Supporting Information

Large-scale asymmetric synthesis of the bioprotective agent JP4-039 and analogs

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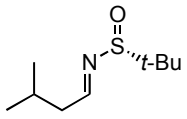
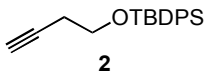
General information. All moisture- and air-sensitive reactions were performed using syringe-septum cap techniques under an inert atmosphere (N_2 or argon) in glassware that was dried in an oven at 140 °C for at least 2 h prior to use. Reactions carried out at a temperature below 0 °C employed a brine/ice bath or a CO_2/acetone bath. All reagents and solvents were used as received unless otherwise specified. THF and Et_2O were distilled over sodium/benzophenone ketyl; MeOH was distilled over magnesium; benzene, acetonitrile and DME were distilled over CaH_2; DMF was distilled and stored over 4Å molecular sieves; pyridine and triethylamine were distilled over CaH_2 and stored over KOH; CH_2Cl_2 and toluene were purified using an alumina column filtration system. Analytical thin-layer chromatography (TLC) was performed on pre-coated SiO_2 60 F_{254} plates (250 μm layer thickness) available from Merck. Visualization was accomplished by UV irradiation at 254 nm and/or by staining with Vaughn's reagent (4.8 g $(NH_4)_6Mo_7O_{24}\bullet 4H_2O$ and 0.2 g $Ce(SO_4)_2\bullet 4H_2O$ in 100 mL of a 3.5 N H_2SO_4 solution), a $KMnO_4$ solution (1.5 g $KMnO_4$ and 1.5 g K_2CO_3 in 100 mL of a 0.1% NaOH solution), a ninhydrin solution (2 g ninhydrin in 100 mL EtOH), a PMA solution (5 g phosphomolybdic acid in 100 mL EtOH), or a *p*-anisaldehyde solution (2.5 mL *p*-anisaldehyde, 2 mL AcOH and 3.5 mL conc. aq. H_2SO_4 in 100 mL EtOH). Flash column chromatography was performed using SiO_2 60 (particle size 0.040–0.055 mm, 230–400 mesh, or Silicycle SiliaFlash® P60, 40-63 μm). Melting points were determined on a Laboratory Devices Mel-Temp II capillary melting point apparatus fitted with a Fluke 51 II digital thermometer. Optical rotations were determined using a Perkin-Elmer 241 polarimeter. Chiral analytical SFC was performed on a Mettler Toledo instrument under the following conditions: column: Chiralpak-IC (250 x 4.6 mm); elution: 7% MeOH in CO_2; pressure: 100 bar; flow: 3 mL/min; sample concentration: 20 mg/mL in MeOH; injection volume: 4 μL; detection: UV λ = 195 nm. Infrared spectra were recorded on a Smiths IdentifyIR ATR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker Avance 300 or 400 instrument at 300/75 MHz or 400/100 MHz, respectively. Chemical shifts were reported in parts per million (ppm) as referenced to residual solvent. ^{1}H NMR spectra are tabulated as follows: chemical shift, multiplicity (app = apparent, b = broad, s = singlet, d = doublet, t = triplet, q = quartet, quint = quintuplet, sext, = sextuplet, m = multiplet), number of protons, coupling constant(s). ^{13}C NMR were obtained using a proton-decoupled pulse sequence and are tabulated by observed peak. ^{19}F NMR were obtained on a Bruker Avance 400 instrument at 376 MHz, using a proton-coupled pulse sequence without internal standard. Mass spectra were obtained on a Waters Autospec double focusing mass spectrometer (EI), a Waters Q-Tof mass spectrometer (ESI), or a Waters Q-Tof Ultima API mass spectrometer (APCI) at the University of Pittsburgh Mass Spectrometry facility.



(*R*)-1

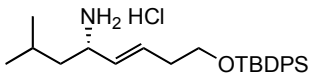
(*R*,*E*)-2-Methyl-*N*-(3-methylbutylidene)propane-2-sulfinamide ((*R*)-1).[1] To a solution of isovaleraldehyde (3.21 mL, 29.1 mmol) in CH_2Cl_2 (150 mL) were added successively (*R*)-2-methylpropane-2-sulfinamide (3.00 g, 24.3 mmol), $MgSO_4$ (14.60 g, 121 mmol) and PPTS (622 mg, 2.43 mmol). The resulting white suspension was stirred at rt for 23 h, then filtered through a pad of Celite and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (8:2, heptane/EtOAc) afforded 4.12 g (90%) of **(*R*)-1** as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.07 (t, 1 H, *J* = 5.2 Hz), 2.48-2.35 (m, 2 H), 2.15-1.96 (m, 1 H), 1.21 (s, 9 H), 1.00 (d, 6 H, *J* = 6.6 Hz). As an alternative, filtration through a pad of SiO_2 provides crude imine that functions equally well in subsequent reactions.



2

(But-3-ynyloxy)(*tert*-butyl)diphenylsilane (2).[2] To a solution of 3-butyn-1-ol (3.00 g, 41.5 mmol) in CH_2Cl_2 (240 mL) were added successively imidazole (3.14 g, 45.7 mmol) and TBDPSCl (12.1 mL, 45.7 mmol). The resulting white suspension was stirred at rt for 23 h, then filtered through a pad of SiO_2, the SiO_2 washed with CH_2Cl_2 and the colorless solution concentrated *in vacuo* to yield 14.6 g of crude **2** as a clear oil that was carried on without further purification.

Large Scale Procedure: To a solution of 3-butyn-1-ol (75.0 g, 1.07 mol) in CH_2Cl_2 (3000 mL) was added imidazole (79.7 g, 1.15 mol) in one portion, followed by TBDPSCl (264.7 g, 0.96 mol) dropwise over 45 min, with the temperature controlled at 25~30 ^{o}C during the addition by a cool water bath. After the addition, the reaction mixture was stirred at 25-30 ^{o}C until the reaction was complete. The suspension was filtered through a pad of SiO_2 (500 g), the filter cake was washed with CH_2Cl_2 (1000 mL) and the filtrate was concentrated to afford **2** as a light yellow oil (304.3 g, GC purity 98.5%, yield >100%, KF = 300 ppm), which was used in the next reaction without further purification.



(*S*)-3

(*S*,*E*)-8-(*tert*-Butyldiphenylsilyloxy)-2-methyloct-5-en-4-amine hydrochloride ((*S*)-3). To a solution of alkyne **2** (9.81 g, 27.9 mmol, crude) in dry CH_2Cl_2 (162 mL) was added zirconocene hydrochloride (7.67 g, 29.7 mmol) in 3 portions and the resulting suspension was stirred at rt for 10 min. The resulting yellow solution was cooled to 0 °C and Me_3Al (freshly prepared, 2.0 M in CH_2Cl_2, 14.9 mL, 29.7 mmol) was added slowly. Stirring was continued for 5 min, then followed by slow addition of a solution of imine **(*R*)-1** (3.52 g, 18.6 mmol) in dry CH_2Cl_2 (27 mL). The resulting orange solution was stirred for 4 h while allowed to warm to rt. The reaction was quenched carefully with a small amount of water, further diluted with water and CH_2Cl_2, and 10% aq. HCl was added to break up the emulsion. The organic layer was separated and the aqueous phase extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The resulting residue was dissolved in a minimum amount of Et_2O, allowed to sit for 2 h, then filtered through a

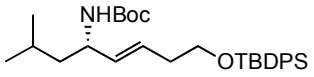
[1] Staas, D. D.; Savage, K. L.; Homnick, C. F.; Tsou, N.; Ball, R. G. *J. Org. Chem.* **2002**, *67*, 8276-8279.
[2] Nicolaou, K. C.; Lizos, D. E.; Kim, D. W.; Schlawe, D.; de Noronha, R. G.; Longbottom, D. A.; Rodriquez, M.; Bucci, M.; Cirino, G. *J. Am. Chem. Soc.* **2006**, *128*, 4460-4470.

pad of Celite and concentrated *in vacuo* to remove the metal salts. Crude *t*-Butyl-sulfinamide (14.2 g) was obtained as a yellow oil. Analysis of the crude residue by ^{1}H NMR showed only 1 diastereomer (> 20:1 *dr*).

To a solution of this crude product in dry Et_2O (500 mL) was added a 4.0 M solution of HCl in 1,4-dioxane (10.6 mL, 42.4 mmol). The reaction mixture was stirred at rt for 1 h. The resulting white cloudy suspension was filtered and the white solid was rinsed with dry Et_2O then dried under high vacuum to afford 7.40 g (81%, 3 steps) of **(*S*)-3** as a white powder. Representative experimental data are as follows: Mp 151-154 °C; $[\alpha]_D^{23}$ –2.9 (*c* 1.0, CH_2Cl_2); IR (neat) 3012 (br), 2950, 2926, 2868, 1601, 1506, 1468, 1427, 1386, 1366, 1099, 982, 824, 753, 738, 708, 701, 688 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.42 (bs, 3 H), 7.70-7.55 (m, 4 H), 7.48-7.30 (m, 6 H), 5.90 (dt, 1 H, *J* = 14.9, 7.5 Hz), 5.52 (dd, 1 H, *J* = 15.4, 8.4 Hz), 3.69 (app t, 3 H, *J* = 6.5 Hz), 2.45-2.20 (m, 2 H), 1.80-1.50 (m, 3 H), 1.03 (s, 9 H), 0.95-0.84 (m, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.5, 134.5, 133.7, 129.5, 127.6, 127.3, 63.0, 52.9, 42.1, 35.6, 26.7, 24.4, 22.9, 21.5, 19.1; EI-MS *m/z* 395 (M^+, 40), 338 (86), 198 (100); HRMS (EI) *m/z* calcd for $C_{25}H_{37}NOSi$ 395.2644, found 395.2640.

Large Scale Procedure: To a solution of (but-3-ynyloxy)-(*tert*-butyl)diphenylsilane (**2**, 156.4 g, 0.50 mol) in CH_2Cl_2 (1.564 L) was added zirconocene hydrochloride (148.0 g, amount based on use test with alkyne to determine potency, hydrochloride versus over-reduced dihydride) in three portions at 20-25 °C. After stirring for 10 min at 20-25 °C, the solution was cooled to -5 – 0 °C, and Me_3Al (2 M solution in hexane, 271 mL, 0.54 mol) was added dropwise at this temperature over 1 h. After stirring for 30 min at -5 – 0 °C, a solution of (*R, E*)-2-methyl-*N*-(3-methylbutylidene)propane-2-sulfinamide (64.0 g, 0.34 mol) in CH_2Cl_2 (100 mL) was added dropwise over 60 min. After the addition was complete, the reaction mixture was warmed to 15-20 °C and stirred for a further 3 h. Methanol (80 mL) was added dropwise, maintaining the temperature below 30 °C. The reaction mixture was then diluted with water (200 mL) and 1 N HCl (100 mL). The mixture was filtered to improve phase separation. The aqueous phase was removed and extracted with CH_2Cl_2 (2 x 200 mL). The combined organic phase was washed with water (600 mL) and brine (600 mL), filtered through celite and the filtrate concentrated to afford the crude product which was redissolved in MTBE (1200 mL) and then filtered through a celite pad. A solution of HCl in dioxane (3.5 M, 188 mL, 0.66 mol) was added dropwise to the filtrate solution at 20-25 °C. Stirring was continued for 40 min after which time a solid precipitated from the solution which was collected by filtration and washed with MTBE (500 mL) to afford **(*S*)-3** (140.5 g, 96%) as a white powder.

(*R*,*E*)-8-(*tert*-Butyldiphenylsilyloxy)-2-methyloct-5-en-4-amine hydrochloride ((*R*)-3): $[\alpha]_D^{22}$ +2.7 (*c* 1.0, CH_2Cl_2).

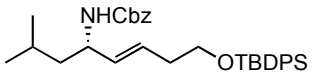


(*S*)-4a

(*S*,*E*)-*tert*-Butyl 8-(*tert*-butyldiphenylsilyloxy)-2-methyloct-5-en-4-ylcarbamate ((*S*)-4a). To a solution of the amine **(*S*)-3** (3.00 g, 6.94 mmol) in dry CH_2Cl_2 (114 mL) were added Et_3N (2.93 mL, 20.8 mmol) and then Boc_2O (1.68 g, 7.64 mmol) at 0 °C. The reaction mixture was stirred at rt for 15 h, then quenched with sat. aq. NH_4Cl and the aqueous phase extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (8:2, heptane/EtOAc) afforded 3.47 g (quant) of crude **(*S*)-4a** as a yellow oil that was carried on without further purification.

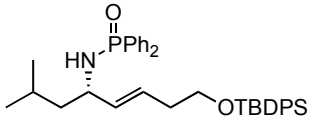
Large Scale Procedure: To a solution of **(*S*)-3** (140.5 g, 0.32 mol) in CH_2Cl_2 (2,100 mL) was added dropwise Et_3N (98.7 g, 0.97 mol) at 10-15 °C over 10 min to give a clear light yellow solution. Boc_2O (74.4 g, 0.34 mmol) was added portionwise at 15-20 °C over 35 min. The resulting solution was stirred for 18 h at this temperature. After the reaction was

complete, saturated NH_4Cl solution (500 mL) was added, and the aqueous phase was removed and extracted with CH_2Cl_2 (2 x 200 mL). The combined organic phases were washed with water (200 mL) and brine (200 mL), then concentrated to afford crude **(*S*)-4a** as a red oil (138.3 g, 85.9%) which was used without further purification.



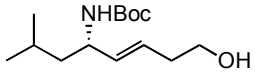
(*S*)-4b

(*S*,*E*)-Benzyl 8-(*tert*-butyldiphenylsilyloxy)-2-methyloct-5-en-4-ylcarbamate ((*S*)-4b). To a mixture of the amine **(*S*)-3** (1.50 g, 3.47 mmol) in dry THF (15 mL) were added Et_3N (1.65 mL, 11.8 mmol), and then a solution of benzyl chloroformate (0.59 mL, 4.17 mmol) in dry THF (4 mL) at 0 °C. The resulting white suspension was allowed to warm to rt and stirred for 5 h, then diluted with CH_2Cl_2 and water. The aqueous phase was extracted twice with CH_2Cl_2, and the combined organic layers were washed with 10% aq. HCl and sat. aq. $NaHCO_3$, dried ($MgSO_4$), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (8:2, hexanes/EtOAc) afforded 1.45 g (79%) of crude **(*S*)-4b** as a yellow oil that was carried on without further purification.



(*S*)-4c

(*S*,*E*)-*N*-(8-(*tert*-Butyldiphenylsilyloxy)-2-methyloct-5-en-4-yl)-*P*,*P*-diphenylphosphinic amide ((*S*)-4c). To a solution of the amine **(*S*)-3** (400 mg, 0.926 mmol) in dry CH_2Cl_2 (7 mL) were added Et_3N (0.44 mL, 3.13 mmol), and then a solution of diphenylphosphinic chloride (0.22 mL, 1.11 mmol) in dry CH_2Cl_2 (3 mL) at 0 °C. After being stirred at 0 °C for 15 min, the reaction mixture was allowed to warm to rt and stirred for 4 h, then diluted with CH_2Cl_2 and 10% aq. HCl. The aqueous phase was extracted with CH_2Cl_2 and the combined organic layers were washed with sat. aq. $NaHCO_3$, dried ($MgSO_4$), filtered and concentrated *in vacuo* to afford 720 mg of crude **(*S*)-4c** as a pale yellow, viscuous oil that was carried on without further purification.



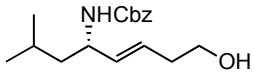
(*S*)-5a

(*S*,*E*)-*tert*-Butyl 8-hydroxy-2-methyloct-5-en-4-ylcarbamate ((*S*)-5a). To a solution of the silyl ether **(*S*)-4a** (2.80 g, 5.60 mmol, crude) in dry THF (46 mL) at 0 °C was added TBAF (1.0 M in THF, 7.00 mL, 7.00 mmol), and the reaction mixture was allowed to warm to rt while stirring for 4 h, then quenched with sat. aq. NH_4Cl and diluted with EtOAc. The aqueous phase was separated and extracted with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (5:5, hexanes/EtOAc) afforded 1.35 g (94%, 2 steps) of **(*S*)-5a** as a colorless oil. Representative experimental data are as follows: Chiral SFC t_R 4.06 min, 96.6% *ee*; $[\alpha]_D^{23}$ –12.7 (*c* 1.0, CH_2Cl_2); IR (CH_2Cl_2) 3327 (br), 2952, 2930, 2866, 1683, 1521, 1468, 1452, 1388, 1364, 1247, 1165, 1042, 1019, 967, 870, 738 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.53 (dt, 1 H, *J* = 15.4, 6.9 Hz), 5.37 (dd, 1 H, *J* = 15.4, 6.5 Hz), 4.50 (bs, 1 H), 4.11-3.95 (m, 1 H), 3.60 (t, 2 H, *J* = 6.2 Hz), 2.42 (bs, 1 H), 2.25 (app q, 2 H, *J* = 6.4 Hz), 1.70-1.51 (m, 1 H), 1.41 (s, 9 H), 1.37-1.20 (m, 2 H), 0.89 (d, 3 H, *J* = 6.6 Hz), 0.88 (d, 3 H, *J* = 6.6 Hz); ^{13}C NMR

($CDCl_3$, 75 MHz) δ 155.4, 134.3, 126.9, 79.2, 61.5, 50.9, 44.5, 35.6, 28.3, 24.6, 22.5; EI-MS *m/z* 257 (M^+, 10), 227 (55), 171 (65); HRMS (EI) *m/z* calcd for $C_{14}H_{27}NO_3$ 257.1991, found 257.1994.

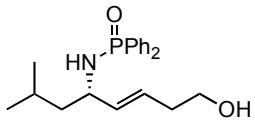
Large Scale Procedure: To a 5-L 4-neck flask was added silyl ether **(*S*)-4a** (138.3 g, 0.27 mol) and THF (2.300 L). A solution of TBAF monohydrate (91.1 g, 0.34 mol) in THF (500 mL) was added dropwise at -5~0 °C over 50 min. After the addition, the reaction mixture was warmed to 20-25 °C and stirred at this temperature for 2 h until the reaction was complete. The reaction was quenched by addition of a saturated solution of NH_4Cl (500 mL). The organic layer was removed, washed with brine (2 x 200 mL), dried ($MgSO_4$), filtered, concentrated and purified by chromatography on SiO_2 (ethyl acetate/petroleum ether, 1:20 to 1:2) to afford **(*S*)-5a** (39.3 g, 45%, 4 steps) as a colorless oil.

(*R*,*E*)-*tert*-Butyl 8-hydroxy-2-methyloct-5-en-4-ylcarbamate ((*R*)-5a): Chiral SFC t_R 3.02 min, 98.0% *ee*; $[\alpha]_D^{24}$ +12.5 (*c* 1.0, CH_2Cl_2).



(*S*)-5b

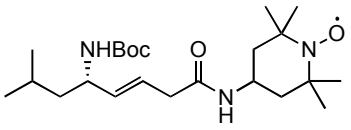
(*S*,*E*)-Benzyl 8-hydroxy-2-methyloct-5-en-4-ylcarbamate ((*S*)-5b). To a solution of the silyl ether **(*S*)-4b** (584 mg, 1.10 mmol, crude) in dry THF (9 mL) at 0 °C was added TBAF (1.0 M in THF, 1.38 mL, 1.38 mmol), and the reaction mixture was allowed to warm to rt while stirring for 3.5 h, then quenched with sat. aq. NH_4Cl and diluted with EtOAc. The aqueous phase was separated and extracted with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (5:5, hexanes/EtOAc) afforded 194 mg (58%, 2 steps) of **(*S*)-5b** as a colorless oil: $[\alpha]_D^{23}$ –6.4 (*c* 1.0, CH_2Cl_2); IR (CH_2Cl_2) 3410 (br), 3317 (br), 3032, 2952, 2933, 2868, 1694, 1532, 1498, 1467, 1454, 1329, 1282, 1254, 1116, 1079, 1042, 1027, 967, 751, 736, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40-7.20 (m, 5 H), 5.58 (dt, 1 H, *J* = 15.3, 6.6 Hz), 5.43 (dd, 1 H, *J* = 15.3, 6.6 Hz), 5.09 (s, 2 H), 4.75-4.55 (m, 1 H), 4.23-4.05 (m, 1 H), 3.70-3.50 (m, 2 H), 2.28 (app q, 2 H, *J* = 6.0 Hz), 1.82 (bs, 1 H), 1.72-1.54 (m, 1 H), 1.43-1.22 (m, 2 H), 1.00-0.80 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.0, 136.7, 134.3, 128.7, 128.3, 127.5, 66.8, 61.8, 51.7, 44.7, 35.8, 24.9, 22.8, 22.6; ESI-MS *m/z* 314 ($[M+Na]^+$, 100); HRMS (ESI) *m/z* calcd for $C_{17}H_{25}NO_3Na$ (M+Na) 314.1732, found 314.1739.



(*S*)-5c

(*S*,*E*)-*N*-(8-Hydroxy-2-methyloct-5-en-4-yl)-*P*,*P*-diphenylphosphinic amide ((*S*)-5c). To a solution of the silyl ether **(*S*)-4c** (700 mg, 0.900 mmol, crude) in dry THF (8 mL) at 0 °C was added TBAF (1.0 M in THF, 1.23 mL, 1.23 mmol), and the reaction mixture was allowed to warm to rt while stirring. As completion was not reached after 4 h, 0.75 equiv. of TBAF (0.75 mL) was added at 0 °C. The reaction mixture was stirred further at rt for 3 h, then quenched with sat. aq. NH_4Cl and diluted with EtOAc. The aqueous phase was separated and extracted with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (95:5, EtOAc/MeOH) afforded 272 mg (85%, 2 steps) of **(*S*)-5c** as a white solid: Mp 124.0-124.2 °C; $[\alpha]_D^{23}$ –12.1 (*c* 1.0, CH_2Cl_2); IR (neat) 3399 (br), 3237 (br), 3054, 2954, 2932, 2902, 2881, 2866, 2848, 1468, 1433, 1165, 1124, 1107, 1094, 1046, 1023, 1004, 995, 986, 965, 921, 749, 727, 691 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.00-7.83 (m, 4 H), 7.58-7.35

(m, 6 H), 5.52 (dd, 1 H, *J* = 15.3, 9.0 Hz), 5.22 (ddd, 1 H, *J* = 15.0, 8.6, 6.3), 4.58 (bs, 1 H), 3.78-3.47 (m, 3 H), 2.80 (app dd, 1 H, *J* = 9.2, 3.8 Hz), 2.22-2.07 (m, 2 H), 1.80-1.60 (m, 1 H), 1.55-1.43 (m, 1 H), 1.43-1.31 (m, 1 H), 0.89 (d, 3 H, *J* = 6.3 Hz), 0.86 (d, 3 H, *J* = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.8, 136.8, 134.4, 133.0, 132.9, 132.8, 132.8, 132.1, 132.1, 132.0, 131.9, 131.2, 129.4, 129.0, 128.8, 128.6, 61.5, 53.6, 53.6, 47.0, 46.8, 36.0, 24.8, 22.9, 22.6; ESI-MS *m/z* 380 ([M+Na]$^+$, 80), 396 ([M+K]$^+$, 20); HRMS (ESI) *m/z* calcd for $C_{21}H_{28}NO_2PNa$ (M+Na) 380.1755, found 380.1725.



(*S*)-6a

(*S*,*E*)-*N*-(2,2,6,6-Tetramethyl-1-oxo-piperidin-4-yl)-5-(*tert*-butoxycarbonylamino)-7-methyloct-3-enamide ((*S*)-6a). To a solution of alcohol **(*S*)-5a** (1.00 g, 3.89 mmol) in acetone (40 mL) at 0 °C was added slowly a freshly prepared solution of Jones reagent (2.5 M, 3.89 mL, 9.71 mmol). The resulting dark suspension was stirred at 0 °C for 1 h, then diluted with Et_2O and water. The aqueous phase was separated and extracted twice with Et_2O. The combined organic layers were washed with water (2x) and brine (1x), dried (Na_2SO_4), filtered and concentrated *in vacuo* to yield 990 mg (94%) of the crude acid as a yellow oil that was carried on without further purification.

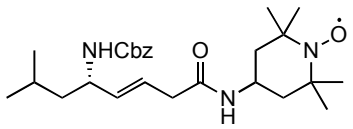
To a solution of this acid (678 mg, 2.50 mmol, crude) in dry CH_2Cl_2 (35 mL) at 0 °C were added successively 4-amino-TEMPO (662 mg, 3.75 mmol), DMAP (339 mg, 2.75 mmol), HOBt•H_2O (377 mg, 2.75 mmol) and EDCI (575 mg, 3.00 mmol). The resulting orange solution was stirred at rt for 14 h, and then washed with sat. aq. NH_4Cl. The aqueous phase was separated and extracted once with CH_2Cl_2, and the combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (1:1 to 1:2, hexanes/EtOAc) afforded 857 mg (81%) of **(*S*)-6a** as a peach colored solid: Mp 61 °C (softening point: 51 °C); $[\alpha]_D^{23}$ +35.6 (*c* 0.5, CH_2Cl_2); IR (neat) 3302 (br), 2969, 2954, 2932, 2866, 1685, 1670, 1644, 1523, 1457, 1386, 1275, 1362, 1316, 1297, 1241, 1165, 1042, 971 cm^{-1}; ESI-MS *m/z* 527 (20), 447 ([M+Na]$^+$, 100), 391 (50), 365 (40); HRMS (ESI) *m/z* calcd for $C_{23}H_{42}N_3O_4Na$ (M+Na) 447.3073, found 447.3109.

A sample of this nitroxide (14.8 mg, 0.035 mmol) was dissolved in dry MeOH (0.5 mL) and L-ascorbic acid (6.2 mg, 0.035 mmol) was added. Complete discoloration of the solution occured within a few seconds. After stirring at rt for 10 min, the solvent was removed *in vacuo*. The resulting residue was dissolved in EtOAc and washed with water. The aqueous phase was extracted twice with EtOAc, and the combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo* to yield 13.0 mg (88%) of the corresponding hydroxylamine as a white foam: ^{1}H NMR (300 MHz, CD_3OD) δ 6.65 (bd, 1 H, *J* = 6.6 Hz), 5.64 (ddt, 1 H, *J* = 15.3, 6.9, 0.9 Hz), 5.50 (dd, 1 H, *J* = 15.3, 6.2 Hz), 4.16-3.95 (m, 2 H), 2.89 (d, 2 H, *J* = 6.9 Hz), 1.80-1.70 (m, 2 H), 1.70-1.55 (m, 1 H), 1.44 (s, 9 H), 1.48-1.25 (m, 4 H), 1.19 (s, 6 H), 1.17 (s, 6 H), 0.91 (app d, 6 H, *J* = 6.6 Hz); ^{13}C NMR (75 MHz, CD_3OD) δ 173.4, 158.0, 136.8, 124.5, 80.1, 60.7, 51.8, 45.9, 45.4, 42.3, 40.8, 32.6, 29.0, 26.0, 23.2, 22.8, 20.4.

Large scale procedure: To a solution of alcohol **(*S*)-5a** (135 g, 0.52 mol)) in acetone (4.000 L) was added dropwise a solution of freshly prepared Jones reagent (1.38 L, 1.81 M, 1.3 mol) at 0 °C. The reaction mixture was stirred at 0 °C until TLC analysis showed the completion of the reaction. The mixture was extracted with MTBE (3x 1000 mL) and the combined organic layers were washed with water (2x 1000 mL), brine (100 mL), dried ($MgSO_4$), filtered and concentrated to afford the crude acid (115 g) which was used in the next step without further purification.

GMP procedure of last step: To a dry and clean 20-L flask was added crude acid (280 g, 83 wt%, 0.85 mol) and CH_2Cl_2 (10.8 kg). A solution of 4-AT (154.6 g, 1.05 equiv, 0.90 mol) in CH_2Cl_2 (1.53 kg) was added over 60 min whilst maintaining the internal reaction temperature at -5 ~0 °C, resulting in a brown-red solution. Subsequently, EDCI•HCl (197.5 g, 1.02 mol), DMAP (115.0 g, 0.93 mol) and HOBT (127.5 g, 0.93 mol) were added successively at -5~0 °C. The resulting deep red solution was then allowed to warm up gradually and stirred at 15-25 °C for 15 h. After the completion of the reaction (by TLC analysis), the reaction mixture was quenched with a solution of NH_4Cl (0.25 kg in 3 kg of water). The organic layer was separated and then extracted with CH_2Cl_2 (4 kg). The combined organic layers were washed with 20% brine (3.8 kg), dried (Na_2SO_4, 1.5 kg), filtered and concentrated. The crude product was purified by chromatography on SiO_2 (1.2 – 1.4 kg, 200-300 mesh; hexane/ethyl acetate, 1:10 to 1:1, collecting fractions of 200-250 mL size) to afford product of 90% purity. A significant impurity at RT = 0.95 was persistent and difficult to remove by chromatography. The partially purified product was then treated with ethyl acetate (1.5 vol) and *n*-hexane (10 vol). The solid was filtered and then washed with *n*-hexane (1.5 vol), and dried in the filter until organic solvent residue was <0.38% to afford the desired **(*S*)-6a** (162 g, 73%) as a peach colored solid: Mp 139 °C (softening point 134 °C), $[\alpha]_D^{23}$ +36.5 (*c* 0.5, CH_2Cl_2), HPLC purity 99%, *ee* 100%.

(*R*,*E*)-*N*-(2,2,6,6-Tetramethyl-1-oxo-piperidin-4-yl)-5-(*tert*-butoxycarbonylamino)-7-methyloct-3-enamide ((*R*)-6a): $[\alpha]_D^{24}$ –34.9 (*c* 0.5, CH_2Cl_2).



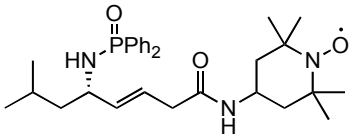
(*S*)-6b

(*S*,*E*)-*N*-(2,2,6,6-Tetramethyl-1-oxo-piperidin-4-yl)-5-(benzyloxycarbonylamino)-7-methyloct-3-enamide ((*S*)-6b). To a solution of the alcohol **(*S*)-5b** (158 mg, 0.543 mmol) in acetone (5 mL) at 0 °C was added slowly a freshly prepared solution of Jones reagent (2.5 M, 0.54 mL, 1.36 mmol). The resulting dark suspension was stirred at 0 °C for 1 h, then diluted with Et_2O and water. The aqueous phase was separated and extracted twice with Et_2O. The combined organic layers were washed with water (2x) and brine (1x), dried (Na_2SO_4), filtered and concentrated *in vacuo* to yield 166 mg (quant.) of the crude acid as a slighly yellow oil, that was carried on without further purification.

To a solution of this acid (160 mg, 0.524 mmol, crude) in dry CH_2Cl_2 (7 mL) at 0 °C were added successively a solution of 4-amino-TEMPO (139 mg, 0.786 mmol) in dry CH_2Cl_2 (0.5 mL), DMAP (71.1 mg, 0.576 mmol), HOBt•H_2O (77.9 mg, 0.576 mmol) and EDCI (123 mg, 0.629 mmol). The resulting orange solution was stirred at rt for 15 h, and then washed with sat. aq. NH_4Cl. The aqueous phase was separated and extracted once with CH_2Cl_2, and the combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (5:5 to 3:7, hexanes/EtOAc) afforded 171 mg (71%) of the title compound as a peach colored foam: mp 60.5 °C (softening point: 44 °C); $[\alpha]_D^{23}$ +26.5 (*c* 0.5, CH_2Cl_2); IR (neat) 3302 (br), 3062, 3028, 2952, 2930, 2866, 1698, 1644, 1526, 1454, 1362, 1316, 1295, 1277, 1239, 1196, 1178, 1116, 1085, 1040, 1027, 971, 736, 697 cm^{-1}; EI-MS *m*/*z* 458 (M^+, 37), 281 (19), 154 (28), 124 (47), 91 (100), 84 (41); HRMS (EI) *m*/*z* calcd for $C_{26}H_{40}N_3O_4$ 458.3019, found 458.3035.

