Development of a Method for the *N*-Arylation of Amino Acid Esters with Aryl Triflates

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Supporting Information

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I. General Information

A) Procedures: All reactions were performed in oven-dried Fisher Scientific 20 Å~ 125 mm screw-cap tubes (Cat. No. 14-959-37A) using Thermo Scientific PTFE/silicon septa (Cat. No. B7995-18), unless otherwise noted. Intermediates were purified using a Biotage® Isolera system, employing polypropylene cartridges preloaded with silica gel (Silicycle SiliaFlash® F60 silica gel) or with new Biotage® SNAP cartridges. Samples were eluted using a flow rate of 18–50 mL/min, with detection by UV (254 nm). Analytical thin-layered chromatography (TLC) was performed using glass plates pre-coated with silica gel (0.25 mm, 60 Å pore size) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light (UV) and/or submersion in aqueous ceric ammonium molybdate solution (CAM), or aqueous potassium permanganate solution ($KMnO_4$).

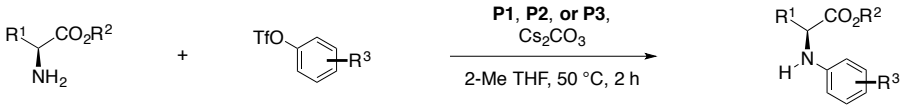
B) Materials: Commercial solvents and reagents were purchased from Aldrich Chemical Company, Strem Chemicals, Acros Organics, Alfa Aesar, TCI America, Combi Blocks, Oakwood Chemical, Matrix Scientific, and Chem-Impex and used as received with the following exceptions. *t*-BuBrettPhos (**L1**) was a gift from Aldrich. Anhydrous 1,4-dioxane and 2-methyltetrahydrofuran were purchased from Aldrich Chemical Co. in Sure-Seal™ bottles and used as received. THF and CH_2Cl_2 were purchased from J.T. Baker in CYCLE-TAINER® solvent-delivery kegs and vigorously purged with argon for 2 h, followed by passing it under argon pressure through two packed columns of neutral alumina. Cesium carbonate, sodium *tert*-butoxide, sodium phenoxide, and potassium phosphate were stored in a nitrogen-filled glovebox. Small quantities of cesium carbonate were stored on the bench in a desiccator for up to one week. Unless otherwise noted, amino acid ester free bases were prepared from the corresponding hydrochloride salt by washing with 10% aqueous sodium carbonate. Precatalyst **P3** was prepared by a modified literature procedure (vide infra).[1] Precatalyst **P1**,[2] precatalyst **P2**,[1] *N*-methyl-2-aminobiphenylpalladium methanesulfonate dimer (**S1**)[1] L-Trp-(Boc)-OMe (**5m**),[3] L-Gln-(Trt)-OMe•HCl (**5l**),[4] L-β-Phe-OMe•HCl (**5n**),[5] 4-*n*-butylphenyl trifluoromethanesulfonate (**7a**),[6] *m*-tolyl trifluoromethanesulfonate (**7b**),[7] 2-methoxy-4-propylphenyl trifluoromethanesulfonate (**7c**),[8] 4-acetamidophenyl trifluoromethanesulfonate (**7e**),[9] methyl 3-trifluoromethanesulfonyloxy-benzoate (**7g**),[10] 4-chlorophenyl trifluoromethanesulfonate (**7h**),[11] 3-acetylphenyl trifluoromethanesulfonate (**7j**),[12] 4-(trifluoromethyl)phenyl trifluoromethanesulfonate (**7k**),[9] 3-quinolinyl trifluoromethanesulfonate (**7l**),[13] estrone trifluoromethanesulfonate (**7m**),[14] and 1-bromo-4-(methoxymethyl)benzene[15] were prepared according to published procedures.

C) Instrumentation: Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded at 400 or 500 MHz at 24 °C, unless otherwise noted. Chemical shifts are expressed in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$, δ 7.26; CHD_2OD, δ 3.31). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiple resonances, br = broad, app = apparent), coupling constant in Hertz, and integration. Proton-decoupled carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded at 100 or 125 MHz at 24 °C, unless otherwise noted. Chemical shifts are expressed in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$, δ 77.2; CD_3OD, δ 49.0). Proton-decoupled fluorine nuclear magnetic resonance spectra (^{19}F NMR) were recorded at 375 MHz at 24 °C, unless otherwise noted. Chemical shifts are expressed in parts per million (ppm, δ scale) downfield from fluorotrichloromethane (0.00 ppm). Proton-decoupled phosphorous nuclear magnetic resonance spectra (^{31}P NMR) were recorded at 162 MHz at 24 °C, unless otherwise noted. Chemical shifts are expressed in parts per million (ppm, δ scale) downfield from 85% aq. phosphoric acid (0.00 ppm). Attenuated total reflectance Fourier transform infrared spectra (ATR-FTIR) were obtained using a Thermo

Scientific iD5 ATR Nicolet iS5 FT-IR spectrometer referenced to a polystyrene standard and data are reported as frequency of absorption (cm^{-1}). Melting points were obtained on a Mel-Temp capillary melting point apparatus. Elemental analyses were carried out by Atlantic Microlab, Inc., Norcross, GA. High Resolution Mass Spectra were obtained on a Bruker Daltonics APEXIV 4.7 Tesla Fourier transform ion cyclotron resonance mass spectrometer (FT-ICR-MS). High-pressure liquid chromatography (HPLC) was performed on Agilent 1200 Series chromatographs using chiral columns (25 cm) as noted for each compound. (Note: In some instances DL material was prepared by mixing a 1:1 ratio of the L- and D-amino acid ester. As this was often done on a small scale, the ratios of the enantiomeric products shown below may differ from 1:1). Optical rotations were measured on a Jasco P-1010 polarimeter equipped with a sodium (589 nm, D) lamp. Optical rotation data are represented as follows: specific rotation ($[\alpha]_D^T$), concentration (g/100 mL), and solvent.

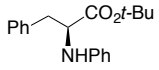
II. Experimental Procedures and Characterization Data[16]

A) *N*-Arylation of Amino Acid Esters



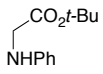
amino acid ester free base **5a–5t** | PhOTf or **7a–7m** | *N*-arylation product **6a–6t**, **8a–8m**

General Procedure: A 25 mL screw-cap tube equipped with a stir bar and Teflon septum was charged sequentially with amino acid ester, if solid, (1.00 mmol, 1.00 equiv), triflate, if solid, (1.00 mmol, 1.00 equiv), **P1** (43.0 mg, 50.0 μmol, 5.0 mol%) or **P3** (43.0 mg, 50.0 μmol, 5.0 mol%), and cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv). The reaction test tube was capped and then evacuated and backfilled with argon by piercing with a needle attached to a Schlenk line (this process was repeated a total of three times). Amino acid ester and/or triflate, if liquid, and 2-methyltetrahydrofuran (2.00 mL) were added sequentially to the reaction test tube. The reaction test tube was placed in an oil bath that had been preheated to 50 °C. The reaction mixture was stirred and heated at 50 °C for 2 h. The reaction mixture was allowed to cool over 20 min to rt. The cooled product mixture was diluted with CH_2Cl_2 (5.00 mL). The diluted product mixture was filtered through Celite and concentrated to dryness. The residue obtained was purified by automated flash-column chromatography. The yields reported are the average of two experiments. The enantiomeric excesses (% ee) were determined by HPLC analysis using chiral stationary phases.



6a

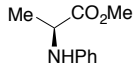
Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a**, 221 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 μL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 2% acetone–hexanes initially, grading to 20% acetone–hexanes, linear gradient) to afford **6a** as a white solid. Yield: 268 mg, 90%. mp = 83–85 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.25 (m, 5H), 7.22 (dd, *J* = 8.5, 7.4 Hz, 2H), 6.79 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 7.7 Hz, 2H), 4.31 (t, *J* = 6.4 Hz, 1H), 3.16 (d, *J* = 6.4 Hz, 2H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 146.7, 136.8, 129.6, 129.4, 128.4, 126.9, 118.3, 113.7, 81.8, 58.3, 38.7, 28.0. IR (neat, cm^{-1}): 3358, 2976, 1704, 1601, 1157, 693. Anal. Calcd. for $C_{19}H_{23}NO_2$: C, 76.74; H, 7.80, Found: C, 76.86; H, 7.87. $[\alpha]_D^{24}$ +18.6 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 94% ee: tR (minor) = 14.4 min, tR (major) = 19.0 min.



6b

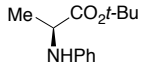
Following the general procedure, a mixture of Gly-O*t*-Bu (**5b**, 131 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 μL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 2% acetone–hexanes initially, grading to 20% acetone–hexanes, linear gradient) to afford **6b** as a clear oil. Yield: 200 mg, 97%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.22 (m, 2H), 6.82 (t, *J* = 7.3 Hz, 1H), 6.67 (d, *J* = 7.8 Hz, 2H), 4.38 (s, 1H), 3.85 (s, 2H),

1.57 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 147.2, 129.2, 117.9, 112.9, 81.8, 46.5, 28.0. IR (neat, cm^{-1}): 3401, 2977, 1732, 1604, 1508, 1150. Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27, Found: C, 69.26; H, 8.25.



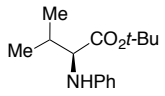
6c

Following the general procedure, a mixture of L-Ala-OMe (**5c**, 103 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 μL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography with a new column (eluting with 1% acetone–pentane initially, grading to 10% acetone–pentane, linear gradient) to afford **6c** as a yellow oil. Yield: 157 mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (dd, J = 8.5, 7.4 Hz, 2H), 6.77 (t, J = 7.3 Hz, 1H), 6.64 (d, J = 7.7 Hz, 2H), 4.25 (br s, 1H), 4.19 (q, J = 7.0 Hz, 1H), 3.75 (s, 3H), 1.50 (d, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 146.6, 129.3, 118.3, 113.3, 52.2, 51.9, 18.9. IR (neat, cm^{-1}): 3394, 2951, 1732, 1602, 1506, 1156, 748, 692. Anal. Calcd. for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31, Found: C, 67.14; H, 7.15. $[\alpha]_D^{24}$ –53.6 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 95% ee: tR (minor) = 16.2 min, tR (major) = 24.2 min.



6d

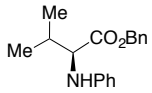
Following the general procedure, a mixture of L-Ala-O*t*-Bu (**5d**, 145 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 μL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 1% acetone–pentane initially, grading to 10% acetone–pentane, linear gradient) to afford **6d** as a clear oil. Yield: 198 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09–7.03 (m, 2H), 6.62 (t, J = 7.3 Hz, 1H), 6.51 (d, J = 7.7 Hz, 2H), 4.16 (br s, 1H), 3.92 (q, J = 6.9 Hz, 1H), 1.33 (s, 9H), 1.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 146.8, 129.2, 118.1, 113.5, 81.4, 52.6, 28.0, 18.8. IR (neat, cm^{-1}): 3395, 2977, 1726, 1603, 1505, 1145, 746, 691. Anal. Calcd. for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65, Found: C, 70.70; H, 8.47. $[\alpha]_D^{24}$ –38.6 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 96% ee: tR (minor) = 8.7 min, tR (major) = 9.3 min.



6e

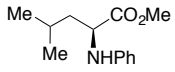
Following the general procedure, a mixture of L-Val-O*t*-Bu (**5e**, 173 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 μL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 14 h. The crude product was purified by automated flash-column chromatography (eluting with 1% EtOAc–hexanes initially, grading to 10% EtOAc–hexanes, linear gradient) to afford **6e** as a white solid. Yield: 208 mg, 83%. mp = 82–84 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.14 (m, 2H), 6.73 (t, J = 7.3 Hz, 1H), 6.65 (d, J = 7.7 Hz, 2H), 4.22 (br s, 1H), 3.77 (d, J = 5.6 Hz, 1H), 2.13 (dp, J = 13.5, 6.8 Hz, 1H), 1.44 (s, 9H), 1.05 (dd, J = 8.9, 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 147.7, 129.3, 118.1, 113.8, 81.6, 63.0, 31.6, 28.2, 19.1, 18.8. IR (neat, cm^{-1}): 3382, 2970, 1707, 1604, 1257, 1156, 745, 691. Anal. Calcd. for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30, Found: C, 72.35; H, 9.44. $[\alpha]_D^{24}$ –70.1 (*c* 1.0, $CHCl_3$). HPLC

analysis (OJ-H, 0.5% IPA–hexanes, 0.5 mL/min, 254 nm) indicated 87% ee: tR (major) = 12.3 min, tR (minor) = 13.3 min.



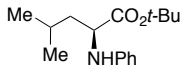
6f

Following the general procedure, a mixture of L-Val-OBn (**5f**, 207 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 14 h. The crude product was purified by automated flash-column chromatography (eluting with 2% ether–pentane initially, grading to 20% ether–pentane, linear gradient) to afford **6f** as a clear oil. Yield: 216 mg, 76%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.36 (m, 5H), 7.27 (t, *J* = 7.9 Hz, 2H), 6.85 (t, *J* = 7.3 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 2H), 5.25 (app d, *J* = 2.9 Hz, 2H), 4.27 (br d, *J* = 7.8 Hz, 1H), 4.04 (t, *J* = 7.1 Hz, 1H), 2.31–2.18 (m, *J* = 6.7 Hz, 1H), 1.13 (dd, *J* = 10.2, 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 147.4, 135.6, 129.3, 128.6, 128.4, 128.3, 118.3, 113.7, 66.7, 62.6, 31.6, 19.2, 18.7. IR (neat, cm^{-1}): 3384, 2961, 1729, 1601, 1145, 746, 691. Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47, Found: C, 76.34; H, 7.39. $[\alpha]_D^{24}$ –40.6 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 94% ee: tR (minor) = 19.0 min, tR (major) = 24.0 min.



6g

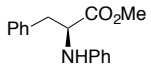
Following the general procedure, a mixture of L-Leu-OMe (**5g**, 145 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 1% acetone–pentane initially, grading to 10% acetone–pentane, linear gradient) to afford **6g** as a white solid. Yield: 198 mg, 90%. mp = 49–50 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (dd, *J* = 8.6, 7.3 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 2H), 4.17–4.11 (m, 1H), 4.08 (br s, 1H), 3.72 (s, 3H), 1.84 (hept, *J* = 6.3 Hz, 1H), 1.69 (td, *J* = 7.0, 2.7 Hz, 2H), 1.01 (dd, *J* = 18.1, 6.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 147.0, 129.4, 118.4, 113.5, 55.2, 52.0, 42.4, 24.9, 22.8, 22.3. IR (neat, cm^{-1}): 3383, 2954, 1718, 1602, 745, 689. Anal. Calcd. for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65, Found: C, 70.68; H, 8.67. $[\alpha]_D^{24}$ –70.7 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 96% ee: tR (minor) = 10.2 min, tR (major) = 15.0 min.



6h

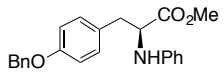
Following the general procedure, a mixture of L-Leu-O*t*-Bu (**5h**, 187 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 2% EtOAc–hexanes initially, grading to 10% EtOAc–hexanes, linear gradient) to afford **6h** as a white solid. Yield: 231 mg, 88%. mp = 68–70 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23–7.15 (m, 2H), 6.75 (t, *J* = 7.3 Hz, 1H), 6.66 (d, *J* = 7.7 Hz, 2H), 4.06 (br s, 1H), 4.03–3.98 (m, 1H), 1.87 (dp, *J* = 13.4, 6.7 Hz, 1H), 1.67 (tt, *J* = 13.9, 6.5 Hz, 2H), 1.45 (s, 9H), 1.02 (dd, *J* = 20.8, 6.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 147.3, 129.2, 118.1, 113.6, 81.3, 55.9, 42.4, 28.0, 25.0, 22.8, 22.5. IR (neat, cm^{-1}): 3378, 2955, 1703, 1604, 1305,

1149, 761, 693. Anal. Calcd. for $C_{16}H_{25}NO_2$: C, 72.97; H, 9.57, Found: C, 73.16; H, 9.69. $[\alpha]_D^{24}$ –70.1 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 1% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 97% ee: tR (minor) = 6.3 min, tR (major) = 7.0 min.



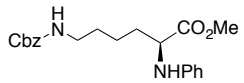
6i

Following the general procedure, a mixture of L-Phe-OMe (**5i**, 179 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography with a new column (eluting with 2% acetone–hexanes initially, grading to 20% acetone–hexanes, linear gradient) to afford **6i** as a yellow oil. Yield: 244 mg, 96%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dt, *J* = 14.7, 6.9 Hz, 3H), 7.32–7.25 (m, 4H), 6.87 (t, *J* = 7.3 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 2H), 4.50 (t, *J* = 6.2 Hz, 1H), 4.39 (br s, 1H), 3.75 (s, 3H), 3.31–3.18 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 146.3, 136.3, 129.3, 129.2, 128.5, 127.0, 118.4, 113.6, 57.8, 52.0, 38.6. IR (neat, cm^{-1}): 3353, 3026, 1731, 1601, 1496, 692. Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.72; H, 6.71, Found: C, 75.42; H, 6.80. $[\alpha]_D^{24}$ +38.2 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 87% ee: tR (minor) = 30.7 min, tR (major) = 42.8 min.



6j

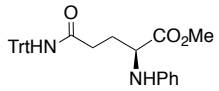
Following the general procedure, a mixture of L-Tyr-(Bn)-OMe (**5j**, 285 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography with a new column (eluting with 10% ether–pentane initially, grading to 20% ether–pentane, linear gradient) to afford **6j** as a clear oil. Yield: 343 mg, 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–7.39 (m, 5H), 7.32–7.25 (m, 2H), 7.21–7.15 (m, 2H), 7.03–6.99 (m, 2H), 6.85 (tt, *J* = 7.4, 1.0 Hz, 1H), 6.73–6.68 (m, 2H), 5.12 (s, 2H), 4.44 (s, 1H), 4.29 (s, 1H), 3.75 (s, 3H), 3.24–3.10 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 157.9, 146.4, 137.0, 130.3, 129.4, 128.6 (2C), 128.0, 127.5, 118.4, 114.9, 113.6, 70.0, 57.8, 52.1, 37.7. IR (neat, cm^{-1}): 3397, 3030, 1736, 1602, 1506, 1239, 1175, 748, 693. Anal. Calcd. for $C_{23}H_{23}NO_3$: C, 76.43; H, 6.41, Found: C, 76.23; H, 6.44. $[\alpha]_D^{24}$ +47.6 (*c* 1.0, $CHCl_3$). HPLC analysis (OD-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 96% ee: tR (major) = 29.8 min, tR (minor) = 54.4 min.



6k

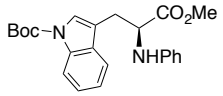
Following the general procedure, a mixture of L-Lys-(Cbz)-OMe (**5k**, 294 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 8% EtOAc–hexanes initially, grading to 66% EtOAc–hexanes, linear gradient) to afford **6k** as a yellow oil. Yield: 340 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.29 (m, 5H), 7.21–7.15 (m, 2H), 6.75 (tt, *J* = 7.3, 1.0 Hz, 1H), 6.64–6.59 (m, 2H), 5.11 (s, 2H), 4.94 (s, 1H), 4.21 (s, 1H), 4.06 (s, 1H), 3.71 (s, 3H), 3.19 (q, *J* = 6.4 Hz, 2H), 1.93–1.68 (m, 2H), 1.59–1.38 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 156.5, 146.8, 136.6,

129.4, 128.5, 128.1 (2 C), 118.3, 113.4, 66.6, 56.4, 52.2, 40.7, 32.6, 29.7, 22.8. IR (neat, cm^{-1}): 3357, 2949, 1702, 1603, 1506, 1242, 693. Anal. Calcd. for $C_{21}H_{26}N_2O_4$: C, 68.09; H, 7.07, Found: C, 68.25; H, 6.99. $[\alpha]_D^{24}$ –20.3 (*c* 1.0, $CHCl_3$). HPLC analysis (OD-H, 20% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 94% ee: tR (major) = 19.7 min, tR (minor) = 40.3 min.



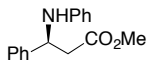
6l

Following the general procedure, a mixture of L-Gln-(Trt)-OMe (**5l**, 402 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 1% acetone–CH_2Cl_2 initially, grading to 10% acetone–CH_2Cl_2, linear gradient) to afford **6l** as a white solid. Yield: 420 mg, 88%. mp = 187–190 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.24 (m, 9H), 7.24–7.15 (m, 8H), 6.78 (t, *J* = 7.3 Hz, 1H), 6.66 (s, 1H), 6.60 (d, *J* = 7.7 Hz, 2H), 4.43 (br s, 1H), 4.13 (dd, *J* = 8.4, 5.3 Hz, 1H), 3.70 (s, 3H), 2.60–2.39 (m, 2H), 2.26–2.05 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 170.8, 146.9, 144.8, 129.5, 128.8, 128.1, 127.2, 118.7, 113.8, 70.8, 56.5, 52.4, 33.6, 28.0. IR (neat, cm^{-1}): 3271, 1741, 1647, 1536, 748, 697. Anal. Calcd. for $C_{31}H_{30}N_2O_3$: C, 77.80; H, 6.32, Found: C, 77.40; H, 6.39. $[\alpha]_D^{24}$ –17.1 (*c* 1.0, $CHCl_3$). HPLC analysis (AD-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 92% ee: tR (minor) = 10.5 min, tR (major) = 30.1 min.



6m

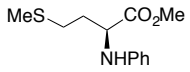
Following the general procedure, a mixture of L-Trp-(Boc)-OMe (**5m**, 318 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography with a new column (eluting with 10% ether–pentane initially, grading to 20% ether–pentane, linear gradient) to afford **6m** as a white solid. Yield: 378 mg, 96%. mp = 94–96 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 7.7 Hz, 1H), 7.34 (s, 1H), 7.22 (t, *J* = 7.7 Hz, 1H), 7.16–7.05 (m, 3H), 6.66 (t, *J* = 7.3 Hz, 1H), 6.53 (d, *J* = 7.7 Hz, 2H), 4.38 (t, *J* = 5.9 Hz, 1H), 4.17 (s, 1H), 3.55 (s, 3H), 3.16 (qd, *J* = 14.6, 5.8 Hz, 2H), 1.57 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 149.7, 146.4, 135.5, 130.6, 129.5, 124.6, 124.3, 122.6, 118.9, 118.6, 115.4, 115.3, 113.7, 83.8, 56.6, 52.3, 28.3, 28.2. IR (neat, cm^{-1}): 3349, 2970, 1711, 1251, 1149, 745. Anal. Calcd. for $C_{23}H_{26}N_2O_4$: C, 70.03; H, 6.64, Found: C, 69.50; H, 6.67. $[\alpha]_D^{24}$ +33.3 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 93% ee: tR (major) = 13.4 min, tR (minor) = 16.7 min.



6n

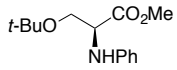
Following the general procedure, a mixture of L-β-Phe-OMe (**5n**, 179 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 14 h. The crude product was purified by automated flash-column chromatography with a new column (eluting with 5% ether–pentane initially, grading to 10% ether–pentane, linear gradient) to afford **6n** as a white solid. Yield: 198 mg, 78%. mp = 102–103 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.41 (m, 2H), 7.40–7.36 (m, 2H), 7.33–7.27 (m,

1H), 7.20–7.13 (m, 2H), 6.74 (t, J = 7.3 Hz, 1H), 6.63 (d, J = 7.7 Hz, 2H), 4.91 (t, J = 6.7 Hz, 1H), 4.61 (s, 1H), 3.70 (s, 3H), 2.88 (dd, J = 6.7, 1.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 146.8, 142.3, 129.2, 128.9, 127.6, 126.3, 117.9, 113.8, 55.0, 52.0, 42.7. IR (neat, cm^{-1}): 3375, 1716, 1603, 1289, 749, 693. Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71, Found: C, 75.01; H, 6.73. $[\alpha]_D^{24}$ +1.3 (*c* 1.0, $CHCl_3$). HPLC analysis (OD-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 99% ee: tR (major) = 19.8 min, tR (minor) = 21.6 min.



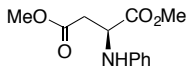
6o

Following the general procedure, a mixture of L-Met-OMe (**5o**, 163 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography with a new column (eluting with 5% EtOAc–pentane) to afford **6o** as a yellow oil. Yield: 202 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (dd, J = 8.6, 7.3 Hz, 2H), 6.76 (tt, J = 7.3, 1.1 Hz, 1H), 6.67 (dd, J = 8.7, 1.1 Hz, 2H), 4.28 (dd, J = 7.6, 5.3 Hz, 1H), 4.24 (br s, 1H), 3.73 (s, 3H), 2.64 (t, J = 7.2 Hz, 2H), 2.20–2.12 (m, 1H), 2.11 (s, 3H), 2.03 (dt, J = 14.1, 7.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 146.7, 129.4, 118.5, 113.6, 55.5, 52.3, 32.3, 30.3, 15.5. IR (neat, cm^{-1}): 3379, 2916, 1733, 1602, 1506, 1167, 748, 692. Anal. Calcd. for $C_{12}H_{17}NO_2S$: C, 60.22; H, 7.16, Found: C, 60.34; H, 6.97. $[\alpha]_D^{24}$ –21.9 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 80% ee: tR (minor) = 20.3 min, tR (major) = 29.6 min.



6p

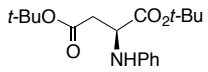
Following the general procedure, a mixture of L-Ser-(*t*-Bu)-OMe (**5p**, 175 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 1% acetone–pentane initially, grading to 10% acetone–pentane, linear gradient) to afford **6p** as a white solid. Yield: 233 mg, 93%. mp = 47–50 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.14 (m, 2H), 6.75 (t, J = 7.3 Hz, 1H), 6.67–6.60 (m, 2H), 4.20 (t, J = 4.1 Hz, 1H), 3.79 (dd, J = 8.8, 4.0 Hz, 1H), 3.73 (s, 3H), 3.69 (dd, J = 8.8, 4.2 Hz, 1H), 1.17 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 146.9, 129.4, 118.5, 113.8, 73.6, 62.5, 57.4, 52.2, 27.5. IR (neat, cm^{-1}): 3401, 2978, 1748, 1604, 1508, 1147, 1102, 755. Anal. Calcd. for $C_{14}H_{21}NO_3$: C, 66.91; H, 8.42, Found: C, 67.20; H, 8.48. $[\alpha]_D^{24}$ –10.7 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 71% ee: tR (minor) = 7.1 min, tR (major) = 10.9 min.



6q

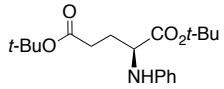
Following the general procedure, a mixture of L-Asp-(Me)-OMe (**5q**, 161 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 6% EtOAc–hexanes initially, grading to 50% EtOAc–hexanes, linear gradient) to afford **6q** as a yellow oil. Yield: 231 mg, 98%. ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.23–7.15 (m, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.67 (d, *J* = 7.7 Hz, 2H), 4.56–4.42 (m, 2H), 3.75 (s, 3H), 3.70 (s, 3H), 2.89 (d, *J* = 5.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 171.0, 146.2, 129.4, 118.7, 113.7, 53.4, 52.6, 52.0, 37.1. IR (neat, cm^{-1}): 3383, 2952, 1729, 1602, 1168, 749. Anal. Calcd. for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37, Found: C, 61.03; H, 6.46. $[\alpha]_D^{24}$ +6.8 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 74% ee: tR (minor) = 34.0 min, tR (major) = 58.1 min.



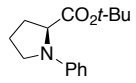
6r

Following the general procedure, a mixture of L-Asp-(*t*-Bu)-O*t*-Bu (**5r**, 245 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 1% acetone–hexanes initially, grading to 10% acetone–hexanes, linear gradient) to afford **6r** as a white solid. Yield: 290 mg, 90%. mp = 72–74 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22–7.14 (m, 2H), 6.78–6.71 (m, 1H), 6.68–6.63 (m, 2H), 4.49 (app d, *J* = 8.4 Hz, 1H), 4.28 (dt, *J* = 8.4, 5.6 Hz, 1H), 2.75 (d, *J* = 5.6 Hz, 2H), 1.46 (s, 9H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 169.9, 146.8, 129.3, 118.4, 113.8, 82.1, 81.3, 54.1, 38.6, 28.2, 28.0. IR (neat, cm^{-1}): 3400, 2977, 1732, 1140, 747, 696. Anal. Calcd. for $C_{18}H_{27}NO_4$: C, 67.26; H, 8.47, Found: C, 67.42; H, 8.54. $[\alpha]_D^{24}$ –1.1 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 80% ee: tR (minor) = 4.7 min, tR (major) = 6.0 min.



6s

Following the general procedure, a mixture of L-Glu-(*t*-Bu)-O*t*-Bu (**5s**, 259 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 1% acetone–pentane initially, grading to 10% acetone–pentane, linear gradient) to afford **6s** as a yellow solid. Yield: 313 mg, 93%. mp = 61–64 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, *J* = 8.5, 7.3 Hz, 2H), 6.75–6.70 (m, 1H), 6.65–6.60 (m, 2H), 4.23 (br s, 1H), 4.00 (dd, *J* = 7.6, 5.5 Hz, 1H), 2.47–2.31 (m, 2H), 2.17–1.95 (m, 2H), 1.45 (s, 9H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 172.4, 147.1, 129.3, 118.2, 113.6, 81.8, 80.6, 56.8, 31.7, 28.2, 28.1 (2C). IR (neat, cm^{-1}): 3363, 2977, 1722, 1704, 1605, 1155, 752, 693. Anal. Calcd. for $C_{19}H_{29}NO_4$: C, 68.03; H, 8.71, Found: C, 68.03; H, 8.70. $[\alpha]_D^{24}$ –27.7 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 97% ee: tR (minor) = 6.4 min, tR (major) = 7.8 min.

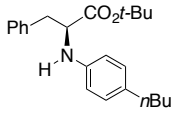


6t

Following the general procedure, a mixture of L-Pro-O*t*-Bu (**5t**, 171 mg, 1.00 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (162 µL, 1.00 mmol, 1 equiv), **P2** (46.0 mg, 50.0 µmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 80 °C for 14 h. The crude product was purified by automated flash-column chromatography with a new column (eluting with 1% ether–pentane initially, grading to 10% ether–pentane, linear gradient) to afford **6t** as a clear oil. Yield: 177 mg, 72%. ^{1}H NMR (400

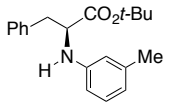
MHz, $CDCl_3$) δ 7.30 (td, *J* = 7.3, 2.0 Hz, 2H), 6.78 (tt, *J* = 7.2, 1.1 Hz, 1H), 6.64 (d, *J* = 7.9 Hz, 2H), 4.21 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.60 (dt, *J* = 7.9, 4.1 Hz, 1H), 3.44 (q, *J* = 7.8 Hz, 1H), 2.36–2.05 (m, 4H), 1.51 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 146.8, 129.1, 116.3, 111.9, 80.9, 61.6, 48.1, 30.7, 28.0, 23.8. IR (neat, cm^{-1}): 2975, 1737, 1598, 1505, 1365, 1144, 745, 670. Anal. Calcd. for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56, Found: C, 72.75; H, 8.53. $[\alpha]_D^{24}$ –53.0 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 44% ee: tR (minor) = 7.0 min, tR (major) = 10.3 min.

Repeating the reaction with stirring at 50 °C for 2 h afforded **6t** as a clear oil. Yield 20.6 mg, 9%. HPLC analysis (OJ-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 97% ee: tR (minor) = 7.2 min, tR (major) = 10.7 min.



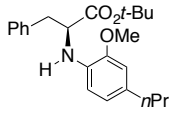
8a

Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a**, 221 mg, 1.00 mmol, 1.00 equiv), 4-*n*-butylphenyl trifluoromethanesulfonate (**7a**, 282 mg, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 5% ether–hexanes initially, grading to 40% ether–hexanes, linear gradient) to afford **8a** as a yellow solid. Yield: 318 mg, 90%. mp = 50–52 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.28 (m, 5H), 7.11–7.05 (m, 2H), 6.69–6.62 (m, 2H), 4.32 (t, *J* = 6.4 Hz, 1H), 4.19 (br s, 1H), 3.24–3.12 (m, 2H), 2.64–2.55 (m, 2H), 1.65 (tt, *J* = 8.9, 6.8 Hz, 2H), 1.43 (br s, 11H), 1.02 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 144.5, 136.9, 132.6, 129.5, 129.1, 128.3, 126.8, 113.8, 81.5, 58.6, 38.8, 34.8, 34.0, 27.9, 22.3, 14.0. IR (neat, cm^{-1}): 3368, 2924, 1726, 1518, 1149, 699. Anal. Calcd. for $C_{23}H_{31}NO_2$: C, 77.80; H, 6.32, Found: C, 77.40; H, 6.39. $[\alpha]_D^{24}$ +18.1 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 90% ee: tR (minor) = 8.4 min, tR (major) = 10.6 min.



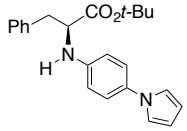
8b

Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a**, 221 mg, 1.00 mmol, 1.00 equiv), *m*-tolyl trifluoromethanesulfonate (**7b**, 282 mg, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 2% EtOAc–hexanes initially, grading to 20% EtOAc–hexanes, linear gradient) to afford **8b** as a clear oil. Yield: 288 mg, 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.33 (m, 2H), 7.33–7.26 (m, 3H), 7.13 (td, *J* = 7.4, 1.1 Hz, 1H), 6.63 (d, *J* = 7.5 Hz, 1H), 6.51 (app d, *J* = 7.6 Hz, 2H), 4.31 (t, *J* = 6.4 Hz, 1H), 4.23 (br s, 1H), 3.16 (d, *J* = 6.4 Hz, 2H), 2.34 (s, 3H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 146.7, 139.0, 136.8, 129.6, 129.2, 128.4, 126.9, 119.2, 114.5, 110.8, 81.7, 58.3, 38.8, 28.0, 21.7. IR (neat, cm^{-1}): 3366, 2923, 1716, 1605, 1148, 699. Anal. Calcd. for $C_{20}H_{25}NO_2$: C, 77.14; H, 8.09, Found: C, 77.42; H, 8.08. $[\alpha]_D^{24}$ +14.9 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 87% ee: tR (minor) = 16.1 min, tR (major) = 20.3 min.



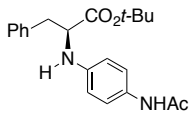
8c

Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a**, 221 mg, 1.00 mmol, 1.00 equiv), 2-methoxy-4-propylphenyl trifluoromethanesulfonate (**7c**, 298 mg, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 2% ether–hexanes initially, grading to 20% ether–hexanes, linear gradient) to afford **8c** as a clear oil. Yield: 344 mg, 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 6.76–6.68 (m, 2H), 6.61 (d, *J* = 7.9 Hz, 1H), 4.80 (br s, 1H), 4.31 (t, *J* = 6.6 Hz, 1H), 3.90 (s, 3H), 3.21 (qd, *J* = 13.6, 6.6 Hz, 2H), 2.63–2.55 (m, 2H), 1.70 (dq, *J* = 14.8, 7.4 Hz, 2H), 1.41 (s, 9H), 1.03 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 147.2, 137.1, 134.5, 132.0, 129.5, 128.3, 126.7, 120.6, 110.7, 110.5, 81.3, 58.5, 55.5, 39.0, 37.8, 27.9, 24.9, 13.9. IR (neat, cm^{-1}): 3420, 2930, 1728, 1521, 1142, 699. Anal. Calcd. for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46, Found: C, 74.48; H, 8.40. $[\alpha]_D^{24}$ +7.8 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 88% ee: tR (minor) = 8.9 min, tR (major) = 10.8 min.



8d

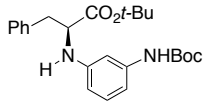
Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a,** 221 mg, 1.00 mmol, 1.00 equiv), 4-(1*H*-pyrrol-1-yl)phenyl trifluoromethanesulfonate (**7d**, 291 mg, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography with a new column (eluting with 5% acetone–pentane initially, grading to 10% acetone–pentane, linear gradient) to afford **8d** as a white solid. Yield: 316 mg, 87%. mp = 102–103 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.22 (m, 7H), 7.03–7.01 (m, 2H), 6.72–6.67 (m, 2H), 6.37–6.34 (m, 2H), 4.35 (br s, 1H), 4.30 (t, *J* = 6.4 Hz, 1H), 3.17 (d, *J* = 6.3 Hz, 2H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 144.9, 136.6, 132.7, 129.6, 128.5, 127.0, 122.4, 119.7, 114.3, 109.5, 82.1, 58.5, 38.7, 28.1. IR (neat, cm^{-1}): 3355, 2977, 1703, 1522, 699. Anal. Calcd. for $C_{23}H_{26}N_2O_2$: C, 76.21; H, 7.23, Found: C, 76.36; H, 7.30. $[\alpha]_D^{24}$ +28.3 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 91% ee: tR (major) = 38.3 min, tR (minor) = 50.5 min.



8e

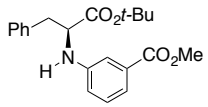
Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a**, 221 mg, 1.00 mmol, 1.00 equiv), 4-acetamidophenyl trifluoromethanesulfonate (**7e**, 283 mg, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 8% acetone–hexanes initially, grading to 66% acetone–hexanes, linear gradient) to afford **8e** as a white solid. Yield: 312 mg, 88%. mp = 148–149 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.35–7.18 (m, 7H), 6.54 (d, *J* = 8.8 Hz, 2H), 4.22 (t, *J* = 6.4 Hz, 1H), 4.19 (br s, 1H), 3.09 (dd, *J* = 6.4, 2.2 Hz, 2H), 2.07 (s, 3H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 168.6, 143.5, 136.6, 129.5, 129.3, 128.4, 126.8, 122.1,

113.8, 81.8, 58.5, 38.6, 27.9, 24.1. IR (neat, cm^{-1}): 3301, 1722, 1670, 1517, 1146, 826, 693. HRMS. Calcd. for $C_{21}H_{27}N_2O_3$, [M+H]: 355.2016, Found: [M+H]: 355.2024. $[\alpha]_D^{24}$ +21.4 (*c* 1.0, $CHCl_3$). HPLC analysis (AD-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 86% ee: tR (minor) = 17.4 min, tR (major) = 23.7 min.



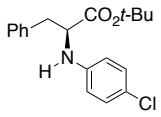
8f

Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a**, 221 mg, 1.00 mmol, 1.00 equiv), 3-((tert-butoxycarbonyl)amino)phenyl trifluoromethanesulfonate (**7f**, 341 mg, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography with a new column (eluting with 10% ether–pentane initially, grading to 20% ether–pentane, linear gradient) to afford **8f** as a white solid. Yield: 404 mg, 98%. mp = 86–88 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.22 (m, 5H), 7.08 (t, *J* = 8.0 Hz, 1H), 6.62–6.55 (m, 2H), 6.33 (ddd, *J* = 8.1, 2.2, 0.9 Hz, 1H), 4.35 (br s, 1H), 4.30 (t, *J* = 6.3 Hz, 1H), 3.13 (d, *J* = 6.3 Hz, 2H), 1.56 (s, 9H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 152.7, 147.3, 139.5, 136.6, 129.7, 129.6, 128.3, 126.8, 108.3, 108.2, 103.6, 81.8, 80.2, 58.0, 38.6, 28.4, 27.9. IR (neat, cm^{-1}): 3317, 2976, 1691, 1596, 1533, 1150. Anal. Calcd. for $C_{24}H_{32}N_2O_4$: C, 69.88; H, 7.82, Found: C, 70.00; H, 7.86. $[\alpha]_D^{24}$ +11.7 (*c* 1.0, $CHCl_3$). HPLC analysis (AD-H, 10% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 80% ee: tR (major) = 12.8 min, tR (minor) = 15.0 min.



8g

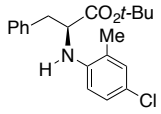
Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a**, 221 mg, 1.00 mmol, 1.00 equiv), methyl 3-trifluoromethanesulfonyloxy-benzoate (**7g**, 284 mg, 1.00 mmol, 1 equiv), **P3** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 2% EtOAc–hexanes initially, grading to 20% EtOAc–hexanes, linear gradient) to afford **8g** as a yellow oil. Yield: 343 mg, 97%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (ddd, *J* = 7.6, 1.6, 1.0 Hz, 1H), 7.36–7.21 (m, 7H), 6.81 (ddd, *J* = 8.1, 2.6, 1.0 Hz, 1H), 4.42 (br s, 1H), 4.32 (t, *J* = 6.4 Hz, 1H), 3.91 (s, 3H), 3.15 (d, *J* = 6.4 Hz, 2H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 167.4, 146.7, 136.5, 131.2, 129.6, 129.3, 128.5, 127.0, 119.4, 118.3, 114.0, 82.1, 58.1, 52.1, 38.6, 28.0. IR (neat, cm^{-1}): 3367, 2978, 1717, 1245, 1149, 752. HRMS. Calcd. for $C_{21}H_{26}NO_4$, [M+H]: 356.1856, Found: [M+H]: 356.1845 $[\alpha]_D^{24}$ +6.4 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 82% ee: tR (major) = 11.9 min, tR (minor) = 18.8 min.



8h

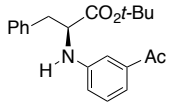
Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a**, 221 mg, 1.00 mmol, 1.00 equiv), 4-chlorophenyl trifluoromethanesulfonate (**7h**, 261 mg, 1.00 mmol, 1 equiv), **P3** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-

methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 2% ether–hexanes initially, grading to 20% ether–hexanes, linear gradient) to afford **8h** as a white solid. Yield: 307 mg, 93%. mp = 75–78 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.26 (m, 5H), 7.21–7.15 (m, 2H), 6.62–6.56 (m, 2H), 4.37 (br s, 1H), 4.28 (t, *J* = 6.4 Hz, 1H), 3.16 (d, *J* = 6.3 Hz, 2H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 145.3, 136.4, 129.5, 129.1, 128.4, 126.9, 122.6, 114.7, 81.9, 58.2, 38.5, 27.9. IR (neat, cm^{-1}): 3359, 2985, 1709, 1600, 817, 698. Anal. Calcd. for $C_{19}H_{22}ClNO_2$: C, 68.77; H, 6.68, Found: C, 68.88; H, 6.79. $[\alpha]_D^{24}$ +25.8 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 91% ee: tR (minor) = 15.7 min, tR (major) = 19.8 min.



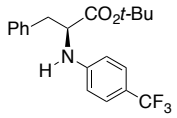
8i

Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a**, 221 mg, 1.00 mmol, 1.00 equiv), 4-chloro-2-methylphenyl trifluoromethanesulfonate (**7i**, 275 mg, 1.00 mmol, 1 equiv), **P3** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 1% ether–pentane initially, grading to 10% ether–pentane, linear gradient) to afford **8i** as a yellow oil. Yield: 291 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.26 (m, 3H), 7.26–7.21 (m, 2H), 7.12–7.05 (m, 2H), 6.52 (d, *J* = 8.2 Hz, 1H), 4.29 (t, *J* = 6.2 Hz, 1H), 4.11 (s, 1H), 3.19 (dd, *J* = 6.2, 2.3 Hz, 2H), 2.12 (s, 3H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 143.3, 136.5, 130.1, 129.6, 128.5, 127.0, 126.7, 124.6, 122.2, 111.5, 82.0, 58.0, 38.4, 28.0, 17.3. IR (neat, cm^{-1}): 3424, 2977, 1726, 1505, 1147, 690. Anal. Calcd. for $C_{20}H_{24}ClNO_2$: C, 69.45; H, 6.99, Found: C, 69.71; H, 6.96. $[\alpha]_D^{24}$ +14.7 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 88% ee: tR (minor) = 11.9 min, tR (major) = 18.0 min.



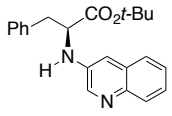
8j

Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a**, 221 mg, 1.00 mmol, 1.00 equiv), 3-acetylphenyl trifluoromethanesulfonate (**7j**, 268 mg, 1.00 mmol, 1 equiv), **P3** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography with a new column (eluting with 2% acetone–hexanes initially, grading to 20% acetone–hexanes, linear gradient) to afford **8j** as a yellow oil. Yield: 305 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.29 (m, 3H), 7.29–7.20 (m, 5H), 6.81 (ddd, *J* = 7.9, 2.6, 1.0 Hz, 1H), 4.43 (br s, 1H), 4.32 (t, *J* = 6.4 Hz, 1H), 3.14 (d, *J* = 6.1 Hz, 2H), 2.56 (s, 3H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 172.1, 147.0, 138.2, 136.5, 129.5, 129.4, 128.5, 127.0, 118.6, 118.5, 112.2, 82.1, 58.0, 38.6, 28.0, 26.7. IR (neat, cm^{-1}): 3361, 2977, 1725, 1679, 1601, 1149, 699. HRMS. Calcd. for $C_{21}H_{26}NO_3$, [M+H]: 340.1907, Found: [M+H]: 340.1920 $[\alpha]_D^{24}$ +3.1 (*c* 1.0, $CHCl_3$). HPLC analysis (AD-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 85% ee: tR (minor) = 13.9 min, tR (major) = 20.2 min.



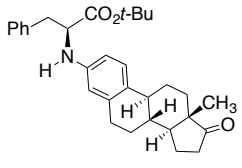
8k

Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a**, 221 mg, 1.00 mmol, 1.00 equiv), 4-(trifluoromethyl)phenyl trifluoromethanesulfonate (**7k**, 294 mg, 1.00 mmol, 1 equiv), **P3** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 2% ether–hexanes initially, grading to 20% ether–hexanes, linear gradient) to afford **8k** as a white solid. Yield: 283 mg, 77%. mp = 80–81 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.5 Hz, 2H), 7.37–7.25 (m, 3H), 7.25–7.19 (m, 2H), 6.63 (d, *J* = 8.5 Hz, 2H), 4.57 (br s, 1H), 4.31 (t, *J* = 6.2 Hz, 1H), 3.15 (dd, *J* = 6.2, 3.4 Hz, 2H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 149.2, 136.3, 129.6, 128.6, 127.2, 126.8 (q, *J* = 3.0 Hz), 125.0 (q, *J* = 270.0 Hz), 119.8 (q, *J* = 30.0 Hz), 112.7, 82.4, 57.6, 38.5, 28.1. ^{19}F NMR (375 MHz, $CDCl_3$) –61.12. IR (neat, cm^{-1}): 3382, 2988, 1708, 1616, 1317, 1104. Anal. Calcd. for $C_{20}H_{22}F_3NO_2$: C, 65.74; H, 6.07, Found: C, 65.89; H, 6.03. $[\alpha]_D^{24}$ +16.4 (*c* 1.0, $CHCl_3$). HPLC analysis (OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 55% ee: tR (minor) = 18.4 min, tR (major) = 24.4 min.



8l

Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a**, 221 mg, 1.00 mmol, 1.00 equiv), 3-quinolinyl trifluoromethanesulfonate (**7l**, 277 mg, 1.00 mmol, 1 equiv), **P3** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 12% EtOAc–hexanes initially, grading to 100% EtOAc–hexanes, linear gradient) to afford **8l** as an orange oil. Yield: 241 mg, 69%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 2.8 Hz, 1H), 8.01–7.94 (m, 1H), 7.63–7.56 (m, 1H), 7.44 (dt, *J* = 6.0, 3.6 Hz, 2H), 7.36–7.23 (m, 5H), 7.03 (d, *J* = 2.8 Hz, 1H), 4.69 (d, *J* = 8.3 Hz, 1H), 4.37 (dt, *J* = 8.3, 6.3 Hz, 1H), 3.29–3.14 (m, 2H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 143.5, 142.4, 140.1, 136.3, 129.5, 129.3, 129.1, 128.5, 127.1, 127.0, 126.0, 125.3, 111.4, 82.4, 57.9, 38.2, 28.0. IR (neat, cm^{-1}): 3365, 2977, 1725, 1608, 1148, 732. HRMS. Calcd. for $C_{22}H_{25}N_2O_2$, [M+H]: 349.1911, Found: [M+H]: 349.1926 $[\alpha]_D^{24}$ +18.0 (*c* 1.0, $CHCl_3$). HPLC analysis (AD-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 97% ee: tR (minor) = 12.3 min, tR (major) = 25.7 min.

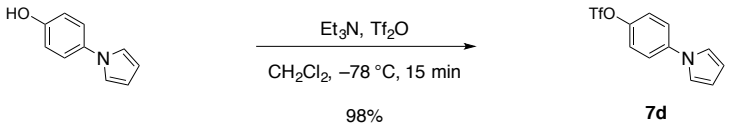


8m

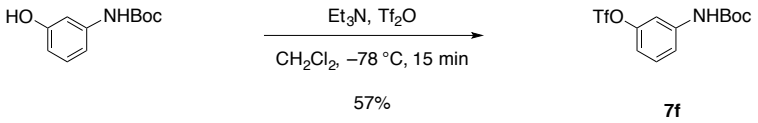
Following the general procedure, a mixture of L-Phe-O*t*-Bu (**5a**, 221 mg, 1.00 mmol, 1.00 equiv), estrone trifluoromethanesulfonate (**7m**, 402 mg, 1.00 mmol, 1 equiv), **P1** (43.0 mg, 50.0 μmol, 5.0 mol%), cesium carbonate (977 mg, 3.00 mmol, 3.00 equiv), and 2-methyltetrahydrofuran (2.00 mL) was stirred at 50 °C for 2 h. The crude product was purified by automated flash-column chromatography (eluting with 8% ether–hexanes initially, grading to 66% ether–hexanes, linear gradient) to afford **8m** as a clear oil. Yield: 463 mg, 98%. ^{1}H NMR (400 MHz, $CDCl_3$) δ

7.39–7.24 (m, 5H), 7.15–7.04 (m, 1H), 6.49 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.41 (d, *J* = 2.4 Hz, 1H), 4.26 (app t, *J* = 6.5 Hz, 2H), 3.13 (d, *J* = 6.4 Hz, 2H), 2.99–2.80 (m, 2H), 2.52 (dd, *J* = 18.8, 8.8 Hz, 1H), 2.45–2.34 (m, 1H), 2.28–1.95 (m, 5H), 1.74–1.46 (m, 6H), 1.42 (s, 9H), 0.94 (app d, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, *denotes rotamer, when observed) δ 220.6, 219.9*, 172.2, 147.4*, 144.5, 140.2*, 139.2*, 137.0, 136.7, 129.4 (2C), 128.1, 127.1*, 126.6, 126.0, 121.0*, 120.2*, 118.1*, 117.0*, 113.4, 111.4, 81.3, 58.1, 50.2, 50.1*, 47.8, 47.6*, 43.9*, 43.8, 38.7, 38.3, 37.5*, 36.5*, 35.7, 35.6*, 31.5, 31.3*, 29.5, 29.2*, 27.8, 26.5, 25.9*, 25.8, 25.5*, 21.4, 13.7, 13.6*. IR (neat, cm^{-1}): 3378, 2928, 1733, 1615, 1149, 732, 700. HRMS. Calcd. for $C_{31}H_{40}NO_3$, [M+H]: 474.3003, Found: [M+H]: 474.3016 $[\alpha]_D^{24}$ +77.7 (*c* 1.0, $CHCl_3$). The product **9m** prepared in this way was 19.6:1.0 d.r. [as determined by inverse-gated ^{13}C NMR (relaxation delay = 20 s)].

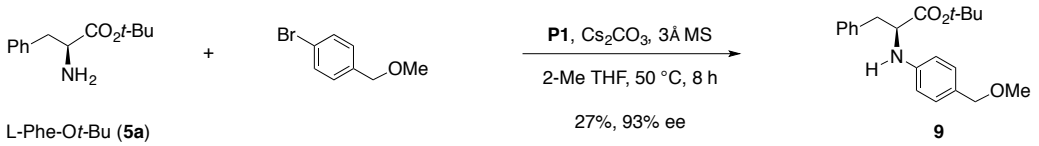
B) Preparation of Starting Materials



*Preparation of 4-(1H-pyrrol-1-yl)phenyl trifluoromethanesulfonate (**7d**):* Triethylamine (607 mg, 6.00 mmol, 1.20 equiv) and trifluoromethanesulfonic anhydride (1.55 g, 5.50 mmol, 1.10 equiv) were added in sequence to a solution of 4-(1*H*-pyrrol-1-yl)phenol (796 mg, 5.00 mmol, 1 equiv) in CH_2Cl_2 (30 mL) at –78 °C. The reaction mixture was stirred for 15 min at –78 °C. After warming to room temperature, the product mixture was transferred to a separatory funnel that had been charged with CH_2Cl_2 (20 mL). The diluted product mixture was washed with saturated aqueous sodium bicarbonate solution (50 mL). The aqueous layer was isolated and the isolated aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The organic layers were combined and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue obtained was purified by automated flash-column chromatography (eluting with 2% EtOAc–hexanes initially, grading to 20% EtOAc–hexanes, linear gradient) to afford 4-(1*H*-pyrrol-1-yl)phenyl trifluoromethanesulfonate (**7d**) as a white solid. Yield: 1.43g, 98%. mp = 49–51 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.42 (m, 2H), 7.39–7.33 (m, 2H), 7.09 (t, *J* = 2.2 Hz, 2H), 6.42 (t, *J* = 2.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 140.6, 122.7, 121.6, 119.4, 118.9 (q, *J* = 320.0 Hz), 111.5. ^{19}F NMR (375 MHz, $CDCl_3$) δ –72.74. IR (neat, cm^{-1}): 1515, 1426, 1207, 1133, 881, 835, 723, 605. Anal. Calcd. for $C_{11}H_8F_3NO_3S$: C, 45.36; H, 2.77, Found: C, 45.53; H, 2.86.

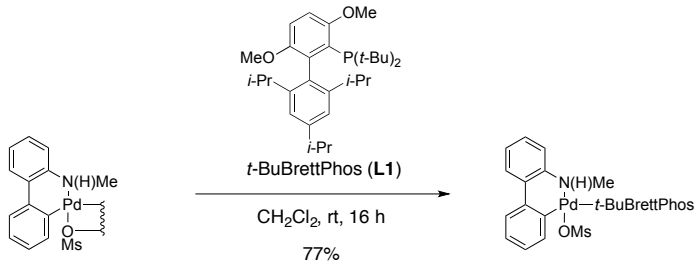


*Preparation of 3-((tert-butoxycarbonyl)amino)phenyl trifluoromethanesulfonate (**7f**):* Triethylamine (607 mg, 6.00 mmol, 1.20 equiv) and trifluoromethanesulfonic anhydride (1.55 g, 5.50 mmol, 1.10 equiv) were added in sequence to a solution of *N*-Boc-3-aminophenol (1.05 g, 5.00 mmol, 1 equiv) in CH_2Cl_2 (30 mL) at –78 °C. The reaction mixture was stirred for 15 min at –78 °C. After warming to room temperature, the product mixture was transferred to a separatory funnel that had been charged with CH_2Cl_2 (20 mL). The diluted product mixture was washed with saturated aqueous sodium bicarbonate solution (50 mL). The aqueous layer was isolated and the isolated aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The organic layers were combined and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue obtained was purified by automated flash-column chromatography (eluting with 5% EtOAc–hexanes initially, grading to 40% EtOAc–hexanes, linear gradient) to afford 3-((*tert*-butoxycarbonyl)amino)phenyl trifluoromethanesulfonate (**7f**) as a white solid. Yield: 1.16 g, 57%. mp = 74–76 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.32 (t, *J* = 8.2 Hz, 1H), 7.25 (d, *J* = 8.3 Hz, 1H), 7.01–6.90 (m, 2H), 1.54 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.5, 150.0, 140.6, 130.4, 118.8 (q, J = 320.0 Hz), 118.0, 115.3, 111.5, 81.5, 28.3. ^{19}F NMR (375 MHz, $CDCl_3$) –73.04. IR (neat, cm^{-1}): 3326, 2976, 1693, 1533, 1417, 1288, 1206, 1138. Anal. Calcd. for $C_{12}H_{14}F_3NO_5S$: C, 42.23; H, 4.13, Found: C, 42.49; H, 4.09.



L-Phe-O*t*-Bu (**5a**) **9**

*Preparation of the N-arylation product **9**:* A 25 mL screw-cap tube equipped with a stir bar and Teflon septum was charged sequentially with L-Phe-O*t*-Bu, (**5a**, 443 mg, 2.00 mmol, 1.00 equiv), 1-bromo-4-(methoxymethyl)benzene, (402 mg, 2.00 mmol, 1.00 equiv), **P1** (85.4 mg, 100 μmol, 5.0 mol%), and cesium carbonate (1.95 g, 6.00 mmol, 3.00 equiv). The reaction test tube was capped and then evacuated and backfilled with argon by piercing with a needle attached to a Schlenk line (this process was repeated a total of three times). 2-Methyltetrahydrofuran (4.00 mL) was added to the reaction test tube. The reaction test tube was placed in an oil bath that had been preheated to 50 °C. The reaction mixture was stirred and heated at 50 °C for 8 h. The reaction mixture was allowed to cool over 20 min to rt. The cooled product mixture was diluted with CH_2Cl_2 (5.00 mL). The diluted product mixture was filtered through Celite and concentrated. The residue obtained was purified by automated flash-column chromatography (eluting with 8% ether–hexanes initially, grading to 66% ether–hexanes, linear gradient) to afford **9** as a yellow oil. Yield: 186 mg, 27%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22–7.09 (m, 5H), 7.08–7.02 (m, 2H), 6.53–6.47 (m, 2H), 4.24 (s, 2H), 4.20–4.11 (m, 1H), 3.24 (s, 3H), 3.00 (d, J = 6.0 Hz, 2H), 1.25 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 146.3, 136.7, 129.6 (2 C), 128.4, 127.7, 126.9, 113.5, 81.8, 74.7, 58.2, 57.7, 38.6, 28.0. IR (neat, cm^{-1}): 3365, 2977, 1726, 1615, 1521, 1367, 1149, 1088, 699. Anal. Calcd. for $C_{21}H_{27}NO_3$: C, 73.87; H, 7.97, Found: C, 74.04; H, 7.88. $[\alpha]_D^{24}$ +24.4 (*c* 1.0, $CHCl_3$). HPLC analysis (OD-H, 10% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 93% ee: tR (minor) = 7.8 min, tR (major) = 10.6 min.

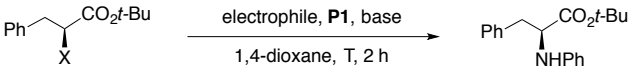


S1 **P3**

*Preparation of **P3** [Prepared from a modified literature procedure]*[1]: A 25 mL screw-cap tube equipped with a stir bar and Teflon septum was charged sequentially with *N*-methyl-2-aminobiphenylpalladium methanesulfonate dimer (**S1**) (384 mg, 0.50 mmol, 0.50 equiv), *t*-BuBrettPhos (**L1**) (485 mg, 1.00 mmol, 1.00 equiv), and CH_2Cl_2 (5.00 mL). The reaction mixture was stirred at rt for 16 h. The product mixture was concentrated, and pentane (25 mL) was added to precipitate the precatalyst, which was isolated via vacuum filtration and dried under vacuum overnight to provide **P3** as a yellow solid. Yield: 665 mg, 77%. ^{1}H NMR (400 MHz, CD_3OD) Complex Spectrum – See Attached. ^{13}C NMR (125 MHz, CD_3OD) δ 161.48, 160.98, 159.09, 155.70, 155.69, 153.00, 152.88, 151.93, 148.77, 146.26, 143.27, 141.87, 141.85, 140.60, 137.66, 137.62, 136.22, 129.91, 129.17, 128.94, 128.75, 128.72, 127.96, 126.83, 125.93, 125.36, 124.65, 122.73, 122.56, 122.54, 121.02, 119.94, 116.59, 116.58, 113.57, 113.54, 112.79, 56.72, 55.62, 55.29, 54.70, 41.02, 41.01, 40.72, 40.59, 40.55, 40.42, 39.50, 35.82, 35.48, 34.24, 33.05, 33.00, 32.59, 32.55, 32.44, 32.31, 31.72, 29.61, 29.59, 26.51, 26.11, 25.87, 25.36, 24.83, 24.74, 24.38, 24.19, 23.51 (observed complexity due to C–P splitting). ^{31}P NMR (162 MHz, CD_3OD) δ 79.03, 42.26, 41.84, 41.42, 32.61. IR (neat, cm^{-1}): 3222, 2960, 1575, 1456, 1421, 1250, 1144, 1037, 1017, 764, 740.

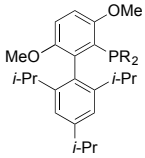
C) Reaction Optimization

Table S1. Summary of initial *N*-arylation experiments.

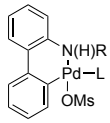


X = NH_2 L-Phe-O*t*-Bu (**5a**) **6a**
X = $NH_3^+Cl^-$ L-Phe-O*t*Bu•HCl (**5a•HCl**)

entry	amino acid ester	electrophile	base	T	yield[e]	ee[f]
1[a]	**5a•HCl**	PhBr	NaO*t*-Bu	rt	99%	0%
2[a]	**5a•HCl**	PhBr	NaOPh	70 °C	16%	41%
3[a]	**5a•HCl**	PhBr	Cs_2CO_3	70 °C	0%	–
4[b]	**5a**	PhBr	NaO*t*-Bu	rt	29%	0%
5[b]	**5a**	PhBr	NaOPh	70 °C	9%	72%
6[b]	**5a**	PhBr	Cs_2CO_3	70 °C	19%	73%
7[c]	**5a**	PhCl	Cs_2CO_3	70 °C	12%	78%
8[d]	**5a**	PhOTf	Cs_2CO_3	70 °C	61%	84%



R = *t*-Bu *t*-BuBrettPhos (**L1**)
R = Cy BrettPhos (**L2**)



R = H, L = L1 *t*-BuBrettPhos Pd G3 (**P1**)
R = Me, L = L2 Brett Phos Pd G4 (**P2**)
R = Me, L = L1 *t*-BuBrettPhos Pd G4 (**P3**)

[a] Reaction Conditions: L-Phe-O*t*-Bu•HCl (**5a•HCl**, 1.2 equiv), base (2.4 equiv), bromobenzene (1 equiv), **P1** (1 mol%). [b] Reaction Conditions: L-Phe-O*t*-Bu (**5a**, 1.2 equiv), base (1.2 equiv), bromobenzene (1 equiv), **P1** (1 mol%). [c] Reaction Conditions: L-Phe-O*t*-Bu (**5a**, 1.2 equiv), base (1.2 equiv), chlorobenzene (1 equiv), **P1** (1 mol%). [d] Reaction Conditions: L-Phe-O*t*-Bu (**5a**, 1.2 equiv), base (1.2 equiv), phenyl trifluoromethanesulfonate (1 equiv), **P1** (1 mol%). [e] Isolated yields. [f] Enantiomeric excess (ee) was determined by HPLC analysis using chiral stationary phases.

Procedure for entries 1–3: A 10 mL screw-cap tube equipped with a stir bar and Teflon septum was charged sequentially with L-Phe-O*t*-Bu•HCl (**5a•HCl**, 155 mg, 600 µmol, 1.20 equiv) and **P1** (4.3 mg, 5.0 µmol, 1.0 mol%). The reaction tube was transferred into a nitrogen-filled drybox. Base [sodium *tert*-butoxide (115 mg, 1.20 mol, 2.40 equiv), sodium phenoxide (139 mg, 1.20 mmol, 2.40 equiv) or cesium carbonate (391 mg, 1.20 mmol, 2.40 equiv)] was added and the reaction tube was sealed. The sealed reaction tube was removed from the drybox. The reaction test tube was evacuated and backfilled with argon by piercing with a needle attached to a Schlenk line (this process was repeated a total of three times). Bromobenzene (52.7 µL, 500 µmol, 1.00 equiv) and 1,4-dioxane (1.0 mL) were added sequentially to the reaction tube. The reaction mixture was stirred at rt for 2 h (entry 1) or stirred and heated at 70 °C for 2 h (entries 2 and 3). The reaction mixture was allowed to cool over 20 min to rt. The cooled product mixture was diluted with CH_2Cl_2 (3.00 mL). The diluted product mixture was filtered through Celite and concentrated to dryness. The crude product was purified by automated flash-column chromatography (eluting with 2% EtOAc–hexanes initially, grading to 20% EtOAc–hexanes, linear gradient) to afford **6a** as a white solid.

Procedure for entries 4–8: A 10 mL screw-cap tube equipped with a stir bar and Teflon septum was charged sequentially with L-Phe-O*t*-Bu (**5a**, 53.1 mg, 240 µmol, 1.20 equiv) and **P1** (1.7 mg, 2.0 µmol, 1.0 mol%). The reaction tube was transferred into a nitrogen-filled drybox. Base [sodium *tert*-butoxide (23.1 mg, 240 µmol, 1.20 equiv), sodium phenoxide (27.9 mg, 240 µmol, 1.20 equiv) or cesium carbonate (78.2 mg, 240 µmol, 1.20 equiv)] was added and the reaction tube was sealed. The sealed reaction tube was removed from the drybox. The reaction test tube

was evacuated and backfilled with argon by piercing with a needle attached to a Schlenk line (this process was repeated a total of three times). Electrophile [bromobenzene (21.1 μL, 200 μmol, 1.00 equiv), chlorobenzene (20.4 μL, 200 μmol, 1.00 equiv), or phenyl trifluoromethane sulfonate (32.4 μL, 200 μmol, 1.00 equiv)] and 1,4-dioxane (400 μL) were added sequentially to the reaction tube. The reaction mixture was stirred at rt for 2 h (entry 4) or stirred and heated at 70 °C for 2 h (entries 5–8). The reaction mixture was allowed to cool over 20 min to rt. The cooled product mixture was diluted with CH_2Cl_2 (3.00 mL). The diluted product mixture was filtered through Celite and concentrated to dryness. The crude product was purified by automated flash-column chromatography (eluting with 2% EtOAc–hexanes initially, grading to 20% EtOAc–hexanes, linear gradient) to afford **6a** as a white solid.

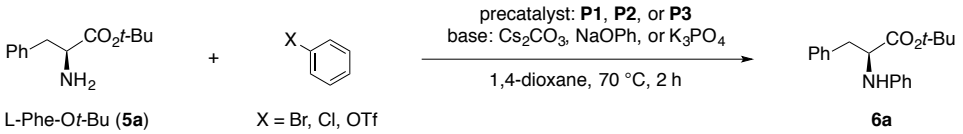
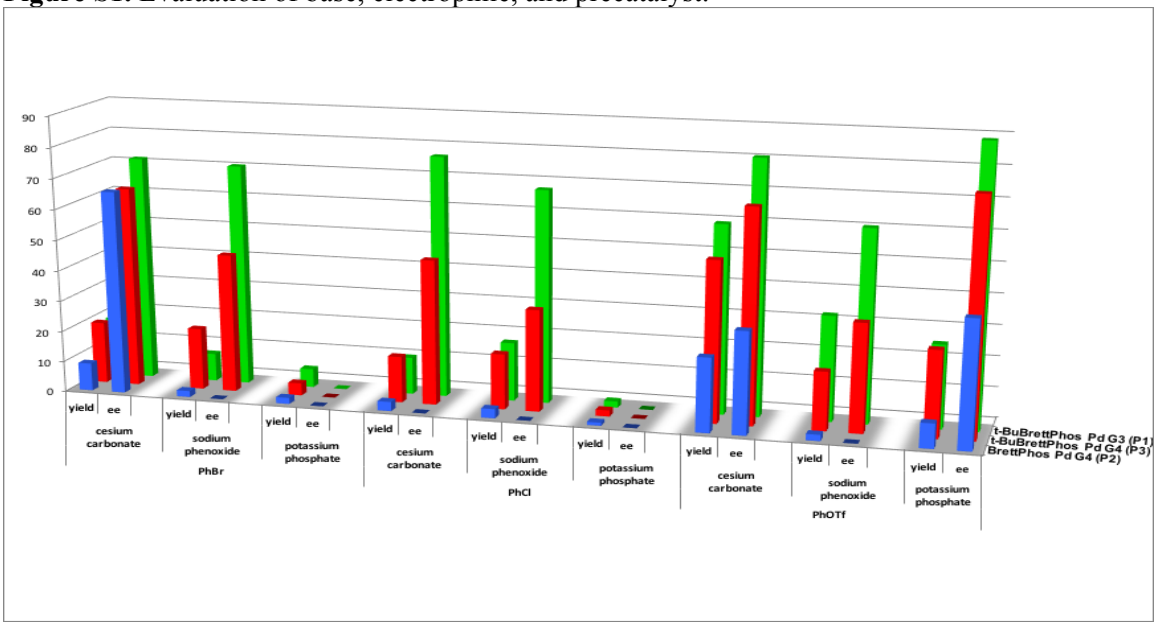


Figure S1. Evaluation of base, electrophile, and precatalyst.



Z axis: % yield and % ee for each reaction. Y axis: Green = reactions with precatalyst **P1**. Red = reactions with precatalyst **P3**. Blue = reactions with precatalyst **P2**. X axis: electrophile and base for each reaction. Optimal combination: cesium carbonate, phenyl trifluoromethanesulfonate, and precatalyst **P1** (61% yield, 84% ee).

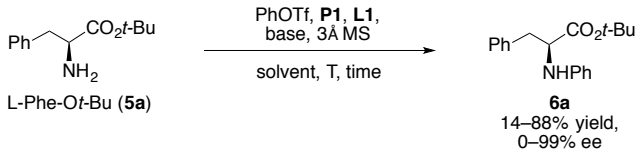
Procedure for Figure S1: A 10 mL screw-cap tube equipped with a stir bar and Teflon septum was charged sequentially with L-Phe-O*t*-Bu (**5a**, 53.1 mg, 240 µmol, 1.20 equiv) and precatalyst [**P1** (1.7 mg, 2.0 µmol, 1.0 mol%) or **P3** (2.1 mg, 2.0 µmol, 1.0 mol%) or **P2** (1.8 mg, 2.0 µmol, 1.0 mol%)]. The reaction tube was transferred into a nitrogen-filled drybox. Base [cesium carbonate (78.2 mg, 240 µmol, 1.20 equiv) or sodium phenoxide (27.9 mg, 240 µmol, 1.20 equiv) or potassium phosphate (50.9 mg, 240 µmol, 1.20 equiv)] was added and the reaction tube was sealed. The sealed reaction tube was removed from the drybox. The reaction test tube was evacuated and backfilled with argon by piercing with a needle attached to a Schlenk line (this process was repeated a total of three times). Electrophile [bromobenzene (21.1 µL, 200 µmol, 1.00 equiv) or chlorobenzene (20.4 µL, 200 µmol, 1.00 equiv) or phenyl trifluoromethanesulfonate (32.4 µL, 200 µmol, 1.00 equiv)] and 1,4-dioxane (400 µL) were added sequentially to the reaction tube. The reaction test tube was placed in an oil bath that had been preheated to 70 °C. The reaction mixture was stirred and heated at 70 °C for 2 h. The reaction mixture was allowed to cool over 20 min to rt. The cooled product mixture was diluted with CH_2Cl_2 (3.00 mL). The diluted product mixture was filtered through Celite and concentrated to dryness. The crude product was purified by automated flash-column chromatography (eluting with 2% EtOAc–hexanes initially, grading to 20% EtOAc–hexanes, linear gradient) to afford **6a** as a white solid.

D) Design of Experiment (DOE) Analysis

DOE analysis was carried out using JMP® Software.

Table 2. Summary of reaction optimization by DOE.[a] **A.** Initial analysis of eleven reaction variables.

A.



L-Phe-O*t*-Bu (**5a**) — **6a** 14–88% yield, 0–99% ee

variable	effect on yield	effect on ee	conclusion
ligand additive	0	0	omit
base treatment	0	0	omit
ratio **5a** : PhOTf	0	0	1 : 1
precatalyst loading	+	0	2 mol%
time	0	–	2 h
solvent (mL)	–	0	0.5 M
solvent	THF, 2-Me THF	dioxane, 2-Me THF	2-Me THF
T (°C)	+	–	optimize further
equiv base (to **5a**)	+	–	optimize further
3Å MS	–	+	optimize further
base	Cs_2CO_3 (minor)	K_3PO_4 (minor)	optimize further

[a] For categorical variables, highest yield/ee obtained with listed entry. For continuous variables: 0 = variable has no effect on yield/ee, + = highest yield/ee obtained at highest value of variable, – = highest yield/ee obtained at lowest value of variable.

Variable Legend:
ligand additive: 0 (none added), 1 (added same mol% as the mol% precatalyst in reaction)
precatalyst loading (mol%): 1 or 5
solvent volume (mL): 1 or 5
T (°C) = 50 or 90
time (h) = 2 or 12
3 Å MS: 0 (none added) or 1 (50 mg added)
base: K_3PO_4 or Cs_2CO_3
base treatment: no treatment or finely ground
ratio **5a** to phenyl trifluoromethanesulfonate: 0.83 or 1.2
equiv base (to **5a**): 1 or 3
solvent: 1,4-dioxane, 2-methyltetrahydrofuran, or THF

Table S2: Reactions run in initial DOE analysis.

Pattern	ligand additive (mol%)	catalyst loading (mol%)	volume (mL)	T (C)	time (h)	3A MS (mg)	base	base treatment	ratio AA : PhOTf	equiv base (to AA)	solvent	Yield	ee
----------	0	1	1	50	2	0	K3PO4	bottle	0.83	1	dioxane	40	97
---------0	0	1	1	50	2	0	K3PO4	bottle	0.83	1	THF	17	97
---------+	0	1	1	50	2	0	K3PO4	bottle	0.83	1	2-MeTHF	42	96
++++++++++	1	5	5	50	12	1	K3PO4	finely ground	0.83	1	dioxane	23	88
-+++-----+-	0	5	5	50	12	0	K3PO4	bottle	1.2	3	dioxane	82	66
-+++-----++0	0	5	5	50	12	0	K3PO4	bottle	1.2	3	THF	51	79
+++-++++---0	1	5	5	50	12	1	K3PO4	finely ground	0.83	1	THF	39	79
+++-++++---+	1	5	5	50	12	1	K3PO4	finely ground	0.83	1	2-MeTHF	25	92
-++-+----+++	0	5	5	50	12	0	K3PO4	bottle	1.2	3	2-MeTHF	61	81
++-+---++--	1	1	5	50	2	0	Cs2CO3	finely ground	1.2	1	dioxane	23	98
-+----++++-	0	5	1	50	2	1	Cs2CO3	finely ground	0.83	3	dioxane	30	98
-+----++++0	0	5	1	50	2	1	Cs2CO3	finely ground	0.83	3	THF	85	87
++-+----+++0	1	1	5	50	2	0	Cs2CO3	finely ground	1.2	1	THF	34	99
++-+----++++	1	1	5	50	2	0	Cs2CO3	finely ground	1.2	1	2-MeTHF	17	98
-+----++++++	0	5	1	50	2	1	Cs2CO3	finely ground	0.83	3	2-MeTHF	88	89
+----+++-++-	1	1	1	50	12	1	Cs2CO3	bottle	1.2	3	dioxane	16	89
+----+++-++0	1	1	1	50	12	1	Cs2CO3	bottle	1.2	3	THF	59	41
+----+++-+++	1	1	1	50	12	1	Cs2CO3	bottle	1.2	3	2-MeTHF	26	62
++-+----++--	1	5	1	90	2	0	K3PO4	finely ground	1.2	3	dioxane	79	56
++-++-----+-	1	1	5	90	2	1	K3PO4	bottle	0.83	3	dioxane	28	70
++-++-----+0	1	1	5	90	2	1	K3PO4	bottle	0.83	3	THF	26	67
++-+----++++	1	5	1	90	2	0	K3PO4	finely ground	1.2	3	THF	78	45
++-+----++++	1	5	1	90	2	0	K3PO4	finely ground	1.2	3	2-MeTHF	83	59
+-++-----++-	1	1	5	90	2	1	K3PO4	bottle	0.83	3	2-MeTHF	26	70
---++-++---	0	1	1	90	12	1	K3PO4	finely ground	1.2	1	dioxane	14	52
---++-++-0	0	1	1	90	12	1	K3PO4	finely ground	1.2	1	THF	31	51
---++-++-+	0	1	1	90	12	1	K3PO4	finely ground	1.2	1	2-MeTHF	28	39
-++-++-+--	0	5	5	90	2	1	Cs2CO3	bottle	1.2	1	dioxane	51	74
-++-++-+-0	0	5	5	90	2	1	Cs2CO3	bottle	1.2	1	THF	41	85
-++-++-+-+	0	5	5	90	2	1	Cs2CO3	bottle	1.2	1	2-MeTHF	37	86
++-++-+----	1	5	1	90	12	0	Cs2CO3	bottle	0.83	1	dioxane	81	32
---++-++-+-	0	1	5	90	12	0	Cs2CO3	finely ground	0.83	3	dioxane	54	4
++-++-+---0	1	5	1	90	12	0	Cs2CO3	bottle	0.83	1	THF	83	1
---++-++-+0	0	1	5	90	12	0	Cs2CO3	finely ground	0.83	3	THF	53	0
++-++-+---+	1	5	1	90	12	0	Cs2CO3	bottle	0.83	1	2-MeTHF	80	61
---++-++-++	0	1	5	90	12	0	Cs2CO3	finely ground	0.83	3	2-MeTHF	67	4

Figure S2: Statistical analysis of 11 reaction variables.

