Supporting Information

for

Selective Esterifications of Primary Alcohols in a Water Containing Solvent

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General

All reactions were carried out using oven-dried glassware, assembled hot and cooled under a stream of nitrogen before use. Reactions with air sensitive materials were carried out by standard syringe techniques. Commercially available reagents were used as received without further purification. Analytical thin-layer chromatography was performed with 0.25 mm coated commercial silica gel plates (EMD, Silica Gel $60F_{254}$) visualizing at 254 nm, or developed with ceric ammonium molybdate or anisaldehyde solutions by heating on a hot plate. Specified products were purified by flash column chromatography using silica gel 60 (230-400 mesh, Merck). IR absorptions on NaCl plates were run on a FT-IR 1600 spectrometer. 1H-NMR spectral data were obtained using 400, and 500 MHz instruments. 13C NMR spectral data were obtained using a 100, 125 MHz spectrometer. For all NMR spectra, δ values are given in ppm and *J* values in Hz.

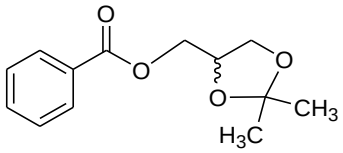
Experimental Procedures

General Procedure (A).

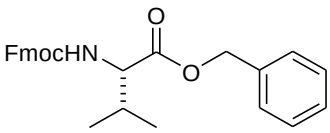
To a stirred solution of carboxylic acid (1 equiv) in (0.2-0.3M) $CH_3CN:H_20$ (95:5) was added oxyma (1.5 equiv), EDCI (1.5 equiv), alcohol (2 equiv) followed by $NaHCO_3$ (6 equiv). The reaction mixture was stirred at rt. Upon completion, all volatiles were evaporated *in vacuo*, and the crude material was dissolved in EtOAc. The crude material was washed with aq. NaHCO3 (3x). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The crude material was purified by silica gel column chromatography (Hexanes:EtOAc 75:25) to give the desired ester.

General Procedure (B).

To a stirred solution of alcohol (1 equiv) in (0.2-0.3M) $CH_3CN:H_20$ (95:5) was added oxyma (3 equiv), EDCI (3 equiv), carboxylic acid (2 equiv) followed by $NaHCO_3$ (10 equiv). The reaction mixture was stirred at rt. Upon completion, all volatiles were evaporated *in vacuo*, and the crude material was dissolved in EtOAc. The crude material was washed with aq. NaHCO3 (3x). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The crude material was purified by silica gel column chromatography (Hexanes:EtOAc 75:25) to give the desired ester.

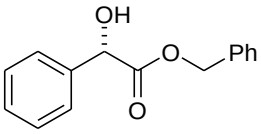


(2,2-dimethyl-1,3-dioxolan-4-yl)methyl benzoate (30a). General Procedure B; Yield: 95%; white solid; TLC (Hexanes:EtOAc 75:25): R_f = 0.75; IR (thin film) υ_{max} = 3453, 1723, 1440, 1215, 1175, 1036, 1054 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.07 (d, *J* = 8.5 Hz, 2H), 7.57 (m, 1H), 7.46 (m, 2H), 4.47 (m, 1H), 4.42 (m, 2H), 4.17 (m, 1H), 3.89 (m, 1H), 1.48 (s, 3H), 1.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.4, 133.2, 129.8, 129.7, 128.4, 109.9, 73.7, 66.4, 65.0, 26.8, 25.4; HRMS (ESI^+): *m/z* calcd for $C_{13}H_{16}O_4$, 236.1049; found 236.1052. Melting Point = 39-40 ^0C.

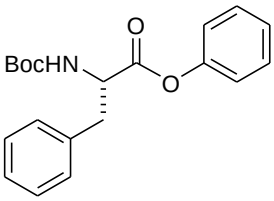


(*S*)-benzyl 2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-methylbutanoate (25). General Procedure A; Yield: 96%; white foam; TLC (Hexanes:EtOAc 75:25): R_f = 0.65; $[\alpha]^{22}_D$ -3.16 (*c* = 0.3, $CHCl_3$); IR (thin film) υ_{max} = 3351, 2963, 1724, 1613, 1516 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.79 (d, *J* = 7.5 Hz, 2H), 7.63 (d, *J* = 7.5 Hz, 2H), 7.38 (m, 9H), 5.36 (d, *J* = 9.0 Hz, 1H), 5.23 (m, 2H), 4.39 (m, 3H), 4.25 (m, 1H), 2.22 (m, 1H),

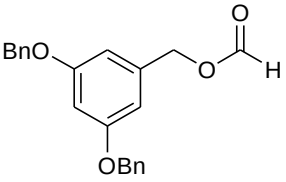
0.98 (m, 3H), 0.90 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.9, 156.2, 143.9, 143.8, 141.3, 135.3, 128.6, 128.5, 128.4, 127.7, 127.1, 125.1, 119.9, 67.1, 58.9, 47.2, 31.4, 19.0, 17.5; HRMS (ESI$^+$): *m/z* calcd for $C_{27}H_{27}NO_4$, 429.1940; found 429.1942.



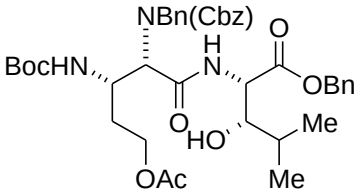
(*S*)-benzyl 2-hydroxy-2-phenylacetate (27). General Procedure A; Yield: 98%; white solid; TLC (Hexanes:EtOAc 75:25): R_f = 0.50; $[\alpha]^{22}_D$ -53.7 (*c* = 1, $CHCl_3$); IR (thin film) υ_{max} = 3447 (br), 1727, 1445, 1210, 1180, 1096, 1066, 710 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.45-7.33 (m, 8H), 7.22 (m, 2H), 5.26 (d, *J* = 12.5 Hz, 1H), 3.45 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 173.6, 138.2, 134.9, 128.6, 128.5, 128.4, 128.3, 128.0, 126.6, 72.9, 67.7; HRMS (ESI$^+$): *m/z* calcd for $C_{15}H_{14}O_3$, 242.0943; found 242.0943. Melting Point = 92-93 ^{0}C.



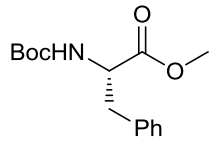
(*S*)-phenyl 2-((tert-butoxycarbonyl)amino)-3-phenylpropanoate (23e). General Procedure A; Yield: 95%; colorless liquid; TLC (Hexanes:EtOAc 75:25): R_f = 0.80; $[\alpha]^{22}_D$ -2.5 (*c* = 0.3, $CHCl_3$); IR (thin film) υ_{max} = 3361, 1735, 1703, 1506, 1366, 1220, 1174 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.39-7.24 (m, 8H), 7.02-7.00 (m, 2H), 5.08 (d, *J* = 6.5 Hz, 1H), 4.84 (d, *J* = 7.0 Hz, 1H), 3.26 (d, *J* = 5.0 Hz, 1H), 1.47 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.6, 155.2, 150.4, 135.8, 129.5, 128.8, 127.3, 126.1, 121.3, 80.2, 54.7, 38.4, 28.4; HRMS (ESI$^+$): *m/z* calcd for $C_{20}H_{23}NO_4$, 341.1627; found 341.1627.



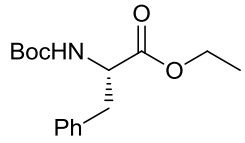
3,5-bis(benzyloxy)benzyl formate (31). General Procedure B; Yield: 95%; colorless liquid; TLC (Hexanes:EtOAc 75:25): R_f = 0.70; IR (thin film) υ_{max} = 3309, 3234, 1888, 1786, 1776, 1548, 1494, 1468, 1294, 855 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.17 (s, 1H,), 7.45-7.36 (m, 10H), 6.62 (m, 3H), 5.16 (s, 2H), 5.06 (s, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 160.8, 160.2, 137.5, 136.7, 128.7, 128.5, 128.1, 127.6, 107.2, 102.1, 70.2, 65.6; HRMS (ESI$^+$): *m/z* calcd for $C_{22}H_{20}O_4$, 348.1362; found 348.1363.



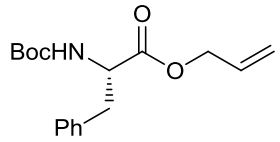
(2*S*,3*S*)-benzyl 2-((2*S*,3*S*)-5-acetoxy-2-(benzyl((benzyloxy)carbonyl)amino)-3-((tert-butoxycarbonyl)amino)pentanamido)-3-hydroxy-4-methylpentanoate (3a). General Procedure A; Yield: 95%; colorless liquid; TLC (Hexanes:EtOAc 50:50): R_f = 0.50; $[\alpha]^{22}_D$ +0.6 (*c* = 0.8, $CHCl_3$); IR (thin film) υ_{max} = 3350 (br), 3015, 2975, 2962, 1728, 1510, 1464, 1412, 1182, 1109, 1063, 1035, 769, 735, 687 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.18-7.48 (m, 15H), 6.62 (s, 1H), 5.16-5.26 (m, 6H),), 4.64-4.61 (m, 2H), 4.41-4.49 (m, 3H), 4.11 (s, 3H), 3.84-3.88 (m, 1H), 3.53-3.57 (m, 1H), 2.19 (s, 1H), 2.08 (s, 3H), 1.69 (m, 1H), 1.39 (s, 9H), 0.89-1.03 (m, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.7, 171.1, 168.4, 155.5, 137.7, 135.9, 128.5, 128.4, 128.2, 128.1, 127.9, 127.8, 127.6, 79.5, 68.1, 64.1, 61.3, 52.2, 20.7, 47.3, 41.8, 41.3, 30.8, 29.7, 28.3, 24.9, 22.8, 22.7, 21.9, 21.8, 20.9, 14.19; HRMS (ESI^+): *m/z* calcd for $C_{40}H_{51}N_3O_{10}$, 733.3574; found 733.3574.



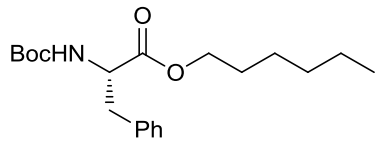
2-tert-Butoxycarbonylamino-3-phenyl-propionic acid methyl ester (11a). General Procedure A; Yield: 96%; colorless liquid; TLC (Hexanes:EtOAc 70:30): R_f = 0.75; $[\alpha]^{22}_D$ -20.1 (*c* = 0.9, $CHCl_3$); IR (thin film) υ_{max} = 3384, 1944, 1840, 1677, 1355, 877 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.31 (m, 3H), 7.14 (d, *J* = 6.5 Hz, 2H), 4.97 (bs, 1H), 4.61 (d, *J* = 5.5 Hz, 1H), 3.72 (s, 3H), 3.10 (m, 2H), 1.43 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.4, 155.1, 136.0, 129.3, 128.6, 127.0, 79.9, 54.4, 52.2, 38.4, 28.3; HRMS (ESI^+): *m/z* calcd for $C_{15}H_{21}NO_4$, 279.1471; found 279.1476.



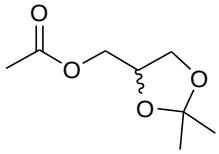
2-tert-Butoxycarbonylamino-3-phenyl-propionic acid ethyl ester (23a). General Procedure A; Yield: 95%; colorless liquid; TLC (Hexanes:EtOAc 70:30): R_f = 0.75; $[\alpha]^{22}_D$ -12.5 (*c* = 0.9, $CHCl_3$); IR (thin film) υ_{max} = 3394, 1949, 1843, 1676, 1345, 879 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.27 (m, 3H), 7.13 (d, *J* = 6.8 Hz, 2H), 4.97 (d, *J* = 7.2 Hz, 1H), 4.56 (q, 1H), 4.15 (q, 2H), 3.08 (m, 2H), 1.42 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.9, 155.1, 136.1, 129.4, 128.5, 127.0, 79.9, 61.4, 54.5, 38.3, 14.1; HRMS (ESI^+): *m/z* calcd for $C_{16}H_{23}NO_4$, 293.1627; found 293.1622.



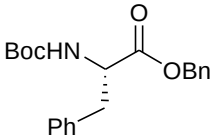
2-tert-Butoxycarbonylamino-3-phenyl-propionic acid allyl ester (23c). General Procedure A; Yield: 98%; colorless liquid; TLC (Hexanes:EtOAc 70:30): R_f = 0.70; $[\alpha]^{22}_D$ -10.1 (*c* = 1.7, $CHCl_3$); IR (thin film) υ_{max} = 3384, 1939, 1833, 1677, 1508, 1348, 1333, 877 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.27 (m, 3H), 7.13 (d, *J* = 7.2 Hz, 2H), 5.86 (m, 1H), 5.26 (dd, 2H), 4.96 (d, *J* = 7.2 Hz, 1H), 4.60 (d, *J* = 6.0 Hz, 1H), 3.09 (m, 2H), 1.41 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.6, 155.1, 136.0, 131.5, 129.4, 128.5, 127.0, 118.9, 79.9, 65.9, 54.5, 38.4, 28.3; HRMS (ESI^+): *m/z* calcd for $C_{17}H_{23}NO_4$, 305.1627; found 305.1621.



2-tert-Butoxycarbonylamino-3-phenyl-propionic acid hexyl ester (23b). General Procedure A; Yield: 97%; colorless liquid; TLC (Hexanes:EtOAc 70:30): R_f = 0.85; $[\alpha]^{22}_D$ -20.6 (*c* = 0.8, $CHCl_3$); IR (thin film) υ_{max} = 3280, 1938, 1842, 1679, 1510, 1349, 877 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.20 (m, 3H), 7.06 (d, *J* = 6.8 Hz, 2H), 4.91 (d, *J* = 8.0 Hz, 1H), 4.50 (q, 1H), 4.01 (m, 2H), 3.01 (m, 2H), 1.52 (m, 2H), 1.35 (s, 9H), 1.21 (m, 6H), 0.82 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.0, 155.1, 136.1, 129.4, 128.5, 127.0, 79.8, 65.5, 54.5, 38.5, 31.4, 28.4, 22.5, 14.0; HRMS (ESI^+): *m/z* calcd for $C_{20}H_{31}NO_4$, 349.2253; found 349.2259.

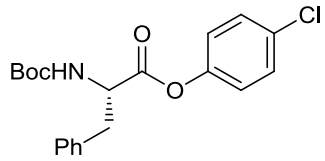


Acetic acid 2,2-dimethyl-[1,3]dioxolan-4-ylmethyl ester (30b). General Procedure B; Yield: 99%; colorless liquid; TLC (Hexanes:EtOAc 70:30): R_f = 0.70; IR (thin film) υ_{max} = 1945, 1376, 1189 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 4.30 (m, 1H), 4.15 (dd, *J* = 4.4 Hz, 1H), 4.06 (m, 2H), 3.71 (dd, *J* = 6.0 Hz, 1H), 2.07 (s, 3H), 1.41 (s, 3H), 1.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.8, 109.9, 73.6, 66.3, 64.9, 26.7, 25.4, 20.9; HRMS (ESI^+): *m/z* calcd for $C_8H_{14}O_4$, 174.0892; found 174.0889.

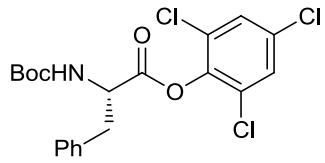


2-tert-Butoxycarbonylamino-3-phenyl-propionic acid benzyl ester (23d). General Procedure A; Yield: 99%; amorphous solid; TLC (Hexanes:EtOAc 70:30): R_f = 0.70; $[\alpha]^{22}_D$ -28.6 (*c* = 1.4, $CHCl_3$); IR (thin film) υ_{max} = 3370, 1918, 1832, 1681, 1351, 1340, 887 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.3 (bs, 3H), 7.31 (m, 2H), 7.24(bs, 3H), 7.06 (bs, 2H), 5.15 (q, 2H), 4.98 (bs, 1H), 4.64 (d, *J* = 5.5 Hz, 1H), 3.10 1.43 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.9, 155.3, 136.1, 135.4, 129.6, 128.8, 127.2, 80.1, 67.3,

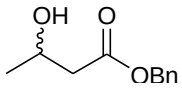
54.6, 54.6, 38.5, 28.5; HRMS (ESI^+): *m/z* calcd for $C_{21}H_{25}NO_4$, 355.1784; found 355.1788.



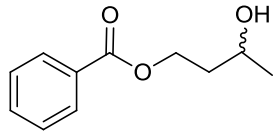
2-tert-Butoxycarbonylamino-3-phenyl-propionic acid 4-chloro-phenyl ester (23f). General Procedure A; Yield: 95%; amorphous solid; TLC (Hexanes:EtOAc 70:30): R_f = 0.65; $[\alpha]^{22}_D$ -30.9 (*c* = 0.8, $CHCl_3$); IR (thin film) υ_{max} = 3381, 1945, 1845, 1672, 1510, 1390, 1350, 870 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.34 (m, 5H), 7.24 (d, *J* = 6.5 Hz, 2H), 6.93 (m, 2H), 5.05 (bs, 1H), 4.81 (bs, 1H), 3.23 (m, 2H), 1.46 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 155.1, 148.8, 135.6, 131.5, 129.5, 128.8, 127.4, 122.7, 80.3, 54.7, 38.3, 28.3; HRMS (ESI^+): *m/z* calcd for $C_{20}H_{22}ClNO_4$, 375.1237; found 375.1233.



2-tert-Butoxycarbonylamino-3-phenyl-propionic acid 2,4,6-trichloro-phenyl ester(23g). General Procedure A; Yield: 90%; amorphous solid; TLC (Hexanes:EtOAc 70:30): R_f = 0.65; $[\alpha]^{22}_D$ -25.9 (*c* = 0.9, $CHCl_3$); IR (thin film) υ_{max} = 3371, 2008, 1843, 1675, 1610, 1516, 1392, 1352, 1148, 1083, 686 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.39 (s, 2H), 7.30 (m, 5H), 4.95 (bs, 2H), 3.43 (m, 1H), 3.15 (m, 1H), 1.40 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.8, 155.0, 142.6, 135.6, 132.4, 129.5, 128.7, 128.1, 127.2, 80.3, 54.3, 38.0, 28.3; HRMS (ESI^+): *m/z* calcd for $C_{20}H_{20}Cl_3NO_4$, 443.0458; found 443.0452.

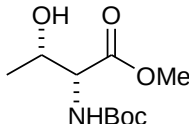


3-Hydroxy-butyric acid benzyl ester (28). General Procedure A; Yield: 99%; Amorphous solid; TLC (Hexanes:EtOAc 70:30): R_f = 0.45; IR (thin film) υ_{max} = 3283, 1955, 1440, 1377, 1301, 311 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36 (m, 5H), 5.16 (s, 2H), 4.22 (m, 1H), 2.94 (s, 1H), 2.51 (m, 2H), 1.23 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.8, 135.6, 128.7, 128.3, 66.6, 64.3, 42.9, 22.5;HRMS (ESI^+): *m/z* calcd for $C_{11}H_{14}O3$, 194.0943; found 194.0950.

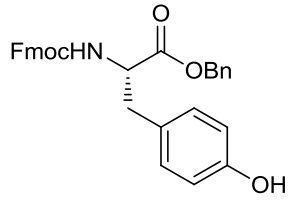


Benzoic acid 3-hydroxy-butyl ester (32). General Procedure B; Yield: 80%; amorphous solid; TLC (Hexanes:EtOAc 70:30): R_f = 0.45; IR (thin film) υ_{max} = 3299, 1910, 1453, 1400, 1244, 819, 321 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.04 (d, *J* = 7.5 Hz, 2H), 7.57

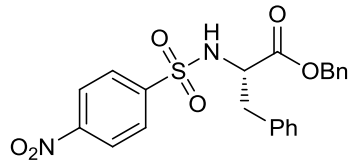
(m, 1H), 7.45 (m, 2H), 4.62 (m, 1H), 4.39 (m, 1H), 3.98 (m, 1H), 2.05 (bs, 1H), 1.97 (m, 1H), 1.86 (m, 1H), 1.27 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.0, 133.1, 130.1, 129.6, 128.4, 64.9, 62.2, 38.3, 23.5; HRMS (ESI^+): *m/z* calcd for $C_{11}H_{14}O_3$, 194.0943; found 194.0949.



2-tert-Butoxycarbonylamino-3-hydroxy-butyric acid methyl ester (29). General Procedure A; Yield: 95%; amorphous solid; TLC (Hexanes:EtOAc 70:30): R_f = 0.45; $[\alpha]^{22}_D$ 20.9 (*c* = 0.8, $CHCl_3$); IR (thin film) υ_{max} = 3301, 1905, 1450, 1403, 1250, 811 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.36 (d, *J* = 8.0 Hz, 1H), 4.27 (m, 2H), 3.76 (s, 3H), 2.37 (bs, 1H), 1.44 (s, 9H), 1.23 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.0, 156.2, 80.1, 68.1, 58.7, 52.5, 28.3, 19.9; HRMS (ESI^+): *m/z* calcd for $C_{10}H_{19}NO_5$, 233.1263; found 233.1268.

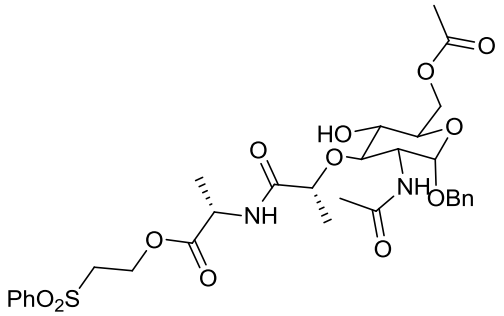


2-(9H-Fluoren-9-ylmethoxycarbonylamino)-3-(4-hydroxy-phenyl)-propionic acid benzyl ester (24). General Procedure A, except 8 eqiv. Of BnOH used; Yield: 95%; amorphous solid; TLC (Hexanes:EtOAc 70:30): R_f = 0.40; $[\alpha]^{22}_D$ -29.9 (*c* = 1.0, $CHCl_3$); IR (thin film) υ_{max} = 3801, 3377, 1915, 1866, 1670, 1433, 1377, 1312, 1220, 881 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.55 (bs, 2H), 7.41-7.30 (m, 8H), 6.84 (d, *J* = 8.0 Hz, 2H), 6.66 (d, *J* = 8.0 Hz, 2H), 5.25 (d, *J* = 8.0 Hz, 1H), 5.16 (q, 2H), 4.79 (bs, 1H), 4.67 (m, 1H), 4.43 (m, 1H), 4.35 (t, *J* = 8.5 Hz, 1H), 4.20 (m, 1H), 3.04 (bs, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.6, 155.8, 154.9, 144.1, 141.5, 135.3, 130.8, 128.9, 127.8, 127.3, 125.3, 120.2, 115.7, 67.5, 67.2, 55.1, 47.4, 37.6; HRMS (ESI^+): *m/z* calcd for $C_{31}H_{27}NO_5$, 493.1889; found 493.1892.

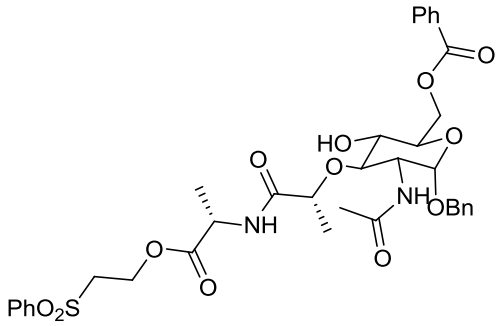


2-(4-Nitro-benzenesulfonylamino)-3-phenyl-propionic acid benzyl ester (26). General Procedure A; Yield: 98%; amorphous solid; TLC (Hexanes:EtOAc 70:30): R_f = 0.55; $[\alpha]^{22}_D$ -26.8 (*c* = 1.0, $CHCl_3$); IR (thin film) υ_{max} = 3733, 3367, 1921, 1866, 1603, 1433, 1357, 1270, 801 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.12 (d, *J* = 8.5 Hz, 2H), 7.80 (d, *J* = 9.0 Hz, 2H), 7.35 (m, 3H), 7.18 (m, 5H), 7.01 (d, *J* = 6.5 Hz, 2H), 5.19 (d, *J* = 9.0 Hz, 1H), 4.97 (q, 2H), 4.30 (m, 1H), 3.13-3.06 (ddd, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ

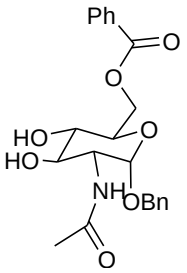
170.4, 149.9, 145.4, 134.6, 134.4, 129.4, 128.9, 128.8, 128.7, 128.2, 127.5, 124.1, 67.8, 57.0, 39.3; HRMS (ESI$^+$): *m/z* calcd for $C_{22}H_{20}N_2O_6S$, 440.1042; found 440.1046.



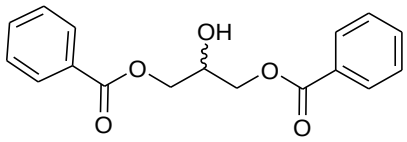
2-[2-(2-Acetoxymethyl-5-acetylamino-6-benzyloxy-3-hydroxy-tetrahydro-pyran-4-yloxy)-propionylamino]-propionic acid 2-benzenesulfonyl-ethyl ester (36a). General Procedure A; Yield: 95%; amorphous solid; TLC (Hexanes:EtOAc 70:30): R_f = 0.50; $[\alpha]^{22}_D$ + 125 (*c* = 1.1, $CHCl_3$); IR (thin film) υ_{max} = 3798, 3267, 3211, 1941, 1909, 1876, 1683, 1655, 1470, 1397, 1375, 1274, 721 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.08 (d, *J* = 7.0 Hz, 2H), 7.90 (d, *J* = 6.5 Hz, 2H), 7.67 (m, 1H), 7.60-7.56 (m, 3H), 7.46 (m, 2H), 7.39-7.32 (m, 5H), 6.95 (d, *J* = 5.5 Hz, 1H), 6.27 (dd, 1H), 4.97 (s, 1H), 4.72 (m, 2H), 4.52-4.39 (m, 4H), 4.28-4.10 (m, 4H), 3.93 (bs, 1H), 3.60 (m, 2H), 3.44 (bs, 1H), 3.38 (m, 2H), 1.93 (d, *J* = 3.0 Hz, 3H), 1.42 (dd, 3H), 1.32 (dd, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.8, 171.9, 170.4, 139.1, 136.9, 134.2, 129.5, 128.7, 128.3, 128.1, 97.2, 80.0, 77.9, 70.5, 58.0, 54.9, 52.6, 47.9, 23.4, 20.9, 19.0, 17.2; HRMS (ESI$^+$): *m/z* calcd for $C_{31}H_{40}N_2O_{12}S$, 664.2302; found 664.2305.



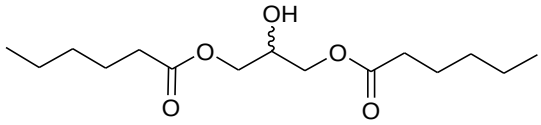
Benzoic acid 5-acetylamino-4-{1-[1-(2-benzenesulfonyl-ethoxycarbonyl)-ethylcarbamoyl]-ethoxy}-6-benzyloxy-3-hydroxy-tetrahydro-pyran-2-ylmethyl ester (36b). General Procedure A; Yield: 98%; amorphous solid; TLC (Hexanes:EtOAc 70:30): R_f = 0.50; $[\alpha]^{22}_D$ + 122 (*c* = 1.2, $CHCl_3$); IR (thin film) υ_{max} = 3808, 3271, 3231, 1941, 1930, 1709, 1681, 1402, 1357, 1270, 1214, 818 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.93 (d, *J* = 8.5 Hz, 2H), 7.70 (t, *J* = 7.0 Hz, 1H), 7.60 (t, *J* = 7.5 Hz, 2H), 7.39-7.32 (m, 5H), 6.92 (d, *J* = 7.0 Hz, 1H), 6.13 (d, *J* = 7.0 Hz, 1H), 4.95 (s, 1H), 4.70 (d, *J* = 12.0 Hz, 1H), 4.53-4.40 (m, 4H), 4.30-4.13 (m, 4H), 3.81 (d, *J* = 8.5 Hz, 1H), 3.58-3.50 (m, 2H), 3.47-3.36 (m, 2H), 3.14 (s, 1H), 2.15 (s, 3H), 1.93 (s, 3H), 1.43 (d, *J* = 6.5 Hz, 3H), 1.34 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 173.2, 171.9, 170.5, 166.8, 139.4, 137.1, 134.2, 132.8, 129.7, 128.9, 128.3, 128.1, 127.9, 127.5, 97.2, 80.2, 77.9, 70.5, 70.0, 63.5, 58.1, 54.9, 53.0, 47.9, 23.5, 19.0, 17.2; HRMS (ESI$^+$): *m/z* calcd for $C_{36}H_{42}N_2O_{12}S$, 726.2458; found 726.2454.



Benzoic acid 5-acetylamino-6-benzyloxy-3,4-dihydroxy-tetrahydro-pyran-2-ylmethyl ester (34). General Procedure B; Yield: 90%; amorphous solid; TLC (Hexanes:EtOAc 70:30): R_f = 0.30; $[\alpha]^{22}_D$ +210 (*c* = 1.2, $CHCl_3$); IR (thin film) υ_{max} = 3788, 3776, 3260, 1902, 1870, 1689, 1431, 1420, 1398, 1242, 1184, 819 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.06 (d, *J* = 7.2 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.34 (m, 5H), 5.84, (d, *J* = 8.4 Hz, 1H), 4.92 (d, *J* = 4.0 Hz, 4.74 (m, 2H), 4.49 (m, 2H), 4.11 (m, 1H), 3.91 (m, 1H), 3.76 (m, 1H), 3.55 (m, 1H), 3.43 (d, *J* = 3.5 Hz, 1H), 1.99 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.9, 167.1, 136.8, 133.4, 129.8, 128.7, 128.5, 128.4, 128.1, 96.7, 73.9, 71.2, 70.3, 69.8, 63.5, 53.6, 23.3; HRMS (ESI^+): *m/z* calcd for $C_{22}H_{25}NO_7$, 415.1631; found 415.1635.