A sample of this nitroxide (65.0 mg, 0.142 mmol) was dissolved in dry MeOH (1 mL) and L-ascorbic acid (25.2 mg, 0.142 mmol) was added. Complete discoloration of the solution occured within a few seconds. After stirring at rt for 10 min, the solvent was removed *in vacuo*. The resulting residue was taken up in Et_2O and washed with water. The aqueous phase was extracted twice with Et_2O, and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered

and concentrated *in vacuo* to yield 63.3 mg (97%) of the corresponding hydroxylamine as a solidified colorless oil: ^{1}H NMR (300 MHz, CD_3OD) δ 7.40-7.22 (m, 5 H), 7.10 (bd, 1 H, *J* = 7.8 Hz), 5.68 (dt, 1 H, *J* = 15.3, 6.3 Hz), 5.51 (dd, 1 H, *J* = 15.3, 6.3 Hz), 5.07 (s, 2 H), 4.18-4.00 (m, 2 H), 2.89 (d, 2 H, *J* = 6.6 Hz), 1.79-1.68 (m, 2 H), 1.70-1.54 (m, 1 H), 1.49-1.22 (m, 4 H), 1.17 (s, 6 H), 1.16 (s, 3 H), 1.15 (s, 3 H), 0.91 (d, 6 H, *J* = 6.0 Hz); ^{13}C NMR (75 MHz, CD_3OD) δ 173.3, 158.4, 138.6, 136.5, 129.6, 129.1, 128.8, 124.9, 67.5, 60.4, 52.5, 46.0, 45.2, 42.3, 40.7, 32.8, 25.9, 23.2, 22.7, 20.4.

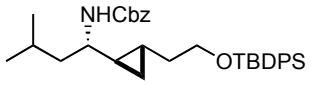


(*S*)-6c

(*S*,*E*)-*N*-(2,2,6,6-Tetramethyl-1-oxo-piperidin-4-yl)-5-(diphenylphosphorylamino)-7-methyloct-3-enamide ((*S*)-6c). To a solution of the alcohol **(*S*)-5c** (166 mg, 0.466 mmol) in acetone (5 mL) at 0 °C was slowly added a freshly prepared solution of Jones reagent (2.5 M, 0.47 mL, 1.16 mmol). The resulting dark suspension was stirred at 0 °C for 2 h, then diluted with Et_2O and water. The aqueous phase was separated and extracted twice with Et_2O. The combined organic layers were washed with water (2x) and brine (1x), dried (Na_2SO_4), filtered and concentrated *in vacuo* to yield 114 mg (66%) of the crude acid as a white foam, that was carried on without further purification.

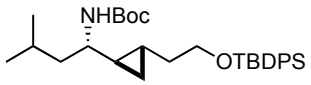
To a solution of this acid (110 mg, 0.296 mmol, crude) in dry CH_2Cl_2 (3.5 mL) at 0 °C were added successively a solution of 4-amino-TEMPO (78.4 mg, 0.444 mmol) in dry CH_2Cl_2 (0.5 mL), DMAP (40.2 mg, 0.326 mmol), HOBt•H_2O (44.0 mg, 0.326 mmol) and EDCI (69.5 mg, 0.355 mmol). The resulting orange solution was stirred at rt for 13 h, and then washed with sat. aq. NH_4Cl. The aqueous phase was separated and extracted once with CH_2Cl_2, and the combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (EtOAc to 97:3, EtOAc/MeOH) afforded 91.2 mg (59%) of **(*S*)-6c)** as an orange oil which solidified very slowly upon high vacuum: Mp 168.0-168.8 °C (softening point: ~75 °C); $[\alpha]_D^{23}$ –14.1 (*c* 0.5, CH_2Cl_2); IR (neat) 3222 (br), 3056, 2950, 2933, 2866, 1541, 1459, 1437, 1362, 1241, 1183, 1122, 1109, 1085, 1068, 1051, 1042, 995, 969, 922, 749, 723, 695, 638 cm^{-1}; EI-MS *m/z* 524 (M^+, 5), 371 (27), 218 (28), 201 (74), 124 (100), 91 (35), 84 (26); HRMS (EI) *m/z* calcd for $C_{30}H_{43}N_3O_3P$ 524.3042, found 524.3040.

A sample of this nitroxide (35.0 mg, 0.067 mmol) was dissolved in dry MeOH (0.8 mL) and L-ascorbic acid (11.9 mg, 0.067 mmol) was added. Complete discoloration of the solution occured within a few seconds. After stirring at rt for 10 min, the solvent was removed *in vacuo*. The resulting residue was taken up in EtOAc with a few amount of MeOH to achieve a complete dissolution, and washed with water. The aqueous phase was extracted twice with EtOAc, and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo* to yield 30.0 mg (86%) of the corresponding hydroxylamine as a solidified slighly yellow oil: ^{1}H NMR (300 MHz, CD_3OD) δ 7.93-7.77 (m, 4 H), 7.60-7.43 (m, 6 H), 5.63-5.44 (m, 2 H), 4.20-4.03 (m, 1 H), 3.57-3.43 (m, 1 H), 2.86 (d, 2 H, *J* = 5.7 Hz), 1.86-1.72 (m, 2 H), 1.79-1.63 (m, 1 H), 1.60-1.46 (m, 3 H), 1.46-1.34 (m, 1 H), 1.34-1.25 (m, 1 H), 1.23 (s, 6 H), 1.21 (s, 3 H), 1.20 (s, 3 H), 0.86-0.77 (m, 6 H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.4, 138.4, 138.3, 134.8, 134.7, 133.6, 133.5, 133.4, 133.3, 133.3, 133.3, 133.0, 132.9, 129.9, 129.8, 129.7, 129.7, 124.8, 61.4, 53.3, 48.1, 48.0, 45.8, 45.7, 42.2, 40.8, 32.3, 25.8, 23.4, 22.7, 20.5.



7b

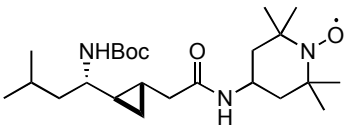
Benzyl (*S*)-1-((1*R*,2*S*)-2-(2-(*tert*-butyldiphenylsilyloxy)ethyl)cyclopropyl)-3-methylbutylcarbamate (7b). To a solution of $ZnEt_2$ (827 mg, 6.36 mmol) in dry CH_2Cl_2 (15 mL) was added DME (freshly distilled, 0.67 mL, 6.36 mmol). The reaction mixture was stirred at rt for 15 min, then cooled to –20 °C and CH_2I_2 (1.03 mL, 12.7 mmol) was added dropwise *via* syringe over 10 min. After stirring for 15 min, a solution of the alkene **(*S*)-4b** (1.12 g, 2.12 mmol) in dry CH_2Cl_2 (6 mL) was added dropwise *via* syringe over 10 min. The reaction mixture was allowed to warm to rt while stirring. After 10 h, the reaction mixture was quenched with sat. aq. NH_4Cl and diluted with CH_2Cl_2 and water, the aqueous phase was separated and extracted with EtOAc. The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (9:1, hexanes/Et_2O) afforded 785 mg (68%) **7b** as a colorless oil, and 195 mg of recovered starting material (82% yld b.r.s.m.). ^{1}H NMR analysis showed only 1 diastereomer (> 20:1 *dr*). Representative experimental data are as follows: $[\alpha]_D^{23}$ –26.8 (*c* 1.0, CH_2Cl_2); IR (CH_2Cl_2) 3338 (br), 3067, 2995, 2952, 2928, 2898, 2857, 1702, 1506, 1470, 1426, 1262, 1245, 1217, 1105, 1092, 1053, 1027, 1006, 999, 822, 734, 699 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73-7.66 (m, 4 H), 7.48-7.28 (m, 11 H), 5.09, 5.03 (ABq, 2 H, J_{AB} = 12.2 Hz), 4.62 (bd, 1 H, *J* = 8.4 Hz), 3.72 (bt, 2 H, *J* = 6.4 Hz), 3.28-3.10 (m, 1 H), 1.80-1.63 (m, 1 H), 1.60-1.25 (m, 4 H), 1.08 (s, 9 H), 0.92 (d, 6 H, *J* = 6.3 Hz), 0.84-0.70 (m, 1 H), 0.58-0.46 (m, 1 H), 0.46-0.35 (m, 1 H), 0.31 (dt, 1 H, *J* = 8.4, 4.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3, 136.9, 135.8, 134.2, 129.8, 128.6, 128.2, 127.8, 66.6, 64.3, 53.2, 45.4, 37.0, 27.1, 24.9, 24.5, 23.3, 22.6, 19.4, 13.2, 10.6; ESI-MS *m/z* 566 ([M+Na]$^+$, 100), 582 ([M+K]$^+$, 60); HRMS (ESI) *m/z* calcd for $C_{34}H_{45}NO_3SiNa$ (M+Na) 566.3066, found 566.3103.



7a

***tert*-Butyl (*S*)-1-((1*R*,2*S*)-2-(2-(*tert*-butyldiphenylsilyloxy)ethyl)cyclopropyl)-3-methylbutylcarbaate (7a).** A flask containing a solution of the Cbz-protected amine **7b** (460 mg, 0.846 mmol) in a 5:1 MeOH/EtOAc mixture (12 mL) was purged and filled 3 times with argon, then 10% Pd/C (50 mg) was added. The flask was purged and filled 3 times with H_2, and the resulting black suspension was stirred at rt under H_2 (1 atm). Since the reaction did not reach completion after 3 h, an additional amount of 10% Pd/C (30 mg) was added and stirring under H_2 was continued for 5 h. The reaction mixture was then filtered through a pad of Celite, the Celite washed with MeOH and AcOEt, and the solution concentrated *in vacuo* to yield 317 mg (92%) of the crude amine as a pale yellow oil, that was carried on without further purification.

To a solution of this amine (309 mg, 0.755 mmol) in dry CH_2Cl_2 (12 mL) was added Et_3N (0.21 mL, 0.153 mmol) and then Boc_2O (183 mg, 0.830 mmol) at 0 °C. The reaction mixture was stirred at rt for 28 h. The reaction was quenched with sat. aq. NH_4Cl and the aqueous phase extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo* to yield 471 mg of **7a** as a colorless oil, that was carried on without further purification.



8a

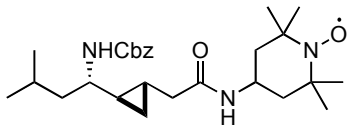
***N*-(2,2,6,6-Tetramethyl-1-oxo-piperidin-4-yl)-2-((1*R*,2*S*)-2-((*S*)-1-(*tert*-butoxycarbonylamino)-3-methylbutyl)cyclopropyl)acetamide (8a).** To a solution of the silyl ether **7a** (464 mg, 0.742 mmol, crude) in dry THF (6 mL) at 0 °C was added TBAF (1.0 M in THF, 0.93 mL, 0.927 mmol), and the reaction mixture was allowed to warm to rt while stirring. Since TLC showed uncomplete reaction after 5 h, 0.75 equiv. TBAF (0.56 mL) was added. After 9 h, the reaction mixture was quenched with sat. aq. NH_4Cl and diluted with EtOAc. The aqueous phase was separated and extracted with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (5:5, hexanes/EtOAc) afforded 177 mg (88%, 2 steps) of *tert*-butyl (*S*)-1-((1*R*,2*S*)-2-(2-hydroxyethyl)cyclopropyl)-3-methylbutylcarbamate as a colorless oil which solidified upon high vacuum to give a white powder: Mp 49.8-50.2 °C; $[\alpha]_D^{22}$ –30.8 (*c* 1.0, CH_2Cl_2); IR (neat) 3354, 3272 (br), 2976, 2950, 2926, 2868, 1675, 1517, 1456, 1442, 1386, 1364, 1327, 1299, 1271, 1245, 1168, 1066, 1049, 1029, 1006, 993, 894, 885, 775, 758, 744 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.50 (bd, 1 H, *J* = 4.5 Hz), 3.66 (app bs, 2 H), 3.00-2.87 (m, 1 H), 2.36 (bs, 1 H), 1.82 (app bs, 1 H), 1.77-1.60 (m, 1 H), 1.45 (s, 9 H), 1.39 (t, 2 H, *J* = 7.2 Hz), 1.01 (app bs, 2 H), 0.91 (d, 3 H, *J* = 6.6 Hz), 0.88 (d, 3 H, *J* = 6.6 Hz), 0.56-0.44 (m, 1 H), 0.39 (dt, 1 H, *J* = 8.4, 4.8 Hz), 0.32 (dt, 1 H, *J* = 8.4, 4.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4, 79.3, 62.7, 53.3, 44.9, 36.8, 28.6, 24.8, 23.4, 22.2, 14.5, 9.8; ESI-MS *m/z* 294 ([M+Na]$^+$, 100); HRMS (ESI) *m/z* calcd for $C_{15}H_{29}NO_3Na$ (M+Na) 294.2045, found 294.2064.

To a solution of this alcohol (130 mg, 0.477 mmol) in acetone (5 mL) at 0 °C was slowly added a solution of Jones reagent (2.5 M, 0.48 mL, 1.19 mmol). The resulting dark suspension was stirred at 0 °C for 1 h, then diluted with Et_2O and water. The aqueous phase was separated and extracted twice with Et_2O. The combined organic layers were washed with water (2x) and brine (1x), dried (Na_2SO_4), filtered and concentrated *in vacuo* to yield 133 mg (97%) of the crude acid as a colorless oil, that was carried on without further purification.

To a solution of this acid (128 mg, 0.447 mmol, crude) in dry CH_2Cl_2 (5.5 mL) at 0 °C were added successively a solution of 4-amino-TEMPO (118 mg, 0.671 mmol) in dry CH_2Cl_2 (0.5 mL), DMAP (60.7 mg, 0.492 mmol), HOBt•H_2O (66.4 mg, 0.492 mmol) and EDCI (105 mg, 0.536 mmol). The resulting orange solution was stirred at rt for 15 h, and then washed with sat. aq. NH_4Cl. The aqueous phase was separated and extracted once with CH_2Cl_2, and the combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (5:5 to 3:7, hexanes/EtOAc) afforded 150 mg (76%) of **8a** as a peach colored foam: Mp 139.5 °C; $[\alpha]_D^{23}$ –15.7 (*c* 0.5, CH_2Cl_2); IR (neat) 3312 (br), 2969, 2959, 2948, 2944, 2930, 2905, 2866, 1685, 1653, 1530, 1457, 1437, 1386, 1375, 1362, 1321, 1303, 1265, 1243, 1219, 1168, 1098, 1086, 1055, 1042, 1027, 995 cm^{-1}; EI-MS *m/z* 438 (M$^+$, 6), 252 (57), 140 (67), 124 (80), 91 (48), 84 (59), 57 (100); HRMS (EI) *m/z* calcd for $C_{24}H_{44}N_3O_4$ 438.3332, found 438.3352.

A sample of this nitroxide (51.4 mg, 0.117 mmol) was dissolved in dry MeOH (1 mL) and L-ascorbic acid (20.8 mg, 0.117 mmol) was added. Complete discoloration of the solution occured within a few seconds. After stirring at rt for 10 min, the solvent was removed *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 and washed with water. The aqueous phase was extracted with CH_2Cl_2 (3x), and the combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo* to yield 48.0 mg (93%) of the corresponding hydroxylamine as a white solid: ^1H NMR (300 MHz, CD_3OD) δ 7.73 (bd, 1 H, *J* = 6.9 Hz), 6.40 (bd, 1 H, *J* = 7.2 Hz), 4.22-4.43 (m, 1 H), 3.26 (app bs, 1 H), 2.12 (dd, 1 H, *J* = 13.8, 6.0 Hz), 1.97 (dd, 1 H, *J* = 14.1, 7.8 Hz), 1.88-1.74 (m, 2 H), 1.74-1.57 (m, 1 H), 1.55-1.46 (m, 2 H), 1.43 (s, 9 H),

1.35-1.25 (m, 2 H), 1.23 (s, 6 H), 1.22 (s, 6 H), 1.06-0.94 (m, 1 H), 0.92 (d, 3 H, J = 6.6 Hz), 0.89 (d, 3 H, J = 6.3 Hz), 0.76-0.65 (m, 1 H), 0.46-0.32 (m, 2 H); ^{13}C NMR (75 MHz, CD_3OD) δ 174.8, 158.4, 79.8, 61.4, 52.2, 45.9, 45.8, 45.7, 42.0, 41.6, 32.3, 29.0, 26.1, 25.1, 23.9, 22.6, 20.5, 20.5, 13.3, 10.6.



8b

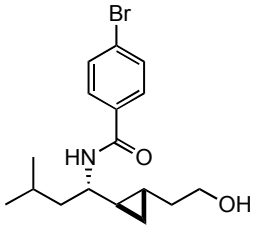
***N*-(2,2,6,6-Tetramethyl-1-oxo-piperidin-4-yl)-2-((1*R*,2*S*)-2-((*S*)-1-(benzyloxycarbonylamino)-3-methylbutyl)cyclopropyl)acetamide (8b).** To a solution of the silyl ether **7b** (320 mg, 0.588 mmol) in dry THF (5 mL) at 0 °C was added TBAF (1.0 M in THF, 0.74 mL, 0.735 mmol), and the reaction mixture was allowed to warm to rt while stirring for 7 h, then quenched with sat. aq. NH_4Cl and diluted with EtOAc. The aqueous phase was separated and extracted with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (5:5, hexanes/EtOAc) afforded 166 mg (92%) of benzyl (*S*)-1-((1*R*,2*S*)-2-(2-hydroxyethyl)cyclopropyl)-3-methylbutylcarbamate as a colorless oil: $[\alpha]_D^{23}$ –21.6 (*c* 1.0, CH_2Cl_2); IR (CH_2Cl_2) 3401 (br), 3315 (br), 3062, 3030, 2991, 2952, 2926, 2866, 1688, 1530, 1467, 1454, 1321, 1297, 1250, 1118, 1099, 1047, 1027, 1003, 773, 734, 695, 680, 669, 656 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.28 (m, 5 H), 5.11, 5.09 (ABq, 2 H, J_{AB} = 12.3 Hz), 4.76 (bd, 1 H, J = 5.7 Hz), 3.70-3.53 (m, 2 H), 3.10-2.97 (m, 1 H), 2.12-1.98 (app bs, 1 H), 1.83-1.62 (m, 2 H), 1.42 (t, 2 H, J = 7.0 Hz), 1.16-0.95 (m, 2 H), 0.91 (app d, 3 H, J = 6.9 Hz), 0.88 (app d, 3 H, J = 7.2 Hz), 0.58-0.47 (m, 1 H), 0.42 (dt, 1 H, J = 8.4, 4.5 Hz), 0.34 (dt, 1 H, J = 8.4, 5.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.8, 136.8, 128.6, 128.2, 66.7, 62.8, 54.0, 44.9, 36.7, 24.8, 24.8, 23.4, 22.3, 14.4, 10.0; ESI-MS *m/z* 328 ([M+Na]$^+$, 100); HRMS (ESI) *m/z* calcd for $C_{18}H_{27}NO_3Na$ (M+Na) 328.1889, found 328.1860.

To a solution of this alcohol (110 mg, 0.362 mmol) in acetone (5 mL) at 0 °C was slowly added a solution of Jones reagent (2.5 M, 0.36 mL, 0.904 mmol). The resulting dark suspension was stirred at 0 °C for 1 h, then diluted with Et_2O and water. The aqueous phase was separated and extracted twice with Et_2O. The combined organic layers were washed with water (2x) and brine (1x), dried (Na_2SO_4), filtered and concentrated *in vacuo* to yield 114 mg (98%) of crude acid as a colorless oil that was carried on without further purification.

To a solution of this acid (110 mg, 0.344 mmol, crude) in dry CH_2Cl_2 (4.5 mL) at 0 °C were added successively a solution of 4-amino-TEMPO (91.2 mg, 0.517 mmol) in dry CH_2Cl_2 (0.5 mL), DMAP (46.7 mg, 0.379 mmol), HOBt•H_2O (51.2 mg, 0.379 mmol) and EDCI (80.8 mg, 0.413 mmol). The resulting orange solution was stirred at rt for 18 h, and then washed with sat. aq. NH_4Cl. The aqueous phase was separated and extracted once with CH_2Cl_2, and the combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (4:6, hexanes/EtOAc) afforded 123 mg (75%) of **8b** as a peach colored foam: Mp 51.8 °C (softening point: 44 °C); $[\alpha]_D^{23}$ –15.3 (*c* 0.5, CH_2Cl_2); IR (neat) 3310 (br), 3062, 2948, 2866, 1696, 1646, 1528, 1455, 1437, 1375, 1362, 1321, 1297, 1241, 1196, 1178, 1118, 1096, 1086, 1057, 1040, 1027, 1001, 978, 773, 736, 697 cm^{-1}; EI-MS *m/z* 472 (M$^+$, 42), 415 (58), 322 (43), 168 (47), 140 (46), 124 (75), 91 (100), 84 (53); HRMS (EI) *m/z* calcd for $C_{27}H_{42}N_3O_4$ 472.3175, found 472.3165.

A sample of this nitroxide (51.0 mg, 0.108 mmol) was dissolved in dry MeOH (1 mL) and L-ascorbic acid (19.2 mg, 0.108 mmol) was added. Complete discoloration of the solution occured within a few seconds. After stirring at rt for 10 min, the solvent was removed *in vacuo*. The resulting residue was dissolved in EtOAc and washed with water. The aqueous phase was extracted twice with EtOAc, and the combined organic layers were washed with brine, dried (Na_2SO_4),

filtered and concentrated *in vacuo* to yield 51.0 mg (quant.) of the corresponding hydroxylamine as a white foam: ^{1}H NMR (300 MHz, CD_3OD) δ 7.68 (bd, 1 H, *J* = 7.2 Hz), 7.38-7.23 (m, 5 H), 6.88 (bd, 1 H, *J* = 8.4 Hz), 5.10, 5.04 (ABq, 2 H, J_{AB} = 12.6 Hz), 4.29-4.03 (m, 1 H), 3.30-3.17 (m, 1 H), 2.14 (dd, 1 H, *J* = 14.1, 6.6 Hz), 1.95 (dd, 1 H, *J* = 14.1, 7.8 Hz), 1.79 (app dd, 2 H, *J* = 12.3, 2.4 Hz), 1.72-1.68 (m, 1 H), 1.56-1.28 (m, 4 H), 1.18 (s, 12 H), 1.10-0.95 (m, 1 H), 0.91 (d, 3 H, *J* = 6.6 Hz), 0.87 (d, 3 H, *J* = 6.6 Hz), 0.80-0.67 (m, 1 H), 0.47-0.34 (m, 2 H); ^{13}C NMR (75 MHz, CD_3OD) δ 174.8, 158.9, 138.7, 129.6, 129.0, 128.7, 67.4, 61.1, 53.6, 53.5, 45.8, 45.7, 42.1, 41.5, 32.4, 26.1, 25.3, 23.9, 22.5, 20.5, 13.8, 10.8.

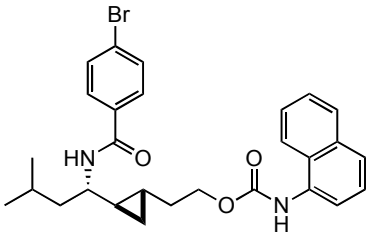


9

4-Bromo-*N*-((*S*)-1-((1*R*,2*S*)-2-(2-hydroxyethyl)cyclopropyl)-3-methylbutyl)benzamide (9). A flask containing a solution of the Cbz-protected amine **7b** (70.5 mg, 0.130 mmol) in MeOH (2 mL) was purged and filled 3 times with argon, then 10% Pd/C (14 mg) was added. The flask was purged and filled 3 times with H_2, and the resulting black suspension was stirred at rt under H_2 (1 atm) for 13 h. The reaction mixture was then filtered through a pad of Celite, the Celite washed with MeOH, and the solution concentrated *in vacuo* to yield 51.5 mg (97%) of the crude amine as a colorless oil, that was carried on without further purification.

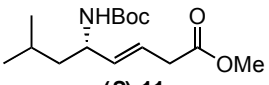
To a solution of this amine (51.5 mg, 0.126 mmol, crude) and Et_3N (35 μL, 0.251 mmol) in dry CH_2Cl_2 (0.8 mL) at 0 °C was added a suspension of 4-bromobenzoyl chloride (30.4 mg, 0.138 mmol) in dry CH_2Cl_2 (0.2 mL). The resulting reaction mixture was allowed to warm to rt and stirred for 1.5 h, then diluted with CH_2Cl_2 and washed with 1 N aq. HCl. The aqueous phase was separated and extracted again with CH_2Cl_2, and the combined organic layers were washed with sat. aq. $NaHCO_3$, dried (Na_2SO_4), filtered and concentrated *in vacuo* to yield 73.8 mg (99%) of the crude amide as a slighly yellow gum that was carried on without further purification.

To a solution of this amide (70.0 mg, 0.118 mmol) in dry THF (1 mL) at 0 °C was added TBAF (1.0 M in THF, 0.15 mL, 0.148 mmol), and the reaction mixture was allowed to warm to rt while stirring for 3 h, then quenched with sat. aq. NH_4Cl and diluted with EtOAc. The aqueous phase was separated and extracted with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (5:5, hexanes/EtOAc) afforded 24.7 mg (59%) of **9** as a white powder: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, 2 H, *J* = 8.7 Hz), 7.56 (d, 2 H, *J* = 8.4 Hz), 6.50 (bd, 1 H, *J* = 6.9 Hz), 3.73-3.57 (m, 2 H), 3.52-3.39 (m, 1 H), 2.18 (bs, 1 H), 1.93-1.80 (m, 1 H), 1.80-1.69 (m, 1 H), 1.69-1.57 (m, 1 H), 1.57-1.44 (m, 1 H), 1.10-0.90 (m, 2 H), 0.96 (d, 3 H, *J* = 6.9 Hz), 0.93 (d, 3 H, *J* = 6.6 Hz), 0.69-0.57 (m, 1 H), 0.52 (dt, 1 H, *J* = 8.1, 4.8 Hz), 0.42 (dt, 1 H, *J* = 8.4, 4.8 Hz).



10

2-((1*S*,2*R*)-2-((*S*)-1-(4-Bromobenzamido)-3-methylbutyl)cyclopropyl)ethyl naphthalen-1-ylcarbamate (10). To a solution of the alcohol **9** (7.7 mg, 0.0217 mmol) and dry pyridine (44 μL, 0.543 mmol) in dry CH_2Cl_2 (0.2 mL) at 0 °C was added 1-naphtylisocyanate (18.4 mg, 0.109 mmol). The reaction mixture was stirred at 0 °C for 1 h then allowed to warm to rt. After 4 h, the reaction was quenched with water and vigorous stirring was continued for 20 min. The mixture was then filtered though Celite, the layers separated, and the aqueous phase extracted with CH_2Cl_2. The combined organic layers were washed with 1 N aq. HCl and sat. aq. $NaHCO_3$, dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (7:3 to 5:5, hexanes/EtOAc) afforded 11.3 mg (99%) of **10** as a white powder. Slow vapor diffusion of pentane in a dilute solution of the product in THF at 4 °C gave fine colorless needles: Mp 198.5-199.0 °C; $[\alpha]_D^{23}$ +6.6 (*c* 0.57, CH_2Cl_2); IR (neat) 3287, 3259, 3062, 3047, 2993, 2948, 2918, 2902, 2864, 2846, 1688, 1623, 1534, 1502, 1476, 1463, 1448, 1437, 1427, 1342, 1256, 1237, 1213, 1198, 1174, 1152, 1142, 1124, 1105, 1077, 1068, 1008, 995, 965, 954, 939, 896, 848, 839, 783, 766, 725, 686, 673, 669 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 9.41 (s, 1 H), 8.31 (d, 1 H, *J* = 8.7 Hz), 8.03-7.96 (m, 1 H), 7.94-7.88 (m, 1 H), 7.77 (app d, 2 H, *J* = 8.4 Hz), 7.72 (d, 1 H, *J* = 7.8 Hz), 7.60 (app d, 2 H, *J* = 8.4 Hz), 7.55-7.41 (m, 4 H), 4.07 (t, 2 H, *J* = 6.6 Hz), 3.60-3.45 (m, 1 H), 1.72-1.52 (m, 3 H), 1.47-1.31 (m, 2 H), 0.86 (d, 3 H, *J* = 6.6 Hz), 0.84 (d, 3 H, *J* = 6.6 Hz), 0.90-0.71 (m, 2 H), 0.44-0.33 (m, 2 H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 164.9, 154.9, 134.1, 133.7, 133.7, 131.2, 129.4, 128.0, 127.8, 126.0, 125.7, 125.6, 124.8, 124.6, 122.7, 121.0, 64.6, 50.7, 43.7, 32.7, 24.5, 24.0, 23.3, 21.9, 12.8, 10.3; EI-MS *m/z* 524 (M^+, 47), 522 (M^+, 46), 185 (46), 183 (65), 169 (69), 157 (43), 155 (43), 143 (100), 115 (87), 67 (47); HRMS (EI) *m/z* calcd for $C_{28}H_{31}BrN_2O_3$ 522.1518, found 522.1526.

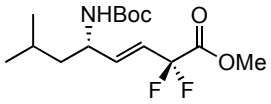


(*S*)-11

(*S*,*E*)-Methyl 5-(*tert*-butoxycarbonylamino)-7-methyloct-3-enoate ((*S*)-11). To a solution of the alcohol **(*S*)-5a** (183 mg, 0.711 mmol) in acetone (7 mL) at 0 °C was slowly added a fresh solution of Jones reagent (2.5 M, 0.71 mL, 1.78 mmol). The resulting dark suspension was stirred at 0 °C for 1 h, then diluted with Et_2O and water. The aqueous phase was separated and extracted with Et_2O (3x). The combined organic layers were washed with water (2x) and brine (1x), dried (Na_2SO_4), filtered and concentrated *in vacuo* to yield 155 mg (80%) of the crude acid as a colorless oil, that was carried on without further purification.

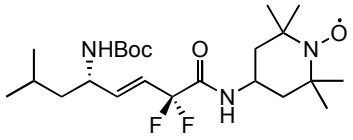
A solution of this acid (153 mg, 0.562 mmol, crude) in 4:1 benzene/MeOH (3.2 mL) was treated at 0 °C with $TMSCHN_2$ (2 M in hexanes, 1.4 mL, 2.81 mmol). The resulting yellow reaction mixture was stirred at rt for 20 min under argon, then concentrated *in vacuo*. Chromatography of the residue on SiO_2 (9:1, hexanes/EtOAc) afforded 126 mg (78%) of **(*S*)-11** as a colorless oil: $[\alpha]_D^{20}$ –13.0 (*c* 1.0, CH_2Cl_2); IR (CH_2Cl_2) 3351 (br), 2952, 2932, 2867, 1737, 1692, 1512, 1452, 1435, 1389, 1364, 1327, 1245, 1159, 1118, 1081, 1042, 1016, 967 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.69 (dtd, 1 H, *J* = 15.5, 6.9, 1.2 Hz), 5.49 (dd, 1 H, *J* = 15.2, 4.9 Hz), 4.39 (bs, 1 H), 4.23-4.00 (m, 1 H), 3.68 (s, 3 H), 3.07 (d, 2 H, *J* = 6.9 Hz),

1.72-1.59 (m, 1 H), 1.44 (s, 9 H), 1.39-1.25 (m, 2 H), 0.92 (d, 3 H, *J* = 6.6 Hz), 0.91 (d, 3 H, *J* = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 155.5, 135.6, 122.0, 79.5, 52.0, 50.4, 44.8, 37.7, 28.6, 24.9, 22.9, 22.6; ESI-MS m/z 308 ($[M+Na]^+$, 100); HRMS (ESI) m/z calcd for $C_{15}H_{27}NO_4Na$ (M+Na) 308.1838, found 308.1860.



(*S*)-12

(*S*,*E*)-Methyl 5-(*tert*-butoxycarbonylamino)-2,2-difluoro-7-methyloct-3-enoate ((*S*)-12). To a solution of ester **(*S*)-11** (104 mg, 0.365 mmol) and *N*-fluorobenzenesulfonimide (NFSi, 356 mg, 1.10 mmol) in dry THF (5 mL) at –78 °C was added a solution of NaHMDS (162 mg, 0.840 mmol) in dry THF (2 mL). The resulting reaction mixture was stirred under N_2 from –78 to –50 °C for 5 h, then quenched with sat. aq. NH_4Cl and extracted twice with CH_2Cl_2. The mixture was filtered through Celite to break the emulsion. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (9:1, hexanes/EtOAc) afforded 106 mg (86%, ~95% estimated purity by ^{1}H NMR) of **((*S*)-12** as a colorless oil: $[\alpha]_D^{22}$ –5.7 (*c* 1.0, CH_2Cl_2); IR (CH_2Cl_2) 3331 (br), 2956, 2930, 2868, 1767, 1687, 1514, 1469, 1452, 1437, 1389, 1366, 1305, 1264, 1247, 1165, 1079, 1044, 1021, 966 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 (app bd, 1 H, *J* = 14.6 Hz), 5.80 (dtd, 1 H, *J* = 15.8, 11.2, 1.5 Hz), 4.40 (app bs, 1 H), 4.36-4.20 (m, 1 H), 3.87 (s, 3 H), 1.75-1.62 (m, 1 H), 1.45 (s, 9 H), 1.37 (app t, 2 H, *J* = 7.2 Hz), 0.94 (d, 3 H, *J* = 6.6 Hz), 0.94 (d, 3 H, *J* = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5 (t, *J* = 35.0 Hz), 155.3, 140.6 (t, *J* = 8.5 Hz), 120.6 (t, *J* = 24.5 Hz), 112.5 (t, *J* = 246.5 Hz), 80.0, 53.7, 49.7, 44.1, 28.5, 24.9, 23.0, 22.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ –103.3 (dd, *J* = 64.7, 10.5 Hz); APCI-MS m/z 344 ($[M+Na]^+$, 100), 337 (52), 335 (60), 330 (43), 321 (45); HRMS (APCI) m/z calcd for $C_{15}H_{25}F_2NO_4Na$ (M+Na) 344.1649, found 344.1672.



