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Supporting Information

Total Synthesis of the Core Tetrasaccharide of *Neisseria meningitidis* Lipopolysaccharide, a Potential Vaccine Candidate for Meningococcal Diseases

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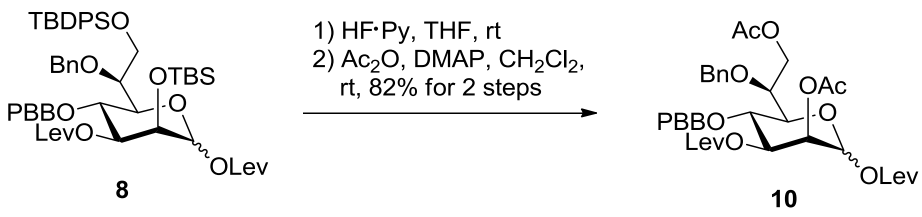
Contents

1. General information for chemical synthesis. Commercial reagents were used without further purification except where noted. Solvents were dried and redistilled prior to use in the usual way. All reactions were performed in oven-dried glassware under an inert atmosphere unless noted otherwise. Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F254 glass plates precoated with a 0.25 mm thickness of silica gel. The TLC plates were visualized with UV light and by staining with Hanessian solution (ceric sulfate and ammonium molybdate in aqueous sulfuric acid) or sulfuric acid-ethanol solution. Column chromatography was performed on Fluka Kieselgel 60 (230-400 mesh). Optical rotations (OR) were measured with a Schmidt & Haensch UniPol L1000 polarimeter at a concentration (c) expressed in g/100 mL. ^{1}H and ^{13}C NMR spectra were measured with a Varian 400-MR or Varian 600 spectrometer with Me_4Si as the internal standard. NMR chemical shifts (δ) were recorded in ppm and coupling constants (*J*) were reported in Hz. High-resolution mass spectra (HRMS) were recorded with an Agilent 6210 ESI-TOF mass spectrometer at the Freie Universität Berlin, Mass Spectrometry Core Facility.

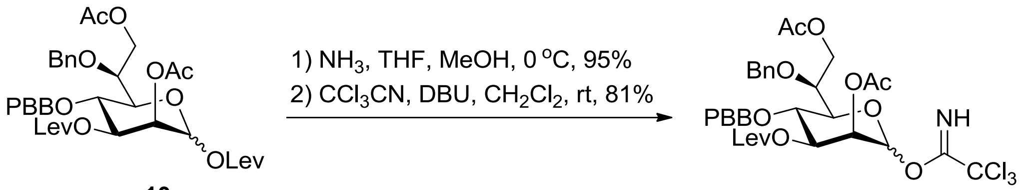
2. Experimental details and characterization data of new compounds

2.1. Synthesis of 2,7-di-*O*-acetyl-3-*O*-levulinoyl-4-*O*-*para*-bromobenzyl-6-*O*-benzyl-L-*glycero*-D-*manno*-heptopyranosyl levulinoate 10



Compound **8**[1] (500 mg, 0.49 mmol) was dissolved in THF (2 mL) at room temperature, followed by addition of 70% HF-pyridine (0.4 mL). After stirring for 2 days, the reaction mixture was carefully quenched with sat. aq. $NaHCO_3$ and the resulting solution was diluted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to give the corresponding diol as a colorless syrup. To a solution of the above diol and DMAP (12 mg, 0.1 mmol) in CH_2Cl_2 (20 mL), was added Ac_2O (1 mL). After being stirred at room temperature for overnight, the mixture was washed with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (cyclohexane/EtOAc: 1/1) to give **10** (300 mg, 82% for 2 steps) as a pale yellow syrup: $[\alpha]^{20}_{D}$ = +53.3 (*c* 0.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.27 (m, 7 H, Ar), 7.03 (m, 2 H, Ar), 6.06 (d, *J* = 2.4 Hz, 1 H, H-1), 5.31 (dd, *J* = 3.6, 9.2 Hz, 1 H, H-3), 5.21 (dd, *J* = 2.4, 3.6 Hz, 1 H, H-2), 4.80 (d-like, *J* = 12.0 Hz, 1 H, OCH_2Ar), 4.50 (t, *J* = 11.6 Hz, 2 H, OCH_2Ar), 4.44 (dd, *J* = 6.0, 11.6 Hz, 1 H, H-7), 4.21 (dd, *J* = 6.0, 11.6 Hz, 1 H, H-7), 4.14 (d-like, *J* = 11.6 Hz, 1 H, OCH_2Ar), 4.03 (t, *J* = 9.6 Hz, 1 H, H-4), 3.98 (m, 1 H, H-6), 3.89 (dd, *J* = 1.6, 9.6 Hz, 1 H, H-5), 2.77 – 2.57 (m, 6 H, $C(O)CH_2$), 2.42 (m, 2 H, $C(O)CH_2$), 2.17 (s, 3 H, $C(O)CH_3$), 2.14 (s, 3 H, $C(O)CH_3$), 2.13 (s, 3 H, $C(O)CH_3$), 2.04 (s, 3 H, $C(O)CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.1, 205.9, 171.8, 170.6, 170.2, 169.8, 137.9, 137.0, 131.5, 129.0, 128.5, 128.0, 127.9, 121.5, 90.9 (C-1), 73.5, 73.4, 73.3, 73.1, 72.4, 72.2, 72.1, 68.5, 62.8, 37.7, 29.7, 29.6, 27.8, 27.7, 20.9, 20.8; HRMS (ESI) *m/z* calcd for $C_{35}H_{41}BrO_{13}Na$ $[M+Na]^+$ 773.1608, found 773.1645.

2.2. Synthesis of 2,7-di-*O*-acetyl-3-*O*-levulinoyl-4-*O*-*para*-bromobenzyl-6-*O*-benzyl-1-thio-L-*glycero*-D-*manno*-heptopyranosyl trichloroacetimidate 4



10 **4**

To a solution of compound **10** (170 mg, 0.227 mmol) in THF and methanol (7:3, 10 mL) at 0 °C, was bubbled through gaseous ammonium at a modest rate. After stirring for 30 min at 0 °C, the solution was evaporated *in vacuo* to give a residue, which was purified by silica gel column chromatography (CH_2Cl_2/MeOH: 20/1) to afford the corresponding hemiacetal (140 mg, 95%) as a colorless syrup. To a solution of the above hemiacetal (140 mg, 0.215 mmol) in CH_2Cl_2 (5 mL) was added CCl_3CN (107 μL, 1.07 mmol) and DBU (7 μL, 0.046 mmol). After being stirred at room temperature for 2 h, TLC revealed almost complete conversion of the starting material. The solution was concentrated *in vacuo* to a residue, which was purified by silica gel

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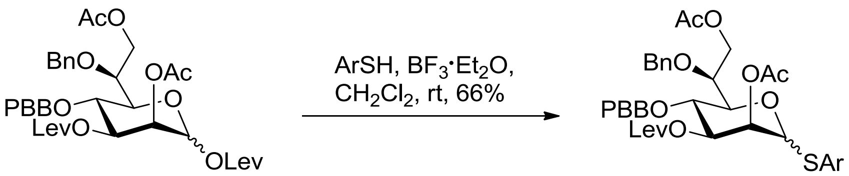
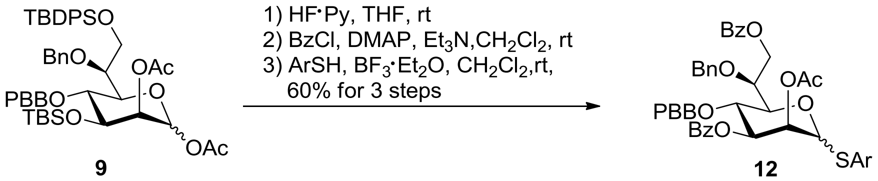
column chromatography (cyclohexane/EtOAc: 2/1) to give **4** (138 mg, 81%) as a colorless syrup: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1 H, C(NH)), 7.44 – 7.30 (m, 7 H, Ar), 7.06 (d, *J* = 8.4 Hz, 2 H, Ar), 6.28 (d, *J* = 2.0 Hz, 1 H, H-1), 5.44 (dd, *J* = 2.0, 3.2 Hz, 1 H, H-2), 5.40 (dd, *J* = 3.2, 9.2 Hz, 1 H, H-3), 4.82 (d-like, *J* = 12.0 Hz, 1 H, OCH_2Ar), 4.56 (d-like, *J* = 11.6 Hz, 1 H, OCH_2Ar), 4.47 (m, 2 H), 4.17 (m, 3 H), 4.02 (m, 2 H), 2.68 (m, 2 H, $C(O)CH_2$), 2.45 (m, 2 H, $C(O)CH_2$), 2.18 (s, 3 H, $C(O)CH_3$), 2.16 (s, 3 H, $C(O)CH_3$), 2.01 (s, 3 H, $C(O)CH_3$); LRMS (ESI) *m/z* calcd for $C_{32}H_{35}BrCl_3NO_{11}Na$ $[M+Na]^+$ 816.0, found 815.9.

2.3. Synthesis of 5-*tert*-butyl-2-methylphenyl 2,7-di-*O*-acetyl-3-*O*-levulinoyl-4-*O*-*para*-bromobenzyl-6-*O*-benzyl-1-thio-L-*glycero*-D-*manno*-heptopyranoside 11



To a solution of compound **10** (50 mg, 0.067 mmol) in CH_2Cl_2 (2.5 mL), was added 5-*tert*-butyl-2-methylbenzenethiol (61 μL, 0.33 mmol) and BF_3OEt_2 (18 μL, 0.14 mmol). After being stirred at room temperature for overnight, the mixture was quenched with Et_3N and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (cyclohexane/EtOAc: 3/1) to give **11** (36 mg, 66%) as a colorless syrup: $[\alpha]^{20}_D$ = +98.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.29 (m, 8 H, Ar), 7.18 (dd, *J* = 2.0, 8.0 Hz, 1 H, Ar), 7.07 (m, 3 H, Ar), 5.54 (d, *J* = 2.0 Hz, 1 H, H-1), 5.51 (dd, *J* = 2.0, 3.2 Hz, 1 H, H-2), 5.37 (dd, *J* = 3.2, 9.2 Hz, 1 H, H-3), 4.79 (d-like, *J* = 11.6 Hz, 1 H, OCH_2Ar), 4.54 (d-like, *J* = 12.0 Hz, 1 H, OCH_2Ar), 4.50 (d-like, *J* = 12.0 Hz, 1 H, OCH_2Ar), 4.44 (dd, *J* = 6.0, 11.2 Hz, 1 H, H-7), 4.27 (dd, *J* = 1.2, 9.6 Hz, 1 H, H-5), 4.18 (d-like, *J* = 12.0 Hz, 1 H, OCH_2Ar), 4.09 (t, *J* = 9.6 Hz, 1 H, H-4), 4.06 (m, 1 H), 3.99 (m, 1 H), 2.69 (m, 2 H, $C(O)CH_2$), 2.44 (m, 2 H, $C(O)CH_2$), 2.36 (s, 3 H, $ArCH_3$), 2.17 (s, 3 H, $C(O)CH_3$), 2.16 (s, 3 H, $C(O)CH_3$), 1.91 (s, 3 H, $C(O)CH_3$), 1.29 (s, 9 H, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.1, 171.8, 170.4, 170.1, 150.0, 137.8, 137.1, 135.8, 132.1, 131.5, 130.1, 128.9, 128.5, 128.1, 128.0, 127.8, 124.9, 121.5, 85.3 (C-1), 73.5, 73.4, 73.0, 72.9, 72.4, 72.3, 71.6, 62.6, 37.7, 34.5, 31.3, 29.8, 27.8, 26.9, 21.0, 20.7, 20.2; HRMS (ESI) *m/z* calcd for $C_{41}H_{49}BrSO_{10}Na$ $[M+Na]^+$ 837.2107, found 837.2085.

2.4. Synthesis of 5-*tert*-butyl-2-methylphenyl 2-*O*-acetyl-3,7-di-*O*-benzoyl-4-*O*-*para*-bromobenzyl-6-*O*-benzyl-1-thio-L-*glycero*-D-*manno*-heptopyranoside 12

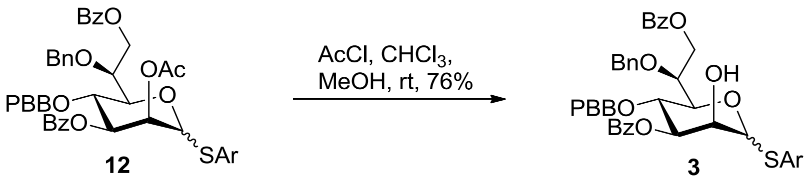


9 12

Compound **9**[1] (930 mg, 1.03 mmol) was dissolved in THF (4 mL) at room temperature, followed by addition of 70% HF-pyridine (0.8 mL). After stirring for 2 days, the reaction mixture was carefully quenched with sat. aq. $NaHCO_3$ and the resulting solution was diluted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to give the corresponding diol as a colorless syrup. To a solution of the above diol and DMAP (200 mg, 1.64 mmol) in CH_2Cl_2 (20 mL), was added Et_3N (2.0 mL) and benzoyl chloride (1.0 mL). After being stirred at room temperature for overnight, the mixture was concentrated *in vacuo* to give a residue, which was purified by silica gel column chromatography (cyclohexane/EtOAc: 5/1 to 3/1) to give the corresponding ester (709 mg) as a white solid. To a solution of the above ester (709 mg, 0.93 mmol) and freshly activated 4Å MS in CH_2Cl_2 (20 mL), was added 5-*tert*-butyl-2-methylbenzenethiol (0.98 mL, 5.31 mmol) and BF_3OEt_2 (0.73 mL, 5.77 mmol). After being stirred at room temperature for overnight, the mixture was quenched with Et_3N and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (cyclohexane/EtOAc: 10/1 to 8/1) to provide **12** (531 mg, α/β = 4.0, 60% for 3 steps) as a white foam: $[\alpha]^{20}_{D}$ α-anomer: +64.0 (*c* 0.3, $CHCl_3$); β-anomer: +52.3 (*c* 1.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) α-anomer: δ 7.88 – 7.81 (m, 4 H, Ar), 7.51 – 7.15 (m, 14 H, Ar), 7.06 (dd, *J* = 2.0, 8.0 Hz, 1 H, Ar), 6.96 – 6.81 (m, 3 H, Ar), 5.59 (m, 3 H, H-1/2/3), 4.82 (d-like, *J* = 11.6 Hz, 1 H, OCH_2Ar), 4.70 (dd, *J* = 5.6, 10.8 Hz, 1 H, H-7), 4.51 (d-like, *J* = 12.0 Hz, 1 H, OCH_2Ar), 4.42 (m, 2 H), 4.18 (m, 4 H), 2.26 (s, 3 H, $ArCH_3$), 2.09 (s, 3 H, $C(O)CH_3$), 1.20 (s, 9 H, $C(CH_3)_3$); β-anomer: δ 8.07 – 7.92 (m, 4 H, Ar), 7.61 – 7.36 (m, 14 H, Ar), 7.14 (dd, *J* = 2.0, 8.0 Hz, 1 H, Ar), 7.04 (m, 3 H, Ar), 5.78 (dd, *J* = 2.0, 3.2 Hz, 1 H, H-2), 5.63 (d, *J* = 2.0 Hz, 1 H, H-1), 5.51 (dd, *J* = 3.2, 9.6 Hz, 1 H, H-3), 4.92 (d-like, *J* = 11.6 Hz, 1 H, OCH_2Ar), 4.80 (dd, *J* = 6.0, 10.8 Hz, 1 H, H-7), 4.52 (m, 2 H), 4.47 (dd, *J* = 1.6, 9.6 Hz, 1 H, H-5), 4.32 (m, 3 H), 4.28 (m, 1 H), 2.38 (s, 3 H, $ArCH_3$), 1.91 (s, 3 H, $C(O)CH_3$), 1.25 (s, 9 H, $C(CH_3)_3$); ^{13}C NMR (100 MHz,

$CDCl_3$) α-anomer: δ 169.8, 165.9, 165.2, 149.9, 137.8, 136.7, 135.5, 133.4, 133.0, 132.2, 131.3, 130.1, 129.6, 129.5, 129.4, 129.3, 128.8, 128.5, 128.4, 128.3, 128.1, 128.0, 127.3, 124.7, 121.5, 85.2 (C-1), 73.6, 73.5, 73.4, 72.8, 72.6, 72.3, 72.1, 62.3, 34.5, 31.3, 21.0, 20.1; β-anomer: δ 169.8, 166.0, 165.4, 149.9, 138.0, 137.0, 136.1, 133.4, 133.1, 132.1, 131.5, 130.1, 129.9, 129.6, 129.5, 128.7, 128.5, 128.4, 128.3, 127.8, 127.7, 125.0, 121.5, 85.5 (C-1), 74.0, 73.6, 73.3, 72.6, 72.5, 72.4, 72.3, 62.6, 34.5, 31.3, 20.8, 20.3; HRMS (ESI) *m/z* calcd for $C_{48}H_{49}BrSO_9Na$ $[M+Na]^+$ 905.2158, found 905.2164.

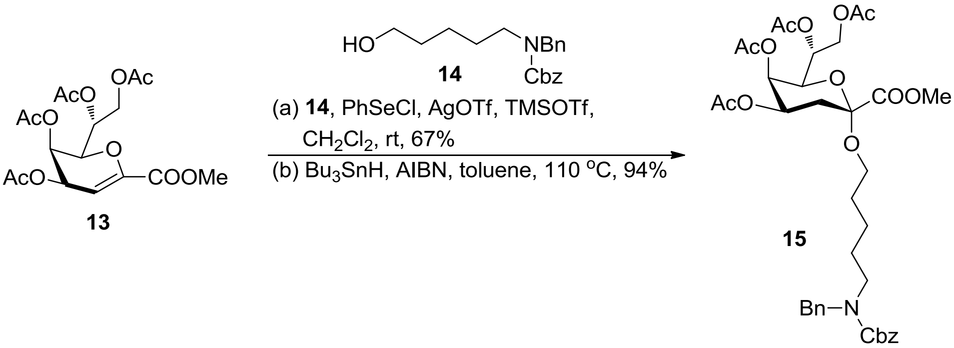
2.5. Synthesis of 5-*tert*-butyl-2-methylphenyl 3,7-di-*O*-benzoyl-4-*O*-*para*-bromobenzyl-6-*O*-benzyl-1-thio-L-*glycero*-D-*manno*-heptopyranoside 3



To a solution of thioglycoside **12** (220 mg, 0.249 mmol) in $MeOH/CHCl_3$ (5/2, v/v, 12.3 mL), was added acetyl chloride (0.53 mL). After being stirred at room tempearature for 1 d, the mixture was diluted with CH_2Cl_2, washed with saturated aqueous $NaHCO_3$, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/EtOAc: 6/1) to afford **3** (160 mg, 76%) as a white solid: $[\alpha]^{20}_D$ = +79.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.83 (m, 4 H, Ar), 7.58 – 7.21 (m, 14 H, Ar), 7.10 (dd, *J* = 2.0, 8.0 Hz, 1 H, Ar), 7.01 – 6.87 (m, 3 H, Ar), 5.67 (d, *J* = 2.0 Hz, 1 H, H-1), 5.56 (dd, *J* = 3.2, 9.2 Hz, 1 H, H-3), 4.85 (d-like, *J* = 12.0 Hz, 1 H, OCH_2Ar), 4.76 (dd, *J* = 6.0, 11.2 Hz, 1 H, H-7), 4.54 (d-like, *J* = 11.6 Hz, 1 H, OCH_2Ar), 4.46 (m, 3 H), 4.28 (m, 3 H), 4.19 (m, 1 H), 2.30 (s, 3 H, $ArCH_3$), 1.27 (s, 9 H, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 165.5, 149.9, 137.7, 136.8, 134.9, 133.5, 133.0, 132.7, 131.3, 130.0, 129.7, 129.6, 129.5, 129.0, 128.5, 128.2, 128.1, 128.0, 126.4, 124.3, 121.5, 86.9 (C-1), 73.7, 73.5, 73.1, 72.6, 72.2, 71.4, 62.4, 34.5, 31.3, 20.1; HRMS (ESI) *m/z* calcd for $C_{46}H_{47}BrSO_8Na$ $[M+Na]^+$ 863.2052, found 863.2017.

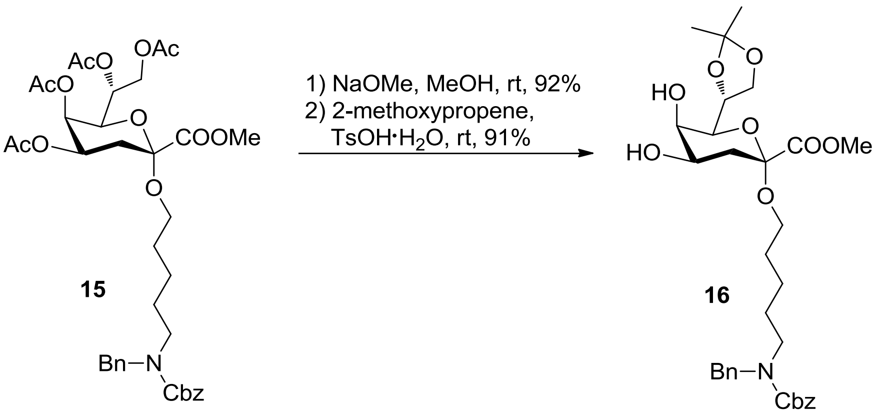
2.6. Synthesis of methyl (*N*-benzyl-benzyloxycarbonyl-5-aminopentyl 4,5,7,8-

tetra-*O*-acetyl-3-deoxy-α-D-*manno*-oct-2-ulopyranosid)onate 15

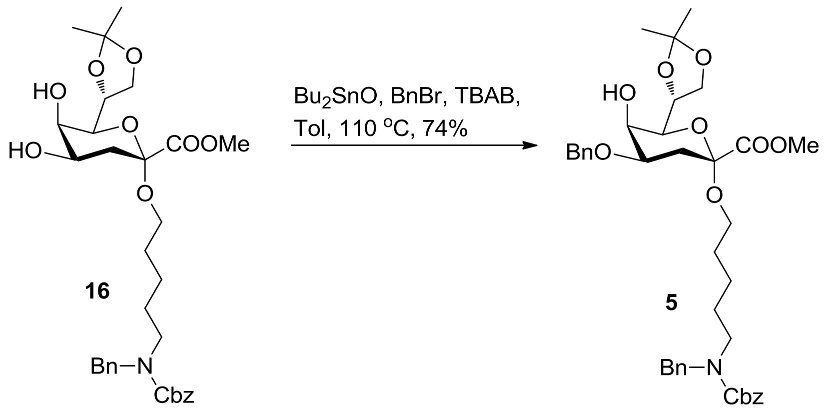


To a stirred solution of phenylselenyl chloride (2.73 g, 14.3 mmol) in CH_2Cl_2 (50 mL) was added AgOTf (2.55 g, 9.92 mmol) and TMSOTf (0.16 mL, 0.86 mmol). After stirring at room temperature for 30 min, a solution of glycal **13**[2] (2.85 g, 7.08 mmol) and linker **14**[3] (3.25 g, 9.92 mmol) in CH_2Cl_2 (70 mL) was added dropwise. After being stirred at room temperature for 2 h, the mixture was diluted with CH_2Cl_2, washed with saturated aqueous $NaHCO_3$, and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (cyclohexane/EtOAc: 3/1) to give a white solid (4.2 g, 67%). To a solution of the above solid (4.2 g, 4.75 mmol) in toluene (140 mL), was added tri-*n*-butyltin hydride (3.8 mL, 14.24 mmol) and AIBN (779 mg, 4.75 mmol). After being refluxed for 1.5 h, the mixture was concentrated *in vacuo* and purified by silica gel column chromatography (cyclohexane/EtOAc: 5/2 to 2/1) to afford **15** (3.26 g, 94%) as a colorless syrup: $[\alpha]^{20}_D$ = +43.5 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.11 (m, 10 H, Ar), 5.29 (br s, 1 H), 5.24 (m, 1 H, H-4), 5.13 (m, 3 H), 4.51 (d-like, *J* = 12.0 Hz, 1 H), 4.43 (br s, 2 H), 4.05 (dd, *J* = 3.6, 12.4 Hz, 1 H), 3.98 (m, 1 H), 3.71 (s, 3 H, $C(O)OCH_3$), 3.37 (m, 1 H, OCH_2), 3.16 (m, 3 H, OCH_2/NCH_2), 2.09 (dd, *J* = 4.8, 13.2 Hz, 1 H, H-3*e*), 2.00 (s, 3 H, $C(O)CH_3$), 1.95 (m, 1 H, H-3*a*), 1.91 (s, 6 H, $C(O)CH_3$), 1.90 (s, 3 H, $C(O)CH_3$), 1.47 (m, 4 H, CCH_2C), 1.22 (m, 2 H, CCH_2C); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 170.3, 169.9, 169.6, 167.8, 137.8, 128.5, 128.4, 127.9, 127.8, 127.3, 127.2, 98.8 (C-2), 68.1, 67.6, 67.1, 66.4, 64.3, 63.8, 62.0, 52.6, 32.1 (C-3), 29.7, 29.2, 23.4, 20.8, 20.7, 20.6; HRMS (ESI) *m/z* calcd for $C_{37}H_{47}NO_{14}Na$ $[M+Na]^+$ 752.2894, found 752.2921.

2.7. Synthesis of methyl (*N*-benzyl-benzyloxycarbonyl-5-aminopentyl 4-*O*-benzyl-7,8-O-isopropylidene-3-deoxy-α-D-*manno*-oct-2-ulopyranosid)onate 5



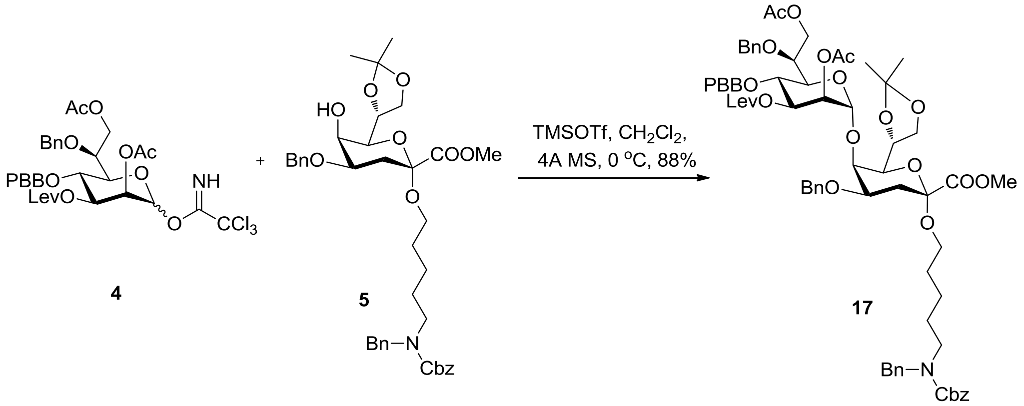
To a stirred solution of compound **15** (1 g, 1.37 mmol) in MeOH (25 mL) was added NaOMe (74 mg, 1.37 mmol). The mixture was stirred at room temperature for 4 h, and then neutralized with Amberlite IR120 H^+ resin. Filtration, concentration *in vacuo*, and purification by silica gel column chromatography (CH_2Cl_2/MeOH: 12/1) gave the corresponding alcohol (710 mg, 92%) as a white solid. To a stirred solution of the above alcohol (500 mg, 0.89 mmol) in DMF (9 mL), was added 2-methoxypropene (153 µL, 1.60 mmol) and *p*-toluenesulfonic acid monohydrate (40 mg, 0.21 mmol). The mixture was stirred at room temperature for 2 h, and then neutralized with sodium hydrogencarbonate. Filtration, concentration *in vacuo*, and purification by silica gel column chromatography (CH_2Cl_2/MeOH: 40/1) afforded **16** (490 mg, 91%) as a colorless syrup: $[\alpha]^{20}_{D}$ = +30.3 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.10 (m, 10 H, Ar), 5.09 (d-like, *J* = 12.0 Hz, 2 H), 4.42 (br s, 2 H), 4.32 (m, 1 H), 4.07 (dd, *J* = 6.0, 8.4 Hz, 1 H), 3.97 (m, 1 H, H-4), 3.88 (m, 2 H), 3.67 (s, 3 H, C(O)OCH_3), 3.42 (m, 1 H), 3.31 (m, 1 H, OCH_2), 3.15 (m, 3 H, OCH_2/NCH_2), 2.05 (dd, *J* = 4.8, 12.8 Hz, 1 H, H-3*e*), 1.78 (t, *J* = 12.0 Hz, 1 H, H-3*a*), 1.44 (m, 4 H, CCH_2C), 1.32 (s, 3 H, $C(CH_3)_2$), 1.29 (s, 3 H, $C(CH_3)_2$), 1.18 (m, 2 H, CCH_2C); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 137.8, 128.5, 128.4, 127.9, 127.8, 127.3, 127.2, 109.4 (*C*$(CH_3)_2$), 99.0 (C-2), 73.6, 72.8, 67.2, 67.1, 66.7, 65.7, 63.6, 52.5, 35.0 (C-3), 29.7, 29.2, 26.9, 25.3; HRMS (ESI) *m/z* calcd for $C_{32}H_{43}NO_{10}Na$ $[M+Na]^+$ 624.2785, found 624.2736.



A mixture of compound **16** (490 mg, 0.81 mmol), dibutyltin oxide (304 mg, 1.22 mmol) and 4Å MS (500 mg) in toluene (15 mL) was heated at 110 ^{o}C for 2 h. After cooling to room temperature, benzyl bromide (0.17 mL, 1.47 mmol) and tetrabutylammonium bromide (158 mg, 0.49 mmol) were added, and the mixture was heated at 110 ^{o}C for overnight. The cooling mixture was then filtered and the filrate was evaporated. The residue was dissolved in CH_2Cl_2 and washed with water. The organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo* to give a residue, which was purified by silica gel column chromatography (cyclohexane/ EtOAc: 4/1) to give a syrup, which was dissolved in MeOH (8 mL) and treated with NaOMe (24 mg, 0.44 mmol). The mixture was stirred at room temperature for 3 h, and then neutralized with Amberlite IR120 H^+ resin. Filtration, concentration *in vacuo*, and purification by silica gel column chromatography (cyclohexane/EtOAc: 3/1) provided **5** (418 mg, 74%) as a colorless syrup: $[\alpha]^{20}_{D}$ = +21.7 (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.12 (m, 15 H, Ar), 5.12 (d-like, *J* = 13.2 Hz, 2 H), 4.53 (dd, *J* = 11.6, 16.4 Hz, 2 H), 4.41 (m, 3 H), 4.09 (m, 2 H), 3.92 (dd, *J* = 4.8, 8.8 Hz, 1 H), 3.85 (m, 1 H, H-4), 3.69 (s, 3 H, $C(O)OCH_3$), 3.42 (m, 1 H), 3.34 (m, 1 H, OCH_2), 3.20 (m, 3 H, OCH_2/NCH_2), 2.16 (dd, *J* = 4.8, 12.8 Hz, 1 H, H-3*e*), 1.93 (t, *J* = 12.8 Hz, 1 H, H-3*a*), 1.48 (m, 4 H, CCH_2C), 1.35 (s, 3 H, $C(CH_3)_2$), 1.32 (s, 3 H, $C(CH_3)_2$), 1.20 (m, 2 H, CCH_2C); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 137.9, 137.7, 128.5, 128.4, 127.9, 127.8, 127.7, 127.6, 127.3, 127.1, 109.2 (*C*$(CH_3)_2$), 98.9 (C-2), 73.5, 72.9, 72.7, 70.3, 67.1, 67.0, 64.1, 63.5, 52.5, 32.2 (C-3), 29.2, 26.9, 25.3, 23.4; HRMS (ESI) *m/z* calcd for $C_{39}H_{49}NO_{10}Na$ $[M+Na]^+$ 714.3254, found 714.3221.

