Carboxylic Acids as a Traceless Activation Group for Conjugate Additions: A Three-Step Synthesis of (±)-Lyrica

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Supporting Information

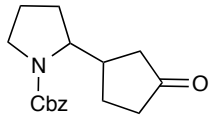
Contents

1. General Information

Commercial reagents were purchased from Sigma Aldrich and purified prior to use following the guidelines of Perrin and Armarego (*1*). All solvents were purified by passage through columns of activated alumina. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using an acetone-dry ice bath for volatile compounds. Chromatographic purification of products was accomplished by flash chromatography on silica gel (Fluka, 230-400 mesh). Thin layer chromatography (TLC) was performed on Analtech Uniplate 250 m silica gel plates. Visualization of the developed chromatogram was performed by fluorescence quenching, *p*-anisaldehyde, potassium permanganate, or ceric ammonium molybdate stain. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 500 (500 and 125 MHz) instrument, and are internally referenced to residual protio solvent signals (note: $CDCl_3$ referenced at 7.26 and 77.0 ppm respectively). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz) and assignment. Data for ^{13}C NMR are reported in terms of chemical shift and no special nomenclature is used for equivalent carbons. High resolution mass spectra were obtained at Princeton University mass spectrometry facilities. All amino acids were used from commercial suppliers or prepared using standard literature procedures. All olefins were used from commercial suppliers or prepared using standard literature procedures.

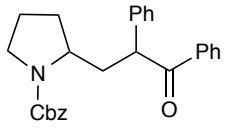
2. Experimental Procedures and Characterization of the Decarboxylative Michael Products

General Procedure for the Decarboxylative Michael: An oven-dried 8 mL vial equipped with a Teflon septum and magnetic stir bar was charged with $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2 μmol, 0.01 equiv), Cbz-Pro-OH (0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (0.2 mmol, 1.0 equiv), K_2HPO_4 (0.24 mmol, 1.2 equiv), and 0.5 mL of DMF. The reaction mixture was degassed by bubbling nitrogen stream for 15 min, then irradiated with a 26 W fluorescent lamp (at approximately 2 cm away from the light source). After 36h, the reaction mixture was diluted with saturated aqueous $NaHCO_3$ solution, extracted with Et_2O (3 × 50 mL). The combined organic extracts were washed with water and brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired product.



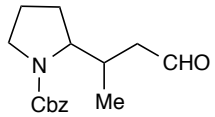
(±)-Benzyl 2-(3-oxocyclopentyl)pyrrolidine-1-carboxylate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Cbz-Pro-OH (50.0 mg, 0.2 mmol, 1.0 equiv), 2-cyclopenten-1-one (16.4 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow oil (51 mg, 88%). ^1H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 7.37-7.30 (m, 5H), 5.16-5.10 (m, 2H), 4.06-3.96 (m, 1H), 3.62-3.52 (m, 1H), 3.38 (br, 1H), 2.35-1.79 (m, 10H), 1.69-1.64 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 218.79, 218.42, 155.93, 155.85, 155.62, 155.45, 136.97,

136.55, 128.57, 128.41, 128.25, 128.02, 127.84, 67.22, 66.82, 60.90, 60.76, 60.27, 60.18, 46.75, 46.66, 42.84, 42.08, 41.65, 41.46, 41.35, 38.70, 38.52, 38.34, 29.49, 28.88, 28.54, 28.13, 26.82, 26.12, 24.04, 23.96, 23.12, 23.04; HRMS (ESI) m/z calcd for $C_{17}H_{22}NO_3$ $[(M+H)^+]$ 288.1600, found 288.1609. IR (film) 2961, 1738, 1693, 1405, 1102, 698 cm^{-1};

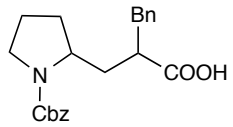


(±)-Benzyl 2-(3-oxo-2,3-diphenylpropyl)pyrrolidine-1-carboxylate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Cbz-Pro-OH (49.9 mg, 0.2 mmol, 1.0 equiv.), CsF (36.5 mg, 0.24 mmol, 1.2 equiv.), 1,2-diphenylprop-2-en-1-one (41.7 mg, 0.2 mmol, 1.0 equiv.) and DMF (0.5 mL) were used. The product was isolated by flash chromatography (30% ethyl acetate in hexanes) as a colourless powder (67 mg, 81%). ^1H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers : δ 8.06-7.84 (m, 2H), 7.50-7.14 (m, 13H), 5.20-5.03 (m, 1.2H), 5.03-4.90 (m, 0.6H), 4.82-4.75 (m, 0.2H), 4.74-4.67 (m, 0.2H), 4.67-4.58 (m, 0.6H), 4.41 (d, *J* = 12.5 Hz, 0.2H), 4.26-4.18 (m, 0.4H), 4.05-3.94 (m, 0.35H), 3.94-3.85 (m, 0.25H), 3.55-3.20 (m, 2H), 2.79-2.67 (m, 0.5H), 2.41-2.32 (m, 0.15H), 2.30-2.21 (m, 0.2H), 2.21-1.71 (m, 4.5H), 1.55-1.44 (m, 0.65H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 199.40, 199.15, 198.95, 198.57, 155.43, 155.28, 154.93, 139.86, 139.70, 139.52, 139.31, 137.28, 136.87, 136.79, 136.60, 136.46, 136.40, 132.87, 132.73, 132.60, 129.05, 128.96, 128.88, 128.77, 128.63, 128.52, 128.47, 128.38, 128.24, 128.14, 128.06, 127.86, 127.81, 127.69, 127.11, 126.99, 66.86, 66.53, 66.48, 56.49, 56.20, 55.64, 51.09, 50.89, 50.39, 46.45, 46.25, 45.76, 40.15, 39.58, 39.05, 31.77, 31.41, 31.26, 30.99, 23.83,

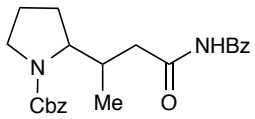
23.55, 22.90; HRMS (ESI) *m/z* calcd for $C_{27}H_{28}NO_3$ $[(M+H)^+]$ 414.20637, found 414.20623. IR (film) 2958, 1686, 1407, 1353, 1206, 1177, 1096, 953, 747, 694 cm^{-1};



(±)-Benzyl 2-(4-oxobutan-2-yl)pyrrolidine-1-carboxylate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (11 mg, 10.0 μmol, 0.01 equiv), Cbz-Pro-OH (250.0 mg, 1.0 mmol, 1.0 equiv), crotonaldehyde (70.9 mg, 1.0 mmol, 1.0 equiv), K_2HPO_4 (210.0 mg, 1.2 mmol, 1.2 equiv), and 2.5 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow oil (253 mg, 92%). ^1H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 9.70 (br, 0.3H), 9.59-9.57 (m, 0.5H), 9.50 (br, 0.2H), 7.37-7.30 (m, 5H), 5.16-5.09 (m, 2H), 3.90 (br, 0.55H), 3.81 (br, 0.45H), 3.65-3.48 (m, 1H), 3.31-3.26 (m, 0.45H), 3.22-3.17 (m, 0.55H), 2.95 (br, 0.3H), 2.69 (br, 0.2H), 2.59-2.49 (m, 0.6H), 2.39-2.34 (m, 0.6H), 2.26-2.11 (m, 0.9H), 1.93-1.63 (m, 4.4H), 0.96-0.86 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 202.10, 201.83, 201.61, 201.42, 155.43, 155.38, 155.16, 136.78, 136.52, 128.32, 127.93, 127.76, 127.60, 66.87, 66.54, 61.91, 61.66, 61.00, 47.93, 47.66, 47.20, 47.08, 46.61, 46.16, 45.77, 31.06, 30.98, 30.96, 30.37, 27.19, 26.82, 25.79, 24.18, 23.85, 23.55, 23.24, 16.91, 15.68, 15.25; HRMS (ESI) m/z calcd for $C_{16}H_{21}NNaO_3$ $[(M+Na)^+]$ 298.1419, found 298.1422. IR (film) 2962, 1692, 1404, 1097, 697 cm^{-1};

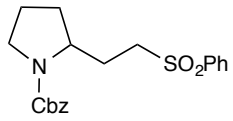


(±)-2-Benzyl-3-(1-((benzyloxy)carbonyl)pyrrolidin-2-yl)propanoic acid: According to the general procedure, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Cbz-Pro-OH (50.0 mg, 0.2 mmol, 1.0 equiv), 2-benzylacrylic acid (32.4 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (50% ethyl acetate/hexane) as a pale yellow solid (42 mg, 57%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 7.41-7.08 (m, 10H), 5.23-5.01 (m, 2H), 4.16-4.12 (m, 0.6H), 3.98-3.92 (m, 0.4H), 3.46-3.42 (m, 1H), 3.32-3.27 (m, 1H), 3.12-2.60 (m, 3H), 2.20-1.53 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 179.80, 179.56, 177.13, 157.21, 155.39, 155.22, 139.26, 139.05, 138.75, 138.70, 136.90, 136.36, 129.37, 129.16, 129.04, 128.96, 128.71, 128.57, 128.53, 128.42, 128.34, 128.17, 128.04, 127.97, 126.62, 126.53, 126.45, 67.82, 67.11, 66.97, 56.24, 55.93, 55.63, 46.66, 46.45, 46.28, 44.89, 44.58, 44.43, 38.85, 38.56, 38.42, 36.75, 36.37, 36.04, 31.53, 31.24, 30.82, 30.40, 29.83, 23.71, 23.47, 23.16, 22.93; HRMS (ESI) m/z calcd for $C_{22}H_{26}NO_4$ $[(M+H)^+]$ 368.1862, found 368.1868. IR (film) 2957, 1700, 1419, 1105, 698 cm^{-1};



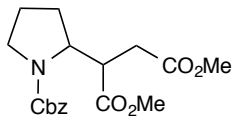
(±)-Benzyl 2-(4-benzamido-4-oxobutan-2-yl)pyrrolidine-1-carboxylate: According to the general procedure, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Cbz-

Pro-OH (50.0 mg, 0.2 mmol, 1.0 equiv), (*E*)-*N*-(but-2-enoyl)benzamide (37.8 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (30% ethyl acetate/hexane) as a pale yellow solid (67 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 9.41 (s, 0.2H), 9.03 (s, 0.4H), 8.45 (s, 0.14H), 8.39 (m, 0.26H), 7.91-7.78 (m, 2H), 7.62-7.56 (m, 1H), 7.51-7.45 (m, 2H), 7.37-7.22 (m, 5H), 5.16-5.00 (m, 2H), 4.04 (br, 0.2H), 3.92-3.91 (m, 0.8H), 3.68-3.59 (m, 0.6H), 3.55-3.50 (m, 0.4H), 3.36-3.29 (m, 1H), 3.09-2.88 (m, 1H), 2.81-2.68 (m, 1H), 2.61-2.49 (m, 1H), 2.00-1.73 (m, 4H), 1.02-0.93 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 175.46, 175.21, 174.58, 174.23, 165.63, 165.57, 156.11, 155.93, 155.76, 155.57, 136.98, 136.89, 133.25, 133.03, 129.02, 128.86, 128.57, 128.52, 128.46, 128.12, 127.96, 127.84, 127.77, 67.00, 66.91, 66.81, 62.15, 61.37, 61.32, 47.83, 47.32, 46.80, 41.74, 41.40, 40.01, 34.02, 32.73, 32.50, 27.82, 27.71, 27.45, 24.42, 24.02, 23.77, 23.51, 17.00, 16.59, 15.84, 15.60; HRMS (ESI) m/z calcd for $C_{23}H_{27}N_2O_4$ [$(M+H)^+$] 395.1971, found 395.1961. IR (film) 2964, 1686, 1411, 1242, 1102, 705 cm^{-1};



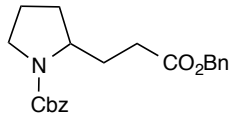
(±)-Benzyl 2-(2-(phenylsulfonyl)ethyl)pyrrolidine-1-carboxylate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Cbz-Pro-OH (50.0 mg, 0.2 mmol, 1.0 equiv), phenyl vinylsulfone (33.6 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (50% ethyl acetate/hexane) as a pale yellow solid

(52 mg, 69%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 7.90 (d, *J* = 7.5 Hz, 1H), 7.83 (d, *J* = 7.0 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.57-7.52 (m, 2H), 7.33-7.30 (m, 4H), 7.26-7.22 (m, 1H), 5.09-5.04 (m, 2H), 3.96-3.89 (m, 1H), 3.49-3.35 (m, 2H), 3.20 (d, *J* = 8.0 Hz, 1H), 3.03-3.02 (m, 1H), 2.09-1.94 (m, 2H), 1.90-1.82 (m, 3H), 1.65-1.62 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 155.47, 155.00, 139.20, 139.02, 136.81, 136.39, 133.78, 129.37, 128.64, 128.57, 128.22, 128.10, 128.06, 127.87, 67.20, 66.85, 56.49, 55.87, 53.93, 53.60, 46.87, 46.48, 31.14, 30.68, 27.90, 27.83, 23.75, 23.02; HRMS (ESI) m/z calcd for $C_{20}H_{24}NO_4S$ $[(M+H)^+]$ 374.1426, found 374.1431. IR (film) 2956, 1691, 1408, 1304, 1143, 1086, 742 cm^{-1};

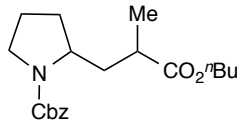


(±)-Diethyl 2-(1-(1-benzoylpyrrolidin-2-yl)ethyl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Cbz-Pro-OH (50.0 mg, 0.2 mmol, 1.0 equiv), dimethyl maleate (28.8 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (25% ethyl acetate/hexane) as a pale yellow oil (65 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 7.41-7.29 (m, 5H), 5.21-5.08 (m, 2H), 4.31-4.28 (m, 0.55H), 4.17-4.09 (m, 0.45H), 3.69-3.64 (m, 6.8H), 3.56-3.47 (m, 0.8H), 3.37-3.33 (m, 0.8H), 3.28-3.22 (m, 0.6H), 2.81-2.70 (m, 1H), 2.54-2.29 (m, 1H), 1.95-1.72 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 173.60, 173.27, 173.03, 172.37, 172.30, 172.14, 155.40,

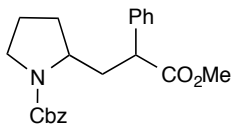
155.03, 136.89, 136.77, 136.56, 128.52, 128.22, 128.08, 128.03, 127.99, 127.86, 67.22, 66.86, 59.02, 58.35, 58.24, 57.42, 52.13, 52.11, 51.92, 51.86, 47.79, 47.19, 46.96, 46.60, 44.57, 44.31, 44.13, 43.65, 33.60, 31.15, 30.54, 28.14, 28.10, 27.42, 24.17, 23.64, 23.57, 22.85; HRMS (ESI) m/z calcd for $C_{18}H_{24}NO_6$ $[(M+H)^+]$ 350.1604, found 350.1600. IR (film) 2953, 1697, 1732, 1408, 1165, 1110, 699 cm^{-1};



(±)-Benzyl 2-(3-(benzyloxy)-3-oxopropyl)pyrrolidine-1-carboxylate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Cbz-Pro-OH (49.9 mg, 0.2 mmol, 1.0 equiv.), benzyl acrylate (32.4 mg, 0.2 mmol, 1.0 equiv.), K_2HPO_4 (41.8 mg, 0.24 mmol, 1.2 equiv.) and DMF (0.5 mL) were used. The product was isolated by flash chromatography (30% ethyl acetate in hexanes) as a colorless oil (55 mg, 75%). ^1H NMR (500 MHz, $CDCl_3$) mixture of rotamers: δ 7.31-7.19 (m, 10H), 5.08-4.94 (m, 4H), 3.89-3.80 (m, 1H), 3.46-3.26 (m, 2 H), 2.40-2.22 (m, 2H), 2.05-1.95 (m, 0.5H), 1.95-1.62 (m, 4.5H), 1.60-1.50 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of rotamers: δ 173.25, 173.03, 155.14, 137.03, 136.84, 136.01, 135.94, 128.54, 128.46, 128.26, 128.20, 127.97, 127.88, 127.85, 66.84, 66.59, 66.28, 57.25, 56.54, 46.65, 46.32, 31.36, 31.17, 30.75, 30.05, 29.80, 29.44, 23.77, 23.00; HRMS (ESI) *m/z* calcd for $C_{22}H_{26}NO_4$ $[(M+H)^+]$ 368.18563, found 368.18568. IR (film) 2957, 1733, 1695, 1455, 1409, 1355, 1165, 1151, 1098, 743, 697 cm^{-1};

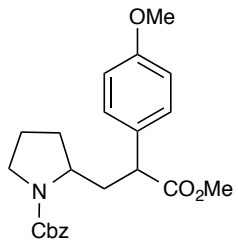


(±)-Benzyl 2-(3-butoxy-2-methyl-3-oxopropyl)pyrrolidine-1-carboxylate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Cbz-Pro-OH (50.0 mg, 0.2 mmol, 1.0 equiv), butyl methacrylate (28.4 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow oil (48 mg, 69%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 7.39-7.26 (m, 5H), 5.18-5.07 (m, 2H), 4.06-3.91 (m, 3H), 3.49-3.33 (m, 2H), 2.56-2.38 (m, 1H), 2.18-1.60 (m, 6H), 1.39-1.31 (m, 3H), 1.24-1.20 (m, 1.4H), 1.10-1.09 (m, 2H), 0.95-0.90 (m, 3.6H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 176.76, 176.38, 155.28, 155.02, 154.69, 137.25, 137.17, 136.94, 128.55, 128.53, 128.29, 128.07, 128.01, 127.96, 127.94, 127.93, 127.83, 66.95, 66.91, 66.90, 66.65, 66.61, 64.65, 64.33, 64.31, 55.92, 55.45, 46.57, 46.45, 46.28, 46.26, 46.20, 38.98, 38.52, 37.49, 37.17, 30.73, 30.71, 30.69, 30.57, 23.89, 23.81, 22.99, 19.37, 19.25, 19.24, 17.95, 17.80, 13.89, 13.86, 13.85; HRMS (ESI) m/z calcd for $C_{20}H_{30}NO_4$ $[(M+H)^+]$ 348.2175, found 348.2183. IR (film) 2959, 1698, 1408, 1110, 697 cm^{-1};



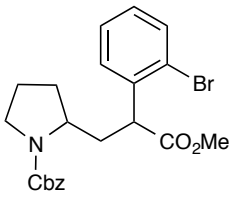
(±)-Benzyl 2-(3-methoxy-3-oxo-2-phenylpropyl)pyrrolidine-1-carboxylate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 10.0 μmol, 0.01 equiv), Cbz-Pro-OH (50.0 mg, 0.2 mmol, 1.0 equiv), methyl 2-phenylacrylate (32.4

mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow oil (65 mg, 89%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 7.46-7.15 (m, 10H), 5.15-5.03 (m, 2H), 3.99-3.31 (s, 7H), 2.59-2.55 (br, 0.7H), 2.34-2.22 (m, 0.3H), 2.10-2.05 (m, 0.3H), 1.91-1.70 (m, 3.7H), 1.57-1.48 (m, 0.8H), 1.27-1.20 (m, 0.2H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 174.25, 174.00, 173.91, 155.26, 155.12, 155.01, 139.40, 139.12, 138.57, 138.14, 137.04, 136.90, 136.82, 128.71, 128.53, 128.43, 128.38, 128.36, 128.06, 127.94, 127.84, 127.39, 127.31, 126.67, 67.04, 66.96, 66.65, 66.59, 56.52, 56.06, 55.97, 55.24, 56.52, 56.06, 55.97, 55.24, 52.14, 52.09, 48.97, 48.75, 46.60, 46.35, 46.05, 38.68, 38.60, 37.62, 37.24, 31.15, 30.80, 30.70, 30.15, 23.88, 23.72, 23.07, 22.90; HRMS (ESI) m/z calcd for $C_{22}H_{26}NO_4$ [$(M+H)^+$] 368.1862, found 368.1869. IR (film) 2952, 2693, 1408, 1097, 697 cm^{-1};



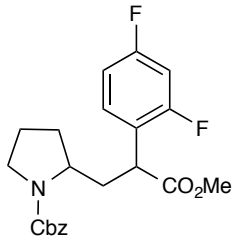
(±)-Benzyl 2-(3-methoxy-2-(4-methoxyphenyl)-3-oxopropyl)pyrrolidine-1-carboxylate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Cbz-Pro-OH (49.9 mg, 0.2 mmol, 1.0 equiv.), CsF (36.5 mg, 0.24 mmol, 1.2 equiv.), methyl 2-(4-methoxyphenyl)acrylate (38.4 mg, 0.2 mmol, 1.0 equiv.) and DMF (0.5 mL) were used. The product was isolated by flash chromatography (30% ethyl acetate in hexanes) as a colorless oil (60 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$)

mixture of diastereomers and rotamers: δ 7.50-7.28 (m, 6H), 7.16 (d, *J* = 7.5 Hz, 0.8H), 7.08 (d, *J* = 7.5 Hz, 0.2H), 6.90-6.81 (m, 1.8H), 6.71 (d, *J* = 8.5 Hz, 0.2H), 5.21-5.05 (m, 2H), 4.04-3.89 (m, 0.8H), 3.85-3.75 (m, 3.5H), 3.75-3.52 (m, 3.5H), 3.52-3.30 (m, 2.2H), 2.62-2.49 (m, 0.8H), 2.43-2.33 (m, 0.1H), 2.29-2.20 (m, 0.1H), 2.10-1.42 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 174.48, 174.22, 174.15, 158.79, 155.20, 155.04, 154.99, 136.99, 136.86, 136.77, 131.36, 131.09, 129.03, 128.80, 128.00, 127.88, 127.78, 114.00, 66.97, 66.60, 56.43, 55.93, 55.26, 55.23, 55.10, 52.07, 52.00, 48.06, 47.81, 46.55, 46.29, 46.02, 38.69, 38.58, 37.36, 36.96, 31.20, 30.79, 30.53, 29.99, 23.84, 23.69, 23.03, 22.86; HRMS (ESI) *m/z* calcd for $C_{23}H_{28}NO_5$ $[(M+H)^+]$ 398.1962, found 398.19642. IR (film) 2952, 1731, 1694, 1511, 1409, 1351, 1248, 1178, 1161, 1097, 1032, 698cm^{-1};



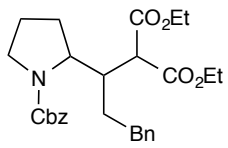
(±)- Benzyl 2-(2-(2-bromophenyl)-3-methoxy-3-oxopropyl)pyrrolidine-1-carboxylate: According to the general procedure, Ir[dF(CF_3)ppy)]$_2$(dtbbpy)PF_6 (2.2 mg, 2 μmol, 0.01 equiv.), Cbz-Pro-OH (49.9 mg, 0.20 mmol, 1.0 equiv.), K_2HPO_4 (41.8 mg, 0.24 mmol, 1.2 equiv.), methyl 2-(2-bromophenyl)acrylate (48.2 mg, 0.2 mmol, 1.0 equiv.) and DMF (0.5 mL) were used. The product was isolated by flash chromatography (30% ethyl acetate in hexanes) as a colorless oil (77 mg, 87%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 7.60-7.53 (m, 1H), 7.52-7.25 (m, 6.5H), 7.18-6.98 (m, 1.5H), 5.23-5.03 (m, 2H), 4.37-4.20 (m, 1H), 4.12-4.03 (m, 0.65H), 3.90-

3.83 (m, 0.16H), 3.77-3.75 (m, 0.19H), 3.74-3.55 (m, 3H), 3.54-3.33 (m, 2H), 2.71-2.62 (m, 0.3H), 2.57-2.47 (m, 0.3H), 2.37-2.28 (m, 0.2H), 2.23-2.16 (m, 0.2H), 2.12-1.60 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers : δ 173.61, 173.45, 173.30, 173.18, 155.13, 154.99, 154.94, 138.94, 138.67, 138.05, 137.74, 137.04, 136.85, 136.78, 133.07, 132.95, 128.97, 128.93, 128.77, 128.72, 128.66, 128.49, 128.44, 128.32, 128.29, 128.00, 127.81, 124.82, 124.79, 124.34, 66.95, 66.53, 56.61, 55.96, 55.73, 55.08, 55.22, 47.73, 47.55, 47.23, 47.06, 46.57, 46.33, 46.27, 46.11, 38.20, 37.51, 37.34, 36.89, 30.94, 30.71, 30.27, 30.12, 23.81, 23.76, 22.98, 22.88; HRMS (ESI) *m/z* calcd for $C_{22}H_{25}BrNO_4$ [$(M+H)^+$] 446.09615, found 446.09693. IR (film) 2951, 1734, 1694, 1408, 1350, 1187, 1166, 1096, 1022, 748, 697 cm^{-1};



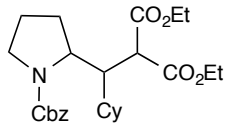
(±)-Benzyl 2-(2-(2,4-difluorophenyl)-3-methoxy-3-oxopropyl)pyrrolidine-1-carboxylate: According to the general procedure, Ir[dF(CF_3)ppy)]$_2$(dtbbpy)PF_6 (2.2 mg, 2 μmol, 0.01 equiv.), Cbz-Pro-OH (74.8 mg, 0.30 mmol, 1.5 equiv.), K_2HPO_4 (52.3 mg, 0.3 mmol, 1.5 equiv.), methyl 2-(2,4-difluorophenyl)acrylate (39.6 mg, 0.2 mmol, 1.0 equiv.) and DMF (0.5 mL) were used. The product was isolated by flash chromatography (30% ethyl acetate in hexanes) as a colorless oil (73 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers : δ 7.55-7.23 (m, 5.9H), 7.11-7.03 (m, 0.3H), 6.89-6.70 (m, 1.6H), 6.54 (t, J = 8.0 Hz, 0.2H), 5.22-5.03 (m, 2H), 4.14-4.06 (m,

0.3H), 4.06-3.93 (m, 1H), 3.93-3.86 (m, 0.2H), 3.82-3.74 (m, 0.2H), 3.70-3.57 (m, 3H), 3.54-3.31 (m, 2H), 2.69-2.61 (m, 0.3H), 2.58-2.50 (m, 0.3H), 2.45-2.35 (m, 0.2H), 2.28-2.19 (m, 0.2H), 2.11-1.52 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 173.32, 173.22, 173.12, 173.04, 163.06, 162.95, 162.87, 161.53, 161.44, 161.35, 161.20, 160.97, 159.56, 159.46, 159.37, 159.27, 155.13, 155.01, 154.91, 136.92, 136.76, 136.59, 130.37, 130.12, 129.82, 129.66, 128.46, 128.27, 128.13, 127.93, 127.83, 127.80, 127.70, 122.56, 122.44, 122.27, 122.15, 121.32, 121.20, 120.95, 120.82, 111.85, 111.66, 111.50, 111.36, 104.08, 103.95, 103.87, 103.75, 103.67, 103.54, 67.06, 66.61, 56.32, 55.76, 54.96, 52.30, 52.24, 46.58, 46.31, 46.14, 41.06, 40.48, 40.23, 40.09, 37.76, 37.19, 36.45, 35.89, 31.00, 30.36, 29.82, 23.82, 23.75, 23.01, 22.87; HRMS (ESI) *m/z* calcd for $C_{22}H_{24}F_2NO_4$ [$(M+H)^+$] 404.16679, found 404.16672. IR (film) 2954, 2883, 1736, 1694, 1503, 1409, 1352, 1279, 1196, 1156, 1140, 1098, 964, 850, 698 cm^{-1};



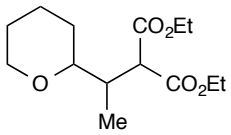
(±)-Diethyl 2-(1-(1-benzoylpyrrolidin-2-yl)ethyl)malonate: According to the general procedure, Ir[dF(CF_3)ppy)]$_2$(dtbbpy)PF_6 (2.2 mg, 20.0 μmol, 0.01 equiv), Cbz-Pro-OH (50.0 mg, 0.2 mmol, 1.0 equiv), diethyl 2-(3-phenylpropylidene)malonate (55.5 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (25% ethyl acetate/hexane) as a pale yellow oil (89 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 7.45-7.29 (m, 5H), 7.27-7.23 (m, 2H), 7.18-7.04 (m, 3H), 5.20-5.05 (m, 2H), 4.22-3.99 (m, 5H), 3.76-3.57 (m, 1H), 3.50-3.47 (m, 0.5H), 3.40-3.36 (m, 0.5H), 3.25-

3.14 (m, 1H), 3.07 (br, 0.6H), 2.72-2.38 (m, 2.4H), 2.00-1.95 (m, 1H), 1.91-1.84 (m, 1H), 1.82-1.58 (m, 4H), 1.27-1.19 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 169.02, 168.93, 168.76, 168.61, 155.67, 155.35, 142.35, 142.23, 142.00, 141.92, 136.83, 136.76, 136.64, 136.40, 128.52, 128.46, 128.40, 128.37, 128.29, 128.22, 128.15, 128.00, 127.92, 127.79, 125.89, 67.43, 67.31, 66.93, 66.80, 61.63, 61.42, 61.36, 60.50, 59.79, 59.56, 58.88, 54.13, 53.73, 53.37, 52.86, 48.16, 47.74, 47.49, 47.01, 42.22, 41.93, 40.58, 34.53, 34.25, 33.04, 32.75, 31.87, 31.75, 31.25, 29.77, 29.49, 27.47, 27.24, 24.32, 23.75, 23.65, 23.00, 14.13, 14.09, 14.02; HRMS (ESI) m/z calcd for $C_{28}H_{36}NO_6$ [$(M+H)^+$] 482.2543, found 482.2557. IR (film) 2947, 1697, 1405, 1096, 749, 698 cm^{-1};



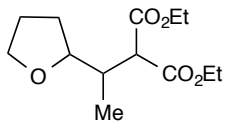
(±)-Diethyl 2-((1-((benzyloxy)carbonyl)pyrrolidin-2-yl)(cyclohexyl)methyl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.2 mg, 10.0 μmol, 0.01 equiv), Cbz-Pro-OH (50.0 mg, 0.2 mmol, 1.0 equiv), diethyl 2-(cyclohexylmethylene)malonate (50.8 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (25% ethyl acetate/hexane) as a pale yellow oil (80 mg, 87%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 7.47-7.29 (m, 5H), 5.22-5.01 (m, 2H), 4.21-4.06 (m, 4H), 3.96-3.87 (m, 0.25H), 3.70-3.53 (m, 1.75H), 3.29-3.17 (m, 1H), 3.07-3.00 (m, 1H), 1.97-1.56 (m, 11H), 1.27 (d, J = 7.0 Hz, 3H), 1.20 (d, J = 7.0 Hz, 3H), 1.13-0.96 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and

rotamers: δ 169.69, 169.63, 169.53, 169.03, 168.73, 156.83, 155.73, 155.68, 155.47, 137.04, 136.74, 136.64, 136.06, 129.35, 128.53, 128.46, 128.31, 127.98, 127.90, 127.75, 67.87, 67.36, 67.00, 66.66, 61.60, 61.43, 61.31, 61.05, 58.35, 57.85, 57.55, 57.06, 52.98, 52.71, 51.20, 50.80, 49.67, 49.26, 47.83, 47.72, 47.33, 47.22, 45.83, 45.19, 40.27, 40.21, 38.96, 38.70, 33.85, 33.27, 32.02, 31.49, 30.86, 28.28, 27.68, 27.63, 27.43, 27.37, 27.05, 26.86, 26.71, 26.59, 26.48, 24.40, 23.82, 23.33, 22.42, 14.22, 14.12, 14.00; HRMS (ESI) m/z calcd for $C_{26}H_{38}NO_6$ [$(M+H)^+$] 460.2699, found 460.2697. IR (film) 2926, 1698, 1404, 1097, 698 cm^{-1};

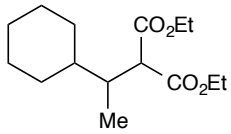


(±)-Diethyl 2-(1-(tetrahydro-2*H*-pyran-2-yl)ethyl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), tetrahydro-2*H*-pyran-4-carboxylic acid (26 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.20 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane) as a pale yellow oil (50 mg, 90%). ^1H NMR (500 MHz, $CDCl_3$) mixture of diastereomers: δ 4.23-4.15 (m, 4H), 3.94 (d, *J* = 10.5 Hz, 1H), 3.73 (d, *J* = 5.5 Hz, 0.4H), 3.51 (d, *J* = 9.0 Hz, 0.6H), 3.37-3.26 (m, 1.6H), 3.16 (t, *J* = 9.5 Hz, 0.4H), 2.33-2.27 (m, 1H), 1.87-1.84 (m, 1H), 1.74 and 1.72 (2 brs, 0.4H), 1.53-1.42 (m, 4H), 1.28-1.17 (m, 6.6H), 1.00-0.97 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers: δ 169.66, 169.11, 169.05, 168.88, 79.27, 78.47, 68.69, 68.54, 61.13, 61.08, 60.98, 60.79, 54.94, 52.92, 39.03, 38.14, 29.16, 28.65, 26.02, 26.00, 23.71, 23.46, 14.16,

14.11, 14.08, 12.88, 11.70; HRMS (ESI) m/z calcd for $C_{14}H_{25}O_5$ [$(M+H)^+$] 273.1702, found 273.1703. IR (film) 2939, 1749, 1729, 1088, 1029, 895 cm^{-1};

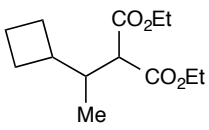


(±)-Diethyl 2-(1-(tetrahydrofuran-2-yl)ethyl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), tetrahydro-2-furoic acid (24 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane) as a pale yellow oil (47.5 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers: δ 4.24-4.16 (m, 4H), 3.86-3.68 (m, 3H), 3.61 (d, *J* = 6.0 Hz, 0.55H), 3.42 (d, *J* = 9.0 Hz, 0.45H), 2.52-2.45 (m, 0.45H), 2.33-2.26 (m, 0.55H), 2.03-1.82 (m, 3H), 1.64-1.57 (m, 1H), 1.28-1.25 (m, 6H), 0.98 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers: δ 169.31, 168.86, 168.83, 168.77, 81.25, 80.35, 68.32, 67.75, 61.22, 61.17, 61.09, 61.00, 54.93, 54.42, 39.09, 37.36, 30.00, 28.46, 25.98, 25.86, 14.13, 14.09, 14.06, 14.05, 13.49, 12.31; HRMS (ESI) m/z calcd for $C_{13}H_{23}O_5$ [$(M+H)^+$] 259.1545, found 259.1525. IR (film) 2978, 1748, 1728, 1153, 1065, 1030 cm^{-1};



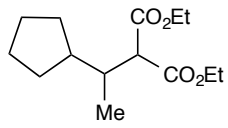
(±)-Diethyl 2-(1-cyclohexylethyl)malonate [known compound (*2*)]**:** According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.),

cyclohexanecarboxylic acid (26 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), 0.5 mL of DMF and 34 W Blue LED (instead of 26 W fluorescent light bulb) were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane) as a pale yellow oil (41 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.23-4.16 (m, 4H), 3.39 (d, J = 9.5 Hz, 1H), 2.21-2.14 (m, 1H), 1.76-1.71 (m, 2H), 1.67-1.57 (m, 3H), 1.30-1.08 (m, 11H), 0.98-0.92 (m, 1H), 0.90 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.30, 169.05, 61.14, 61.06, 55.81, 40.24, 38.56, 31.52, 27.37, 26.73, 26.53, 26.46, 14.13, 12.89; HRMS (ESI) m/z calcd for $C_{15}H_{26}NaO_4$ [$(M+Na)^+$] 293.1729, found 293.1727. IR (film) 2925, 1753, 1729, 1147, 1031 cm^{-1};

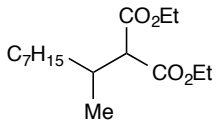


(±)-Diethyl 2-(1-cyclobutylethyl)malonate: According to the general procedure, Ir[dF(CF_3)ppy)]$_2$(dtbbpy)PF_6 (2.2 mg, 2 μmol, 0.01 equiv.), cyclobutanecarboxylic acid (20 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (54 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.3 mmol, 1.2 equiv), 0.5 mL of DMF and 34 W Blue LED (instead of 26 W fluorescent light bulb) were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane) as a pale yellow oil (33 mg, 68%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.20-4.14 (m, 4H), 3.22 (d, J = 6.5 Hz, 1H), 2.27-2.13 (m, 2H), 2.01-1.89 (m, 2H), 1.83-1.74 (m, 1H), 1.72-1.62 (m, 3H), 1.27 (t, J = 7.5 Hz, 6H), 0.91 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.26, 168.71, 61.16, 60.96, 55.03, 40.10, 39.95, 27.28, 27.05, 17.50, 14.14, 14.06, 13.96; HRMS (ESI) m/z calcd for

$C_{13}H_{22}NaO_4$ [$(M+Na)^+$] 265.1416, found 265.1400. IR (film) 2970, 1750, 1729, 1148, 1032 cm^{-1}.

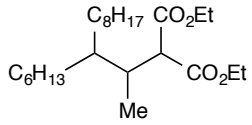


(±)-Diethyl 2-(1-cyclopentylethyl)malonate: According to the general procedure, Ir[dF(CF_3)ppy)]$_2$(dtbbpy)PF_6 (2.2 mg, 2 μmol, 0.01 equiv.), cyclopentanecarboxylic acid (24 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of 1,4-dioxane were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane) as a pale yellow oil (30 mg, 58%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.19 (q, *J* = 7.5 Hz, 4H), 3.41 (d, *J* = 6.5 Hz, 1H), 2.17-2.10 (m, 1H), 1.79-1.71 (m, 3H), 1.64-1.58 (m, 2H), 1.53-1.50 (m, 2H), 1.27 (td, *J* = 7.5 Hz, *J* = 2.5 Hz, 6H), 1.19-1.13 (m, 2H), 1.02 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.48, 168.86, 61.15, 60.91, 56.32, 43.82, 38.48, 30.96, 29.66, 25.32, 25.28, 14.61, 14.16, 14.10; HRMS (ESI) m/z calcd for $C_{14}H_{25}O_4$ [$(M+H)^+$] 257.1753, found 257.1770. IR (film) 2952, 1750, 1728, 1124, 1150, 1030 cm^{-1};

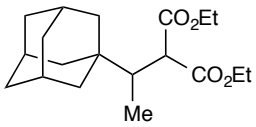


(±)-Diethyl 2-(nonan-2-yl)malonate: According to the general procedure, Ir[dF(CF_3)ppy)]$_2$(dtbbpy)PF_6 (2.2 mg, 2 μmol, 0.01 equiv.), octanoic acid (29 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), 0.5 mL of DMF and 34 W Blue LED (instead of 26 W

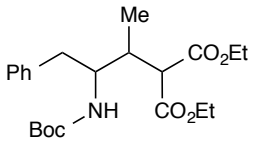
fluorescent light bulb) were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane) as a colorless oil (22 mg, 38%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.19 (q, *J* = 7.0 Hz, 4H), 3.22 (d, *J* = 8.0 Hz, 1H), 2.27-2.19 (m, 1H), 1.42-1.18 (m, 18H), 0.98 (d, *J* = 7.0 Hz, 3H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.05, 168.89, 61.12, 61.06, 57.84, 34.34, 33.39, 31.83, 29.59, 29.24, 26.81, 22.66, 16.96, 14.14, 14.12, 14.11; HRMS (ESI) m/z calcd for $C_{16}H_{30}NaO_4$ [$(M+Na)^+$] 309.2036, found 309.2026. IR (film) 2927, 1753, 1731, 1148, 1031 cm^{-1}.