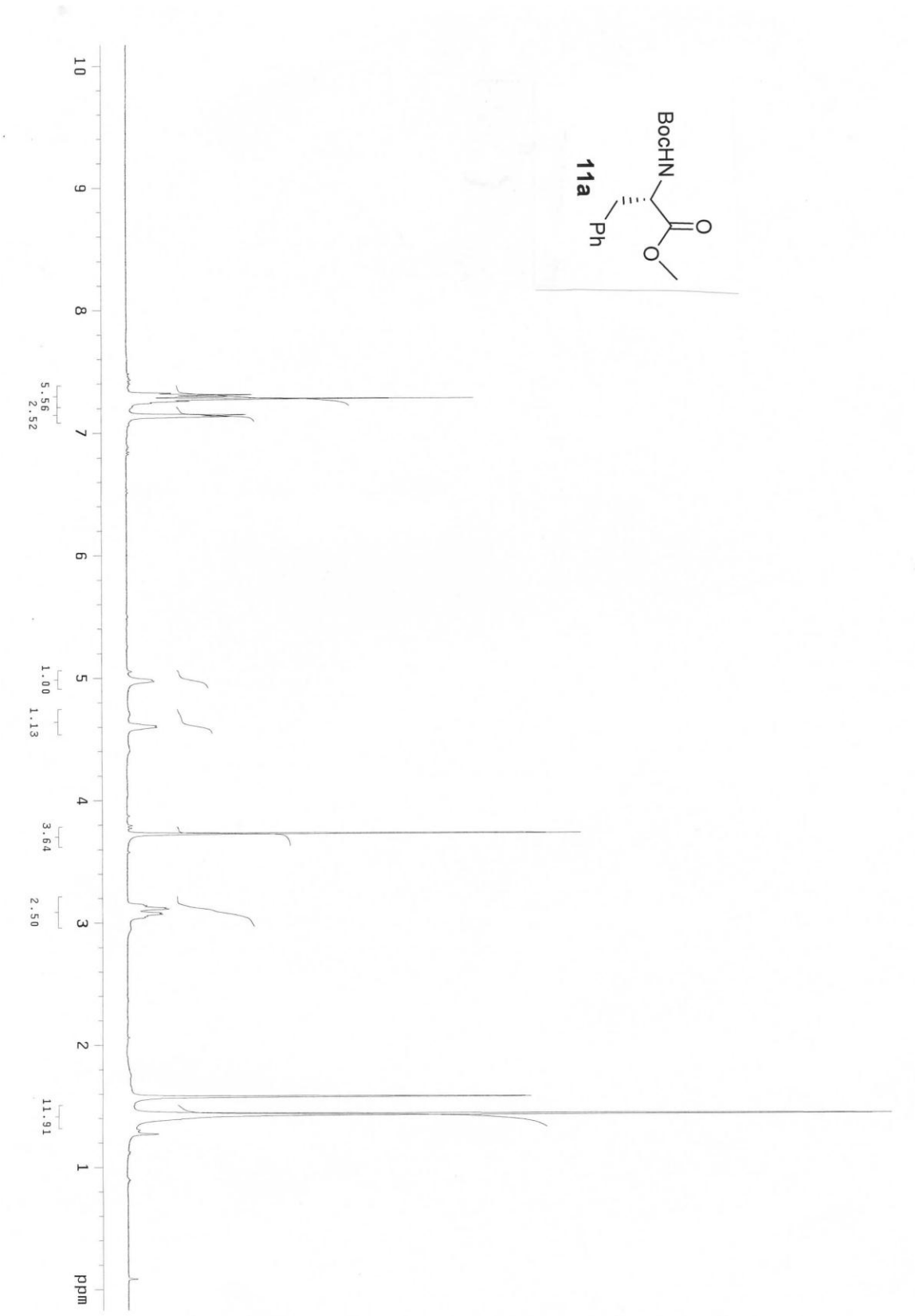


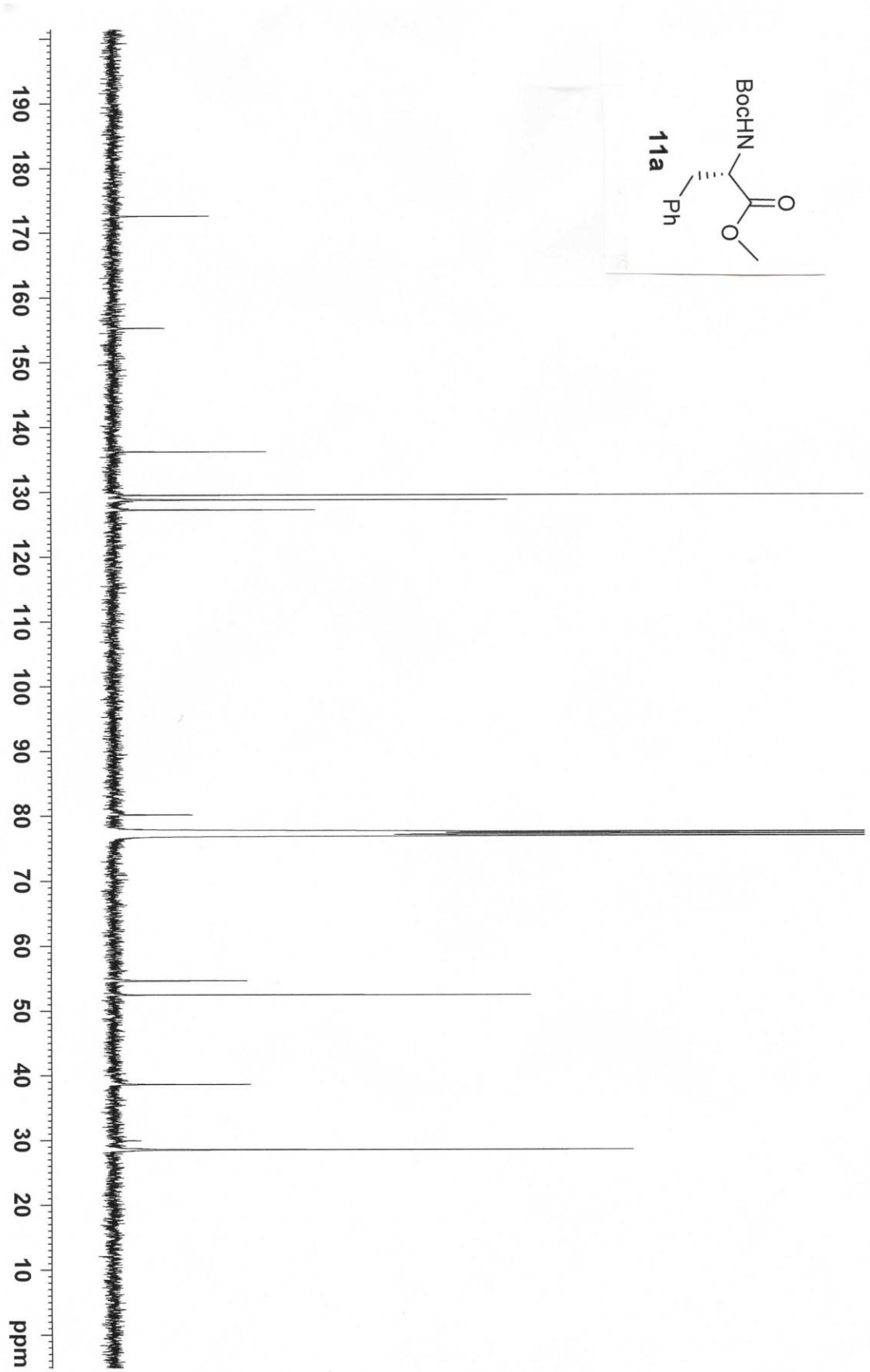
Benzoic acid 3-hexanoyloxy-2-hydroxy-propyl ester (33a). General Procedure B; Yield: 85%; amorphous solid; TLC (Hexanes:EtOAc 70:30): R_f = 0.55; IR (thin film) υ_{max} = 3693, 1915, 1400, 1387, 1231, 819 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.05 (d, *J* = 7.2 Hz, 4H), 7.57 (t, *J* = 7.2 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 4H), 4.51 (m, 4H), 4.39 (m, 1H), 2.68 (d, *J* = 4.2Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.7, 133.4, 129.5, 128.5, 68.7, 65.9; HRMS (ESI^+): *m/z* calcd for $C_{17}H_{16}O_5$, 300.0998; found 300.0993.



Hexanoic acid 3-hexanoyloxy-2-hydroxy-propyl ester (33b). General Procedure B; Yield: 90%; amorphous solid; TLC (Hexanes:EtOAc 70:30): R_f = 0.60; IR (thin film) υ_{max} = 3701, 1971, 1888, 1692, 1415, 1348, 1270, 654 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 4.17 (m, 4H), 4.07 (m, 1H), 2.41 (d, *J* = 4.2 Hz, 1H), 2.33 (t, *J* = 7.6 Hz, 4H), 1.62 (m, 4H), 1.30 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 74.0, 68.4, 65.0, 34.1, 31.3, 24.6, 22.4, 13.9; HRMS (ESI^+): *m/z* calcd for $C_{17}H_{16}O_5$, 300.0998; found 300.0993.