2.8. Synthesis of methyl [*N*-benzyl-benzyloxycarbonyl-5-aminopentyl (2,7-di-*O*-acetyl-3-*O*-levulinoyl-4-*O*-*para*-bromobenzyl-6-*O*-benzyl-L-*glycero*-α-D-*manno*-

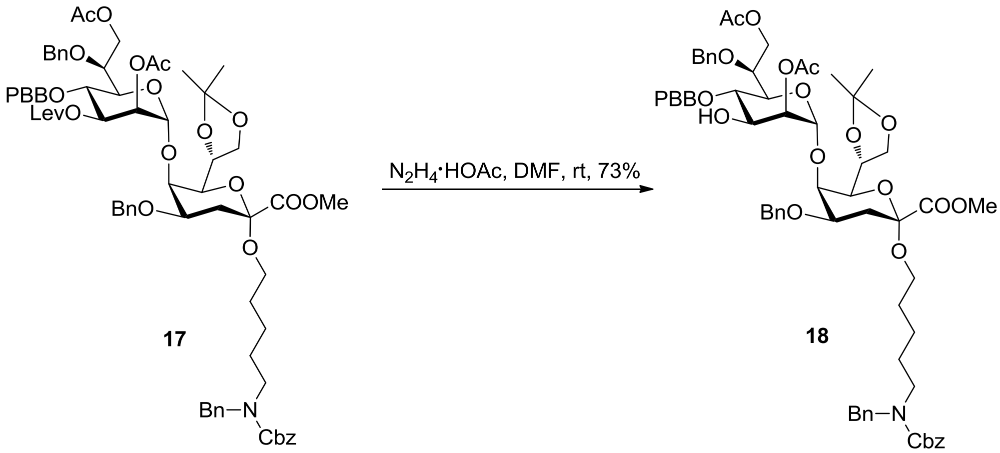
heptopyranosyl)-(1→5)-4-*O*-benzyl-7,8-*O*-isopropylidene-3-deoxy-α-D-*manno*-oct-2-ulopyranosid]onate 17



To a stirred mixture of the donor **4** (100 mg, 0.126 mmol), acceptor **5** (65 mg, 0.094 mmol), and freshly activated 4Å MS in dry CH_2Cl_2 (5.5 mL) at 0 °C, was added dropwise TMSOTf in CH_2Cl_2 (0.05 M, 138 μL) under nitrogen. After being stirred at 0 °C for 1 h, the mixture was quenched with Et_3N, filtered and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (cyclohexane/EtOAc: 2/1 to 3/2) to afford **17** (110 mg, 88%) as a colorless syrup: $[\alpha]^{20}_D$ = +35.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.05 (m, 24 H, Ar), 5.40 (dd, *J* = 3.2, 9.6 Hz, 1 H, H-3), 5.33 (dd, *J* = 2.0, 3.2 Hz, 1 H, H-2), 5.19 (d, *J* = 1.6 Hz, 1 H, H-1), 5.16 (m, 2 H), 4.76 (d-like, *J* = 12.0 Hz, 1 H), 4.64 (d-like, *J* = 11.6 Hz, 1 H), 4.50 (m, 3 H), 4.42 (m, 2 H), 4.33 (m, 2 H), 4.19 (m, 3 H), 4.09 (br s, 1 H), 4.01 (t, *J* = 9.6 Hz, 1 H), 3.92 (dd, *J* = 2.8, 12.4 Hz, 1 H), 3.86 (m, 1 H, H-4'), 3.77 (m, 1 H), 3.76 (s, 3 H, $C(O)OCH_3$), 3.65 (m, 1 H), 3.25 (m, 5 H), 2.67 (m, 2 H, $C(O)CH_2$), 2.43 (m, 2 H, $C(O)CH_2$), 2.30 (dd, *J* = 3.6, 12.4 Hz, 1 H, H-3'*e*), 2.15 (s, 3 H, $C(O)CH_3$), 2.11 (s, 3 H, $C(O)CH_3$), 2.00 (t, *J* = 12.0 Hz, 1 H, H-3'*a*), 1.95 (s, 3 H, $C(O)CH_3$), 1.49 (m, 4 H, CCH_2C), 1.25 (s, 3 H, $C(CH_3)_2$), 1.24 (s, 3 H, $C(CH_3)_2$), 1.23 (m, 2 H, CCH_2C); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.2, 171.5, 170.4, 170.0, 168.4, 138.5, 137.7, 137.5, 131.3, 128.9, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.2, 121.3, 109.6 (*C*($CH_3)_2$), 98.8 (C-2'), 97.4 (C-1, $J_{C,H}$ = 173.0 Hz), 77.2, 74.5, 74.4, 73.2, 73.0, 72.6, 72.3, 72.2, 72.1, 71.9, 71.7, 70.2, 70.0, 67.9, 67.1, 66.3, 63.5, 52.4, 37.8, 31.8 (C-3'), 29.8, 29.7, 29.3, 27.9, 26.8, 24.7, 23.4, 22.7, 21.0, 20.9; HRMS (ESI) *m/z* calcd for $C_{69}H_{82}BrNO_{20}Na$ $[M+Na]^+$ 1346.4511, found 1346.4506.

2.9. Synthesis of methyl [*N*-benzyl-benzyloxycarbonyl-5-aminopentyl (2,7-di-*O*-

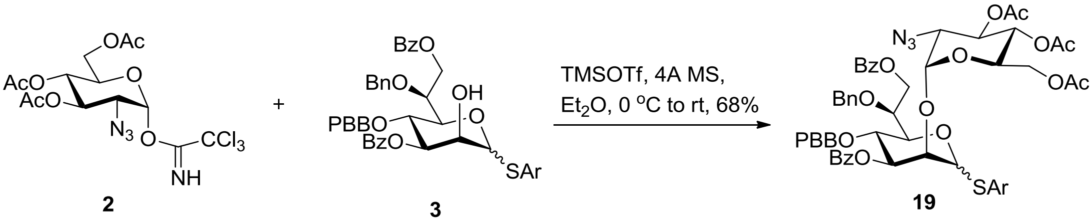
acetyl-4-*O*-*para*-bromobenzyl-6-*O*-benzyl-L-*glycero*-α-D-*manno*-heptopyranosyl)-(1→5)-4-*O*-benzyl-7,8-*O*-isopropylidene-3-deoxy-α-D-*manno*-oct-2-ulopyranosid]onate 18



To a solution of **17** (105 mg, 0.079 mmol) in DMF (3 mL) at room temperature, was added hydrazine acetate (30 mg, 0.324 mmol). After being stirred at room temperature for 40 min, the mixture was diluted with EtOAc, washed with saturated aqueous $NaHCO_3$, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/EtOAc: 1/1) to give **18** (71 mg, 73 %) as a colorless syrup: $[\alpha]^{20}_{D}$ = +28.6 (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.10 (m, 24 H, Ar), 5.26 (d, *J* = 1.2 Hz, 1 H, H-1), 5.20 (m, 3 H), 4.76 (d-like, *J* = 12.0 Hz, 2 H), 4.65 (d-like, *J* = 11.6 Hz, 1 H), 4.50 – 4.43 (m, 4 H), 4.38 – 4.20 (m, 6 H), 4.11 (m, 2 H), 3.95 (dd, *J* = 2.4, 12.0 Hz, 1 H), 3.83 (m, 2 H), 3.76 (s, 3 H, $C(O)OCH_3$), 3.68 (m, 1 H), 3.35 (m, 2 H), 3.25 (m, 3 H), 2.32 (dd, *J* = 4.0, 12.8 Hz, 1 H, H-3'*e*), 2.13 (s, 3 H, $C(O)CH_3$), 1.96 (s, 3 H, $C(O)CH_3$), 1.94 (t, *J* = 12.0 Hz, 1 H, H-3'*a*), 1.51 (m, 4 H, CCH_2C), 1.27 (s, 3 H, $C(CH_3)_2$), 1.26 (s, 3 H, $C(CH_3)_2$), 1.25 (m, 2 H, CCH_2C); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 170.6, 170.5, 168.5, 138.5, 137.9, 137.8, 137.7, 131.4, 131.2, 129.0, 128.6, 128.5, 128.4, 128.2, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.3, 127.1, 121.3, 109.6 ($C(CH_3)_2$), 98.8 (C-2'), 97.0 (C-1), 77.2, 75.7, 74.8, 74.5, 73.4, 72.7, 72.6, 72.2, 72.1, 71.6, 70.6, 70.2, 67.9, 67.1, 66.8, 63.6, 60.4, 52.5, 31.9 (C-3'), 29.2, 26.9, 24.8, 23.4, 21.1, 21.0; HRMS (ESI) *m/z* calcd for $C_{64}H_{76}BrNO_{18}Na$ $[M+Na]^+$ 1250.4123, found 1250.4144.

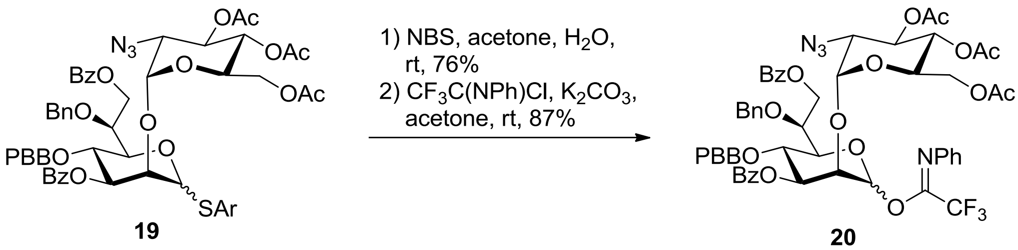
2.10. Synthesis of 5-*tert*-butyl-2-methylphenyl (3,4,6-tri-*O*-acetyl-2-azido-

2-deoxy-α-D-glucopyranosyl)-(1→2)-3,7-di-*O*-benzoyl-4-*O*-*para*-bromobenzyl-6-*O*-benzyl-1-thio-L-*glycero*-D-*manno*-heptopyranoside 19



To a stirred mixture of the donor **2**[4] (70 mg, 0.147 mmol), acceptor **3** (28 mg, 0.033 mmol), and freshly activated 4Å MS in dry Et_2O (3 mL) at 0 °C, was added dropwise TMSOTf in CH_2Cl_2 (0.05 M, 0.34 mL) under nitrogen. After 0.5 h, the temperature was allowed to warm up naturally to room temperature and the stirring continued for overnight. The mixture was then filtered and concentrated *in vacuo*. The residue was purified silica gel column chromatography (hexane/EtOAc: 7/1 to 6/1) provided **19** (26 mg, 68%) as a white solid: $[\alpha]^{20}_{D}$ = +78.61 (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 7.91 (m, 4 H, Ar), 7.58 – 7.21 (m, 14 H, Ar), 7.16 (dd, *J* = 2.0, 8.0 Hz, 1 H, Ar), 7.08 – 6.85 (m, 3 H, Ar), 5.83 (d, *J* = 2.0 Hz, 1 H, H-1'), 5.66 (dd, *J* = 9.2, 10.4 Hz, 1 H, H-3/H-4), 5.58 (m, 1 H, H-3'), 5.07 (dd, *J* = 9.2, 10.4 Hz, 1 H, H-3/H-4), 5.05 (d, *J* = 3.2 Hz, 1 H, H-1), 4.85 (d-like, *J* = 12.0 Hz, 1 H), 4.77 (dd, *J* = 5.6, 10.8 Hz, 1 H), 4.58 (m, 2 H), 4.55 (m, 1 H), 4.42 (m, 3 H), 4.32 (m, 2 H), 4.17 (t, *J* = 6.8 Hz, 1 H), 3.98 (m, 2 H), 3.41 (dd, *J* = 3.6, 10.4 Hz, 1 H, H-2), 2.36 (s, 3 H, $ArCH_3$), 2.13 (s, 3 H, $C(O)CH_3$), 1.95 (s, 3 H, $C(O)CH_3$), 1.85 (s, 3 H, $C(O)CH_3$), 1.28 (s, 9 H, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 169.8, 169.7, 166.0, 165.9, 150.0, 137.9, 136.9, 135.7, 133.4, 133.0, 132.6, 131.2, 130.2, 129.7, 129.6, 129.5, 129.3, 129.0, 128.7, 128.5, 128.3, 128.1, 127.9, 124.9, 121.3, 99.1 (C-1), 85.9 (C-1'), 73.3, 73.1, 72.6, 72.2, 71.7, 70.7, 70.5, 68.6, 68.4, 68.2, 62.6, 61.6, 61.2, 34.5, 31.3, 20.7, 20.5, 20.3, 20.2; HRMS (ESI) *m/z* calcd for $C_{58}H_{62}BrSN_3O_{15}Na$ $[M+Na]^+$ 1176.2962, found 1176.2992.

2.11. Synthesis of *N*-Phenyl Trifluoroacetimidate (3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→2)-3,7-di-*O*-benzoyl-4-*O*-*para*-bromobenzyl-6-*O*-benzyl-L-*glycero*-D-*manno*-heptopyranoside 20

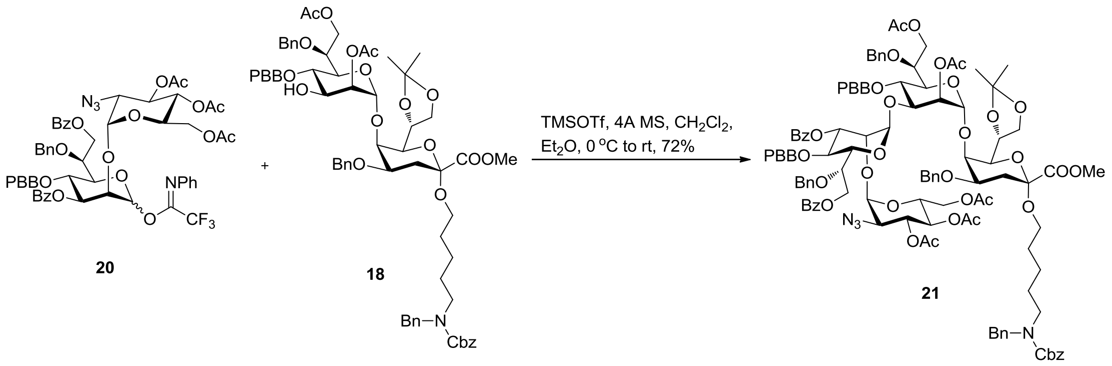


19 **20**

To a solution of compound **19** (83 mg, 0.072 mmol) in acetone/H_2O (10/1, v/v, 2.2 mL), was added NBS (38 mg, 0.22 mmol). After being stirred at room tempearature for 1 h, the mixture was diluted with EtOAc, washed with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/ EtOAc: 2/1) to afford the corresponding hemiacetal (54 mg, 76%) as a colorless syrup. To a solution of the above hemiacetal (69 mg, 0.070 mmol) and K_2CO_3 (27 mg, 0.195 mmol) in acetone (1.5 mL), was added 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride[5] (100 mg, 0.482 mmol). After being stirred at room temperature for 30 min, the solution was filtered and concentrated *in vacuo* to a residue, which was purified by silica gel column chromatography (hexane/EtOAc: 3/1) to afford **20** (70 mg, 87%) as a colorless syrup: $[\alpha]^{20}_D$ = +47.32 (*c* 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 – 8.01 (m, 4 H, Ar), 7.61 – 7.09 (m, 18 H, Ar), 6.86 – 6.81 (m, 4 H, Ar), 5.62 (dd, *J* = 9.2, 10.4 Hz, 1 H), 5.59 (dd, *J* = 2.8, 9.2 Hz, 1 H), 5.05 (dd, *J* = 9.6, 10.4 Hz, 1 H), 4.85 (d-like, *J* = 12.0 Hz, 1 H, OCH_2Ar), 4.77 (dd, *J* = 5.2, 10.8 Hz, 1 H), 4.60 (d-like, *J* = 12.4 Hz, 1 H, OCH_2Ar), 4.49 – 4.40 (m, 5 H), 4.27 (dd, *J* = 4.0, 12.4 Hz, 1 H), 4.15 (t, *J* = 6.4 Hz, 1 H), 4.08 (d-like, *J* = 9.6 Hz, 1 H), 3.99 (d-like, *J* = 12.4 Hz, 1 H), 3.40 (dd, *J* = 4.0, 10.8 Hz, 1 H, H-2), 2.12 (s, 3 H, C(O)CH_3), 2.01 (s, 3 H, C(O)CH_3), 1.95 (s, 3 H, C(O)CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 169.8, 169.7, 166.2, 165.9, 143.2, 137.8, 136.7, 133.6, 133.3, 131.4, 129.8, 129.7, 129.6, 129.3, 129.2, 128.9, 128.8, 128.6, 128.5, 128.2, 128.1, 124.6, 121.6, 119.4, 99.3 (C-1), 77.3, 73.6, 73.5, 72.7, 72.5, 72.2, 70.4, 68.5, 68.2, 62.3, 61.5, 61.1, 20.8, 20.7, 20.6; HRMS (ESI) *m/z* calcd for $C_{55}H_{52}BrF_3N_4O_{16}Na$ $[M+Na]^+$ 1185.2400, found 1185.2423.

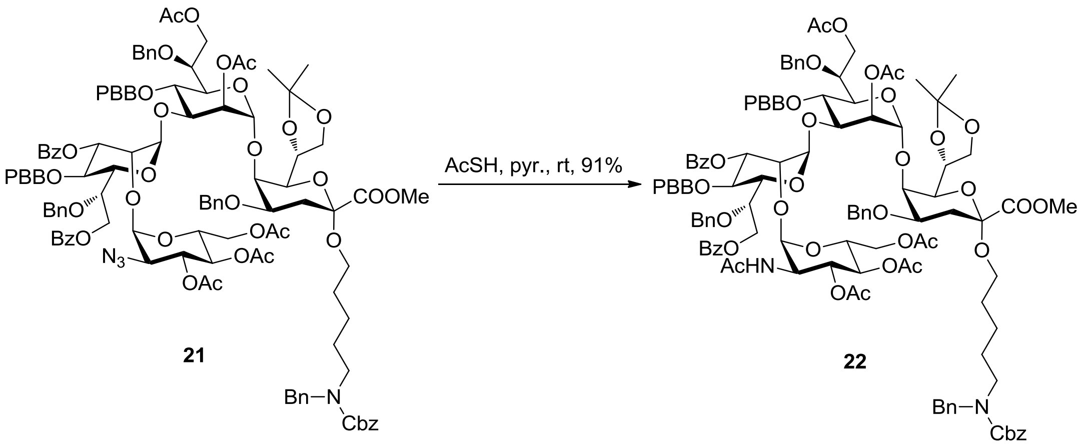
2.12. Synthesis of methyl [*N*-benzyl-benzyloxycarbonyl-5-aminopentyl (3,4,6-tri -*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→2)-(3,7-di-*O*-benzoyl-4-*O*-*para*-bromobenzyl-6-*O*-benzyl-1-thio-L-*glycero*-α-D-*manno*-heptopyranosyl)-

(1→3)-(2,7-di-*O*-acetyl-4-*O*-*para*-bromobenzyl-6-*O*-benzyl-L-*glycero*-α-D-*manno*-heptopyranosyl)-(1→5)-4-*O*-benzyl-7,8-*O*-isopropylidene-3-deoxy-α-D-*manno*-oct-2-ulopyranosid]onate 21



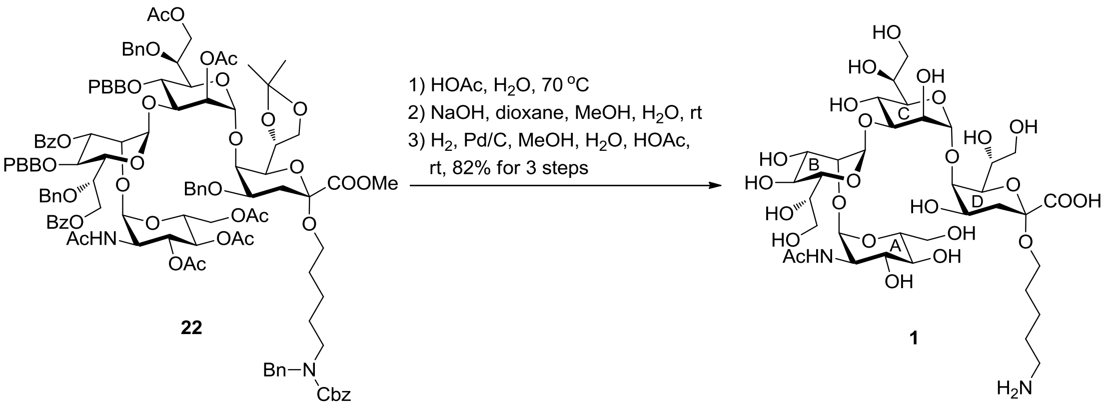
To a stirred mixture of the disaccharide donor **20** (49 mg, 42 μmol), disaccharide acceptor **18** (38 mg, 31 μmol), and freshly activated 4Å MS in dry diethyl ether and dichloromethane (1/1, v/v, 3.6 mL) at 0 °C, was added TMSOTf in CH_2Cl_2 (0.05 M, 90 μL) under nitrogen. The temperature was allowed to warm up naturally to room temperature and the stirring continued for 1 h. The mixture was quenched with Et_3N, and filtered. The filtrate was concentrated *in vacuo* to give a residue, which was purified by silica gel column chromatography (hexane/EtOAc/TEA: 5/2/0.07) to afford **21** (49 mg, 72%) as a white solid: $[\alpha]^{20}_{D}$ = +19.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, Pyridine-d_5) δ 8.49 – 8.33 (m, 4 H, Ar), 7.85 (m, 2 H, Ar), 7.66 – 7.31 (m, 33 H, Ar), 7.16 (d, *J* = 7.8 Hz, 2 H, Ar), 6.96 (d, *J* = 7.8 Hz, 2 H, Ar), 6.11 (dd, *J* = 2.4, 9.0 Hz, 1 H), 6.04 (m, 1 H), 6.02 (br s, 1 H, H-1"), 5.84 (br s, 1 H, H-1), 5.50 (t, *J* = 9.6 Hz, 1 H), 5.45 – 5.37 (m, 3 H), 5.20 (m, 2 H), 5.02 (m, 4 H), 4.93 – 4.83 (m, 7 H), 4.77 (d-like, *J* = 11.4 Hz, 2 H), 4.73 – 4.62 (m, 6 H), 4.56 (m, 3 H), 4.48 (m, 1 H), 4.43 (m, 2 H), 4.28 (d-like, *J* = 11.4 Hz, 1 H), 4.18 (m, 2 H), 4.07 – 4.01 (m, 3 H), 3.91 (m, 1 H), 3.89 (s, 3 H, $C(O)OCH_3$), 3.76 (m, 1 H), 3.42 (m, 3 H), 3.29 (m, 1 H), 2.62 (d-like, *J* = 9.6 Hz, 1 H, H-3'''*e*), 2.32 (t, *J* = 12.0 Hz, 1 H, H-3'''*a*), 2.27 (s, 3 H, $C(O)CH_3$), 2.16 (s, 3 H, $C(O)CH_3$), 2.15 (s, 3 H, $C(O)CH_3$), 2.01 (s, 3 H, $C(O)CH_3$), 1.99 (s, 3 H, $C(O)CH_3$), 1.55 (m, 4 H, CCH_2C), 1.41 (s, 3 H, $C(CH_3)_2$), 1.35 (s, 3 H, $C(CH_3)_2$), 1.26 (m, 2 H, CCH_2C); ^{13}C NMR (150 MHz, Pyridine-d_5) δ 171.1, 171.0, 170.9, 170.7, 170.4, 169.1, 167.2, 166.7, 150.7, 140.2, 139.4, 139.3, 139.0, 138.9, 138.5, 138.3, 136.3, 134.1, 134.0, 132.3, 131.8, 131.2, 130.9, 130.8, 130.5, 130.3, 129.7, 129.6, 129.5, 129.4, 129.3, 129.2, 129.1, 128.7, 128.6, 128.2, 128.0, 124.3, 123.6, 122.1, 121.7, 110.4 (*C*$(CH_3)_2$), 101.1 (C-1"), 99.8 (C-2'''), 98.1 (C-1), 76.7, 76.1, 75.3, 75.0, 74.5, 73.7, 73.5, 73.2, 73.1, 72.5, 72.3, 71.6, 70.9, 69.5, 69.4, 68.5, 67.7, 67.6, 67.3, 64.4, 62.7, 62.3, 54.7, 53.0, 51.2, 50.8, 47.9, 47.0, 30.5 (C-3'''), 30.0, 27.4, 25.6, 24.1, 23.4, 21.5, 21.3, 21.1, 21.0, 20.9; HRMS (ESI) *m/z* calcd for $C_{111}H_{122}Br_2N_4O_{33}Na$ $[M+Na]^+$ 2222.6275, found 2222.6349.

2.13. Synthesis of methyl [*N*-benzyl-benzyloxycarbonyl-5-aminopentyl (3,4,6-tri-*O*-acetyl-2-*N*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→2)-(3,7-di-*O*-benzoyl-4-*O*-*para*-bromobenzyl-6-*O*-benzyl-L-*glycero*-α-D-*manno*-heptopyranosyl)-(1→3)-(2,7-di-*O*-acetyl-4-*O*-*para*-bromobenzyl-6-*O*-benzyl-L-*glycero*-α-D-*manno*-heptopyranosyl)-(1→5)-4-*O*-benzyl-7,8-*O*-isopropylidene-3-deoxy-α-D-*manno*-oct-2-ulopyranosid]onate 22



To a solution of compound **21** (37 mg, 0.017 mmol) in dry pyridine (0.3 mL), was added thioacetic acid (0.3 mL, 4.18 mmol). After being stirred at room temperature for 24 h, the solution was coevaporated with toluene to give a residue, which was purified by silica gel column chromatography (hexane/EtOAc/TEA: 3/2/0.05 to 1/1/0.02) to give **22** (34 mg, 91%) as a pale yellow solid: $[\alpha]^{20}_D$ = +26.1 (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, Pyridine-d_5) δ 8.51 – 8.19 (m, 4 H, Ar), 7.79 – 7.18 (m, 37 H, Ar), 6.99 (d, *J* = 8.4 Hz, 2 H, Ar), 6.12 (m, 2 H, H-1"), 6.04 (br s, 1 H), 5.88 (m, 1 H), 5.83 (br s, 1 H, H-1), 5.56 (t, *J* = 10.0 Hz, 1 H), 5.39 (m, 4 H), 5.24 (d-like, *J* = 12.0 Hz, 1 H), 5.05 – 4.89 (m, 9 H), 4.86 – 4.68 (m, 8 H), 4.64 – 4.54 (m, 6 H), 4.39 (m, 2 H), 4.17 (m, 2 H), 4.07 (m, 2 H), 4.00 (m, 2 H), 3.93 (s, 3 H, $C(O)OCH_3$), 3.75 (d-like, *J* = 8.8 Hz, 1 H), 3.46 (m, 3 H), 3.29 (m, 1 H), 2.63 (m, 1 H, H-3'''*e*), 2.28 (s, 3 H, $C(O)CH_3$), 2.25 (m, 1 H, H-3'''*a*), 2.23 (s, 3 H, $C(O)CH_3$), 2.02 (s, 3 H, $C(O)CH_3$), 1.98 (s, 3 H, $C(O)CH_3$), 1.97 (s, 6 H, $C(O)CH_3$), 1.55 (m, 4 H, CCH_2C), 1.41 (s, 3 H, $C(CH_3)_2$), 1.34 (s, 3 H, $C(CH_3)_2$), 1.25 (m, 2 H, CCH_2C); ^{13}C NMR (100 MHz, Pyridine-d_5) δ 171.6, 171.1, 171.0, 170.4, 170.3, 169.0, 167.3, 166.2, 140.2, 139.5, 139.4, 138.9, 138.6, 138.3, 134.4, 134.0, 132.4, 131.9, 131.2, 130.8, 130.5, 130.4, 130.2, 129.7, 129.6, 129.5, 129.4, 129.3, 129.2, 128.7, 128.6, 128.3, 128.1, 128.0, 122.2, 110.4 (*C*($CH_3)_2$), 100.6 (C-1'), 99.8 (C-2'''), 98.2 (C-1), 76.0, 75.3, 74.8, 73.7, 73.5, 73.1, 72.5, 72.0, 70.9, 69.7, 68.5, 67.7, 67.2, 64.4, 62.9, 60.7, 53.5, 53.0, 51.2, 50.8, 48.0, 47.1, 30.5 (C-3'''), 30.0, 27.4, 25.7, 24.1, 22.8, 21.6, 21.4, 21.3, 21.2, 21.1, 20.9; HRMS (ESI) *m/z* calcd for $C_{113}H_{126}Br_2N_2O_{34}Na$ $[M+Na]^+$ 2238.6476, found 2238.6545.

2.14. Synthesis of 2-*N*-acetyl-2-deoxy-α-D-glucopyranosyl-(1→2)-L-*glycero*-α-D-*manno*-heptopyranosyl-(1→3)-L-*glycero*-α-D-*manno*-heptopyranosyl-(1→5)-2-(5-amino)pentyl-3-deoxy-α-D-*manno*-oct-2-ulopyranosidonic acid 1



A solution of compound **22** (35 mg, 0.016 mmol) in acetic acid/water (8/1, v/v, 1.80 mL) was stirred at 70 °C for overnight. TLC indicated complete conversion of starting material. The mixture was covaporated with toluene and dried *in vacuo* to give the corresponding diol as a pale yellow syrup. The above diol was dissolved in a mixture of dioxane, methanol and 1 M aq NaOH (3/1/1, v/v/v, 1.25 mL). After being stirred at room temperature for overnight, the reaction mixture was diluted with methanol and neutralized with Amberlite IR120 H^+ resin. After filtration, the filtrate was concentrated *in vacuo* to give the corresponding tetrasaccharide as a white solid. A mixture of the above tetrasaccharide and Pd/C (70 mg, 10%) in methanol, water and acetic acid (50/25/1, v/v/v, 3.04 mL) was stirred under an atmosphere of H_2 at room temperature for 24 h. Filtration, concentration *in vacuo* and elution through Sephadex LH-20 column (H_2O) provided **1** (12 mg, 82% for 3 steps) as a white solid:

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$[\alpha]^{20}_{D}$ = +64.2 (*c* 0.3, H_2O); ^{1}H NMR (600 MHz, D_2O) δ 5.42 (br s, 1 H, H-1' of B ring), 5.12 (d, *J* = 3.6 Hz, 1 H, H-1 of A ring), 5.09 (d, *J* = 1.2 Hz, 1 H, H-1" of C ring), 4.16 (m, 2 H, H-4'''), 4.09 (m, 2 H), 4.06 – 4.01 (m, 4 H), 3.98 (m, 3 H), 3.95 (dd, *J* = 3.0, 12.0 Hz, 1 H), 3.91 (dd, *J* = 3.6, 10.8 Hz, 1 H), 3.85 – 3.76 (m, 6 H), 3.73 – 3.63 (m, 6 H), 3.49 (t, *J* = 9.6 Hz, 1 H), 3.44 (m, 1 H, OCH_2), 3.30 (m, 1 H, OCH_2), 3.01 (t, *J* = 7.8 Hz, 2 H, NCH_2), 2.10 (dd, *J* = 4.8, 12.6 Hz, 1 H, H-3'''*e*), 2.07 (s, 3 H, $C(O)CH_3$), 1.84 (t, *J* = 12.6 Hz, 1 H, H-3'''*a*), 1.69 (m, 2 H, CCH_2C), 1.62 (m, 2 H, CCH_2C), 1.44 (m, 2 H, CCH_2C); ^{13}C NMR (150 MHz, D_2O) δ 175.0, 174.4, 101.3 (C-1" of C ring, $J_{C,H}$ = 169.7 Hz), 100.3 (C-1' of B ring, $J_{C,H}$ = 172.1 Hz), 99.7 (C-2''' of D ring), 99.2 (C-1 of A ring, $J_{C,H}$ = 171.6 Hz), 78.6, 76.7, 75.0, 72.2, 71.9, 71.6, 71.3, 70.6, 70.4, 70.1, 69.9, 69.2, 68.7, 68.5, 66.3, 65.9, 65.6, 63.3, 63.2, 62.9, 60.4, 53.9, 39.3(NCH_2),, 34.8 (C-3'''), 28.1, 26.4, 22.4, 21.9; HRMS (ESI) *m/z* calcd for $C_{35}H_{61}N_2O_{25}$ $[M–H]^-$ 909.3563, found 909.3629.