(±)-Diethyl 2-(3-hexylundecan-2-yl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), 2-hexyldecanoic acid (52 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), 0.5 mL of DMF and 34 W Blue LED (instead of 26 W fluorescent light bulb) were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane) as a pale yellow oil (42 mg, 53%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.21-4.16 (m, 4H), 3.34 (d, *J* = 10.5 Hz, 1H), 2.46-2.38 (m, 1H), 1.36-1.17 (m, 30H), 1.00-0.94 (m, 1H), 0.88 (t, *J* = 7.0 Hz, 6H), 0.81 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.12, 168.97, 61.16, 56.63, 39.69, 35.09, 31.93, 31.89, 31.79, 30.32, 30.09, 29.96, 29.75, 29.64, 29.59, 29.38, 29.31, 28.06, 28.02, 27.42, 27.39, 22.70, 14.13, 11.61; HRMS (ESI) m/z calcd for $C_{24}H_{46}NaO_4$ [$(M+Na)^+$] 421.3294, found 421.3293. IR (film) 2924, 2855, 1757, 1733, 1175, 1032 cm^{-1};

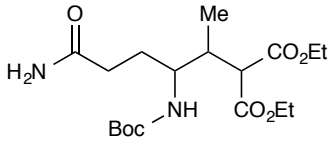


(±)-Diethyl 2-(1-((3*r*,5*r*,7*r*)-adamantan-1-yl)ethyl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), 1-adamantanecarboxylic acid (36 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.7 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), 0.5 mL of DMF and 34 W Blue LED (instead of 26 W fluorescent light bulb) were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane) as a pale yellow oil (60 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.21-4.14 (m, 4H), 3.57 (d, *J* = 5.5 Hz, 1H), 2.09-2.04 (m, 1H), 1.98-1.95 (m, 3H), 1.69-1.67 (m, 3H), 1.61-1.59 (m, 3H), 1.53-1.47 (m, 6H), 1.27 (q, *J* = 7.0 Hz, 6H), 0.98 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.38, 169.79, 61.32, 60.89, 51.83, 43.08, 39.36, 37.02, 35.23, 28.61, 14.09, 14.05, 10.40; HRMS (ESI) m/z calcd for $C_{19}H_{30}NaO_4$ [$(M+Na)^+$] 345.2042, found 345.2024. IR (film) 2901, 2848, 1728, 1218, 1148, 1137, 1031 cm^{-1};



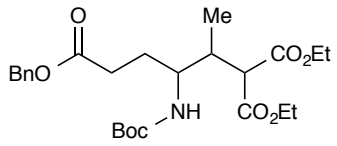
(±)-Diethyl 2-(3-((*tert*-butoxycarbonyl)amino)-4-phenylbutan-2-yl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Boc-Phe-OH (53.0 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (15% ethyl acetate/hexane)

as a pale yellow oil (77 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers: δ 7.29-7.25 (m, 2H), 7.21-7.15 (m, 3H), 4.49 (d, *J* = 9.5 Hz, 0.43H), 4.32-3.98 (m, 5H), 3.86-3.72 (m, 0.57H), 3.51-3.46 (m, 0.55H), 3.39-3.33 (m, 0.45H), 2.99-2.95 (m, 0.6H), 2.81-2.73 (m, 0.8H), 2.66-2.61 (m, 0.6H), 2.50-2.39 (m, 1H), 1.32-1.19 (m, 15H), 1.15 (d, *J* = 6.5 Hz, 1.7H), 0.95 (d, *J* = 7.0 Hz, 1.3H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers: δ 169.67, 169.01, 168.43, 155.56, 155.34, 138.03, 137.97, 129.41, 129.17, 128.51, 128.48, 126.48, 79.30, 79.21, 61.60, 61.48, 61.46, 61.43, 55.65, 55.26, 54.28, 52.81, 39.93, 39.08, 37.18, 35.76, 28.36. 15.12, 14.20, 14.18, 14.12, 11.15; HRMS (ESI) m/z calcd for $C_{22}H_{34}NO_6$ [$(M+H)^+$] 408.2386, found 408.2388. IR (film) 2978, 1704, 1365, 1165, 1026, 699 cm^{-1};



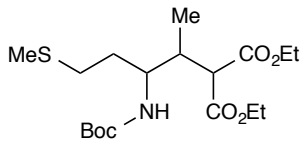
(±)-Diethyl 2-(6-amino-3-((*tert*-butoxycarbonyl)amino)-6-oxohexan-2-yl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)$ (2.2 mg, 2 μmol, 0.01 equiv.), Boc-Gln-OH (49 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (60% ethyl acetate/hexane) as a pale yellow solid (65 mg, 84%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers: δ 6.35 (s, 0.5H), 6.14 (s, 0.5H), 5.40 (s, 1H), 4.76 (d, *J* = 10.0 Hz, 0.5H), 4.46 (d, *J* = 10.5 Hz, 0.5H), 4.23-4.17 (m, 4H), 3.87-3.81 (m, 0.5H), 3.64-3.59 (m, 0.5H), 3.44 (d, *J* = 6.5 Hz, 0.5H), 3.20 (d, *J* = 10.0 Hz, 0.5H), 2.46-2.34 (m, 1H), 2.29-2.24 (m, 2H), 2.02-1.96 (m, 0.5H), 1.83-1.77 (m, 2H), 1.63-1.55 (m, 0.5H), 1.42 (s, 9H), 1.29-1.24

(m, 6H), 1.06 (d, *J* = 7.0 Hz, 1.5H), 0.91 (d, *J* = 7.0 Hz, 1.5H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers: δ 175.61, 175.55, 169.42, 168.91, 168.81, 168.52, 156.35, 156.30, 79.56, 79.49, 61.64, 61.53, 61.48, 61.47, 55.53, 54.25, 53.49, 51.50, 37.90, 36.96, 32.96, 32.65, 29.75, 29.28, 28.39, 28.36, 14.73, 14.13, 14.09, 14.03, 11.14; HRMS (ESI) m/z calcd for $C_{18}H_{33}N_2O_7$ [$(M+H)^+$] 389.2288, found 389.2296. IR (film) 3347, 2978, 1670, 1165, 1026, 735 cm^{-1};

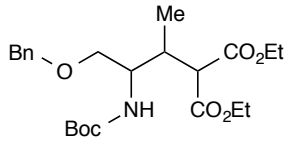


(±)-5-Benzyl 1,1-diethyl 3-((*tert*-butoxycarbonyl)amino)-2-methylpentane-1,1,5-tricarboxylate: According to the general procedure, Ir[dF(CF_3)ppy)]$_2$(dtbbpy)PF_6 (2.2 mg, 2 μmol, 0.01 equiv.), Boc-Glu(OBzl)-OH (67 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow oil (89 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers: δ 7.38-7.31 (m, 5H), 5.15-5.08 (m, 2H), 4.52 (d, *J* = 10.0 Hz, 0.4H), 4.31 (d, *J* = 10.5 Hz, 0.4H), 4.22-4.16 (m, 4.2H), 3.86-3.74 (m, 0.5H), 3.62-3.49 (m, 0.5H), 3.42 (d, *J* = 7.0 Hz, 0.5H), 3.28 (d, *J* = 10.0 Hz, 0.5H), 2.50-2.34 (m, 3H), 2.03-1.96 (m, 0.5H), 1.85-1.74 (m, 1H), 1.65-1.60 (m, 0.5H), 1.41 (m, 5H), 1.40 (s, 4H), 1.27 (qd, *J* = 7.0 Hz, *J* = 3.0 Hz, 6H), 1.05 (d, *J* = 7.0 Hz, 1.6H), 0.89 (d, *J* = 7.0 Hz, 1.4H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers: δ 173.23, 173.20, 169.45, 168.82, 168.78, 168.38, 155.70, 155.51, 135.90, 135.89, 128.56, 128.24, 128.21, 128.20, 79.37, 79.26, 66.37, 66.34, 61.56, 61.43, 61.37, 55.41, 54.26, 53.59,

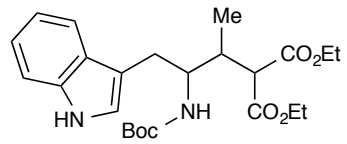
51.52, 37.87, 36.83, 31.47, 31.02, 28.70, 28.35, 28.32, 28.14, 14.69, 14.10, 14.06, 14.01, 11.12; HRMS (ESI) m/z calcd for $C_{25}H_{38}NO_8$ $[(M+H)^+]$ 480.2597, found 480.2604. IR (film) 2978, 1727, 1710, 1161, 1026, 698 cm^{-1};



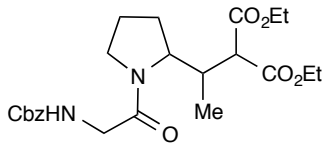
(±)-Diethyl 2-(3-((*tert*-butoxycarbonyl)amino)-5-(methylthio)pentan-2-yl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Boc-Met-OH (50.0 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow oil (74 mg, 94%). ^1H NMR (500 MHz, $CDCl_3$) mixture of diastereomers: δ 4.56 (d, J = 9.5 Hz, 0.5H), 4.31 (d, J = 10.5 Hz, 0.3H), 4.23-4.17 (m, 4.2H), 3.92-3.87 (m, 0.4H), 3.68-3.63 (m, 0.6H), 3.42 (d, J = 7.0 Hz, 0.6H), 3.29 (d, J = 10.0 Hz, 0.4H), 2.59-1.67 (m, 8H), 1.43 (s, 5H), 1.42 (s, 4H), 1.29-1.25 (m, 6H), 1.05 (d, J = 7.0 Hz, 1.7H), 0.89 (d, J = 7.0 Hz, 1.3H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers: δ 169.53, 168.90, 168.45, 155.74, 155.58, 79.46, 79.32, 61.64, 61.53, 61.46, 55.49, 54.33, 53.58, 51.41, 37.66, 36.80, 34.02, 33.02, 31.16, 30.85, 28.42, 28.39, 15.76, 15.74, 14.81, 14.17, 14.14, 14.08, 11.20; HRMS (ESI) m/z calcd for $C_{18}H_{33}NNaO_6S$ $[(M+Na)^+]$ 414.1926, found 414.1940. IR (film) 2978, 1715, 1366, 1168, 1031 cm^{-1};



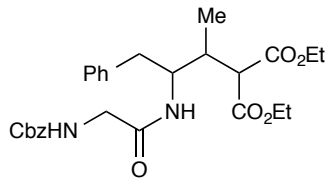
(±)-Diethyl 2-(4-(benzyloxy)-3-((*tert*-butoxycarbonyl)amino)butan-2-yl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Boc-Ser(Bzl)-OH (59 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (25% ethyl acetate/hexane) as a pale yellow oil (83 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers: δ 7.36-7.27 (m, 5H), 4.94 (d, *J* = 9.5 Hz, 0.5H), 4.68 (d, *J* = 9.5 Hz, 0.5H), 4.53-4.46 (m, 2H), 4.23-4.14 (m, 4H), 4.04-3.92 (m, 0.5H), 3.78-3.75 (m, 0.5H), 3.63-3.55 (m, 1.5H), 3.50-3.46 (m, 1H), 3.41 (d, *J* = 9.0 Hz, 0.5H), 2.61-2.56 (m, 1H), 1.43 (s, 4.3H), 1.42 (s, 4.7H), 1.26 (td, *J* = 7.0 Hz, *J* = 2.5 Hz, 6H), 1.05 (d, *J* = 7.0 Hz, 1.6H), 0.96 (d, *J* = 7.0 Hz, 1.4H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers: δ 169.76, 168.99, 168.88, 168.76, 155.80, 155.61, 138.11, 128.50, 128.49, 127.81, 127.76, 127.69, 79.45, 79.35, 73.29, 73.06, 70.96, 70.20, 61.48, 61.38, 61.26, 55.12, 53.89, 53.50, 51.23, 34.94, 34.91, 28.46, 14.41, 14.21, 14.18, 14.14, 12.31; HRMS (ESI) m/z calcd for $C_{23}H_{36}NO_7$ $[(M+H)^+]$ 438.2492, found 438.2496. IR (film) 2978, 1715, 1164, 1028, 698 cm^{-1};



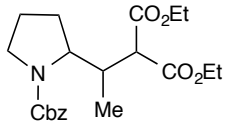
(±)-Diethyl 2-(3-((*tert*-butoxycarbonyl)amino)-4-(1*H*-indol-3-yl)butan-2-yl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Boc-Trp-OH (61 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow solid (51 mg, 57%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers: δ 8.02 (br, 1H), 7.60 (dd, *J* = 17.5 Hz, *J* = 8.0 Hz, 1H), 7.60 (dd, *J* = 8.0 Hz, *J* = 3.5 Hz, 1H), 7.20-7.16 (m, 1H), 7.13-7.05 (m, 2H), 4.59 (d, *J* = 9.5 Hz, 0.3H), 4.41 (d, *J* = 9.5 Hz, 0.3H), 4.30-4.28 (m, 0.4H), 4.22-4.15 (m, 4.5H), 3.95 (br, 0.5H), 3.54 (d, *J* = 6.5 Hz, 0.5H), 3.39 (d, *J* = 10.0 Hz, 0.5H), 3.10-3.06 (m, 0.5H), 2.95-2.78 (m, 1.5H), 2.62-2.56 (m, 0.5H), 2.48 (q, *J* = 7.0 Hz, 0.5H), 1.35-1.33 (m, 6H), 1.29-1.17 (m, 9H), 1.10-1.03 (m, 1.5H), 0.97 (d, *J* = 7.0 Hz, 1.5H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers: δ 169.80, 169.20, 169.12, 168.65, 155.85, 155.63, 136.57, 136.27, 128.07, 127.82, 127.54, 122.78, 122.63, 122.46, 121.97, 121.88, 119.40, 119.30, 118.86, 118.69, 111.98, 111.47, 111.25, 79.31, 79.11, 61.57, 61.51, 61.45, 55.77, 54.56, 54.16, 52.07, 36.86, 36.42, 35.76, 28.36, 27.73, 15.15, 14.18, 14.14, 14.05, 11.09; HRMS (ESI) m/z calcd for $C_{24}H_{35}N_2O_6$ $[(M+H)^+]$ 447.2495, found 447.2498. IR (film) 3387, 2978, 1721, 1169, 1027, 741 cm^{-1};



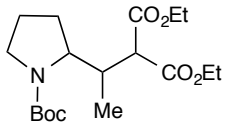
(±)-Diethyl 2-(1-(1-(((benzyloxy)carbonyl)glycyl)pyrrolidin-2-yl)ethyl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Z-Gly-Pro (61.1 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.20 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow solid (79 mg, 88%). ^1H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 7.36-7.229 (m, 5H), 5.80-5.59 (m, 1H), 5.14-5.09 (m, 2H), 4.31-4.28 (m, 0.4H), 4.23-4.13 (m, 4H), 4.09-4.00 (m, 0.6H), 4.00 (d, *J* = 4.0 Hz, 0.15H), 3.96 (dd, *J* = 7.0 Hz, *J* = 7.0 Hz, 0.55H), 3.91 (q, *J* = 4.5 Hz, 0.6H), 3.87 (d, *J* = 4.0 Hz, 0.3H), 3.81 (d, *J* = 4.0 Hz, 0.2H), 3.78 (q, *J* = 4.5 Hz, 0.2H), 3.64 (q, *J* = 9.5 Hz, 0.4H), 3.50-3.47 (m, 0.6H), 3.46-3.44 (m, 0.4H), 3.32-3.18 (m, 1.6H), 2.70-2.65 (m, 1H), 2.10-1.76 (m, 4H), 1.29-1.19 (m, 6H), 1.01 (d, *J* = 7.0 Hz, 0.2H), 0.95 (d, *J* = 6.5 Hz, 1.3H), 0.92 (d, *J* = 7.0 Hz, 0.2H), 0.88 (d, *J* = 7.0 Hz, 1.3H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ169.01, 168.84, 168.67, 168.46, 168.37, 168.11, 168.05, 167.92, 167.70, 167.58, 156.25, 156.21, 136.56, 136.54, 128.55, 128.12, 128.03, 66.86, 62.04, 62.00, 61.81, 61.79, 61.51, 61.38, 61.36, 61.07, 60.26, 60.05, 59.05, 55.70, 55.09, 53.30, 46.93, 46.82, 46.39, 46.06, 43.78, 43.48, 43.37, 37.25, 36.78, 36.35, 36.16, 29.14, 27.60, 24.47, 23.84, 22.73, 22.32, 14.26, 14.17, 14.11, 14.05, 13.38; HRMS (ESI) m/z calcd for $C_{23}H_{33}N_2O_7$ $[(M+H)^+]$ 449.2288, found 449.2278. IR (film) 2976, 1721, 1647, 1243, 1028, 698 cm^{-1};



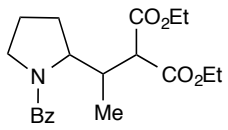
(±)-Diethyl 2-(3-(2-(((benzyloxy)carbonyl)amino)acetamido)-4-phenylbutan-2-yl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Z-Gly-Phe (71.3 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 1.0 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow solid (90 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 7.37-7.30 (m, 5H), 7.27-7.24 (m, 2H), 7.21-7.17 (m, 1H), 7.16-7.12 (m, 2H), 6.44 (d, *J* = 9.0 Hz, 0.6H), 5.92 (d, *J* = 8.0 Hz, 0.4H), 5.21 (br, 1H), 5.13 (s, 2H), 4.47 (q, *J* = 8.0 Hz, 0.4H), 4.24-4.14 (m, 4.6H), 3.76-3.67 (m, 2H), 3.50 (d, *J* = 6.5 Hz, 0.6H), 3.29 (d, *J* = 9.5 Hz, 0.4H), 2.93-2.89 (m, 0.6H), 2.84-2.80 (m, 0.4H), 2.75-2.71 (m, 1H), 2.53-2.41 (m, 1H), 1.27-1.22 (m, 6H), 1.14 (d, *J* = 6.5 Hz, 1.7H), 0.94 (d, *J* = 7.0 Hz, 1.3H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 169.24, 168.99, 168.82, 168.48, 168.38, 156.73, 156.51, 137.73, 137.57, 136.27, 136.21, 129.24, 128.97, 128.60, 128.57, 128.50, 128.48, 128.29, 128.24, 128.03, 126.62, 126.58, 67.12, 67.07, 61.72, 61.64, 61.53, 61.43, 55.59, 53.95, 53.59, 51.67, 44.62, 44.47, 39.32, 38.14, 36.23, 35.91, 15.01, 14.12, 14.07, 14.06, 11.14; HRMS (ESI) m/z calcd for $C_{27}H_{35}N_2O_7$ $[(M+H)^+]$ 449.2444, found 449.2420. IR (film) 3321, 2980, 1722, 1230, 1027, 733, 697 cm^{-1};



(±)-Diethyl 2-(1-(1-((benzyloxy)carbonyl)pyrrolidin-2-yl)ethyl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Z-Pro-OH (50.0 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow oil (72 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 7.42-7.29 (m, 5H), 5.21-5.03 (m, 2H), 4.20-3.84 (m, 5H), 3.69-3.36 (m, 2H), 3.24-3.17 (m, 1H), 2.80-2.73 (m, 0.6H), 2.68-2.63 (m, 0.4H), 2.02-1.72 (m, 4H), 1.28-1.18 (m, 6H), 0.96-0.87 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 169.05, 168.93, 168.87, 168.81, 168.71, 168.56, 168.47, 155.95, 155.85, 155.70, 155.27, 136.87, 136.81, 136.72, 136.65, 128.44, 128.20, 128.14, 127.92, 127.83, 127.77, 67.11, 66.79, 61.70, 61.46, 61.23, 60.56, 60.47, 59.96, 55.58, 55.13, 55.00, 54.50, 47.95, 47.66, 47.26, 46.76, 37.13, 37.05, 29.15, 28.78, 28.27, 28.16, 24.41, 23.79, 23.65, 23.19, 14.22, 14.12, 14.06, 14.02, 13.87, 13.68, 13.48; HRMS (ESI) m/z calcd for $C_{21}H_{30}NO_6$ [$(M+H)^+$] 392.2073, found 392.2066. IR (film) 2977, 1695, 1405, 1096, 1027, 697 cm^{-1};

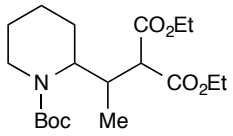


(±)-Diethyl 2-(1-(1-(*tert*-butoxycarbonyl)pyrrolidin-2-yl)ethyl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Boc-Pro-OH (43.0 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow oil (69 mg, 97%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 4.22-4.11 (m, 4H), 3.97-3.30 (m, 3H), 3.17-3.12 (m, 0.55H), 3.11-3.06 (m, 0.45H), 2.75-2.71 (m, 0.83H), 2.60-2.53 (m, 0.17H), 2.00-1.67 (m, 4H), 1.46 (s, 9H), 1.28-1.23 (m, 6H), 0.94-0.88 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 168.88, 168.73, 168.36, 155.43, 155.20, 154.79, 79.77, 79.07, 61.29, 61.12, 60.52, 60.26, 59.91, 55.52, 54.74, 54.00, 47.72, 47.14, 46.95, 46.81, 37.00, 36.77, 28.45, 28.42, 24.37, 23.77, 23.48, 23.26, 14.08, 14.02; HRMS (ESI) m/z calcd for $C_{18}H_{32}NO_6$ [$(M+H)^+$] 358.2230, found 358.2235. IR (film) 2975, 1729, 1689, 1381, 1365, 1162, 1105, 1030, 773 cm^{-1};



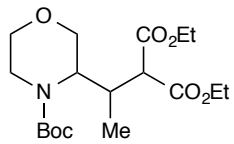
(±)-Diethyl 2-(1-(1-benzoylpyrrolidin-2-yl)ethyl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (5.5 mg, 5 μmol, 0.01 equiv.), Benzoyl-*L*-proline (110 mg, 0.5 mmol, 1.0 equiv.), K_2HPO_4 (105 mg, 0.6 mmol, 1.2 equiv.), diethyl 2-ethylidenemalonate (93 mg, 0.5 mmol, 1.0 equiv.) and DMF (1.25 mL) were used. The product was isolated by flash chromatography (30% ethyl acetate in hexanes) as a pale yellow oil (150 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and

rotamers : δ 7.56-7.48 (m, 2H), 7.44-7.34 (m, 3H), 4.57 (td, *J* = 8.0, 3.0 Hz, 0.4H), 4.48-4.42 (m, 0.6H), 4.30-4.10 (m, 4H), 3.82 (d, *J* = 10.0 Hz, 0.4H), 3.54-3.47 (m, 1H), 3.44-3.36 (m, 1.6H), 3.02-2.93 (m, 0.6H), 2.80-2.71 (m, 0.4 H), 2.26-2.17 (m, 0.4H), 2.20-1.56 (m, 3.6 H), 1.29-1.19 (m, 6H), 1.01-0.99 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 171.51, 170.63, 169.34, 169.20, 168.88, 168.68, 136.88, 136.82, 130.24, 130.14, 128.16, 128.10, 127.69, 127.61, 61.37, 61.25, 61.21, 61.17, 59.92, 59.05, 55.48, 51.99, 50.81, 37.31, 35.29, 29.42, 26.82, 25.40, 25.12, 14.12, 14.09, 14.02, 14.00, 12.97, 12.49; HRMS (ESI) *m/z* calcd for $C_{20}H_{28}NO_5$ [$(M+H)^+$] 362.1962, found 362.19642. IR (film) 2977, 1747, 1726, 1627, 1394, 1265, 1174, 1150, 1027, 792, 700 cm^{-1}.

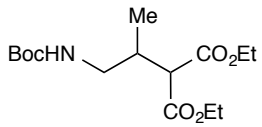


(±)-Diethyl 2-(1-(1-(*tert*-butoxycarbonyl)piperidin-2-yl)ethyl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Boc-Pip-OH (45.8 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow oil (70 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers: δ 4.26-3.95 (m, 6H), 3.43 (d, *J* = 4.5 Hz, 1H), 2.79-2.68 (m, 2H), 1.80-1.78 (m, 0.4H), 1.71-1.69 (m, 0.6H), 1.58-1.49 (m, 5H), 1.44 (s, 9H), 1.30-1.24 (m, 6H), 1.07 (d, *J* = 6.5 Hz, 1.3H), 0.99 (d, *J* = 7.0 Hz, 1.7H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers: δ 169.87, 169.24, 168.52, 168.24, 155.16, 155.14, 79.50, 79.39, 61.49, 61.39, 61.17, 60.91,

53.37, 53.14, 31.97, 31.70, 28.49, 28.45, 26.18, 25.39, 19.04, 18.89, 14.21, 14.14, 14.11, 13.80, 12.90; HRMS (ESI) m/z calcd for $C_{19}H_{33}NNaO_6$ [$(M+Na)^+$] 394.2206, found 394.2192. IR (film) 2977, 2935, 1687, 1150, 1028, 866 cm^{-1};

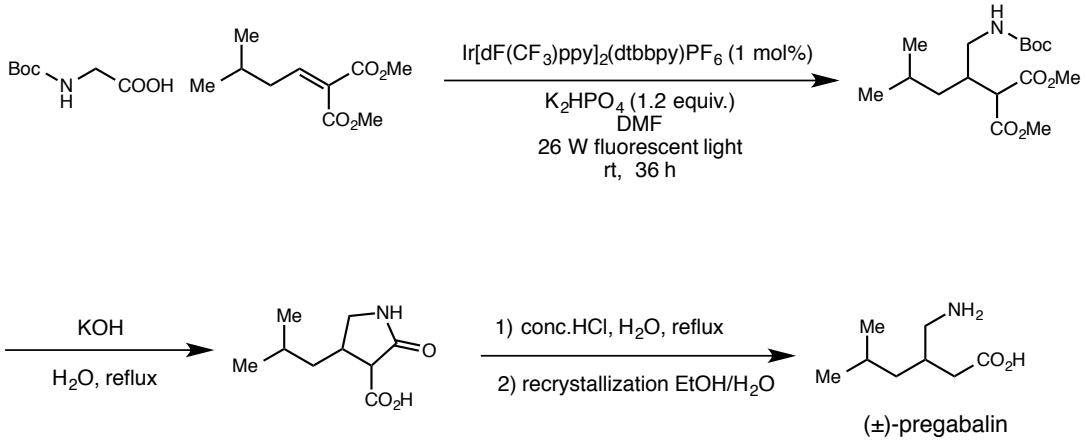


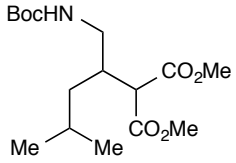
(±)-Diethyl 2-(1-(4-(*tert*-butoxycarbonyl)morpholin-3-yl)ethyl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Boc-Morph-OH (46.2 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.20 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow oil (71 mg, 95%). ^1H NMR (500 MHz, $CDCl_3$) mixture of diastereomers: δ 4.23-4.10 (m, 4H), 4.01-3.78 (m, 4H), 3.51-3.44 (m, 3H), 3.13-3.03 (m, 1H), 2.93-2.85 (m, 1H), 1.46 (s, 4.5H), 1.45 (s, 4.5H); 1.30-1.25 (m, 6H), 1.16 (d, J = 7.0 Hz, 1.5H), 1.05 (d, J = 7.0 Hz, 1.5H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers: δ 168.83, 168.26, 168.22, 154.76, 154.59, 80.28, 67.21, 67.14, 61.48, 61.27, 60.97, 52.90, 52.66, 31.21, 28.40, 28.36, 14.21, 14.16, 14.14, 14.09, 13.67, 12.80; HRMS (ESI) m/z calcd for $C_{18}H_{31}NNaO_7$ [$(M+Na)^+$] 396.1998, found 396.1995. IR (film) 2978, 1729, 1690, 1103, 866 cm^{-1};



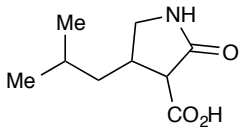
(±)-Diethyl 2-(1-((*tert*-butoxycarbonyl)amino)propan-2-yl)malonate: According to the general procedure, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Boc-Gly-OH (35.0 mg, 0.2 mmol, 1.0 equiv), diethyl ethylidenemalonate (37.3 mg, 0.2 mmol, 1.0 equiv), K_2HPO_4 (42.0 mg, 0.24 mmol, 1.2 equiv), and 0.5 mL of DMF were used. The product was isolated by flash chromatography (25% ethyl acetate/hexane) as a pale yellow oil (60 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers: δ 4.71 (s, 1H), 4.20 (qd, J = 7.0 Hz, J = 2.0 Hz, 4H), 3.31 (d, J = 7.5 Hz, 1H), 3.22-3.12 (m, 2H), 2.48-2.43 (m, 1H), 1.43 (s, 9H), 1.27 (d, J = 7.5 Hz, 6H), 1.01 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers: δ 168.78, 168.56, 155.96, 79.21, 61.41, 61.35, 55.02, 44.18, 34.08, 28.37, 15.52, 14.09, 14.06; HRMS (ESI) m/z calcd for $C_{15}H_{27}NNaO_6$ [$(M+Na)^+$] 340.1736, found 340.1739. IR (film) 2978, 1714, 1515, 1246, 1164, 1030 cm^{-1};

3. Synthetic Procedures and Characterization of (±)-Lyrica



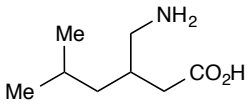


(±)-Dimethyl 2-(1-((*tert*-butoxycarbonyl)amino)-4-methylpentan-2-yl)malonate: According to the general procedure of decarboxylative alkylation, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (2.2 mg, 2 μmol, 0.01 equiv.), Boc-Gly-OH (35 mg, 0.2 mmol, 1.0 equiv.), K_2HPO_4 (41.8 mg, 0.24 mmol, 1.2 equiv.), dimethyl 2-(3-methylbutylidene)malonate (42.4 mg, 0.2 mmol, 1.0 equiv.) and DMF (0.5 mL) were used. The product was isolated by flash chromatography (30% ethyl acetate in hexanes) as a pale yellow oil (64 mg, 96%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of rotamers : δ 4.80 (br, 0.8H), 4.66 (br, 0.2H), 3.66 (d, *J* = 2.5 Hz, 6H), 3.36 (d, *J* = 6.5 Hz, 1H), 3.23-3.18 (m, 1H), 3.22-3.19 (m, 1H), 3.11-3.01 (m, 1H), 2.40-2.33 (m, 1H), 1.65-1.54 (m, 1H), 1.45 (s, 9H), 1.19-1.13 (m, 1H), 1.06-0.99 (m, 1H), 0.82 (m, 6H); ^{13}C NMR mixture of rotamers (125 MHz, $CDCl_3$): δ 169.29, 155.83, 79.01, 53.62, 52.36, 52.33, 41.51, 39.14, 36.96, 28.31, 25.26, 23.21, 21.85; HRMS (ESI) *m/z* calcd for $C_{16}H_{29}NNaO_6$ $[(M+Na)^+]$ 354.1887, found 354.1888. IR (film) 2956, 1732, 1713, 1509, 1435, 1366, 1246, 1159, 1018 cm^{-1};



(±)-4-Isobutyl-2-oxopyrrolidine-3-carboxylic acid: A flask was charged with (±)-Dimethyl 2-(1-((*tert*-butoxycarbonyl)amino)-4-methylpentan-2-yl)mlonate (450 mg, 1.36 mmol) and KOH (229 mg, 4.07 mmol, 3 equiv.) solution in water (2 mL) and the mixture

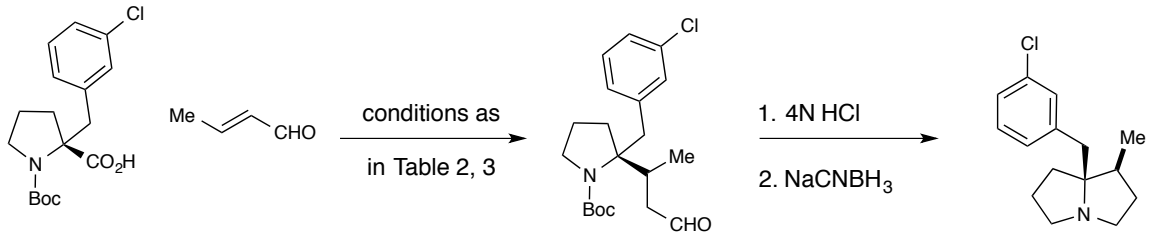
was heated to reflux for 20 h and then cooled to room temperature. The pH of the solution was adjusted to 2 with conc. HCl and diluted with ethyl acetate. The solution was extracted twice with ethyl acetate and concentrated. The residue was purified by column chromatography (3% methanol in dichloromethane then 10% methanol in dichloromethane) to give a colorless powder (200 mg, 80%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.87 (br, 1H), 7.47 (s, 1H), 3.52 (t, *J* = 9.0 Hz, 1H), 3.02 (t, *J* = 9.0 Hz, 1H), 2.97 (t, *J* = 8.0 Hz, 1H), 2.88-2.79 (m, 1H), 1.57-1.47 (m, 2H), 1.35-1.26 (m, 1H), 0.86 (d, *J* = 6.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.24, 172.14, 53.81, 47.18, 43.31, 36.87, 25.94, 22.90, 22.19; HRMS (ESI) *m/z* calcd for $C_9H_{16}NO_3$ [$(M+H)^+$] 186.1125, found 186.1125;

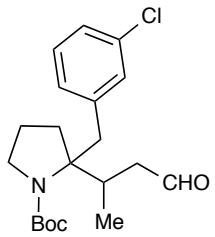


(±)-3-(Aminomethyl)-5-methylhexanoic acid [known compound (*3*)]**:** A flask was charged with (±)-4-isobutyl-2-oxopyrrolidine-3-carboxylic acid (200 mg, 1.08 mmol), solution of conc. HCl (240 mg, 2.37 mmol, 2.2 equiv.) in water (2 mL) and acetic acid (20 mg, 0.33 mmol, 0.31 equiv.). The mixture was heated to reflux for 48 h and then cooled to room temperature. The solution was concentrated and the residue was purified by ion-exchange chromatography on Dowex 50W-8 (H^+) (H_2O until pH 7 and then 0.5 mol/L NH_4OH). Fractions containing product were concentrated and crystallized from ethanol and water to give a colorless powder (121 mg, 70%). mp 166.5-167.7 °C. ^{1}H NMR (500 MHz, D_2O): δ 2.93-2.82 (m 2H), 2.24-2.05 (m, 3H), 1.58-1.53 (m, 1H), 1.12 (t, *J* = 7.5 Hz, 2H), 0.79 (dd, *J* = 6 Hz, 6H); ^{13}C NMR (125 MHz, D_2O): δ 181.18, 43.63,

40.69, 40.54, 31.66, 24.35, 21.94, 21.47; HRMS (ESI) *m/z* calcd for $C_8H_{18}NO_2$ $[(M+H)^+]$ 160.1332, found 160.1331;

4. Synthetic Procedures and Characterization of Pyrrolizidine

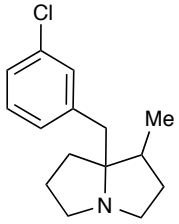




(±)-*tert*-Butyl-2-(3-chlorobenzyl)-2-(4-oxobutan-2-yl)pyrrolidine-1-carboxylate:

According to the general procedure of decarboxylative alkylation, $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (4.4 mg, 4 μmol, 0.01 equiv.), 1-(*tert*-butoxycarbonyl)-2-(3-chlorobenzyl)pyrrolidine-2-carboxylic acid (136.0 mg, 0.4 mmol, 1.0 equiv), crotonaldehyde (28.0 mg, 0.4 mmol, 1.0 equiv), K_2HPO_4 (84.0 mg, 0.48 mmol, 1.2 equiv), and 1.4 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow oil (135 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 9.79-9.77 (m, 0.3H), 9.74-9.73 (m, 0.3H), 9.61 (t, *J* = 2.5 Hz, 0.4H), 7.22-7.12 (m, 3H), 7.05-7.02 (m, 0.7H),

7.00-6.98 (m, 0.3H), 3.65-3.62 (m, 0.6H), 3.49-3.45 (m, 0.4H), 3.36-3.22 (m, 1H), 3.11-2.90 (m, 2H), 2.75-2.56 (m, 1.4H), 2.42-2.05 (m, 1.6H), 1.88-1.68 (m, 2H), 1.58-1.15 (m, 8H), 1.34-1.28 (m, 1H), 1.05-1.03 (m, 1.7H), 0.91-0.86 (m, 1.3H), 0.68-0.45 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 202.48, 202.31, 201.37, 201.29, 153.93, 153.89, 153.81, 153.77, 140.64, 140.55, 140.38, 140.20, 134.05, 134.02, 133.98, 133.96, 130.46, 130.42, 130.32, 130.24, 129.59, 129.57, 129.22, 128.57, 128.43, 128.25, 126.76, 126.73, 126.54, 80.66, 80.42, 79.51, 79.25, 69.48, 69.02, 68.92, 68.48, 49.43, 49.39, 49.29, 49.10, 47.70, 47.33, 47.14, 46.13, 41.62, 41.28, 40.52, 40.26, 34.59, 34.51, 34.50, 34.09, 32.47, 32.07, 31.07, 30.82, 28.76, 28.69, 28.65, 28.54, 21.73, 21.51, 21.11, 20.87, 16.74, 16.58, 14.66, 14.56; HRMS (ESI) m/z calcd for $C_{20}H_{28}ClNNaO_3$ [$(M+Na)^+$] 388.1655, found 388.1657.



7a-(3-Chlorobenzyl)-1-methylhexahydro-1*H*-pyrrolizine: To a stirring solution of (±)-*tert*-Butyl-2-(3-chlorobenzyl)-2-(4-oxobutan-2-yl)pyrrolidine-1-carboxylate (80 mg, 0.2 mmol, 1.0 equiv.) in CH_2Cl_2 (2 mL) at room temperature was added 4N HCl in dioxane (1 mL). The reaction mixture was stirred at room temperature for 4 hours, and then evaporated in vacuo. The crude aldehyde was dissolved in THF/H_2O (3 mL, 2:1) and added $NaCNBH_4$ (42 mg, 0.6 mmol, 3.0 equiv.). The reaction mixture was stirred at room temperature until the reaction was completed (judged by TLC). Saturated aqueous

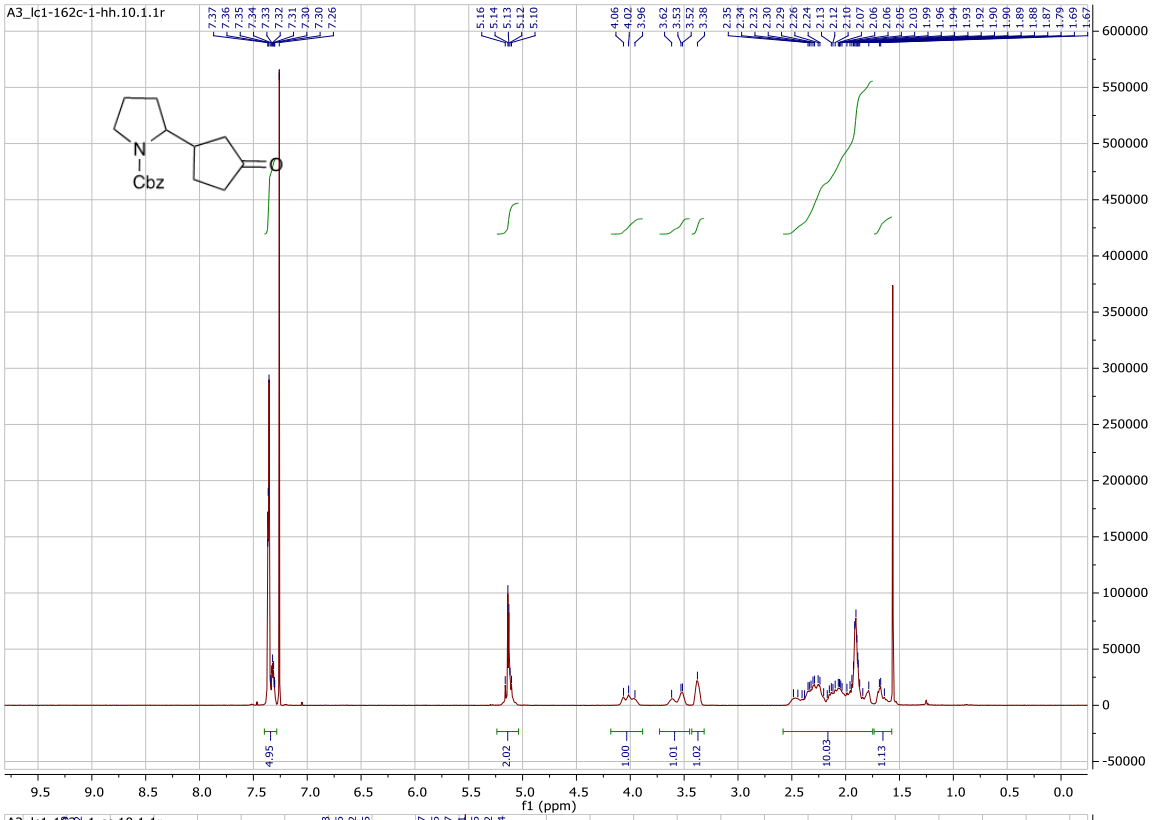
$NaHCO_3$ solution was added to the reaction mixture. The layers were separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated. The residue was purified by flash chromatography (5% MeOH/CH_2Cl_2). Two separated isomers were isolated (23 mg and 12 mg, 71% yield in total). Major isomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 (s, 1H), 7.23-7.20 (m, 1H), 7.17-7.14 (m, 2H), 3.24 (t, *J* = 8.0 Hz, 1H), 2.58-2.56 (m, 1H), 2.49-2.36 (m, 4H), 1.93-1.88 (m, 1H), 1.84-1.76 (m, 1H), 1.64-1.45 (m, 4H), 1.19-1.15 (m, 1H), 1.06 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.00, 133.10, 131.41, 129.68, 128.53, 125.73, 56.15, 54.67, 44.60, 40.86, 35.02, 34.20, 29.85, 25.00, 14.39; Minor isomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (br, 1H), 7.19-7.18 (m, 3H), 3.25-3.21 (m, 1H), 2.84-2.79 (m, 1H), 2.67 (s, 2H), 2.56-2.48 (m, 2H), 2.02-1.94 (m, 1H), 1.77-1.71 (m, 1H), 1.66-1.50 (m, 4H), 1.44-1.37 (m, 1H), 0.81 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.49, 133.58, 130.66, 129.03, 128.93, 126.24, 56.88, 53.67, 46.13, 40.79, 32.30, 31.40, 29.85, 25.42, 15.17; HRMS (ESI) m/z calcd for $C_{15}H_{21}ClN$ [$(M+H)^+$] 250.1363, found 250.1359. IR (film) 2942, 1471, 1081, 780, 708 cm^{-1};

