Ligand-Enabled β-C–H Arylation of Alpha-Amino Acids Using a Simple and Practical Auxiliary

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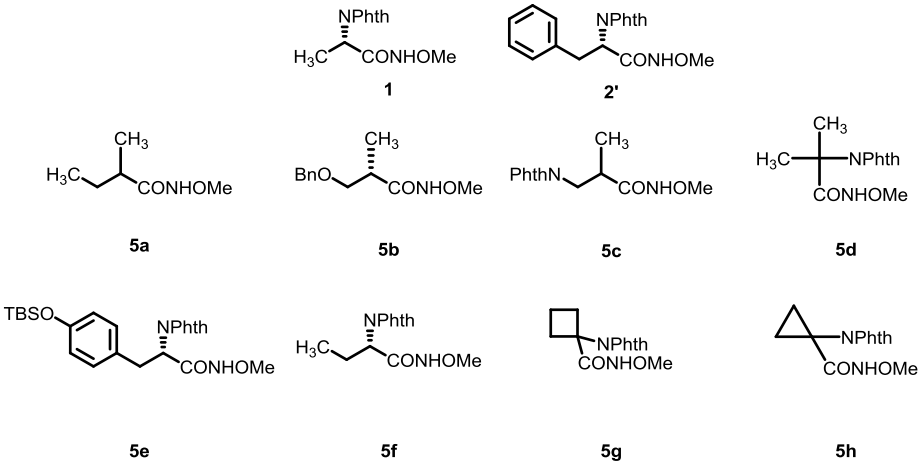
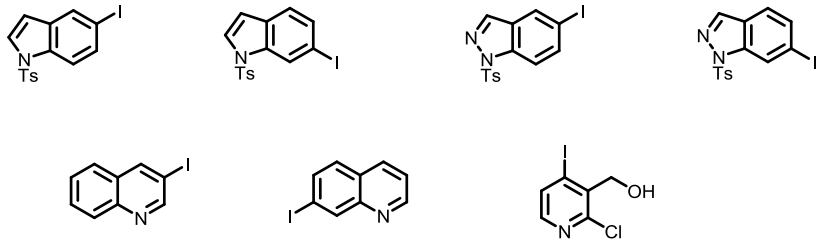
General Information: Solvents were obtained from Sigma-Aldrich, Alfa-Aesar and Acros and used directly without further purification. Carboxylic acids and carboxylic acid chlorides were obtained from the commercial sources or synthesized following literature procedures, and used to prepare the corresponding amides. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light and Vogel's permanganate. ^{1}H NMR spectra were recorded on Bruker AMX-400 instrument (400 MHz) or Bruker DRX-600 instrument (600 MHz). When the ^{1}H NMR solvent was $CDCl_3$, chemical shifts were quoted in parts per million (ppm) referenced to 0.00 ppm for tetramethylsilane; When the ^{1}H NMR solvent was MeOD, chemical shifts were quoted in parts per million (ppm) referenced to 3.31 ppm for solvent MeOD; When the ^{1}H NMR solvent was Acetone-*d*-6, chemical shifts were quoted in parts per million (ppm) referenced to 2.05 ppm for solvent Acetone-*d*-6. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants, *J*, were reported in Hertz unit (Hz). ^{13}C NMR spectra were recorded on Bruker DRX-600 instrument (150 MHz), and were fully decoupled by broad band proton decoupling. When the ^{13}C NMR solvent was $CDCl_3$, chemical shifts were reported in ppm referenced to 0.0 ppm for tetramethylsilane; When the ^{13}C NMR solvent was MeOD, chemical shifts were quoted in parts per million (ppm) referenced to 49.1 ppm for solvent MeOD; When the ^{13}C NMR solvent was Acetone-*d*-6, chemical shifts were quoted in parts per million (ppm) referenced to 29.9 ppm for solvent Acetone-*d*-6. High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight). Melting points were obtained from a Mel-temp II apparatus (uncorrected). HPLC profiles were obtained on a Hitachi LaChrom Elite HPLC system using commercially available chiral columns.

Structures of Substrates



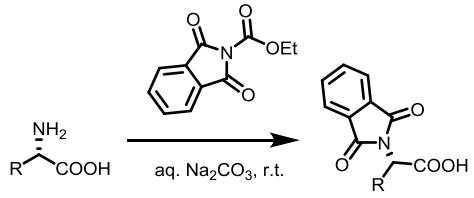
Structures of Heterocyclic Iodides prepared in our laboratory



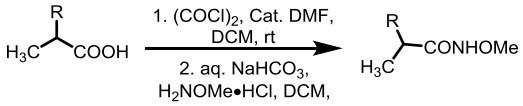
Experimental Section

A. Preparation of Substrates

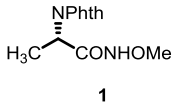
General Method A (Amino Acid Substrates):



Synthesis of phthalimide-protected amino acids:[1] amino acid (1 equiv) and Na_2CO_3 (1 equiv) were dissolved in water (1M) at room temperature and *N*-ethoxycarbonylphthalimide (1 equiv) was added to the solution in small portions. The reaction was stirred for 3 hours at room temperature, and then the aqueous solution was cooled to ^{o}C and slowly acidified with aqueous HCl (6 M) until pH of 1-2 was attained and white precipitate was observed. The precipitate was collected and washed with aqueous HCl (20 mL, 1M) and EtOAc/hexanes = 1/5 (20 mL) to give phthalimide-protected amino acid in high yields.



Synthesis of *N*-methoxy amides from acids: To a 250 mL round-bottom flask were added the acid (50 mmol, 1 equiv), DCM (100 mL), and 0.05 mL DMF, oxalyl chloride (100 mmol, 8.5 mL, 2 equiv) was added slowly to the mixture, the above mixture were reacted for 3 h at room temperature. Then, the excess of oxalyl chloride and DCM were removed *in vacuo*, and the crude acid chloride in DCM (60 mL) was added slowly to a vigorously stirring solution of $H_2NOMe•HCl$ (60 mmol, 5.0 g, 1.2 equiv) and $NaHCO_3$ (120 mmol, 2.4 equiv), in DCM (60 mL) and water (60 mL) in ice cooled bath. The reaction mixture was stirred for 3 h at 0 ^{o}C (monitored by TLC), after which H_2O and DCM was added to the reaction mixture. The aqueous layer was then extracted with DCM (3 ×) and the combined organics were washed with brine, dried over Na_2SO_4, filtered and concentrated. The product was recrystallized in DCM/hexanes to give the pure amide (over 90% yield).

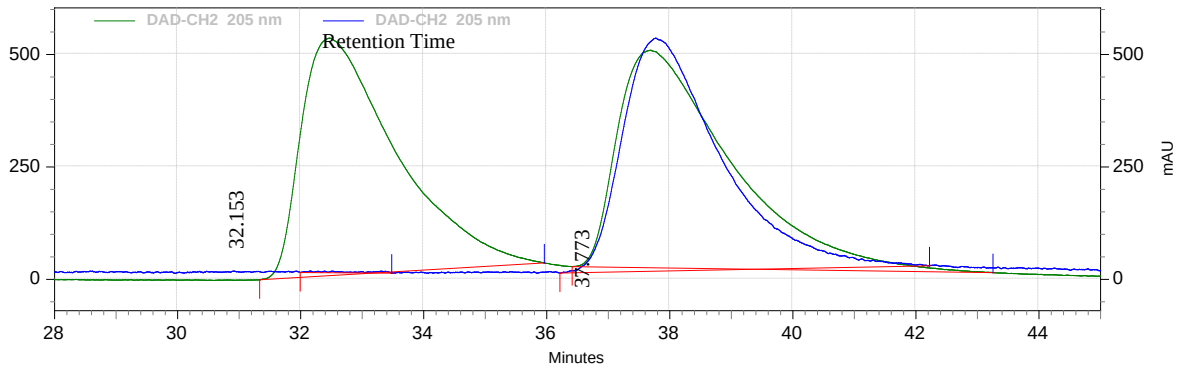


1

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxypropanamide (1)

White solid. m.p. = 126-127 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 7.89-7.86 (m, 2H), 7.78-7.75 (m, 2H), 4.97 (m, 1H), 3.77 (s, 3H), 1.70 (d, J = 7.4 Hz, 3H). The ee value was determined by HPLC analysis on a Chiralcel OD-H column (20% isopropanol in hexanes, 0.4 mL/min) with t_r = 32.2 min (minor), 37.8 min (major): 99% ee.

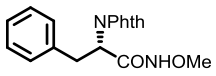
Area % Report



DAD-CH2 205 nm
Results

Retention Time	Area	Area %	Height	Height %
32.153	208785	0.34	3727	0.67
37.773	61441667	99.66	552430	99.33

Totals	61650452	100.00	556157	100.00

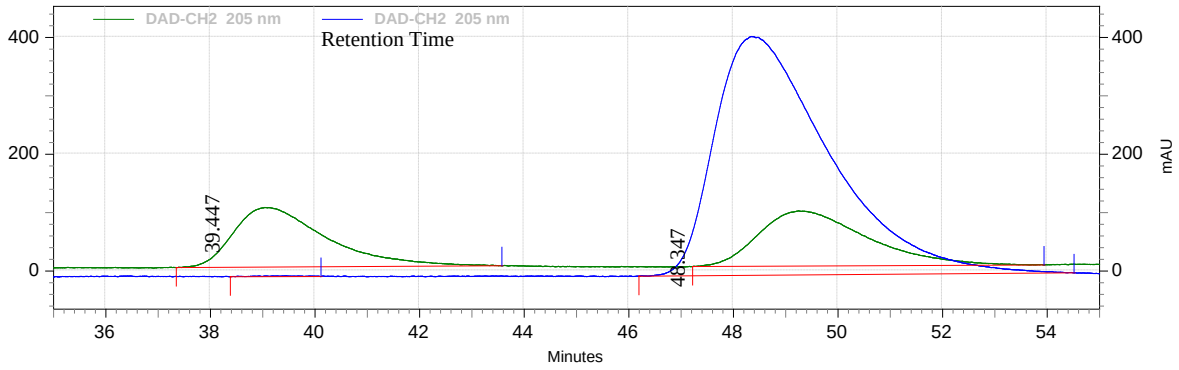


2'

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-phenylpropanamide (2′)

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.31 (s, 1H), 7.78-7.75 (m, 2H), 7.71-7.68 (m, 2H), 7.18-7.11 (m, 5H), 5.08 (m, 1H), 3.75 (s, 3H), 3.54-3.40 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.90, 166.58, 136.07, 134.40, 131.25, 128.89, 128.67, 127.10, 123.60, 64.52, 54.57, 34.75; HRMS (ESI-TOF) Calcd for $C_{18}H_{17}N_2O_4$ $[M+H]^+$: 325.1183; found: 325.1185. The ee value was determined by HPLC analysis on a Chiralcel OD-H column (20% isopropanol in hexanes, 0.4 mL/min) with t_r = 39.4 min (minor), 48.3 min (major): 99% ee.

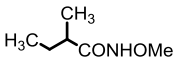
Area % Report



DAD-CH2 205 nm
Results

Retention Time	Area	Area %	Height	Height %
39.447	287676	0.12	5658	0.34
48.347	249491625	99.88	1635575	99.66

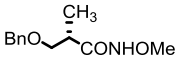
Totals	249779301	100.00	1641233	100.00



5a

_N_-Methoxy-2-methylbutanamide (5a)

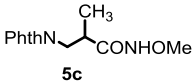
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38 (s, 1H), 3.77 (s, 3H), 1.99 (m, 1H), 1.73-1.66 (m, 1H), 1.49-1.42 (m, 1H), 1.15 (d, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.32, 64.47, 39.92, 27.00, 17.26, 11.78; HRMS (ESI-TOF) Calcd for $C_6H_{14}NO_2$ $[M+H]^+$: 132.1019; found: 132.1020.



5b

(*S*)-3-(Benzyloxy)-*N*-methoxy-2-methylpropanamide (5b)

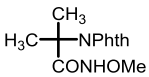
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.37-7.30 (m, 5H), 4.55-4.50 (m, 2H), 3.73 (s, 3H), 3.53-3.50 (m, 2H), 2.49 (m, 1H), 1.15 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.91, 137.44, 128.54, 127.97, 127.77, 73.48, 71.82, 64.31, 38.84, 13.36; HRMS (ESI-TOF) Calcd for $C_{12}H_{18}NO_3$ $[M+H]^+$: 224.1281; found: 224.1284.



5c

3-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-2-methylpropanamide (5c)

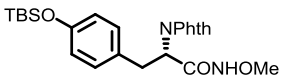
White solid. m.p. = 182-184 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.86-7.85 (m, 2H), 7.74-7.72 (m, 2H), 3.93 (dd, *J* = 13.5, 7.5 Hz, 1H), 3.77 (dd, *J* = 14.1, 6.5 Hz, 1H), 3.70 (s, 3H), 2.73 (m, 1H), 1.23 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.23, 168.26, 134.19, 131.82, 123.44, 64.43, 40.88, 37.36, 15.31; HRMS (ESI-TOF) Calcd for $C_{13}H_{15}N_2O_4$ $[M+H]^+$: 263.1026; found: 263.1027.



5d

2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-2-methylpropanamide (5d)

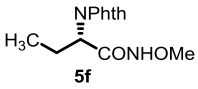
White solid. m.p. = 172-175 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.81-7.78 (m, 2H), 7.73-7.70 (m, 2H), 3.81 (s, 3H), 1.84 (s, 6H), 1.67 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.35, 168.44, 134.19, 131.77, 123.19, 64.15, 60.26, 24.51; HRMS (ESI-TOF) Calcd for $C_{13}H_{15}N_2O_4$ $[M+H]^+$: 263.1026; found: 263.1022.



5e

(*S*)-3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxy propanamide (5e)

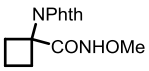
^{1}H NMR (600 MHz, $CDCl_3$) δ 9.30 (s, 1H), 7.77-7.74 (m, 2H), 7.70-7.67 (m, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.63 (d, *J* = 8.4 Hz, 2H), 5.05 (m, 1H), 3.75 (s, 3H), 3.43-3.41 (m, 2H), 0.89 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.90, 166.70, 154.60, 134.33, 131.24, 129.90, 128.65, 123.54, 120.37, 64.50, 54.76, 34.05, 25.62, 18.15, -4.55; HRMS (ESI-TOF) Calcd for $C_{24}H_{31}N_2O_5Si$ $[M+H]^+$: 455.1997; found: 455.2000.



5f

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxybutanamide (5f)

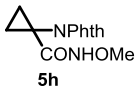
White solid. m.p. = 153-155 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.22 (s, 1H), 7.89-7.88 (m, 2H), 7.78-7.76 (m, 2H), 4.76 (m, 1H), 3.76 (s, 3H), 2.23-2.18 (m, 2H), 0.94 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.15, 161.93, 134.54, 131.44, 123.75, 64.57, 55.29, 22.43, 10.77; HRMS (ESI-TOF) Calcd for $C_{13}H_{15}N_2O_4$ $[M+H]^+$: 263.1026; found: 263.1023.



5g

1-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxycyclobutane-1-carboxamide (5g)

White solid. m.p. = 196-200 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.93 (s, 1H), 7.85-7.82 (m, 2H), 7.76-7.73 (m, 2H), 3.76 (s, 3H), 3.02-2.98 (m, 2H), 2.74-2.68 (m, 2H), 2.13-2.10 (m, 1H), 1.98-1.95 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.35, 167.87, 134.42, 131.77, 123.46, 64.45, 59.19, 31.78, 17.58; HRMS (ESI-TOF) Calcd for $C_{14}H_{15}N_2O_4$ $[M+H]^+$: 275.1026; found: 275.1029.

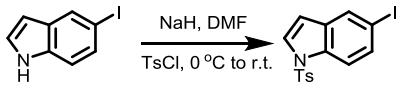


5h

1-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxycyclopropane-1-carboxamide (5h)

White solid. m.p. = 208-212 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.90-7.88 (m, 2H), 7.80-7.79 (m, 2H), 3.70 (s, 3H), 1.87-1.85 (m, 2H), 1.33-1.31 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.56, 167.81, 134.74, 131.29, 123.78, 64.53, 31.86, 16.25; HRMS (ESI-TOF) Calcd for $C_{13}H_{13}N_2O_4$ $[M+H]^+$: 261.0870; found: 261.0871.

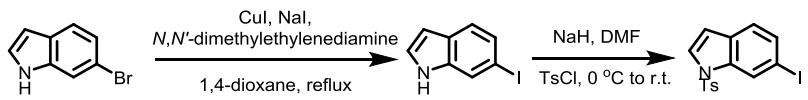
B. Preparation of Heterocyclic Iodides



Sodium hydride (60% dispersion in mineral oil, 2.4 g, 60.0 mmol) was suspended in 50 ml N,N-dimethylformamide (DMF) and the mixture was cooled in an ice-bath. A solution of 5-iodo-1 *H*-indole (9.72 g, 40.0 mmol) in 25 ml DMF was added dropwise over 10 min and the mixture was stirred for 30 min. A solution of 4-methylbenzene-1-sulfonyl chloride (9.17 g, 48.0 mmol) in 25 ml DMF was added dropwise and the mixture was stirred for 2 h, warming to room temperature. The mixture was partitioned between water and ethyl acetate. The organic layer was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered and evaporated. The residue was purified using the hexanes/EtOAc as eluent (100: 0 to 90:10) to give 14.69 g (93%) of the title compound as a white solid.

5-Iodo-1-tosyl-1*H*-indole

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 1.2 Hz, 1H), 7.76-7.72 (m, 3H), 7.68-7.56 (m, 1H), 7.52 (d, *J* = 3.6 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.57 (d, *J* = 3.6 Hz, 1H), 2.35 (s, 3H).

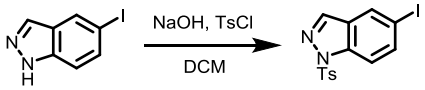


An oven dried, sealable glass tube was charged with a magenetic stirbar, 6-bromoindole (0.98 g, 5.0 mmol), freshly ground sodium iodide (1.52 g, 10.0 mmol), and copper(I) iodide (100 mg, 0.5 mmol). The vessel was then fitted with a rubber septum, evacuated under vacuum and backfilled with argon. This process was repeated three times. The vessel was then charged with 1,4-dioxane (5 mL) followed by *N*,*N*'-dimethylethylenediamine (0.12 mL, 1.0 mmol) via syringe. The rubber septum was removed and the reaction vessel immediately sealed tightly with a Teflon screw cap and heated to 110 ˚C for 22 h. After cooling to room temperature, the reaction was diluted with saturated aqueous NH_4Cl (30 mL) and extracted with DCM (4 × 25 mL). The combined organic layers were washed with brine (30 mL) and dried over Na_2SO_4, then concentrated to a brown residue. The residue was triturated in hexanes and concentrated to provide 6-iodo-1*H*-indole as a crude product.[2]

Sodium hydride (60% dispersion in mineral oil, 0.3 g, 7.5 mmol) was suspended in 5 ml DMF and the mixture was cooled in an ice-bath. A solution of 6-iodo-1*H*-indole in 1 ml DMF was added dropwise over 5 min and the mixture was stirred for 30 min. A solution of 4-methylbenzene-1-sulfonyl chloride (1.18 g, 6.0 mmol) in 2 ml DMF was added dropwise and the mixture was stirred for 2 h, warming to room. The mixture was partitioned between water and ethyl acetate. The organic layer was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered and evaporated. The residue was purified using the hexanes/EtOAc as eluent (100/0 to 90/10) to give 1.51 g (76%) of the title compound as a gray solid.

6-Iodo-1-tosyl-1*H*-indole

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.52 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.48 (d, *J* = 3.6 Hz, 1H), 7.28-7.25 (m, 4H), 6.60 (d, *J* = 3.6 Hz, 1H), 2.36 (s, 3H).



Sodium hydroxide (0.3 g, 6 mmol) was suspended in 10 ml DCM. 5-iodo-1*H*-indazole (448 mg, 2 mmol) was added, and the mixture was stirred for 30 min. A solution of 4-methylbenzene-1-sulfonyl chloride (456 mg, 2.4 mmol) in 2 mL DCM was added dropwise and the mixture was stirred for several hours. The mixture was partitioned with water. The organic layer was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered and evaporated. The residue was purified via colum chromatography on silca gel using the hexanes/EtOAc as eluent (100/0 to 90/10) to give 517 mg (65%) of the title compound as a gray solid.

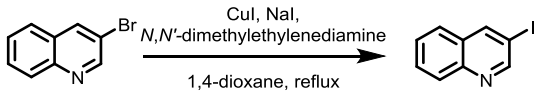
5-Iodo-1-tosyl-1*H*-indazole

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (d, *J* = 1.2 Hz, 1H), 8.05-8.04 (m, 1H), 8.00-7.99 (m, 1H), 7.86-7.84 (m, 2H), 7.81-7.79 (m, 1H), 7.26-7.25 (m, 2H), 2.37 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.72, 139.85, 139.53, 137.64, 134.28, 130.22, 129.95, 128.01, 127.60, 114.90, 87.92, 21.67; HRMS (ESI-TOF) Calcd for $C_{14}H_{12}IN_2O_2S$ $[M+H]^+$: 398.9659; found: 398.9663.

Sodium hydroxide (0.3 g, 6 mmol) was suspended in 10 ml DCM. 5-iodo-1*H*-indazole (448 mg, 2 mmol) was added, and the mixture was stirred for 30 min. A solution of 4-methylbenzene-1-sulfonyl chloride (456 mg, 2.4 mmol) in 2 mL DCM was added dropwise and the mixture was stirred for several hours. The mixture was partitioned with water. The organic layer was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered and evaporated. The residue was purified via colum chromatography on silca gel using the hexanes/EtOAc as eluent (100/0 to 90/10) to give 358 mg (45%) of the title compound as a gray solid.

6-Iodo-1-tosyl-1*H*-indazol

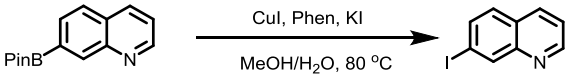
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.64 (d, *J* = 0.6 Hz, 1H), 8.12 (d, *J* = 0.6 Hz, 1H), 7.89-7.87 (m, 2H), 7.64-7.62 (m, 1H), 7.43-7.41 (m, 1H), 7.29-7.27 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.73, 141.06, 140.90, 134.34, 133.33, 129.98, 127.68, 125.00, 122.37, 122.18, 95.55, 21.68; HRMS (ESI-TOF) Calcd for $C_{14}H_{12}IN_2O_2S$ $[M+H]^+$: 398.9659; found: 398.9662.



An oven dried, sealable glass tube was charged with a magenetic stirbar, 3-bromoqunoline (1.04 g, 5.0 mmol), freshly ground sodium iodide (1.52 g, 10.0 mmol), and copper(I) iodide (100 mg, 0.5 mmol). The vessel was then fitted with a rubber septum, evacuated under vacuum and backfilled with argon. This process was repeated three times. The vessel was then charged with 1,4-dioxane (5 mL) followed by *N*,*N*'-dimethylethylenediamine (0.12 mL, 1.0 mmol) via syringe. The rubber septum was removed and the reaction vessel immediately sealed tightly with a Teflon screw cap and heated to 110 ˚C for 22 hours. After cooling to room temperature, the reaction was diluted with saturated aqueous NH_4Cl (30 mL) and extracted with DCM (4 × 25 mL). The combined organic layers were washed with brine (30 mL) and dried over Na_2SO_4, then concentrated to a brown residue. The residue was recrystallized in hexanes/EtOAc to provide 3-iodoqunoline (1.15g, 90%).

3-Iodoquinoline

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.04 (d, *J* = 1.8 Hz, 1H), 8.55-8.54 (m, 1H), 8.08-8.06 (m, 1H), 7.75-7.71 (m, 2H), 7.58-7.56 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.57, 146.34, 143.71, 130.03, 130.01, 129.50, 127.41, 126.79, 89.77; HRMS (ESI-TOF) Calcd for C_9H_7IN $[M+H]^+$: 255.9618; found: 255.9623.

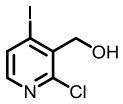


The starting material (638 mg, 2.5 mmol) was dissolved in methanol (20 mL), and the methanol solution was transferred to a 250 mL pressure vessel containing CuI (47.6 mg, 0.25 mmol, 10.0 mol%), phenanthroline (90.0 mg, 0.5 mmol, 20.0 mol%) and KI (0.622 g, 3.76 mmol, 1.50 equiv). The mixture was stirred at room temperature, and water (5 mL) was added. The flask was sealed under air, and the mixture was heated at 80 °C for 1 h, over which time the reaction was monitored by TLC. The reaction was cooled to room temperature, water (25 mL) was added, and the mixture was extracted with Et_2O (3 × 25 mL). The combined organic phases were washed with brine (25 mL), dried with $MgSO_4$, and concentrated in vacuo. After purification by column

chromatography using hexanes/EtOAc (20/1) as the eluent, the product was obtained as a white solid (593 mg, 93%).[3]

7-Iodoquinoline

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.91 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.55-8.54 (m, 1H), 8.13-8.11 (m, 1H), 7.81 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.42 (dd, *J* = 8.4, 4.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 151.07, 148.94, 138.53, 135.99, 135.30, 128.90, 127.25, 121.60, 95.47; HRMS (ESI-TOF) Calcd for C_9H_7IN $[M+H]^+$: 255.9618; found: 255.9621.

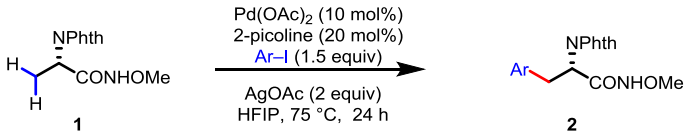


(2-Chloro-4-iodopyridin-3-yl)methanol

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 4.8 Hz, 1H), 7.75 (d, *J* = 5.4 Hz, 1H), 5.00-4.99 (m, 2H), 2.22 (br, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 150.89, 149.05, 136.86, 134.34, 113.30, 66.94; HRMS (ESI-TOF) Calcd for C_6H_6ClINO $[M+H]^+$: 269.9177; found: 269.9181.

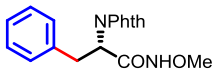
General Reaction Scheme:

Monoarylation



General procedure for monoarylation with aryl iodides: The starting material **1** (0.1 mmol, 24.8 mg), $Pd(OAc)_2$ (10 mol%, 2.2 mg), and AgOAc (0.2 mmol, 33.4 mg) were weighed in air and placed in a sealed tube (10 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (0.15 mmol), 2-picoline (20 mol%, 2 μL), HFIP (1.0 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 75 °C for 24 hours under vigorous

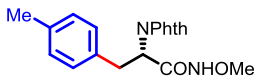
stirring. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent.



2'

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-phenylpropanamide (2')

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2'** was obtained as a white solid (29.8 mg, 90%). (For the NMR data, see the previous one in the substrate preparation section)

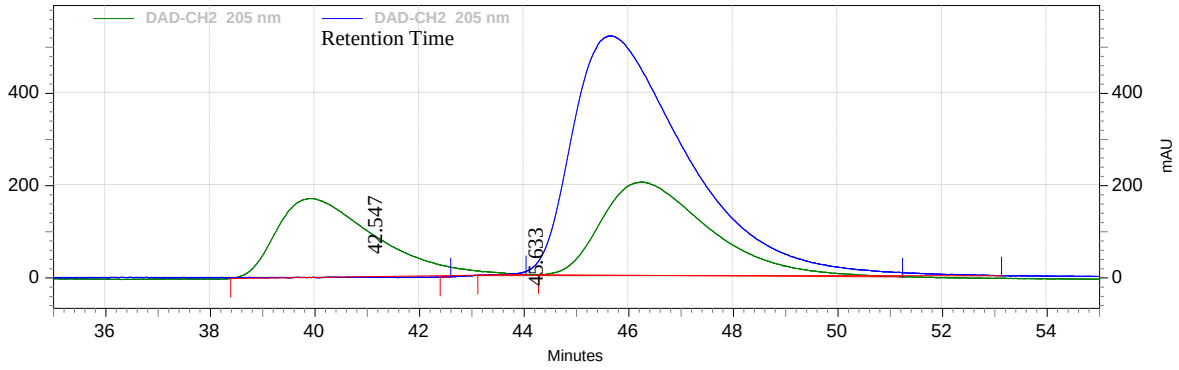


2a

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(*p*-tolyl)propanamide (2a)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2a** was obtained as a white solid (31.0 mg, 92%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.34 (s, 1H), 7.78-7.75 (m, 2H), 7.70-7.68 (m, 2H), 7.03 (d, *J* = 7.8 Hz, 2H), 6.97 (d, *J* = 7.8 Hz, 2H), 5.06 (m, 1H), 3.74 (s, 3H), 3.47 (m, 2H), 2.21 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.93, 166.64, 136.63, 134.34, 132.90, 131.31, 129.35, 128.71, 123.57, 64.49, 54.62, 34.34, 20.99; HRMS (ESI-TOF) Calcd for $C_{19}H_{19}N_2O_4$ $[M+H]^+$: 339.1339; found: 339.1338. The ee value was determined by HPLC analysis on a Chiralcel OD-H column (20% isopropanol in hexanes, 0.4 mL/min) with t_r = 42.5 min (minor), 45.6 min (major): 99% ee.

Area % Report



DAD-CH2 205 nm

Results

Retention Time	Area	Area %	Height	Height %
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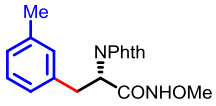
45.633	316582855	99.99	2077420	99.91

Totals	316599838	100.00	2079208	100.00

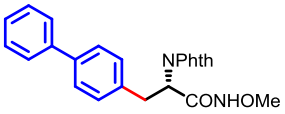


2b

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(*m*-tolyl)propanamide (2b)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2b** was obtained as a white solid (22.1 mg, 65%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.29 (s, 1H), 7.78-7.75 (m, 2H), 7.70-7.67 (m, 2H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.95-6.92 (m, 3H), 5.06 (m, 1H), 3.74 (s, 3H), 3.52-

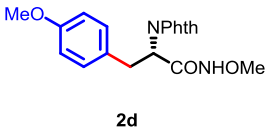
3.44 (m, 2H), 2.17 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.92, 166.59, 138.28, 135.98, 134.36, 131.31, 129.69, 128.53, 127.81, 125.85, 123.56, 64.50, 54.65, 34.70, 21.19; HRMS (ESI-TOF) Calcd for $C_{19}H_{19}N_2O_4$ $[M+H]^+$: 339.1339; found: 339.1337.



2c

(*S*)-3-([1,1'-Biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxypropanamide (2c)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2c** was obtained as a yellow solid (25.4 mg, 64%). m.p. = 107-110 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.32 (s, 1H), 7.79-7.76 (m, 2H), 7.70-7.67 (m, 2H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.40-7.36 (m, 2H), 7.31-7.28 (m, 1H), 7.23 (d, *J* = 7.8 Hz, 2H), 5.13 (m, 1H), 3.76 (s, 3H), 3.57 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.93, 166.56, 140.44, 139.81, 135.09, 134.41, 131.25, 129.30, 128.68, 127.29, 127.25, 126.87, 123.63, 64.54, 54.46, 34.40; HRMS (ESI-TOF) Calcd for $C_{24}H_{21}N_2O_4$ $[M+H]^+$: 401.1496; found 401.1497.

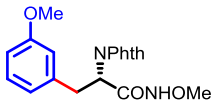


2d

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(4-methoxyphenyl)propanamide (2d)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2d** was obtained as a white solid (25.3 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.32 (s, 1H), 7.79-7.76 (m, 2H), 7.71-7.68 (m, 2H), 7.06 (d, *J* = 8.4 Hz, 2H), 6.70 (d, *J* = 8.4 Hz, 2H), 5.05 (m, 1H), 3.75 (s, 3H), 3.69 (s, 3H), 3.45 (m, 2H); ^{13}C NMR (150MHz, $CDCl_3$) δ 167.94, 166.67, 158.51, 134.37,

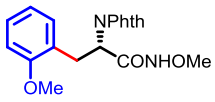
131.27, 129.90, 127.93, 123.60, 114.06, 64.51, 55.15, 54.75, 33.94; HRMS (ESI-TOF) Calcd for $C_{19}H_{19}N_2O_5$ $[M+H]^+$: 355.1288; found: 355.1289.



2e

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(3-methoxyphenyl)propanamide (2e)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2e** was obtained as a white solid (29.3 mg, 83%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.36 (s, 1H), 7.79-7.76 (m, 2H), 7.71-7.68 (m, 2H), 7.07 (t, *J* = 7.8 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 6.69 (s, 1H), 6.67-6.65 (m, 1H), 5.10 (m, 1H), 3.75 (s, 3H), 3.66 (s, 3H), 3.55-3.41 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.89, 166.52, 159.66, 137.61, 134.38, 131.29, 129.66, 123.58, 121.18, 114.07, 113.02, 64.50, 55.08, 54.43, 34.75; HRMS (ESI-TOF) Calcd for $C_{19}H_{19}N_2O_5$ $[M+H]^+$: 355.1288; found: 355.1291.

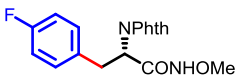


2f

(*S*)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxy-3-(2-methoxyphenyl)propanamide (2f)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2f** was obtained as a white solid (27.0 mg, 76%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.23 (s, 1H), 7.77-7.75 (m, 2H), 7.70-7.67 (m, 2H), 7.14-7.13 (m, 1H), 7.03 (dd, *J* = 7.2, 1.8 Hz, 1H), 6.76-6.74 (m, 1H), 6.73-6.70 (m, 1H), 5.26 (m, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 3.54-3.40 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.83, 166.89, 157.47, 134.18, 131.47, 131.01, 128.62, 124.44, 123.42, 120.54,

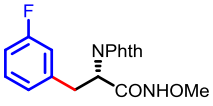
110.28, 64.49, 55.18, 52.75, 30.40; HRMS (ESI-TOF) Calcd for $C_{19}H_{19}N_2O_5$ $[M+H]^+$: 355.1288; found: 355.1291.



2g

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-3-(4-fluorophenyl)-*N*-methoxypropanamide (2g)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2g** was obtained as a white solid (27.8 mg, 81%). m.p. = 135-137 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.44 (s, 1H), 7.80-7.76 (m, 2H), 7.72-7.68 (m, 2H), 7.12-7.10 (m, 2H), 6.85 (t, J = 8.4 Hz, 2H), 5.04 (m, 1H), 3.74 (s, 3H), 3.56-3.40 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.84, 166.40, 161.80 (d, J_{FC} = 243.9 Hz), 134.47, 131.80, 131.17, 130.43 (d, J_{FC} = 8.0 Hz), 123.63, 115.52 (d, J_{FC} = 21.3 Hz), 64.50, 54.39, 33.88; HRMS (ESI-TOF) Calcd for $C_{18}H_{16}FN_2O_4$ $[M+H]^+$: 343.1089; found:. 343.1086.

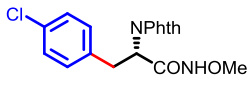


2h

(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(3-fluorophenyl)-*N*-methoxypropanamide (2h)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2h** was obtained as a white solid (24.3 mg, 71%). m.p. = 125-127 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.47 (s, 1H), 7.78-7.77 (m, 2H), 7.71-7.70 (m, 2H), 7.15-7.12 (m, 1H), 6.94 (d, J = 7.8 Hz, 1H), 6.87 (d, J = 10.2 Hz, 1H), 6.82 (t, J = 8.4 Hz, 1H), 5.05 (m, 1H), 3.74 (s, 3H), 3.52 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.80, 166.25, 162.72 (d, J_{FC} = 245.1 Hz), 138.69, 134.47, 131.19, 130.14 (d,

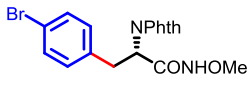
J_{FC} = 8.4 Hz), 124.57 (d, J_{FC} = 2.9 Hz), 123.64, 115.89 (d, J_{FC} = 20.7 Hz), 114.04 (d, J_{FC} = 20.9 Hz), 64.48, 54.03, 34.34; HRMS (ESI-TOF) Calcd for $C_{18}H_{16}FN_2O_4$ $[M+H]^+$: 343.1089; found: 343.1087.



2i

(*S*)-3-(4-Chlorophenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxypropanamide (2i)

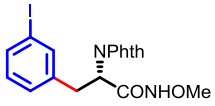
Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2i** was obtained as a white solid (22.6 mg, 63%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.33 (s, 1H), 7.80-7.77 (m, 2H), 7.73-7.70 (m, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 5.04 (m, 1H), 3.75 (s, 3H), 3.49 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.82, 166.33, 134.53, 132.92, 131.14, 130.24, 128.81, 123.70, 64.55, 54.19, 34.00; HRMS (ESI-TOF) Calcd for $C_{18}H_{16}ClN_2O_4$ $[M+H]^+$: 359.0793; found: 359.0791.



2j

(*S*)-3-(4-Bromophenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxypropanamide (2j)

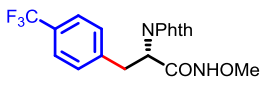
Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2j** was obtained as a white solid (28.6 mg, 71%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.27 (s, 1H), 7.80-7.77 (m, 2H), 7.73-7.70 (m, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 7.2 Hz, 2H), 5.06 (m, 1H), 3.75 (s, 3H), 3.48 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.82, 166.31, 135.06, 134.55, 131.77, 131.12, 130.60, 123.72, 121.05, 64.57, 54.15, 34.08; HRMS (ESI-TOF) Calcd for $C_{18}H_{16}BrN_2O_4$ $[M+H]^+$: 403.0288; found: 403.0284.



2k

(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(3-iodophenyl)-*N*-methoxypropanamide (2k)

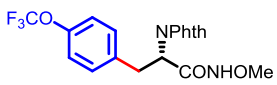
Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2k** was obtained as a white solid (22.1 mg, 49%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.27 (s, 1H), 7.82-7.79 (m, 2H), 7.74-7.72 (m, 2H), 7.47-7.45 (m, 2H), 7.14 (d, *J* = 7.2 Hz, 1H), 6.93 (t, *J* = 7.8 Hz, 1H), 5.01 (m, 1H), 3.75 (s, 3H), 3.47-3.45 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.82, 166.14, 138.53, 137.98, 136.18, 134.55, 131.15, 130.36, 128.16, 123.73, 94.39, 64.58, 54.25, 34.23; HRMS (ESI-TOF) Calcd for $C_{18}H_{16}IN_2O_4$ $[M+H]^+$: 451.0149; found: 451.0143.



2l

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(4-(trifluoromethyl)phenyl)propanamide (2l)

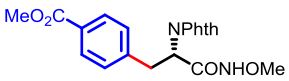
Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2l** was obtained as a white solid (28.0 mg, 71%). m.p. = 137-139 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.43 (s, 1H), 7.79-7.76 (m, 2H), 7.73-7.70 (m, 2H), 7.43 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 2H), 5.10 (m, 1H), 3.75 (s, 3H), 3.59 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.78, 166.16, 140.33, 134.57, 131.12, 129.67-129.03, 125.57 (q, J_{FC} = 3.5 Hz) 123.98 (q, J_{FC} = 270.4 Hz), 123.70, 64.53, 53.84, 34.41; HRMS (ESI-TOF) Calcd for $C_{19}H_{16}F_3N_2O_4$ $[M+H]^+$: 393.1057; found 393.1060.



2m

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(4-(trifluoromethoxy)phenyl)propanamide (2m)

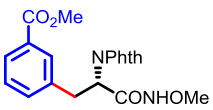
Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2m** was obtained as a white solid (33.6 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.41 (s, 1H), 7.79-7.76 (m, 2H), 7.72-7.69 (m, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 7.02 (d, *J* = 7.8 Hz, 2H), 5.07 (m, 1H), 3.74 (s, 3H), 3.53 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.83, 166.34, 148.19, 134.88, 134.53, 131.15, 130.34, 123.65, 121.11, 120.32 (q, J_{FC} = 255.5 Hz), 64.51, 54.14, 33.99; HRMS (ESI-TOF) Calcd for $C_{19}H_{16}F_3N_2O_5$ $[M+H]^+$: 409.1006; found: 409.1013.



2n

Methyl (*S*)-4-(2-(1,3-dioxoisoindolin-2-yl)-3-(methoxyamino)-3-oxopropyl)benzoate (2n)

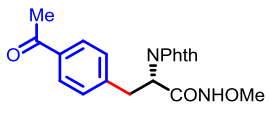
Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2n** was obtained as a white solid (31.3 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.49 (s, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.76-7.63 (m, 2H), 7.70-7.66 (m, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 5.10 (m, 1H), 3.83 (s, 3H), 3.58 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.72, 166.82, 166.18, 141.64, 134.48, 131.12, 129.91, 128.97, 128.89, 123.65, 64.50, 53.83, 52.07, 34.56; HRMS (ESI-TOF) Calcd for $C_{20}H_{19}N_2O_6$ $[M+H]^+$: 383.1238; found: 383.1238.



2o

methyl (*S*)-3-(2-(1,3-dioxoisoindolin-2-yl)-3-(methoxyamino)-3-oxopropyl)benzoate (2o)

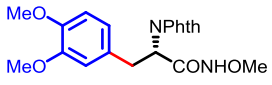
Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2o** was obtained as a white solid (30.9 mg, 81%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.40 (s, 1H), 7.82-7.79 (m, 2H), 7.78-7.76 (m, 2H), 7.71-7.69 (m, 2H), 7.37 (d, *J* = 7.2 Hz, 1H), 7.26-7.25 (m, 1H), 5.10 (m, 1H), 3.82 (s, 3H), 3.76 (s, 3H), 3.59-3.57 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.78, 166.72, 166.14, 136.64, 134.44, 133.50, 131.21, 130.44, 130.06, 128.76, 128.37, 123.65, 64.51, 54.27, 52.10, 34.42; HRMS (ESI-TOF) Calcd for $C_{20}H_{19}N_2O_6$ $[M+H]^+$: 383.1238; found: 383.1240.



2p

(*S*)-3-(4-Acetylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxypropanamide (2p)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2p** was obtained as a white solid (26.3 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.55 (s, 1H), 7.76-7.74 (m, 4H), 7.71-7.68 (m, 2H), 7.25 (d, *J* = 7.8 Hz, 2H), 5.11 (m, 1H), 3.75 (s, 4H), 3.59 (m, 2H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.90, 167.72, 166.11, 141.94, 135.84, 134.51, 131.14, 129.17, 128.70, 123.67, 64.49, 53.80, 34.54, 26.52; HRMS (ESI-TOF) Calcd for $C_{20}H_{19}N_2O_5$ $[M+H]^+$: 367.1288; found: 367.1286.

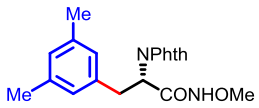


2q

(*S*)-3-(2,3-Dimethoxyphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxypropanamide (2q)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2q** was obtained

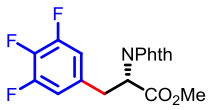
as a white solid (22.8 mg, 60%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.27 (s, 1H), 7.79-7.76 (m, 2H), 7.71-7.69 (m, 2H), 6.68-6.63 (m, 3H), 5.08 (m, 1H), 3.76 (s, 6H), 3.70 (s, 3H), 3.47-3.44 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.95, 166.70, 148.79, 147.89, 134.45, 131.24, 128.33, 123.59, 121.06, 111.68, 111.19, 64.56, 55.72, 55.66, 54.75, 34.37; HRMS (ESI-TOF) Calcd for $C_{20}H_{21}N_2O_6$ $[M+H]^+$: 385.1394; found: 385.140



2r

(*S*)-3-(3,5-Dimethylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxypropanamide (2r)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2r** was obtained as a white solid (36.4 mg, 75%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.26 (s, 1H), 7.80-7.77 (m, 2H), 7.71-7.69 (m, 2H), 6.75 (s, 3H), 5.04 (m, 1H), 3.74 (s, 3H), 3.46-3.36 (m, 2H), 2.13 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.95, 166.60, 138.15, 135.92, 134.32, 131.38, 128.68, 126.70, 123.52, 64.48, 54.70, 34.66, 21.04; HRMS (ESI-TOF) Calcd for $C_{20}H_{21}N_2O_4$ $[M+H]^+$: 353.1496; found: 353.1498.

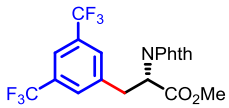


2s'

Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(3,4,5-trifluorophenyl)propanoate (2s')

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. The solvents were removed under reduced pressure and the resulting mixture was added $PhI(OAc)_2$ (0.1 mmol, 32.2 mg) and MeOH (1 mL) in a sealed tube (10 mL) with a magnetic stir bar, the reaction mixture was heated to 80 °C for 3 hours. Upon completion, the reaction mixture was cooled to room

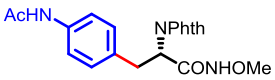
temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using hexanes/EtOAc (5/1 to 4/1 to 2/1) as the eluent. **2s'** was obtained as a white solid (22.5 mg, 62%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85-7.82 (m, 2H), 7.76-7.73 (m, 2H), 6.83-6.78 (m, 2H), 5.09-5.07 (m, 1H), 3.78 (s, 3H), 3.56-3.46 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.67, 167.39, 151.06 (ddd, J_{FC} = 248.8 Hz, 9.8 Hz, 4.0 Hz), 138.76 (dt, J_{FC} = 249.0 Hz, 15.1 Hz), 134.43, 133.11-132.98, 131.39, 123.73, 112.96 (dd, J_{FC} = 16.4 Hz, 4.4 Hz), 53.12, 52.59, 34.16; HRMS (ESI-TOF) Calcd for $C_{18}H_{13}F_3NO_4$ $[M+H]^+$: 364.0791; found: 364.0794.



2t'

Methyl (*S*)-3-(3,5-bis(trifluoromethyl)phenyl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (2t')

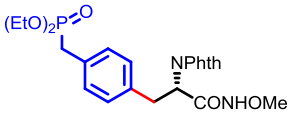
Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. The solvents were removed under reduced pressure and the resulting mixture was added $PhI(OAc)_2$ (0.1 mmol, 32.2 mg) and MeOH (1 mL) in a sealed tube (10 mL) with a magnetic stir bar. The reaction mixture was heated to 80 °C for 3 hours. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using Hexanes/EtOAc (5/1 to 4/1 to 2/1) as the eluent. **2t'** was obtained as a white solid (23.6 mg, 53%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83-7.80 (m, 2H), 7.75-7.72 (m, 2H), 7.68 (s, 1H), 7.63 (s, 2H), 5.15 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.80 (s, 3H), 3.73 (dd, *J* = 14.4, 5.4 Hz, 1H), 3.64 (dd, *J* = 14.4, 10.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.57, 167.31, 139.40, 134.48, 131.83 (q, J_{FC} = 33.2 Hz), 131.31, 129.24 (q, J_{FC} = 4.3 Hz), 123.69, 123.26 (q, J_{FC} = 271.2 Hz), 121.14-120.97, 53.17, 52.42, 34.56; HRMS (ESI-TOF) Calcd for $C_{20}H_{14}F_6NO_4$ $[M+H]^+$: 446.0822; found: 446.0820.



2u

(*S*)-3-(4-Acetamidophenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxypropanamide (2u)

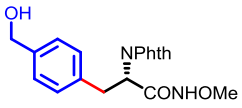
Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (4/1 to 2/1 to 0/1) as the eluent, **2u** was obtained as a white solid (20.2 mg, 53%). ^{1}H NMR (600 MHz, MeOD) δ 7.82-7.79 (m, 4H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 5.08 (dd, *J* = 11.4, 5.4 Hz, 1H), 4.63 (br, 1H), 3.72 (s, 3H), 3.52-3.43 (m, 2H), 2.07 (s, 3H); ^{13}C NMR (150 MHz, MeOD) δ 171.60, 169.10, 168.09, 138.78, 135.68, 133.73, 132.97, 130.51, 124.36, 121.13, 64.47, 54.31, 34.62, 23.83; HRMS (ESI-TOF) Calcd for $C_{20}H_{20}N_3O_5$ $[M+H]^+$: 382.1397; found: 382.1401.



2v

Diethyl (*S*)-(4-(2-(1,3-dioxoisoindolin-2-yl)-3-(methoxyamino)-3-oxopropyl)benzyl) phosphonate (2v)

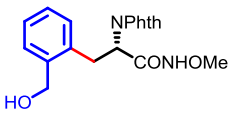
Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (4/1 to 2/1 to 0/1) as the eluent, **2v** was obtained as a white solid (44.4 mg, 94%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.20 (s, 1H), 7.76-7.73 (m, 2H), 7.69-7.67 (m, 2H), 7.07 (m, 4H), 5.05 (m, 1H), 3.89-3.82 (m, 4H), 3.72 (s, 3H), 3.57-3.45 (m, 2H), 3.05-2.89 (m, 2H), 1.15-1.12 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.79, 166.27, 135.26, 134.17, 131.48, 129.99, 129.95, 129.10, 123.42, 64.20, 62.21-62.11, 54.09, 34.20, 33.16 (d, J_{PC} = 137.4 Hz), 16.28-16.23; HRMS (ESI-TOF) Calcd for $C_{23}H_{28}N_2O_7P$ $[M+H]^+$: 475.1629; found: 475.1630.



2w

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-3-(4-(hydroxymethyl)phenyl)-*N*-methoxypropanamide (2w)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2w** was obtained as a white solid (22.1 mg, 62%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.41 (s, 1H), 7.78-7.75 (m, 2H), 7.71-7.68 (m, 2H), 7.17-7.12 (m, 4H), 5.05 (m, 1H), 4.55 (s, 2H), 3.73 (s, 3H), 3.53-3.43 (m, 2H), 2.02-1.78 (br, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.90, 166.51, 139.68, 135.44, 134.43, 131.23, 129.03, 127.28, 123.63, 64.82, 64.48, 54.44, 34.40; HRMS (ESI-TOF) Calcd for $C_{19}H_{19}N_2O_5$ $[M+H]^+$: 355.1288; found: 355.1288.



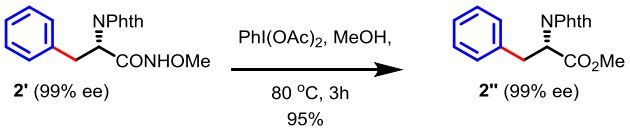
2x

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-3-(2-(hydroxymethyl)phenyl)-*N*-methoxypropanamide (2x)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **2x** was obtained as a white solid (15.0 mg, 42%). m.p. = 122-124 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.71 (s, 1H), 7.79-7.76 (dm, 2H), 7.71-7.68 (m, 2H), 7.30 (d, *J* = 7.5 Hz, 1H), 7.15-7.14 (m, 1H), 7.07-7.06 (m, 2H), 5.22 (m, 1H), 4.84 (d, *J* = 12.6 Hz, 1H), 4.69 (d, *J* = 12.0 Hz, 1H), 3.69 (s, 3H), 3.69-3.64 (m, 1H), 3.53 (dd, *J* = 14.4, 10.0 Hz, 1H), 1.85 (br, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.04, 166.45, 138.58, 135.53, 134.33, 131.38, 130.09, 129.95, 128.34, 127.48, 123.58, 64.37, 63.67, 53.67, 31.85; HRMS (ESI-TOF) Calcd for $C_{19}H_{19}N_2O_5$ $[M+H]^+$: 355.1288; found: 355.1287.

Removal of the directing group:

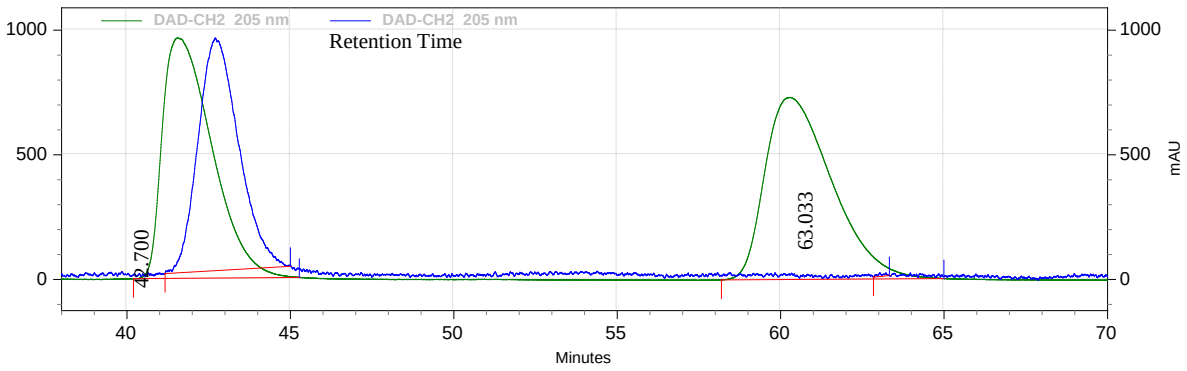
Method A: $PhI(OAc)_2$



Methyl (S)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoate (2'')

The substrate **2'** (0.1 mmol, 32.8 mg) was dissolved in MeOH (1 mL), followed by the addition of $PhI(OAc)_2$ (0.1 mmol, 32.2 mg). The reaction mixture was heated to 80 °C for 3 hours. The reaction mixture was then cooled to room temperature and then saturated aq. Na_2SO_3 and saturated aq. $NaHCO_3$ were added. The aqueous layer was then extracted with EtOAc and the combined organic layers washed with brine, dried over $MgSO_4$, filtered and concentrated. Purify by column chromatography (hexanes/ EtOAc = 2:1 to 1:1) to provide product **2''**, (29.4 mg. 95%). ^1H NMR (600 MHz, $CDCl_3$) δ 7.79-7.77 (m, 2H), 7.70-7.68 (m, 2H), 7.19-7.13 (m, 5H), 5.16 (dd, *J* = 11.4, 5.4 Hz, 1H), 3.78 (s, 3H), 3.61-3.52 (m, 2H). The ee value was determined by HPLC analysis on a Chiralcel OJ column (25% isopropanol in hexanes, 0.4 mL/min) with t_r = 42.7 min (major), 63.0 min (minor): 99% ee.

Area % Report

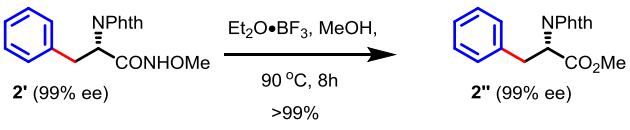


DAD-CH2 205 nm

Results

Retention Time	Area	Area %	Height	Height %
42.700	18924298	99.77	218886	98.38
63.033	43990	0.23	3603	1.62
Totals	18968288	100.00	222489	100.00

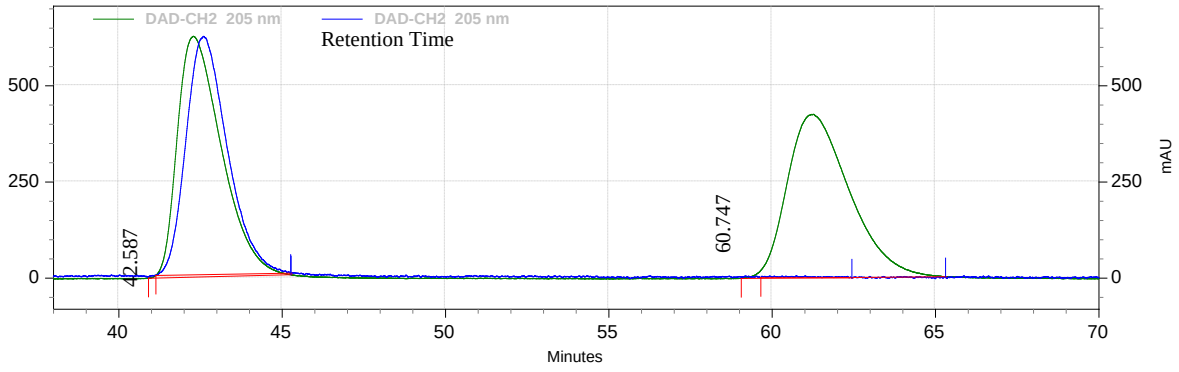
Method B: $Et_2O \bullet BF_3$



A sealable pressure flask was charged with MeOH (1 mL) and amide **2'** (0.1 mmol, 32.8 mg)**.** $BF_3 \bullet OEt_2$ (5 equiv.) was added and the reaction vessel sealed. The reaction mixture was heated to 90 °C for 8 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The solvents were removed under reduced pressure and H_2O and EtOAc were added, organic layers were removed and the aqueous layer was then extracted with EtOAc

and the combined organics washed with brine, dried over $MgSO_4$, filtered and concentrated. Purify by column chromatography (hexanes/ EtOAc = 2:1 to 1:1) to provide **2''** white solid (30.9 mg, >99%). The ee value was determined by HPLC analysis on a Chiralcel OJ column (25% isopropanol in hexanes, 0.4 mL/min) with t_r = 42.6 min (major), 60.7 min (minor): 99% ee.

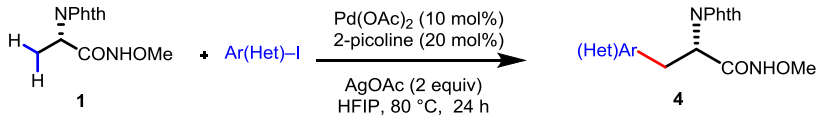
Area % Report



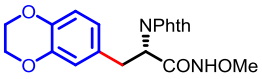
DAD-CH2 205 nm
Results

Retention Time	Area	Area %	Height	Height %
42.587	50142197	99.32	568129	99.24
60.747	344863	0.68	4334	0.76
Totals	50487060	100.00	572463	100.00

Arylation with heteroaryl iodides



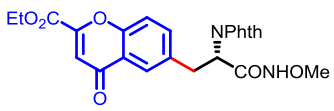
General procedure for monoarylation of 1 with heterocyclic iodides: The starting material **l** (0.1 mmol, 24.8 mg), $Pd(OAc)_2$ (10 mol%, 2.2 mg), and AgOAc (0.2 mmol, 33.4 mg) were weighed in air and placed in a sealed tube (10 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (0.15 mmol), 2-picoline (20 mol%, 2 μL), HFIP (1.0 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 80 °C for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent.



4a

(*S*)-3-(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxy propanamide (4a)

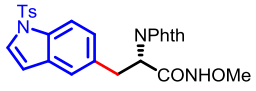
Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **4a** was obtained as a white solid (29.0 mg, 76%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.23 (s, 1H), 7.81-7.78 (m, 2H), 7.72-7.70 (m, 2H), 6.68 (s, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 6.60 (d, *J* = 7.8 Hz, 1H), 5.02 (m, 1H), 4.16-4.14 (m, 4H), 3.74 (s, 3H), 3.40 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.93, 166.58, 143.49, 142.54, 134.36, 131.34, 129.16, 123.63, 121.75, 117.68, 117.35, 64.51, 64.16, 54.64, 34.10; HRMS (ESI-TOF) Calcd for $C_{20}H_{19}N_2O_6$ $[M+H]^+$: 383.1238; found: 383.1244.



4b

Ethyl (*S*)-6-(2-(1,3-dioxoisoindolin-2-yl)-3-(methoxyamino)-3-oxopropyl)-4-oxo-4*H*-chromene-3-carboxylate (4b)

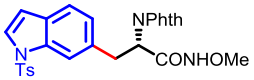
Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **4b** was obtained as a white solid (31.5 mg, 70%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.95 (s, 1H), 7.76-7.74 (m, 2H), 7.69-7.67 (m, 2H), 7.60 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.44 (d, *J* = 8.7 Hz, 1H), 6.96 (s, 1H), 5.13 (m, 1H), 4.43 (q, *J* = 7.2 Hz, 2H), 3.77 (s, 3H), 3.68-3.67 (m, 2H), 1.41 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.24, 167.67, 166.00, 160.38, 154.92, 152.19, 135.79, 134.86, 134.43, 131.23, 125.68, 124.12, 123.66, 119.18, 114.50, 64.45, 63.05, 53.83, 34.04, 14.07; HRMS (ESI-TOF) Calcd for $C_{24}H_{21}N_2O_8$ $[M+H]^+$: 465.1292; found: 465.1295.



4c

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(1-tosyl-1H-indol-5-yl)propanamide (4c)

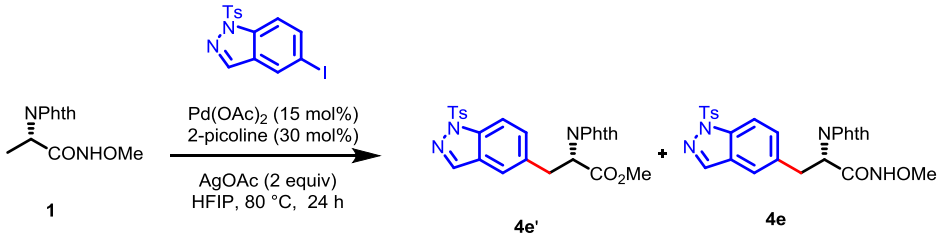
Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **4c** was obtained as a white solid (25.6 mg, 62%). m.p. = 194-196 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.12 (s, 1H), 7.79 (d, *J* = 9.0 Hz, 1H), 7.75-7.73 (m, 2H), 7.69-7.67 (m, 4H), 7.46 (d, *J* = 3.6 Hz, 1H), 7.33 (s, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 1H), 6.50 (d, *J* = 3.6 Hz, 1H), 5.10 (m, 1H), 3.72 (s, 3H), 3.59-3.55 (m, 2H), 2.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.90, 166.71, 144.92, 135.16, 134.41, 133.88, 131.20, 131.08, 129.87, 126.73, 126.71, 125.37, 123.62, 121.67, 113.67, 108.82, 64.52, 54.80, 34.63, 21.55; HRMS (ESI-TOF) Calcd for $C_{27}H_{24}N_3O_6S$ $[M+H]^+$: 518.1380; found 518.1386.



4d

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(1-tosyl-1H-indol-6-yl)propanamide (4d)

Substrate **1** was arylated following the general arylation procedure. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **4d** was obtained as a white solid (33.7 mg, 65%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.24 (s, 1H), 7.83 (s, 1H), 7.77-7.75 (m, 2H), 7.72-7.68 (m, 4H), 7.42 (d, *J* = 3.6 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 7.8 Hz, 1H), 6.51 (d, *J* = 3.0 Hz, 1H), 5.16 (m, 1H), 3.78 (s, 3H), 3.67-3.66 (m, 2H), 2.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.92, 166.51, 144.87, 135.19, 135.04, 134.36, 132.82, 131.29, 129.94, 129.71, 126.80, 126.37, 124.33, 123.64, 121.54, 113.81, 108.73, 64.56, 54.94, 35.11, 21.55; HRMS (ESI-TOF) Calcd for $C_{27}H_{24}N_3O_6S$ $[M+H]^+$: 518.1380; found: 518.1386.

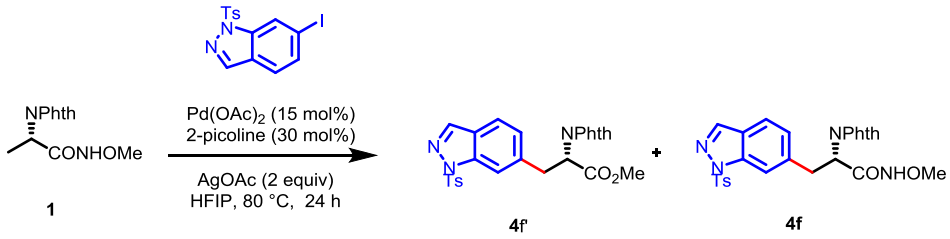


Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(1-tosyl-1*H*-indazol-5-yl)propanoate (4e')

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(1-tosyl-1*H*-indazol-5-yl)propanamide (4e)

Substrate **1** was arylated following the general arylation procedure except $Pd(OAc)_2$ (15 mol%, 3.3 mg) and 2-picoline (30 mol%, 3 μL). Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **4 e'** was obtained as a white solid (8.5 mg, 16%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05-8.03 (m, 2H), 7.82-7.80 (m, 2H), 7.78-7.75 (m, 2H), 7.71-7.67 (m, 2H), 7.48 (s, 1H), 7.38 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 5.18 (dd,

J = 10.8, 5.4 Hz, 1H), 3.78 (s, 3H), 3.72-3.63 (m, 2H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.09, 167.45, 145.36, 140.97, 139.41, 134.52, 134.27, 132.96, 131.43, 130.28, 129.81, 127.55, 126.11, 123.58, 121.24, 113.34, 53.15, 53.02, 34.40, 21.63; HRMS (ESI-TOF) Calcd for $C_{26}H_{22}N_3O_6S$ $[M+H]^+$: 504.1224; found: 504.1225. **4e** was obtained as a white solid (21.8 mg, 42%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.28 (s, 1H), 8.03-8.01 (m, 2H), 7.80-7.79 (m, 2H), 7.75-7.73 (m, 2H), 7.69-7.68 (m, 2H), 7.48 (s, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.22-7.20 (m, 2H), 5.12 (m, 1H), 3.74 (s, 3H), 3.64 (m, 2H), 2.34 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.81, 166.25, 145.44, 140.94, 139.40, 134.56, 134.42, 132.38, 131.07, 130.26, 129.83, 127.52, 126.10, 123.69, 121.43, 113.39, 64.57, 54.35, 34.38, 21.63; HRMS (ESI-TOF) Calcd for $C_{26}H_{23}N_4O_6S$ $[M+H]^+$: 519.1333; found: 519.1339.

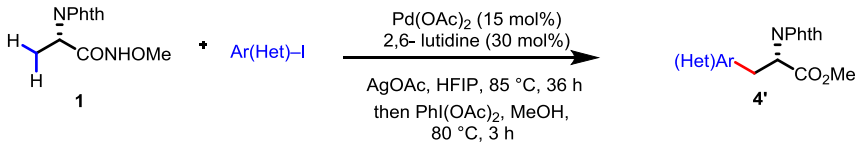


Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(1-tosyl-1H-indazol-6-yl)propanoate (4f')

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(1-tosyl-1H-indazol-6-yl)propanamide (4f)

Substrate **1** was arylated following the general arylation procedure except $Pd(OAc)_2$ (15 mol%, 3.3 mg) and 2-picoline (30 mol%, 3 μL). Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent, **4f'** was obtained as a white solid (11.6 mg, 22%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (m, 2H), 7.80-7.76 (m, 4H), 7.72-7.70 (m, 2H), 7.51 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.19-7.15 (m, 3H), 5.24 (dd, *J* = 11.4, 5.4 Hz, 1H), 3.82 (s, 3H), 3.80-3.75 (m, 2H), 2.34 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.98, 167.38, 145.22, 141.02, 140.63, 138.82, 134.53, 134.23, 131.52, 129.81, 127.53, 125.44, 124.84, 123.61, 121.41, 113.28, 53.33, 53.08, 35.13, 21.64; HRMS (ESI-TOF) Calcd for $C_{26}H_{22}N_3O_6S$ $[M+H]^+$: 504.1224; found: 504.1225. **4f** was obtained as a white solid (23.0 mg, 44%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.40

(s, 1H), 8.03 (s, 1H), 7.80 (s, 1H), 7.78-7.76 (m, 4H), 7.71-7.69 (m, 2H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 1H), 5.21 (m, 1H), 3.80 (s, 3H), 3.77-3.68 (m, 2H), 2.34 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.81, 165.93, 145.33, 140.96, 140.50, 138.28, 134.52, 134.43, 131.16, 129.85, 127.51, 125.50, 124.88, 123.73, 121.56, 113.24, 64.69, 54.44, 35.13, 21.64; HRMS (ESI-TOF) Calcd for $C_{26}H_{23}N_4O_6S$ $[M+H]^+$: 519.1333; found: 519.1340.

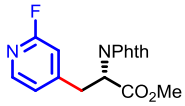


General procedure for monoarylation of 1 with heterocyclic iodides:

Method A. The starting material **1** (0.1 mmol, 24.8 mg), $Pd(OAc)_2$ (15 mol%, 3.3 mg), and AgOAc (0.2 mmol, 33.4 mg) were weighed in air and placed in a sealed tube (10 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (0.15 mmol), 2,6-lutidine (30 mol%, 3 μL), HFIP (1.0 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 80 °C for 36 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture was added $PhI(OAc)_2$ (0.1 mmol, 32.2 mg) and MeOH (1 mL) in a sealed tube (10 mL) with a magnetic stir bar. The reaction mixture was heated to 80 °C for 3 hours. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using hexanes/EtOAc (5/1 to 4/1 to 2/1) as the eluent.

Method B. The starting material **1** (0.2 mmol, 49.6 mg), $Pd(OAc)_2$ (15 mol%, 3.3 mg), and AgOAc (0.2 mmol, 33.4 mg) were weighed in air and placed in a sealed tube (10 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (0.1 mmol), 2,6-lutidine (30 mol%, 3 μL), HFIP (1.0 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 80 °C for 36 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were

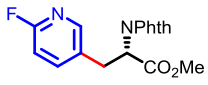
removed under reduced pressure and the resulting mixture was added $PhI(OAc)_2$ (0.2 mmol, 64.4 mg) and MeOH (1 mL) in a sealed tube (10 mL) with a magnetic stir bar, The reaction mixture was heated to 80 °C for 3 hours, Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using hexanes/EtOAc (5/1 to 4/1 to 2/1) as the eluent.



4h'

Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(2-fluoropyridin-4-yl)propanoate (4h')

Substrate **1** was arylated following the general arylation and deprotection (method A). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4h'** was obtained as a white solid (16.0 mg, 47%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (d, J = 5.4 Hz, 1H), 7.82-7.81 (m, 2H), 7.75-7.73 (m, 2H), 7.03 (d, J = 5.4 Hz, 1H), 6.77 (m, 1H), 5.20 (dd, J = 10.5, 5.7 Hz, 1H), 3.79 (s, 3H), 3.64-3.62 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.58, 167.34, 163.98 (d, J_{FC} = 87.6 Hz), 151.79 (d, J_{FC} = 7.8 Hz), 147.85 (d, J_{FC} = 15.2 Hz), 134.48, 131.34, 123.77, 121.69 (d, J_{FC} = 4.1 Hz), 109.85 (d, J_{FC} = 37.1 Hz), 53.22, 51.80, 34.03 (d, J_{FC} = 2.9 Hz); HRMS (ESI-TOF) Calcd for $C_{17}H_{14}FN_2O_4$ $[M+H]^+$: 329.0932; found: 329.0929.

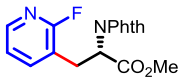


4i'

Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(6-fluoropyridin-3-yl)propanoate (4i')

Substrate **1** was arylated following the general arylation and deprotection (method A). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4i'** was obtained as a white solid (18.5mg, 56%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98-7.97 (m, 1H), 7.81-7.80 (m, 2H), 7.74-7.72 (m, 2H), 7.68-7.65 (m, 1H), 6.82 (dd, J = 8.4, 3.0 Hz, 1H), 5.09 (dd, J =

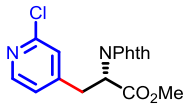
10.2, 6.6 Hz, 1H), 3.80 (s, 3H), 3.58-3.56 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.73, 167.35, 162.80 (d, J_{FC} = 237.3 Hz), 147.79 (d, J_{FC} = 14.1 Hz), 141.50 (d, J_{FC} = 6.3 Hz), 134.43, 131.36, 129.94 (d, J_{FC} = 4.2 Hz), 123.75, 109.56 (d, J_{FC} = 37.5 Hz), 53.13, 52.62, 31.40; HRMS (ESI-TOF) Calcd for $C_{17}H_{14}FN_2O_4$ $[M+H]^+$: 329.0932; found: 329.0942.



4j'

Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(2-fluoropyridin-3-yl)propanoate (4j')

Substrate **1** was arylated following the general arylation and deprotection (method A). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4j'** was obtained as a white solid (9.8 mg, 30%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05-8.04 (m, 1H), 7.82-7.81 (m, 2H), 7.73-7.72 (m, 2H), 7.62-7.59 (m, 1H), 7.05-7.02 (m, 1H), 5.19 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.79 (s, 3H), 3.64 (dd, *J* = 14.7, 5.1 Hz, 1H), 3.55 (dd, *J* = 14.4, 10.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.76, 167.26, 162.15 (d, J_{FC} = 88.4 Hz), 146.50 (d, J_{FC} = 14.7 Hz), 141.82 (d, J_{FC} = 5.6 Hz), 134.32, 131.47, 123.67, 121.53 (d, J_{FC} = 4.8 Hz), 118.88 (d, J_{FC} = 30.5 Hz), 53.09, 51.34, 28.80 (d, J_{FC} = 3.2 Hz); HRMS (ESI-TOF) Calcd for $C_{17}H_{14}FN_2O_4$ $[M+H]^+$: 329.0932; found: 329.0940.

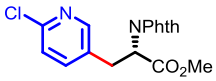


4k'

Methyl (*S*)-3-(2-chloropyridin-4-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (4k')

Substrate **1** was arylated following the general arylation and deprotection (method A). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4k'** was obtained as a white solid (19.8 mg, 57%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (d, *J* = 4.8 Hz, 1H), 7.83-7.82 (m, 2H), 7.75-7.73 (m, 2H), 7.18 (s, 1H), 7.07 (dd, *J* = 5.1, 1.5 Hz, 1H), 5.18 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.79 (s, 3H), 3.62-3.54 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.54,

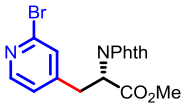
167.34, 151.90, 149.81, 149.23, 134.49, 131.33, 124.66, 123.77, 122.70, 53.22, 51.72, 33.93; HRMS (ESI-TOF) Calcd for $C_{17}H_{14}ClN_2O_4$ $[M+H]^+$: 345.0637; found: 345.0635.



4l'

Methyl (*S*)-3-(6-chloropyridin-3-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (4l')

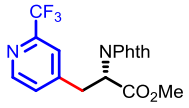
Substrate **1** was arylated following the general arylation and deprotection (method A). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4l'** was obtained as a white solid (21.0 mg, 61%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (dd, *J* = 2.4, 0.6 Hz, 1H), 7.82-7.80 (m, 2H), 7.74-7.73 (m, 2H), 7.54 (dd, *J* = 8.2, 2.5 Hz, 1H), 7.21 (dd, *J* = 8.2, 0.7 Hz, 1H), 5.09 (dd, *J* = 10.0, 6.4 Hz, 1H), 3.79 (s, 3H), 3.57-3.55 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.66, 167.35, 150.28, 150.03, 139.14, 134.45, 131.35, 131.27, 124.23, 123.76, 53.16, 52.47, 31.35; HRMS (ESI-TOF) Calcd for $C_{17}H_{14}ClN_2O_4$ $[M+H]^+$: 345.0637; found: 345.0638.



4m'

Methyl (*S*)-3-(2-bromopyridin-4-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (4m')

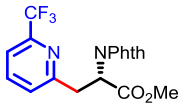
Substrate **1** was arylated following the general arylation and deprotection (method A). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4m'** was obtained as a white solid (18.3 mg, 47%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 (d, *J* = 5.4 Hz, 1H), 7.83-7.82 (m, 2H), 7.75-7.74 (m, 2H), 7.34 (s, 1H), 7.11 (d, *J* = 4.8 Hz, 1H), 5.17 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.79 (s, 3H), 3.60-3.51 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.52, 167.33, 150.22, 148.95, 142.60, 134.49, 131.33, 128.47, 123.78, 123.06, 53.22, 51.70, 33.85; HRMS (ESI-TOF) Calcd for $C_{17}H_{14}BrN_2O_4$ $[M+H]^+$: 389.0131; found: 389.0132.



4n'

Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)propanoate (4n')

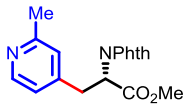
Substrate **1** was arylated following the general arylation and deprotection (method A). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4n'** was obtained as a white solid (25.0 mg, 66%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.8 Hz, 1H), 7.84-7.81 (m, 2H), 7.76-7.72 (m, 2H), 7.52 (s, 1H), 7.35 (d, *J* = 4.8 Hz, 1H), 5.21 (dd, *J* = 11.1, 5.7 Hz, 1H), 3.79 (s, 3H), 3.73-3.63 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.48, 167.32, 150.21, 148.57 (q, J_{FC} = 34.0 Hz), 148.02, 134.54, 131.30, 126.66, 123.78, 121.32 (q, J_{FC} = 272.5 Hz), 121.00-120.95, 53.26, 51.70, 34.33; HRMS (ESI-TOF) Calcd for $C_{18}H_{14}F_3N_2O_4$ $[M+H]^+$: 379.0900; found: 379.0910.



4o'

Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(6-(trifluoromethyl)pyridin-2-yl)propanoate (4o')

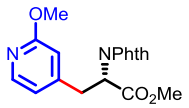
Substrate **1** was arylated following the general arylation and deprotection (method A). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4o'** was obtained as a white solid (17.6 mg, 47%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82-7.79 (m, 2H), 7.74-7.70 (m, 3H), 7.45 (d, *J* = 7.2 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 5.46 (dd, *J* = 8.4, 7.2 Hz, 1H), 3.79-3.78 (m, 2H), 3.78 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.31, 167.39, 158.02, 147.82 (q, J_{FC} = 34.5 Hz), 137.82, 134.07, 131.76, 126.44, 123.46, 121.14 (q, J_{FC} = 272.7 Hz), 118.48-118.40, 52.98, 51.23, 36.11; HRMS (ESI-TOF) Calcd for $C_{18}H_{14}F_3N_2O_4$ $[M+H]^+$: 379.0900; found: 379.0898.



4p'

Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(2-methylpyridin-4-yl)propanoate (4p')

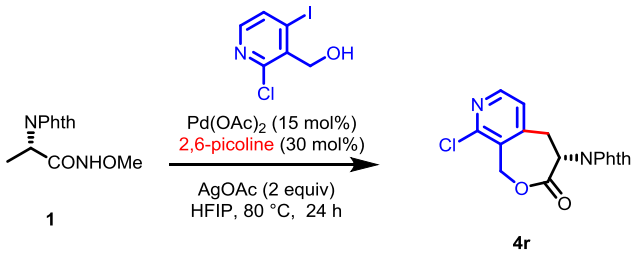
Substrate **1** was arylated following the general arylation and deprotection (method B). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4p'** was obtained as a white solid (13.7 mg, 42%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (d, *J* = 4.8 Hz, 1H), 7.81-7.80 (m, 2H), 7.73-7.71 (m, 2H), 6.99 (s, 1H), 6.92 (dd, *J* = 5.4, 1.2 Hz, 1H), 5.20 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.79 (s, 3H), 3.56-3.53 (m, 2H), 2.43 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.92, 167.40, 158.66, 149.24, 146.08, 134.33, 131.43, 123.69, 123.63, 121.07, 53.10, 52.05, 34.04, 24.24; HRMS (ESI-TOF) Calcd for $C_{18}H_{17}N_2O_4$ $[M+H]^+$: 325.1183; found: 325.1184.



4q'

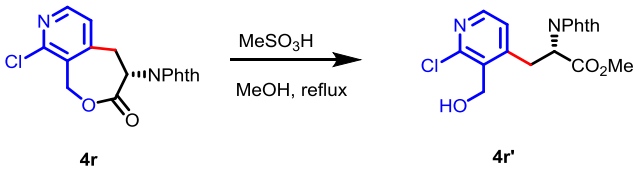
Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(2-methoxypyridin-4-yl)propanoate (4q')

Substrate **1** was arylated following the general arylation and deprotection (method B). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4q'** was obtained as a white solid (17.1 mg, 50%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (d, *J* = 5.4 Hz, 1H), 7.82-7.79 (m, 2H), 7.73-7.70 (m, 2H), 6.71 (dd, *J* = 5.1, 1.5 Hz, 1H), 6.56 (s, 1H), 5.18 (dd, *J* = 10.2, 6.0 Hz, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.55-3.53 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.92, 167.38, 164.51, 148.56, 147.02, 134.28, 131.49, 123.66, 117.21, 110.91, 53.34, 53.09, 52.07, 33.96; HRMS (ESI-TOF) Calcd for $C_{18}H_{17}N_2O_5$ $[M+H]^+$: 341.1132; found 341.1134.



(*S*)-2-(9-chloro-3-oxo-1,3,4,5-tetrahydrooxepino[3,4-c]pyridin-4-yl)isoindoline-1,3-dione (4r)

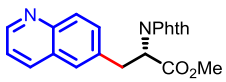
Substrate **1** was arylated following the general arylation (method A). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4r** was obtained as a white solid (11.0 mg, 32%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (d, *J* = 4.8 Hz, 1H), 7.92-7.91 (m, 2H), 7.80-7.79 (m, 2H), 7.17 (d, *J* = 5.4 Hz, 1H), 5.81 (d, *J* = 15.6 Hz, 1H), 5.63 (d, *J* = 15.0 Hz, 1H), 5.56 (dd, *J* = 12.6, 4.8 Hz, 1H), 4.32 (dd, *J* = 16.5, 12.9 Hz, 1H), 3.25 (dd, *J* = 16.8, 4.8 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.26, 167.20, 150.72, 149.68, 147.86, 134.66, 131.61, 128.16, 123.95, 123.94, 65.52, 49.10, 33.87; HRMS (ESI-TOF) Calcd for $C_{17}H_{12}ClN_2O_4$ $[M+H]^+$: 343.0480; found: 343.0482.



Methyl (*S*)-3-(2-chloro-3-(hydroxymethyl)pyridin-4-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (4r')

To a solution of **4r** (0.032 mmol, 11.0 mg) in MeOH (1 mL) was added $MeSO_3H$ (1.5 equiv). After the mixture was heated to reflux for one to two hours, the reaction was cooled to room temperature. The solvents were removed under reduced pressure and the resulting mixture was purified by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4r'** was obtained as a white solid (11.5 mg, >99%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 (d, *J* = 4.8 Hz, 1H), 7.82-7.81 (m, 2H), 7.75-7.73 (m, 2H), 7.02 (d, *J* = 4.8 Hz, 1H), 5.35 (dd, *J* = 11.1, 5.1 Hz, 1H), 4.95 (d, *J* = 12.6 Hz, 1H), 4.88 (d, *J* = 12.6 Hz, 1H), 3.81 (dd, *J* = 14.4, 5.4 Hz, 1H), 3.79 (s, 3H), 3.61 (dd, *J* = 14.7, 11.1 Hz, 1H), 2.49 (br, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.62, 167.52,

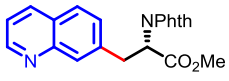
152.81, 148.72, 148.70, 134.49, 133.06, 131.35, 124.46, 123.80, 59.01, 53.23, 52.15, 32.24; HRMS (ESI-TOF) Calcd for $C_{18}H_{16}ClN_2O_5$ $[M+H]^+$: 375.0742; found: 375.0743.



4s'

Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(quinolin-6-yl)propanoate (4s')

Substrate **1** was arylated following the general arylation and deprotection (method B). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4s'** was obtained as a white solid (15.6 mg, 43%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.82 (dd, *J* = 3.6, 1.2 Hz, 1H), 8.03-8.01 (m, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.76-7.74 (m, 2H), 7.67-7.62 (m, 2H), 7.62 (d, *J* = 1.2 Hz, 1H), 7.56 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.32 (dd, *J* = 8.4, 4.2 Hz, 1H), 5.30 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.83 (s, 3H), 3.82-3.74 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.18, 167.47, 150.10, 147.24, 135.85, 135.24, 134.19, 131.45, 130.53, 129.64, 128.21, 127.50, 123.56, 121.25, 53.04, 52.93, 34.67; HRMS (ESI-TOF) Calcd for $C_{21}H_{17}N_2O_4$ $[M+H]^+$: 361.1183; found: 361.1185.

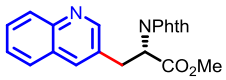


4t'

Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(quinolin-7-yl)propanoate (4t')

Substrate **1** was arylated following the general arylation and deprotection (method B). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4t'** was obtained as a white solid (14.9 mg, 42%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.82 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.07-8.05 (m, 1H), 7.87 (s, 1H), 7.76-7.73 (m, 2H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.67-7.64 (m, 2H), 7.44 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.31 (dd, *J* = 8.4, 4.2 Hz, 1H), 5.29 (dd, *J* = 11.1, 5.1 Hz, 1H), 3.84-3.74 (m, 2H), 3.80 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.17, 167.41, 150.52,

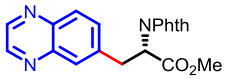
148.21, 138.51, 135.80, 134.12, 131.52, 129.29, 128.15, 127.53, 127.11, 123.58, 120.87, 53.06, 53.03, 35.01; HRMS (ESI-TOF) Calcd for $C_{21}H_{17}N_2O_4$ $[M+H]^+$: 361.1183; found: 361.1188.



4u'

Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(quinolin-3-yl)propanoate (4u')

Substrate **1** was arylated following the general arylation and deprotection (method B). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4u'** was obtained as a white solid (11.0 mg, 31%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.75 (d, *J* = 2.4 Hz, 1H), 8.02-8.00 (m, 2H), 7.79-7.76 (m, 2H), 7.72-7.71 (m, 1H), 7.70-767 (m, 2H), 7.66-7.63 (m, 1H), 7.50-7.47 (m, 1H), 5.27 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.86-3.73 (m, 2H), 3.81 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.93, 167.47, 151.45, 147.21, 135.53, 134.30, 131.44, 129.63, 129.23, 129.15, 127.84, 127.53, 126.78, 123.68, 53.11, 52.83, 32.23; HRMS (ESI-TOF) Calcd for $C_{21}H_{17}N_2O_4$ $[M+H]^+$: 361.1183; found: 361.1185.

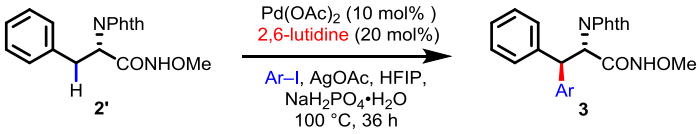


4v'

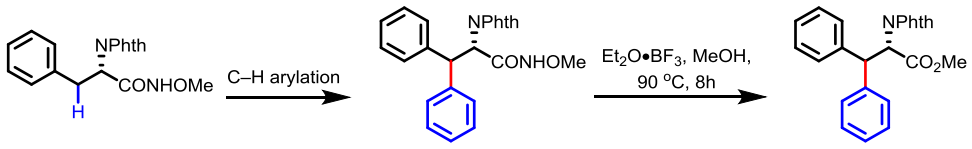
Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(quinoxalin-6-yl)propanoate (4v')

Substrate **1** was arylated following the general arylation and deprotection (method B). After purification by column chromatography using hexanes/EtOAc (3/1) as the eluent, **4v'** was obtained as a white solid (16.2 mg, 45%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.76 (s, 2H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.90-7.89 (m, 1H), 7.77-7.76 (m, 2H), 7.69-7.65 (m, 3H), 5.30 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.88-3.75 (m, 2H), 3.81 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.99, 167.39, 145.12, 144.73, 142.89, 142.04, 139.41, 134.23, 131.44, 131.17, 129.75, 129.22, 123.64, 53.10, 52.86, 34.89; HRMS (ESI-TOF) Calcd for $C_{20}H_{16}N_3O_4$ $[M+H]^+$: 362.1135; found: 362.1139.

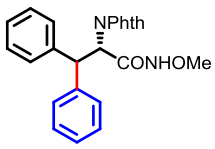
Arylation of methylene C–H bonds



General procedure: The substrate **2'** (0.1 mmol, 24.8 mg), $Pd(OAc)_2$ (0.01 mmol, 2.2 mg), $NaH_2PO_4•H_2O$ (0.3 mmol, 42 mg) and AgOAc (0.2 mmol, 33.4 mg) were weighed in air and placed in a sealed tube (10 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (0.3 mmol), 2,6-lutidine (0.02 mmol, 2 μL), HFIP (1 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 36 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column.



2', (99% ee) **3q**, 82% (99% ee) **3q'**, 90% (99% ee)



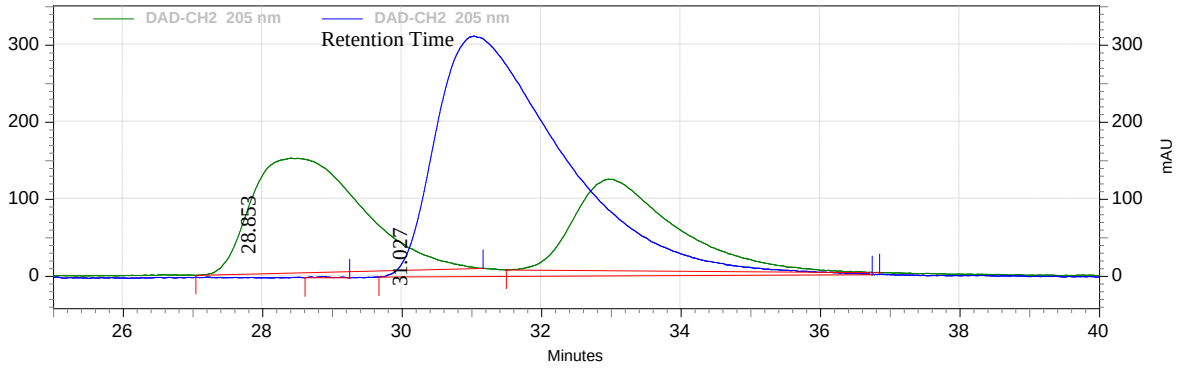
3q

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-N-methoxy-3,3-diphenylpropanamide (3q)

Substrate **1** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3q** was obtained as a white solid (30.7 mg, 77%). m.p. = 220-222 °C. ^{1}H NMR (600 MHz, CDCl3) δ 9.14 (s, 1H), 7.73-7.71 (m, 2H), 7.66-7.63 (m, 2H), 7.52-7.50 (m, 2H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.28-7.26 (m, 2H), 7.24 (t, *J* = 7.2 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 2H), 7.03 (t, *J* = 7.2 Hz, 1H), 5.57 (d, *J* = 12.6 Hz, 1H), 5.32 (t, *J* = 12.6 Hz, 1H), 3.48 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.90, 164.99, 139.78, 139.73,

134.30, 131.07, 129.07, 128.73, 128.16, 127.63, 127.54, 127.13, 123.55, 64.14, 56.91, 50.20; HRMS (ESI-TOF) Calcd for $C_{24}H_{21}N_2O_4$ $[M+H]^+$: 401.1496; found: 401.1493. The ee value was determined by HPLC analysis on a Chiralcel OD-H column (20% isopropanol in hexanes, 0.4 mL/min) with t_r = 28.9 min (minor), 31.0 min (major): 99% ee.

Area % Report

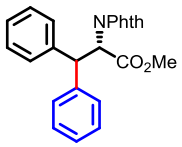


DAD-CH2 205 nm

Results

Retention Time	Area	Area %	Height	Height %
28.853	102668	0.06	6381	0.51
31.027	159396134	99.94	1248555	99.49

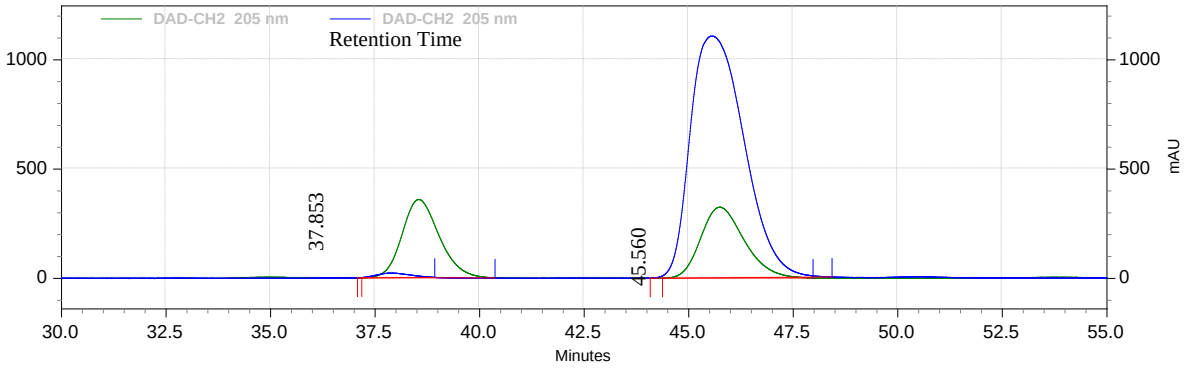
Totals	159498802	100.00	1254936	100.00



3q'

Methyl (S)-2-(1,3-dioxoisoindolin-2-yl)-3,3-diphenylpropanoate (3q')

A sealable pressure flask was charged with MeOH (1 mL) and amide **3q** (0.1 mmol, 40 mg)**.** BF_3•OEt_2 (5 equiv.) was added and the reaction vessel sealed. The reaction mixture was heated to 90 °C for 8 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The solvents were removed under reduced pressure and H_2O and EtOAc was added, organic layers were removed and the aqueous layer was then extracted with EtOAc and the combined organics washed with brine, dried over $MgSO_4$, filtered and concentrated. Purified by column chromatography (hexanes/EtOAc = 2/1 to 1/1) to provide **3q'** as a white solid (34.7 mg, 90%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74-7.72 (m, 2H), 7.66-7.64 (m, 2H), 7.49 (d, *J* = 7.8 Hz, 2H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.26-7.20 (m, 3H), 7.09 (t, *J* = 7.8 Hz, 2H), 6.98 (t, *J* = 7.2 Hz, 1H), 5.75 (d, *J* = 12.0 Hz, 1H), 5.27 (d, *J* = 12.0 Hz, 1H), 3.57 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.67, 167.29, 141.49, 140.35, 134.07, 131.31, 128.73, 128.49, 127.98, 127.70, 126.89, 126.87, 123.41, 54.81, 52.63, 50.56. The ee value was determined by HPLC analysis on a Chiralcel ADH column (10% isopropanol in hexanes, 0.5 mL/min) with t_r = 37.9 min (minor), 45.6 min (major): 98% ee.



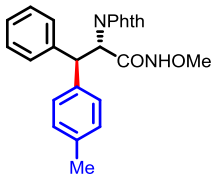
DAD-CH2 205 nm

Results

Retention Time	Area	Area %	Height	Height %
37.853	4729873	1.18	85311	1.89

45.560	395751505	98.82	4421105	98.11

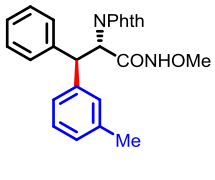
Totals	400481378	100.00	4506416	100.00



3a

(2*S*, 3*R*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-phenyl-3-(p-tolyl)propanamide (3a)

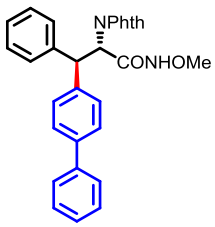
Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3a** was obtained as a white solid (33.6 mg, 81%). m.p. = 215-218 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.09 (s, 1H), 7.73-7.71 (m, 2H), 7.65-7.63 (m, 2H), 7.41-7.39 (m, 2H), 7.25 (d, *J* = 7.8 Hz, 2H), 7.15-7.11 (m, 4H), 7.03-7.00 (m, 1H), 5.56 (d, *J* = 12.6 Hz, 1H), 5.25 (d, *J* = 12.6 Hz, 1H), 3.52 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.92, 165.12, 140.05, 137.37, 136.68, 134.27, 131.09, 129.81, 128.70, 127.95, 127.45, 127.04, 123.53, 64.20, 56.95, 49.92, 21.04; HRMS (ESI-TOF) Calcd for $C_{25}H_{23}N_2O_4$ $[M+H]^+$: 415.1652; found: 415.1649.



3b

(2*S*, 3*R*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-phenyl-3-(m-tolyl)propanamide (3b)

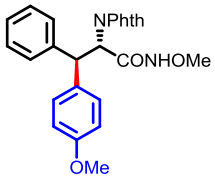
Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3b** was obtained as a white solid (33.6 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.07 (s, 1H), 7.74 (m, 2H), 7.66-7.63 (m, 2H), 7.32-7.26 (m, 4H), 7.22 (t, *J* = 7.8 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 2H), 7.05-7.01 (m, 2H), 5.56 (d, *J* = 12.6 Hz, 1H), 5.27 (d, *J* = 12.6 Hz, 1H), 3.52 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.88, 165.03, 139.92, 139.66, 138.76, 134.25, 131.09, 128.98, 128.93, 128.69, 128.43, 127.53, 127.06, 125.00, 123.51, 64.12, 56.79, 50.14, 45.20, 21.49; HRMS (ESI-TOF) Calcd for $C_{25}H_{23}N_2O_4$ $[M+H]^+$: 415.1652; found: 415.1651.



3c

(2*S*, 3*R*)-3-([1,1'-Biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxy-3-phenyl propanamide (3c)

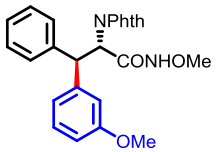
Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3c** was obtained as a yellow solid (27.6 mg, 61%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.28 (s, 1H), 7.73-7.71 (m, 2H), 7.65-7.62 (m, 2H), 7.60-7.55 (m, 4H), 7.54-7.52 (m, 2H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.33-7.30 (m, 3H), 7.15 (t, *J* = 7.8 Hz, 2H), 7.04 (t, *J* = 7.2 Hz, 1H), 5.61 (d, *J* = 12.6 Hz, 1H), 5.39 (d, *J* = 12.6 Hz, 1H), 3.51 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.92, 165.01, 140.41, 139.73, 138.73, 134.32, 134.26, 131.05, 128.82, 128.79, 128.75, 128.57, 127.69, 127.58, 127.36, 127.20, 126.98, 123.55, 64.18, 56.83, 49.85; HRMS (ESI-TOF) Calcd for $C_{30}H_{25}N_2O_4$ $[M+H]^+$: 477.1809; found: 477.1809.



3d

(2*S*, 3*R*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(4-methoxyphenyl)-3-phenyl propanamide (3d)

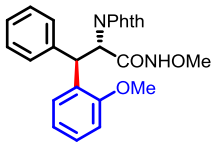
Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3d** was obtained as a white solid (35.2 mg, 80%). m.p. = 175-178 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.15 (s, 1H), 7.74-7.71 (m, 2H), 7.66-7.63 (m, 2H), 7.44-7.41 (m, 2H), 7.27-7.24 (m, 2H), 7.14-7.12 (m, 2H), 7.04-7.01 (m, 1H), 6.89-6.88 (m, 2H), 5.52 (d, *J* = 12.6 Hz, 1H), 5.25 (d, *J* = 12.6 Hz, 1H), 3.76 (s, 3H), 3.53 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.94, 165.16, 158.94, 140.12, 134.30, 131.70, 131.08, 129.24, 129.21, 128.72, 127.40, 127.03, 123.54, 114.46, 64.23, 57.09, 55.24, 49.46; HRMS (ESI-TOF) Calcd for $C_{25}H_{23}N_2O_5$ $[M+H]^+$: 431.1601; found: 431.1601.



3e

(2*S*, 3*R*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(3-methoxyphenyl)-3-phenylpropanamide (3e)

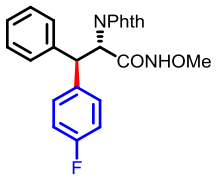
Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3e** was obtained as a white solid (32.1 mg, 75%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.08 (s, 1H), 7.73-7.70 (m, 2H), 7.65-7.62 (m, 2H), 7.27-7.24 (m, 3H), 7.14-7.10 (m, 3H), 7.04-7.01 (m, 2H), 6.783-6.77 (m, 1H), 5.54 (d, *J* = 12.6 Hz, 1H), 5.30 (d, *J* = 12.6 Hz, 1H), 3.79 (s, 3H), 3.52 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.87, 165.00, 159.96, 141.35, 139.70, 134.27, 131.09, 130.13, 128.72, 127.55, 127.15, 123.53, 120.23, 114.21, 112.81, 64.17, 56.67, 55.26, 50.10; HRMS (ESI-TOF) Calcd for $C_{25}H_{23}N_2O_5$ $[M+H]^+$: 431.1601; found: 431.1606.



3f

(2*S*, 3*R*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(2-methoxyphenyl)-3-phenyl propanamide (3f)

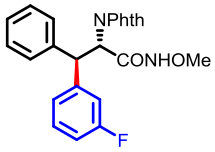
Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3f** was obtained as a yellow solid (25.5 mg, 59%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.33 (s, 1H), 7.75-7.72 (m, 2H), 7.66-7.63 (m, 2H), 7.59-7.58 (m, 1H), 7.31-7.29 (m, 2H), 7.23-7.21 (m, 1H), 7.10 (t, *J* = 7.8 Hz, 2H), 7.01-6.98 (m, 2H), 6.88-6.87 (m, 1H), 5.80 (d, *J* = 13.2 Hz, 1H), 5.68 (d, *J* = 13.2 Hz, 1H), 3.90 (s, 3H), 3.46 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.21, 165.08, 156.76, 139.62, 134.23, 131.15, 128.70, 128.40, 128.34, 127.93, 126.87, 123.49, 121.25, 111.32, 110.02, 63.95, 56.61, 55.71, 42.80; HRMS (ESI-TOF) Calcd for $C_{25}H_{23}N_2O_5$ $[M+H]^+$: 431.1601; found: 431.1597.



3g

(2*S*, 3*R*)-2-(1,3-Dioxoisoindolin-2-yl)-3-(4-fluorophenyl)-*N*-methoxy-3-phenylpropanamide (3g)

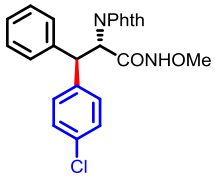
Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3g** was obtained as a white solid (30.1 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.37 (s, 1H), 7.73-7.70 (m, 2H), 7.67-7.64 (m, 2H), 7.49-7.47 (m, 2H), 7.24 (d, *J* = 7.8 Hz, 2H), 7.14 (t, *J* = 7.8 Hz, 2H), 7.06-7.00 (m, 3H), 5.51 (d, *J* = 12.6 Hz, 1H), 5.34 (d, *J* = 12.6 Hz, 1H), 3.52 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.90, 164.92, 162.02 (d, J_{FC} = 245.1 Hz), 139.51, 135.51, 134.40, 130.98, 129.84 (d, J_{FC} = 8.0 Hz), 128.83, 127.47, 127.28, 123.60, 115.83 (d, J_{FC} = 21.2 Hz), 64.20, 56.98, 49.35; HRMS (ESI-TOF) Calcd for $C_{24}H_{20}FN_2O_4$ $[M+H]^+$: 419.1402; found: 419.1402.



3h

(2*S*, 3*R*)-2-(1,3-Dioxoisoindolin-2-yl)-3-(3-fluorophenyl)-*N*-methoxy-3-phenylpropanamide (3h)

Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3h** was obtained as a white solid (29.2 mg, 70%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.33 (s, 1H), 7.73-7.71 (m, 2H), 7.67-7.64 (m, 2H), 7.32-7.29 (m, 2H), 7.27-7.25 (m, 2H), 7.21 (d, J = 10.2 Hz, 1H), 7.15 (t, J = 7.5 Hz, 2H), 7.06 (t, J = 7.2 Hz, 1H), 6.93 (t, J = 7.2 Hz, 1H), 5.51 (d, J = 12.6 Hz, 1H), 5.37 (d, J = 12.6 Hz, 1H), 3.53 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.83, 164.79, 162.91 (d, J_{FC} = 245.4 Hz), 142.28, 139.10, 134.39, 130.98, 130.48 (d, J_{FC} = 7.5 Hz), 128.85, 127.59, 127.39, 123.87, 123.60, 115.30 (d, J_{FC} = 21.8 Hz), 114.51 (d, J_{FC} = 20.7 Hz), 64.19, 56.60, 49.74; HRMS (ESI-TOF) Calcd for $C_{24}H_{20}FN_2O_4$ $[M+H]^+$: 419.1402; found: 419.1402.

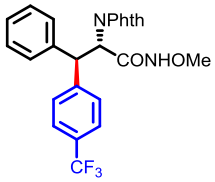


3i

(2*S*, 3*R*)-3-(4-chlorophenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxy-3-phenylpropanamide (3i)

Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3i** was obtained as a white solid (32.6 mg, 75%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.40 (s, 1H), 7.72-7.70 (m, 2H), 7.66-7.64 (m, 2H), 7.45-7.44 (m, 2H), 7.30-7.28 (m, 2H), 7.24-7.23 (m, 2H), 7.14 (t, J = 7.5 Hz, 2H), 7.06-7.03 (m, 1H), 5.51 (d, J = 12.6 Hz, 1H), 5.33 (d, J = 12.6 Hz, 1H), 3.53 (s, 3H); ^{13}C NMR (150 MHz,

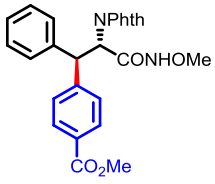
$CDCl_3$) δ 167.86, 164.84, 139.25, 138.24, 134.41, 133.38, 130.95, 129.56, 129.08, 128.85, 127.49, 127.35, 123.60, 64.22, 56.71, 49.46; HRMS (ESI-TOF) Calcd for $C_{24}H_{20}ClN_2O_4$ $[M+H]^+$: 435.1106; found: 435.1107.



3j

(2*S*, 3*R*)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxy-3-phenyl-3-(4-(trifluoromethyl)phenyl) propanamide (3j)

Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3j** was obtained as a white solid (34.9 mg, 75%). m.p. = 120-123 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.48 (s, 1H), 7.73-7.71 (m, 2H), 7.67-7.64 (m, 4H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.26-7.25 (m, 2H), 7.15 (t, *J* = 7.5 Hz, 2H), 7.07-7.05 (m, 1H), 5.58 (d, *J* = 12.6 Hz, 1H), 5.45 (d, *J* = 12.6 Hz, 1H), 3.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.86, 164.75, 143.81, 138.81, 134.48, 130.93, 129.67 (q, J_{FC} = 32.4 Hz), 128.94, 128.64, 127.62, 127.54, 125.93-125.75, 123.97 (q, J_{FC} = 270.5 Hz), 123.65, 64.17, 56.47, 49.82; HRMS (ESI-TOF) Calcd for $C_{25}H_{20}F_3N_2O_4$ $[M+H]^+$: 469.1370; found: 469.1372.

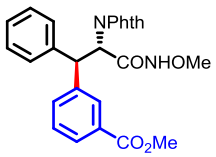


3k

Methyl 4-((1*R*, 2*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(methoxyamino)-3-oxo-1-phenylpropyl) benzoate (3k)

Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3k** was obtained as a white solid (34.7 mg, 76%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.49 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.72-7.69 (m, 2H), 7.66-7.63 (m, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 7.2 Hz, 3H), 7.14 (t, *J* = 7.8 Hz, 3H), 7.05 (t, *J* = 7.2 Hz, 1H), 5.58 (d, *J* = 12.6 Hz, 1H), 5.45 (d, *J* = 12.6 Hz, 1H), 3.88 (s, 3H),

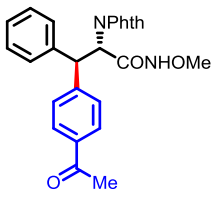
3.48 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.83, 166.71, 164.74, 144.99, 138.98, 134.40, 130.97, 130.20, 129.24, 128.86, 128.28, 127.66, 127.42, 123.59, 64.15, 56.39, 52.13, 49.94; HRMS (ESI-TOF) Calcd for $C_{26}H_{23}N_2O_6$ $[M+H]^+$: 459.1551; found: 459.1554.



3l

Methyl 3-((1*R*, 2*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(methoxyamino)-3-oxo-1-phenylpropyl) benzoate (3l)

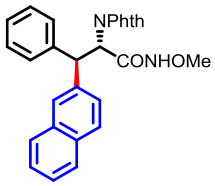
Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3l** was obtained as a white solid (37.8 mg, 83%). m.p. = 107-109 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.42 (s, 1H), 8.17 (s, 1H), 7.91 (d, *J* = 7.2 Hz, 1H), 7.75-7.72 (m, 3H), 7.67-7.64 (m, 2H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 7.2 Hz, 2H), 7.15 (t, *J* = 7.2 Hz, 2H), 7.05 (t, *J* = 7.5 Hz, 1H), 5.59 (d, *J* = 12.6 Hz, 1H), 5.43 (d, *J* = 12.6 Hz, 1H), 3.89 (s, 3H), 3.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.87, 166.77, 164.72, 140.24, 139.15, 134.41, 132.88, 130.98, 130.69, 129.27, 129.11, 128.89, 128.76, 127.60, 127.38, 123.62, 64.18, 56.73, 52.21, 49.88; HRMS (ESI-TOF) Calcd for $C_{26}H_{23}N_2O_6$ $[M+H]^+$: 459.1551; found: 459.1550.



3m

(2*S*, 3*R*)-3-(4-Acetylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxy-3-phenylpropanamide (3m)

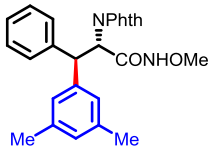
Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3m** was obtained as a white solid (24.3 mg, 55%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.44 (s, 1H), 7.92 (d, *J* = 8.4 Hz, 2H), 7.75-7.72 (m, 2H), 7.68-7.66 (m, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.29-7.27 (m, 2H), 7.14 (t, *J* = 7.2 Hz, 2H), 7.08-7.05 (m, 1H), 5.59 (d, *J* = 12.6 Hz, 1H), 5.41 (d, *J* = 12.6 Hz, 1H), 3.51 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.61, 167.86, 164.79, 145.08, 138.84, 136.17, 134.47, 130.93, 128.99, 128.90, 128.41, 127.61, 127.49, 123.65, 64.23, 56.51, 50.04, 26.60; HRMS (ESI-TOF) Calcd for $C_{26}H_{23}N_2O_5$ $[M+H]^+$: 443.1601; found: 443.1601.



3n

(2*S*, 3*R*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(naphthalen-2-yl)-3-phenyl propanamide (3n)

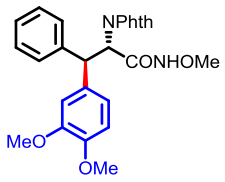
Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3n** was obtained as a yellow solid (27.6 mg, 61%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.20 (s, 1H), 8.01 (s, 1H), 7.85-7.76 (m, 3H), 7.75-7.72 (m, 2H), 7.66-7.63 (m, 2H), 7.58 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.47-7.43 (m, 2H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.14 (t, *J* = 7.8 Hz, 2H), 7.04-7.01 (m, 1H), 5.71 (d, *J* = 12.6 Hz, 1H), 5.50 (d, *J* = 12.6 Hz, 1H), 3.39 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.96, 165.03, 139.69, 137.12, 134.32, 133.48, 132.63, 131.08, 128.92, 128.76, 127.95, 127.67, 127.60, 127.19, 126.87, 126.37, 126.14, 126.01, 123.58, 64.13, 56.74, 50.20; HRMS (ESI-TOF) Calcd for $C_{28}H_{23}N_2O_4$ $[M+H]^+$: 451.1652; found: 451.1651.



3o

(2*S*, 3*R*)-3-(3,5-Dimethylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxy-3-phenyl propanamide (3o)

Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3o** was obtained as a white solid (32.2 mg, 75%). m.p. = 108-110 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.91 (s, 1H), 7.73-7.71 (m, 2H), 7.65-7.63 (m, 2H), 7.27-7.25 (m, 2H), 7.14-7.11 (m, 4H), 7.03-7.01 (m, 1H), 6.87 (s, 1H), 5.55 (d, *J* = 12.6 Hz, 1H), 5.19 (d, *J* = 12.6 Hz, 1H), 3.52 (s, 3H), 2.29 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.90, 165.10, 140.05, 139.59, 138.70, 134.21, 131.14, 129.43, 128.67, 127.51, 127.02, 125.80, 123.50, 64.14, 56.74, 50.13, 21.38; HRMS (ESI-TOF) Calcd for $C_{26}H_{25}N_2O_4$ $[M+H]^+$: 429.1809; found: 429.1806.



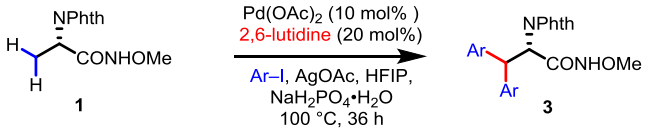
3p

(2*S*, 3*R*)-3-(3,4-Dimethoxyphenyl)-2-(1, 3-dioxoisoindolin-2-yl)-*N*-methoxy-3-phenyl propanamide (3p)

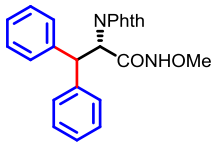
Substrate **2'** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3p** was obtained as a yellow solid (31.6 mg, 69%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.10 (s, 1H), 7.73-7.71 (m, 2H), 7.66-7.63 (m, 2H), 7.27-7.25 (m, 2H), 7.15-7.13 (m, 2H), 7.07 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.05-7.02 (m, 1H), 6.98 (d, *J* = 2.4 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 5.51 (d, *J* = 12.6 Hz, 1H), 5.26 (d, *J* = 12.6 Hz, 1H), 3.89 (s, 3H), 3.83 (s, 3H), 3.53 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.92, 165.20, 149.21, 148.41, 140.054, 134.30, 132.21, 131.08, 128.73, 127.41, 127.11, 123.54, 119.95, 111.61,

111.52, 64.24, 56.94, 56.02, 55.85, 49.69; HRMS (ESI-TOF) Calcd for $C_{26}H_{25}N_2O_6$ $[M+H]^+$: 461.1707; found: 461.1708.

Homo-diarylation of Alanine



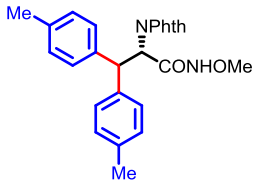
General procedure: The substrate **1** (0.1 mmol, 24.8 mg), $Pd(OAc)_2$ (0.01 mmol, 2.2 mg), $NaH_2PO_4•H_2O$ (0.3 mmol, 42 mg) and AgOAc (0.2 mmol, 33.4 mg) were weighed in air and placed in a sealed tube (10 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (0.3 mmol), 2,6-lutidine (0.2 mmol, 2 μL), HFIP (1 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 36 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using hexanes/EtOAc (5/1 to 3/1 to 2/1) as the eluent.



3q

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3,3-diphenylpropanamide (3q)

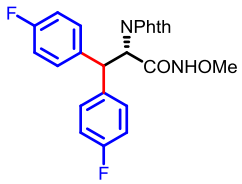
Substrate **1** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3q** was obtained as a white solid (26.7 mg, 67%). (For the NMR data, please see the previous one in section of Arylation of Methylene C–H Bonds)



3r

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3,3-di-p-tolylpropanamide (3r)

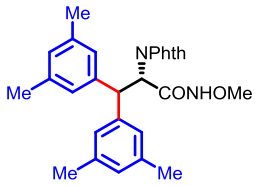
Substrate **1** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3r** was obtained as a white solid (26.8 mg, 63%). m.p. = 120-122 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.08 (s, 1H), 7.75-7.72 (m, 2H), 7.66-7.63 (m, 2H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.14 (dd, *J* = 7.8, 1.8 Hz, 4H), 6.92 (d, *J* = 7.8 Hz, 2H), 5.53 (d, *J* = 12.6 Hz, 1H), 5.21 (d, *J* = 12.6 Hz, 1H), 3.51 (s, 3H), 2.28 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.94, 165.20, 137.24, 137.05, 137.00, 136.57, 134.23, 131.16, 129.78, 129.40, 127.89, 127.23, 123.54, 64.17, 57.01, 49.50, 21.03, 20.88; HRMS (ESI-TOF) Calcd for $C_{26}H_{25}N_2O_4$ $[M+H]^+$: 429.1809; found: 429.1803.



3s

(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-3,3-bis(4-fluorophenyl)-*N*-methoxypropanamide (3s)

Substrate **1** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3s** was obtained as a white solid (31.4 mg, 72%). m.p. = 102-104 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.33 (s, 1H), 7.75-7.72 (m, 2H), 7.69-7.67 (m, 2H), 7.47-7.45 (m, 2H), 7.23-7.21 (m, 2H), 7.03 (t, *J* = 8.4 Hz, 2H), 6.84 (t, *J* = 8.4 Hz, 2H), 5.45 (d, *J* = 12.6 Hz, 1H), 5.35 (d, *J* = 12.6 Hz, 1H), 3.51 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.86, 164.74, 162.07 (d, J_{FC} = 245.4 Hz), 161.74 (d, J_{FC} = 245.0 Hz), 135.40, 135.30, 134.53, 130.91, 129.75 (d, J_{FC} = 8.0 Hz), 129.09 (d, J_{FC} = 17.7 Hz), 123.68, 116.00-115.71, 64.21, 56.90, 48.56; HRMS (ESI-TOF) Calcd for $C_{24}H_{19}F_2N_2O_4$ $[M+H]^+$: 437.1307; found: 437.1308.

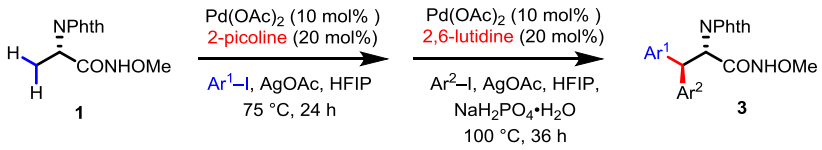


3t

(*S*)-3,3-Bis(3,5-Dimethylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxypropanamide (3t)

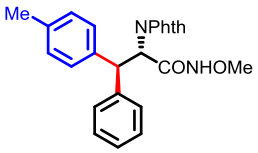
Substrate **1** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3t** was obtained as a white solid (34.4 mg, 75%). m.p. = 100-102 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.95 (s, 1H), 7.75-7.72 (m, 2H), 7.65-7.53 (m, 2H), 7.10 (s, 2H), 6.86 (s, 1H),6.84 (s, 2H), 6.63 (s, 1H), 5.53 (d, *J* = 12.6 Hz, 1H), 5.10 (d, *J* = 12.6 Hz, 1H), 3.51 (s, 3H), 2.30 (s, 6H), 2.11 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.91, 165.22, 139.80, 139.76, 138.60, 137.99, 134.17, 131.26, 129.34, 128.71, 125.83, 125.26, 123.44, 64.09, 56.87, 49.97, 21.40, 21.21; HRMS (ESI-TOF) Calcd for $C_{28}H_{29}N_2O_4$ $[M+H]^+$: 457.2122; found: 457.2118.

Hetero-diarylation of Alanine



General procedure: The starting material **1** (0.1 mmol, 24.8 mg), $Pd(OAc)_2$ (10 mol%, 2.2 mg), and AgOAc (0.2 mmol, 33.4 mg) were weighed in air and placed in a sealed tube (10 mL) with a magnetic stir bar. To the reaction mixture, the first aryl iodide (0.12 mmol), 2-picoline (20 mol%, 2 μL), HFIP (1.0 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 75 °C for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, to the reaction mixture, $Pd(OAc)_2$ (0.01mmol, 2.2mg), NaH_2PO_4•H_2O (0.3 mmol, 42 mg), AgOAc (0.2 mmol, 33.4mg), the second aryl iodide (0.3 mmol) and 2,6-lutidine (0.02 mmol, 2 μL), were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 36 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture

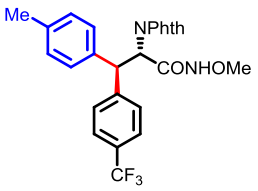
was purified by a silica gel-packed flash chromatography column using hexanes/EtOAc (5/1 to 3/1 to 2/1) as the eluent.



3u

(2*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-phenyl-3-(*p*-tolyl)propanamide (3u)

Substrate **1** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3u** was obtained as a white solid (29.4 mg, 71%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.07 (s, 1H), 7.75-7.73 (m, 2H), 7.67-7.65 (m, 2H), 7.50-7.49 (m, 2H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 2H), 6.94 (d, *J* = 7.8 Hz, 2H), 5.54 (d, *J* = 12.6 Hz, 1H), 5.27 (d, *J* = 12.6 Hz, 1H), 3.47 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.93, 165.08, 140.01, 136.75, 136.71, 134.28, 131.14, 129.45, 129.06, 128.10, 127.55, 127.31, 123.59, 64.14, 57.02, 49.81, 20.90; HRMS (ESI-TOF) Calcd for $C_{25}H_{23}N_2O_4$ $[M+H]^+$: 415.1652; found: 415.1656.

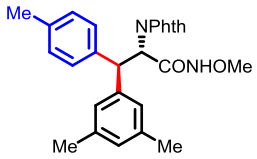


3v

(2*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(*p*-tolyl)-3-(4-(trifluoromethyl)phenyl) propanamide (3v)

Substrate **1** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3v** was obtained as a white solid (23.1 mg, 48%). m.p. = 111-113 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.35 (s, 1H), 7.77-7.74 (m, 2H), 7.69-7.67 (m, 2H), 7.62-7.59 (m, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 6.96 (d, *J* = 7.8 Hz, 2H), 5.54 (d, *J* = 12.6 Hz, 1H), 5.37 (d, *J* = 12.6 Hz, 1H), 3.50 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.89, 164.82, 144.04, 137.24, 135.74, 134.48, 130.98, 129.96-129.30, 129.66,

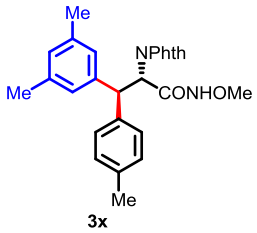
128.53, 127.37, 125.85-125.83, 123.97 (q, J_{FC} = 270.5 Hz), 123.71, 64.21, 56.69, 49.50, 20.91; HRMS (ESI-TOF) Calcd for $C_{26}H_{22}F_3N_2O_4$ $[M+H]^+$: 483.1526; found 483.1523.



3w

(2*S*)-3-(3,5-Dimethylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxy-3-(*p*-tolyl) propanamide (3w)

Substrate **1** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3w** was obtained as a white solid (29.9 mg, 67%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.74-7.72 (m, 2H), 7.66-7.63 (m, 2H), 7.14 (d, *J* = 8.4, 2H), 7.10 (s, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.86 (s, 1H), 5.53 (d, *J* = 12.6 Hz, 1H), 5.16 (d, *J* = 12.6 Hz, 1H), 3.51 (s, 3H), 2.28 (s, 6H), 2.13 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.92, 165.18, 139.89, 138.66, 137.04, 136.56, 134.18, 131.22, 129.39, 129.34, 127.29, 125.74, 123.53, 64.12, 56.81, 49.73, 21.38, 20.90; HRMS (ESI-TOF) Calcd for $C_{27}H_{27}N_2O_4$ $[M+H]^+$: 443.1965; found: 443.1962.

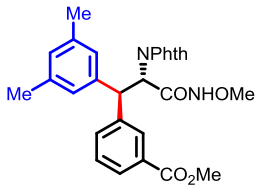


3x

(2*S*)-3-(3,5-Dimethylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxy-3-(*p*-tolyl) propanamide (3x)

Substrate **1** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3x** was obtained as a white solid (22.5 mg, 51%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.08 (s, 1H), 7.76-7.73 (m, 2H), 7.67-7.64 (m, 2H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 6.84 (s, 2H), 6.63 (s, 1H), 5.53 (d, *J* = 12.6 Hz,

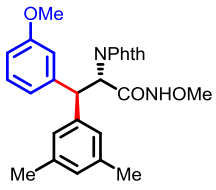
1H), 5.13 (d, *J* = 12.6 Hz, 1H), 3.51 (s, 3H), 2.29 (s, 3H), 2.10 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.98, 165.25, 139.81, 138.03, 137.25, 136.85, 134.22, 131.22, 129.77, 128.70, 127.97, 125.20, 123.48, 64.17, 57.14, 49.81, 21.19, 21.05; HRMS (ESI-TOF) Calcd for $C_{27}H_{27}N_2O_4$ $[M+H]^+$: 443.1965; found: 443.1962.



3y

Methyl 3-((2*S*)-1-(3,5-dimethylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-(methoxyamino)-3-oxopropyl)benzoate (3y)

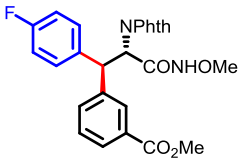
Substrate **1** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3y** was obtained as a white solid (23.2 mg, 48%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.39 (s, 1H), 8.15 (s, 1H), 7.92-7.90 (m, 1H), 7.76-7.73 (m, 3H), 7.69-7.66 (m, 2H), 7.42 (t, *J* = 7.8 Hz, 1H), 6.86 (s, 2H), 6.66 (s, 1H), 5.56 (d, *J* = 12.6 Hz, 1H), 5.29 (d, *J* = 12.6 Hz, 1H), 3.91 (s, 3H), 3.48 (s, 3H), 2.12 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.94, 166.82, 164.85, 140.35, 138.91, 138.29, 134.38, 132.77, 131.09, 130.62, 129.39, 129.05, 128.67, 125.32, 123.58, 64.16, 56.96, 52.20, 49.81, 21.19; HRMS (ESI-TOF) Calcd for $C_{28}H_{27}N_2O_6$ $[M+H]^+$: 487.1864; found: 487.1862.



3z

(2*S*,2*S*)-3-(3,5-Dimethylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxy-3-(3-methoxyphenyl) propanamide (3z)

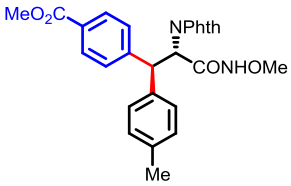
Substrate **1** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3z** was obtained as a white solid (25.1 mg, 55%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.77-7.73 (m, 2H), 7.67-7.64 (m, 2H), 7.10 (s, 2H), 7.04 (t, *J* = 8.1 Hz, 1H), 6.88 (s, 1H), 6.85 (d, *J* = 7.8 Hz, 1H), 6.80 (t, *J* = 1.8 Hz, 1H), 6.57 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.54 (d, *J* = 12.6 Hz, 1H), 5.15 (d, *J* = 12.6 Hz, 1H), 3.67 (s, 3H), 3.52 (s, 3H), 2.30 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.94, 165.07, 159.54, 141.54, 139.46, 138.70, 134.25, 131.21, 129.67, 129.49, 125.79, 123.56, 119.73, 113.07, 112.76, 64.16, 56.73, 55.10, 50.12, 21.40; HRMS (ESI-TOF) Calcd for $C_{27}H_{27}N_2O_5$ $[M+H]^+$: 459.1914; found: 459.1917.



3aa

Methyl 3-((2*S*)-2-(1,3-dioxoisoindolin-2-yl)-1-(4-fluorophenyl)-3-(methoxyamino)-3-oxopropyl) benzoate (3aa)

Substrate **1** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3aa** was obtained as a white solid (25.1 mg, 53%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.33 (s, 1H), 8.14 (s, 1H), 7.93 (d, *J* = 7.2 Hz, 1H), 7.77-7.74 (m, 2H), 7.77-7.68 (m, 3H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.27-7.25 (m, 2H), 6.84 (t, *J* = 8.4 Hz, 2H), 5.53 (d, *J* = 12.6 Hz, 1H), 5.43 (d, *J* = 12.6 Hz, 1H), 3.91 (s, 3H), 3.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.85, 166.70, 164.54, 161.80 (d, J_{FC} = 245.0 Hz), 140.02, 135.02, 134.55, 132.75, 130.85 (d, J_{FC} = 17.3 Hz), 129.25, 129.19, 129.11, 128.87, 123.71, 115.86 (d, J_{FC} = 21.3 Hz), 64.21, 56.70, 52.26, 49.09; HRMS (ESI-TOF) Calcd for $C_{26}H_{22}FN_2O_6$ $[M+H]^+$: 477.1456; found: 477.1459.