NMR spectra

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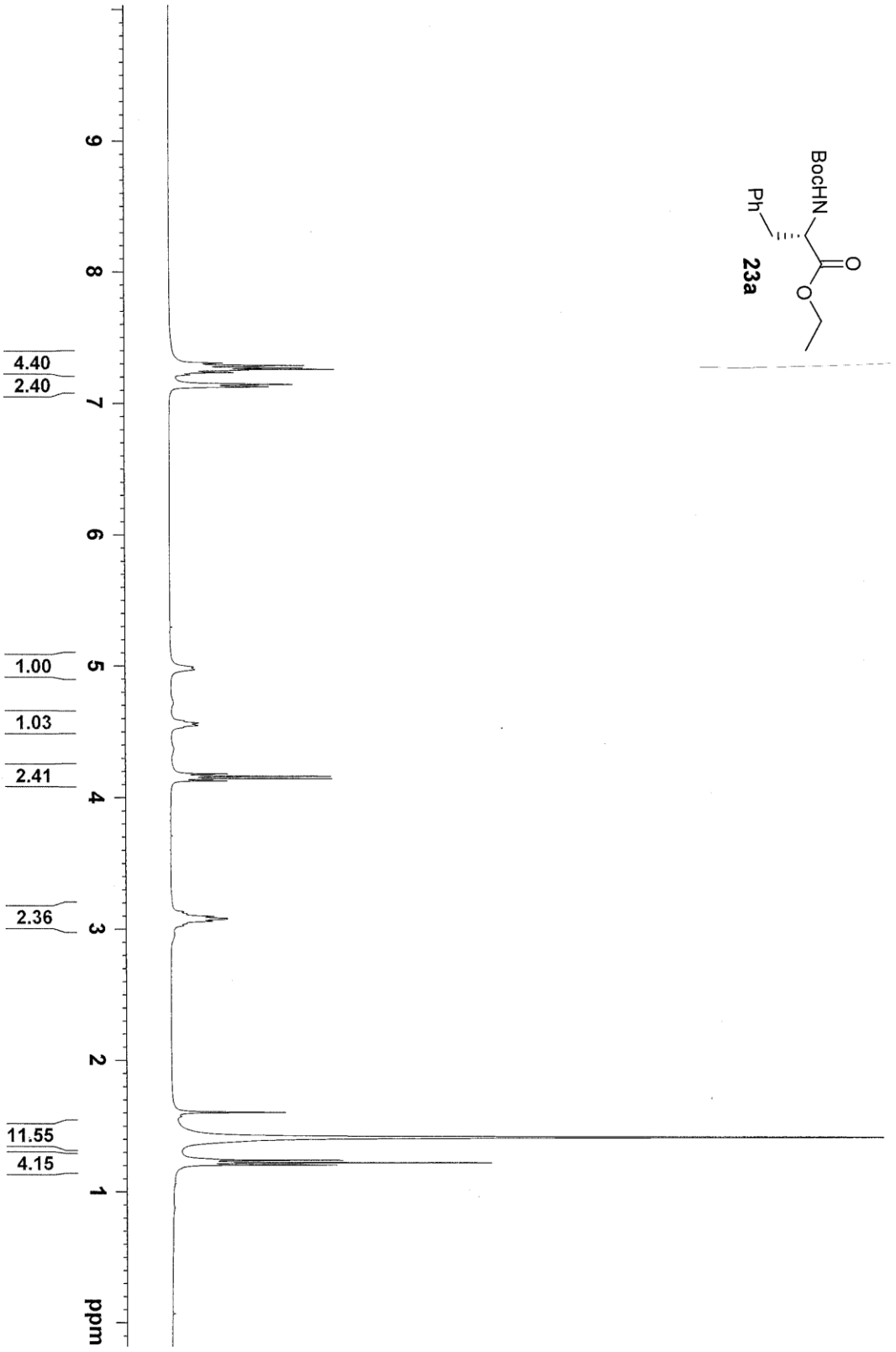
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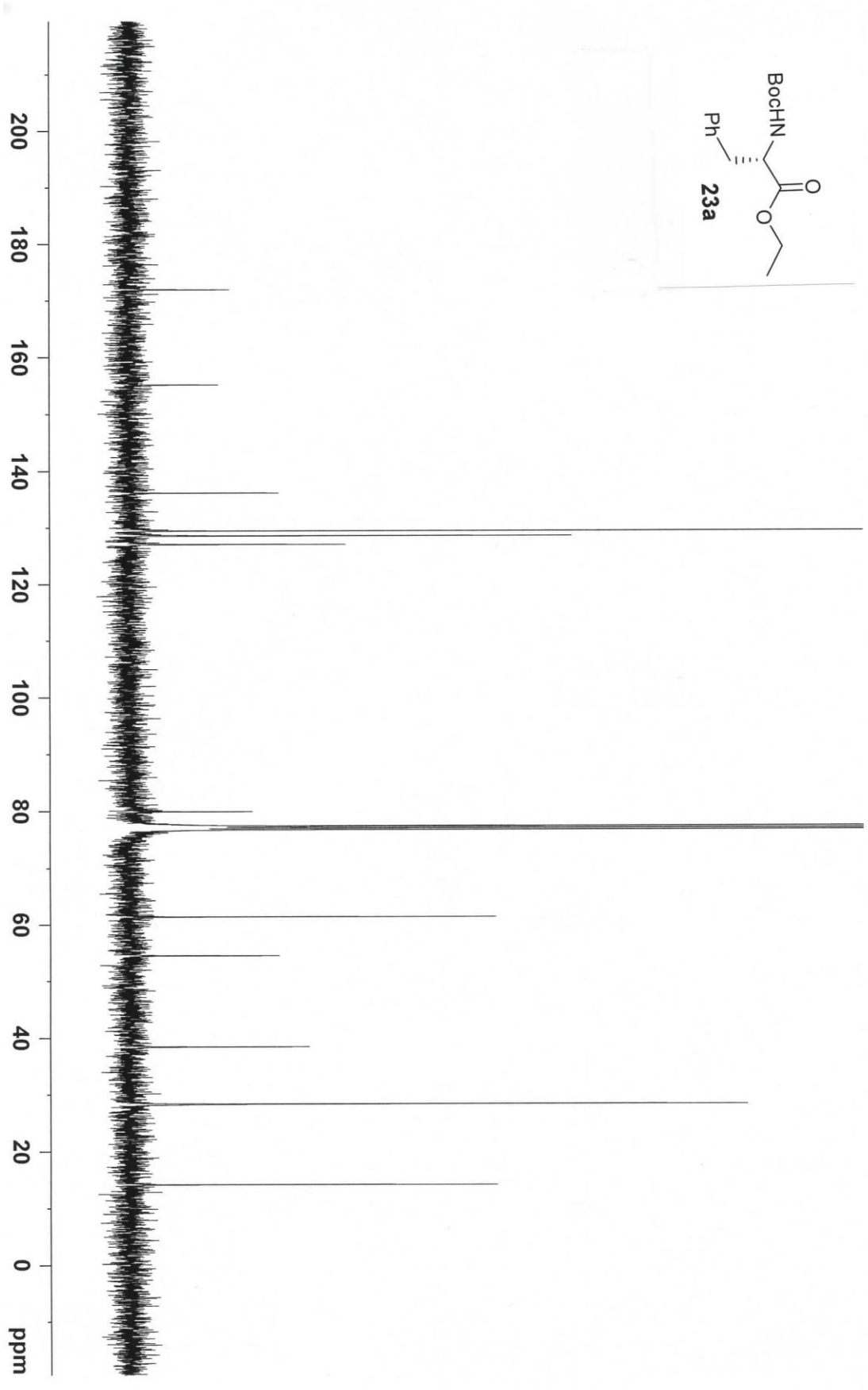
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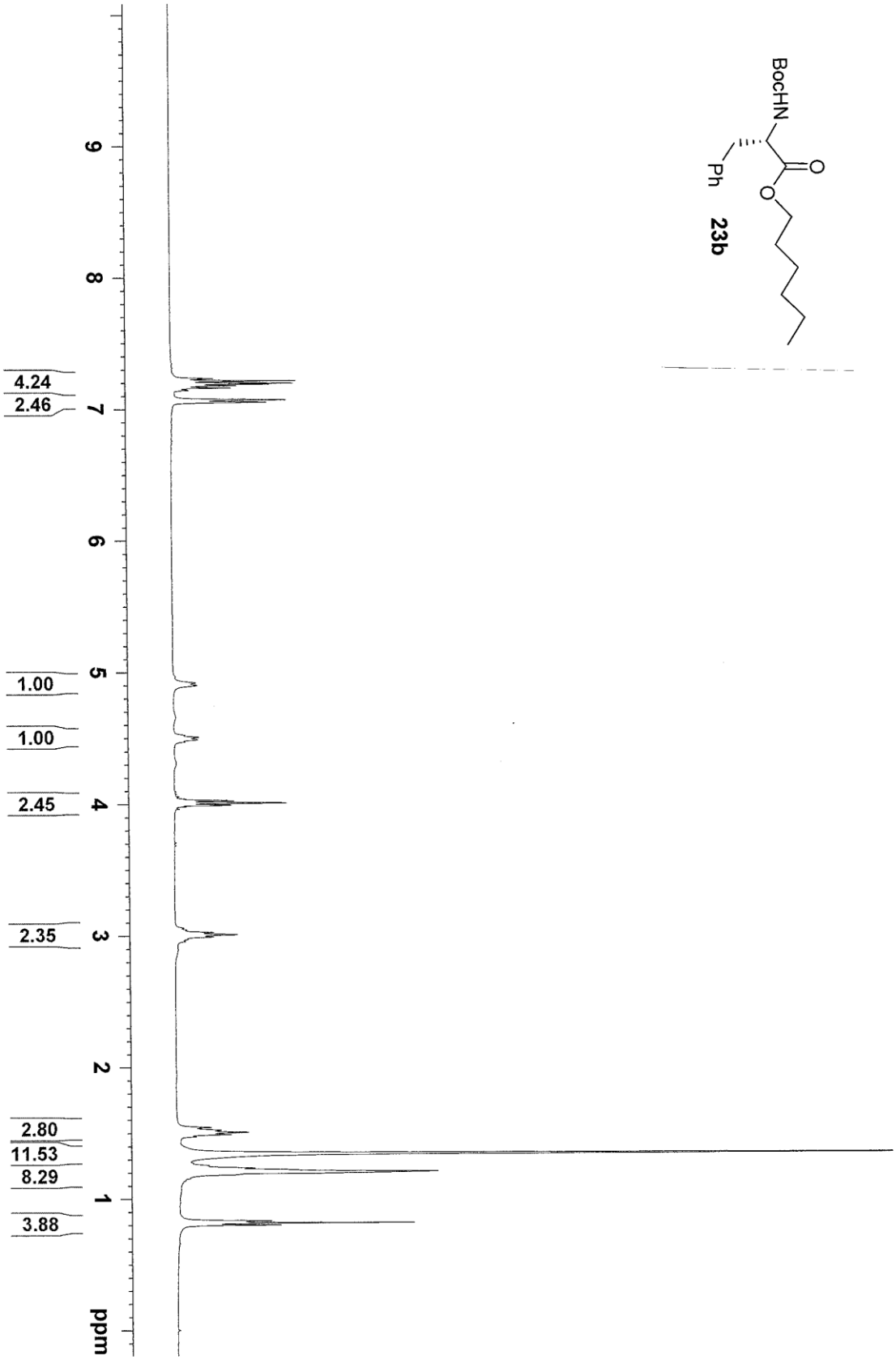
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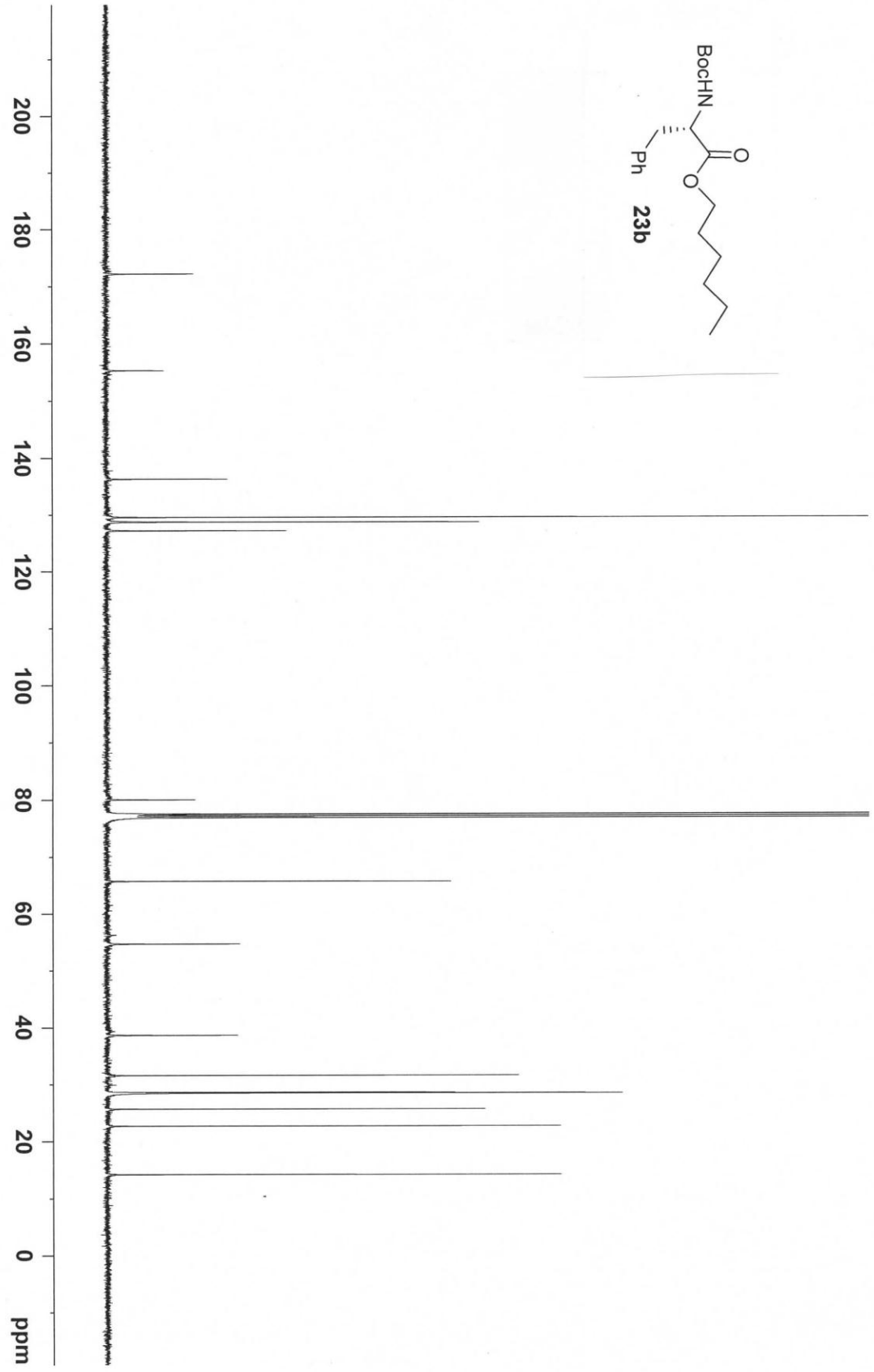
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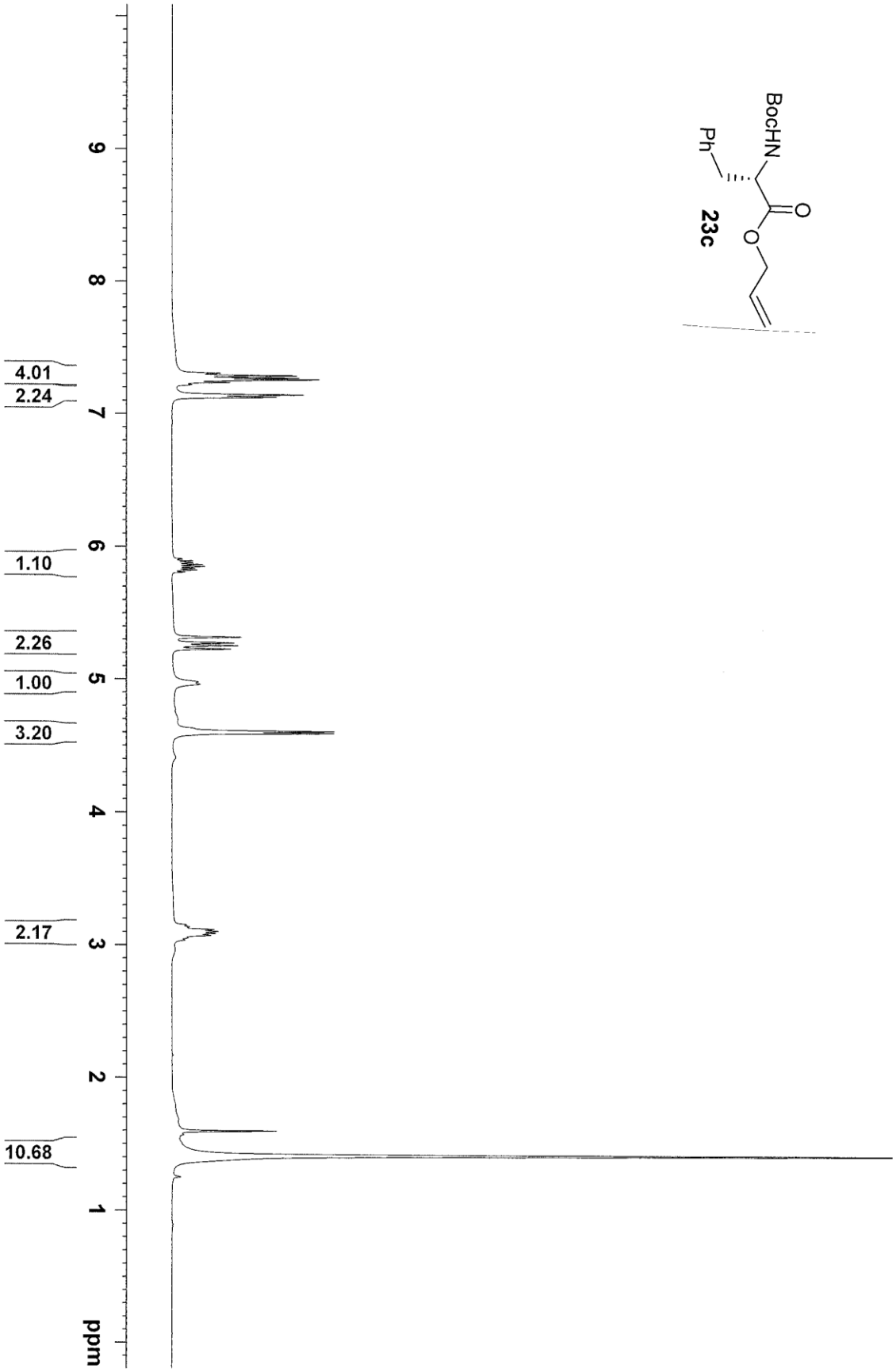
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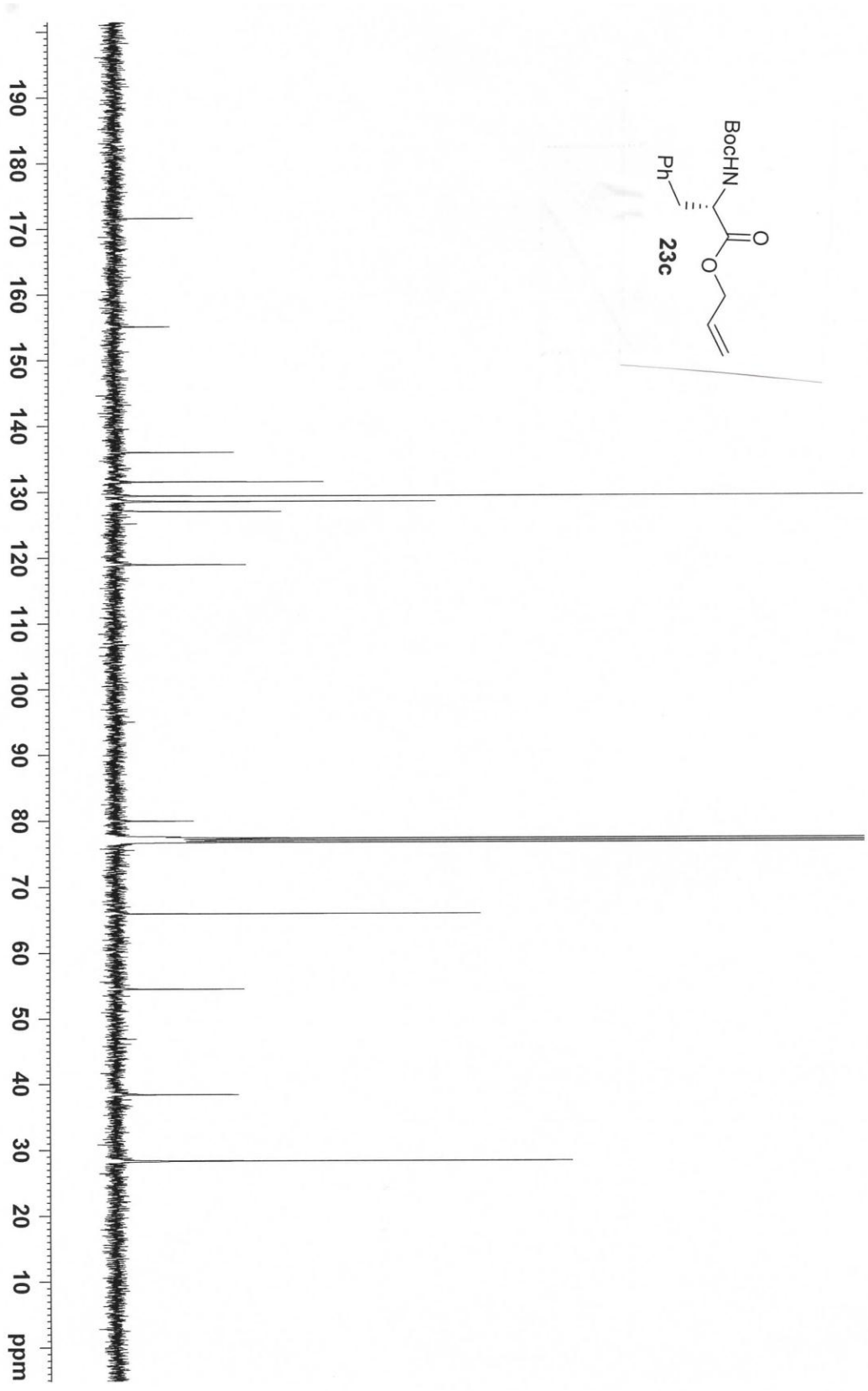
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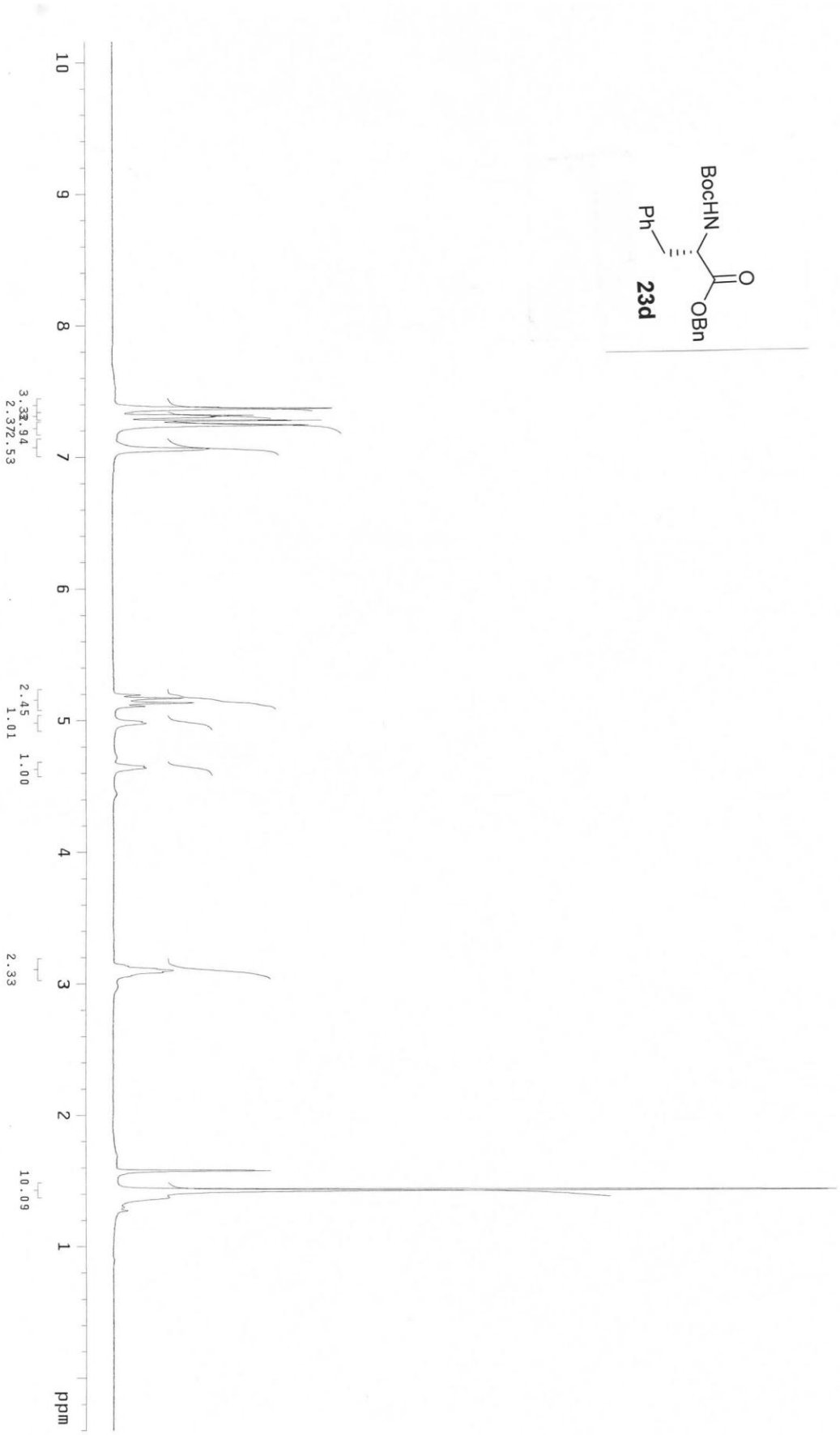
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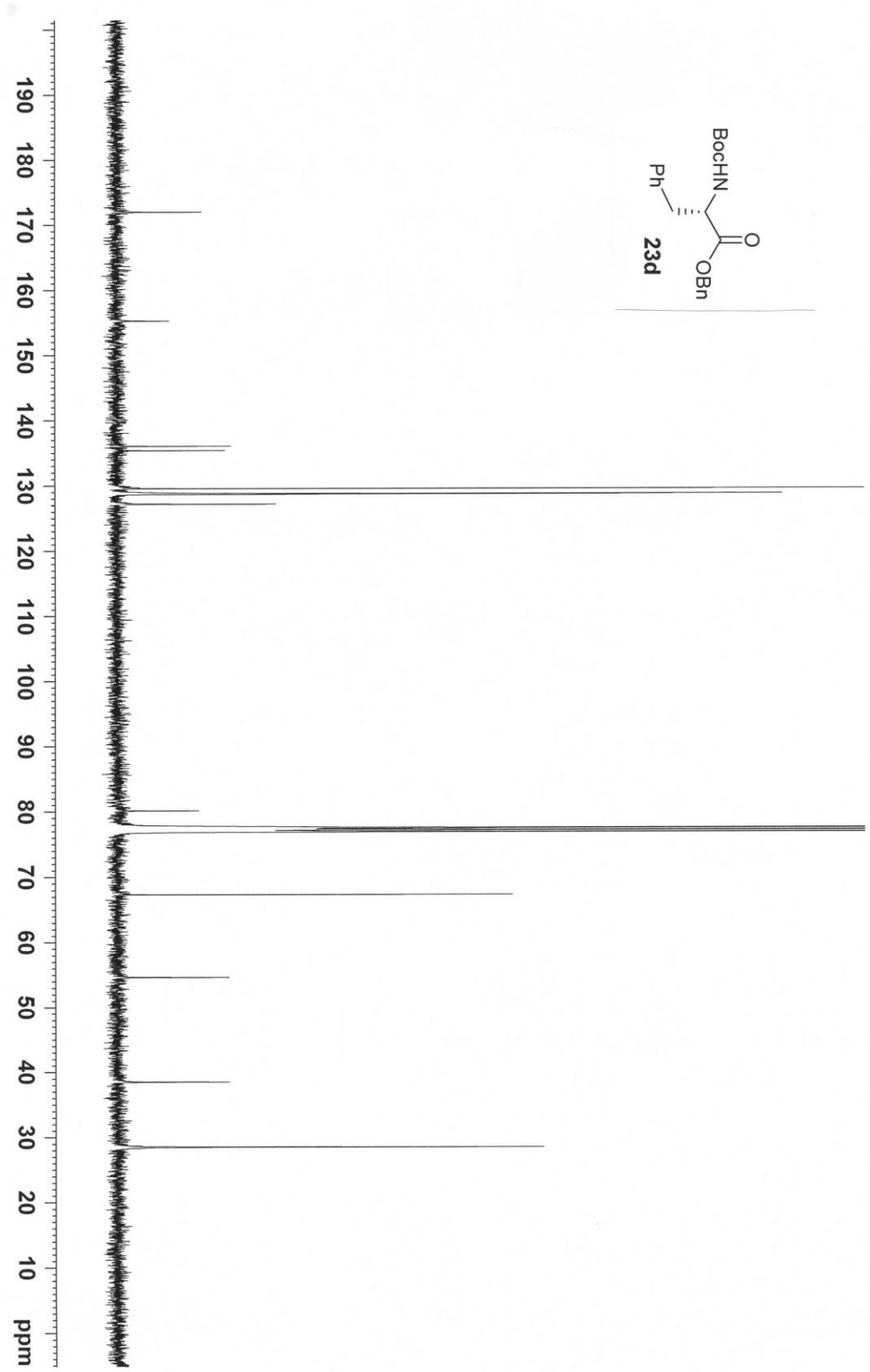
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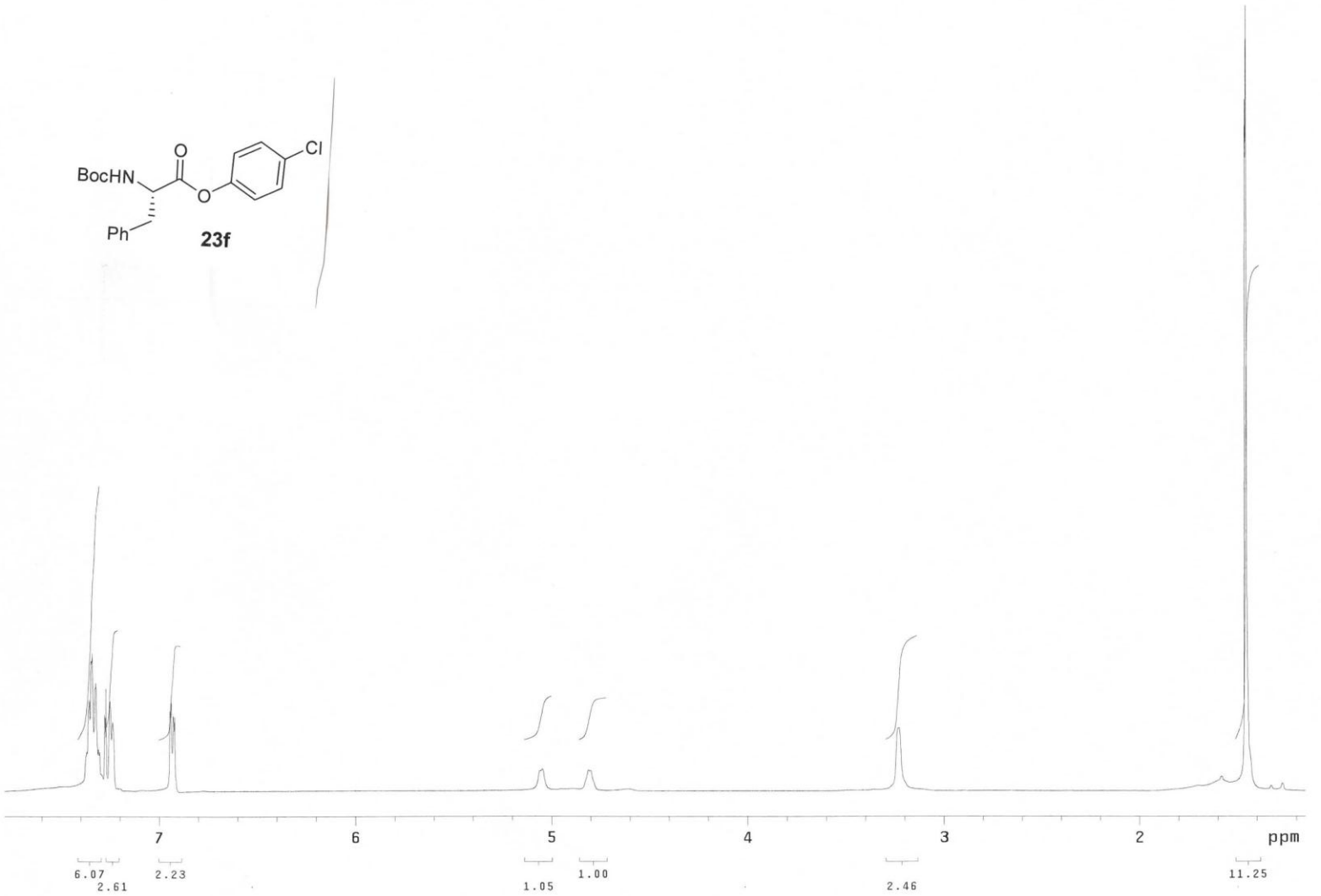
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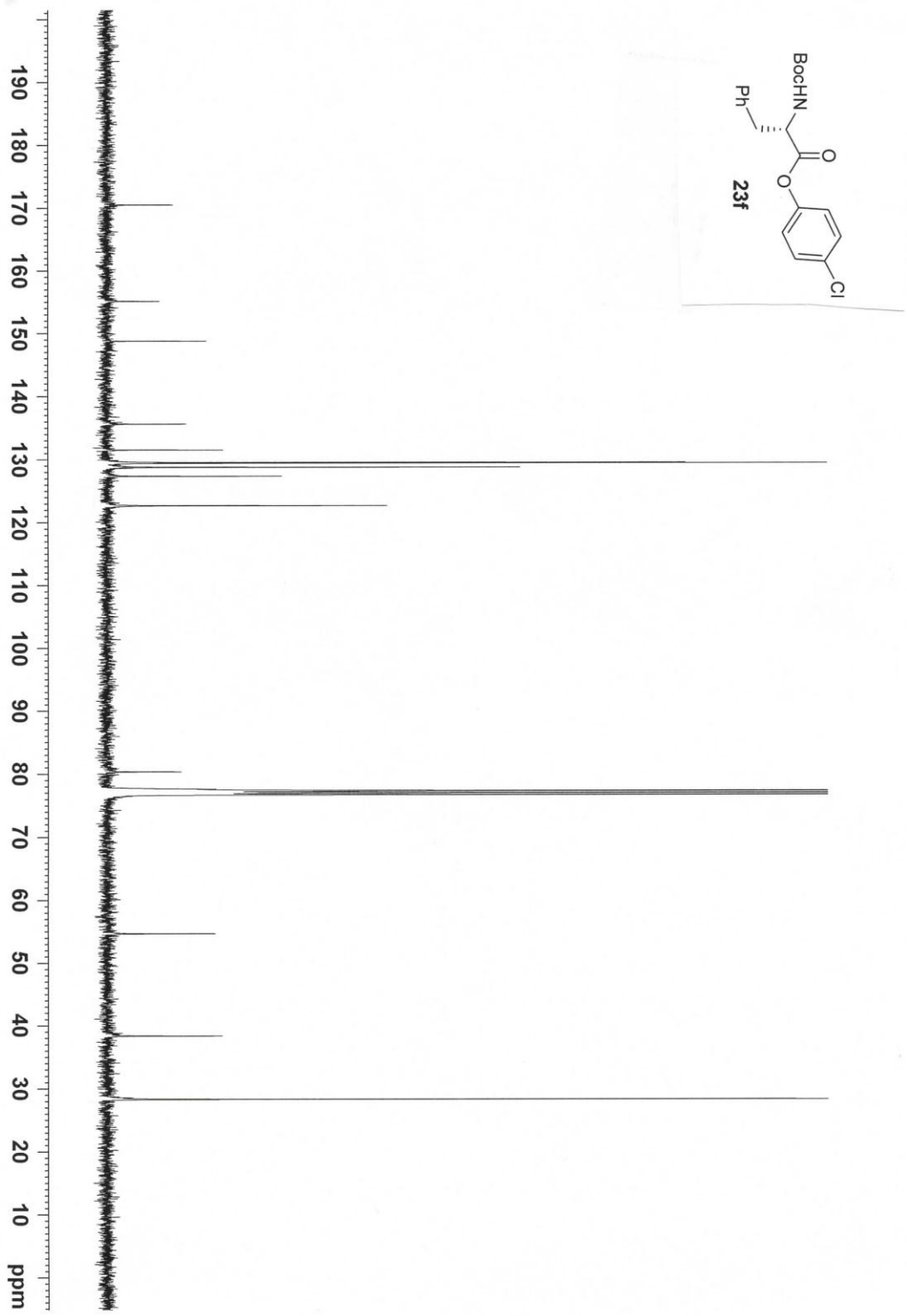
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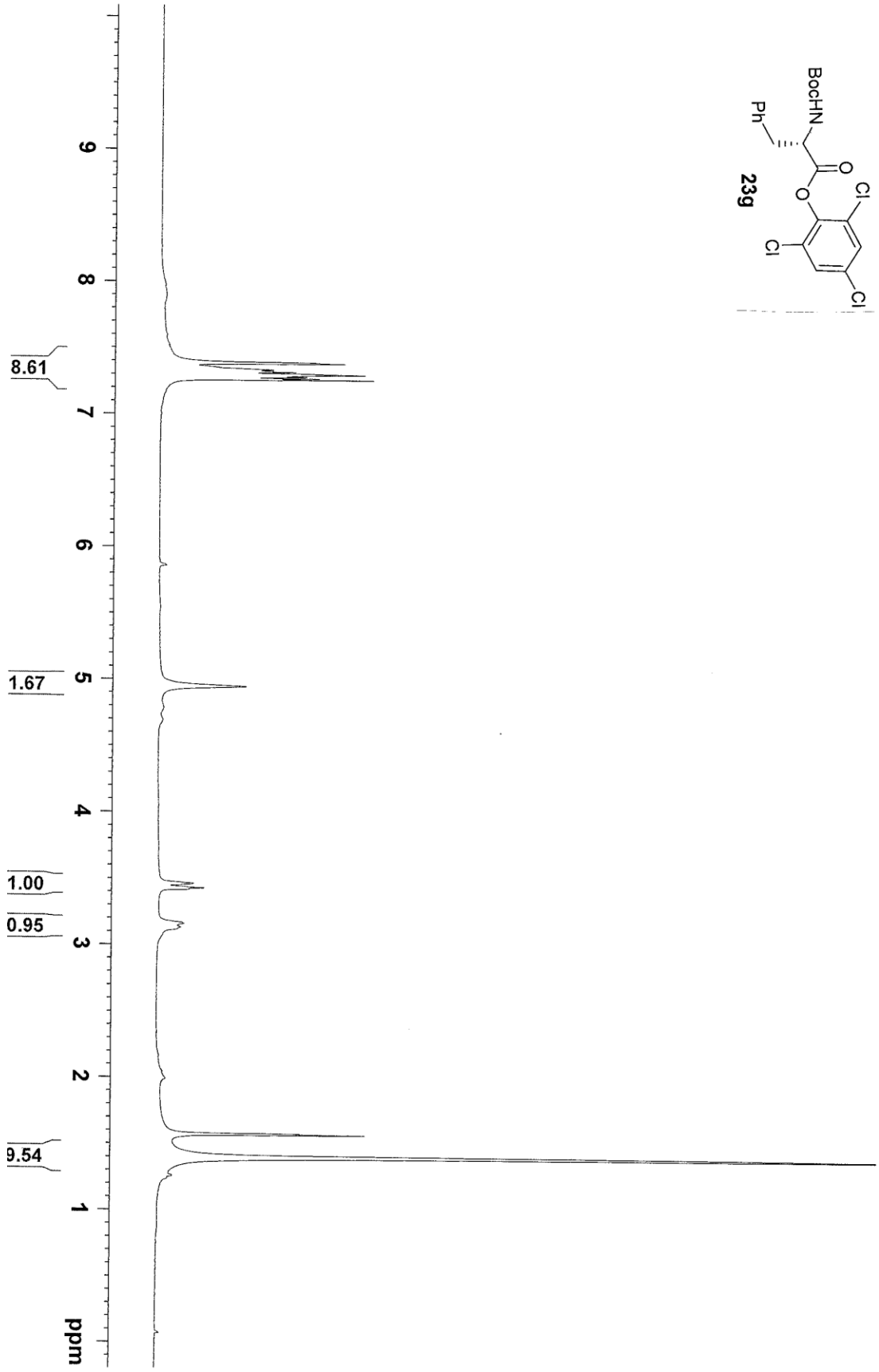
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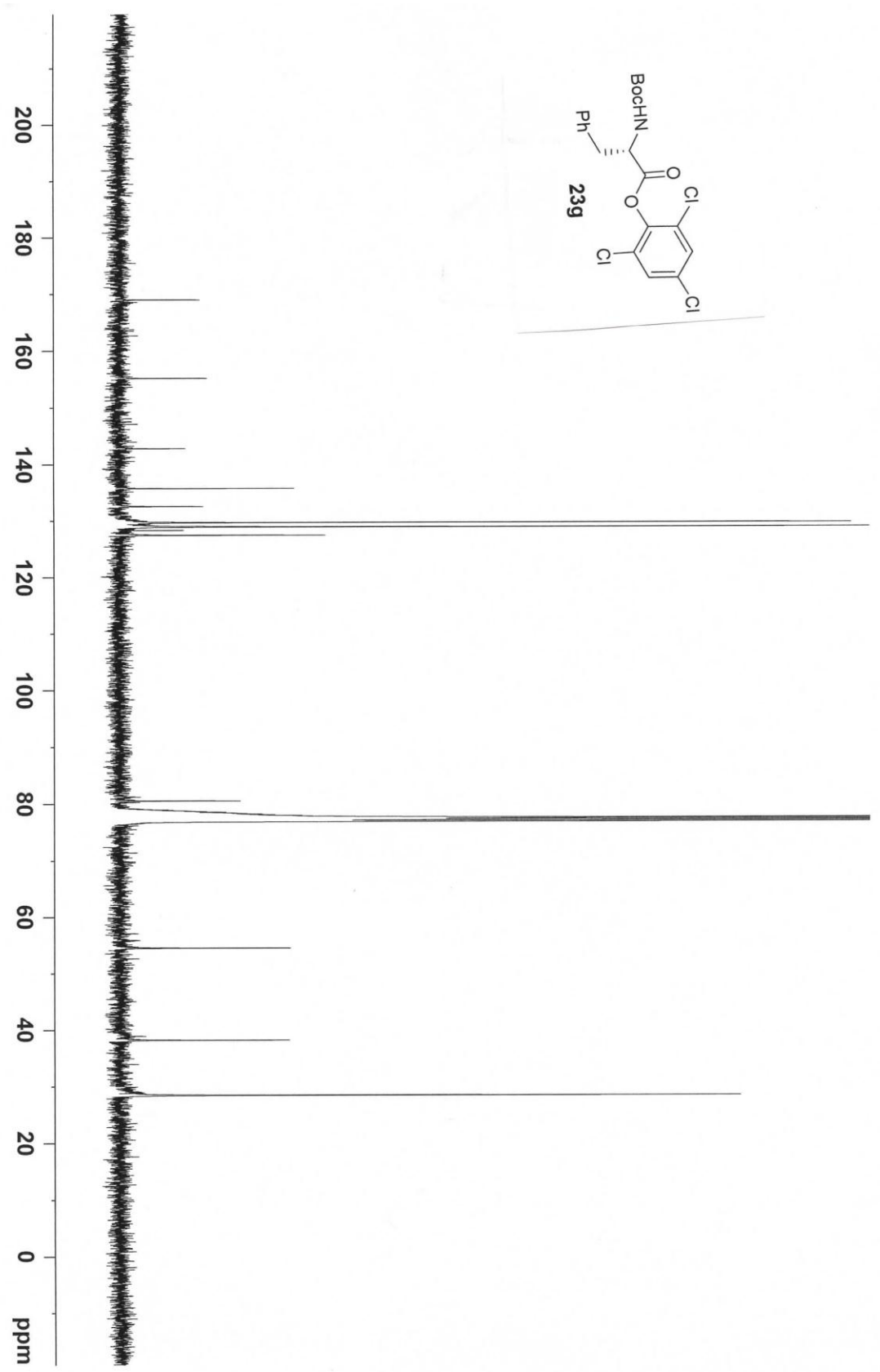
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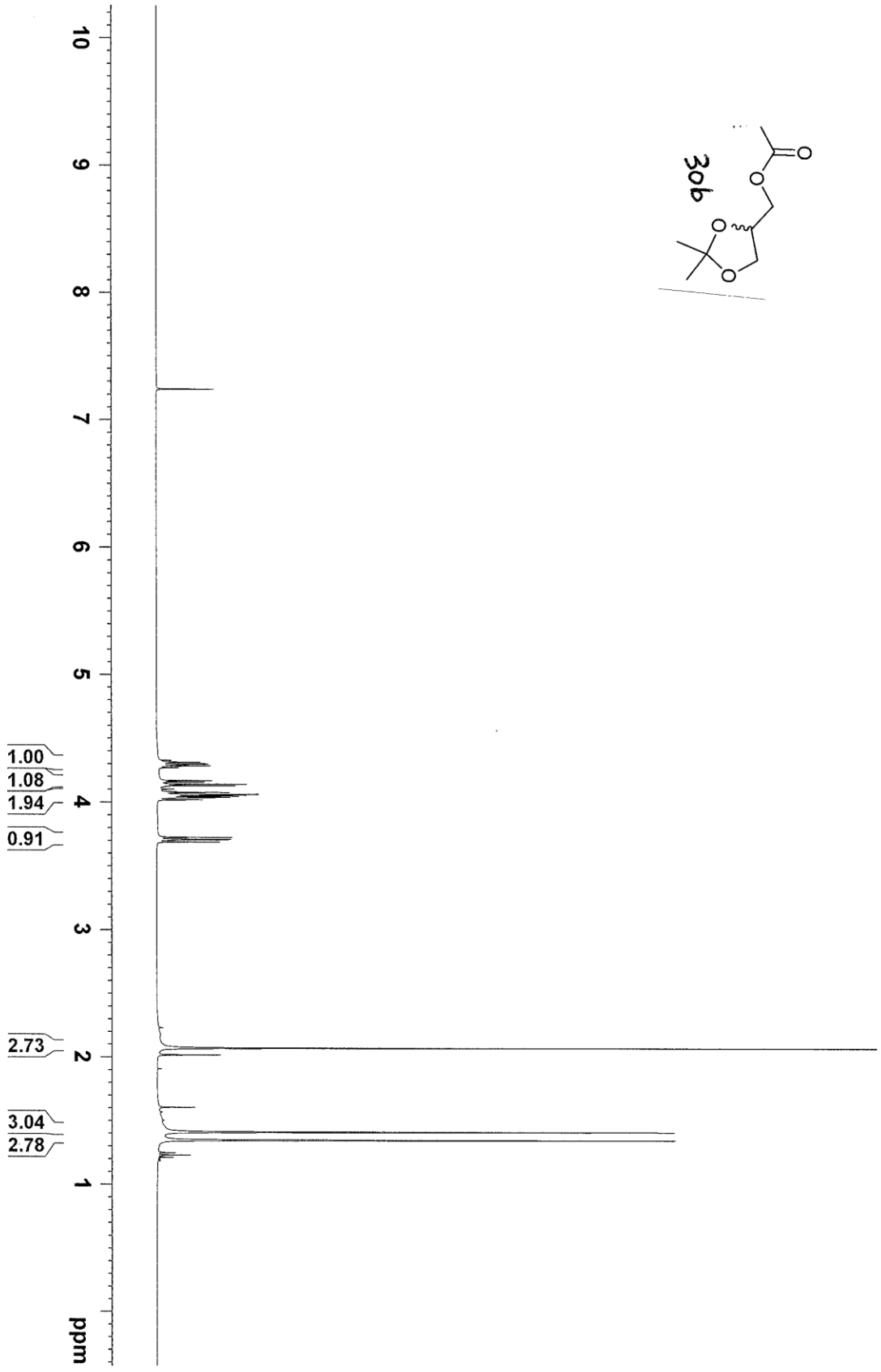
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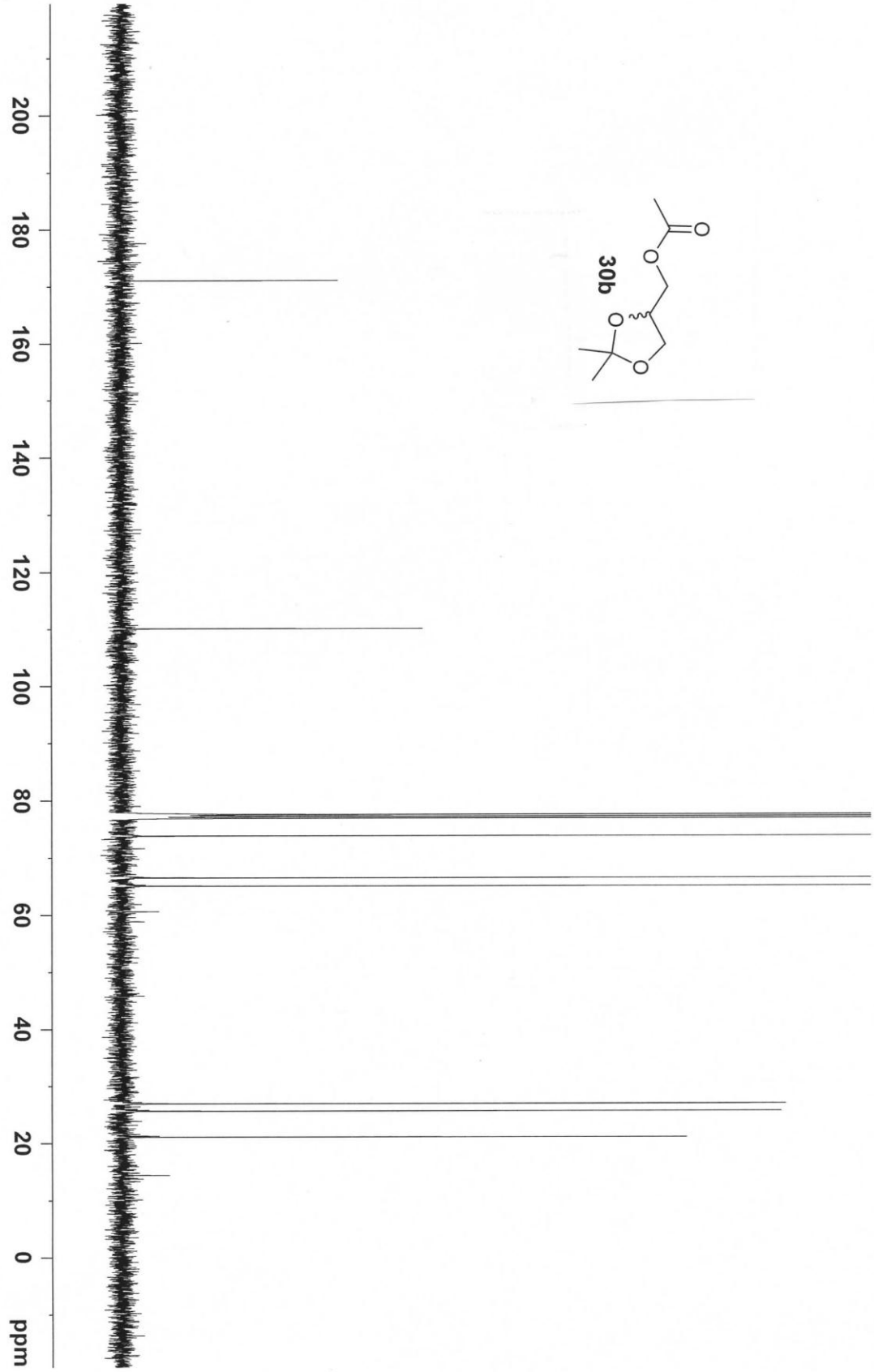
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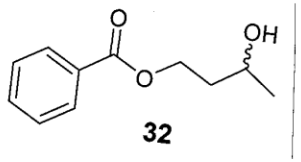