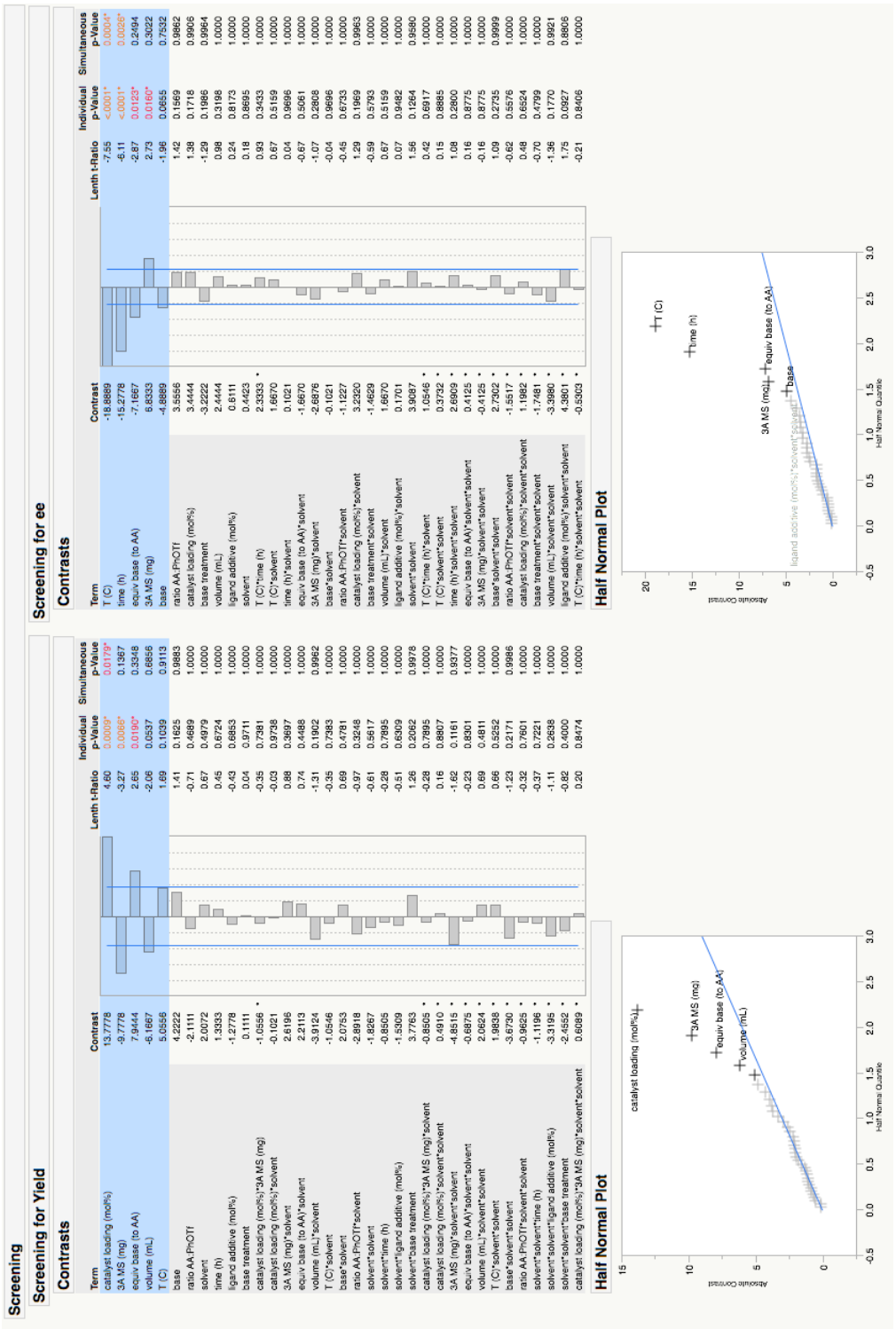
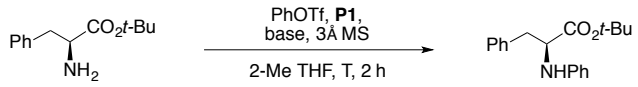


Table 2. Summary of reaction optimization by DOE.[a] **B.** Subsequent analysis of four reaction variables.

B.



L-Phe-O*t*-Bu (**5a**) — **6a** 18–88% yield, 61–99% ee

variable	effect on yield	effect on ee	conclusion
T (°C)	+	–	optimize further
equiv base (to **5a**)	+	–	optimize further
3Å MS	–	+ (minor)	omit
base	Cs_2CO_3	0	Cs_2CO_3

[a] For categorical variables, highest yield/ee obtained with listed entry. For continuous variables: 0 = variable has no effect on yield/ee, + = highest yield/ee obtained at highest value of variable, – = highest yield/ee obtained at lowest value of variable.

Variable Legend:
T (°C) = 50, 60, or 70
equiv base (to **5a**): 1 or 3
3 Å MS (mg): 0 or 50
base: K_3PO_4 or Cs_2CO_3

Table S3. Subset of reactions from subsequent DOE analysis.

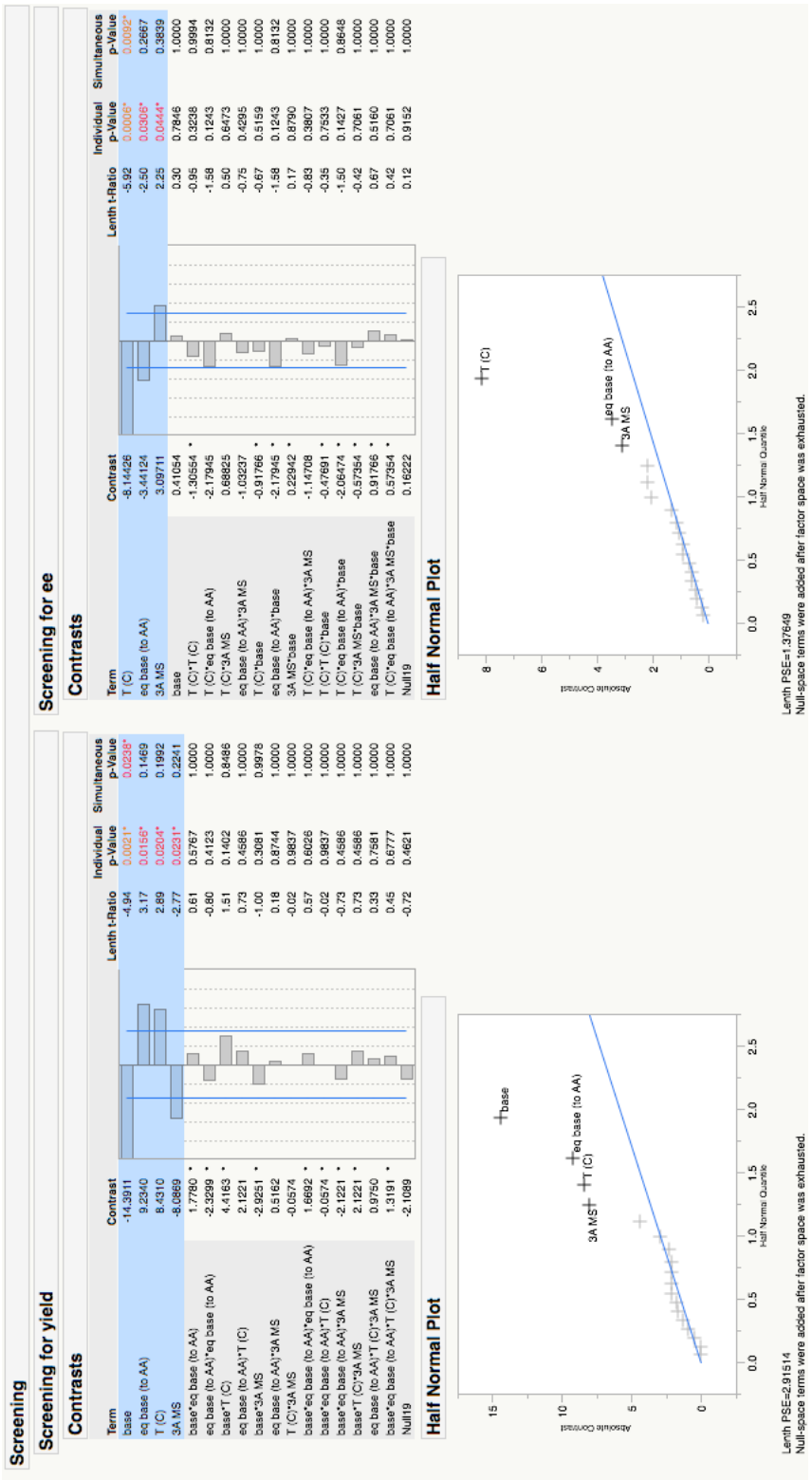
					2 mol% precatalyst		**5 mol% precatalyst**	
entry	**T**	**base**	**equiv base (to 5a)**	**3 Å MS**	**yield**	**ee**	**yield**	**ee**
1	50 °C	Cs_2CO_3	1	0 mg	64%	91%	89%	94%
2	50 °C	Cs_2CO_3	1	50 mg	51%	95%	80%	92%
3	50 °C	Cs_2CO_3	3	0 mg	69%	89%	93%	91%
4	50 °C	Cs_2CO_3	3	50 mg	69%	92%	95%	94%

Yellow indicates optimized reaction conditions.

Table S4: Reactions run in subsequent DOE analysis.

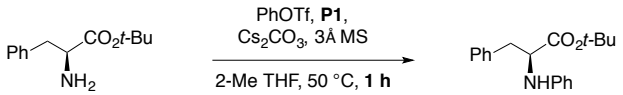
Pattern	T (C)	eq base (to AA)	3A MS	base	yield	ee
−+++	50	3	50	K3PO4	18	97
−−+−	50	1	50	Cs2CO3	51	95
−−−+	50	1	0	K3PO4	27	93
−++−	50	3	50	Cs2CO3	69	92
−−++	50	1	50	K3PO4	7	99
−+−−	50	3	0	Cs2CO3	69	89
−+−+	50	3	0	K3PO4	55	89
−−−−	50	1	0	Cs2CO3	64	91
000−	60	2	25	Cs2CO3	71	86
000+	60	2	25	K3PO4	41	90
000−	60	2	25	Cs2CO3	84	87
++++	70	3	50	K3PO4	60	67
+−−+	70	1	0	K3PO4	51	81
+++−	70	3	50	Cs2CO3	77	75
+−+−	70	1	50	Cs2CO3	51	86
++−−	70	3	0	Cs2CO3	88	74
+−−−	70	1	0	Cs2CO3	72	69
++−+	70	3	0	K3PO4	78	61
+−++	70	1	50	K3PO4	30	90

Figure S3: Statistical analysis of four reaction variables.



E) Experiments to Determine Mechanism of Racemization

A.



L-Phe-O*t*-Bu (**5a**) **6a**

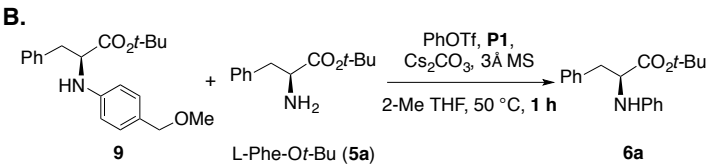
	ee before reaction	ee after reaction[a]
5a	99%	81%
6a	–	97%

[a] Enantiomeric excess (ee) was determined directly from the crude reaction mixture by HPLC analysis using chiral stationary phases.

Scheme 3. A. Experiment determining the enantiomeric excess before and after the reaction.

Procedure for Scheme 3A: A 10 mL screw-cap tube equipped with a stir bar and Teflon septum was charged sequentially with L-Phe-O*t*-Bu (**5a**, 111 mg, 500 μmol, 1.00 equiv), **P1** (21.4 mg, 30.0 μmol, 5.0 mol%), and activated 3Å MS (50.0 mg). The reaction tube was transferred into a nitrogen-filled drybox. Cesium carbonate (489 mg, 1.50 mmol, 3.00 equiv) was added and the reaction tube was sealed. The sealed reaction tube was removed from the drybox. The reaction test tube was evacuated and backfilled with argon by piercing with a needle attached to a Schlenk line (this process was repeated a total of three times). Phenyl trifluoromethanesulfonate (81.0 μL, 500 μmol, 1.00 equiv) and 2-methyltetrahydrofuran (1.00 mL) were added sequentially to the reaction tube. The reaction test tube was placed in an oil bath that had been preheated to 50 °C. The reaction mixture was stirred and heated at 50 °C for 1 h. The reaction mixture was allowed to cool over 20 min to rt. The cooled product mixture was diluted with CH_2Cl_2 (5.00 mL). The diluted product mixture was filtered through Celite and concentrated to dryness. The crude product mixture was analyzed by HPLC. The crude product mixture was then purified by automated flash-column chromatography (eluting with 8% ether–hexanes initially, grading to 100% ether–hexanes, linear gradient, followed by elution with 1% MeOH–ether, grading to 10% MeOH–ether, linear gradient) to afford **6a** as a white solid. Yield: 116 mg, 78%.

B.

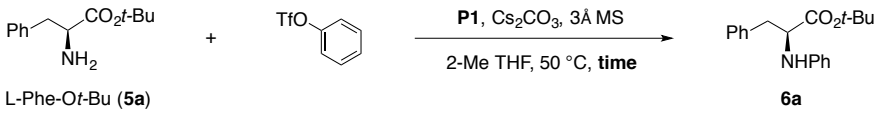


	ee before reaction	ee after reaction[a]
9	93%	93%
5a	99%	81%
6a	–	93%

[a] Enantiomeric excess (ee) was determined after purification by silica gel chromatography.

Scheme 3. B. Experiment to test for product racemization with exogenous and different product added.

Procedure for Scheme 3B: A 10 mL screw-cap tube equipped with a stir bar and Teflon septum was charged sequentially with the *N*-arylation product **9**, (85.4 mg, 250 μmol, 1.00 equiv), L-Phe-O*t*-Bu (**5a**, 55.3 mg, 250 μmol, 1.00 equiv), **P1** (10.7 mg, 10.0 μmol, 5.0 mol%), and activated 3Å MS (25.0 mg). The reaction tube was transferred into a nitrogen-filled drybox. Cesium carbonate (244 mg, 750 μmol, 3.00 equiv) was added and the reaction tube was sealed. The sealed reaction tube was removed from the drybox. The reaction test tube was evacuated and backfilled with argon by piercing with a needle attached to a Schlenk line (this process was repeated a total of three times). Phenyl trifluoromethanesulfonate (40.5 μL, 250 μmol, 1.00 equiv) and 2-methyltetrahydrofuran (1.00 mL) were added sequentially to the reaction tube. The reaction test tube was placed in an oil bath that had been preheated to 50 °C. The reaction mixture was stirred and heated at 50 °C for 1 h. The reaction mixture was allowed to cool over 20 min to rt. The cooled product mixture was diluted with CH_2Cl_2 (5.00 mL). The diluted product mixture was filtered through Celite and concentrated to dryness. The residue obtained was purified by automated flash-column chromatography (eluting with 8% ether–hexanes initially, grading to 100% ether–hexanes, linear gradient, followed by elution with 1% MeOH:ether, grading to 10% MeOH–ether, linear gradient) to afford **9** as a yellow oil (85.3 mg, 99% recovered), L-Phe-O-*t*-Bu (**5a**) as a yellow oil (19.7 mg, 36% recovered), and **6a** as a white solid (43.1 mg, 58%).



L-Phe-O*t*-Bu (**5a**) **6a**

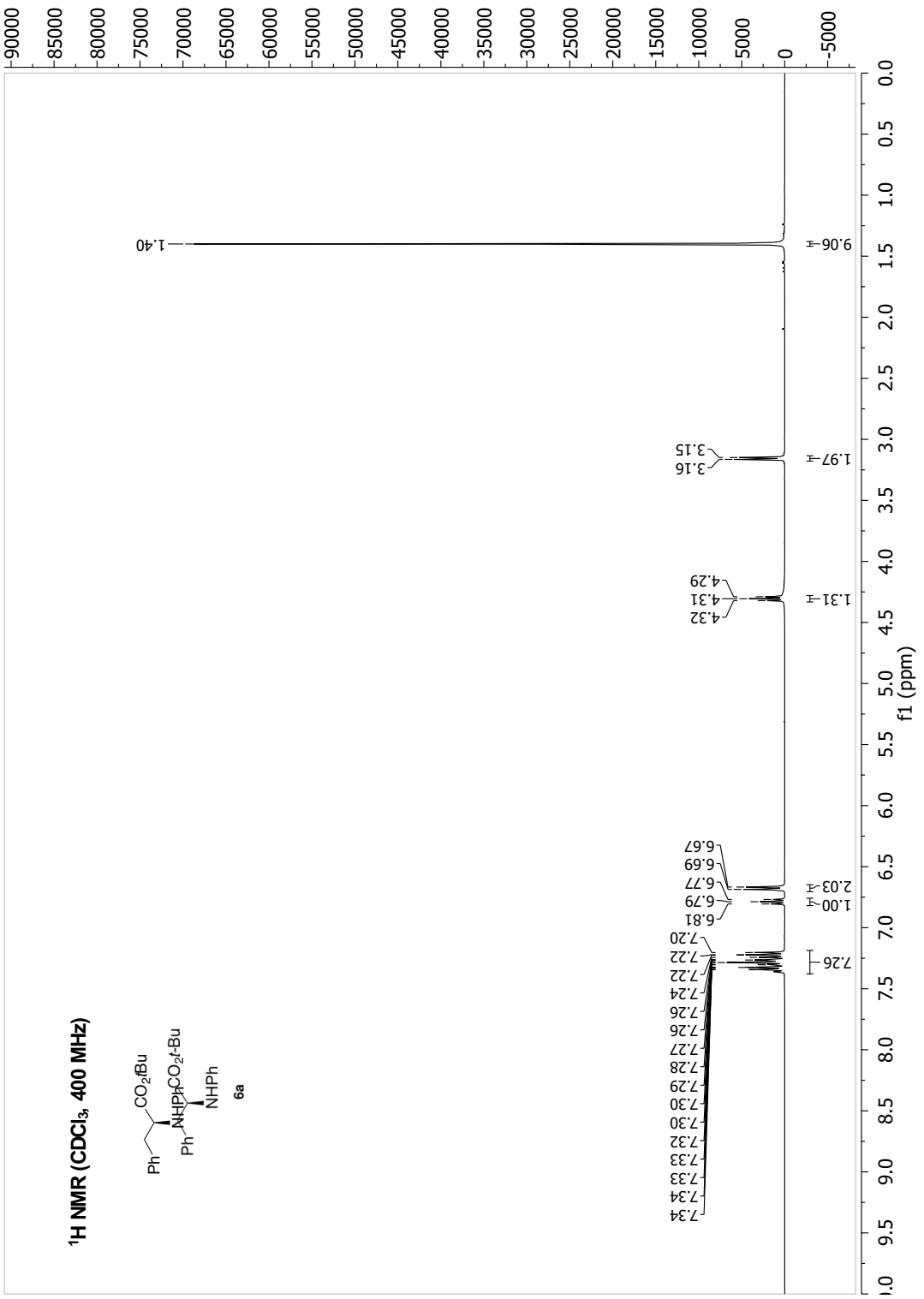
Table S5. Evaluation of yield and ee over reaction time.

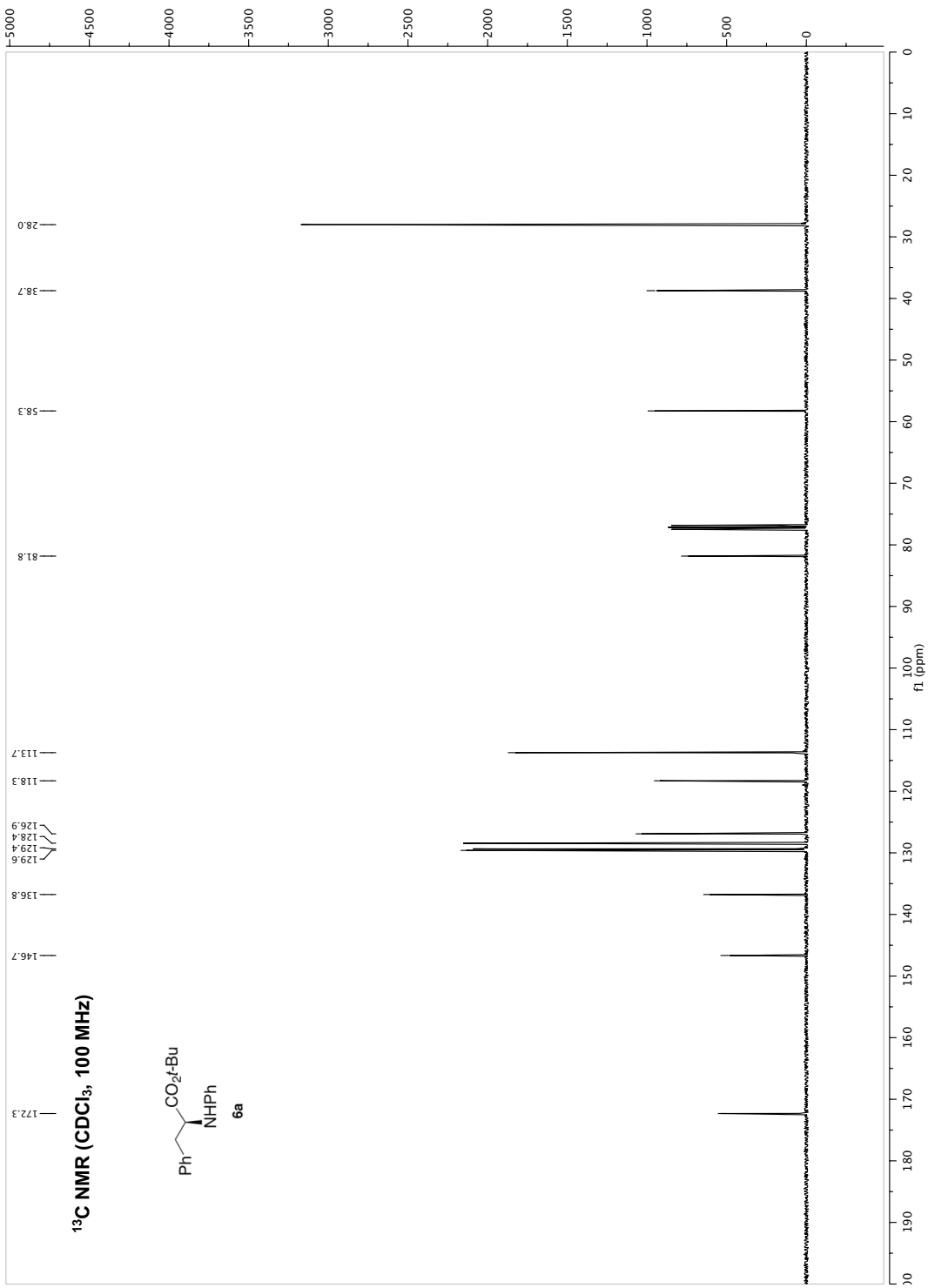
entry	time	yield	ee
1	30 min	67%	98%
2	1 h	73%	97%
3	1.5 h	90%	95%
4	2 h	92%	95%
5	4 h	96%	93%
6	16 h	99%	88%
7	10 d	91%	10%

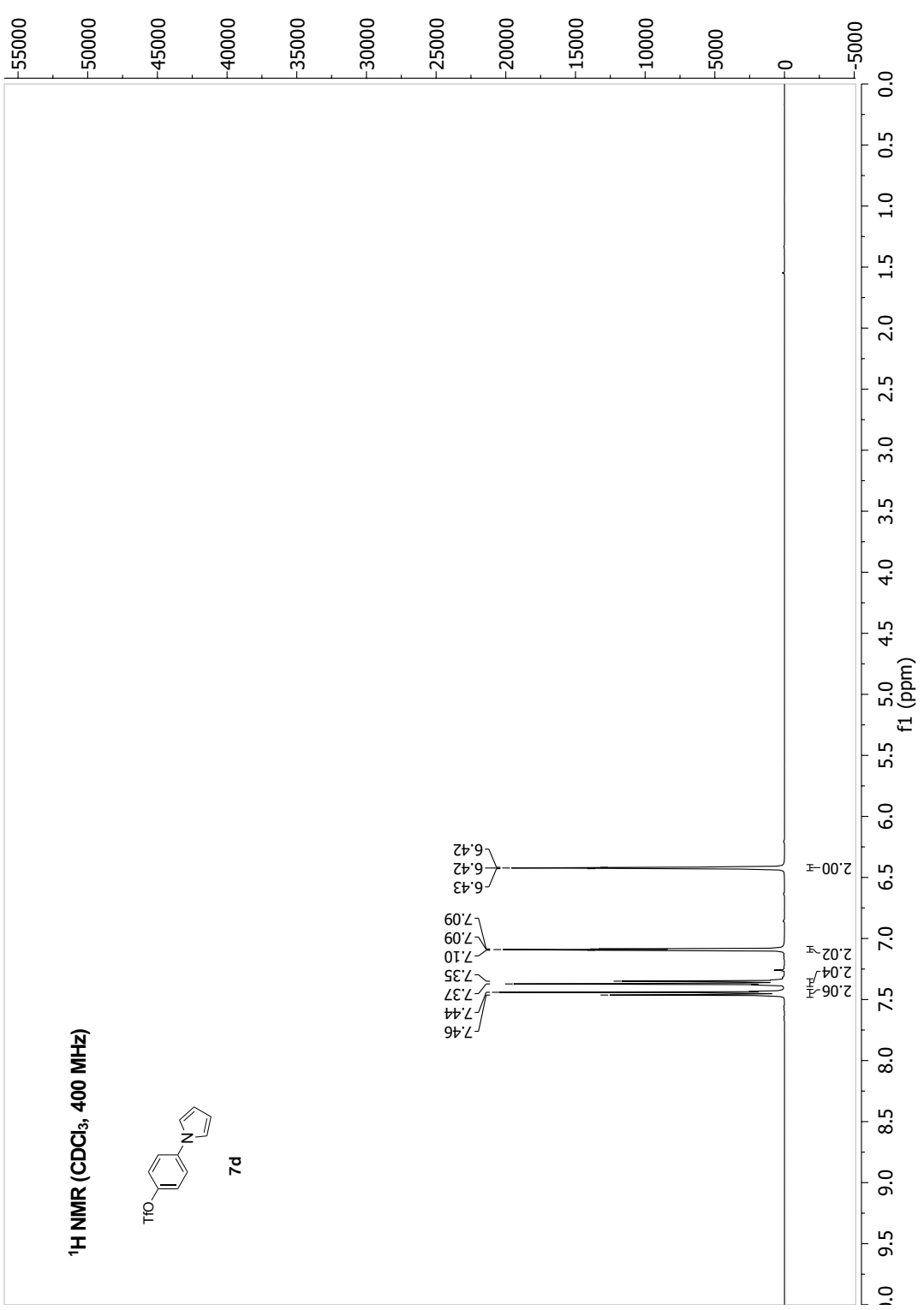
Procedure for Table S5: A 10 mL screw-cap tube equipped with a stir bar and Teflon septum was charged sequentially with L-Phe-O*t*-Bu (**5a**, 111 mg, 500 μmol, 1.00 equiv), **P1** (21.4 mg, 30.0 μmol, 5.0 mol%), and activated 3Å MS (50.0 mg). The reaction tube was transferred into a nitrogen-filled drybox. Cesium carbonate (489 mg, 1.50 mmol, 3.00 equiv) was added and the reaction tube was sealed. The sealed reaction tube was removed from the drybox. The reaction test tube was evacuated and backfilled with argon by piercing with a needle attached to a Schlenk line (this process was repeated a total of three times). Phenyl trifluoromethanesulfonate (81.0 μL, 500 μmol, 1.00 equiv) and 2-methyltetrahydrofuran (1.00 mL) were added sequentially to the reaction tube. The reaction test tube was placed in an oil bath that had been preheated to 50 °C. The reaction mixture was stirred and heated at 50 °C for the indicated time. The reaction mixture was allowed to cool over 20 min to rt. The cooled product mixture was diluted with CH_2Cl_2 (5.00 mL). The diluted product mixture was filtered through Celite and concentrated to dryness. The crude product was purified by automated flash-column chromatography (eluting with 2% EtOAc–hexanes initially, grading to 20% EtOAc–hexanes, linear gradient) to afford **6a** as a white solid.

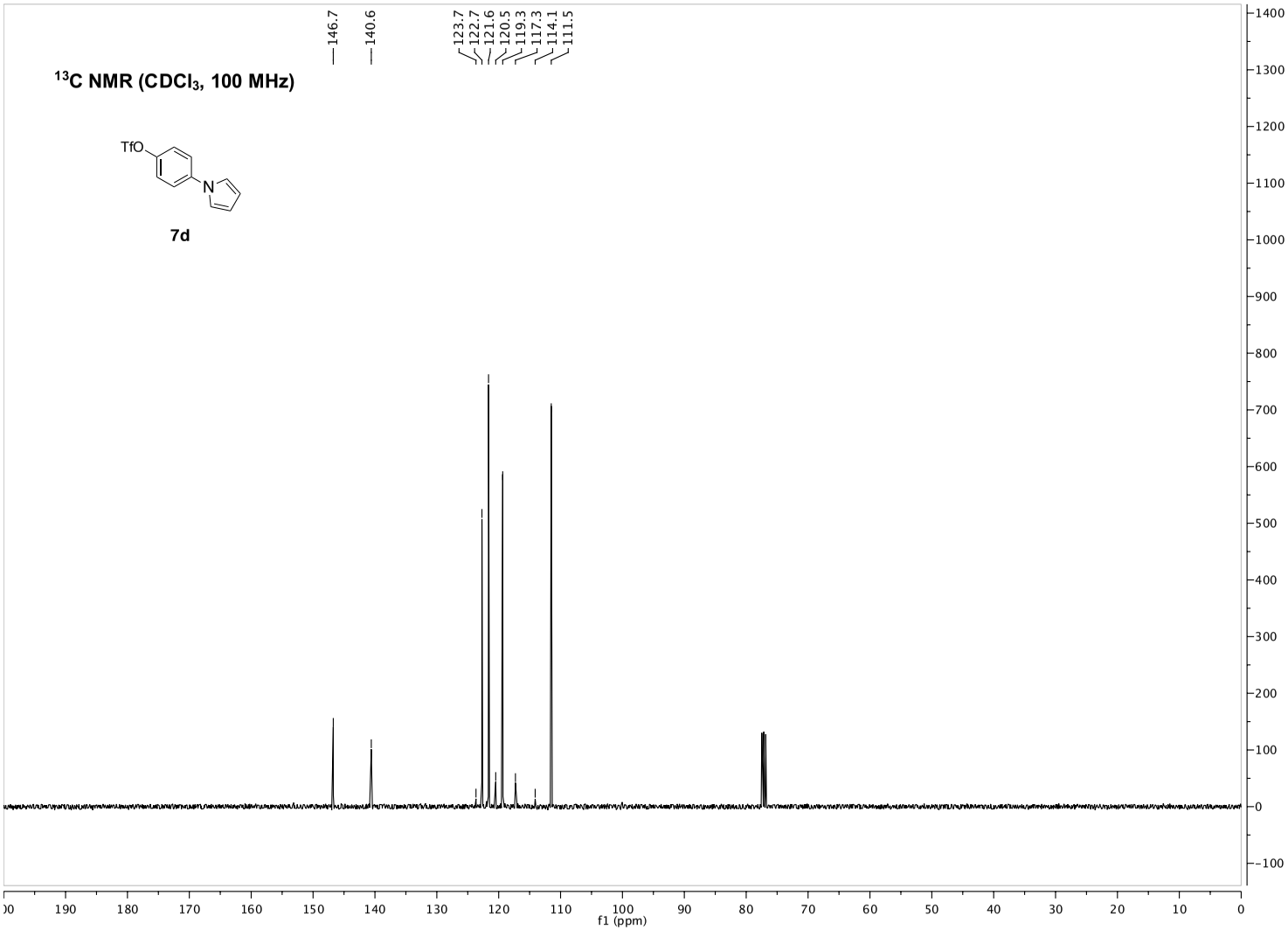
III. Catalog of Spectra

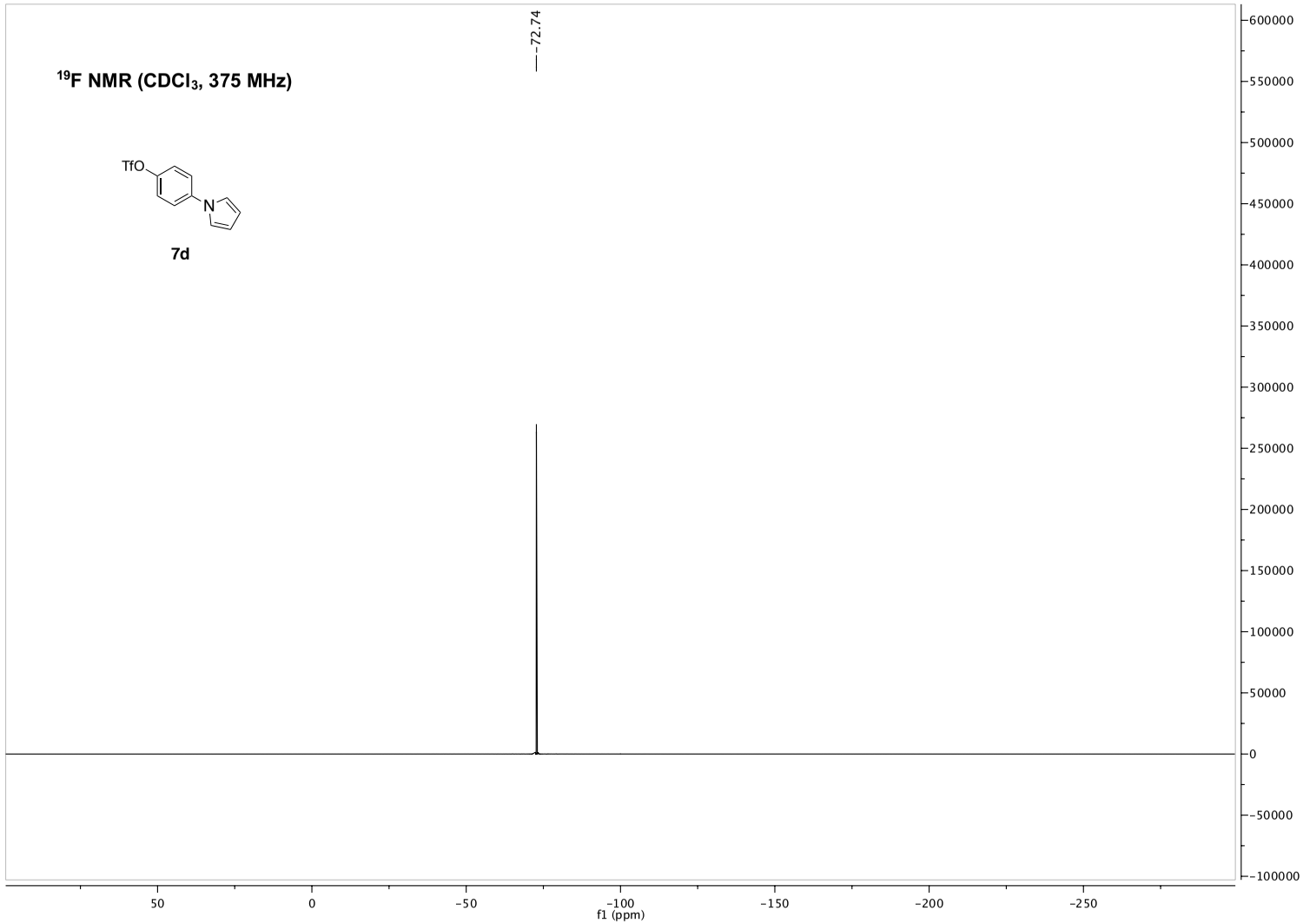
A) Catalog of NMR Spectra

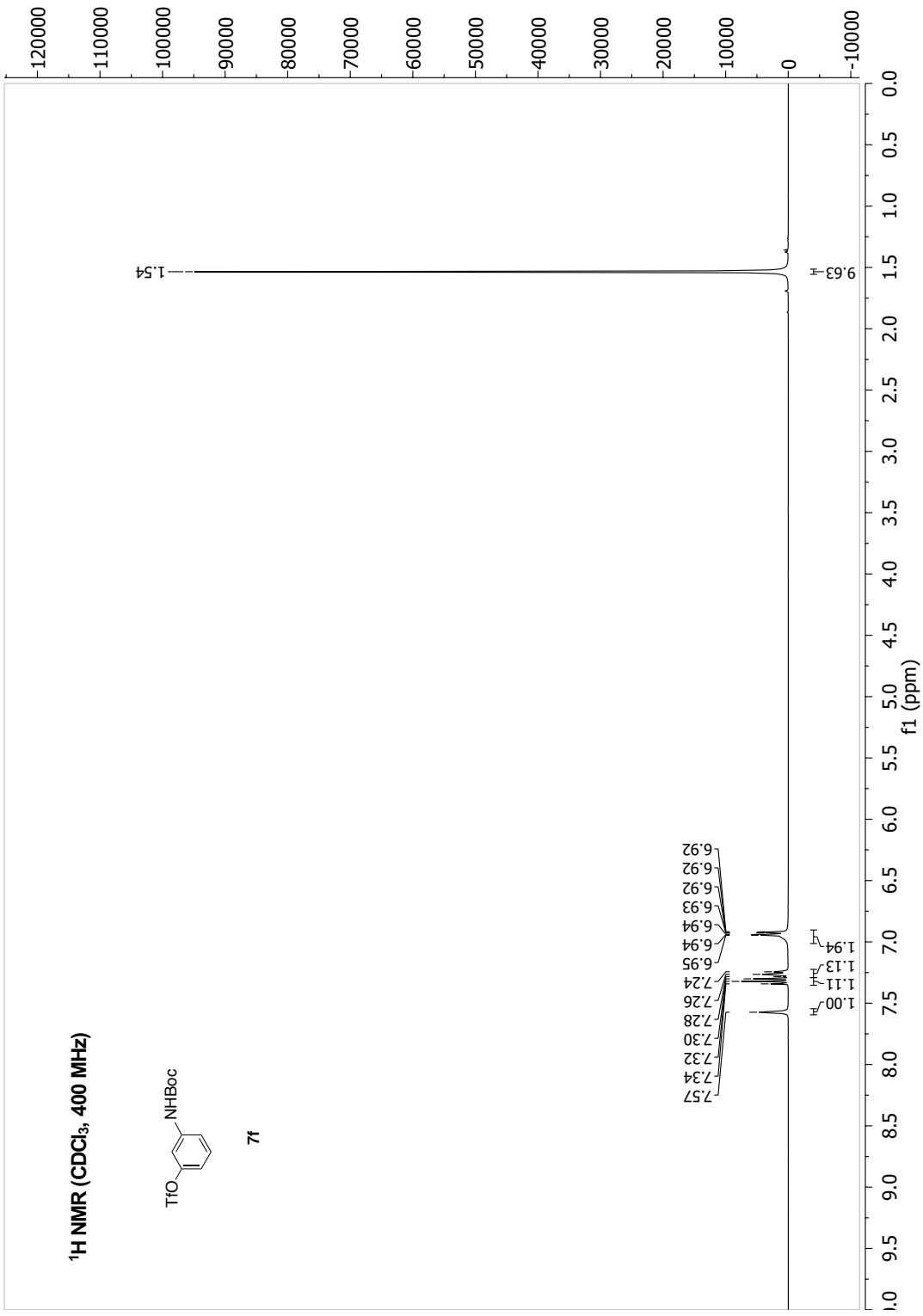


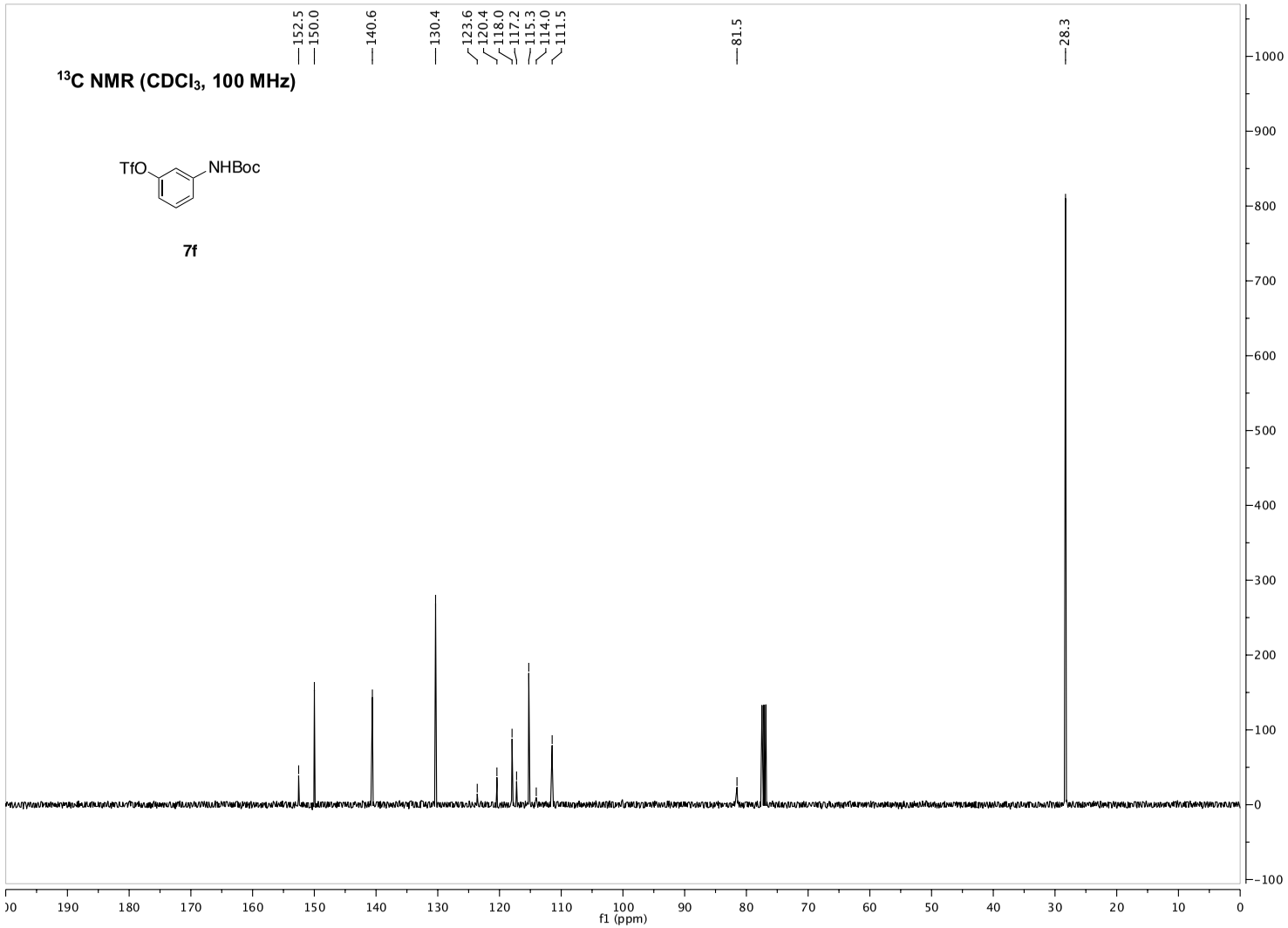

13C NMR (CDCl3, 100 MHz)
Ph
NHPh
CO2t-Bu
6a
172.3
146.7
136.8
129.6
129.4
128.4
126.9
118.3
113.7
81.8
58.3
38.7
28.0
f1 (ppm)

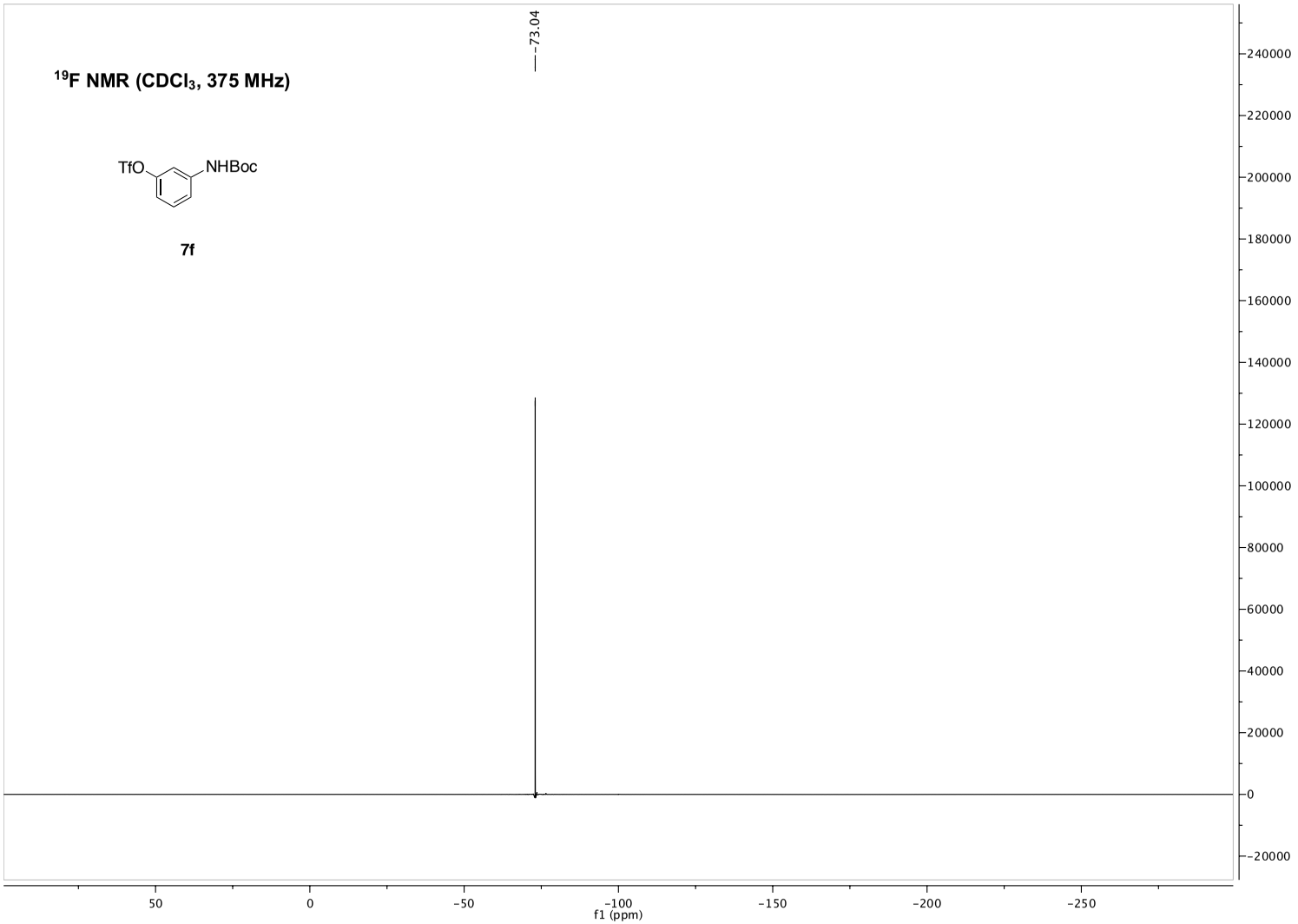

1H NMR (CDCl3, 400 MHz)
TfO
7d
p2
7.46
7.44
7.37
7.35
7.10
7.09
6.43
6.42
6.42
2.06
2.04
2.02
2.00
f1 (ppm)

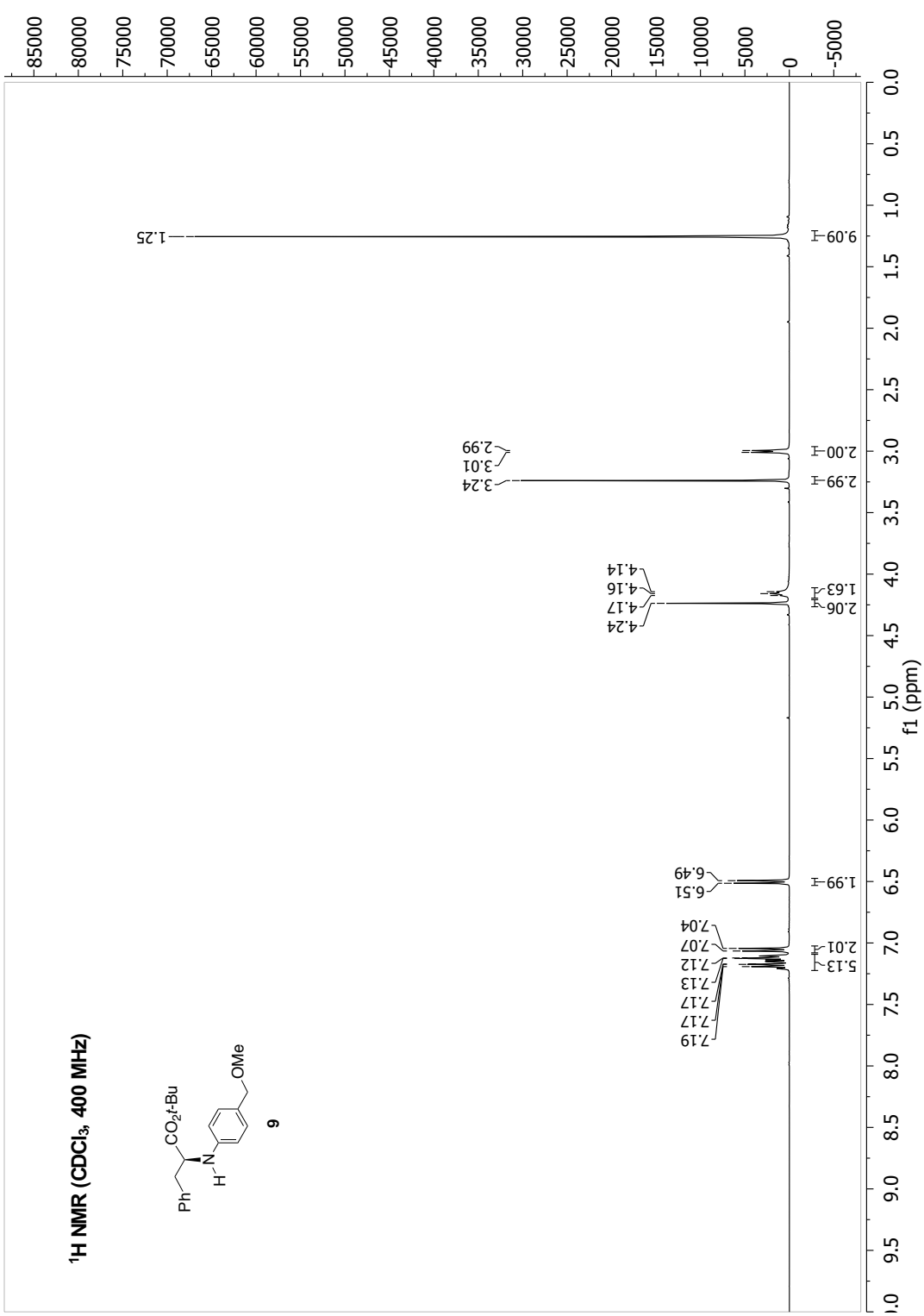

146.7
140.6
123.7
122.7
121.6
120.5
119.3
117.3
114.1
111.5
^{13}C NMR ($CDCl_3$, 100 MHz)
TfO
N
7d
f1 (ppm)


^{19}F NMR (CDCl$_3$, 375 MHz)
TfO
N
7d
-72.74
600000
550000
500000
450000
400000
350000
300000
250000
200000
150000
100000
50000
0
-50000
-100000
50
0
-50
-100
-150
-200
-250
f1 (ppm)


^{1}H NMR ($CDCl_3$, 400 MHz)
NHBoc
TfO
7f
1.54
9.63
7.57
7.34
7.32
7.30
7.28
7.26
7.24
6.95
6.94
6.94
6.93
6.92
6.92
6.92
1.94
1.13
1.11
1.00
f1 (ppm)


152.5
150.0
140.6
130.4
123.6
120.4
118.0
117.2
115.3
114.0
111.5
81.5
28.3
^{13}C NMR ($CDCl_3$, 100 MHz)
TfO
NHBoc
7f
f1 (ppm)


^{19}F NMR ($CDCl_3$, 375 MHz)
TfO
NHBoc
7f
-73.04
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000
50
0
-50
-100
-150
-200
-250
f1 (ppm)


^{1}H NMR ($CDCl_3$, 400 MHz)
Ph
CO_2t-Bu
N
H
OMe
9
1.25
9.09
3.24
3.01
2.99
2.00
2.99
4.24
4.17
4.16
4.14
2.06
1.63
1.99
6.51
6.49
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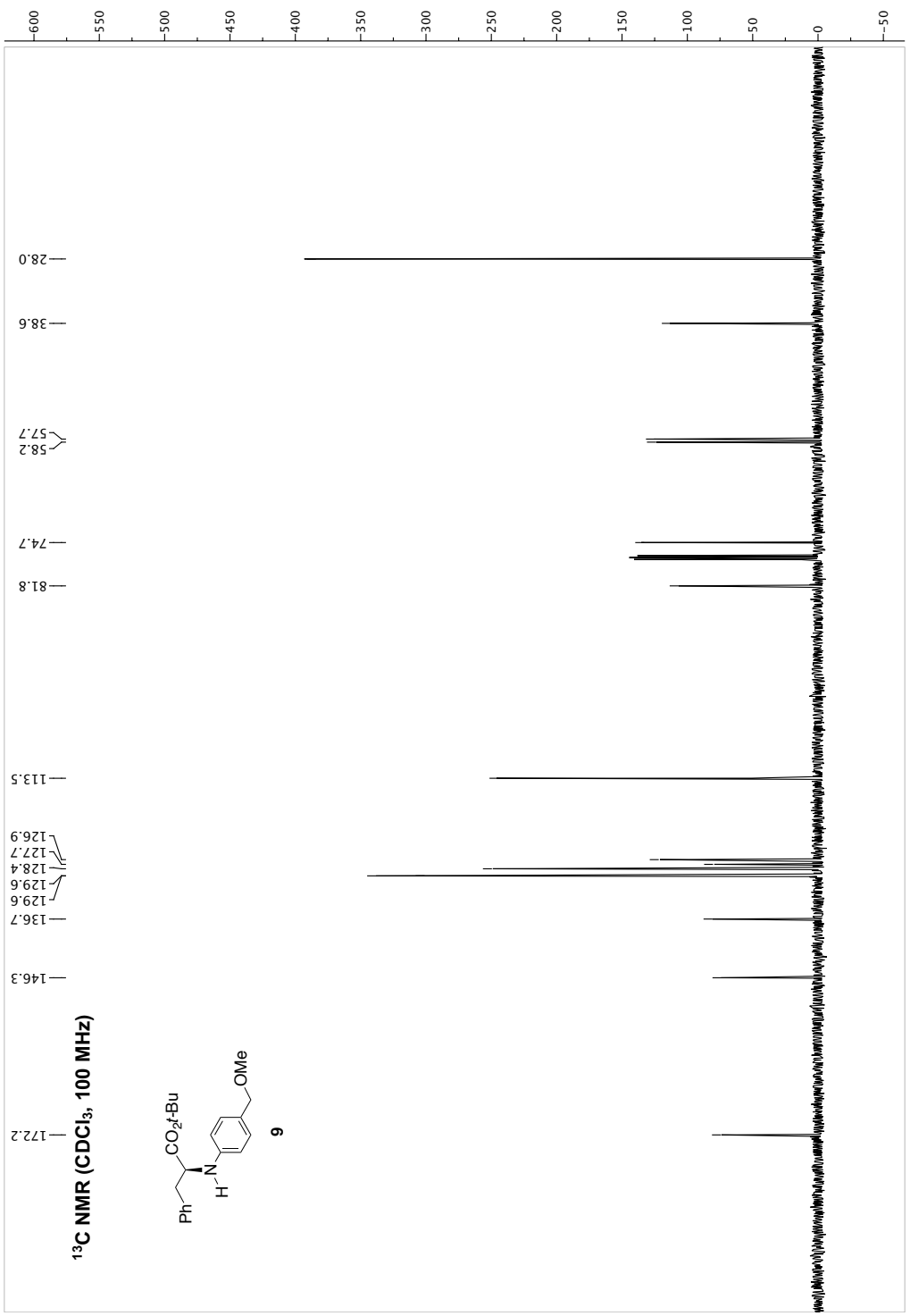
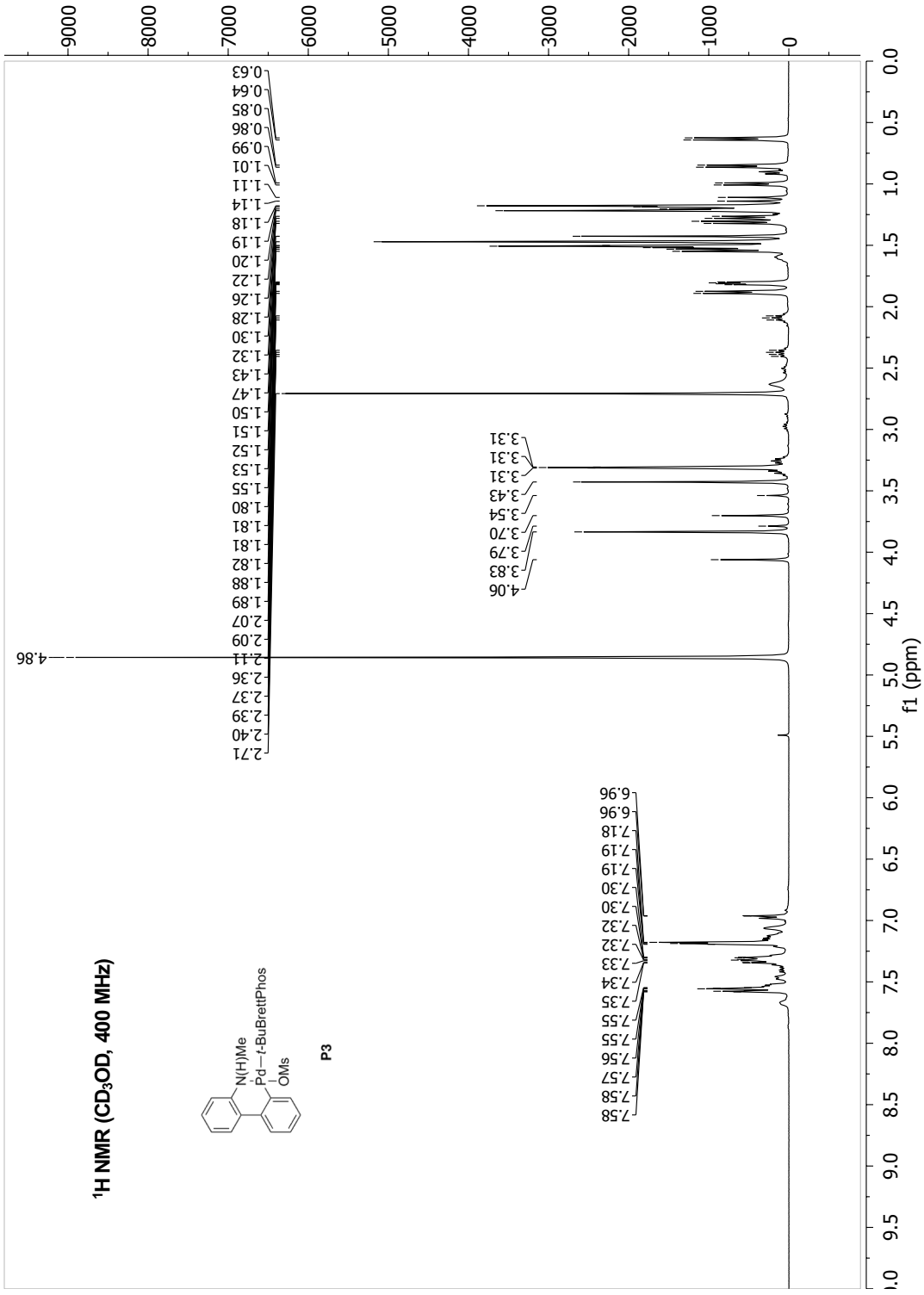
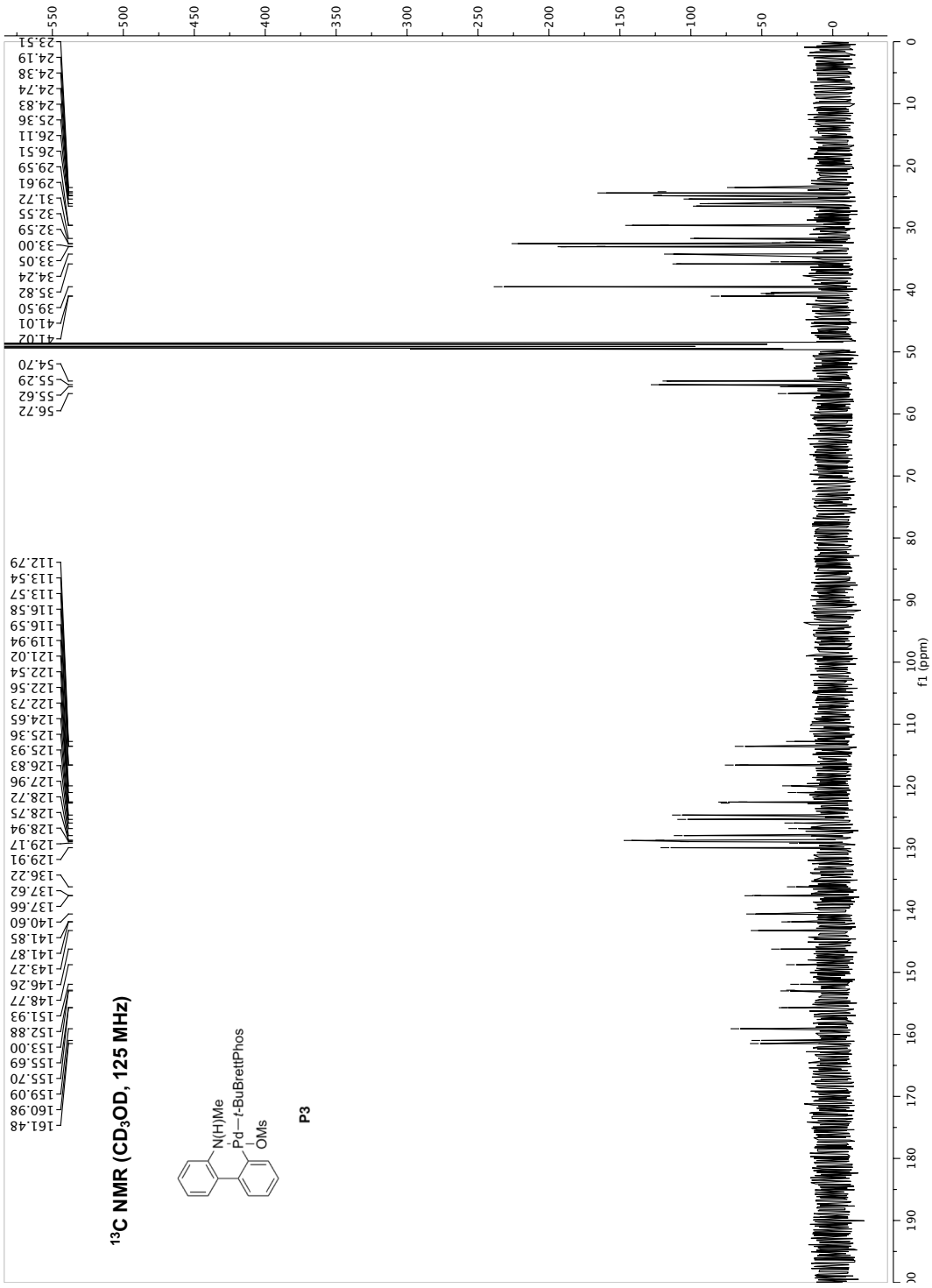
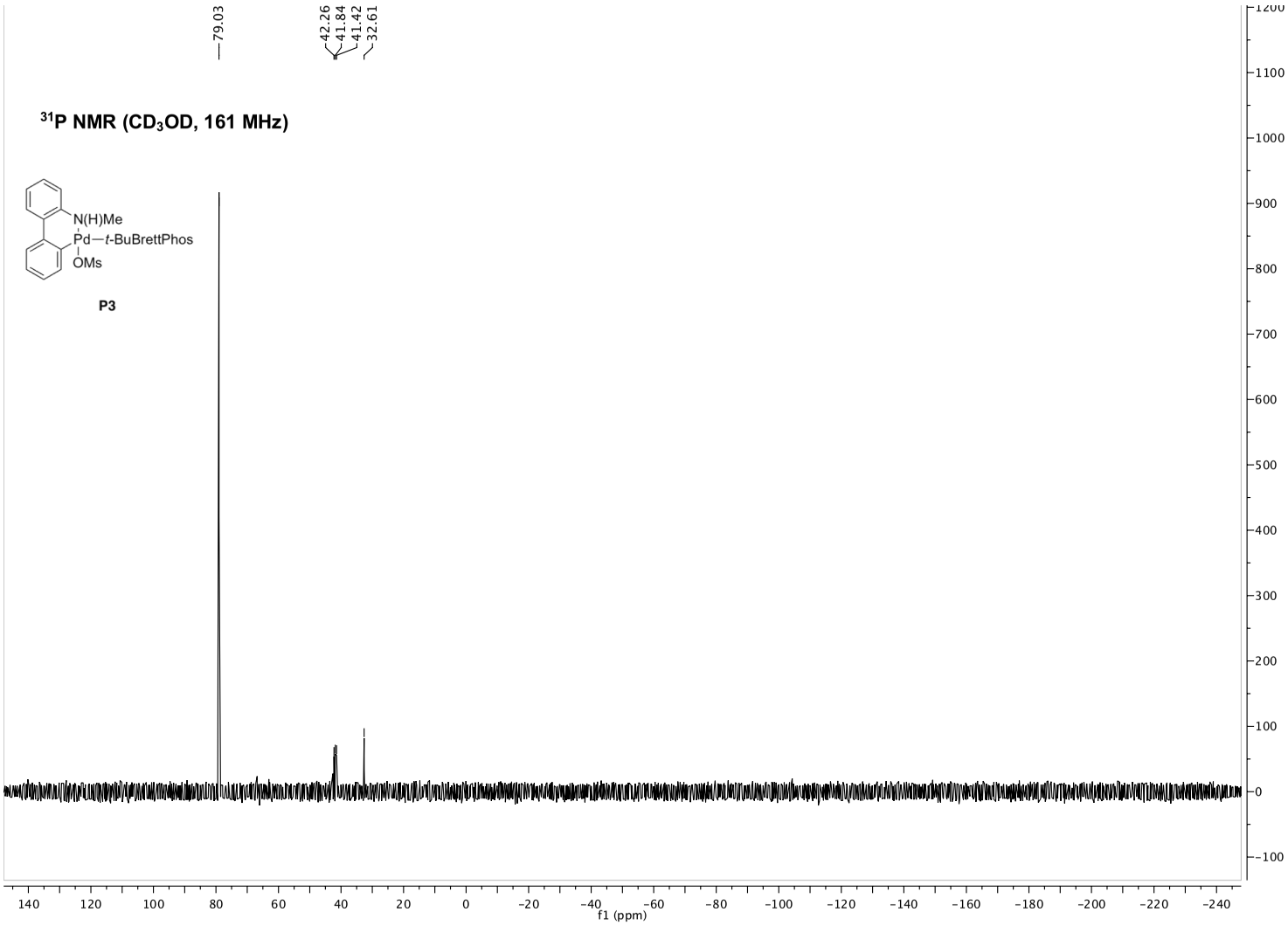
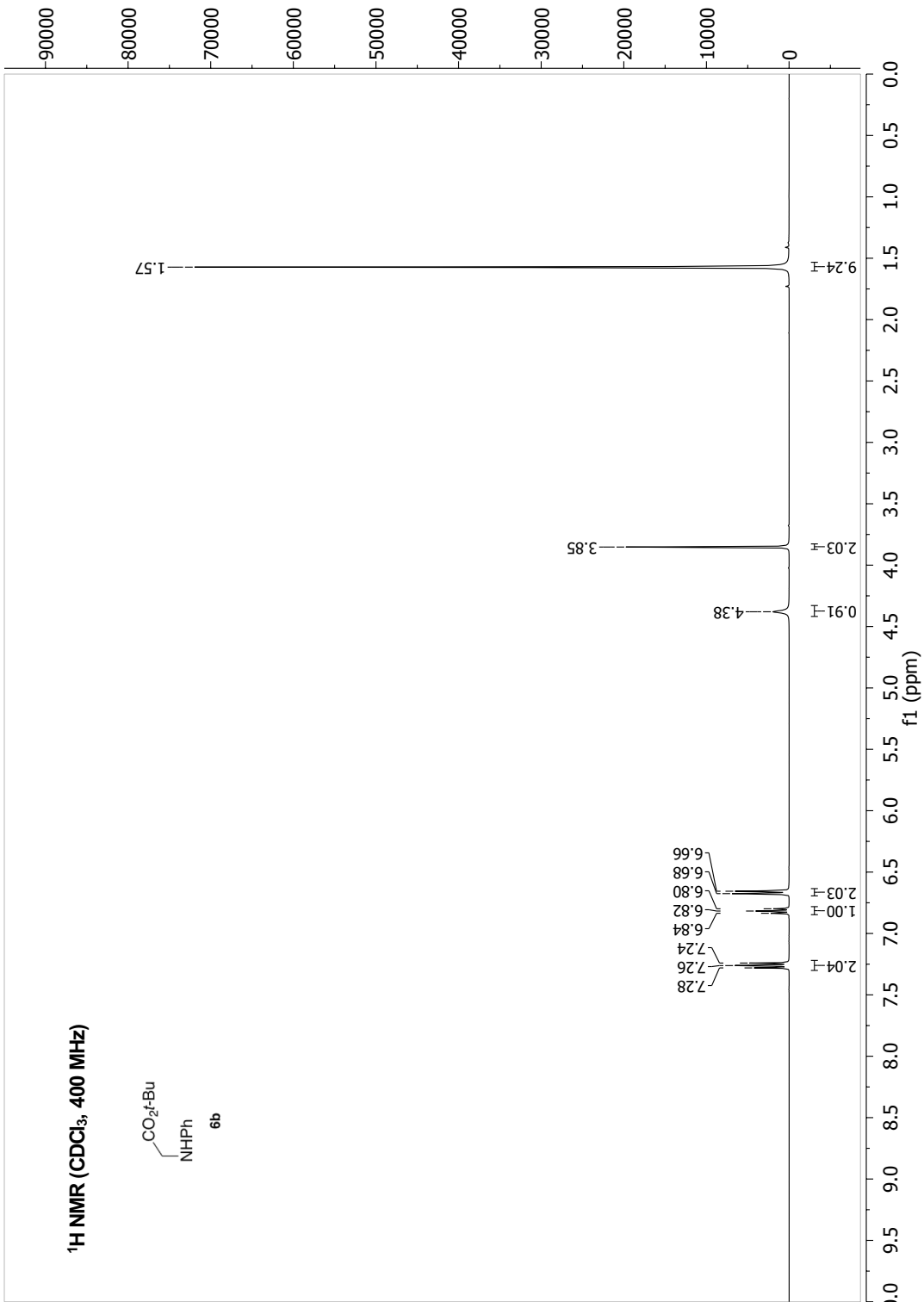
7.17
7.17
7.13
7.12
7.07
7.04
2.01
5.13
f1 (ppm)

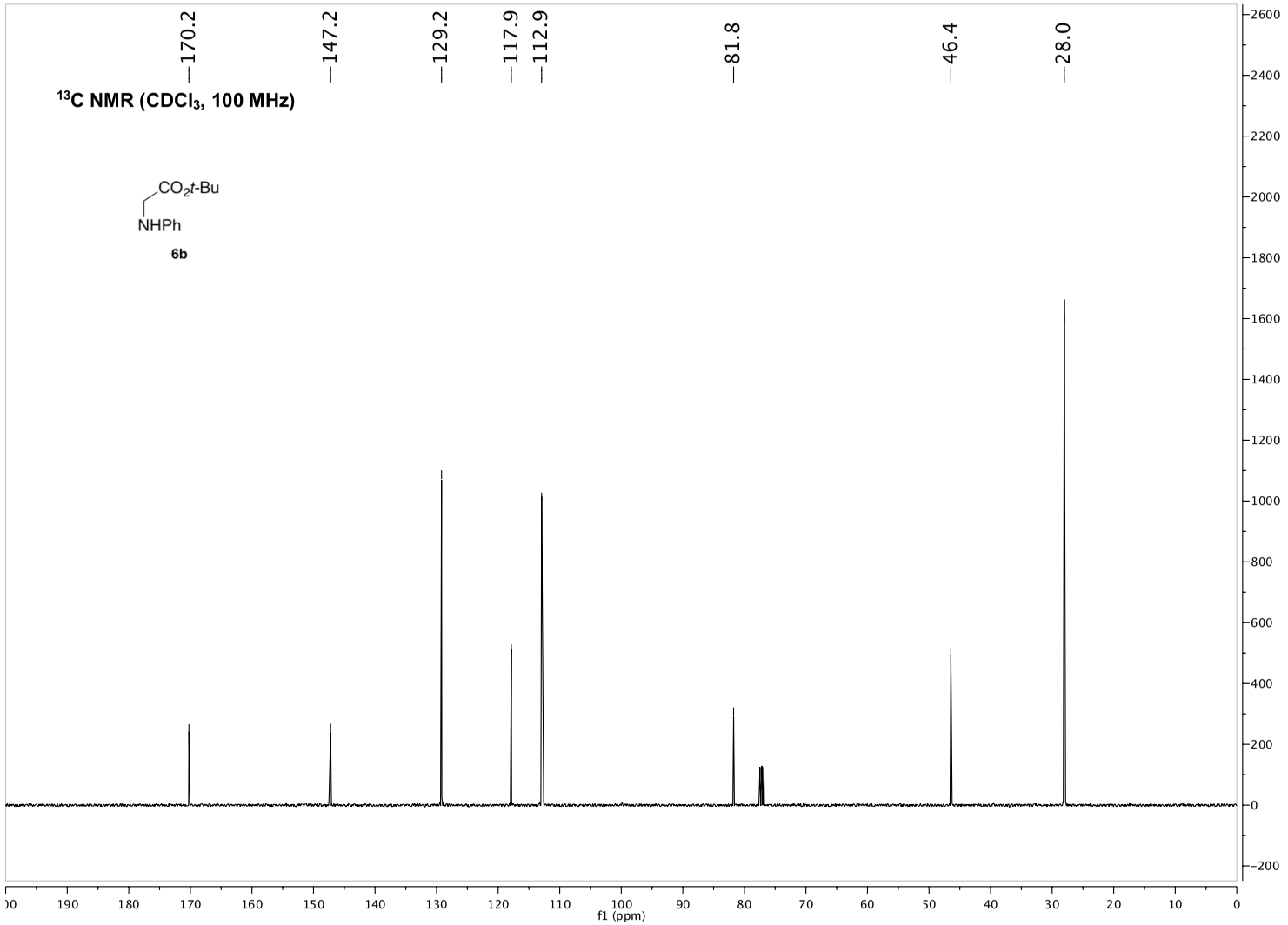

13C NMR (CDCl3, 100 MHz)
9
Ph
CO2t-Bu
OMe
172.2
146.3
136.7
129.6
129.6
128.4
127.7
126.9
113.5
81.8
74.7
58.2
57.7
38.6
28.0
f1 (ppm)