(*S*)-13

(*S*,*E*)-*N*-(2,2,6,6-Tetramethyl-1-oxo-piperidin-4-yl)-5-(*tert*-butoxycarbonylamino)-2,2-difluoro-7-methyloct-3-enamide ((*S*)-13). A solution of ester **(*S*)-12** (86.4 mg, 0.255 mmol) in THF (3 mL) was treated by a slow addition of TBAH (40% in water, 0.16 mL, 0.255 mmol) at –10 °C. Stirring was continued under argon from –10 to –5 °C for 30 min, then the solvent was removed *in vacuo*. The residue was dissolved in water, the solution acidified (pH 1) with 1 N aq. HCl, and extracted twice with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo* to afford 255 mg of the crude acid as a colorless thick oil, that was carried on without further purification.

To a solution of this acid (248 mg, 0.248 mmol, crude) and 4-amino-TEMPO (64 mg, 0.37 mmol) in dry CH_2Cl_2 (4 mL) at 0 °C were added successively HOBt•H_2O (36.9 mg, 0.273 mmol), DMAP (33.7 mg, 0.273 mmol), and EDCI (58.3 mg, 0.298 mmol). The resulting orange solution was stirred at rt under N_2 for 17 h, and then washed with sat. aq. NH_4Cl. The aqueous phase was separated and extracted once with CH_2Cl_2, and the combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residue on SiO_2 (8:2 to 7:3, hexanes/EtOAc) afforded 71.2 mg (62%, 2 steps) of **((*S*)-13** as a peach colored foam: Mp 65-66 °C (softening point: ~59 °C); $[\alpha]_D^{22}$ +4.3 (*c* 1.0, CH_2Cl_2); IR (neat) 3314 (br), 2971, 2956, 2936, 2868, 1681, 1523, 1459, 1389, 1377, 1364, 1331, 1243, 1217, 1165, 1113, 1085, 1042,

1021, 967 cm^{-1}; ESI-MS m/z 483 ($[M+Na]^+$, 100); HRMS (ESI) m/z calcd for $C_{23}H_{40}F_2N_3O_4Na$ (M+Na) 483.2885, found 483.2892.

A sample of this nitroxide (10.0 mg, 0.0217 mmol) was dissolved in dry MeOH (0.5 mL) and L-ascorbic acid (3.9 mg, 0.0217 mmol) was added. Complete discoloration of the solution occured within a few seconds. After stirring at rt for 15 min under argon, the solvent was removed *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 and washed once with water. The aqueous layers was extracted once with CH_2Cl_2, and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo* to yield 9.6 mg (96%) of the corresponding hydroxylamine as a colorless oil that forms a white foam: ^{1}H NMR (400 MHz, CD_3OD) δ 6.87 (bd, 1 H, *J* = 8.1 Hz), 6.22-6.08 (m, 1 H), 5.81 (dtd, 1 H, *J* = 15.8, 10.9, 1.2 Hz), 4.24-4.10 (m, 2 H), 1.78 (app bd, 2 H, *J* = 11.0 Hz), 1.73-1.60 (m, 1 H), 1.59 (app bt, 2 H, *J* = 12.6 Hz), 1.44 (s, 9 H), 1.42-1.30 (m, 2 H), 1.23 (s, 6 H), 1.22 (s, 6 H), 0.94 (d, 3 H, *J* = 6.6 Hz), 0.93 (d, 3 H, *J* = 6.6 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 165.8 (t, *J* = 31.0 Hz), 158.0, 141.5 (t, *J* = 8.5 Hz), 122.3 (t, *J* = 25.0 Hz), 115.4 (t, *J* = 246.0 Hz), 80.4, 61.7, 51.0, 44.9, 44.5, 42.7, 32.2, 28.9, 26.1, 23.3, 22.4, 20.4; ^{19}F NMR (376 MHz, CD_3OD) δ –105.0 (dd, *J* = 21.8, 10.2 Hz).

Table 1. Crystal data and structure refinement for JP4-039 ((*S*)-**6a**)

Identification code	klw_as4s	
Empirical formula	C23 H42 N3 O4	
Formula weight	424.60	
Temperature	203(2) K	
Wavelength	0.71073 Å	
Crystal system	Tetragonal	
Space group	P4(1)	
Unit cell dimensions	a = 12.9391(15) Å	a= 90°.
	b = 12.9391(15) Å	b= 90°.
	c = 15.758(3) Å	g = 90°.
Volume	2638.3(6) Å3	
Z	4	
Density (calculated)	1.069 Mg/m3	
Absorption coefficient	0.073 mm-1	
F(000)	932	
Crystal size	0.15 x 0.10 x 0.08 mm3	
Theta range for data collection	2.04 to 24.99°	
Index ranges	-15<=h<=15, -15<=k<=15, -18<=l<=18	
Reflections collected	21146	
Independent reflections	2423 [R(int) = 0.1028]	
Completeness to theta = 25.00°	100.0 %	
Absorption correction	None	
Max. and min. transmission	0.9942 and 0.9892	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	2423 / 1 / 296	
Goodness-of-fit on F2	0.919	
Final R indices [I>2sigma(I)]	R1 = 0.0438, wR2 = 0.1065	
R indices (all data)	R1 = 0.0647, wR2 = 0.1176	
Absolute structure parameter	0.5(17)	
Largest diff. peak and hole	0.143 and -0.125 e.Å-3	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for JP4-039 ((*S*)-**6a**). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	3499(3)	3267(2)	3293(2)	44(1)
N(1)	1649(2)	3707(2)	3213(2)	52(1)
O(1)	928(2)	4387(2)	3181(2)	77(1)
C(2)	2690(3)	4096(3)	3461(2)	48(1)
N(2)	4016(2)	1468(2)	3445(2)	44(1)
O(2)	3508(2)	408(2)	4494(1)	49(1)
C(3)	1295(3)	2620(3)	3311(3)	59(1)
N(3)	6034(2)	999(2)	944(2)	39(1)
O(3)	5126(2)	2213(2)	1664(1)	44(1)
C(4)	2201(3)	1887(3)	3152(3)	51(1)
O(4)	4855(2)	1897(2)	260(2)	51(1)
C(5)	3184(2)	2201(2)	3598(2)	40(1)
C(6)	2915(4)	5039(3)	2923(3)	75(1)
C(7)	2681(3)	4401(3)	4399(3)	66(1)
C(8)	833(4)	2464(4)	4190(4)	84(2)
C(9)	462(4)	2431(4)	2635(4)	96(2)
C(10)	4110(3)	609(2)	3914(2)	40(1)
C(11)	4985(3)	-115(3)	3700(2)	50(1)
C(12)	5769(3)	313(3)	3101(2)	41(1)
C(13)	5818(3)	105(3)	2290(2)	41(1)
C(14)	6567(2)	562(2)	1678(2)	36(1)
C(15)	7323(3)	-252(3)	1348(2)	52(1)
C(16)	8012(4)	-758(4)	2016(3)	67(1)
C(17)	8598(6)	-1646(6)	1605(4)	141(3)
C(18)	8727(4)	-4(6)	2422(4)	117(2)
C(19)	5322(2)	1740(2)	1013(2)	35(1)
C(20)	4159(3)	2770(2)	107(2)	44(1)
C(21)	3212(3)	2700(4)	656(3)	72(1)
C(22)	3857(4)	2619(4)	-817(3)	80(2)
C(23)	4721(4)	3766(3)	241(4)	81(1)

Table 3. Bond lengths [Å] and angles [°] for JP4-039 ((*S*)-**6a**).

C(1)-C(2)	1.521(5)
C(1)-C(5)	1.517(5)
C(1)-H(1A)	0.9800
C(1)-H(1B)	0.9800
N(1)-O(1)	1.284(4)
N(1)-C(3)	1.487(5)
N(1)-C(2)	1.490(5)
C(2)-C(6)	1.514(5)
C(2)-C(7)	1.530(6)
N(2)-C(10)	1.340(4)
N(2)-C(5)	1.455(4)
N(2)-H(2N)	0.88(4)
O(2)-C(10)	1.228(4)
C(3)-C(8)	1.521(7)
C(3)-C(4)	1.529(5)
C(3)-C(9)	1.534(6)
N(3)-C(19)	1.334(4)
N(3)-C(14)	1.461(4)
N(3)-H(3N)	0.83(3)
O(3)-C(19)	1.222(4)
C(4)-C(5)	1.509(5)
C(4)-H(4A)	0.9800
C(4)-H(4B)	0.9800
O(4)-C(19)	1.347(4)
O(4)-C(20)	1.463(4)
C(5)-H(5A)	0.9900
C(6)-H(6A)	0.9700
C(6)-H(6B)	0.9700
C(6)-H(6C)	0.9700
C(7)-H(7A)	0.9700
C(7)-H(7B)	0.9700
C(7)-H(7C)	0.9700
C(8)-H(8A)	0.9700
C(8)-H(8B)	0.9700
C(8)-H(8C)	0.9700
C(9)-H(9A)	0.9700

C(9)-H(9B)	0.9700
C(9)-H(9C)	0.9700
C(10)-C(11)	1.507(5)
C(11)-C(12)	1.491(5)
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(12)-C(13)	1.309(5)
C(12)-H(12)	0.92(3)
C(13)-C(14)	1.489(5)
C(13)-H(13)	0.97(4)
C(14)-C(15)	1.528(5)
C(14)-H(14A)	0.9900
C(15)-C(16)	1.527(5)
C(15)-H(15A)	0.9800
C(15)-H(15B)	0.9800
C(16)-C(18)	1.489(8)
C(16)-C(17)	1.521(7)
C(16)-H(16A)	0.9900
C(17)-H(17A)	0.9700
C(17)-H(17B)	0.9700
C(17)-H(17C)	0.9700
C(18)-H(18A)	0.9700
C(18)-H(18B)	0.9700
C(18)-H(18C)	0.9700
C(20)-C(23)	1.495(6)
C(20)-C(21)	1.503(5)
C(20)-C(22)	1.520(6)
C(21)-H(21A)	0.9700
C(21)-H(21B)	0.9700
C(21)-H(21C)	0.9700
C(22)-H(22A)	0.9700
C(22)-H(22B)	0.9700
C(22)-H(22C)	0.9700
C(23)-H(23A)	0.9700
C(23)-H(23B)	0.9700
C(23)-H(23C)	0.9700

C(2)-C(1)-C(5)	113.7(3)

C(2)-C(1)-H(1A)	108.8
C(5)-C(1)-H(1A)	108.8
C(2)-C(1)-H(1B)	108.8
C(5)-C(1)-H(1B)	108.8
H(1A)-C(1)-H(1B)	107.7
O(1)-N(1)-C(3)	115.4(3)
O(1)-N(1)-C(2)	115.8(3)
C(3)-N(1)-C(2)	124.8(3)
N(1)-C(2)-C(1)	109.8(3)
N(1)-C(2)-C(6)	107.4(3)
C(1)-C(2)-C(6)	109.8(3)
N(1)-C(2)-C(7)	109.5(3)
C(1)-C(2)-C(7)	110.8(3)
C(6)-C(2)-C(7)	109.5(4)
C(10)-N(2)-C(5)	121.0(3)
C(10)-N(2)-H(2N)	116(2)
C(5)-N(2)-H(2N)	123(2)
N(1)-C(3)-C(8)	110.0(4)
N(1)-C(3)-C(4)	109.4(3)
C(8)-C(3)-C(4)	111.6(3)
N(1)-C(3)-C(9)	107.2(3)
C(8)-C(3)-C(9)	109.5(4)
C(4)-C(3)-C(9)	109.0(4)
C(19)-N(3)-C(14)	122.6(3)
C(19)-N(3)-H(3N)	117(2)
C(14)-N(3)-H(3N)	118(2)
C(5)-C(4)-C(3)	113.8(3)
C(5)-C(4)-H(4A)	108.8
C(3)-C(4)-H(4A)	108.8
C(5)-C(4)-H(4B)	108.8
C(3)-C(4)-H(4B)	108.8
H(4A)-C(4)-H(4B)	107.7
C(19)-O(4)-C(20)	122.6(2)
N(2)-C(5)-C(4)	111.8(3)
N(2)-C(5)-C(1)	110.0(3)
C(4)-C(5)-C(1)	108.8(3)
N(2)-C(5)-H(5A)	108.7
C(4)-C(5)-H(5A)	108.7

C(1)-C(5)-H(5A)	108.7
C(2)-C(6)-H(6A)	109.5
C(2)-C(6)-H(6B)	109.5
H(6A)-C(6)-H(6B)	109.5
C(2)-C(6)-H(6C)	109.5
H(6A)-C(6)-H(6C)	109.5
H(6B)-C(6)-H(6C)	109.5
C(2)-C(7)-H(7A)	109.5
C(2)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
C(2)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(3)-C(8)-H(8A)	109.5
C(3)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5
C(3)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
C(3)-C(9)-H(9A)	109.5
C(3)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(3)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
O(2)-C(10)-N(2)	121.9(3)
O(2)-C(10)-C(11)	120.7(3)
N(2)-C(10)-C(11)	117.3(3)
C(12)-C(11)-C(10)	115.0(3)
C(12)-C(11)-H(11A)	108.5
C(10)-C(11)-H(11A)	108.5
C(12)-C(11)-H(11B)	108.5
C(10)-C(11)-H(11B)	108.5
H(11A)-C(11)-H(11B)	107.5
C(13)-C(12)-C(11)	125.1(4)
C(13)-C(12)-H(12)	114(2)
C(11)-C(12)-H(12)	121(2)
C(12)-C(13)-C(14)	125.7(4)

C(12)-C(13)-H(13)	121(2)
C(14)-C(13)-H(13)	113(2)
N(3)-C(14)-C(13)	111.1(3)
N(3)-C(14)-C(15)	107.4(3)
C(13)-C(14)-C(15)	111.3(3)
N(3)-C(14)-H(14A)	109.0
C(13)-C(14)-H(14A)	109.0
C(15)-C(14)-H(14A)	109.0
C(14)-C(15)-C(16)	115.8(3)
C(14)-C(15)-H(15A)	108.3
C(16)-C(15)-H(15A)	108.3
C(14)-C(15)-H(15B)	108.3
C(16)-C(15)-H(15B)	108.3
H(15A)-C(15)-H(15B)	107.4
C(18)-C(16)-C(15)	112.2(4)
C(18)-C(16)-C(17)	111.5(5)
C(15)-C(16)-C(17)	108.7(4)
C(18)-C(16)-H(16A)	108.1
C(15)-C(16)-H(16A)	108.1
C(17)-C(16)-H(16A)	108.1
C(16)-C(17)-H(17A)	109.5
C(16)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(16)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(16)-C(18)-H(18A)	109.5
C(16)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(16)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
O(3)-C(19)-N(3)	124.9(3)
O(3)-C(19)-O(4)	124.8(3)
N(3)-C(19)-O(4)	110.3(3)
O(4)-C(20)-C(23)	110.1(3)
O(4)-C(20)-C(21)	111.1(3)
C(23)-C(20)-C(21)	111.6(4)

O(4)-C(20)-C(22)	102.6(3)
C(23)-C(20)-C(22)	111.7(4)
C(21)-C(20)-C(22)	109.5(4)
C(20)-C(21)-H(21A)	109.5
C(20)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(20)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(20)-C(22)-H(22A)	109.5
C(20)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(20)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(20)-C(23)-H(23A)	109.5
C(20)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(20)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for JP4-039 ((*S*)-**6a**). The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + \ldots + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	43(2)	41(2)	47(2)	5(2)	5(2)	5(2)
N(1)	47(2)	53(2)	56(2)	7(2)	-4(2)	11(2)
O(1)	60(2)	83(2)	89(2)	3(2)	-11(2)	33(2)
C(2)	47(2)	42(2)	53(2)	4(2)	4(2)	6(2)
N(2)	52(2)	39(2)	41(2)	9(1)	13(2)	9(1)
O(2)	53(1)	50(1)	44(1)	13(1)	11(1)	4(1)
C(3)	43(2)	67(3)	67(3)	13(2)	-5(2)	-1(2)
N(3)	48(2)	38(2)	32(2)	-3(1)	-4(1)	6(1)
O(3)	52(1)	41(1)	38(1)	-5(1)	-5(1)	9(1)
C(4)	54(2)	46(2)	54(2)	6(2)	-1(2)	-5(2)
O(4)	67(2)	44(1)	41(1)	-7(1)	-13(1)	25(1)
C(5)	38(2)	42(2)	38(2)	3(1)	4(1)	6(2)
C(6)	75(3)	48(2)	102(4)	22(2)	10(3)	12(2)
C(7)	62(3)	65(3)	72(3)	-18(2)	-7(2)	17(2)
C(8)	54(3)	101(4)	98(4)	22(3)	23(3)	-1(3)
C(9)	65(3)	98(4)	125(5)	17(3)	-37(3)	-14(3)
C(10)	50(2)	39(2)	33(2)	4(1)	-1(2)	2(2)
C(11)	66(2)	43(2)	43(2)	10(2)	13(2)	14(2)
C(12)	46(2)	38(2)	40(2)	4(2)	1(2)	9(2)
C(13)	47(2)	34(2)	41(2)	-1(2)	-1(2)	4(2)
C(14)	39(2)	37(2)	32(2)	-1(1)	-4(1)	3(1)
C(15)	59(2)	62(2)	36(2)	1(2)	-1(2)	24(2)
C(16)	73(3)	81(3)	47(2)	7(2)	-3(2)	34(2)
C(17)	170(6)	167(6)	87(4)	-21(4)	-33(4)	125(6)
C(18)	89(4)	159(6)	103(4)	2(4)	-51(4)	28(4)
C(19)	43(2)	30(2)	33(2)	-1(1)	-5(1)	1(1)
C(20)	52(2)	36(2)	44(2)	0(2)	-6(2)	13(2)
C(21)	57(3)	100(3)	60(3)	4(2)	-8(2)	17(2)
C(22)	118(4)	78(3)	44(2)	-3(2)	-21(2)	54(3)
C(23)	94(3)	46(2)	102(4)	16(2)	-21(3)	2(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{-3}) for JP4-039 ((*S*)-**6a**).

	x	y	z	U(eq)
H(1A)	4144	3465	3576	52
H(1B)	3635	3236	2682	52
H(2N)	4480(30)	1550(30)	3050(30)	49(10)
H(3N)	6050(20)	670(20)	500(20)	28(9)
H(4A)	2006	1192	3339	62
H(4B)	2334	1856	2540	62
H(5A)	3049	2232	4216	47
H(6A)	2919	4845	2328	112
H(6B)	3584	5320	3077	112
H(6C)	2385	5556	3019	112
H(7A)	2548	3795	4744	100
H(7B)	2143	4910	4496	100
H(7C)	3346	4693	4552	100
H(8A)	1375	2513	4613	126
H(8B)	513	1787	4221	126
H(8C)	317	2992	4295	126
H(9A)	-119	2888	2736	144
H(9B)	232	1719	2666	144
H(9C)	748	2566	2077	144
H(11A)	5335	-310	4228	61
H(11B)	4693	-745	3452	61
H(12)	6260(30)	780(30)	3280(20)	38(9)
H(13)	5350(30)	-390(30)	2030(30)	65(12)
H(14A)	6960	1116	1966	43
H(15A)	7768	73	921	63
H(15B)	6926	-795	1062	63
H(16A)	7560	-1050	2464	80
H(17A)	9001	-2004	2033	212
H(17B)	9056	-1375	1171	212
H(17C)	8111	-2123	1349	212
H(18A)	8330	499	2741	175
H(18B)	9125	347	1987	175
H(18C)	9192	-367	2802	175

H(21A)	3411	2746	1248	108
H(21B)	2867	2045	556	108
H(21C)	2745	3262	519	108
H(22A)	4472	2641	-1169	120
H(22B)	3388	3166	-988	120
H(22C)	3518	1956	-884	120
H(23A)	4854	3862	841	121
H(23B)	4301	4334	32	121
H(23C)	5371	3750	-65	121

Table 6. Crystal data and structure refinement for **10**.

Identification code	mcf807s	
Empirical formula	C28 H31 Br N2 O3	
Formula weight	523.46	
Temperature	203(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2	
Unit cell dimensions	a = 29.131(12) Å	α= 90°.
	b = 4.9265(19) Å	β= 126.463(8)°.
	c = 22.228(9) Å	γ = 90°.
Volume	2565.5(17) $Å^3$	
Z	4	
Density (calculated)	1.355 Mg/m^3	
Absorption coefficient	1.634 mm^{-1}	
F(000)	1088	
Crystal size	0.23 x 0.06 x 0.04 mm^3	
Theta range for data collection	1.74 to 25.00°.	
Index ranges	-34<=h<=34, -5<=k<=5, -26<=l<=26	
Reflections collected	10092	
Independent reflections	4496 [R(int) = 0.0968]	
Completeness to theta = 25.00°	99.8 %	
Absorption correction	None	
Max. and min. transmission	0.9375 and 0.7051	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4496 / 1 / 308	
Goodness-of-fit on F^2	1.136	
Final R indices [I>2sigma(I)]	R1 = 0.0887, wR2 = 0.2195	
R indices (all data)	R1 = 0.1507, wR2 = 0.2389	
Absolute structure parameter	0.07(3)	
Largest diff. peak and hole	1.381 and -0.320 e.$Å^{-3}$	

Table 7. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **10**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br	-3346(1)	-8051(4)	-4543(1)	84(1)
C(1)	-2021(3)	-8557(19)	-1773(5)	37(2)
N(1)	-1453(3)	-9077(14)	-1535(4)	39(2)
O(1)	-1177(4)	-4665(16)	-1455(5)	71(2)
O(2)	-580(2)	-8172(17)	-1168(3)	45(2)
N(2)	-468(3)	-8497(16)	-2913(4)	37(2)
C(2)	-2355(5)	-6700(20)	-2310(6)	56(3)
O(3)	-637(3)	-12853(17)	-2852(4)	59(2)
C(3)	-2910(5)	-6220(20)	-2527(7)	61(3)
C(4)	-3104(4)	-7460(20)	-2172(6)	56(3)
C(5)	-2773(4)	-9430(20)	-1606(5)	42(2)
C(6)	-2965(4)	-10820(20)	-1258(6)	51(3)
C(7)	-2639(4)	-12650(30)	-715(6)	54(3)
C(8)	-2091(4)	-13310(30)	-505(5)	48(2)
C(9)	-1874(4)	-11929(18)	-814(5)	40(2)
C(10)	-2211(3)	-9934(19)	-1399(5)	35(2)
C(11)	-1089(4)	-7060(20)	-1395(5)	43(3)
C(12)	-138(4)	-6170(20)	-969(6)	49(3)
C(13)	409(4)	-7640(30)	-635(5)	50(3)
C(14)	421(4)	-9280(20)	-1194(5)	40(2)
C(15)	969(4)	-9450(20)	-1110(6)	50(3)
C(16)	474(3)	-7860(20)	-1740(4)	39(2)
C(17)	154(4)	-8818(19)	-2521(5)	41(3)
C(18)	350(4)	-7430(20)	-2940(5)	49(3)
C(19)	291(5)	-8960(30)	-3579(6)	75(4)
C(20)	558(5)	-7220(40)	-3881(7)	91(6)
C(22)	-814(4)	-10539(19)	-3034(5)	38(2)
C(23)	-1700(4)	-7760(30)	-3916(5)	47(2)
C(24)	-2269(5)	-7220(20)	-4257(6)	65(4)
C(25)	-2561(4)	-8780(20)	-4061(5)	48(3)
C(26)	-2297(4)	-10810(20)	-3547(6)	55(3)
C(27)	-1727(4)	-11410(20)	-3218(6)	53(3)
C(28)	-1431(4)	-9856(19)	-3392(5)	38(2)
C(21)	-289(6)	-9830(30)	-4175(7)	92(5)

Table 8. Bond lengths [Å] and angles [°] for **10**.

Br-C(25)	1.894(9)
C(1)-C(2)	1.351(13)
C(1)-C(10)	1.417(13)
C(1)-N(1)	1.430(11)
N(1)-C(11)	1.344(11)
N(1)-H(1A)	0.8700
O(1)-C(11)	1.200(11)
O(2)-C(11)	1.366(12)
O(2)-C(12)	1.467(11)
N(2)-C(22)	1.333(12)
N(2)-C(17)	1.479(11)
N(2)-H(2B)	0.8700
C(2)-C(3)	1.404(16)
C(2)-H(2A)	0.9400
O(3)-C(22)	1.217(12)
C(3)-C(4)	1.358(15)
C(3)-H(3A)	0.9400
C(4)-C(5)	1.419(14)
C(4)-H(4A)	0.9400
C(5)-C(6)	1.375(15)
C(5)-C(10)	1.434(12)
C(6)-C(7)	1.348(15)
C(6)-H(6A)	0.9400
C(7)-C(8)	1.410(13)
C(7)-H(7A)	0.9400
C(8)-C(9)	1.357(13)
C(8)-H(8A)	0.9400
C(9)-C(10)	1.450(13)
C(9)-H(9A)	0.9400
C(12)-C(13)	1.486(14)
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(13)-C(14)	1.501(14)
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(14)-C(16)	1.484(13)
C(14)-C(15)	1.496(13)
C(14)-H(14A)	0.9900

C(15)-C(16)	1.499(13)
C(15)-H(15A)	0.9800
C(15)-H(15B)	0.9800
C(16)-C(17)	1.477(12)
C(16)-H(16A)	0.9900
C(17)-C(18)	1.515(13)
C(17)-H(17A)	0.9900
C(18)-C(19)	1.525(14)
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(19)-C(21)	1.462(17)
C(19)-C(20)	1.551(18)
C(19)-H(19A)	0.9900
C(20)-H(20A)	0.9700
C(20)-H(20B)	0.9700
C(20)-H(20C)	0.9700
C(22)-C(28)	1.509(13)
C(23)-C(24)	1.378(14)
C(23)-C(28)	1.398(14)
C(23)-H(23A)	0.9400
C(24)-C(25)	1.394(15)
C(24)-H(24A)	0.9400
C(25)-C(26)	1.363(15)
C(26)-C(27)	1.393(14)
C(26)-H(26A)	0.9400
C(27)-C(28)	1.369(14)
C(27)-H(27A)	0.9400
C(21)-H(21A)	0.9700
C(21)-H(21B)	0.9700
C(21)-H(21C)	0.9700

C(2)-C(1)-C(10)	120.9(8)
C(2)-C(1)-N(1)	121.0(9)
C(10)-C(1)-N(1)	117.9(8)
C(11)-N(1)-C(1)	122.2(8)
C(11)-N(1)-H(1A)	118.9
C(1)-N(1)-H(1A)	118.9
C(11)-O(2)-C(12)	114.1(8)
C(22)-N(2)-C(17)	123.5(8)
C(22)-N(2)-H(2B)	118.2

C(17)-N(2)-H(2B)	118.2
C(1)-C(2)-C(3)	119.7(10)
C(1)-C(2)-H(2A)	120.2
C(3)-C(2)-H(2A)	120.2
C(4)-C(3)-C(2)	121.1(10)
C(4)-C(3)-H(3A)	119.4
C(2)-C(3)-H(3A)	119.4
C(3)-C(4)-C(5)	121.6(10)
C(3)-C(4)-H(4A)	119.2
C(5)-C(4)-H(4A)	119.2
C(6)-C(5)-C(4)	123.3(9)
C(6)-C(5)-C(10)	120.2(10)
C(4)-C(5)-C(10)	116.6(10)
C(7)-C(6)-C(5)	122.0(9)
C(7)-C(6)-H(6A)	119.0
C(5)-C(6)-H(6A)	119.0
C(6)-C(7)-C(8)	120.4(10)
C(6)-C(7)-H(7A)	119.8
C(8)-C(7)-H(7A)	119.8
C(9)-C(8)-C(7)	119.6(11)
C(9)-C(8)-H(8A)	120.2
C(7)-C(8)-H(8A)	120.2
C(8)-C(9)-C(10)	121.5(9)
C(8)-C(9)-H(9A)	119.3
C(10)-C(9)-H(9A)	119.3
C(1)-C(10)-C(5)	119.9(9)
C(1)-C(10)-C(9)	123.9(7)
C(5)-C(10)-C(9)	116.1(9)
O(1)-C(11)-N(1)	128.0(10)
O(1)-C(11)-O(2)	123.1(10)
N(1)-C(11)-O(2)	108.9(9)
O(2)-C(12)-C(13)	108.0(8)
O(2)-C(12)-H(12A)	110.1
C(13)-C(12)-H(12A)	110.1
O(2)-C(12)-H(12B)	110.1
C(13)-C(12)-H(12B)	110.1
H(12A)-C(12)-H(12B)	108.4
C(12)-C(13)-C(14)	113.2(8)
C(12)-C(13)-H(13A)	108.9
C(14)-C(13)-H(13A)	108.9

C(12)-C(13)-H(13B)	108.9
C(14)-C(13)-H(13B)	108.9
H(13A)-C(13)-H(13B)	107.7
C(16)-C(14)-C(15)	60.4(6)
C(16)-C(14)-C(13)	119.3(9)
C(15)-C(14)-C(13)	118.4(8)
C(16)-C(14)-H(14A)	115.8
C(15)-C(14)-H(14A)	115.8
C(13)-C(14)-H(14A)	115.8
C(14)-C(15)-C(16)	59.4(6)
C(14)-C(15)-H(15A)	117.8
C(16)-C(15)-H(15A)	117.8
C(14)-C(15)-H(15B)	117.8
C(16)-C(15)-H(15B)	117.8
H(15A)-C(15)-H(15B)	115.0
C(17)-C(16)-C(14)	120.8(9)
C(17)-C(16)-C(15)	121.0(9)
C(14)-C(16)-C(15)	60.2(6)
C(17)-C(16)-H(16A)	114.7
C(14)-C(16)-H(16A)	114.7
C(15)-C(16)-H(16A)	114.7
C(16)-C(17)-N(2)	110.8(7)
C(16)-C(17)-C(18)	112.0(8)
N(2)-C(17)-C(18)	111.6(7)
C(16)-C(17)-H(17A)	107.4
N(2)-C(17)-H(17A)	107.4
C(18)-C(17)-H(17A)	107.4
C(17)-C(18)-C(19)	118.4(10)
C(17)-C(18)-H(18A)	107.7
C(19)-C(18)-H(18A)	107.7
C(17)-C(18)-H(18B)	107.7
C(19)-C(18)-H(18B)	107.7
H(18A)-C(18)-H(18B)	107.1
C(21)-C(19)-C(18)	114.7(10)
C(21)-C(19)-C(20)	112.2(10)
C(18)-C(19)-C(20)	108.9(11)
C(21)-C(19)-H(19A)	106.9
C(18)-C(19)-H(19A)	106.9
C(20)-C(19)-H(19A)	106.9
C(19)-C(20)-H(20A)	109.5

C(19)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(19)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
O(3)-C(22)-N(2)	121.3(9)
O(3)-C(22)-C(28)	121.4(9)
N(2)-C(22)-C(28)	117.3(8)
C(24)-C(23)-C(28)	119.7(10)
C(24)-C(23)-H(23A)	120.2
C(28)-C(23)-H(23A)	120.2
C(23)-C(24)-C(25)	118.7(10)
C(23)-C(24)-H(24A)	120.6
C(25)-C(24)-H(24A)	120.6
C(26)-C(25)-C(24)	121.5(9)
C(26)-C(25)-Br	120.1(8)
C(24)-C(25)-Br	118.4(8)
C(25)-C(26)-C(27)	119.9(10)
C(25)-C(26)-H(26A)	120.0
C(27)-C(26)-H(26A)	120.0
C(28)-C(27)-C(26)	119.2(10)
C(28)-C(27)-H(27A)	120.4
C(26)-C(27)-H(27A)	120.4
C(27)-C(28)-C(23)	120.9(9)
C(27)-C(28)-C(22)	118.6(8)
C(23)-C(28)-C(22)	120.4(9)
C(19)-C(21)-H(21A)	109.5
C(19)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(19)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5