References

1. D. D. Perrin, W. L. F. Armarego, *Purification of Laboratory Chemicals* (Pergamon, Oxford, ed. 3, 1988).

2. Maas, S.; Stamm, A.; Kunz, H. *Synthesis* **1999**, 1792.

3. Martinez, C. A.; Hu, S.; Dumond, Y.; Tao, J.; Kelleher, P.; Tully, L. *Org. Process Res. Dev.* **2008**, *12*, 392.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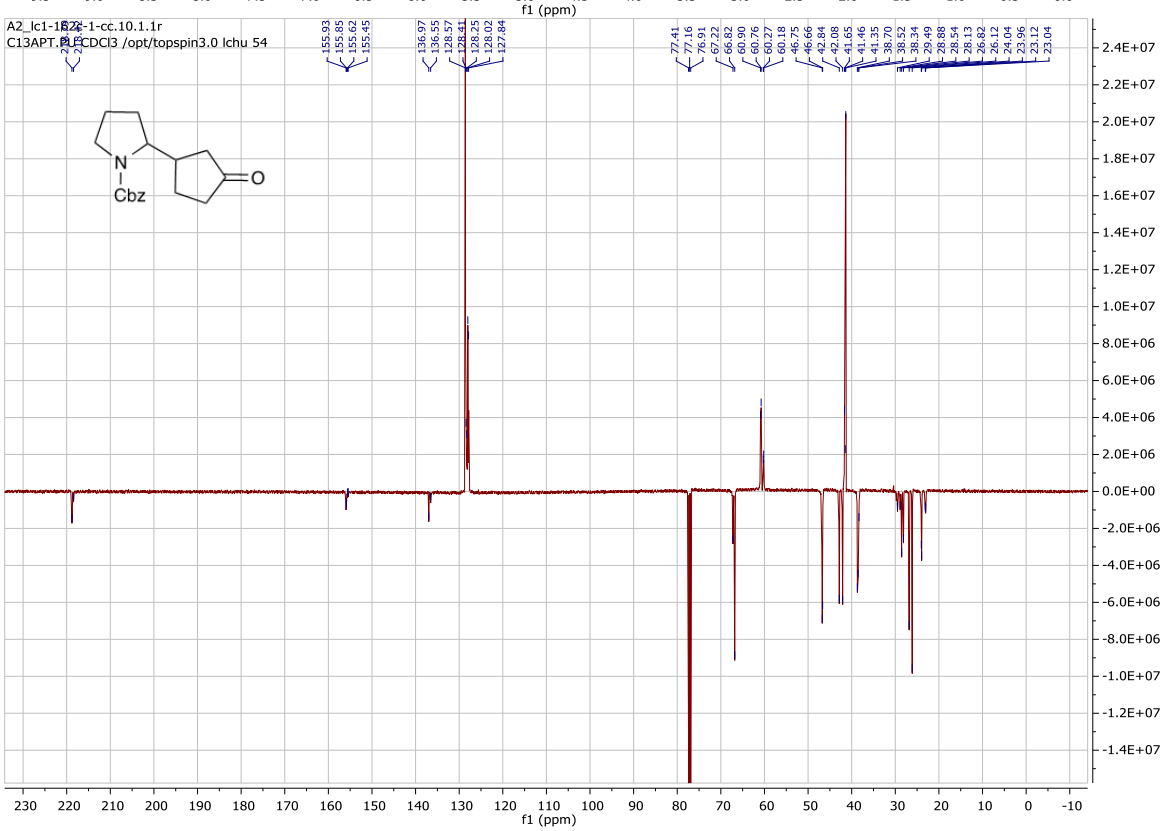
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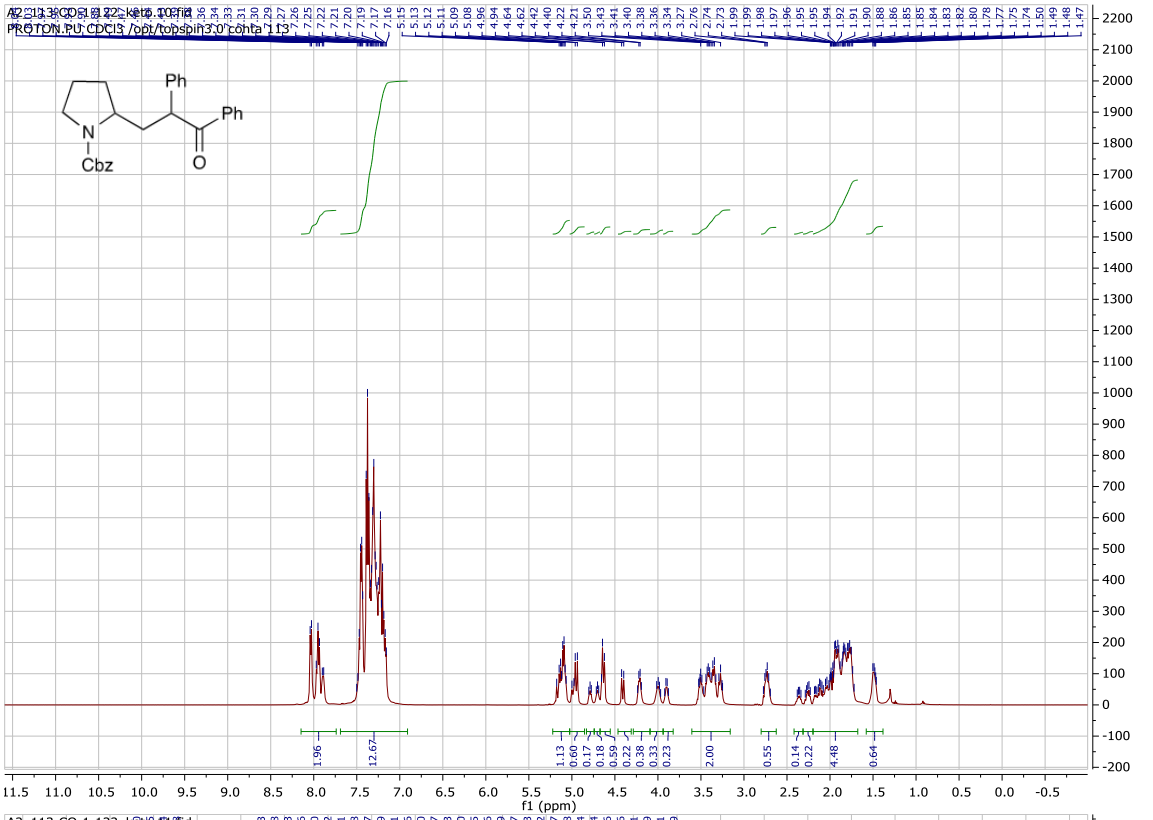
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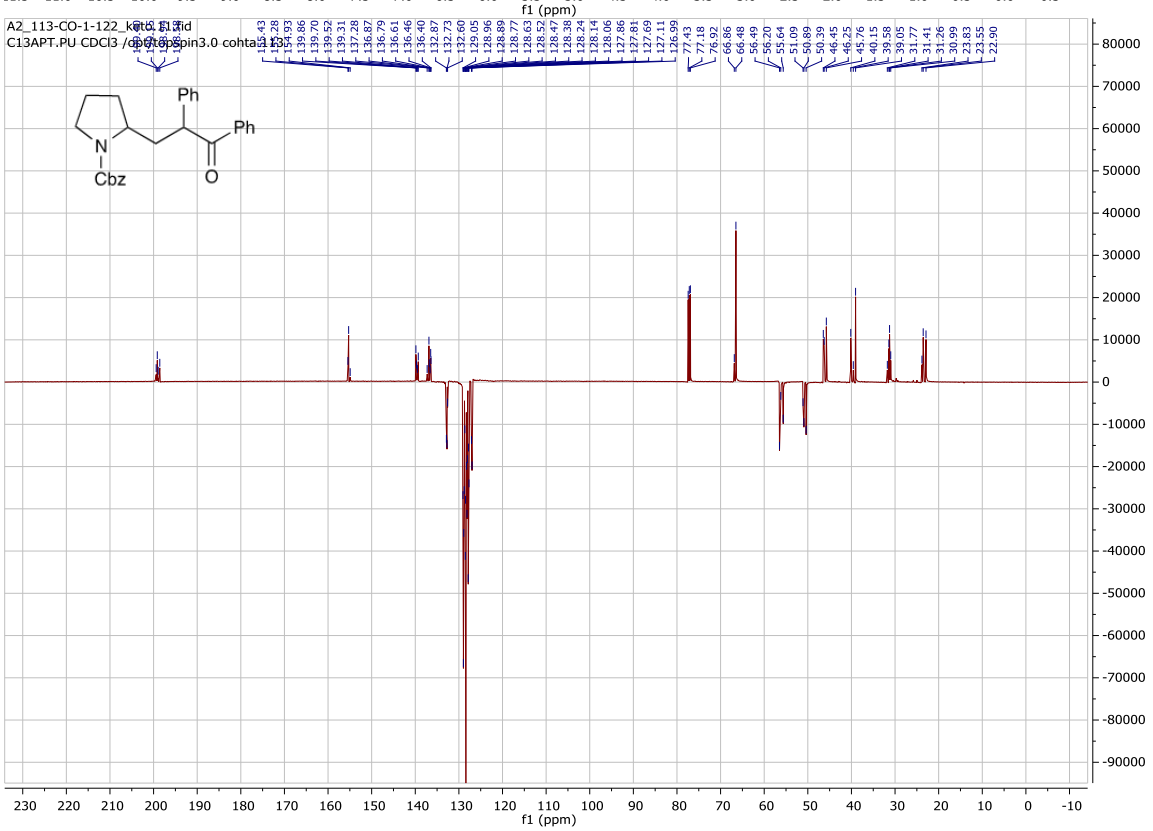
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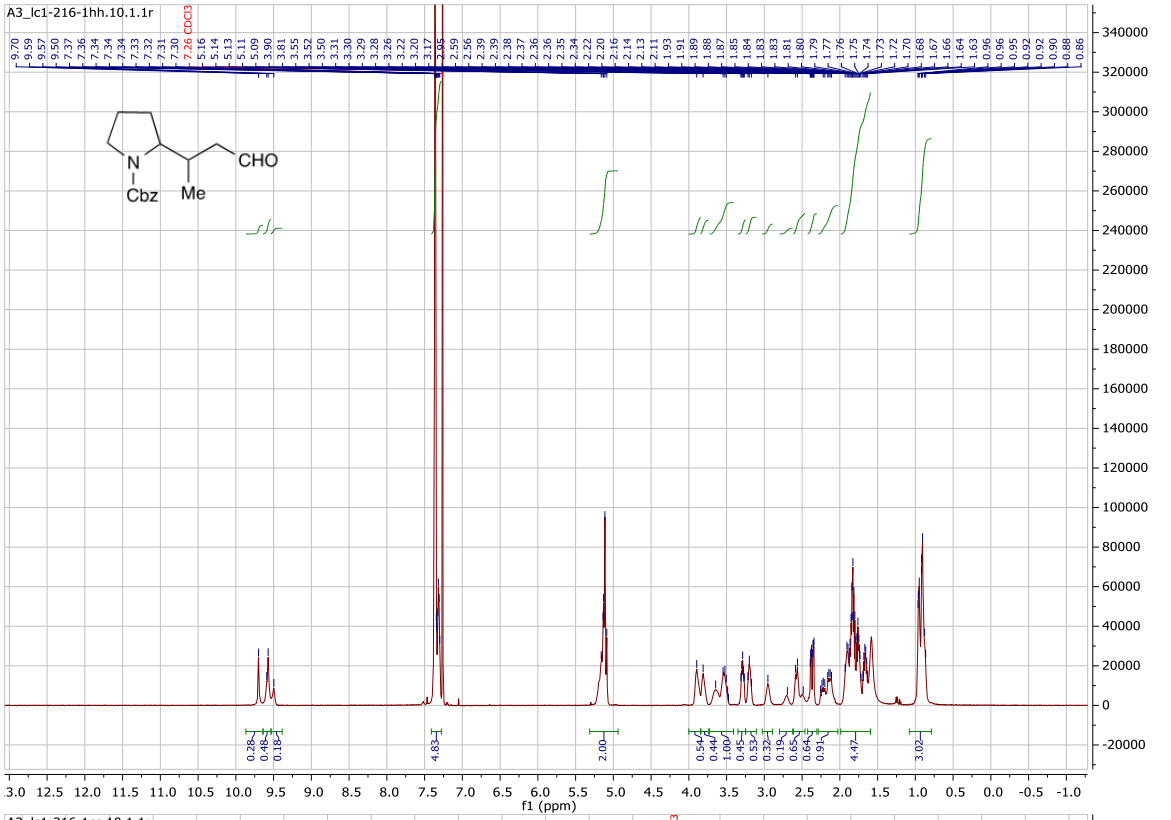
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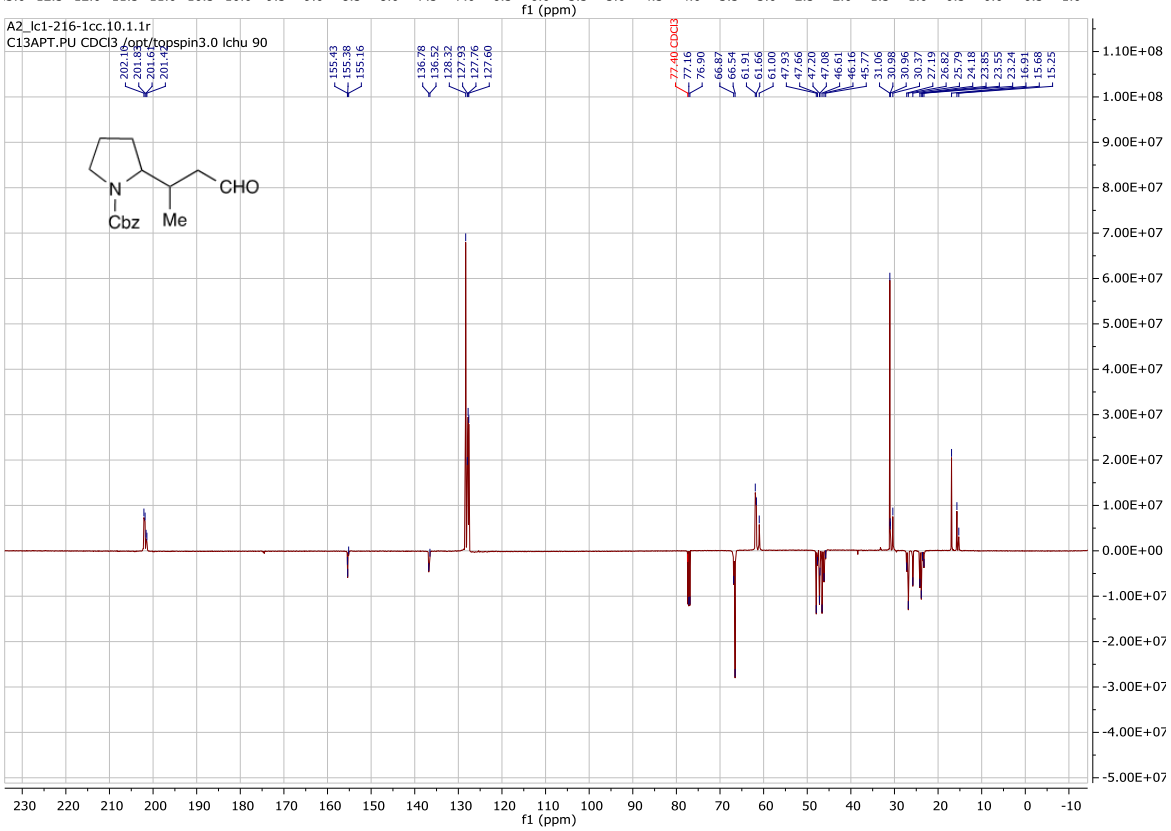
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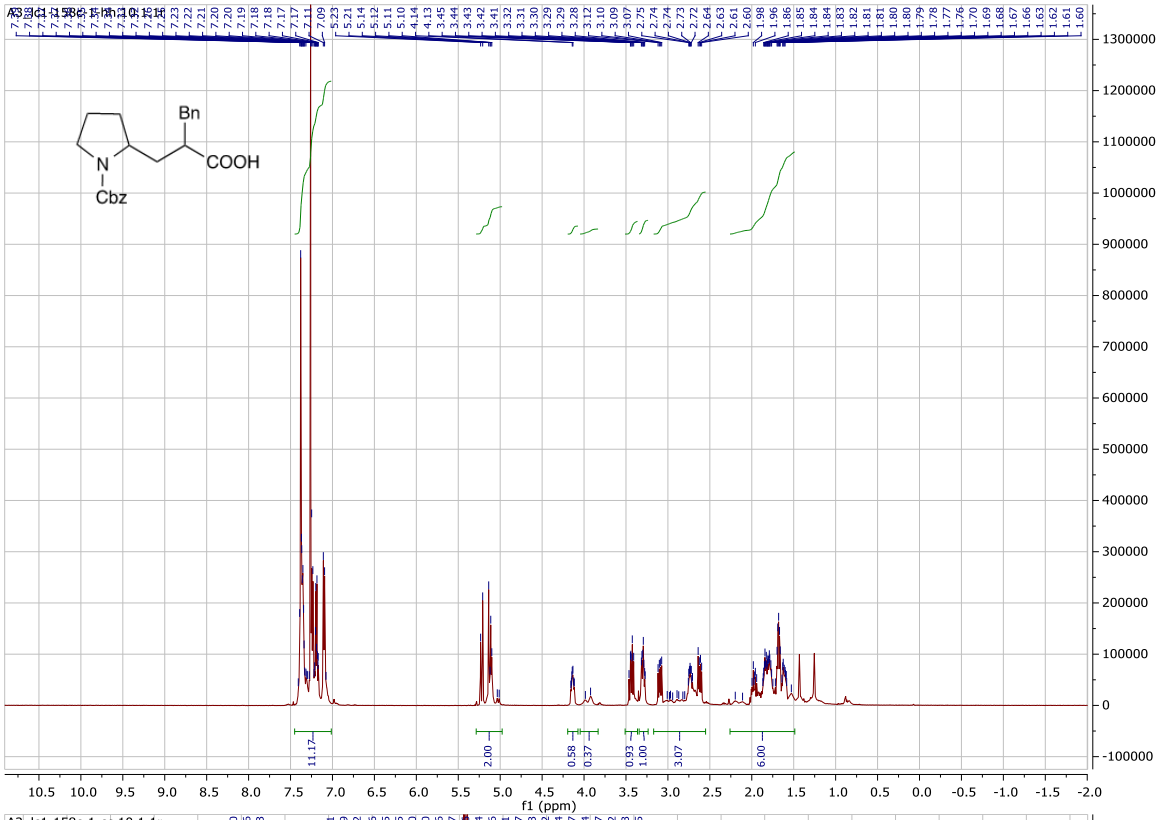
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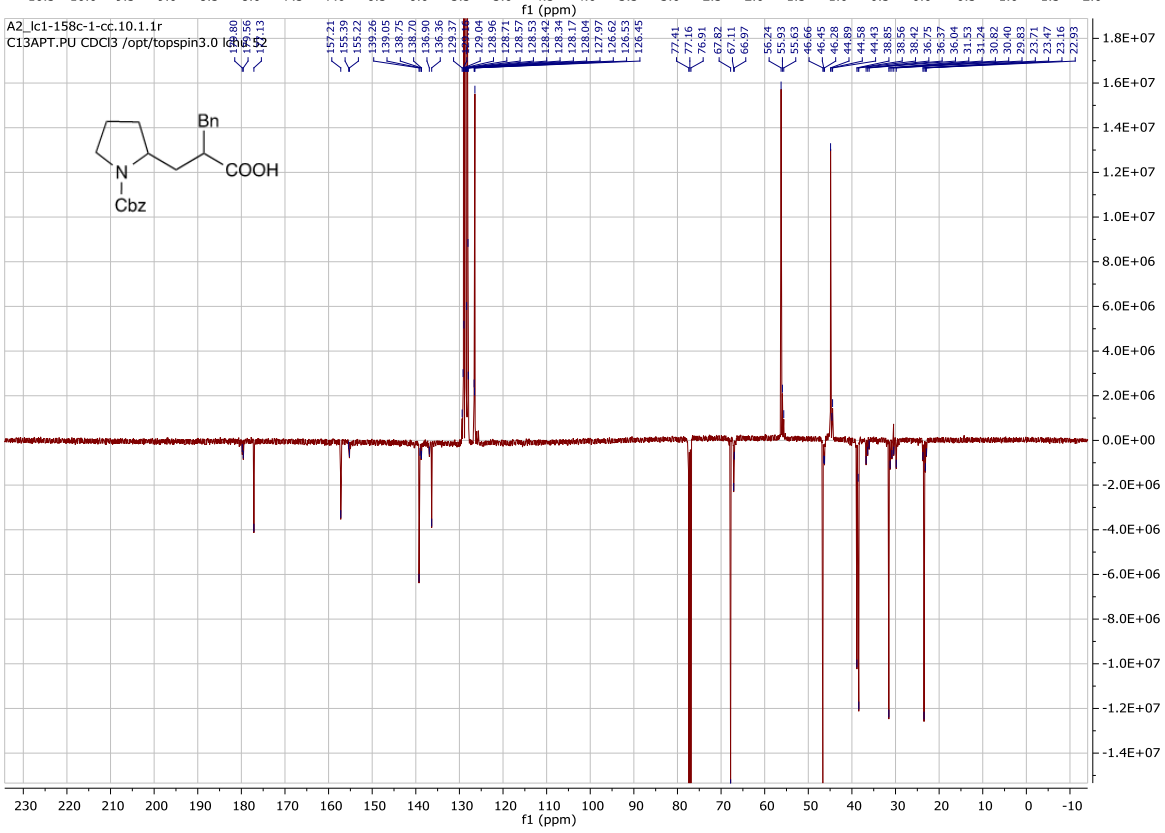
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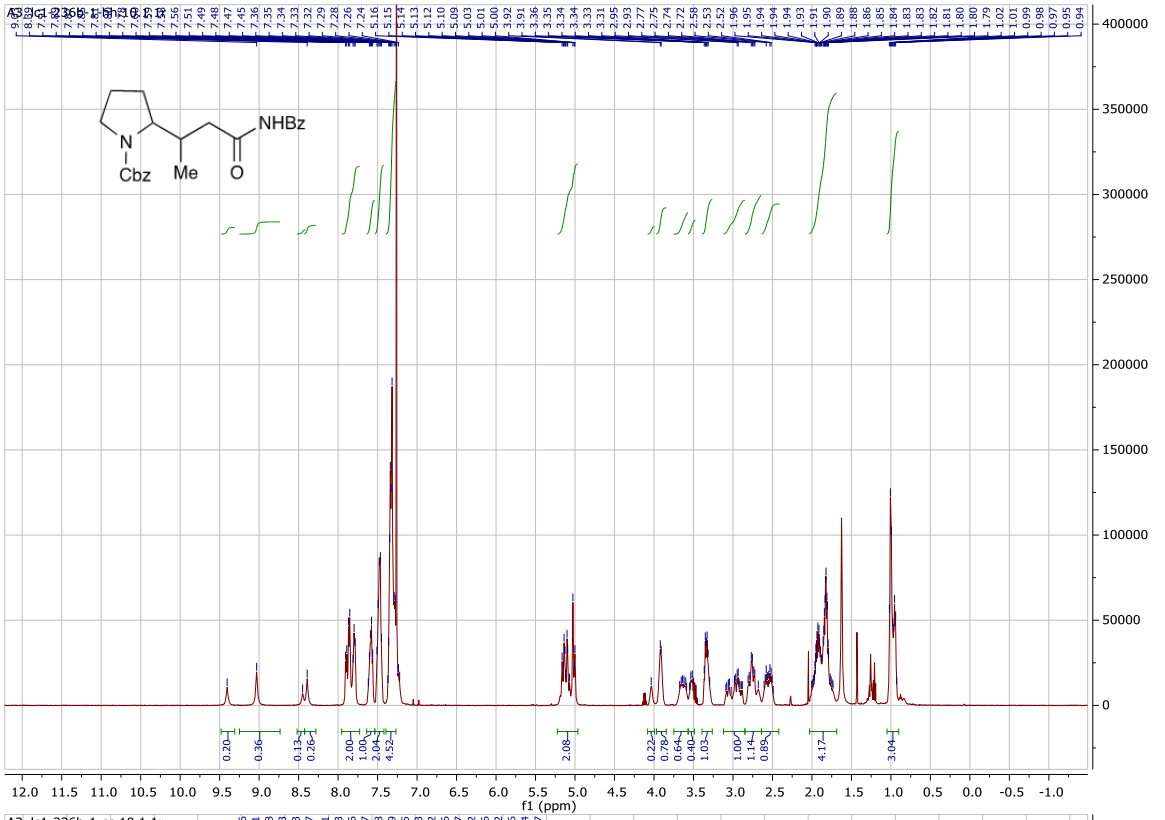
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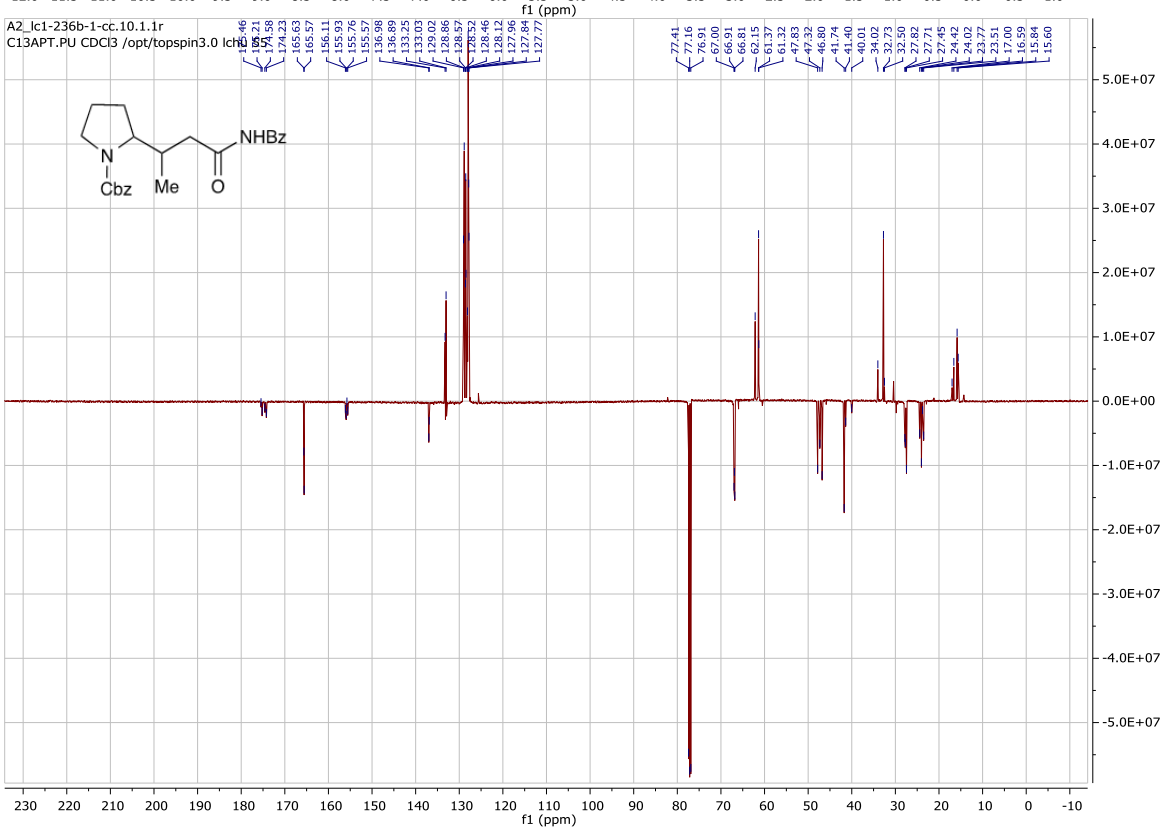
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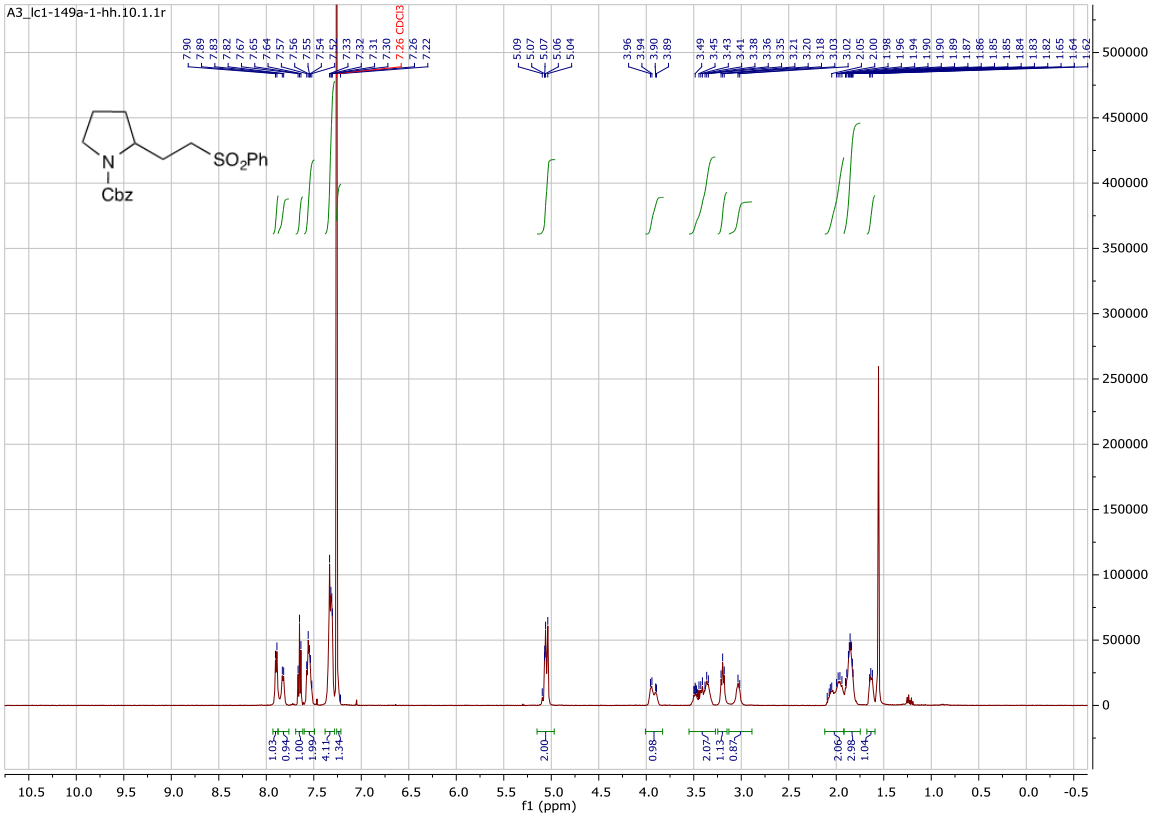
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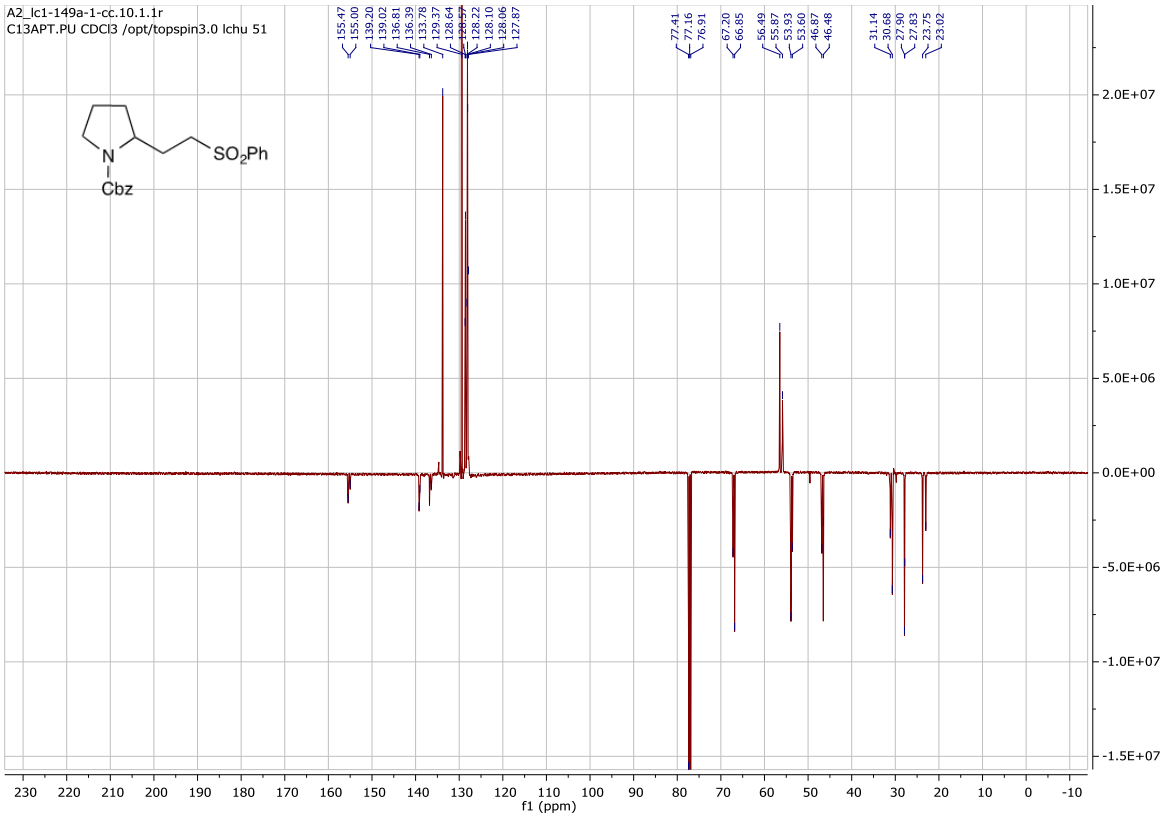
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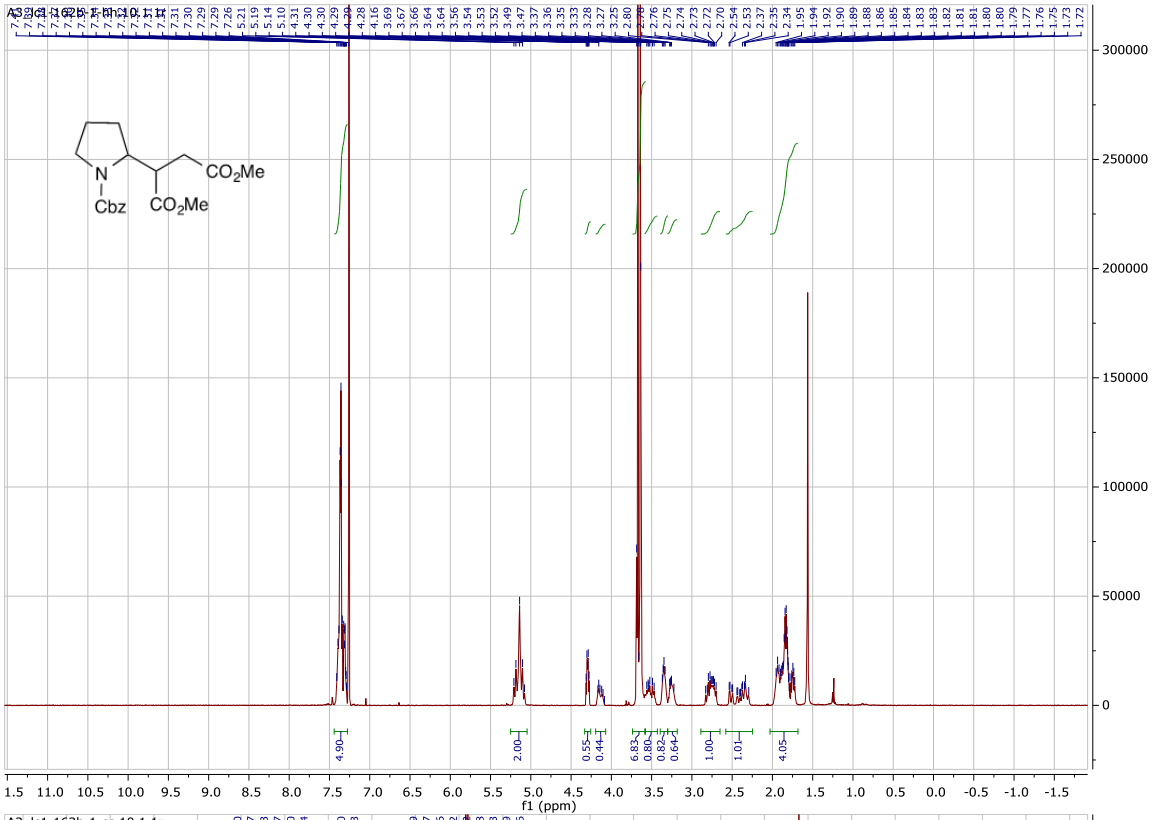