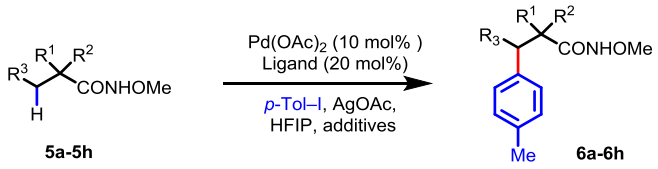


3ab

Methyl 4-((2*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(methoxyamino)-3-oxo-1-(*p*-tolyl)propyl) benzoate (3ab)

Substrate **1** was arylated following the general arylation procedure. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **3ab** was obtained as a white solid (22.3 mg, 47%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.99 (s, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.74-7.71 (m, 2H), 7.67-7.65 (m, 2H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 5.55 (d, *J* = 12.6 Hz, 1H), 5.37 (d, *J* = 12.6 Hz, 1H), 3.79 (s, 3H), 3.52 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.86, 166.64, 164.78, 145.32, 137.77, 135.91, 134.43, 130.98, 130.08, 129.97, 128.91, 127.98, 127.55, 123.67, 64.24, 56.50, 52.02, 49.76, 21.05; HRMS (ESI-TOF) Calcd for $C_{27}H_{25}N_2O_6$ $[M+H]^+$: 473.1707; found: 473.1710.

Arylation of Other Carboxylic Acid:



5a-5h **6a-6h**

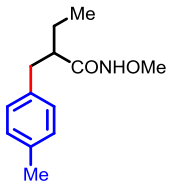
General procedure for arylation with aryl iodides:

Method A: The starting material (0.2 mmol), $Pd(OAc)_2$ (10 mol%, 4.4 mg), and AgOAc (0.4 mmol, 66.8 mg) were weighed in air and placed in a sealed tube (10 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (0.3 mmol), 2-picoline (20 mol%, 4 μL), HFIP (2.0 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 75 °C for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under

reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column.

Method B: The substrate (0.1 mmol), $Pd(OAc)_2$ (0.01 mmol, 2.2 mg), $NaH_2PO_4•H_2O$ (0.3 mmol, 42 mg) and AgOAc (0.2 mmol, 33.4 mg) were weighed in air and placed in a sealed tube (10 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (0.3 mmol), 2,6-lutidine (0.02 mmol, 2 μL), HFIP (1 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 36 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using.

Method C: The substrate (0.1 mmol, 24.8 mg), $Pd(OAc)_2$ (0.015 mmol, 3.3 mg) and AgOAc (0.2 mmol, 33.4 mg) were weighed in air and placed in a sealed tube (10 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (0.3 mmol), **L1** (0.03 mmol, 8.1 mg), TFA (2 μL) and DCE (1 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 90 °C for 36 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column.

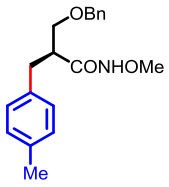


6a

***N*-Methoxy-2-(4-methylbenzyl)butanamide (6a)**

Substrate **5a** was arylated following the general arylation procedure of Method A. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **6a** was obtained as a white solid (26.5 mg, 60%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.08-7.05 (m, 4H), 3.58 (s, 3H), 2.87 (dd, *J* = 13.2, 9.6 Hz, 1H), 2.71 (dd, *J* = 13.2, 5.4 Hz, 1H), 2.32 (s, 3H), 2.01-2.00 (m, 1H), 1.78-1.74 (m, 1H), 1.57-1.53 (m, 1H), 0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C

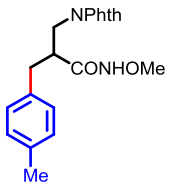
NMR (150 MHz, $CDCl_3$) δ 172.78, 136.35, 135.91, 129.15, 128.80, 64.32, 48.72, 38.43, 25.46, 21.02, 11.96; HRMS (ESI-TOF) Calcd for $C_{13}H_{20}NO_2$ $[M+H]^+$: 222.1489; found: 222.1489.



6b

(*S*)-O-(3-(Benzyloxy)-2-(4-methylbenzyl)-1l2-propyl)-*N*-methoxyhydroxylamine (6b)

Substrate **5b** was arylated following the general arylation procedure of **Method A**. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **6b** was obtained as a white solid (16.6 mg, 53%).^{1}H NMR (600 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.36-7.29 (m, mH), 7.10-7.04 (m, 4H), 4.51-4.46 (m, 2H), 3.65 (s, 3H), 3.59-3.53 (m, 2H), 2.97 (dd, *J* = 13.6, 7.8 Hz, 1H), 2.73 (dd, *J* = 13.6, 7.5 Hz, 1H), 2.54 (m, 1H), 2.31 (s, 3H).; ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.75, 137.50, 136.08, 135.54, 129.23, 128.83, 128.53, 127.95, 127.81, 73.53, 69.66, 64.32, 47.16, 34.17, 21.03; HRMS (ESI-TOF) Calcd for $C_{19}H_{24}NO_3$ $[M+H]^+$: 314.1751; found: 314.1747.

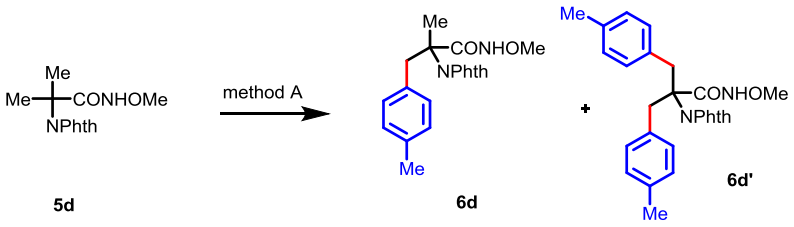


6c

2-(3-((Methoxyamino)oxy)-2-(4-methylbenzyl)-3l2-propyl)isoindoline-1,3-dione (6c)

Substrate **5c** was arylated following the general arylation procedure of **Method A**. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **6c** was obtained as a white solid (25.3 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.82-7.81 (m, 2H), 7.71-7.70 (m, 2H), 7.06-7.01 (m, 4H), 4.00 (dd, *J* = 14.4, 7.8 Hz, 1H), 3.87 (dd, *J* =

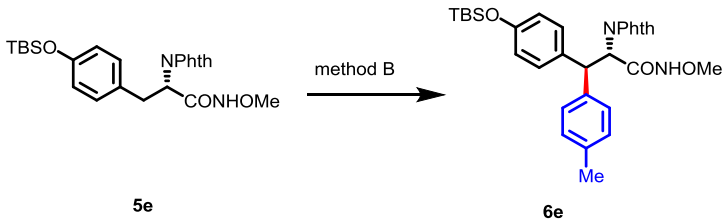
14.4, 7.2 Hz, 1H), 3.49 (s, 3H), 3.03-2.99 (m, 1H), 2.91-2.86 (m, 1H), 2.79 (dd, *J* = 13.2, 5.4 Hz, 1H), 2.24 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.83, 168.18, 136.22, 134.90, 134.13, 131.78, 129.24, 128.74, 123.38, 64.21, 44.78, 39.88, 35.96, 20.97; HRMS (ESI-TOF) Calcd for $C_{20}H_{21}N_2O_4$ $[M+H]^+$: 353.1496; found: 353.1493.



2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-2-methyl-3-(*p*-tolyl)propanamide (6d)

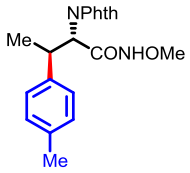
2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-2-(4-methylbenzyl)-3-(*p*-tolyl)propanamide (6d')

Substrate **5d** was arylated following the general arylation procedure of **Method A**. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **6d** was obtained as a white solid (20.3 mg, 29%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.78-7.75 (m, 2H), 7.77-7.69 (m, 2H), 7.02-6.93 (m, 4H), 3.79 (d, *J* = 13.2 Hz, 1H), 3.75 (s, 3H), 3.25 (d, *J* = 13.2 Hz, 1H), 2.26 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.76, 168.57, 136.80, 134.23, 131.79, 135.53, 130.50, 128.98, 123.22, 64.26, 64.15, 40.24, 21.84, 21.05; HRMS (ESI-TOF) Calcd for $C_{20}H_{21}N_2O_4$ $[M+H]^+$: 353.1496; found: 353.1497. **6d'** was obtained as a white solid (30.4 mg, 35%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.72 -7.67 (m, 4H), 7.15-7.14 (m, 4H), 7.05-7.02 (m, 4H), 3.71 (d, *J* = 13.8 Hz, 2H), 3.65 (s, 3H), 3.44 (d, *J* = 13.8 Hz, 2H), 2.27 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.24, 168.70, 136.92, 134.09, 131.83, 131.39, 130.71, 129.12, 123.14, 68.86, 63.97, 37.47, 21.05; HRMS (ESI-TOF) Calcd for $C_{27}H_{27}N_2O_4$ $[M+H]^+$: 443.1965; found: 443.1963.



(2*S*, 3*S*)-3-(4-((Tert-butyldimethylsilyl)oxy)phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxy-3-(p-tolyl)propanamide (6e)

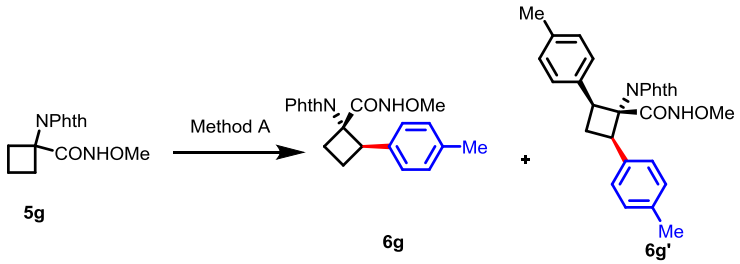
Substrate **5e** was arylated following the general arylation procedure of **Method B**. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **6e** was obtained as a white solid (31.6 mg, 58%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.15 (s, 1H), 7.73-7.71(m, 2H), 7.66-7.63 (m, 2H), 7.42-7.40(m, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 6.58-6.56 (m, 2H), 5.49 (d, *J* = 12.6 Hz, 1H), 5.12 (d, *J* = 12.6 Hz, 1H), 3.53 (s, 3H), 2.30 (s, 3H), 0.82 (s, 9H), -0.031 (s, 3H), -0.034 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.92, 165.20, 154.47, 137.26, 136.84, 134.24, 132.82, 131.09, 129.76, 128.53, 127.90, 123.50, 120.31, 64.19, 57.30, 49.36, 25.55, 21.05, 18.08, -4.62; HRMS (ESI-TOF) Calcd for $C_{31}H_{37}N_2O_5Si$ $[M+H]^+$: 545.2466; found: 545.2464.



6f

(2*S*, 3*R*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(p-tolyl)butanamide (6f)

Substrate **5f** was arylated following the general arylation procedure of **Method B**. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **6f** was obtained as a white solid (19.2 mg, 55%). m.p. = 152-154 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.86 (s, 1H), 7.91-7.88 (m, 2H), 7.79-7.76 (m, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 4.86 (d, *J* = 12.0 Hz, 1H), 3.98-3.97 (m, 1H), 3.48 (s, 3H), 2.34 (s, 3H), 1.20 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.26, 165.34, 138.59, 137.34, 134.50, 131.42, 129.75, 127.57, 123.76, 64.12, 59.55, 38.44, 21.09, 19.74; HRMS (ESI-TOF) Calcd for $C_{20}H_{21}N_2O_4$ $[M+H]^+$: 353.1496; found: 353.1495.

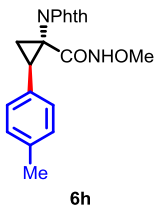


5g 6g 6g'

(1*S*, 2*R*)-1-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-2-(p-tolyl)cyclobutane-1-carboxamide (6g)

(1*S*, 2*R*)-1-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-2,4-di-p-tolylcyclobutane-1-carboxamide (6g')

Substrate **5g** was arylated following the general arylation procedure of Method A. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **6g** was obtained as a white solid (16.8 mg, 23%). m.p. = 209-211 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.86-7.83 (m, 2H), 7.77-7.74 (m, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 7.8 Hz, 2H), 4.48 (t, *J* = 10.2 Hz, 1H), 3.39-3.36 (m, 4H), 2.56-2.49 (m, 1H), 2.43-2.36 (m, 1H), 2.33 (s, 3H), 2.32-2.26 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.90, 167.85, 137.23, 135.37, 134.45, 131.69, 129.13, 128.76, 123.45, 65.49, 63.98, 47.41, 27.98, 23.56, 21.10; HRMS (ESI-TOF) Calcd for $C_{21}H_{21}N_2O_4$ $[M+H]^+$: 365.1496; found: 365.1491. **6g'** was obtained as a white solid (57.3 mg, 63%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.88-7.85 (m, 2H), 7.77-7.74 (m, 2H), 7.38 (d, *J* = 8.4 Hz, 4H), 7.15 (d, *J* = 7.8 Hz, 4H), 4.85-4.82 (m, 2H), 3.28 (s, 3H), 3.03-2.97 (m, 1H), 2.63-2.59 (m, 1H), 2.33 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.65, 165.86, 136.99, 134.60, 134.41, 131.63, 128.89, 128.61, 123.46, 71.61, 63.78, 44.41, 25.91, 21.11; HRMS (ESI-TOF) Calcd for $C_{28}H_{27}N_2O_4$ $[M+H]^+$: 455.1965; found: 455.1962.

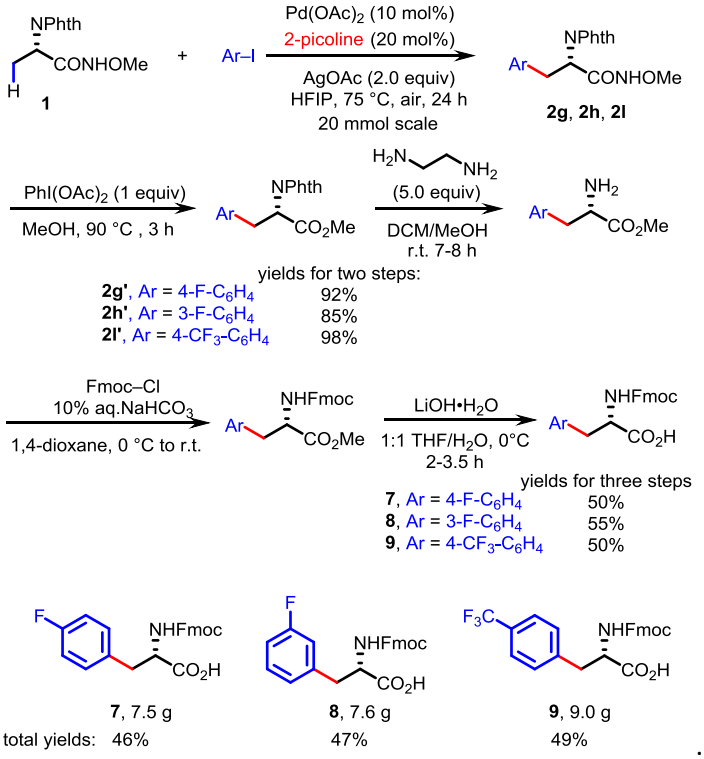


6h

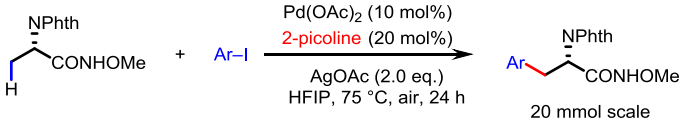
2-((1*S*, 2*R*)-1-(((Methoxyamino)oxy)-l2-methyl)-2-(*p*-tolyl)cyclopropyl)isoindoline-1,3-dione (6h)

Substrate **5h** was arylated following the general arylation procedure of Method C. After purification by column chromatography using hexanes/EtOAc (2/1) as the eluent, **6h** was obtained as a white solid 15.8 mg (45%). m.p. = 203-206 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.927.89 (m, 2H), 7.80-7.77 (m, 2H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 7.8 Hz, 2H), 3.26 (s, 3H), 2.84 (t, *J* = 9.6 Hz, 1H), 2.50 (dd, *J* = 8.4, 6.6 Hz, 1H), 2.33 (s, 3H), 1.83 (dd, *J* = 9.6, 7.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.30, 164.66, 137.40, 134.67, 131.41, 130.80, 129.21, 128.90, 123.76, 63.96, 38.50, 32.19, 21.15, 16.14; HRMS (ESI-TOF) Calcd for $C_{20}H_{19}N_2O_4$ $[M+H]^+$: 351.1339; found: 351.1339

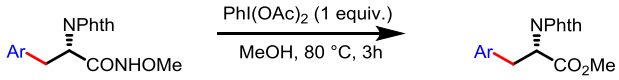
Gram-Scale Synthesis of Unnatural Amino Acids



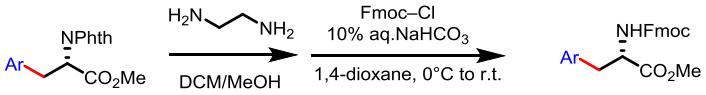
Gerenal procedure for scale up synthesis of unnatural amino acid



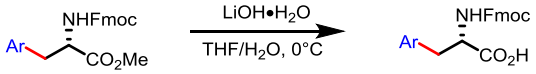
The starting material (20.0 mmol, 4.96 g), $Pd(OAc)_2$ (3.0 mmol, 674 mg), and AgOAc (40.0 mmol, 6.68 g) were weighed in air and placed in a sealed tube (350 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (30 mmol), 2-picoline (6.00 mmol, 0.6 mL), and HFIP (150 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 90 °C for 36 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, and HFIP was recovered by distillation. The residue was filtered with DCM and concentrated as crude product.



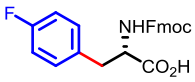
The above crude product substrate was dissolved in MeOH (120 mL), followed by the addition of $PhI(OAc)_2$ (20 mmol, 6.44 g). The reaction mixture was heated to 80 °C for 3 hours. The reaction mixture was then cooled to room temperature and then saturated aq. Na_2SO_3 and saturated aq. $NaHCO_3$ were added. The aqueous layer was then extracted with EtOAc and the combined organic layers washed with brine, dried over $MgSO_4$, filtered and concentrated. Purified by column chromatography (hexanes/ EtOAc = 2/1) to provide product.



The substrate (5 mmol) was dissolved in a 1:1 mixture of DCM/MeOH (50 mL total), and ethylenediamine (5-6 equiv.) was added. The reaction mixture was heated to 40 °C for 3 h, and then cooled to room temperature. The reaction mixture was stirred at room temperature for 7 h (monitored by TLC). Then reaction mixture (with solvent) was transferred to a column with silica gel directly and purified by column chromatography (DCM/MeOH =10/1). Crude product was obtained as oil (yield 85-95%) and used directly for next step. Amino ester was dissolved in 1,4-dioxane, and 10% aq. $NaHCO_3$ was added. The mixture was cooled to 0 °C and Fmoc–Cl (1.2 equiv) was added. The ice bath was allowed to warm to room temperature overnight, after which H_2O and EtOAc was added to the reaction mixture. The aqueous layer was then extracted with EtOAc twice and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. Purify by column chromatography (hexanes/EtOAc = 3/1 to 2/1).



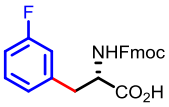
The substrate was dissolved in THF. The solution was cooled to 0 °C, and a cold solution of LiOH•H_2O (2 equiv) in H_2O were added. The reaction was maintained at 0 °C for 1 hour. The reaction was acidified with 2N HCl and extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (hexanes/EtOAc/AcOH= 10/10/1).



7

(*S*)-2-((((9*H*-Fluoren-9-yl)methoxy)carbonyl)amino)-3-(4-fluorophenyl)propanoic acid (7)

Total yield (46%), white solid (7.5 g). m.p. = 162-165 °C. ^{1}H NMR (600 MHz, Acetone *d*-6) δ 7.85 (d, *J* = 7.8 Hz, 2H), 7.65 (t, *J* = 7.8 Hz, 2H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.35-7.29 (m, 4H), 7.04 (t, *J* = 9.0 Hz, 2H), 4.49 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.32-4.25 (m, 2H), 4.19 (t, *J* = 7.8 Hz, 1H), 3.24 (dd, *J* = 13.8, 4.8 Hz, 1H), 3.03 (dd, *J* = 13.8, 9.6 Hz, 1H); ^{13}C NMR (150 MHz, Acetone *d*-6) δ 173.19, 162.69 (d, J_{FC} = 241.1 Hz), 156.81, 145.08, 145.02, 142.14, 134.58, 132.05 (d, J_{FC} = 8.0 Hz), 128.57, 127.96, 126.21, 126.17, 120.85, 115.82 (d, J_{FC} = 21.3 Hz), 67.17, 56.13, 48.00, 37.34; HRMS (ESI-TOF) Calcd for $C_{24}H_{21}FNO_4$ $[M+H]^+$: 406.1449; found: 406.1446.

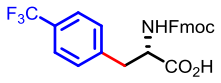


8

(*S*)-2-((((9*H*-Fluoren-9-yl)methoxy)carbonyl)amino)-3-(3-fluorophenyl)propanoic acid (8)

Total yield (47%), white solid (7.6 g). m.p. = 145-148 °C. ^{1}H NMR (600 MHz, Acetone *d*-6) δ 7.84 (d, *J* = 7.2 Hz, 2H), 7.65 (t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.34-7.29 (m, 3H), 7.16-7.12 (m, 2H), 6.99 (dt, *J* = 8.5, 2.4 Hz, 1H), 4.57-4.53 (m, 1H), 4.31-4.24 (m, 2H), 4.19 (t, *J*

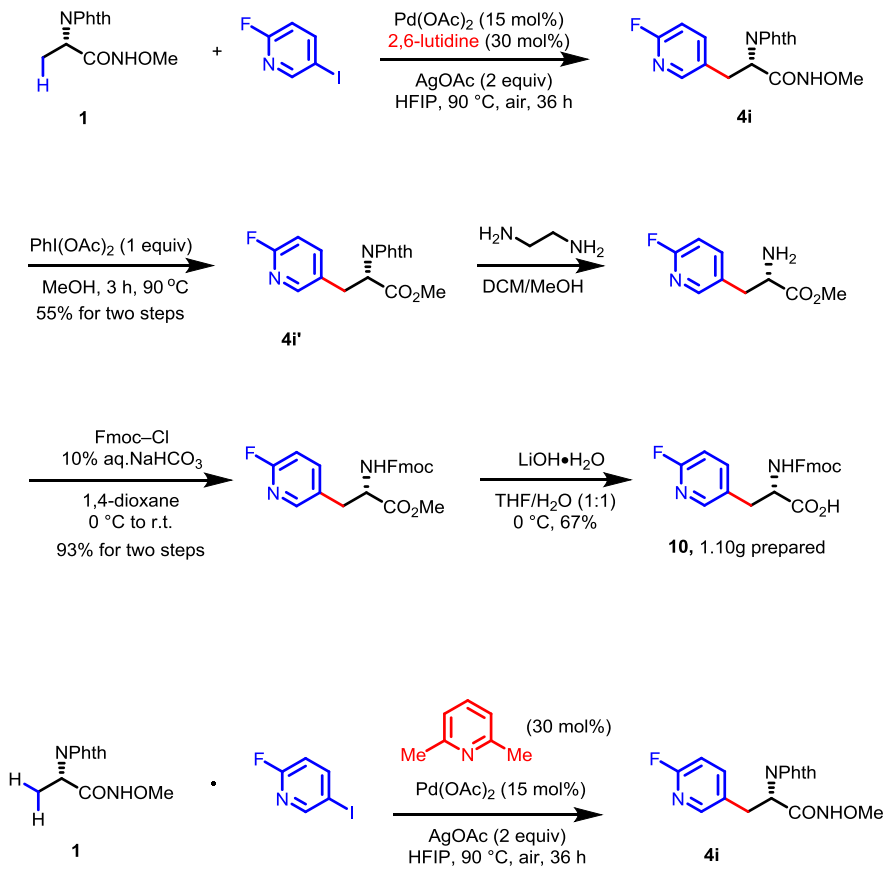
= 7.2 Hz, 1H), 3.29 (dd, *J* = 13.8, 4.8 Hz, 1H), 3.08 (dd, *J* = 13.8, 9.6 Hz, 1H); ^{13}C NMR (150 MHz, Acetone *d*-6) δ 173.13, 163.66 (d, J_{FC} = 242.0 Hz), 156.88, 145.04, 145.01, 142.11, 141.47, 141.42, 130.94 (d, J_{FC} = 8.4 Hz), 128.57, 127.97, 126.26 (d, J_{FC} = 2.6 Hz), 126.22, 126.16, 120.84, 116.98 (d, J_{FC} = 21.3 Hz), 114.24 (d, J_{FC} = 21.0 Hz), 67.26, 55.99, 47.97, 37.86; HRMS (ESI-TOF) Calcd for $C_{24}H_{21}FNO_4$ [M+H]$^+$: 406.1449; found: 406.1450.



9

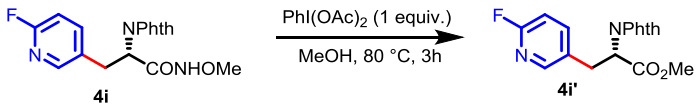
(*S*)-2-((((9*H*-Fluoren-9-yl)methoxy)carbonyl)amino)-3-(4-(trifluoromethyl)phenyl) propanoic acid (9)

Total yield (49%), white solid (9.0 g). m.p. = 170-174 °C. ^{1}H NMR (600 MHz, MeOD) δ 7.78 (d, *J* = 7.8 Hz, 2H), 7.59-7.52 (m, 4H), 7.40-7.36 (m, 4H), 7.29-7.25 (m, 2H), 4.40 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.36-4.31 (m, 1H), 4.23 (dd, *J* = 10.8, 6.6 Hz, 1H), 4.14 (t, *J* = 6.6 Hz, 1H), 3.31-3.28 (m, 1H), 3.02 (dd, *J* = 13.8, 9.0 Hz, 1H); ^{13}C NMR (150 MHz, MeOD) δ 176.16, 158.36, 145.33, 145.26, 143.86, 142.65, 131.16, 130.47- 129.80, 128.84, 128.20, 126.32, 126.27-126.20, 125.91(q, J_{FC} = 269.3 Hz), 120.98, 120.97, 67.91, 57.13, 48.42, 38.61; HRMS (ESI-TOF) Calcd for $C_{25}H_{21}F_3NO_4$ [M+H]$^+$: 456.1417; found: 456.1415.



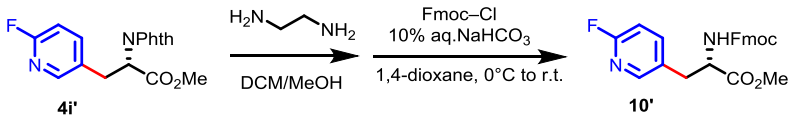
(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-3-(6-fluoropyridin-3-yl)-*N*-methoxypropanamide (4i)

The starting material **1** (10.0 mmol, 2.48 g), $Pd(OAc)_2$ (1.50 mmol, 337 mg), and AgOAc (20.0 mmol, 3.34 g) were weighed in air and placed in a sealed tube (350 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (15 mmol), 2,6-lutidine (3.00 mmol, 0.3 mL), and HFIP (100 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 90 °C for 36 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, and HFIP was recovered by distillation. The residue was filtered with DCM and concentrated as crude product. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.16 (s, 1H), 7.96 (s, 1H), 7.82-7.79 (m, 2H), 7.5-7.74 (m, 2H), 7.70-7.67 (m, 1H), 6.81 (dd, J = 8.4, 2.4 Hz, 1H), 5.04 (m, 1H), 3.76 (s, 3H), 3.58-3.49 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.71, 165.97, 162.87 (d, J_{FC} = 237.9 Hz), 147.78 (d, J_{FC} = 14.4 Hz), 141.68 (d, J_{FC} = 8.0 Hz), 134.78, 131.01, 129.49, 123.89, 109.69 (d, J_{FC} = 37.2 Hz), 64.66, 53.84, 30.98; HRMS (ESI-TOF) Calcd for $C_{17}H_{15}FN_3O_4$ $[M+H]^+$: 343.0968; found: 343.1047.



Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(6-fluoropyridin-3-yl)propanoate (4i')

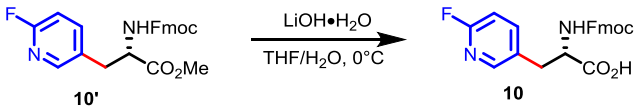
The above crude product substrate was dissolved in MeOH (100 mL), followed by the addition of $PhI(OAc)_2$ (10 mmol, 3.22 g). The reaction mixture was heated to 80 °C for 3 hours. The reaction mixture was then cooled to room temperature and then saturated aq. Na_2SO_3 and saturated aq. $NaHCO_3$ were added. The aqueous layer was then extracted with EtOAc and the combined organic layers washed with brine, dried over $MgSO_4$, filtered and concentrated. After purified by column chromatography (hexanes/ EtOAc = 2/1 to 1/1) to provide product as white solid **4i'** (1.81g, 55%). (For the NMR data, please see the previous one in the section of Arylation with Heterocylic Iodides)



Methyl (*S*)-2-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-3-(6-fluoropyridin-3-yl) propanoate (10')

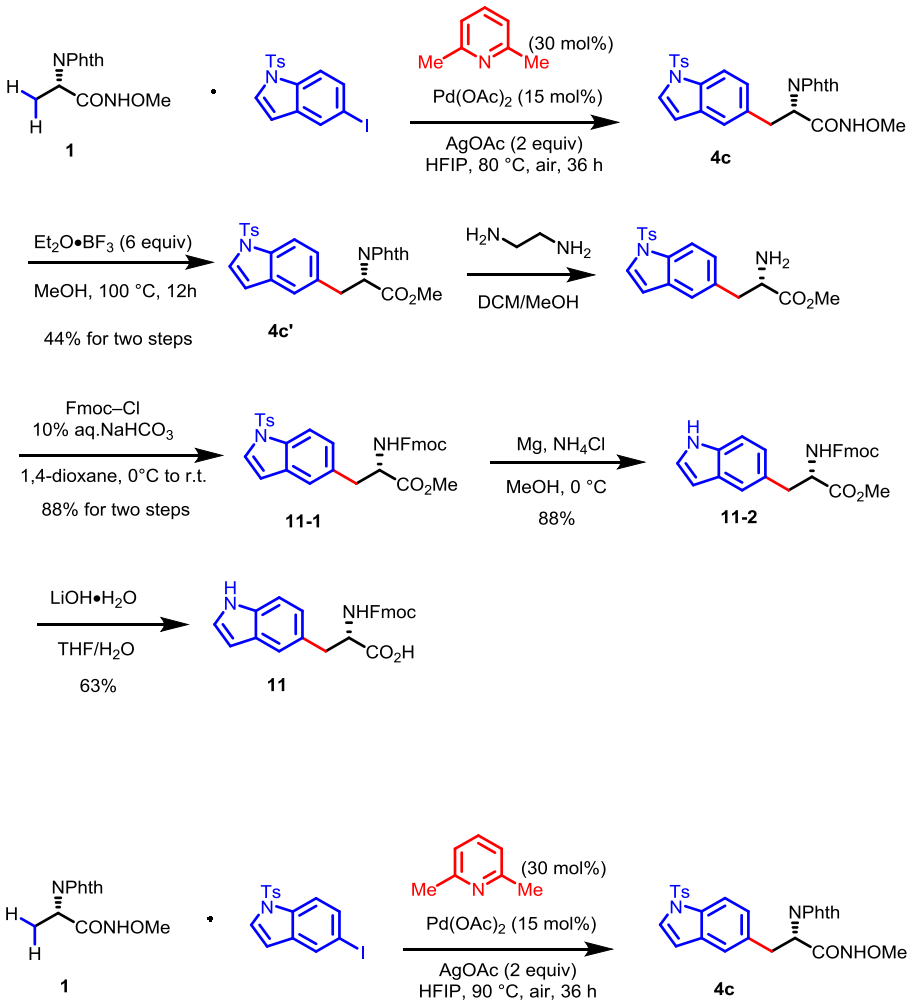
The substrate **4i'** (3.63 mmol, 1.19 g) was dissolved in a 1:1 mixture of DCM/MeOH (25 mL total), and ethylenediamine (18.2 mmol, 1.09 g) was added. The reaction mixture was heated to 40 °C for 3 h, and then cooled to room temperature. After removing the solvent *in vacuo*, the residue was purified by column chromatography (DCM/MeOH = 20:1 to 10:1). Amino ester was dissolved in 1,4-dioxane (22 mL), and 10% aq. $NaHCO_3$ (14 mL) was added. The mixture was cooled to 0 °C and Fmoc-Cl (3.99 mmol, 1.03 g) was added. The ice bath was allowed to warm to room temperature overnight, after which H_2O and EtOAc was added to the reaction mixture. The aqueous layer was then extracted with EtOAc (2 x) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. After purified by column chromatography (hexanes/EtOAc = 3/1 to 2/1 to 1/1). white solid **10'** (1.42 g, 93%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.78 (d, *J* = 7.2 Hz, 2H), 7.57 (d, *J* = 7.8 Hz, 2H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.42-7.40 (m, 2H), 7.35-7.31 (m, 2H), 6.85 (d, *J* = 6.0 Hz, 1H), 5.31 (d, *J* = 6.6 Hz,

1H), 4.64 (dd, *J* = 13.2, 6.0 Hz, 1H), 4.49 (dd, *J* = 10.8, 6.6 Hz, 1H), 4.42-4.39 (m, 1H), 4.21 (t, *J* = 6.6 Hz, 1H), 3.75 (s, 3H), 3.16 (dd, *J* = 14.4, 6.0 Hz, 1H), 3.07 (dd, *J* = 14.4, 6.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.21, 162.96 (d, J_{FC} = 237.5 Hz), 155.46, 147.92 (d, J_{FC} = 14.3 Hz), 143.70, 143.54, 141.93 (d, J_{FC} = 8.0 Hz), 141.38, 141.32, 129.12 (d, J_{FC} = 4.4 Hz), 127.79, 127.12, 127.08, 124.99, 124.90, 120.05, 120.02, 109.42 (d, J_{FC} = 37.2 Hz), 66.91, 54.48, 52.68, 47.16, 34.51; HRMS (ESI-TOF) Calcd for $C_{24}H_{22}FN_2O_4$ $[M+H]^+$: 421.1558; found: 421.1562.



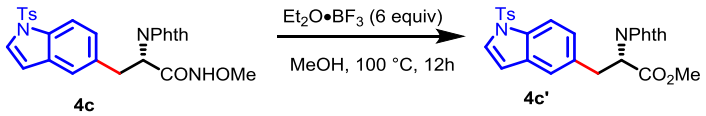
(*S*)-2-((((9*H*-Fluoren-9-yl)methoxy)carbonyl)amino)-3-(6-fluoropyridin-3-yl)propanoic acid (10)

The substrate (4.02 mmol, 1.69 g) was dissolved in THF (20 mL). The solution was cooled to 0 °C, and a cold solution of LiOH•H_2O (8.04 mmol, 0.338 g) in H_2O (20 mL) were added. The reaction was maintained at 0 °C for 1 hour. The reaction was acidified with 2N HCl and extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (hexanes/EtOAc/AcOH = 10/10/1). Pale yellow solid **10** (1.10 g, 67%). m.p. = 136-138 °C. ^{1}H NMR (600 MHz, MeOD) δ 8.06 (d, *J* = 2.4 Hz, 1H), 7.81-7.77 (m, 3H), 7.60-7.57 (m, 2H), 7.38 (t, *J* = 7.2 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 2H), 6.97 (dd, *J* = 8.4, 2.4 Hz, 1H), 4.43 (dd, *J* = 9.6, 4.8 Hz, 1H), 4.34-4.27 (m, 2H), 4.17 (t, *J* = 7.2 Hz, 1H), 3.24 (dd, *J* = 14.4, 4.8 Hz, 1H), 2.98 (dd, *J* = 14.4, 9.6 Hz, 1H); ^{13}C NMR (150 MHz, MeOD) δ 174.48, 164.14 (J_{FC} = 236.9 Hz), 158.47, 148.82 (J_{FC} = 13.4 Hz), 145.32, 145.19, 144.15 (J_{FC} = 8.6 Hz), 142.65, 132.81 (J_{FC} = 5.4 Hz), 128.86, 128.24, 126.29, 126.24, 121.00, 120.99, 110.37 (J_{FC} = 36.8 Hz), 67.99, 56.29, 48.42, 34.76; HRMS (ESI-TOF) Calcd for $C_{23}H_{20}FN_2O_4$ $[M+H]^+$: 407.1402; found: 407.1401.



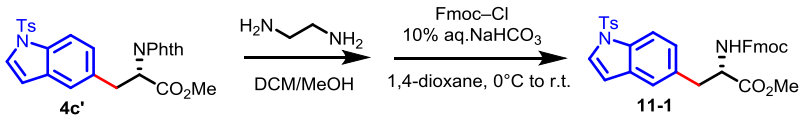
(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(1-tosyl-1H-indol-5-yl)propanamide (4c)

Substrate **1** (25 mmol, 6.2 g), $Pd(OAc)_2$ (3.75 mmol, 844 mg), and AgOAc (50 mmol, 8.35 g) were weighed in air and placed in a sealed tube (350 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (37.5 mmol, 14.9 g), 2,6-lutidine (7.5 mmol, 0.75 mL), and HFIP (130 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 90 °C for 36 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The solvents were removed under reduced pressure and recovered for next use, and the resulting mixture was used directly for next step.



Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(1-tosyl-1*H*-indol-5-yl)propanoate (4c')

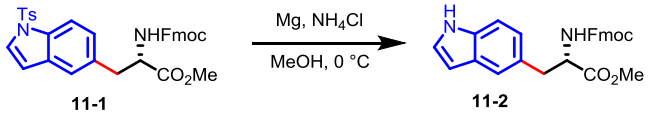
A sealable pressure flask was charged with MeOH (120 mL) and crude amide **4c**. $Et_2O•BF_3$ (105 mmol, 14 mL) was added and the reaction vessel sealed. The reaction mixture was heated to 100 °C for 12 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The solvents were removed under reduced pressure and H_2O and EtOAc was added, organic layers were removed and the aqueous layer was then extracted with EtOAc (3 x) and the combined organics washed with brine, dried over $MgSO_4$, filtered and concentrated. After purified by column chromatography (hexanes/ EtOAc = 2/1 to 1/1) to provide **4c'** white solid (5.53 g, 44%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 1H), 7.76-7.73 (m, 2H), 7.69-7.66 (m, 3H), 7.45 (d, *J* = 3.6 Hz, 1H), 7.33-7.30 (m, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.10 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.50 (d, *J* = 3.6 Hz, 1H), 5.17 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.77 (s, 3H), 3.66-3.58 (m, 3H), 2.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.36, 167.49, 144.84, 135.23, 134.10, 133.86, 131.79, 131.56, 131.01, 129.82, 126.73, 126.56, 125.41, 123.49, 121.54, 113.56, 108.89, 53.46, 52.92, 34.46, 21.56; HRMS (ESI-TOF) Calcd for $C_{27}H_{23}N_2O_6S$ $[M+H]^+$: 503.1271; found: 503.1271.



Methyl (*S*)-2-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-3-(1-tosyl-1*H*-indol-5-yl) propanoate (11-1)

4c' (15 mmol, 7.5 g) was dissolved in a 1:1 mixture of DCM/MeOH (80 mL total), followed by the addition of ethylenediamine (75 mmol, 5 mL). The reaction mixture was heated to 40 °C for 3 h, and then cooled to room temperature. Then reaction mixture (with solvent) was transferred to a column with silica gel directly and purified by column chromatography (DCM/MeOH =10/1). Amino ester was dissolved in 1,4-dioxane (60 mL), and 10% aq. $NaHCO_3$ (45 mL) was added. The mixture was cooled to 0 °C and Fmoc–Cl (16.5 mmol, 4.3 g) was added. The ice bath

was allowed to warm to room temperature overnight, after which H_2O and EtOAc was added to the reaction mixture. The aqueous layer was then extracted with EtOAc (3 x) and the combined organics washed with brine, dried over $MgSO_4$, filtered and concentrated. After purified by column chromatography (hexanes/EtOAc = 3/1 to 2/1 to 1/1). **11-1** was obtained as white solid (8.1 g, 88%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 7.2 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.56-7.52 (m, 4H), 7.41-7.39 (m, 2H), 7.31-7.28 (m, 2H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.58 (d, *J* = 3.6 Hz, 1H), 5.22 (d, *J* = 7.8 Hz, 1H), 4.67 (dd, *J* = 13.8, 6.0 Hz, 1H), 4.43-4.41 (m, 1H), 4.32 (dd, *J* = 10.2, 6.6 Hz, 1H), 4.19 (t, *J* = 6.6 Hz, 1H), 3.71 (s, 3H), 3.20-3.13 (m, 2H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.91, 155.54, 144.99, 143.81, 143.71, 141.31, 135.28, 133.99, 131.06, 130.73, 129.91, 127.76, 127.09, 126.79, 126.75, 125.88, 125.10, 125.03, 121.92, 120.02, 120.00, 113.56, 108.77, 66.95, 54.97, 52.39, 47.15, 38.07, 21.54; HRMS (ESI-TOF) Calcd for $C_{34}H_{31}N_2O_6S$ $[M+H]^+$: 595.1897; found: 595.1897.

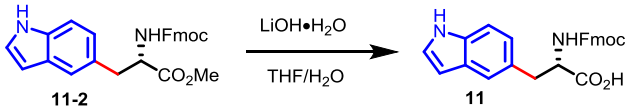


11-1 **11-2**

Methyl (*S*)-2-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-3-(1*H*-indol-5-yl)propanoate (11-2)

A solution of the *N*-Ts methyl ester (12 mmol, 7.13g) and NH_4Cl (120 mmol, 6.5g) in MeOH (240 mL) was cooled to 0 ^{o}C, Mg powder (325 mesh) (240 mmol, 5.8g) was added in small portions under vigorous stirring. Upon completion (about 4h), a solution of AcOH (30 mL) in ethylacetate (150 mL) was added at 0 ^{o}C and the resulting mixture stirred for 30 min. After filtration by celite, filtrate was concentrated. The residue was dissolved in ethylacetate and water (400 mL/150 mL). The aq. layer was extracted with EtOAc (100 mL × 2). The combined ethylacetate phase was dried over Na_2SO_4, filtrated and concentrated. After purified by column chromatography (EtOAc/hexanes/DCM = 1/10/10 to 2/10/10). **11-2** was obtained as white solid (4.4 g, 83%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.76 (d, *J* = 7.2 Hz, 2H), 7.55 (dd, *J* = 13.8, 7.2 Hz, 2H), 7.40-7.38 (m, 2H), 7.33-7.28 (m, 3H), 7.21 (t, *J* = 3.0 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.51 (s, 1H), 5.26 (d, *J* = 8.4 Hz, 1H), 4.71 (dd, *J* = 13.8, 6.0 Hz, 1H), 4.41 (dd, *J* = 10.2,

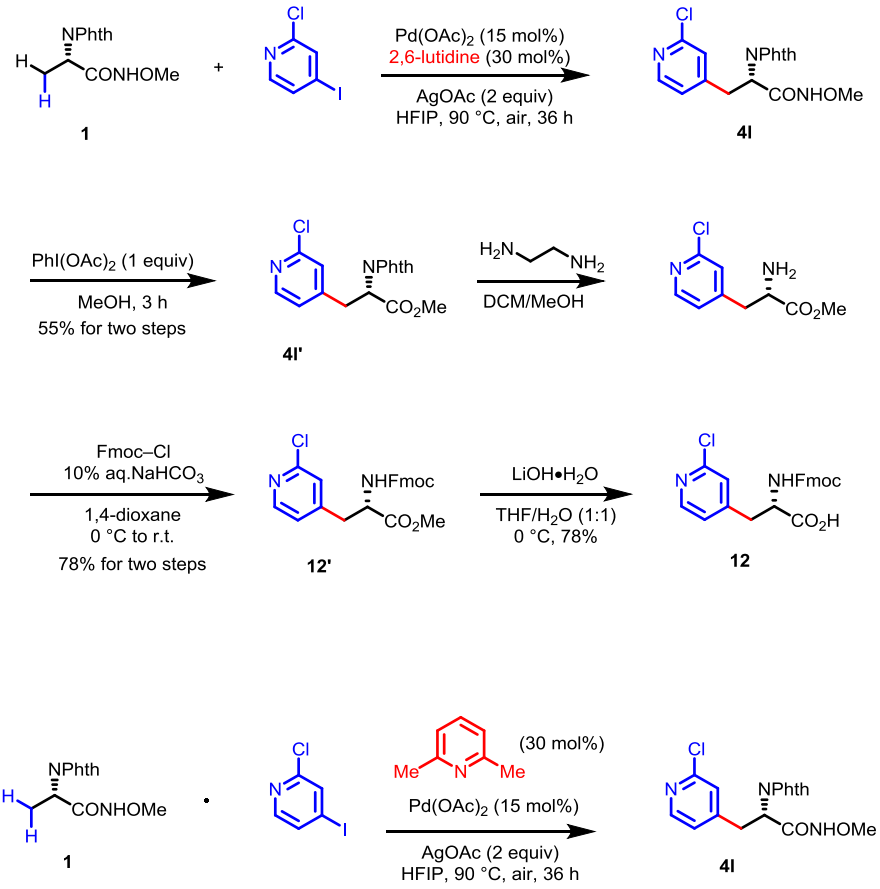
7.2 Hz, 1H), 4.31 (dd, *J* = 10.8, 7.2 Hz, 1H), 4.21 (t, *J* = 7.2 Hz, 1H), 3.74 (s, 3H), 3.23 (dd, *J* = 5.4, 3.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.29, 170.66, 155.66, 143.90, 143.84, 141.29, 135.03, 128.20, 127.67, 127.05, 126.81, 125.21, 125.13, 124.62, 123.35, 121.29, 119.96, 119.94, 111.21, 102.56, 67.01, 55.19, 52.30, 47.17, 38.32; HRMS (ESI-TOF) Calcd for $C_{27}H_{25}N_2O_4$ $[M+H]^+$: 441.1809; found: 441.1810.



11-2 11

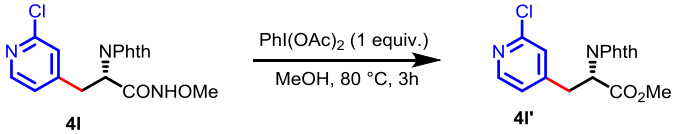
(*S*)-2-((((9*H*-Fluoren-9-yl)methoxy)carbonyl)amino)-3-(1*H*-indol-5-yl)propanoic acid (11)

The substrate **11** (21.3 mmol, 9.4 g) was dissolved in THF (100 mL). The solution was cooled to 0 °C, and a cold solution of LiOH•H_2O (42.6 mmol, 1.79 g) in H_2O (100 mL) were added. The reaction was maintained at 0 °C for 1 hour. The reaction was acidified with 2N HCl and extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (hexanes/EtOAc/AcOH = 10/10/1). **11** was obtained as white solid (5.7 g, 63%). m.p. = 119-121 °C. ^{1}H NMR (600 MHz, MeOD) δ 7.75 (d, *J* = 7.2 Hz, 2H), 7.53 (t, *J* = 8.4 Hz, 2H), 7.44 (s, 1H), 7.34 (dd, *J* = 13.8, 6.6 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.19-7.16 (m, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.36 (d, *J* = 3.0 Hz, 1H), 4.46 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.27 (dd, *J* = 9.6, 6.6 Hz, 1H), 4.16-4.11 (m, 2H), 3.28 (dd, *J* = 13.8, 4.8 Hz, 1H), 3.02 (dd, *J* = 13.8, 9.6 Hz, 1H); ^{13}C NMR (150 MHz, MeOD) δ 175.77, 158.49, 145.30, 142.58, 136.86, 129.74, 128.79, 128.23, 126.48, 126.32, 125.92, 123.75, 121.84, 120.92, 112.22, 102.28, 68.10, 57.60, 48.39, 39.03; HRMS (ESI-TOF) Calcd for $C_{26}H_{23}N_2O_4$ $[M+H]^+$: 427.1652; found: 427.16.



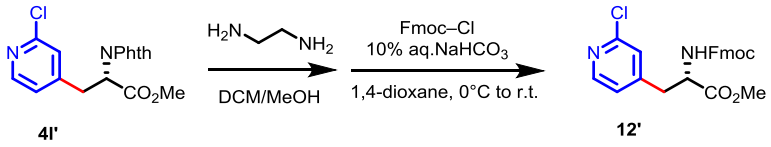
(*S*)-3-(2-Chloropyridin-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-methoxypropanamide (4l)

The starting material **1** (10.0 mmol, 2.48 g), $Pd(OAc)_2$ (1.50 mmol, 337 mg), and AgOAc (20.0 mmol, 3.34 g) were weighed in air and placed in a sealed tube (350 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (15 mmol), 2,6-lutidine (3.00 mmol, 0.3 mL), and HFIP (100 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 90 °C for 36 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, and HFIP was recovered by distillation. The residue was filtered with DCM and concentrated as crude product **4l**.



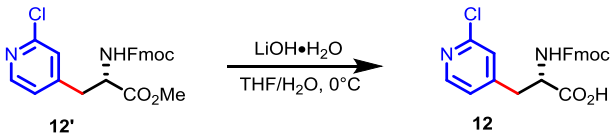
Methyl (*S*)-3-(2-chloropyridin-4-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (4l')

The above crude product substrate was dissolved in MeOH (100 mL), followed by the addition of $PhI(OAc)_2$ (10 mmol, 3.22 g). The reaction mixture was heated to 80 °C for 3 hours. The reaction mixture was then cooled to room temperature and then saturated aq. Na_2SO_3 and saturated aq. $NaHCO_3$ were added. The aqueous layer was then extracted with EtOAc and the combined organic layers washed with brine, dried over $MgSO_4$, filtered and concentrated. After purified by column chromatography (hexanes/ EtOAc = 2/1 to 1/1) to provide product **4l'** (2.00 g, 55%).



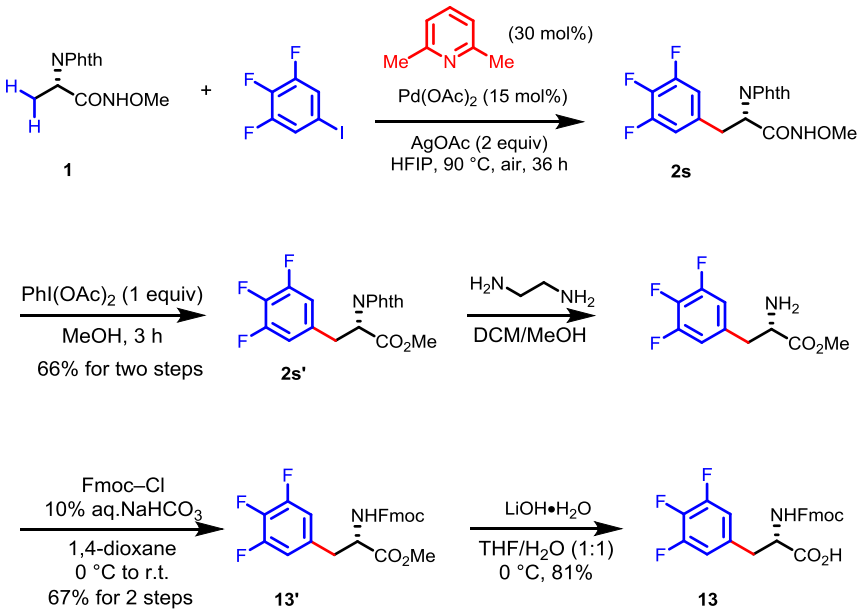
Methyl (*S*)-2-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-3-(2-chloropyridin-4-yl) propanoate (12')

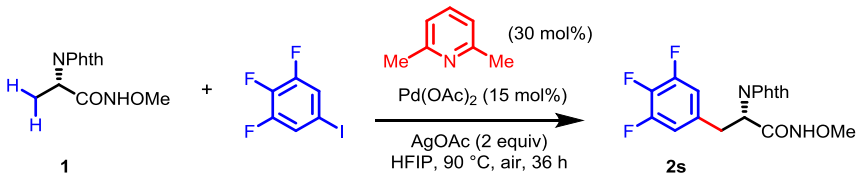
The substrate **4l'** (24.6 mmol, 8.5 g) was dissolved in a 1:1 mixture of DCM/MeOH (100 mL total), and ethylenediamine (123 mmol, 7.36 g) was added. The reaction mixture was heated to 40 °C for 3 h, and then cooled to room temperature. Then reaction mixture (with solvent) was transferred to a column with silica gel directly and purified by column chromatography (DCM/MeOH = 10/1). Amino ester was dissolved in 1,4-dioxane (100 mL), and 10% aq. $NaHCO_3$ (75 mL) was added. The mixture was cooled to 0 °C and Fmoc–Cl (30 mmol, 7.69 g) was added. The ice bath was allowed to warm to room temperature overnight, after which H_2O and EtOAc was added to the reaction mixture. The aqueous layer was then extracted with EtOAc and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. After purified by column chromatography (hexanes/EtOAc = 3/1 to 2/1 to 1/1). **12'** was obtained as white solid (8 g, 78%).



(*S*)-2-((((9*H*-Fluoren-9-yl)methoxy)carbonyl)amino)-3-(2-chloropyridin-4-yl)propanoic acid (12)

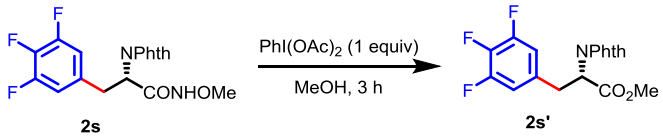
The substrate **12'** (18.3 mmol, 8.0 g) was dissolved in THF (100 mL). The solution was cooled to 0 °C, and a cold solution of LiOH•H_2O (36.6 mmol, 1.53 g) in H_2O (100 mL) were added. The reaction was maintained at 0 °C for 1 hour. The reaction was acidified with 2N HCl and extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (hexanes/EtOAc/AcOH = 10/10/1). **12** was obtained as white solid (6.0 g, 78%). m.p. = 202-204 °C. ^{1}H NMR (600 MHz, MeOD) δ 8.17 (d, *J* = 4.8 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 2H), 7.60 (dd, *J* = 12.0, 7.8 Hz, 2H), 7.39-7.35 (m, 3H), 7.31-7.28 (m, 2H), 7.23 (d, *J* = 4.8 Hz, 1H), 4.38 (dd, *J* = 10.2, 6.6 Hz, 1H), 4.30 (dd, *J* = 7.8, 4.8 Hz, 1H), 4.21 (dd, *J* = 10.2, 6.6 Hz, 1H), 4.17-4.15 (m, 1H), 3.23 (dd, *J* = 13.2, 4.8 Hz, 1H), 2.99 (dd, *J* = 13.8, 8.4 Hz, 1H); ^{13}C NMR (150 MHz, MeOD) δ 176.85, 158.00, 153.94, 152.04, 150.01, 145.40, 145.29, 142.64, 128.84, 128.25, 128.23, 126.75, 126.35, 126.22, 125.53, 120.98, 120.96, 67.85, 57.82, 48.47, 38.91; HRMS (ESI-TOF) Calcd for $C_{23}H_{20}ClN_2O_4$ $[M+H]^+$: 423.1106; found: 423.1107.





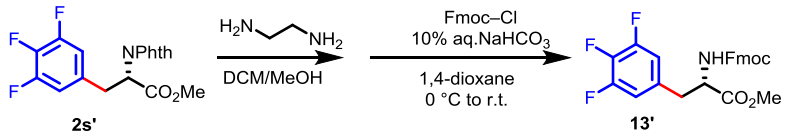
(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(3,4,5-trifluorophenyl)propanamide (2s)

The starting material **1** (10.0 mmol, 2.48 g), $Pd(OAc)_2$ (1.50 mmol, 337 mg), and AgOAc (20.0 mmol, 3.34 g) were weighed in air and placed in a sealed tube (350 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (15 mmol), 2,6-lutidine (3.00 mmol, 0.3 mL), and HFIP (100 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 90 °C for 36 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, and HFIP was recovered by distillation. The residue was filtered with DCM and concentrated as crude product **2s**.



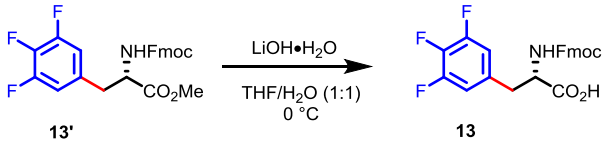
Methyl (*S*)-2-(1,3-Dioxoisoindolin-2-yl)-3-(3,4,5-trifluorophenyl)propanoate (2s')

The above crude product substrate **2s** was dissolved in MeOH (100 mL), followed by the addition of $PhI(OAc)_2$ (10 mmol, 3.22 g). The reaction mixture was heated to 80 °C for 3 hours. The reaction mixture was then cooled to room temperature and then saturated aq. Na_2SO_3 and saturated aq. $NaHCO_3$ were added. The aqueous layer was then extracted with EtOAc and the combined organic layers washed with brine, dried over $MgSO_4$, filtered and concentrated. After purified by column chromatography (hexanes/ EtOAc = 2/1 to 1/1) to provide product **2s'** 2.49 g (66%). (For the NMR Data, please see the previous one in the section of Mono-arylation)



Methyl (*S*)-2-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-3-(3,4,5-trifluorophenyl) propanoate (13')

The substrate **2s'** (5.11 mmol, 1.86 g) was dissolved in a 1:1 mixture of DCM/MeOH (40 mL total), and ethylenediamine (25 mmol, 1.47 g) was added. The reaction mixture was heated to 40 °C for 3 h, and then cooled to room temperature. Then reaction mixture (with solvent) was transferred to a column with silica gel directly and purified by column chromatography (DCM/MeOH = 10/1). Amino ester was dissolved in 1,4-dioxane (20 mL), and 10% aq. $NaHCO_3$ (15 mL) was added. The mixture was cooled to 0 °C and Fmoc–Cl (6.22 mmol, 0.94 g) was added. The ice bath was allowed to warm to room temperature overnight, after which H_2O and EtOAc was added to the reaction mixture. The aqueous layer was then extracted with EtOAc (2 x) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography (hexanes/EtOAc = 3/1 to 2/1 to 1/1). **13'** was obtained as white solid (3.43 g, 67%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.2 Hz, 2H), 7.56 (t, *J* = 6.6 Hz, 2H), 7.40 (dd, *J* = 13.2, 7.2 Hz, 2H), 7.33-7.30 (m, 2H), 6.69 (t, *J* = 6.6 Hz, 2H), 5.33 (d, *J* = 6.6 Hz, 1H), 4.61 (dd, *J* = 13.2, 6.0 Hz, 1H), 4.50 (dd, *J* = 10.2, 7.2 Hz, 1H), 4.39 (dd, *J* = 10.8, 6.6 Hz, 1H), 4.20 (t, *J* = 6.6 Hz, 1H), 3.74 (s, 3H), 3.06 (dd, *J* = 13.8, 5.4 Hz, 1H), 2.98 (dd, *J* = 13.8, 6.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.19, 155.45, 151.03 (ddd, J_{FC} = 249.0, 9.6, 3.2 Hz), 143.74, 143.48, 141.51, 141.35, 141.33, 138.98 (dt, J_{FC} = 249.9, 14.7 Hz), 132.22-132.10, 127.79, 127.10, 127.07, 127.04, 124.97, 124.87, 120.06, 113.36 (dd, J_{FC} = 16.6, 3.9 Hz), 66.92, 54.44, 52.64, 47.16, 37.60; HRMS (ESI-TOF) Calcd for $C_{25}H_{21}F_3NO_4$ $[M+H]^+$: 456.1417; found: 456.1419.



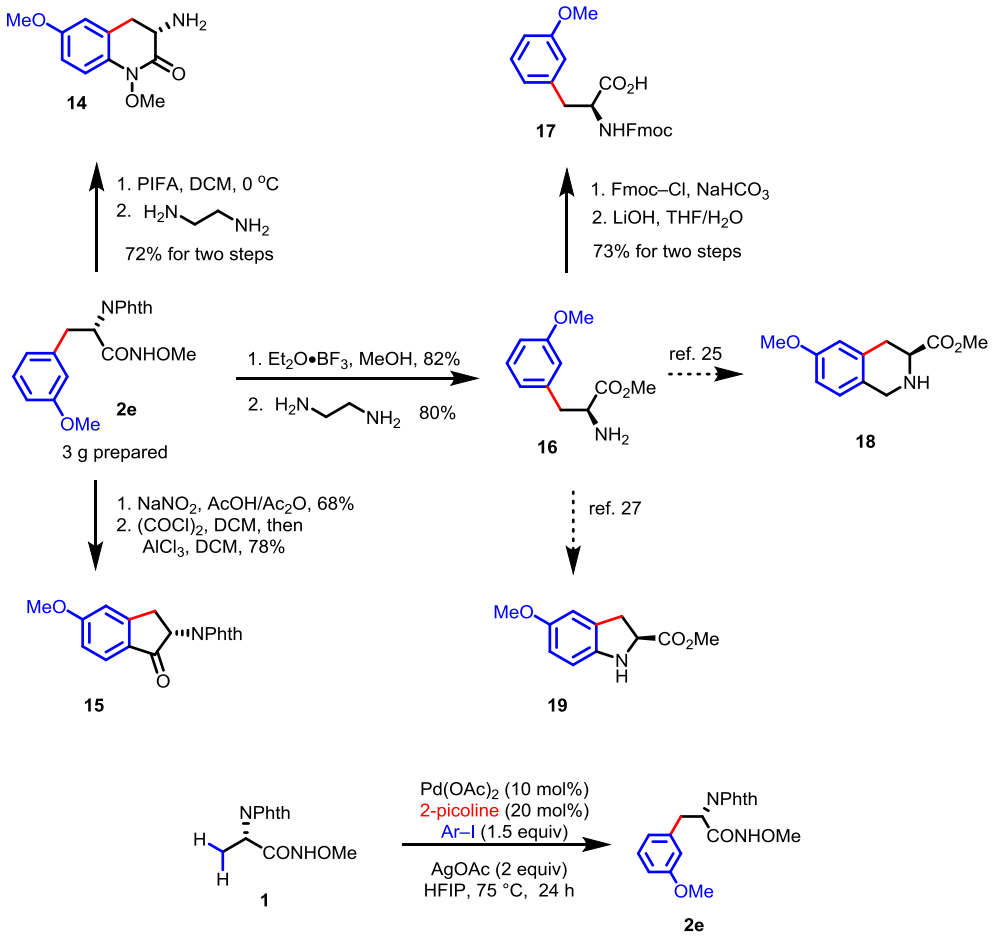
13' 13

(*S*)-2-((((9*H*-Fluoren-9-yl)methoxy)carbonyl)amino)-3-(3,4,5-trifluorophenyl)propanoic acid (13)

The substrate 13' (3.43 mmol, 1.56 g) was dissolved in THF (20 mL). The solution was cooled to 0 °C, and a cold solution of $LiOH•H_2O$ (6.86 mmol, 0.288 g) in H_2O (20 mL) were added. The reaction was maintained at 0 °C for 1 hour. The reaction was acidified with 2N HCl and extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (hexanes/EtOAc/AcOH = 10/10/1). **13** was obtained as white solid (1.23 g, 81%). m.p. = 165-168 °C. ^{1}H NMR (600 MHz, MeOD) δ 7.78

(d, J = 7.2 Hz, 2H), 7.62-7.56 (m, 2H), 7.39-7.36 (m, 2H), 7.28 (t, J = 7.8 Hz, 2H), 6.98 (t, J = 7.8 Hz, 2H), 4.39-4.33 (m, 2H), 4.26 (dd, J = 10.8, 6.6 Hz, 1H), 4.19 (t, J = 6.6 Hz, 1H), 3.17 (dd, J = 13.8, 4.2 Hz, 1H), 2.90 (dd, J = 13.2, 9.6 Hz, 1H); ^{13}C NMR (150 MHz, MeOD) δ 175.88, 158.34, 152.16 (ddd, J_{FC} = 246.5, 9.8, 3.9 Hz), 145.37, 145.21, 142.67, 139.79 (dt, J_{FC} = 246.2, 10.5 Hz), 136.51-136.37, 128.85, 128.20, 126.29, 126.19, 121.00, 120.98, 114.71 (dd, J_{FC} = 16.7, 4.2 Hz), 67.91, 57.10, 48.45, 38.26; HRMS (ESI-TOF) Calcd for $C_{24}H_{19}F_3NO_4$ $[M+H]^+$: 442.1261; found: 442.1264.

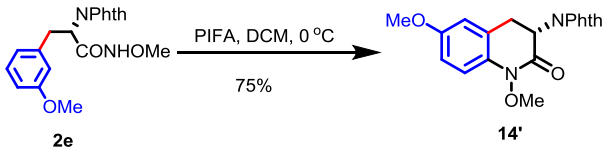
Diverse Synthetic Applications:



(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-methoxy-3-(3-methoxyphenyl)propanamide (2e)

The starting material **1** (10.0 mmol, 2.48 g), $Pd(OAc)_2$ (1.0 mmol, 220 mg), and AgOAc (20.0 mmol, 3.34 g) were weighed in air and placed in a sealed tube (350 mL) with a magnetic stir bar.

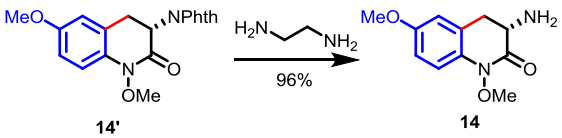
To the reaction mixture, aryl iodide (15 mmol), 2-picoline (2.00 mmol, 0.2 mL), HFIP (100 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 75 °C for 24 h under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using DCM/EtOAc (1/0 to 4/1 to 2/1) as the eluent. **2e** was obtained as yellow oil (2.90 g, 82%).



2e **14'**

(*S*)-2-(1,6-Dimethoxy-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)isoindoline-1,3-dione (14')

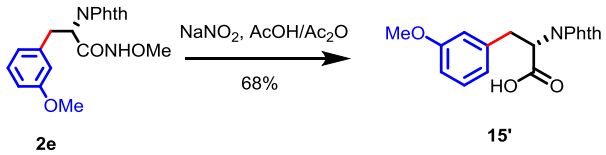
Amide **2e** (0.3 mmol, 106.2 mg) was dissolved in DCM (2 mL), in an ice-cooled flask. Phenyliodine(III) bis(trifluoroacetate) (PIFA, 0.45 mmol) was added in one portion and the reaction mixture was stirred at 0 °C, and monitored by TLC.. After completion of the reaction (about 3h), the mixture was diluted with DCM (4 mL) and washed with a saturated aqueous $NaHCO_3$ solution, then with saturated aqueous sodium chloride solution, dried over sodium sulfate, filtered and concentrated *in vacuo*. The resulting yellow oil was purified by silica gel chromatography using hexanes/EtOAc (5/1 to 3/1 to 2/1) as the eluent. **14'** was obtained as white solid (79.2 mg, 75%).[4] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90-7.89 (m, 2H), 7.77-7.75 (m, 2H), 7.19 (d, *J* = 9.0 Hz, 1H), 6.86 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.76 (dd, *J* = 3.0, 1.2 Hz, 1H), 5.14 (dd, *J* = 15.0, 6.0 Hz, 1H), 4.03-3.93 (m, 4H), 3.81 (s, 3H), 2.92 (dd, *J* = 15.0, 6.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.59, 161.03, 156.33, 134.25, 131.91, 130.75, 123.64, 122.54, 114.23, 113.90, 112.92, 62.73, 55.64, 48.86, 29.92; HRMS (ESI-TOF) Calcd $C_{19}H_{17}N_2O_5$ $[M+H]^+$: 353.1132; found: 353.1135.



14' **14**

(*S*)-3-Amino-1,6-dimethoxy-3,4-dihydroquinolin-2(1*H*)-one (14)

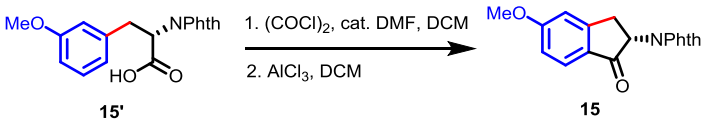
The substrate **14'** (0.2 mmol, 70.4 mg) was dissolved in a 1:1 mixture of DCM/MeOH (2 mL total), and ethylenediamine (0.4 mmol) was added. The reaction mixture was heated to 40 °C for 3 h, and then cooled to room temperature. After removing the solvent *in vacuo*, the residue was purified by column chromatography (DCM/MeOH = 20/1 to 10/1). **14** was obtained as gray solid (42.8 mg, 96%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.8 Hz, 1H), 6.83 (dd, *J* = 8.7, 2.7, Hz, 1H), 6.77 (d, *J* = 9.0 Hz, 1H), 3.91 (s, 3H), 3.80 (s, 3H), 3.63 (dd, *J* = 13.2, 6.0 Hz, 1H), 3.05 (dd, *J* = 15.6, 6.0 Hz, 1H), 2.86-2.81 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.17, 156.20, 130.74, 123.82, 114.34, 113.75, 112.69, 62.37, 55.60, 51.06, 34.21; HRMS (ESI-TOF) Calcd for $C_{11}H_{14}N_2O_3$ $[M+H]^+$: 222.1004; found: 223.1079.



2e **15'**

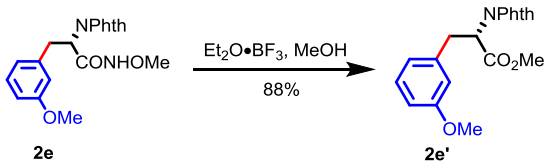
(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-3-(3-methoxyphenyl)propanoic acid (15')

The mono-arylated product **2e** (0.3 mmol, 106mg) was dissolved in the mixed solvents (3 mL, $AcOH/Ac_2O$ = 1/2), and then cooled to 0 °C. $NaNO_2$ (414 mg, 6 mmol) was slowly added into the reaction mixture in portions. The reaction mixture was first stirred at 0 °C for 3 h and then at room temperature for 17 hours. Upon completion, the solvents were removed under reduced pressure, and the mixture was neutralized by slow addition of saturated $NaHCO_3$ solution to pH 8. The aqueous phase was extracted with ether (4 × 10 mL), and then carefully acidified with cold HCl solution (1 N) to pH 2, and then extracted with ether (4 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to afford the desired product **15'** as yellow oil (66.3 mg, 68%).[5] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78-7.76 (m, 2H), 7.68-7.67 (m, 2H), 7.09 (t, *J* = 7.8 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 6.69-6.67 (m, 2H), 5.23-5.20 (m, 1H), 3.67 (s, 3H), 3.56-3.54 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.71, 167.41, 159.61, 138.01, 134.15, 131.52, 129.57, 123.53, 121.12, 114.03, 112.80, 60.48, 55.08, 34.44; HRMS (ESI-TOF) Calcd for $C_{18}H_{14}NO_5$ $[M-H]^-$: 324.0877; found: 324.0880.



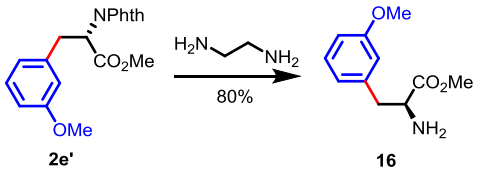
(*S*)-2-(5-Methoxy-1-oxo-2,3-dihydro-1H-inden-2-yl)isoindoline-1,3-dione (15)

To a solution of **15'** (0.2 mmol, 65 mg) in DCM (2 mL) was added a drop of DMF and oxalyl chloride (0.6 mmol) at room temperature. Stirring was continued for 3 h at that temperature. After concentration of the mixture *in vacuo*, the residue was dissolved in DCM (2 mL) and added dropwise rapidly to a suspension of $AlC1_3$ (0.6 mol, 79.7 mg) in DCM (2 mL). Stirring was continued for 1-2 h after the addition had been completed. The mixture was poured into ice-cold dilute HC1 with vigorous stirring which was continued for 1 h. The layers were separated, and the aqueous phase was extracted several times with DCM. The combined organic phase was dried by adding Na_2SO_4 and silica gel, filtered, and concentrated to give **15** as white solid (47.9 mg, 78%).[6] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86-7.85 (m, 2H), 7.78 (d, *J* = 9.0 Hz, 1H), 7.75-7.72 (m, 2H), 6.98-6.97 (m, 1H), 6.93-6.92 (m, 1H), 5.08 (dd, *J* = 8.7, 5.7 Hz, 1H), 3.91 (s, 3H), 3.57-3.52 (m, 1H), 3.39-3.36 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.02, 167.55, 165.95, 153.86, 134.16, 132.02, 128.14, 126.27, 123.50, 115.94, 109.77, 55.74, 53.68, 31.89; HRMS (ESI-TOF) Calcd for $C_{18}H_{14}NO_4$ $[M+H]^+$: 308.0917; found: 308.0917.



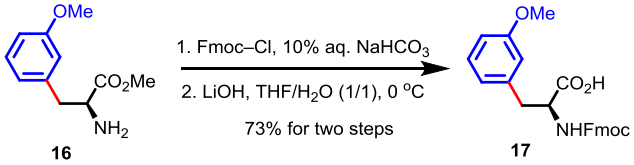
Methyl (*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(3-methoxyphenyl)propanoate (2e')

The scale-up procedure followed. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80-7.77 (m, 2H), 7.71-7.67 (m, 2H), 7.09 (t, *J* = 8.0 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 6.70-6.66 (m, 2H), 5.17 (dd, *J* = 11.4, 5.4 Hz, 1H), 3.78 (s, 3H), 3.67 (s, 3H), 3.60-3.50 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.33, 167.42, 159.60, 138.23, 134.10, 131.61, 129.54, 123.47, 121.13, 114.08, 112.70, 55.06, 53.13, 52.91, 34.64; HRMS (ESI-TOF) Calcd for $C_{19}H_{18}NO$ $[M+H]^+$: 340.1179; found: 340.1177.



Methyl (*S*)-2-amino-3-(3-methoxyphenyl)propanoate (16)

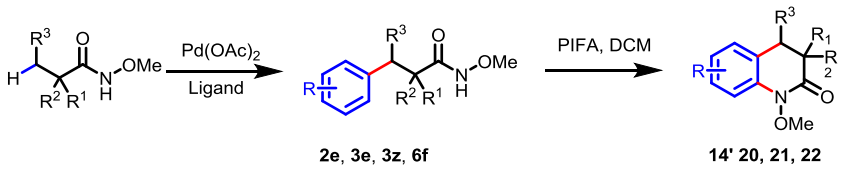
The scale-up procedure followed. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (t, *J* = 7.8 Hz, 1H), 6.80-6.77 (m, 2H), 6.74 (t, *J* = 1.8 Hz, 1H), 3.79 (s, 3H), 3.75-3.73 (m, 1H), 3.73 (s, 3H), 3.08 (dd, *J* = 13.2, 5.1 Hz, 1H), 2.83 (dd, *J* = 13.5, 8.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.38, 159.72, 138.78, 129.56, 121.60, 114.96, 112.19, 55.77, 55.16, 52.01, 41.13; HRMS (ESI-TOF) Calcd for $C_{11}H_{15}NO_3$ $[M+H]^+$: 209.1052; found: 210.1125.



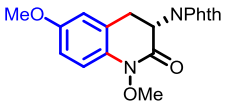
(*S*)-2-((((9H-Fluoren-9-yl)methoxy)carbonyl)amino)-3-(3-methoxyphenyl)propanoic acid (17)

The scale-up procedure followed. ^{1}H NMR (600 MHz, MeOD) δ 7.74 (d, *J* = 7.8 Hz, 2H), 7.55 (d, *J* = 6.6 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.27-7.23 (m, 2H), 7.16 (t, *J* = 7.8 Hz, 1H), 6.83-6.81 (m, 2H), 6.74 (dd, *J* = 8.1, 2.7 Hz, 1H), 4.44 (dd, *J* = 9.6, 4.8 Hz, 1H), 4.27 (dd, *J* = 10.8, 7.2 Hz, 1H), 4.17 (dd, *J* = 10.2, 7.2 Hz, 1H), 4.12-4.10 (m, 1H), 3.71 (s, 3H), 3.19 (dd, *J* = 13.9, 4.5 Hz, 1H), 2.91 (dd, *J* = 13.8, 9.6 Hz, 1H); ^{13}C NMR (150 MHz, MeOD) δ 175.46, 161.19, 158.41, 145.25, 142.56, 142.54, 140.25, 130.47, 128.80, 128.21, 126.41, 126.29, 122.67, 120.95, 120.92, 115.99, 113.30, 68.10, 56.91, 55.63, 48.35, 38.72; HRMS (ESI-TOF) Calcd for $C_{25}H_{24}NO_5$ $[M+H]^+$: 418.1649; found: 418.1647.

Lactamization of different substrates:



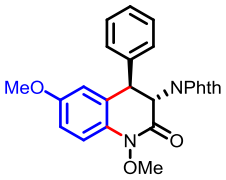
General procedure: Amide (0.1 mmol) was dissolved in DCM (2 mL), in an ice-cooled flask. Phenyliodine(III) bis(trifluoroacetate) (PIFA, 0.15 mmol) was added in one portion and the reaction mixture was stirred at 0 °C, and monitored by TLC. After completion of the reaction (about 3h), the mixture was diluted with DCM (4 mL) and washed with a saturated aqueous $NaHCO_3$ solution, then with saturated aqueous sodium chloride solution, dried over sodium sulfate, filtered and concentrated *in vacuo*. The resulting yellow oil was purified by silica gel chromatography using hexanes/EtOAc (5/1 to 3/1 to 2/1) as the eluent.



14'

(*S*)-2-(1,6-Dimethoxy-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)isoindoline-1,3-dione (14')

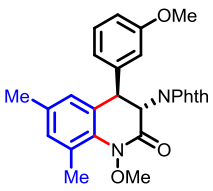
White solid, 75% yield. (For the NMR data, please see the previous one in the section of Diverse Synthetic Application)



20

(*S*)-2-(1,6-Dimethoxy-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)isoindoline-1,3-dione compound with 2-((3*S*,4*R*)-1,6-dimethoxy-2-oxo-4-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)isoindoline-1,3-dione (1:1) (20)

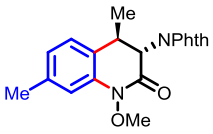
White solid, 82% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76-7.73 (m, 2H), 7.67-7.64 (m, 2H), 7.31-7.22 (m, 6H), 6.86 (dd, *J* = 8.7, 2.7 Hz, 1H), 6.18-6.17 (m, 1H), 5.36 (d, *J* = 14.4 Hz, 1H), 5.20 (d, *J* = 14.4 Hz, 1H), 4.01 (s, 3H), 3.66 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.48, 160.67, 156.41, 136.46, 134.02, 131.59, 130.29, 129.16, 129.04, 128.08, 127.67, 123.49, 114.95, 113.82, 112.44, 62.84, 55.47, 54.23, 44.90; HRMS (ESI-TOF) Calcd for $C_{25}H_{21}N_2O_5$ $[M+H]^+$: 429.1445; found: 429.1449.



21

2-((3*S*,4*R*)-1-Methoxy-4-(3-methoxyphenyl)-6,8-dimethyl-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)isoindoline-1,3-dione (21)

White solid, 94% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75-7.73 (m, 2H), 7.65-7.63 (m, 2H), 7.20 (t, *J* = 7.8 Hz, 1H), 6.96 (s, 1H), 6.81-6.80 (m, 1H), 6.77-6.75 (m, 2H), 6.21 (s, 1H), 5.36 (d, *J* = 13.8 Hz, 1H), 5.21 (d, *J* = 14.4 Hz, 1H), 3.84 (s, 3H), 3.72 (s, 3H), 2.45 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.53, 162.41, 159.83, 138.15, 135.05, 133.99, 132.66, 132.39, 131.59, 130.17, 129.93, 127.60, 125.88, 123.45, 121.62, 113.99, 61.95, 55.22, 54.20, 45.33, 20.79, 20.73; HRMS (ESI-TOF) Calcd for $C_{27}H_{25}N_2O_5$ $[M+H]^+$: 457.1758; found: 457.1756.

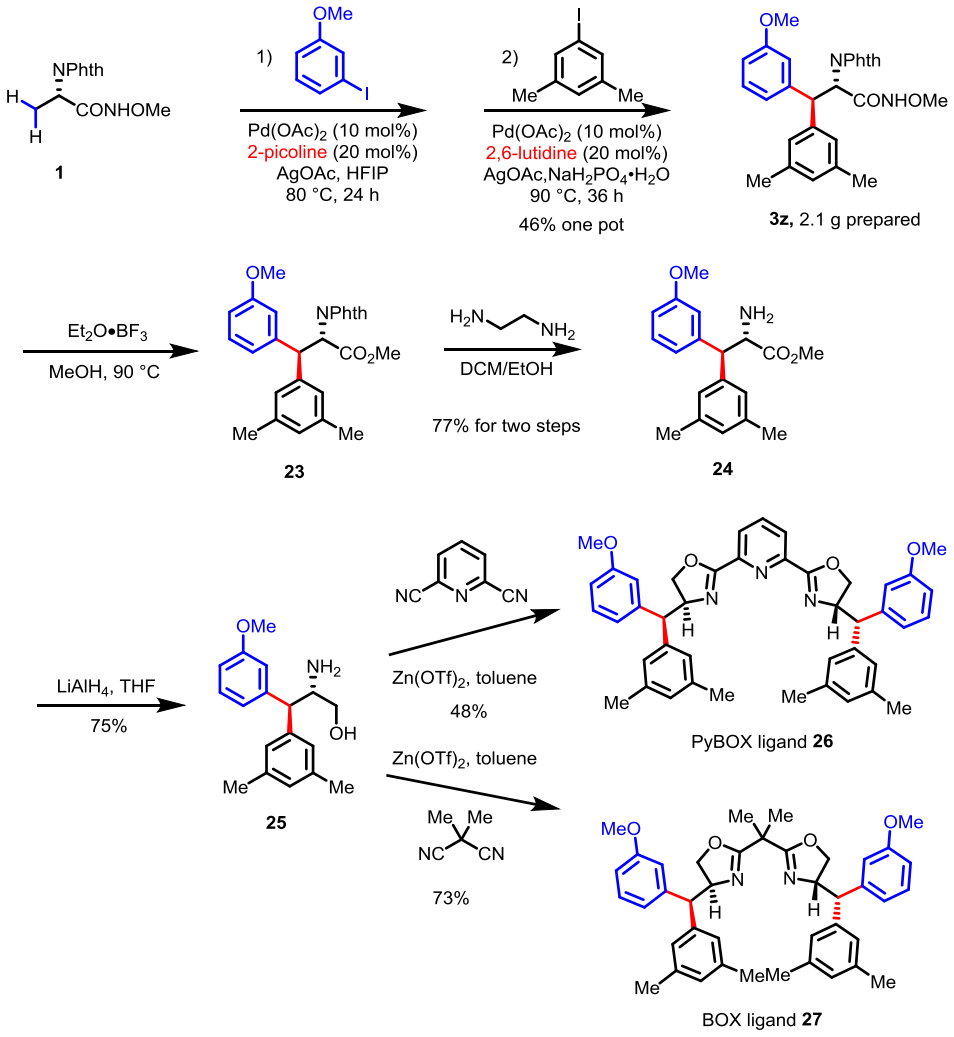


22

2-((3*S*)-1-Methoxy-4,7-dimethyl-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)isoindoline-1,3-dione (22)

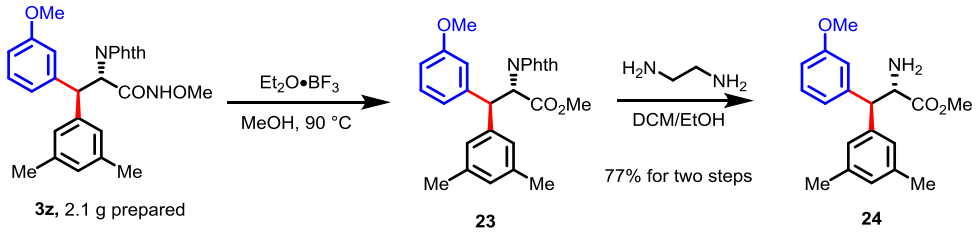
White solid, 39% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92-7.89 (m, 2H), 7.78-7.76 (m, 2H), 7.18 (d, *J* = 7.8 Hz, 1H), 7.13 (s, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 4.72 (d, *J* = 13.8 Hz, 1H), 3.98 (s, 3H), 3.95-3.89 (m, 1H), 2.41 (s, 3H), 1.34 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.85, 161.80, 138.45, 136.59, 134.27, 131.86, 125.46, 124.95, 123.66, 122.90, 113.12, 62.90, 55.27, 31.71, 21.39, 14.35; HRMS (ESI-TOF) Calcd for $C_{20}H_{19}N_2O_4$ $[M+H]^+$: 351.1339; found: 351.1340.

Synthesis of PyBOX and BOX ligands.



(2*R*, 3*S*)-3-(3,5-Dimethylphenyl)-2-(1,3-dioxo-2,3-dihydro-1H-inden-2-yl)-*N*-methoxy-3-(3-methoxyphenyl)propanamide (3z)

The starting material **1** (10.0 mmol, 2.48 g), $Pd(OAc)_2$ (1.0 mmol, 220 mg), and AgOAc (20.0 mmol, 3.34 g) were weighed in air and placed in a sealed tube (350 mL) with a magnetic stir bar. To the reaction mixture, aryl iodide (12 mmol), 2-picoline (2.00 mmol, 0.2 mL), HFIP (100 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 75 °C for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. To the reaction mixture, $Pd(OAc)_2$ (1.0 mmol, 220 mg), $NaH_2PO_4•H_2O$ (30 mmol, 4.2 g), AgOAc (20 mmol, 3.34 g), the second aryl iodide (30 mmol) and 2,6-lutidine (2 mmol, 0.2 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C for another 36 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, filtered with celite using DCM. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using hexanes/EtOAc (5/1 to 3/1 to 2/1) as the eluent to afford **3z (**2.1 g, 46% overall yield). (For the NMR data, please see the previous one in the section of Hetero-Diarylation).



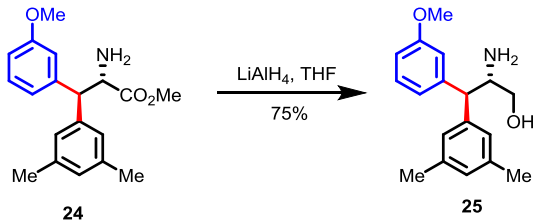
(2*R*, 3*S*)-Methyl 3-(3,5-dimethylphenyl)-2-(1,3-dioxo-2,3-dihydro-1H-inden-2-yl)-3-(3-methoxyphenyl)propanoate (23)

A sealable pressure flask was charged with MeOH (120 mL) and crude amide **3z** (4.57 mmol, 2.1 g). $Et_2O•BF_3$ (27.4 mmol) was added and the reaction vessel sealed. The reaction mixture was heated to 100 °C for 12 hours under vigorous stirring. Upon completion, the reaction

mixture was cooled to room temperature. The solvents were removed under reduced pressure and H_2O and EtOAc was added, organic layers were removed and the aqueous layer was then extracted with EtOAc and the combined organics washed with brine, dried over $MgSO_4$, filtered and concentrated.

(2*S*, 3*S*)-Methyl 2-amino-3-(3,5-dimethylphenyl)-3-(3-methoxyphenyl)propanoate (24)

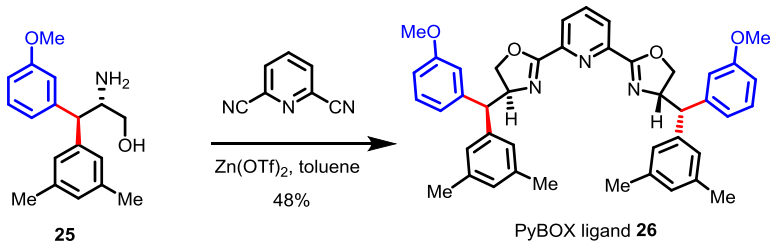
The crude **23** was dissolved in a 1:1 mixture of DCM/MeOH (40 mL total), and ethylenediamine (22.9 mmol) was added. The reaction mixture was heated to 40 °C for 6 h, and then cooled to room temperature. After removing the solvent *in vacuo*, the residue was purified by column chromatography (DCM/MeOH = 20/1 to 10/1). **24** was obtained as gray solid (1.1 g, 77% yield for two steps). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.8 Hz, 1H), 6.90-6.89 (m, 3H), 6.85 (t, *J* = 2.1 Hz, 1H), 6.81 (s, 1H), 6.77 (dd, *J* = 8.1, 2.1 Hz, 1H), 4.19-4.14 (m, 2H), 3.78 (s, 3H), 3.54 (s, 3H), 2.25 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.84, 159.75, 142.20, 140.98, 137.81, 129.69, 128.49, 125.82, 120.98, 114.97, 111.84, 58.84, 56.36, 55.15, 51.80, 21.37; HRMS (ESI-TOF) Calcd for $C_{19}H_{24}NO_3$ $[M+H]^+$: 314.1751; found: 314.1749.



(2*S*, 3*S*)-2-Amino-3-(3,5-dimethylphenyl)-3-(3-methoxyphenyl)propan-1-ol (25)

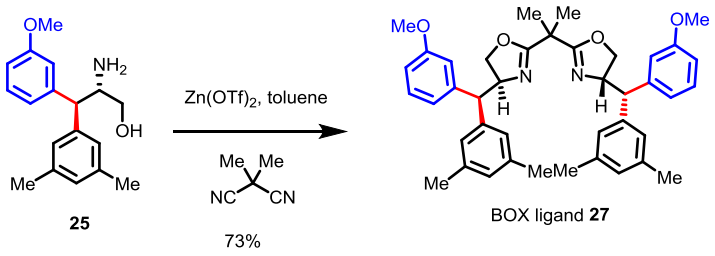
To a suspension of LAH (5 mL, 1M in THF) in THF (10 mL) at 0 °C was added dropwise a solution of the ester (535 mg, 1.70 mmol) in THF (10 mL). The mixture was reacted less than 15 min and then cooled to 0 °C. The mixture was then treated dropwise with water (3 mL) and 10% aqueous sodium hydroxide (3 mL). Note: extreme care should be practiced during the quenching process. *As this process is exothermic and produces flammable hydrogen gas, it is highly advisable to cool the reaction mixture to 0 °C prior to quenching and to add the water and aqueous solution of sodium hydroxide cautiously.* The mixture was filtered over Na_2SO_4, and the filtrate was evaporated under reduced pressure, purified by column chromatography

(DCM/MeOH = 20/1 to 10/1). **25** was obtained as white solid (363 mg, 75%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.8 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 6.90-6.88 (m, 2H), 6.81 (s,1H), 6.75-6.73 (m, 1H), 3.79 (s, 3H), 3.65-3.63 (m, 2H), 3.57-3.55 (m, 1H), 3.30-3.27 (m, 1H), 2.25 (s, 6H), 1.93 (br, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.91, 143.95, 141.67, 138.16, 129.94, 128.45, 125.55, 120.43, 114.54, 111.51, 64.76, 56.58, 55.58, 55.18, 21.38; HRMS (ESI-TOF) Calcd for $C_{18}H_{24}NO_2$ $[M+H]^+$: 286.1802; found: 286.1803.



2,6-Bis((*S*)-4-((*S*)-(3,5-dimethylphenyl)(3-methoxyphenyl)methyl)-4,5-dihydrooxazol-2-yl)pyridine (26)

A 10-mL two-necked round-bottomed flask fitted with a reflux condenser was charged pyridine-2,6-dicarbonitrile (13 mg, 0.1 mmol) and the adequate amount of zinc triflate (40 mg, 0.1 mmol). The system was purged with argon and dry toluene (1 mL) was added. The solution was stirred for 5 min and a solution of the *β*-amino alcohol (62 mg, 0.1 mmol) in dry toluene (1.5 mL) was added. The solution was heated under reflux for 48 h. The system was allowed to cool, and reaction was diluted with 25 mL of EtOAc. The solution was then washed with brine (3 × 25 mL) and Saturated aq. $NaHCO_3$ (3 × 25 mL), dried with $MgSO_4$ and the solvent evaporated, and the crude product was purified by silica gel chromatography with EtOAc/hexanes (1/5 to 1/3) as the eluent, producing a yellow solid **26** (32.0 mg, 48%).[7] ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (d, *J* = 7.8 Hz, 2H), 7.78 (t, *J* = 8.1 Hz, 1H), 7.22 (t, *J* = 7.8 Hz, 2H), 6.96-6.94 (m, 2H), 6.90 (t, *J* = 2.1 Hz, 2H), 6.87 (s, 4H), 6.83 (s, 2H), 6.75-6.73 (m, 2H), 5.13-5.11 (m, 2H), 4.51 (t, *J* = 9.3 Hz, 2H), 4.17 (t, *J* = 8.4 Hz, 2H), 3.91 (d, *J* = 9.6 Hz, 2H), 3.77 (s, 6H), 2.26 (s, 12H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.81, 159.44, 146.73, 143.96, 141.42, 138.17, 137.07, 129.26, 128.61, 126.22, 126.19, 120.92, 114.94, 111.27, 72.35, 70.36, 57.10, 55.12, 21.39; HRMS (ESI-TOF) Calcd for $C_{43}H_{44}N_3O_4$ $[M+H]^+$: 666.3326; found 666.3326.



(*S*, 4*S*, 4'*S*)-2,2'-(propane-2,2-diyl)bis(4-((*S*)-(3,5-dimethylphenyl)(3-methoxyphenyl)methyl)-4,5-dihydrooxazole) (27)

A 10-mL two-necked round-bottomed flask fitted with a reflux condenser was charged with 2,2-dimethyl malononitrile (10 mg, 0.1 mmol) and zinc triflate (40 mg, 0.1 mmol). The system was purged with argon and dry toluene (1 mL) was added. The solution was stirred during 5 min and a solution of the *β*-amino alcohol **25** (57 mg, 0.2 mmol) in dry toluene (1 mL) was added. The solution was heated under reflux for 48 h. The system was allowed to cool. The reaction was then washed with brine (3 × 25 mL) and saturated aq. $NaHCO_3$ (3 × 20 mL), dried with $MgSO_4$ and the solvent evaporated, and the crude product was purified by silica gel chromatography, with EtOAc/hexanes (1/5 to 1/3) as the eluent, producing a yellow solid **27** (45.9 mg, 73%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 (d, *J* = 2.4 Hz, 1H), 7.18-7.15 (m, 2H), 6.84-6.80 (m, 9H), 6.72-6.71 (m, 2H), 4.84-4.80 (m, 2H), 4.27-4.24 (m, 2H), 4.00-3.97 (m, 2H), 3.89 (d, *J* = 7.8 Hz, 2H), 3.74 (s, 6H), 2.25 (s, 12H), 1.32 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.25, 159.26, 143.81, 141.32, 137.74, 128.99, 128.33, 126.72, 121.31, 115.27, 111.13, 71.50, 69.28, 56.20, 55.07, 38.60, 23.93, 21.38; HRMS (ESI-TOF) Calcd for $C_{41}H_{47}N_2O_4$ $[M+H]^+$: 631.3530; found: 631.3527.