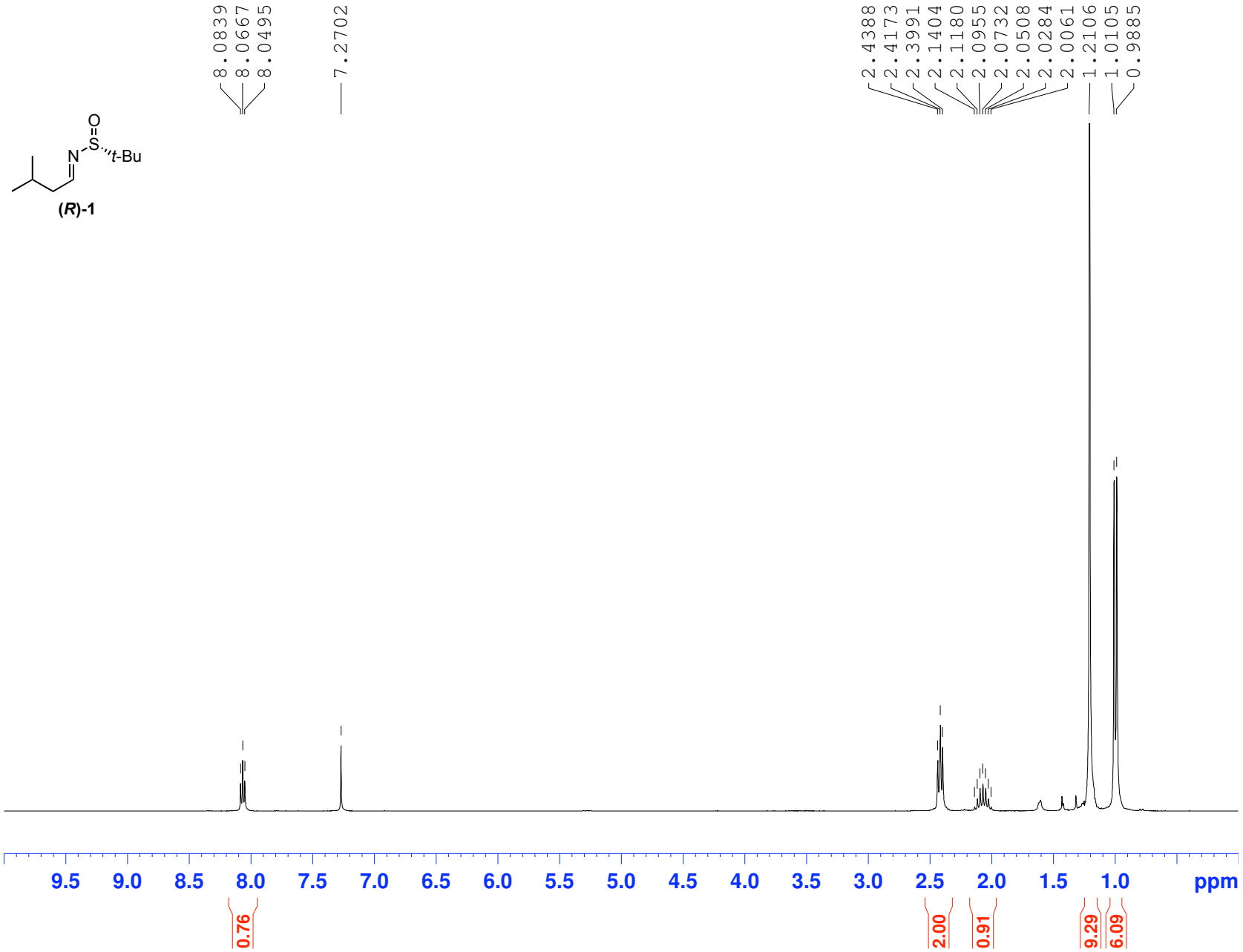
Symmetry transformations used to generate equivalent atoms:

Table 9. Anisotropic displacement parameters ($Å^2$ x 10^3) for **10**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br	44(1)	112(1)	75(1)	-3(1)	24(1)	22(1)
C(1)	34(4)	22(5)	54(5)	-6(5)	26(4)	7(5)
N(1)	48(5)	28(5)	51(5)	2(3)	35(4)	9(4)
O(1)	85(6)	29(4)	133(8)	1(5)	83(6)	-1(4)
O(2)	47(3)	35(3)	65(4)	2(4)	40(3)	-2(4)
N(2)	39(4)	19(4)	46(4)	-7(4)	21(3)	-1(4)
C(2)	66(7)	58(7)	46(6)	11(6)	35(6)	-1(6)
O(3)	47(3)	22(4)	78(4)	-5(4)	20(3)	2(4)
C(3)	49(7)	44(7)	62(7)	22(6)	17(6)	9(6)
C(4)	50(6)	41(8)	62(7)	-4(6)	25(6)	22(6)
C(5)	31(5)	45(6)	41(6)	-16(5)	17(5)	-1(5)
C(6)	41(6)	52(7)	58(7)	-17(6)	28(6)	0(6)
C(7)	55(6)	62(8)	62(6)	-9(7)	43(5)	-12(7)
C(8)	43(5)	54(7)	53(5)	14(6)	32(4)	8(6)
C(9)	45(5)	36(6)	50(6)	-4(5)	34(5)	-5(5)
C(10)	25(4)	41(6)	46(5)	-10(5)	25(4)	1(4)
C(11)	56(6)	47(8)	47(6)	-1(5)	42(5)	-6(6)
C(12)	58(6)	44(6)	75(7)	-7(6)	56(6)	-21(5)
C(13)	61(6)	52(7)	50(5)	-7(6)	41(5)	-22(6)
C(14)	34(5)	41(6)	50(6)	-2(5)	27(5)	-4(4)
C(15)	39(5)	57(7)	53(6)	9(5)	27(5)	-2(5)
C(16)	45(5)	29(5)	43(5)	-2(5)	26(4)	-8(6)
C(17)	40(5)	42(7)	41(5)	-11(4)	25(4)	-2(5)
C(18)	46(5)	59(8)	45(5)	-7(5)	29(5)	-8(6)
C(19)	72(7)	118(14)	51(6)	-10(7)	47(6)	-1(8)
C(20)	77(8)	149(18)	63(7)	-34(9)	49(7)	-16(9)
C(22)	59(6)	23(6)	36(5)	-5(4)	30(5)	-6(5)
C(23)	41(5)	48(7)	46(5)	-5(6)	23(4)	8(6)
C(24)	56(7)	60(9)	40(6)	9(6)	7(5)	14(6)
C(25)	39(5)	55(8)	41(5)	-3(5)	18(5)	14(5)
C(26)	43(6)	64(8)	50(6)	3(6)	23(5)	-8(6)
C(27)	44(6)	48(7)	56(7)	6(5)	24(6)	1(6)
C(28)	37(5)	26(5)	35(5)	-5(4)	12(4)	8(4)
C(21)	97(10)	124(12)	49(7)	-25(8)	40(8)	-22(10)

Table 10. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for **10**.

	x	y	z	U(eq)
H(1A)	-1338	-10750	-1479	46
H(2B)	-616	-6890	-3073	45
H(2A)	-2217	-5741	-2537	67
H(3A)	-3150	-5026	-2924	73
H(4A)	-3467	-7002	-2305	67
H(6A)	-3336	-10469	-1404	61
H(7A)	-2778	-13504	-474	65
H(8A)	-1876	-14687	-153	58
H(9A)	-1498	-12277	-645	48
H(12A)	-99	-4861	-609	58
H(12B)	-241	-5174	-1416	58
H(13A)	473	-8856	-242	60
H(13B)	722	-6325	-400	60
H(14A)	184	-10943	-1379	48
H(15A)	1063	-11175	-1232	59
H(15B)	1297	-8430	-701	59
H(16A)	515	-5868	-1678	47
H(17A)	232	-10783	-2506	49
H(18A)	754	-6958	-2575	58
H(18B)	139	-5723	-3142	58
H(19A)	526	-10620	-3362	89
H(20A)	531	-8197	-4281	137
H(20B)	956	-6870	-3480	137
H(20C)	354	-5514	-4072	137
H(23A)	-1493	-6723	-4036	56
H(24A)	-2456	-5829	-4614	79
H(26A)	-2500	-11806	-3414	67
H(27A)	-1547	-12866	-2881	64
H(21A)	-437	-10936	-3964	138
H(21B)	-286	-10880	-4541	138
H(21C)	-531	-8247	-4416	138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N
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7.0
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6.0
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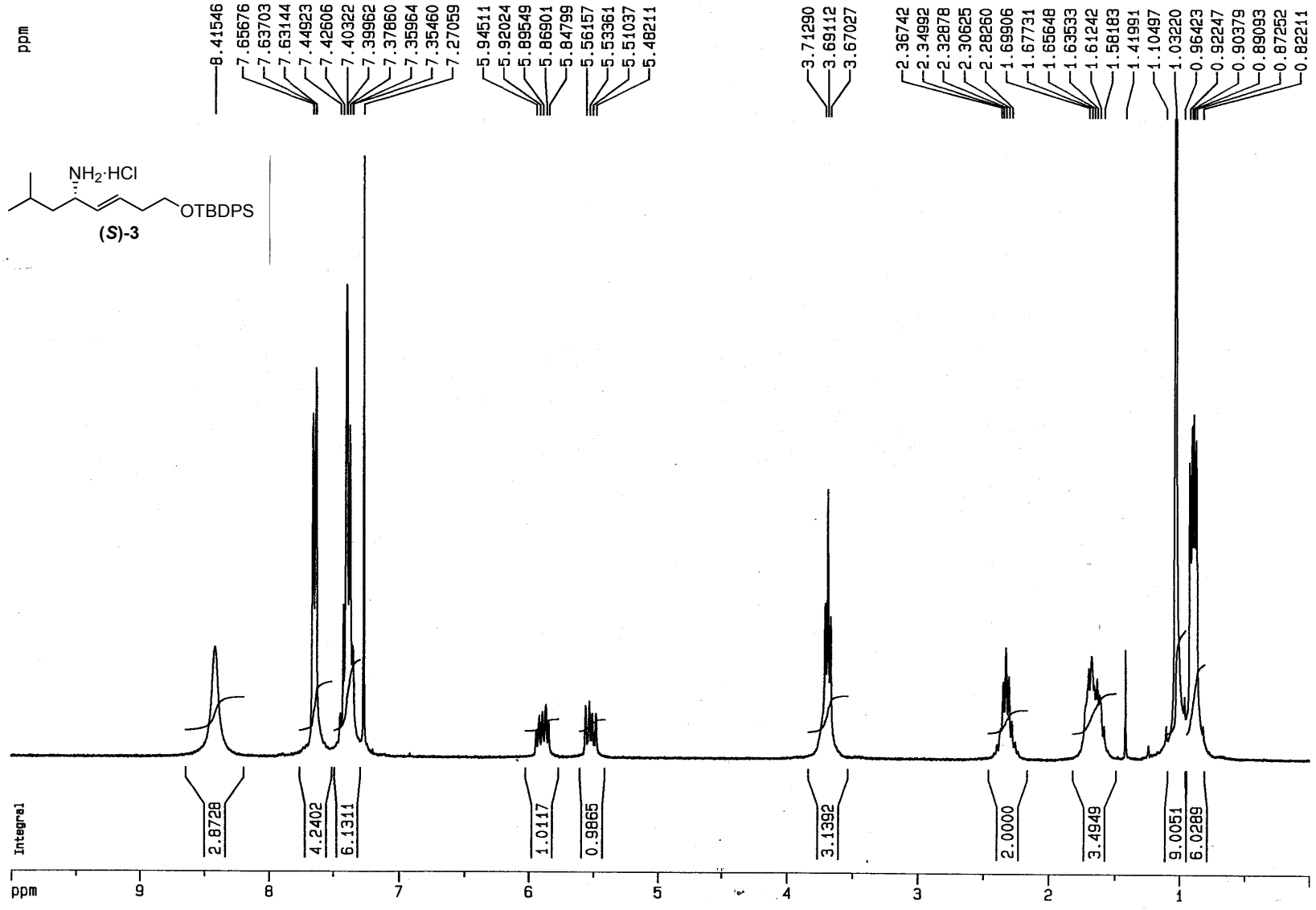
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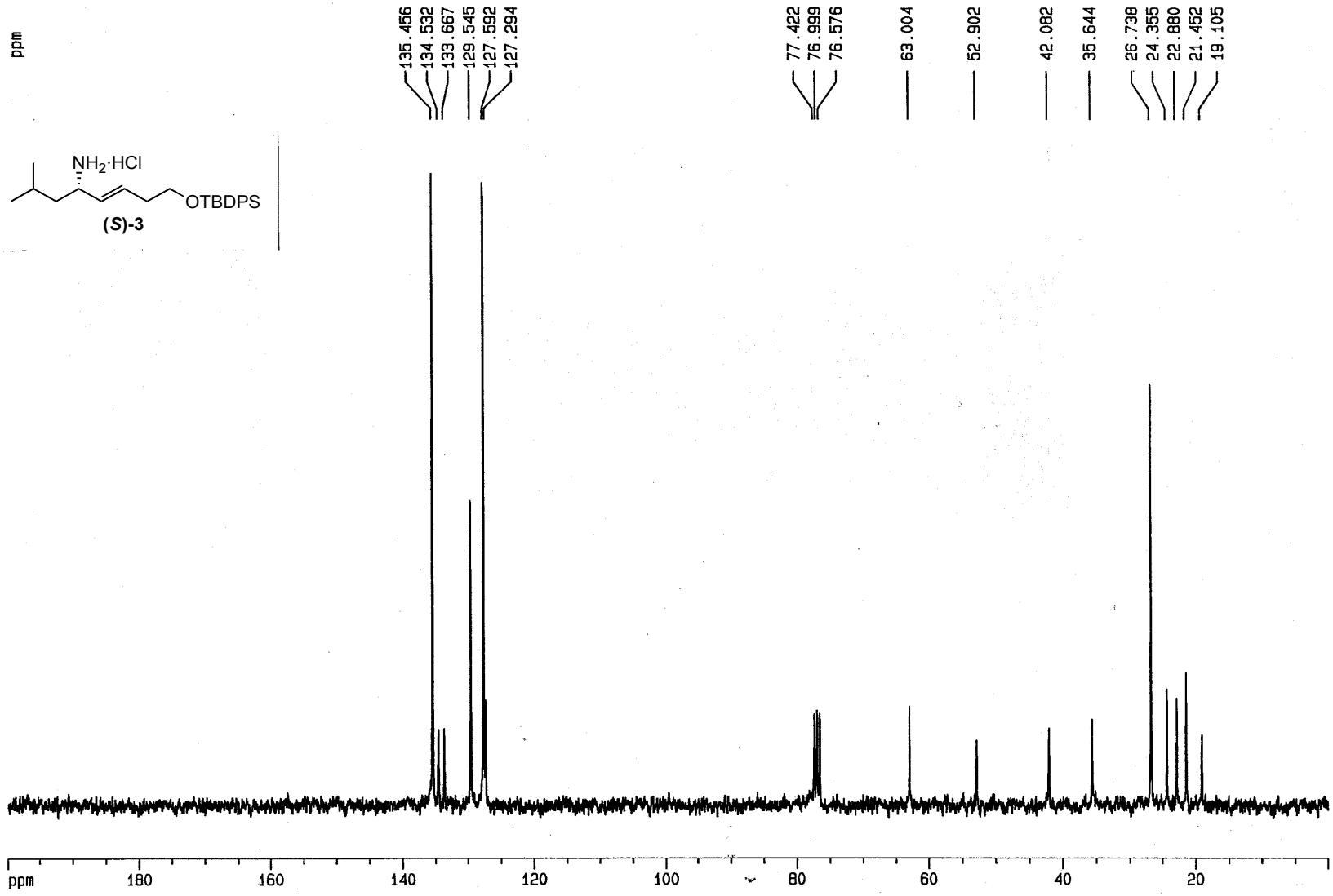
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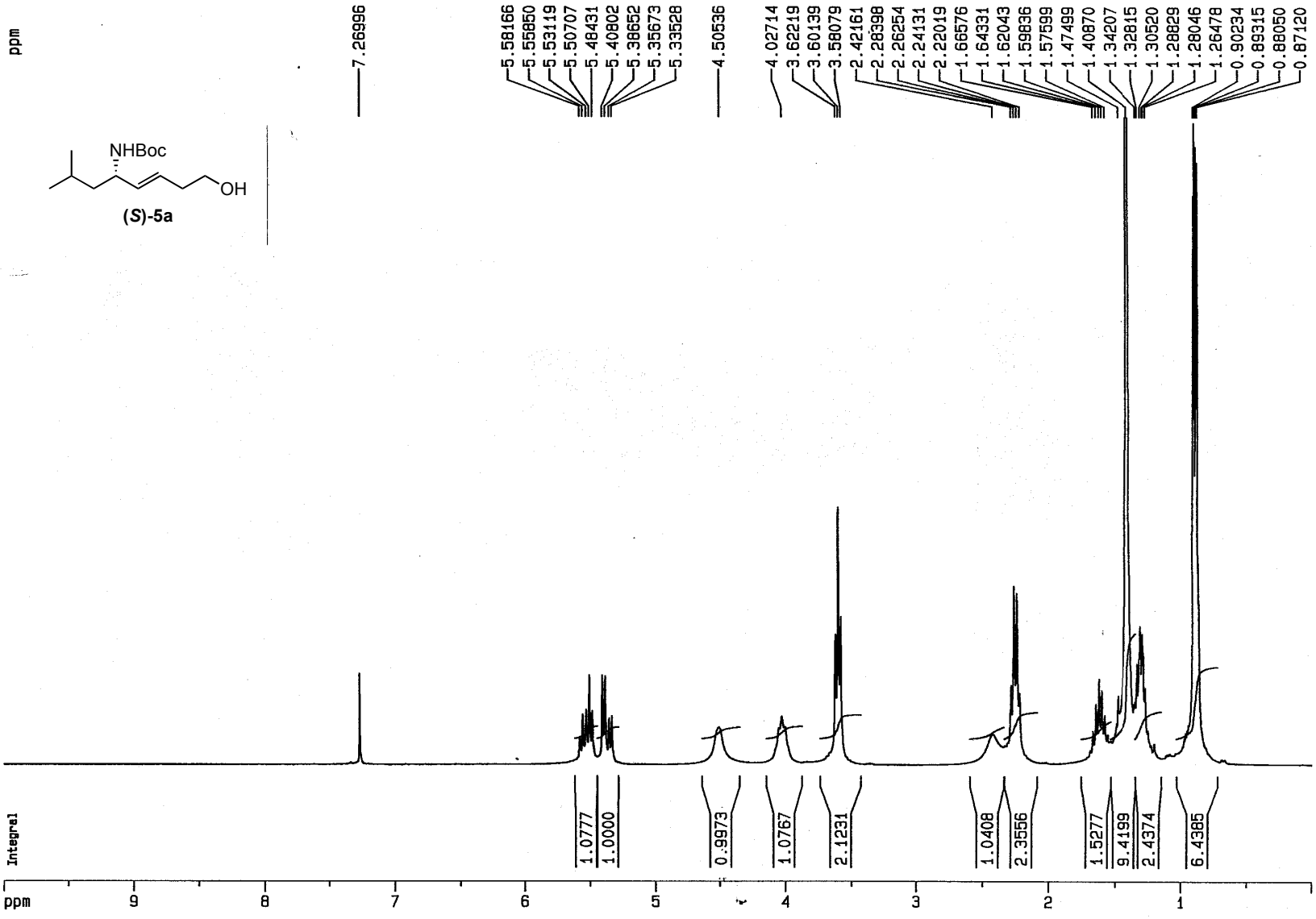
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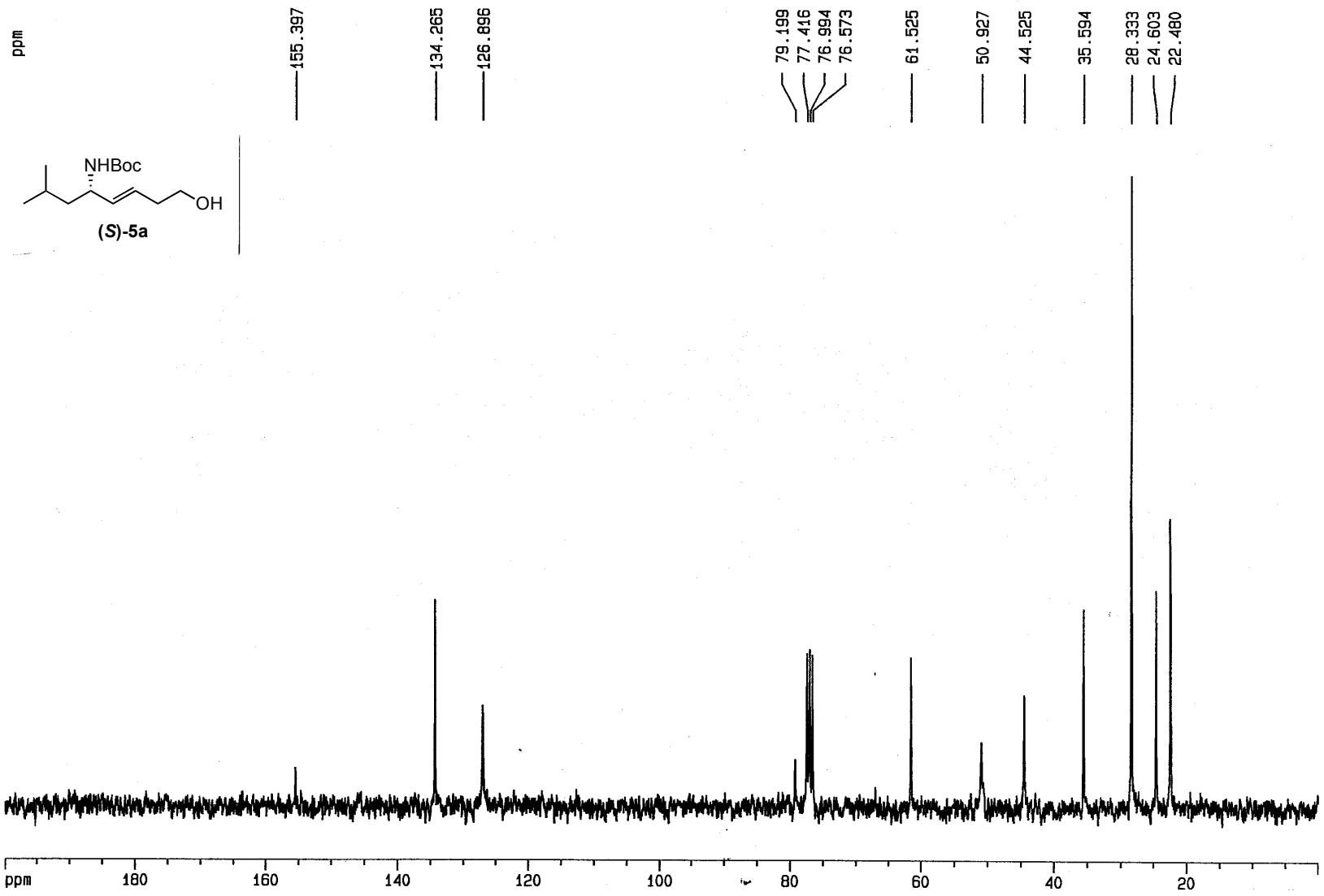
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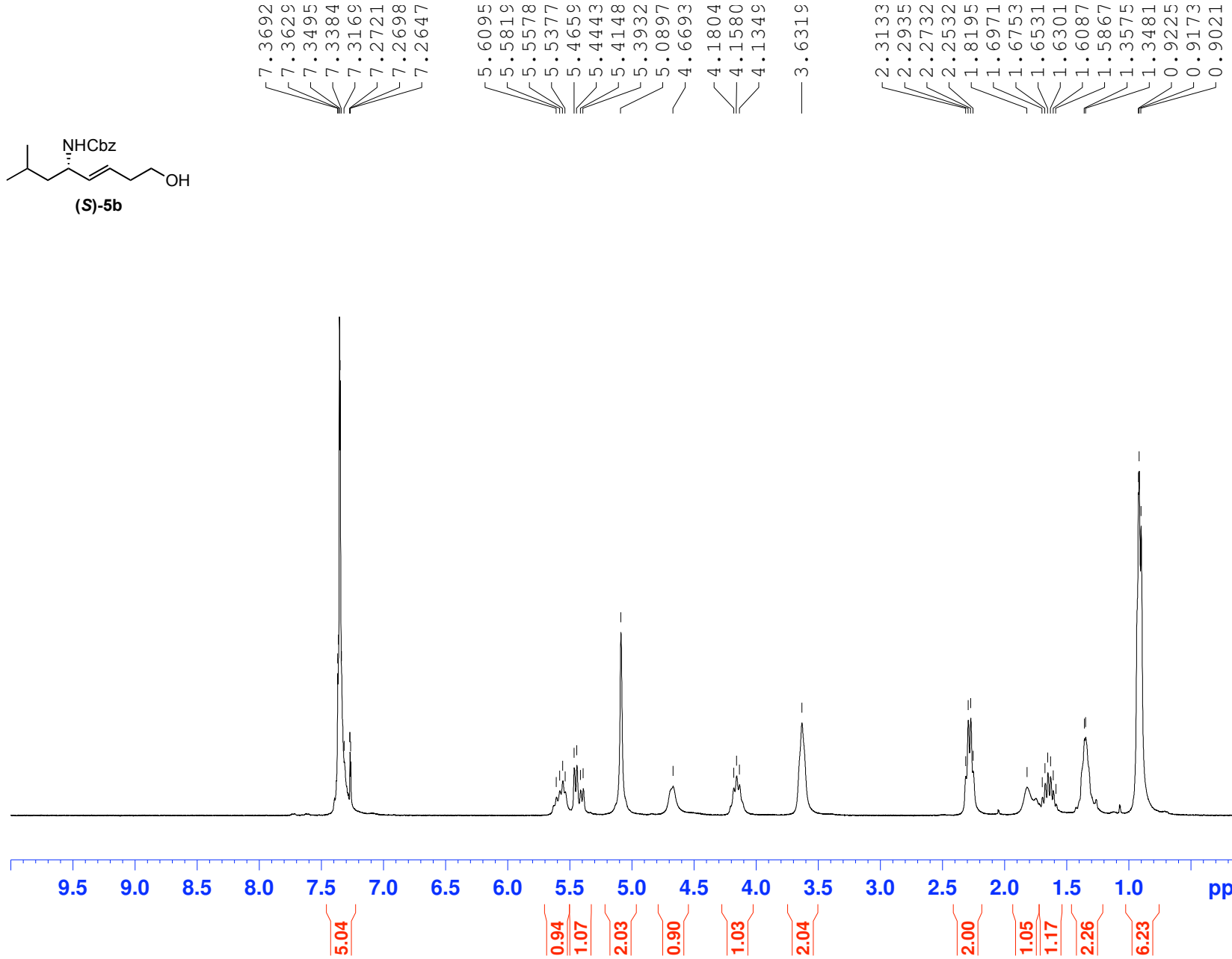
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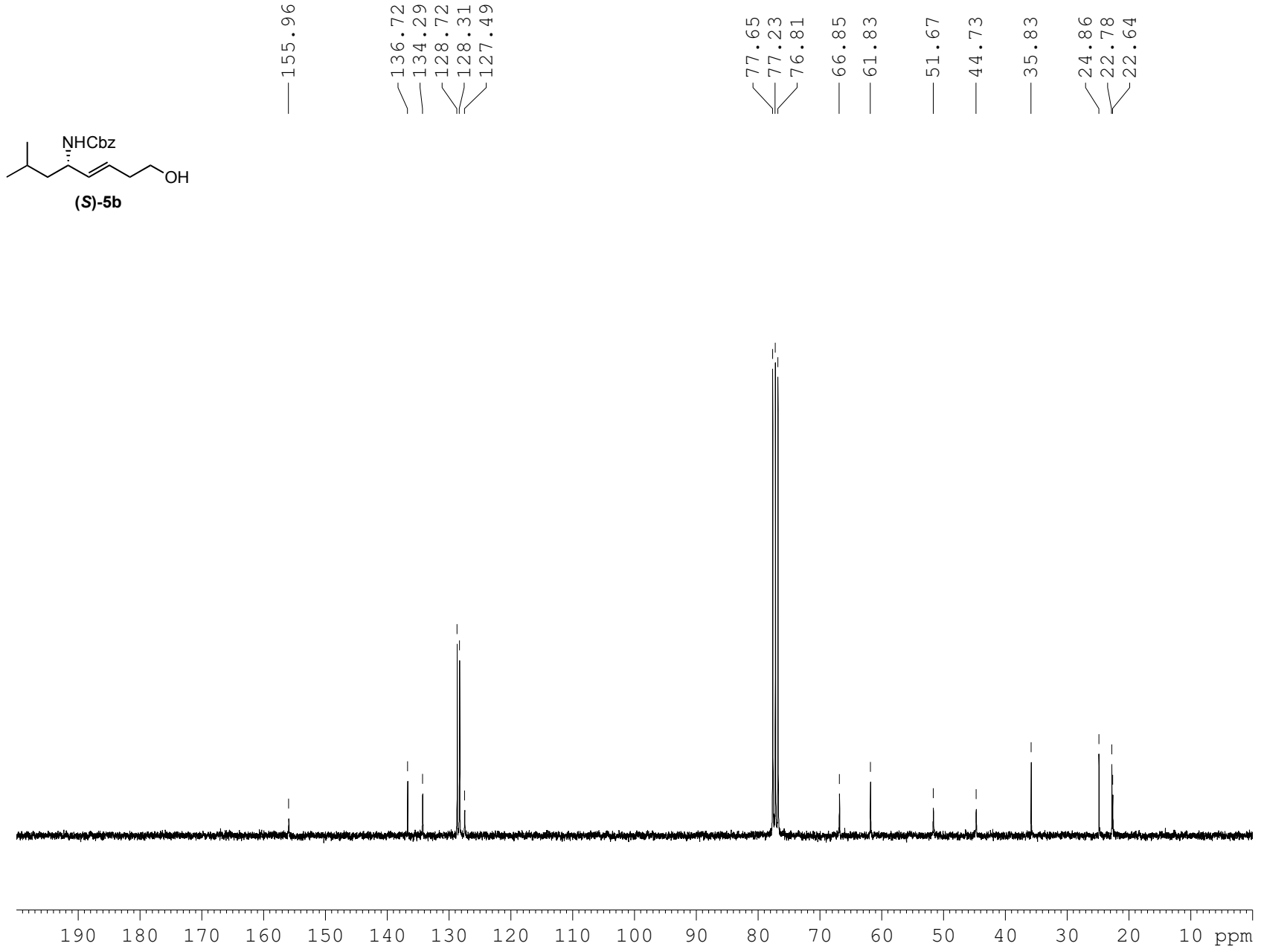
5.5819
5.5578
5.5377
5.4659
5.4443
5.4148
5.3932
5.0897
4.6693
4.1804
4.1580
4.1349
3.6319
2.3133
2.2935
2.2732
2.2532
1.8195
1.6971
1.6753
1.6531
1.6301
1.6087
1.5867
1.3575
1.3481
0.9225
0.9173
0.9021
NHCbz
OH
(S)-5b
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
5.04
0.94
1.07
2.03
0.90
1.03
2.04
2.00
1.05
1.17
2.26
6.23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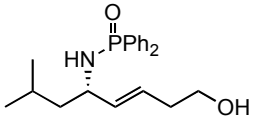
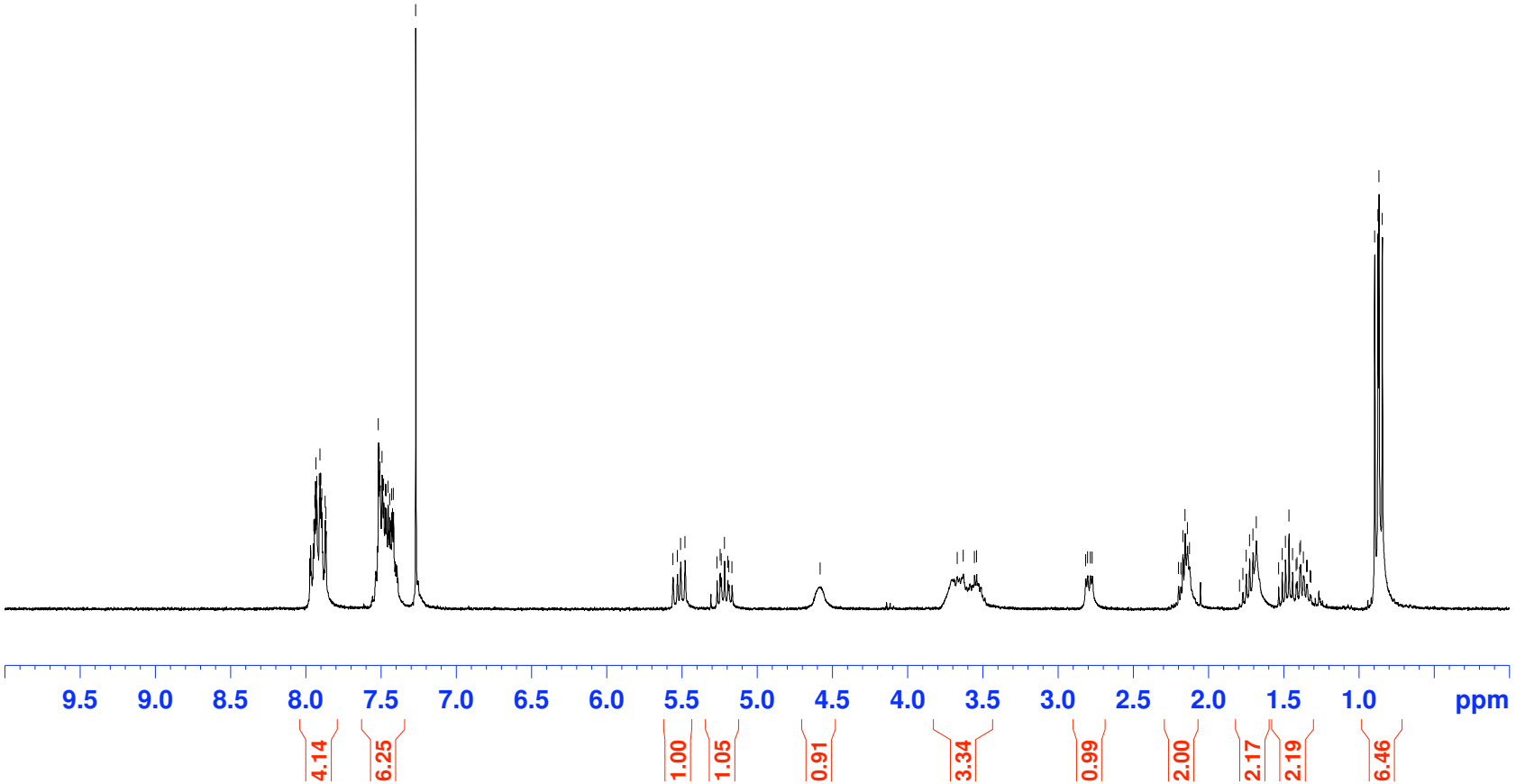
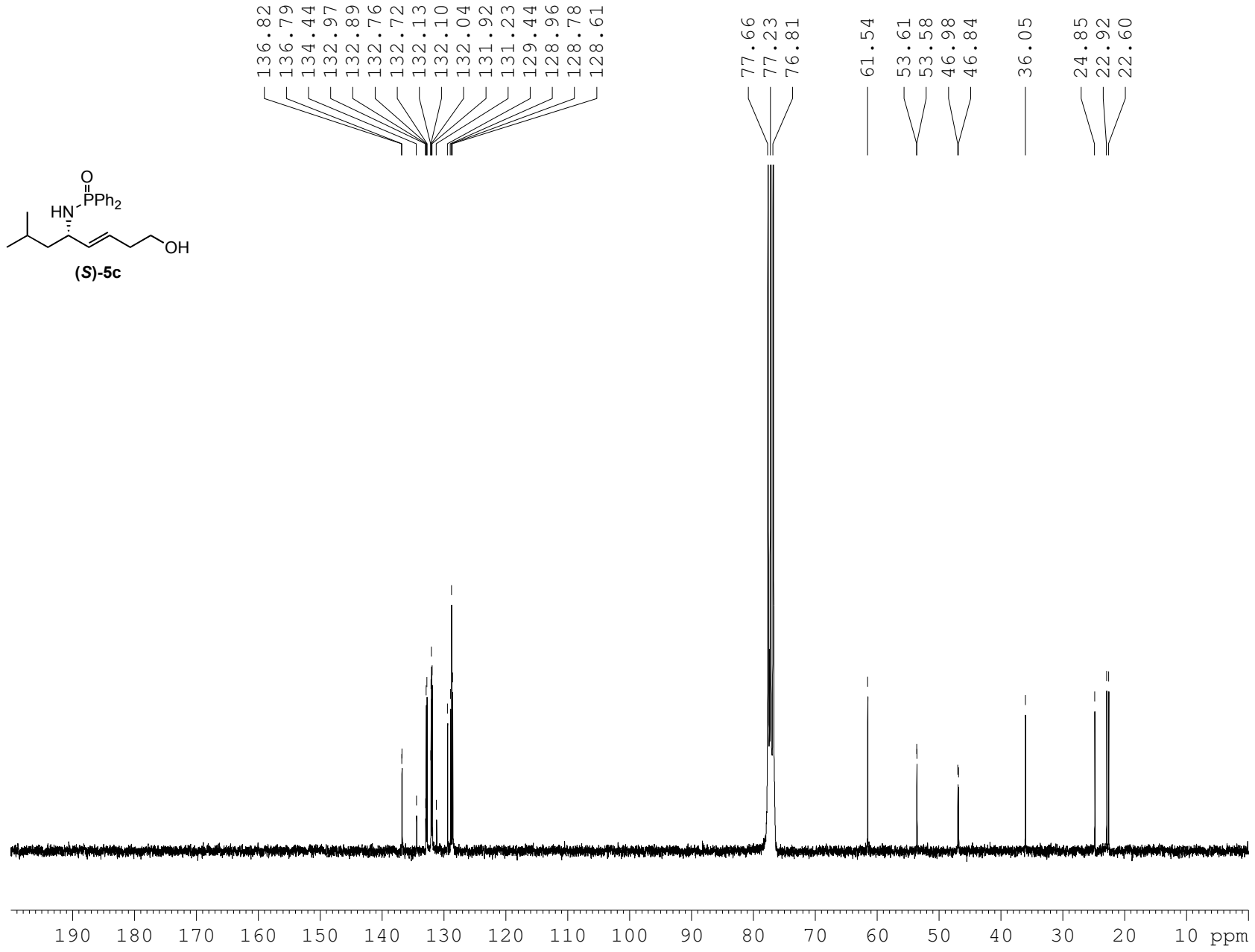
136.72
134.29
128.72
128.31
127.49
77.65
77.23
76.81
66.85
61.83
51.67
44.73
35.83
24.86
22.78
22.64
NHCbz
OH
(S)-5b
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