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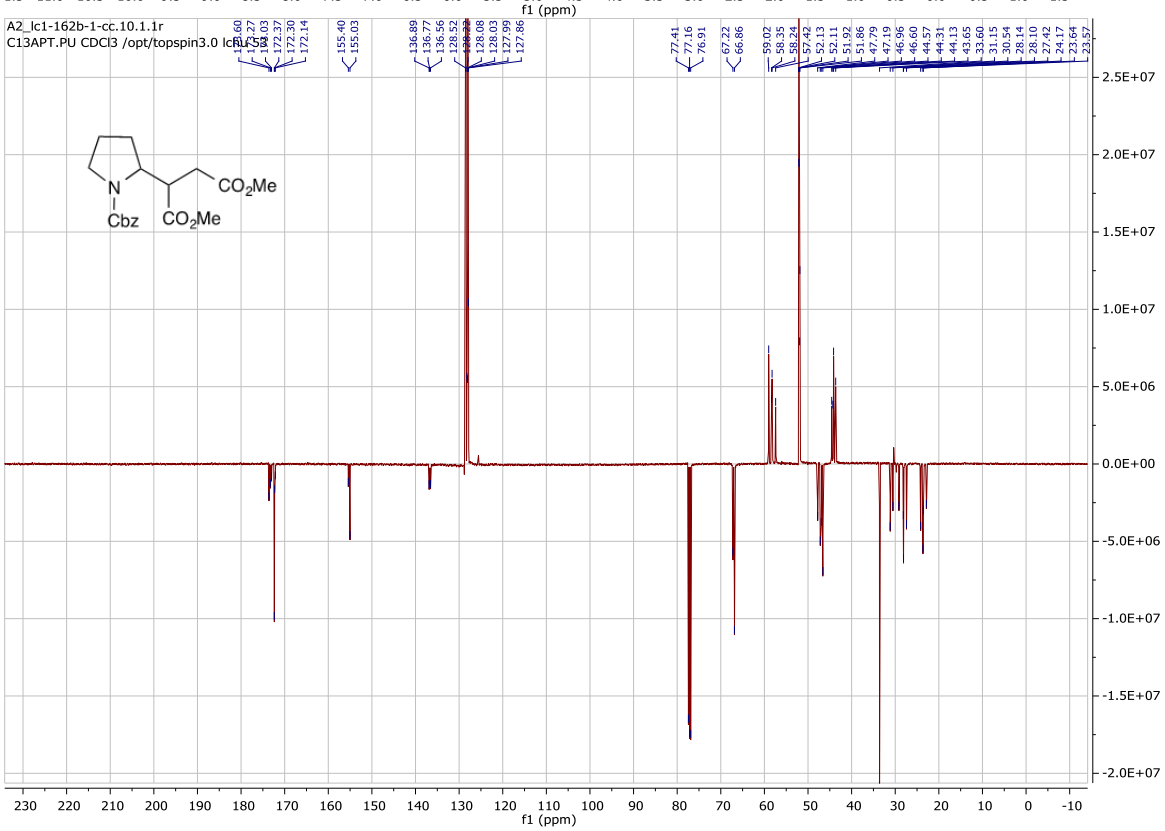
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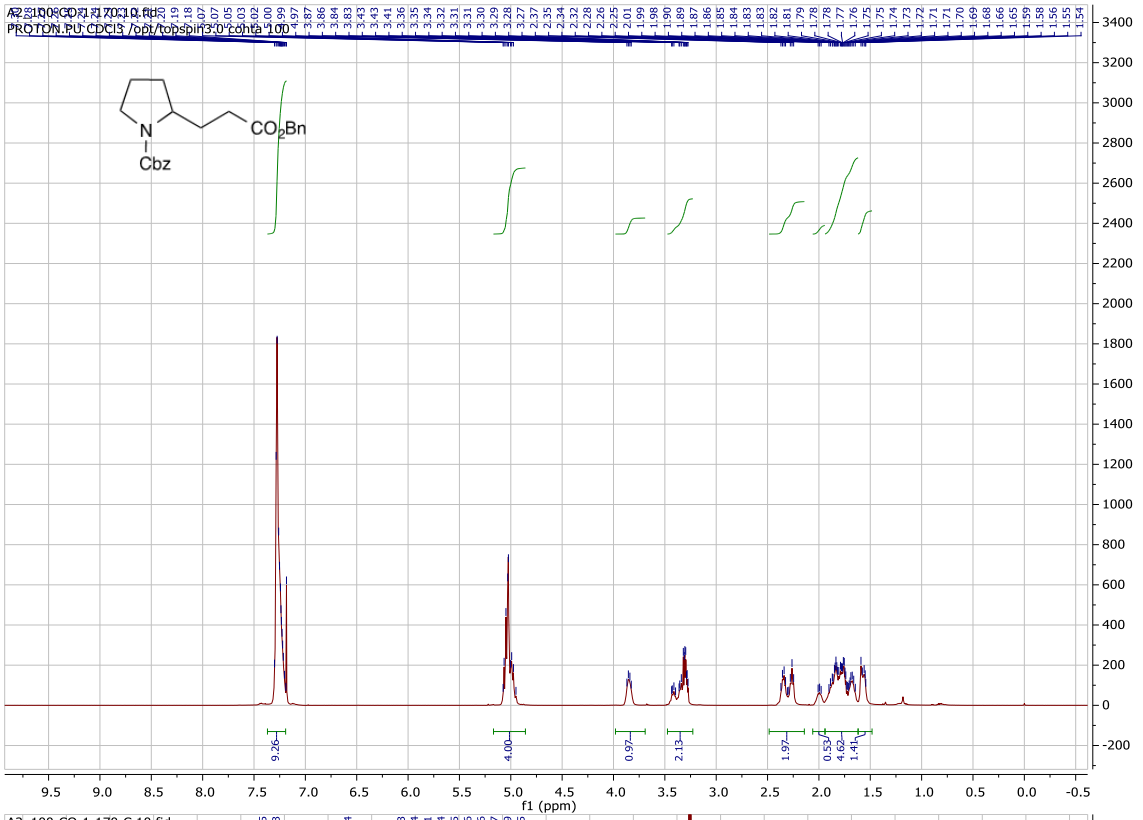
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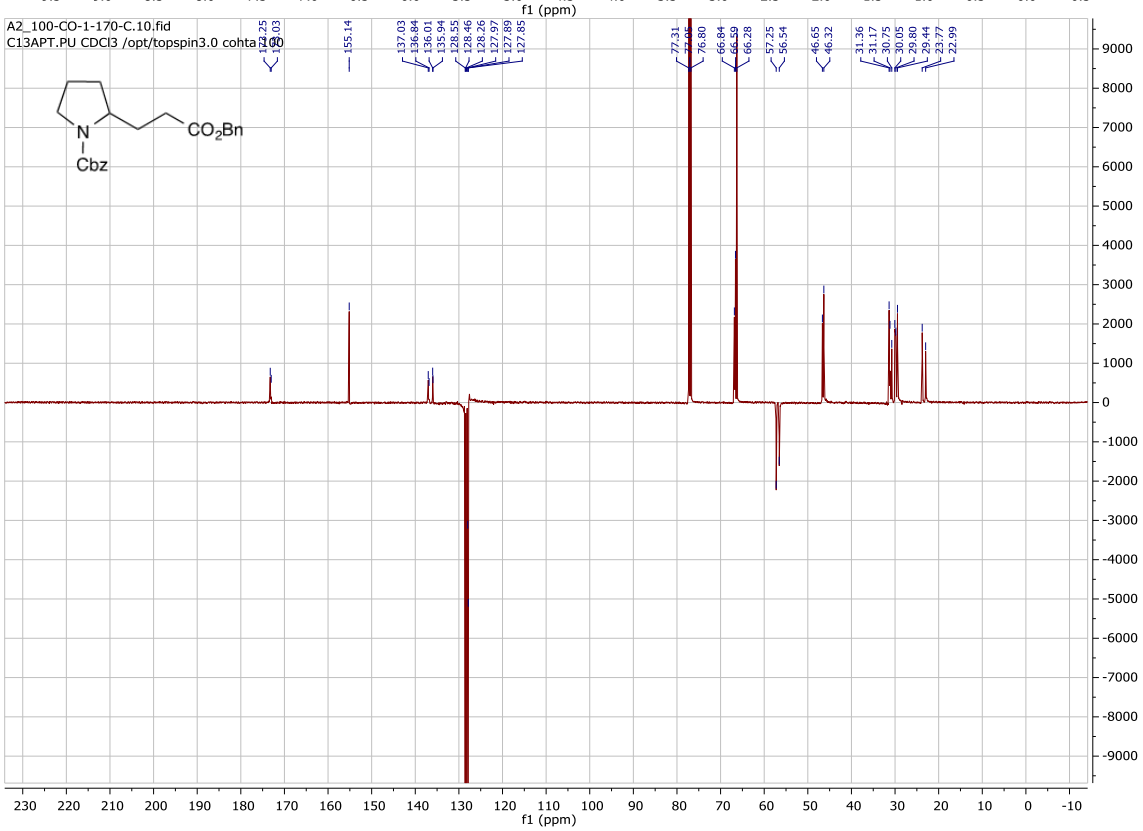
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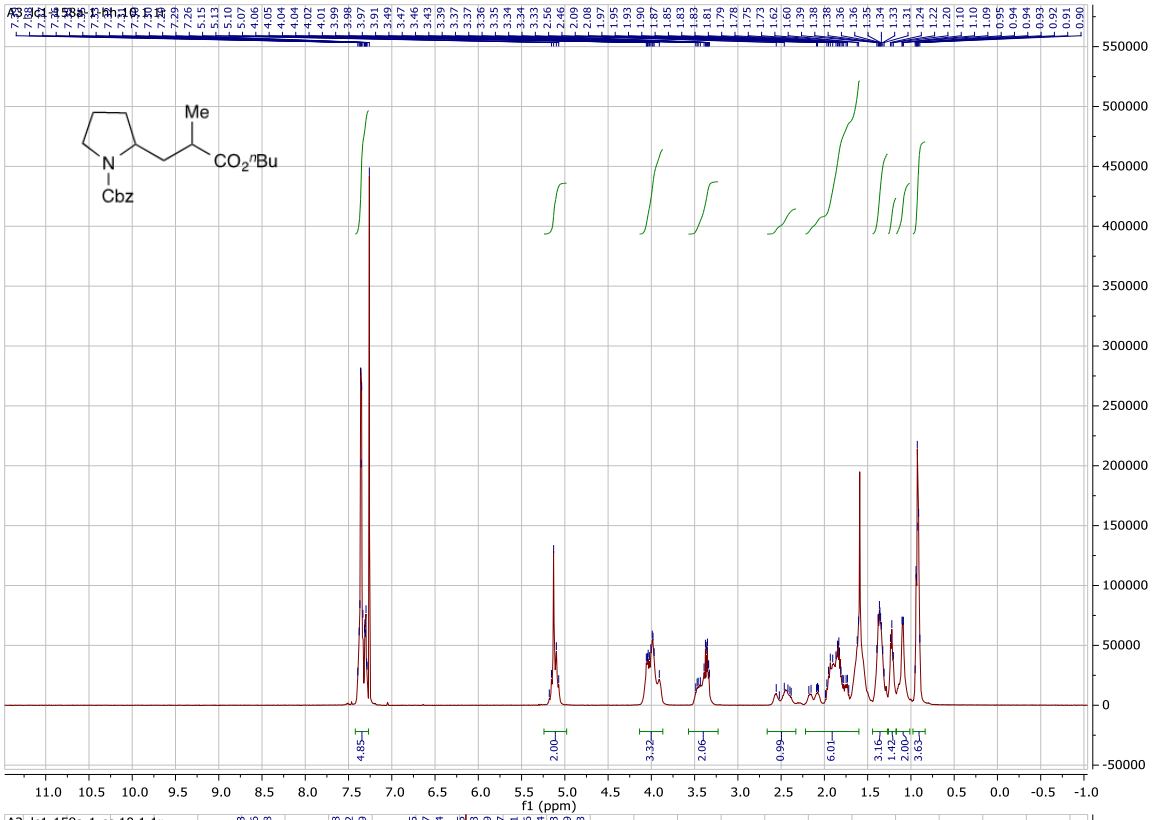
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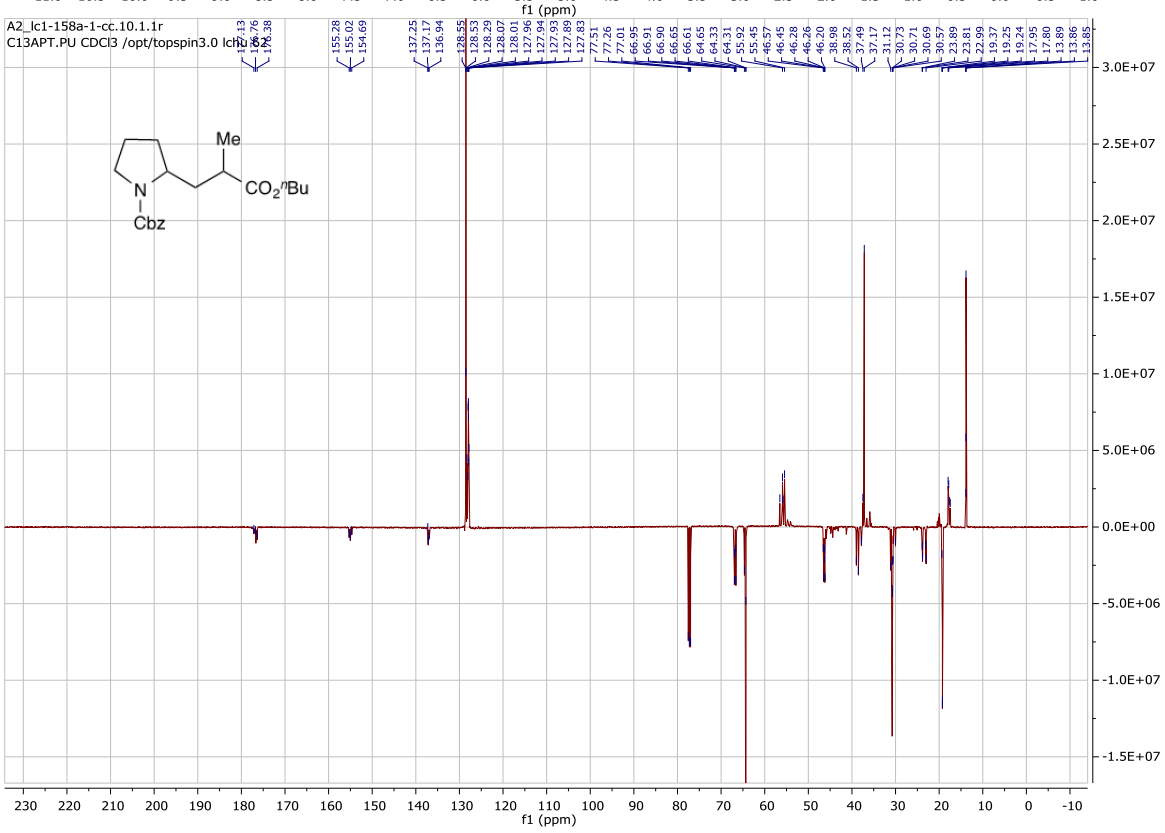
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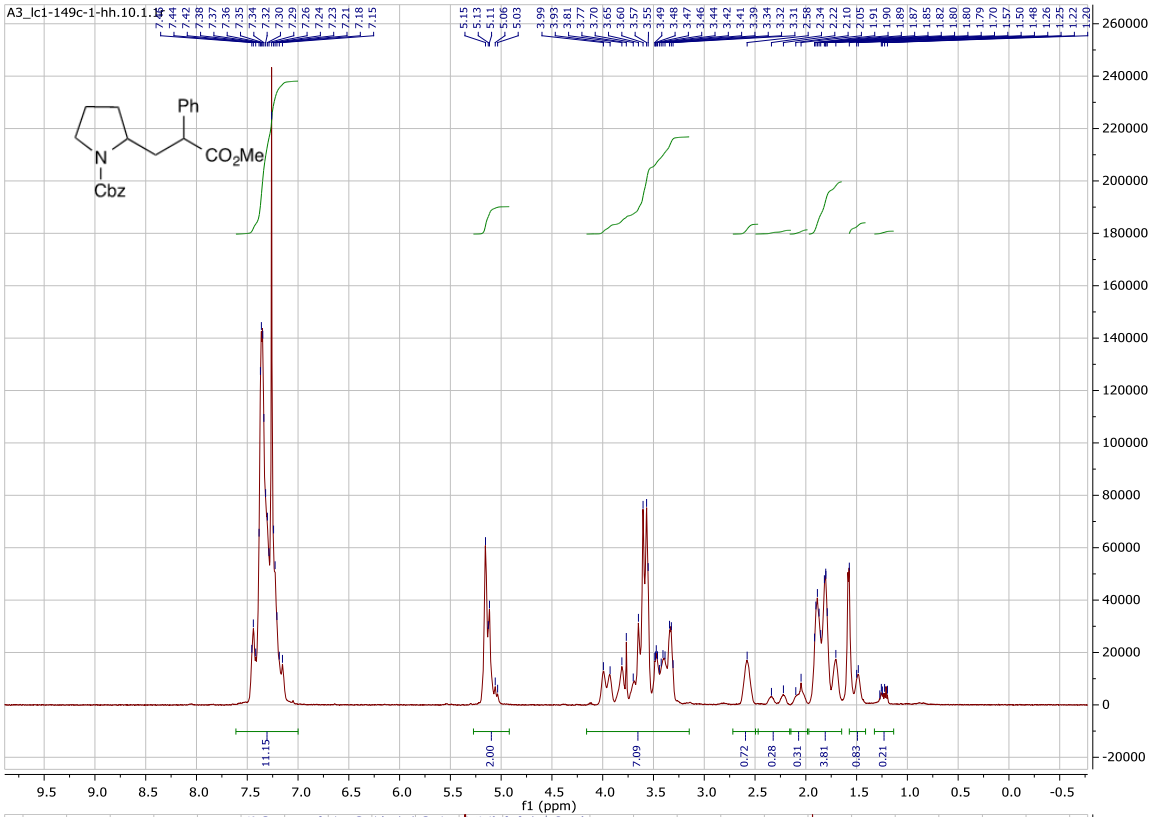
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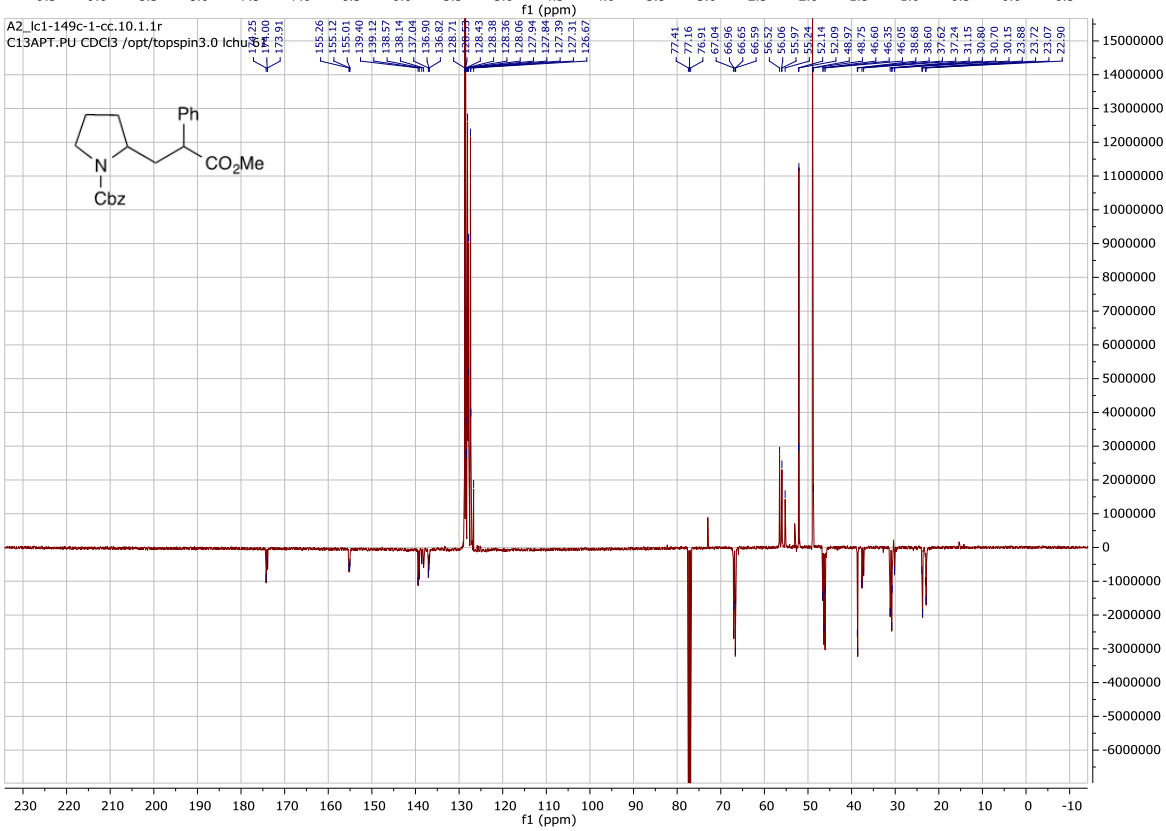
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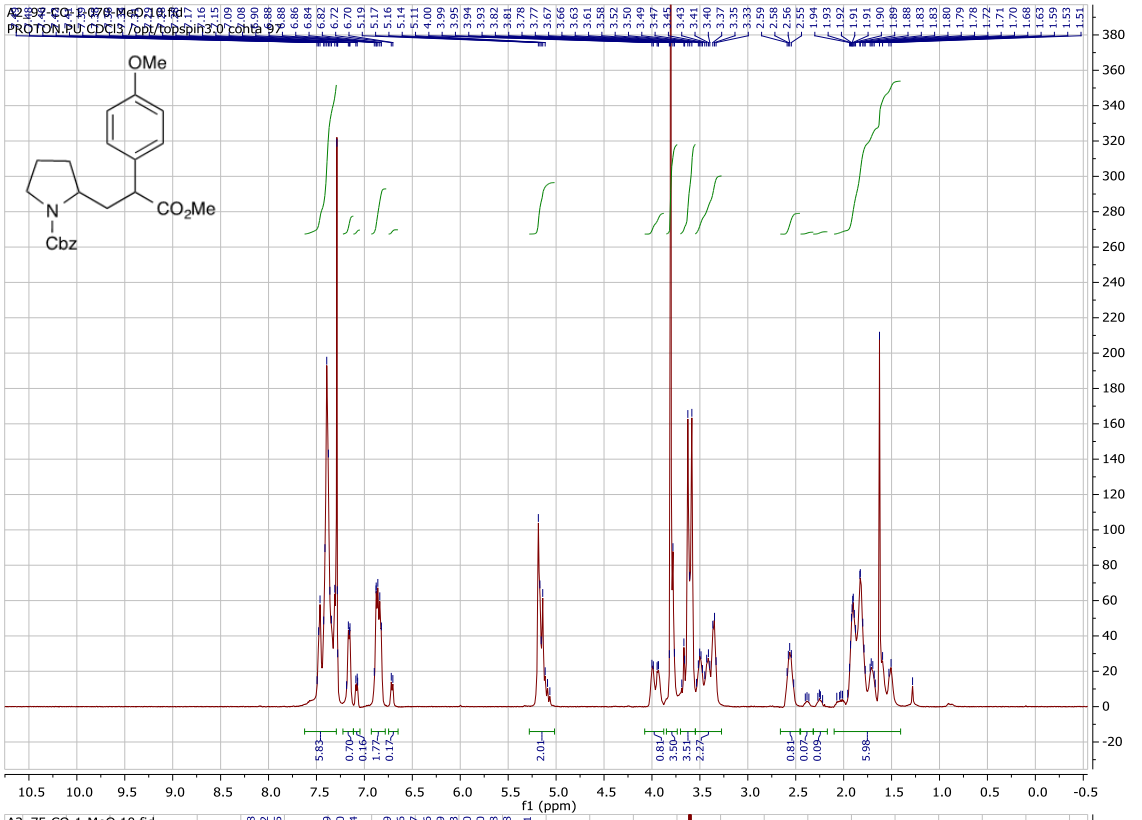
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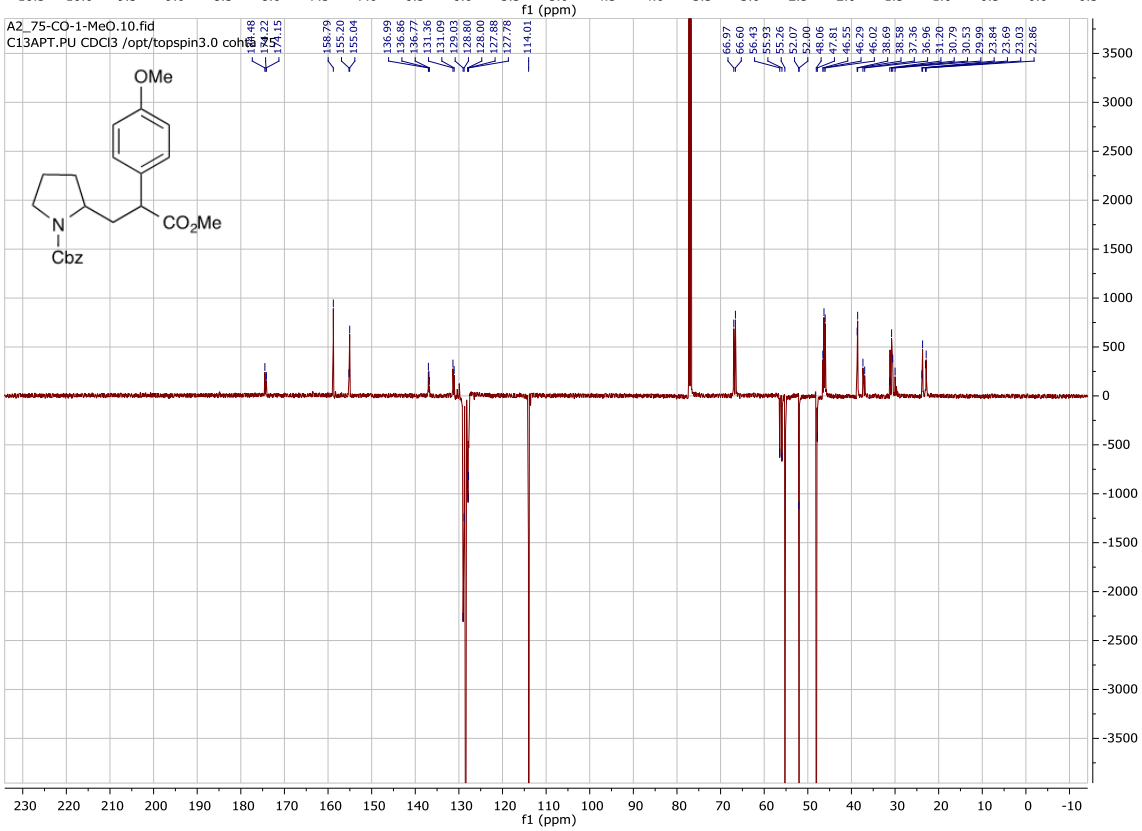
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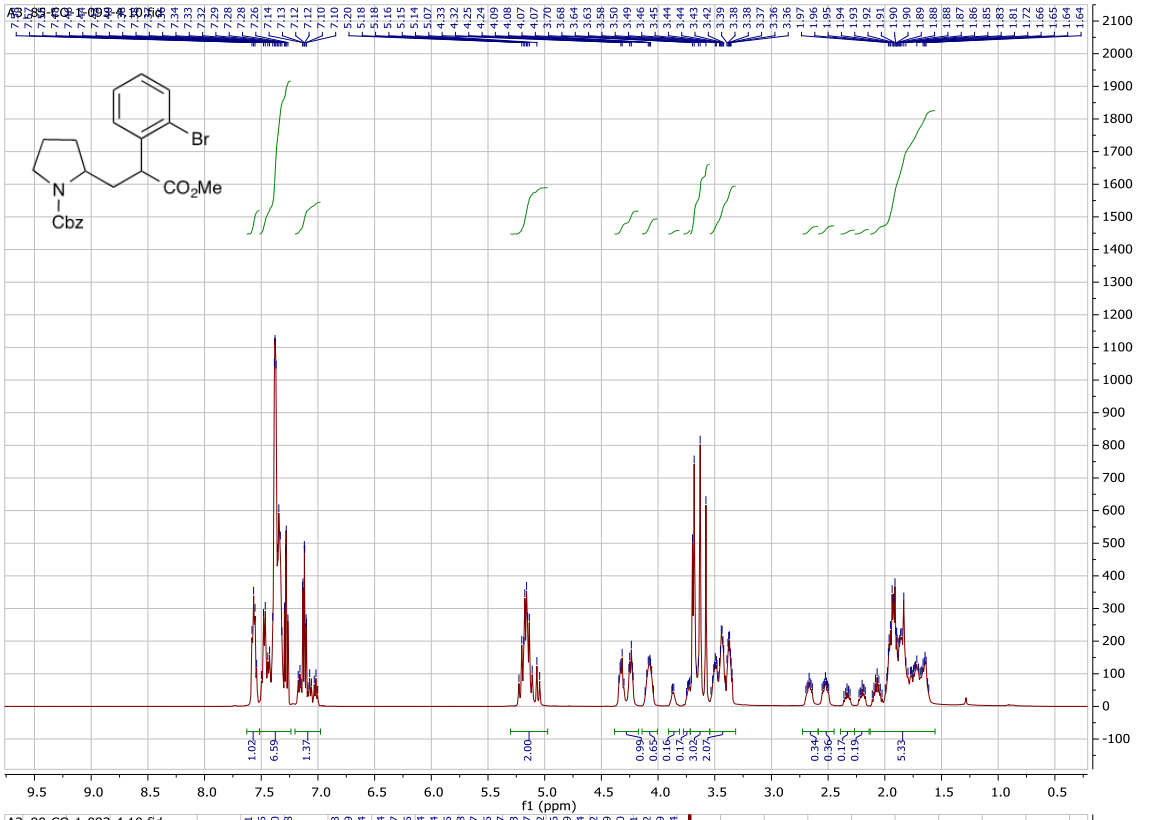
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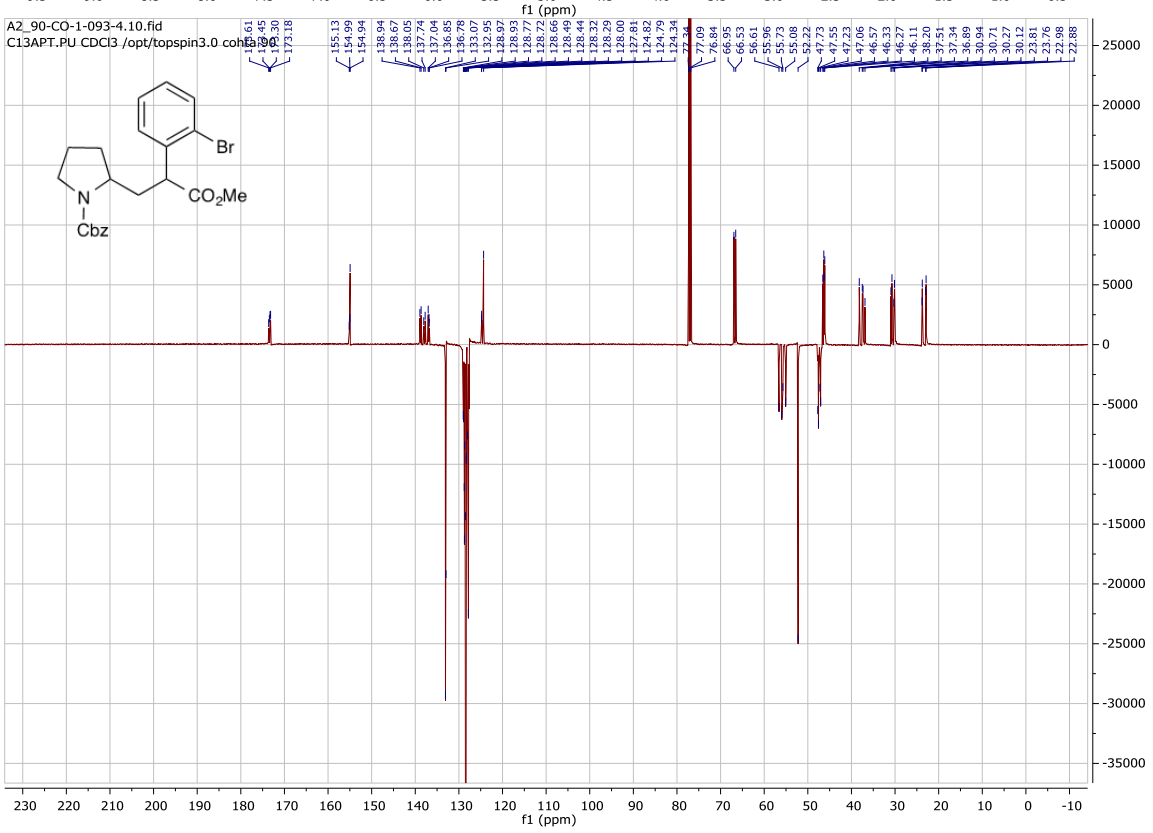
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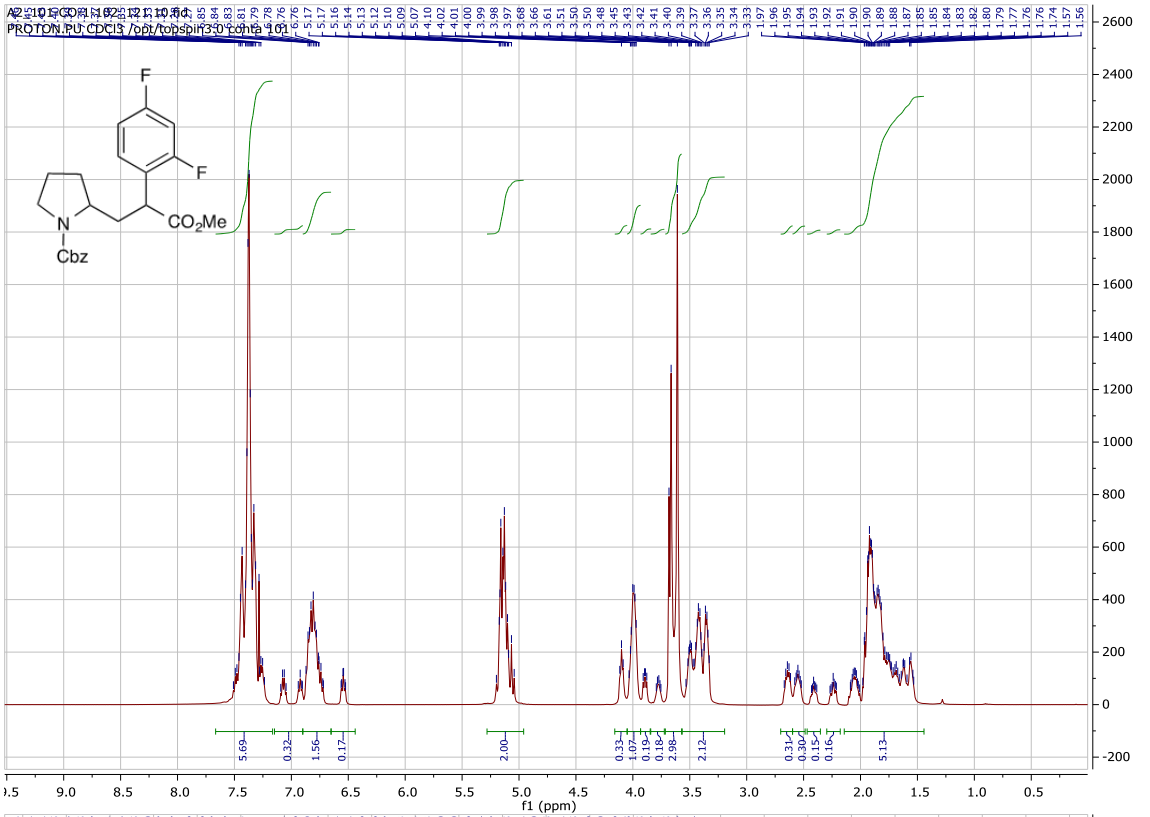
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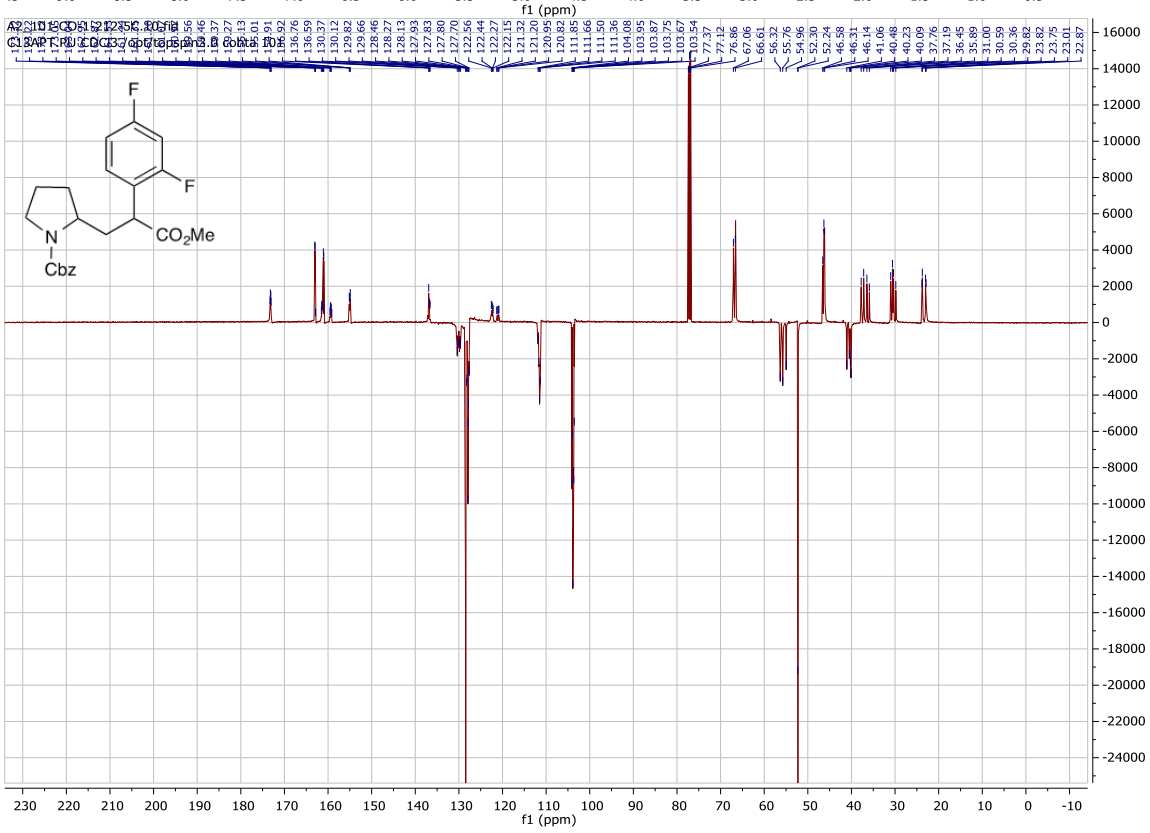
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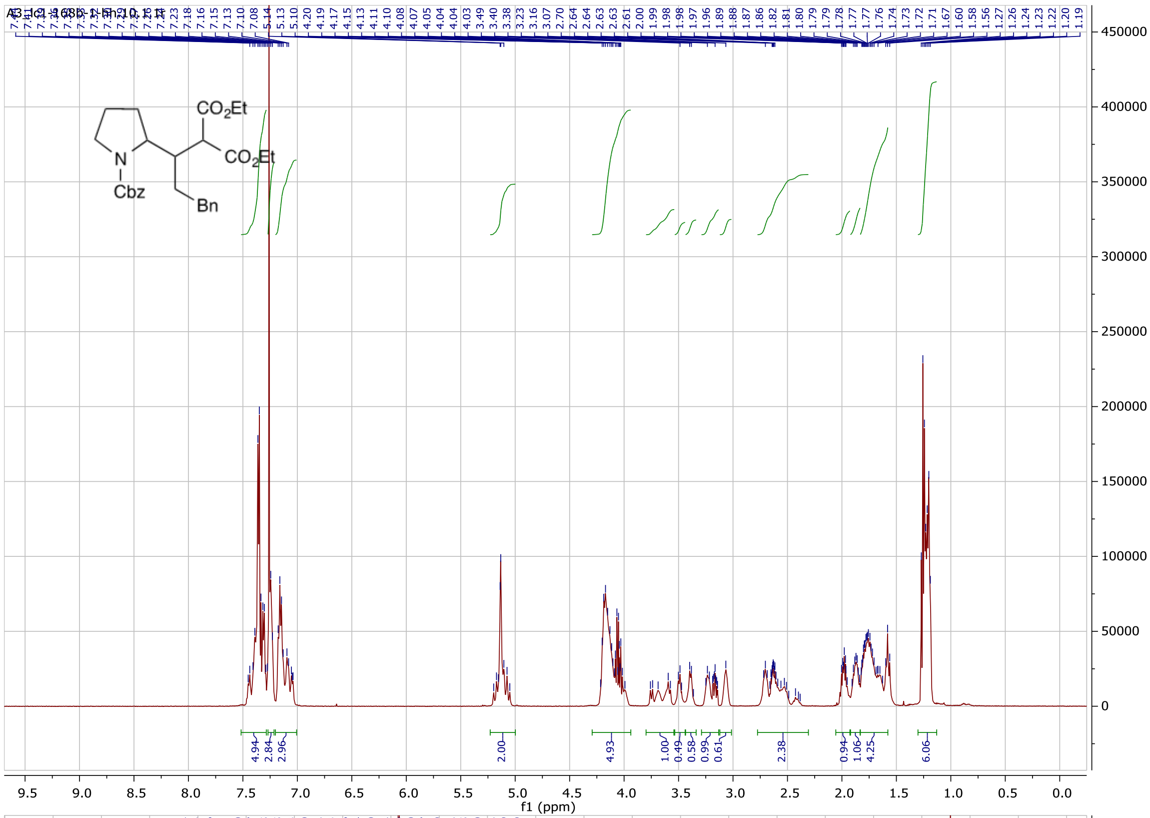
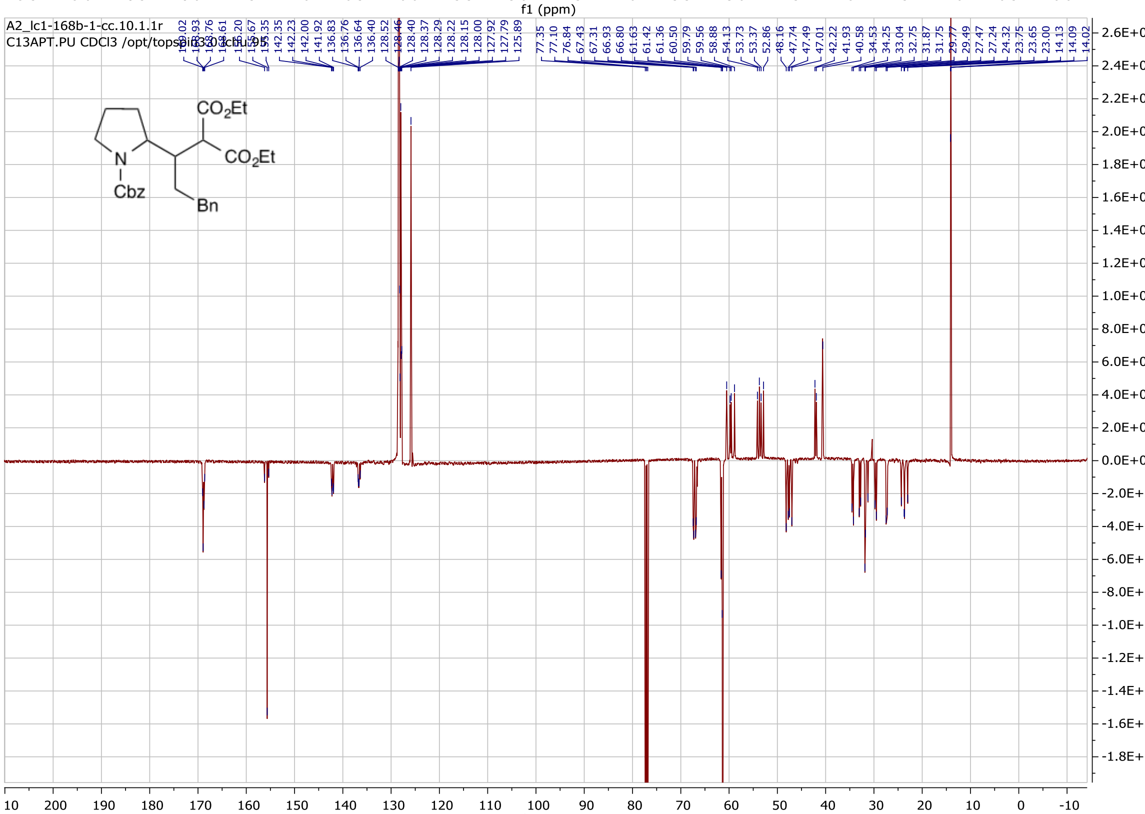
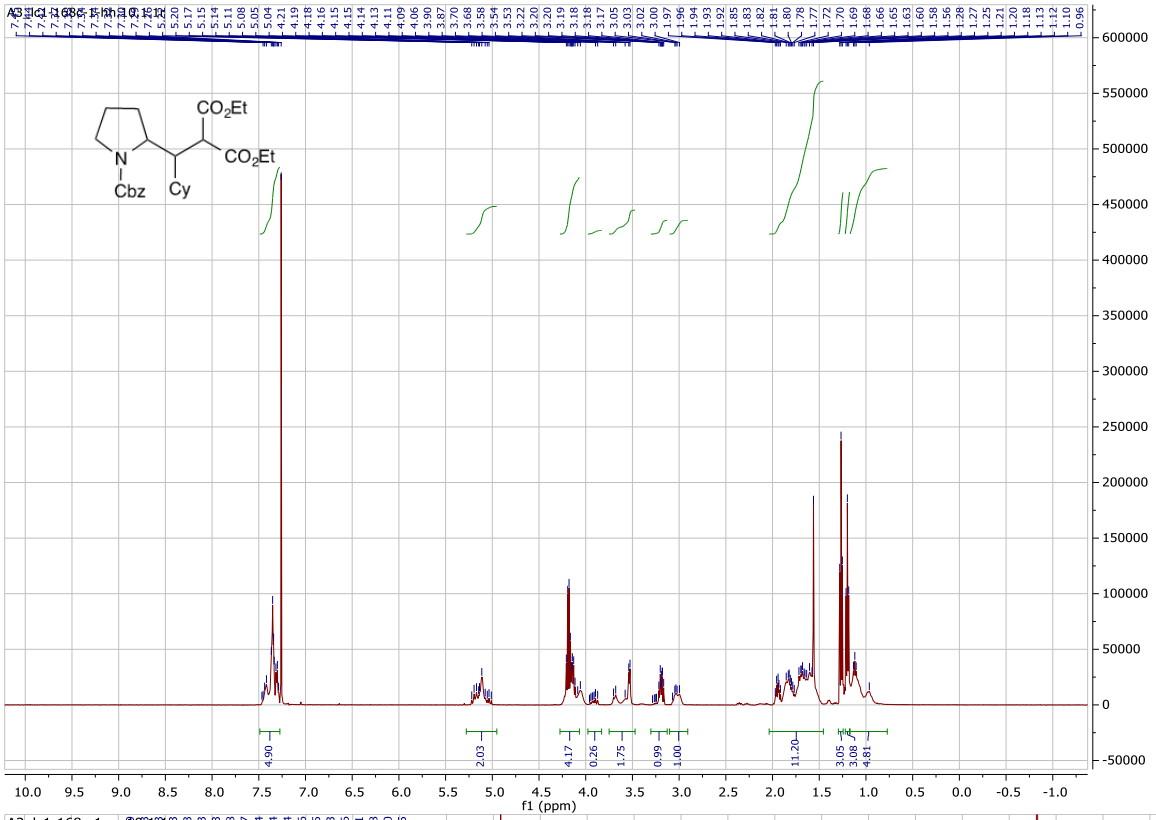
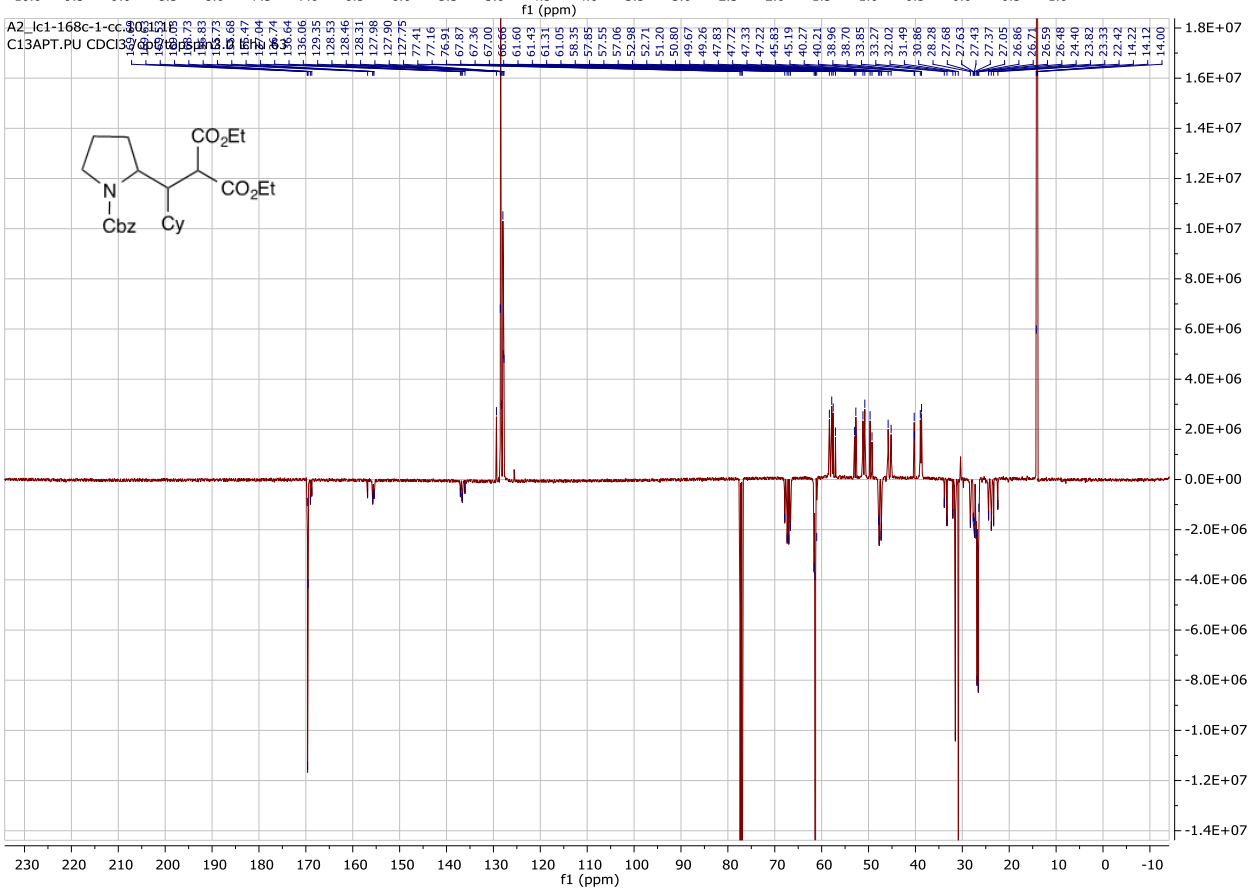
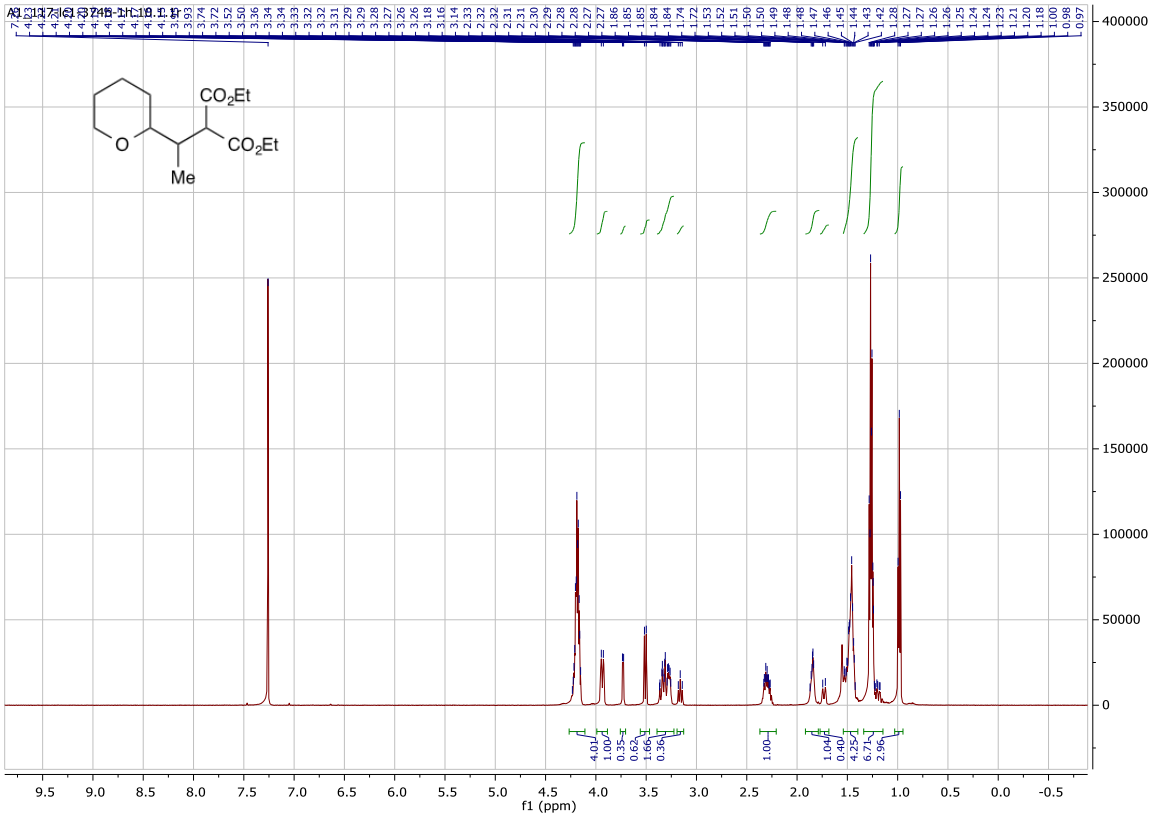