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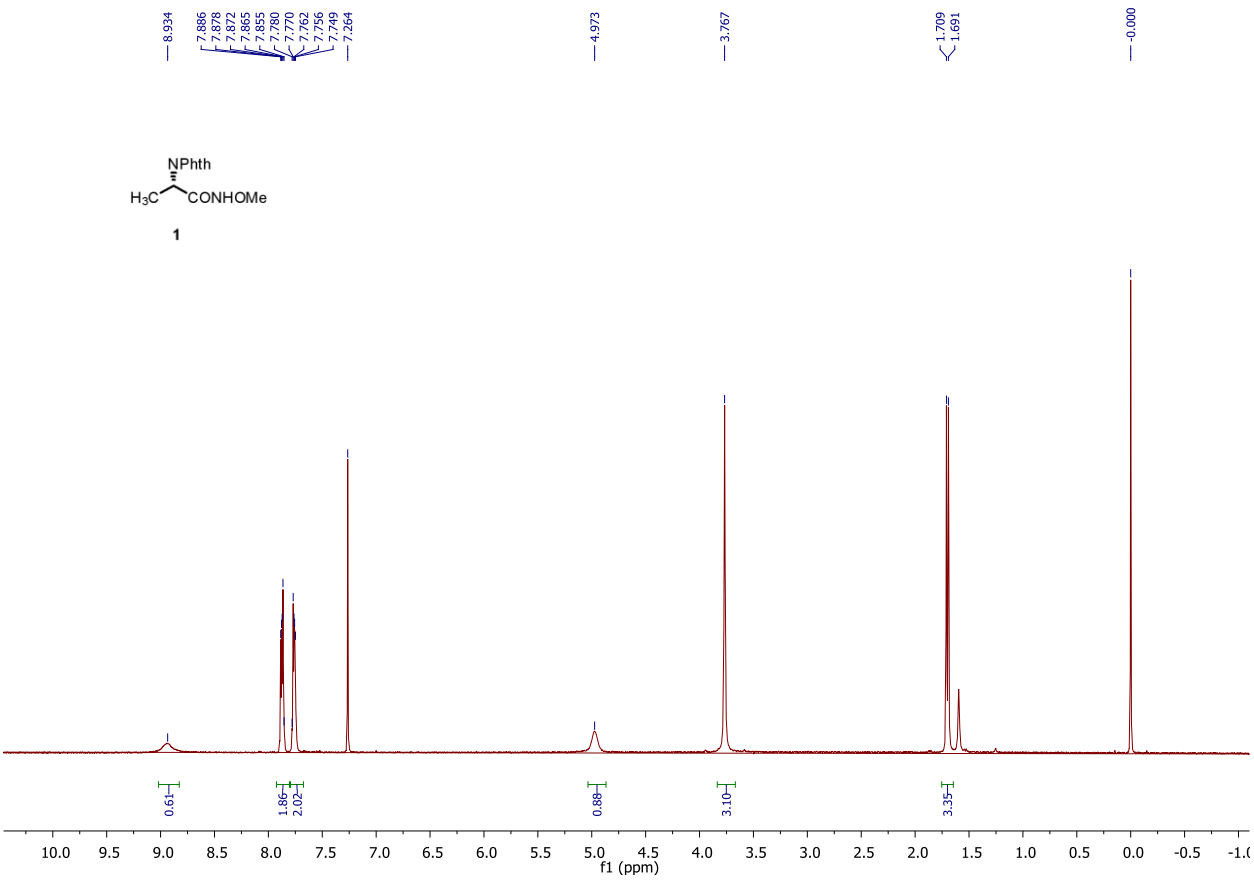
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7.872
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7.756
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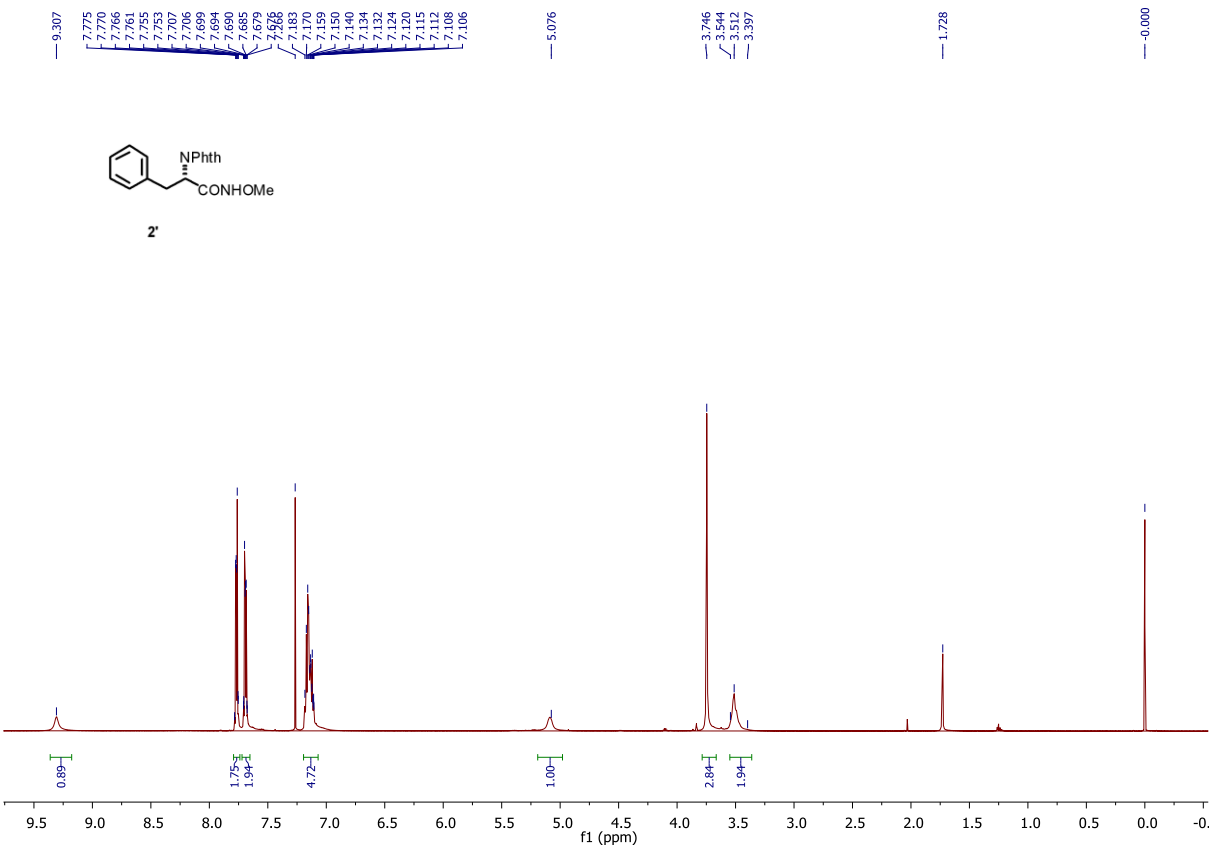
7.264
4.973
3.767
1.709
1.691
0.000
NPhth
H3C
CONHOMe
1
0.61
1.86
2.02
0.88
3.10
3.35
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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7.685
7.679
7.676
7.668
7.183
7.170
7.159
7.150
7.140
7.134
7.132
7.124
7.120
7.115
7.112
7.108
7.106
5.076
3.746
3.544
3.512
3.397
1.728
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2'
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1.75
1.94
4.72
1.00
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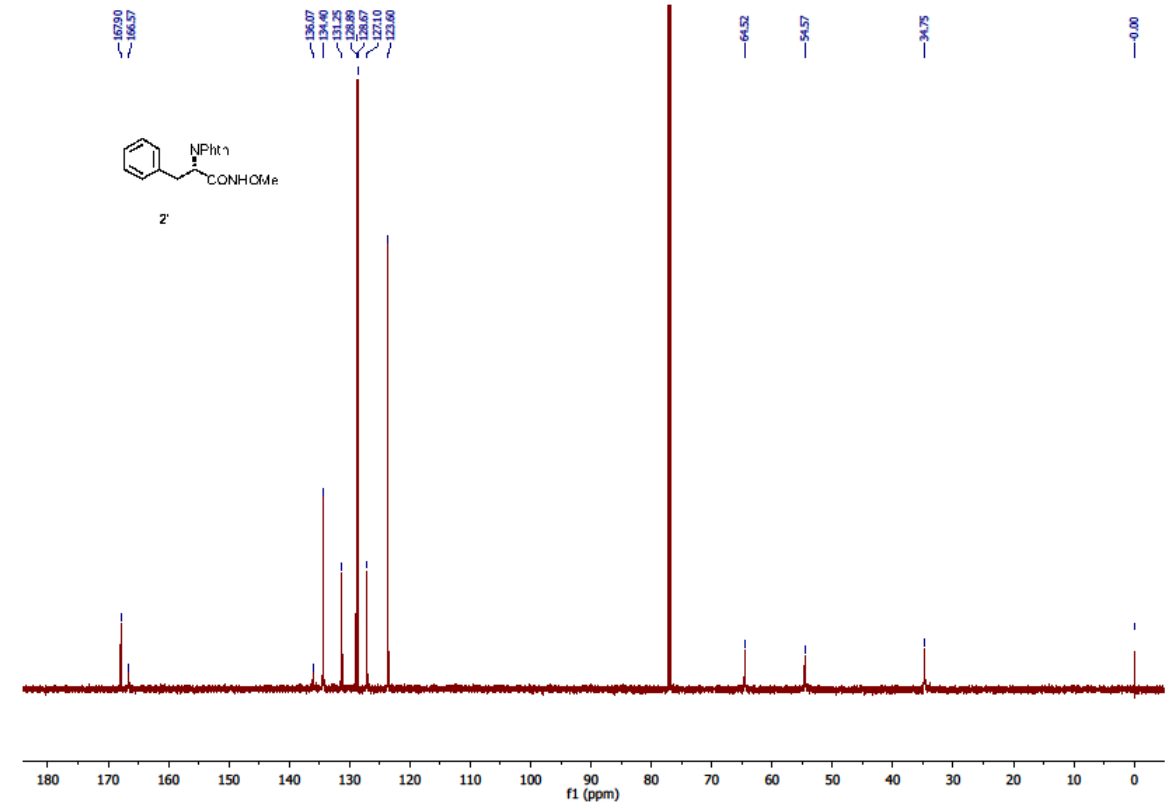
1.94
f1 (ppm)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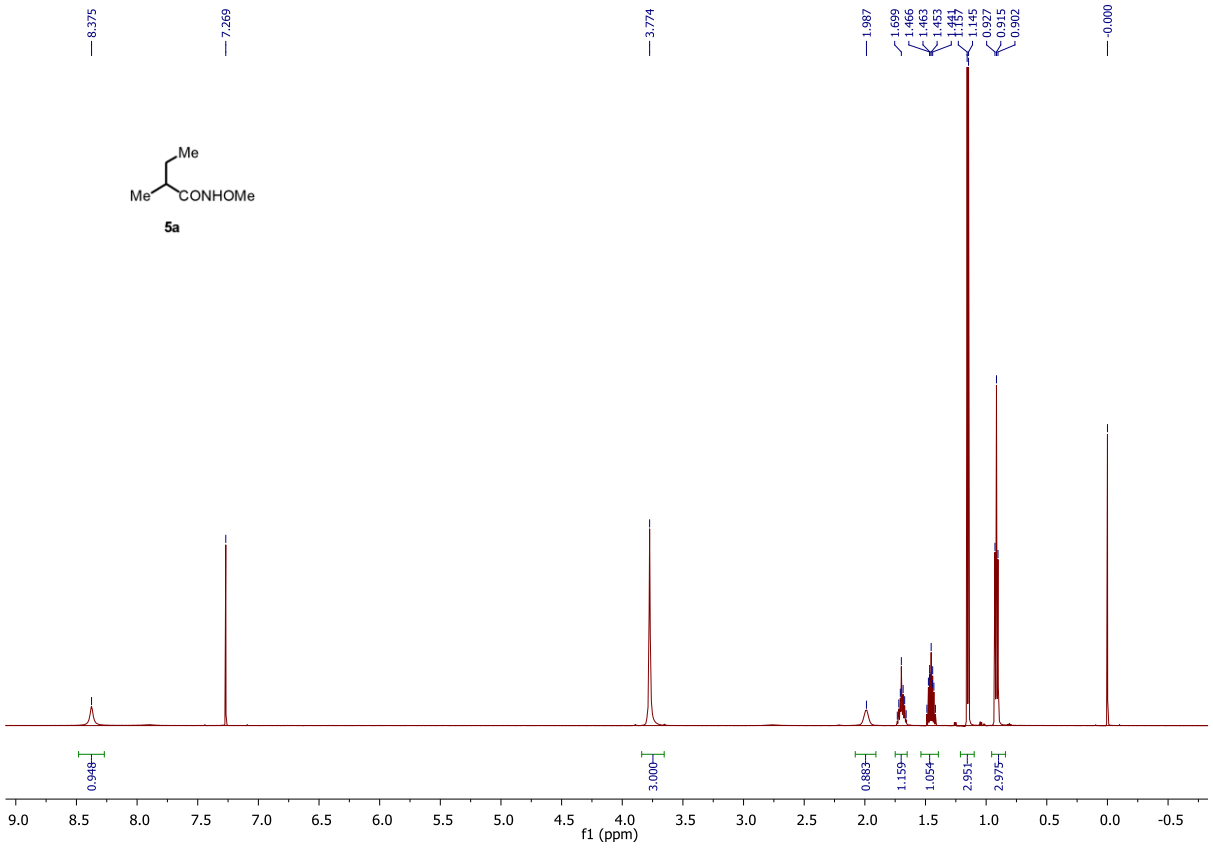
CONHOMe
2'
f1 (ppm)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1.466
1.463
1.453
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1.145
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0.915
0.902
-0.000
Me
Me
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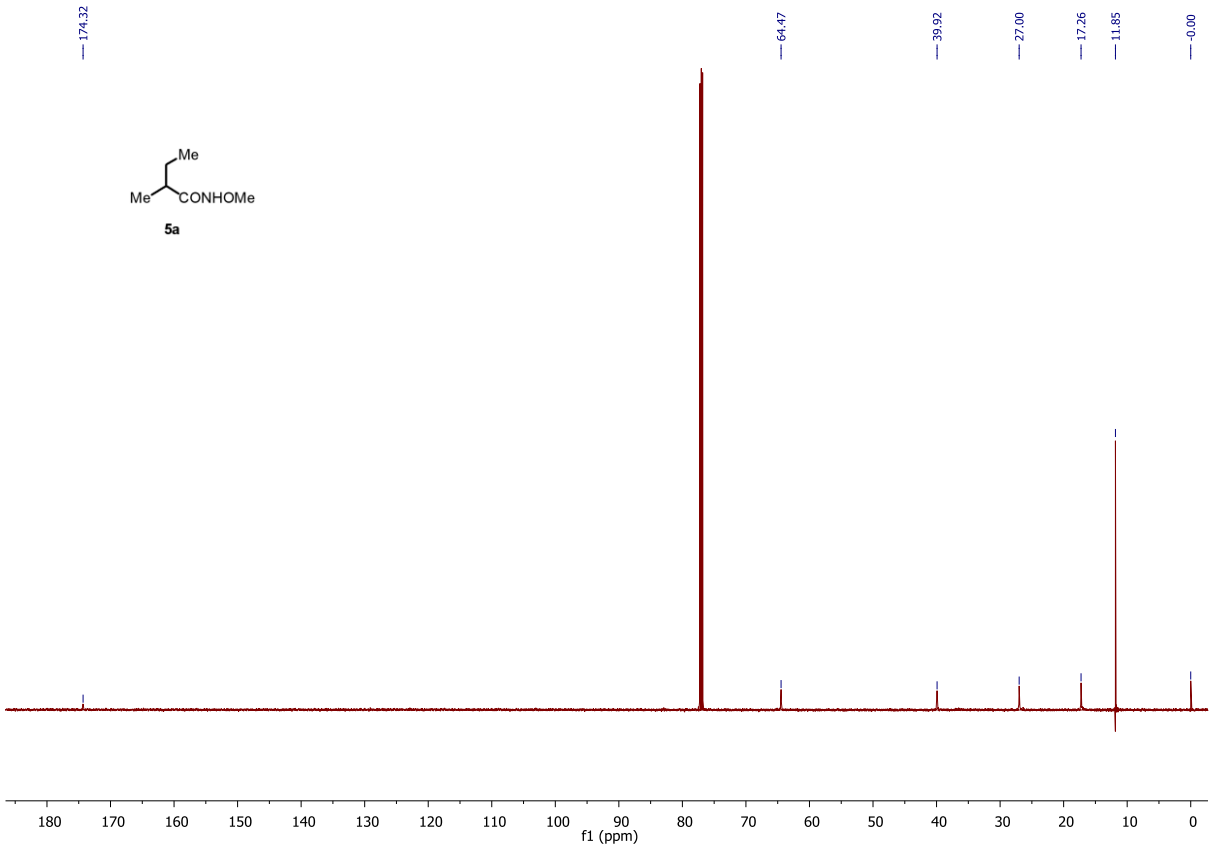
5a
0.949
3.000
0.883
1.159
1.054
2.951
2.975
f1 (ppm)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Me
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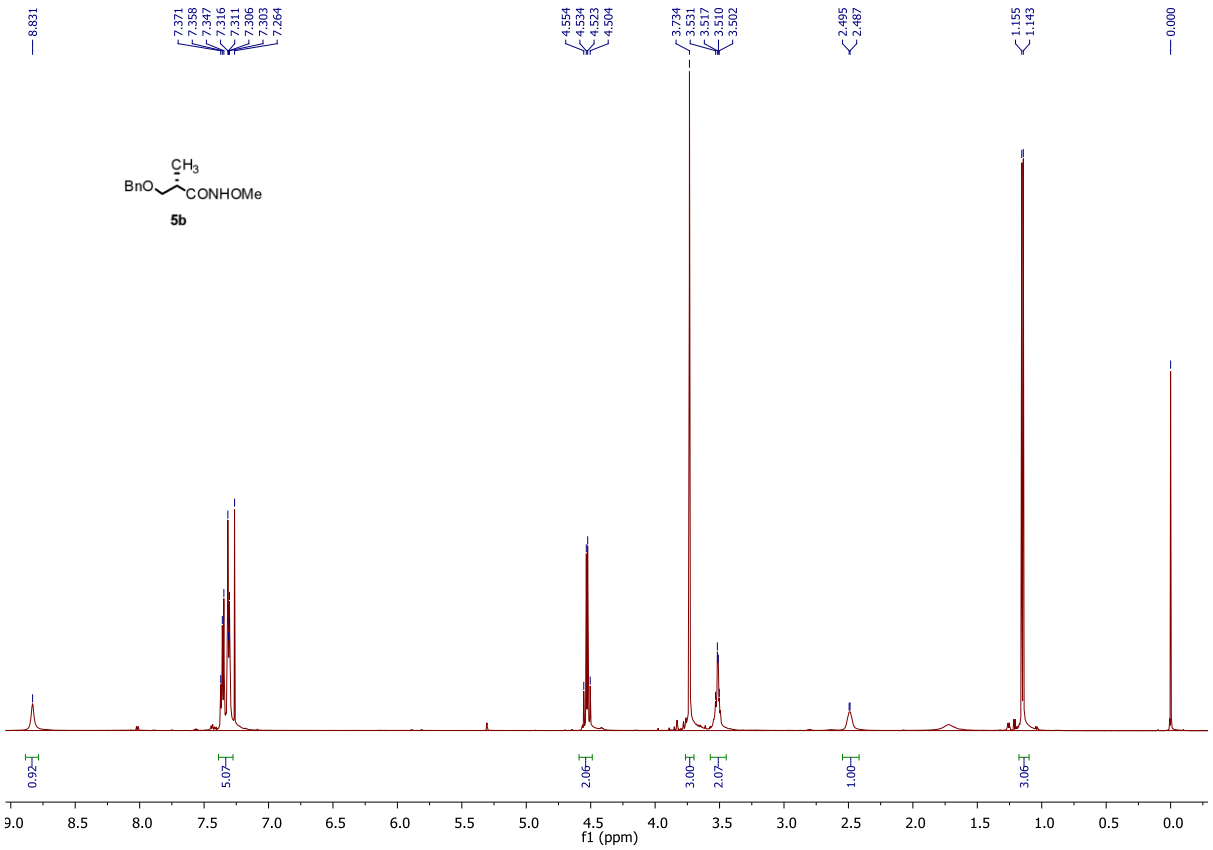
f1 (ppm)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3.531
3.517
3.510
3.502
2.495
2.487
1.155
1.143
0.000
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CH3
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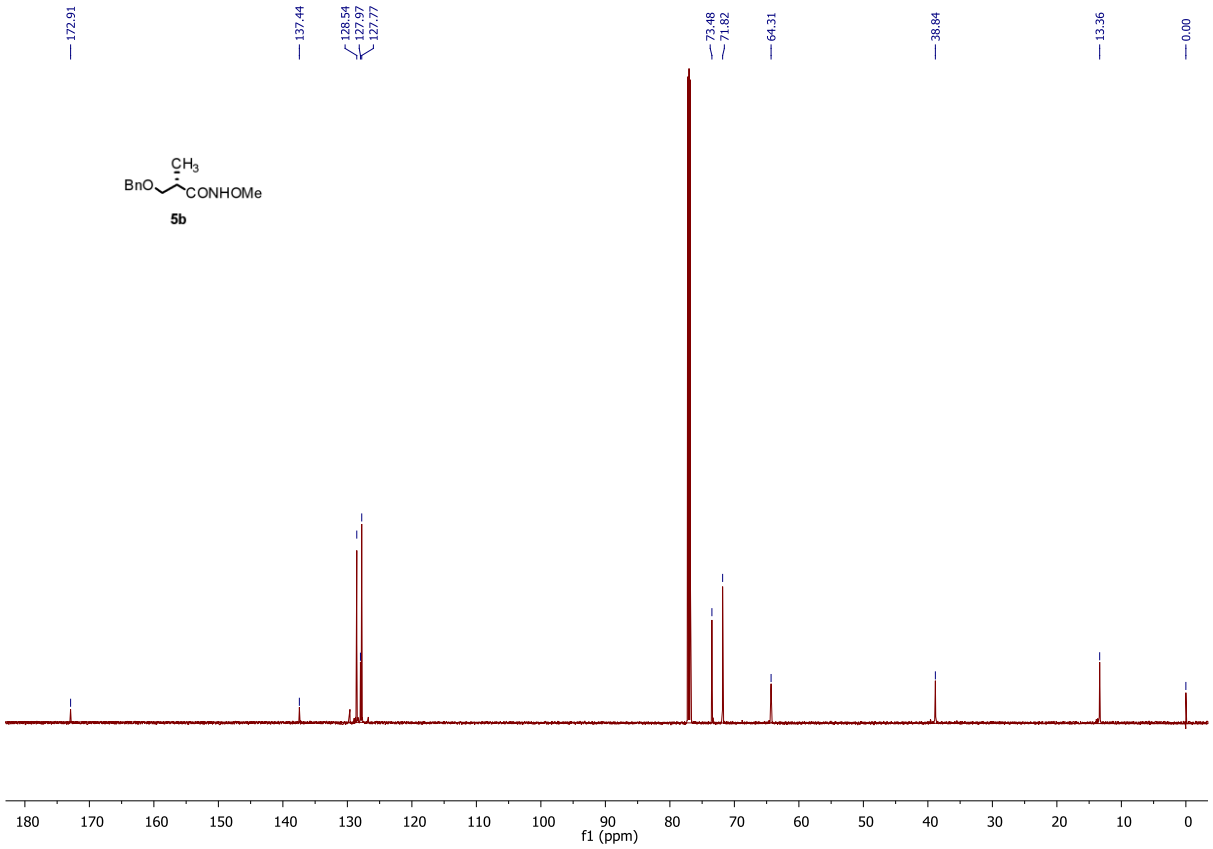
f1 (ppm)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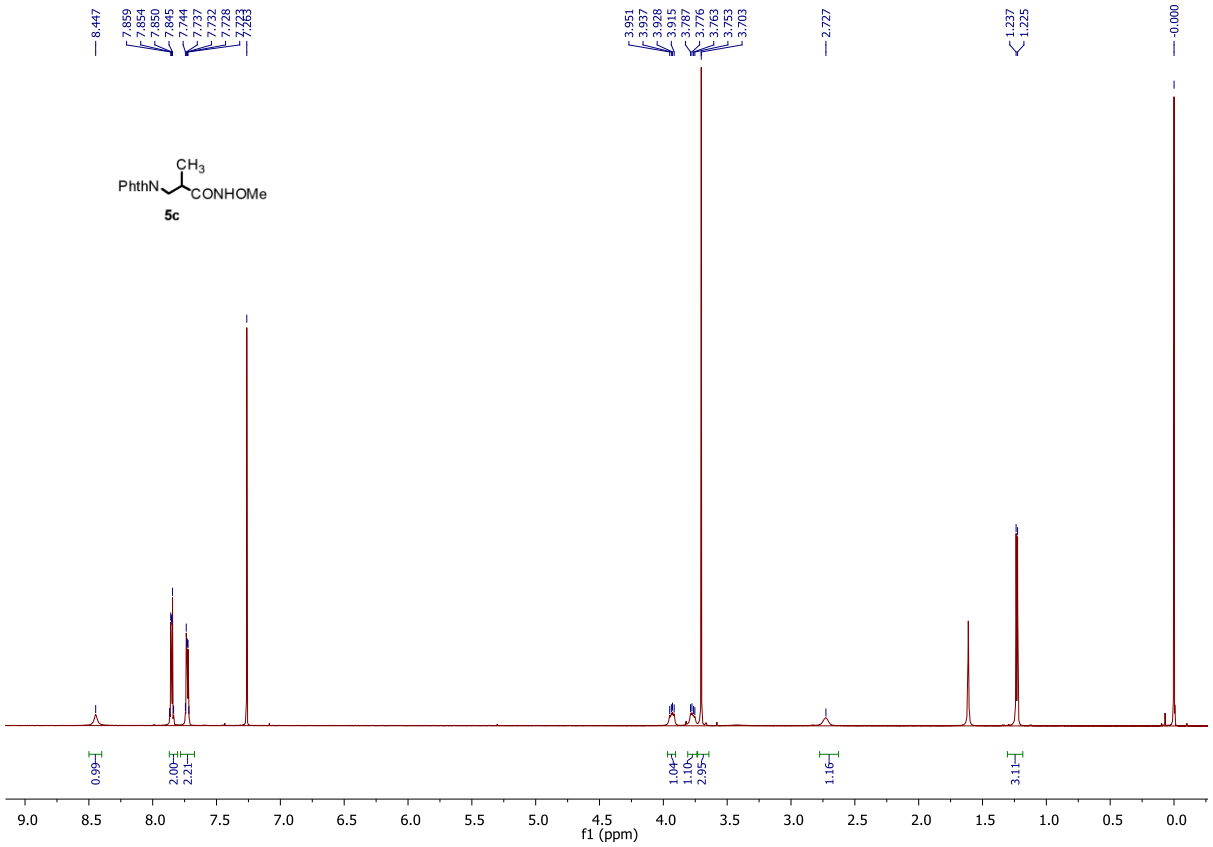
BnO
CH3
CONHOMe
5b
f1 (ppm)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3.928
3.915
3.787
3.776
3.763
3.753
3.703
2.727
1.237
1.225
0.000
PhthN
CH3
CONHOMe
5c
0.99
2.00
2.21
1.04
1.10
2.95
1.16
3.11
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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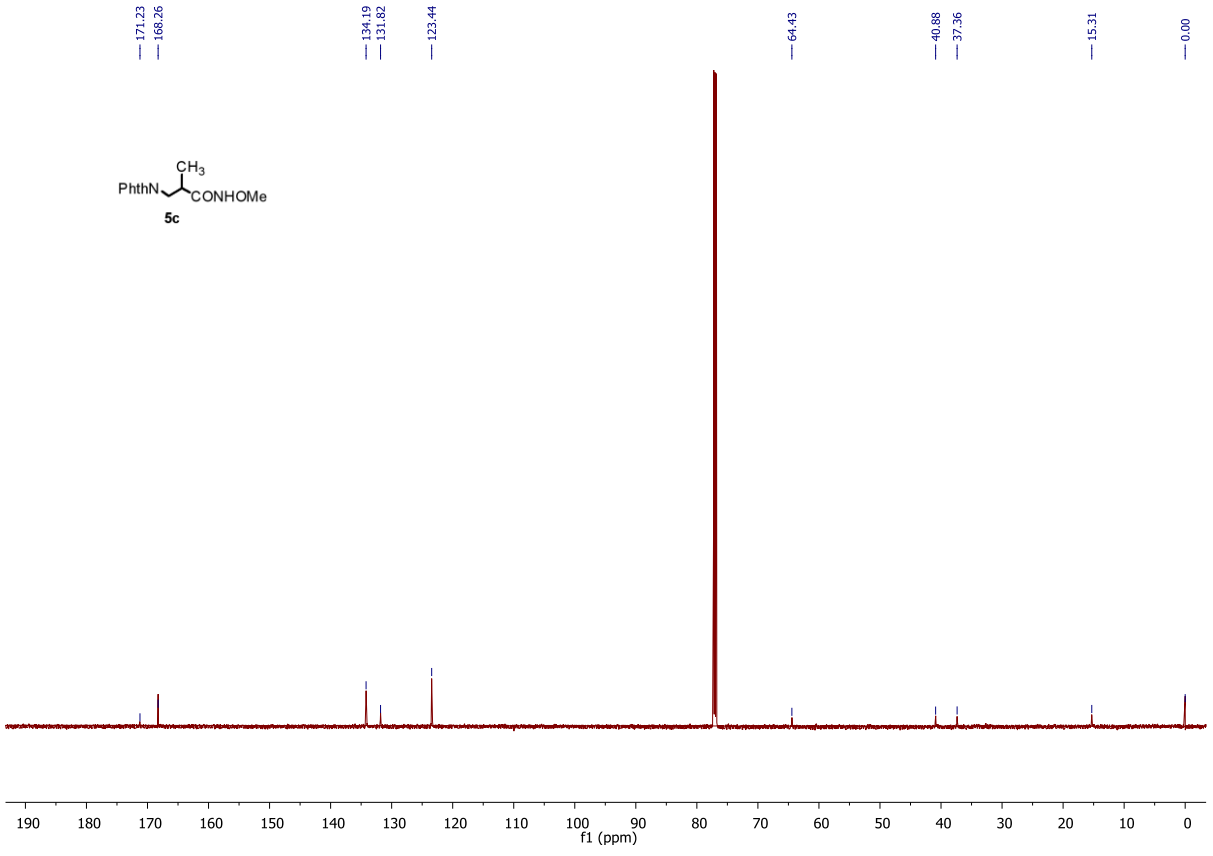
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CH3
CONHOMe
5c
190
180
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90
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70
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50
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30
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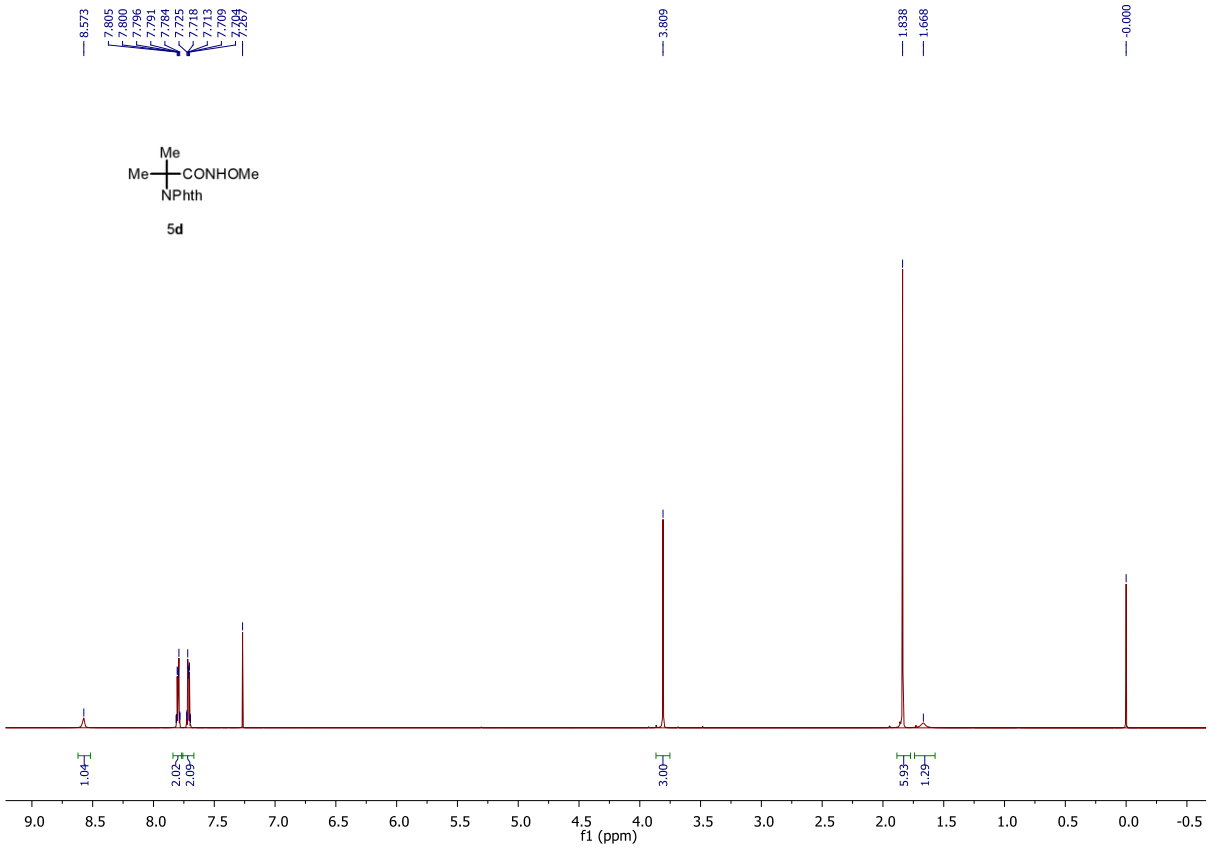
10
0
f1 (ppm)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Me
CONHOMe
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5d
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2.02
2.09
3.00
5.93
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8.5
8.0
7.5
7.0
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6.0
5.5
5.0
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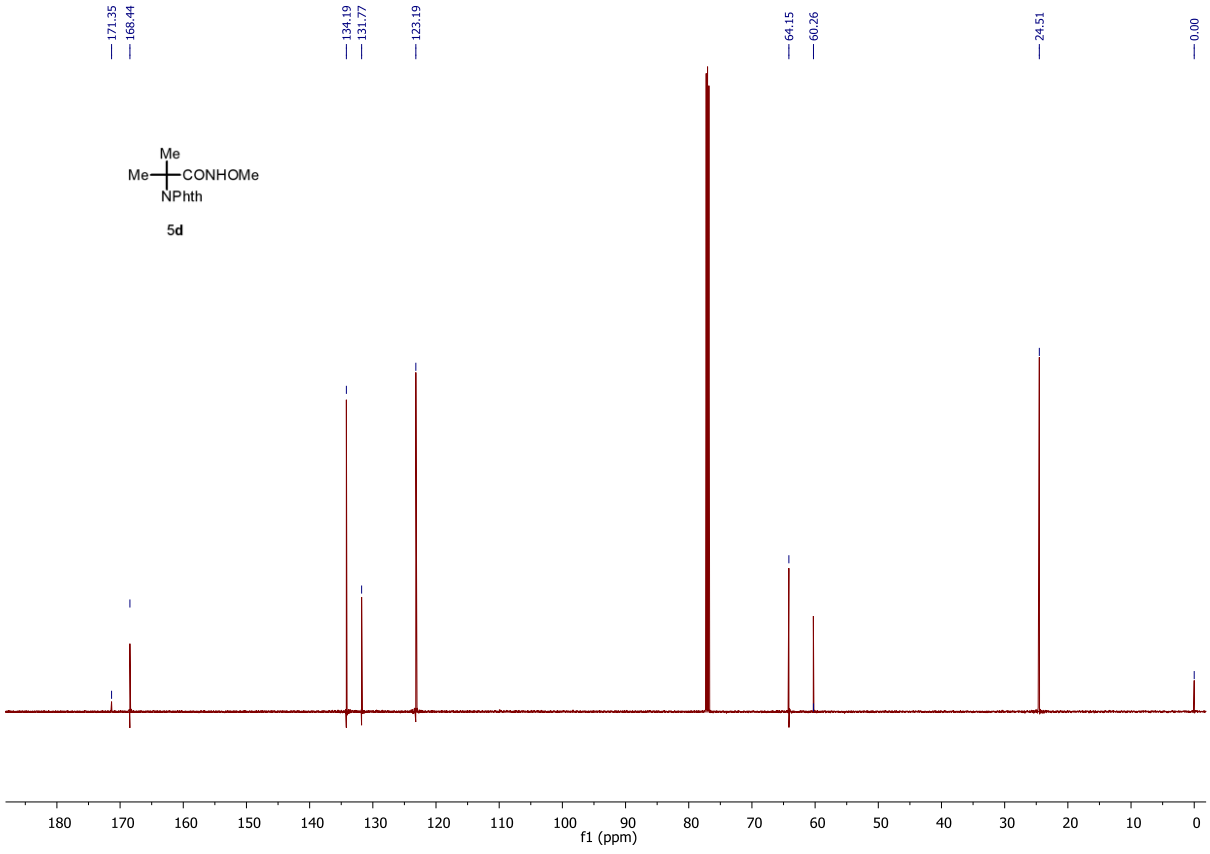
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Me
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5d
180
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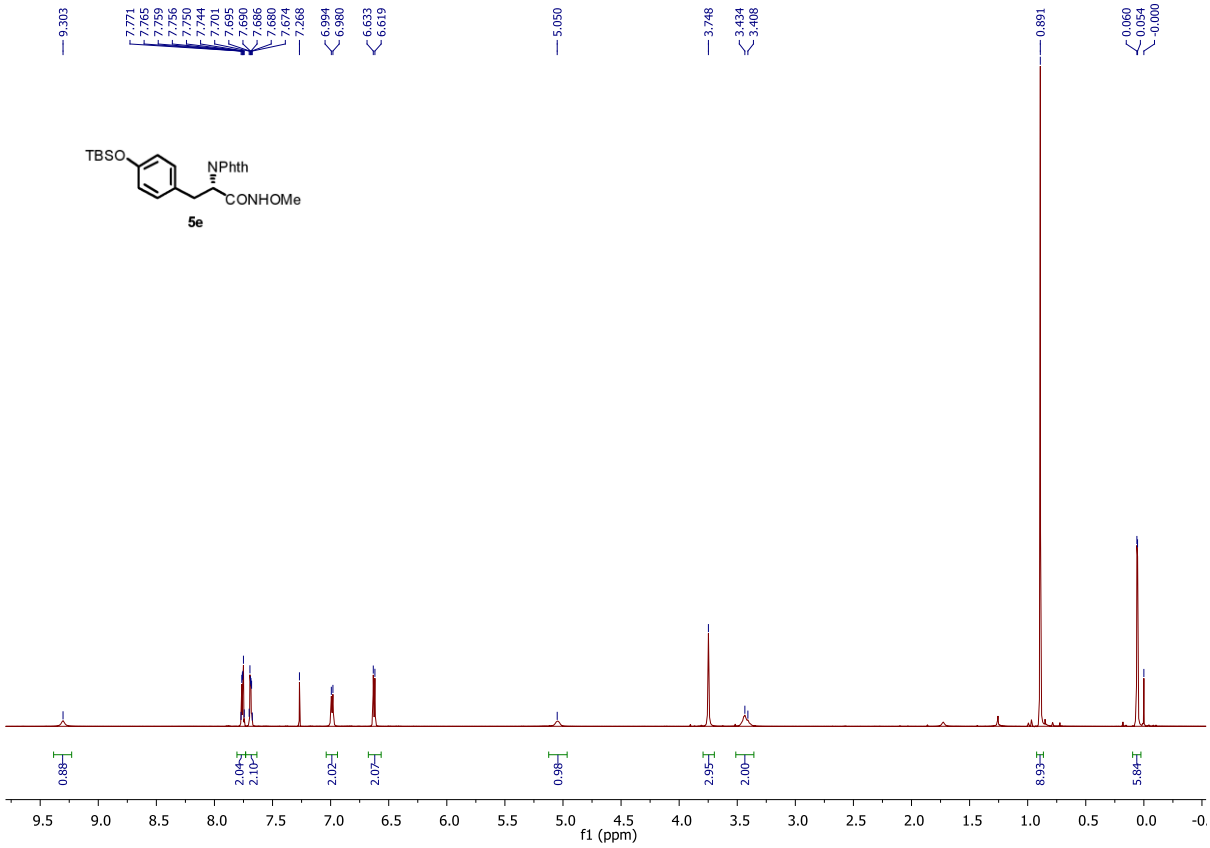
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7.674
7.268
6.994
6.980
6.633
6.619
5.050
3.748
3.434
3.408
0.891
0.060
0.054
-0.000
TBSO
NPhth
CONHOMe
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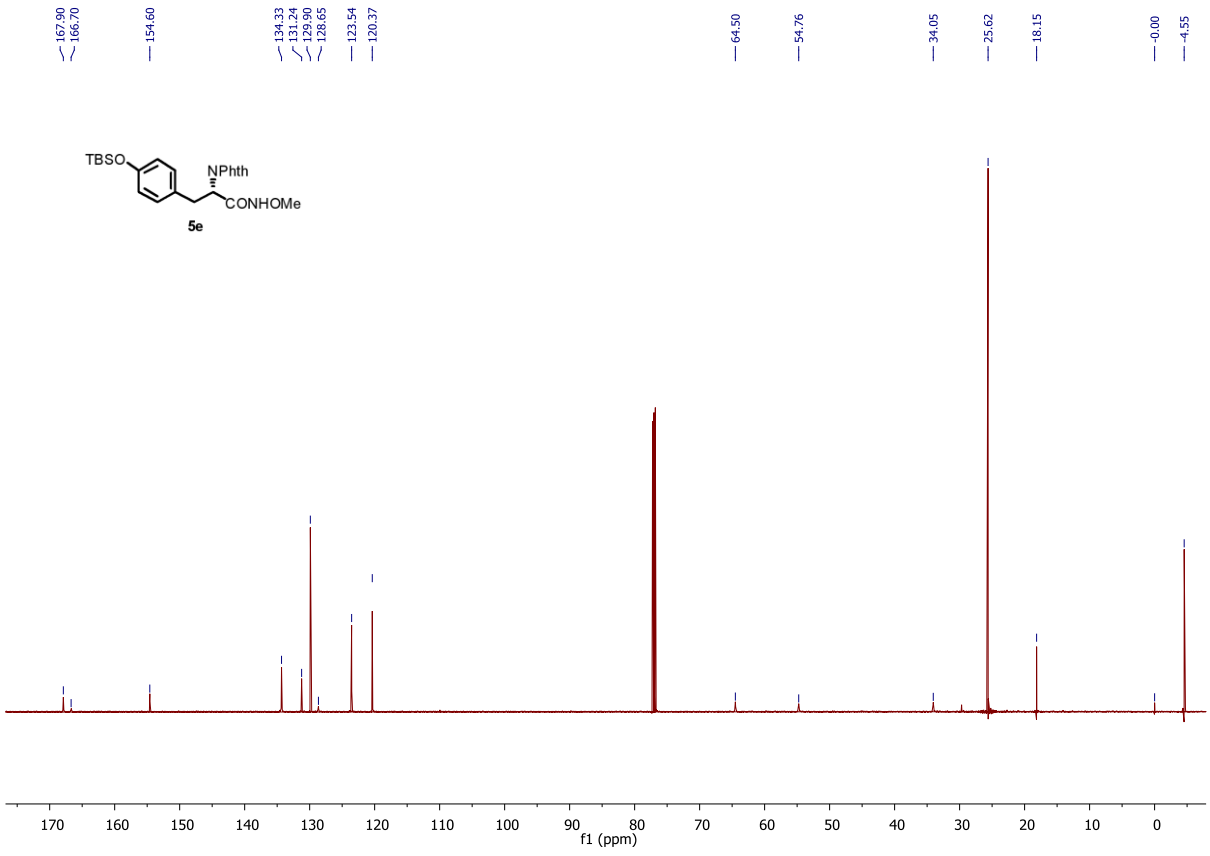
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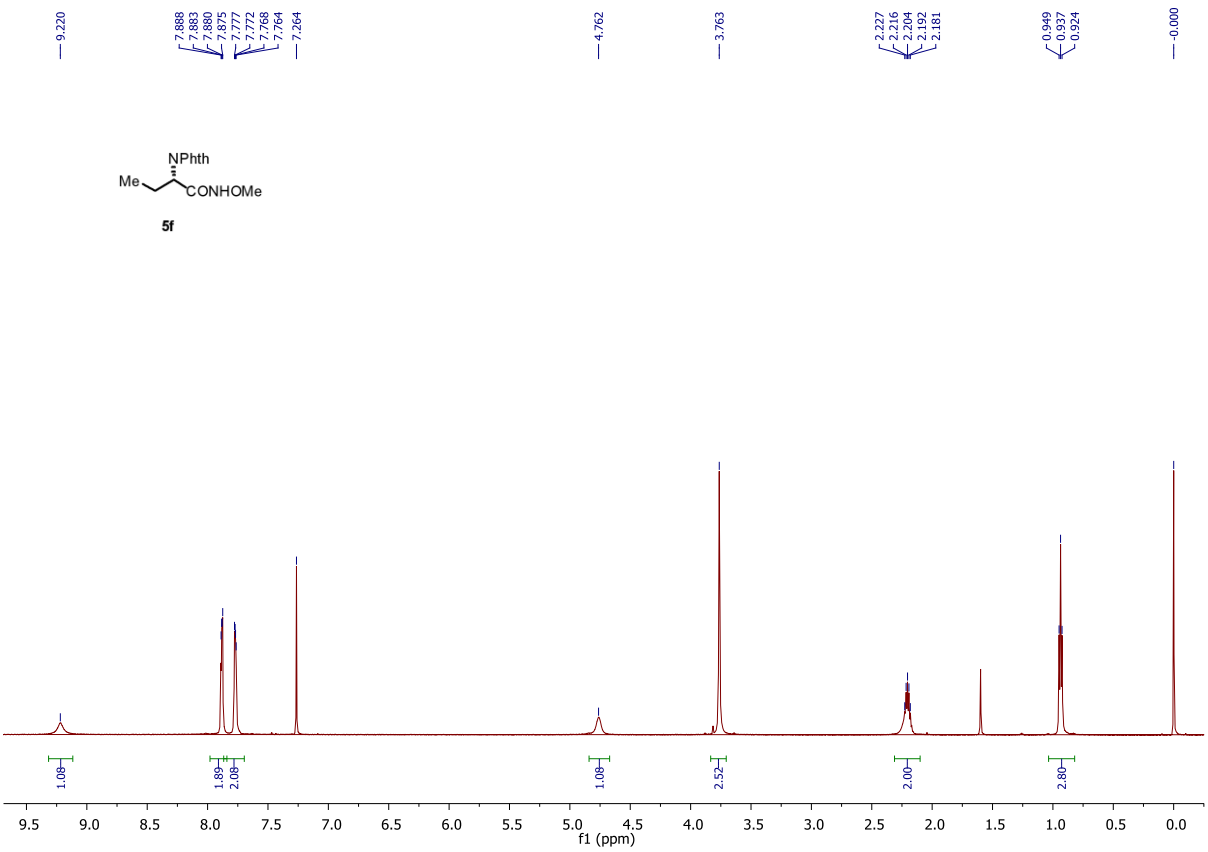
TBSO
NPhth
CONHOMe
5e
f1 (ppm)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2.216
2.204
2.192
2.181
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0.924
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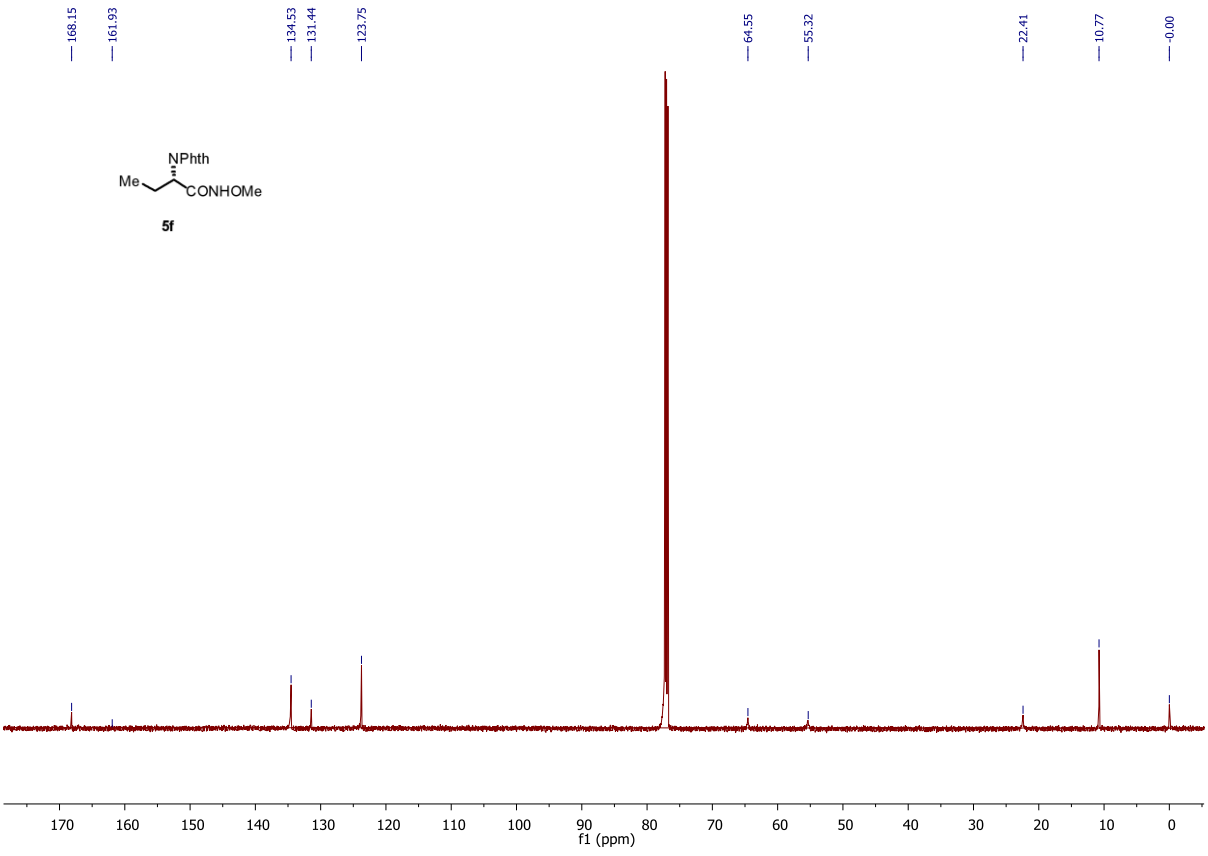
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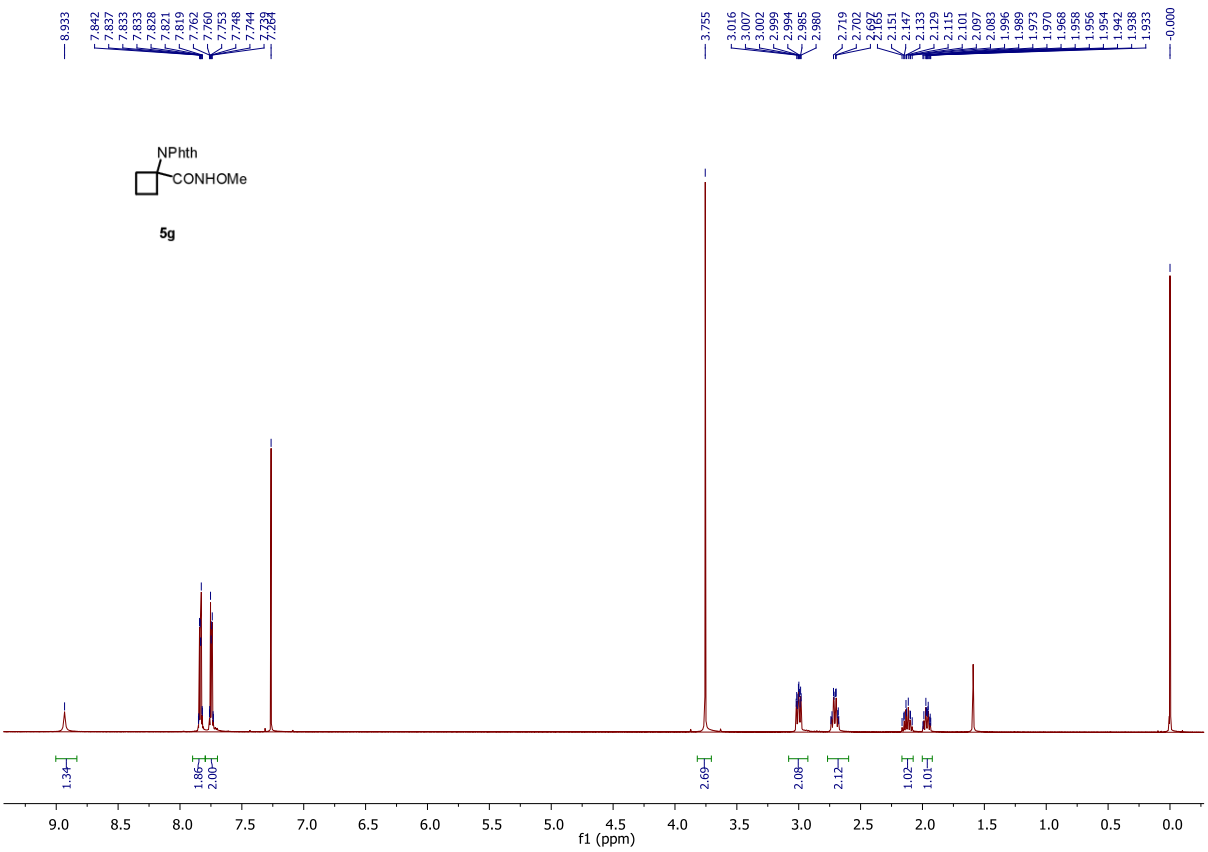
f1 (ppm)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7.744
7.284
3.755
3.016
3.007
3.002
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2.985
2.980
2.719
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2.133
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2.115
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1.956
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1.01
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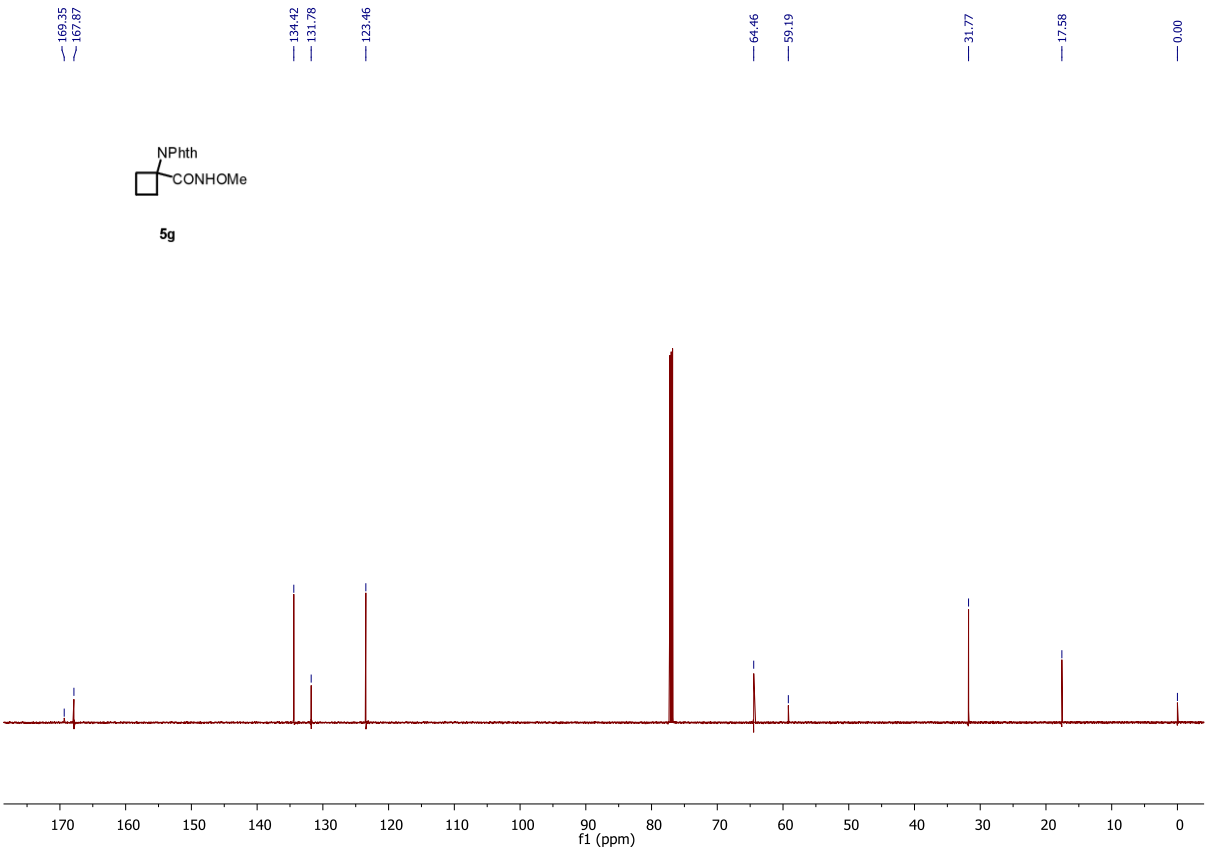
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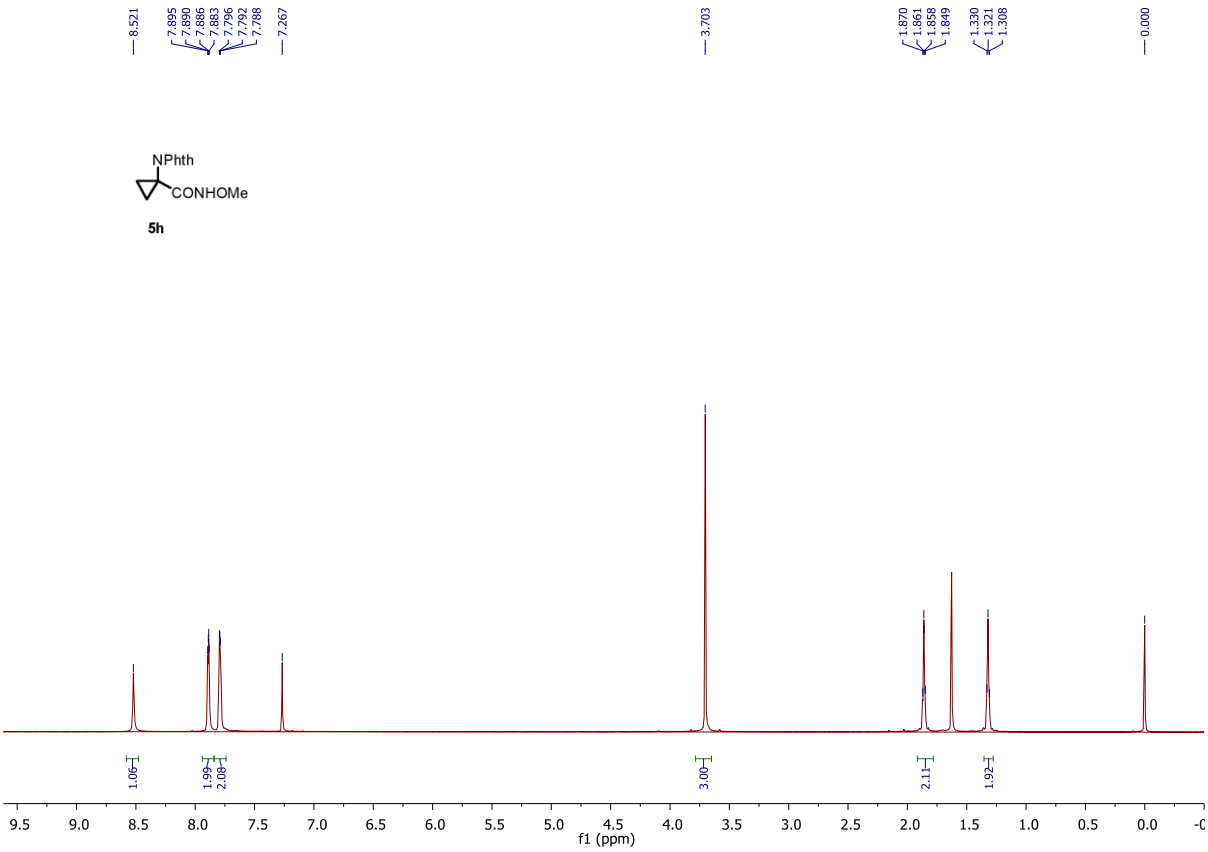
5g
f1 (ppm)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1.849
1.330
1.321
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2.11
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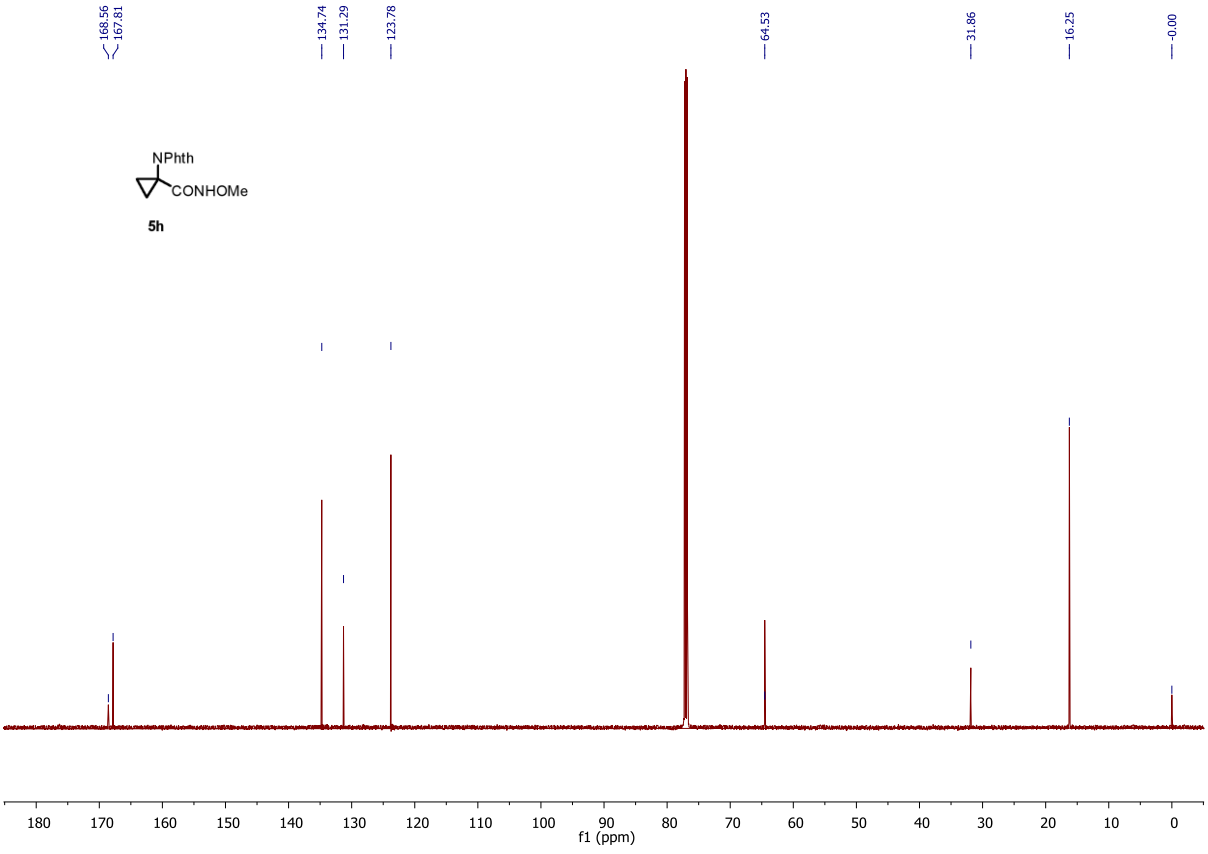
f1 (ppm)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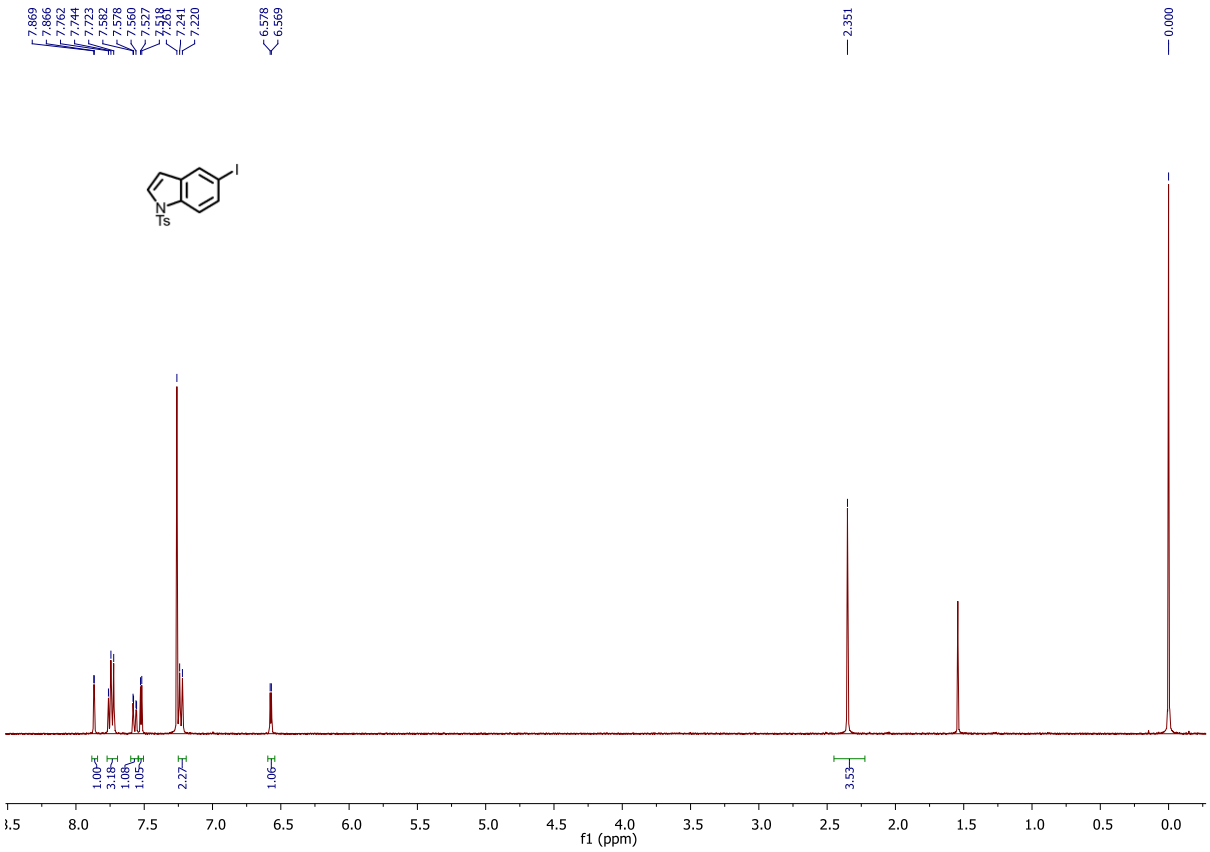
5h
f1 (ppm)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7.241
7.220
6.578
6.569
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N
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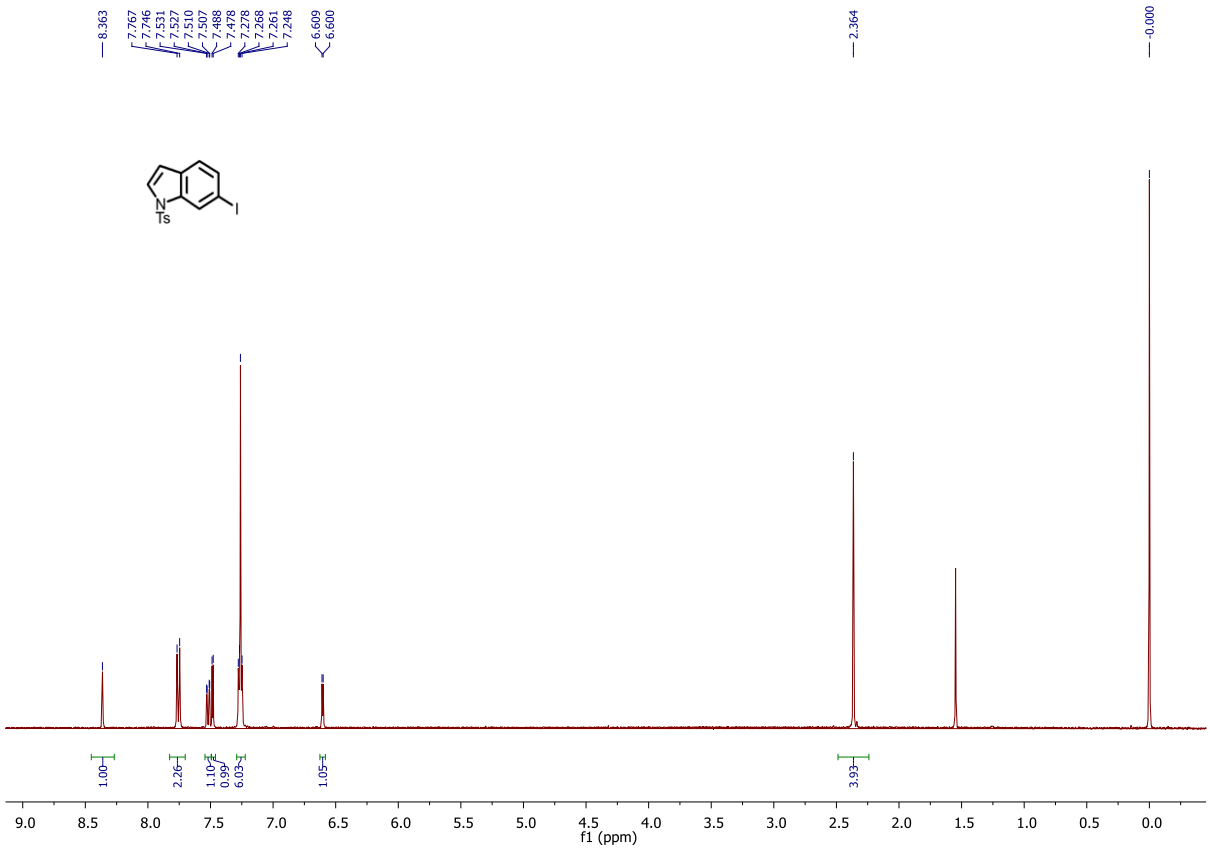
f1 (ppm)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7.507
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7.278
7.268
7.261
7.248
6.609
6.600
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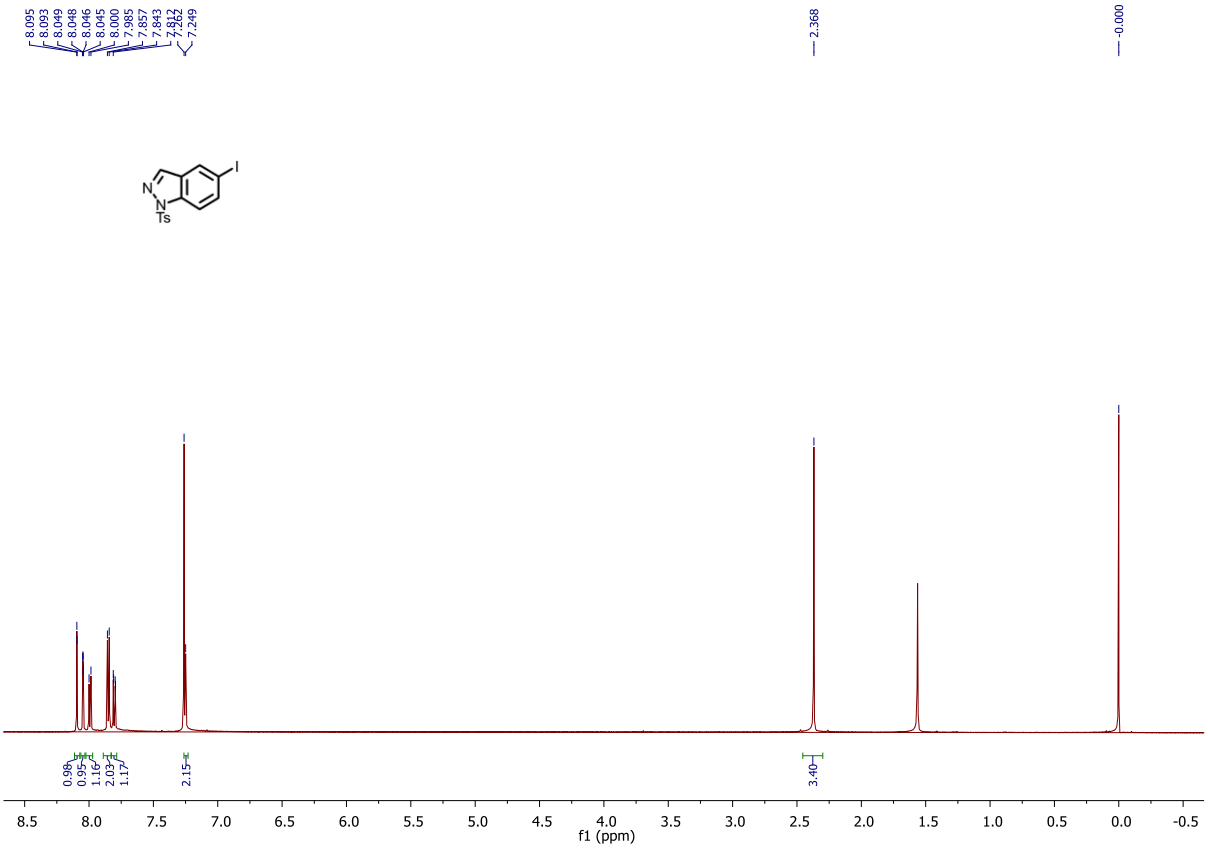
1.05
3.93
f1 (ppm)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8.048
8.046
8.045
8.000
7.985
7.857
7.843
7.812
7.262
7.249
2.368
-0.000
I
N
N
Ts
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0.95
1.16
2.03
1.17
2.15
3.40
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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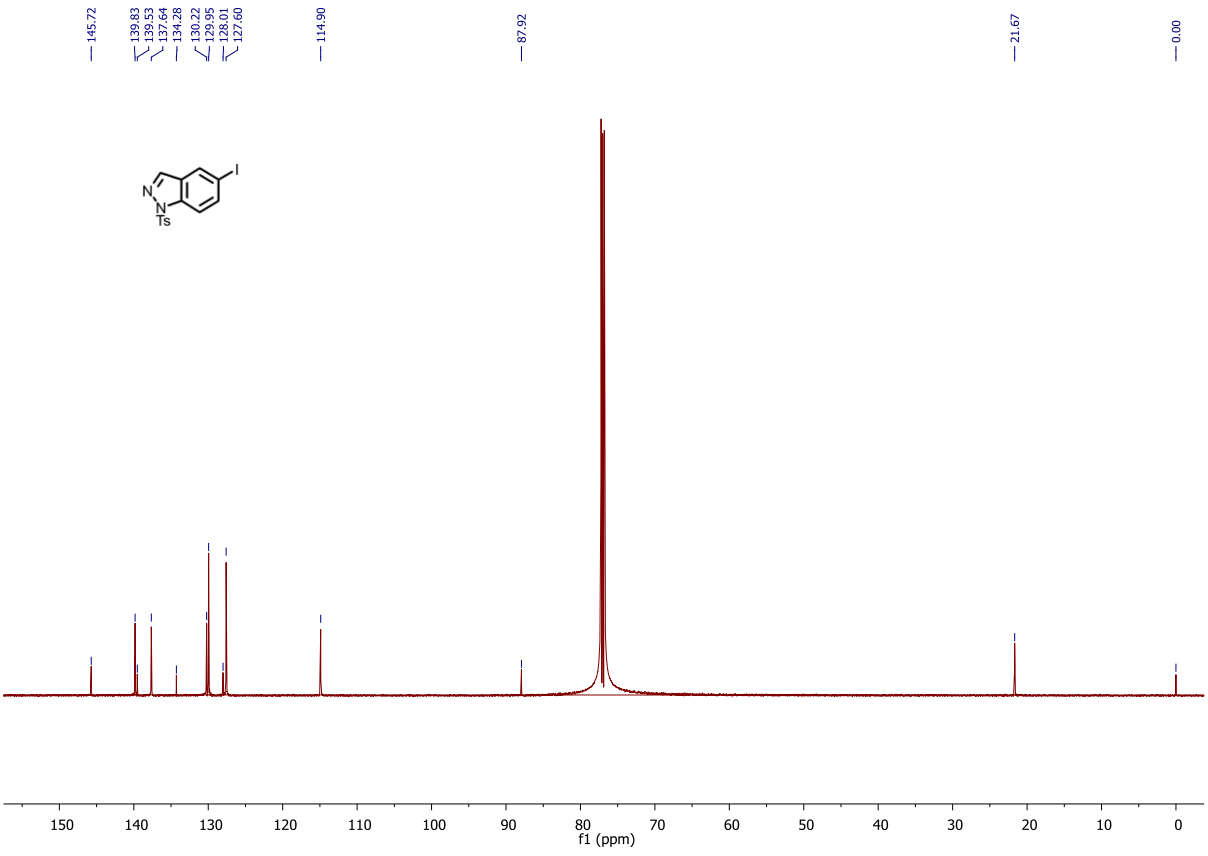
f1 (ppm)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87.92
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0.00
I
N
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Ts
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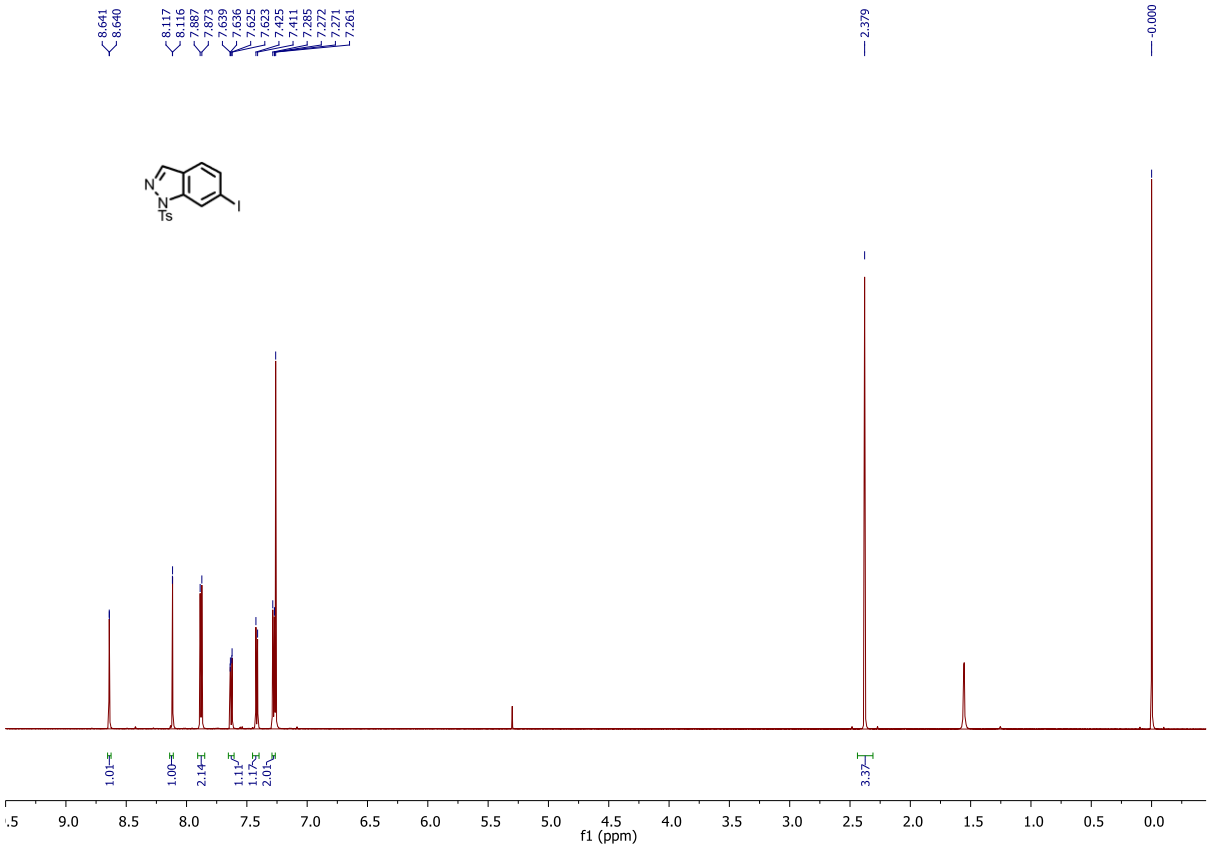
f1 (ppm)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7.272
7.271
7.261
2.379
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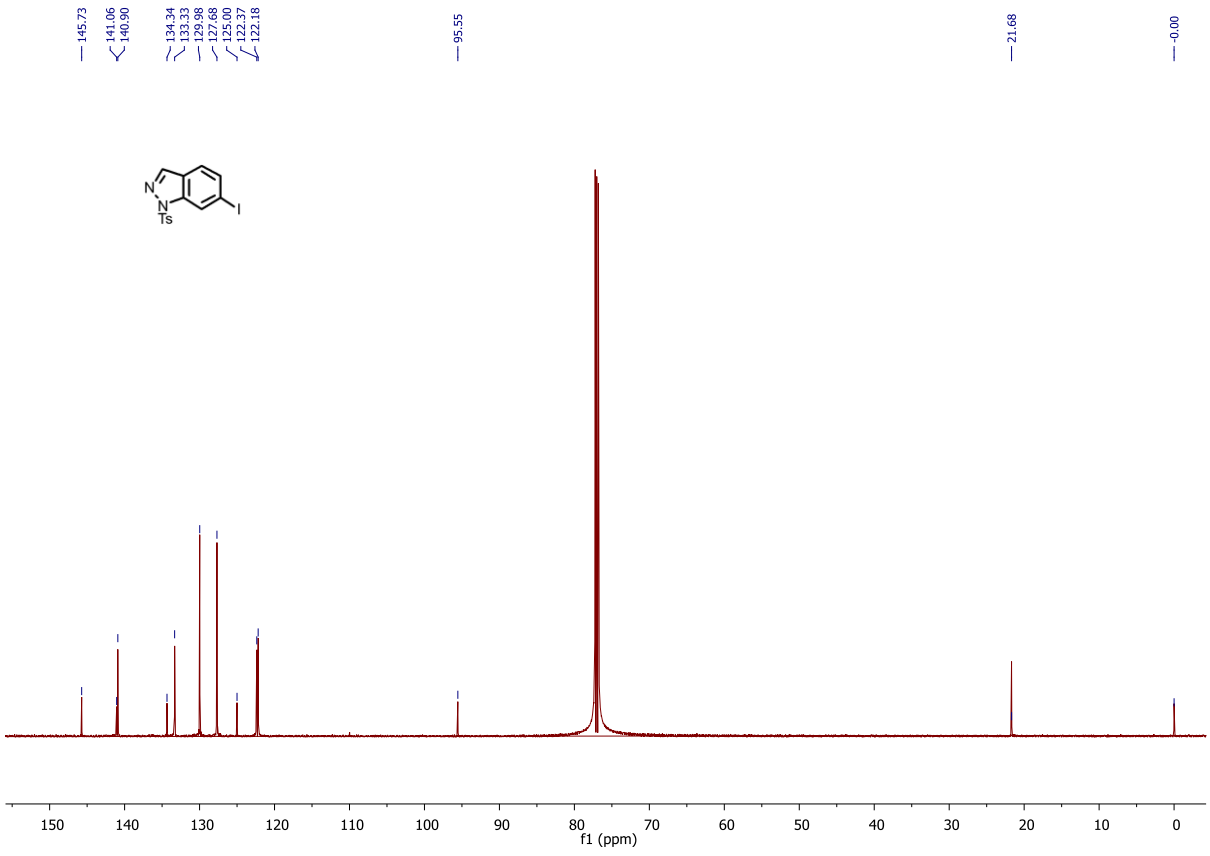
2.01
3.37
f1 (ppm)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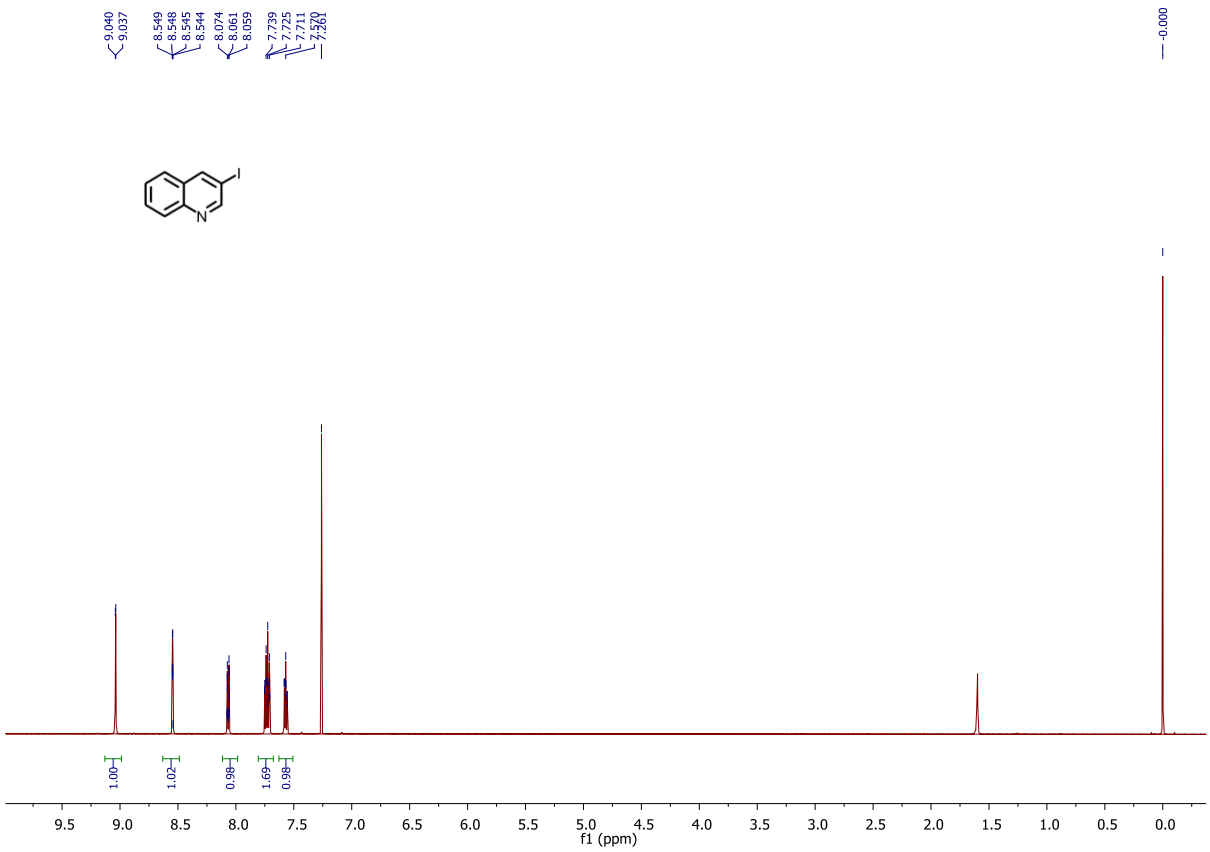
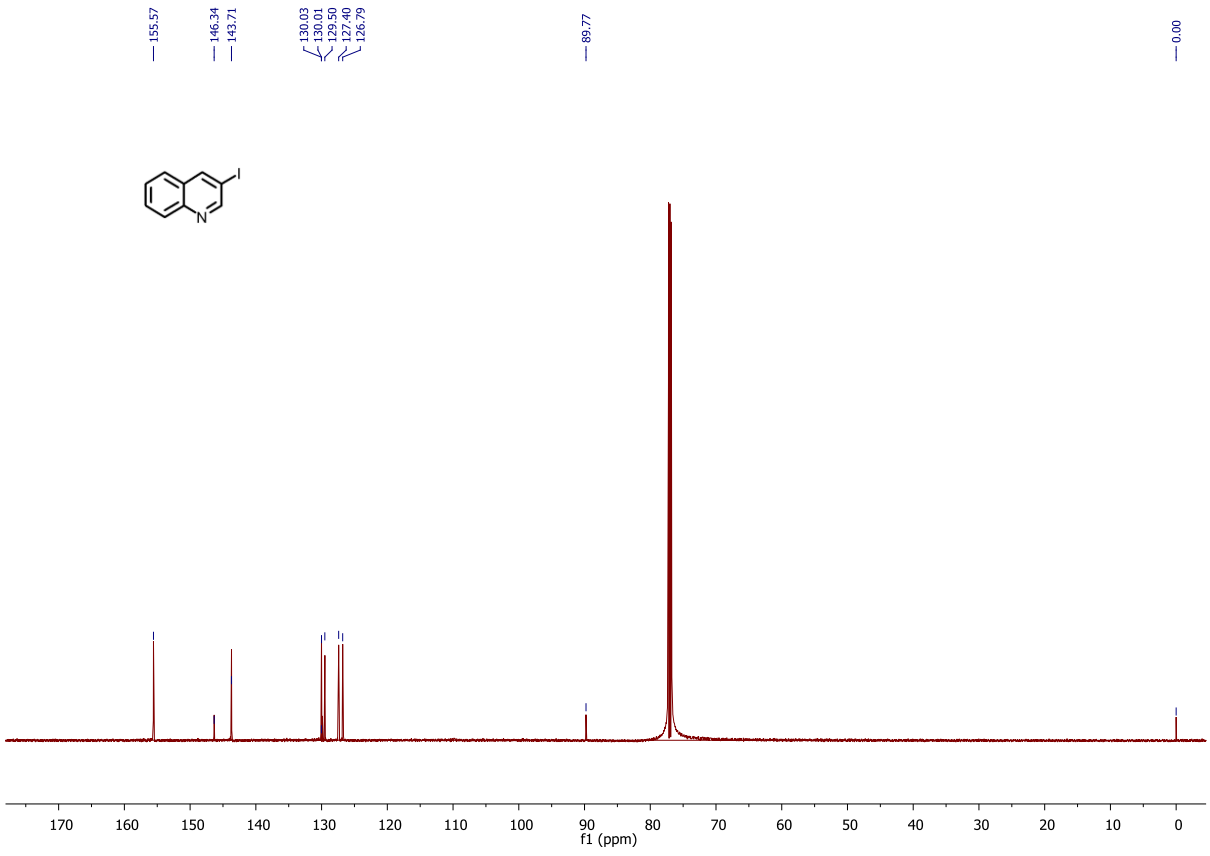
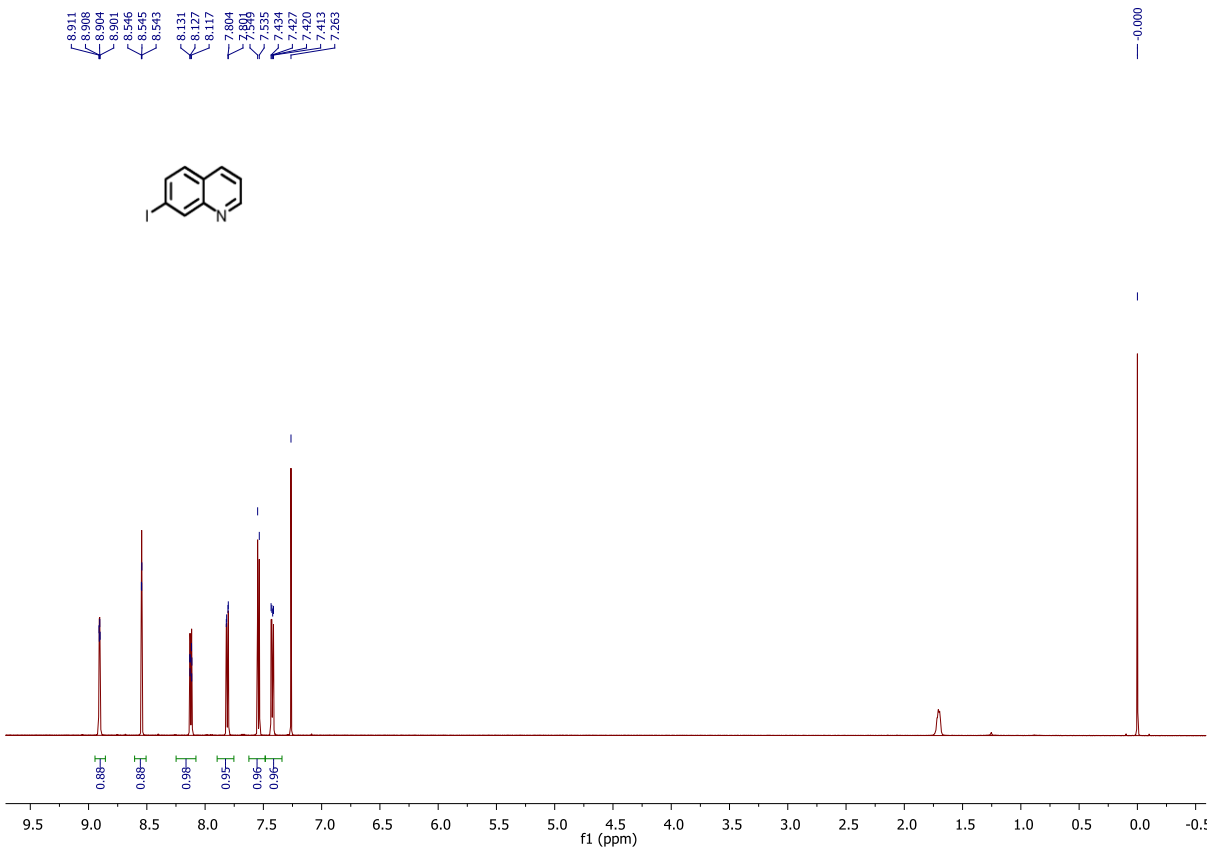
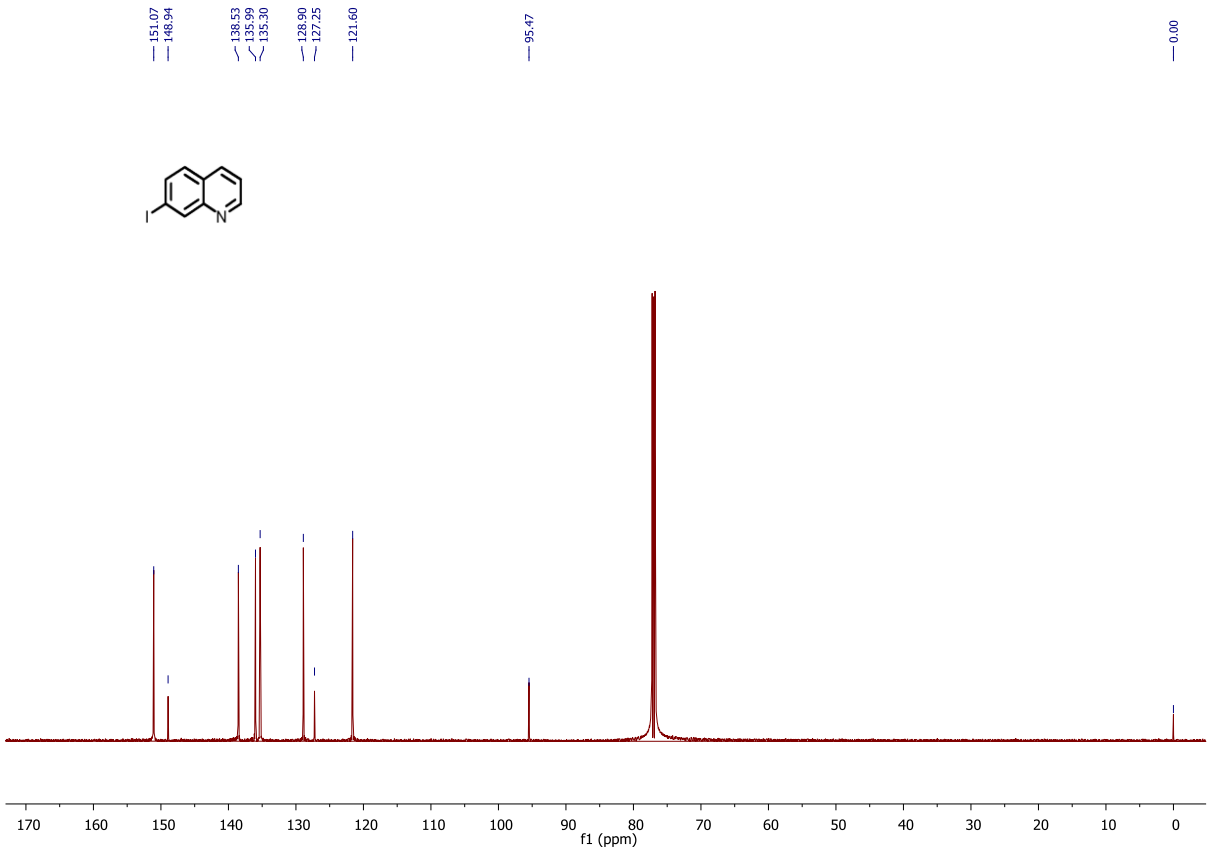
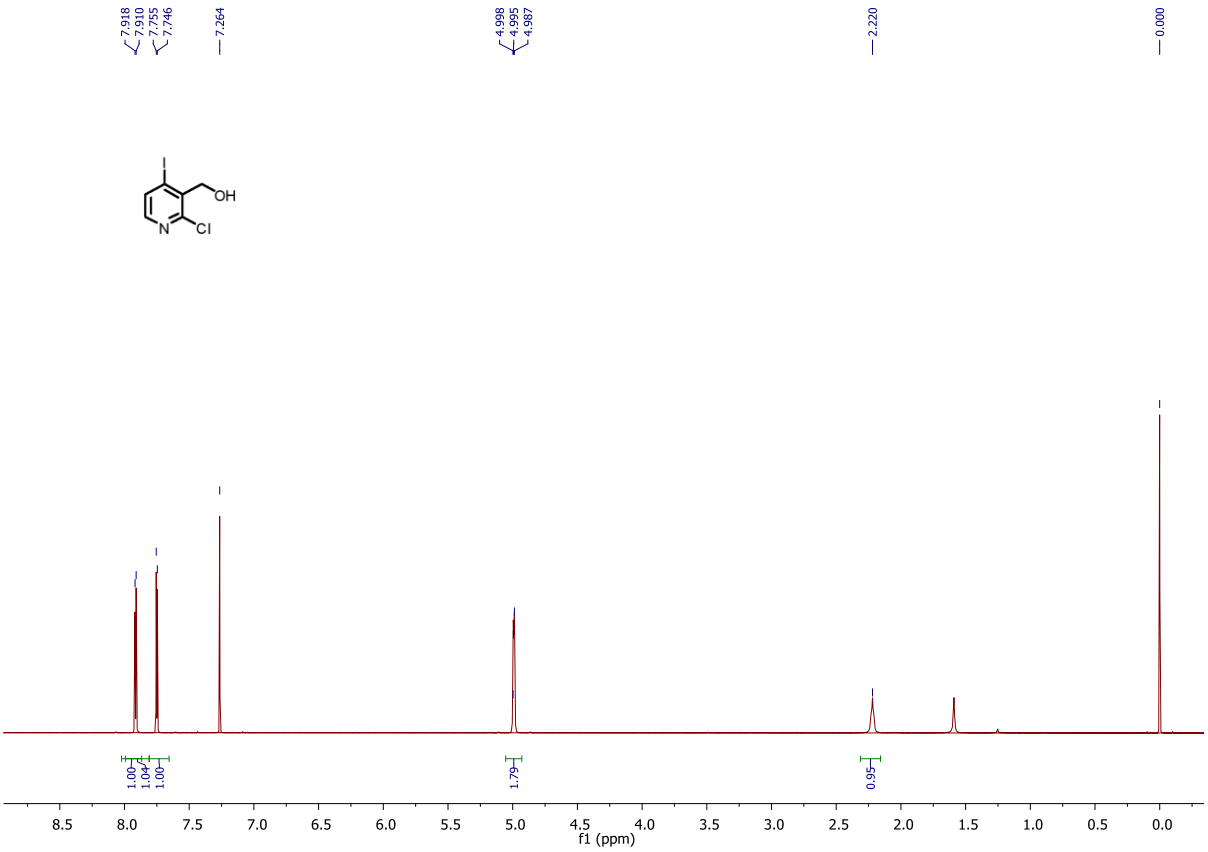
133.33
129.98
127.68
125.00
122.37
122.18
95.55
21.68
-0.00
N
N
Ts
I
f1 (ppm)

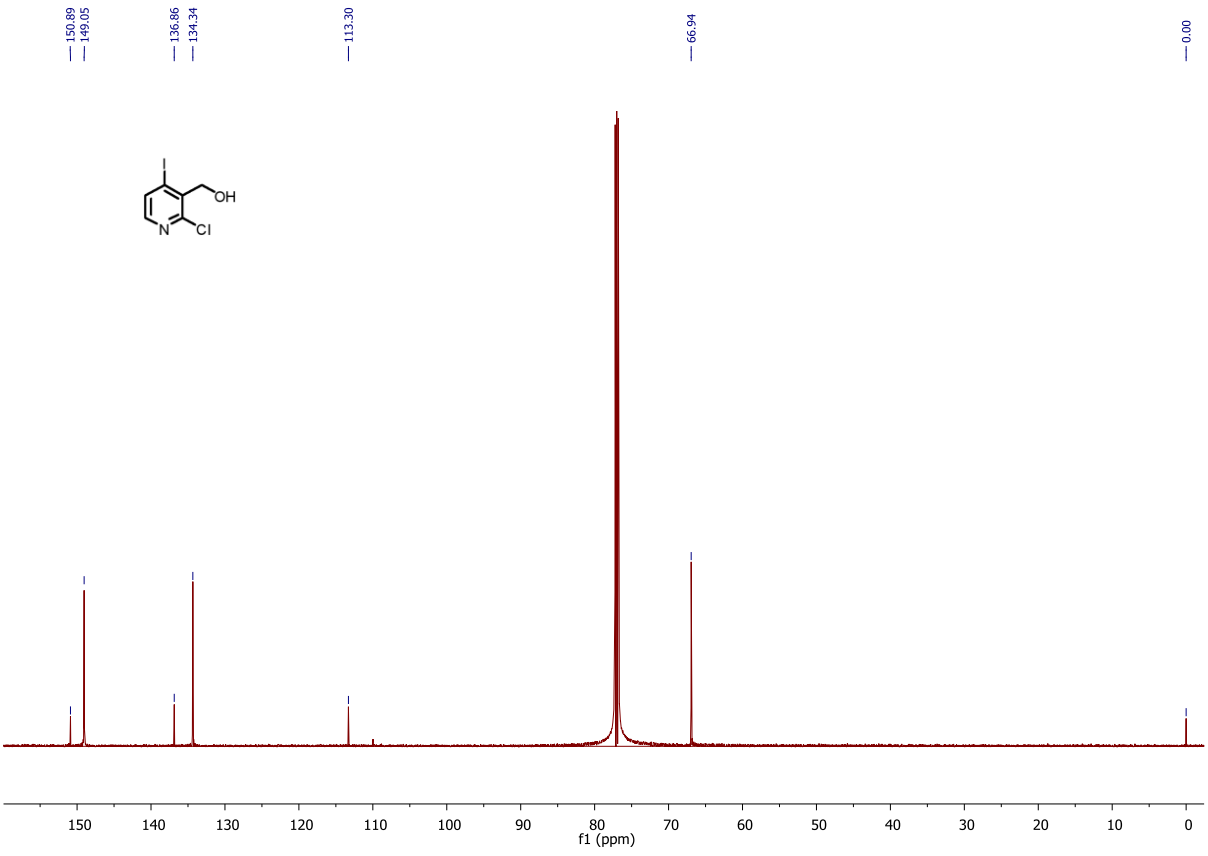

9.040
9.037
8.549
8.548
8.545
8.544
8.074
8.061
8.059
7.739
7.725
7.711
7.570
7.261
0.000
1.00
1.02
0.98
1.69
0.98
f1 (ppm)

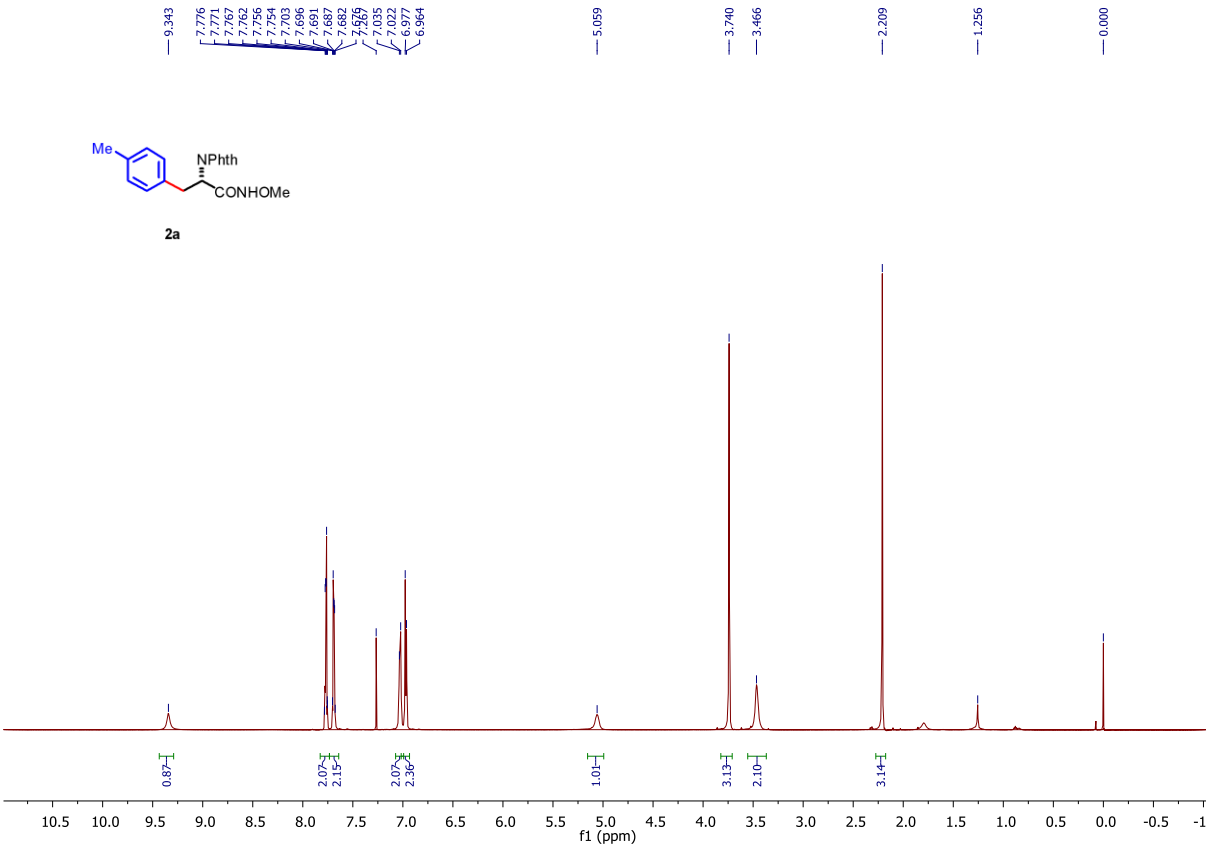

155.57
146.34
143.71
130.03
130.01
129.50
127.40
126.79
89.77
0.00
f1 (ppm)

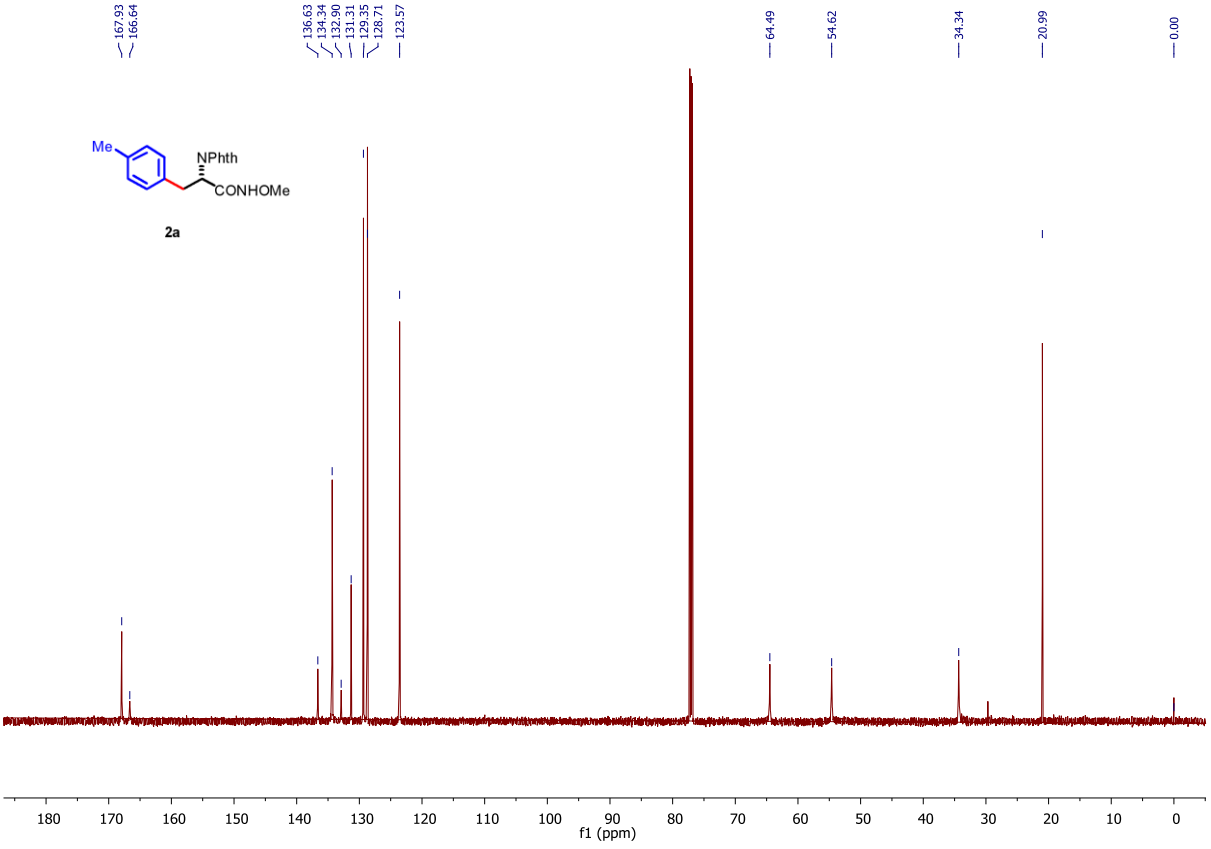

8.911
8.908
8.904
8.901
8.546
8.545
8.543
8.131
8.127
8.117
7.804
7.801
7.549
7.535
7.434
7.427
7.420
7.413
7.263
-0.000
I
N
0.88
0.88
0.98
0.95
0.96
0.96
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

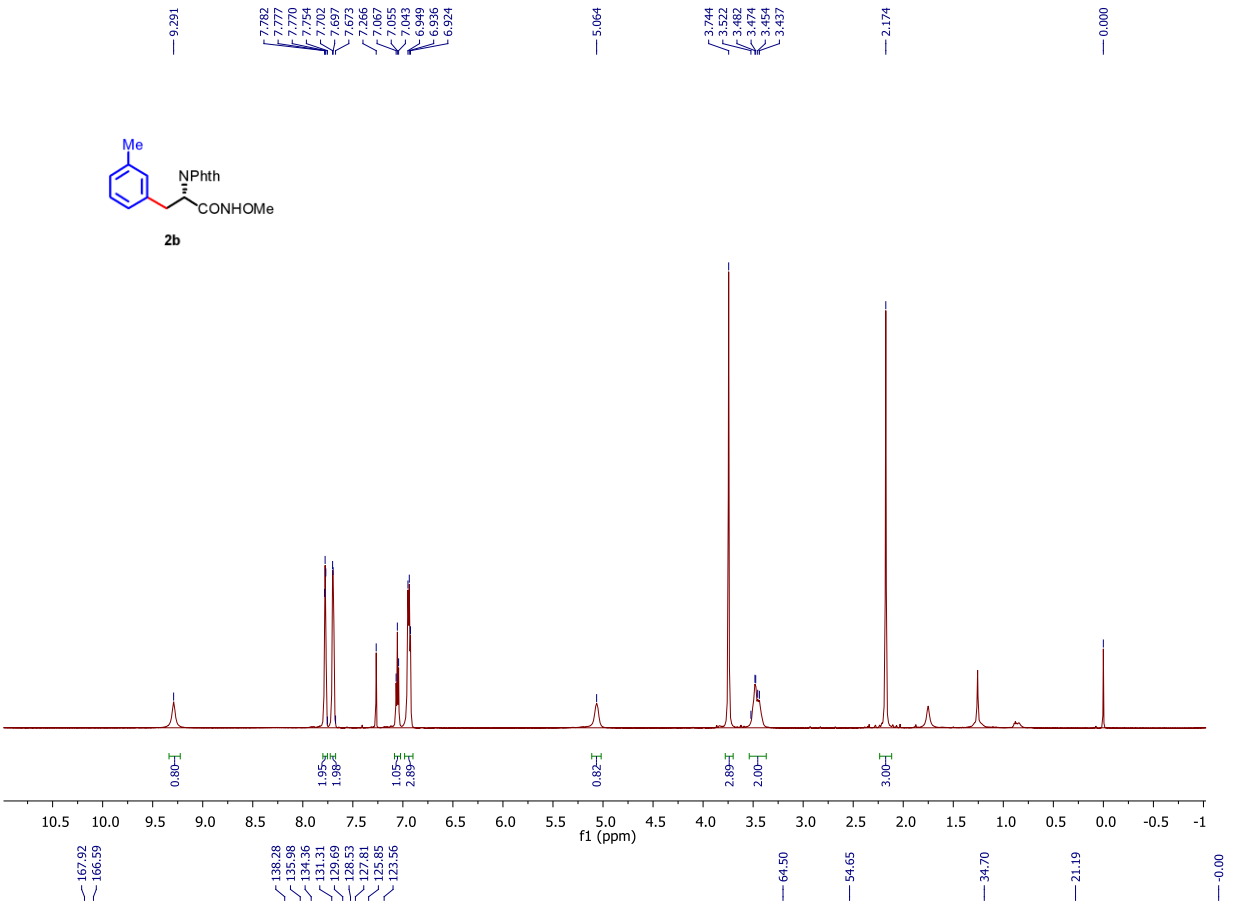

151.07
148.94
138.53
135.99
135.30
128.90
127.25
121.60
95.47
0.00
I
N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

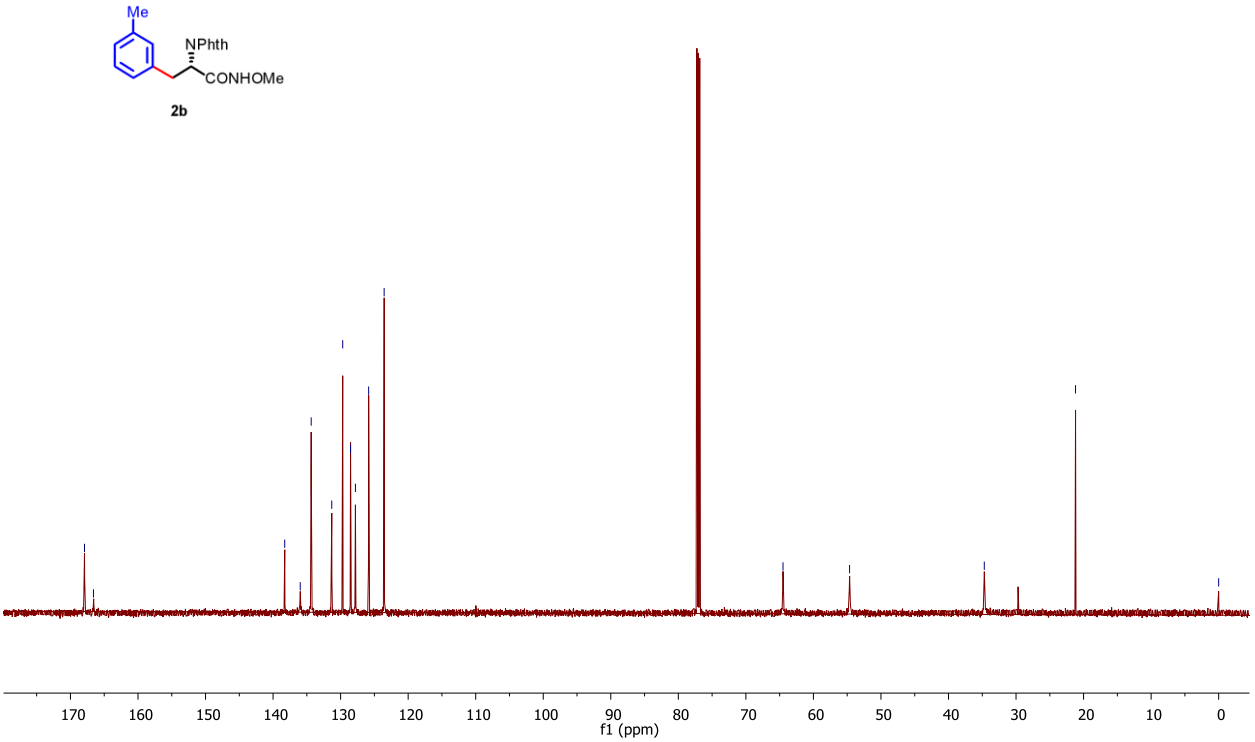

7.918
7.910
7.755
7.746
7.264
4.998
4.995
4.987
2.220
0.000
OH
Cl
N
1.00
1.04
1.00
1.79
0.95
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

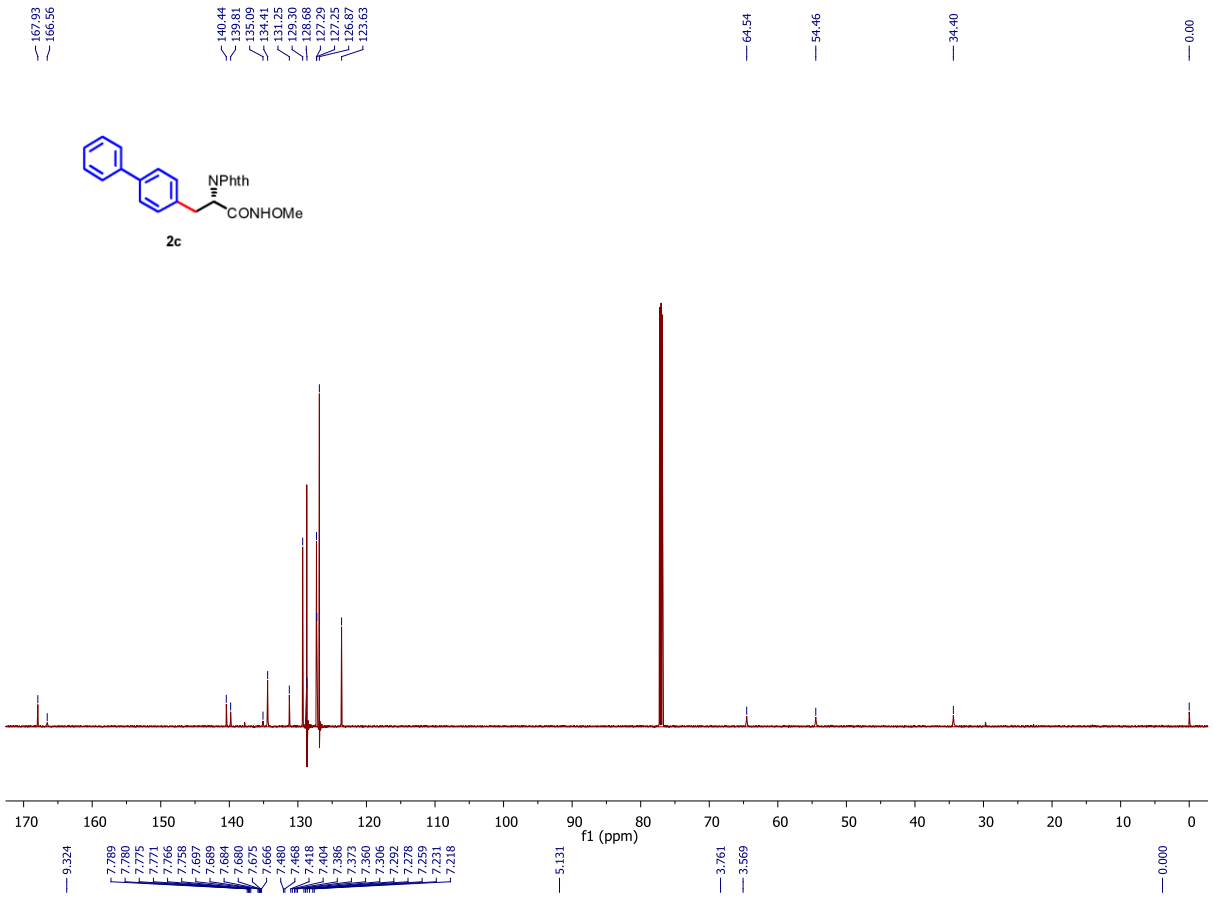

150.89
149.05
136.86
134.34
113.30
66.94
0.00
OH
Cl
N
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

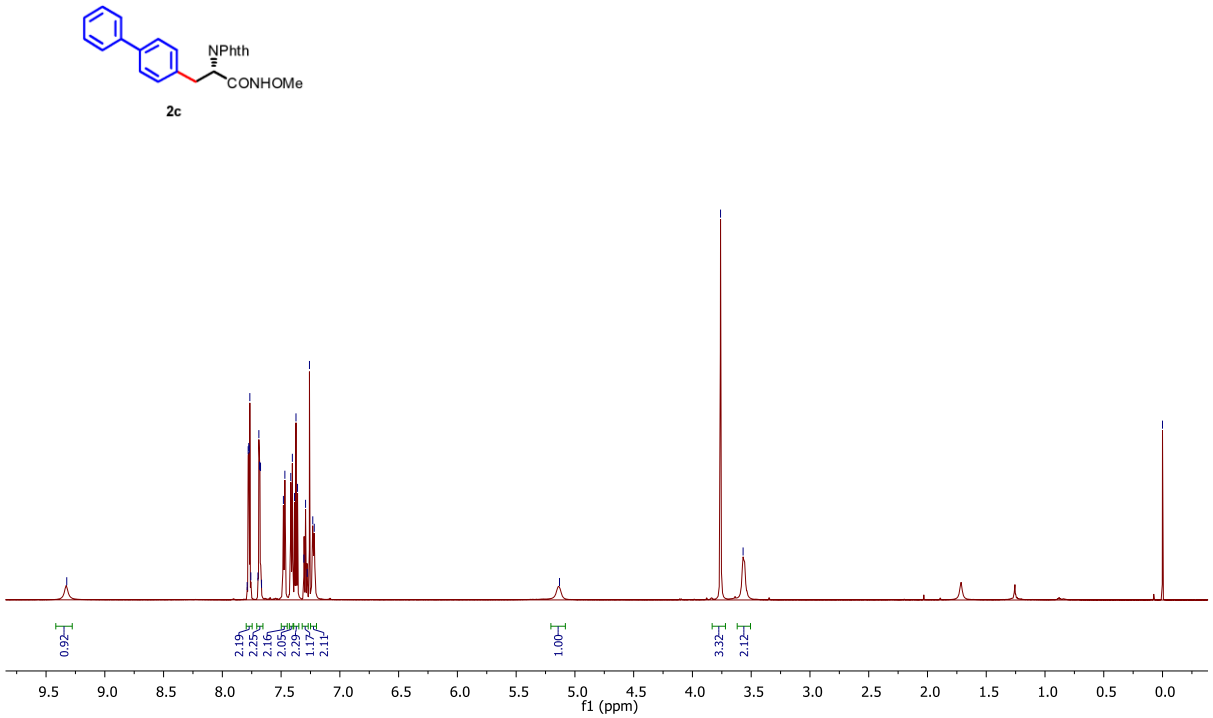

9.343
7.776
7.771
7.767
7.762
7.756
7.754
7.703
7.696
7.691
7.687
7.682
7.679
7.675
7.669
7.035
7.022
6.977
6.964
5.059
3.740
3.466
2.209
1.256
0.000
Me
NPhth
CONHOMe
2a
0.87
2.07
2.15
2.07
2.36
1.01
3.13
2.10
3.14
f1 (ppm)

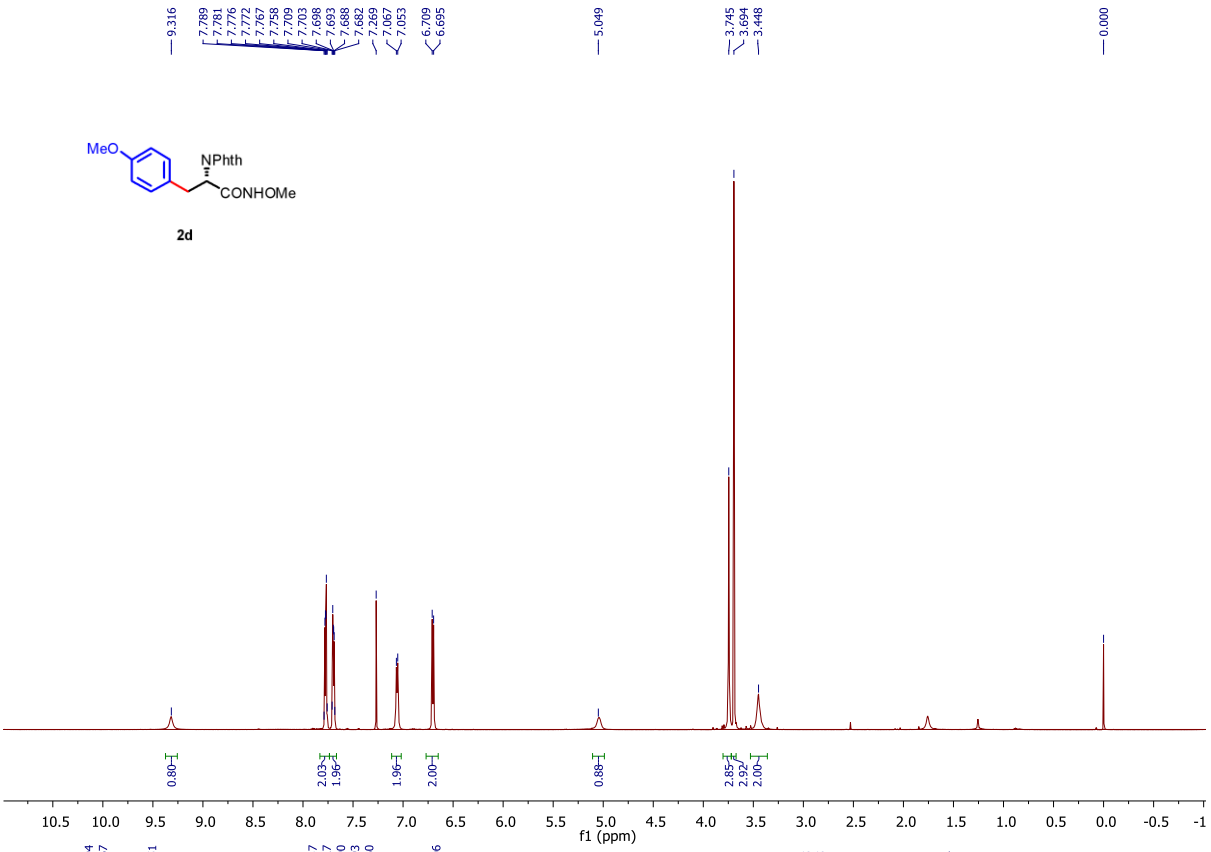

167.93
166.64
136.63
134.34
132.90
131.31
129.35
128.71
123.57
64.49
54.62
34.34
20.99
0.00
Me
NPhth
CONHOMe
2a
f1 (ppm)

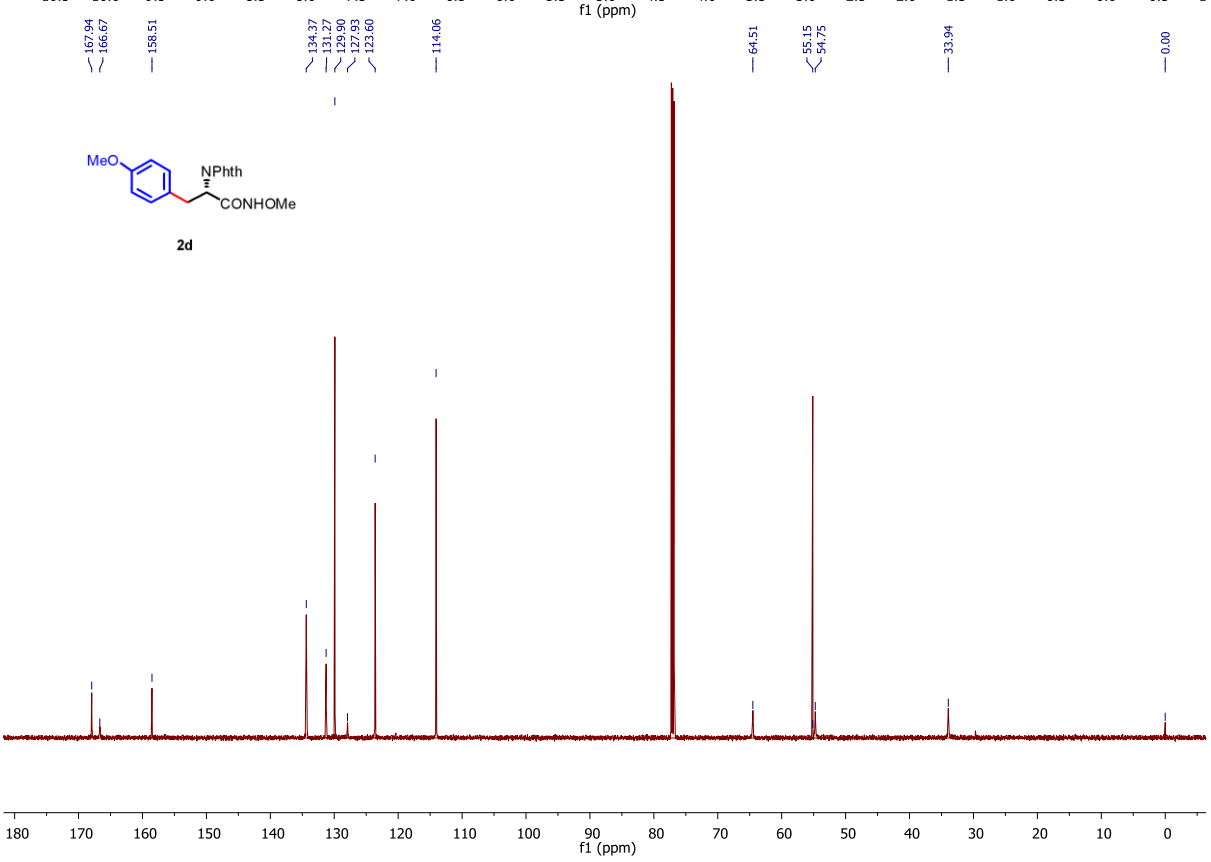

9.291
7.782
7.777
7.770
7.754
7.702
7.697
7.673
7.266
7.067
7.055
7.043
6.949
6.936
6.924
5.064
3.744
3.522
3.482
3.474
3.454
3.437
2.174
0.000
Me
NPhth
CONHOMe
2b
0.80
1.95
1.98
1.05
2.89
0.82
2.89
2.00
3.00
f1 (ppm)
167.92
166.59
138.28
135.98
134.36
131.31
129.69
128.53
127.81
125.85
123.56
64.50
54.65
34.70
21.19
-0.00

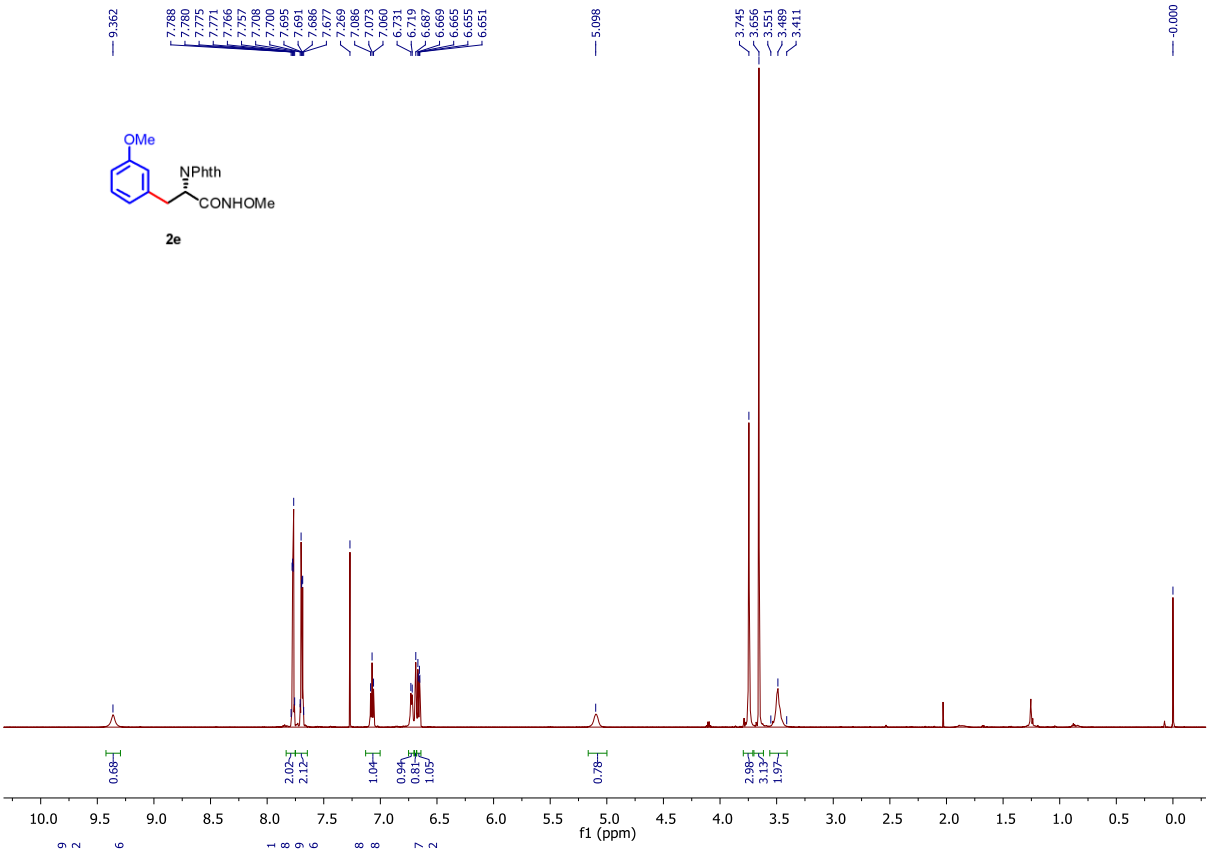

Me
NPhth
CONHOMe
2b
f1 (ppm)

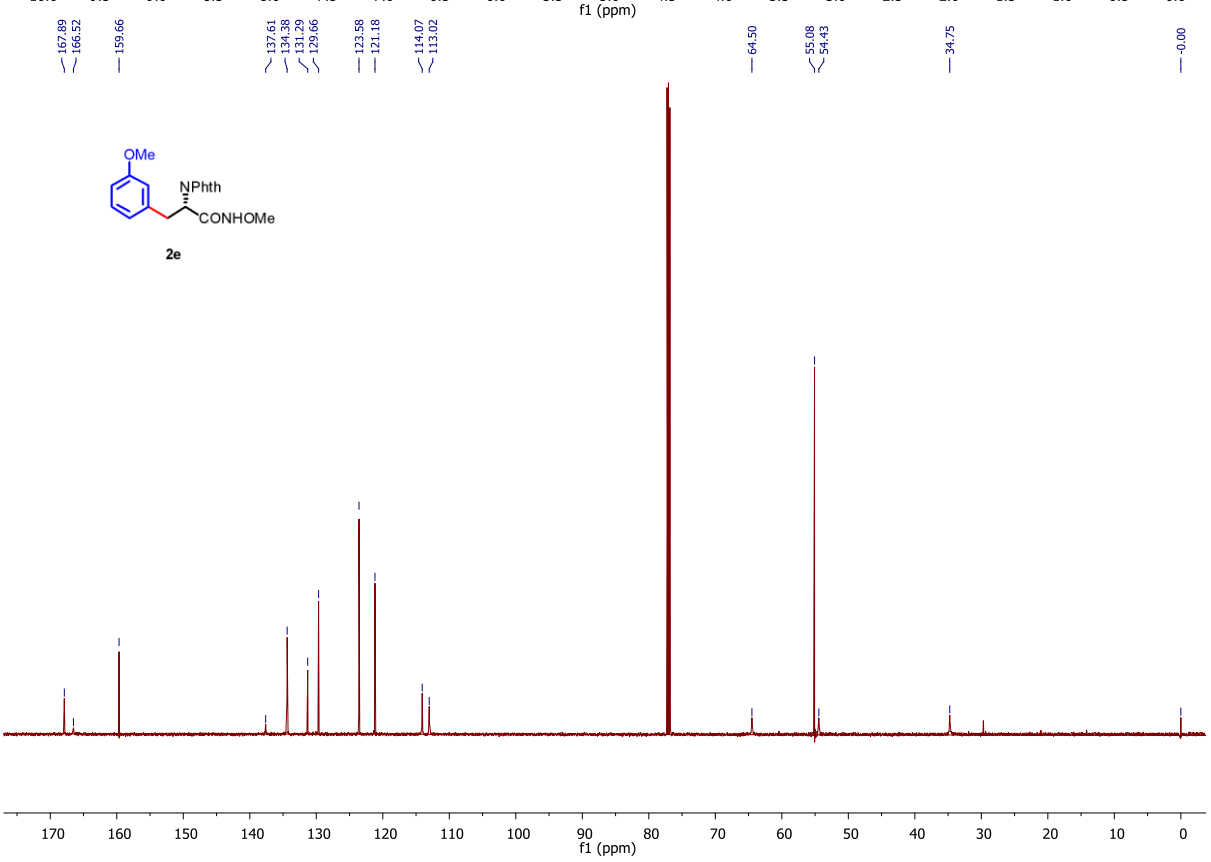

167.93
166.56
140.44
139.81
135.09
134.41
131.25
129.30
128.68
127.29
127.25
126.87
123.63
64.54
54.46
34.40
0.00
NPhth
CONHOMe
2c
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
9.324
7.789
7.780
7.775
7.771
7.766
7.758
7.697
7.689
7.684
7.680
7.675
7.666
7.480
7.468
7.418
7.404
7.386
7.373
7.360
7.306
7.292
7.278
7.259
7.231
7.218
5.131
3.761
3.569
0.000

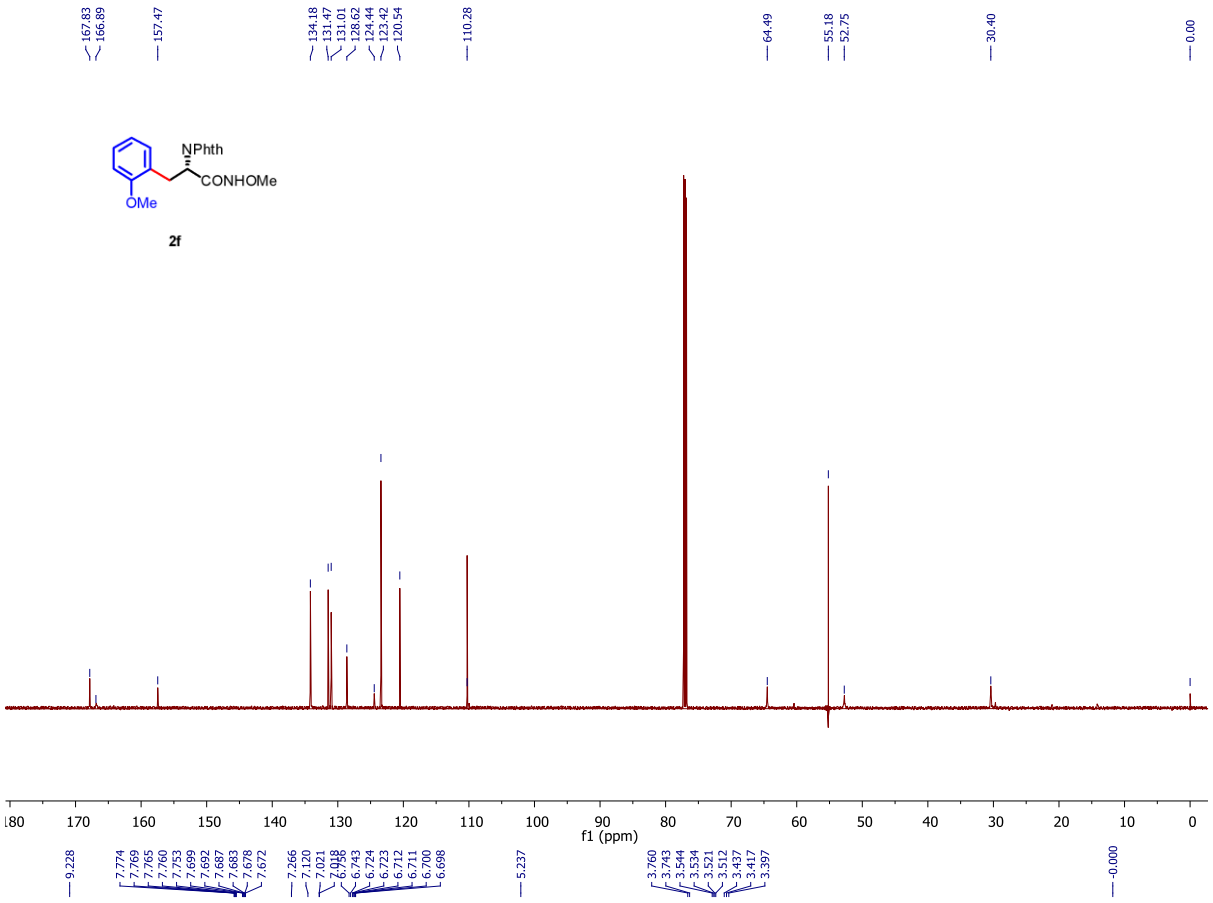

NPhth
CONHOMe
2c
0.92
2.19
2.25
2.16
2.05
2.29
1.17
2.11
1.00
3.32
2.12
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

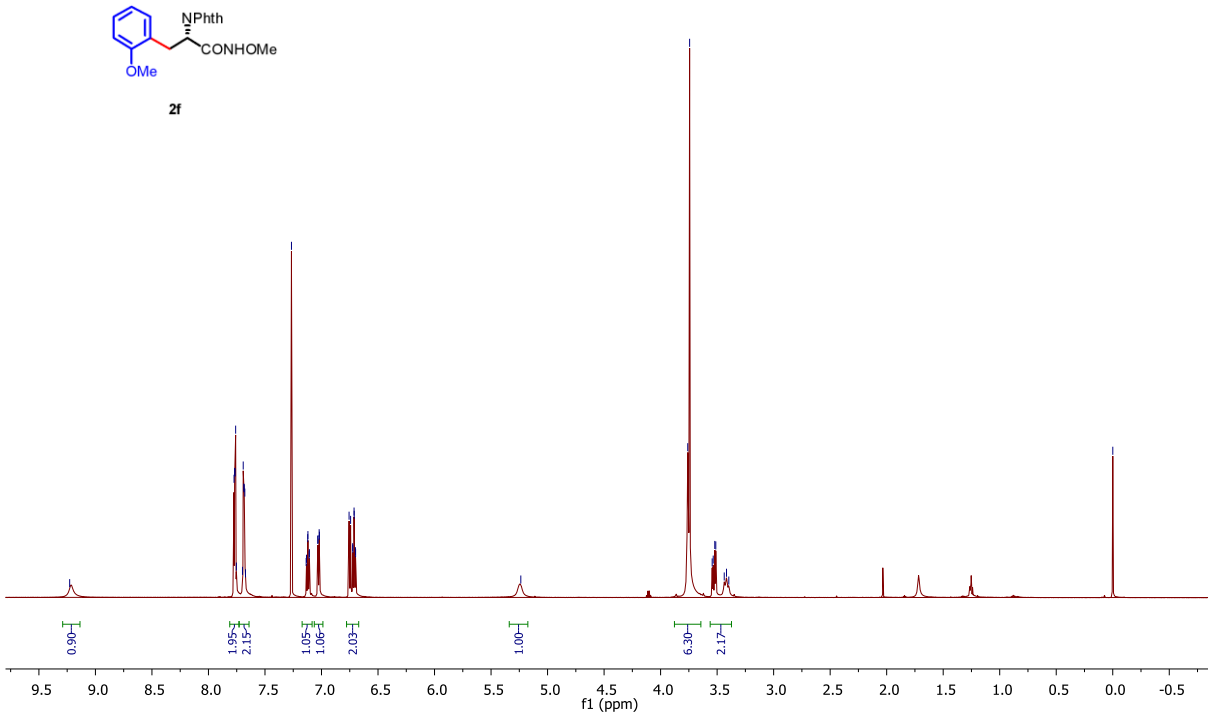

9.316
7.789
7.781
7.776
7.772
7.767
7.758
7.709
7.703
7.698
7.693
7.688
7.682
7.269
7.067
7.053
6.709
6.695
5.049
3.745
3.694
3.448
0.000
MeO
NPhth
CONHOMe
2d
0.80
2.03
1.96
1.96
2.00
0.88
2.85
2.92
2.00
f1 (ppm)

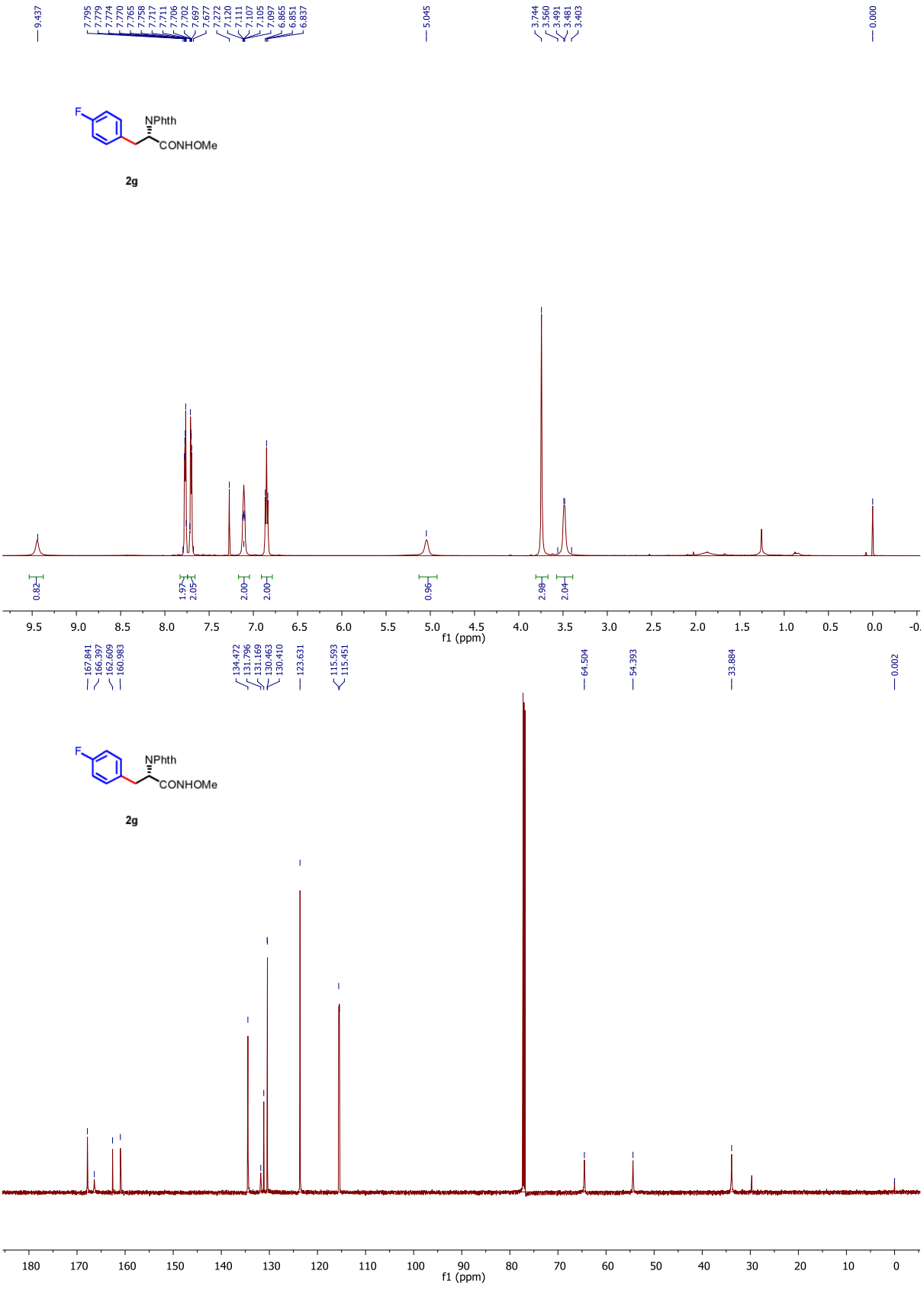

167.94
166.67
158.51
134.37
131.27
129.90
127.93
123.60
114.06
64.51
55.15
54.75
33.94
0.00
MeO
NPhth
CONHOMe
2d
f1 (ppm)

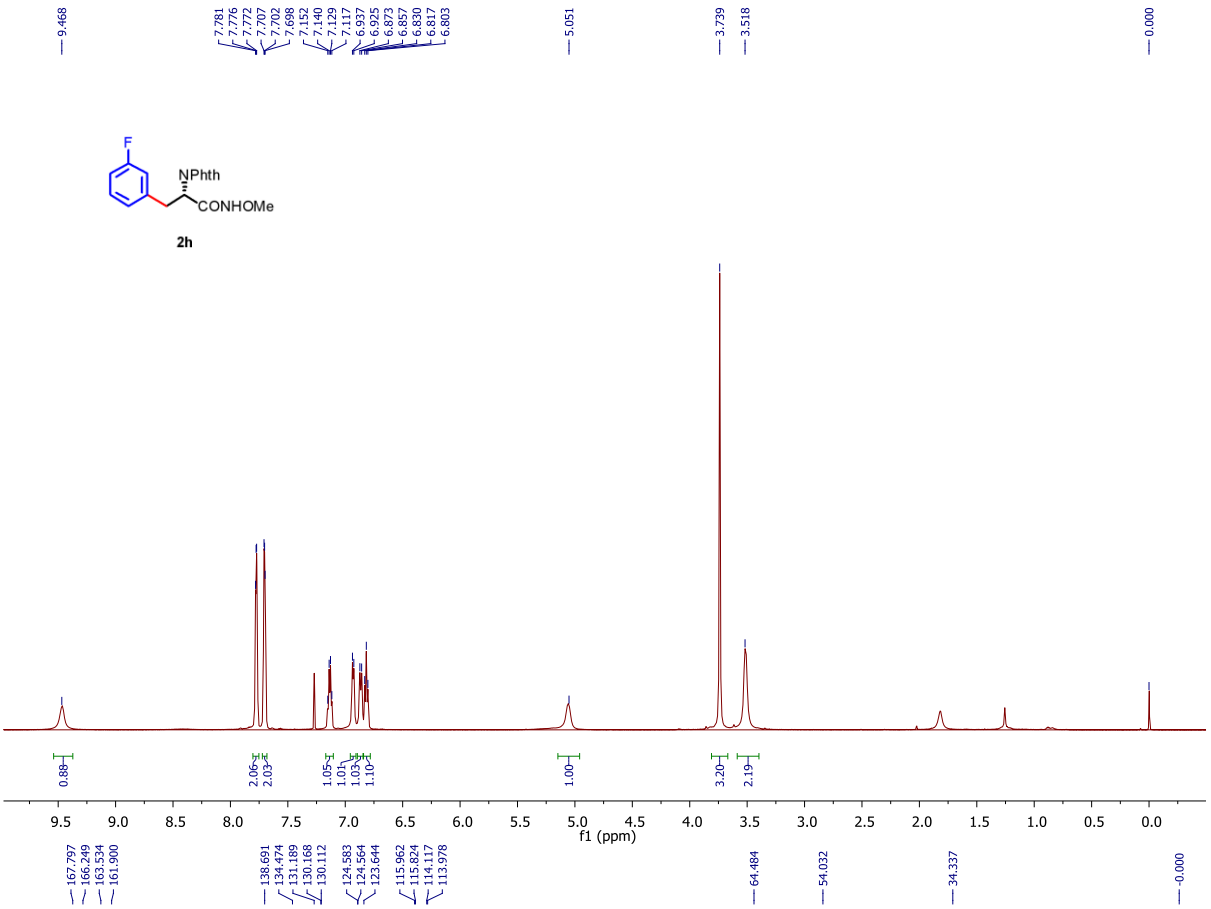

9.362
7.788
7.780
7.775
7.771
7.766
7.757
7.708
7.700
7.695
7.691
7.686
7.677
7.269
7.086
7.073
7.060
6.731
6.719
6.687
6.669
6.665
6.655
6.651
5.098
3.745
3.656
3.551
3.489
3.411
-0.000
OMe
NPhth
CONHOMe
2e
0.68
2.02
2.12
1.04
0.94
0.81
1.05
0.78
2.98
3.13
1.97
f1 (ppm)

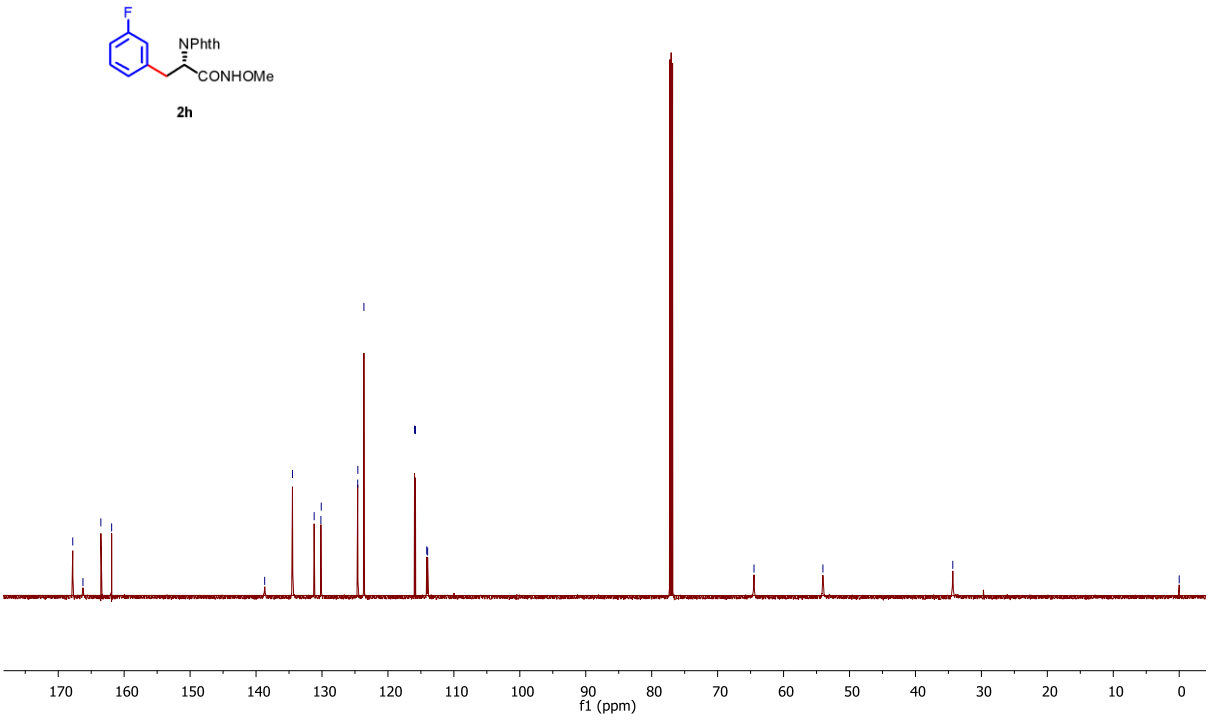

167.89
166.52
159.66
137.61
134.38
131.29
129.66
123.58
121.18
114.07
113.02
64.50
55.08
54.43
34.75
-0.00
OMe
NPhth
CONHOMe
2e
f1 (ppm)

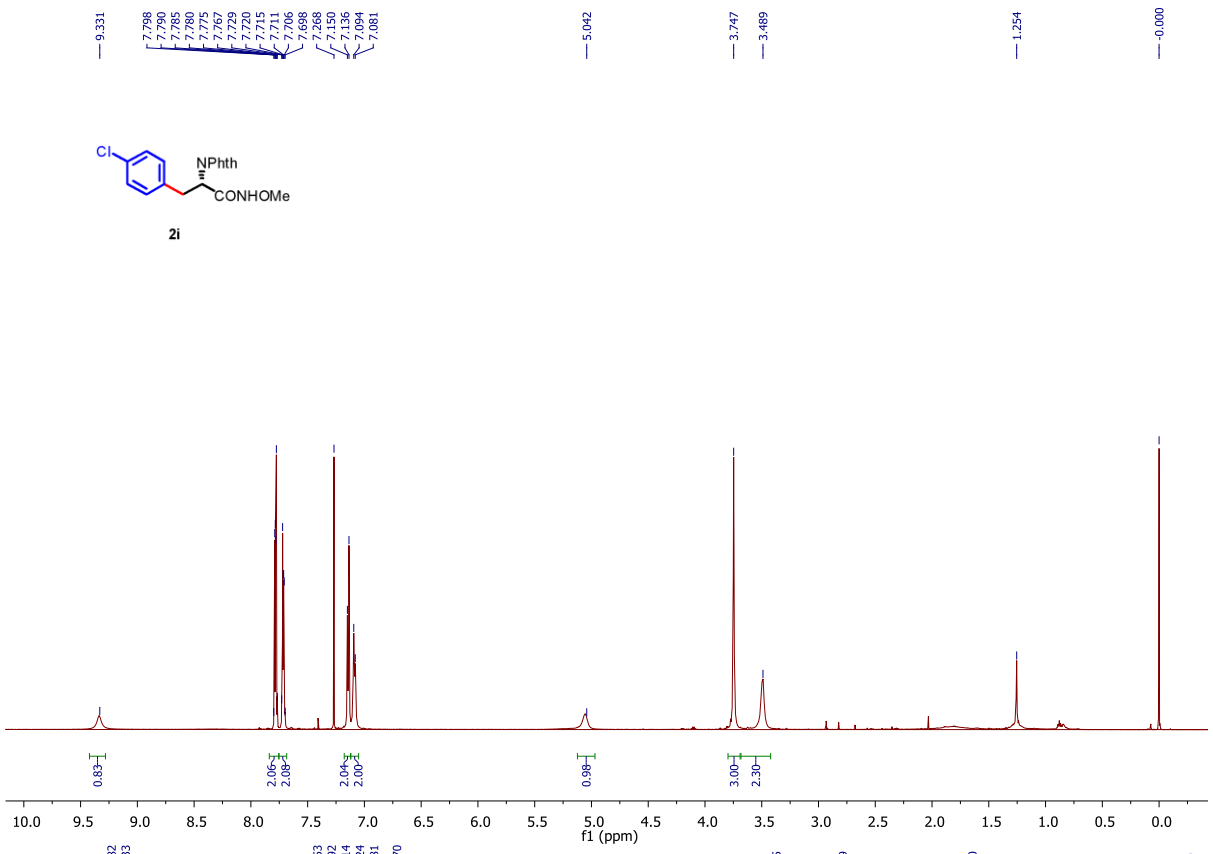

167.83
166.89
157.47
134.18
131.47
131.01
128.62
124.44
123.42
120.54
110.28
64.49
55.18
52.75
30.40
0.00
NPhth
CONHOMe
OMe
2f
f1 (ppm)
9.228
7.774
7.769
7.765
7.760
7.753
7.699
7.692
7.687
7.683
7.678
7.672
7.266
7.120
7.021
6.748
6.743
6.724
6.723
6.712
6.711
6.700
6.698
5.237
3.760
3.743
3.544
3.534
3.521
3.512
3.437
3.417
3.397
-0.000