7.9474
7.9405
7.9382
7.9329
7.9278
7.9111
7.9063
7.9002
7.8942
7.8721
7.8667
7.5188
7.5122
7.5074
7.4939
7.4836
7.4720
7.4665
7.4541
7.4432
7.4360
7.4298
7.4241
7.4189
7.2703
5.5310
5.5096
5.4804
5.2466
5.2179
3.6309
3.5566
3.5424
2.8043
2.7860
2.7739
2.1709
2.1569
2.1408
2.1270
1.7501
1.7279
1.7053
1.6831
1.5108
1.4895
1.4660
1.4420
1.3943
1.3888
1.3700
0.8965
0.8745
0.8679
0.8459



(*S*)-5c

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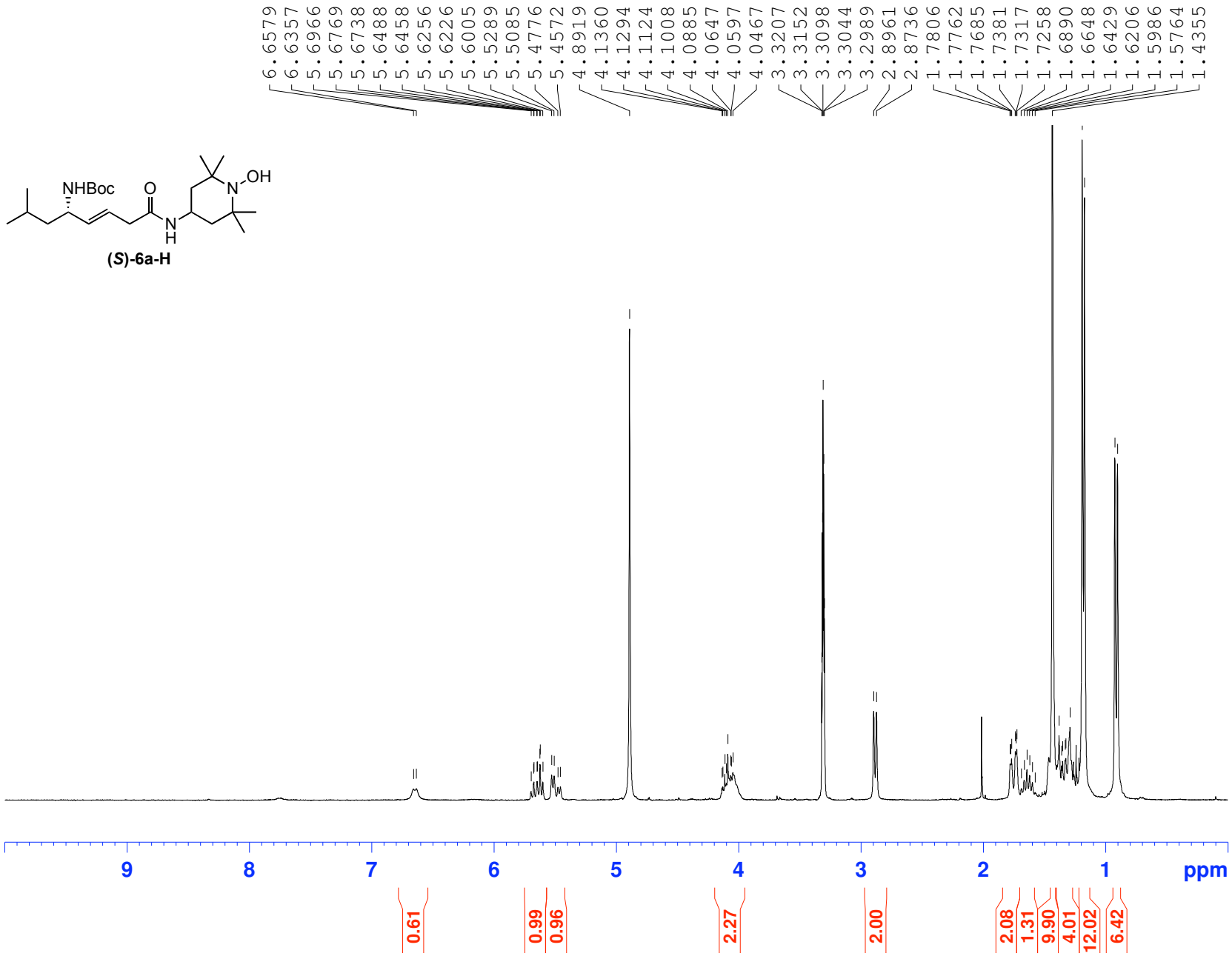
136.79
134.44
132.97
132.89
132.76
132.72
132.13
132.10
132.04
131.92
131.23
129.44
128.96
128.78
128.61
77.66
77.23
76.81
61.54
53.61
53.58
46.98
46.84
36.05
24.85
22.92
22.60
O
PPh2
HN
OH
(S)-5c
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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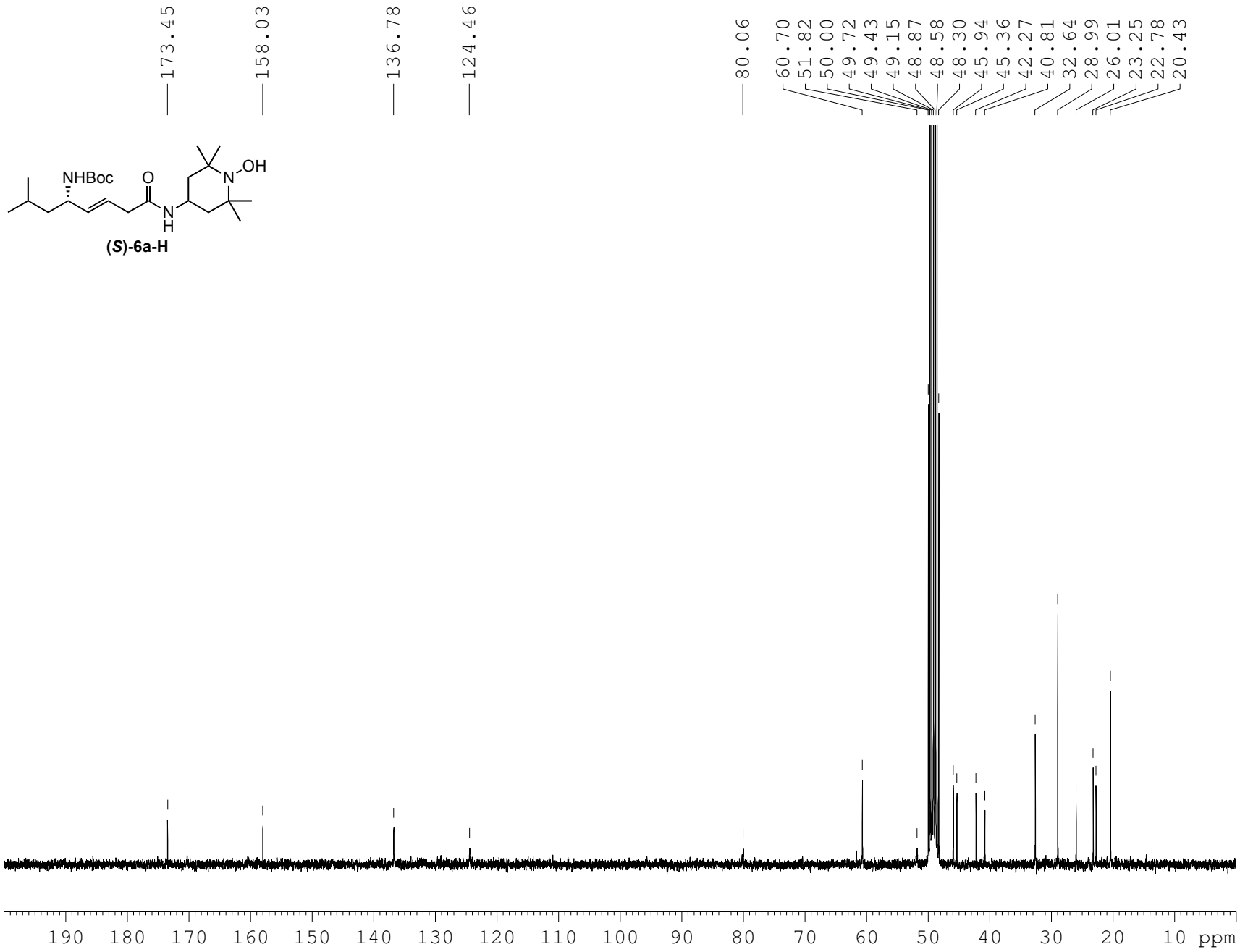
6.6357
5.6966
5.6769
5.6738
5.6488
5.6458
5.6256
5.6226
5.6005
5.5289
5.5085
5.4776
5.4572
4.8919
4.1360
4.1294
4.1124
4.1008
4.0885
4.0647
4.0597
4.0467
3.3207
3.3152
3.3098
3.3044
3.2989
2.8961
2.8736
1.7806
1.7762
1.7685
1.7381
1.7317
1.7258
1.6890
1.6648
1.6429
1.6206
1.5986
1.5764
1.4355
NHBoc
O
N
OH
N
H
(S)-6a-H
9
8
7
6
5
4
3
2
1
ppm
0.61
0.99
0.96
2.27
2.00
2.08
1.31
9.90
4.01
12.02
6.42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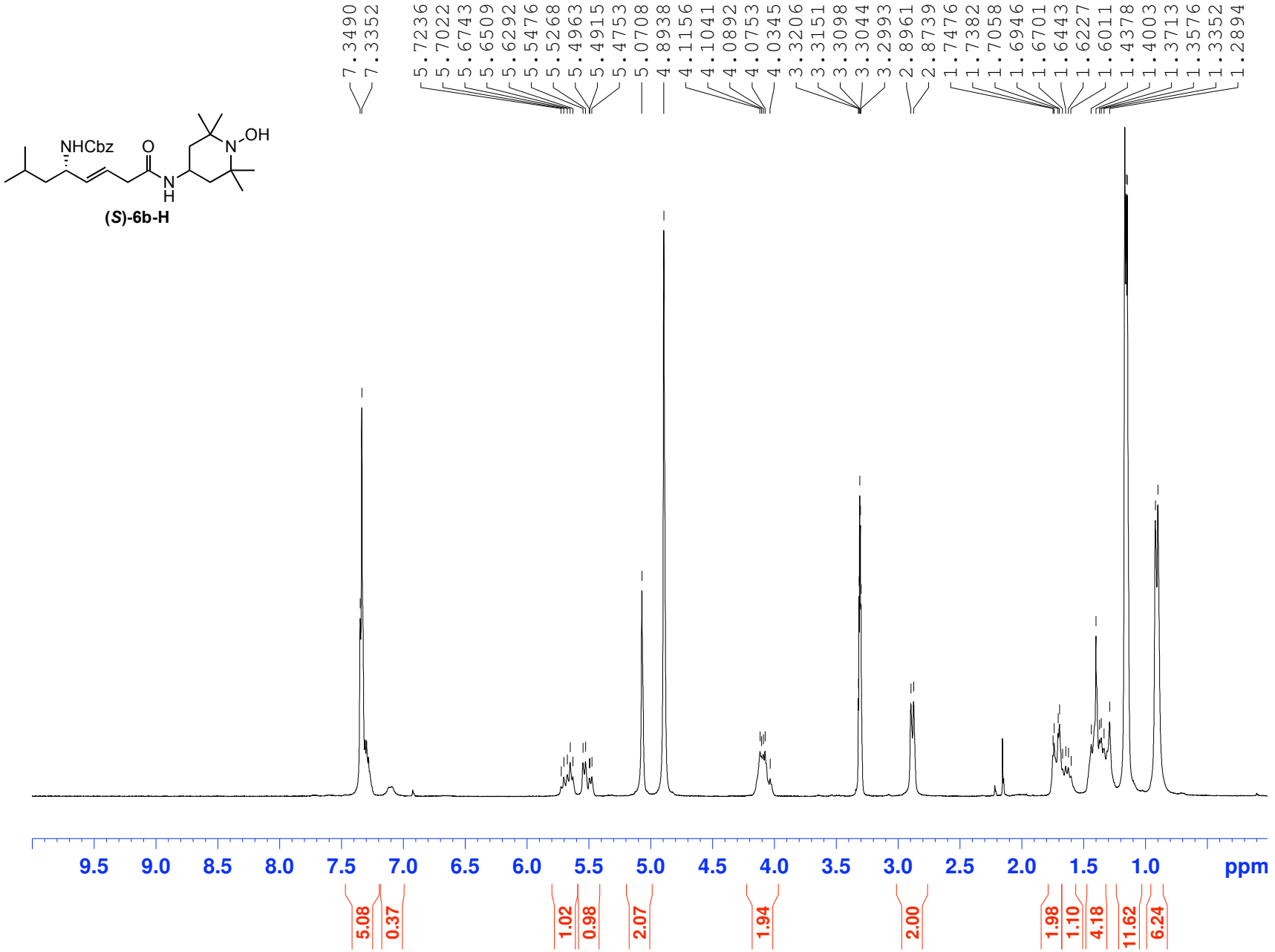
158.03
136.78
124.46
80.06
60.70
51.82
50.00
49.72
49.43
49.15
48.87
48.58
48.30
45.94
45.36
42.27
40.81
32.64
28.99
26.01
23.25
22.78
20.43
NHBoc
O
N
H
N
OH
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

(*S*)-6a-H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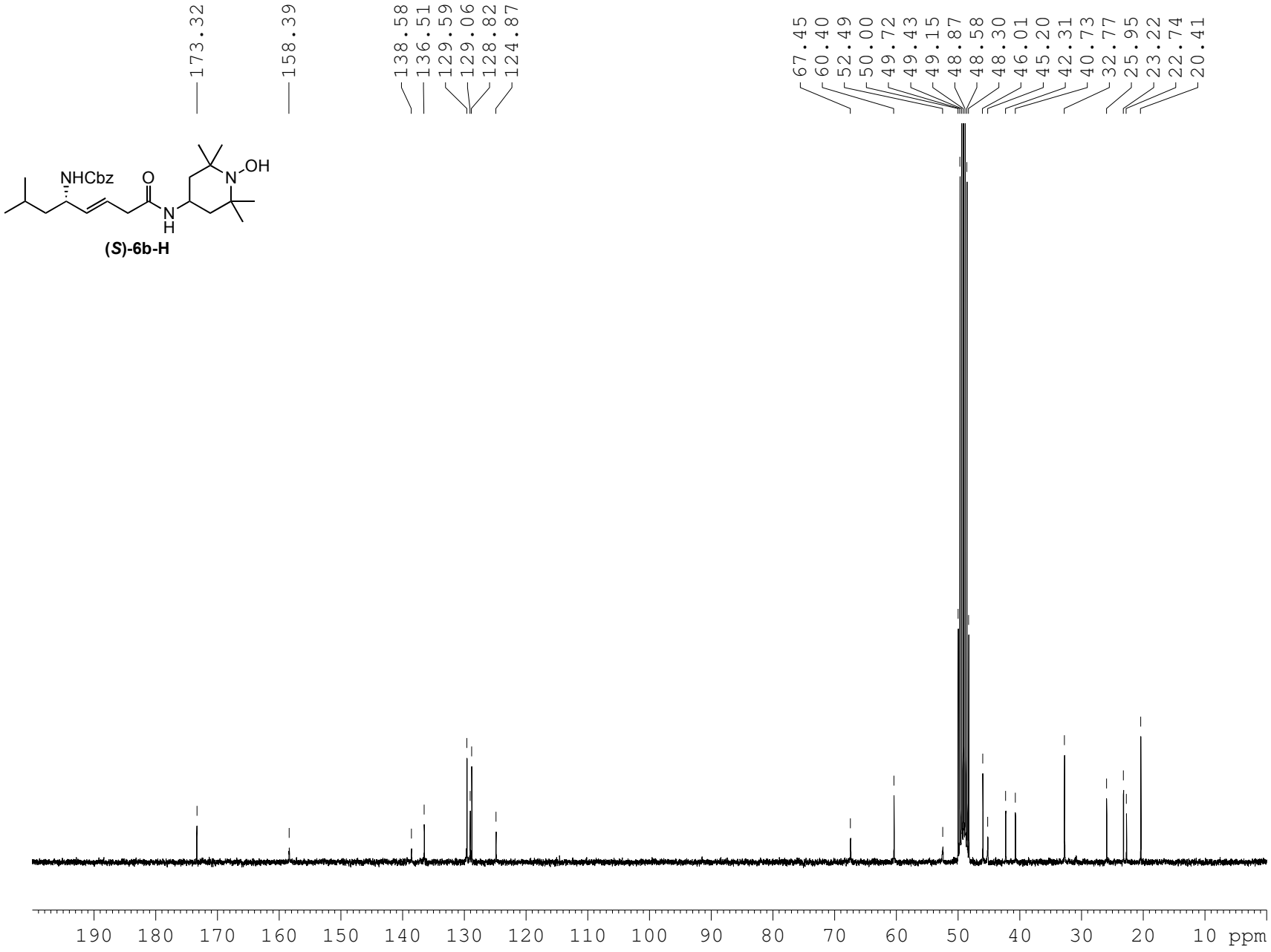
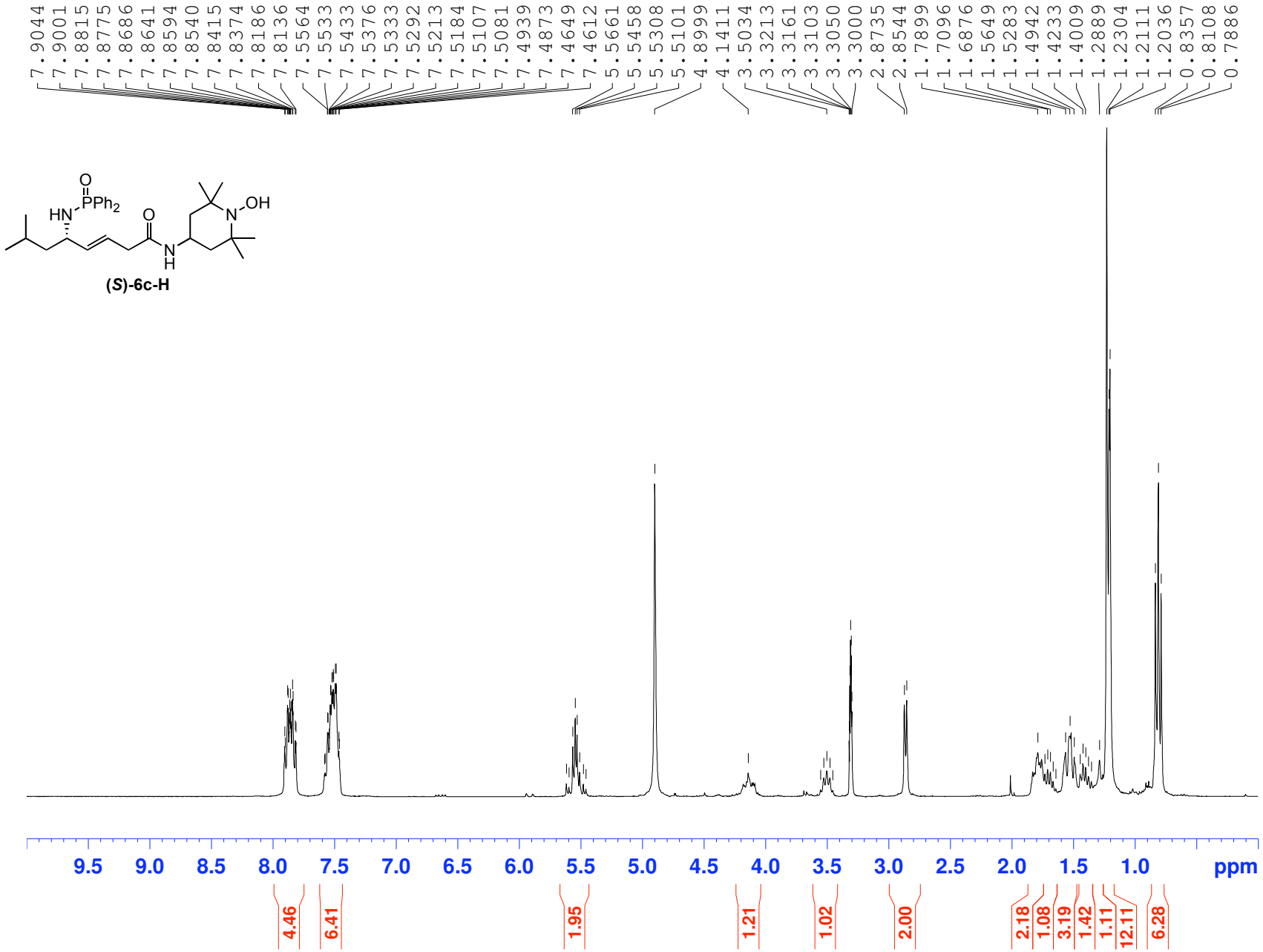
7.3352
5.7236
5.7022
5.6743
5.6509
5.6292
5.5476
5.5268
5.4963
5.4915
5.4753
5.0708
4.8938
4.1156
4.1041
4.0892
4.0753
4.0345
3.3206
3.3151
3.3098
3.3044
3.2993
2.8961
2.8739
1.7476
1.7382
1.7058
1.6946
1.6701
1.6443
1.6227
1.6011
1.4378
1.4003
1.3713
1.3576
1.3352
1.2894
NHCbz
O
N
OH
N
H
(S)-6b-H
9.5
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
ppm
5.08
0.37
1.02
0.98
2.07
1.94
2.00
1.98
1.10
4.18
11.62
6.24