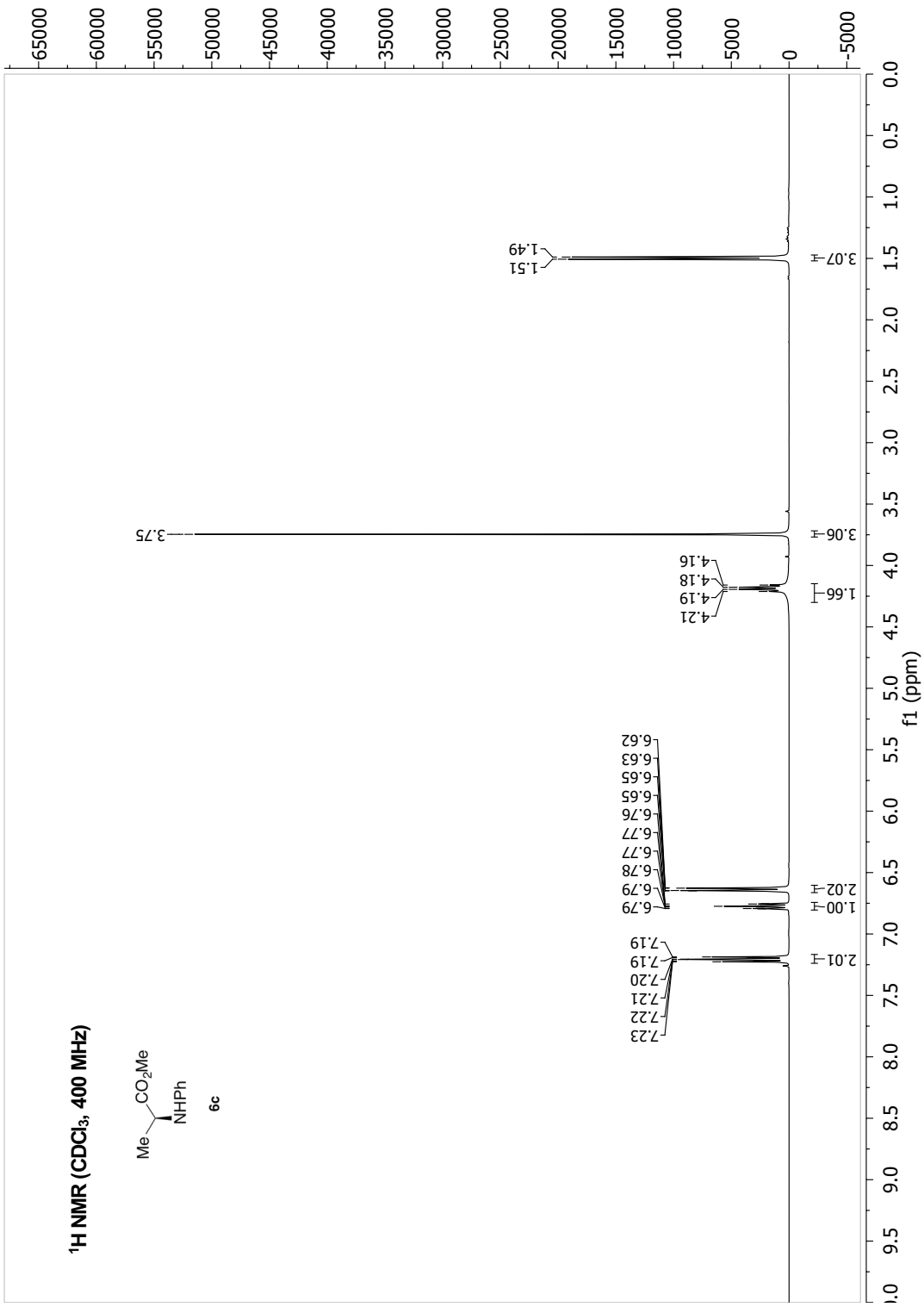

^{1}H NMR (CD_3OD, 400 MHz)
N(H)Me
Pd—t-BuBrettPhos
OMs
P3
f1 (ppm)

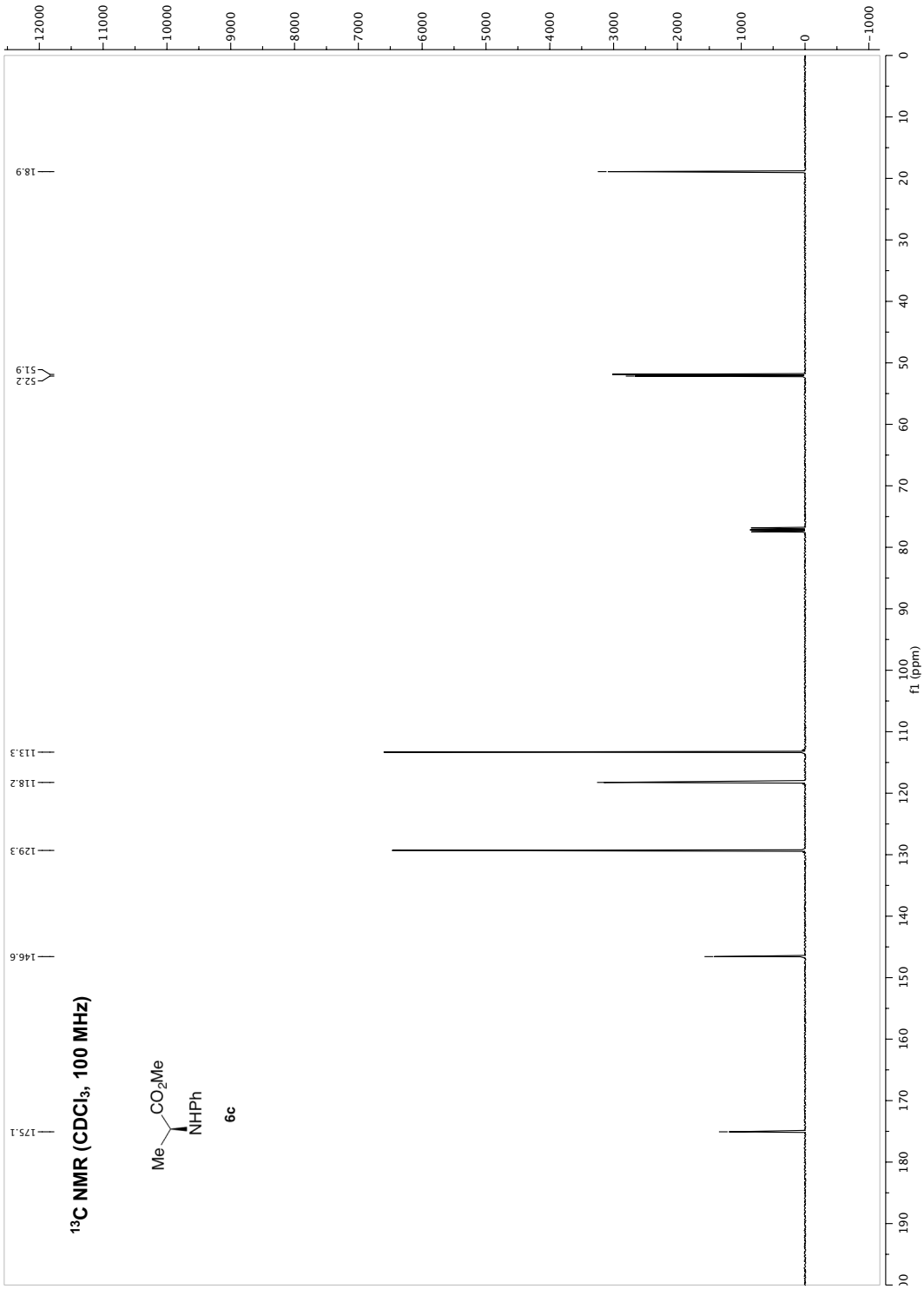

13C NMR (CD3OD, 125 MHz)
P3
N(H)Me
Pd
t-BuBrettPhos
OMs
f1 (ppm)

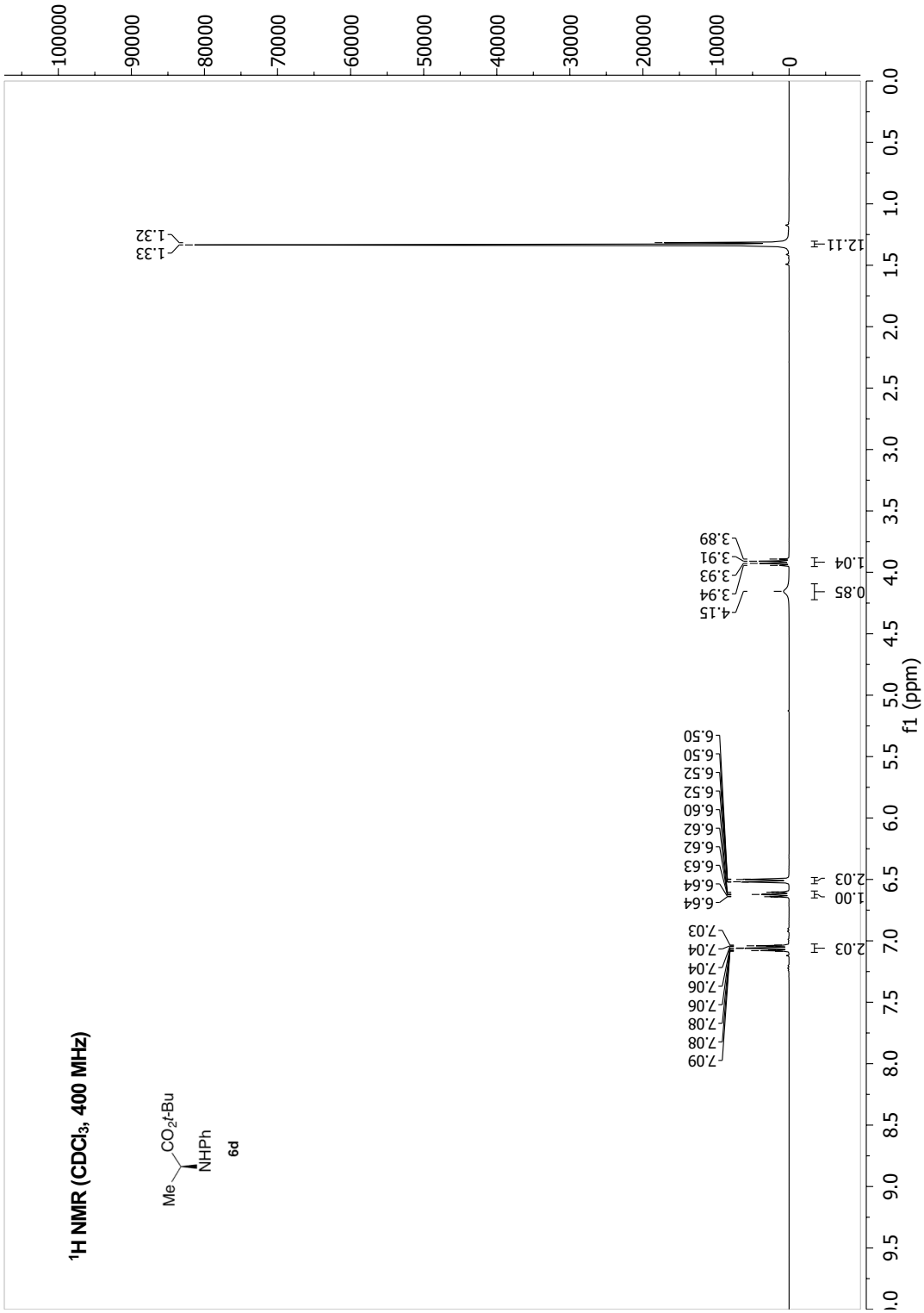

79.03
42.26
41.84
41.42
32.61
31P NMR (CD3OD, 161 MHz)
N(H)Me
Pd—t-BuBrettPhos
OMs
P3
f1 (ppm)

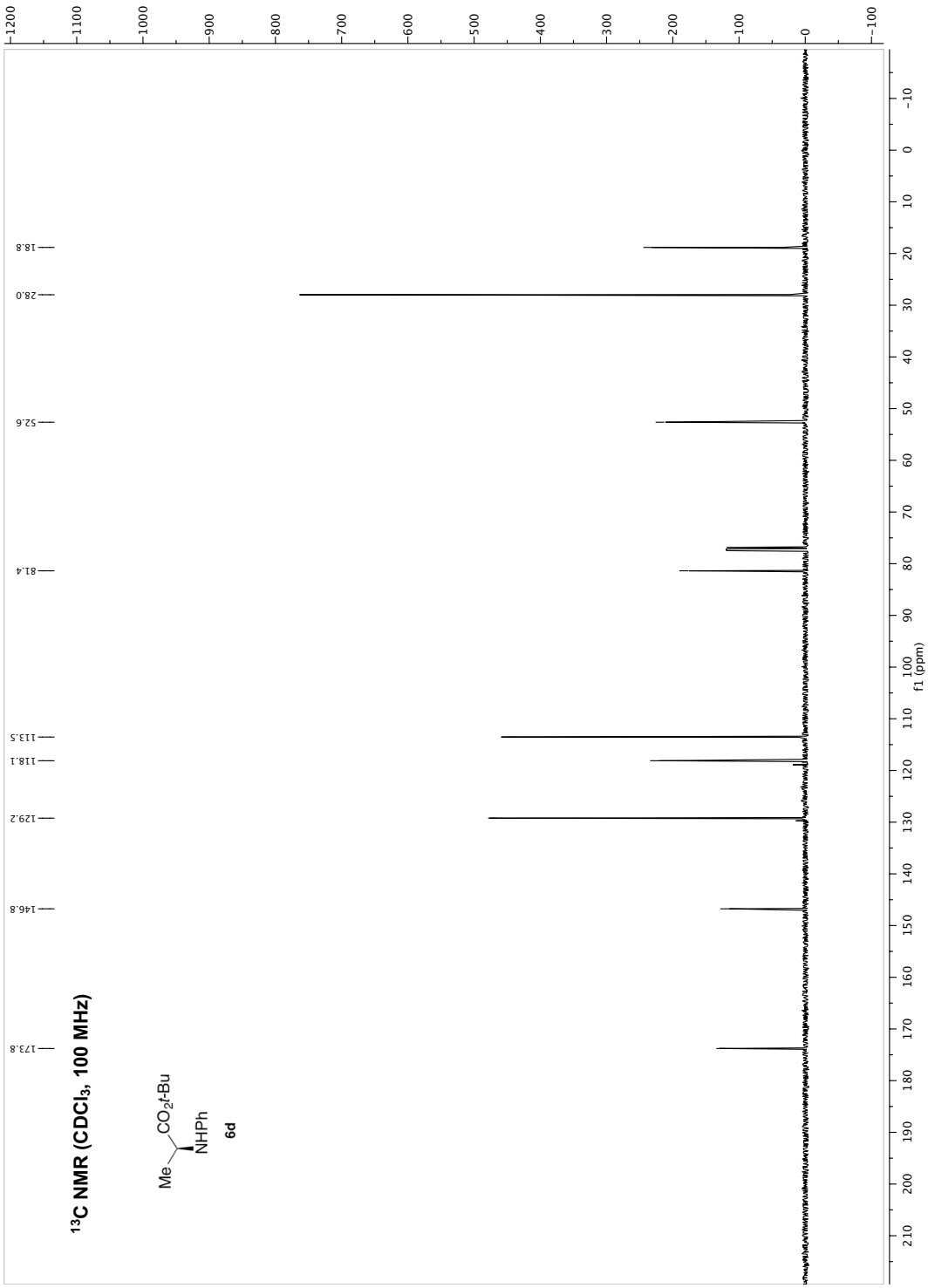

1H NMR (CDCl3, 400 MHz)
CO2t-Bu
NHPh
6b
1.57
3.85
4.38
7.28
7.26
7.24
6.84
6.82
6.80
6.68
6.66
9.24
2.03
0.91
2.04
1.00
2.03
f1 (ppm)

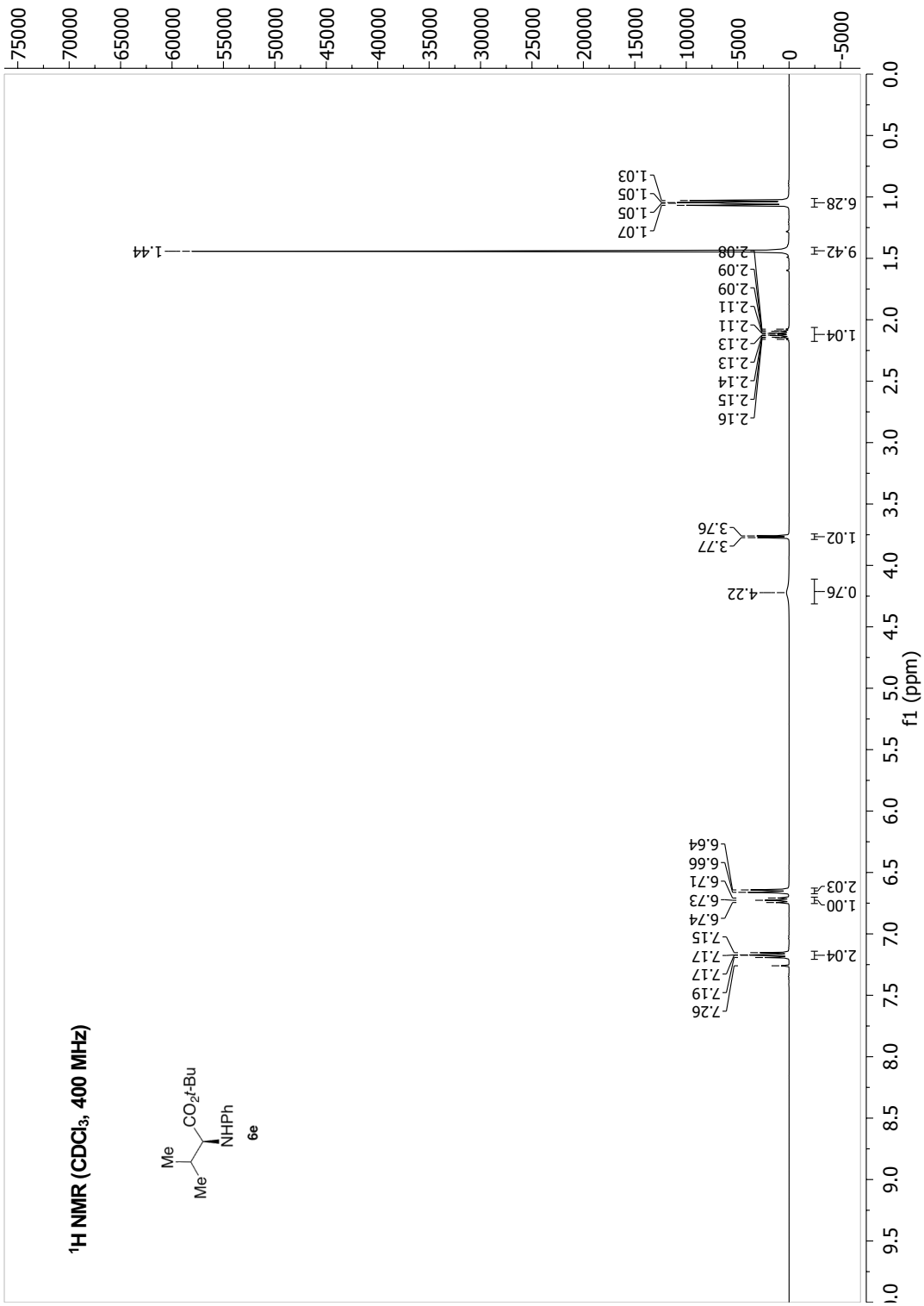

170.2
147.2
129.2
117.9
112.9
81.8
46.4
28.0
^{13}C NMR ($CDCl_3$, 100 MHz)
CO_2t-Bu
NHPh
6b
f1 (ppm)

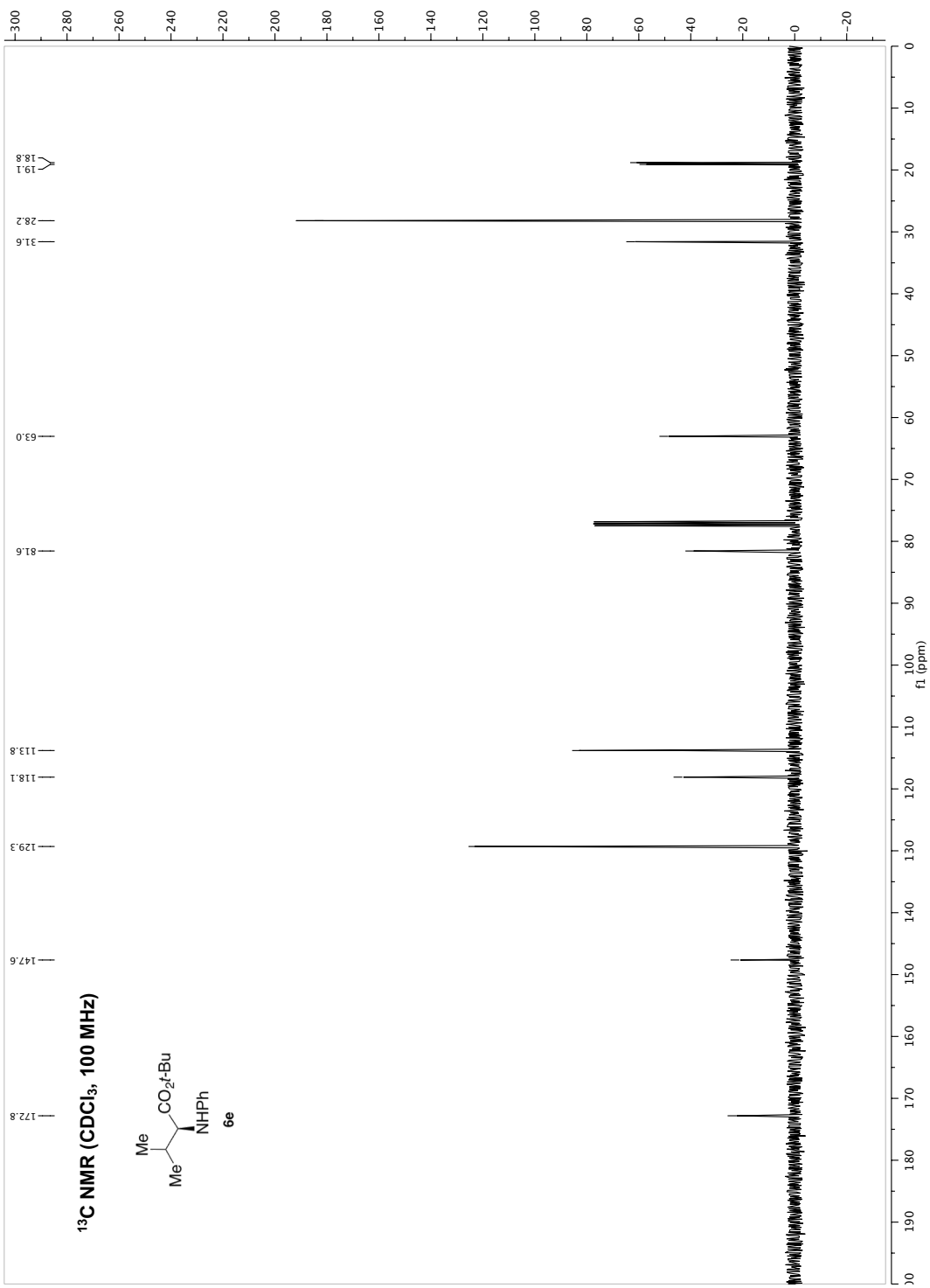

1H NMR (CDCl3, 400 MHz)
Me
CO2Me
NHPh
6c
f1 (ppm)

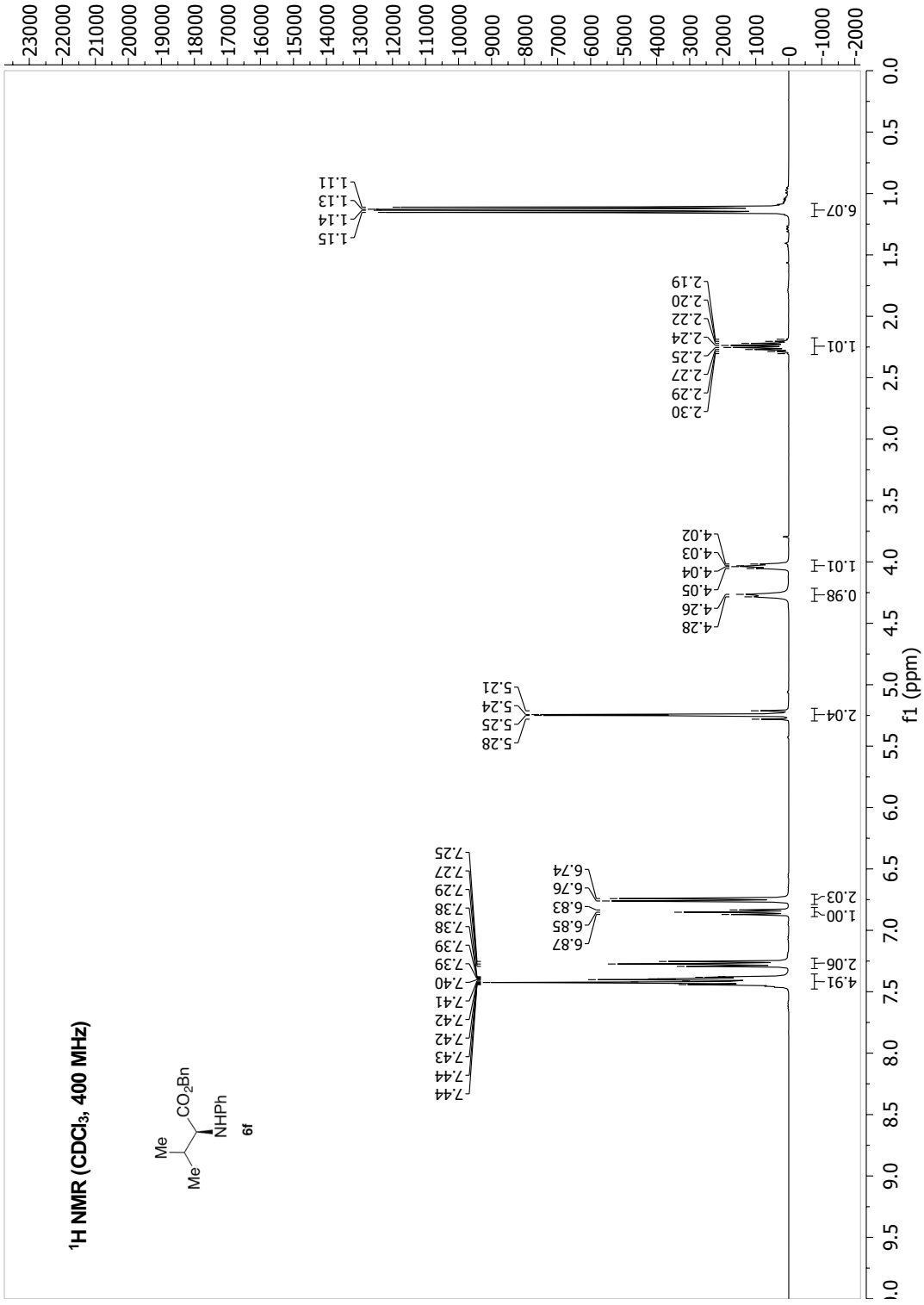

^{13}C NMR (CDCl$_3$, 100 MHz)
Me
CO$_2$Me
NHPh
6c
175.1
146.6
129.3
118.2
113.3
52.2
51.9
18.9
f1 (ppm)

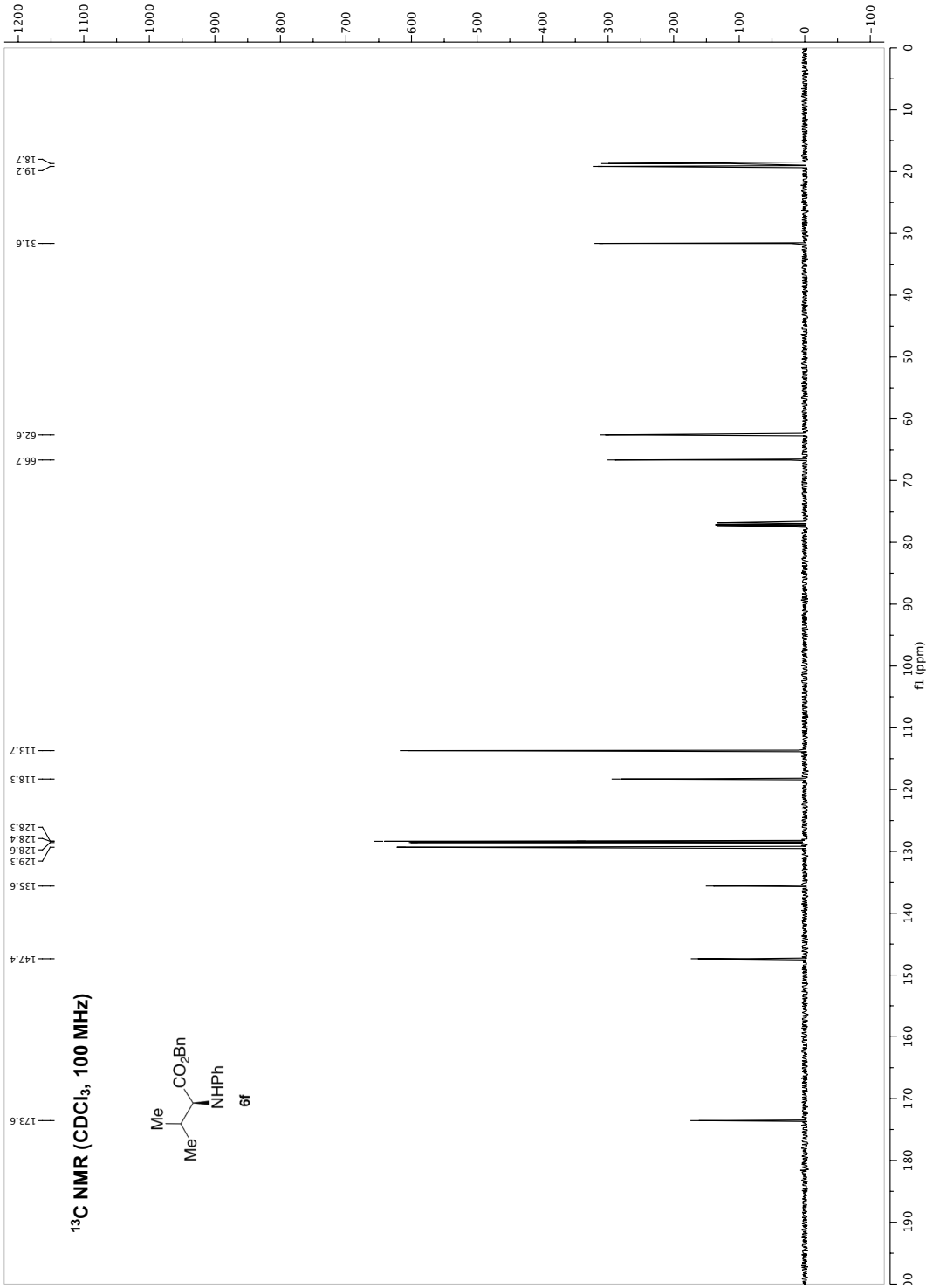

1H NMR (CDCl3, 400 MHz)
Me
CO2t-Bu
NHPh
6d
f1 (ppm)

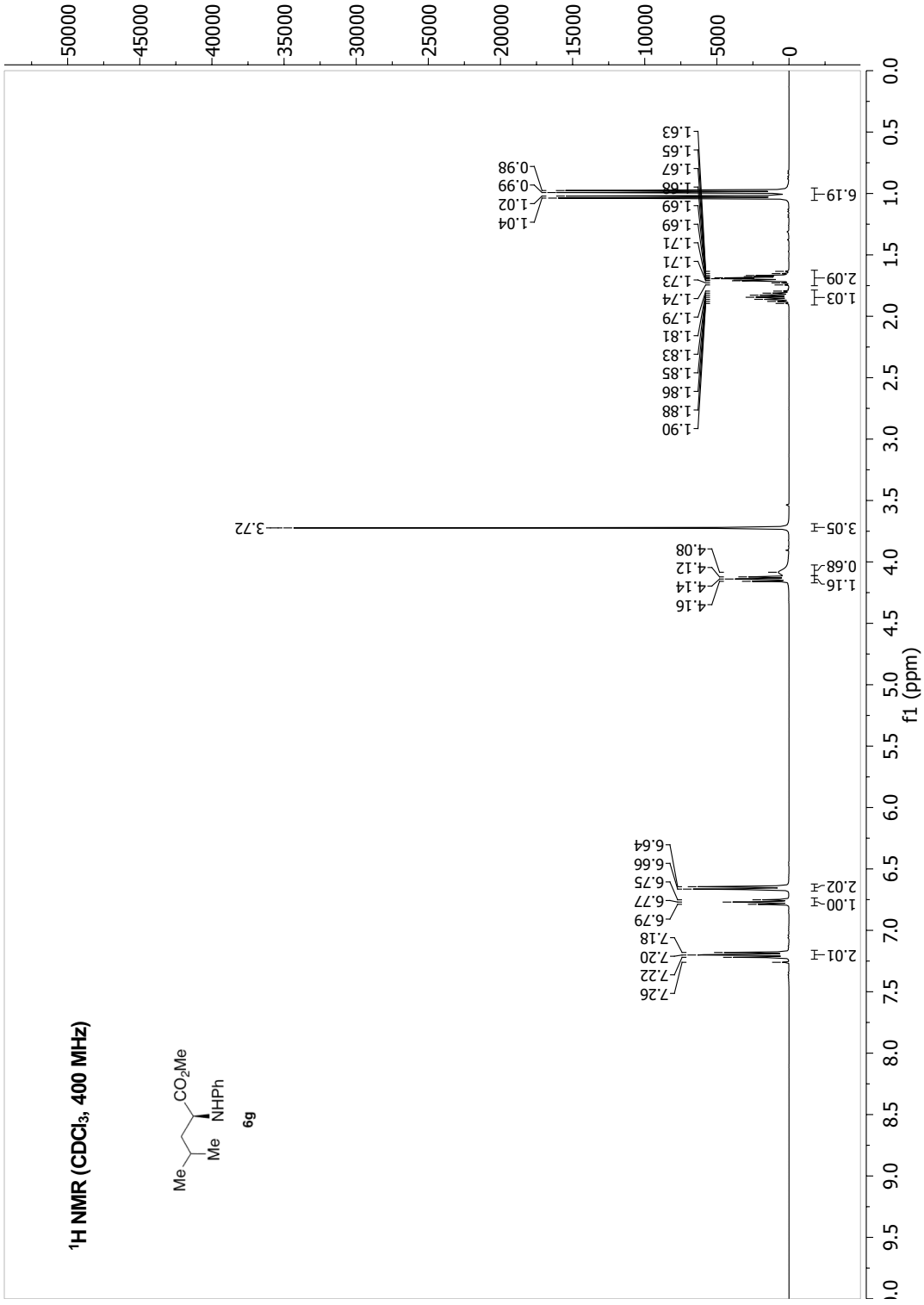

^{13}C NMR ($CDCl_3$, 100 MHz)
Me
CO_2t-Bu
NHPh
6d
173.8
146.8
129.2
118.1
113.5
81.4
52.6
28.0
18.8
f1 (ppm)

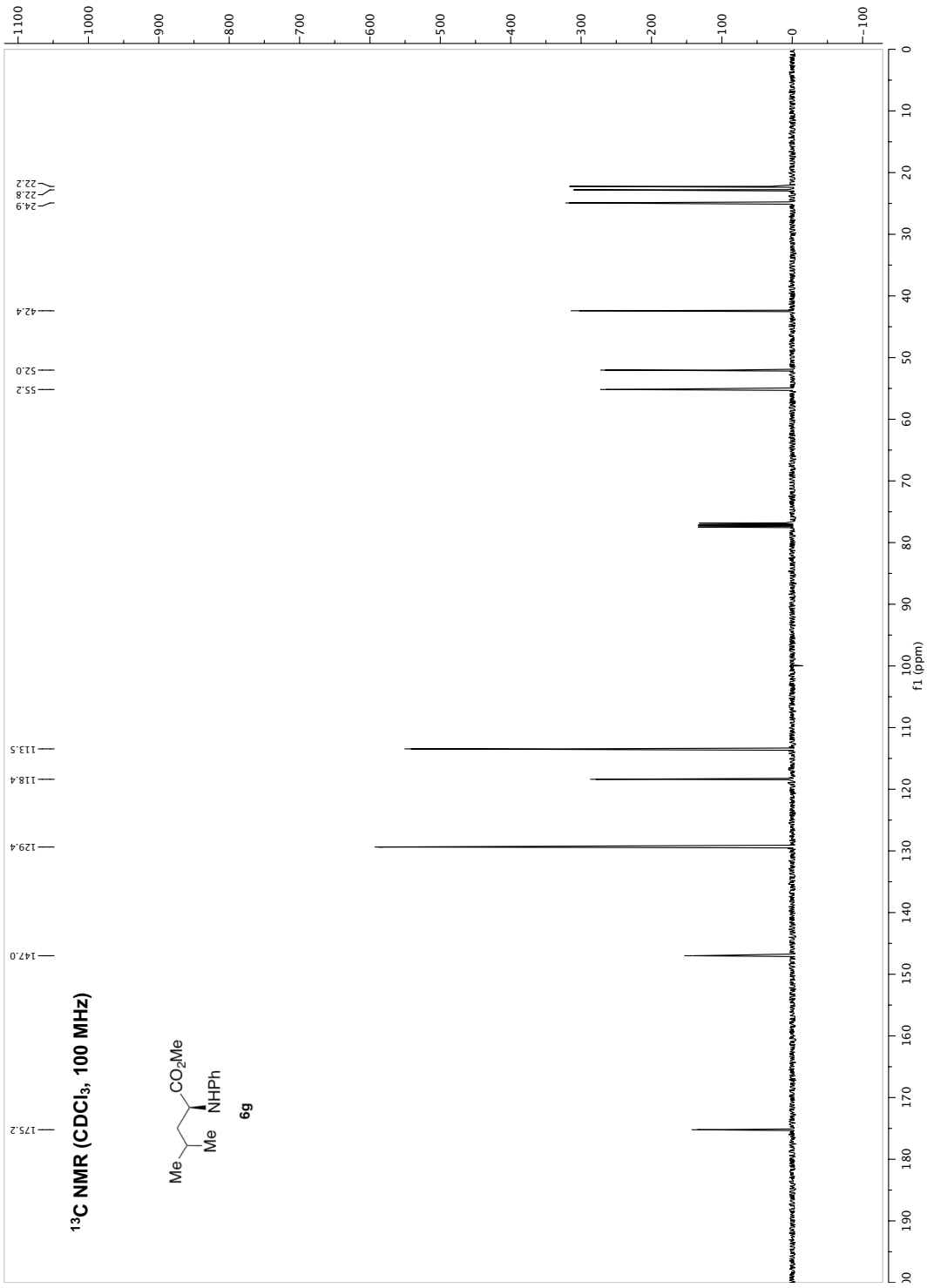

^{1}H NMR ($CDCl_3$, 400 MHz)
Me
Me
CO_2t-Bu
NHPh
6e
f1 (ppm)

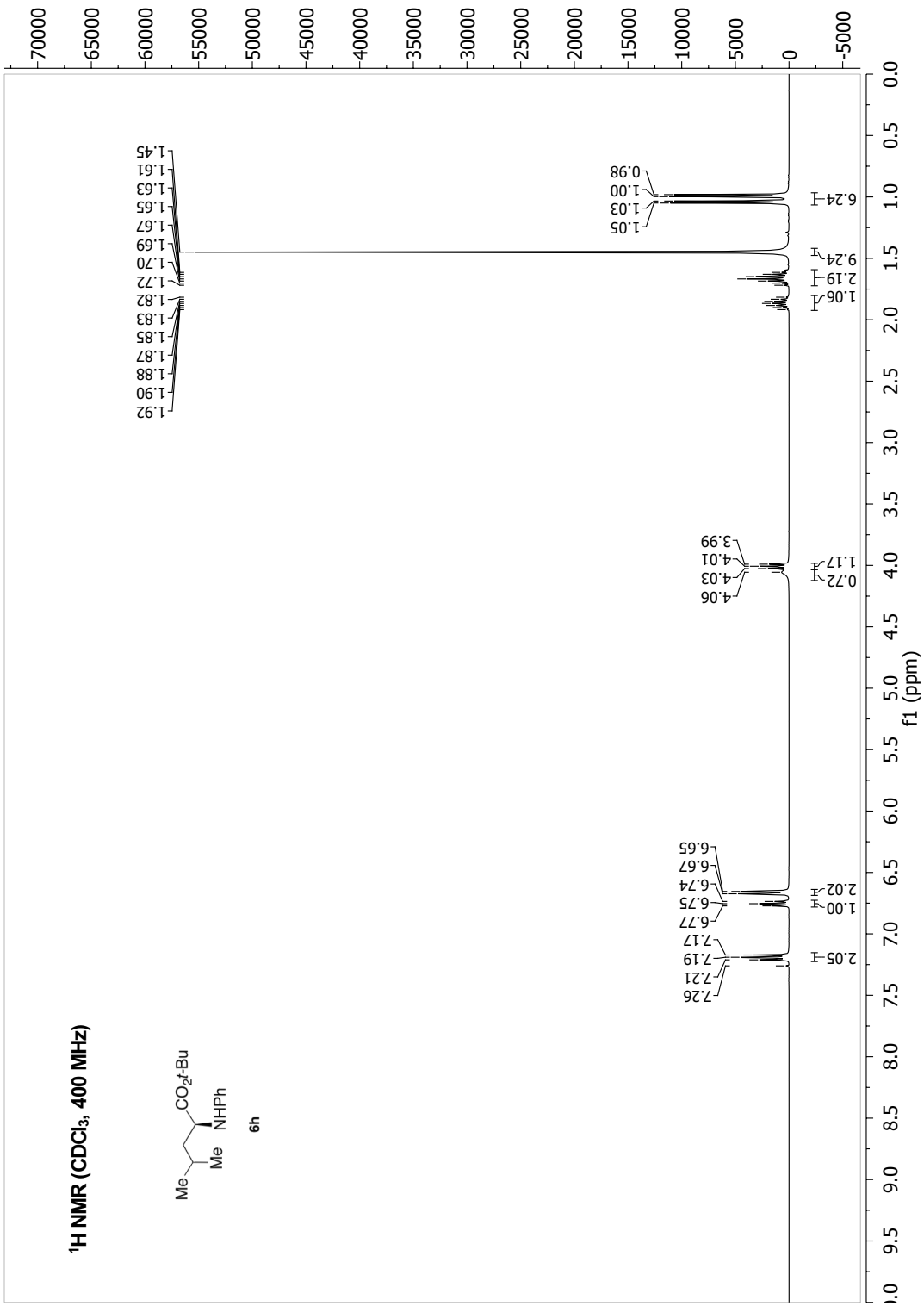

^{13}C NMR (CDCl$_3$, 100 MHz)
Me
Me
CO$_2$t-Bu
NHPh
6e
172.8
147.6
129.3
118.1
113.8
81.6
63.0
31.6
28.2
19.1
18.8
f1 (ppm)

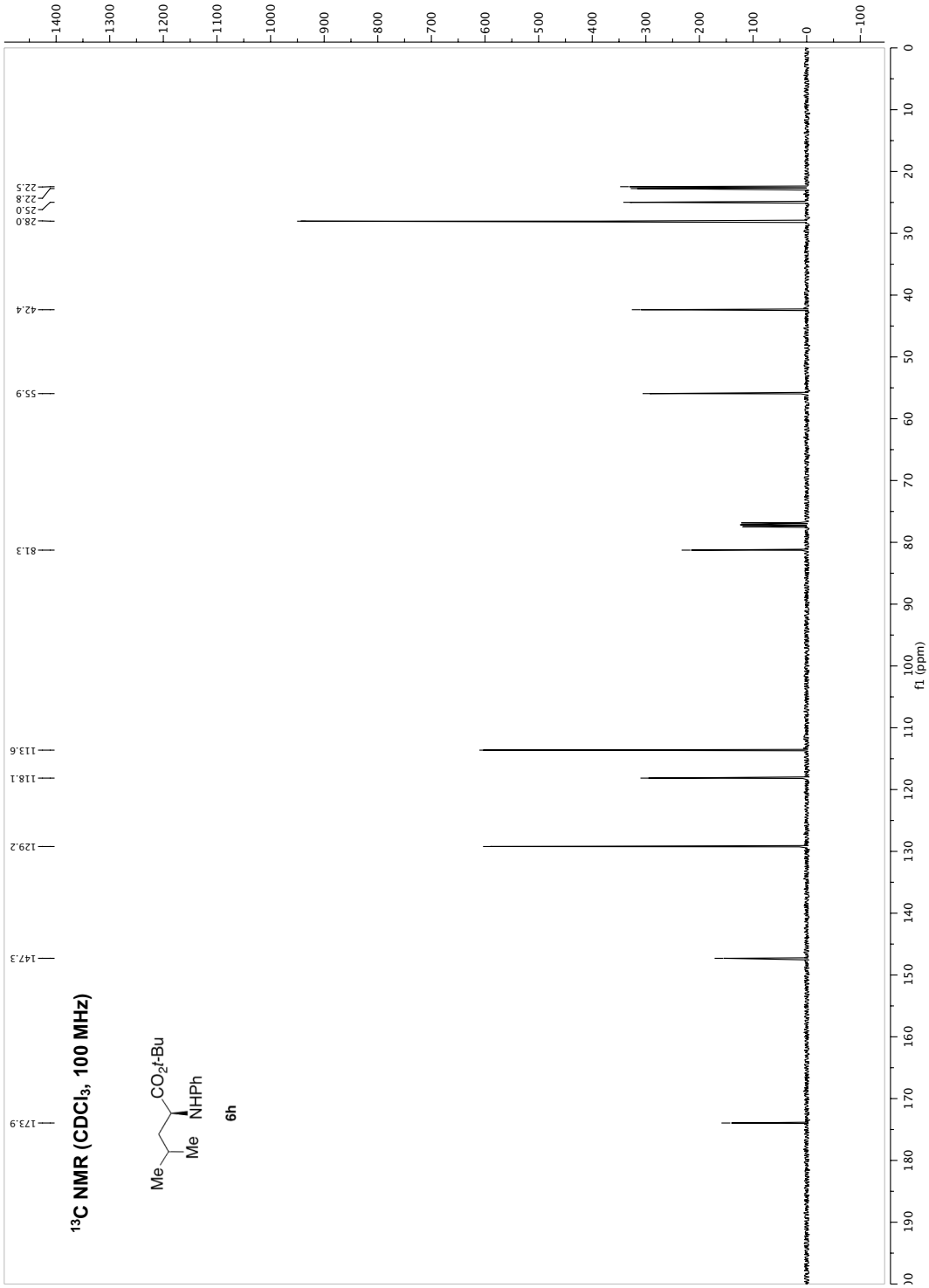

^{1}H NMR ($CDCl_3$, 400 MHz)
Me
Me
CO_2Bn
NHPh
6f
f1 (ppm)

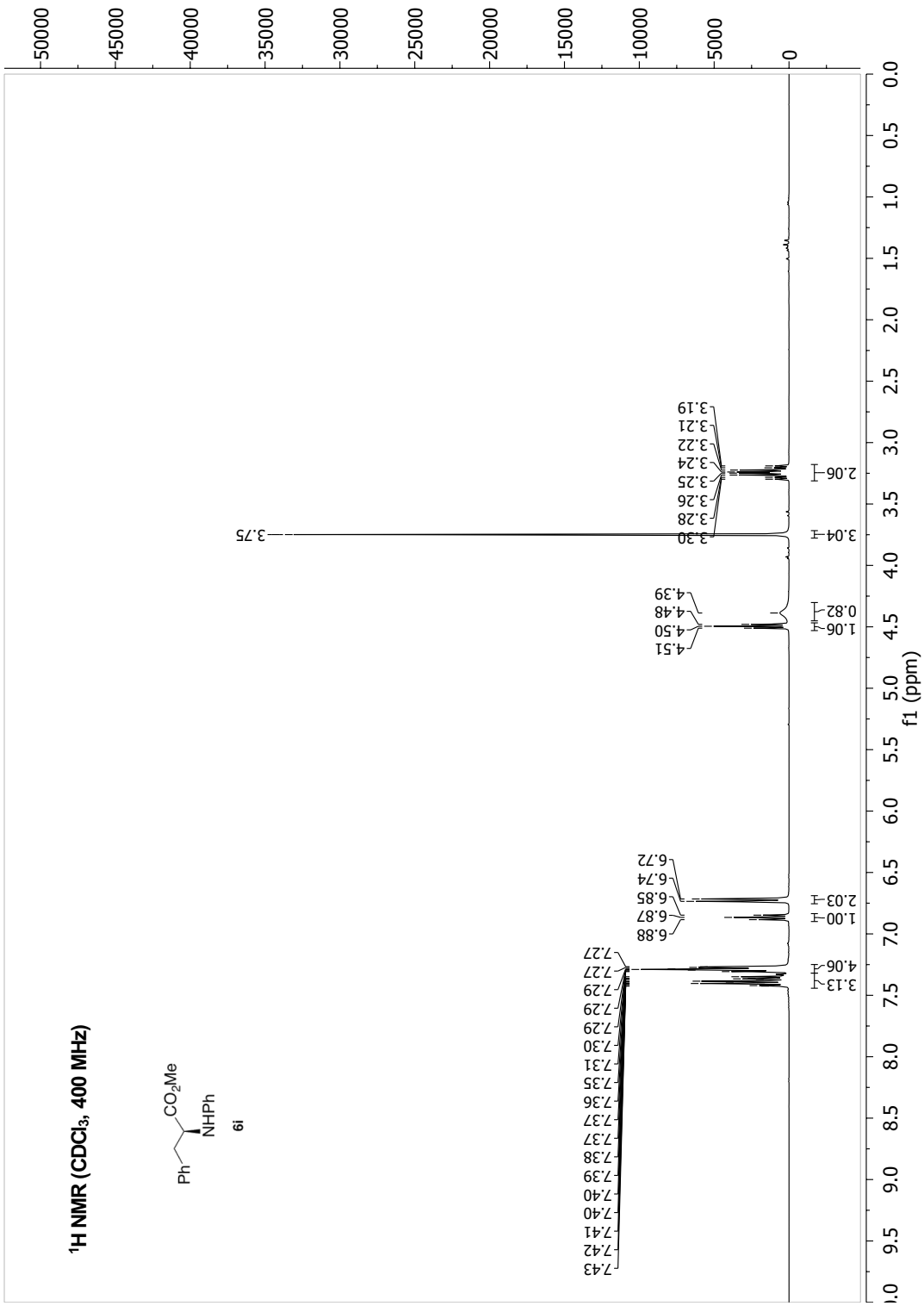

13C NMR (CDCl3, 100 MHz)
Me
Me
CO2Bn
NHPh
6f
173.6
147.4
135.6
129.3
128.6
128.4
128.3
118.3
113.7
66.7
62.6
31.6
19.2
18.7
f1 (ppm)

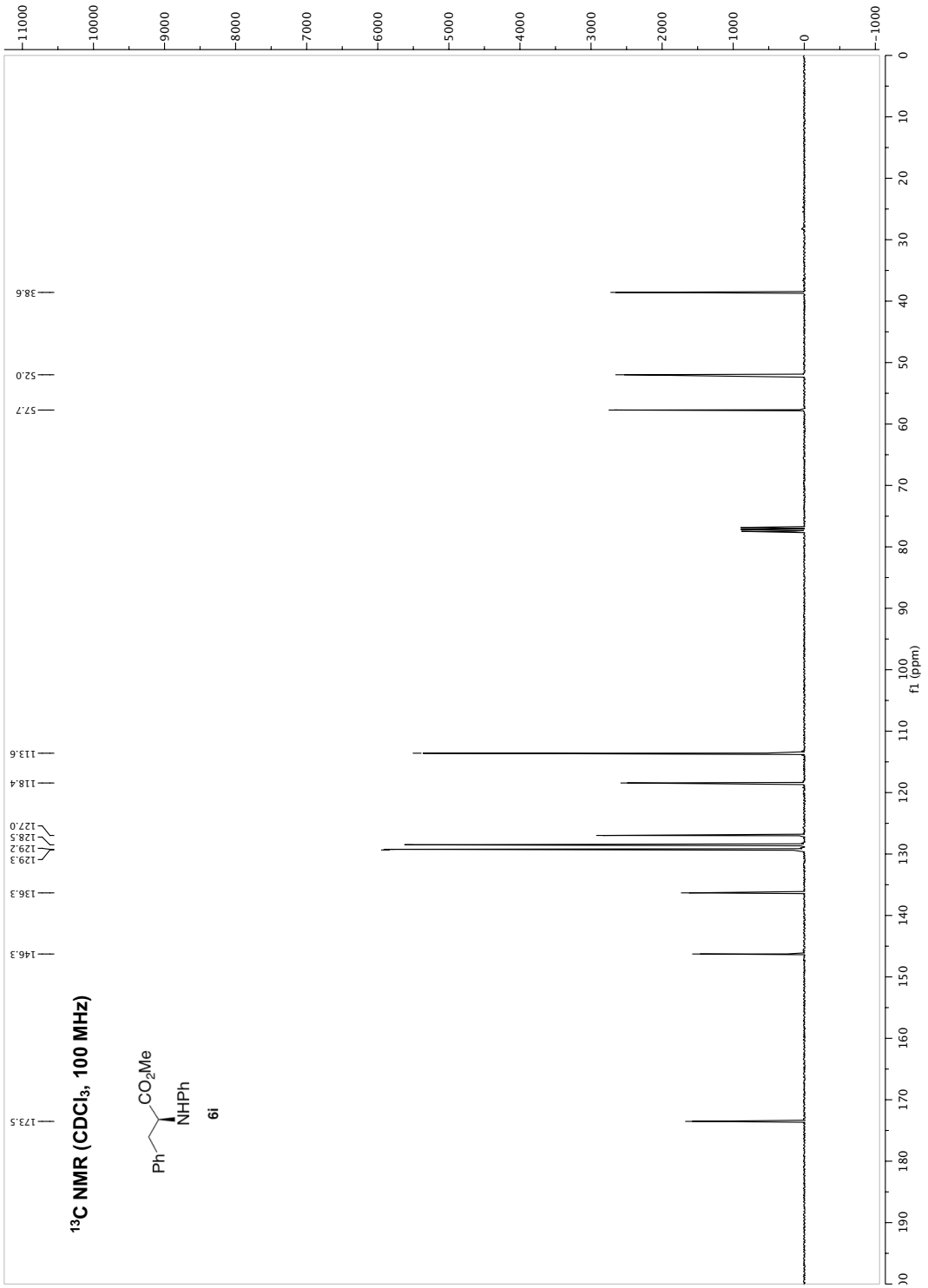

^{1}H NMR ($CDCl_3$, 400 MHz)
CO_2Me
NHPh
Me
Me
6g
f1 (ppm)

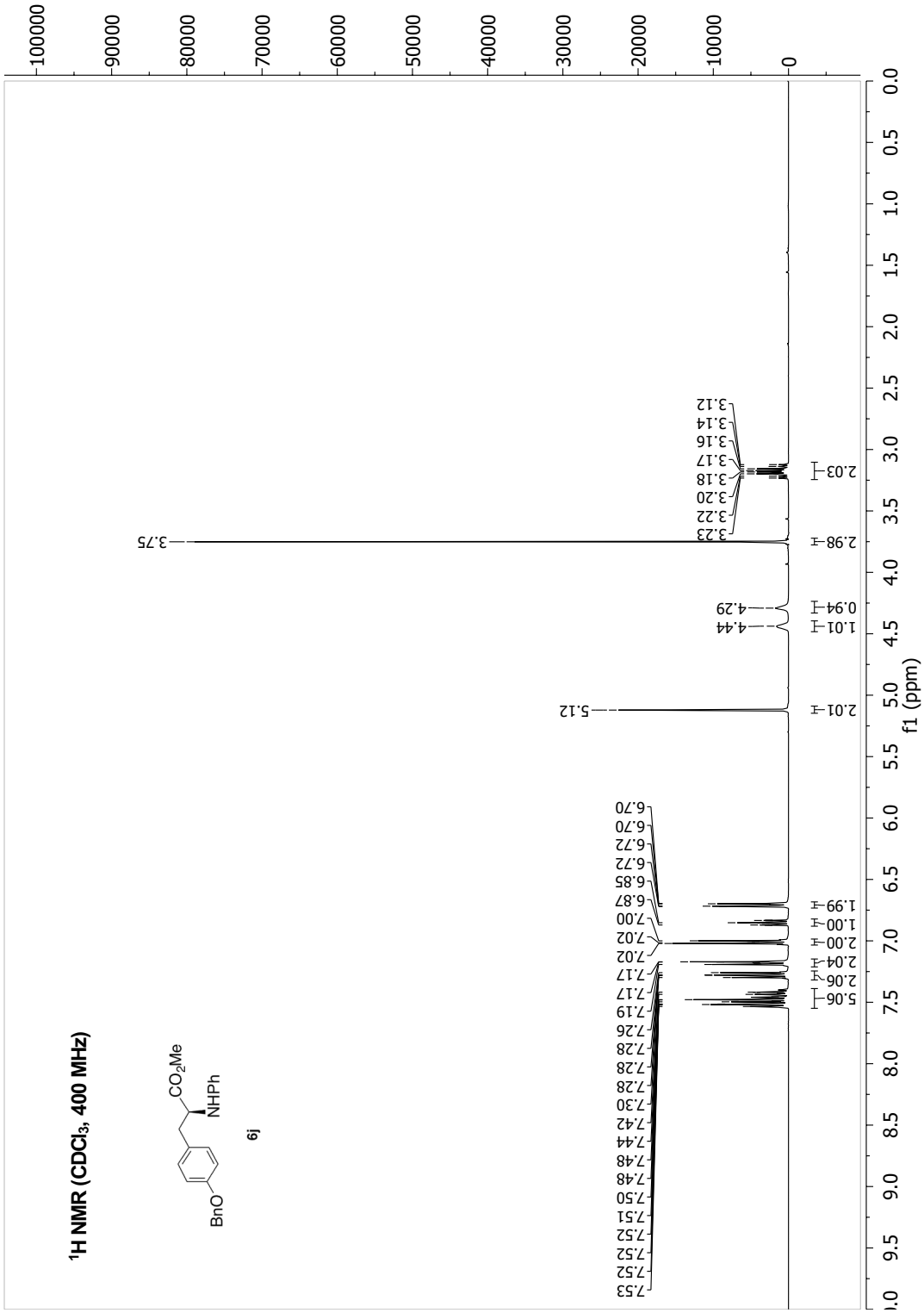

13C NMR (CDCl3, 100 MHz)
Me
CO2Me
Me
NHPh
6g
175.2
147.0
129.4
118.4
113.5
55.2
52.0
42.4
24.9
22.8
22.2
f1 (ppm)

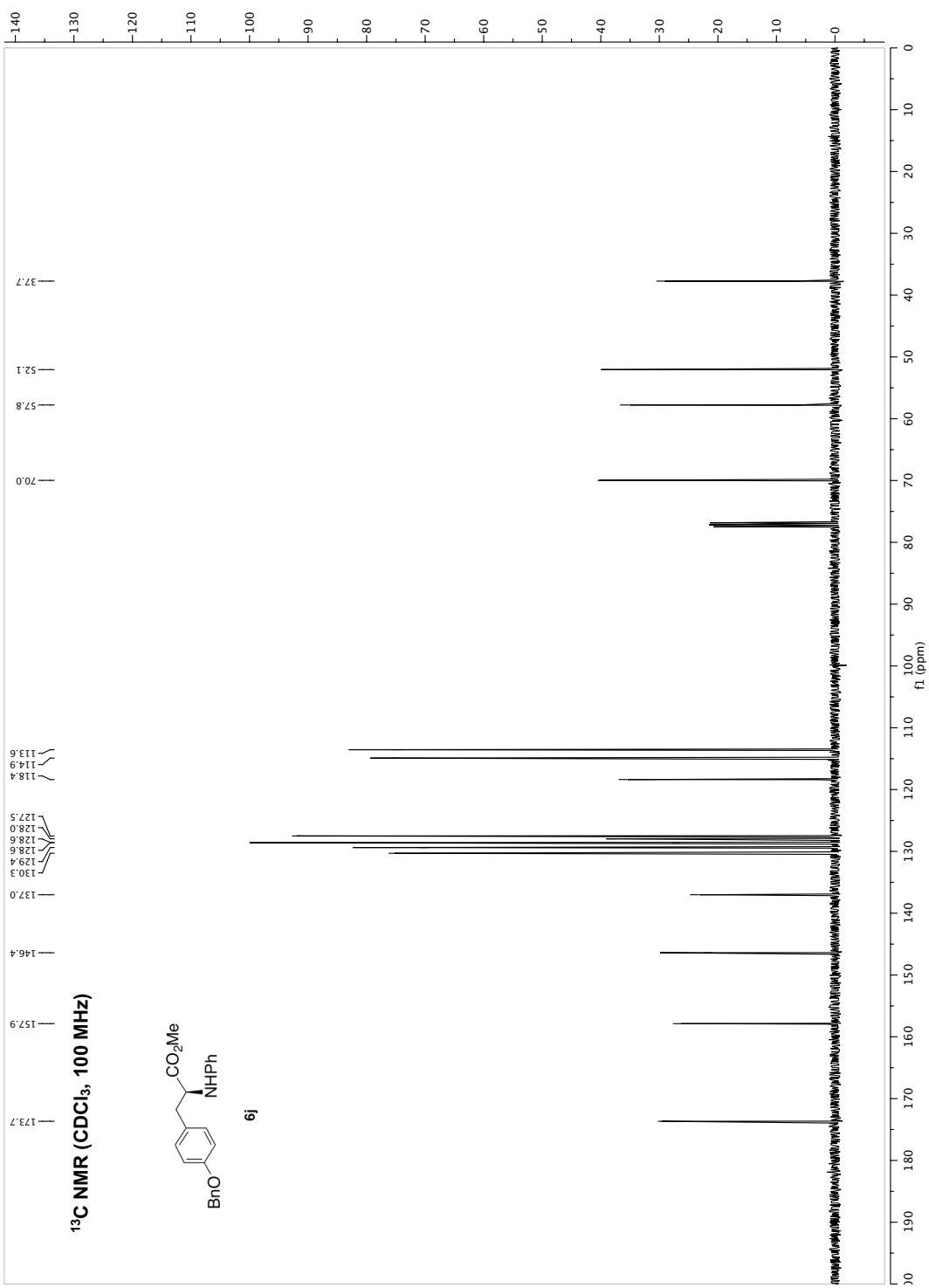

1H NMR (CDCl3, 400 MHz)
Me
CO2t-Bu
Me
NHPh
6h
f1 (ppm)

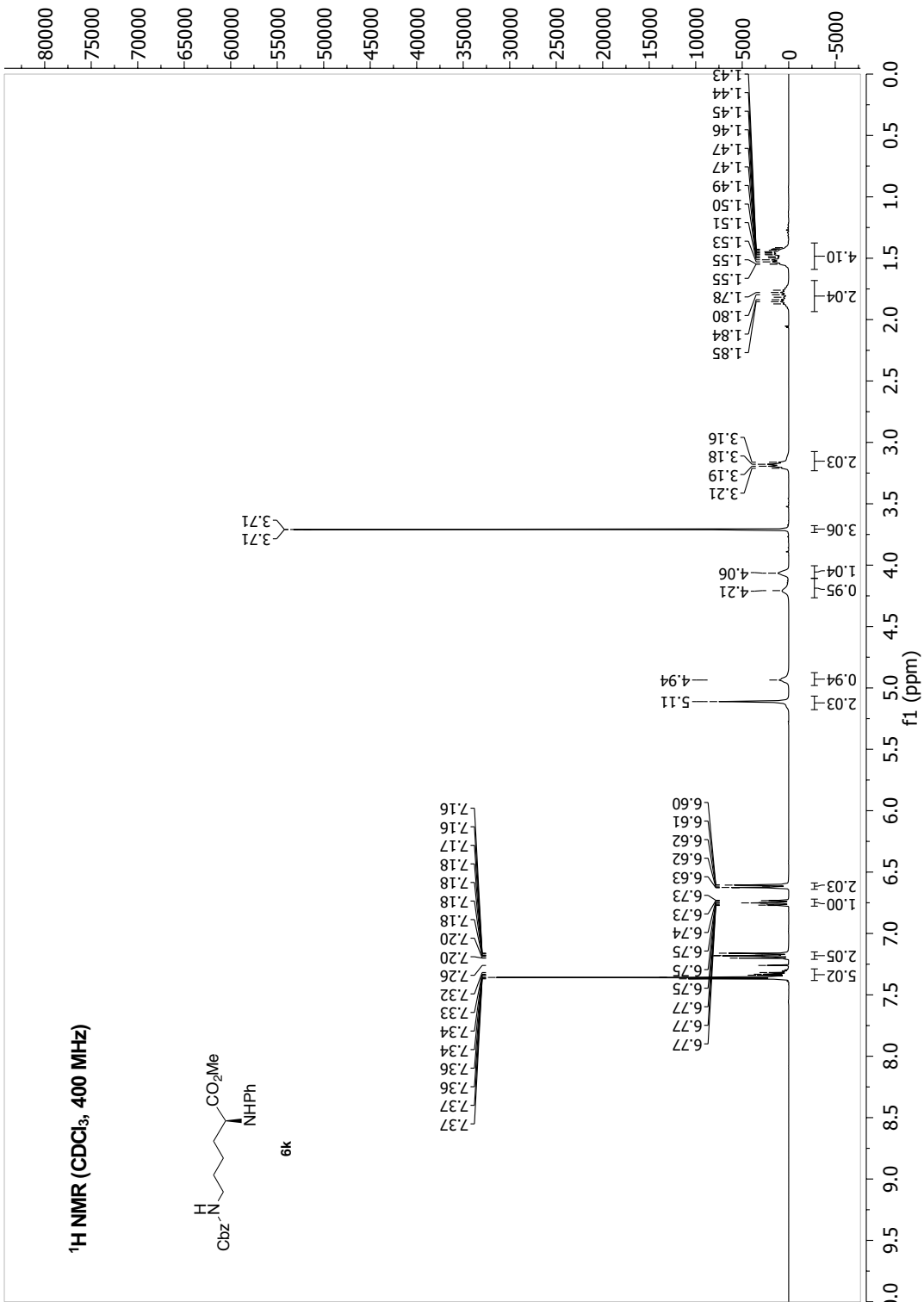

13C NMR (CDCl3, 100 MHz)
Me
CO2t-Bu
Me
NHPh
6h
173.9
147.3
129.2
118.1
113.6
81.3
55.9
42.4
28.0
25.0
22.8
22.5
f1 (ppm)

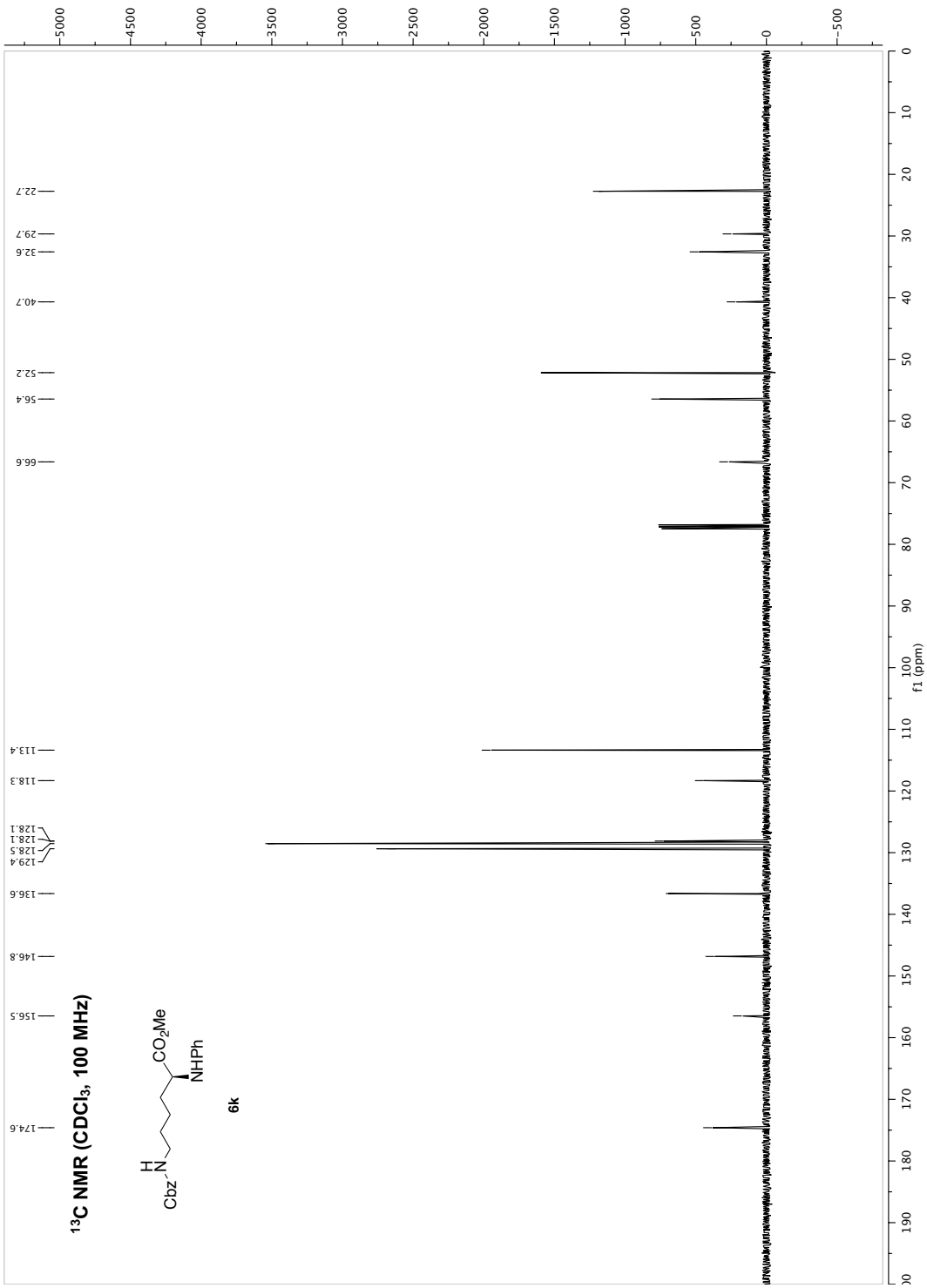

^{1}H NMR ($CDCl_3$, 400 MHz)
Ph
CO_2Me
NHPh
6i
f1 (ppm)

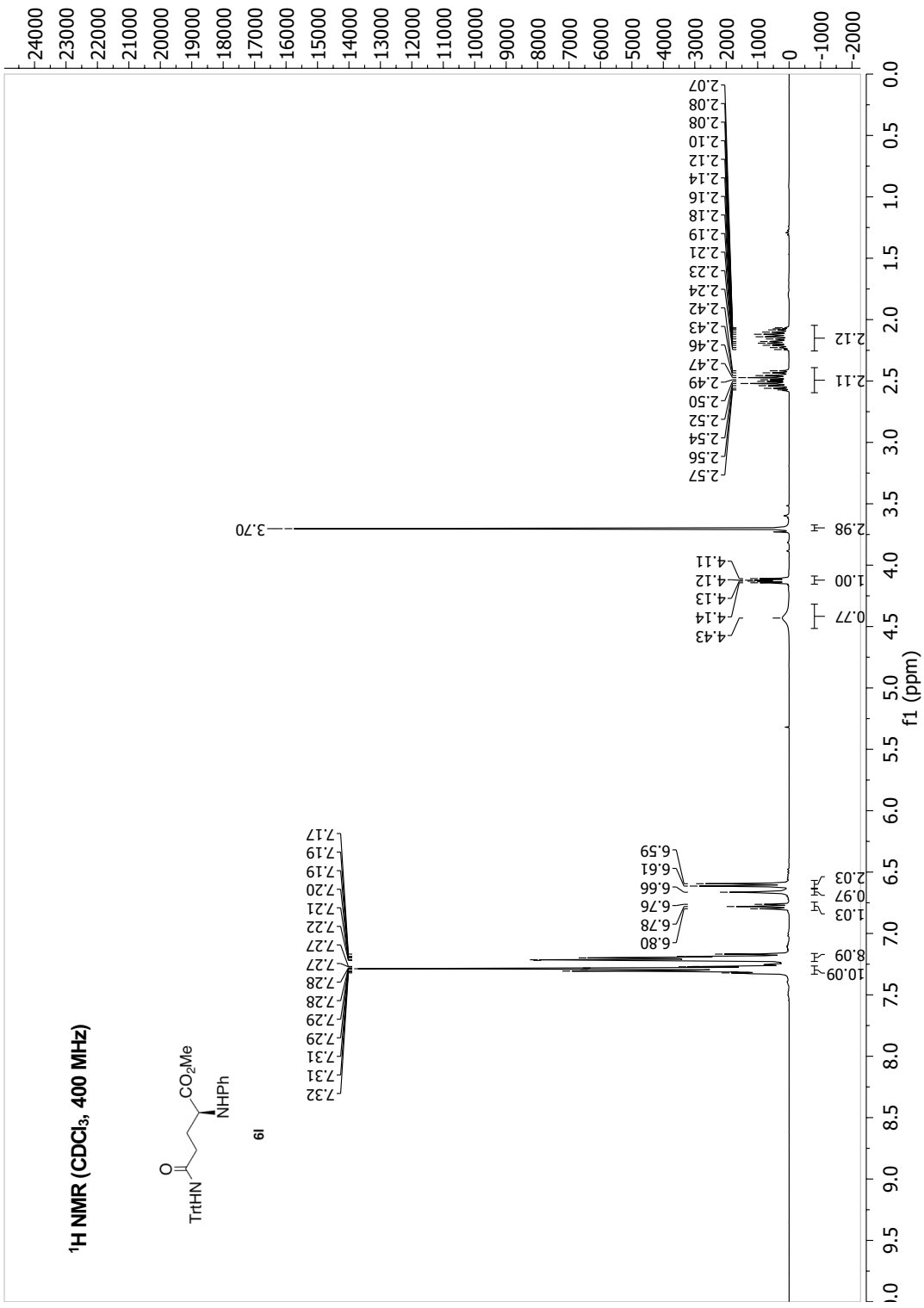

^{13}C NMR (CDCl$_3$, 100 MHz)
CO$_2$Me
NHPh
Ph
6i
173.5
146.3
136.3
129.3
129.2
128.5
127.0
118.4
113.6
57.7
52.0
38.6
f1 (ppm)