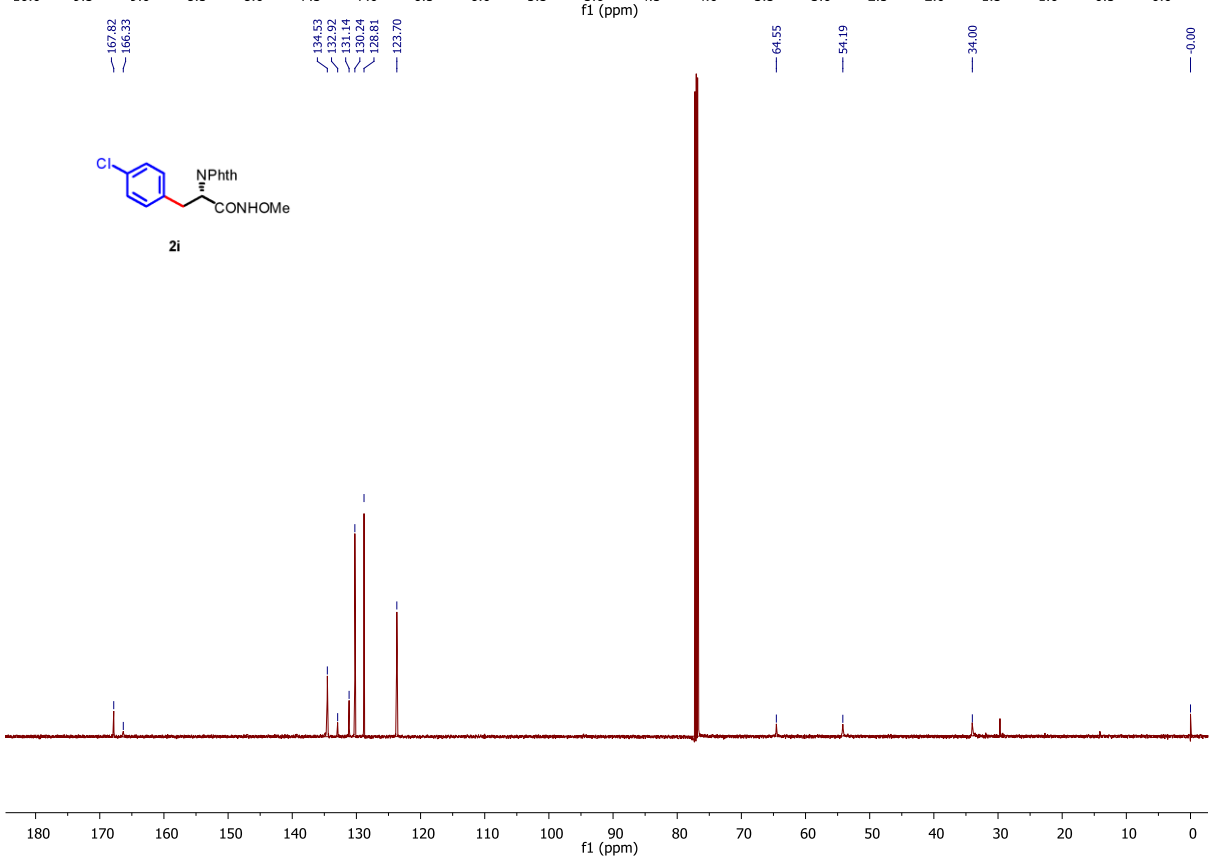

NPhth
CONHOMe
OMe
2f
0.90
1.95
2.15
1.05
1.06
2.03
1.00
6.30
2.17
f1 (ppm)

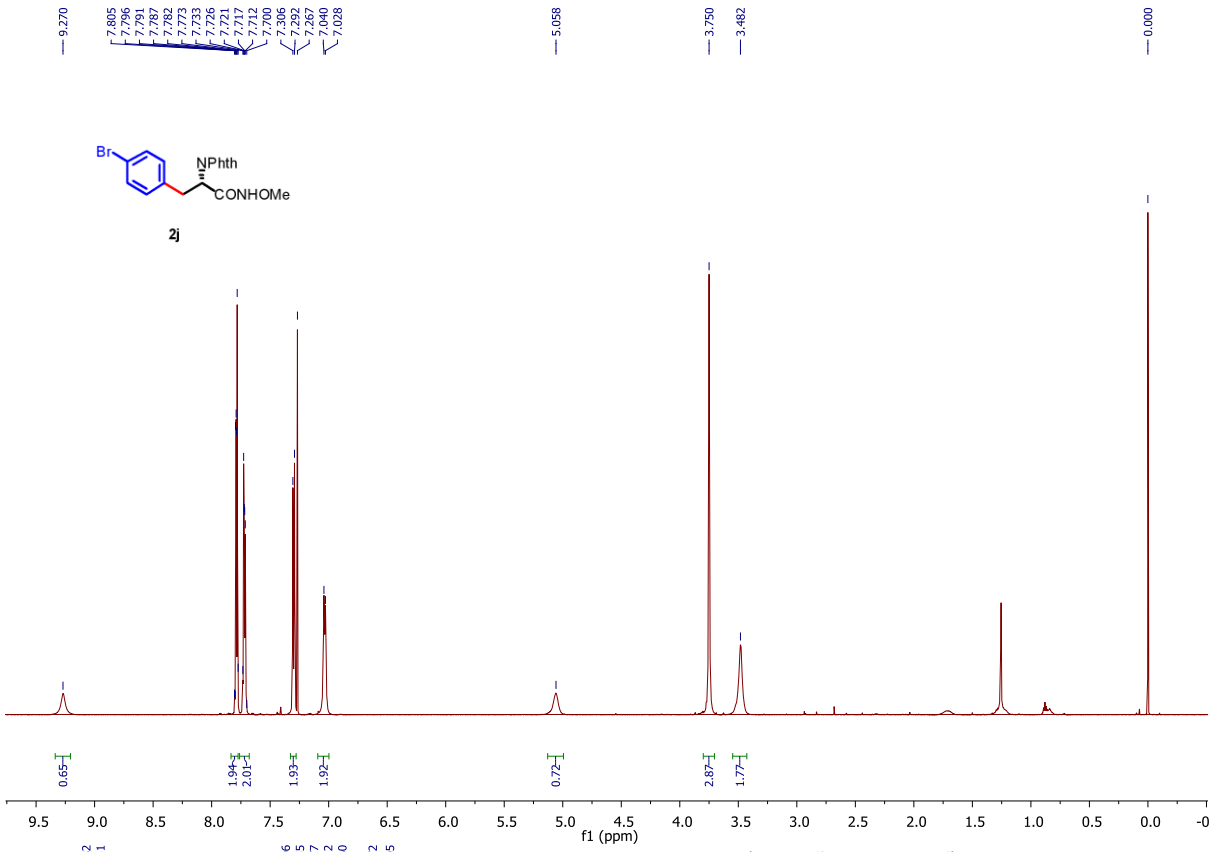

9.437
7.795
7.779
7.774
7.770
7.765
7.758
7.717
7.711
7.706
7.702
7.697
7.677
7.272
7.120
7.111
7.107
7.105
7.097
6.865
6.851
6.837
5.045
3.744
3.560
3.491
3.481
3.403
0.000
F
NPhth
CONHOMe
2g
0.82
1.97
2.05
2.00
2.00
0.96
2.98
2.04
f1 (ppm)
167.841
166.397
162.609
160.983
134.472
131.796
131.169
130.463
130.410
123.631
115.593
115.451
64.504
54.393
33.884
0.002
F
NPhth
CONHOMe
2g
f1 (ppm)

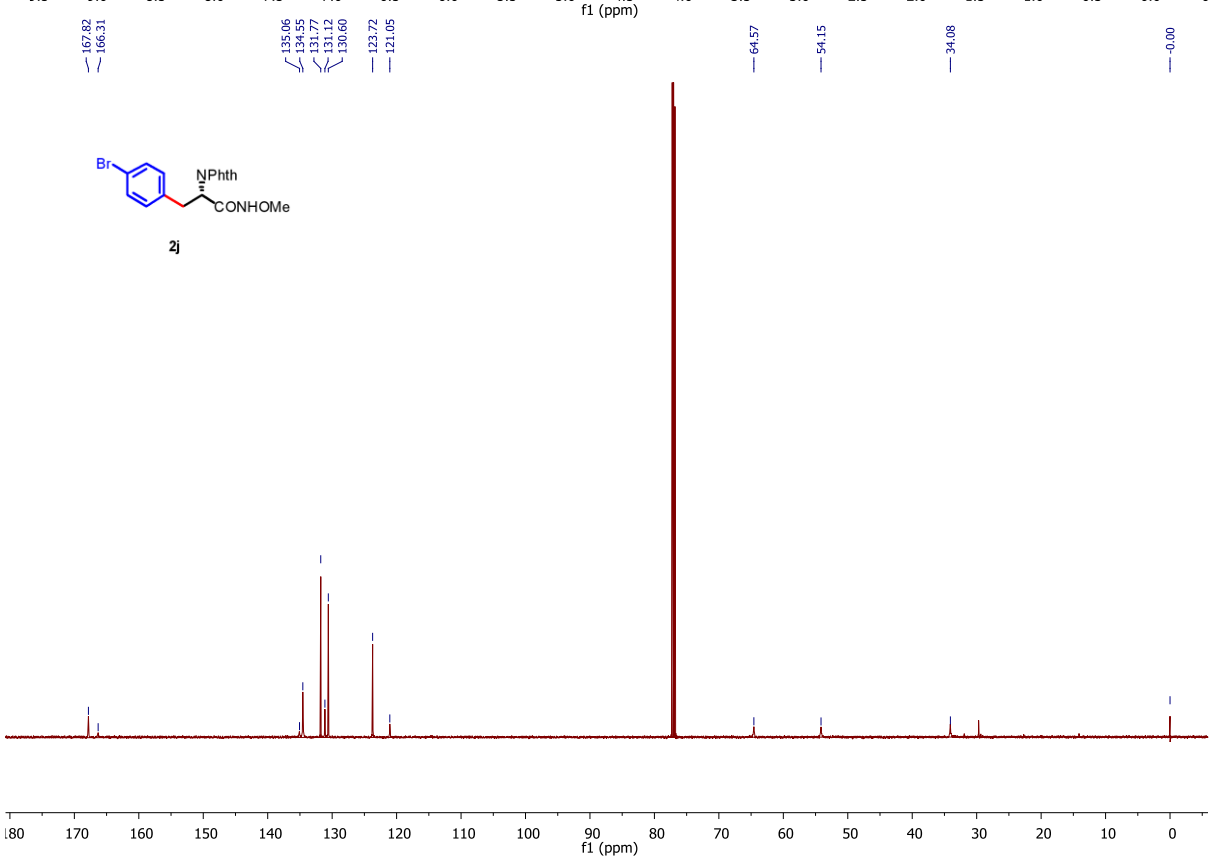

9.468
7.781
7.776
7.772
7.707
7.702
7.698
7.152
7.140
7.129
7.117
6.937
6.925
6.873
6.857
6.830
6.817
6.803
5.051
3.739
3.518
0.000
F
NPhth
CONHOMe
2h
0.88
2.06
2.03
1.05
1.01
1.03
1.10
1.00
3.20
2.19
f1 (ppm)

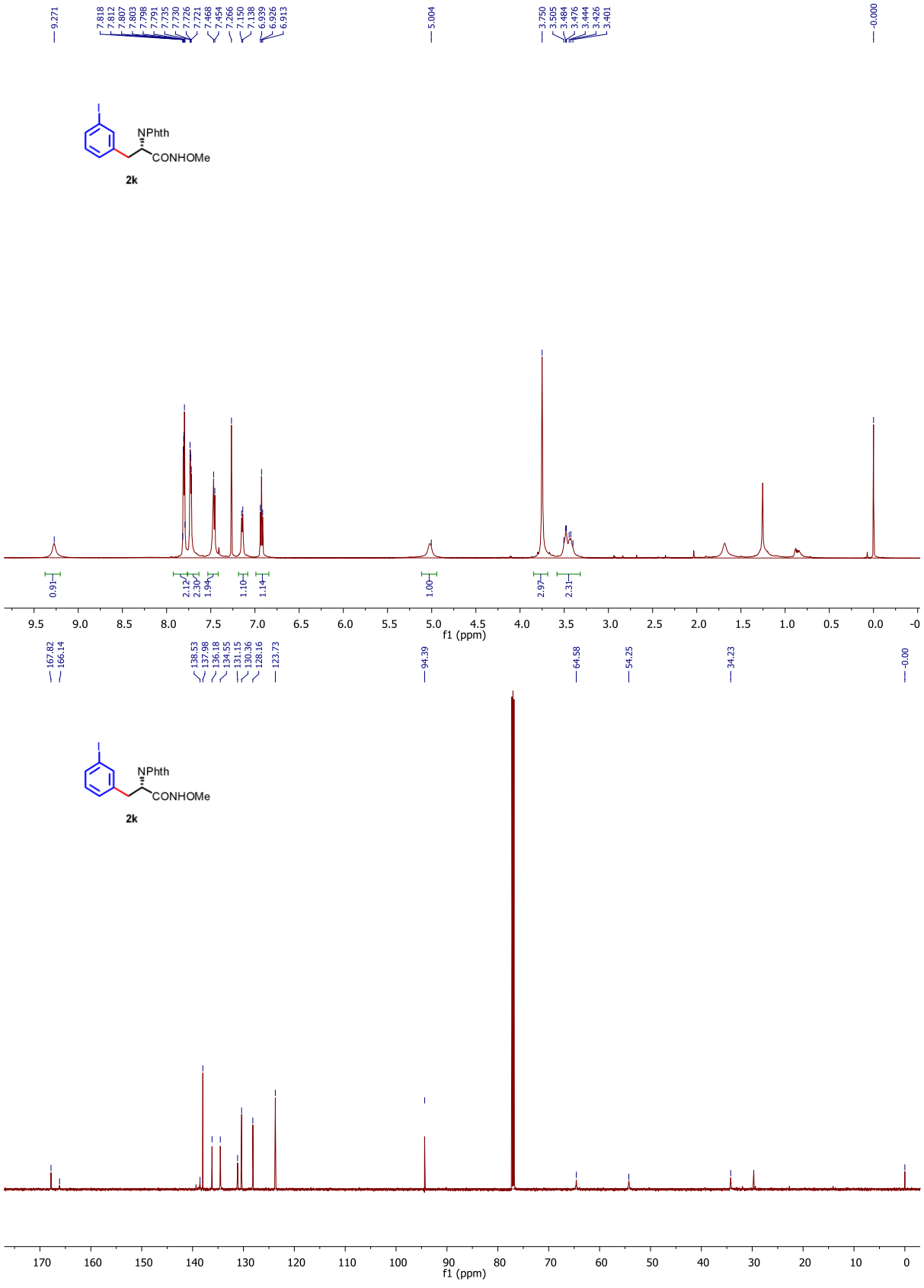

167.797
166.249
163.534
161.900
138.691
134.474
131.189
130.168
130.112
124.583
124.564
123.644
115.962
115.824
114.117
113.978
64.484
54.032
34.337
-0.000
F
NPhth
CONHOMe
2h
f1 (ppm)

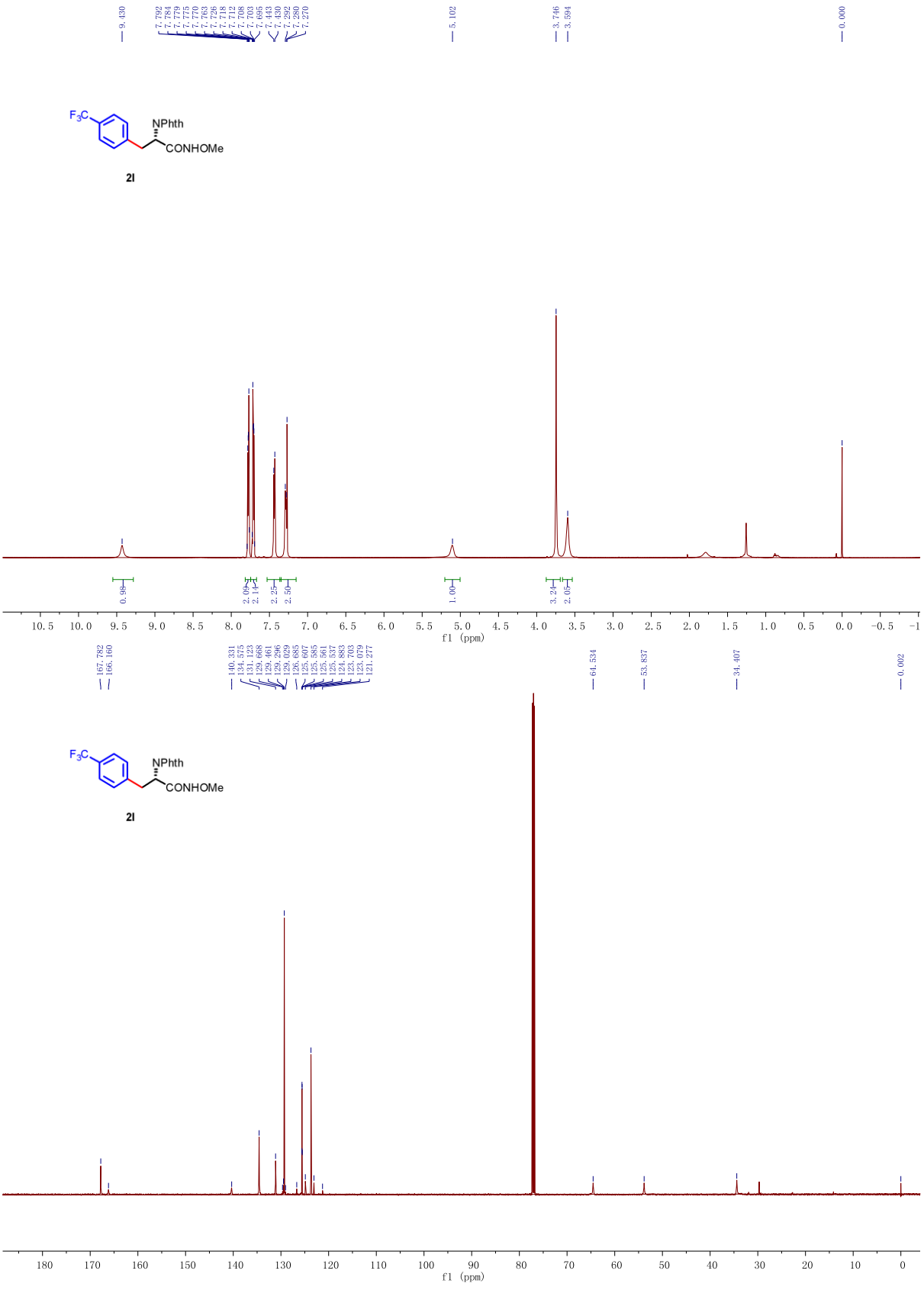

9.331
7.798
7.790
7.785
7.780
7.775
7.767
7.729
7.720
7.715
7.711
7.706
7.698
7.268
7.150
7.136
7.094
7.081
5.042
3.747
3.489
1.254
0.000
Cl
NPhth
CONHOMe
2i
0.83
2.06
2.08
2.04
2.00
0.98
3.00
2.30
f1 (ppm)

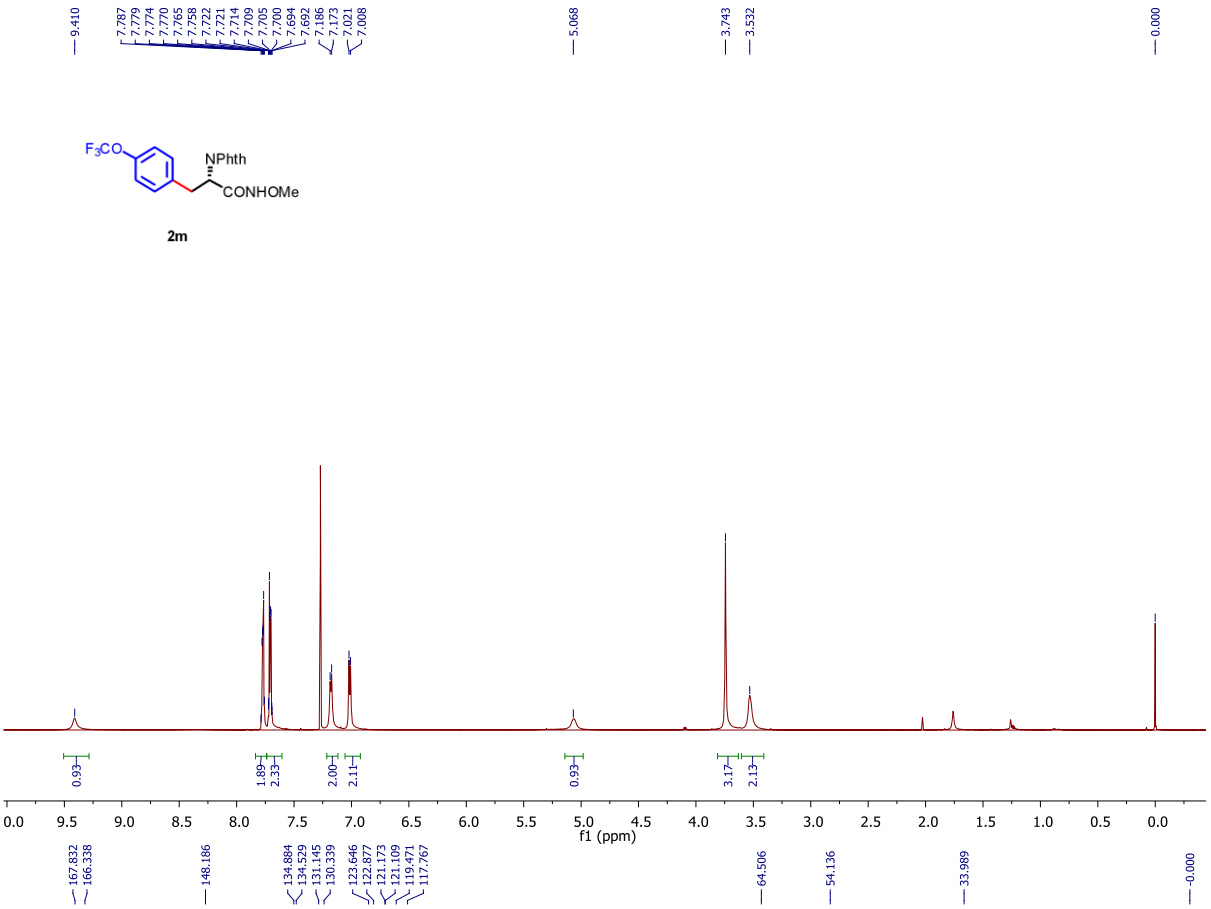

167.82
166.33
134.53
132.92
131.14
130.24
128.81
123.70
64.55
54.19
34.00
0.00
Cl
NPhth
CONHOMe
2i
f1 (ppm)


9.270
7.805
7.796
7.791
7.787
7.782
7.773
7.733
7.726
7.721
7.717
7.712
7.700
7.306
7.292
7.267
7.040
7.028
5.058
3.750
3.482
0.000
Br
NPhth
CONHOMe
2j
0.65
1.94
2.01
1.93
1.92
0.72
2.87
1.77
f1 (ppm)


167.82
166.31
135.06
134.55
131.77
131.12
130.60
123.72
121.05
64.57
54.15
34.08
-0.00
Br
NPhth
CONHOMe
2j
f1 (ppm)


9.271
7.818
7.812
7.807
7.803
7.798
7.791
7.735
7.730
7.726
7.721
7.468
7.454
7.266
7.150
7.138
6.939
6.926
6.913
5.004
3.750
3.505
3.484
3.476
3.444
3.426
3.401
-0.000
NPhth
CONHOMe
2k
0.91
2.12
2.30
1.94
1.10
1.14
1.00
2.97
2.31
f1 (ppm)
167.82
166.14
138.53
137.98
136.18
134.55
131.15
130.36
128.16
123.73
94.39
64.58
54.25
34.23
-0.00
NPhth
CONHOMe
2k
f1 (ppm)


9.430
7.792
7.784
7.779
7.775
7.770
7.763
7.726
7.718
7.712
7.708
7.701
7.695
7.443
7.430
7.292
7.280
7.270
5.102
3.746
3.594
0.000
F3C
NPhth
CONHOMe
2l
0.89
2.09
2.14
2.25
2.50
1.00
3.24
2.07
f1 (ppm)
167.782
166.160
140.331
134.575
131.123
129.668
129.461
129.296
129.029
126.685
125.607
125.585
125.561
125.537
124.883
123.703
123.079
121.277
64.534
53.837
34.407
0.002
f1 (ppm)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7.779
7.774
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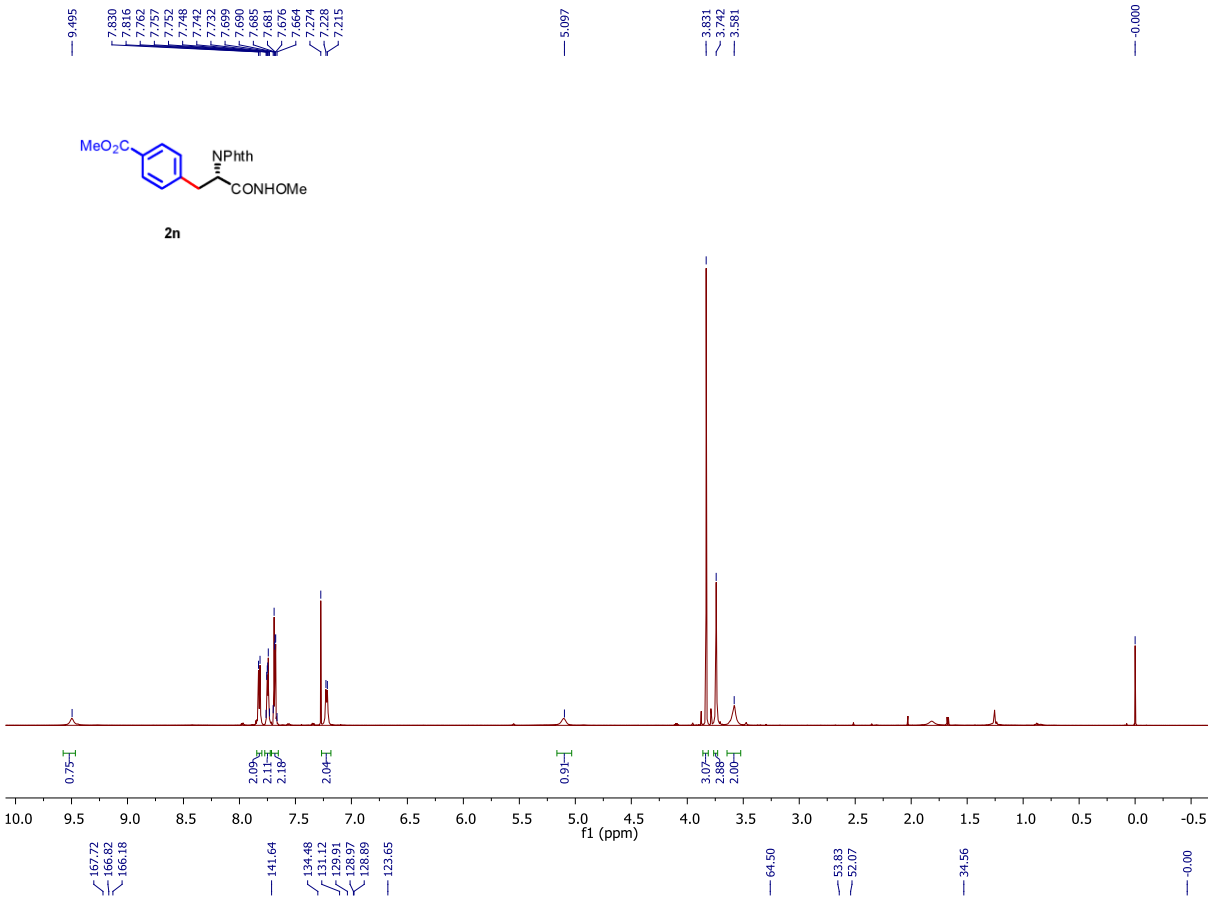
7.765
7.758
7.722
7.721
7.714
7.709
7.705
7.700
7.694
7.692
7.186
7.173
7.021
7.008
5.068
3.743
3.532
0.000
F3CO
NPhth
CONHOMe
2m
0.93
1.89
2.33
2.00
2.11
0.93
3.17
2.13
f1 (ppm)
167.832
166.338
148.186
134.884
134.529
131.145
130.339
123.646
122.877
121.173
121.109
119.471
117.767
64.506
54.136
33.989
-0.000
f1 (ppm)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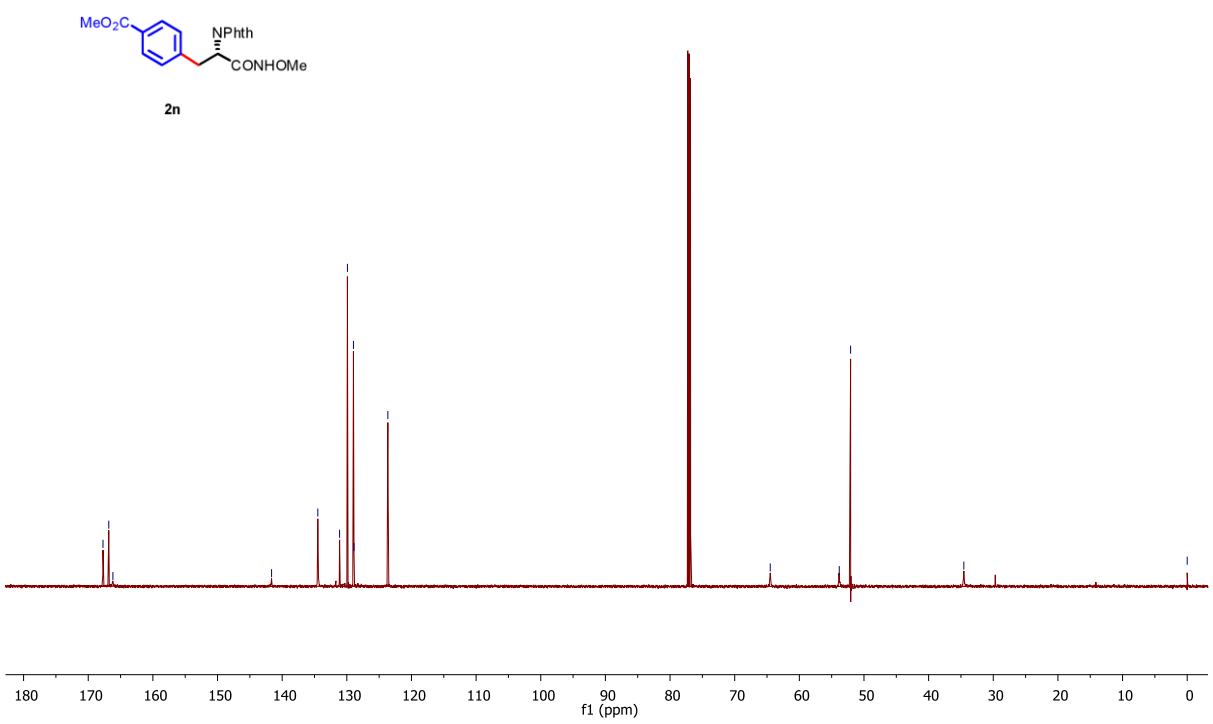
7.830
7.816
7.762
7.757
7.752
7.748
7.742
7.732
7.699
7.690
7.685
7.681
7.676
7.664
7.274
7.228
7.215
5.097
3.831
3.742
3.581
-0.000
MeO2C
NPhth
CONHOMe
2n
0.75
2.09
2.11
2.18
2.04
0.91
3.07
2.88
2.00
f1 (ppm)


167.72
166.82
166.18
141.64
134.48
131.12
129.91
128.97
128.89
123.65
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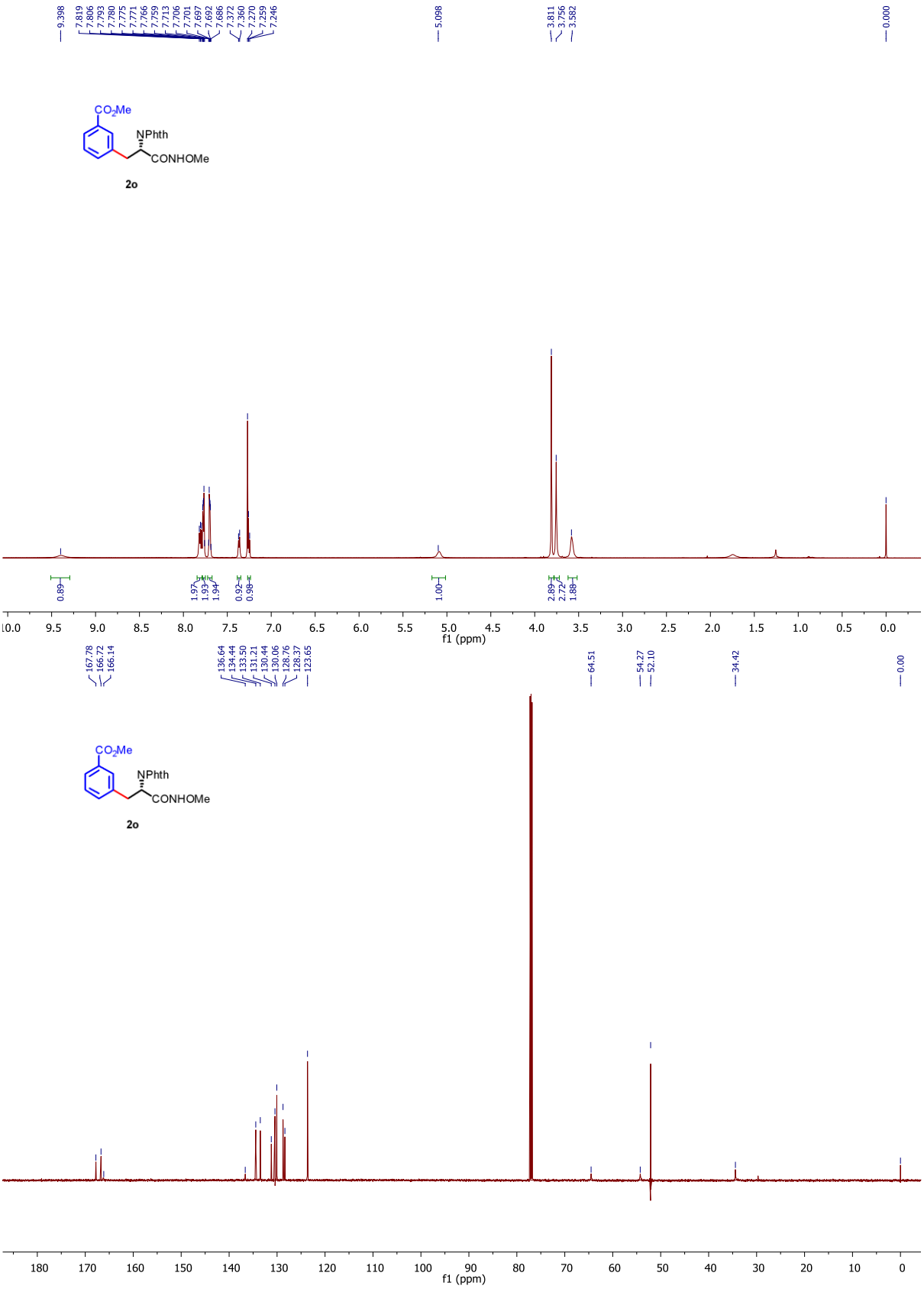
53.83
52.07
34.56
-0.00
MeO2C
NPhth
CONHOMe
2n
f1 (ppm)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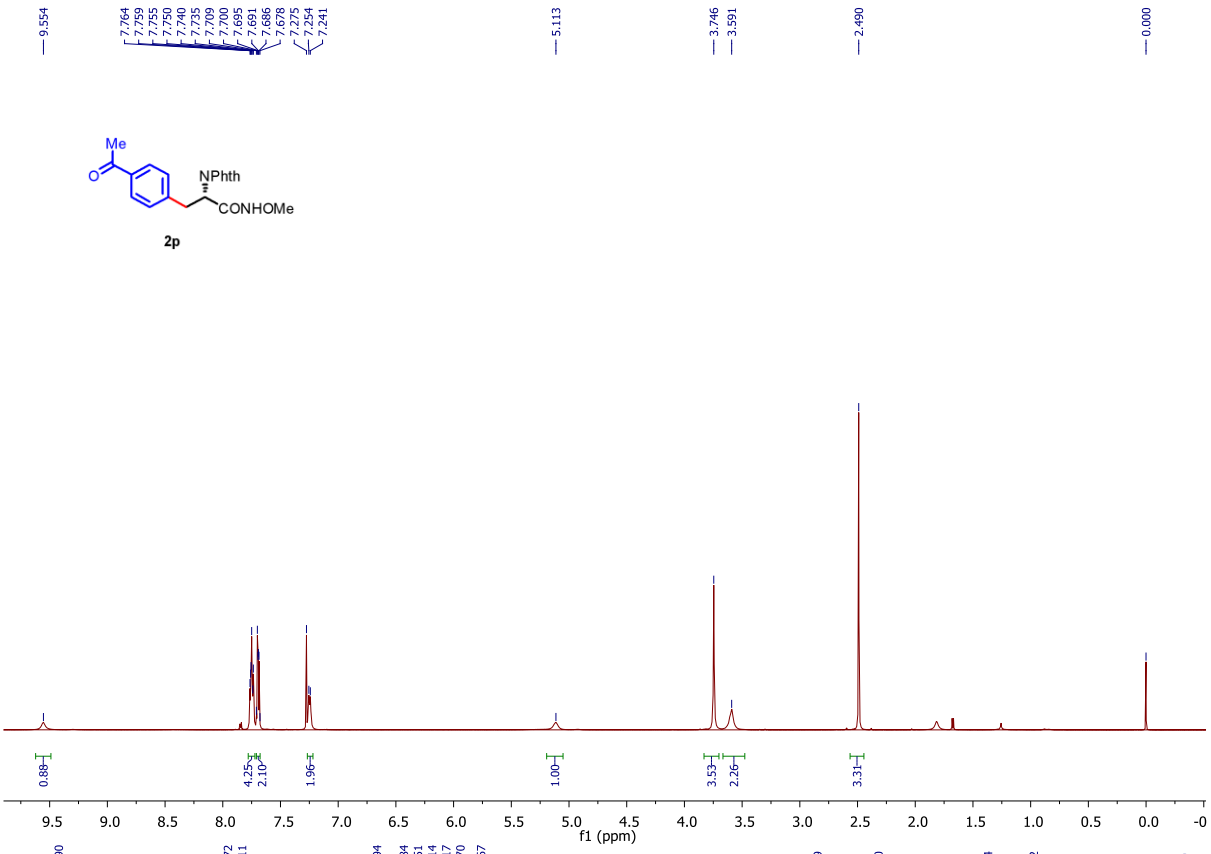
7.806
7.793
7.780
7.775
7.771
7.766
7.759
7.713
7.706
7.701
7.697
7.692
7.686
7.372
7.360
7.270
7.259
7.246
5.098
3.811
3.756
3.582
0.000
CO2Me
NPhth
CONHOMe
2o
0.89
1.97
1.93
1.94
0.92
0.98
1.00
2.89
2.72
1.88
f1 (ppm)
167.78
166.72
166.14
136.64
134.44
133.50
131.21
130.44
130.06
128.76
128.37
123.65
64.51
54.27
52.10
34.42
0.00
CO2Me
NPhth
CONHOMe
2o
f1 (ppm)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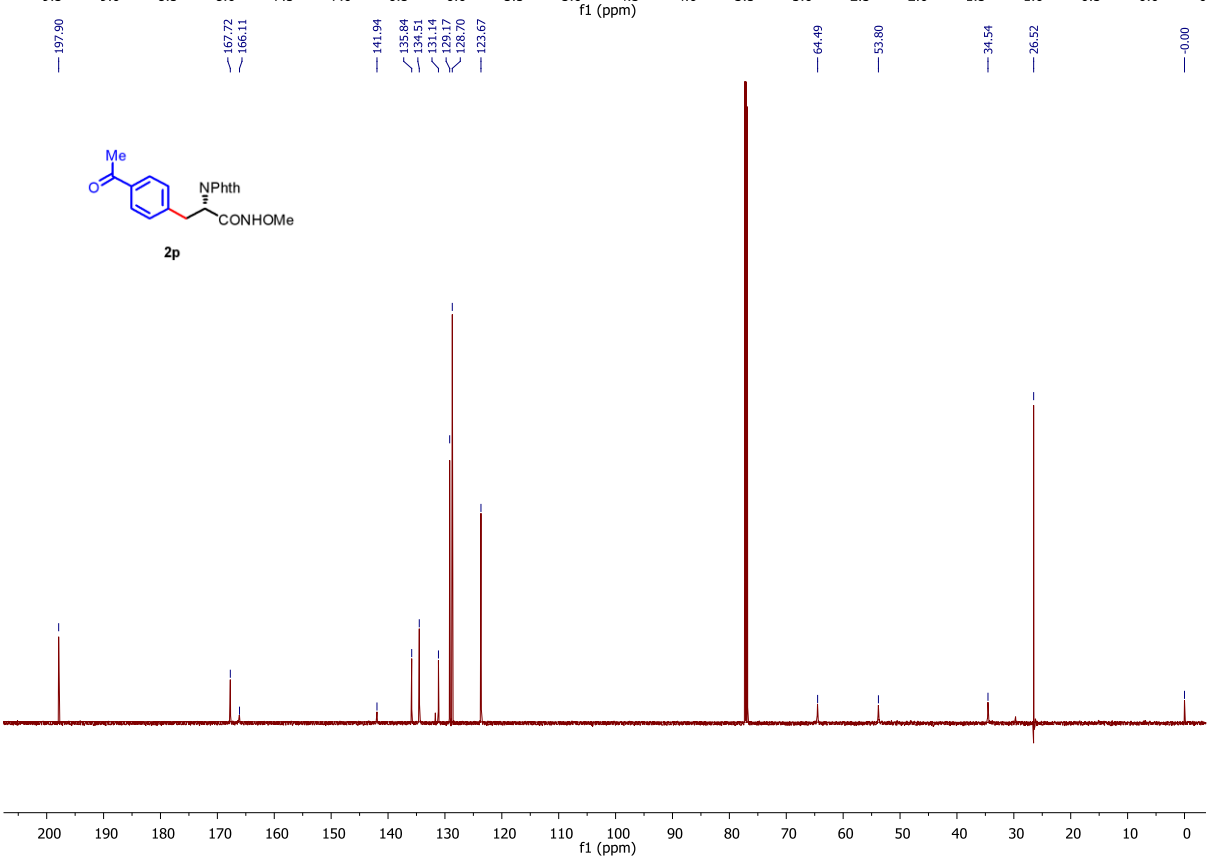
7.759
7.755
7.750
7.740
7.735
7.709
7.700
7.695
7.691
7.686
7.678
7.275
7.254
7.241
5.113
3.746
3.591
2.490
0.000
Me
NPhth
CONHOMe
2p
0.88
4.25
2.10
1.96
1.00
3.53
2.26
3.31
f1 (ppm)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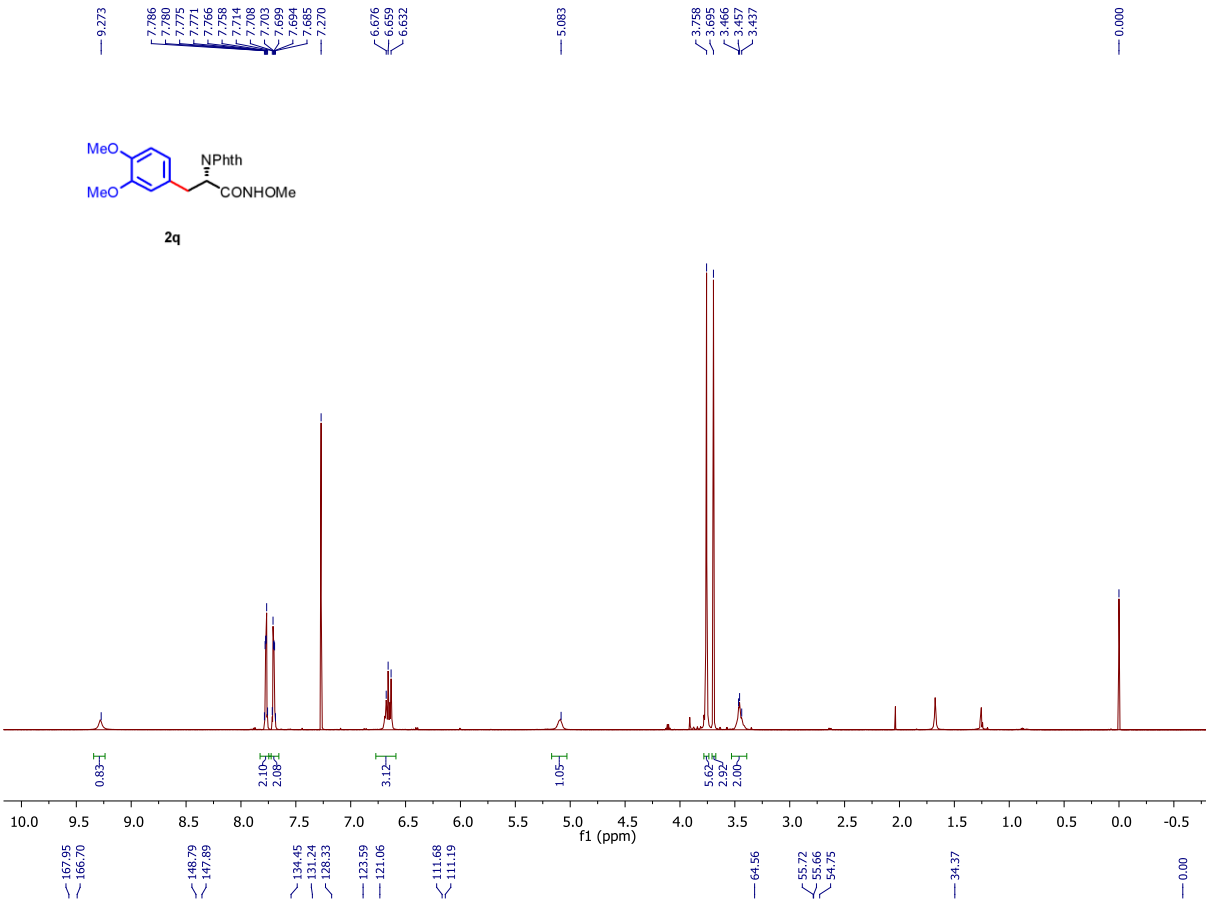
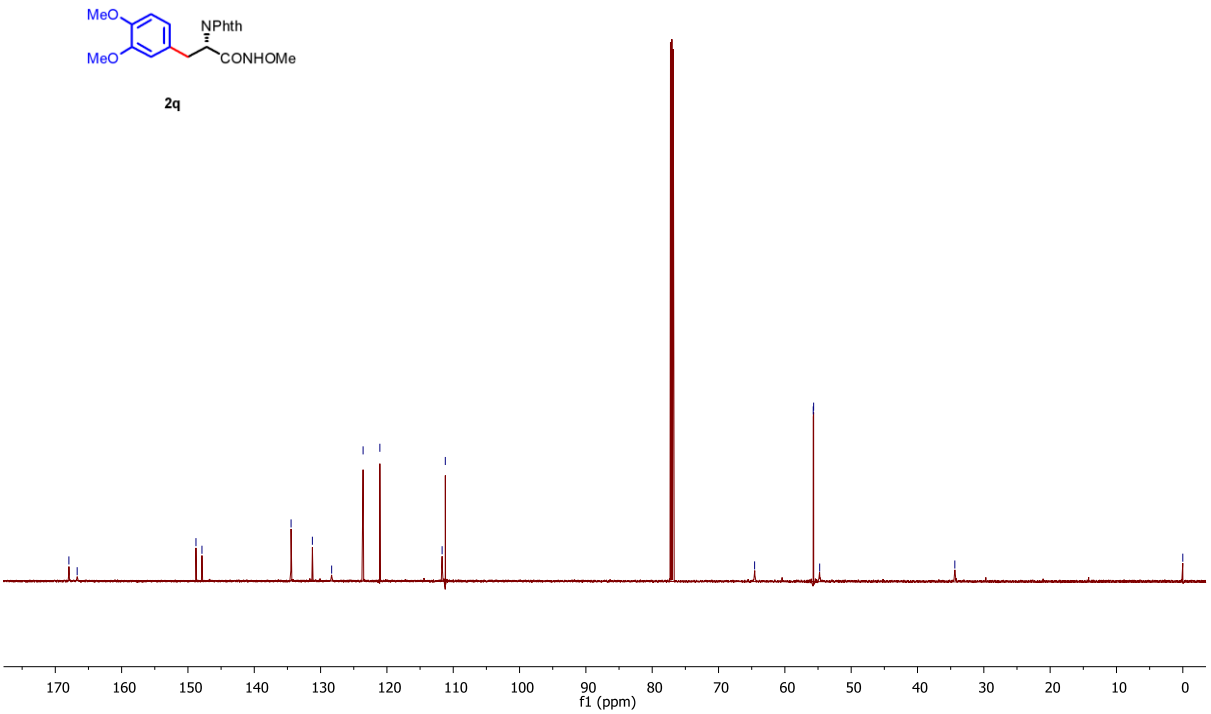
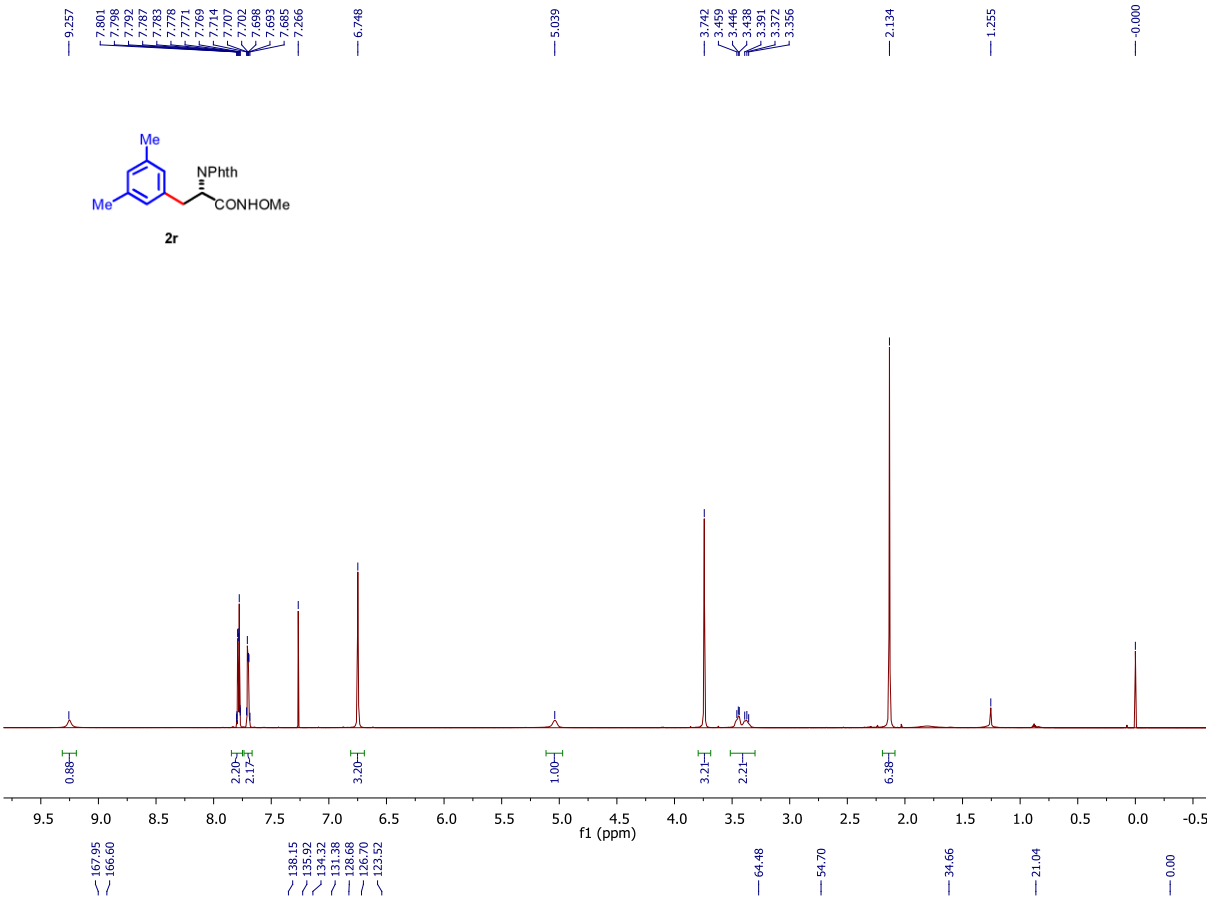
167.72
166.11
141.94
135.84
134.51
131.14
129.17
128.70
123.67
64.49
53.80
34.54
26.52
-0.00
Me
NPhth
CONHOMe
2p
f1 (ppm)


9.273
7.786
7.780
7.775
7.771
7.766
7.758
7.714
7.708
7.703
7.699
7.694
7.685
7.270
6.676
6.659
6.632
5.083
3.758
3.695
3.466
3.457
3.437
0.000
MeO
MeO
NPhth
CONHOMe
2q
0.83
2.10
2.08
3.12
1.05
5.62
2.92
2.00
f1 (ppm)
167.95
166.70
148.79
147.89
134.45
131.24
128.33
123.59
121.06
111.68
111.19
64.56
55.72
55.66
54.75
34.37
0.00


MeO
MeO
NPhth
CONHOMe
2q
f1 (ppm)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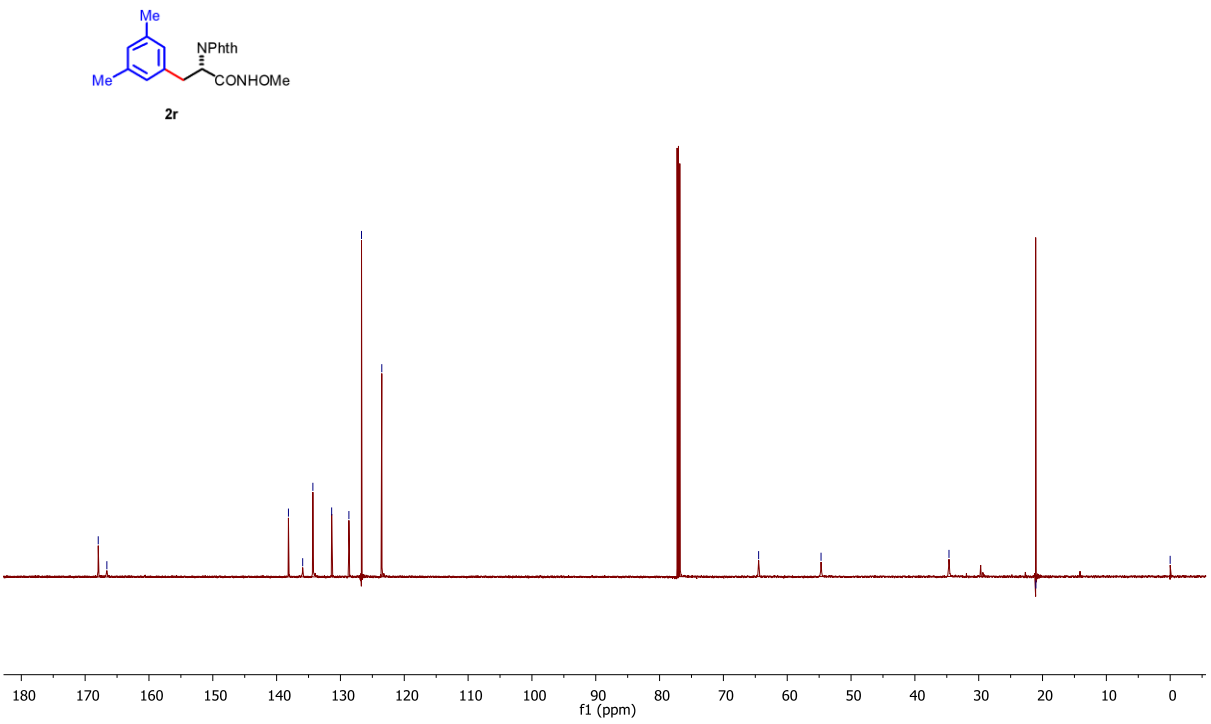
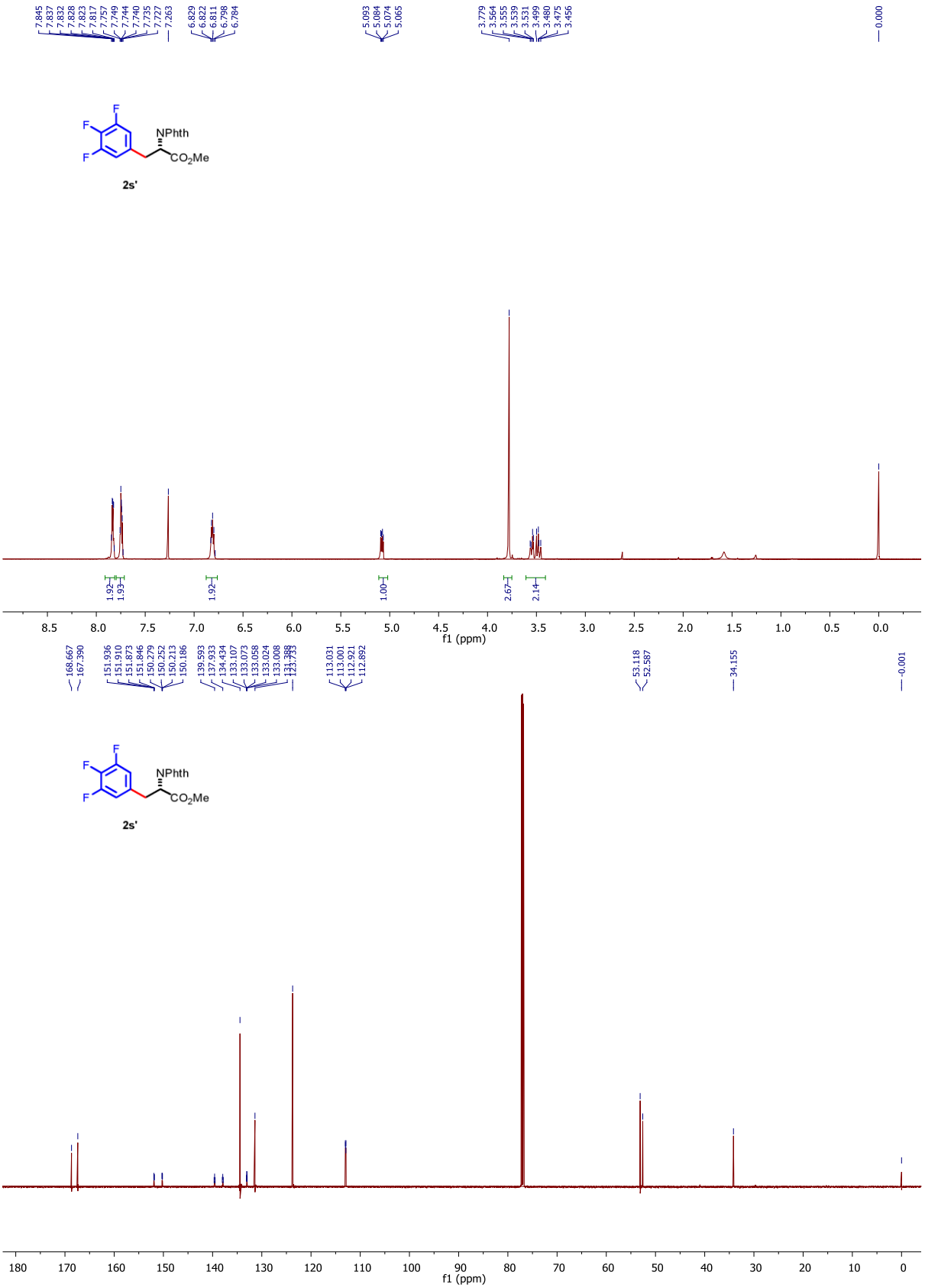
7.801
7.798
7.792
7.787
7.783
7.778
7.771
7.769
7.714
7.707
7.702
7.698
7.693
7.685
7.266
6.748
5.039
3.742
3.459
3.446
3.438
3.391
3.372
3.356
2.134
1.255
-0.000
Me
NPhth
Me
CONHOMe
2r
0.88
2.20
2.17
3.20
1.00
3.21
2.21
6.38
f1 (ppm)


167.95
166.60
138.15
135.92
134.32
131.38
128.68
126.70
123.52
64.48
54.70
34.66
21.04
0.00
Me
NPhth
Me
CONHOMe
2r
f1 (ppm)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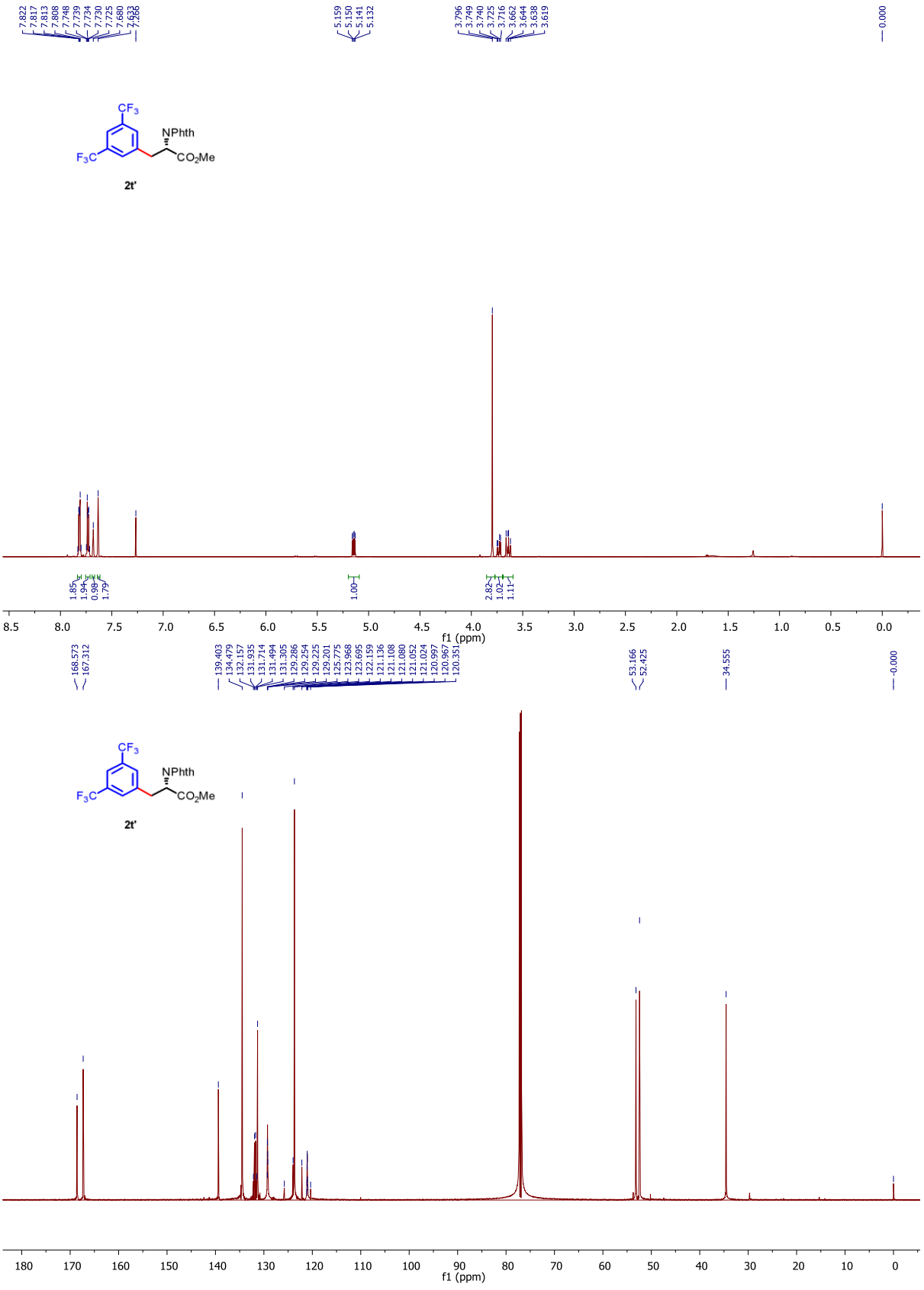
7.837
7.832
7.828
7.823
7.817
7.757
7.749
7.744
7.740
7.735
7.727
7.263
6.829
6.822
6.811
6.798
6.784
5.093
5.084
5.074
5.065
3.779
3.564
3.555
3.539
3.531
3.499
3.480
3.475
3.456
0.000
F
F
F
NPhth
CO2Me
2s'
1.92
1.93
1.92
1.00
2.67
2.14
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
168.667
167.390
151.936
151.910
151.873
151.846
150.279
150.252
150.213
150.186
139.593
137.933
134.434
133.107
133.073
133.058
133.024
133.008
123.733
113.031
113.001
112.921
112.892
53.118
52.587
34.155
-0.001
F
F
F
NPhth
CO2Me
2s'
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.822
7.817
7.813
7.808
7.748
7.739
7.734
7.730
7.725
7.680
7.633
7.266
5.159
5.150
5.141
5.132
3.796
3.749
3.740
3.725
3.716
3.662
3.644
3.638
3.619
0.000
CF3
NPhth
F3C
CO2Me
2t'
1.85
1.94
0.98
1.79
1.00
2.82
1.02
1.11
f1 (ppm)
168.573
167.312
139.403
134.479
132.157
131.935
131.714
131.494
131.305
129.286
129.254
129.225
129.201
125.775
123.968
123.695
122.159
121.136
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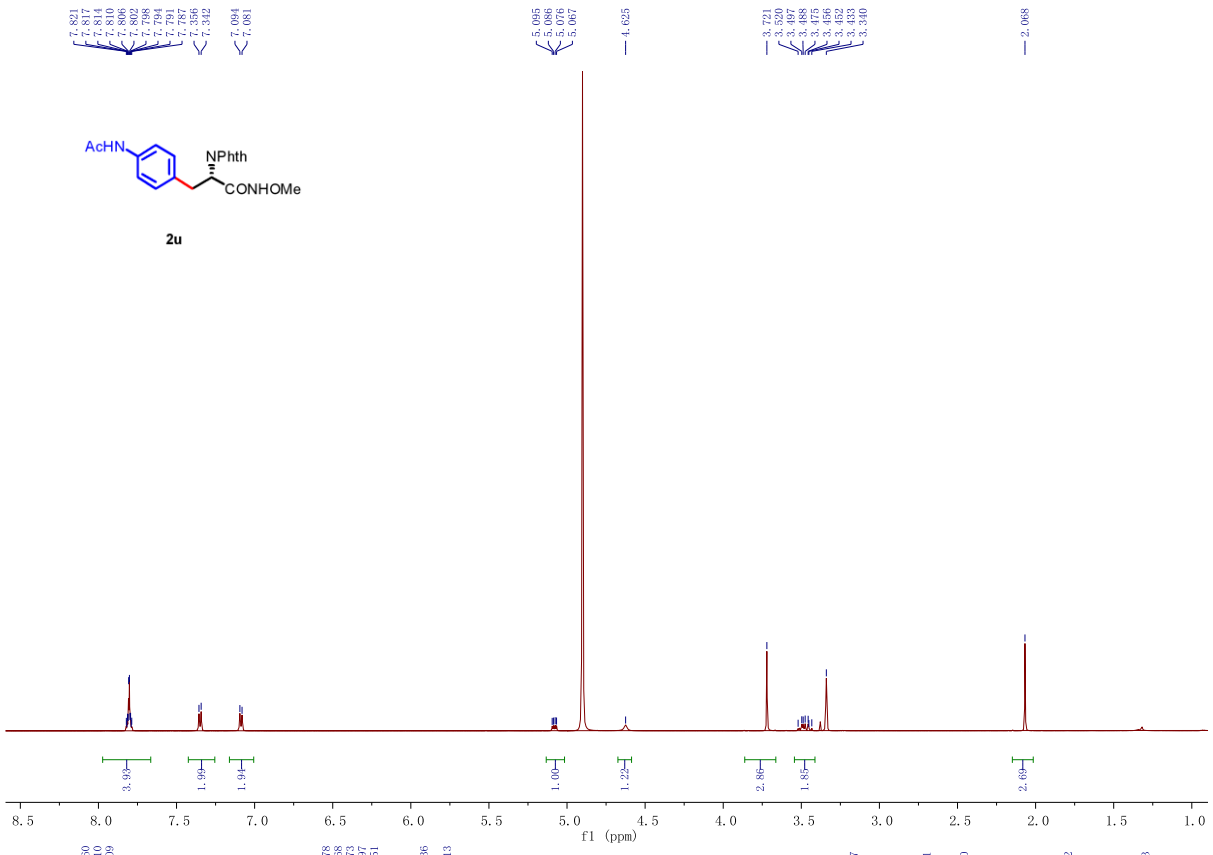
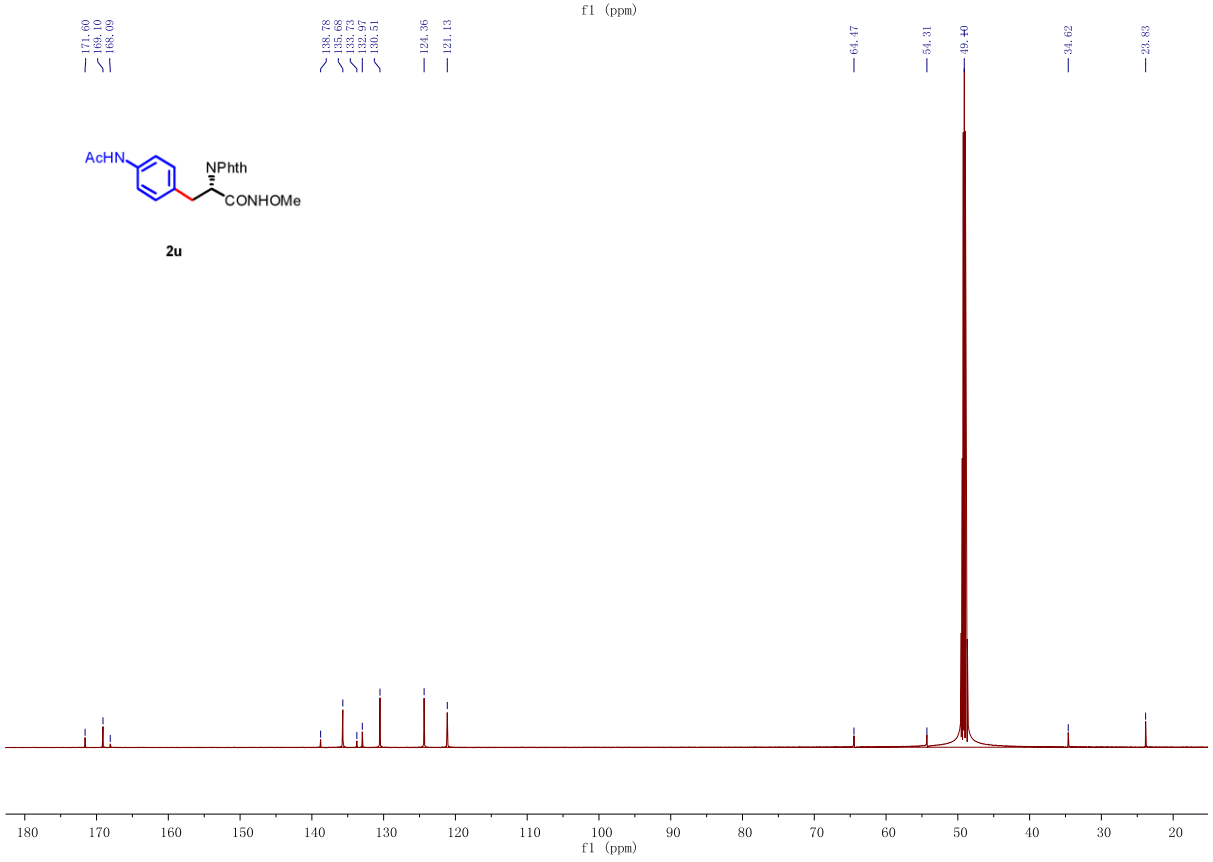
121.080
121.052
121.024
120.997
120.967
120.351
53.166
52.425
34.555
-0.000
f1 (ppm)


7.821
7.817
7.814
7.810
7.806
7.802
7.798
7.794
7.791
7.787
7.586
7.342
7.094
7.061
5.095
5.086
5.076
5.067
4.625
3.721
3.709
3.497
3.488
3.475
3.456
3.452
3.433
3.340
2.068
AcHN
NPhth
CONHOMe
2u
3.93
1.99
1.94
1.00
1.22
2.88
1.85
2.69
f1 (ppm)


171.60
169.10
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138.78
135.68
133.73
132.97
130.51
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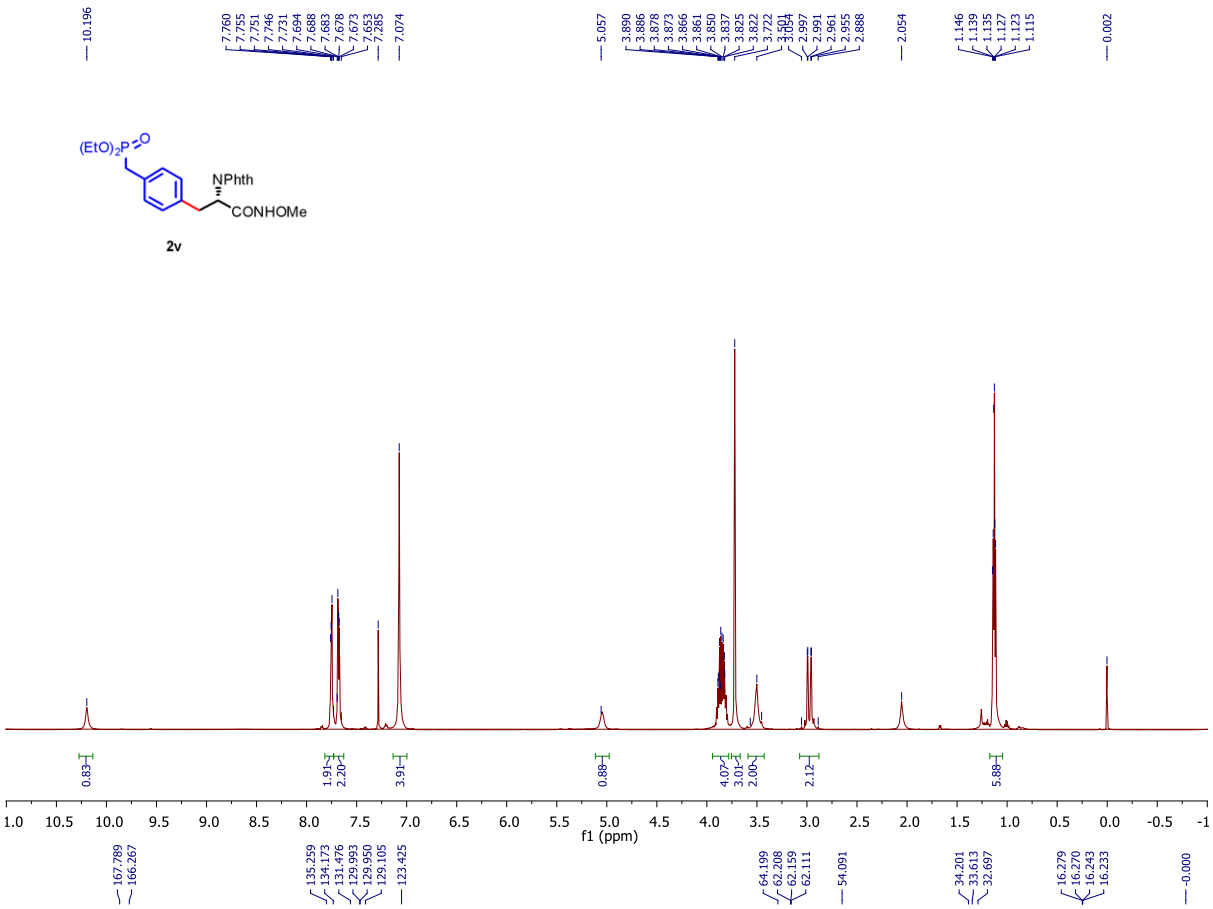
121.13
64.47
54.31
49.40
34.62
23.83
AcHN
NPhth
CONHOMe
2u
f1 (ppm)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7.755
7.751
7.746
7.731
7.694
7.688
7.683
7.678
7.673
7.653
7.285
7.074
5.057
3.890
3.886
3.878
3.873
3.866
3.861
3.850
3.837
3.825
3.822
3.722
3.054
2.997
2.991
2.961
2.955
2.888
2.054
1.146
1.139
1.135
1.127
1.123
1.115
0.002
(EtO)2P
O
NPhth
CONHOMe
2v
0.83
1.91
2.20
3.91
0.88
4.07
3.01
2.00
2.12
5.88
f1 (ppm)
167.789
166.267
135.259
134.173
131.476
129.993
129.950
129.105
123.425
64.199
62.208
62.159
62.111
54.091
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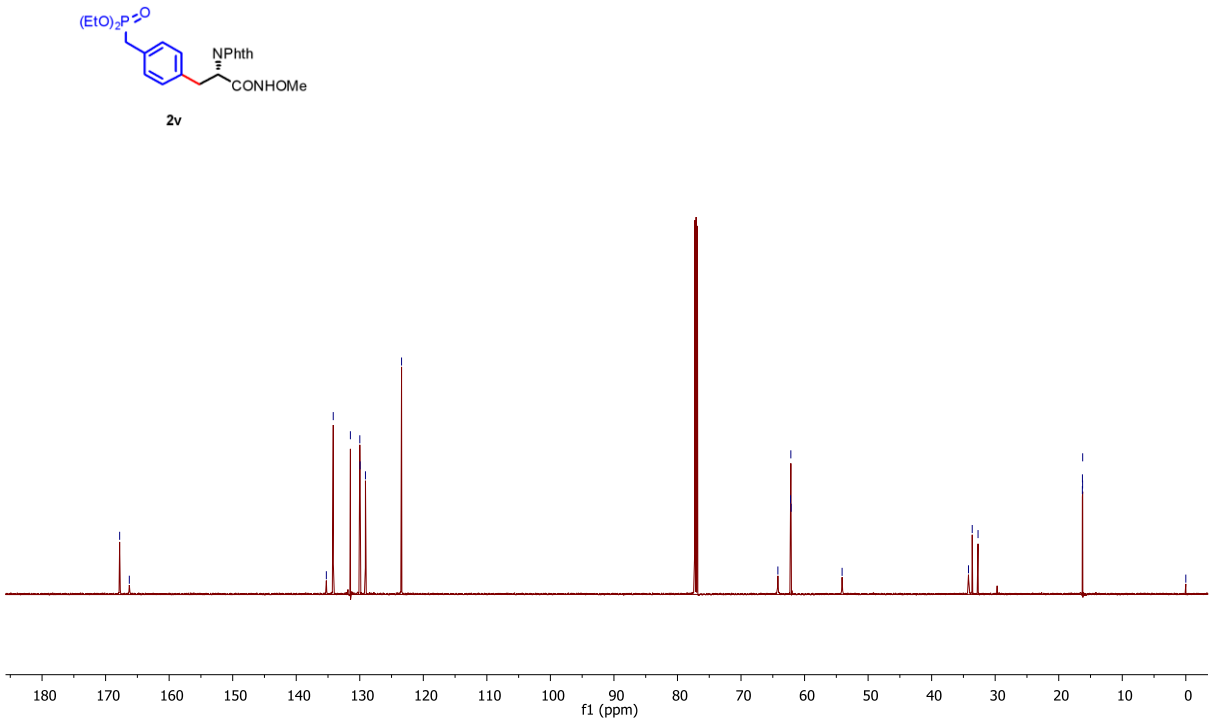
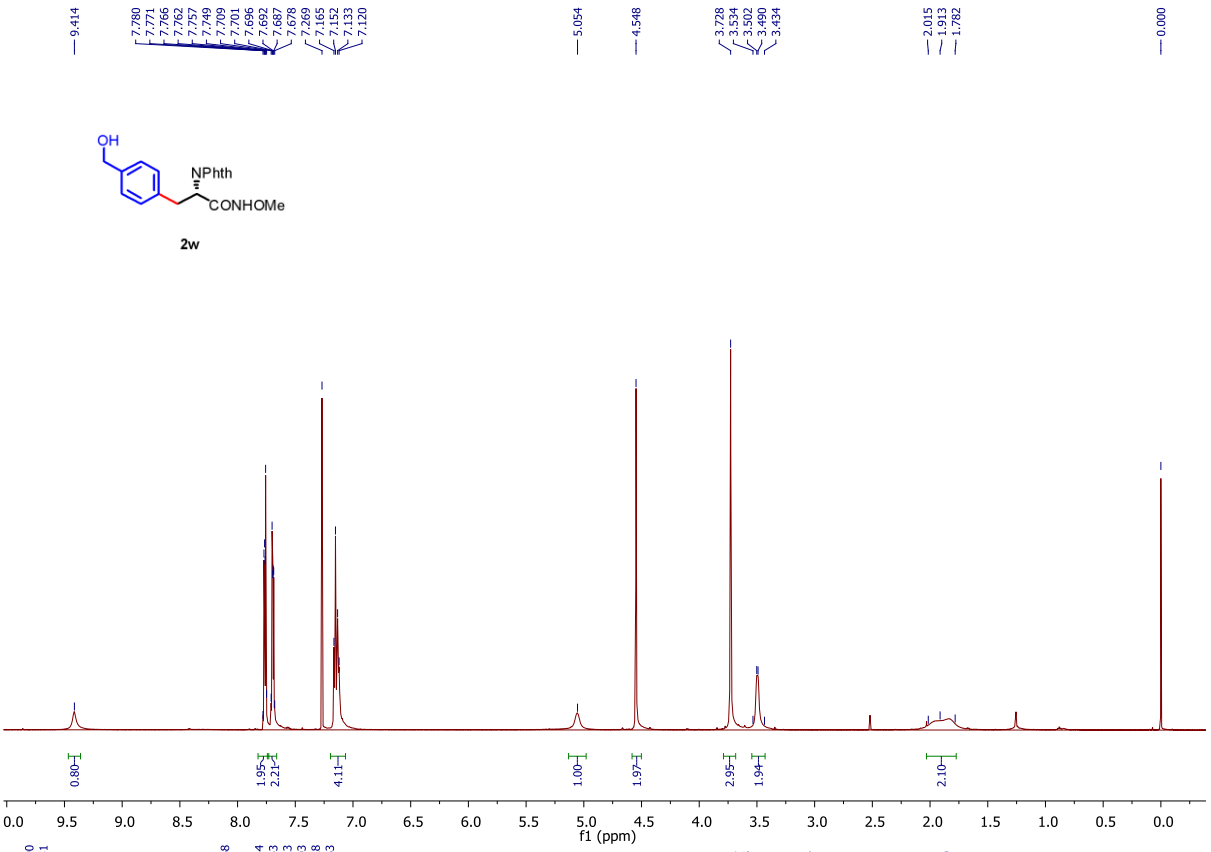
33.613
32.697
16.279
16.270
16.243
16.233
-0.000


(EtO)2P
O
NPhth
CONHOMe
2v
f1 (ppm)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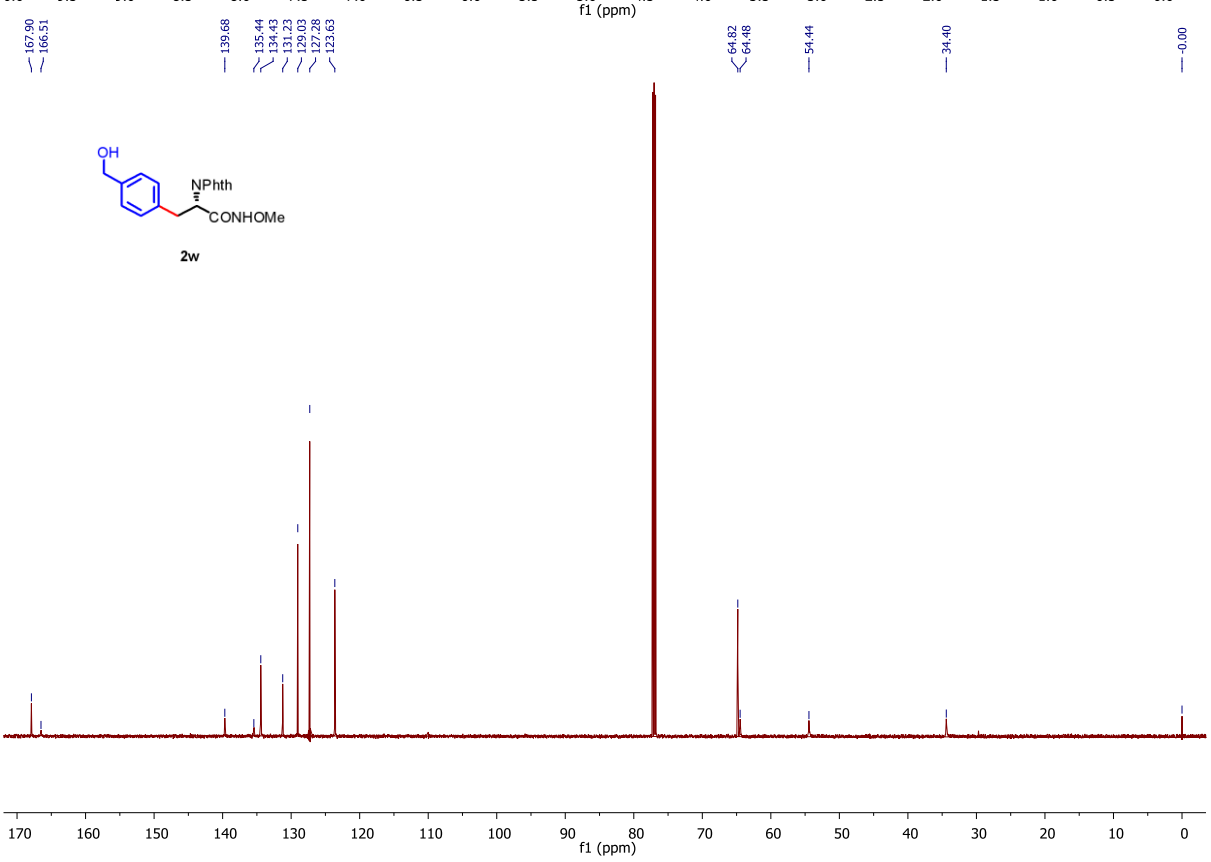
7.771
7.766
7.762
7.757
7.749
7.709
7.701
7.696
7.692
7.687
7.678
7.269
7.165
7.152
7.133
7.120
5.054
4.548
3.728
3.534
3.502
3.490
3.434
2.015
1.913
1.782
0.000
OH
NPhth
CONHOMe
2w
0.80
1.95
2.21
4.11
1.00
1.97
2.95
1.94
2.10
f1 (ppm)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135.44
134.43
131.23
129.03
127.28
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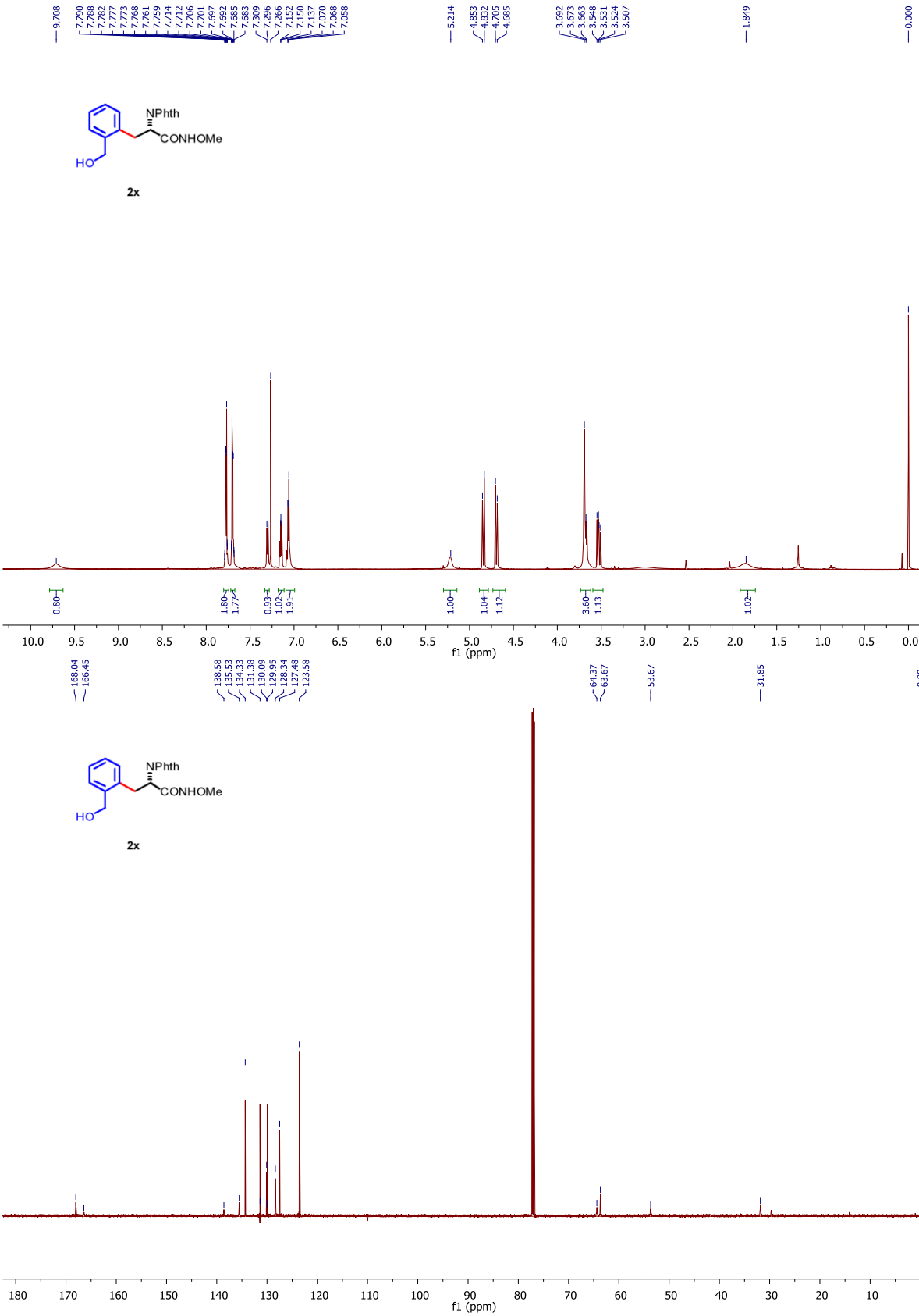
64.48
54.44
34.40
-0.00
OH
NPhth
CONHOMe
2w
f1 (ppm)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7.768
7.761
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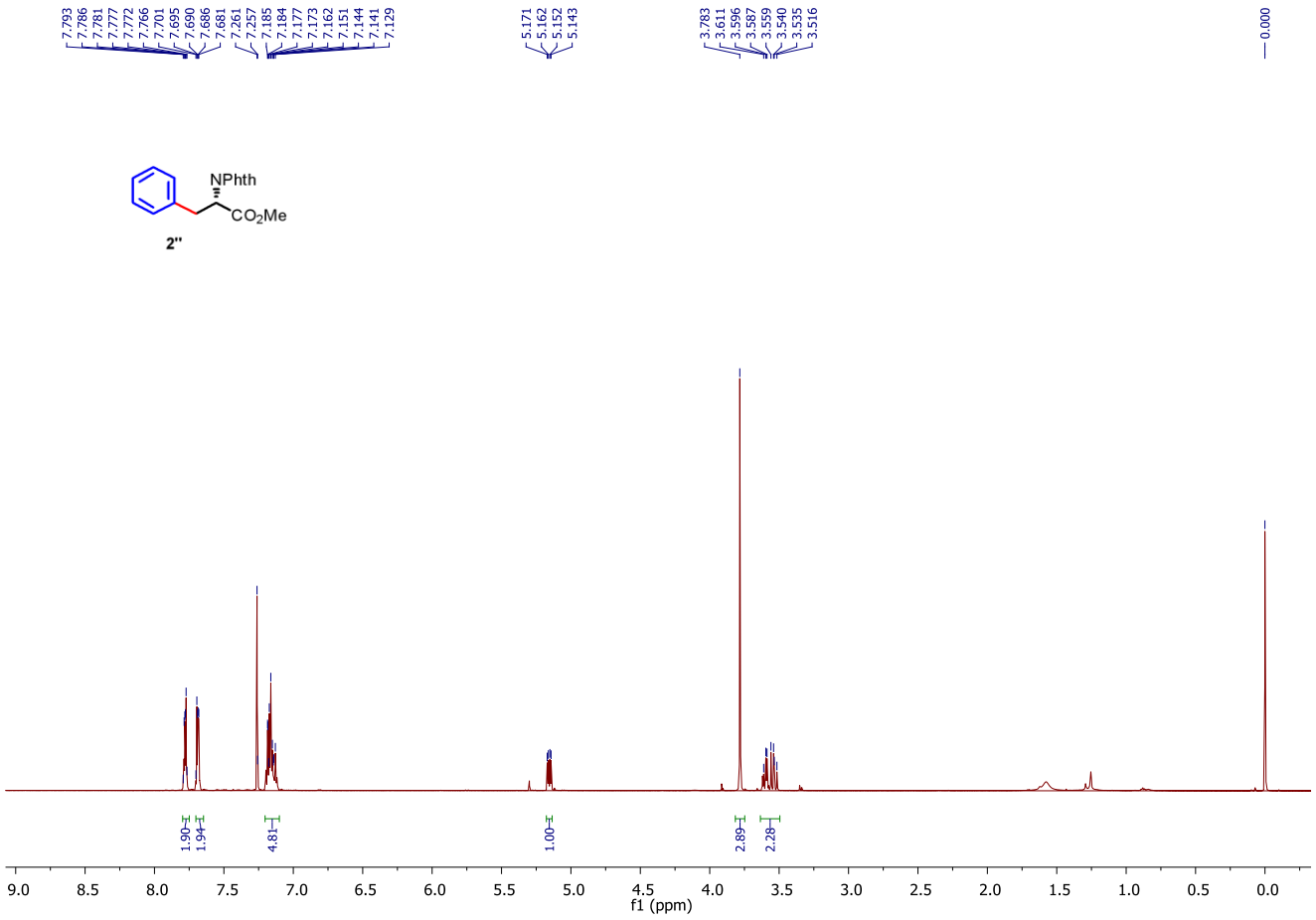
7.714
7.712
7.706
7.701
7.697
7.692
7.685
7.683
7.309
7.296
7.266
7.152
7.150
7.137
7.070
7.068
7.058
5.214
4.853
4.832
4.705
4.685
3.692
3.673
3.663
3.548
3.531
3.524
3.507
1.849
0.000
NPhth
CONHOMe
HO
2x
0.80
1.80
1.77
0.93
1.02
1.91
1.00
1.04
1.12
3.60
1.13
1.02
f1 (ppm)
168.04
166.45
138.58
135.53
134.33
131.38
130.09
129.95
128.34
127.48
123.58
64.37
63.67
53.67
31.85
0.00
NPhth
CONHOMe
HO
2x
f1 (ppm)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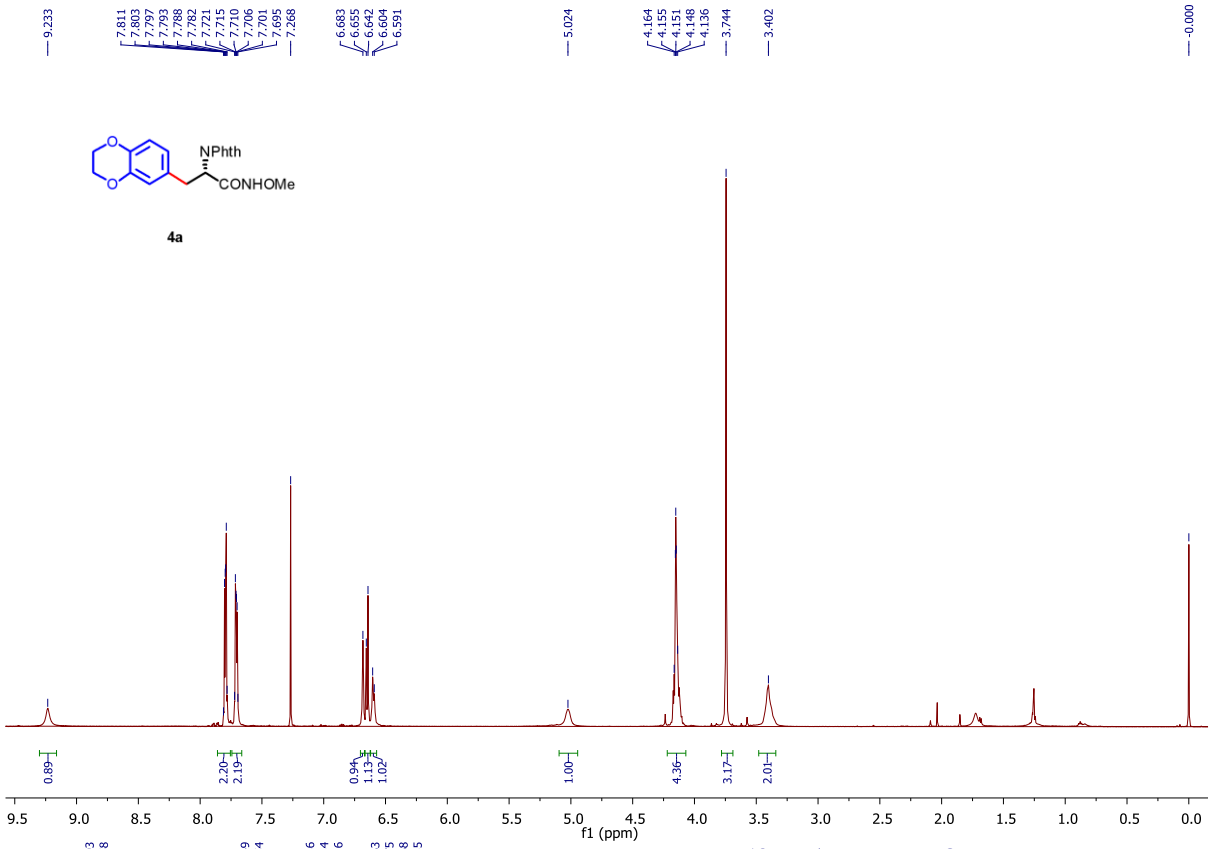
7.766
7.701
7.695
7.690
7.686
7.681
7.261
7.257
7.185
7.184
7.177
7.173
7.162
7.151
7.144
7.141
7.129
5.171
5.162
5.152
5.143
3.783
3.611
3.596
3.587
3.559
3.540
3.535
3.516
0.000
NPhth
CO2Me
2''
1.90
1.94
4.81
1.00
2.89
2.28
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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7.797
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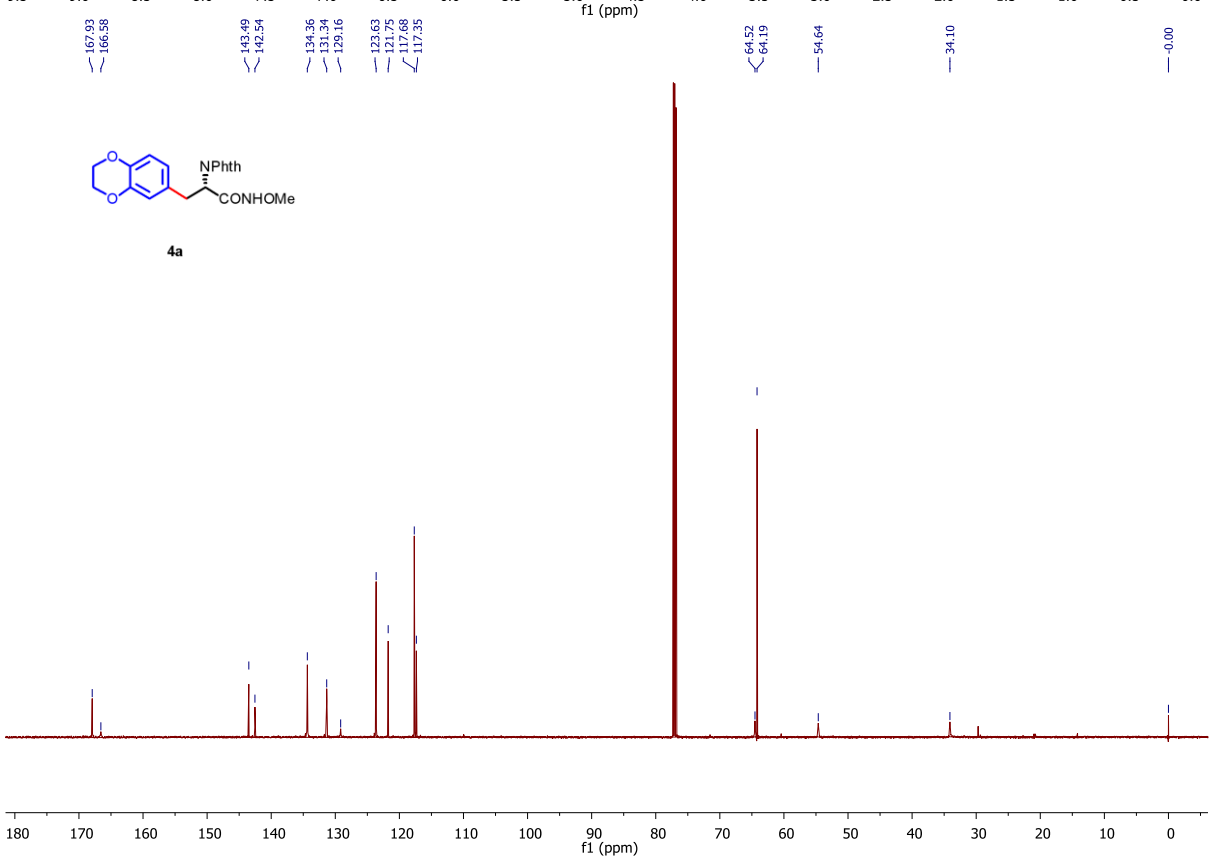
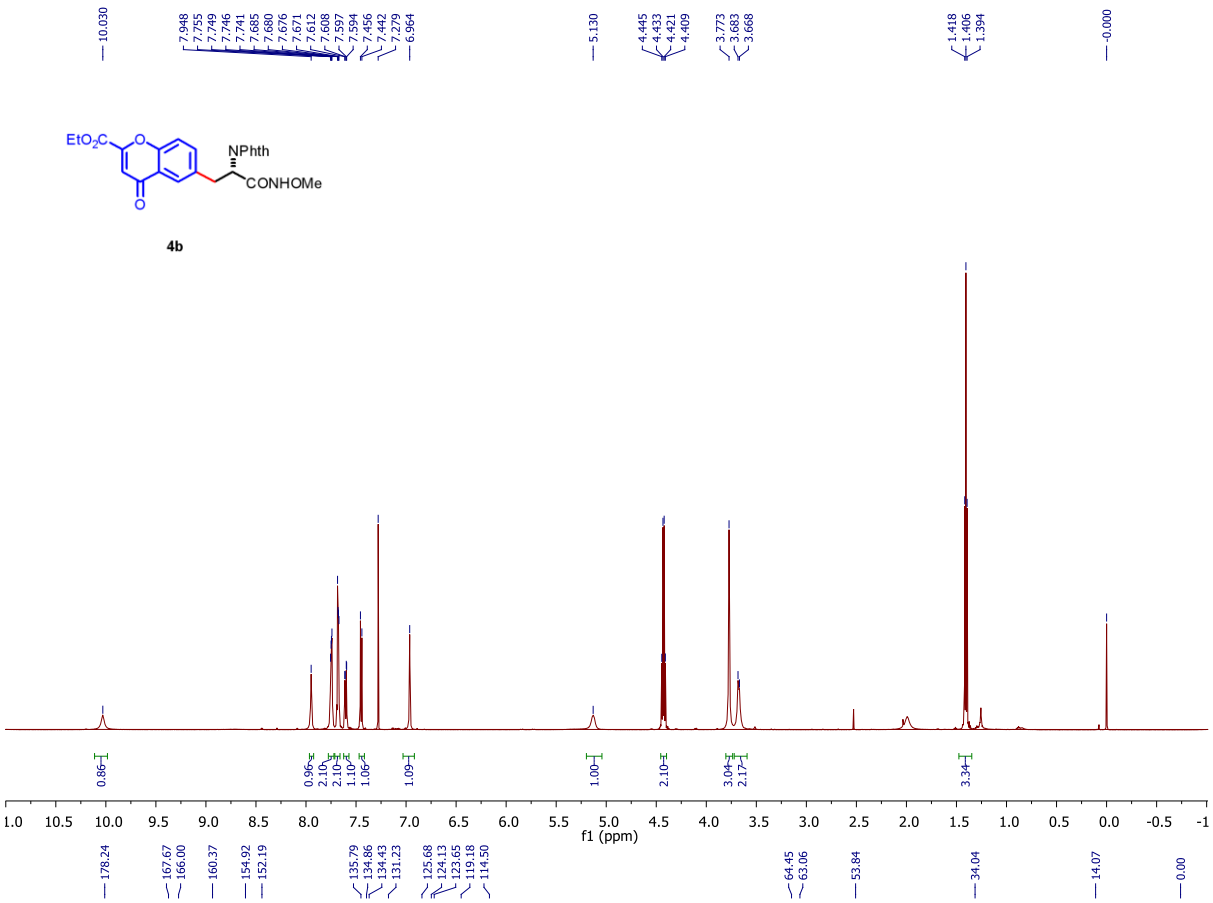
7.788
7.782
7.721
7.715
7.710
7.706
7.701
7.695
7.268
6.683
6.655
6.642
6.604
6.591
5.024
4.164
4.155
4.151
4.148
4.136
3.744
3.402
-0.000
NPhth
CONHOMe
4a
0.89
2.20
2.19
0.94
1.13
1.02
1.00
4.36
3.17
2.01
f1 (ppm)


167.93
166.58
143.49
142.54
134.36
131.34
129.16
123.63
121.75
117.68
117.35
64.52
64.19
54.64
34.10
-0.00
NPhth
CONHOMe
4a
f1 (ppm)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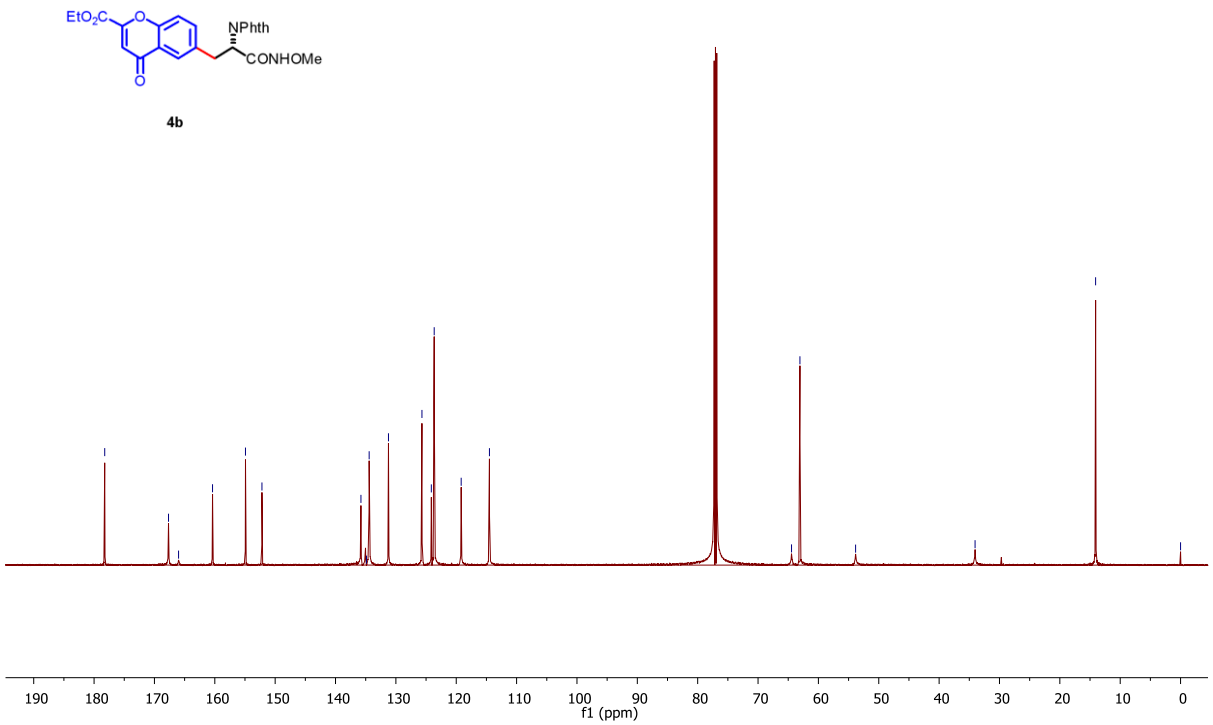
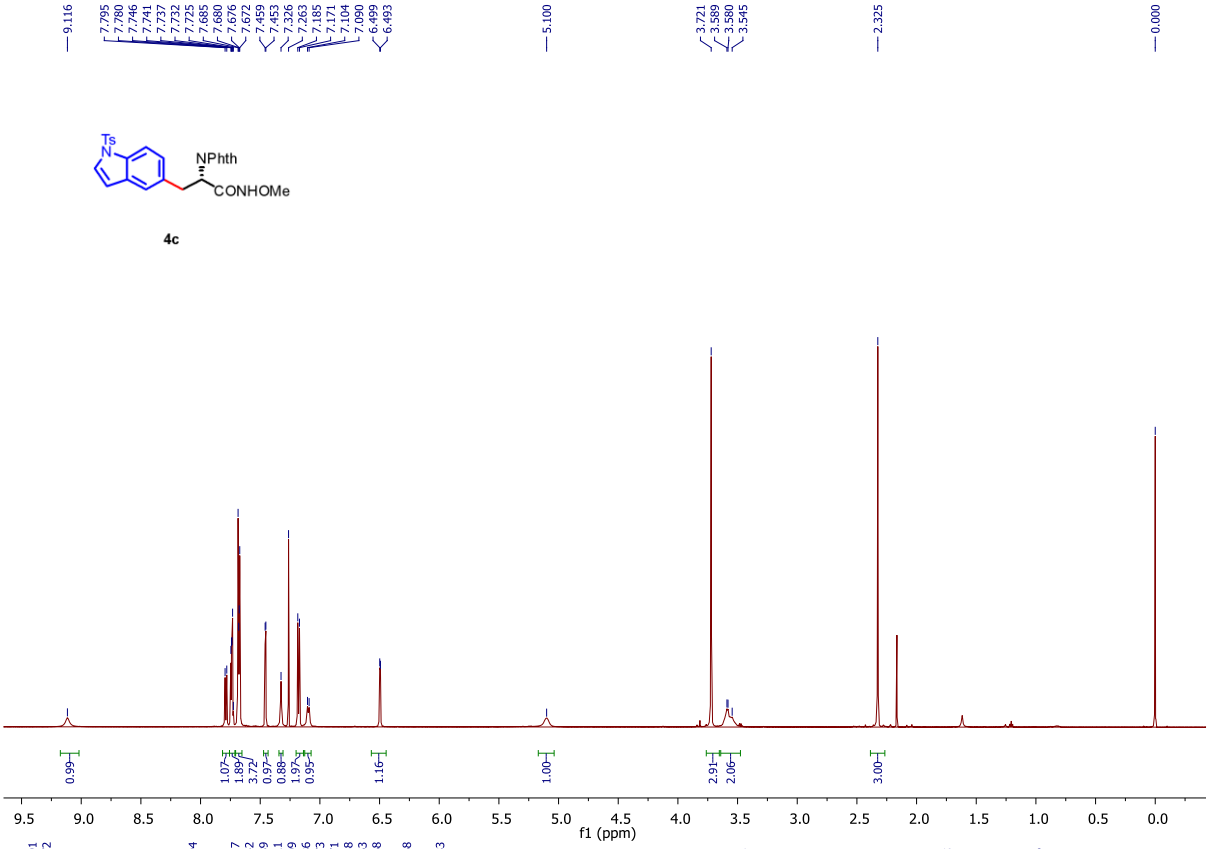
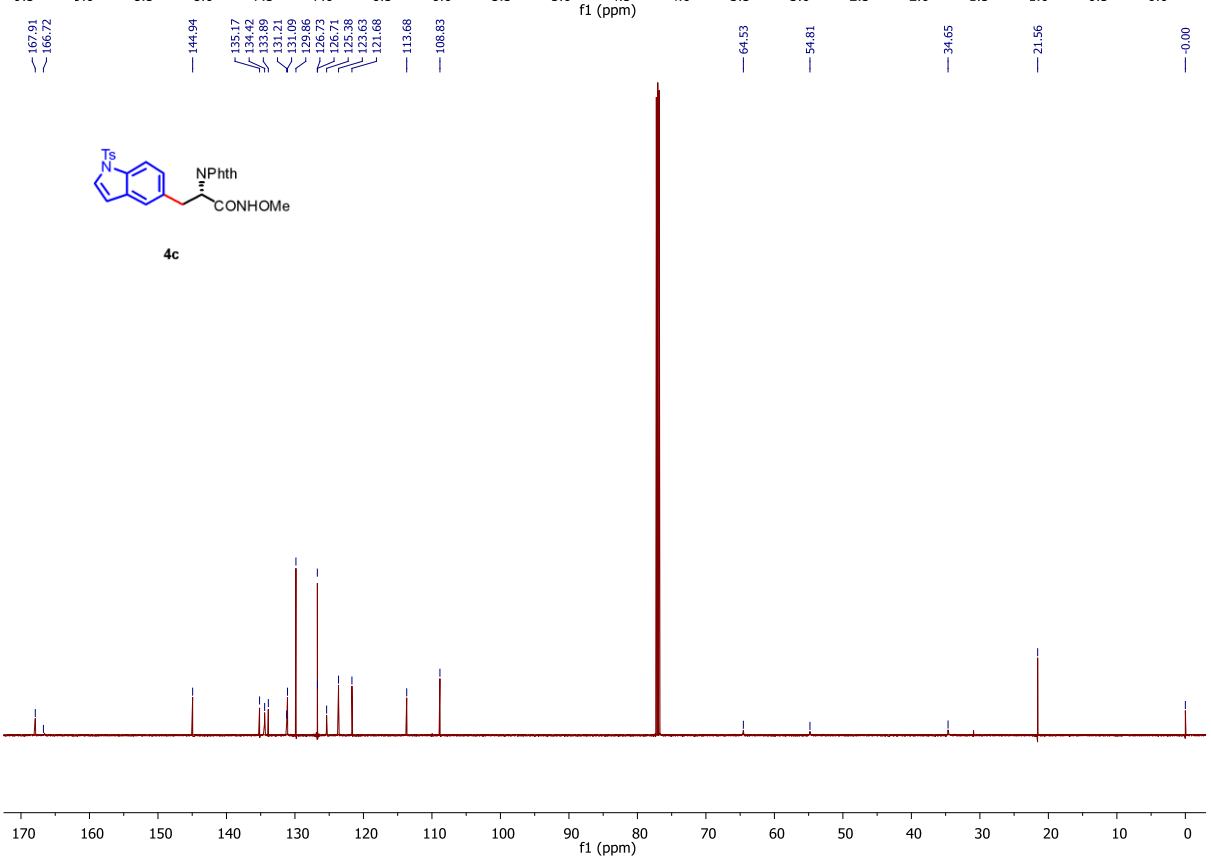
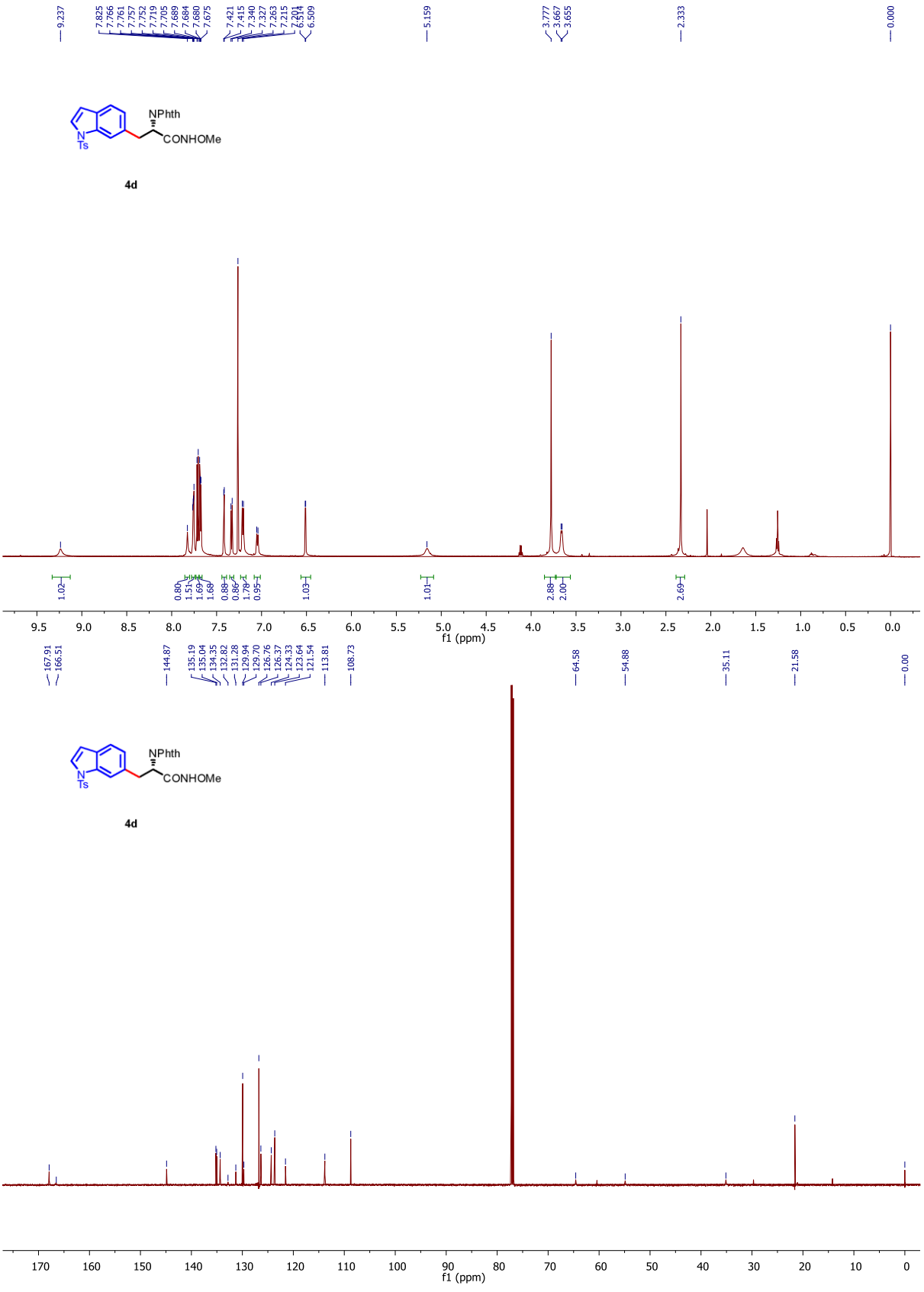
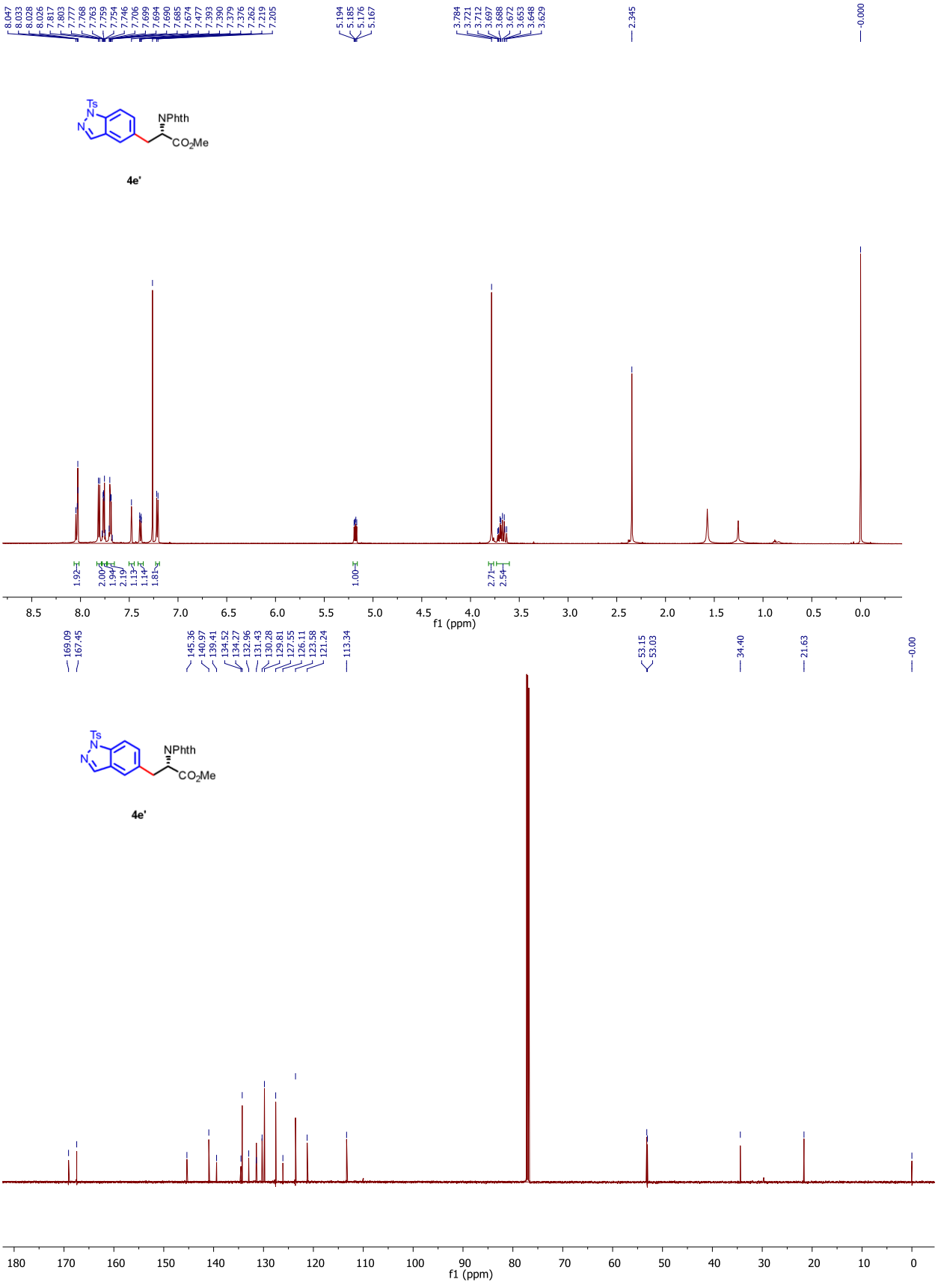
7.749
7.746
7.741
7.685
7.680
7.676
7.671
7.612
7.608
7.597
7.594
7.456
7.442
7.279
6.964
5.130
4.445
4.433
4.421
4.409
3.773
3.683
3.668
1.418
1.406
1.394
-0.000
EtO2C
NPhth
CONHOMe
4b
0.86
0.96
2.10
2.10
1.10
1.06
1.09
1.00
2.10
3.04
2.17
3.34
f1 (ppm)
178.24
167.67
166.00
160.37
154.92
152.19
135.79
134.86
134.43
131.23
125.68
124.13
123.65
119.18
114.50
64.45
63.06
53.84
34.04
14.07
0.00

