 50WX8 Na^+ resin using methanol as eluent to provide **19** (60.3 mg, 99%) as a white solid. $[\alpha]_D^{25}$ = –38.4 (*c* 0.31, CH_3OH); ^{1}H NMR (600 MHz, CD_3OD) δ 8.12 (m, 2 H), 8.09 (m, 2 H), 8.05 (m, 2 H), 7.98 (m, 2 H), 7.62–7.60 (m, 2 H), 7.57 (t, *J* = 7.8 Hz, 1 H), 7.53–7.44 (m, 7 H), 7.42–7.15 (m, 22 H), 5.79 (s, 1 H), 5.61 (br s, 2 H), 5.55 (s, 1 H), 5.53 (t, *J* = 3.0 Hz, 1 H), 5.23 (s, 1 H), 5.18–5.14 (m, 2 H), 5.12 (s, 1 H), 5.00 (d, *J* = 2.4 Hz, 1 H), 4.93 (d, *J* = 8.4 Hz, 1 H), 4.89–4.82 (m, 4 H), 4.71 (t, *J* = 10.2 Hz, 2 H), 4.63 (d, *J* = 1.8 Hz,

1 H), 4.55 (d-like, *J* = 10.8 Hz, 1 H), 4.51 (s, 2 H), 4.10 (br s, 1 H), 4.04 (t, *J* = 9.0 Hz, 1 H), 4.00 (t, *J* = 3.0 Hz, 1 H), 3.94 (s, 3 H), 3.90 (t, *J* = 2.4 Hz, 1 H), 3.84–3.81 (m, 2 H), 3.76 (s, 3 H), 3.67–3.54 (m, 2 H), 3.44–3.24 (m, 3 H), 1.75 (s, 3 H), 1.61–1.52 (m, 4 H), 1.30 (m, 5 H), 0.61 (d, *J* = 6.0 Hz, 3 H); ^{13}C NMR (150 MHz, CD_3OD) δ 171.3, 171.2, 170.4, 167.3, 167.1, 167.0, 166.5, 139.2, 138.8, 138.1, 134.4, 134.3, 131.3, 131.2, 131.1, 131.0, 130.9, 129.8, 129.7, 129.6, 129.5, 129.4, 129.3, 129.2, 129.1, 129.0, 128.8, 128.7, 128.4, 101.6, 100.9, 100.5, 98.5, 78.7, 78.2, 77.5, 77.1, 74.7, 73.4, 73.3, 73.1, 72.8, 70.0, 69.2, 69.0, 68.9, 68.5, 68.4, 67.8, 53.6, 52.9, 51.7, 51.5, 47.7, 29.0, 28.5, 24.3, 20.5, 18.8, 18.4; HRMS (ESI) *m/z* calcd for $C_{90}H_{94}NO_{34}S_2$ $[M - H]^-$ 1796.5104, found 1796.5125.

2.16. Synthesis of α-L-idopyanosyl uronate-(1→4)-3-*O*-sulfo-α-L-rhamno pyranosyl-(1→4)-α-L-idopyranosyl uronate-(1→4)-3-*O*-sulfo-5-aminopentyl-α-L-rhamnopyranoside 1



A premixed solution of 30% aqueous H_2O_2 (674 μL, 6.6 mmol, 100 equiv per CO_2Me) and 1 M aqueous LiOH (3.3 mL, 3.3 mmol, 50 equiv per CO_2Me) was added to the solution of **19** (59.2 mg, 0.033 mmol) in THF (1.65 mL). After stirring at room temperature for 24 h, 3 M aqueous KOH was added until pH 14. The mixture was stirred for another 24 h at room temperature, adjusted to pH 8 by Amberlite IR-120 H^+ resin, filtered, and concentrated under reduced pressure. The residue was purified by RP-18 column chromatography (MeOH/H_2O: 1/3→2/1) to afford the corresponding polyol **S2** (37.9 mg, 88%) as a white solid. $[\alpha]_D^{25}$ = –81.6 (*c* 0.29, H_2O); ^{1}H NMR (600 MHz, D_2O) δ 7.45–7.18 (m, 20 H), 5.21 (s, 1 H), 5.13 (br s, 2 H), 5.09 (s, 1 H), 4.87 (s, 1 H), 4.77–4.74 (m, 2 H), 4.68–4.64 (m, 3 H), 4.56 (dd, *J* = 3.0, 9.6 Hz, 1 H), 4.54 (d, *J* = 1.8 Hz, 1 H), 4.49–4.45 (m, 4 H), 4.29 (m, 1 H), 4.25 (s, 1 H), 4.15 (s, 2 H), 4.05 (dd, *J* = 2.4, 4.2 Hz, 1 H), 3.99 (m, 1 H), 3.78–3.70 (m, 5 H), 3.66 (br s, 1 H), 3.60–3.37 (m, 2 H), 3.24–3.21 (m, 2 H), 1.53–1.44 (m, 4 H), 1.30–1.20 (m, 5 H), 1.03 (br s, 3 H); ^{13}C NMR (150 MHz, D_2O) δ 176.0, 175.3, 158.1, 157.7, 137.6, 137.5, 137.2, 136.3, 128.7, 128.6, 128.5, 128.2, 128.1, 127.9, 127.8, 127.5, 127.3,

127.1, 102.4, 102.2, 101.0, 99.3, 79.2, 78.9, 76.9, 76.8, 76.3, 75.9, 74.5, 71.7, 71.5, 70.1, 69.2, 68.9, 68.7, 68.1, 67.7, 67.5, 67.3, 66.7, 66.5, 50.5, 50.4, 47.6, 46.8, 28.3, 28.1, 27.1, 26.9, 22.8, 22.6, 17.1, 17.0; HRMS (ESI) m/z calcd for $C_{58}H_{72}O_{29}NS_2$ [M – H]$^-$ 1310.3631, found 1310.3637.

To a solution of the above polyol **S2** (77.9 mg, 0.059 mmol) in CH_3OH/H_2O (1/3, v/v, 14.4 mL) was added palladium hydroxide on carbon (10%, 623 mg). After purged with hydrogen for five times, the mixture was stirred under an atmosphere of hydrogen for 24 h. The mixture was filtered and concentrated under reduced pressure. The residue was immediately passed through a column of Dowex 50WX8 Na^+ resin using H_2O as eluent. The fractions containing product were concentrated *in vacuo*. The residue was eluted through Sephadex LH-20 column (H_2O) to provide **1** (52.2 mg, 98%) as a slightly orange solid. $[\alpha]_D^{25}$ = –76.9 (*c* 0.20, H_2O); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.12 (d, *J* = 4.2 Hz, 1 H), 5.08 (d, *J* = 3.6 Hz, 1 H), 4.87 (d, *J* = 1.2 Hz, 1 H), 4.81 (d, *J* = 1.8 Hz, 1 H), 4.61–4.59 (m, 2 H), 4.55 (d, *J* = 3.6 Hz, 1 H), 4.51 (d, *J* = 3.6 Hz, 1 H), 4.29 (t, *J* = 2.4 Hz, 1 H), 4.25 (t, *J* = 3.0 Hz, 1 H), 4.10–4.05 (m, 1 H), 4.00 (t, *J* = 3.6 Hz, 1 H), 3.95 (t-like, *J* = 4.8 Hz, 1 H), 3.88–3.83 (m, 3 H), 3.82–3.78 (m, 2 H), 3.75–3.69 (m, 3 H), 3.57–3.53 (m, 1 H), 3.02 (t, *J* = 7.2 Hz, 2 H), 1.74–1.62 (m, 2 H), 1.55–1.42 (m, 2 H), 1.27 (d, *J* = 6.0 Hz, 3 H), 1.26 (d, *J* = 6.0 Hz, 3 H); ^{13}C NMR (150 MHz, D_2O) δ 175.7, 174.6, 103.0, 102.7, 101.2, 99.3, 79.0, 78.8, 76.5, 76.1, 71.4, 71.3, 71.2, 70.9, 70.7, 70.3, 69.9, 68.8, 68.7, 67.8, 67.6, 67.4, 39.4, 28.0, 26.6, 22.6, 16.9, 16.8; HRMS (ESI) m/z calcd for $C_{29}H_{48}O_{27}NS_2$ [M – H]$^-$ 906.1855, found 906.1810.

3. Materials and method biology

3.1 Reagents

Neutral red was purchased from J&K scientific. LPS was purchased from Sigma.

3.2 Cell culture

The murine macrophage RAW264.7 cell line was purchased from the Cell Bank of the Chinese Academy of Sciences (Shanghai, China) and cultured in DMEM (Gibco, USA) supplemented with 10% fetal bovine serum (FBS, Gibco) at 37 ℃ in a moisturized atmosphere of 5% CO_2 and 95% air.

3.3 Cell viability analysis

The effect of the sulfated tetrasaccharide **1** on the viability of RAW264.7 cells was measured by MTT (3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide) assays. RAW264.7 cells were seeded in 96-well plates for 12 h, and then treated with tetrasaccharide **1** (0, 18.75, 37.5, 75, 150, 300 μg/mL) for an additional 24 h. Next, the medium containing **1** was removed, and fresh medium containing MTT (200 μL per well) was added. After 4 h, the formazan crystals were dissolved in 100 μL DMSO and the optical density at 540 nm was measured by multi-mode microplate reader (BioTek's Synergy Neo2). The cell viability was analyzed by this equation: Cell Viability (%) = [OD (Samples)-OD (Blank)/OD (Control)-OD (Blank)]*100%.

3.4 Phagocytosis assay

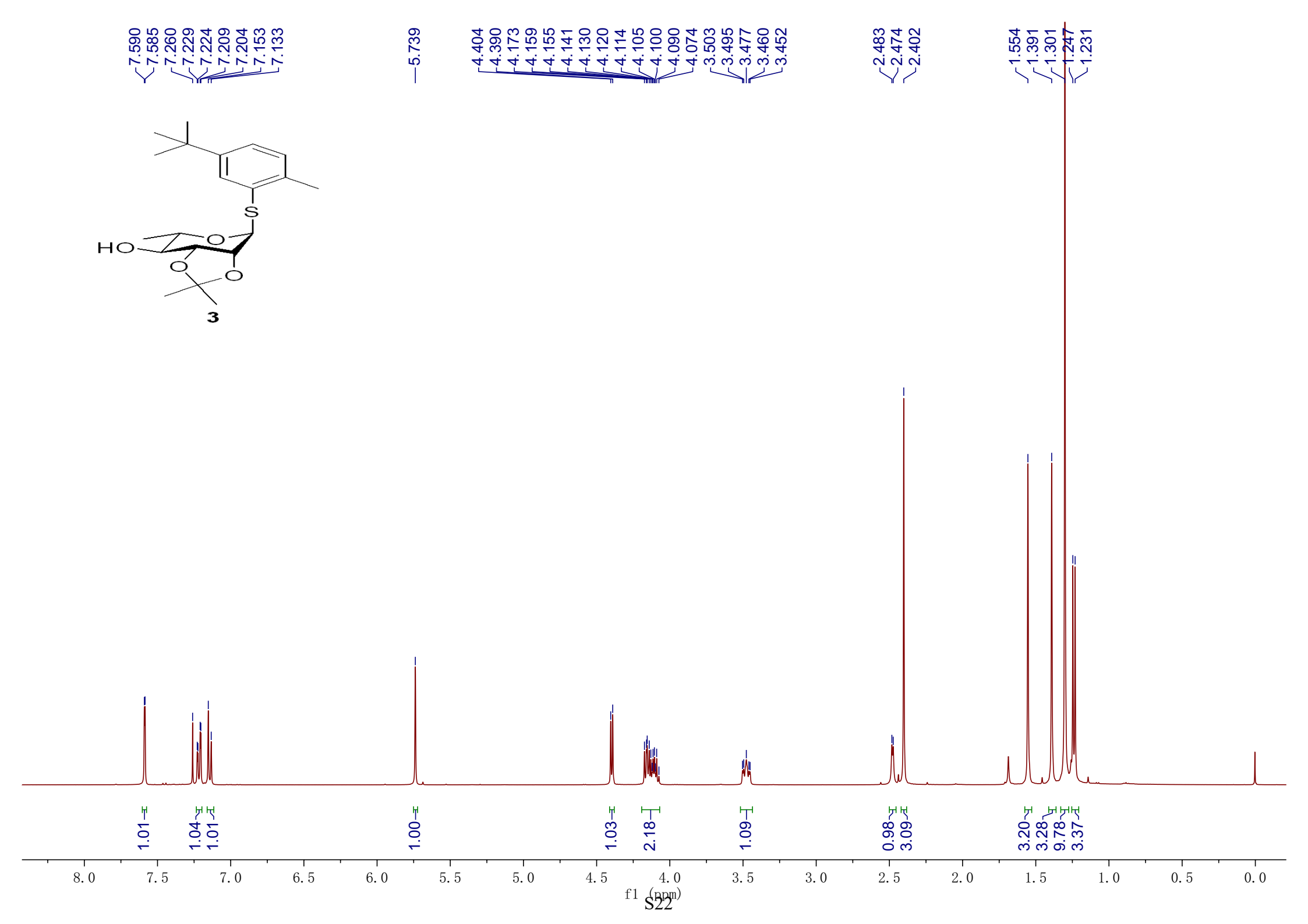
The phagocytic ability of RAW264.7 cells was evaluated by neutral red uptake assay. RAW264.7 cells were seeded in a 96-well plate and incubated at 37 ℃ for 12 h. After cells were incubated with the sulfated tetrasaccharide **1** (0, 37.5, 75, 150, 300 μg/mL) or LPS (1 μg/mL) for 24 h, 100 μL of neutral red solution (0.075%) was added into wells and incubated for 4 min. Next, these cells were washed with PBS twice and lysed by cell lysates (ethanol and acetic acid at the ratio of 1:1, 100 μL/well) at room temperature for 2 h. The optical density at 540 nm was measured by multi-mode microplate reader (BioTek's Synergy Neo2).

3.5 Statistical analysis

Statistical analysis was performed with Graphpad Prism 8.0.1 software. Experimental results were expressed by the mean ± standard deviation (SD) of three independent experiments. The data were statistically analyzed by Student's t test to detect significant difference between two groups. The p-value less than 0.05 was considered significant.

4. References

1. Q. Liu, P. Wang, L. Zhang, T. Guo, G. Lv and Y. Li, *Carbohydr. Res.* 2009, **344**, 1276−1281.
2. (a) X. Dai, W. Liu, Q. Zhou, C. Cheng, C. Yang, S. Wang, M. Zhang, P. Tang, H. Song, D. Zhang and Y. Qin, *J. Org. Chem.* 2016, **81**, 162–184; (b) S.-C. Hung, X.-A. Lu, J.-C. Lee, M. D.-T. Chang, S.-l. Fang, T.-c. Fan, M. M. L. Zulueta and Y.-Q. Zhong, *Org. Biomol. Chem.* 2012, **10**, 760–772; (c) J.-C. Lee, X.-A. Lu, S. S. Kulkarni, Y.-S. Wen, S.-C. Hung, *J. Am. Chem. Soc.* 2004, **126**, 476–477.
3. E. Piers, T. Wong, P. D. Coish and C. Rogers, *Can. J. Chem.* 1994, **72**, 1816–1819.
4. (a) T. K. K. Mong, M. K. Lee, S. G. Duron and C. H. Wong, *Proc. Natl. Acad. Sci. USA* 2003, **100**, 797–802; (b) C. Noti, J. L. de Paz, L. Polito and P. H. Seeberger, *Chem. Eur. J.* 2006, **12**, 8664–8686.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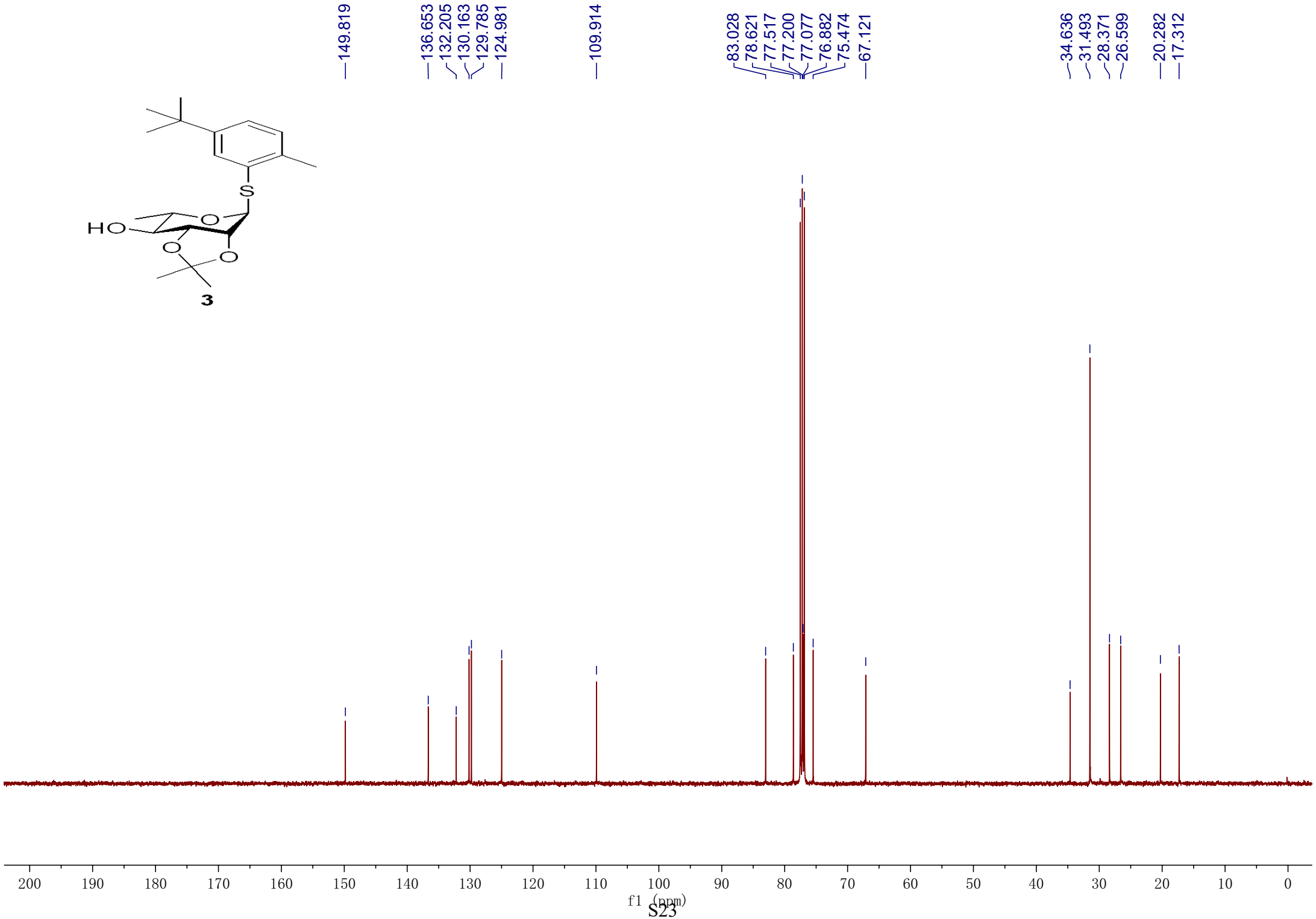
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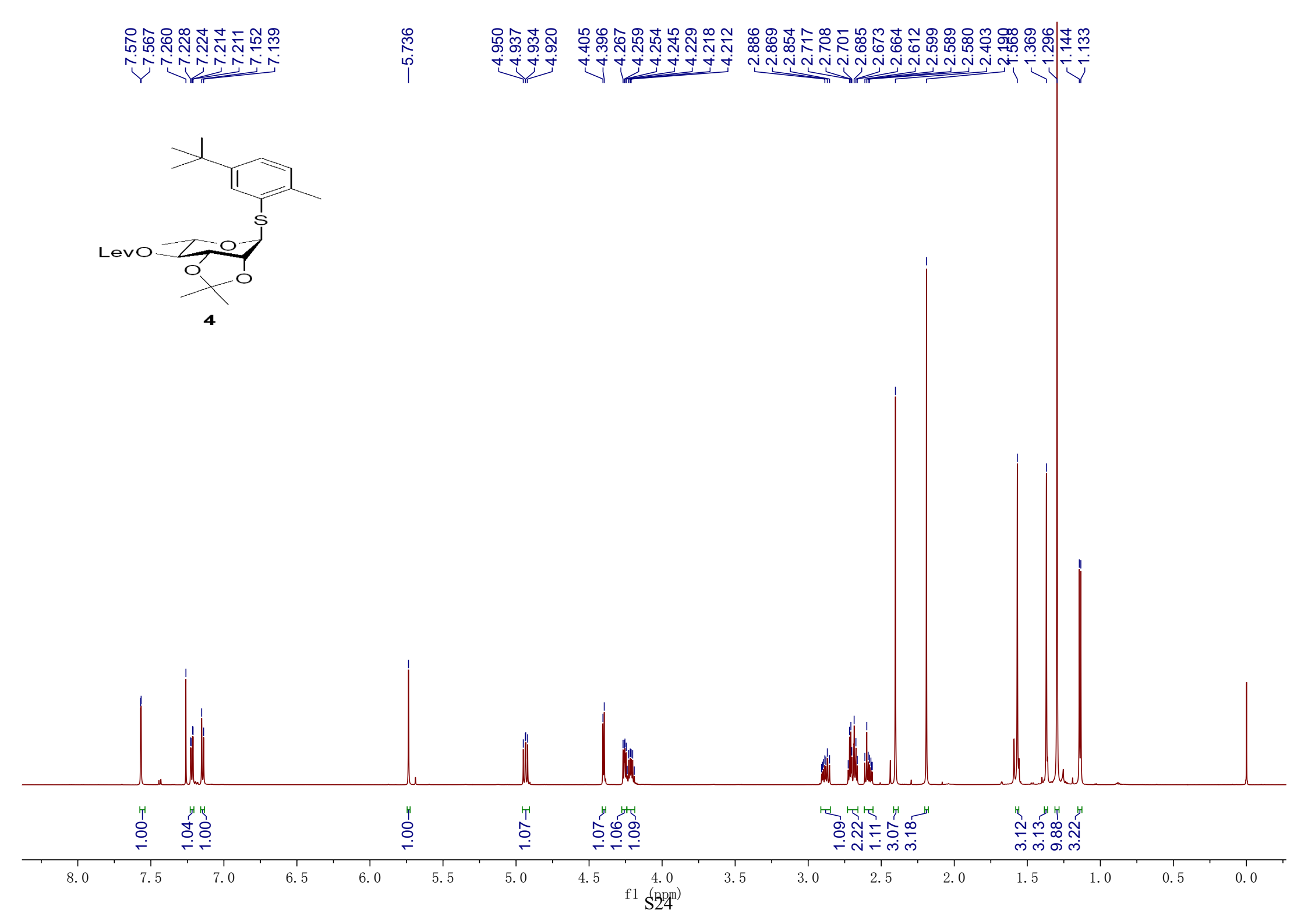
67.121
34.636
31.493
28.371
26.599
20.282
17.312
HO
O
O
O
S
3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.567
7.260
7.228
7.224
7.214
7.211
7.152
7.139
5.736
4.950
4.937
4.934
4.920
4.405
4.396
4.267
4.259
4.254
4.245
4.229
4.218
4.212
2.886
2.869
2.854
2.717
2.708
2.701
2.685
2.673
2.664
2.612
2.599
2.589
2.580
2.403
1.369
1.296
1.144
1.133
LevO
O
O
O
O
S
4
1.00
1.04
1.00
1.00
1.07
1.07
1.06
1.09
1.09
2.22
1.11
3.07
3.18
3.12
3.13
9.88
3.22
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
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1.0
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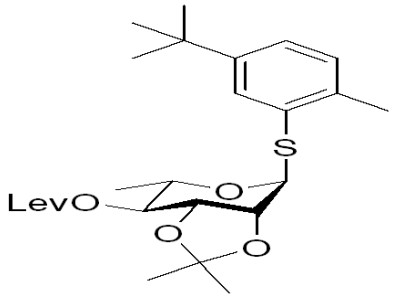
0.0
f1 (ppm)