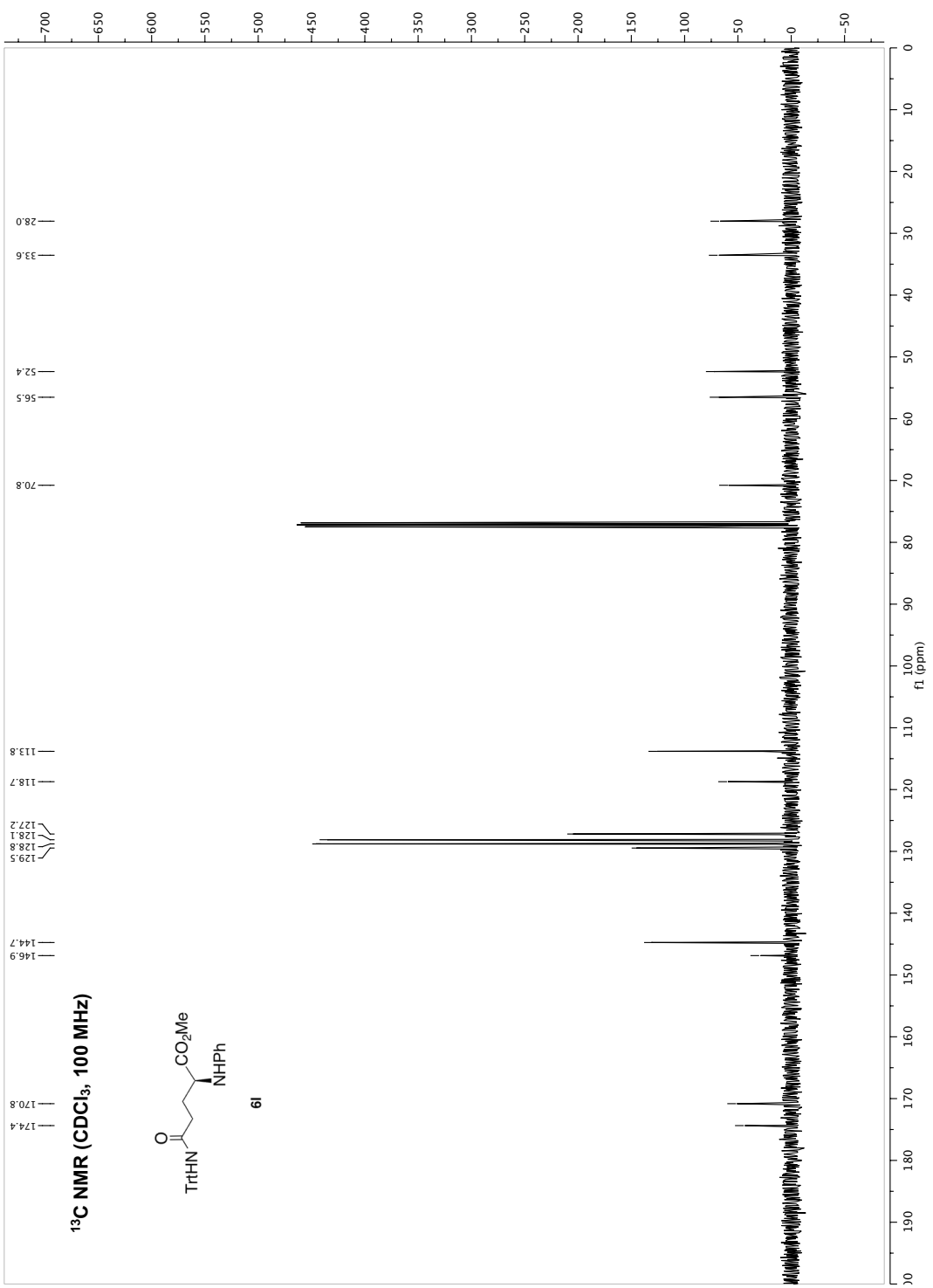

^{1}H NMR ($CDCl_3$, 400 MHz)
CO_2Me
NHPh
BnO
6j
7.53
7.52
7.52
7.52
7.51
7.50
7.48
7.48
7.44
7.42
7.30
7.28
7.28
7.28
7.26
7.19
7.17
7.17
7.02
7.02
7.00
6.87
6.85
6.72
6.72
6.70
6.70
5.12
4.44
4.29
3.75
3.23
3.22
3.20
3.18
3.17
3.16
3.14
3.12
5.06
2.06
2.04
2.00
1.00
1.99
2.01
1.01
0.94
2.98
2.03
f1 (ppm)

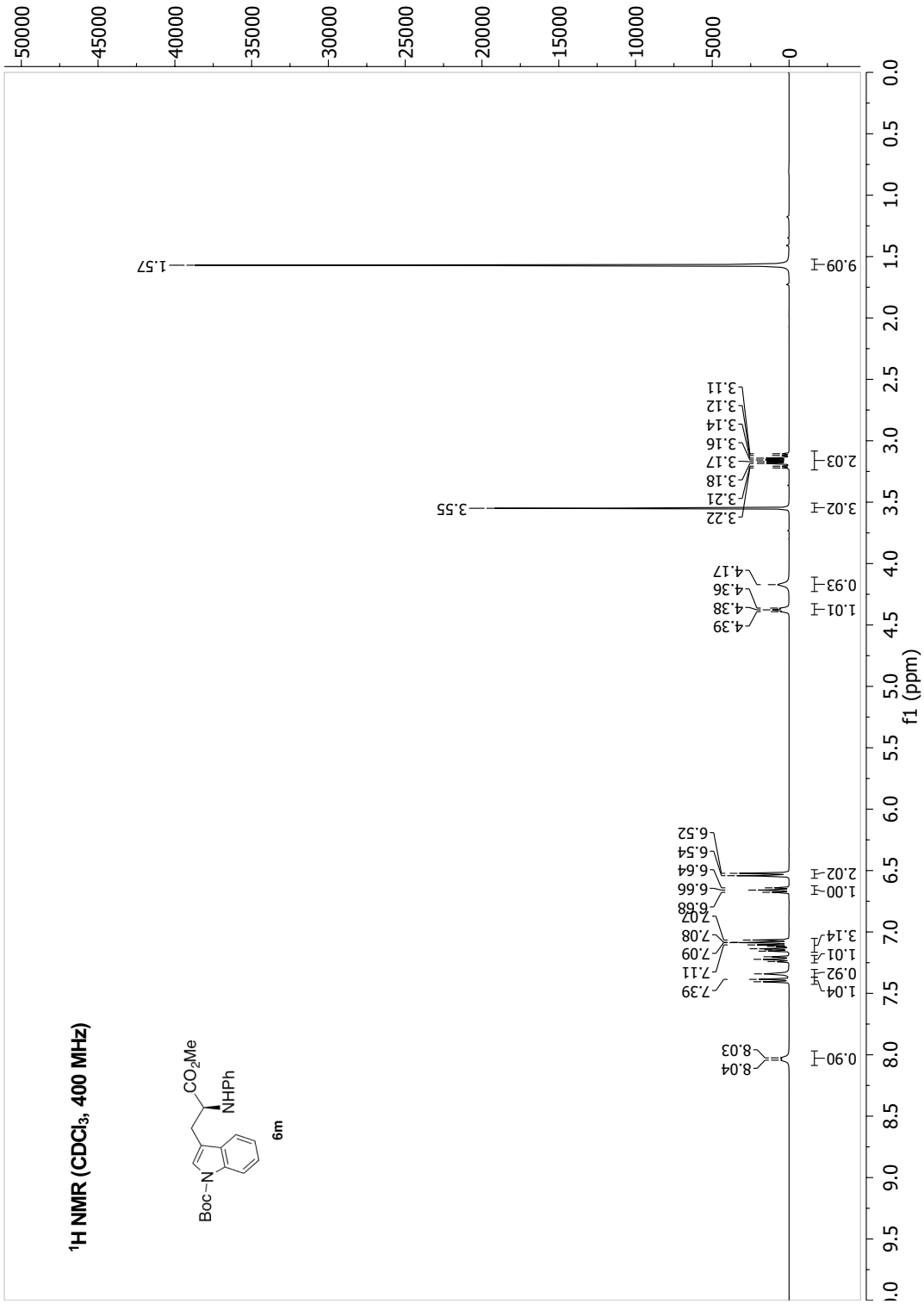

13C NMR (CDCl3, 100 MHz)
6j
CO2Me
NHPh
BnO
173.7
157.9
146.4
137.0
130.3
129.4
128.6
128.6
128.0
127.5
118.4
114.9
113.6
70.0
57.8
52.1
37.7
f1 (ppm)

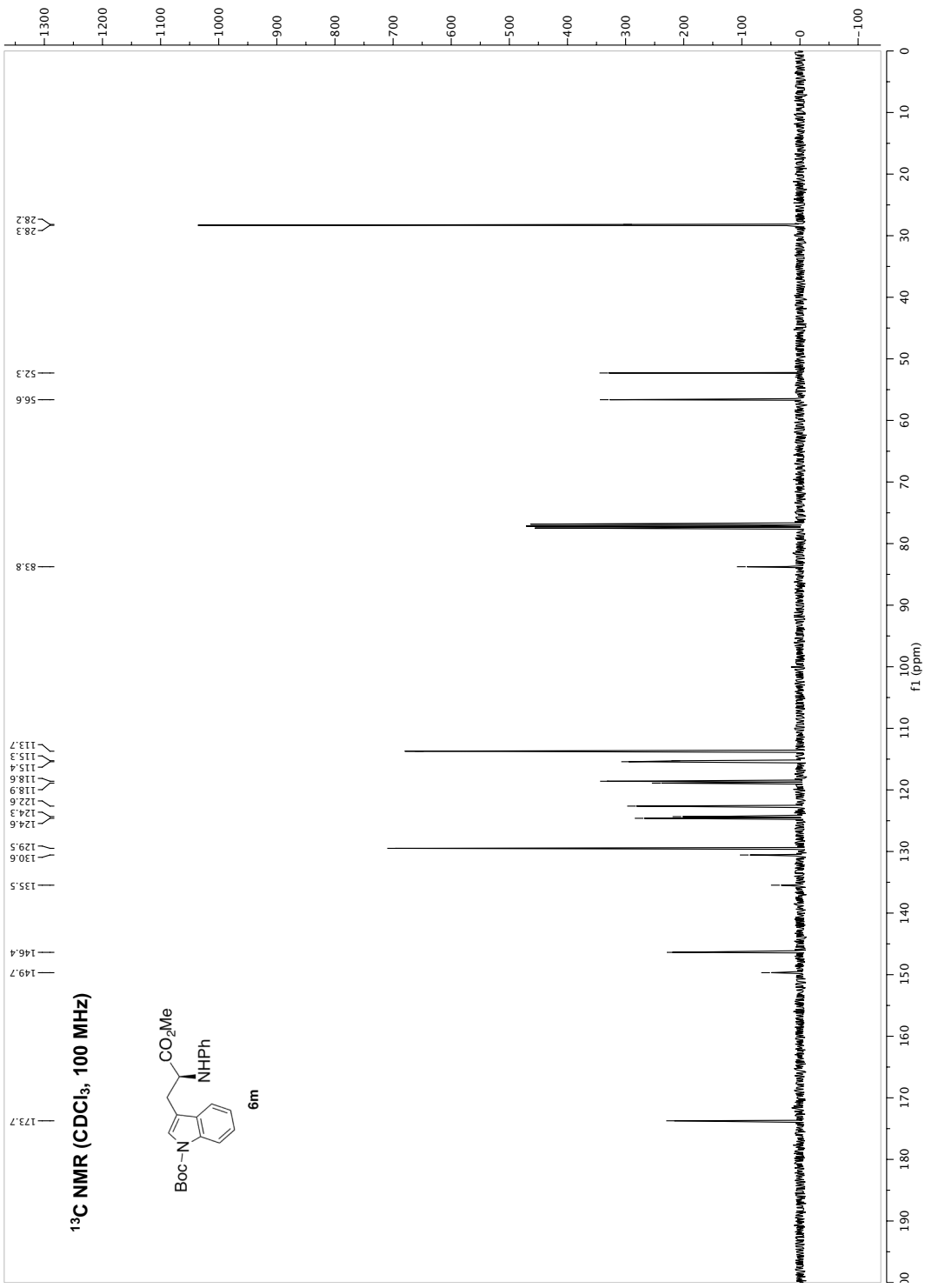

^{1}H NMR ($CDCl_3$, 400 MHz)
Cbz
N
H
CO_2Me
NHPh
6k
f1 (ppm)

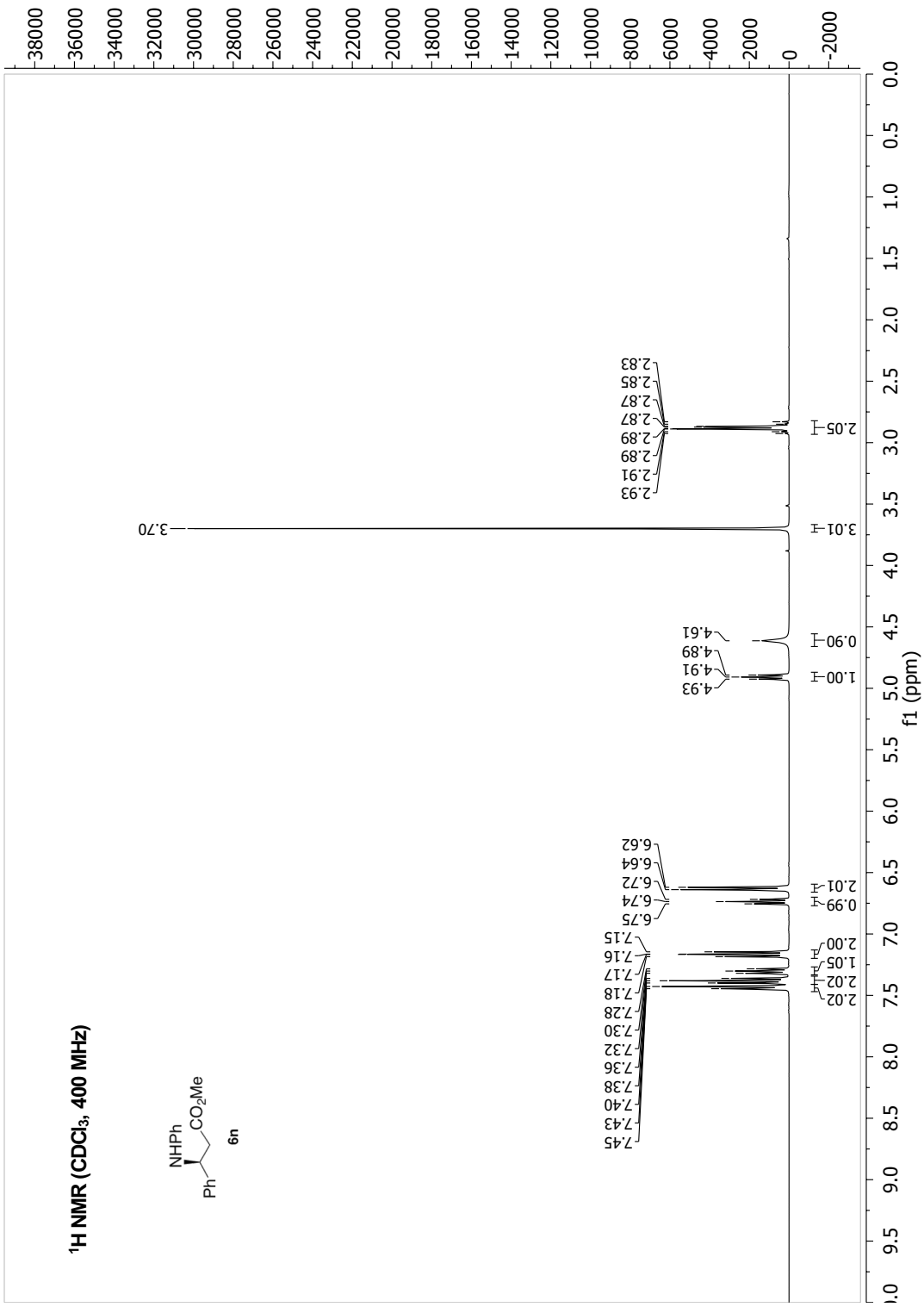

13C NMR (CDCl3, 100 MHz)
6k
Cbz
H
N
CO2Me
NHPh
174.6
156.5
146.8
136.6
129.4
128.5
128.1
128.1
118.3
113.4
66.6
56.4
52.2
40.7
32.6
29.7
22.7
f1 (ppm)

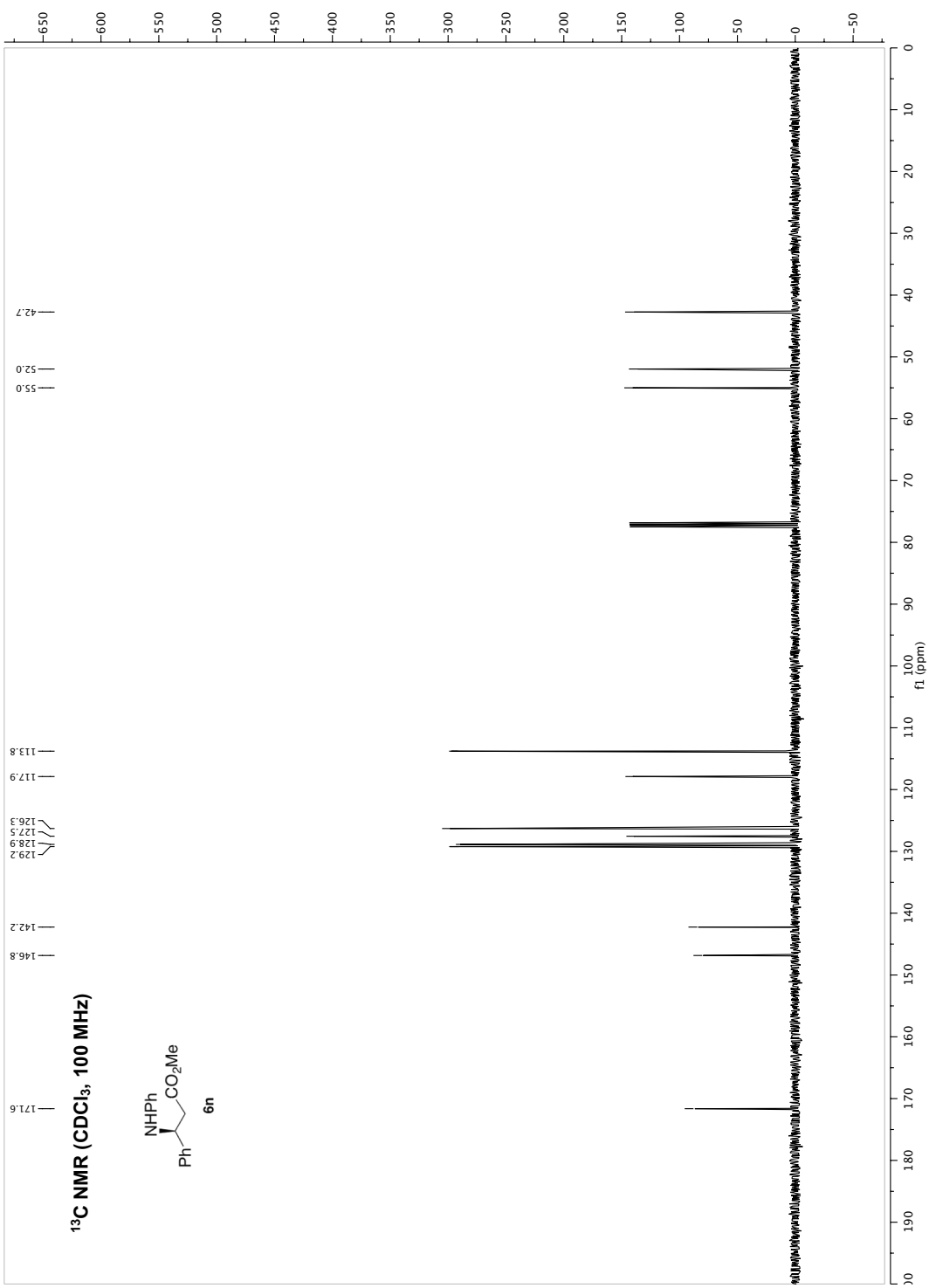

^{1}H NMR ($CDCl_3$, 400 MHz)
TrtHN
O
CO_2Me
NHPh
6l
f1 (ppm)

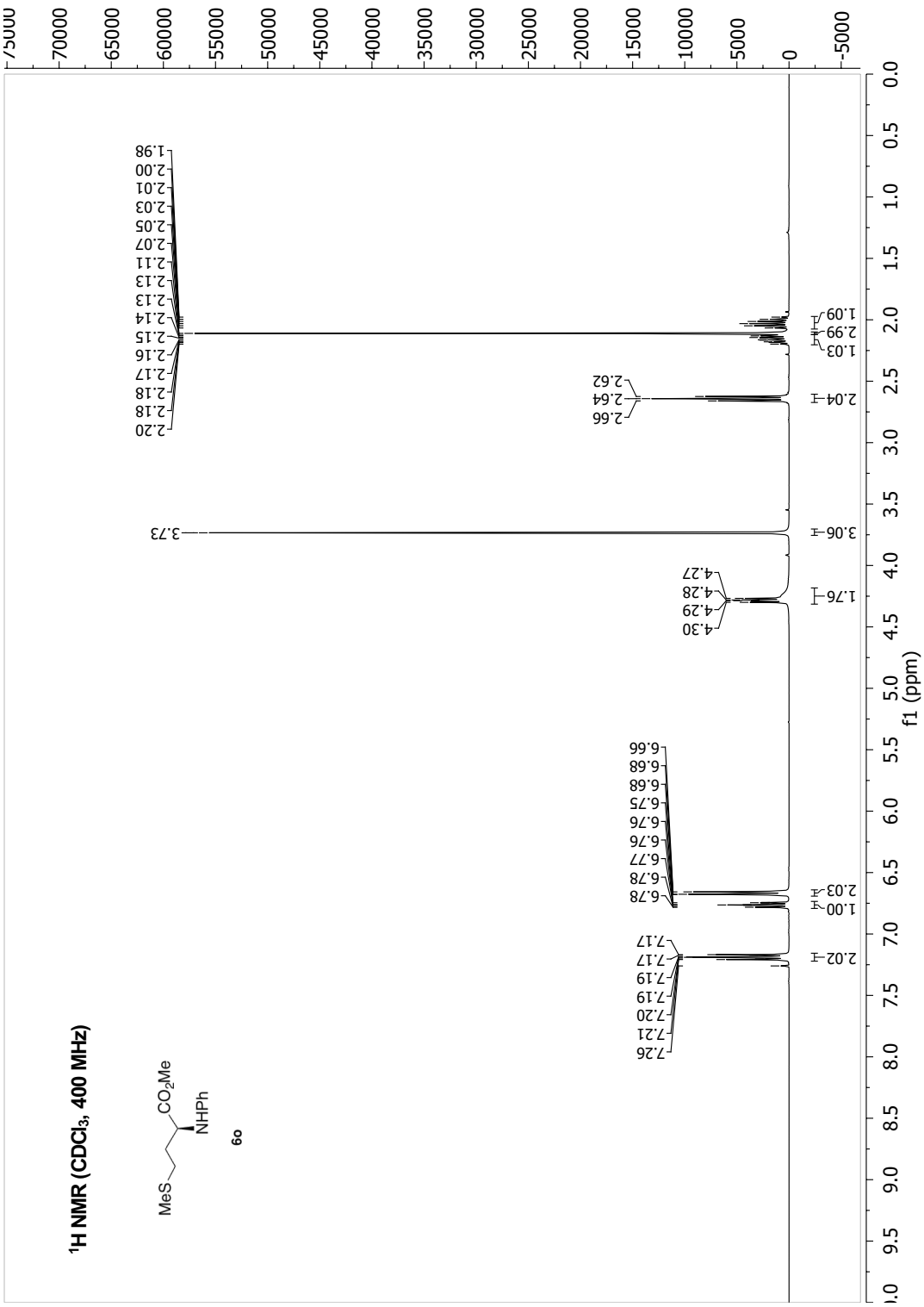

13C NMR (CDCl3, 100 MHz)
TrtHN
O
CO2Me
NHPh
6l
174.4
170.8
146.9
144.7
129.5
128.8
128.1
127.2
118.7
113.8
70.8
56.5
52.4
33.6
28.0
f1 (ppm)

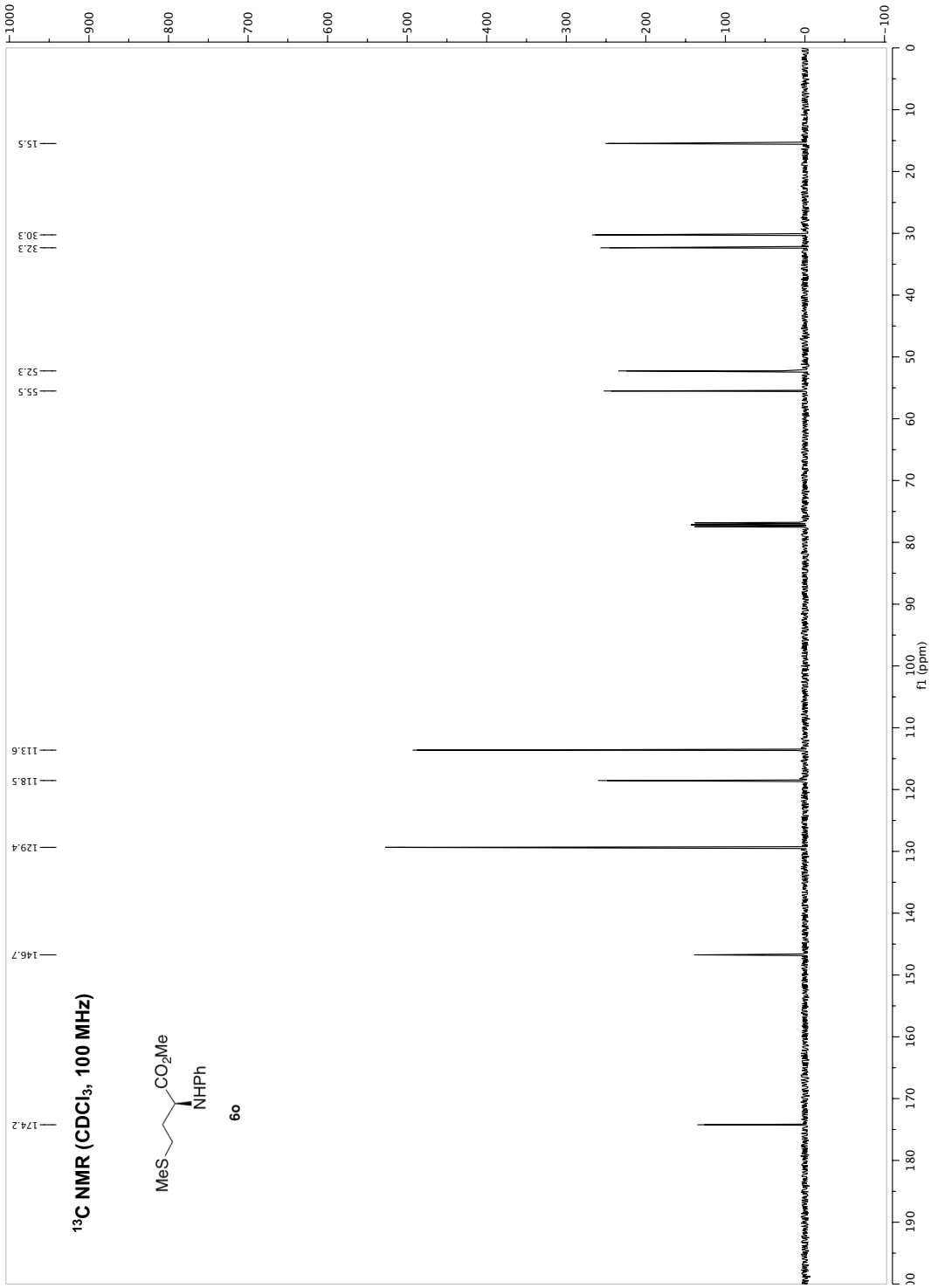

^{1}H NMR ($CDCl_3$, 400 MHz)
CO_2Me
NHPh
Boc–N
6m
f1 (ppm)

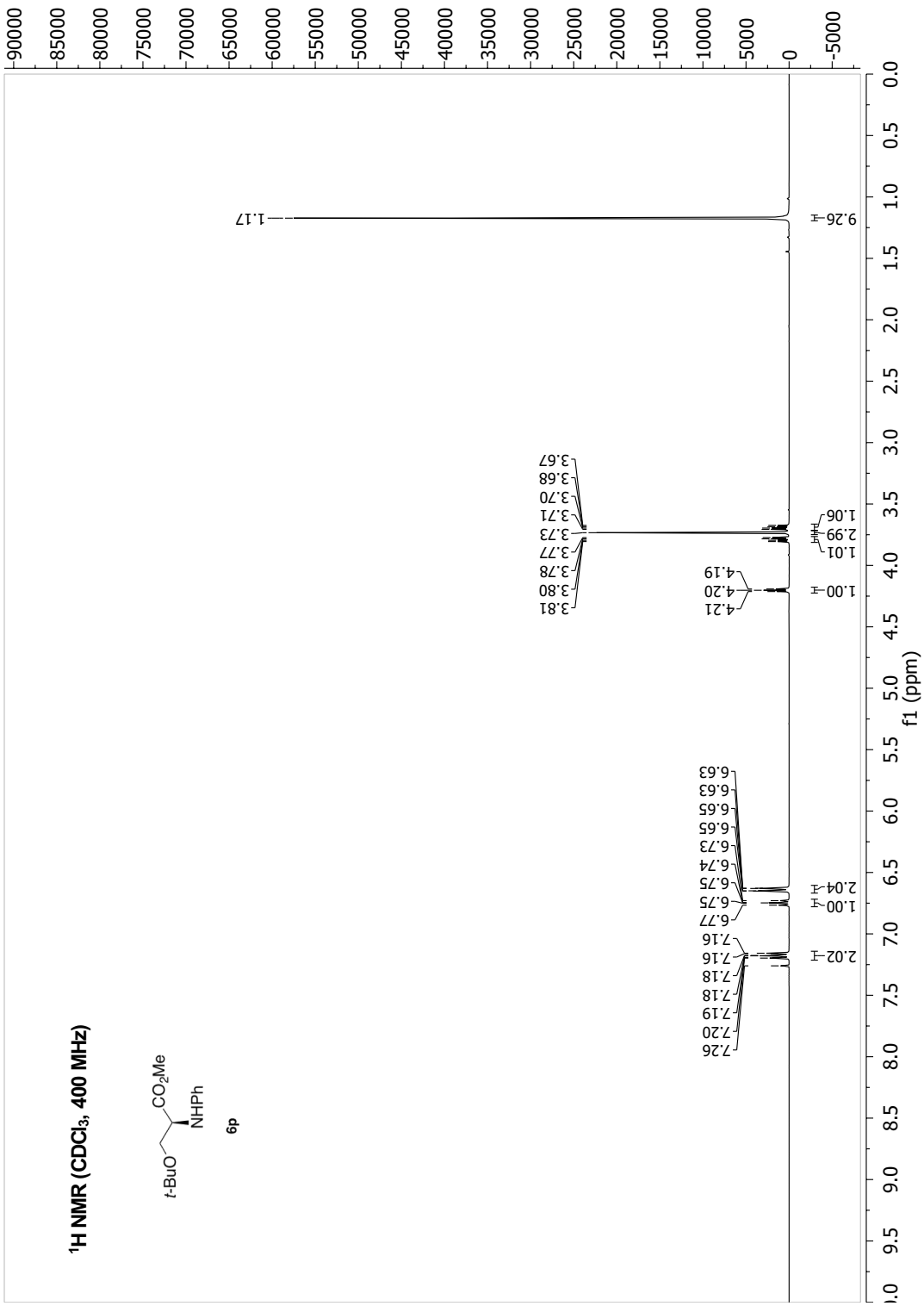

^{13}C NMR (CDCl$_3$, 100 MHz)
CO$_2$Me
NHPh
Boc–N
6m
173.7
149.7
146.4
135.5
130.6
129.5
124.6
124.3
122.6
118.9
118.6
115.4
115.3
113.7
83.8
56.6
52.3
28.3
28.2
f1 (ppm)

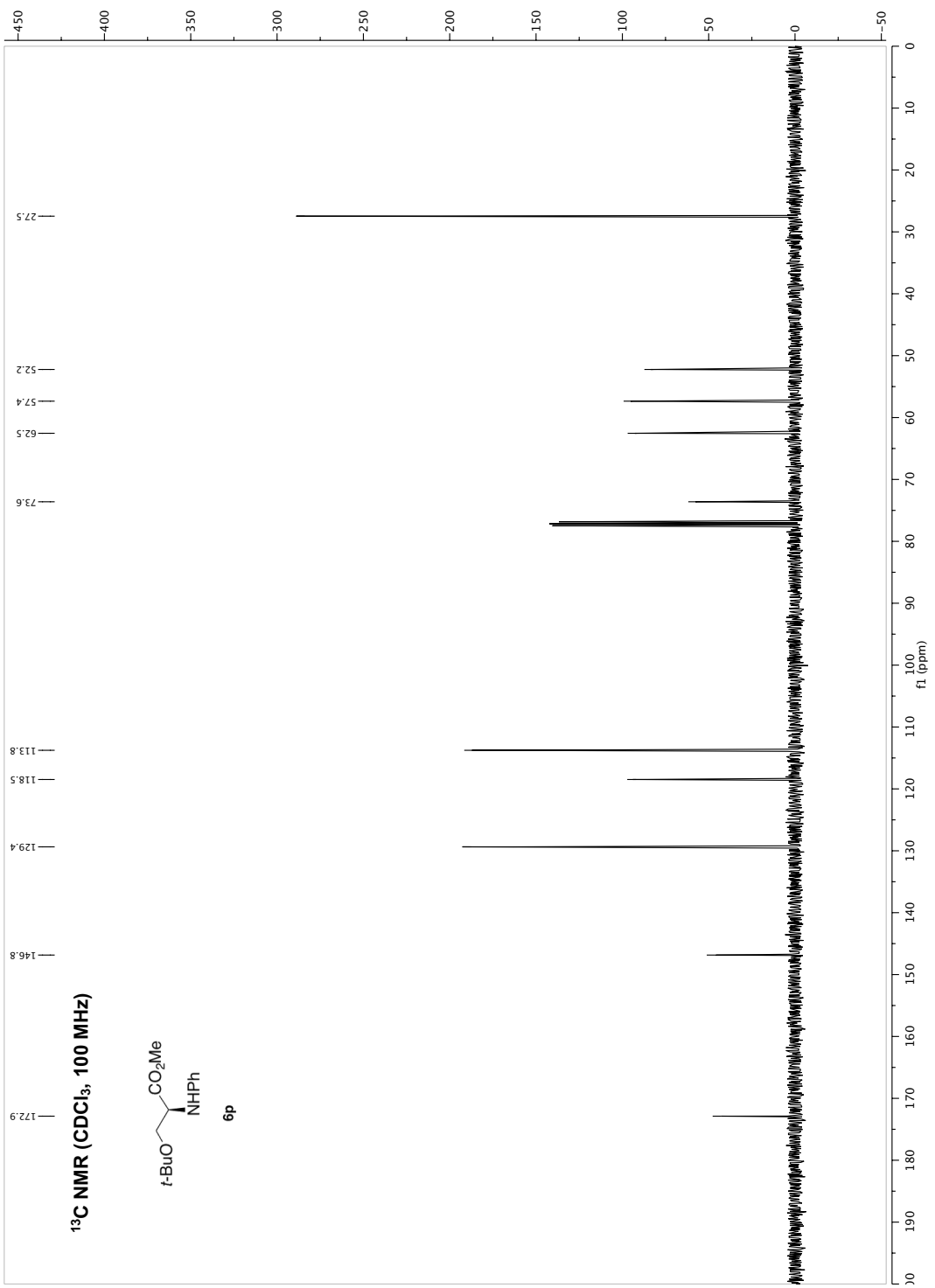

^{1}H NMR ($CDCl_3$, 400 MHz)
NHPh
CO_2Me
Ph
6n
7.45
7.43
7.40
7.38
7.36
7.32
7.30
7.28
7.18
7.17
7.16
7.15
6.75
6.74
6.72
6.64
6.62
4.93
4.91
4.89
4.61
3.70
2.93
2.91
2.89
2.89
2.87
2.87
2.85
2.83
2.02
2.02
1.05
2.00
0.99
2.01
2.05
3.01
0.90
1.00
f1 (ppm)

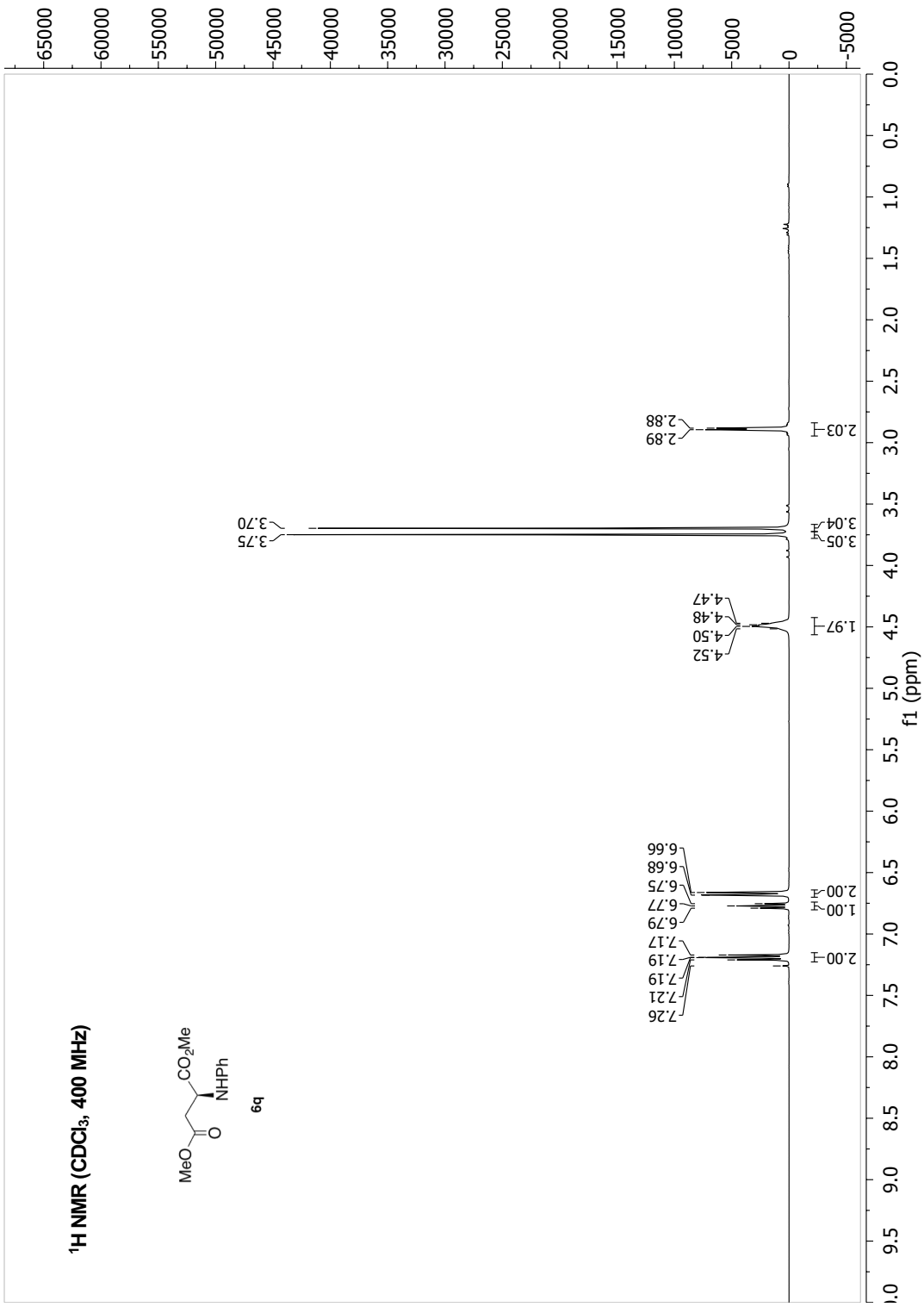

13C NMR (CDCl3, 100 MHz)
NHPh
CO2Me
Ph
6n
171.6
146.8
142.2
129.2
128.9
127.5
126.3
117.9
113.8
55.0
52.0
42.7
f1 (ppm)

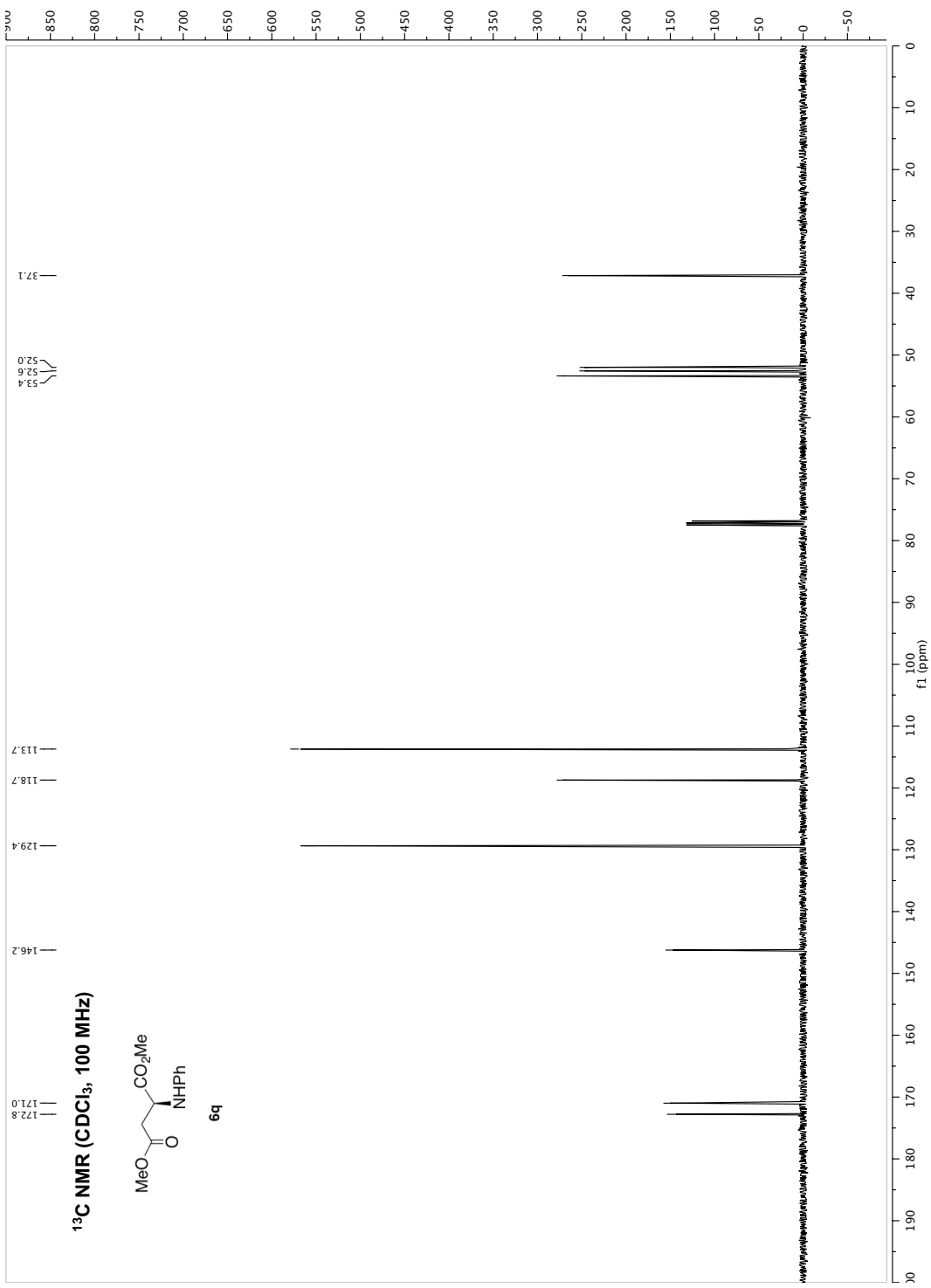

^{1}H NMR ($CDCl_3$, 400 MHz)
MeS
CO_2Me
NHPh
6o
f1 (ppm)

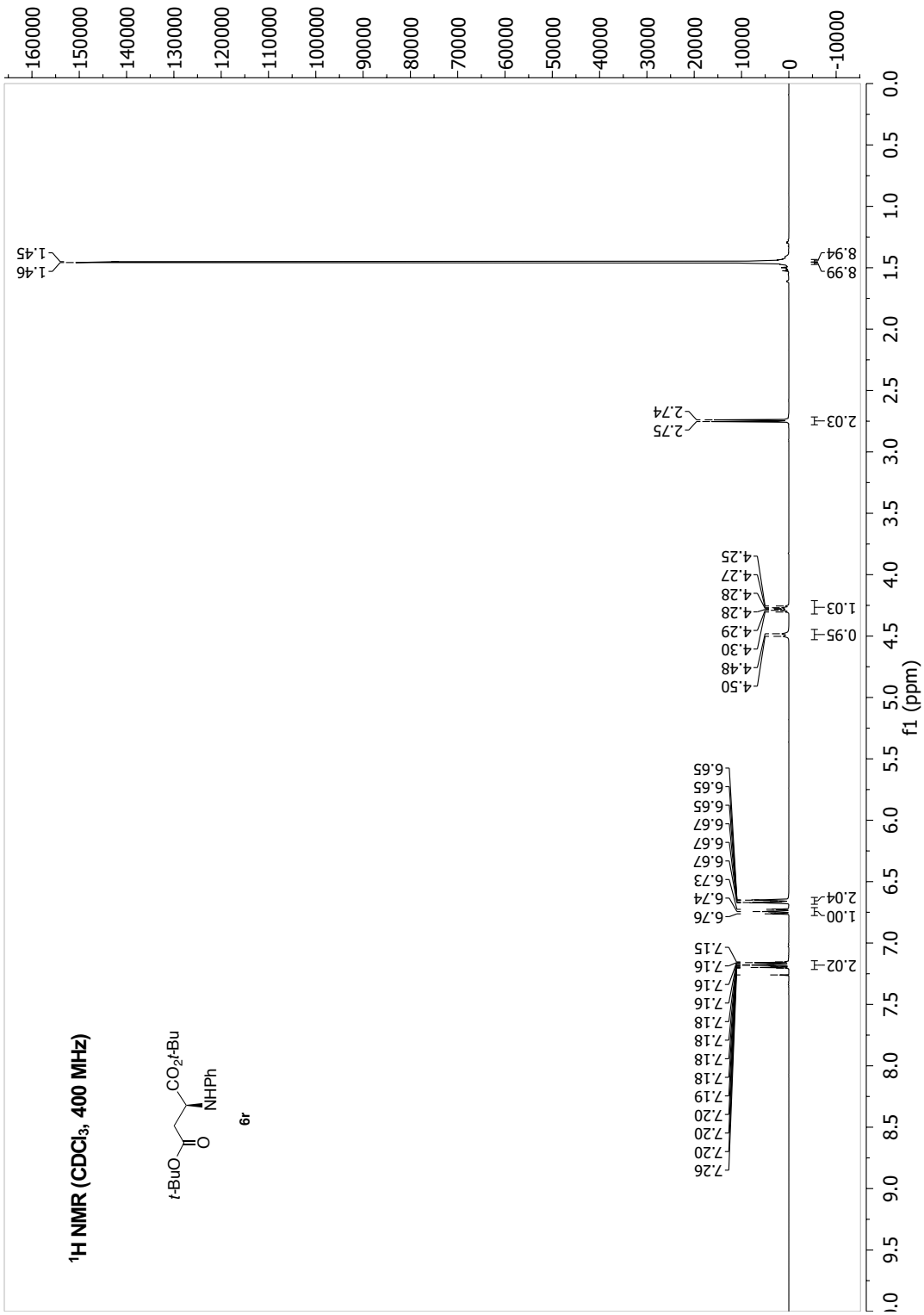

^{13}C NMR (CDCl$_3$, 100 MHz)
MeS
CO$_2$Me
NHPh
6o
174.2
146.7
129.4
118.5
113.6
55.5
52.3
32.3
30.3
15.5
f1 (ppm)

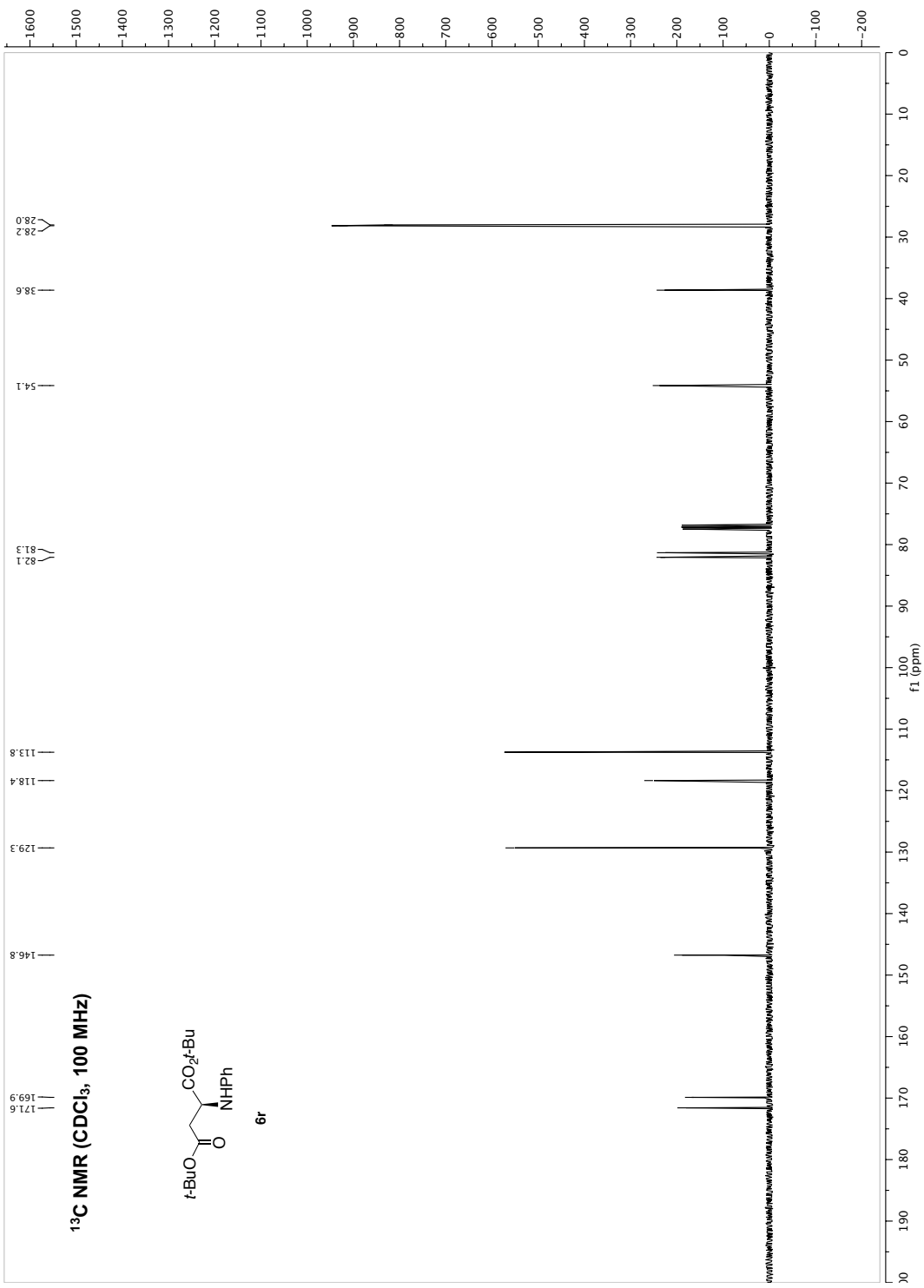

1H NMR (CDCl3, 400 MHz)
t-BuO
CO2Me
NHPh
6p
1.17
3.67
3.68
3.70
3.71
3.73
3.77
3.78
3.80
3.81
4.19
4.20
4.21
6.63
6.63
6.65
6.65
6.73
6.74
6.75
6.75
6.77
7.16
7.16
7.18
7.18
7.19
7.20
7.26
9.26
1.00
2.99
1.06
1.01
1.00
2.04
2.02
f1 (ppm)

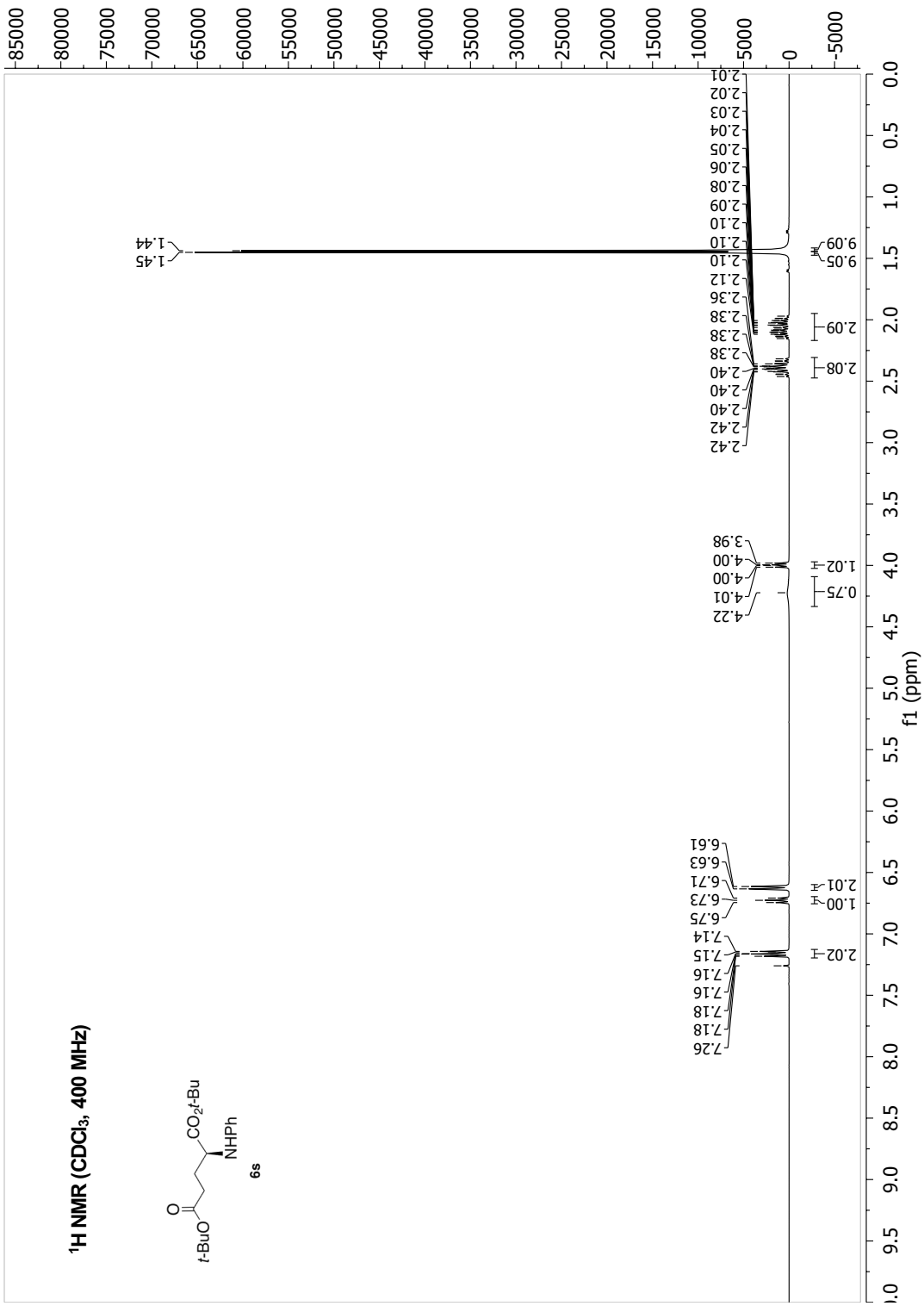

^{13}C NMR (CDCl$_3$, 100 MHz)
t-BuO
CO$_2$Me
NHPh
6p
172.9
146.8
129.4
118.5
113.8
73.6
62.5
57.4
52.2
27.5
f1 (ppm)

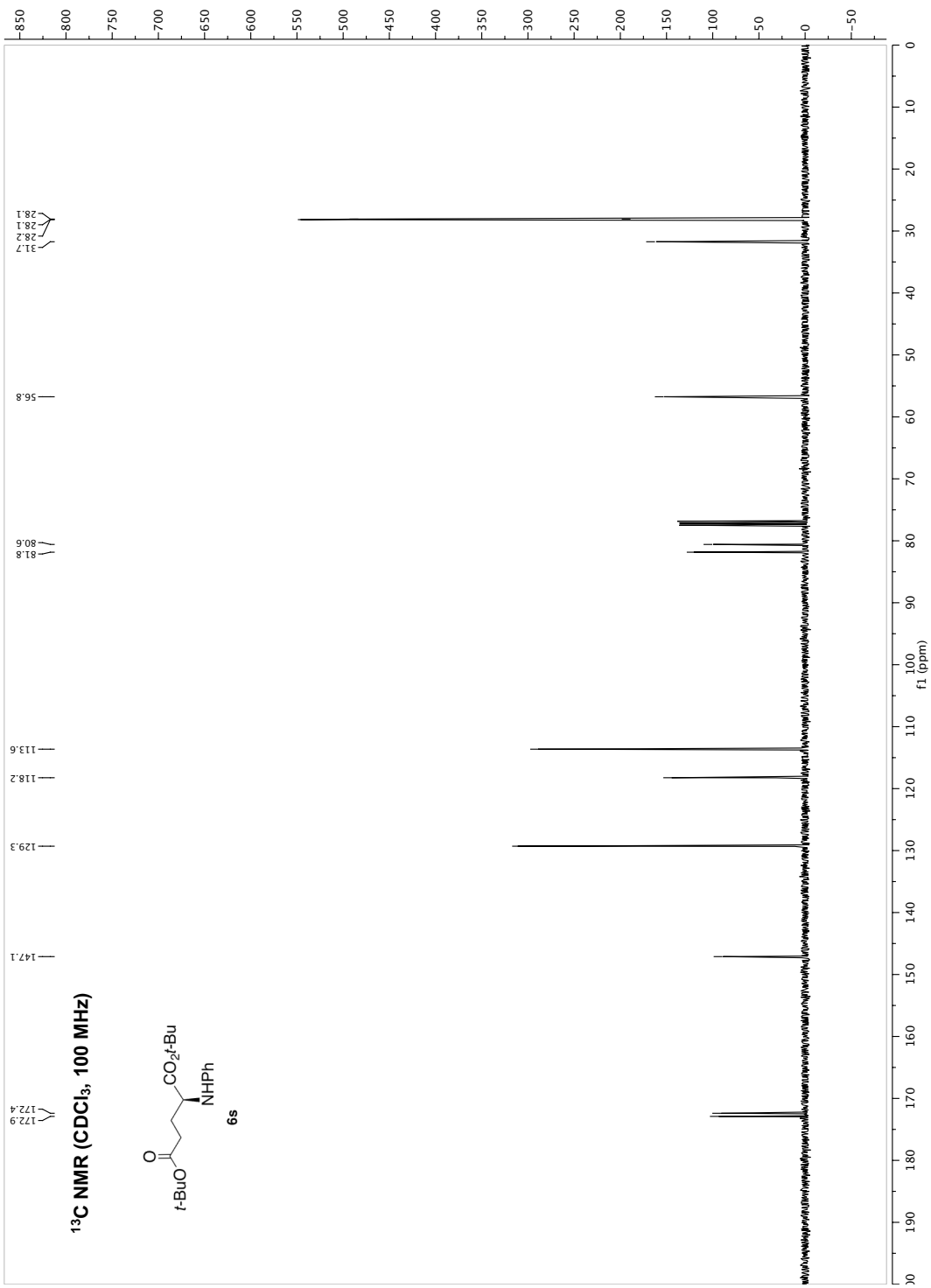

^{1}H NMR ($CDCl_3$, 400 MHz)
MeO
O
CO_2Me
NHPh
6q
7.26
7.21
7.19
7.19
7.17
6.79
6.77
6.75
6.68
6.66
4.52
4.50
4.48
4.47
3.75
3.70
2.89
2.88
2.00
1.00
2.00
1.97
3.05
3.04
2.03
f1 (ppm)

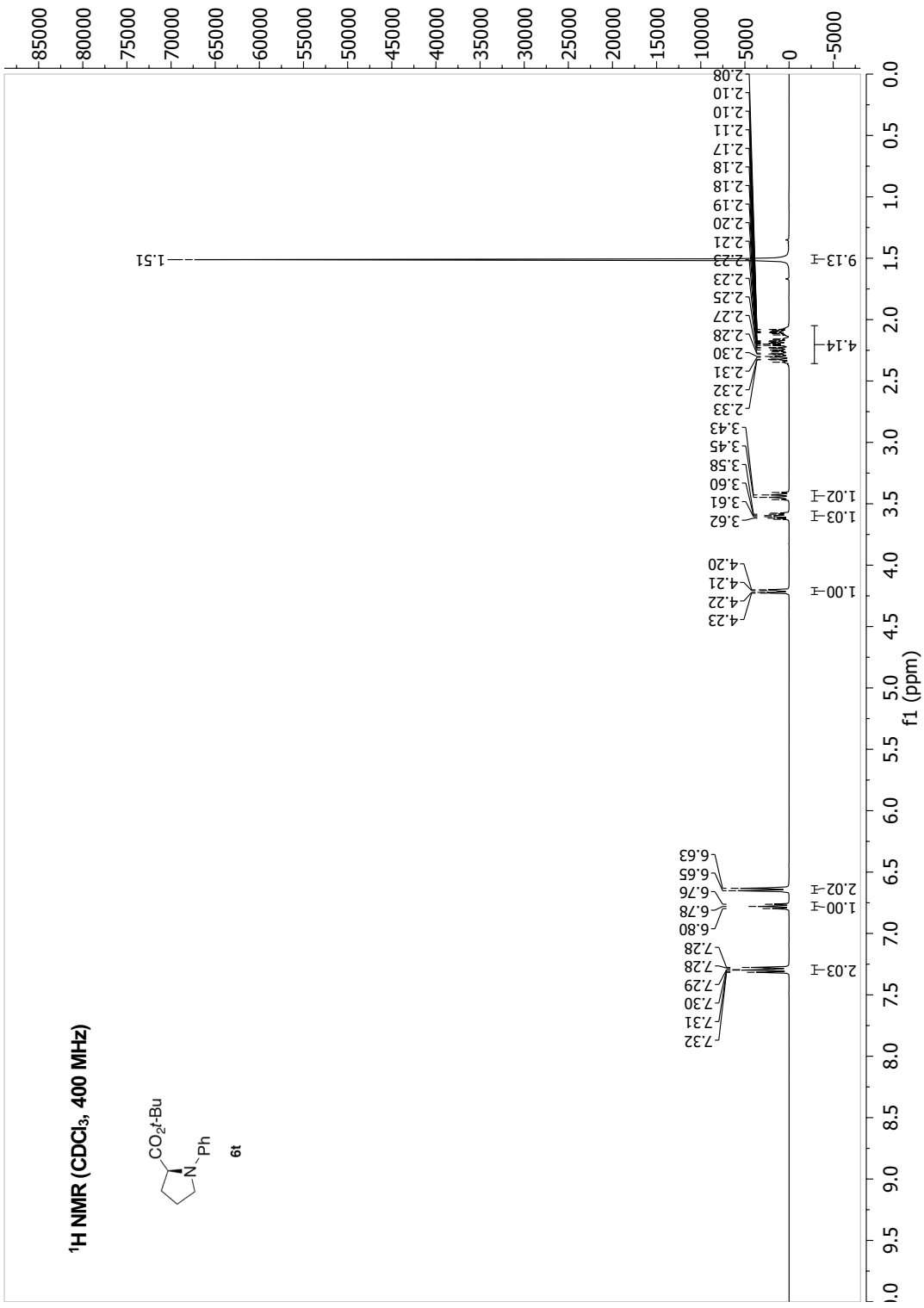

13C NMR (CDCl3, 100 MHz)
MeO
O
CO2Me
NHPh
6q
172.8
171.0
146.2
129.4
118.7
113.7
53.4
52.6
52.0
37.1
f1 (ppm)

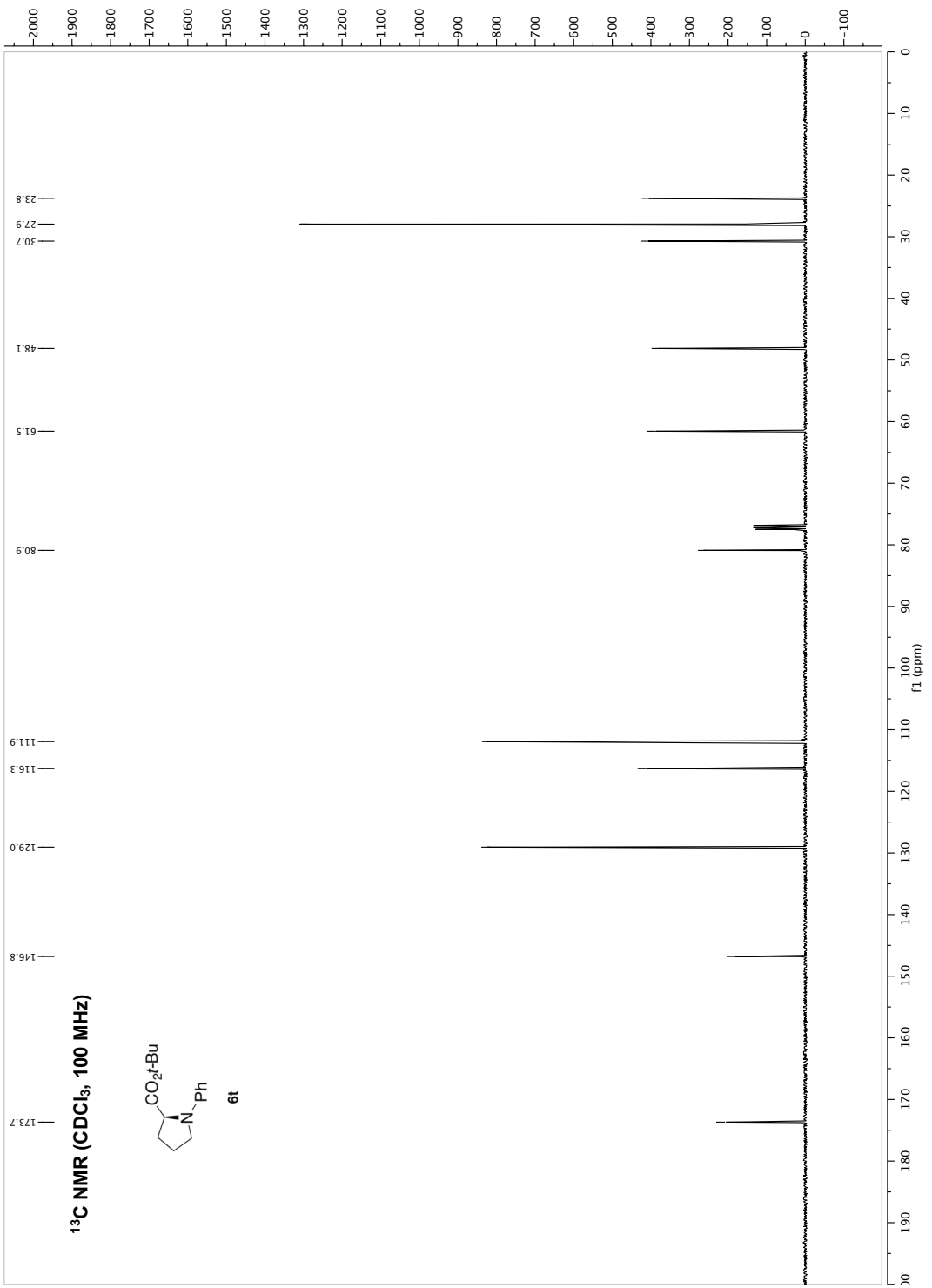

¹H NMR (CDCl₃, 400 MHz)
t-BuO
O
NHPh
CO₂t-Bu
6r
f1 (ppm)

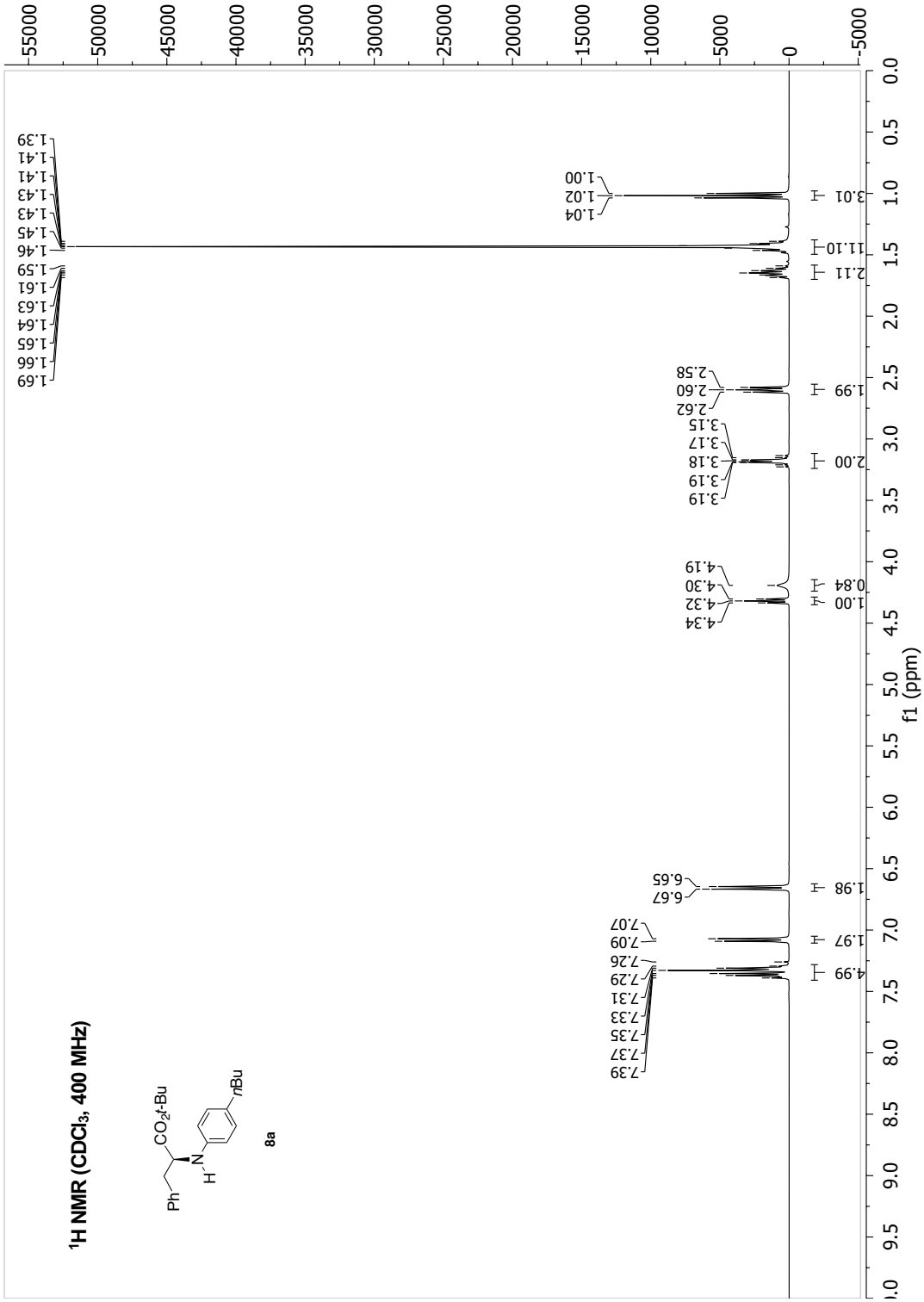

13C NMR (CDCl3, 100 MHz)
t-BuO
CO2t-Bu
NHPh
O
6r
171.6
169.9
146.8
129.3
118.4
113.8
82.1
81.3
54.1
38.6
28.2
28.0
f1 (ppm)

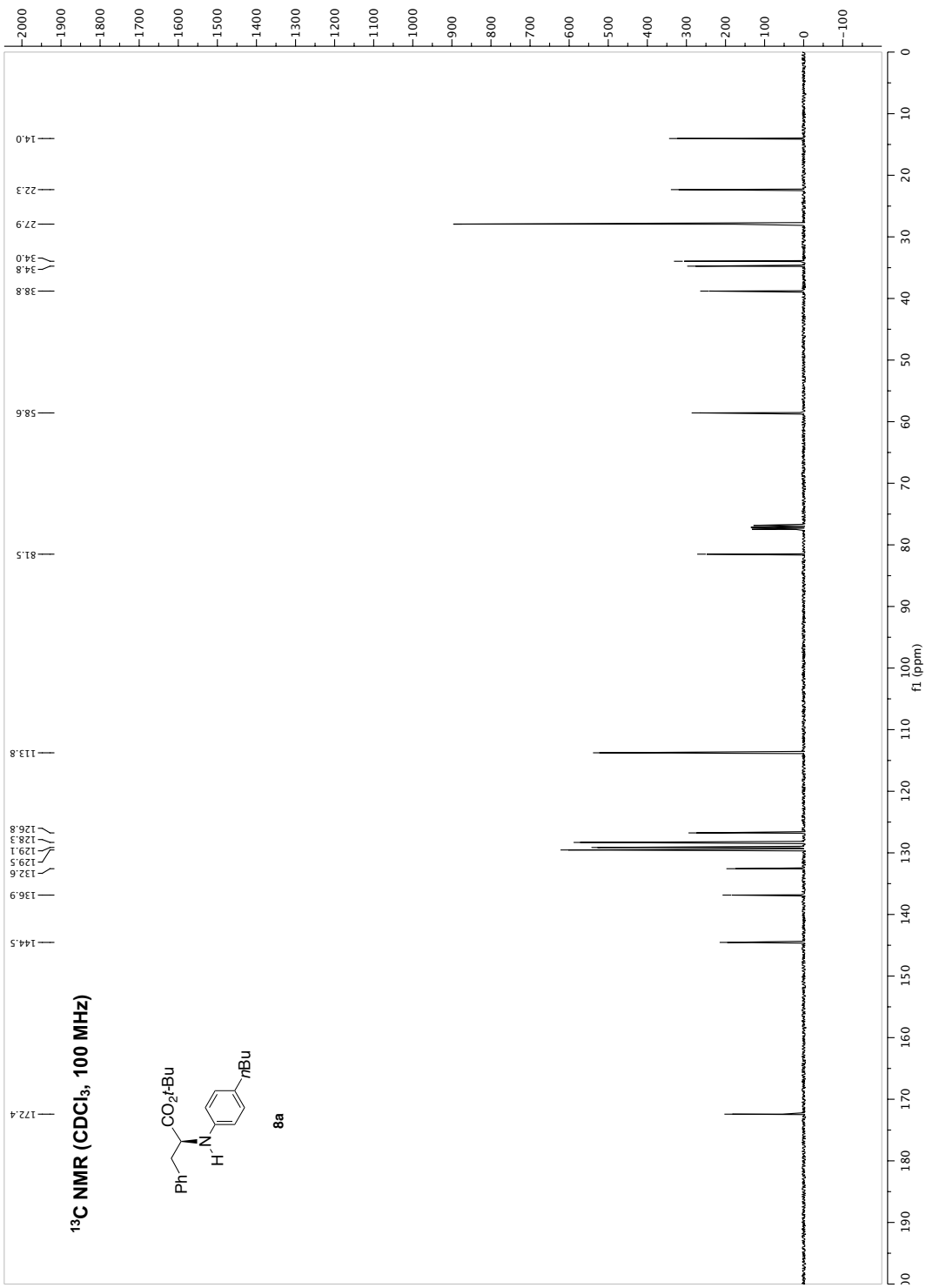

1H NMR (CDCl3, 400 MHz)
t-BuO
O
CO2t-Bu
NHPh
6s
f1 (ppm)