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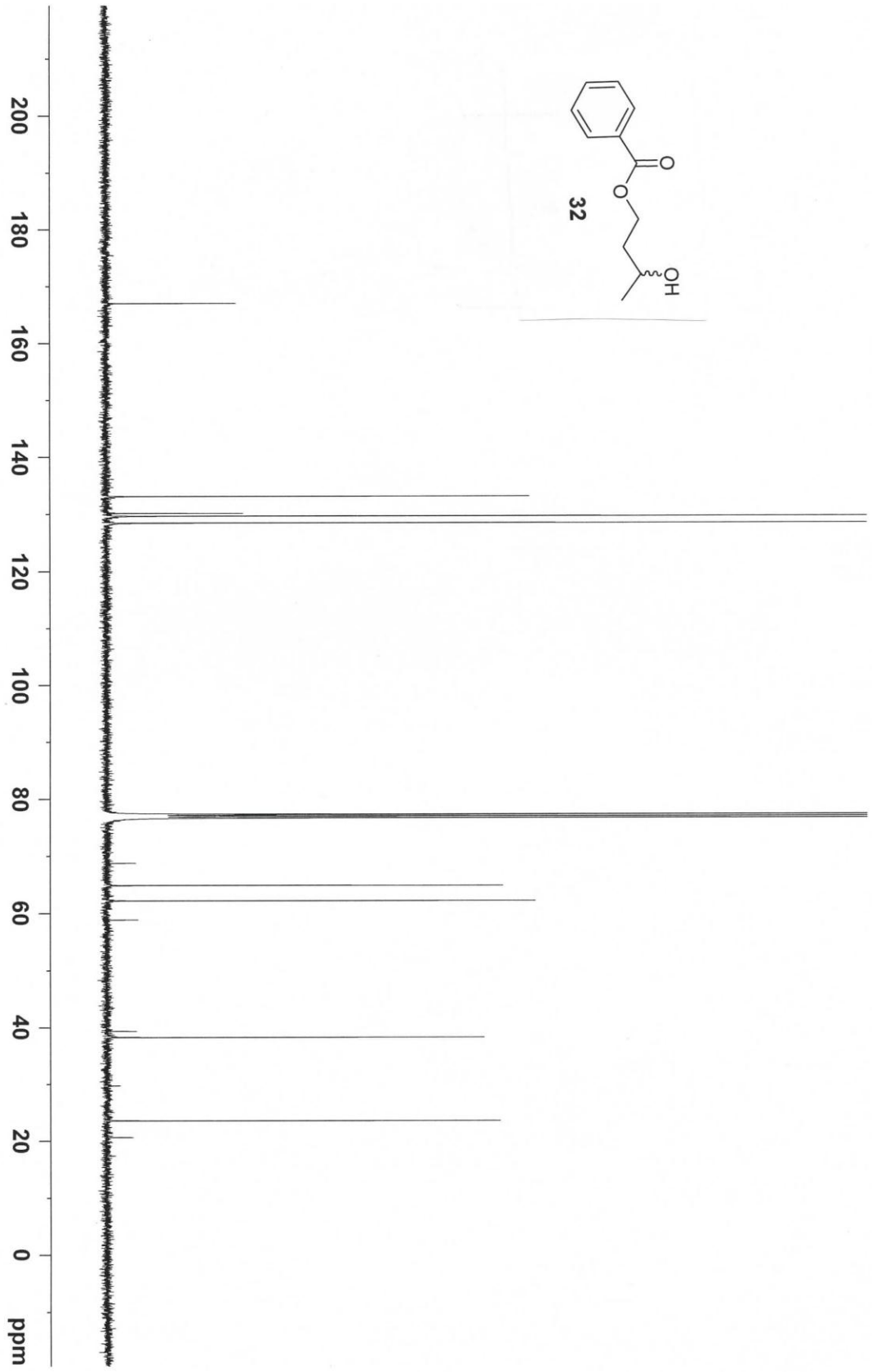
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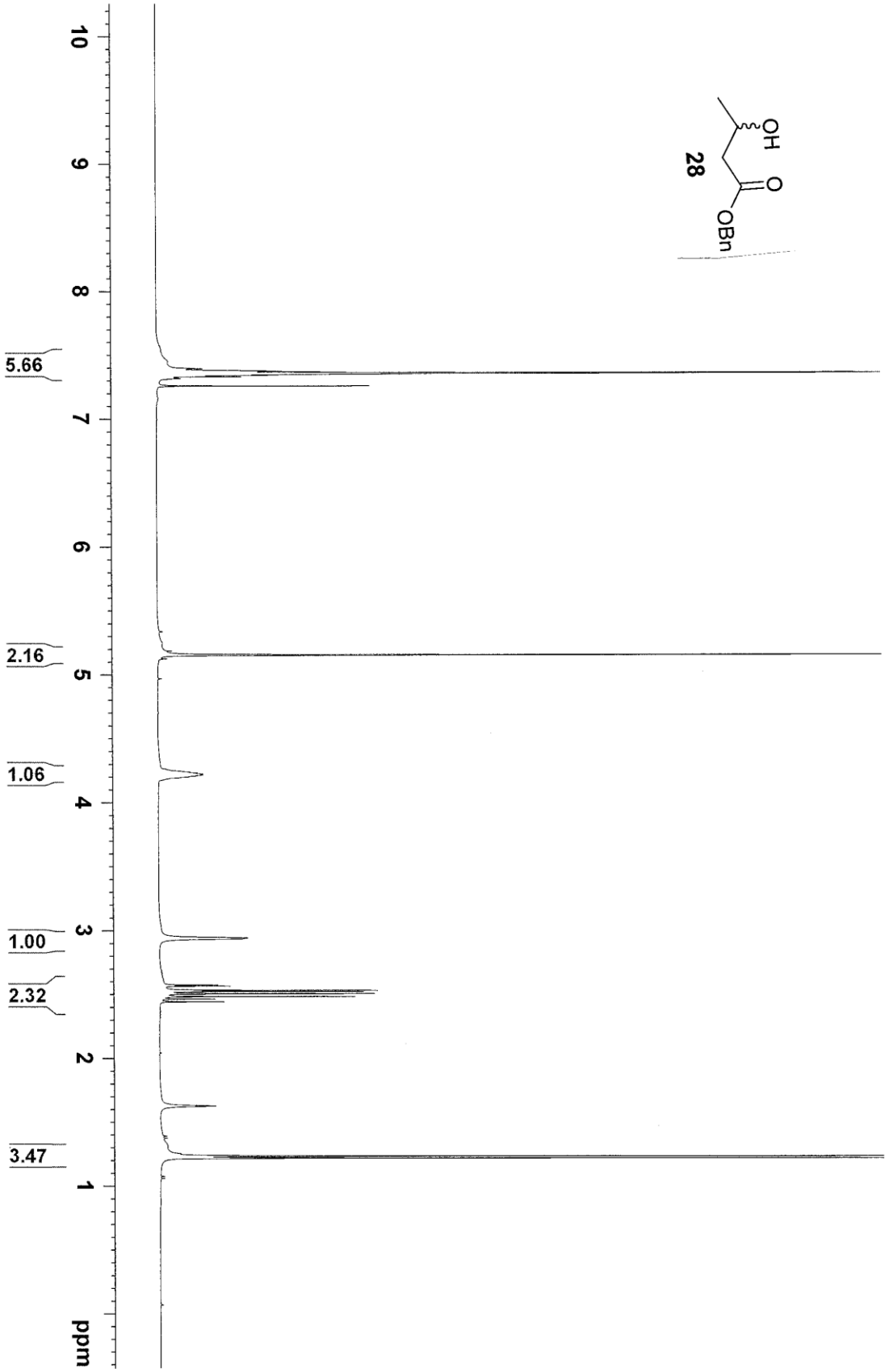
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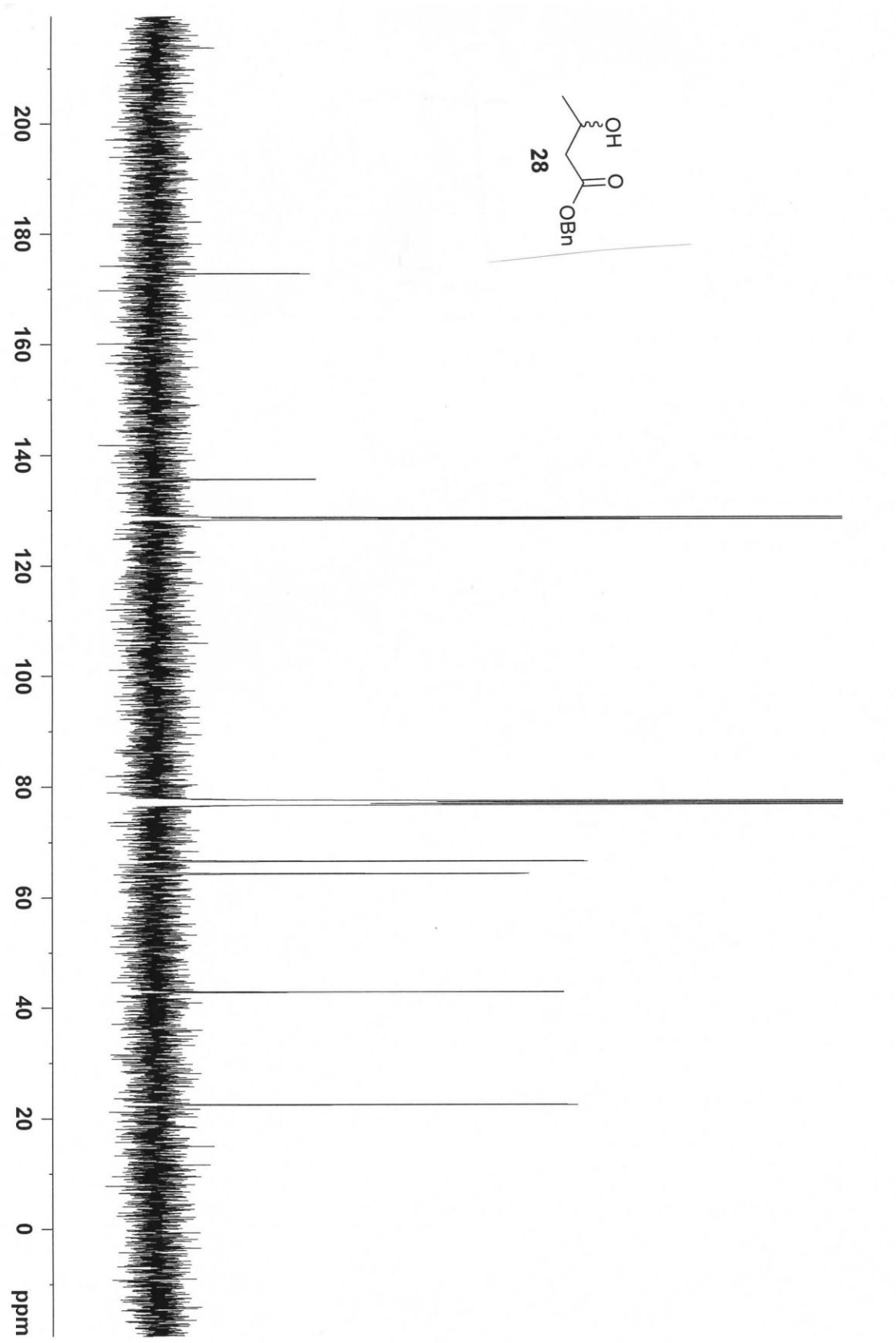
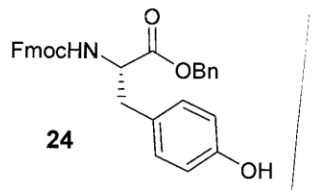
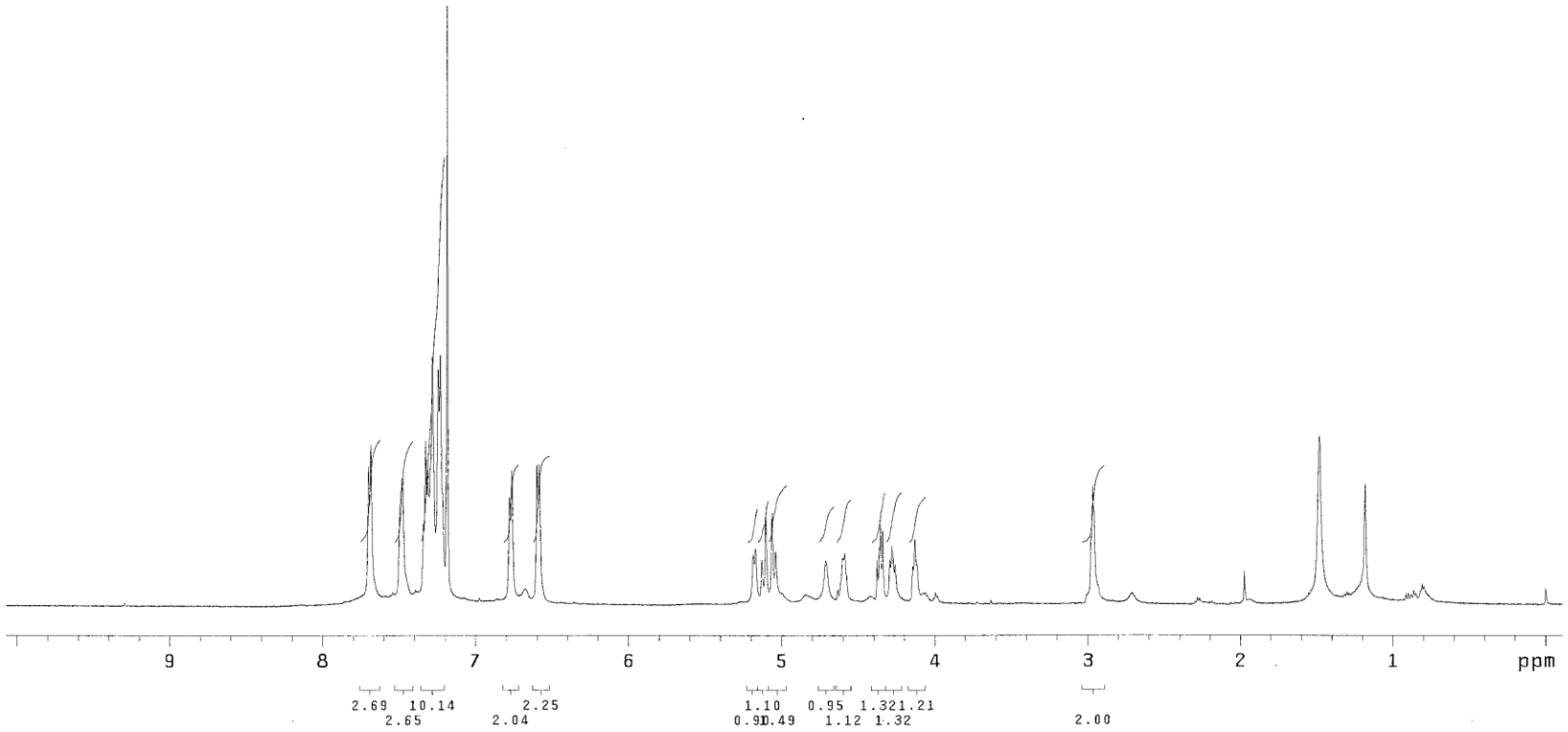
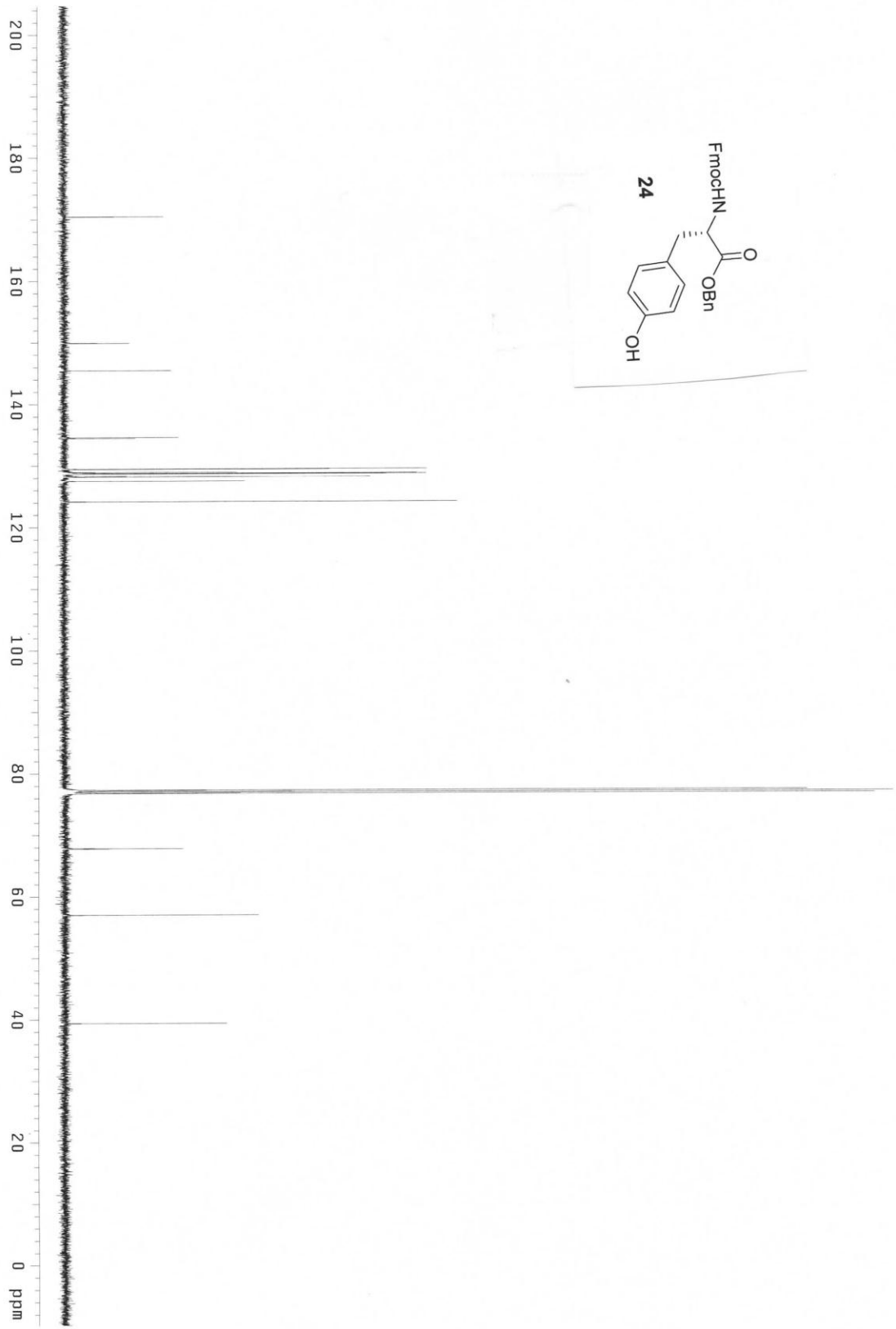
7
6
5
4
3
2
1
ppm

