Supplementary Material (ESI) for Chemical Communications
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Supporting Information for:

Stereocontrolled synthesis of fully functionalized D-glucosamine monosaccharides via a domino nitro-Michael/Henry reaction

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General information : All chemicals used were reagent grade and used as supplied except where noted. Dichloromethane (CH_2Cl_2), toluene and tetrahydrofuran (THF) were purified by a Cycle-Tainer Solvent Delivery System. Pyridine and triethylamine were distilled over CaH_2 prior to use. Analytical thin layer chromatography (TLC) was performed on Merck silica gel 60 F254 plates (0.25 mm). Compounds were visualized by UV irradiation or dipping the plate in an anisaldehyde solution followed by heating. Flash column chromatography was carried out using forced flow of the indicated solvent on Fluka Kieselgel 60 (230–400 mesh). ^1H and ^{13}C NMR spectra were recorded on a Varian VXR-300 (300 MHz) or Bruker DRX500 (500 MHz) spectrometer. High-resolution mass spectra (MALDI-HRMS) were performed by the MS-service at the Laboratory for Organic Chemistry (ETH Zürich). ESI-MS were run on an Agilent 1100 Series LC/MSD instrument. IR spectra were recorded on a Perkin-Elmer 1600 FTIR spectrometer. Optical rotations were measured using a Perkin-Elmer 241 polarimeter.

2,4-*O*-Benzylidene-D-erythrose (8), 1,3-*O*-benzylidene-6-deoxy-6-nitro-L-arabitol (10) and 1,3-*O*-benzylidene-6-deoxy-6-nitro-D-xylitol (11): $NaIO_4$ (984 mg, 4.6 mmol, 2.2 equiv.) was added portionwise to a vigorously stirred mixture of $NaHCO_3$ (168 mg, 2.0 mmol, 1 equiv.) in H_2O (4 mL) and 4,6-*O*-benzylidene-D-glucose (536 mg, 2.0 mmol) in CH_2Cl_2 (8 mL). After stirring for 45 min the reaction mixture was diluted with water and extracted three times with CH_2Cl_2. The combined extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield the crude aldehyde **8** (315 mg, 1.51 mmol, 76%) as a colourless oil. Sodium methoxide (4.5 mL of a 0.5 M solution in methanol, 2.26 mmol, 1.5 eq) was added to the crude aldehyde. Nitromethane (0.5 mL, 7.5 mmol, 5 equiv.) was slowly added and the mixture was stirred for 2 h. The mixture was quenched by adding sat. aq. NH_4Cl (20 mL). The mixture was extracted with ethyl acetate and the filtrate was washed with sat. aq. $NaHCO_3$ (10 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated. Purification of the residue by column chromatography (hexanes → ethyl acetate/hexanes, 1/3) gave 241 mg, (0.90 mmol, 59%) of isomer **10** and 92 mg (0.33 mmol, 23%) of isomer **11**, both as white solids. **L-Arabitol (10):** Mp: 101 °C; $[\alpha]_D^{rt}$ = -39.4 (c = 1.0, $CHCl_3$); IR (thin film on NaCl): ν = 3339, 3036, 2863, 1557, 1456, 1377, 1275,

1103, 1042, 999 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.45-7.36 (m, 5H), 5.49 (s, 1H), 4.75 (d, *J* = 11.5 Hz, 1H), 4.64-4.59 (m, 2H), 4.34 (dd, *J* = 5.4, 11.1 Hz, 1H), 3.98 (ddd, *J* = 2.6, 5.4, 8.8, 10.1 Hz, 1H), 3.64 (dd, *J* = 11.1, 10.1 Hz, 1H), 3.64 (dd, *J* = 8.8, 2.5 Hz, 1H), 3.50 (d, *J* = 4.1 Hz, 1H), 3.07 (d, *J* = 2.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.5, 129.2, 128.2, 125.9, 100.9, 79.1, 76.8, 71.6, 70.3, 65.1; ESI-HRMS m/z calcld. for $C_{12}H_{15}NO_6Na^+$: 292.0792, obsd. 292.0796 $[M+Na]^+$. **D-Xylitol (11):** Mp: 137°C; $[\alpha]_D^{rt}$ = -15.9 (c = 1.0, $CHCl_3$); IR (thin film on NaCl): ν = 3562, 3376, 3009, 2862, 1558, 1456, 1382, 1094, 1077, 1043, 1028 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.46-7.36 (m, 5H), 5.53 (s, 1H), 4.80-4.72 (m, 1H), 4.67 (d, *J* = 1.1 Hz, 1H), 4.65 (d, *J* = 0.7 Hz, 1H), 4.37 (dd, *J* = 5.4, 10.8 Hz, 1H), 4.08 (ddd, *J* = 4.9, 5.4, 9.3, 10.3 Hz, 1H), 3.74 (dd, *J* = 2.7, 9.3 Hz, 1H), 3.66 (dd, *J* = 10.3, 10.8 Hz, 1H), 2.72 (d, *J* = 8.1 Hz, 1H,), 2.14 (d, *J* = 4.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.7, 129.4, 128.6, 127.0, 101.9, 82.9, 79.5, 71.9, 67.6, 61.1; ESI-HRMS m/z calcld. for $C_{12}H_{15}NO_6Na^+$: 292.0792, obsd. 292.0801 $[M+Na]^+$.