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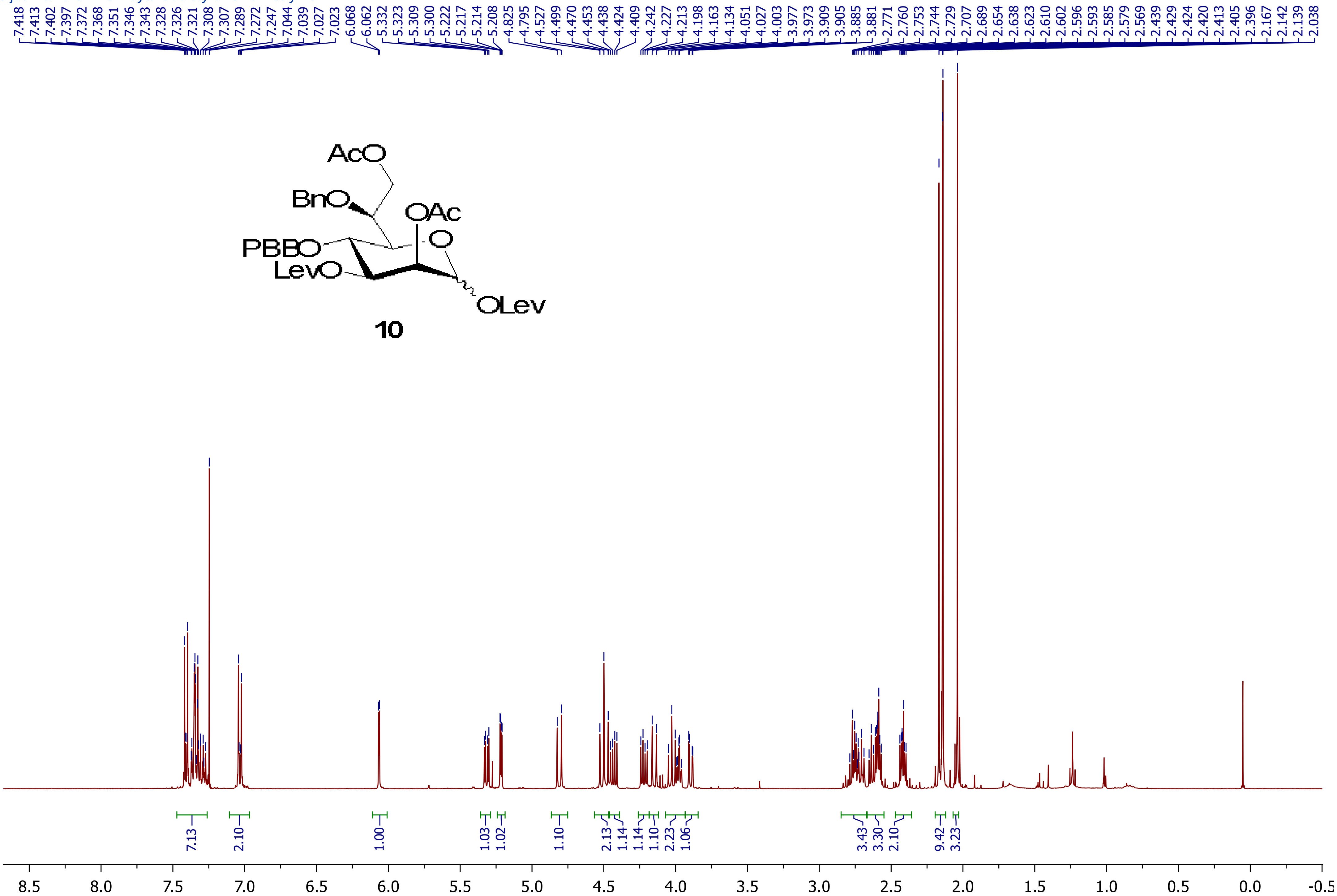
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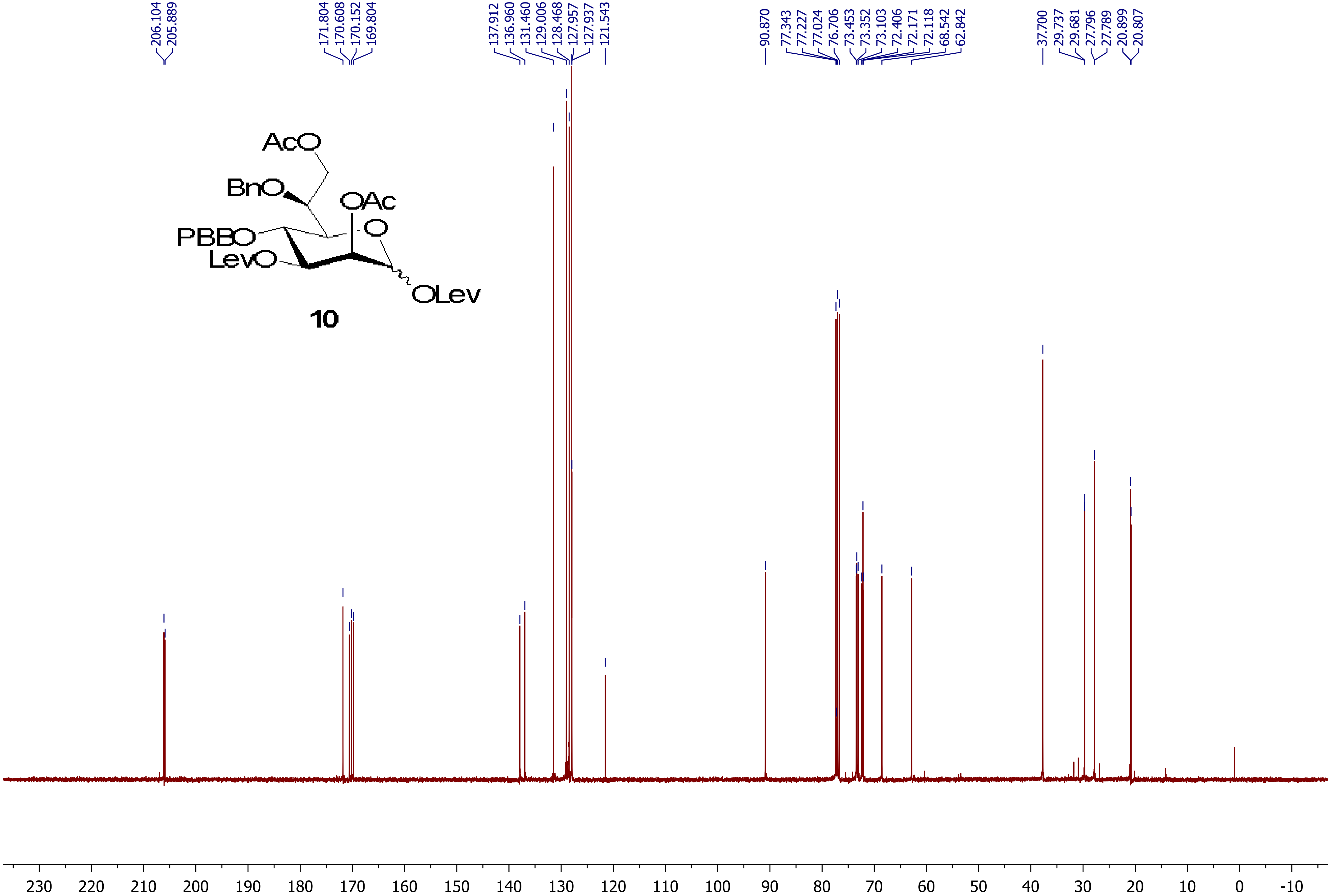
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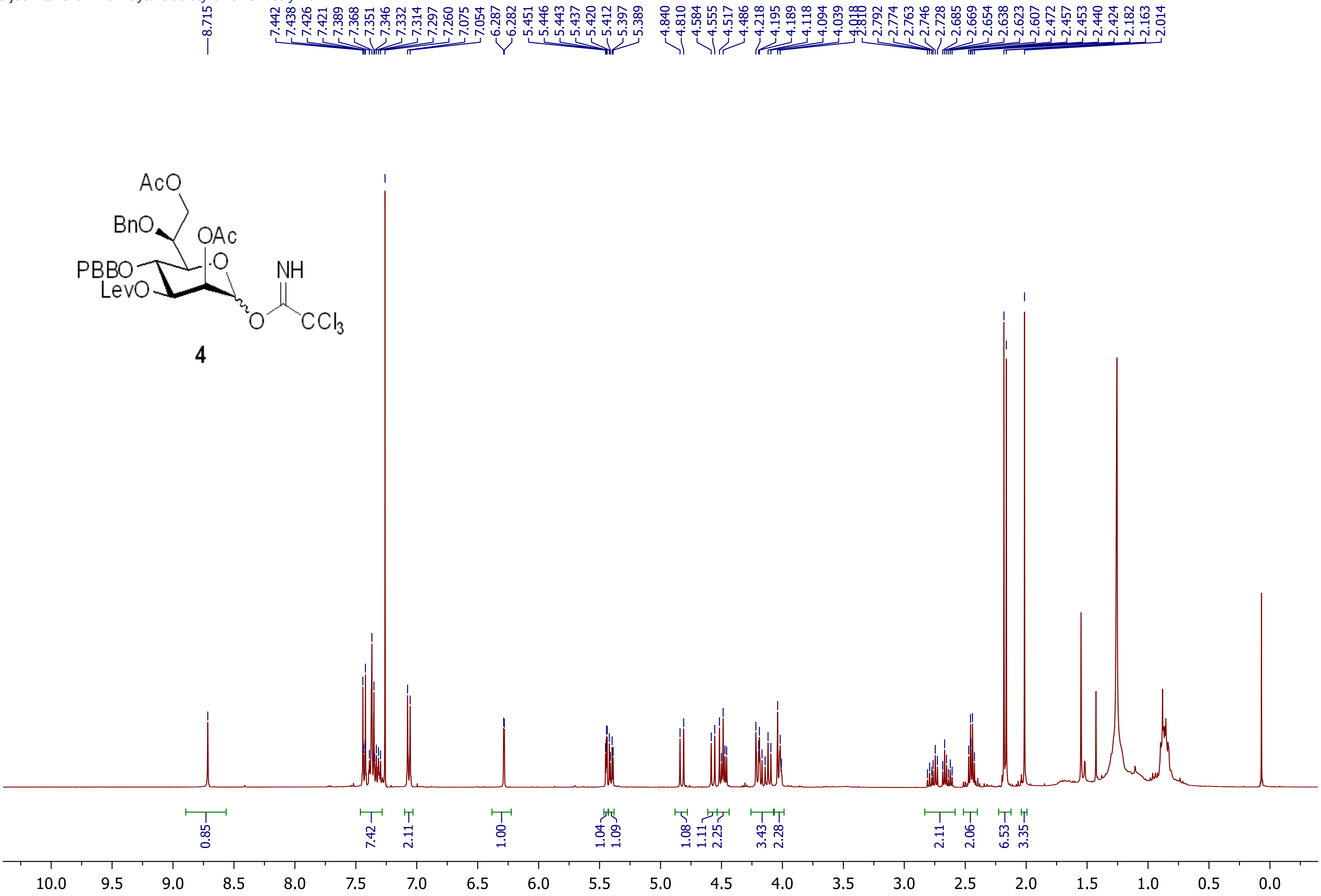
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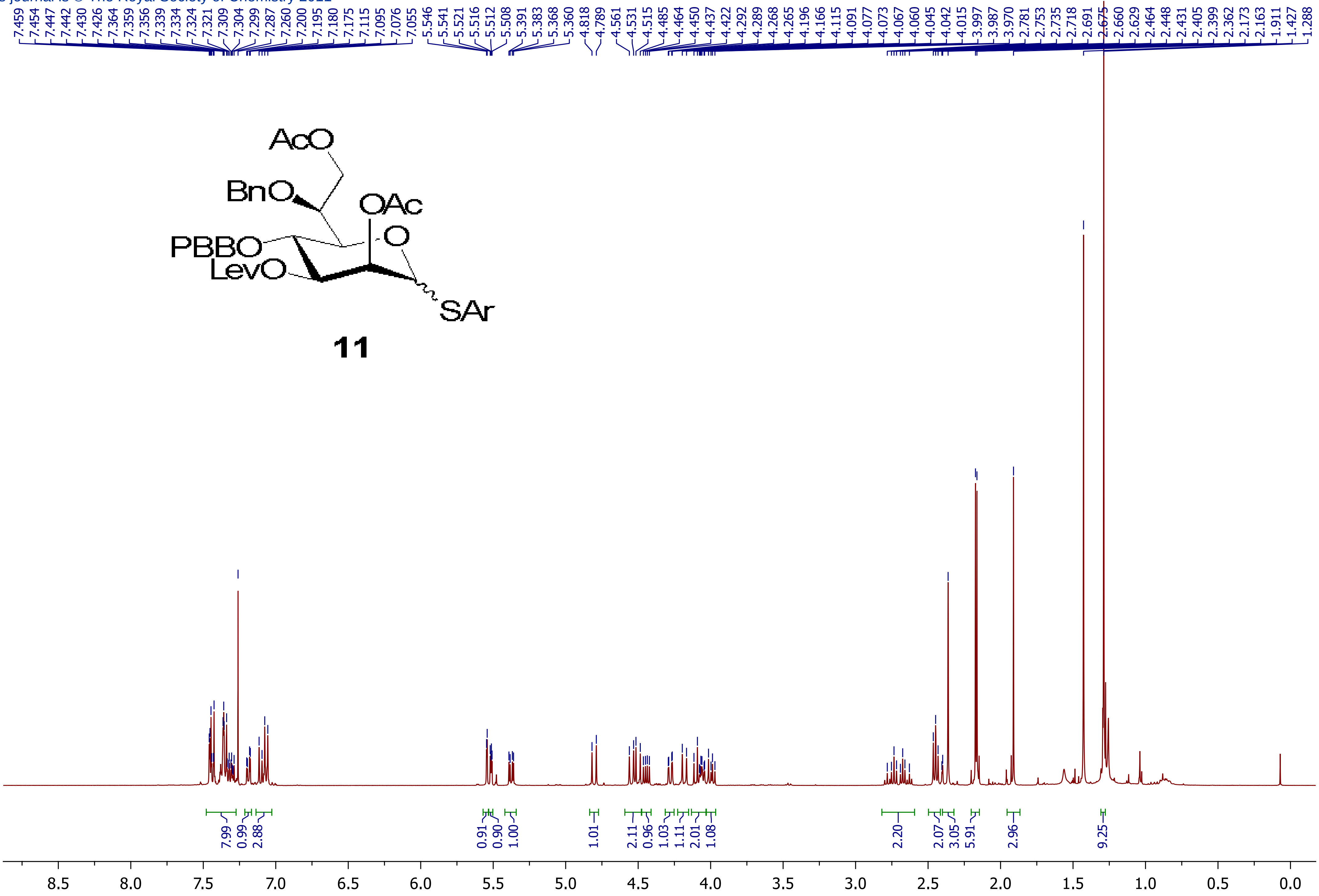
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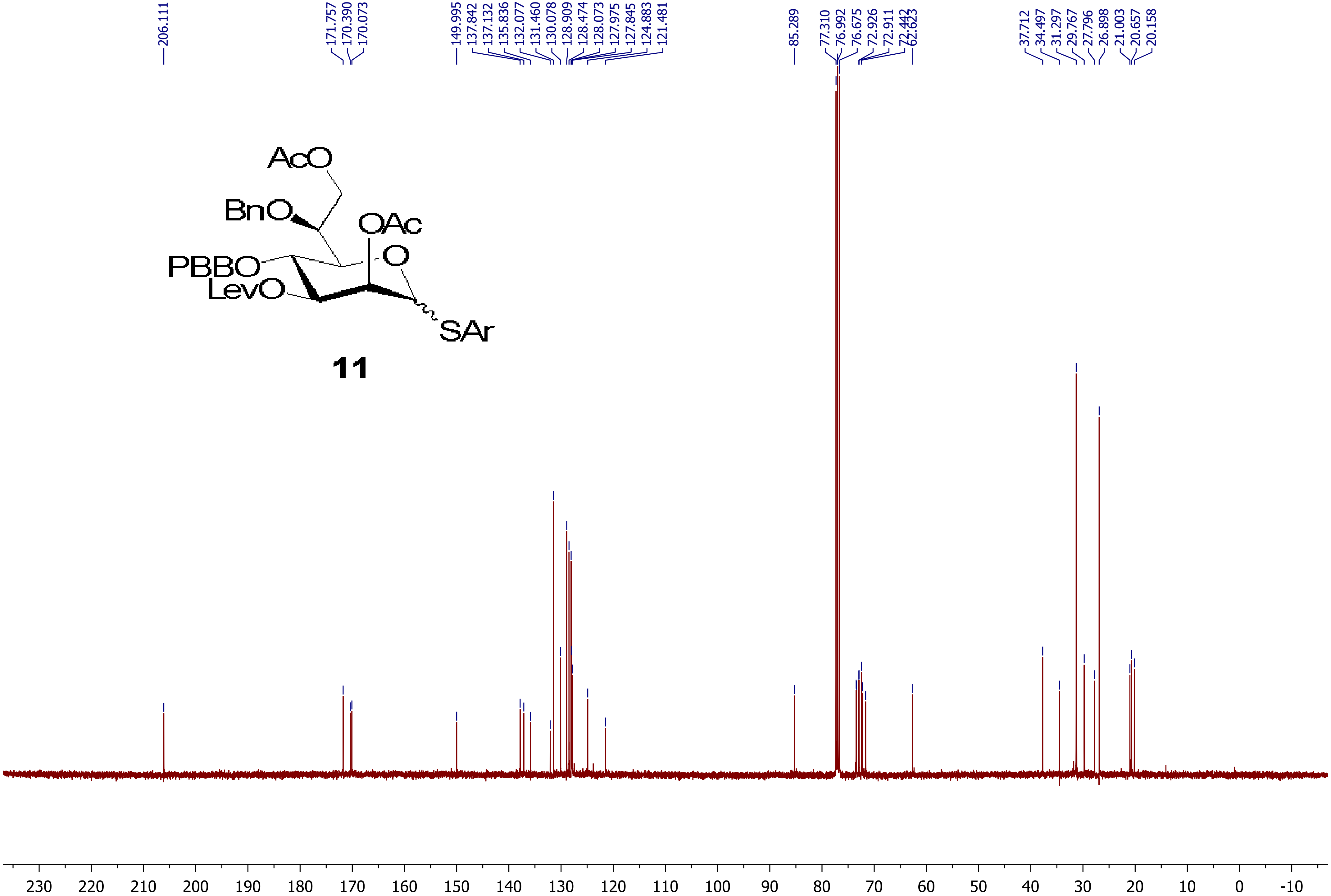
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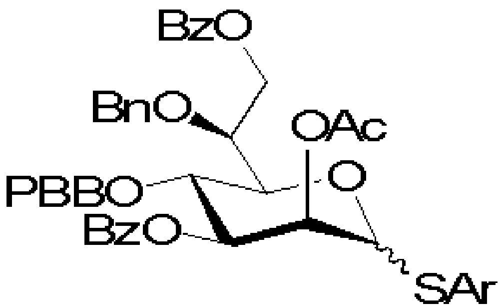
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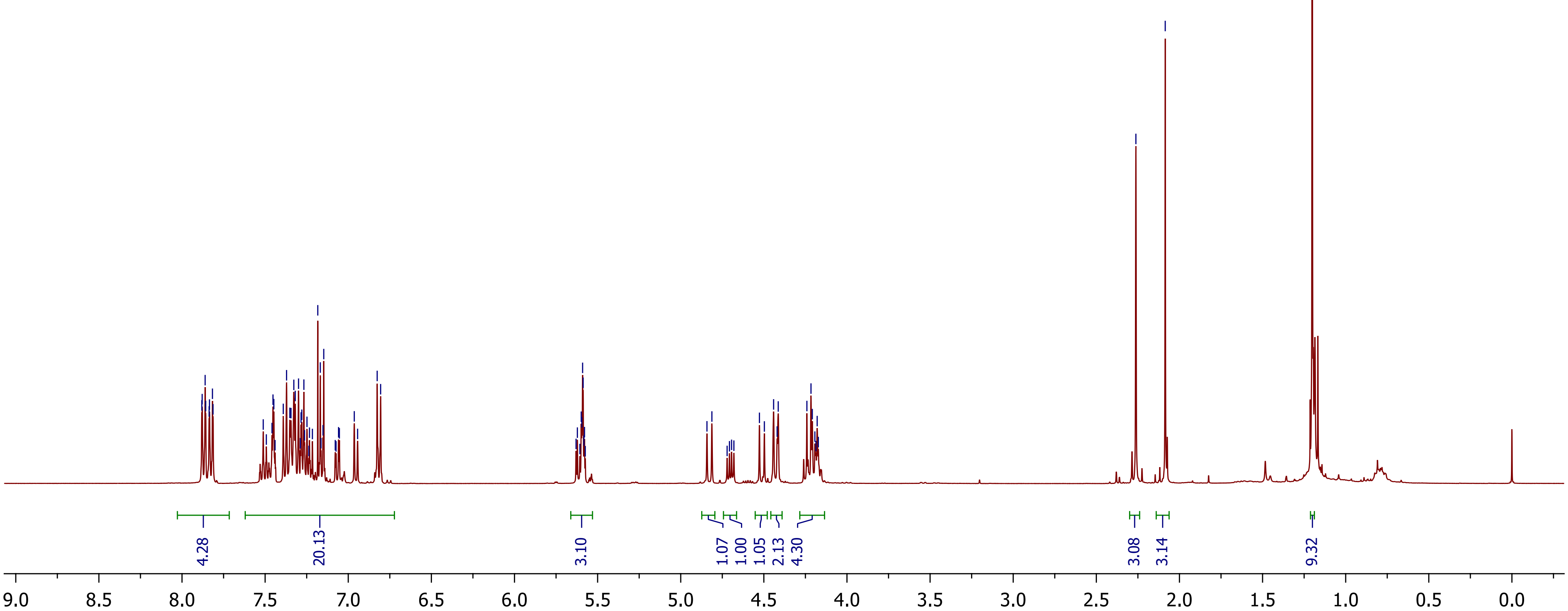
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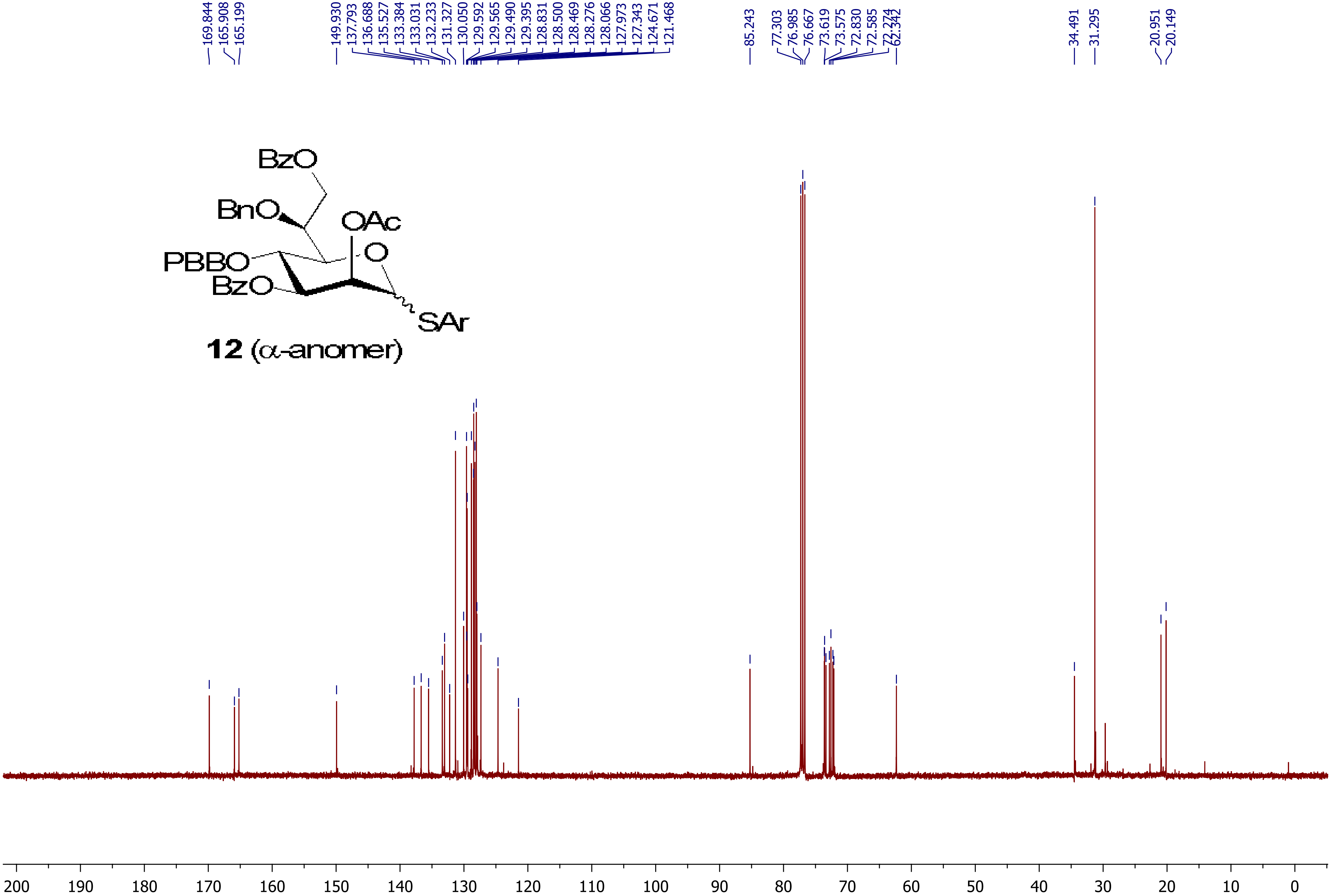
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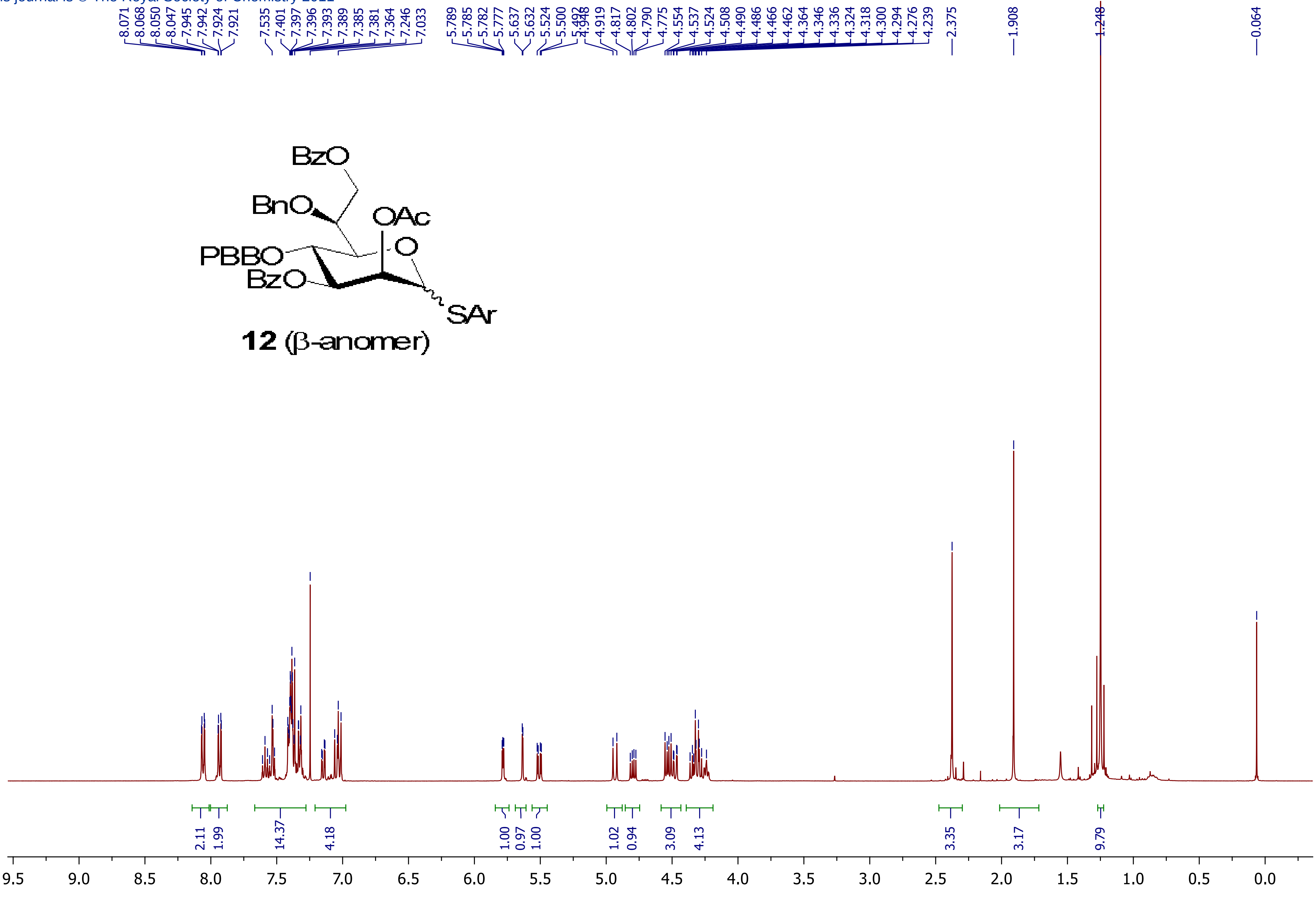
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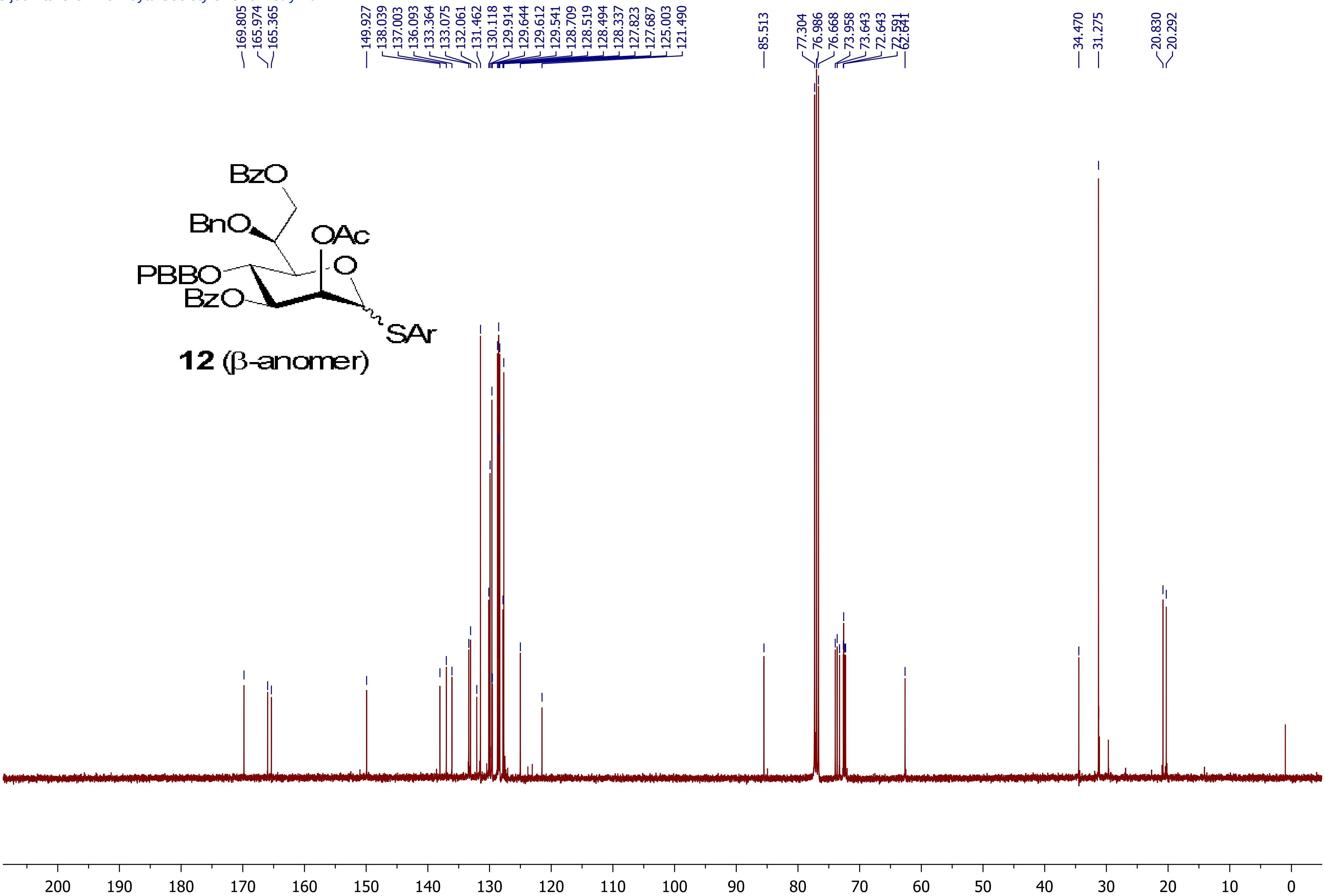