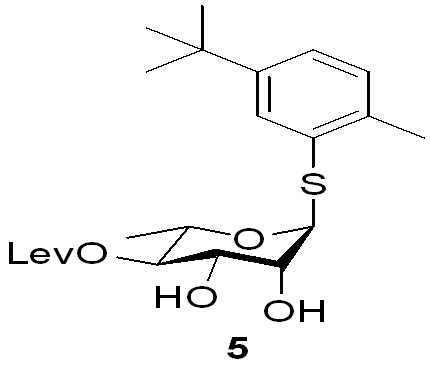


4

206.559
172.218
149.922
136.703
132.015
130.235
129.879
125.151
110.168
83.096
77.412
77.200
77.041
76.989
75.724
75.191
65.852
38.099
34.652
31.499
29.984
28.150
27.914
26.755
20.303
17.035

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)



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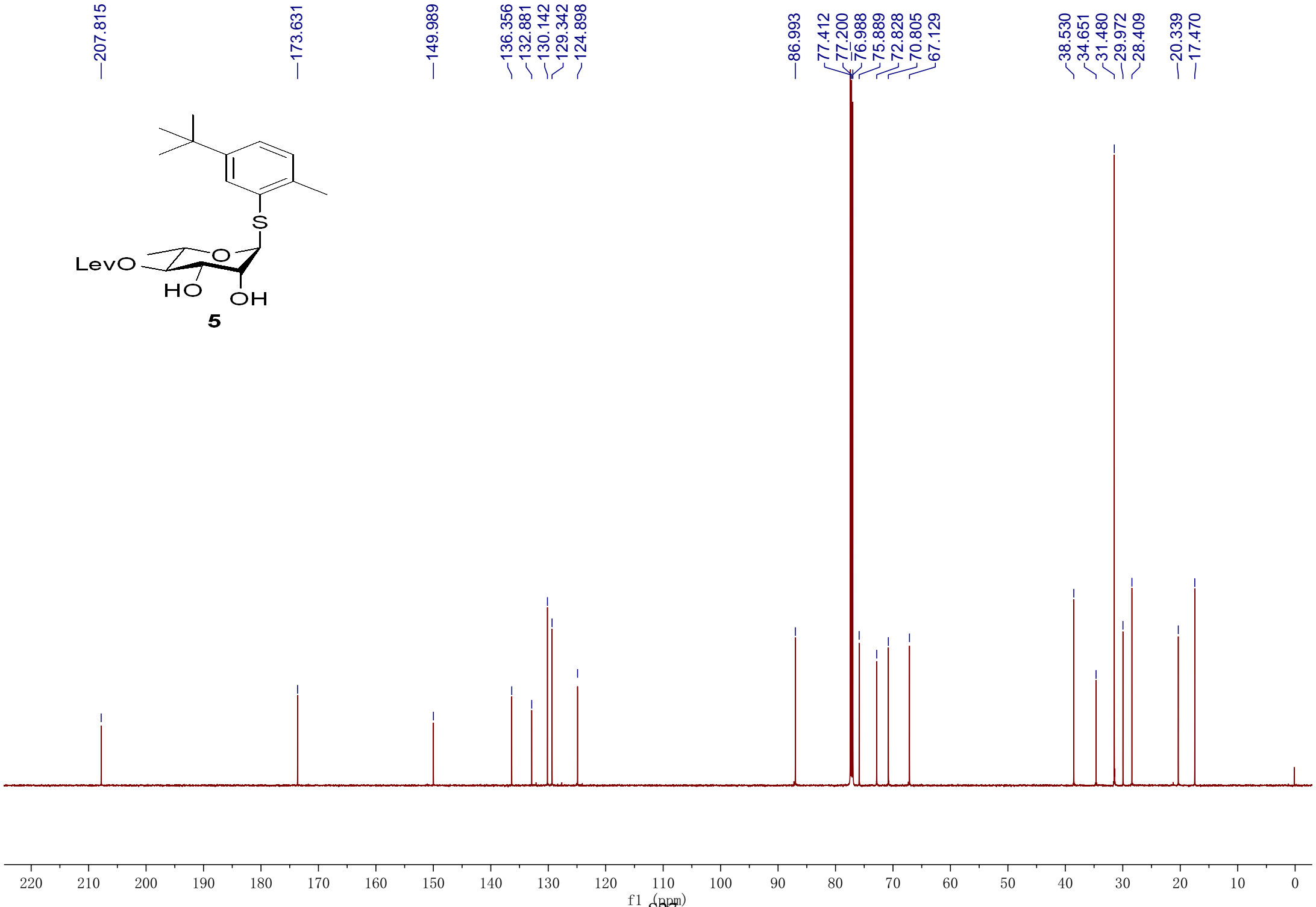
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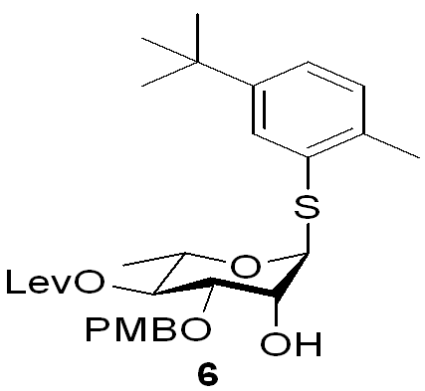
129.342
124.898
86.993
77.412
77.200
76.988
75.889
72.828
70.805
67.129
38.530
34.651
31.480
29.972
28.409
20.339
17.470
LevO
O
HO
OH
S
5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



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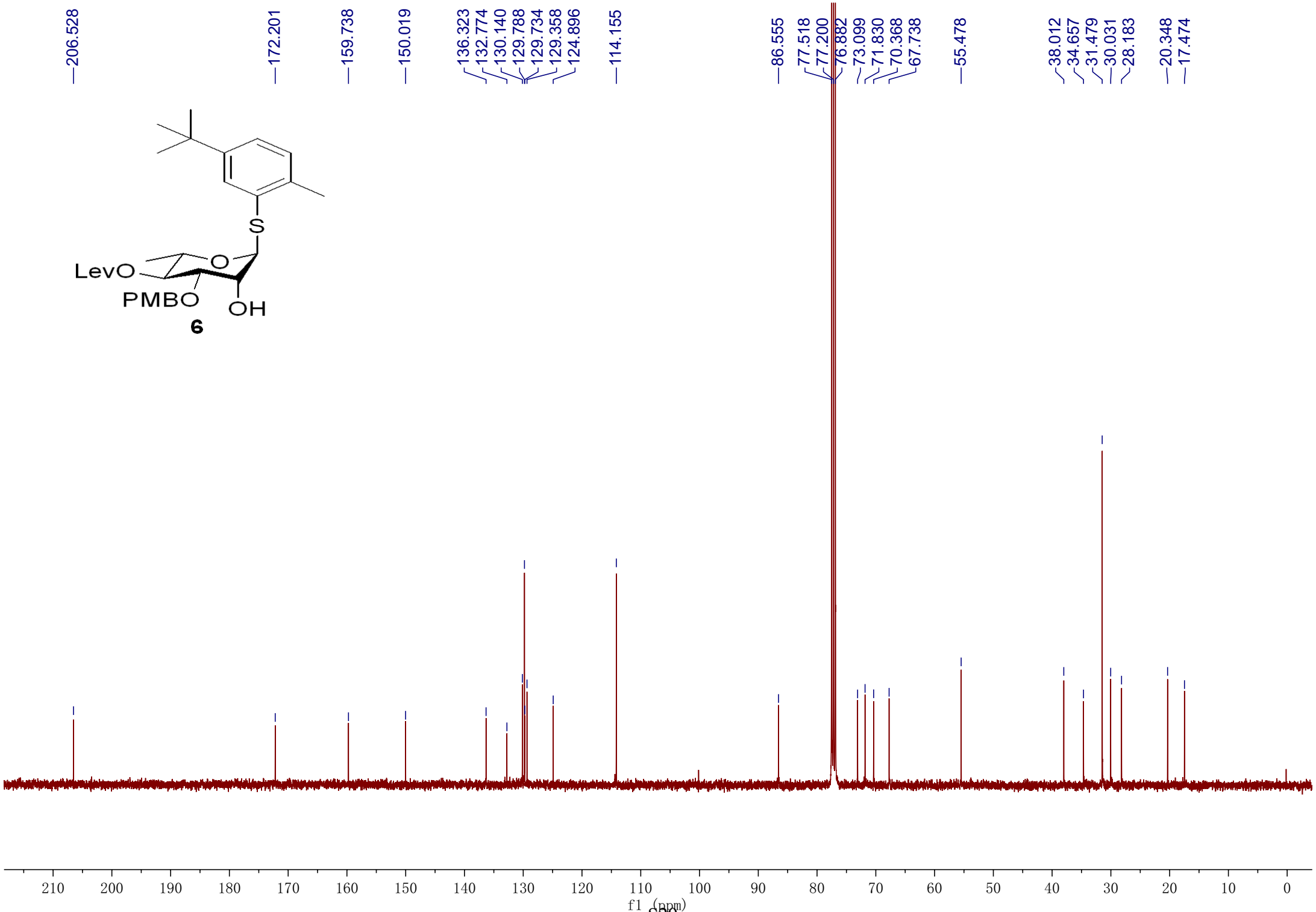
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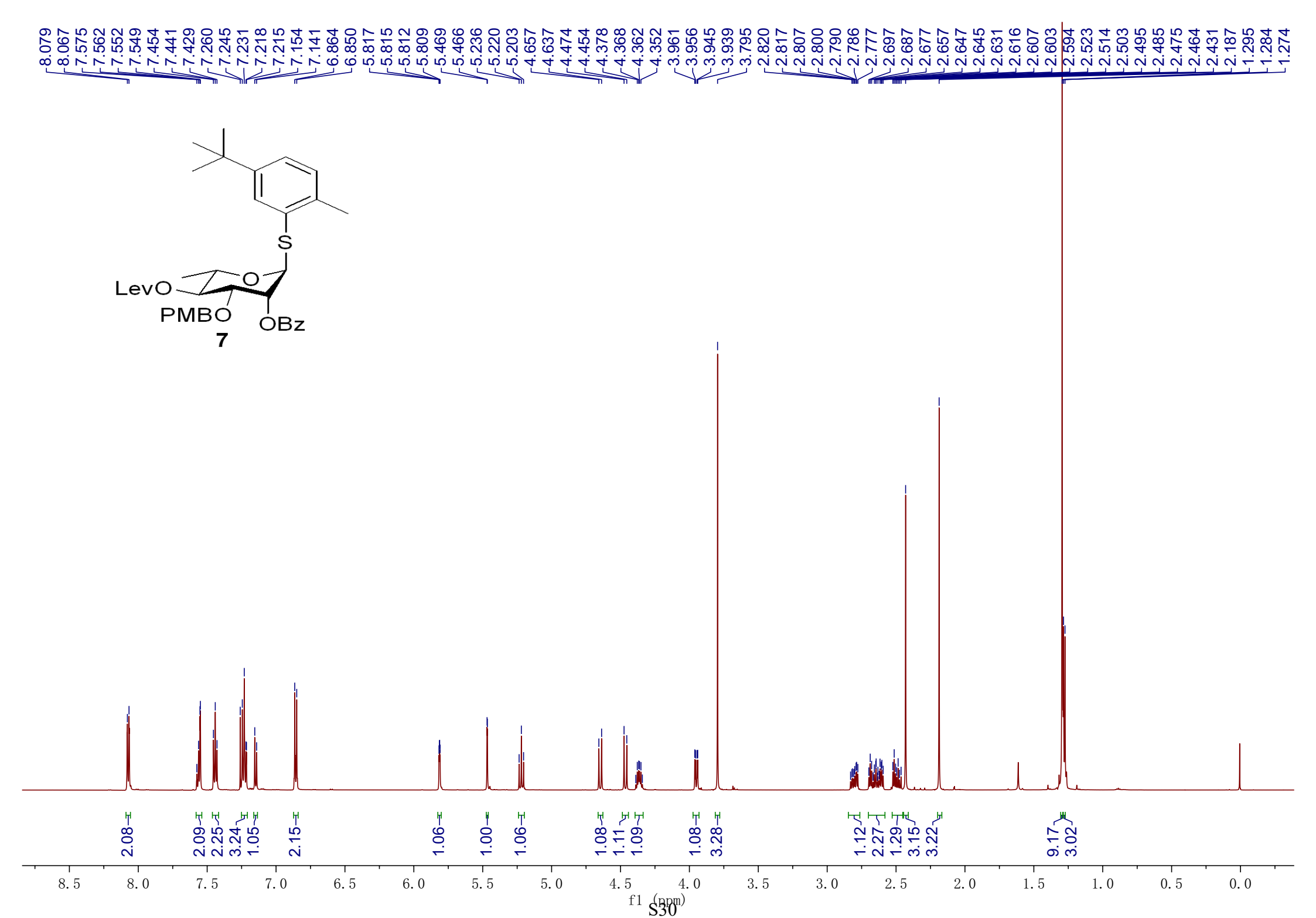
172.201
159.738
150.019
136.323
132.774
130.140
129.788
129.734
129.358
124.896
114.155
86.555
77.518
77.200
76.882
73.099
71.830
70.368
67.738
55.478
38.012
34.657
31.479
30.031
28.183
20.348
17.474
S
O
LevO
PMBO
OH
6
f1 (ppm)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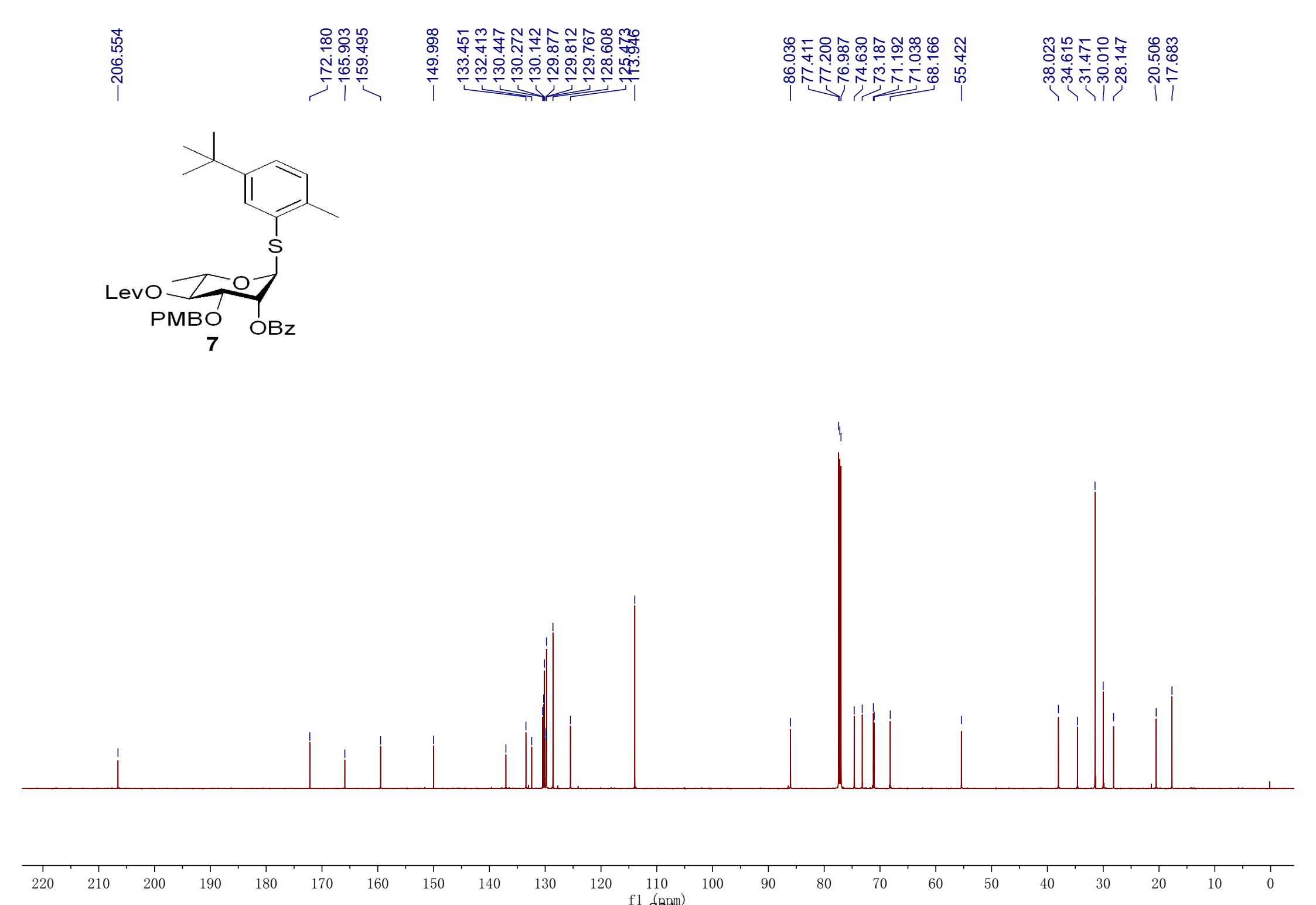
8.067
7.575
7.562
7.552
7.549
7.454
7.441
7.429
7.260
7.245
7.231
7.218
7.215
7.154
7.141
6.864
6.850
5.817
5.815
5.812
5.809
5.469
5.466
5.236
5.220
5.203
4.657
4.637
4.474
4.454
4.378
4.368
4.362
4.352
3.961
3.956
3.945
3.939
3.795
2.820
2.817
2.807
2.800
2.790
2.786
2.777
2.697
2.687
2.677
2.657
2.647
2.645
2.631
2.616
2.607
2.603
2.594
2.523
2.514
2.503
2.495
2.485
2.475
2.464
2.431
2.187
1.295
1.284
1.274
S
O
LevO
PMBO
OBz
7
2.08
2.09
2.25
3.24
1.05
2.15
1.06
1.00
1.06
1.08
1.11
1.09
1.08
3.28
1.12
2.27
1.29
3.15
3.22
9.17
3.02
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)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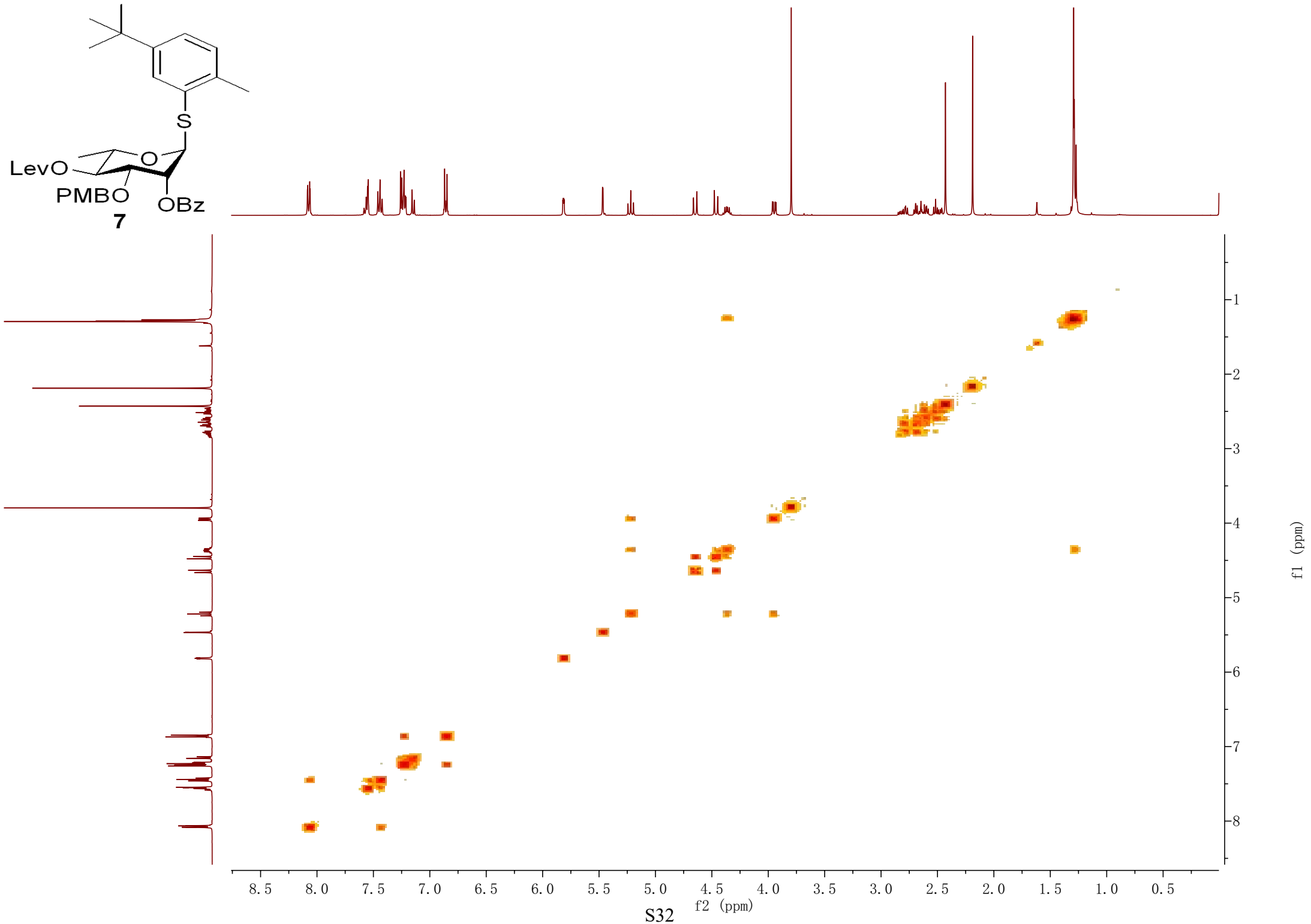
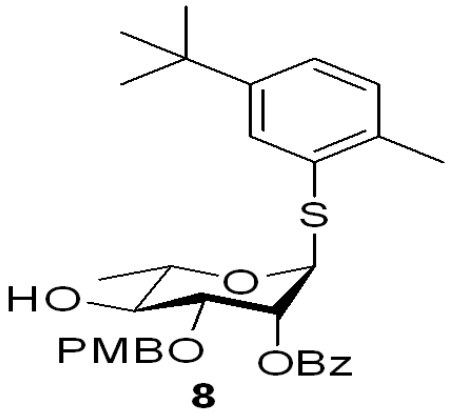
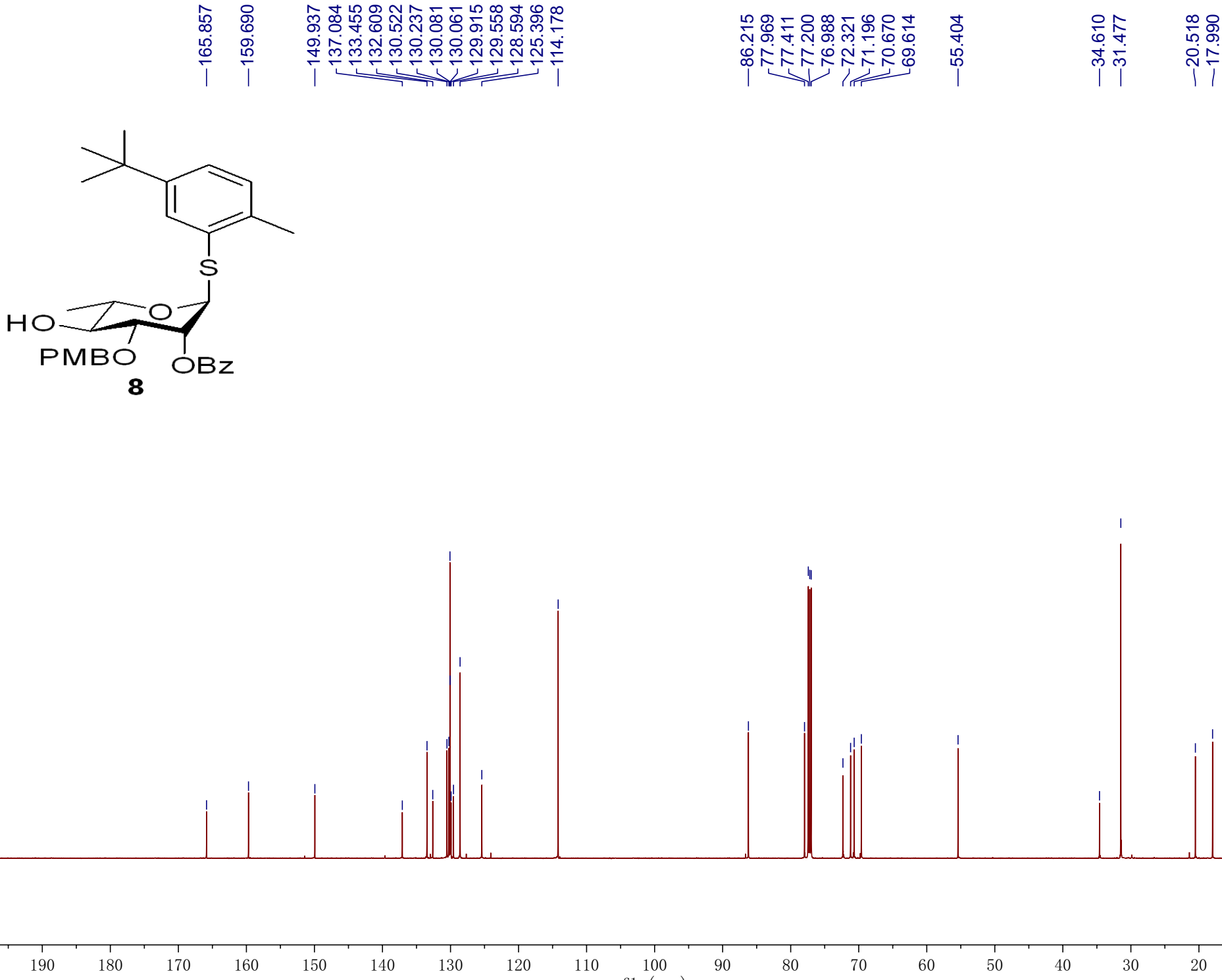
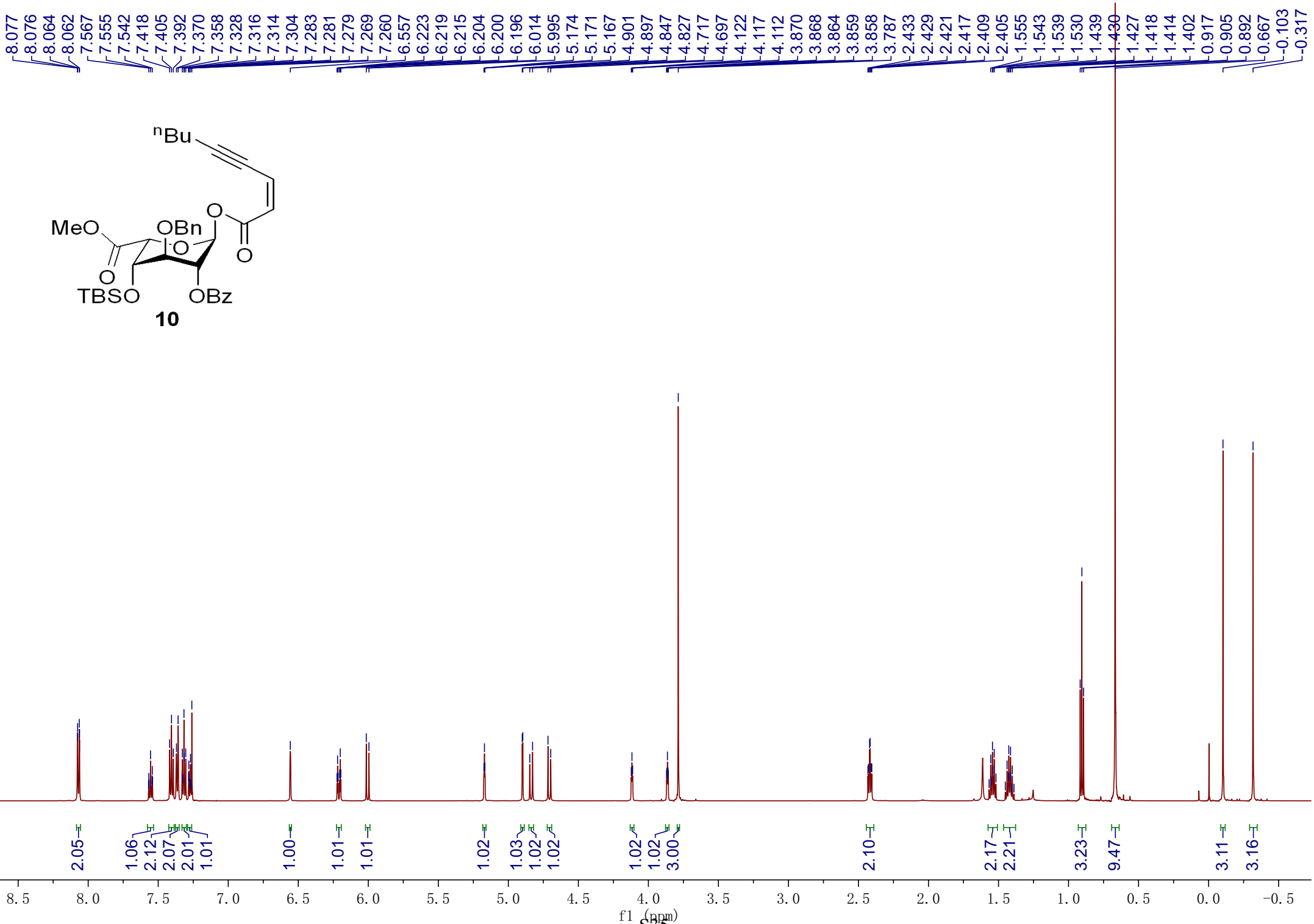
172.180
165.903
159.495
149.998
133.451
132.413
130.447
130.272
130.142
129.877
129.812
129.767
128.608
125.473
113.946
86.036
77.411
77.200
76.987
74.630
73.187
71.192
71.038
68.166
55.422
38.023
34.615
31.471
30.010
28.147
20.506
17.683
S
O
LevO
PMBO
OBz
7
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