173.32
158.39
138.58
136.51
129.59
129.06
128.82
124.87
67.45
60.40
52.49
50.00
49.72
49.43
49.15
48.87
48.58
48.30
46.01
45.20
42.31
40.73
32.77
25.95
23.22
22.74
20.41
NHCbz
O
N
OH
H
(S)-6b-H
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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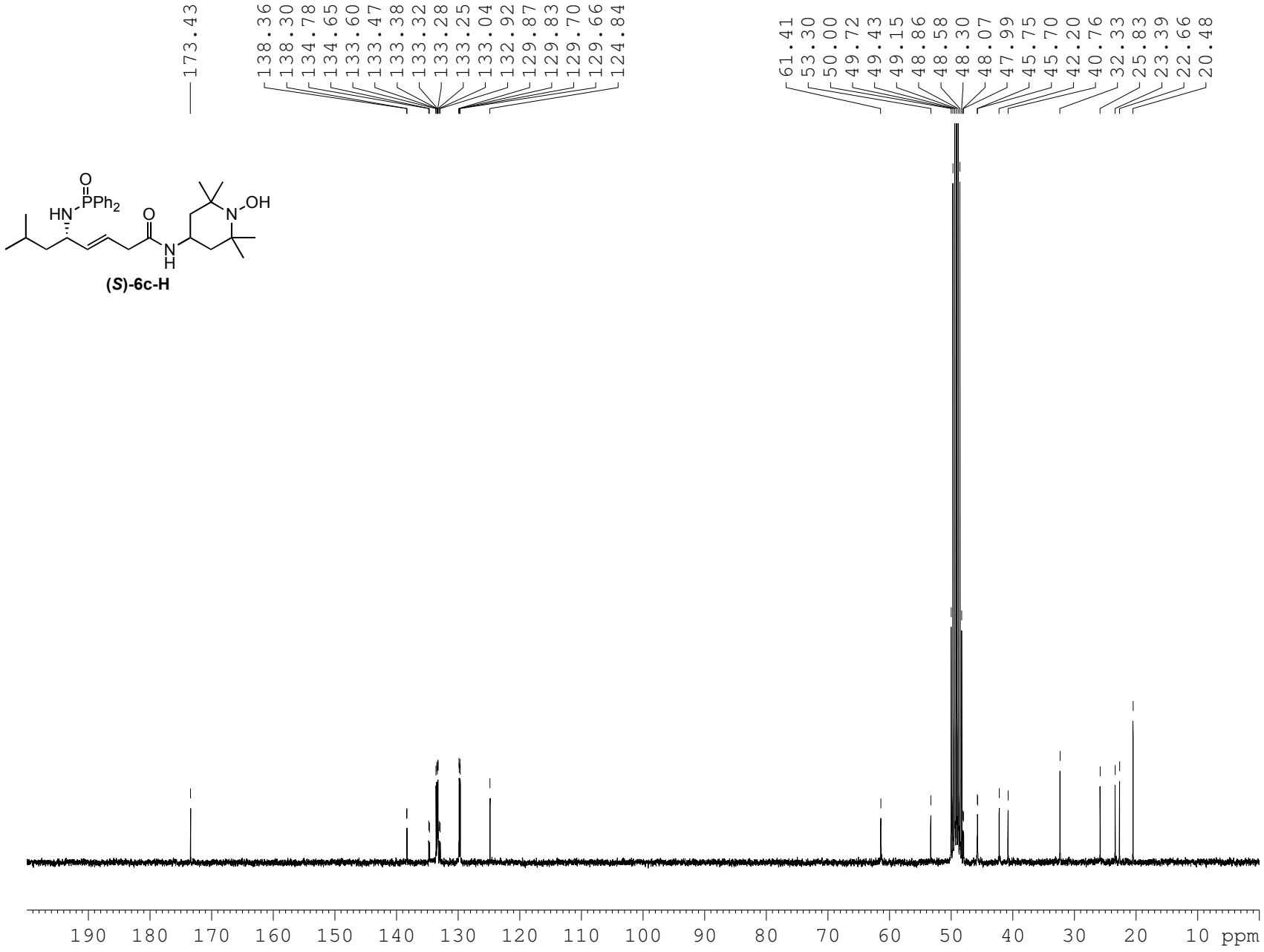
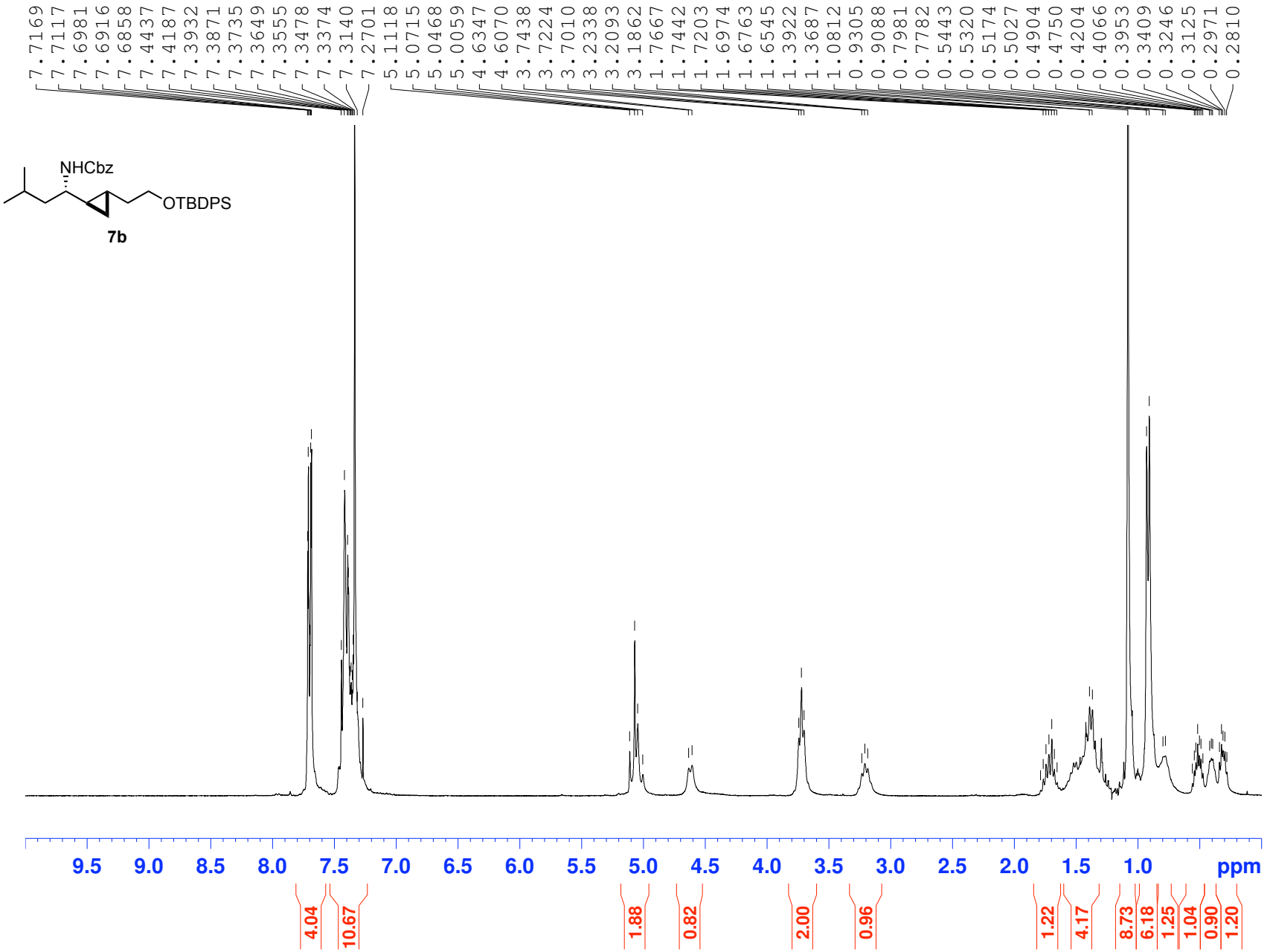
7.8815
7.8775
7.8686
7.8641
7.8594
7.8540
7.8415
7.8374
7.8186
7.8136
7.5564
7.5533
7.5433
7.5376
7.5333
7.5292
7.5213
7.5184
7.5107
7.5081
7.4939
7.4873
7.4649
7.4612
5.5661
5.5458
5.5308
5.5101
4.8999
4.1411
3.5034
3.3213
3.3161
3.3103
3.3050
3.3000
2.8735
2.8544
1.7899
1.7096
1.6876
1.5649
1.5283
1.4942
1.4233
1.4009
1.2889
1.2304
1.2111
1.2036
0.8357
0.8108
0.7886
HN
O
PPh2
O
N
H
N
OH
(S)-6c-H
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
ppm
4.46
6.41
1.95
1.21
1.02
2.00
2.18
1.08
3.19
1.42
1.11
12.11
6.28


173.43
138.36
138.30
134.78
134.65
133.60
133.47
133.38
133.32
133.28
133.25
133.04
132.92
129.87
129.83
129.70
129.66
124.84
61.41
53.30
50.00
49.72
49.43
49.15
48.86
48.58
48.30
48.07
47.99
45.75
45.70
42.20
40.76
32.33
25.83
23.39
22.66
20.48
O
PPh2
HN
O
N
H
N
OH
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

(*S*)-6c-H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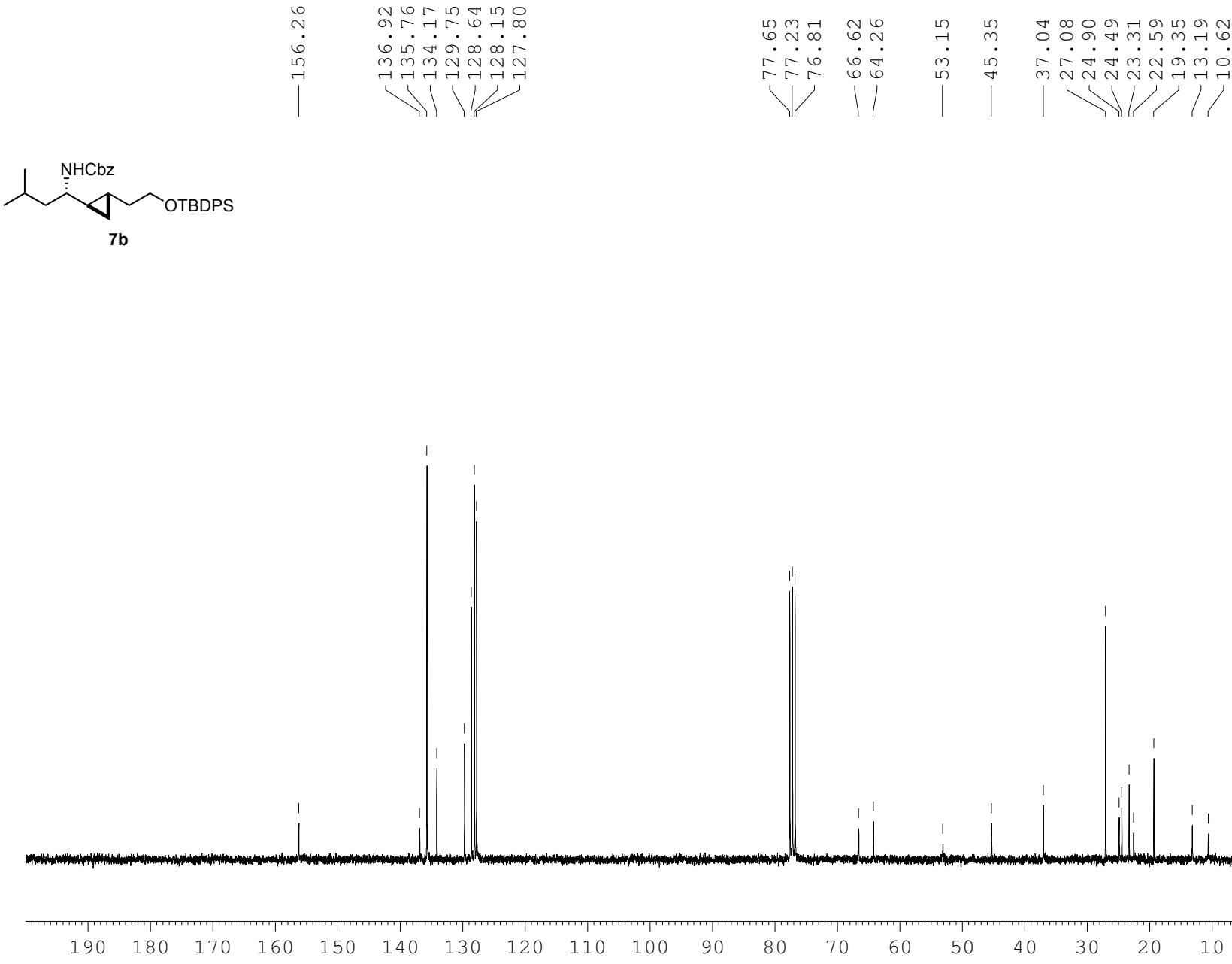
7.6981
7.6916
7.6858
7.4437
7.4187
7.3932
7.3871
7.3735
7.3649
7.3555
7.3478
7.3374
7.3140
7.2701
5.1118
5.0715
5.0468
5.0059
4.6347
4.6070
3.7438
3.7224
3.7010
3.2338
3.2093
3.1862
1.7667
1.7442
1.7203
1.6974
1.6763
1.6545
1.3922
1.3687
1.0812
0.9305
0.9088
0.7981
0.7782
0.5443
0.5320
0.5174
0.5027
0.4904
0.4750
0.4204
0.4066
0.3953
0.3409
0.3246
0.3125
0.2971
0.2810
NHCbz
OTBDPS
7b
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
ppm
4.04
10.67
1.88
0.82
2.00
0.96
1.22
4.17
8.73
6.18
1.25
1.04
0.90
1.20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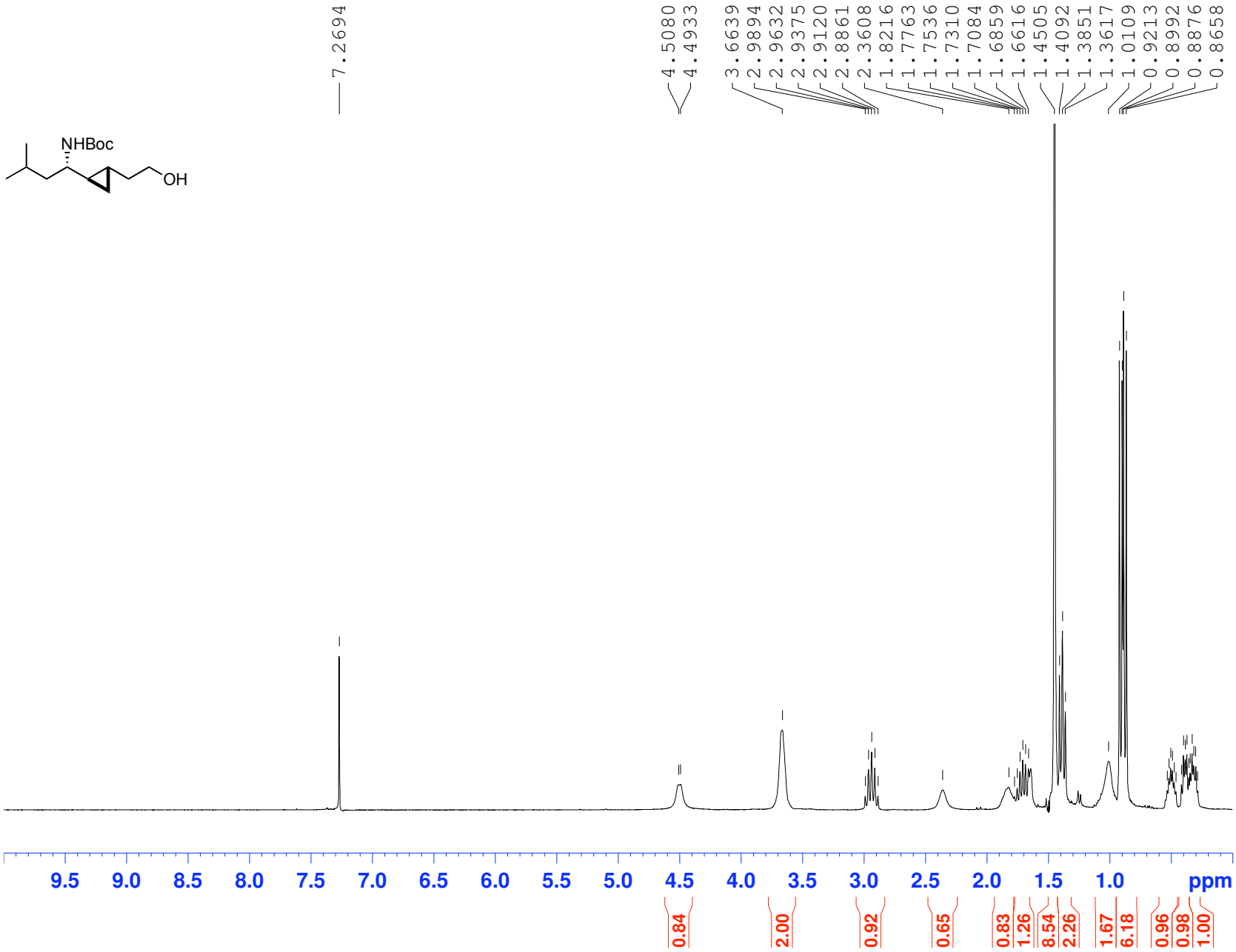
136.92
135.76
134.17
129.75
128.64
128.15
127.80
77.65
77.23
76.81
66.62
64.26
53.15
45.35
37.04
27.08
24.90
24.49
23.31
22.59
19.35
13.19
10.62
NHCbz
OTBDPS
7b
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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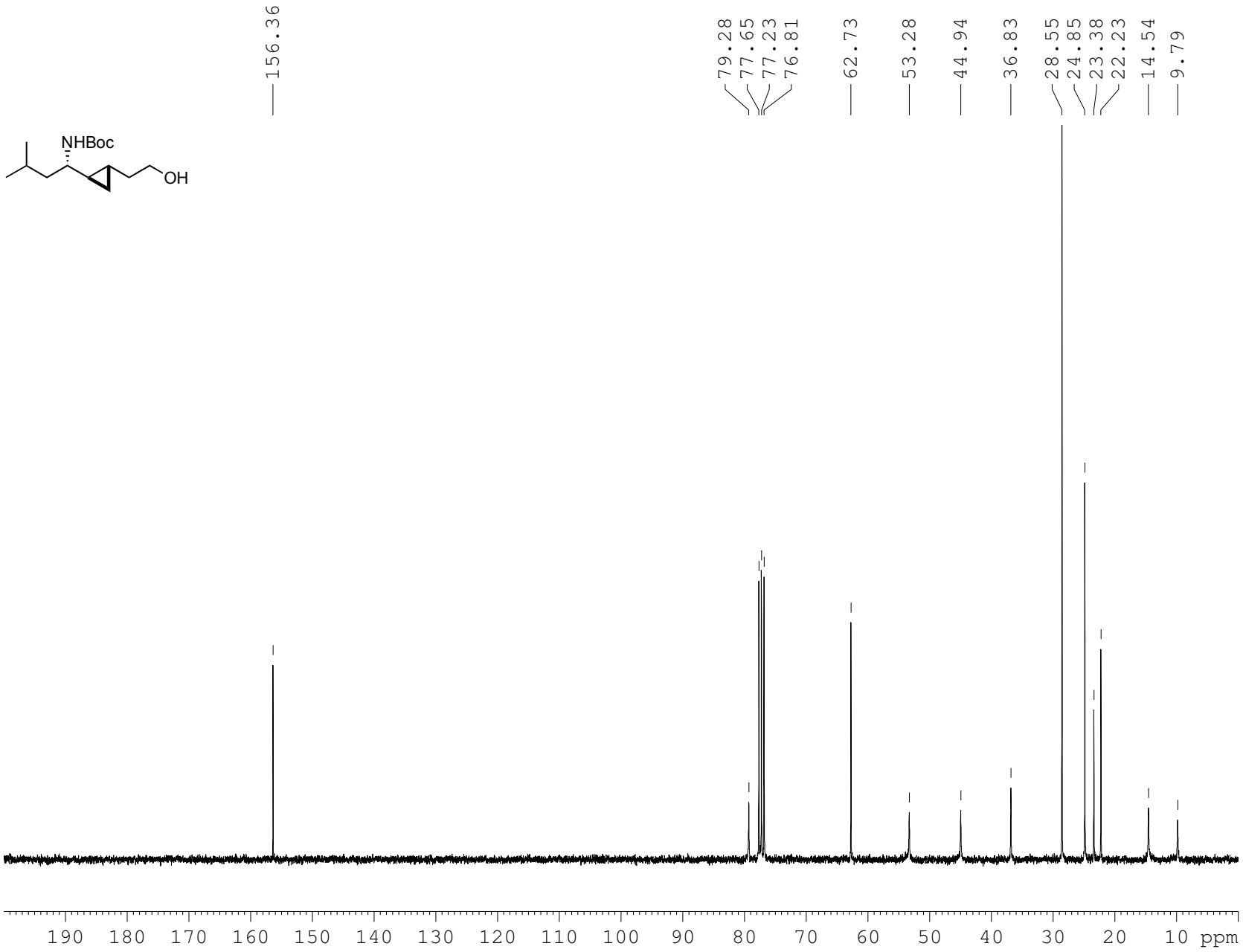
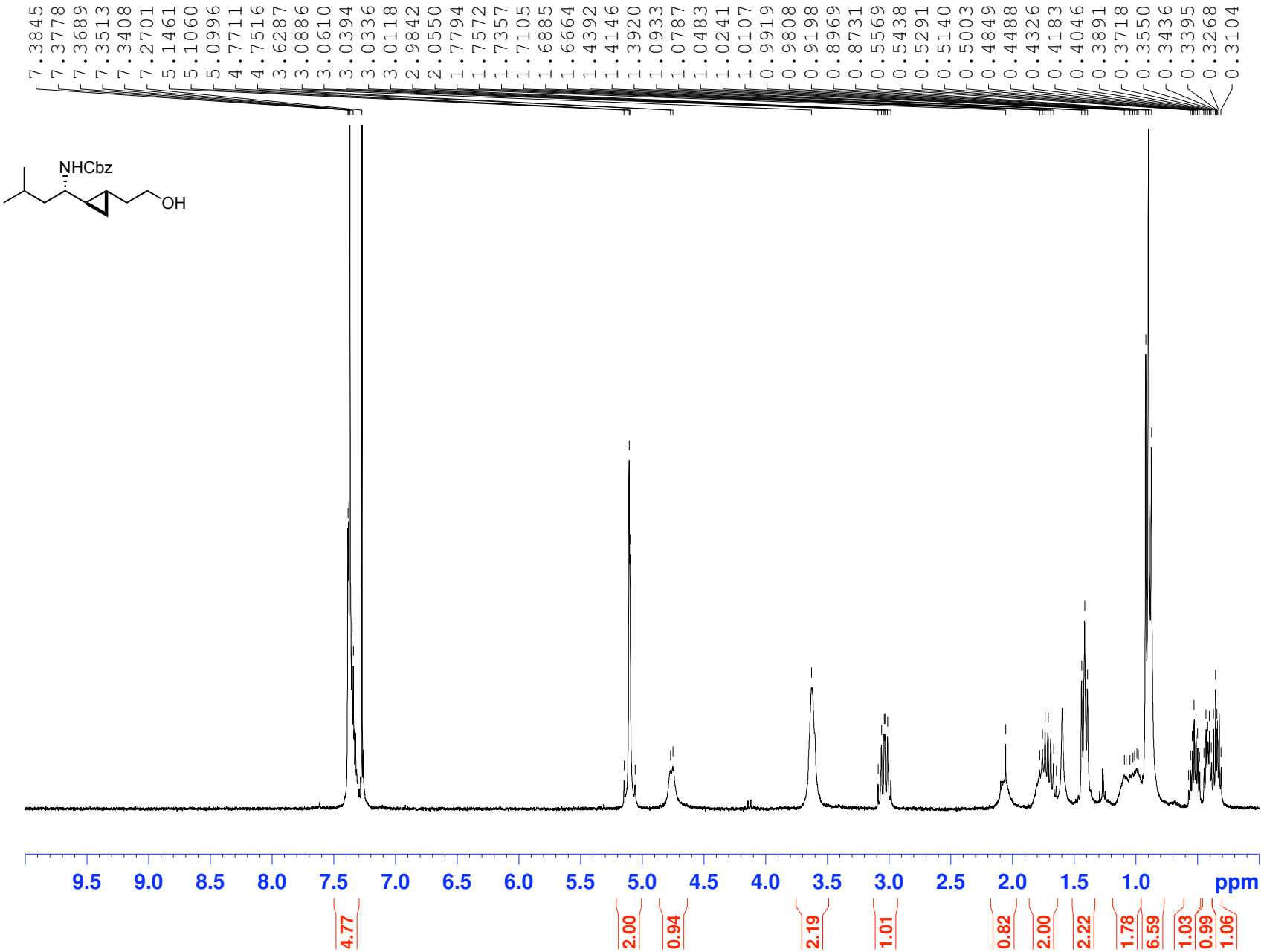
4.5080
4.4933
3.6639
2.9894
2.9632
2.9375
2.9120
2.8861
2.3608
1.8216
1.7763
1.7536
1.7310
1.7084
1.6859
1.6616
1.4505
1.4092
1.3851
1.3617
1.0109
0.9213
0.8992
0.8876
0.8658
NHBoc
OH
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.84
2.00
0.92
0.65
0.83
1.26
8.54
2.26
1.67
6.18
0.96
0.98
1.00


156.36
79.28
77.65
77.23
76.81
62.73
53.28
44.94
36.83
28.55
24.85
23.38
22.23
14.54
9.79
NHBoc
OH
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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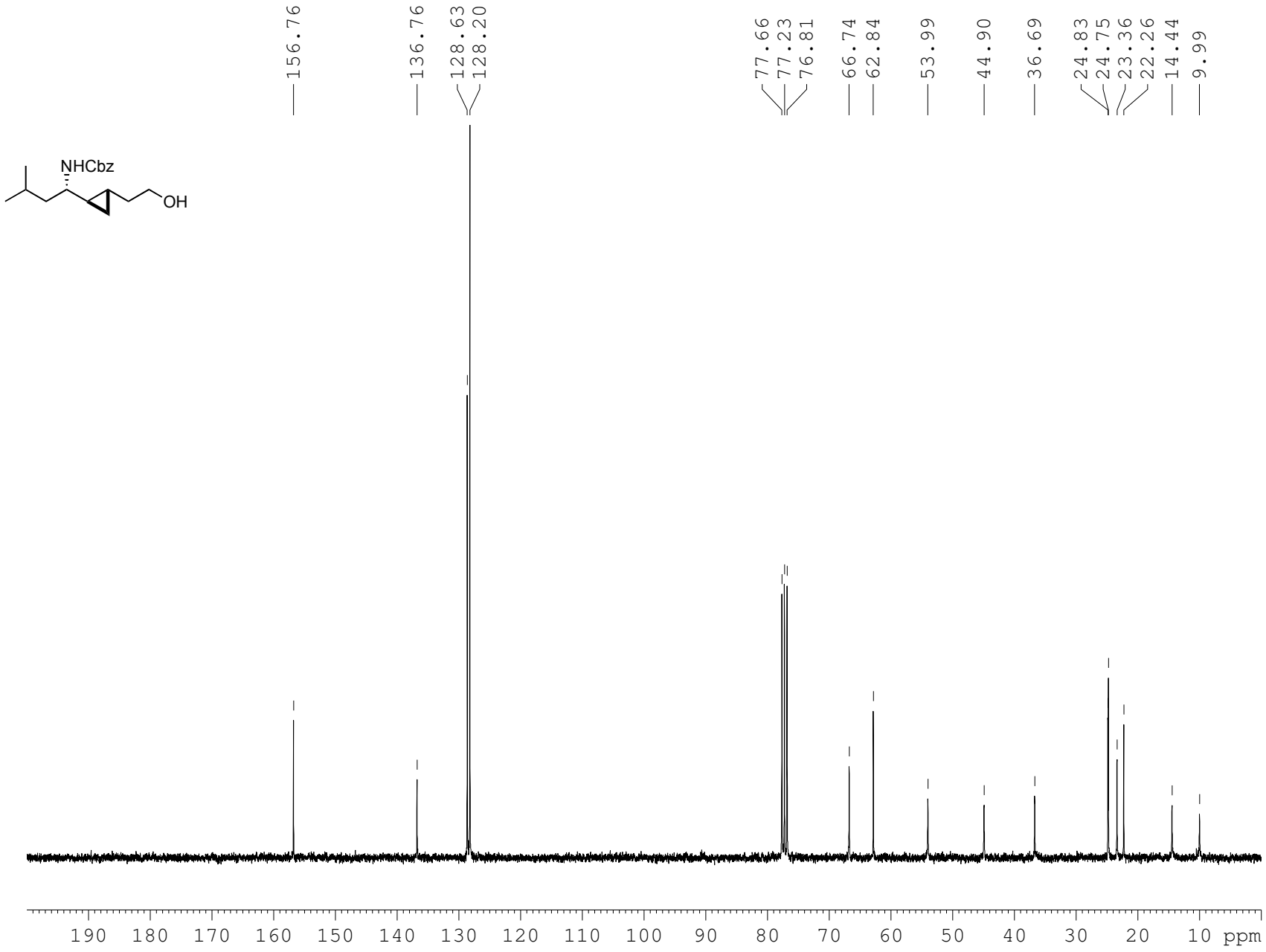
7.3778
7.3689
7.3513
7.3408
7.2701
5.1461
5.1060
5.0996
4.7711
4.7516
3.6287
3.0886
3.0610
3.0394
3.0336
3.0118
2.9842
2.0550
1.7794
1.7572
1.7357
1.7105
1.6885
1.6664
1.4392
1.4146
1.3920
1.0933
1.0787
1.0483
1.0241
1.0107
0.9919
0.9808
0.9198
0.8969
0.8731
0.5569
0.5438
0.5291
0.5140
0.5003
0.4849
0.4488
0.4326
0.4183
0.4046
0.3891
0.3718
0.3550
0.3436
0.3395
0.3268
0.3104
NHCbz
OH
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
ppm
4.77
2.00
0.94
2.19
1.01
0.82
2.00
2.22
1.78
6.59
1.03
0.99
1.06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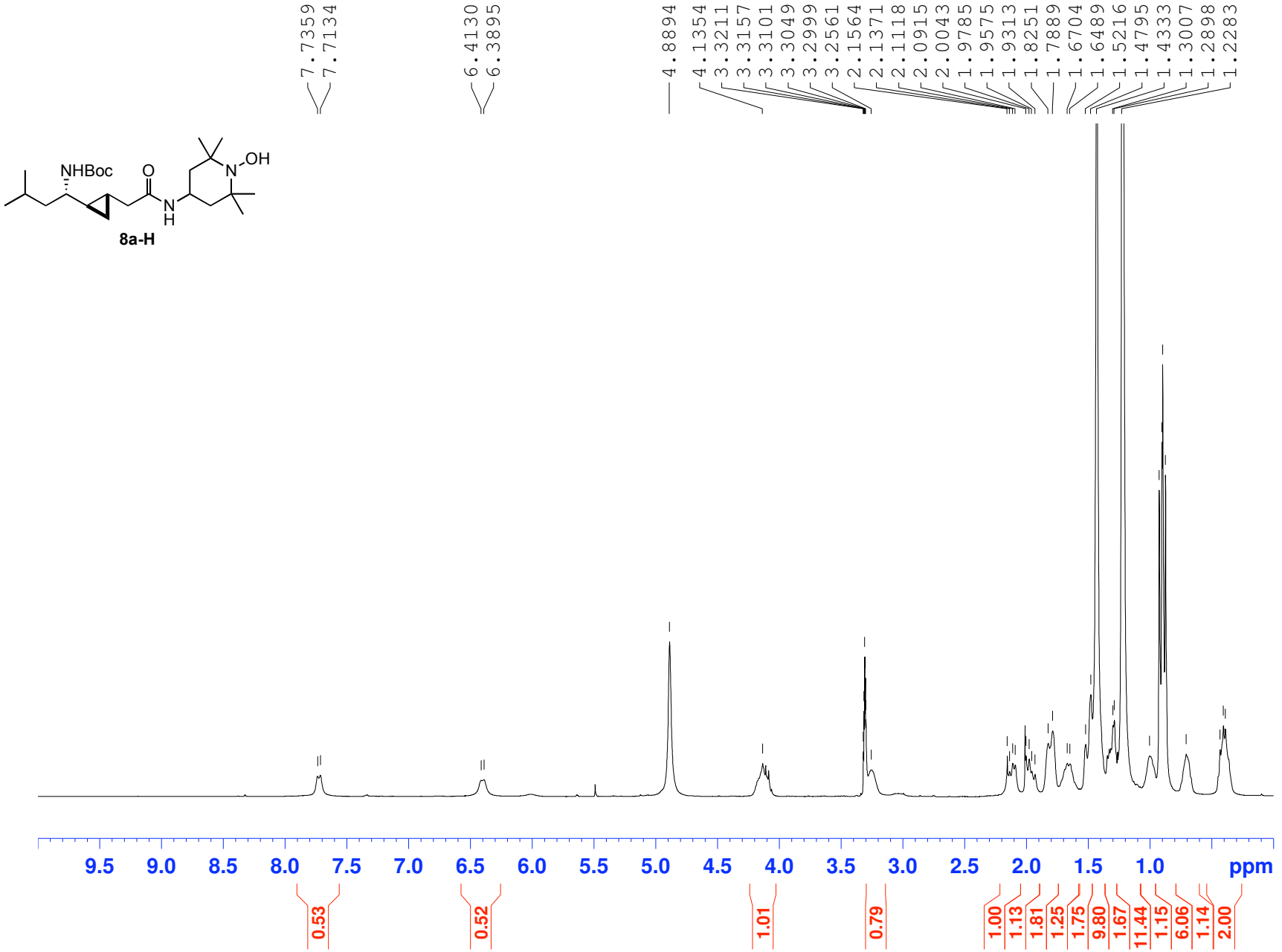
136.76
128.63
128.20
77.66
77.23
76.81
66.74
62.84
53.99
44.90
36.69
24.83
24.75
23.36
22.26
14.44
9.99
NHCbz
OH
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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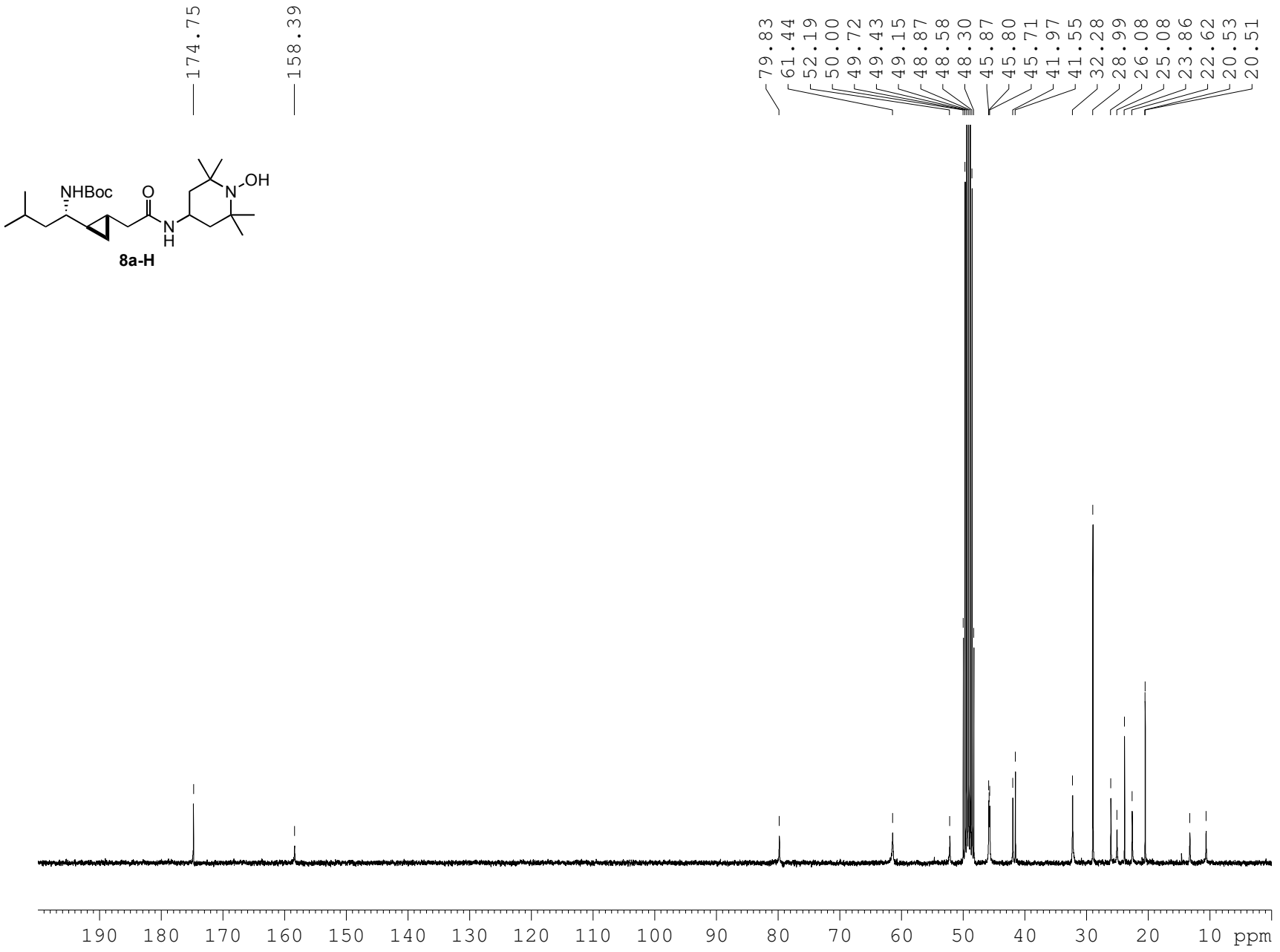
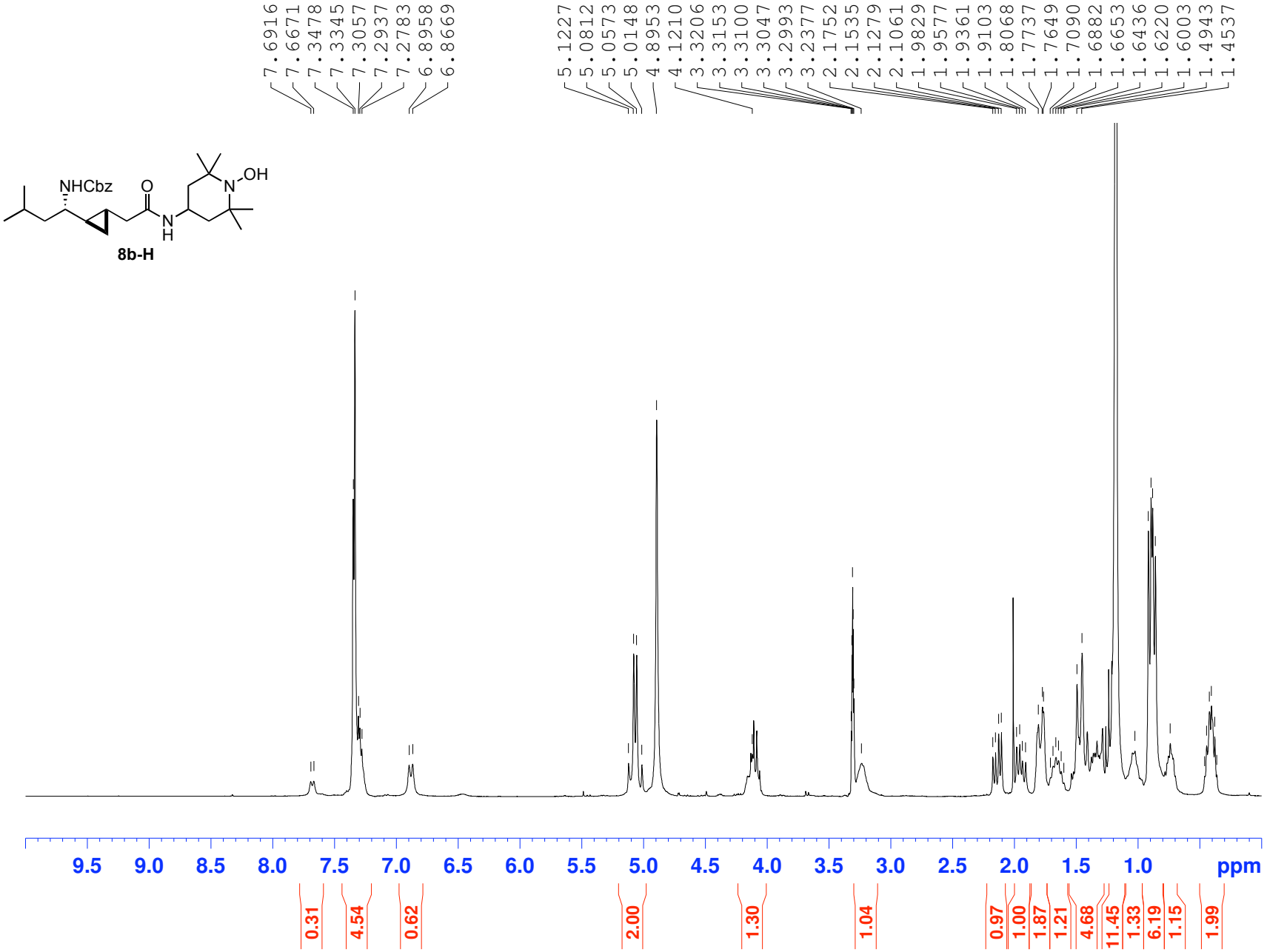
7.7134
6.4130
6.3895
4.8894
4.1354
3.3211
3.3157
3.3101
3.3049
3.2999
3.2561
2.1564
2.1371
2.1118
2.0915
2.0043
1.9785
1.9575
1.9313
1.8251
1.7889
1.6704
1.6489
1.5216
1.4795
1.4333
1.3007
1.2898
1.2283
NHBoc
O
N
OH
N
H
8a-H
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.53
0.52
1.01
0.79
1.00
1.13
1.81
1.25
1.75
9.80
1.67
11.44
1.15
6.06
1.14
2.00