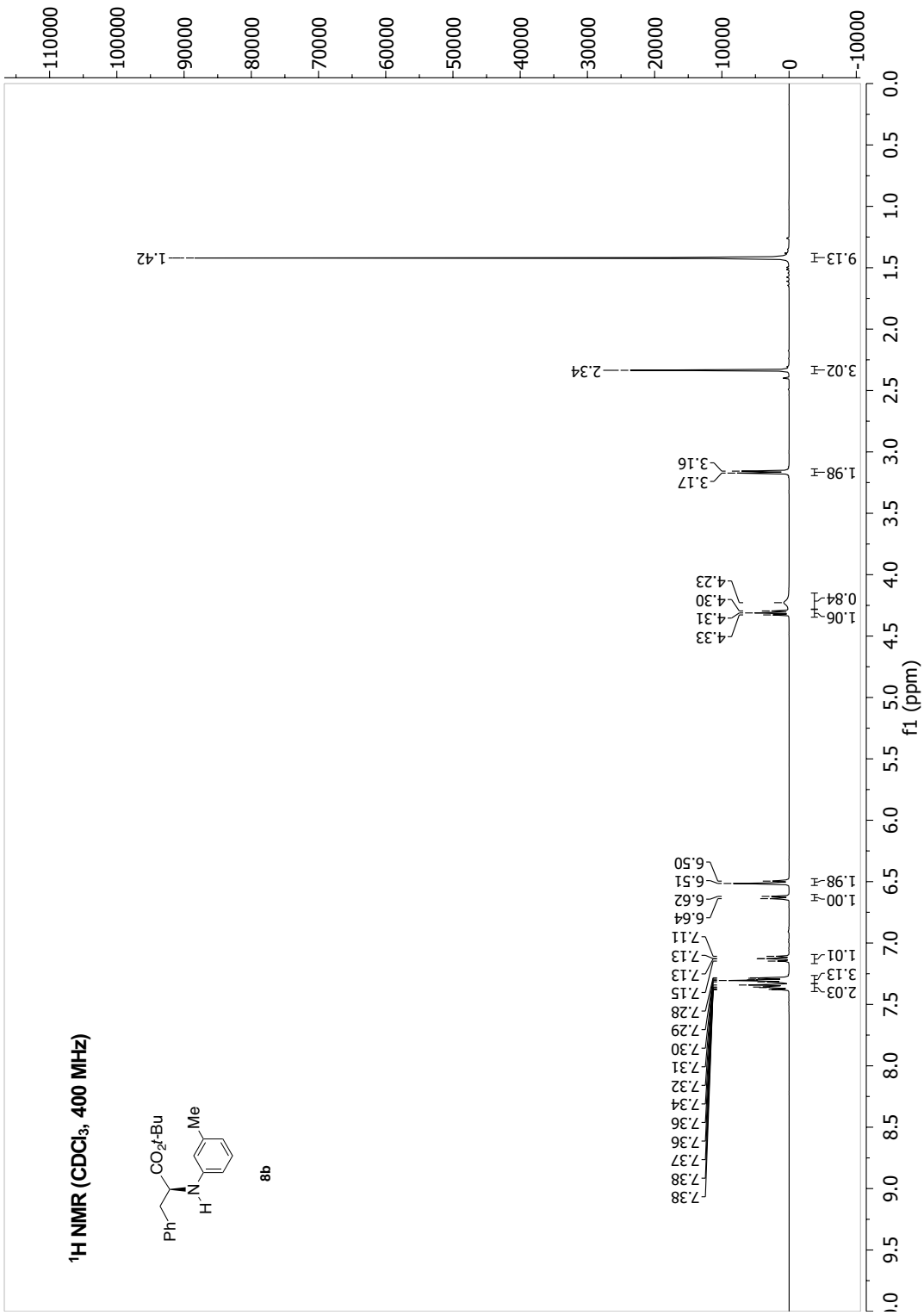

13C NMR (CDCl3, 100 MHz)
t-BuO
O
CO2t-Bu
NHPh
6s
172.9
172.4
147.1
129.3
118.2
113.6
81.8
80.6
56.8
31.7
28.2
28.1
28.1
f1 (ppm)

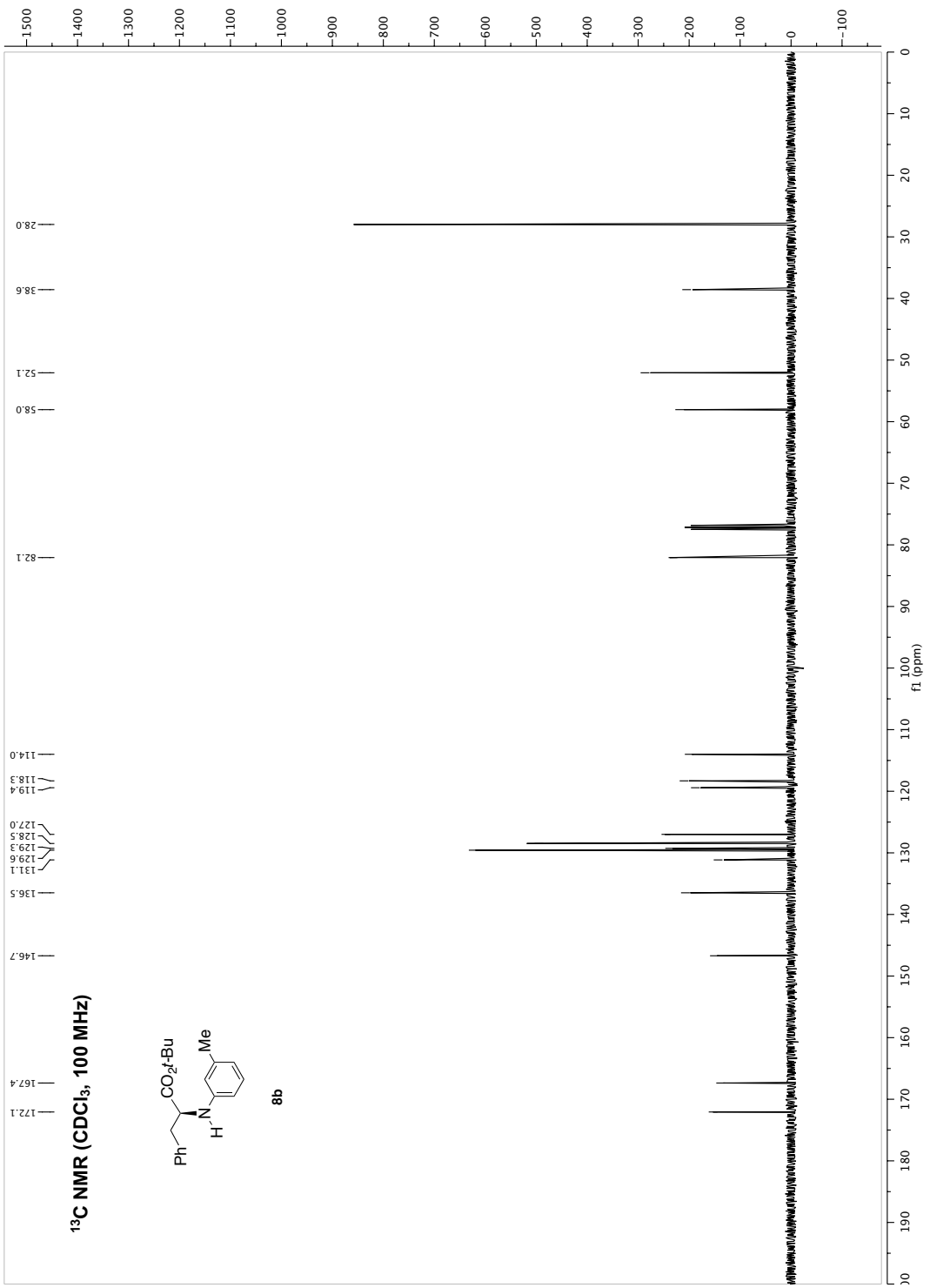

^{1}H NMR ($CDCl_3$, 400 MHz)
CO_2t-Bu
N
Ph
6t
f1 (ppm)

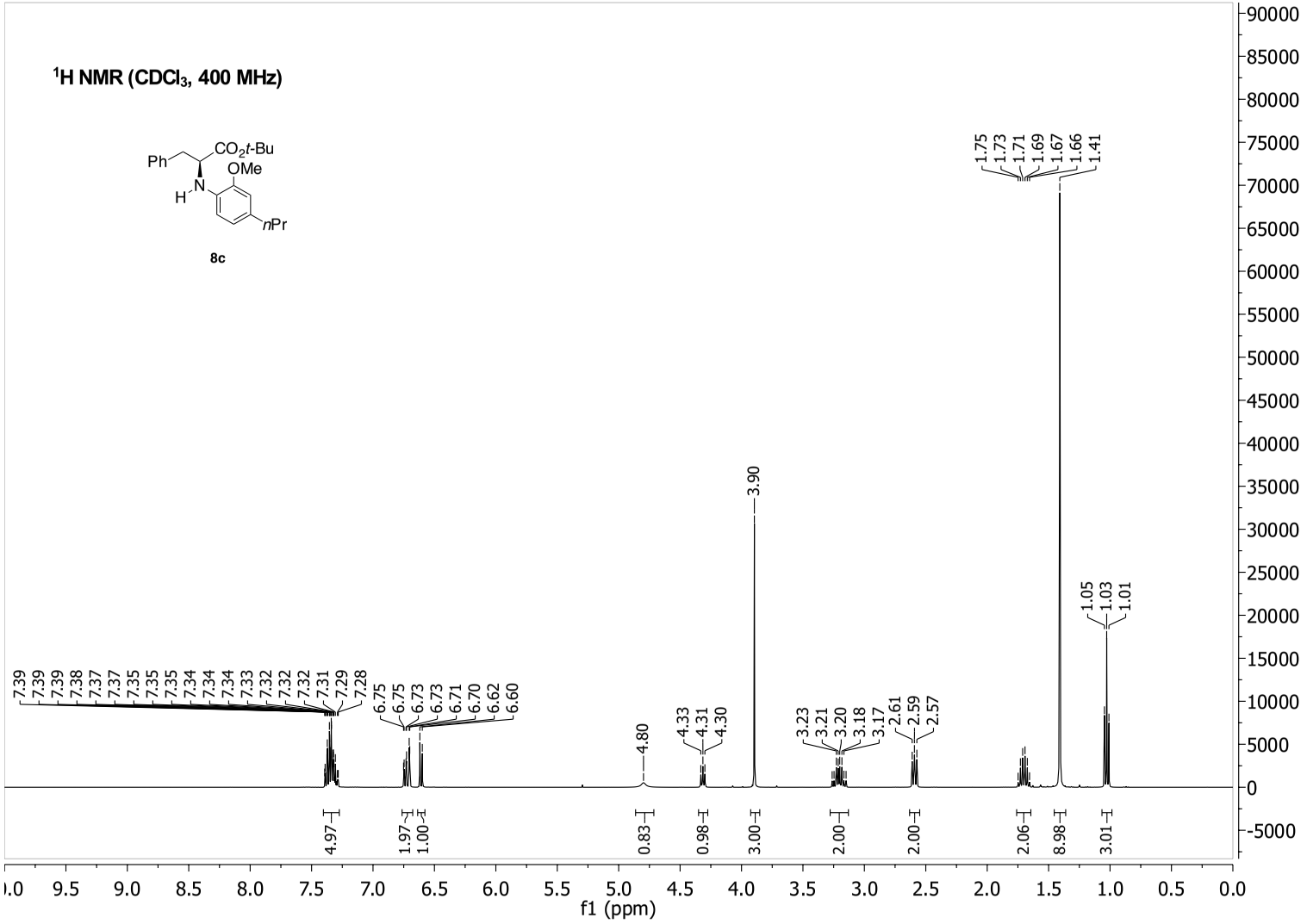

^{13}C NMR ($CDCl_3$, 100 MHz)
CO_2t-Bu
N
Ph
6t
173.7
146.8
129.0
116.3
111.9
80.9
61.5
48.1
30.7
27.9
23.8
f1 (ppm)

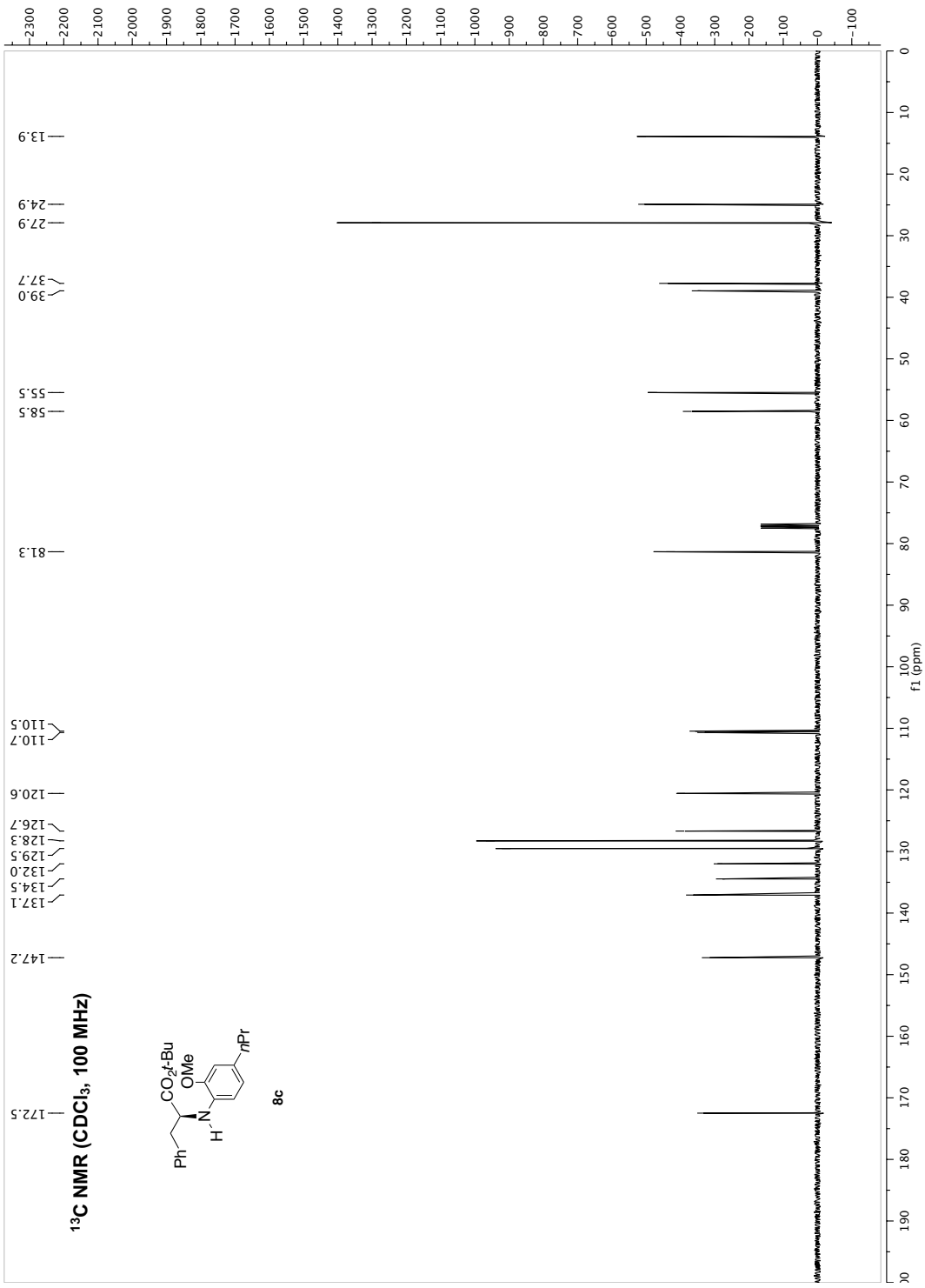

1H NMR (CDCl3, 400 MHz)
8a
f1 (ppm)

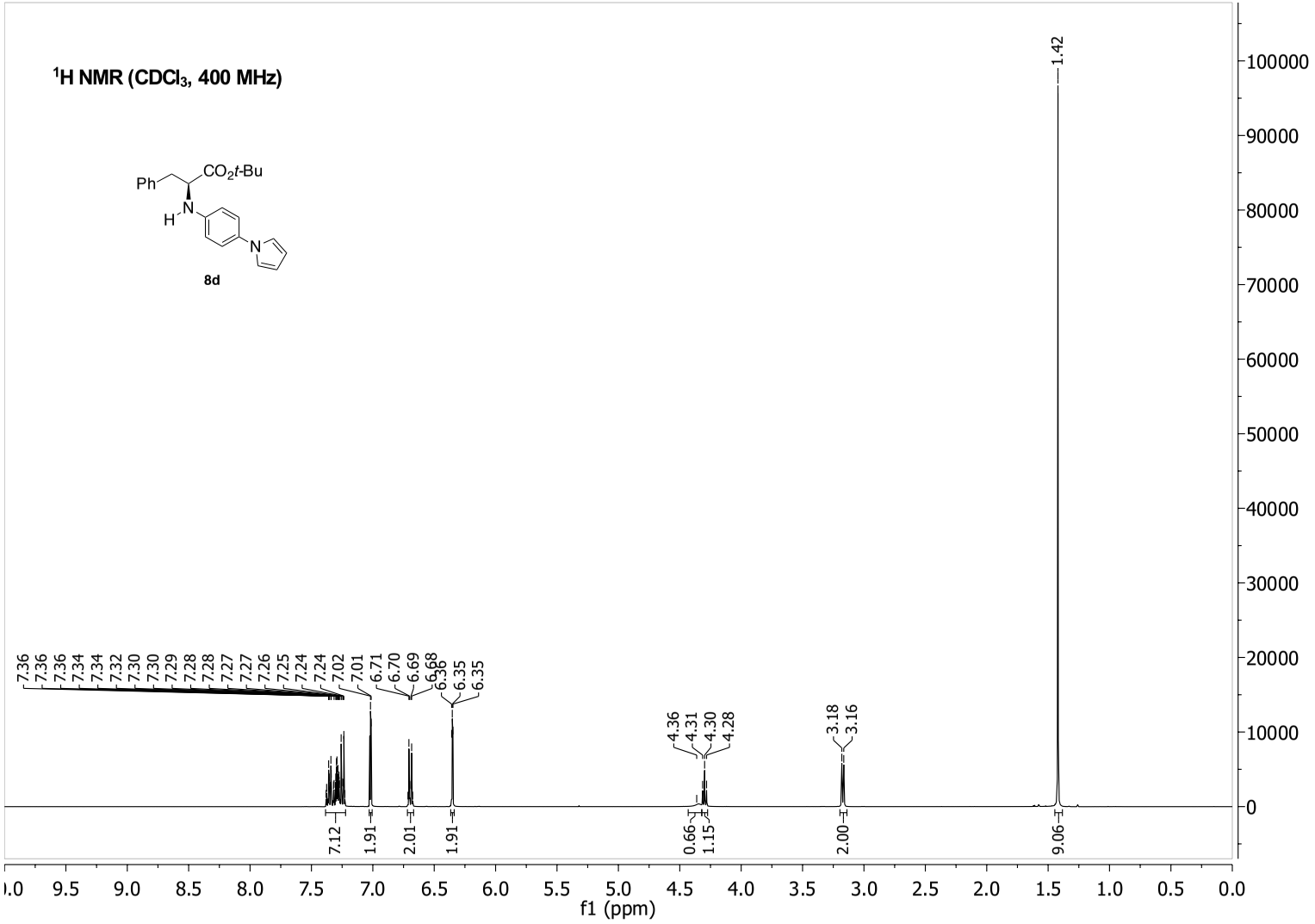

^{13}C NMR (CDCl$_3$, 100 MHz)
Ph
CO$_2$t-Bu
N
H
nBu
8a
172.4
144.5
136.9
132.6
129.5
129.1
128.3
126.8
113.8
81.5
58.6
38.8
34.8
34.0
27.9
22.3
14.0
f1 (ppm)

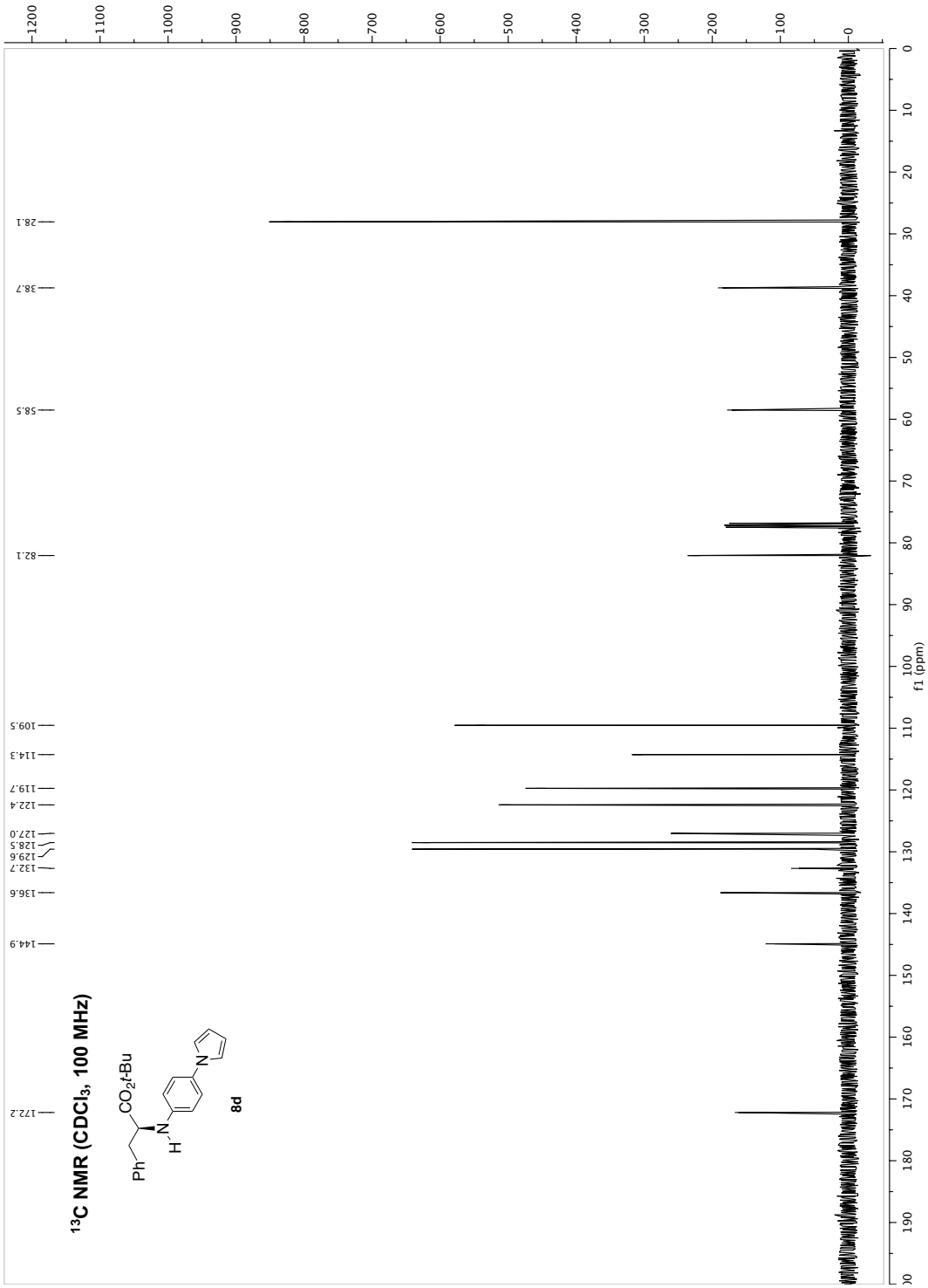

1H NMR (CDCl3, 400 MHz)
8b
Ph
CO2t-Bu
N
H
Me
f1 (ppm)

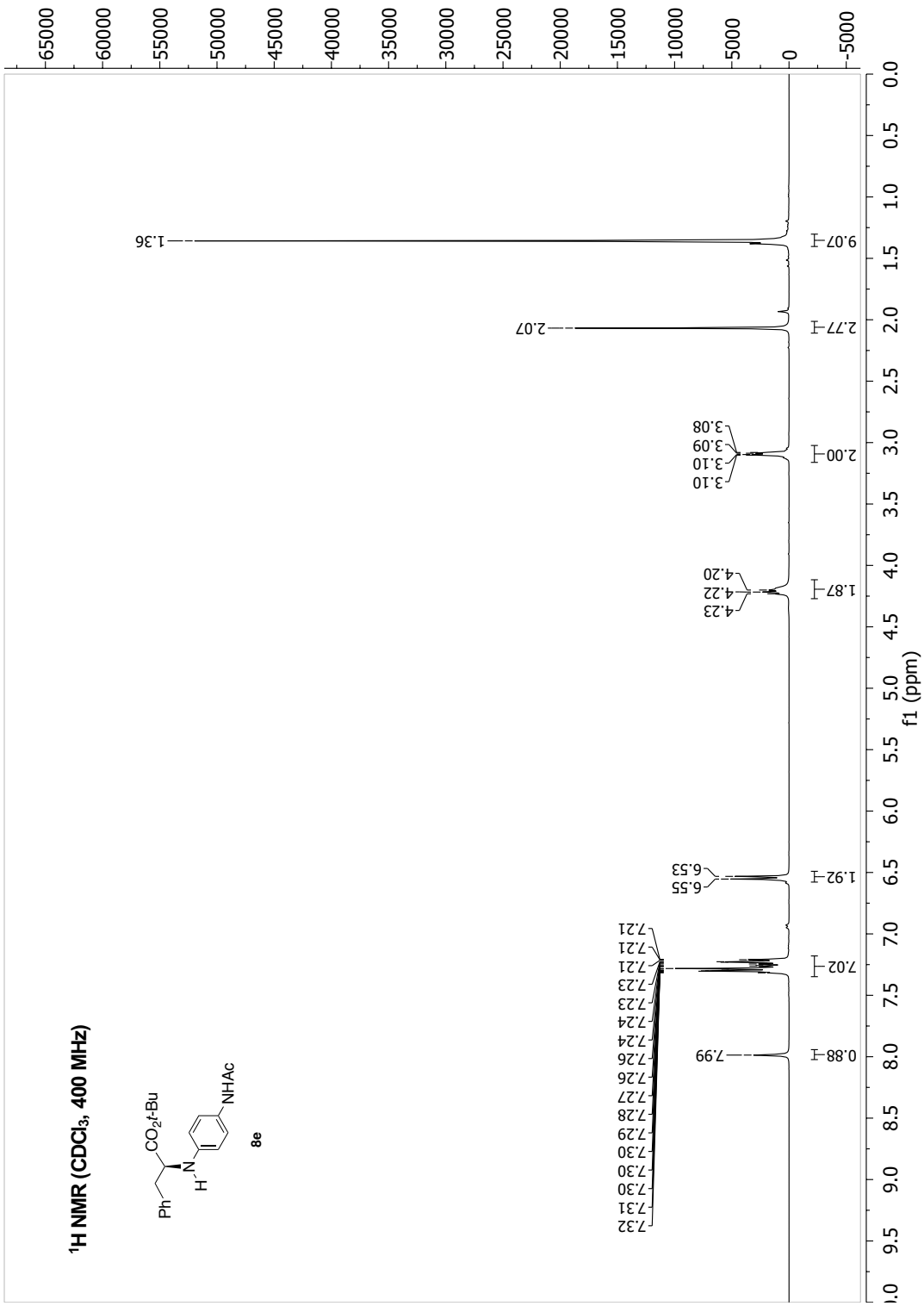

13C NMR (CDCl3, 100 MHz)
CO2t-Bu
Ph
N
H
Me
8b
172.1
167.4
146.7
136.5
131.1
129.6
129.3
128.5
127.0
119.4
118.3
114.0
82.1
58.0
52.1
38.6
28.0
f1 (ppm)

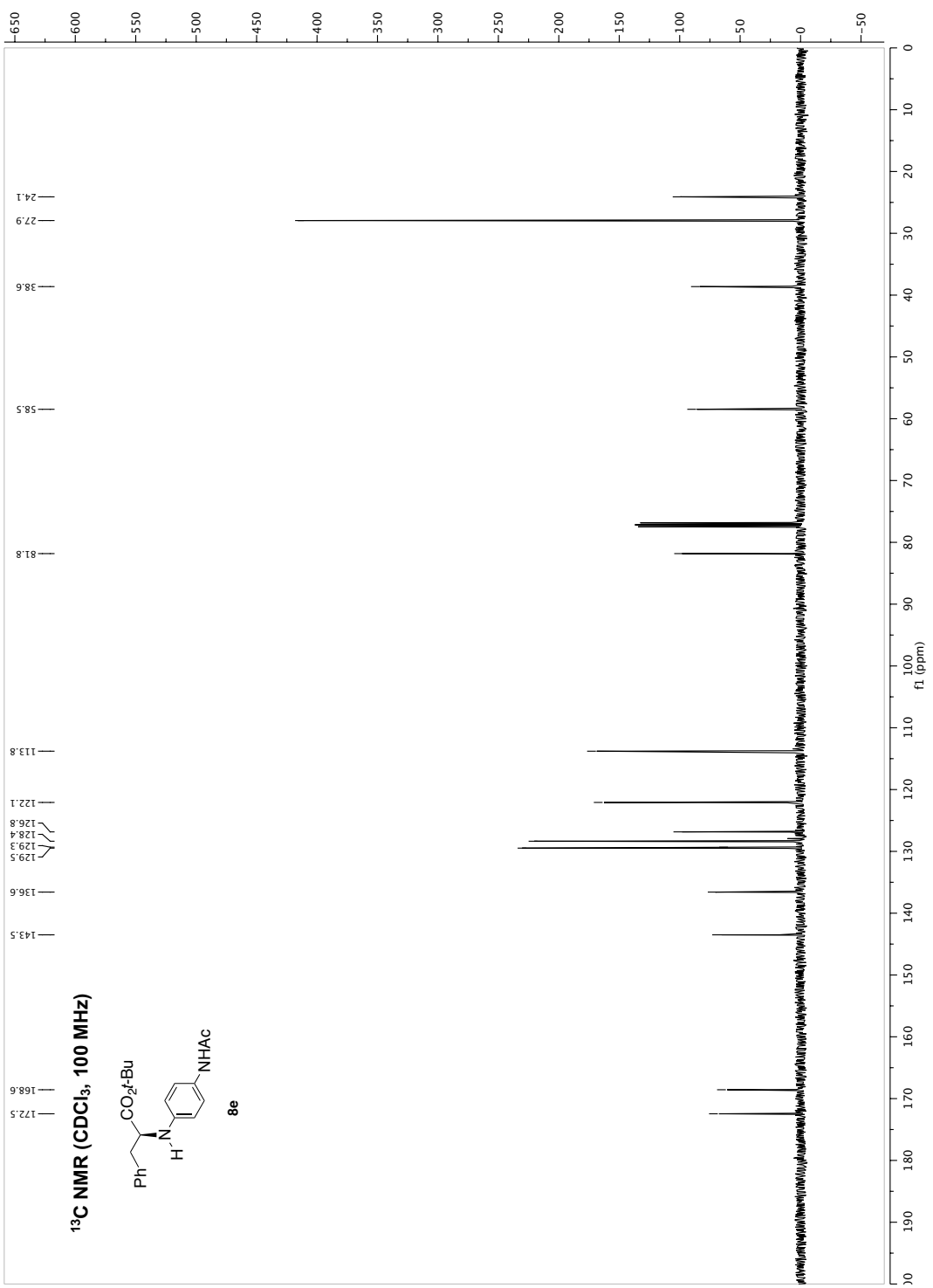

1H NMR (CDCl3, 400 MHz)
Ph
CO2t-Bu
OMe
N
H
nPr
8c
f1 (ppm)

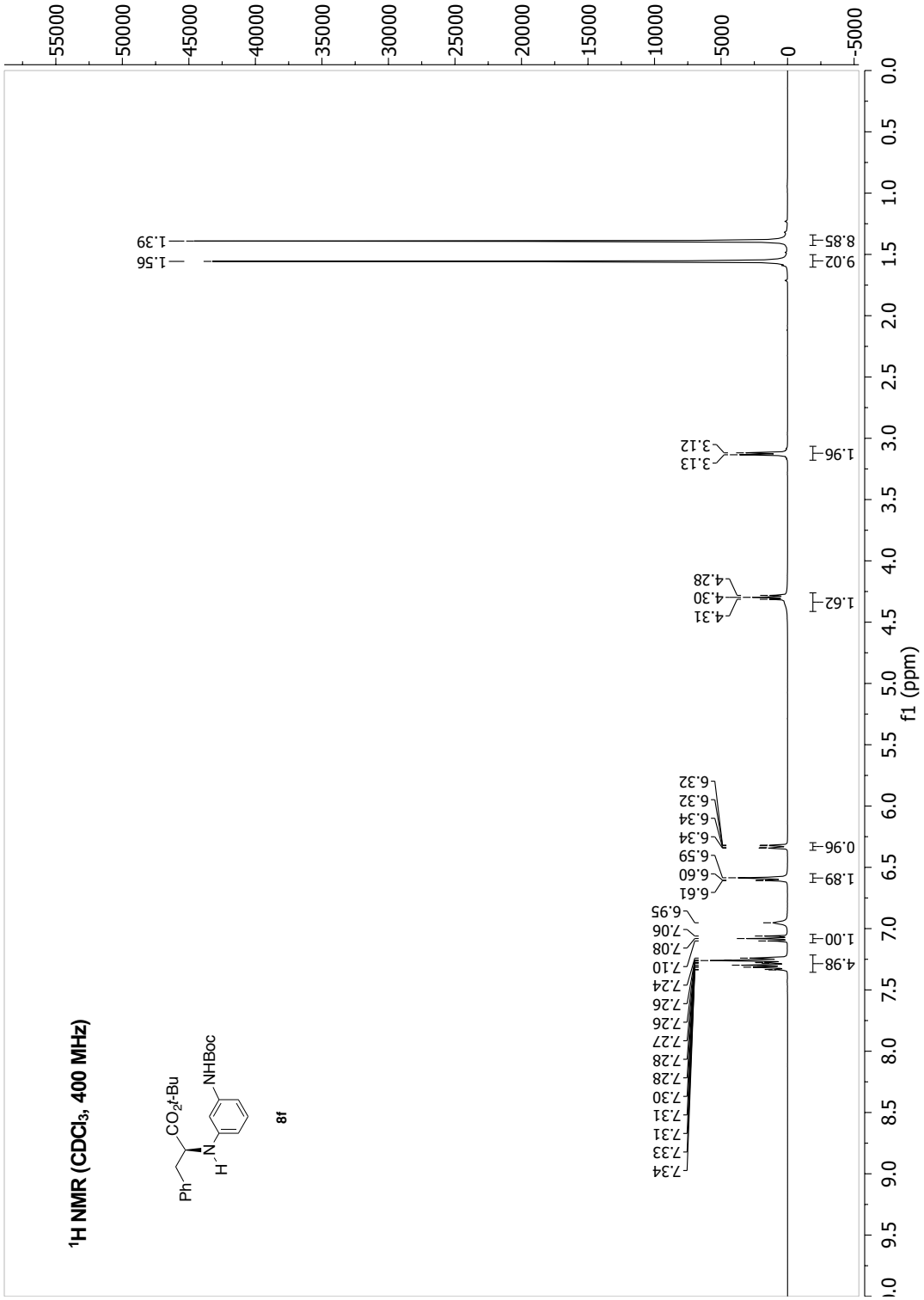

13C NMR (CDCl3, 100 MHz)
8c
Ph
CO2t-Bu
OMe
nPr
H
N
172.5
147.2
137.1
134.5
132.0
129.5
128.3
126.7
120.6
110.7
110.5
81.3
58.5
55.5
39.0
37.7
27.9
24.9
13.9
f1 (ppm)


1H NMR (CDCl3, 400 MHz)
Ph
CO2t-Bu
H
N
N
8d
7.36
7.36
7.36
7.34
7.34
7.32
7.30
7.30
7.29
7.28
7.28
7.27
7.27
7.26
7.25
7.24
7.24
7.02
7.01
6.71
6.70
6.69
6.68
6.36
6.35
6.35
4.36
4.31
4.30
4.28
3.18
3.16
1.42
7.12
1.91
2.01
1.91
0.66
1.15
2.00
9.06
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
f1 (ppm)


13C NMR (CDCl3, 100 MHz)
CO2t-Bu
Ph
H
N
8d
172.2
144.9
136.6
132.7
129.6
128.5
127.0
122.4
119.7
114.3
109.5
82.1
58.5
38.7
28.1
f1 (ppm)


^{1}H NMR ($CDCl_3$, 400 MHz)
Ph
CO_2t-Bu
N
H
NHAc
8e
1.36
2.07
3.10
3.09
3.08
4.23
4.22
4.20
6.55
6.53
7.32
7.31
7.30
7.30
7.29
7.28
7.27
7.26
7.26
7.24
7.24
7.23
7.23
7.21
7.21
7.21
7.99
9.07
2.77
2.00
1.87
1.92
7.02
0.88
f1 (ppm)


13C NMR (CDCl3, 100 MHz)
Ph
CO2t-Bu
N
H
NHAc
8e
172.5
168.6
143.5
136.6
129.5
129.3
128.4
126.8
122.1
113.8
81.8
58.5
38.6
27.9
24.1
f1 (ppm)


^{1}H NMR ($CDCl_3$, 400 MHz)
Ph
CO_2t-Bu
NHBoc
H
N
8f
1.39
1.56
8.85
9.02
1.96
3.12
3.13
1.62
4.28
4.30
4.31
0.96
6.32
6.32
6.34
6.34
1.89
6.59
6.60
6.61
1.00
6.95
7.06
7.08
4.98
7.10
7.24
7.26
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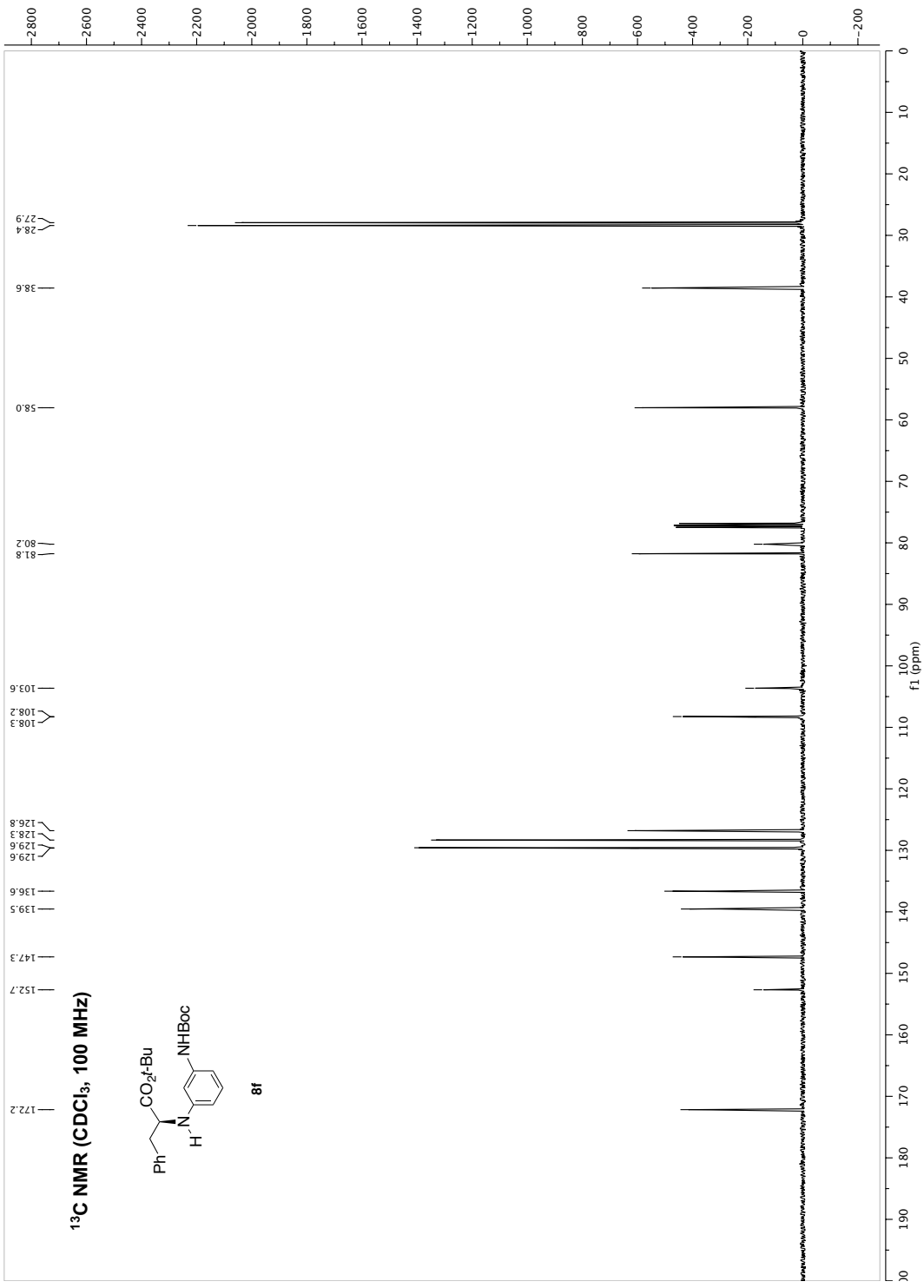
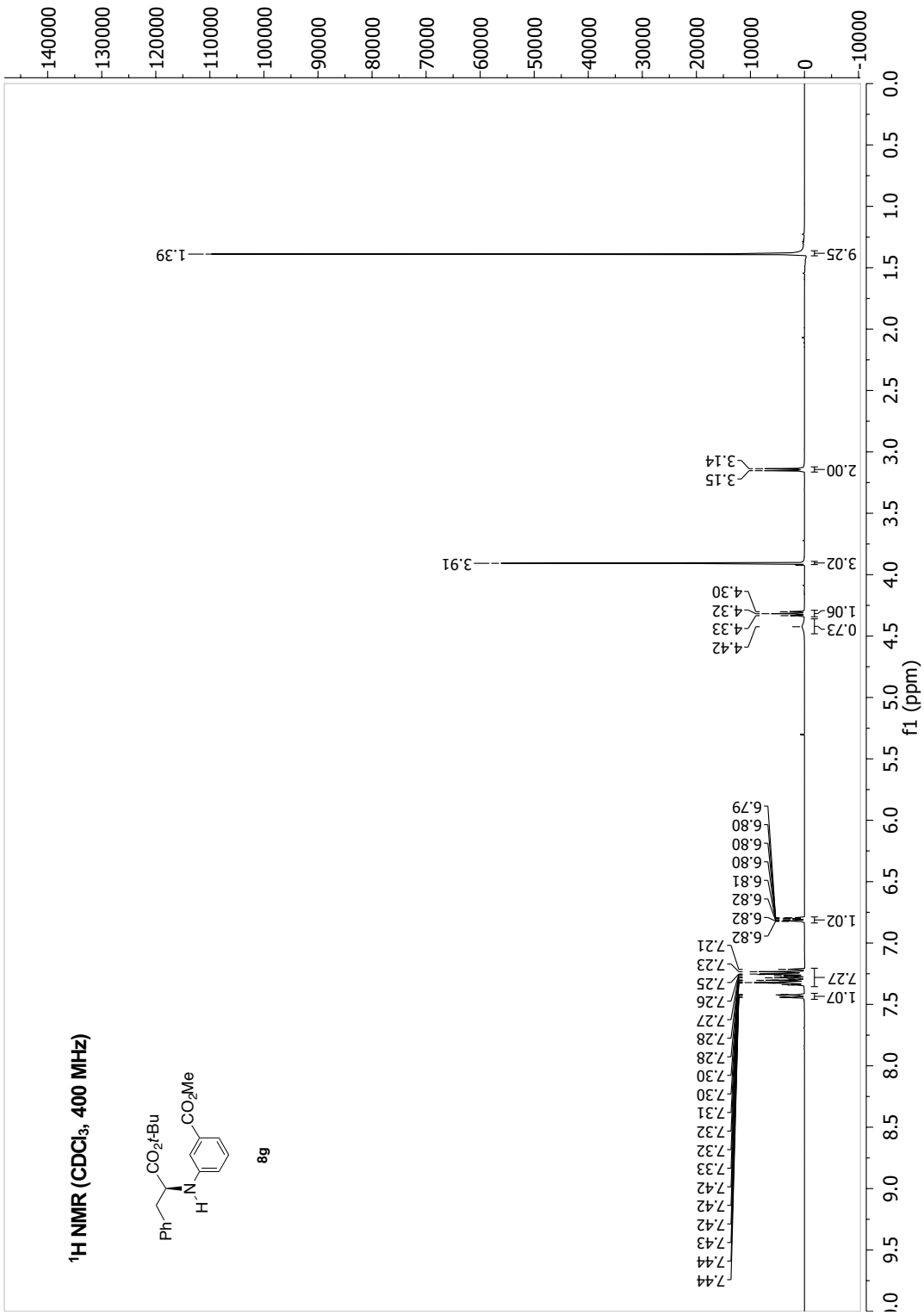
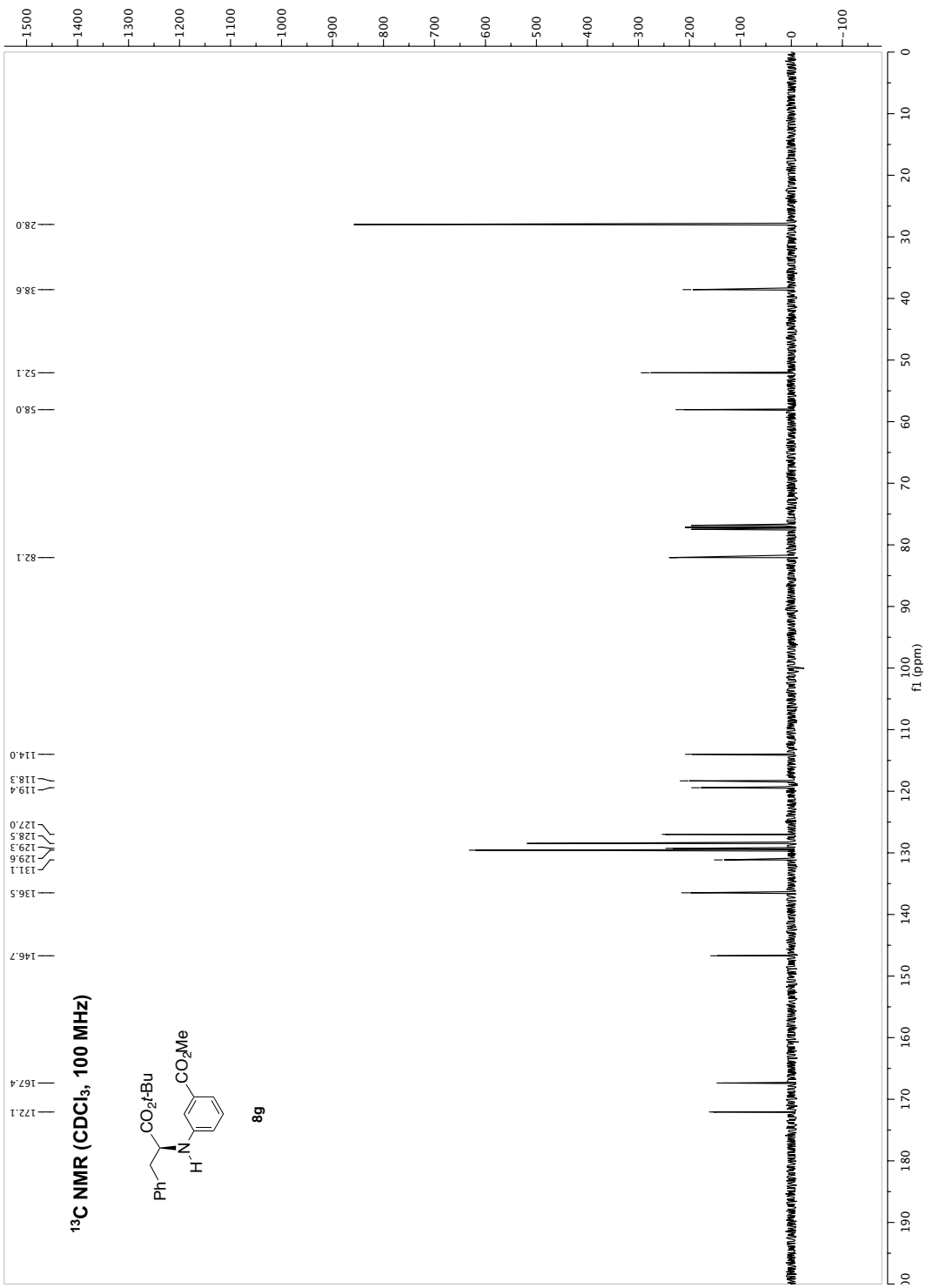
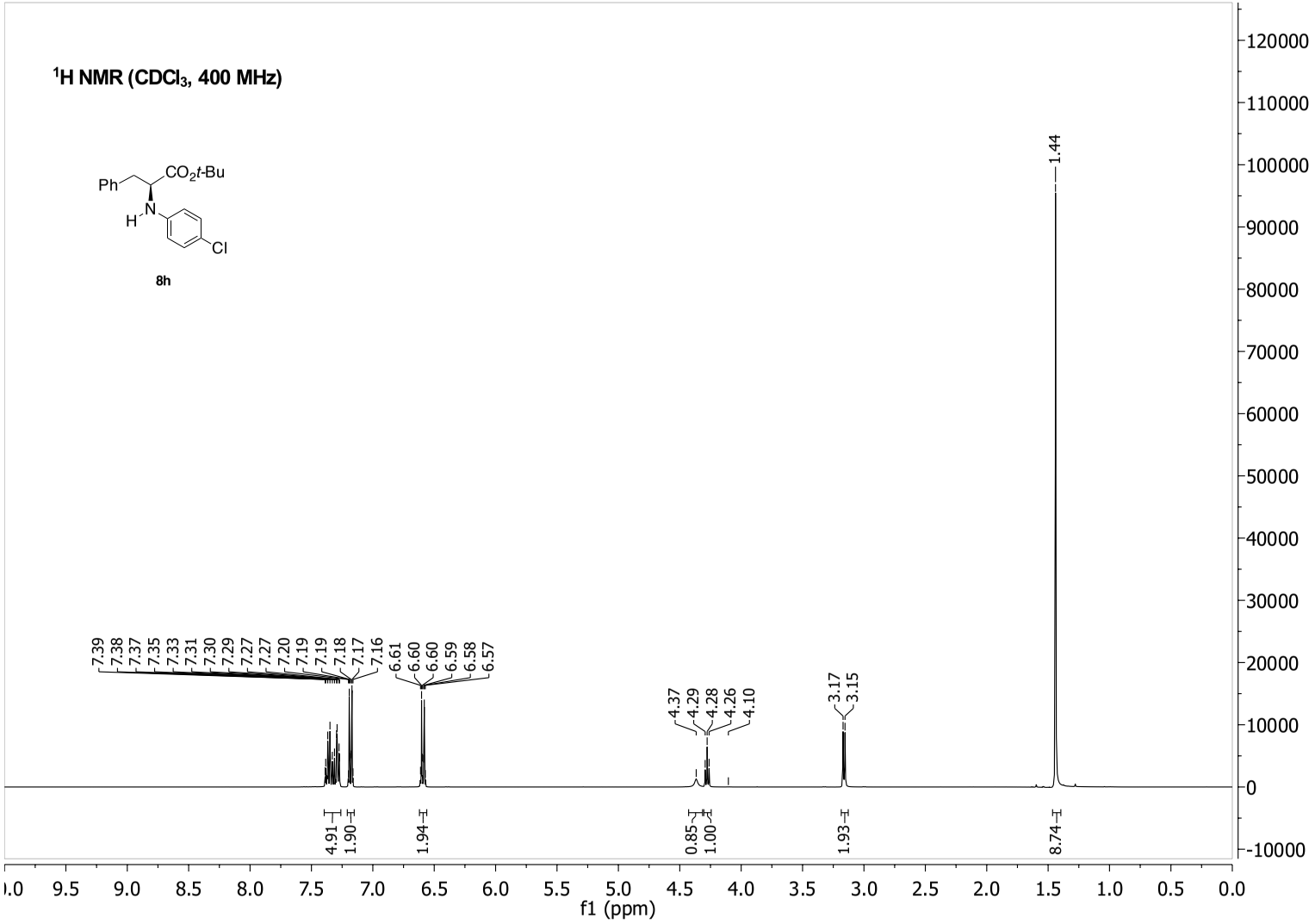
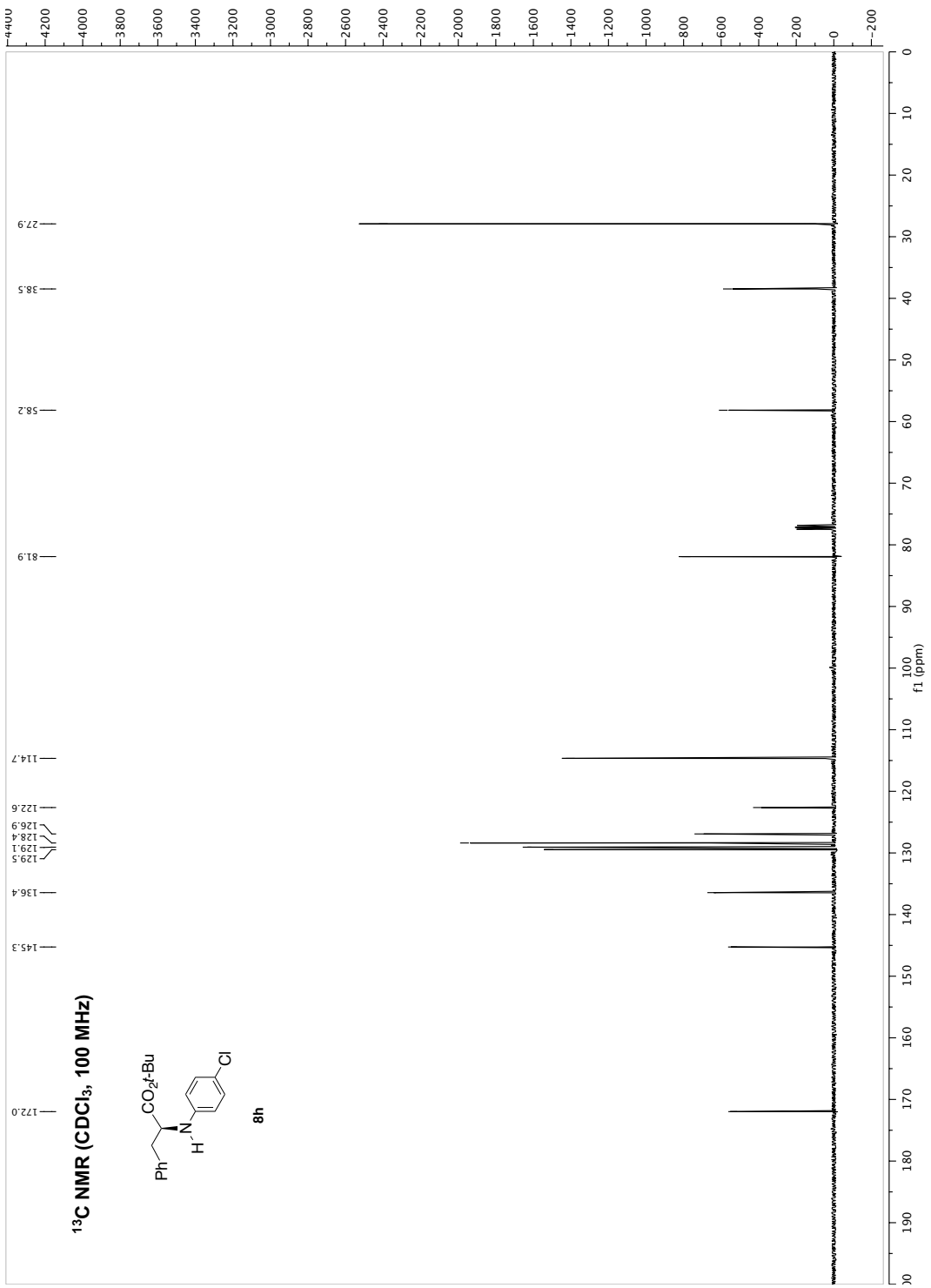
7.27
7.28
7.28
7.30
7.31
7.31
7.33
7.34
f1 (ppm)

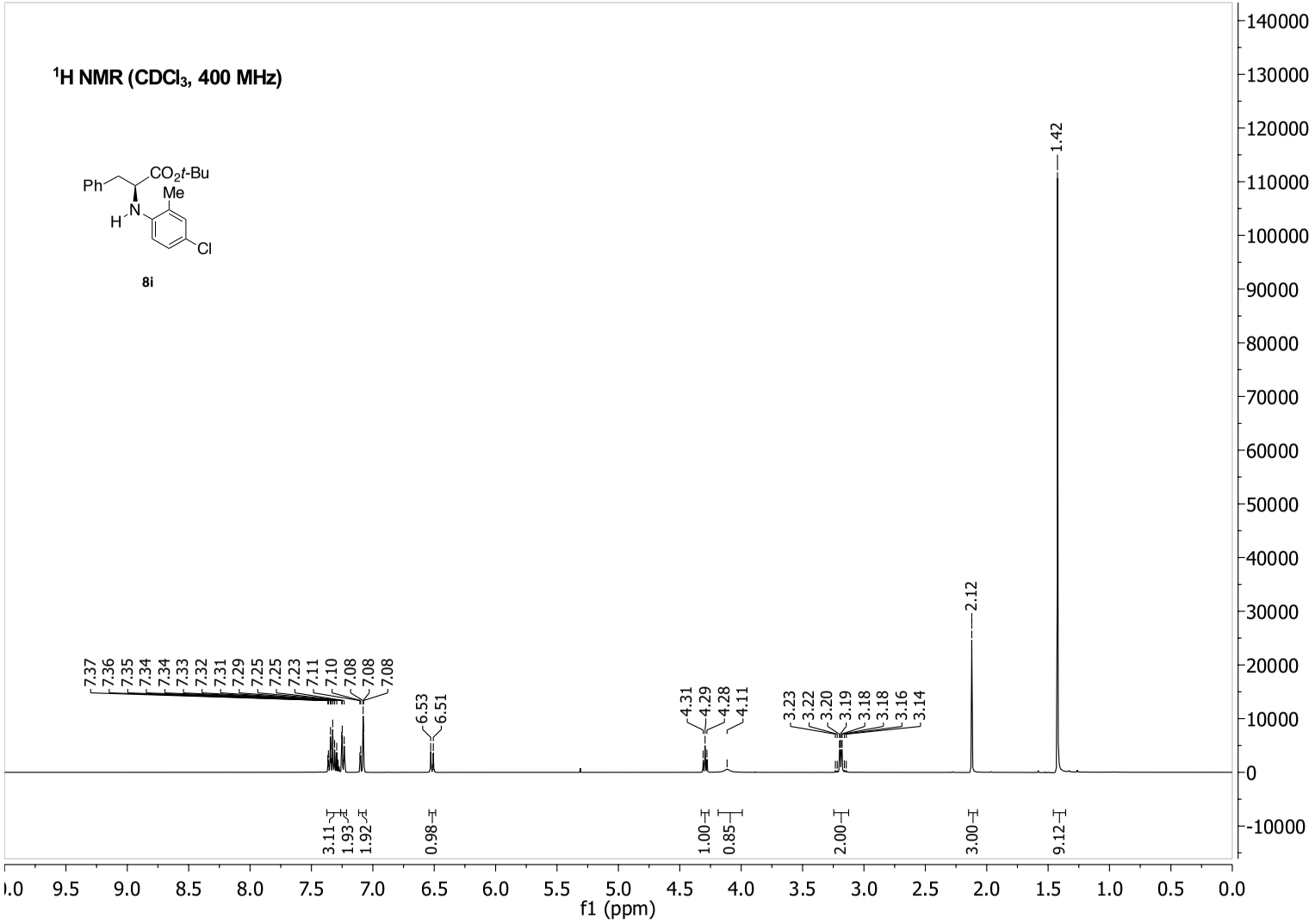

13C NMR (CDCl3, 100 MHz)
8f
Ph
CO2t-Bu
NHBoc
H
N
172.2
152.7
147.3
139.5
136.6
129.6
129.6
128.3
126.8
108.3
108.2
103.6
81.8
80.2
58.0
38.6
28.4
27.9
f1 (ppm)

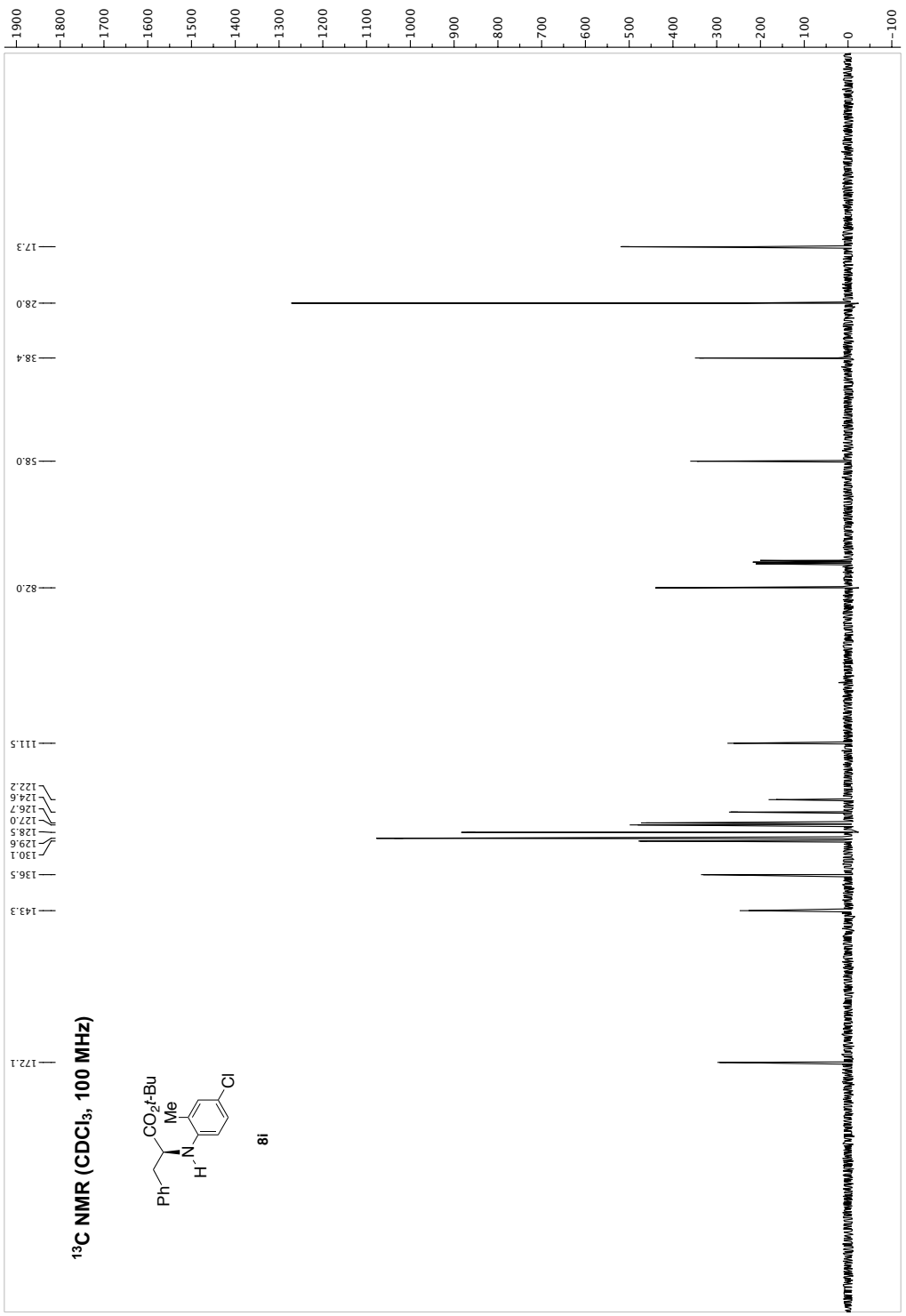

^{1}H NMR ($CDCl_3$, 400 MHz)
8g
f1 (ppm)

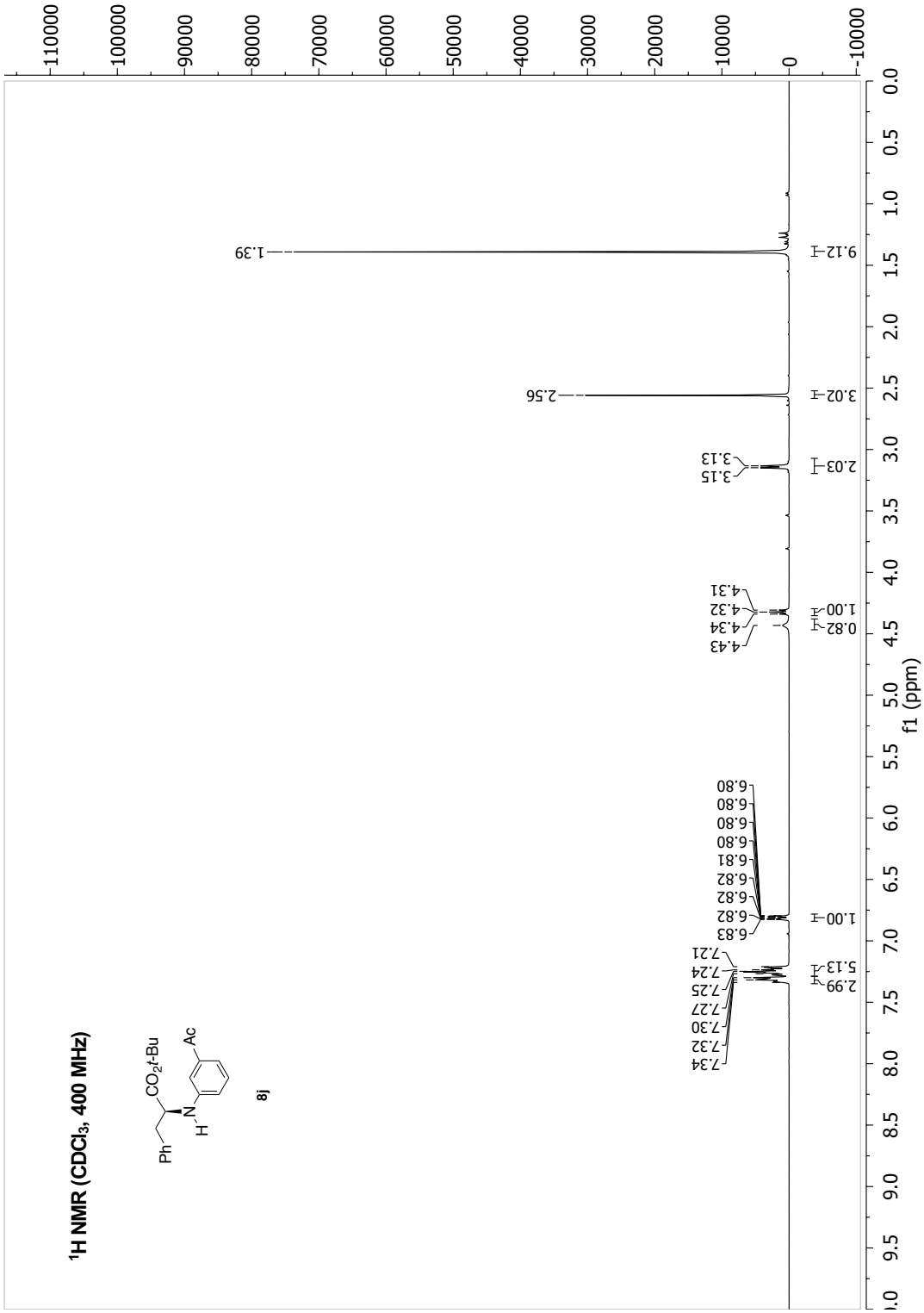

13C NMR (CDCl3, 100 MHz)
8g
Ph
CO2t-Bu
CO2Me
H
N
172.1
167.4
146.7
136.5
131.1
129.6
129.3
128.5
127.0
119.4
118.3
114.0
82.1
58.0
52.1
38.6
28.0
f1 (ppm)

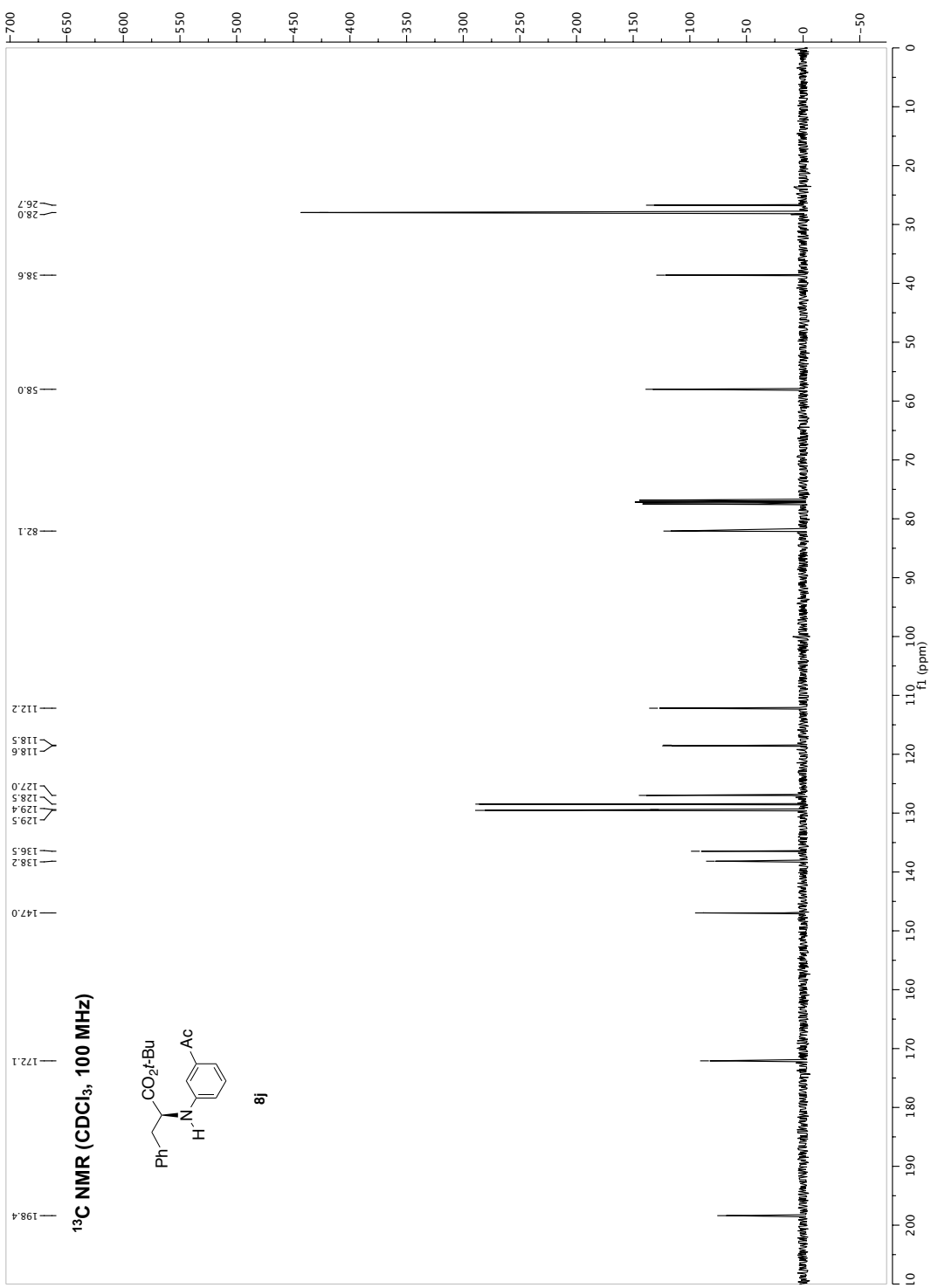

1H NMR (CDCl3, 400 MHz)
Ph
CO2t-Bu
H
N
Cl
8h
7.39
7.38
7.37
7.35
7.33
7.31
7.30
7.29
7.27
7.27
7.20
7.19
7.19
7.18
7.17
7.16
6.61
6.60
6.60
6.59
6.58
6.57
4.37
4.29
4.28
4.26
4.10
3.17
3.15
1.44
4.91
1.90
1.94
0.85
1.00
1.93
8.74
f1 (ppm)

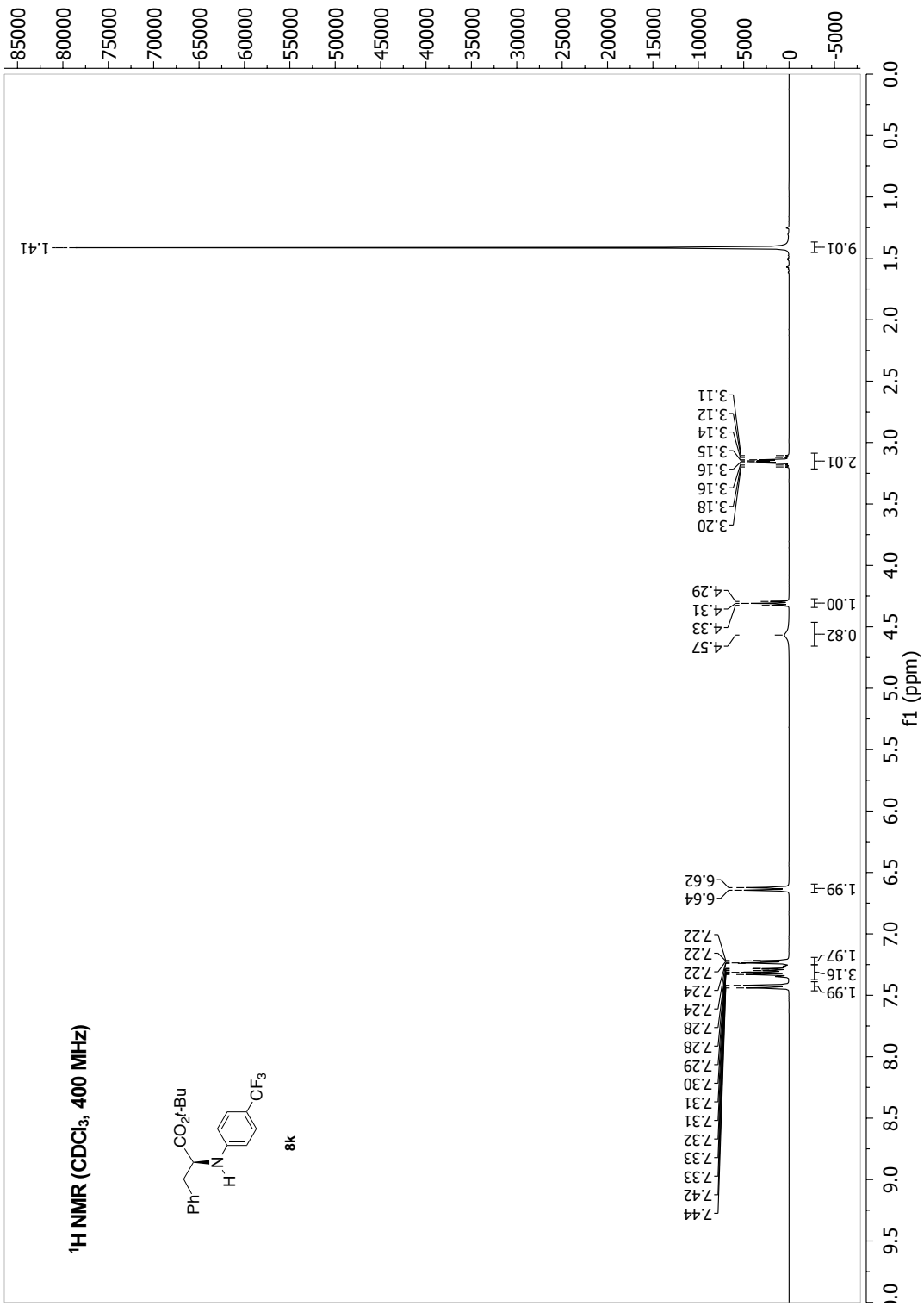

13C NMR (CDCl3, 100 MHz)
8h
172.0
145.3
136.4
129.5
129.1
128.4
126.9
122.6
114.7
81.9
58.2
38.5
27.9
f1 (ppm)