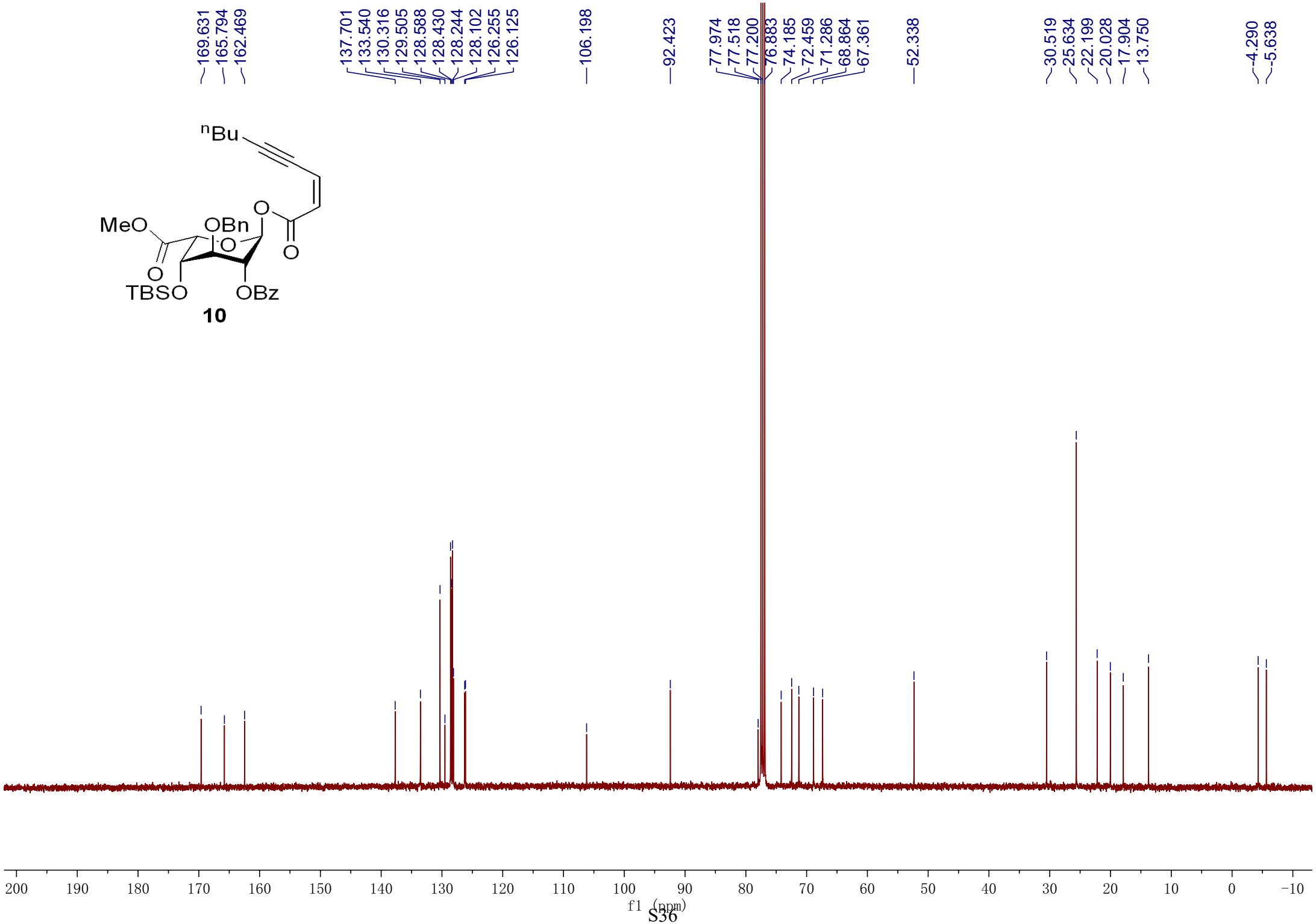

S
O
LevO
PMBO
OBz
7
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)
1
2
3
4
5
6
7
8
f1 (ppm)



8


165.857
159.690
149.937
137.084
133.455
132.609
130.522
130.237
130.081
130.061
129.915
129.558
128.594
125.396
114.178
86.215
77.969
77.411
77.200
76.988
72.321
71.196
70.670
69.614
55.404
34.610
31.477
20.518
17.990
HO
O
S
PMBO
OBz
8
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.077
8.076
8.064
8.062
7.567
7.555
7.542
7.418
7.405
7.392
7.370
7.358
7.328
7.316
7.314
7.304
7.283
7.281
7.279
7.269
7.260
6.557
6.223
6.219
6.215
6.204
6.200
6.196
6.014
5.995
5.174
5.171
5.167
4.901
4.897
4.847
4.827
4.717
4.697
4.122
4.117
4.112
3.870
3.868
3.864
3.859
3.858
3.787
2.433
2.429
2.421
2.417
2.409
2.405
1.555
1.543
1.539
1.530
1.439
1.430
1.427
1.418
1.414
1.402
0.917
0.905
0.892
0.667
-0.103
-0.317
nBu
MeO
OBn
O
TBSO
OBz
10
2.05
1.06
2.12
2.07
2.01
1.01
1.00
1.01
1.01
1.02
1.03
1.02
1.02
1.02
1.02
3.00
2.10
2.17
2.21
3.23
9.47
3.11
3.16
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
-0.5
f1 (ppm)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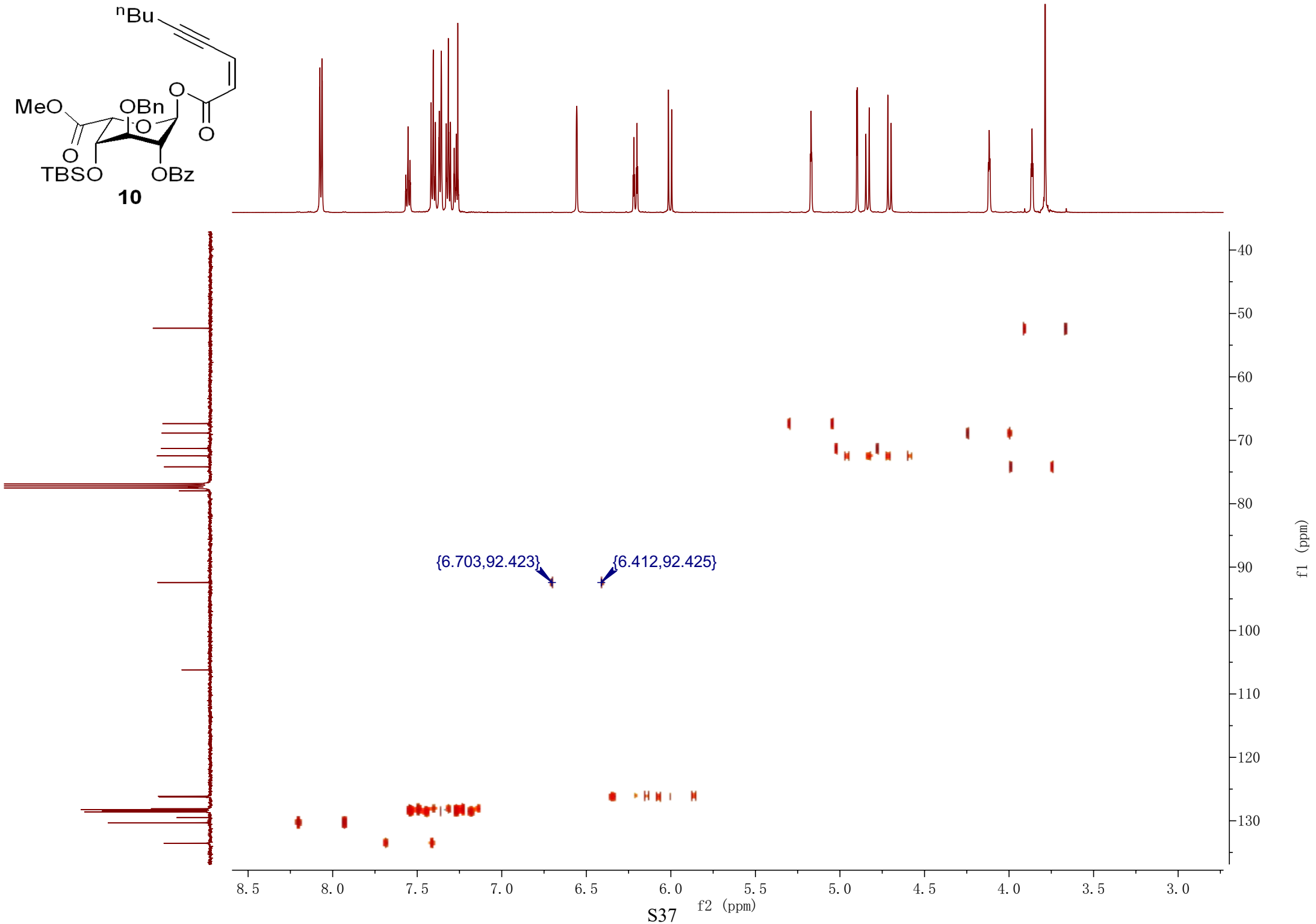
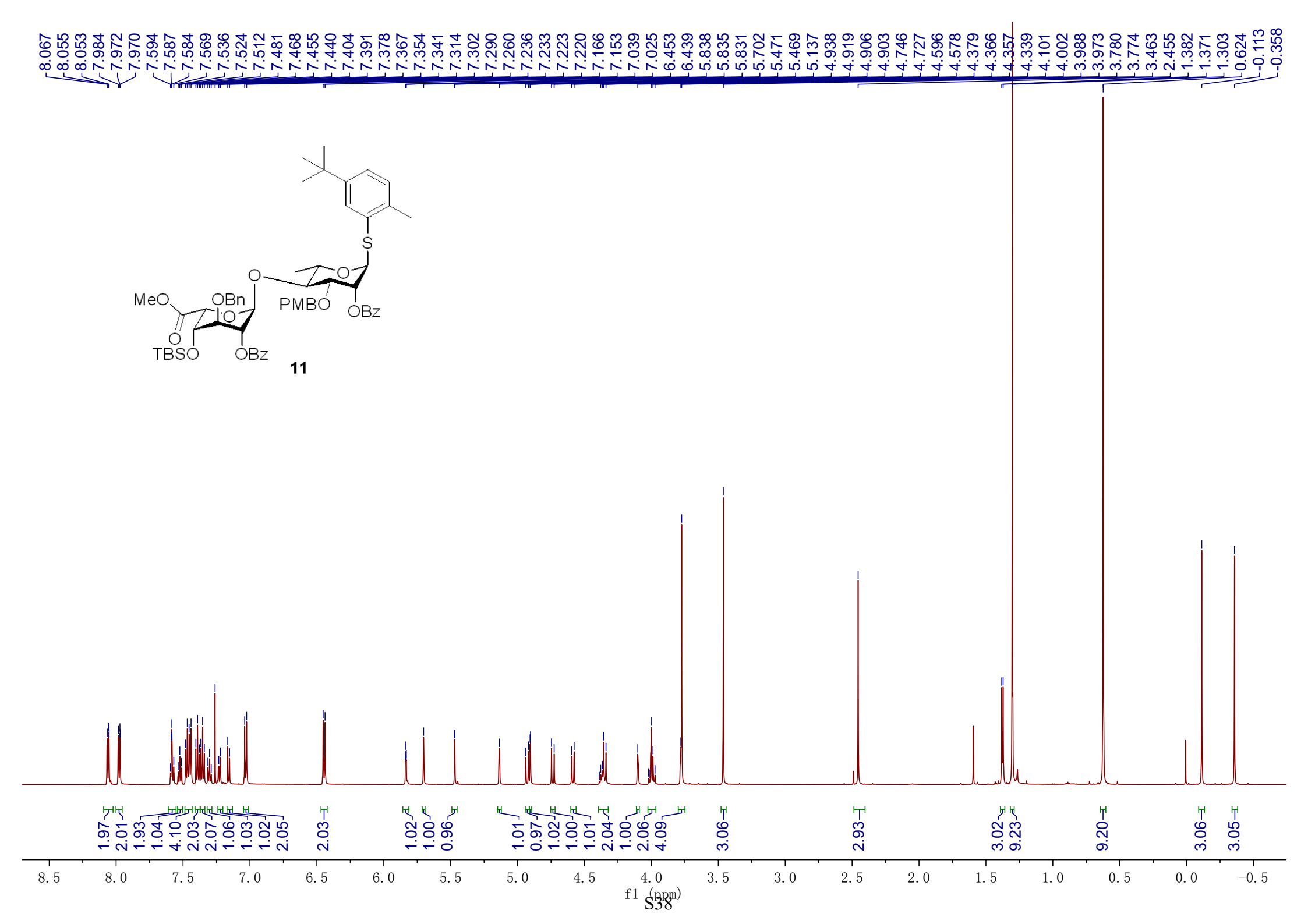
162.469
137.701
133.540
130.316
129.505
128.588
128.430
128.244
128.102
126.255
126.125
106.198
92.423
77.974
77.518
77.200
76.883
74.185
72.459
71.286
68.864
67.361
52.338
30.519
25.634
22.199
20.028
17.904
13.750
-4.290
-5.638
nBu
MeO
OBn
O
O
O
O
TBSO
OBz
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