CO2Et
CO2Et
N
Cbz
Cy
f1 (ppm)


CO2Et
CO2Et
N
Cbz
Cy
f1 (ppm)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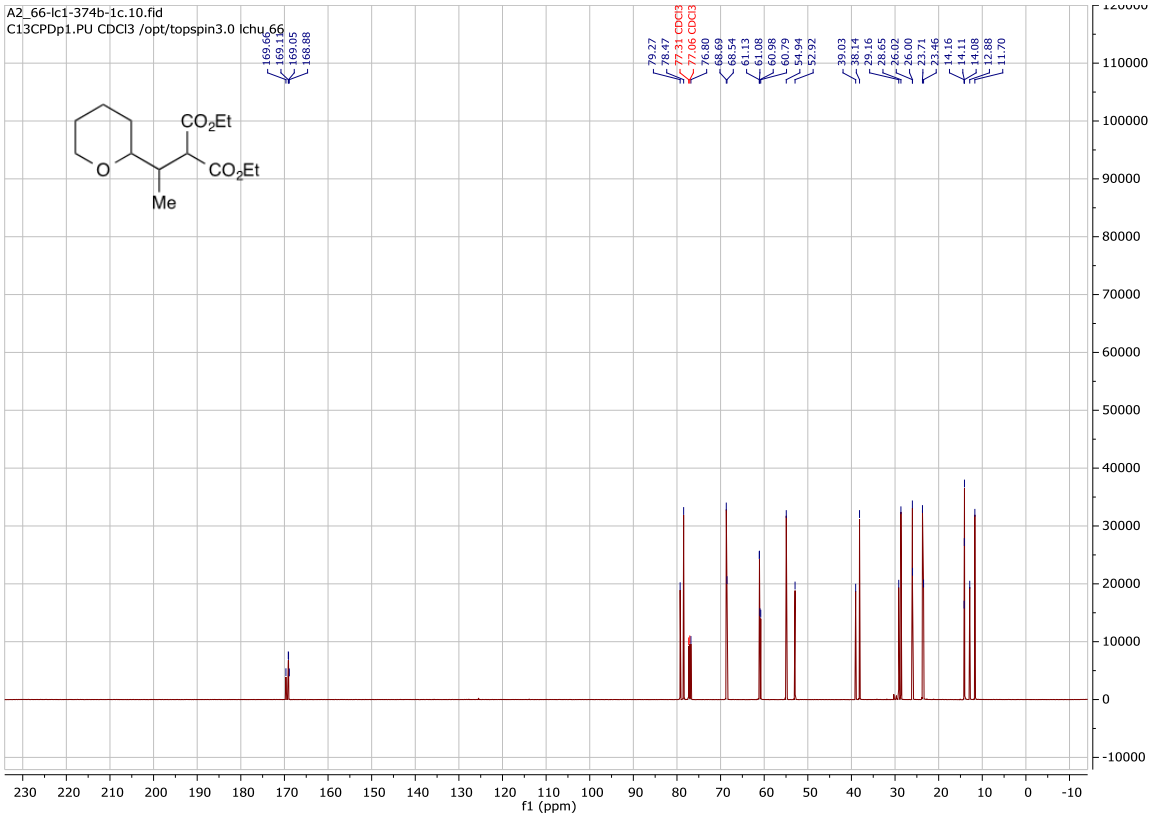
CO2Et
O
Me
f1 (ppm)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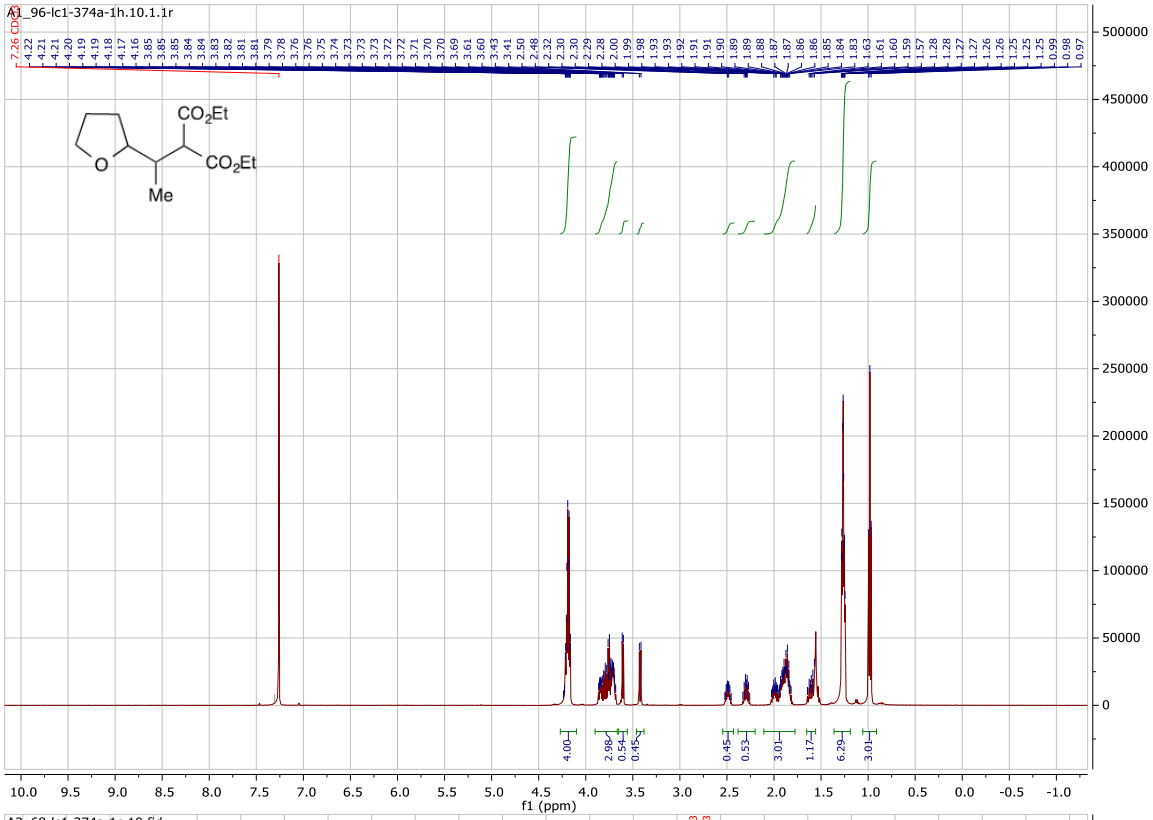
CO2Et
CO2Et
O
Me
f1 (ppm)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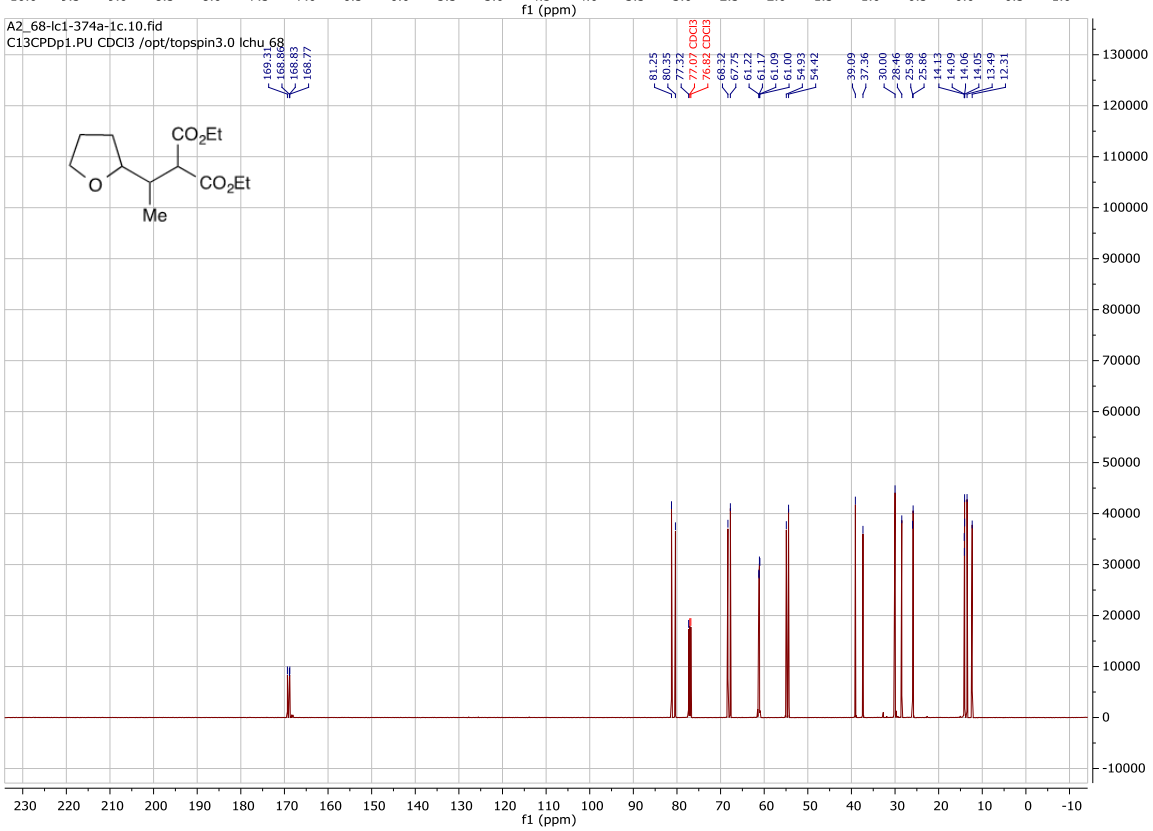
CO2Et
O
Me
f1 (ppm)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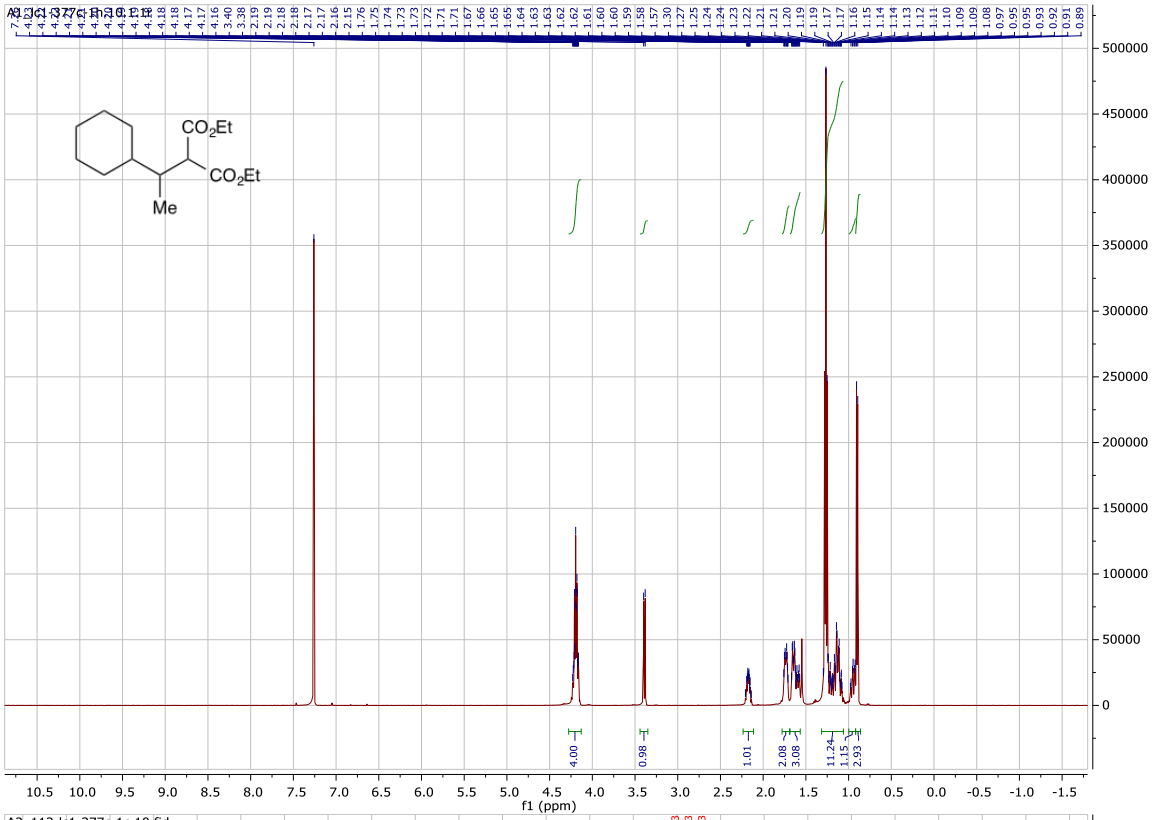
CO2Et
O
Me
f1 (ppm)


A2_112-lc1-377c-1h.10.fid
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CO2Et
Me
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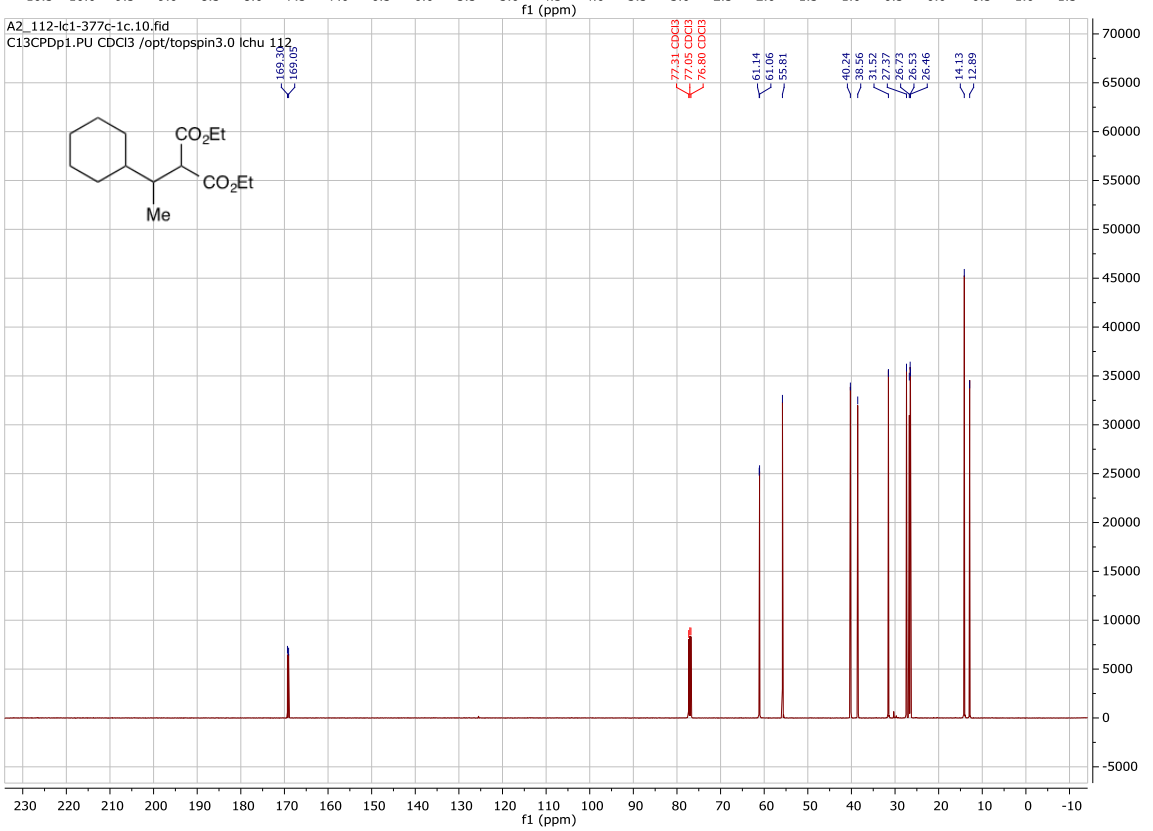
0.98
1.01
2.08
3.08
11.24
1.15
2.93
f1 (ppm)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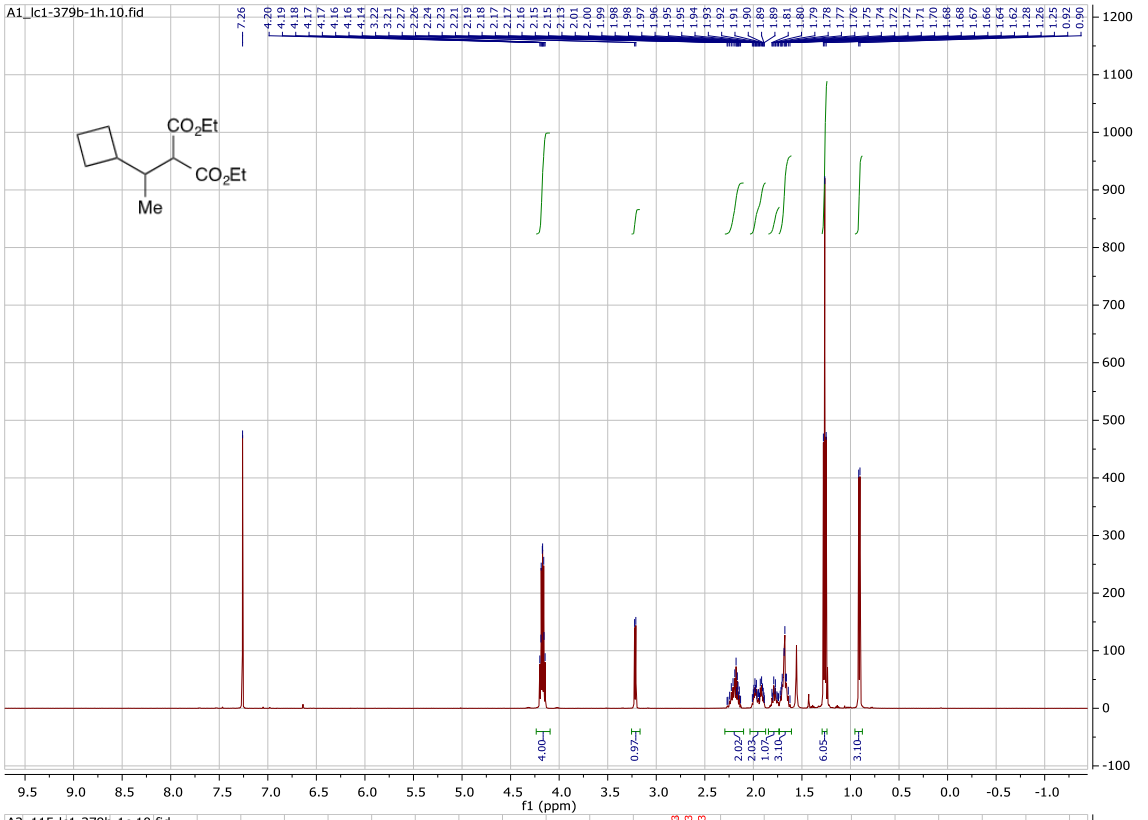
C13CPDp1.PU CDCl3 /opt/topspin3.0 lchu 112
169.30
169.03
77.31 CDCl3
77.05 CDCl3
76.80 CDCl3
61.14
61.06
55.81
40.24
38.56
31.52
27.37
26.73
26.53
26.46
14.13
12.89
CO2Et
CO2Et
Me
f1 (ppm)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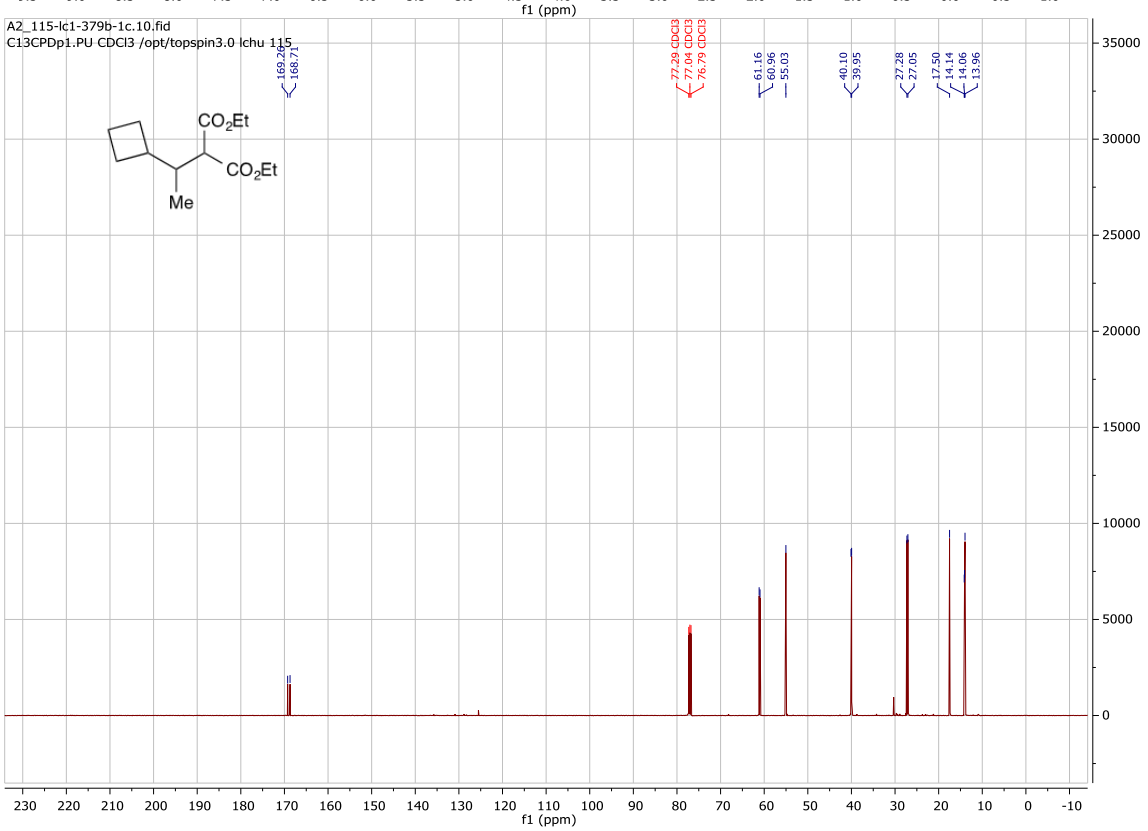
CO2Et
Me
f1 (ppm)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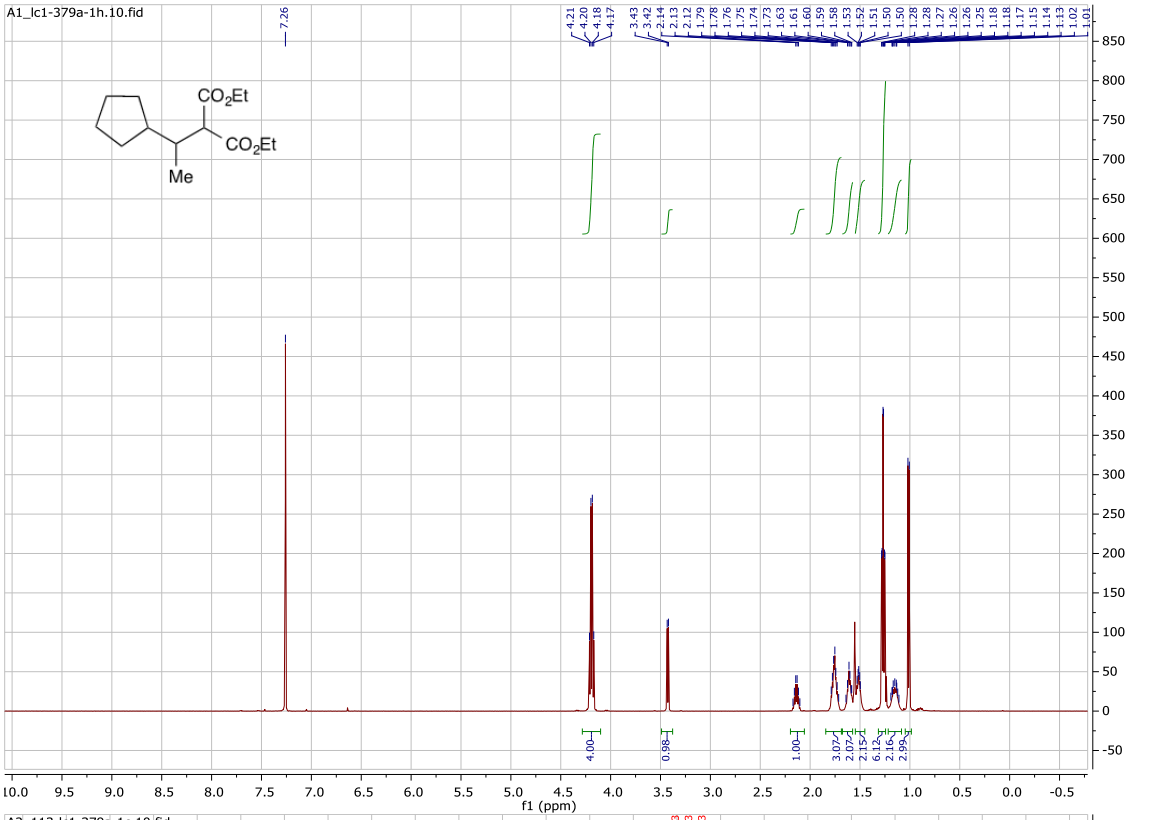
CO2Et
CO2Et
Me
f1 (ppm)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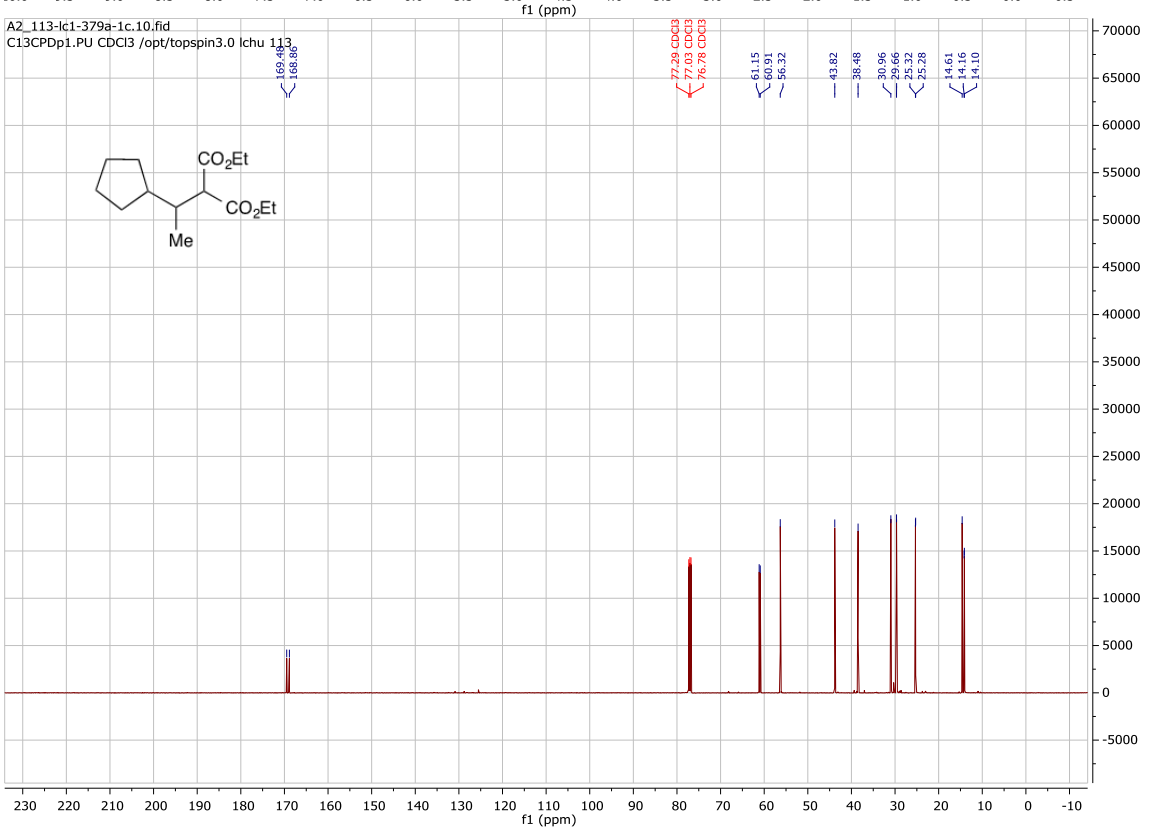
CO2Et
Me
f1 (ppm)


A2_113-lc1-379a-1c.10.fid
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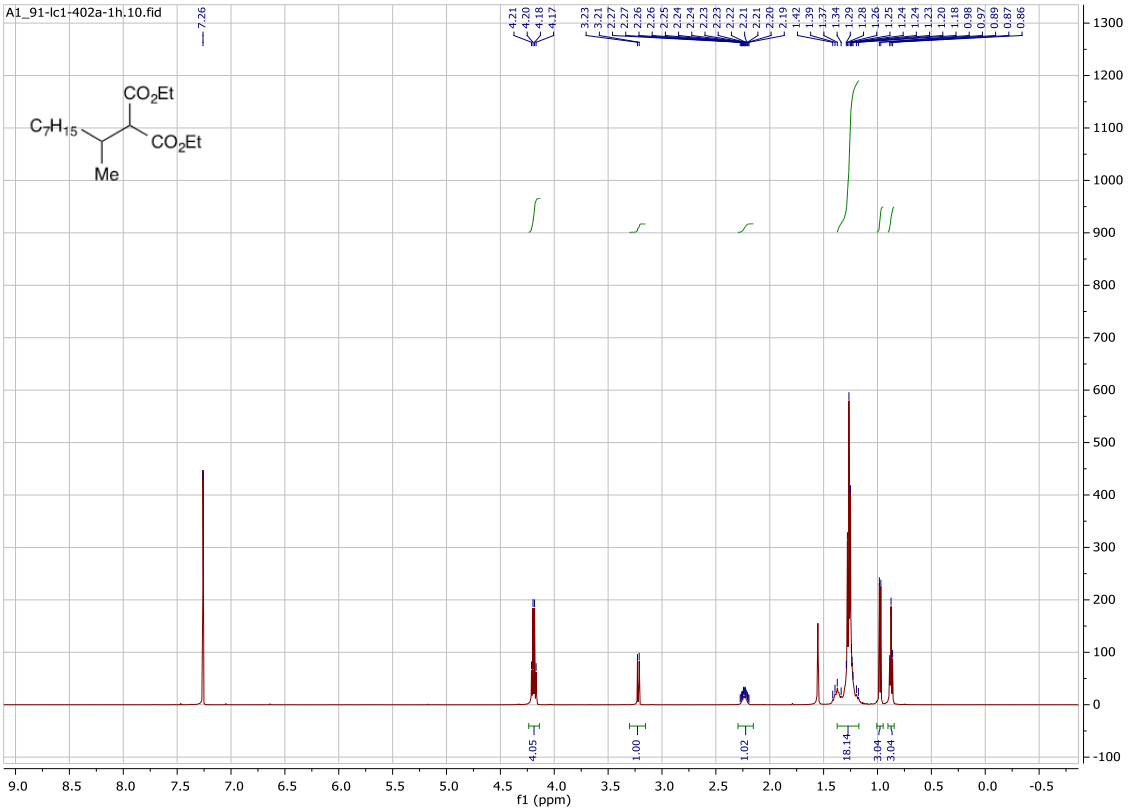
CO2Et
CO2Et
Me
f1 (ppm)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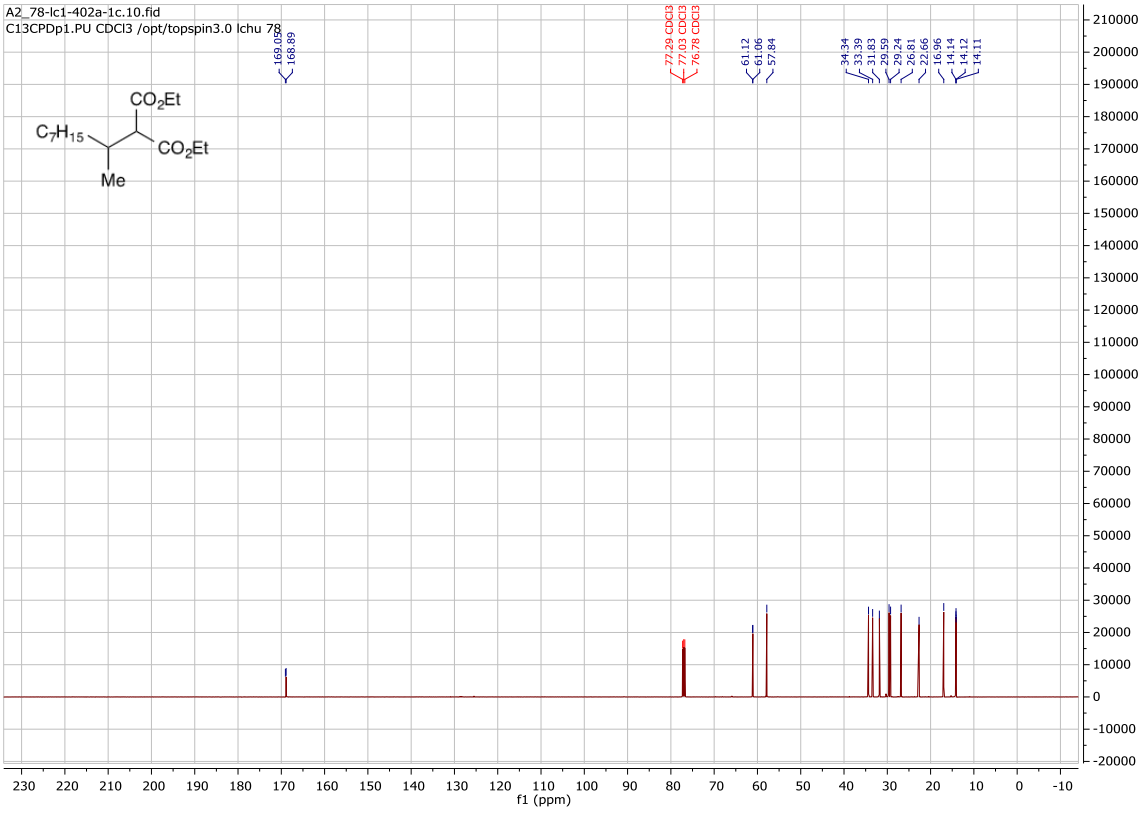
CO2Et
C7H15
CO2Et
Me
f1 (ppm)


A2_78-lc1-402a-1c.10.fid
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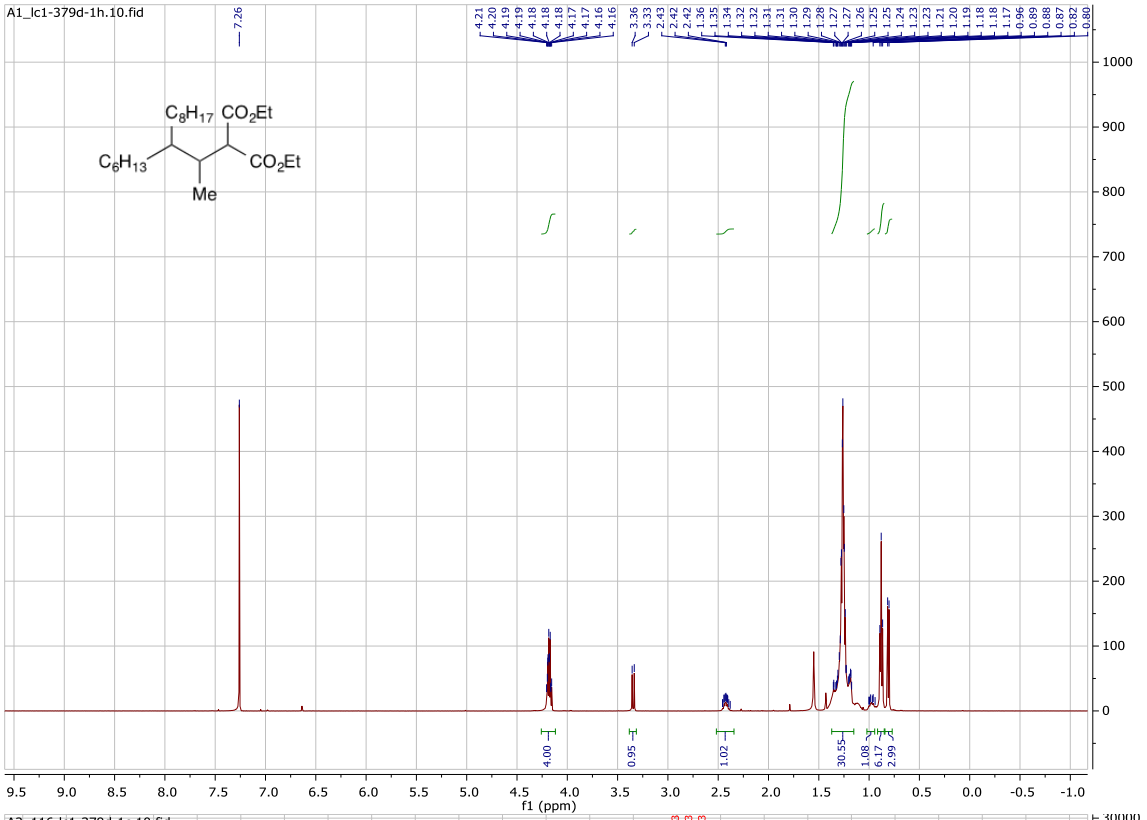
CO2Et
C7H15
CO2Et
Me
f1 (ppm)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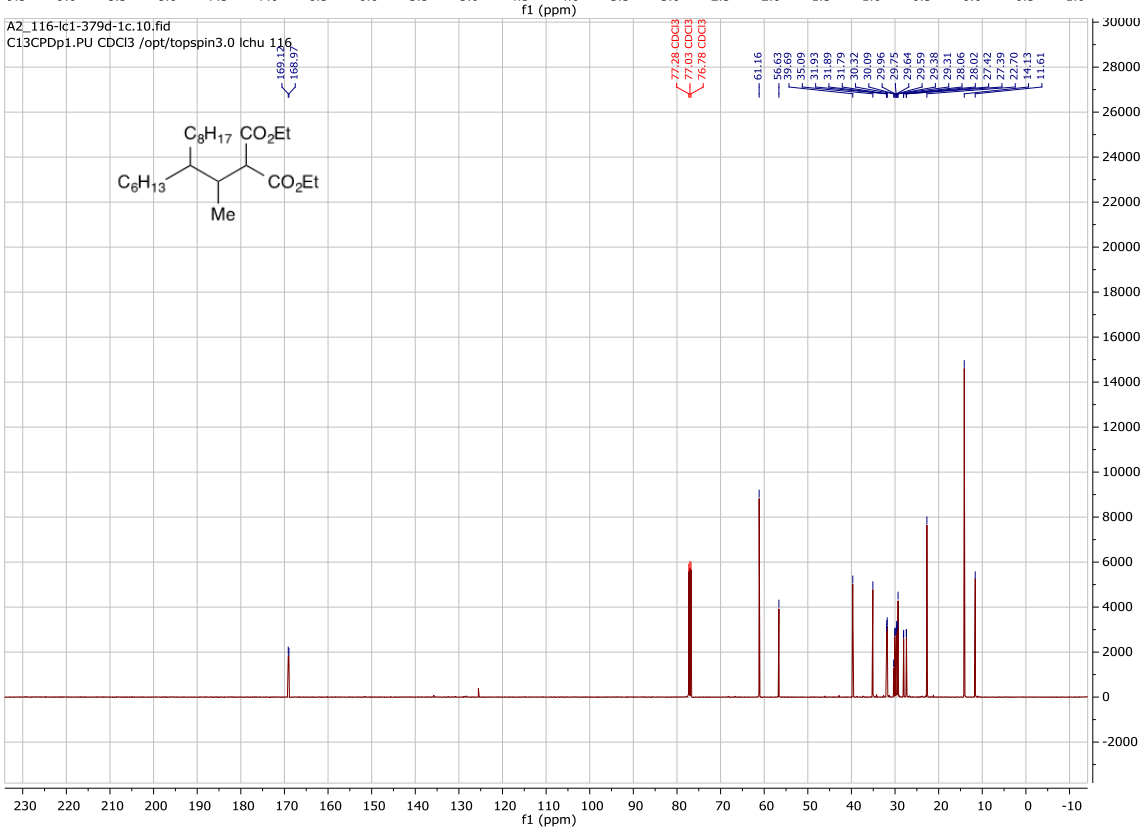
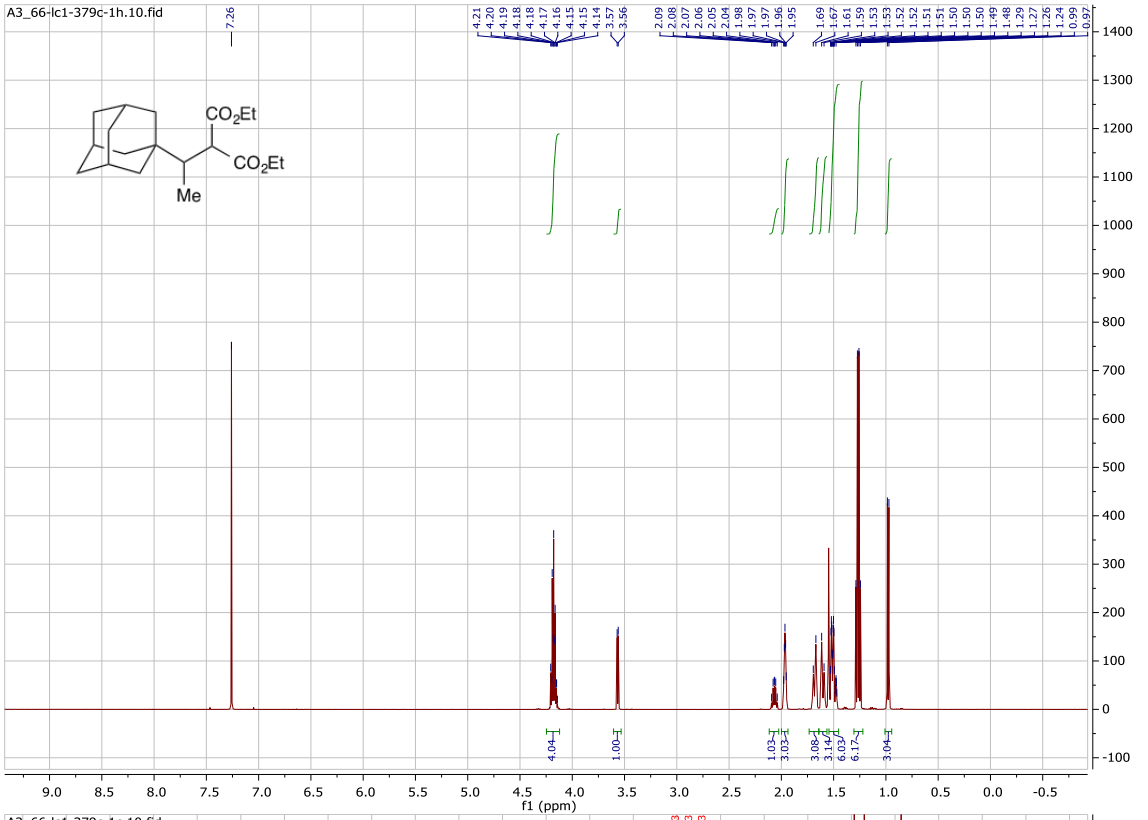
7.26
4.21 4.20 4.19 4.19 4.18 4.18 4.18 4.17 4.17 4.16 4.16
3.36 3.33 2.43 2.42 2.42 1.36 1.35 1.34 1.32 1.32 1.31 1.31 1.30 1.29 1.28 1.27 1.27 1.26 1.25 1.25 1.24 1.23 1.23 1.21 1.20 1.19 1.18 1.18 1.17 0.96 0.89 0.88 0.87 0.82 0.80
C8H17 CO2Et
C6H13
CO2Et
Me
4.00
0.95
1.02
30.55
1.08
6.17
2.99
f1 (ppm)