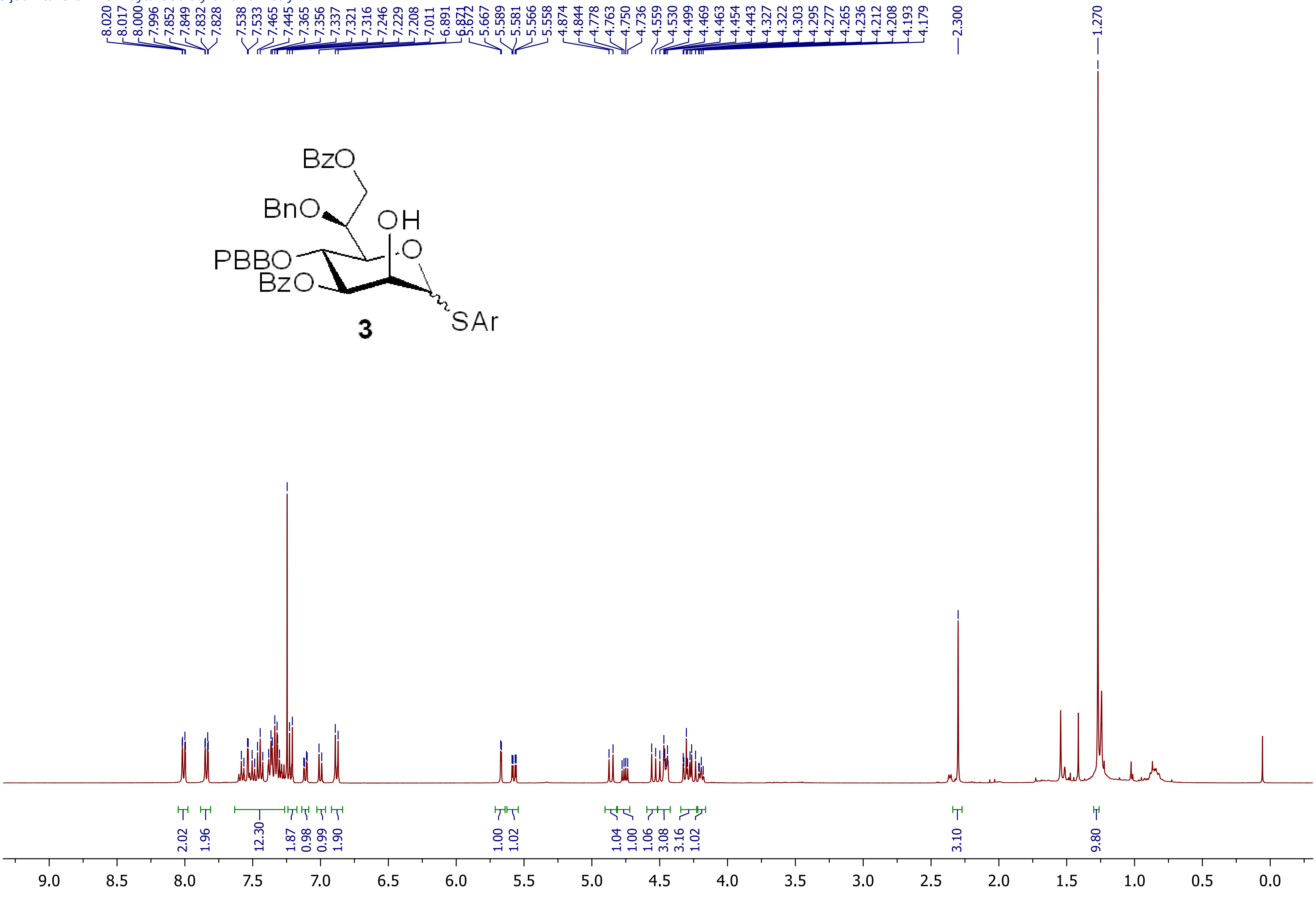
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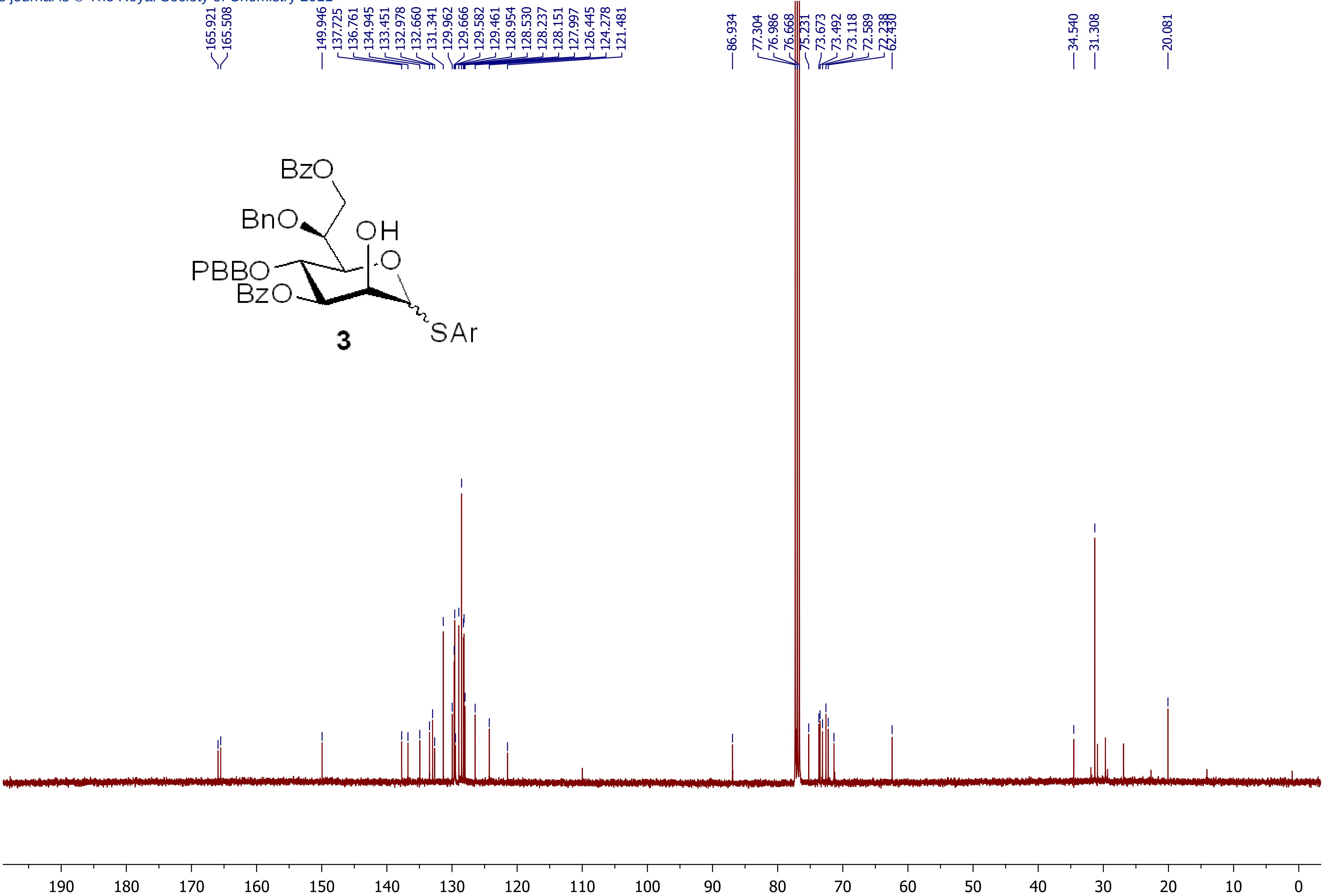

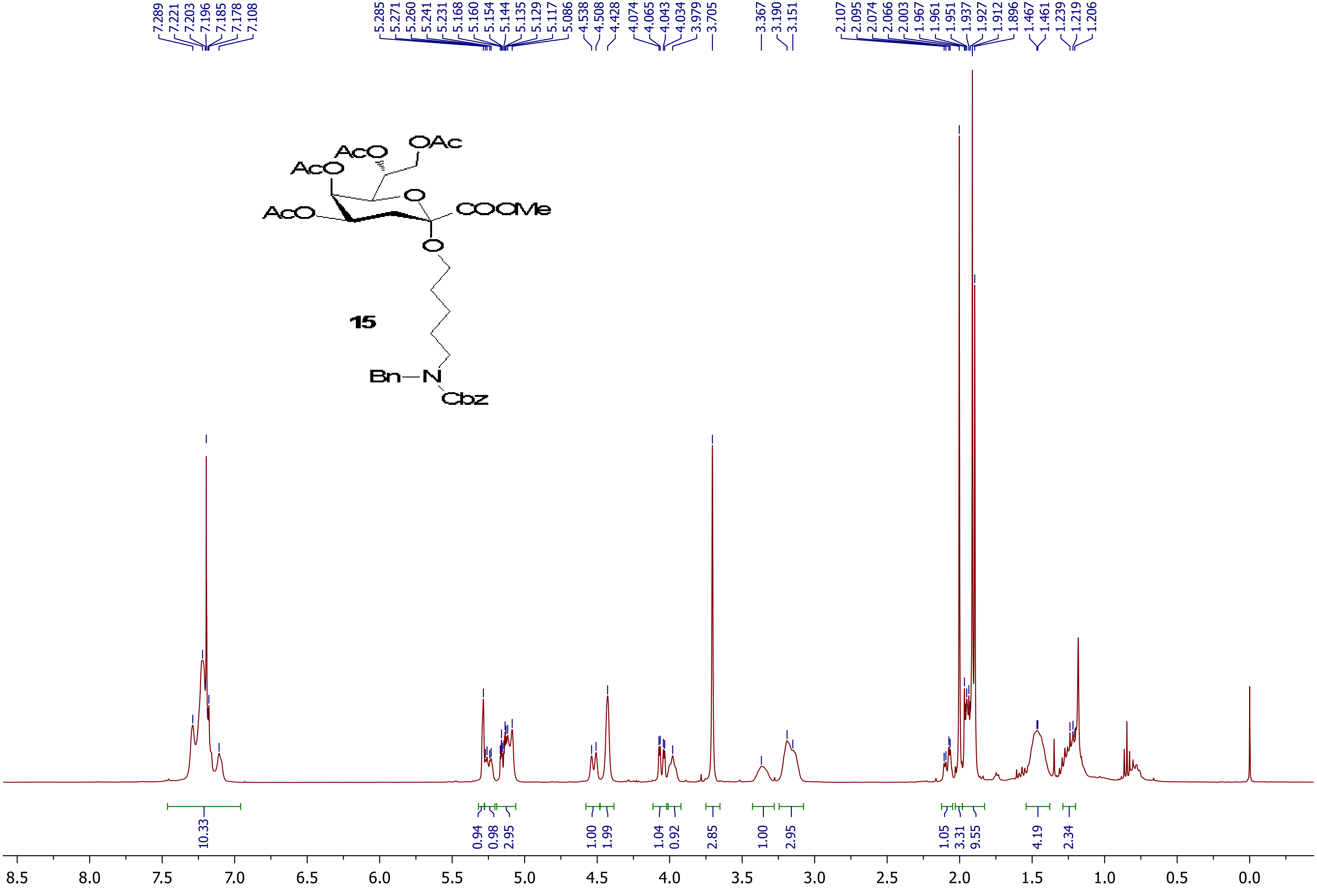
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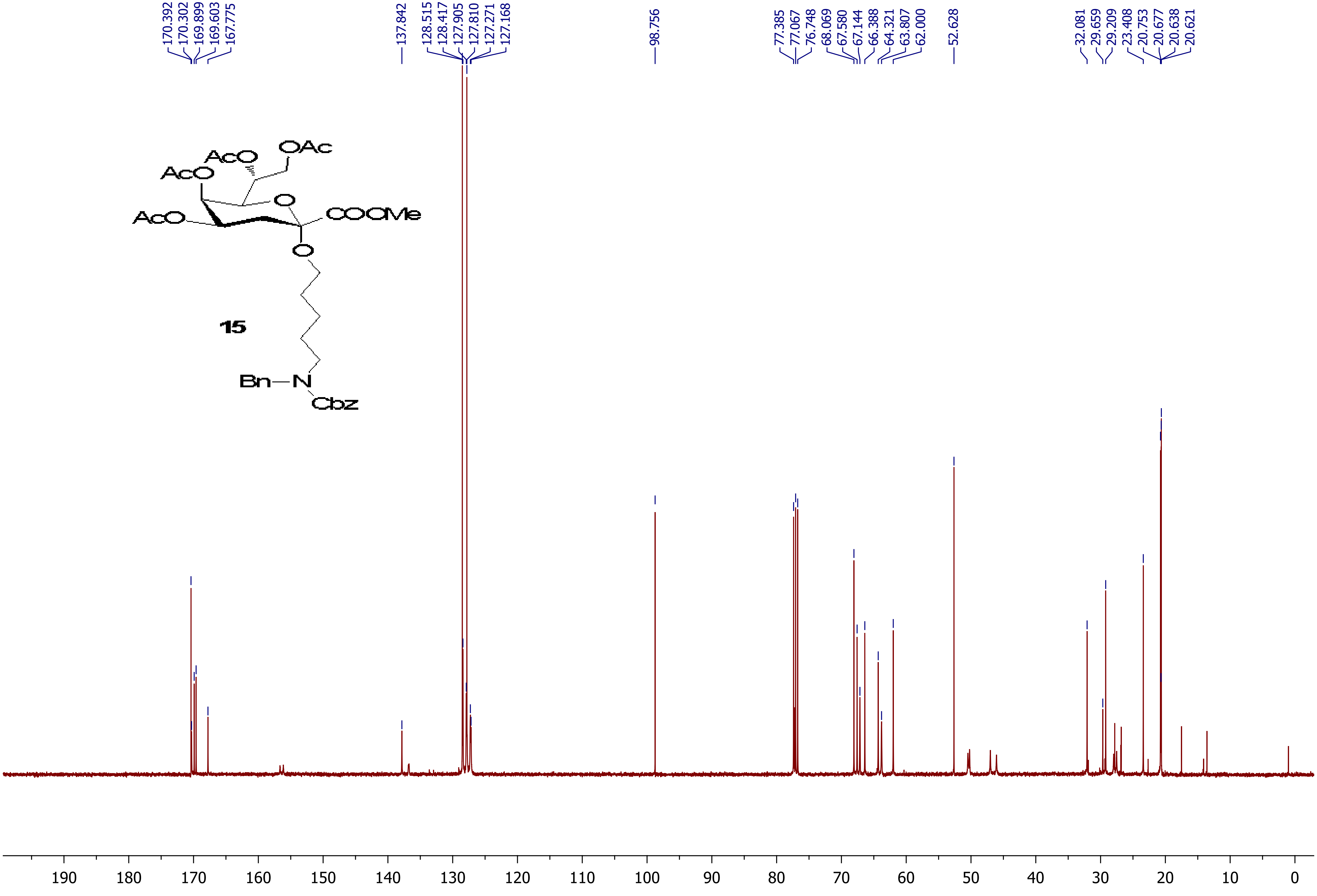
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AcO
OAc
O
COOMe
O
Bn—N
Cbz
15
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169.603
167.775
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128.417
127.905
127.810
127.271
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77.385
77.067
76.748
68.069
67.580
67.144
66.388
64.321
63.807
62.000
52.628
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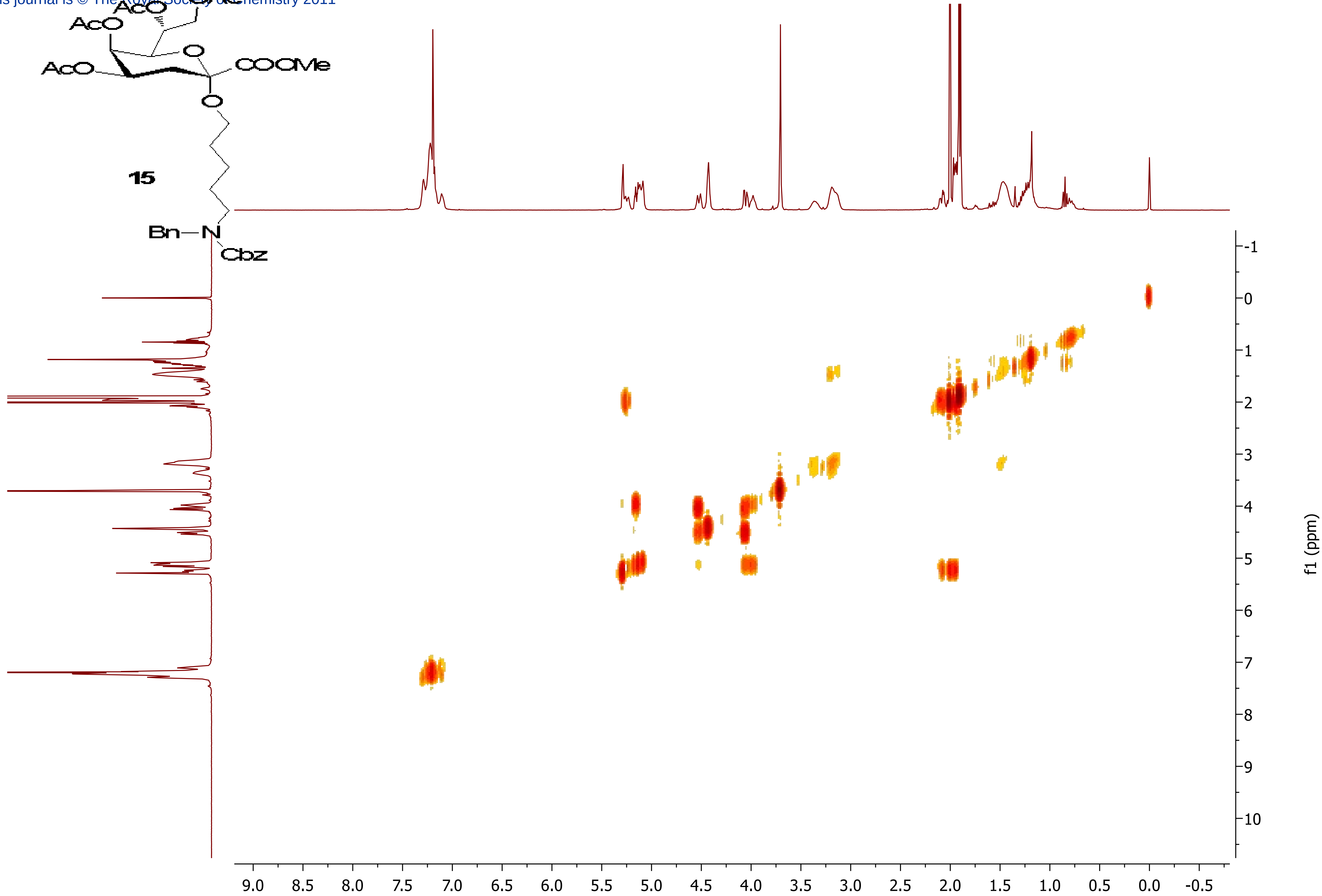
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AcO
O
COOMe
O
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Bn—N
Cbz
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
0
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2
3
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9
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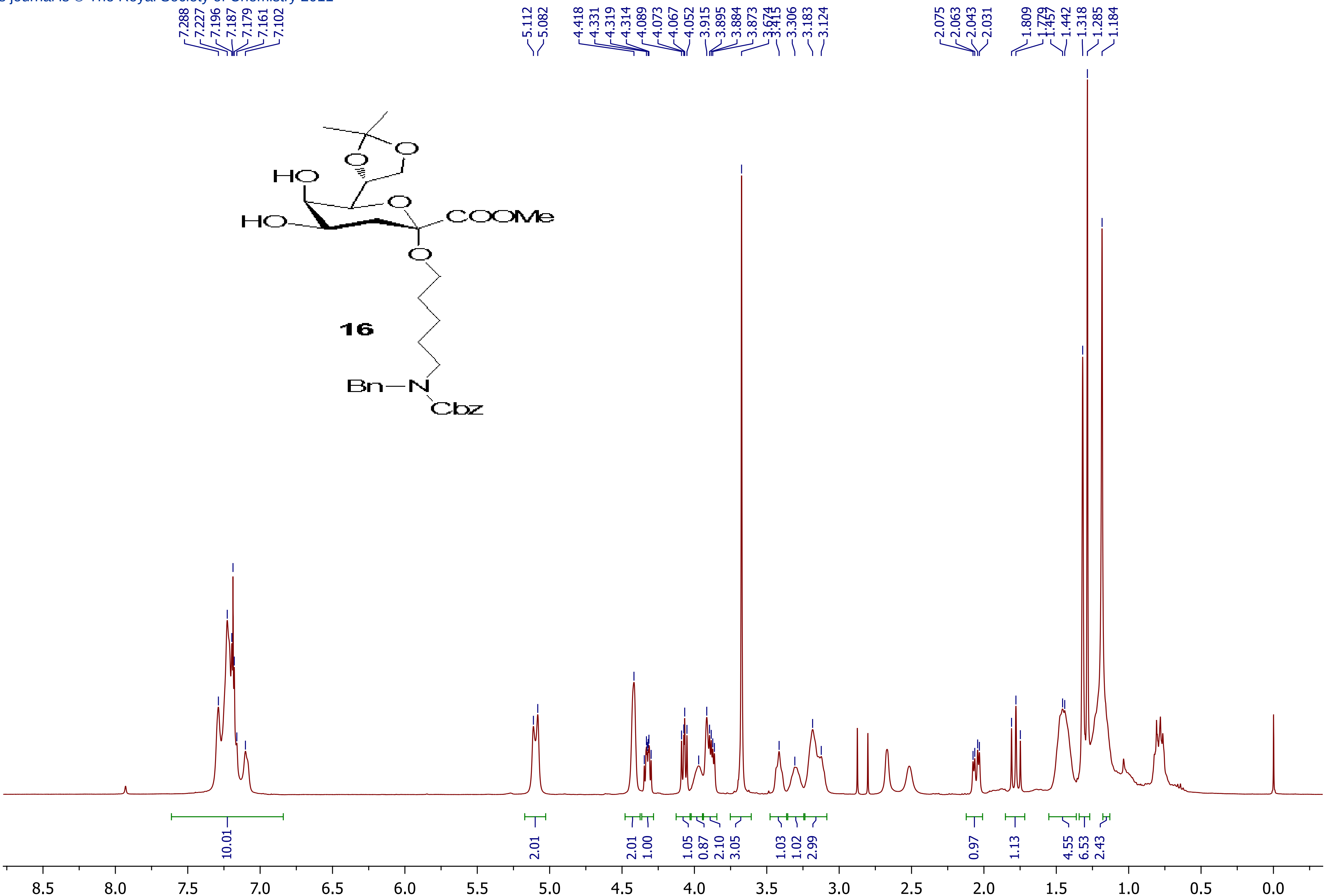