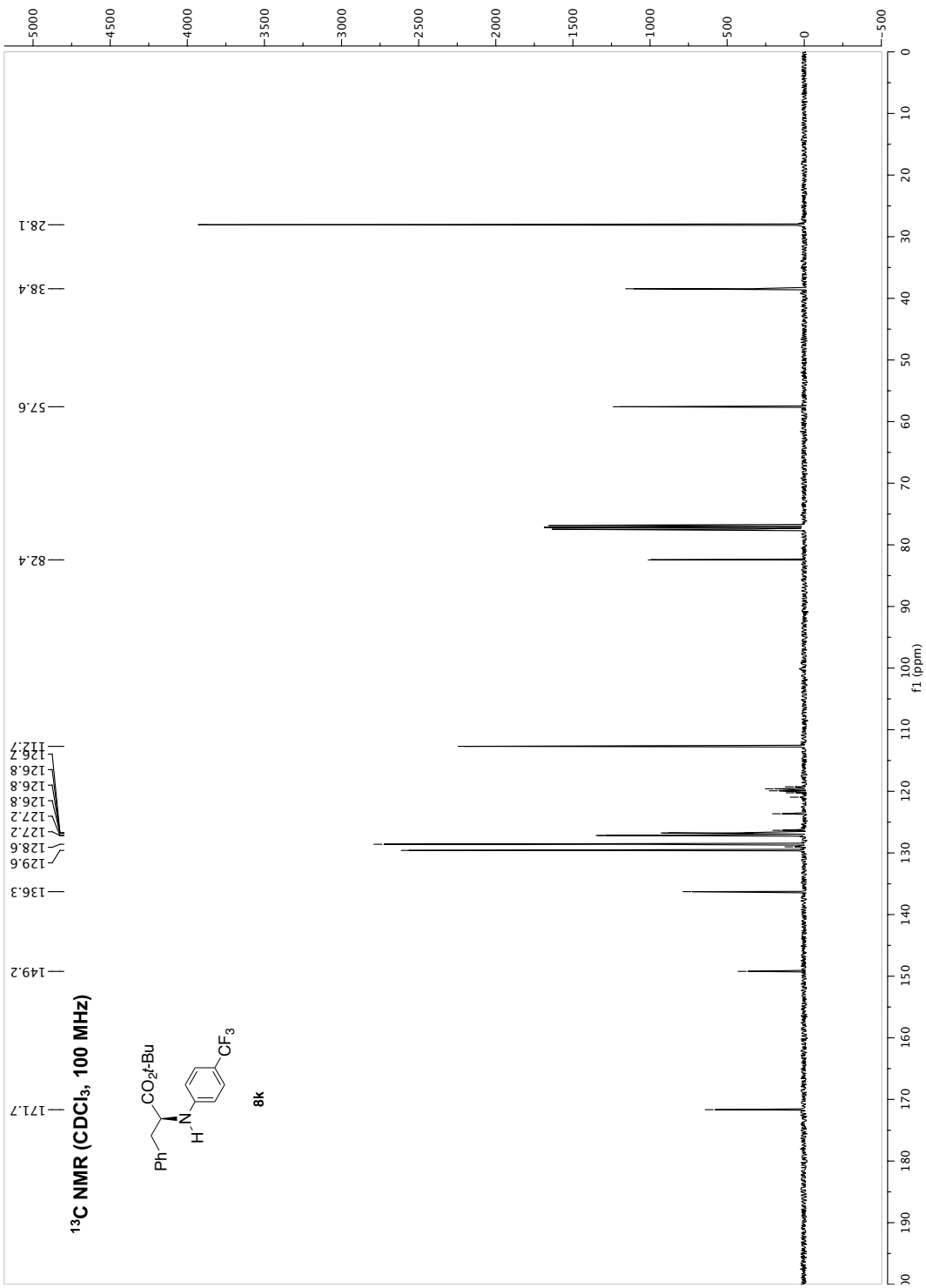

1H NMR (CDCl3, 400 MHz)
Ph
CO2t-Bu
Me
N
H
Cl
8i
7.37
7.36
7.35
7.34
7.34
7.33
7.32
7.31
7.29
7.25
7.25
7.23
7.11
7.10
7.08
7.08
7.08
6.53
6.51
4.31
4.29
4.28
4.11
3.23
3.22
3.20
3.19
3.18
3.18
3.16
3.14
2.12
1.42
3.11
1.93
1.92
0.98
1.00
0.85
2.00
3.00
9.12
f1 (ppm)

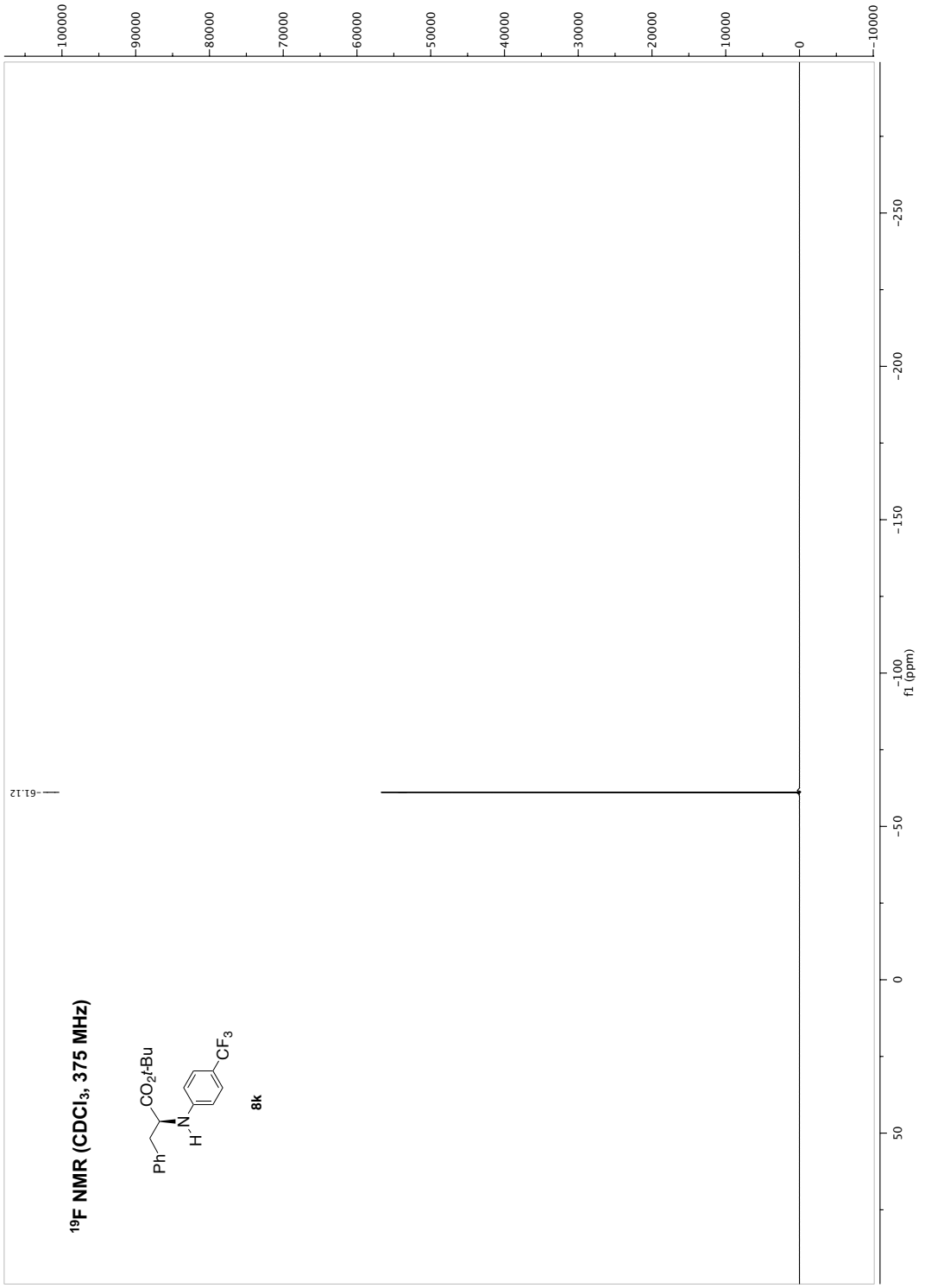

13C NMR (CDCl3, 100 MHz)
172.1
143.3
136.5
130.1
129.6
128.5
127.0
126.7
124.6
122.2
111.5
82.0
58.0
38.4
28.0
17.3
CO2t-Bu
Me
Ph
N
H
Cl
8l
f1 (ppm)

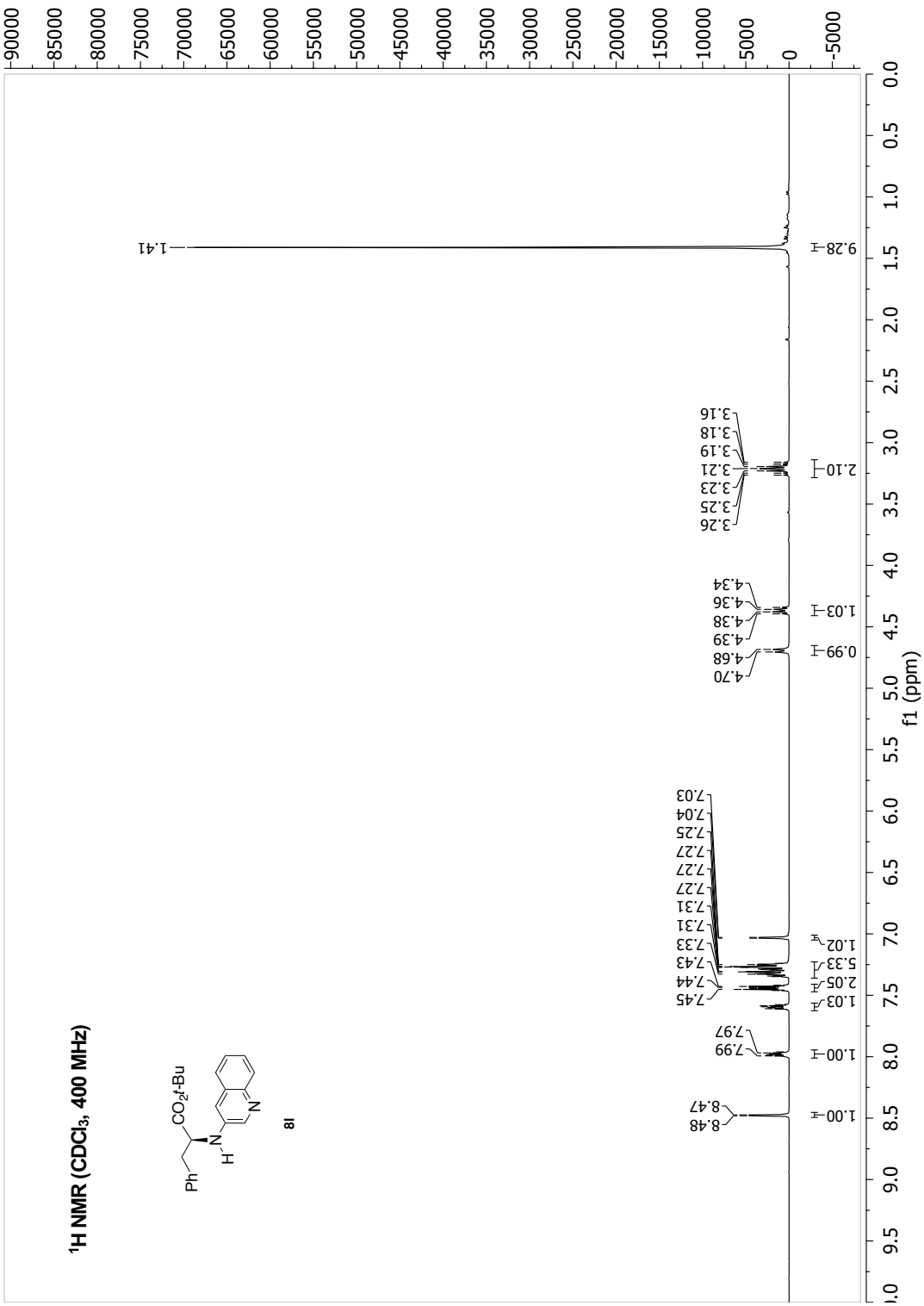

1H NMR (CDCl3, 400 MHz)
8j
Ph
CO2t-Bu
Ac
H
N
f1 (ppm)

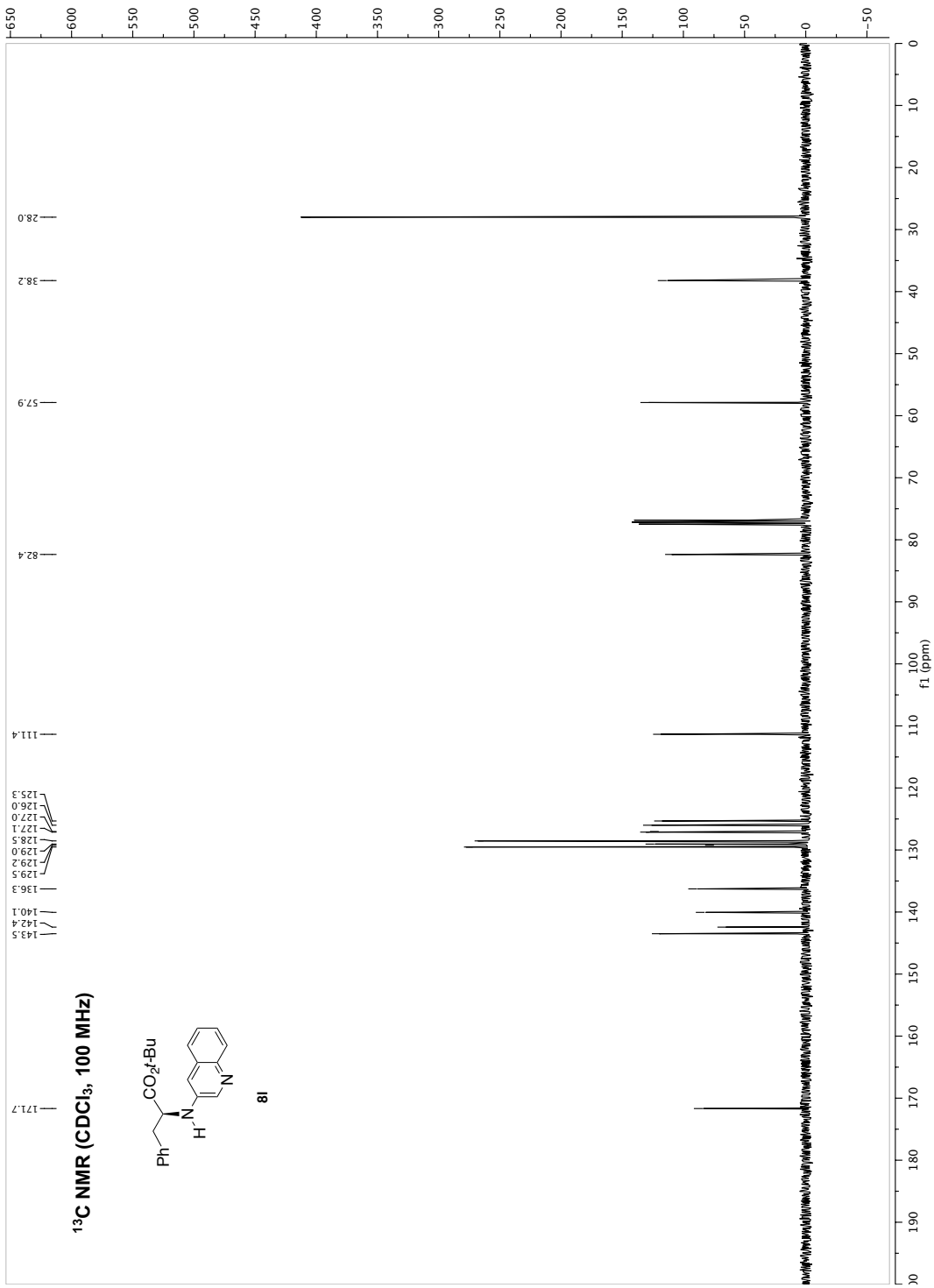

13C NMR (CDCl3, 100 MHz)
198.4
172.1
147.0
138.2
136.5
129.5
129.4
128.5
127.0
118.6
118.5
112.2
82.1
58.0
38.6
28.0
26.7
CO2t-Bu
Ac
Ph
N
H
8j
f1 (ppm)

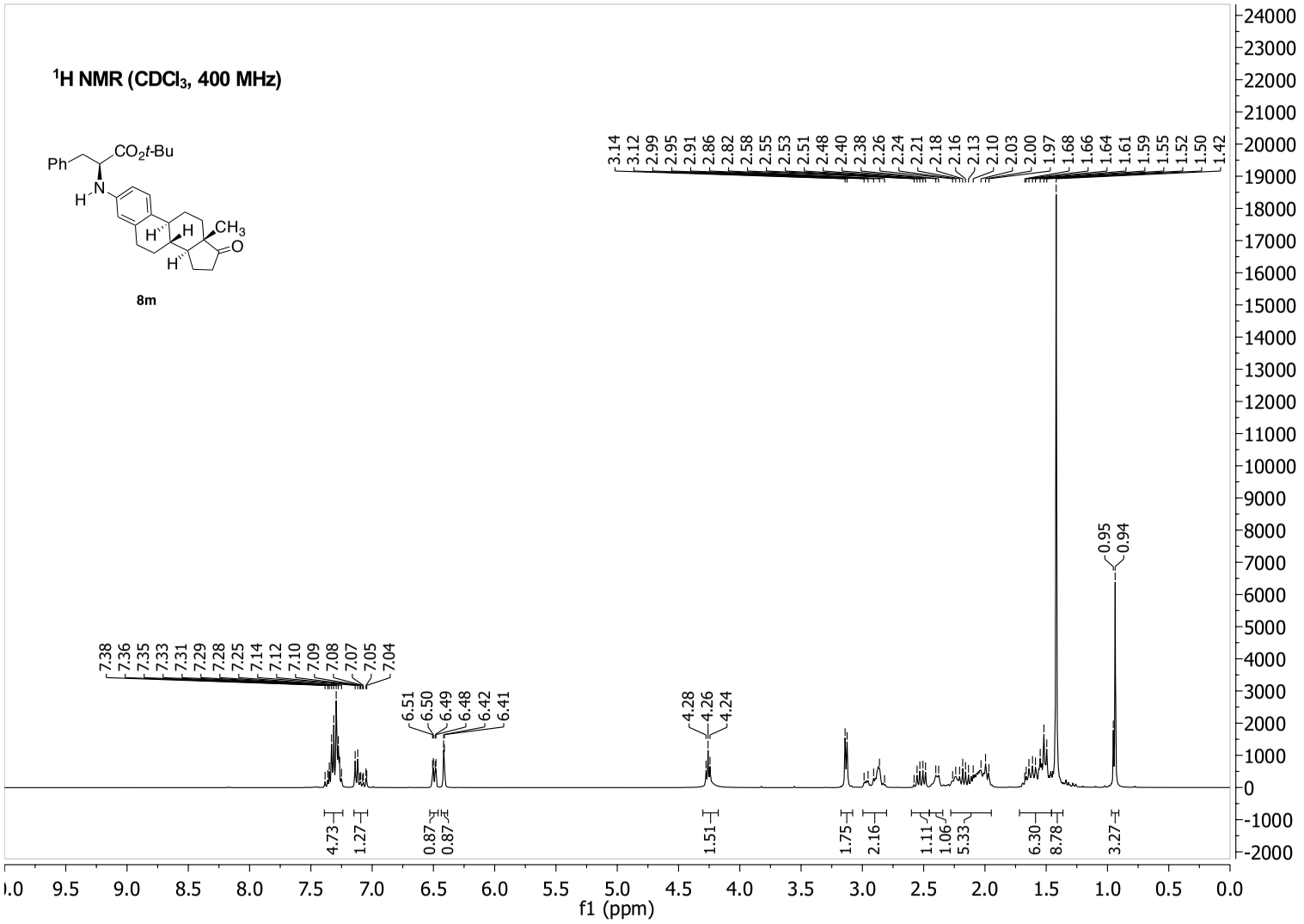

1H NMR (CDCl3, 400 MHz)
8k
f1 (ppm)

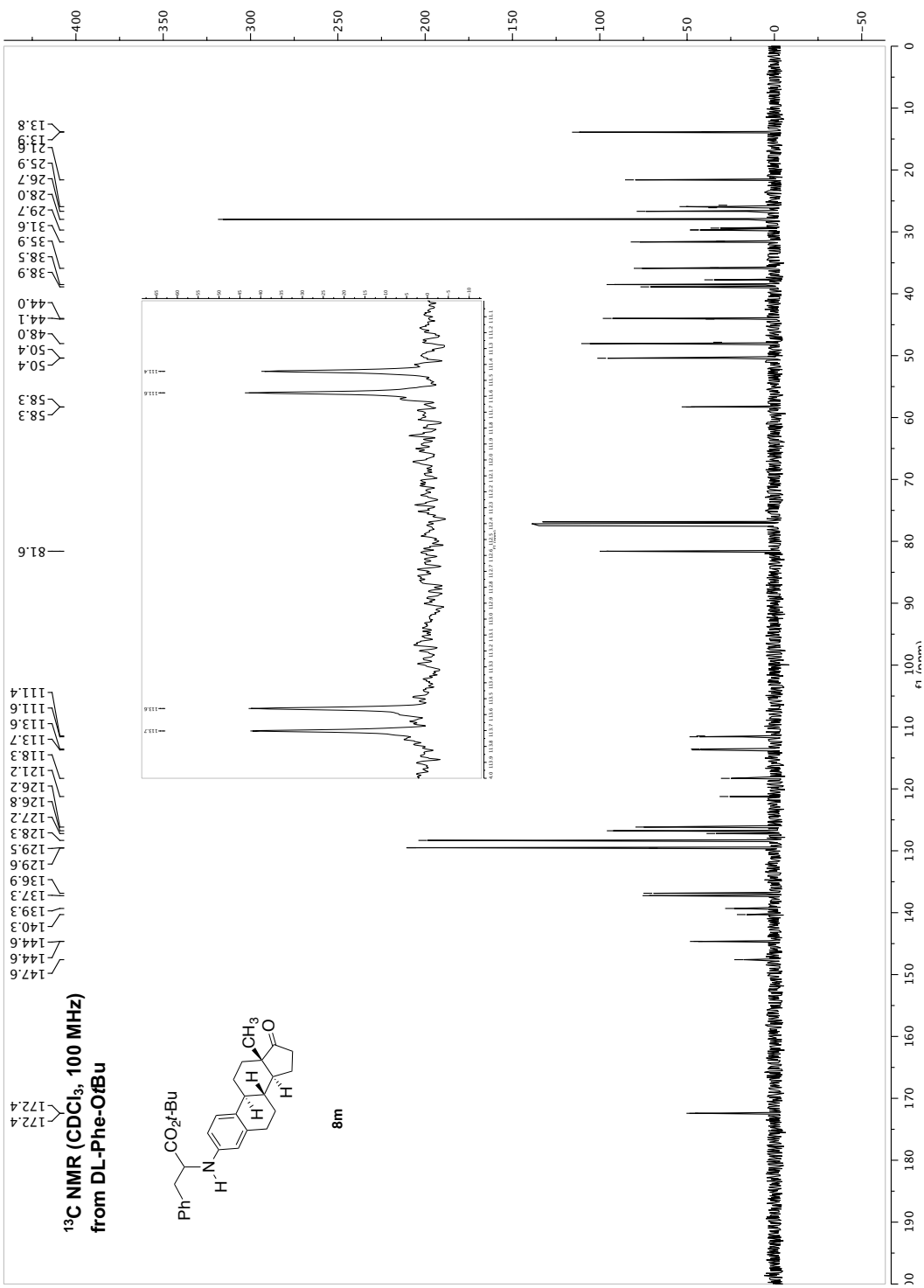

^{13}C NMR ($CDCl_3$, 100 MHz)
8k
Ph
CO_2t-Bu
CF_3
171.7
149.2
136.3
129.6
128.6
127.2
127.2
126.8
126.8
126.8
126.7
112.7
82.4
57.6
38.4
28.1
f1 (ppm)

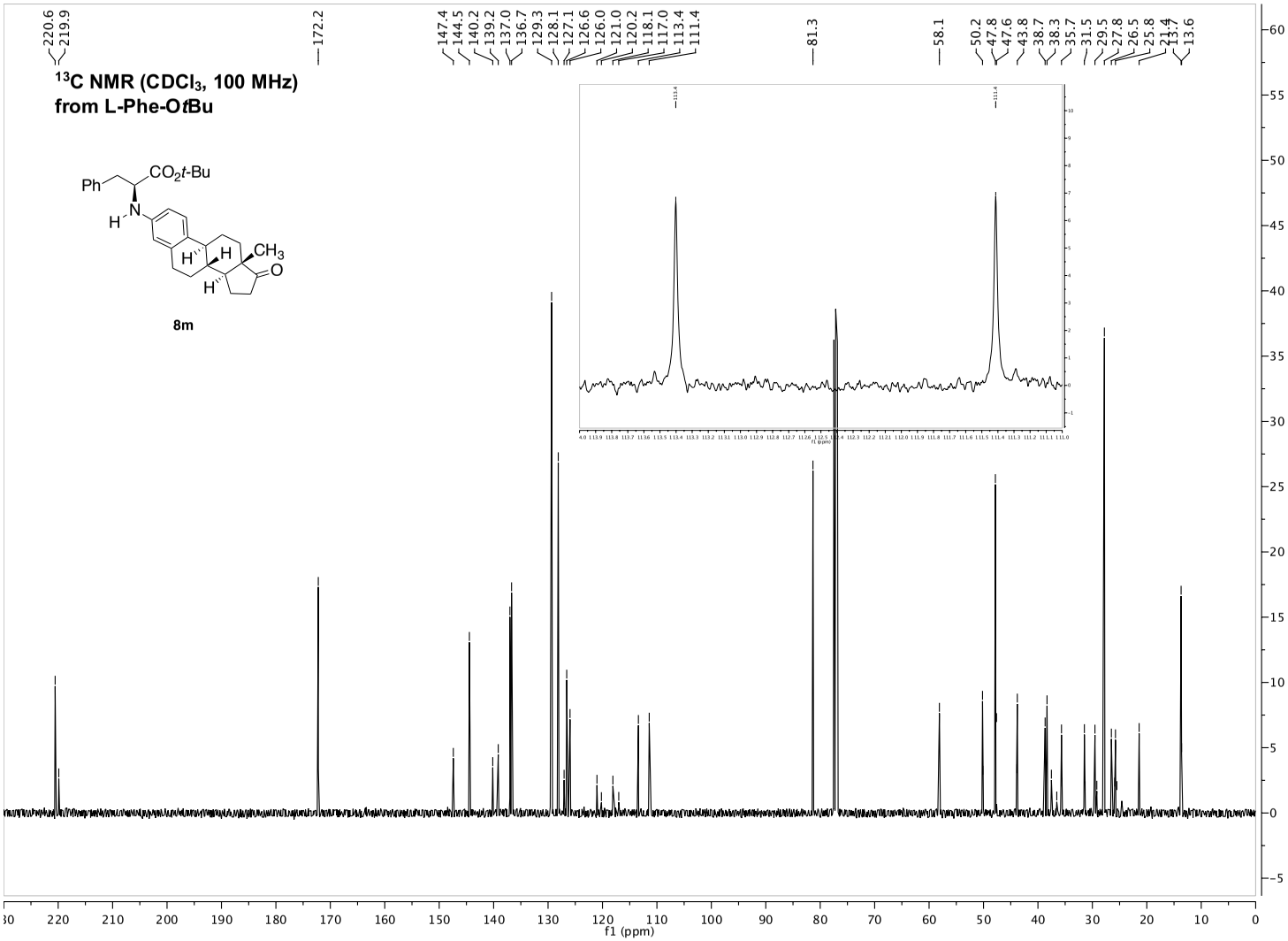

19F NMR (CDCl3, 375 MHz)
-61.12
CO2t-Bu
Ph
N
H
CF3
8k
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
50
0
-50
-100
-150
-200
-250
f1 (ppm)

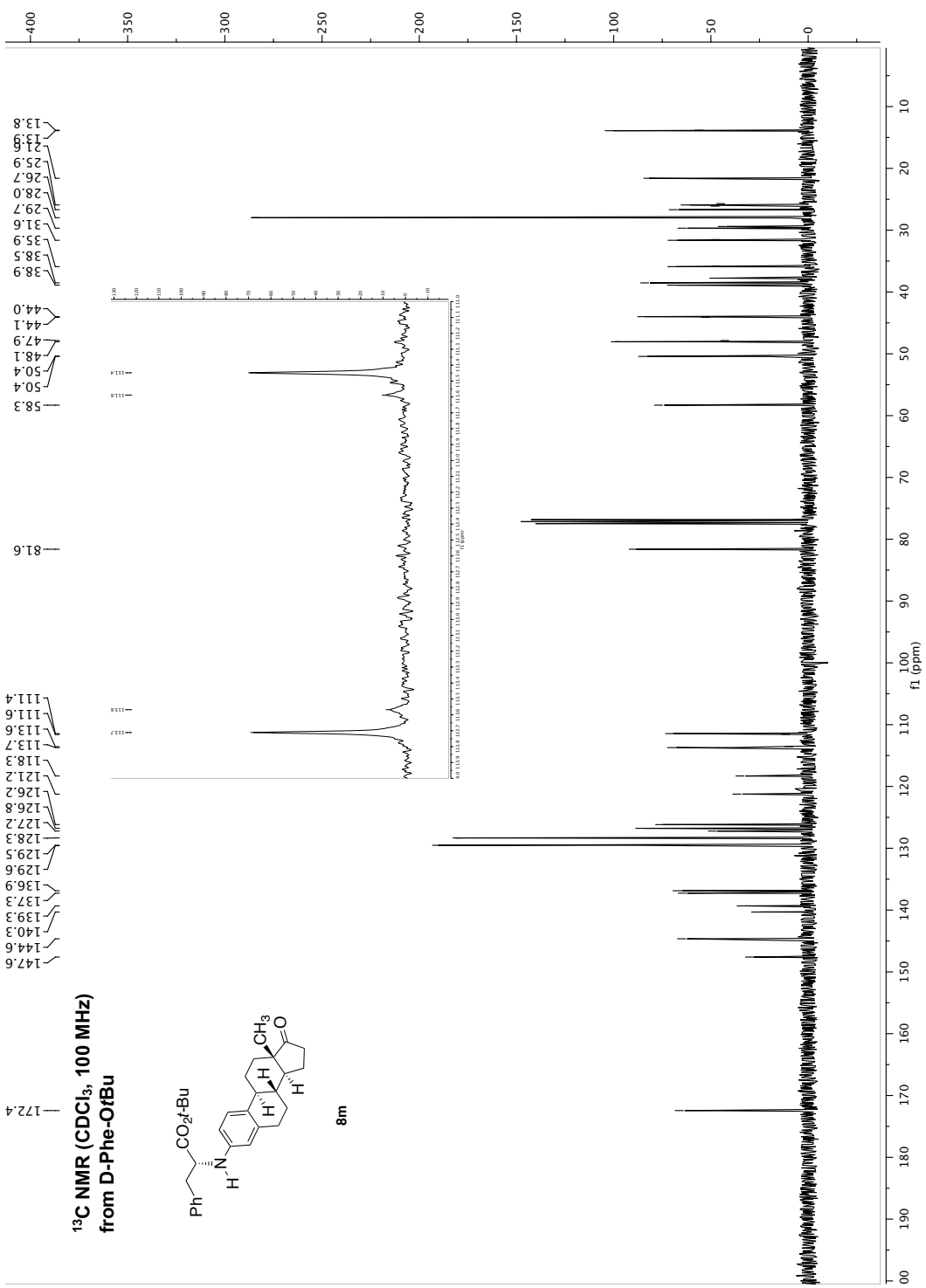

1H NMR (CDCl3, 400 MHz)
Ph
CO2t-Bu
N
H
8l
f1 (ppm)

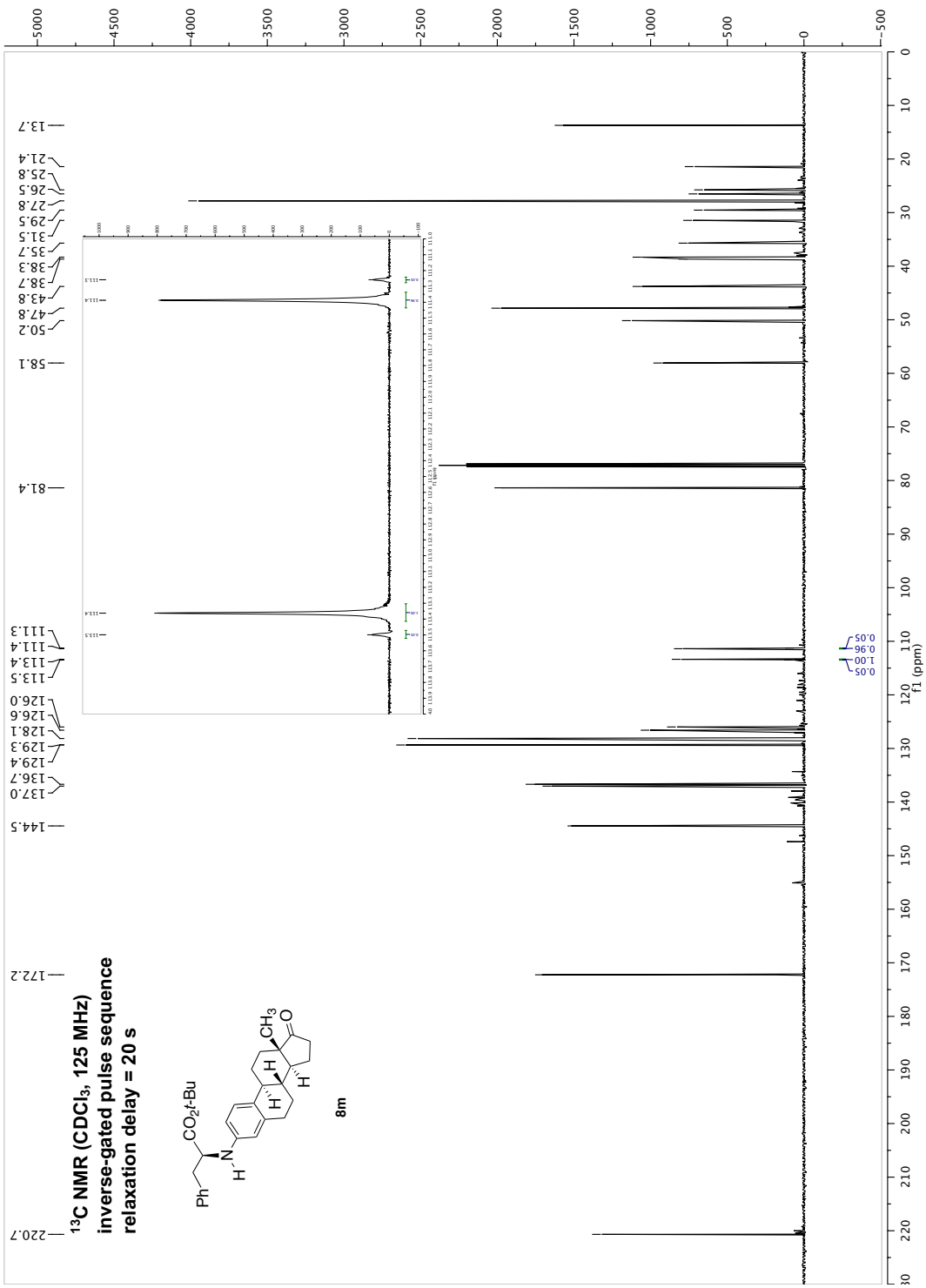

13C NMR (CDCl3, 100 MHz)
8l
Ph
CO2t-Bu
H
N
171.7
143.5
142.4
140.1
136.3
129.5
129.2
129.0
128.5
127.1
127.0
126.0
125.3
111.4
82.4
57.9
38.2
28.0
f1 (ppm)


1H NMR (CDCl3, 400 MHz)
Ph
CO2t-Bu
N
H
H
H
CH3
O
8m
3.14
3.12
2.99
2.95
2.91
2.86
2.82
2.58
2.55
2.53
2.51
2.48
2.40
2.38
2.26
2.24
2.21
2.18
2.16
2.13
2.10
2.03
2.00
1.97
1.68
1.66
1.64
1.61
1.59
1.55
1.52
1.50
1.42
0.95
0.94
7.38
7.36
7.35
7.33
7.31
7.29
7.28
7.25
7.14
7.12
7.10
7.09
7.08
7.07
7.05
7.04
6.51
6.50
6.49
6.48
6.42
6.41
4.28
4.26
4.24
4.73
1.27
0.87
0.87
1.51
1.75
2.16
1.11
1.06
5.33
6.30
8.78
3.27
f1 (ppm)

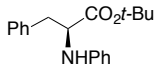

13C NMR (CDCl3, 100 MHz)
from DL-Phe-OtBu
8m
Ph
CO2t-Bu
CH3
O
H
N
172.4
147.6
144.6
144.6
140.3
139.3
137.3
136.9
129.6
129.5
128.3
127.2
126.8
126.2
121.2
118.3
113.7
113.6
111.6
111.4
81.6
58.3
58.3
50.4
50.4
48.0
44.1
44.0
38.9
38.5
35.9
31.6
29.7
28.0
26.7
25.9
21.6
13.9
13.8


220.6
219.9
172.2
147.4
144.5
140.2
139.2
137.0
136.7
129.3
128.1
127.1
126.6
126.0
121.0
120.2
118.1
117.0
113.4
111.4
81.3
58.1
50.2
47.8
47.6
43.8
38.7
38.3
35.7
31.5
29.5
27.8
26.5
25.8
21.4
13.6
^{13}C NMR ($CDCl_3$, 100 MHz)
from L-Phe-O*t*Bu
Ph
CO_2t-Bu
N
H
H
H
CH_3
O
8m
f1 (ppm)


13C NMR (CDCl3, 100 MHz)
from D-Phe-OtBu
8m
Ph
CO2t-Bu
CH3
O
H
N
172.4
147.6
144.6
140.3
139.3
137.3
136.9
129.6
129.5
128.3
127.2
126.8
126.2
121.2
118.3
113.7
113.6
111.6
111.4
81.6
58.3
50.4
50.4
48.1
47.9
44.1
44.0
38.9
38.5
35.9
31.6
29.7
28.0
26.7
25.9
21.6
13.9
13.8
f1 (ppm)


13C NMR (CDCl3, 125 MHz)
inverse-gated pulse sequence
relaxation delay = 20 s
8m
Ph
CO2t-Bu
CH3
O
f1 (ppm)

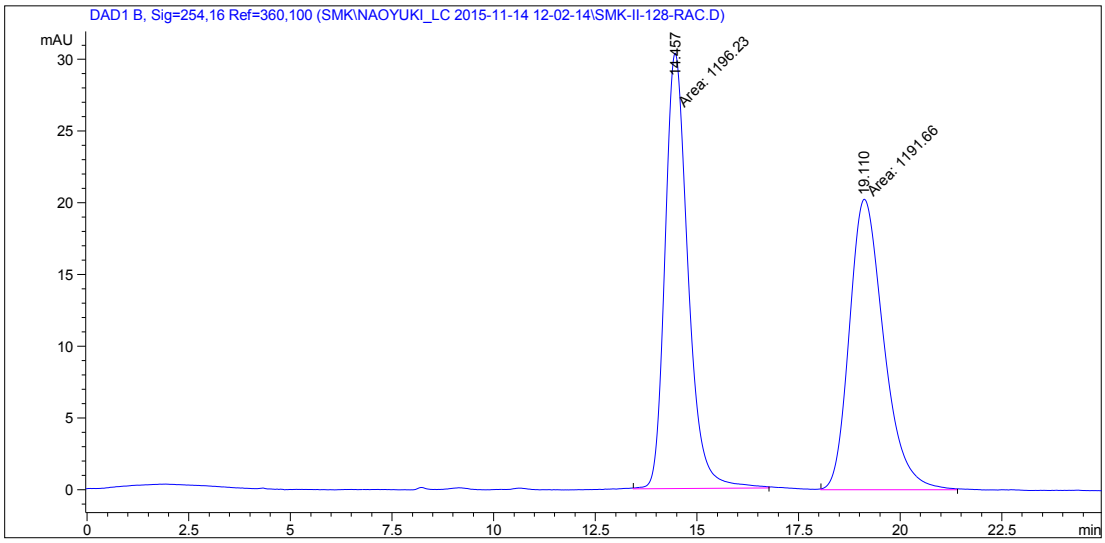
B) Catalog of HPLC Spectra



6a

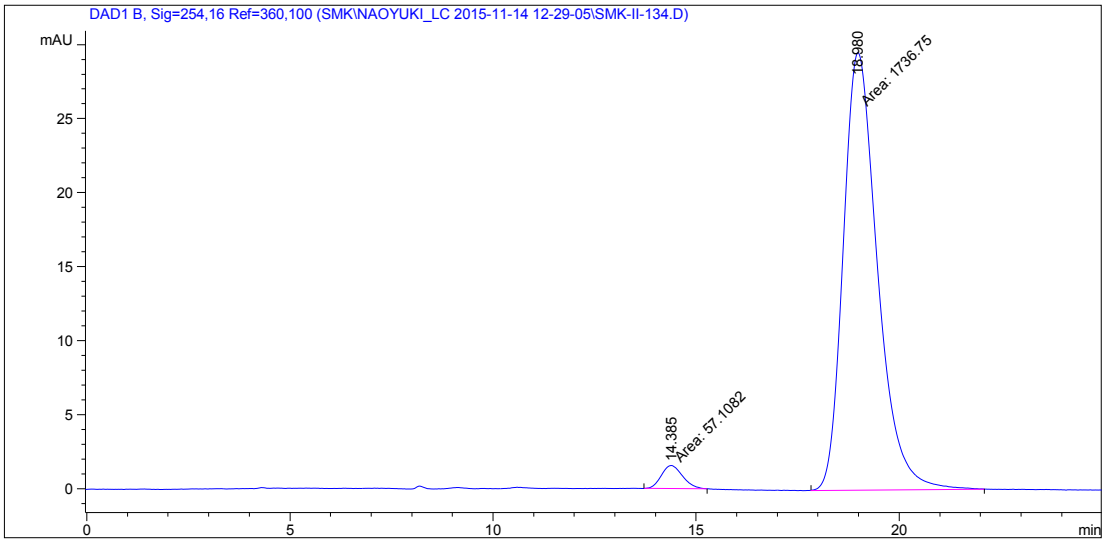
HPLC analysis (OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 94% ee: tR (minor) = 14.4 min, tR (major) = 19.0 min.

DL-6a

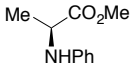


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.457	MM T	0.6566	1196.22986	30.36582	50.0957
2	19.110	MM T	0.9799	1191.65881	20.26895	49.9043

L-6a: 94% ee



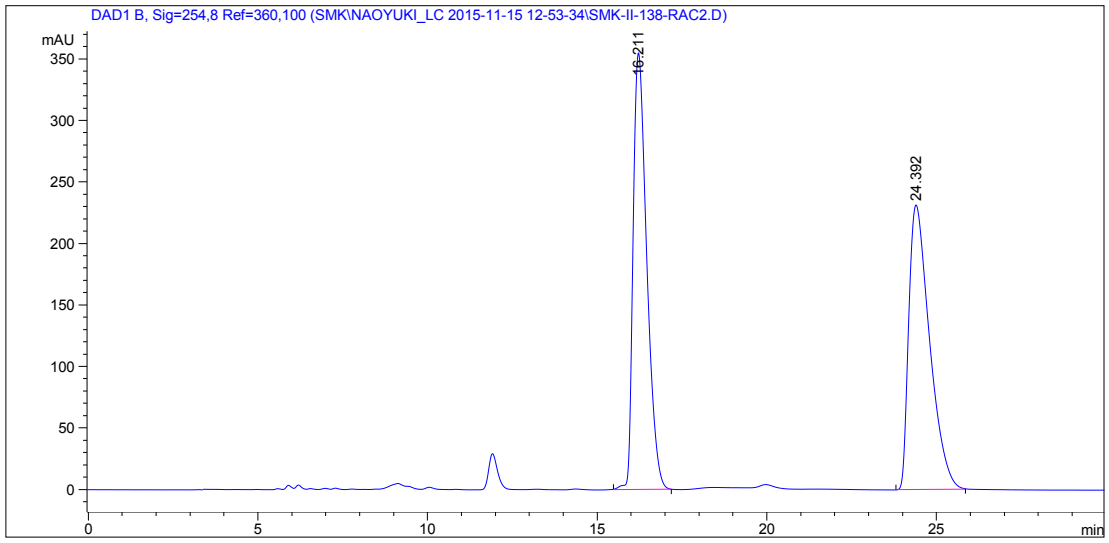
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.385	MM T	0.6089	57.10818	1.56307	3.1835
2	18.980	MM T	0.9790	1736.74756	29.56627	96.8165



6c

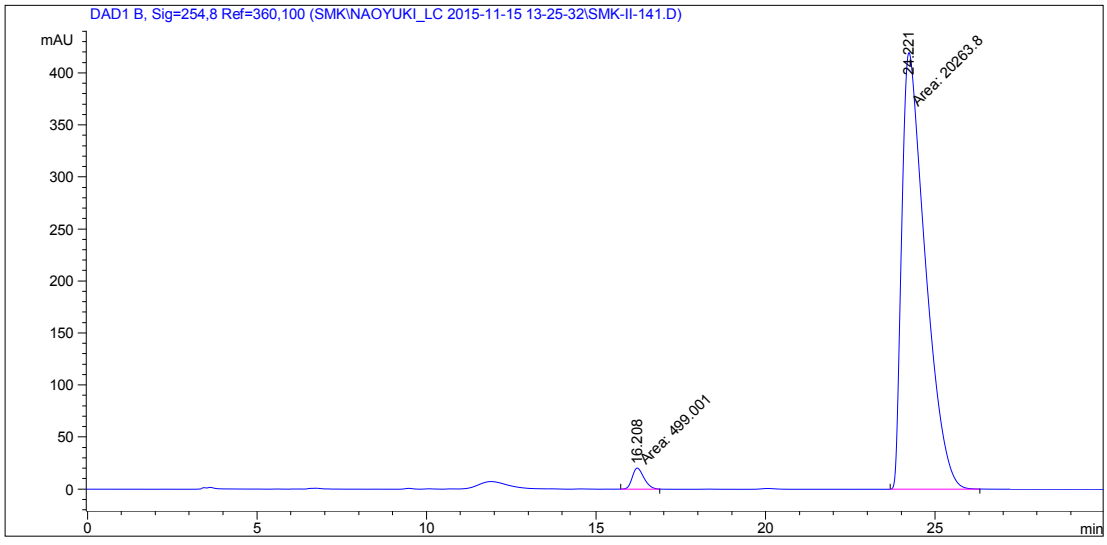
HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 95% ee: tR (minor) = 16.2 min, tR (major) = 24.2 min.

DL-6c

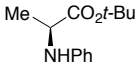


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.211	BB	0.4341	9921.71094	354.91168	50.1313
2	24.392	BB	0.6515	9869.74414	231.46831	49.8687

L-6c: 95% ee



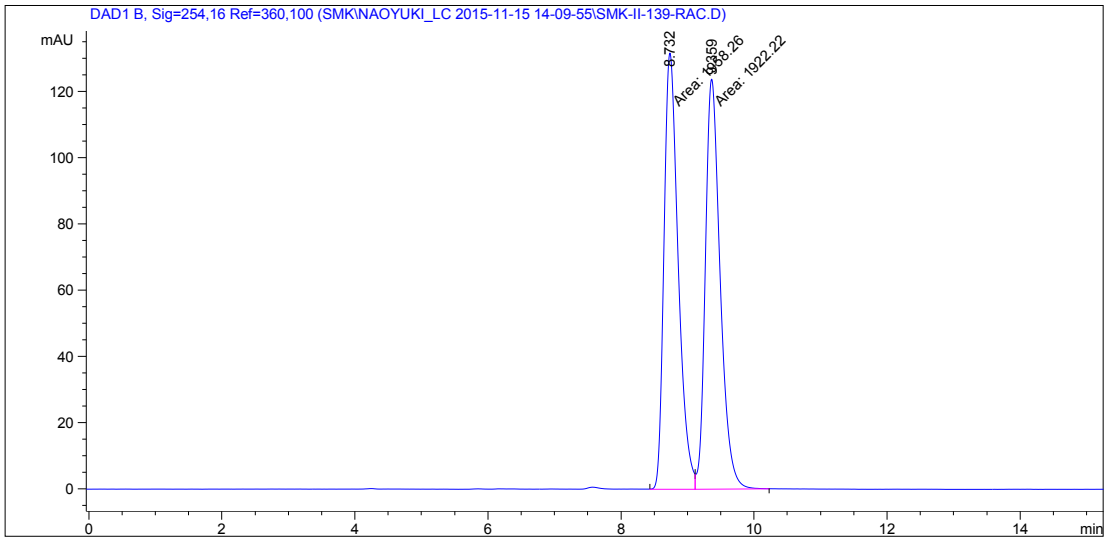
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.208	MM T	0.4076	499.00128	20.40226	2.4033
2	24.221	MM T	0.8045	2.02638e4	419.81766	97.5967



6d

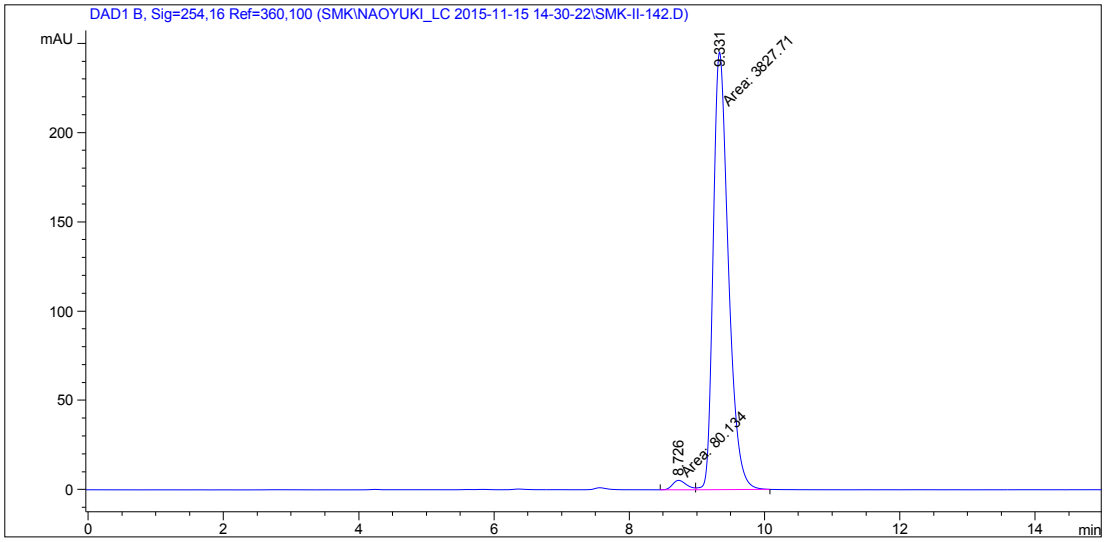
HPLC analysis (OJ-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 96% ee: tR (minor) = 8.7 min, tR (major) = 9.3 min.

DL-6d

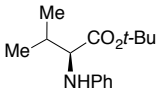


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.732	MF T	0.2475	1958.25598	131.87755	50.4643
2	9.359	FM T	0.2585	1922.22168	123.92563	49.5357

L-6d: 96% ee



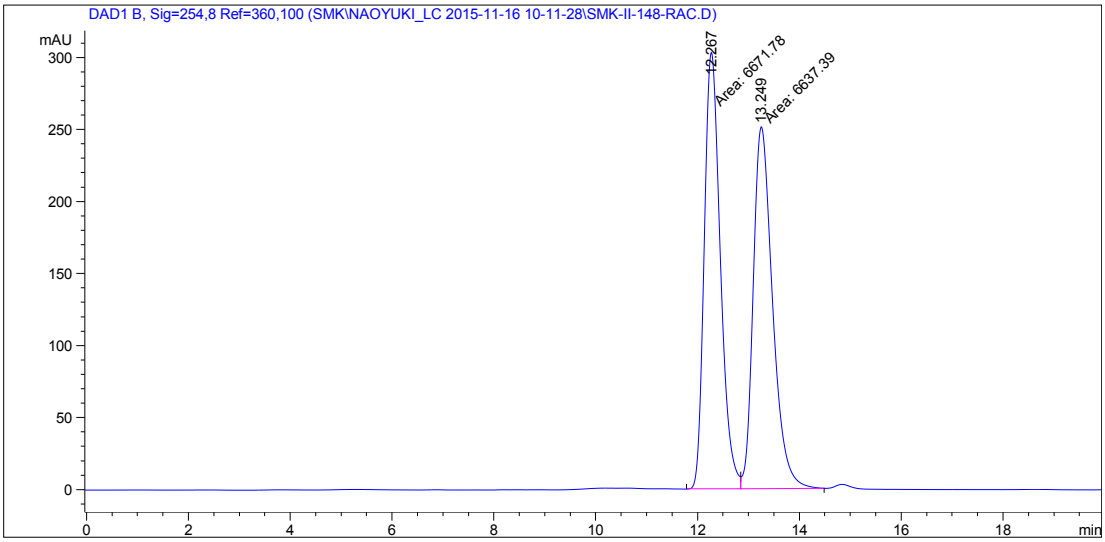
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.726	MF T	0.2472	80.13400	5.40341	2.0506
2	9.331	FM T	0.2601	3827.71411	245.30026	97.9494



6e

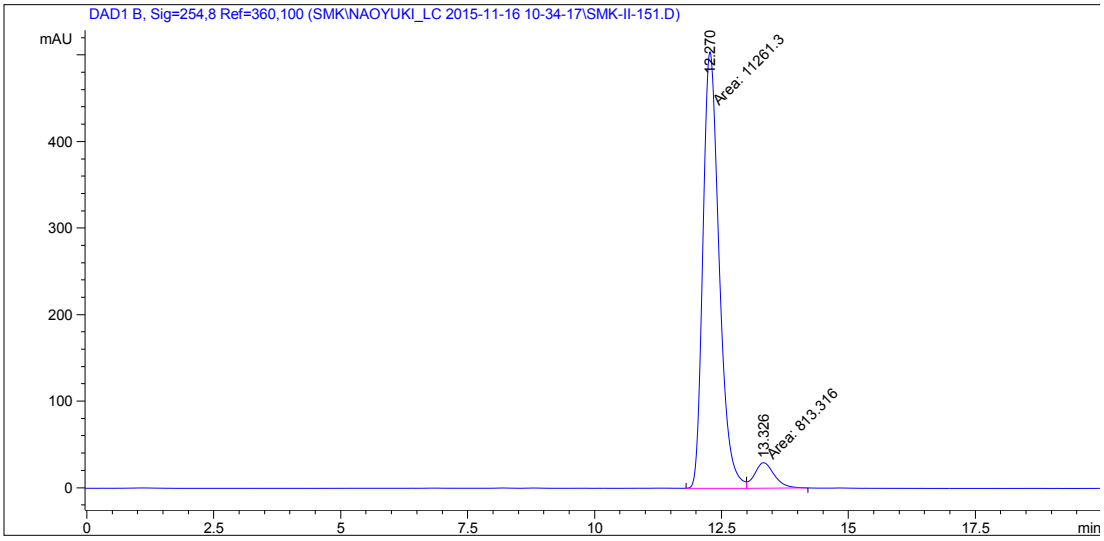
HPLC analysis (OJ-H, 0.5% IPA–hexanes, 0.5 mL/min, 254 nm) indicated 87% ee: tR (major) = 12.3 min, tR (minor) = 13.3 min.

DL-6e

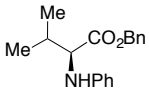


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.267	MF T	0.3669	6671.77686	303.05771	50.1292
2	13.249	FM T	0.4403	6637.38916	251.25612	49.8708

L-6e: 87% ee



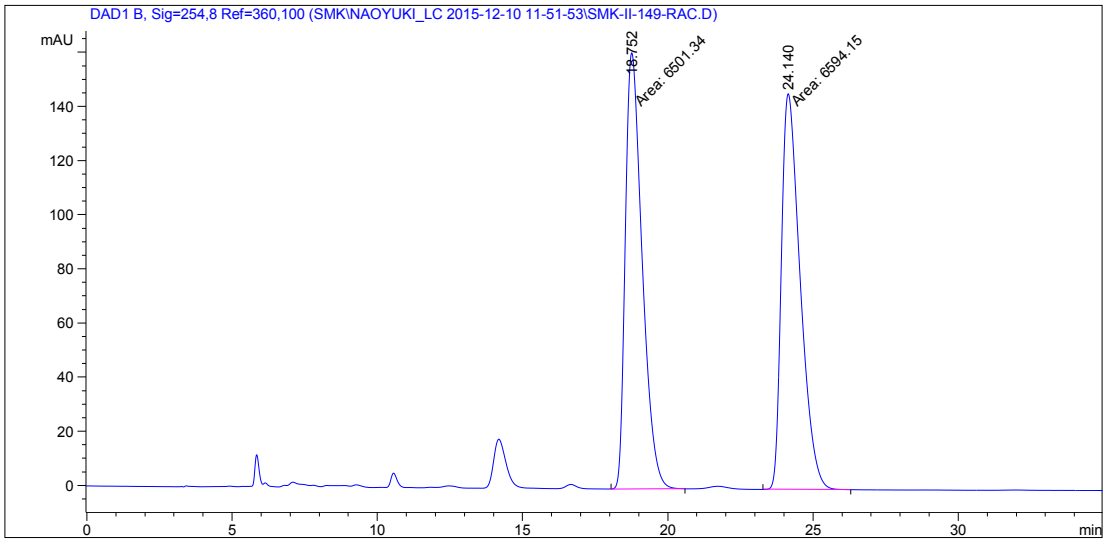
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.270	MF T	0.3721	1.12613e4	504.38626	93.2643
2	13.326	FM T	0.4577	813.31567	29.61808	6.7357



6f

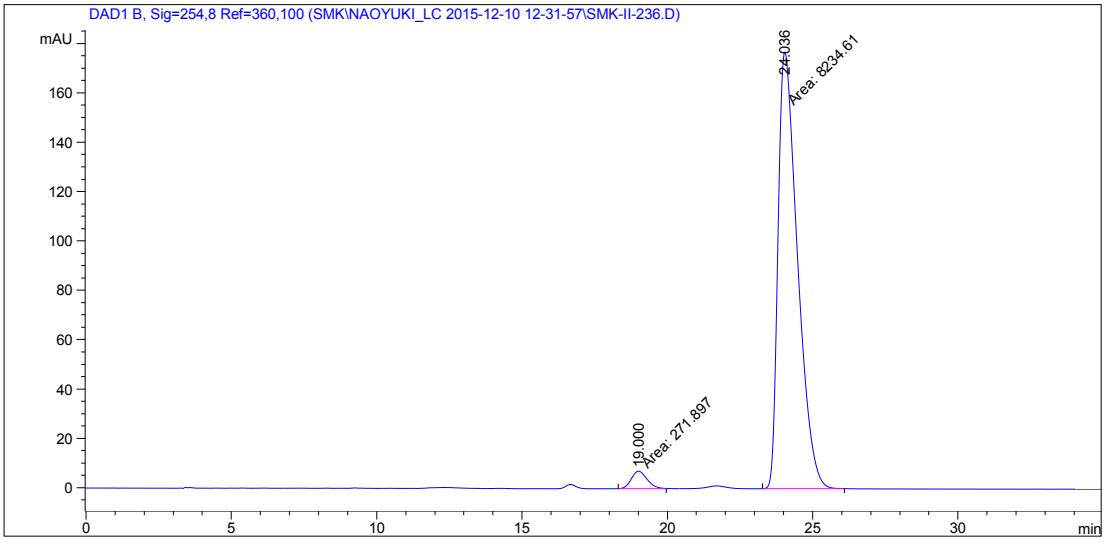
HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 94% ee: tR (minor) = 19.0 min, tR (major) = 24.0 min.

DL-6f

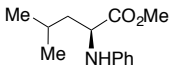


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.752	MM T	0.6722	6501.33789	161.18393	49.6456
2	24.140	MM T	0.7516	6594.14844	146.21629	50.3544

L-6f: 94% ee



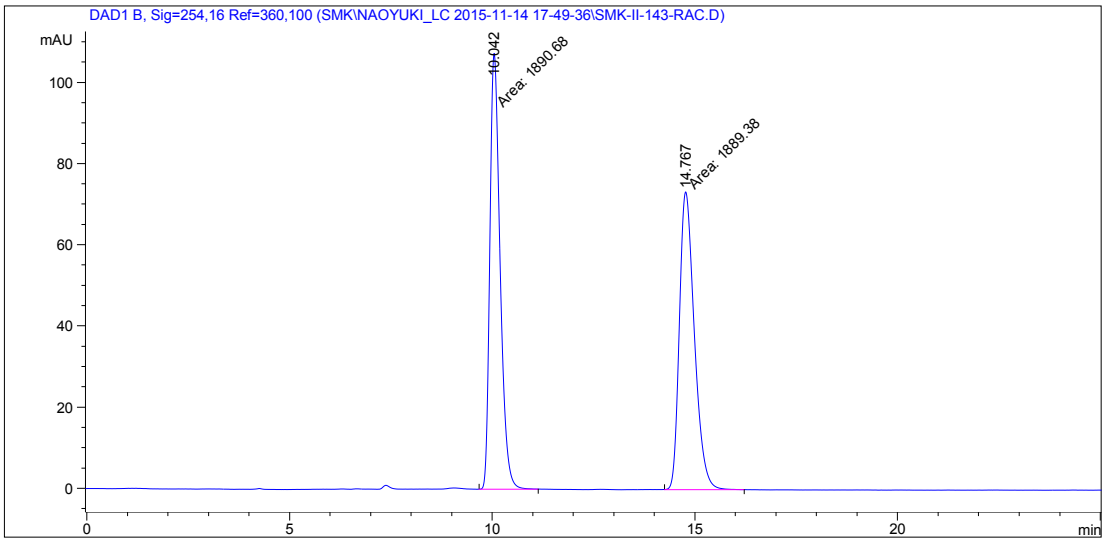
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.000	MM T	0.6356	271.89746	7.12991	3.1963
2	24.036	MM T	0.7751	8234.60547	177.05835	96.8037



6g

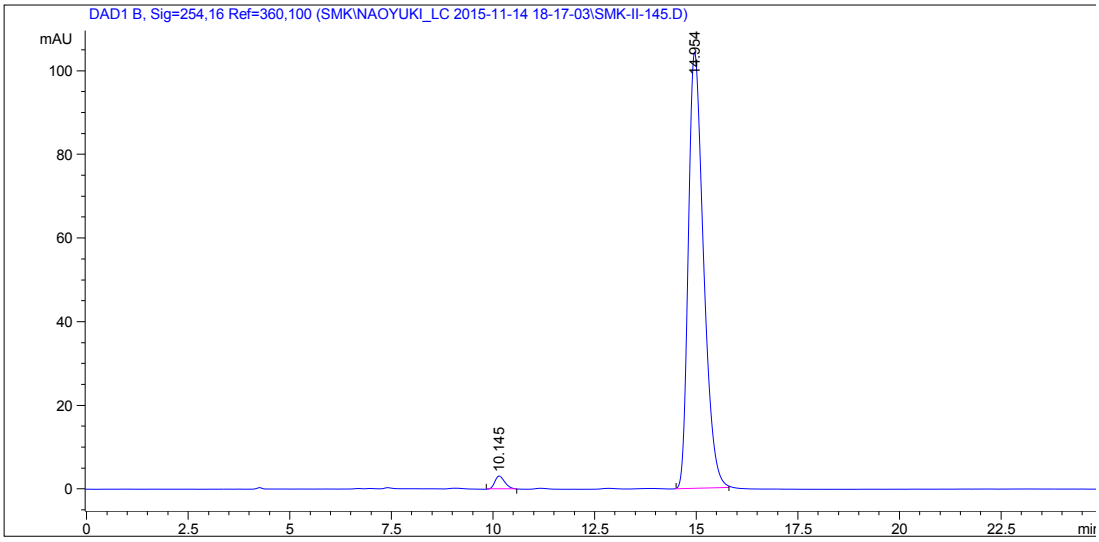
HPLC analysis (OJ-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 96% ee: tR (minor) = 10.2 min, tR (major) = 15.0 min.

DL-6g

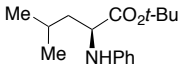


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.042	MM T	0.2932	1890.68164	107.46779	50.0173
2	14.767	MM T	0.4291	1889.37646	73.38699	49.9827

L-6g: 96% ee



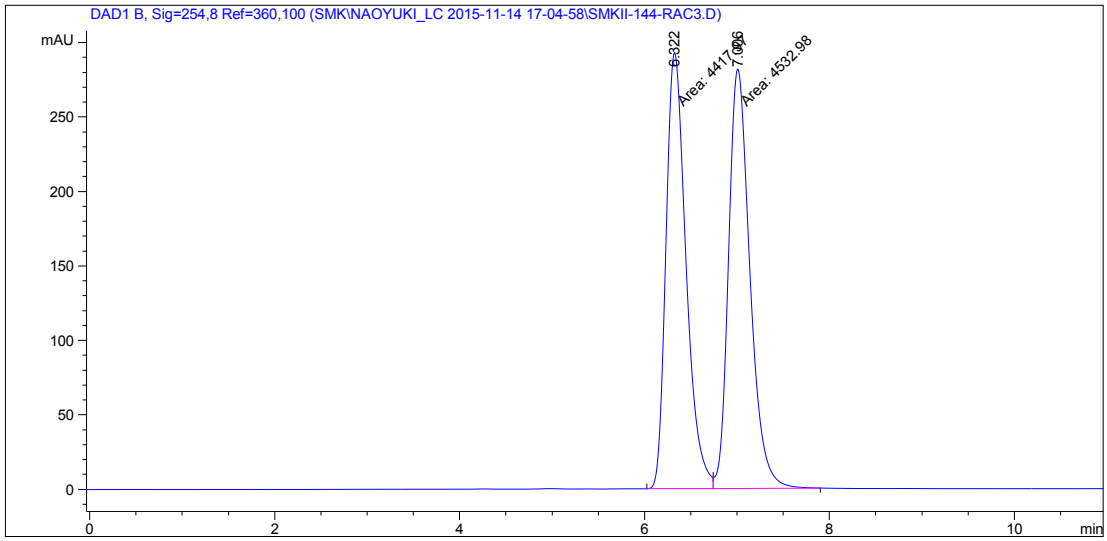
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.145	BB	0.2609	54.09112	3.14050	1.9569
2	14.954	BB	0.3992	2710.00024	104.27953	98.0431



6h

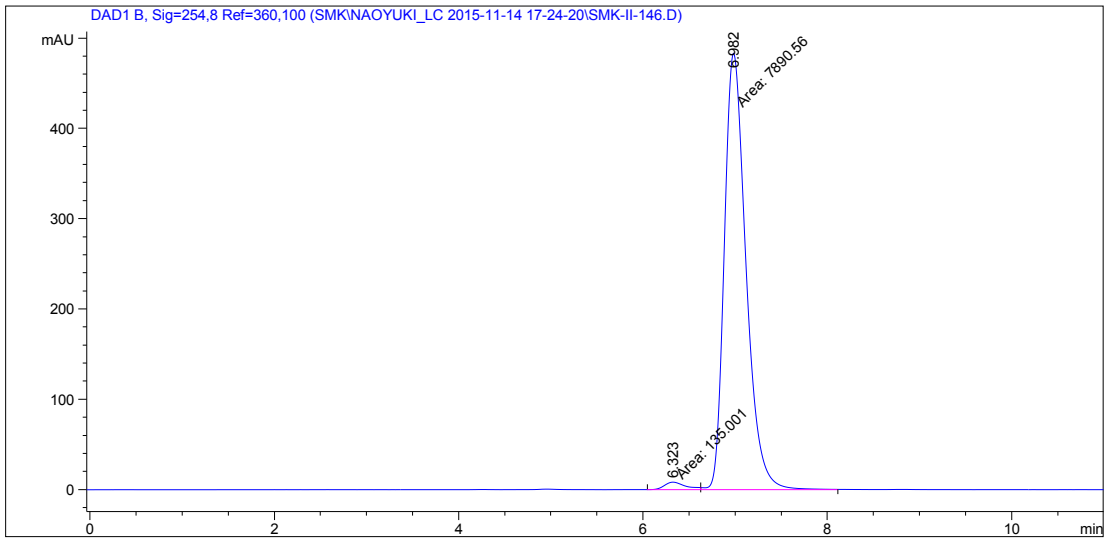
HPLC analysis (OJ-H, 1% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 97% ee: tR (minor) = 6.3 min, tR (major) = 7.0 min.

DL-6h

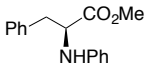


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.322	MF T	0.2513	4417.97314	292.96231	49.3576
2	7.006	FM T	0.2681	4532.97559	281.83261	50.6424

L-6h: 97% ee



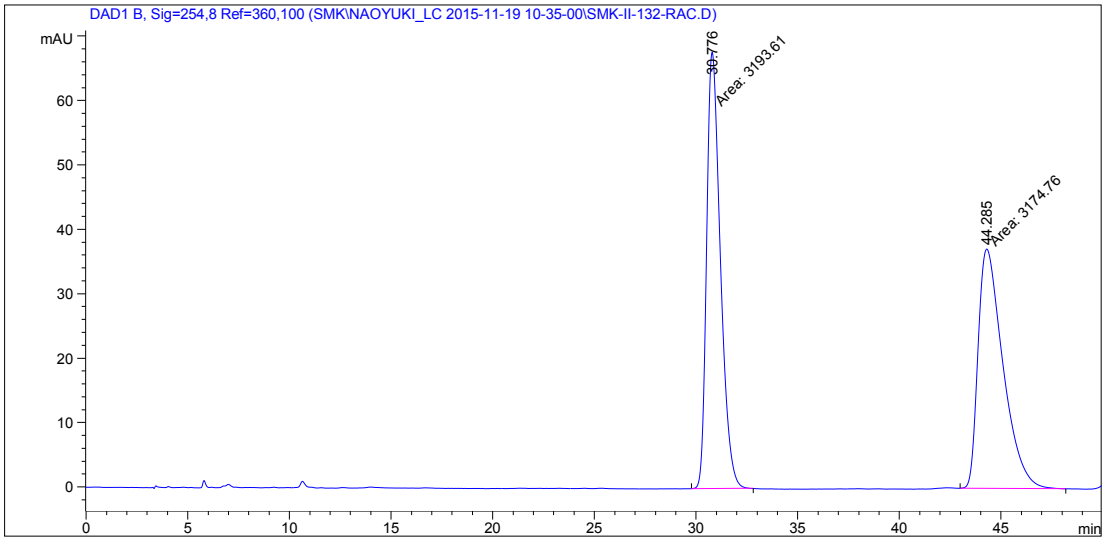
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.323	MF T	0.2697	135.00081	8.34301	1.6821
2	6.982	FM T	0.3253	7890.55957	483.25766	98.3179



6i

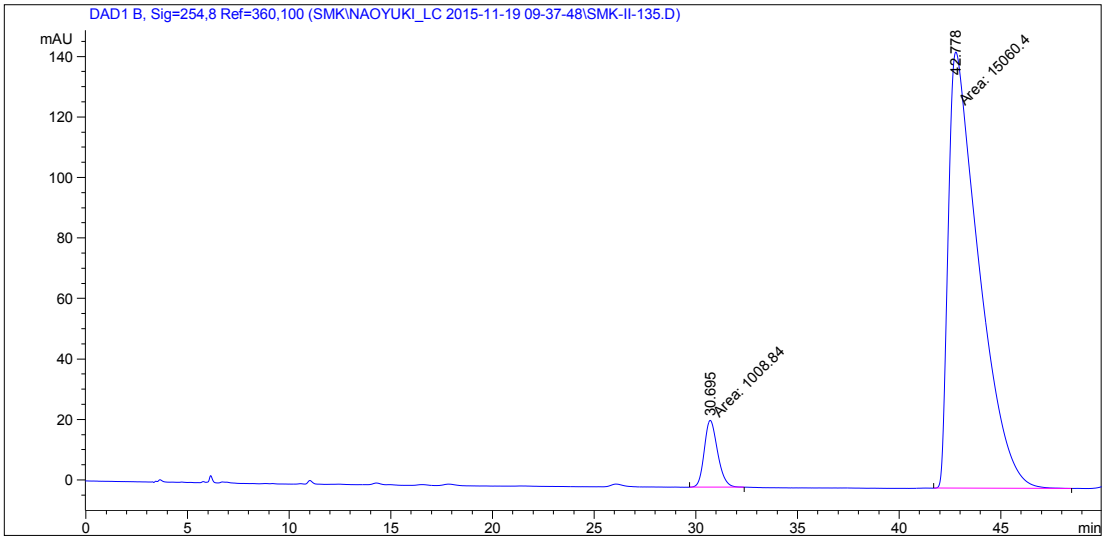
HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 87% ee: tR (minor) = 30.7 min, tR (major) = 42.8 min.

DL-6i

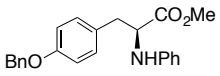


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.776	MM T	0.7855	3193.60840	67.76417	50.1480
2	44.285	MM T	1.4228	3174.75586	37.18823	49.8520

L-6i: 87% ee



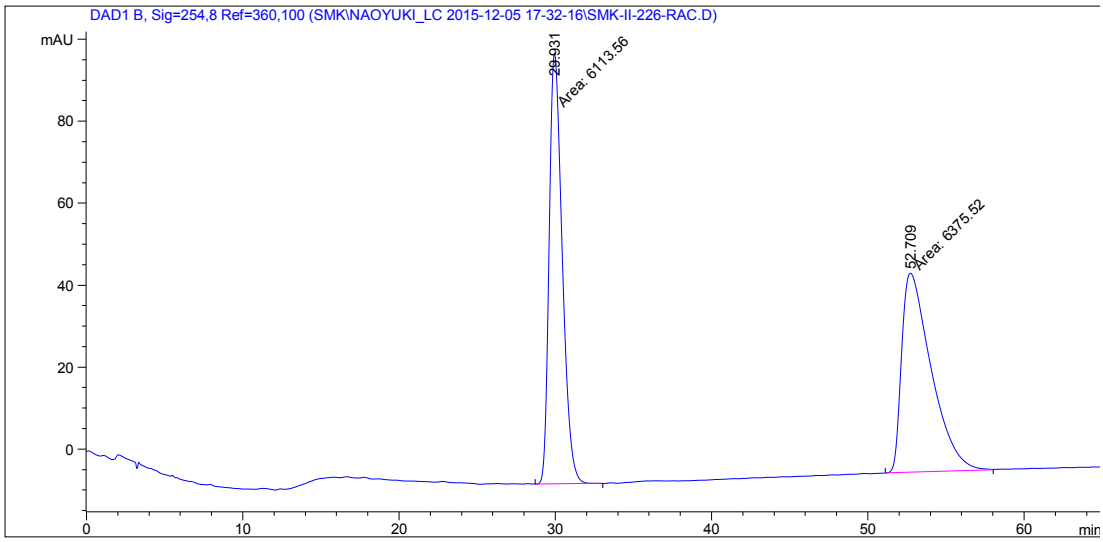
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.695	MM T	0.7608	1008.83502	22.10026	6.2780
2	42.778	MM T	1.7406	1.50604e4	144.20990	93.7220



6j

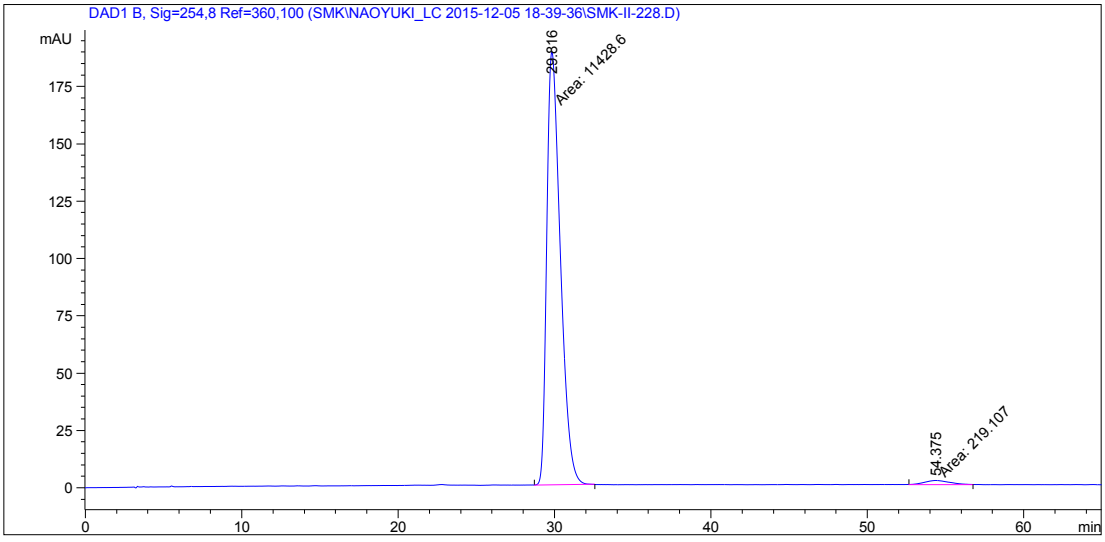
HPLC analysis (OD-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 96% ee: tR (major) = 29.8 min, tR (minor) = 54.4 min.