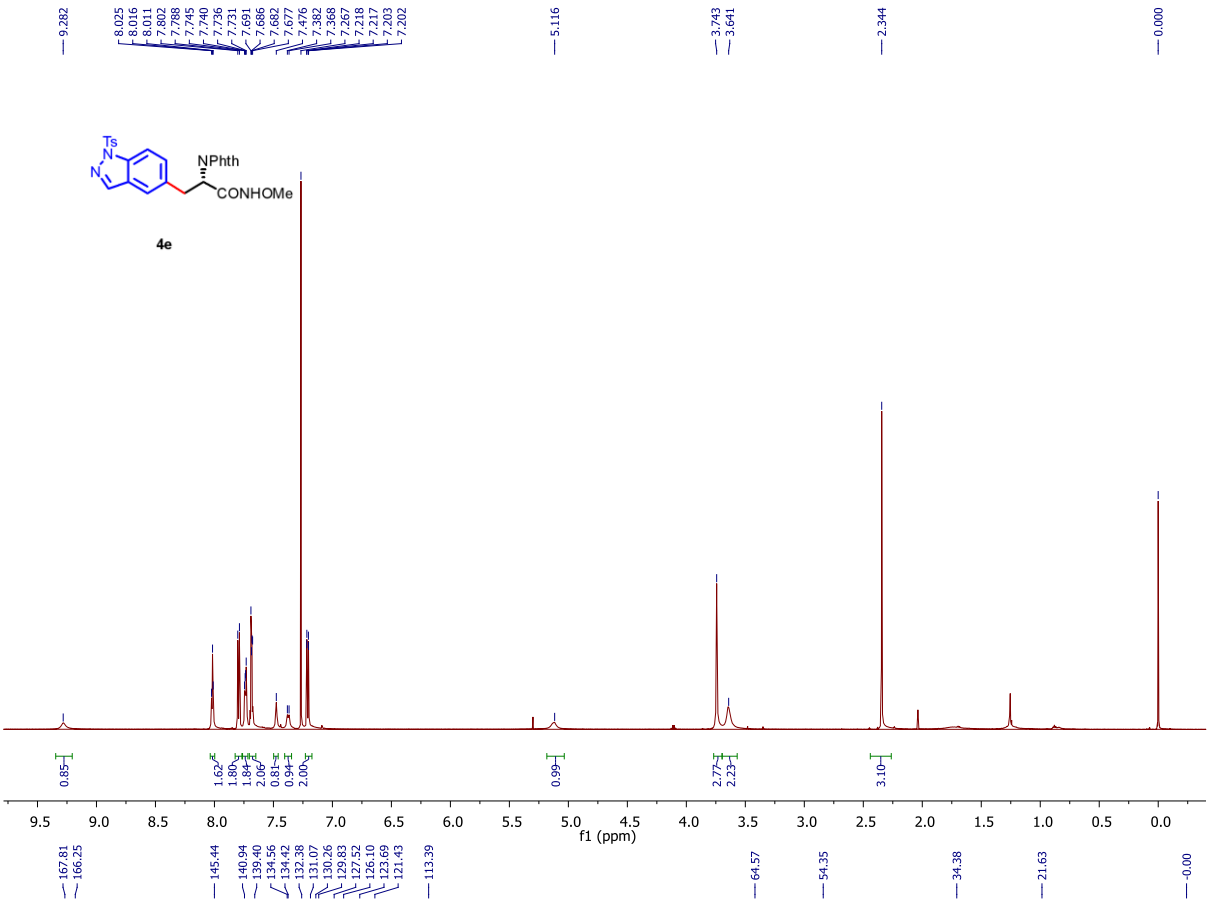

EtO2C
NPhth
CONHOMe
4b
f1 (ppm)

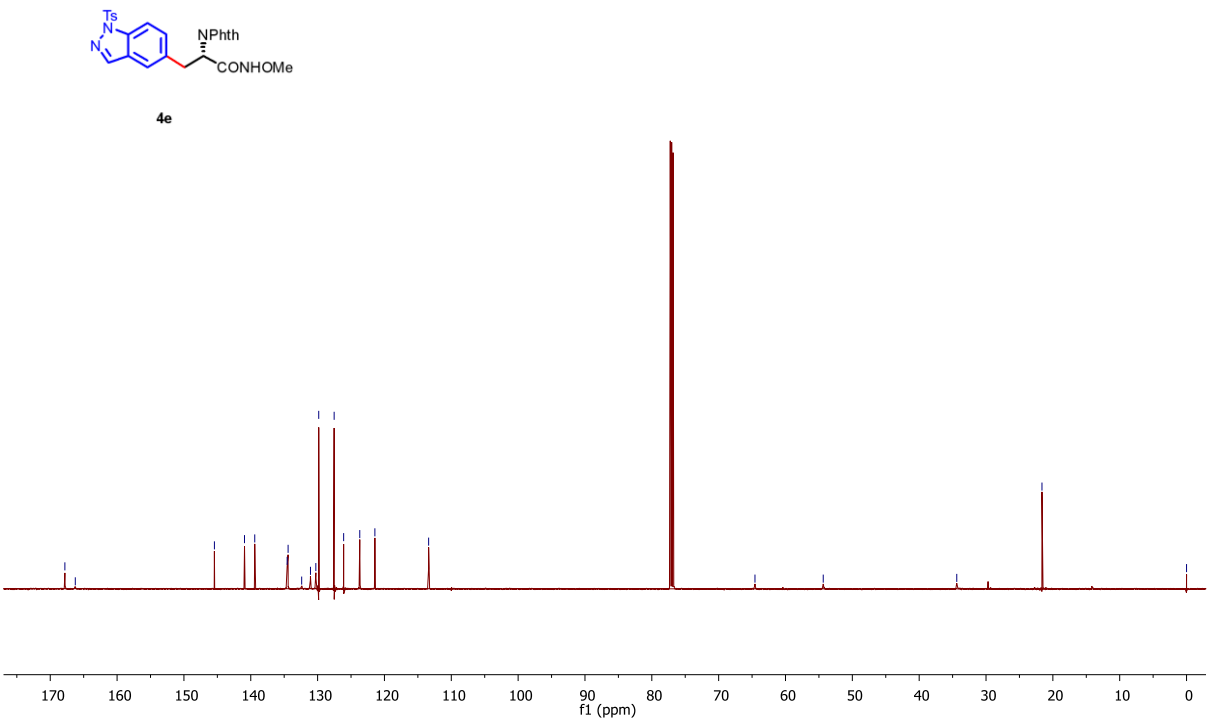

9.116
7.795
7.780
7.746
7.741
7.737
7.732
7.725
7.685
7.680
7.676
7.672
7.459
7.453
7.326
7.263
7.185
7.171
7.104
7.090
6.499
6.493
5.100
3.721
3.589
3.580
3.545
2.325
0.000
Ts
N
NPhth
CONHOMe
4c
0.99
1.07
1.89
3.72
0.97
0.88
1.97
0.95
1.16
1.00
2.91
2.06
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

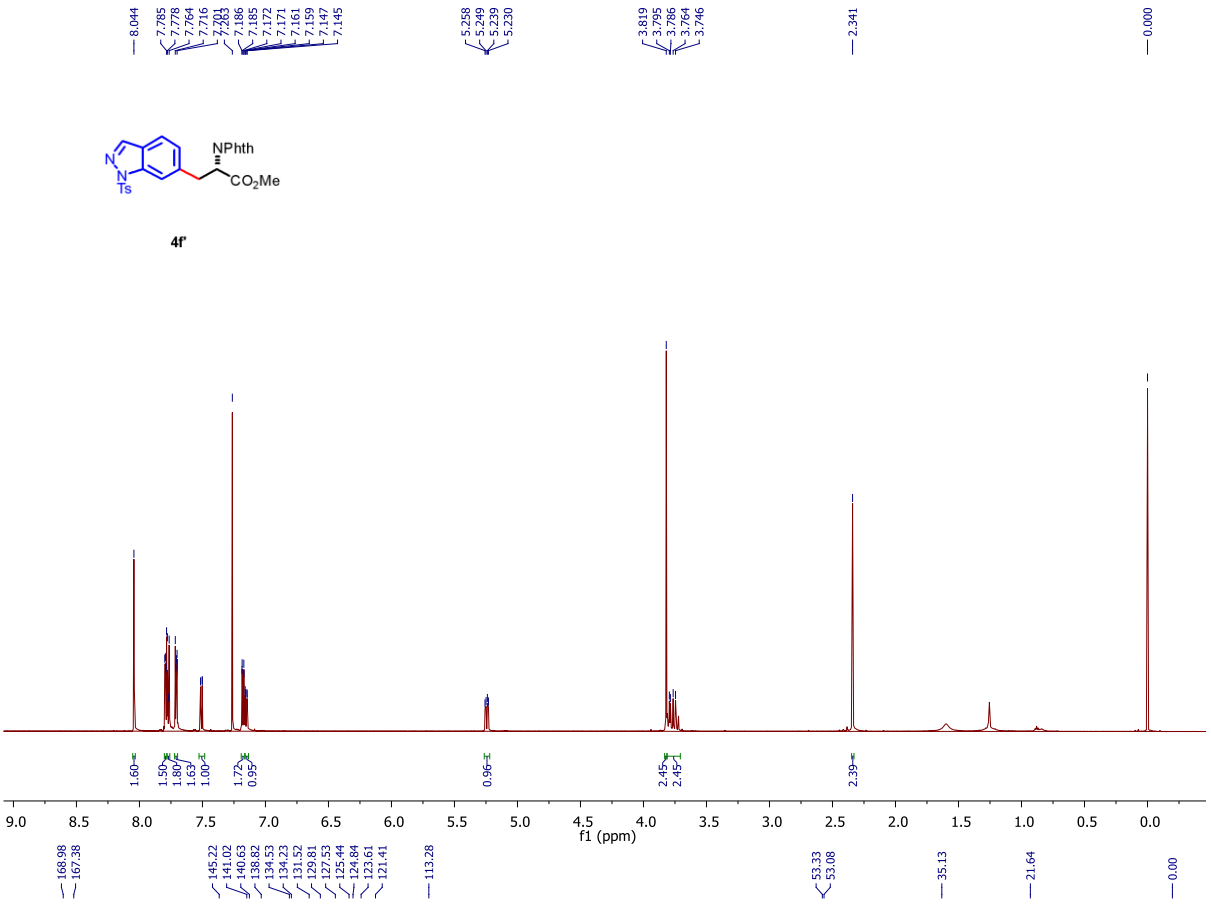

167.91
166.72
144.94
135.17
134.42
133.89
131.21
131.09
129.86
126.73
126.71
125.38
123.63
121.68
113.68
108.83
64.53
54.81
34.65
21.56
-0.00
Ts
N
NPhth
CONHOMe
4c
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

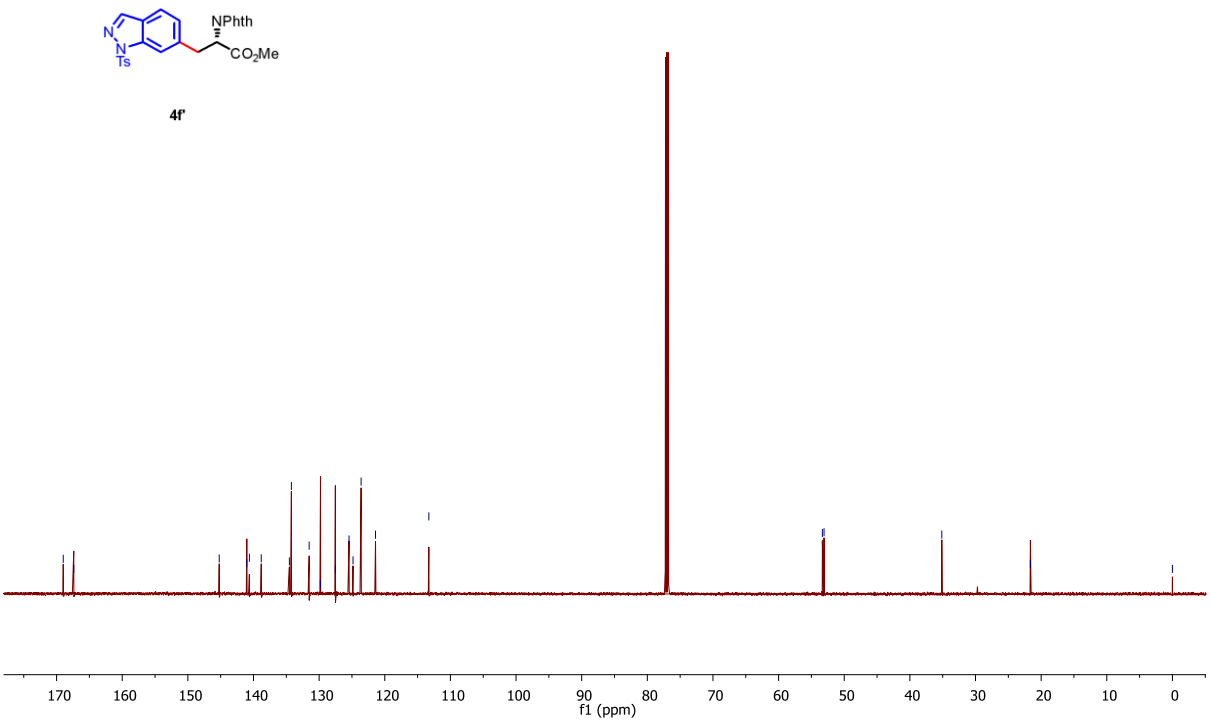

9.237
7.825
7.766
7.761
7.757
7.752
7.719
7.705
7.689
7.684
7.680
7.675
7.421
7.415
7.340
7.327
7.263
7.215
6.514
6.509
5.159
3.777
3.667
3.655
2.333
0.000
NPhth
CONHOMe
Ts
4d
1.02
0.80
1.51
1.69
1.68
0.88
0.86
1.78
0.95
1.03
1.01
2.88
2.00
2.69
f1 (ppm)
167.91
166.51
144.87
135.19
135.04
134.35
132.82
131.28
129.94
129.70
126.76
126.37
124.33
123.64
121.54
113.81
108.73
64.58
54.88
35.11
21.58
0.00
NPhth
CONHOMe
Ts
4d
f1 (ppm)

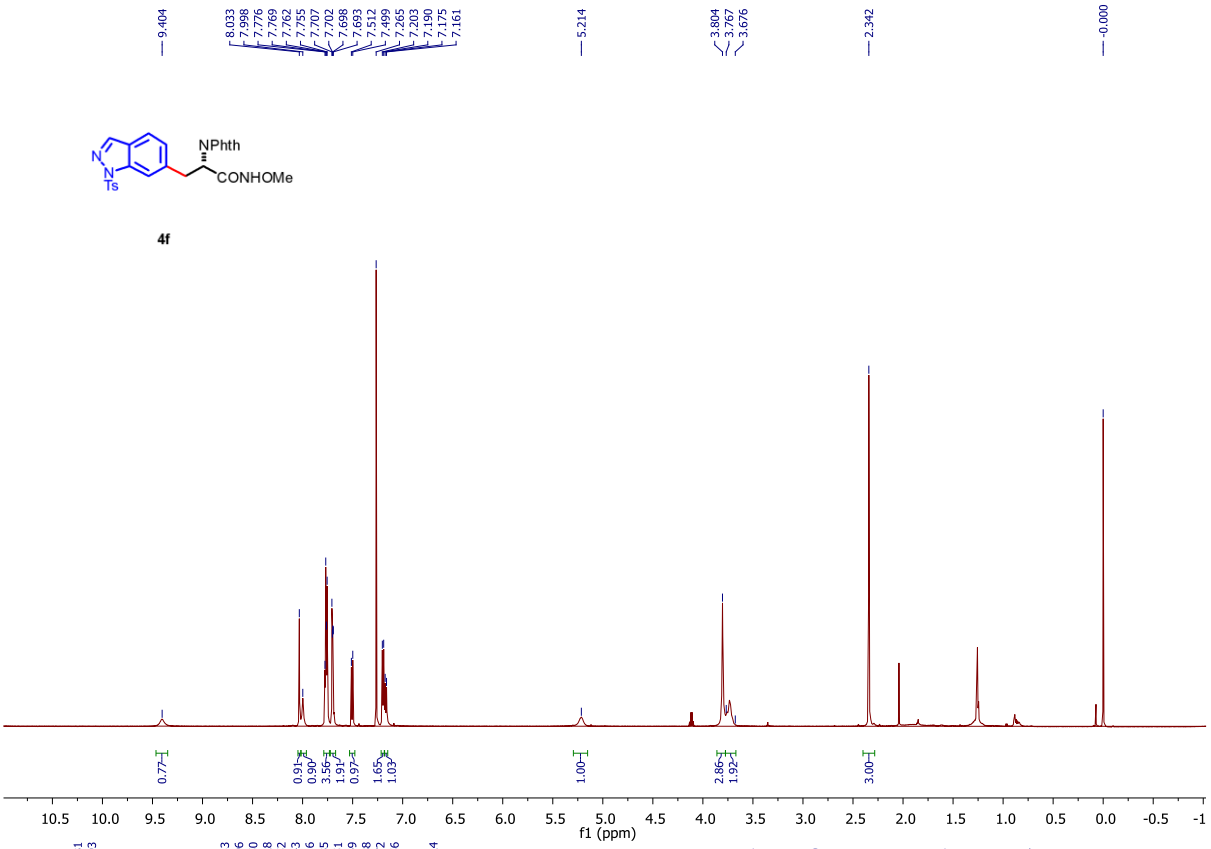

8.047
8.033
8.028
8.026
8.026
7.817
7.803
7.777
7.768
7.763
7.759
7.754
7.746
7.706
7.699
7.694
7.690
7.685
7.674
7.477
7.393
7.390
7.379
7.376
7.262
7.219
7.205
5.194
5.185
5.176
5.167
3.784
3.721
3.712
3.697
3.688
3.672
3.653
3.648
3.629
2.345
-0.000
Ts
N
N
NPhth
CO2Me
4e'
1.92
2.00
1.94
2.19
1.13
1.14
1.81
1.00
2.71
2.54
f1 (ppm)
169.09
167.45
145.36
140.97
139.41
134.52
134.27
132.96
131.43
130.28
129.81
127.55
126.11
123.58
121.24
113.34
53.15
53.03
34.40
21.63
-0.00
Ts
N
N
NPhth
CO2Me
4e'
f1 (ppm)

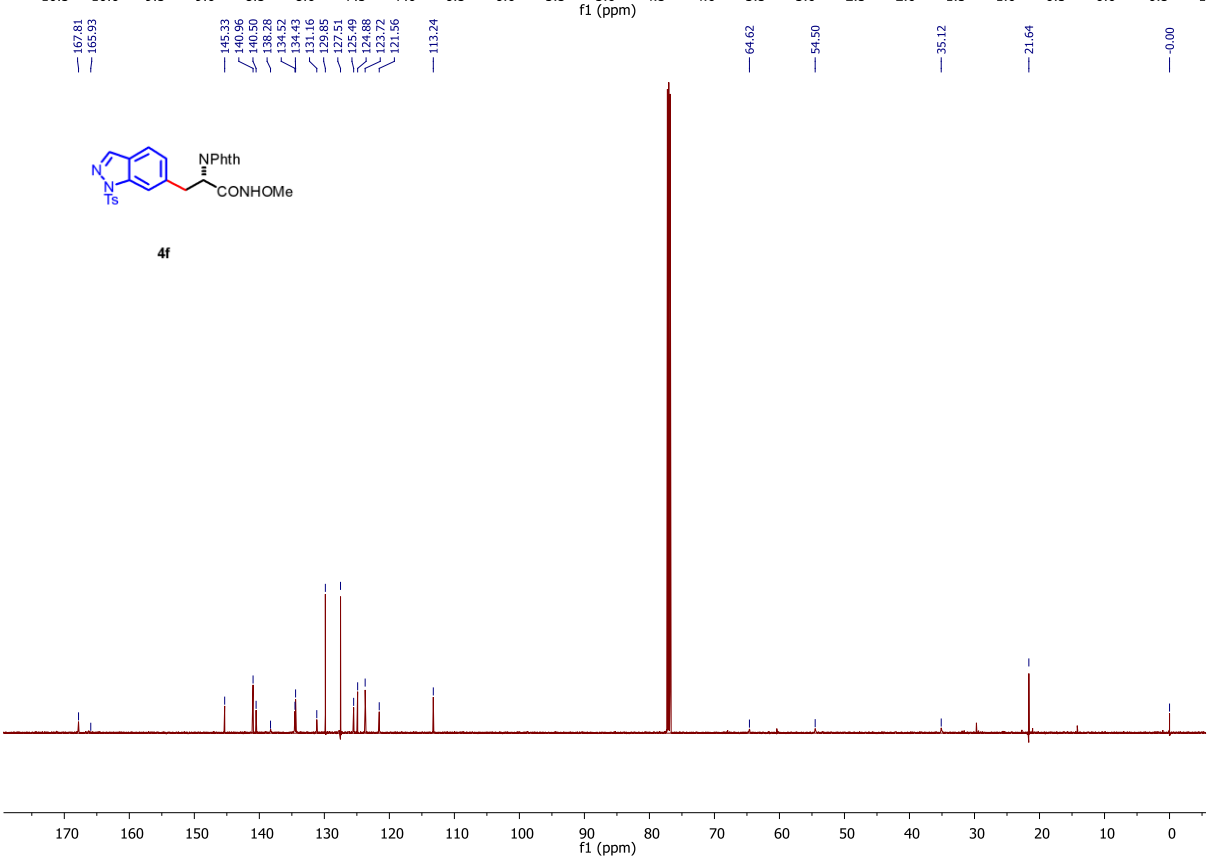

9.282
8.025
8.016
8.011
7.802
7.788
7.745
7.740
7.736
7.731
7.691
7.686
7.682
7.677
7.476
7.382
7.368
7.267
7.218
7.217
7.203
7.202
5.116
3.743
3.641
2.344
0.000
Ts
N
N
NPhth
CONHOMe
4e
0.85
1.62
1.80
1.84
2.06
0.81
0.94
2.00
0.99
2.77
2.23
3.10
f1 (ppm)

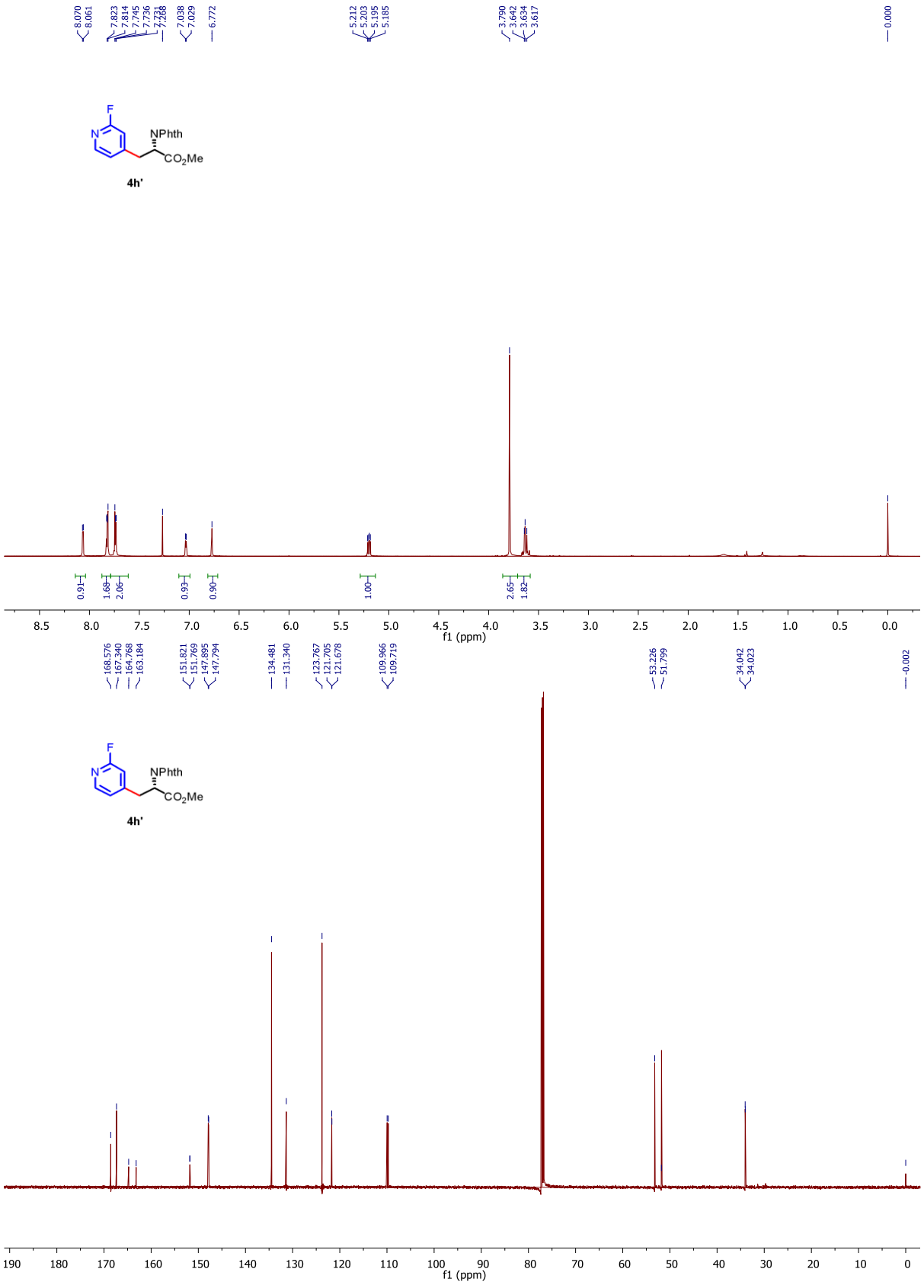

167.81
166.25
145.44
140.94
139.40
134.56
134.42
132.38
131.07
130.26
129.83
127.52
126.10
123.69
121.43
113.39
64.57
54.35
34.38
21.63
-0.00
Ts
N
N
NPhth
CONHOMe
4e
f1 (ppm)

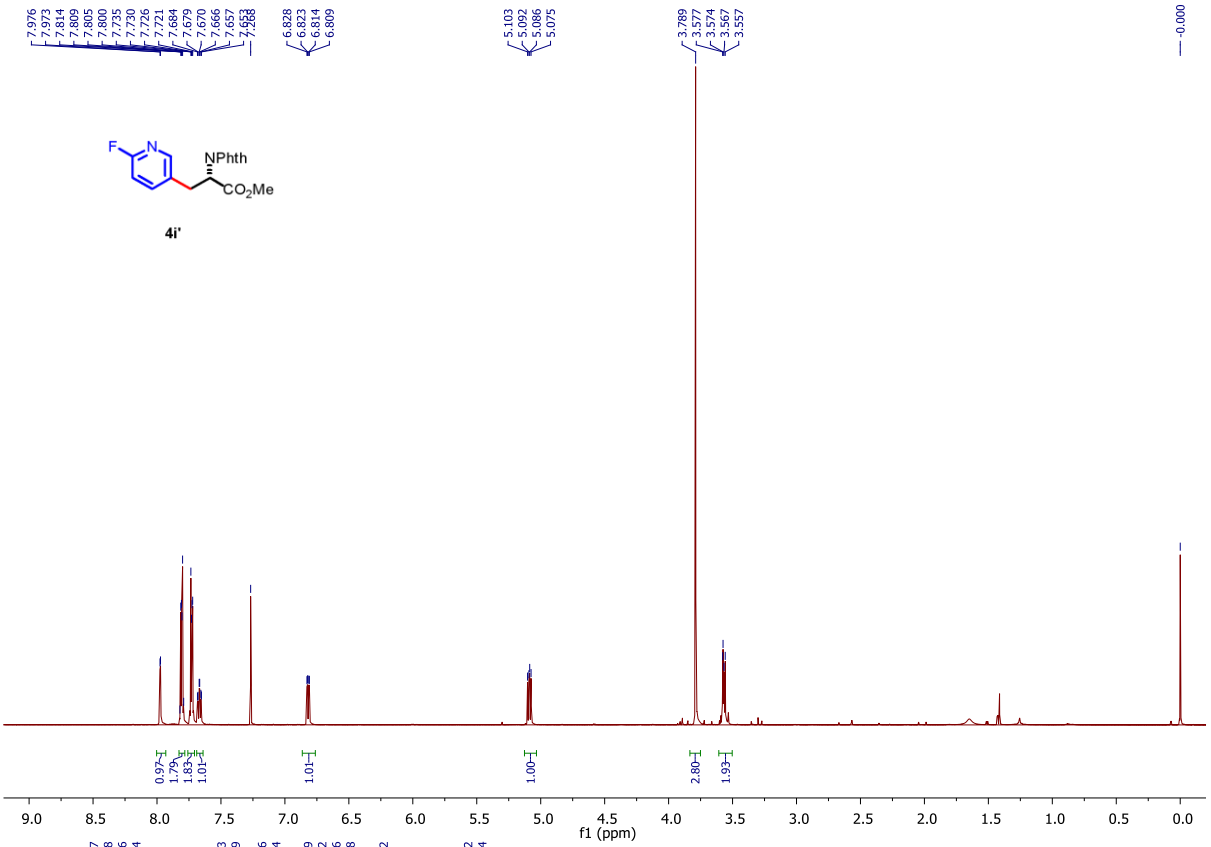

8.044
7.785
7.778
7.764
7.716
7.203
7.186
7.185
7.172
7.171
7.161
7.159
7.147
7.145
5.258
5.249
5.239
5.230
3.819
3.795
3.786
3.764
3.746
2.341
0.000
NPhth
N
N
Ts
CO2Me
4f'
1.60
1.50
1.80
1.63
1.00
1.72
0.95
0.96
2.45
2.45
2.39
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

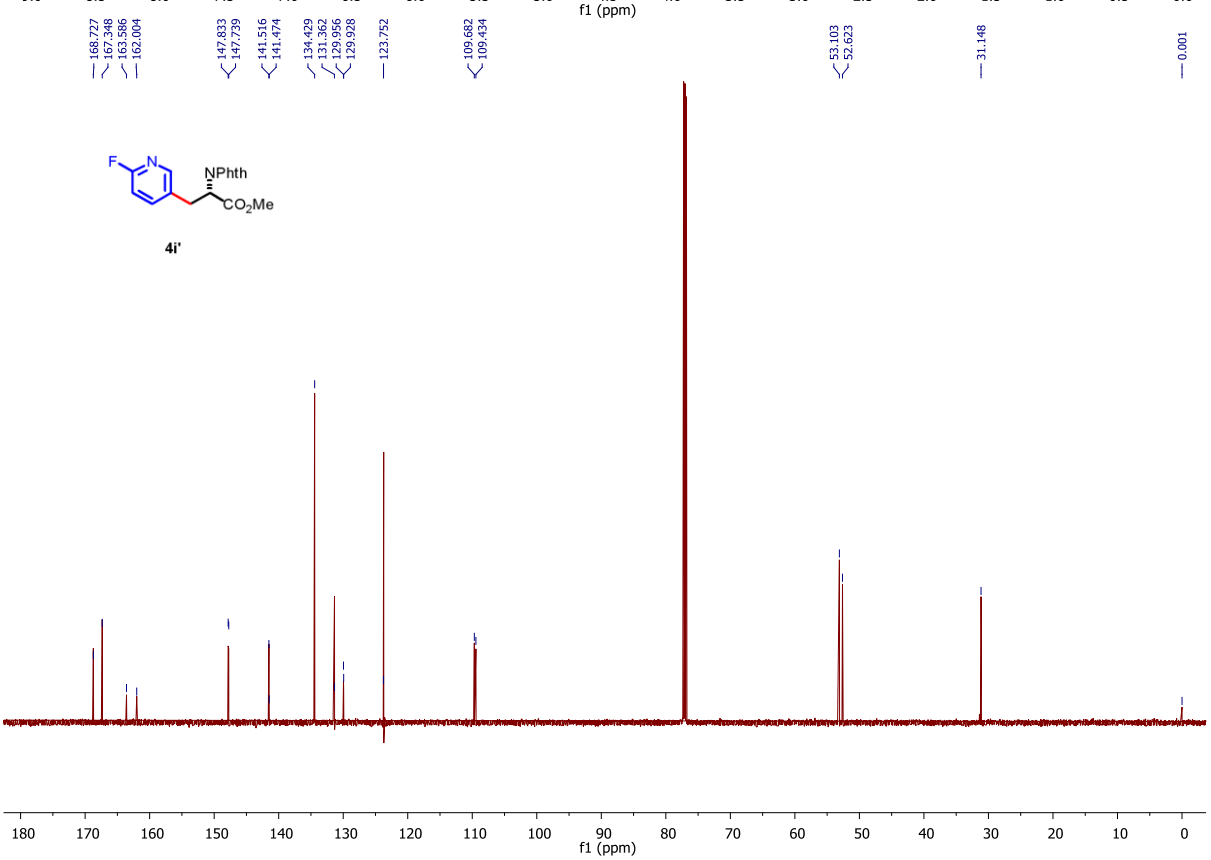

168.98
167.38
145.22
141.02
140.63
138.82
134.53
134.23
131.52
129.81
127.53
125.44
124.84
123.61
121.41
113.28
53.33
53.08
35.13
21.64
0.00
NPhth
N
N
Ts
CO2Me
4f'
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

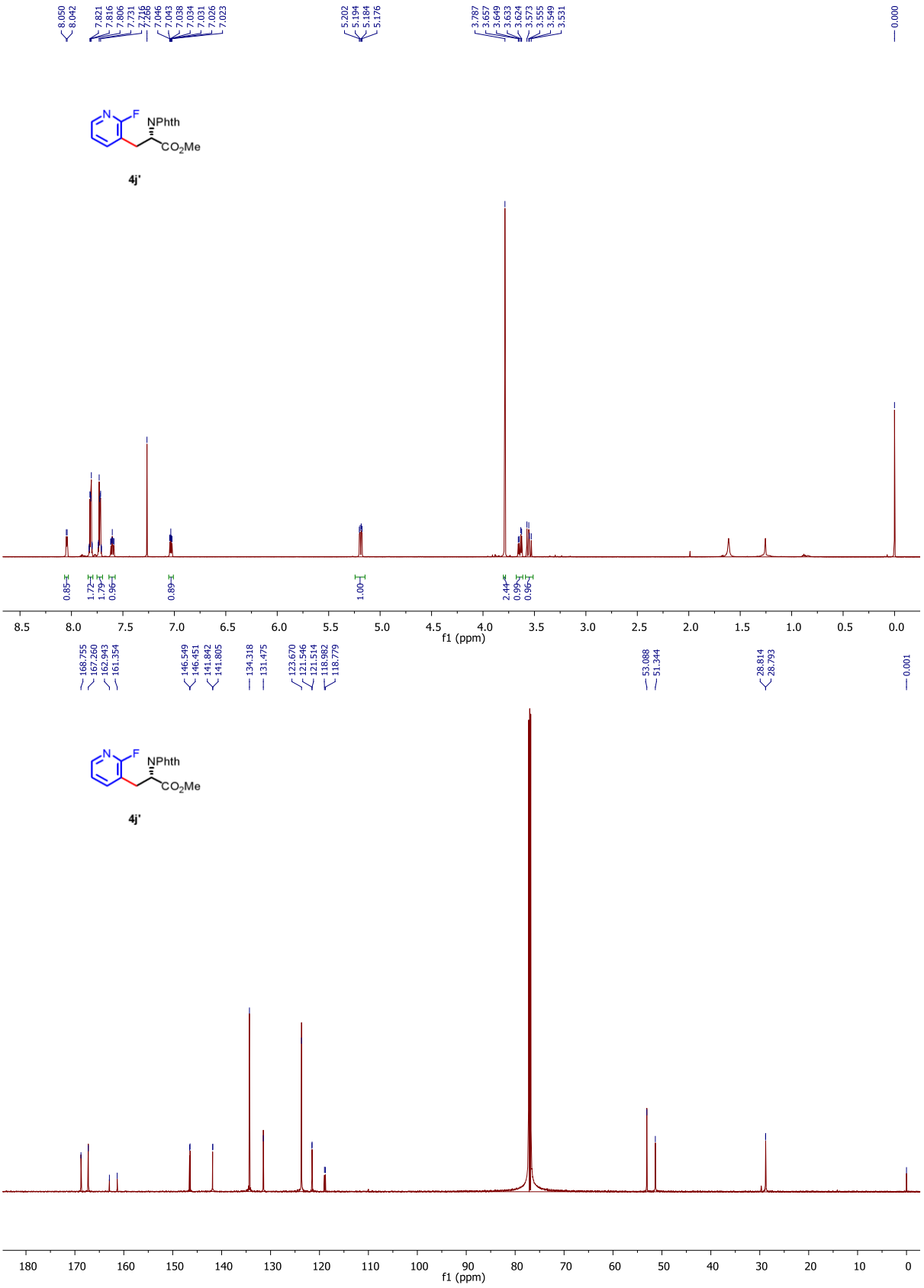

9.404
8.033
7.998
7.776
7.769
7.762
7.755
7.707
7.702
7.698
7.693
7.512
7.499
7.265
7.203
7.190
7.175
7.161
5.214
3.804
3.767
3.676
2.342
-0.000
NPhth
CONHOMe
Ts
4f
0.77
0.91
0.90
3.56
1.91
0.97
1.65
1.03
1.00
2.86
1.92
3.00
f1 (ppm)

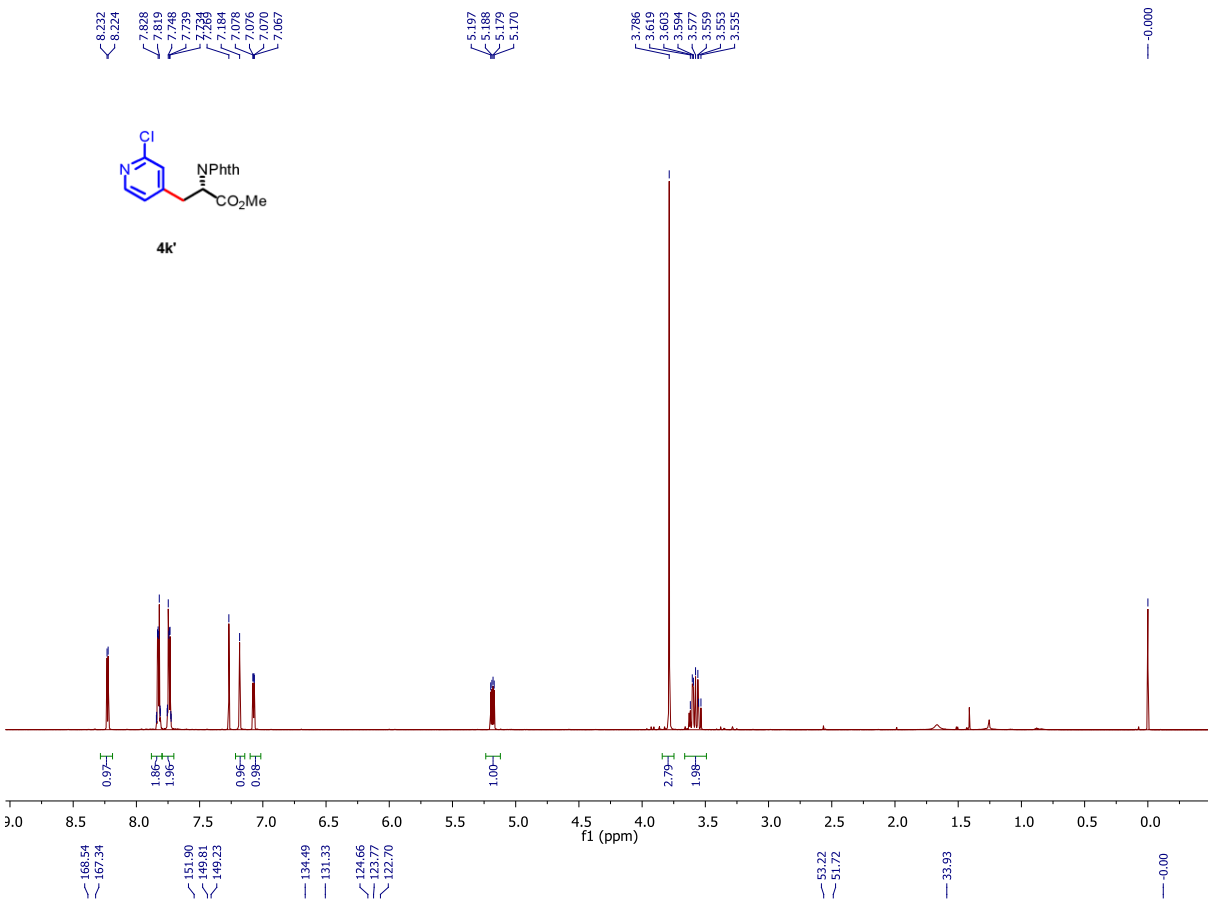

167.81
165.93
145.33
140.96
140.50
138.28
134.52
134.43
131.16
129.85
127.51
125.49
124.88
123.72
121.56
113.24
64.62
54.50
35.12
21.64
-0.00
NPhth
CONHOMe
Ts
4f
f1 (ppm)

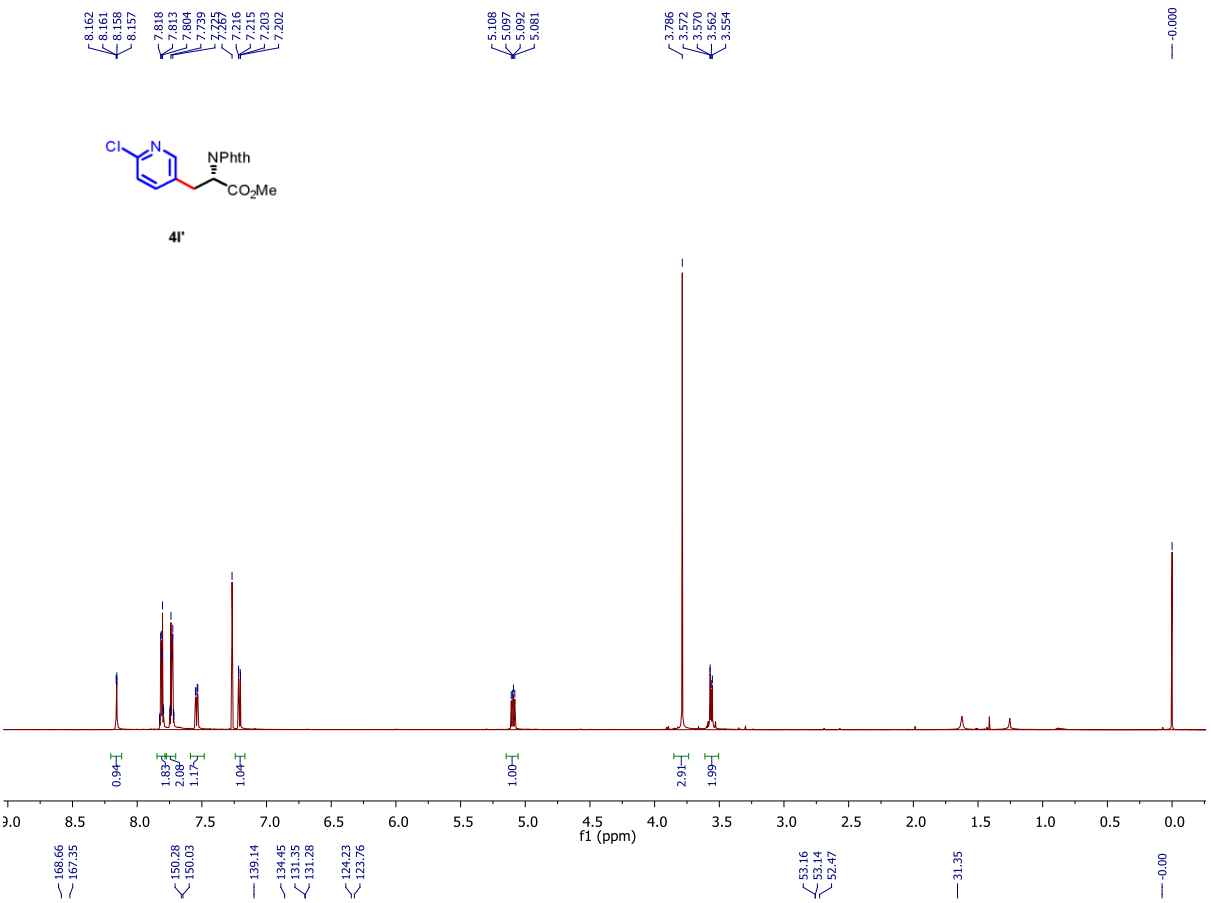

8.070
8.061
7.823
7.814
7.745
7.736
7.268
7.038
7.029
6.772
5.212
5.203
5.195
5.185
3.790
3.642
3.634
3.617
0.000
F
N
NPhth
CO2Me
4h'
0.91
1.68
2.06
0.93
0.90
1.00
2.65
1.82
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
168.576
167.340
164.768
163.184
151.821
151.769
147.895
147.794
134.481
131.340
123.767
121.705
121.678
109.966
109.719
53.226
51.799
34.042
34.023
-0.002
F
N
NPhth
CO2Me
4h'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

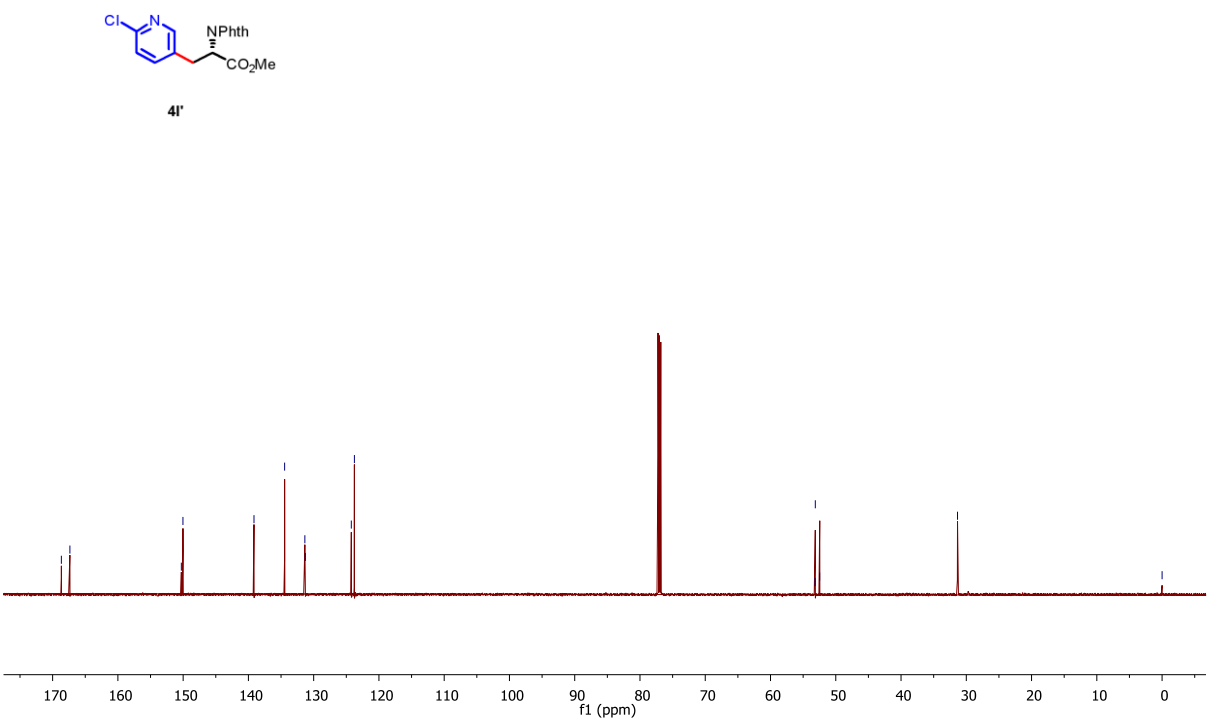

7.976
7.973
7.814
7.809
7.805
7.800
7.735
7.730
7.726
7.721
7.684
7.679
7.670
7.666
7.657
7.653
7.268
6.828
6.823
6.814
6.809
5.103
5.092
5.086
5.075
3.789
3.577
3.574
3.567
3.557
-0.000
F
N
NPhth
CO2Me
4i'
0.97
1.79
1.83
1.01
1.01
1.00
2.80
1.93
f1 (ppm)

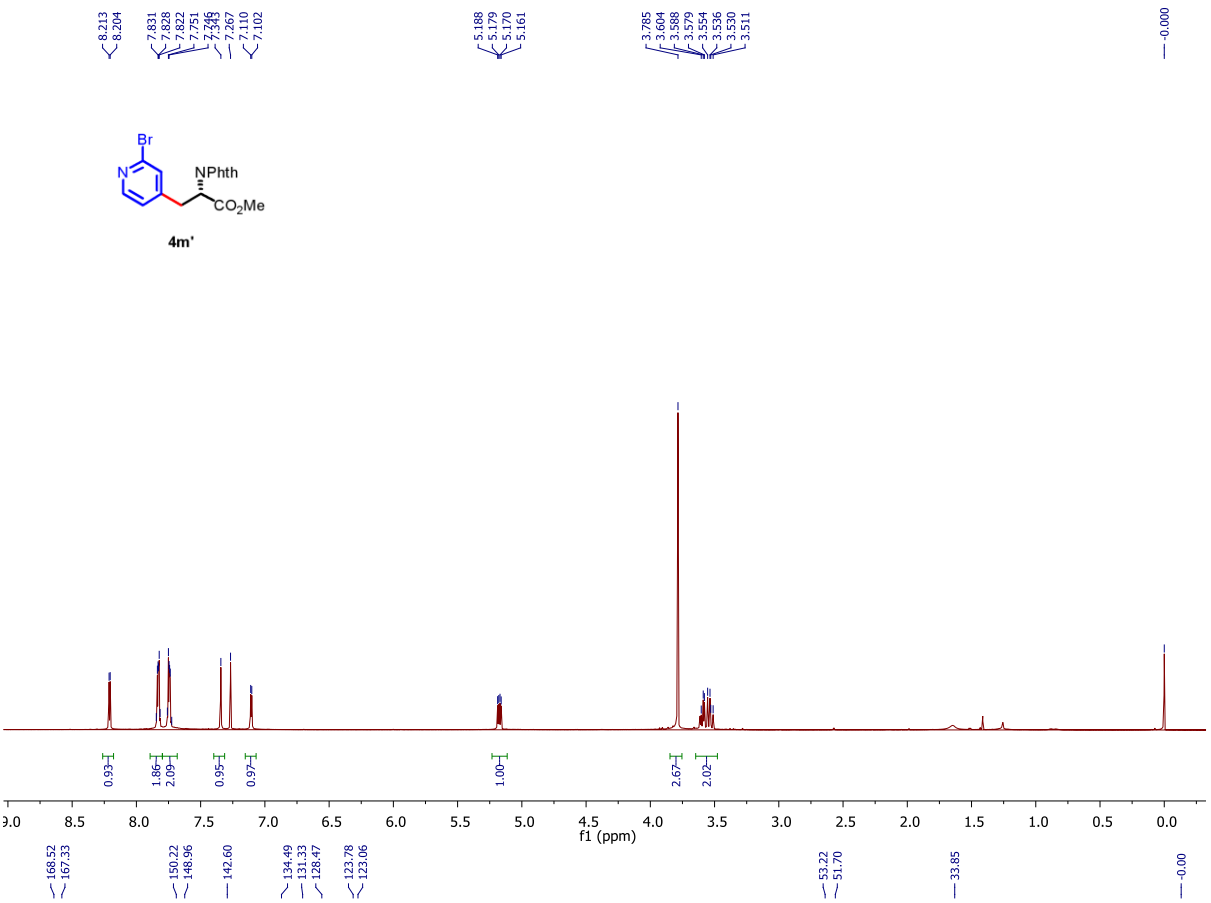

168.727
167.348
163.586
162.004
147.833
147.739
141.516
141.474
134.429
131.362
129.956
129.928
123.752
109.682
109.434
53.103
52.623
31.148
0.001
F
N
NPhth
CO2Me
4i'
f1 (ppm)

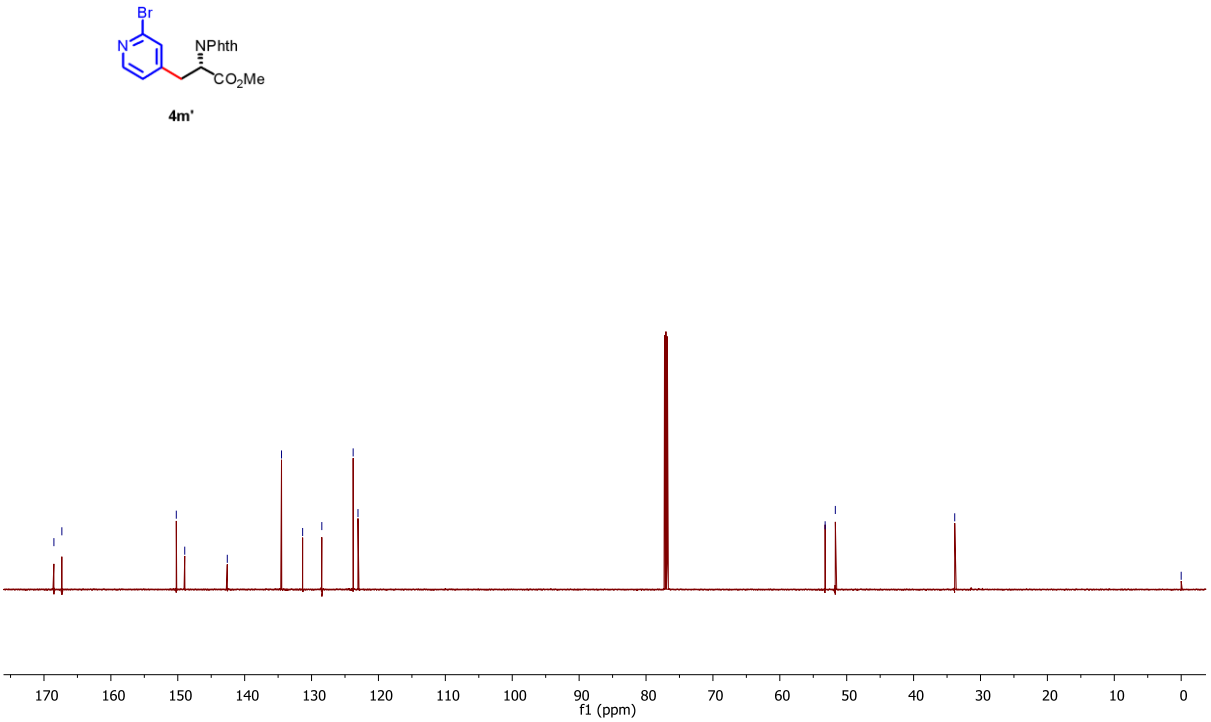

8.050
8.042
7.821
7.816
7.806
7.731
7.716
7.268
7.046
7.043
7.038
7.034
7.031
7.026
7.023
5.202
5.194
5.184
5.176
3.787
3.657
3.649
3.633
3.624
3.573
3.555
3.549
3.531
0.000
N
F
NPhth
CO2Me
4j'
0.85
1.72
1.79
0.96
0.89
1.00
2.44
0.99
0.96
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
168.755
167.260
162.943
161.354
146.549
146.451
141.842
141.805
134.318
131.475
123.670
121.546
121.514
118.982
118.779
53.088
51.344
28.814
28.793
0.001
N
F
NPhth
CO2Me
4j'
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

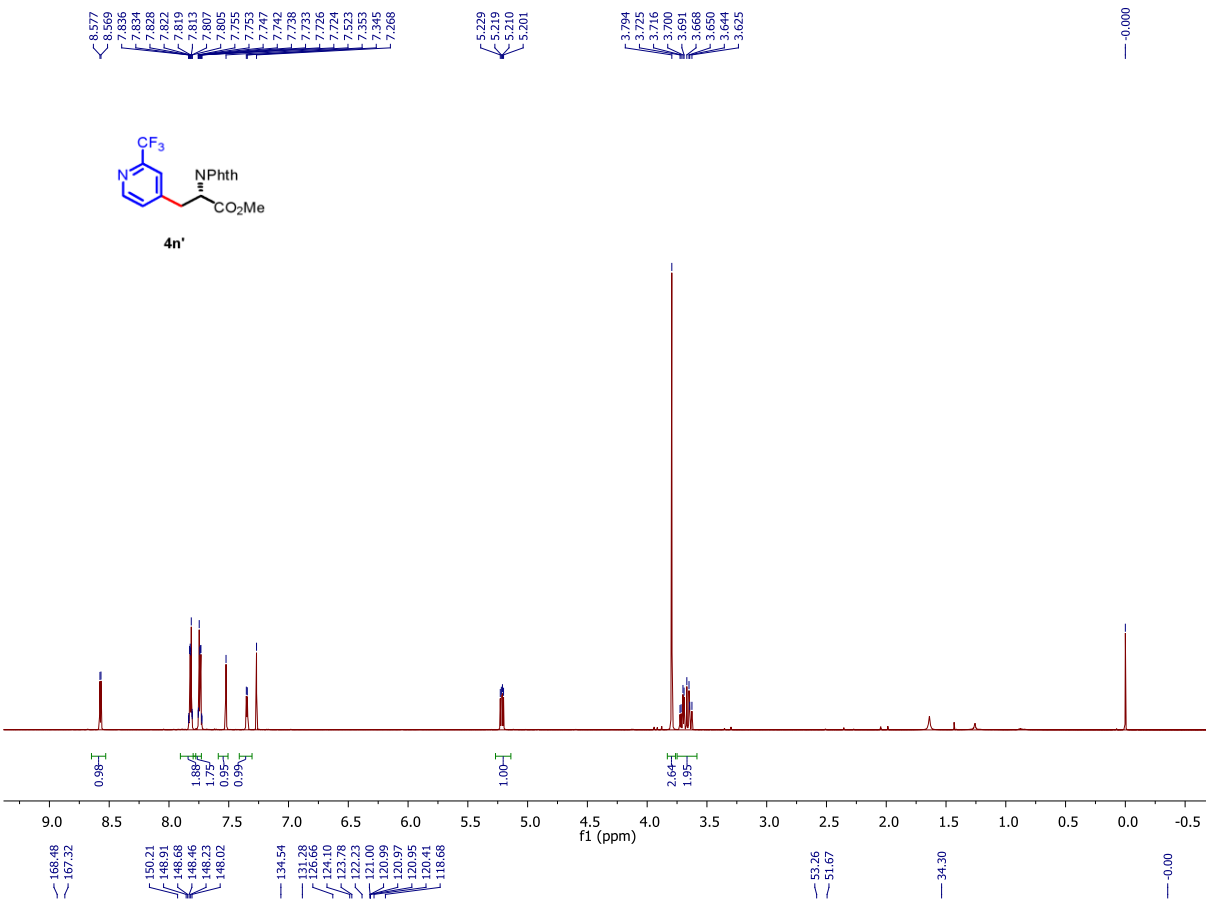

8.232
8.224
7.828
7.819
7.748
7.739
7.269
7.184
7.078
7.076
7.070
7.067
5.197
5.188
5.179
5.170
3.786
3.619
3.603
3.594
3.577
3.559
3.553
3.535
-0.000
Cl
N
NPhth
CO2Me
4k'
0.97
1.86
1.96
0.96
0.98
1.00
2.79
1.98
f1 (ppm)
168.54
167.34
151.90
149.81
149.23
134.49
131.33
124.66
123.77
122.70
53.22
51.72
33.93
-0.00
Cl
N
NPhth
CO2Me
4k'
f1 (ppm)

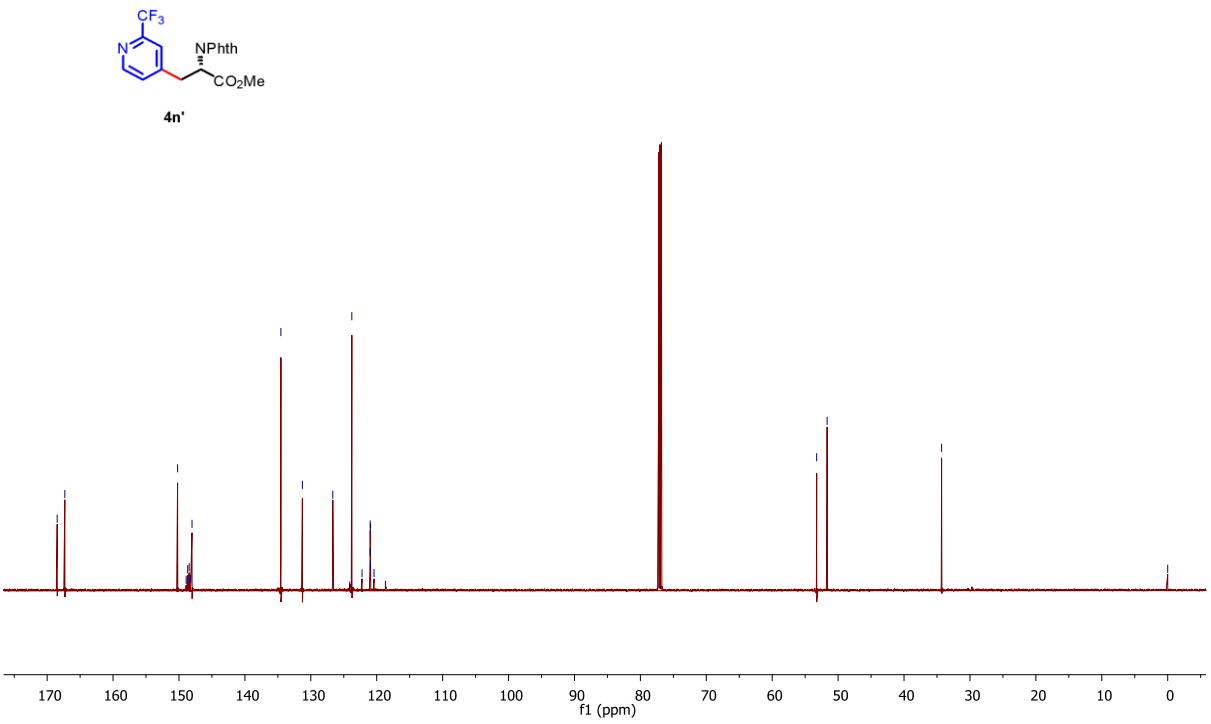

8.162
8.161
8.158
8.157
7.818
7.813
7.804
7.739
7.725
7.267
7.216
7.215
7.203
7.202
5.108
5.097
5.092
5.081
3.786
3.572
3.570
3.562
3.554
-0.000
Cl
N
NPhth
CO2Me
4l'
0.94
1.83
2.08
1.17
1.04
1.00
2.91
1.99
f1 (ppm)

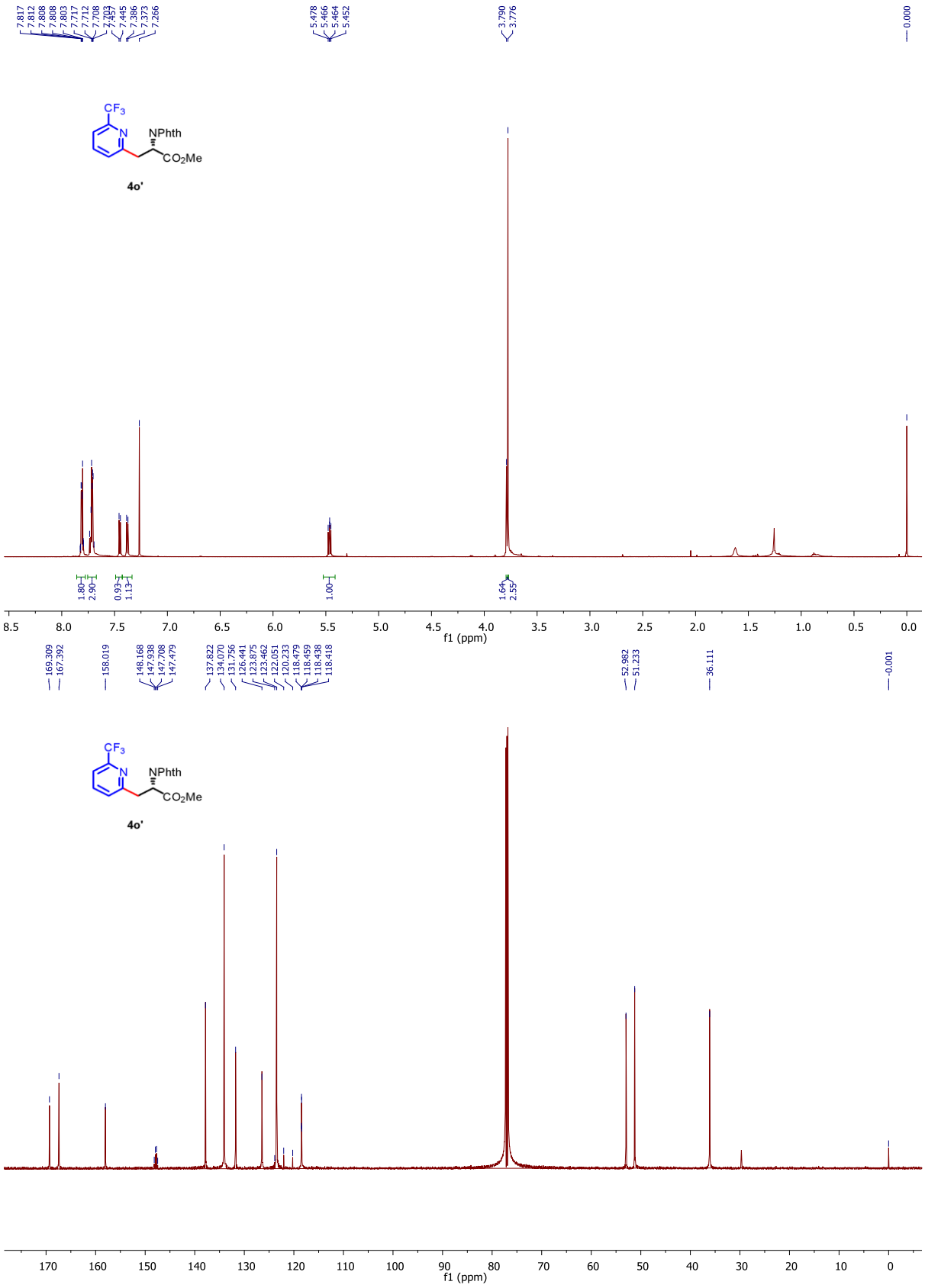

168.66
167.35
150.28
150.03
139.14
134.45
131.35
131.28
124.23
123.76
53.16
53.14
52.47
31.35
-0.00
Cl
N
NPhth
CO2Me
4l'
f1 (ppm)

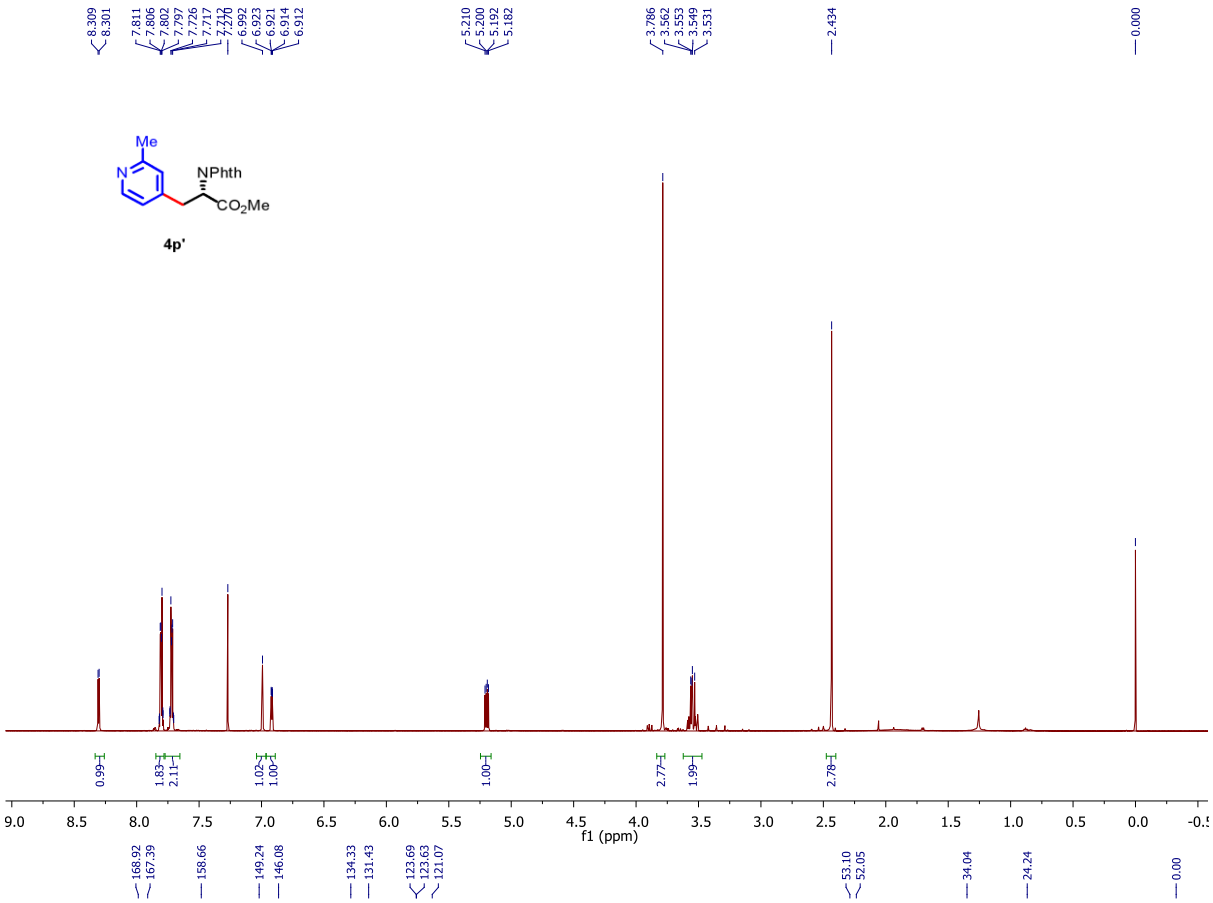

8.213
8.204
7.831
7.828
7.822
7.751
7.346
7.267
7.110
7.102
5.188
5.179
5.170
5.161
3.785
3.604
3.588
3.579
3.554
3.536
3.530
3.511
0.000
Br
N
NPhth
CO2Me
4m'
0.93
1.86
2.09
0.95
0.97
1.00
2.67
2.02
f1 (ppm)
168.52
167.33
150.22
148.96
142.60
134.49
131.33
128.47
123.78
123.06
53.22
51.70
33.85
0.00

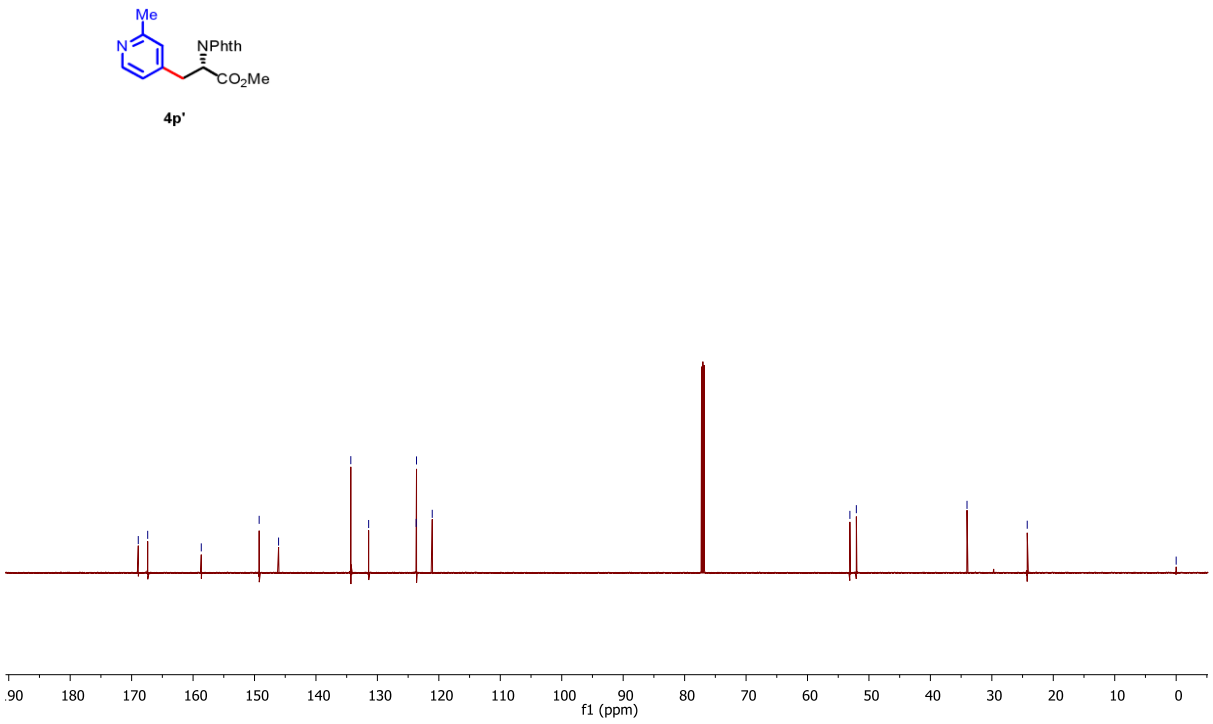

Br
N
NPhth
CO2Me
4m'
f1 (ppm)

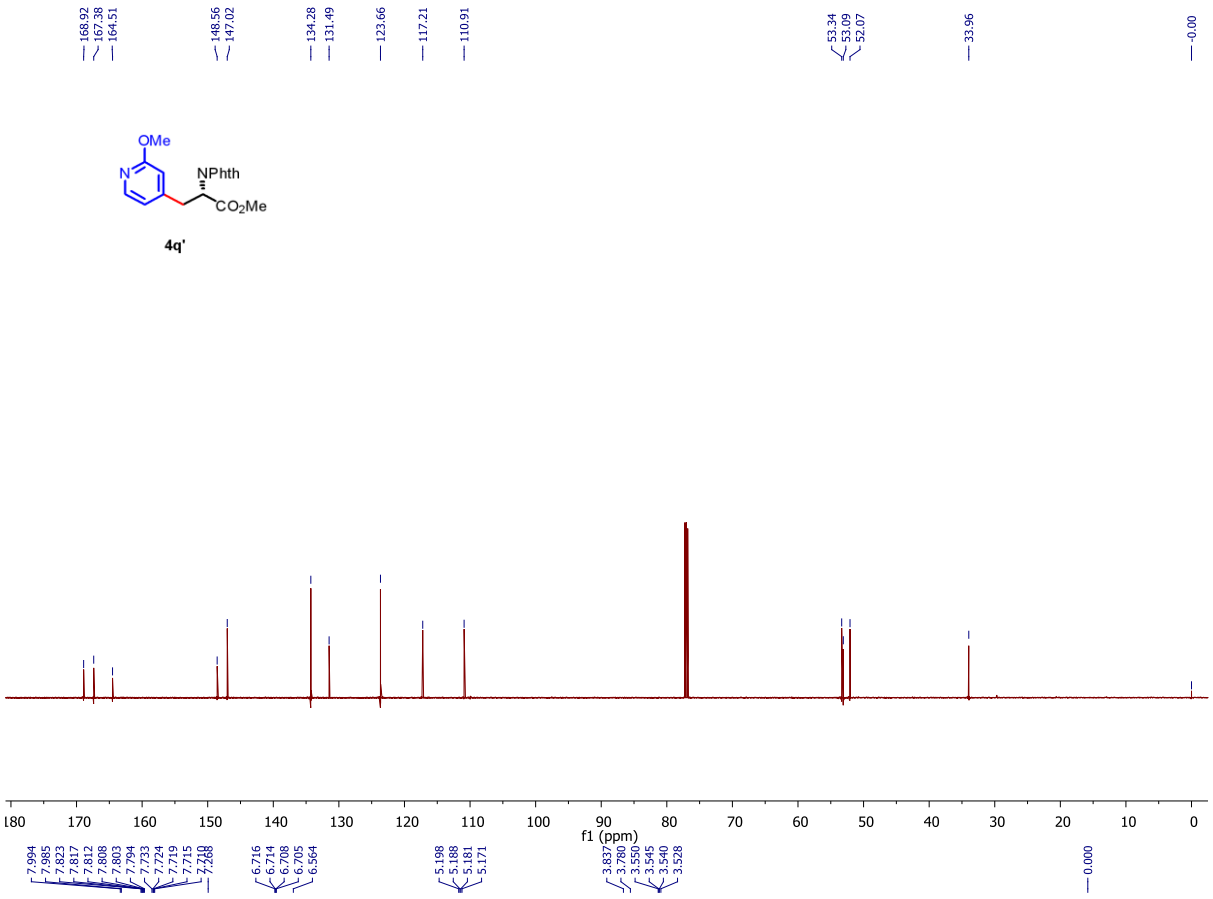

8.577
8.569
7.836
7.834
7.828
7.822
7.819
7.813
7.807
7.805
7.755
7.753
7.747
7.742
7.738
7.733
7.726
7.724
7.523
7.353
7.345
7.268
5.229
5.219
5.210
5.201
3.794
3.725
3.716
3.700
3.691
3.668
3.650
3.644
3.625
-0.000
CF3
N
NPhth
CO2Me
4n'
0.98
1.89
1.75
0.95
0.99
1.00
2.64
1.95
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

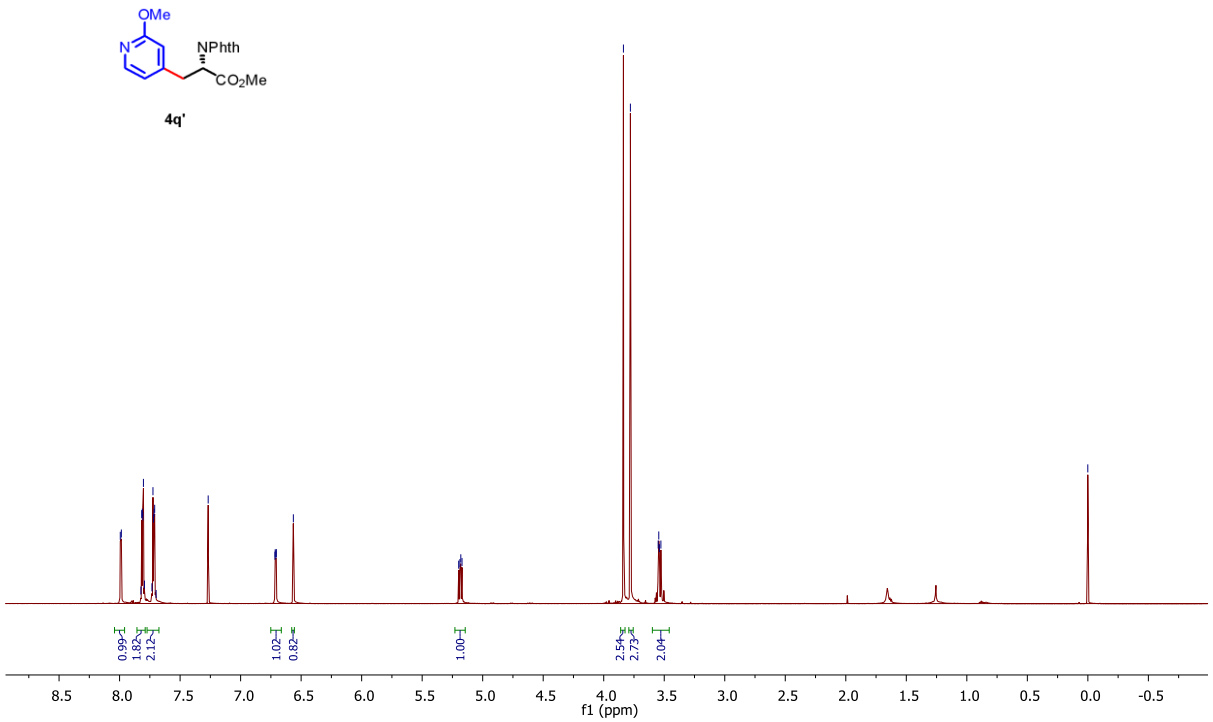

168.48
167.32
150.21
148.91
148.68
148.46
148.23
148.02
134.54
131.28
126.66
124.10
123.78
122.23
121.00
120.99
120.97
120.95
120.41
118.68
53.26
51.67
34.30
-0.00
CF3
N
NPhth
CO2Me
4n'
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

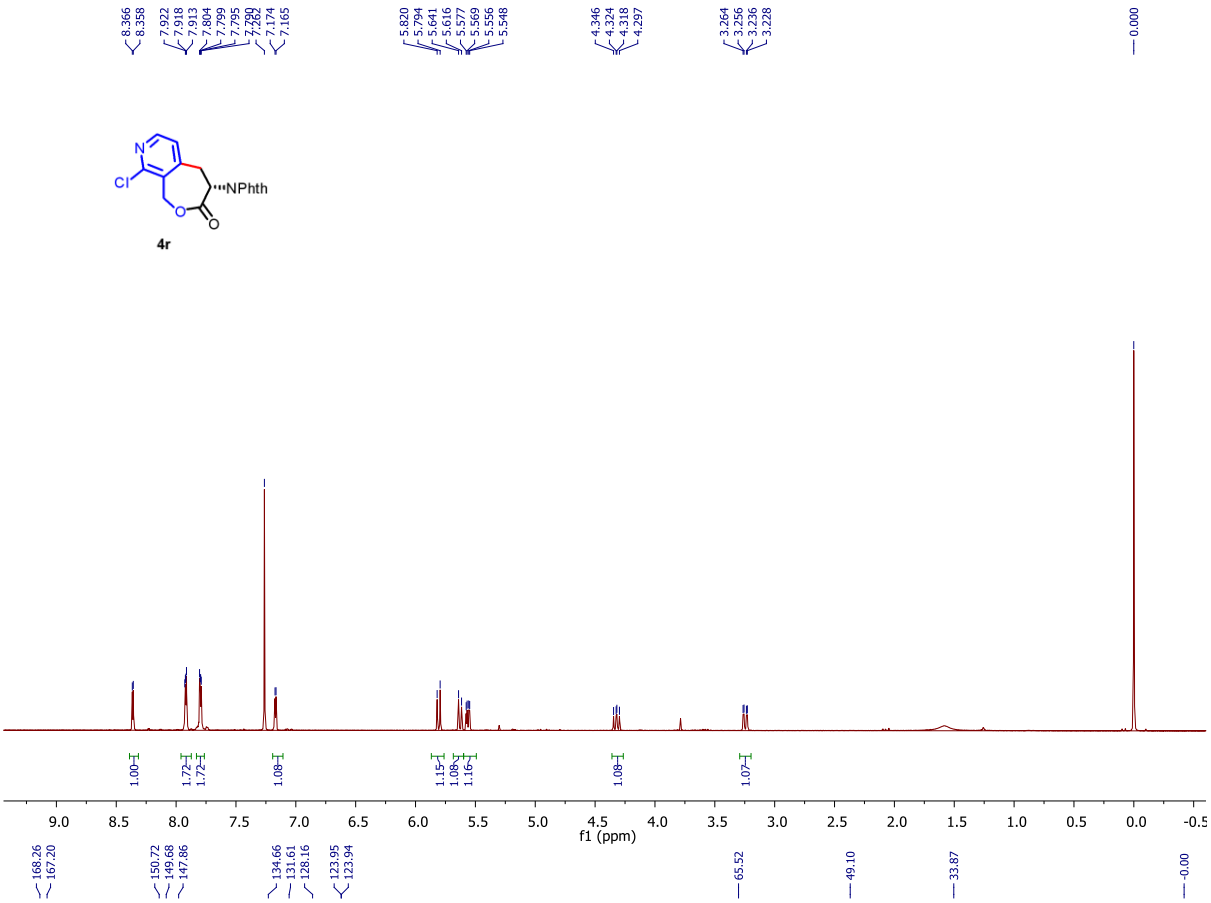

7.817
7.812
7.808
7.808
7.803
7.717
7.712
7.708
7.453
7.445
7.386
7.373
7.266
5.478
5.466
5.464
5.452
3.790
3.776
0.000
CF3
N
NPhth
CO2Me
4o'
1.80
2.90
0.93
1.13
1.00
1.64
2.55
f1 (ppm)
169.309
167.392
158.019
148.168
147.938
147.708
147.479
137.822
134.070
131.756
126.441
123.875
123.462
122.051
120.233
118.479
118.459
118.438
118.418
52.982
51.233
36.111
-0.001
f1 (ppm)

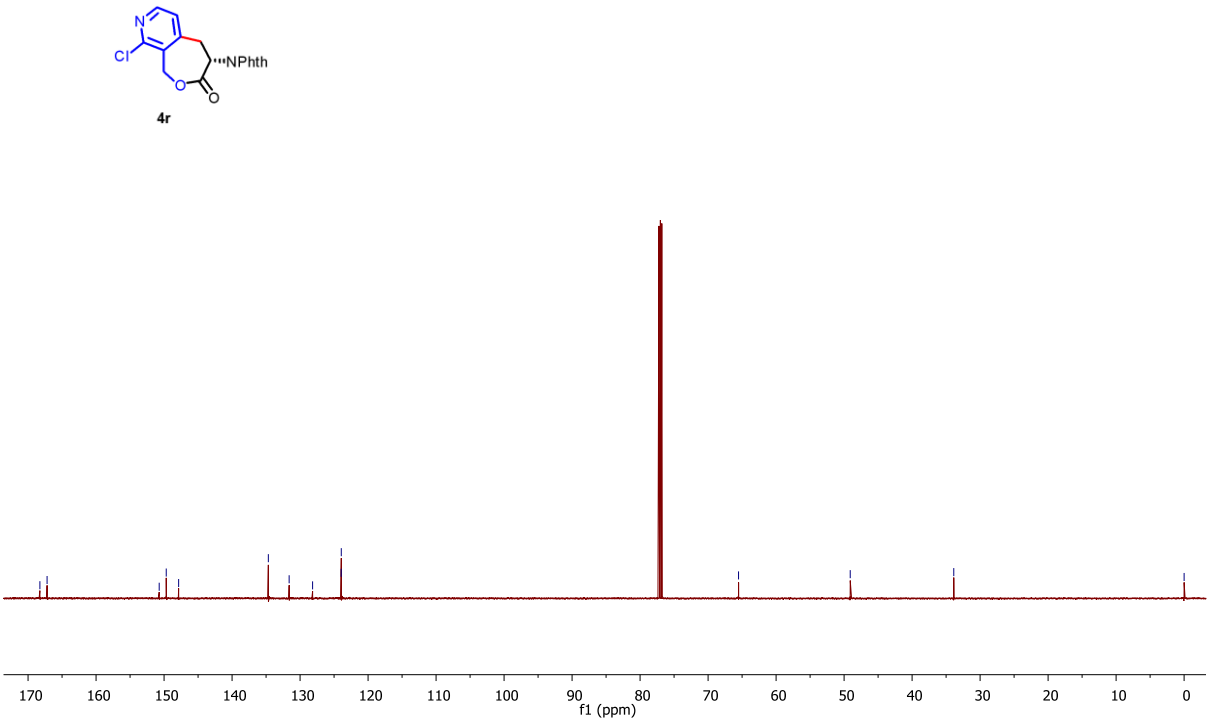

8.309
8.301
7.811
7.806
7.802
7.797
7.726
7.717
7.270
6.992
6.923
6.921
6.914
6.912
5.210
5.200
5.192
5.182
3.786
3.562
3.553
3.549
3.531
2.434
0.000
Me
N
NPhth
CO2Me
4p'
0.99
1.83
2.11
1.02
1.00
1.00
2.77
1.99
2.78
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

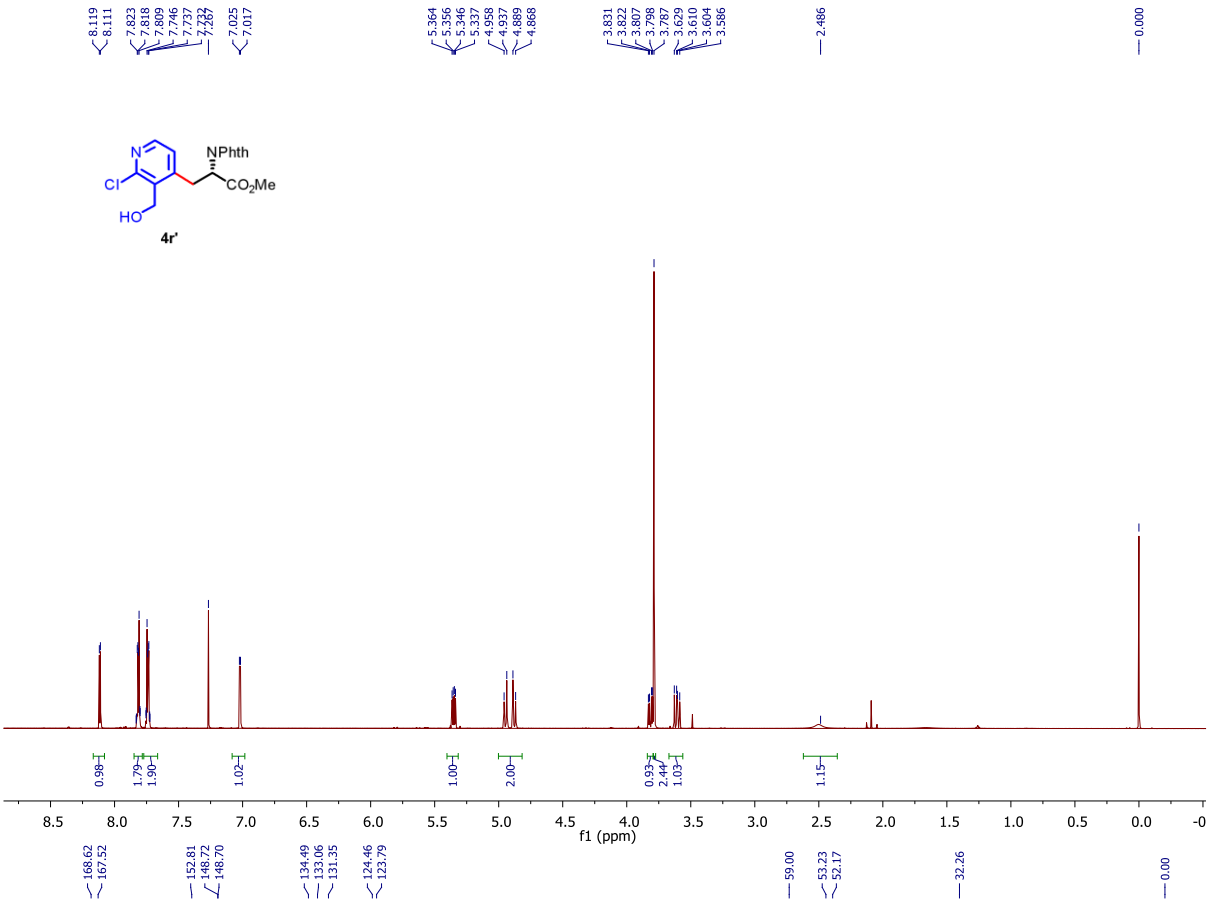

168.92
167.39
158.66
149.24
146.08
134.33
131.43
123.69
123.63
121.07
53.10
52.05
34.04
24.24
0.00
Me
N
NPhth
CO2Me
4p'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

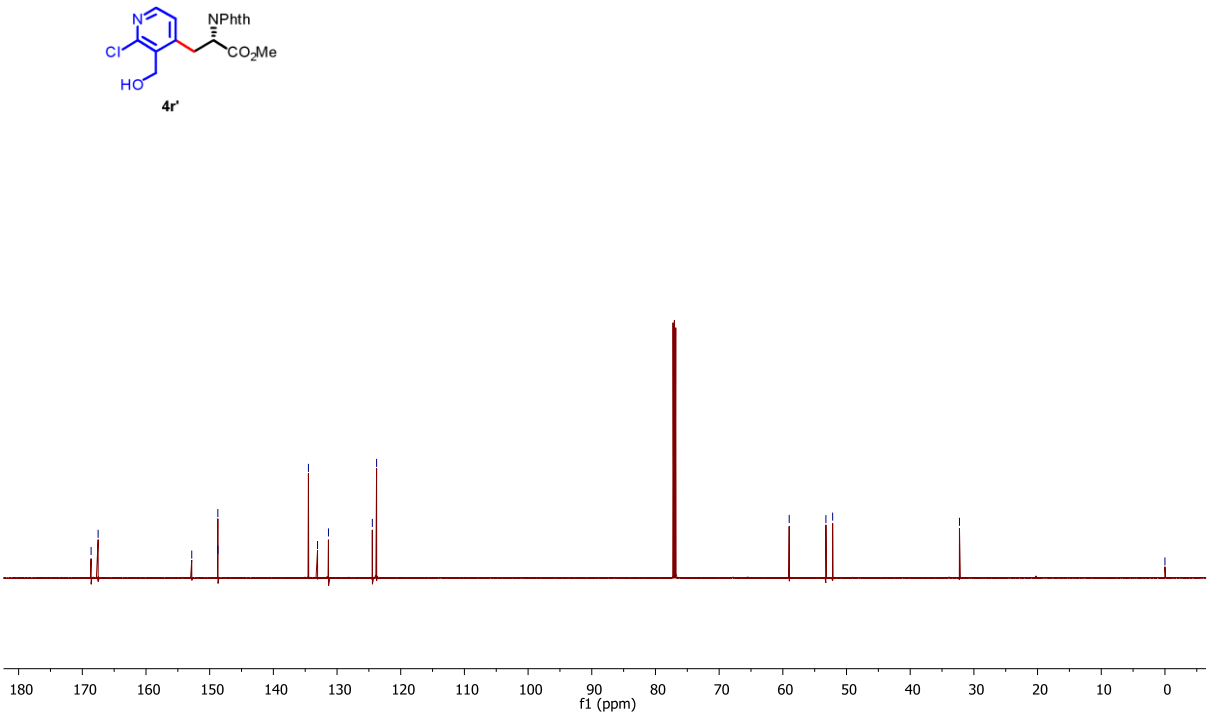

168.92
167.38
164.51
148.56
147.02
134.28
131.49
123.66
117.21
110.91
53.34
53.09
52.07
33.96
-0.00
OMe
N
NPhth
CO2Me
4q'
f1 (ppm)
7.994
7.985
7.823
7.817
7.812
7.808
7.803
7.794
7.733
7.724
7.719
7.715
7.710
7.268
6.716
6.714
6.708
6.705
6.564
5.198
5.188
5.181
5.171
3.837
3.780
3.550
3.545
3.540
3.528
0.000

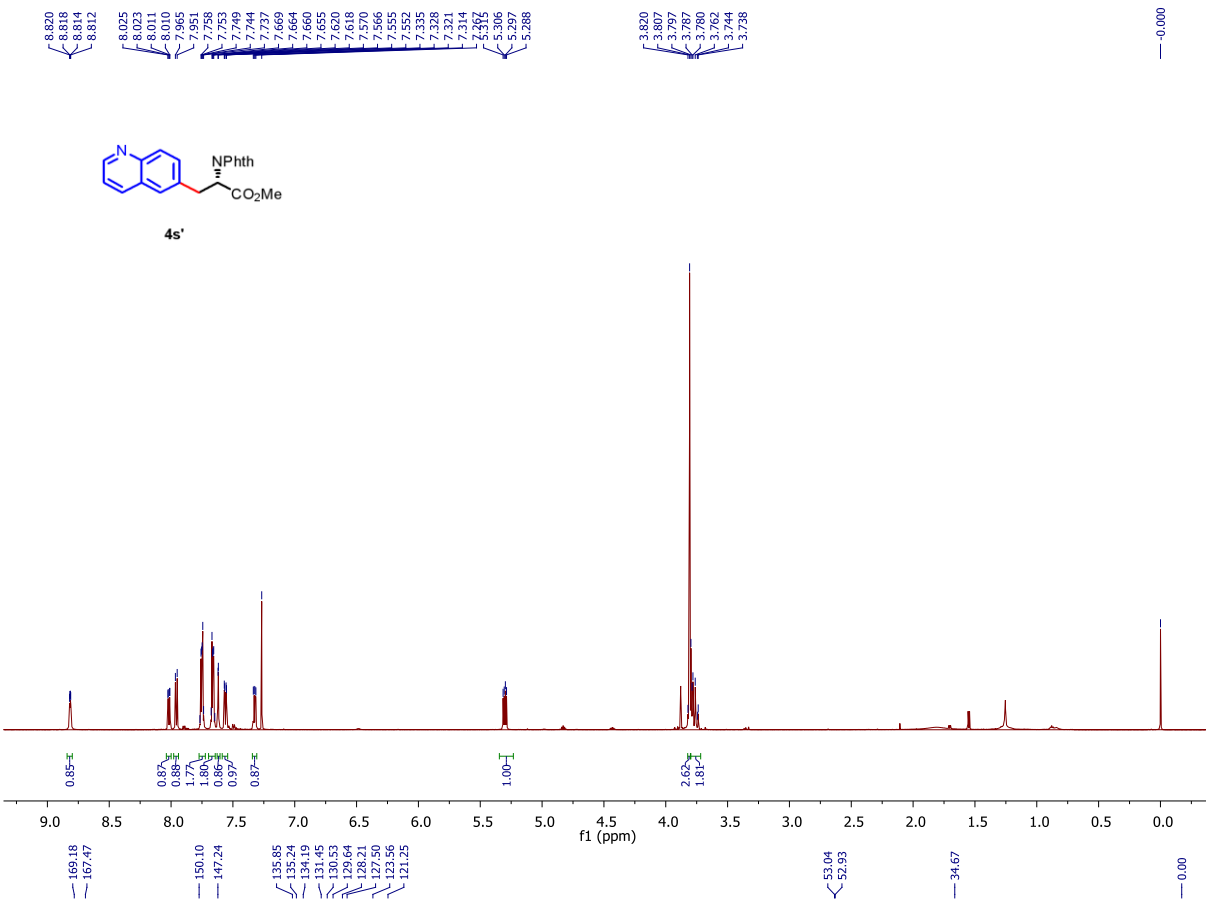

OMe
N
NPhth
CO2Me
4q'
0.99
1.82
2.12
1.02
0.82
1.00
2.54
2.73
2.04
f1 (ppm)

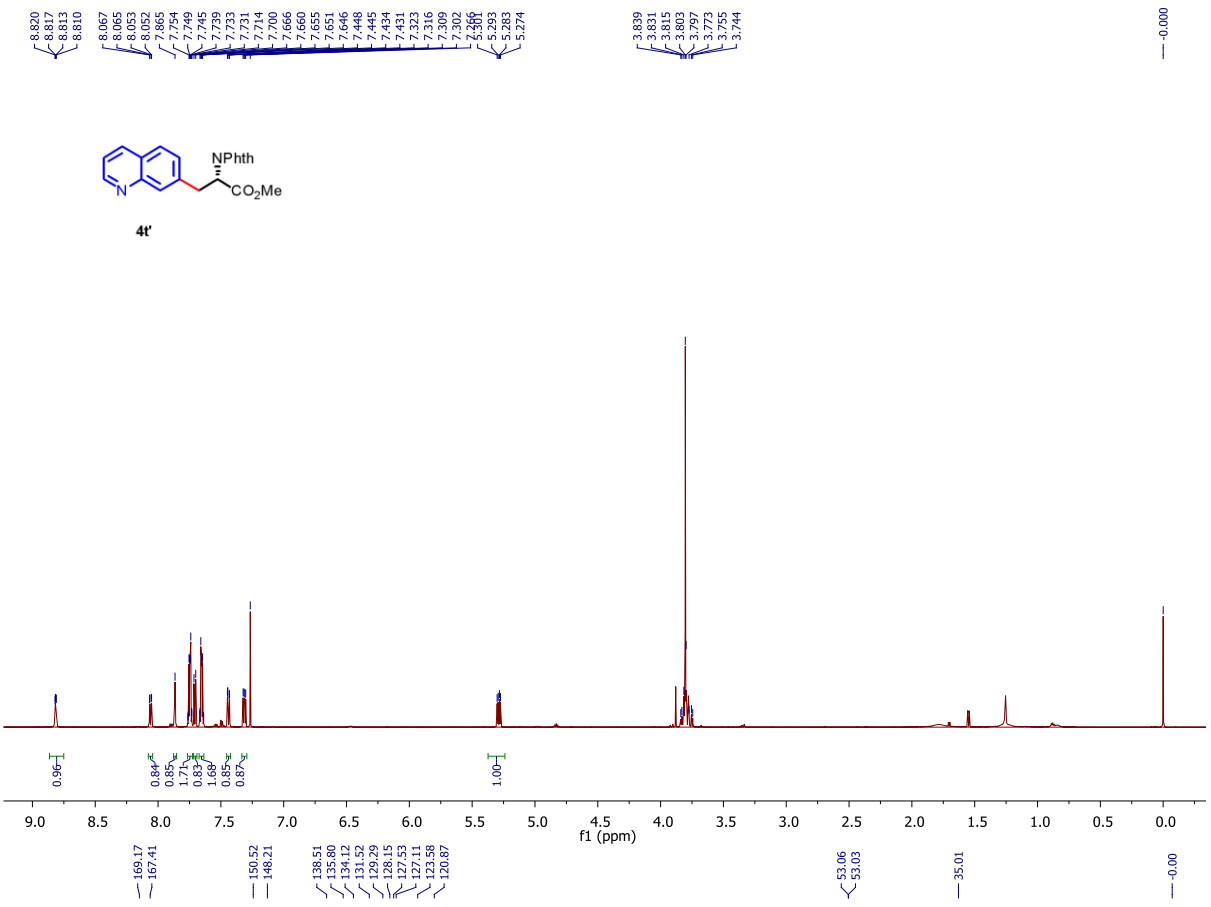

8.366
8.358
7.922
7.918
7.913
7.804
7.799
7.795
7.290
7.286
7.174
7.165
5.820
5.794
5.641
5.616
5.577
5.569
5.556
5.548
4.346
4.324
4.318
4.297
3.264
3.256
3.236
3.228
0.000
Cl
N
O
O
NPhth
4r
1.00
1.72
1.72
1.08
1.15
1.08
1.16
1.08
1.07
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
168.26
167.20
150.72
149.68
147.86
134.66
131.61
128.16
123.95
123.94
65.52
49.10
33.87
-0.00

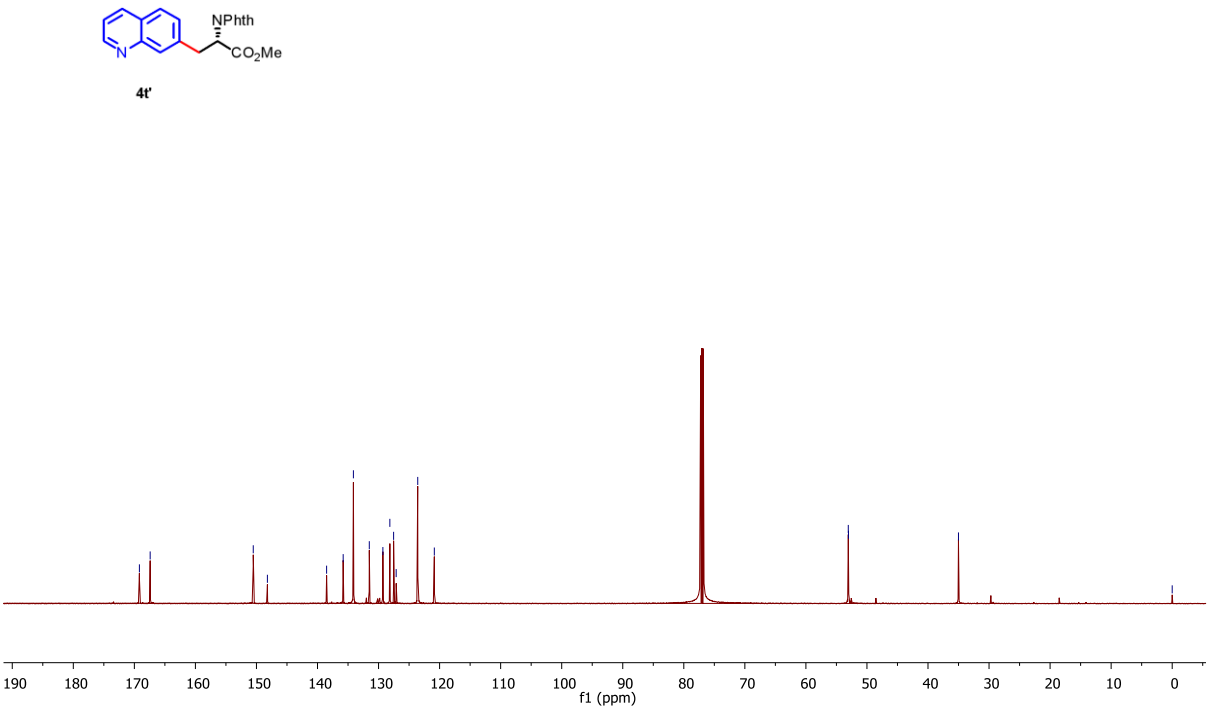

Cl
N
O
O
NPhth
4r
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

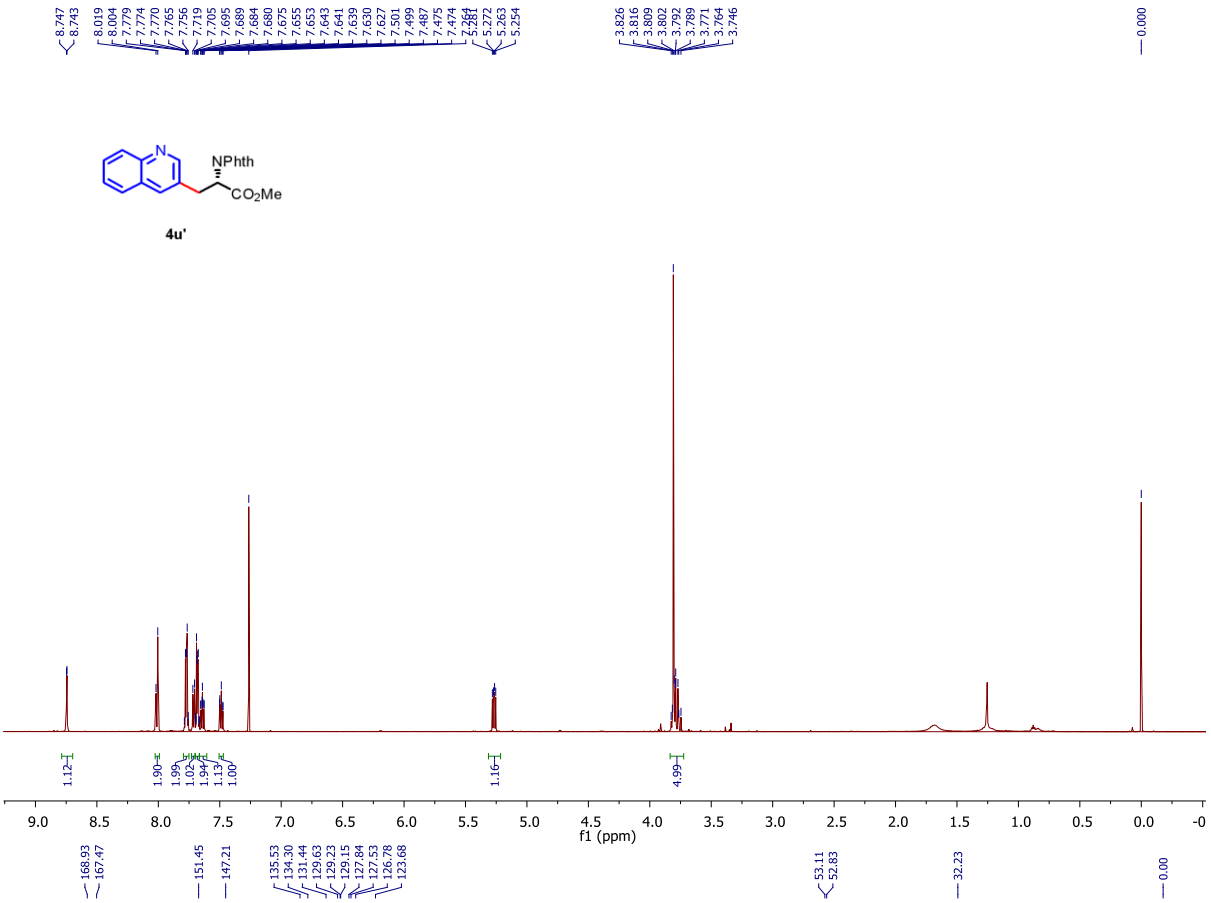

8.119
8.111
7.823
7.818
7.809
7.746
7.737
7.732
7.267
7.025
7.017
5.364
5.356
5.346
5.337
4.958
4.937
4.889
4.868
3.831
3.822
3.807
3.798
3.787
3.629
3.610
3.604
3.586
2.486
0.000
NPhth
CO2Me
Cl
HO
4r'
0.98
1.79
1.90
1.02
1.00
2.00
0.93
2.44
1.03
1.15
f1 (ppm)
168.62
167.52
152.81
148.72
148.70
134.49
133.06
131.35
124.46
123.79
59.00
53.23
52.17
32.26
0.00

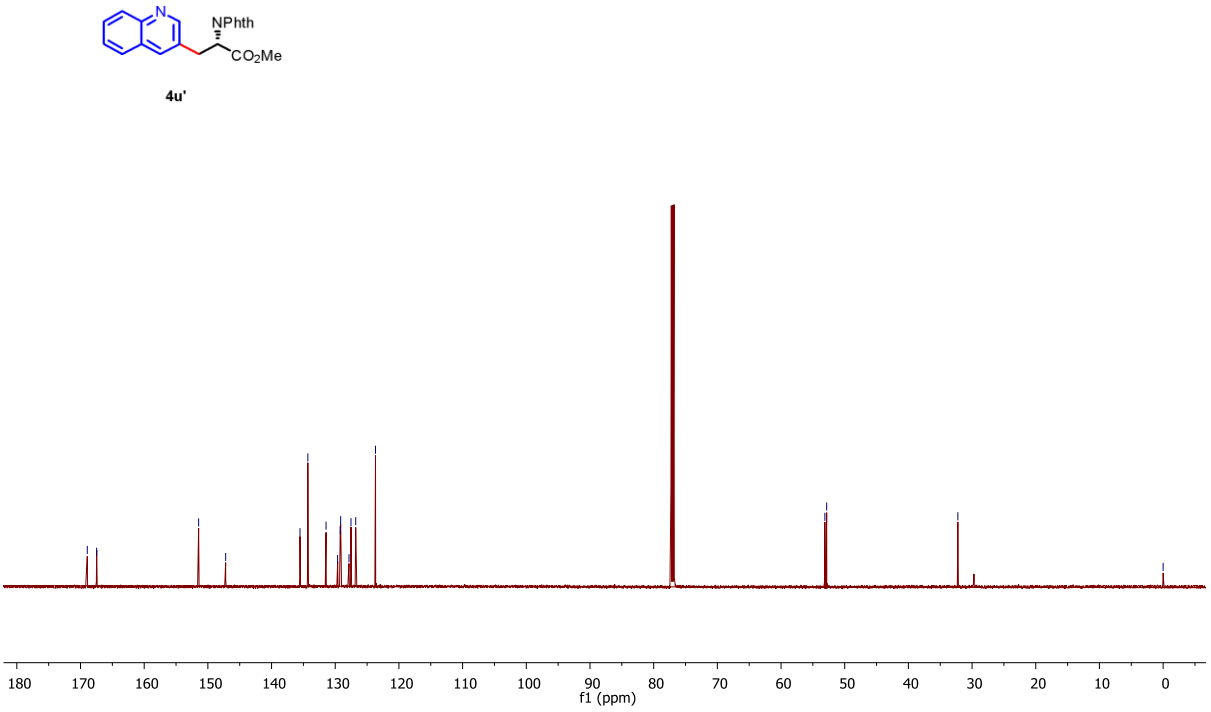

NPhth
CO2Me
Cl
HO
4r'
f1 (ppm)

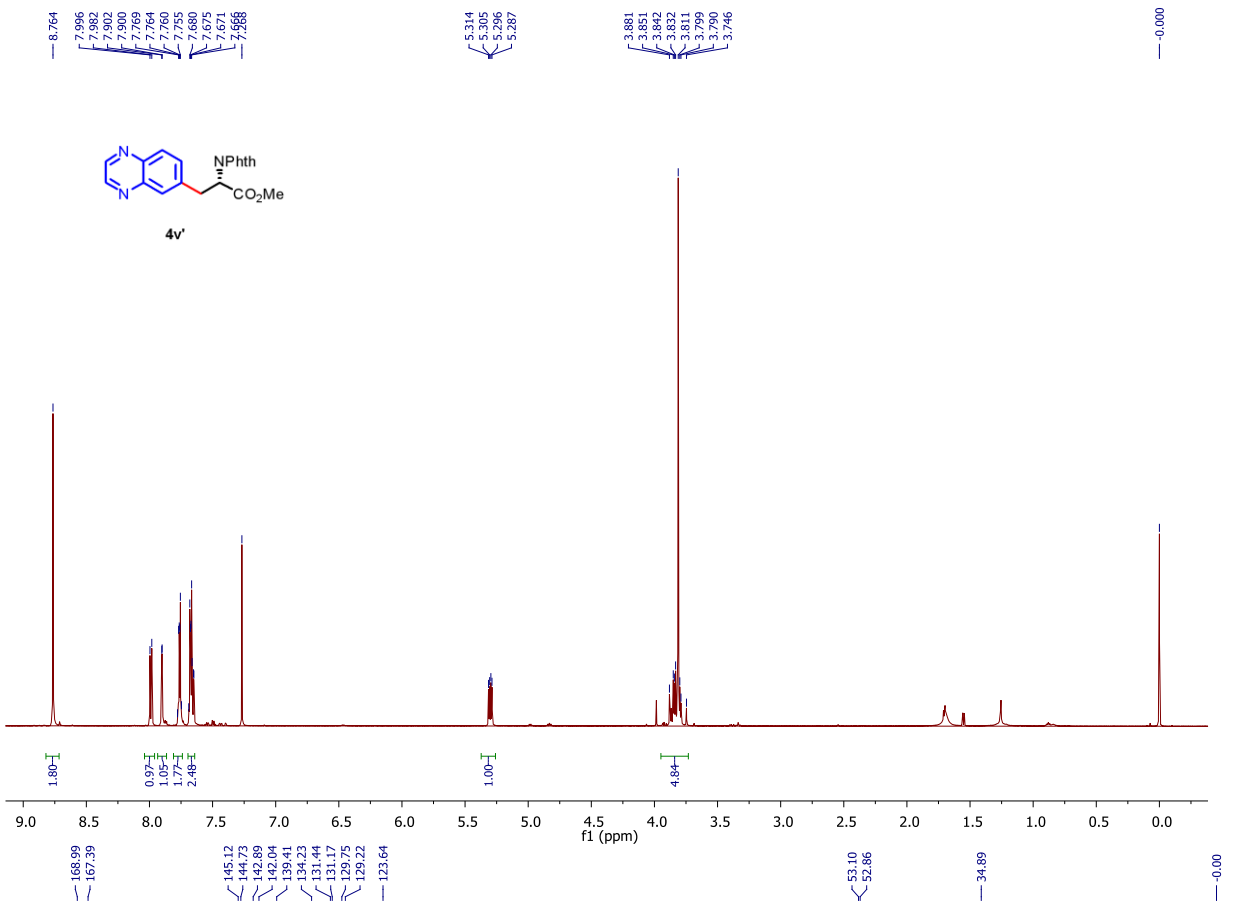

8.820
8.818
8.814
8.812
8.025
8.023
8.011
8.010
7.965
7.951
7.758
7.753
7.749
7.744
7.737
7.669
7.664
7.660
7.655
7.620
7.618
7.570
7.566
7.555
7.552
7.335
7.328
7.321
7.314
7.267
5.315
5.306
5.297
5.288
3.820
3.807
3.797
3.787
3.780
3.762
3.744
3.738
-0.000
NPhth
CO2Me
4s'
0.85
0.87
0.88
1.77
1.80
0.86
0.97
0.87
1.00
2.62
1.81
f1 (ppm)
169.18
167.47
150.10
147.24
135.85
135.24
134.19
131.45
130.53
129.64
128.21
127.50
123.56
121.25
53.04
52.93
34.67
0.00
NPhth
CO2Me
4s'
f1 (ppm)

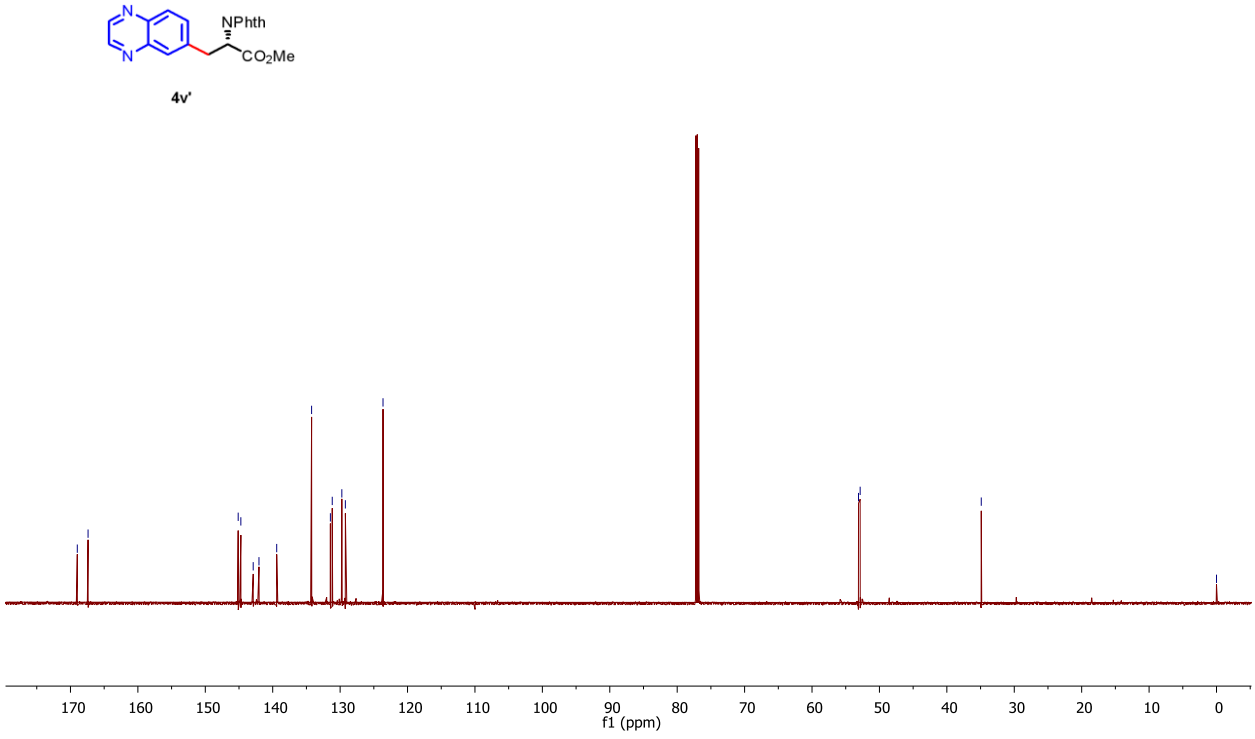

8.820
8.817
8.813
8.810
8.067
8.065
8.053
8.052
7.865
7.754
7.749
7.745
7.739
7.733
7.731
7.714
7.700
7.666
7.660
7.655
7.651
7.646
7.448
7.445
7.434
7.431
7.323
7.316
7.309
7.302
5.293
5.283
5.274
3.839
3.831
3.815
3.803
3.797
3.773
3.755
3.744
-0.000
NPhth
CO2Me
4t'
0.96
0.84
0.85
1.71
0.83
1.68
0.85
0.87
1.00
f1 (ppm)
169.17
167.41
150.52
148.21
138.51
135.80
134.12
131.52
129.29
128.15
127.53
127.11
123.58
120.87
53.06
53.03
35.01
-0.00


NPhth
CO2Me
4t'
f1 (ppm)


8.747
8.743
8.019
8.004
7.779
7.774
7.770
7.765
7.756
7.719
7.705
7.695
7.689
7.684
7.680
7.675
7.655
7.653
7.643
7.641
7.639
7.630
7.627
7.501
7.499
7.487
7.475
7.474
5.272
5.263
5.254
3.826
3.816
3.809
3.802
3.792
3.789
3.771
3.764
3.746
0.000
NPhth
CO2Me
4u'
1.12
1.90
1.99
1.02
1.94
1.13
1.00
1.16
4.99
f1 (ppm)
168.93
167.47
151.45
147.21
135.53
134.30
131.44
129.63
129.23
129.15
127.84
127.53
126.78
123.68
53.11
52.83
32.23
0.00


NPhth
CO2Me
4u'
f1 (ppm)

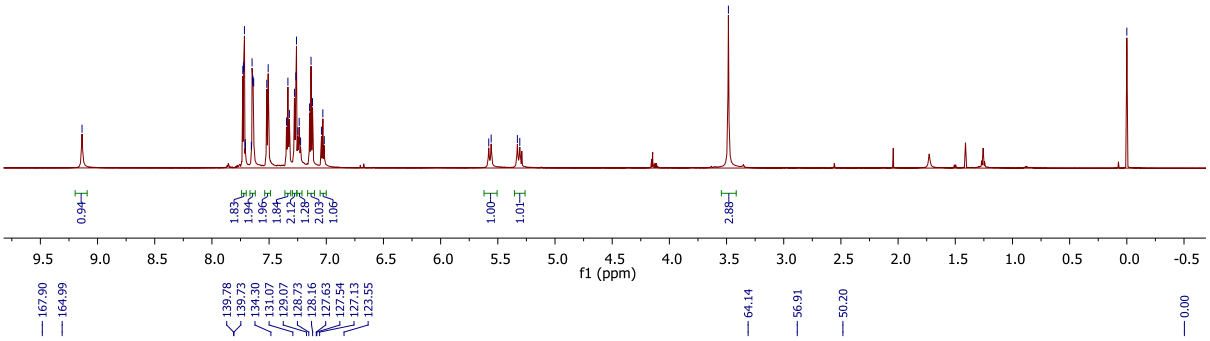

8.764
7.996
7.982
7.902
7.900
7.769
7.764
7.760
7.755
7.680
7.675
7.671
5.314
5.305
5.296
5.287
3.881
3.851
3.842
3.832
3.811
3.799
3.790
3.746
-0.000
NPhth
CO2Me
4v'
1.80
0.97
1.05
1.77
2.48
1.00
4.84
f1 (ppm)


168.99
167.39
145.12
144.73
142.89
142.04
139.41
134.23
131.44
131.17
129.75
129.22
123.64
53.10
52.86
34.89
-0.00
NPhth
CO2Me
4v'
f1 (ppm)

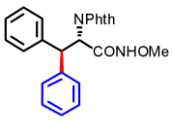

9.136
7.730
7.725
7.720
7.715
7.709
7.655
7.649
7.644
7.640
7.635
7.520
7.508
7.348
7.335
7.323
7.278
7.266
7.261
7.249
7.237
7.225
7.146
7.133
7.120
7.042
7.030
5.558
5.329
5.308
3.484
0.000

NPhth
CONHOMe

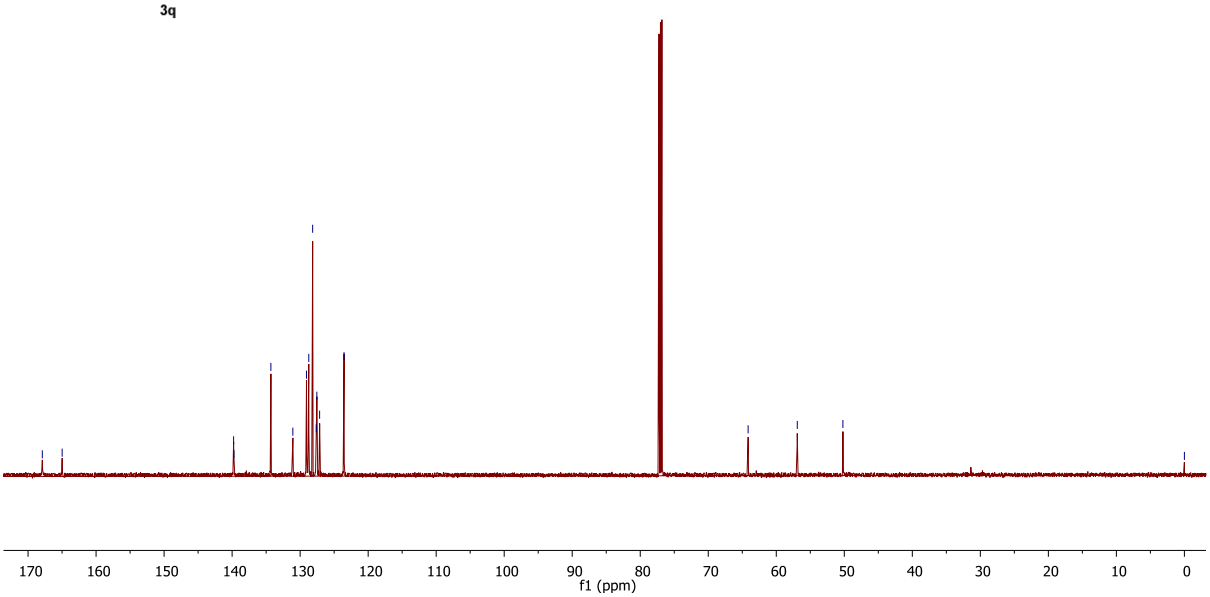
3q

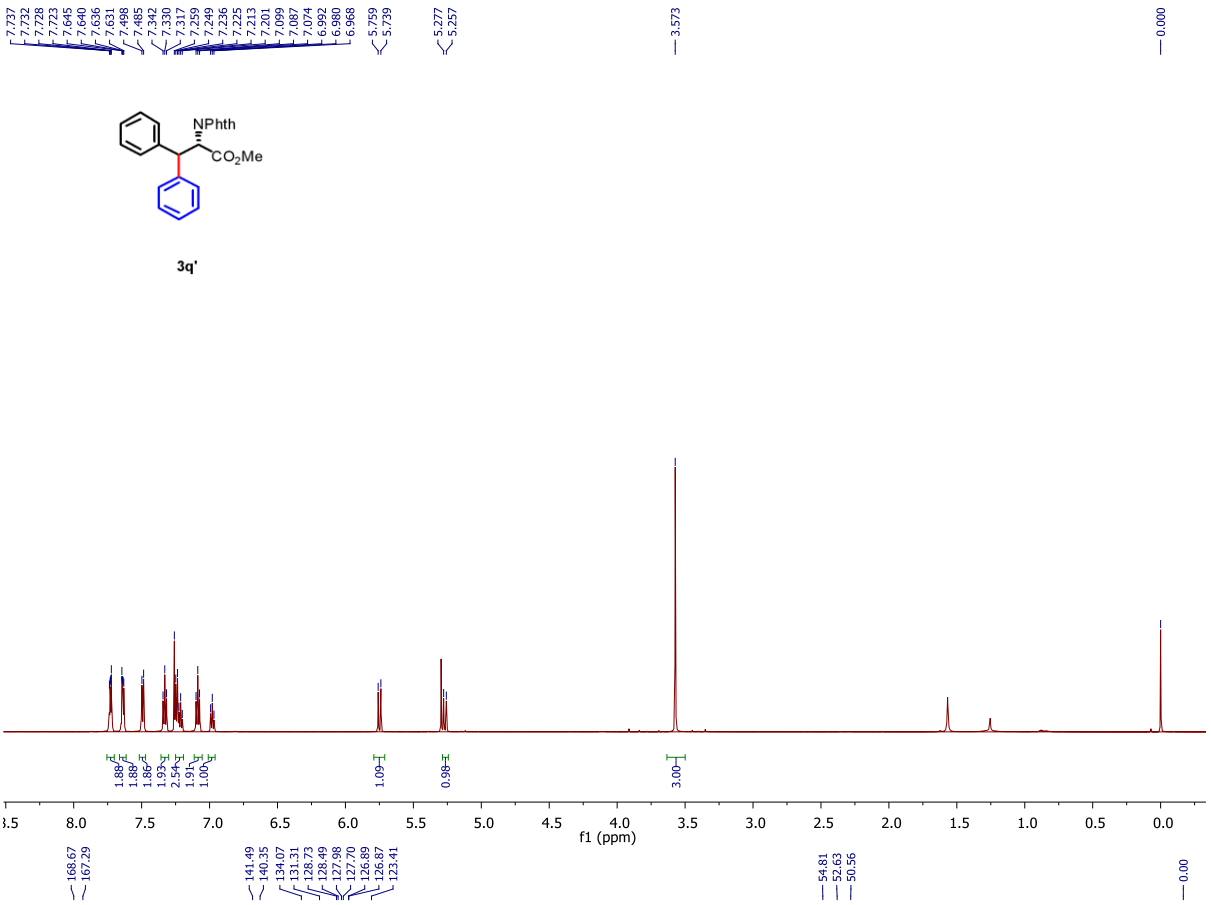

0.94
1.83
1.94
1.96
1.84
2.12
1.28
2.03
1.06
1.00
1.01
2.88
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