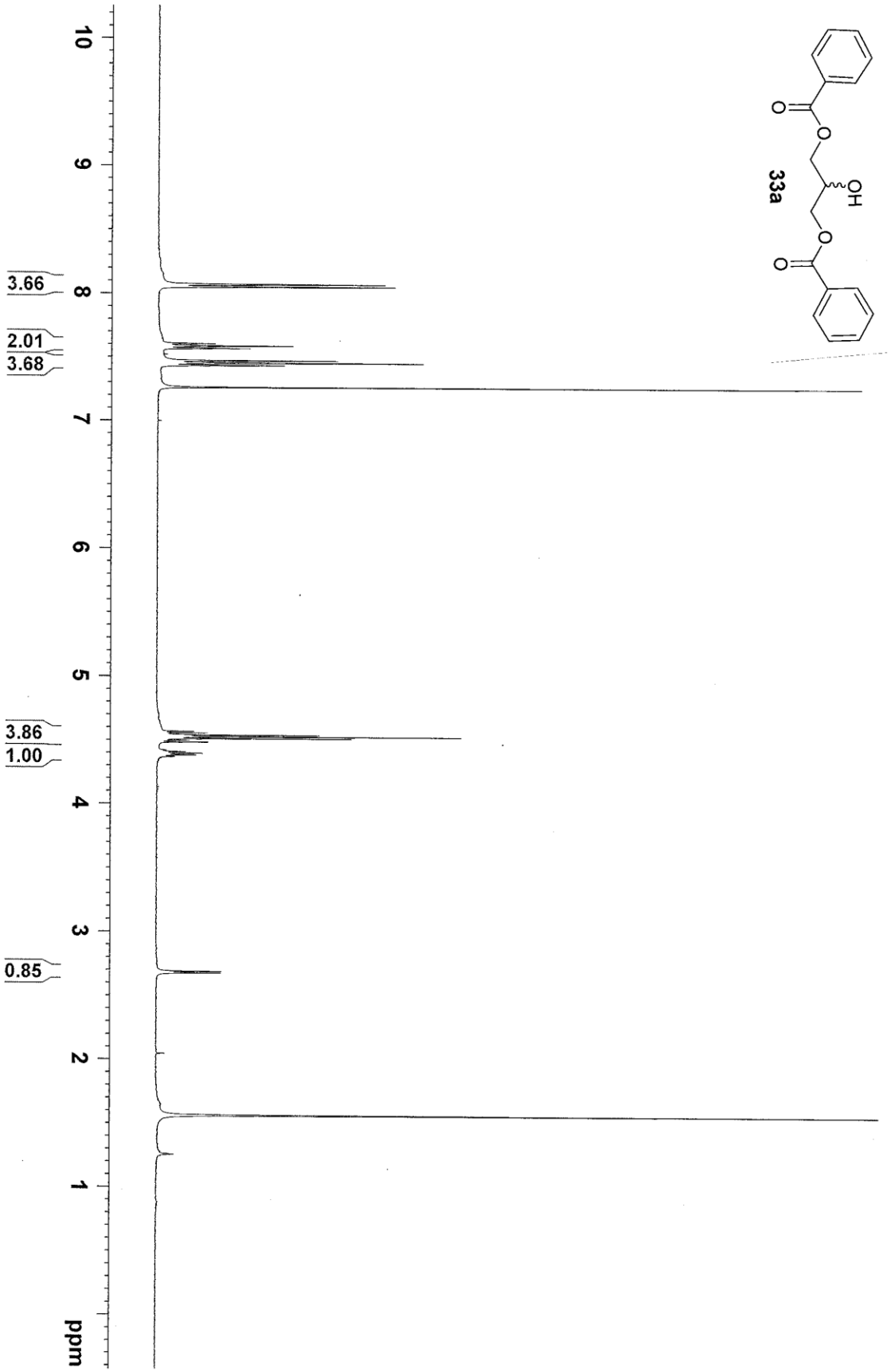

28
OH
O
OBn
200
180
160
140
120
100
80
60
40
20
0
ppm

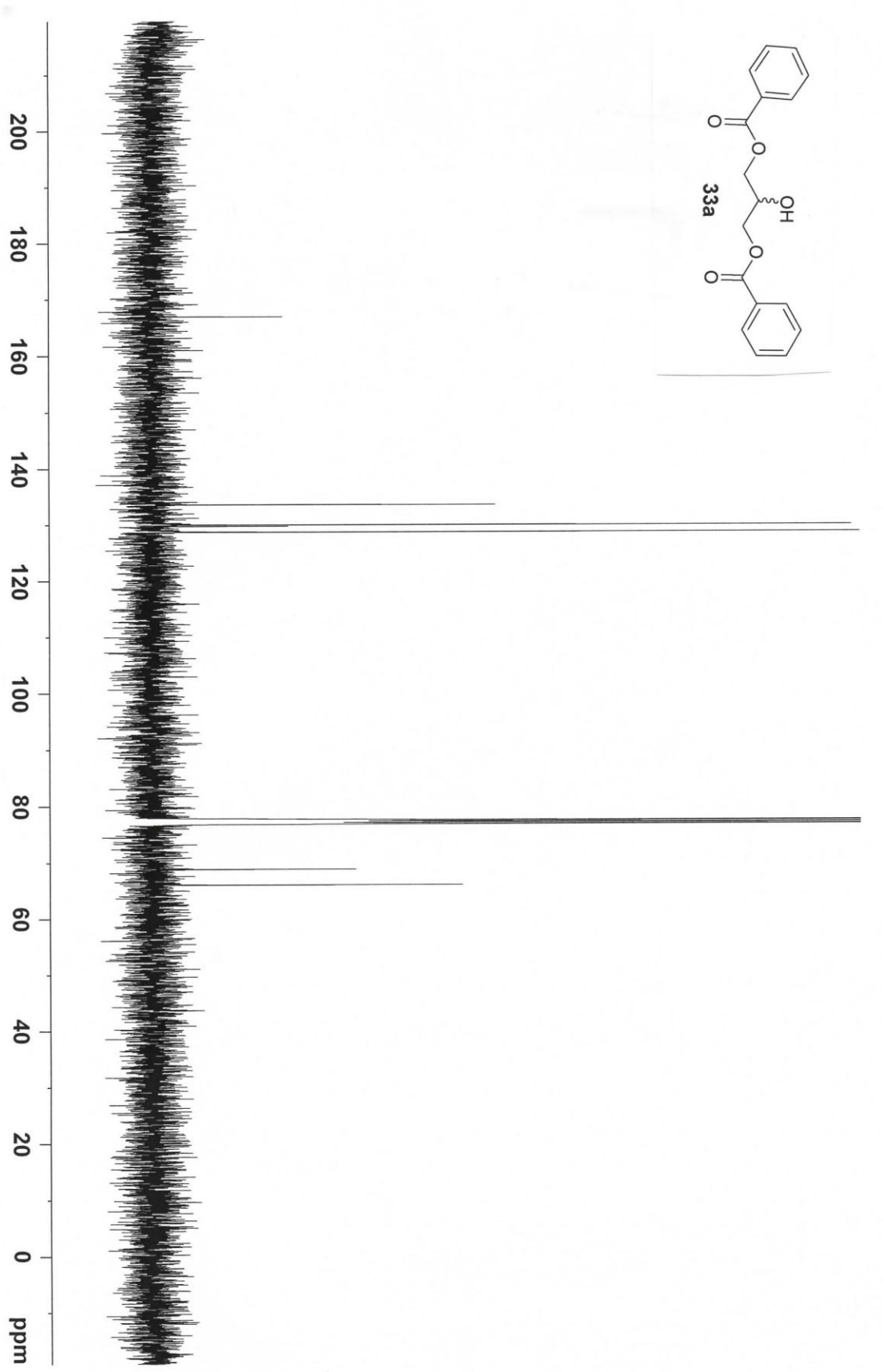

FmocHN
O
OBn
OH

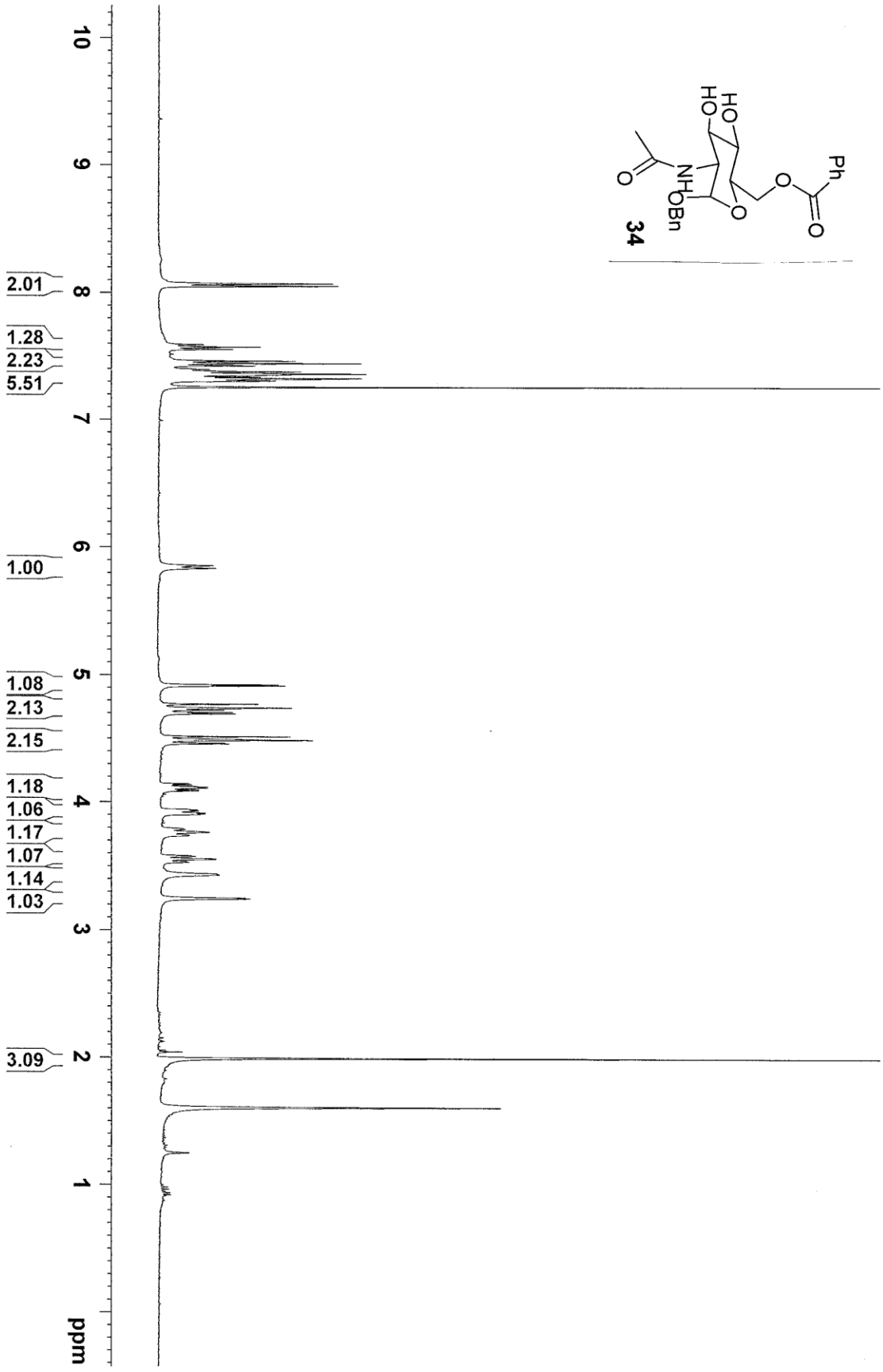
24

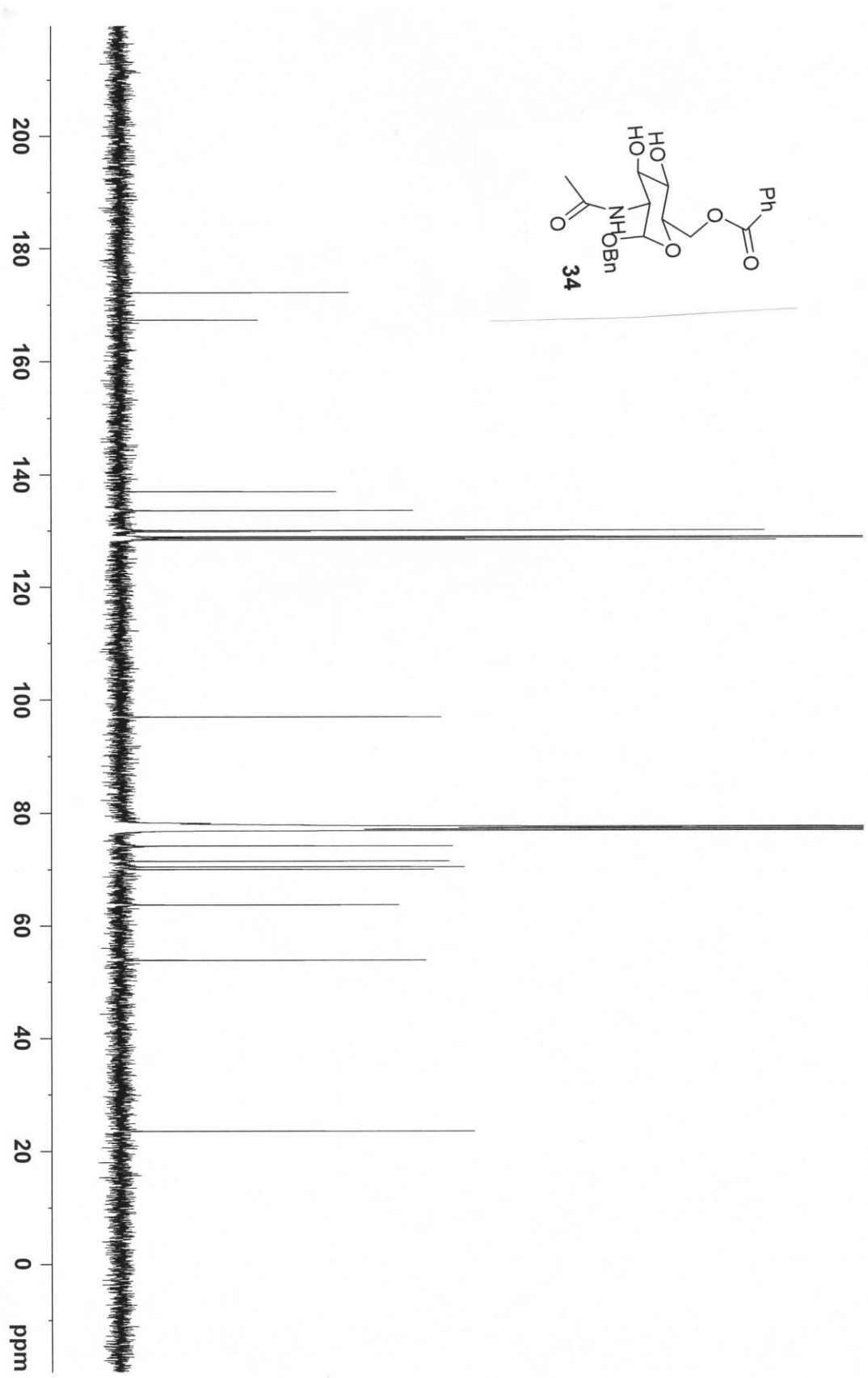

9
8
7
6
5
4
3
2
1
ppm
2.69
10.14
2.65
2.25
2.04
1.10
0.91
0.49
0.95
1.12
1.32
1.21
1.32
2.00

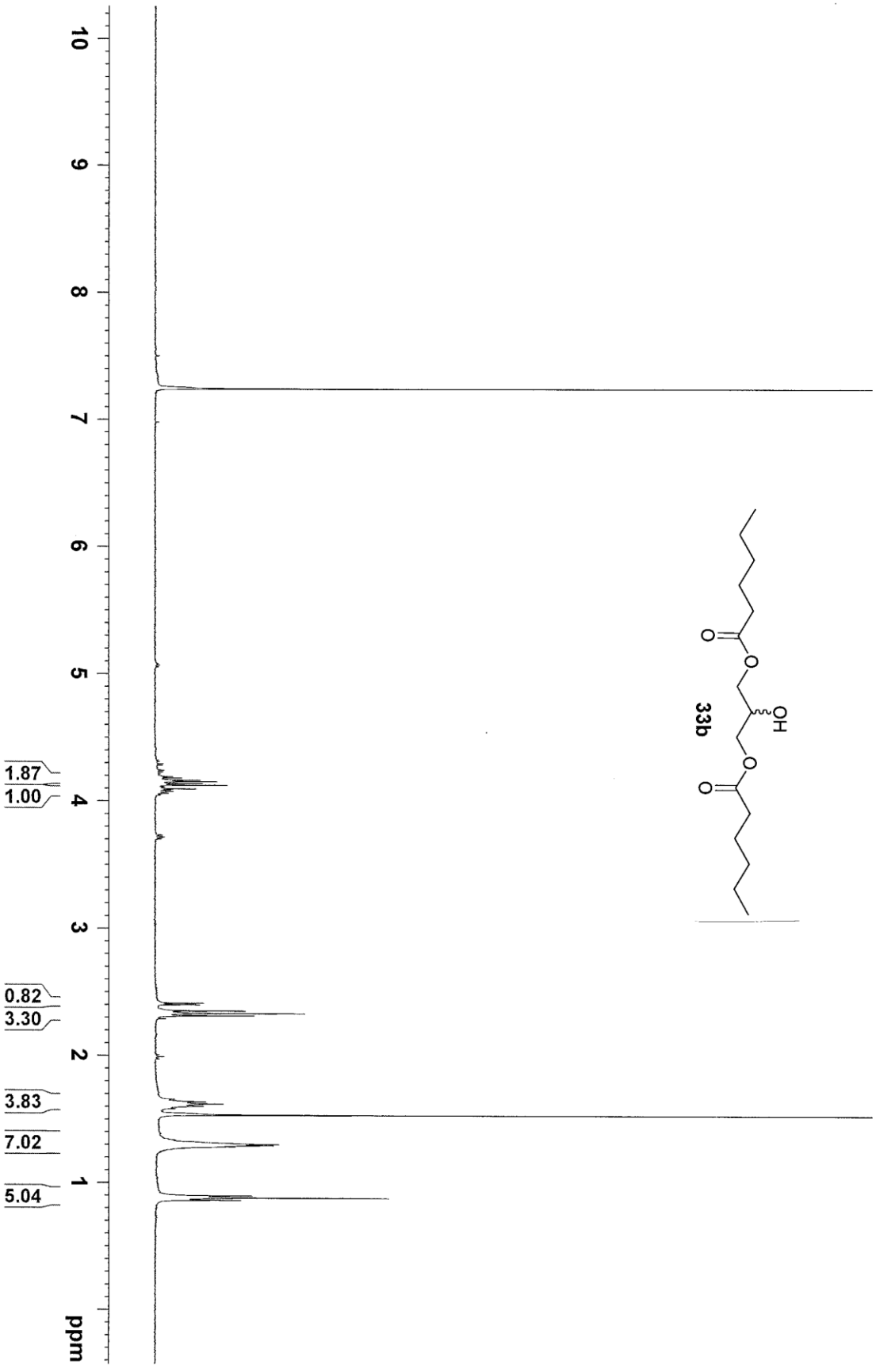

FmocHN
O
OBn
OH
24
200
180
160
140
120
100
80
60
40
20
0
ppm

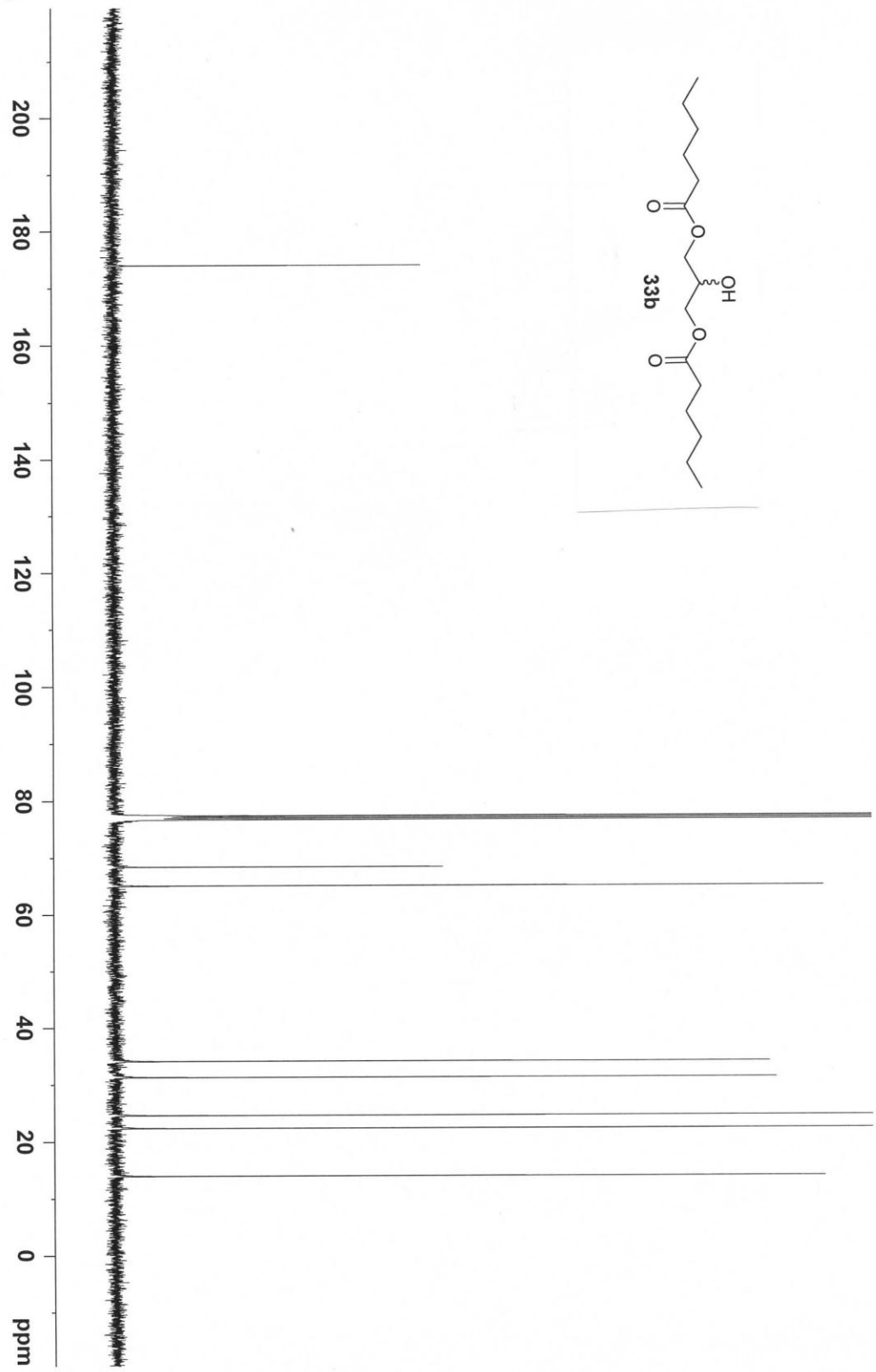

3.66
2.01
3.68
3.86
1.00
0.85
ppm
33a
OH

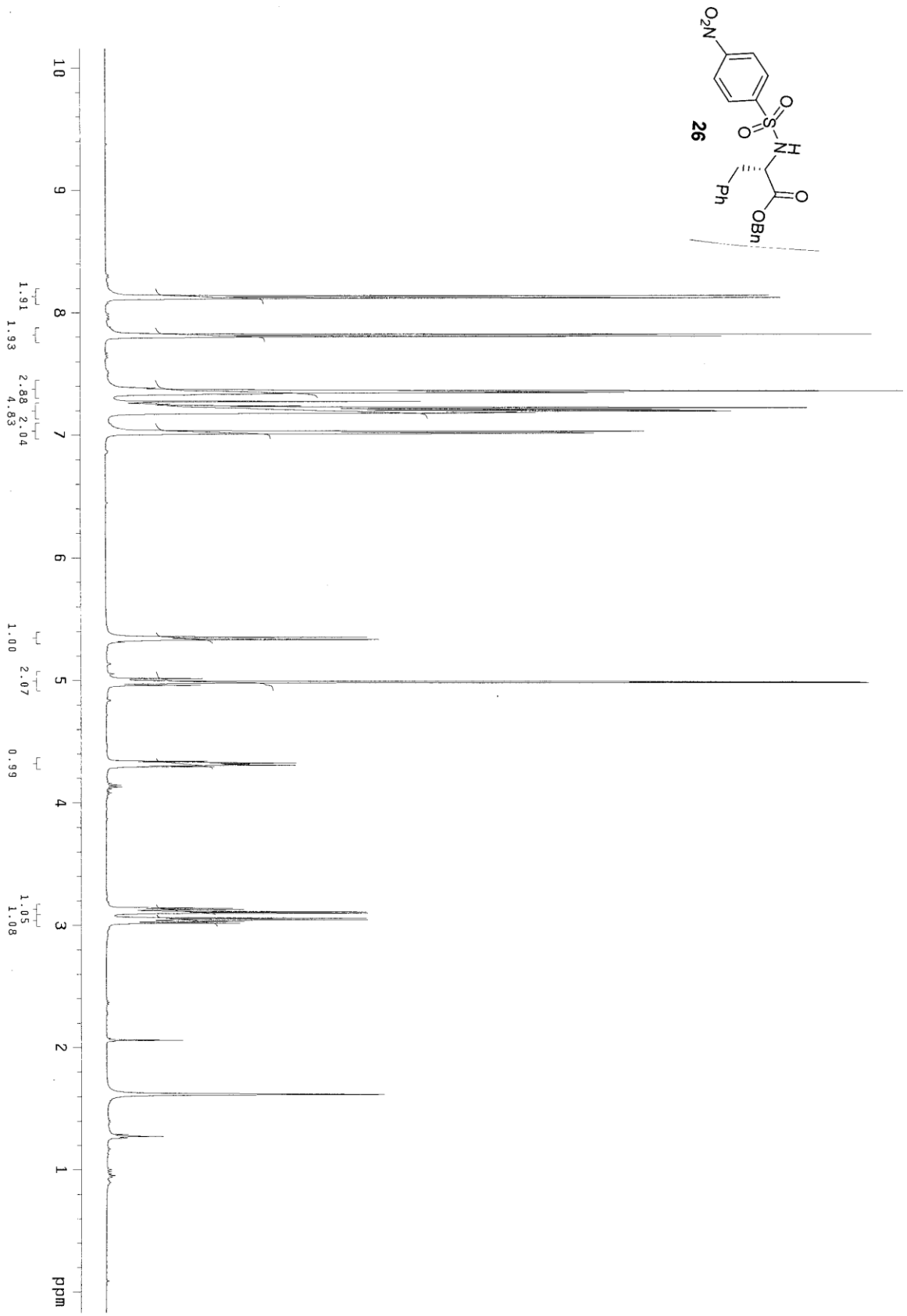

33a
OH
O
O
O
O
200
180
160
140
120
100
80
60
40
20
0
ppm

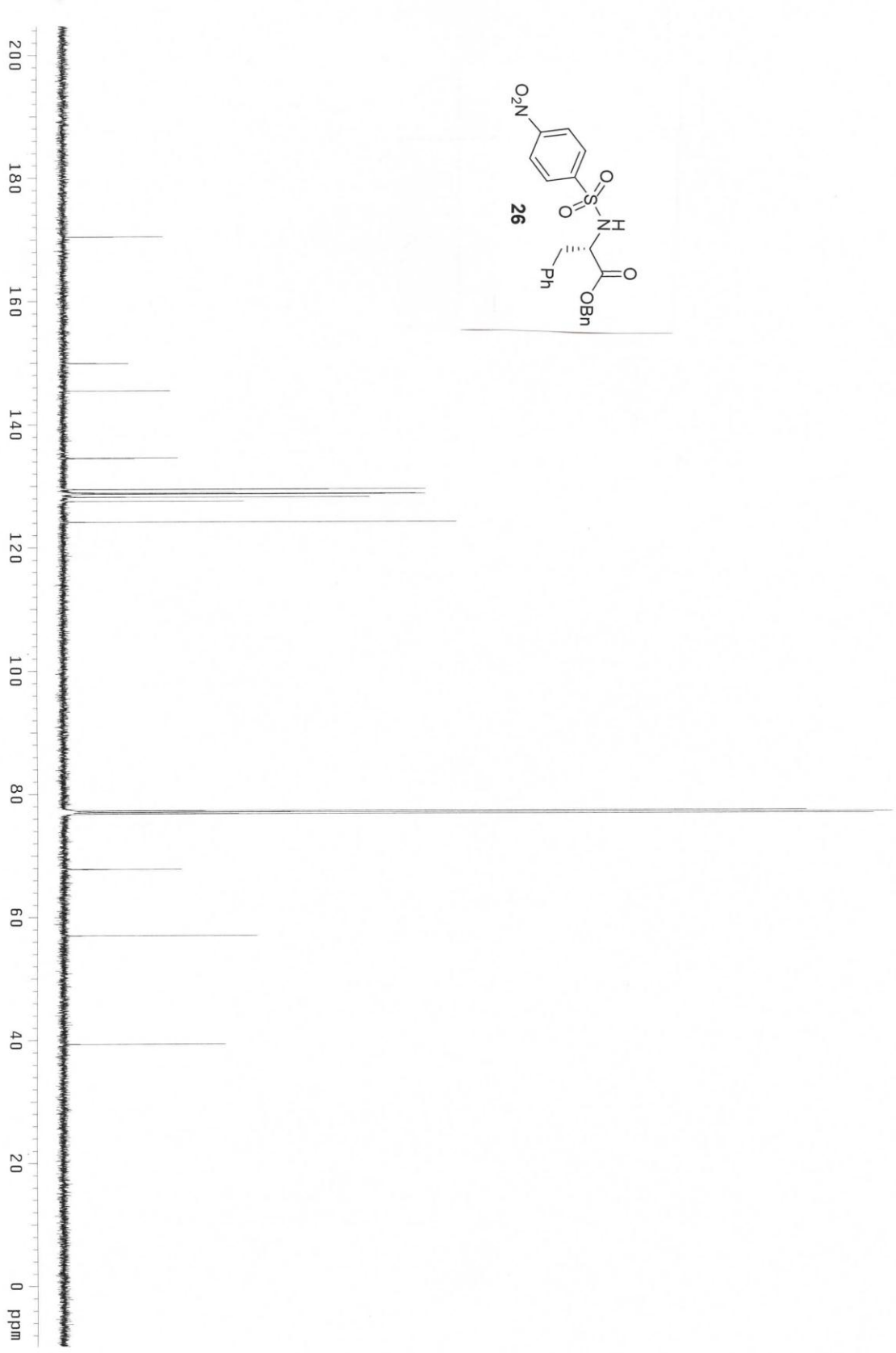

2.01
1.28
2.23
5.51
1.00
1.08
2.13
2.15
1.18
1.06
1.17
1.07
1.14
1.03
3.09
10
9
8
7
6
5
4
3
2
1
ppm
HO
HO
NH
OBn
O
O
O
O
Ph
34