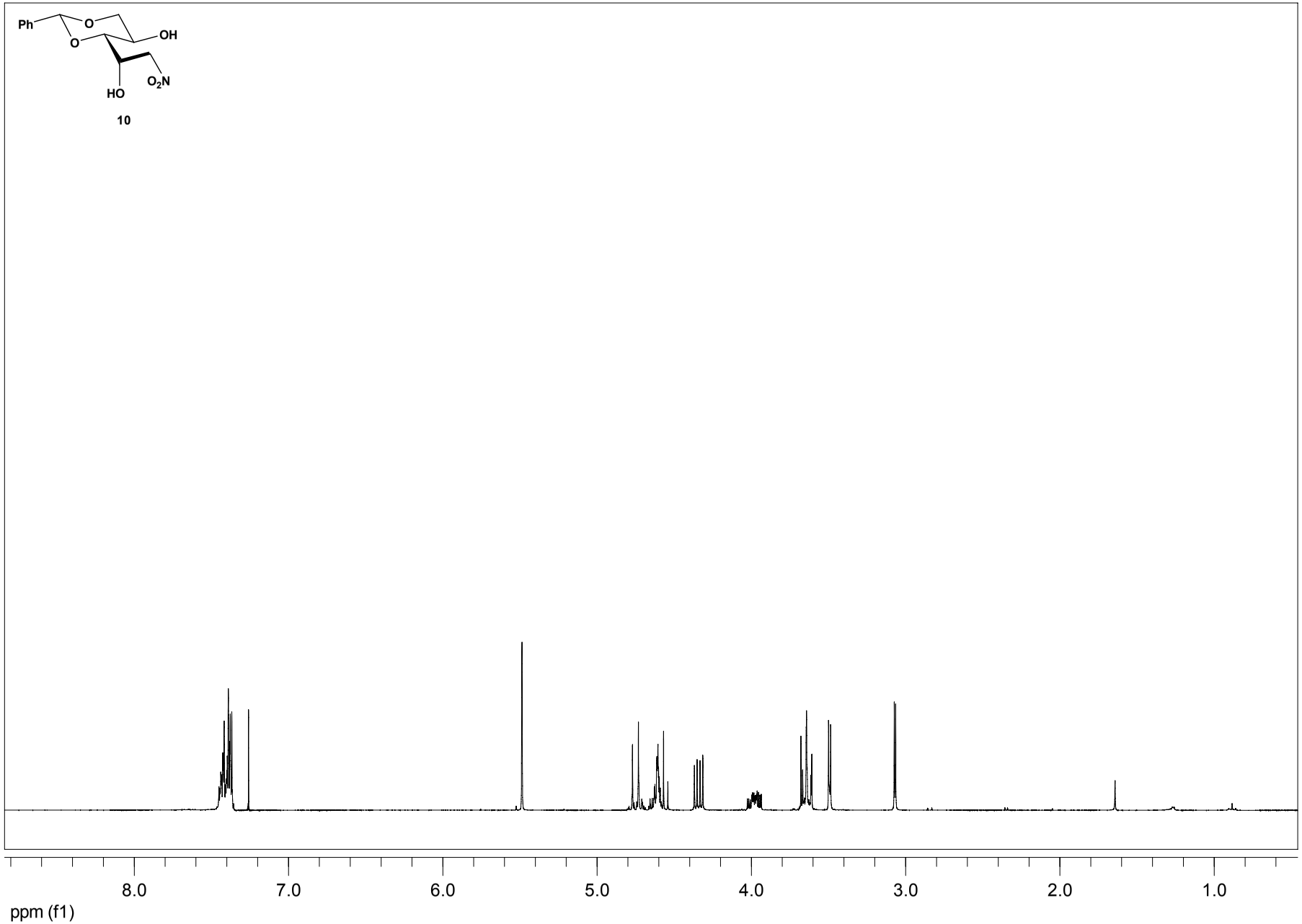
Ethyl 4,6-*O*-benzylidene-2-deoxy-2-nitro-α-D-glucopyranoside (14): LiHMDS (0.28 mL 1.0 M in hexanes, 0.28 mmol, 1.5 equiv.) was added to a cooled (-78 °C) solution of the aldehyde **8** (40 mg, 0.19 mmol) in THF (10 mL). After stirring for 5 min, 2-nitrovinyl ethyl ether **7** (0.02 mL, 0.19 mmol, 1.0 equiv.) was added and stirring was continued for 1 h at the same temperature. The mixture was allowed to warm up to 0 °C, stirred for 1 h, then warmed to rt and stirred for another 30 min. The reaction was quenched by the addition of sat. aq. NH_4Cl. The aqueous layer was extracted with ethyl acetate and the combined extracts were washed with brine, dried ($MgSO_4$), filtered and concentrated. Purification of the residue by column chromatography (hexanes → ethyl acetate/hexanes, 1/4) and subsequent recrystallization from ethyl acetate/hexanes yielded 2-nitropyranoside **14** (51 mg, 0.16 mmol, 83%) as white solid. Mp: 157 °C; $[\alpha]_D^{rt}$ = 33.5 (c = 1.0, $CHCl_3$); IR (thin film on NaCl): ν = 3682, 3618, 3010, 2926, 2854, 2434, 1563, 1522, 1423, 1378, 1248, 1047 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.53-7.48 (m, 2H), 7.31-7.37 (m, 3H), 5.57 (s, 1H), 5.36 (d, *J* = 4.2 Hz, 1H), 4.79 (ddd, *J* = 3.5, 9.5, 9.7 Hz, 1H), 4.53 (dd, *J* = 4.2, 9.7 Hz, 1H), 4.31 (dd, *J* = 4.9, 10.3 Hz, 1H), 3.97 (ddd, *J* = 4.9, 9.6, 9.8 Hz, 1H), 3.78 (dq, *J* = 9.8, 7.1 Hz, 1H), 3.77 (dd, *J* = 9.8, 10.3 Hz, 1H), 3.60 (dd, *J* = 9.5, 9.8 Hz, 1H), 3.52 (dq, *J* = 9.8, 7.1 Hz, 1H), 2.86 (d, *J* = 3.5 Hz, 1H), 1.20 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.5, 129.2, 128.2, 126.0, 102.1, 96.2, 87.1, 80.2, 68.5, 66.7, 64.7, 62.3, 14.6; MALDI-HRMS m/z calcld. for $C_{15}H_{19}NO_7Na^+$: 348.1054, obsd. 348.1051 $[M+Na]^+$.