DL-6j

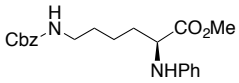


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.931	MM T	0.9698	6113.56494	105.06756	48.9513
2	52.709	MM T	2.1865	6375.51855	48.59669	51.0487

L-6j: 96% ee



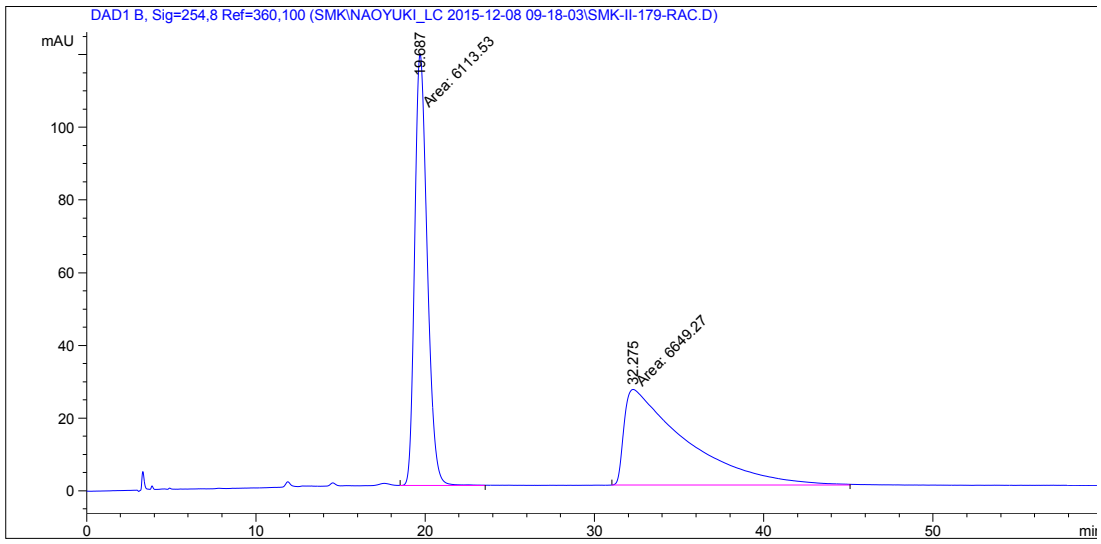
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.816	MM T	1.0084	1.14286e4	188.89705	98.1189
2	54.375	MM T	1.9436	219.10712	1.87883	1.8811



6k

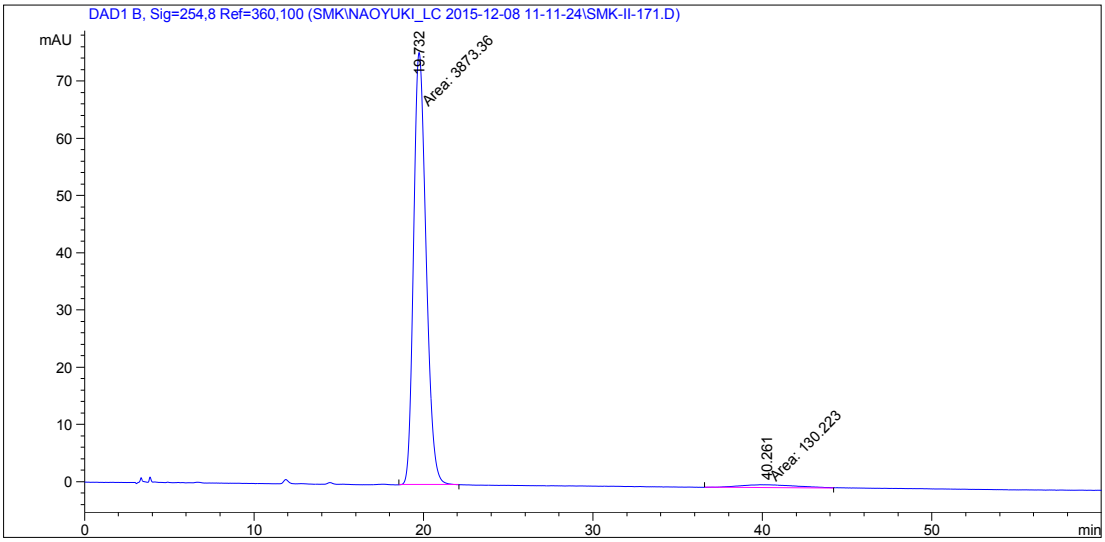
HPLC analysis (OD-H, 20% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 94% ee: tR (major) = 19.7 min, tR (minor) = 40.3 min.

DL-6k

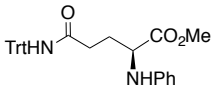


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.687	MM T	0.8580	6113.52637	118.76188	47.9011
2	32.275	MM T	4.2124	6649.27490	26.30807	52.0989

L-6k: 94%



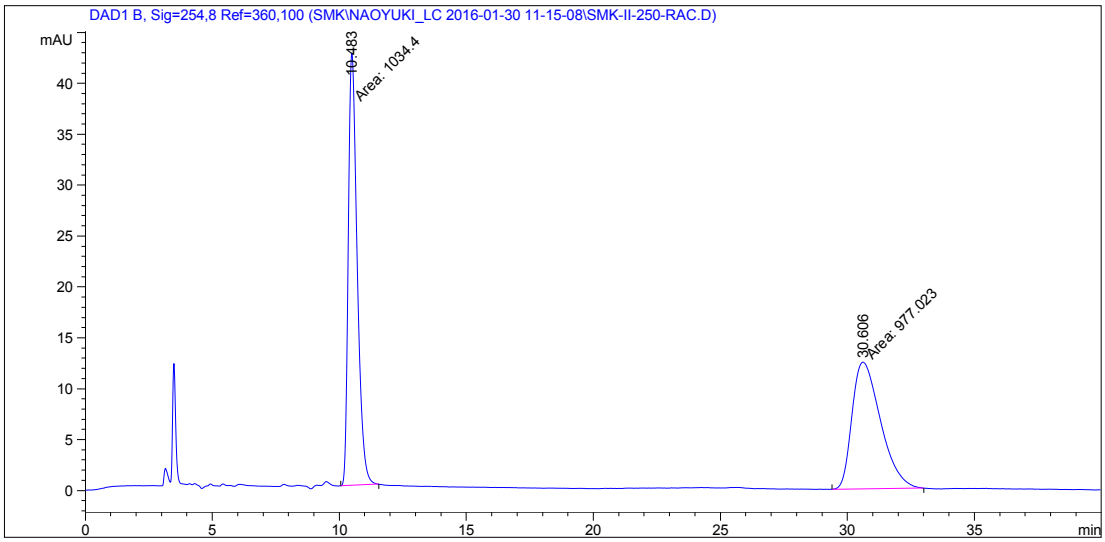
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.732	MM T	0.8546	3873.36255	75.53883	96.7473
2	40.261	MM T	4.1188	130.22308	5.26940e-1	3.2527



6l

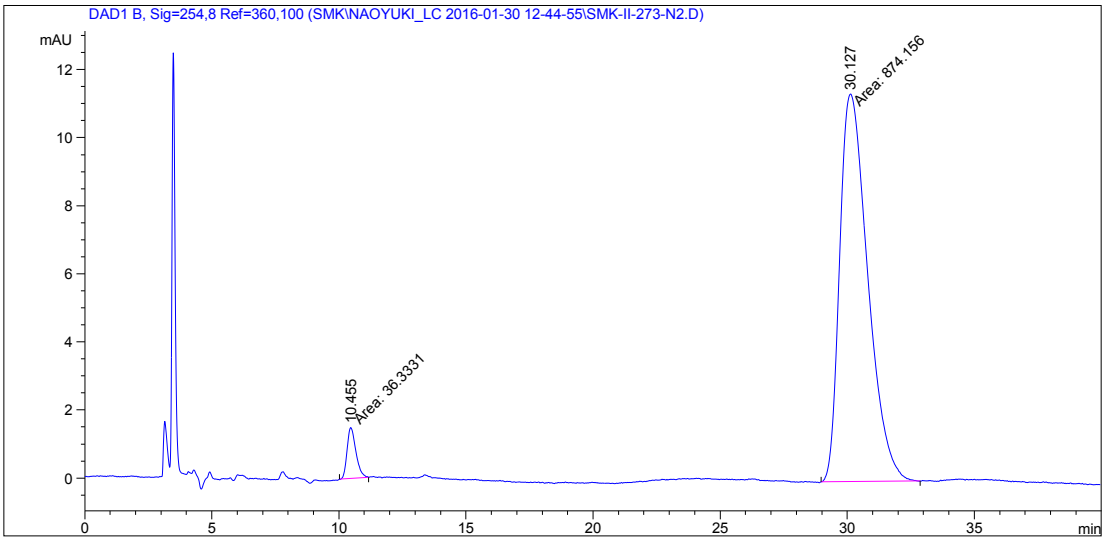
HPLC analysis (AD-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 92% ee: tR (minor) = 10.5 min, tR (major) = 30.1 min.

DL-6l

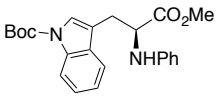


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.483	MM T	0.4058	1034.40479	42.48903	51.4264
2	30.606	MM T	1.3053	977.02319	12.47537	48.5736

L-6l: 92%



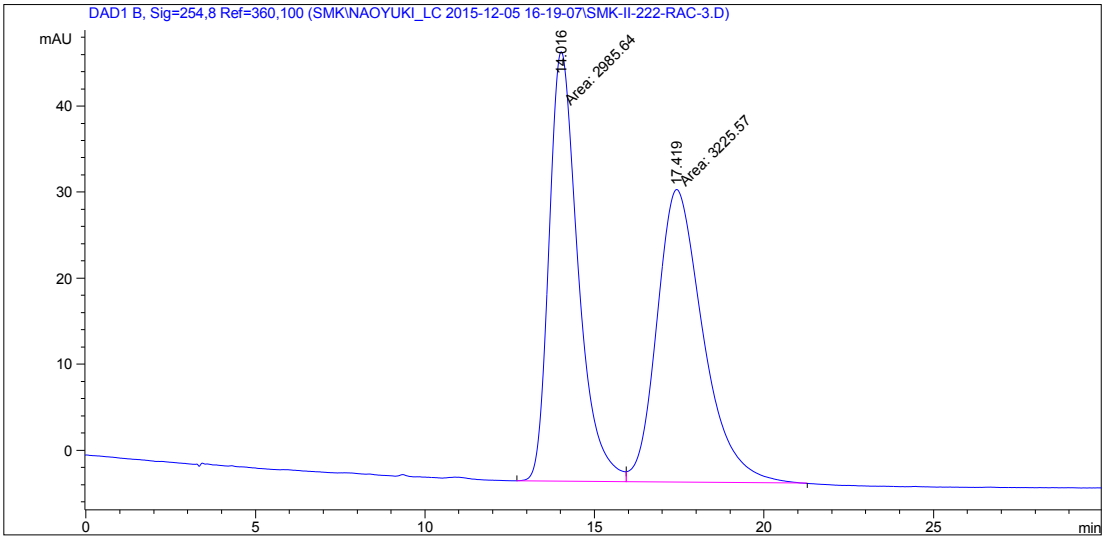
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.455	MM T	0.4036	36.33312	1.50054	3.9905
2	30.127	MM T	1.2795	874.15619	11.38695	96.0095



6m

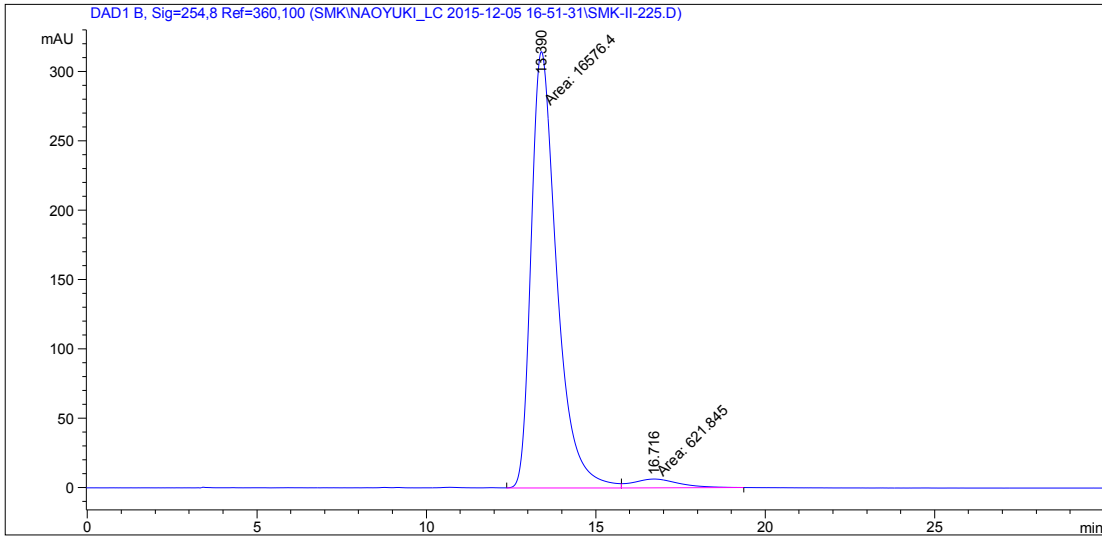
HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 93% ee: tR (major) = 13.4 min, tR (minor) = 16.7 min.

DL-6m

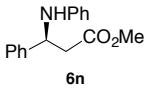


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.016	MF T	0.9965	2985.64014	49.93752	48.0686
2	17.419	FM T	1.5793	3225.56665	34.03899	51.9314

L-6m: 93% ee



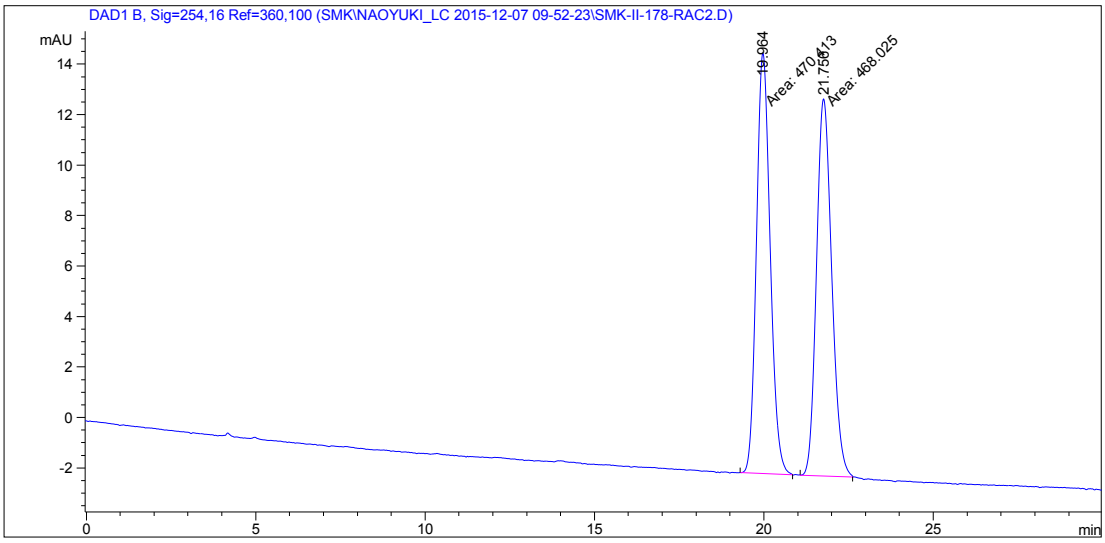
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.390	MF T	0.8785	1.65764e4	314.49765	96.3843
2	16.716	FM T	1.6117	621.84534	6.43063	3.6157



6n

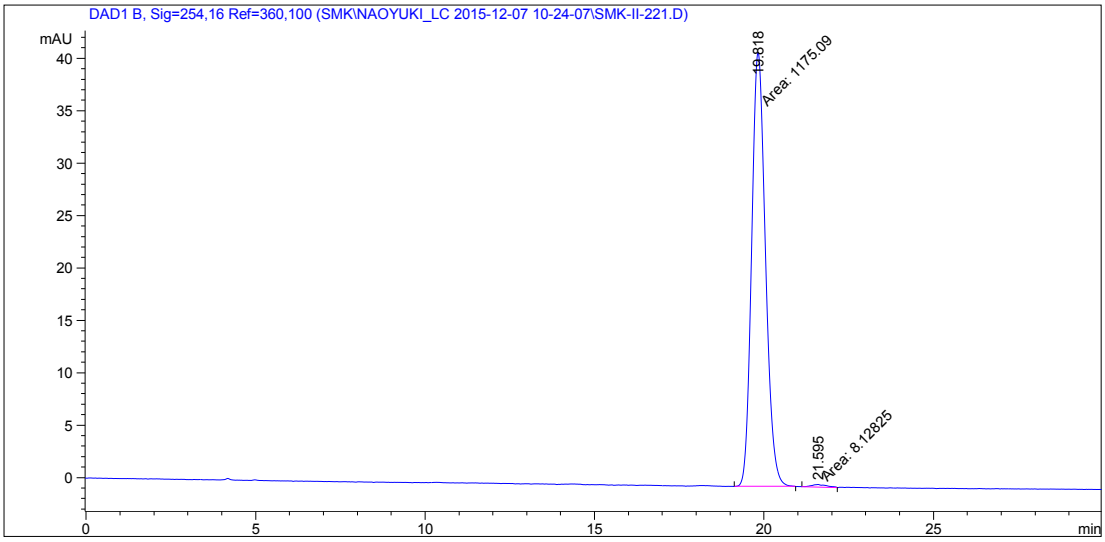
HPLC analysis (OD-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 99% ee: tR (major) = 19.8 min, tR (minor) = 21.6 min.

DL-6n

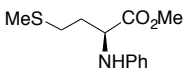


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.964	MM T	0.4703	470.41306	16.67086	50.1272
2	21.756	MM T	0.5217	468.02487	14.95182	49.8728

L-6n: 99% ee



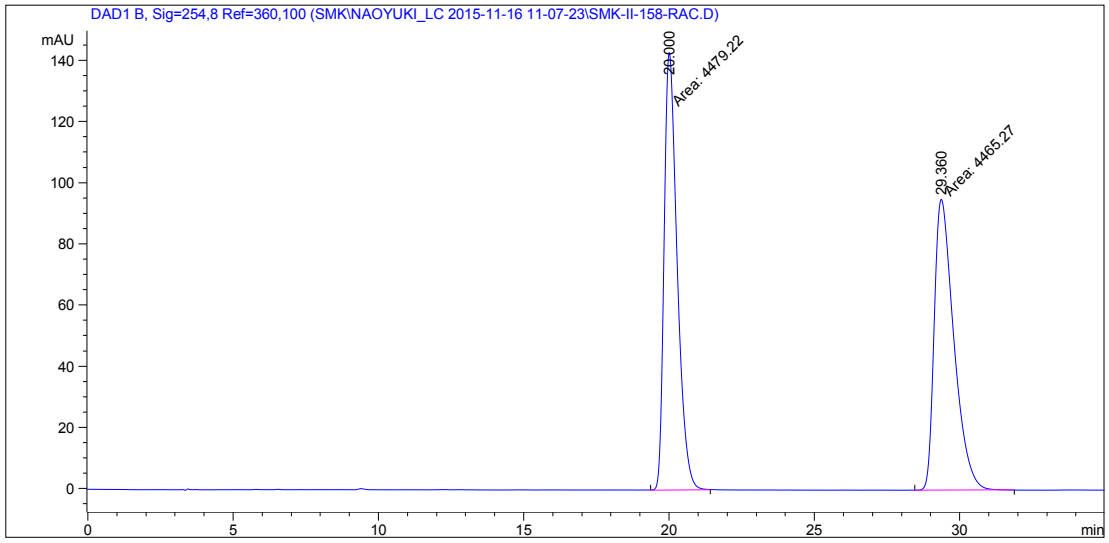
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.818	MM T	0.4728	1175.09338	41.42310	99.3130
2	21.595	MM T	0.5334	8.12825	2.53999e-1	0.6870



6o

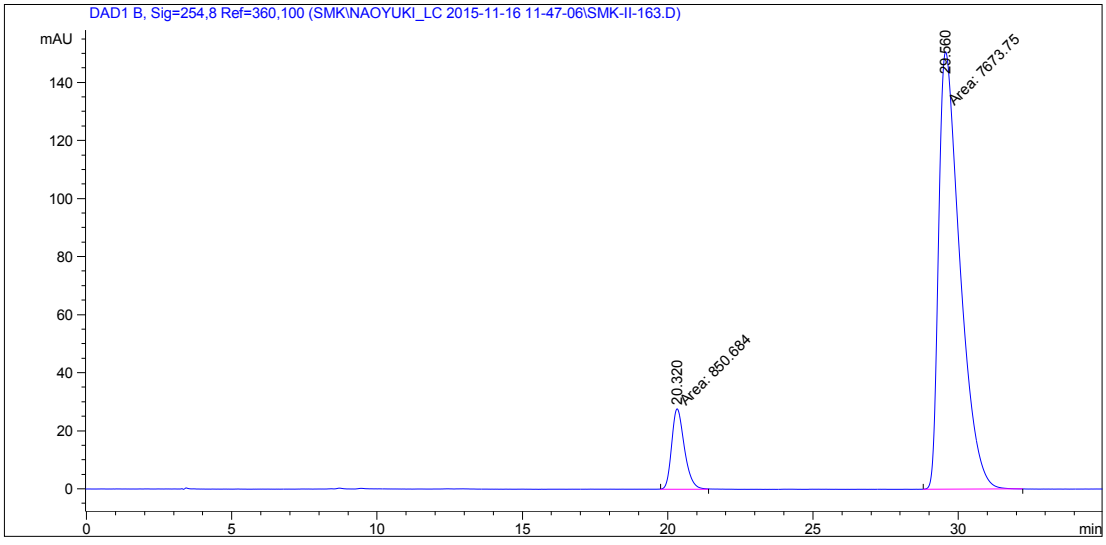
HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 80% ee: tR (minor) = 20.3 min, tR (major) = 29.6 min.

DL-6o

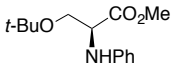


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.000	MM T	0.5215	4479.21973	143.14674	50.0780
2	29.360	MM T	0.7828	4465.26514	95.07150	49.9220

L-6o: 80% ee



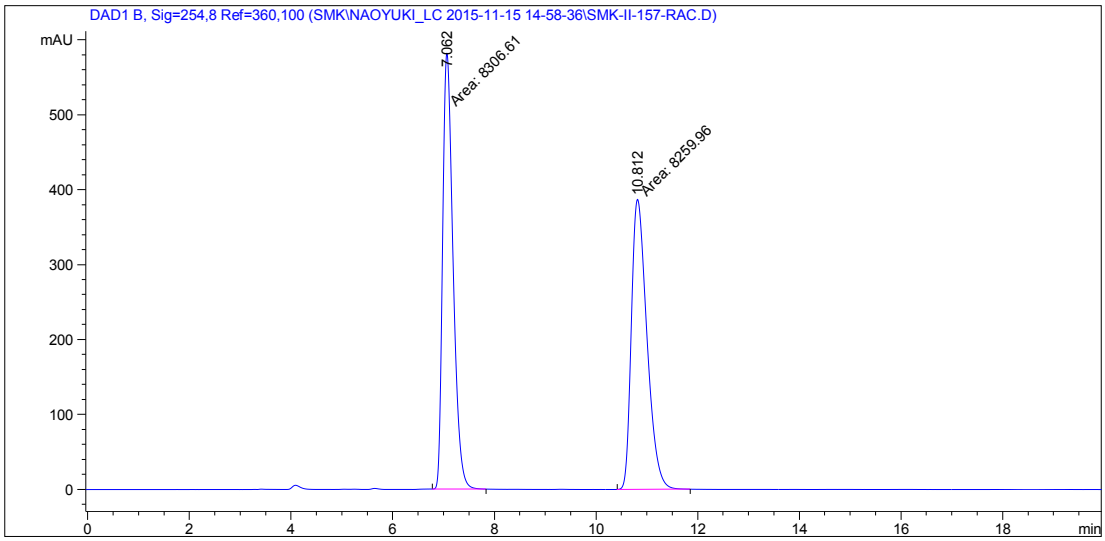
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.320	MM T	0.5105	850.68414	27.77098	9.9794
2	29.560	MM T	0.8488	7673.74561	150.67964	90.0206



6p

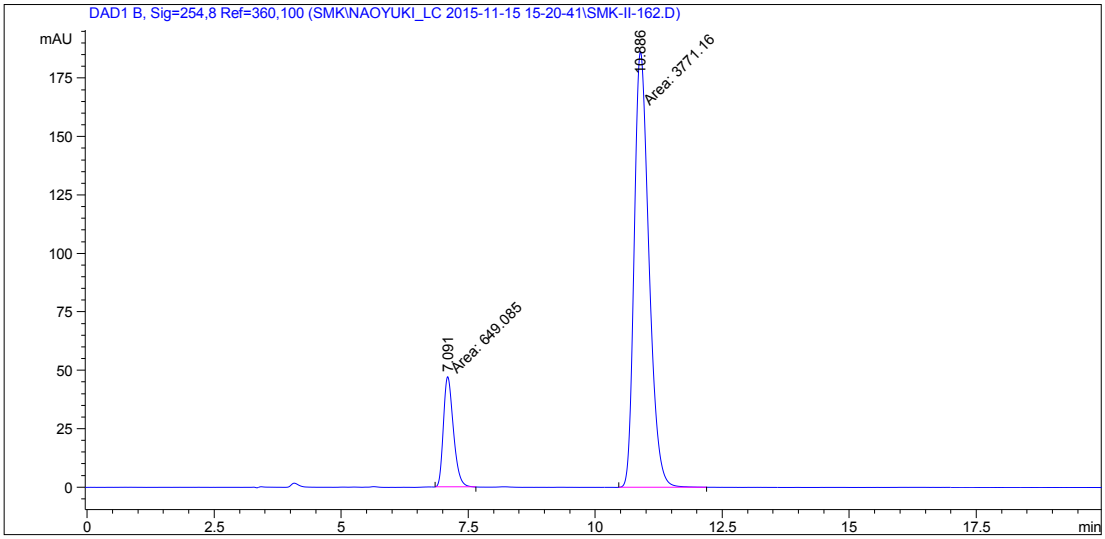
HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 71% ee: tR (minor) = 7.1 min, tR (major) = 10.9 min.

DL-6p

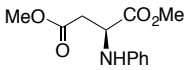


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.062	MM T	0.2377	8306.60547	582.36609	50.1408
2	10.812	MM T	0.3553	8259.96094	387.49521	49.8592

L-6p: 71% ee



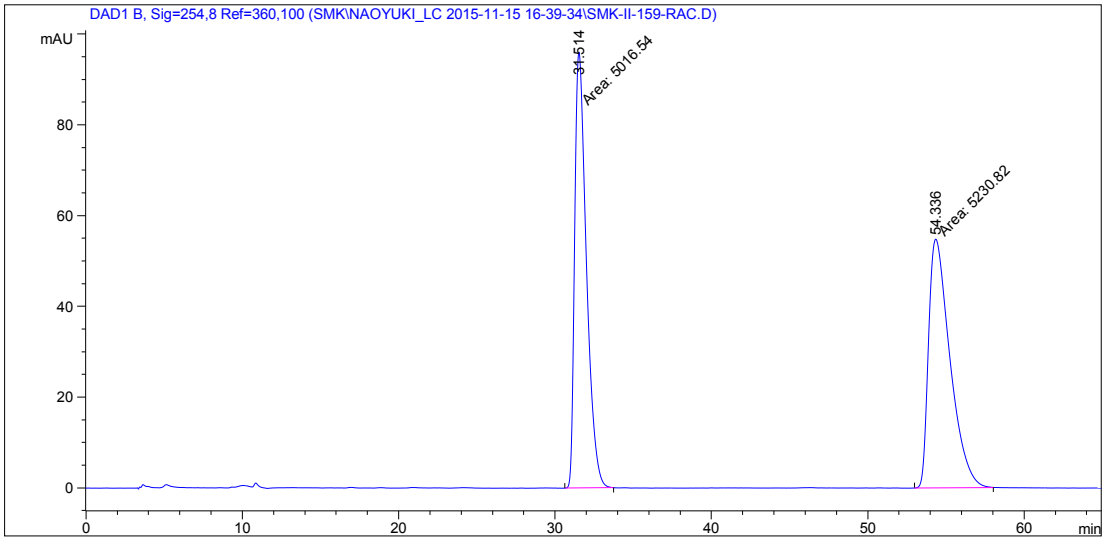
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.091	MM T	0.2289	649.08466	47.25744	14.6844
2	10.886	MM T	0.3371	3771.16309	186.42711	85.3156



6q

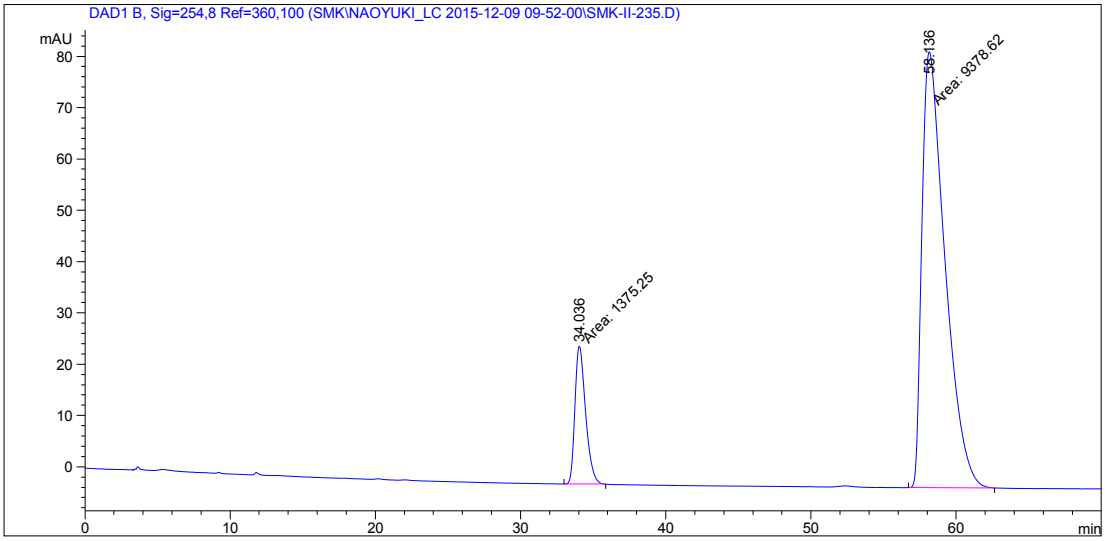
HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 74% ee: tR (minor) = 34.0 min, tR (major) = 58.1 min.

DL-6q

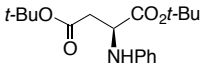


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.514	MM T	0.8702	5016.53857	96.08055	48.9545
2	54.336	MM T	1.5890	5230.82080	54.86498	51.0455

L-6q: 74% ee



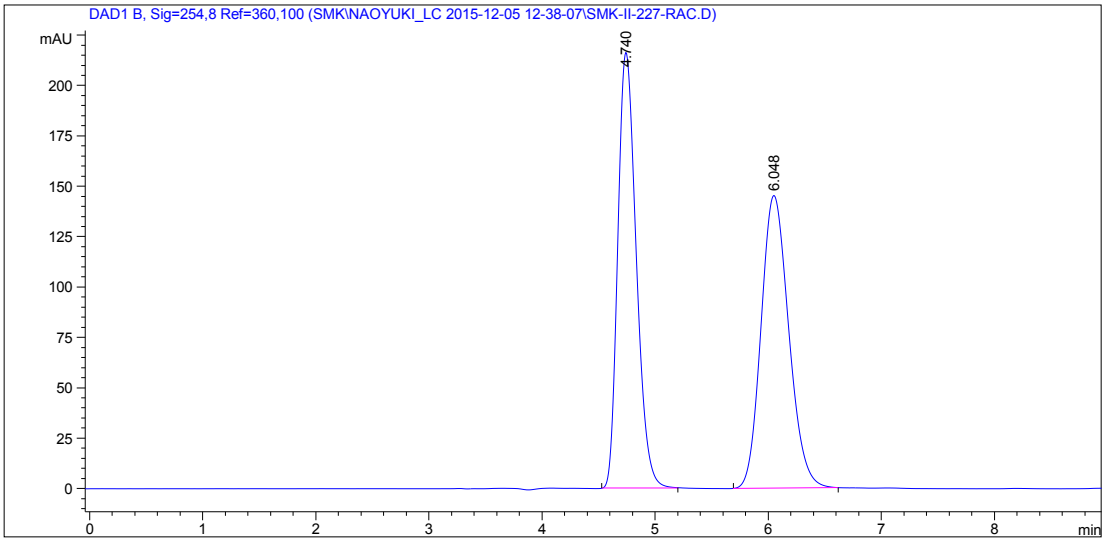
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.036	MM T	0.8524	1375.24902	26.88844	12.7884
2	58.136	MM T	1.8396	9378.61816	84.97053	87.2116



6r

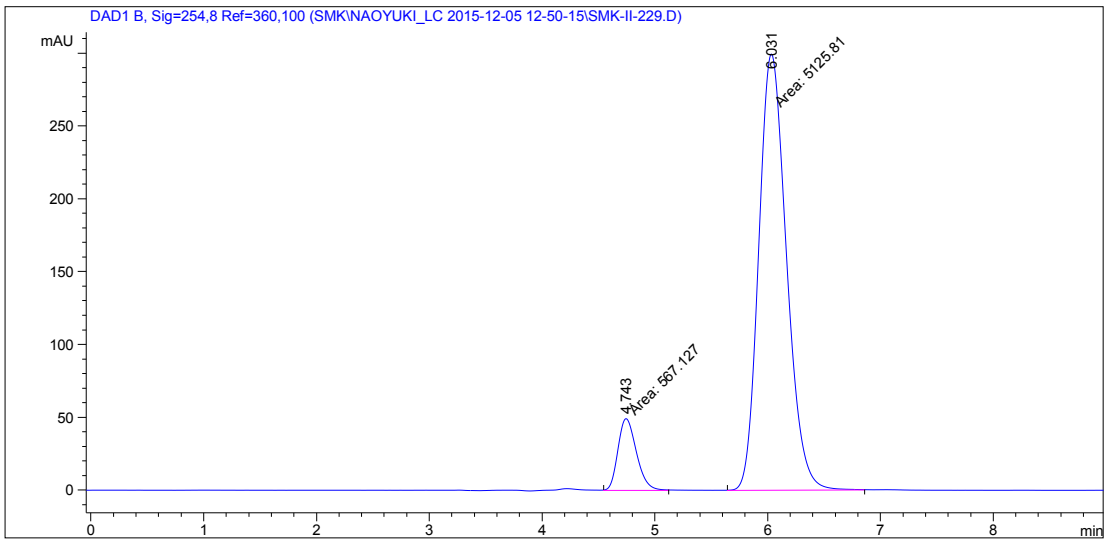
HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 80% ee: tR (minor) = 4.7 min, tR (major) = 6.0 min.

DL-6r

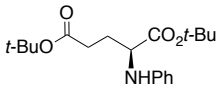


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.740	BB	0.1762	2451.02417	216.31883	49.7712
2	6.048	BB	0.2647	2473.56104	145.26938	50.2288

L-6r: 80% ee



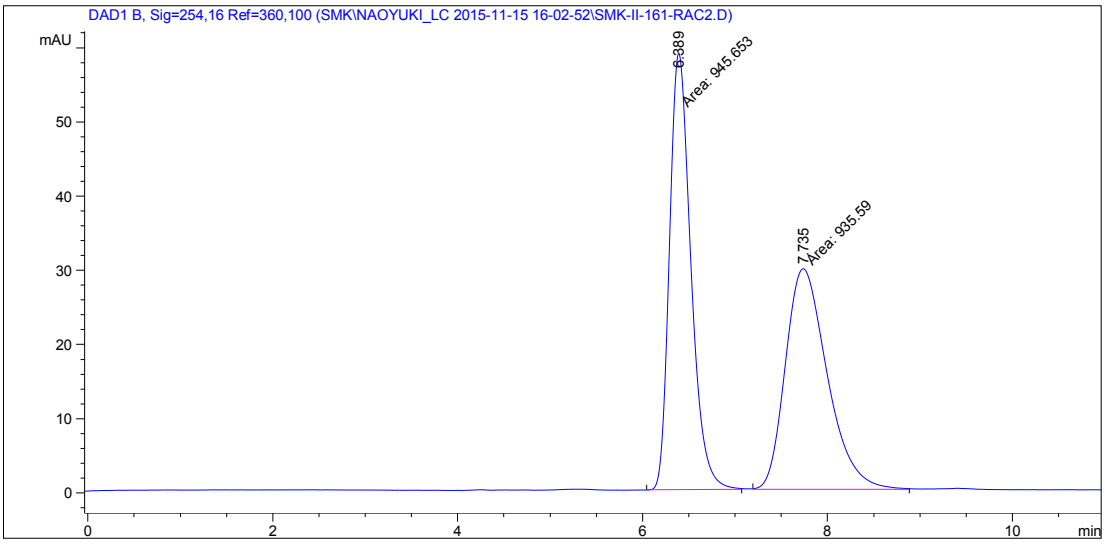
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.743	MM T	0.1911	567.12701	49.45195	9.9619
2	6.031	MM T	0.2850	5125.80957	299.72882	90.0381



6s

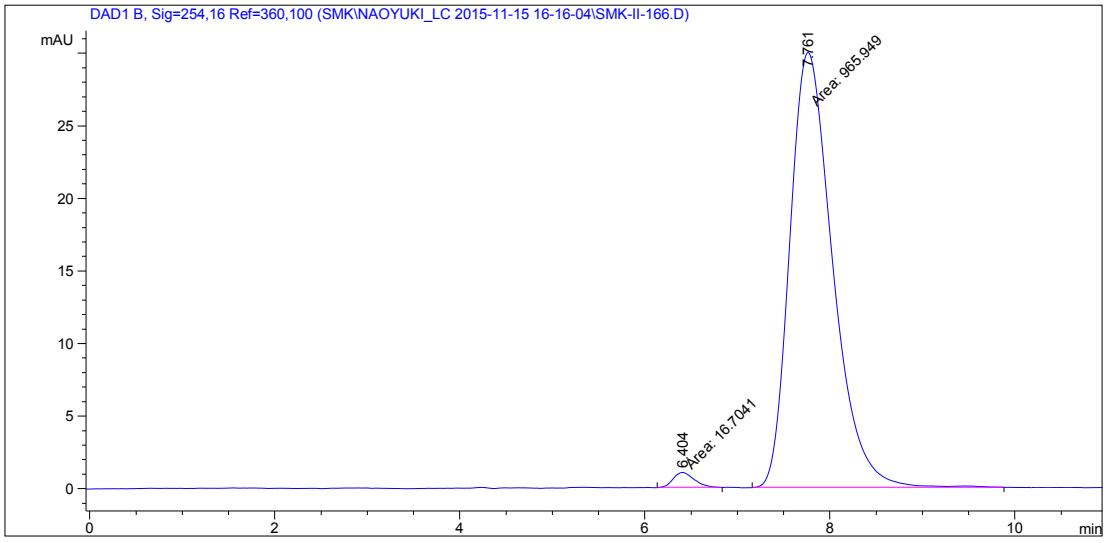
HPLC analysis (OJ-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 97% ee: tR (minor) = 6.4 min, tR (major) = 7.8 min.

DL-6s

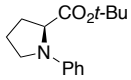


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.389	MM T	0.2678	945.65277	58.85315	50.2674
2	7.735	MM T	0.5243	935.59015	29.74061	49.7326

L-6s: 97% ee



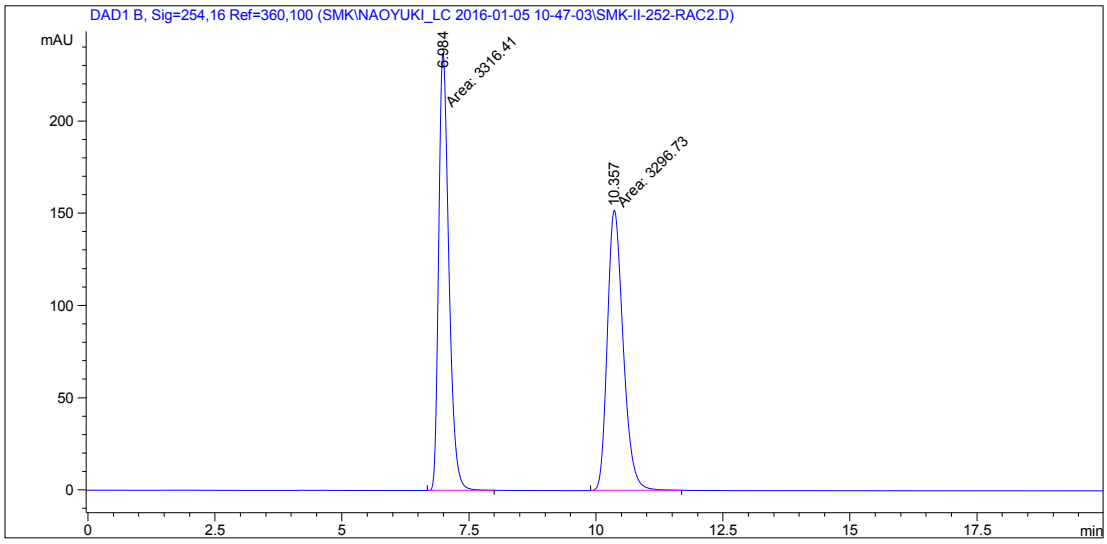
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.404	MM T	0.2662	16.70407	1.04569	1.6999
2	7.761	MM T	0.5371	965.94861	29.97613	98.3001



6t

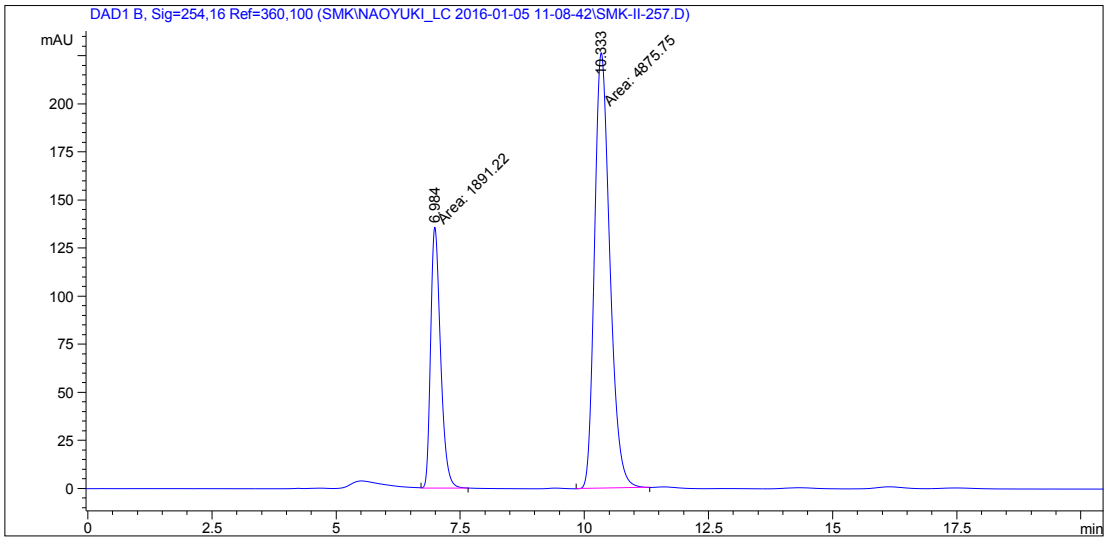
HPLC analysis (OJ-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 44% ee: tR (minor) = 7.0 min, tR (major) = 10.3 min.

DL-6t



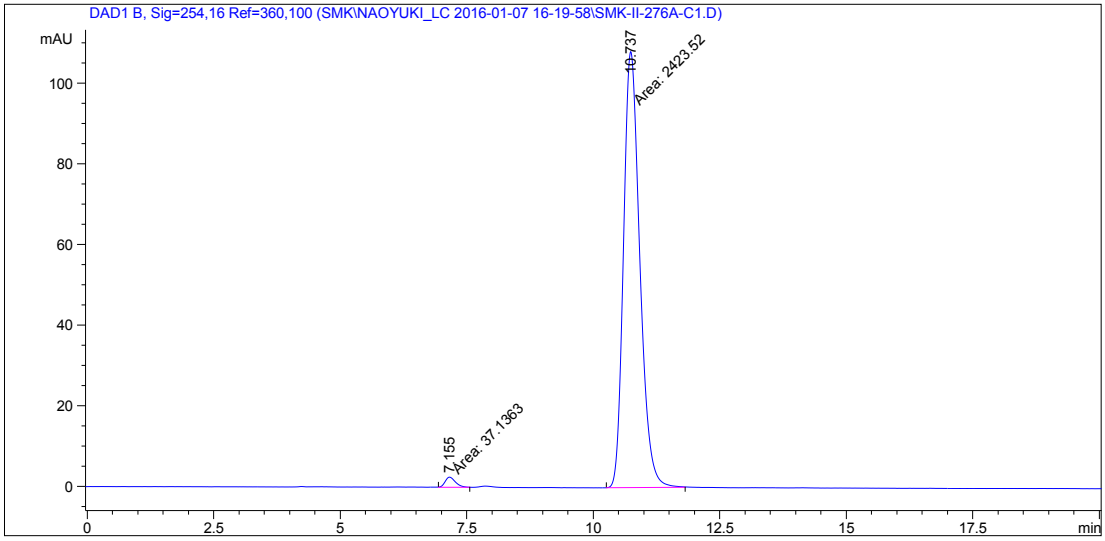
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.984	MM T	0.2330	3316.41333	237.21582	50.1488
2	10.357	MM T	0.3614	3296.72925	152.01476	49.8512

L-6t: 44% ee

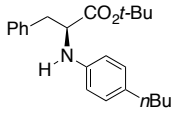


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.984	MM T	0.2321	1891.22009	135.79919	27.9478
2	10.333	MM T	0.4395	4875.75342	226.49168	72.0522

L-6t: 97% ee



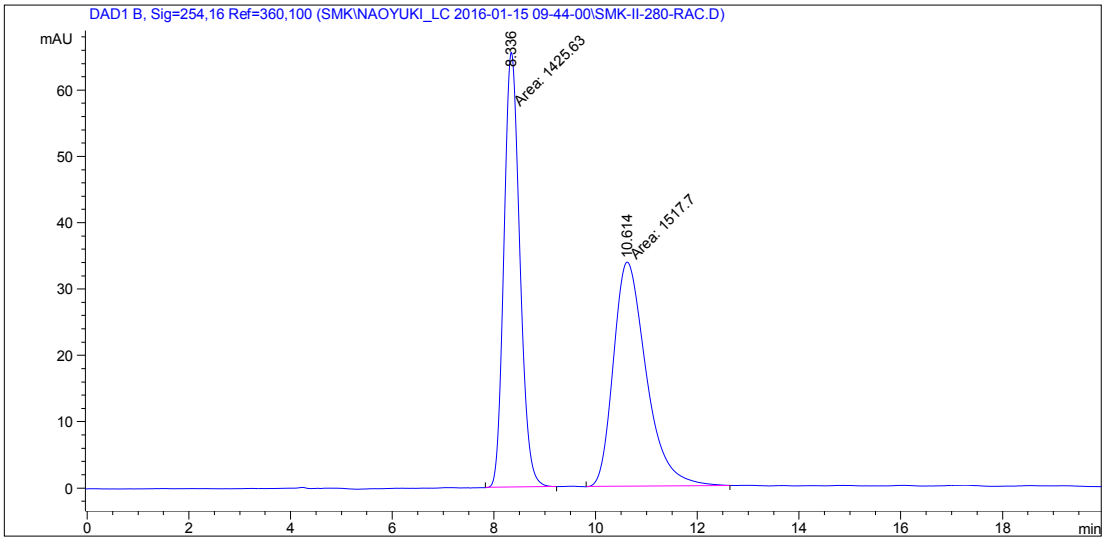
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.155	MM T	0.2426	37.13628	2.55177	1.5092
2	10.737	MM T	0.3735	2423.52246	108.15245	98.4908



8a

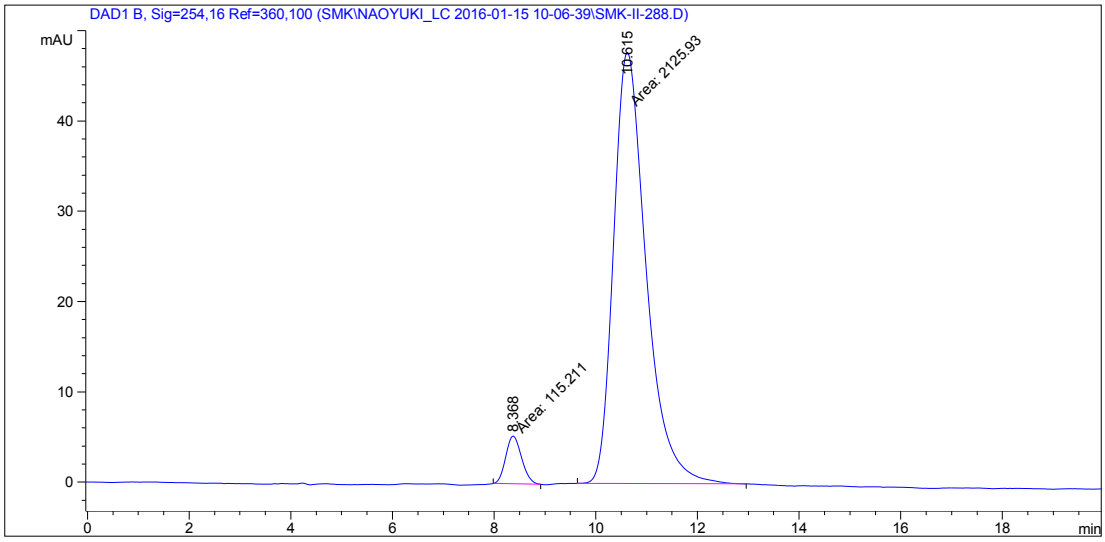
HPLC analysis (OJ-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 90% ee: tR (minor) = 8.4 min, tR (major) = 10.6 min.

DL-8a

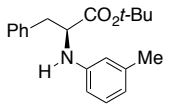


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.336	MM T	0.3623	1425.62817	65.58488	48.4360
2	10.614	MM T	0.7479	1517.69531	33.81954	51.5640

L-8a: 90% ee



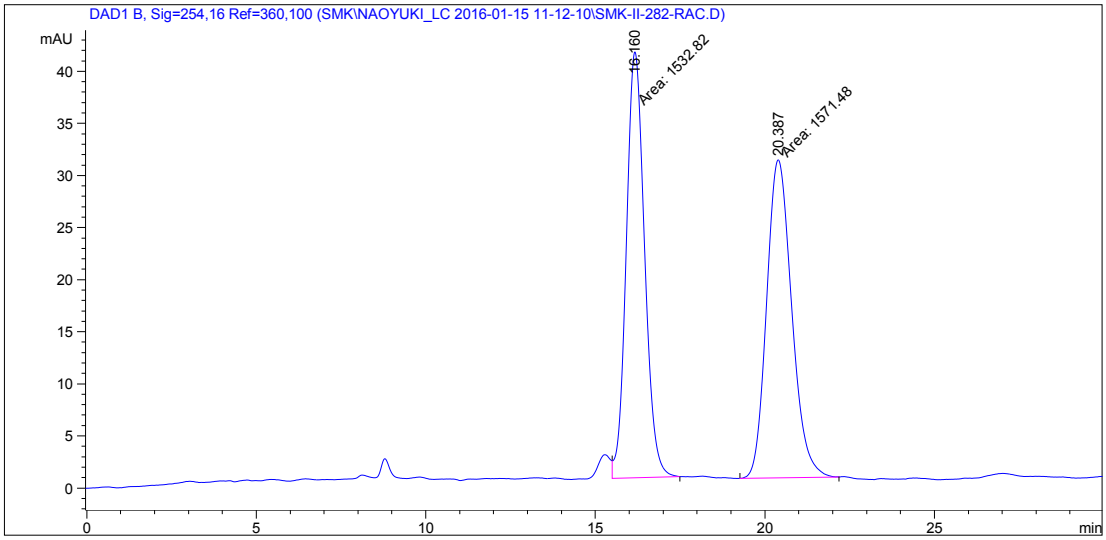
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.368	MM T	0.3632	115.21096	5.28719	5.1407
2	10.615	MM T	0.7421	2125.93457	47.74479	94.8593



8b

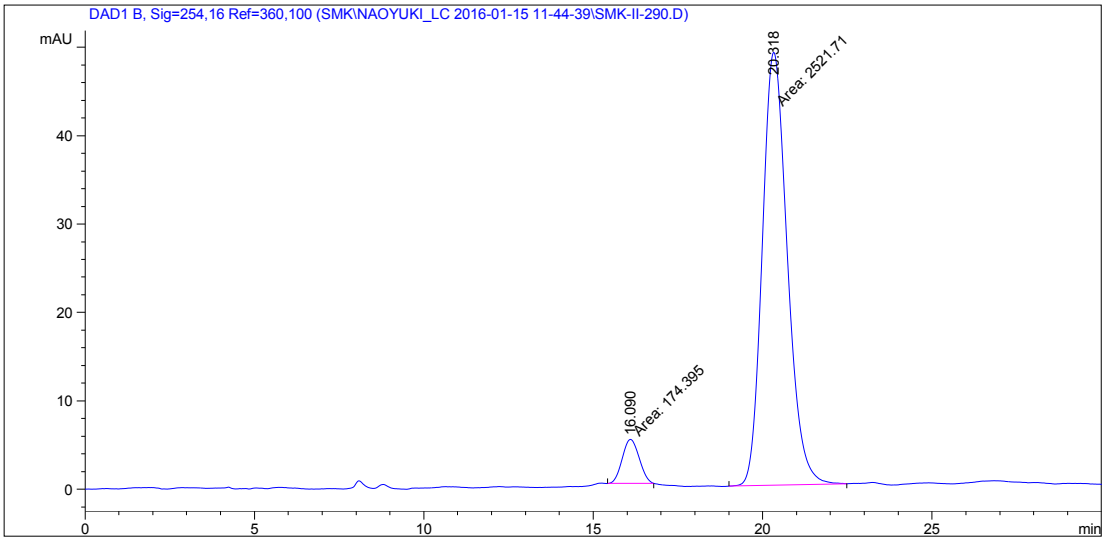
HPLC analysis (OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 87% ee: tR (minor) = 16.1 min, tR (major) = 20.3 min.

DL-8b

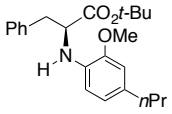


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.160	FM T	0.6248	1532.82227	40.88693	49.3773
2	20.387	MM T	0.8578	1571.48206	30.53393	50.6227

L-8b: 87% ee



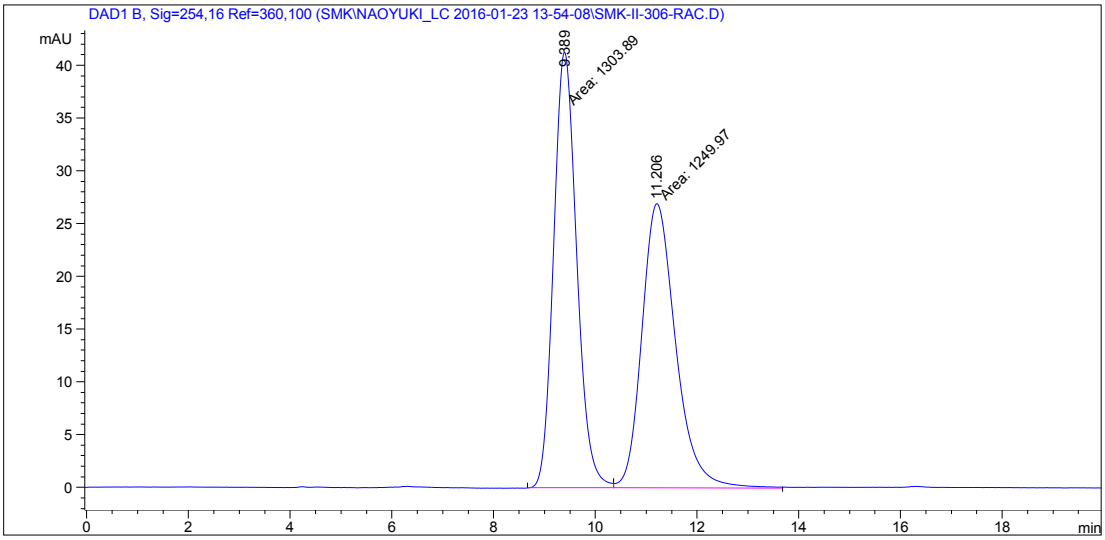
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.090	MM T	0.5819	174.39456	4.99514	6.4684
2	20.318	MM T	0.8576	2521.71191	49.00652	93.5316



8c

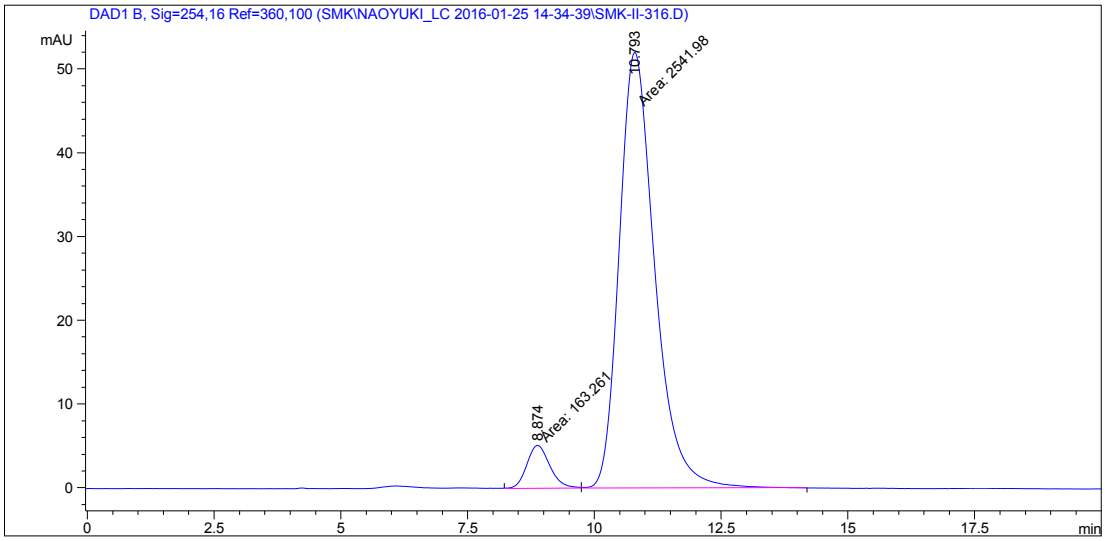
HPLC analysis (OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 88% ee: tR (minor) = 8.9 min, tR (major) = 10.8 min.

DL-8c

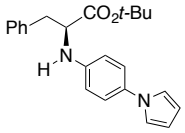


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.389	MF T	0.5263	1303.88879	41.29055	51.0556
2	11.206	FM T	0.7730	1249.97083	26.95138	48.9444

L-8c: 88% ee



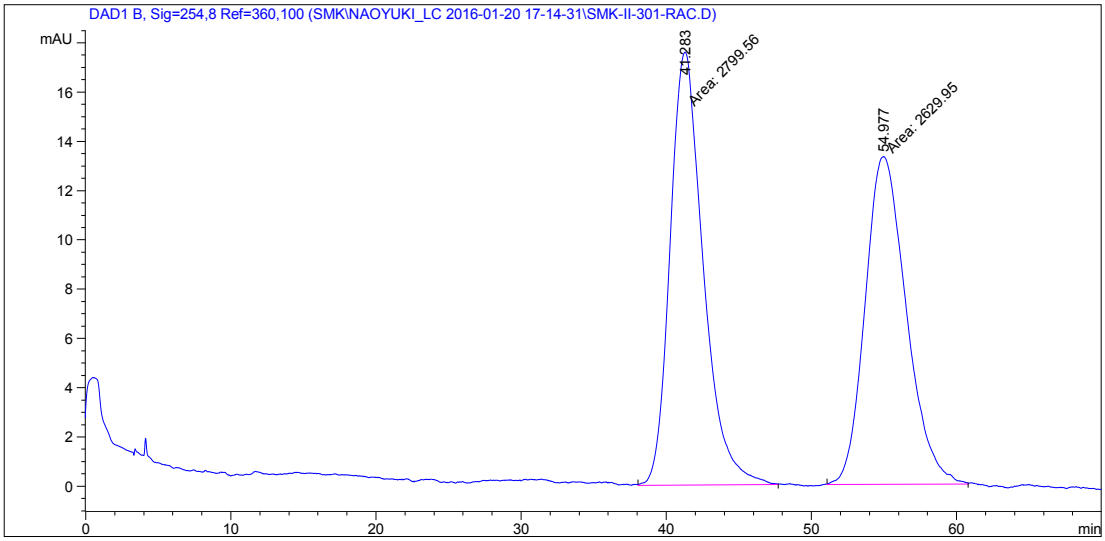
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.874	MF T	0.5294	163.26129	5.13948	6.0350
2	10.793	FM T	0.8144	2541.97607	52.01950	93.9650



8d

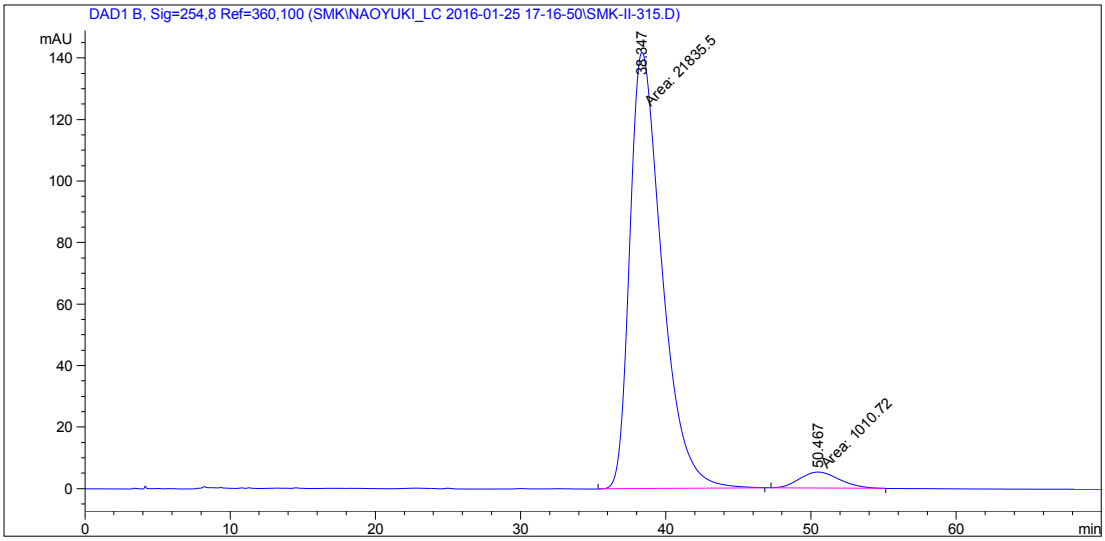
HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 91% ee: tR (major) = 38.3 min, tR (minor) = 50.5 min.

DL-8d

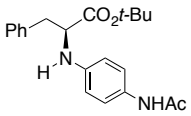


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.283	MM T	2.6534	2799.55811	17.58467	51.5619
2	54.977	MM T	3.2915	2629.95483	13.31691	48.4381

L-8d: 91% ee



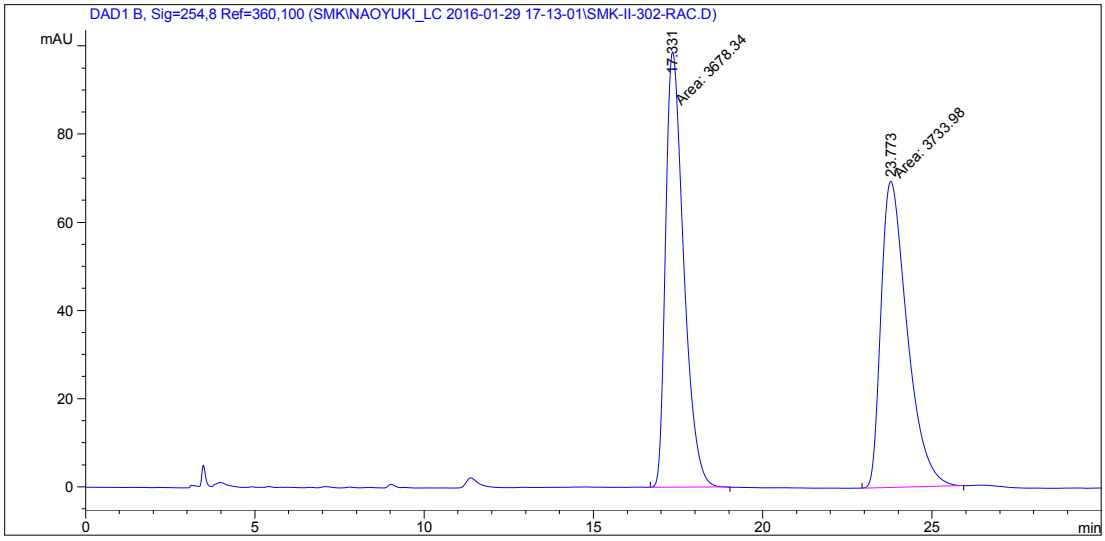
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	38.347	MM T	2.5646	2.18355e4	141.90234	95.5760
2	50.467	MM T	3.2115	1010.72095	5.24537	4.4240



8e

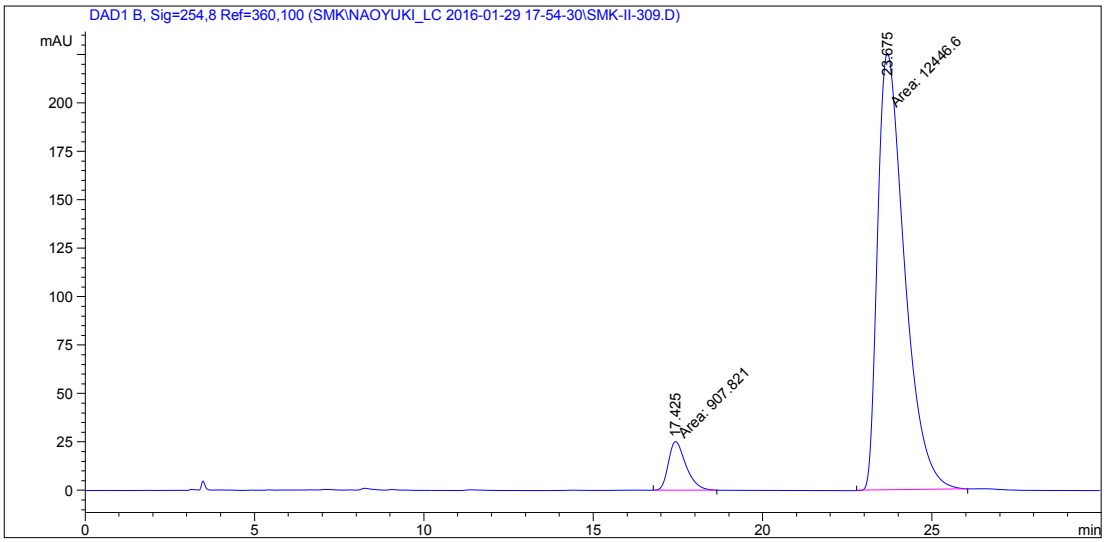
HPLC analysis (AD-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 86% ee: tR (minor) = 17.4 min, tR (major) = 23.7 min.

DL-8e

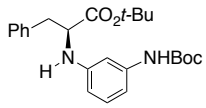


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.331	MM T	0.6205	3678.34009	98.80273	49.6247
2	23.773	MM T	0.8958	3733.97754	69.47446	50.3753

L-8e: 86% ee



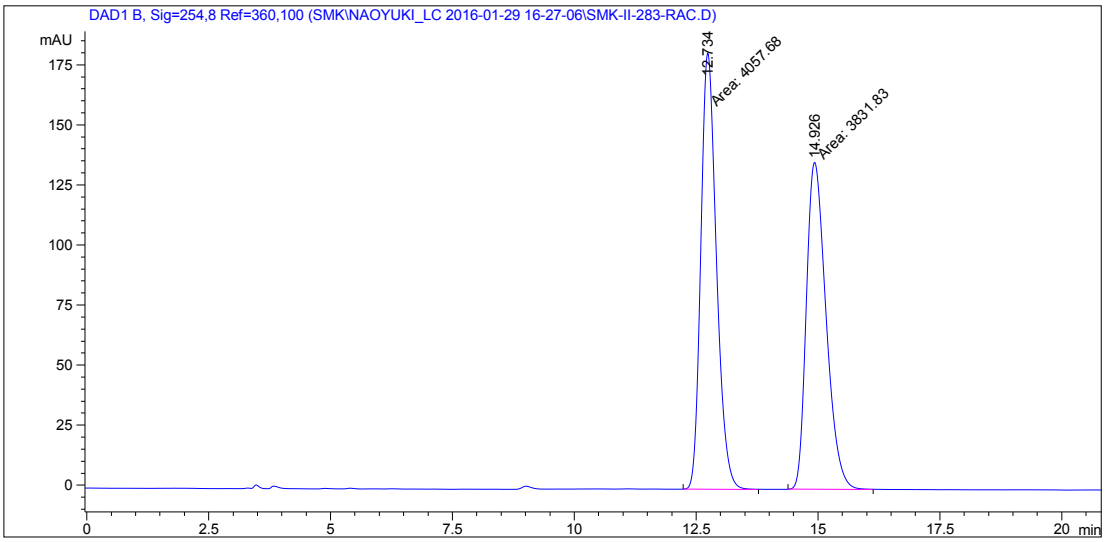
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.425	MM T	0.6017	907.82111	25.14801	6.7979
2	23.675	MM T	0.9202	1.24466e4	225.43025	93.2021



8f

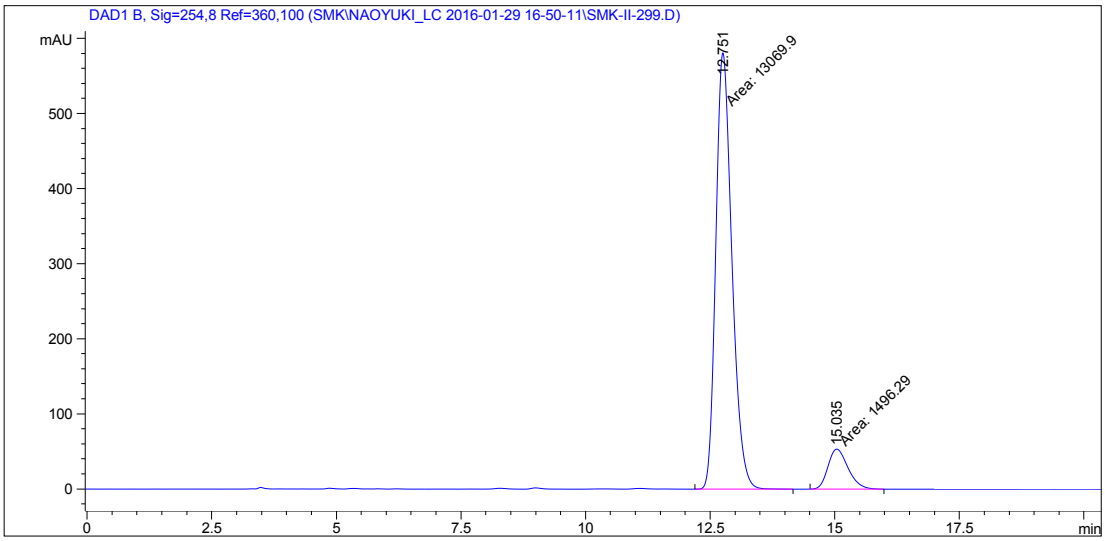
HPLC analysis (AD-H, 10% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 80% ee: tR (major) = 12.8 min, tR (minor) = 15.0 min.

DL-8f

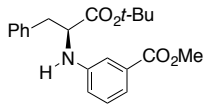


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.734	MM T	0.3722	4057.68433	181.69006	51.4314
2	14.926	MM T	0.4689	3831.82544	136.19818	48.5686

L-8f: 80% ee



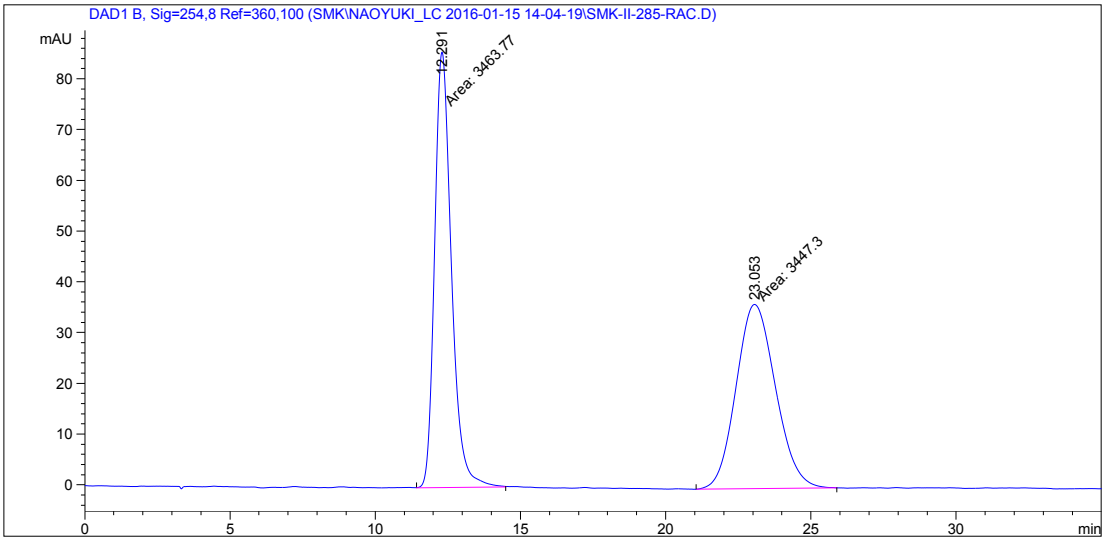
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.751	MM T	0.3749	1.30699e4	580.98706	89.7276
2	15.035	MM T	0.4674	1496.29407	53.35979	10.2724



8g

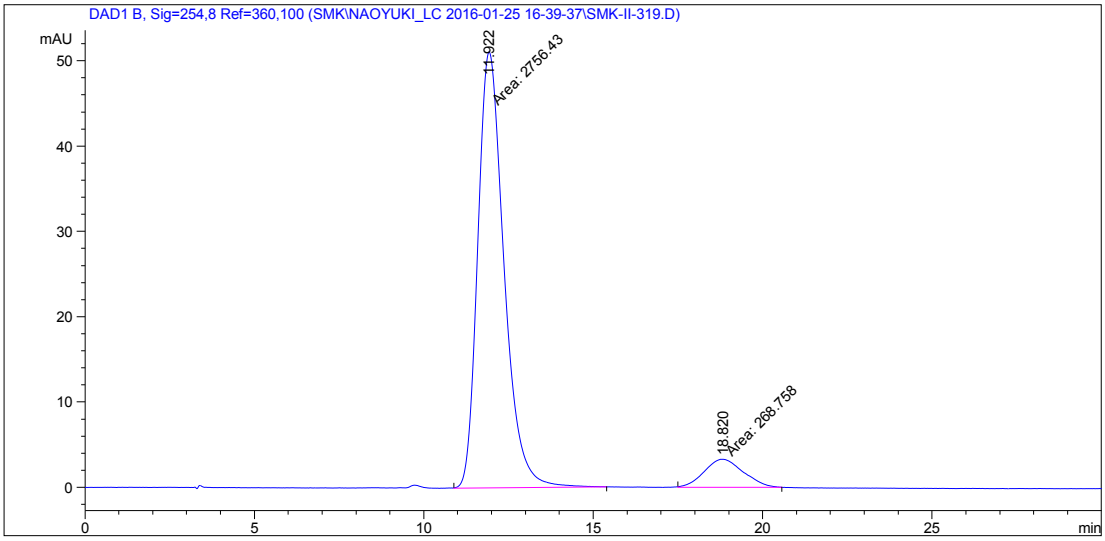
HPLC analysis (OJ-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 82% ee: tR (major) = 11.9 min, tR (minor) = 18.8 min.