A2_116-lc1-379d-1c.10.fid
C13CPDp1.PU CDCl3 /opt/topspin3.0 lchu 116
169.12
168.97
77.28 CDCl3
77.03 CDCl3
76.78 CDCl3
61.16
56.63
39.69
35.09
31.93
31.89
31.79
30.32
30.09
29.96
29.75
29.64
29.59
29.38
29.31
28.06
28.02
27.42
27.39
22.70
14.13
11.61
C8H17 CO2Et
C6H13
CO2Et
Me
f1 (ppm)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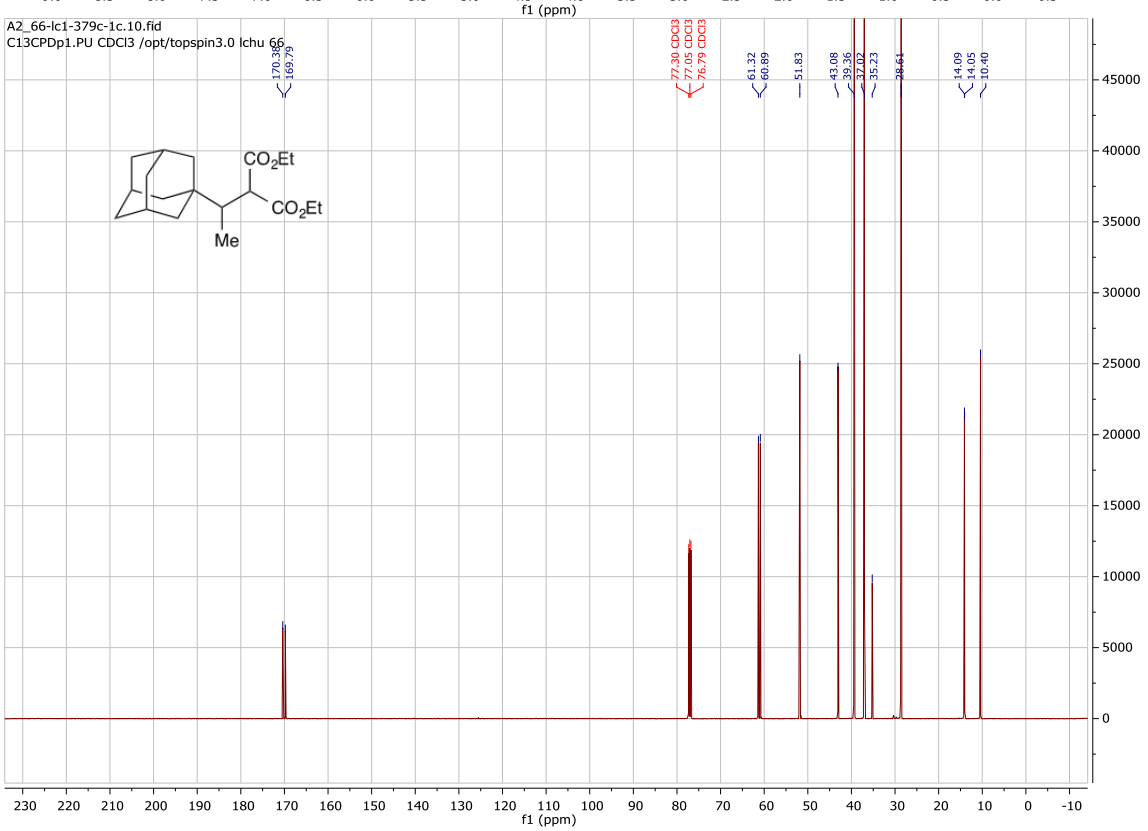
CO2Et
CO2Et
Me
f1 (ppm)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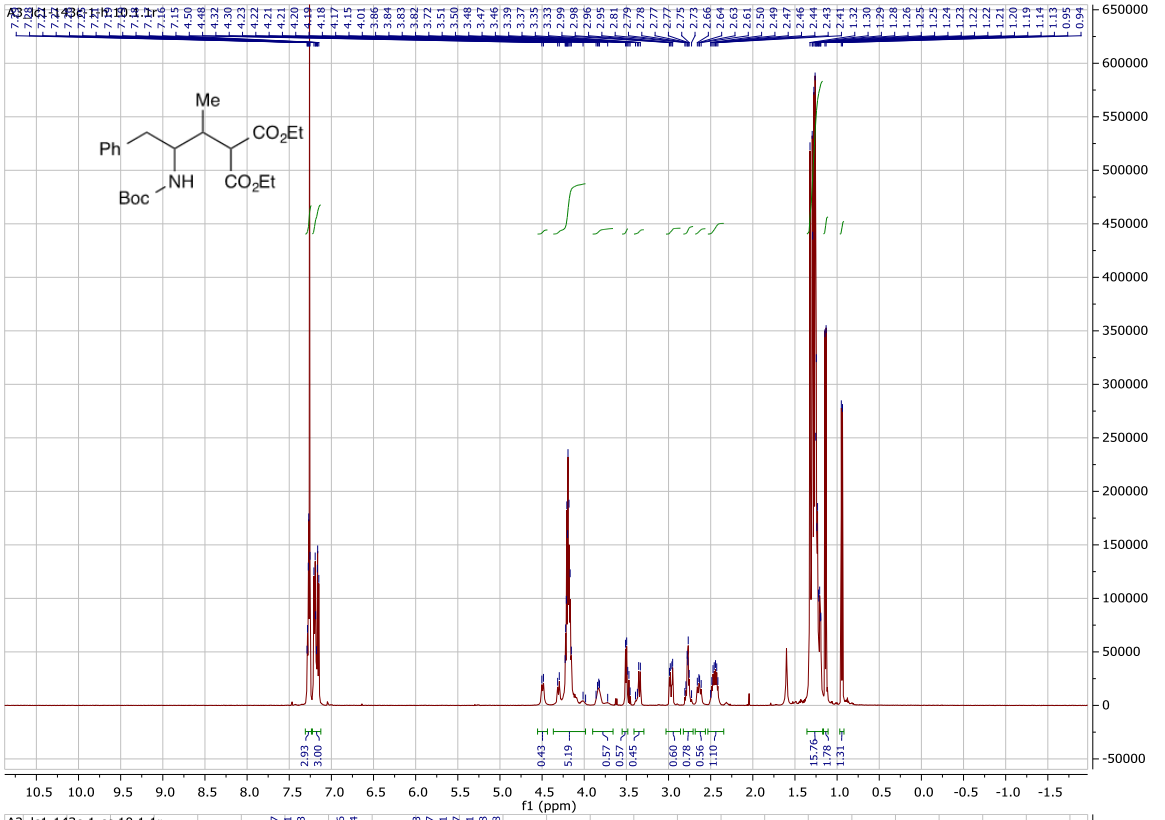
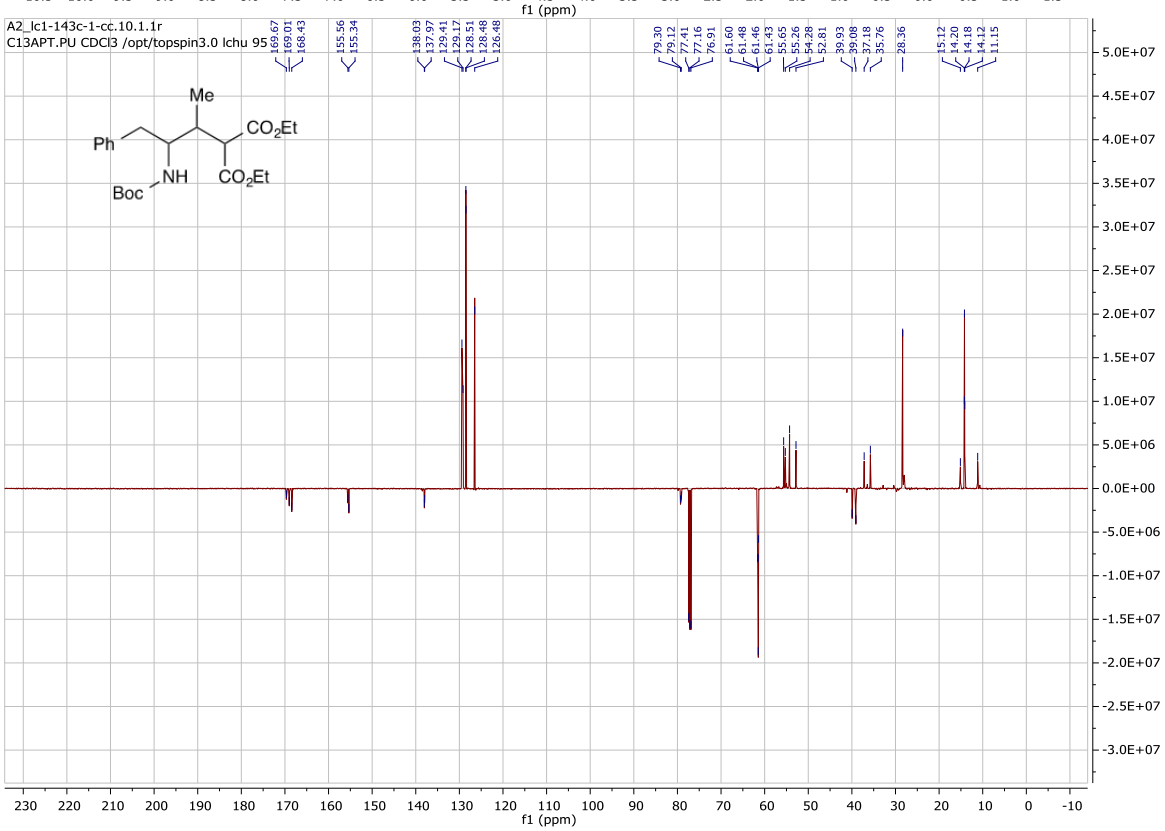
CO2Et
CO2Et
Me
f1 (ppm)


Me
Ph
CO2Et
NH
Boc
CO2Et
f1 (ppm)


A2_lc1-143c-1-cc.10.1.1r
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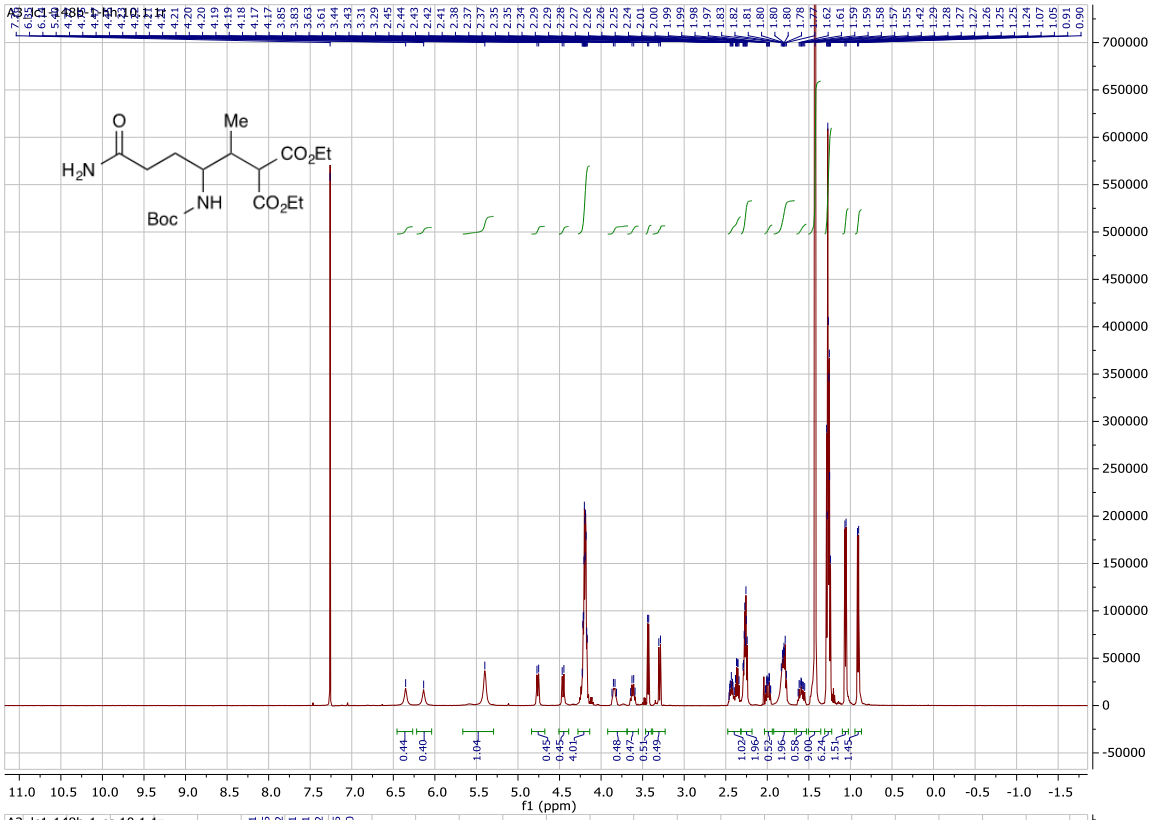
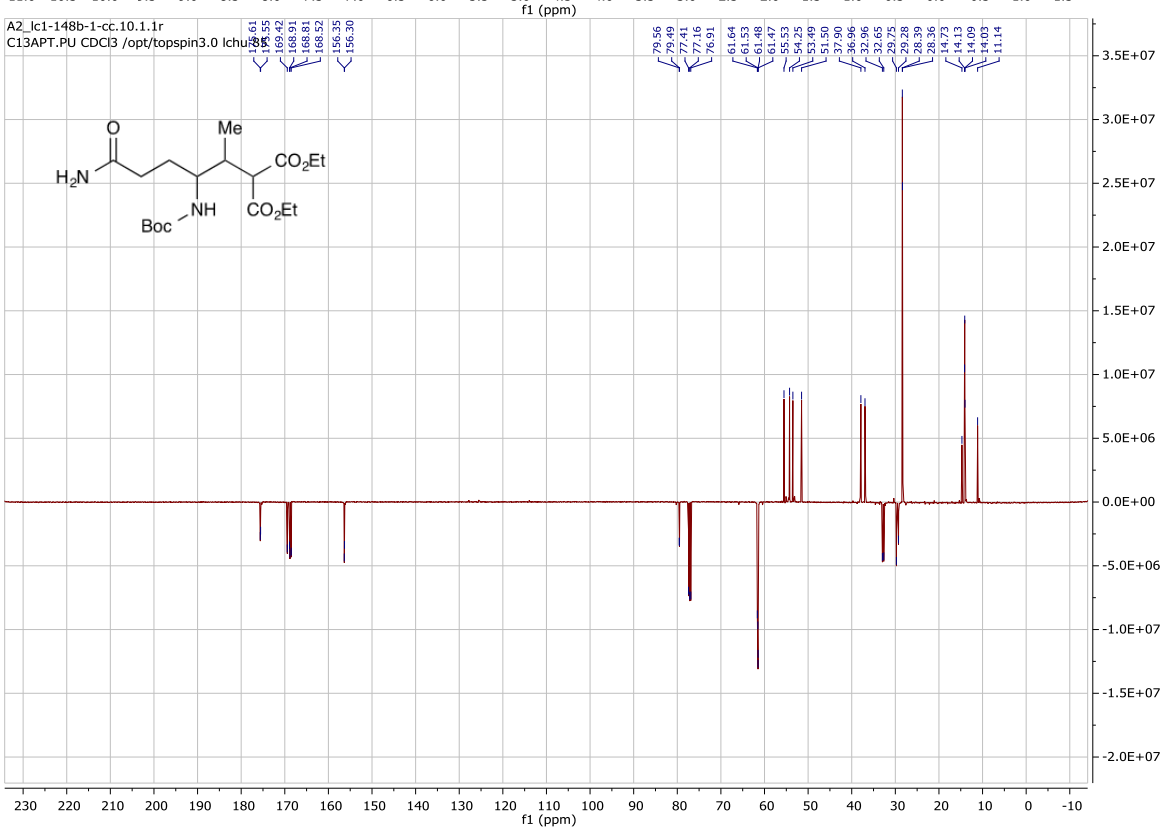
Me
Ph
CO2Et
NH
Boc
CO2Et
f1 (ppm)


O
Me
H_2N
CO_2Et
NH
Boc
CO_2Et
f1 (ppm)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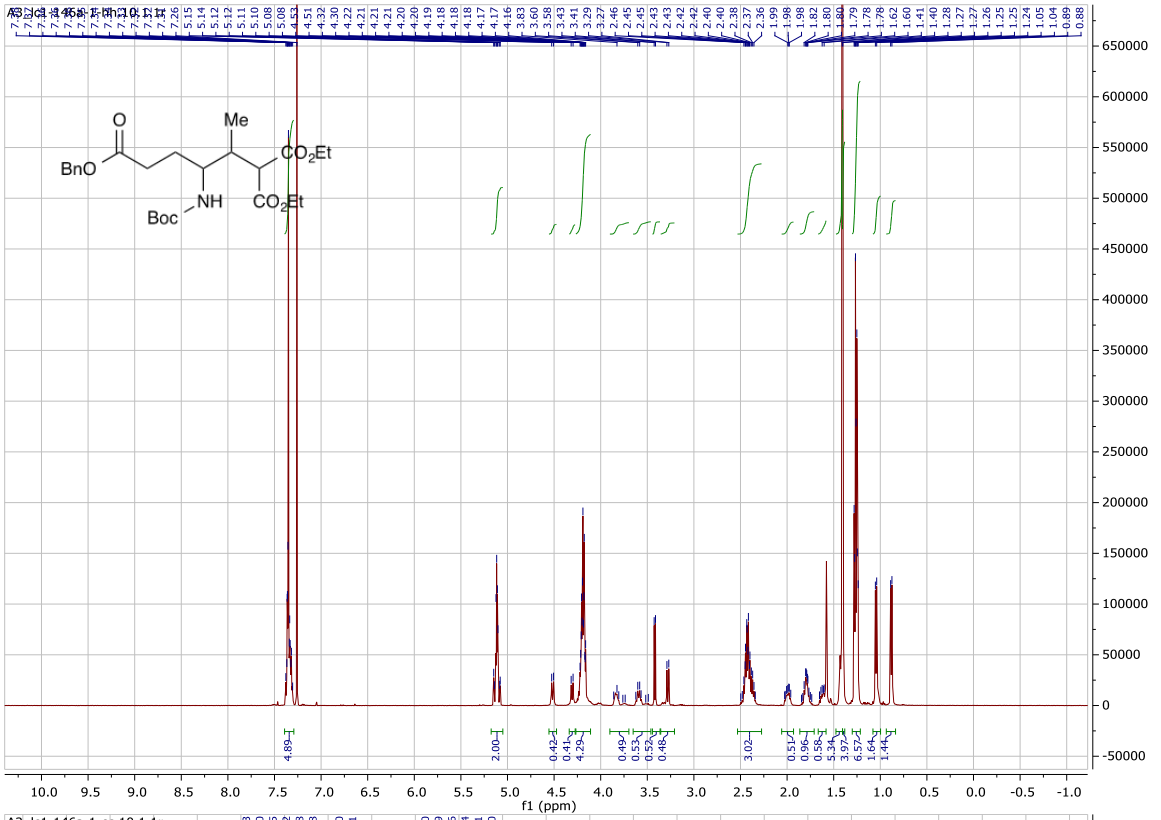
Me
H_2N
CO_2Et
NH
Boc
CO_2Et
f1 (ppm)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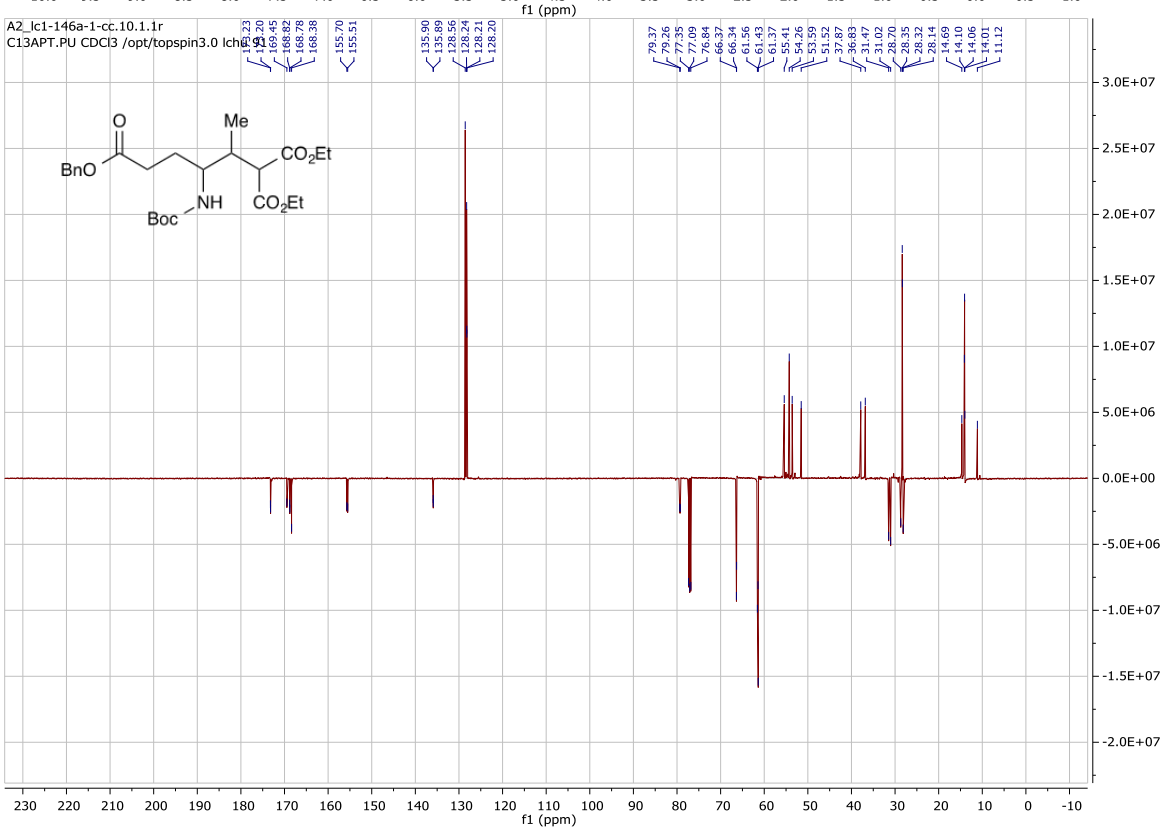
Me
BnO
CO2Et
NH
CO2Et
Boc
f1 (ppm)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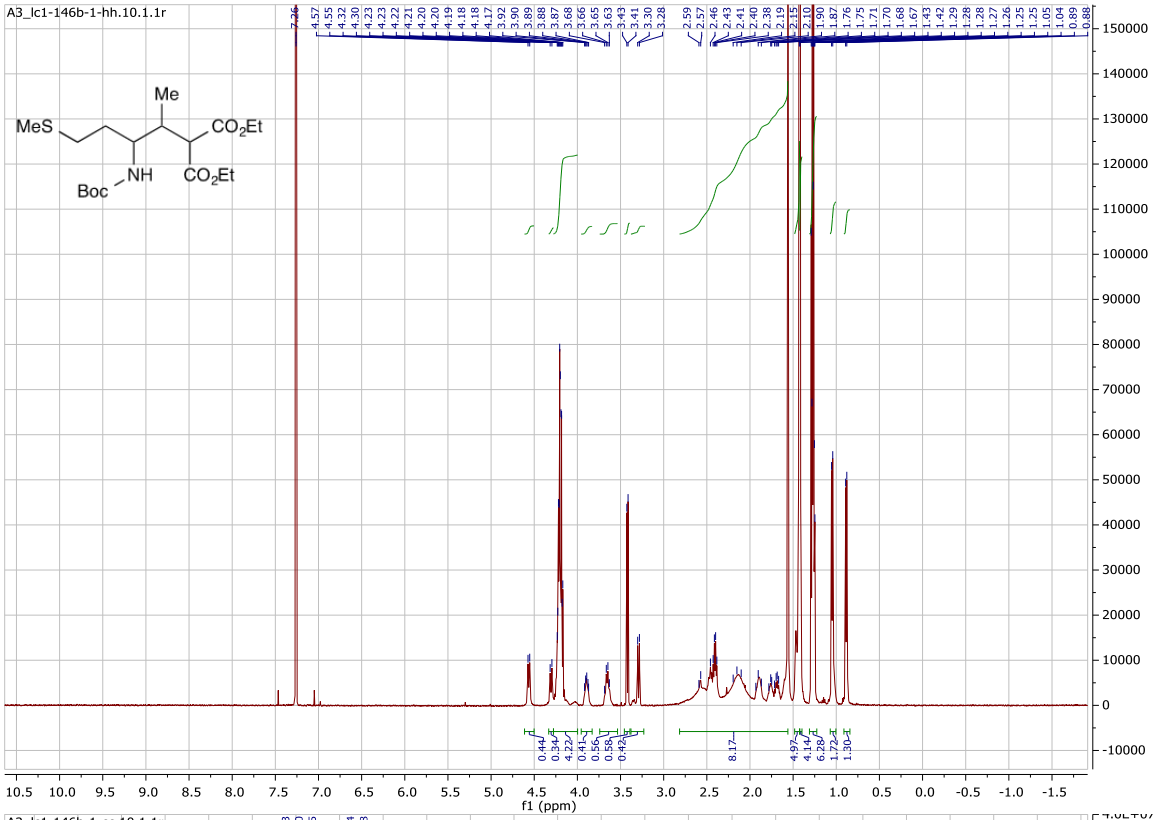
O
Me
BnO
CO2Et
NH
CO2Et
Boc
f1 (ppm)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Me
MeS
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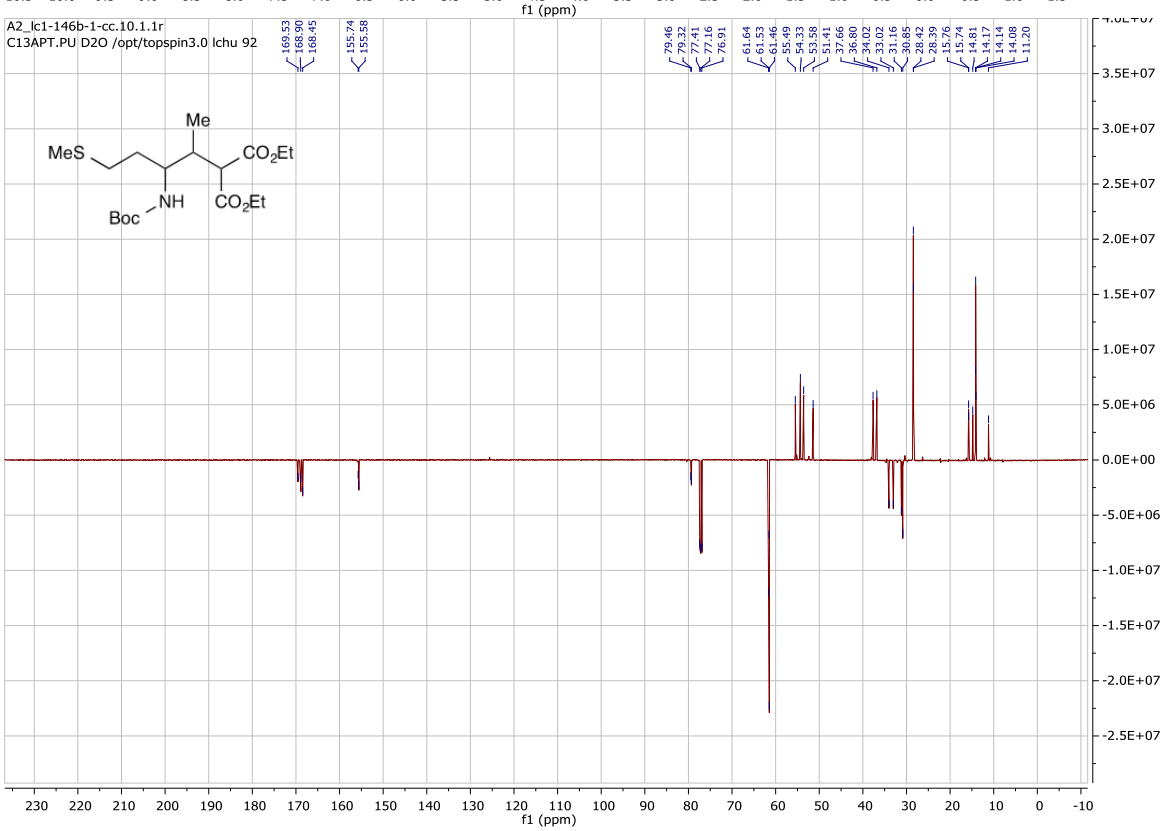
NH
CO2Et
Boc
f1 (ppm)


A2_lc1-146b-1-cc.10.1.1r
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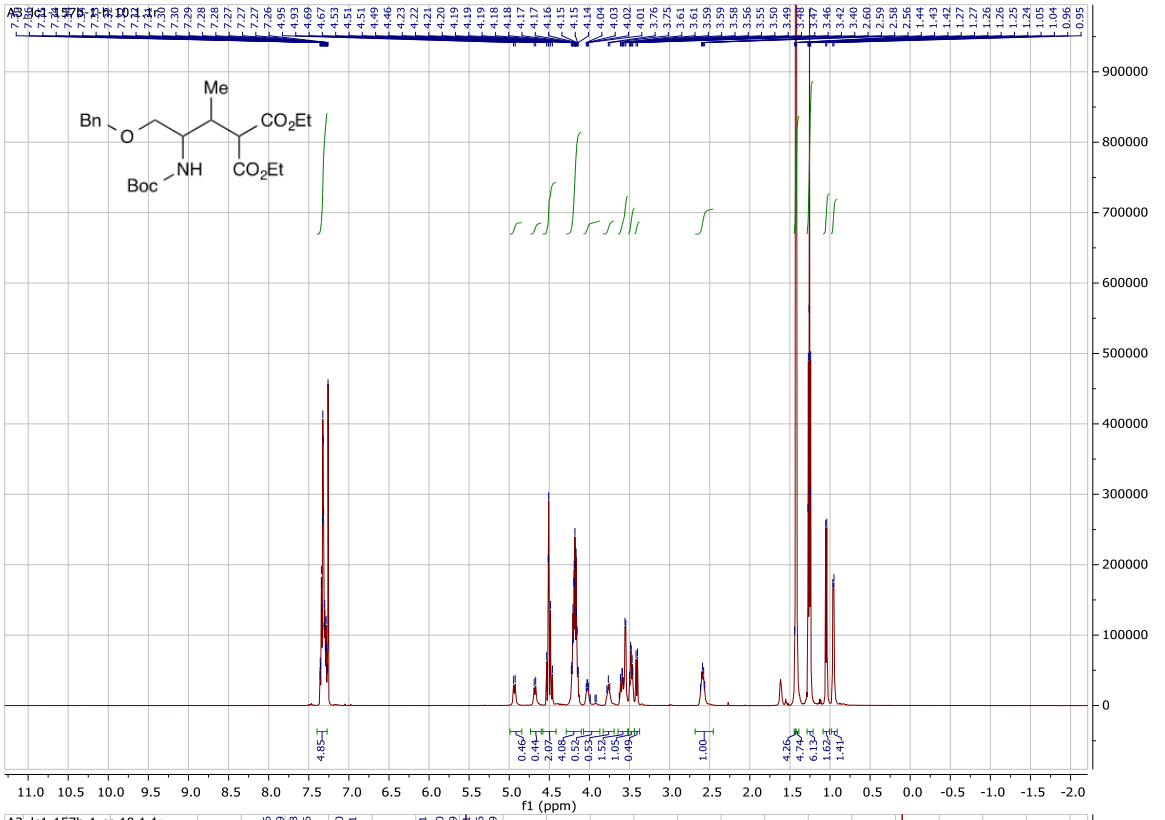
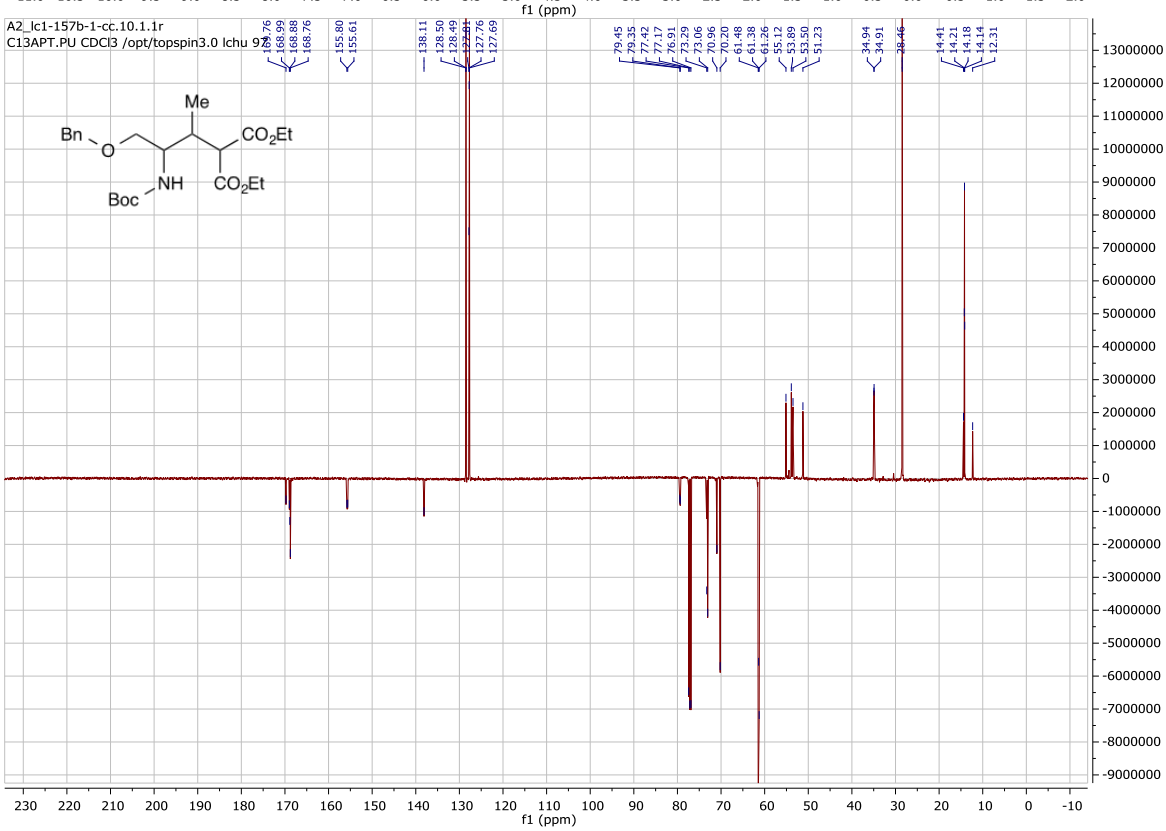
Me
MeS
CO2Et
NH
CO2Et
Boc
f1 (ppm)