174.75
158.39
79.83
61.44
52.19
50.00
49.72
49.43
49.15
48.87
48.58
48.30
45.87
45.80
45.71
41.97
41.55
32.28
28.99
26.08
25.08
23.86
22.62
20.53
20.51
NHBoc
O
N
H
N
OH
8a-H
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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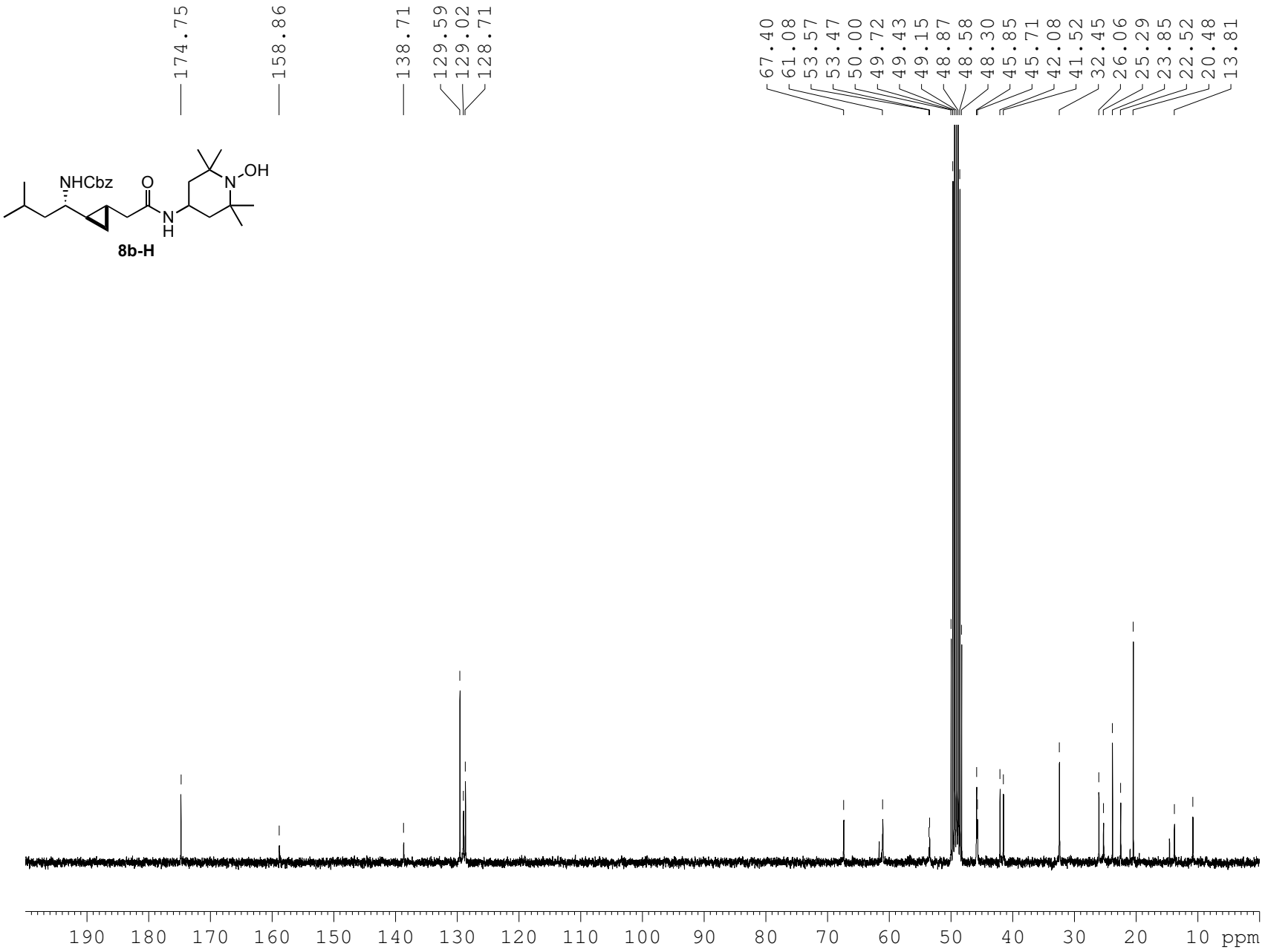
7.6671
7.3478
7.3345
7.3057
7.2937
7.2783
6.8958
6.8669
5.1227
5.0812
5.0573
5.0148
4.8953
4.1210
3.3206
3.3153
3.3100
3.3047
3.2993
3.2377
2.1752
2.1535
2.1279
2.1061
1.9829
1.9577
1.9361
1.9103
1.8068
1.7737
1.7649
1.7090
1.6882
1.6653
1.6436
1.6220
1.6003
1.4943
1.4537
NHCbz
O
N
H
N
OH
8b-H
9.5
9.0
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
ppm
0.31
4.54
0.62
2.00
1.30
1.04
0.97
1.00
1.87
1.21
4.68
11.45
1.33
6.19
1.15
1.99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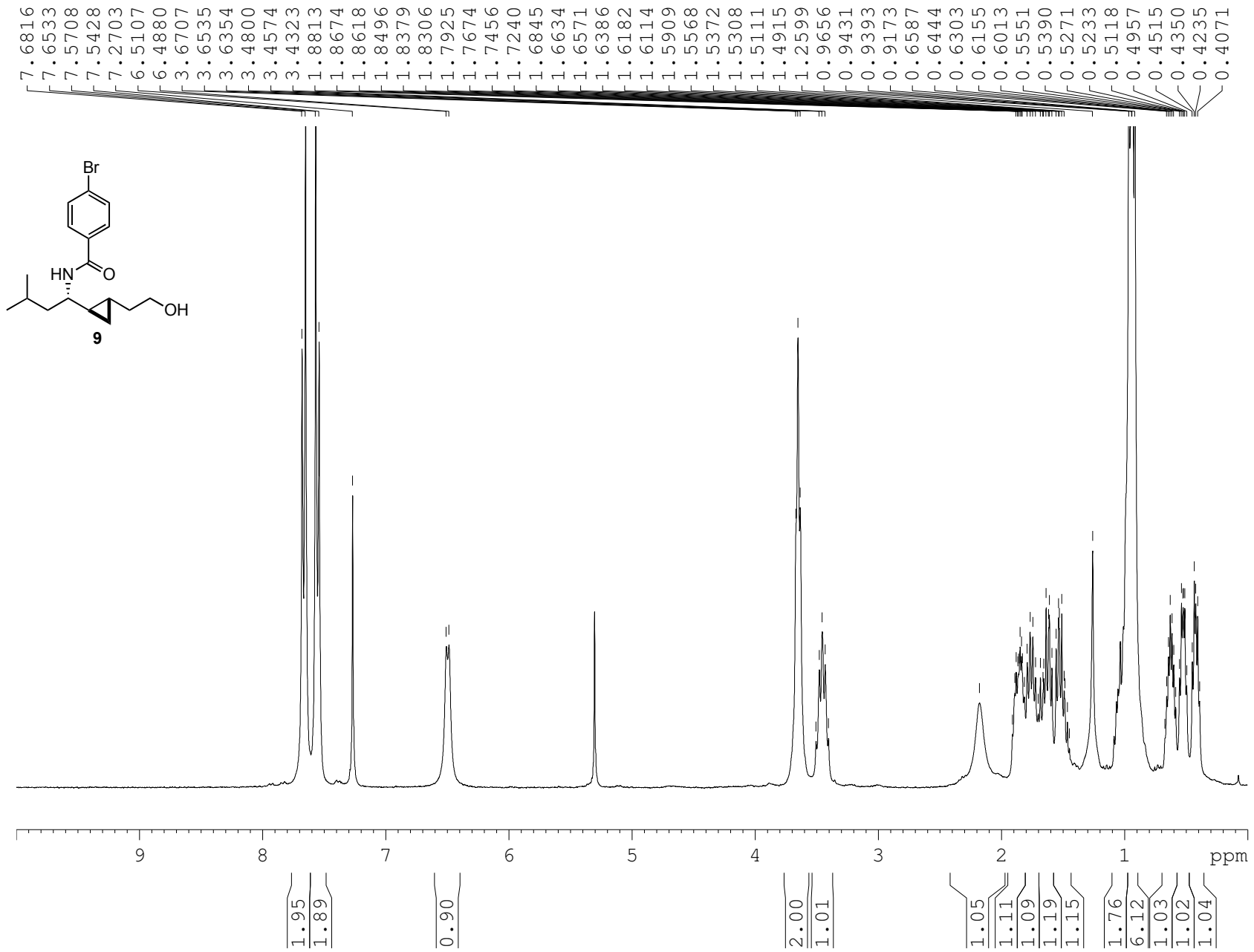
158.86
138.71
129.59
129.02
128.71
67.40
61.08
53.57
53.47
50.00
49.72
49.43
49.15
48.87
48.58
48.30
45.85
45.71
42.08
41.52
32.45
26.06
25.29
23.85
22.52
20.48
13.81
NHCbz
O
N
H
N
OH
8b-H
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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7.5708
7.5428
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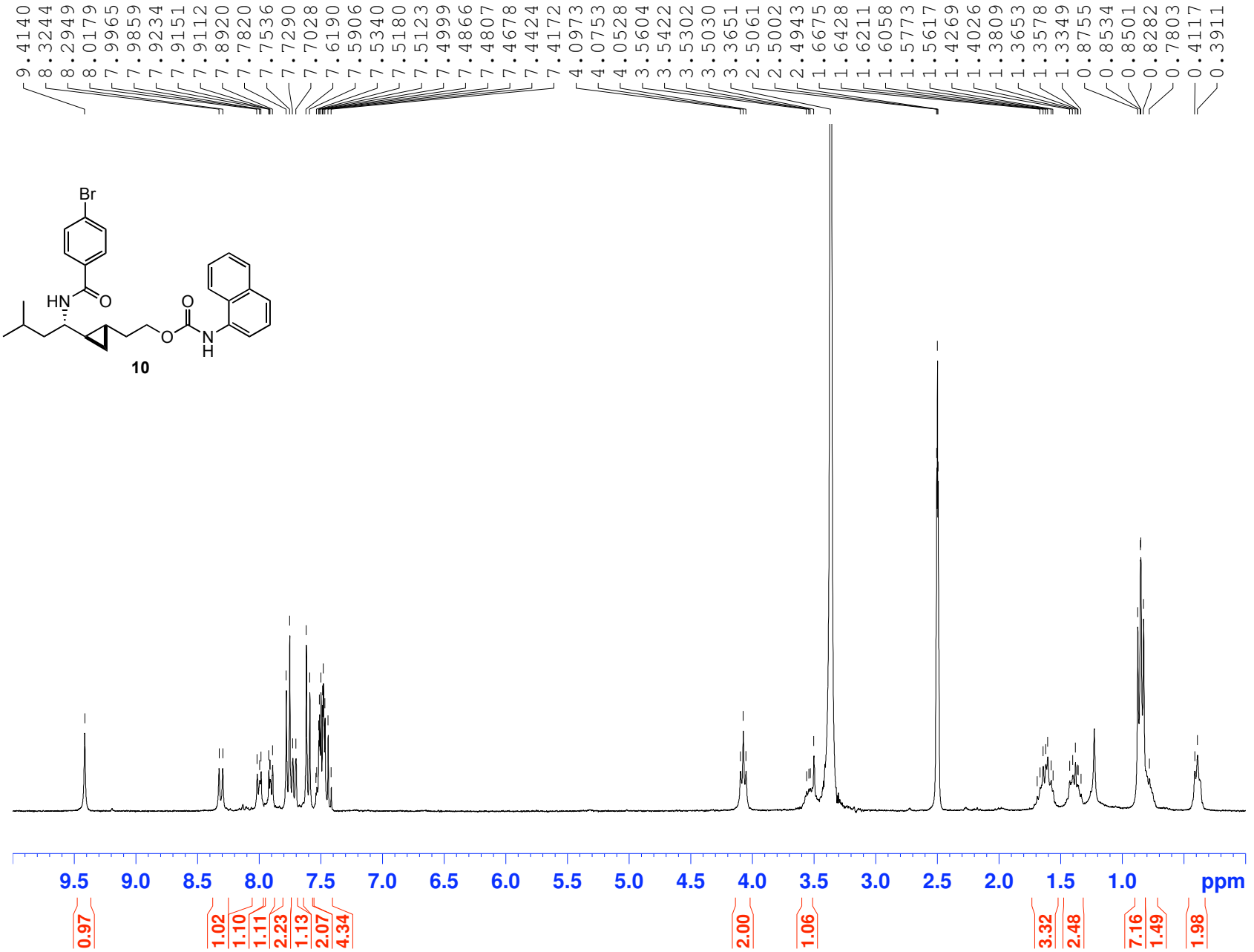
3.6707
3.6535
3.6354
3.4800
3.4574
3.4323
1.8813
1.8674
1.8618
1.8496
1.8379
1.8306
1.7925
1.7674
1.7456
1.7240
1.6845
1.6634
1.6571
1.6386
1.6182
1.6114
1.5909
1.5568
1.5372
1.5308
1.5111
1.4915
1.2599
0.9656
0.9431
0.9393
0.9173
0.6587
0.6444
0.6303
0.6155
0.6013
0.5551
0.5390
0.5271
0.5233
0.5118
0.4957
0.4515
0.4350
0.4235
0.4071
Br
HN
O
OH
9
9
8
7
6
5
4
3
2
1
ppm
1.95
1.89
0.90
2.00
1.01
1.05
1.11
1.09
1.19
1.15
1.76
6.12
1.03
1.02
1.04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8.3244
8.2949
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7.9234
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7.9112
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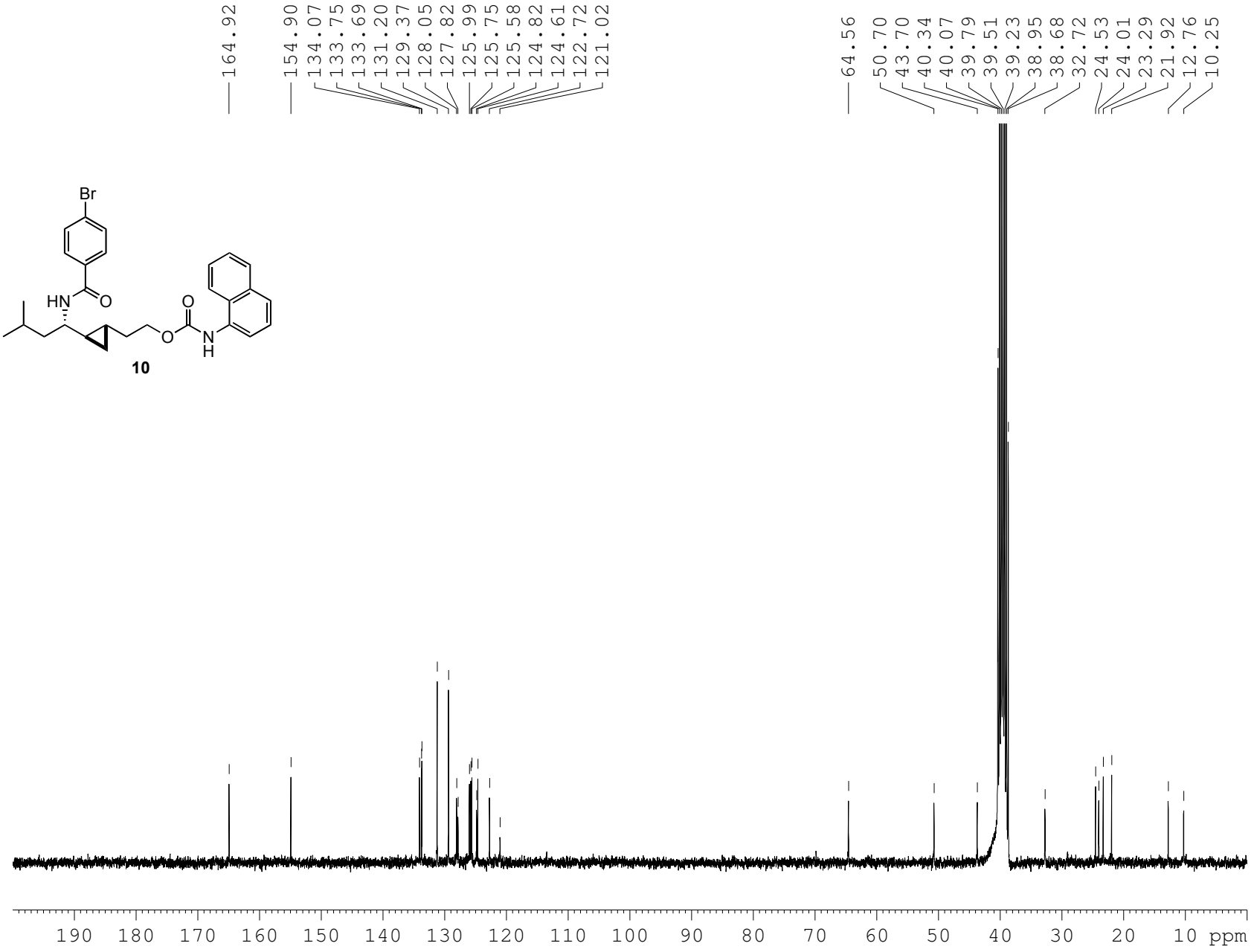
7.7820
7.7536
7.7290
7.7028
7.6190
7.5906
7.5340
7.5180
7.5123
7.4999
7.4866
7.4807
7.4678
7.4424
7.4172
4.0973
4.0753
4.0528
3.5604
3.5422
3.5302
3.5030
3.3651
2.5061
2.5002
2.4943
1.6675
1.6428
1.6211
1.6058
1.5773
1.5617
1.4269
1.4026
1.3809
1.3653
1.3578
1.3349
0.8755
0.8534
0.8501
0.8282
0.7803
0.4117
0.3911
Br
HN
O
O
O
N
H
10
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
ppm
0.97
1.02
1.10
1.11
2.23
1.13
2.07
4.34
2.00
1.06
3.32
2.48
7.16
1.49
1.98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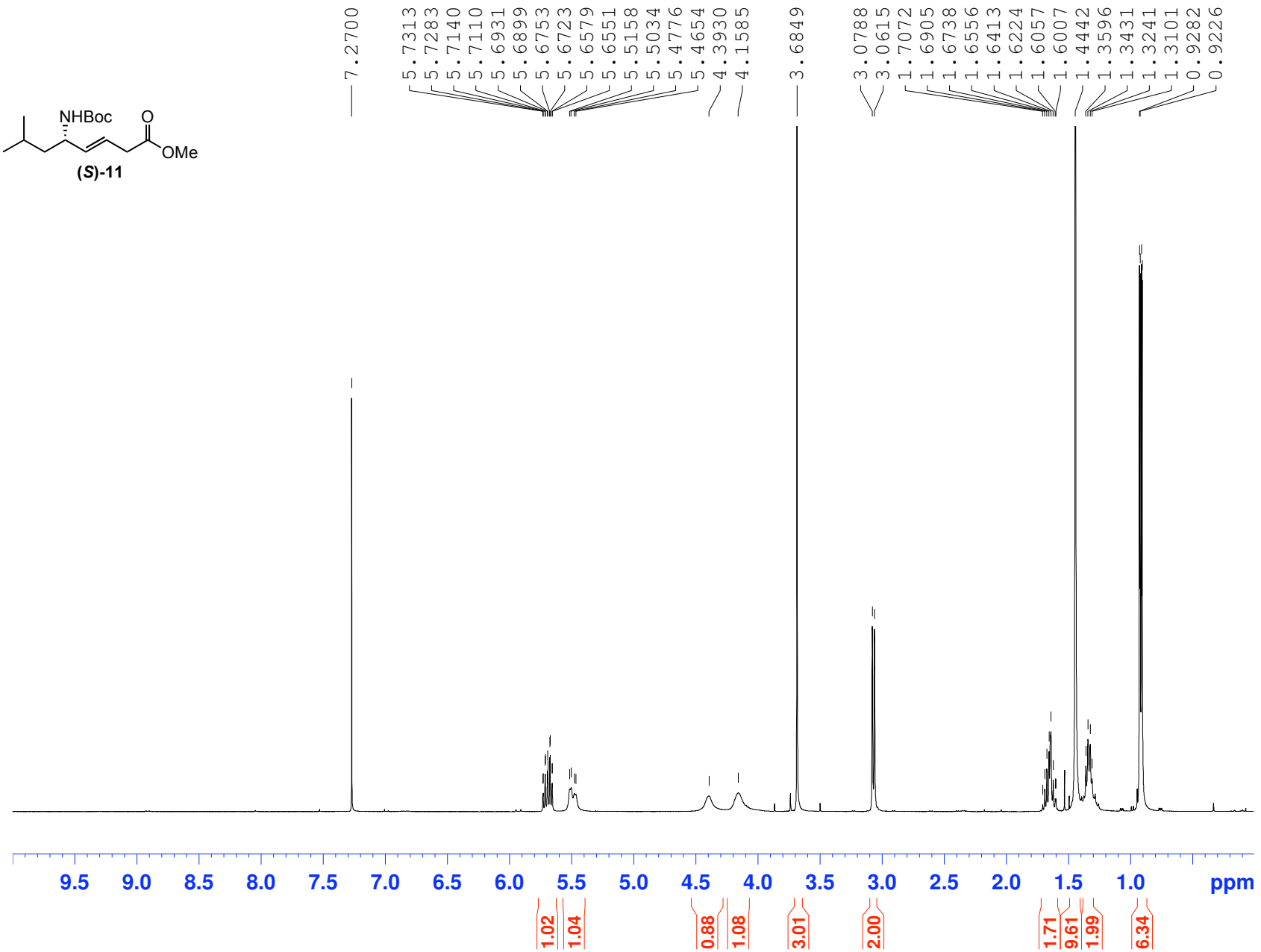
154.90
134.07
133.75
133.69
131.20
129.37
128.05
127.82
125.99
125.75
125.58
124.82
124.61
122.72
121.02
64.56
50.70
43.70
40.34
40.07
39.79
39.51
39.23
38.95
38.68
32.72
24.53
24.01
23.29
21.92
12.76
10.25
Br
HN
O
O
O
N
H
10
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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O
OMe
(S)-11
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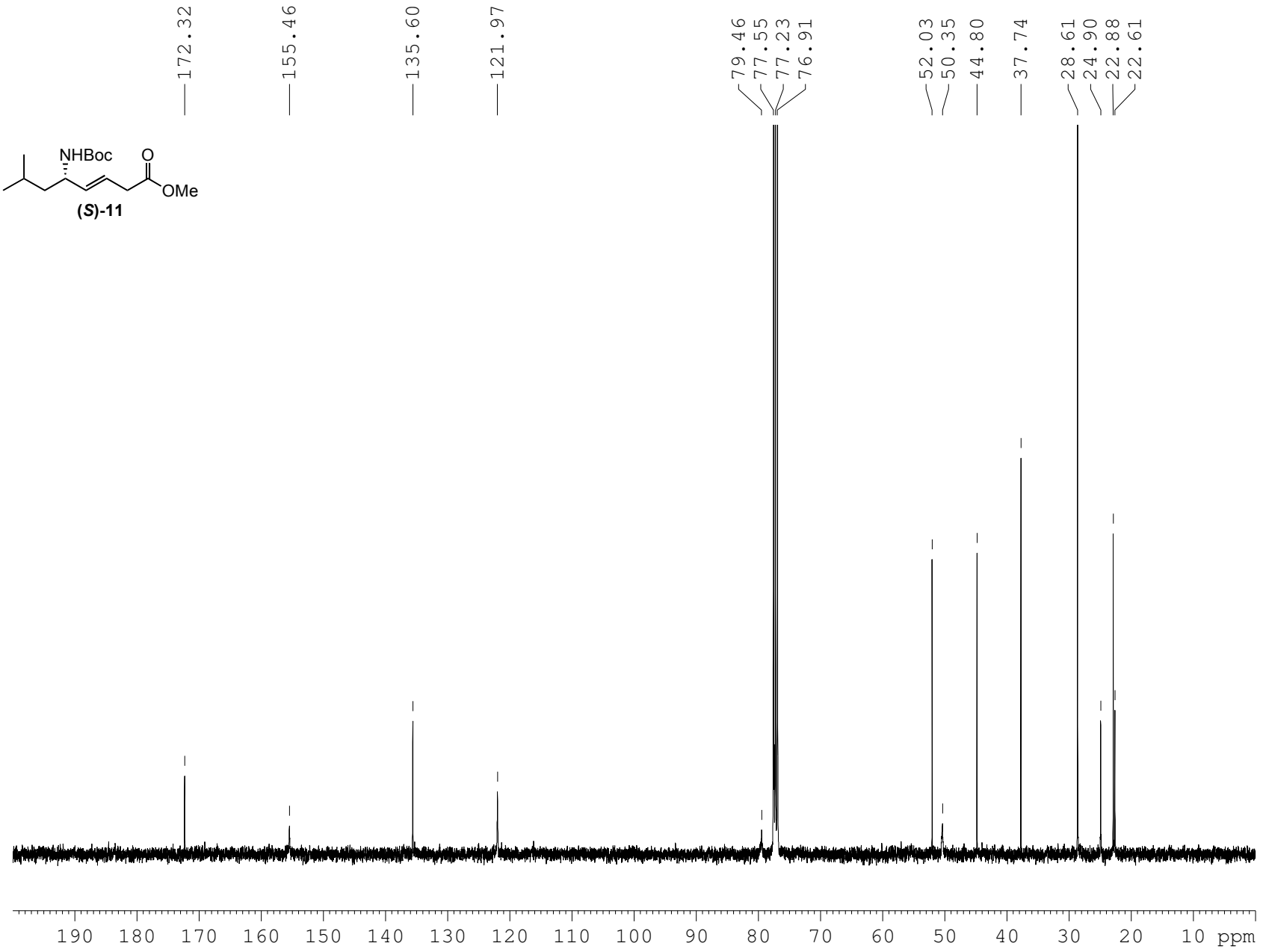
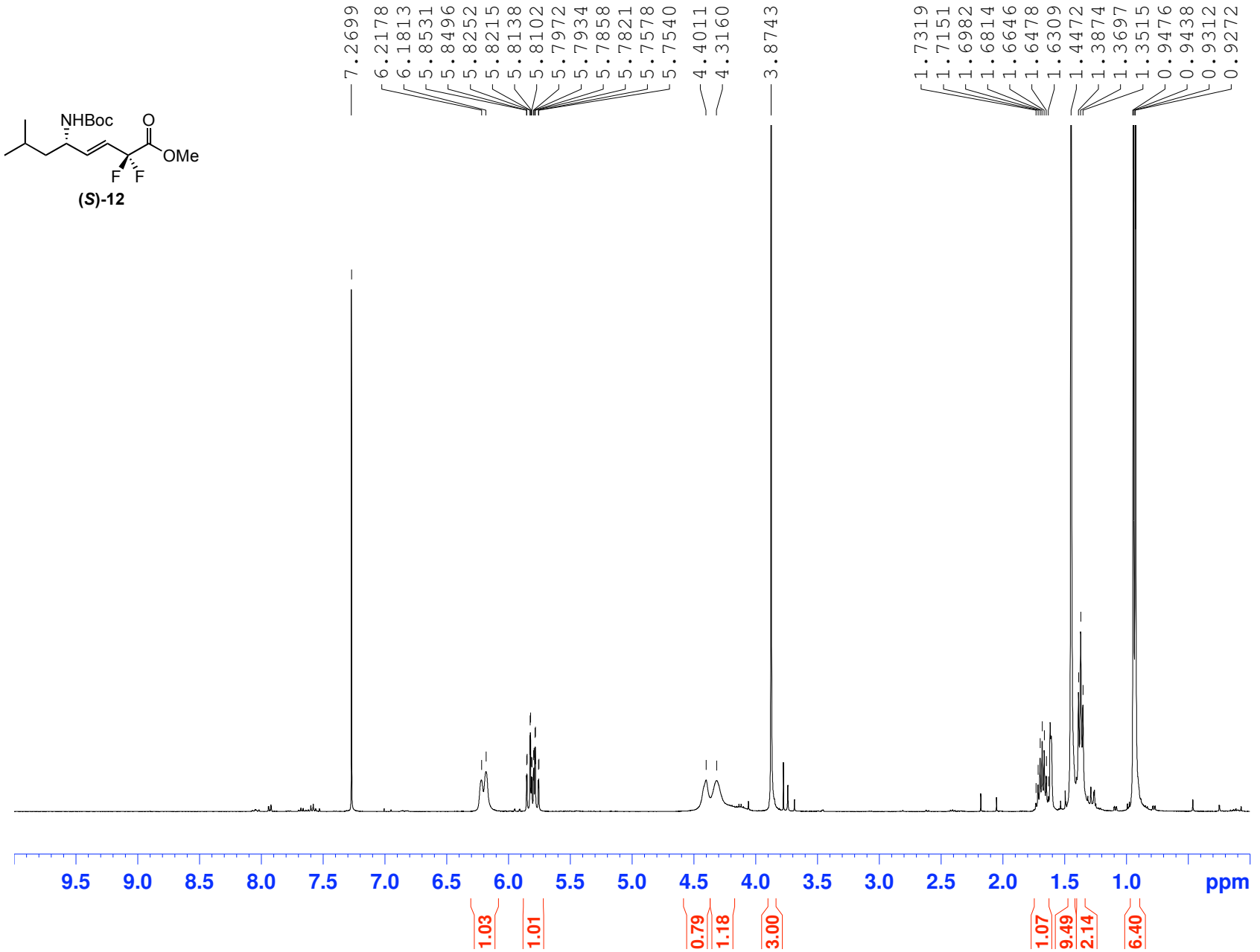
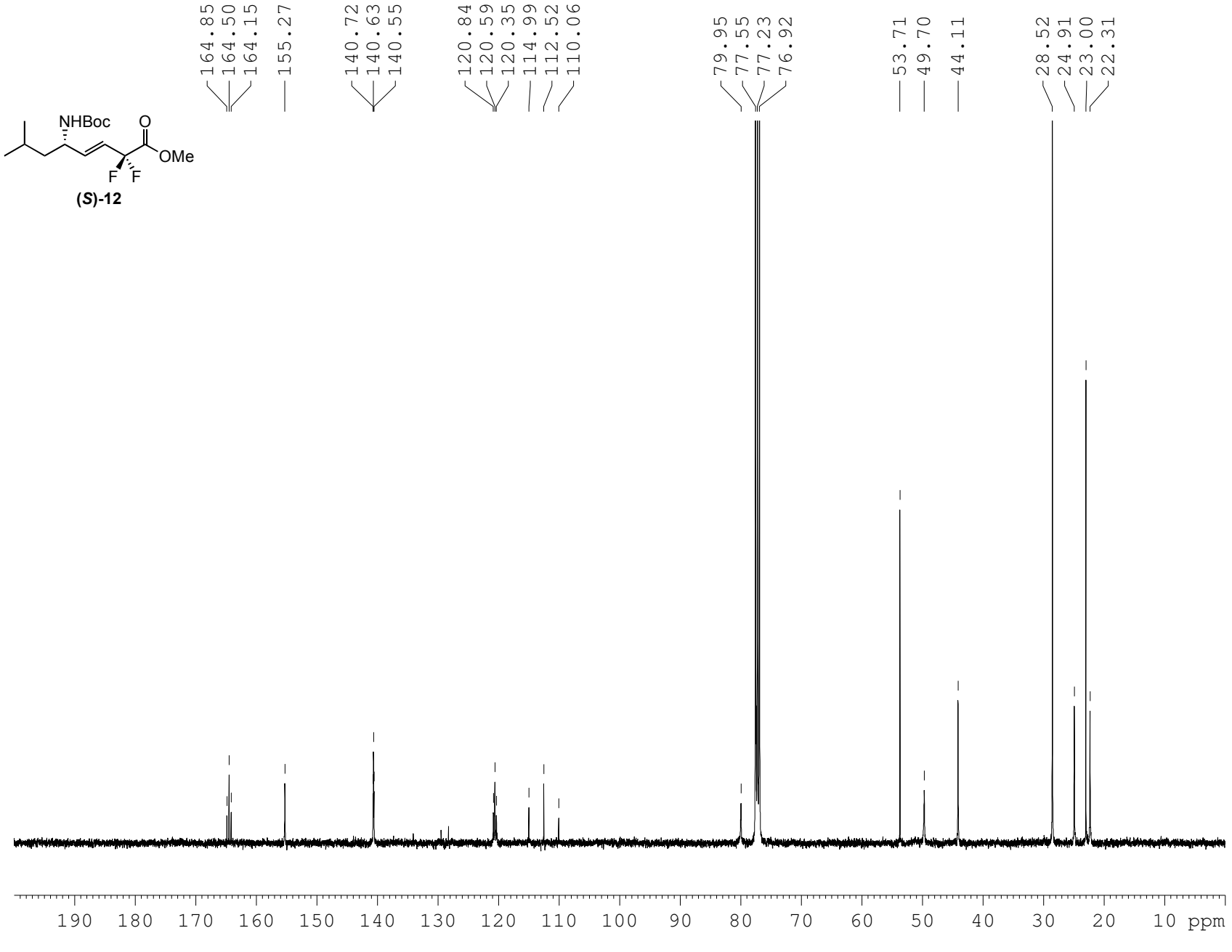
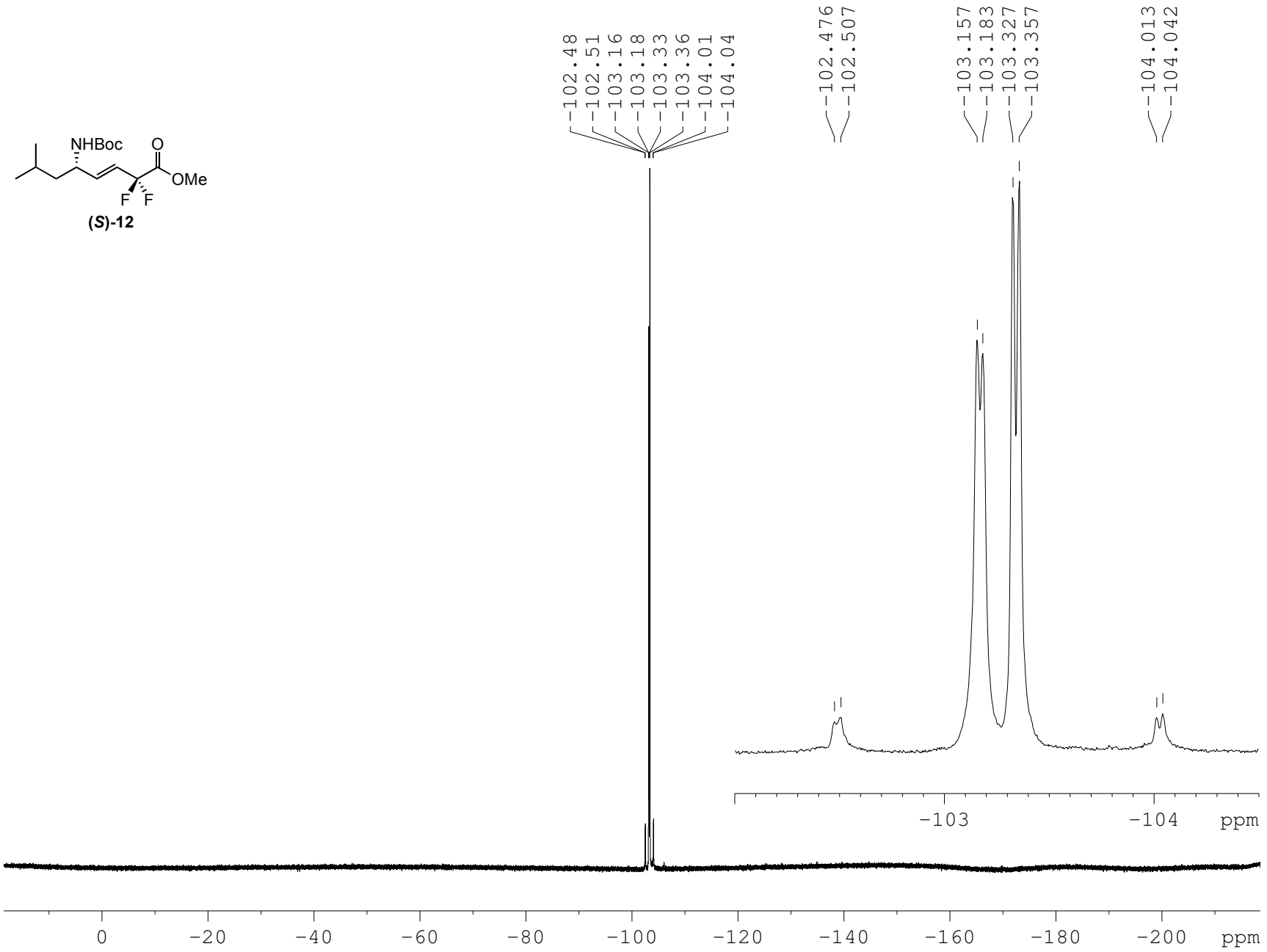
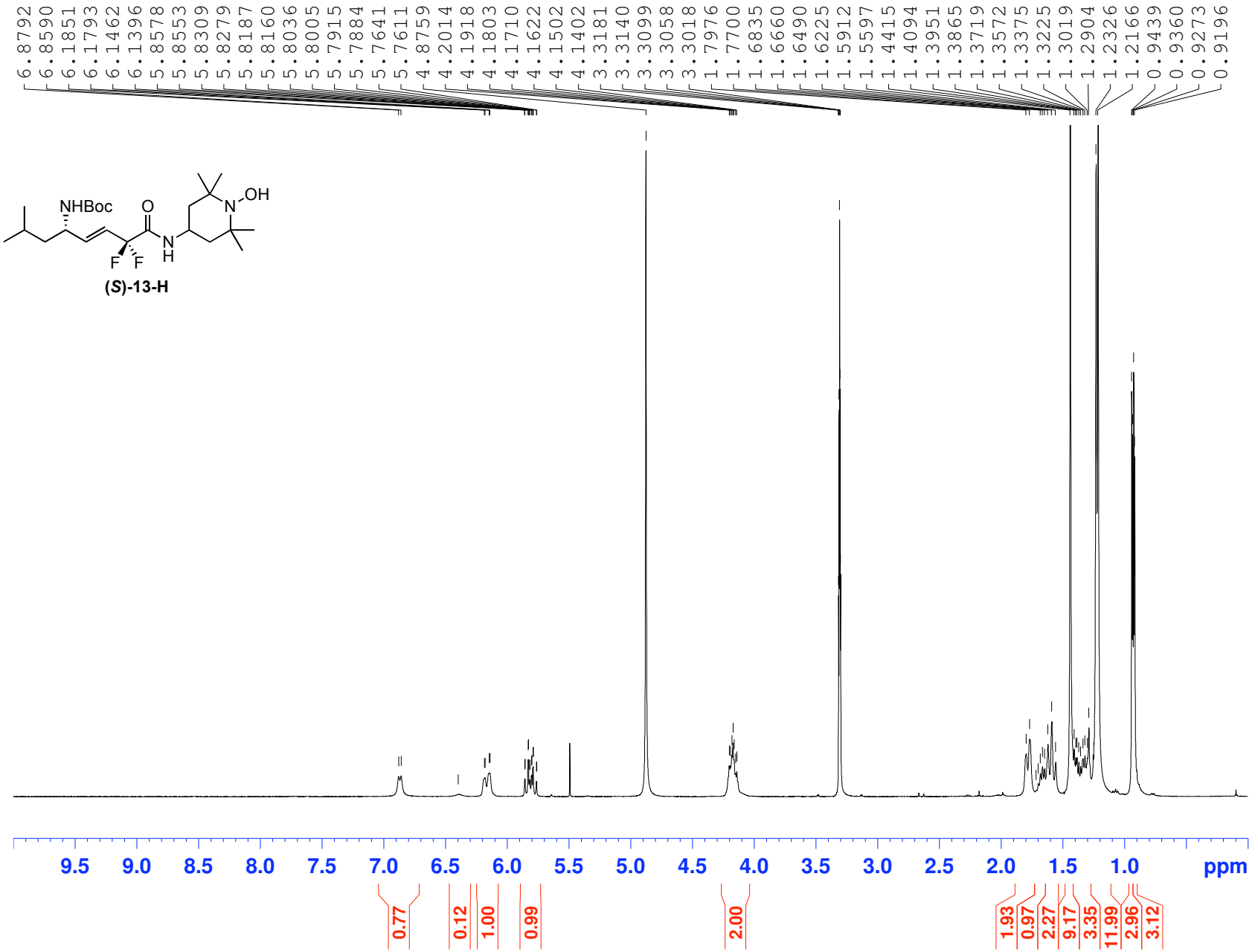
5.7313
5.7283
5.7140
5.7110
5.6931
5.6899
5.6753
5.6723
5.6579
5.6551
5.5158
5.5034
5.4776
5.4654
4.3930
4.1585
3.6849
3.0788
3.0615
1.7072
1.6905
1.6738
1.6556
1.6413
1.6224
1.6057
1.6007
1.4442
1.3596
1.3431
1.3241
1.3101
0.9282
0.9226
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.02
1.04
0.88
1.08
3.01
2.00
1.71
9.61
1.99
6.34