Ethyl 4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-α-D-glucopyranoside: Zinc dust (342 mg, 5.23 mmol, 20.0 equiv.) was added to a cooled (0 °C) solution of the nitropyranoside **14** (85 mg, 0.26 mmol, 1.0 equiv.) in THF (2 mL), conc. HCl (0.1 mL), acetic acid (0.5 mL) and water (1 mL). After stirring for 2 h, the mixture was diluted with CH_2Cl_2 (100 mL), filtered over celite, washed with H_2O, sat. aq. $NaHCO_3$, and dried over $MgSO_4$. The solvent was removed and the residue was dissolved in THF (2 mL). NEt_3 (0.18 mL, 1.3 mmol, 5.0 equiv.) and trichloroacetyl chloride (0.11 mL, 1 mmol, 4.0 equiv.) were added and the solution was stirred at rt for 2 h. Sat. aq. $NaHCO_3$ solution was added and the mixture was stirred for another hour. The phases were separated and the organic layer was was washed with brine, dried ($MgSO_4$), filtered and concentrated. Purification of the residue by column chromatography (hexanes → ethyl acetate/hexanes, 1/2) delivered 93 mg (0.21 mmol, 81%) of trichloroacetamide as colourless oil. R_f = 0.6 (ethyl acetate/hexanes, 2/3); $[\alpha]_D^{rt}$ = 55.6 (c = 1.0, $CHCl_3$); IR (thin film on NaCl): ν = 3421, 2929, 2352, 2183, 1714, 1516, 1376, 1122, 1073, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.44 (m, 5H), 6.96 (d, *J* = 8.7 Hz, 1H, N*H*), 5.55 (s, 1H, PhC*H*O_2), 4.93 (d, *J* = 3.8 Hz, 1H, 1-H), 4.27 (dd, *J* = 9.8, 4.5 Hz, 1H, H-6a), 4.14 (ddd, *J* = 10.1, 8.8, 3.8 Hz, 1H, H-2),

3.99 (t, *J* = 9.6 Hz, 1H, H-6b), 3.81 (m, 3H, H-3, OC*H*$_2$CH$_3$), 3.51 (m, 2H, H-4, H-5), 2.75 (s, 1H, OH), 1.24 (t, *J* = 7.1 Hz, 3H, OCH$_2$C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.2, 136.9, 129.2, 128.3, 126.2, 101.8, 96.8, 92.3, 81.5, 77.4, 77.0, 76.5, 69.8, 68.6, 64.0, 62.5, 55.3, 14.9; MALDI-HRMS m/z calcld. for $C_{17}H_{20}Cl_3NO_6Na^+$: 462.0248, obsd. 462.0241 $[M+Na]^+$.

Ethyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-α-D-glucopyranoside (15): Trichloroacetamide (77 mg, 0.175 mmo, 1.0 equiv.) was dissolved in DMF (2 mL) and cooled to -20 °C. Benzyl bromide (21 µL, 0.175 mmol, 1.0 equiv.) was added, followed by NaH (60 % dispersion, 15 mg, 0.385 mmol, 2.2 equiv.). After 2 h of stirring at -20 °C, the reaction was quenched by addition of ethanol (1 mL). Solvents were removed at reduced pressure; the residue was dissolved in EtOAc (100 mL) and washed with water and brine. The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed and the residue was purified by column chromatography (hexanes → ethyl acetate/hexanes, 1/4) to afford 89 mg (0.168 mmol, 96%) of benzyl ether **15** as colourless oil. R_f = 0.5 (ethyl acetate/hexanes, 1/4); $[\alpha]_D^{rt}$ = 70.2 (c = 1.0, $CHCl_3$); IR (thin film on NaCl): ν = 2927, 2332, 2174, 1694, 1532, 1451, 1369, 1129, 1107, 1076, 1015 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38 (m, 10H), 6.82 (d, *J* = 9.1 Hz, 1H, N*H*), 5.62 (s, 1H, PhC*H*O$_2$), 4.93 (d, *J* = 11.7 Hz, 1H, PhC*H*O), 4.92 (d, *J* = 3.9 Hz, 1H, H-1), 4.73 (d, *J* = 11.7 Hz, 1H, PhC*H*O), 4.27 (m, 2H, H-6a, H-6b), 3.82 (m, 5H, H-2, H-3, H-4, OC*H*$_2$CH$_3$), 3.53 (m, 1H, H-5), 1.23 (t, *J* = 7.1 Hz, 3H, OCH$_2$C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.5, 137.8, 137.1, 128.9, 128.3, 128.2, 127.7, 127.6, 125.8, 101.2, 97.0, 92.5, 82.6, 76.0, 74.4, 68.9, 64.0, 62.8, 54.6, 15.1; MALDI-HRMS m/z calcld. for $C_{24}H_{26}Cl_3NO_6Na^+$: 552.0718, obsd. 552.0709 $[M+Na]^+$.

Ethyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (16): α-Ethyl glycoside **15** (37 mg, 84 µmol, 1.0 equiv.) was dissolved in dichloroethane (2 mL). Thioethyl-trimethylsilane (68 µL, 0.42 mmol, 5 equiv.), ZnI_2 (134 mg, 0.42 mmol, 5 equiv.) and Bu_4NI (47 mg, 0.126 mmol, 1.5 equiv.) were added. The reaction mixture was stirred at rt for 2 h, benzaldehyde (85 µL, 0.84 mmol, 10 equiv.) was added and the mixture stirred for another 2 h. Reaction was quenched with triethylamine (0.5 mL) and the solvent was removed. The residue was dissolved in CH_2Cl_2 (100 mL) and washed with sat. aq. NH_4Cl solution and brine. The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed and the residue was purified by column chromatography (hexanes → ethyl acetate/hexanes, 1/4) to afford 28 mg (62 µmol, 74%) of β-thioglycoside **16** as colourless oil. The analytical data were in agreement with those reported in the literature (A. A. Sherman, O. N. Yudina, Y. V. Mironov, E. V. Sukhova, A. S. Shashkov, V. M. Menshov, N. E. Nifantiev, *Carbohydr. Res.* **2001**, *336*, 13-46).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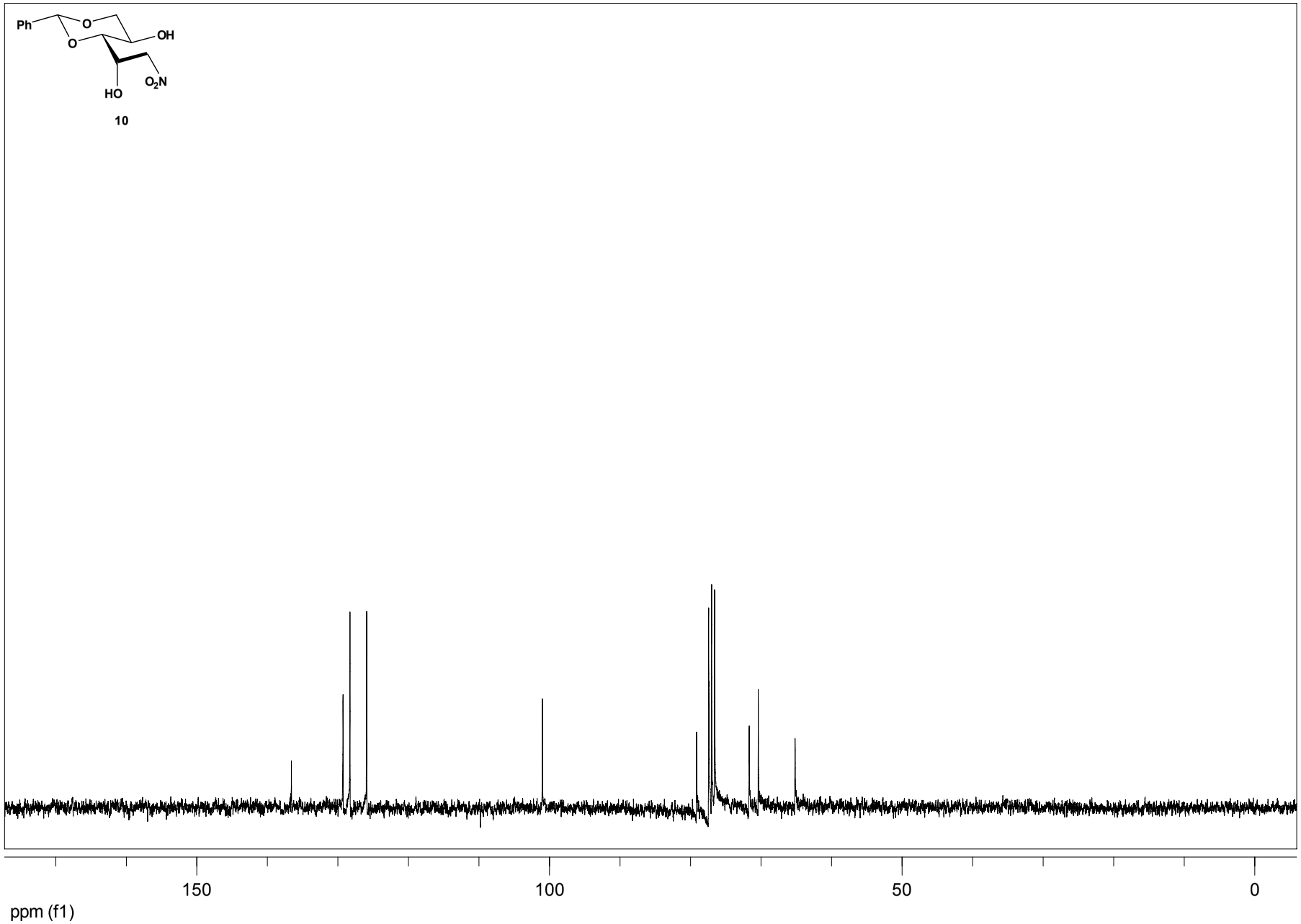
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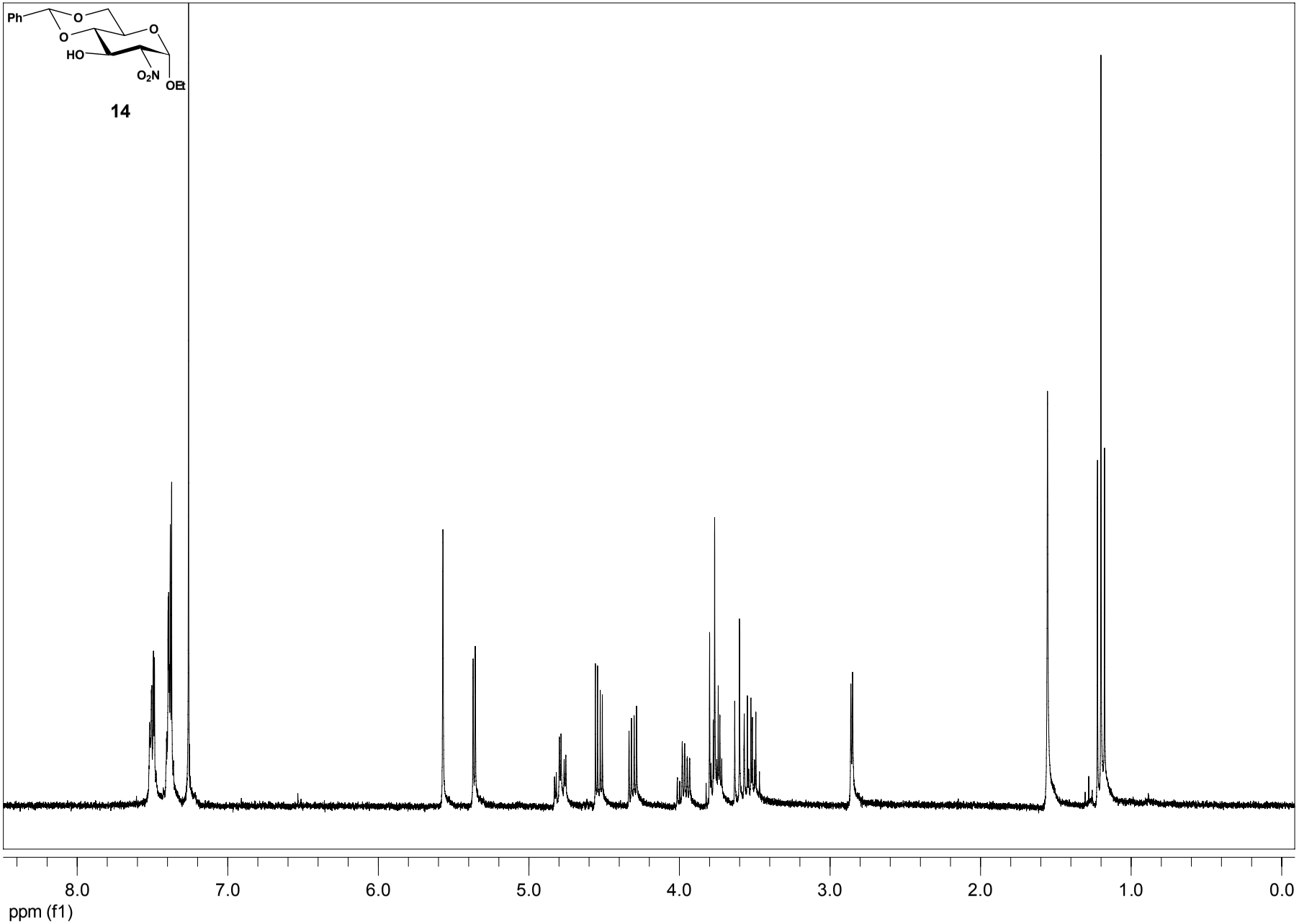
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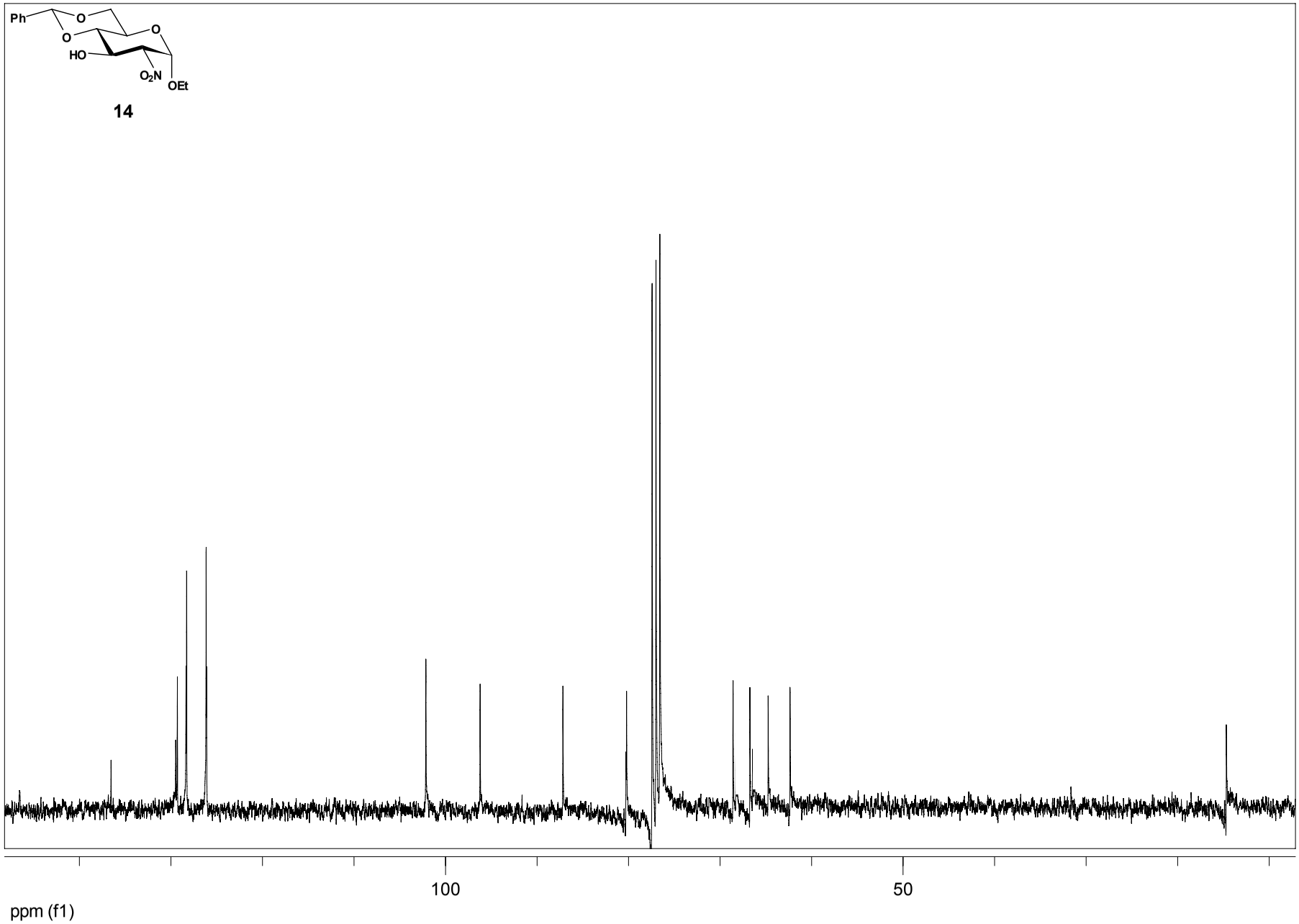
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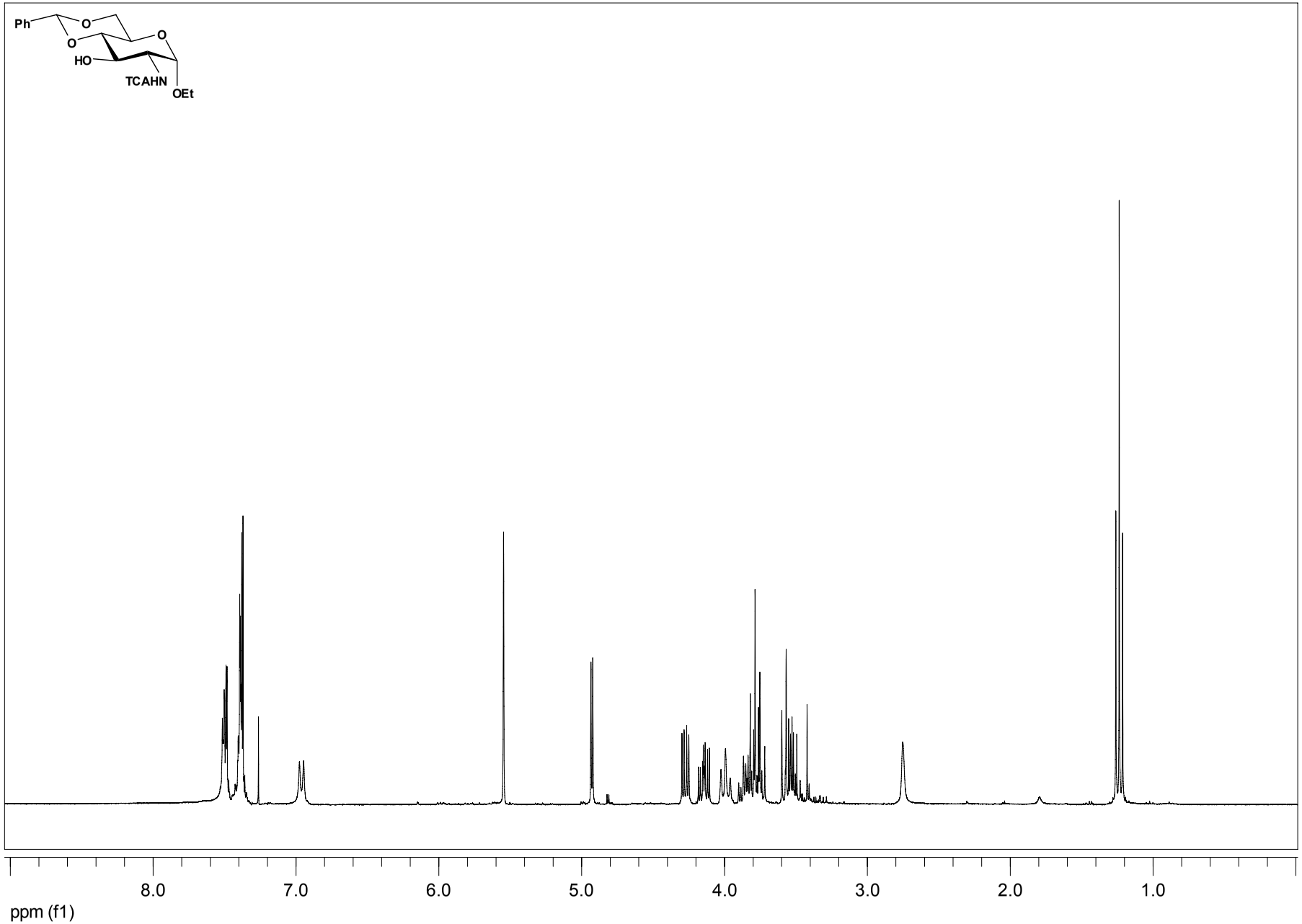