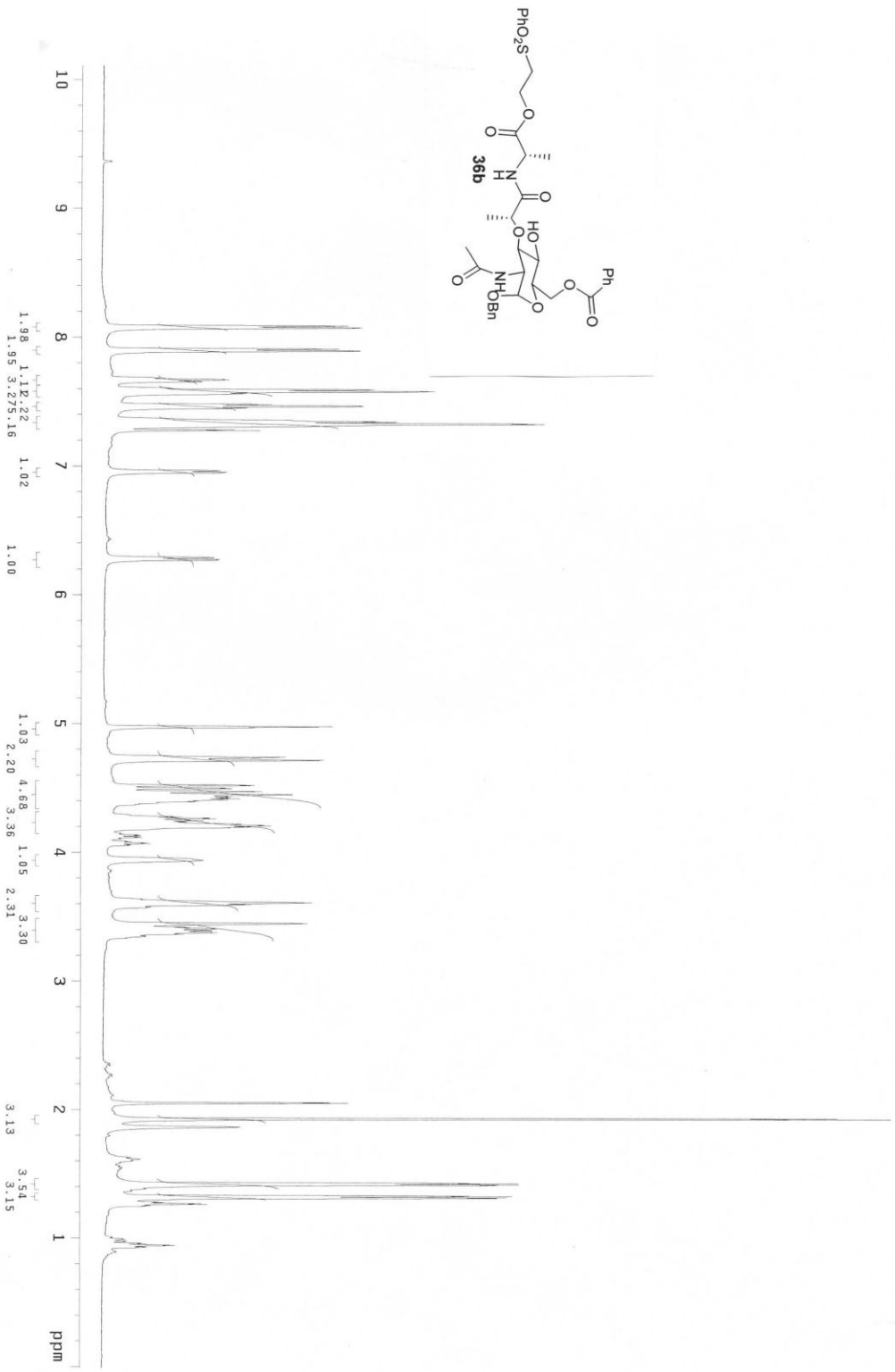

200
180
160
140
120
100
80
60
40
20
0
ppm
HO
HO
O
NH
O
OBn
O
O
Ph
O
34

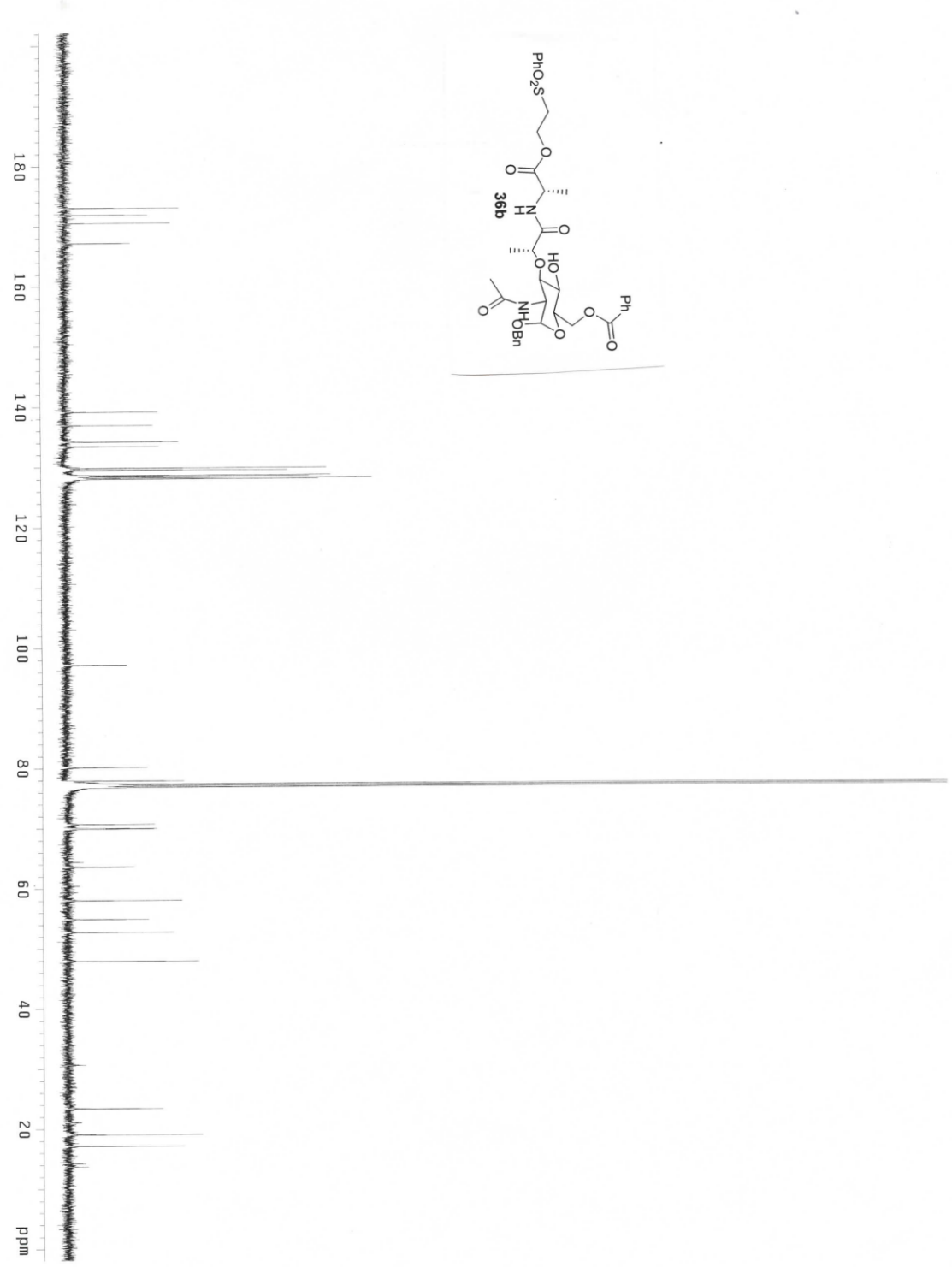

10
9
8
7
6
5
4
3
2
1
ppm
1.87
1.00
0.82
3.30
3.83
7.02
5.04
33b
OH
O
O
O
O
O

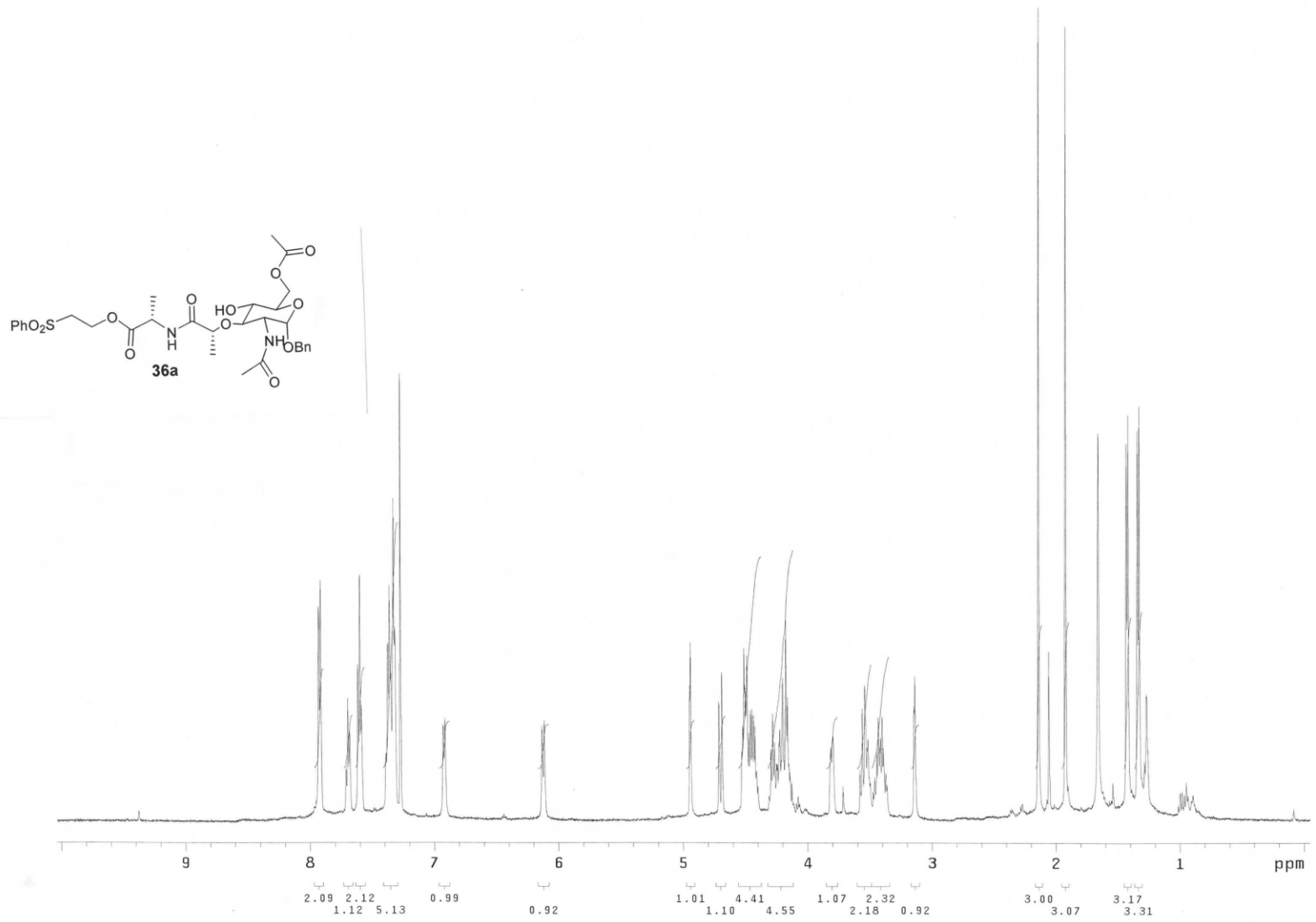

200
180
160
140
120
100
80
60
40
20
0
ppm
33b
OH
O
O
O
O
O

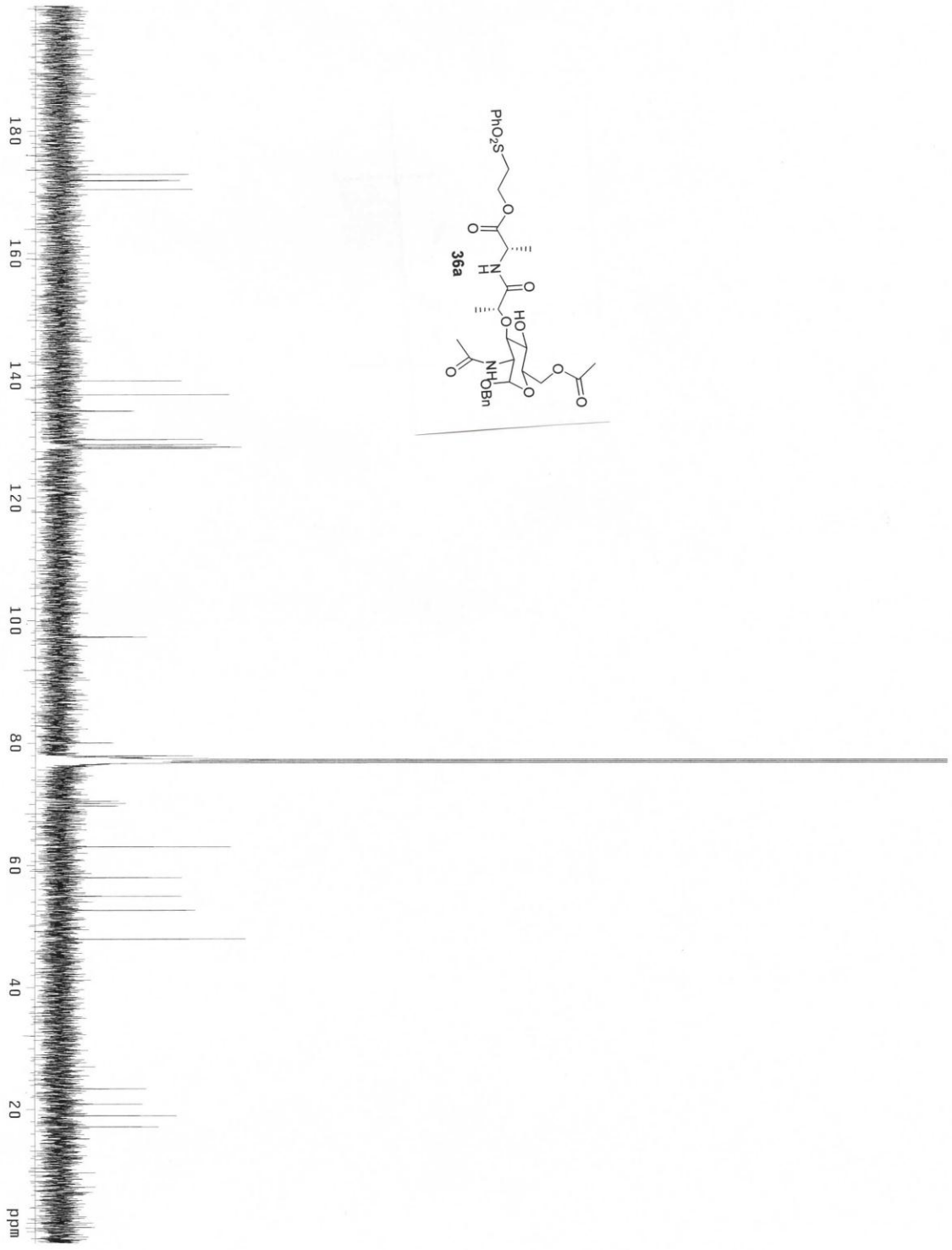

O2N
O
S
O
N
H
O
Ph
OBn
26
10
9
8
7
6
5
4
3
2
1
ppm
1.91
1.93
2.88
2.04
4.83
1.00
2.07
0.99
1.05
1.08

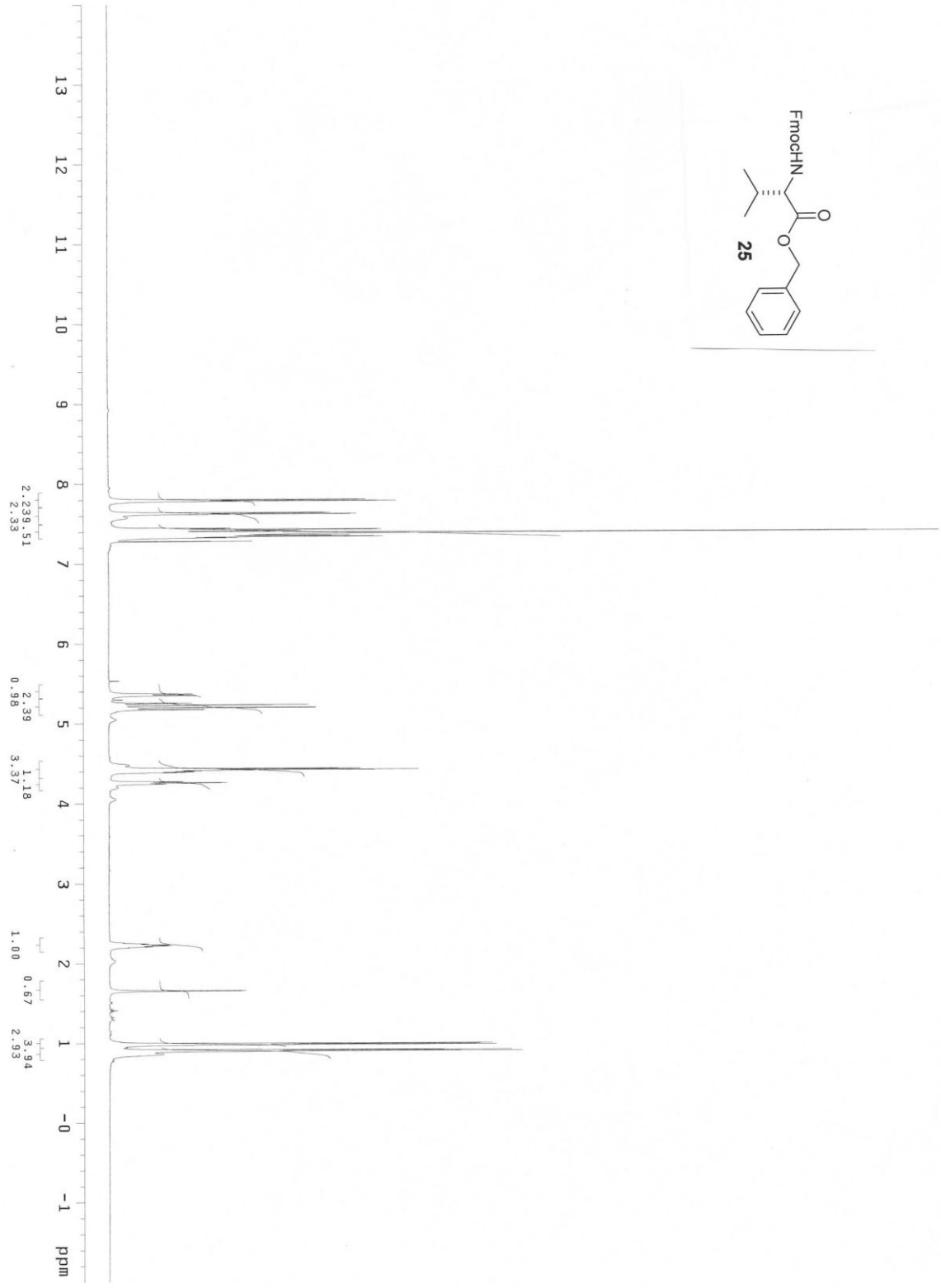

200
180
160
140
120
100
80
60
40
20
0 ppm
O2N
S
O
O
H
N
O
OBn
Ph
26

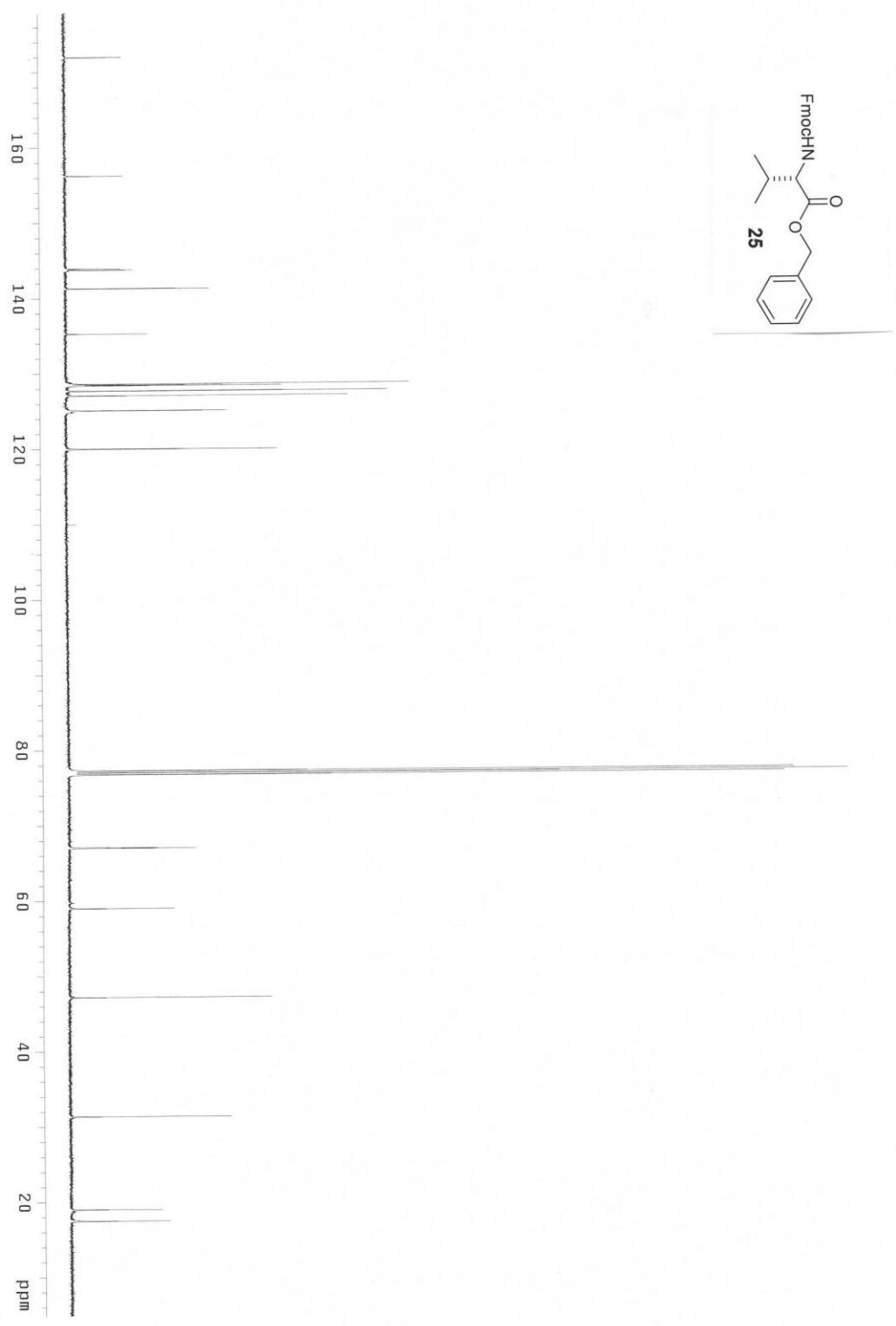

PhO2S
O
O
N
H
36b
O
HO
O
NH
Bn
O
O
Ph
O
10
9
8
7
6
5
4
3
2
1
ppm
1.98
1.95
1.11
3.27
2.22
5.16
1.02
1.00
1.03
2.20
4.68
3.36
1.05
2.31
3.30
3.13
3.54
3.15

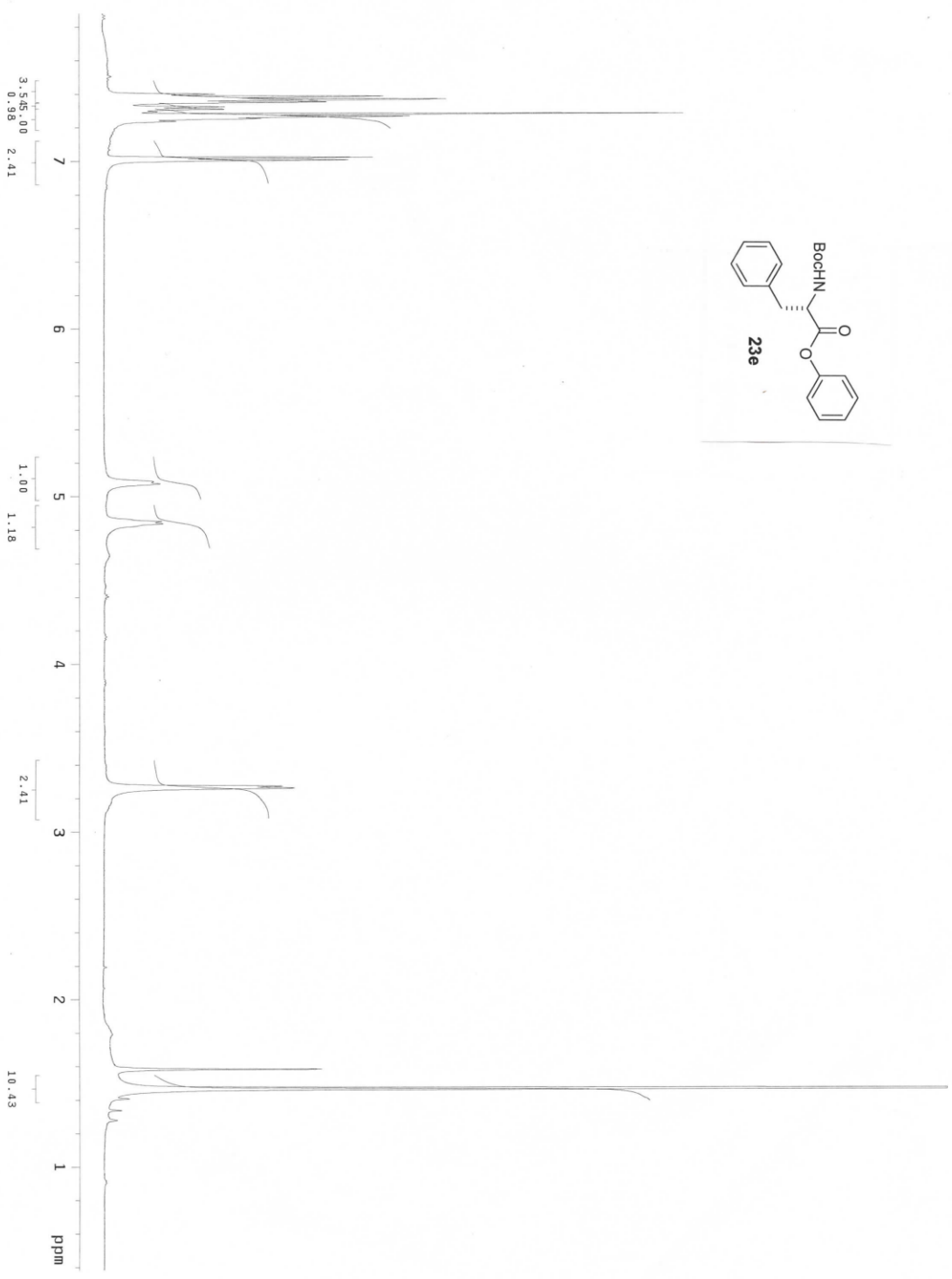

PhO2S
36b
HO
NH
OBn
Ph
180
160
140
120
100
80
60
40
20
ppm

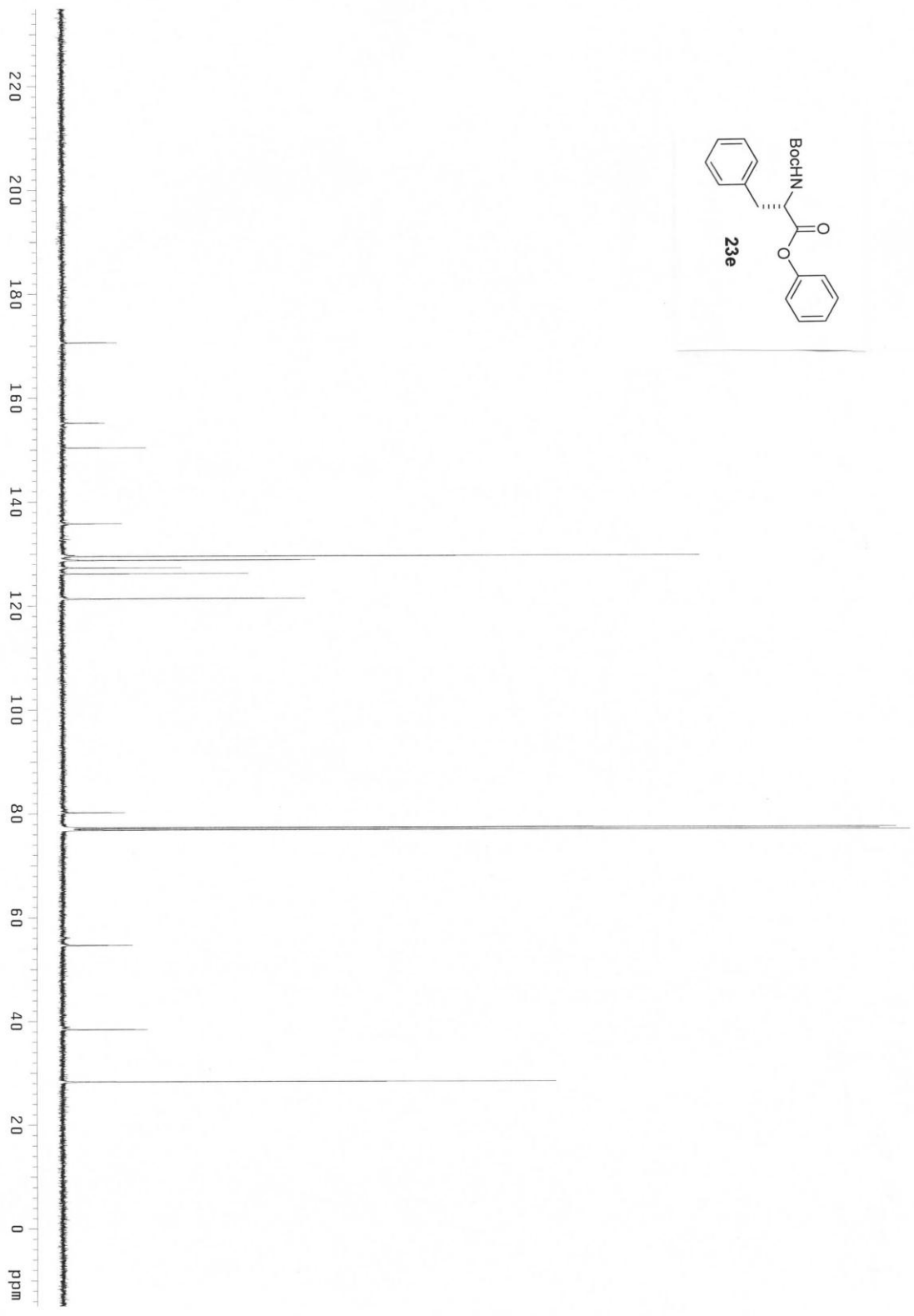

PhO2S
HO
NH
OBn
36a
9
8
7
6
5
4
3
2
1
ppm
2.09 2.12 0.99
1.12 5.13
0.92
1.01 4.41 1.07 2.32
1.10 4.55 2.18 0.92
3.00 3.17
3.07 3.31

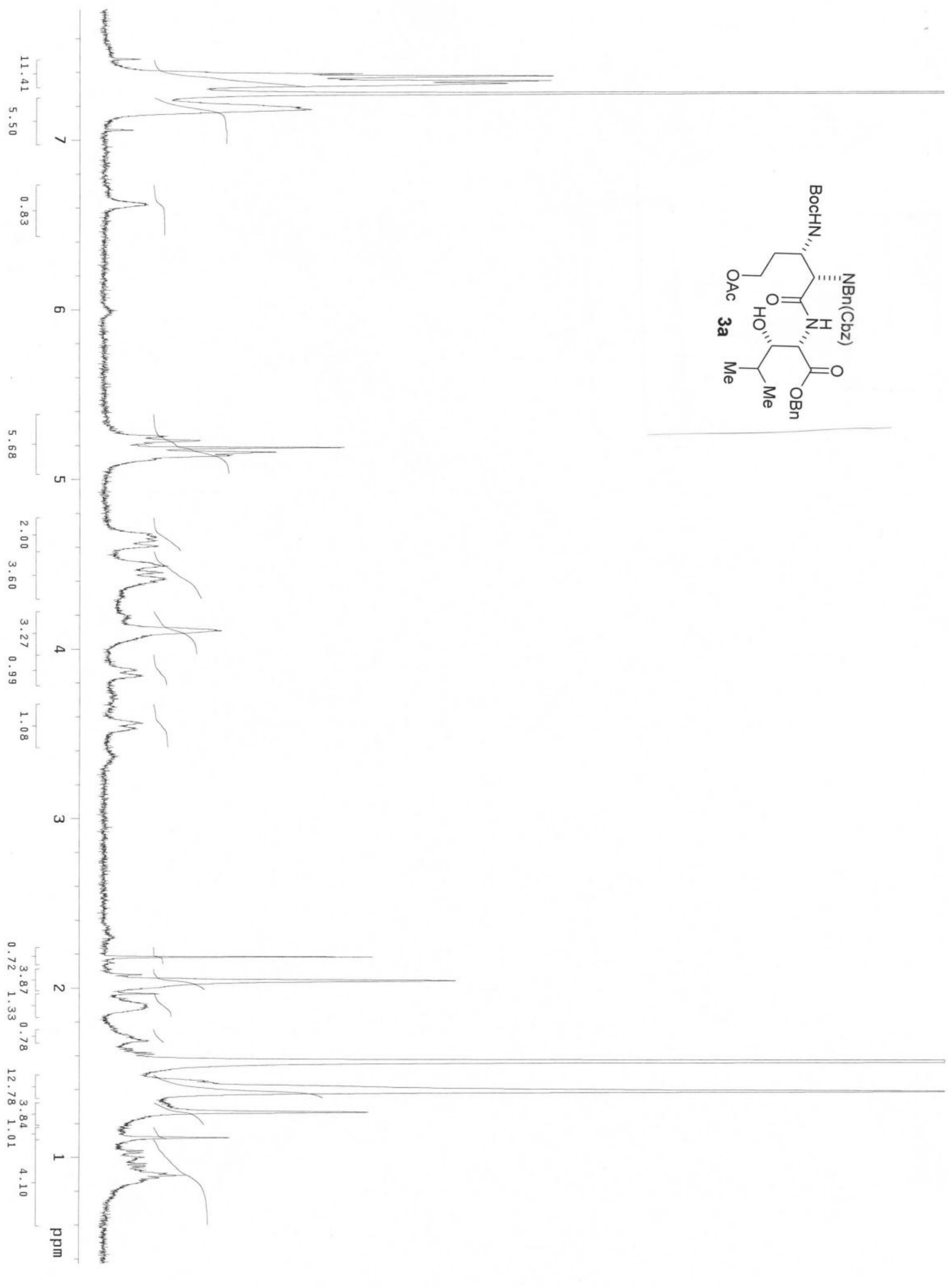

PhO2S
O
O
O
36a
N
H
O
O
HO
O
NHO
Bn
O
O
O
180
160
140
120
100
80
60
40
20
ppm

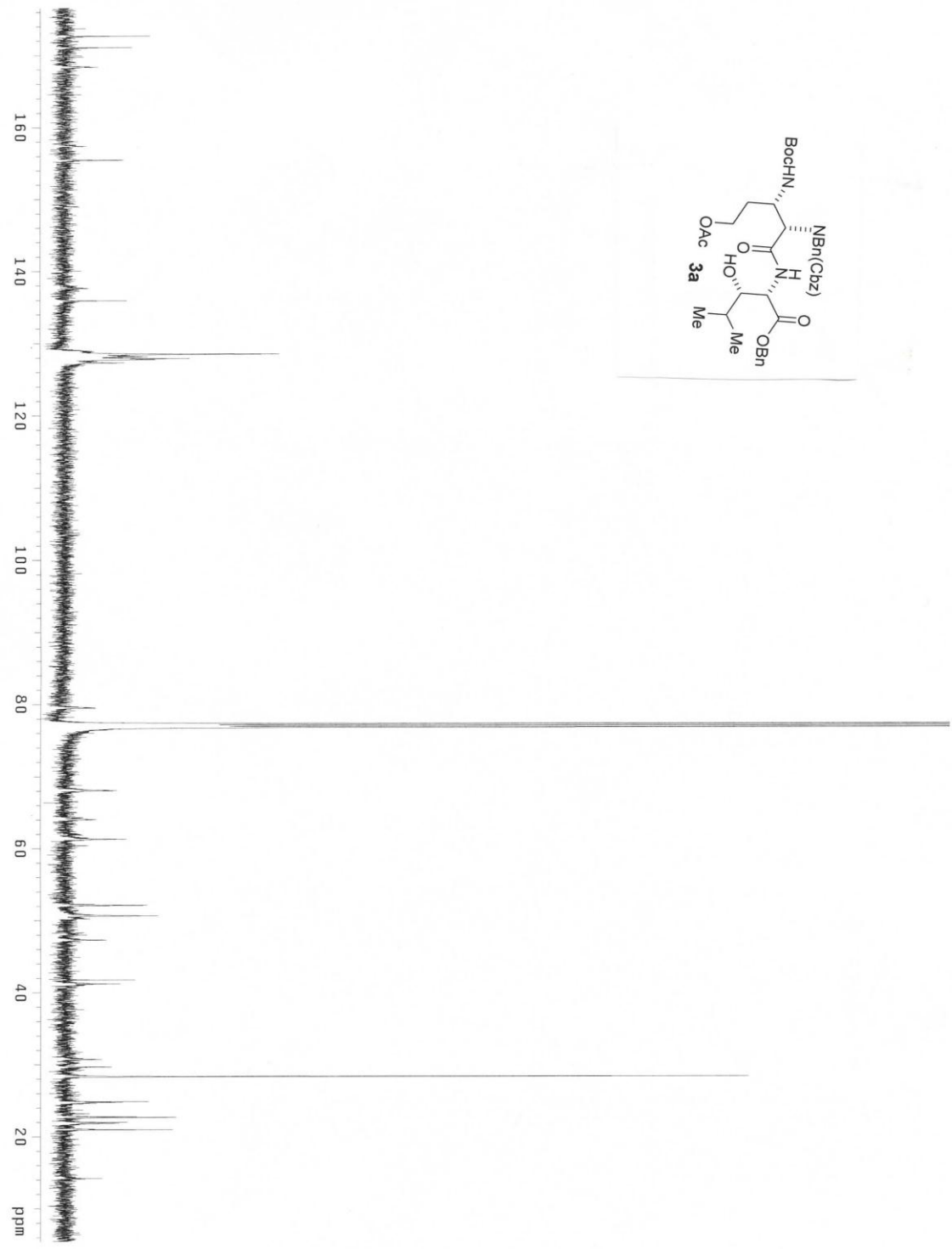

FmocHN
O
O
25
13
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm
2.33
2.23
9.51
0.98
2.39
3.37
1.18
1.00
0.67
2.93
3.94