nBu
MeO
OBn
O
O
TBSO
OBz
10
{6.703,92.423}
{6.412,92.425}
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
f2 (ppm)
40
50
60
70
80
90
100
110
120
130
f1 (ppm)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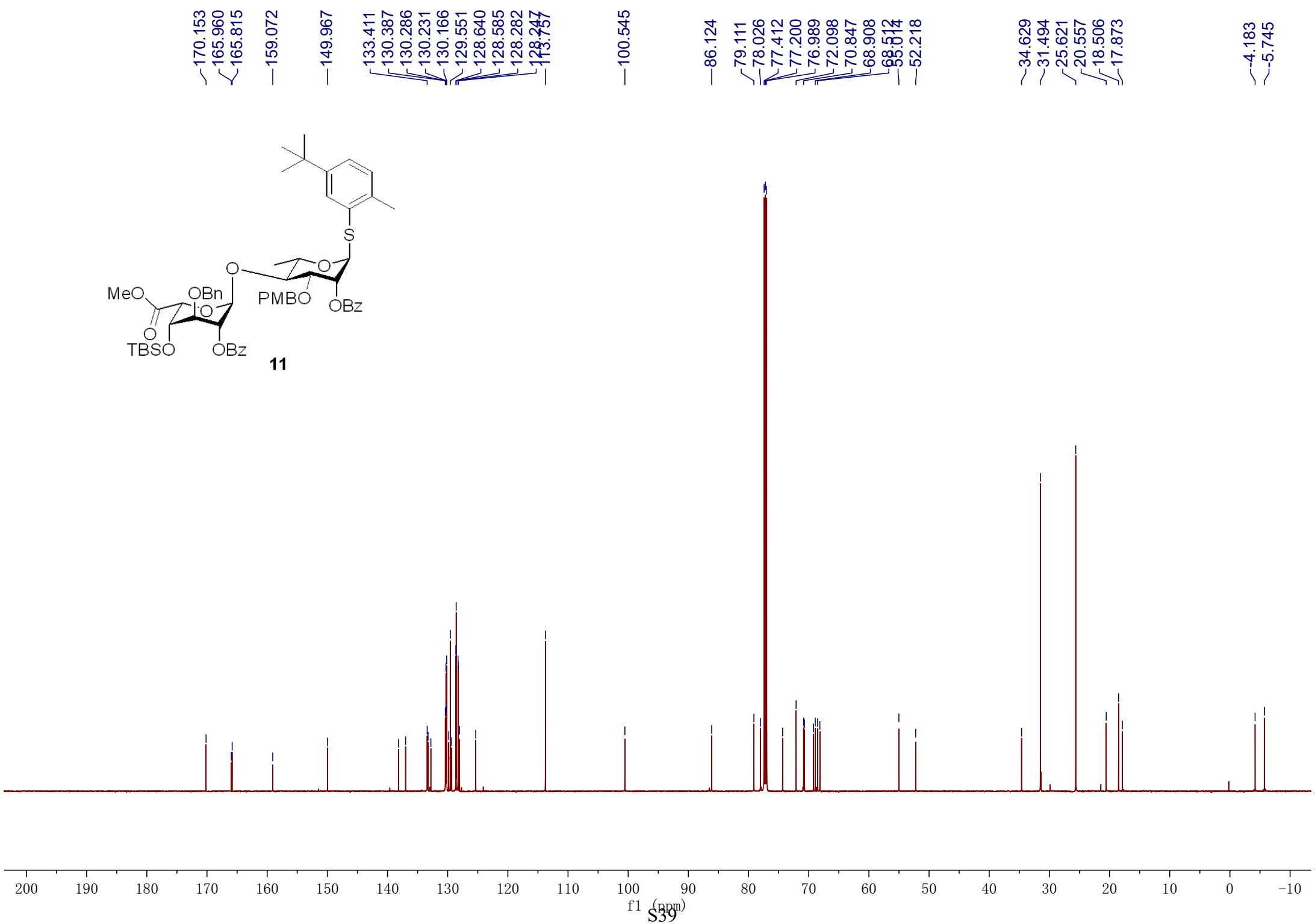
8.055
8.053
7.984
7.972
7.970
7.594
7.587
7.584
7.569
7.536
7.524
7.512
7.481
7.468
7.455
7.440
7.404
7.391
7.378
7.367
7.354
7.341
7.314
7.302
7.290
7.260
7.236
7.233
7.223
7.220
7.166
7.153
7.039
7.025
6.453
6.439
5.838
5.835
5.831
5.702
5.471
5.469
5.137
4.938
4.919
4.906
4.903
4.746
4.727
4.596
4.578
4.379
4.366
4.357
4.339
4.101
4.002
3.988
3.973
3.780
3.774
3.463
2.455
1.382
1.371
1.303
0.624
-0.113
-0.358
MeO
OBn
O
TBSO
OBz
O
PMBO
O
S
OBz
11
1.97
2.01
1.93
1.04
4.10
2.03
2.07
1.06
1.03
1.02
2.05
2.03
1.02
1.00
0.96
1.01
0.97
1.02
1.00
1.01
2.04
1.00
2.06
4.09
3.06
2.93
3.02
9.23
9.20
3.06
3.05
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
-0.5
f1 (ppm)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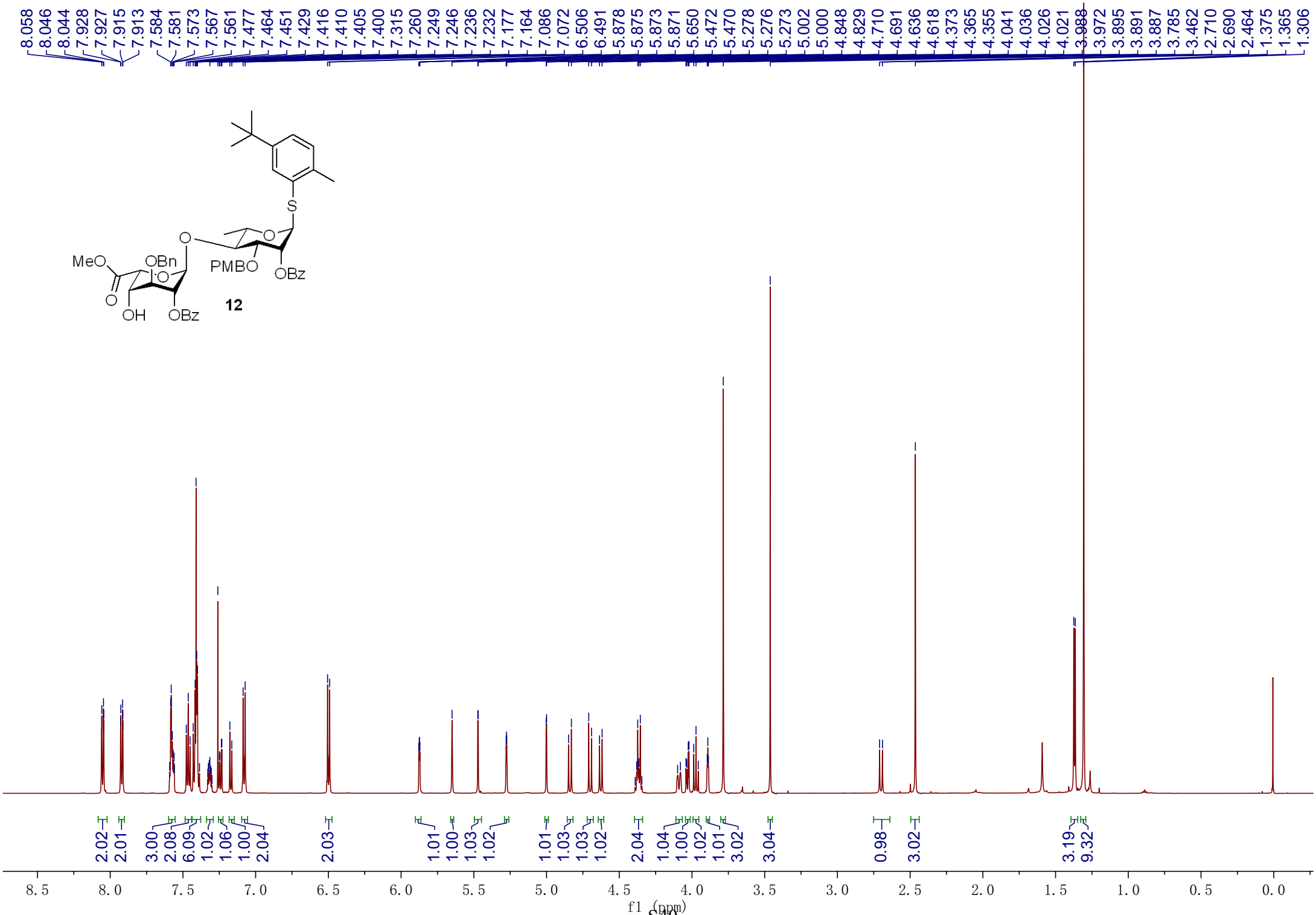
130.286
130.231
130.166
129.551
128.640
128.585
128.282
128.247
113.757
100.545
86.124
79.111
78.026
77.412
77.200
76.989
72.098
70.847
68.908
68.512
55.014
52.218
34.629
31.494
25.621
20.557
18.506
17.873
-4.183
-5.745
MeO
OBn
O
O
TBSO
OBz
O
PMBO
O
S
OBz
11
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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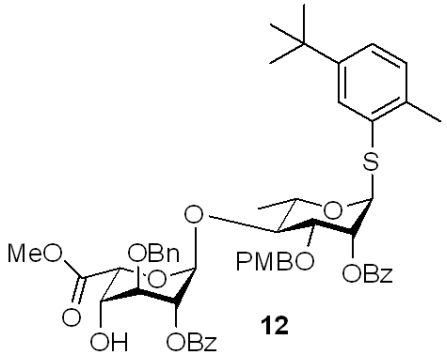
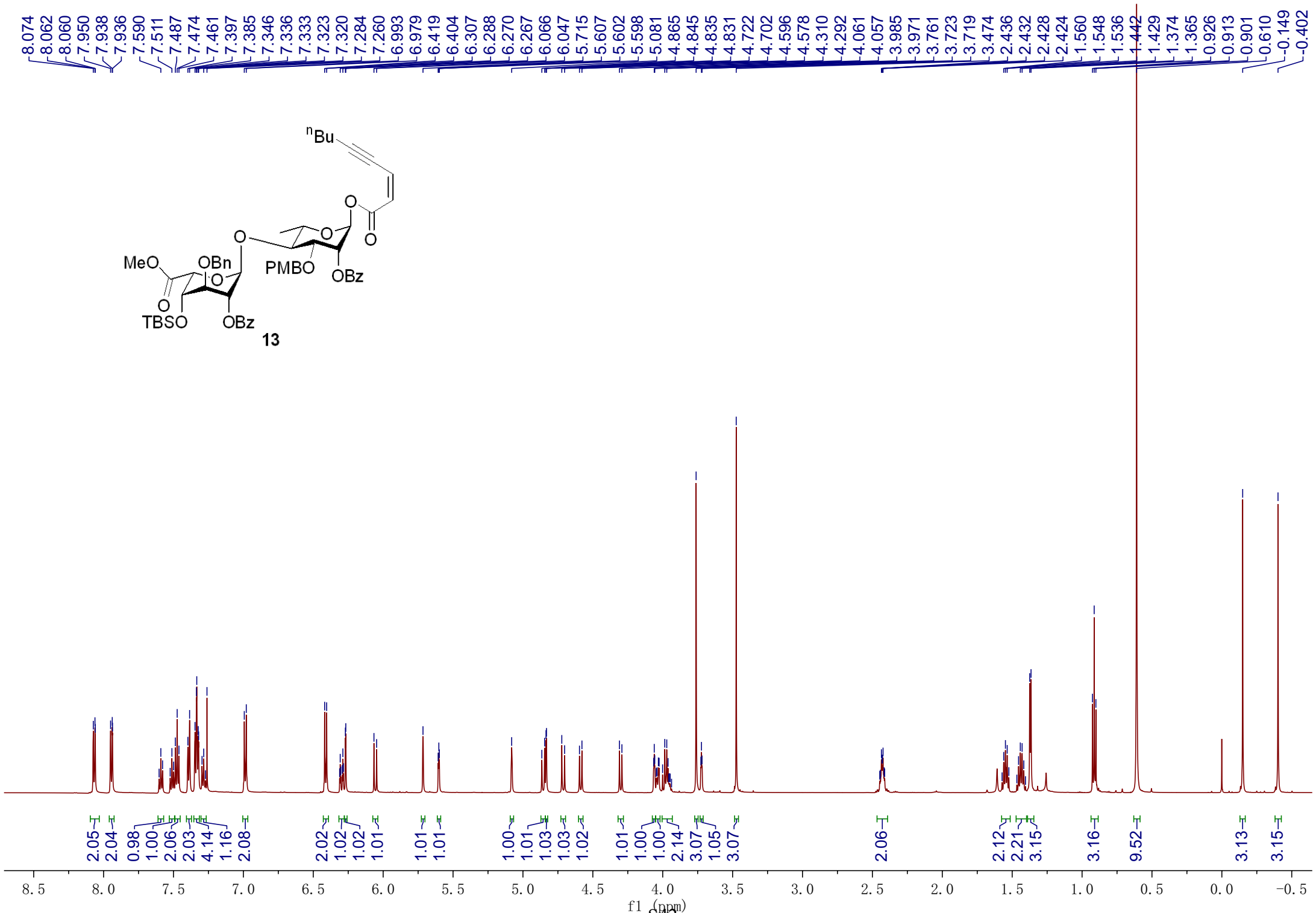
8.046
8.044
7.928
7.927
7.915
7.913
7.584
7.581
7.573
7.567
7.561
7.477
7.464
7.451
7.429
7.416
7.410
7.405
7.400
7.315
7.260
7.249
7.246
7.236
7.232
7.177
7.164
7.086
7.072
6.506
6.491
5.878
5.875
5.873
5.871
5.650
5.472
5.470
5.278
5.276
5.273
5.002
5.000
4.848
4.829
4.710
4.691
4.636
4.618
4.373
4.365
4.355
4.041
4.036
4.026
4.021
3.988
3.972
3.895
3.891
3.887
3.785
3.462
2.710
2.690
2.464
1.375
1.365
1.306
MeO
OBn
O
O
OH
OBz
O
PMBO
O
S
OBz
12
2.02
2.01
3.00
2.08
6.09
1.02
1.06
1.00
2.04
2.03
1.01
1.00
1.03
1.02
1.01
1.03
1.03
1.02
2.04
1.04
1.00
1.02
1.01
3.02
3.04
0.98
3.02
3.19
9.32
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)


MeO
OBn
PMBO
OBz
OH
OBz
12


8.074
8.062
8.060
7.950
7.938
7.936
7.590
7.511
7.487
7.474
7.461
7.397
7.385
7.346
7.336
7.333
7.323
7.320
7.284
7.260
6.993
6.979
6.419
6.404
6.307
6.288
6.270
6.267
6.066
6.047
5.715
5.607
5.602
5.598
5.081
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4.845
4.835
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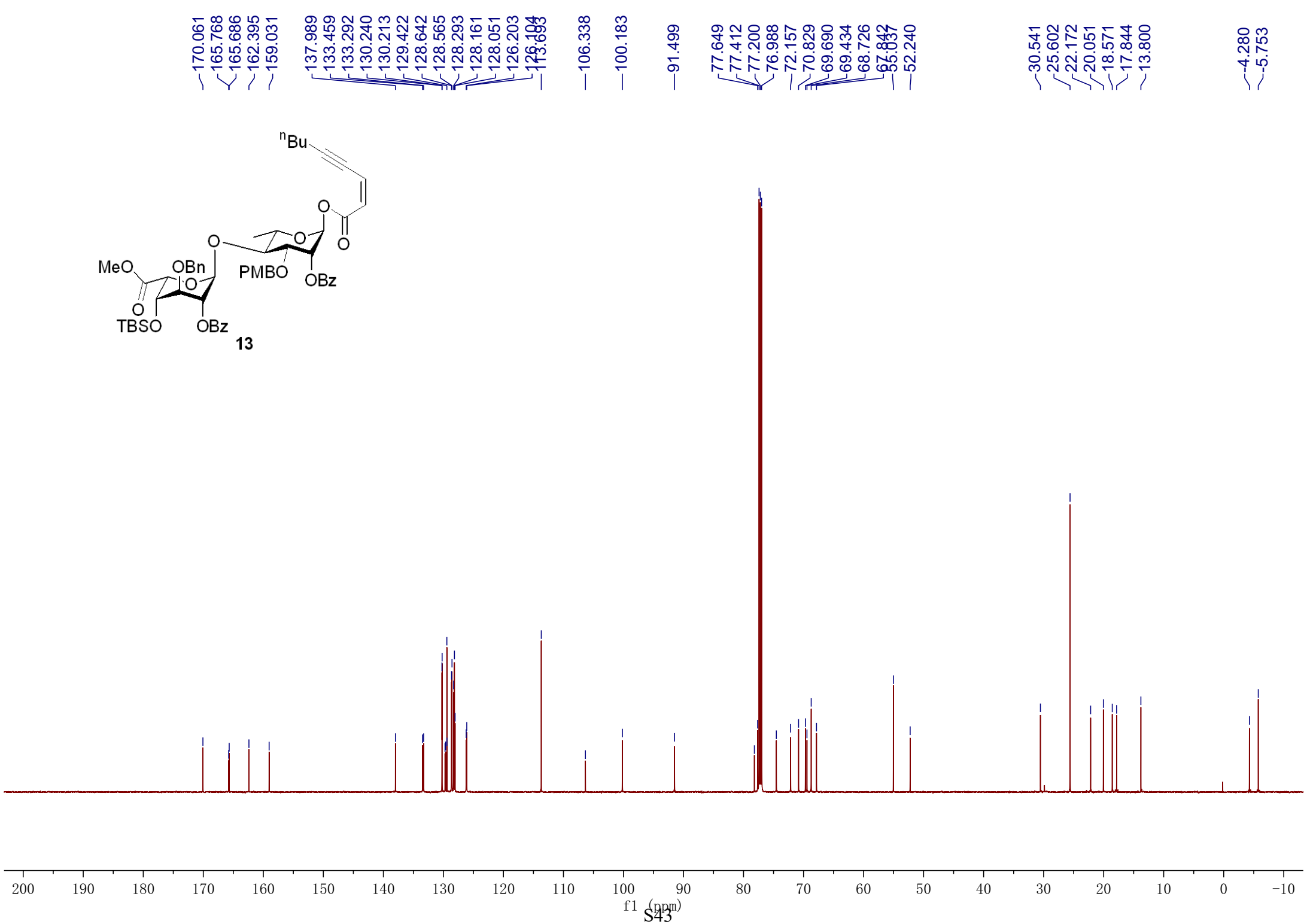
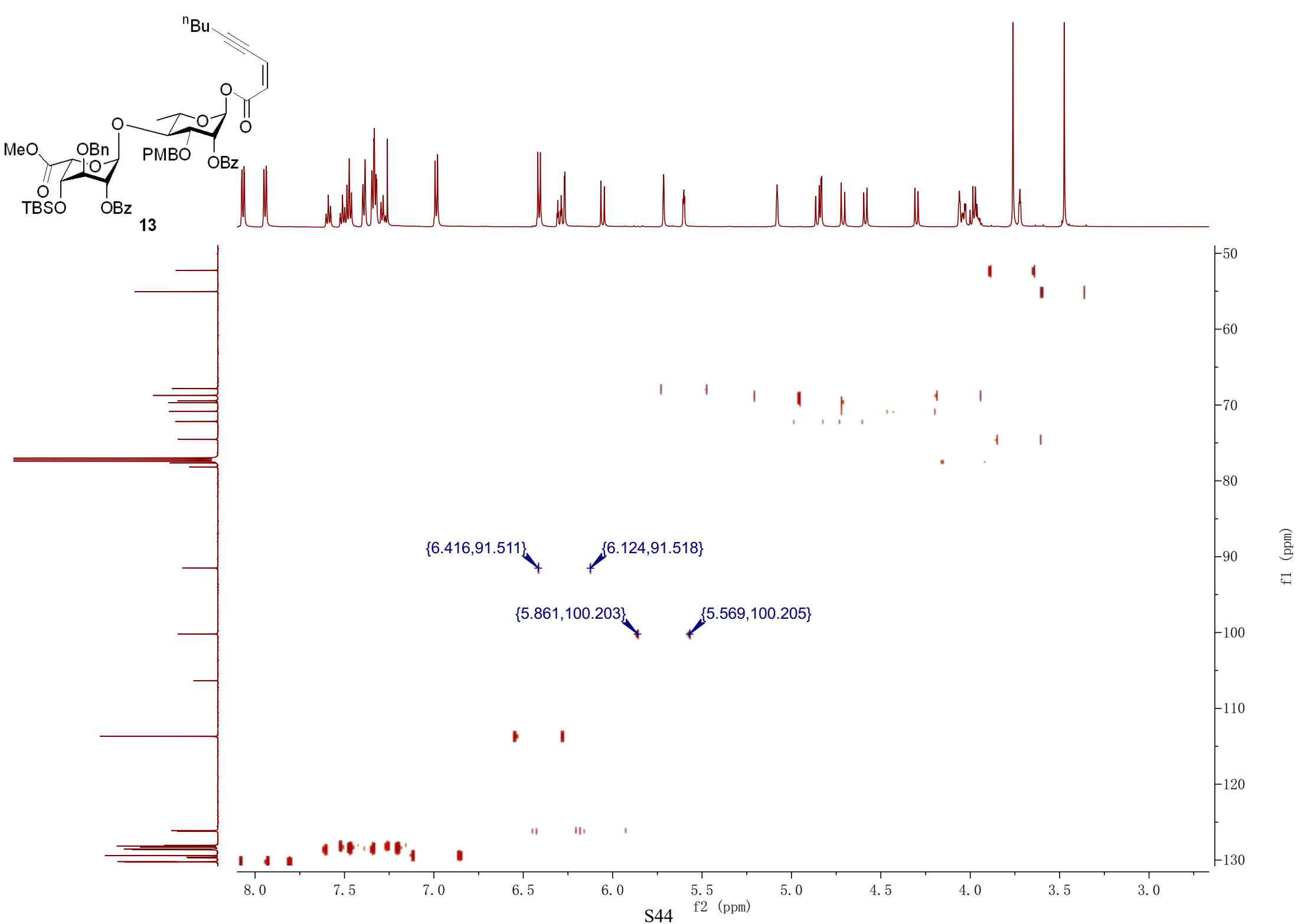
4.596
4.578
4.310
4.292
4.061
4.057
3.985
3.971
3.761
3.723
3.719
3.474
2.436
2.432
2.428
2.424
1.560
1.548
1.536
1.442
1.429
1.374
1.365
0.926
0.913
0.901
0.610
-0.149
-0.402
nBu
O
O
O
O
MeO
OBn
O
PMBO
OBz
O
TBSO
OBz
13
2.05
2.04
0.98
1.00
2.06
2.03
4.14
1.16
2.08
2.02
1.02
1.02
1.01
1.01
1.01
1.00
1.01
1.03
1.03
1.02
1.01
1.00
1.00
2.14
3.07
1.05
3.07
2.06
2.12
2.21
3.15
3.16
9.52
3.13
3.15
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
−0.5
f1 (ppm)