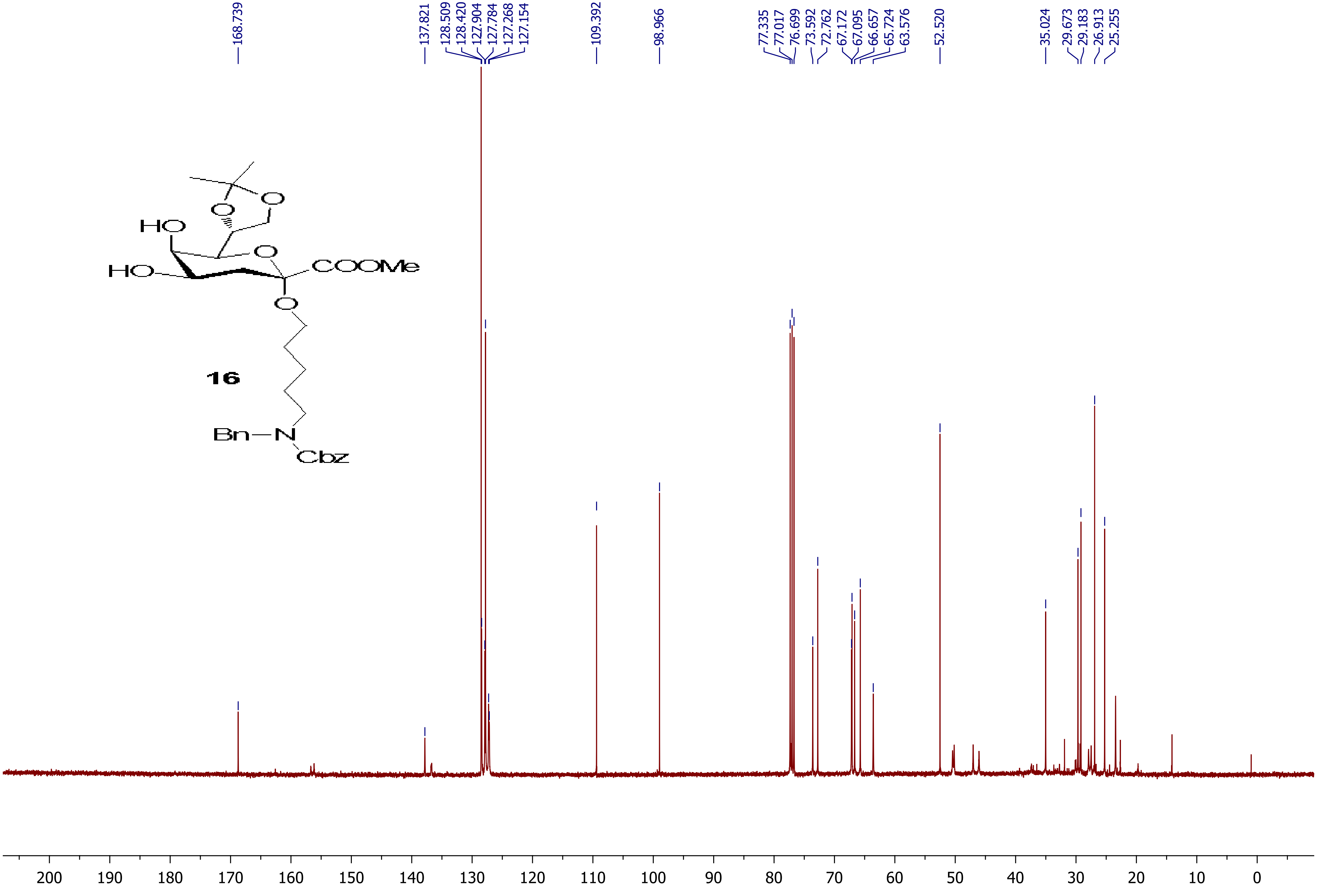
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77.017
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73.592
72.762
67.172
67.095
66.657
65.724
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35.024
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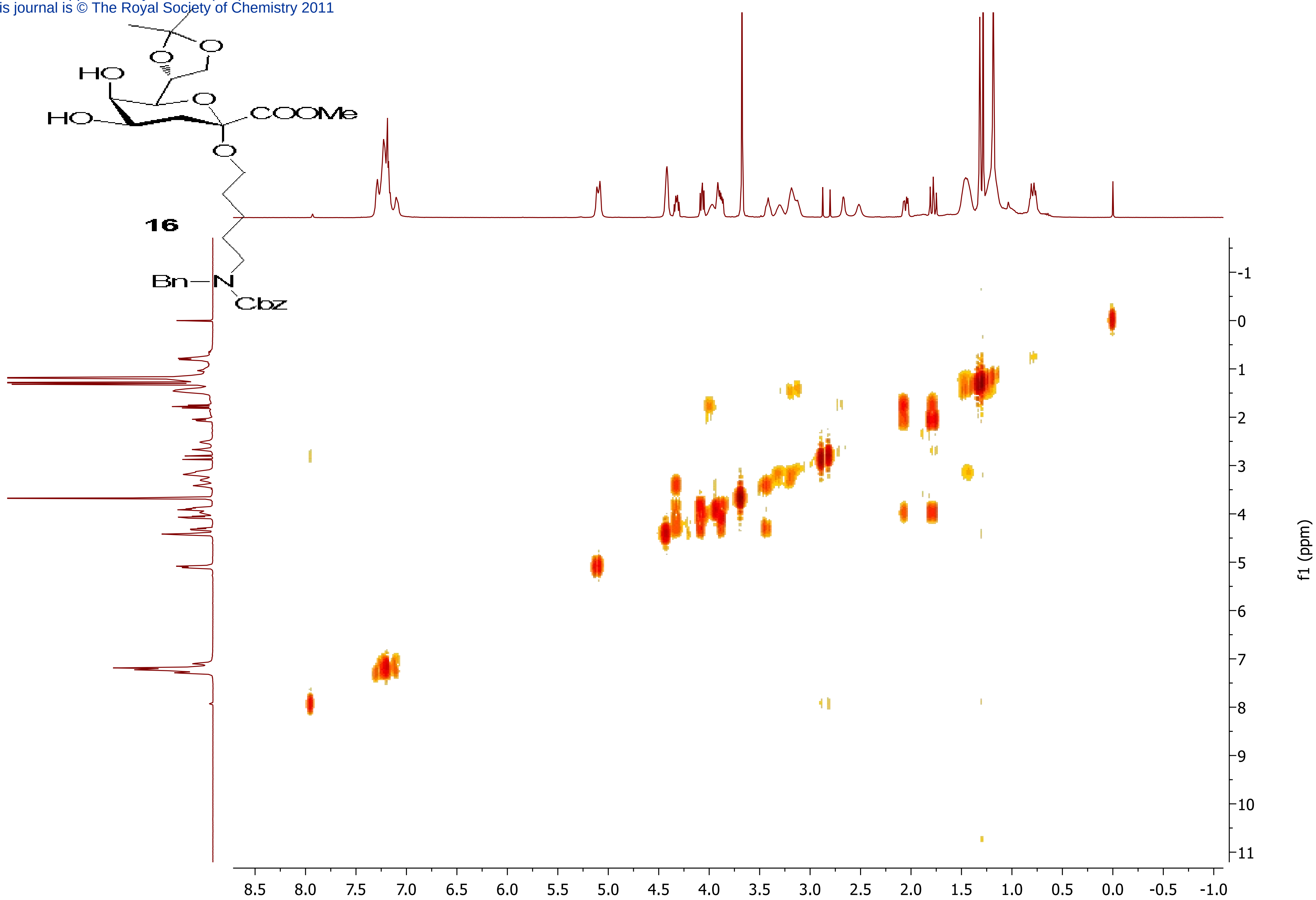
HO
HO
O
O
O
COOMe
O
16
Bn
N
Cbz
f1 (ppm)
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0
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2
3
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5
6
7
8
9
10
11
8.5
8.0
7.5
7.0
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6.0
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5.0
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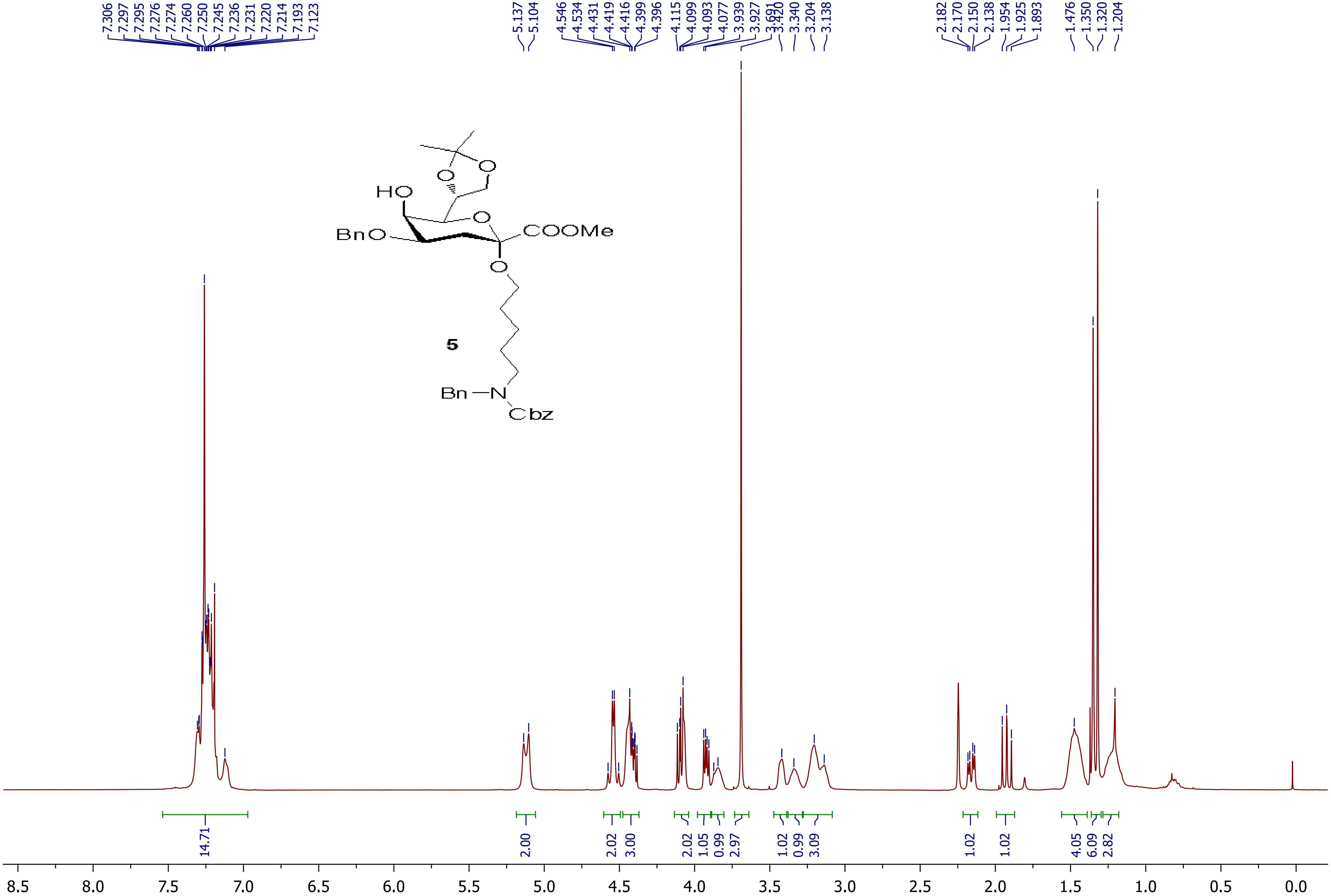
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BnO
COOMe
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Bn
N
Cbz
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5.137 5.104
4.546 4.534 4.431 4.419 4.416 4.399 4.396
4.115 4.099 4.093 4.077 3.939 3.927 3.691 3.420 3.340 3.204 3.138
2.182 2.170 2.150 2.138 1.954 1.925 1.893
1.476 1.350 1.320 1.204
14.71
2.00
2.02 3.00
2.02 1.05 0.99 2.97
1.02 0.99 3.09
1.02
1.02
4.05 6.09 2.82
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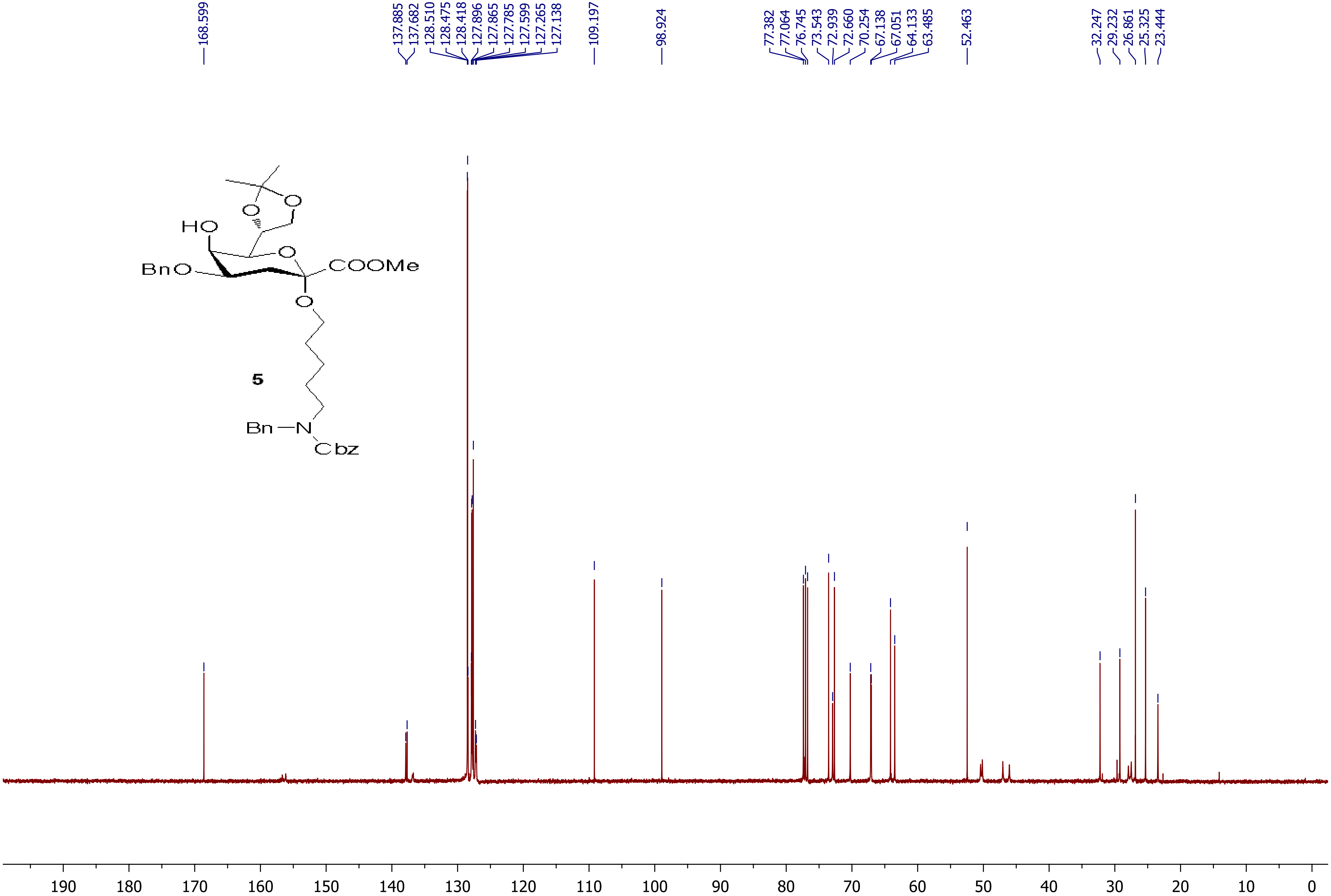
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98.924
77.382
77.064
76.745
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72.939
72.660
70.254
67.138
67.051
64.133
63.485
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32.247
29.232
26.861
25.325
23.444
HO
BnO
COOMe
Bn
N
Cbz
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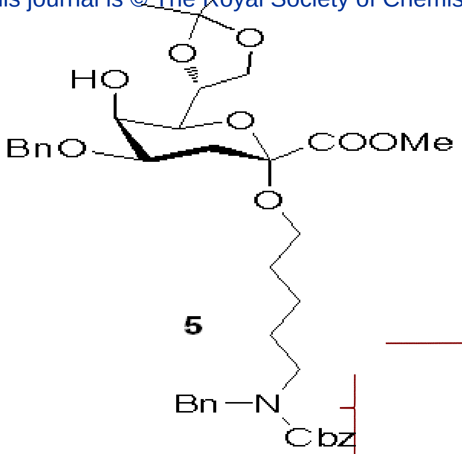
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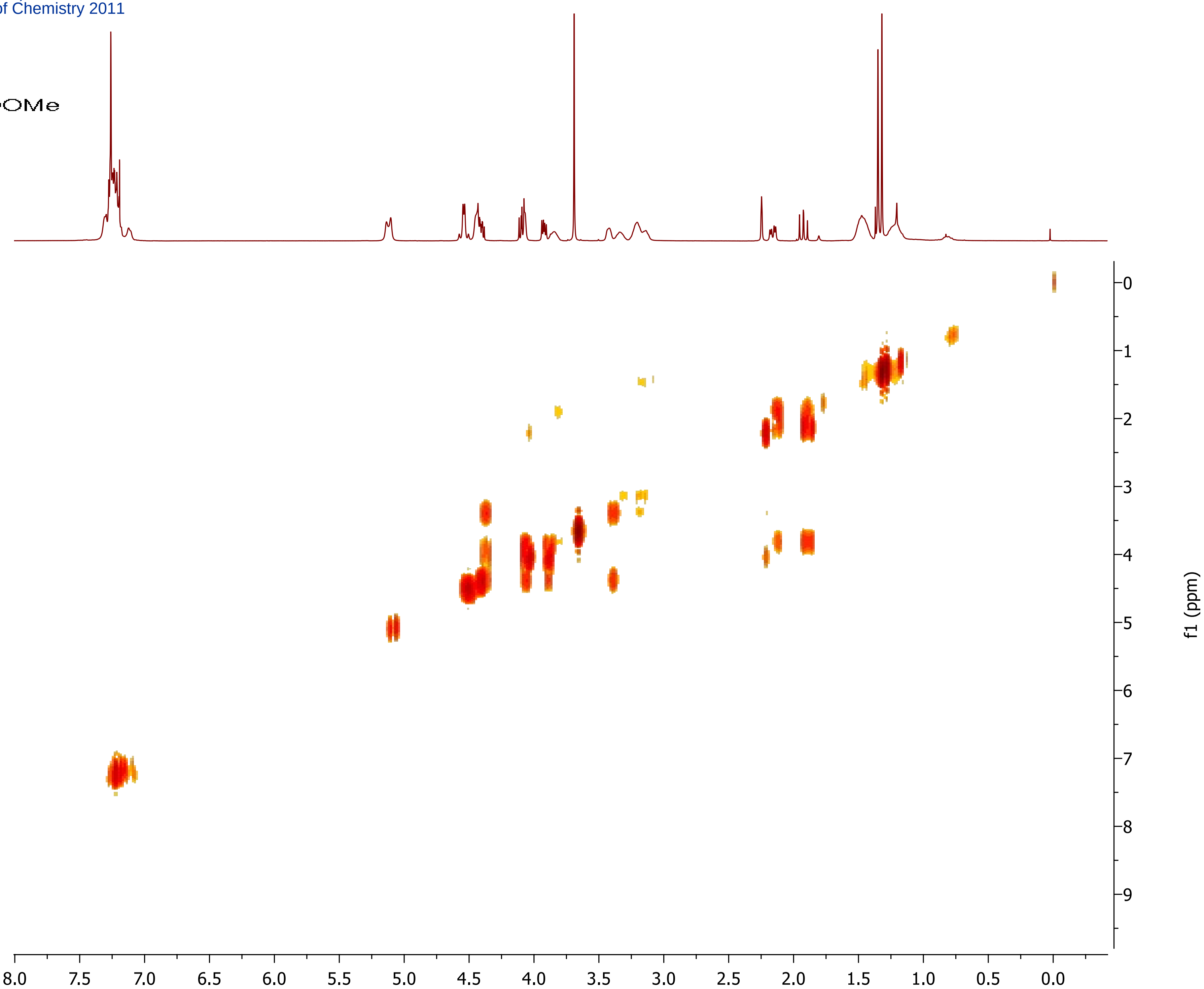
BnO
COOMe
Bn
N
Cbz

5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f1 (ppm)
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6.0
5.5
5.0
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3.0
2.5
2.0
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1.0
0.5
0.0

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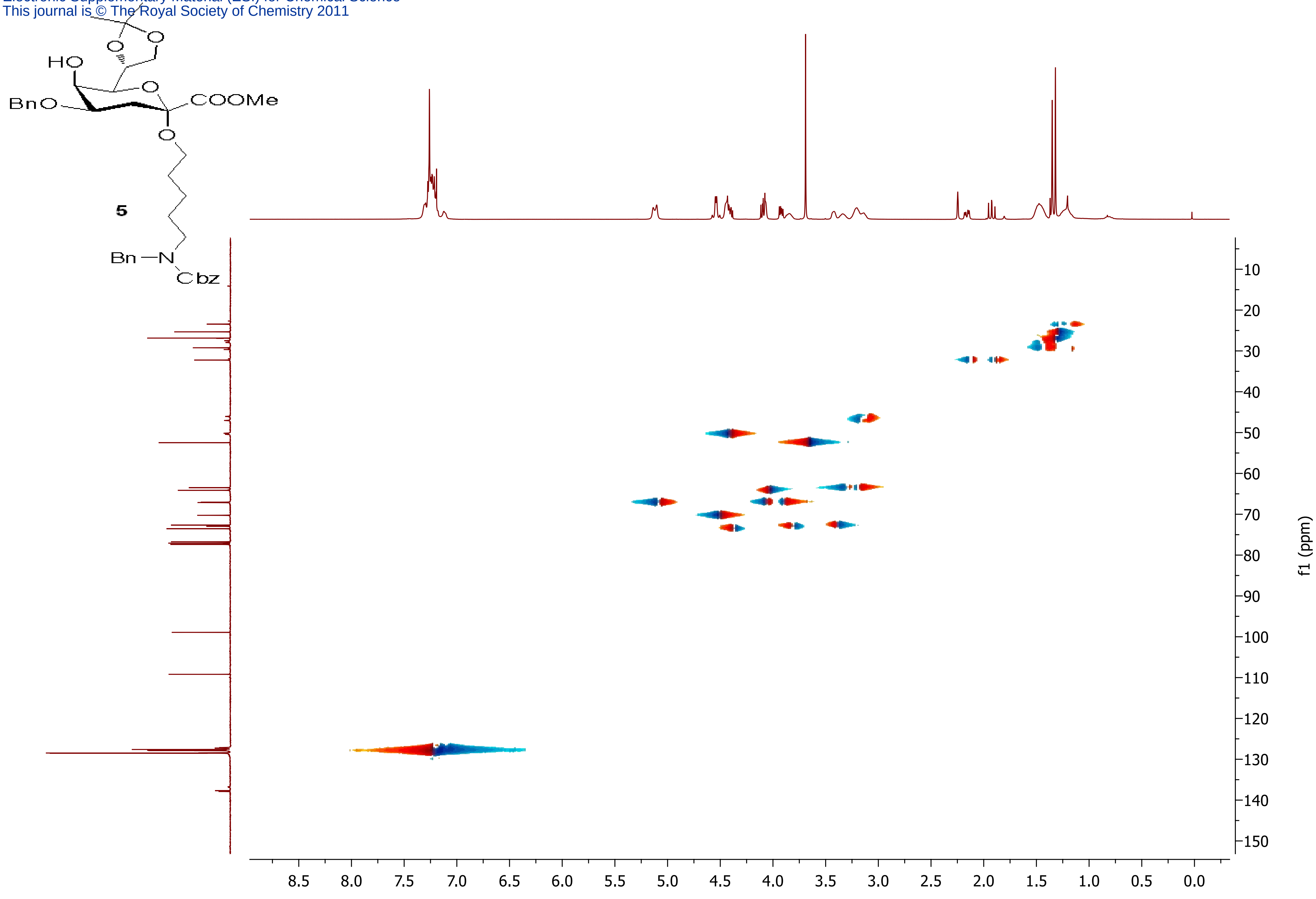

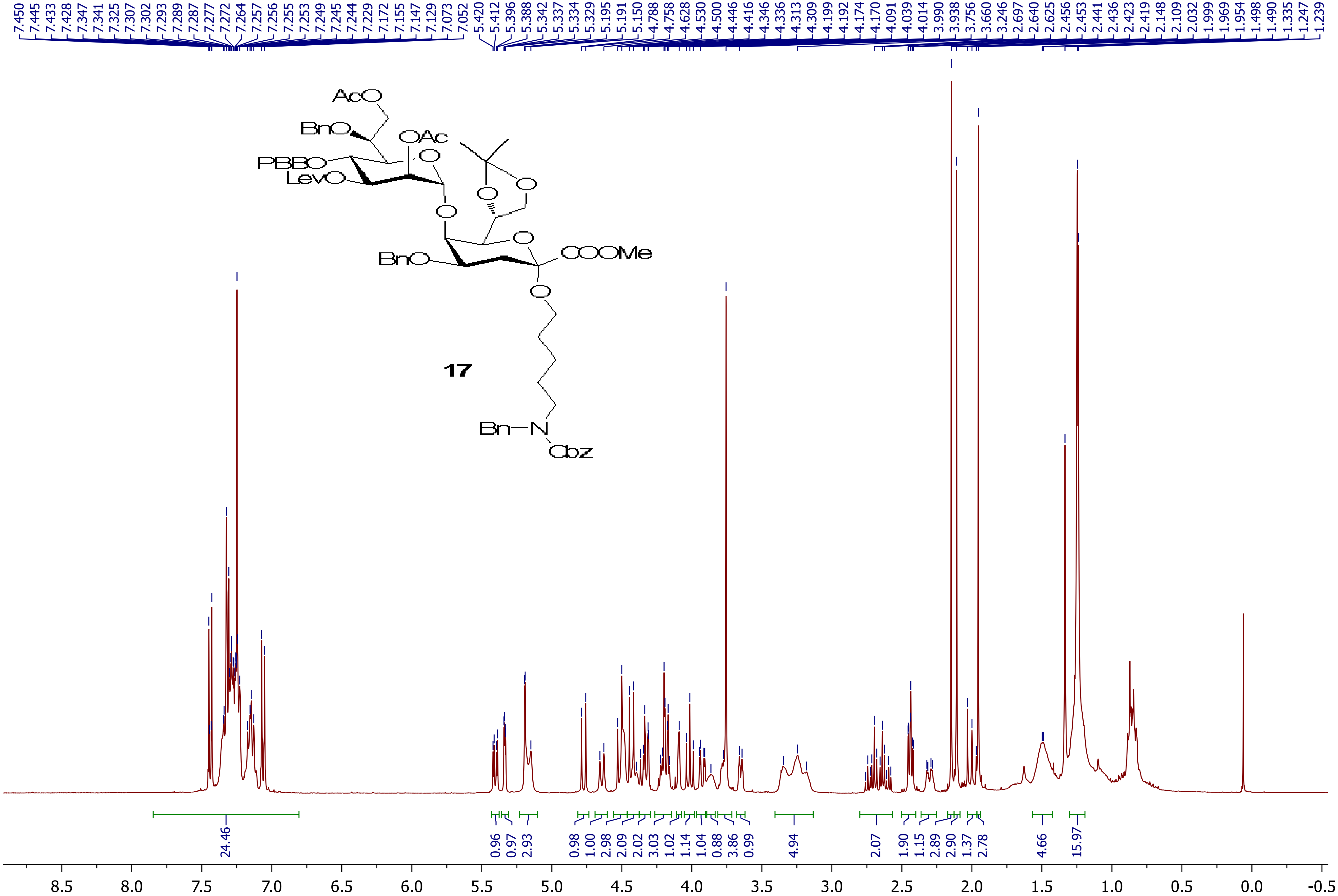
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AcO
BnO
OAc
PBBO
LevO
O
BnO
COOMe
17
Bn—N
Cbz
24.46
0.96 0.97 2.93
0.98 1.00 2.98 2.09 2.02 3.03 1.02 1.14 1.04 0.88 3.86 0.99
4.94
2.07 1.90 1.15 2.89 2.90 1.37 2.78
4.66 15.97
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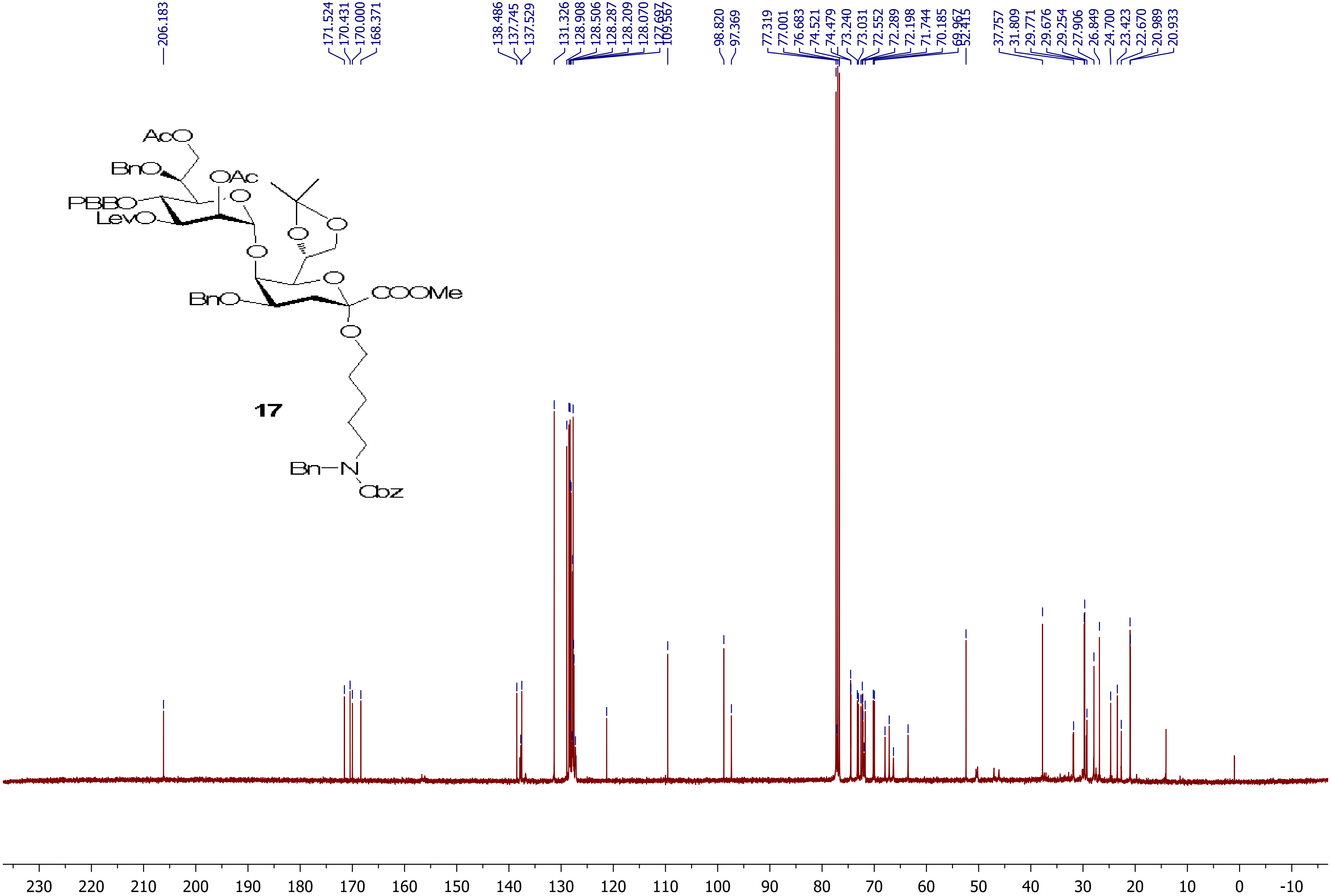
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128.209
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77.001
76.683
74.521
74.479
73.240
73.031
72.552
72.289
72.198
71.744
70.185
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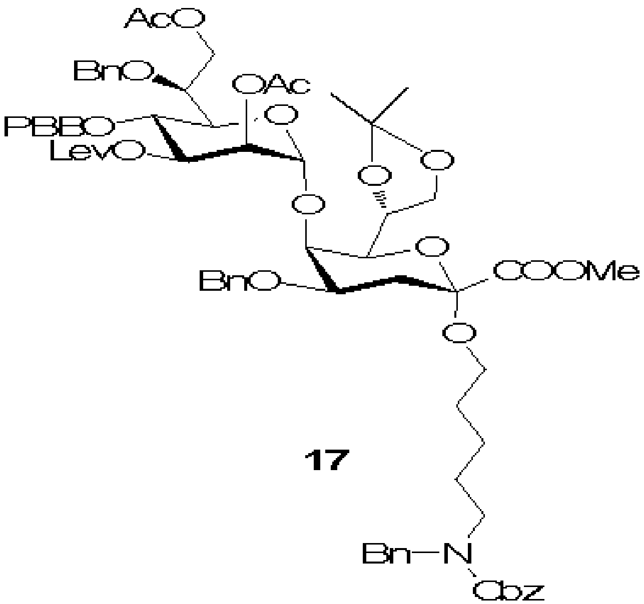
27.906
26.849
24.700
23.423
22.670
20.989
20.933
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
AcO
BnO
OAc
O
PBBO
LevO
O
O
O
O
BnO
COOMe
O
Bn
N
Cbz