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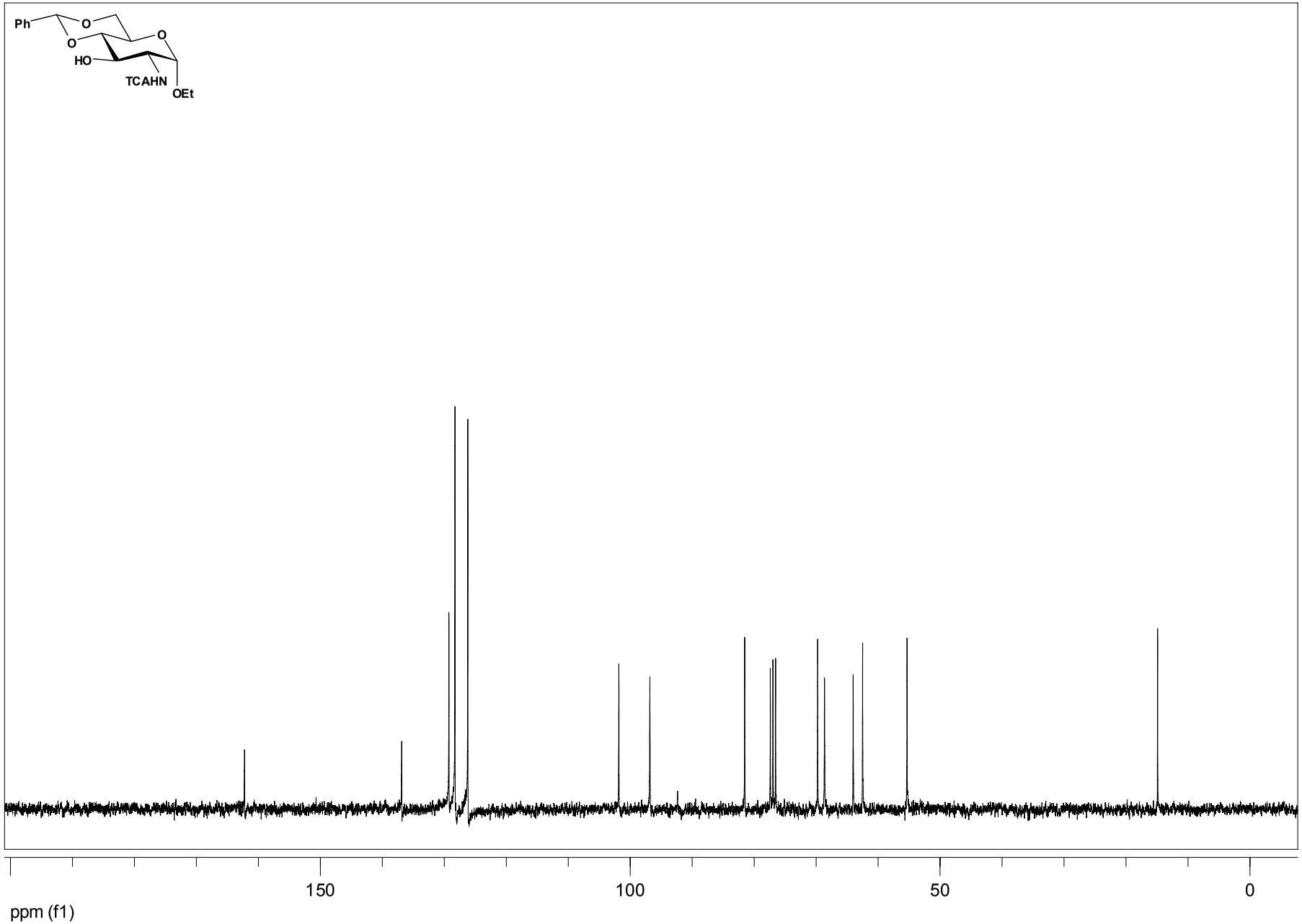
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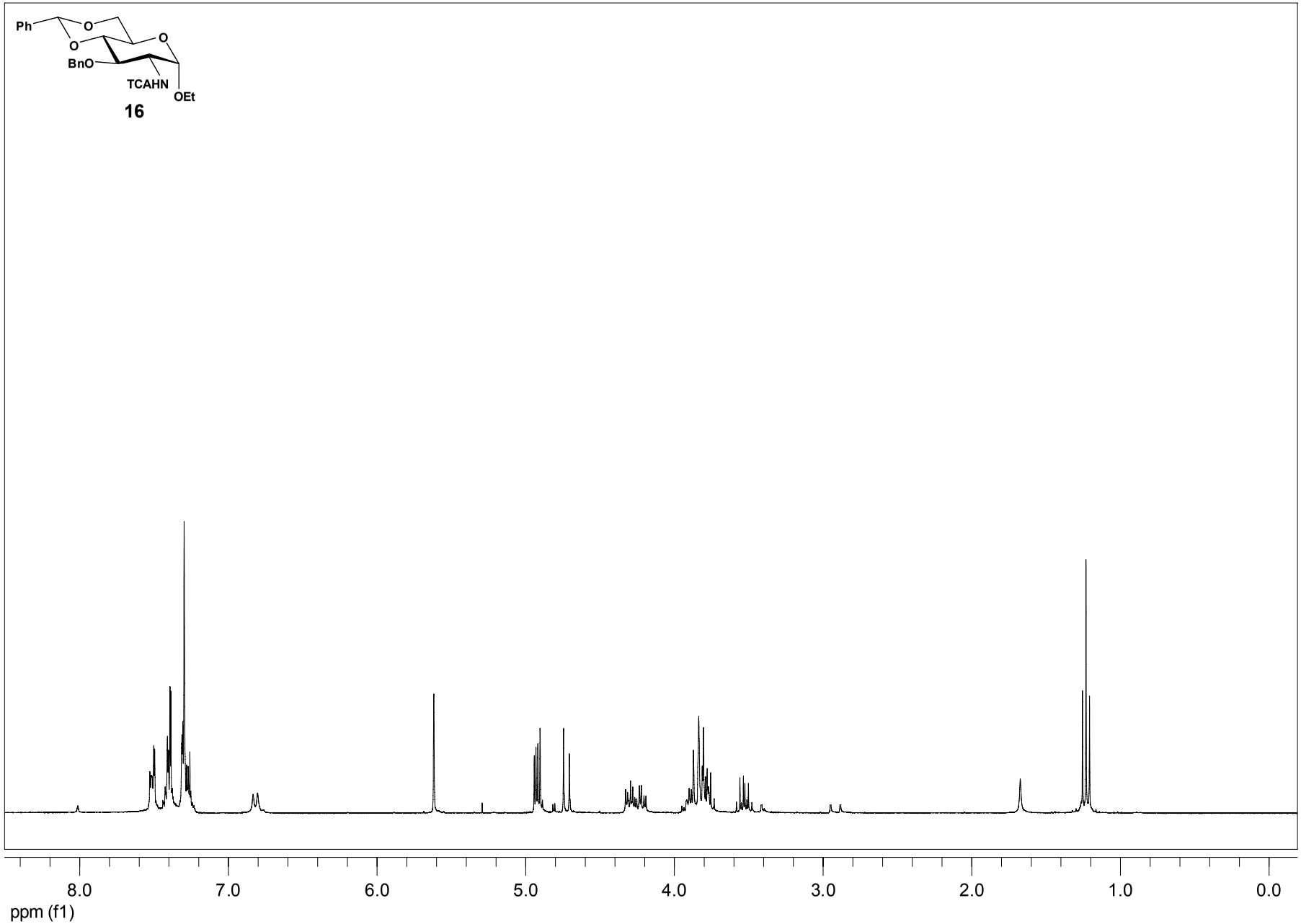
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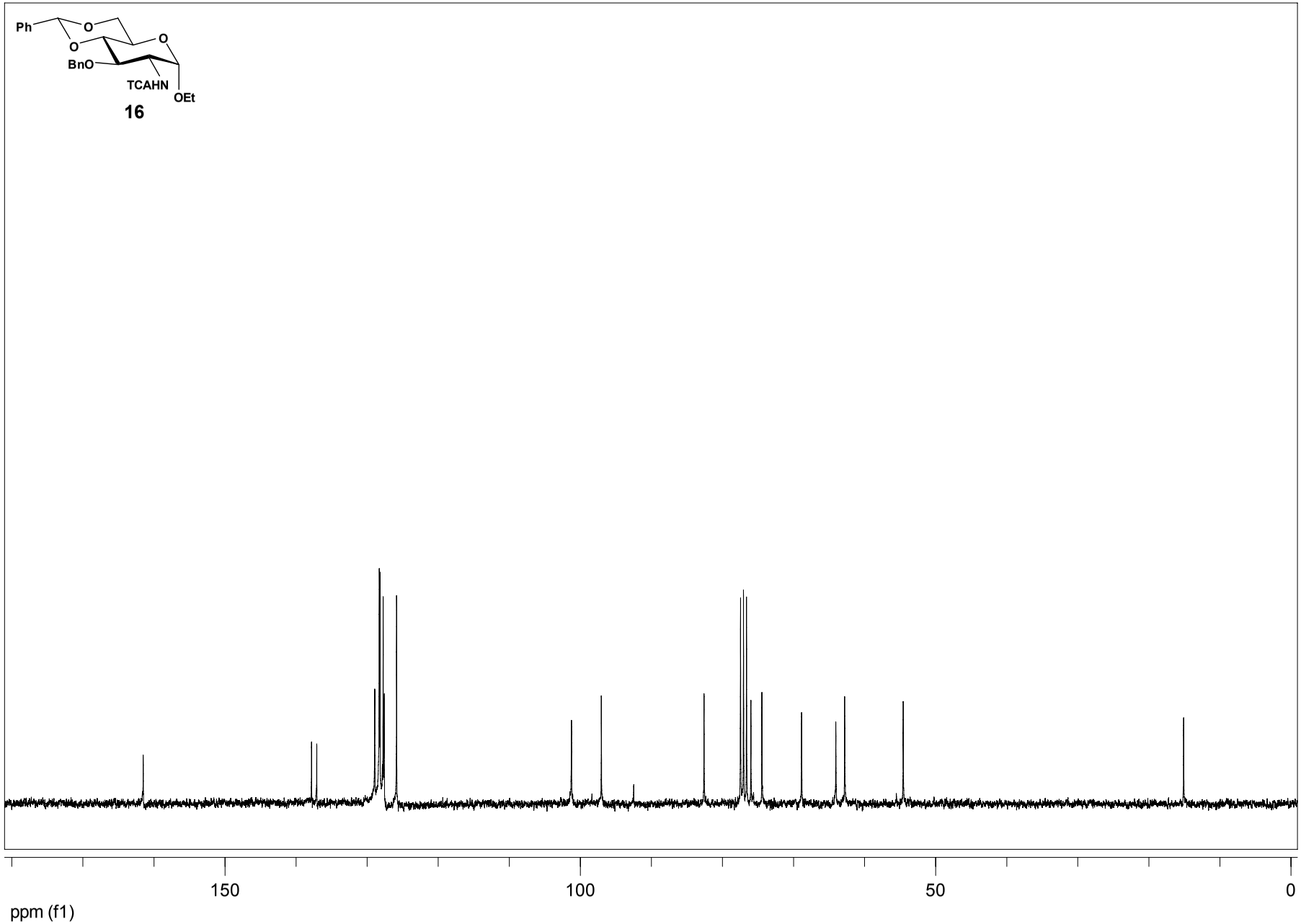
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