170.061
165.768
165.686
162.395
159.031
137.989
133.459
133.292
130.240
130.213
129.422
128.642
128.565
128.293
128.161
128.051
126.203
106.338
100.183
91.499
77.649
77.412
77.200
76.988
72.157
70.829
69.690
69.434
68.726
52.240
30.541
25.602
22.172
20.051
18.571
17.844
13.800
-4.280
-5.753
nBu
MeO
OBn
PMBO
OBz
TBSO
OBz
13
f1 (ppm)


nBu
MeO
OBn
PMBO
OBz
TBSO
OBz
13
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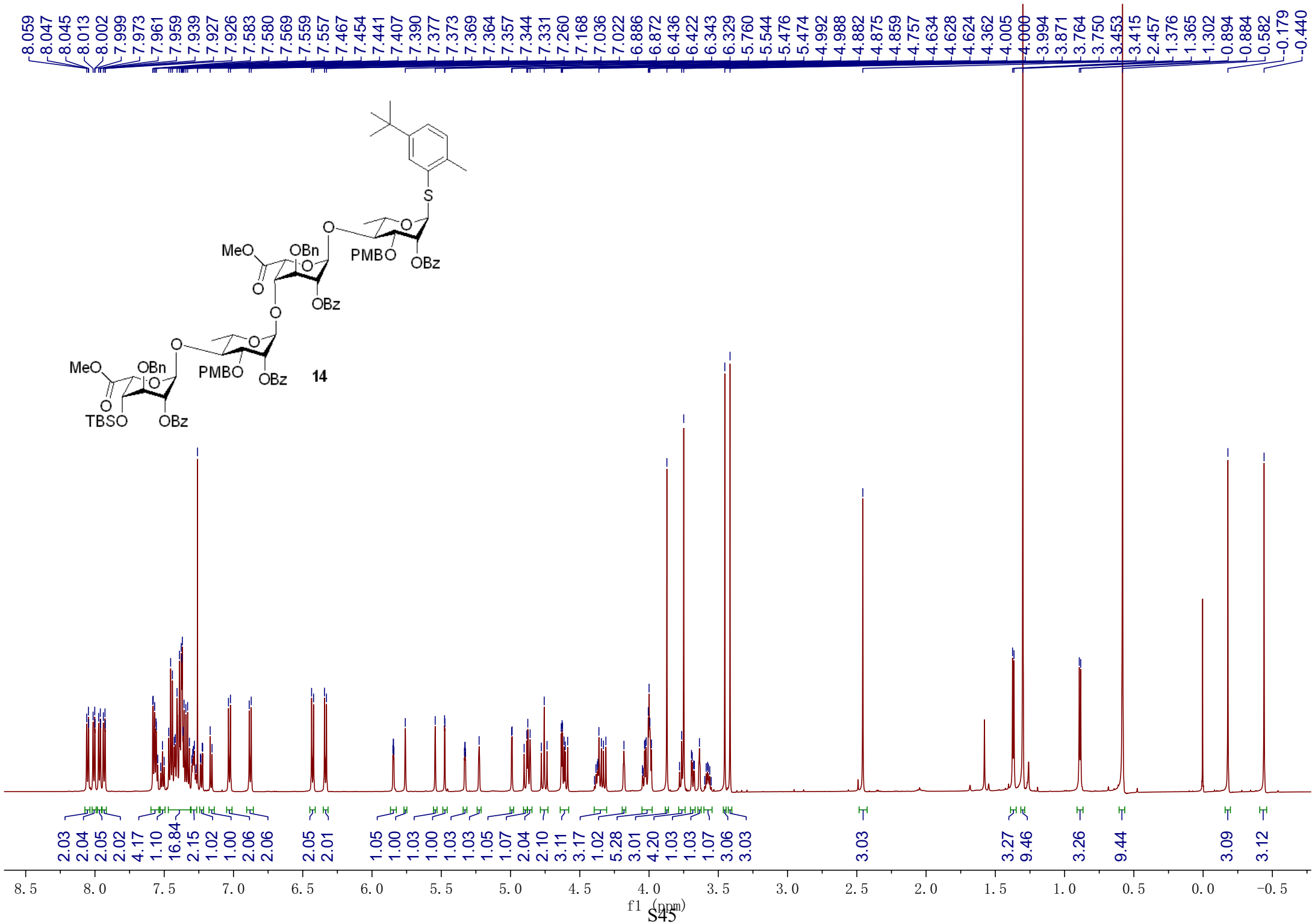
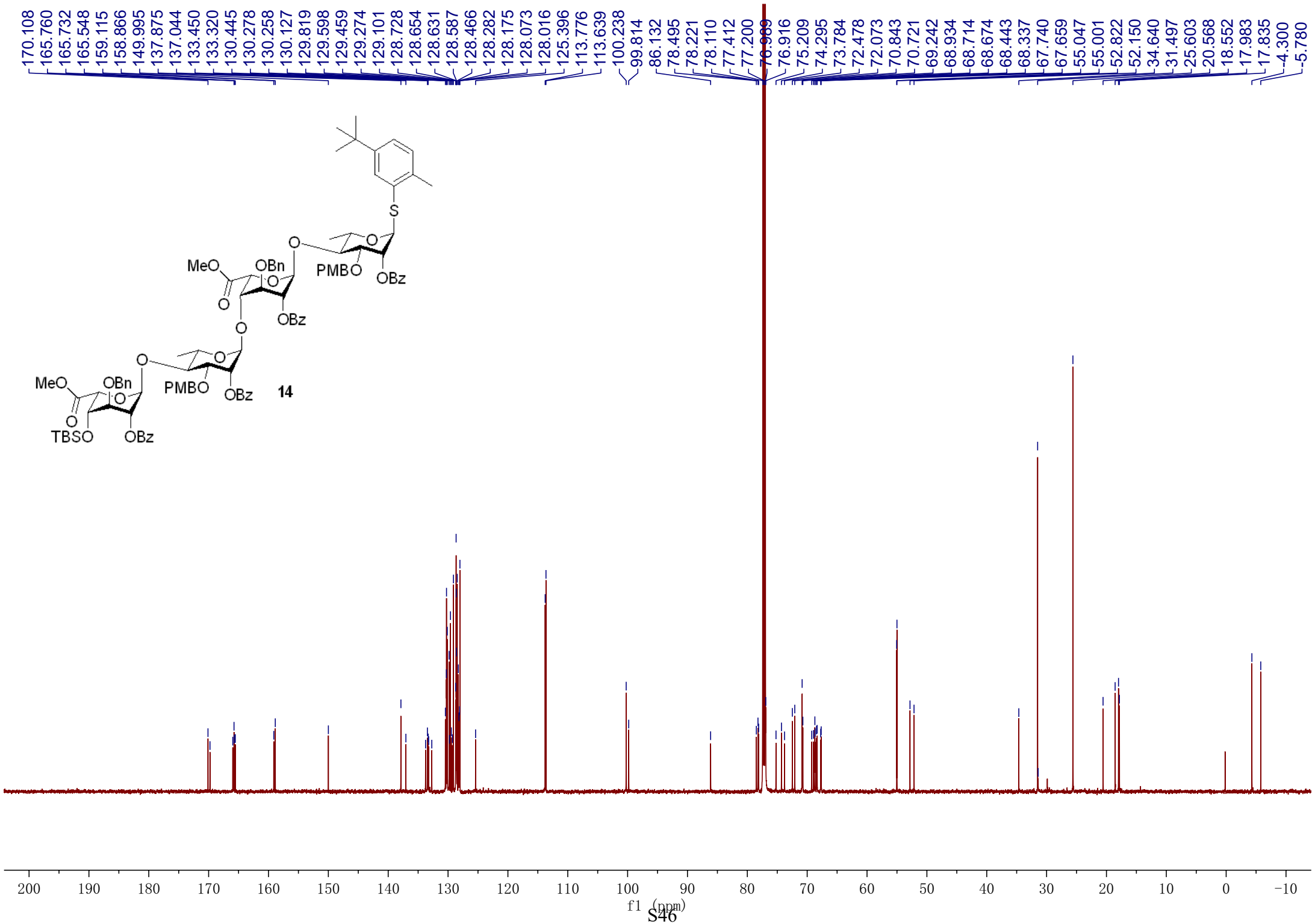
{6.124,91.518}
{5.861,100.203}
{5.569,100.205}
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
f2 (ppm)
50
60
70
80
90
100
110
120
130
f1 (ppm)


8.059 8.047 8.045 8.013 8.002 7.999 7.973 7.961 7.959 7.939 7.927 7.926 7.583 7.580 7.569 7.559 7.557 7.467 7.454 7.441 7.407 7.390 7.377 7.373 7.369 7.364 7.357 7.344 7.331 7.260 7.168 7.036 7.022 6.886 6.872 6.436 6.422 6.343 6.329 5.760 5.544 5.476 5.474 4.992 4.988 4.882 4.875 4.859 4.757 4.634 4.628 4.624 4.362 4.005 4.000 3.994 3.871 3.764 3.750 3.453 3.415 2.457 1.376 1.365 1.302 0.894 0.884 0.582 -0.179 -0.440
MeO
OBn
PMBO
OBz
S
TBSO
14
2.03 2.04 2.05 2.02 4.17 1.10 16.84 2.15 1.02 1.00 2.06 2.06 2.05 2.01 1.05 1.00 1.03 1.00 1.03 1.03 1.05 1.07 2.04 2.10 3.11 3.17 1.02 5.28 3.01 4.20 1.03 1.03 1.07 3.06 3.03 3.03 3.27 9.46 3.26 9.44 3.09 3.12
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 −0.5
f1 (ppm)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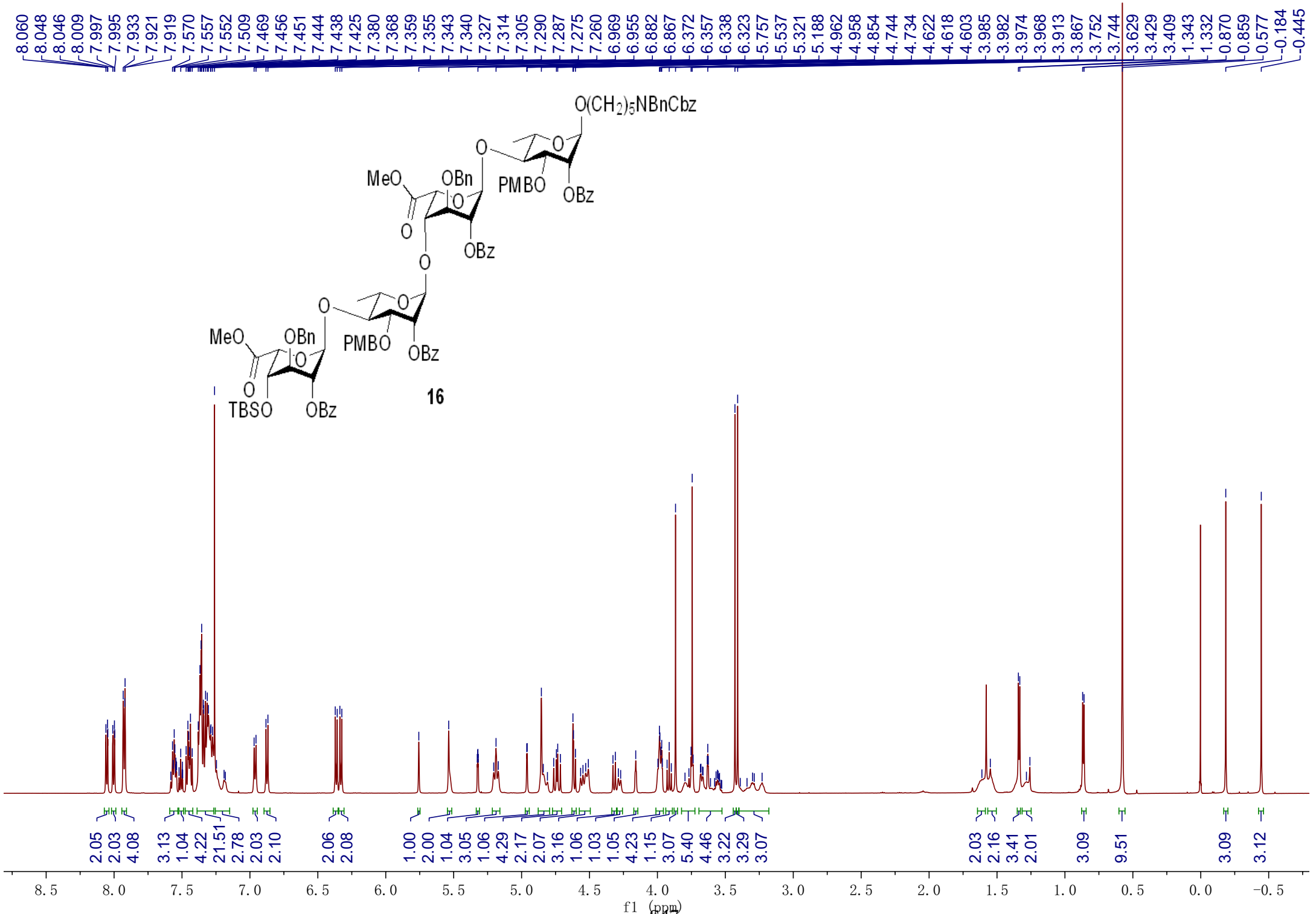
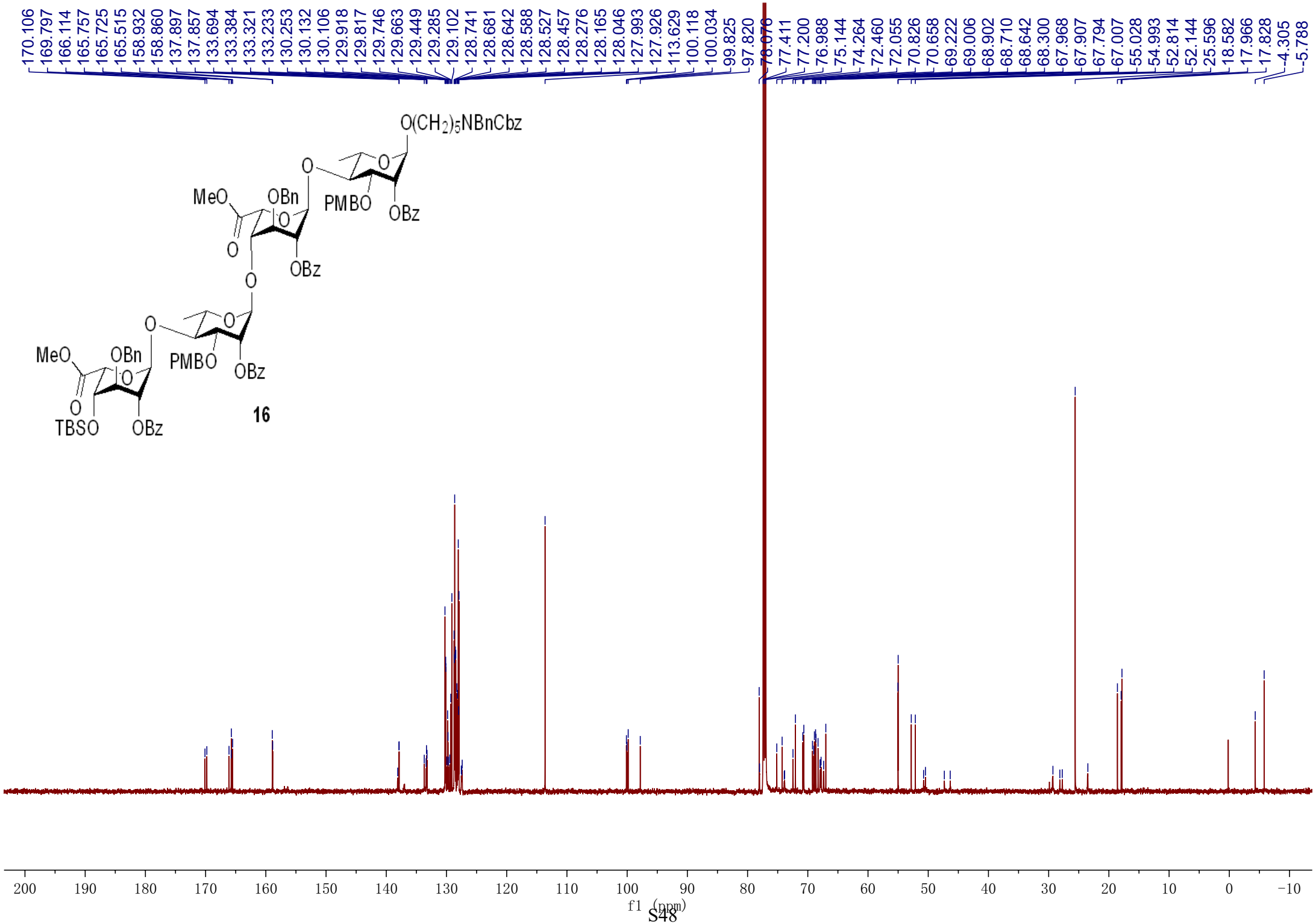
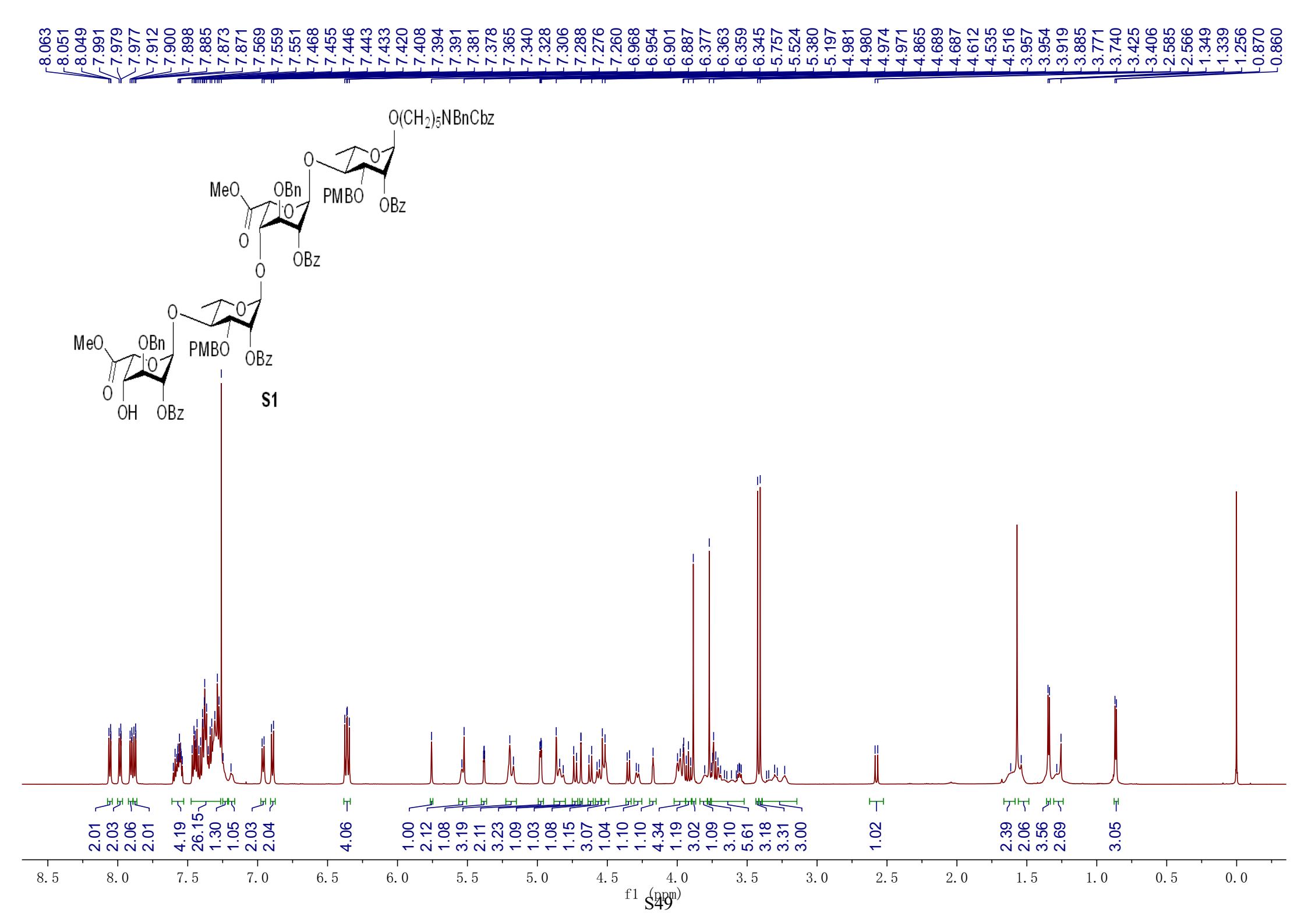
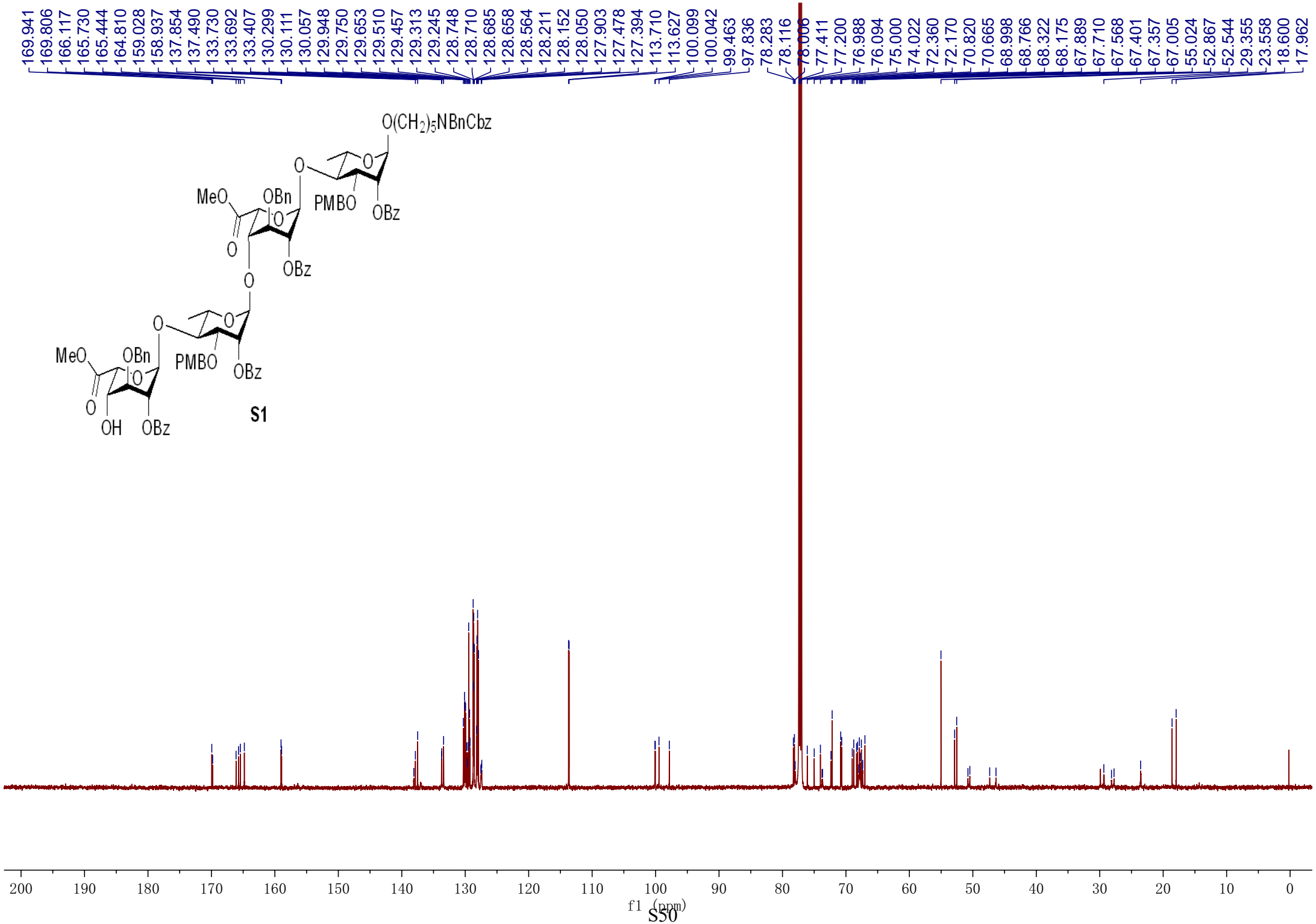
165.760
165.732
165.548
159.115
158.866
149.995
137.875
137.044
133.450
133.320
130.445
130.278
130.258
130.127
129.819
129.598
129.459
129.274
129.101
128.728
128.654
128.631
128.587
128.466
128.282
128.175
128.073
128.016
125.396
113.776
113.639
100.238
99.814
86.132
78.495
78.221
78.110
77.412
77.200
76.989
76.916
75.209
74.295
73.784
72.478
72.073
70.843
70.721
69.242
68.934
68.714
68.674
68.443
68.337
67.740
67.659
55.047
55.001
52.822
52.150
34.640
31.497
25.603
20.568
18.552
17.983
17.835
-4.300
-5.780
S
O
MeO
OBn
O
PMBO
OBz
O
OBz
O
O
MeO
OBn
O
PMBO
OBz
14
O
TBSO
OBz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)