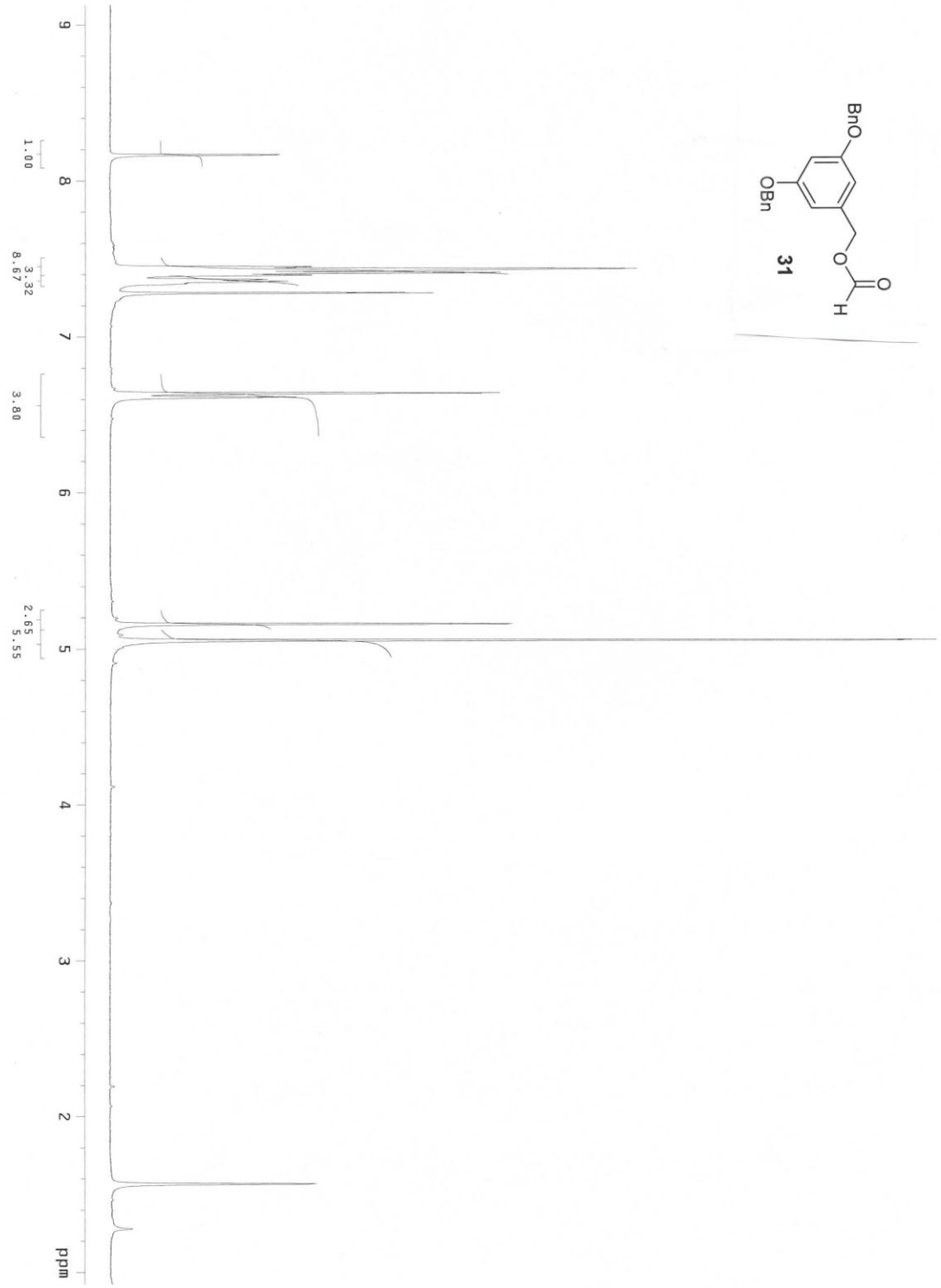

FmocHN
O
O
25
160
140
120
100
80
60
40
20
ppm

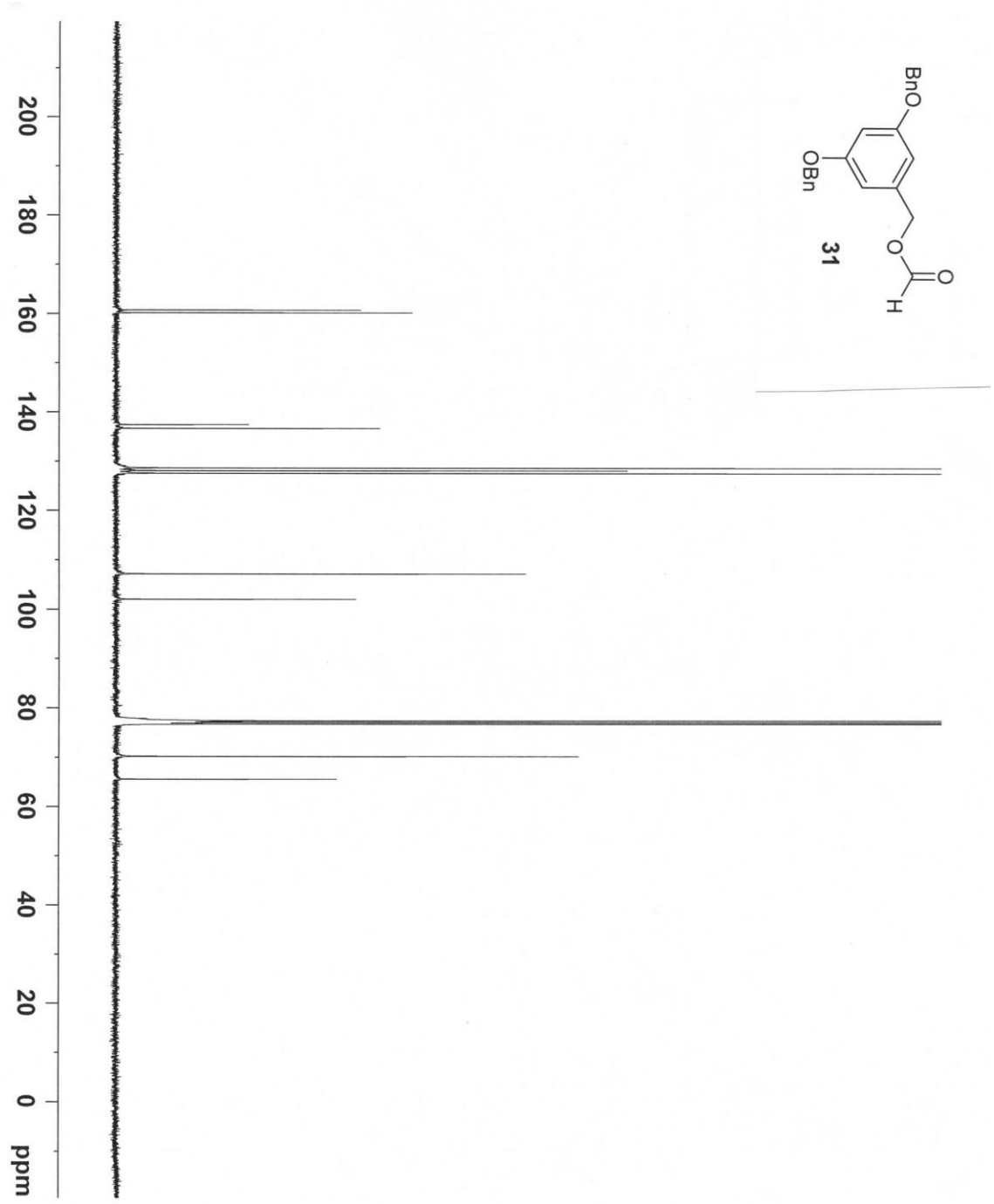

BocHN
O
O
23e
3.54
5.00
0.98
2.41
1.00
1.18
2.41
10.43
7
6
5
4
3
2
1
ppm

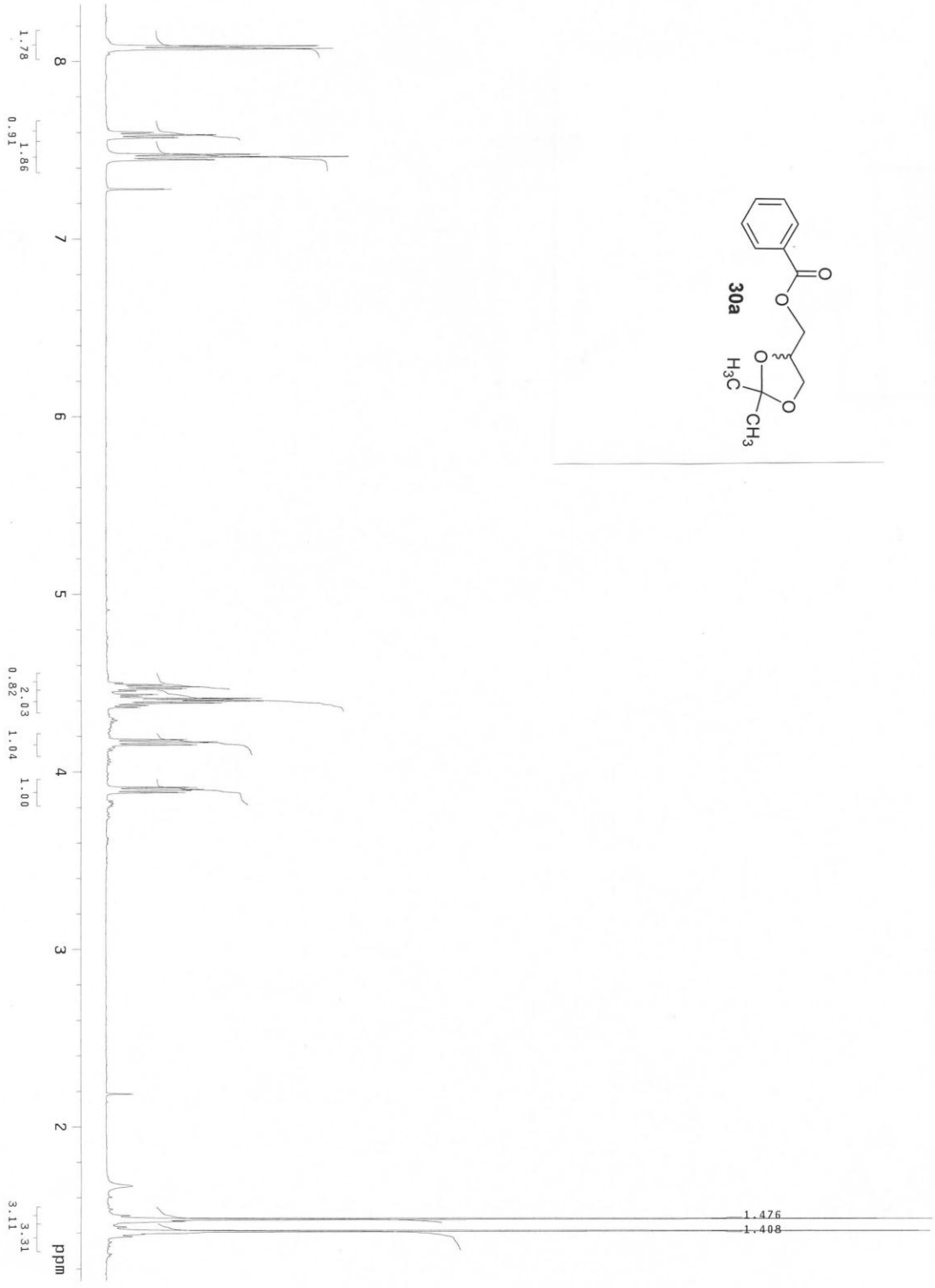

BocHN
O
O
23e
220
200
180
160
140
120
100
80
60
40
20
0
ppm

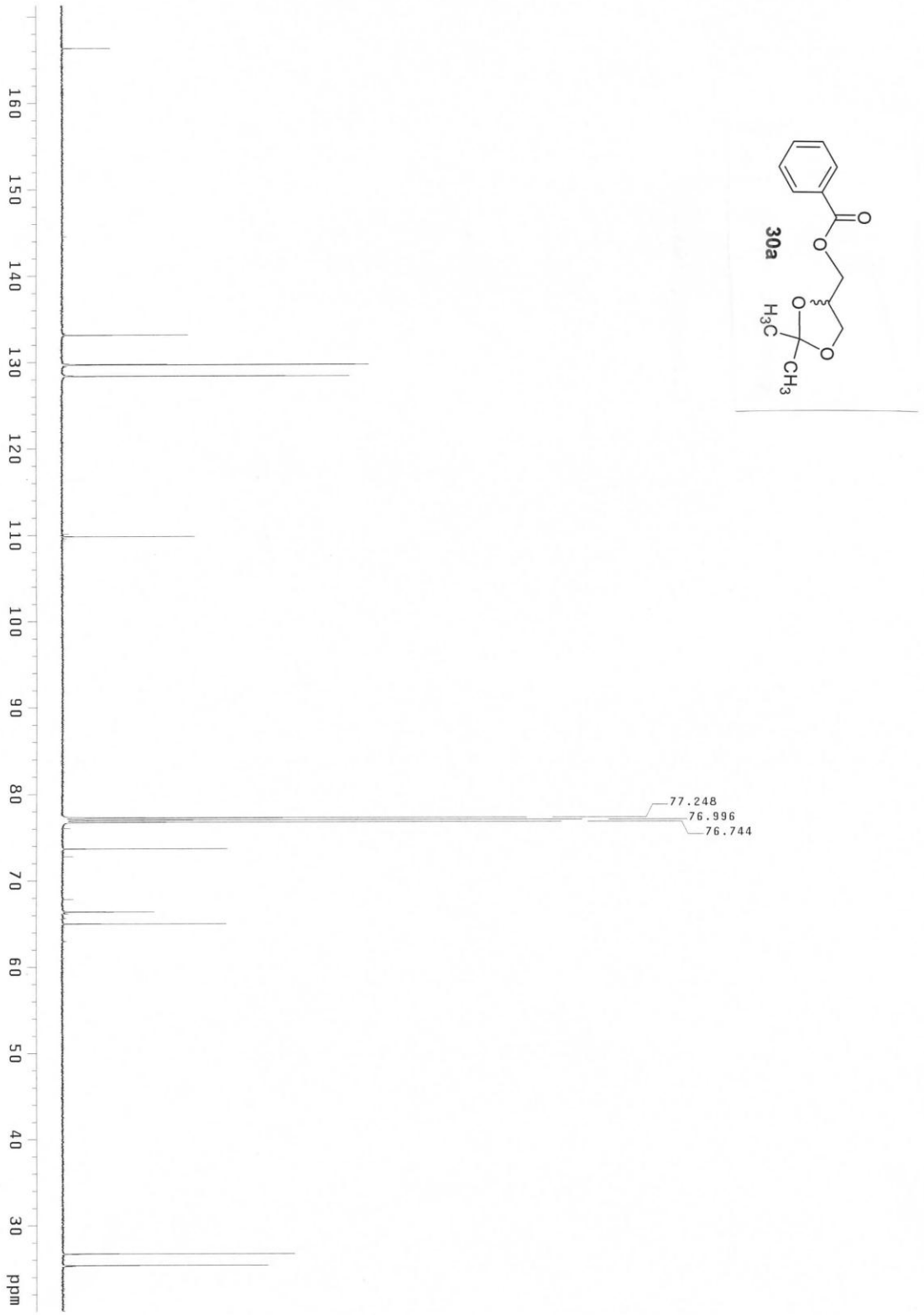

BocHN
NBn(Cbz)
H
N
O
O
OBn
HO
Me
Me
OAc
3a
ppm

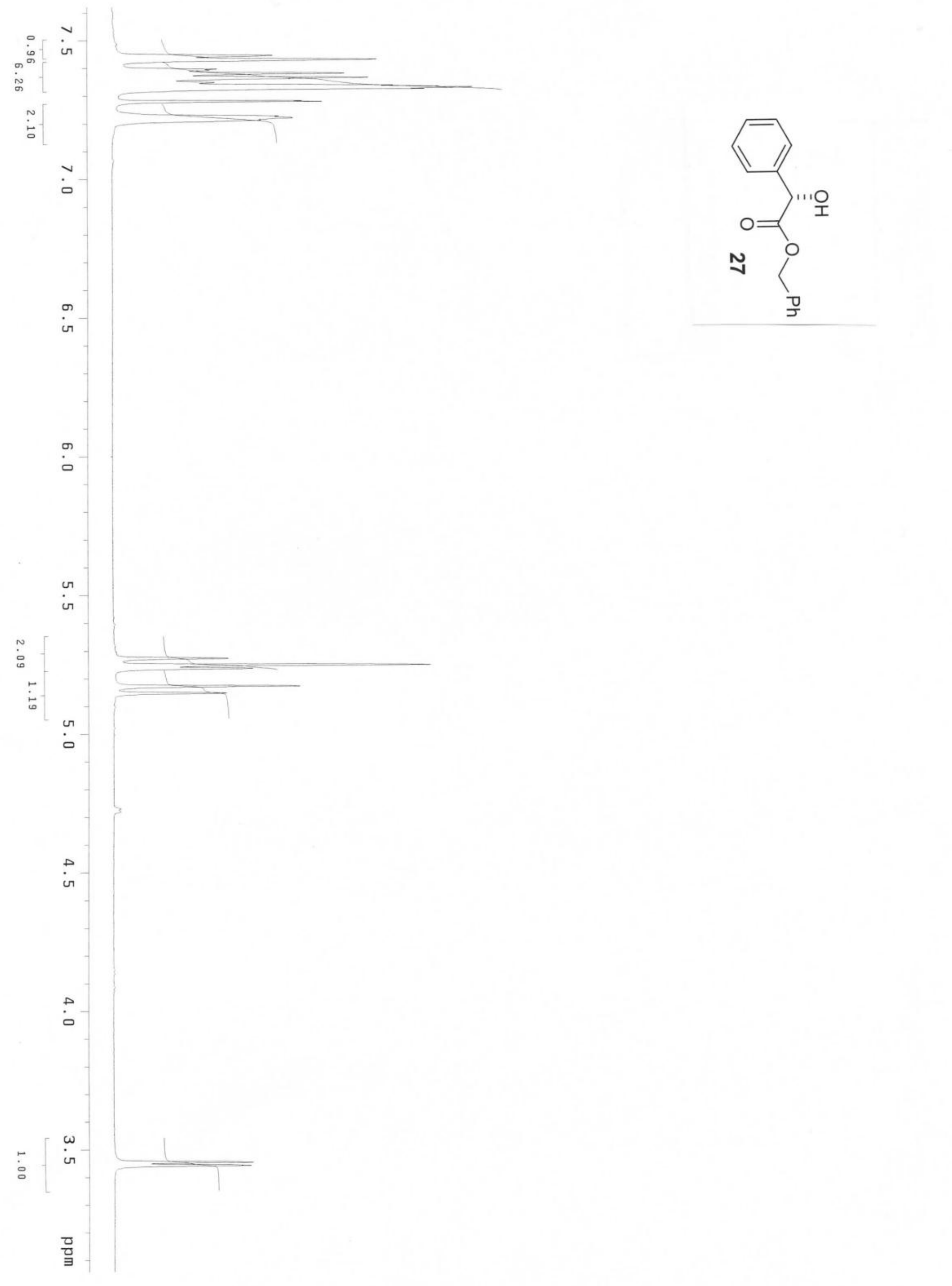

BocHN
NBn(Cbz)
OAc
3a
HO
Me
Me
OBn
160
140
120
100
80
60
40
20
ppm

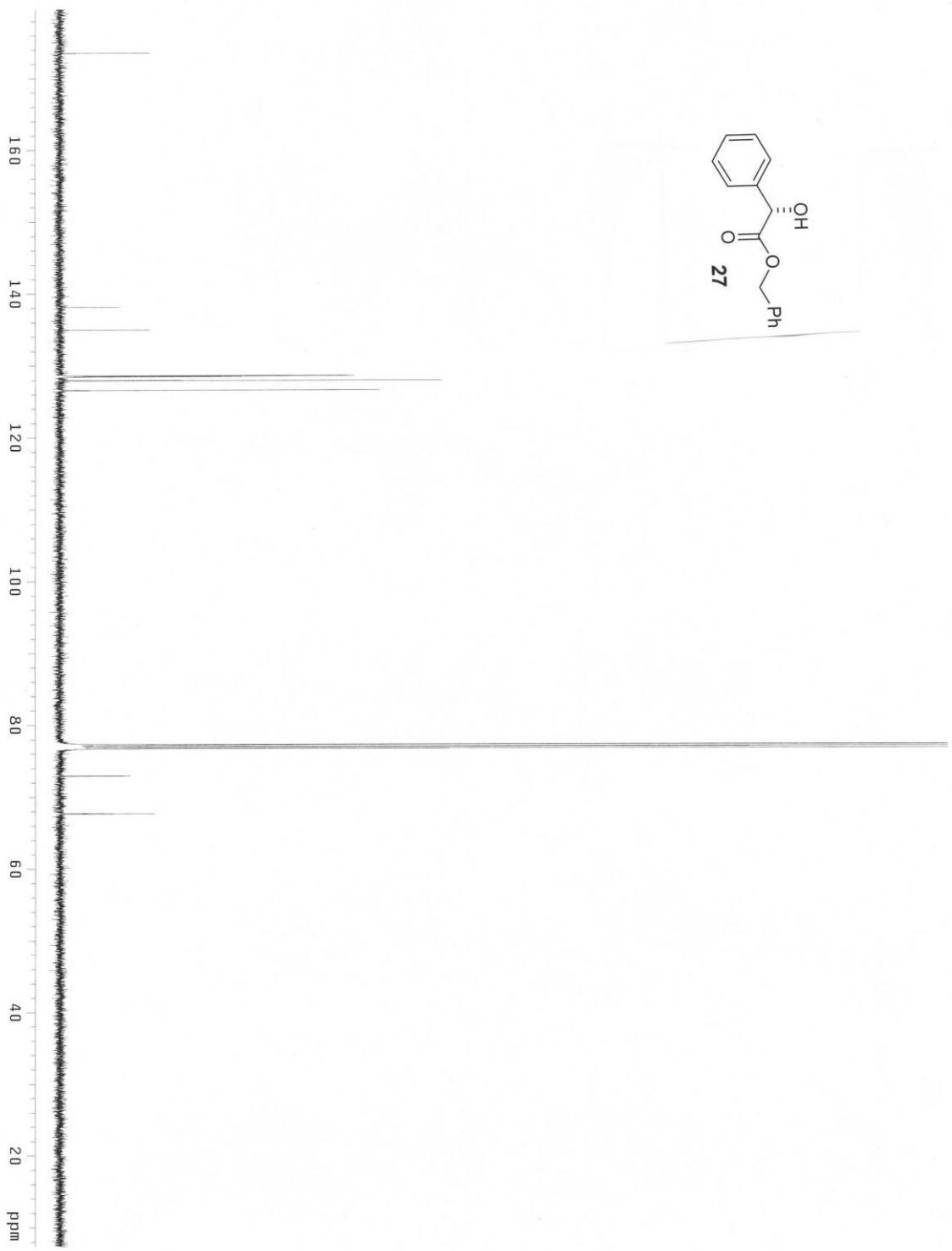

BnO
OBn
31
O
H
O
9
8
7
6
5
4
3
2
ppm
1.00
3.32
8.67
3.80
2.65
5.55

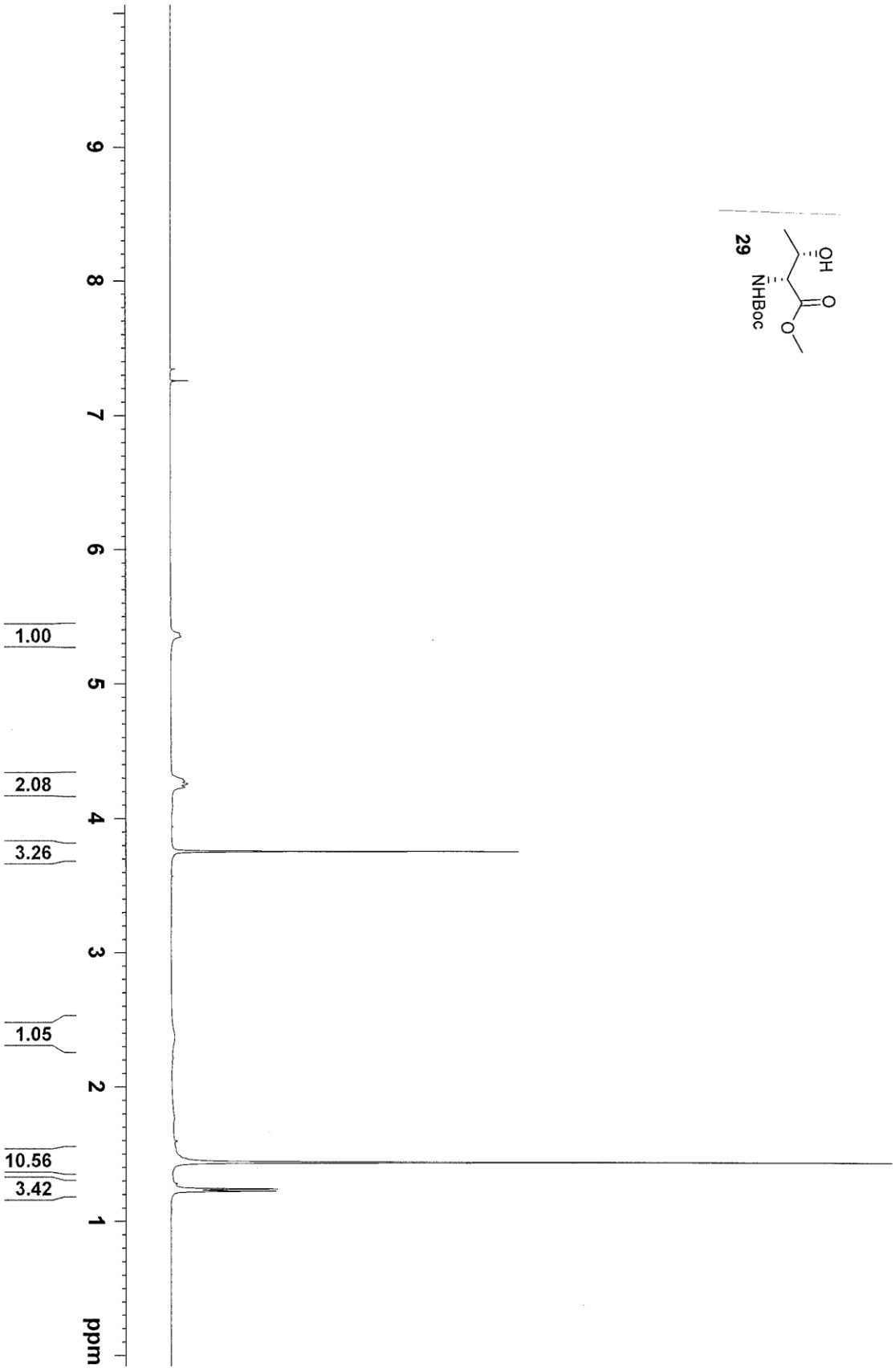

BnO
OBn
31
O
H
200
180
160
140
120
100
80
60
40
20
0
ppm

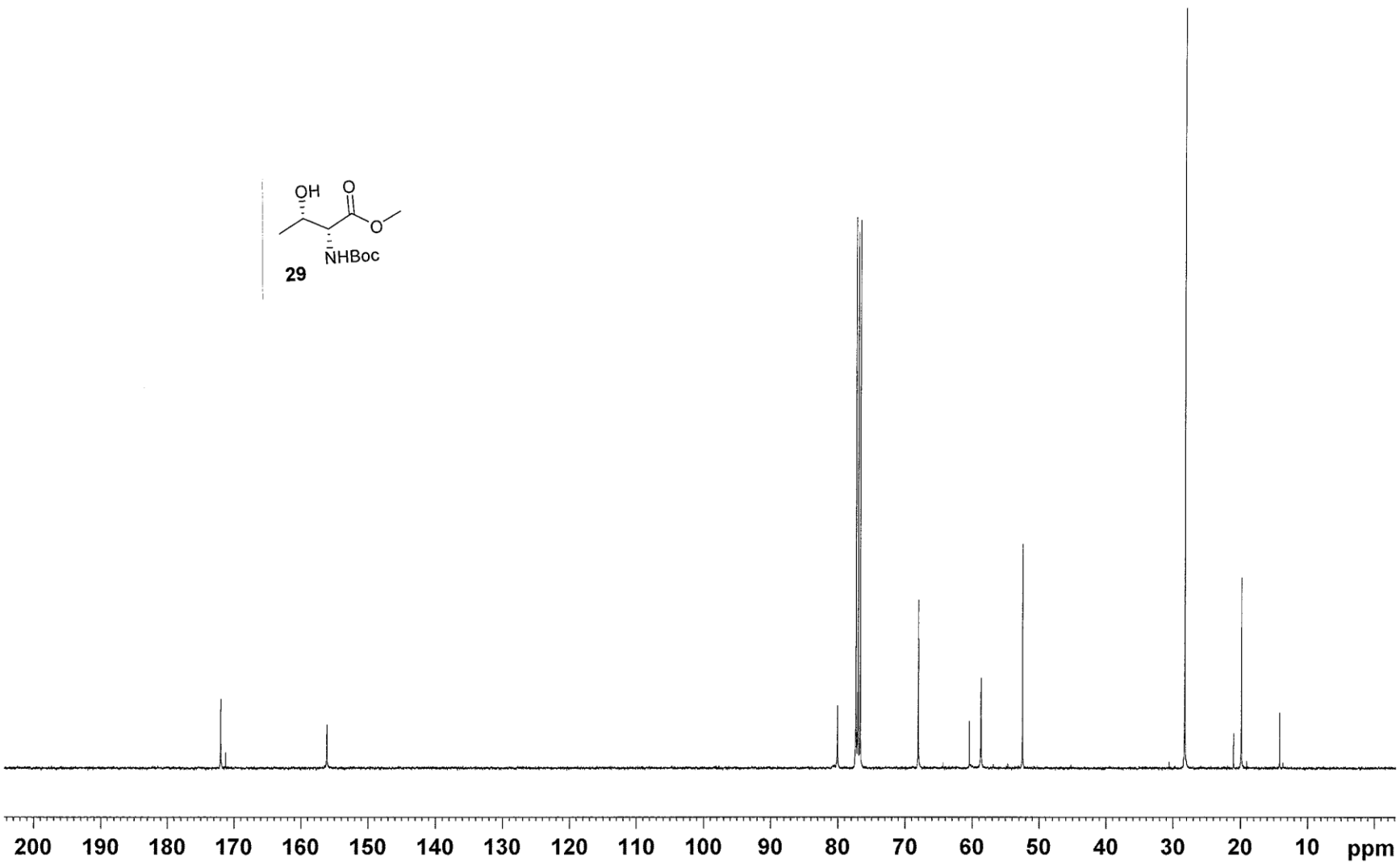

30a
1.78
1.86
0.91
2.03
0.82
1.04
1.00
3.31
3.11
1.476
1.408
ppm


30a
77.248
76.996
76.744
ppm


7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
ppm
0.96
6.26
2.10
2.09
1.19
1.00
OH
O
O
Ph
27