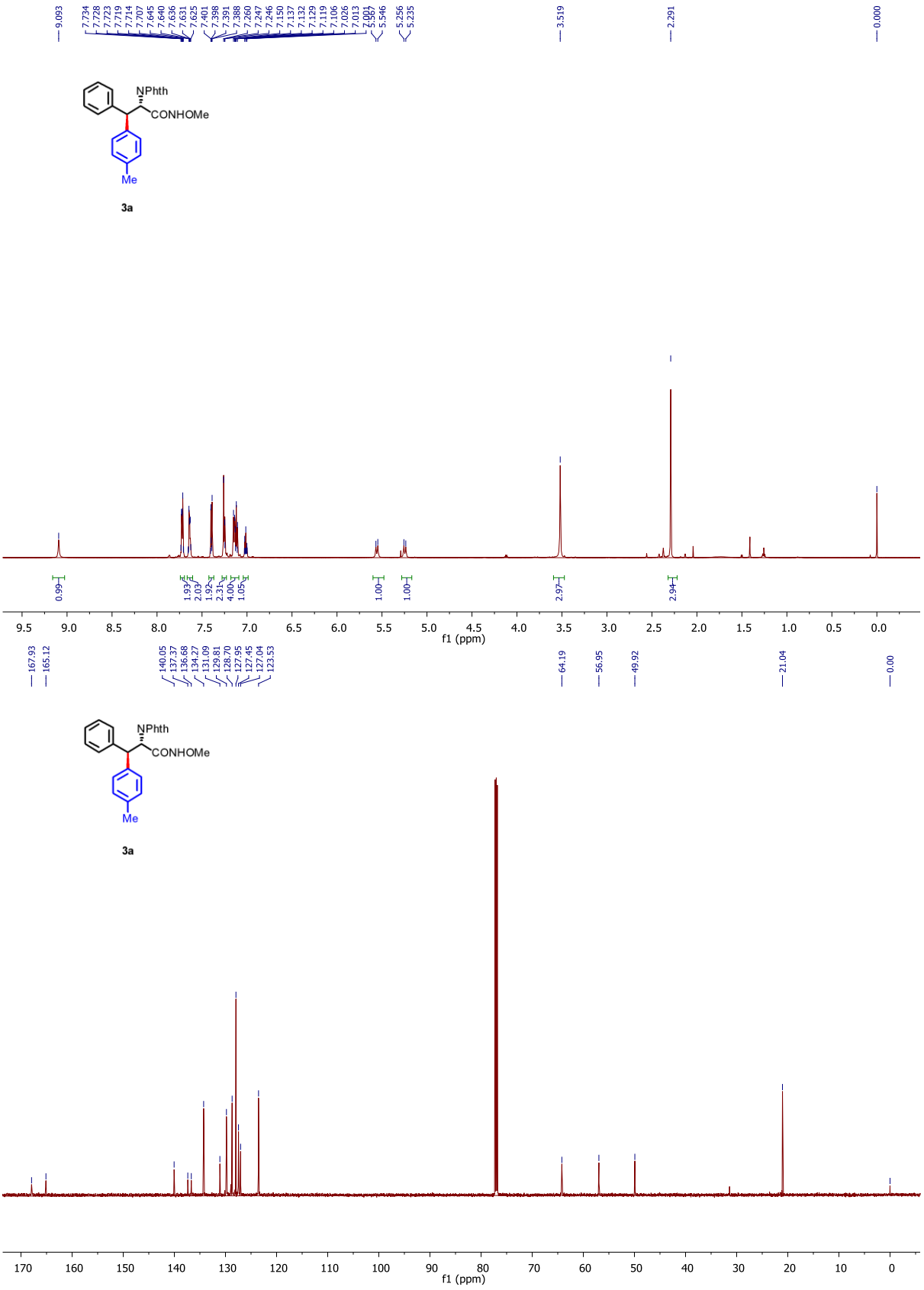
167.90
164.99
139.78
139.73
134.30
131.07
129.07
128.73
128.16
127.63
127.54
127.13
123.55
64.14
56.91
50.20
0.00

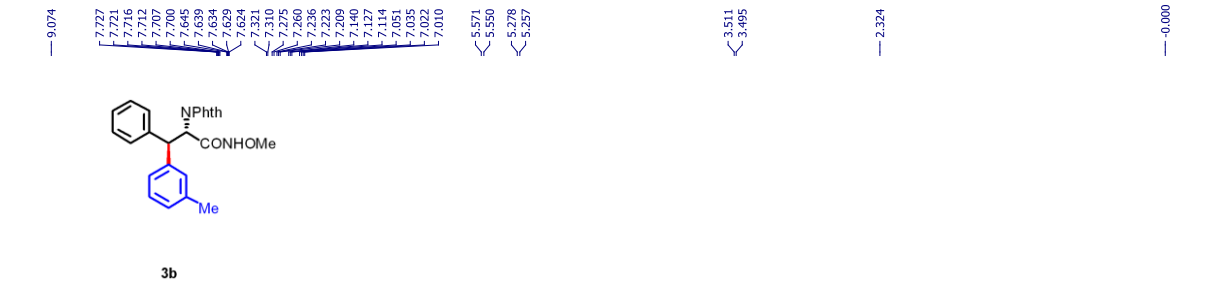

NPhth
CONHOMe

3q

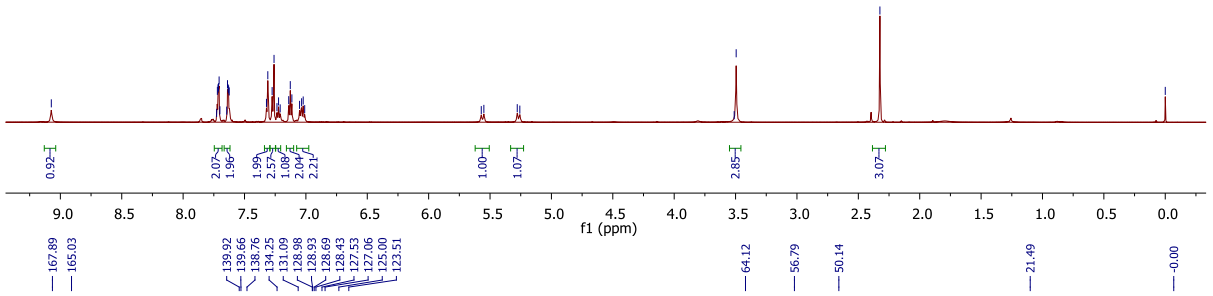

170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.737
7.732
7.728
7.723
7.645
7.640
7.636
7.631
7.498
7.485
7.342
7.330
7.317
7.259
7.249
7.236
7.225
7.213
7.201
7.099
7.087
7.074
6.992
6.980
6.968
5.759
5.739
5.277
5.257
3.573
0.000
NPhth
CO2Me
3q'
1.89
1.89
1.88
1.86
1.93
2.54
1.91
1.00
1.09
0.98
3.00
f1 (ppm)
168.67
167.29
141.49
140.35
134.07
131.31
128.73
128.49
127.98
127.70
126.89
126.87
123.41
54.81
52.63
50.56
0.00
NPhth
CO2Me
3q'
f1 (ppm)


9.093
7.734
7.728
7.723
7.719
7.714
7.707
7.645
7.640
7.636
7.631
7.625
7.401
7.398
7.391
7.388
7.260
7.247
7.246
7.150
7.137
7.132
7.129
7.119
7.106
7.026
7.013
7.001
5.567
5.546
5.256
5.235
3.519
2.291
0.000
NPhth
CONHOMe
Me
3a
0.99
1.93
2.03
1.92
2.31
4.00
1.05
1.00
1.00
2.97
2.94
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
167.93
165.12
140.05
137.37
136.68
134.27
131.09
129.81
128.70
127.95
127.45
127.04
123.53
64.19
56.95
49.92
21.04
0.00
NPhth
CONHOMe
Me
3a
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


9.074
7.727
7.721
7.716
7.712
7.707
7.700
7.645
7.639
7.634
7.629
7.624
7.321
7.310
7.275
7.260
7.236
7.223
7.209
7.140
7.127
7.114
7.051
7.035
7.022
7.010
5.571
5.550
5.278
5.257
3.511
3.495
2.324
-0.000
NPhth
CONHOMe
Me

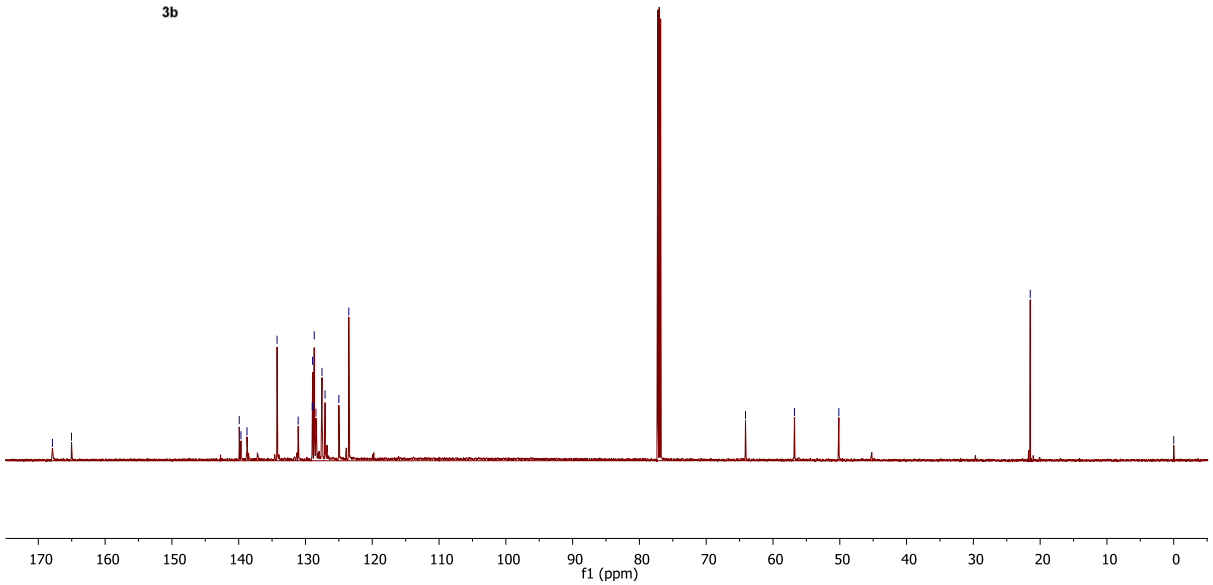
3b

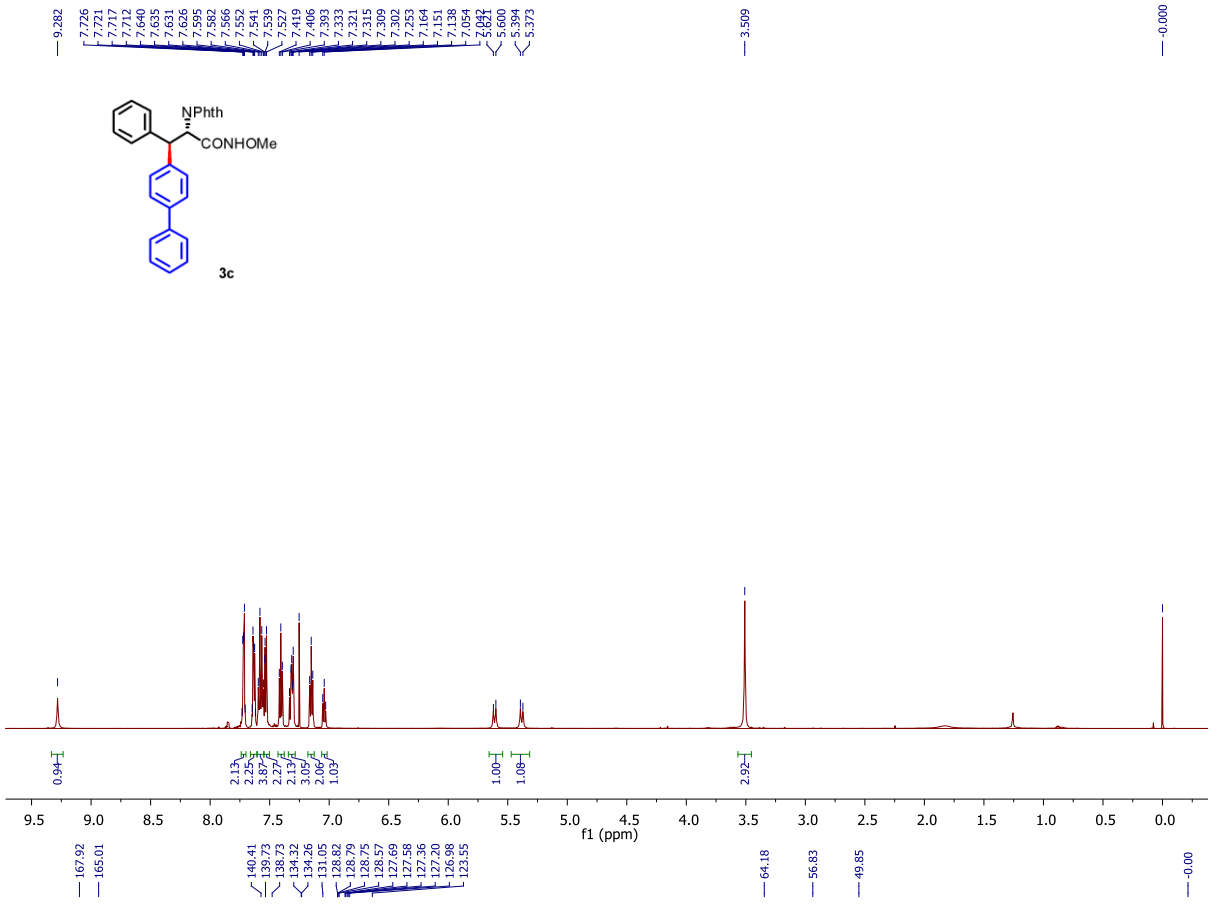

0.92
2.07
1.96
1.99
2.57
1.08
2.04
2.21
1.00
1.07
2.85
3.07
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

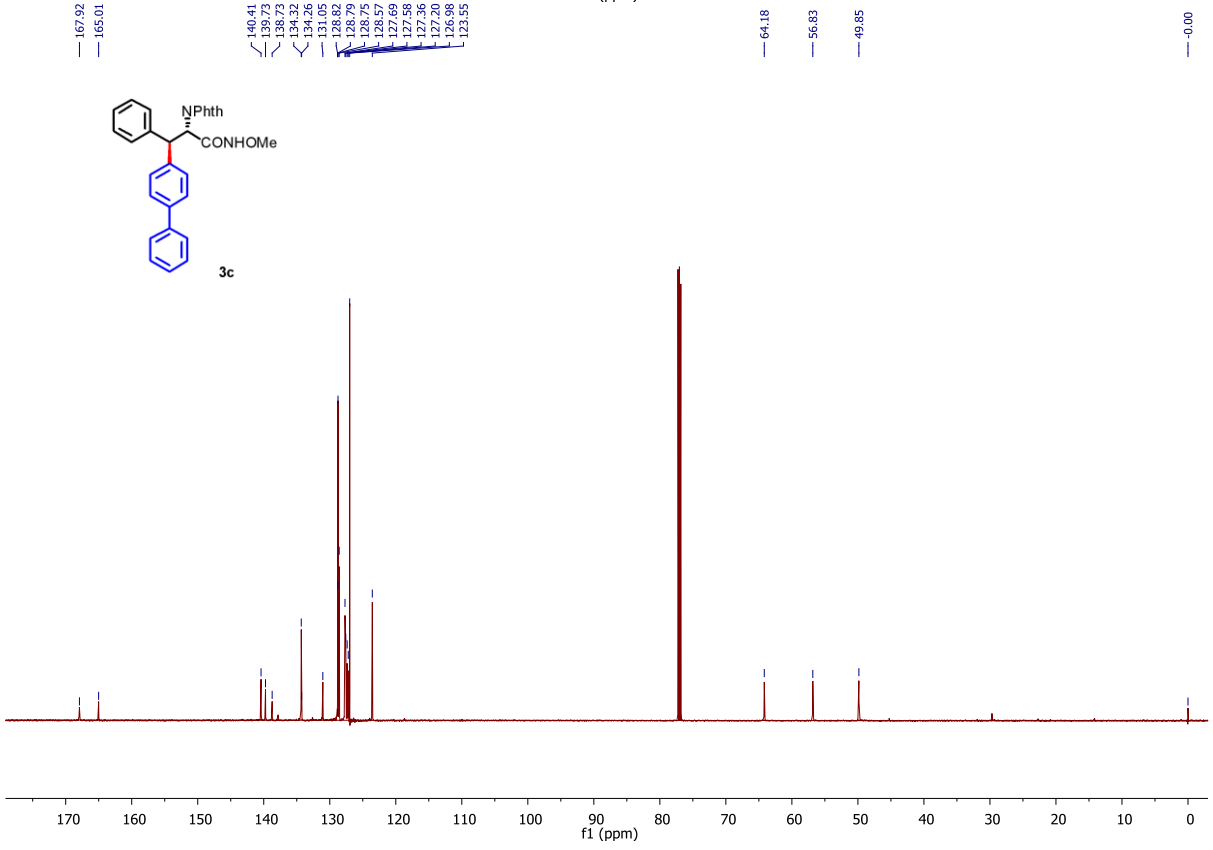
167.89
165.03
139.92
139.66
138.76
134.25
131.09
128.98
128.93
128.69
128.43
127.53
127.06
125.00
123.51
64.12
56.79
50.14
21.49
-0.00

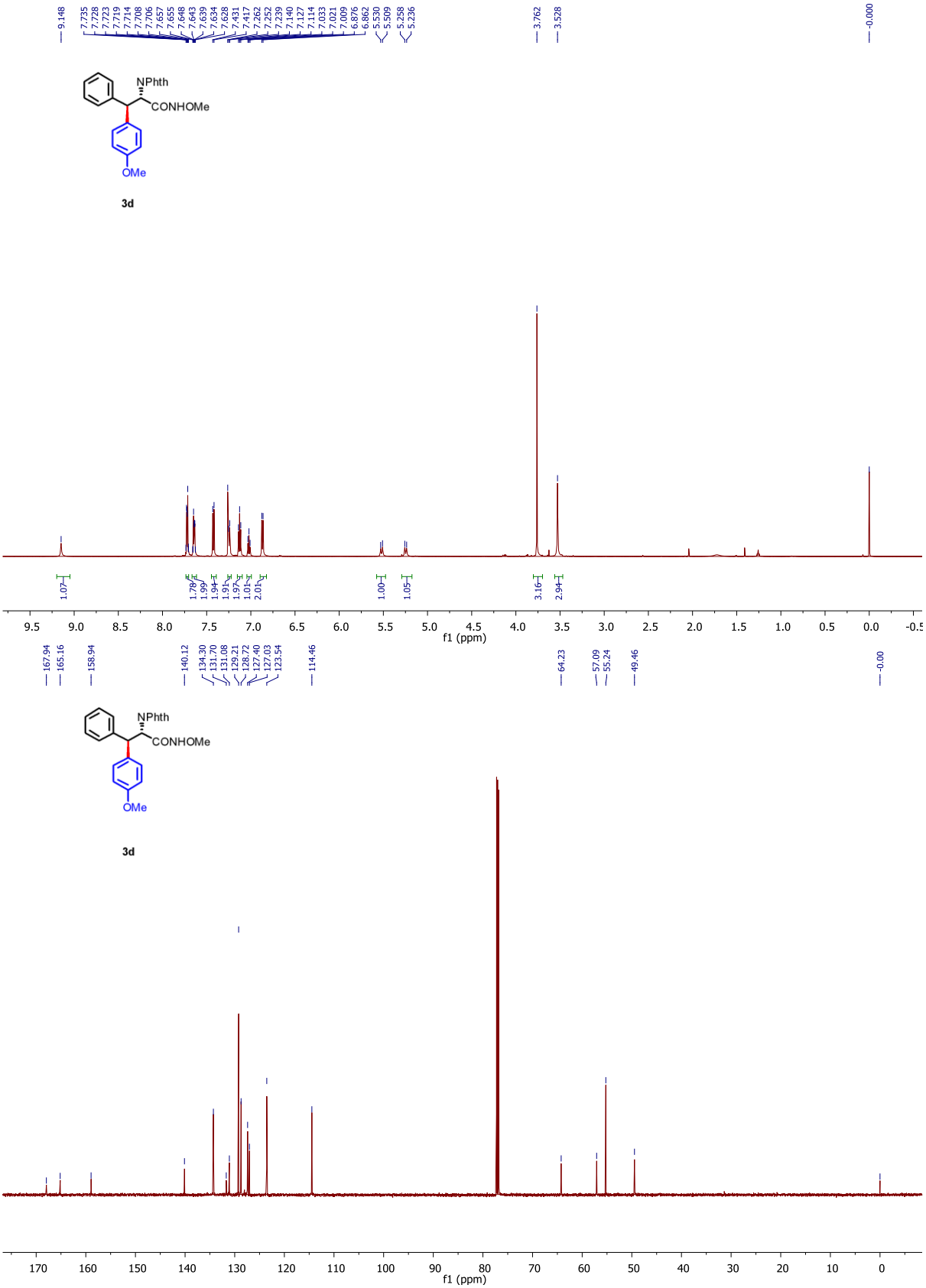

NPhth
CONHOMe
Me

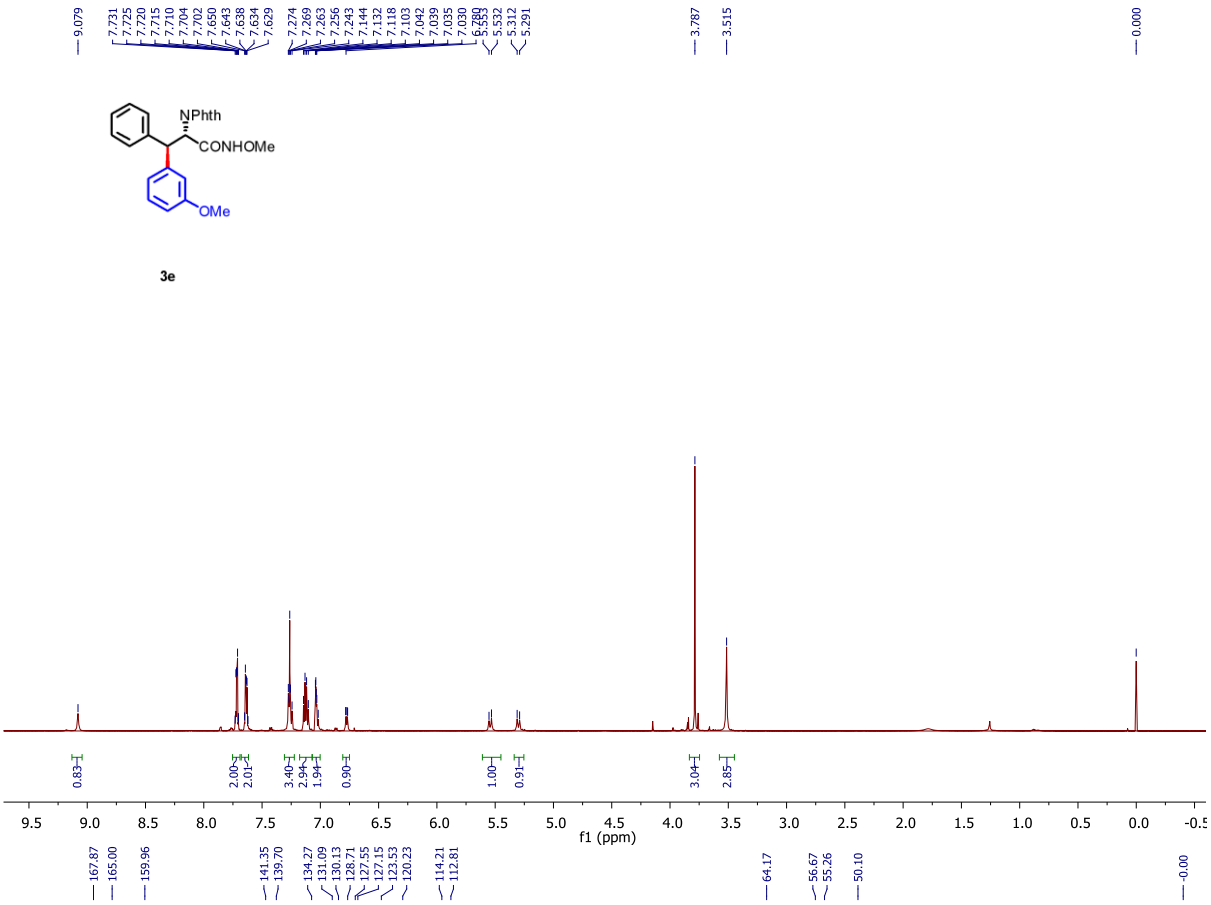
3b


170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.282
7.726
7.721
7.717
7.712
7.640
7.635
7.631
7.626
7.595
7.582
7.566
7.552
7.541
7.539
7.527
7.419
7.406
7.393
7.333
7.321
7.315
7.309
7.302
7.253
7.164
7.151
7.138
7.054
5.621
5.600
5.394
5.373
3.509
-0.000
NPhth
CONHOMe
3c
0.94
2.13
2.25
3.87
2.27
2.13
3.05
2.06
1.03
1.00
1.08
2.92
f1 (ppm)


167.92
165.01
140.41
139.73
138.73
134.32
134.26
131.05
128.82
128.79
128.75
128.57
127.69
127.58
127.36
127.20
126.98
123.55
64.18
56.83
49.85
-0.00
NPhth
CONHOMe
3c
f1 (ppm)

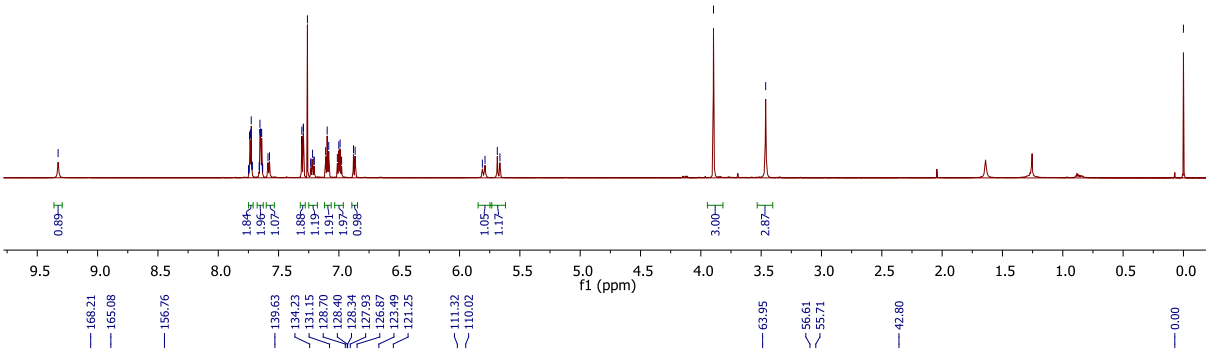

9.148
7.735
7.728
7.723
7.719
7.714
7.708
7.706
7.657
7.655
7.648
7.643
7.639
7.634
7.628
7.431
7.417
7.262
7.252
7.239
7.140
7.127
7.114
7.033
7.021
7.009
6.876
6.862
5.530
5.509
5.258
5.236
3.762
3.528
-0.000
NPhth
CONHOMe
OMe
3d
1.07
1.78
1.99
1.94
1.91
1.97
1.01
2.01
1.00
1.05
3.16
2.94
f1 (ppm)
167.94
165.16
158.94
140.12
134.30
131.70
131.08
129.21
128.72
127.40
127.03
123.54
114.46
64.23
57.09
55.24
49.46
-0.00
NPhth
CONHOMe
OMe
3d
f1 (ppm)


9.079
7.731
7.725
7.720
7.715
7.710
7.704
7.702
7.650
7.643
7.638
7.634
7.629
7.274
7.269
7.263
7.256
7.243
7.144
7.132
7.118
7.103
7.042
7.039
7.035
7.030
6.280
5.553
5.532
5.312
5.291
3.787
3.515
0.000
NPhth
CONHOMe
OMe
3e
0.83
2.00
2.01
3.40
2.94
1.94
0.90
1.00
0.91
3.04
2.85
f1 (ppm)
167.87
165.00
159.96
141.35
139.70
134.27
131.09
130.13
128.71
127.55
127.15
123.53
120.23
114.21
112.81
64.17
56.67
55.26
50.10
-0.00
NPhth
CONHOMe
OMe
3e
f1 (ppm)

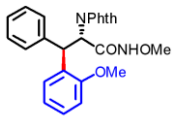

9.327
7.741
7.736
7.731
7.727
7.720
7.718
7.661
7.654
7.649
7.645
7.640
7.634
7.632
7.588
7.575
7.309
7.307
7.295
7.294
7.261
7.110
7.097
7.084
7.001
6.990
6.879
6.865
6.811
5.789
5.687
5.665
3.895
3.463
-0.000

NPhth
CONHOMe
OMe

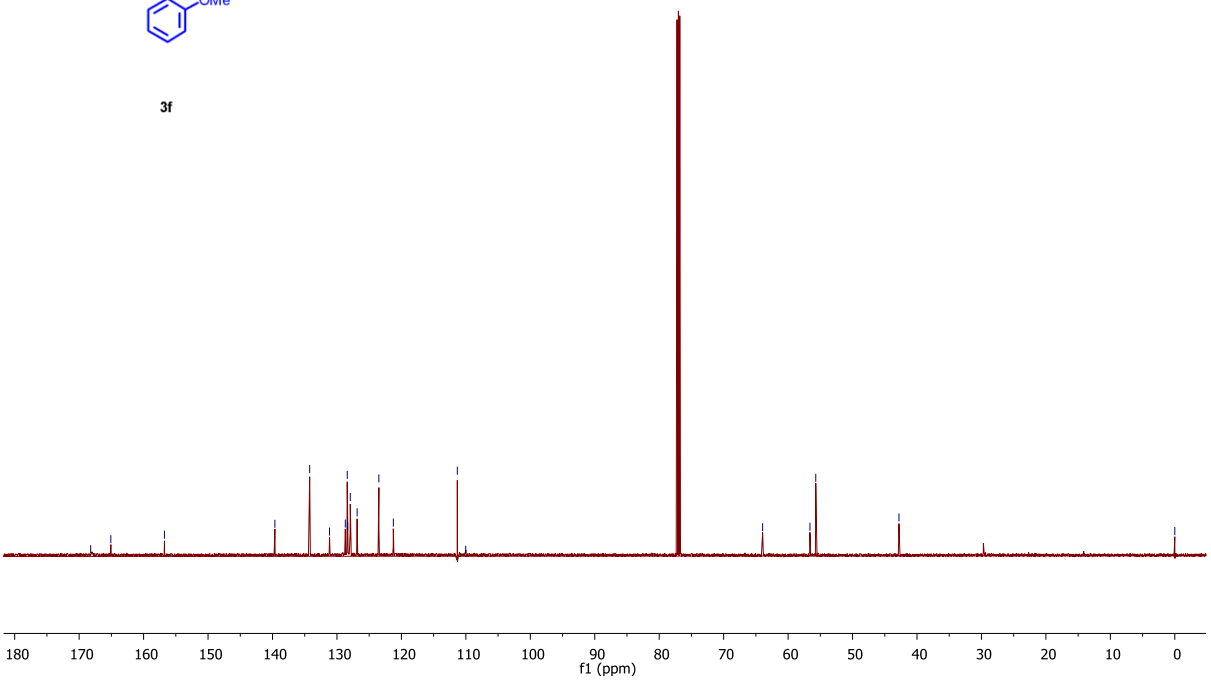
3f

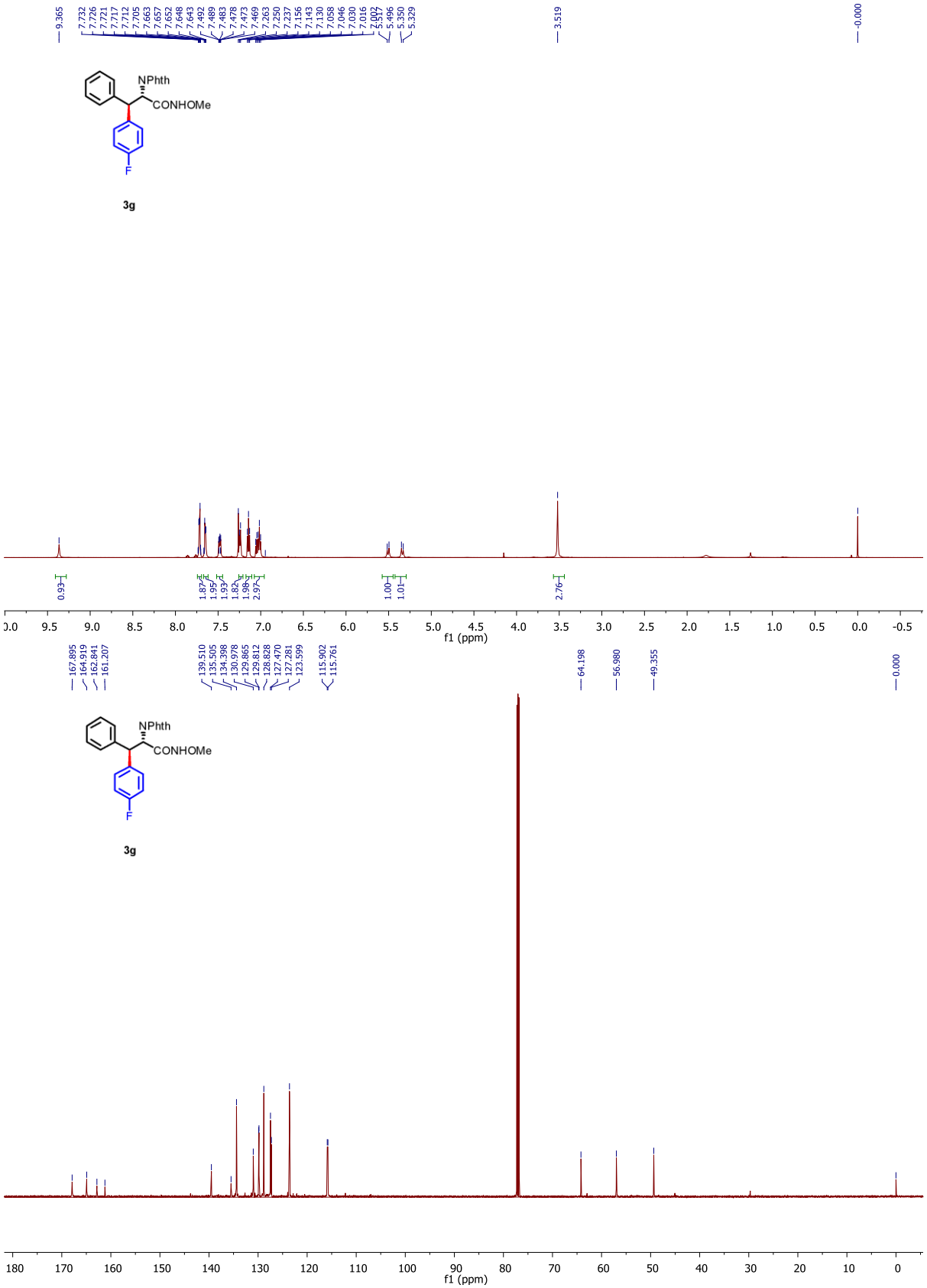

0.89
1.84
1.96
1.07
1.88
1.19
1.91
1.97
0.98
1.05
1.17
3.00
2.87
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

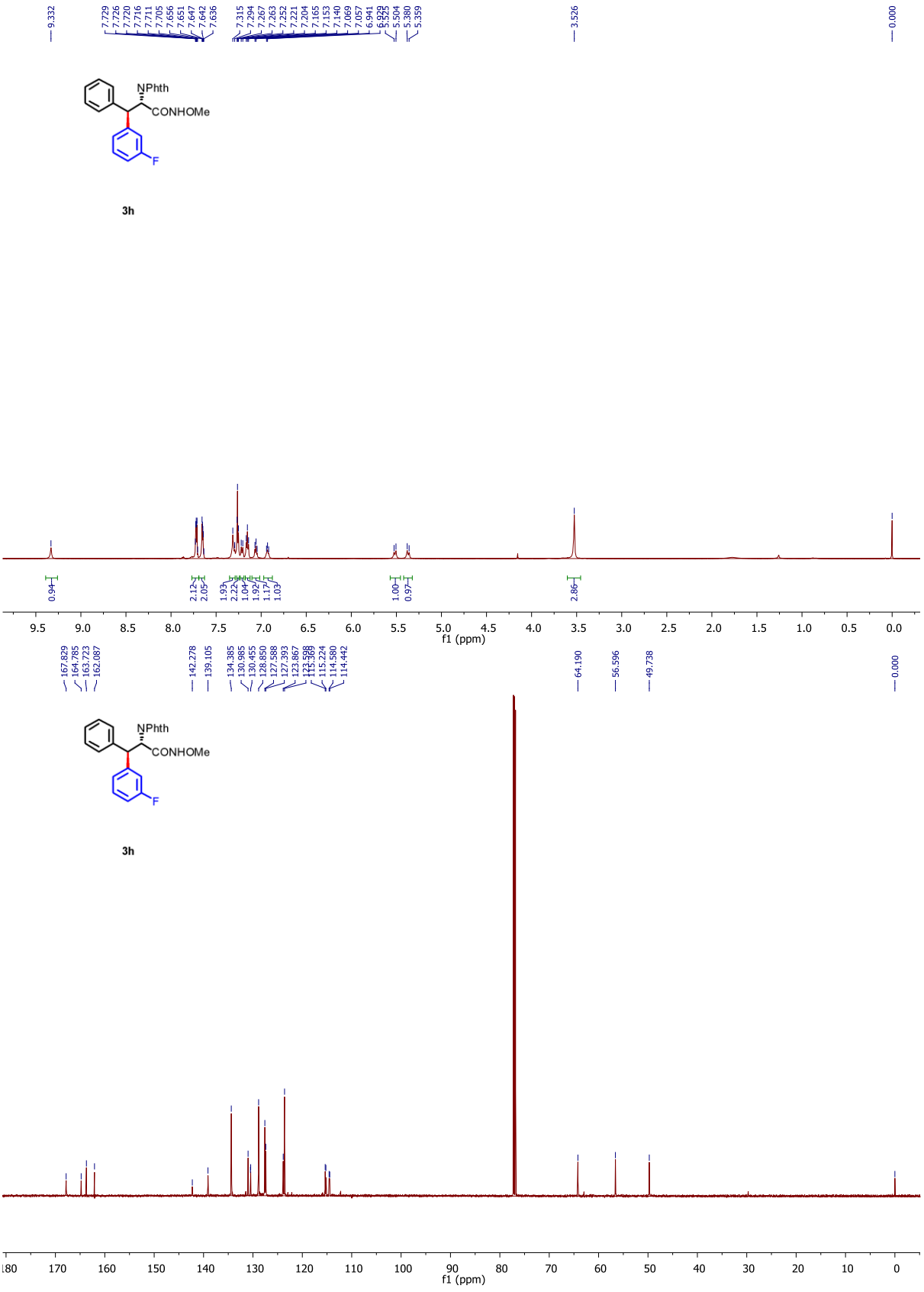
168.21
165.08
156.76
139.63
134.23
131.15
128.70
128.40
128.34
127.93
126.87
123.49
121.25
111.32
110.02
63.95
56.61
55.71
42.80
0.00

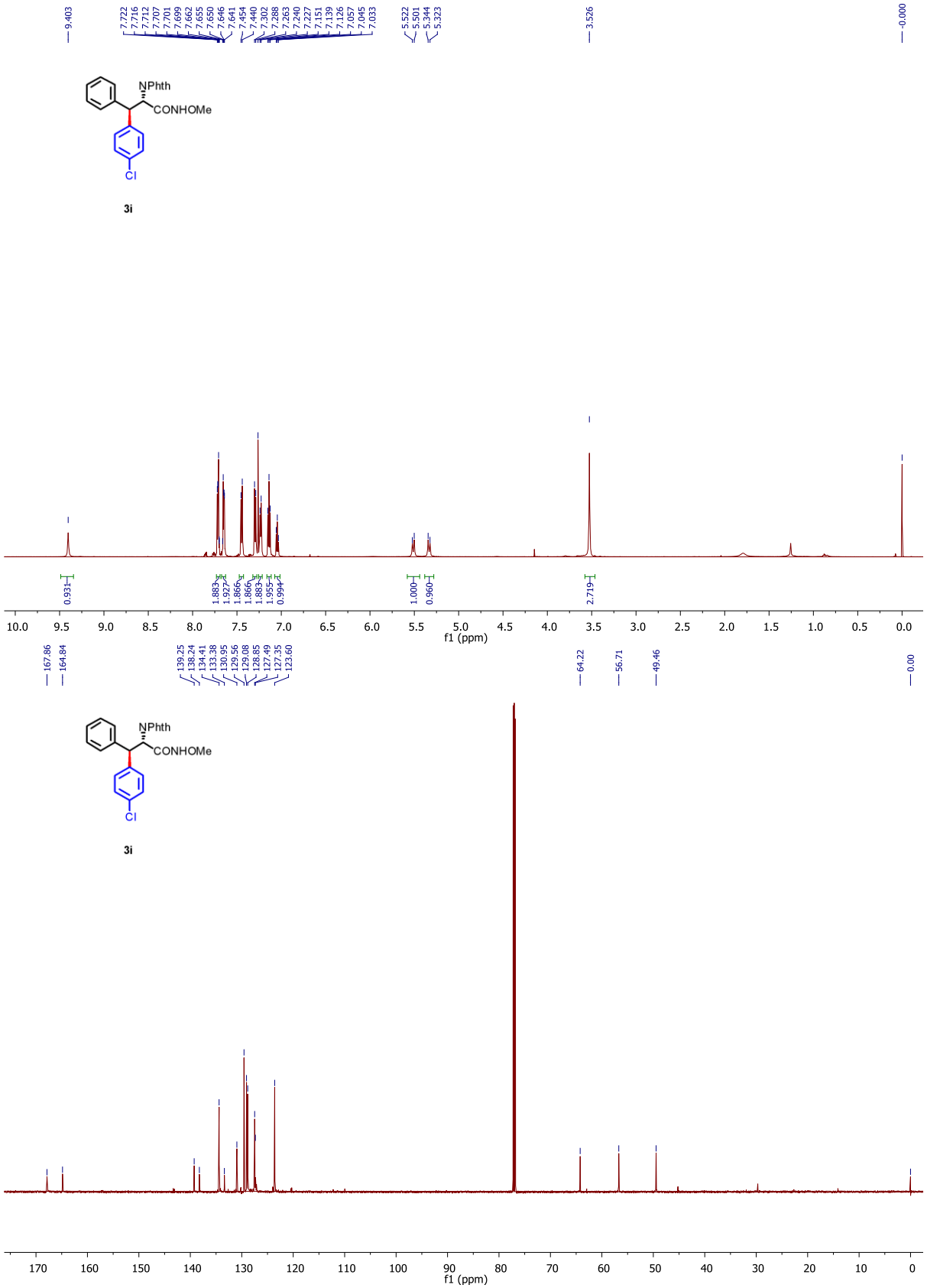

NPhth
CONHOMe
OMe

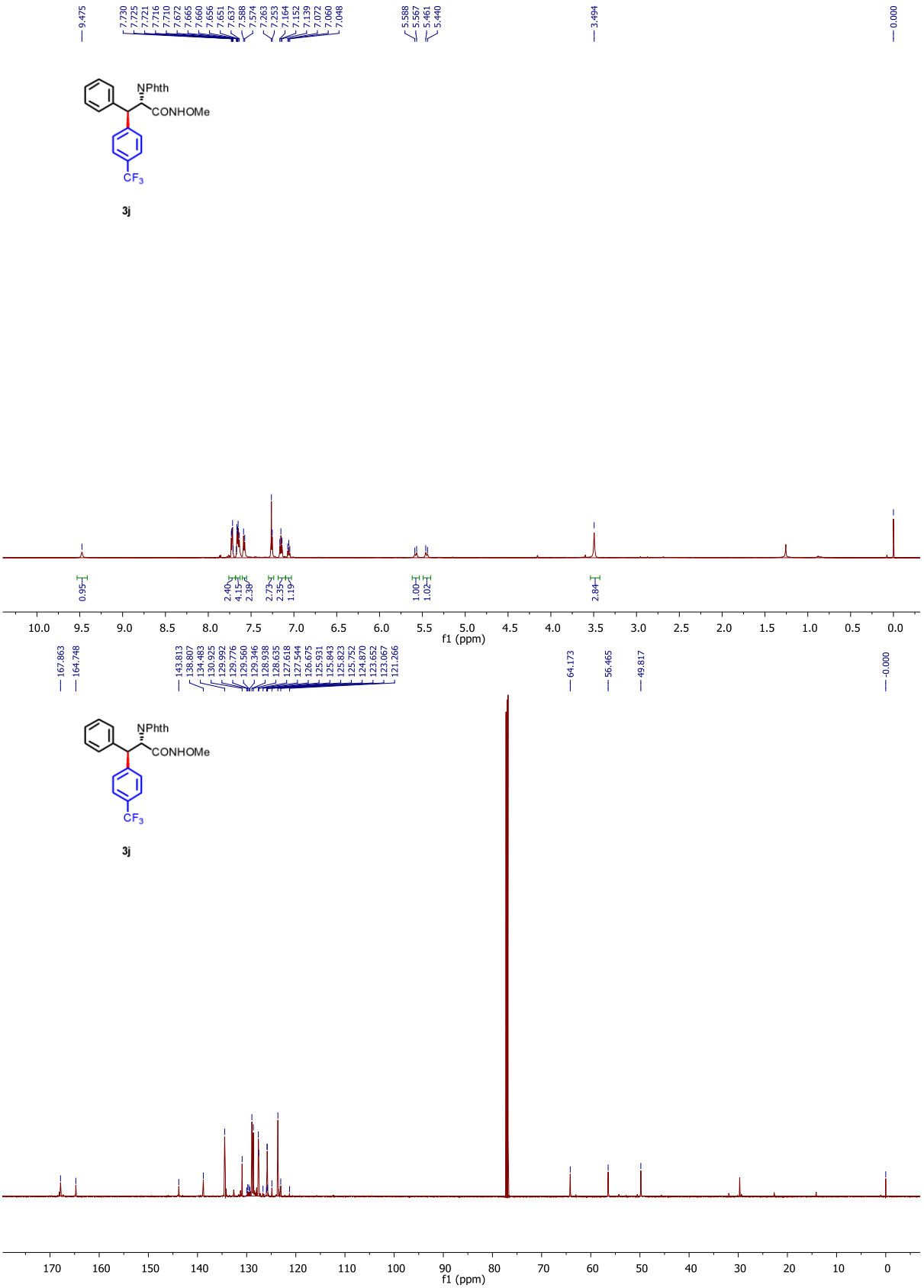
3f

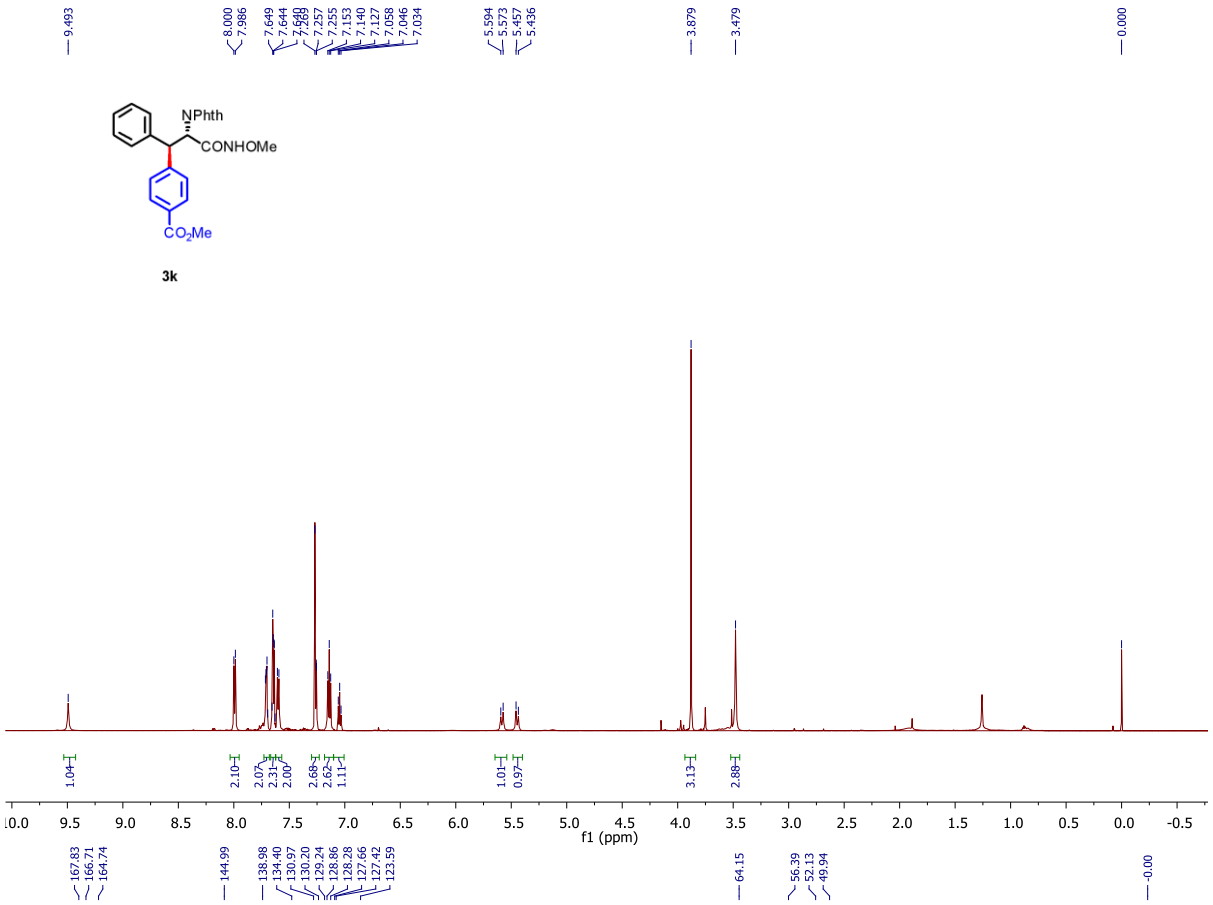

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

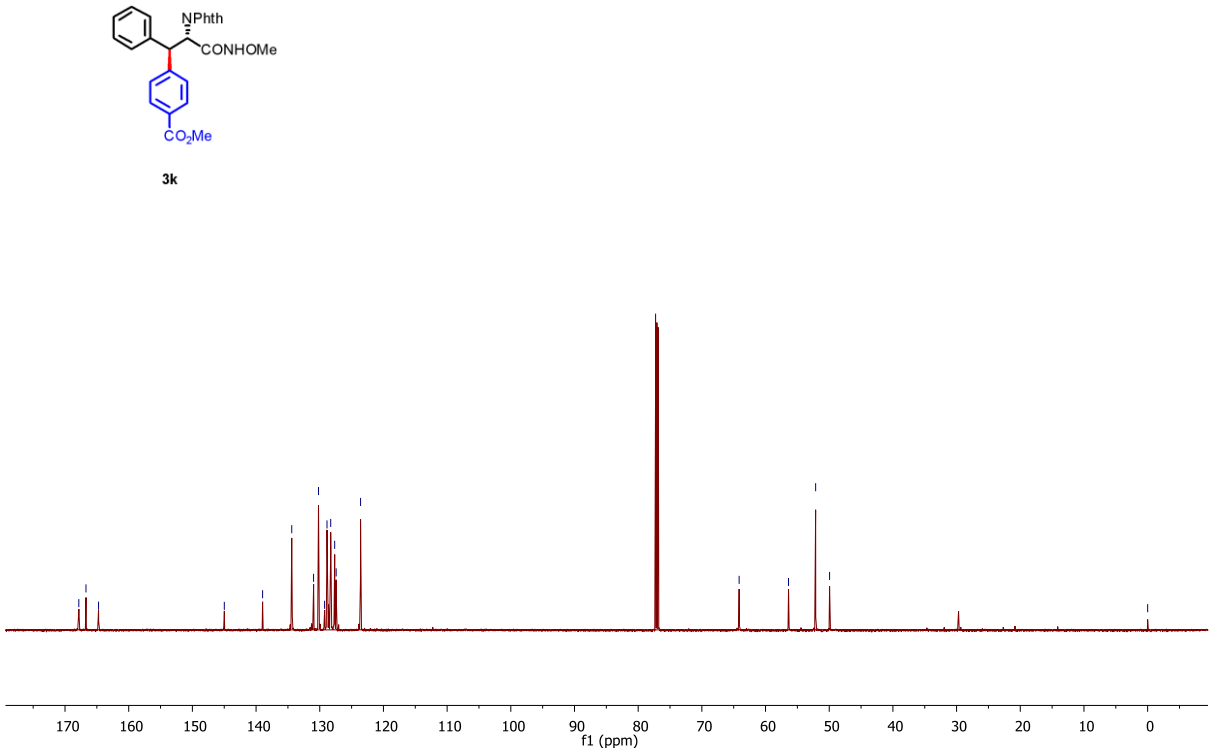

9.365
7.732
7.726
7.721
7.717
7.712
7.705
7.663
7.657
7.652
7.648
7.643
7.492
7.489
7.483
7.478
7.473
7.469
7.263
7.250
7.237
7.156
7.143
7.130
7.058
7.046
7.030
7.016
5.496
5.350
5.329
3.519
-0.000
NPhth
CONHOMe
F
3g
0.93
1.87
1.95
1.93
1.82
1.98
2.97
1.00
1.01
2.76
f1 (ppm)
167.895
164.919
162.841
161.207
139.510
135.505
134.398
130.978
129.865
129.812
128.828
127.470
127.281
123.599
115.902
115.761
64.198
56.980
49.355
0.000
NPhth
CONHOMe
F
3g
f1 (ppm)

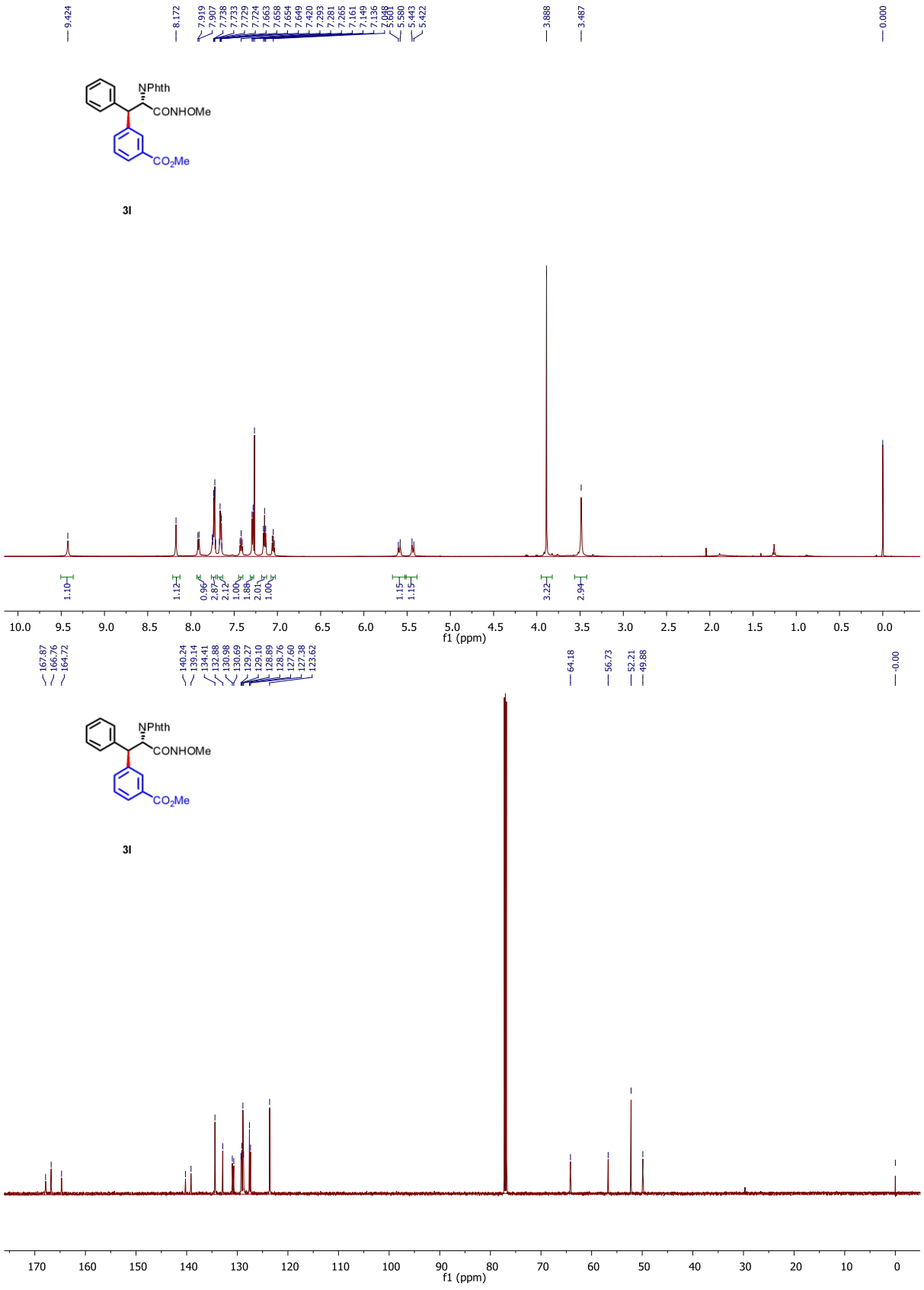

9.332
7.729
7.726
7.720
7.716
7.711
7.705
7.656
7.651
7.647
7.642
7.636
7.315
7.294
7.267
7.263
7.252
7.221
7.204
7.165
7.153
7.140
7.069
7.057
6.941
5.523
5.504
5.380
5.359
3.526
0.000
NPhth
CONHOMe
F
3h
0.94
2.12
2.05
1.93
2.22
1.04
1.92
1.17
1.03
1.00
0.97
2.86
f1 (ppm)
167.829
164.785
163.723
162.087
142.278
139.105
134.385
130.985
130.455
128.850
127.588
127.393
123.867
115.224
114.580
114.442
64.190
56.596
49.738
0.000
NPhth
CONHOMe
F
3h
f1 (ppm)

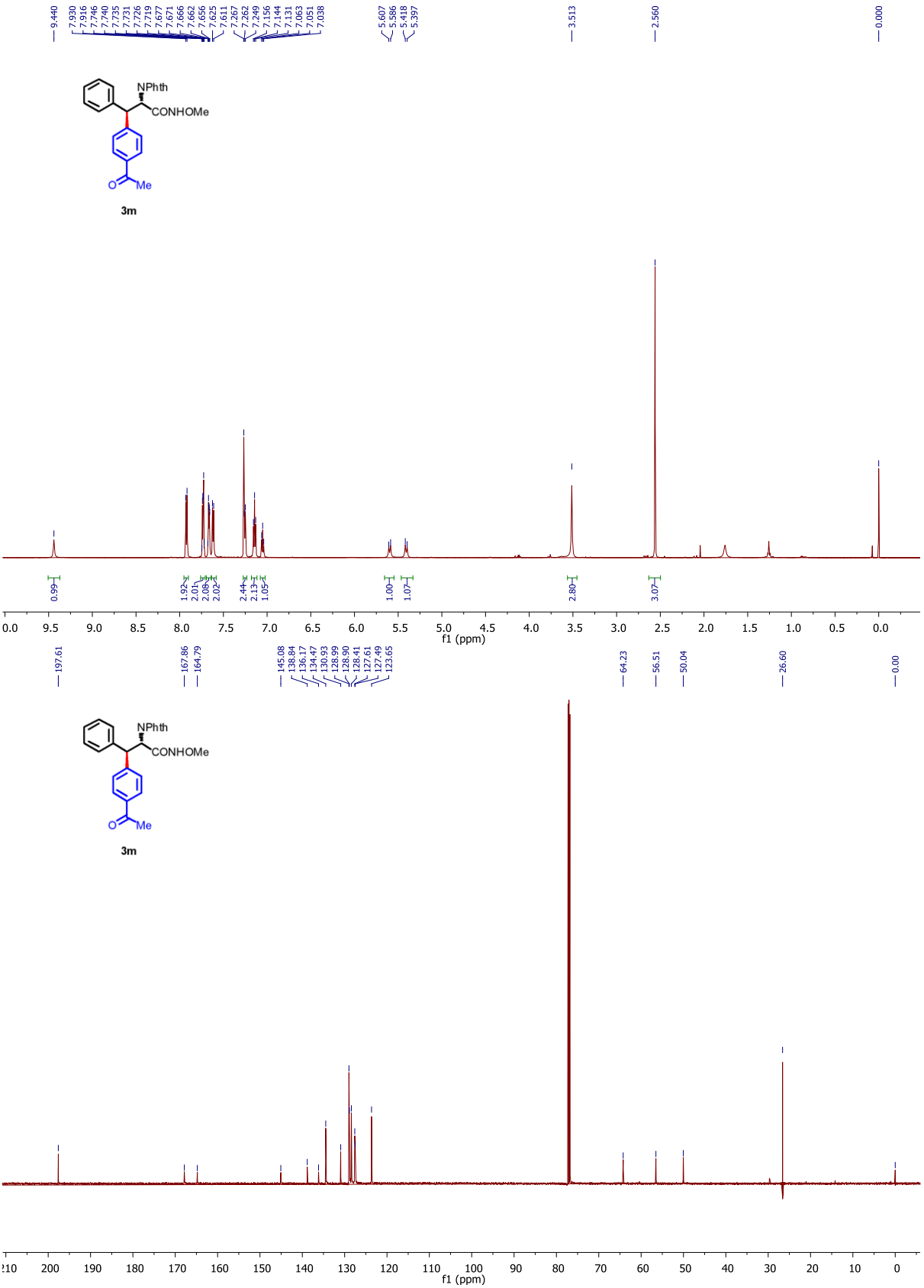

9.403
7.722
7.716
7.712
7.707
7.701
7.699
7.662
7.655
7.650
7.646
7.641
7.454
7.440
7.302
7.288
7.263
7.240
7.227
7.151
7.139
7.126
7.057
7.045
7.033
5.522
5.501
5.344
5.323
3.526
-0.000
NPhth
CONHOMe
Cl
3i
0.931
1.883
1.927
1.866
1.866
1.883
1.955
0.994
1.000
0.960
2.719
f1 (ppm)
167.86
164.84
139.25
138.24
134.41
133.38
130.95
129.56
129.08
128.85
127.49
127.35
123.60
64.22
56.71
49.46
0.00
NPhth
CONHOMe
Cl
3i
f1 (ppm)

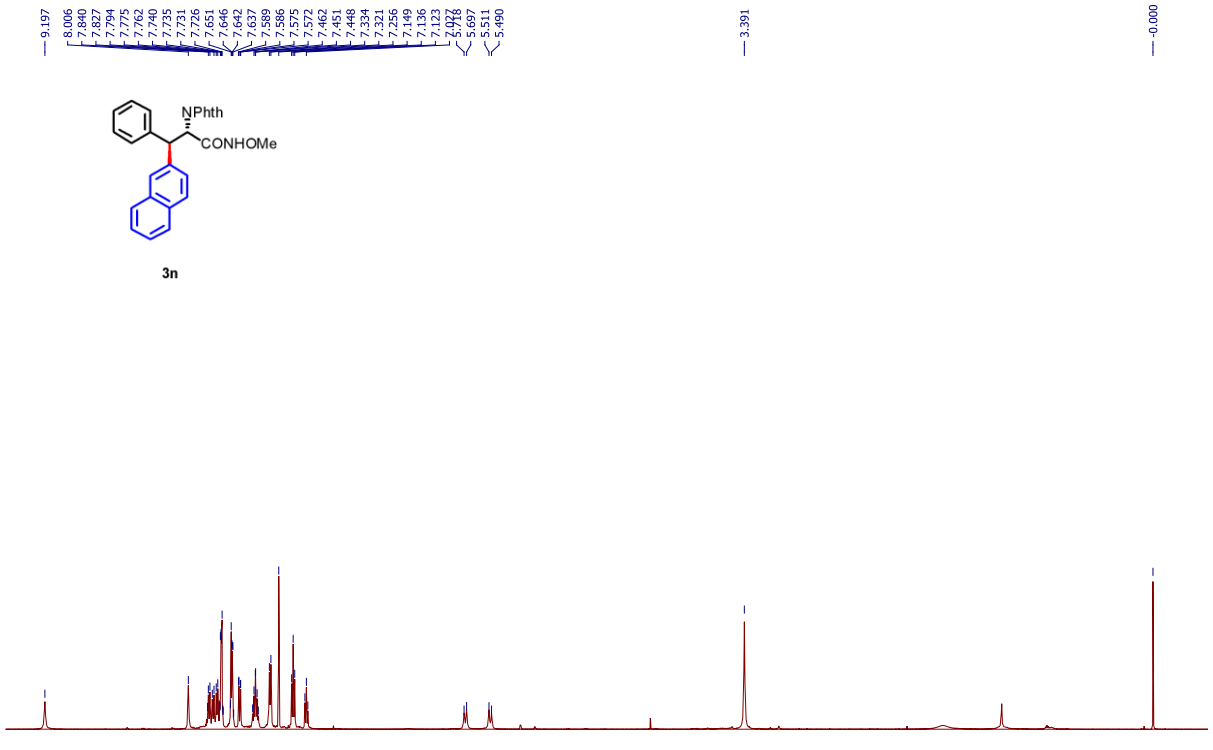

9.475
7.730
7.725
7.721
7.716
7.710
7.672
7.665
7.660
7.656
7.651
7.637
7.588
7.574
7.263
7.253
7.164
7.152
7.139
7.072
7.060
7.048
5.588
5.567
5.461
5.440
3.494
0.000
NPhth
CONHOMe
CF3
3j
0.95
2.40
4.15
2.38
2.73
2.35
1.19
1.00
1.02
2.84
f1 (ppm)
167.863
164.748
143.813
138.807
134.483
130.925
129.992
129.776
129.560
129.346
128.938
128.635
127.618
127.544
126.675
125.931
125.843
125.823
125.752
124.870
123.652
123.067
121.266
64.173
56.465
49.817
-0.000
NPhth
CONHOMe
CF3
3j
f1 (ppm)

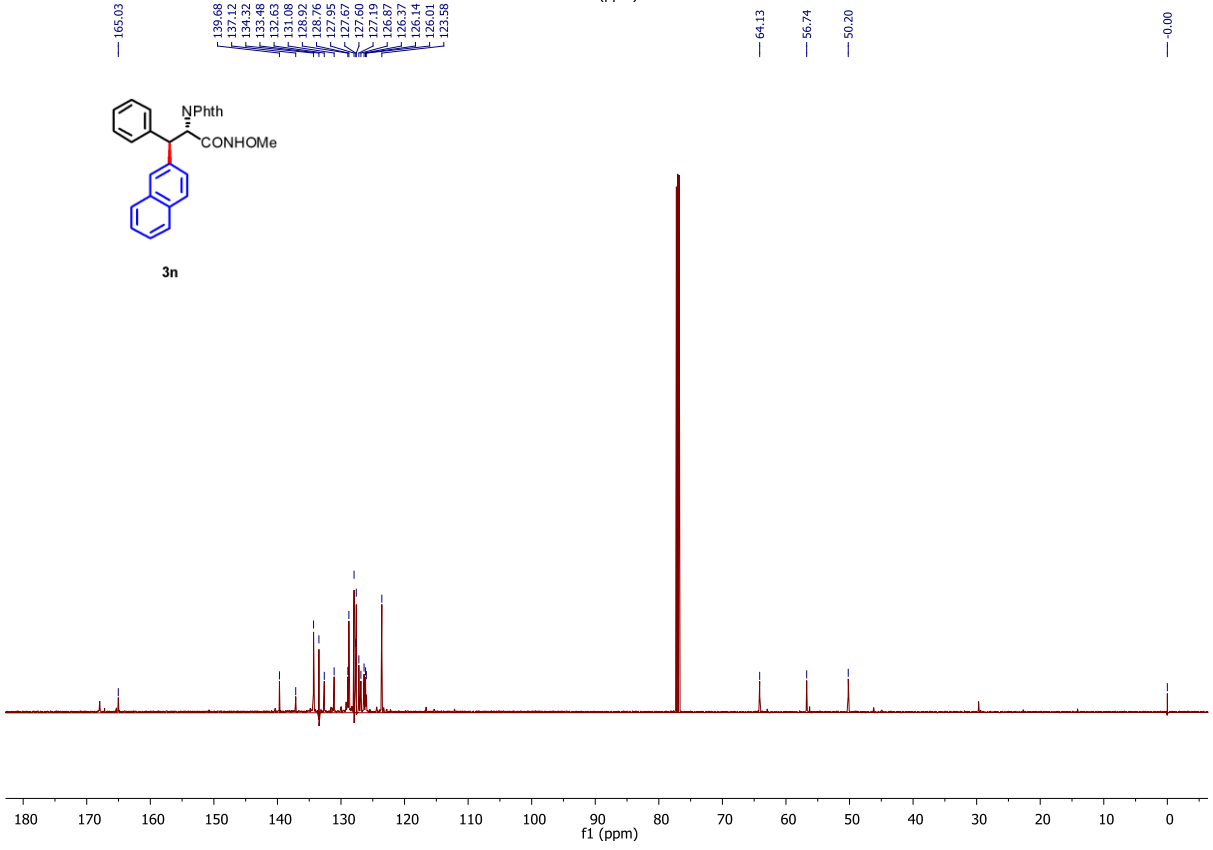

9.493
8.000
7.986
7.649
7.644
7.640
7.289
7.257
7.255
7.153
7.140
7.127
7.058
7.046
7.034
5.594
5.573
5.457
5.436
3.879
3.479
0.000
NPhth
CONHOMe
CO2Me
3k
1.04
2.10
2.07
2.31
2.00
2.68
2.62
1.11
1.01
0.97
3.13
2.89
f1 (ppm)

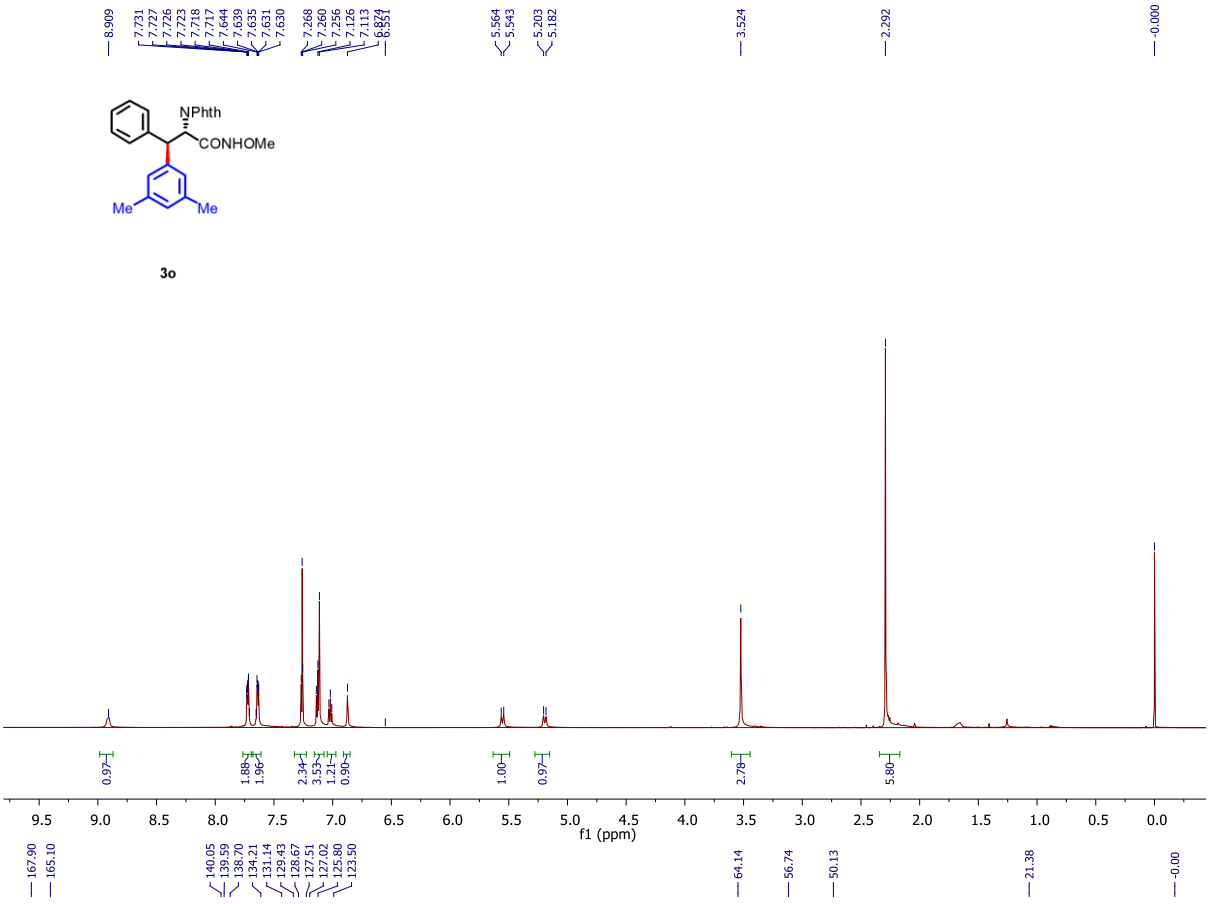

167.83
166.71
164.74
144.99
138.98
134.40
130.97
130.20
129.24
128.86
128.28
127.66
127.42
123.59
64.15
56.39
52.13
49.94
-0.00
NPhth
CONHOMe
CO2Me
3k
f1 (ppm)

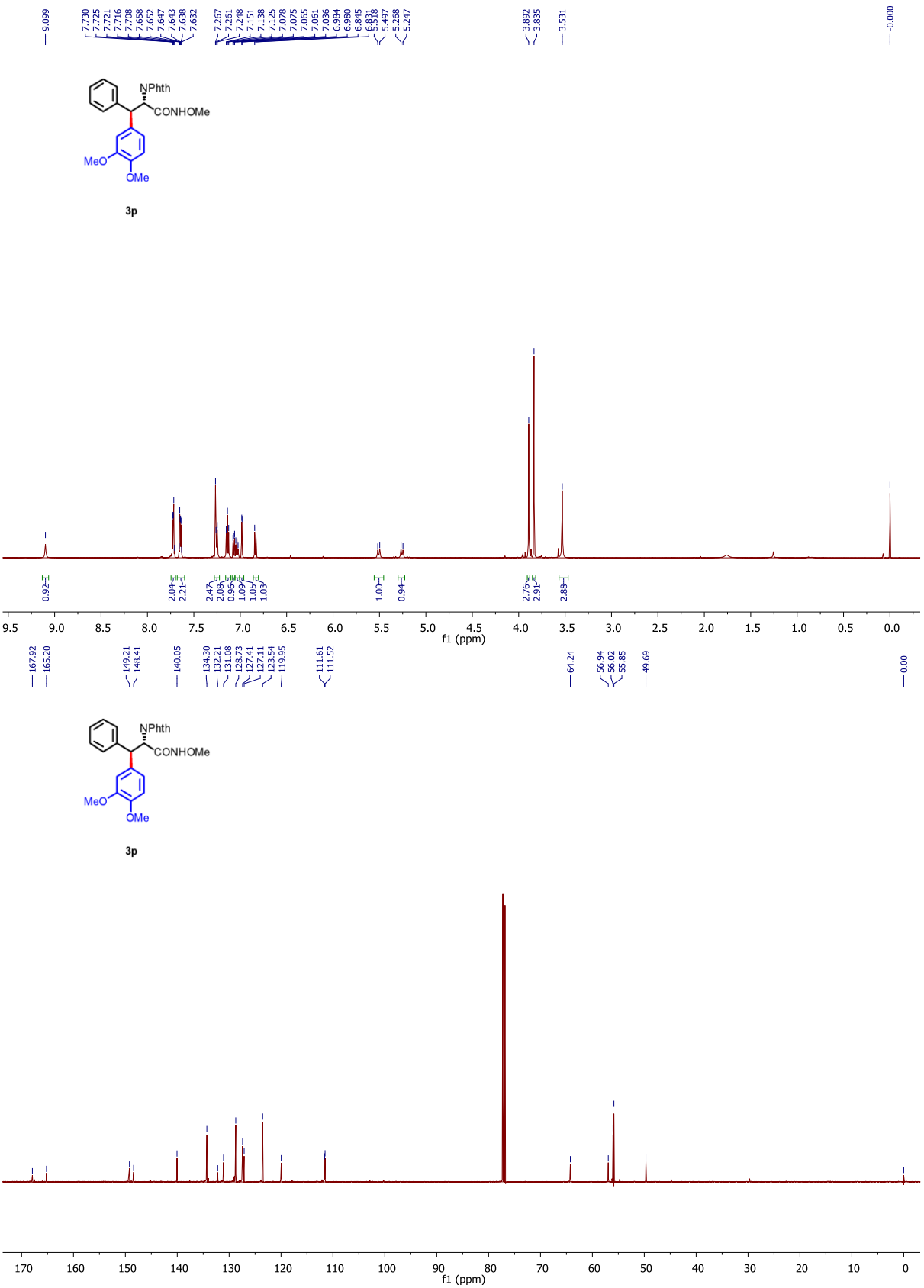

9.424
8.172
7.919
7.907
7.738
7.733
7.729
7.724
7.663
7.658
7.654
7.649
7.420
7.293
7.281
7.265
7.161
7.149
7.136
5.580
5.443
5.422
3.888
3.487
0.000
NPhth
CONHOMe
CO2Me
3l
1.10
1.12
0.96
2.87
2.12
1.00
1.88
2.01
1.00
1.15
1.15
3.22
2.94
f1 (ppm)
167.87
166.76
164.72
140.24
139.14
134.41
132.88
130.98
130.69
129.27
129.10
128.89
128.76
127.60
127.38
123.62
64.18
56.73
52.21
49.88
-0.00
NPhth
CONHOMe
CO2Me
3l
f1 (ppm)

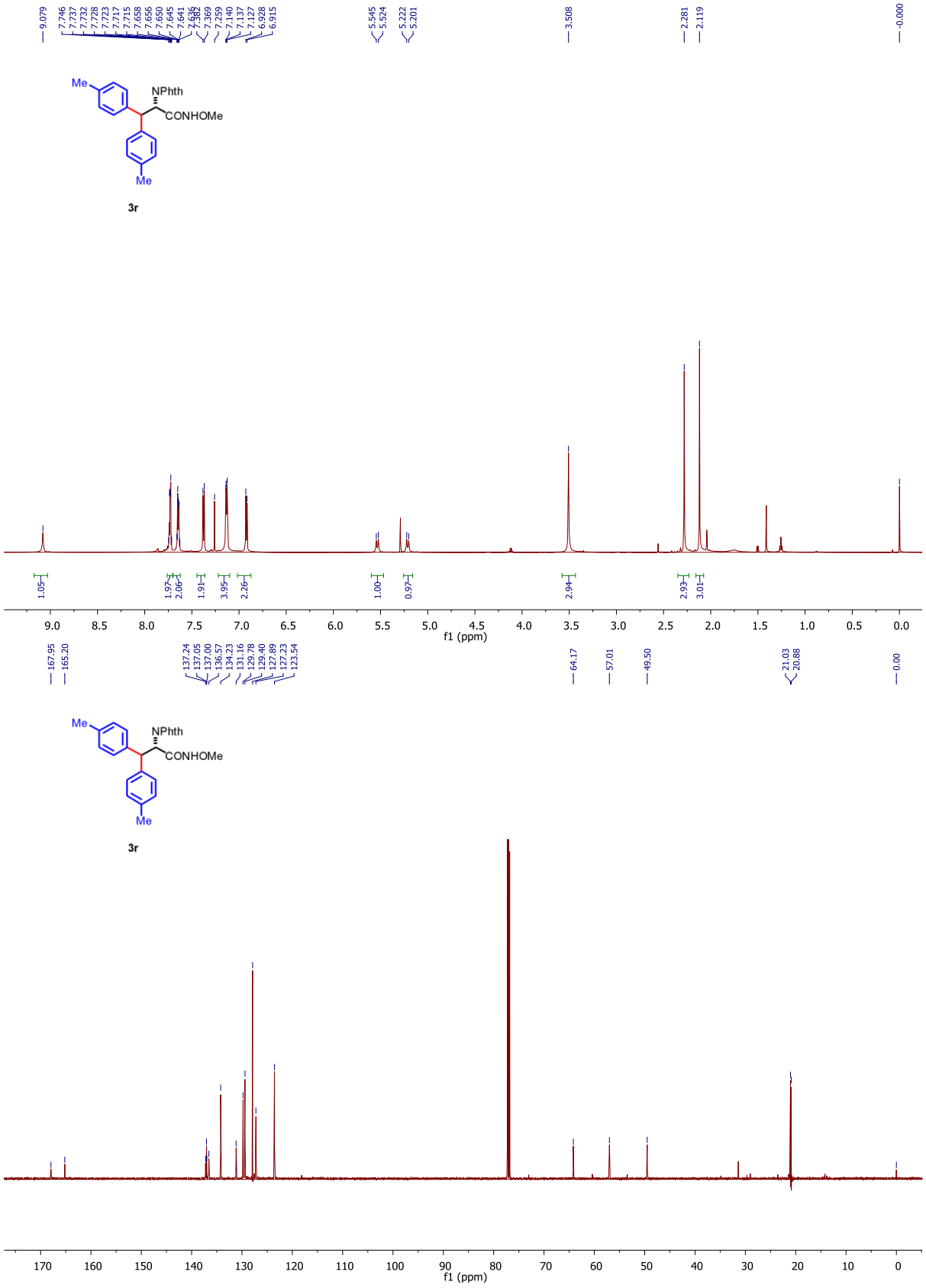

9.440
7.930
7.916
7.746
7.740
7.735
7.731
7.726
7.719
7.677
7.671
7.666
7.662
7.656
7.625
7.611
7.267
7.262
7.249
7.156
7.144
7.131
7.063
7.051
7.038
5.607
5.586
5.418
5.397
3.513
2.560
0.000
NPhth
CONHOMe
O
Me
3m
0.99
1.92
2.01
2.08
2.02
2.44
2.13
1.05
1.00
1.07
2.80
3.07
f1 (ppm)
197.61
167.86
164.79
145.08
138.84
136.17
134.47
130.93
128.99
128.90
128.41
127.61
127.49
123.65
64.23
56.51
50.04
26.60
0.00
NPhth
CONHOMe
O
Me
3m
f1 (ppm)


9.197
8.006
7.840
7.827
7.794
7.775
7.762
7.740
7.735
7.731
7.726
7.651
7.646
7.642
7.637
7.589
7.586
7.575
7.572
7.462
7.451
7.448
7.334
7.321
7.256
7.149
7.136
7.123
5.738
5.697
5.511
5.490
3.391
0.000
NPhth
CONHOMe
3n
0.76
0.90
3.09
1.98
1.93
1.09
1.96
1.85
1.80
0.95
1.00
0.91
2.45
f1 (ppm)


165.03
139.68
137.12
134.32
133.48
132.63
131.08
128.92
128.76
128.95
127.67
127.60
127.19
126.87
126.37
126.14
126.01
123.58
64.13
56.74
50.20
0.00
NPhth
CONHOMe
3n
f1 (ppm)


8.909
7.731
7.727
7.726
7.723
7.718
7.717
7.644
7.639
7.635
7.631
7.630
7.268
7.260
7.256
7.126
7.113
6.874
6.851
5.564
5.543
5.203
5.182
3.524
2.292
-0.000
NPhth
CONHOMe
Me
Me
3o
0.97
1.88
1.96
2.34
3.55
1.21
0.90
1.00
0.97
2.78
5.80
f1 (ppm)
167.90
165.10
140.05
139.59
138.70
134.21
131.14
129.43
128.67
127.51
127.02
125.80
123.50
64.14
56.74
50.13
21.38
-0.00
NPhth
CONHOMe
Me
Me
3o
f1 (ppm)


9.099
7.730
7.725
7.721
7.716
7.708
7.658
7.652
7.647
7.643
7.638
7.632
7.267
7.261
7.248
7.151
7.138
7.125
7.078
7.075
7.065
7.061
7.036
6.984
6.980
6.845
6.831
5.497
5.268
5.247
3.892
3.835
3.531
-0.000
NPhth
CONHOMe
MeO
OMe
3p
0.92
2.04
2.21
2.47
2.08
0.96
1.09
1.05
1.03
1.00
0.94
2.76
2.91
2.88
f1 (ppm)
167.92
165.20
149.21
148.41
140.05
134.30
132.21
131.08
128.73
127.41
127.11
123.54
119.95
111.61
111.52
64.24
56.94
56.02
55.85
49.69
0.00
NPhth
CONHOMe
MeO
OMe
3p
f1 (ppm)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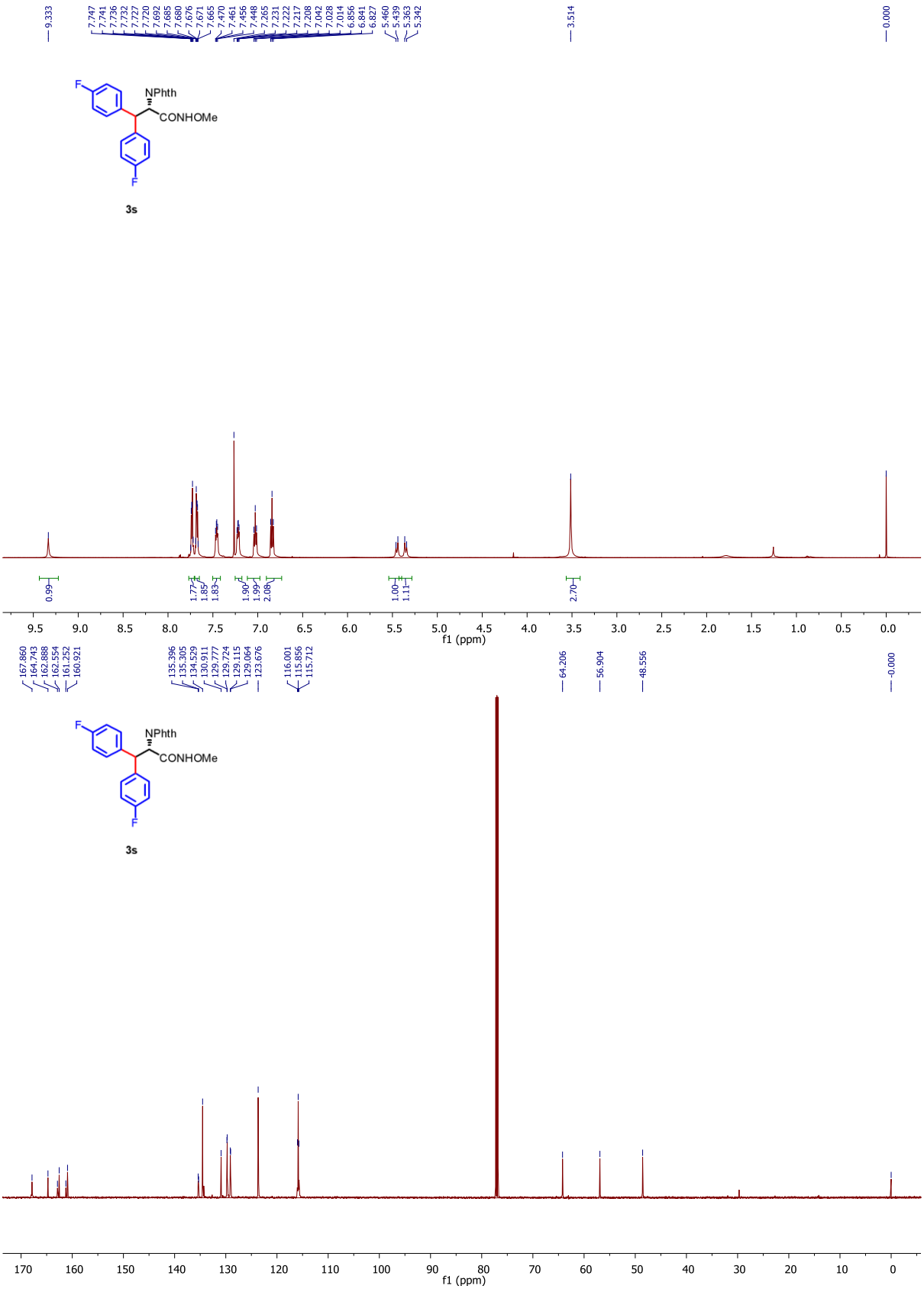
7.746
7.737
7.732
7.728
7.723
7.717
7.715
7.658
7.656
7.650
7.645
7.641
7.369
7.259
7.140
7.137
7.127
6.928
6.915
5.545
5.524
5.222
5.201
3.508
2.281
2.119
-0.000
Me
NPhth
CONHOMe
Me
3r
1.05
1.97
2.06
1.91
3.95
2.26
1.00
0.97
2.94
2.93
3.01
f1 (ppm)
167.95
165.20
137.24
137.05
137.00
136.57
134.23
131.16
129.78
129.40
127.89
127.23
123.54
64.17
57.01
49.50
21.03
20.88
0.00
f1 (ppm)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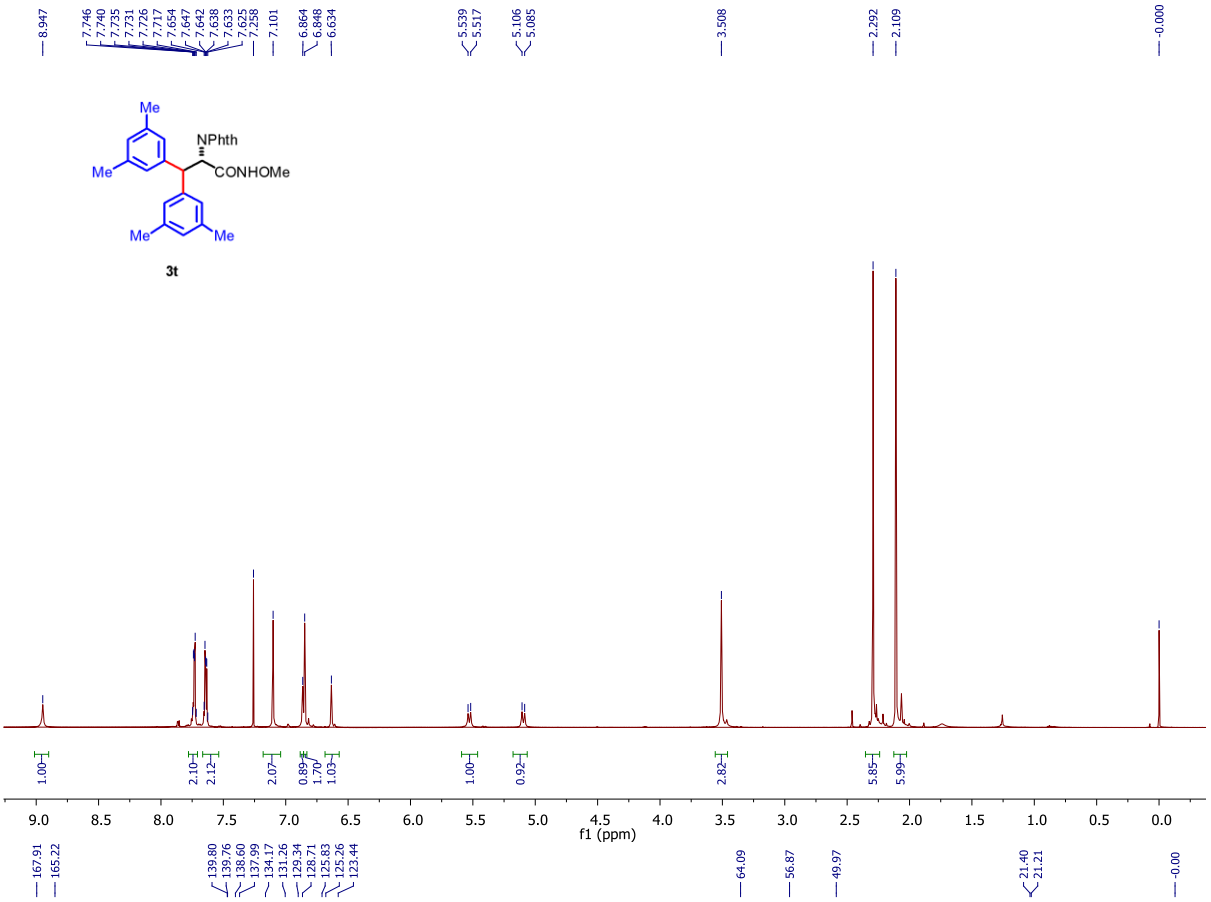
7.747
7.741
7.736
7.732
7.727
7.720
7.692
7.685
7.680
7.676
7.671
7.665
7.470
7.461
7.456
7.448
7.265
7.231
7.222
7.217
7.208
7.042
7.028
7.014
6.856
6.841
6.827
5.460
5.439
5.363
5.342
3.514
0.000
F
NPhth
CONHOMe
F
3s
0.99
1.77
1.85
1.83
1.90
1.99
2.08
1.00
1.11
2.70
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
167.860
164.743
162.888
162.554
161.252
160.921
135.396
135.305
134.529
130.911
129.777
129.724
129.115
129.064
123.676
116.001
115.856
115.712
64.206
56.904
48.556
-0.000
F
NPhth
CONHOMe
F
3s
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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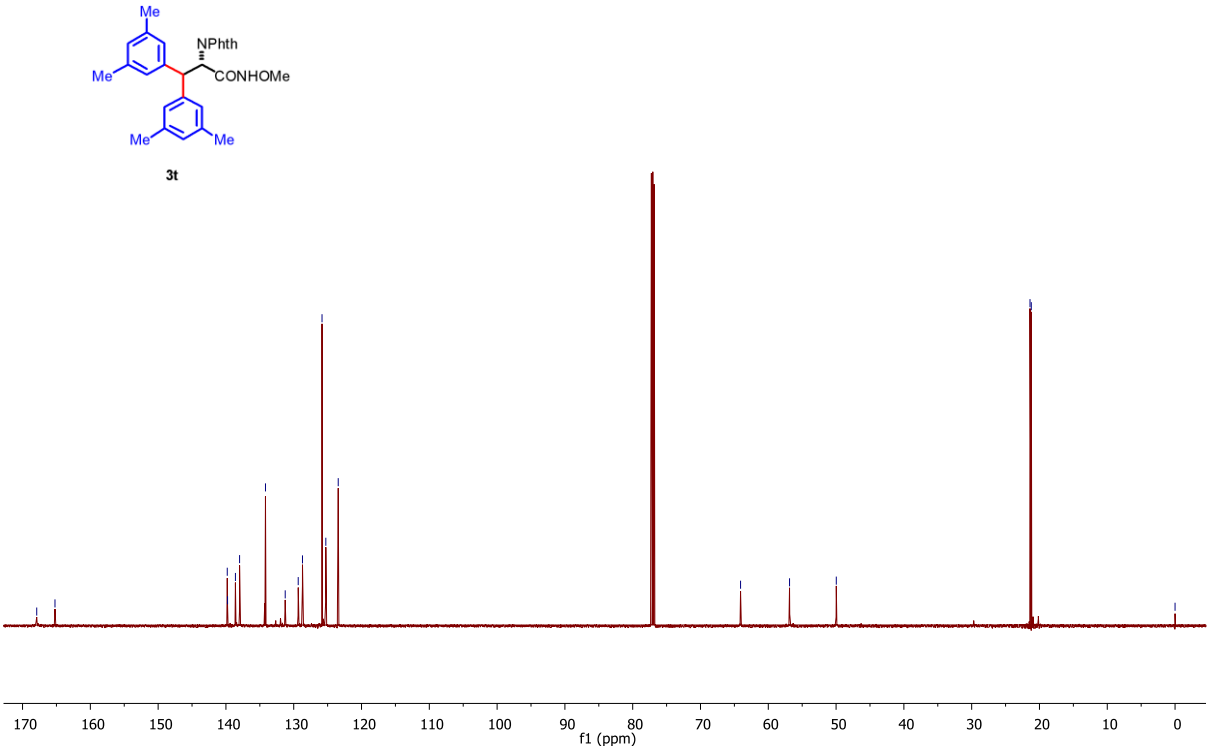
7.746
7.740
7.735
7.731
7.726
7.717
7.654
7.647
7.642
7.638
7.633
7.625
7.258
7.101
6.864
6.848
6.634
5.539
5.517
5.106
5.085
3.508
2.292
2.109
-0.000
Me
NPhth
CONHOMe
Me
Me
Me
3t
1.00
2.10
2.12
2.07
0.89
1.70
1.03
1.00
0.92
2.82
5.85
5.99
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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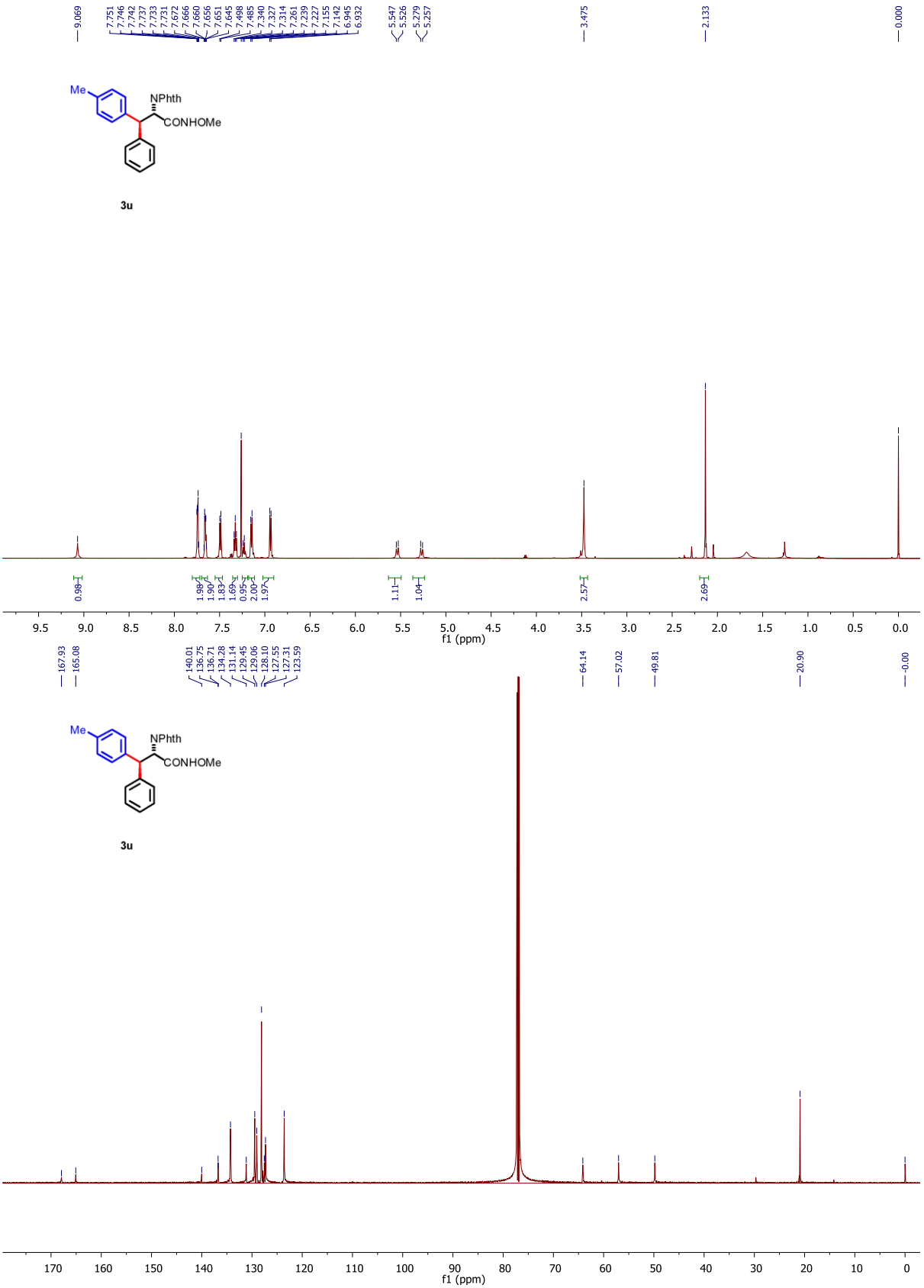
165.22
139.80
139.76
138.60
137.99
134.17
131.26
129.34
128.71
125.83
125.26
123.44
64.09
56.87
49.97
21.40
21.21
-0.00
Me
NPhth
CONHOMe
Me
Me
Me
3t
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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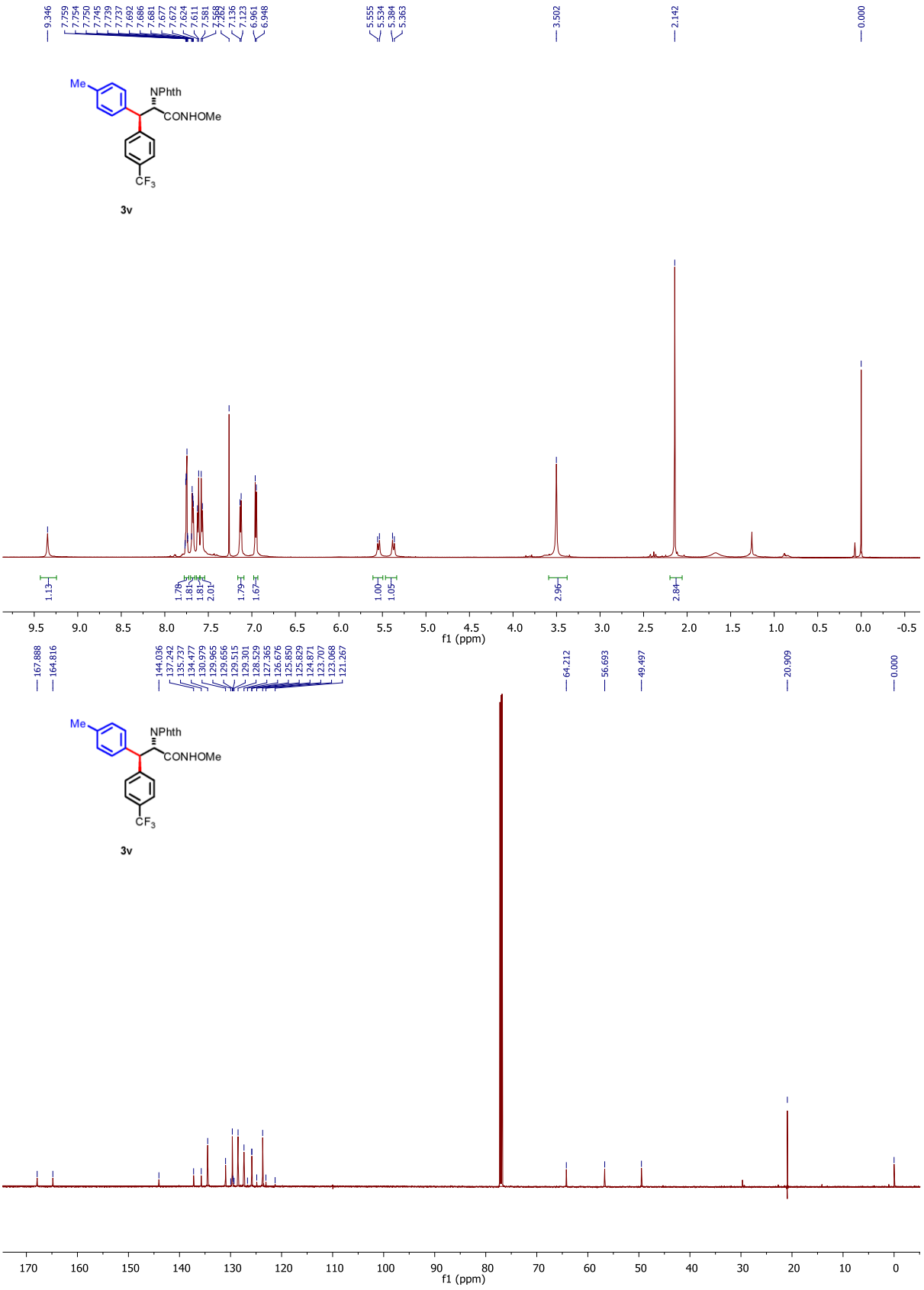
7.751
7.746
7.742
7.737
7.733
7.731
7.672
7.666
7.660
7.656
7.651
7.645
7.498
7.485
7.340
7.327
7.314
7.261
7.239
7.227
7.155
7.142
6.945
6.932
5.547
5.526
5.279
5.257
3.475
2.133
0.000
Me
NPhth
CONHOMe
3u
0.98
1.98
1.90
1.83
1.69
0.95
2.00
1.97
1.11
1.04
2.57
2.69
f1 (ppm)
167.93
165.08
140.01
136.75
136.71
134.28
131.14
129.45
129.06
128.10
127.55
127.31
123.59
64.14
57.02
49.81
20.90
-0.00
Me
NPhth
CONHOMe
3u
f1 (ppm)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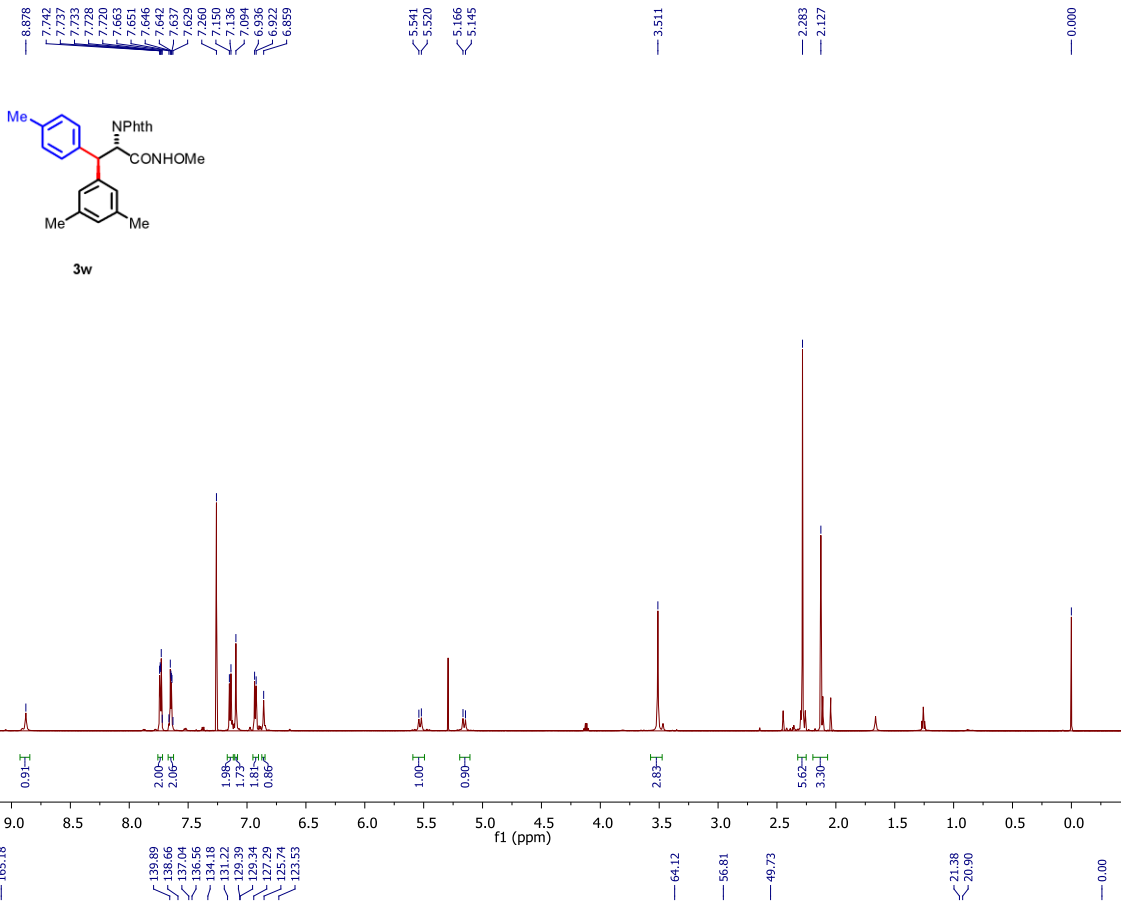
7.754
7.750
7.745
7.739
7.737
7.692
7.686
7.681
7.677
7.672
7.624
7.611
7.581
7.568
7.282
7.136
7.123
6.961
6.948
5.555
5.534
5.384
5.363
3.502
2.142
0.000
Me
NPhth
CONHOMe
CF3
3v
1.13
1.78
1.81
1.81
2.01
1.79
1.67
1.00
1.05
2.96
2.84
f1 (ppm)
167.888
164.816
144.036
137.242
135.737
134.477
130.979
129.965
129.656
129.515
129.301
128.529
127.365
126.676
125.850
125.829
124.871
123.707
123.068
121.267
64.212
56.693
49.497
20.909
0.000
Me
NPhth
CONHOMe
CF3
3v
f1 (ppm)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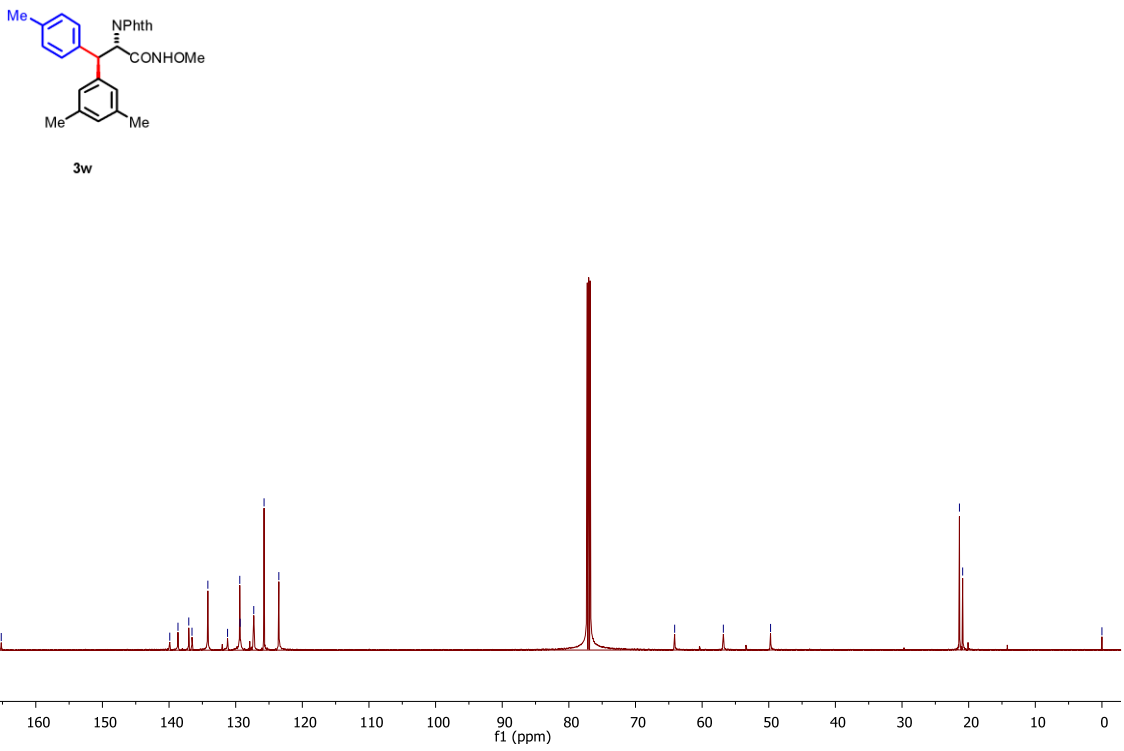
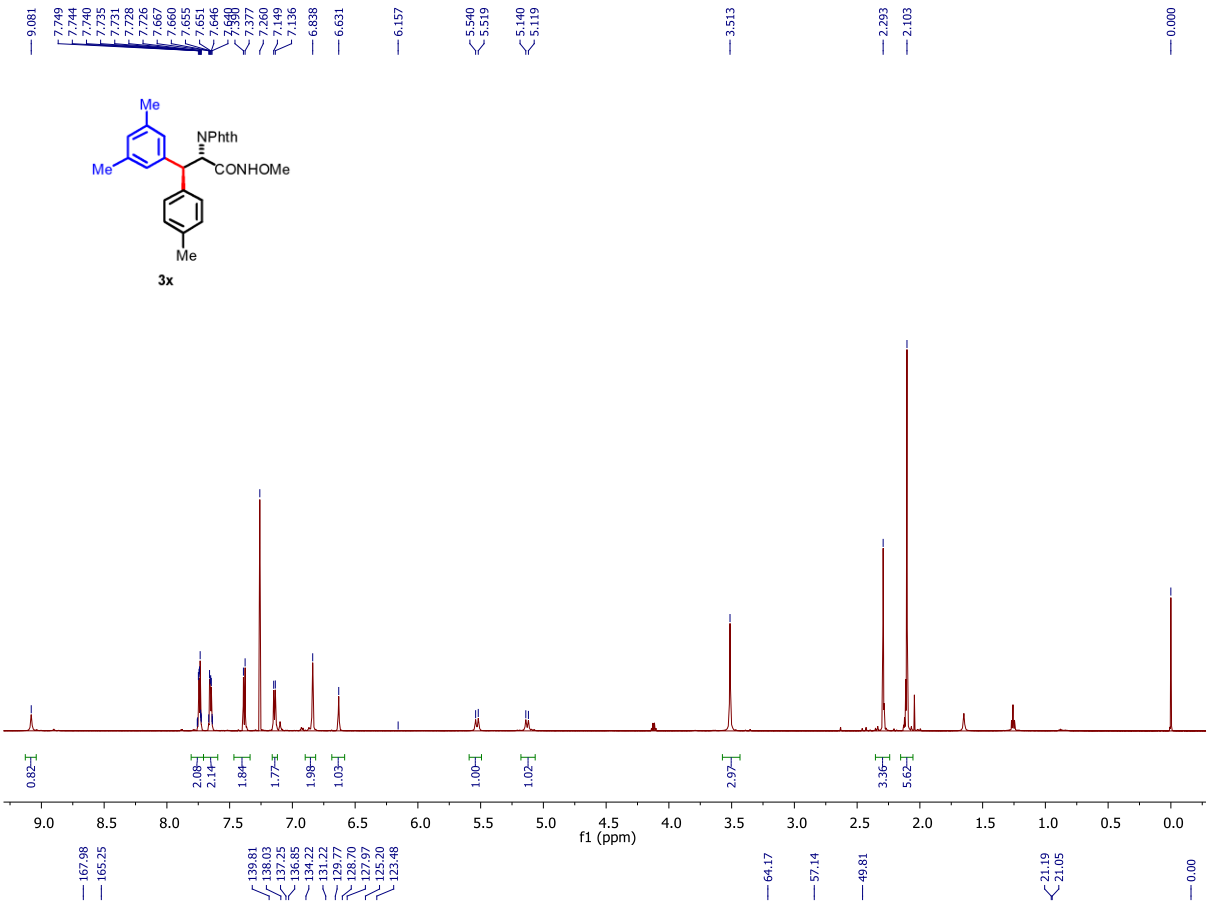
7.737
7.733
7.728
7.720
7.663
7.651
7.646
7.642
7.637
7.629
7.260
7.150
7.136
7.094
6.936
6.922
6.859
5.541
5.520
5.166
5.145
3.511
2.283
2.127
0.000
Me
NPhth
CONHOMe
Me
Me
3w
0.91
2.00
2.06
1.98
1.73
1.81
0.86
1.00
0.90
2.83
5.62
3.30
f1 (ppm)


167.92
165.18
139.89
138.66
137.04
136.56
134.18
131.22
129.39
129.34
127.29
125.74
123.53
64.12
56.81
49.73
21.38
20.90
0.00
Me
NPhth
CONHOMe
Me
Me
3w
f1 (ppm)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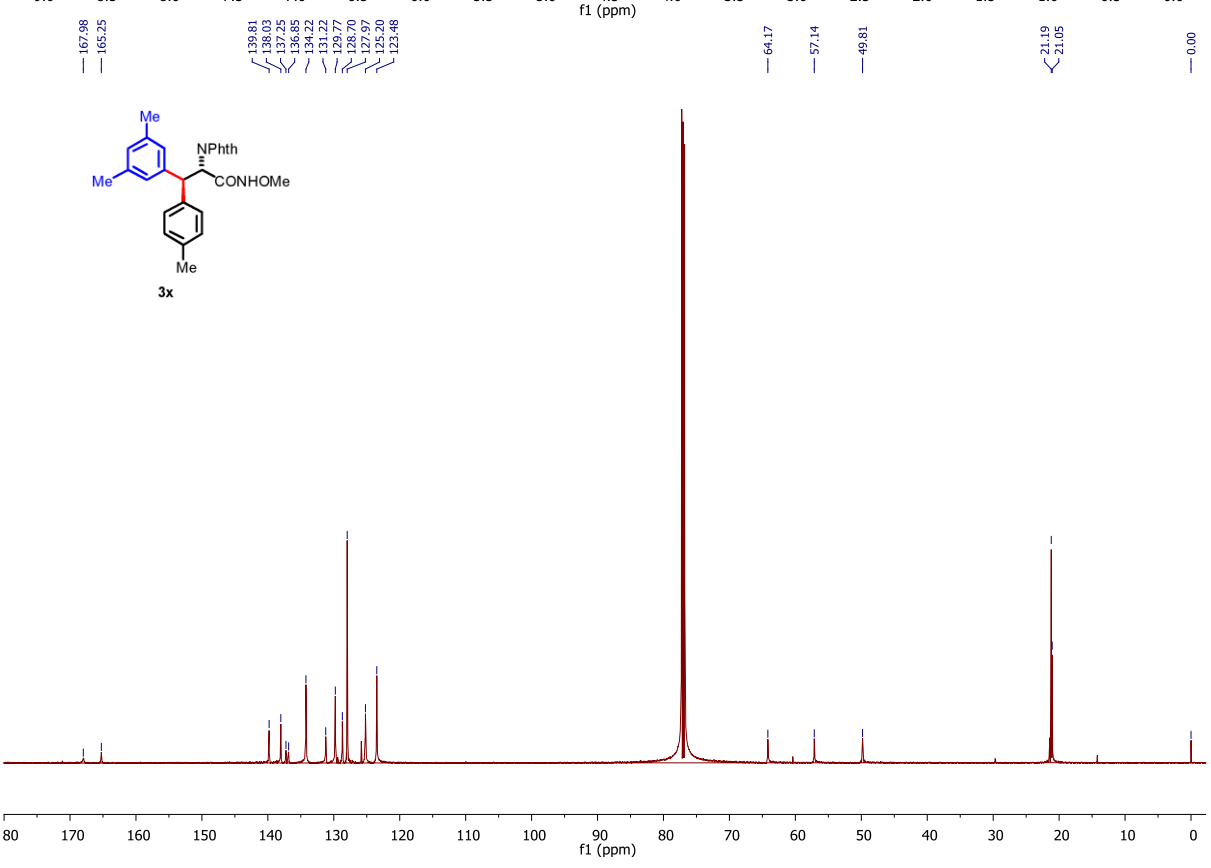
7.749
7.744
7.740
7.735
7.731
7.728
7.726
7.667
7.660
7.655
7.651
7.646
7.390
7.377
7.260
7.149
7.136
6.838
6.631
6.157
5.540
5.519
5.140
5.119
3.513
2.293
2.103
0.000
Me
NPhth
Me
CONHOMe
Me
3x
0.82
2.08
2.14
1.84
1.77
1.98
1.03
1.00
1.02
2.97
3.36
5.62
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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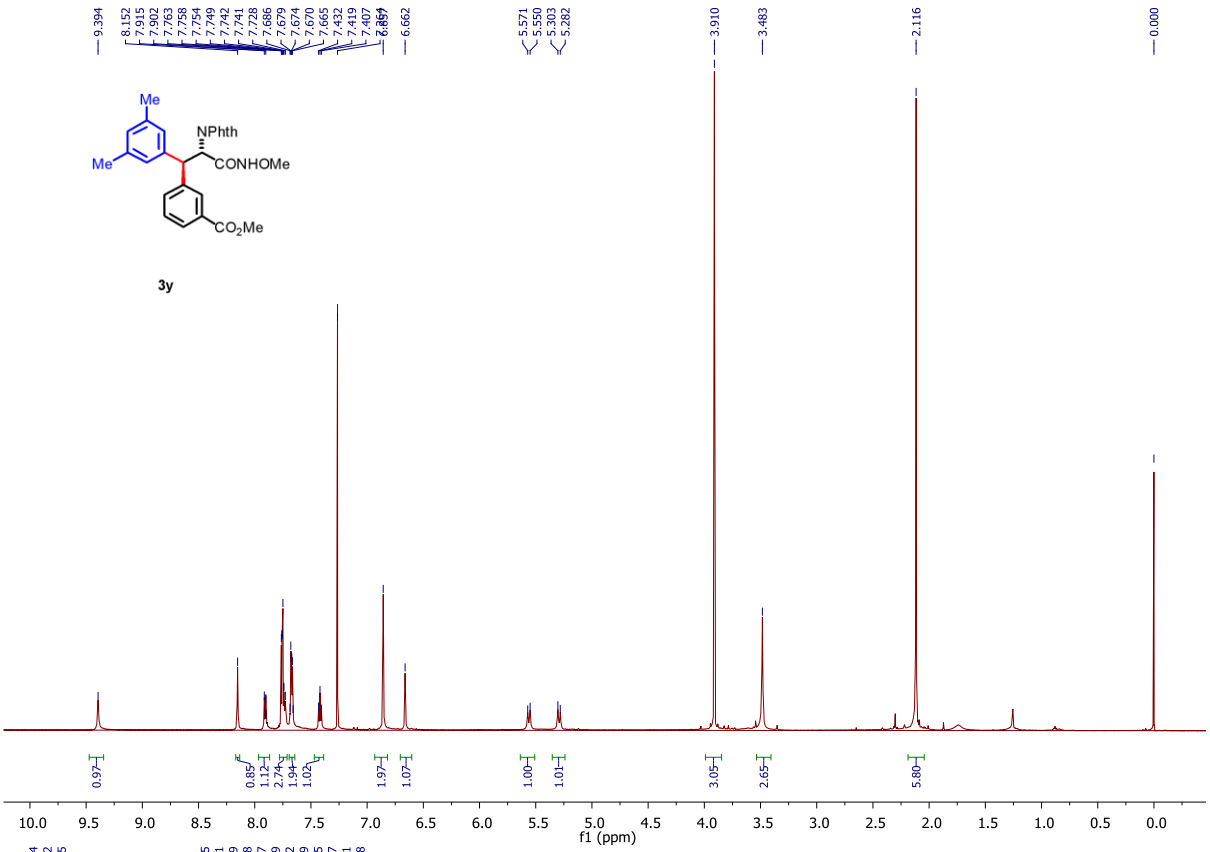
139.81
138.03
137.25
136.85
134.22
131.22
129.77
128.70
127.97
125.20
123.48
64.17
57.14
49.81
21.19
21.05
0.00
Me
NPhth
Me
CONHOMe
Me
3x
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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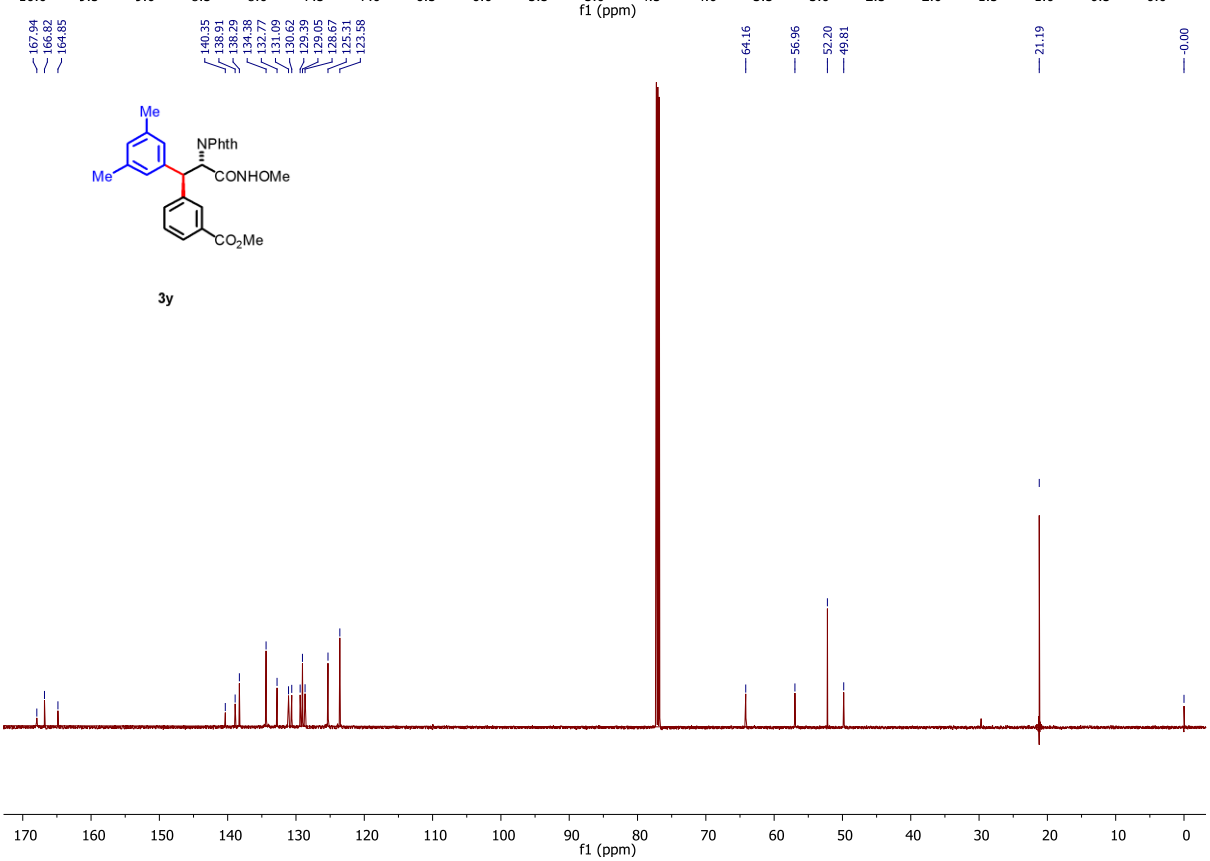
7.915
7.902
7.763
7.758
7.754
7.749
7.742
7.741
7.728
7.686
7.679
7.674
7.670
7.665
7.432
7.419
7.407
6.867
6.662
5.571
5.550
5.303
5.282
3.910
3.483
2.116
0.000
Me
Me
NPhth
CONHOMe
CO2Me
3y
0.97
0.85
1.12
2.74
1.94
1.02
1.97
1.07
1.00
1.01
3.05
2.65
5.80
f1 (ppm)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166.82
164.85
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138.91
138.29
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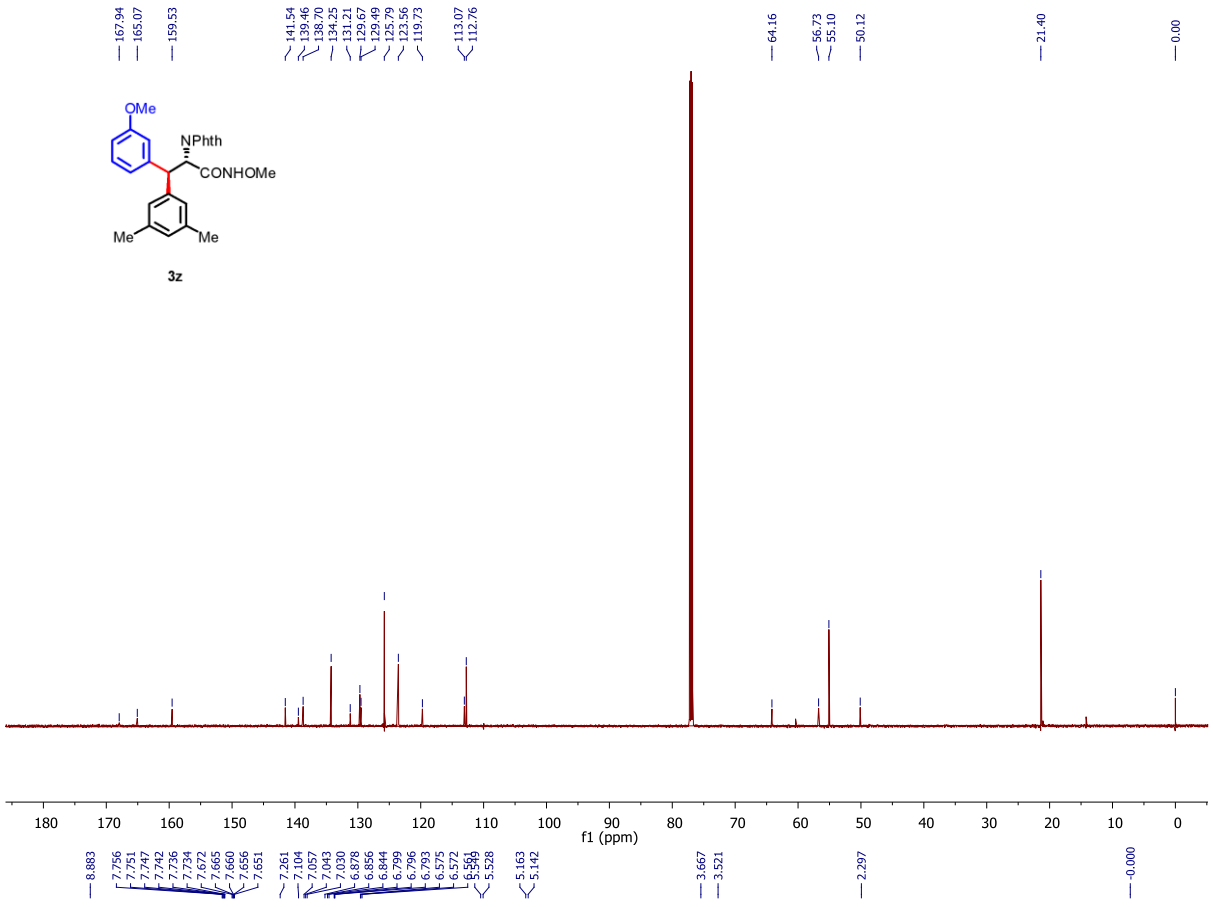
132.77
131.09
130.62
129.39
129.05
128.67
125.31
123.58
64.16
56.96
52.20
49.81
21.19
-0.00
Me
Me
NPhth
CONHOMe
CO2Me
3y
f1 (ppm)