17

Coupled carbon



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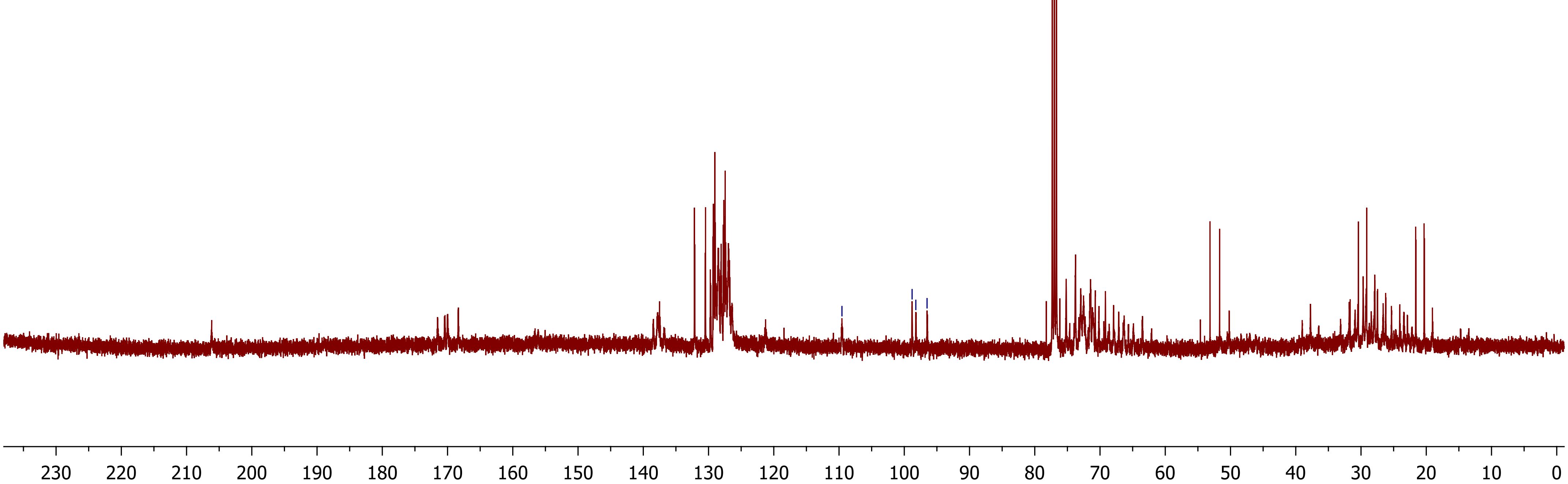
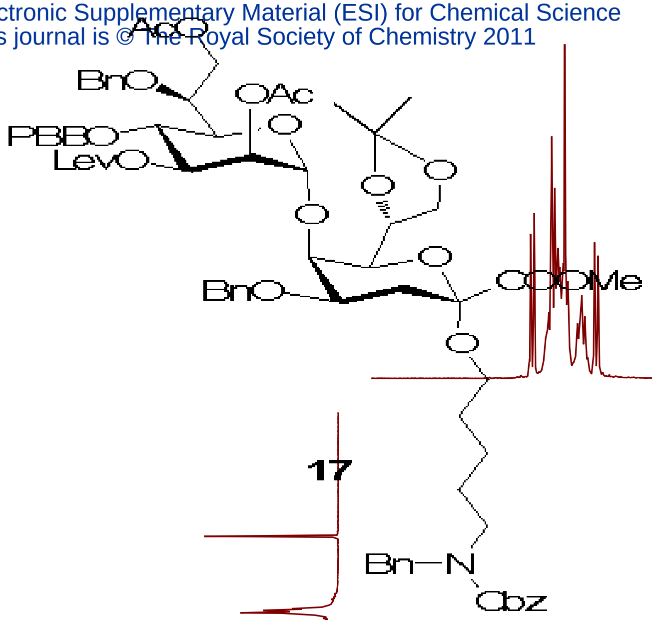
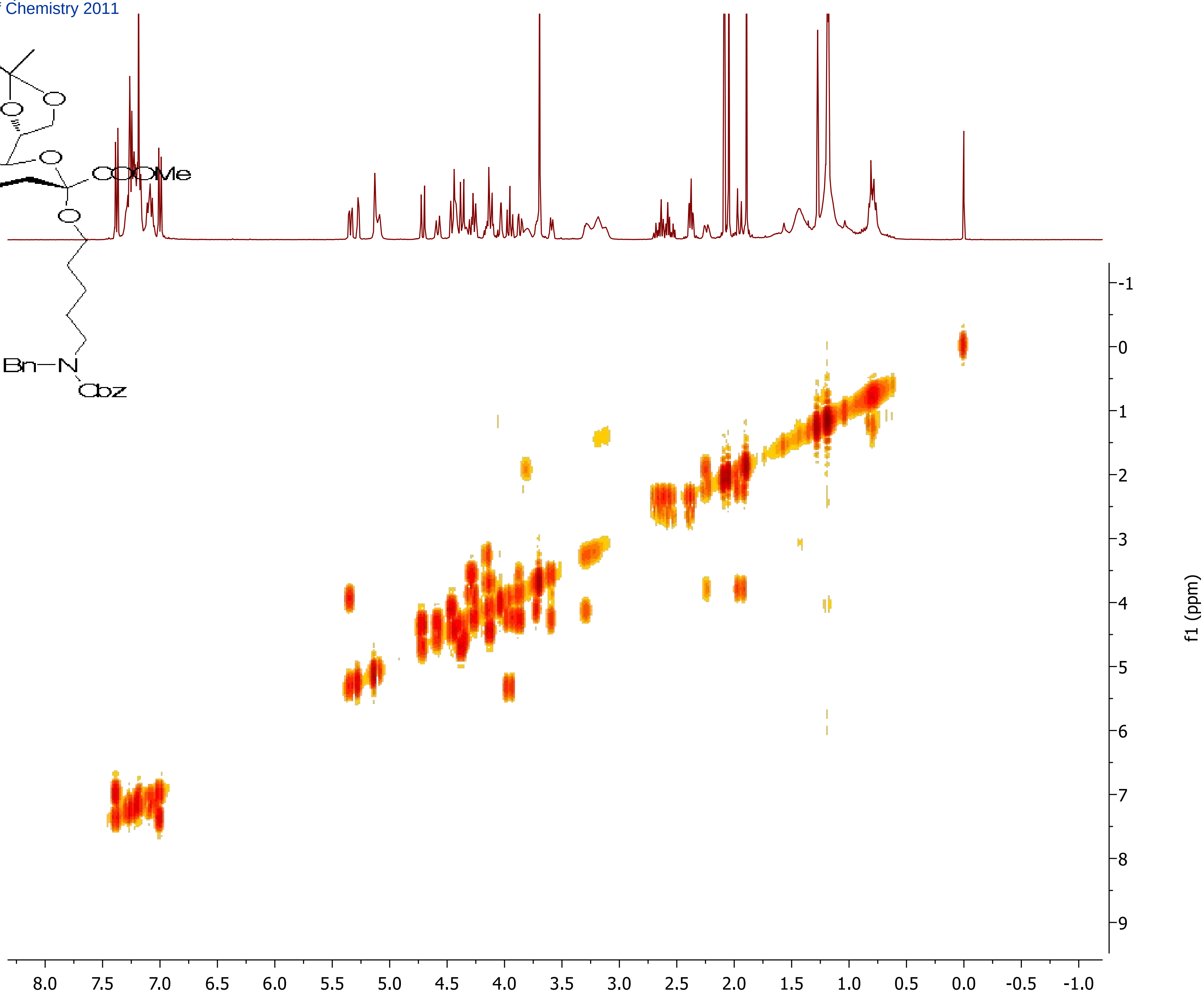



AcO
BnO
OAc
PBBO
LevO
BnO
COOMe
Bn—N
Cbz

17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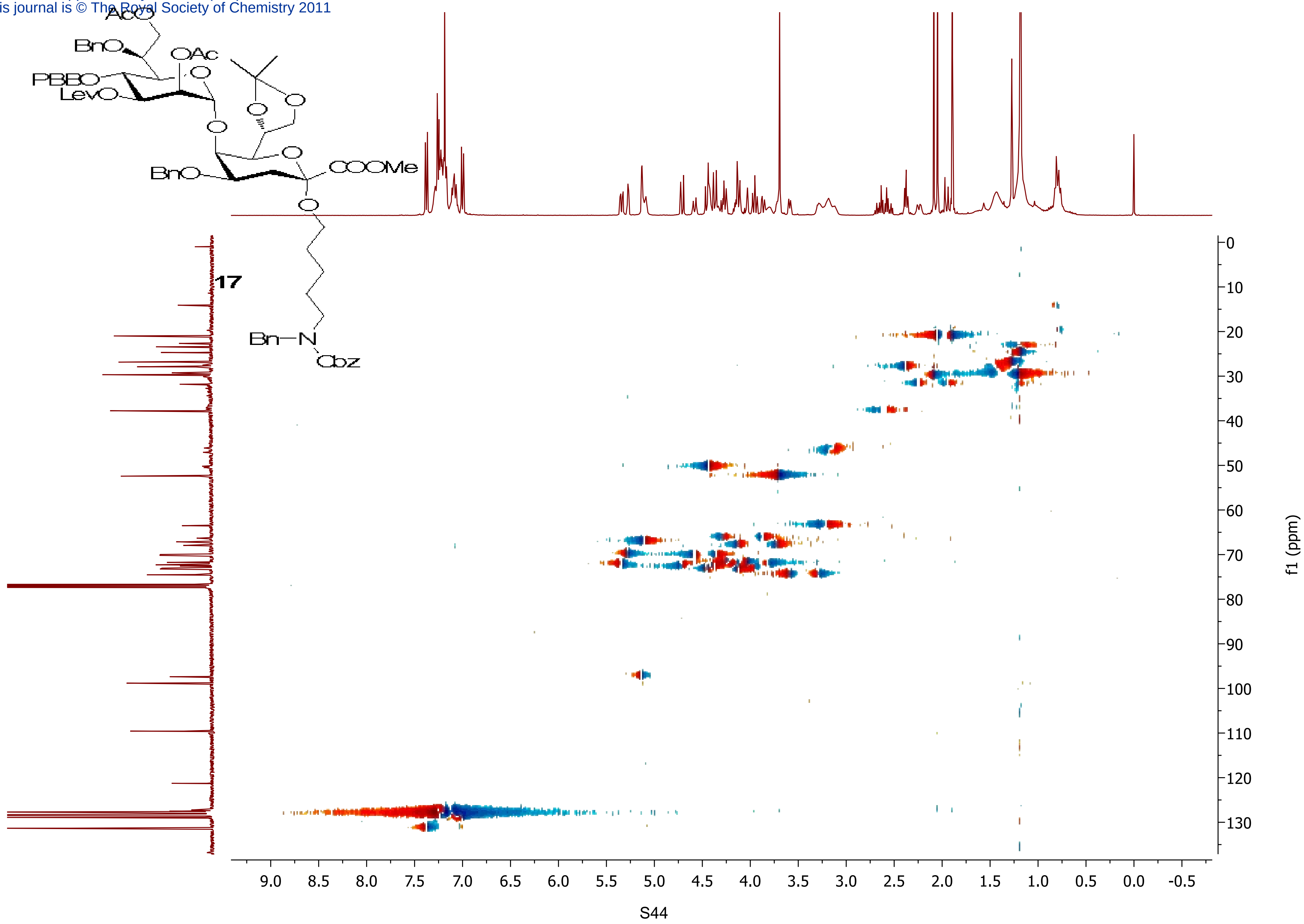
-0.5
-1.0


AcO
BnO
OAc
PBBO
LevO
BnO
COOMe
Bn—N
Cbz
17
9.0
8.5
8.0
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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)
0
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20
30
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60
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120
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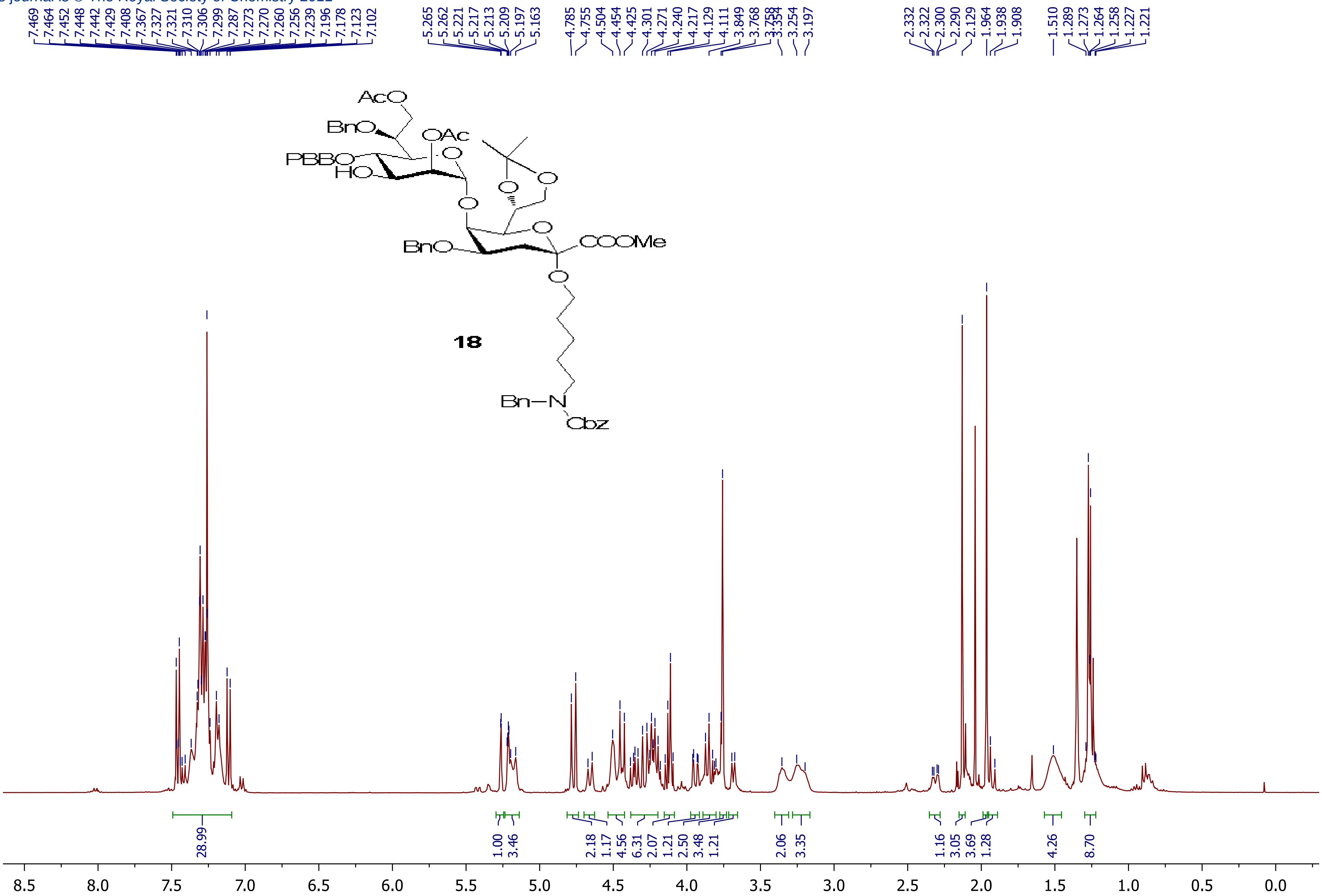
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OAc
PBBO
HO
BnO
COOMe
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Bn—N
Cbz
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1.17
4.56
6.31
2.07
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1.21
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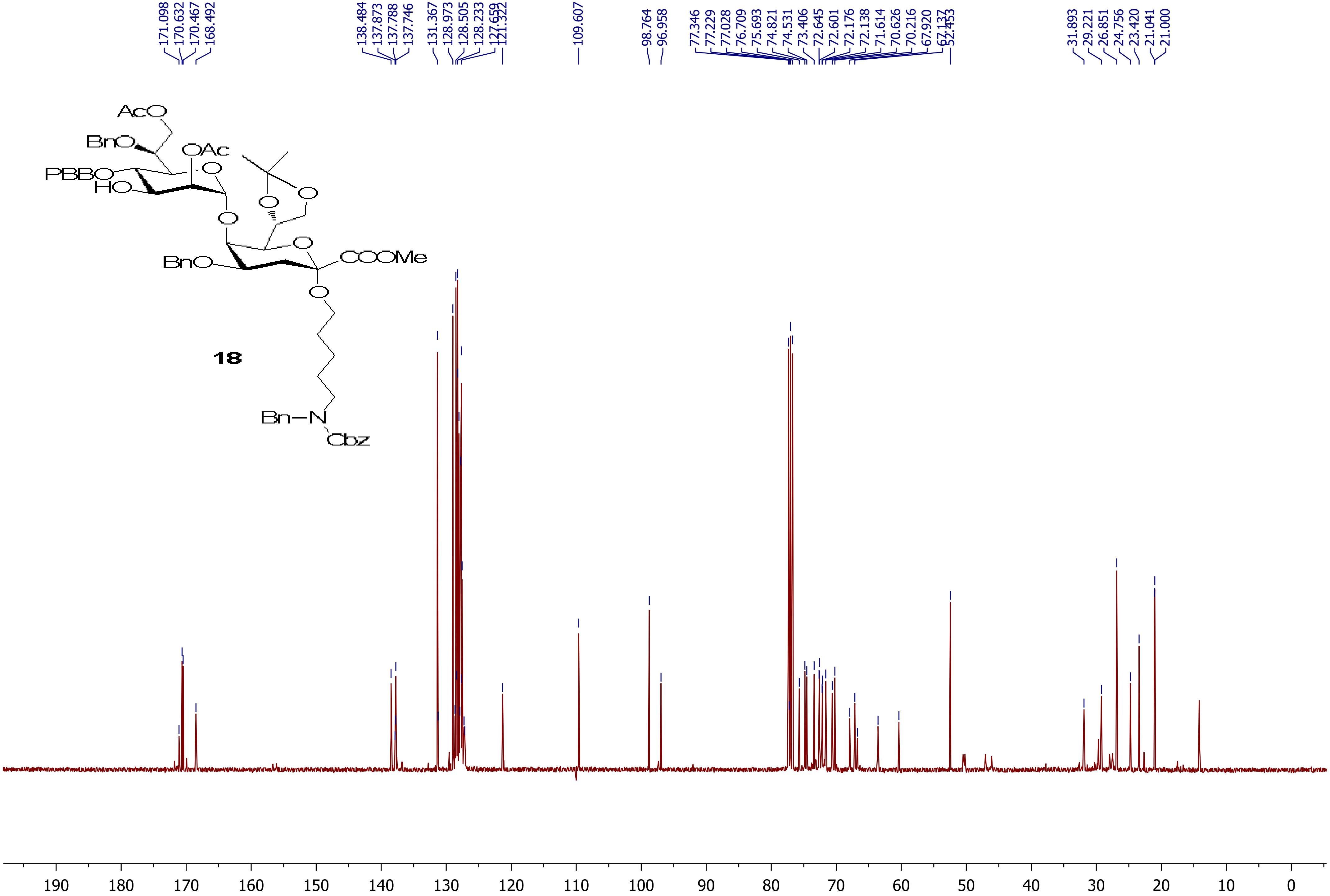
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74.531
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72.176
72.138
71.614
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70.216
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67.137
52.453
31.893
29.221
26.851
24.756
23.420
21.041
21.000
AcO
BnO
OAc
PBBO
HO
O
BnO
COOMe
18
Bn—N
Cbz
190
180
170
160
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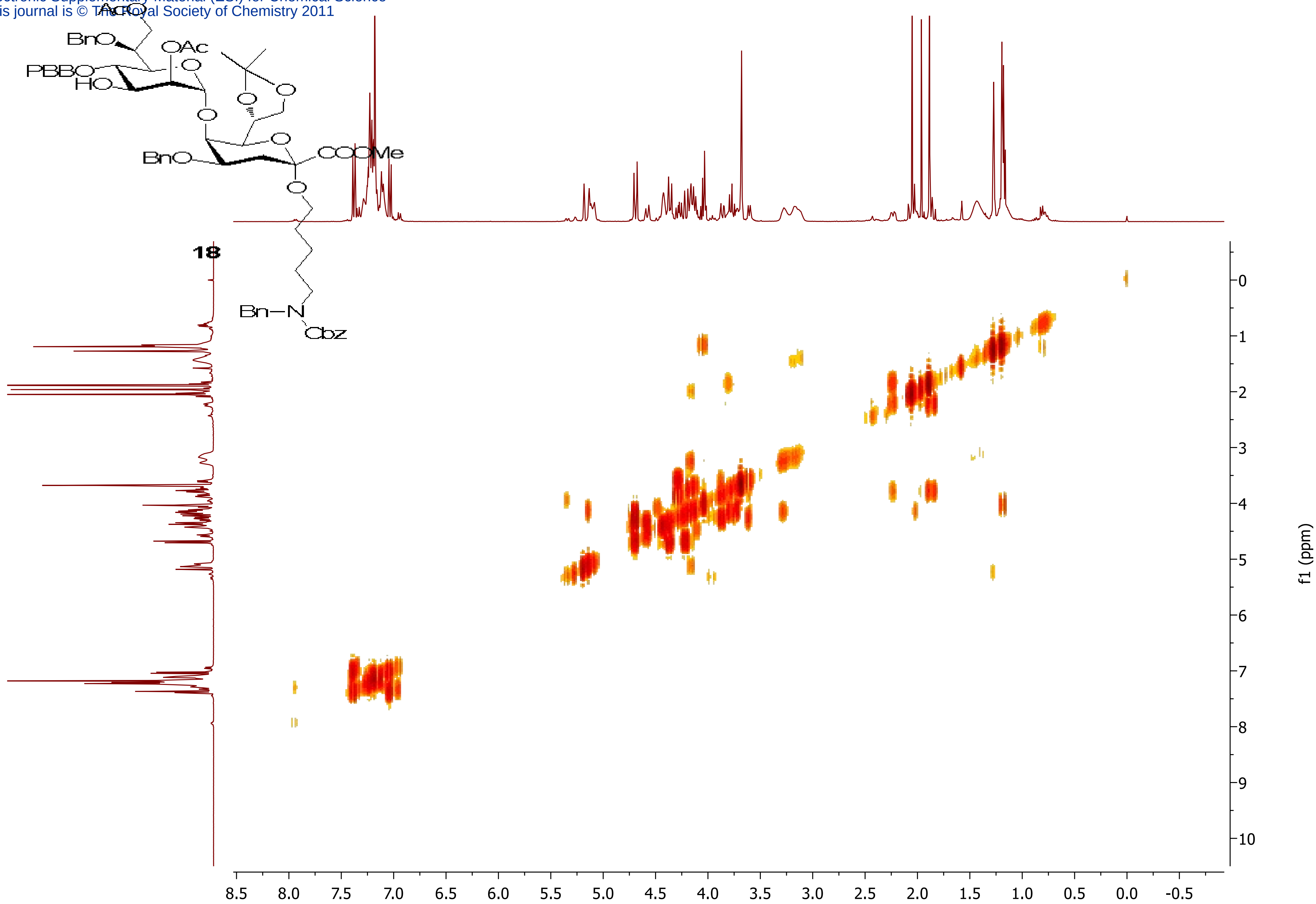

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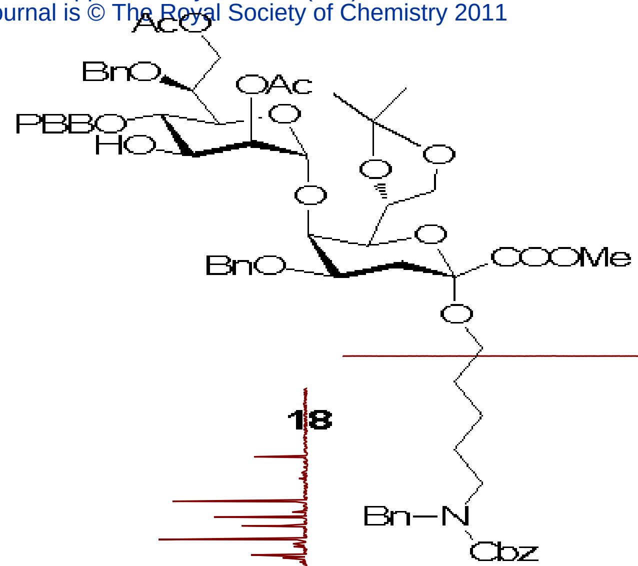

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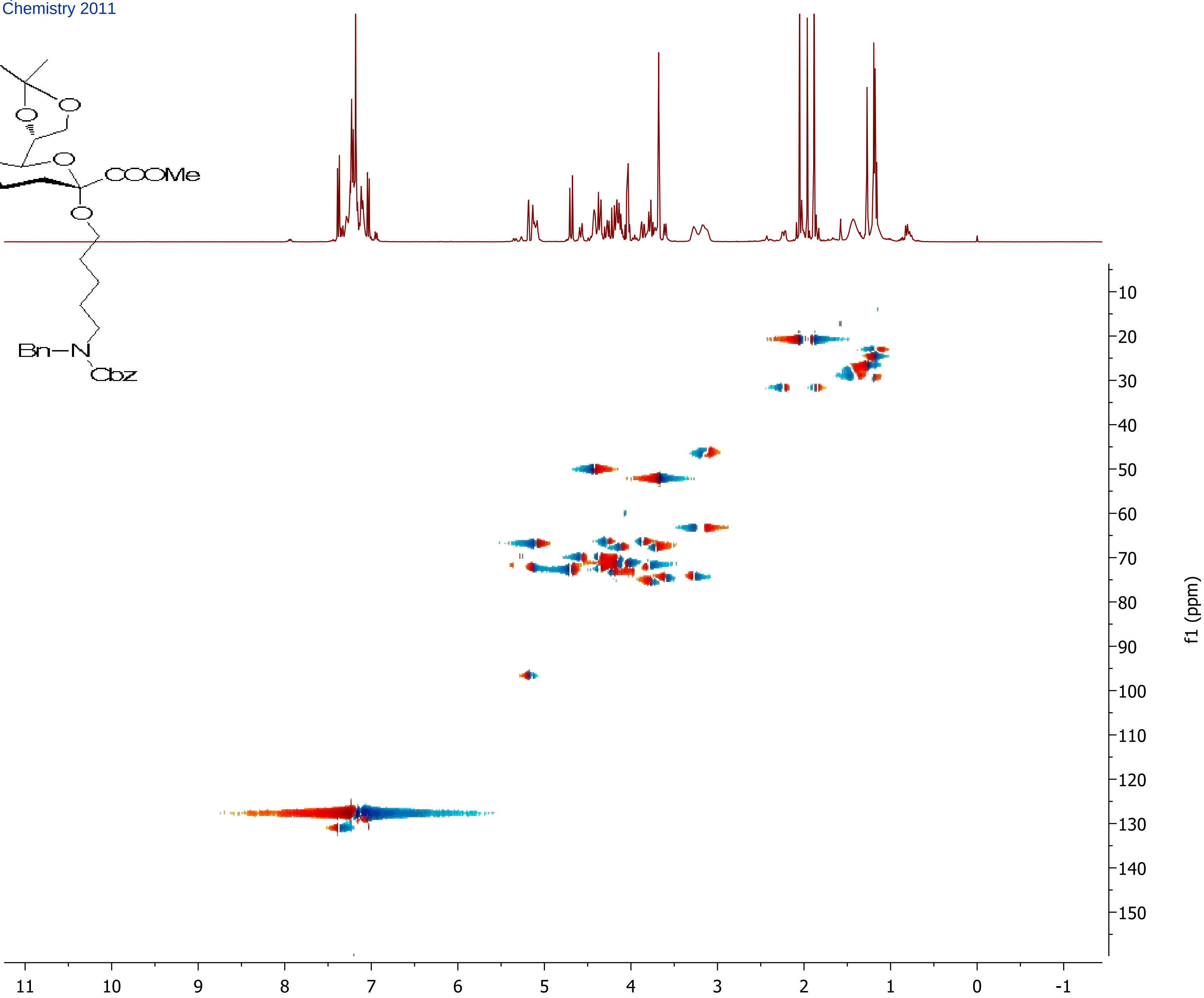