O(CH2)5NBnCbz
MeO
OBn
PMBO
OBz
TBSO
16
f1 (ppm)


170.106
169.797
166.114
165.757
165.725
165.515
158.932
158.860
137.897
137.857
133.694
133.384
133.321
133.233
130.253
130.132
130.106
129.918
129.817
129.746
129.663
129.449
129.285
129.102
128.741
128.681
128.642
128.588
128.527
128.457
128.276
128.165
128.046
127.993
127.926
113.629
100.118
100.034
99.825
97.820
78.076
77.411
77.200
76.988
75.144
74.264
72.460
72.055
70.826
70.658
69.222
69.006
68.902
68.710
68.642
68.300
67.968
67.907
67.794
67.007
55.028
54.993
52.814
52.144
25.596
18.582
17.966
17.828
-4.305
-5.788
O(CH2)5NBnCbz
MeO
OBn
PMBO
OBz
TBSO
16
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.063 8.051 8.049 7.991 7.979 7.977 7.912 7.900 7.898 7.885 7.873 7.871 7.569 7.559 7.551 7.468 7.455 7.446 7.443 7.433 7.420 7.408 7.394 7.391 7.381 7.378 7.365 7.340 7.328 7.306 7.288 7.276 7.260 6.968 6.954 6.901 6.887 6.377 6.363 6.359 6.345 5.757 5.524 5.380 5.197 4.981 4.980 4.974 4.971 4.865 4.689 4.687 4.612 4.535 4.516 3.957 3.954 3.919 3.885 3.771 3.740 3.425 3.406 2.585 2.566 1.349 1.339 1.256 0.870 0.860
O(CH2)5NBnCbz
MeO
OBn
PMBO
OBz
OBz
MeO
OBn
PMBO
OBz
OH
OBz
S1
2.01 2.03 2.06 2.01 4.19 26.15 1.30 1.05 2.03 2.04 4.06 1.00 2.12 1.08 3.19 2.11 3.23 1.09 1.03 1.08 1.15 3.07 1.04 1.10 1.10 4.34 1.19 3.02 1.09 3.10 5.61 3.18 3.31 3.00 1.02 2.39 2.06 3.56 2.69 3.05
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)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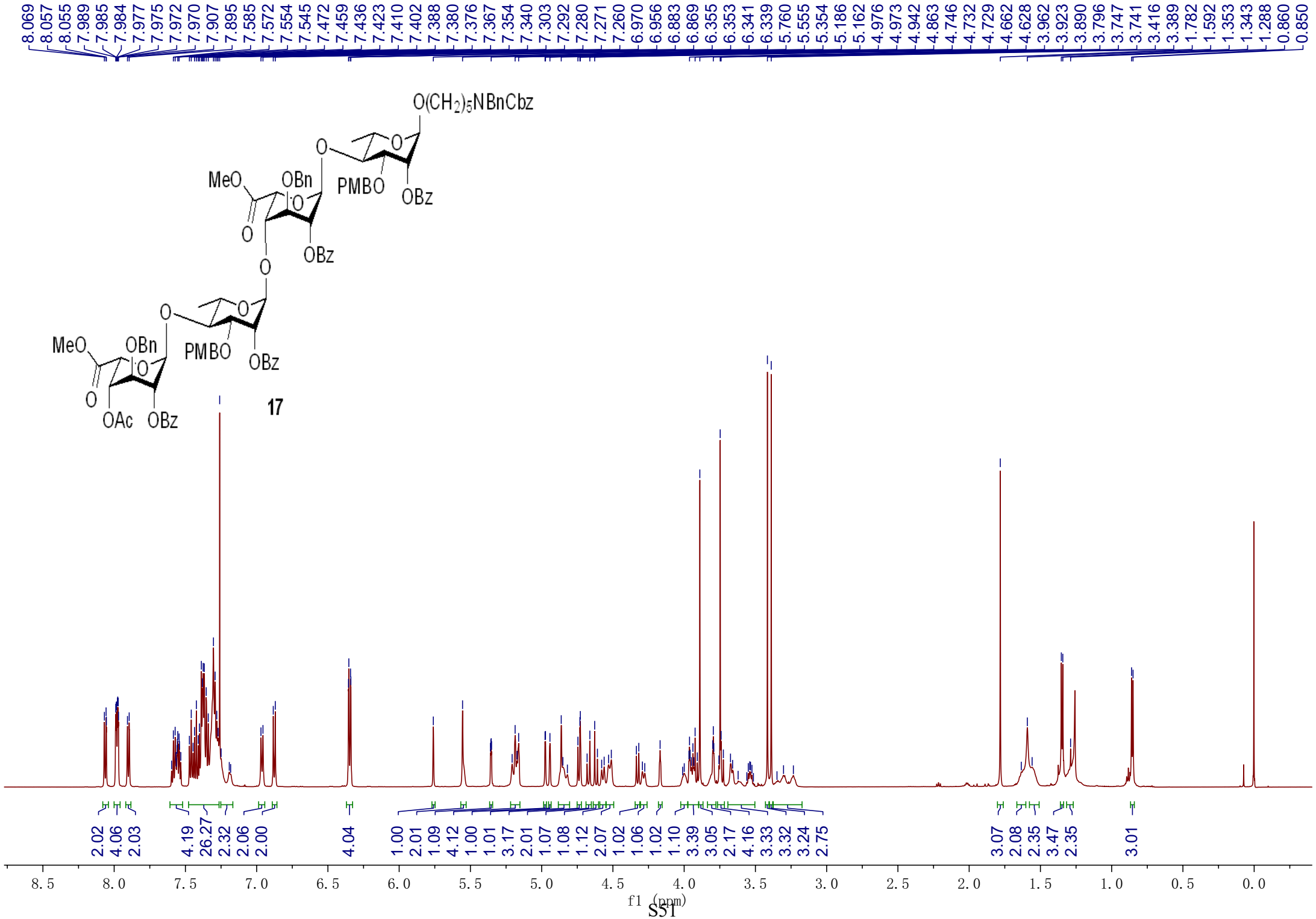
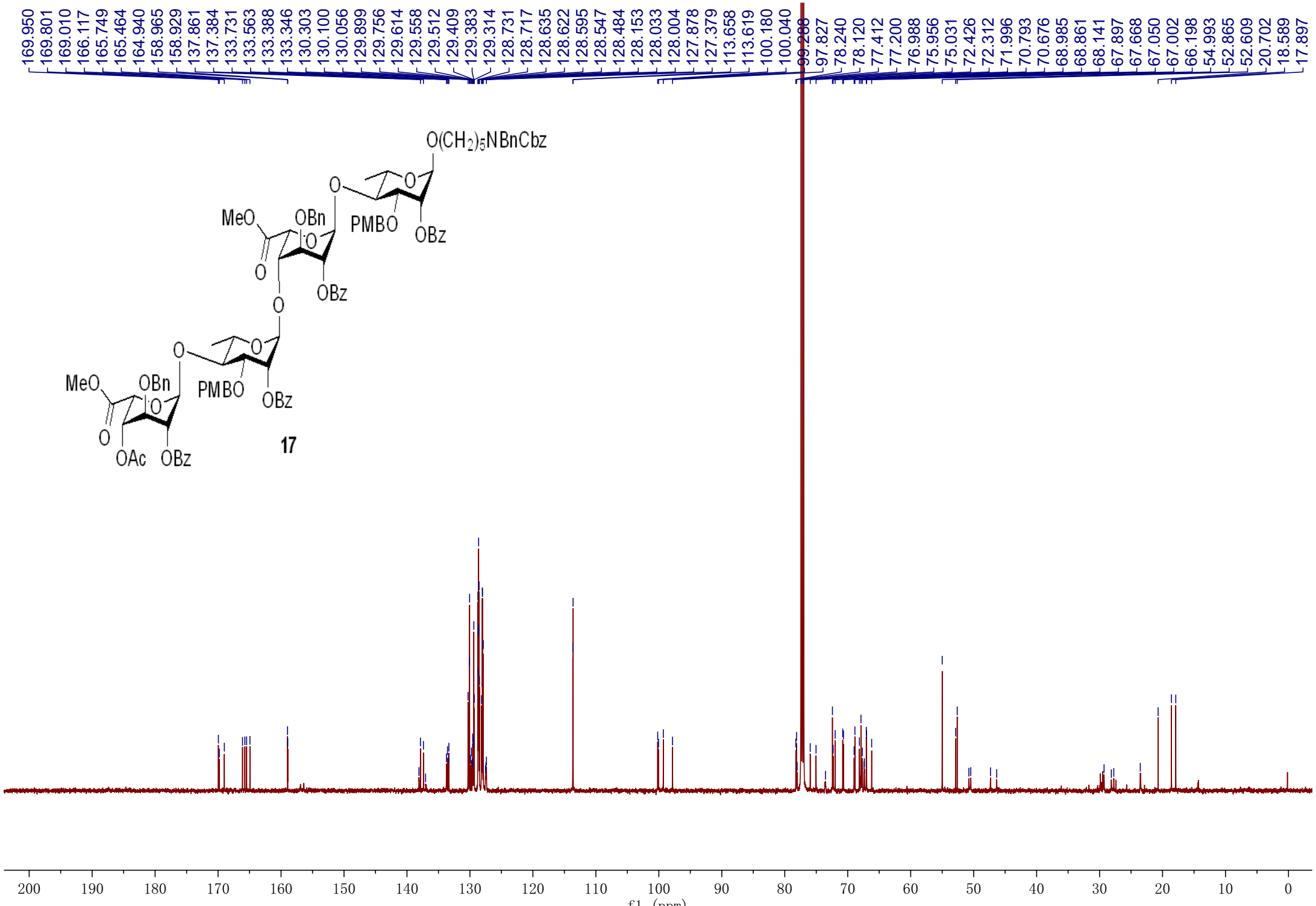
169.806
166.117
165.730
165.444
164.810
159.028
158.937
137.854
137.490
133.730
133.692
133.407
130.299
130.111
130.057
129.948
129.750
129.653
129.510
129.457
129.313
129.245
128.748
128.710
128.685
128.658
128.564
128.211
128.152
128.050
127.903
127.478
127.394
113.710
113.627
100.099
100.042
99.463
97.836
78.283
78.116
78.006
77.411
77.200
76.988
76.094
75.000
74.022
72.360
72.170
70.820
70.665
68.998
68.766
68.322
68.175
67.889
67.710
67.568
67.401
67.357
67.005
55.024
52.867
52.544
29.355
23.558
18.600
17.962
O(CH2)5NBnCbz
MeO
OBn
PMBO
OBz
OBz
MeO
OBn
PMBO
OBz
OH
OBz
S1
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.069 8.057 8.055 7.989 7.985 7.984 7.977 7.975 7.972 7.970 7.907 7.895 7.585 7.572 7.554 7.545 7.472 7.459 7.436 7.423 7.410 7.402 7.388 7.380 7.376 7.367 7.354 7.340 7.303 7.292 7.280 7.271 7.260 6.970 6.956 6.883 6.869 6.355 6.353 6.341 6.339 5.760 5.555 5.354 5.186 5.162 4.976 4.973 4.942 4.863 4.746 4.732 4.729 4.662 4.628 3.962 3.923 3.890 3.796 3.747 3.741 3.416 3.389 1.782 1.592 1.353 1.343 1.288 0.860 0.850
O(CH2)5NBnCbz
MeO
OBn
PMBO
OBz
OBz
MeO
OBn
PMBO
OBz
OAc
OBz
17
2.02 4.06 2.03 4.19 26.27 2.32 2.06 2.00 4.04 1.00 2.01 1.09 4.12 1.00 1.01 3.17 2.01 1.07 1.08 1.12 2.07 1.02 1.06 1.02 1.10 3.39 3.05 2.17 4.16 3.33 3.32 3.24 2.75 3.07 2.08 2.35 3.47 2.35 3.01
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)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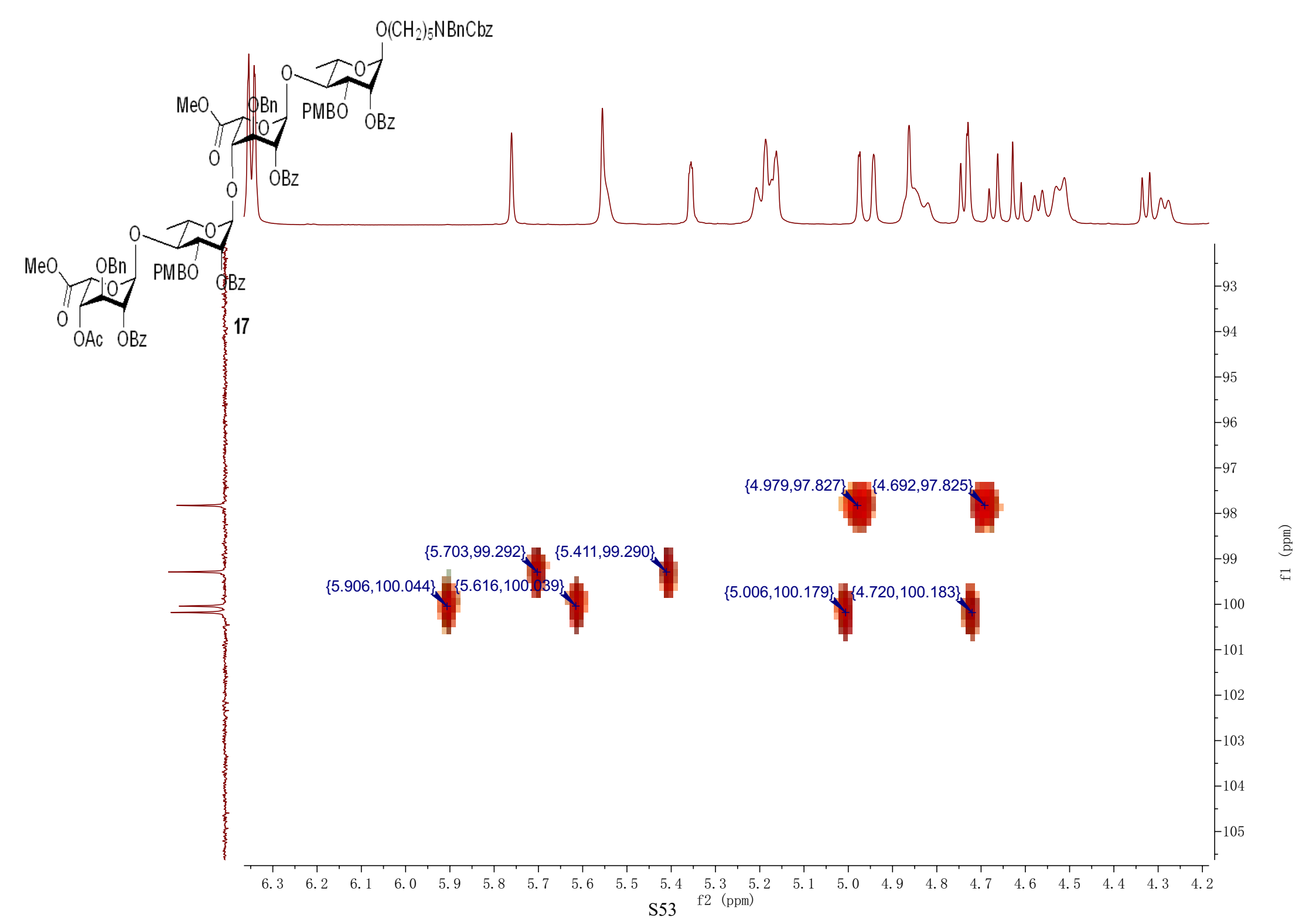
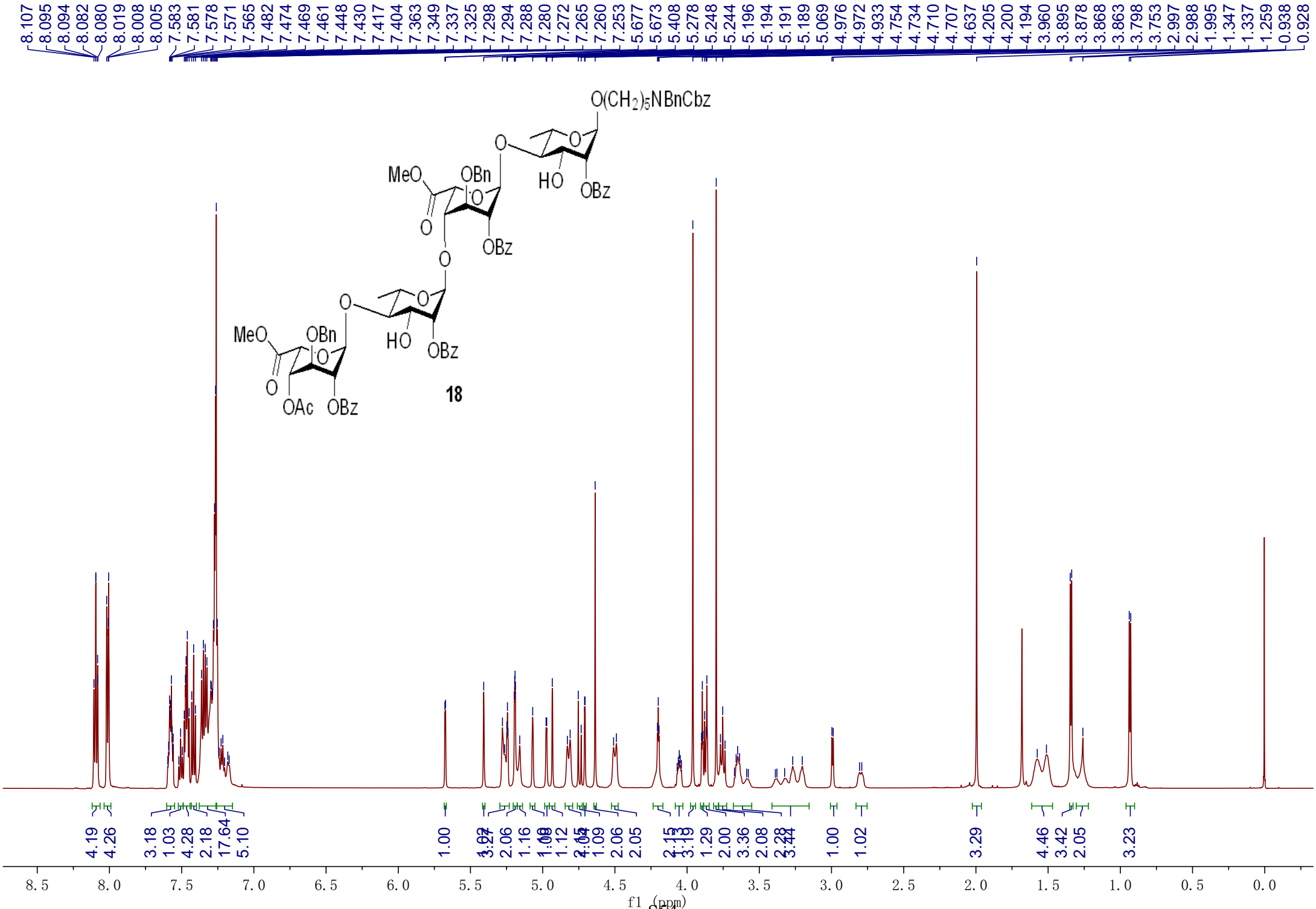
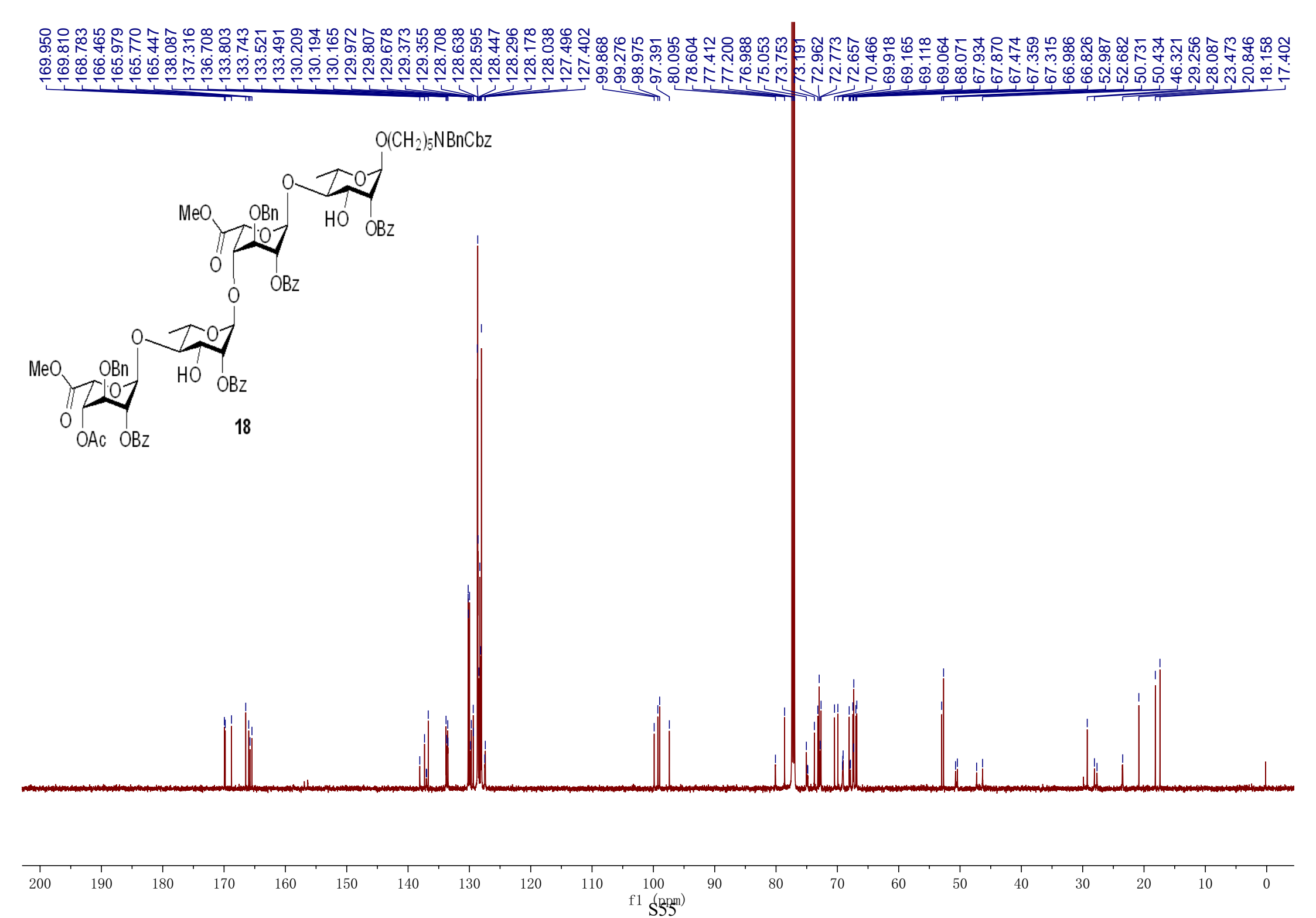
169.801
169.010
166.117
165.749
165.464
164.940
158.965
158.929
137.861
137.384
133.731
133.563
133.388
133.346
130.303
130.100
130.056
129.899
129.756
129.614
129.558
129.512
129.409
129.383
129.314
128.731
128.717
128.635
128.622
128.595
128.547
128.484
128.153
128.033
128.004
127.878
127.379
113.658
113.619
100.180
100.040
99.208
97.827
78.240
78.120
77.412
77.200
76.988
75.956
75.031
72.426
72.312
71.996
70.793
70.676
68.985
68.861
68.141
67.897
67.668
67.050
67.002
66.198
54.993
52.865
52.609
20.702
18.589
17.897
O(CH2)5NBnCbz
MeO
OBn
PMBO
OBz
OBz
MeO
OBn
PMBO
OBz
OAc
OBz
17
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O(CH2)5NBnCbz
MeO
OBn
PMBO
OBz
OBz
MeO
OBn
PMBO
OBz
OAc
OBz
17
{4.979,97.827}
{4.692,97.825}
{5.703,99.292}
{5.411,99.290}
{5.906,100.044}
{5.616,100.039}
{5.006,100.179}
{4.720,100.183}
f2 (ppm)
f1 (ppm)