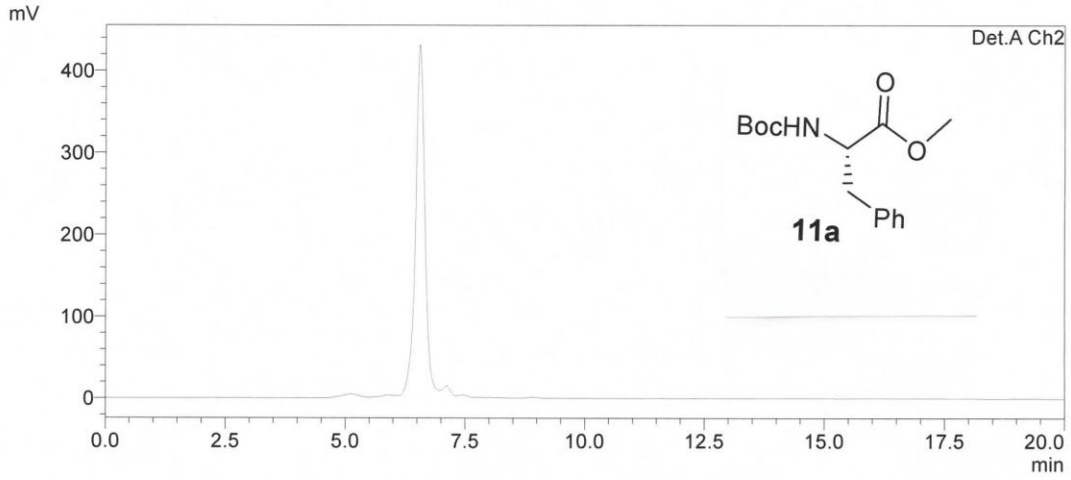

OH
O
O
Ph
27
160
140
120
100
80
60
40
20
ppm


29
OH
NHBoc
O
O
1.00
2.08
3.26
1.05
10.56
3.42
ppm

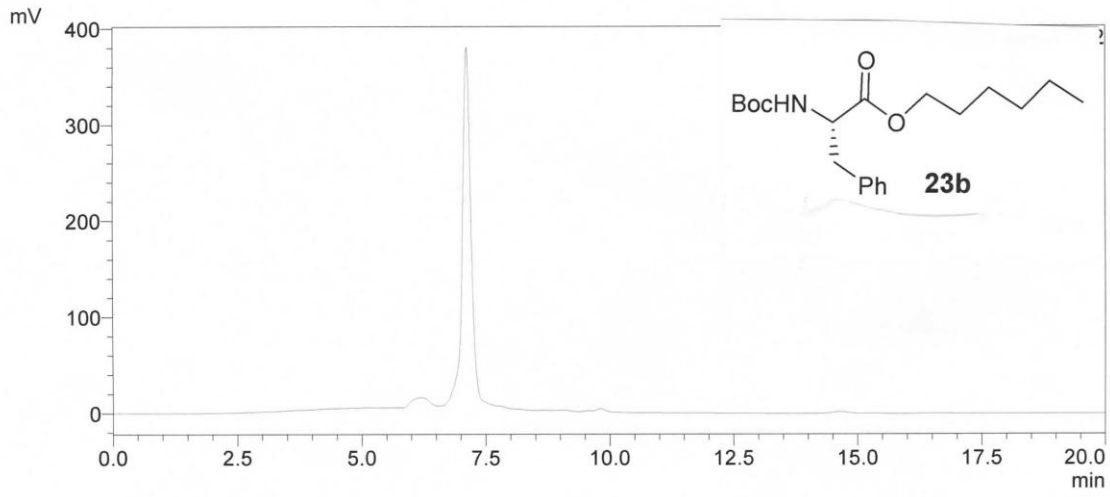

OH
O
O
NHBoc
29
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

Determination of racemization of the optically active esters via HPLC

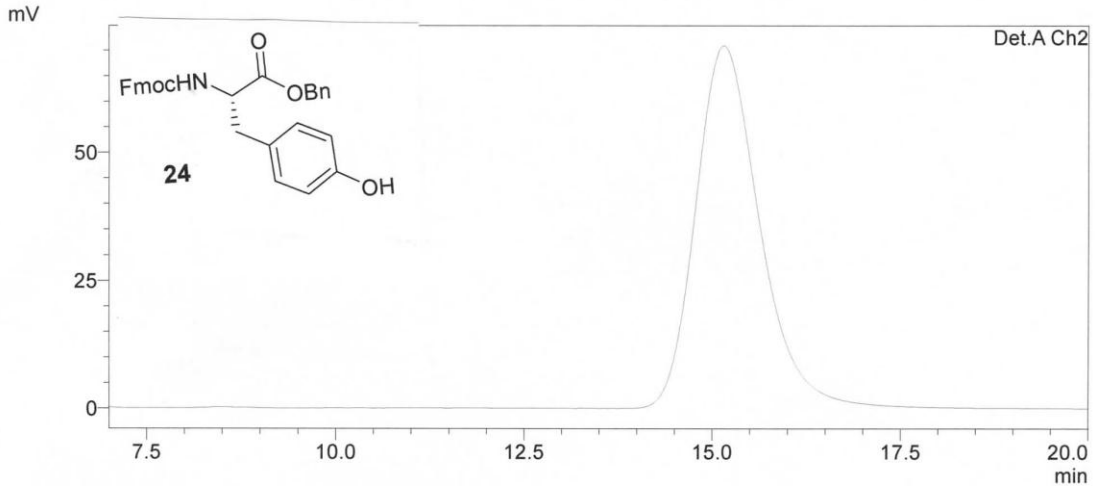
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



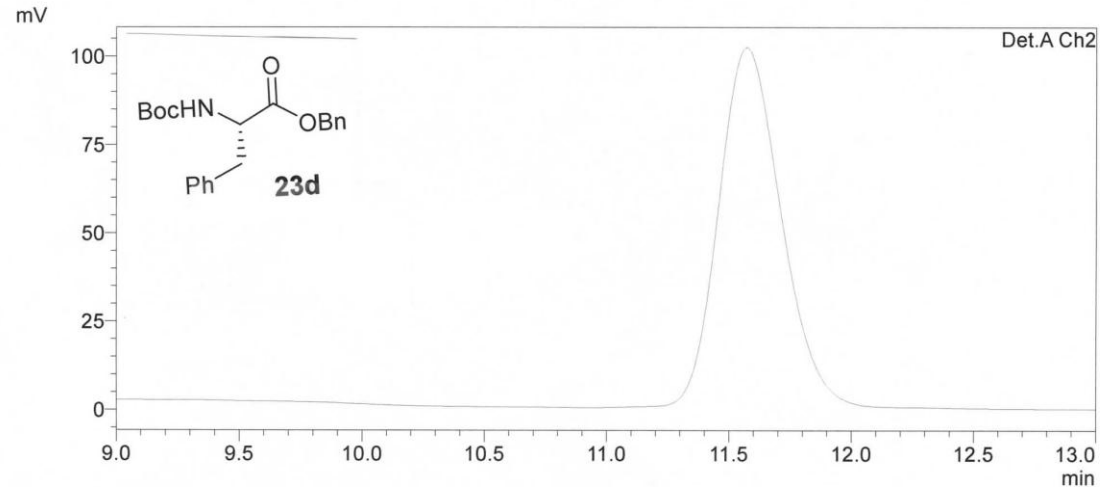
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



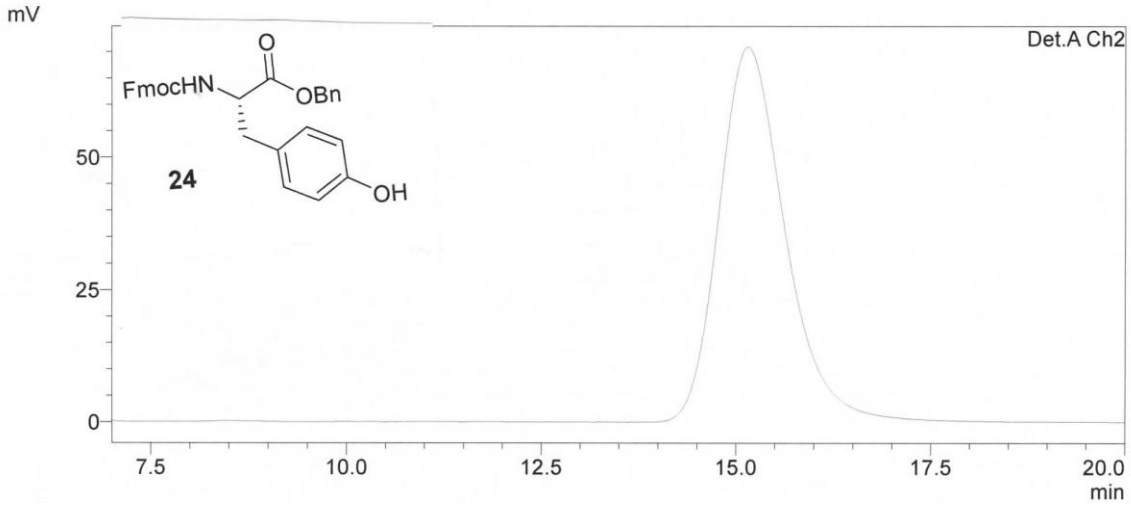
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



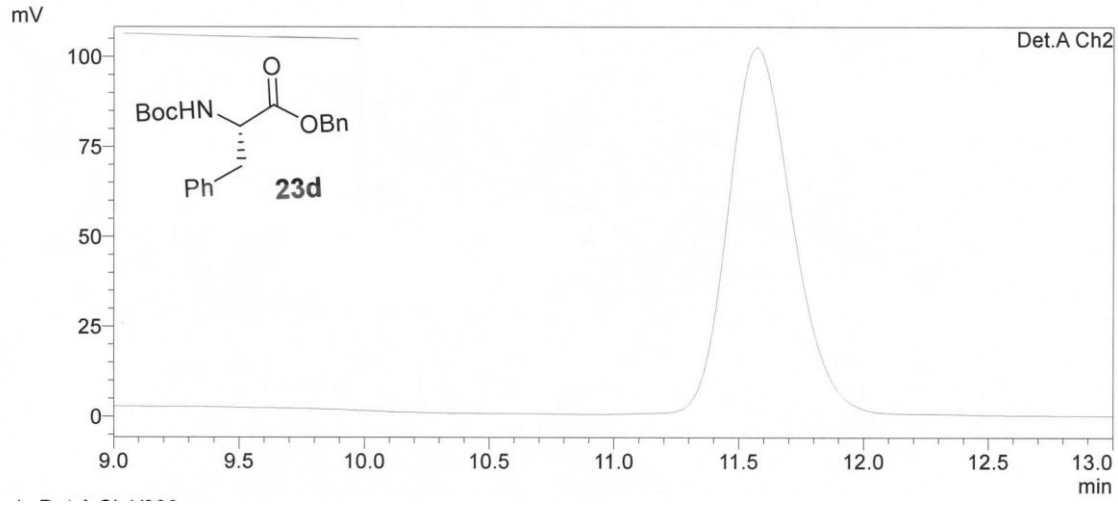
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



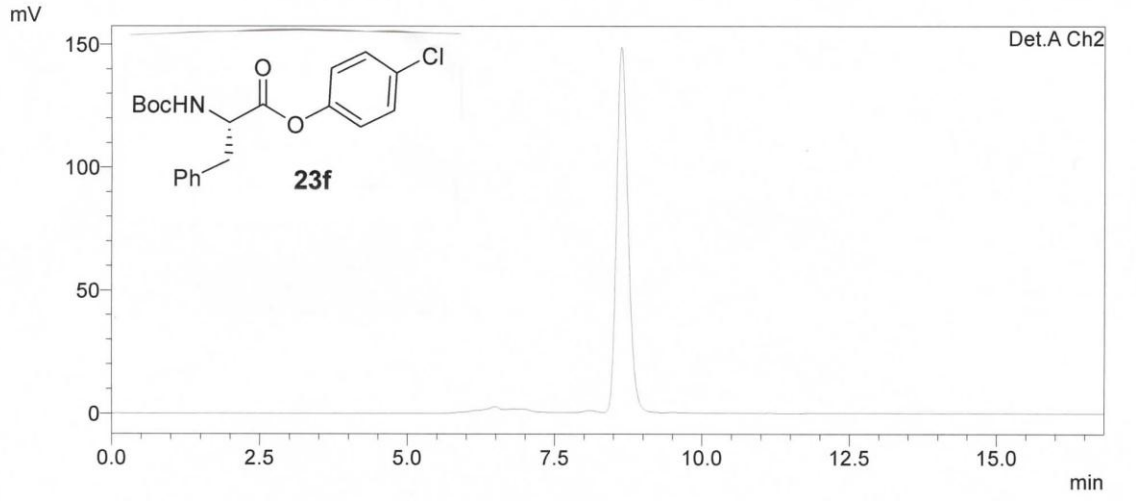
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



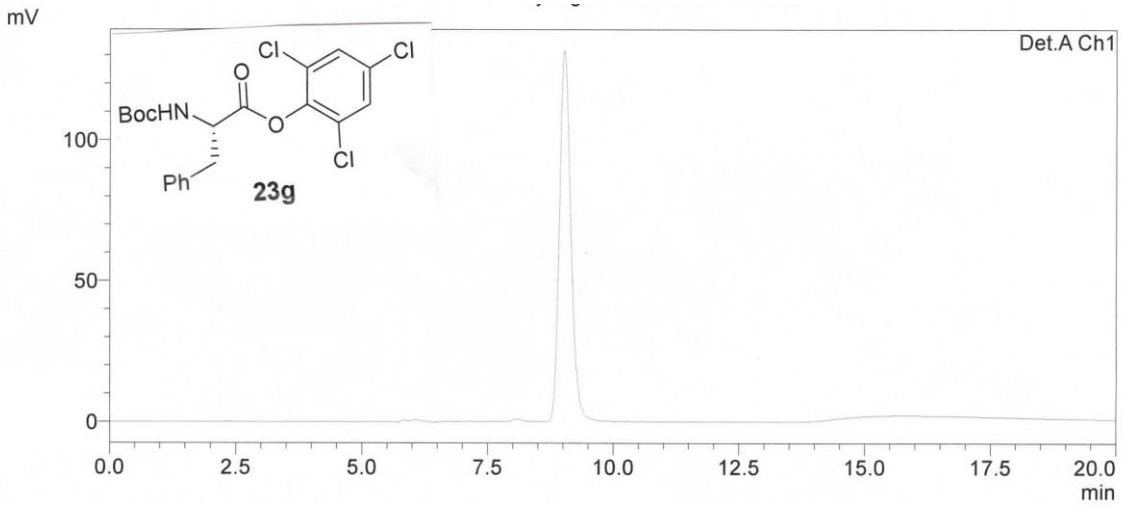
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



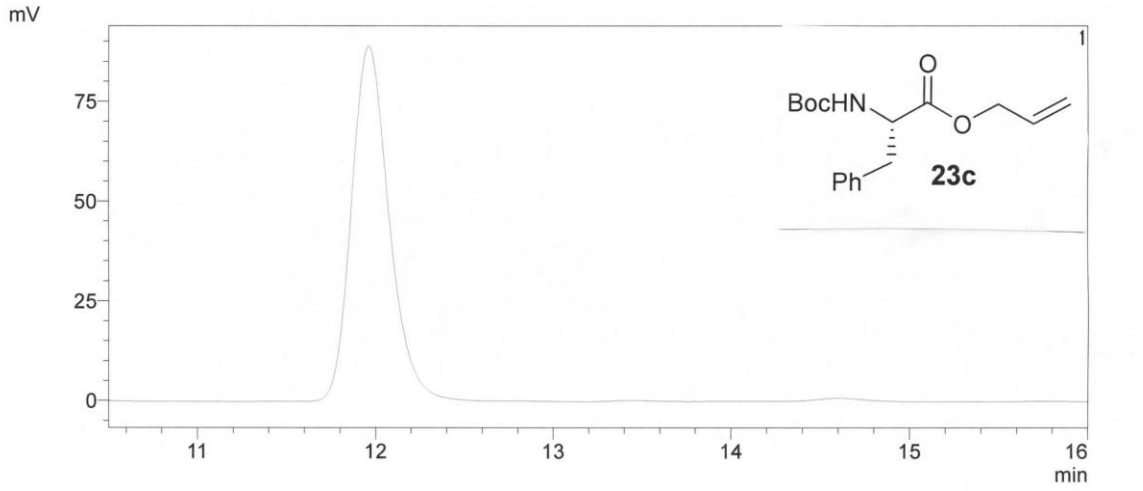
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



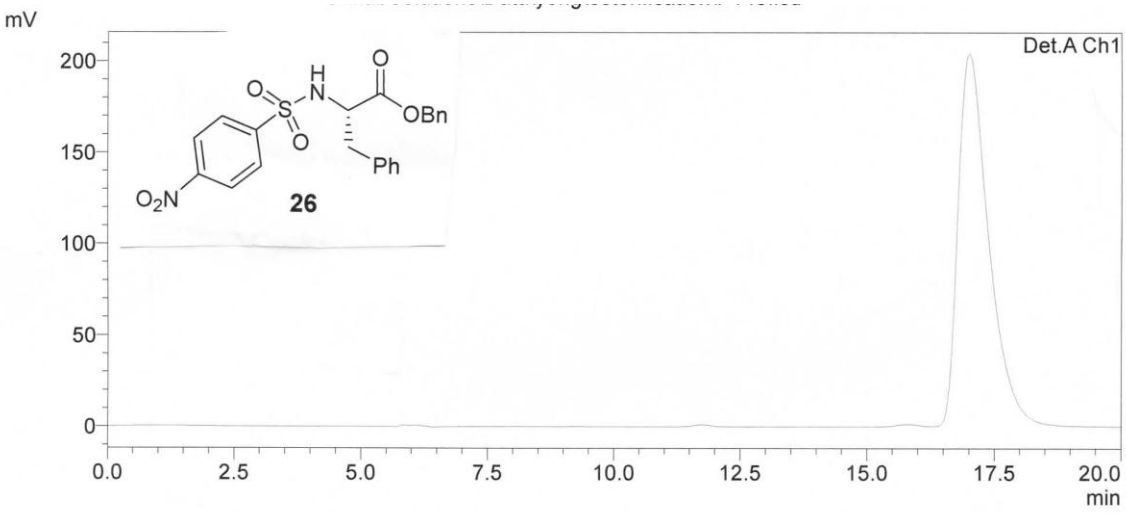
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



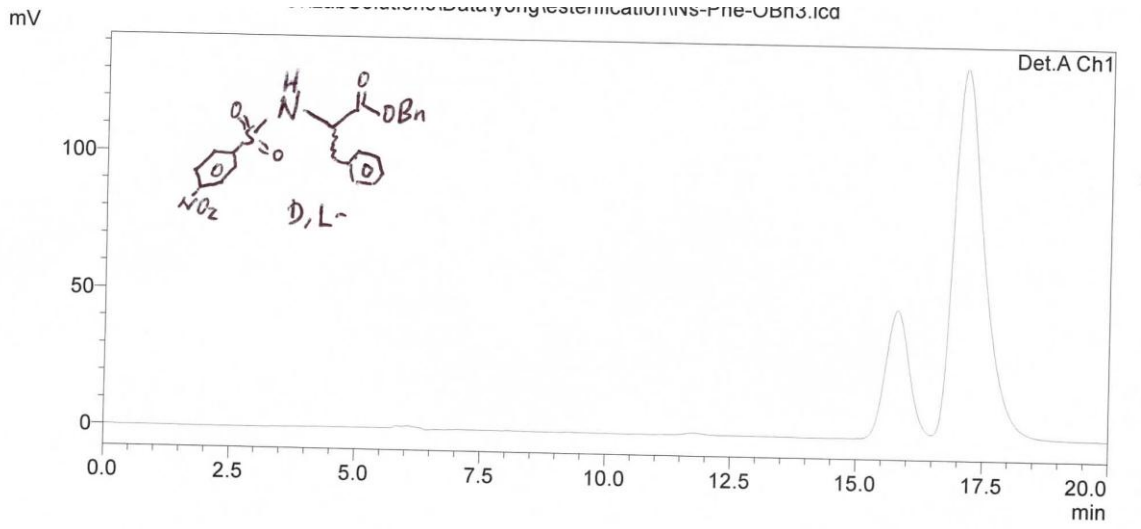
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



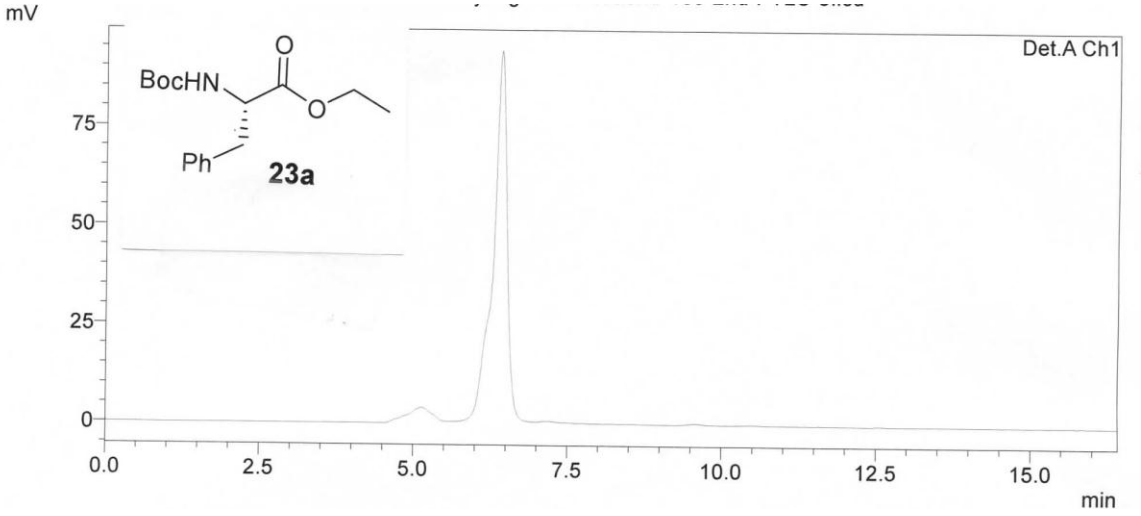
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



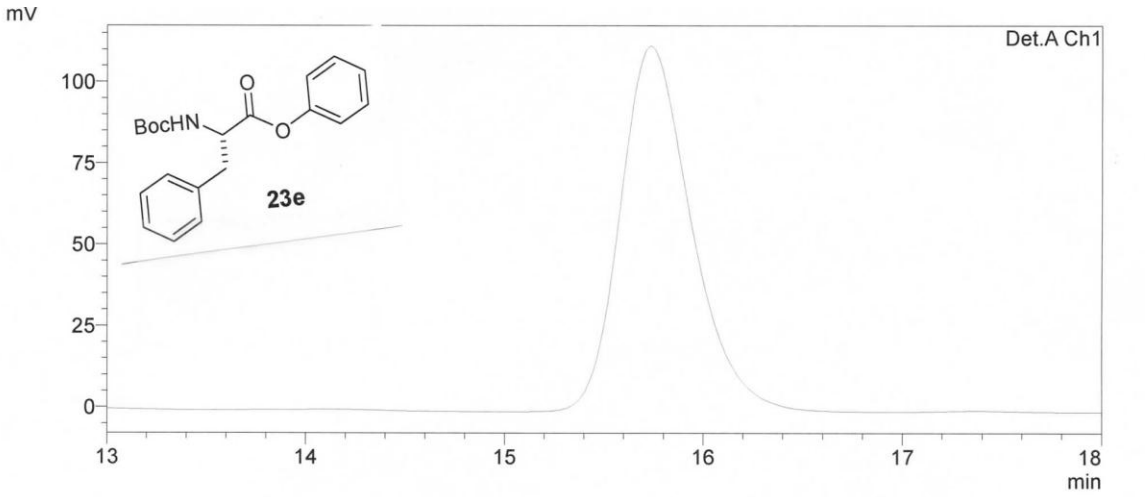
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



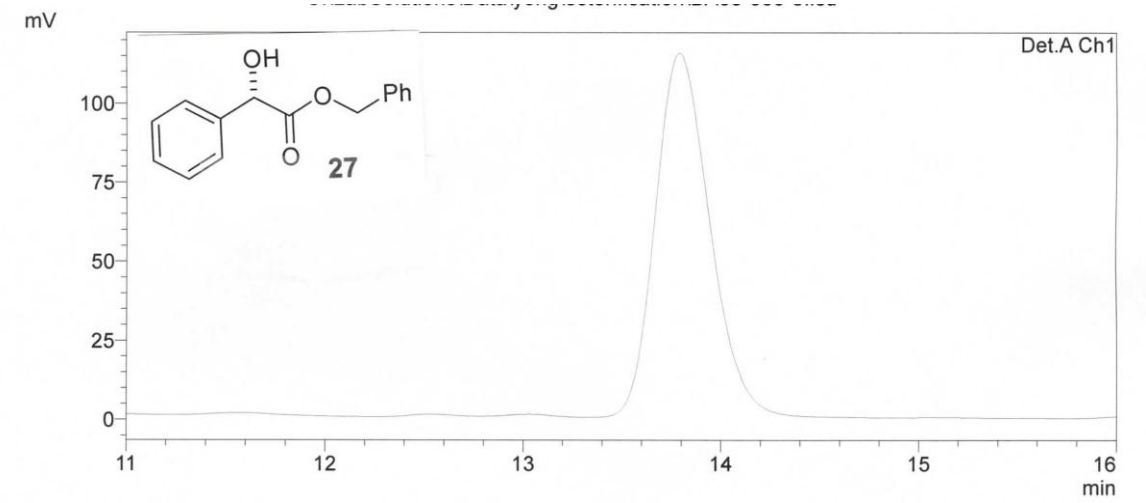
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



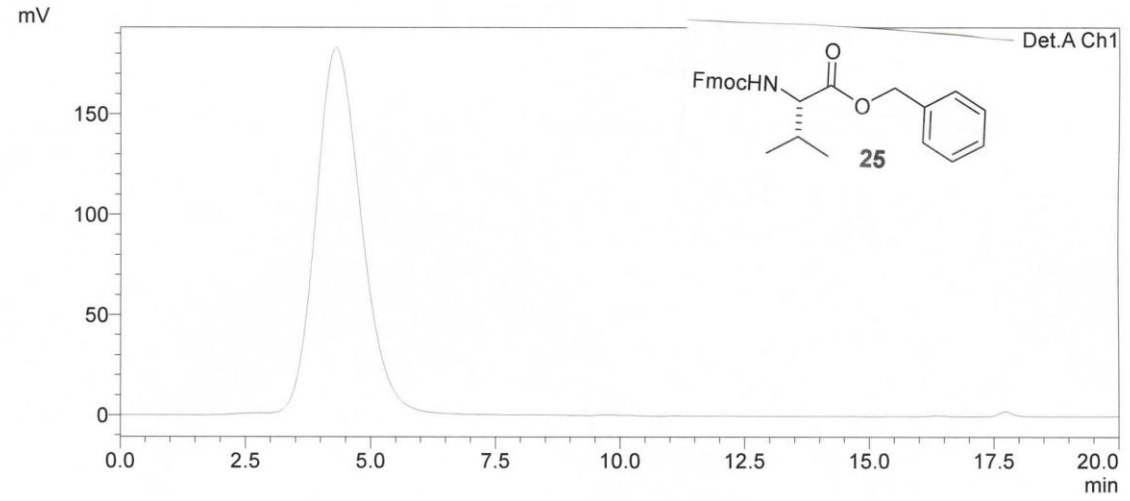
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



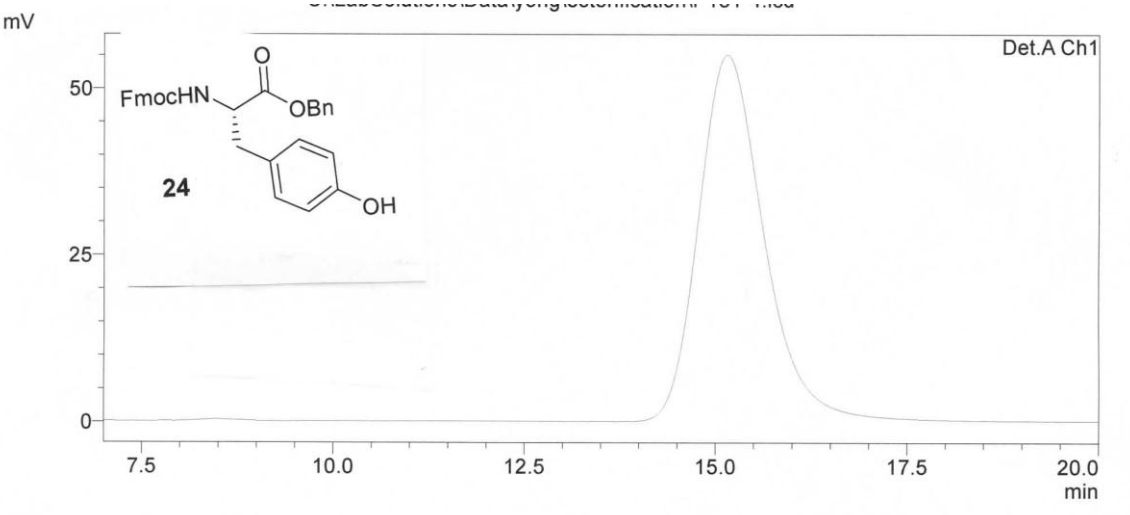
Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



Chromatography condition: ^{i}PrOH:Hexanes (30:70), Daicel Chiralcel OD-H column, 0.5ml/min, 254 nm



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