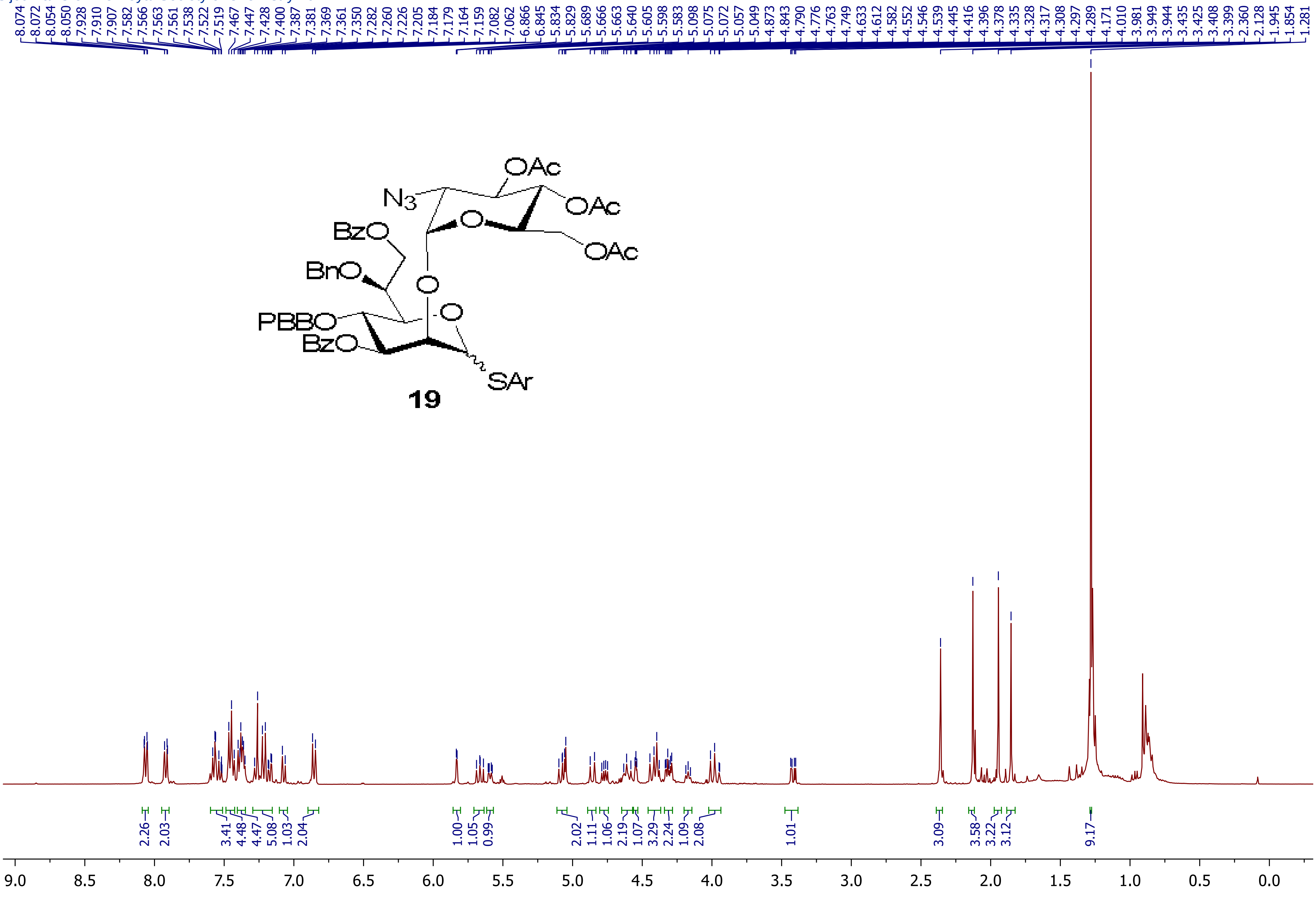
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BzO
OAc
BnO
PBBO
BzO
SAr
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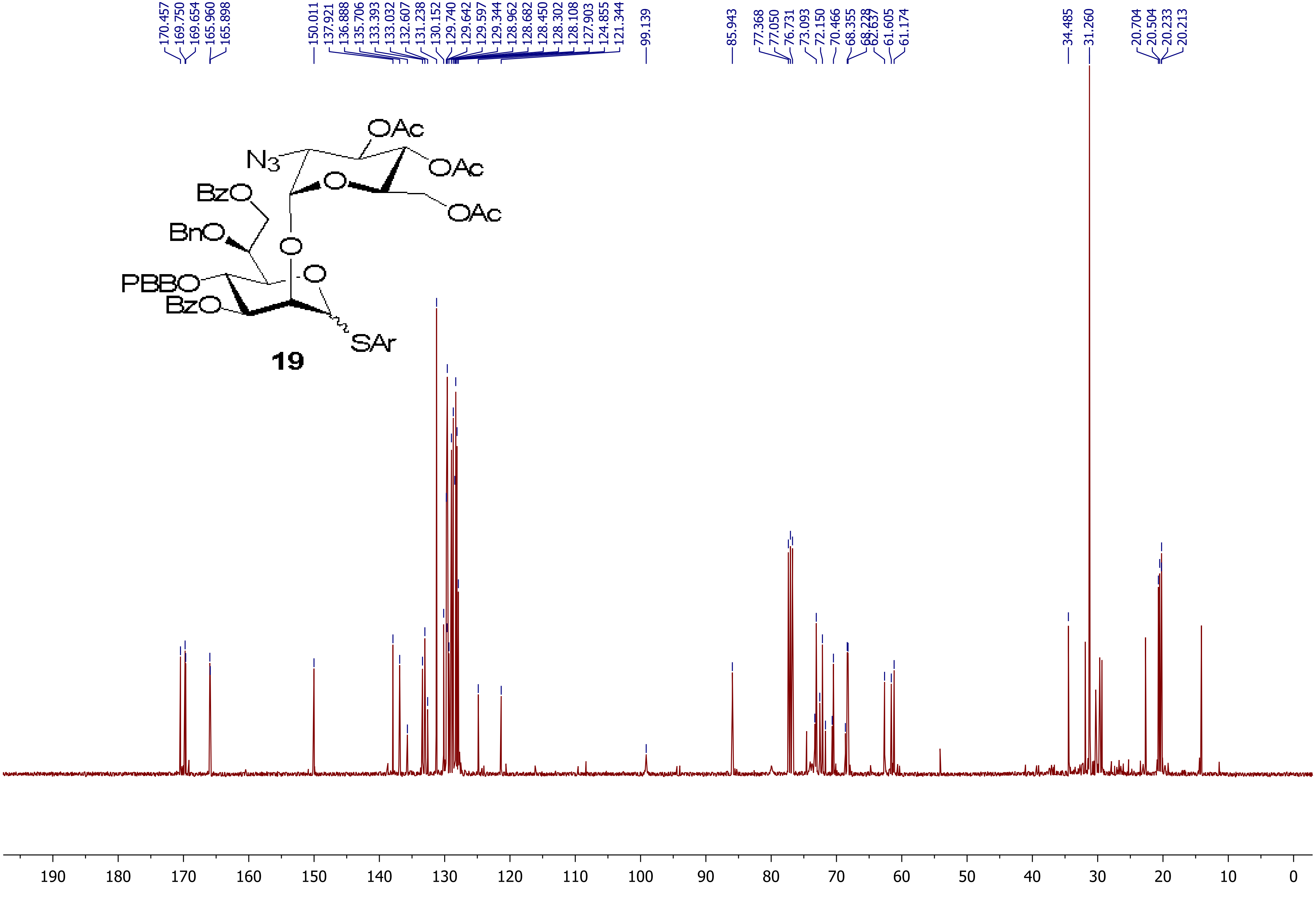
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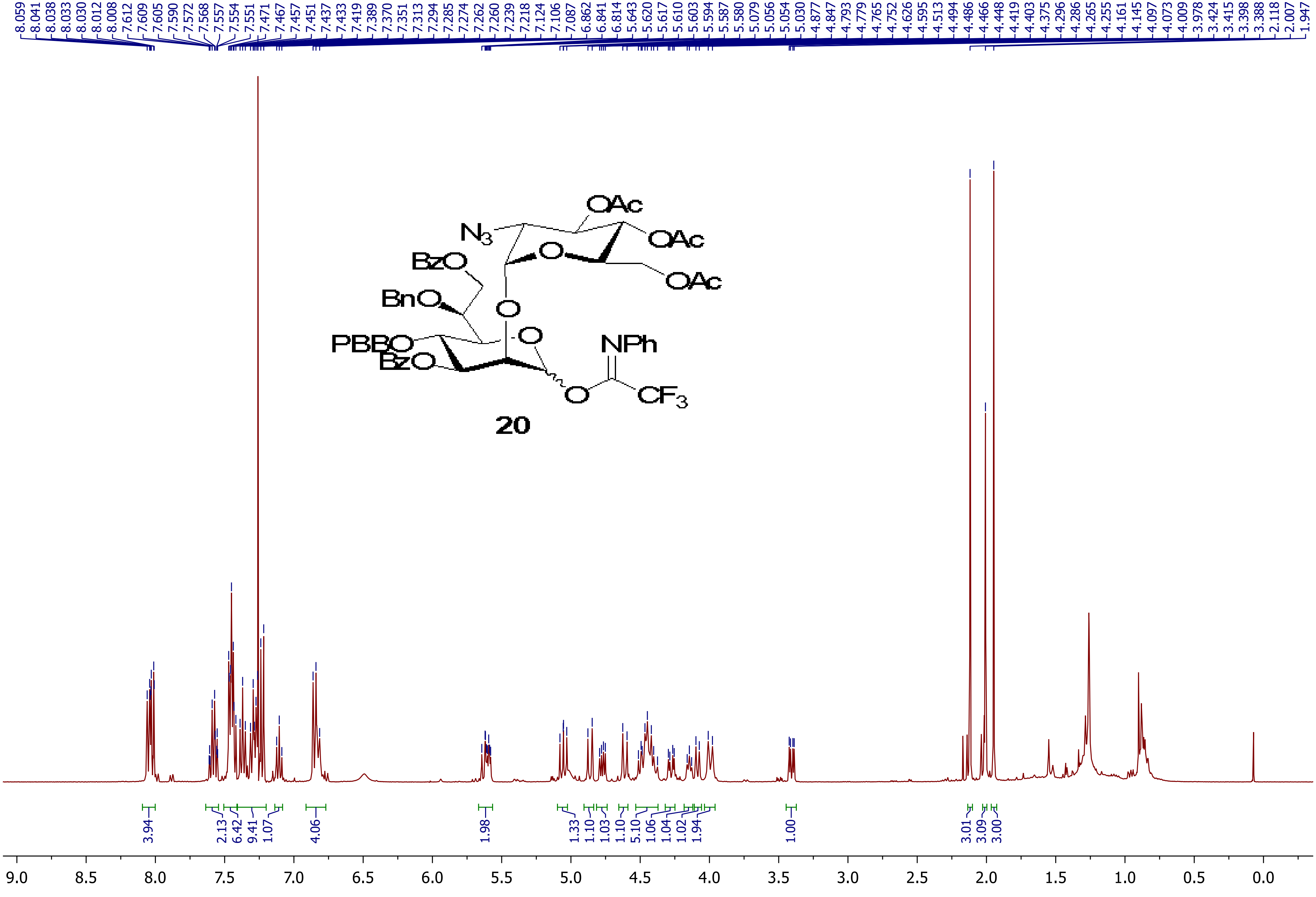
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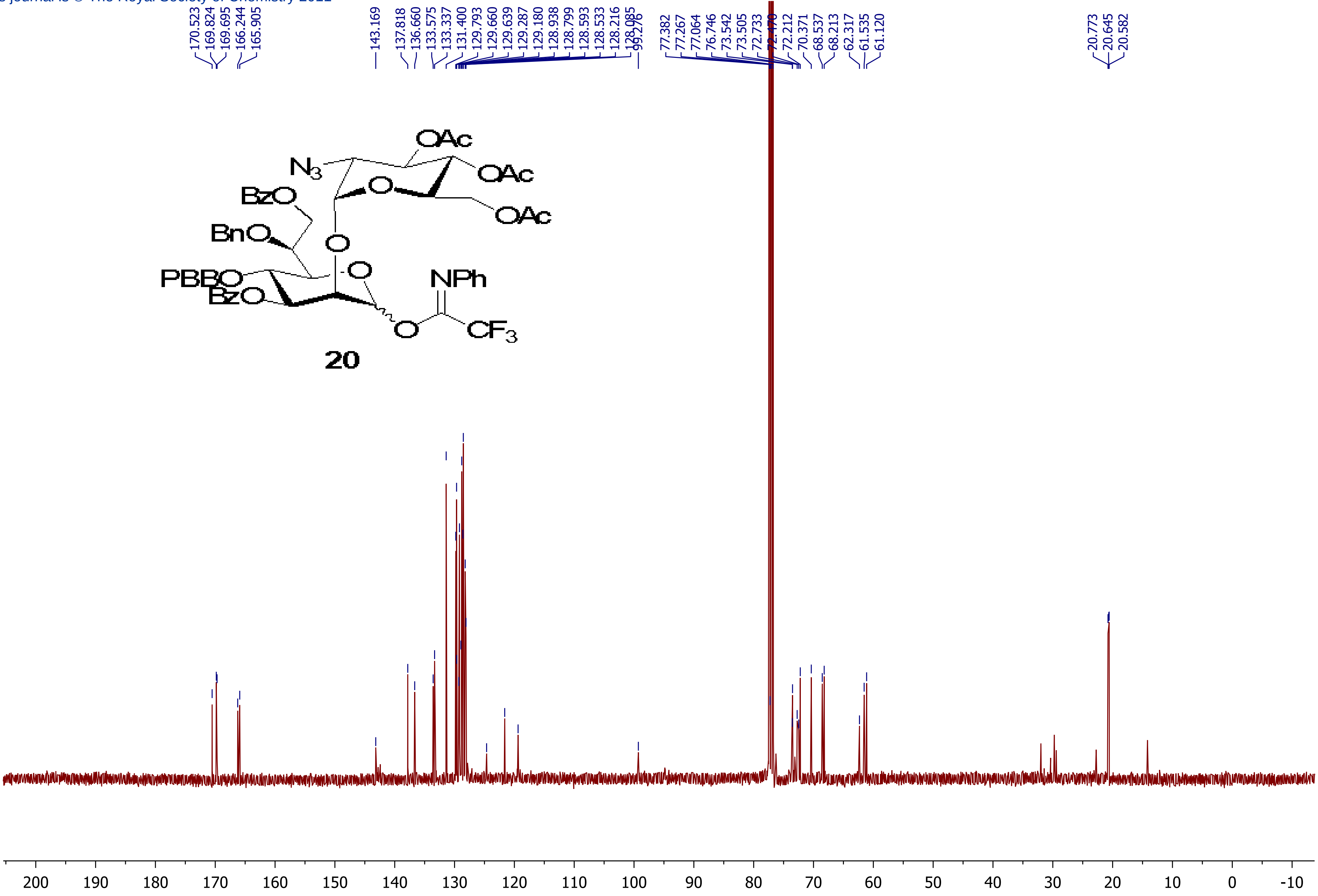
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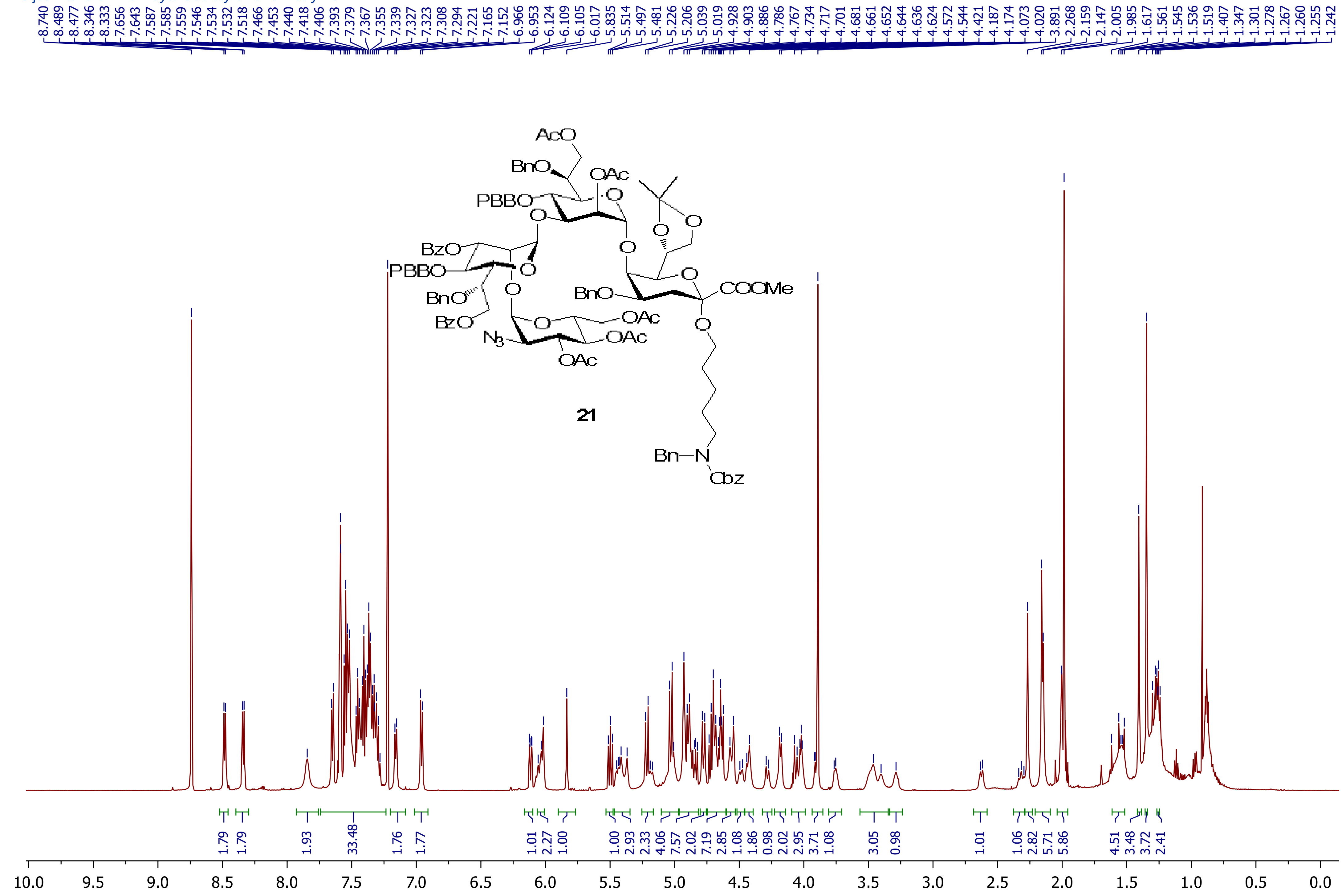

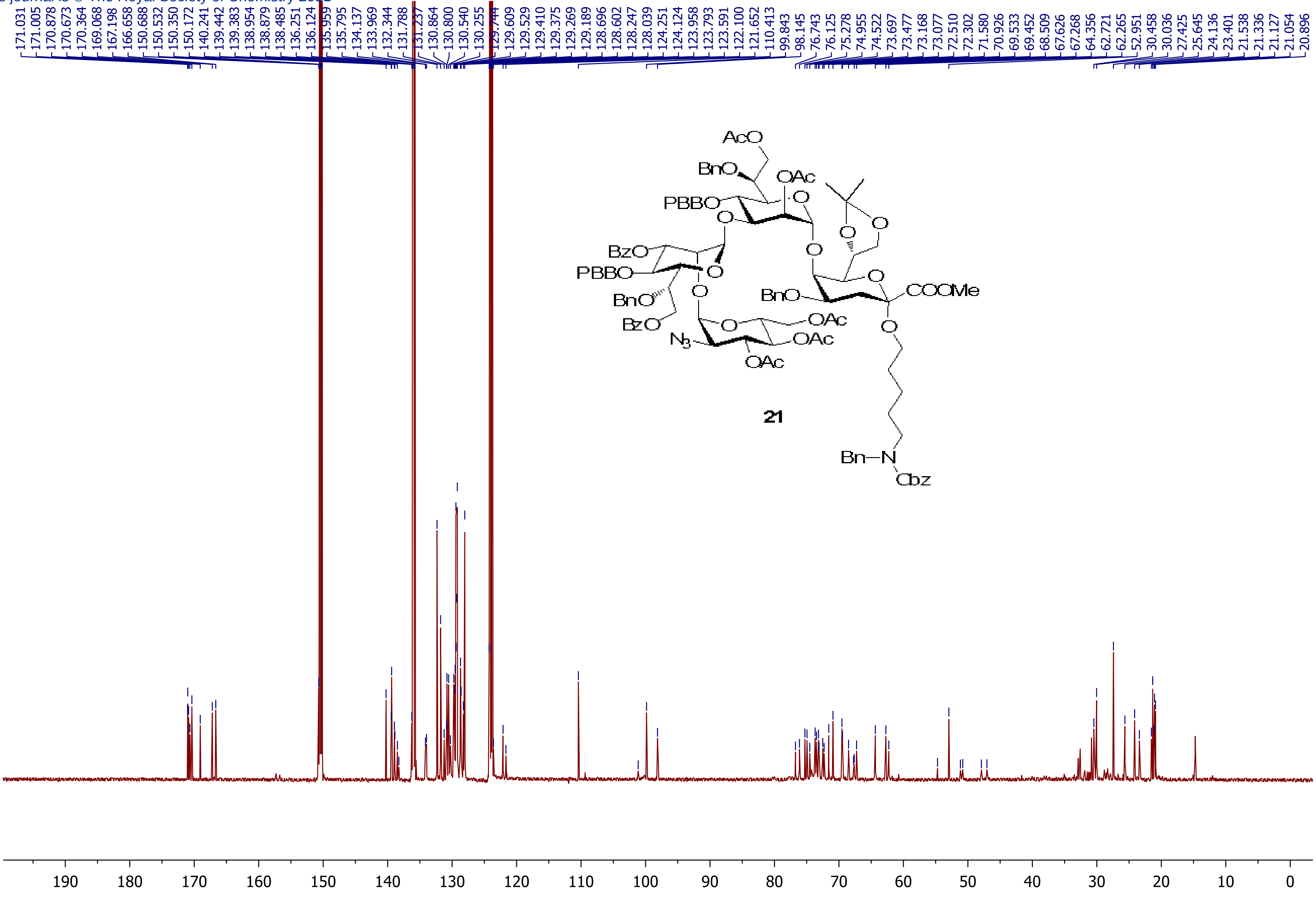
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AcO
BnO
OAc
PBBO
BzO
PBBO
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BzO
N3
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OAc
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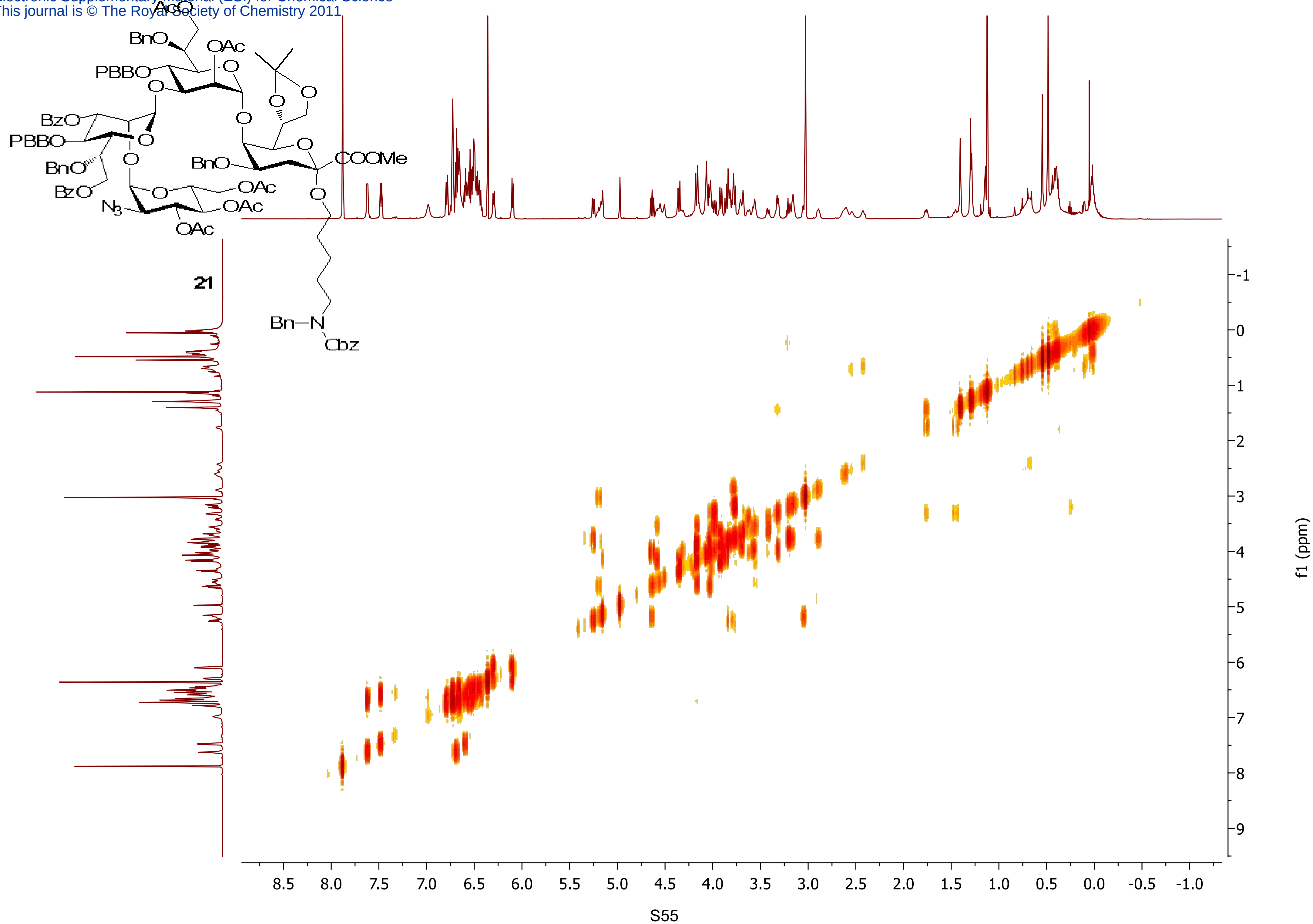
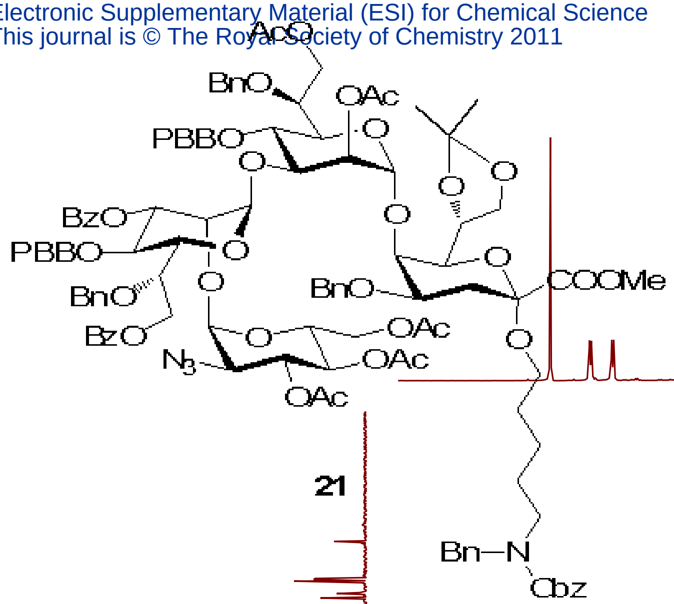
BnO
COOMe
Bn—N
Cbz
21
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

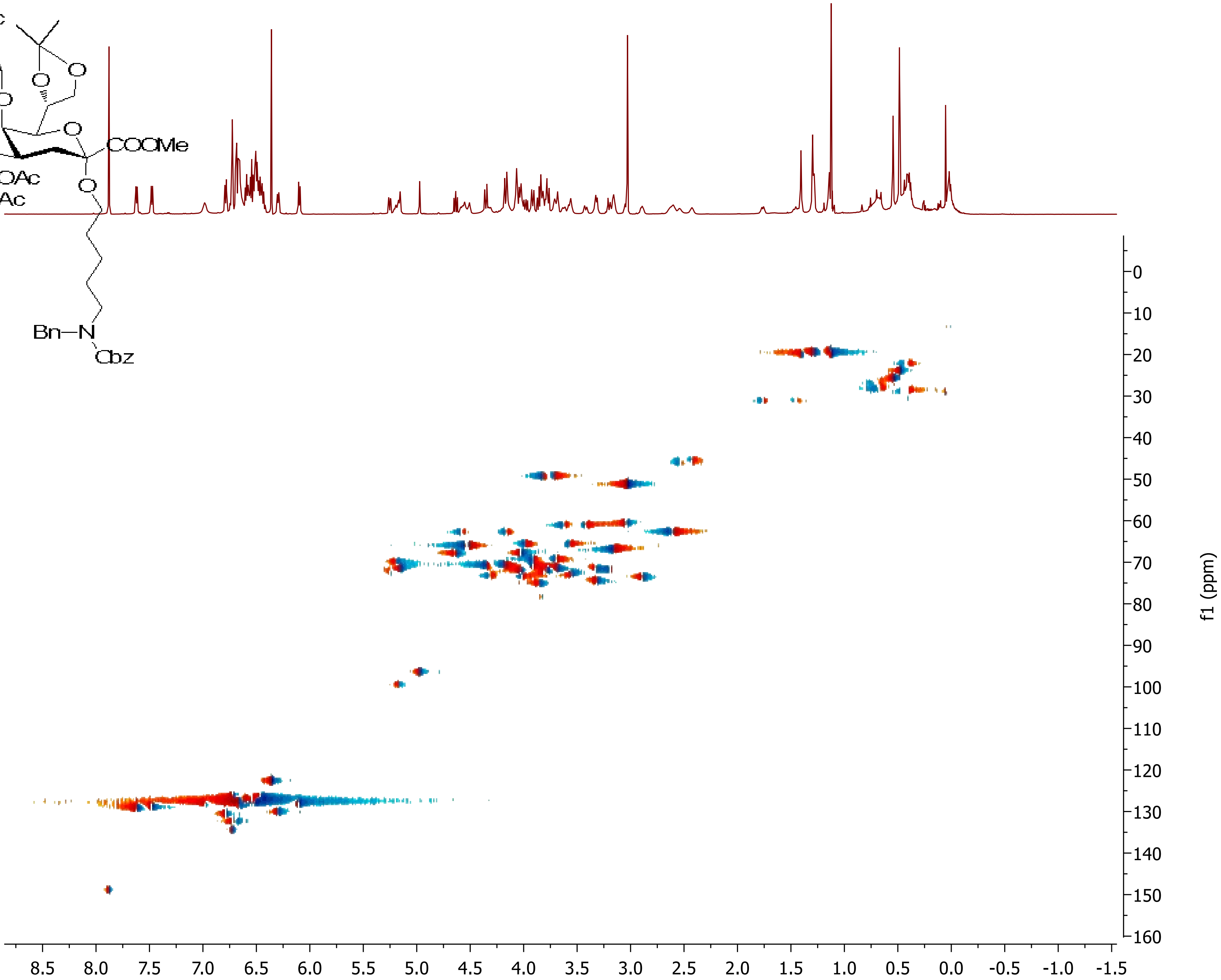


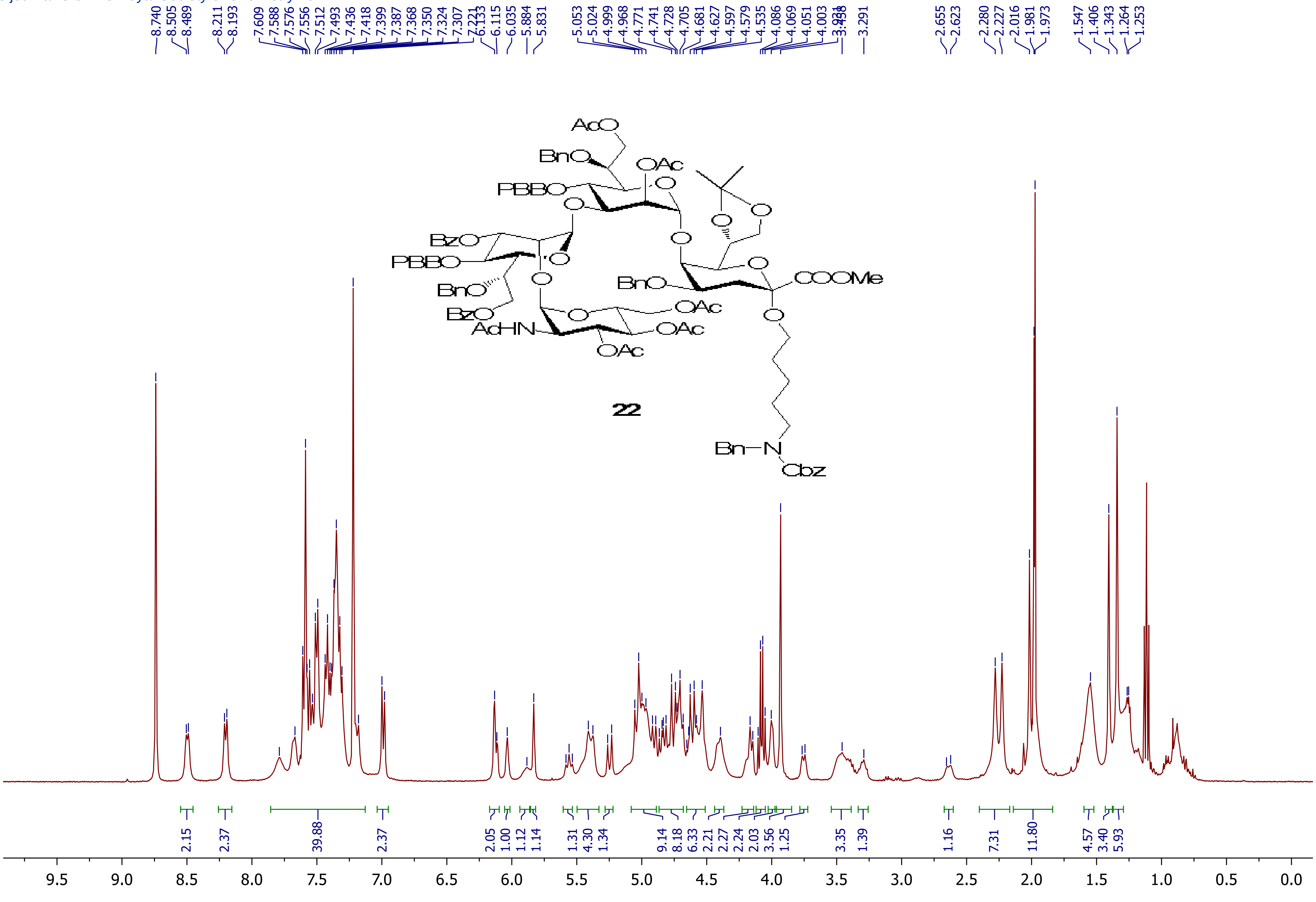
f1 (ppm)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
-1 0 1 2 3 4 5 6 7 8 9