167.94
165.07
159.53
141.54
139.46
138.70
134.25
131.21
129.67
129.49
125.79
123.56
119.73
113.07
112.76
64.16
56.73
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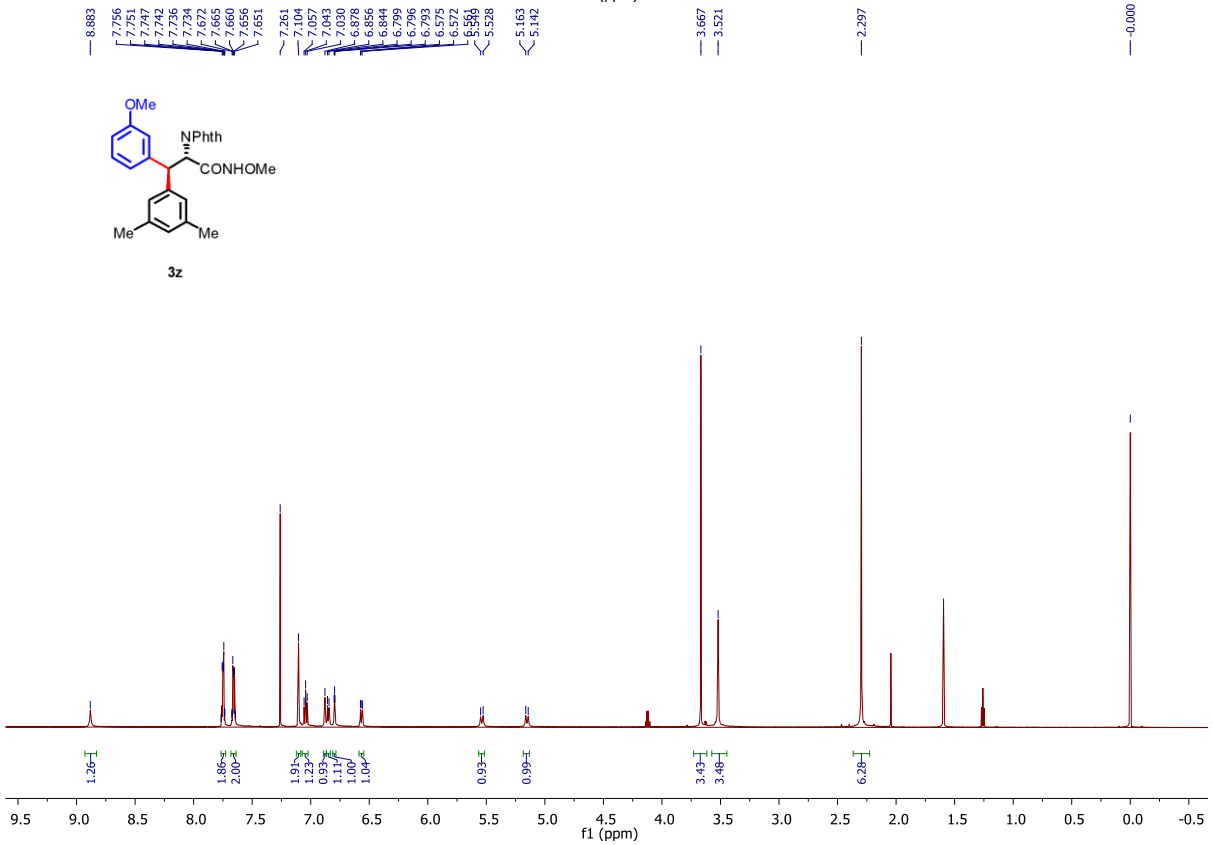
50.12
21.40
0.00
OMe
NPhth
CONHOMe
Me
Me
3z
f1 (ppm)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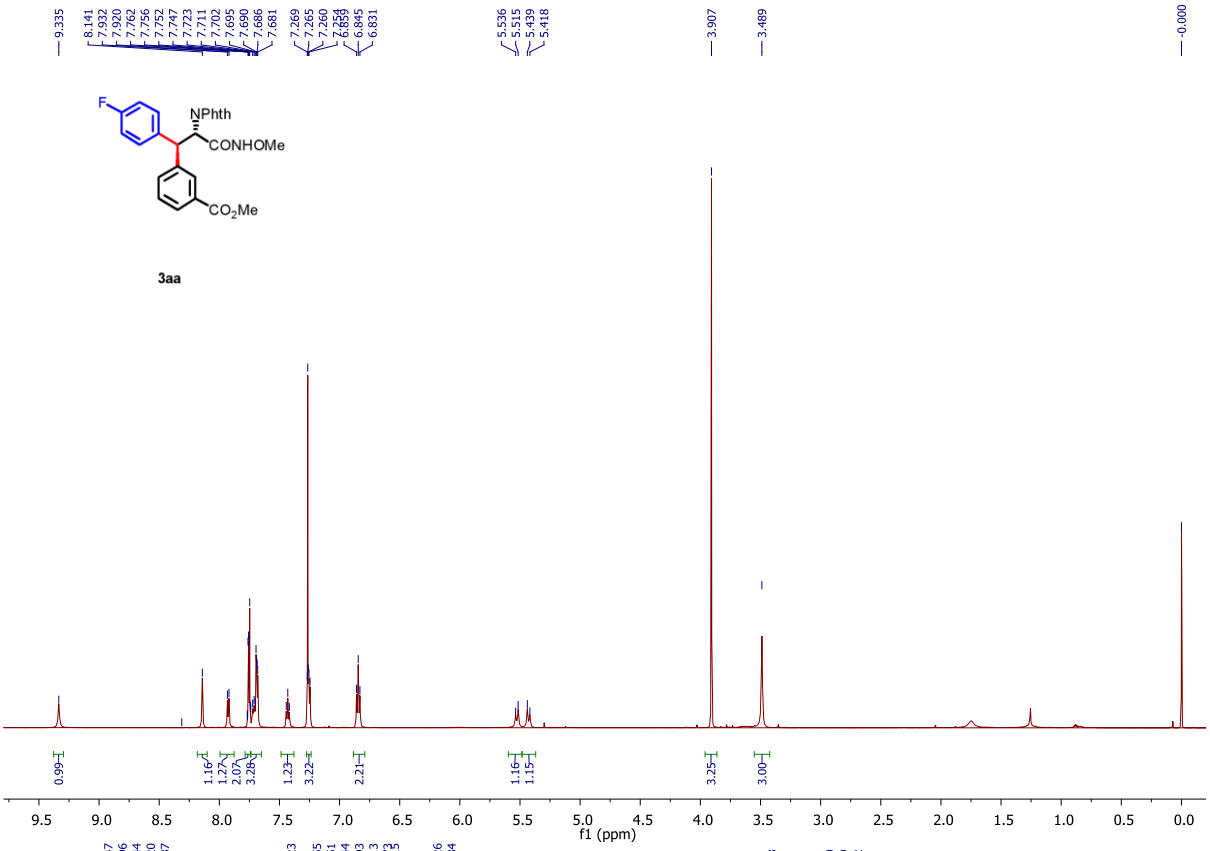
7.734
7.672
7.665
7.660
7.656
7.651
7.261
7.104
7.057
7.043
7.030
6.878
6.856
6.844
6.799
6.796
6.793
6.575
6.572
6.561
6.549
5.528
5.163
5.142
3.667
3.521
2.297
-0.000
OMe
NPhth
CONHOMe
Me
Me
3z
1.26
1.86
2.00
1.91
1.23
0.93
1.11
1.00
1.04
0.93
0.99
3.43
3.48
6.28
f1 (ppm)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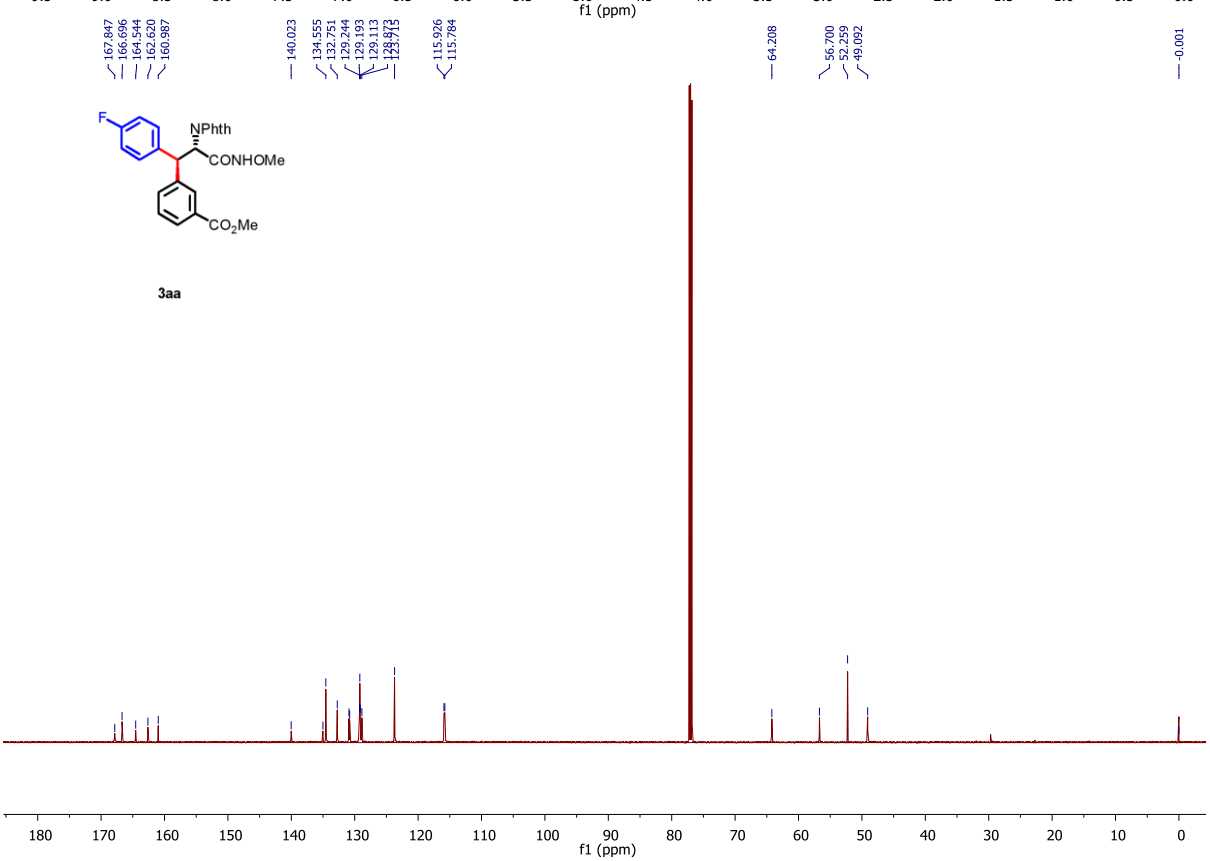
7.752
7.747
7.723
7.711
7.702
7.695
7.690
7.686
7.681
7.269
7.265
7.260
6.859
6.845
6.831
5.536
5.515
5.439
5.418
3.907
3.489
-0.000
F
NPhth
CONHOMe
CO2Me
3aa
0.99
1.16
1.27
2.07
3.28
1.23
3.22
2.21
1.16
1.15
3.25
3.00
f1 (ppm)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132.751
129.244
129.193
129.113
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115.784
64.208
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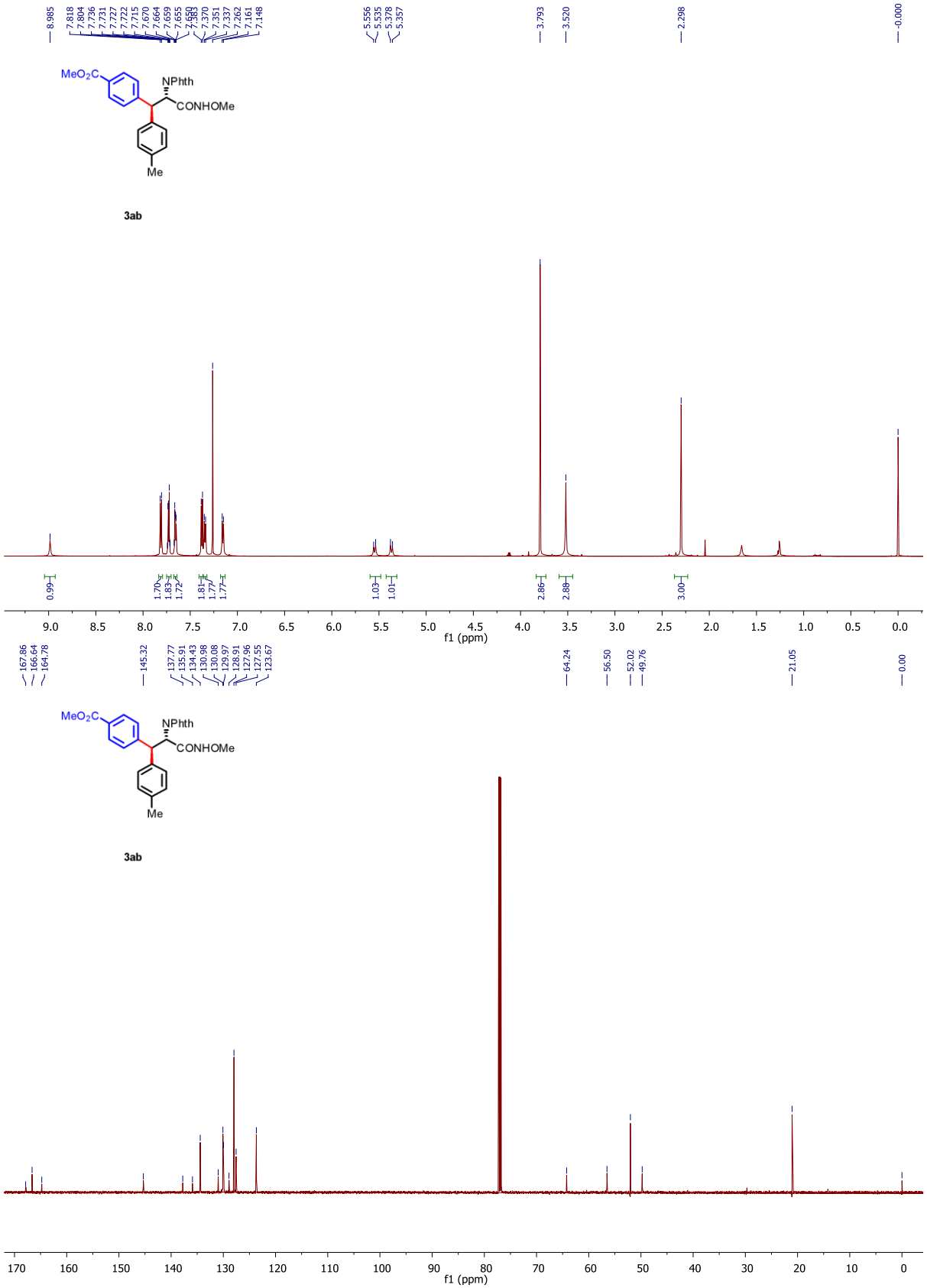
52.259
49.092
-0.001
F
NPhth
CONHOMe
CO2Me
3aa
f1 (ppm)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7.804
7.736
7.731
7.727
7.722
7.715
7.670
7.664
7.659
7.655
7.583
7.370
7.351
7.337
7.262
7.161
7.148
5.556
5.535
5.378
5.357
3.793
3.520
2.298
-0.000
MeO2C
NPhth
CONHOMe
Me
3ab
0.99
1.70
1.83
1.72
1.81
1.77
1.77
1.03
1.01
2.86
2.88
3.00
f1 (ppm)
167.86
166.64
164.78
145.32
137.77
135.91
134.43
130.98
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128.91
127.96
127.55
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56.50
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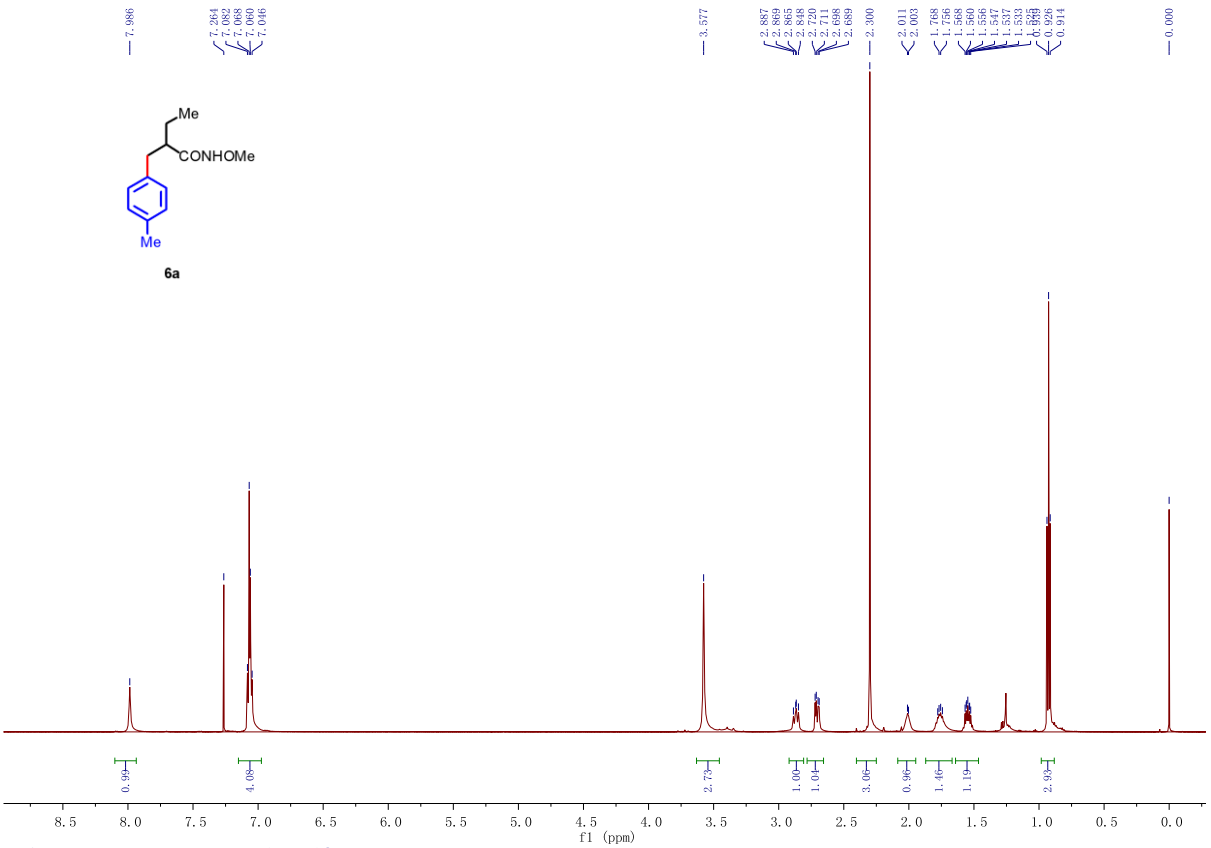
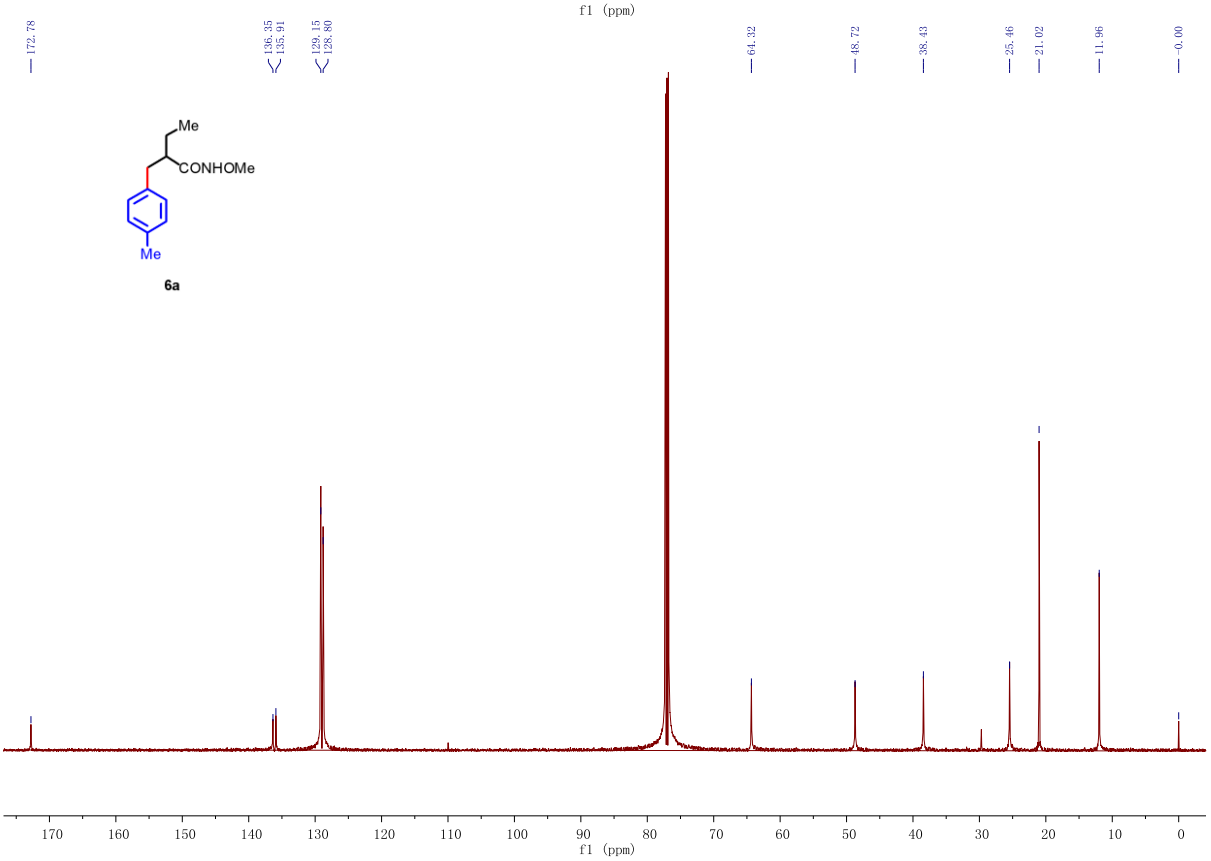
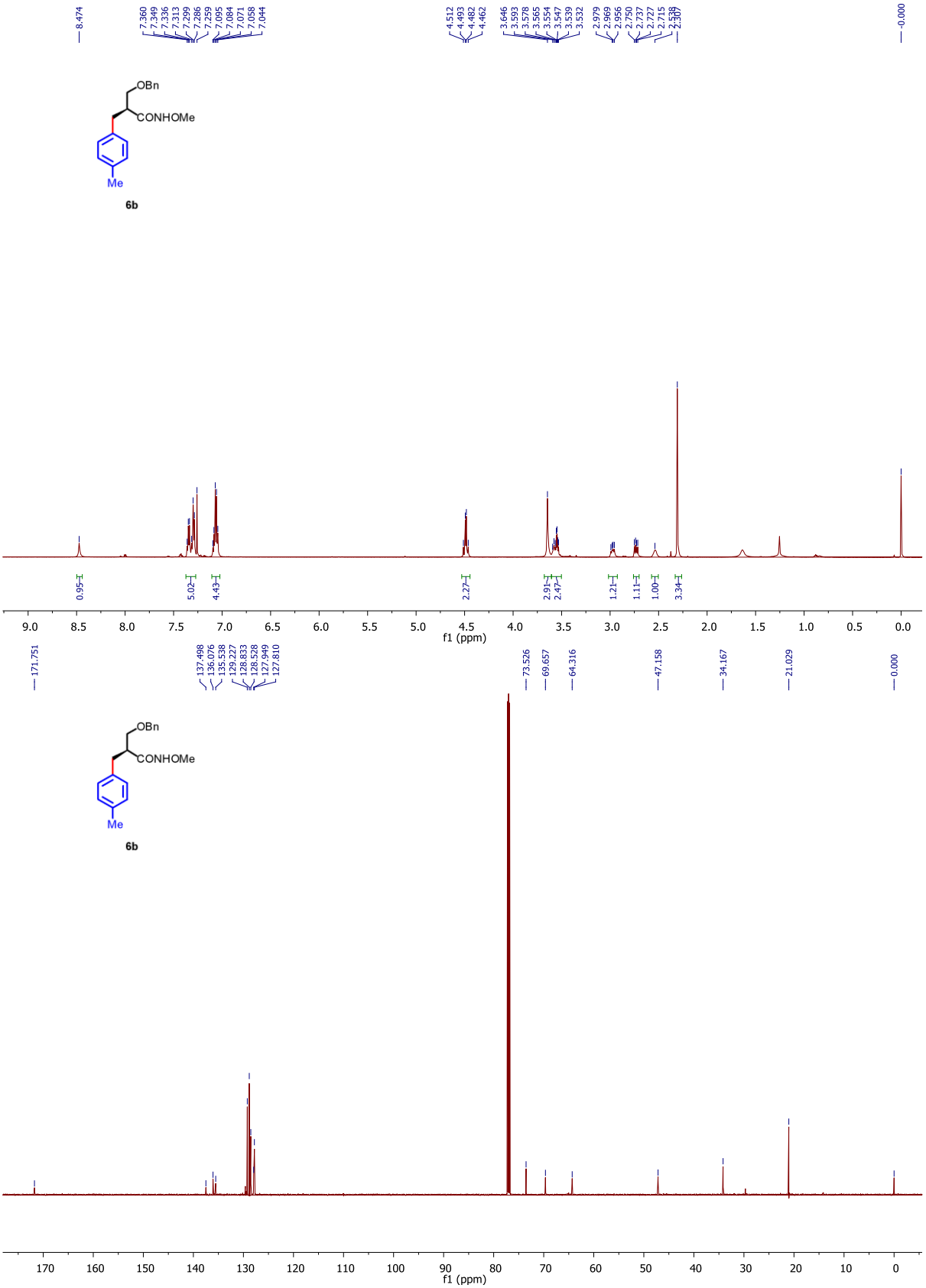
0.00


Me
CONHOMe
Me
6a
f1 (ppm)


Me
CONHOMe
Me
6a
f1 (ppm)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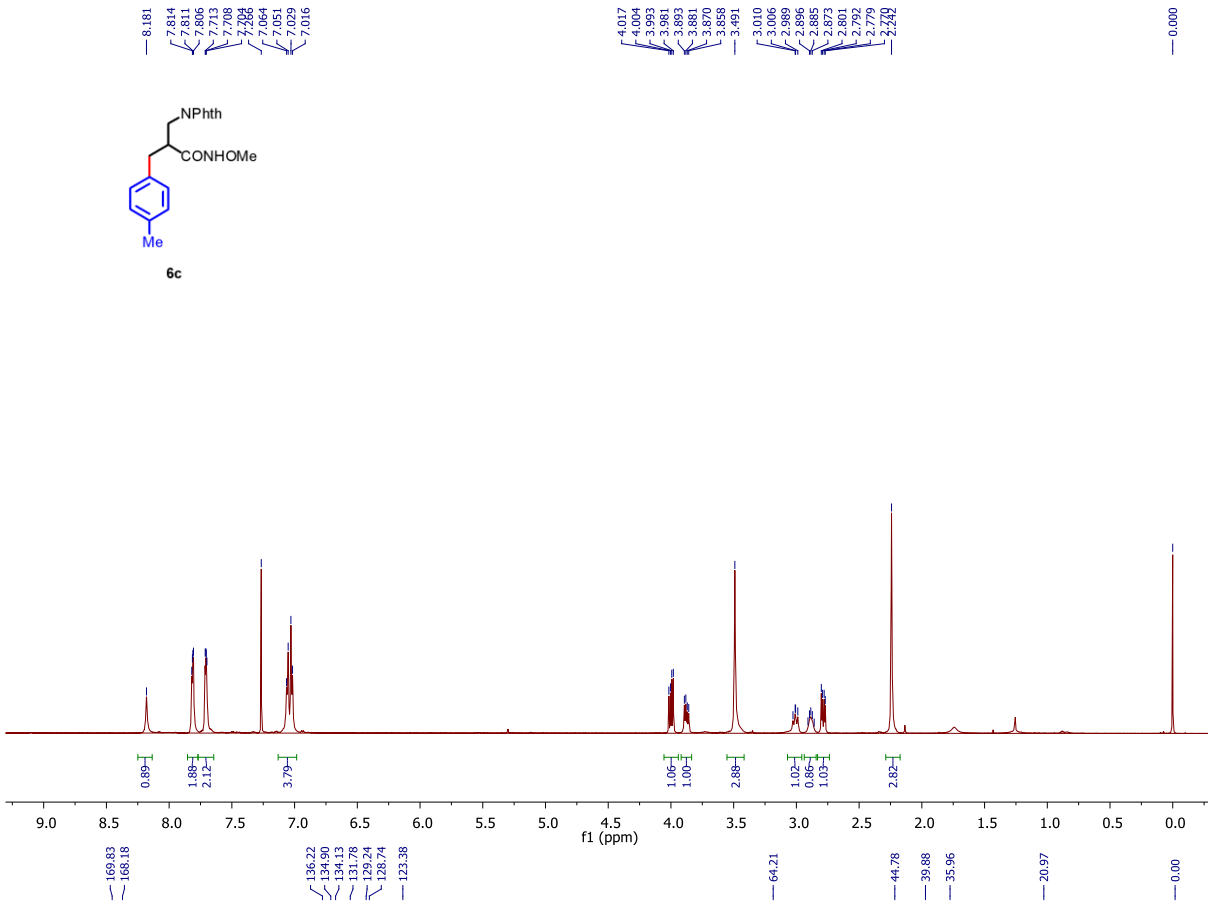
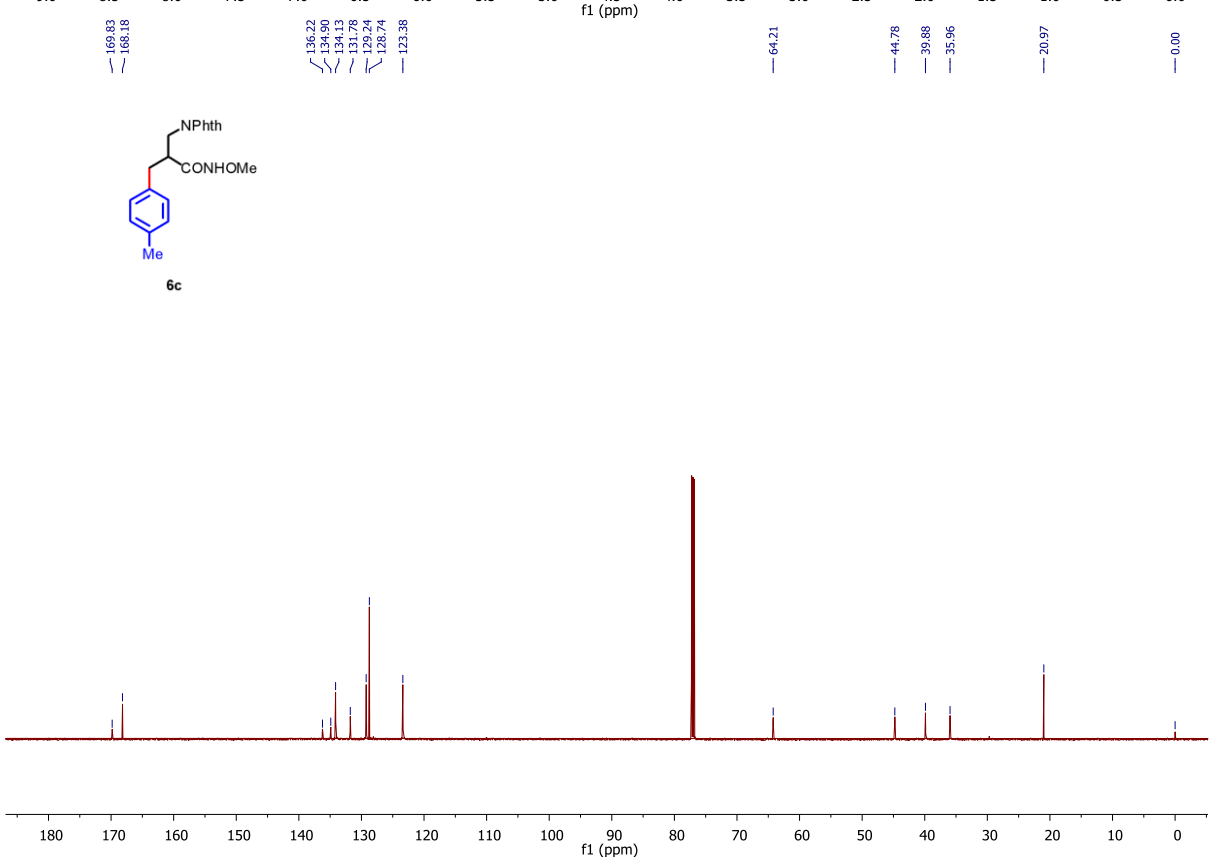
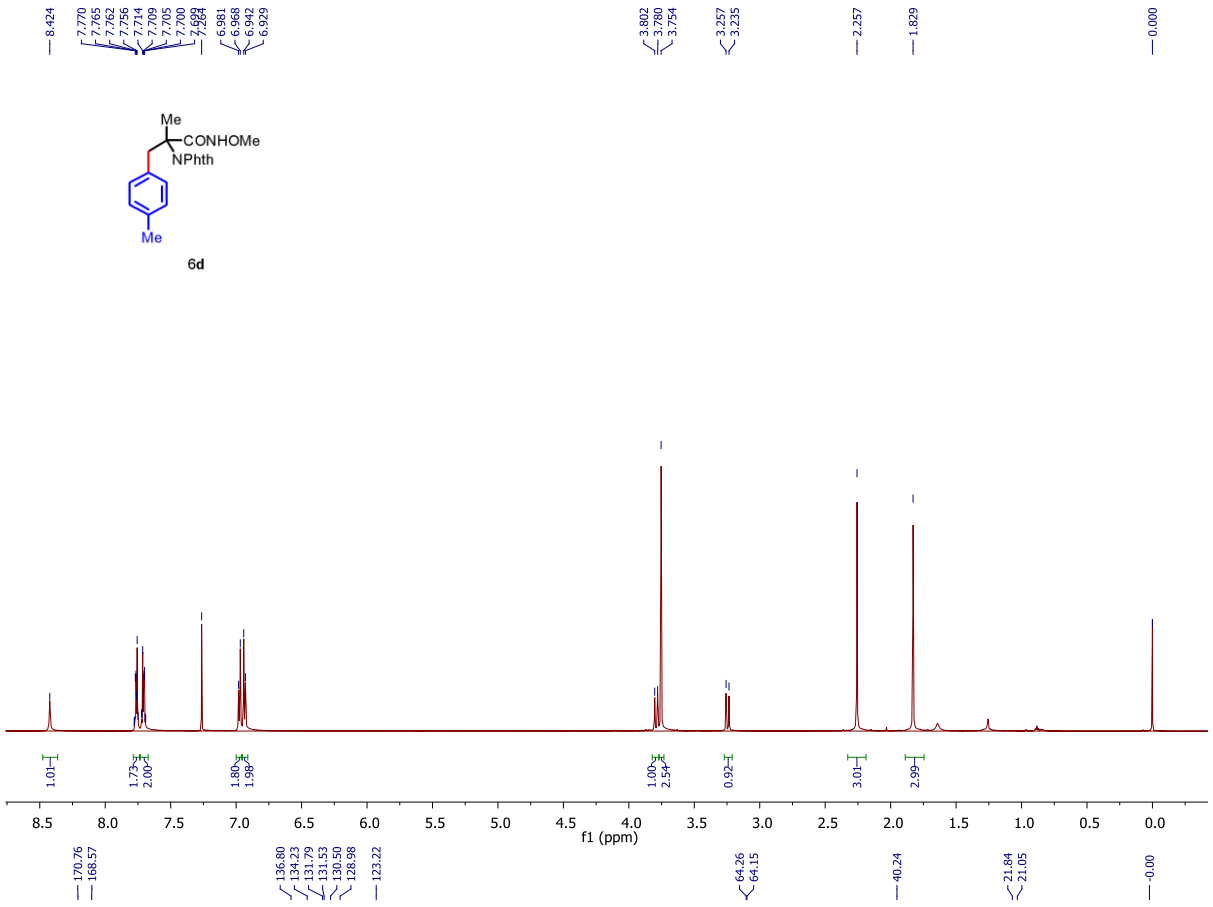
7.286
7.259
7.095
7.084
7.071
7.058
7.044
4.512
4.493
4.482
4.462
3.646
3.593
3.578
3.565
3.554
3.547
3.539
3.532
2.979
2.969
2.956
2.750
2.737
2.727
2.715
2.307
0.000
OBn
CONHOMe
Me
6b
0.95
5.02
4.43
2.27
2.91
2.47
1.21
1.11
1.00
3.34
f1 (ppm)
171.751
137.498
136.076
135.538
129.227
128.833
128.528
127.949
127.810
73.526
69.657
64.316
47.158
34.167
21.029
0.000
OBn
CONHOMe
Me
6b
f1 (ppm)


8.181
7.814
7.811
7.806
7.713
7.708
7.288
7.064
7.051
7.029
7.016
4.017
4.004
3.993
3.981
3.893
3.881
3.870
3.858
3.491
3.010
3.006
2.989
2.896
2.885
2.873
2.801
2.792
2.779
0.000
NPhth
CONHOMe
Me
6c
0.89
1.88
2.12
3.79
1.06
1.00
2.88
1.02
0.86
1.03
2.82
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


169.83
168.18
136.22
134.90
134.13
131.78
129.24
128.74
123.38
64.21
44.78
39.88
35.96
20.97
0.00
NPhth
CONHOMe
Me
6c
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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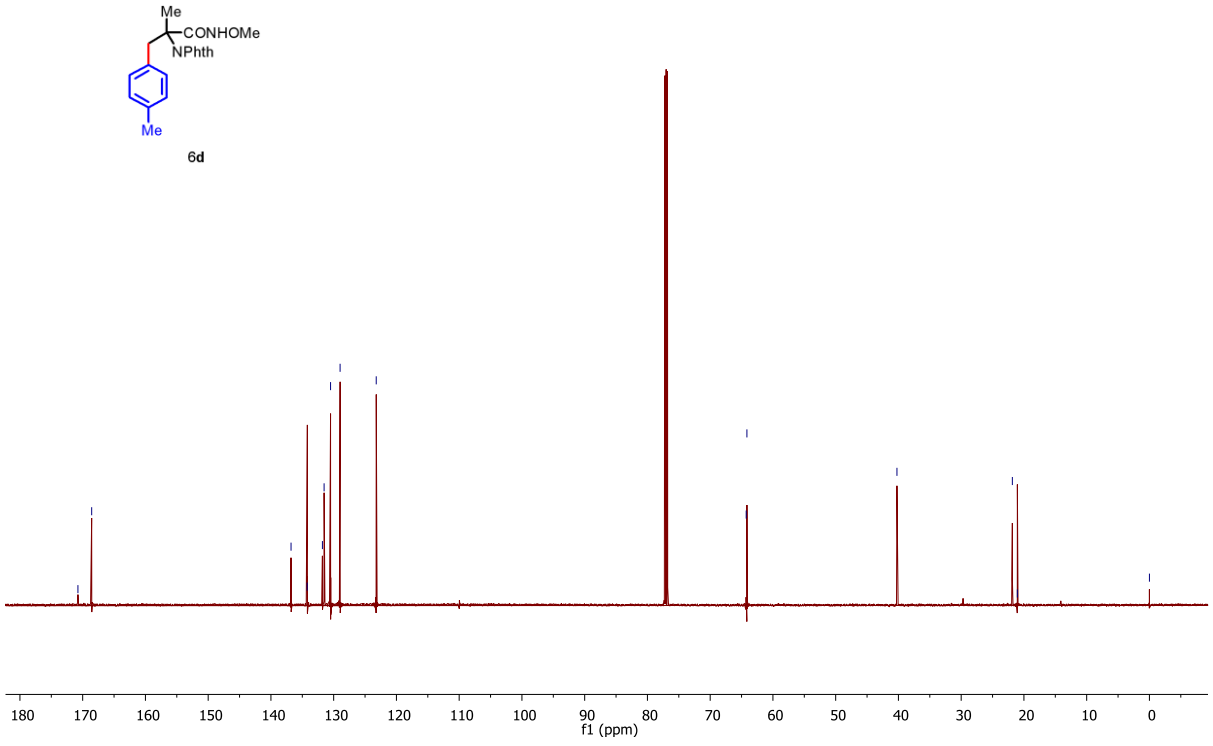
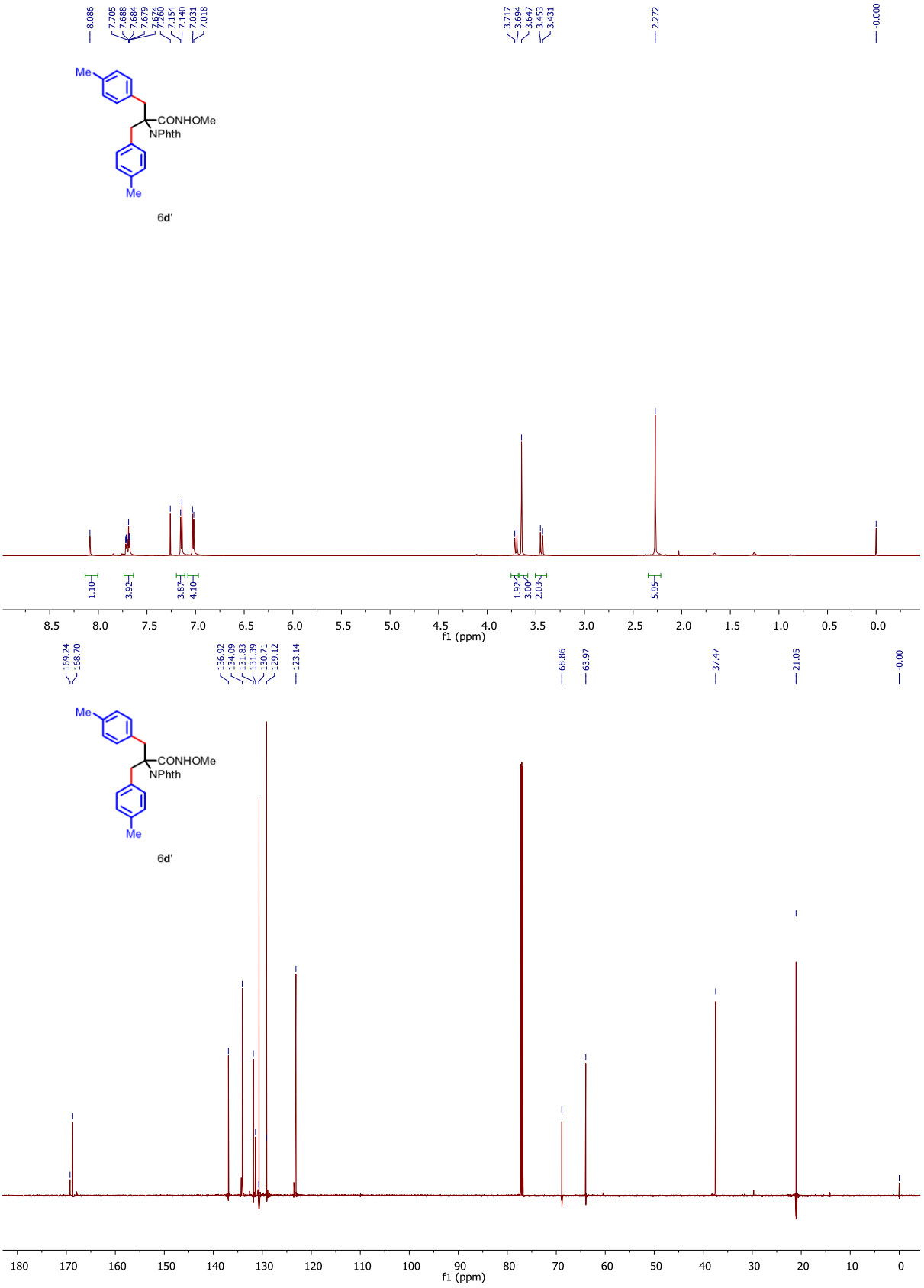
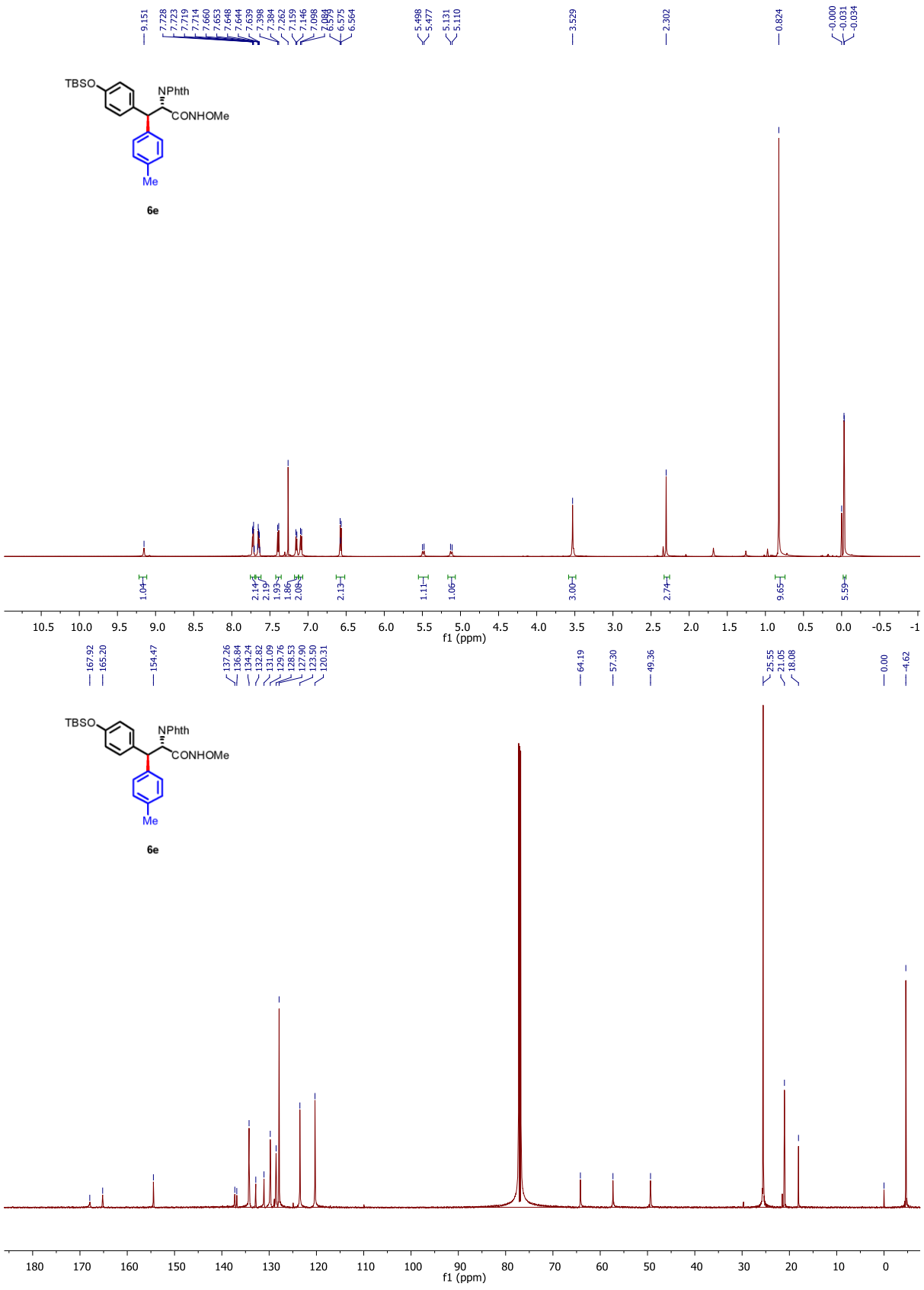
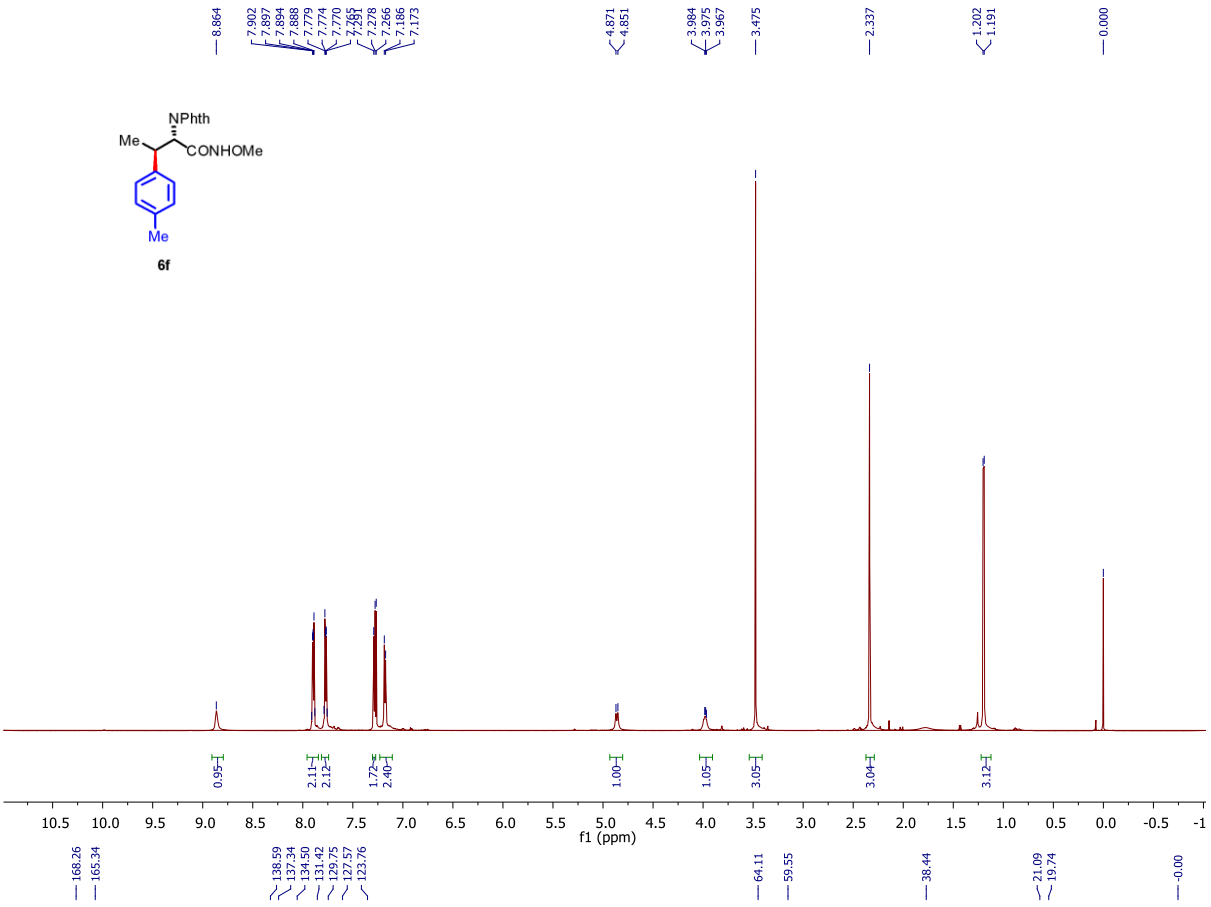
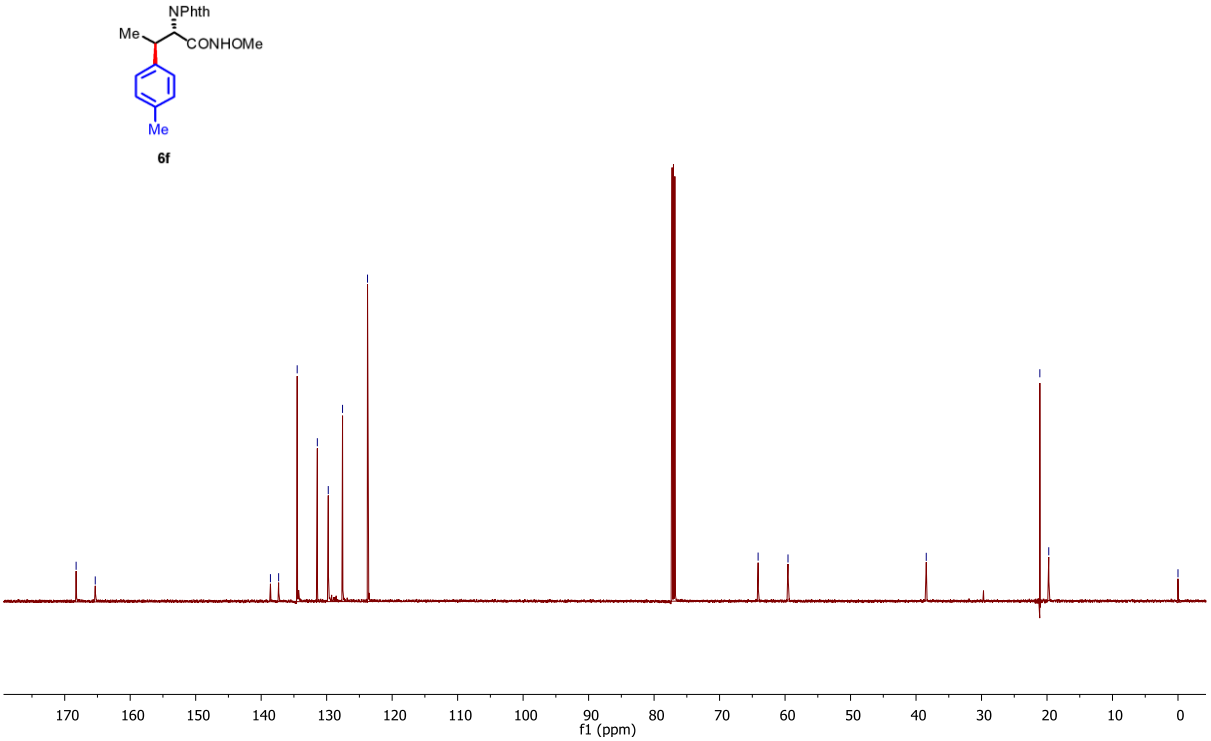
7.770
7.765
7.762
7.756
7.714
7.709
7.705
7.700
7.694
7.688
6.981
6.968
6.942
6.929
3.802
3.780
3.754
3.257
3.235
2.257
1.829
0.000
Me
CONHOMe
NPhth
Me
6d
1.01
1.73
2.00
1.80
1.98
1.00
2.54
0.92
3.01
2.99
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

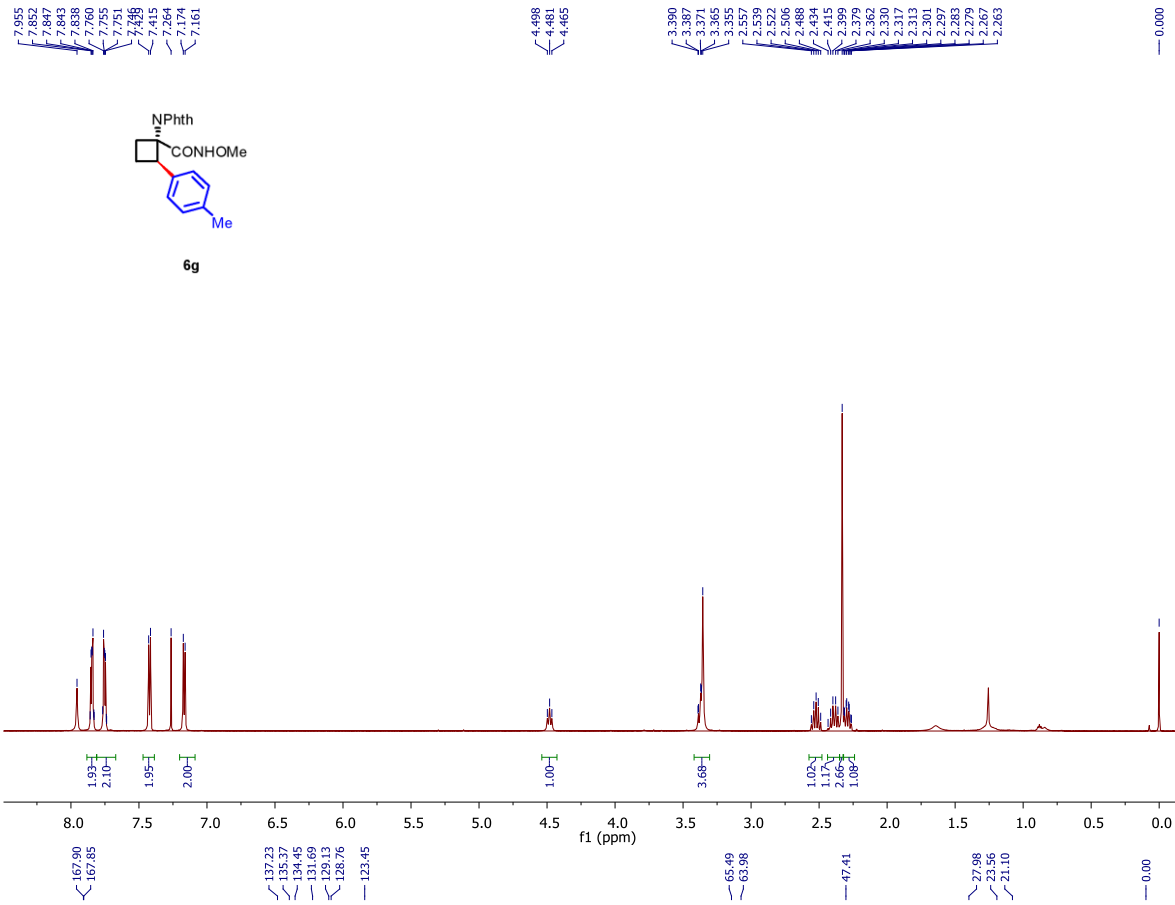

170.76
168.57
136.80
134.23
131.79
131.53
130.50
128.98
123.22
64.26
64.15
40.24
21.84
21.05
-0.00
Me
CONHOMe
NPhth
Me
6d
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

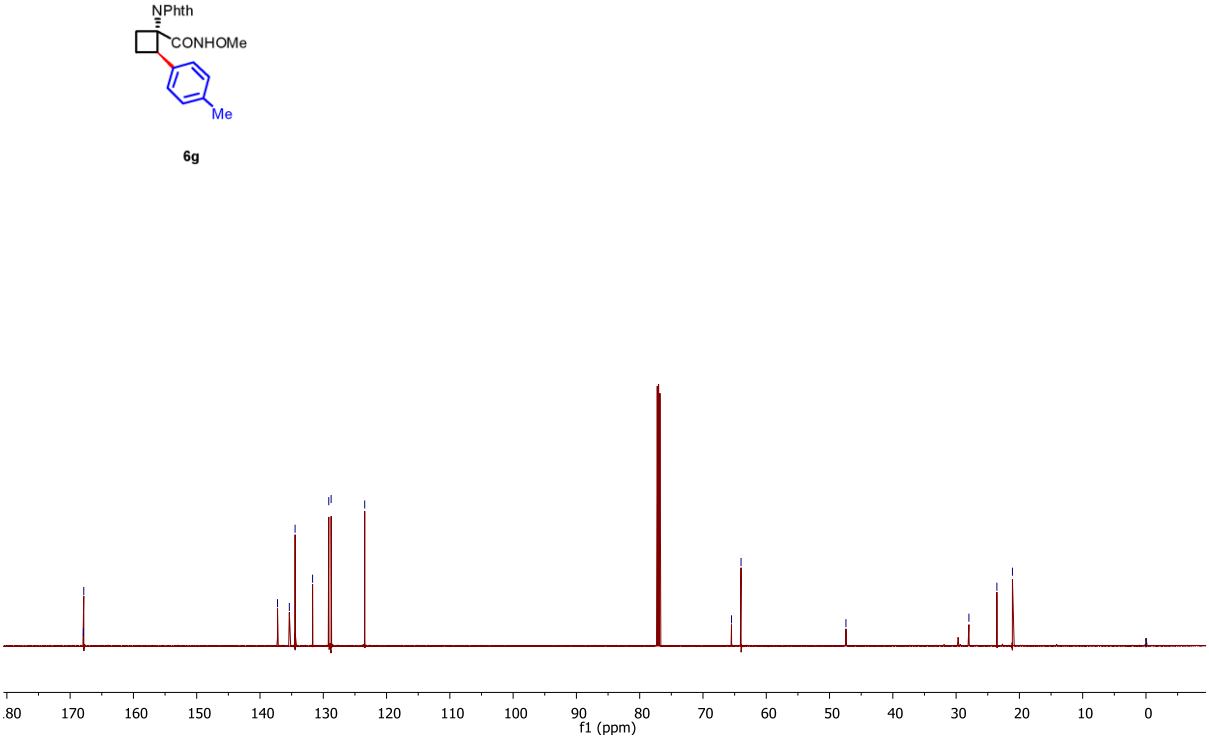

8.086
7.705
7.688
7.684
7.679
7.263
7.154
7.140
7.031
7.018
3.717
3.694
3.647
3.453
3.431
2.272
-0.000
Me
CONHOMe
NPhth
Me
6d'
1.10
3.92
3.87
4.10
1.92
3.00
2.03
5.95
f1 (ppm)
169.24
168.70
136.92
134.09
131.83
131.39
130.71
129.12
123.14
68.86
63.97
37.47
21.05
-0.00
Me
CONHOMe
NPhth
Me
6d'
f1 (ppm)

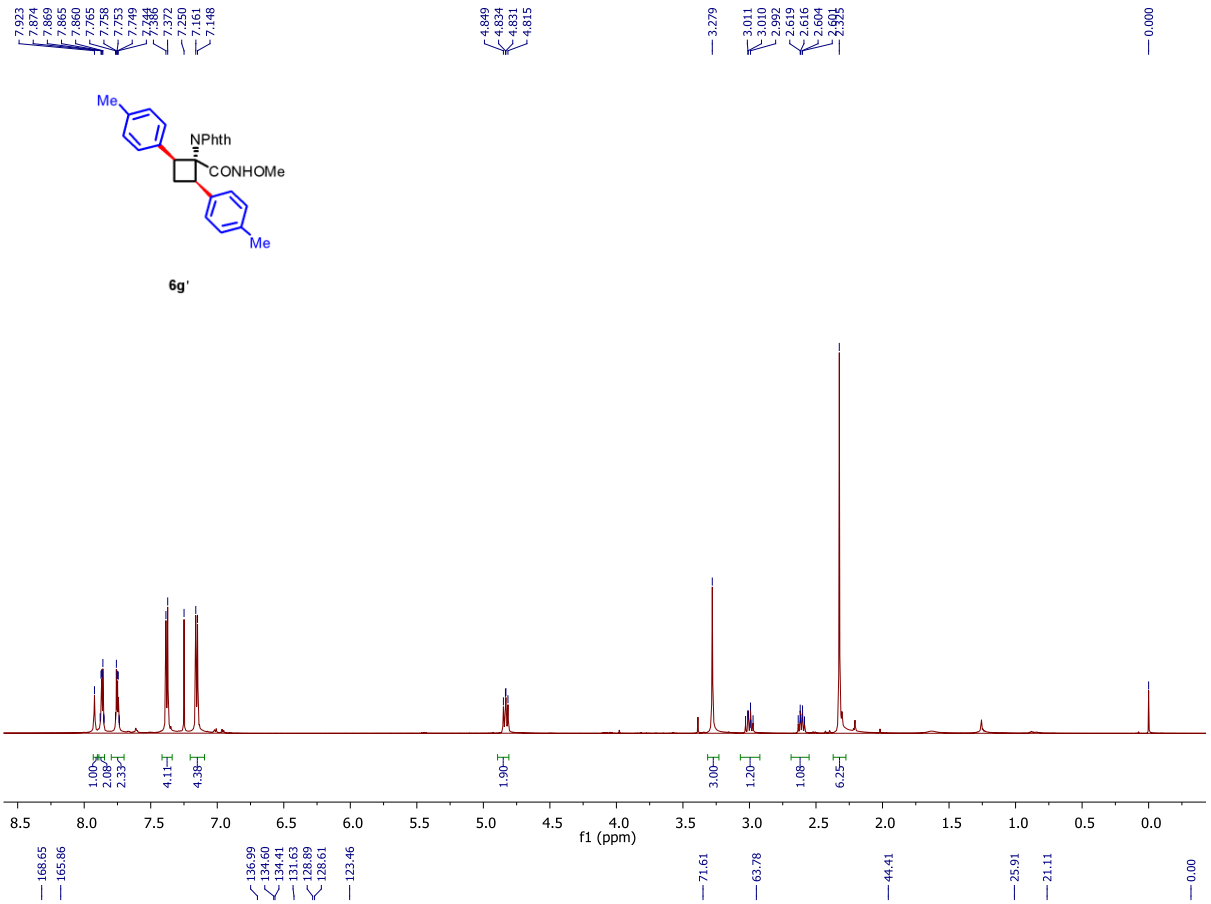

9.151
7.728
7.723
7.719
7.714
7.660
7.653
7.648
7.644
7.639
7.398
7.384
7.262
7.159
7.146
7.098
7.084
6.579
6.575
6.564
5.498
5.477
5.131
5.110
3.529
2.302
0.824
0.000
-0.031
-0.034
TBSO
NPhth
CONHOMe
Me
6e
1.04
2.14
2.19
1.93
1.86
2.08
2.13
1.11
1.06
3.00
2.74
9.65
5.59
f1 (ppm)
167.92
165.20
154.47
137.26
136.84
134.24
132.82
131.09
129.76
128.53
127.90
123.50
120.31
64.19
57.30
49.36
25.55
21.05
18.08
0.00
-4.62
TBSO
NPhth
CONHOMe
Me
6e
f1 (ppm)

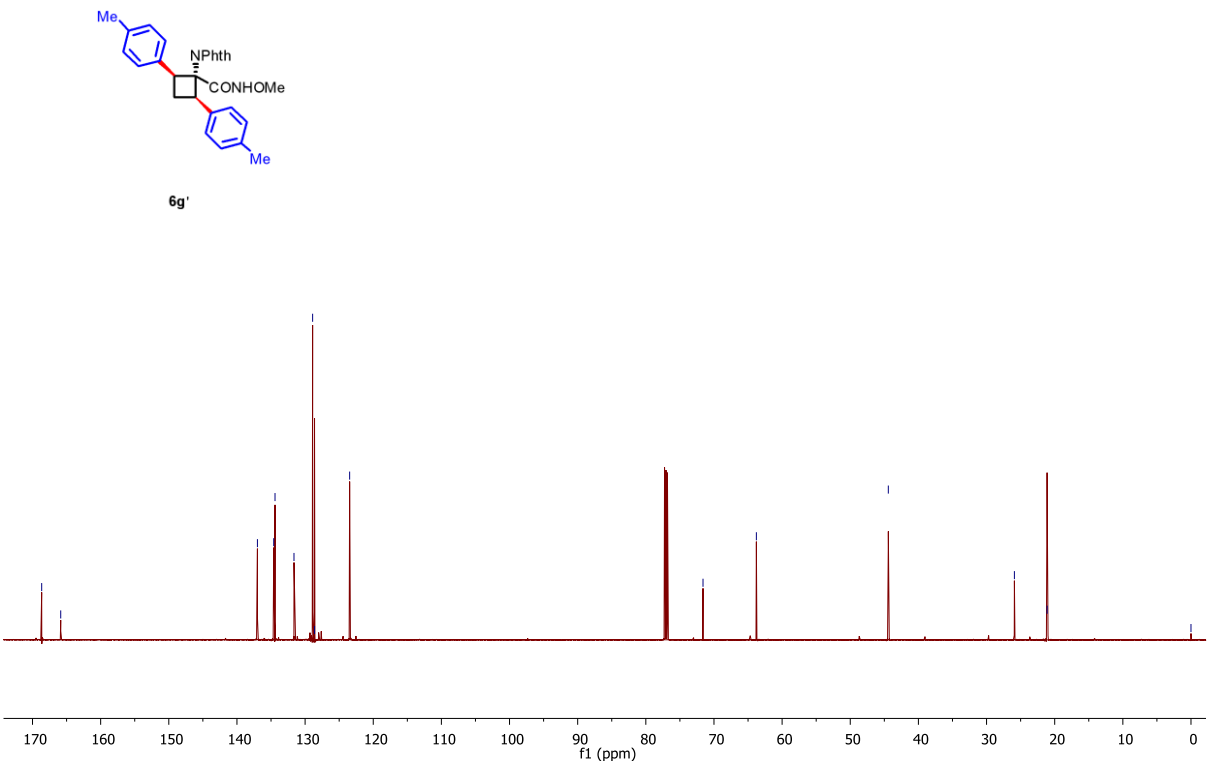

8.864
7.902
7.897
7.894
7.888
7.779
7.774
7.770
7.291
7.278
7.266
7.186
7.173
4.871
4.851
3.984
3.975
3.967
3.475
2.337
1.202
1.191
0.000
NPhth
Me
CONHOMe
Me
6f
0.95
2.11
2.12
1.72
2.40
1.00
1.05
3.05
3.04
3.12
f1 (ppm)
168.26
165.34
138.59
137.34
134.50
131.42
129.75
127.57
123.76
64.11
59.55
38.44
21.09
19.74
-0.00

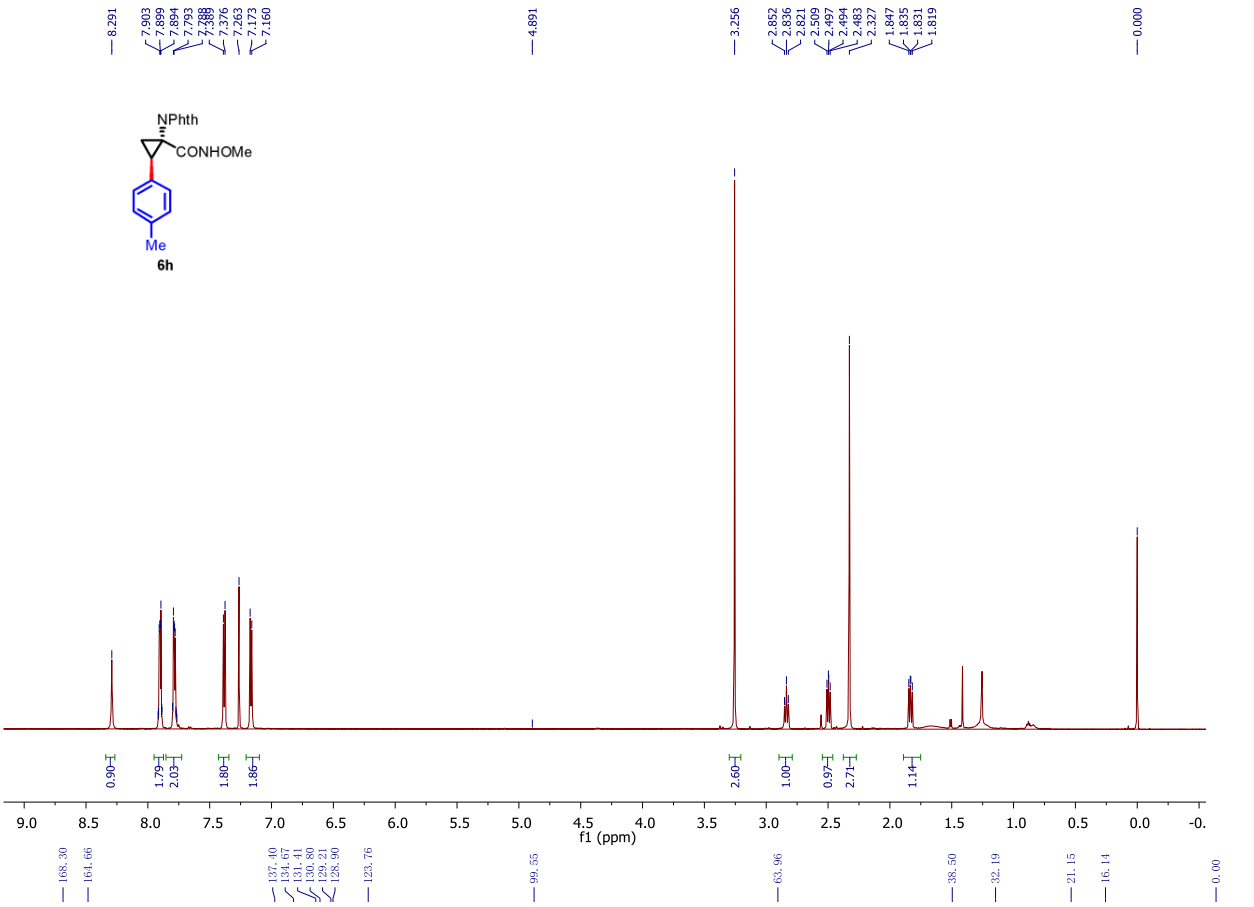

NPhth
Me
CONHOMe
Me
6f
f1 (ppm)

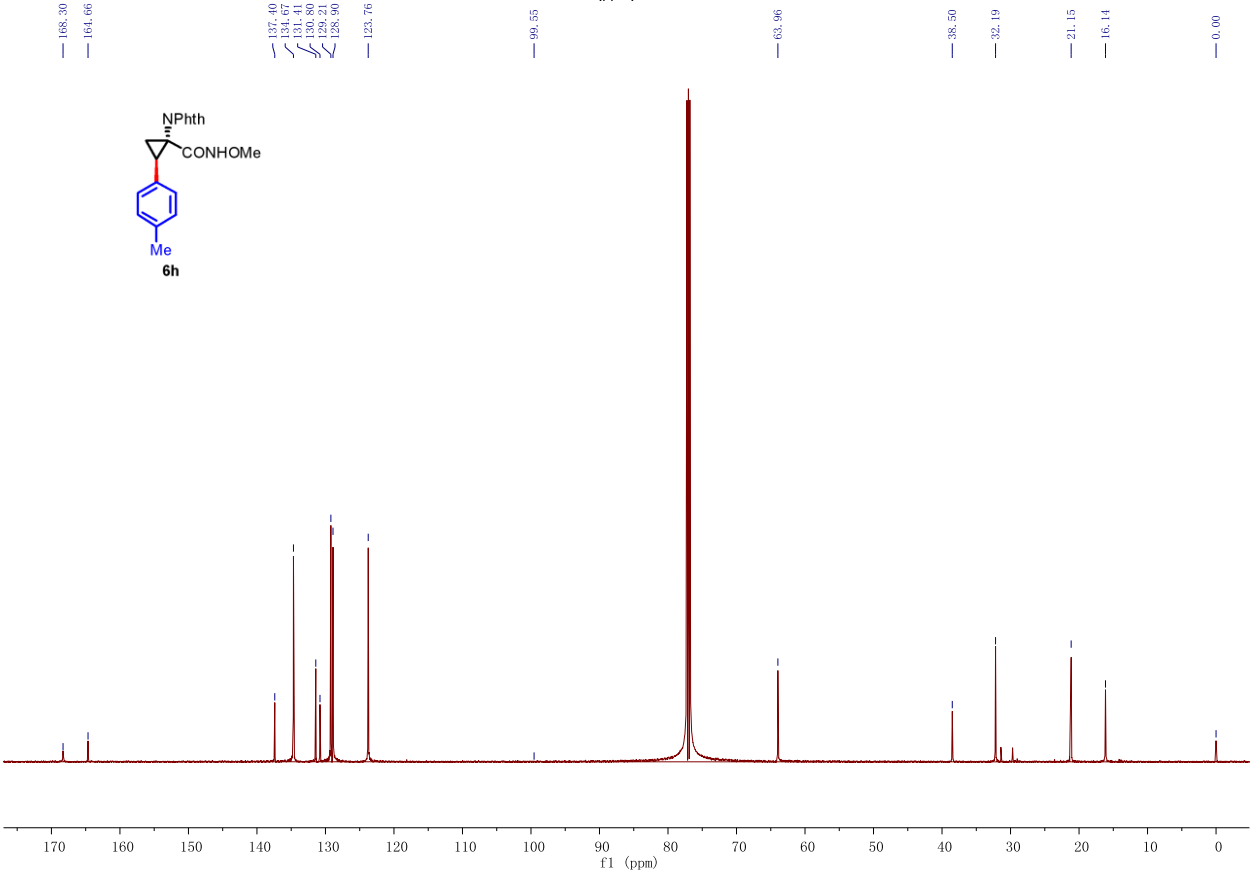

7.955
7.852
7.847
7.843
7.838
7.760
7.755
7.751
7.746
7.439
7.415
7.264
7.174
7.161
4.498
4.481
4.465
3.390
3.387
3.371
3.365
3.355
2.557
2.539
2.522
2.506
2.488
2.434
2.415
2.399
2.379
2.362
2.330
2.317
2.313
2.301
2.297
2.283
2.279
2.267
2.263
0.000
NPhth
CONHOMe
Me
6g
1.93
2.10
1.95
2.00
1.00
3.68
1.02
1.17
2.66
1.08
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
167.90
167.85
137.23
135.37
134.45
131.69
129.13
128.76
123.45
65.49
63.98
47.41
27.98
23.56
21.10
0.00

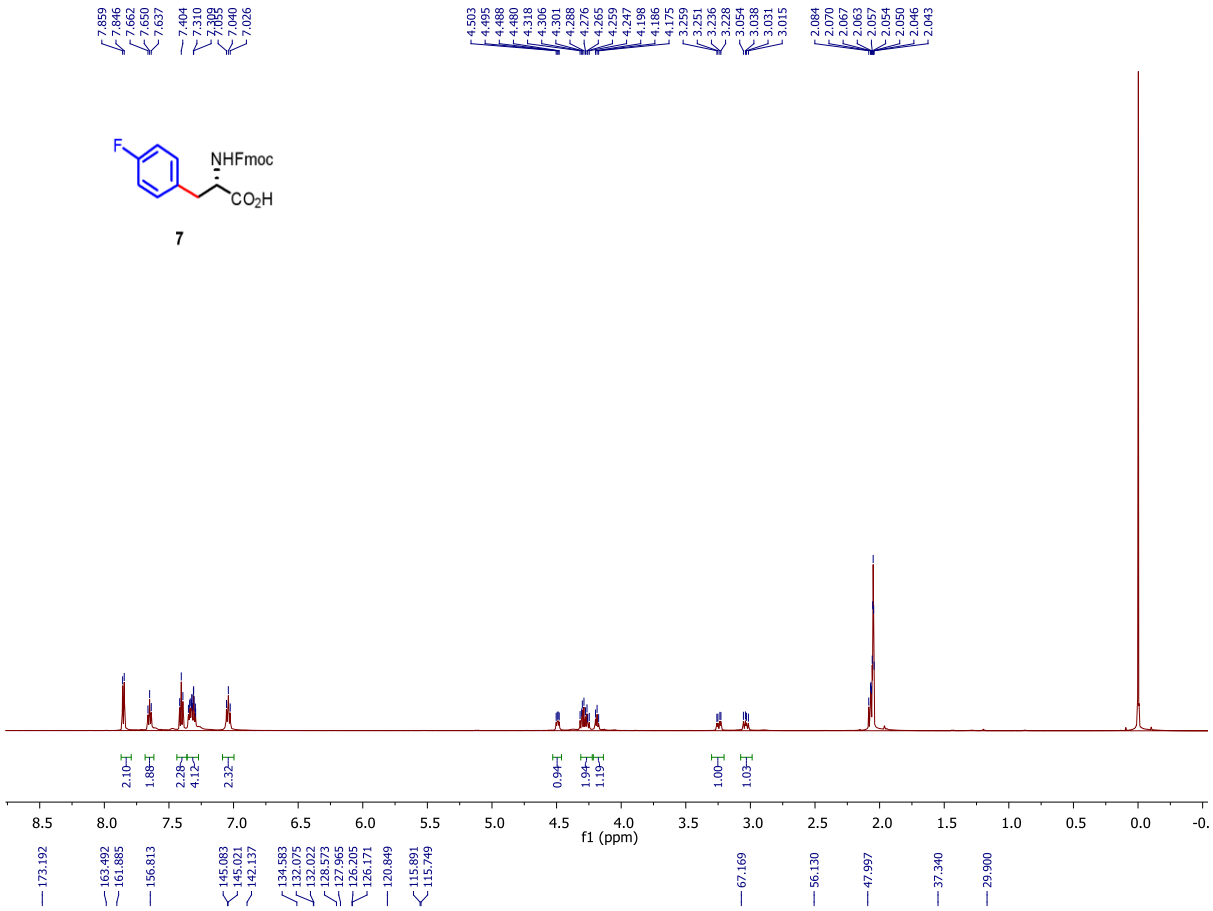

NPhth
CONHOMe
Me
6g
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

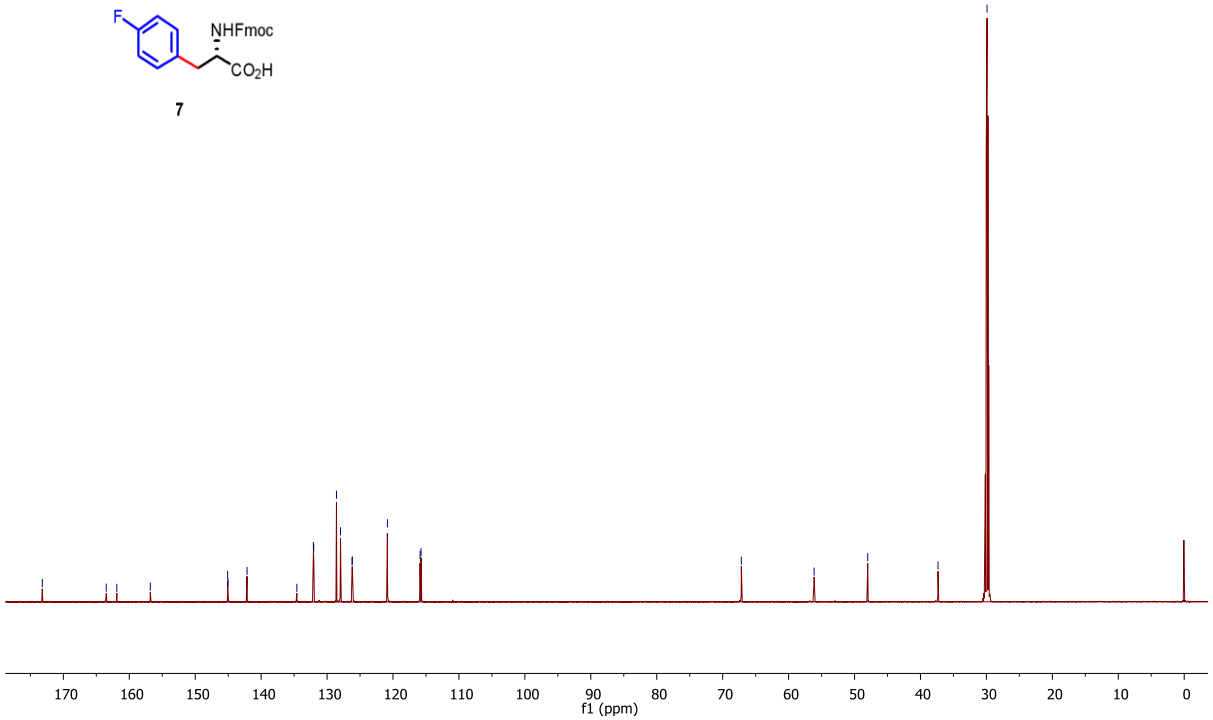

7.923
7.874
7.869
7.865
7.860
7.765
7.758
7.753
7.749
7.744
7.388
7.372
7.250
7.161
7.148
4.849
4.834
4.831
4.815
3.279
3.011
3.010
2.992
2.619
2.616
2.604
2.601
0.000
Me
NPhth
CONHOMe
Me
6g'
1.00
2.08
2.33
4.11
4.38
1.90
3.00
1.20
1.08
6.25
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


168.65
165.86
136.99
134.60
134.41
131.63
128.89
128.61
123.46
71.61
63.78
44.41
25.91
21.11
0.00
Me
NPhth
CONHOMe
Me
6g'
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

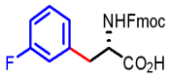

8.291
7.903
7.899
7.894
7.793
7.389
7.376
7.263
7.173
7.160
4.891
3.256
2.852
2.836
2.821
2.509
2.497
2.494
2.483
2.327
1.847
1.835
1.831
1.819
0.000
NPhth
CONHOMe
Me
6h
0.90
1.79
2.03
1.80
1.86
2.60
1.00
0.97
2.71
1.14
f1 (ppm)


168.30
164.66
137.40
134.67
131.41
130.80
129.21
128.90
123.76
99.55
63.96
38.50
32.19
21.15
16.14
0.00
NPhth
CONHOMe
Me
6h
f1 (ppm)

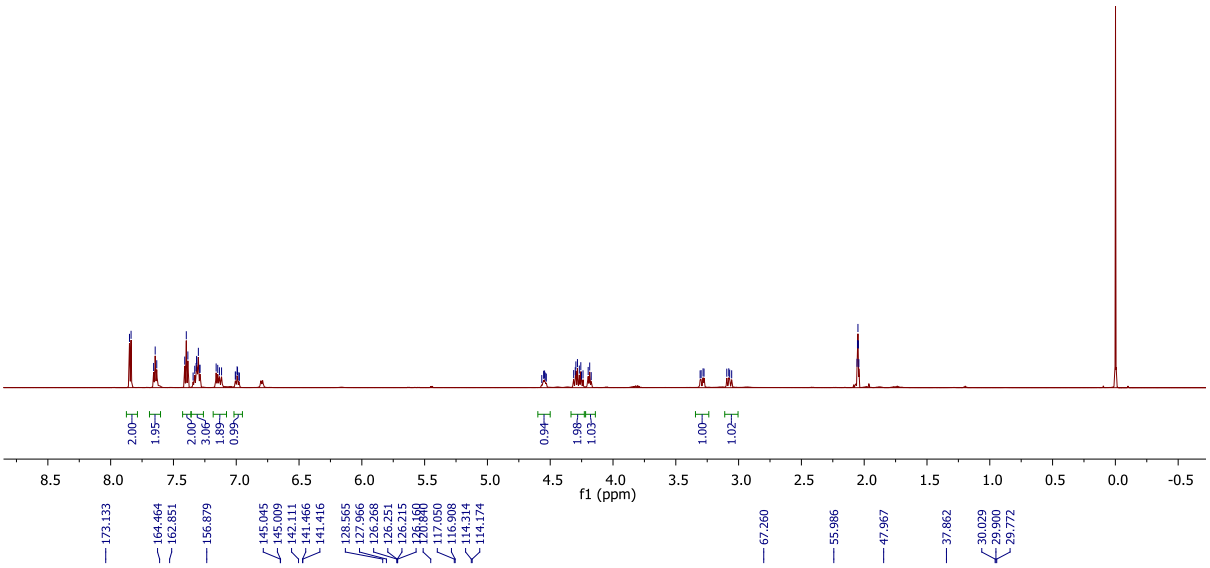

7.859
7.846
7.662
7.650
7.637
7.404
7.310
7.040
7.026
4.503
4.495
4.488
4.480
4.318
4.306
4.301
4.288
4.276
4.265
4.259
4.247
4.198
4.186
4.175
3.259
3.251
3.236
3.228
3.054
3.038
3.031
3.015
2.084
2.070
2.067
2.063
2.057
2.054
2.050
2.046
2.043
F
NHFmoc
CO2H
7
2.10
1.88
2.28
4.12
2.32
0.94
1.94
1.19
1.00
1.03
f1 (ppm)
173.192
163.492
161.885
156.813
145.083
145.021
142.137
134.583
132.075
132.022
128.573
127.965
126.205
126.171
120.849
115.891
115.749
67.169
56.130
47.997
37.340
29.900


F
NHFmoc
CO2H
7
f1 (ppm)

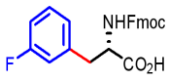

7.850
7.838
7.658
7.645
7.633
7.410
7.398
7.385
7.343
7.331
7.320
7.316
7.314
7.302
7.291
7.289
7.160
7.147
7.134
7.117
7.007
7.004
6.993
6.990
6.979
6.975
4.567
4.553
4.545
4.540
4.531
4.313
4.301
4.296
4.283
4.268
4.256
4.251
4.239
4.198
4.186
4.174
3.306
3.299
3.283
3.275
3.094
3.078
3.071
3.055
2.057
2.053
2.050
2.046
2.042


NHFmoc
F
CO2H

8

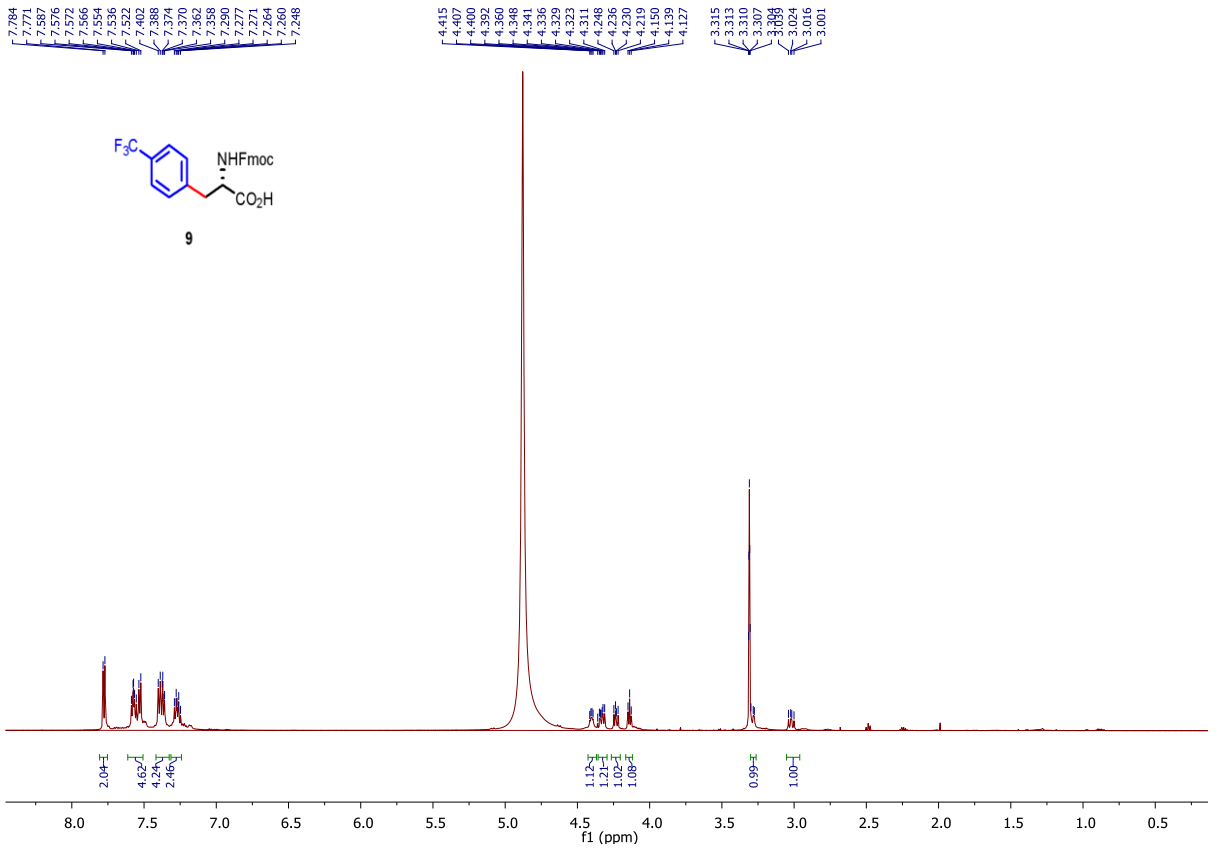

2.00
1.95
2.00
3.06
1.89
0.99
0.94
1.98
1.03
1.00
1.02
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

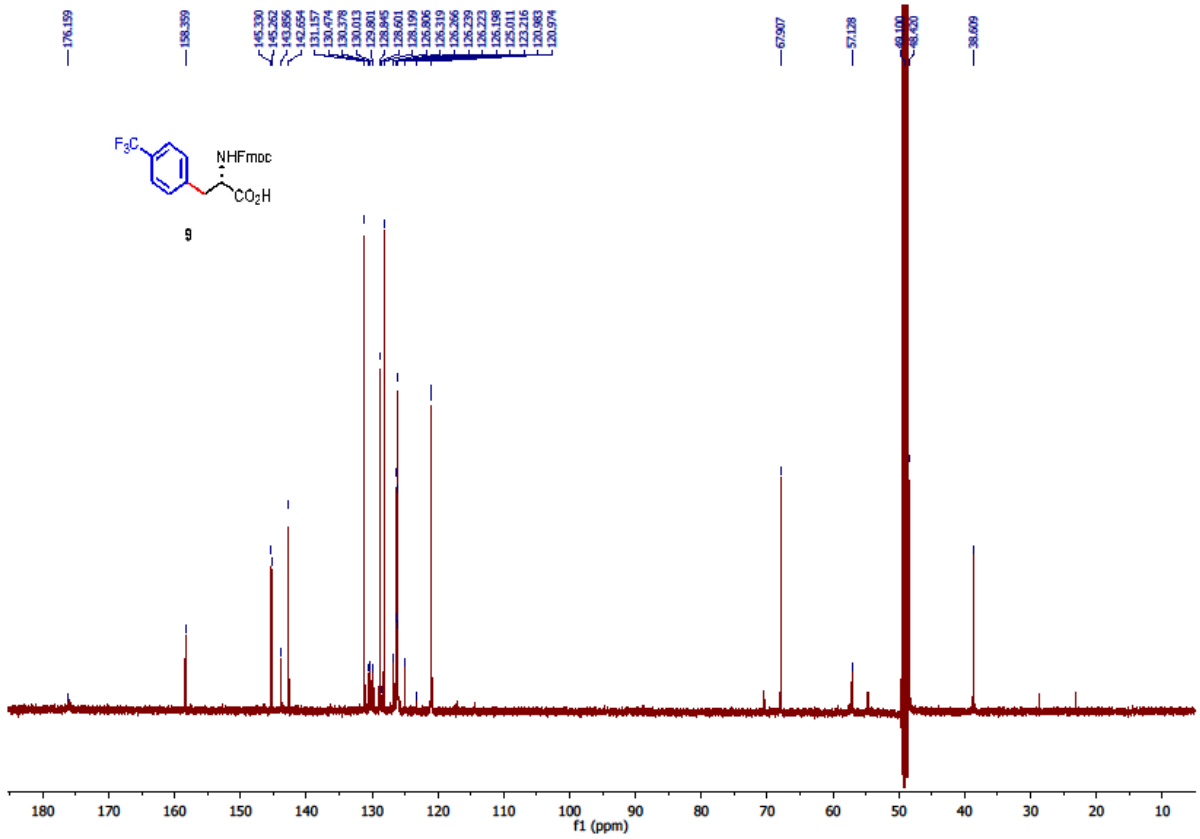
173.133
164.464
162.851
156.879
145.045
145.009
142.111
141.466
141.416
128.565
127.966
126.268
126.251
126.215
117.050
116.908
114.314
114.174
67.260
55.986
47.967
37.862
30.029
29.900
29.772

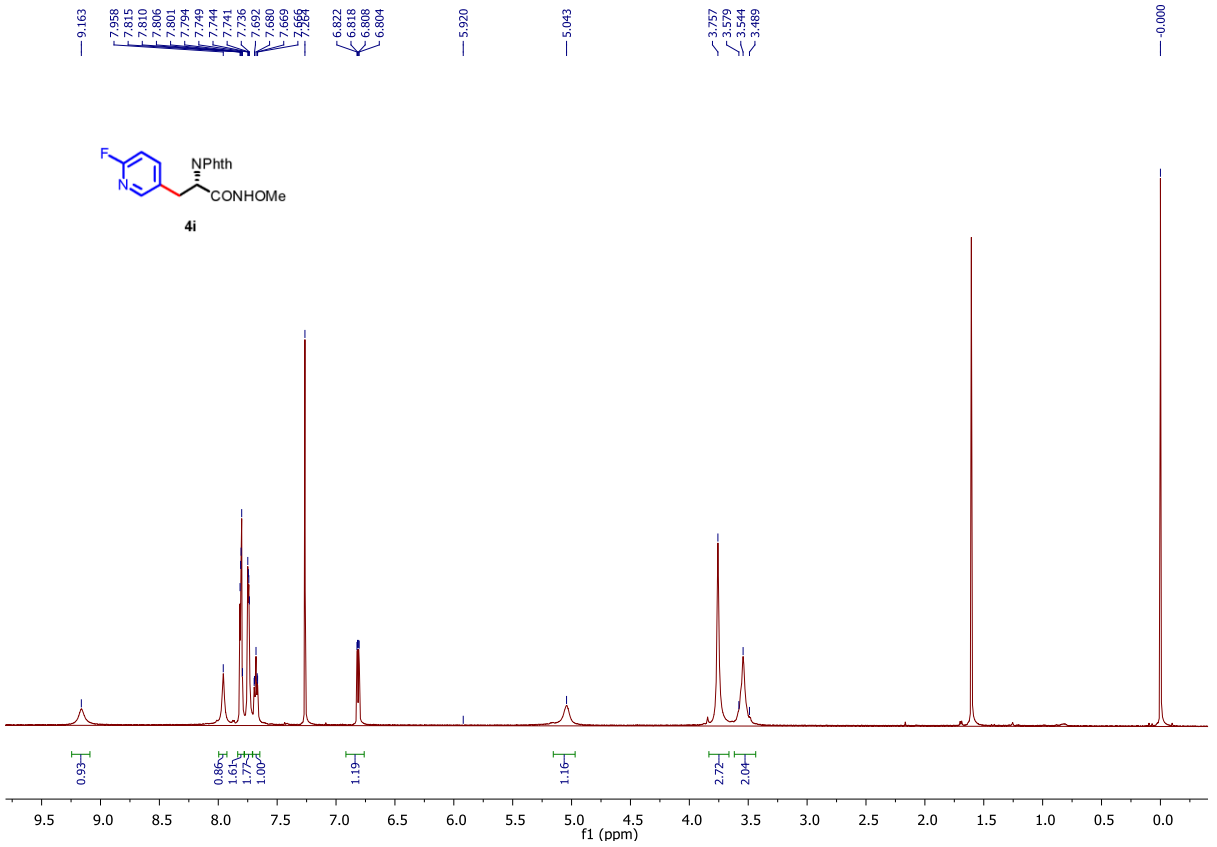

NHFmoc
F
CO2H

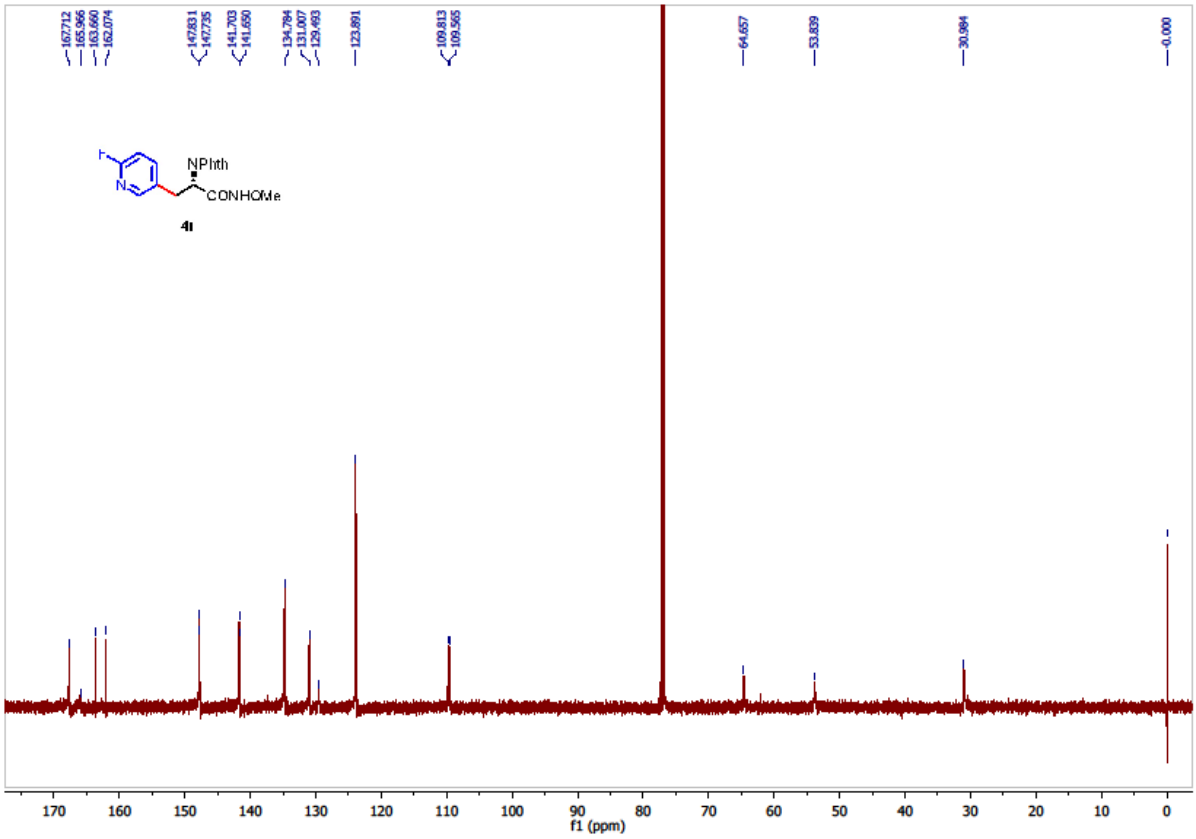
8

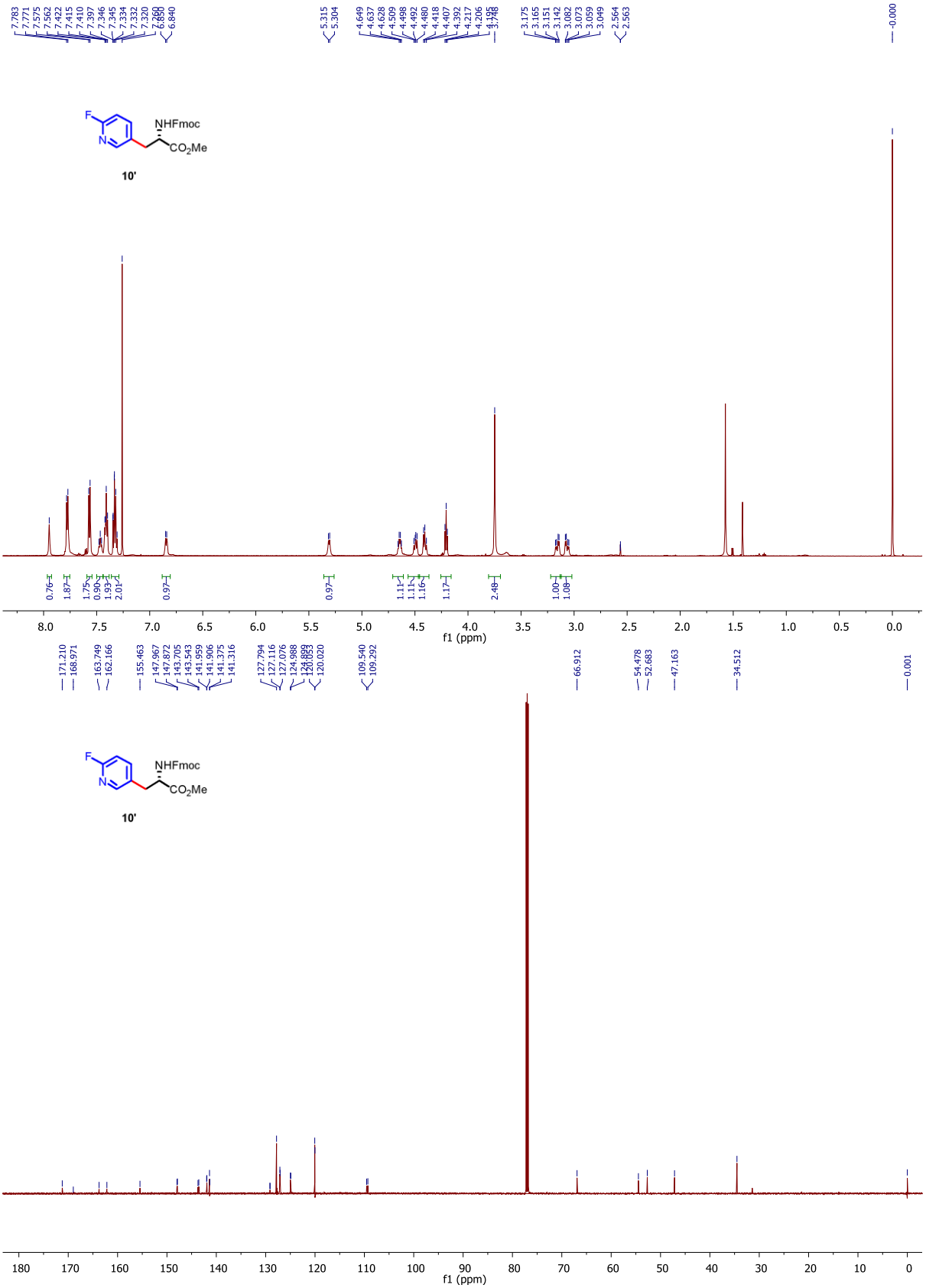
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

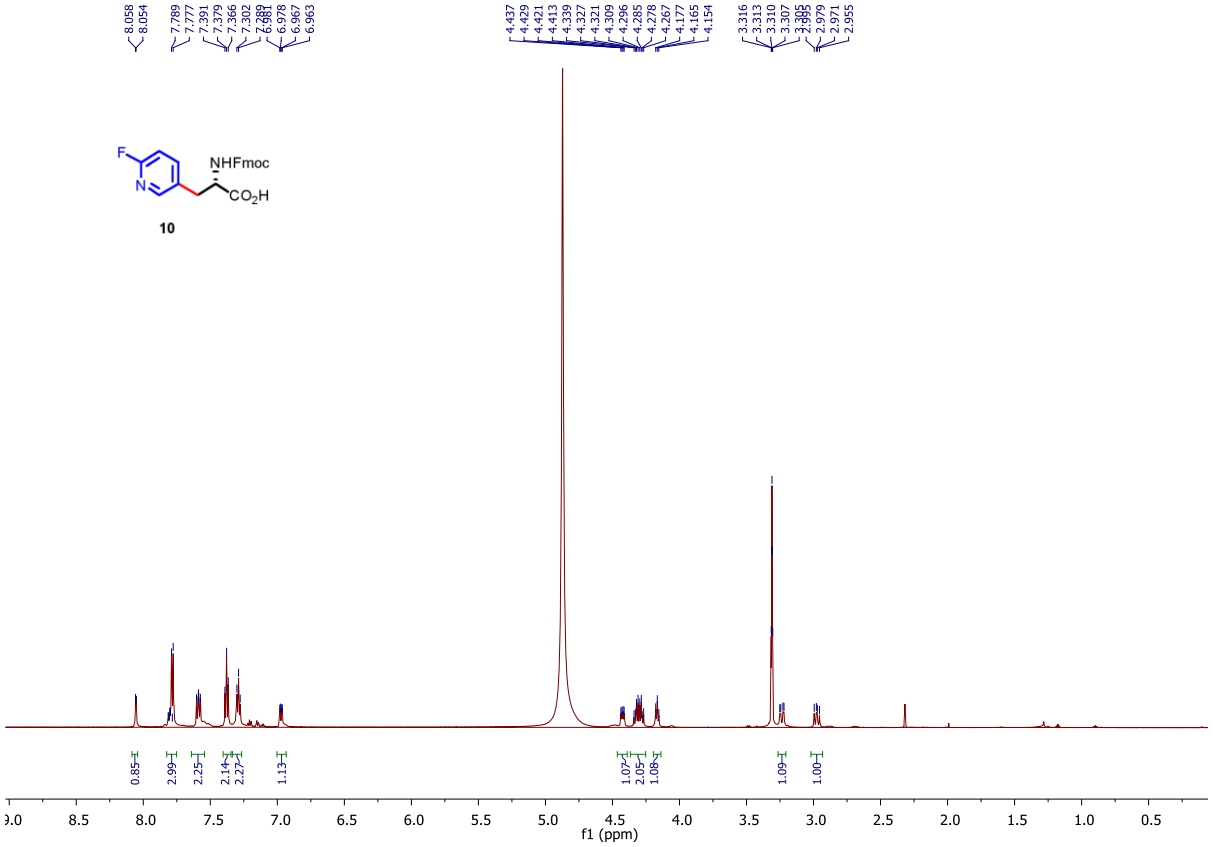

F3C
NHFmoc
CO2H
9
f1 (ppm)

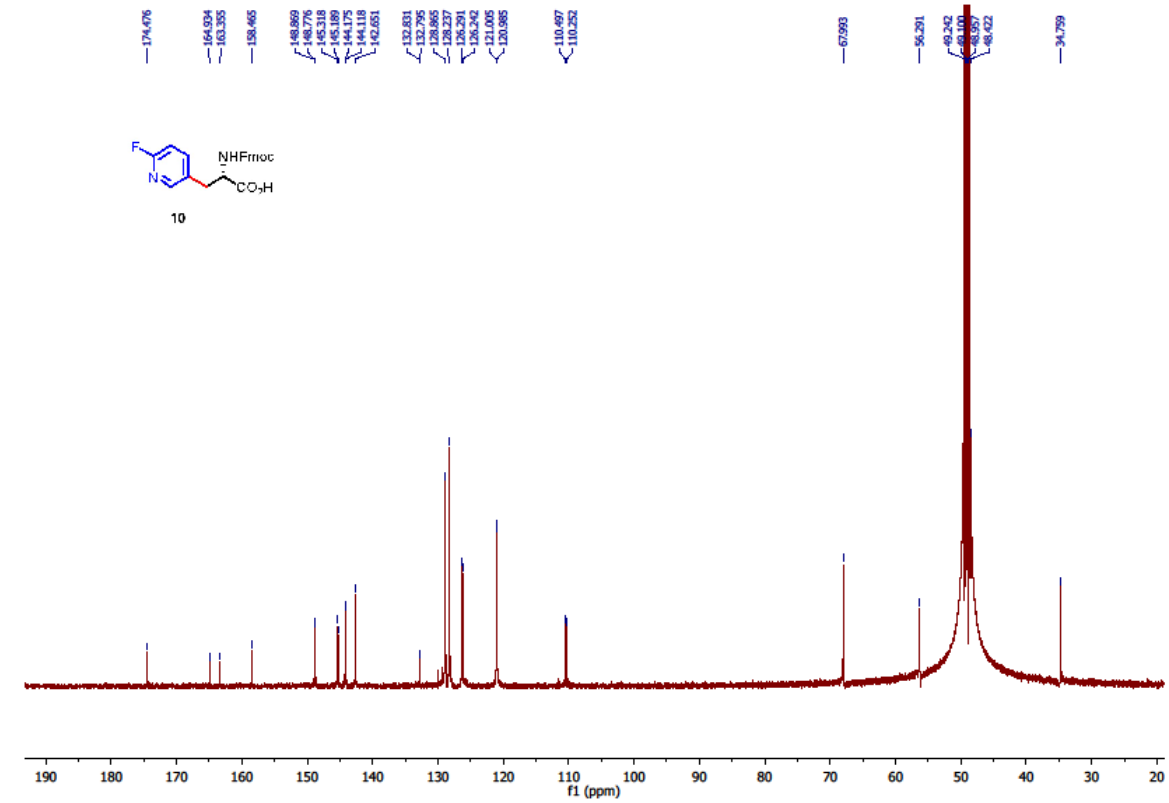

F3C
NHFmoc
CO2H
9
f1 (ppm)


9.163
7.958
7.815
7.810
7.806
7.801
7.794
7.749
7.744
7.741
7.736
7.692
7.680
7.669
7.666
7.264
6.822
6.818
6.808
6.804
5.920
5.043
3.757
3.579
3.544
3.489
0.000
F
N
NPhth
CONHOMe
4i
0.93
0.86
1.65
1.77
1.00
1.19
1.16
2.72
2.04
f1 (ppm)


167.712
165.966
163.660
162.074
147.831
147.735
141.703
141.650
134.784
131.007
129.493
123.891
109.813
109.565
64.657
53.839
30.984
0.000
F
N
NPhth
CONHOMe
4i
f1 (ppm)