Me
Bn
O
CO2Et
NH
Boc
CO2Et
f1 (ppm)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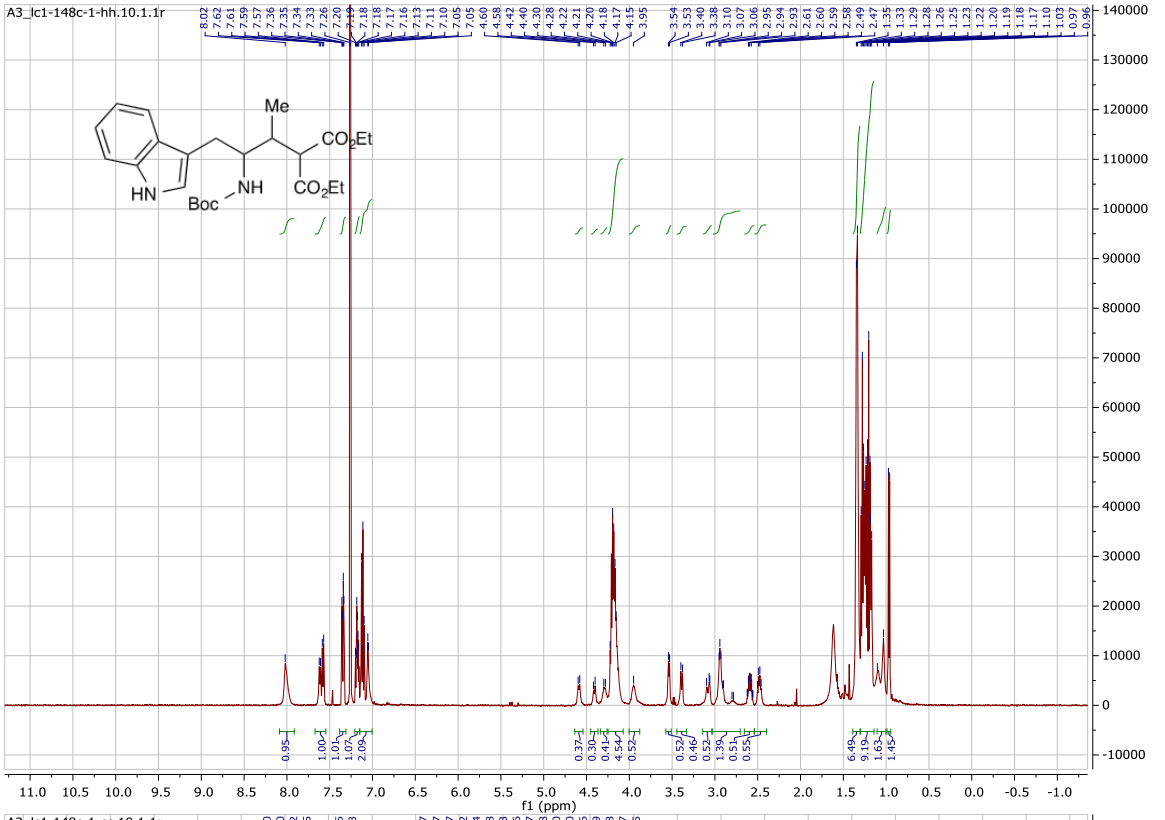
Me
Bn
O
CO2Et
NH
Boc
CO2Et
f1 (ppm)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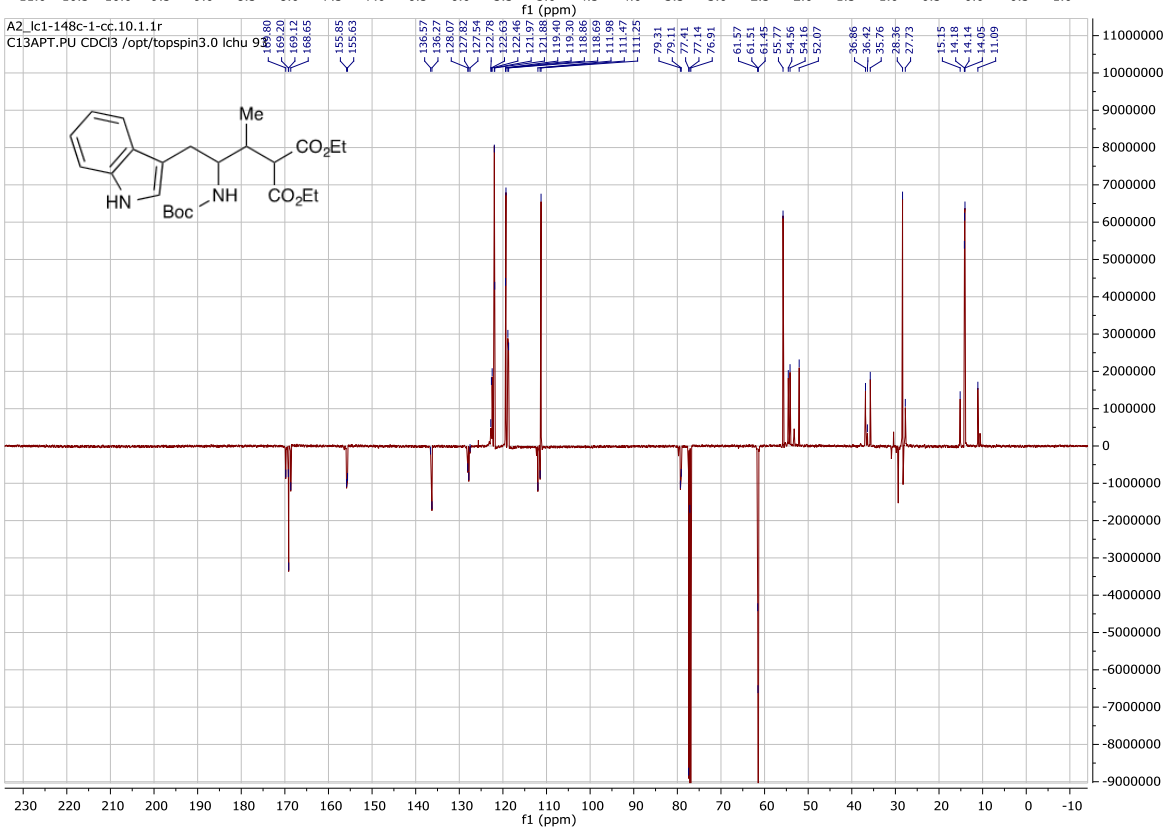
f1 (ppm)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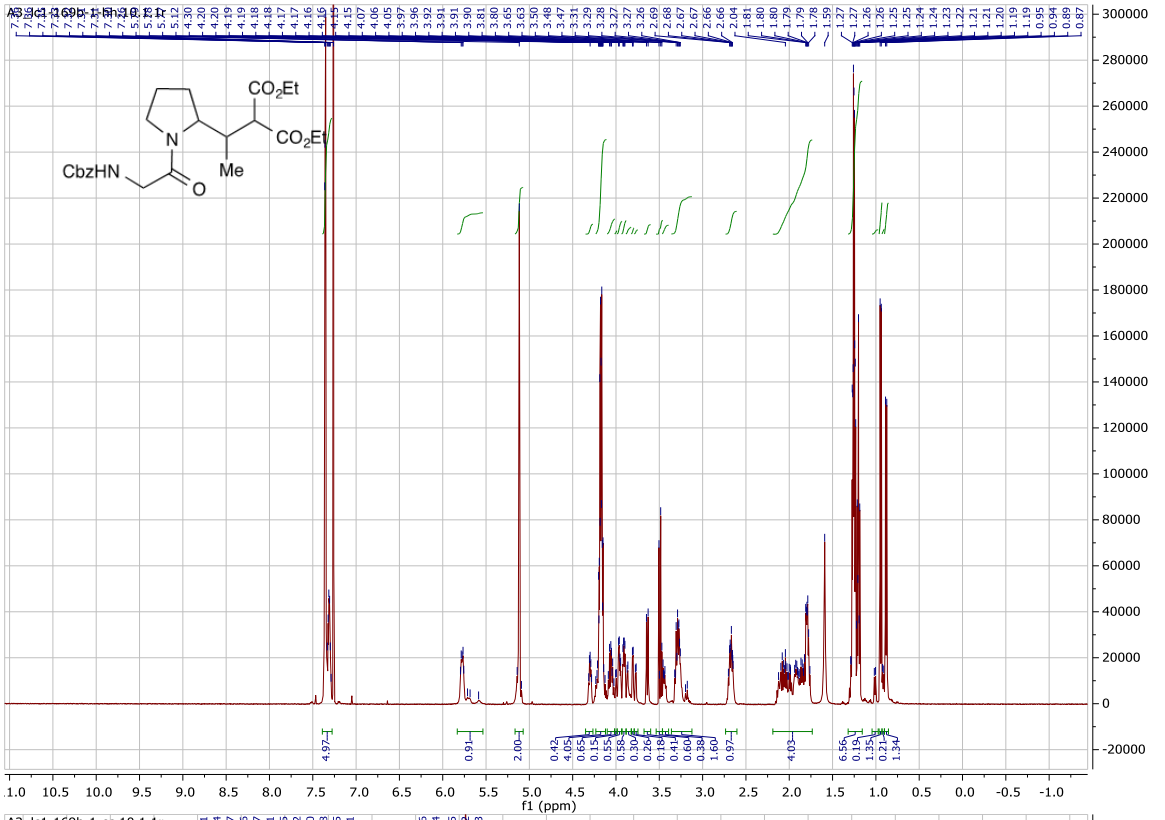
HN
NH
Boc
CO2Et
f1 (ppm)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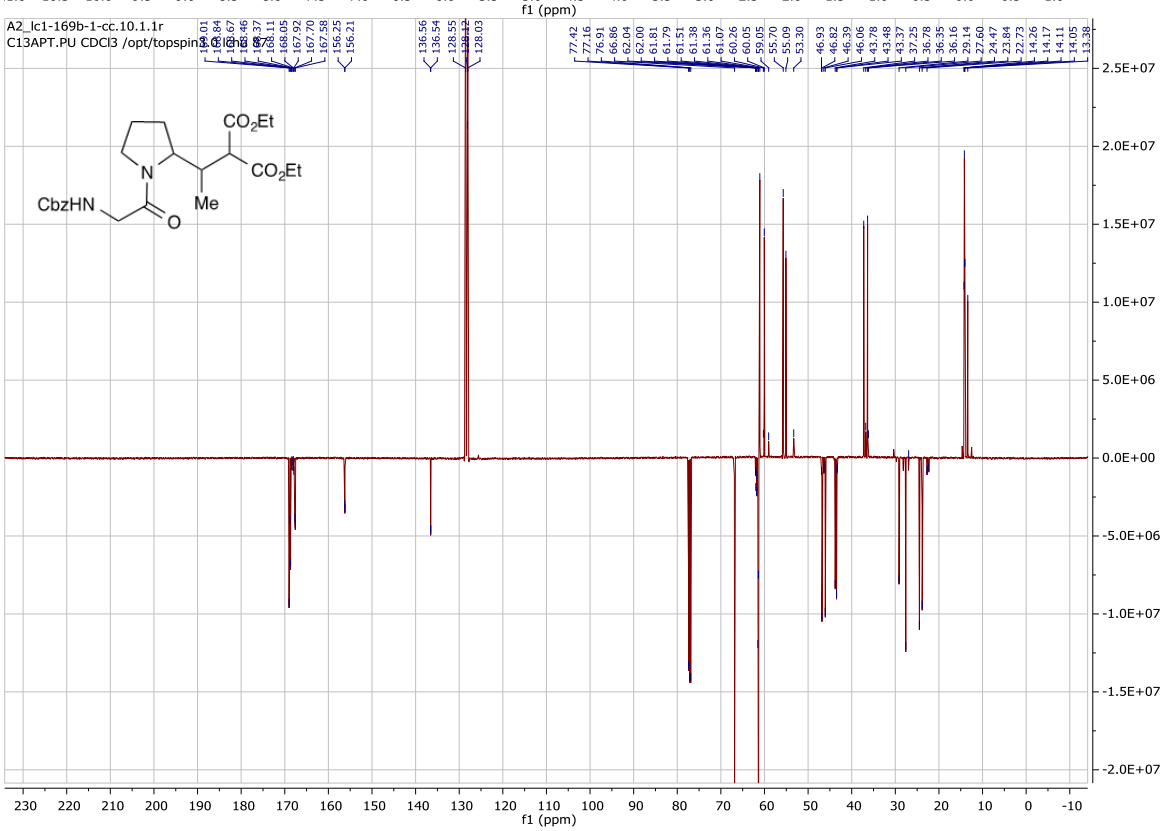
f1 (ppm)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O
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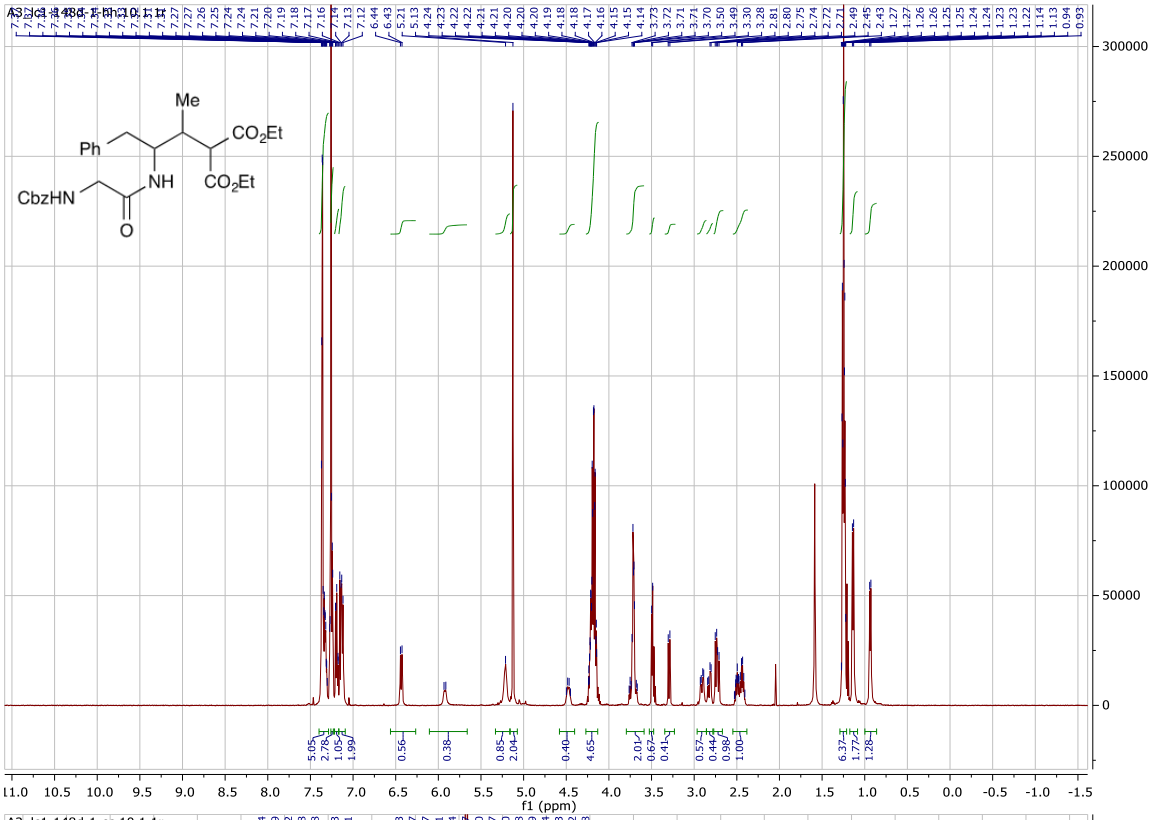
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Ph
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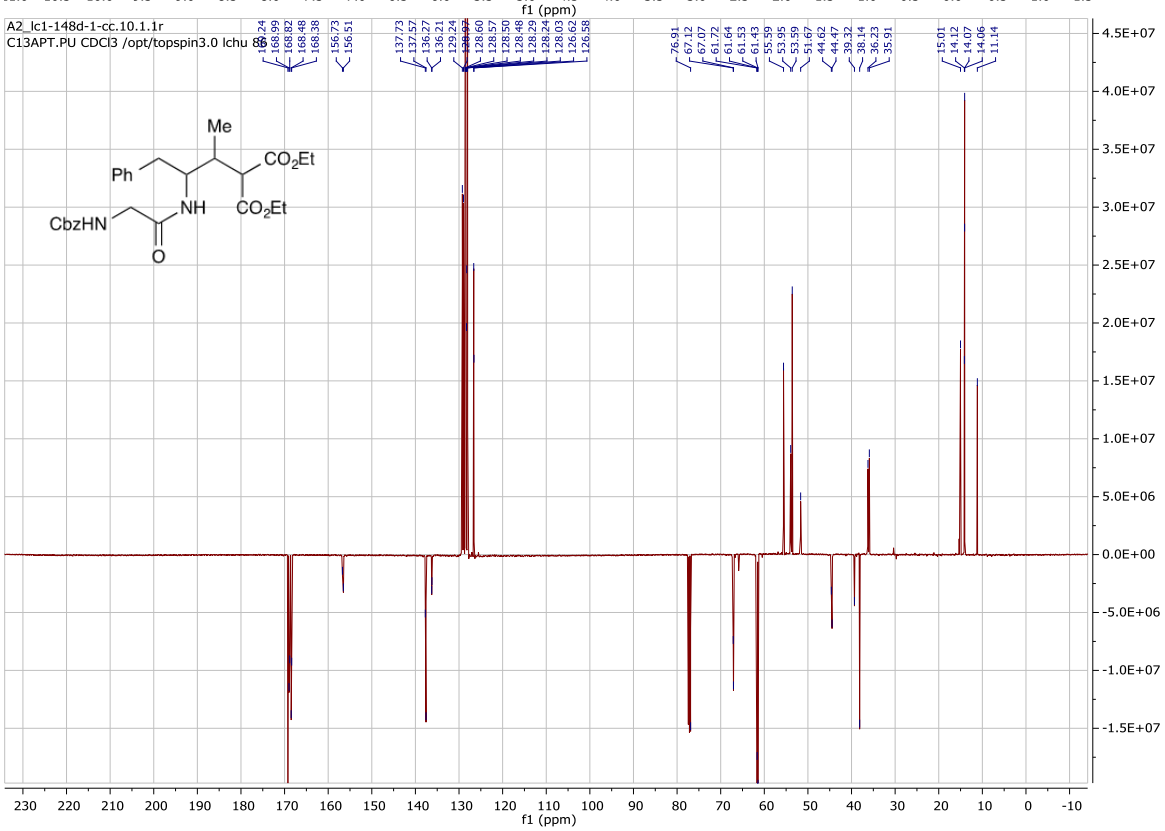
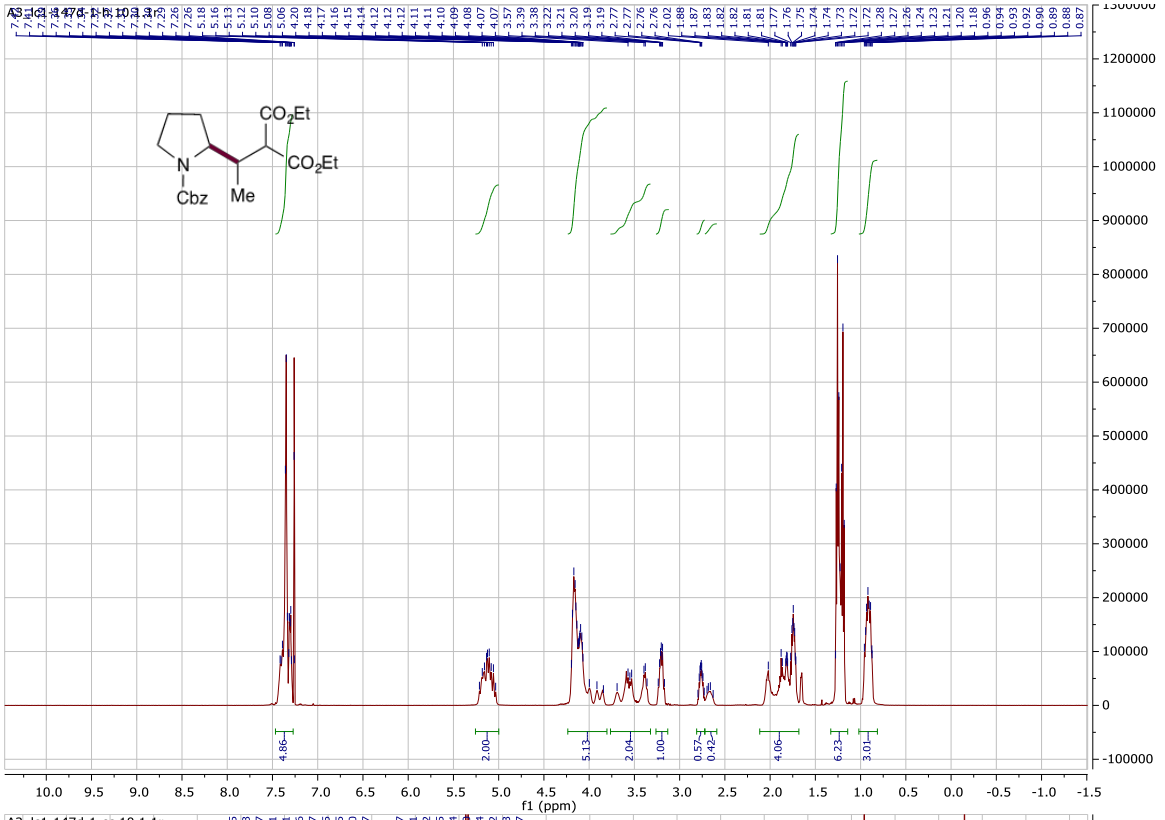
NH
CO2Et
CbzHN
O
f1 (ppm)


A2_lc1-148d-1-cc.10.1.1r
C13APT.PU CDCl3 /opt/topspin3.0 lchu 8
Me
Ph
CO2Et
NH
CO2Et
CbzHN
O
f1 (ppm)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CO2Et
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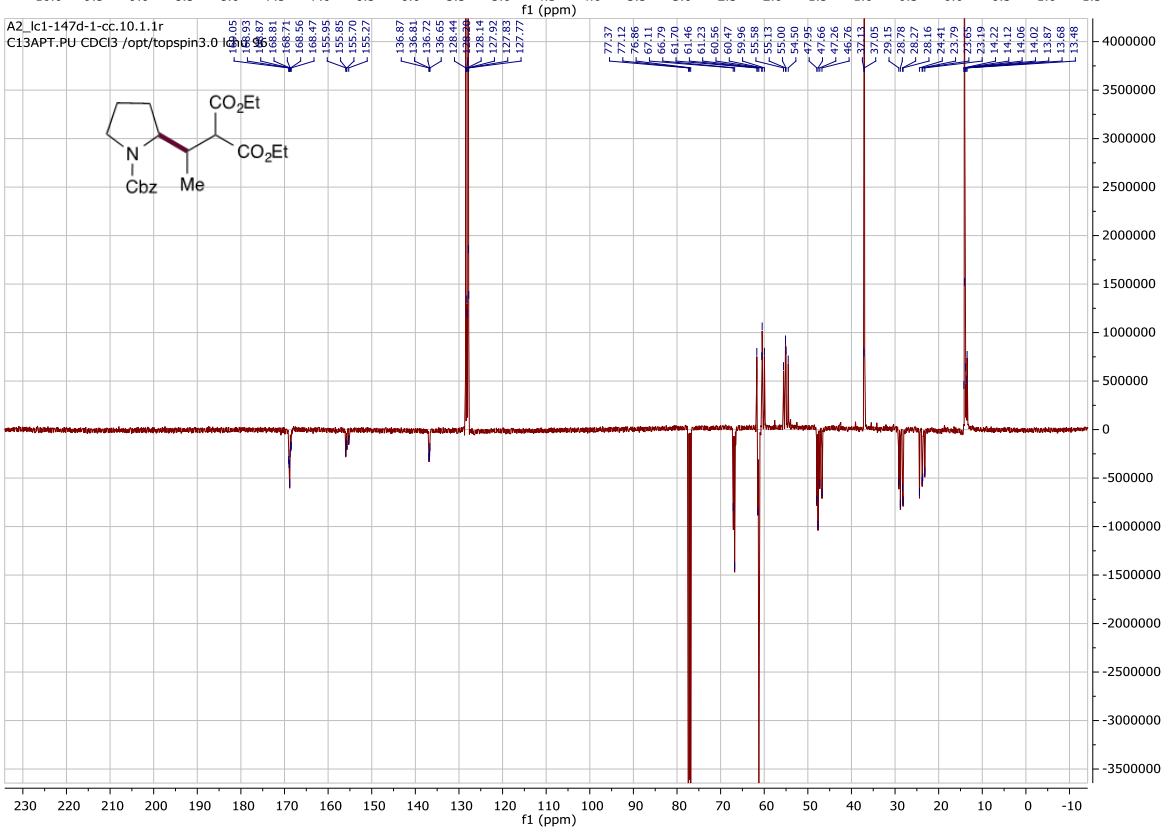
Cbz
Me
f1 (ppm)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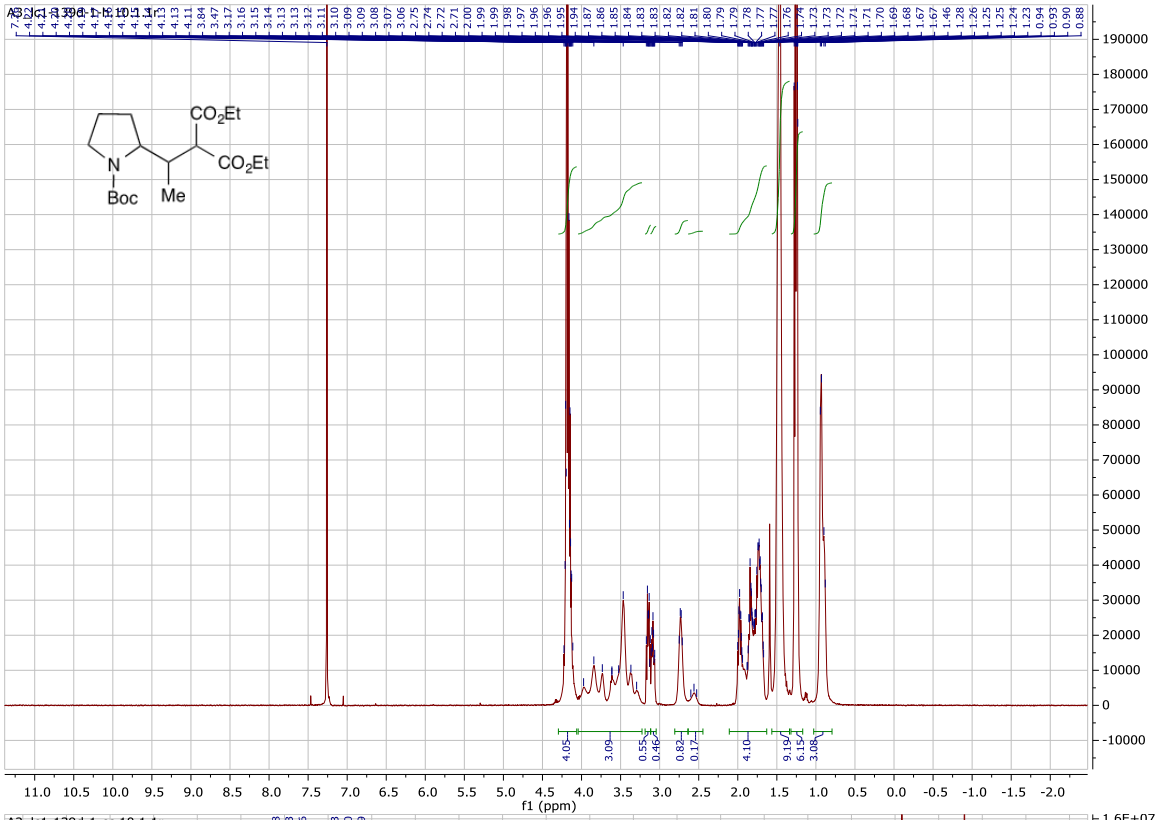
Cbz
Me
f1 (ppm)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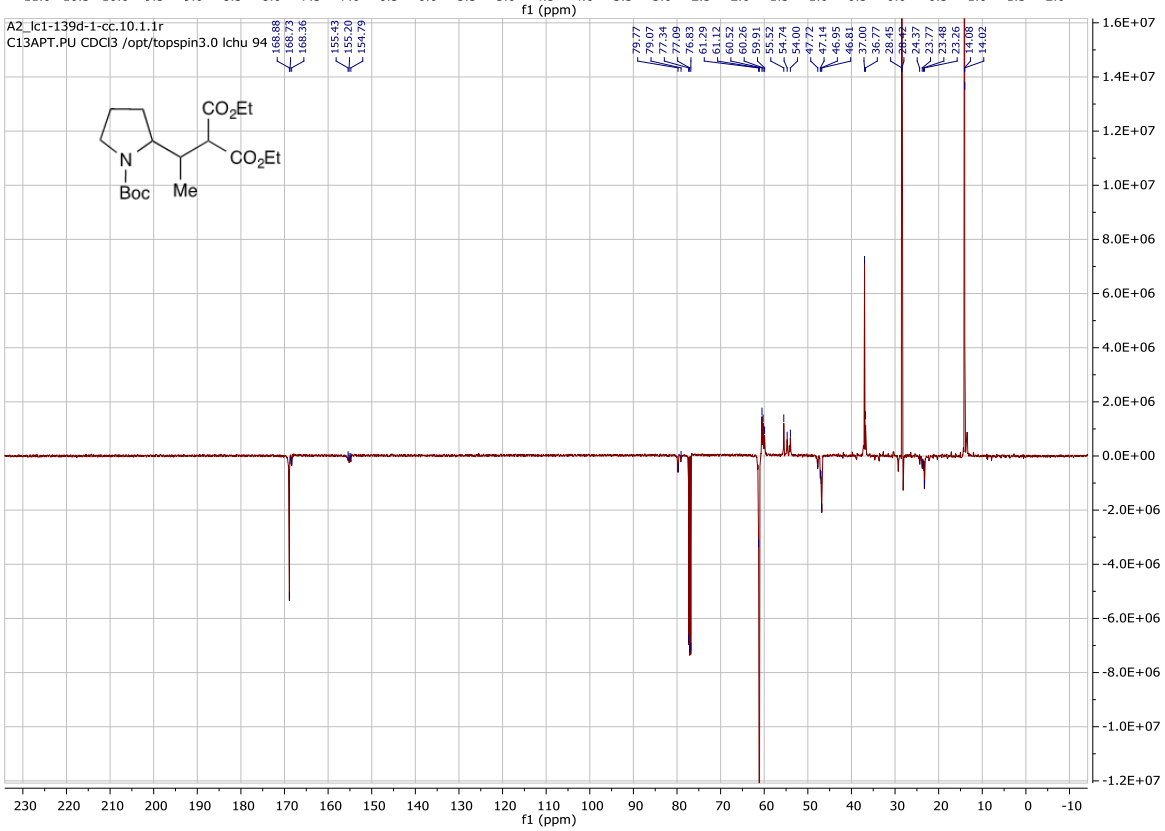
CO2Et
N
Boc
Me
f1 (ppm)


A2_lc1-139d-1-cc.10.1.1r
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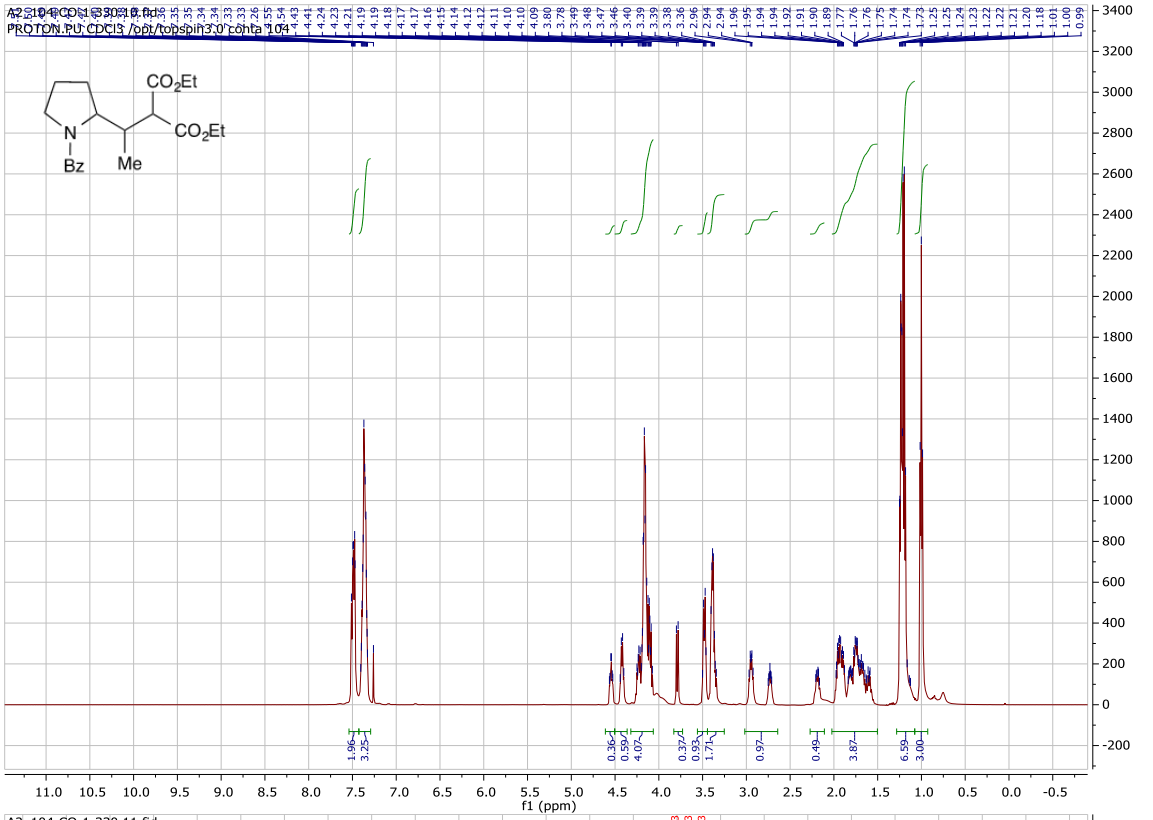
CO2Et
CO2Et
N
Boc
Me
f1 (ppm)


A2_104-CO-1-330.10.fid
PROTON.PU CDCl3 /opt/topspin3.0 conta 104
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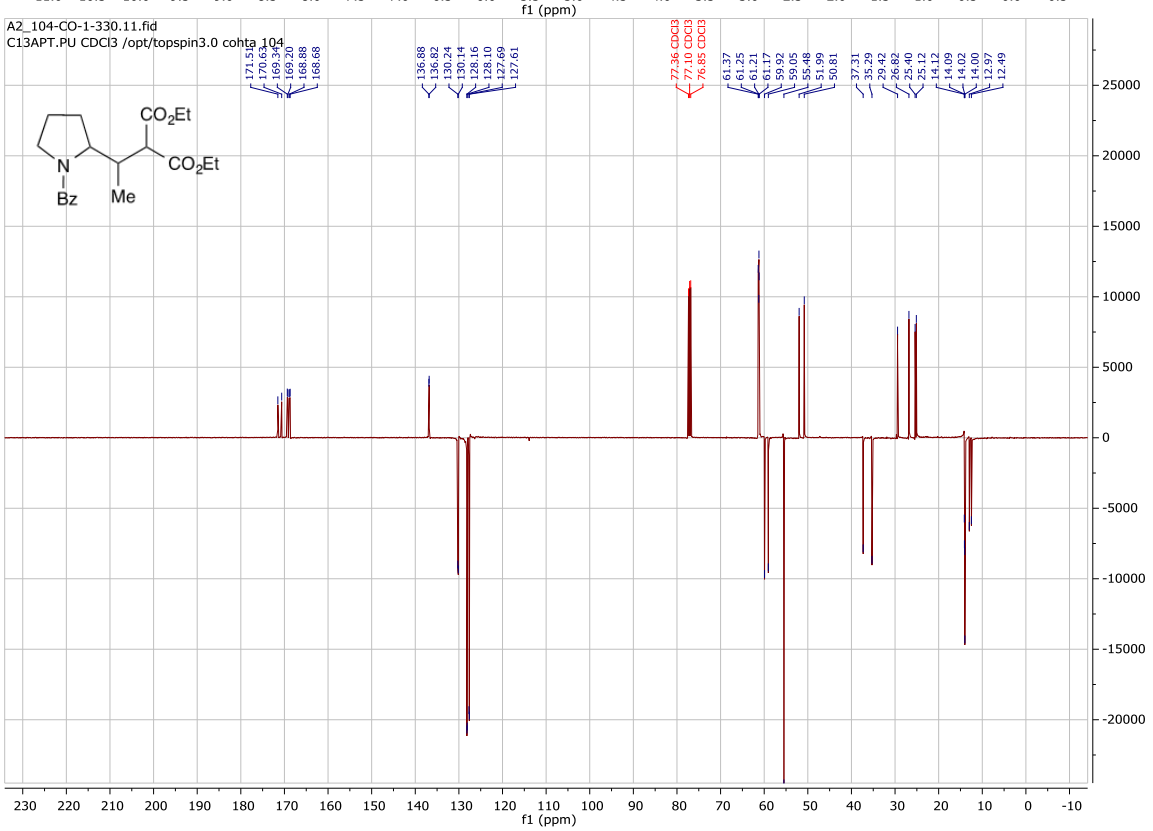
CO2Et
N
Bz
Me
f1 (ppm)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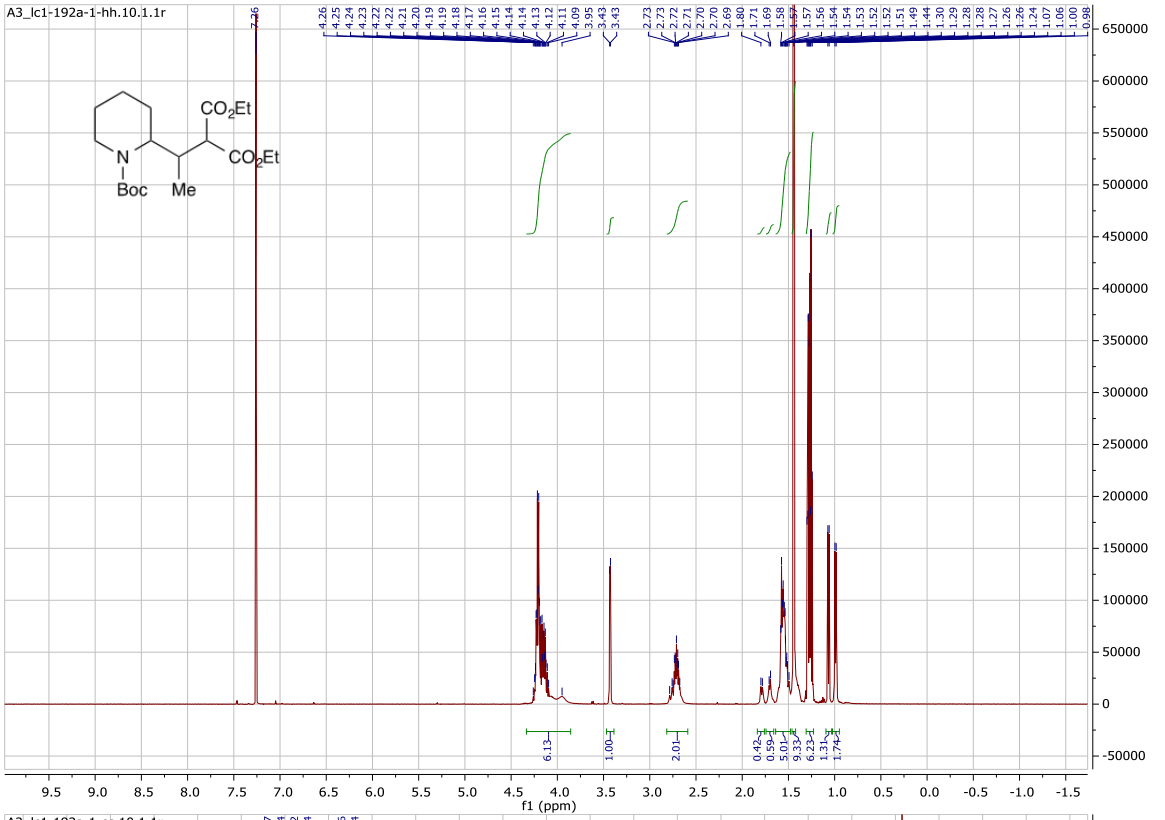
CO2Et
N
Bz
Me
f1 (ppm)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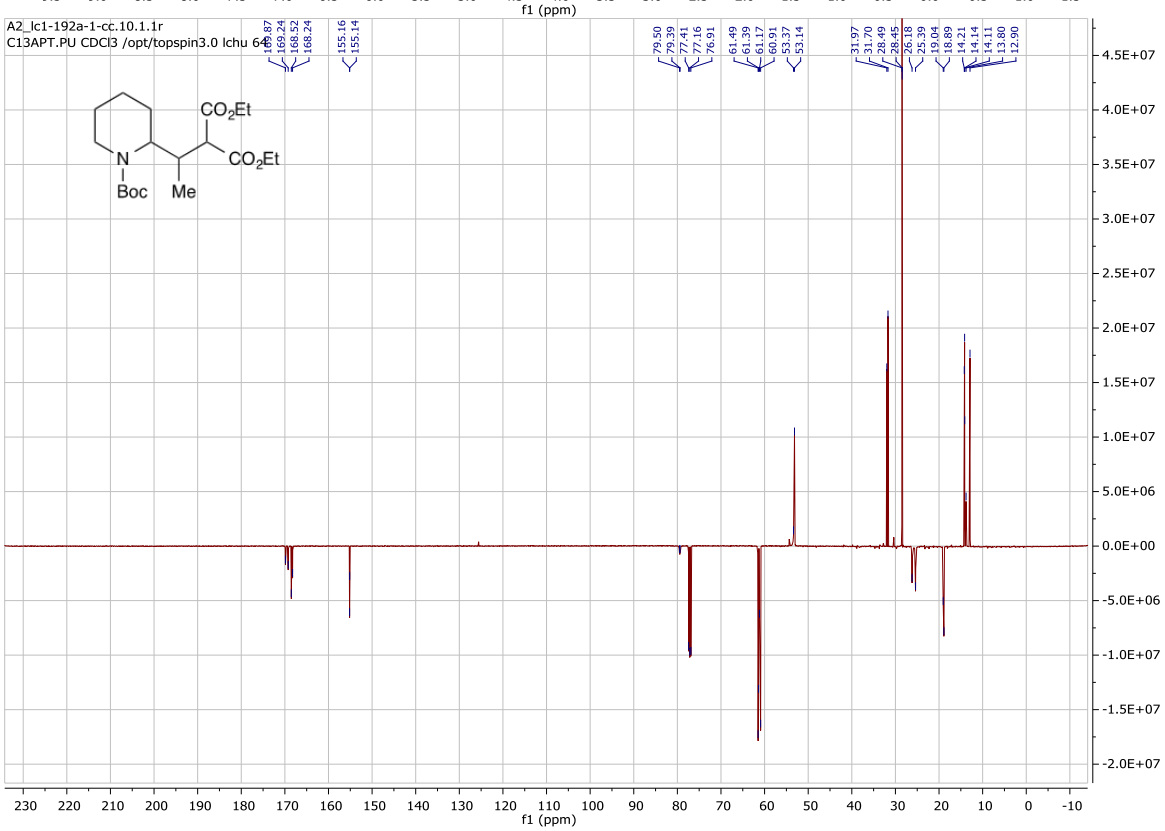
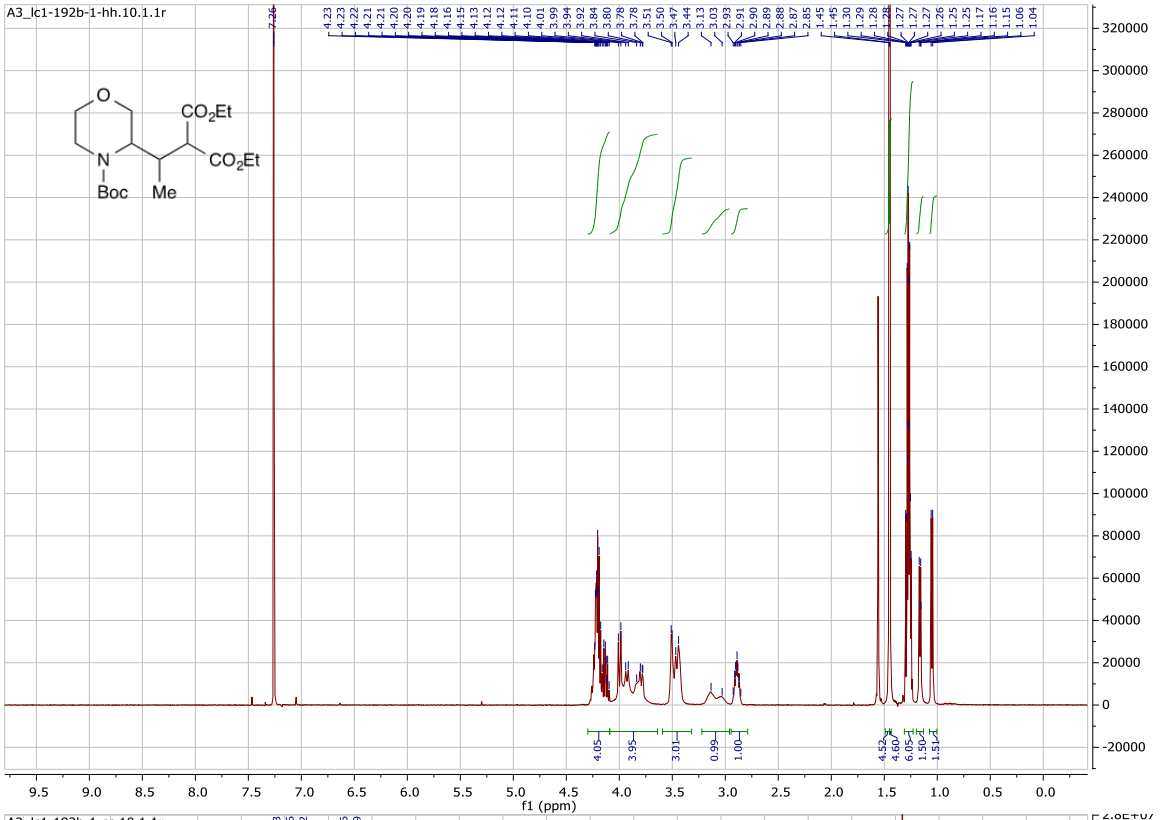
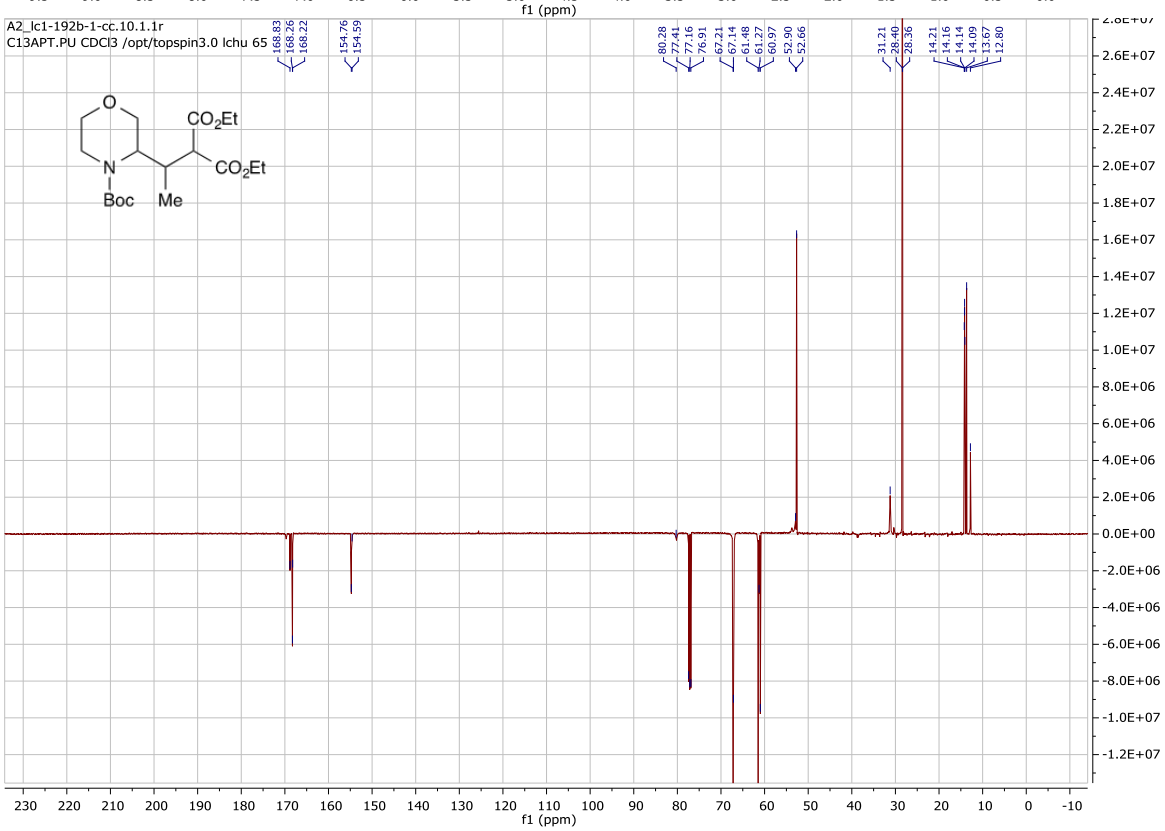
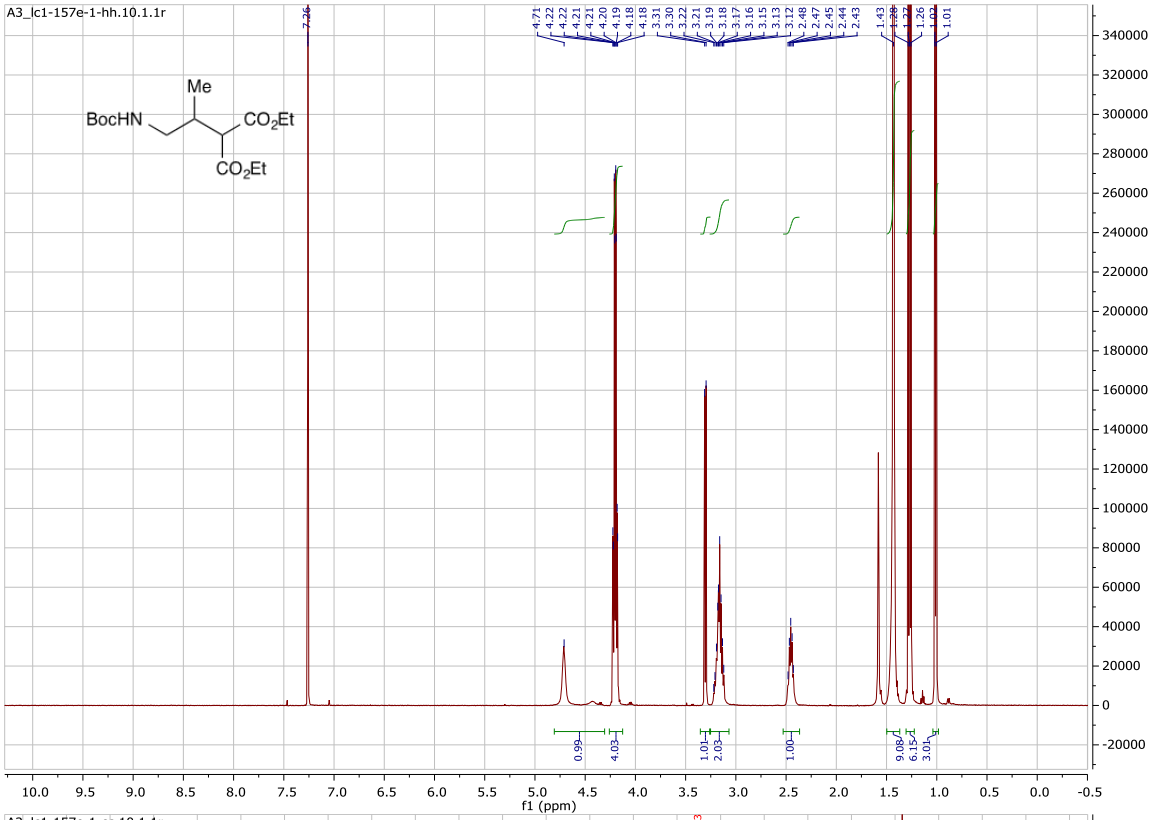
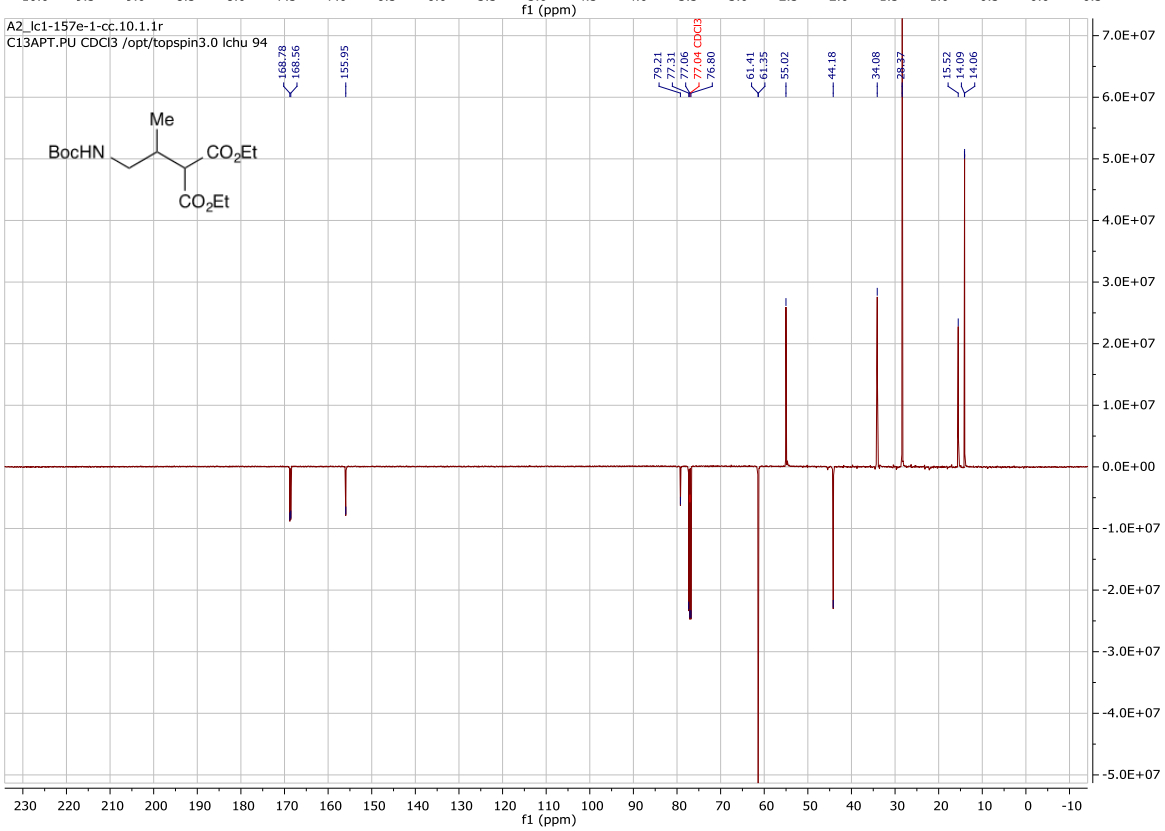
CO2Et
N
Boc
Me
f1 (ppm)