8.107 8.095 8.094 8.082 8.080 8.019 8.008 8.005 7.583 7.581 7.578 7.571 7.565 7.482 7.474 7.469 7.461 7.448 7.430 7.417 7.404 7.363 7.349 7.337 7.325 7.298 7.294 7.288 7.280 7.272 7.265 7.260 7.253 5.677 5.673 5.408 5.278 5.248 5.244 5.196 5.194 5.191 5.189 5.069 4.976 4.972 4.933 4.754 4.734 4.710 4.707 4.637 4.205 4.200 4.194 3.960 3.895 3.878 3.868 3.863 3.798 3.753 2.997 2.988 1.995 1.347 1.337 1.259 0.938 0.928
O(CH2)5NBnCbz
MeO
OBn
HO
OBz
OAc
18
4.19 4.26 3.18 1.03 4.28 2.18 17.64 5.10 1.00 2.06 1.16 1.12 2.09 2.06 2.05 3.29 4.46 3.42 2.05 3.23
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)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165.979
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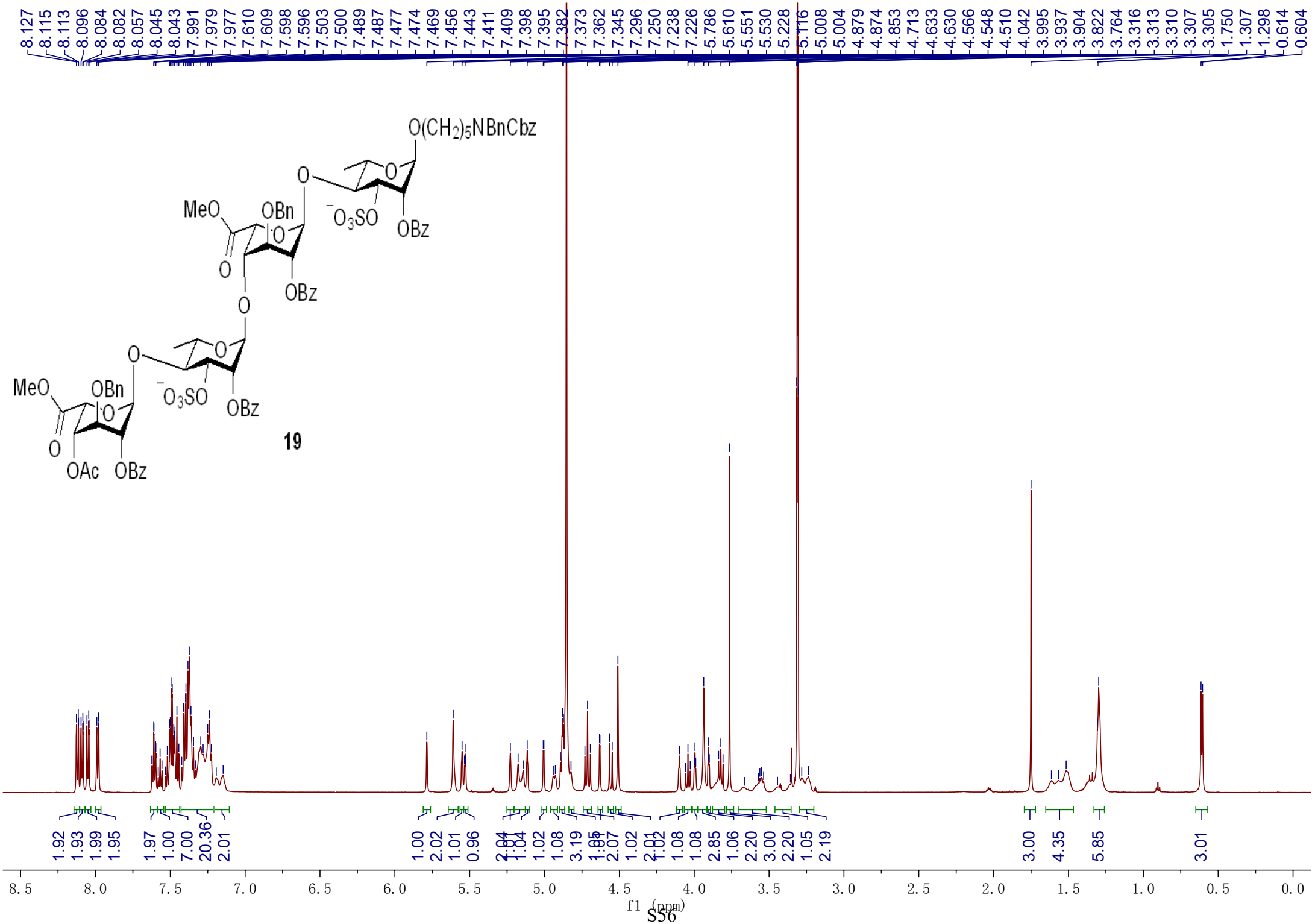
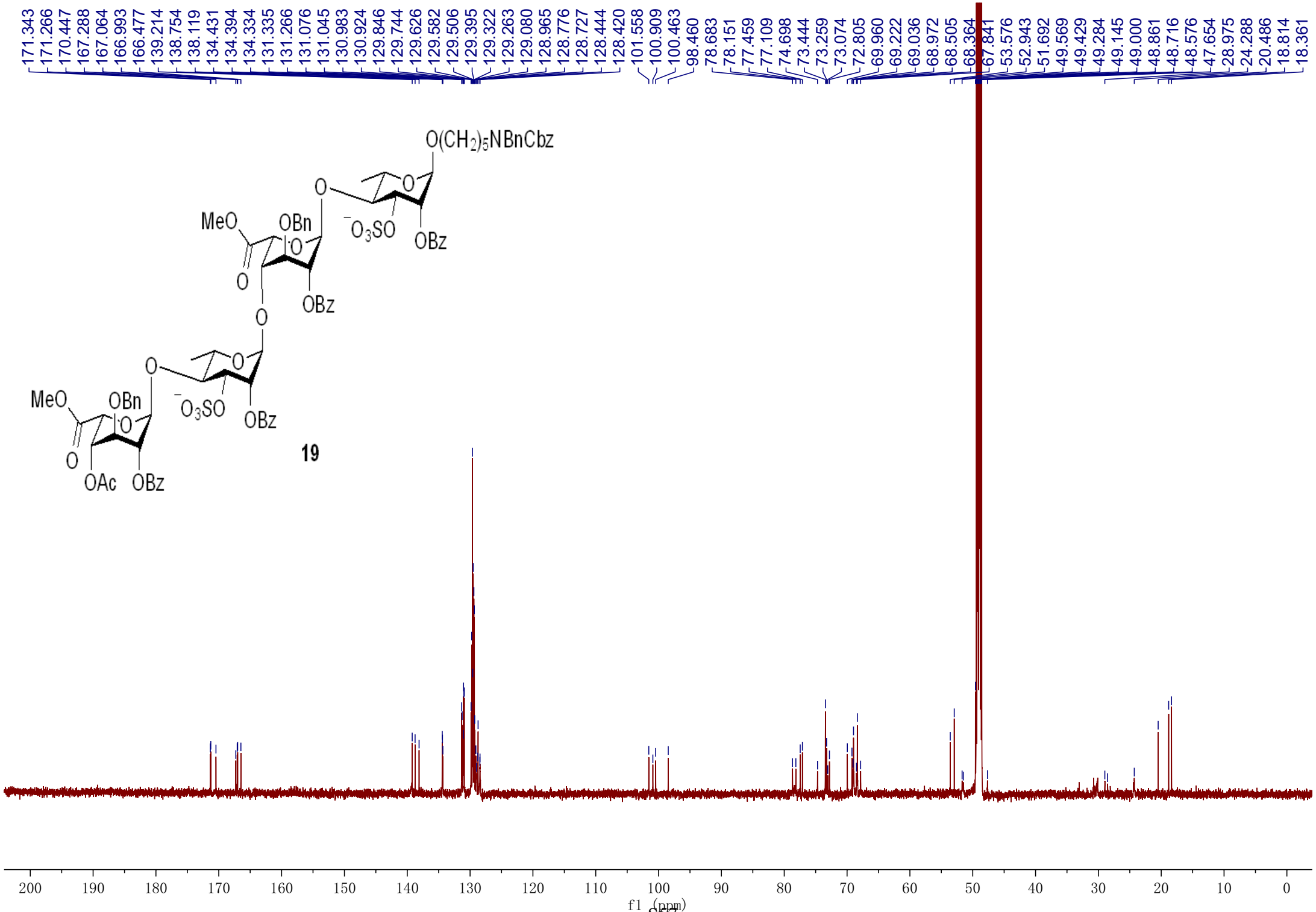
165.447
138.087
137.316
136.708
133.803
133.743
133.521
133.491
130.209
130.194
130.165
129.972
129.807
129.678
129.373
129.355
128.708
128.638
128.595
128.447
128.296
128.178
128.038
127.496
127.402
99.868
99.276
98.975
97.391
80.095
78.604
77.412
77.200
76.988
75.053
73.753
73.191
72.962
72.773
72.657
70.466
69.918
69.165
69.118
69.064
68.071
67.934
67.870
67.474
67.359
67.315
66.986
66.826
52.987
52.682
50.731
50.434
46.321
29.256
28.087
23.473
20.846
18.158
17.402
O(CH2)5NBnCbz
MeO
OBn
HO
OBz
OBz
MeO
OBn
HO
OBz
OAc
OBz
18
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.127 8.115 8.113 8.096 8.084 8.082 8.057 8.045 8.043 7.991 7.979 7.977 7.610 7.609 7.598 7.596 7.503 7.500 7.489 7.487 7.477 7.474 7.469 7.456 7.443 7.411 7.409 7.398 7.395 7.382 7.373 7.362 7.345 7.296 7.250 7.238 7.226 5.786 5.610 5.551 5.530 5.228 5.116 5.008 5.004 4.879 4.874 4.853 4.713 4.633 4.630 4.566 4.548 4.510 4.042 3.995 3.937 3.904 3.822 3.764 3.316 3.313 3.310 3.307 3.305 1.750 1.307 1.298 0.614 0.604
O(CH2)5NBnCbz
MeO
OBn
O3SO
OBz
OAc
19
1.92 1.93 1.99 1.95 1.97 1.00 7.00 20.36 2.01 1.00 2.02 1.01 0.96 1.02 1.08 3.19 2.07 1.02 1.08 1.08 2.85 1.06 2.20 3.00 2.20 1.05 2.19 3.00 4.35 5.85 3.01
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)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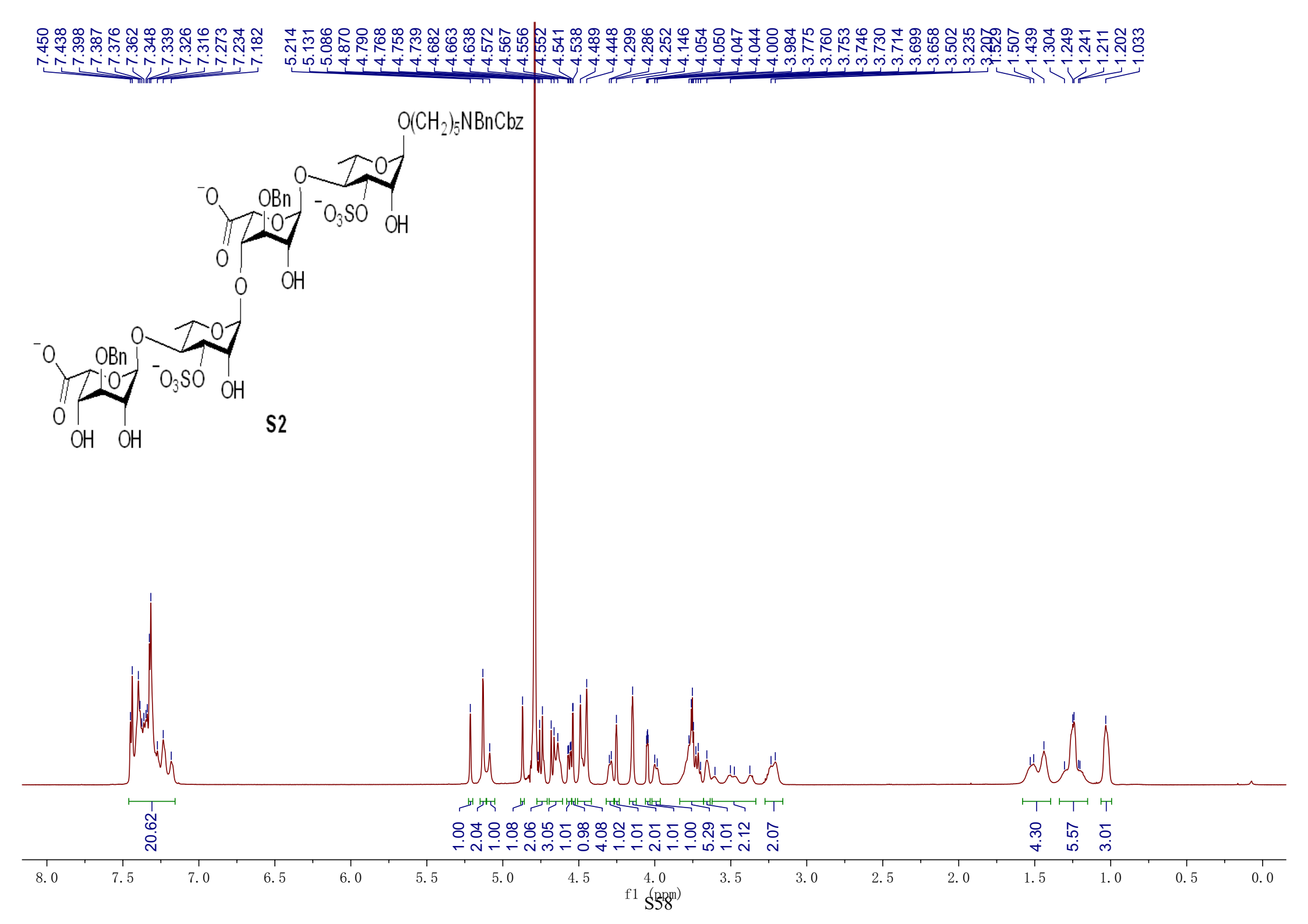
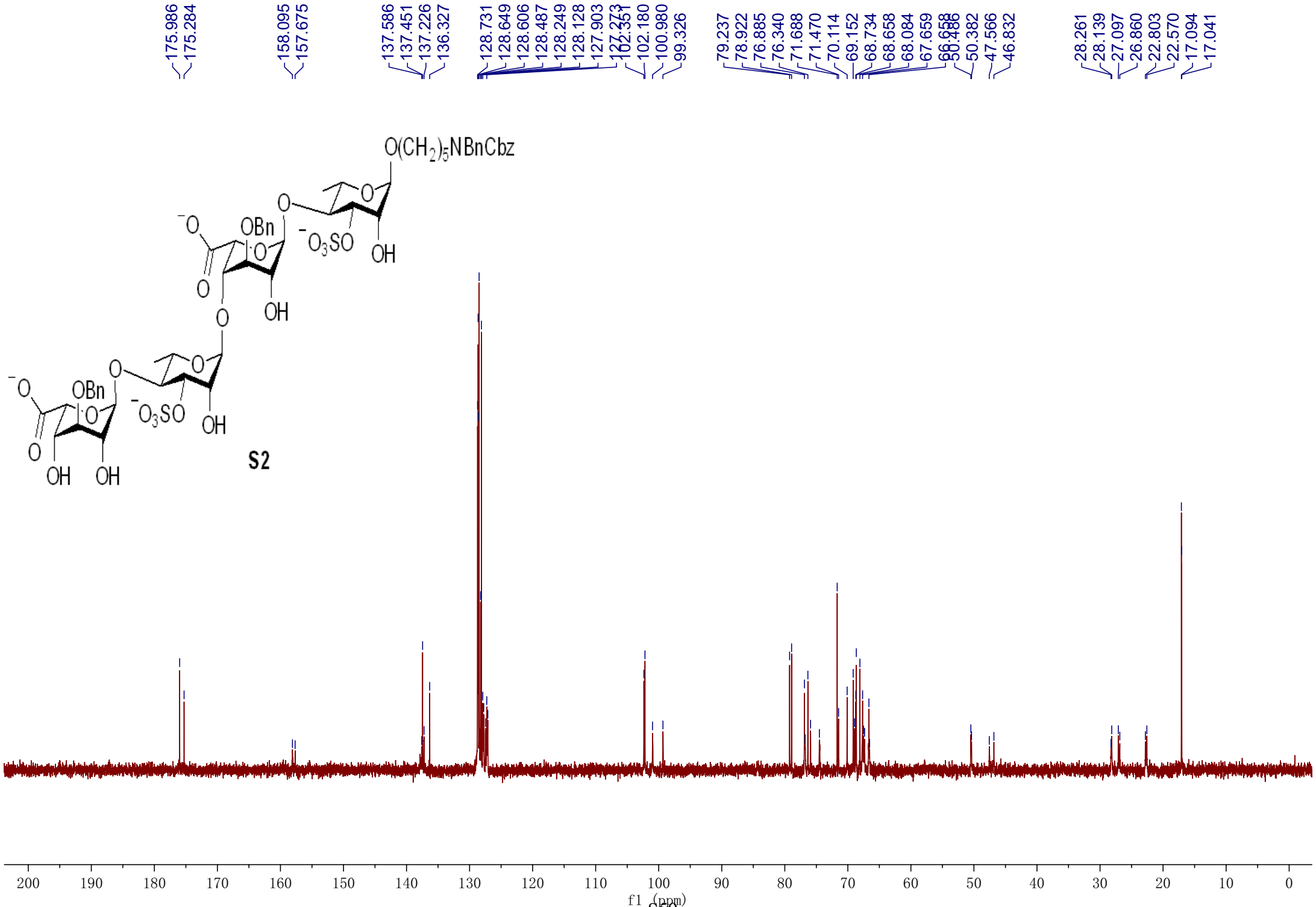
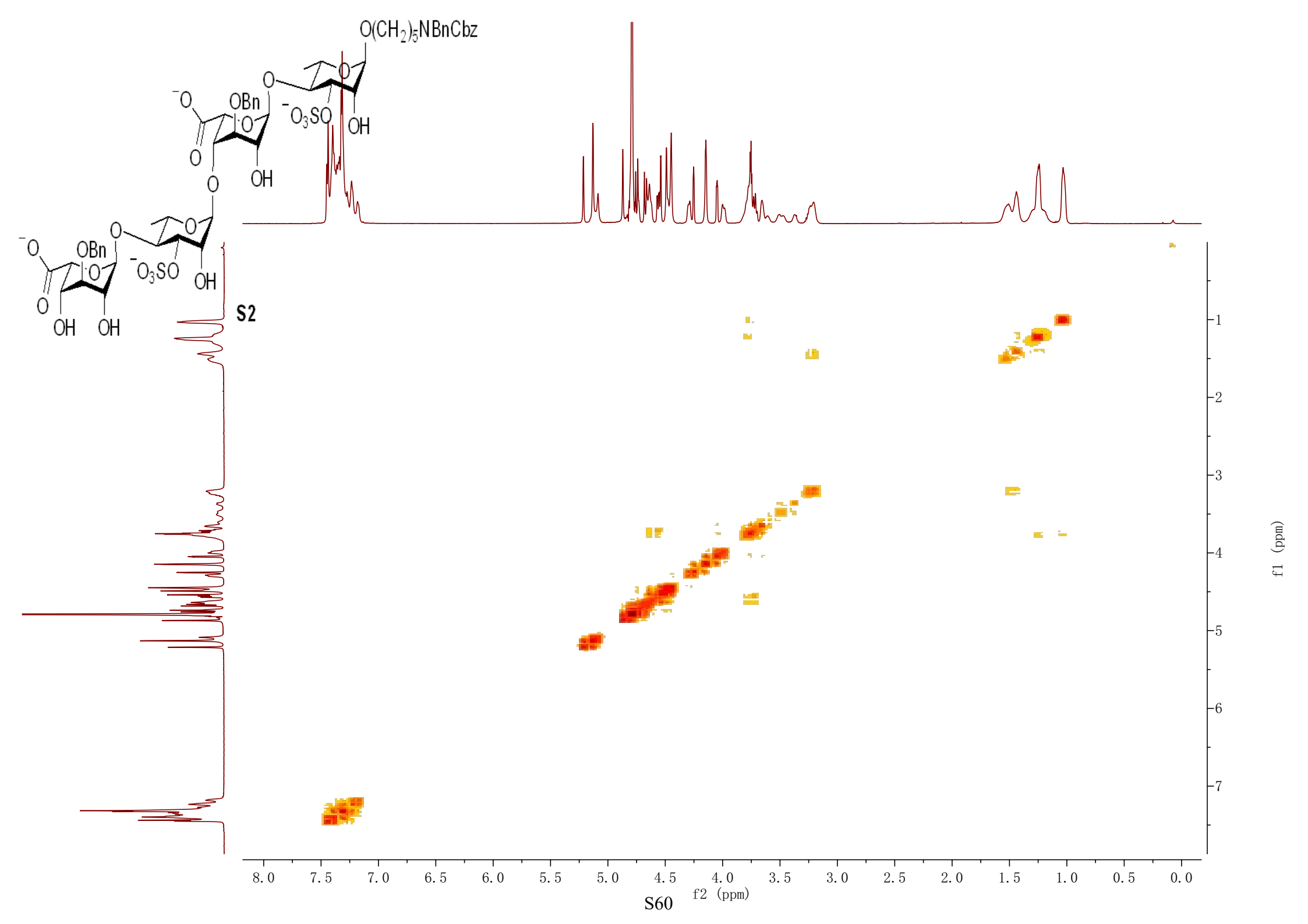
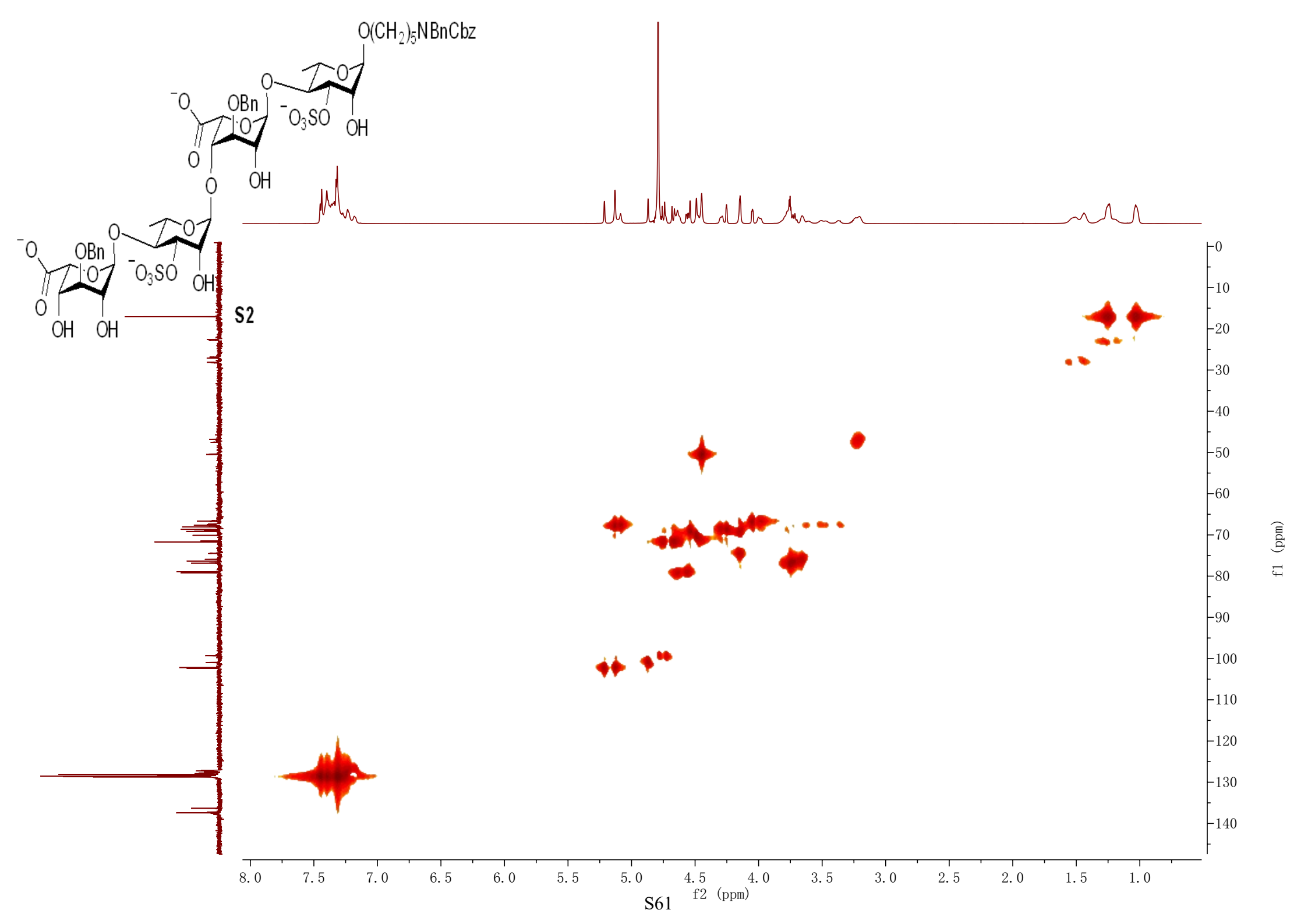
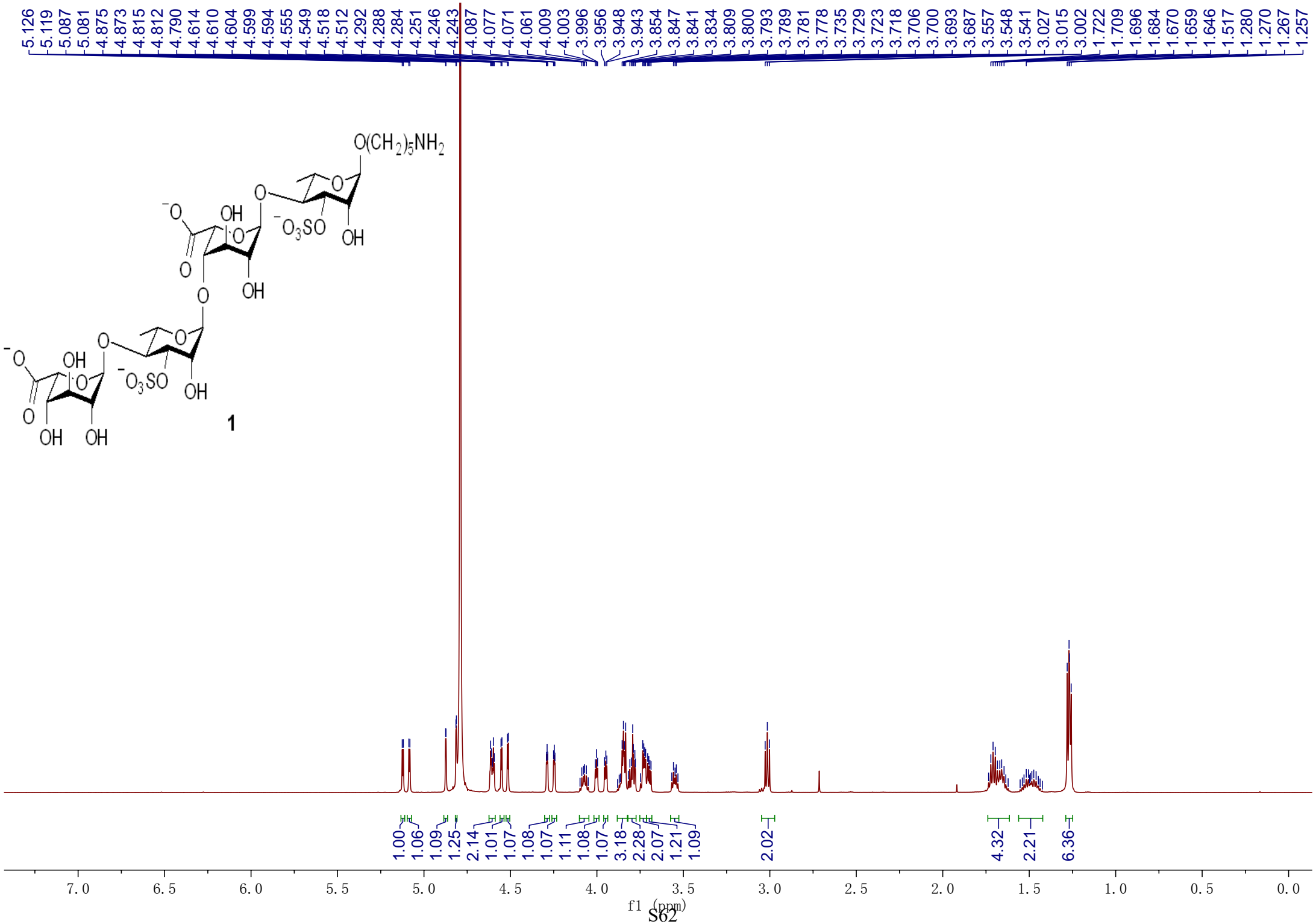
171.266
170.447
167.288
167.064
166.993
166.477
139.214
138.754
138.119
134.431
134.394
134.334
131.335
131.266
131.076
131.045
130.983
130.924
129.846
129.744
129.626
129.582
129.506
129.395
129.322
129.263
129.080
128.965
128.776
128.727
128.444
128.420
101.558
100.909
100.463
98.460
78.683
78.151
77.459
77.109
74.698
73.444
73.259
73.074
72.805
69.960
69.222
69.036
68.972
68.505
68.364
67.841
53.576
52.943
51.692
49.569
49.429
49.284
49.145
49.000
48.861
48.716
48.576
47.654
28.975
24.288
20.486
18.814
18.361
O(CH2)5NBnCbz
MeO
OBn
O3SO
OBz
OBz
MeO
OBn
O3SO
OBz
OAc
OBz
19
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