7.783
7.771
7.575
7.562
7.422
7.415
7.410
7.397
7.346
7.345
7.334
7.332
7.320
6.850
6.840
5.315
5.304
4.649
4.637
4.628
4.509
4.498
4.492
4.480
4.418
4.407
4.392
4.217
4.206
3.175
3.165
3.151
3.142
3.082
3.073
3.059
3.049
2.564
2.563
-0.000
F
N
NHFmoc
CO2Me
10'
0.76
1.87
1.75
0.90
1.93
2.01
0.97
0.97
1.11
1.11
1.16
1.17
2.48
1.00
1.08
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
171.210
168.971
163.749
162.166
155.463
147.967
147.872
143.705
143.543
141.959
141.906
141.375
141.316
127.794
127.116
127.076
124.988
120.053
120.020
109.540
109.292
66.912
54.478
52.683
47.163
34.512
0.001
F
N
NHFmoc
CO2Me
10'
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.058
8.054
7.789
7.777
7.391
7.379
7.366
7.302
6.978
6.967
6.963
4.437
4.429
4.421
4.413
4.339
4.327
4.321
4.309
4.296
4.285
4.278
4.267
4.177
4.165
4.154
3.316
3.313
3.310
3.307
2.979
2.971
2.955
F
N
NHFmoc
CO2H
10
0.85
2.99
2.25
2.14
2.27
1.13
1.07
2.05
1.08
1.09
1.00
f1 (ppm)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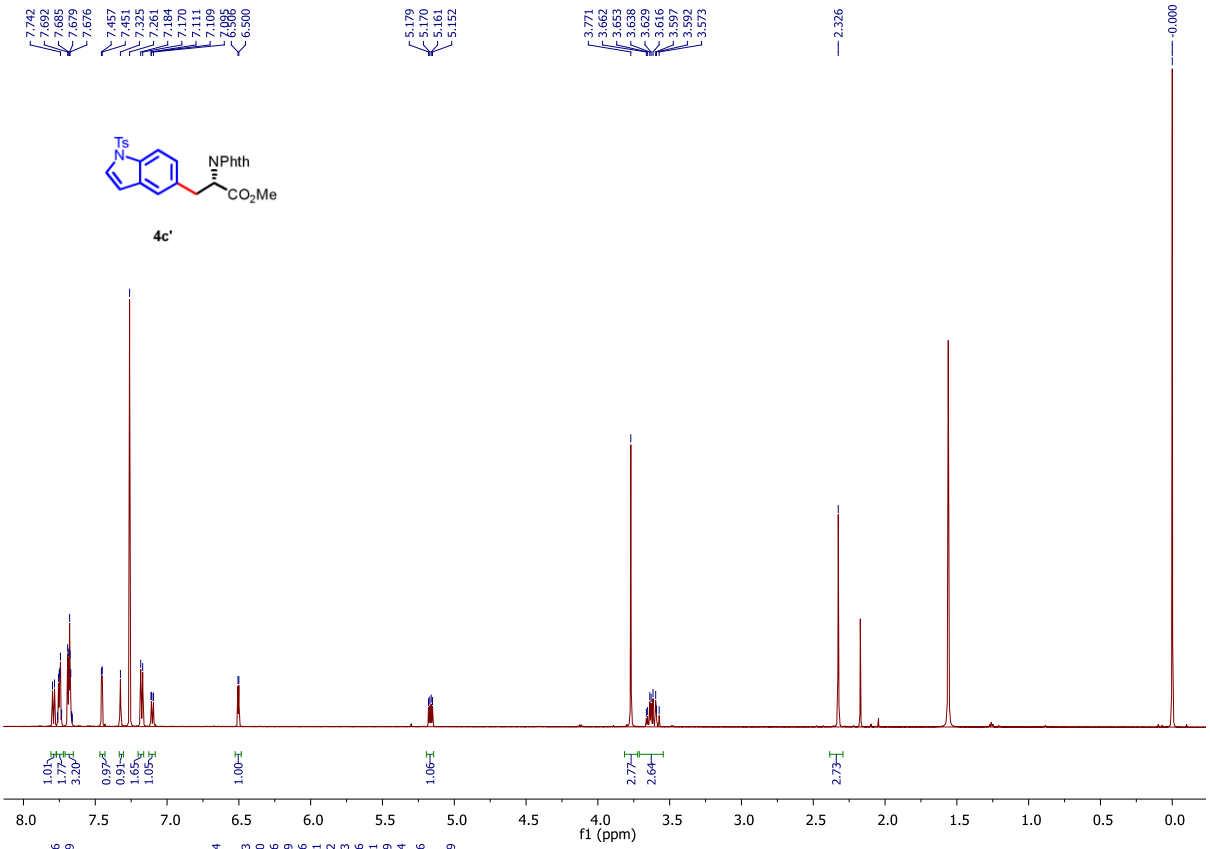
164.934
163.355
158.465
148.869
148.776
145.318
145.189
144.175
144.118
142.651
132.831
132.795
128.865
128.237
126.291
126.242
121.005
120.985
110.497
110.252
67.993
56.291
49.242
48.857
48.422
34.759
F
N
NHFmoc
CO2H
10
f1 (ppm)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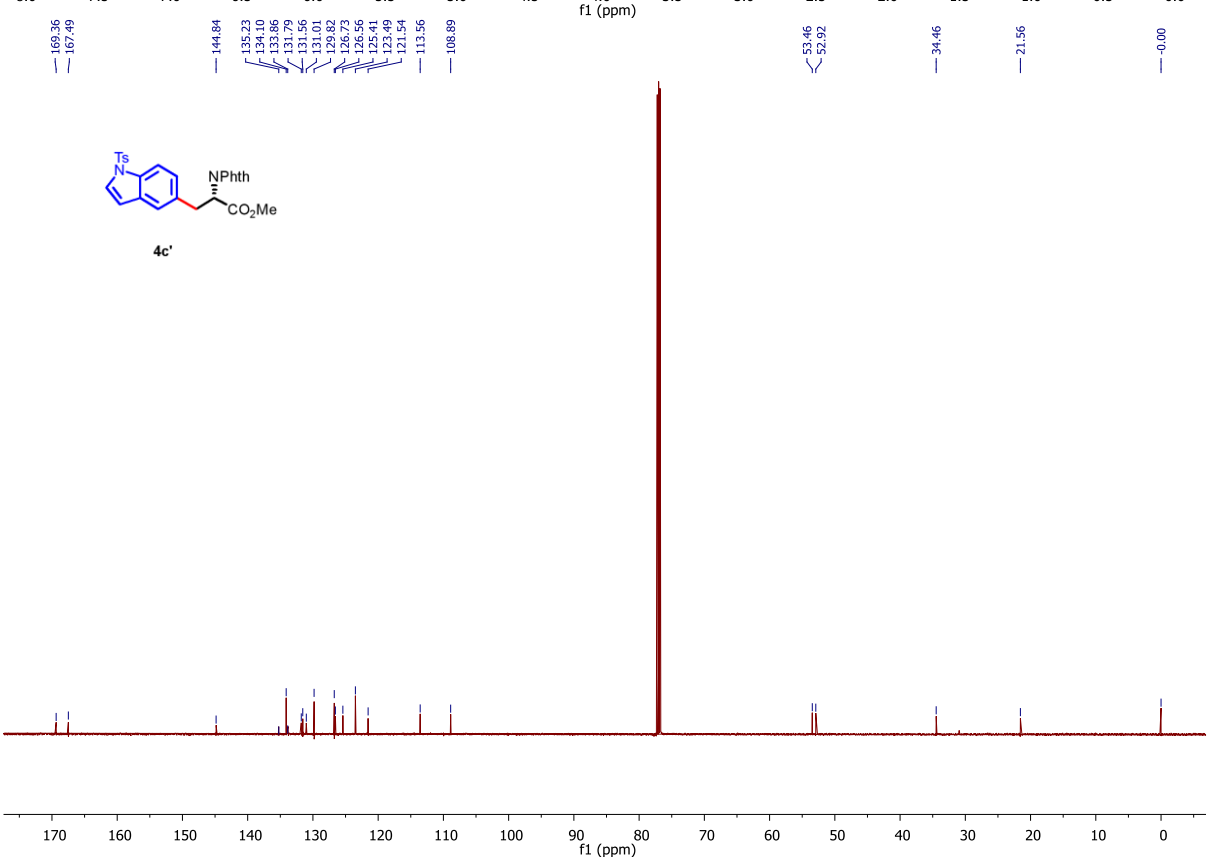
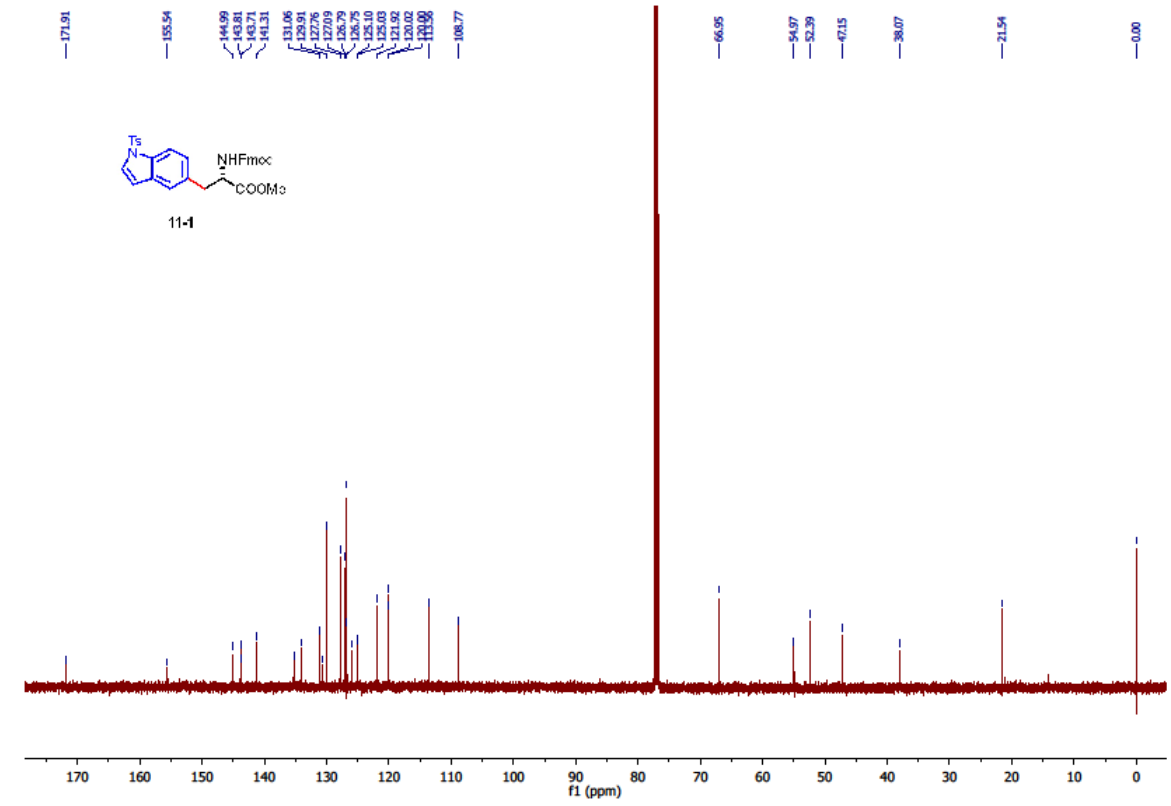
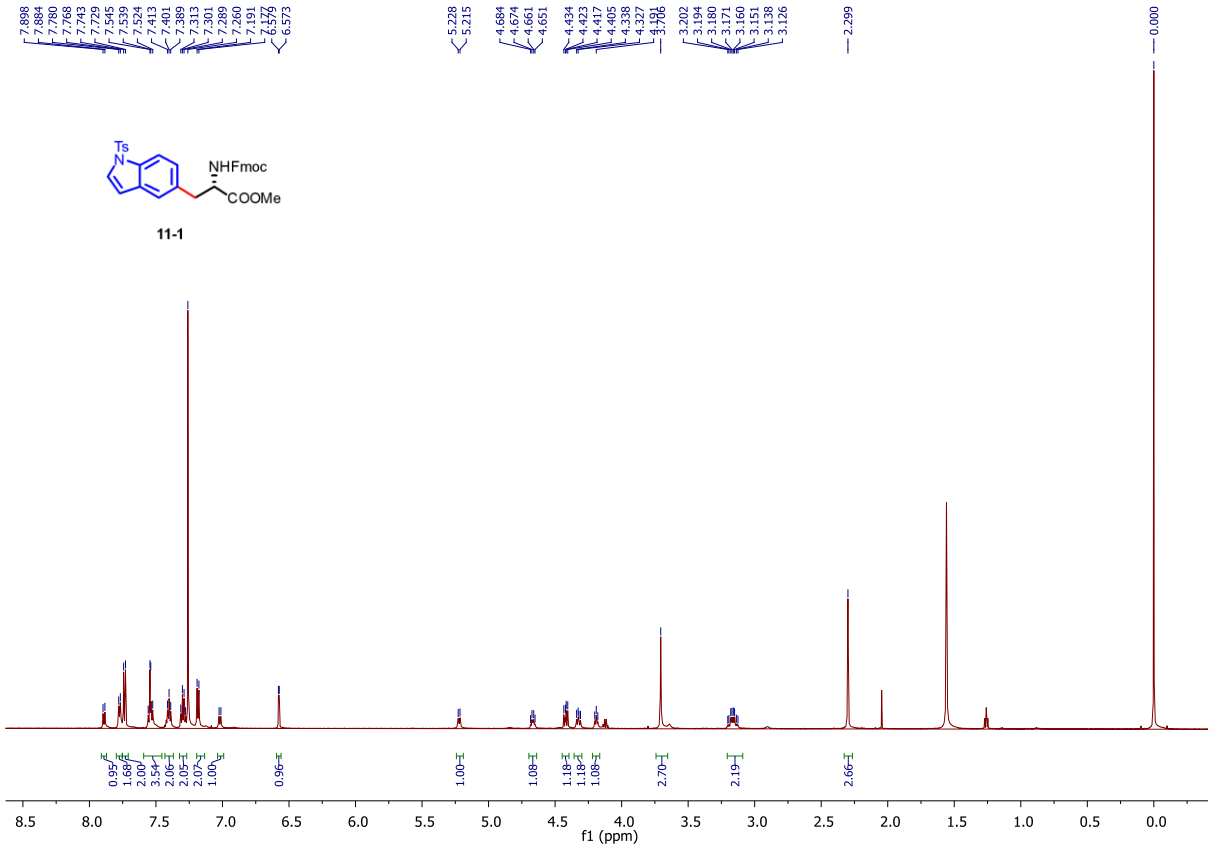
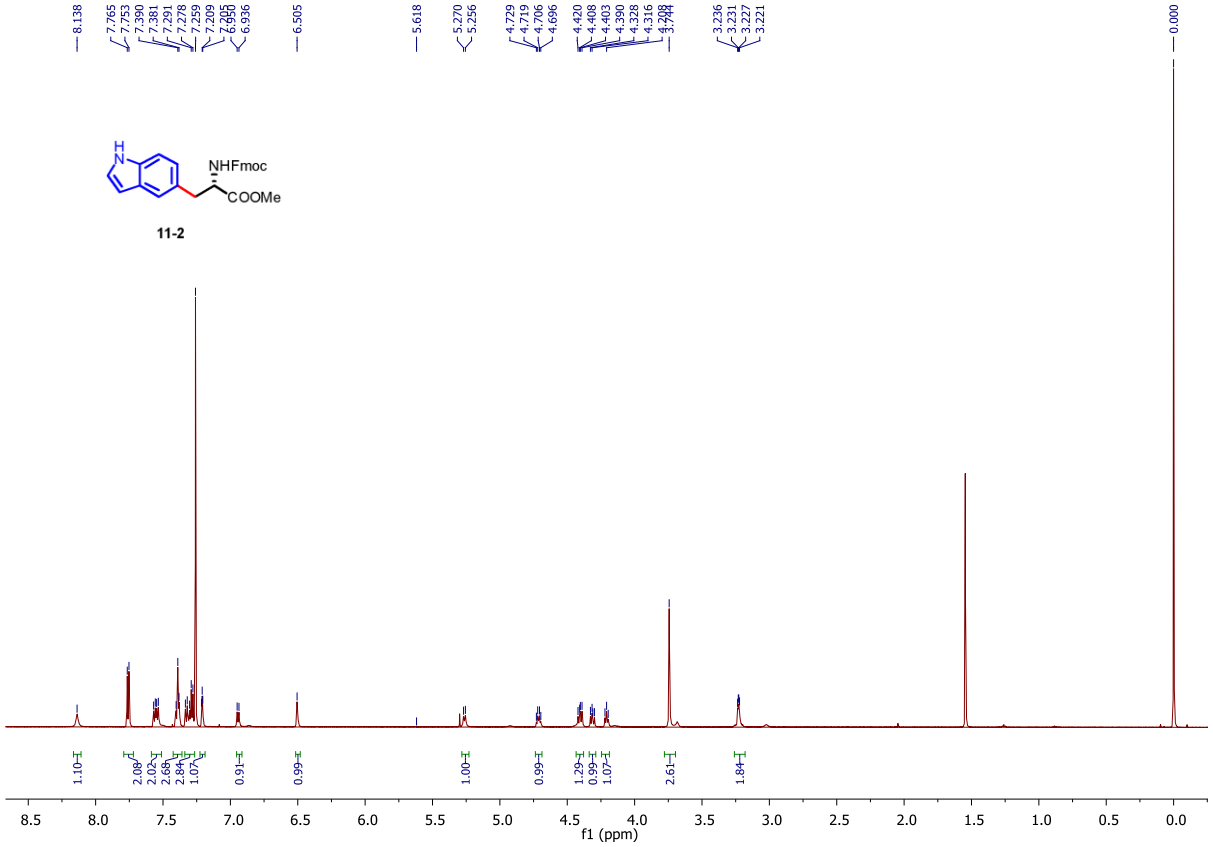
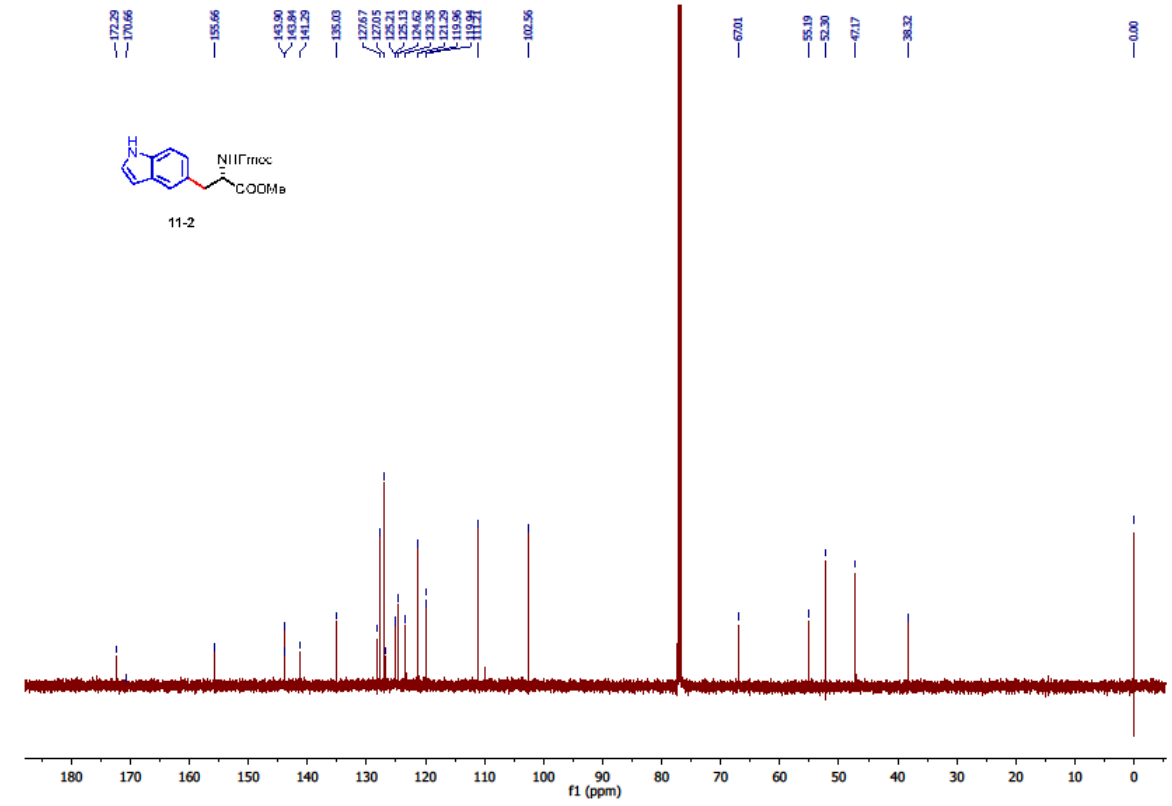
7.692
7.685
7.679
7.676
7.457
7.451
7.325
7.261
7.184
7.170
7.111
7.109
6.508
6.500
5.179
5.170
5.161
5.152
3.771
3.662
3.653
3.638
3.629
3.616
3.597
3.592
3.573
2.326
-0.000
Ts
N
NPhth
CO2Me
4c'
1.01
1.77
3.20
0.97
0.91
1.65
1.05
1.00
1.06
2.77
2.64
2.73
f1 (ppm)

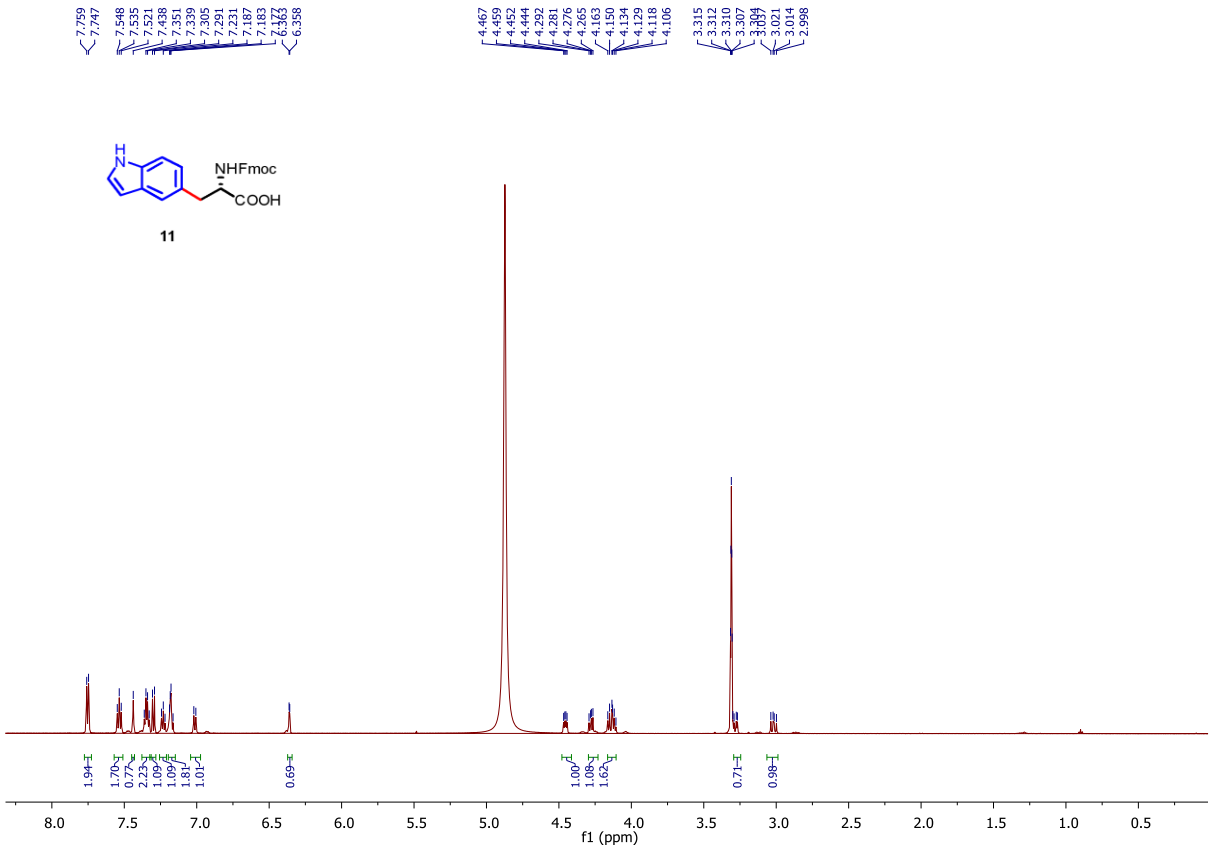

169.36
167.49
144.84
135.23
134.10
133.86
131.79
131.56
131.01
129.82
126.73
126.56
125.41
123.49
121.54
113.56
108.89
53.46
52.92
34.46
21.56
-0.00
Ts
N
NPhth
CO2Me
4c'
f1 (ppm)

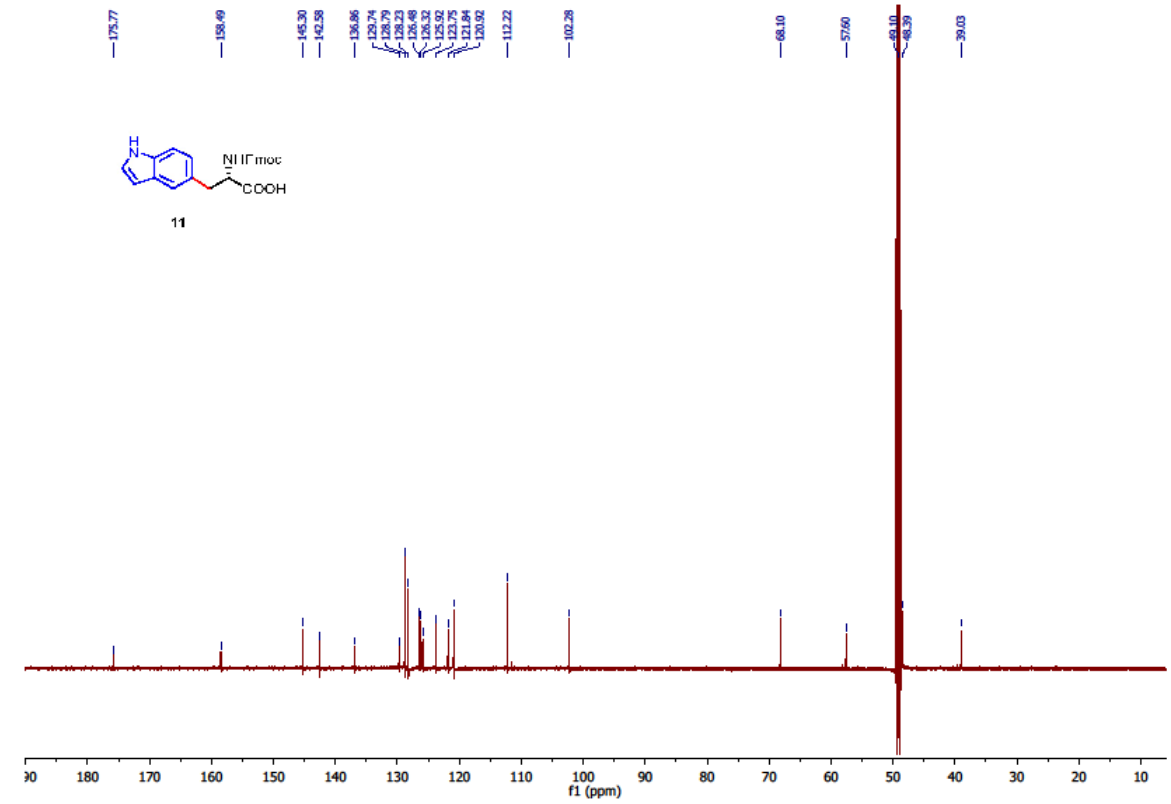

171.91
155.54
144.99
143.81
143.71
141.31
131.06
129.91
127.76
127.09
126.79
126.75
125.10
125.03
121.92
120.02
108.77
66.95
54.97
52.39
47.15
38.07
21.54
0.00
Ts
N
NHFmoc
COOMe
11-1
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

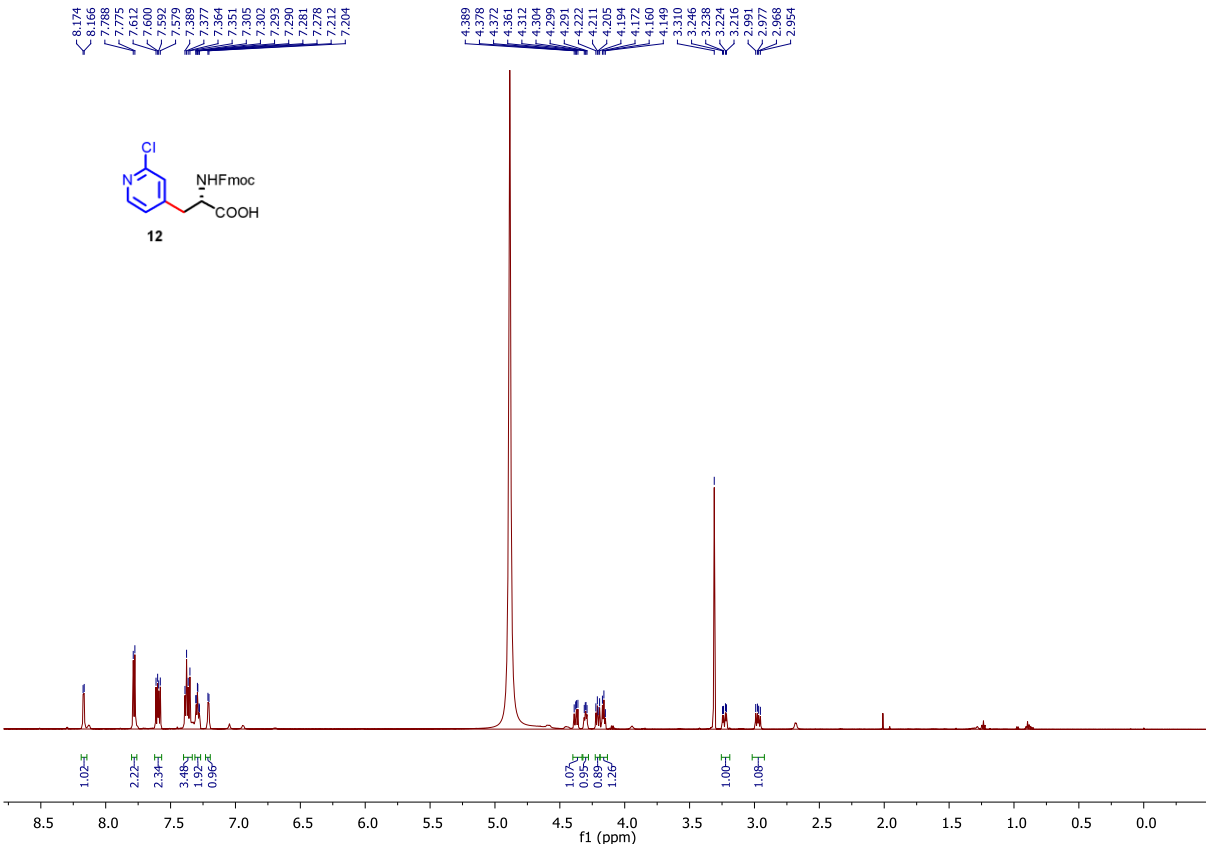

7.898
7.884
7.780
7.768
7.743
7.729
7.545
7.539
7.524
7.413
7.401
7.389
7.313
7.301
7.289
7.260
7.191
6.573
5.228
5.215
4.684
4.674
4.661
4.651
4.434
4.423
4.417
4.405
4.338
4.327
3.202
3.194
3.180
3.171
3.160
3.151
3.138
3.126
2.299
0.000
Ts
N
NHFmoc
COOMe
11-1
0.95
1.68
2.00
3.54
2.06
2.05
2.07
1.00
0.96
1.00
1.08
1.18
1.18
1.08
2.70
2.19
2.66
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

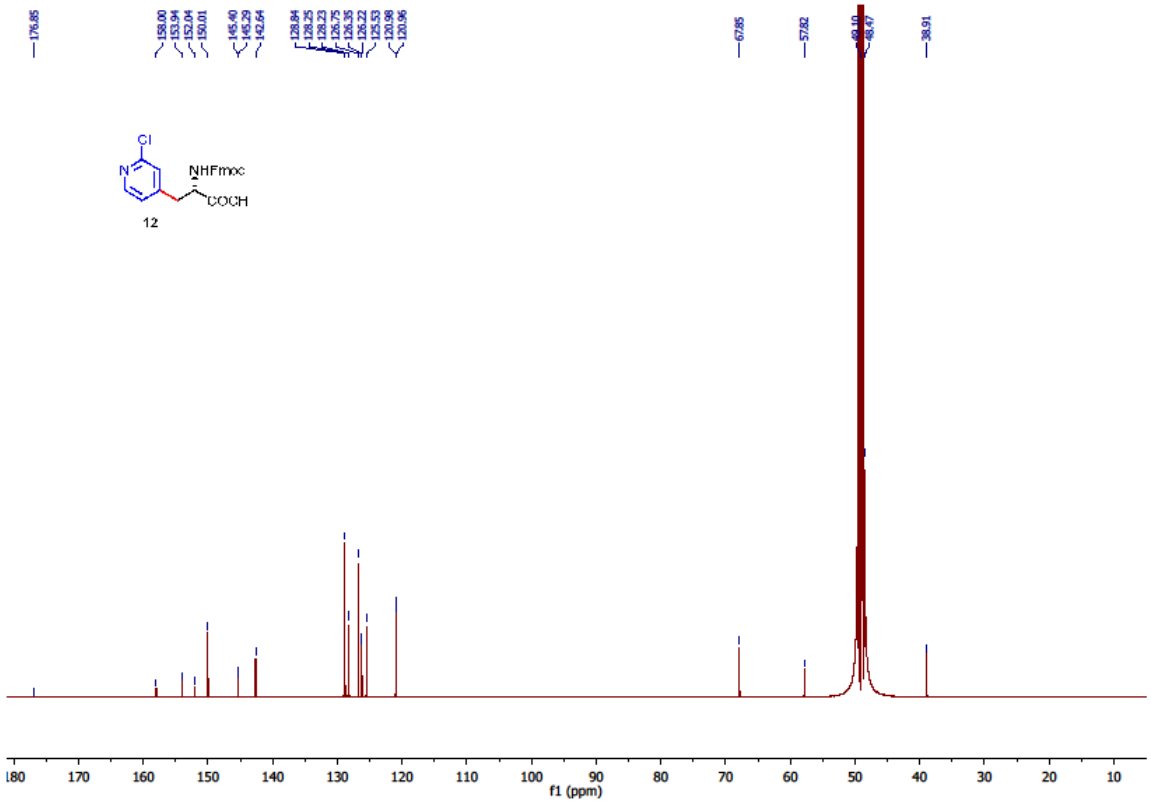

NHFmoc
COOMe
11-2
f1 (ppm)

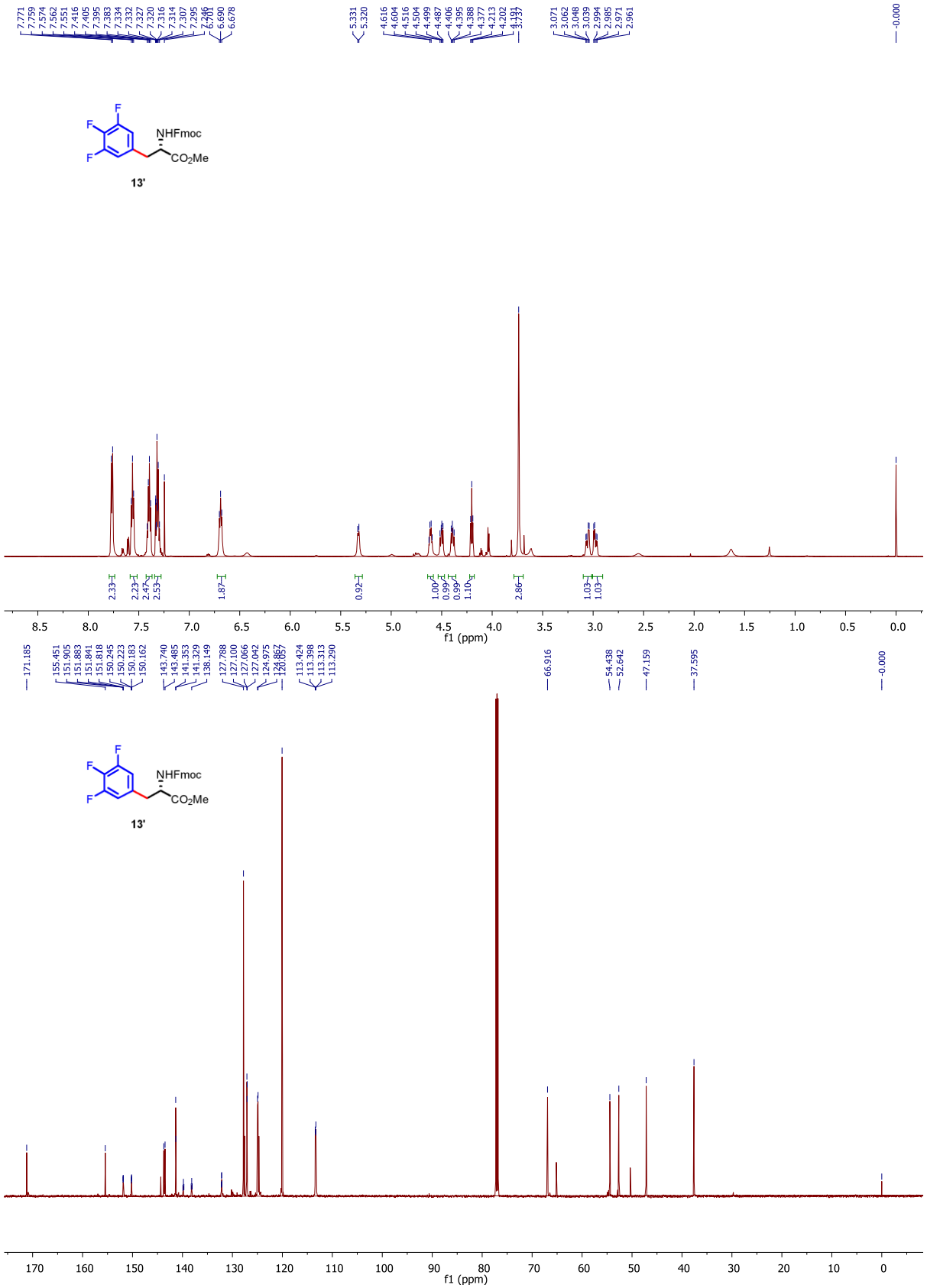

NHFmoc
COOMe
11-2
f1 (ppm)

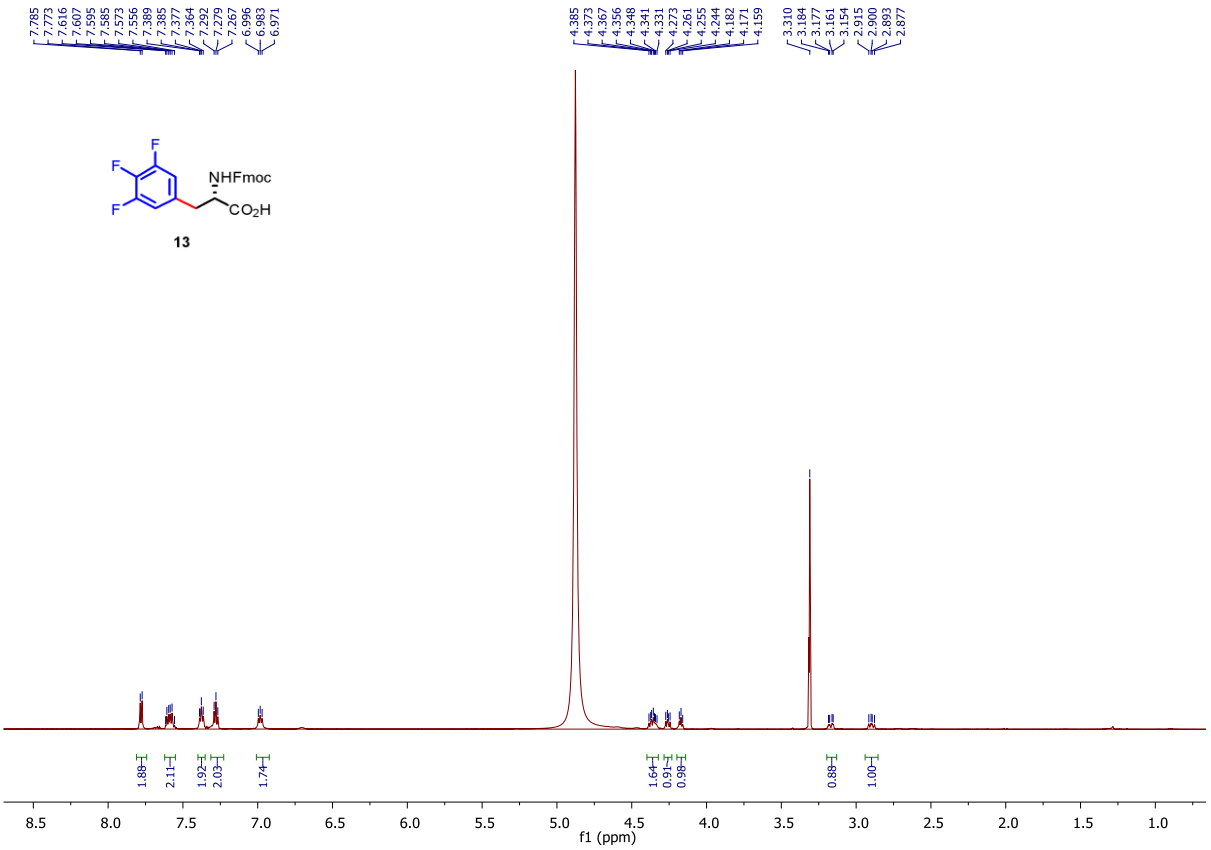

NHFmoc
COOH
11
f1 (ppm)

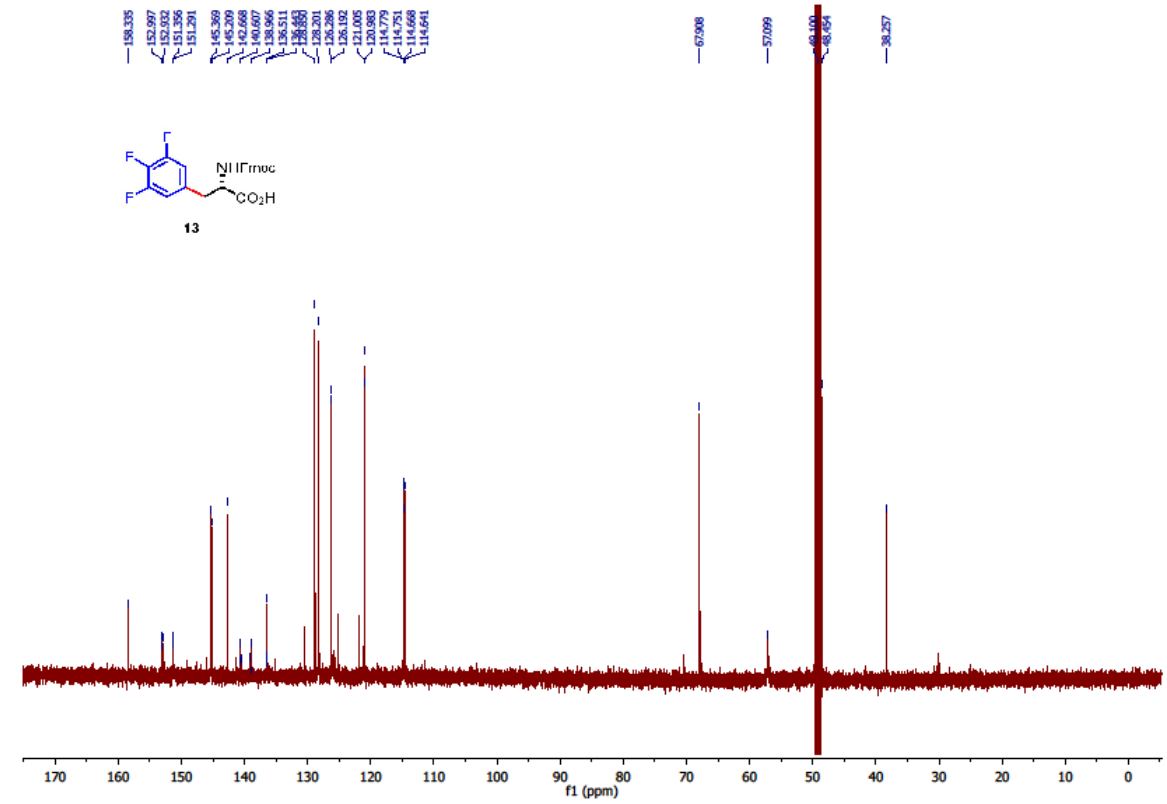

NHFmoc
COOH
11
f1 (ppm)

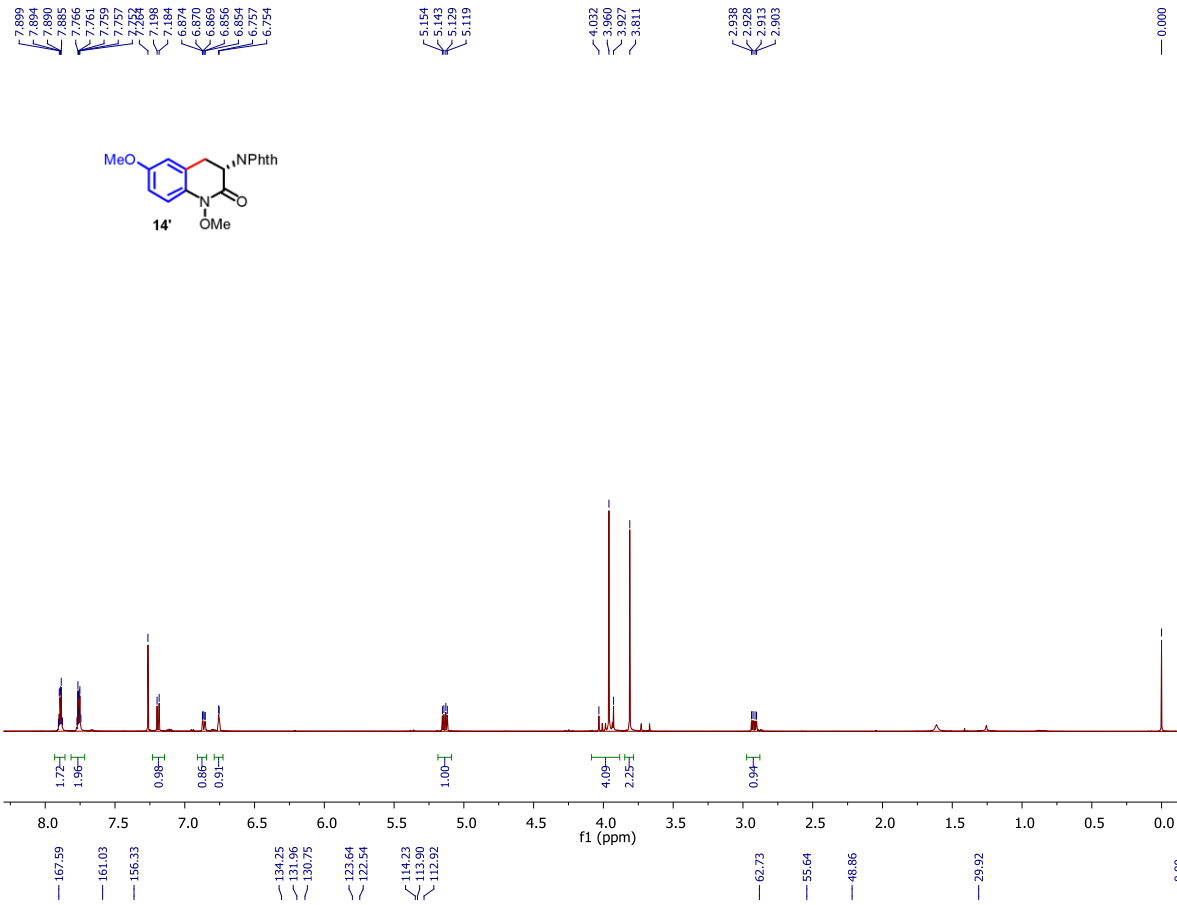

8.174
8.166
7.788
7.775
7.612
7.600
7.592
7.579
7.389
7.377
7.364
7.351
7.305
7.302
7.293
7.290
7.281
7.278
7.212
7.204
4.389
4.378
4.372
4.361
4.312
4.304
4.299
4.291
4.222
4.211
4.205
4.194
4.172
4.160
4.149
3.310
3.246
3.238
3.224
3.216
2.991
2.977
2.968
2.954
Cl
N
NHFmoc
COOH
12
1.02
2.22
2.34
3.48
1.92
0.96
1.07
0.95
0.89
1.26
1.00
1.08
f1 (ppm)

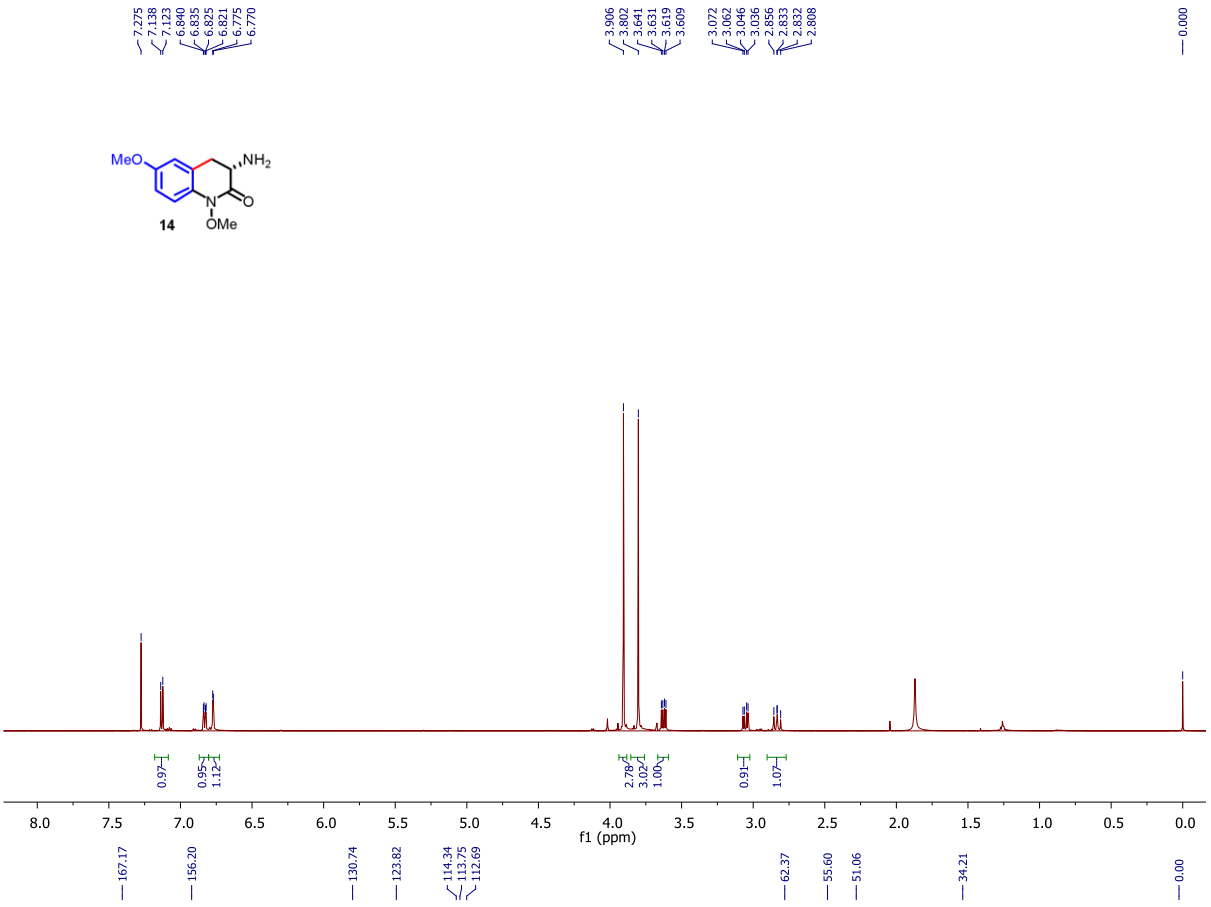

176.85
158.00
153.94
152.04
150.01
145.40
145.29
142.64
128.84
128.25
128.23
126.75
126.35
126.22
125.53
120.98
120.96
67.85
57.82
49.47
38.91
Cl
N
NHFmoc
COOH
12
f1 (ppm)

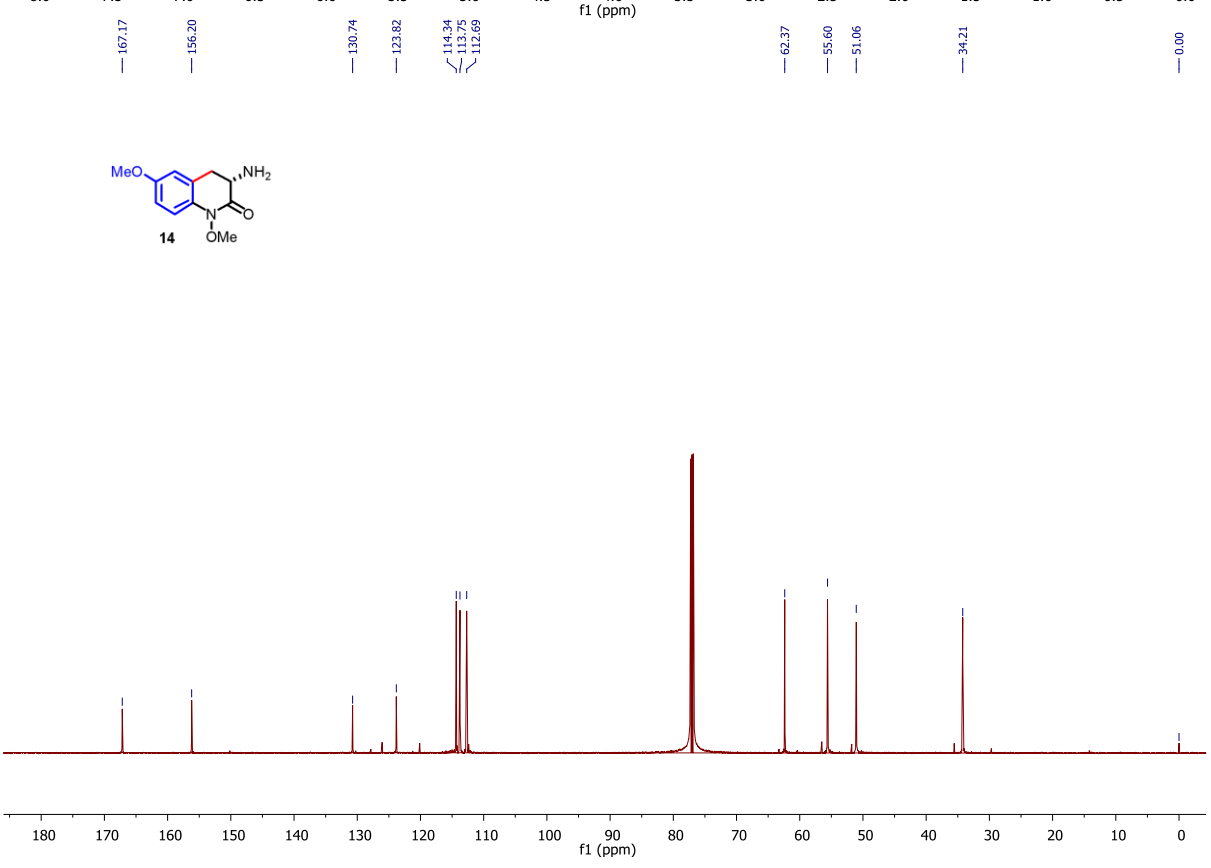

7.771
7.759
7.574
7.562
7.551
7.416
7.405
7.395
7.383
7.334
7.332
7.327
7.320
7.316
7.314
7.307
7.295
6.701
6.690
6.678
5.331
5.320
4.616
4.604
4.516
4.504
4.499
4.487
4.406
4.395
4.388
4.377
4.213
4.202
3.071
3.062
3.048
3.039
2.994
2.985
2.971
2.961
-0.000
F
F
F
NHFmoc
CO2Me
13'
2.33
2.23
2.47
2.53
1.87
0.92
1.00
0.99
0.99
1.10
2.86
1.03
1.03
f1 (ppm)
171.185
155.451
151.905
151.883
151.841
151.818
150.245
150.223
150.183
150.162
143.740
143.485
141.353
141.329
138.149
127.788
127.100
127.066
127.042
124.975
113.424
113.398
113.313
113.290
66.916
54.438
52.642
47.159
37.595
-0.000
f1 (ppm)

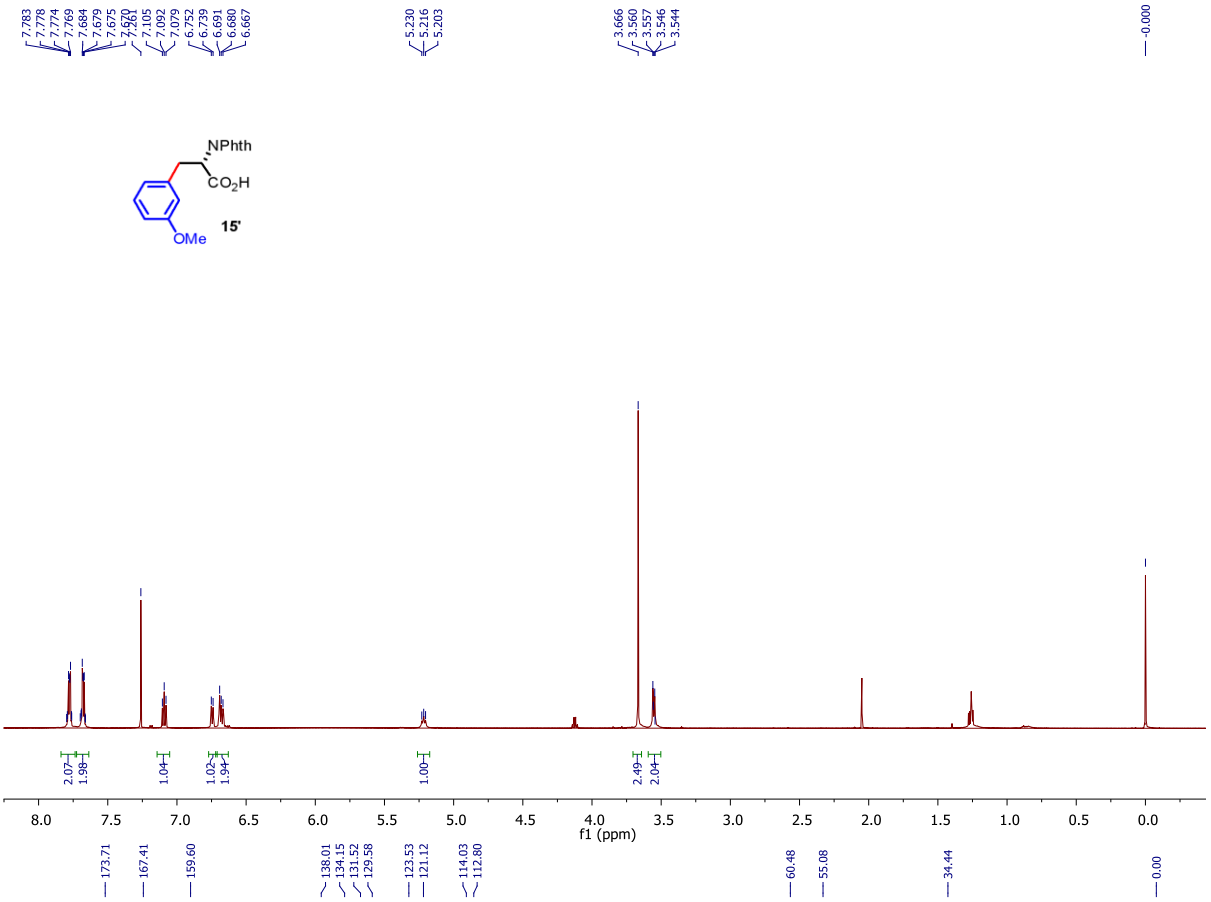

F
F
F
NHFmoc
CO2H
13
f1 (ppm)

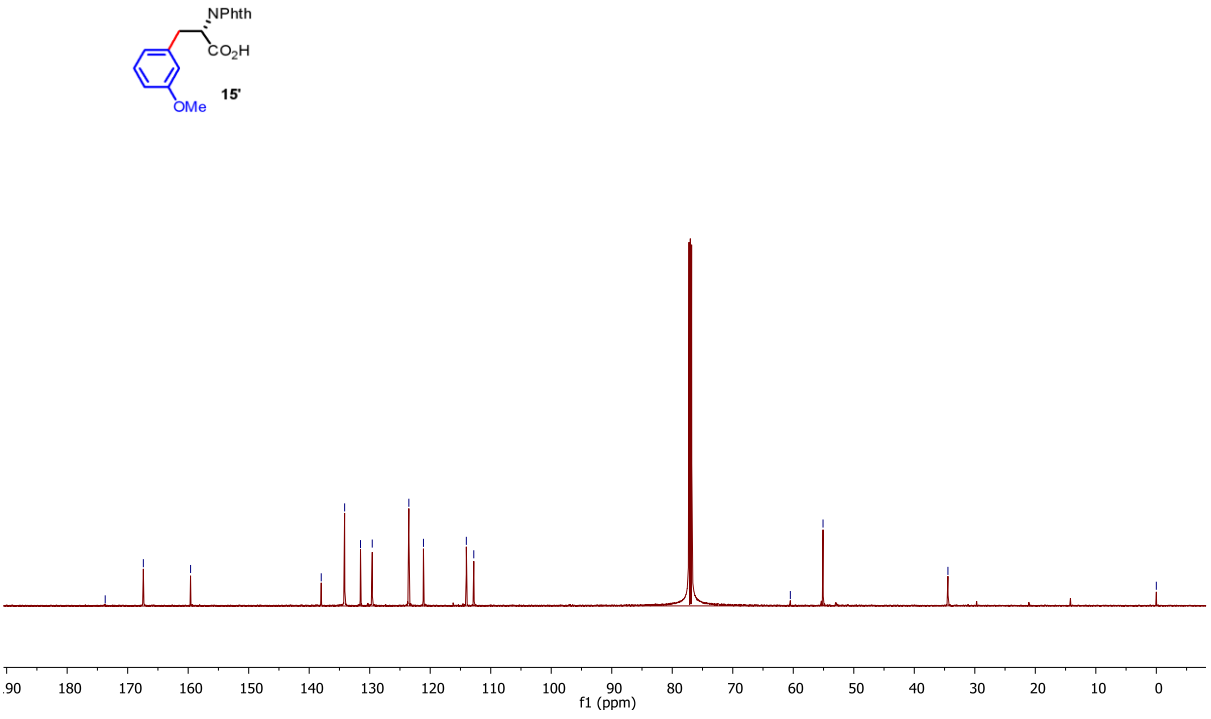

F
F
F
NHFmoc
CO2H
13
f1 (ppm)

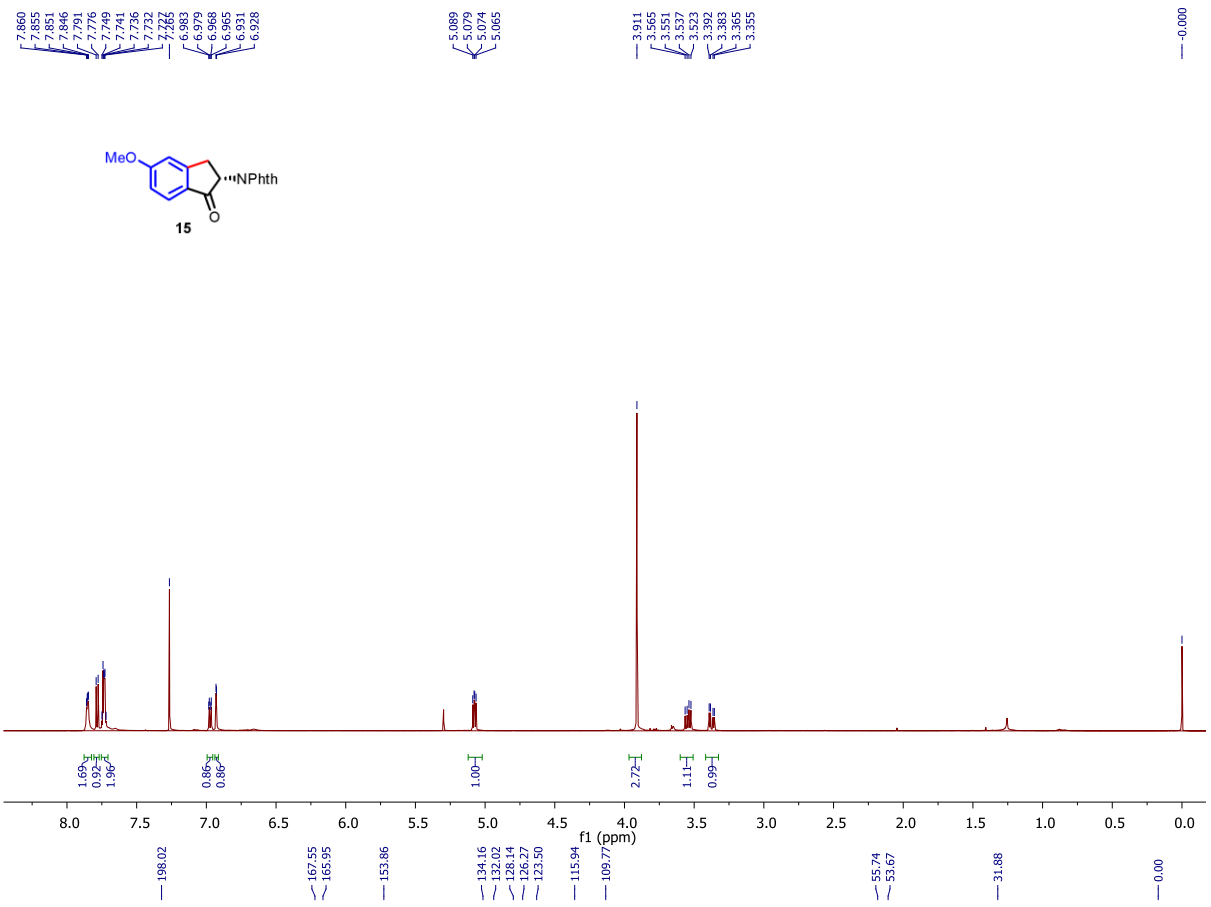

7.899
7.894
7.890
7.885
7.766
7.761
7.759
7.757
7.757
7.254
7.198
7.184
6.874
6.870
6.869
6.856
6.854
6.757
6.754
5.154
5.143
5.129
5.119
4.032
3.960
3.927
3.811
2.938
2.928
2.913
2.903
0.000
MeO
NPhth
N
O
OMe
14'
1.72
1.96
0.98
0.86
0.91
1.00
4.09
2.25
0.94
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
167.59
161.03
156.33
134.25
131.96
130.75
123.64
122.54
114.23
113.90
112.92
62.73
55.64
48.86
29.92
0.00
MeO
NPhth
N
O
OMe
14'
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

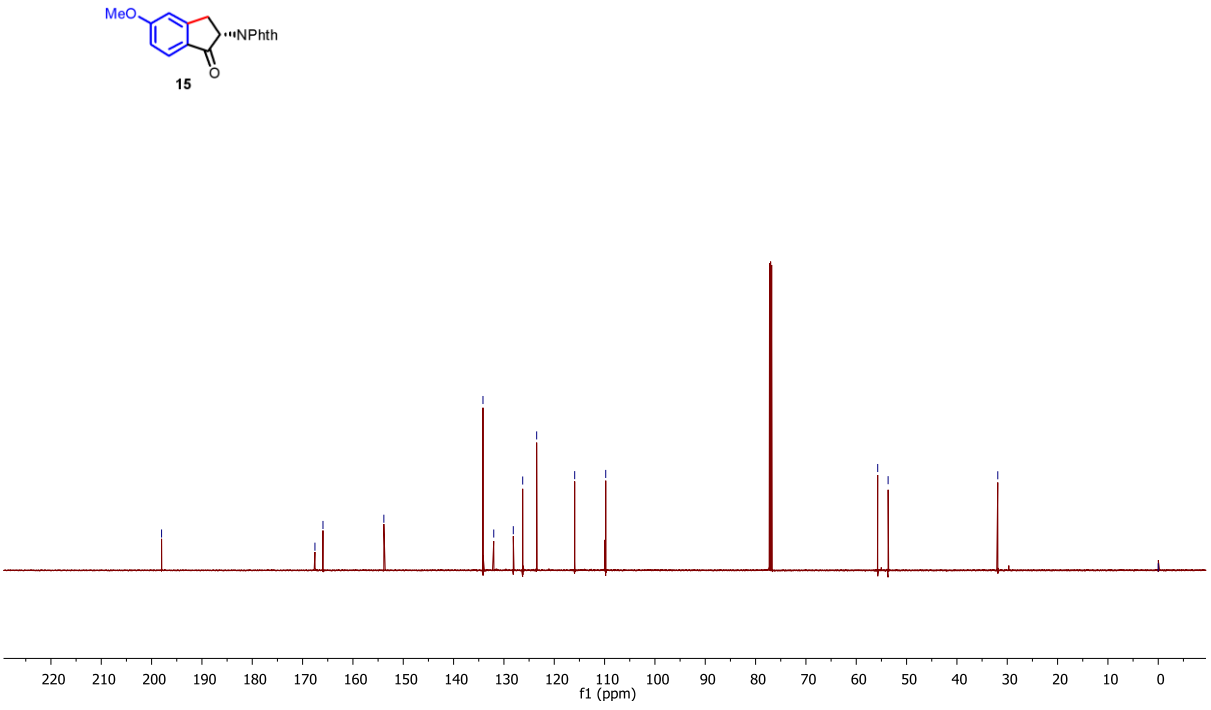

7.275
7.138
7.123
6.840
6.835
6.825
6.821
6.775
6.770
3.906
3.802
3.641
3.631
3.619
3.609
3.072
3.062
3.046
3.036
2.856
2.833
2.832
2.808
0.000
MeO
NH2
N
O
OMe
14
0.97
0.95
1.12
2.78
3.02
1.00
0.91
1.07
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

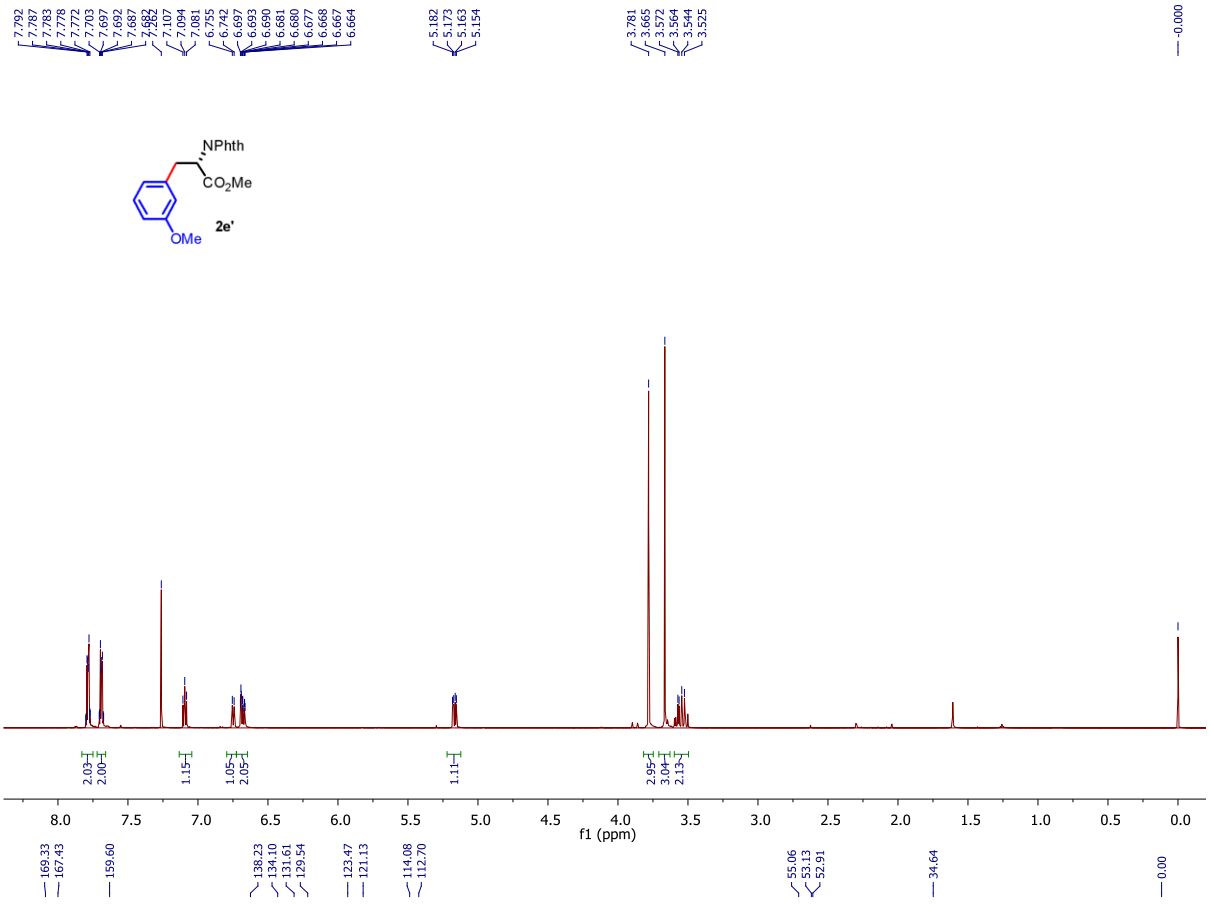

167.17
156.20
130.74
123.82
114.34
113.75
112.69
62.37
55.60
51.06
34.21
0.00
MeO
NH2
N
O
OMe
14
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

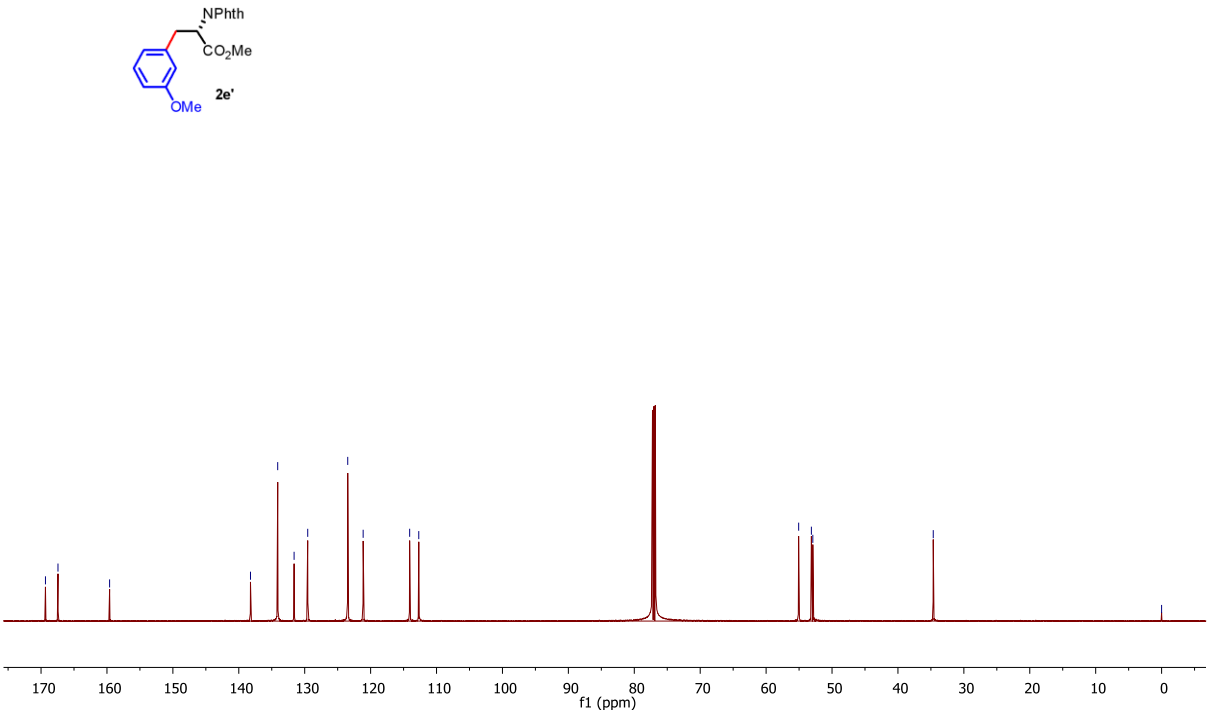

7.783
7.778
7.774
7.769
7.684
7.679
7.675
7.620
7.616
7.105
7.092
7.079
6.752
6.739
6.691
6.680
6.667
5.230
5.216
5.203
3.666
3.560
3.557
3.546
3.544
-0.000
NPhth
CO2H
OMe
15'
2.07
1.98
1.04
1.02
1.94
1.00
2.49
2.04
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

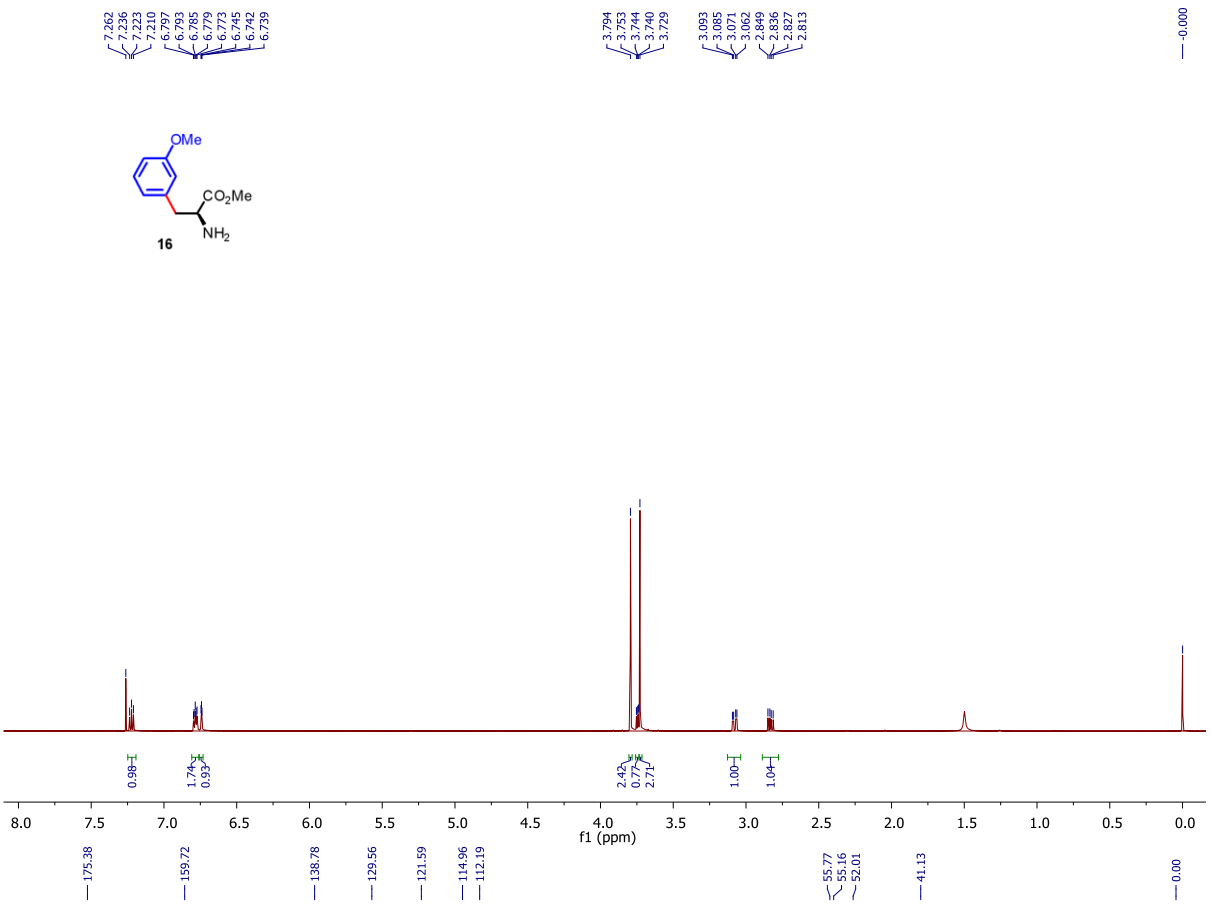

173.71
167.41
159.60
138.01
134.15
131.52
129.58
123.53
121.12
114.03
112.80
60.48
55.08
34.44
0.00
NPhth
CO2H
OMe
15'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

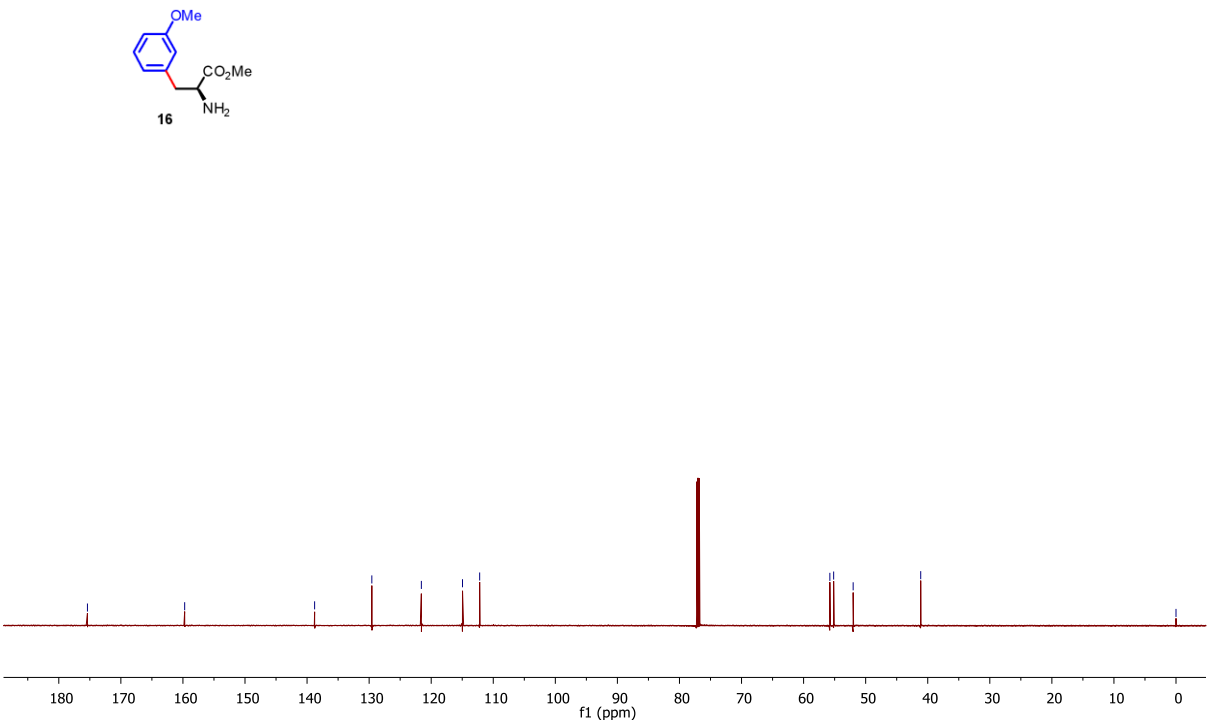

7.860
7.855
7.851
7.846
7.791
7.776
7.749
7.741
7.736
7.732
7.265
6.983
6.979
6.968
6.965
6.931
6.928
5.089
5.079
5.074
5.065
3.911
3.565
3.551
3.537
3.523
3.392
3.383
3.365
3.355
-0.000
MeO
NPhth
O
15
1.69
0.92
1.96
0.86
0.86
1.00
2.72
1.11
0.99
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
198.02
167.55
165.95
153.86
134.16
132.02
128.14
126.27
123.50
115.94
109.77
55.74
53.67
31.88
0.00

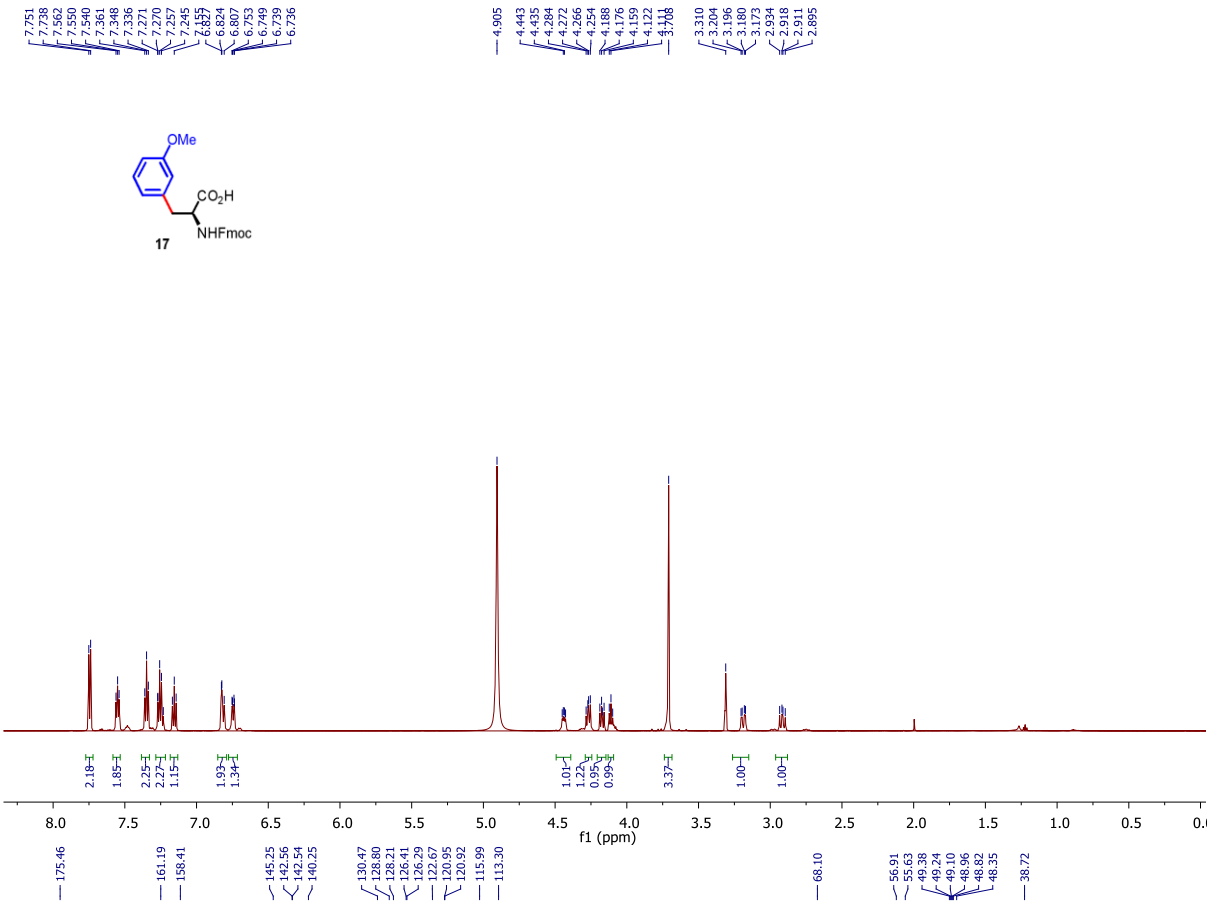

MeO
NPhth
O
15
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

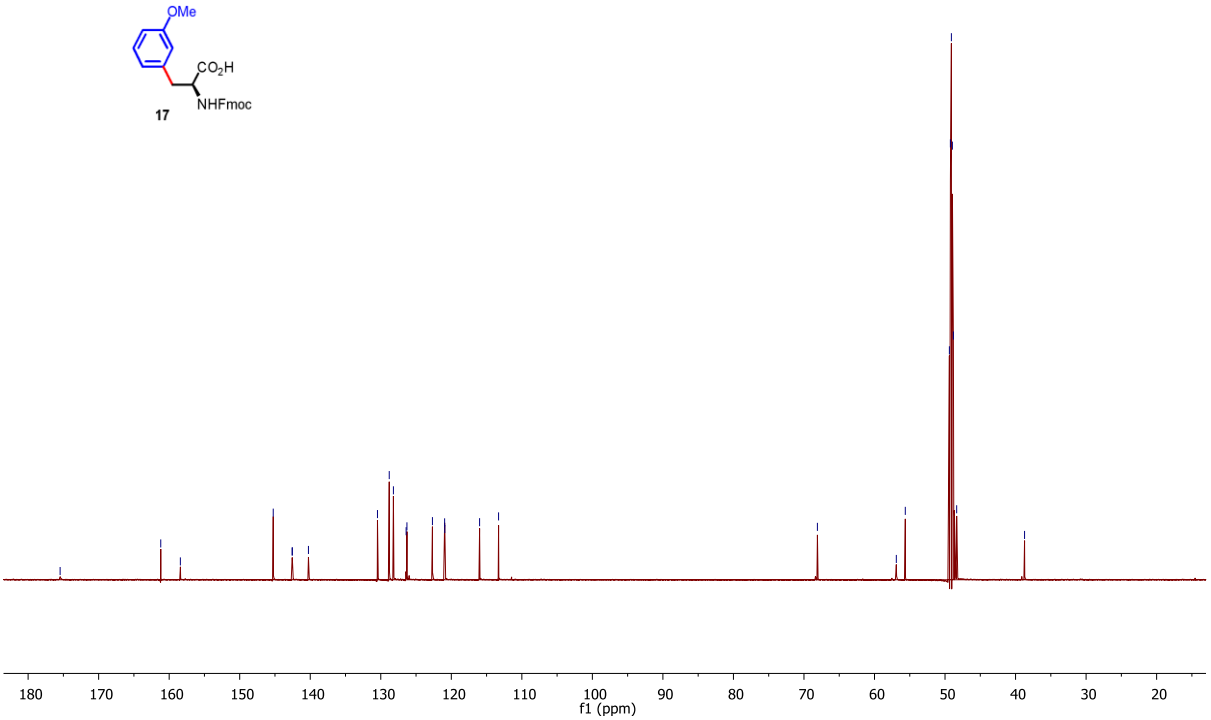

7.792
7.787
7.783
7.778
7.772
7.703
7.697
7.692
7.687
7.682
7.107
7.094
7.081
6.755
6.742
6.697
6.693
6.690
6.681
6.680
6.677
6.668
6.667
6.664
5.182
5.173
5.163
5.154
3.781
3.665
3.572
3.564
3.544
3.525
-0.000
NPhth
CO2Me
OMe
2e'
2.03
2.00
1.15
1.05
2.05
1.11
2.95
3.04
2.13
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
169.33
167.43
159.60
138.23
134.10
131.61
129.54
123.47
121.13
114.08
112.70
55.06
53.13
52.91
34.64
0.00

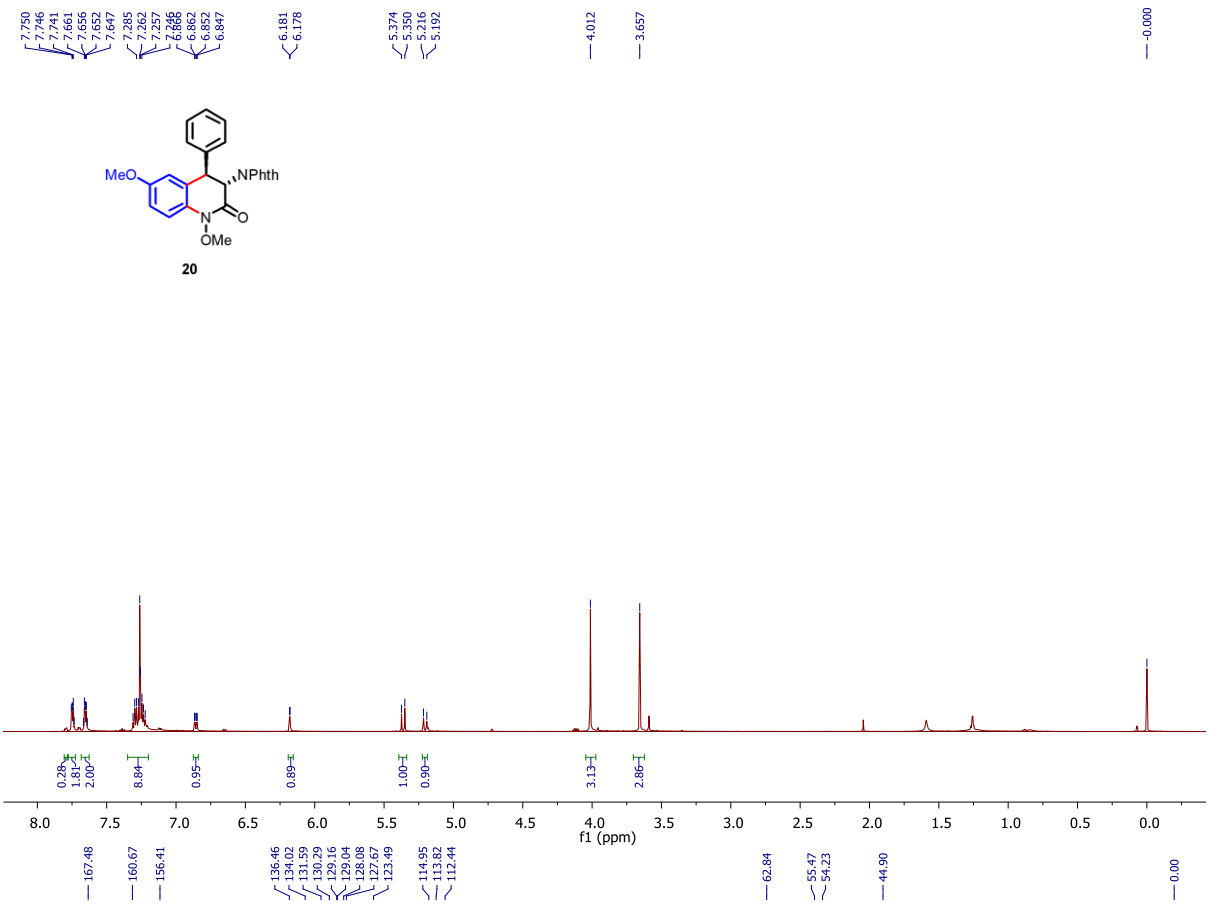

NPhth
CO2Me
OMe
2e'
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

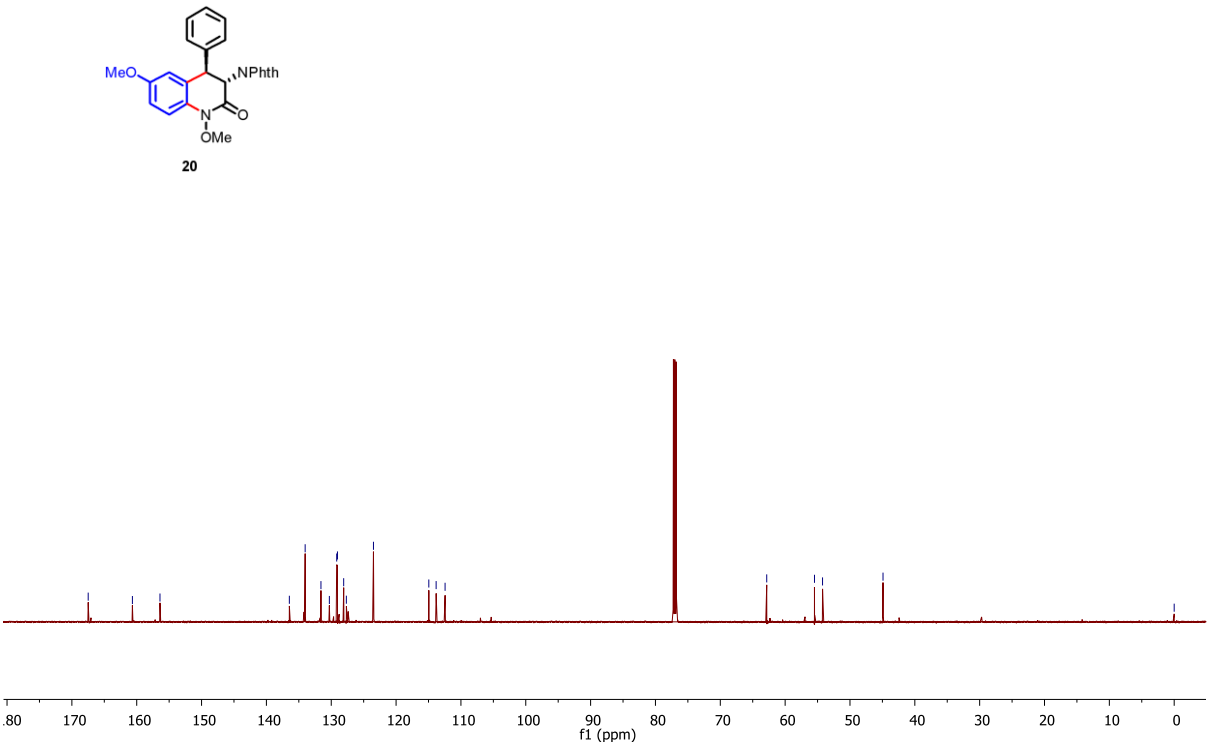

7.262
7.236
7.223
7.210
6.797
6.793
6.785
6.779
6.773
6.745
6.742
6.739
3.794
3.753
3.744
3.740
3.729
3.093
3.085
3.071
3.062
2.849
2.836
2.827
2.813
-0.000
OMe
CO2Me
NH2
16
0.98
1.74
0.93
2.42
0.75
2.71
1.00
1.04
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
175.38
159.72
138.78
129.56
121.59
114.96
112.19
55.77
55.16
52.01
41.13
0.00

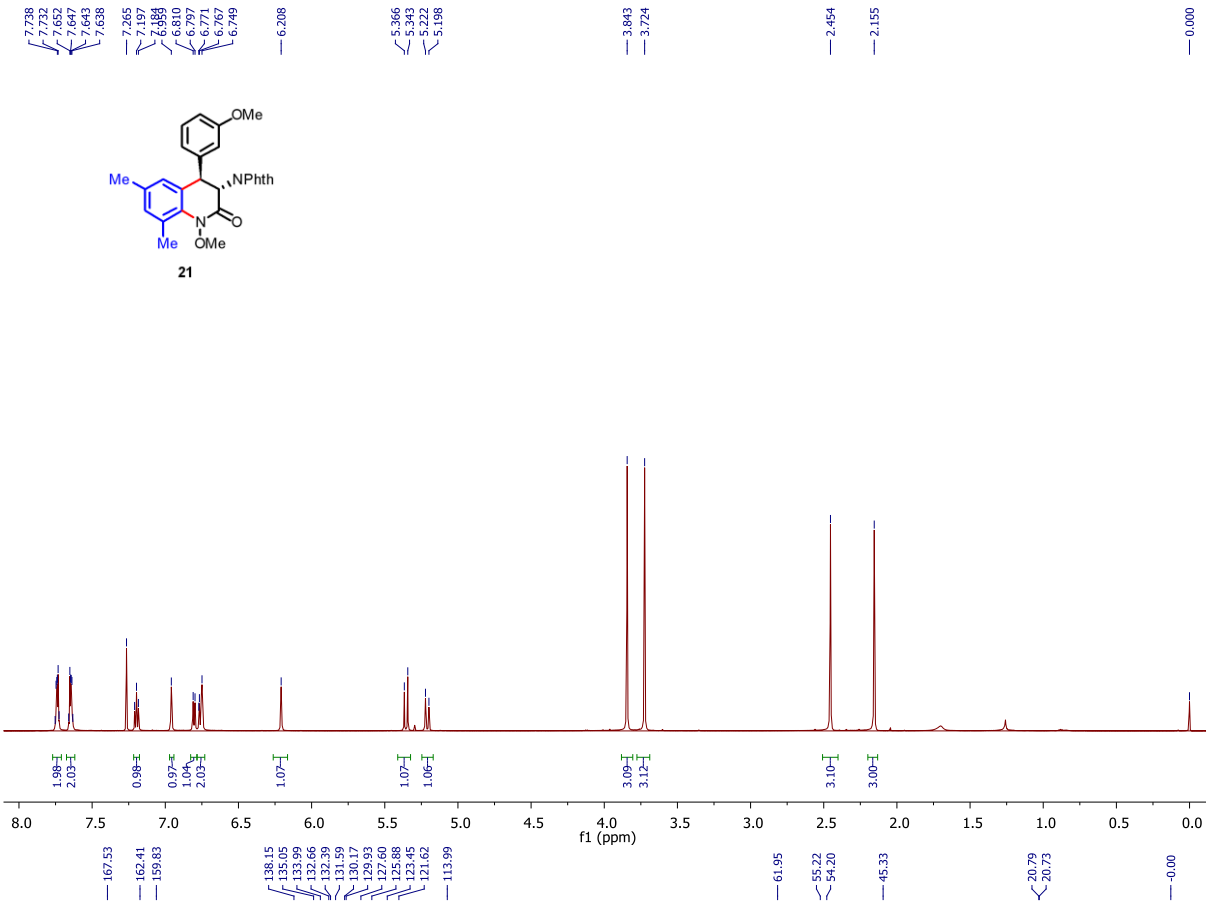

OMe
CO2Me
NH2
16
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

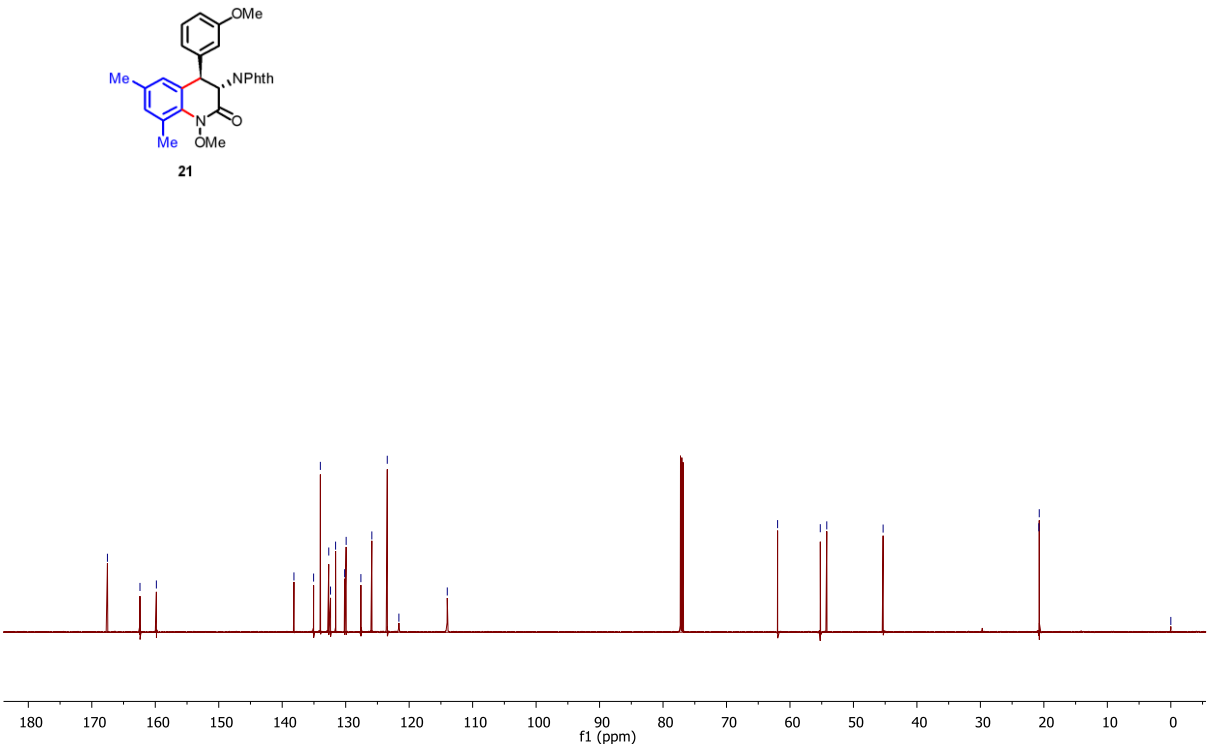

7.751
7.738
7.562
7.550
7.540
7.361
7.348
7.336
7.271
7.270
7.257
7.245
7.155
6.827
6.824
6.807
6.753
6.749
6.739
6.736
4.905
4.443
4.435
4.284
4.272
4.266
4.254
4.188
4.176
4.159
4.122
4.111
3.708
3.310
3.204
3.196
3.180
3.173
2.934
2.918
2.911
2.895
OMe
CO2H
NHFmoc
17
2.18
1.85
2.25
2.27
1.15
1.93
1.34
1.01
1.22
0.95
0.99
3.37
1.00
1.00
f1 (ppm)
175.46
161.19
158.41
145.25
142.56
142.54
140.25
130.47
128.80
128.21
126.41
126.29
122.67
120.95
120.92
115.99
113.30
68.10
56.91
55.63
49.38
49.24
49.10
48.96
48.82
48.35
38.72

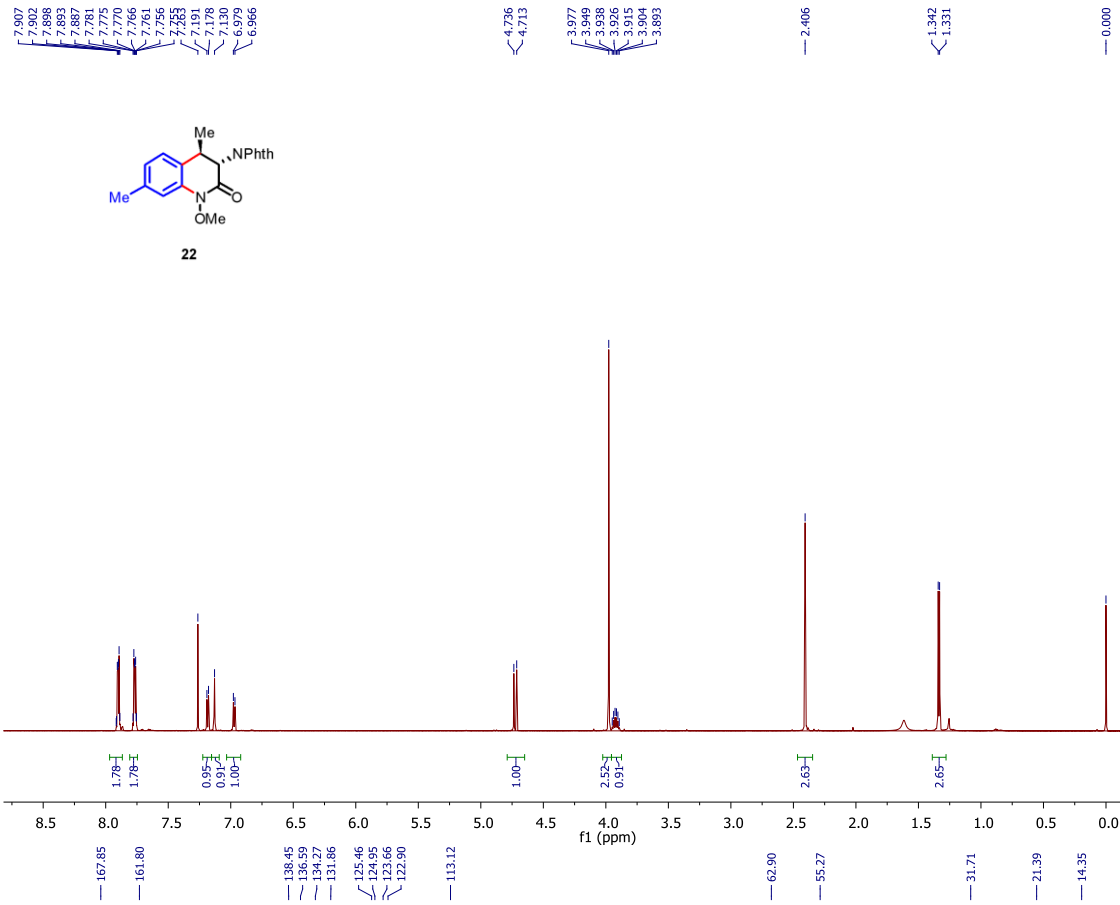

OMe
CO2H
NHFmoc
17
f1 (ppm)

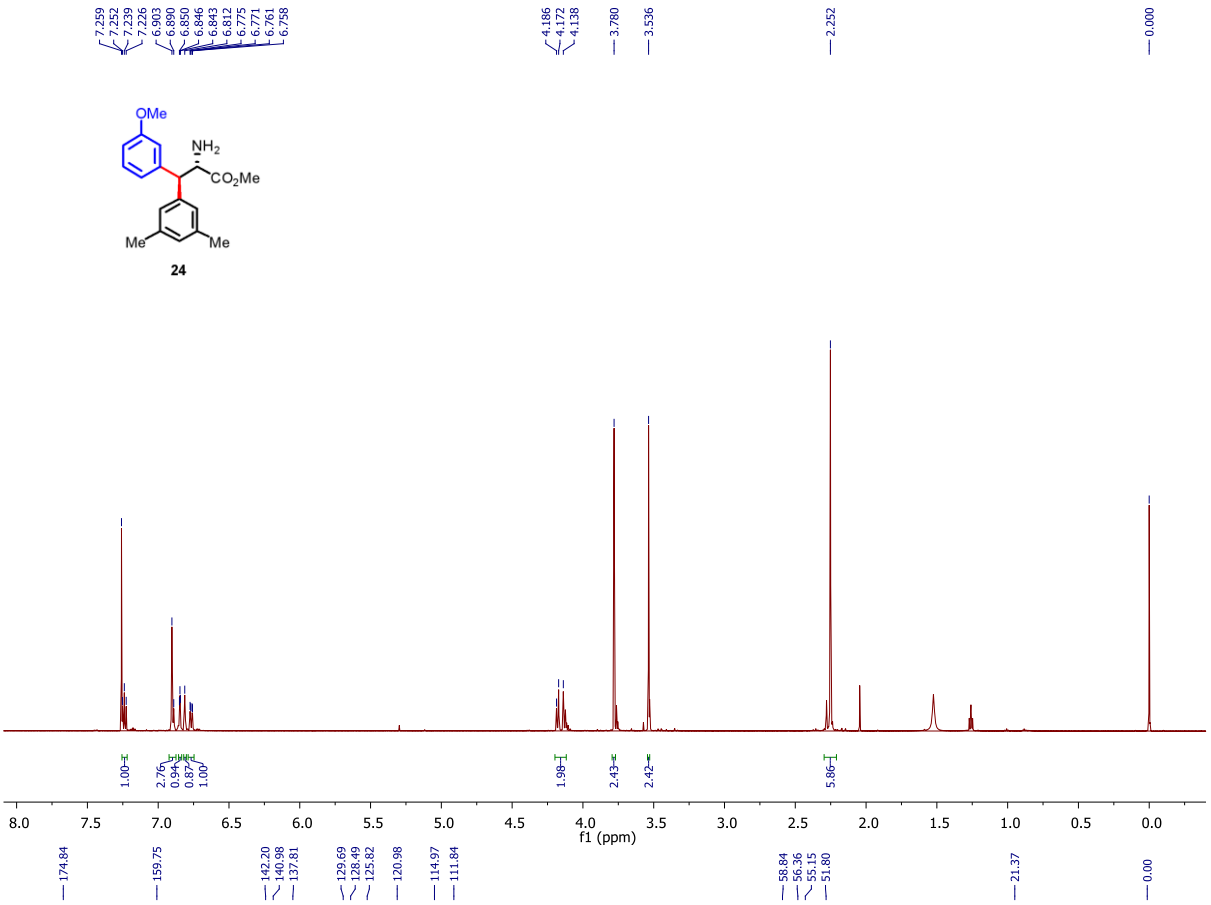

7.750
7.746
7.741
7.661
7.656
7.652
7.647
7.285
7.262
7.257
6.862
6.852
6.847
6.181
6.178
5.374
5.350
5.216
5.192
4.012
3.657
-0.000
MeO
NPhth
N
O
OMe
20
0.28
1.81
2.00
8.84
0.95
0.89
1.00
0.90
3.13
2.86
f1 (ppm)
167.48
160.67
156.41
136.46
134.02
131.59
130.29
129.16
129.04
128.08
127.67
123.49
114.95
113.82
112.44
62.84
55.47
54.23
44.90
0.00

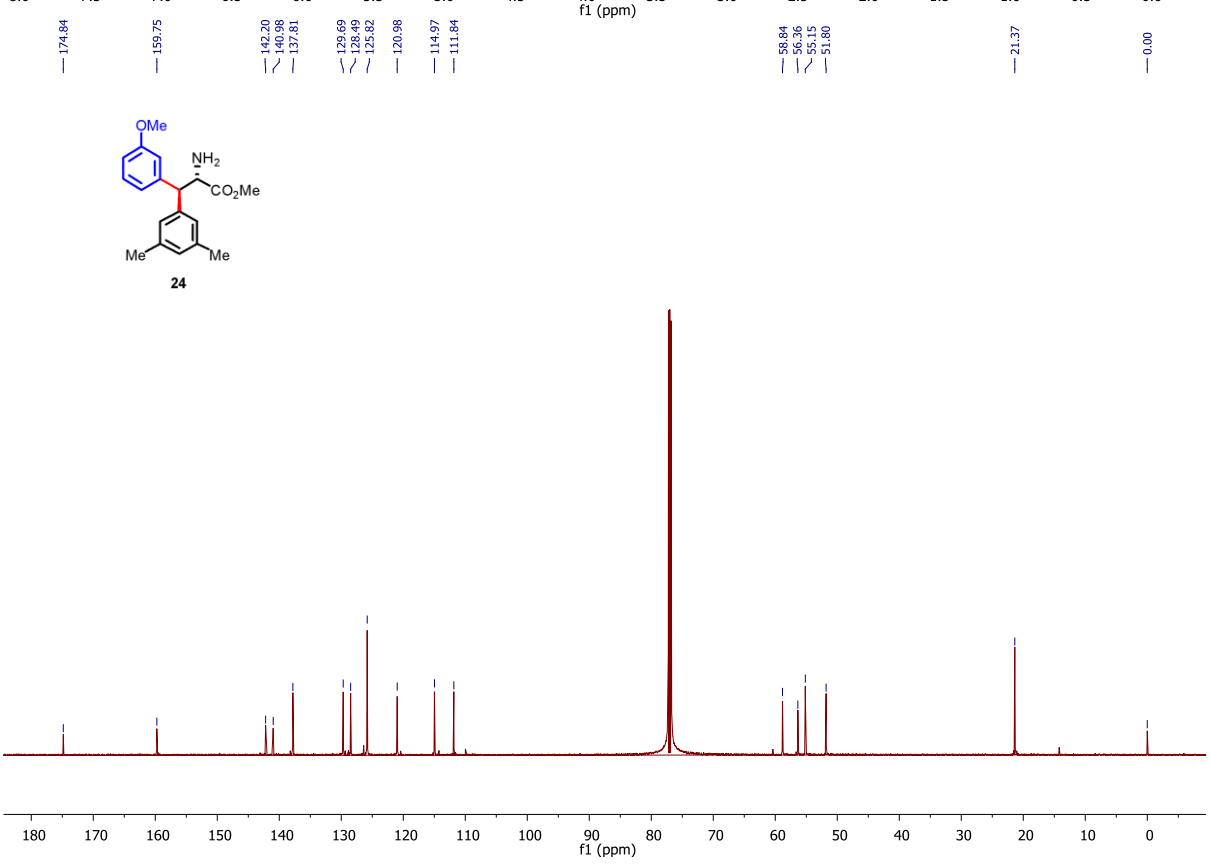

MeO
NPhth
N
O
OMe
20
f1 (ppm)

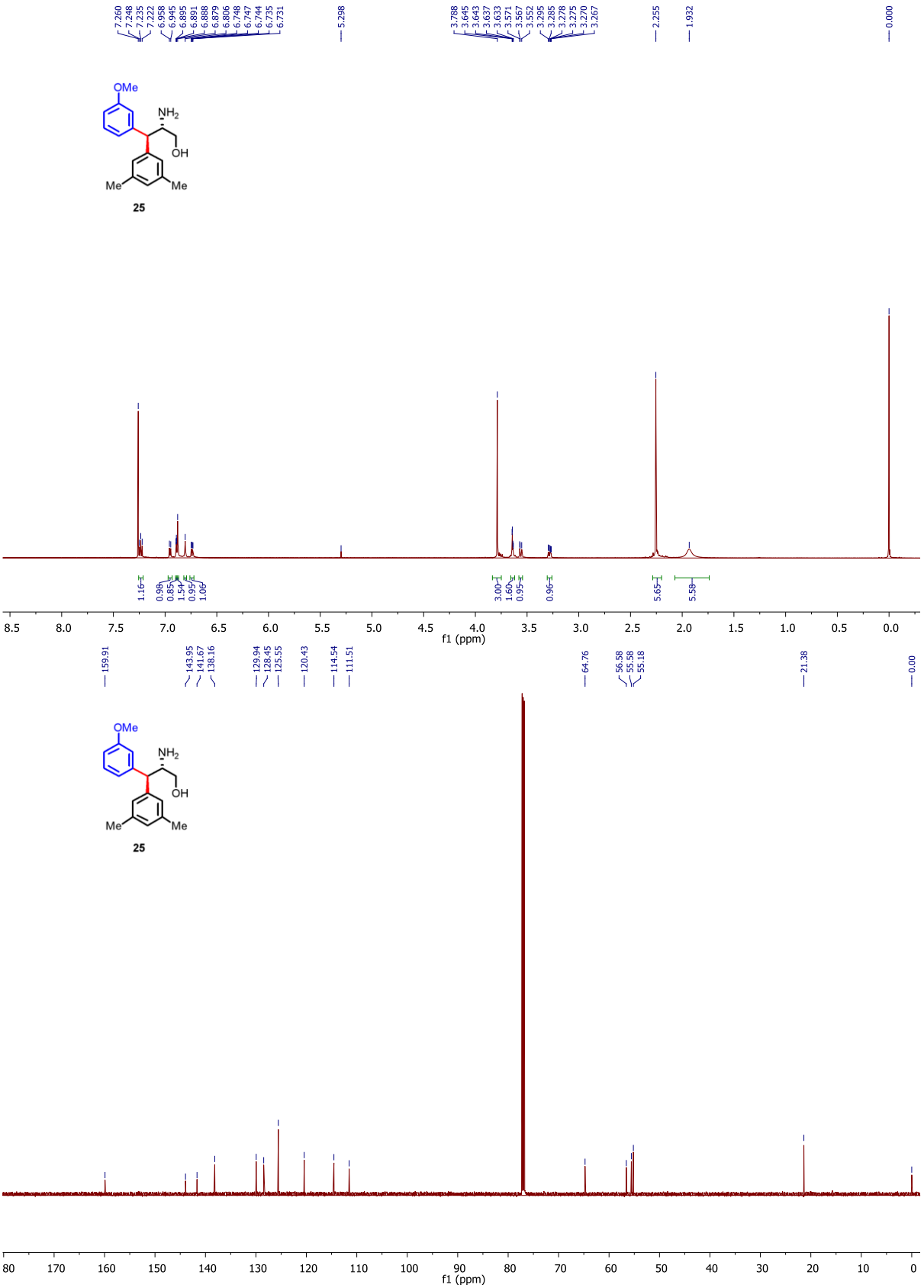

7.738
7.732
7.652
7.647
7.643
7.638
7.265
7.197
6.955
6.810
6.797
6.771
6.767
6.749
6.208
5.366
5.343
5.222
5.198
3.843
3.724
2.454
2.155
0.000
OMe
NPhth
Me
Me
N
O
OMe
21
1.98
2.03
0.98
0.97
1.04
2.03
1.07
1.07
1.06
3.09
3.12
3.10
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

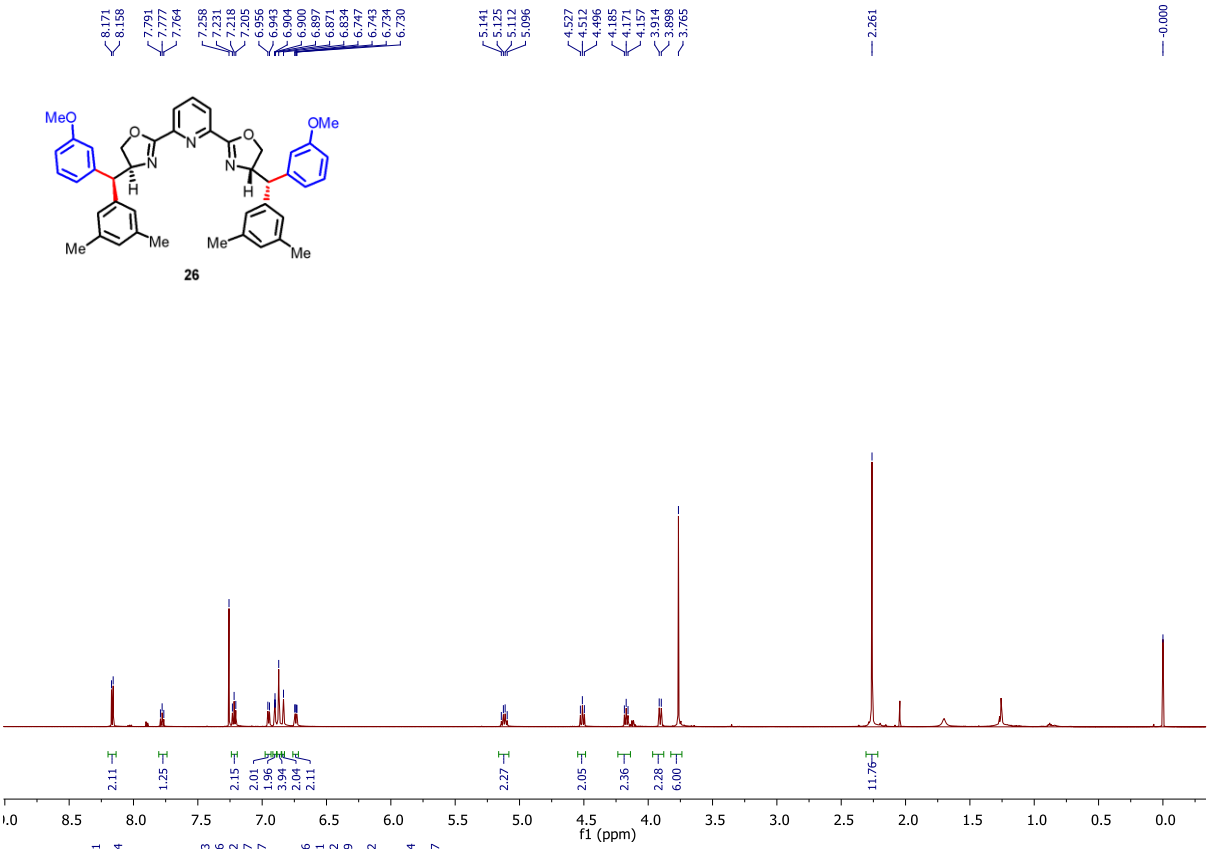

167.53
162.41
159.83
138.15
135.05
133.99
132.66
132.39
131.59
130.17
129.93
127.60
125.88
123.45
121.62
113.99
61.95
55.22
54.20
45.33
20.79
20.73
-0.00
OMe
NPhth
Me
Me
N
O
OMe
21
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

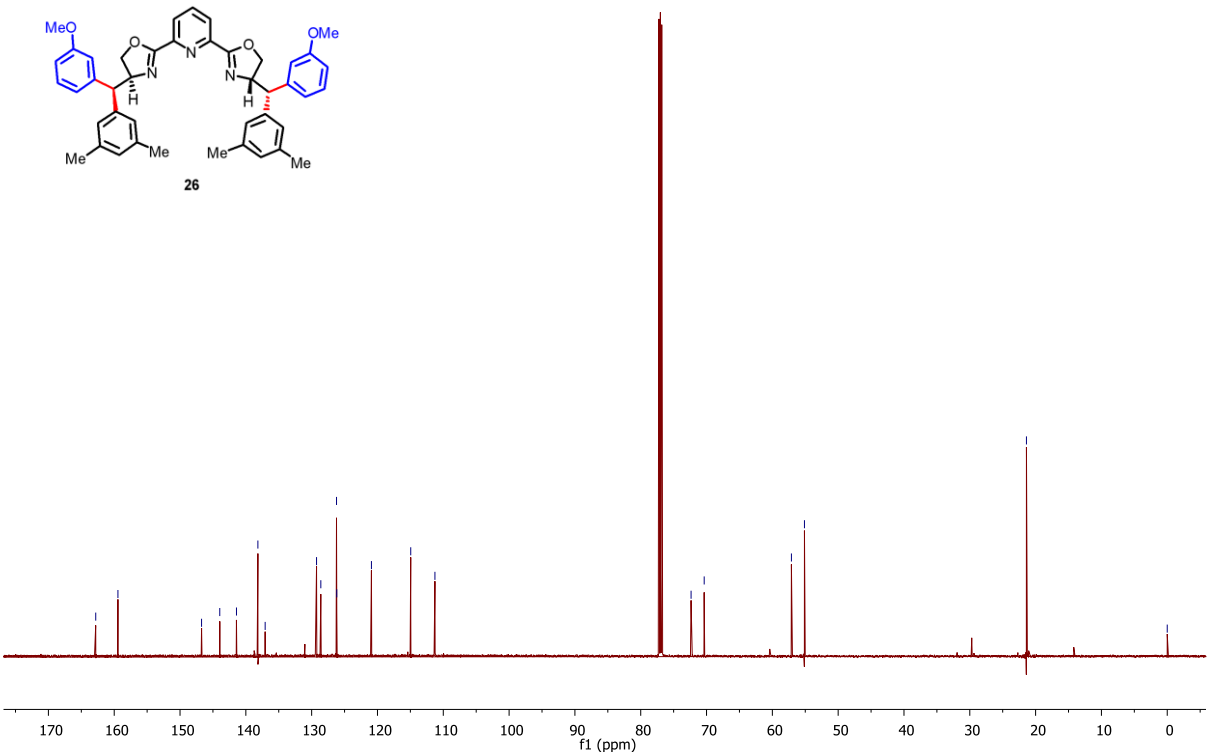

7.907
7.902
7.898
7.893
7.887
7.781
7.775
7.770
7.766
7.761
7.755
7.253
7.191
7.178
7.130
6.979
6.966
4.736
4.713
3.977
3.949
3.938
3.926
3.915
3.904
3.893
2.406
1.342
1.331
0.000
Me
NPhth
Me
N
O
OMe
22
1.78
1.78
0.95
0.91
1.00
1.00
2.52
0.91
2.63
2.65
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
167.85
161.80
138.45
136.59
134.27
131.86
125.46
124.95
123.66
122.90
113.12
62.90
55.27
31.71
21.39
14.35
-0.00
Me
NPhth
Me
N
O
OMe
22
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

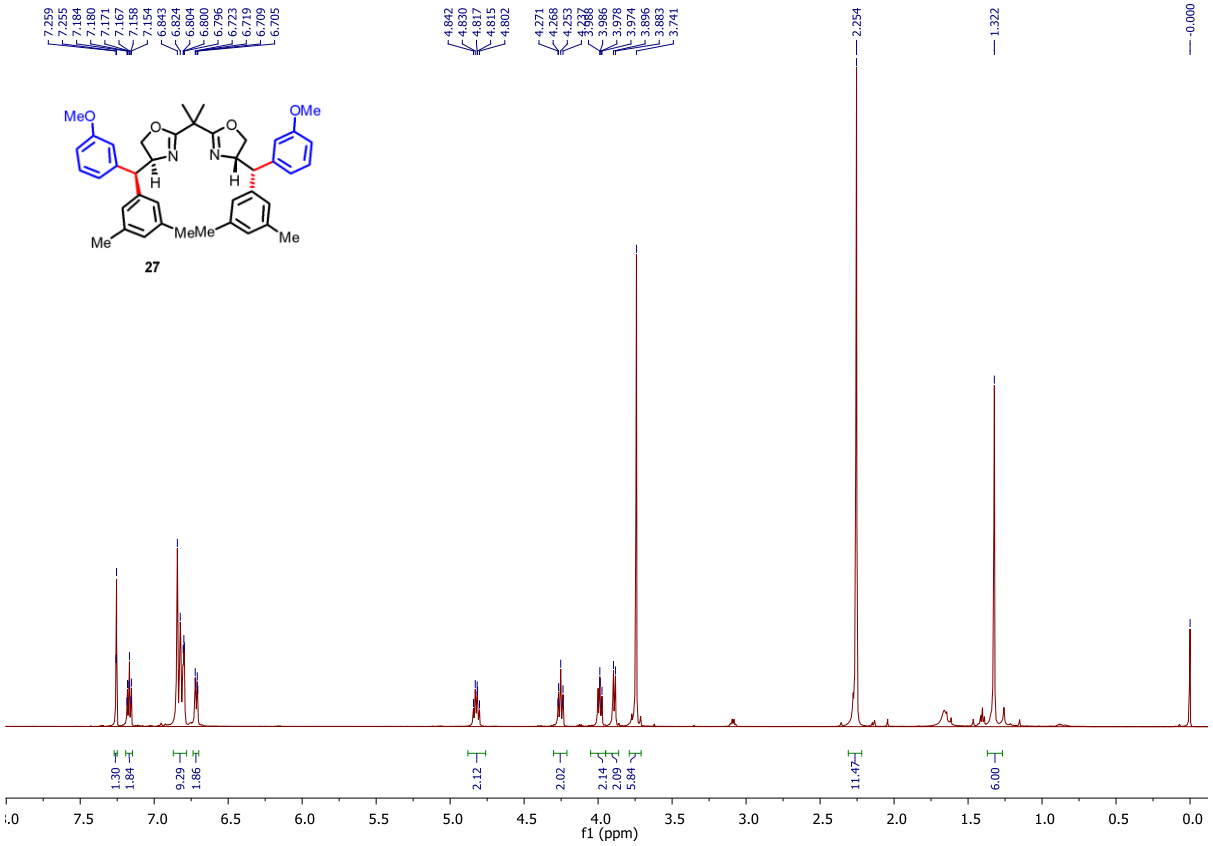

7.259
7.252
7.239
7.226
6.903
6.890
6.850
6.846
6.843
6.812
6.775
6.771
6.761
6.758
4.186
4.172
4.138
3.780
3.536
2.252
0.000
OMe
NH2
CO2Me
Me
Me
24
1.00
2.76
0.94
0.87
1.00
1.98
2.43
2.42
5.86
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

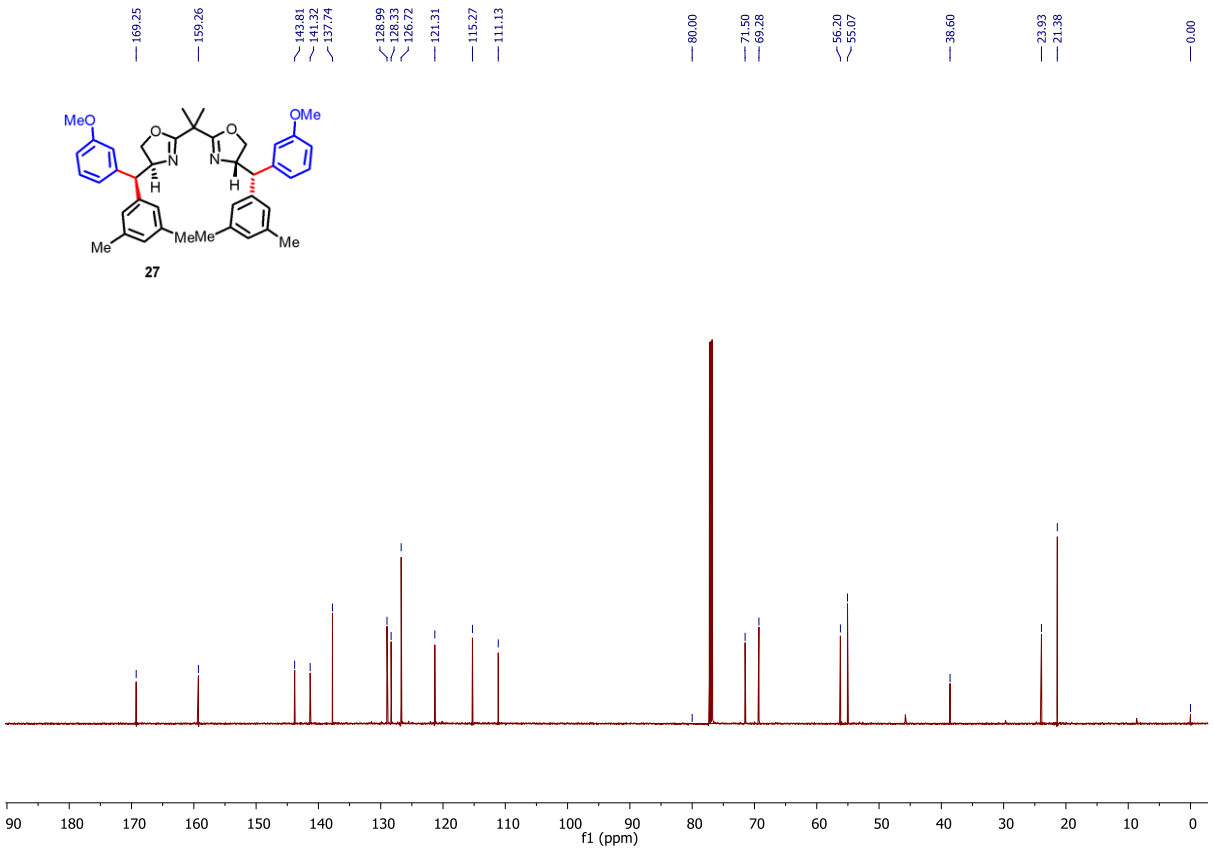

174.84
159.75
142.20
140.98
137.81
129.69
128.49
125.82
120.98
114.97
111.84
58.84
56.36
55.15
51.80
21.37
0.00
OMe
NH2
CO2Me
Me
Me
24
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.260
7.248
7.235
7.222
6.958
6.945
6.895
6.891
6.888
6.879
6.806
6.748
6.747
6.744
6.735
6.731
5.298
3.788
3.645
3.643
3.637
3.633
3.571
3.567
3.552
3.295
3.285
3.278
3.275
3.270
3.267
2.255
1.932
0.000
OMe
NH2
OH
Me
Me
25
1.16
0.98
0.85
1.54
0.95
1.06
3.00
1.60
0.95
0.96
5.65
5.58
f1 (ppm)
159.91
143.95
141.67
138.16
129.94
128.45
125.55
120.43
114.54
111.51
64.76
56.58
55.58
55.18
21.38
0.00
f1 (ppm)


8.171
8.158
7.791
7.777
7.764
7.258
7.231
7.218
7.205
6.956
6.943
6.904
6.900
6.897
6.871
6.834
6.747
6.743
6.734
6.730
5.141
5.125
5.112
5.096
4.527
4.512
4.496
4.185
4.171
4.157
3.914
3.898
3.765
2.261
-0.000
MeO
OMe
Me
Me
Me
Me
26
2.11
1.25
2.15
2.01
1.96
3.94
2.04
2.11
2.27
2.05
2.36
2.28
6.00
11.76
f1 (ppm)


162.81
159.44
146.73
143.96
141.42
138.17
137.07
129.26
128.61
126.22
126.19
120.92
114.94
111.27
72.35
70.36
57.10
55.12
21.39
-0.00
MeO
OMe
Me
Me
Me
Me
26
f1 (ppm)


7.259
7.255
7.184
7.180
7.171
7.167
7.158
7.154
6.843
6.824
6.804
6.800
6.796
6.723
6.719
6.709
6.705
4.842
4.830
4.817
4.815
4.802
4.271
4.268
4.253
4.237
3.988
3.986
3.978
3.974
3.896
3.883
3.741
2.254
1.322
-0.000
MeO
OMe
Me
MeMe
Me
27
1.30
1.84
9.29
1.86
2.12
2.02
2.14
2.09
5.84
11.47
6.00
f1 (ppm)


169.25
159.26
143.81
141.32
137.74
128.99
128.33
126.72
121.31
115.27
111.13
80.00
71.50
69.28
56.20
55.07
38.60
23.93
21.38
0.00
MeO
OMe
Me
MeMe
Me
27
f1 (ppm)