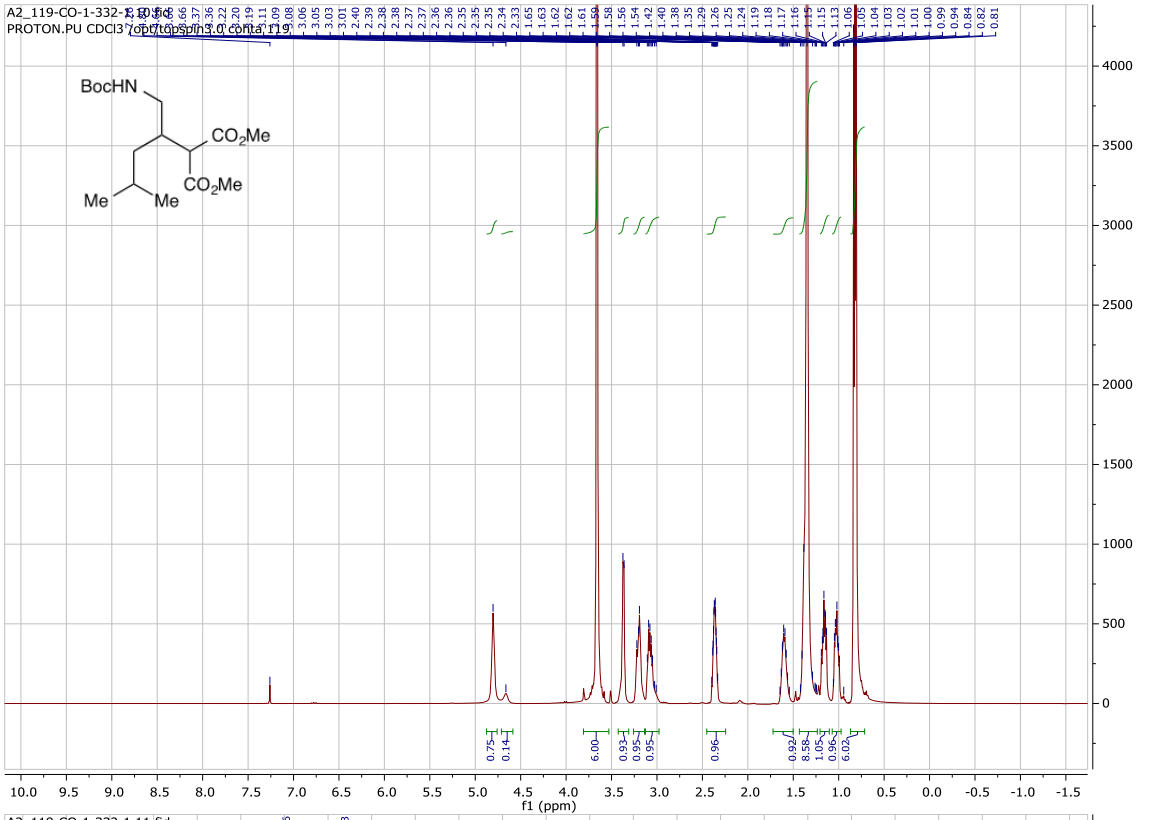

A2_lc1-192a-1-cc.10.1.1r
C13APT.PU CDCl3 /opt/topspin3.0 lchu 64
CO2Et
CO2Et
N
Boc
Me
f1 (ppm)

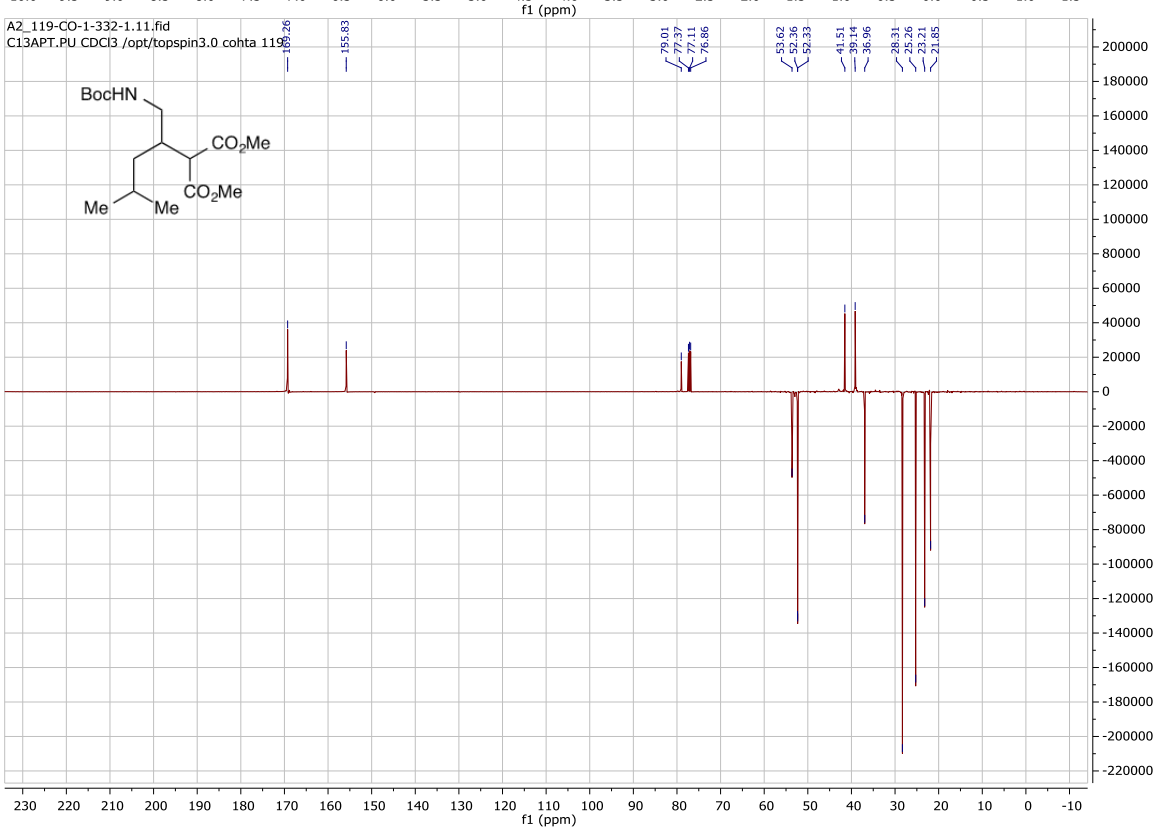

A3_lc1-192b-1-hh.10.1.1r
O
N
Boc
Me
CO2Et
CO2Et
f1 (ppm)

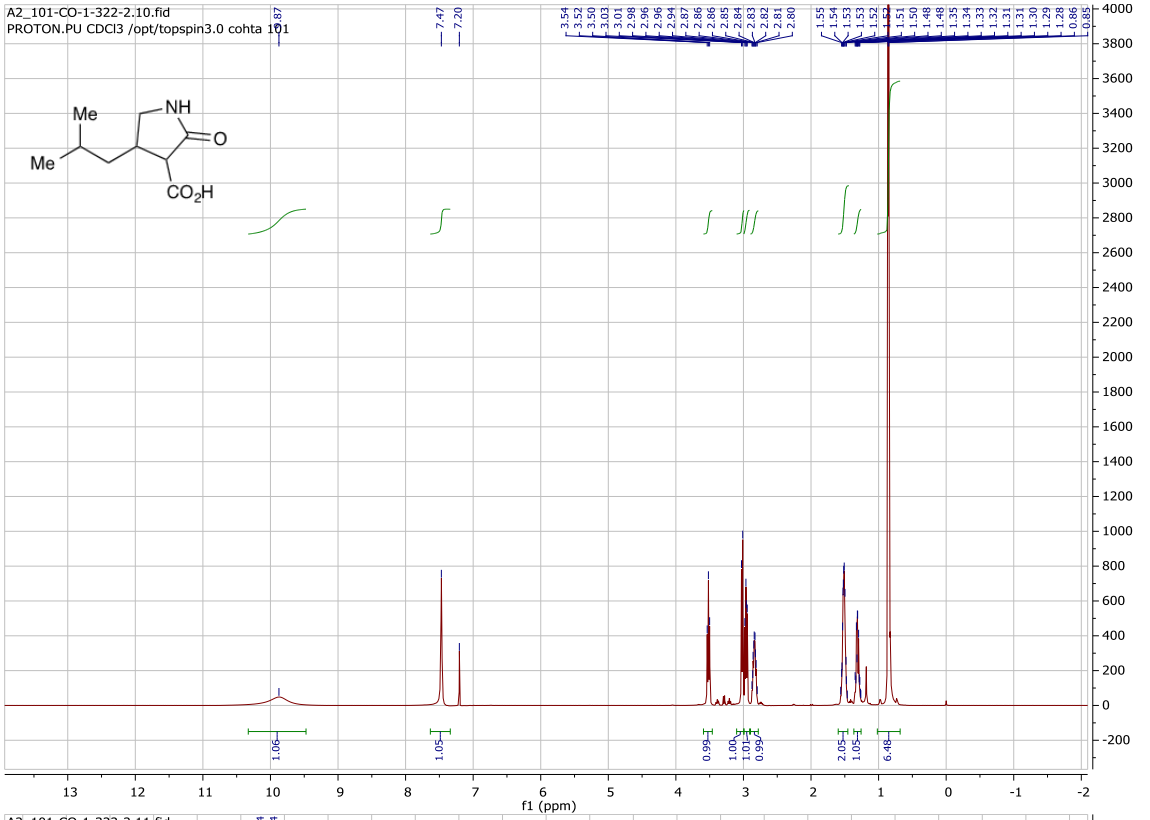

A2_lc1-192b-1-cc.10.1.1r
C13APT.PU CDCl3 /opt/topspin3.0 lchu 65
O
N
Boc
Me
CO2Et
CO2Et
f1 (ppm)

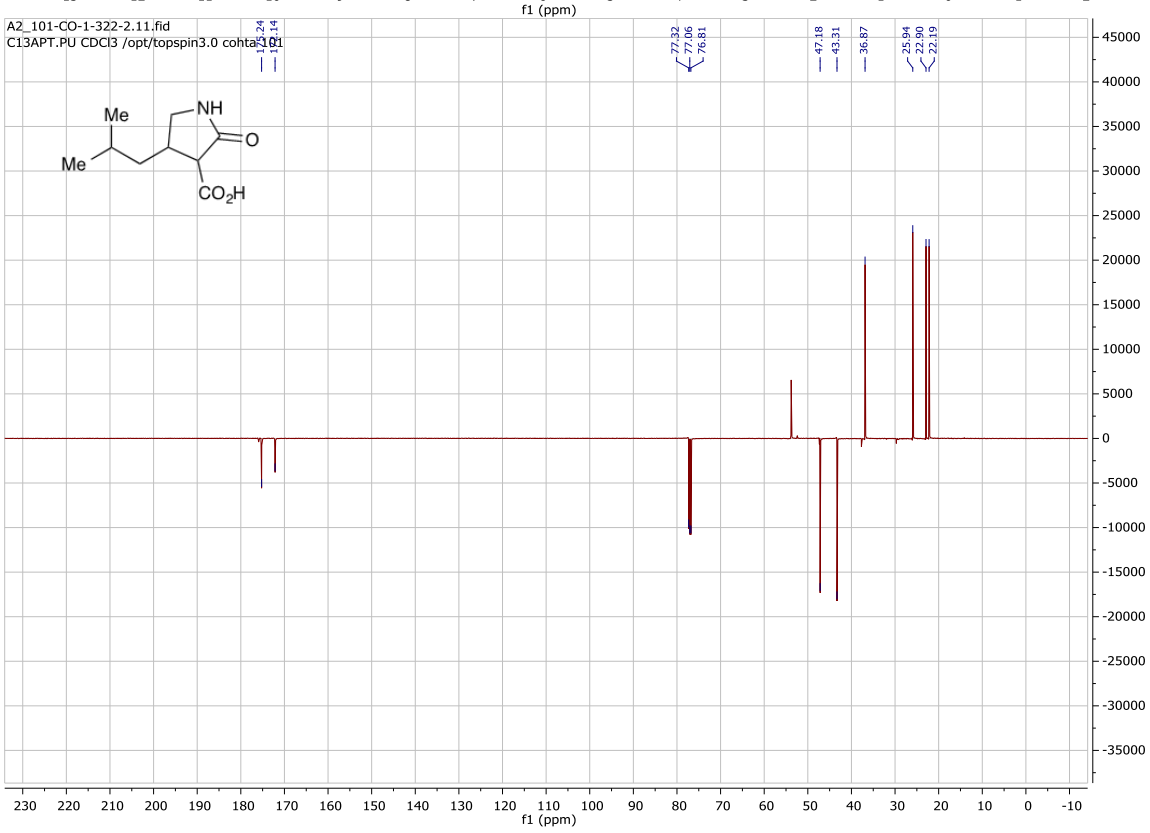

A3_lc1-157e-1-hh.10.1.1r
Me
BocHN
CO2Et
CO2Et
f1 (ppm)

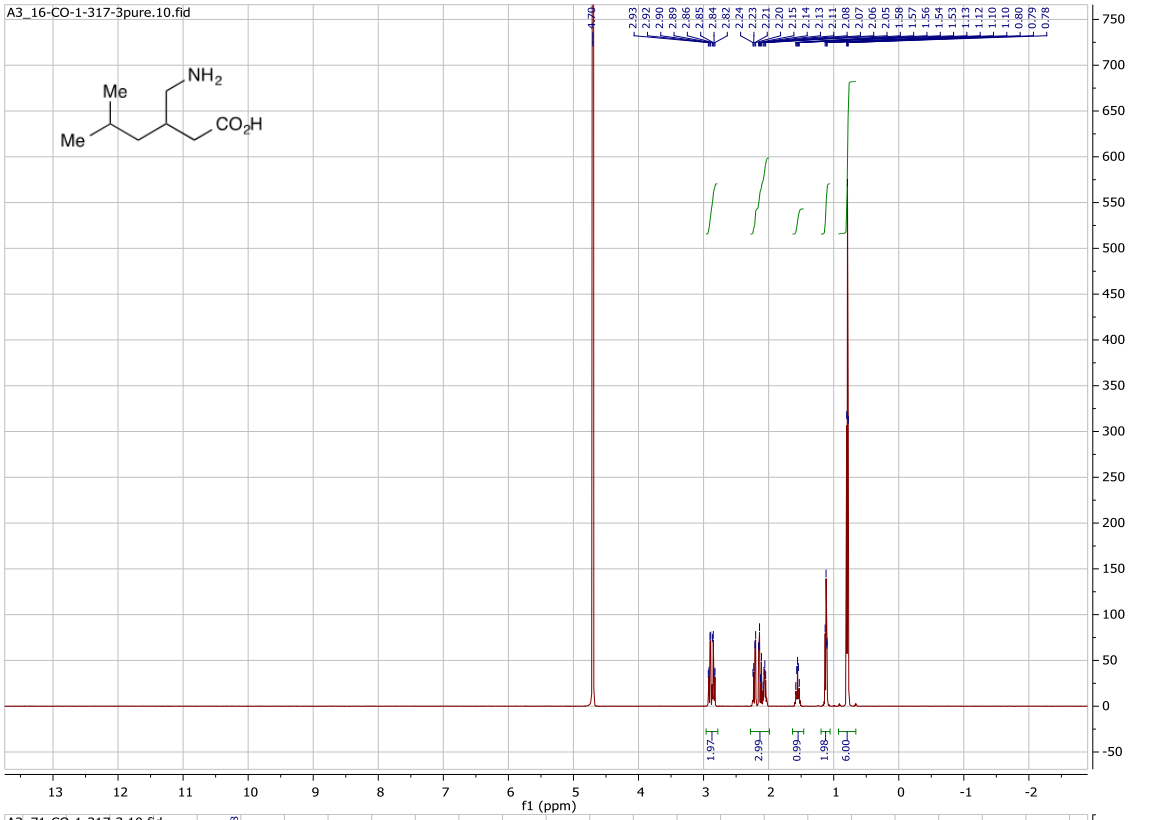

A2_lc1-157e-1-cc.10.1.1r
C13APT.PU CDCl3 /opt/topspin3.0 lchu 94
Me
BocHN
CO2Et
CO2Et
CDCl3
f1 (ppm)

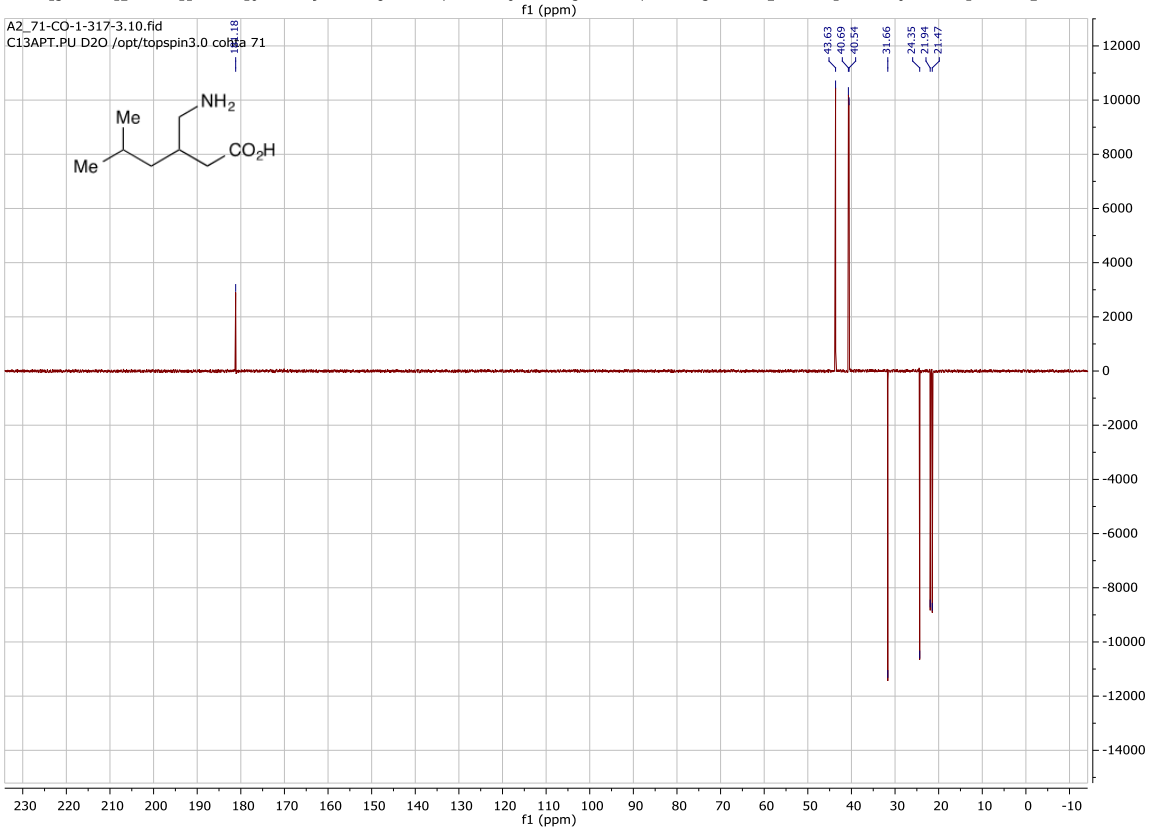

BocHN
CO2Me
CO2Me
Me
Me
f1 (ppm)

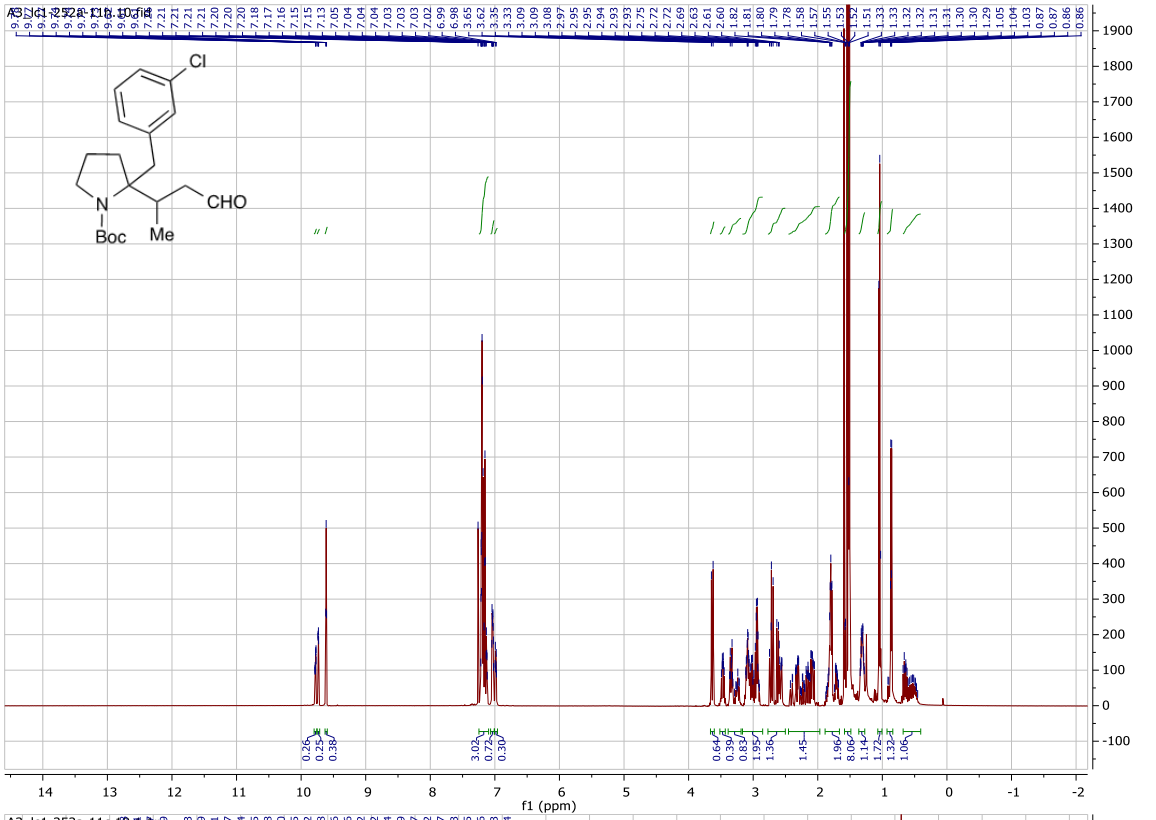

BocHN
CO2Me
CO2Me
Me
Me
f1 (ppm)

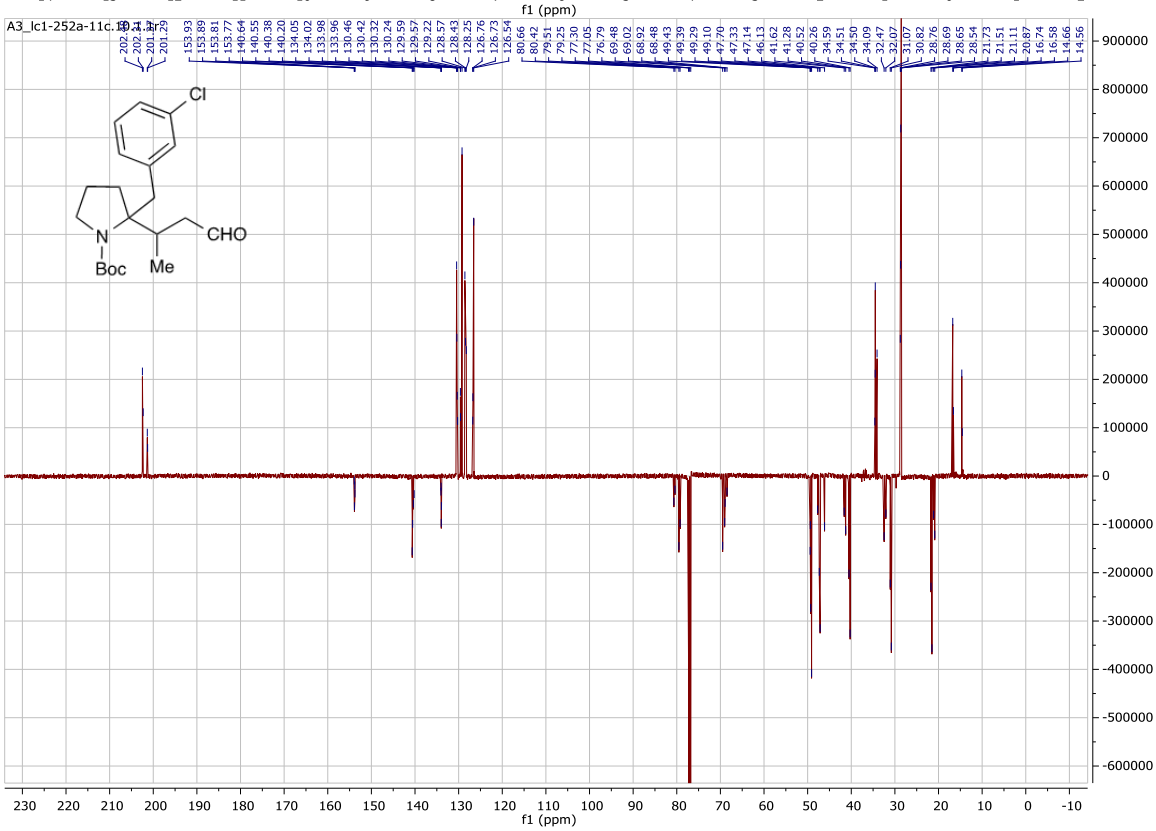

A2_101-CO-1-322-2.10.fid
PROTON.PU CDCl3 /opt/topspin3.0 cohta 101
Me
Me
NH
O
CO2H
f1 (ppm)

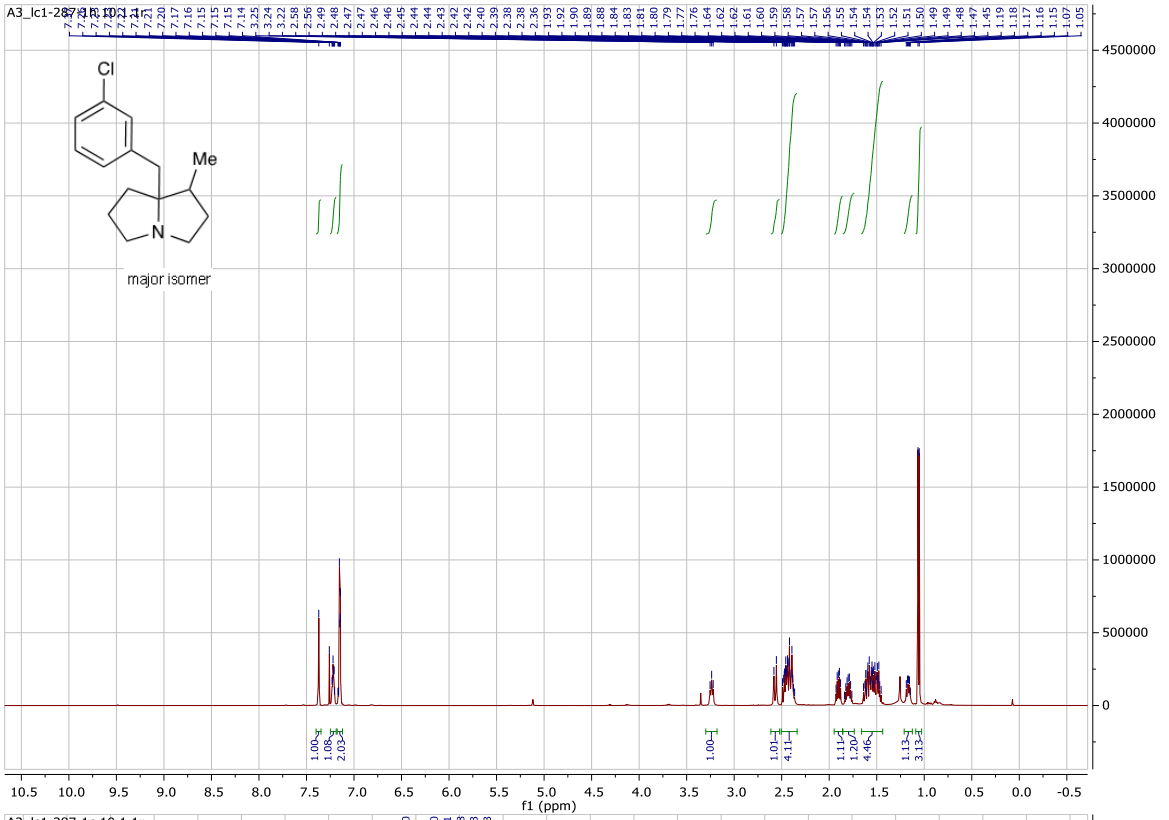

A2_101-CO-1-322-2.11.fid
C13APT.PU CDCl3 /opt/topspin3.0 cohta 101
Me
Me
NH
O
CO2H
f1 (ppm)

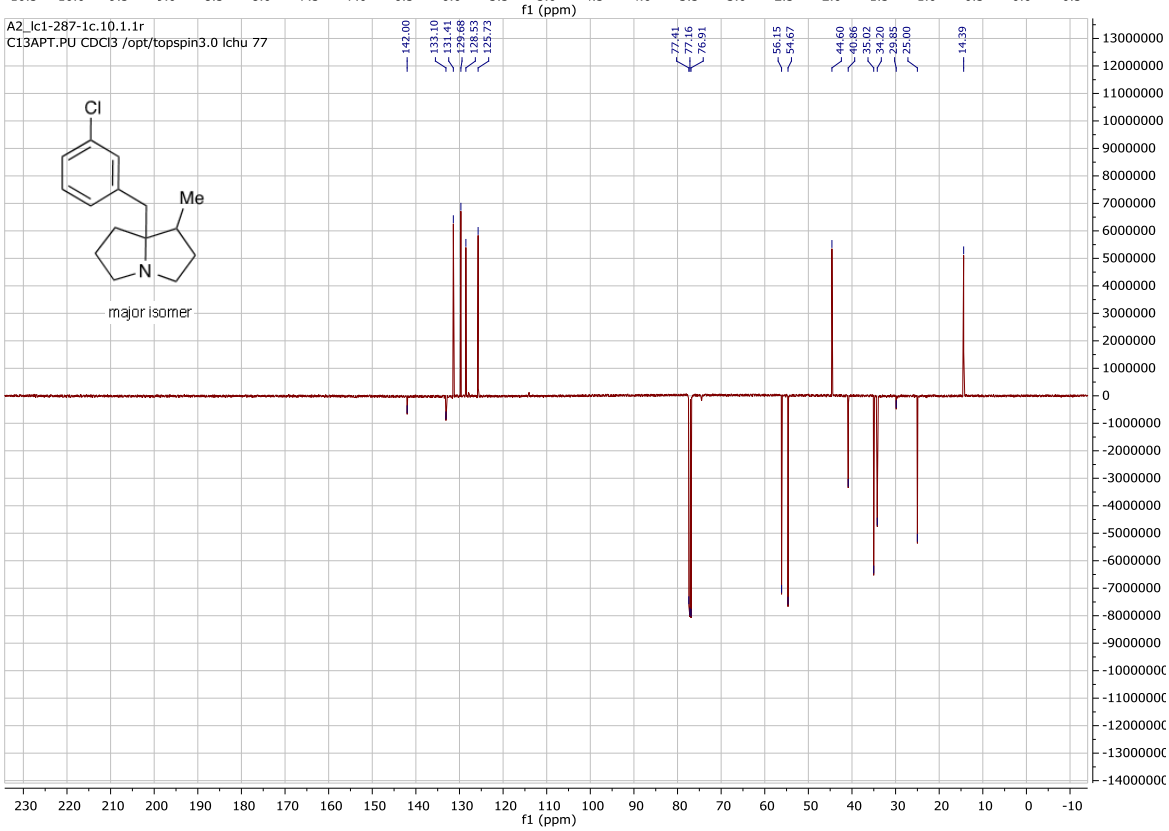

A3_16-CO-1-317-3pure.10.fid
Me
NH2
Me
CO2H
f1 (ppm)

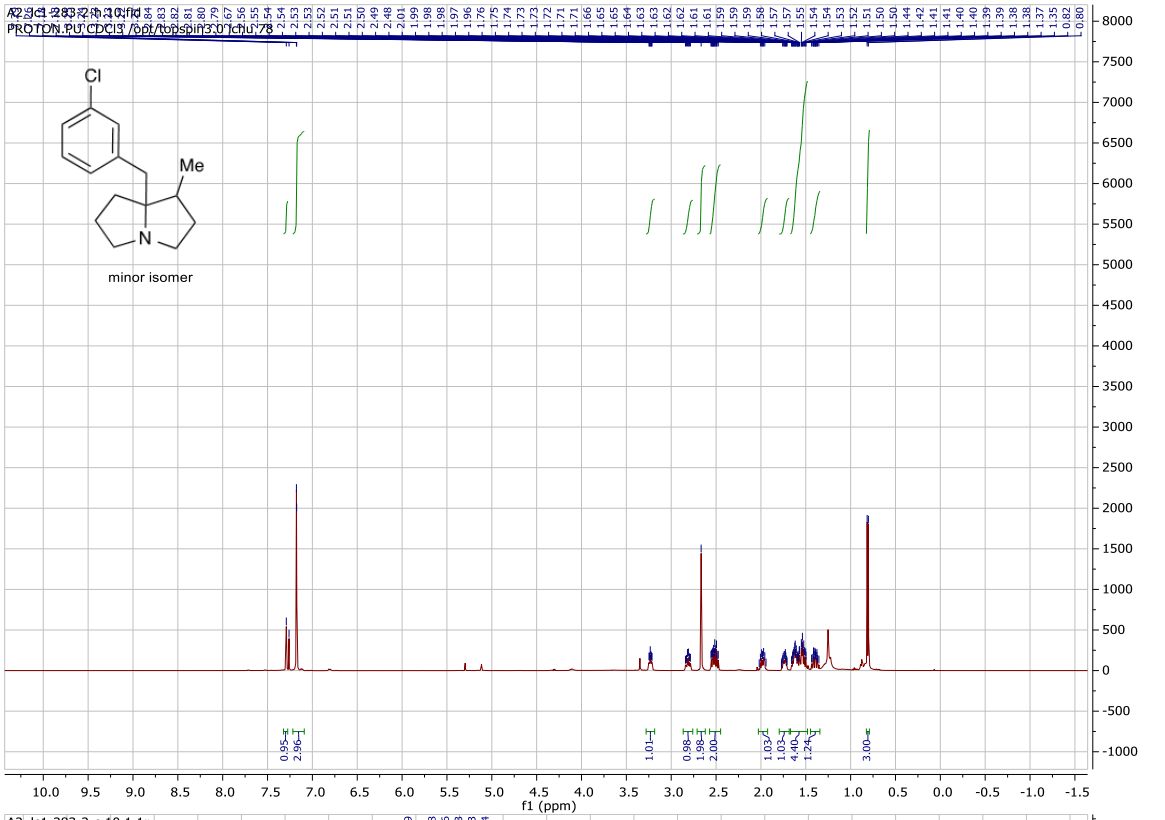

A2_71-CO-1-317-3.10.fid
C13APT.PU D2O /opt/topspin3.0 conta 71
Me
NH2
Me
CO2H
f1 (ppm)

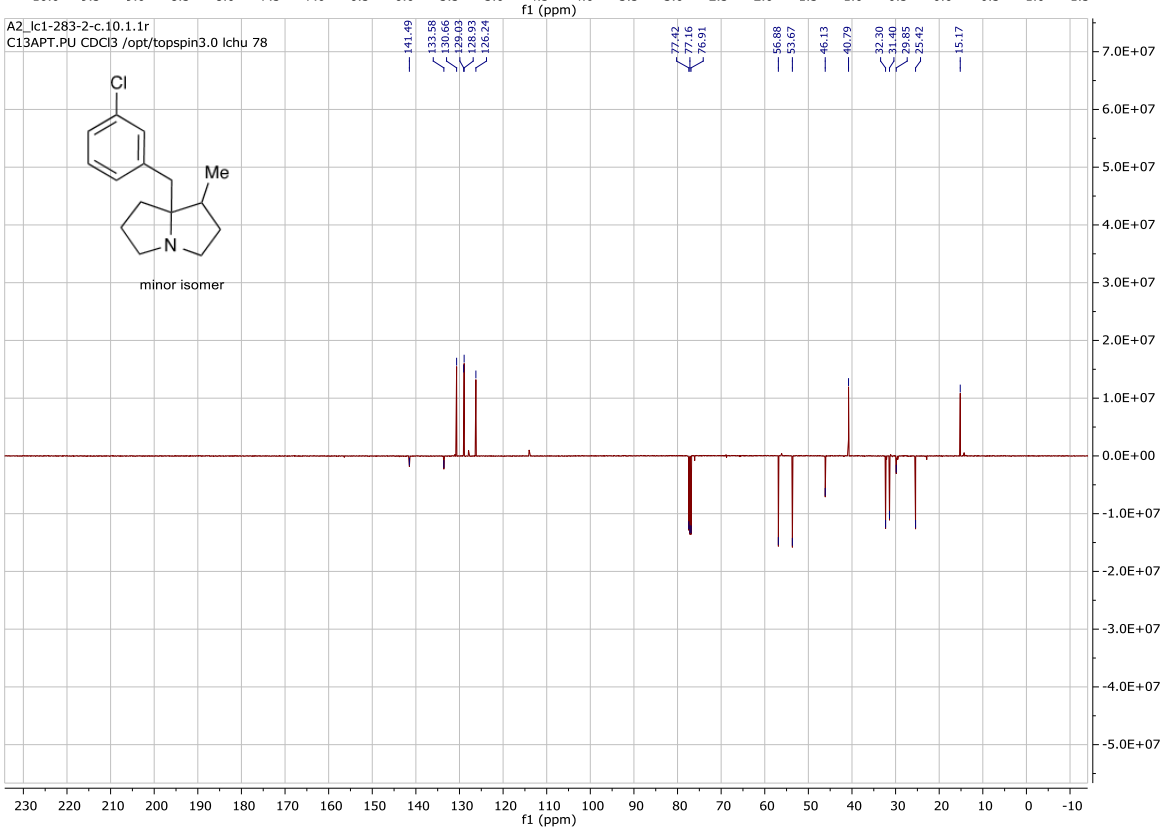

Cl
CHO
N
Boc
Me
f1 (ppm)


Cl
CHO
N
Boc
Me
f1 (ppm)


A3_lc1-287-1H.10.1.1r
Cl
Me
N
major isomer
f1 (ppm)


A2_lc1-287-1c.10.1.1r
C13APT.PU CDCl3 /opt/topspin3.0 lchu 77
Cl
Me
N
major isomer
f1 (ppm)


A2_lc1-283-2-h.10.fid
PROTON.PU CDCl3 /opt/topspin3.0 lchu 78
Cl
Me
N
minor isomer
f1 (ppm)


A2_lc1-283-2-c.10.1.1r
C13APT.PU CDCl3 /opt/topspin3.0 lchu 78
141.49
133.58
130.66
129.03
128.93
126.24
77.42
77.16
76.91
56.88
53.67
46.13
40.79
32.30
31.40
29.85
25.42
15.17
Cl
Me
N
minor isomer
f1 (ppm)