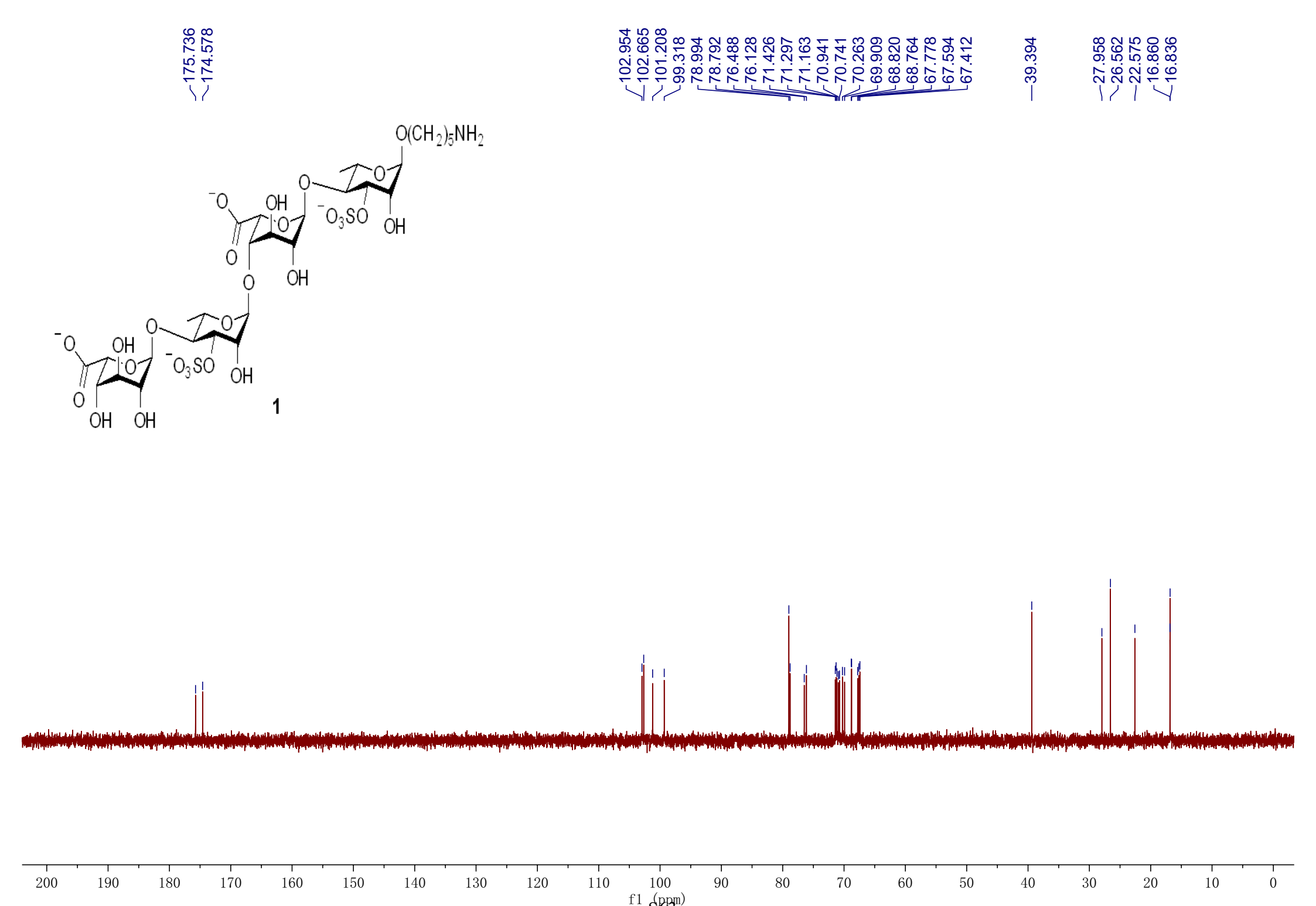

7.450 7.438 7.398 7.387 7.376 7.362 7.348 7.339 7.326 7.316 7.273 7.234 7.182
5.214 5.131 5.086 4.870 4.790 4.768 4.758 4.739 4.682 4.663 4.638 4.572 4.567 4.556 4.552 4.541 4.538 4.489 4.448 4.299 4.286 4.252 4.146 4.054 4.050 4.047 4.044 4.000 3.984 3.775 3.760 3.753 3.746 3.730 3.714 3.699 3.658 3.502 3.235 1.529 1.507 1.439 1.304 1.249 1.241 1.211 1.202 1.033
O(CH2)5NBnCbz
OBn
O3SO
OH
S2
20.62
1.00 2.04 1.00 1.08 2.06 3.05 1.01 0.98 4.08 1.02 1.01 2.01 1.01 1.00 5.29 1.01 2.12 2.07
4.30 5.57 3.01
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)

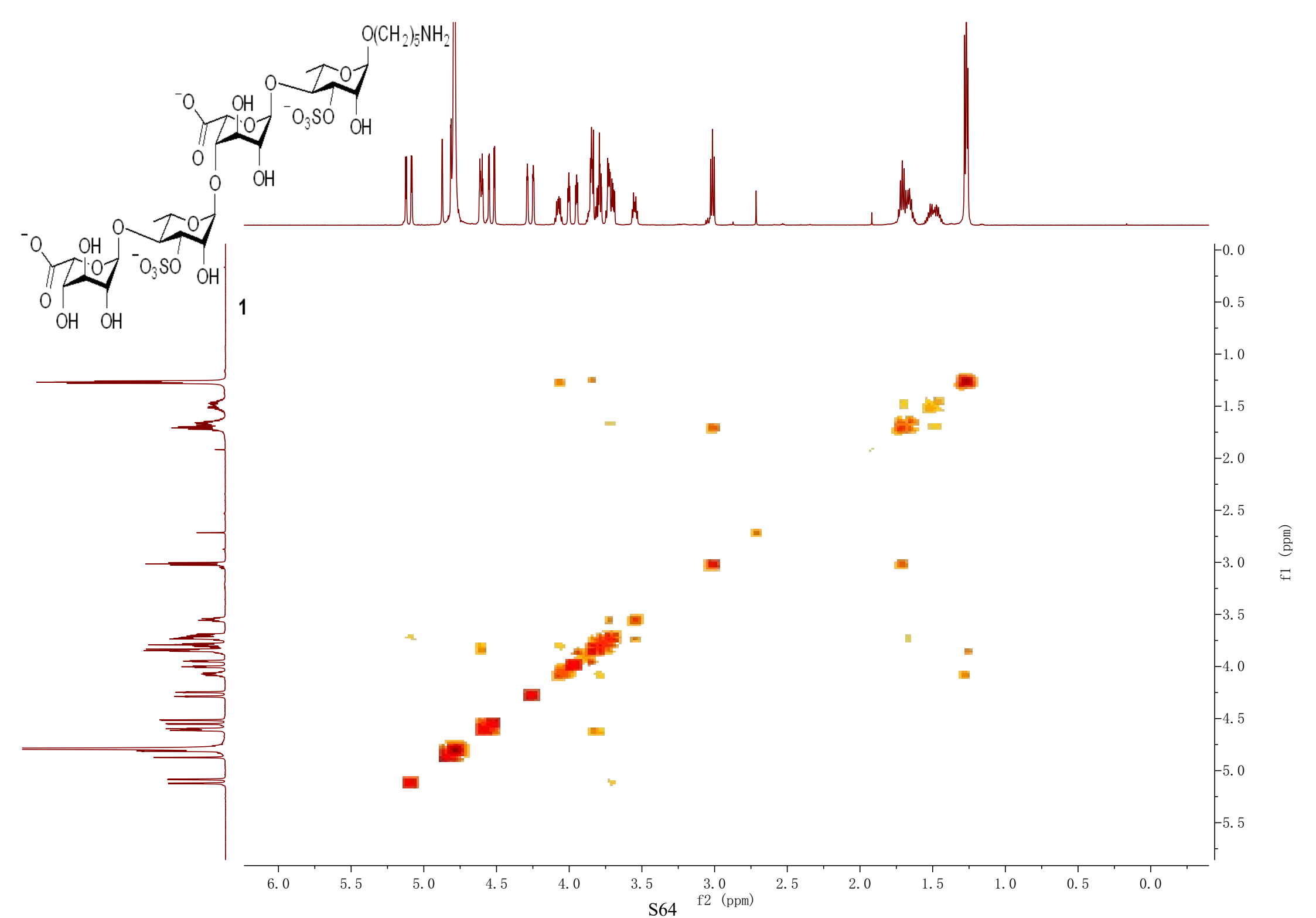

175.986
175.284
158.095
157.675
137.586
137.451
137.226
136.327
128.731
128.649
128.606
128.487
128.249
128.128
127.903
102.351
102.180
100.980
99.326
79.237
78.922
76.885
76.340
71.688
71.470
70.114
69.152
68.734
68.658
68.084
67.659
50.382
47.566
46.832
28.261
28.139
27.097
26.860
22.803
22.570
17.094
17.041
O(CH2)5NBnCbz
OBn
O3SO
OH
S2
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

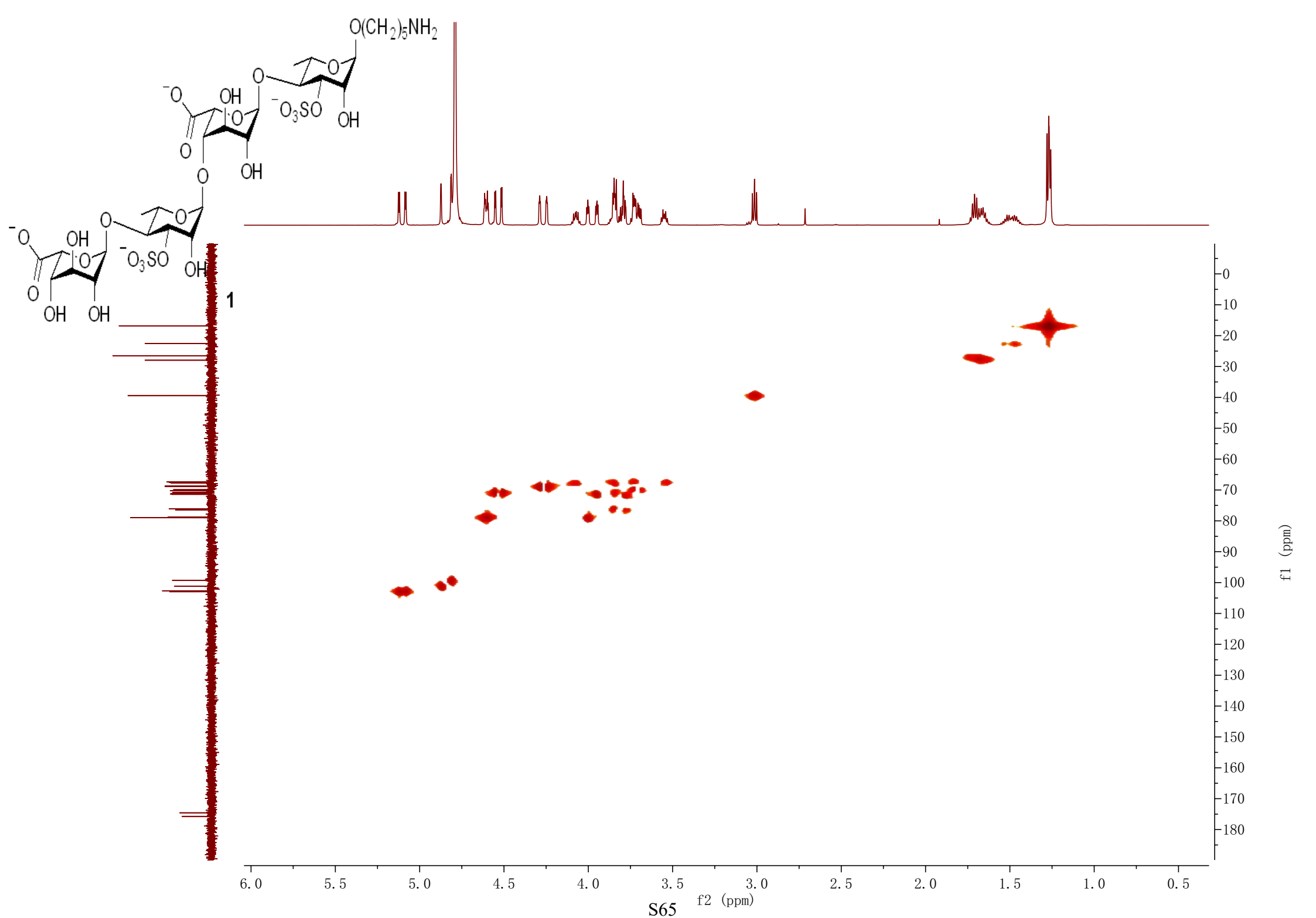

O(CH2)5NBnCbz
OBn
O3SO
OH
S2
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)
f1 (ppm)


O(CH2)5NBnCbz
OBn
O3SO
OH
S2
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
10
20
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)


5.126
5.119
5.087
5.081
4.875
4.873
4.815
4.812
4.790
4.614
4.610
4.604
4.599
4.594
4.555
4.549
4.518
4.512
4.292
4.288
4.284
4.251
4.246
4.243
4.087
4.077
4.071
4.061
4.009
4.003
3.996
3.956
3.948
3.943
3.854
3.847
3.841
3.834
3.809
3.800
3.793
3.789
3.781
3.778
3.735
3.729
3.723
3.718
3.706
3.700
3.693
3.687
3.557
3.548
3.541
3.027
3.015
3.002
1.722
1.709
1.696
1.684
1.670
1.659
1.646
1.517
1.280
1.270
1.267
1.257
O(CH2)5NH2
OH
O3SO
OH
OH
O3SO
OH
OH
OH
1
1.00
1.06
1.09
1.25
2.14
1.01
1.07
1.08
1.07
1.11
1.08
1.07
3.18
2.28
2.07
1.21
1.09
2.02
4.32
2.21
6.36
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)


175.736
174.578
102.954
102.665
101.208
99.318
78.994
78.792
76.488
76.128
71.426
71.297
71.163
70.941
70.741
70.263
69.909
68.820
68.764
67.778
67.594
67.412
39.394
27.958
26.562
22.575
16.860
16.836
O(CH2)5NH2
1
f1 (ppm)


O(CH2)5NH2
1
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)
f1 (ppm)


O(CH2)5NH2
OH
O
O3SO
OH
OH
OH
OH
OH
OH
1
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)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
f1 (ppm)