DL-8g

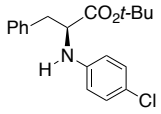


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.291	MM T	0.6723	3463.77002	85.86269	50.1192
2	23.053	MM T	1.5800	3447.29565	36.36466	49.8808

L-8g: 82% ee



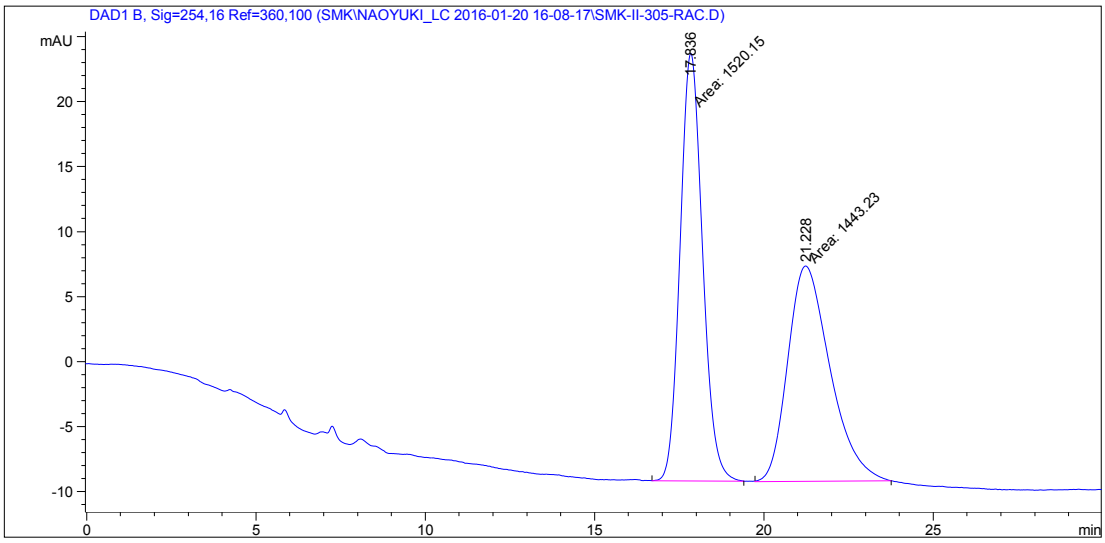
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.922	MM T	0.8989	2756.42700	51.10752	91.1160
2	18.820	MM T	1.3519	268.75815	3.31338	8.8840



8h

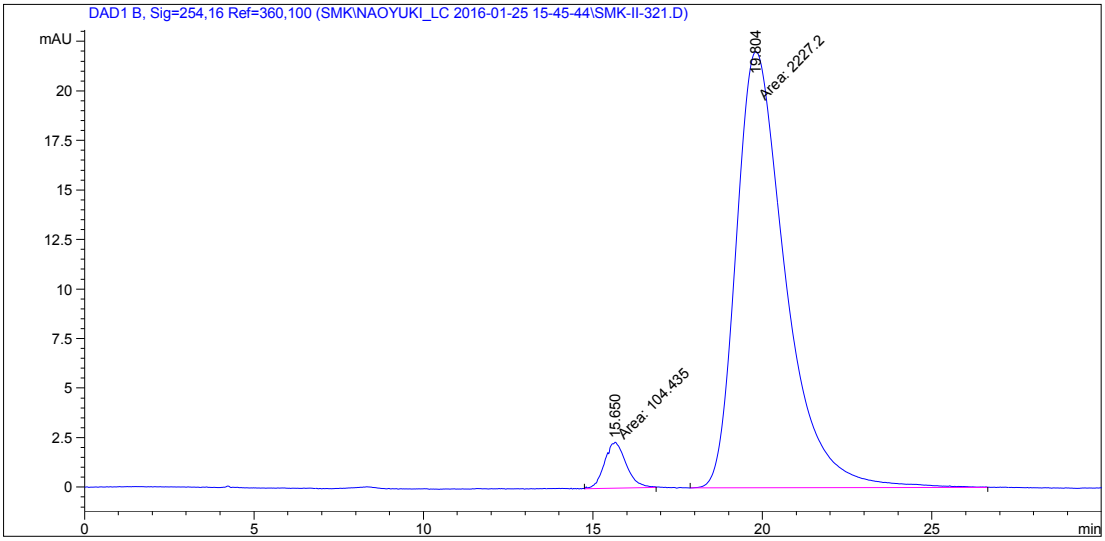
HPLC analysis (OJ-H, 5% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 91% ee: tR (minor) = 15.7 min, tR (major) = 19.8 min.

DL-8h

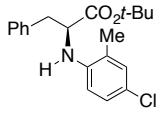


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.836	MM T	0.7699	1520.15405	32.90823	51.2979
2	21.228	MM T	1.4503	1443.23242	16.58567	48.7021

L-8h: 91% ee



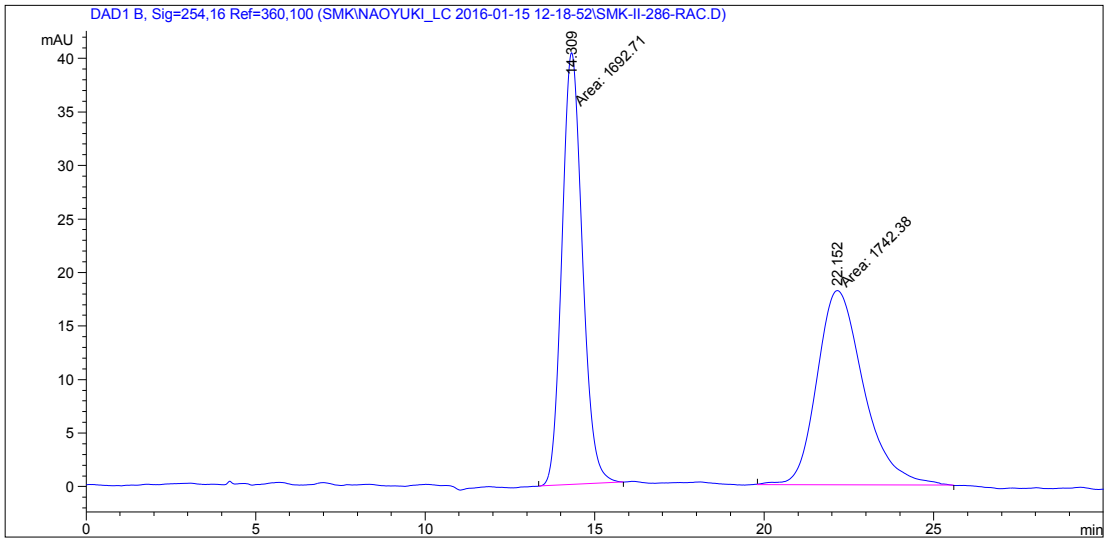
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.650	MM T	0.7462	104.43485	2.33263	4.4790
2	19.804	MM T	1.6858	2227.20020	22.01986	95.5210



8i

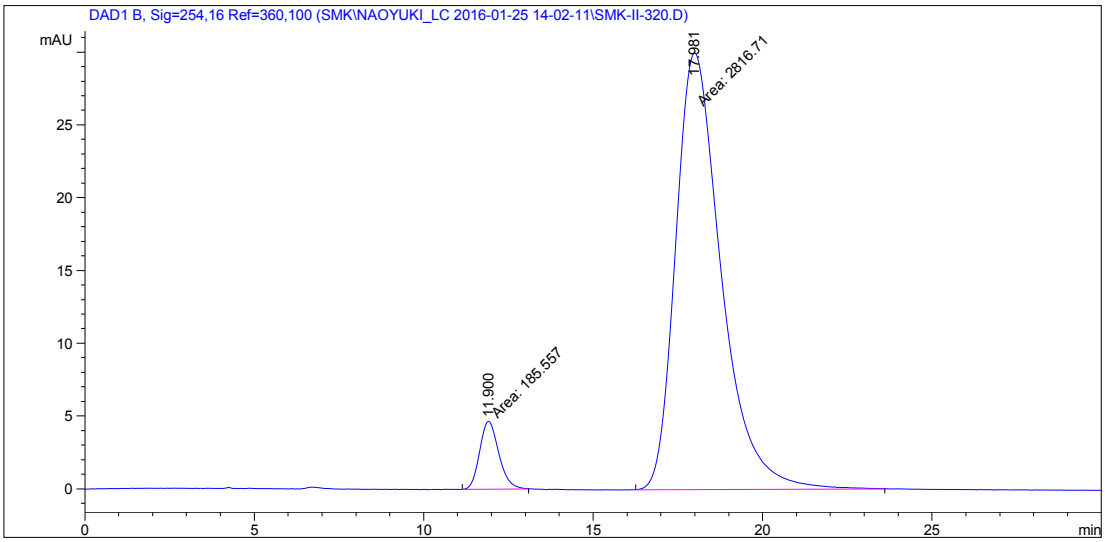
HPLC analysis (OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 88% ee: tR (minor) = 11.9 min, tR (major) = 18.0 min.

DL-8i

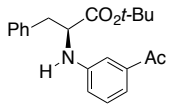


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.309	MM T	0.6993	1692.70593	40.34129	49.2769
2	22.152	MM T	1.5991	1742.38257	18.16058	50.7231

L-8i: 88%



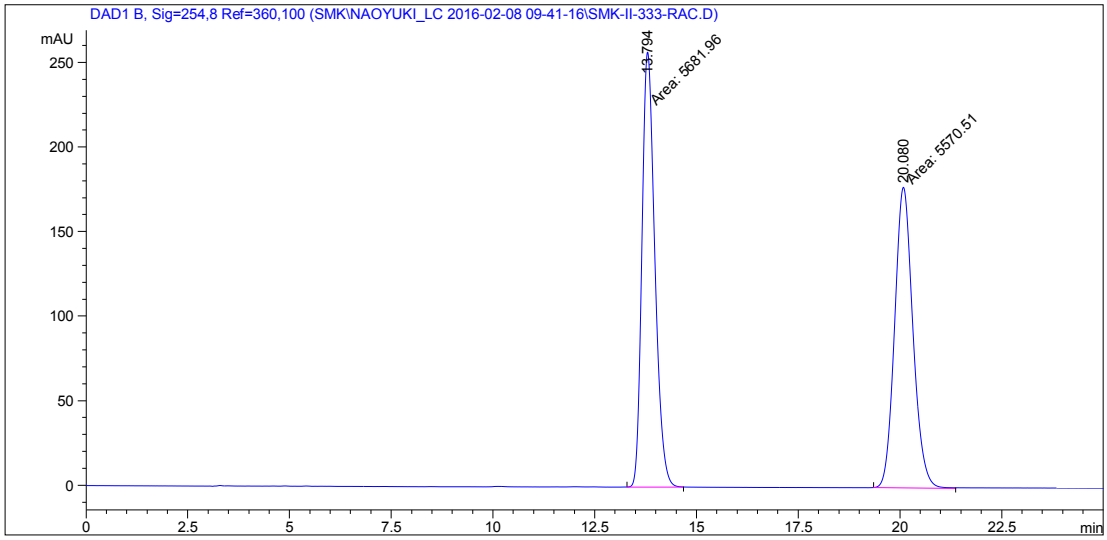
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.900	MM T	0.6610	185.55652	4.67876	6.1805
2	17.981	MM T	1.5645	2816.71094	30.00627	93.8195



8j

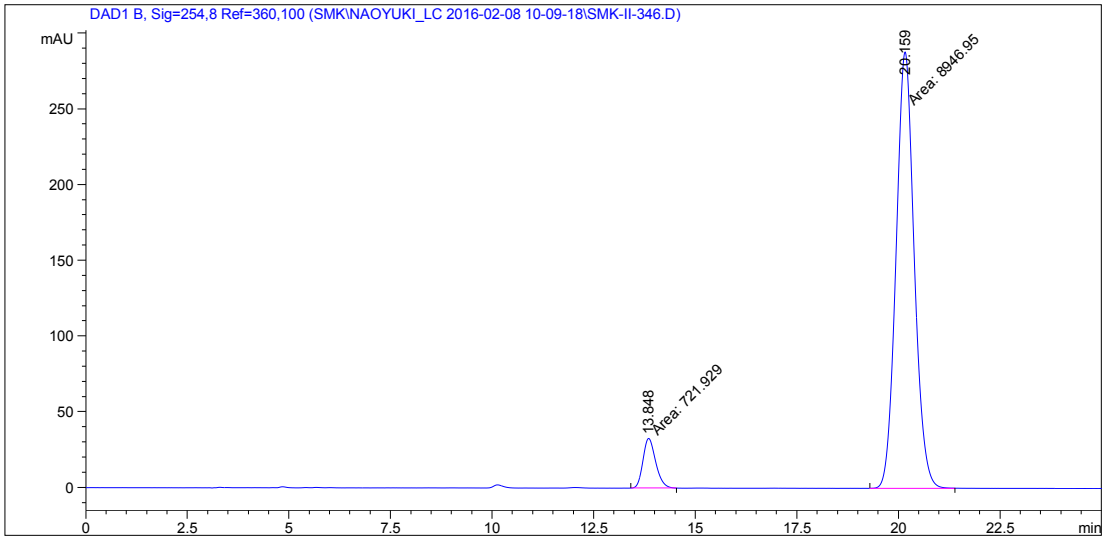
HPLC analysis (AD-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 85% ee: tR (minor) = 13.9 min, tR (major) = 20.2 min.

DL-8j

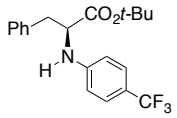


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.794	MM T	0.3679	5681.96191	257.38715	50.4952
2	20.080	MM T	0.5218	5570.51074	177.92102	49.5048

L-8j: 85% ee



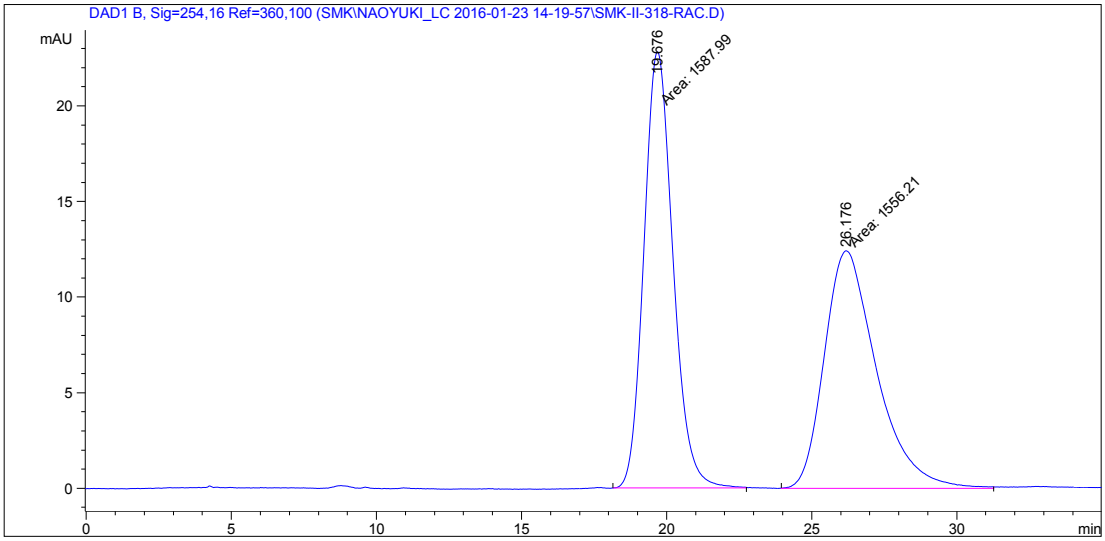
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.848	MM T	0.3658	721.92902	32.89493	7.4665
2	20.159	MM T	0.5174	8946.94922	288.20944	92.5335



8k

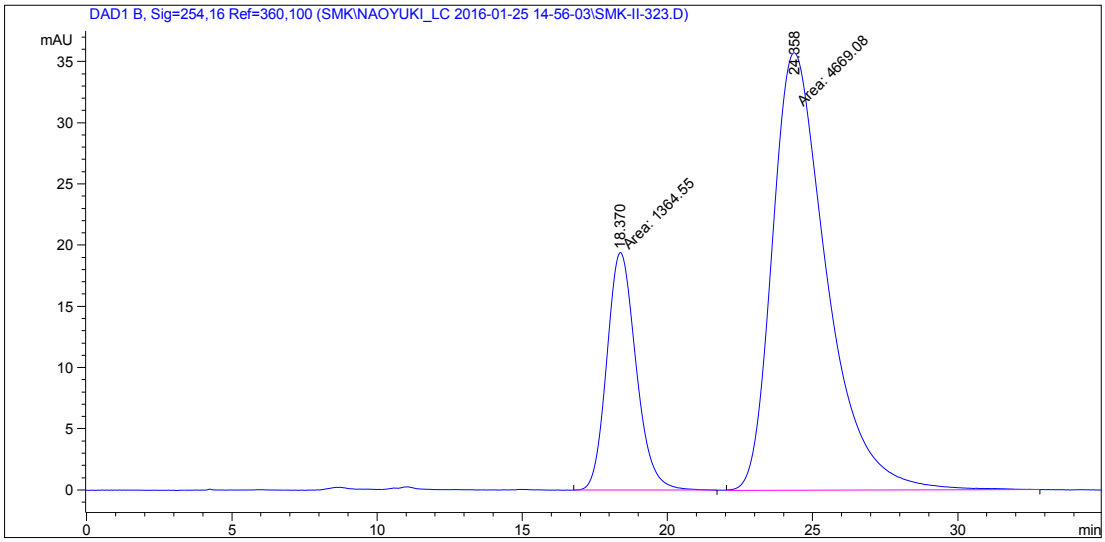
HPLC analysis (OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 55% ee: tR (minor) = 18.4 min, tR (major) = 24.4 min.

DL-8k

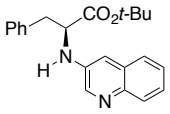


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.676	MM T	1.1603	1587.98938	22.81080	50.5053
2	26.176	MM T	2.1387	1556.21118	12.43672	49.4947

L-8k: 55% ee



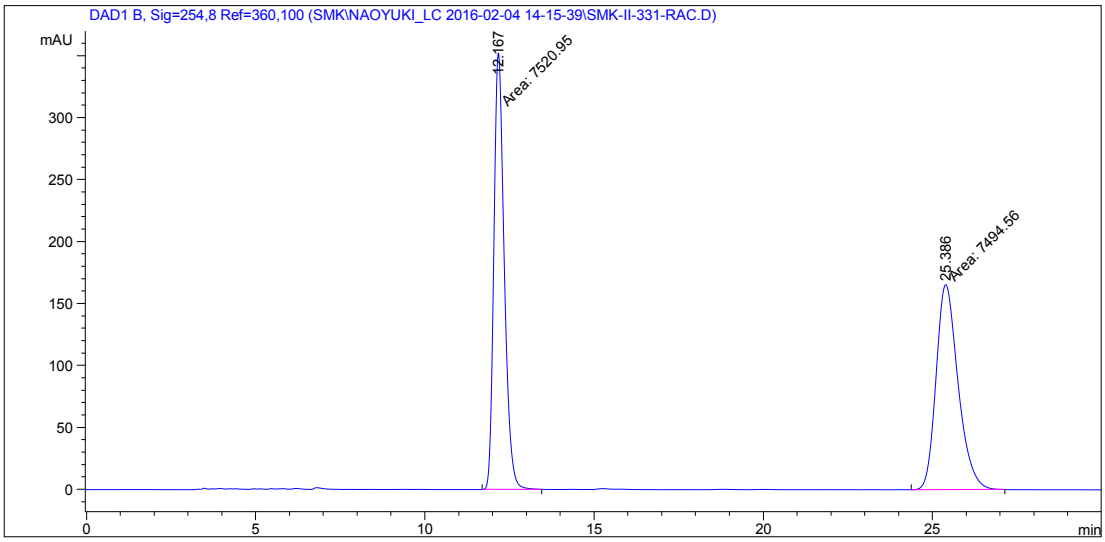
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.370	MM T	1.1711	1364.54626	19.42023	22.6157
2	24.358	MM T	2.1762	4669.08252	35.75946	77.3843



8l

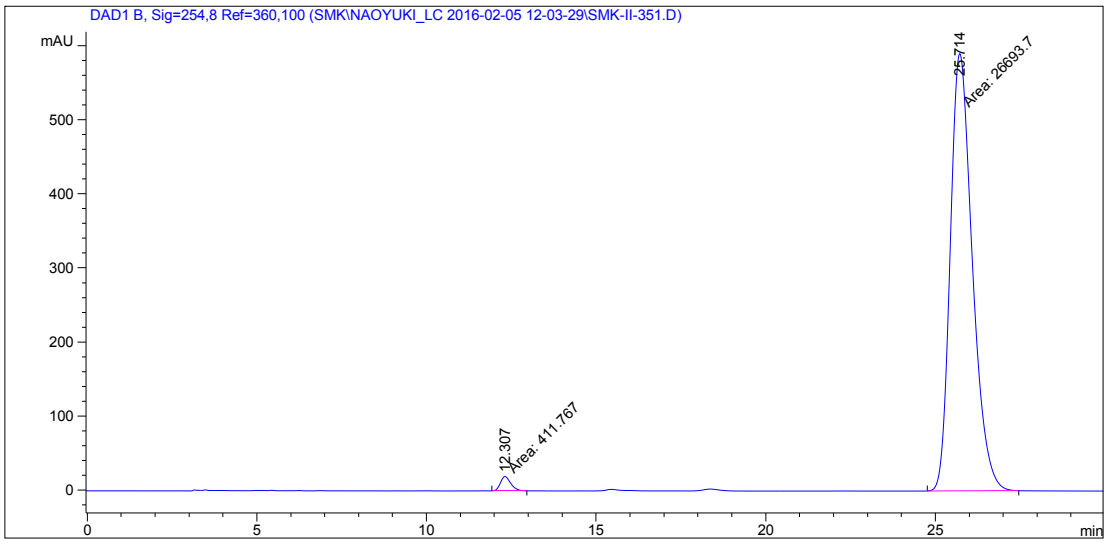
HPLC analysis (AD-H, 10% IPA–hexanes, 1.0 mL/min, 254 nm) indicated 97% ee: tR (minor) = 12.3 min, tR (major) = 25.7 min.

DL-8l



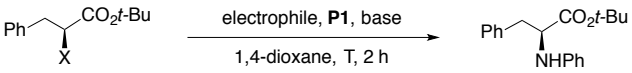
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.167	MM T	0.3558	7520.95361	352.33743	50.0879
2	25.386	MM T	0.7545	7494.55811	165.54926	49.9121

L-8l: 97% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.307	MM T	0.3542	411.76654	19.37539	1.5191
2	25.714	MM T	0.7540	2.66937e4	590.05597	98.4809

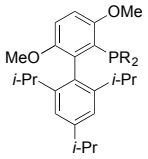
Table S1. Summary of initial *N*-arylation experiments.



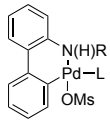
6a

X = NH_2 L-Phe-O*t*-Bu (**5a**)
X = $NH_3^+Cl^-$ L-Phe-O*t*Bu•HCl (**5a•HCl**)

entry	amino acid ester	electrophile	base	T	yield[e]	ee[f]
1[a]	**5a•HCl**	PhBr	NaO*t*-Bu	rt	99%	0%
2[a]	**5a•HCl**	PhBr	NaOPh	70 °C	16%	41%
3[a]	**5a•HCl**	PhBr	Cs_2CO_3	70 °C	0%	–
4[b]	**5a**	PhBr	NaO*t*-Bu	rt	29%	0%
5[b]	**5a**	PhBr	NaOPh	70 °C	9%	72%
6[b]	**5a**	PhBr	Cs_2CO_3	70 °C	19%	73%
7[c]	**5a**	PhCl	Cs_2CO_3	70 °C	12%	78%
8[d]	**5a**	PhOTf	Cs_2CO_3	70 °C	61%	84%

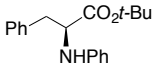


R = *t*-Bu *t*-BuBrettPhos (**L1**)
R = Cy BrettPhos (**L2**)



R = H, L = L1 *t*-BuBrettPhos Pd G3 (**P1**)
R = Me, L = L2 Brett Phos Pd G4 (**P2**)
R = Me, L = L1 *t*-BuBrettPhos Pd G4 (**P3**)

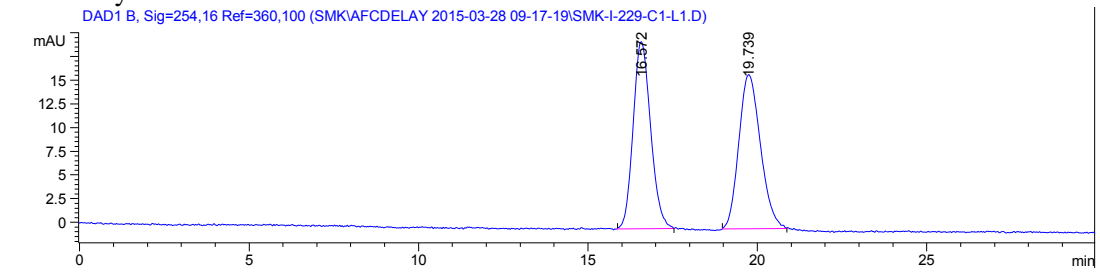
[a] Reaction Conditions: L-Phe-O*t*-Bu•HCl (**5a•HCl**, 1.2 equiv), base (2.4 equiv), bromobenzene (1 equiv), **P1** (1 mol%). [b] Reaction Conditions: L-Phe-O*t*-Bu (**5a**, 1.2 equiv), base (1.2 equiv), bromobenzene (1 equiv), **P1** (1 mol%). [c] Reaction Conditions: L-Phe-O*t*-Bu (**5a**, 1.2 equiv), base (1.2 equiv), chlorobenzene (1 equiv), **P1** (1 mol%). [d] Reaction Conditions: L-Phe-O*t*-Bu (**5a**, 1.2 equiv), base (1.2 equiv), phenyl trifluoromethanesulfonate (1 equiv), **P1** (1 mol%). [e] Isolated yields. [f] Enantiomeric excess (ee) was determined by HPLC analysis using chiral stationary phases.



6a

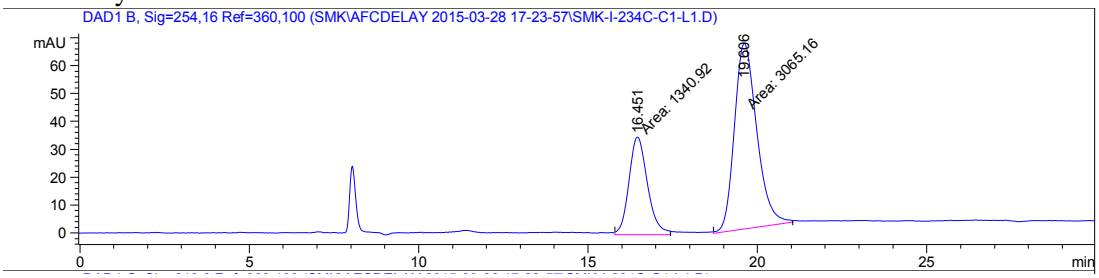
HPLC analysis conditions: OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm

L-6a entry 1: 0% ee



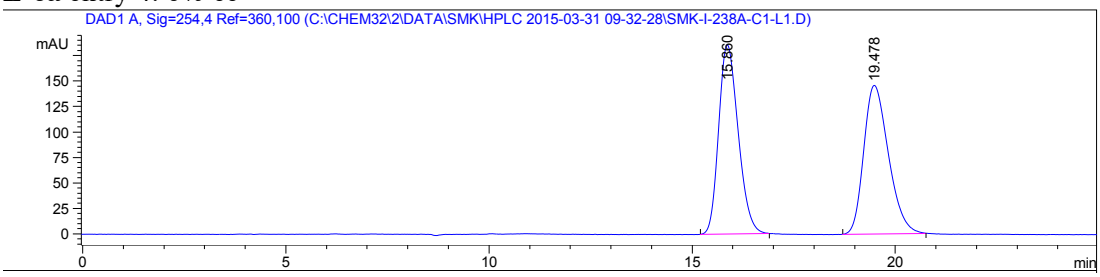
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.572	BB	0.4774	708.99554	19.72478	49.4522
2	19.739	BB	0.5335	724.70392	16.27460	50.5478

L-6a entry 2: 41% ee



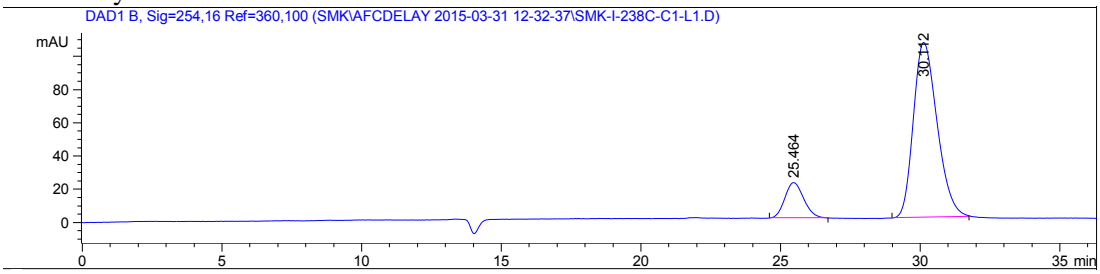
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.451	MM T	0.6377	1340.92188	35.04696	30.4334
2	19.606	MM T	0.7667	3065.15771	66.63328	69.5666

L-6a entry 4: 0% ee



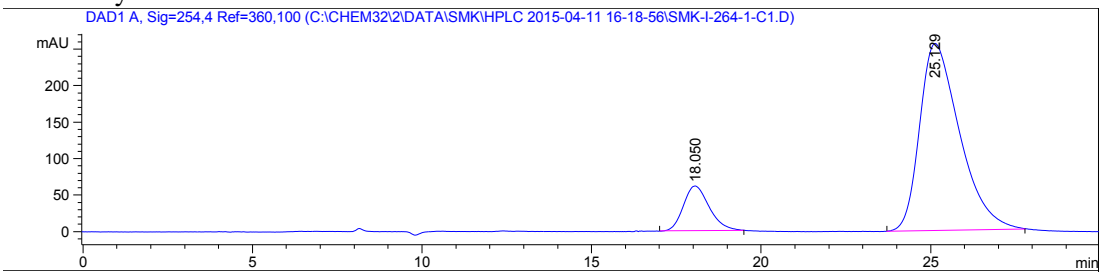
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.860	BB	0.5119	6208.93066	185.78294	50.1237
2	19.478	BB	0.6480	6178.27881	145.90656	49.8763

L-**6a** entry 5: 72% ee



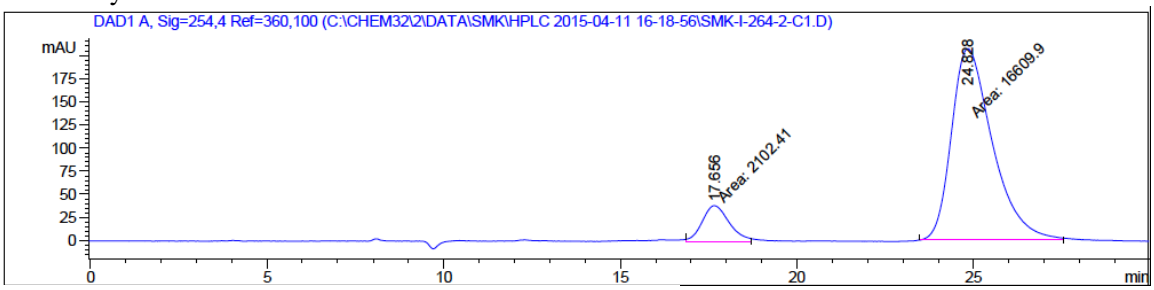
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.464	BB	0.5745	1010.54022	21.33744	13.9433
2	30.112	BB	0.8488	6236.94043	105.33337	86.0567

L-6a entry 6: 73% ee



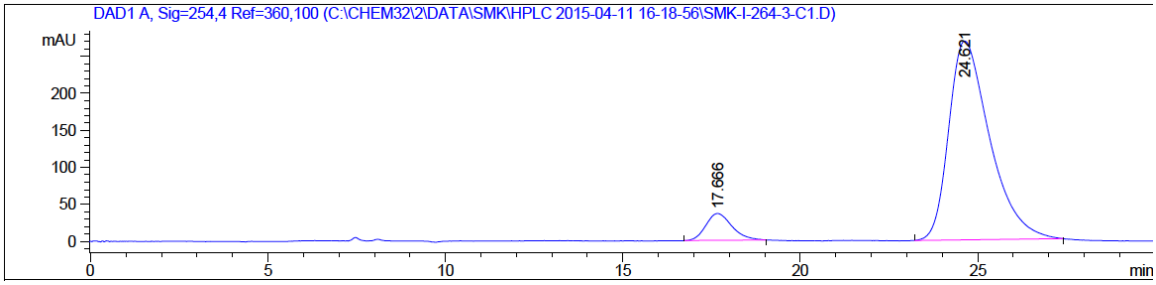
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.050	BB	0.6521	3300.34644	61.69863	13.5605
2	25.129	BB	1.0209	2.10375e4	256.48758	86.4395

L-6a entry 7: 78% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.656	MM	0.8952	2102.41284	39.14093	11.2355
2	24.828	MM	1.3405	1.66099e4	206.50815	88.7645

L-6a entry 8: 84% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.666	BB	0.6531	1867.96472	36.37347	7.9421
2	24.621	BB	1.0675	2.16517e4	268.86987	92.0579

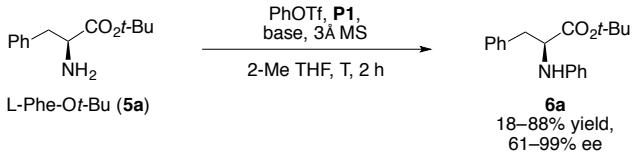
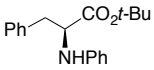


Table S3. Subset of reactions from subsequent DOE analysis.

					2 mol% precatalyst		5 mol% precatalyst	
entry	**T**	**base**	**equiv base (to 5a)**	**3 Å MS**	**yield**	**ee**	**yield**	**ee**
1	50 °C	Cs_2CO_3	1	0 mg	64%	91%	89%	94%
2	50 °C	Cs_2CO_3	1	50 mg	51%	95%	80%	92%
3	50 °C	Cs_2CO_3	3	0 mg	69%	89%	93%	91%
4	50 °C	Cs_2CO_3	3	50 mg	69%	92%	95%	94%

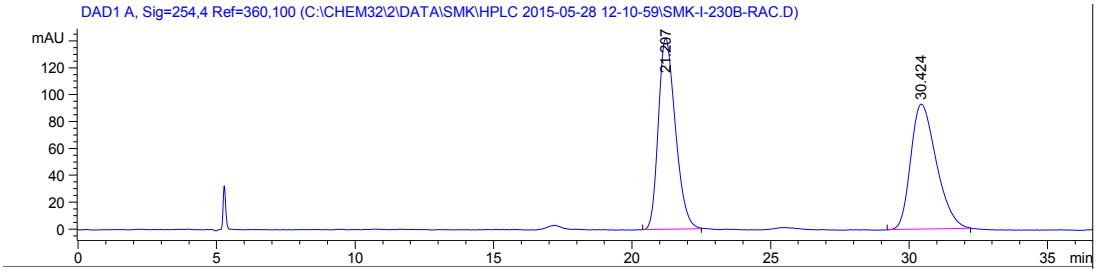
Yellow indicates optimized reaction conditions.



6a

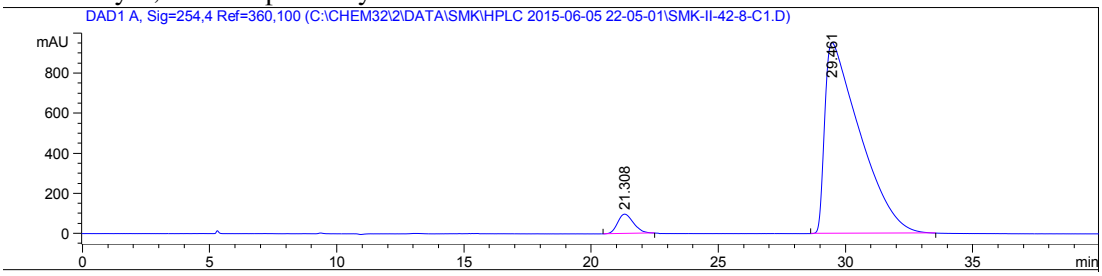
HPLC analysis conditions: OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm

DL-6a



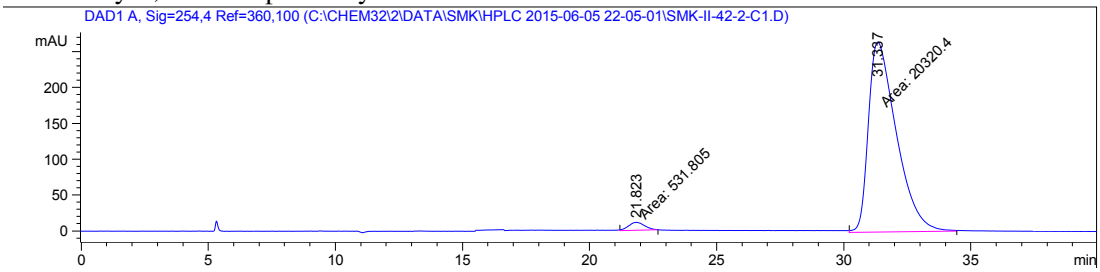
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.207	BB	0.6281	6097.20557	142.23837	50.3170
2	30.424	VB	0.8056	6020.39209	93.20570	49.6830

L-6a entry 1, 2 mol% precatalyst: 91% ee



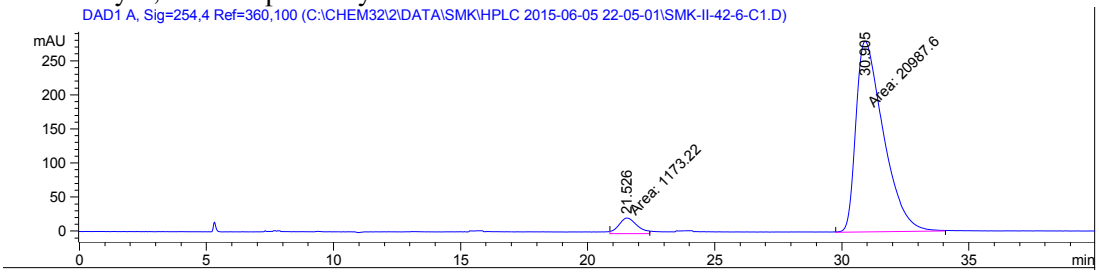
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.308	BB	0.6320	4237.56250	96.93819	4.4197
2	29.461	BB	1.2386	9.16420e4	952.37134	95.5803

L-6a entry 2, 2 mol% precatalyst: 95% ee



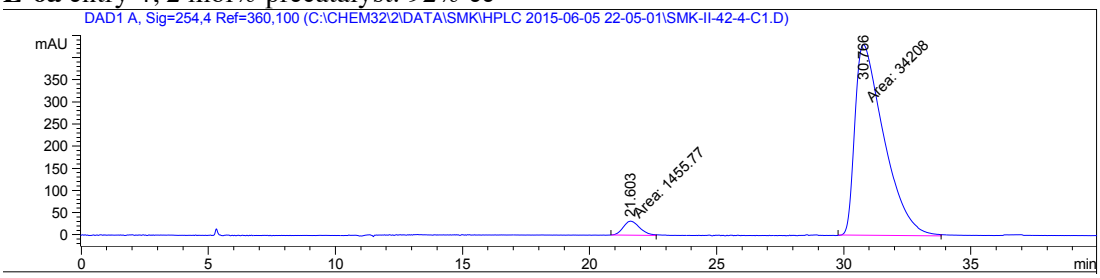
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.823	MM T	0.7247	531.80450	11.60152	2.5504
2	31.337	MM	1.2751	2.03204e4	265.60229	97.4496

L-6a entry 3, 2 mol% precatalyst: 89% ee

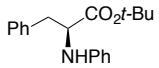


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.526	MM T	0.8447	1173.21558	23.14777	5.2941
2	30.905	MM T	1.2510	2.09876e4	279.60117	94.7059

L-6a entry 4, 2 mol% precatalyst: 92% ee



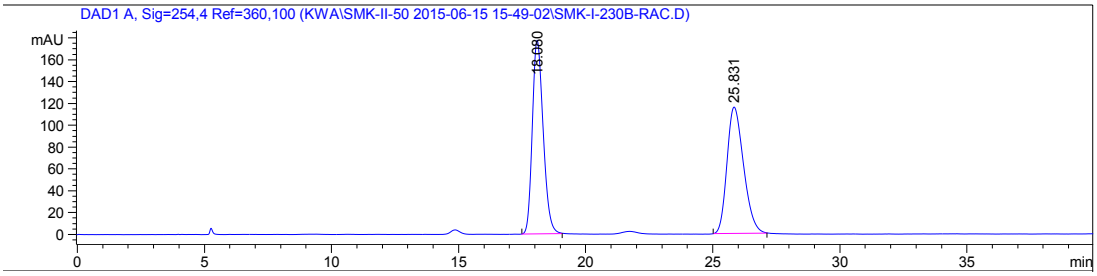
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.603	MM T	0.7598	1455.76648	31.93314	4.0819
2	30.766	MM T	1.3242	3.42080e4	430.54477	95.9181



6a

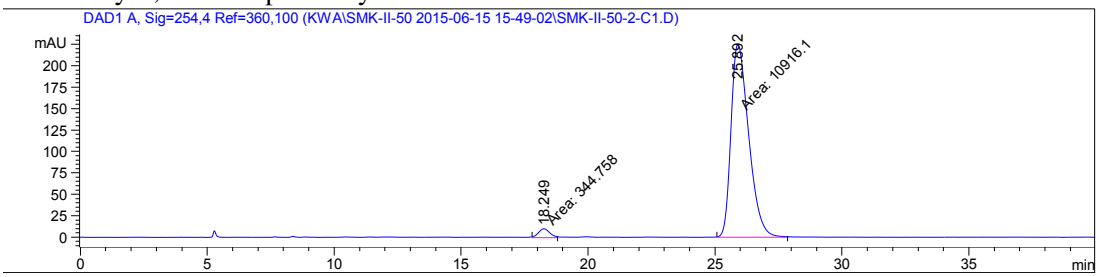
HPLC analysis conditions: OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm

DL-6a



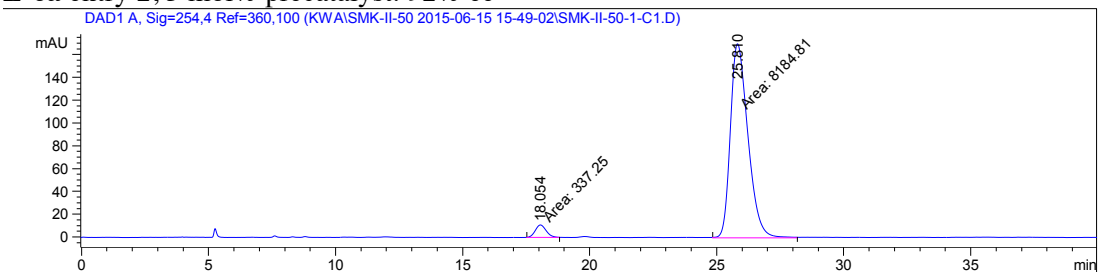
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.080	BB	0.4583	5263.57080	177.31154	49.9466
2	25.831	BB	0.7086	5274.83594	115.97603	50.0534

L-6a entry 1, 5 mol% precatalyst: 94% ee



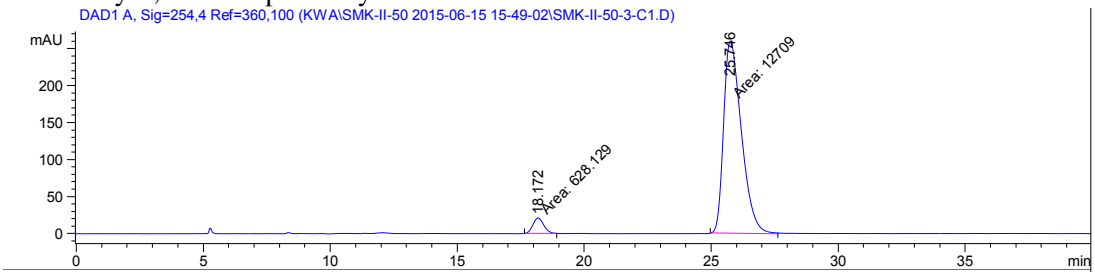
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.249	MM T	0.5363	344.75839	10.71373	3.0616
2	25.892	MM T	0.8067	1.09161e4	225.54106	96.9384

L-6a entry 2, 5 mol% precatalyst: 92% ee



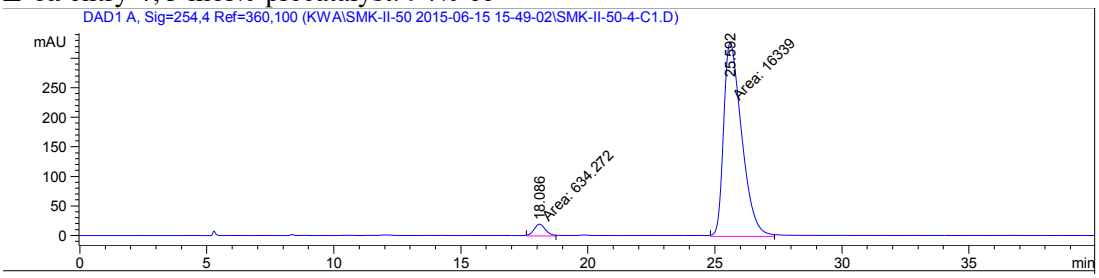
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.054	MM T	0.5078	337.25040	11.06958	3.9574
2	25.810	MM	0.8014	8184.80518	170.22174	96.0426

L-6a entry 3, 5 mol% precatalyst: 91% ee



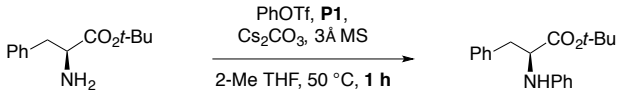
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.172	MM T	0.4976	628.12885	21.03867	4.7096
2	25.746	MM T	0.8142	1.27090e4	260.16263	95.2904

L-6a entry 4, 5 mol% precatalyst: 94% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.086	MM	0.5300	634.27228	19.94557	3.7369
2	25.592	MM T	0.8291	1.63390e4	328.45538	96.2631

A.

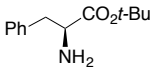


L-Phe-O*t*-Bu (**5a**) **6a**

	ee before reaction	ee after reaction[a]
5a	99%	81%
6a	–	97%

[a] Enantiomeric excess (ee) was determined directly from the crude reaction mixture by HPLC analysis using chiral stationary phases.

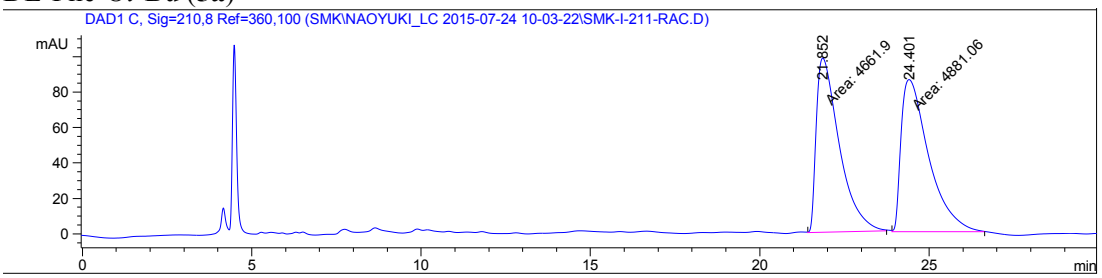
Scheme 3. A. Experiment determining the enantiomeric excess before and after the reaction.



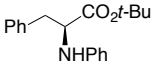
L-Phe-O*t*-Bu (**5a**)

HPLC analysis conditions: AD-H, 1% IPA–hexanes, 0.8 mL/min, 210 nm

DL-Phe-O*t*-Bu (**5a**)



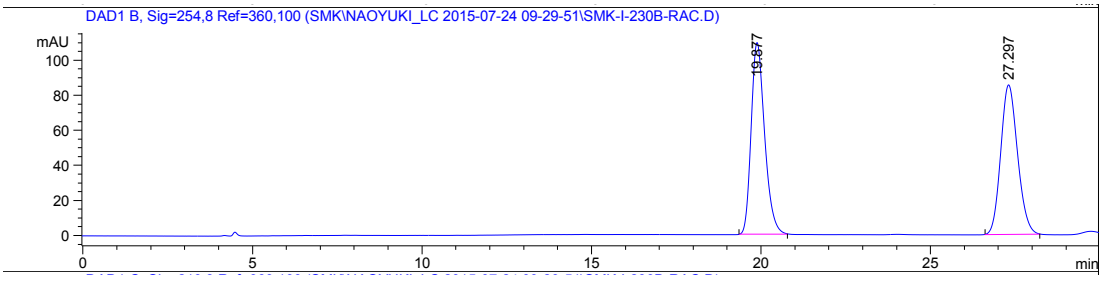
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.852	MM T	0.7892	4661.89600	98.45503	48.8517
2	24.401	MM T	0.9467	4881.06299	85.93376	51.1483



6a

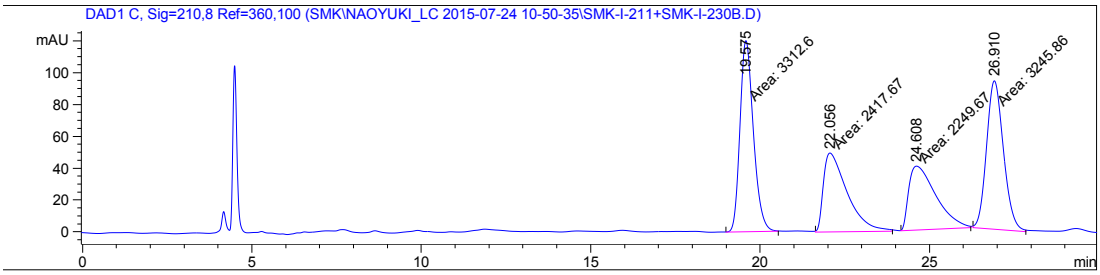
HPLC analysis conditions: AD-H, 1% IPA–hexanes, 0.8 mL/min, 254 nm

DL-6a



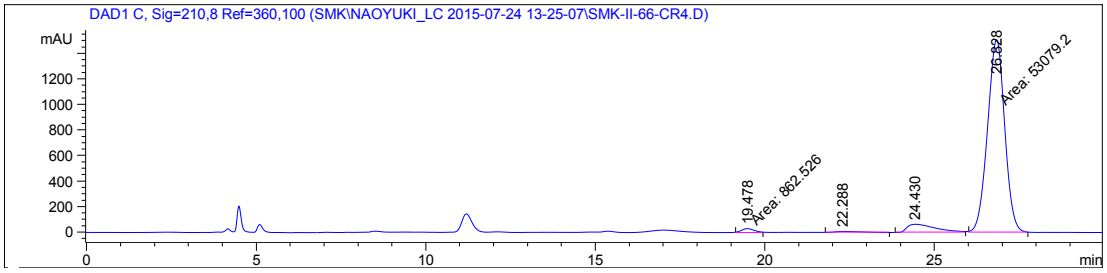
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.877	BB	0.4244	3024.33228	109.42875	50.6032
2	27.297	BB	0.5313	2952.23071	85.39536	49.3968

co-injection of **DL-6a** + DL-Phe-O*t*-Bu (**5a**)

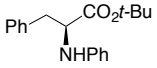


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.575	MM T	0.4594	3312.59814	120.16578	29.5088
2	22.056	MM T	0.8120	2417.67017	49.62156	21.5367
3	24.608	MM T	0.9303	2249.66992	40.30579	20.0402
4	26.910	MM T	0.5796	3245.85571	93.33982	28.9143

HPLC analysis of crude reaction mixture: L-Phe-O-*t*-Bu (**5a**), 81% ee; **L-6a**, 97% ee

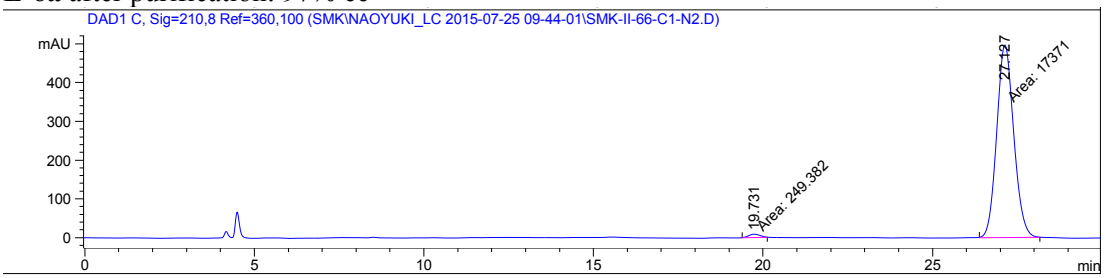


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.478	MM T	0.4527	862.52649	31.75817	1.4838
2	22.288	BB	0.6972	398.70175	7.78851	0.6859
3	24.430	BV	0.9010	3787.77734	63.95182	6.5162
4	26.828	MM T	0.5866	5.30792e4	1508.10205	91.3140



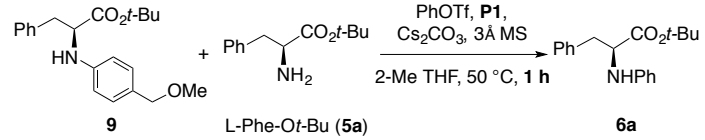
6a

L-6a after purification: 97% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.731	MM T	0.4273	249.38188	9.72712	1.4153
2	27.127	MM T	0.5824	1.73710e4	497.09439	98.5847

B.

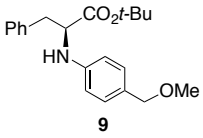


9 L-Phe-O*t*-Bu (**5a**) **6a**

	ee before reaction	ee after reaction[a]
9	93%	93%
5a	99%	81%
6a	–	93%

[a] Enantiomeric excess (ee) was determined after purification by silica gel chromatography.

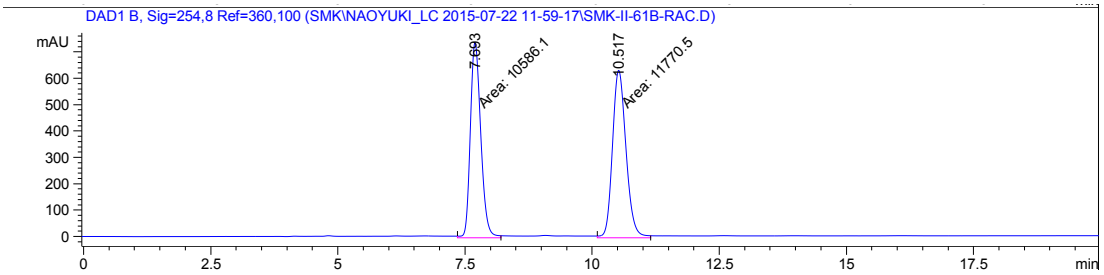
Scheme 3. B. Experiment to test for product racemization with exogenous and different product added.



9

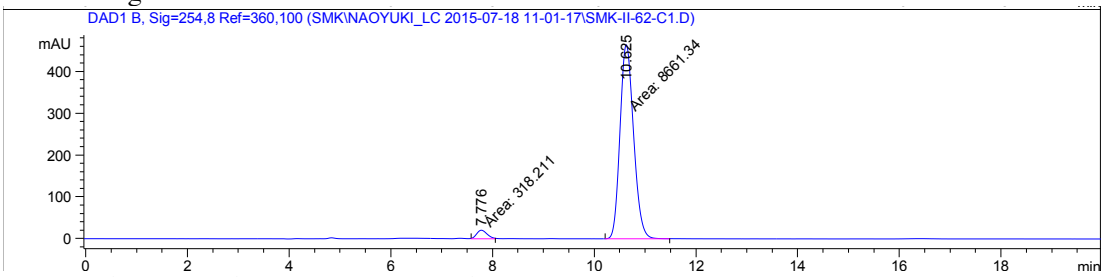
HPLC analysis (OD-H, 10% IPA–hexanes, 0.8 mL/min, 254 nm) indicated 93% ee: tR (minor) = 7.8 min, tR (major) = 10.6 min.

DL-9



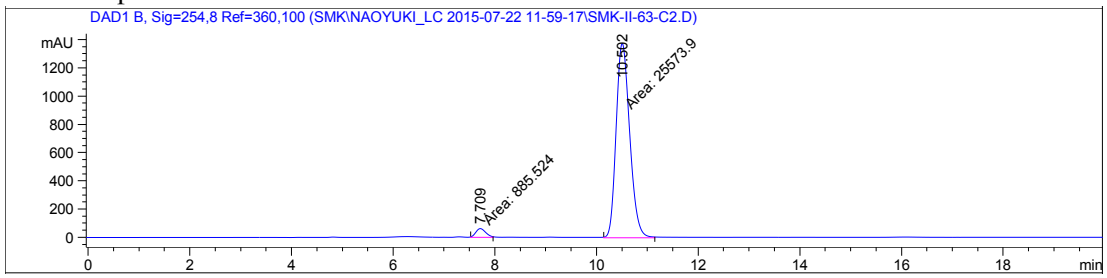
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.693	MM T	0.2382	1.05861e4	740.77106	47.3510
2	10.517	MM T	0.3089	1.17705e4	635.03198	52.6490

L-9 starting material: 93% ee

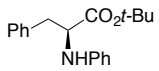


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.776	MM T	0.2477	318.21130	21.41052	3.5437
2	10.625	MM T	0.3104	8661.33594	465.04422	96.4563

L-9 after purification: 93% ee



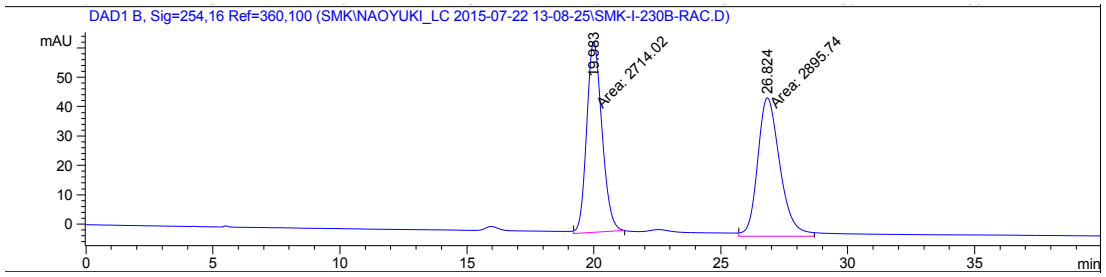
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.709	MM T	0.2325	885.52423	63.46655	3.3467
2	10.502	MM T	0.3095	2.55739e4	1377.27856	96.6533



6a

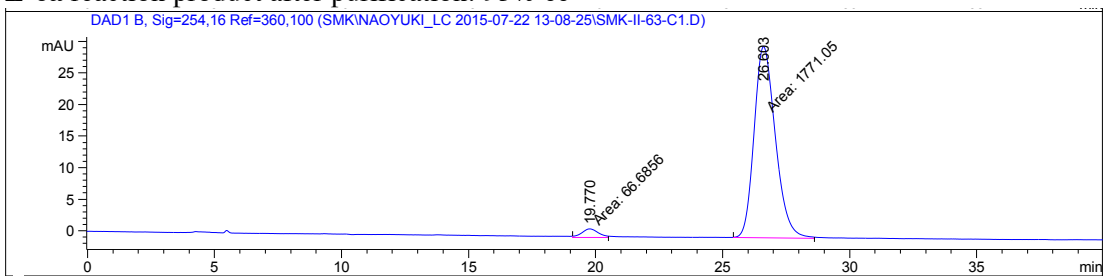
HPLC analysis conditions: AD-H, 1% IPA–hexanes, 0.8 mL/min, 254 nm, tR (minor) = 19.8 min, tR (major) = 26.6 min.

DL-6a

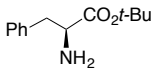


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.983	MM T	0.6977	2714.02490	64.83457	48.3804
2	26.824	MM T	1.0221	2895.74146	47.21736	51.6196

L-6a reaction product after purification: 93% ee



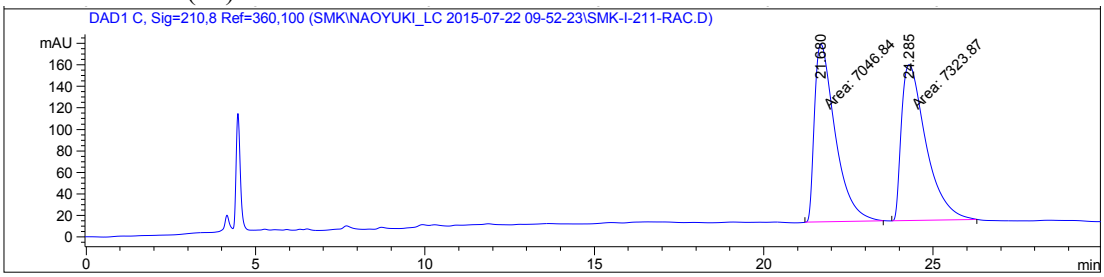
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.770	MM T	0.7872	66.68557	1.41196	3.6287
2	26.603	MM T	0.9742	1771.04736	30.29883	96.3713



L-Phe-O*t*-Bu (**5a**)

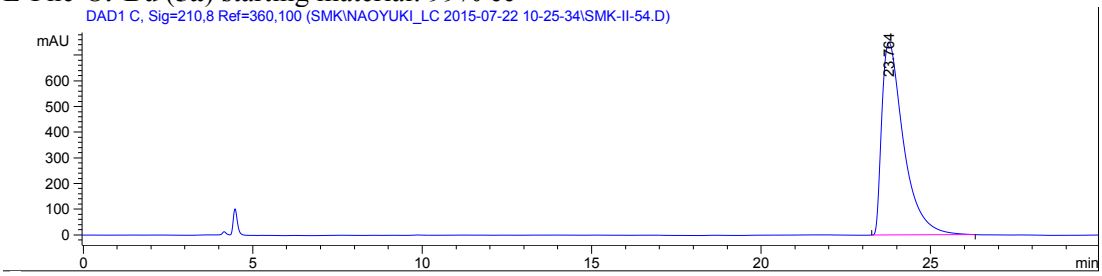
HPLC analysis conditions: AD-H, 1% IPA–hexanes, 0.8 mL/min, 254 nm, tR (minor) = 21.8 min, tR (major) = 23.8 min

DL-Phe-O*t*-Bu (**5a**)



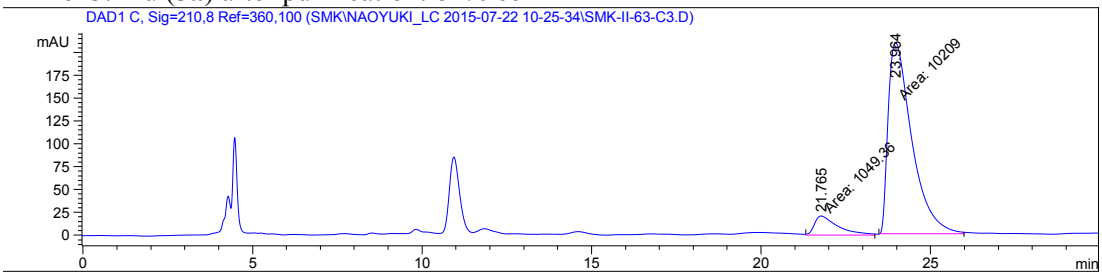
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.680	MM T	0.7096	7046.84131	165.50804	49.0361
2	24.285	MM T	0.8412	7323.87207	145.11440	50.9639

L-Phe-O*t*-Bu (**5a**) starting material: 99% ee

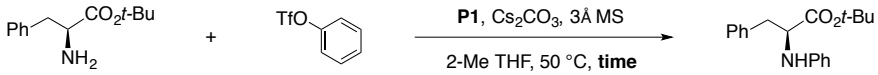


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.764	BB	0.6747	3.35271e4	751.23444	100.0000

L-Phe-O*t*-Bu (**5a**) after purification: 81% ee



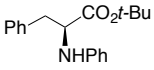
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.765	MM T	0.8216	1049.36023	21.28705	9.3207
2	23.964	MM T	0.8131	1.02090e4	209.26880	90.6793



L-Phe-O*t*-Bu (**5a**) **6a**

Table S5. Evaluation of yield and ee over reaction time.

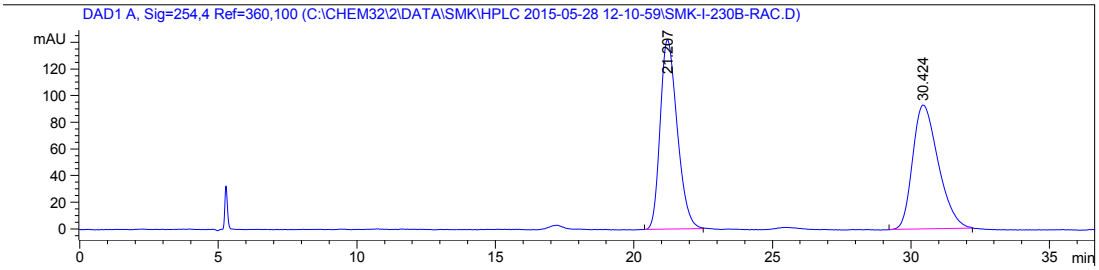
entry	time	yield	ee
1	30 min	67%	98%
2	1 h	73%	97%
3	1.5 h	90%	95%
4	2 h	92%	95%
5	4 h	96%	93%
6	16 h	99%	88%
7	10 d	91%	10%



6a

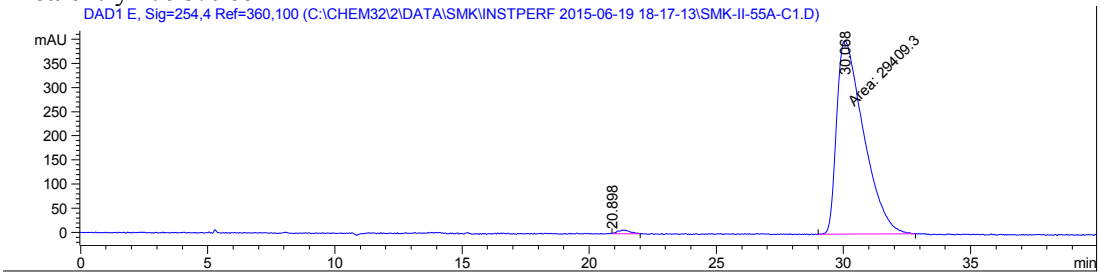
HPLC analysis conditions: OJ-H, 2% IPA–hexanes, 0.8 mL/min, 254 nm

DL-6a



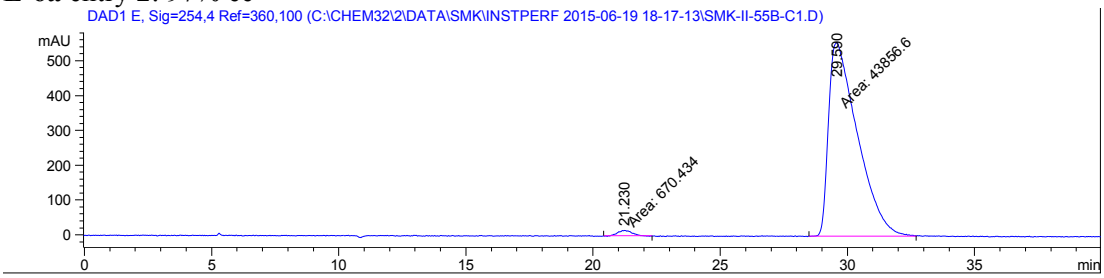
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.207	BB	0.6281	6097.20557	142.23837	50.3170
2	30.424	VB	0.8056	6020.39209	93.20570	49.6830

L-6a entry 1: 98% ee



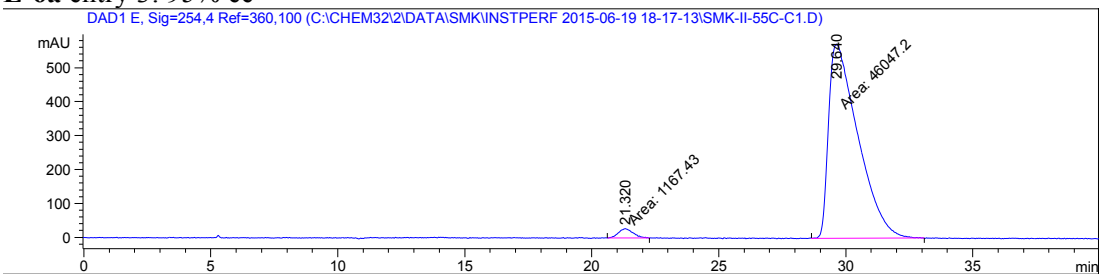
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.898	MM R	0.5826	277.33759	7.35449e-1	0.9342
2	30.068	MM T	1.2234	2.94093e4	400.64212	99.0658

L-6a entry 2: 97% ee



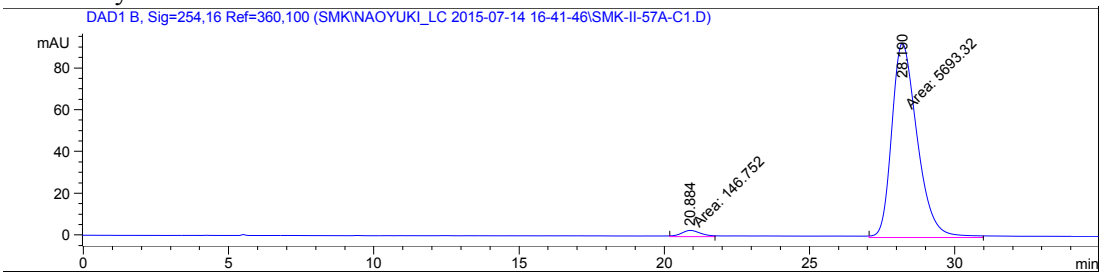
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.230	MM T	0.6844	670.43445	16.32698	1.5057
2	29.590	MM T	1.3119	4.38566e4	557.17871	98.4943

L-6a entry 3: 95% ee



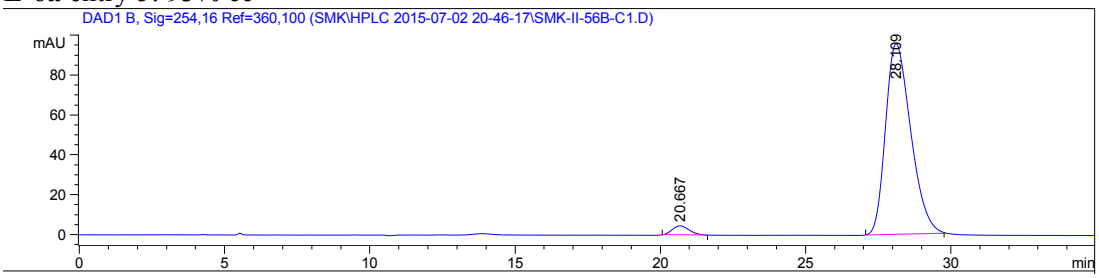
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.320	MM T	0.6894	1167.42615	28.22312	2.4726
2	29.640	MM T	1.3393	4.60472e4	573.04565	97.5274

L-6a entry 4: 95% ee



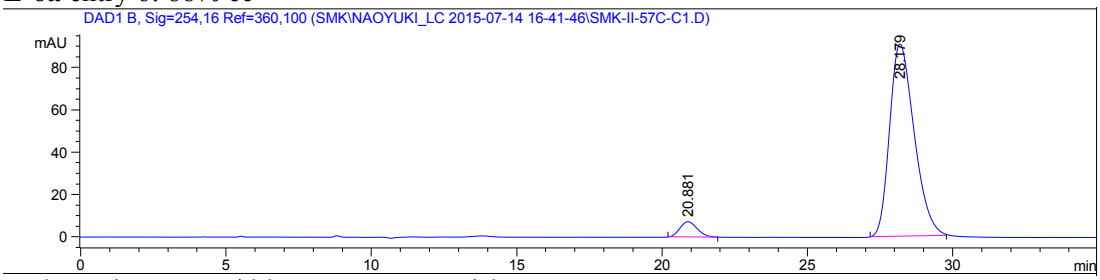
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.884	MM T	0.8044	146.75229	3.04073	2.5129
2	28.190	MM T	1.0193	5693.31689	93.09573	97.4871

L-6a entry 5: 93% ee



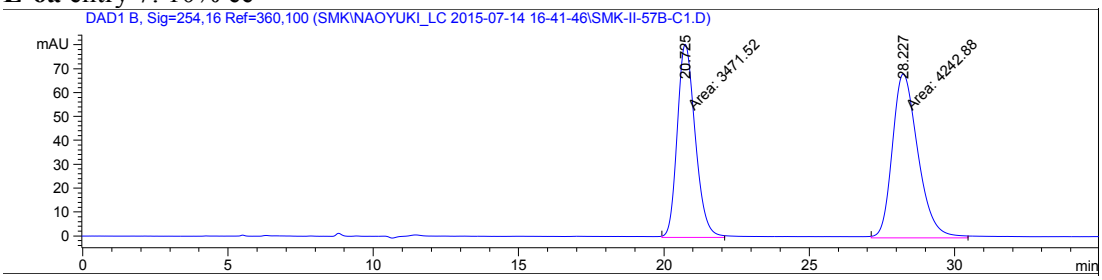
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.667	BB	0.5464	185.99770	4.59382	3.1189
2	28.109	BB	0.9291	5777.48828	95.60141	96.8811

L-6a entry 6: 88% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.881	BB	0.5996	301.59750	7.24530	5.3442
2	28.179	BB	0.9102	5341.89160	90.81699	94.6558

L-6a entry 7: 10% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.725	MM T	0.7158	3471.51953	80.82986	45.0005
2	28.227	MM T	1.0278	4242.88184	68.79994	54.9995

IV. Bibliography

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16. For clarity synthetic intermediates not described in the manuscript are numbered in the Supporting Information beginning with **S1**.