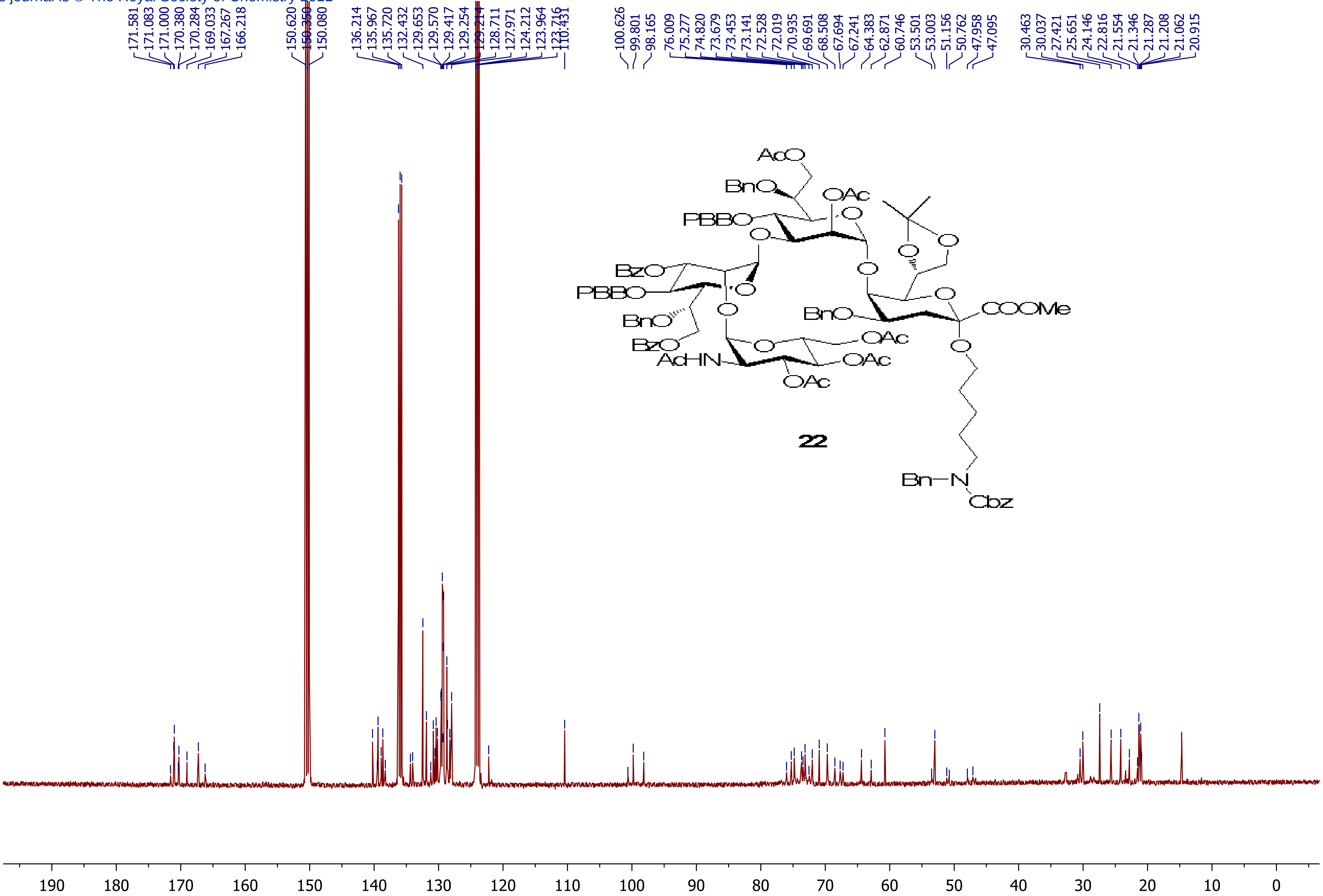
21

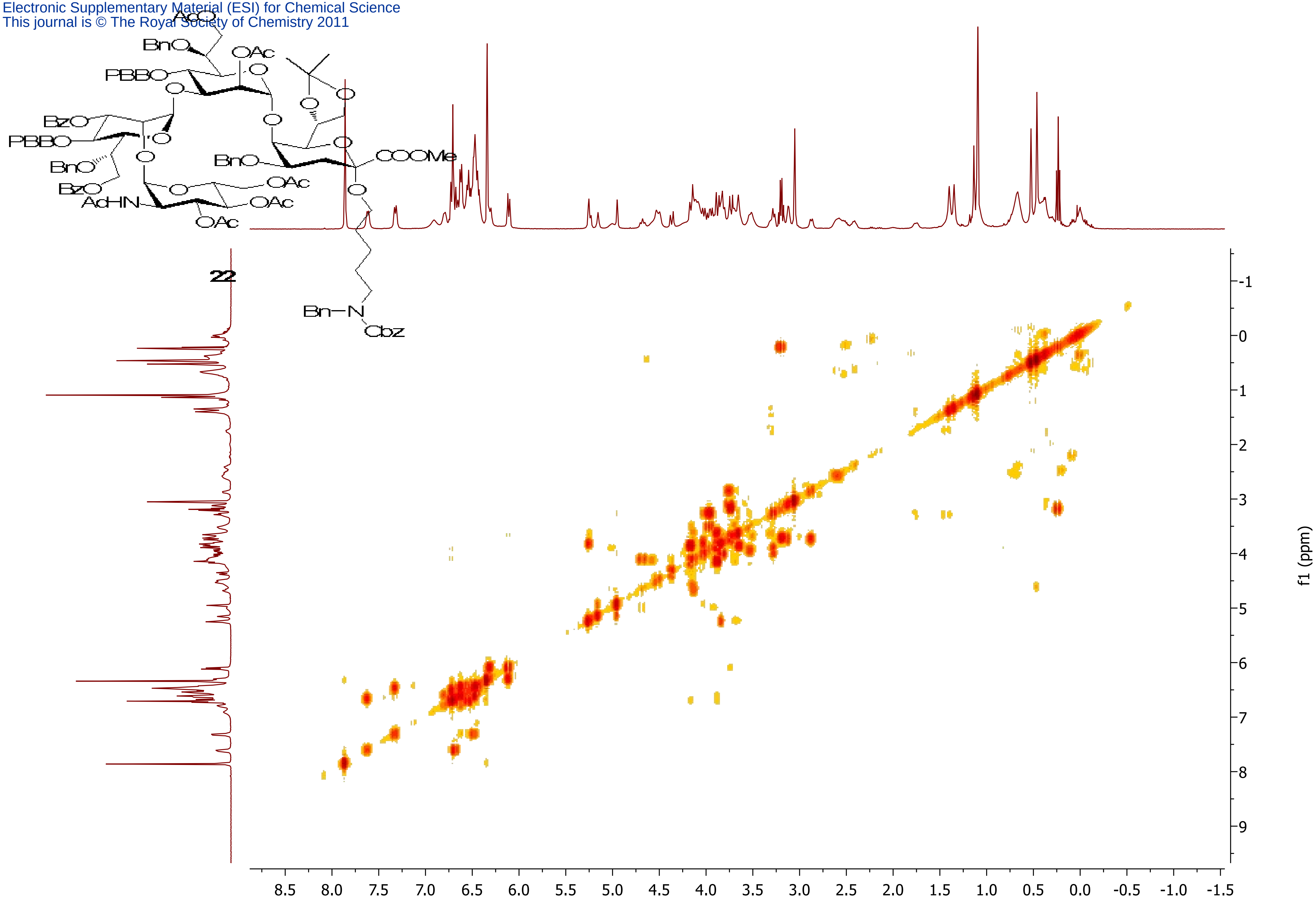

AcO
BnO
OAc
O
PBBO
O
O
O
O
BzO
PBBO
O
O
BnO
COOMe
BnO
O
OAc
BzO
N3
OAc
OAc
O
Bn—N
Cbz

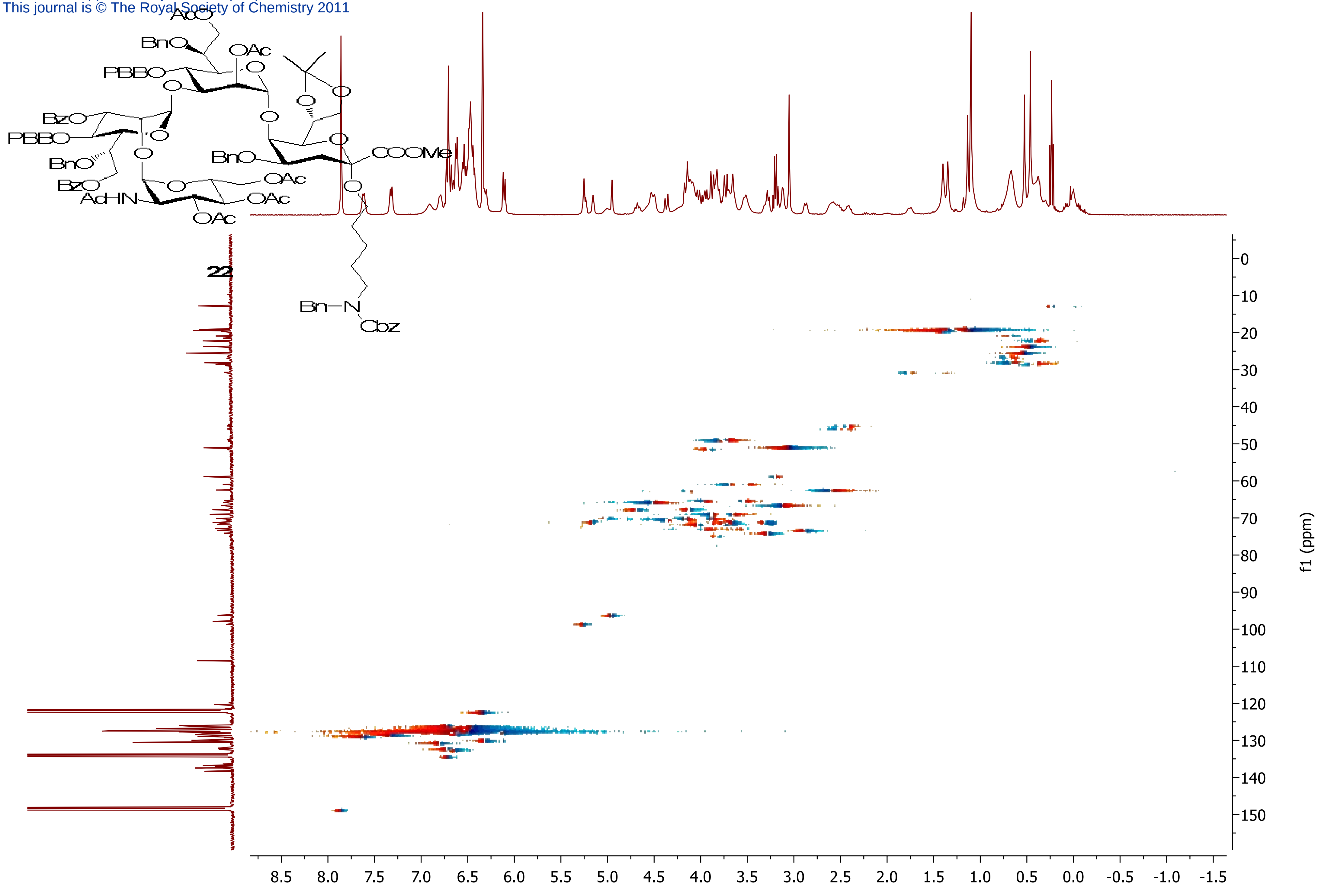
21

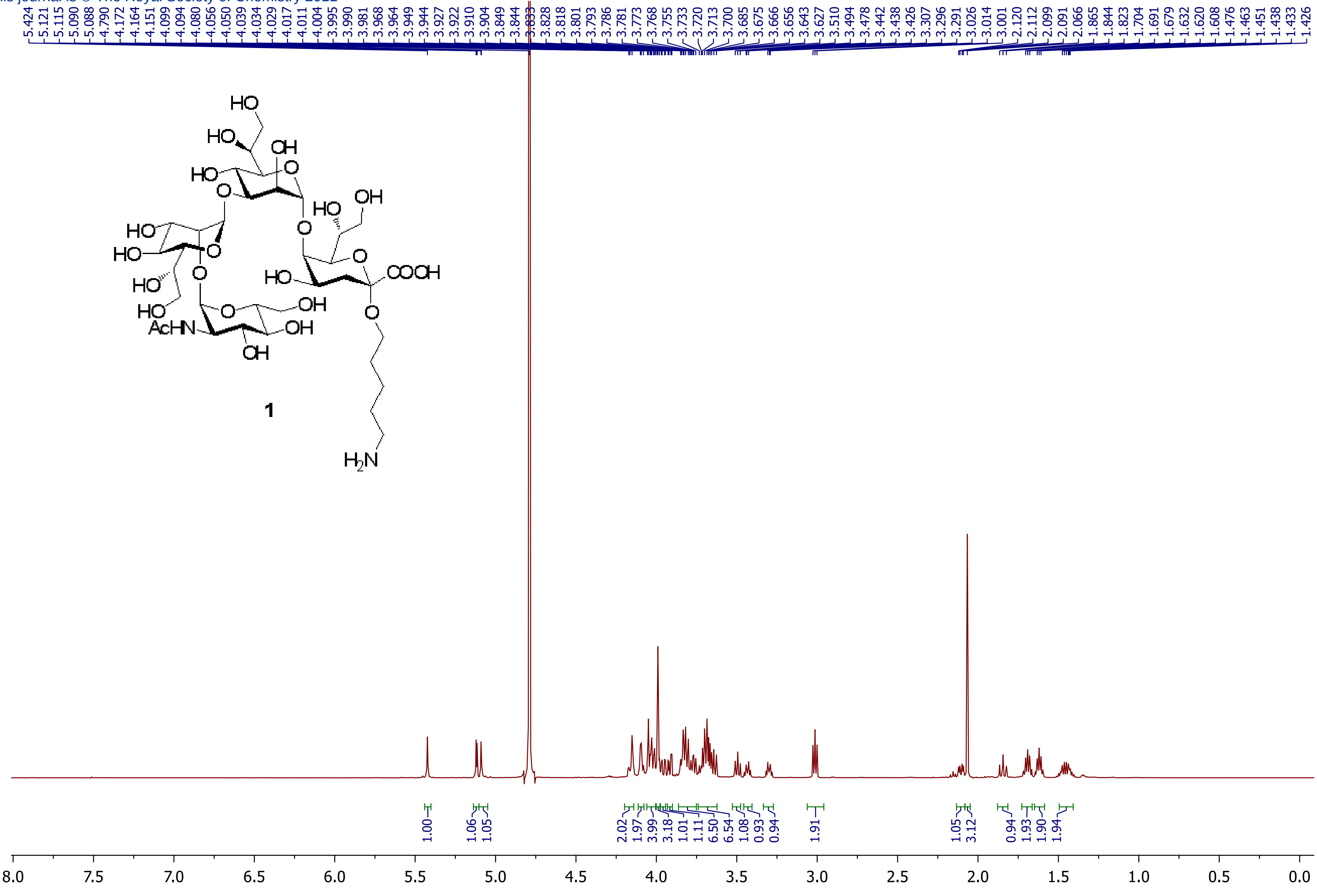

0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5

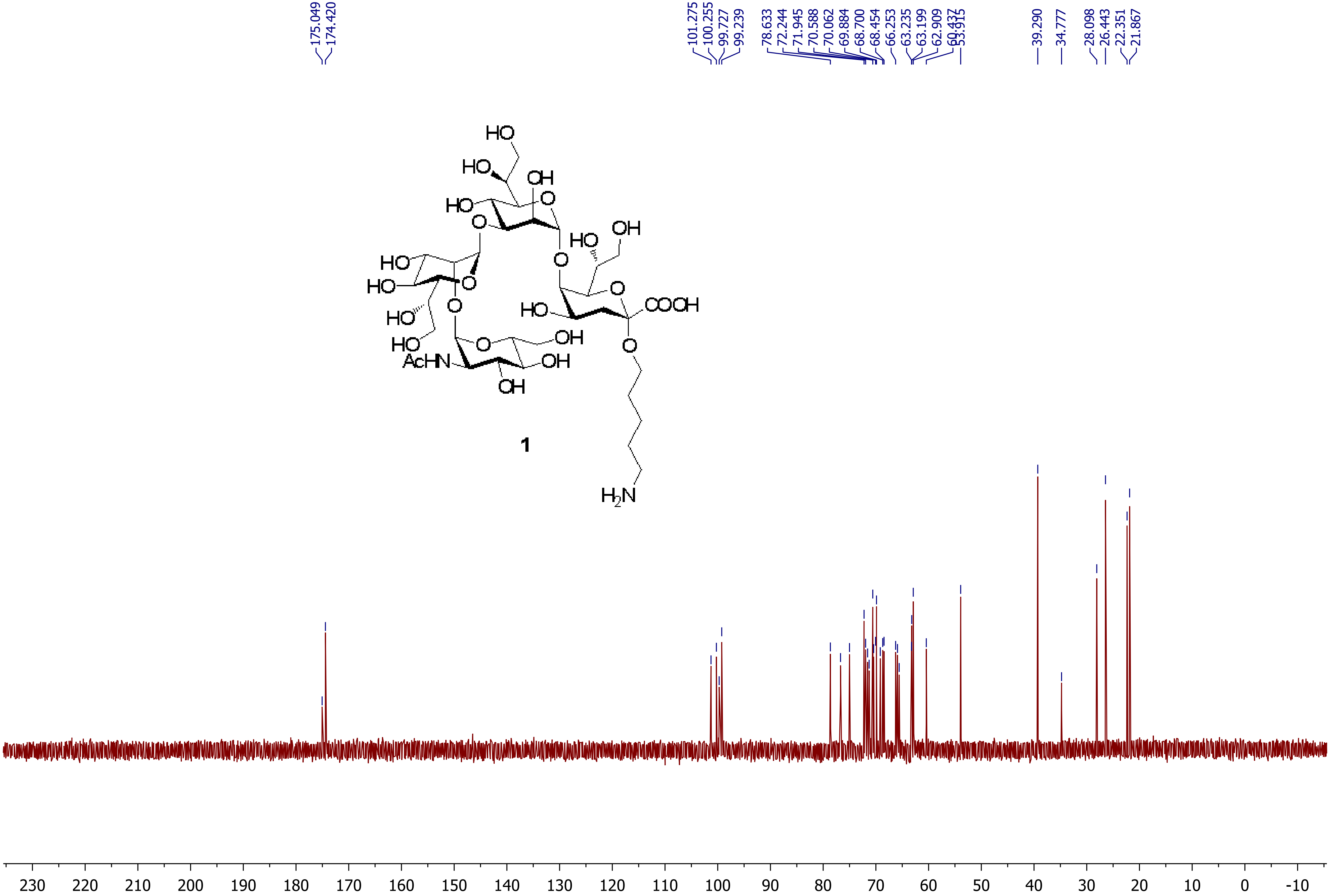

AcO
BnO
OAc
PBBO
BzO
PBBO
BnO
BzO
AcHN
OAc
OAc
OAc
BnO
COOMe
22
Bn—N
Cbz
8.740 8.505 8.489 8.211 8.193 7.609 7.588 7.576 7.556 7.512 7.493 7.436 7.418 7.399 7.387 7.368 7.350 7.324 7.307 7.221 6.133 6.115 6.035 5.884 5.831
5.053 5.024 4.999 4.968 4.771 4.741 4.728 4.705 4.681 4.627 4.597 4.579 4.535 4.086 4.069 4.051 4.003 3.931 3.458 3.291
2.655 2.623 2.280 2.227 2.016 1.981 1.973 1.547 1.406 1.343 1.264 1.253
2.15 2.37 39.88 2.37 2.05 1.00 1.12 1.14 1.31 4.30 1.34 9.14 8.18 6.33 2.21 2.27 2.24 2.03 3.56 1.25 3.35 1.39 1.16 7.31 11.80 4.57 3.40 5.93
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


171.581
171.083
171.000
170.380
170.284
169.033
167.267
166.218
150.620
150.350
150.080
136.214
135.967
135.720
132.432
129.653
129.570
129.417
129.254
129.214
128.711
127.971
124.212
123.964
123.716
110.431
100.626
99.801
98.165
76.009
75.277
74.820
73.679
73.453
73.141
72.528
72.019
70.935
69.691
68.508
67.694
67.241
64.383
62.871
60.746
53.501
53.003
51.156
50.762
47.958
47.095
30.463
30.037
27.421
25.651
24.146
22.816
21.554
21.346
21.287
21.208
21.062
20.915
AcO
BnO
OAc
PBBO
O
BzO
PBBO
BnO
BzO
AcHN
OAc
OAc
OAc
BnO
COOMe
22
Bn
N
Cbz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

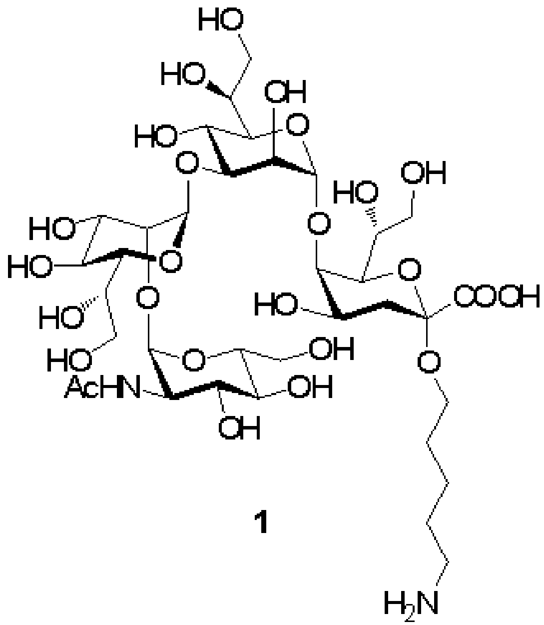

22
f1 (ppm)


AcO
BnO
OAc
PBBO
O
BzO
PBBO
BnO
BzO
AcHN
OAc
OAc
OAc
BnO
COOMe
O
Bn–N
Cbz
22
f1 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
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
-1.0
-1.5

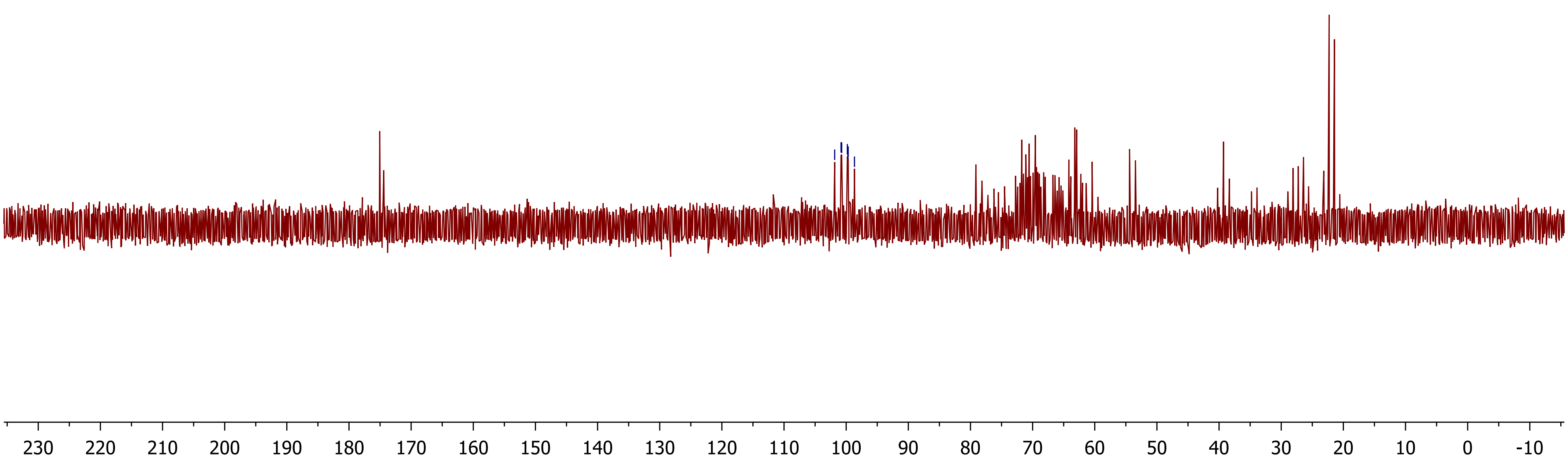


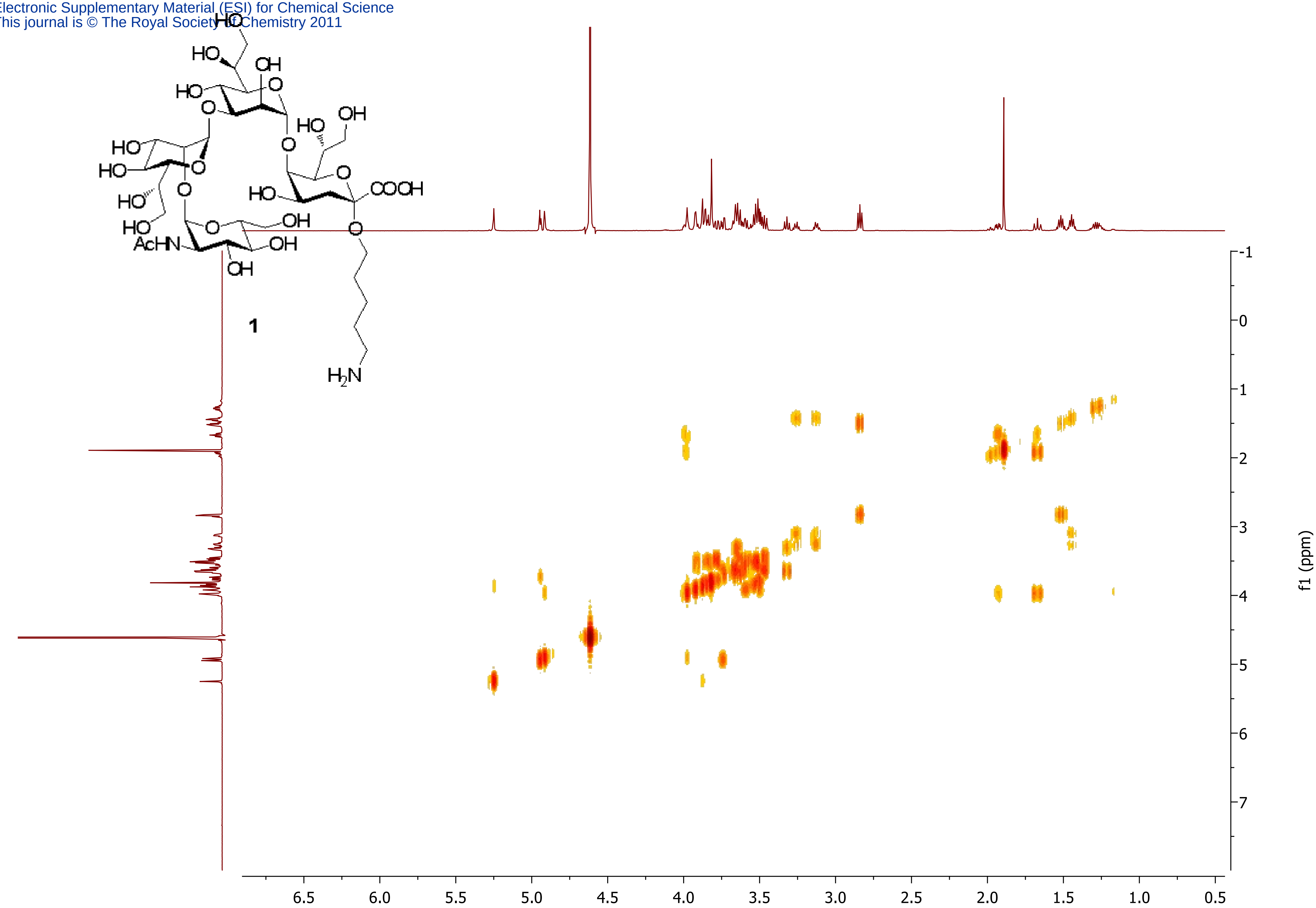

175.049
174.420
101.275
100.255
99.727
99.239
78.633
72.244
71.945
70.588
70.062
69.884
68.700
68.454
66.253
63.235
63.199
62.909
60.437
53.915
39.290
34.777
28.098
26.443
22.351
21.867
HO
HO
OH
O
HO
O
OH
HO
HO
O
HO
O
HO
O
O
COOH
HO
HO
O
OH
HO
AcHN
OH
OH
O
1
H2N
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

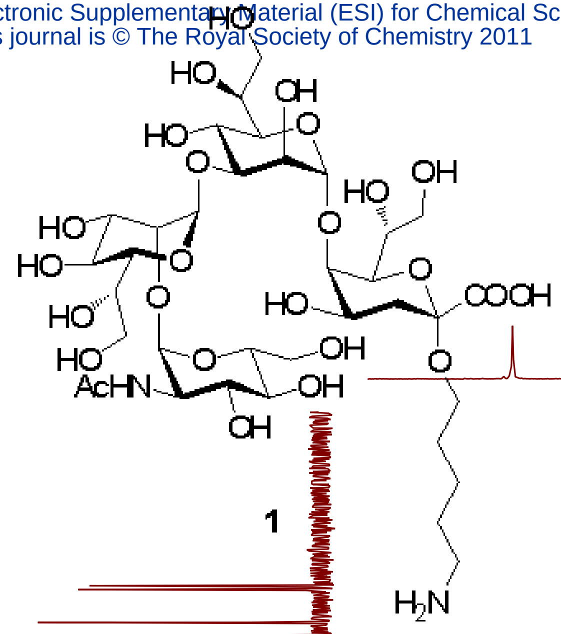
Coupled carbon



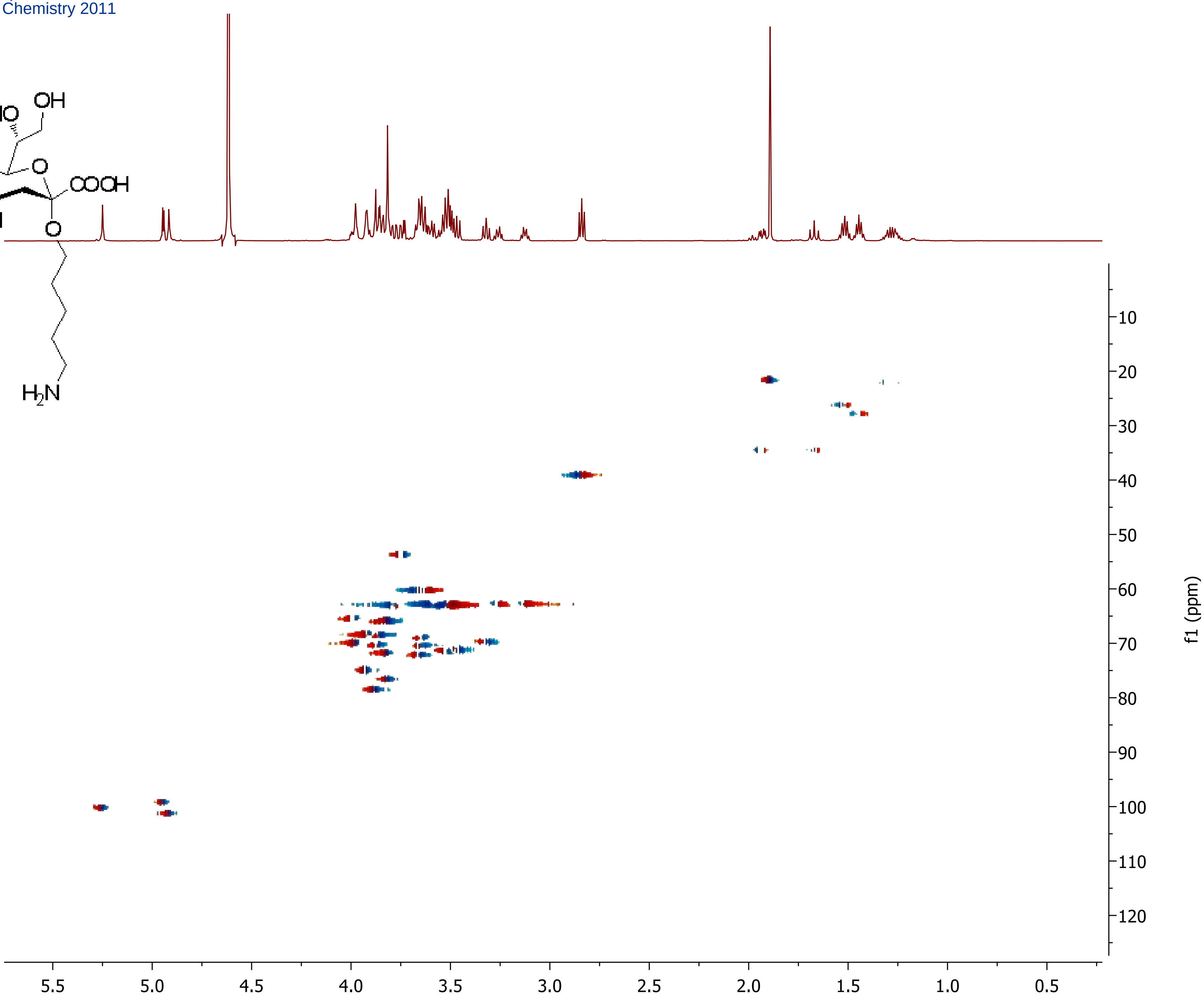
1




HO
HO
OH
O
HO
O
HO
OH
HO
HO
O
O
COOH
HO
HO
O
HO
O
OH
AcHN
O
OH
OH
H2N
1
-1
0
1
2
3
4
5
6
7
f1 (ppm)
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


HO
HO
OH
O
HO
O
OH
HO
HO
O
HO
O
O
COOH
HO
HO
O
OH
HO
AcHN
OH
OH
O
H2N

1


f1 (ppm)
10
20
30
40
50
60
70
80
90
100
110
120
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5