172.32
155.46
135.60
121.97
79.46
77.55
77.23
76.91
52.03
50.35
44.80
37.74
28.61
24.90
22.88
22.61
NHBoc
O
OMe
(S)-11
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


NHBoc
O
OMe
F
F
(S)-12
7.2699
6.2178
6.1813
5.8531
5.8496
5.8252
5.8215
5.8138
5.8102
5.7972
5.7934
5.7858
5.7821
5.7578
5.7540
4.4011
4.3160
3.8743
1.7319
1.7151
1.6982
1.6814
1.6646
1.6478
1.6309
1.4472
1.3874
1.3697
1.3515
0.9476
0.9438
0.9312
0.9272
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
ppm
1.03
1.01
0.79
1.18
3.00
1.07
9.49
2.14
6.40


164.85
164.50
164.15
155.27
140.72
140.63
140.55
120.84
120.59
120.35
114.99
112.52
110.06
79.95
77.55
77.23
76.92
53.71
49.70
44.11
28.52
24.91
23.00
22.31
NHBoc
O
OMe
F
F
(S)-12
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


NHBoc
O
OMe
F F
(S)-12
-102.48
-102.51
-103.16
-103.18
-103.33
-103.36
-104.01
-104.04
-102.476
-102.507
-103.157
-103.183
-103.327
-103.357
-104.013
-104.042
-103
-104
ppm
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm


6.8792
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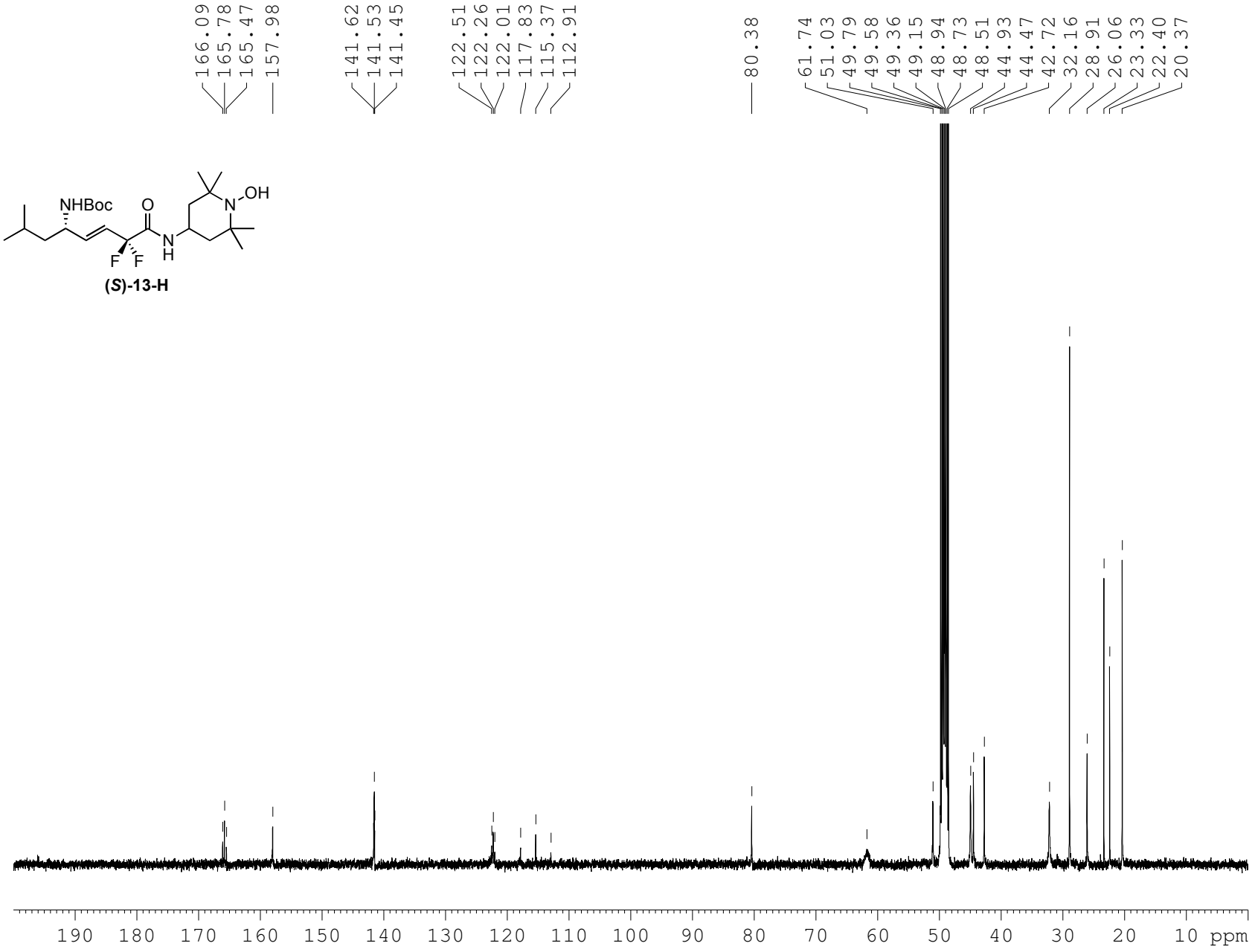
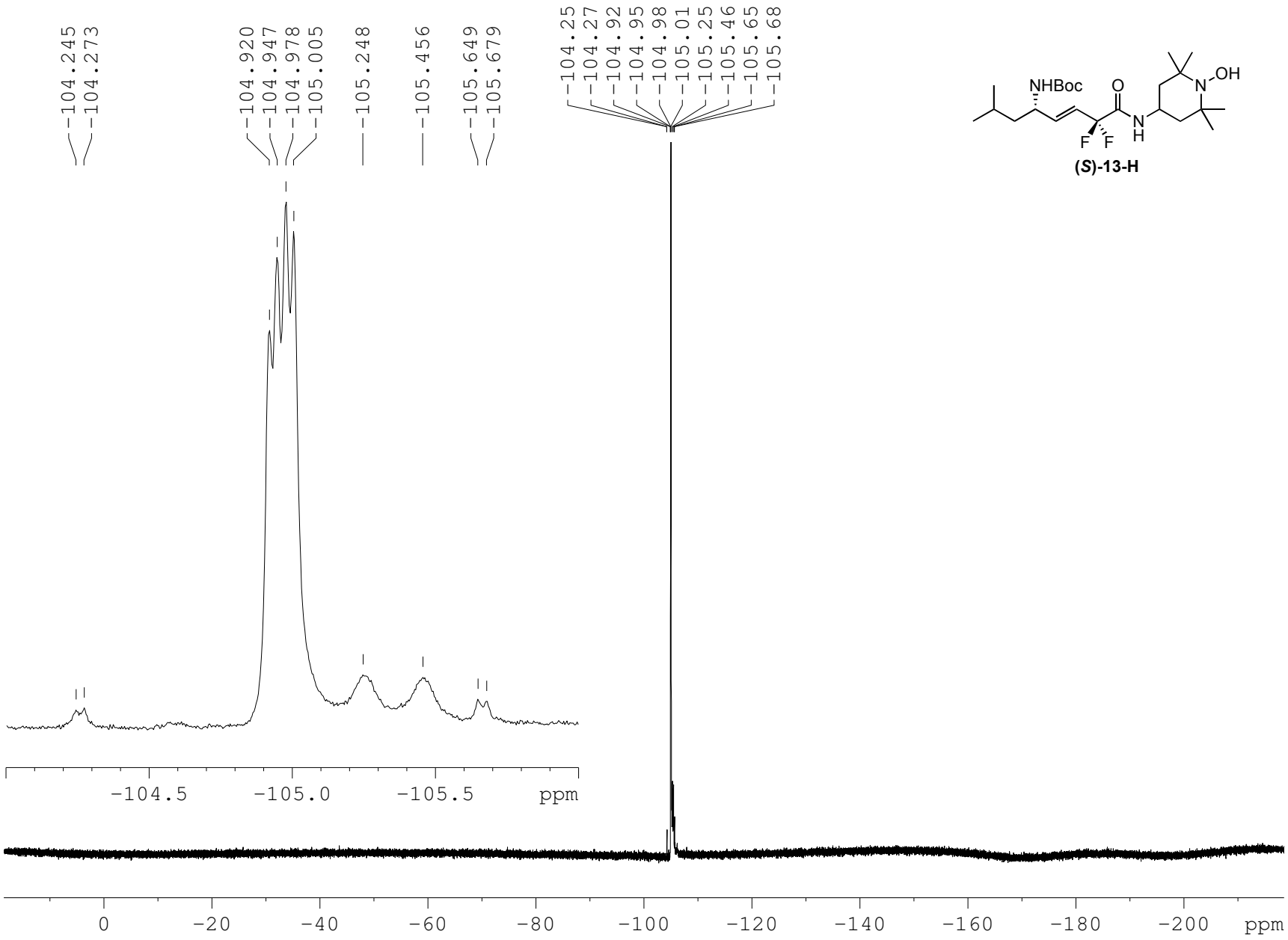
6.1851
6.1793
6.1462
6.1396
5.8578
5.8553
5.8309
5.8279
5.8187
5.8160
5.8036
5.8005
5.7915
5.7884
5.7641
5.7611
4.8759
4.2014
4.1918
4.1803
4.1710
4.1622
4.1502
4.1402
3.3181
3.3140
3.3099
3.3058
3.3018
1.7976
1.7700
1.6835
1.6660
1.6490
1.6225
1.5912
1.5597
1.4415
1.4094
1.3951
1.3865
1.3719
1.3572
1.3375
1.3225
1.3019
1.2904
1.2326
1.2166
0.9439
0.9360
0.9273
0.9196
NHBoc
O
N
OH
N
H
F
F
(S)-13-H
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
ppm
0.77
0.12
1.00
0.99
2.00
1.93
0.97
2.27
9.17
3.35
11.99
2.96
3.12

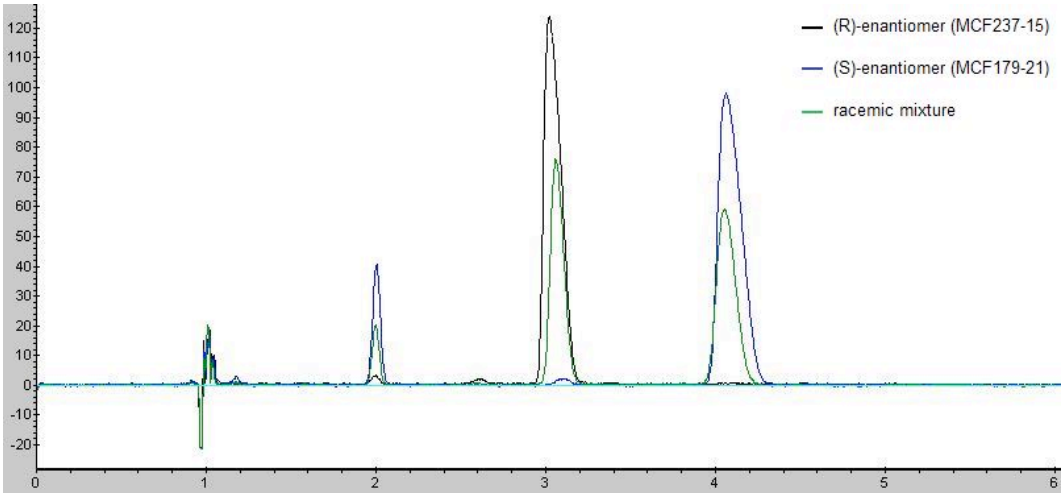

166.09
165.78
165.47
157.98
141.62
141.53
141.45
122.51
122.26
122.01
117.83
115.37
112.91
80.38
61.74
51.03
49.79
49.58
49.36
49.15
48.94
48.73
48.51
44.93
44.47
42.72
32.16
28.91
26.06
23.33
22.40
20.37
NHBoc
O
N
OH
N
H
F
F
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

(*S*)-13-H

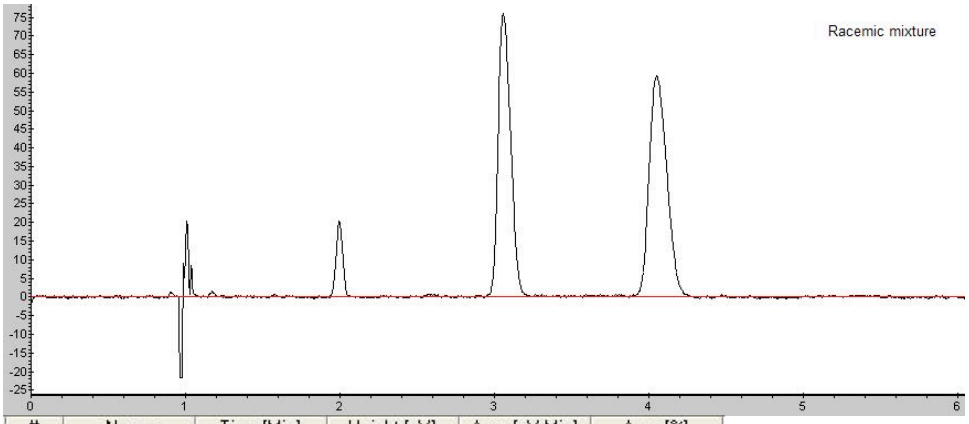

-104.245
-104.273
-104.920
-104.947
-104.978
-105.005
-105.248
-105.456
-105.649
-105.679
-104.25
-104.27
-104.92
-104.95
-104.98
-105.01
-105.25
-105.46
-105.65
-105.68
NHBoc
O
N
OH
H
F
F
(S)-13-H
-104.5
-105.0
-105.5
ppm
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

Chiral SFC analysis of (*S*)-5a and (*R*)-5a for *ee* determination

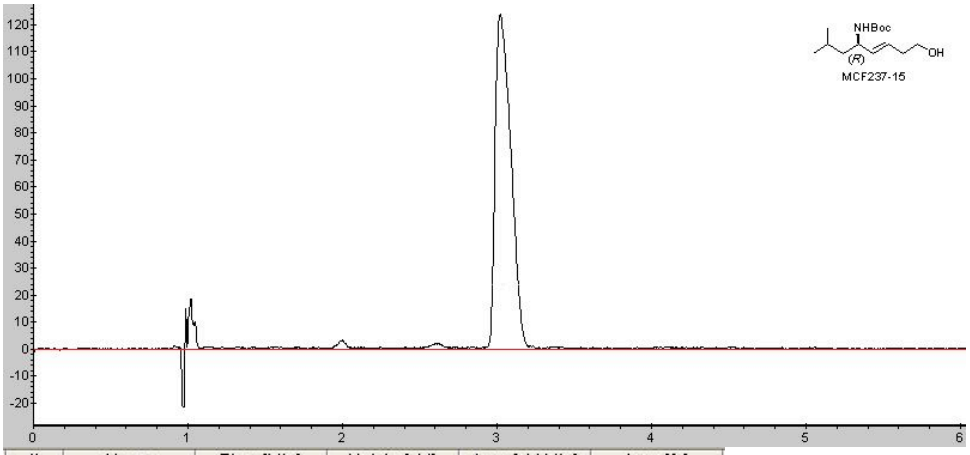
Instrumentation: SFC Mettler Toledo
Column: Chiralpak-IC (250 x 4.6 mm)
Elution: 7% MeOH in CO_2
Pressure: 100 bar
Flow: 3 mL/min
Sample concentration: 20 mg/mL in MeOH
Injection volume: 4 µL
Detection: UV λ = 195 nm



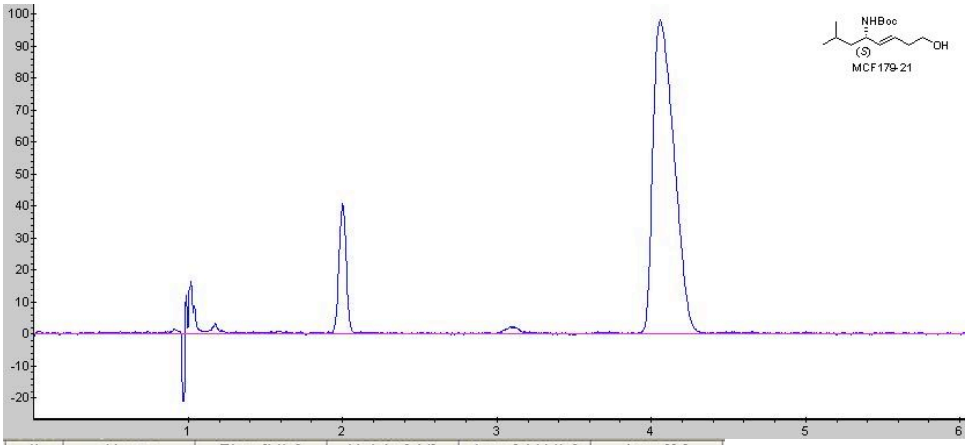
MCF237-15 = **(*R*)-5a**
MCF179-21= **(*S*)-5a**
(*S*)-enantiomer: 96.6% ee
(*R*)-enantiomer: 98.0% ee



#	Name	Time [Min]	Height [µV]	Area [µV.Min]	Area [%]
1	MCF237-15	3.06	76.0	7.2	47.266
2	MCF179-21	4.05	59.5	8.1	52.734
Total			135.6	15.3	100.000



#	Name	Time [Min]	Height [µV]	Area [µV.Min]	Area [%]
1	MCF237-15	3.02	123.7	14.7	98.978
2	MCF179-21	4.10	0.9	0.2	1.022
Total			124.7	14.9	100.000



#	Name	Time [Min]	Height [µV]	Area [µV.Min]	Area [%]
1	MCF237-15	3.10	2.2	0.3	1.697
2	MCF179-21	4.06	98.3	15.7	98.303
Total			100.6	15.9	100.000